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Asymmetric Catalysis with Rhodium Hydrides



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# Asymmetric Catalysis with Rhodium Hydrides

DISSERTATION

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for the degree of

DOCTOR OF PHILOSOPHY

in Chemistry

by

Zhiwei Chen

Dissertation Committee:
Professor Vy M. Dong, Chair
Professor David L. Van Vranken
Professor Christopher D. Vanderwal

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# Curriculum Vitae

## Zhiwei Chen

### Education

**University of California, Irvine**, Irvine, CA
PhD, Chemistry; September 2014 – May 2019; GPA: 3.915

**Queens College CUNY**, Flushing, NY
BA, Chemistry; Mathematics Minor; August 2008 – May 2014; Summa Cum Laude

### Research Experience

**Doctoral Studies**

**Thesis Advisor: Prof. Vy M. Dong,** University of California, Irvine, September 2014 – May 2019

- Expanded the scope of a regioselective hydroamination of alkynes *via* tandem Rh–H catalysis and discovered the origin of the regioselectivity.
- Extended the tandem Rh–H catalysis to C–C bond formation using alkynes and $\beta$-keto acids.
- Accessed cyclohexenes enantio- and diastereoselectively *via* a Rh-catalyzed cycloisomerization of 1,6-dienes triggered by aldehyde C–H activation.
- Prepared bicylic ketolactones enantioselectively utilizing a Rh-catalyzed ketone hydroacylation; both diastereomers of the products can be favored by tuning the reaction conditions.
- Developed an enantio- and regioselective semireduction of allenes using Rh–H catalysis; synthesized and evaluated six Josiphos ligands during reaction optimization.
- Developed an asymmetric olefin hydroacylation via dynamic kinetic resolution

**Summer Internship**

**Supervisor: Dr. Allen Y. Hong,** Genentech, June 2017 – September 2017

- Optimized and expanded the scope of a novel transformation to access polycyclic motifs.

**Undergraduate Studies**

**Advisor: Prof. Yu Chen,** Queens College CUNY, September 2012 – June 2014

- Worked with Prof. Chen to expand the scope of an iodine-mediated annulation of ynones to generate six- or seven-membered rings.
- Worked with Prof. Chen during the optimization of a Pd-catalyzed synthesis of 2-azafluorenones from isoxazoles and electron-deficient alkenes.

**Technical Skills,** 1-D, 2-D NMR spectroscopy, mass spectrometry, chromatography (GC, HPLC, GC-MS, SFC, flash column, TLC), polarimetry, IR spectroscopy, glovebox and Schlenk technique.

## Publications

(11) **Chen, Z.**; Aota, Y.; Nguyen, H. M. H.; Dong, V. M. "Dynamic Kinetic Resolution of Aldehydes by Hydroacylation", *Angew. Chem. Int. Ed.* **2019**, *58*, 4705.

(10) **Chen, Z.**; Dong, V. M. Rhodium(I)-Catalyzed Hydroformylation and Hydroamination. In *Rhodium Catalysis in Organic Synthesis: Methods and Reactions*; Tanaka, K., Ed.; Wiley-VCH: Weinheim, 2019; pp 49-61.

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(5) Park, J.-W.; **Chen, Z.**; Dong, V. M. "Rhodium-Catalyzed Enantioselective Cycloisomerization to Cyclohexenes Bearing Quaternary Carbon Centers." *J. Am. Chem. Soc.* **2016**, *138*, 3310.

(4) Chen, Q.-A.; **Chen, Z.**; Dong, V. M. "Rhodium-Catalyzed Enantioselective Hydroamination of Alkynes with Indolines." *J. Am. Chem. Soc.* **2015**, *137*, 8392.

─ Featured in C&EN news

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(2) Chen, Y.; Huang, C.; Liu, X.; Perl, E.; **Chen, Z.**; Namgung, J.; Subramaniam, G.; Zhang, G.; Hersh, W. H. "Synthesis of Dibenzocyclohepten-5-ones by Electrophilic Iodocyclization of 1-([1,1'-Biphenyl]-2-yl)-alkynones." *J. Org. Chem.* **2014**, *79*, 3452.

(1) Chen, Y.; Liu, X.; Lee, M.; Huang, C.; Inoyatov, I.; **Chen, Z.**; Perl, A. C.; Hersh, W. H. "ICl-Induced Intramolecular Electrophilic Cyclization of 1-(4'-Methoxy-[1,1'-biphenyl]-2-yl)-alkynones − A Facile Approach to Spiroconjugated Molecules." *Chem. Eur. J.* **2013**, *19*, 9795.

**Teaching Experience**

(1) **Teaching Assistant,** University of California, Irvine, September 2014 – present, periodically

- TAed Prof. Dong's general (CHEM 51A) and advanced (CHEM 125) organic chemistry courses, including leading lectures, recitations, and review sessions. Also held office hours.
  ─Received a Teaching Award

- TAed an undergraduate organic chemistry lab course (CHEM 51LB), which involved supervising students performing experiments and holding office hours.

(2) **Chemistry Tutor,** Queens College CUNY, September 2013 – June 2014

- Tutored undergraduate students in general, organic, and physical chemistry courses.

**Awards and Fellowships**

(1) Allergan Graduate Fellowship in Synthetic Organic Chemistry, Fall 2017

(2) UC Irvine's Teaching Award for Most Promising Future Teacher, Department of Chemistry, University of California, Irvine, Spring 2016

(3) NSF Graduate Research Fellowship, Honorable Mention, Spring 2016

(4) ACS Undergraduate Award in Organic Chemistry, Spring 2014

(5) Summa Cum Laude, Queens College CUNY, Spring 2014

(6) Phi Beta Kappa, Queens College CUNY, Spring 2013

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**"**Stereoselective Hydrofunctionalizations and Cycloisomerizations via Rh-Catalysis" (oral presentation)

(7) DOC Graduate Research Symposium, July 26–29, 2018

**"**Asymmetric Intramolecular Hydroacylation via Dynamic Kinetic Resolution" (oral presentation)

(6) Chirality 2018 (ISCD-30), June 10–13, 2018

**"**Asymmetric Intramolecular Hydroacylation via Dynamic Kinetic Resolution" (poster presentation)

(5) Moving Molecules from the Academic Lab to the Clinic, May 25, 2017

"Enantioselective Semireduction of Allenes" (poster presentation)

(4) UC Chemical Symposium, March 27–29, 2017

"Enantioselective Semireduction of Allenes" (oral presentation)

(3) ISACS19: Challenges in Organic Chemistry, March 20–23, 2016

"Rhodium-catalyzed Tandem Isomerization and Hydroamination of Alkynes" (poster presentation)

(2) 5th International Symposium on Organic Synthesis and Drug Development,

October 17–18, 2015

"Rhodium-catalyzed Tandem Isomerization and Hydroamination of Alkynes" (oral presentation)

(1) NSFC-RSC International Symposium on Emerging Frontiers in Organic Synthesis, October 8–10, 2015

"Rhodium-catalyzed Tandem Isomerization and Hydroamination of Alkynes" (poster presentation)

# Abstract of the Dissertation

Asymmetric Catalysis with Rhodium Hydrides

By

Zhiwei Chen

Doctor of Philosophy in Chemistry

University of California, Irvine, 2019

Professor Vy M. Dong, Chair

The efficient and stereoselective conversion of simple chemical building blocks, including olefins, alkynes, and aldehydes, into value-added products represents a modern challenge in synthetic organic chemistry. Significant research efforts have led to the discovery that rhodium-based catalysts can promote a variety of novel transformations. To this end, my co-workers and I have developed new synthetic methods, where we leveraged catalytically generated rhodium-hydride intermediates to achieve stereo- and regiocontrolled hydrofunctionalizations (Chapter 1) and cycloisomerizations (Chapter 2). Both processes are attractive methods that address the need for atom-economical and sustainable chemistry.

Typically, the hydrofunctionalization of alkynes yields achiral olefin products. We showed that rhodium-hydride catalysis can switch the regioselectivity of these processes to generate chiral products by (1) isomerization of an alkyne to an allene, (2) Rh–H reinsertion to generate an electrophilic Rh–allyl intermediate, and (3) allylic substitution with various (pro)nucleophiles. By careful choice of the catalyst, we developed an asymmetric alkyne hydroamination with amines (Chapter 1.1) and a regioselective decarboxylative hydroalkylation with $\beta$-keto acids (Chapter 1.2).

Despite the numerous catalysts available for asymmetric reduction, allenes are challenging substrates for stereo- and regiocontrolled reduction. In light of this challenge, we envisioned that our aforementioned strategy of alkyne hydrofunctionalization could be applied to achieve an asymmetric semireduction of allenes. We described a method that generates a Rh–allyl intermediate from a 1,1-disubstituted allene, which reacts with a Hantzsch ester (a hydride donor) to produce a chiral olefin product (Chapter 1.3). A designer Josiphos ligand was key to generate the products with high regio- and enanatioselectivity.

Desymmetrizations are powerful strategies to form multiple chiral centers in a single step. When coupled with cycloisomerizations, various carbocyclic motifs can be stereoselectively formed. We describe a desymmetrization of prochiral diketoaldehydes by ketone hydroacylation to generate chiral bicylic ketolactones (Chapter 2.1). In this process, a Rh–H intermediate generated from aldehyde C–H activation inserts into one of the carbonyl groups, and subsequent reductive elimination yields the product. By tuning the reaction conditions, we can selectively form each diastereomer of the product. Using aldehyde C–H activation, we showed that prochiral dienyl aldehydes can be transformed into chiral cyclohexenes (Chapter 2.2). This method complements the Diels-Alder cycloaddition and is a rare example of a cycloisomerization to generate six-membered rings.

Dynamic kinetic resolutons have emerged as an attractive to transform racemic building blocks into enantioenriched products. We described a dynamic kinetic resolution (DKR) of racemic $\alpha$-allyl aldehydes by olefin hydroacylation to generate $\alpha,\gamma$-disubstituted cyclopentanones with high enantio- and diastereoselectivity (Chapter 2.3). A bulky primary amine co-catalyst is important for selective racemization of the aldehyde substrate, and a bulky

bisphosphine ligand is needed for cycloisomerization. Three different classes of aldehydes can be efficiently resolved with different amine and ligand combinations.

Fused cyclic ketones (e.g. tetralones) are commonly found in natural products and used as building blocks in chemical synthesis. Several tetralone derivatives were needed by Genentech scientists for the synthesis of drug candidates. However, no satisfactory general method existed for the preparation of these motifs. Toward a solution to this challenge, I collaborated with two process chemists to develop a strategy towards the synthesis of tetralones from aryl iodides and cyclopropane diesters (Chapter 3.1). This strategy proceeds via a homoconjugate addition between the corresponding aryl organocopper intermediate and the cyclopropyl electrophile followed by a decarboxylative Dieckmann annulation.

# Chapter 1 – Rhodium-Catalyzed Hydrofunctionalizations

## 1.1 Rhodium-Catalyzed Enantioselective Hydroamination of Alkynes with Indolines[i]

### 1.1.1 Introduction

Amines are ubiquitous in agrochemicals, fine chemicals, and pharmaceuticals. Thus, developing regio- and enantioselective methods to construct C–N bonds is an important challenge in organic synthesis. Transition-metal catalyzed allylic substitution enables the coupling of amines with allylic electrophiles to afford *N*-allylic amines but requires a pre-installed leaving group that generates stoichiometric waste (Figure 1.1a).[1] Alternatively, alkyne hydroamination has emerged as an atom economical C–N bond forming method.[2] This process typically affords imines and enamines (Figure 1.1b). In contrast, Yamamoto reported an atom-economical Pd-catalyzed hydroamination of internal alkynes to regioselectively afford linear *N*-allylic amines

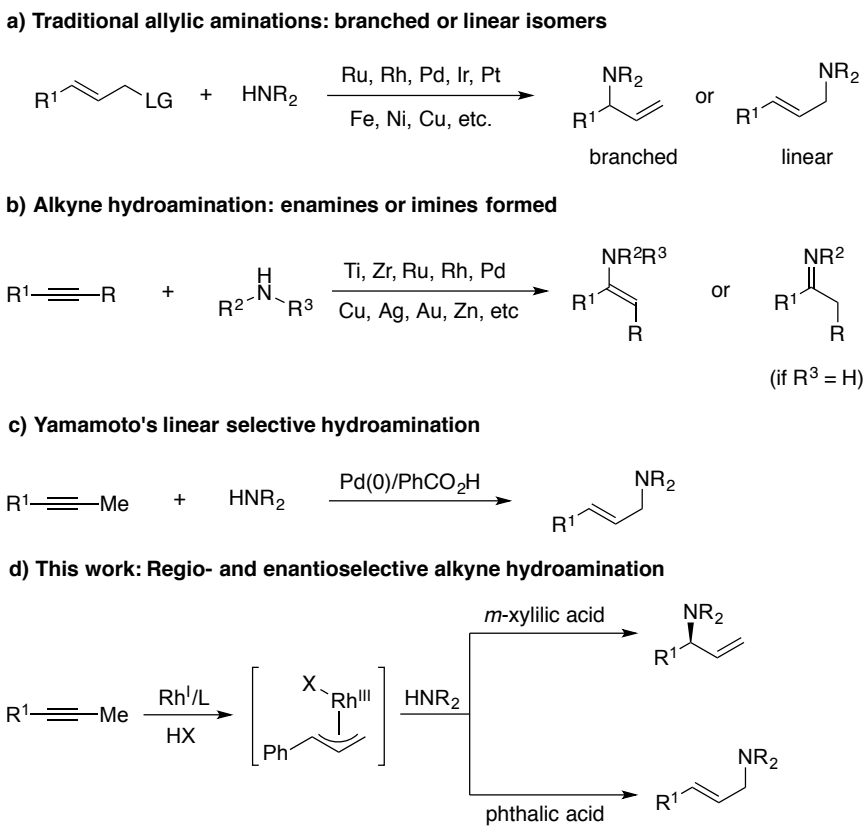



**Figure 1.1.** Allylic aminations versus alkyne hydroaminations

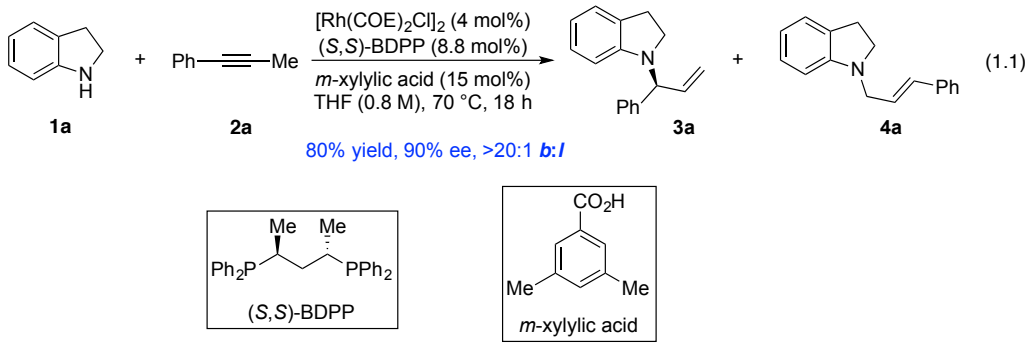
[i] Reproduced in part with permission from Chen. Q.-A.; Chen, Z.; Dong, V. M. *J. Am. Chem. Soc.*, **2015,** *137,* 8392. Copyright 2015 American Chemical Society.

(Figure 1.1c).[3] Although it is a promising approach, there are no intermolecular variants to access the corresponding branched regioisomers. This chapter describes the first example of an enantioselective and intermolecular Rh-catalyzed hydroamination of alkynes[4] that allows access to both branched and linear isomers with high regiocontrol by the choice of the carboxylic acid additive used (Figure 1.1d).

Transition-metal hydrides have been shown to be competent catalysts for the isomerization of alkynes to metal allyl species. Using transition metal-hydride catalysis, Ishii[5], Krische[6], and our group[7] have generated C–C bonds by coupling internal alkynes to alcohols or aldehydes. Breit has used Rh-catalysis to generate allylrhodium intermediates from terminal alkynes that undergo C–O and C–S bond formations.[8] Encouraged by this promising approach, we focused on the regio- and enantioselective formation of C–N bonds through the tandem isomerization and hydroamination of alkynes.

### 1.1.2 Results and Discussion

Dr. Qing-An Chen initiated this project and found that the combination of $[Rh(COE)_2Cl]_2$, (*S*,*S*)-BDPP, and *m*-xylylic acid promoted the coupling of indoline **1a** and 1-phenyl-1-propyne **2a** affording the desired *N*-allylic indoline **3a** in 80% yield, 90% *ee*, and with >20:1 selectivity for the branched regioisomer (eq. 1.1). In addition to optimizing the reaction conditions, he examined the branched-selective hydroamination of 1-phenyl-1-propyne **2a** with various amines **1**. Dr. Chen also examined the branch-selective hydroamination of various alkynes with indoline **1a**.




We proposed a mechanistic pathway involving tandem Rh-catalysis on the basis of literature precedence (Figure 1.2).[1,8] Oxidative addition of a Rh(I) precursor with the carboxylic acid generates a rhodium(III)-hydride catalyst. Insertion of alkyne **2a** into the Rh(III)–H gives Rh-vinyl intermediate **A**, which undergoes $\beta$-hydride elimination to generate intermediate allene **5**. Reinsertion of **5** into the Rh(III)–H affords $\pi$-allyl rhodium complex **B**. Product formation can occur via two competing pathways.[9] In path A (PA), ligand exchange of the amine **1** with the carboxylate (X) on complex **B** generates $\pi$-allyl rhodium complex **C**, which can undergo reductive elimination to yield allylic amine **3**. In path B (PB), **1** undergoes nucleophilic attack on the more substituted carbon of the metal-allyl species **B** to afford **ent-3**.

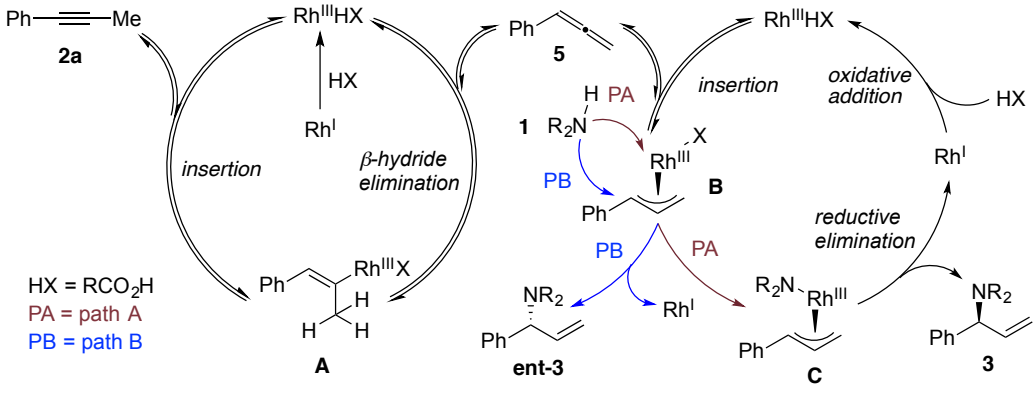
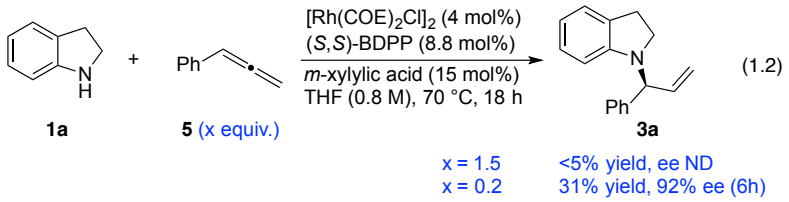
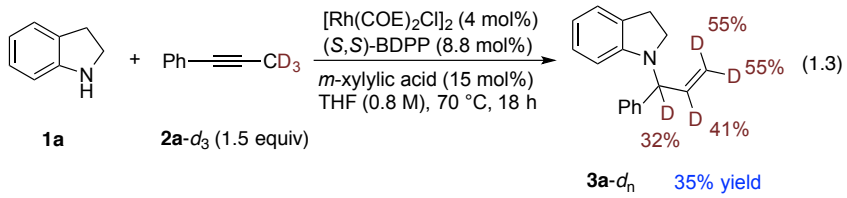



**Figure 1.2.** Proposed mechanism for hydroamination of alkynes

To support the intermediacy of an allene I prepared phenylallene **5**, and Dr. Qing-An Chen subjected it to the reaction conditions with indoline **1a** (eq. 1.2). We observed trace amounts of

the expected product **3**. However, the yield increased when 0.2 equivalents of phenylallene **5** was used. Our results support the formation of an allene intermediate in low equivalents. Dr. Chen also performed the hydroamination of deuterated alkyne **2a**-$d_3$, and found scrambling of the deuterium label into the $\alpha$, $\beta$, and $\gamma$-positions of the allylic amine **3a**-$d_n$ (eq. 1.3), which is consistent with reversible $\beta$-hydride elimination during allene formation.

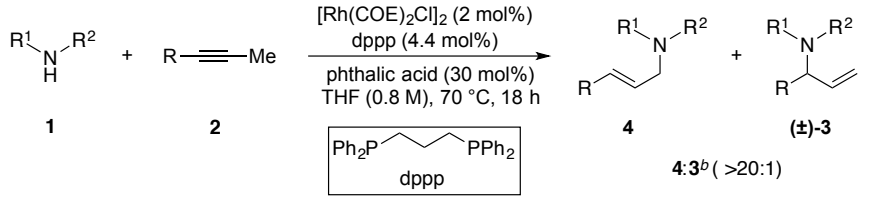



During our optimization studies I found that using phthalic acid (benzene-1,2-dicarboxylic acid) instead of *m*-xylilic acid gave the corresponding linear allylic amines with high regioselectivity (>20:1). Other acids (TFA, tartaric acid, malonic acid) which have pKa's from –0.3 to 3 also promoted the linear selective hydroamination. Phthalic was the optimal acid with respect to substrate generality. I optimized the synthesis of linear allylic amines by finding 1,3-bis(diphenylphosphino)propane (dppp) to be the optimal ligand with respect to reactivity and regioselectivity. Next, I examined the substrate scope for this linear-selective alkyne hydroamination. I found that the hydroamination of 1-phenyl-1-propyne **2a** proceeded with a number of amines affording the linear *N*-allylic amines in yields ranging from 55–99% with >20:1 regioselectivity (Table 1.1). Various secondary amines are accommodated (**4a**-**4e**). I hypothesized that this method could be extended to primary amines such as aniline. Under the

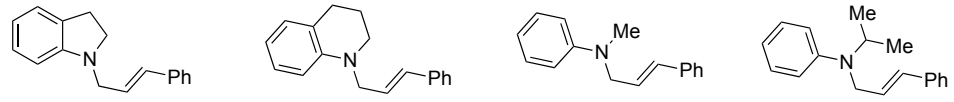
standard stoichiometry, I observed a 1.2:1 mixture of mono- and bisallylated products (**4f** and **4f'**). By tuning the stoichiometry of aniline **1f** and alkyne **2a**, either the monoallylated amine **4f** or the bisallylated amine **4f'**can be formed exclusively. This protocol is not limited to the terminal methyl group on the alkyne. I found that the phthalic acid catalyst can also accommodate 1-phenyl-1-butyne **2g**, which bears an ethyl group, to form allylic amine **4g**.

**Table 1.1.** Linear-selective Hydroamination of Alkynes[a]

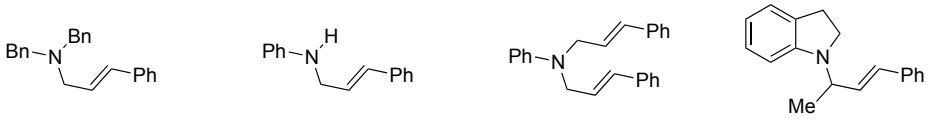



**1** **2** **4** **(±)-3**

**4**:**3**[b] ( >20:1)



**4a**: 80% yield **4b:** 99% yield **4c:** 95% yield **4d:** 85% yield



**4e:** 77% yield **4f:** 77% yield with 0.7 eq of **2a** **4f':** 77% yield with 2.5 eq of **2a** **4g:** 79% yield

[a] **1** (0.20 mmol), **2** (0.30 mmol), $[Rh(COE)_2Cl]_2$ (2.0 mol%), dppp (4.4 mol%), phthalic acid (30 mol%), THF (0.25 mL), 70 °C, 18 h. Isolated yields of **4** are given. [b] Ratio was determined by $^1$H NMR analysis of the unpurified reaction mixture.

While studying the switch in regioselectivity I observed formation of the branched regioisomer followed by its conversion to the linear regioisomer, when I monitored the reaction profile of the linear-selective hydroamination. I isolated and subjected racemic allylic amine **(±)-3a** to various conditions (Figure 1.3). Indeed, I observed full conversion of **(±)-3a** to linear allylic amine **4a** after an hour under the standard reaction conditions using phthalic acid. No isomerization was observed in the absence of either Rh or acid. Isomerization occurred at a slower rate (1:3 **4a**:**3a** after 18 h) when using a less acidic additive. Thus, the branched regioisomer is the kinetic product, which can be obtained in high yield with *m*-xylilic acid. In

contrast, phthalic acid promotes generation of the thermodynamic linear products by an isomerization pathway. The Yudin group previously observed a related isomerization of allylic amines under Pd-catalysis, whereby the kinetic (branched) product was favored by addition of DBU.[10]

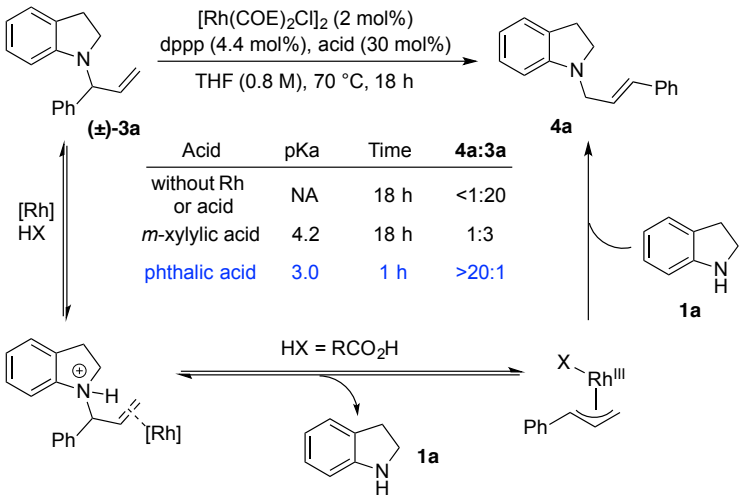



**Figure 1.3.** Acid-promoted isomerization study

### 1.1.3 Conclusion

By tandem Rh-catalysis, an atom economical synthesis of allylic amines via alkyne hydroamination is achieved, which complements traditional allylic amination and alkyne hydroamination. Mechanistic studies support an allene intermediate, which leads to allylic amines instead of the typical imine and enamine products of alkyne hydroamination. Both branched and linear regioisomers can be exclusively obtained by choice of the carboxylic acid additive. Insights from this work will spur further developments in using alkynes as surrogates for allenes and allylic electrophiles. Future studies will focus on extending this strategy to other transformations.

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## 1.2 Tandem Rh-Catalysis: Decarboxylative $\beta$-Keto Acid and Alkyne Cross-Coupling[ii]

### 1.2.1 Introduction

A range of natural processes are driven by the loss of carbon dioxide, from polyketide synthesis to $\gamma$-aminobutyric acid (GABA) production.[1] Various synthetic strategies have emerged using the formation of $CO_2$ gas as the driving force. Tsuji and Saegusa independently reported decarboxylative allylation of $\beta$-keto allyl esters.[2,3] Shair developed a decarboxylative aldol using malonic acid half thioesters,[4] while Gooßen pioneered decarboxylative biaryl cross-couplings.[5] More recently, MacMillan and Doyle have used $CO_2$ gas extrusion and photoredox catalysis to generate a wide range of cross-couplings, including those that generate $Csp^2$–$Csp^3$ bonds.[6] Most relevant to our study, Breit has developed a bioinspired coupling of $\beta$-keto acids with allenes under Rh-hydride catalysis.[7,8] It occurred to us that by using tandem Rh-catalysis, we could achieve a complementary cross-coupling of $\beta$-keto acids with alkynes. We chose alkynes as allyl electrophiles because they are a common and readily accessible functional group. Our approach would enable unique access to ketones under mild conditions, without the need for generating enolates or the use of activated allylating agents.[9-13]

Based on previous studies from Yamamoto,[14] Breit,[15] and our laboratory,[16] we proposed a pathway involving tandem Rh-catalysis to enable decarboxylative coupling between $\beta$-keto acids **1** and alkynes **2** (Figure 1.4).[17] First, $\beta$-keto acid **1** and a Rh(I) species combine to generate a Rh(III)-hydride intermediate.[18] Insertion of alkyne **2** into the Rh(III)–H bond

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gives Rh-vinyl species **5**. Subsequent $\beta$-hydride elimination generates allene **6** and regenerates the Rh(III)-hydride species. Insertion of allene **6** into the Rh(III)-H bond then forms Rh(III)-allyl species **7** that can be trapped with a carbon-based nucleophile.[19] Indeed, Breit recently reported the coupling of 1,3-diketones with terminal alkynes.[20] In the presence of $\beta$-keto acid **1**, C–C bond formation yields allylated $\beta$-keto acid **8**.[21] Finally, decarboxylation affords the desired ketone **3**.

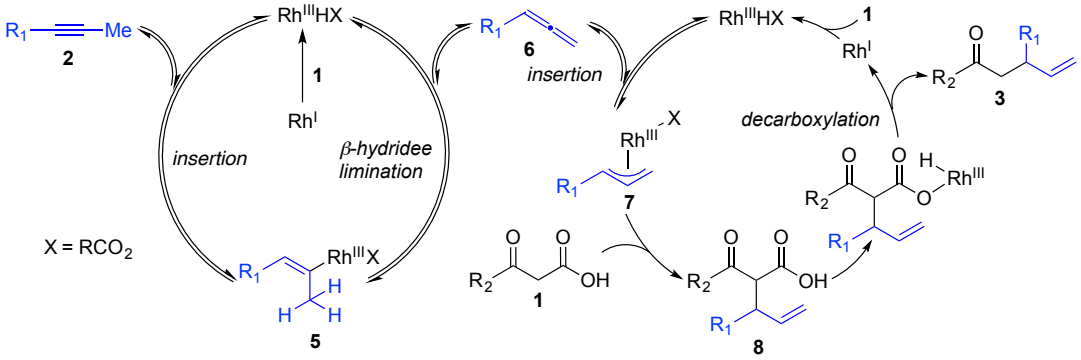
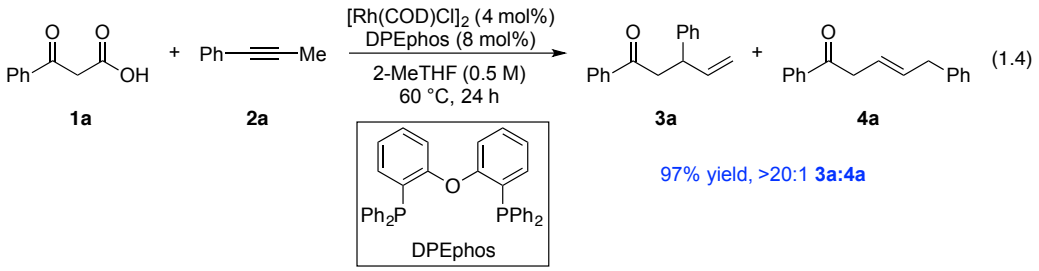



**Figure 1.4.** Proposed decarboxylative $\beta$-keto acid and alkyne coupling

1.2.2 Results and Discussion

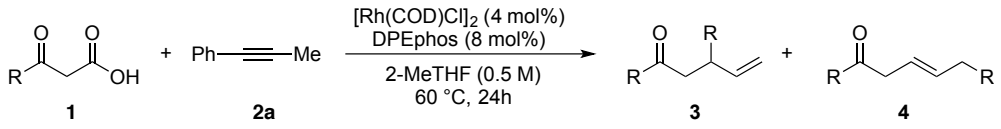
My contributions to this project involved examining the $\beta$-ketoacid substrate scope and mechanistic studies. Faben Cruz initiated this project and optimized the reaction conditions. He found that the combination of $[Rh(COD)Cl]_2$ and DPEphos effected the decarboxylative allylation of benzoylacetic acid **1a** with 1-phenyl-1-propyne **2a** affording the desired $\gamma,\delta$-unsaturated ketone **3a** in 97% yield with >20:1 selectivity for the branched regioisomer (eq. 1.4). In addition, Faben Cruz also performed the decarboxylative allylation of benzoylacetic acid **1a** with various alkynes **2**.

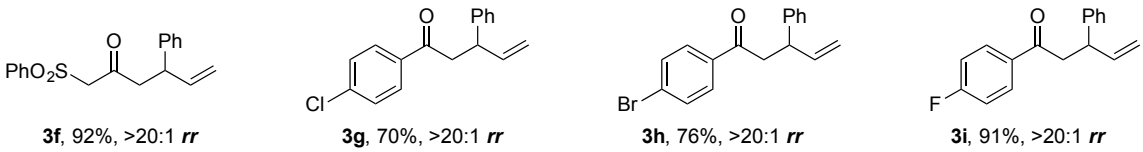



(1.4)

Faben Cruz and I examined the decarboxylative allylation of various $\beta$-ketoacids **1** with 1-phenyl-1-propyne **2a** (Table 1.2). I varied the substituent on the $\beta$-ketoacid and found that various aromatic and heteroaromatic groups underwent efficient decarboxylative allylation affording the desired products in yields ranging from 61–91% with >20:1 regioselectivity for the branched isomer. Notably, ketone **3f** represent site-selective allylation at the less acidic $\alpha$-carbon without the need to add a stoichiometric amount of base. Aryl halides were well tolerated (**3g** and **3h**). Both electron-deficient (**3k**) and electron-rich (**3l**) substrates are well accommodated. $\beta$-Ketoacids bearing heterocycles (**3m** and **3n**) were tolerated.

**Table 1.2.** Decarboxylative Coupling of Various $\beta$-Ketoacids with Alkyne **2a**[a]



**3f**, 92%, >20:1 ***rr***



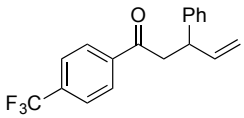
**3g**, 70%, >20:1 ***rr***



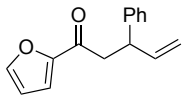
**3h**, 76%, >20:1 ***rr***



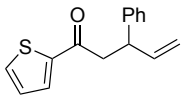
**3i**, 91%, >20:1 ***rr***



**3k**, 63%, >20:1 ***rr***



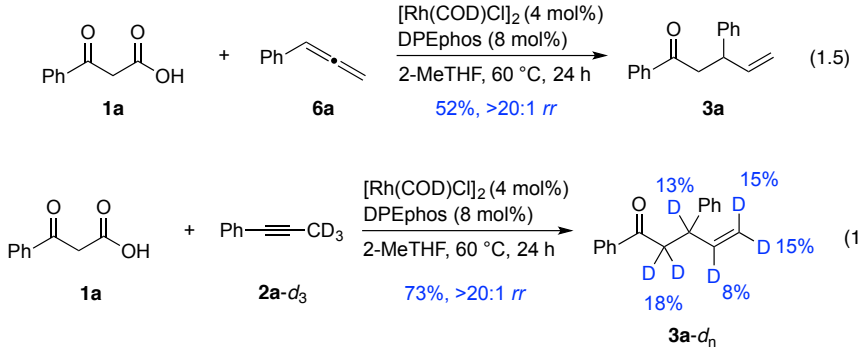
**3m**, 90%, >20:1 ***rr***



**3n**, 89%, >20:1 ***rr***

[a] **1** (0.40 mmol), **2a** (0.20 mmol), $[Rh(COD)Cl]_2$ (4.0 mol%), DPEphos (8.0 mol%), 2-MeTHF (0.40 mL), 60 °C, 24 h. Isolated yields of **3**. Regioselectivity was determined by $^1H$ NMR analysis of the unpurified reaction mixture. Performed by Zhiwei Chen.

To support the proposed allene intermediate, I prepared phenyallene **6a** and subjected it to the standard reaction conditions. The desired ketone **3a** was isolated in 52% yield supporting the intermediacy of an allene. I prepared and subjected deuterated alkyne **2a**-$d_3$ to coupling with **1a** and observed scrambling of the deuterium label. The observed results are consistent with reversible $\beta$-hydride elimination during allene formation (eq. 1.5 and 1.6).




1.2.3 Conclusion

This Rh-catalyzed decarboxylative coupling between $\beta$-keto acids and alkynes provides a complementary approach to generate ketones, without need for enolate generation and activated allylic electrophiles. In addition, alkylation at specific sites can be performed in the presence of multiple reactive sites due to the directing effect of the carboxylic acid. Our study contributes to the emerging use of alkynes in various cross-couplings to generate C–O,[22] C–N,[23] C–S,[24] and C–C bonds.[25] Further studies are underway to expand the scope of carbon pronucleophiles and identify more enantioselective variants for tandem Rh-catalysis.

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(23) For select examples of C–N bond formation from alkynes, see: references 14a, 14b, 14c, 14d, 14e, 14f, 14h, 14i and 16.

(24) For a select example of C–S bond formation from alkynes, see: reference 15c.

(25) For select examples of C–C bond formation from alkynes, see: references 14c, 14f, 14g, 14j, 14k and 19.

## 1.3 Enantioselective Semireduction of Allenes[iii]

### 1.3.1 Introduction

In nature, chemo- and stereocontrolled reduction of unsaturated bonds are catalysed by enzymes and mediated by cofactors such as nicotinamide adenine dinucleotide phosphate (NAD(P)H)[1]. Inspired by this cofactor, chemists have used Hantzsch esters as mild reagents to solve various challenges in asymmetric reductions[2]. It occurred to us that this cofactor mimic could be combined with Rh-hydride catalysis to enable a valuable strategy for reducing allenes to generate benzylic motifs common in medicinal chemistry, which are traditionally made by an allylic substitution between an allylic electrophile and an organometallic reagent[3-7] or a hydride source[8-14] (Figure 1.5A). Since allenes are readily accessible[15], a method to access these motifs through a semireduction of allenes would avoid the pre-installation of a suitable leaving group. Allenes are challenging functional groups for reduction because of problems with chemo-, regio-, and stereoselectivity. Both $\pi$-bonds can be reduced to the corresponding alkane (Figure 1.5B), or one $\pi$-bond can be reduced to afford one or a mixture of alkene isomers (Figure 1.5C). Prior studies in the regioselective semireduction of allenes have shown that the less substituted $\pi$-bond is typically reduced to afford the achiral internal alkene[16-18]. Existing methods that reduce the more substituted $\pi$-bond are limited to monosubstituted and symmetrical allenes, which give rise to achiral terminal alkenes[19-20].

The generation of electrophilic metal-allyl species from allenes using iridium- and rhodium-hydrides is an emerging strategy in allene hydrofunctionalisation[21-22]. These intermediates can undergo allylic substitution with various nucleophiles to afford branched allylated products. We envisioned that a Rh-hydride catalyst would transform an allene to an electrophilic Rh-allyl

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intermediate, which can then be trapped with a hydride nucleophile[23-26]. Given that allenes are known to isomerise to dienes in the presence of transition metal-hydrides[27], we recognize that a key challenge would be identifying a catalyst that promotes semireduction over isomerisation.

Herein, we demonstrate an asymmetric semireduction of allenes enabled by Rh-hydride catalysis as a complementary approach to allylic alkylation and allylic reduction to generate chiral benzylic motifs. Using a designed Josiphos ligand and a Hantzsch ester reductant, various allenes are reduced to the corresponding chiral terminal alkenes with high selectivities.

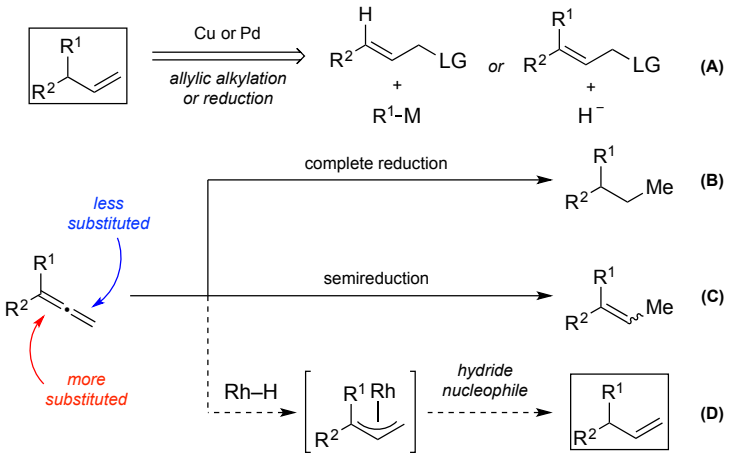
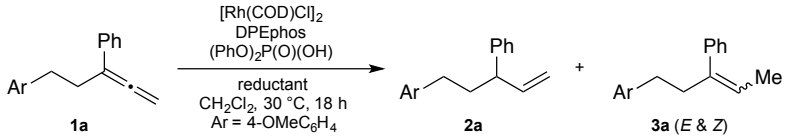



**Figure 1.5. Challenges in the selective reduction of allenes. (A)** Traditional methods to access chiral allylic motifs. **(B)** Complete reduction affords alkanes. **(C)** Existing allene semireductions favour formation of the internal alkene. **(D)** Proposed strategy for regio- and enantioselective semireduction to afford the complementary terminal alkene.

### 1.3.2 Results and Discussion

To test our hypothesis (Figure 1.5D), we chose 1-methoxy-4-(3-phenylpenta-3,4-dien-1-yl)benzene (**1a**) as the model substrate for semireduction in the presence of $[Rh(COD)Cl]_2$, $(PhO)_2P(O)(OH)$, and DPEphos (Figure 1.6). Through a survey of achiral bidentate phosphine ligands, we found DPEphos to be the most promising scaffold for suppressing diene formation, in the presence of various reductants. Tsuji demonstrated that formic acid and formates are competent reductants in the reduction of allylic carbonates[8]. However, these reagents led to

semireduction with little to no regiocontrol (50:50 to 67:33 **2a**:**3a**, entries 1 and 2). Hayashi and Kawabata showed that a combination of formic acid and an amine base, such as 1,8-bis(dimethylamino)naphthalene, reduced allylic carbonates and esters[9-12]. In our system, this combination suppressed semireduction of the more substituted $\pi$-bond (entry 3). $NaBH_4$, a classical nucleophilic hydride source, gave trace reactivity (entry 4), and silanes[13-14] afforded unselective semireduction in low conversion (28%, 50:50 **2a**:**3a**, entry 5). When Hantzsch ester **5a** was used as the reductant (entry 6), the reactivity increased (87% yield), and the desired terminal alkene was obtained as the major product (88:12 **2a**:**3a**).



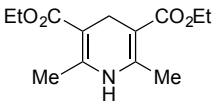

| entry | reductant | yield (%) | **2a**:**3a** |
|---|---|---|---|
| 1 | $HCO_2H$ | 62 | 50:50 |
| 2 | $HCO_2NH_4$ | 63 | 67:33 |
| 3 | $HCO_2H$/ 1,8-bis(dimethylamino)naphthalene[a] | 48 | 0:100 |
| 4 | $NaBH_4$ | trace | ND[b] |
| 5 | $HSiMe(OEt)_2$ | 28 | 50:50 |
| 6 |  **5a** | 87 | 88:12 |



**Figure 1.6. Evaluation of reductants.** Reaction conditions: **1a** (0.050 mmol), reductant (0.10 mmol), $[Rh(COD)Cl]_2$ (4 mol%), DPEphos (8 mol%), $(PhO)_2P(O)(OH)$ (8 mol%), $CH_2Cl_2$ (0.1 mL), 30 °C, 18 h. Yields and regioselectivities were determined by $^1H$ NMR analysis of the unpurified reaction mixture using dimethyl terephthalate as an internal standard. [a] $HCO_2H$ (0.11 mmol), 1,8-bis(dimethylamino)naphthalene (0.060 mmol). [b] ND = not determined

Next, we searched for a chiral ligand that could enable high enantio- and regioselectivities, in combination with Hantzsch ester **5a** as the reductant (Figure 1.7). Axially chiral bisphosphine ligands, such as (*R*)-BINAP (**L1**), afforded a mixture of alkenes **2a** and **3a** as well as competitive

isomerisation to diene **4a** (1:3:2 **2a**:**3a**:**4a**). Ligands bearing point chirality, such as (*R*,*R*)-DIOP (**L2**), promoted semireduction over isomerisation, but with moderate regioselectivity (5:2 **2a**:**3a**).

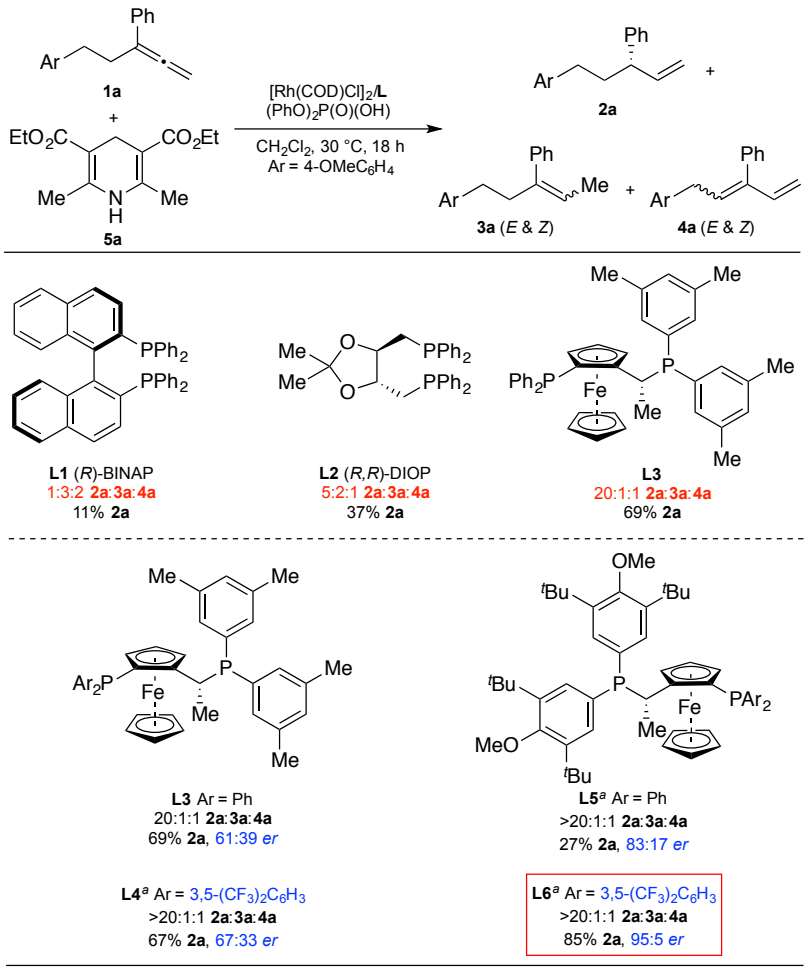



**Figure 1.7. Evaluation of chiral ligands.** Reaction conditions: **1a** (0.10 mmol), **5a** (0.20 mmol), $[Rh(COD)Cl]_2$ (4 mol%), **L** (8 mol%), $(PhO)_2P(O)(OH)$ (8 mol%), $CH_2Cl_2$ (0.2 mL), 30 °C, 18 h. Yields and product ratios were determined by $^1H$ NMR analysis of the unpurified reaction mixture using dimethyl terephthalate as an internal standard. Enantioselectivities (*er*) were determined by chiral SFC analysis. [a] Using $[Rh(COD)Cl]_2$ (2 mol%), **L** (4 mol%), $(PhO)_2P(O)(OH)$ (4 mol%), $CH_2Cl_2$ (0.1 mL).

We discovered that the all-aryl substituted Josiphos ligand scaffold gave high selectivity for **2a**. A significant increase in the reaction selectivity (20:1:1 **2a**:**3a**:**4a**) was observed when commercially available ligand **L3** was employed. Josiphos ligand **L4**, where one phosphine is more electron-deficient, afforded an increase in the reaction rate, so the catalyst loading can be reduced two-fold. In addition, **L4** further improved selectivity for **2a** (>20:1:1 **2a**:**3a**:**4a**), but the enantioselectivity remained low (67:33 *er*). To improve the enantioselectivity, we replaced the

3,5-xylyl groups of **L3** and **L4** with the more electron-rich and sterically encumbered 3,5-di-*tert*-butyl-4-methoxyphenyl groups to afford new Josiphos ligands **L5** and **L6**. With **L5**, the enantioselectivity increased (83:17 *er*), but low reactivity (27%) was observed. However, **L6** afforded the desired terminal alkene in 85% yield and 95:5 *er* while maintaining the high selectivity for **2a** (>20:1:1 **2a**:**3a**:**4a**).

With this protocol, we examined the generality of enantioselective semireduction using other allenes (Figure 1.8). Generally, the terminal alkene was obtained as the sole product; no internal alkene or diene was observed. An allene with an *ortho* substituent (**2b**) on the phenyl group underwent semireduction with lower enantioselectivity (75%, 88:12 *er*). Substrates with *meta* (**2c**) and *para* (**2d**) substituents on the phenyl group reacted with similar efficiencies as the model substrate (88%, 96:4 *er* and 92%, 95:5 *er*, respectively). Allenes bearing electron-rich (**2e**) and electron-deficient (**2f**) substituents underwent semireduction (85–92%, 93:7–97:3 *er*). A benzyl ether is labile under typical hydrogenation conditions, but this protecting group was stable under our semireduction conditions (**2e**). Substrates bearing aryl halide bonds (**2g** and **2h**) were tolerated (87–90%, 94:6–95:5 *er*). Extended aromatic systems, such as a naphthyl group (**2i**), reacted (91%, 94:6 *er*). The semireduction tolerates allenes with heteroaromatic moieties, such as an *N*-tosyl indole (**2j**, 70%, 94:6 *er*) and a thiophene (**2k**, 82%, 94:6 *er*). Chemoselective reduction occurred with substrates containing alkenes (**2l**), alkynes (**2m**), esters (**2s**), and nitriles (**2s**), affording the terminal alkenes selectively (67–81%, 89:11–95:5 *er*). 1-Aryl-1-propynes (**2m**) are reactive substrates towards isomerisation and hydrofunctionalisation[22], but only the allene functionality reacted. Allenes bearing other alkyl groups were accommodated (**2n**–**2s**, 60–99%, 89:11–96:4 *er*). Lastly, the semireduction occurs chemoselectively in the presence of other nucleophiles, such as an alcohol (**2q**, 61%, 96:4 *er*). Allenes bearing dialkyl or diaryl substituents

were unreactive under the present conditions. Notably, the semireduction tolerates acidic and electrophilic functionalities, such as an alcohol (**2q**), ester (**2s**), and nitrile (**2s**). Thus, this method to access benzylic motifs complements allylic substitutions using organometallic reagents. The absolute configuration of **2n** was determined to be (*S*) by comparison of its optical rotation with literature data[28].

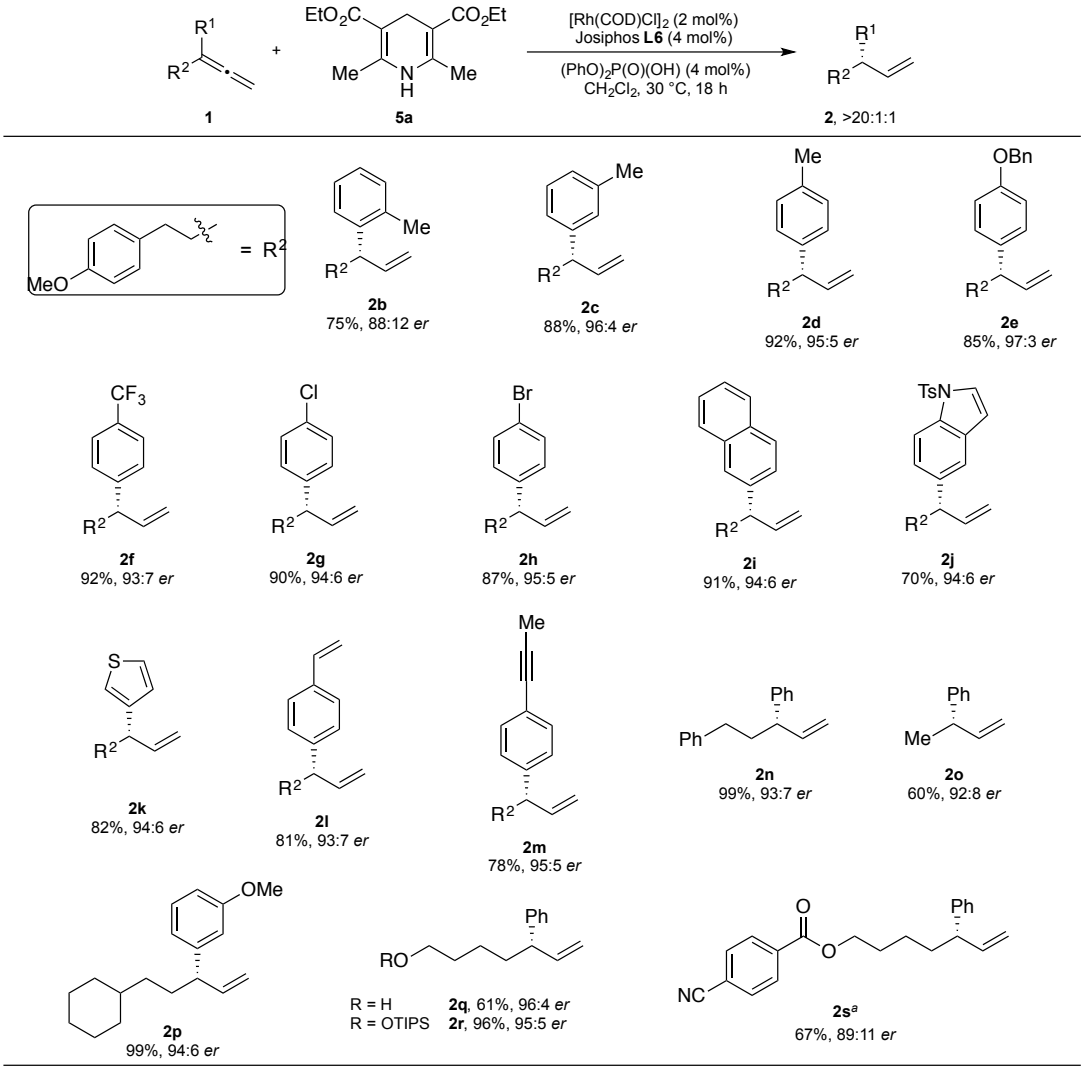



**Figure 1.8. Enantioselective semireduction of allenes.** Reaction conditions: **1** (0.20 mmol), **5a** (0.40 mmol), $[Rh(COD)Cl]_2$ (2 mol%), **L6** (4 mol%), $(PhO)_2P(O)(OH)$ (4 mol%), $CH_2Cl_2$ (0.2 mL), 30 °C, 18 h. Isolated yields. Product ratios were determined by $^1H$ NMR analysis of the unpurified reaction mixture. Enantioselectivities (*er*) were determined by chiral SFC analysis. [a] Reaction performed with 1,2-dichloroethane at 60 °C.

To shed light on the mechanism of this semireduction, we performed deuterium-labelling experiments using deuterated analogues of Hantzsch ester **5a**. Semireduction of **1a** with **5b**

afforded **2ab**, where the deuterium label was completely transferred to the allylic carbon (Figure 1.9a). In addition to its mechanistic significance, this experiment demonstrates a method to prepare chiral isotopically labelled stereogenic centres that complements allylic deuteration using formic acid-$d_2$[29-30]. Using **5c**, **2ac** was obtained, where the deuterium label was incorporated into the internal vinylic carbon (Figure 1.9b). The remaining deuteriums were incorporated into the vinylic methyl groups of the Hantzsch ester **5c** (31% D) and the pyridine byproduct (6% D) presumably as a statistical mixture of products.[31]

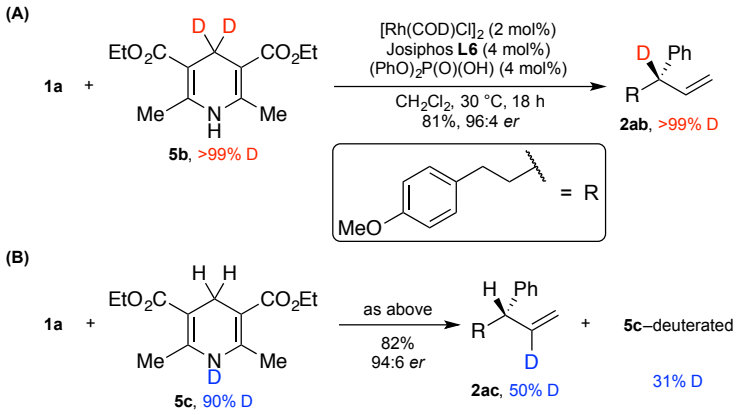



**Figure 1.9. Deuterium labeling studies. (A)** Treatment of allene **1a** with deuterated Hantzsch ester **5b** afforded deuteration in the allylic position. **(B)** Analogous experiment with **5c** gave deuteration in the vinylic position.

On the basis of our observations and literature precedence, we propose the mechanism shown in Figure 1.10. To initiate catalysis, the Rh(I) precursor undergoes oxidative addition to generate a Rh(III)-hydride species **A**. The insertion of allene **1** with **A** forms an electrophilic Rh(III)-allyl intermediate **B**, which undergoes allylic substitution with Hantzsch ester **5a** to furnish the terminal alkene **2** and regenerate the catalyst.

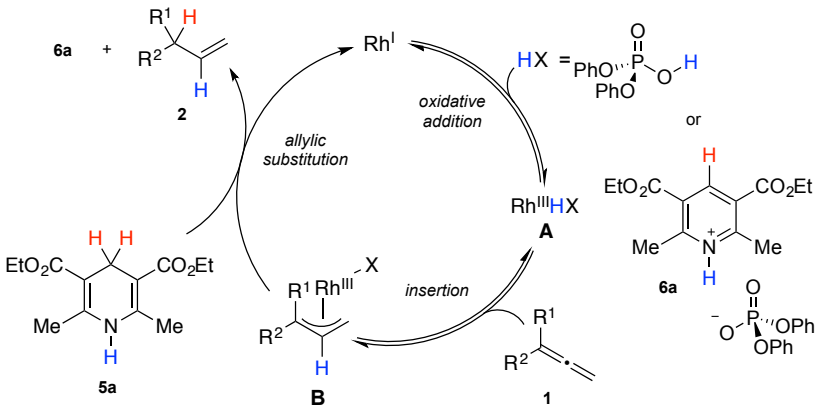



**Figure 1.10.** Proposed mechanism for allene semireduction

### 1.3.3 Conclusion

As a complementary approach to allylic alkylation and allylic reduction, we have demonstrated a Rh-catalysed regio- and enantioselective semireduction of allenes as a strategy to generate chiral benzylic motifs. The high reaction selectivities are enabled by a designed Josiphos ligand and a Hantzsch ester reductant. Given the significance of deuterated pharmaceuticals[32-34], new strategies for asymmetric hydride delivery are especially relevant. Our approach allows access to isotopically labelled stereogenic centres and occurs with excellent chemo- and stereocontrol in the presence of functional groups that are sensitive to conventional hydrogenations.

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# Chapter 2 – Rhodium-Catalyzed Cycloisomerizations

## 2.1 Diastereodivergent Construction of Bicyclic γ-Lactones via Enantioselective Ketone Hydroacylation[iv]

### 2.1.1 Introduction

Cyclic architectures comprise a large number of natural products with diverse biological activity.[1] Nature uses enzymes to access both stereoisomers of any bicycle through kinetic control.[2] The use of metal-catalysis to construct bicyclic motifs with high enantio- and diastereocontrol thus represents a modern challenge for organic synthesis. Inspired by the occurrence of bicyclic γ-lactones in natural products[3] (Figure 2.1a), we sought an atom-economical strategy[4] to access both the *syn* and *anti* diastereomers by ketone hydroacylation[5-7] (Figure 2.1b). Towards this goal, we herein report the construction of bicyclic γ-lactones featuring the rare activation of aliphatic aldehydes, without competitive decarbonylation.[7,8]

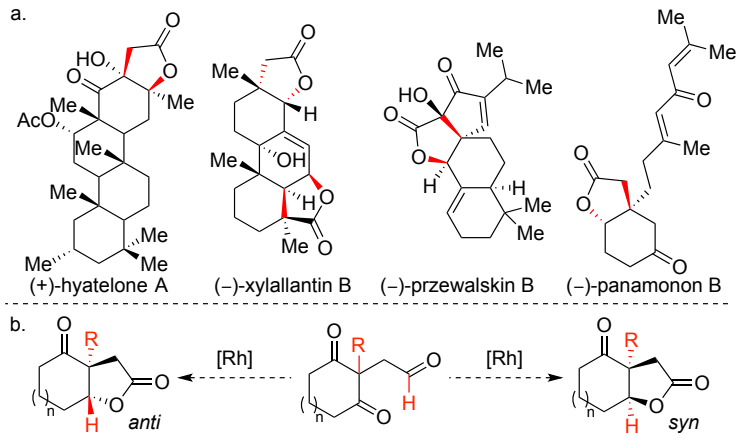


**Figure 2.1.** Inspiration for diastereodivergent ketone hydroacylation

### 2.1.2 Results and Discussion

To begin our studies, we chose 4,4'-diketo aldehyde **1a** bearing a β-quaternary carbon center as the model substrate. This substrate would allow us to address the challenge of preparing quaternary carbon centers with high enantiocontrol using desymmetrization.[9-11] Guided by

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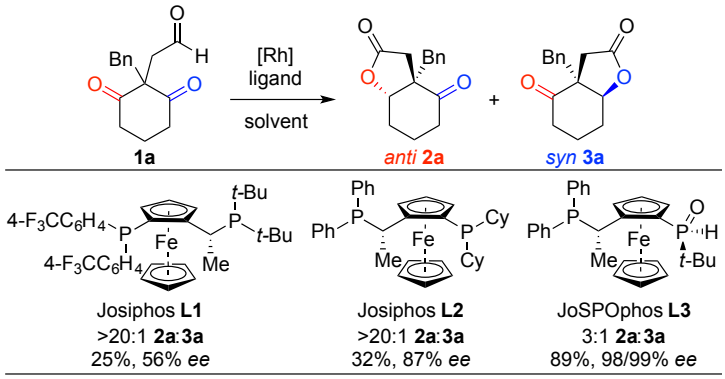
previous hydroacylations,[6,7] we examined $[Rh(C_2H_4)_2Cl]_2$ with a wide range of bidentate phosphine ligands.[12] The Josiphos family of ligands, which we previously found to promote intermolecular hydroacylation with aliphatic aldehydes proved promising (Table 2.1).[12] A combination of $[Rh(C_2H_4)_2Cl]_2$ and Josiphos **L1** in toluene afforded the anti bicyclic γ-lactone **2a** (25% yield, >20:1 *dr*, 56% *ee*). Using Josiphos **L2** improved the enantioselectivity (32% yield, >20:1 *dr*, 87% *ee*). With JoSPOphos **L3**,[13] both diastereomers were observed with excellent enantioselectivities (98% *ee* for **2a** and 99% *ee* for **3a**) in 89% yield as a 3:1 mixture of **2a**:**3a**. Developed by Pugin and Pfaltz for asymmetric hydrogenation, this ligand had yet to be explored for hydroacylation.[13]

**Table 2.1.** Ligand Effects on Stereoselectivity[a,b]




[a] Isolated yields. The *ee* was determined by chiral SFC analysis, and *dr* was determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] Conditions: **1a** (0.20 mmol), $[Rh(C_2H_4)_2Cl]_2$ (2.5 mol%), ligand (5 mol%) in toluene (0.4 mL), 21 °C, 24 h.

While methods for making bicyclic γ-lactones have been reported,[14,15] we aimed to develop a complementary and diastereodivergent strategy. Because the JoSPOphos **L3** ligand provided access to both *anti* and *syn* diastereomers with high enantiocontrol, we chose this ligand for further study. Through a solvent study at 21 ˚C (Table 2.2a), we found that the *anti*

**Table 2.2.** Parameters Impacting Diastereocontrol[a,b]

**a. solvent effect:** ($[Rh(C_2H_4)_2Cl]_2$, at 21 °C)

| | aprotic | | | | protic | | |
|---|---|---|---|---|---|---|---|
| **2a** *anti* | DME 8:1 | toluene 3:1 | DCE 1.7:1 | THF 1.3:1 | *t*-BuOH 1:2 | *t*-AmOH 1:3 | **3a** *syn* |

**b. temperature effect:** ($[Rh(C_2H_4)_2Cl]_2$)

| | in DME | | | in *t*-AmOH | | |
|---|---|---|---|---|---|---|
| | 10 °C | 21 °C | 80 °C | 21 °C | 50 °C | 80 °C |
| **2a** *anti* | 13:1 | 8:1 | 1.5:1 | 1:3 | 1:8 | 1:10 |

**3a** *syn*

**c. counterion effect:** ($(Rh(COD)_2X$ or $[Rh(COD)X]_2$)

| | in DME, at 10 °C | | | | in *t*-AmOH, at 80 °C | | | |
|---|---|---|---|---|---|---|---|---|
| | $Cl^-$ | $Br^-$ | $I^-$ | $SbF_6^-$ | $Cl^-$ | $TfO^-$ | $BF_4^-$ | $SbF_6^-$ |
| **2a** *anti* | 13:1 | 6:1 | 3:1 | 2:1 | 1:11 | 1:>20 | 1:>20 | 1:>20 |

**3a** *syn*

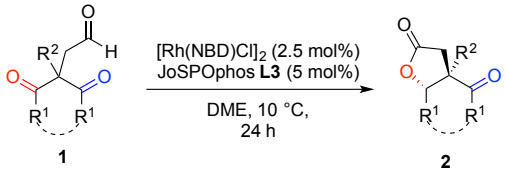
[a] Conditions: **1a** (0.20 mmol), [Rh] (5 mol%), JoSPOphos **L3** (5 mol%) in solvent, 24 h. The diastereomeric ratio (*dr*, **2a**:**3a**) for each case was determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] See Appendix for more details.

diastereomer was favored in polar aprotic solvents, such as 1,2-dimethoxyethane (DME) (8:1 **2a**:**3a**). In contrast, the *syn* diastereomer was preferred in polar protic solvents, such as *tert*-amyl alcohol (*t*-AmOH) (1:3 **2a**:**3a**). Applying these solvents, we discovered a strong temperature dependence (Table 2.2b). At lower temperatures, the *anti* diastereomer was favored (e.g., 13:1 **2a**:**3a** at 10 ˚C in DME), whereas higher temperatures favored the *syn* diastereomer (e.g., 1:10 **2a**:**3a** at 80 ˚C in *t*-AmOH). Finally, tuning of the catalyst counterion revealed that those more coordinating (e.g., $Cl^-$) promote **2a**, whereas those less coordinating (e.g., $SbF6^-$) favor **3a** (Table 2.2c).[16,17] Ultimately, this intramolecular hydroacylation generates the *anti* diastereomer **2a** (91% yield, 17:1 *dr*, 99% *ee*) under $[Rh(NBD)Cl]_2$/**L3** in DME at 10 ˚C and the *syn* diastereomer **3a** (98% yield, >20:1 *dr*, 97% *ee*) under $Rh(COD)_2SbF_6$/**L3** in *t*-AmOH at 80 ˚C.

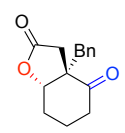
Next, we examined the scope and prepared nineteen *anti* bicyclic γ-lactones in high yields and enantioselectivities (Table 2.3). Keto aldehydes bearing various alkyl groups cyclized to the corresponding *anti* bicyclic γ-lactones in 53–91% yields with 6–17:1 *dr* and 94–>99% *ee* (**2a**-**f**). Dimethyl substituted bicyclic γ-lactone **2g** was obtained in 81% yield, 6:1 *dr*, >99% *ee*, and its absolute configuration was determined by X-ray crystallography.[12] A keto aldehyde containing a seven-membered ring underwent the intramolecular hydroacylation to afford bicyclic[5.3.0]lactone **2h** in 59% yield and 98% *ee* but with lower diastereoselectivity (2:1 *anti*:*syn*). Under the standard conditions, we found that the 3-phenyl substituted keto aldehyde gave the corresponding *syn* bicyclic γ-lactone **3m** rather than the expected *anti* diastereomer **2i**. By using Josiphos **L1** as the ligand in *n*-BuOAc at 100 °C, however, the *anti* diastereomer **2i** was obtained in 81% yield, 10:1 *dr* and 96% *ee*. Using Josiphos **L1**, substrates with either electron-donating (**2j**, **2k**, **2q**, **2r**) or electron-withdrawing groups (**2l**-**p**) on the phenyl ring gave the

desired bicyclic γ-lactones in 67–78% yields with 6–12:1 *dr* and 87–97% *ee*. Aryl halides (**2b**, **2l**, **2m**), ketones (**2e**), esters (**2f**, **2n**) and nitriles (**2o**) were tolerated.

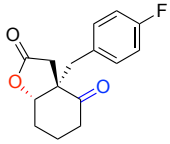
**Table 2.3.** Enantioselective and *anti*-Diastereoselective Ketone Hydroacylation[a]



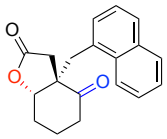

**1** **2**



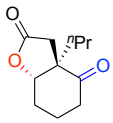
**2a**, 91%
17:1 *dr*, 99% *ee*[b]



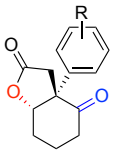
**2b**, 83%
12:1 *dr*, 94% *ee*[b]



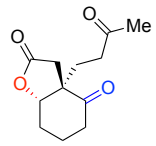
**2c**, 72%
8:1 *dr*, >99% *ee*[b]



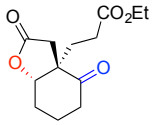
**2d**, 80%
8:1 *dr*, >99% *ee*[b]



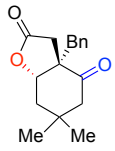
| | |
|---|---|
| R = H | **2i**, 81%, 10:1 *dr*, 96% *ee*[c] |
| 4-OMe | **2j**, 75%, 8:1 *dr*, 95% *ee*[c] |
| 3,4-$(OMe)_2$ | **2k**, 76%, 8:1 *dr*, 97% *ee*[c] |
| 4-Cl | **2l**, 74%, 9:1 *dr*, 94% *ee*[c] |
| 4-F | **2m**, 75%, 11:1 *dr*, 94% *ee*[c] |
| 4-$CO_2Et$ | **2n**, 77%, 12:1 *dr*, 95% *ee*[c] |
| 4-CN | **2o**, 74%, 11:1 *dr*, 90% *ee*[c] |
| 4-$CF_3$ | **2p**, 78%, 10:1 *dr*, 92% *ee*[c] |
| 3-Me | **2q**, 79%, 10:1 *dr*, 94% *ee*[c] |
| 2-Me | **2r**, 67%, 6:1 *dr*, 87% *ee*[c] |



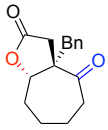
**2e**, 53%
6:1 *dr*, >99% *ee*[b]



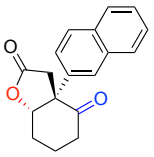
**2f**, 82%
8:1 *dr*, >99% *ee*[b]



**2g**, 81%
6:1 *dr*, >99% *ee*[b]



**2h**, 59%
2:1 *dr*, 98/90% *ee*[b]



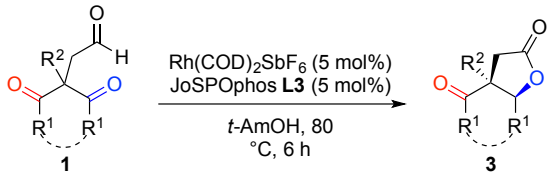
**2s**, 68%
9:1 *dr*, 92% *ee*[c]

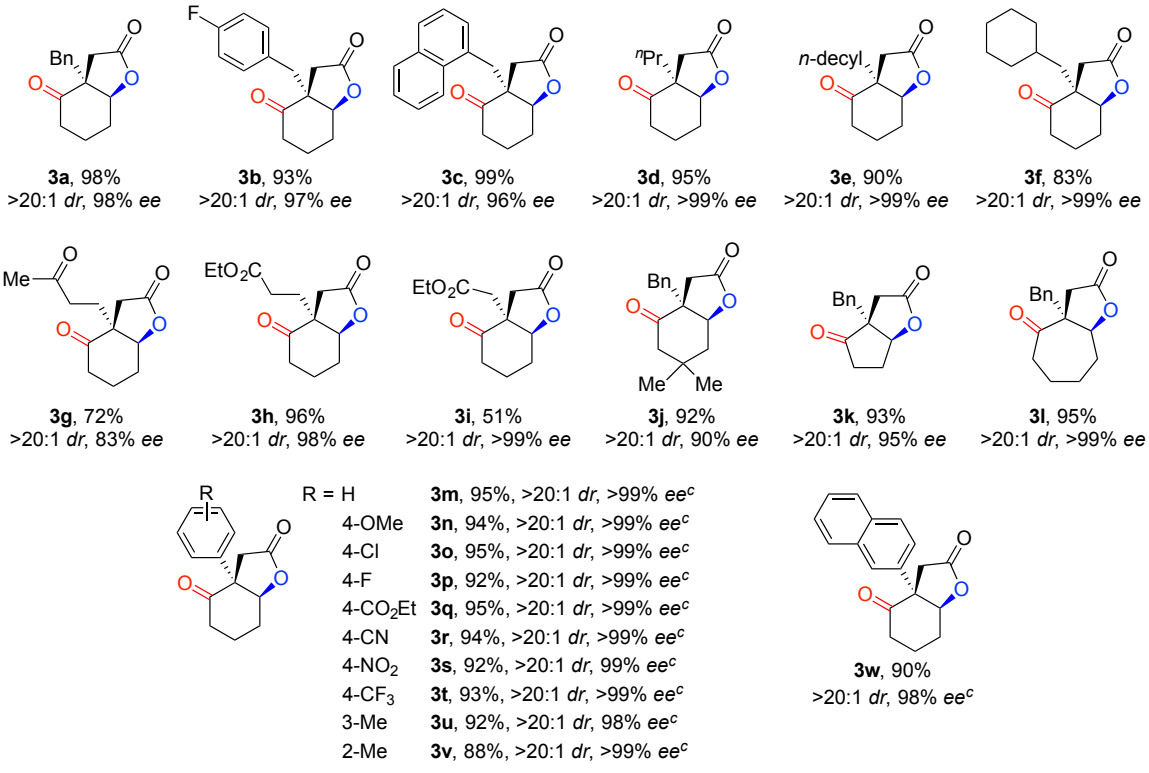
[a] Isolated yields of the major diastereomer **2**. The *ee* was determined by chiral SFC analysis, and *dr* was determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] Conditions: **1** (0.10 or 0.20 mmol), $[Rh(NBD)Cl]_2$ (2.5 mol%), JoSPOphos **L3** (5 mol%) in DME (0.50 M), 10 °C, 24 h. [c] Conditions: **1** (0.10 mmol), $[Rh(COD)Cl]_2$ (2.5 mol%), Josiphos **L1** (5 mol%) in *n*-BuOAc (0.50 M), 100 °C, 24 h.

In a similar fashion, we examined the substrate scope under the *syn* diastereoselective conditions (Table 2.4). Twenty-three 4,4'-diketo aldehydes gave the desired *syn* bicyclic γ-lactones (**3a-w**) in 51–99% yields with >20:1 *dr* and 83–>99% *ee*. Substrates with five- or seven-membered rings efficiently afforded the corresponding *syn* [3.3.0] and [5.3.0] bicyclic γ-lactones (**3k**, 93% yield, >20:1 *dr*, 95% *ee*; **3l**, 95% yield, >20:1 *dr*, >99% *ee*), respectively.[18] Our hydroacylation conditions tolerated ketone (**3g**), ester (**3h-i**, **3q**), halogen (**3b**, **3o**, **3p**, **3t**), nitrile (**3r**), nitro (**3s**) and naphthyl groups (**3c**, **3w**). Some of the aldehydes showcased here (**1e**, **1f**, **1i** and **1k**) were unreactive when tested under the *anti*-selective conditions. The *syn*-selective protocol shows greater scope most likely due to the higher reaction temperature. The absolute configuration of **3j** was confirmed by X-ray crystallography.[12] In comparison to the *anti* selective

hydroacylation, the enantiotopic carbonyl group undergoes reduction to generate the corresponding *syn* diastereomer (see X-ray data for compounds **2g** vs **3j**).[12]

**Table 2.4.** Enantioselective and *syn*-Diastereoselective Ketone Hydroacylation[a,b]




[a] Isolated yields of the major diastereomer **3**. The *ee* was determined by chiral SFC analysis, and *dr* was determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] Conditions: **1** (0.10 or 0.20 mmol), $Rh(COD)_2SbF_6$ (5 mol%), JoSPOphos **L3** (5 mol%) in *t*-AmOH (0.20 M), 80 °C, 6 h. [c] $[Rh(COD)Cl]_2$ (2.5 mol%) was used.

To explore the elaboration of these bicycles, we applied this method to achieve an enantioselective formal synthesis of (–)-mesembrine (Figure 2), which is a potent serotonin reuptake inhibitor isolated from Sceletium tortuosum.[19,20] We chose to intercept a racemic intermediate from Kulkarni's route.[21] Rh-catalyzed desymmetrization of the 4,4'-diketo aldehyde **1x** provided *syn* bicyclic γ-lactone **3x** in 92% yield, >20:1 *dr*, 97% *ee*. The absolute configuration of **3x** was confirmed by X-ray crystallography.[12] Pd-catalyzed aerobic

dehydrogenation[22] and subsequent Luche reduction afforded the allylic alcohol **4**. Sequential, 1,3-transposition of **4** with Osborn's rhenium(VII) catalyst,[23] oxidation, and catalytic hydrogenation afforded isomeric *syn* bicyclic γ-lactone **5**, which has been converted to (–)-mesembrine.[21]

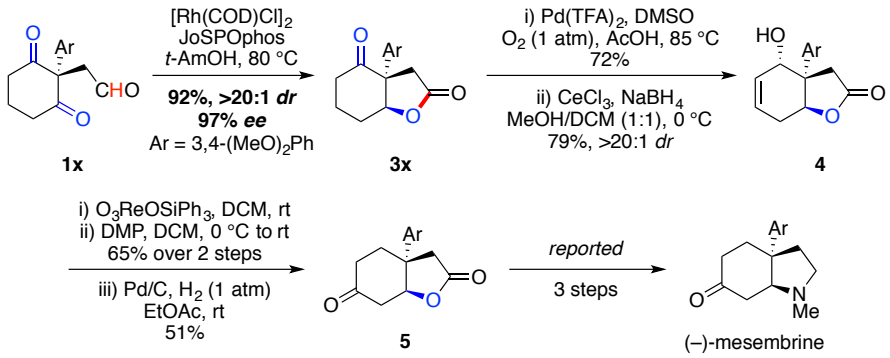



**Figure 2.2.** Formal enantioselective synthesis of (–)-mesembrine

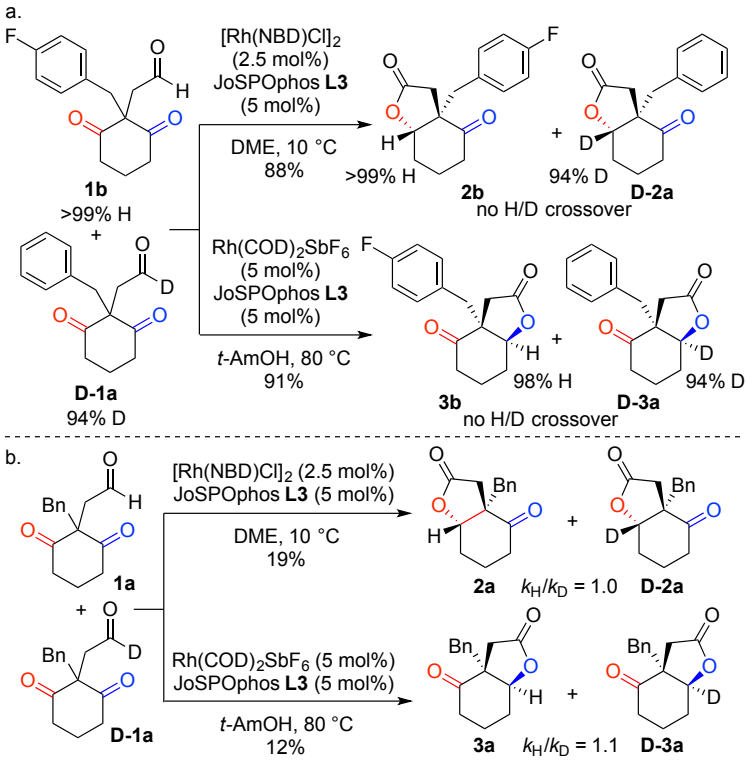



**Figure 2.3.** H/D crossover and kinetic isotope effect experiments

To gain insight into the mechanism, we prepared isotopically labeled substrates and performed crossover and KIE experiments. A crossover experiment with **1b** and **D-1a** suggests that Rh-H insertion is intramolecular, rather than intermolecular.[12] We measured kinetic isotope effects by using a mixture of **1a** and **D-1a**; we observed no KIE under *anti* conditions and a KIE near unity under the *syn* conditions (Figure 2.3). These results suggest that neither aldehyde C–H bond activation nor Rh-hydride insertion are turnover-limiting.[24]

On the basis of our observations and previous reports,[6,7,25] we propose a mechanism in which reductive elimination governs the diastereoselectivity (Figure 2.4).[26] First, oxidative addition of the aldehydic C–H bond in diketo aldehyde **1** to the Rh(I)-catalyst generates an acyl Rh(III)-hydride intermediate **I**. Subsequent insertion of the ketone carbonyl group into the Rh–H bond of **I** generates either rhodacycle **II** or **III**. Because the insertion step is reversible, intermediates **II** and **III** are in equilibrium. The turnover-limiting and stereodetermining step is reductive elimination, which delivers the bicyclic γ-lactone (**2** or **3**) and regenerates the Rh(I)-catalyst. Thus, Curtin-Hammett type kinetics may be operative.[26] Based on our X-ray crystallography results, enantiotopic carbonyl groups are selected for by the same catalyst, which suggests remarkably different transition states leading to the *syn* versus *anti* isomers. The solvent and coordinating ability of the counterion influences these transition state geometries and energies. Notably, we also observe a strong temperature dependence on diastereoselecitvity,[27] which may be due to a marked difference in the entropy of activation for these competing reductive eliminations.

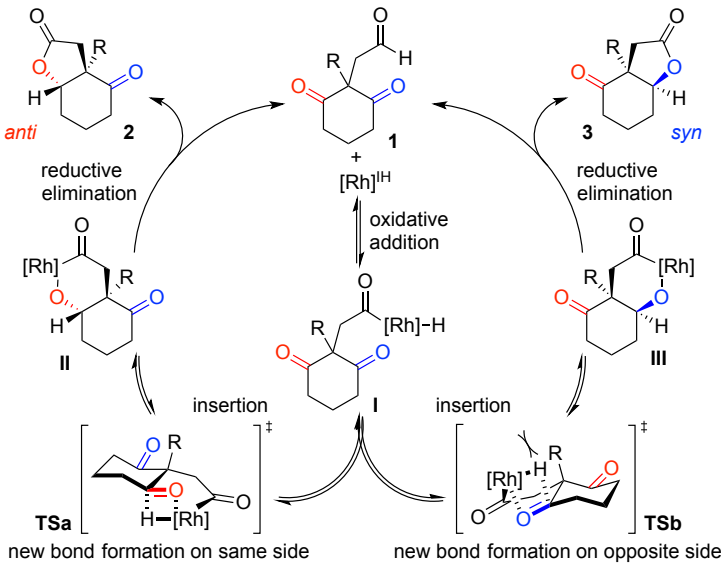



**Figure 2.4.** Reductive elimination governs diastereoselectivity

By computational studies,[28] we find that the *syn* bicycle **3a** is thermodynamically more stable than the *anti* isomer **2a**. We recognize that the *syn* isomer can undergo a chair flip and thus has more conformational degrees of freedom than its *anti* counterpart. A survey of literature reveals that bond formation to generate related fused bicycles typically occurs to the carbonyl via the

same side of the reactive tether, which suggests that such additions are rapid and irreversible.[9b] In contrast, our hydroacylation strategy enables access to both stereoisomers via kinetic control. Under our standard conditions, the *anti* and *syn* products do not interconvert[12] thus further supporting the idea that reductive elimination is irreversible.

### 2.1.3 Conclusion

We have discovered a ketone hydroacylation that desymmetrizes readily accessible 4,4'-diketo aldehydes to generate chiral bicyclic γ-lactones. Both diastereomers can be accessed selectively by tuning the reaction temperature, solvent, and catalyst counterion. Further kinetic and computational studies are underway to better understand these effects to guide development of future stereodivergent strategies.

### 2.1.4 References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(28) DFT calculations show that the free energy of **2a** is 5.8 kcal/mol higher than **3a**. See Appendix 2.1 for more details.

## 2.2 Rhodium-Catalyzed Enantioselective Cycloisomerization to Cyclohexenes Bearing Quaternary Carbon Centers[v]

### 2.2.1 Introduction

The cycloisomerization of dienes represents a powerful and atom-economical route to unsaturated carbocycles that remains relatively limited to the preparation of five-membered rings (Figure 2.5a).[1,2] Cycloisomerizations to six-membered rings have been challenging to achieve with high regio- and enantiocontrol.[1-4] Such strategies remain sought after due to the need for cyclohexenes as building blocks and their common occurrence in nature.[5] Inspired by natural products, including pinnatal, jerantiphylline A, and myricolal (Figure 2.5b),[6] we designed a metal-catalyzed isomerization to generate cyclohex-3-enecarbaldehydes bearing α-quaternary centers.[7] Herein, we disclose a desymmetrization of bisallylaldehydes **1** to generate cyclohexenes **4** via the desymmetrization of prochiral quaternary centers (Figure 2.5c-route A).[7-10] Our Rh-catalyzed method provides enantioselective access to the 3,5,5-trisubstituted cyclohexene motif that is inaccessible by the

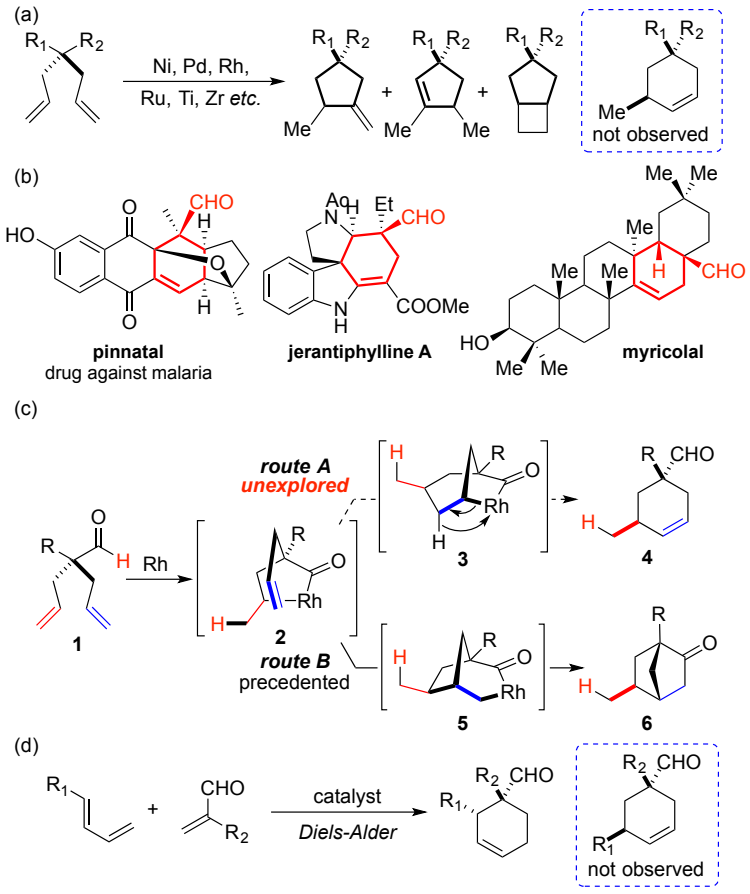


**Figure 2.5.** Inspiration for Rh-catalyzed cycloisomerization

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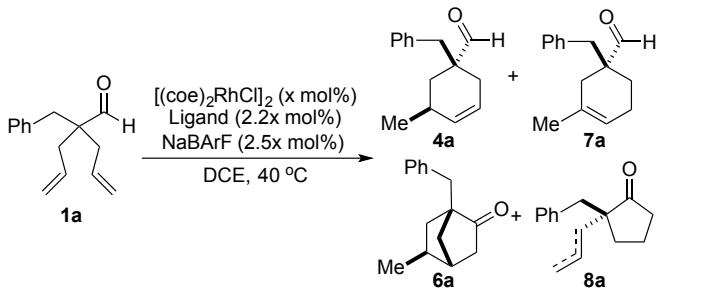
well-established Diels–Alder reaction and therefore complements conventional cycloadditions (Figure 2.5d).[11]

The initial steps of our proposal rely on the well-precedented hydroacylation mechanism, namely aldehyde C–H bond activation and olefin insertion,[12,13] to form intermediate **2** (Figure 2.5c). Next, we imagined that a regioselective carbometallation of the pendant olefin could afford **3**, which upon endocyclic β-hydride elimination[13,14] would lead to the unprecedented cyclohexene **4** (Figure 2.5c-route A). Carbometallation could occur with the opposite regioselectivity to generate **5**, which upon reductive elimination would yield bicyclic heptanones **6** (Figure 2.5c-route B).[15a] On the basis of our previous study,[13] we realized that the key challenge would be to identify a catalyst to favor the proposed cycloisomerization, in preference to the known hydroacylation and carboacylation[15] pathways.

**Table 2.5.** Ligand effects on the desymmetrization of α,α-bisallylaldehyde **1a**




| | | | | |
|---|---|---|---|---|
| Ar= | Ph-DPPF | DTB-DPPF | DTBM-DPPF | DTMS-DPPF |
| yield of **4a**+**7a** | 11%[a] | 66%[b] | 56%[b] | 30%[b] |
| chemoselectivity | (**4a**+**7a**):**6a**:**8a** = 1:1.6:1.4 | (**4a**+**7a**):**6a**:**8a** = 4:1:1 | (**4a**+**7a**):**6a**:**8a** = 3.7:1:1.8 | (**4a**+**7a**):**6a**:**8a** = 6:3:1 |
| Ar= | Ph-SDP | Xyl-SDP | DTB-SDP | DTBM-SDP |
| yield of **4a**[d-f] | 71%, 99% *ee* | 71%, 96% *ee* | 94%, 83% *ee* | 92%, 95% *ee* |
| chemoselectivity[g] | **4a**:**6a** = 3:1 | **4a**:**6a** = 3:1 | **4a**:**6a** = >30:1 | **4a**:**6a** = >30:1 |

[a] x=5, 18 h. [b] x=2.5, 18 h. [c] x=1.25, 12 h. [e] >20:1 *dr*, determined by $^1$H NMR. [f] The aldehyde **4a** was reduced to its corresponding alcohol to determine *ee* by SFC analysis with a chiral stationary phase. [g] Trace amount of **7a** and **8a** was observed. Xyl: 3,5-Me-phenyl, DTB: 3,5-di(*t*-butyl)-phenyl, DTBM: 3,5-di(*t*-butyl)-4-methoxy-phenyl, DTMS: 3,5-di(trimethylsilyl)-phenyl.

## 2.2.2 Results and Discussion

With this hypothesis in mind, we chose 2-allyl-2-benzylpent-4-enal (**1a**) as a model substrate for desymmetrization (Table 2.5). In general, electron-donating bidentate

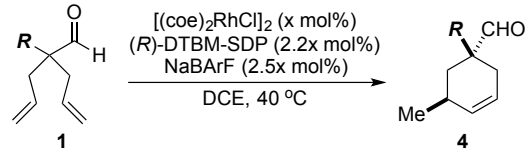
phosphine ligands with bite-angles ranging from 89–91° favored formation of the cyclopentanone **8a** via isomerization-hydroacylation pathways.[13,16] By focusing on ligands with bite-angles ranging from 96–100°,[16] we discovered two ligand classes that resulted in formation of cyclohexenes **4a**/**7a**[17] and bicyclic heptanone **6a** via the carbometallation pathway. By tuning the aryl-substituents on DPPF, we observed a modest increase in selectivity for the generation of cyclohexenes.

Zhou's rigid spiro-bisphosphine ligand, (*S*)-Ph-SDP,[18] gave the most promising lead as we obtained cyclohex-3-enecarbaldehyde **4a** in 71% yield as the major product (99% *ee*, >20:1 *dr*) with generation of **6a** in 23% yield. Transformation of **1a** with Rh-SDP catalyst was efficient with 2.5 mol% catalyst loading. By fine-tuning the aryl-substituents on the Zhou ligand, we observed a dramatic effect on the selectivity for **4a** over **6a**. Commercially available (*S*)-Ph-SDP and (*S*)-Xyl-SDP showed similar ca. 3:1 selectivity for **4a** over **6a**. By changing the meta-substituents on the phenyl group from methyl to *t*-butyl ((*S*)-DTB-SDP), we observed **4a** as the predominant product. There was a drop in enantioselectivity from 96% *ee* to 83% *ee*. We prepared a novel analogue, (*R*)-DTBM-SDP, which bears an additional para-methoxy substituent. This designer ligand gave **4a** as the major product, with high enantioselectivity and diastereoselectivity (95% *ee*, >20:1 *dr*).

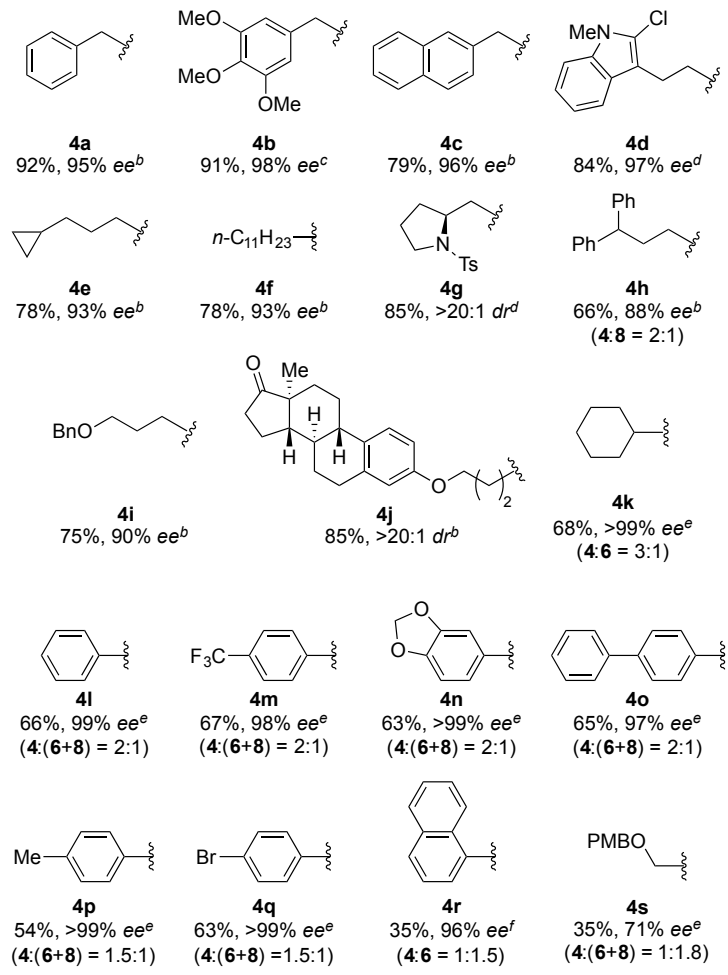
Next, we used this protocol to prepare cyclohex-3-enecarbaldehydes bearing α-quaternary stereocenters (Table 2.6). Aldehydes with α-aliphatic substituents (**1a**–**1j**) underwent cycloisomerization in 71–92% yields with high enantioselectivities and diastereoselectivities (up to 98% *ee*, >20:1 *dr*). Cyclopropyl groups (**1e**), nitrogen heterocycles (**1d** and **1g**), haloaromatics (**1d**), ethers (**1b**, **1i**, and **1j**), and ketones (**1j**) were well tolerated under these conditions.

Aldehydes bearing more sterically encumbered α-substituents such as cyclohexyl (**1k**) and aromatic groups (**1l**–**q**) were challenging to cyclize. However, by using Ph-SDP as the ligand and applying a higher rhodium loading (5%), we obtained the corresponding cyclohexenecarbaldehydes (**4k** and **4l**–**q**) as the major products (about 2:1 chemoselectivity (**4**/(**6**+**8**)), 54−68% isolated yields, and 96−99% *ee*'s). Aldehyde **1r**, bearing the 1-naphthyl group, was unreactive with DTBM-SDP as the ligand, but could be cycloisomerized using the less bulky ligand, Tol-SDP. The aldehyde bearing a β-benzyloxy group (**1s**) transformed to the cyclohexene in only 35% yield because the γ-oxygen directing group promotes hydroacylation over cycloisomerization.[13,14] No reactivity was observed with more hindered, substituted olefin substrates.[19] While further catalyst development is warranted, our study represents a rare example of isomerization of α,ω-heptadienes to generate cyclohexenes with high enantiocontrol.

**Table 2.6.** Enantioselective Cycloisomerization of α,α-Bisallylaldehydes[a]




**1** **4**




**4a** 92%, 95% *ee*[b]

**4b** 91%, 98% *ee*[c]

**4c** 79%, 96% *ee*[b]

**4d** 84%, 97% *ee*[d]

**4e** 78%, 93% *ee*[b]

**4f** 78%, 93% *ee*[b]

**4g** 85%, >20:1 *dr*[d]

**4h** 66%, 88% *ee*[b] (**4**:**8** = 2:1)

**4i** 75%, 90% *ee*[b]

**4j** 85%, >20:1 *dr*[b]

**4k** 68%, >99% *ee*[e] (**4**:**6** = 3:1)

**4l** 66%, 99% *ee*[e] (**4**:(**6**+**8**) = 2:1)

**4m** 67%, 98% *ee*[e] (**4**:(**6**+**8**) = 2:1)

**4n** 63%, >99% *ee*[e] (**4**:(**6**+**8**) = 2:1)

**4o** 65%, 97% *ee*[e] (**4**:(**6**+**8**) = 2:1)

**4p** 54%, >99% *ee*[e] (**4**:(**6**+**8**) = 1.5:1)

**4q** 63%, >99% *ee*[e] (**4**:(**6**+**8**) =1.5:1)

**4r** 35%, 96% *ee*[f] (**4**:**6** = 1:1.5)

**4s** 35%, 71% *ee*[e] (**4**:(**6**+**8**) = 1:1.8)

[a] Isolated yields. The *ee* was determined by chiral SFC analysis after reducing the aldehydes with $NaBH_4$, and *dr* was determined by $^1H$ NMR. [b] Reaction condition: x=1.25, 40 °C, 4-12 h. [c] x=1, rt, 2 h. [d] x=1, 40 °C, 4 h. [e] (*S*)- or (*R*)-SDP, x=2.5, 40 °C, 18 h. [f] (*S*)-Tol-SDP, x=2.5, 40 °C, 18 h.

Aldehydes **4** can be easily oxidized or reduced to generate the corresponding acids or alcohols, respectively (Figure 2.6). Depending on its oxidation state, the resulting cyclohexenes can undergo a number of selective transformations. For example, the aldehyde is necessary to initiate isomerization of the olefin to generate cyclohexenecarbaldehyde **7a** using a Rh(I)/dppf complex (Figure 2.6a).[20] Subjecting ester **9** to the same reaction conditions resulted in no isomerization of the olefin (Figure 2.6b). From this observation, we believe isomerization is triggered by aldehyde C–H bond activation, which generates the requisite Rh-hydride.[13,14,21] By Pinnick oxidation[22] of **4a**, we obtained the carboxylic acid derivative **10**. Iodolactonization of cyclohex-3-enecarboxylic acid **10** afforded [3.2.1]-bicyclic lactone **11** containing four stereogenic centers as a single regio- and diastereomer (Figure 2.6c). Reduction of the aldehyde **4a** to the alcohol resulted in **4a-OH**. The alcohol can be used to direct a diastereoselective cyclopropanation to form bicycloheptane **12** (Figure 2.6d, *dr* >20:1). Alcohol

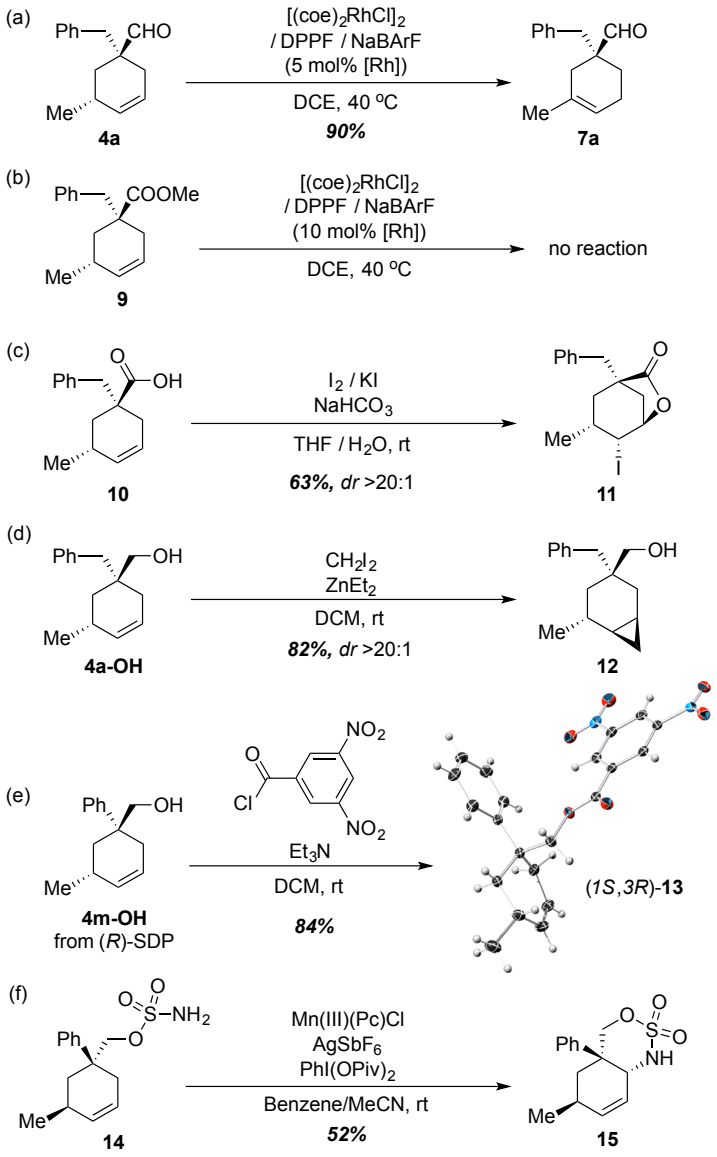



**Figure 2.6.** Elaboration of cyclohexenecarbaldehydes

**4m-OH** can be acylated to generate ester **13** or sulfamylated to give sulfamate **14**. The molecular structure and absolute configuration of **13** was determined by X-ray crystallography (Figure 2.6e).[23] By using White's protocol, sulfamate **14** can undergo a highly diastereoselective allylic C–H bond amina-tion to afford **15** (Figure 2.6f).[24] These simple derivatizations allow a number of different cyclohexanes and cyclohexenes to be prepared with substitution patterns that would otherwise be difficult to access.

On the basis of our observations and literature precedence, we propose the mechanism shown in Scheme 2.7. The cationic Rh(I)-complex activates the aldehyde C–H bond of **1** to form acyl-Rh(III)-hydride **16** which undergoes hydrometallation to generate rhodacycle **2**. Carbometallation onto the pendant olefin in rhodacycle **2** can occur to afford carbometallated intermediate **3**, which would then undergo β-hydride elimination to form acyl-Rh(III)-hydride **17**. Reductive elimination from **17** leads to formation of cycloisomerization product **4**. Reductive elimination from **2** or **3** would result in formation of a strained cyclobutanone, which is not observed. The carbometallation of rhodacycle **2** onto the pendant olefin with opposite regioselectivity would result in rhodabicycle **5** (Figure 2.5c), which undergoes reductive elimination to form **6**.

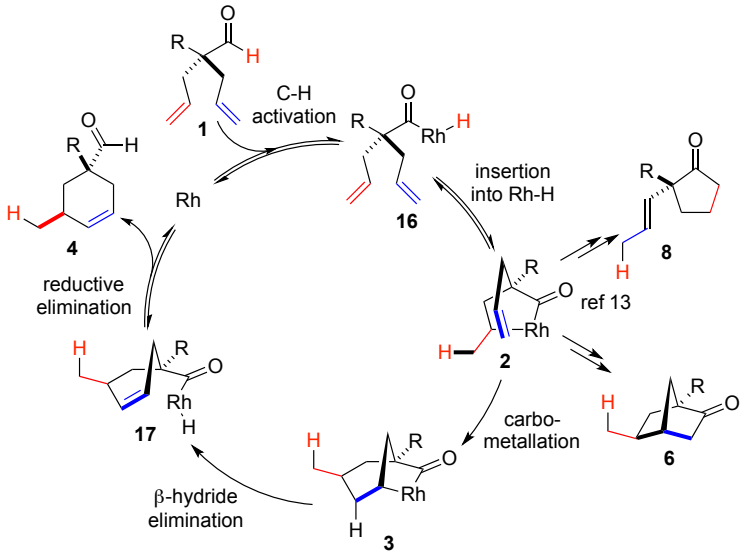
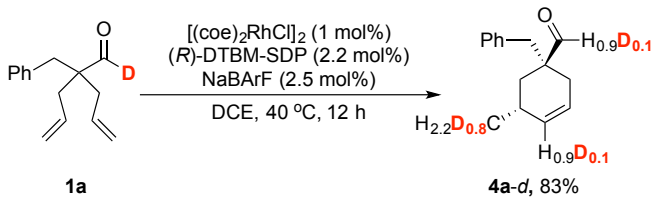



**Figure 2.7.** Proposed mechanism

Our study reveals that the bite angle of the ligand is critical for promoting carboacylation in preference to isomerization-hydroacylation pathways. An electron-donating MeOBiphep ligand

(bite angle: 90.6°) enables an enantioselective hydroacylation to afford cyclopentanone **8**.[13] Phosphine ligands with bite angles ranging from 96-99° promote formation of bicyclic heptanone **6**.[13] Yet, the rigid spiro-bisphosphine ligand, (*S*)-Ph-SDP (bite angle: 96.2°) favors a different carbometallation that leads to cyclohexene **4**.

To gain insight into the mechanism, we performed a deuterium-labeling study with *d*-**1a** (eq. 2.1). The reaction of *d*-**1a**, under standard reaction conditions, led to formation of *d*-**4a** where




**1a** **4a-*d*, 83%** (2.1)

80% of the deuterium label was incorporated into the 5-methyl group and 20% was scrambled between the aldehyde and the 4-position. This deuterium scrambling suggests that the olefin-insertion step (**16**→**2** in Scheme 2) is reversible. As a result, either carbometallation or $\beta$-hydride elimination is the rate- and enantiodetermining step.

### 2.2.3 Conclusion

We have demonstrated a Rh-catalyzed enantioselective cycloisomerization of α,α-bisallylaldehydes to form cyclohex-3-enecarbaldehydes. These products represent versatile intermediates that can be elaborated to a range of structures. Mechanistic studies support an aldehyde-assisted cycloisomerization followed by a regioselective carbometallation. The use of a novel SDP ligand enables high selectivity for cycloisomerization. Further experimental and theoretical studies are underway to elucidate the origin of chemoselectivity and guide development of other cycloisomerizations.

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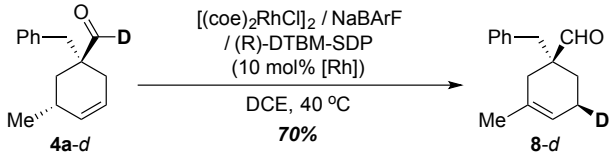
(17) Cyclohexene **7a** arises from olefin isomerization of **4a**.

(18) Xie, J.-H.; Zhou, Q.-L. *Acc. Chem. Res.* **2008**, *41*, 581.

(19) Aldehydes bearing substituted α-allyl groups such as crotyl, cinnamyl, and methallyl groups were unreactive with the Rh/SDP catalyst. We did not observe the desired cycloisomerization product in the reaction of an α,α-bis(homoallyl)aldehyde.

(20) Only some ligands promote this isomerization. DPPF and DPEphos were effective (5% Rh/L, DCE, 40 °C). (*R*)-DTBM-SDP was less reactive even at higher catalyst loading (10% Rh/L).

(21) When D-labeled **4a** (**4a**-*d*) was subjected to the Rh+/(*R*)-DTBM-SDP catalyst (10 mol%), we observed 70% conversion to **8** where the deuterium label was incorporated into the 4-position.




(22) Lindgren, B. O.; Nilsson, T. *Acta Chem. Scand.* **1973**, *27*, 888.

(23) CCDC 1451888 contains the supplementary crystallographic data for compound **13**. See Appendix 2.2. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 879912, Union Road, Cambridge CB879952 879951EZ, UK; fax: +879944 871223 336033.

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## 2.3 Dynamic Kinetic Resolution of Aldehydes by Hydroacylation[vi]

### 2.3.1 Introduction

By merging epimerization with asymmetric catalysis, chemists have developed powerful ways to convert racemic reagents into enantiopure precursors, including those used for making natural products and medicinal targets.[1] While most dynamic kinetic resolutions (DKR's) feature hydrogenation[2a-c] or acylation,[2d,e] variants that exploit C–C bond formation remain rare.[3] Olefin hydroacylation is an atom-economical[4] route to ketones that achieves both C–H bond activation and C–C bond formation.[5] Herein, we disclose a DKR strategy to prepare α,γ-disubstituted cyclopentanones by intramolecular hydroacylation.

The first kinetic resolution of an α-chiral aldehyde was fortuitously discovered by James in 1983. While attempting to develop an enantioselective decarbonylation, the authors observed that 2-methyl-2-phenylpent-4-enal underwent intramolecular hydroacylation to furnish the corresponding cyclopentanone in up to 69% ee (Figure 2.8a).[6a,b] Fu described a parallel kinetic resolution of racemic 4-alkynals to generate a mixture of enantioenriched cyclopentenones and cyclobutanones.[6c] Most recently, Willis disclosed an kinetic resolution of β-thio aldehydes by intermolecular alkyne hydroacylation.[6d]

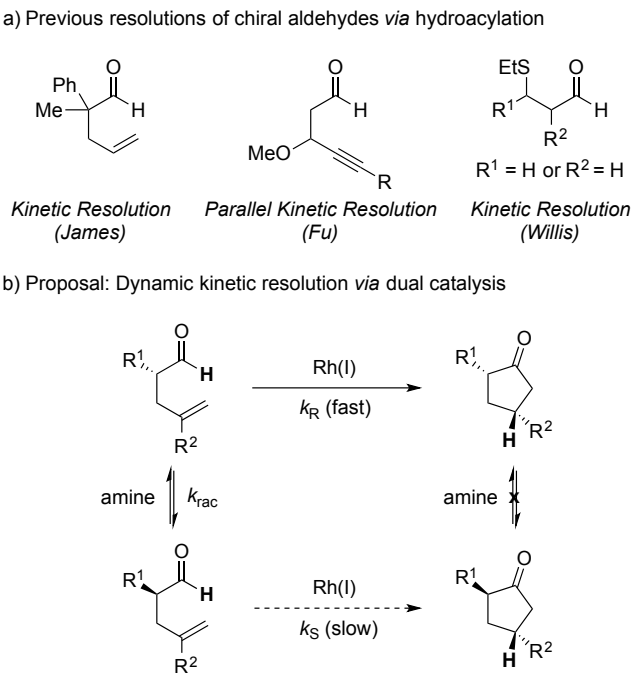



**Figure 2.8.** Resolutions of chrial aldehydes by hydroacylation

Aldehydes bearing either α- or β-stereocenters undergo kinetic resolution. These early studies

[vi] Reproduced from Chen, Z.; Aota, Y.; Nguyen, H. M. H.; Dong, V. M. *Angew. Chem. Int. Ed.*, **2019,** *138*, 3310 with permission from John Wiley & Sons.

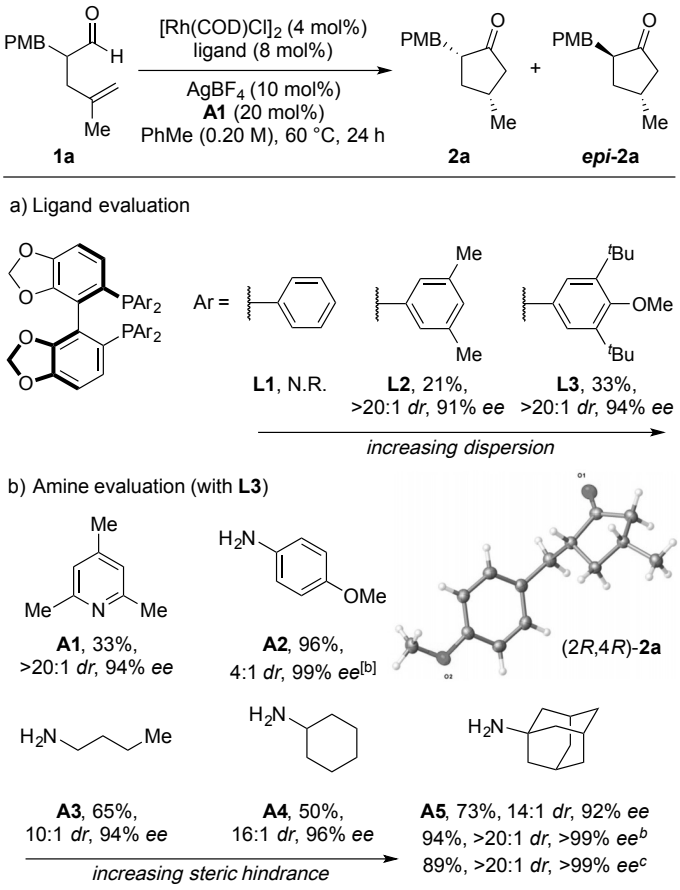
contribute to emerging kinetic resolutions that occur by C–H bond activation,[7] however, the theoretical yield for the enantiopure ketone products is limited to fifty percent. Despite the first resolution over three decades ago, the DKR of aldehydes by hydroacylation had yet to be achieved. In light of this challenge, we imagined combining aldehyde racemization with formyl C–H bond functionalization to invent DKR's via hydroacylation.[8]

We propose using an amine organocatalyst and a Rh-catalyst in tandem to produce α,γ-disubstituted cyclopentanones, a motif not yet accessible by hydroacylation (Figure 2.8b). Given that branched aldehydes readily undergo epimerization,[9] we reasoned a DKR variant of hydroacylation would be feasible. Since the substrate and product have similar acidities, one challenge would be to identify a catalyst that would rapidly and selectively epimerize the aldehyde reagent, in preference to the ketone product. If successful, this DKR by C–C bond formation would complement Buchwald's DKR of cyclopentenones by asymmetric reduction.[10]

### 2.3.2 Results and Discussion

To test our hypothesis, we investigated the cyclization of aldehyde **1a** (Table 2.7). Our initial studies included various bases, such as alkoxides and tertiary amines. The use of pyridine **A1** and a Segphos-derived ligand (Segphos = 5,5'-bis(diphenylphosphino)-4,4'-bi-1,3-benzodioxole) provided an early lead (Table 2.7a), where bulkier phosphine substituents afforded higher reactivity (**L2** and **L3**), presumably due to increased dispersive interactions.[11] The combination of **L3** and **A1** led to cyclopentanone **2a** in 33% yield with high stereoselectivities (>20:1 *dr*, 94% *ee*). Aldehydes are known to form enamines with primary amines, and this reactivity has been used by List to achieve a DKR by reductive amination using aniline **A2**.[9b] We found that **A2** promoted the hydroacylation with excellent reactivity (96%) but gave only 4:1 *dr*. However,

**Table 2.7.** Ligand and Amine Evaluation with α–Alkyl Aldehyde **1a**[a]

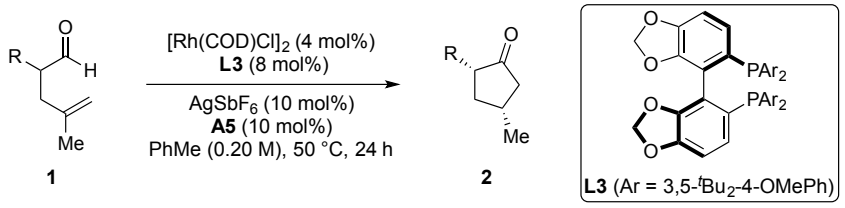


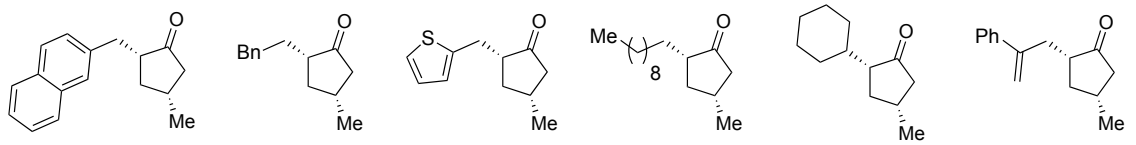

[a] With 0.050 mmol of **1a**. Yields and diastereoselectivities were determined by $^1$H NMR analysis of the unpurified reaction mixture using triphenylmethane as an internal standard. Enantioselectivities (*ee*) were determined by chiral SFC analysis. [b] With 0.10 mmol of **1a**. Reaction performed at 50 °C using $AgSbF_6$ (10 mol%) and 10 mol% of the amine. [c] Isolated yield of **2a** (4.6 mmol scale) using 2 mol% $[Rh(COD)Cl]_2$, 4 mol% **L3**, 5 mol% $AgSbF_6$, and 10 mol% **A5** for 48 h. PMB = *p*-methoxybenzyl. COD = 1,5-cyclooctadiene.

aliphatic primary amines provided higher diastereocontrol with increased steric bulk: *n*-butylamine (**A3**) (65%, 10:1 *dr*), cyclohexylamine (**A4**) (50%, 16:1 *dr*), and 1-adamantylamine (**A5**) (73%, 14:1 *dr*). By using a lower loading of **A5** (10 mol%) and switching the catalyst counter-ion to $SbF_6$, **2a** was obtained in high yield and stereocontrol (94%, >20:1 *dr*, >99% *ee*). The absolute configuration of **2a** was determined to be (2*R*,4*R*) by X-ray crystallography.[12] To demonstrate the scalability of this DKR, we cyclized **1a** on a gram-scale and obtained **2a** in high yield and stereocontrol (89%, >20:1 *dr*, >99% *ee*).

We next examined the cyclization of various α-alkyl aldehydes (Table 2.8). These branched aldehydes undergo DKR with moderate to high reactivity (**2b**–**2k**, 52–94%), diastereocontrol (11–>20:1 *dr*), and enantiocontrol (82–>99% *ee*). This hydroacylation is chemoselective for the terminal olefin as styrenyl olefins (**1g**) and internal alkynes (**1h**), remain intact to afford cyclopentanones **2g** and **2h** (11–>20:1 *dr*, 94–95% *ee*). Placing bulkier alkyl substituents on the olefin led to diminished reactivity and diastereoselectivity (**2j**, 21%, 1:1 *dr*, 88% *ee*). However, high reactivity and stereoselectivities were restored by using JoSPOphos (**L4**) as the chiral ligand

**Table 2.8.** Hydroacylation Scope with α-Alkyl Aldehydes[a]



**2b**, 94%
>20:1 *dr,* 93% *ee*



**2c**, 86%
>20:1 *dr,* 93% *ee*



**2d**, 94%
>20:1 *dr,* 93% *ee*



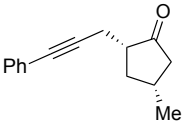
**2e**, 65%[b]
>20:1 *dr,* 96% *ee*[c]



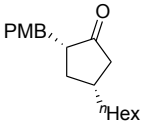
**2f**, 63%[b]
>20:1 *dr,* >99% *ee*[c]



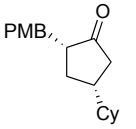
**2g**, 69%
>20:1 *dr,* 94% *ee*



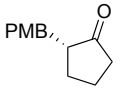
**2h**, 68%[b]
11:1 *dr,* 95% *ee*



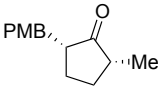
**2i**, 66%
>20:1 *dr,* >99% *ee*



**2j**, 21%[b], 1:1 *dr,* 88% *ee*
89%[d], >20:1 *dr,* >99% *ee*



**2k**, 52%
82% *ee*

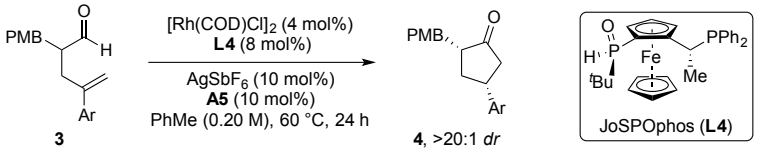


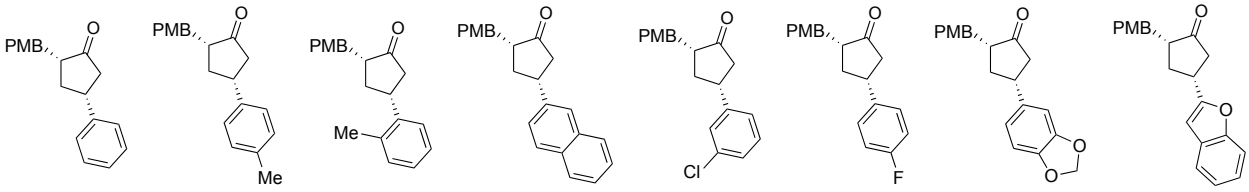
**2l**, 0%

[a] With 0.10 mmol of **1**. Isolated yields are given. Diastereoselectivities were determined by $^1$H NMR analysis of the unpurified reaction mixture. Enantioselectivities (*ee*) were determined by chiral SFC analysis. [b] Reaction performed at 60 °C. [c] SFC analysis performed with the tertiary alcohol after treatment with PhMgBr. [d] Reaction performed with **L4** at 60 °C.

(89%, >20:1 *dr*, >99% *ee*). We also prepared a monosubstituted cyclic ketone (**2k**, 52%, 82% *ee*). A substrate containing an internal olefin (**1l**) failed to cyclize.

**Table 2.9.** Hydroacylation Scope with Styrenyl Olefins[a]



**4a**, 76%
>99% *ee*



**4b**, 90%
95% *ee*



**4c**, 80%
>99% *ee*



**4d**, 88%
96% *ee*



**4e**, 77%
94% *ee*



**4f**, 91%
>99% *ee*



**4g**, 83%
96% *ee*



**4h**, 53%
74% *ee*

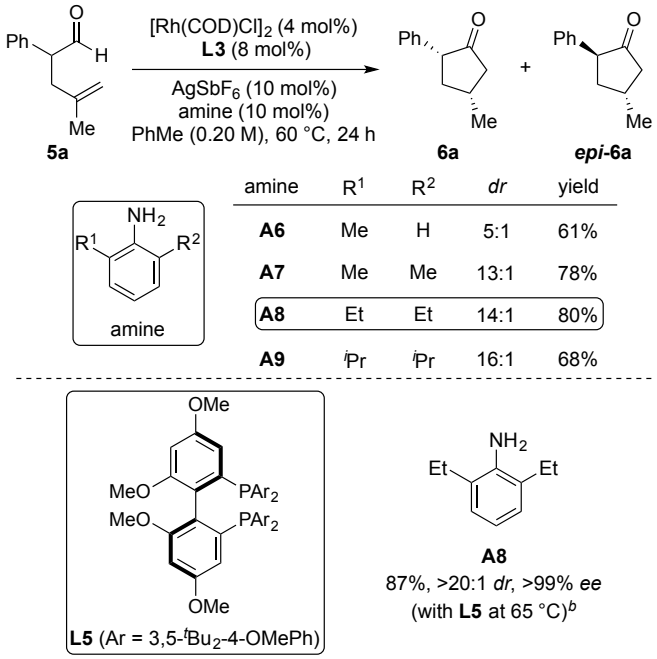
[a] With 0.10 mmol of **3**. Isolated yields are given. Diastereoselectivities were determined by $^1$H NMR analysis of the unpurified reaction mixture. Enantioselectivities (*ee*) were determined by chiral SFC analysis.

Aldehydes with styrenyl olefins (e.g. **3a**) were slow to react with ligand **L3** (Table 2.9). To overcome this limitation, we used amine **A5** and ligand **L4**. This combination enabled the

resolution of chiral aldehydes bearing a range of styrenyl olefins with excellent stereocontrol (**4a**–**4h**, >20:1 *dr*, 74–>99% *ee*). The absolute configuration of **4a** is analogous to that of **2a**, as determined by X-ray crystallography.[12a]

In contrast to the previous aldehydes, we found that the DKR of α-aryl aldehydes **5** requires an aniline co-catalyst (Table 2.10). Using **A5** and **L3**, **5a** transformed into cyclopentanone **6a** with high selectivity (>20:1 *dr*, >99% *ee*), albeit with low yield (24%). Switching to other biaryl ligand scaffolds produced similar results. In contrast, changing the amine to 2,6-disubstituted anilines **A7** and **A8** resulted in improved reactivity and diastereocontrol (78–80%, 13–14:1 *dr*).[13] Aniline **A9**, which is more sterically hindered, provided higher diastereocontrol (16:1 *dr*) but lower yield (68%). Using **A8**, we found that Garphos-derived ligand **L5** promoted the formation of **6a** in 87% yield with high stereoselectivities (>20:1 *dr*, >99% *ee*) (Garphos = 2,2'-bis(diphenylphosphino)-4,4',6,6'-tetramethoxybiphenyl).

**Table 2.10.** Ligand and Amine Evaluation with α-Aryl Aldehyde **5a**[a]




| amine | $R^1$ | $R^2$ | *dr* | yield |
|---|---|---|---|---|
| **A6** | Me | H | 5:1 | 61% |
| **A7** | Me | Me | 13:1 | 78% |
| **A8** | Et | Et | 14:1 | 80% |
| **A9** | *i*Pr | *i*Pr | 16:1 | 68% |

[a] With 0.050 mmol **5a**. Yields and diastereoselectivities were determined by $^1$H NMR analysis of the unpurified reaction mixture using triphenylmethane as an internal standard. Enantioselectivities (*ee*) were determined by chiral SFC analysis. [b] Using 0.10 mmol of **5a**.

We found that **6a** epimerizes on silica and decomposes to form hydroxyketone **6aa** and keto acid **6ab**, which we isolated as the methyl ester (Figure 2.9).[12a] This observation is consistent with those reported by Houminer and others that α-aryl cyclopentanones undergo oxidation via a hydroperoxide intermediate.[14] To circumvent this oxidation, we treat the reaction mixture with

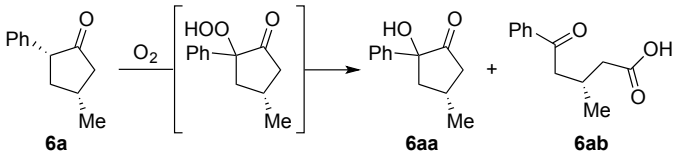
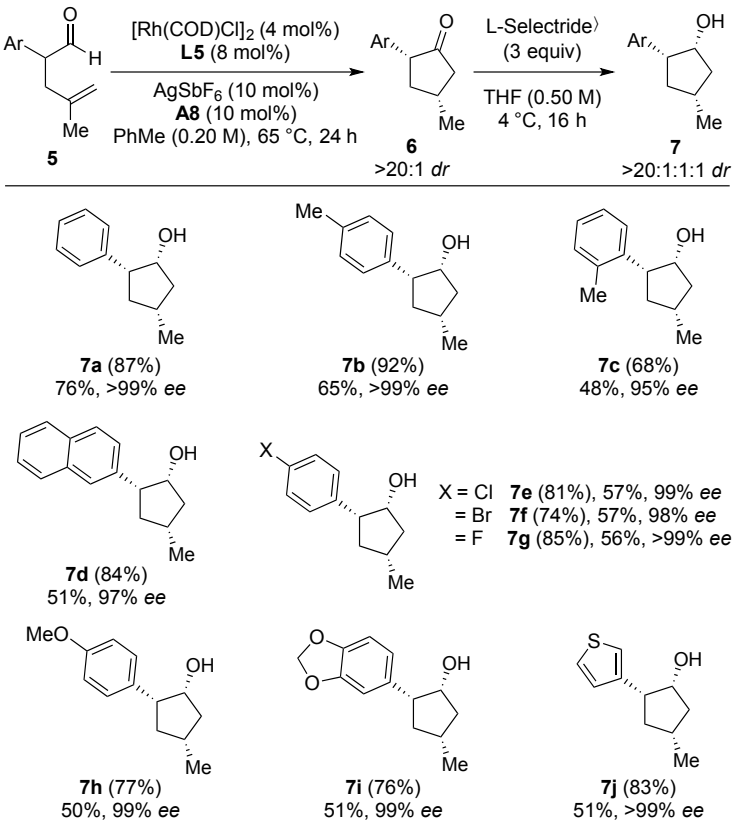



**Figure 2.9.** Decomposition of **6a**

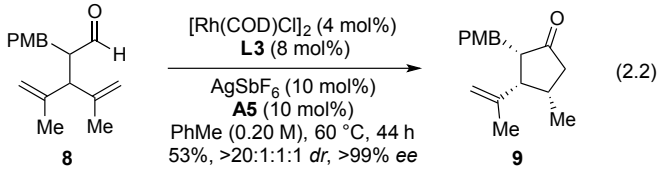
L-Selectride® to produce the all-*syn* cyclopentanol **7a** with high diastereoselectivity (>20:1:1:1 *dr*) (Table 2.11). The absolute configuration of **7a** was determined by X-ray crystallography after derivatization to the corresponding 3,5-dinitrobenzoic ester.[12a]

**Table 2.11.** Hydroacylation Scope with α-Aryl Aldehydes[a]




[a] With 0.10 mmol of **5**. $^1$H NMR yields of **6** are given in parentheses. Isolated yields over two steps are given of **7**. Diastereoselectivities of each step were determined by $^1$H NMR analysis of the unpurified reaction mixture. Enantioselectivities (*ee*) were determined by chiral SFC analysis.

With this two-step protocol, various cyclopentanols can be prepared (**7a**–**7j**, >20:1:1:1 *dr*, 95–>99% *ee*) (Table 2.11). Cyclopentanols containing aryl halides (**7e**–**7g**) can be accessed with high stereoselectivities (>20:1:1:1 *dr*, 98–>99% *ee*). Electron-deficient (**7g**) and electron-rich arenes (**7h** and **7i**) are tolerated. Cyclopentanols bearing heterocycles (**7j**) are obtained with excellent stereocontrol (>20:1:1:1 *dr*, >99% *ee*). By merging DKR with desymmetrization,[15] the α,β,γ-trisubstituted cyclopentanone **9** can be generated in 53% yield as a single stereoisomer (>20:1:1:1 *dr*, >99% *ee*) (eq. 2.2). This example illustrates enantioselective construction of three contiguous stereocenters via a single C–H oxidation.




(2.2)

We propose a mechanism involving two catalysts (Scheme 2). The primary amine catalyst condenses with aldehyde **1** to form an achiral enamine (**A**) that then undergoes hydrolysis. The *R*-enantiomer ((*R*)-**1**) undergoes oxidative addition with the Rh-catalyst to generate the Rh-acyl-hydride **B**. Subsequent migratory insertion makes metallacycle **C**, which undergoes reductive elimination to afford cyclopentanone **2**.

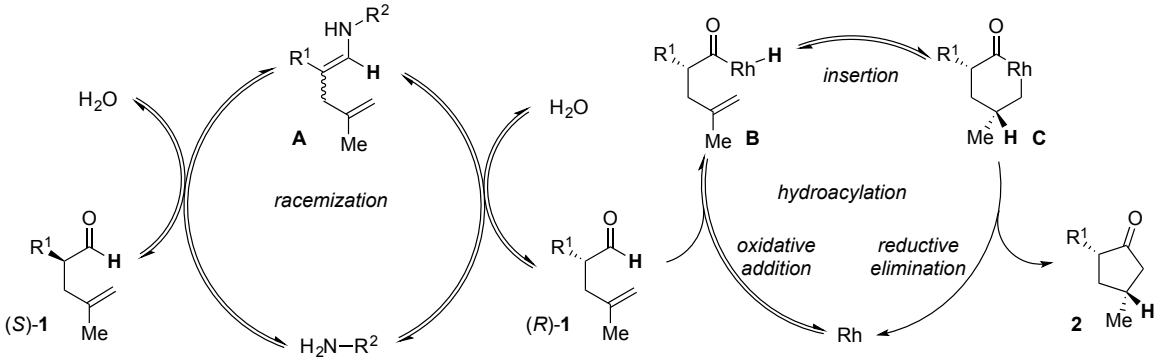



**Figure 2.10.** Amine-catalyzed racemization and Rh-catalyzed hydroacylation

When **1a** was subjected to the Rh-catalyst in the absence of amine **A5**, we observed hydroacylation with the same diastereo- and enantiocontrol (>20:1 *dr*, >99% *ee*), although in lower yield as expected (38%) (Figure 2.11a). This experiment points to the aldehyde as being the substrate for hydroacylation, as opposed to the imine intermediate.[16] In the absence of aldehyde, **2a** can be epimerized. When **2a** (>20:1 *dr*) was subjected to the standard reaction conditions with **L3** and **A5**, it was recovered with lower diastereoselectivity (14:1 *dr*). (Figure 2.11b). When treated with *n*-butylamine (**A3**), **2a** epimerized more rapidly (5:1 *dr*). Due to unfavorable steric interactions, enamine formation with the product should be more challenging

with bulky amines. Moreover, the bulky amine should favor the less substituted enamine **2ab** to avoid allylic strain (Figure 2.11c).

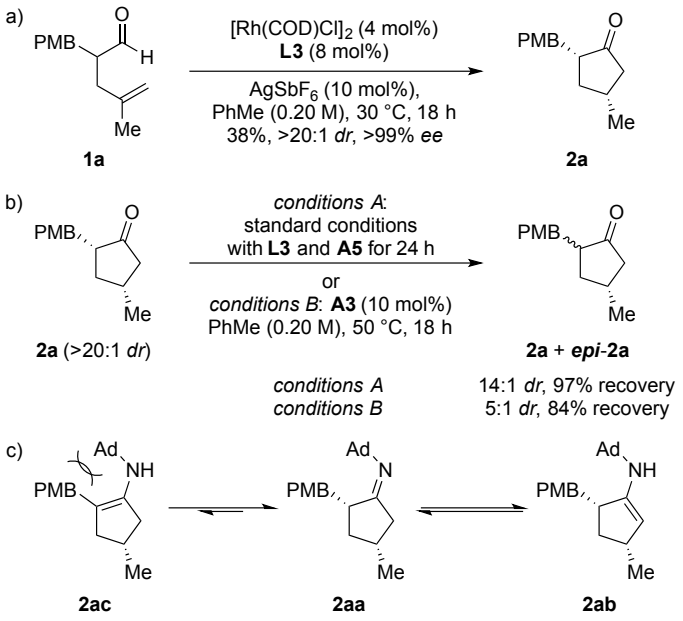



**Figure 2.11.** Amine-free hydroacylation and product epimerization.

An isotope labeling experiment with **1a**-*d* showed that the deuterium label is fully incorporated at the γ-position (Figure 2.12a). This result is consistent with a highly regioselective olefin insertion step. We reason that reductive elimination is the turnover-limiting step. When a 1:1 mixture of **1a** and **1a**-*d* was used for the reaction, no primary kinetic isotope effect (KIE) was observed (Figure 2.12b), which suggests that oxidative addition and migratory insertion are not turnover-limiting.[17]

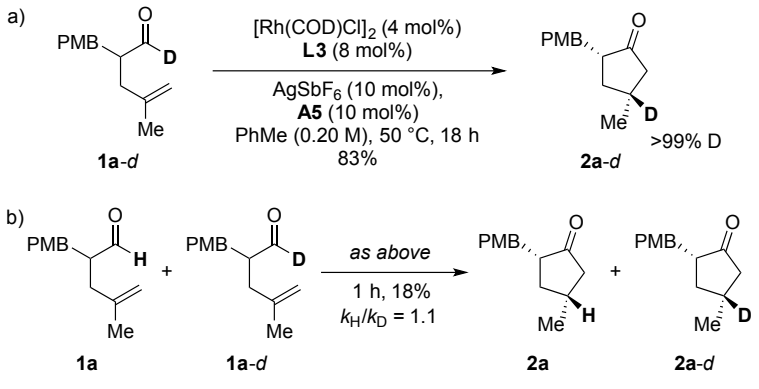



**Figure 2.12.** Isotopic labeling and KIE experiments.

### 2.3.3 Conclusion

By using tandem catalysis,[18] we have added a dynamic twist to hydroacylation. The empirical trends we observed for catalyst choice provides a useful guide for accessing a wide range of enantiopure cyclopentanones that are relatively unique.[19] Our study contributes to a growing class of DKR's that feature aldehyde racemization.[9] The identification of an efficient amine-catalyst for racemization will impact future studies that feature DKR of aldehydes.

### 2.3.4 References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(12) (a) See Appendix 2.3 for more details; (b) CCDC 1869120 contains the supplementary crystallographic data for **2a**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

(13) Sterically encumbered anilines are also effective for racemizing α-alkyl aldehydes. Using **L3** and **A8**, **1a** cyclized to **2a** with high diastereo- and enantioselectivity (86%, >20:1 *dr*, 96% *ee*).

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(19) We evaluated each model aldehyde (**1a**, **3a**, and **5a**) using each of the ligand and amine combinations. See Appendix 2.3 for more details.

# Chapter 3 – Cyclic Ketone Synthesis from Cyclopropanes[a]

## 3.1 Construction of Polycylic β-Ketoesters Using a Homoconjugate Addition/Decarboxylative Dieckmann Annulation Strategy[vii]

### 3.1.1 Introduction

Fused cyclic ketones are integral motifs in biologically active molecules. In particular, α-tetralones and their derivatives are important motifs in natural products and pharmaceuticals, such as nimbiol, tetrahydroaltersolanol B, and tetracycline (Figure 3.1A). During the course of an internal research program in our laboratories, rapid access to a variety of tetralone derivatives became critical for future studies. Synthetic routes often had to be redesigned for different substitution patterns because no satisfactory general synthetic route was available for access to diverse arene and heteroarene scaffolds.[1] To remedy this deficiency, we reasoned that a homoconjugate addition of an organometallic intermediate (generated from metal-halogen exchange of an 2-halobenzoate ester **1**) to a cyclopropyl ester electrophile **2** could provide an intermediate diester **3**, which could then undergo a Dieckmann cyclization to form a polycyclic β-ketoester **4** (Figure 3.1B). We

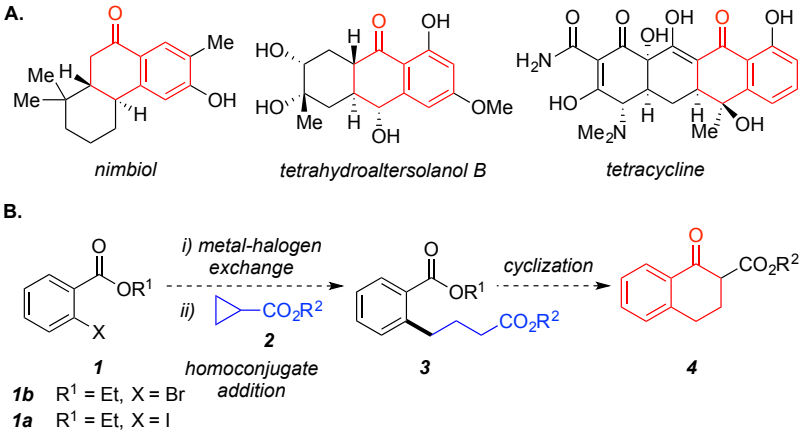



**Figure 3.1.** Inspiration for annulation design strategy

[a] As a part of continued training in pursuit of my doctoral studies at UC Irvine, this work was completed during a summer internship with Genentech in the Small Molecule Process Chemistry Department from June 2017–September 2017.

[vii] Reproduced with permission from Chen, Z.; Hong, A. Y.; Linghu, X. *J. Org. Chem.*, **2018,** *83,* 6225. Copyright 2018 American Chemical Society.

envisioned that this would provide the basis for the preparation of numerous building blocks for analog synthesis.

Our approach was marked by a number of foreseeable challenges. For the first transformation, chemoselective homoconjugate addition over carbonyl addition would be critical. For the second cyclization stage, intramolecular annulation over intermolecular pathways such as ester exchange (R1 ≠ R2) would be an important consideration.

For the metal-halogen exchange and homoconjugate addition processes, we were encouraged by the work of Knochel, which showed that functionalized Grignard reagents can be generated using *i*-PrMgCl·LiCl and aryl halides.[2a,3] Subsequent transmetallation to form an organocuprate could enable coupling with various cyclopropyl electrophiles.[4,5,6] The diesters **3** formed in this manner could cyclize in a straight-forward fashion to provide cyclic β-ketoester products **4**.

### 3.1.2 Results and Discussion

As a starting point, we attempted the coupling of ethyl 2-bromobenzoate **1b** with cyclopropanecarboxylate esters **2** (Figure 3.1B), but avoiding carbonyl addition side reactions during formation of the corresponding Grignard reagent proved difficult.[2a] However, the analogous aryl iodide **1a** underwent facile metal-halogen exchange[2] after 30 min at –40 °C. Transmetallation of Grignard reagent **5** with CuCN generated the corresponding organocuprate, but no homoconjugate addition was observed with ethyl cyclopropanecarboxylate, even in the presence of Lewis acids.[4,6]

Next, we performed the reaction with the more electrophilic doubly activated diethyl cyclopropane-1,1-dicarboxylate (**6a**) and were encouraged upon isolating desired triester **7aa** in 28% yield (Figure 3.2). However, in addition to the desired triester product **7aa**, ethyl benzoate

(**8**), anthraquinone (**9**), and biaryl dimer **10** were formed. Presumably, ethyl benzoate arose from protonation of the organocuprate during aqueous quench of the reaction aliquot. Anthraquinone and the biaryl side product **10** were generated from dimerization via ketone formation and oxidative coupling, respectively, and these hypotheses were confirmed through control experiments.

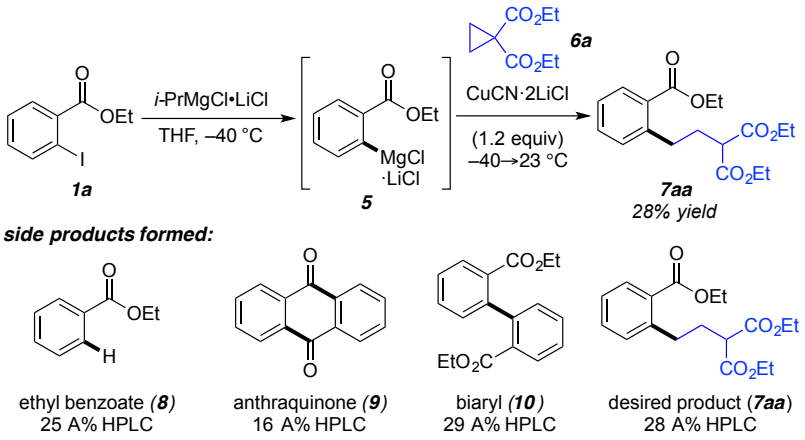



**Figure 3.2.** Side products in unoptimized homoconjugate addition

To improve this challenging transformation, we considered the introduction of additives for controlling the reaction profile. Wicha and co-workers[5c] studied the homoconjugate addition of a methallylcopper intermediate (generated from a methallyl Grignard reagent and CuI·$SMe_2$) to cyclopropane diesters and found that the addition of HMPA led to selective homoconjugate addition over carbonyl addition. HMPA may alter the aggregation state of the organocuprate intermediates and influence their reactivity. Introduction of HMPA additive to our system proved beneficial, and replacement of CuCN with CuI·$SMe_2$ led to an increase in reactivity and selectivity (69% yield, 80:20 homoconjugate addition:biaryl formation). Furthermore, the elimination of hazardous cyanide waste was a positive feature of employing CuI·$SMe_2$. Substitution of HMPA with the less toxic 1,3-dimethyl-2-imidazolidinone (DMI)[7] slightly increased the selectivity (83:17 ratio), but decreased product formation (44% yield). Performing

the metal-halogen exchange at –78 °C with DMI additive further increased the selectivity (96:4 ratio) while maintaining good yield. This positive result was attributed to the suppression of oxygen-mediated homodimerization of the organocuprate relative to the desired homoconjugate addition reaction. An evaluation of solvents revealed that 2-MeTHF was superior to THF and CPME, providing product **7aa** in an optimal manner (79% yield, 98:2 ratio homoconjugate addition:biaryl formation).

Next, we turned our attention toward the Dieckmann cyclization[8] with triesters **7**. While our original design planned for the use of diesters **3**, the triesters **7** were expected to be more challenging for our desired cyclization. Several reports showed that this decarboxylative transformation is feasible for 6-membered ring formation, but also suggested that the alkoxide bases and alcohol solvents in the transformation needed to be matched with the ester moieties of the molecule.[9] These constraints appeared to be a key limitation for the mixed ester substrates we possessed (such as **7ab**) because application of such conditions led to a mixture of methyl and ethyl β-ketoester products (**4b** and **4a**) (Figure 3.3). Additionally, literature examples were isolated and did not delve into a broader study of reaction scope.[9] Clearly, new reaction conditions were needed to accomplish our goal.

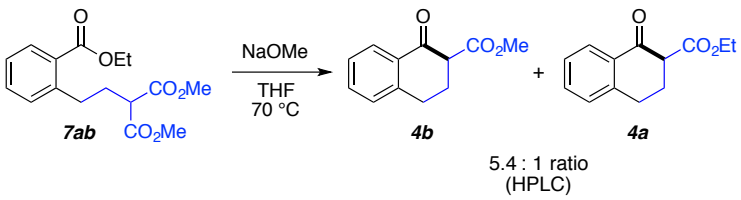


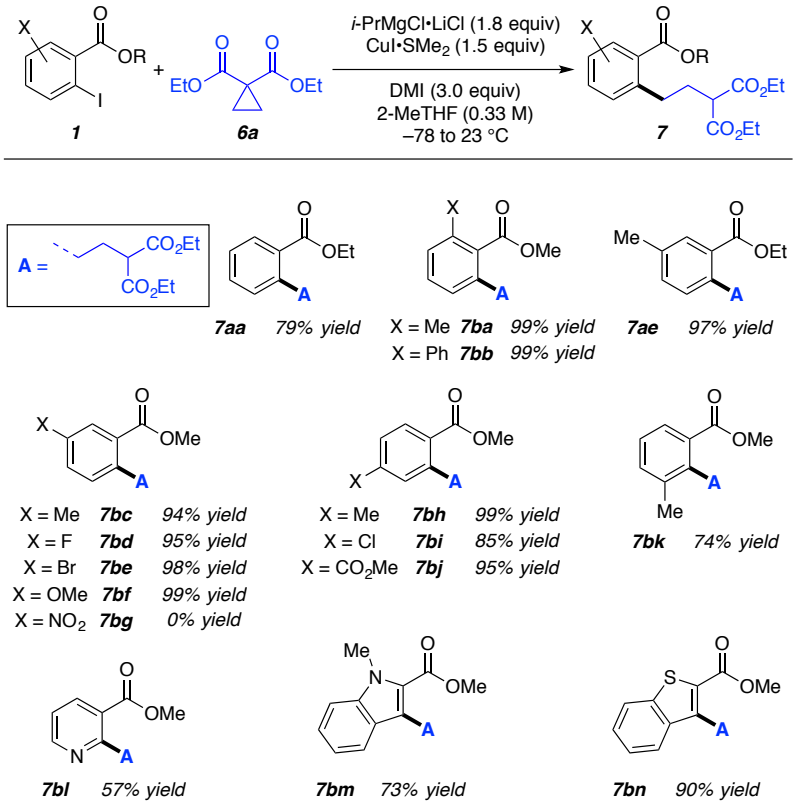

**Figure 3.3.** Formation of β-ketoester mixtures during the unoptimized cyclization

For our optimization studies, we investigated the cyclization of triester **7aa** to β-ketoester **4a**. An initial survey of bases showed that using an excess of Mg(O*t*-Bu)$_2$ in 2-MeTHF afforded the cyclic β-ketoester **4a** in 51% yield. Motivated by the promise of milder organic bases, the use of $Et_3N$ with $MgCl_2$ as an additive increased the yield to 78%. Notably, no reactivity was observed when $MgCl_2$ was omitted or dosed in substoichiometric (0.2 equiv) quantities. Replacing $MgCl_2$

with $MgBr_2$ led to a further increase in the yield to 94%. Gratifyingly, application of the optimal conditions ($Et_3N$, $MgBr_2$, 2-MeTHF) to mixed ester substrates such as **7ab** led to no observable ester exchange.[10]

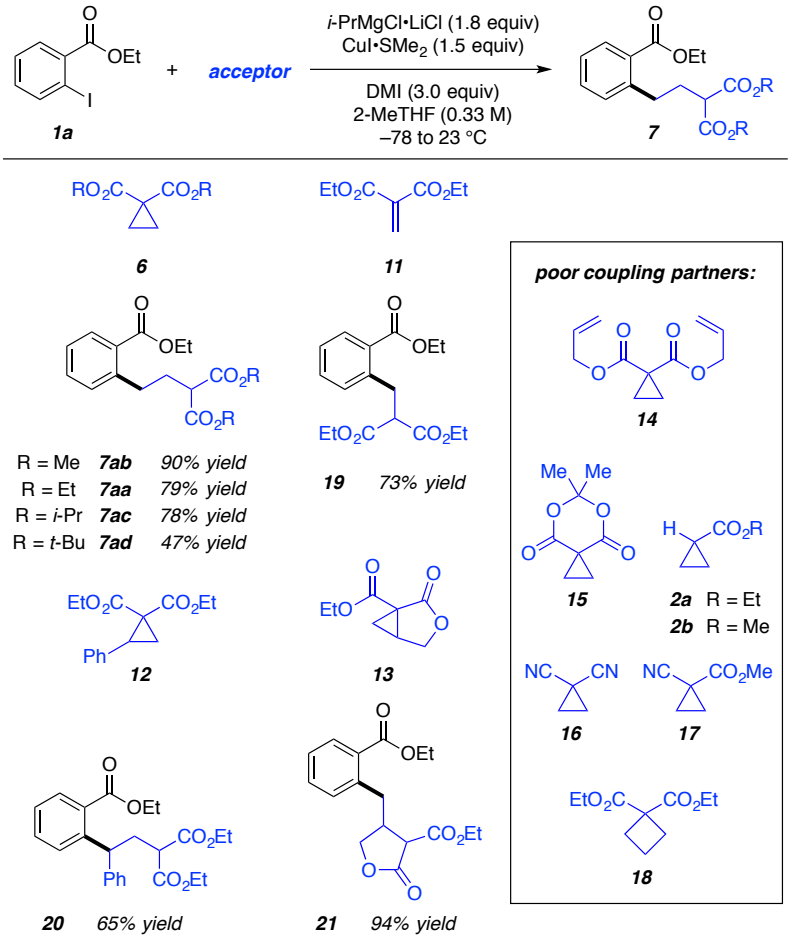
After our optimization studies, we turned our attention to the substrate scope of the Cu-mediated homoconjugate addition step (Table 3.1). We were pleased to find that most substrates performed well in the reaction with variations in the ester and arene. The initial Mg/I exchange was well-tolerated by a range of sensitive functionality, including aryl bromides and esters (**7be** and **7bj**). Nitro groups at the 5-position of the arene, however, did not appear to be tolerated (**7bg**).[11] Transmetallation to copper and addition to diethyl 1,1-cyclopropane dicarboxylate (**6a**) proceeded smoothly in most cases. Electron-rich and electron-deficient arenes afforded product in comparably high yields. We were pleased to see that heterocycles such as pyridine, thiophene, and indole-based starting materials also furnished the corresponding adducts **7bl** (57% yield), **7bm** (73% yield) and **7bn** (90% yield).

**Table 3.1.** Cu-Mediated Homoconjugate Addition: Iodoester Substrate Scope



components had a clear and detrimental effect on the reaction yield (**7aa**–**7ad**). In these transformations, Cu-mediated homodimerization of the aryl fragment became competitive with productive coupling, leading to the decrease in yield. Phenyl-substituted cyclopropane **12** was also tested and the transformation was completely selective for addition at the electronically more activated benzylic cyclopropane position.[12] Lactone-fused cyclopropane **13** was also evaluated and provided adduct in 94% yield. Exploration of diallyl diester cyclopropane **14**, a substrate with competing reactive sites, provided no cyclopropyl addition. Instead, arene allylation product (not shown) was isolated in 58% yield. In contrast to other cyclopropane diesters **6**, Meldrum's acid-derived cyclopropane **15** showed no productive bond formation. Several other cyclopropane electrophiles (**2**, **16**–**17**), which lacked dicarbonyl functionality capable of chelation, showed no reactivity under our developed reaction conditions.

**Table 3.2.** Cu-Mediated Homoconjugate Addition: Electrophile Substrate Scope

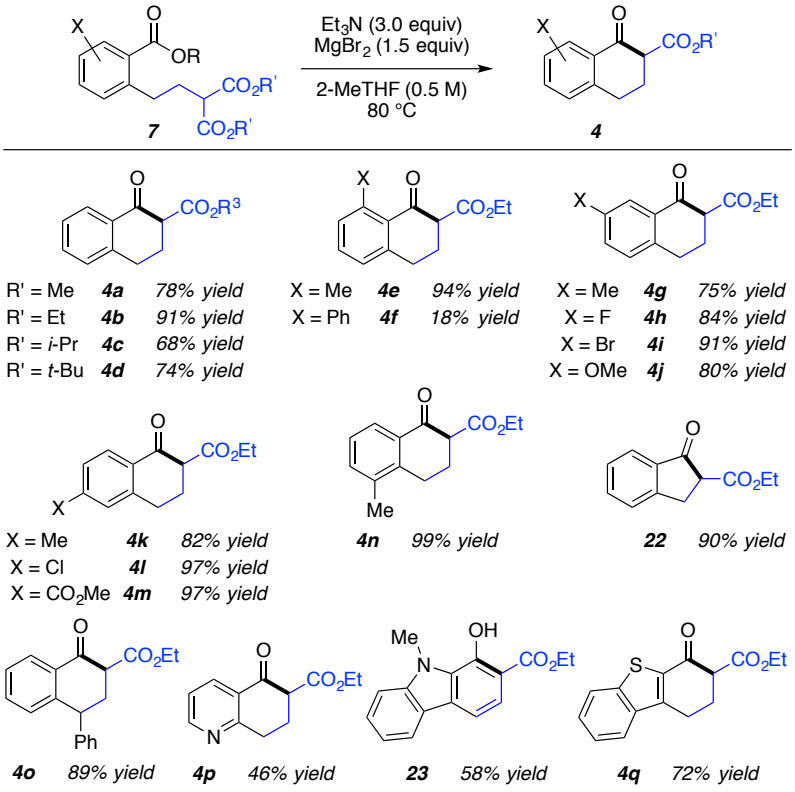



Our interests also extended beyond cyclopropane acceptors because we were also interested in the corresponding analogous indanone and benzosuberone products in addition to our primary

tetralone targets. Toward this end, we tested diethyl methylidene malonate **11** and obtained adduct **19** in 73% yield. In contrast, attempted coupling with diethyl 1,1-cyclobutane dicarboxylate (**18**) did not lead to any desired adduct.

With a variety of adducts in hand, we turned our attention to the cyclization step to evaluate the substrate scope (Table 3.3). The cyclization of triesters **7** containing various malonate and aryl esters proceeded smoothly in most cases to give bicyclic β-ketoesters **4** in good yield. In the cases of mixed esters such as **7ab** and **7ba**, no ester scrambling was observed and the product β-ketoester always retained one of the original malonate esters. For the 6-substituted triester starting materials, a significant drop in yield was apparent with a large phenyl substituent (18% yield) compared to a smaller methyl substituent (94% yield) (cf. **4e** and **4f**). Placing various electronically diverse substituents further away at the arene 5-position, as shown by examples **4g**–**4j**, had a beneficial effect on reaction yields. Excellent results were also obtained with 3-substituted and 4-substituted triesters, as shown by β-ketoesters **4k**–**4n**. Substitution on the aliphatic chain, as shown by product **4o**, also translated to good cyclization yields. Unfortunately, the attempted cyclization of lactone substrate **21** did not provide desired

**Table 3.3.** Decarboxylative Dieckmann Cyclization Scope



product under these conditions and instead led to gradual decomposition during extended reaction times. Finally, heterocyclic scaffolds were also evaluated. Cyclization to the indanone scaffold[13] in **22** proceeded efficiently in 90% yield. Pyridines, indoles, and benzothiophenes could all be incorporated into cyclization products, but the pyridine **4p** was isolated in relatively low yield while carbazole **23** was formed as a result of facile air oxidation during handling and isolation. Thiophene **4q** was formed efficiently under the reaction conditions and was isolated without aromatization.

With the substrate scope of two key transformations explored in detail,[14] we devoted attention to developing working hypotheses for the two transformations based on the observed trends. Chelation appears to be an important feature of both transformations as a means of activating the key reactive functionality for productive bond formation (Figure 3.4). In the case of the Cu-mediated homoconjugate addition, activation of both carbonyls greatly facilitates arylcuprate coupling[6] (Figure 3.4A). Monoesters **2**, dinitrile **16**, nitrile ester **17**, and Meldrum's acid derivative **15** that do not benefit from this type of activation remain unreactive. In a similar manner, the cyclization step benefits from chelation interactions to facilitate enolization of the malonate ester in triester **7** and promote intramolecular nucleophilic attack on the aryl ester

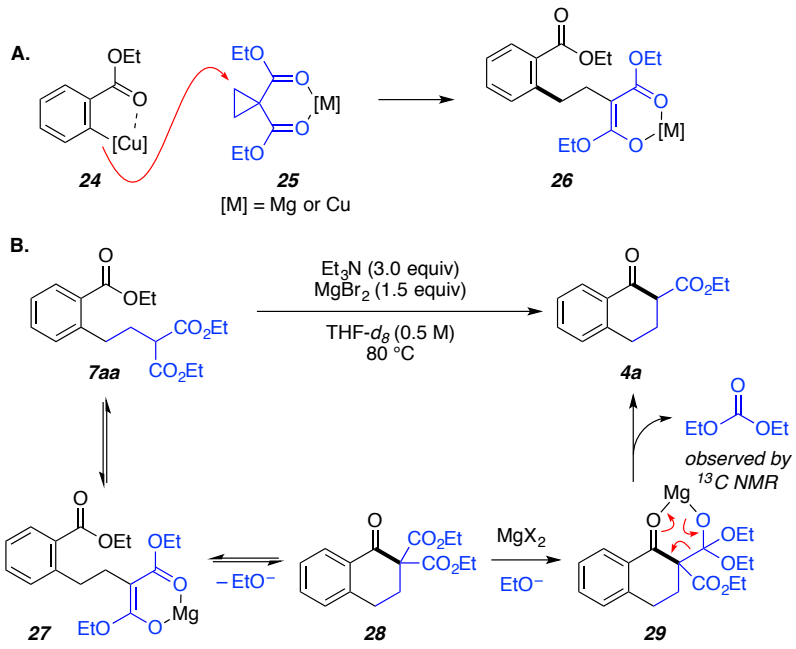



**Figure 3.4.** Mechanistic hypotheses and chelation effect

(Figure 3.4B). Extrusion of diethyl carbonate appeared to be a likely step for the formation of final β-ketoester **4**. We were pleased to observe diethyl carbonate by $^{13}C$ NMR (δ 156.1, 64.1, 14.8 ppm) when the reaction was carried out in THF-$d_8$.

To provide a gram scale demonstration of our synthetic method, we converted 30 mmol of diethyl cyclopropane-1,1-dicarboxylate **6a** to the homoconjugate adduct **7aa** in 79% yield (Figure 3.5). Subsequent decarboxylative Dieckmann cyclization of triester **7aa** on 5.9 mmol scale provided 85% yield of β-ketoester **4a**. Additionally, a simple thermal decarboxylation in the presence of HCl and *i*-PrOH provided 93% yield of tetralone. The synthetic versatility of β-ketoester building blocks in complexity-generating transformations has been well documented. Through a variety of methods, compound **4a** has been elaborated to more complex products, including ring expansion products, heterocycles, and chiral compounds.[15-22]

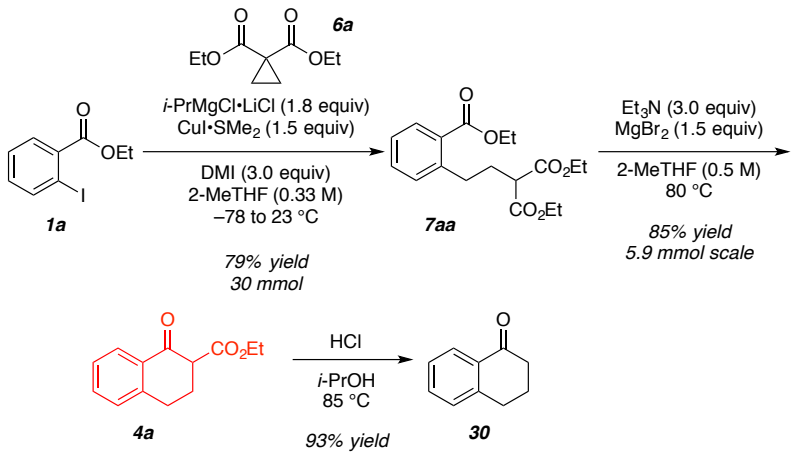



**Figure 3.5.** Gram-scale demonstration and product decarboxylation

## 3.1.3 Conclusion

In summary, we have developed a novel homoconjugate addition/decarboxylative Dieckmann annulation strategy for the efficient formation of a variety of polycyclic β-ketoesters from readily accessible 2-iodoaryl esters and 1,1-cyclopropane diesters. Both transformations appear to benefit from chelation interactions based on reactivity trends. Further evaluation of the

substrate scope, exploration of the mechanism of these transformations, and synthetic applications of the β-ketoester building blocks will be reported in due course.

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# Appendix for Asymmetric Catalysis with Rhodium Hydrides

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## Appendix 1.1: Supporting Information for Chapter 1.1
## Rhodium-Catalyzed Enantioselective Hydroamination of Alkynes with Indolines[i]

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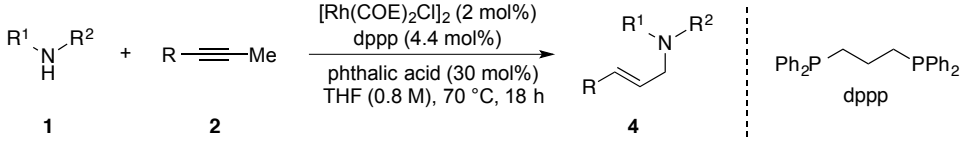
### 1. General

Commercial reagents were purchased from Sigma Aldrich, Strem, or Alfa Aesar and used without further purification. Reactions were monitored using thin-layer chromatography (TLC) or GC-FID. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ stain. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. $^1H$ and $^{13}C$ NMR spectra were recorded on Bruker CRYO-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$) or (400 MHz $^1H$, 100 MHz $^{13}C$) DRX-400 spectrometer. $^{19}F$ NMR spectra were recorded on a Bruker DRX-400 (376.5 MHz $^{19}F$) spectrometer. $^1H$ NMR spectra were internally referenced to the residual solvent signal or TMS. $^{13}C$ NMR spectra were internally referenced to the residual solvent signal. Data for $^1H$ NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for $^{19}F$ and $^{13}C$ NMR are reported in terms of chemical shift (δ ppm). High resolution mass spectra (HRMS) were obtained on a micromass 70S-250 spectrometer (EI) or an ABI/Sciex QStar Mass Spectrometer (ESI). Infrared (IR) spectra were obtained on a Nicolet iS5 FT-IR spectrometer with an iD5 ATR, and are reported in terms of frequency of absorption ($cm^{-1}$). Column chromatography was performed with Silicycle Silia-P Flash Silica Gel using glass columns. Preparatory thin-layer chromatography was performed

[i] See Chen. Q.-A.; Chen, Z.; Dong, V. M. *J. Am. Chem. Soc.,* **2015,** *137,* 8392 for additional details.

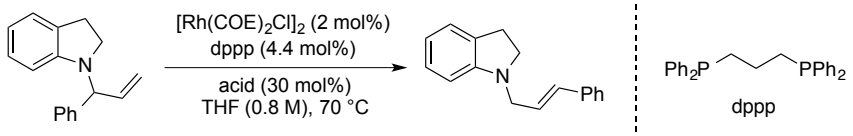
using EMD Silica Gel 60 $F_{254}$ plates. Solvents were purchased from Fisher. Enantiomeric excesses for stereoselective reactions were determined by chiral SFC analysis using an Agilent Technologies HPLC (1200 series) system and Aurora A5 Fusion. Solvents used in hydroaminations were degassed by three freeze-pump-thaw cycles before being taken into a nitrogen-filled glove box.

## 2. Typical procedure for the hydroamination of alkynes



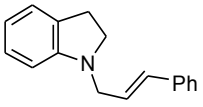

**Method A:** A mixture of $[Rh(COE)_2Cl]_2$ (2.9 mg, 0.0040 mmol), dppp (3.6 mg, 0.0090 mmol), phthalic acid (10 mg, 0.060 mmol), amine **1** (0.20 mmol), alkyne **2** (0.30 mmol), and THF (0.25 mL) were added to a 1-dram vial in the glove box. After heating the reaction mixture at 70 °C for 18 h, the resulting solution was cooled to rt. The selectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. Product **4** was purified by column chromatography on silica gel using hexanes/EtOAc.

## 3. Typical procedure for isomerization of *N*-allylic indoline 3a

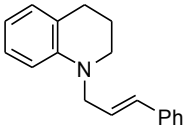



**Method B:** A mixture of $[Rh(COE)_2Cl]_2$ (2.9 mg, 0.0040 mmol), dppp (3.6 mg, 0.0090 mmol), acid (0.060 mmol), racemic branched amine (±)-**3a** (0.20 mmol), and THF (0.25 mL) were added to a 1 dram vial in the glove box. Then the reaction mixture was heated at 70 °C. The reaction progress was monitored by GC. The selectivity (**4a**:**3a**) was determined by $^1$H NMR analysis of the unpurified reaction mixture.

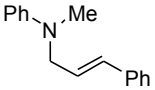
**4. Characterization data of *N*-allylic amines 4**



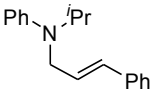
(*E*)-1-(3-Phenyl-2-propenyl)-2,3-dihydroindole (**4a**): (Method **A**) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (42.8 mg, 91% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.9 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.19 (m, 1H), 7.10 – 7.04 (m, 2H), 6.70 – 6.54 (m, 3H), 6.29 (dt, *J* = 15.8, 6.2 Hz, 1H), 3.86 (d, *J* = 6.3 Hz, 2H), 3.37 (t, *J* = 8.3 Hz, 2H), 2.96 (t, *J* = 8.3 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 152.3, 137.0, 132.4, 130.4, 128.7, 127.6, 127.4, 126.5, 126.0, 124.6, 117.9, 107.5, 53.5, 51.7, 28.7. **IR** (ATR): 3024, 2919, 2815, 1605, 1486, 1266, 965, 714, 735, 691cm$^{-1}$.



(*E*)-1-(3-Phenyl-2-propenyl)-1,2,3,4-tetrahydroquinoline (**4b**): (Method **A**) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (49.4 mg, 99% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.07 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.70 – 6.60 (m, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.28 (dt, *J* = 15.8, 5.3 Hz, 1H), 4.05 (d, *J* = 5.5 Hz, 2H), 3.40 – 3.30 (m, 2H), 2.81 (t, *J* = 6.4 Hz, 2H), 2.04 – 1.99 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.4, 137.1, 131.2, 129.2, 128.6, 127.5, 127.3, 126.4, 125.7, 122.7, 116.1, 111.3, 53.6, 49.3, 28.2, 22.4. **IR** (ATR): 3024, 2927, 2840, 1601, 1495, 1344, 1329, 965, 741, 691 cm$^{-1}$.

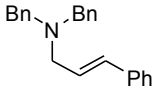


(*E*)-*N*-Methyl-*N*-phenyl-3-phenyl-2-propenylamine (**4c**): (Method **A**) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (42.5 mg, 95% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.31 – 7.19 (m, 5H), 6.78 (d, *J* = 8.2 Hz, 2H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.24 (dt, *J* = 15.9, 5.5 Hz, 1H), 4.06 (dd, *J* = 5.5, 1.5 Hz, 2H), 2.96 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.6, 137.0, 131.4, 129.3, 128.7, 127.5, 126.4, 125.8, 116.7, 112.7, 55.0, 38.2. **IR** (ATR): 3026, 1597, 1505, 1353, 1200, 1117, 991, 964, 728, 690 cm$^{-1}$.

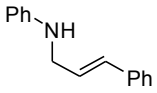


(*E*)-*N*-Isopropyl-*N*-phenyl-3-phenyl-2-propenylamine (**4d**): (Method **A**) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (42.6 mg, 85% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.42 (d, *J* =

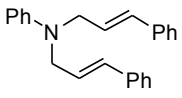
7.9 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.31 – 7.27 (m, 3H), 6.87 (d, *J* = 8.1 Hz, 2H), 6.76 (t, *J* = 7.1 Hz, 1H), 6.63 (d, *J* = 15.9 Hz, 1H), 6.40 – 6.32 (m, 1H), 4.28 – 4.21 (m, 1H), 4.04 (d, *J* = 3.8 Hz, 2H), 1.30 (d, *J* = 6.8 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.3, 137.3, 130.2, 129.3, 128.9, 128.6, 127.3, 126.3, 116.3, 113.1, 48.0, 46.6, 20.1. **IR** (ATR): 3023, 2969, 1596, 1502, 1390, 1184, 964, 745, 731, 689 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{22}N$ $[M+H]^+$ 252.1747, found 252.1754.



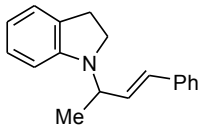

(*E*)-*N*,*N*-Dibenzyl-3-phenyl-2-propenylamine (**4e**): (Method **A**) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (48.1 mg, 77% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 12H), 7.26 – 7.19 (m, 3H), 6.54 (d, *J* = 15.9 Hz, 1H), 6.31 (dt, *J* = 15.8, 6.5 Hz, 1H), 3.65 (s, 4H), 3.24 (d, *J* = 6.4 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 139.7, 137.3, 132.6, 128.9, 128.6, 128.4, 127.9, 127.4, 127.0, 126.4, 58.1, 55.9. **IR** (ATR): 3025, 2792, 1599, 1494, 1451, 1364, 1121, 965, 731, 692 $cm^{-1}$.




(*E*)-*N*-Phenyl-3-phenyl-2-propenylamine (**4f**): (Method **A**, aniline (0.30 mmol), alkyne (0.20 mmol)) The title compound was isolated via column chromatography (10% ethyl acetate in hexanes) as a colorless oil (23.2 mg, 55% yield). **$^{1}$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.42 – 7.37 (m, 2H), 7.34 – 7.30 (m, 2H), 7.27 – 7.21 (m, 1H), 7.21 – 7.14 (m, 2H), 6.73 – 6.60 (m, 4H), 6.36 (dt, *J* = 15.9, 5.8 Hz, 1H), 4.05 – 3.85 (m, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 148.6, 137.4, 131.5, 129.5, 128.9, 127.8, 127.7, 126.6, 117.7, 113.3, 46.4. **IR** (ATR): 3412, 3023, 1600, 1504, 1447, 1316, 1249, 965, 745, 690 $cm^{-1}$.

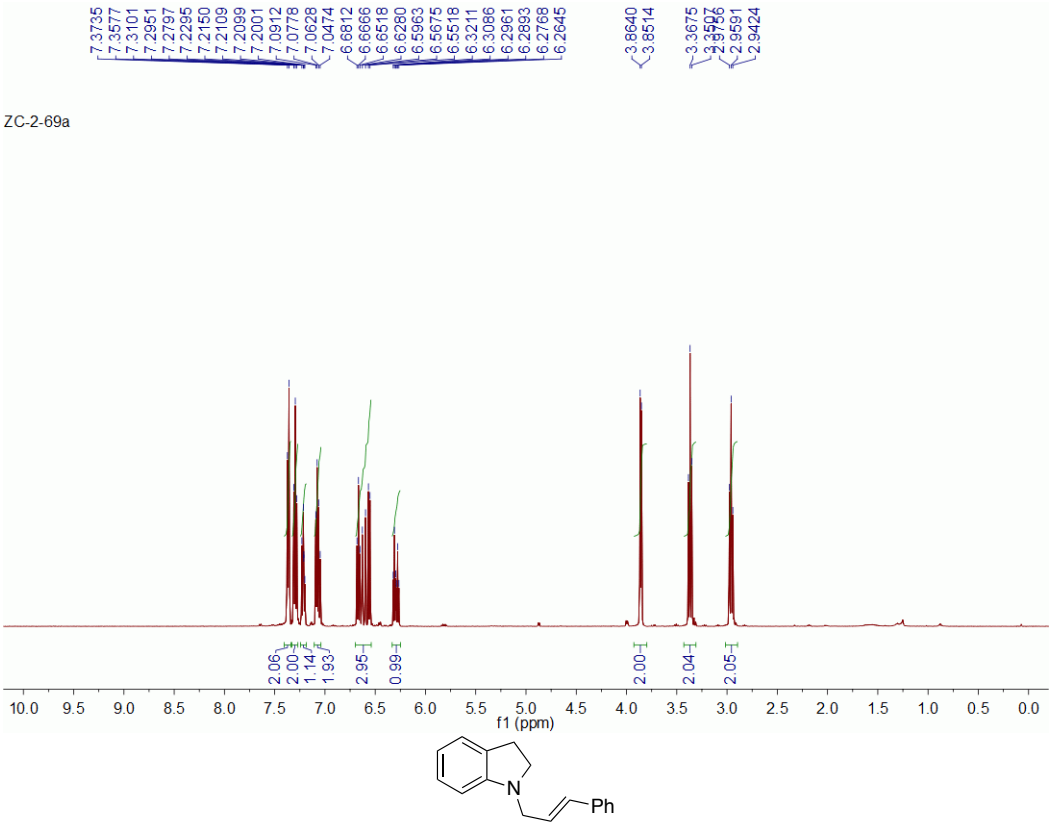



*N*,*N*-Bis[(*E*)-3-phenyl-2-propenyl]benzylamine (**4f'**): (Method **A**, aniline (0.20 mmol), alkyne (0.50 mmol)) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (45.4 mg, 70% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.6 Hz, 4H), 7.30 (t, *J* = 7.6 Hz, 4H), 7.26 – 7.18 (m, 4H), 6.83 (d, *J* = 6.7 Hz, 2H), 6.76 – 6.71 (m, 1H), 6.55 (d, *J* = 15.9 Hz, 2H), 6.29 (dt, *J* = 15.9, 5.1 Hz, 2H), 4.14 (d, *J* = 5.3 Hz, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 148.9, 137.0, 131.3, 129.4, 128.7, 127.5, 126.5, 126.0, 116.7, 112.7, 52.3. **IR** (ATR): 3025, 1597, 1504, 1447, 1354, 1218, 1159, 1066, 964, 908 $cm^{-1}$.




(*E*)-1-(4-Phenylbut-3-en-2-yl)-2,3-dihydroindole (**4g**): (Method **A**) The title compound was isolated via column chromatography (5% ethyl acetate in hexanes) as a colorless oil (39.3 mg, 79% yield). **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.37 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.08 – 6.97 (m, 2H), 6.60 – 6.54 (m, 2H), 6.51 (d, *J* = 7.9 Hz, 1H), 6.33 (dd, *J* = 16.1, 5.9 Hz, 1H), 4.39 – 4.33 (m, 1H), 3.47 – 3.37 (m, 2H), 2.94 (t, *J* = 8.4 Hz, 2H), 1.40 (d, *J* = 6.9 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 151.6, 137.5, 131.0, 130.8, 130.7, 128.9, 127.8, 127.4, 126.6, 124.7, 117.4, 107.9, 52.8, 47.6, 28.6, 16.5. **IR** (ATR): 2971, 2845, 1606, 1486, 1263, 1181, 967, 909, 733, 692 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{20}N$ $[M+H]^+$ 250.1590, found 250.159

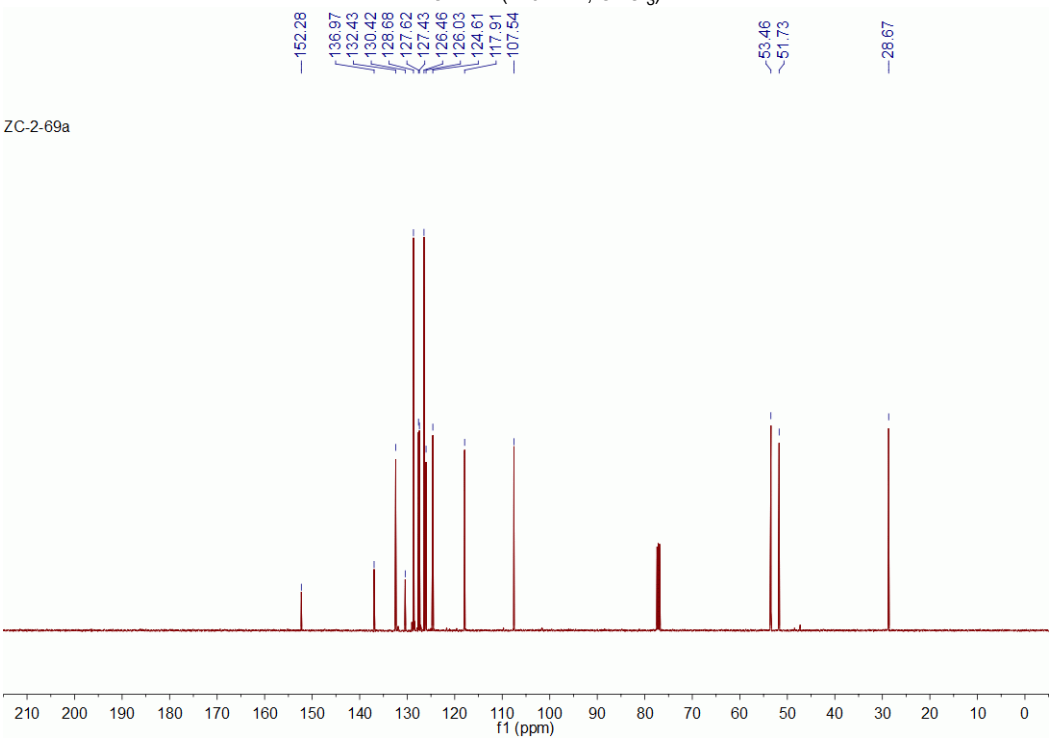
## 5. NMR spectra

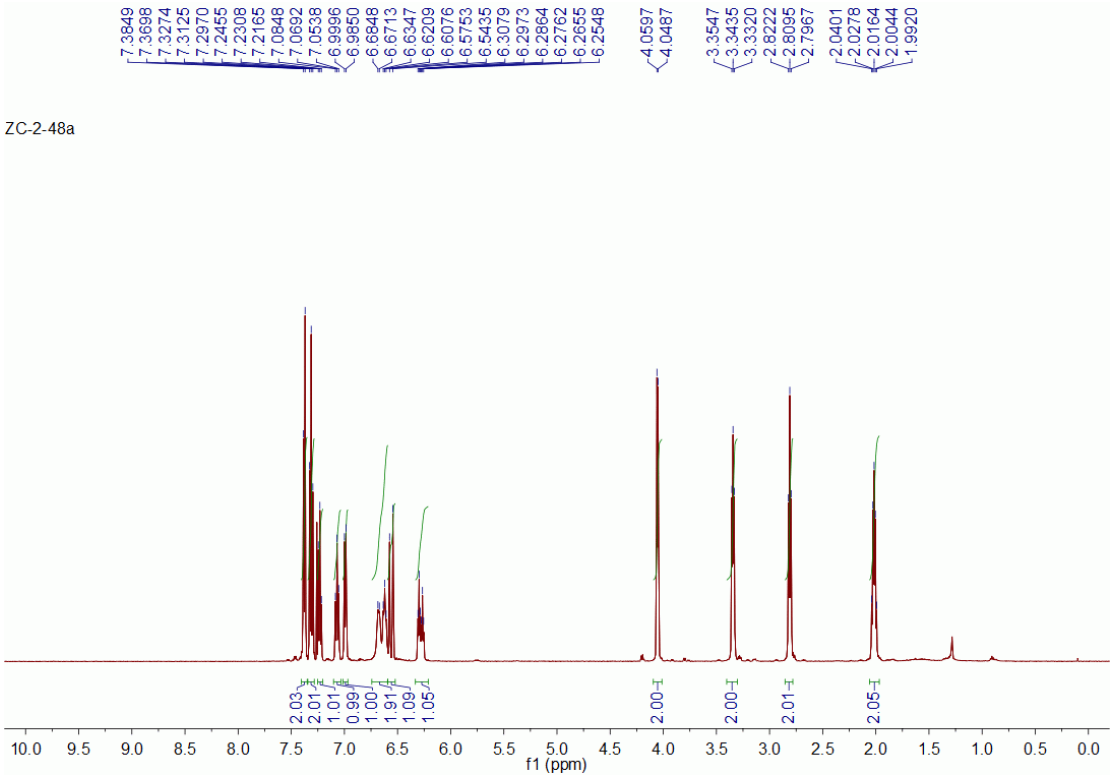


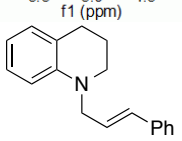




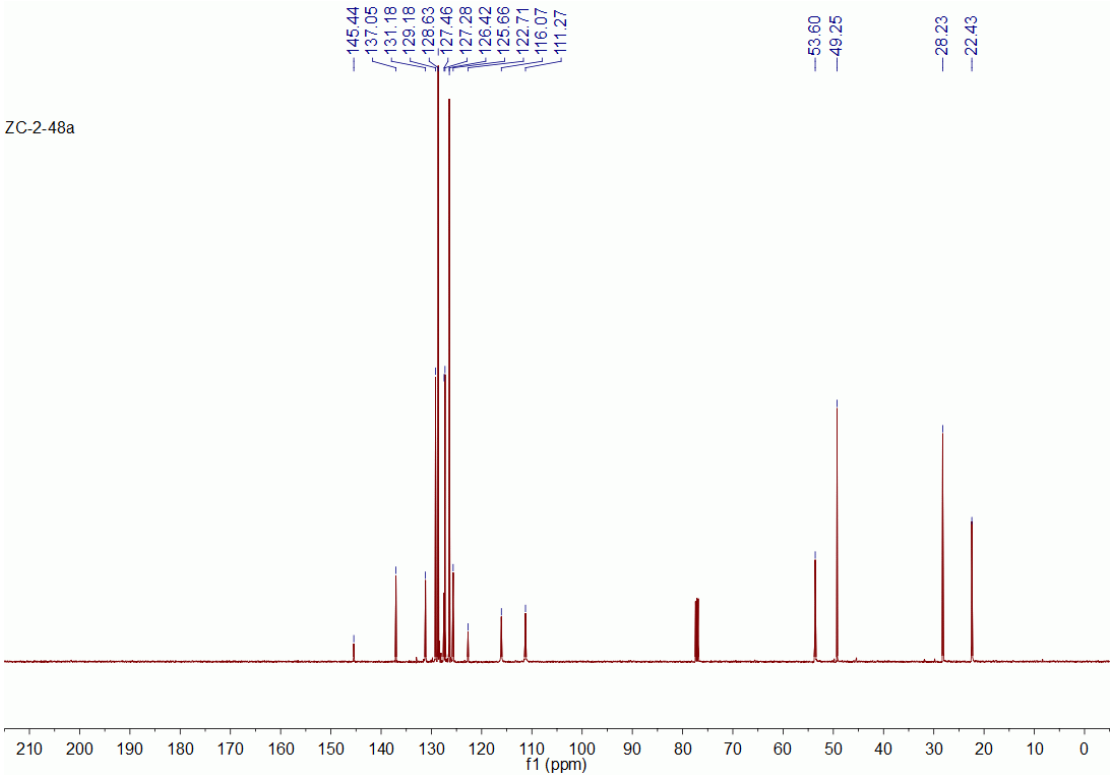
**4a** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)

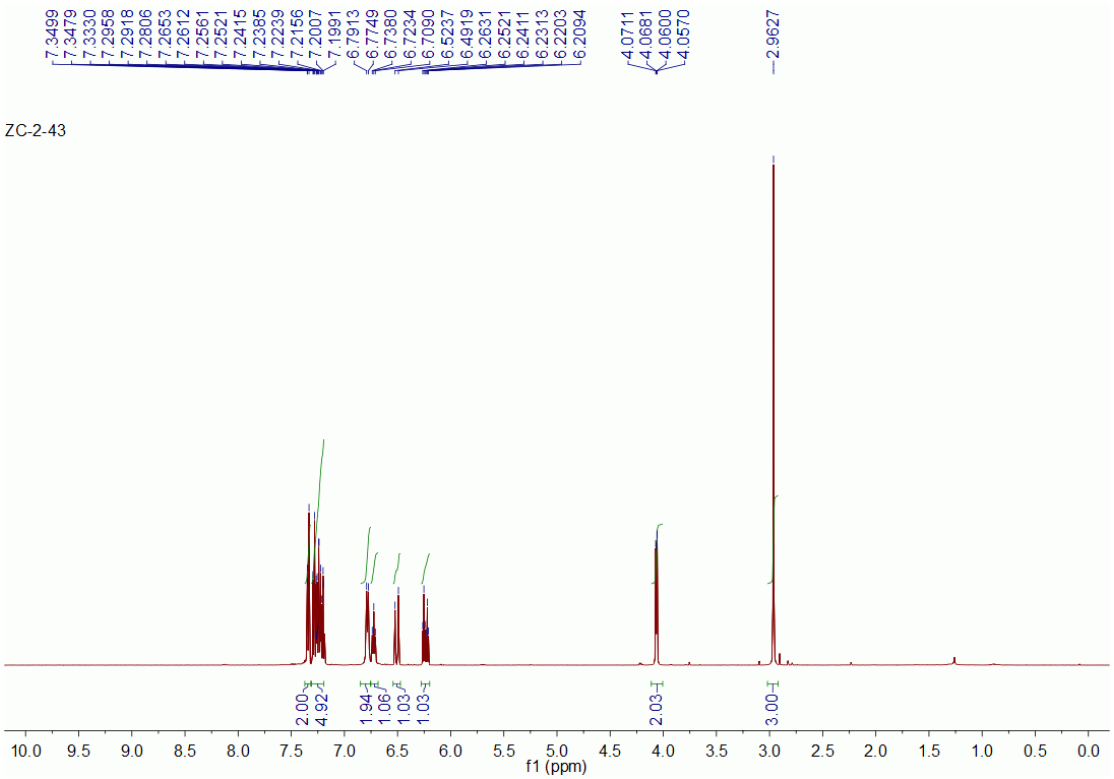


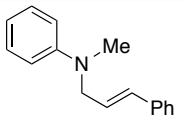


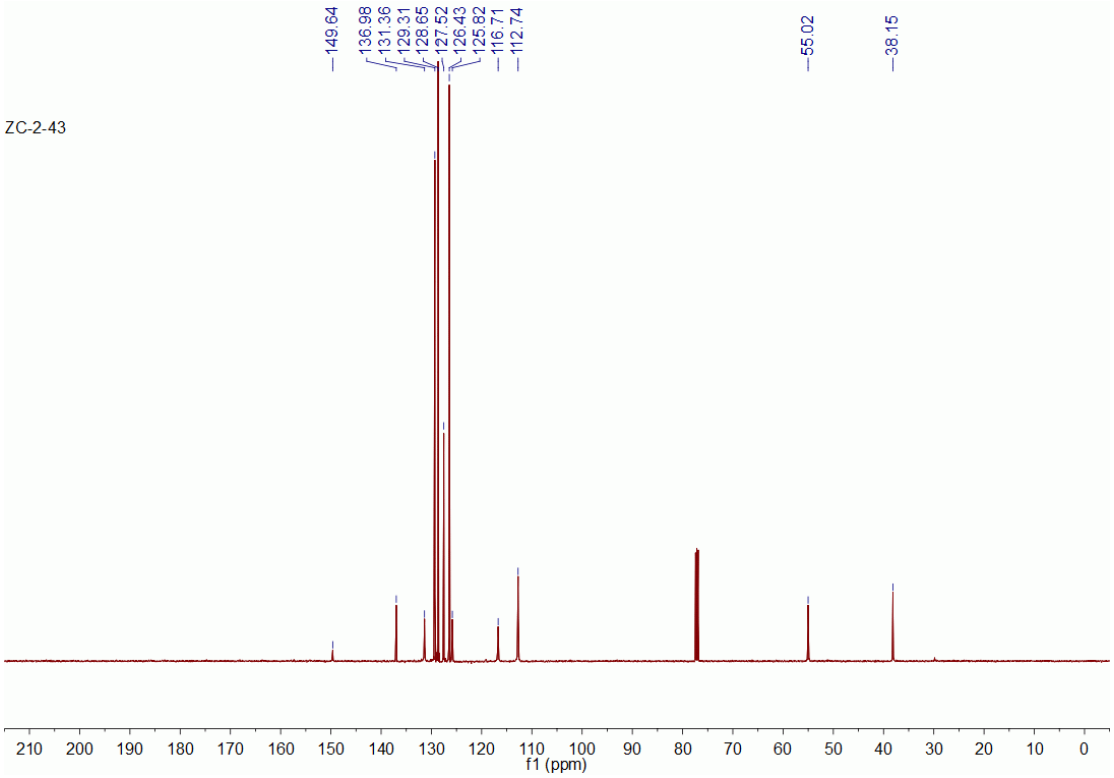

**4b** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)

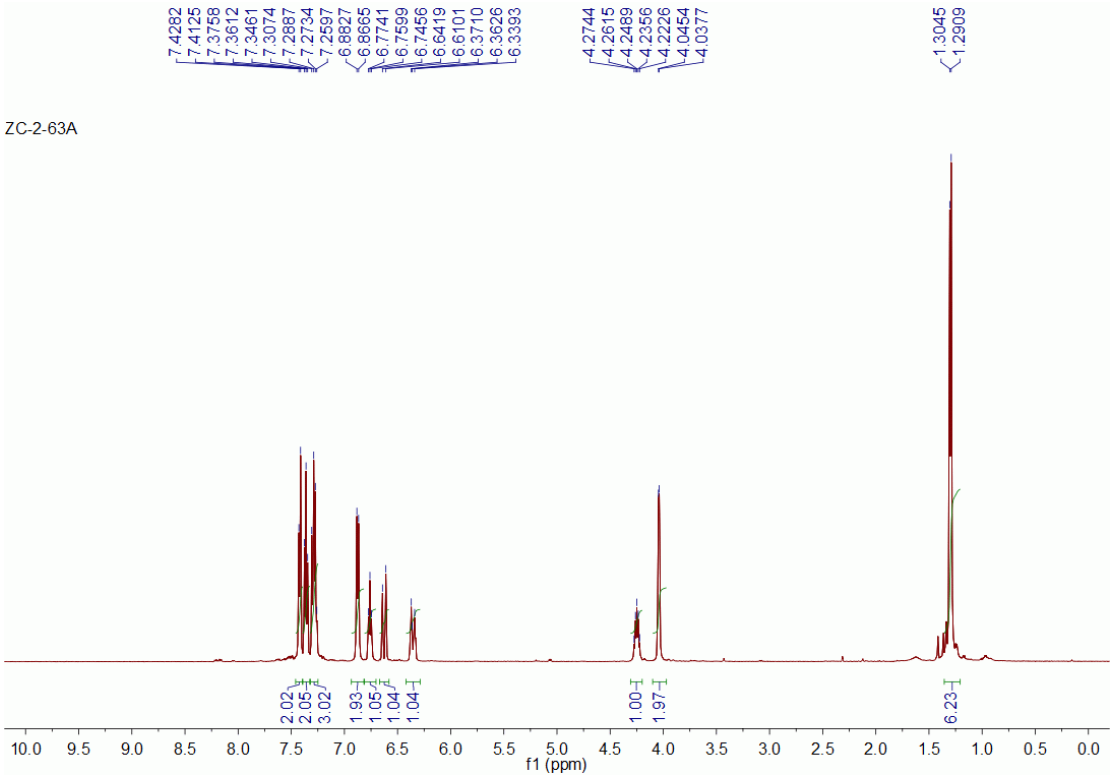


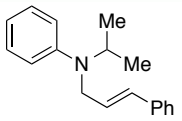


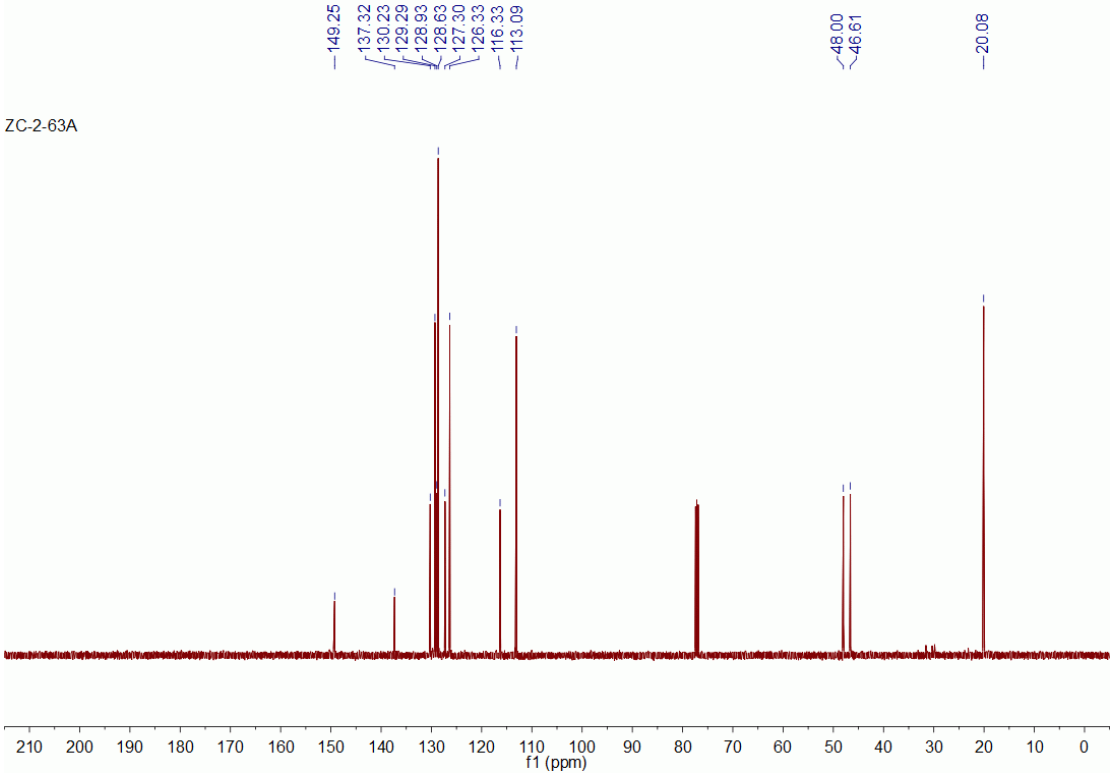

**4c** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)

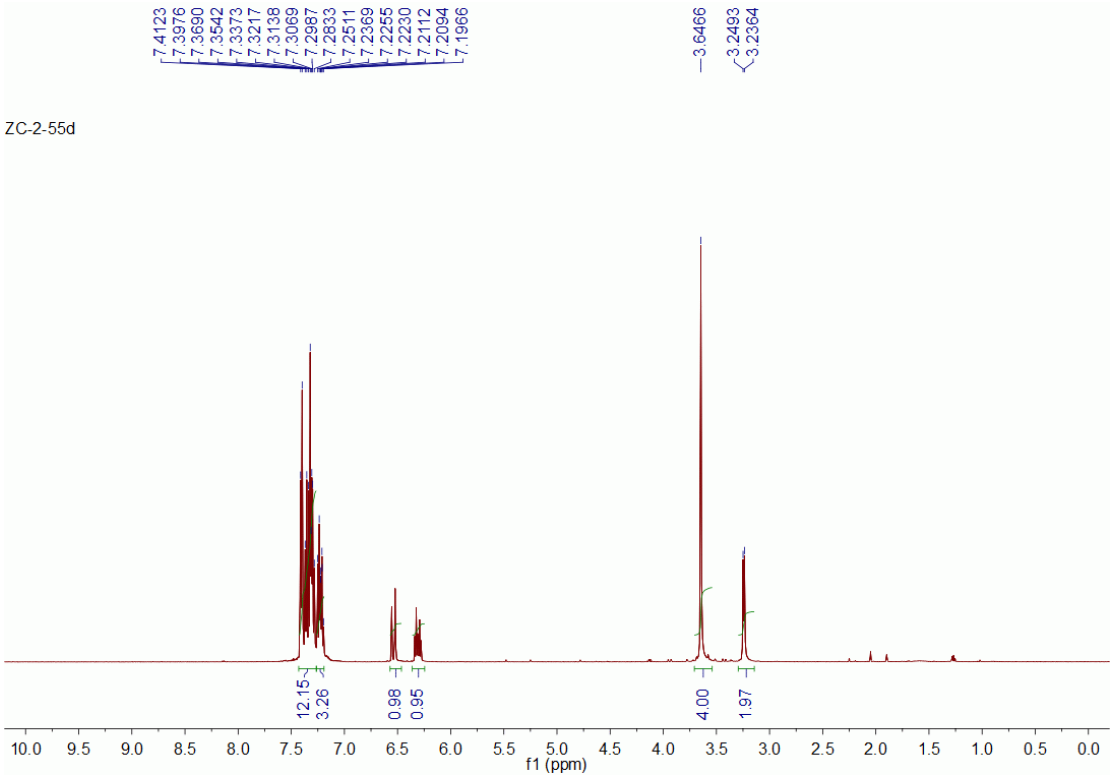


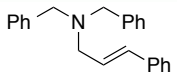


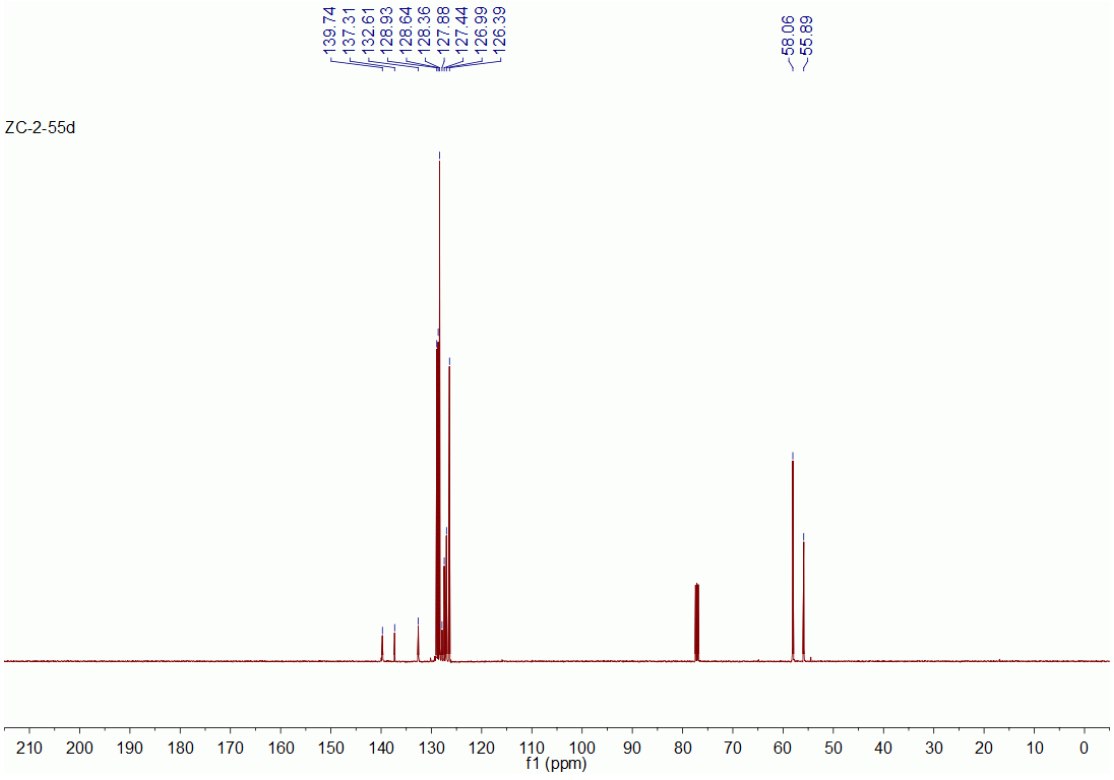

**4d** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)



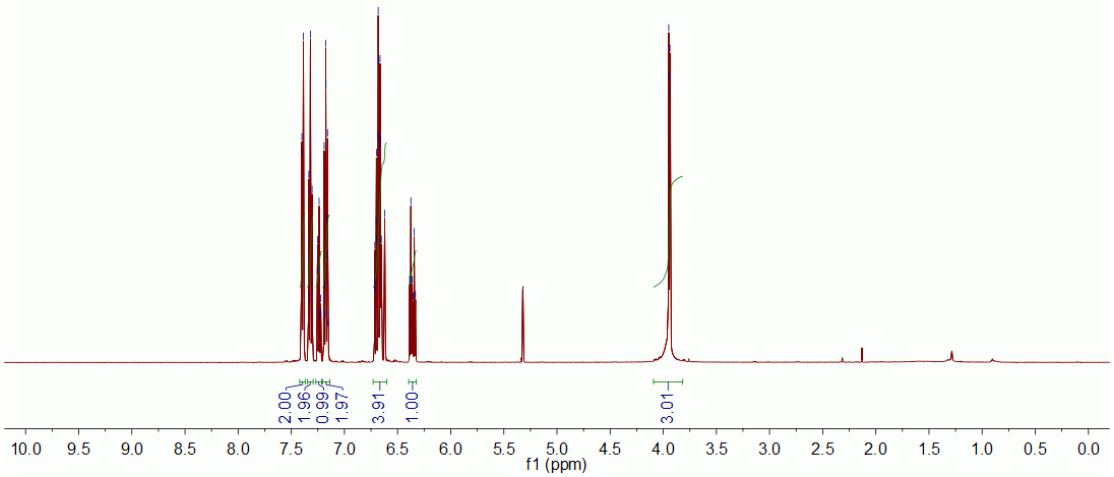


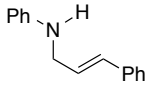




**4e** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)



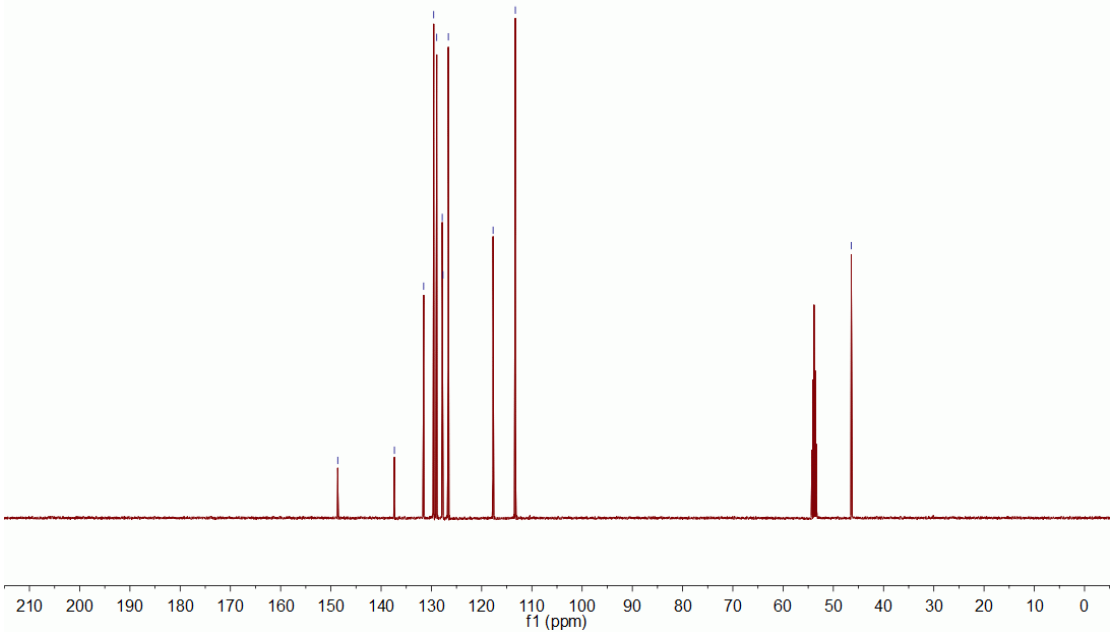

ZC-2-56A

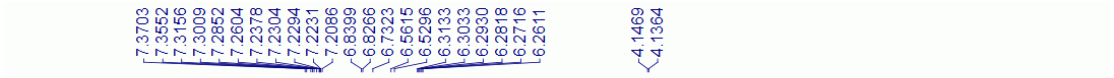


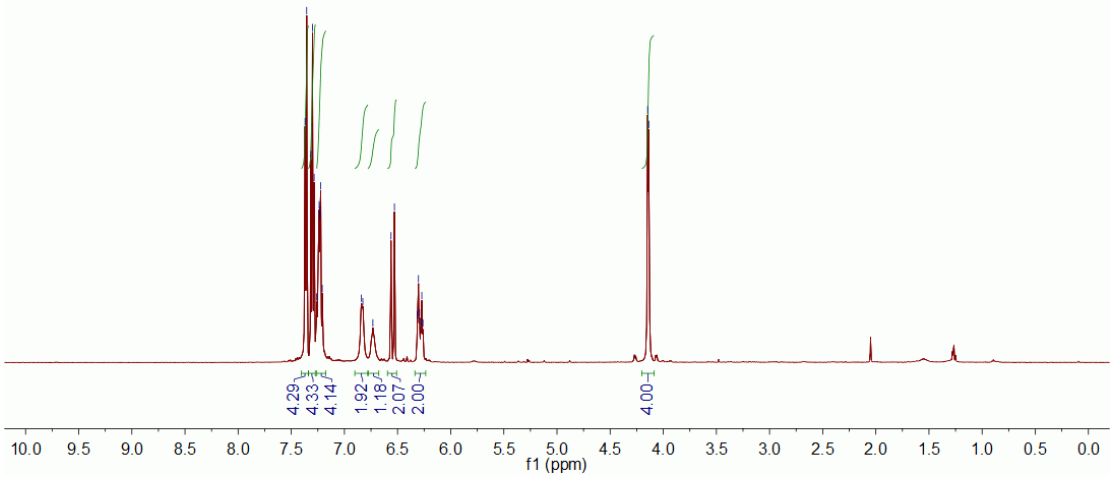

**4f** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)

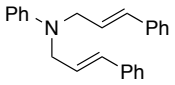

ZC-2-56A





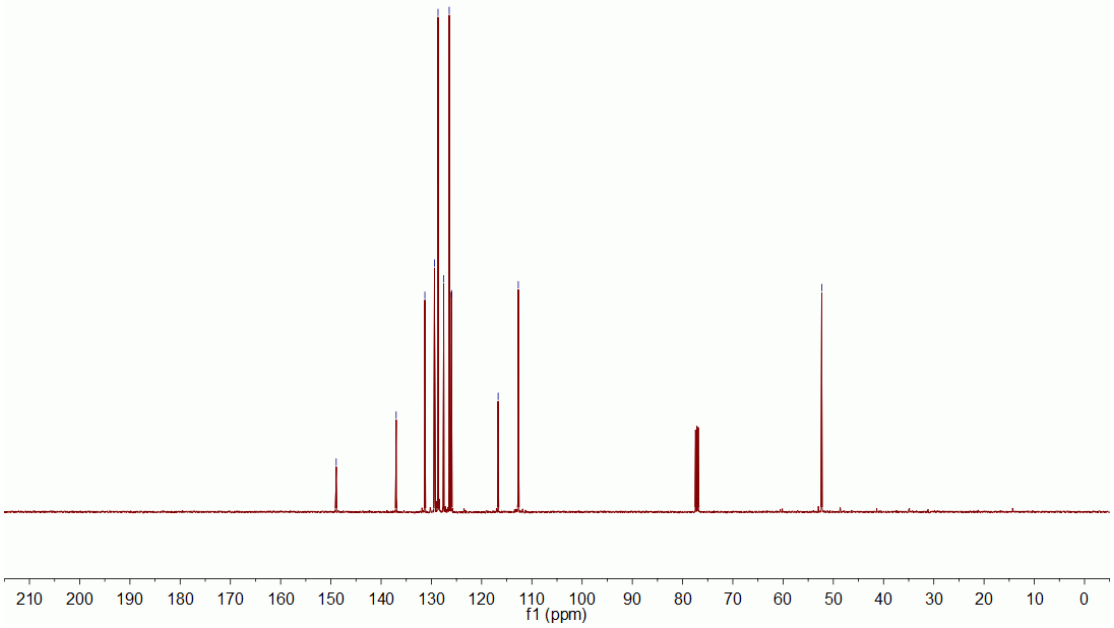

ZC-2-73E

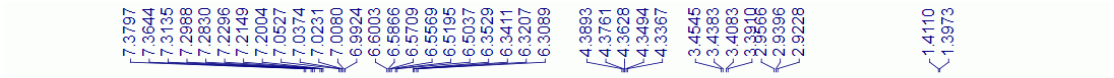


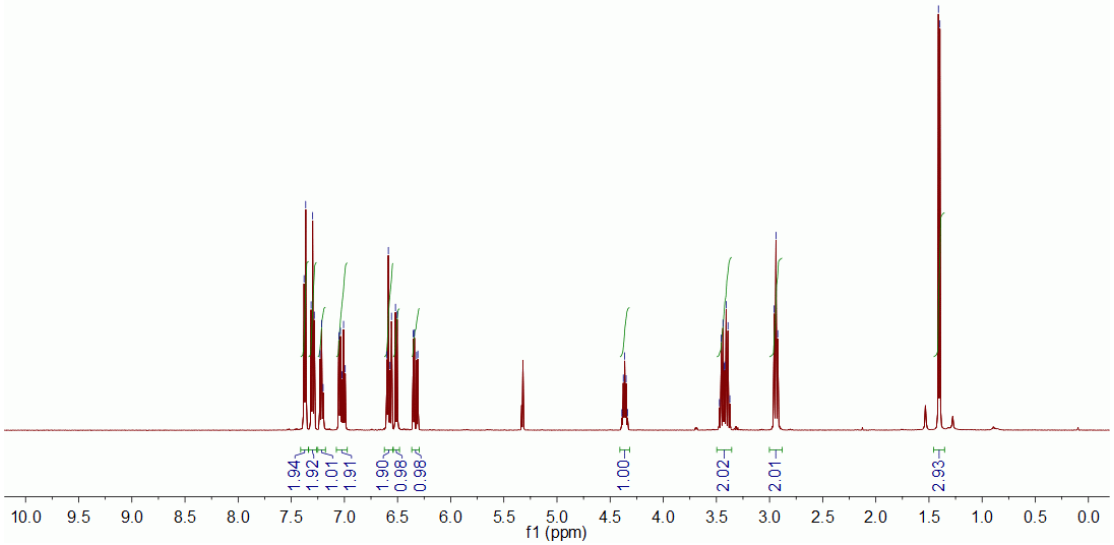

**4f'** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)

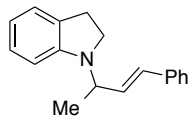

ZC-2-73E





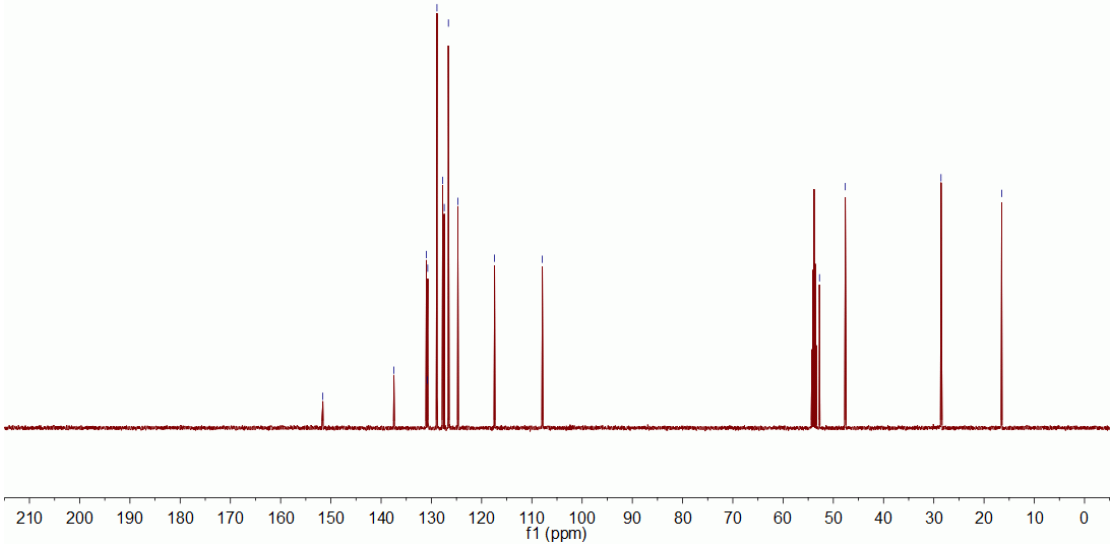

ZC-2-46E




**4g** $^{1}$H NMR (500 MHz, $CDCl_3$)
$^{13}$C NMR (126 MHz, $CDCl_3$)


ZC-2-46E



## Appendix 1.2: Supporting Information for Chapter 1.2
## Tandem Rh-Catalysis: Decarboxylative $\beta$-Keto Acid and Alkyne Cross-Coupling[ii]

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2. Typical procedure for the decarboxylative allylation 80
3. Characterization data of ketones **3** 80
4. References 82
5. NMR spectra 83

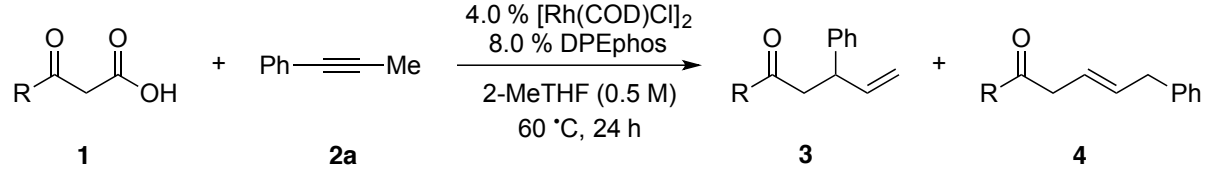

### 1. General

Commercial reagents were purchased from Sigma Aldrich, Strem, or Alfa Aesar and used without further purification. Reactions were monitored using thin-layer chromatography (TLC) or GC-FID. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ stain. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. $^1H$ and $^{13}C$ NMR spectra were recorded on Bruker CRYO-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$) or (400 MHz $^1H$, 100 MHz $^{13}C$) DRX-400 spectrometer. $^{19}F$ NMR spectra were recorded on a Bruker DRX-400 (376.5 MHz $^{19}F$) spectrometer. $^1H$ NMR spectra were internally referenced to the residual solvent signal or TMS. $^{13}C$ NMR spectra were internally referenced to the residual solvent signal. Data for $^1H$ NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for $^{19}F$ and $^{13}C$ NMR are reported in terms of chemical shift (δ ppm). High resolution mass spectra (HRMS) were obtained on a micromass 70S-250 spectrometer (EI) or an ABI/Sciex QStar Mass Spectrometer (ESI). Infrared (IR) spectra were obtained on a Nicolet iS5 FT-IR spectrometer with an iD5 ATR, and are reported in terms of frequency of absorption ($cm^{-1}$). Column chromatography was performed with Silicycle Silia-P Flash Silica Gel using glass columns. Preparatory thin-layer chromatography was performed using EMD Silica Gel 60 $F_{254}$ plates. Solvents were purchased from Fisher. Solvents used in

[ii] See F. A. Cruz, Z. Chen, S. I. Kurtoic and V. M. Dong, *Chem. Commun.*, 2016, **52**, 5836 for additional details.

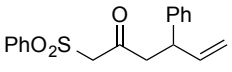
hydroaminations were degassed by three freeze-pump-thaw cycles before being taken into a nitrogen-filled glove box. Alkyne **2a**-$d_3$[1] and 1-phenylallene **6a**[2] were prepared according to literature procedure. *b*-Keto acids **1f**, **1g**, **1h**, **1i**, **1j**, **1k**, **1m**, and **1n** were prepared from the corresponding *b*-keto esters, which were prepared from the corresponding acetophenones.[3]

**2. Typical procedure for the decarboxylative allylation**

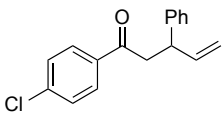



To a 1 dram vial equipped with a magnetic stir bar was added the indicated amount of $[Rh(cod)Cl]_2$ (3.9 mg, 0.008 mmol), DPEphos (8.6 mg, 0.016 mmol), *β*-keto acid (0.20 mmol), alkyne (0.40 mmol), and 2-MeTHF (0.40 mL). The vial was then sealed with a Teflon-lined screw cap and heated at the indicated temperature and time. Regioselectivities were determined by $^1$H NMR analysis of the crude reaction mixture. Ketone products were isolated by preparatory TLC.

**3. Characterization data of ketones 3**

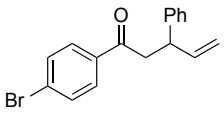


4-phenyl-1-(phenylsulfonyl)hex-5-en-2-one (**3f**): The title compound was isolated via preparatory TLC (10% ethyl acetate in hexanes) as a yellow oil (57.9 mg, 92% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.71 – 7.62 (m, 3H), 7.52 – 7.48 (m, 2H), 7.34 – 7.30 (m, 2H), 7.27 – 7.21 (m, 3H), 5.97 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.10 – 5.03 (m, 2H), 4.06 (q, *J* = 13.4 Hz, 2H), 3.89 (q, *J* = 7.1 Hz, 1H), 3.20 (qd, *J* = 17.6, 7.4 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 196.5, 142.2, 140.1, 138.3, 134.4, 129.4, 128.8, 128.4, 128.0, 127.0, 115.2, 67.4, 49.6, 44.2. **IR** (ATR): 3062, 1721, 1447, 1320, 1310, 1151, 1085, 912, 734, 686 cm$^{-1}$. **HRMS** calculated for $C_{18}H_{18}O_3SNa$ $[M+Na]^+$ 337.0874, found 337.0881.

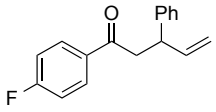


1-(4-chlorophenyl)-3-phenylpent-4-en-1-one (**3g**): The title compound was isolated via preparatory TLC (5% ethyl acetate in hexanes) as a yellow oil (38.1 mg, 70% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.34 – 7.30 (m, 2H), 7.28 – 7.20 (m, 3H), 6.06 (ddd, *J* = 17.2,

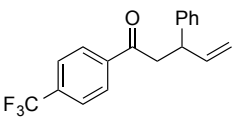
10.4, 6.8 Hz, 1H), 5.11 – 5.02 (m, 2H), 4.13 (q, *J* = 6.8 Hz, 1H), 3.38 (qd, *J* = 16.5, 7.7 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 197.3, 143.1, 140.7, 139.7, 135.6, 129.7, 129.1, 128.8, 127.9, 126.9, 115.0, 44.8, 44.2. **IR** (ATR): 3028, 1684, 1588, 1488, 1399, 1202, 1090, 987, 815, 699 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{19}ClNO$ $[M+NH_4]^+$ 288.1155, found 288.1154.




1-(4-bromophenyl)-3-phenylpent-4-en-1-one (**3h**): The title compound was isolated via preparatory TLC (10% ethyl acetate in hexanes) as a colorless oil (47.6 mg, 76% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.9 Hz, 2H), 7.38 – 7.35 (m, 2H), 7.32 – 7.25 (m, 3H), 6.10 (ddd, *J* = 17.2, 10.4, 6.7 Hz, 1H), 5.15 – 5.08 (m, 2H), 4.18 (q, *J* = 6.9 Hz, 1H), 3.42 (qd, *J* = 16.5, 7.6 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 197.4, 143.1, 140.7, 136.0, 132.1, 130.0, 128.8, 128.4, 127.9, 126.8, 115.0, 44.7, 44.2. **IR** (ATR): 3028, 1685, 1568, 1484, 1396, 1201, 1070, 987, 811, 699 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{15}BrONa$ $[M+Na]^+$ 337.0204, found 339.0211.

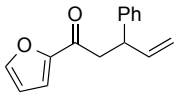



1-(4-fluorophenyl)-3-phenylpent-4-en-1-one (**3i**): The title compound was isolated via preparatory TLC (5% ethyl acetate in hexanes) as a colorless oil (46.4 mg, 91% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.40 – 7.37 (m, 2H), 7.35 – 7.32 (m, 2H), 7.30 – 7.27 (m, 1H), 7.18 (t, *J* = 8.6 Hz, 2H), 6.13 (ddd, *J* = 17.2, 10.4, 6.9 Hz, 1H), 5.17 – 5.09 (m, 2H), 4.21 (q, *J* = 6.9 Hz, 1H), 3.45 (qd, *J* = 16.7, 7.6 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 196.8, 165.9 (d, *J* = 253.9 Hz), 143.2, 140.8, 133.7 (d, *J* = 2.9 Hz), 130.9 (d, *J* = 9.0 Hz), 128.8, 127.9, 126.8, 115.8 (d, *J* = 21.6 Hz), 115.0, 44.8, 44.1. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -105.7. **IR** (ATR): 3028, 1683, 1596, 1505, 1408, 1232, 1155, 989, 829, 699 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{15}FONa$ $[M+Na]^+$ 277.1005, found 277.0999.

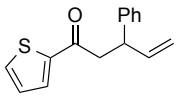



3-phenyl-1-(4-(trifluoromethyl)phenyl)pent-4-en-1-one (**3k**): The title compound was isolated via preparatory TLC (10% ethyl acetate in hexanes) as a colorless oil (38.2 mg, 63% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.30 (m, 2H), 7.28 – 7.20 (m, 3H), 6.06 (ddd, *J* = 17.2, 10.4, 6.7 Hz, 1H), 5.12 – 5.03 (m, 2H), 4.14 (q, *J* = 6.8 Hz, 1H), 3.43 (qd, *J* = 16.7, 7.5 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 197.6, 143.0, 140.54, 140.53, 139.9 (q, *J* = 0.9

Hz), 134.5 (q, *J* = 32.6 Hz), 128.9, 128.6, 127.9, 126.9, 125.9 (q, *J* = 3.8 Hz), 115.2, 44.7, 44.5. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ 63.5. **IR** (ATR): 3029, 1692, 1511, 1410, 1322, 1167, 1126, 1065, 846, 700 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{16}F_3O$ $[M+H]^+$ 305.1153, found 305.1153.




1-(furan-2-yl)-3-phenylpent-4-en-1-one (**3m**): The title compound was isolated via preparatory TLC (10% ethyl acetate in hexanes) as a colorless oil (31.5 mg, 70% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.31 – 7.25 (m, 4H), 7.20 (t, *J* = 7.0 Hz, 1H), 7.15 (d, *J* = 3.2 Hz, 1H), 6.04 (ddd, *J* = 17.0, 10.2, 7.0 Hz, 1H), 5.08 – 5.04 (m, 2H), 4.11 (q, *J* = 6.8 Hz, 1H), 3.29 (dd, *J* = 15.7, 7.9 Hz, 1H), 3.21 (dd, *J* = 15.7, 6.6 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 187.7, 153.1, 146.5, 143.0, 140.6, 128.7, 127.9, 126.8, 117.3, 126.8, 115.0, 112.4, 44.7, 44.0. **IR** (ATR): 3028, 1671, 1567, 1466, 1393, 1268, 1156, 915, 759, 699 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{14}O_2Na$ $[M+Na]^+$ 249.0892, found 249.0895.

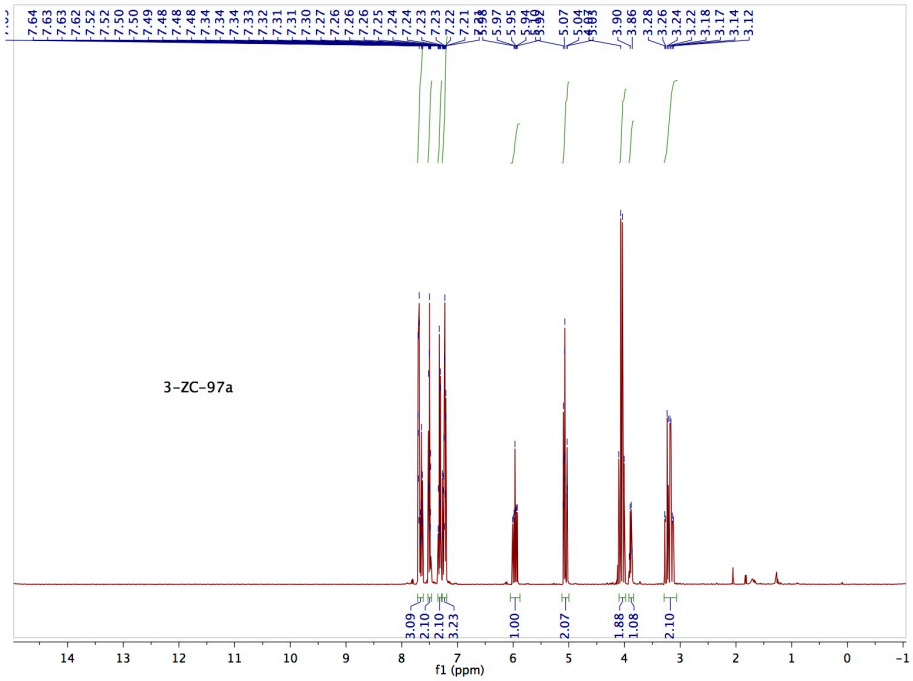


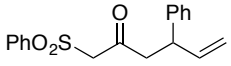

3-phenyl-1-(thiophen-2-yl)pent-4-en-1-one (**3n**): The title compound was isolated via preparatory TLC (10% ethyl acetate in hexanes) as a colorless oil (43.2 mg, 89% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 3.9 Hz, 1H), 7.60 (d, *J* = 5.4 Hz, 1H), 7.32 – 7.25 (m, 4H), 7.20 (t, *J* = 6.9 Hz, 1H), 7.09 (t, *J* = 3.7 Hz, 1H), 6.05 (ddd, *J* = 17.0, 10.3, 6.8 Hz, 1H), 5.09 – 5.04 (m, 2H), 4.13 (q, *J* = 6.9 Hz, 1H), 3.36 (dd, *J* = 15.9, 7.8 Hz, 1H), 3.28 (dd, *J* = 15.9, 6.6 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 191.3, 144.7, 143.0, 140.5, 133.9, 132.0, 128.8, 128.3, 127.9, 126.8, 115.1, 45.0. **IR** (ATR): 3081, 3027, 1657, 1413, 1258, 1061, 916, 857, 723, 699 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{14}OSNa$ $[M+Na]^+$ 265.0663, found 265.0667.

## 4. References

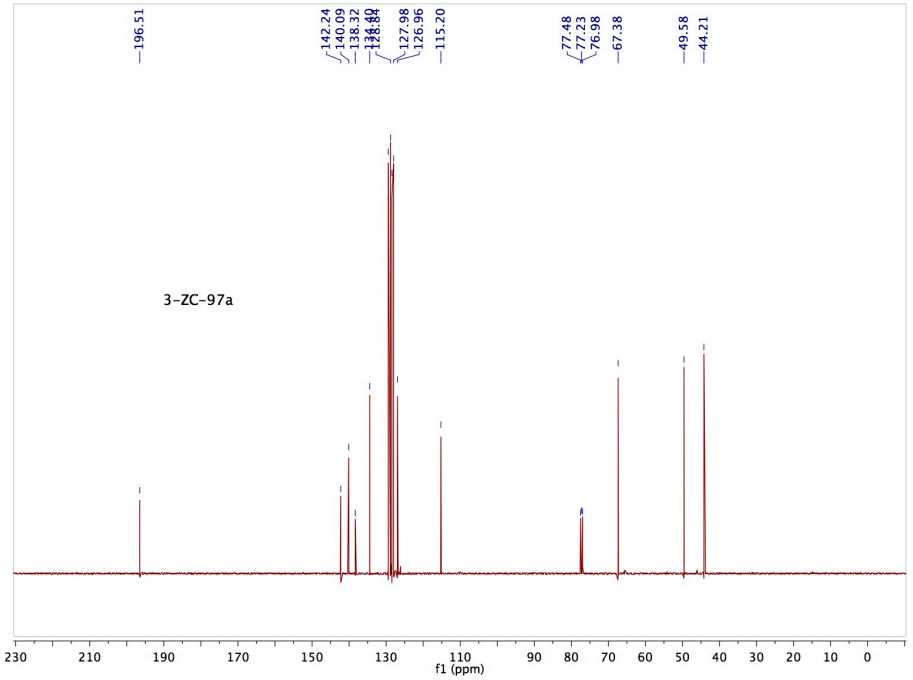

1. Huggins, J. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 3002.
2. Kippo, T.; Fukuyama, T.; Ryu, I. *Org. Lett.* **2011**, *13*, 3864.
3. Evans, D. A.; Mito, S.; Seidel, D. *J. Am. Chem. Soc.* **2007**, *129*, 11583.

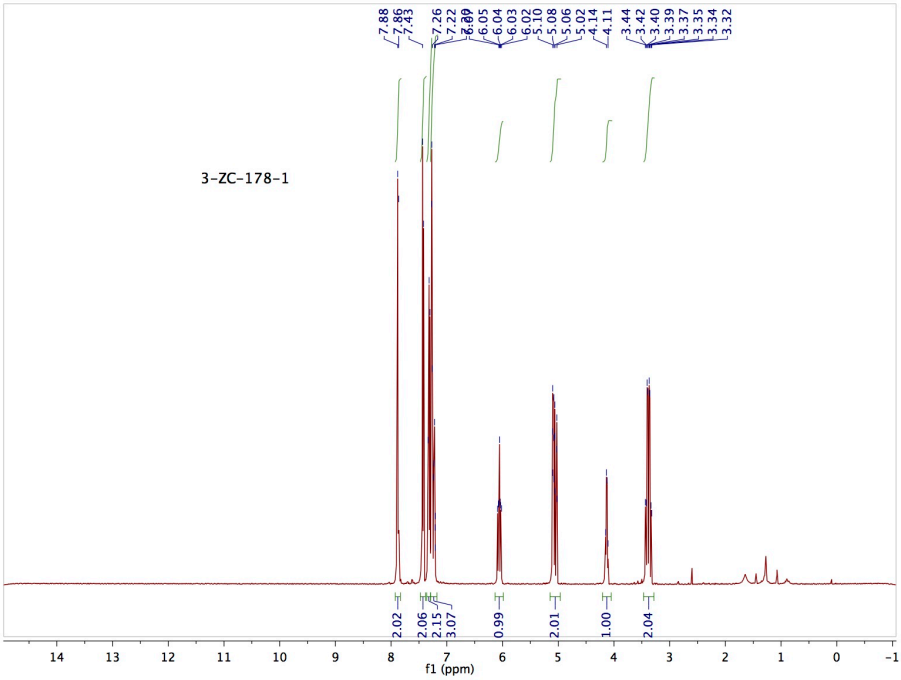
## 5. NMR Spectra

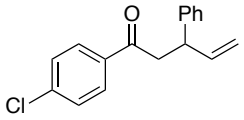


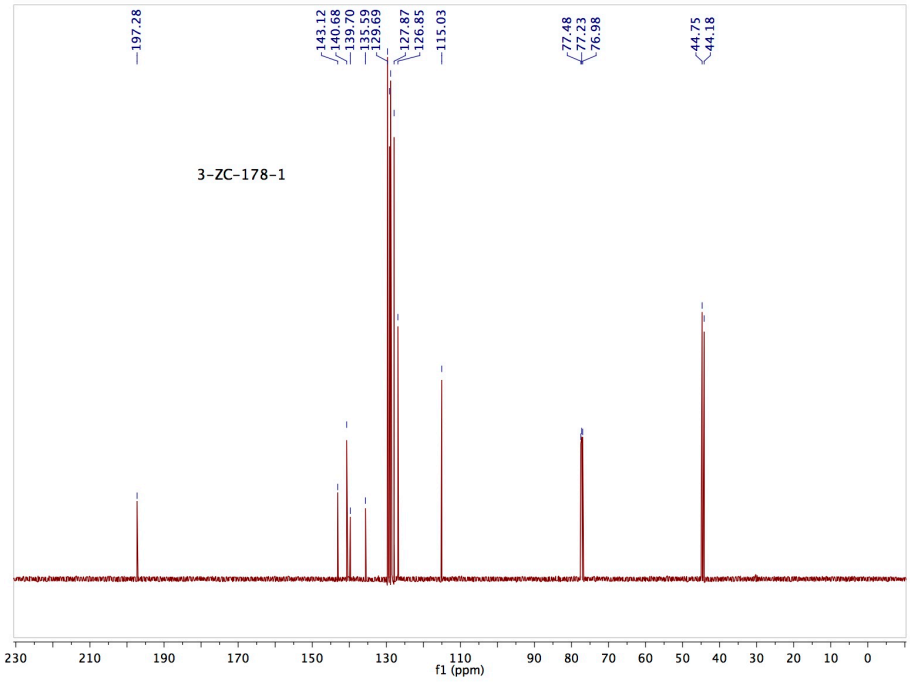

**3f** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)

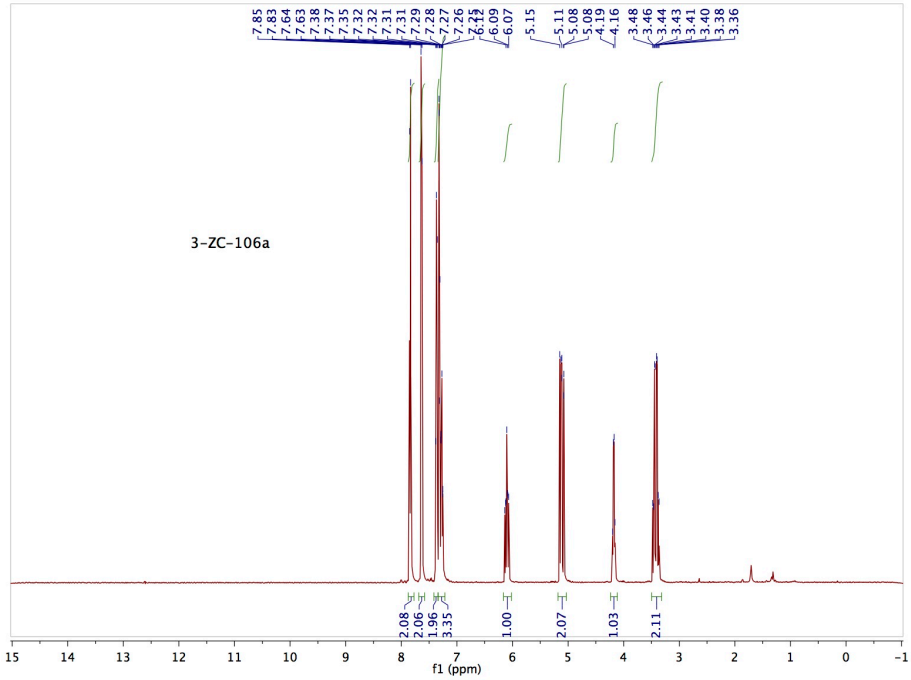


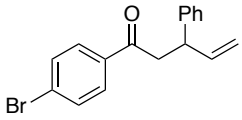


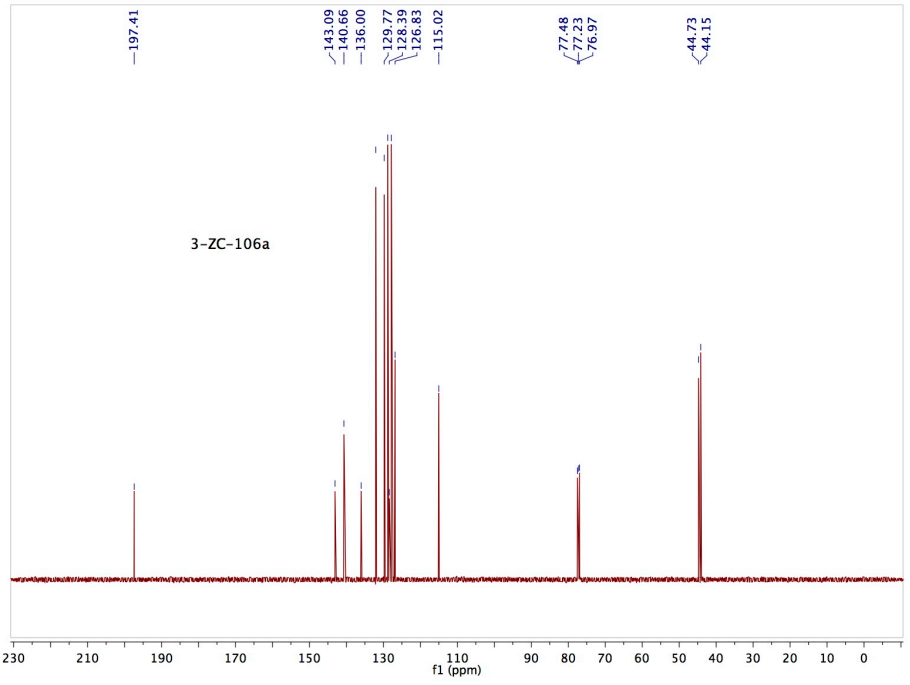

**3g** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)

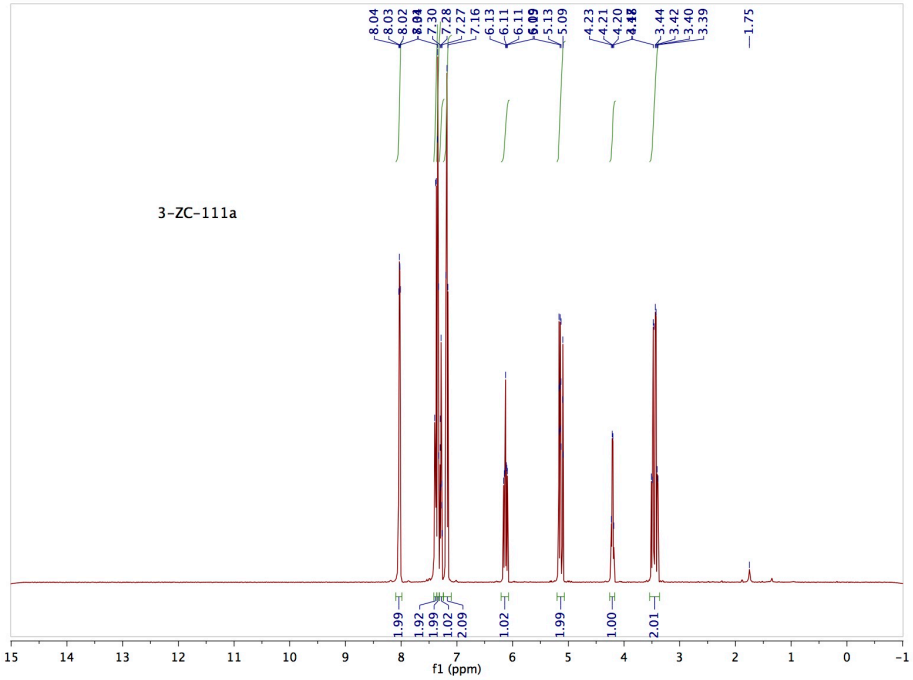


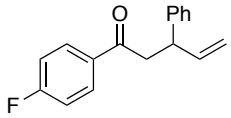


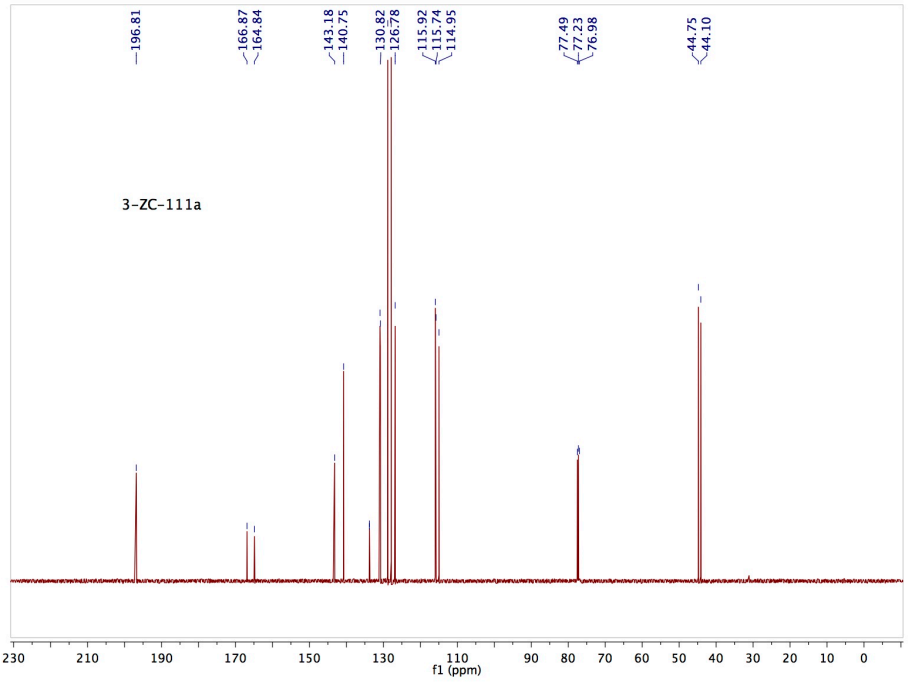

**3h** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)

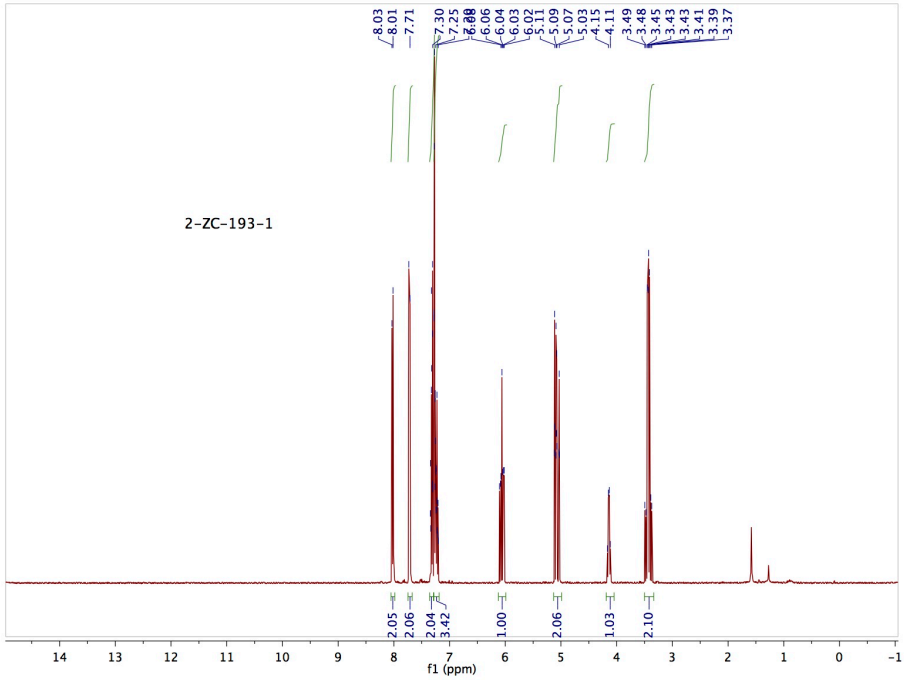


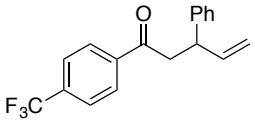


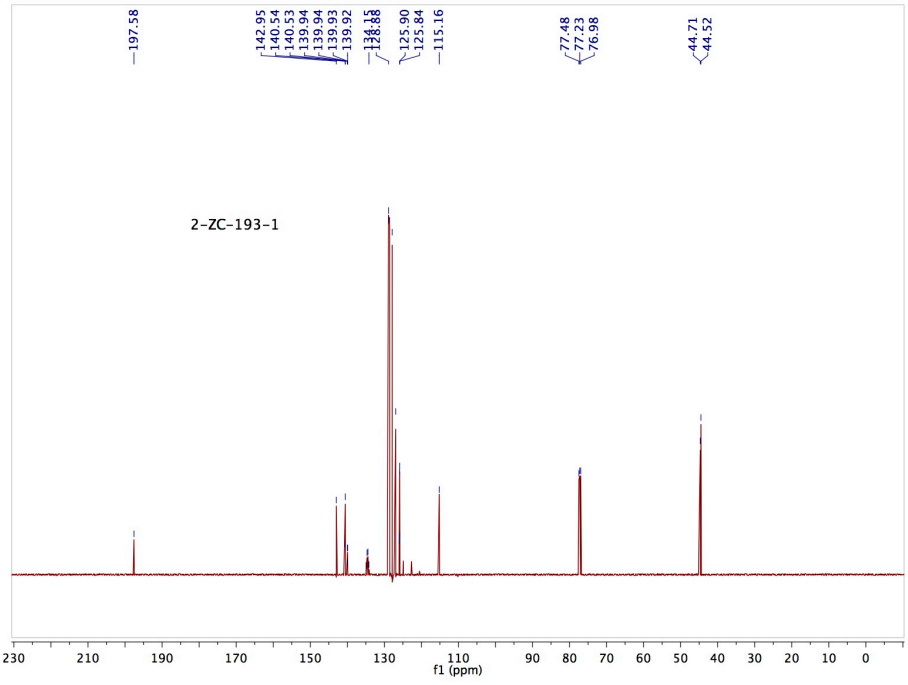

**3i** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)

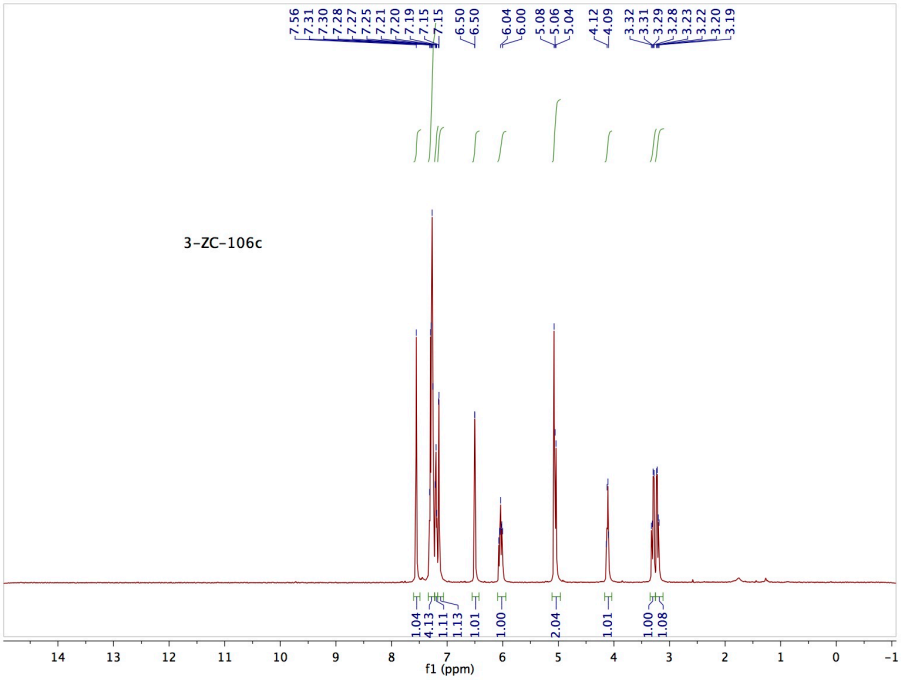


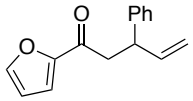


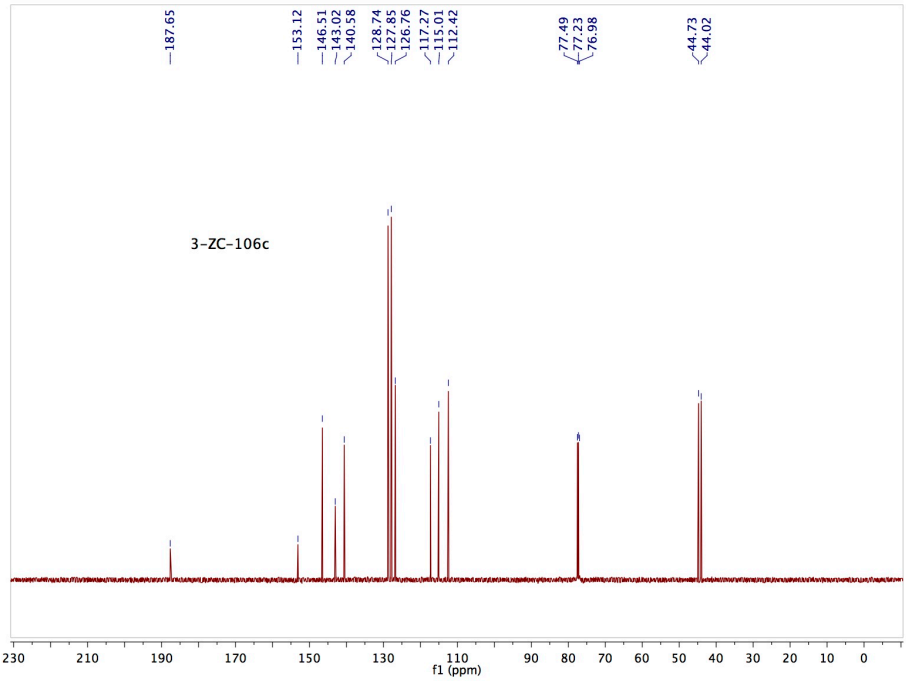

**3k** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)

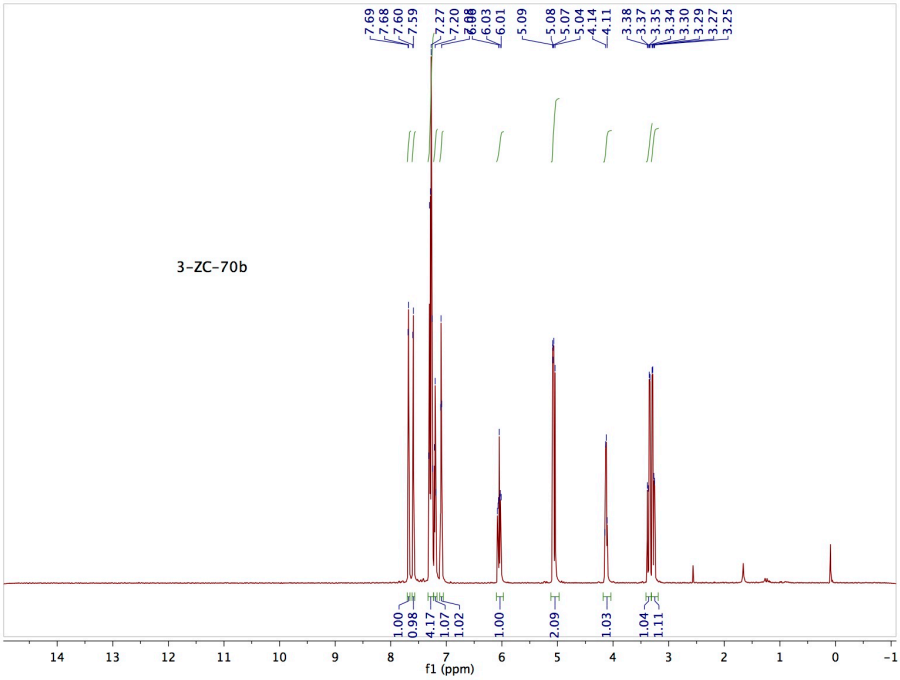


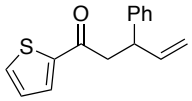


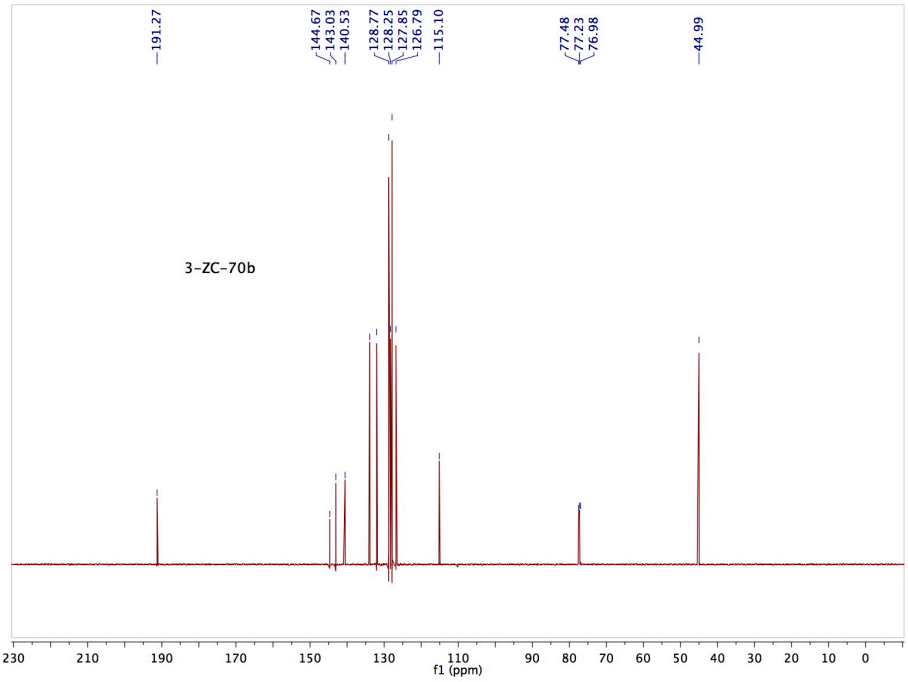

**3m** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)






**3n** $^{1}$H NMR (500 MHz, CDCl3)
$^{13}$C NMR (126 MHz, CDCl3)



## Appendix 1.3: Supporting Information for Chapter 1.3
## Enantioselective Semireduction of Allenes

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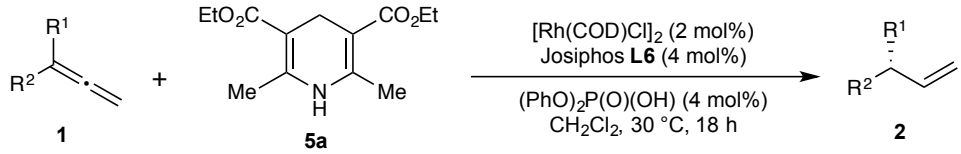
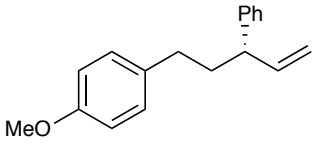
## 1. General Information

Commercially reagents were purchased from Sigma Aldrich, Strem, Acros Organics, TCI or Alfa Aesar and used without further purification. All experiments were performed in oven-dried or flame-dried glassware under an atmosphere of $N_2$. Tetrahydrofuran, diethyl ether, toluene, and dichloromethane were purified using an Innovative Technologies Pure Solv system, degassed by three freeze-pump-thaw cycles, and stored over 3Å MS within a $N_2$ filled glove box. Reactions were monitored either *via* gas chromatography using an Agilent Technologies 7890A GC system equipped with an Agilent Technologies 5975C inert XL EI/CI MSD or by analytical thin-layer chromatography on EMD Silica Gel 60 $F_{254}$ plates. Visualization of the developed plates was performed under UV light (254 nm) or using $KMnO_4$ stain. Purification and isolation of products were performed via silica gel chromatography (both column and preparative thin-layer chromatography). Column chromatography was performed with Silicycle Silia-P Flash Silica Gel using glass columns. $^1H$, $^{13}C$, $^{19}F$, and $^{31}P$ NMR spectra were recorded on a Bruker DRX-400 (400 MHz $^1H$, 100 MHz $^{13}C$, 376.5 MHz $^{19}F$, 162 MHz $^{31}P$), GN-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$, 202 MHz $^{31}P$), or CRYO-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$) spectrometer. $^1H$ NMR spectra were internally referenced to the residual solvent signal or TMS. $^{13}C$ NMR spectra were internally referenced to the residual solvent signal. Data for $^1H$ NMR are reported as follows: chemical shift (δ ppm, δ 7.27 for $CDCl_3$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for $^{13}C$ NMR are reported in terms of chemical shift (δ ppm, δ 77.16 for $CDCl_3$). Infrared spectra were obtained on a Thermo Scientific Nicolet iS5 FT-IR spectrometer equipped with an iD5 ATR accessory, and were reported in terms of frequency of absorption ($cm^{-1}$). Enantioselectivities were determined by chiral SFC analysis using an Agilent Technologies HPLC (1200 series) system and Aurora A5 Fusion. High-resolution mass spectra (HRMS) were obtained on a micromass 70S-250 spectrometer (EI) or an ABI/Sciex QStar Mass Spectrometer (ESI), performed by the University of California, Irvine Mass Spectrometry Centre. Allenes **1o**, **1q**, and **1r** are known compounds and were prepared according to literature procedures[1,2] . Deuterated Hantzsch esters **5b** and **5c** were prepared according to literature procedures[3,4].

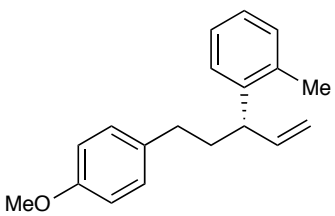
## 2. General Procedure for the Semireduction of Allenes




In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol, 2 mol%), $(PhO)_2P(O)(OH)$ (2.0 mg, 0.0080 mmol, 4 mol%), Josiphos **L6** (9.1 mg, 0.0080 mmol, 4 mol%), Hantzsch ester **5a** (101.3 mg, 0.40 mmol, 2.0 equiv), allene **1** (0.20 mmol, 1 equiv), and $CH_2Cl_2$ (0.20 mL, 1 M) were added to a 1 dram vial equipped with a magnetic stir bar. The vial was then sealed with a Teflon-lined screw cap and stirred at 30 °C for 18 h. The reaction mixture was cooled to rt and concentrated *in vacuo*. Regioselectivities were determined by $^1$H NMR analysis of the unpurified reaction mixture.

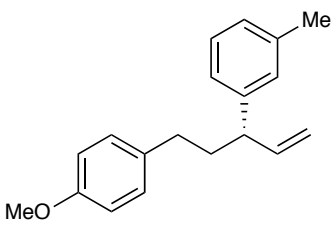



**(*S*)-1-methoxy-4-(3-phenylpent-4-en-1-yl)benzene (2a)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (21.4 mg (from 0.10 mmol of starting material), 85% yield, >20:1 *rr*, 95:5 *er*, $[\alpha]^{24}_D$ = +9.1 (*c* 1.3, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 2H), 7.25 – 7.17 (m, 3H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.05 – 5.92 (m, 1H), 5.10 – 5.01 (m, 2H), 3.80 (s, 3H), 3.29 (q, *J* = 7.6 Hz, 1H), 2.62 – 2.44 (m, 2H), 2.02 (ddd, *J* = 8.7, 8.2, 4.5 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 157.8, 144.3, 142.3, 134.4, 129.5, 128.6, 127.8, 126.4, 114.4, 113.9, 55.4, 49.3, 37.3, 32.8. **IR** (ATR): 3027, 2933, 1611, 1511, 1452, 1243,1176, 1035, 913, 826 cm$^{-1}$. **HRMS** calculated for $C_{18}H_{20}O$ $[M]^+$ 252.1514, found 252.1514. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.1 min, $t_{R2}$ (major) = 2.5 min.

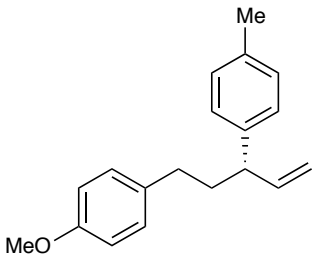



**(*S*)-1-(5-(4-methoxyphenyl)pent-1-en-3-yl)-2-methylbenzene (2b)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (40.0 mg, 75% yield, >20:1 *rr*, 88:12 *er*, $[\alpha]^{24}_D$ =

+23.8 (*c* 0.87, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 2H), 7.18 – 7.10 (m, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.93 (ddd, *J* = 17.4, 10.2, 7.4 Hz, 1H), 5.03 (ddt, *J* = 25.9, 17.1, 1.5 Hz, 2H), 3.81 (s, 3H), 3.53 (q, *J* = 7.4 Hz, 1H), 2.66 – 2.48 (m, 2H), 2.26 (s, 3H), 2.04 (dtd, *J* = 8.9, 7.1, 3.5 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 142.1, 141.8, 136.1, 134.4, 130.5, 129.5, 126.5, 126.3, 126.1, 114.4, 113.9, 55.4, 44.3, 36.9, 32.9, 19.7. **IR** (ATR): 2933, 2833, 1611, 1511, 1441, 1300, 1244, 1176, 1036, 913, 827, 752 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{22}O$ $[M]^+$ 266.1671, found 266.1670. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.3 min, $t_{R2}$ (major) = 10.8 min.

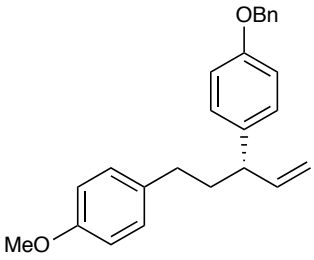



**(*S*)-1-(5-(4-methoxyphenyl)pent-1-en-3-yl)-3-methylbenzene (2c)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (46.6 mg, 88% yield, >20:1 *rr*, 96:4 *er*, $[\alpha]^{24}_D$ = +11.5 (*c* 0.95, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.19 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 7.01 (dd, *J* = 11.1, 5.0 Hz, 3H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.98 (ddd, *J* = 16.9, 10.5, 7.9 Hz, 1H), 5.10 – 4.99 (m, 2H), 3.76 (s, 3H), 3.23 (q, *J* = 7.5 Hz, 1H), 2.60 – 2.41 (m, 2H), 2.33 (s, 3H), 1.98 (td, *J* = 8.7, 1.5 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 158.6, 145.1, 143.3, 138.9, 135.2, 130.1, 129.2, 129.1, 127.7, 125.4, 114.7, 114.4, 56.0, 50.2, 38.2, 33.6, 22.0. **IR** (ATR): 2931, 2858, 1610, 1511, 1455, 1300, 1244, 1176, 1037, 912, 821, 785, 703 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{22}ONH_4$ $[M+NH_4]^+$ 284.2014, found 284.2005. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 8.4 min, $t_{R2}$ (minor) = 9.0 min.

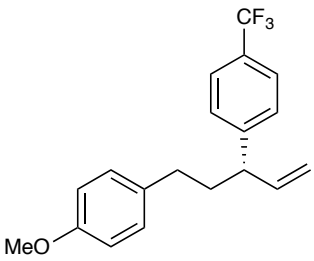



**(*S*)-1-methoxy-4-(3-(*p*-tolyl)pent-4-en-1-yl)benzene (2d)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (49.0 mg, 92% yield, >20:1 *rr*, 95:5 *er*, $[\alpha]^{24}_D$ = +10.2 (*c* 0.65, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.17 – 7.02 (m, 6H), 6.81(d, *J* = 8.7 Hz, 2H), 6.03 – 5.90 (m, 1H), 5.07 – 4.99 (m, 2H), 3.76 (s, 3H), 3.24 (q, *J* = 7.5 Hz, 1H),

2.61 – 2.40 (m, 2H), 2.32 (s, 3H), 2.05 – 1.89 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 158.6, 143.4, 142.1, 136.6, 135.2, 130.1, 129.9, 128.3, 114.5, 114.4, 56.0, 49.8, 38.2, 33.6, 21.5. **IR** (ATR): 2921, 2857, 1611, 1511, 1455, 1300, 1243, 1176, 1036, 912, 815 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{22}O$ $[M]^+$ 266.1671, found 266.1664. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 20% *i*-PrOH, 1.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 3.8 min, $t_{R2}$ (major) = 4.0 min

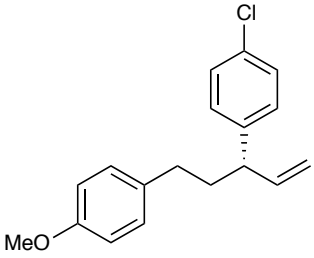



**(*S*)-1-(benzyloxy)-4-(5-(4-methoxyphenyl)pent-1-en-3-yl)benzene (2e)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (61.1 mg, 85% yield, >20:1 *rr*, 97:3 *er*, $[\alpha]^{24}_D$ = +8.8 (*c* 0.83, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.46 (m, 2H), 7.43 (ddt, *J* = 9.5, 7.9, 1.6 Hz, 2H), 7.39 – 7.33 (m, 1H), 7.16 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.99(ddd, *J* = 16.4, 10.9, 7.5 Hz, 1H), 5.11 – 5.02 (m, 4H), 3.82 (s, 3H), 3.27 (q, *J* = 7.4 Hz, 1H), 2.63 – 2.47 (m, 2H), 2.09 – 1.96 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.8, 157.4, 142.6, 137.3, 136.6, 134.4, 129.4, 128.70, 128.68, 128.0, 127.6, 115.0, 114.1, 113.9, 70.2, 55.4, 48.4, 37.4, 32.8. **IR** (ATR): 3031, 2932, 1609, 1509, 1453, 1300, 1241, 1175, 1035, 912, 826, 734 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{22}O$ $[M]^+$ 358.1933, found 358.1942. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 10% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 16.1 min, $t_{R2}$ (minor) = 17.7 min.

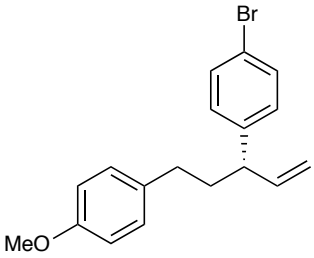



**(*S*)-1-methoxy-4-(3-(4-(trifluoromethyl)phenyl)pent-4-en-1-yl)benzene (2f)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (59.1 mg, 92% yield, >20:1 *rr*, 93:7 *er*, $[\alpha]^{24}_D$ = +7.8 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.09 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.98 (ddd, *J* = 17.1, 10.3, 7.5 Hz, 1H), 5.11 (ddt, *J* = 19.7, 17.1, 1.4 Hz, 2H), 3.82 (s, 3H), 3.37 (q, *J* = 7.4 Hz, 1H), 2.63 – 2.46 (m, 2H), 2.15 – 1.95 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0,

148.4 (q, $J$ = 1.3 Hz), 141.3, 133.9, 129.4, 128.7 (q, $J$ = 32.4 Hz), 128.2, 125.6 (q, $J$ = 3.8 Hz), 124.6 (q, $J$ = 271.8 Hz), 115.3, 114.0, 55.4, 49.1, 37.1, 32.7. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.3. **IR** (ATR): 2936, 1615, 1511, 1324, 1301, 1245, 1162, 1118, 1067, 1036, 1017, 918, 827 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{19}F_3O$ $[M]^+$ 320.1388, found 320.1398. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 1.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.7 min, $t_{R2}$ (major) = 5.1 min.

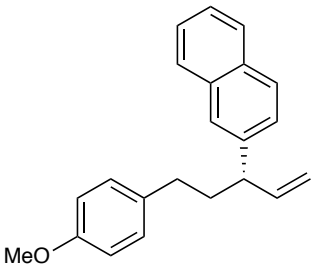



**(*S*)-1-chloro-4-(5-(4-methoxyphenyl)pent-1-en-3-yl)benzene (2g)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (51.2 mg, 90% yield, >20:1 *rr*, 94:6 *er*, $[\alpha]^{24}_D$ = +8.1 (*c* 0.81, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.31 (d, $J$ = 8.4 Hz, 2H), 7.15 (d, $J$ = 8.4 Hz, 2H), 7.08 (d, $J$ = 8.6 Hz, 2H), 6.85 (d, $J$ = 8.6 Hz, 2H), 6.01 – 5.87 (m, 1H), 5.12 – 5.01 (m, 2H), 3.81 (s, 3H), 3.27 (q, $J$ = 7.4 Hz, 1H), 2.60 – 2.44 (m, 2H), 2.11 – 1.91 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 142.7, 141.8, 134.1, 132.0, 129.4, 129.2, 128.7, 114.8, 113.9, 55.4, 48.6, 37.2, 32.7. **IR** (ATR): 2932, 2833, 1611, 1511, 1490, 1300, 1243, 1176, 1090, 1036, 1014, 915, 822 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{19}ClO$ $[M]^+$ 286.1125, found 286.1137. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 0% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 18.8 min, $t_{R2}$ (major) = 19.9 min.

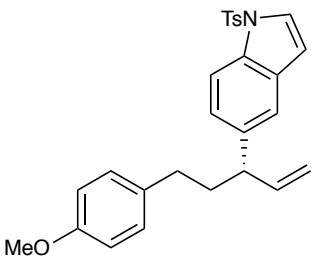



**(*S*)-1-bromo-4-(5-(4-methoxyphenyl)pent-1-en-3-yl)benzene (2h)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (57.6 mg, 87% yield, >20:1 *rr*, 95:5 *er*, $[\alpha]^{24}_D$ = +6.3 (*c* 0.91, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, $J$ = 8.4 Hz, 2H), 7.12 – 7.04 (m, 4H), 6.85 (d, $J$ = 8.7 Hz, 2H), 5.95 (ddd, $J$ = 17.2, 10.3, 7.4 Hz, 1H), 5.07 (ddt, $J$ = 19.9, 17.1, 1.3 Hz, 2H), 3.81 (s, 3H), 3.26 (q, $J$ = 7.5 Hz, 1H), 2.61 – 2.43 (m, 2H), 2.11 – 1.91 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 143.2, 141.7, 134.0, 131.7, 129.6, 129.4, 120.1, 114.9, 113.9, 55.4, 48.6, 37.2, 32.7. **IR** (ATR): 2932, 2833, 1611, 1511, 1486, 1300,1243, 1176, 1073, 1035, 1009, 915, 820 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{19}BrO$ $[M]^+$ 330.0619, found

330.0616. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 10.9 min, $t_{R2}$ (major) = 11.6 min.

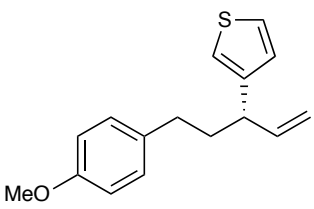



**(*S*)-2-(5-(4-methoxyphenyl)pent-1-en-3-yl)naphthalene (2i)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (54.9 mg, 91% yield, >20:1 *rr*, 94:6 *er*, $[\alpha]^{24}_D$ = +9.4 (*c* 0.71, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.82 (m, 3H), 7.68 (d, *J* = 1.4 Hz, 1H), 7.54 – 7.45 (m, 2H), 7.40 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.16 – 6.04 (m, 1H), 5.17 – 5.09 (m, 2H), 3.83 (s, 3H), 3.49 (q, *J* = 7.5 Hz, 1H), 2.69 – 2.51 (m, 2H), 2.16 (q, *J* = 7.8 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 142.2, 141.7, 134.4, 133.8, 132.4, 129.5, 128.3, 127.8, 127.7, 126.4, 126.2, 126.1, 125.5, 114.7, 113.9, 55.4, 49.4, 37.2, 32.9. **IR** (ATR): 3054, 2932, 2833, 1611, 1511, 1454, 1300, 1243, 1176, 1035, 913, 817, 746 $cm^{-1}$. **HRMS** calculated for $C_{22}H_{22}O$ $[M]^+$ 302.1671, found 302.1658. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 5.7 min, $t_{R2}$ (minor) = 6.3 min.

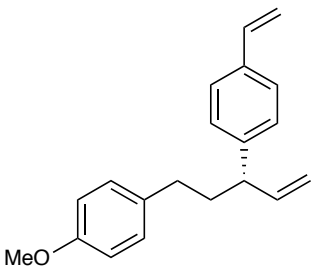



**(*S*)-5-(5-(4-methoxyphenyl)pent-1-en-3-yl)-1-tosyl-1*H*-indole (2j)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (62.4 mg, 70% yield, >20:1 *rr*, 94:6 *er*, $[\alpha]^{24}_D$ = +8.4 (*c* 0.98, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 3.7 Hz, 1H), 7.35 (d, *J* = 1.3 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.16 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.05 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.61(d, *J* = 3.6 Hz, 1H), 5.98 (ddd, *J* = 17.5, 9.8, 7.6 Hz, 1H), 5.10 – 4.98 (m, 2H), 3.79 (s, 3H), 3.34 (q, *J* = 7.4 Hz, 1H), 2.61 – 2.40 (m, 2H), 2.35 (s, 3H), 2.12 – 1.93 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 145.0, 142.5, 139.5, 135.6, 134.3, 133.6, 131.2, 130.0, 129.4, 127.0, 126.6, 124.7, 120.1, 114.4, 113.9, 113.6, 109.1, 55.4, 49.2, 37.6, 32.9, 21.7. **IR** (ATR): 2931, 1611, 1596, 1511, 1456, 1369, 1243, 1170, 1126, 1034, 995, 810, 725, 703, 667 $cm^{-1}$. **HRMS** calculated for $C_{27}H_{27}NO_3SNa$ $[M+Na]^+$ 468.1609, found 468.1622. **Chiral SFC**: 100 mm

CHIRALCEL OJ-H, 10% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 13.3 min, $t_{R2}$ (minor) = 14.1 min.

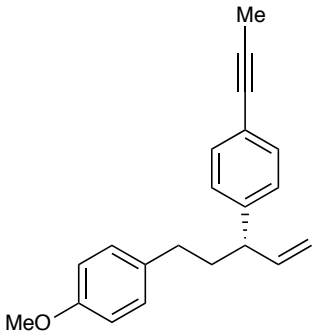



**(*S*)-3-(5-(4-methoxyphenyl)pent-1-en-3-yl)thiophene (2k)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (42.4 mg, 82% yield, >20:1 *rr*, 94:6 *er*, $[\alpha]^{24}_D$ = +23.4 (*c* 1.1,$CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 2H), 7.20 – 7.15 (m, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.72 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.03 – 5.91 (m, 1H), 5.74 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.22 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.09 – 5.01 (m, 2H), 3.80 (s, 3H), 3.28 (q, *J* = 7.5 Hz, 1H), 2.62 – 2.44 (m, 2H), 2.08 – 1.96 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 145.0, 141.7, 134.3, 129.5, 127.3, 125.6, 120.1, 114.7, 113.9, 55.4, 44.7, 37.2, 32.8. **IR** (ATR): 2932, 2833, 1611, 1510, 1441, 1300, 1243, 1176, 1035, 915, 829, 781 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}OS$ $[M]^+$ 258.1078, found 258.1074. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.9 min, $t_{R2}$ (major) = 5.4 min.

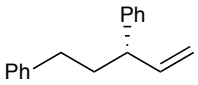



**(*S*)-1-methoxy-4-(3-(4-vinylphenyl)pent-4-en-1-yl)benzene (2l)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (45.0 mg, 81% yield, >20:1 *rr*, 93:7 *er*, $[\alpha]^{24}_D$ = +7.0 (*c* 0.65, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 2H), 7.20 – 7.14 (m, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.72 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.97 (ddd, *J* = 16.5, 10.8, 7.5 Hz, 1H), 5.74 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.22 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.10 – 5.00 (m, 2H), 3.80 (s, 3H), 3.28 (q, *J* = 7.5 Hz, 1H), 2.61 – 2.44 (m, 2H), 2.07 – 1.96 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 144.0, 142.2, 136.8, 135.8, 134.4, 129.5, 128.0, 126.5, 114.5, 113.9, 113.3, 55.4, 49.0, 37.2, 32.8. **IR** (ATR): 3001, 2933, 2833, 1611, 1510, 1441, 1300, 1243, 1176, 1036, 990, 908, 827 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{22}O$ $[M]^+$ 278.1671, found 278.1658. **Chiral SFC**: 100 mm CHIRALCEL AS-H, 1% *i*-

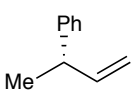
PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 2.8 min, $t_{R2}$ (minor) = 3.3 min.




**(*S*)-1-methoxy-4-(3-(4-(prop-1-yn-1-yl)phenyl)pent-4-en-1-yl)benzene (2m)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (45.4 mg, 78% yield, >20:1 *rr*, 95:5 *er*, $[\alpha]^{24}_D$ = +6.0 (*c* 0.99, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.37(d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.97 (ddd, *J* = 17.0, 10.3, 7.5 Hz, 1H), 5.12 – 5.00 (m, 2H), 3.81 (s, 3H), 3.27 (q, *J* = 7.4 Hz, 1H), 2.60 – 2.45 (m, 2H), 2.07 (s, 3H), 2.06 – 1.92 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 143.7, 141.9, 134.2, 131.8, 129.4, 127.7, 122.0, 114.6, 113.9, 85.4, 79.8, 55.4, 49.1, 37.2, 32.8, 4.5. **IR** (ATR): 2915, 2833, 1611, 1510, 1441, 1300, 1243, 1176, 1036, 915, 830 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{22}O$ $[M]^+$ 290.1671, found 290.1667. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 10.2 min, $t_{R2}$ (minor) = 10.8 min.

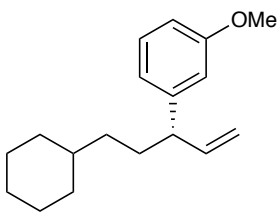



**(*S*)-pent-4-ene-1,3-diyldibenzene (2n)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (hexanes) as a colorless oil (50.2 mg, 99% yield, >20:1 *rr*, 93:7 *er*, $[\alpha]^{24}_D$ = +12.7 (*c* 1.6, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.35 – 7.25 (m, 4H), 7.24 – 7.20 (m, 3H), 7.20 – 7.14 (m, 3H), 6.01 (ddd, *J* = 17.6, 9.8, 7.7 Hz, 1H), 5.12 – 5.00 (m, 2H), 3.30 (q, *J* = 7.6 Hz, 1H), 2.69 – 2.45 (m, 2H), 2.11 – 1.98 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.1, 143.2, 143.1, 129.3, 129.2, 129.1, 128.5, 127.0, 126.5, 114.9, 50.3, 38.0, 34.5. **IR** (ATR): 3026, 2923, 1636, 1601, 1494, 1452, 1029, 993, 912, 765, 746, 697 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{18}$ $[M]^+$ 222.1409, found 222.1418. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 4% *i*-PrOH, 2.3 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.5 min, $t_{R2}$ (major) = 2.7 min.

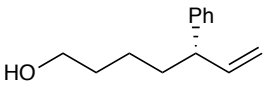



**(*S*)-but-3-en-2-ylbenzene (2o)**: The title compound was synthesized according to the general procedure and isolated by column chromatography (pentanes) as a

colorless liquid (15.9 mg, 60% yield, >20:1 *rr*, 92:8 *er*, $[\alpha]^{24}_D$ = +3.0 (*c* 0.84, $CHCl_3$)). The $^1H$ and $^{13}C$ NMR were in accordance with the literature[5]. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.21 (m, 3H), 6.05 (ddd, *J* = 16.9, 10.3, 6.4 Hz, 1H), 5.15 – 5.02 (m, 2H), 3.51 (p, *J* = 7.0 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.7, 143.4, 128.5, 127.4, 126.3, 113.2, 43.3, 20.9. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 0.1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 1.7 min, $t_{R2}$ (major) = 1.9 min.

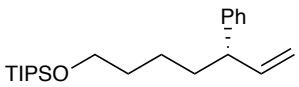



**(*S*)-1-(5-cyclohexylpent-1-en-3-yl)-3-methoxybenzene (2p)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (51.2 mg, 99% yield, >20:1 *rr*, 94:6 *er*, $[\alpha]^{24}_D$ = +20.8 (*c* 0.55, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.20 (m, 1H), 6.85 – 6.79 (m, 1H), 6.79 – 6.71 (m, 2H), 5.96 (ddd, *J* = 17.1, 10.3, 7.7 Hz, 1H), 5.09 – 4.99 (m, 2H), 3.83 (s, 3H), 3.19 (q, *J* = 7.5 Hz,1H), 1.75 – 1.63 (m, 7H), 1.28 – 1.08 (m, 6H), 0.95 – 0.81 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 159.8, 146.6, 142.6, 129.4, 120.1, 114.0, 113.7, 111.2, 55.3, 50.4, 37.9, 35.4, 33.51, 33.49, 32.8, 26.9, 26.56, 26.55. **IR** (ATR): 3026, 2923, 1636, 1601, 1494, 1452, 1029, 993, 912, 765, 746, 697 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{26}OH$ $[M+H]^+$ 259.2062, found 259.2054. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.2 min, $t_{R2}$ (major) = 2.4 min.

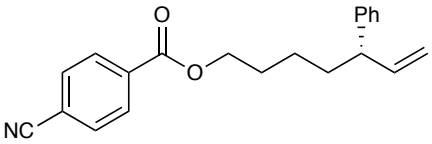



**(*S*)-5-phenylhept-6-en-1-ol (2q)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (25% EtOAc in hexanes) as a colorless oil (23.2 mg, 61% yield, >20:1 *rr*, 96:4 *er*, $[\alpha]^{24}_D$ = +30.1 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H), 7.24 – 7.17 (m, 3H), 6.03 – 5.89 (m, 1H), 5.09 – 4.97 (m, 2H), 3.62 (dd, *J* = 11.9, 6.5 Hz, 2H), 3.26 (q, *J* = 7.5 Hz, 1H), 1.80 – 1.68 (m, 2H), 1.63 – 1.50 (m, 2H), 1.46 – 1.34 (m, 1H), 1.34 – 1.21 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.5, 142.4, 128.6, 127.7, 126.3, 114.2, 63.0, 50.0, 35.3, 32.8, 23.9. **IR** (ATR): 3331, 3026, 2932, 2860, 1636, 1600, 1492, 1452, 1054, 911, 756, 698 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}O$ $[M]^+$ 190.1358, found 190.1356. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-

PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.1 min, $t_{R2}$ (major) = 4.4 min.



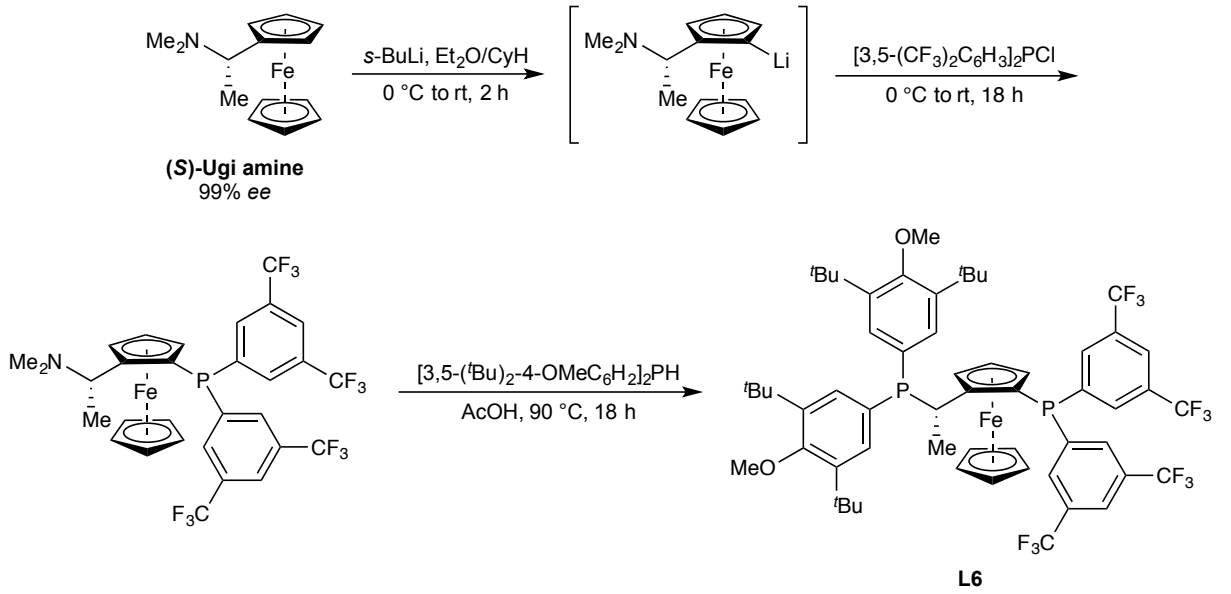

**(*S*)-triisopropyl((5-phenylhept-6-en-1-yl)oxy)silane (2r)**: The title compound was synthesized according to the general procedure and isolated by preparatory TLC (hexanes) as a colorless oil (66.5 mg, 96% yield, >20:1 *rr*, 95:5 *er*, $[\alpha]^{24}_D$ = +12.8 (*c* 0.81, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 2H), 7.25 – 7.17 (m, 3H), 5.99 (ddd, *J* = 16.9, 10.5, 7.6 Hz, 1H), 5.11 – 5.00 (m, 2H), 3.68 (t, *J* = 6.6 Hz, 2H), 3.28 (q, *J* = 7.5 Hz, 1H), 1.83 – 1.69 (m, 2H), 1.59 (ddt, *J* = 13.3, 7.5, 3.8 Hz, 2H), 1.46 – 1.36 (m, 1H), 1.36 – 1.24 (m, 1H), 1.11 – 1.05 (m, 21H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.7, 142.5, 128.5, 127.7, 126.2, 114.1, 63.5, 50.1, 35.4, 33.1, 24.0, 18.2, 12.2. **IR** (ATR): 2940, 2964, 1637, 1462, 1382, 1104, 1068, 994, 911, 881, 698 $cm^{-1}$. **HRMS** calculated for $C_{22}H_{38}OSiH$ $[M+H]^+$ 347.2770, found 347.2783. The enantioselectivity was determined using the corresponding alcohol **2q** after desilyation with TBAF. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.1 min, $t_{R2}$ (major) = 4.3 min.




**(*S*)-5-phenylhept-6-en-1-yl 4-cyanobenzoate (2s)**: The title compound was synthesized according to the general procedure using 1,2-dichloroethane as the solvent and heating at 60 °C. It was isolated by preparatory TLC (10% EtOAc in hexanes) as a colorless oil (43.0 mg, 67% yield, >20:1 *rr*, 89:11 *er*, $[\alpha]^{24}_D$ = +7.9 (*c* 0.47, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.7 Hz, 2H), 7.73 (d, *J* = 8.7 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.21 (td, *J* = 6.9, 1.5 Hz, 3H), 6.03 – 5.90 (m, 1H), 5.09 – 5.00 (m, 2H), 4.33 (td, *J* = 6.6, 1.0 Hz, 2H), 3.28 (q, *J* = 7.5 Hz, 1H), 1.86 – 1.73 (m, 4H), 1.54 – 1.42 (m, 1H), 1.42 – 1.31 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) d 165.0, 144.2, 142.2, 134.3, 132.3, 130.1, 128.6, 127.6, 126.4, 118.1, 116.4, 114.3, 65.7, 49.8, 34.9, 28.5, 23.9. **IR** (ATR): 2924, 2231, 1721, 1636, 1452, 1272, 1107, 913, 860, 767 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{20}NO_2H$ $[M+H]^+$ 319.1572, found 319.1571. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.9 min, $t_{R2}$ (major) = 7.0 min.

## 3. Preparation of the Josiphos Ligand and Substrates

### *Synthesis of Josiphos Ligand L6*

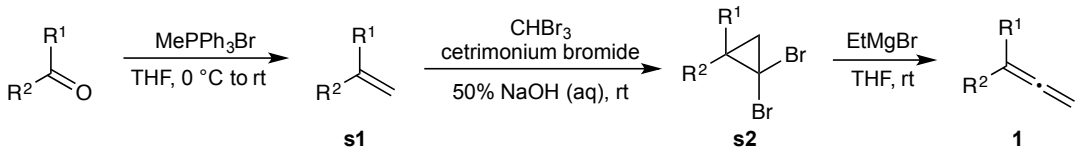



**(*S*)-1-{[(*R*$_p$)-2-[Bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocenyl}ethylbis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine (L6)**: To a flame-dried round bottom flask was charged (*S*)-Ugi amine[6-9] (262.3 mg, 1.02 mmol, 1 equiv) and anhydrous $Et_2O$ (2 mL). The resulting suspension was cooled to 0 °C, and *s*-BuLi (1.4 M in cyclohexane, 0.80 mL, 1.12 mmol, 1.1 equiv) was added dropwise. The resulting red solution was stirred at rt for 2 h. The solution was cooled to 0 °C, and a solution of bis(3,5-di(trifluoromethyl)phenyl)chlorophosphine (502.5 mg, 1.02 mmol, 1 equiv) in anhydrous $Et_2O$ (1 mL) was added dropwise. The resulting mixture was stirred at rt for 18 h. The reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL). The resulting mixture was extracted with $Et_2O$ (3 x 10 mL). The combined organic layers were washed with brine, dried with anhydrous $Na_2SO_4$, filtered, and concentrated *in vacuo*. Purification of the resulting residue by silica gel column chromatography (10% EtOAc in hexanes) gave the ferrocenyl monophosphine as a red oil (563 mg, 77% yield).

A flame-dried round bottom flask equipped with a condenser was charged with the ferrocenyl monophosphine (562.9 mg, 0.789 mmol, 1 equiv), bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine (408.6 mg, 0.868 mmol, 1.1 equiv), and glacial acetic acid (distilled, degassed, 2.6 mL). The resulting mixture was heated at 90 °C for 18 h. The reaction mixture was cooled to rt, and most of the acetic acid was removed under reduced pressure. The resulting

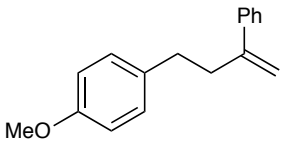
residue was purified by silica gel column chromatography (10% $CH_2Cl_2$ in hexanes) to give the title compound as an orange solid (781 mg, 87% yield). **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 8.16 (d, *J* = 7.1 Hz, 2H), 8.03 (s, 1H), 7.83 – 7.79 (m, 2H), 7.77 (s, 1H), 7.24 (dd, *J* = 6.6, 0.9 Hz, 2H), 6.96 (dd, *J* = 7.2, 0.9 Hz, 2H), 4.46 (t, *J* = 2.5 Hz, 1H), 4.00 (t, *J* = 1.8 Hz, 1H), 3.93 (s, 1H), 3.87 (s, 5H), 3.70 (s, 3H), 3.68 – 3.67 (m, 4H), 1.42 (s, 18H), 1.35 (s, 18H), 1.30 (dd, *J* = 6.9, 4.6 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 161.1, 160.3, 144.3 (d, *J* = 5.1 Hz), 143.5 (d, *J* = 6.9 Hz), 142.6 (d, *J* = 2.9 Hz), 142.5 (d, *J* = 3.0 Hz), 136.1 (d, *J* = 23.7 Hz), 133.8 (d, *J* = 20.8 Hz), 133.3 (d, *J* = 17.6 Hz), 132.2 (qd, *J* = 33.1, 7.8 Hz), 131.4 (qd, *J* = 33.2, 5.1 Hz), 131.0 (d, *J* = 17.3 Hz), 128.0 (d, *J* = 1.8 Hz), 127.9 (d, *J* = 1.8 Hz), 124.3 (dt, *J* = 7.7, 3.9 Hz), 124.2 (q, *J* = 273.0 Hz), 124.1 (q, *J* = 273.3 Hz), 122.7 (p, *J* = 3.6 Hz), 101.6 (d, *J* = 22.1 Hz), 101.3 (d, *J* = 22.2 Hz), 71.19, 71.17 – 70.9 (m), 71.1 – 70.8 (m), 70.3, 65.1, 65.0, 36.5, 36.4, 32.63, 32.55, 32.1 (dd, *J* = 20.0, 10.3 Hz), 15.8 (d, *J* = 3.3 Hz). **$^{31}$P NMR** (162 MHz, $CD_2Cl_2$) δ 12.1 (d, *J* = 34.9 Hz), -21.9 (d, *J* = 36.2 Hz). **$^{19}$F NMR** (376 MHz, $CD_2Cl_2$) δ -63.17, -63.22. **IR** (ATR): 2961, 1352, 1275, 1172, 1136, 1095, 1009, 892, 703, 681 $cm^{-1}$. **HRMS** calculated for $C_{58}H_{64}F_{12}FeO_2P_2$ $[M]^+$ 1138.3541, found 1138.3544. $[\alpha]^{24}_D$ = +184.1 (*c* 0.67, $CHCl_3$)).

***Preparation of Allenes 1***

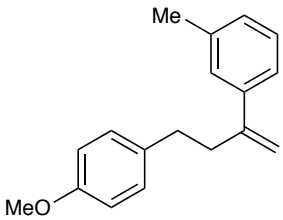



***General Procedure for the Wittig Olefination***

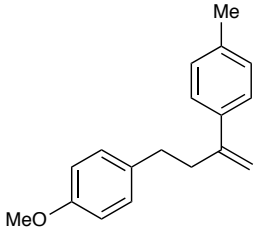
To a flame-dried round bottom flask was added methyltriphenylphosphonium bromide (1.5 equiv) and THF (0.5 M). KO*t*-Bu (1.5 equiv) was added, and the resulting mixture was stirred for 45 minutes at rt. A solution of the ketone (1 equiv) in THF (0.5 M) was added dropwise at 0 °C, and the reaction mixture was stirred at rt for 1 h. The reaction mixture was filtered through celite and concentrated *in vacuo*. The residue was purified by column chromatography to afford the pure 1,1-disubstituted alkene **s1**.




**1-methoxy-4-(3-phenylbut-3-en-1-yl)benzene (s1a)**: The title compound was prepared using the general procedure for the Wittig olefination from 3-(4-methoxyphenyl)-1-phenylpropan-1-one (1.82 g, 7.59 mmol, 1 equiv), methyltriphenylphosphonium bromide (4.07 g, 11.4 mmol, 1.5 equiv), KO*t*-Bu (1.28 g, 11.4 mmol, 1.5 equiv), and THF (30.4 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a colorless oil (1.78 g, 99% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dt, *J* = 3.2, 1.9 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.33 (ddd, *J* = 7.2, 3.7, 1.3 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.34 (d, *J* = 1.2 Hz, 1H), 5.10 (d, *J* = 1.2 Hz, 1H), 3.83 (s, 3H), 2.86 – 2.80 (m, 2H), 2.78 – 2.72 (m, 2H).**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 148.0, 141.3, 134.2, 129.4, 128.5, 127.5, 126.3, 113.9, 112.8, 55.4, 37.7, 34.0. **IR** (ATR): 3030, 2933, 2833, 1611, 1511, 1299, 1243, 1176, 1036, 894, 822, 778, 701 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{18}O$ $[M]^+$ 238.1358, found 238.1358.

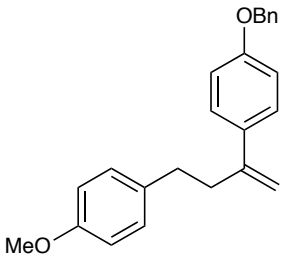



**1-(4-(4-methoxyphenyl)but-1-en-2-yl)-3-methylbenzene (s1b)**: The title compound was prepared using the general procedure for the Wittig olefination from 3-(4-methoxyphenyl)-1-(*m*-tolyl)propan-1-one (763 mg, 3.0 mmol, 1 equiv), methyltriphenylphosphonium bromide (1.68 g, 4.5 mmol, 1.5 equiv), KO*t*-Bu (505 mg, 4.5 mmol, 1.5 equiv), and THF (12.0 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (745 mg, 98% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.33 (m, 3H), 7.21 – 7.18 (m, 3H), 6.93 (d, *J* = 8.5 Hz, 2H), 5.39 (s, 1H), 5.14 (s, 1H), 3.87 (s, 3H), 2.92 – 2.85 (m, 2H), 2.82 (dd, *J* = 8.3, 5.4 Hz, 2H), 2.47 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 148.1, 141.3, 137.9, 134.2, 129.4, 128.34, 128.26, 127.0, 123.4, 113.8, 112.5, 55.3, 37.7, 34.0, 21.6. **IR** (ATR): 2932, 2833, 1611, 1582, 1511, 1454, 1299, 1243, 1176, 1037, 893, 791 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{20}O$ $[M]^+$ 252.1514, found 252.1510.

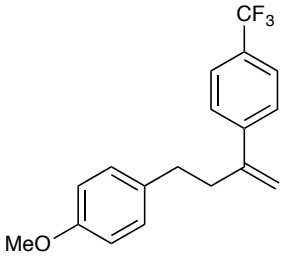



**1-methoxy-4-(3-(*p*-tolyl)but-3-en-1-yl)benzene (s1c)**: The title compound was prepared using the general procedure for the Wittig olefination from 3-(4-methoxyphenyl)-1-(*p*-tolyl)propan-1-one (763 mg, 3.0 mmol, 1 equiv), methyltriphenylphosphonium bromide (1.68 g, 4.5

mmol, 1.5 equiv), KO*t*-Bu (505 mg, 4.5 mmol, 1.5 equiv), and THF (12.0 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a colorless oil (705 mg, 93% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.33 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 5.25 (d, *J* = 1.4 Hz, 1H), 4.99 (d, *J* = 1.3 Hz, 1H), 3.75 (s, 3H), 2.79 – 2.71 (m, 2H), 2.71 – 2.64 (m, 2H), 2.34 (s, 3H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 158.7, 148.6, 138.9, 138.1, 134.9, 130.1, 129.8, 126.7, 114.4, 112.3, 55.9, 38.3, 34.6, 21.6. **IR** (ATR): 2932, 2833, 1611, 1511, 1454, 1299, 1243, 1176, 1037, 891, 821 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{20}OH$ $[M+H]^+$ 253.1592, found 253.1583.

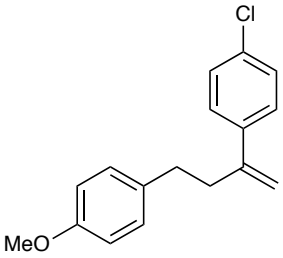



**1-(benzyloxy)-4-(4-(4-methoxyphenyl)but-1-en-2-yl)benzene (s1d)**: The title compound was prepared using the general procedure for the Wittig olefination from 1-(4-(benzyloxy)phenyl)-3-(4-methoxyphenyl)propan-1-one (749 mg, 2.16 mmol, 1 equiv), methyltriphenylphosphonium bromide (1.16 g, 3.24 mmol, 1.5 equiv), KO*t*-Bu (364 mg, 3.24 mmol, 1.5 equiv), and THF (8.7 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a white solid (723 mg, 97% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.45 (m, 2H), 7.45 – 7.32 (m, 5H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.25 (d, *J* = 1.3 Hz, 1H), 5.11 (s, 2H), 5.00 (d, *J* = 1.0 Hz, 1H), 3.81 (s, 3H), 2.83 – 2.68 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.4, 157.9, 147.2, 137.1, 134.3, 133.9, 129.4, 128.7, 128.1, 127.6, 127.4, 114.8, 113.9, 111.3, 70.2, 55.4, 37.7, 34.0. **IR** (ATR): 3038, 2912, 2864, 1603, 1508, 1454, 1379, 1287, 1243, 1179, 1010, 891 $cm^{-1}$. **HRMS** calculated for $C_{24}H_{24}O_2Na$ $[M+Na]^+$ 367.1674, found 367.1686.

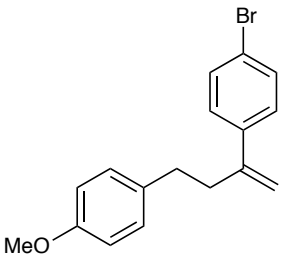



**1-methoxy-4-(3-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)benzene (s1e)**: The title compound was prepared using the general procedure for the Wittig olefination from 3-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)propan-1-one (837 mg, 2.72 mmol, 1 equiv), methyltriphenylphosphonium bromide (1.46 g, 4.07 mmol, 1.5 equiv), KO*t*-Bu (457 mg, 4.07 mmol, 1.5 equiv), and THF (10.9 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a colorless oil (800 mg, 96% yield). **$^1$H NMR** (400

MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 5.36 (s, 1H), 5.17 (s, 1H), 3.81 (s, 3H), 2.80 (dd, *J* = 12.3, 4.6 Hz, 2H), 2.75 – 2.67 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 147.0, 144.9 (q, $J_{C-F}$ = 1.3 Hz), 133.7, 129.5 (q, $J_{C-F}$ = 32.3 Hz), 129.4, 126.6, 125.5 (q, $J_{C-F}$ = 3.8 Hz), 124.2 (q, $J_{C-F}$ = 272.3 Hz), 114.8, 113.9, 55.4, 37.5, 33.8. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.9. **IR** (ATR): 2936, 1615, 1512, 1323, 1301, 1244, 1163, 1115, 1066, 1037, 1014, 903 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{17}F_3O$ $[M]^+$ 306.1231, found 306.1235.

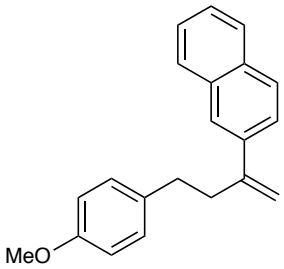



**1-chloro-4-(4-(4-methoxyphenyl)but-1-en-2-yl)benzene (s1f)**: The title compound was prepared using the general procedure for the Wittig olefination from 1-(4-chlorophenyl)-3-(4-methoxyphenyl)propan-1-one (586 mg, 2.13 mmol, 1 equiv), methyltriphenylphosphonium bromide (1.14 g, 3.20 mmol, 1.5 equiv), KO*t*-Bu (359 mg, 3.20 mmol, 1.5 equiv), and THF (8.5 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a colorless oil (494 mg, 85% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.6 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.29 (s, 1H), 5.08 (s, 1H), 3.81 (s, 3H), 2.77 (dd, *J* = 9.7, 7.0 Hz, 2H), 2.74 – 2.66 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.0, 146.9, 139.7, 133.9, 133.3, 129.4, 128.6, 127.6, 113.9, 113.4, 55.4, 37.5, 33.8. **IR** (ATR): 2933, 2833, 1611, 1511, 1491, 1300, 1243, 1176, 1096, 1036, 1011, 897 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{17}ClO$ $[M]^+$ 272.0968, found 272.0974.

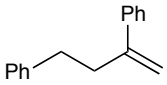



**1-bromo-4-(4-(4-methoxyphenyl)but-1-en-2-yl)benzene (s1g)**: The title compound was prepared using the general procedure for the Wittig olefination from 1-(4-bromophenyl)-3-(4-methoxyphenyl)propan-1-one (580 mg, 1.82 mmol, 1 equiv), methyltriphenylphosphonium bromide (973 mg, 2.73 mmol, 1.5 equiv), KO*t*-Bu (306 mg, 2.73 mmol, 1.5 equiv), and THF (8.5 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a colorless oil (559 mg, 97% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.29 (s, 1H), 5.08 (s, 1H), 3.80 (s, 3H), 2.75 (d, *J* = 4.7 Hz, 2H), 2.73 – 2.65 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ

158.0, 146.9, 140.2, 133.8, 131.6, 129.4, 128.0, 121.5, 113.9, 113.5, 55.4, 37.5, 33.8. **IR** (ATR): 2932, 2833, 1611, 1511, 1487, 1300, 1243, 1176, 1036, 1007, 897, 822 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{17}BrO$ $[M]^+$ 316.0463, found 316.0451.



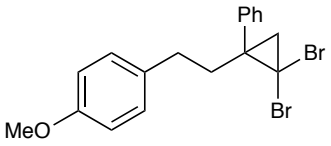

**2-(4-(4-methoxyphenyl)but-1-en-2-yl)naphthalene (s1h)**: The title compound was prepared using the general procedure for the Wittig olefination from 3-(4-methoxyphenyl)-1-(naphthalen-2-yl)propan-1-one (1.18 g, 4.08 mmol, 1 equiv), methyltriphenylphosphonium bromide (2.19 g, 6.12 mmol, 1.5 equiv), KO*t*-Bu (687 mg, 6.12 mmol, 1.5 equiv), and THF (16.3 mL, 0.25 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (1.13 g, 96% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.93 – 7.80 (m, 4H), 7.64 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.55 – 7.44 (m, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.48 (s, 1H), 5.20 (s, 1H), 3.82 (s, 3H), 2.98 – 2.89 (m, 2H), 2.81(dd, *J* = 9.5, 6.1 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 157.9, 147.8, 138.5, 134.2, 133.5, 132.9, 129.5, 128.3, 128.0, 127.7, 126.3, 126.0, 124.9, 124.8, 113.9, 113.4, 55.4, 37.7, 34.0. **IR** (ATR): 3055, 2932, 2833, 1611, 1511, 1299, 1242, 1177, 1036, 890, 858, 818 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{20}O$ $[M]^+$ 288.1514, found 288.1526.




**but-3-ene-1,3-diyldibenzene (s1i)**: The title compound was prepared using the general procedure for the Wittig olefination from 1,3-diphenylpropan-1-one (1.40 g, 6.68 mmol, 1 equiv), methyltriphenylphosphonium bromide (3.58 g, 10.0 mmol, 1.5 equiv), KO*t*-Bu (1.12 g, 10.0 mmol, 1.5 equiv), and THF (26.7 mL, 0.25 M). Isolated by column chromatography (hexanes) as a colorless oil (1.34 g, 96% yield). The $^1$H NMR was in accordance with the literature[10]. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.44 (m, 2H), 7.41 – 7.35 (m, 2H), 7.34 – 7.28 (m, 3H), 7.25 – 7.18 (m, 3H), 5.33 (d, *J* = 1.4 Hz, 1H), 5.10 (d, *J* = 1.3 Hz, 1H), 2.88 – 2.82 (m, 2H), 2.82 – 2.77 (m, 2H).

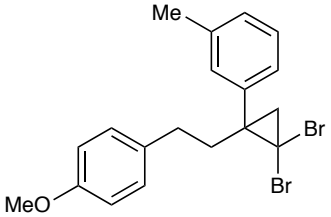
***General Procedure for the Alkene Cyclopropanation***

To a round bottom flask containing the 1,1-disubstituted alkene **s1** (1 equiv) was added cetrimonium bromide (2.0 mol%) and $CHBr_3$ (2.0 equiv). While stirring, a 50% aqueous solution of NaOH (1.3 M) was added dropwise. The resulting solution was vigorously stirred for 24 h at rt. The reaction mixture was quenched with water and extracted with $CH_2Cl_2$. The combined organic layers were washed with brine, dried with anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford the pure dibromocyclopropane **s2**.



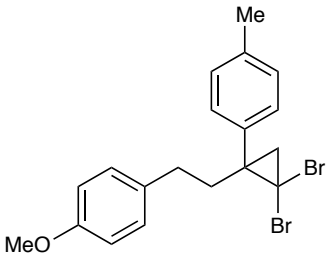

**1-(2-(2,2-dibromo-1-phenylcyclopropyl)ethyl)-4-methoxybenzene (s2a)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1a** (1.12 g, 4.69 mmol, 1 equiv), cetrimonium bromide (34.2 mg, 0.094 mmol, 2.0 mol%), $CHBr_3$ (0.82 mL, 9.39 mmol, 2.0 equiv), and 50% aqueous NaOH (3.5 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (1.78 g, 92% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.37 – 7.29 (m, 3H), 7.00 (d, $J$ = 8.6 Hz, 2H), 6.80 (d, $J$ = 8.7 Hz, 2H), 3.78 (s, 3H), 2.56 – 2.36 (m, 3H), 2.10 (dd, $J$ = 7.6, 1.0 Hz, 1H), 2.07 – 1.97 (m, 1H), 1.73 (d, $J$ = 7.6 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 140.4, 133.5, 129.6, 129.4, 128.5, 127.6, 113.9, 55.4, 42.8, 39.8, 36.4, 33.2, 32.6. **IR** (ATR): 3026, 2952, 2833, 1610, 1511, 1445, 1300, 1243, 1176, 1034, 820, 751 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{18}Br_2O$ $[M]^+$ 407.9724, found 407.9727.

**1-(2,2-dibromo-1-(4-methoxyphenethyl)cyclopropyl)-3-methylbenzene (s2b)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1b** (505 mg, 2.0 mmol, 1 equiv), cetrimonium bromide (14.6 mg, 0.040 mmol, 2.0 mol%), $CHBr_3$ (0.35 mL, 4.0 mmol, 2.0 equiv), and 50% aqueous NaOH (1.5 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (622 mg, 73% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, $J$ = 7.8 Hz, 1H), 7.14 (d, $J$ = 14.2 Hz, 3H), 7.01 (d, $J$ = 8.5 Hz, 2H), 6.80 (d, $J$ = 8.5 Hz, 2H), 3.78 (s, 3H), 2.50 (tdd, $J$ = 20.6, 14.5, 6.3 Hz, 3H), 2.41 (s, 3H), 2.08 (d, $J$ = 7.6 Hz, 1H), 2.06 –

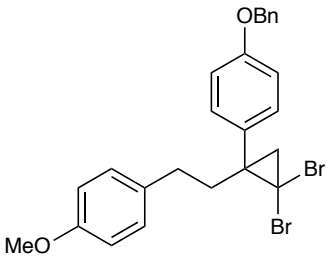


1.96 (m, 1H), 1.72 (d, $J$ = 7.6 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 140.2, 138.1, 133.6, 130.2, 129.4, 128.32, 128.28, 126.6, 113.9, 55.4, 42.8, 39.8, 36.7, 33.2, 32.6, 21.7. **IR** (ATR): 2952, 2833, 1609, 1511, 1453, 1300, 1243, 1176, 1035, 821, 788 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{20}Br_2O$ $[M]^+$ 421.9881, found 421.9893.

**1-(2,2-dibromo-1-(4-methoxyphenethyl)cyclopropyl)-4-methylbenzene (s2c)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1c** (685 mg, 2.71 mmol, 1 equiv), cetrimonium bromide (19.8 mg, 0.054 mmol, 2.0 mol%), $CHBr_3$ (0.47 mL, 5.43 mmol, 2.0 equiv), and 50% aqueous NaOH (2.0 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (1.01 g, 88% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.23 (s, 4H), 7.00 (d, $J$ = 8.7 Hz, 2H), 6.79 (d, $J$ = 8.7 Hz, 2H), 2.52 – 2.41 (m, 3H), 2.39 (s, 3H), 2.09 (dd, $J$ = 7.7, 1.3 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.74 (d, $J$ = 7.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 158.8, 138.02, 137.98, 134.3, 130.1, 130.0, 129.8, 114.5, 56.0, 43.4, 40.2, 37.8, 33.8, 33.2, 21.7. **IR** (ATR): 2952, 2833, 1611, 1511, 1454, 1300, 1243, 1176, 1035, 818, 689 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{20}Br_2O$ $[M]^+$ 421.9881, found 421.9884.

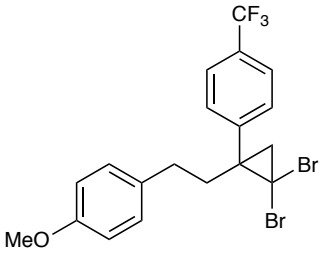



**1-(benzyloxy)-4-(2,2-dibromo-1-(4-methoxyphenethyl)cyclopropyl)benzene (s2d)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1d** (704 mg, 2.04 mmol, 1 equiv), cetrimonium bromide (14.9 mg, 0.041 mmol, 2.0 mol%), $CHBr_3$ (0.36 mL, 4.09 mmol, 2.0 equiv), and 50% aqueous NaOH (1.5 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (780 mg, 74% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.45 (m, 2H), 7.42 (ddd, $J$ = 6.4, 2.6, 0.9 Hz, 2H), 7.36 (ddd, $J$ = 7.0, 3.7, 1.5 Hz, 1H), 7.24 (d, $J$ = 8.8 Hz, 2H), 7.04 – 6.98 (m, 4H), 6.80 (d, $J$ = 8.7 Hz, 2H), 5.09 (s, 2H), 3.79 (s, 3H), 2.47 (qdd, $J$ = 13.9, 11.8, 4.0 Hz, 3H), 2.08 – 1.96 (m, 2H), 1.70 (d,$J$ = 7.6 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.2, 158.0, 137.0, 133.5, 132.8, 130.6, 129.4, 128.8, 128.2, 127.8, 114.7, 113.9, 70.2, 55.4, 42.7, 39.2, 37.1, 33.3, 32.6. **IR** (ATR): 3032, 2951, 1608,



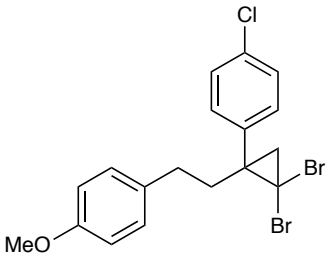
1510, 1453, 1299, 1241, 1175, 1034, 828 $cm^{-1}$. The title compound was unstable under HRMS conditions.

**1-(2-(2,2-dibromo-1-(4-(trifluoromethyl)phenyl)cyclopropyl)ethyl)-4-methoxybenzene (s2e)**:

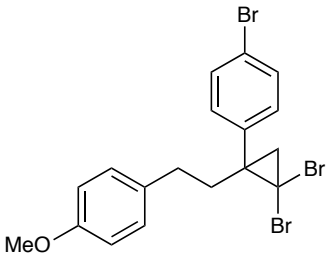



The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1e** (800 mg, 2.61 mmol, 1 equiv), cetrimonium bromide (19.0 mg, 0.052 mmol, 2.0 mol%), $CHBr_3$ (0.46 mL, 5.22 mmol, 2.0 equiv), and 50% aqueous NaOH (2.0 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (989 mg, 79% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, $J$ = 8.1 Hz, 2H), 7.44 (d, $J$ = 8.0 Hz, 2H), 6.99 (d, $J$ = 8.5 Hz, 2H), 6.80 (d, $J$ = 8.5 Hz, 2H), 3.78 (s, 3H), 2.56 – 2.39 (m, 3H), 2.13 – 2.01 (m, 2H), 1.79 (d, $J$ = 7.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.1, 144.4 (q, $J_{C\text{-}F}$ = 1.3 Hz), 132.9, 130.0, 129.8 (q, $J_{C\text{-}F}$ = 32.5 Hz), 129.3, 125.5 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.2 (q, $J_{C\text{-}F}$ = 272.3 Hz), 114.0, 55.4, 42.6, 39.6, 34.9, 33.3, 32.5. **$^{19}$F NMR** (376 MHz, $CDCl_3$) d -62.9. **IR** (ATR): 2955, 2835, 1616, 1511, 1322, 1301, 1244, 1163, 1113, 1065, 1035, 1016, 842 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{17}Br_2F_3O$ $[M]^+$ 475.9598, found 475.9594.

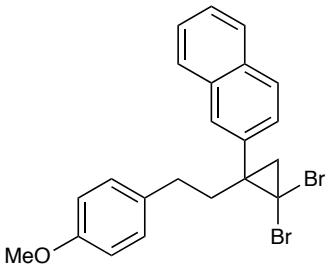
**1-chloro-4-(2,2-dibromo-1-(4-methoxyphenethyl)cyclopropyl)benzene (s2f)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1f** (467 mg, 1.71 mmol, 1 equiv), cetrimonium bromide (12.5 mg, 0.034 mmol, 2.0 mol%), $CHBr_3$ (0.30 mL, 3.43 mmol, 2.0 equiv), and 50% aqueous NaOH (1.3 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (560 mg, 73% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, $J$ = 8.2 Hz, 2H), 7.25 (d, $J$ = 8.4 Hz, 2H), 6.99 (d, $J$ = 8.5 Hz, 2H), 6.80 (d, $J$ = 8.4 Hz, 2H), 3.78 (s, 3H), 2.59 – 2.32 (m, 3H), 2.08 – 1.97 (m, 2H), 1.74 (d, $J$ = 7.7 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.1, 138.9, 133.4, 133.1, 130.9, 129.3, 128.8, 114.0, 55.4, 42.6, 39.2, 35.7, 33.3, 32.5. **IR** (ATR): 2953, 2833, 1611, 1511, 1492, 1300, 1243, 1176, 1087, 1034, 1013, 825 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{17}Br_2ClO$ $[M]^+$ 441.9335, found 441.9333.

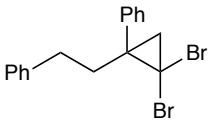


**1-bromo-4-(2,2-dibromo-1-(4-methoxyphenethyl)cyclopropyl)benzene (s2g)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1g** (534 mg, 1.69 mmol, 1 equiv), cetrimonium bromide (12.3 mg, 0.034 mmol, 2.0 mol%), $CHBr_3$ (0.29 mL, 3.37 mmol, 2.0 equiv), and 50% aqueous NaOH (1.3 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (675 mg, 82% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.99 (d, *J* = 8.3 Hz, 2H), 6.80 (d, *J* = 8.1 Hz, 2H), 3.78 (s, 3H), 2.58 – 2.32 (m, 3H), 2.02 (dd, *J* = 17.1, 6.7 Hz, 2H), 1.73 (d, *J* = 7.7 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.1, 139.4, 133.1, 131.7, 131.3, 129.3, 121.6, 114.0, 55.4, 42.6, 39.3, 35.5, 33.3, 32.5. **IR** (ATR): 2952, 2833, 1610, 1511, 1489, 1300, 1243, 1177, 1070, 1034, 1009, 821 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{17}Br_3O$ $[M]^+$ 485.8829, found 485.8834.




**2-(2,2-dibromo-1-(4-methoxyphenethyl)cyclopropyl)naphthalene (s2h)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1h** (1.10 g, 3.81 mmol, 1 equiv), cetrimonium bromide (27.8 mg, 0.076 mmol, 2.0 mol%), $CHBr_3$ (0.67 mL, 7.62 mmol, 2.0 equiv), and 50% aqueous NaOH (2.8 mL, 1.3 M). Isolated by column chromatography (5% EtOAc in hexanes) as a yellow oil (1.27 g, 73% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.94 – 7.83 (m, 3H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.56 – 7.49 (m, 3H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 3.77 (s, 3H), 2.61 – 2.47 (m, 3H), 2.24 (dd, *J* = 7.6, 1.1 Hz, 1H), 2.17 – 2.07 (m, 1H), 1.82 (d, *J* = 7.6 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 138.0, 133.4, 133.3, 132.8, 129.4, 128.4, 128.3, 128.0, 127.9, 127.4, 126.4, 126.3, 113.9, 55.4, 42.6, 40.0, 36.3, 33.3, 32.7. **IR** (ATR): 2952, 2832, 1610, 1511, 1453, 1300, 1242, 1176, 1034, 818 $cm^{-1}$. **HRMS** calculated for $C_{22}H_{20}Br_2O$ $[M]^+$ 459.9862, found 459.9844.

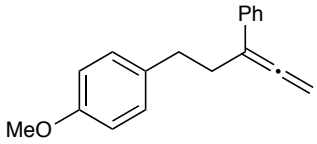





**(2,2-dibromo-1-phenethylcyclopropyl)benzene (s2i)**: The title compound was prepared using the general procedure for the alkene cyclopropanation from 1,1-disubstituted alkene **s1i** (1.32 g, 6.36 mmol, 1 equiv), cetrimonium bromide (46.3 mg, 0.127 mmol, 2.0 mol%), $CHBr_3$ (1.1 mL, 12.7 mmol, 2.0 equiv), and 50% aqueous NaOH (4.7 mL, 1.3 M). Isolated by column chromatography (hexanes) as a yellow oil (2.21 g, 91% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.38 (m, 2H), 7.38 – 7.31 (m, 3H), 7.29 – 7.22 (m, 2H), 7.21 – 7.15 (m, 1H), 7.12 – 7.06 (m, 2H), 2.66 – 2.53 (m, 2H), 2.53 – 2.44 (m, 1H), 2.16 – 2.04 (m, 2H), 1.75 (d, *J* = 7.6 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.4, 140.3, 129.6, 128.51, 128.50, 128.5, 127.6, 126.1, 42.6, 39.9, 36.3, 33.5, 33.2. **IR** (ATR): 3026, 2926, 1602, 1495, 1447, 1101, 1055, 1021, 1003, 777, 762, 744 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{16}Br_2NH_4$ $[M+ NH_4]^+$ 395.9962, found 395.9979.

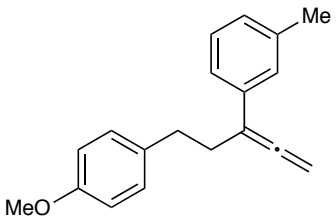
***General Procedure for the Skattebøl Rearrangement***

To a flame-dried round bottom flask was added dibromocyclopropane **s2** (1 equiv) and THF (0.5 M). EtMgBr (1.7 equiv, 1.0 M in THF) was added dropwise, and the resulting mixture was stirred for 1 h at rt. The reaction mixture was quenched with water and extracted with $Et_2O$. The combined organic layers were washed with brine, dried with anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford the desired allene **1**.

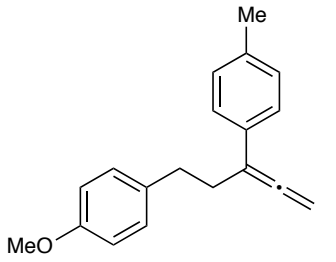



**1-methoxy-4-(3-phenylpenta-3,4-dien-1-yl)benzene (1a)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2a** (1.75 g, 4.27 mmol, 1 equiv), EtMgBr (7.3 mL, 7.3 mmol, 1.7 equiv, 1.0 M in THF), and THF (8.5 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a yellow oil (920 mg, 86% yield). **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.44 (d, *J* = 7.7 Hz, 2H), 7.39 – 7.30 (m, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 6.8 Hz, 2H), 6.85 (d, *J* = 6.8 Hz, 2H), 5.10 (d, *J* = 3.0 Hz, 2H), 3.79 (s, 3H), 2.88 – 2.78 (m, 2H), 2.77 – 2.66 (m, 2H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 209.4, 158.8, 137.1, 134.9, 130.2, 129.2, 127.4, 126.7, 114.5, 105.3, 79.2, 56.0, 34.1,

32.4. **IR** (ATR): 2931, 1939, 1611, 1511, 1493, 1450, 1300, 1243, 1176, 1035, 820 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{17}O$ $[M-H]^-$ 249.1279, found 249.1273.

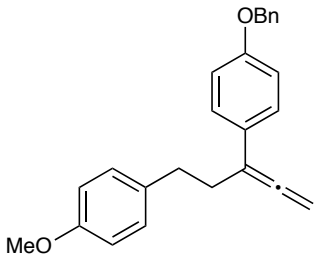



**1-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)-3-methylbenzene (1c)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2b** (593 mg, 1.40 mmol, 1 equiv), EtMgBr (2.4 mL, 2.4 mmol, 1.7 equiv, 1.0 M in THF), and THF (2.8 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a yellow oil (327 mg, 88% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.30 – 7.22 (m, 3H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.09 – 7.03 (m, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.10 (t, *J* = 3.3 Hz, 2H), 3.80 (s, 3H), 2.82 (dd, *J* = 9.3, 5.9 Hz, 2H), 2.70 (ttd, *J* = 8.4, 3.3, 1.0 Hz, 2H), 2.37 (s, 3H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.4, 158.8, 138.8, 137.0, 135.0, 130.2, 129.1, 128.2, 127.5, 123.8, 114.5, 105.4, 79.1, 56.0, 34.1, 32.5, 22.0. **IR** (ATR): 2930, 2833, 1938, 1610, 1511, 1441, 1300, 1243, 1176, 1036, 851, 821, 786 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{20}O$ $[M]^+$ 264.1514, found 264.1517.



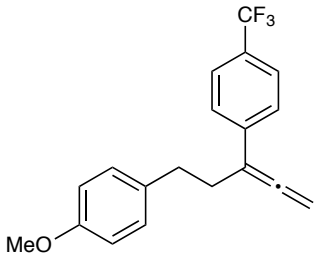

**1-methoxy-4-(3-(*p*-tolyl)penta-3,4-dien-1-yl)benzene (1d)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2c** (509 mg, 1.20 mmol, 1 equiv), EtMgBr (2.0 mL, 2.0 mmol, 1.7 equiv, 1.0 M in THF), and THF (2.4 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a yellow oil (264 mg, 83% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.33 (d, *J* = 8.1 Hz, 2H), 7.23 – 7.11 (m, 4H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.08 (t, *J* = 3.3 Hz, 2H), 3.80 (s, 3H), 2.81 (dd, *J* = 9.6, 6.1 Hz, 2H), 2.73 – 2.64 (m, 2H), 2.35 (s, 3H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.2, 158.8, 137.3, 135.0, 134.0, 130.2, 129.9, 126.6, 114.4, 105.2, 79.0, 56.0, 34.1, 32.5, 21.6. **IR** (ATR): 2930, 2833, 1940, 1611, 1510, 1440, 1300, 1244, 1176, 1036, 849, 817 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{20}OH$ $[M+H]^+$ 265.1592, found 265.1585.

**1-(benzyloxy)-4-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)benzene (1e)**: The title compound

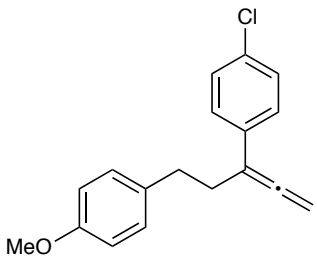



was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2d** (757 mg, 1.47 mmol, 1 equiv), EtMgBr (2.5 mL, 2.5 mmol, 1.7 equiv, 1.0 M in THF), and THF (2.9 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a yellow solid (393 mg, 75% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.47 – 7.43 (m, 2H), 7.40 (ddd, $J$ = 7.8, 6.8, 1.0 Hz, 2H), 7.37 – 7.33 (m, 3H), 7.18 – 7.13 (m, 2H), 6.95 (d, $J$ = 8.9 Hz, 2H), 6.84 (d, $J$ = 8.7 Hz, 2H), 5.08 – 5.05 (m, 4H), 3.78 (s, 3H), 2.79 (dd, $J$ = 9.7, 6.4 Hz, 2H), 2.71 – 2.59 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.1, 158.5, 138.0, 135.0, 130.1, 129.5, 129.3, 128.7, 128.3, 127.8, 124.6, 115.6, 114.4, 104.8, 79.1, 70.8, 56.0, 34.0, 32.6. **IR** (ATR): 2936, 2837, 1939, 1608, 1510, 1465, 1383, 1240, 1177, 1037, 999, 859, 837 cm$^{-1}$. **HRMS** calculated for $C_{25}H_{24}O_2$ $[M]^+$ 356.1776, found 356.1778.

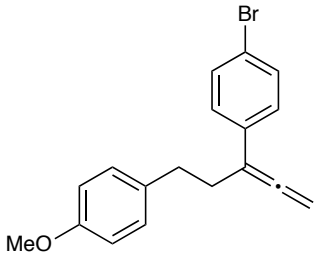
**1-methoxy-4-(3-(4-(trifluoromethyl)phenyl)penta-3,4-dien-1-yl)benzene (1f)**: The title



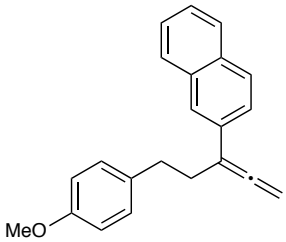

compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2e** (937 mg, 1.96 mmol, 1 equiv), EtMgBr (3.3 mL, 3.3 mmol, 1.7 equiv, 1.0 M in THF), and THF (3.9 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a colorless oil (618 mg, 99% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.60 (d, $J$ = 8.5 Hz, 2H), 7.55 (d, $J$ = 8.5 Hz, 2H), 7.16 (d, $J$ = 8.8 Hz, 2H), 6.85 (d, $J$ = 8.6 Hz, 2H), 5.17 (d, $J$ = 3.3 Hz, 2H), 3.79 (s, 3H), 2.87 – 2.79 (m, 2H), 2.75 – 2.65 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 210.0, 158.9, 141.3 (q, $J_{C\text{-}F}$ = 1.5 Hz), 134.6, 130.2, 129.1 (q, $J_{C\text{-}F}$ = 32.3 Hz), 127.0, 126.05 (q, $J_{C\text{-}F}$ = 3.9 Hz), 125.3 (q, $J_{C\text{-}F}$ = 271.8 Hz), 114.5, 104.7, 79.9, 56.0, 33.9, 32.2. **$^{19}$F NMR** (376 MHz, $CD_2Cl_2$) δ -62.67. **IR** (ATR): 2934, 1939, 1614, 1512, 1324, 1301, 1245, 1163, 1110, 1068, 1036, 1015, 842, 821 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{17}F_3OH$ $[M+H]^+$ 319.1310, found 319.1320.




**1-chloro-4-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)benzene (1g)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2f** (526 mg, 1.18 mmol, 1 equiv), EtMgBr (2.0 mL, 2.0 mmol, 1.7 equiv, 1.0 M in THF), and THF (2.4 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a yellow oil (278 mg, 83% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.38 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.7 Hz, 2H), 7.18 – 7.13 (m, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.11 (t, *J* = 3.3 Hz, 2H), 3.79 (s, 3H), 2.84 – 2.76 (m, 2H), 2.72 – 2.61 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.4, 158.8, 135.8, 134.7, 133.0, 130.1, 129.3, 128.1, 114.5, 104.6, 79.7, 56.0, 33.9, 32.3. **IR** (ATR): 2954, 2912, 1937, 1611, 1511, 1491, 1300, 1244, 1178, 1091, 1031, 1010, 859, 832 cm$^{-1}$. **HRMS** calculated for $C_{18}H_{17}ClONH_4$ $[M+NH_4]^+$ 302.1312, found 302.1313.

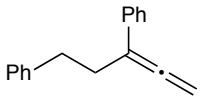



**1-bromo-4-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)benzene (1h)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2g** (653 mg, 1.34 mmol, 1 equiv), EtMgBr (2.3 mL, 2.3 mmol, 1.7 equiv, 1.0 M in THF), and THF (2.7 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a yellow oil (376 mg, 85% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.46 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.10 (t, *J* = 3.3 Hz, 2H), 3.79 (s, 3H), 2.80 (dd, *J* = 9.2, 5.9 Hz, 2H), 2.70 – 2.62 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.4, 158.8, 136.3, 134.7, 132.2, 130.1, 128.4, 121.1, 114.5, 104.6, 79.7, 56.0, 33.9, 32.3. **IR** (ATR): 2933, 1934, 1611, 1511, 1487, 1300, 1241, 1175, 1032, 1005, 950, 863 cm$^{-1}$. **HRMS** calculated for $C_{18}H_{17}BrO$ $[M]^+$ 328.0463, found 328.0458.

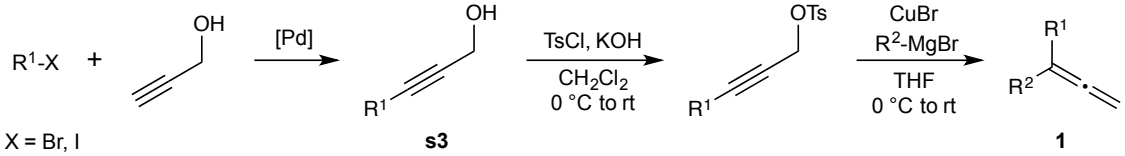


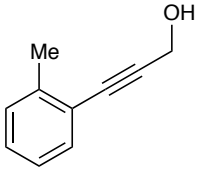

**2-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)naphthalene (1i)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2h** (1.25 g, 2.71 mmol, 1 equiv), EtMgBr (4.6 mL, 4.6 mmol, 1.7 equiv, 1.0 M in THF), and THF (5.4 mL, 0.50 M). Isolated by column chromatography (10% $CH_2Cl_2$ in hexanes) as a

yellow oil (807 mg, 99% yield). **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.82 (t, *J* = 10.0 Hz, 4H), 7.66 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.20 (t, *J* = 3.2 Hz, 2H), 3.80 (s, 3H), 2.90 (ddd, *J* = 8.9, 6.3, 1.9 Hz, 2H), 2.87 – 2.78 (m, 2H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 210.1, 158.8, 135.0, 134.45, 134.44, 133.2, 130.2, 128.7, 128.6, 128.3, 126.9, 126.5, 126.0, 124.3, 114.5, 105.6, 79.7, 56.0, 34.1, 32.4. **IR** (ATR): 3055, 2931, 2833, 1936, 1611, 1511, 1300, 1243, 1177, 1036, 854, 817, 747 $cm^{-1}$. **HRMS** calculated for $C_{22}H_{20}O$ $[M]^+$ 300.1514, found 300.1521.



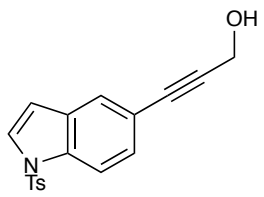

**penta-3,4-diene-1,3-diyldibenzene (1n)**: The title compound was prepared using the general procedure for the Skattebøl rearrangement from dibromocyclopropane **s2i** (2.18 g, 5.73 mmol, 1 equiv), EtMgBr (9.7 mL, 9.7 mmol, 1.7 equiv, 1.0 M in THF), and THF (11.5 mL, 0.50 M). Isolated by column chromatography (hexanes) as a colorless oil (1.19 g, 94% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.48 – 7.42 (m, 2H), 7.38 – 7.29 (m, 4H), 7.28 – 7.24 (m, 2H), 7.24 – 7.19 (m, 2H), 5.11 (t, *J* = 3.3 Hz, 2H), 2.93 – 2.83 (m, 2H), 2.80 – 2.70 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.4, 142.9, 137.1, 129.3, 129.2, 129.1, 127.5, 126.73, 126.65, 105.4, 79.3, 35.0, 32.2. **IR** (ATR): 3026, 2924, 1940, 1596, 1494, 1452, 1076, 1029, 850, 758, 723, 693 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{17}$ $[M+H]^+$ 221.1330, found 221.1325.



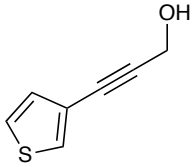




**3-(*o*-tolyl)prop-2-yn-1-ol (s3a)**: Under a gentle flow of nitrogen, an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(PPh_3)_2Cl_2$ (126 mg, 0.180 mmol, 3.0 mol%), CuI (68.6 mg, 0.360 mmol, 6.0 mol%), toluene (6.0 mL, 1.0 M), piperidine (1.2 mL, 12 mmol, 2.0 equiv), 2-iodotoluene (0.76 mL, 6.0 mmol, 1 equiv), and freshly distilled propargyl alcohol (0.36 mL, 6.24 mmol, 1.04 equiv). The resulting mixture was stirred at rt for 4 h. The reaction mixture was filtered through silica and concentrated *in vacuo*. The residue was purified by column chromatography (20% EtOAc in hexanes) to afford the title compound as a red oil (778 mg, 89%

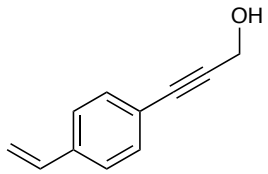
yield). The $^1$H NMR was in accordance with the literature[11]. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.27 – 7.18 (m, 2H), 7.14 (td, *J* = 7.4, 2.1 Hz, 1H), 4.55 (d, *J* = 6.2 Hz, 2H), 2.44 (s, 3H), 1.65 (s, 1H).



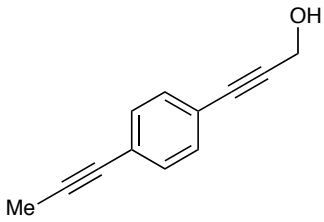

**3-(1-tosyl-1*H*-indol-5-yl)prop-2-yn-1-ol (s3b)**: Under a gentle flow of nitrogen, an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(PPh_3)_4$ (165 mg, 0.143 mmol, 6.0 mol%), pyrrolidine (6.0 mL, 0.40 M), 5-bromo-1-tosyl-1*H*-indole (835 mg, 2.38 mmol, 1 equiv), and freshly distilled propargyl alcohol (0.21 mL, 3.58 mmol, 1.50 equiv). The resulting mixture was stirred overnight at 50 °C. The reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was purified by column chromatography (30% EtOAc in hexanes) to afford the title compound as a yellow oil (702 mg, 91% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.58 (dd, *J* = 12.2, 2.6 Hz, 2H), 7.37 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 6.59 (dd, *J* = 3.7, 0.8 Hz, 1H), 4.50 (s, 2H), 2.32 (s, 3H), 2.05 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.3, 135.1, 134.5, 130.8, 130.0, 128.2, 127.3, 126.9, 125.1, 117.6, 113.6, 108.9, 86.6, 85.8, 51.7, 21.7. **IR** (ATR): 3370, 2924, 1595, 1455, 1370, 1288, 1173, 1158, 1091, 1024, 995, 894, 725 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{15}NO_3SNa$ $[M+Na]^+$ 348.0670, found 348.0685.



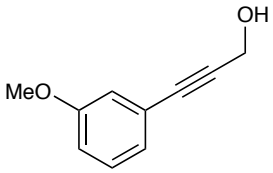

**3-(thiophen-3-yl)prop-2-yn-1-ol (s3c)**: Under a gentle flow of nitrogen, an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(PPh_3)_2Cl_2$ (126 mg, 0.180 mmol, 3.0 mol%), CuI (68.6 mg, 0.360 mmol, 6.0 mol%), $Et_3N$ (6.0 mL, 1.0 M), 3-bromothiophene (0.56 mL, 6.0 mmol, 1 equiv), and freshly distilled propargyl alcohol (0.70 mL, 12.0 mmol, 2.0 equiv). The resulting mixture was stirred at 70 °C for 12 h. The reaction mixture was filtered through celite and concentrated *in vacuo*. The residue was purified by column chromatography (20% EtOAc in hexanes) to afford the title compound as a yellow oil (427 mg, 52% yield). The $^1$H NMR was in accordance with the literature[12]. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 3.0 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.12 (dd, *J* = 4.9, 1.1 Hz, 1H), 4.49 (d, *J* = 5.0 Hz, 2H), 1.62 (s, 1H).




**3-(4-vinylphenyl)prop-2-yn-1-ol (s3d)**: Under a gentle flow of nitrogen, an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (13.5 mg, 0.060 mmol, 1.0 mol%), $PPh_3$(47.2 mg, 0.18 mmol, 3.0 mol%), CuI (11.4 mg, 0.060 mmol, 1.0 mol%), $Et_3N$ (12.0 mL, 0.50 M), 4-bromostyrene (0.78 mL, 6.0 mmol, 1 equiv), and freshly distilled propargyl alcohol (0.35 mL, 6.0 mmol, 1.0 equiv). The resulting mixture was stirred overnight at 80 °C. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The residue was purified by column chromatography (20% EtOAc in hexanes) to afford the title compound as a yellow oil (366 mg, 39% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 6.70 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.78 (dd, *J* = 17.6, 0.8 Hz, 1H), 5.30 (dd, *J* = 10.9, 0.8 Hz, 1H), 4.52 (d, *J* = 6.0 Hz, 2H), 1.66 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.8, 136.3, 132.0, 126.2, 121.9, 115.0, 88.0, 85.8, 51.8. **IR** (ATR): 3305, 1627,1507, 1402, 1356, 1262, 1113, 1018, 998, 952, 911, 841 $cm^{-1}$. **HRMS** calculated for $C_{11}H_{10}O$ $[M]^+$ 158.0732, found 158.0729.




**3-(4-(prop-1-yn-1-yl)phenyl)prop-2-yn-1-ol (s3e)**: Under a gentle flow of nitrogen, an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(PPh_3)_2Cl_2$ (99.8 mg, 0.142 mmol, 3.0 mol%), CuI (54.1 mg, 0.284 mmol, 6.0 mol%), $Et_3N$ (4.7 mL, 1.0 M), 1-bromo-4-(prop-1-yn-1-yl)benzene (924 mg, 4.7 mmol, 1 equiv), and freshly distilled propargyl alcohol (0.41 mL, 7.1 mmol, 1.5 equiv). The resulting mixture was stirred overnight at 80 °C. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The residue was purified by column chromatography (20% EtOAc in hexanes) to afford the title compound as a yellow solid (588 mg, 73% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 4H), 4.50 (s, 2H), 2.06 (s, 3H), 1.86 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 131.6, 131.5, 124.4, 121.7, 88.6, 88.1, 85.6, 79.5, 51.8, 4.6. **IR** (ATR): 3317, 2910, 2863, 1506, 1418, 1370, 1259, 1103, 1016, 950, 832 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{10}O$ $[M]^+$ 170.0732, found 170.0733.




**3-(3-methoxyphenyl)prop-2-yn-1-ol (s3f)**: Under a gentle flow of nitrogen, an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(PPh_3)_4$ (173 mg, 0.150 mmol, 3.0 mol%), CuI (57.1 mg, 0.300 mmol, 6.0 mol%), $Et_3N$ (10.0 mL, 0.50 M), 3-bromoanisole (0.63 mL, 5.0 mmol, 1 equiv), and freshly distilled propargyl alcohol (0.35 mL, 6.0 mmol, 1.2 equiv). The resulting mixture was stirred overnight at 80 °C. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The residue was purified by column chromatography (20% EtOAc in hexanes) to afford the title compound as a yellow oil (652 mg, 80% yield). The $^1$H NMR was in accordance with the literature[13]. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 1H), 7.04 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.98 (dd, *J* = 2.7, 1.4 Hz, 1H), 6.90 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 4.51 (d, *J* = 6.2 Hz, 2H), 3.81 (s, 3H), 1.67 (t, *J* = 5.8 Hz, 1H).

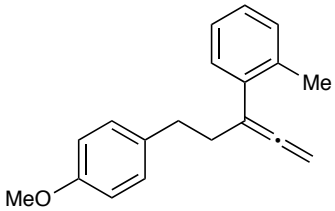
***General Procedure for Alcohol Tosylation***

A flame-dried round bottom flask equipped with a magnetic stir bar was charged with alcohol **s3** (1 equiv) and $CH_2Cl_2$ (0.63 M). The resulting solution was cooled to 0 °C. TsCl (1.20 equiv) was added, followed by freshly crushed KOH (300 mg/mmol of alcohol) portionwise. The resulting mixture was stirred for 1 h at rt. The reaction mixture was poured into ice and extracted with $CH_2Cl_2$. The combined organic layers were washed with brine, dried with anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The obtained crude propargyl tosylate was used without further purification.

***General Procedure for the Cu-catalysed Nucleophilic Substitution***

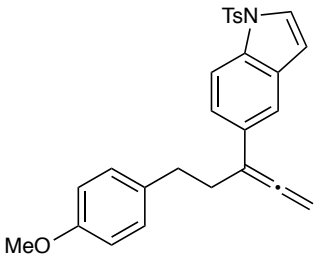
A flame-dried round bottom flask equipped with a magnetic stir bar was charged with propargyl tosylate (1 equiv), CuBr (10 mol%), and THF (0.50 M). The resulting solution was cooled to 0 °C, and a freshly prepared solution of the Grignard reagent (1.25 equiv, 1 M in THF) was added dropwise. (The Grignard reagent solution was prepared by stirring the appropriate alkyl bromide (1 equiv) in the presence of Mg (1.5 equiv) and a catalytic amount of $I_2$ in THF (1 M) at rt for 2 h). The resulting mixture was stirred for 2 h at rt. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with $Et_2O$. The combined organic layers were washed

with brine, dried with anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford the desired allene **1**.




**1-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)-2-methylbenzene (1b)**: The title compound was prepared according to the general procedures for alcohol tosylation and Cu-catalysed nucleophilic substitution using alcohol **s3a** (332 mg, 2.0 mmol, 1 equiv), TsCl (458 mg, 2.4 mmol, 1.2 equiv), KOH (600 mg, 300 mg/mmol of alcohol) and $CH_2Cl_2$ (3.2 mL, 0.63 M). The crude propargyl tosylate was used without further purification.

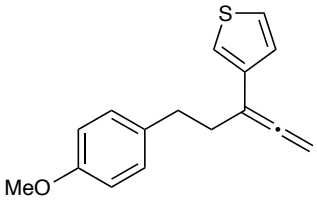
Crude 3-(*o*-tolyl)prop-2-yn-1-yl 4-methylbenzenesulfonate (601 mg, 2.0 mmol, 1 equiv) was reacted with (4-methoxyphenethyl)magnesium bromide (2.5 mL, 1.25 equiv, 1 M in THF) using CuBr (28.7 mg, 0.20 mmol, 10 mol%) and THF (4.0 mL, 0.50 M). Purification by column chromatography (10% $CH_2Cl_2$ in hexanes) afforded the desired allene as a yellow oil (89.8 mg, 17% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.25 – 7.16 (m, 4H), 7.13 (d, $J$ = 8.8 Hz, 2H), 6.83 (d, $J$ = 8.7 Hz, 2H), 4.83 (t, $J$ = 3.2 Hz, 2H), 3.78 (s, 3H), 2.78 – 2.69 (m, 2H), 2.60 (ddtd, $J$ = 9.6, 7.6, 3.2, 1.0 Hz, 2H), 2.32 (s, 3H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 207.7, 158.7, 138.1, 137.0, 134.8, 131.2, 130.1, 128.7, 127.7, 126.6, 114.4, 104.2, 76.3, 56.0, 36.2, 33.8, 20.8. **IR** (ATR): 2930, 2833, 1950, 1611, 1511, 1440, 1300, 1244, 1176, 1036, 845, 821 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{20}O$ $[M]^+$ 264.1514, found 264.1503.




**5-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)-1-tosyl-1*H*-indole (1j)**: The title compound was prepared according to the general procedures for alcohol tosylation and Cu-catalysed nucleophilic substitution using alcohol **s3b** (702 mg, 2.2 mmol, 1 equiv), TsCl (494 mg, 2.6 mmol, 1.2 equiv), KOH (647 mg, 300 mg/mmol of alcohol) and $CH_2Cl_2$ (3.4 mL, 0.63 M). The crude propargyl tosylate was used without further purification.

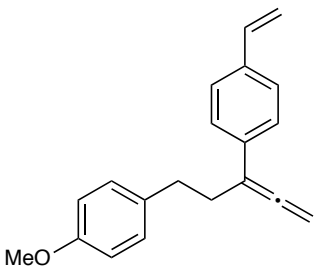
Crude 3-(1-tosyl-1*H*-indol-5-yl)prop-2-yn-1-yl 4-methylbenzenesulfonate (894 mg, 1.9 mmol, 1 equiv) was reacted with (4-methoxyphenethyl)magnesium bromide (2.3 mL, 1.25 equiv, 1 M in THF) using CuBr (26.8 mg, 0.19 mmol, 10 mol%) and THF (3.7 mL, 0.50 M). Purification by column chromatography (5% EtOAc in hexanes) afforded the desired allene as a

colorless oil (159 mg, 19% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.91 (d, *J* = 8.7 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.60 – 7.52 (m, 2H), 7.43 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.65 (d, *J* = 3.7 Hz, 1H), 5.09 (t, *J* = 3.3 Hz, 2H), 3.78 (s, 3H), 2.80 (dd, *J* = 9.7, 6.0 Hz, 2H), 2.70 (td, *J* = 7.5, 6.5, 3.6 Hz, 2H), 2.34 (s, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 209.4, 158.7, 146.2, 135.8, 134.8, 134.4, 132.5, 131.9, 130.7, 130.1, 127.54, 127.48, 124.1, 119.0, 114.4, 114.1, 110.0, 105.2, 79.2, 55.9, 34.0, 32.7, 22.1. **IR** (ATR): 2930, 1938, 1611, 1596, 1512, 1457, 1370, 1244, 1174, 1128, 1035, 994, 812 $cm^{-1}$. **HRMS** calculated for $C_{27}H_{25}NO_3SNa$ $[M+Na]^+$ 466.1453, found 466.1471.



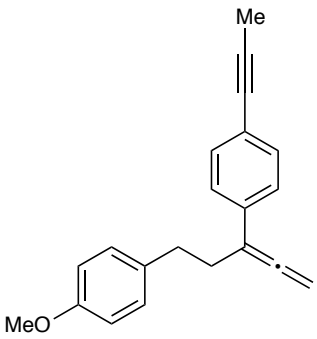

**3-(5-(4-methoxyphenyl)penta-1,2-dien-3-yl)thiophene (1k)**: The title compound was prepared according to the general procedures for alcohol tosylation and Cu-catalysed nucleophilic substitution using alcohol **s3c** (542 mg, 3.9 mmol, 1 equiv), TsCl (897 mg, 4.7 mmol, 1.2 equiv), KOH (1.18 g, 300 mg/mmol of alcohol) and $CH_2Cl_2$ (6.2 mL, 0.63 M). The crude propargyl tosylate was used without further purification.

Crude 3-(thiophen-3-yl)prop-2-yn-1-yl 4-methylbenzenesulfonate (585 mg, 2.0 mmol, 1 equiv) was reacted with (4-methoxyphenethyl)magnesium bromide (2.5 mL, 1.25 equiv, 1 M in THF) using CuBr (28.7 mg, 0.20 mmol, 10 mol%) and THF (4.0 mL, 0.50 M). Purification by column chromatography (10% $CH_2Cl_2$ in hexanes) afforded the desired allene as a colorless oil (128 mg, 25% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 77.31 (dd, *J* = 5.1, 2.9 Hz, 1H), 7.21 – 7.14 (m, 3H), 7.13 (dt, *J* = 3.0, 1.1 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.09 (t, *J* = 2.9 Hz, 2H), 3.80 (s, 3H), 2.84 (dd, *J* = 9.5, 6.3 Hz, 2H), 2.73 – 2.61 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.6, 158.8, 138.9, 134.9, 130.2, 127.5, 126.2, 119.6, 114.5, 101.8, 79.1, 56.0, 33.9, 33.1. **IR** (ATR): 2923, 2855, 1940, 1611, 1511, 1440, 1300, 1244, 1176, 1036, 854 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{16}OS$ $[M]^+$ 256.0922, found 256.0912.




**1-methoxy-4-(3-(4-vinylphenyl)penta-3,4-dien-1-yl)benzene (1l)**: The title compound was prepared according to the general procedures for alcohol tosylation and Cu-catalysed nucleophilic substitution using alcohol **s3d** (332 mg, 2.1 mmol, 1 equiv), TsCl (480 mg, 2.5 mmol, 1.2 equiv), KOH (630 mg, 300 mg/mmol of alcohol) and $CH_2Cl_2$ (3.3 mL, 0.63 M). The crude propargyl tosylate was used without further purification.

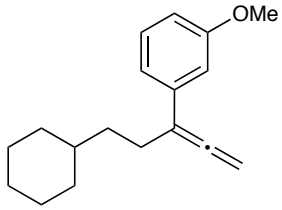
Crude 3-(4-vinylphenyl)prop-2-yn-1-yl 4-methylbenzenesulfonate (638 mg, 2.0 mmol, 1 equiv) was reacted with (4-methoxyphenethyl)magnesium bromide (2.5 mL, 1.25 equiv, 1 M in THF) using CuBr (28.7 mg, 0.20 mmol, 10 mol%) and THF (4.0 mL, 0.50 M). Purification by column chromatography (10% $CH_2Cl_2$ in hexanes) afforded the desired allene as a yellow oil (91 mg, 16% yield). **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.39 (s, 4H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.72 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.76 (dd, *J* = 17.5, 1.0 Hz, 1H), 5.23 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.10 (t, *J* = 3.3 Hz, 2H), 3.78 (s, 3H), 2.80 (dd, *J* = 9.6, 6.2 Hz, 2H), 2.68 (ddt, *J* = 8.3, 4.2, 2.2 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.5, 158.7, 137.2, 136.7, 136.6, 134.8, 130.1, 127.0, 126.8, 114.4, 114.0, 105.1, 79.3, 56.0, 34.0, 32.3. **IR** (ATR): 3038, 2933, 2838, 1935, 1611, 1510, 1441, 1300, 1243, 1175, 1030, 905, 842 cm$^{-1}$. **HRMS** calculated for $C_{20}H_{20}ONH_4$ $[M+NH_4]^+$ 294.1858, found 294.1851.




**1-methoxy-4-(3-(4-(prop-1-yn-1-yl)phenyl)penta-3,4-dien-1-yl)benzene (1m)**: The title compound was prepared according to the general procedures for alcohol tosylation and Cu-catalysed nucleophilic substitution using alcohol **s3e** (340 mg, 2.0 mmol, 1 equiv), TsCl (458 mg, 2.4 mmol, 1.2 equiv), KOH (600 mg, 300 mg/mmol of alcohol) and $CH_2Cl_2$ (3.2 mL, 0.63 M). The crude propargyl tosylate was used without further purification.

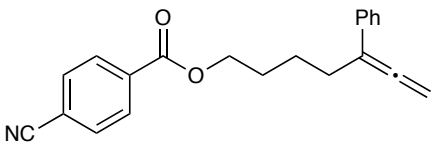
Crude 3-(4-(prop-1-yn-1-yl)phenyl)prop-2-yn-1-yl 4-methylbenzenesulfonate (622 mg, 1.9 mmol, 1 equiv) was reacted with (4-methoxyphenethyl)magnesium bromide (2.4 mL, 1.25 equiv, 1 M in THF) using CuBr (27.5 mg, 0.19 mmol, 10 mol%) and THF (3.8 mL, 0.50 M). Purification by column chromatography (10% $CH_2Cl_2$ in hexanes) afforded the desired allene as

a colorless oil (256 mg, 46% yield). **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.35 (s, 4H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.11 (t, *J* = 3.3 Hz, 2H), 3.78 (s, 3H), 2.80 (dd, *J* = 9.6, 6.2 Hz, 2H), 2.71 – 2.63 (m, 2H), 2.06 (s, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 209.6, 158.8, 136.4, 134.8, 132.3, 130.1, 126.6, 123.0, 114.5, 105.1, 86.9, 80.2, 79.5, 56.0, 34.0, 32.2, 4.8. **IR** (ATR): 2914, 2833, 1937, 1611, 1510, 1440, 1300, 1244, 1176, 1107, 1036, 838, 821 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{20}O$ $[M]^+$ 288.1514, found 288.1513.




**1-(5-cyclohexylpenta-1,2-dien-3-yl)-3-methoxybenzene (1p)**: The title compound was prepared according to the general procedures for alcohol tosylation and Cu-catalysed nucleophilic substitution using alcohol **s3f** (652 mg, 4.0 mmol, 1 equiv), TsCl (920 mg, 4.8 mmol, 1.2 equiv), KOH (1.21 g, 300 mg/mmol of alcohol) and $CH_2Cl_2$ (6.4 mL, 0.63 M). The crude propargyl tosylate was used without further purification.

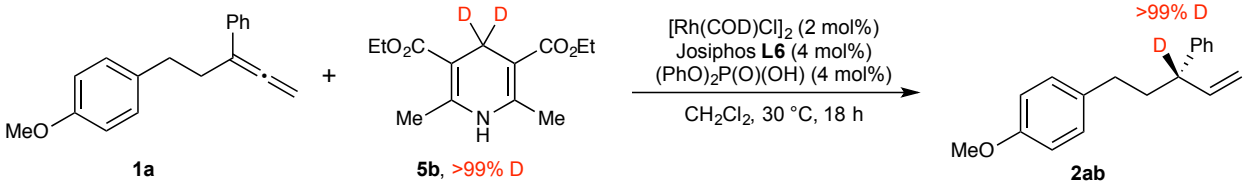
Crude 3-(3-methoxyphenyl)prop-2-yn-1-yl 4-methylbenzenesulfonate (1.27 g, 4.0 mmol, 1 equiv) was reacted with (2-cyclohexylethyl)magnesium bromide (5.0 mL, 1.25 equiv, 1 M in THF) using CuBr (57.7 mg, 0.40 mmol, 10 mol%) and THF (8.0 mL, 0.50 M). Purification by column chromatography (10% $CH_2Cl_2$ in hexanes) afforded the desired allene as a colorless oil (167 mg, 16% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.24 (t, *J* = 8.0 Hz, 1H), 7.06 – 7.00 (m, 1H), 6.97 (t, *J* = 2.1 Hz, 1H), 6.76 (ddd, *J* = 8.1, 2.6, 0.9 Hz, 1H), 5.08 (t, *J* = 3.3 Hz, 2H), 3.81 (s, 3H), 2.47 – 2.38 (m, 2H), 1.83 – 1.63 (m, 5H), 1.51 – 1.43 (m, 2H), 1.43 – 1.31 (m, 1H), 1.31 – 1.13 (m, 3H), 1.03 – 0.90 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.4, 160.6, 139.0, 130.0, 119.3, 112.63, 112.61, 106.0, 78.7, 55.9, 38.4, 36.4, 34.2, 27.8, 27.6, 27.3. **IR** (ATR): 2919, 2849, 1939, 1597, 1580, 1487, 1448, 1286, 1262, 1245, 1165, 1051, 846 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}OH$ $[M+H]^+$ 257.1906, found 257.1902.

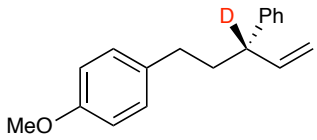



**5-phenylhepta-5,6-dien-1-yl 4-cyanobenzoate (1s)**: An oven-dried round bottom flask equipped with a magnetic stir bar was charged with EDC hydrochloride (249 mg, 1.30 mmol, 1.3 equiv), DMAP (12.2 mg, 0.10 mmol, 10 mol%), and $CH_2Cl_2$ (2.5 mL, 0.40 M). After cooling the resulting mixture to 0 °C, 4-cyanobenzoic acid (147 mg, 1.0 mmol, 1 equiv) and

allene **1q** (226 mg, 1.2 mmol, 1.2 equiv) were added. The resulting mixture was warmed to rt and stirred for 12 h. The reaction mixture was diluted with ether (10 mL) and washed with 1 M HCl (10 mL). The organic layer was washed with brine, dried with anhydrous $Na_2SO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (10% EtOAc in hexanes) to afford the title compound as a yellow solid (265 mg, 83% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 8.12 (d, $J$ = 8.7 Hz, 2H), 7.75 (d, $J$ = 8.7 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.34 (dddd, $J$ = 8.3, 6.8, 1.3, 0.7 Hz, 2H), 7.27 – 7.20 (m, 1H), 5.13 (t, $J$ = 3.4 Hz, 2H), 4.40 (t, $J$ = 6.5 Hz, 2H), 2.58 – 2.49 (m, 2H), 1.97 – 1.87 (m, 2H), 1.82 – 1.70 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.2, 165.6, 137.0, 135.1, 133.0, 130.7, 129.1, 127.4, 126.7, 118.8, 117.0, 105.3, 79.0, 66.4, 29.7, 29.0, 24.9. **IR** (ATR): 2915, 2229, 1937, 1716, 1452, 1278, 1122, 1110, 1032, 1022, 855, 762 cm$^{-1}$. **HRMS** calculated for $C_{21}H_{19}NO_2H$ $[M+H]^+$ 318.1494, found 318.1497.

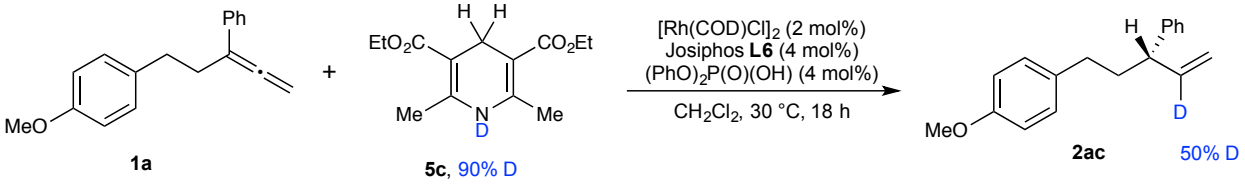
## 4. Deuterium Labelling Experiments

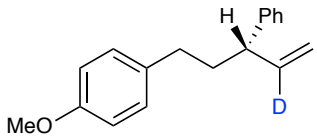



**(*S*)-1-methoxy-4-(3-phenylpent-4-en-1-yl-3-*d*)benzene (2ab)**: In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (1.0 mg, 0.0020 mmol, 2 mol%), $(PhO)_2P(O)(OH)$ (1.0 mg, 0.0040 mmol, 4 mol%), Josiphos **L6** (4.6 mg, 0.0040 mmol, 4 mol%), Hantzsch ester **5b** (51.1 mg, 0.20 mmol, 2.0 equiv), allene **1a** (25.0 mg, 0.10 mmol, 1 equiv), and $CH_2Cl_2$ (0.10 mL, 1 M) were added to a 1 dram vial equipped with a magnetic stir bar. The vial was then sealed with a Teflon-lined screw cap and stirred at 30 °C for 18 h. The reaction mixture was cooled to rt and concentrated *in vacuo*. The regioselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The title compound was isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (20.5 mg, 81% yield, >20:1 *rr*, 96:4 *er*, $[\alpha]^{24}_D$ = +11.6 (*c* 1.3, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.26 – 7.20 (m, 3H), 7.10 (d, $J$ = 8.8 Hz, 2H), 6.85 (d, $J$ = 8.7 Hz, 2H), 6.06 – 5.94

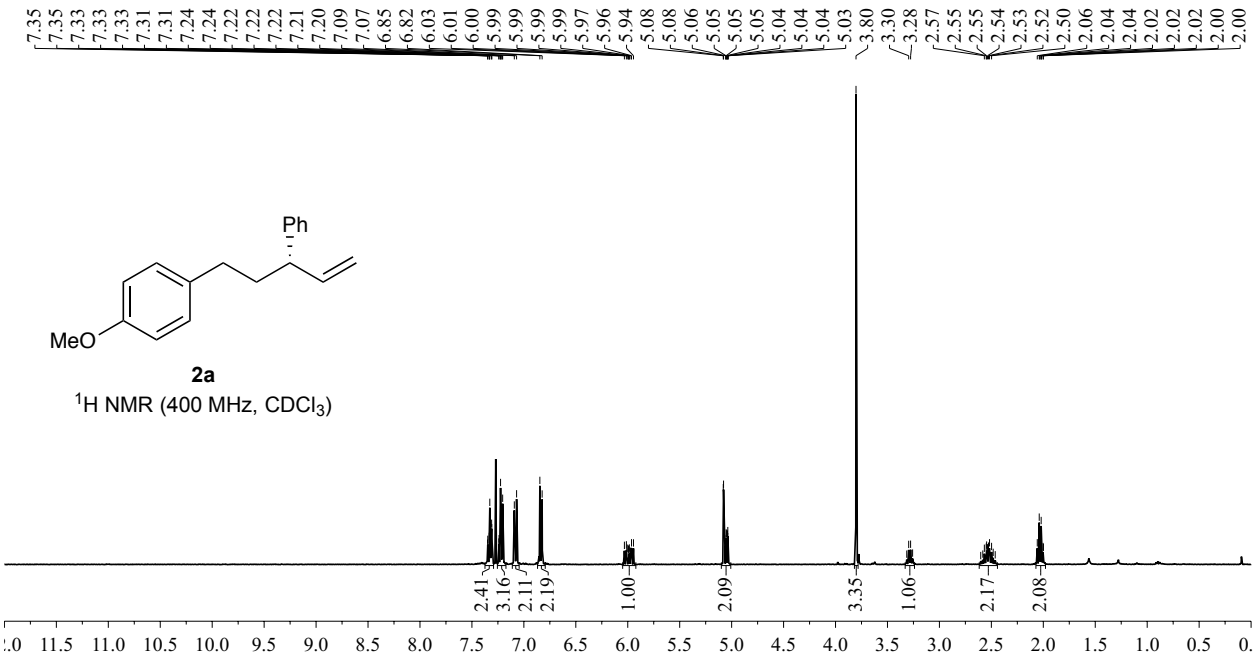
(m, 1H), 5.12 – 5.03 (m, 2H), 3.81 (s, 3H), 2.63 – 2.45 (m, 2H), 2.10 – 1.97 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 144.3, 142.3, 134.4, 129.4, 128.6, 127.8, 126.4, 114.4, 113.9, 55.4, 49.1 – 48.7 (m), 37.2, 32.8. **IR** (ATR): 2932, 2833, 1611, 1511, 1447, 1300, 1243, 1176, 1035, 913, 828, 750 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{19}DONH_4$ $[M+NH_4]^+$ 271.1921, found 271.1922. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.2 min, $t_{R2}$ (major) = 2.6 min.

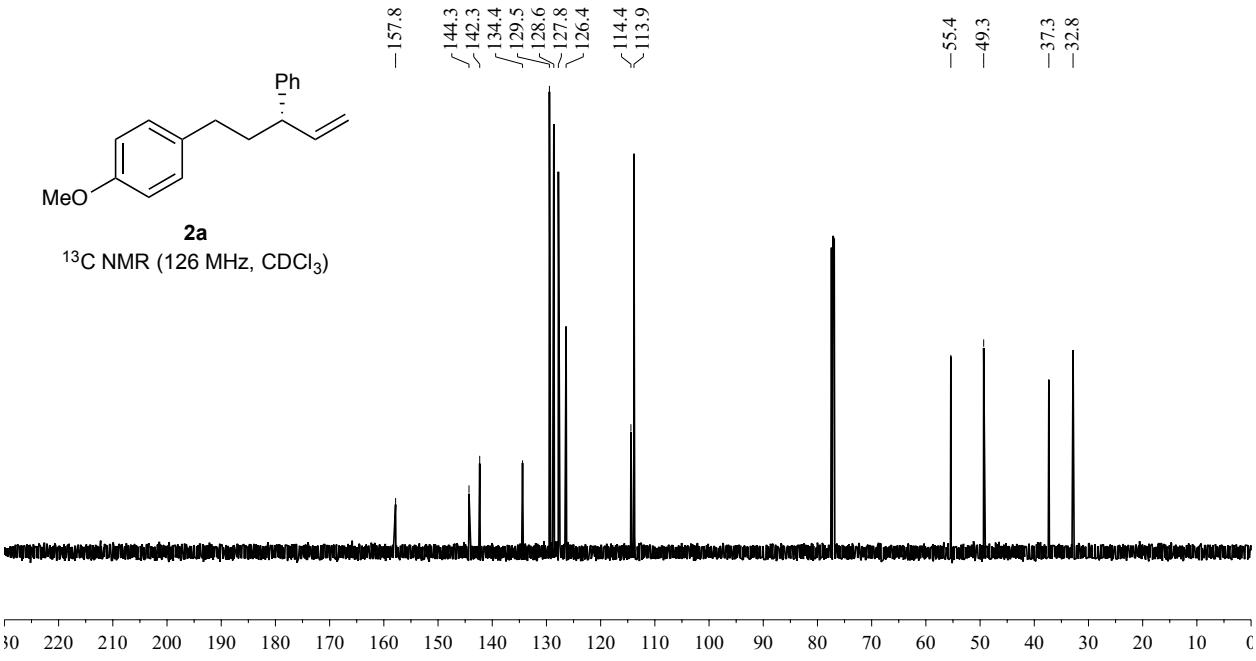


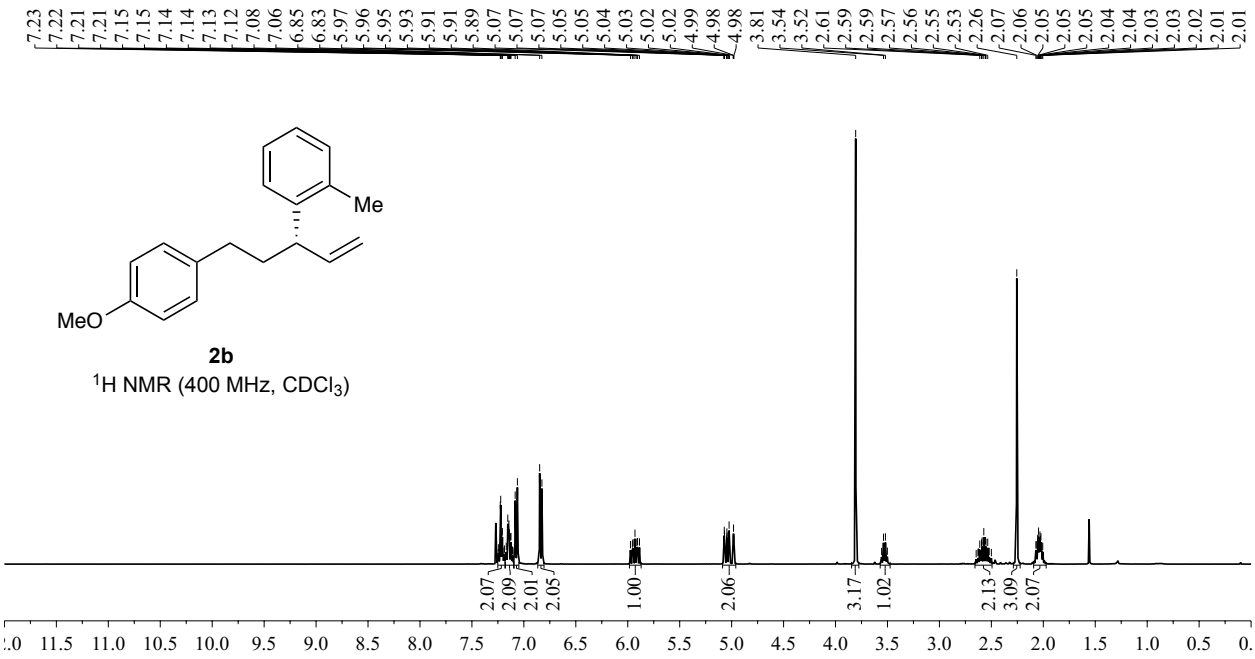



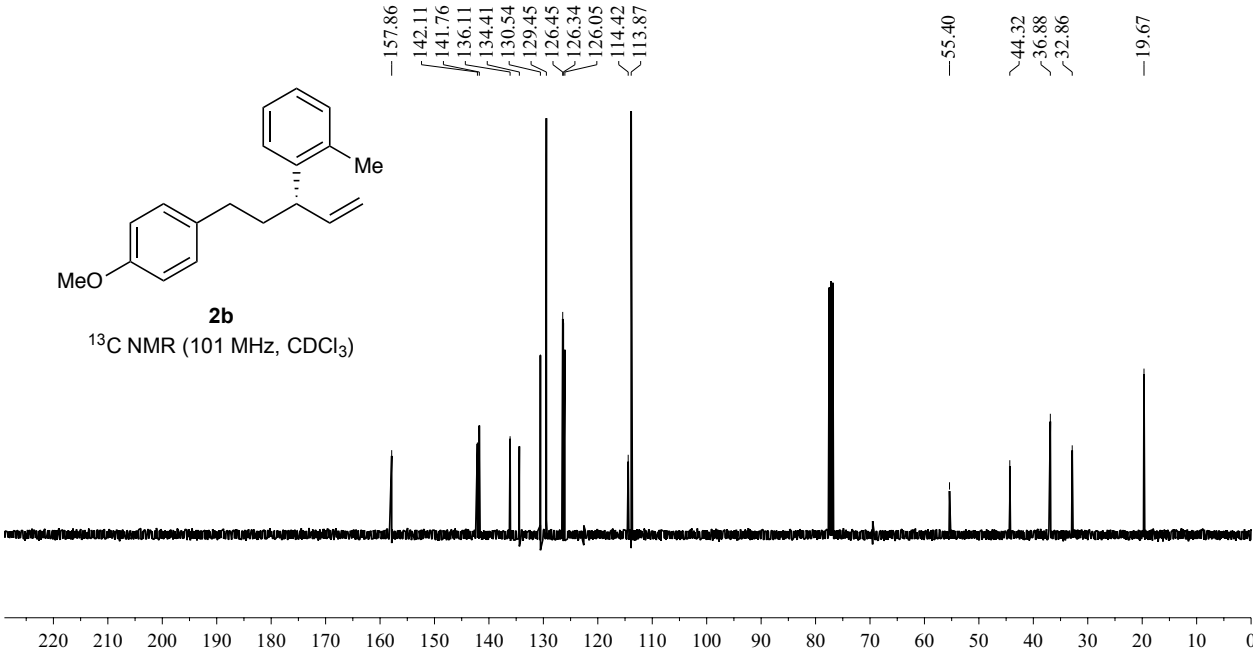

**(*S*)-1-methoxy-4-(3-phenylpent-4-en-1-yl-4-*d*)benzene (2ac)**: In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (1.0 mg, 0.0020 mmol, 2 mol%), $(PhO)_2P(O)(OH)$ (1.0 mg, 0.0040 mmol, 4 mol%), Josiphos **L6** (4.6 mg, 0.0040 mmol, 4 mol%), Hantzsch ester **5c** (50.9 mg, 0.20 mmol, 2.0 equiv), allene **1a** (25.0 mg, 0.10 mmol, 1 equiv), and $CH_2Cl_2$ (0.10 mL, 1 M) were added to a 1 dram vial equipped with a magnetic stir bar. The vial was then sealed with a Teflon-lined screw cap and stirred at 30 °C for 18 h. The reaction mixture was cooled to rt and concentrated *in vacuo*. The regioselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The title compound was isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (20.7 mg, 82% yield, >20:1 *rr*, 94:6 *er*, $[\alpha]^{24}_D$ = +10.8 (*c* 1.3, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.7, 6.8 Hz, 2H), 7.26 – 7.19 (m, 3H), 7.12 – 7.06 (m, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.06 – 5.94 (m, 0.5H), 5.12 – 5.01 (m, 2H), 3.81 (s, 3H), 3.30 (q, *J* = 7.2 Hz, 1H), 2.63 – 2.46 (m, 2H), 2.04 (td, *J* = 8.7, 8.2, 6.9 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.9, 144.3, 142.3, 134.4, 129.4, 128.6, 127.8, 126.4, 114.4, 113.9, 55.4, 49.3, 37.3, 32.9. **IR** (ATR): 3027, 2933, 2833, 1611, 1510, 1452, 1243, 1176, 1035, 913, 824, 752 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{19}DONH_4$ $[M+NH_4]^+$ 271.1921, found 271.1909. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.2 min, $t_{R2}$ (major) = 2.6 min.

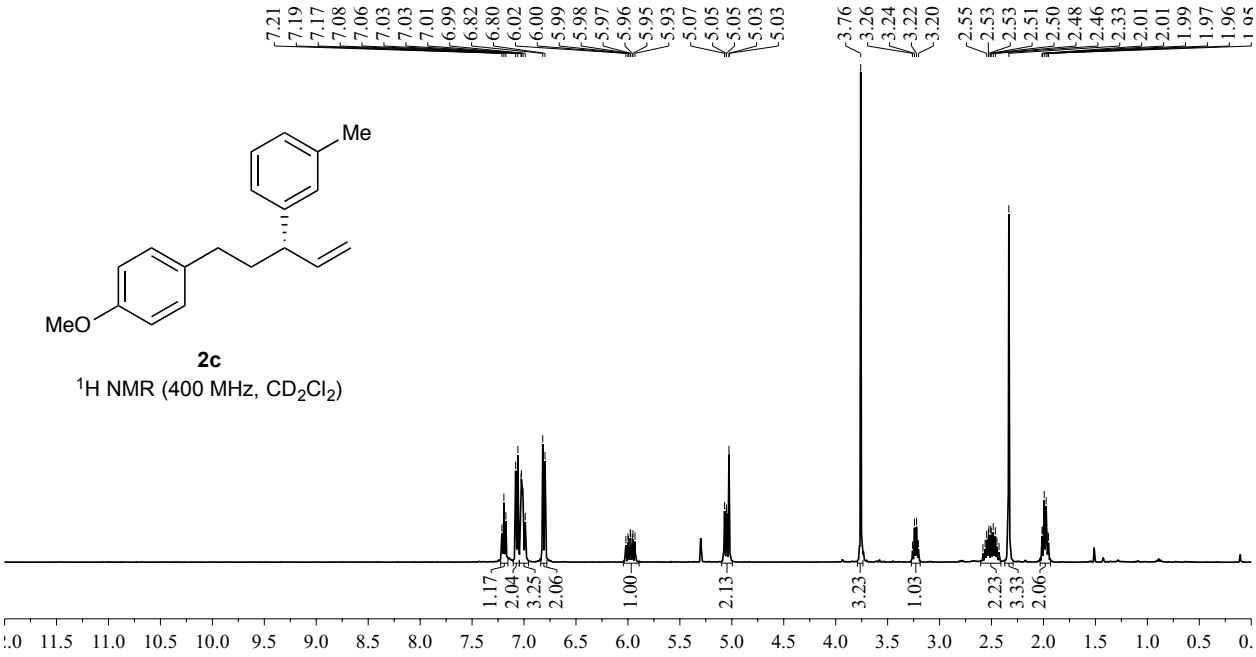
## 5. NMR Spectra

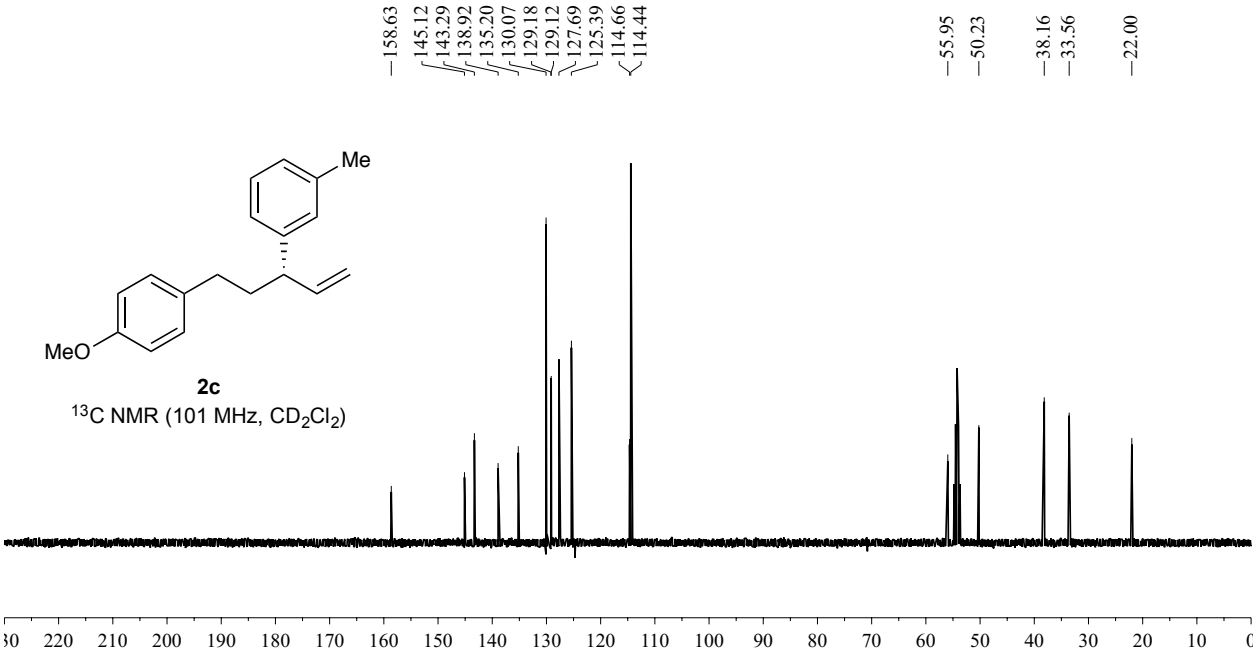



Me
MeO
2b
1H NMR (400 MHz, CDCl3)


Me
MeO
2b
13C NMR (101 MHz, CDCl3)


Me
MeO
2c
1H NMR (400 MHz, CD2Cl2)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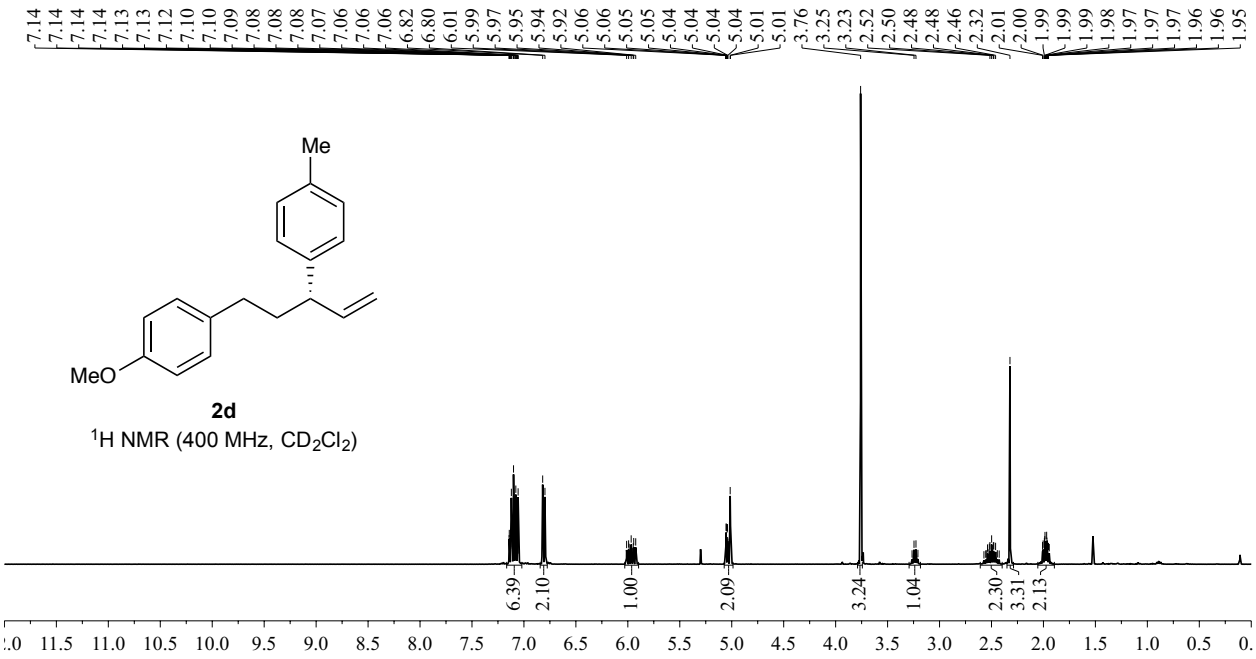
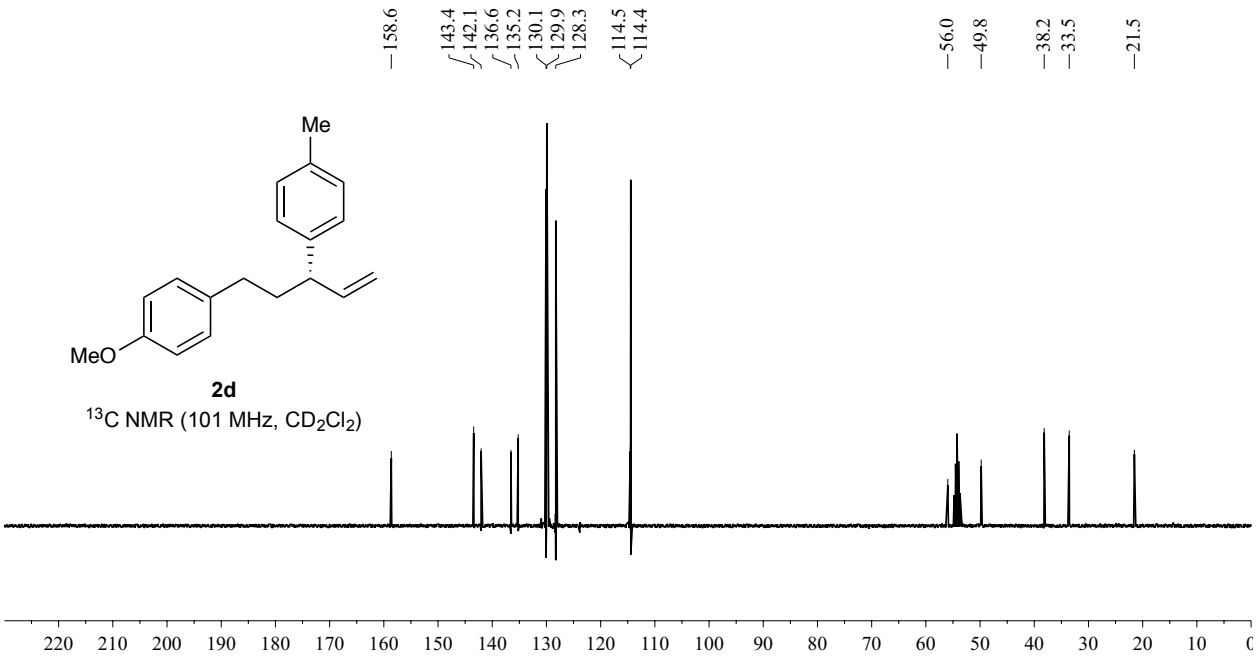
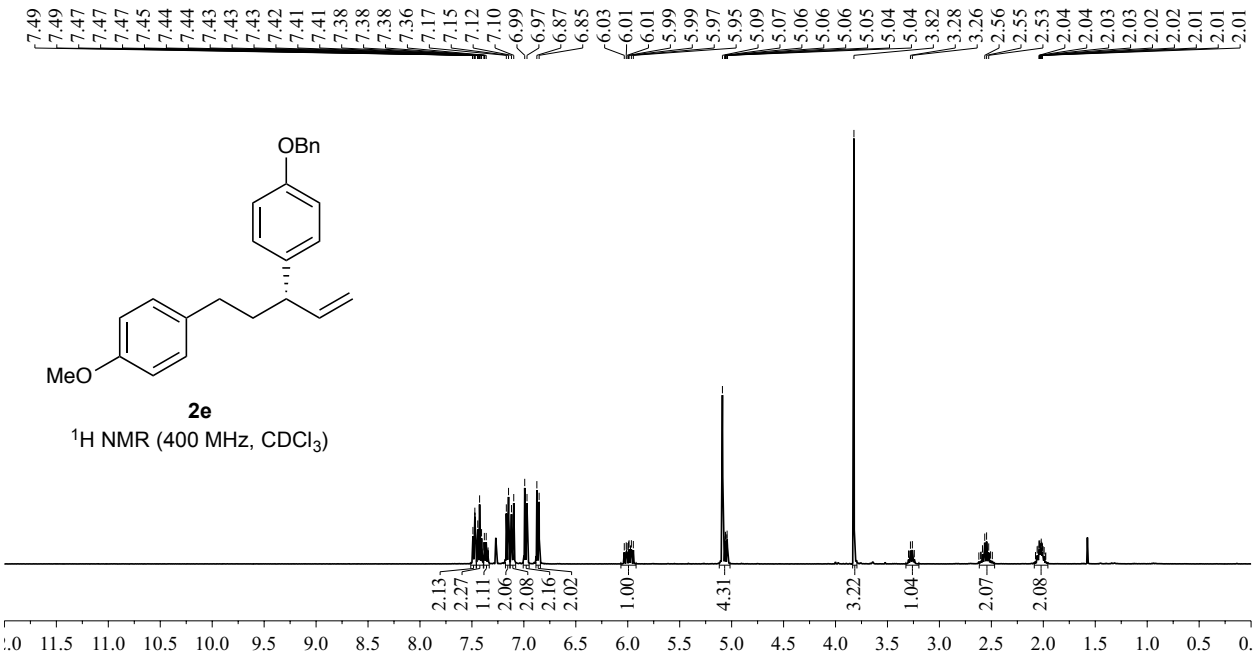
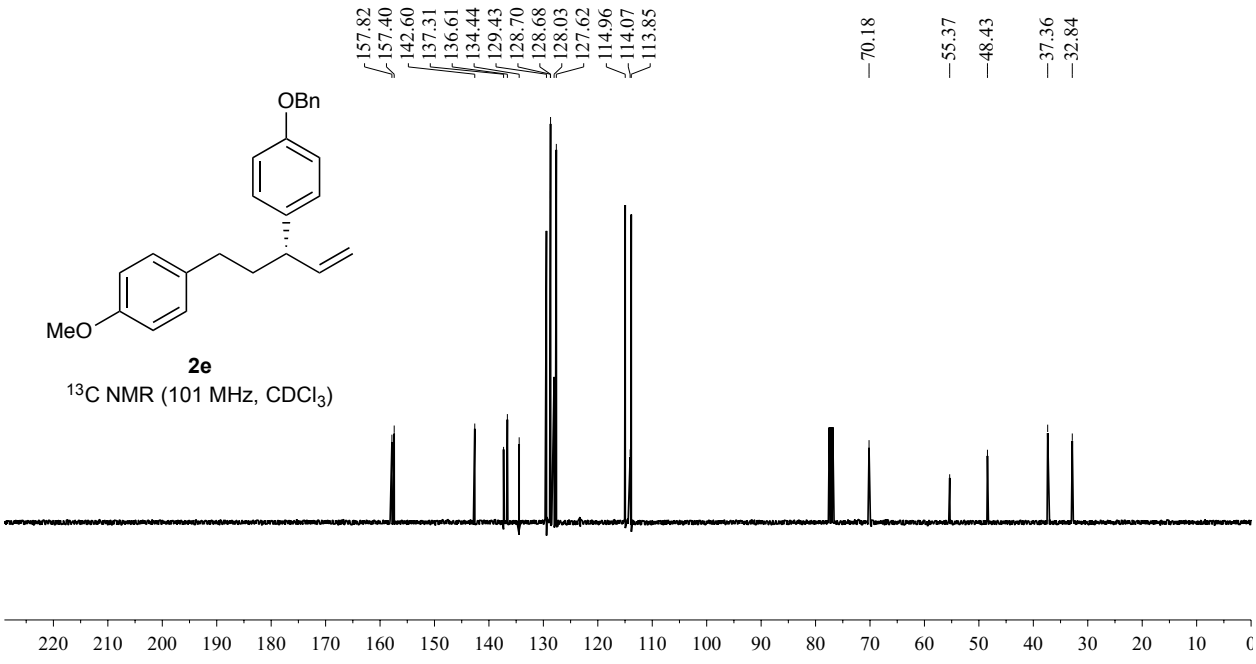
MeO
2c
13C NMR (101 MHz, CD2Cl2)


Me
MeO
2d
1H NMR (400 MHz, CD2Cl2)


Me
MeO
2d
13C NMR (101 MHz, CD2Cl2)


OBn
MeO
2e
1H NMR (400 MHz, CDCl3)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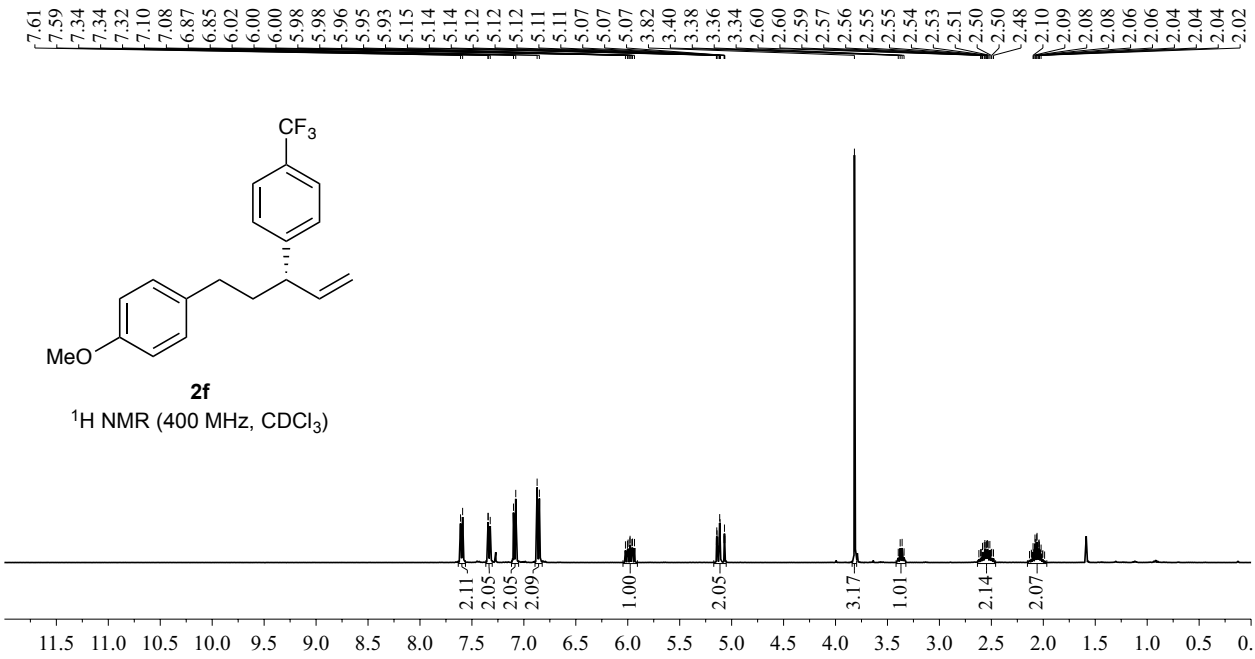
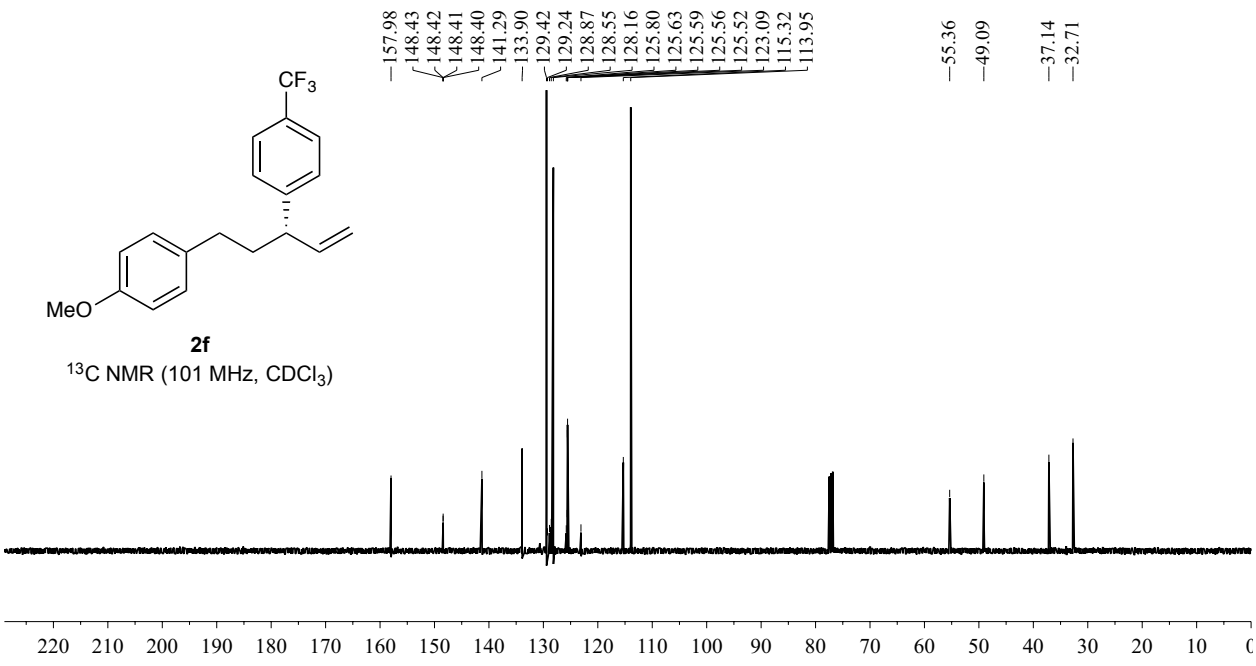
MeO
2e
13C NMR (101 MHz, CDCl3)



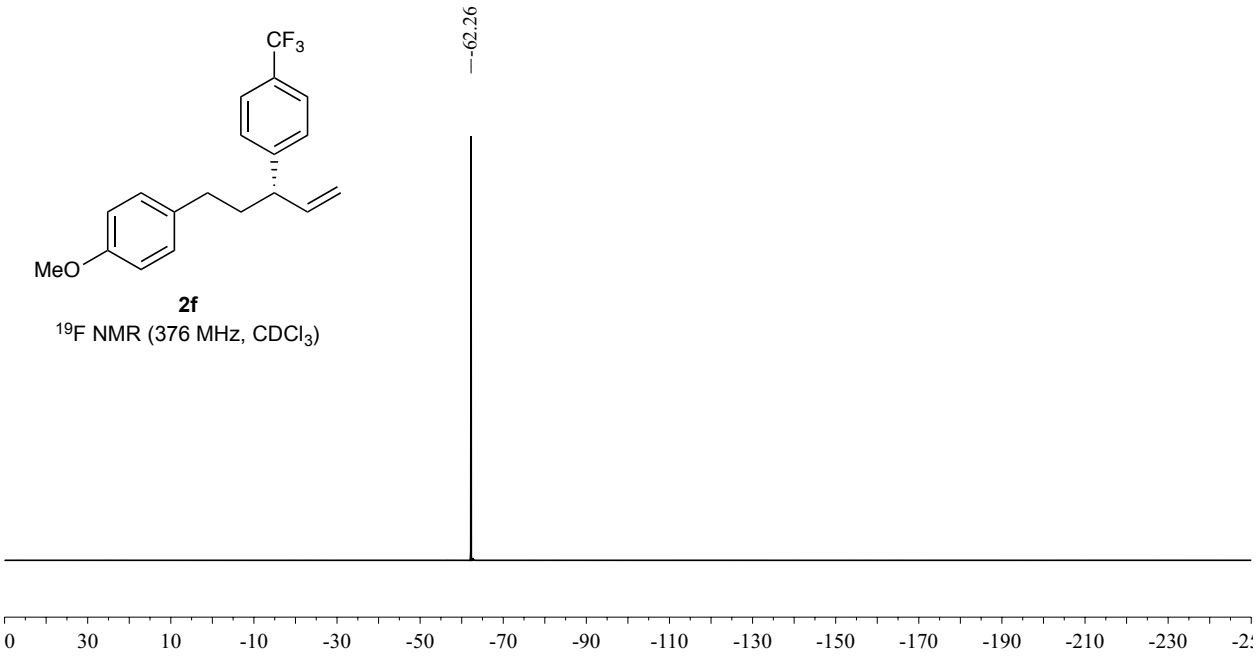

**2f**

$^{1}$H NMR (400 MHz, $CDCl_3$)



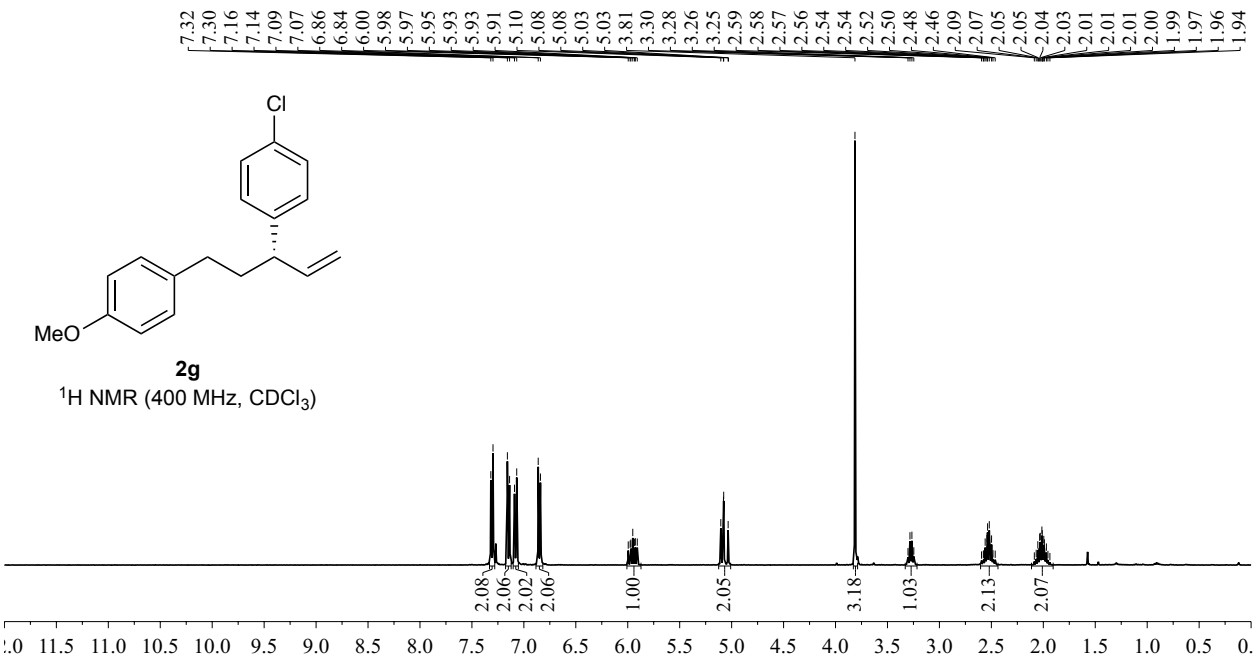

**2f**

$^{13}$C NMR (101 MHz, $CDCl_3$)



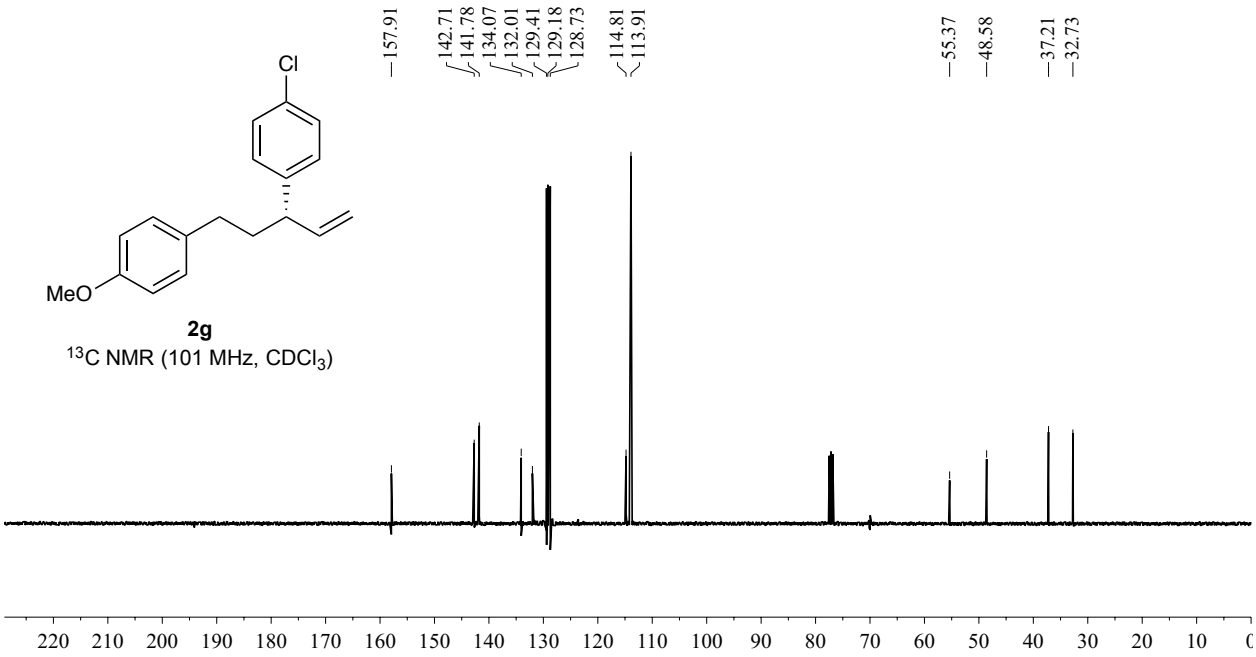

**2f**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



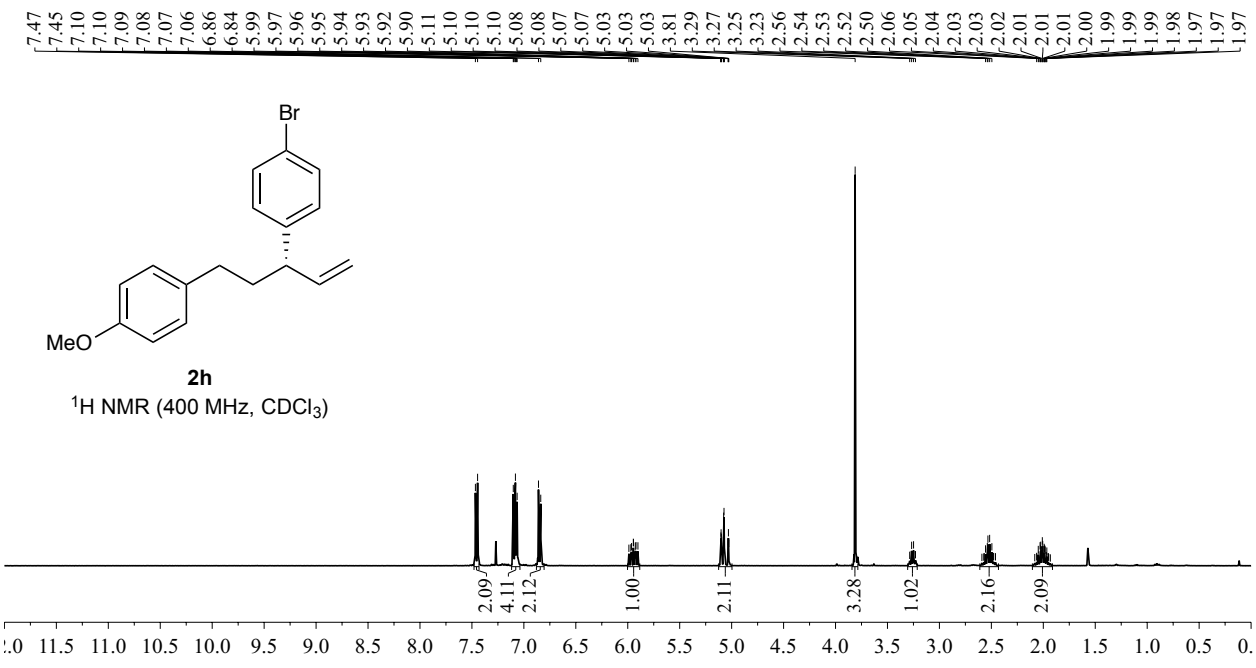

**2g**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



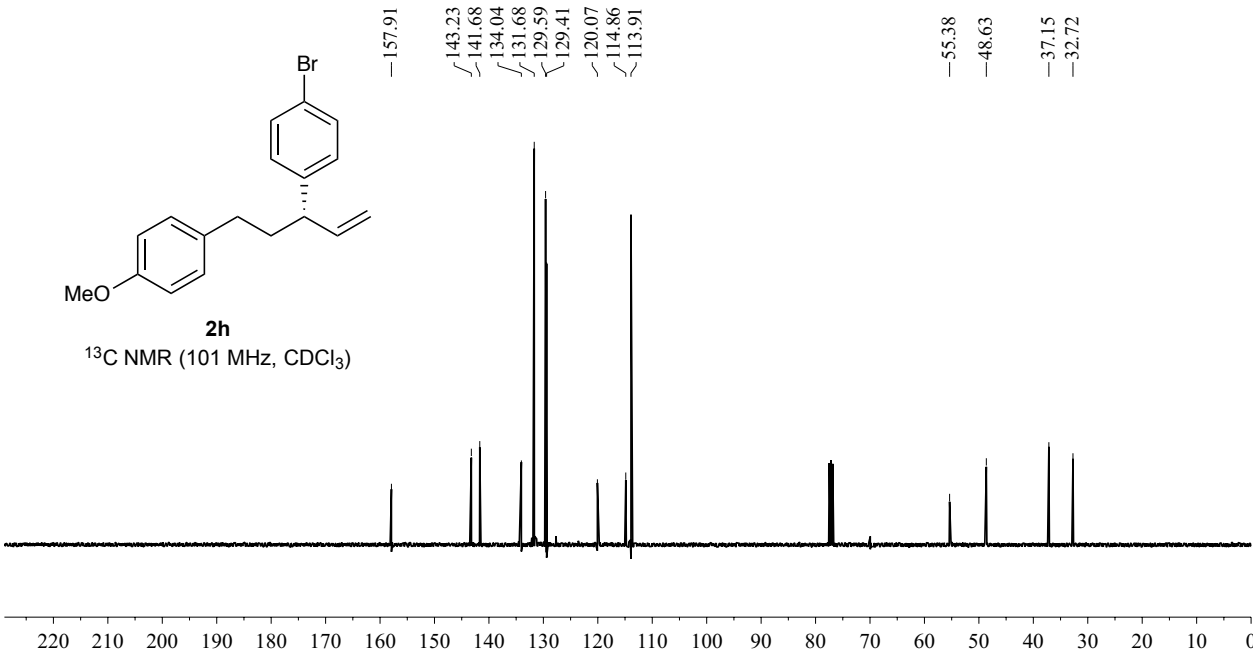

**2g**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



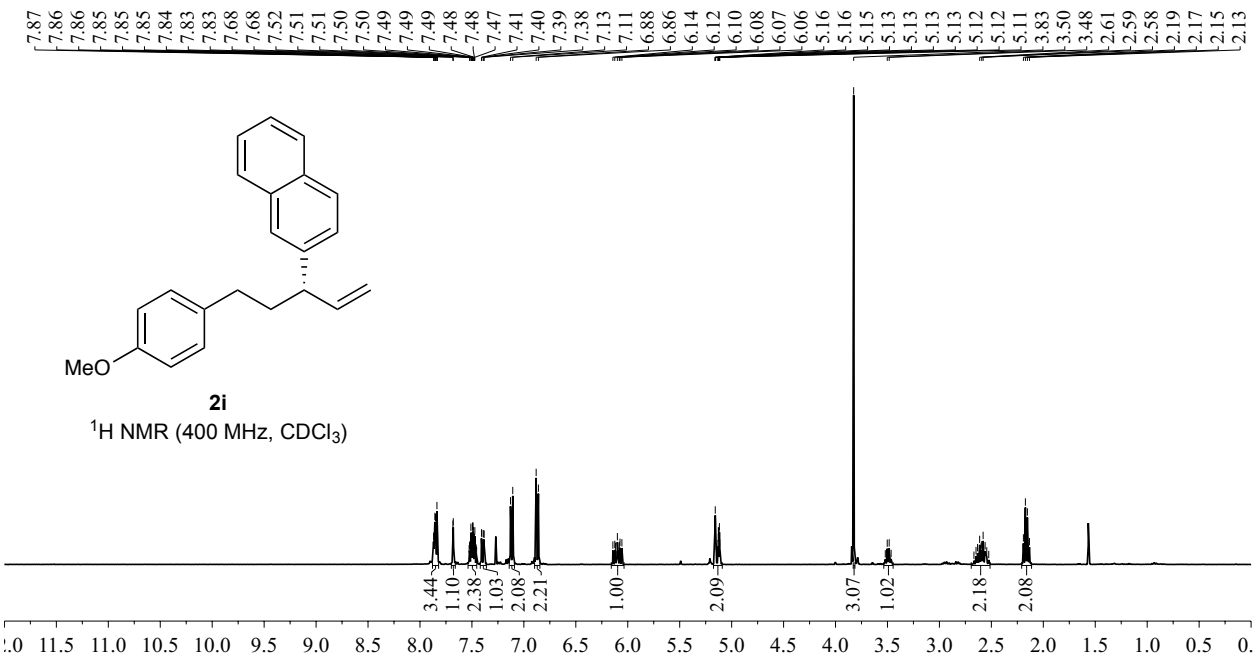

**2h**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



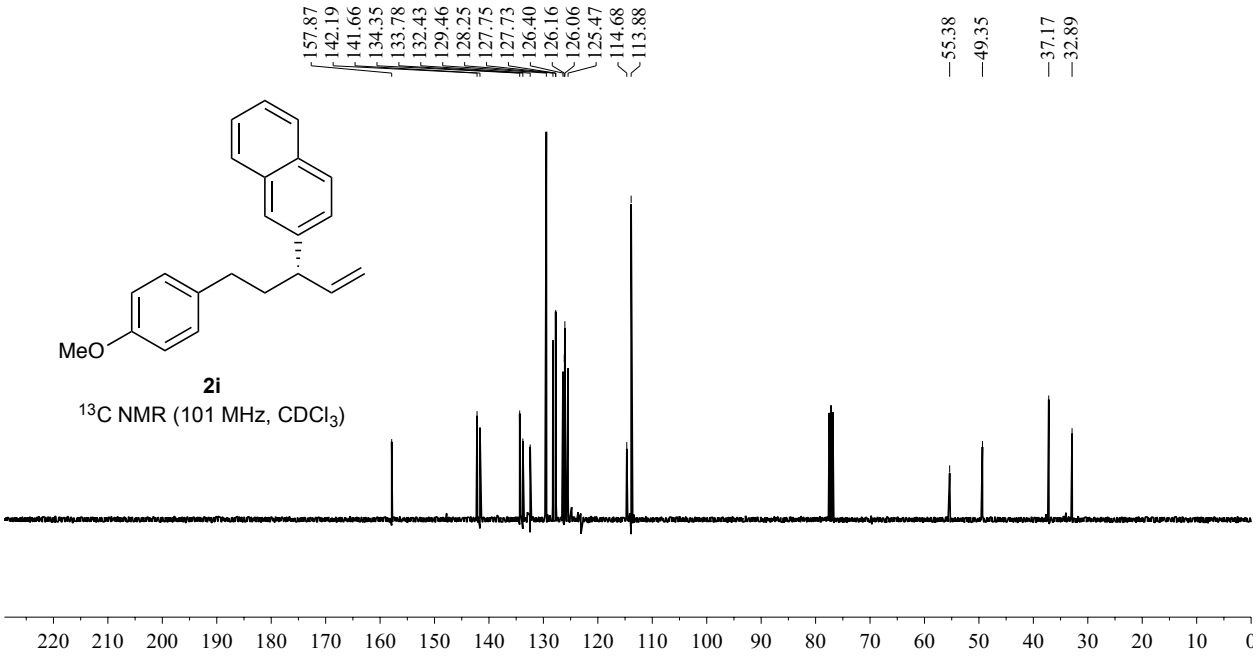

**2h**

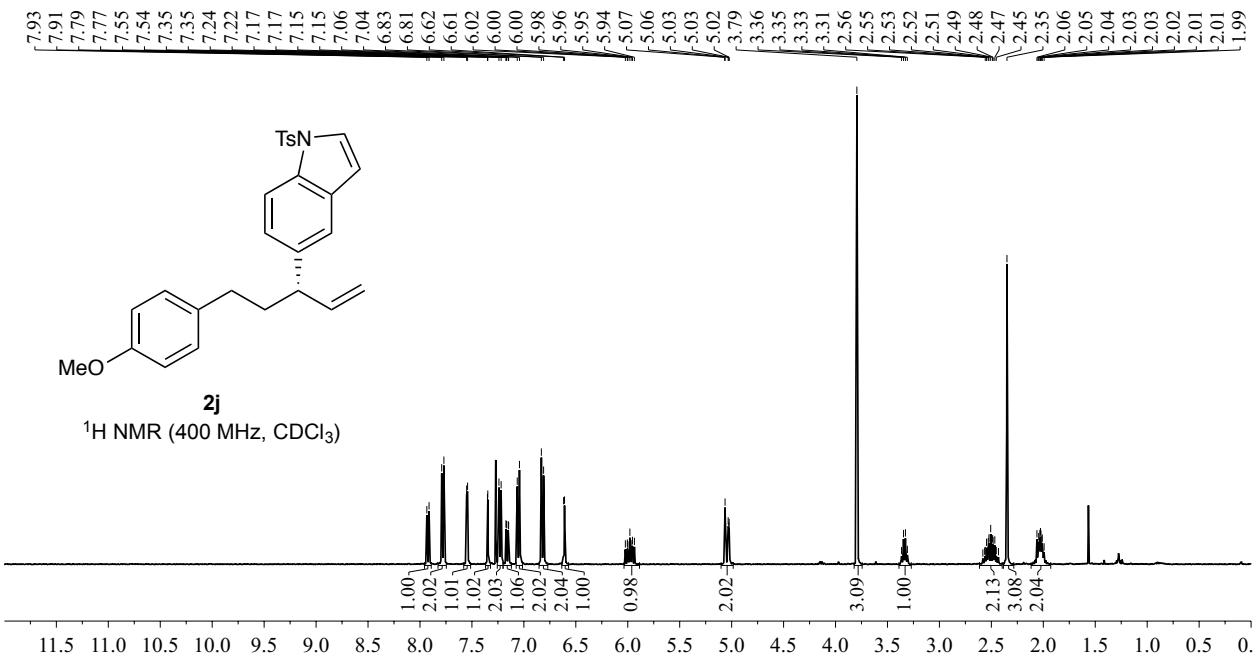
$^{13}C$ NMR (101 MHz, $CDCl_3$)

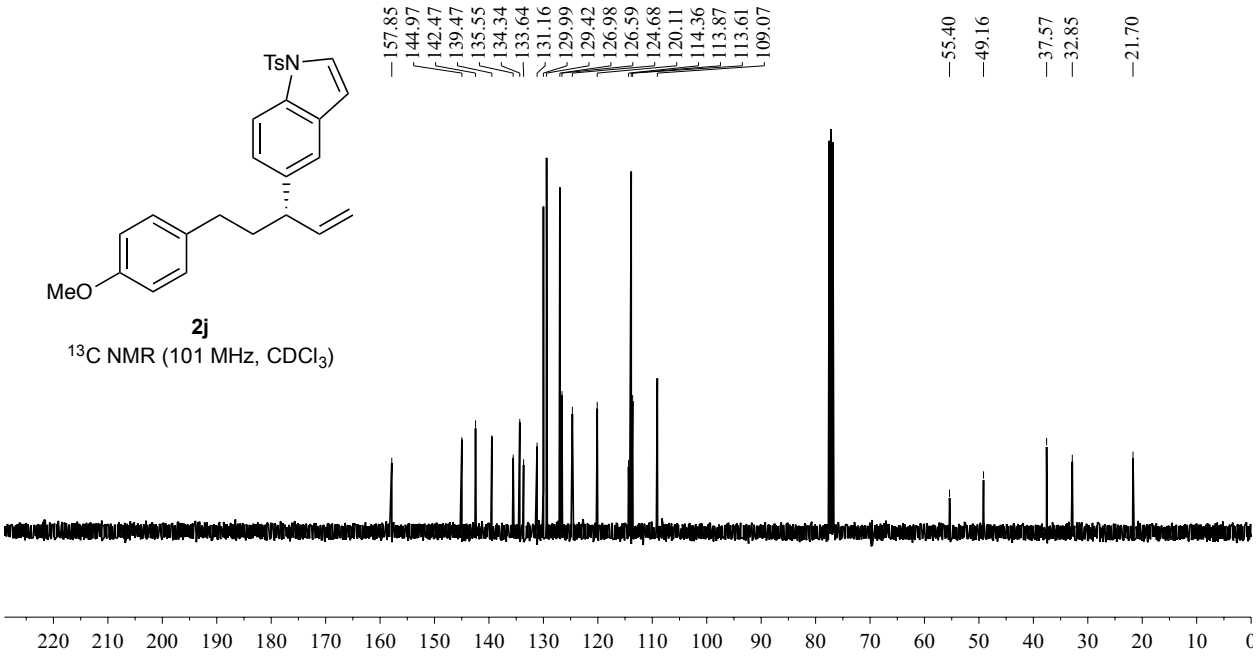



**2i**

$^{1}H$ NMR (400 MHz, $CDCl_3$)

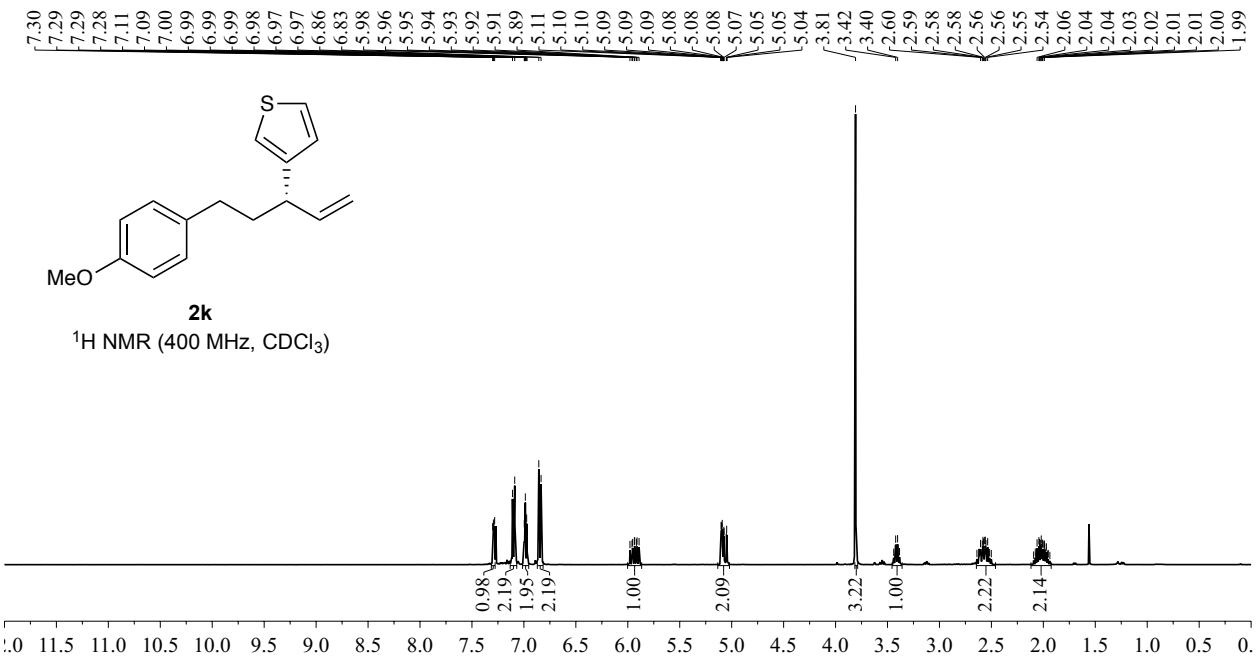

157.87
142.19
141.66
134.35
133.78
132.43
129.46
128.25
127.75
127.73
126.40
126.16
126.06
125.47
114.68
113.88
55.38
49.35
37.17
32.89
MeO
2i
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10


7.93
7.91
7.79
7.77
7.55
7.54
7.35
7.35
7.24
7.22
7.17
7.17
7.15
7.15
7.06
7.04
6.83
6.81
6.62
6.61
6.02
6.00
6.00
5.98
5.96
5.95
5.94
5.07
5.06
5.03
5.03
5.02
3.79
3.36
3.35
3.33
3.31
2.56
2.55
2.53
2.52
2.51
2.49
2.48
2.47
2.45
2.35
2.06
2.05
2.04
2.03
2.03
2.02
2.01
2.01
1.99
TsN
MeO
2j
1H NMR (400 MHz, CDCl3)
1.00
2.02
1.01
1.02
2.03
1.06
2.02
2.04
1.00
0.98
2.02
3.09
1.00
2.13
3.08
2.04
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5



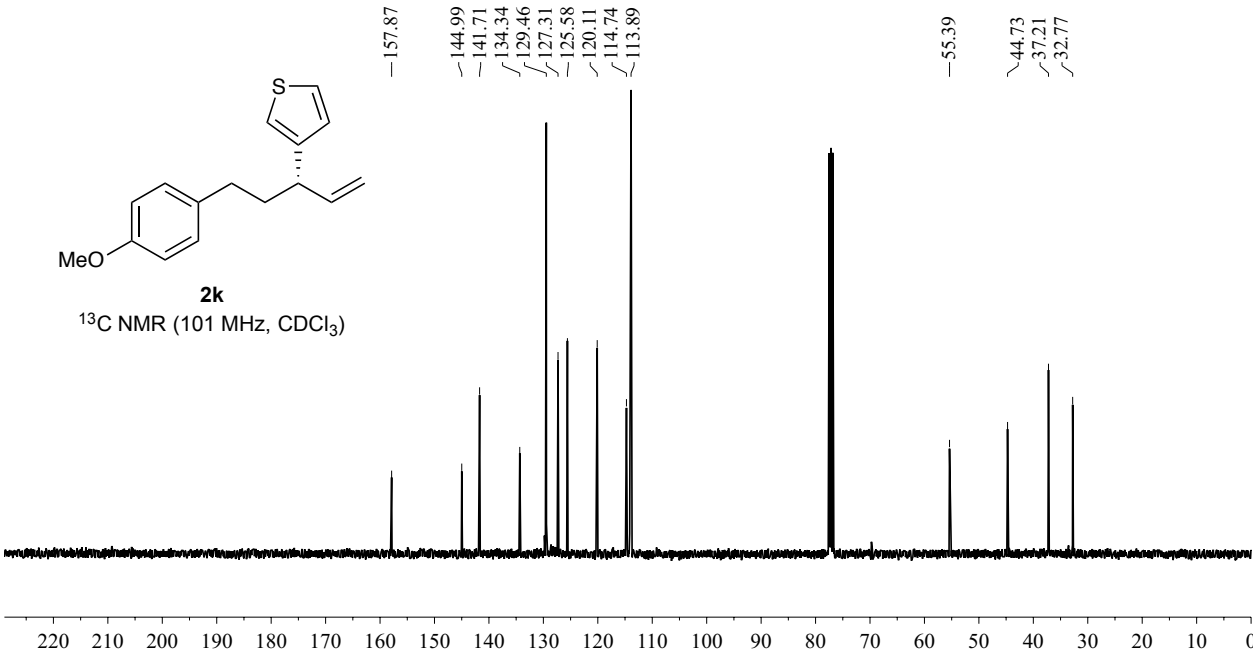

**2j**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



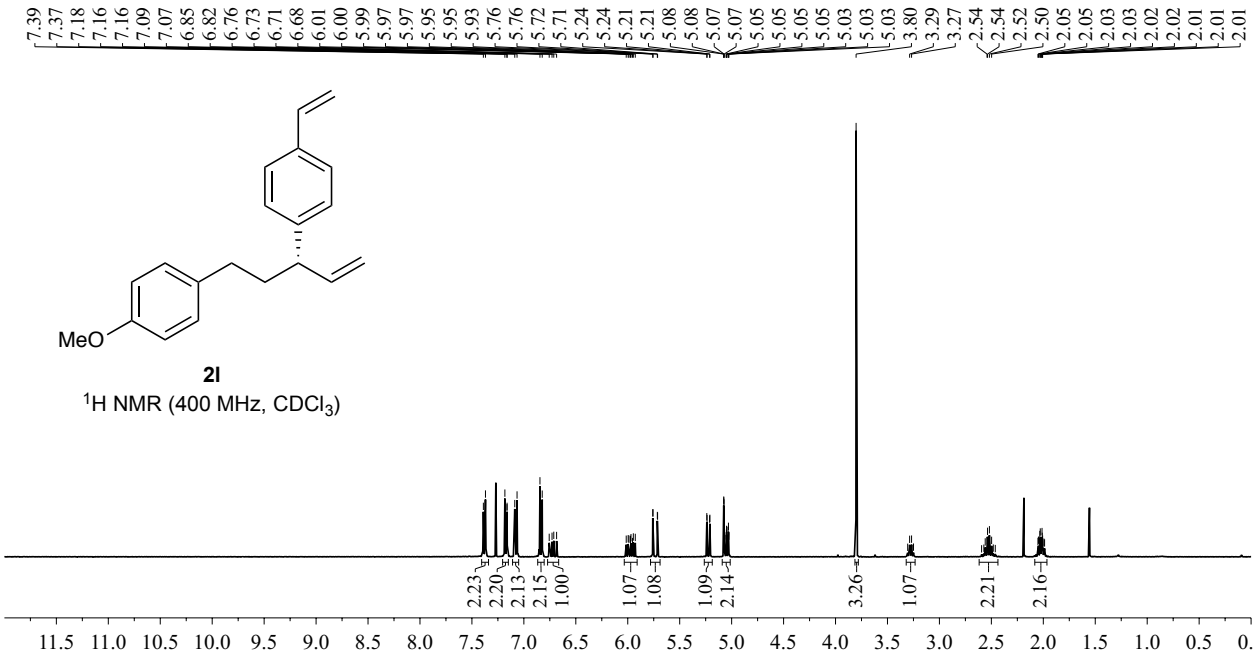

**2k**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



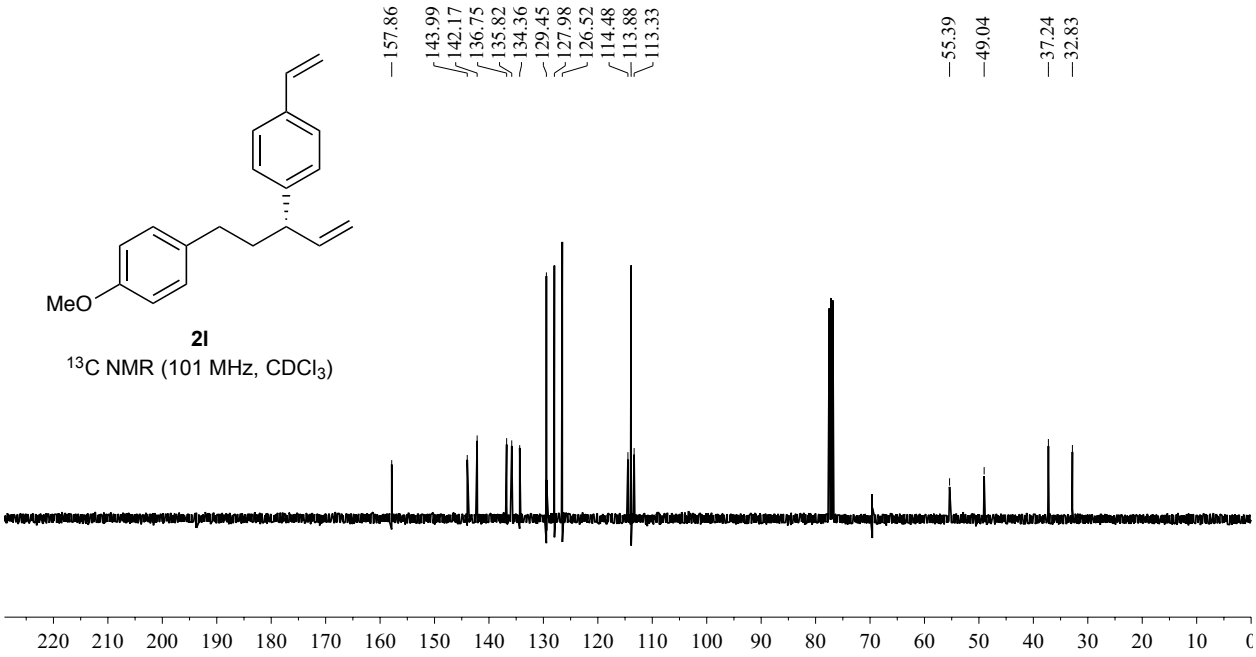

**2k**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



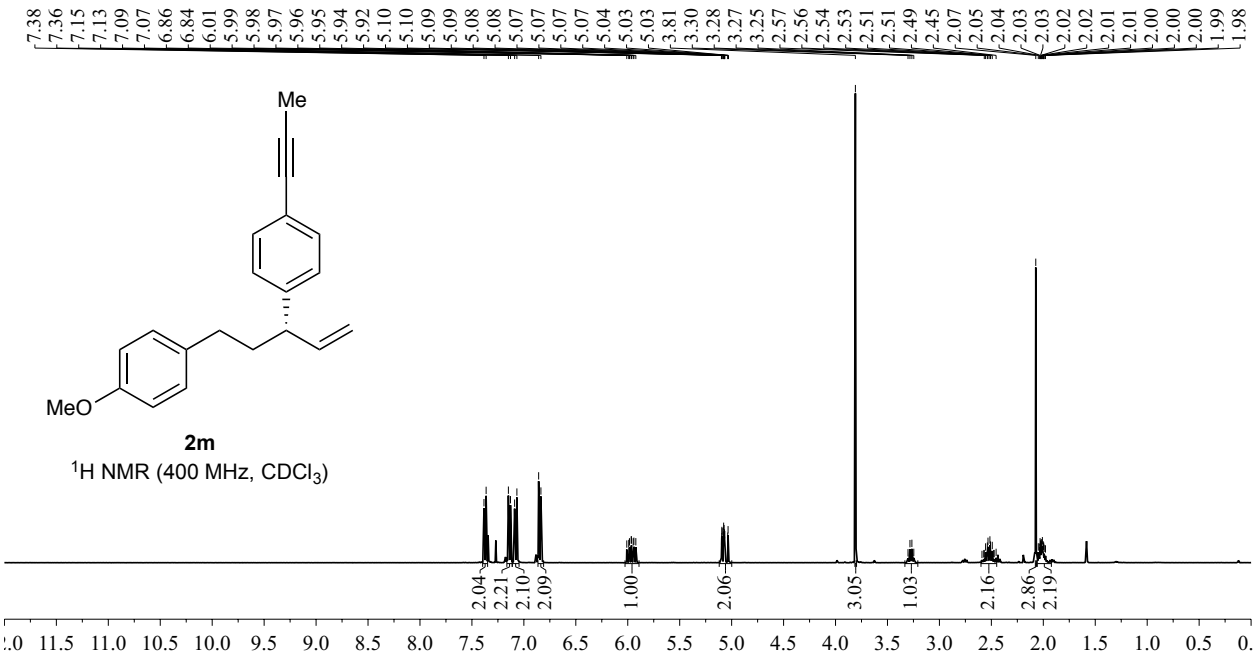

**2l**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



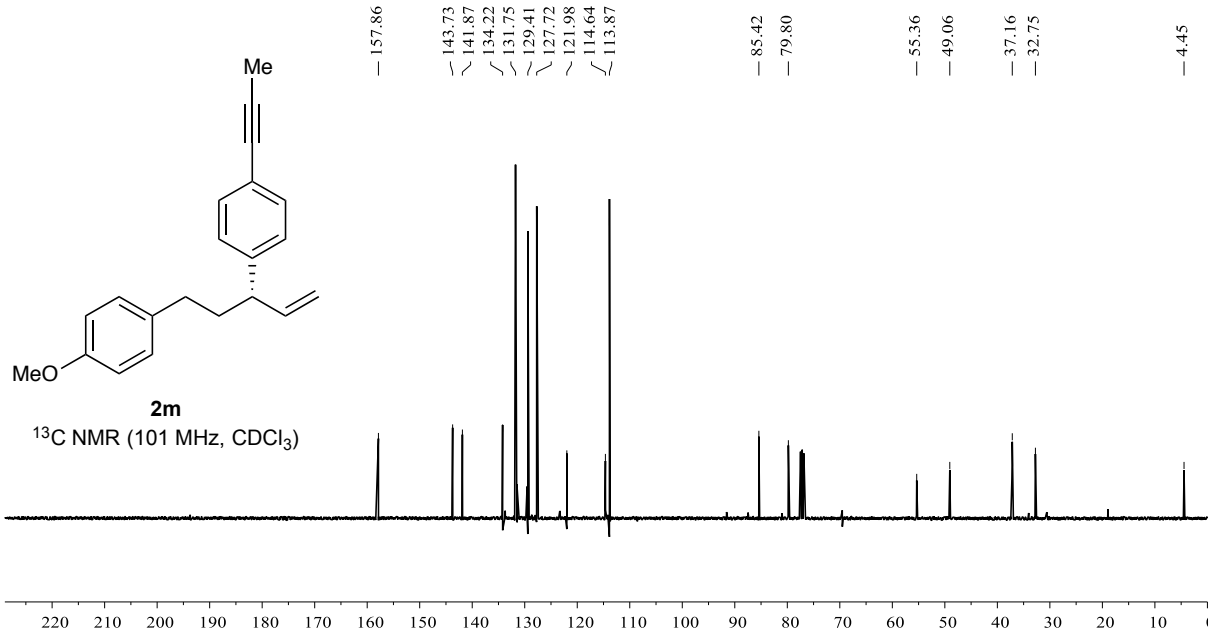

**2l**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



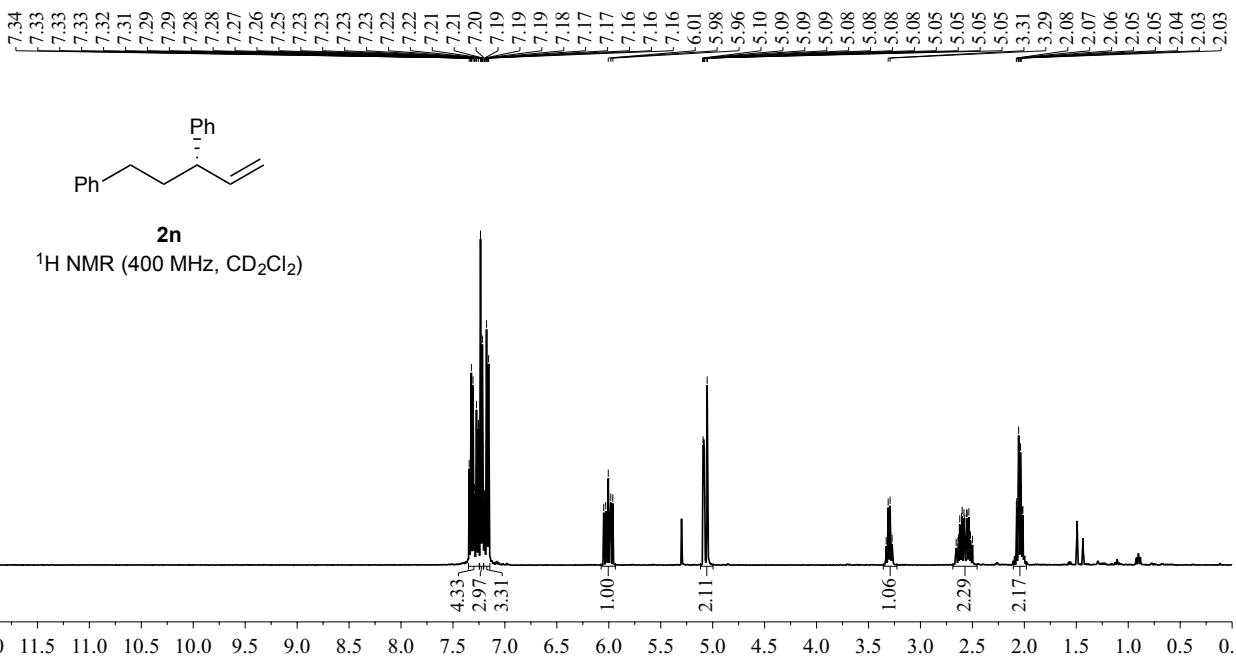

**2m**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



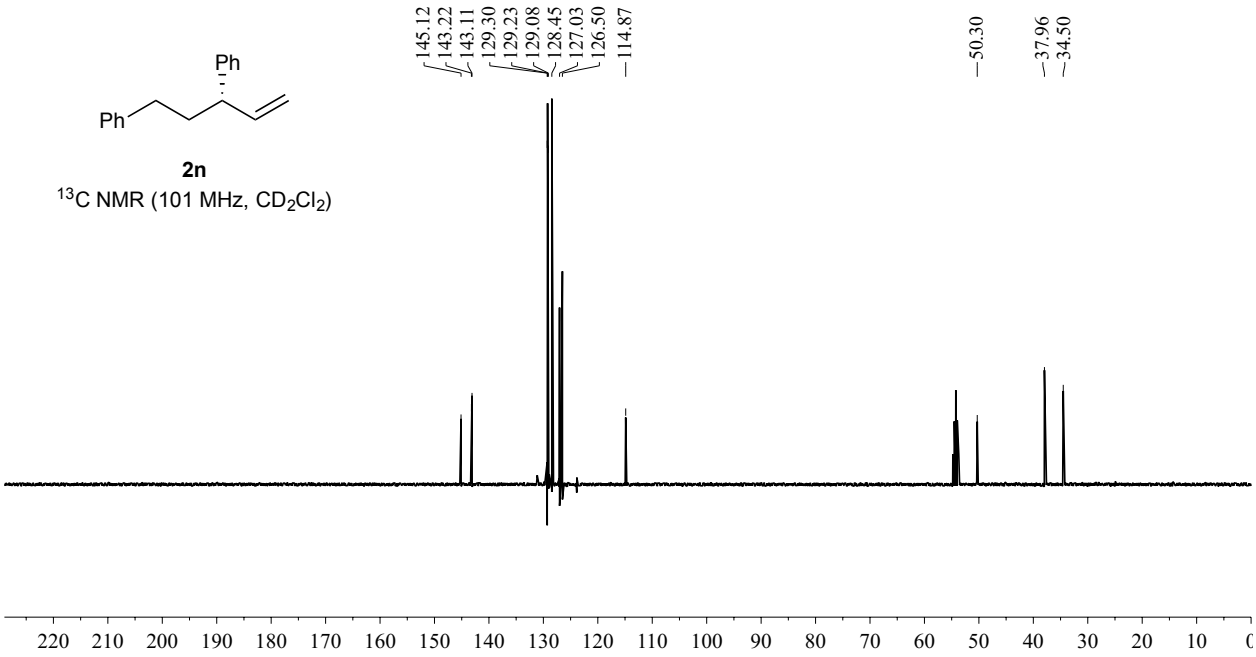

**2m**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



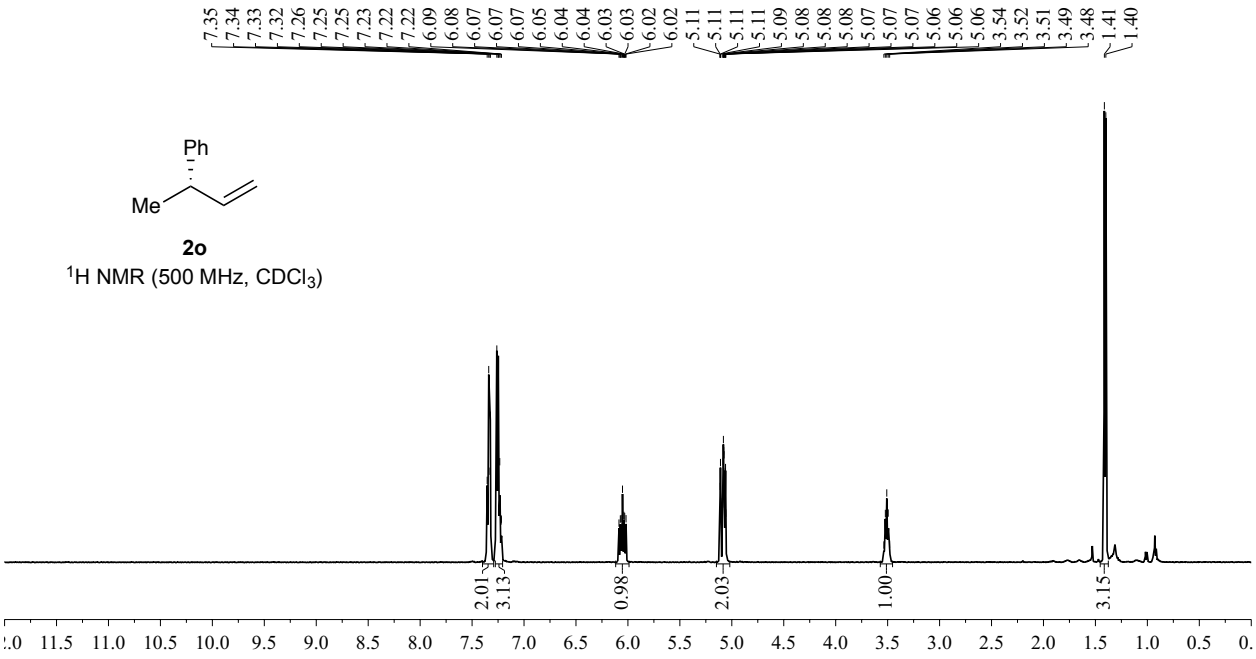

**2n**

$^{1}H$ NMR (400 MHz, $CD_2Cl_2$)



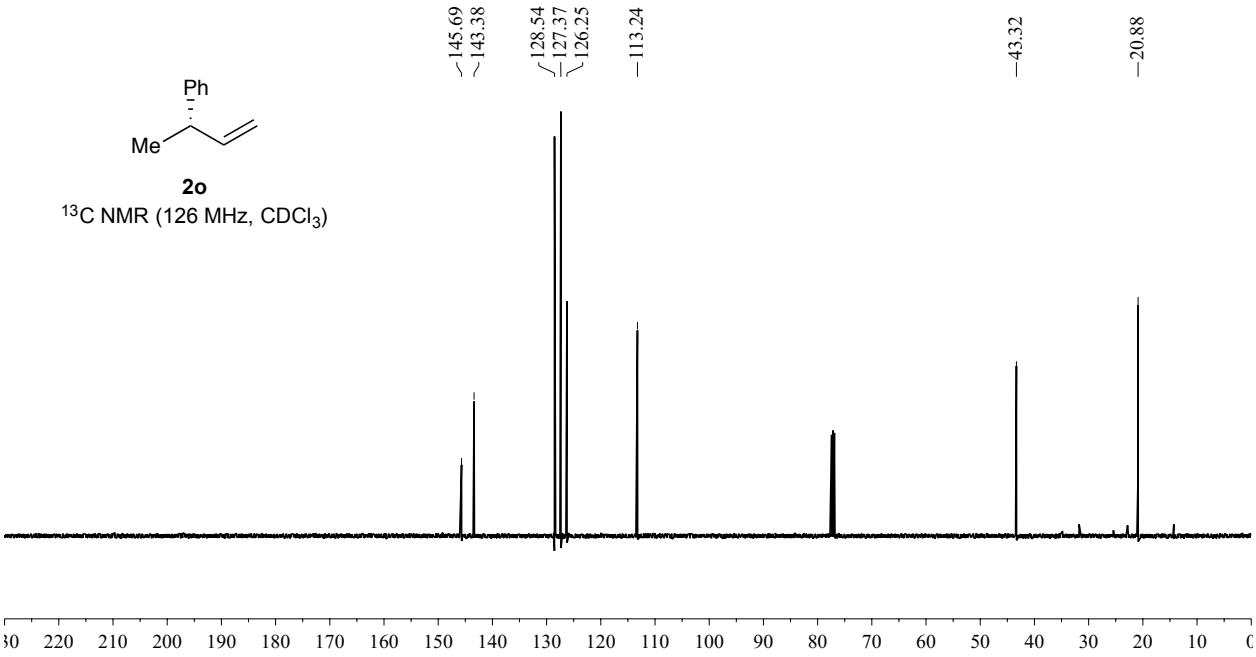

**2n**

$^{13}C$ NMR (101 MHz, $CD_2Cl_2$)



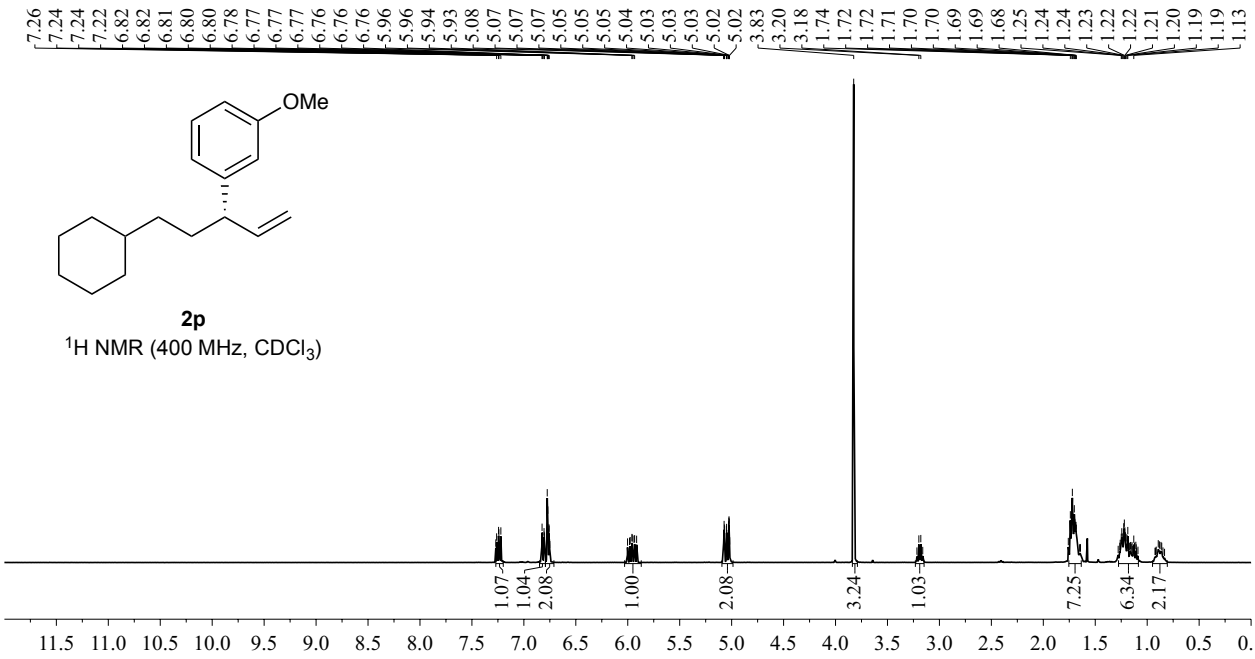

**2o**

$^{1}H$ NMR (500 MHz, $CDCl_3$)



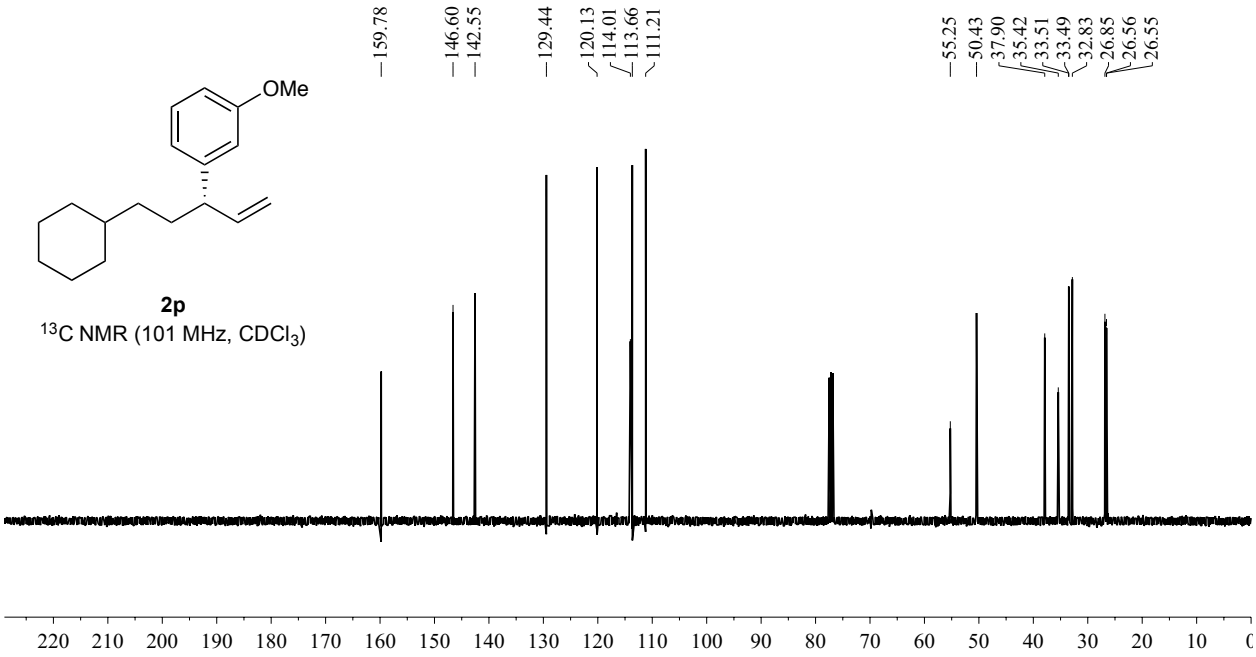

**2o**

$^{13}C$ NMR (126 MHz, $CDCl_3$)



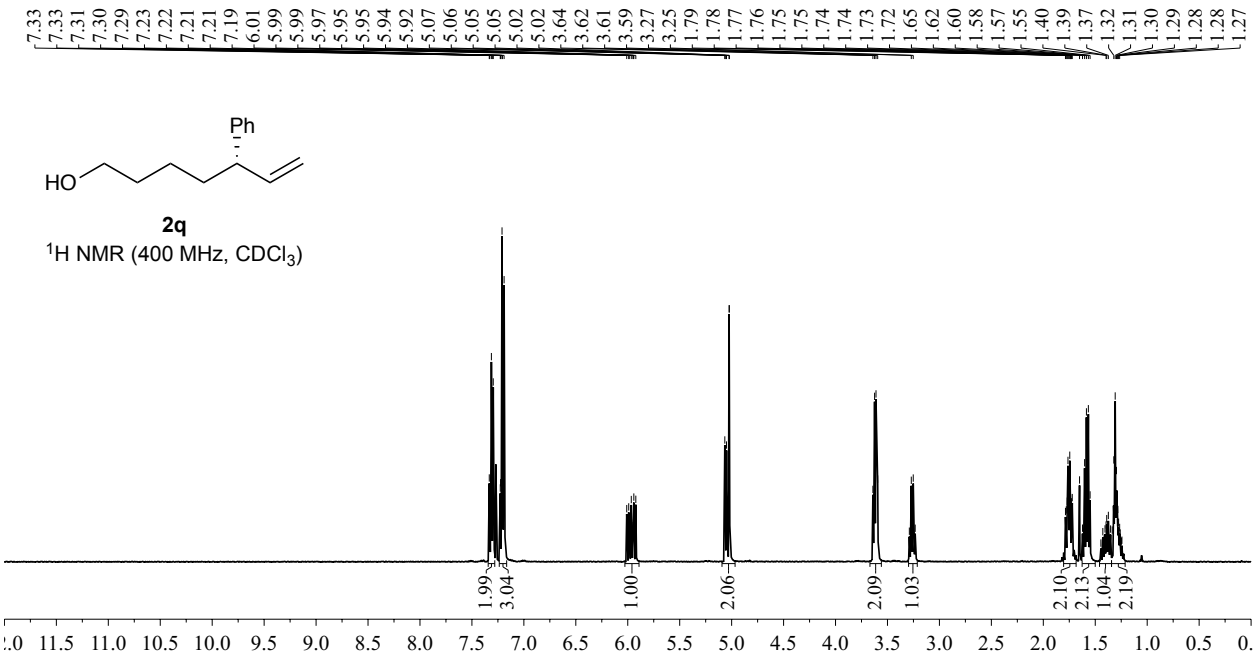

**2p**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



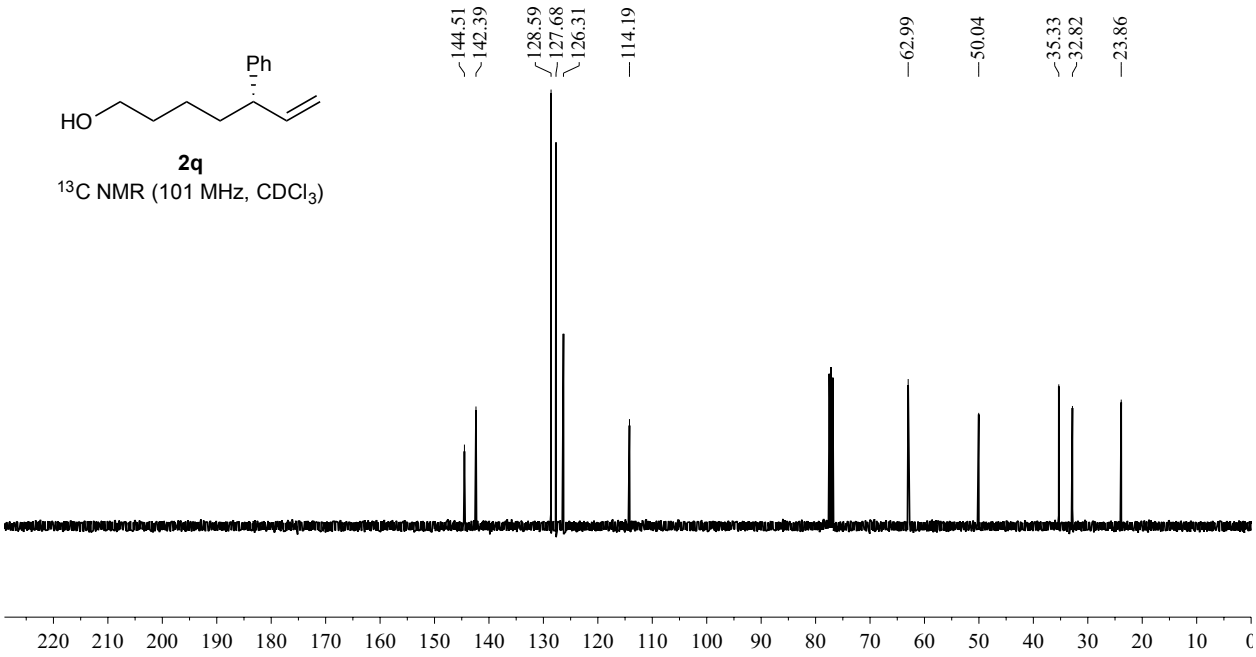

**2p**

$^{13}$C NMR (101 MHz, $CDCl_3$)



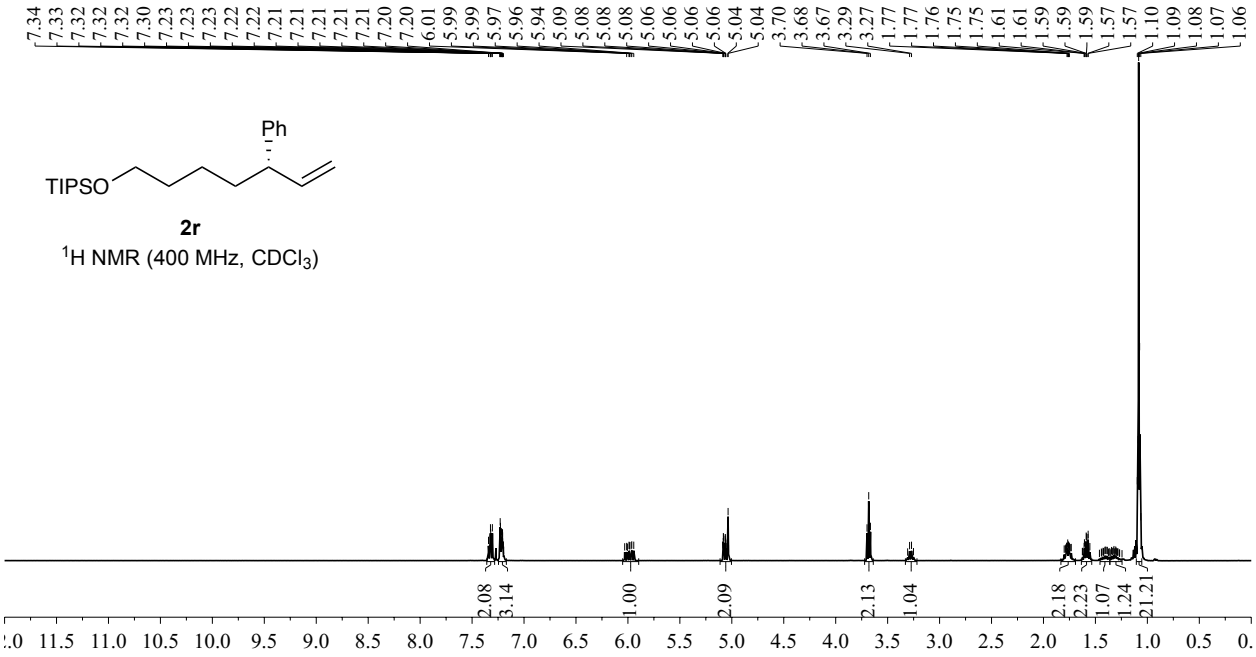

**2q**

$^{1}$H NMR (400 MHz, $CDCl_3$)



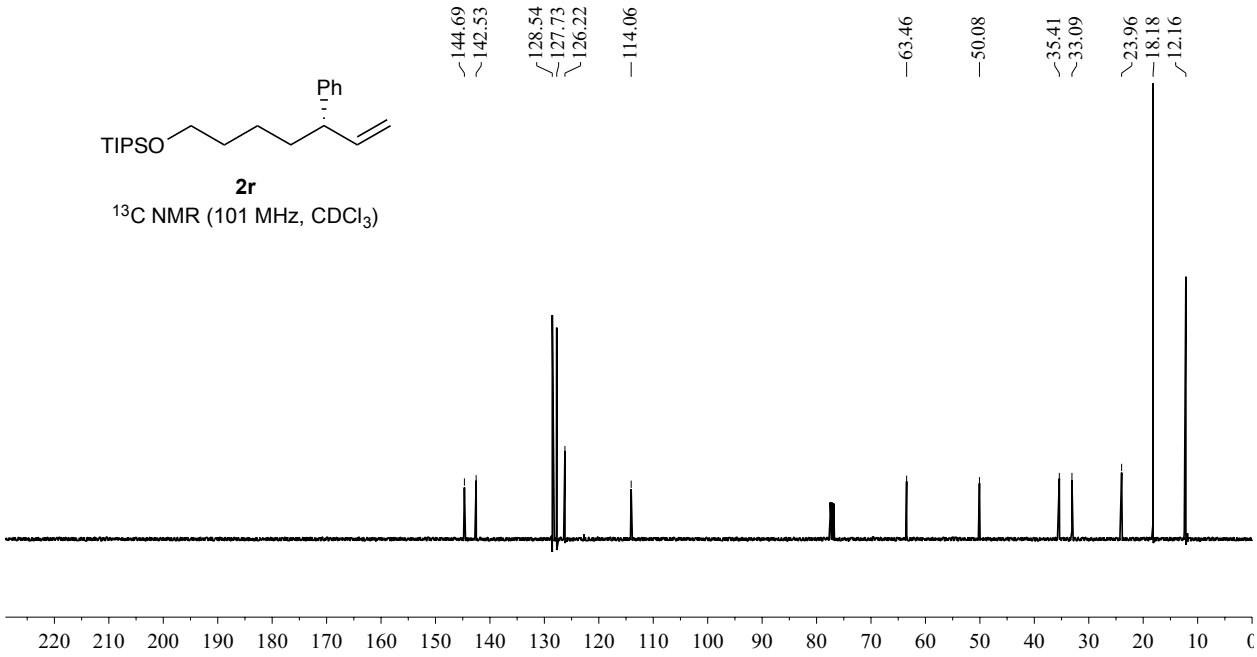

**2q**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



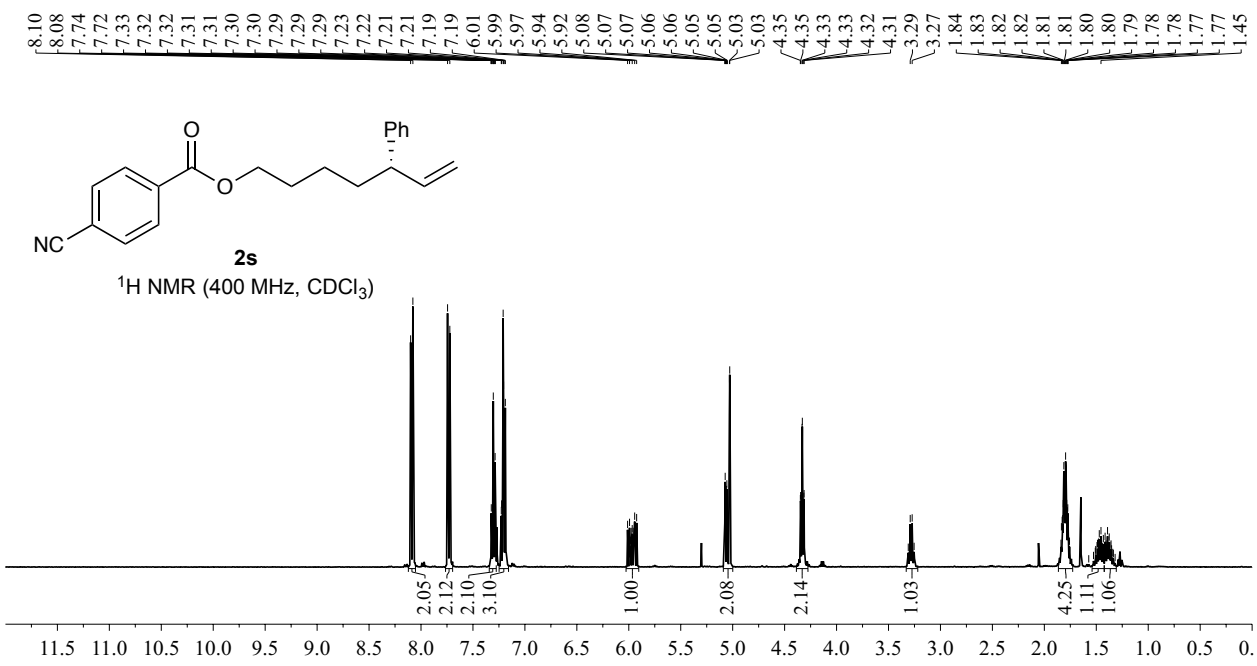

**2r**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



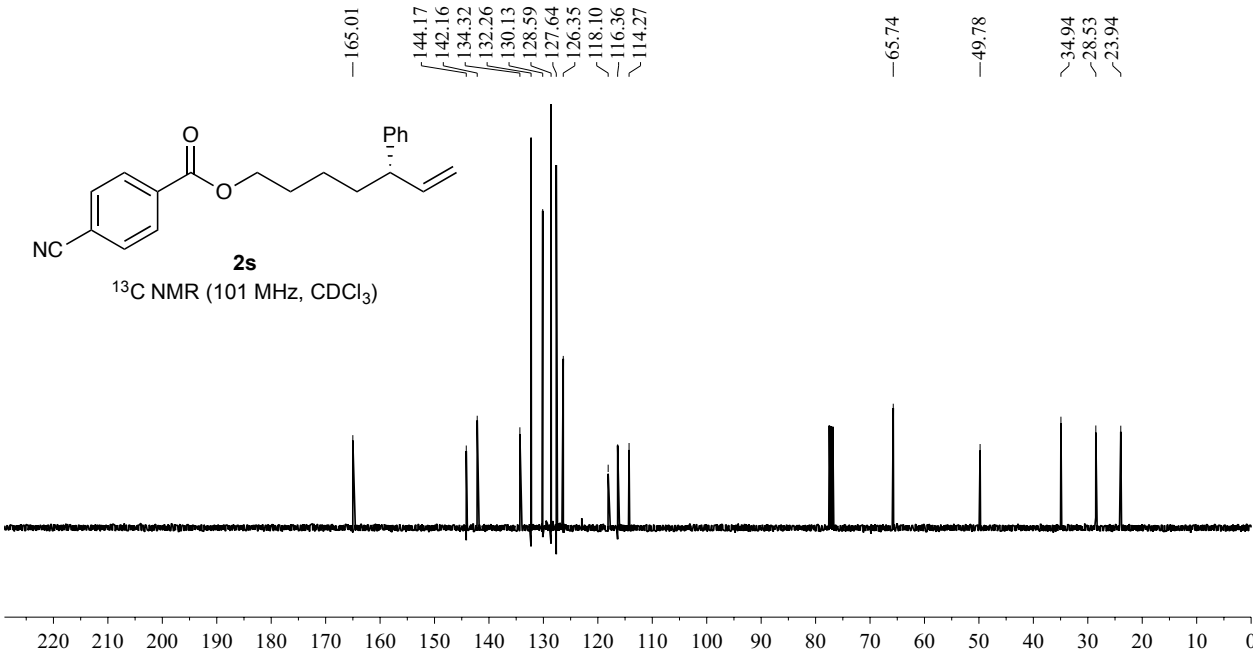

**2r**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



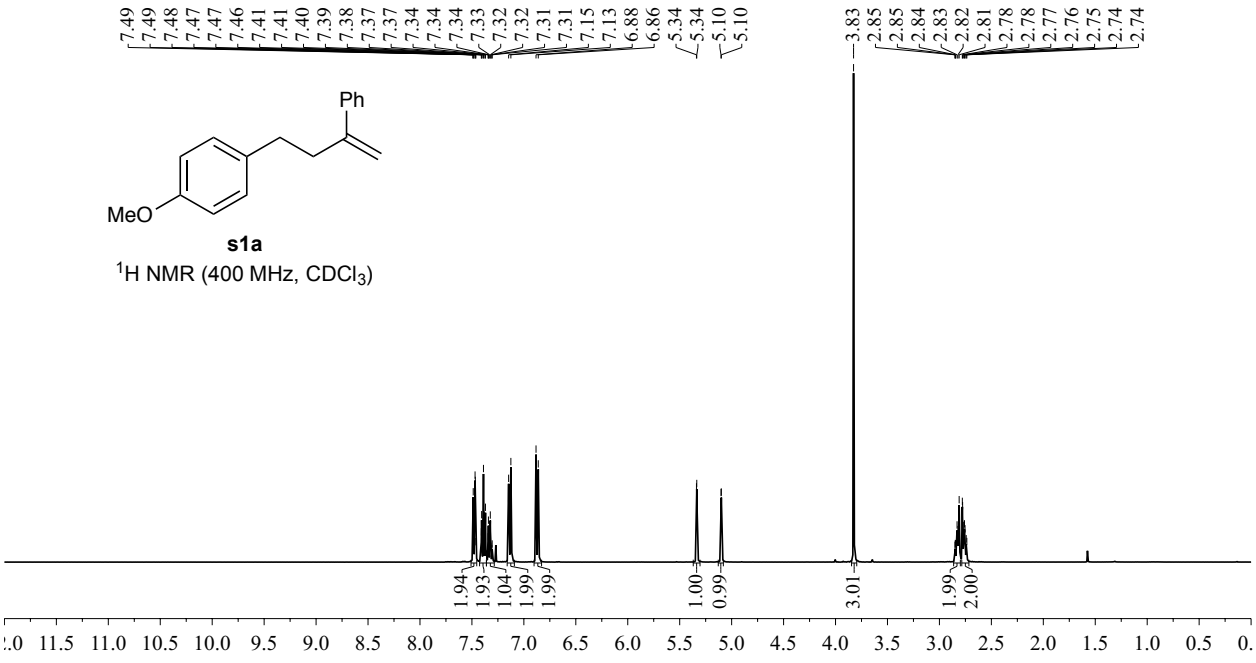

**2s**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



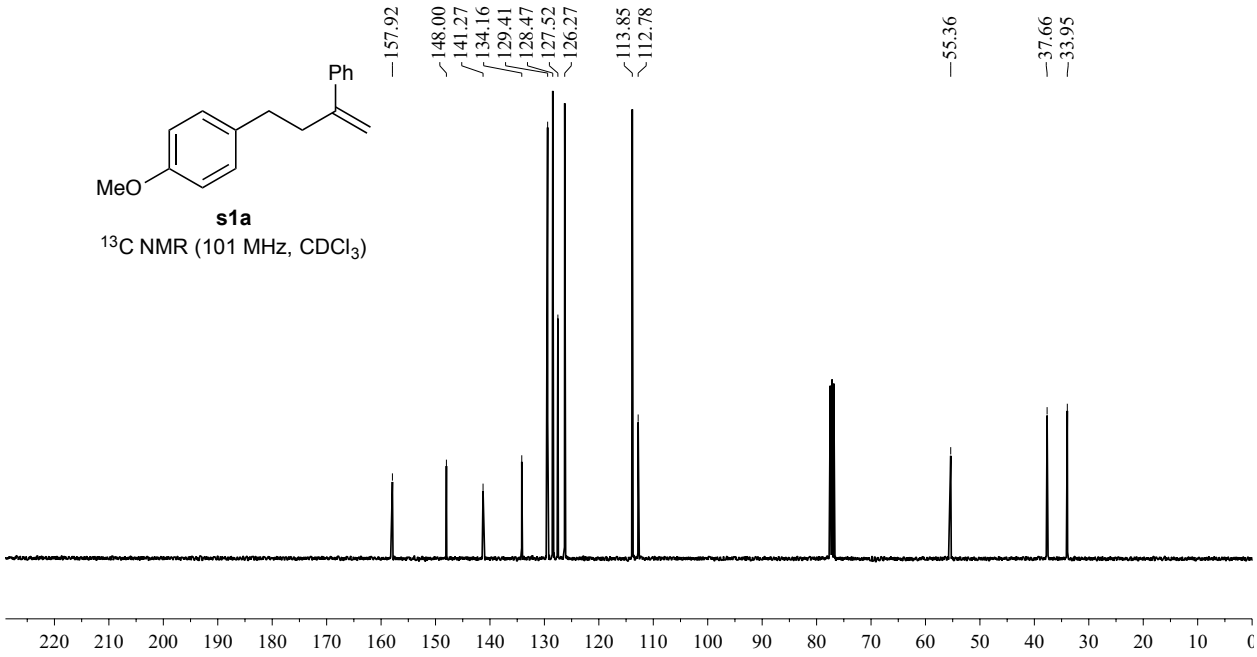

**2s**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



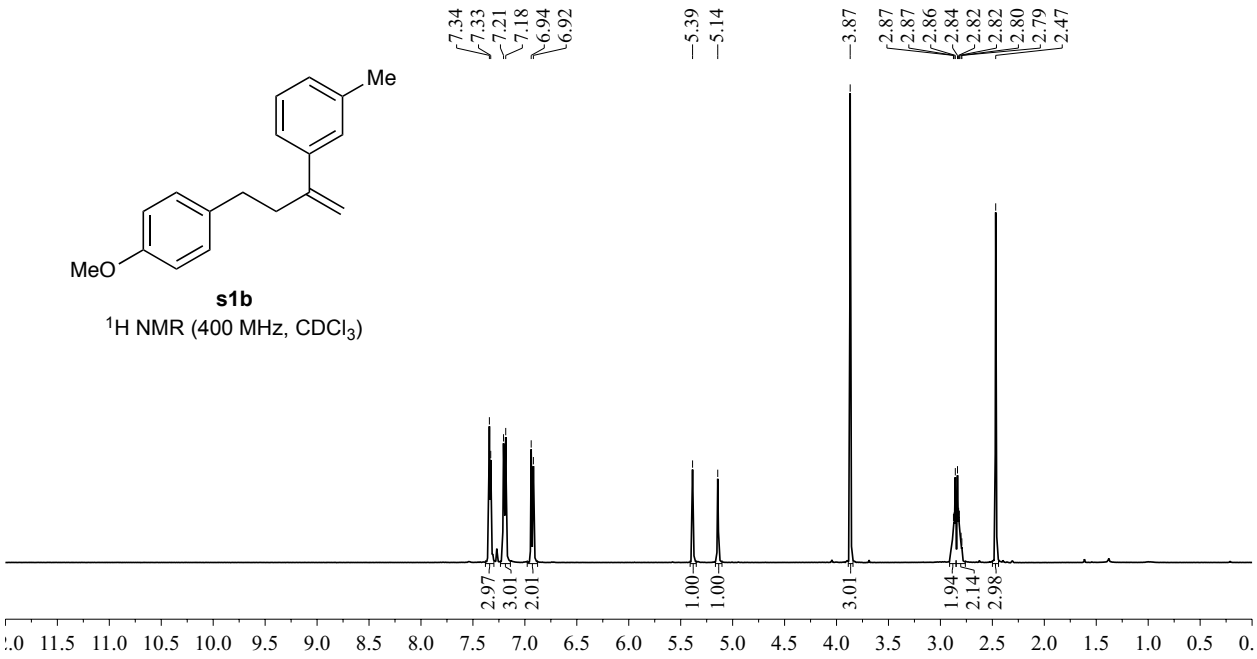

**s1a**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



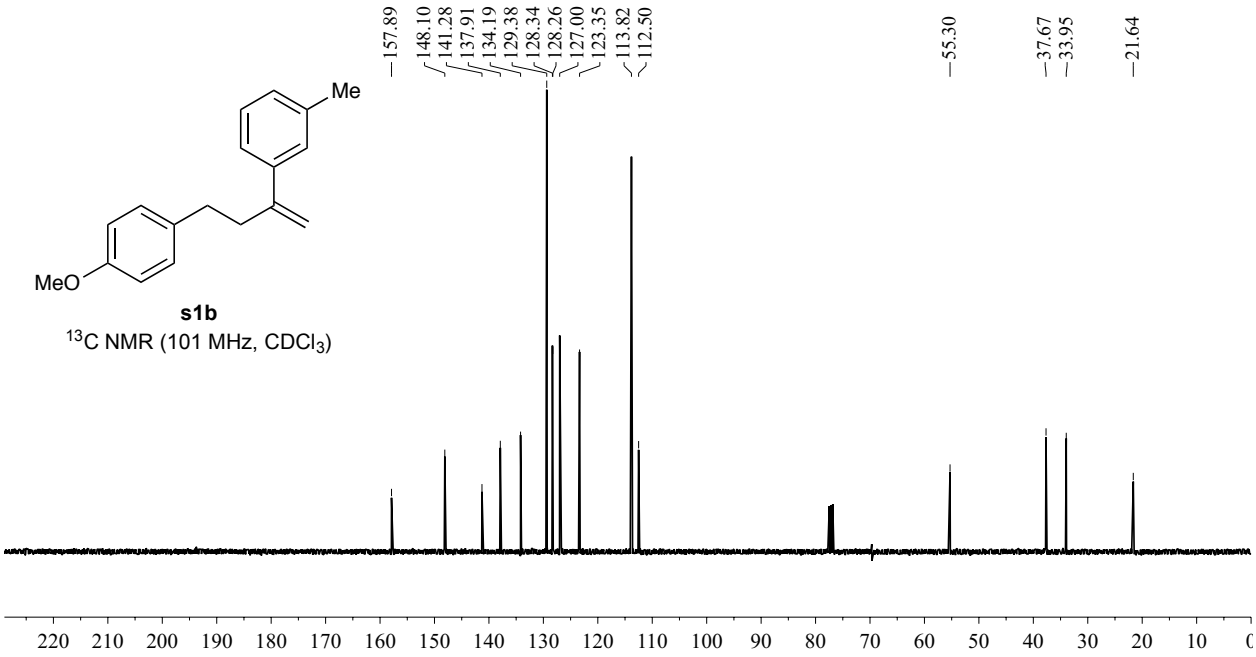

**s1a**

$^{13}$C NMR (101 MHz, $CDCl_3$)



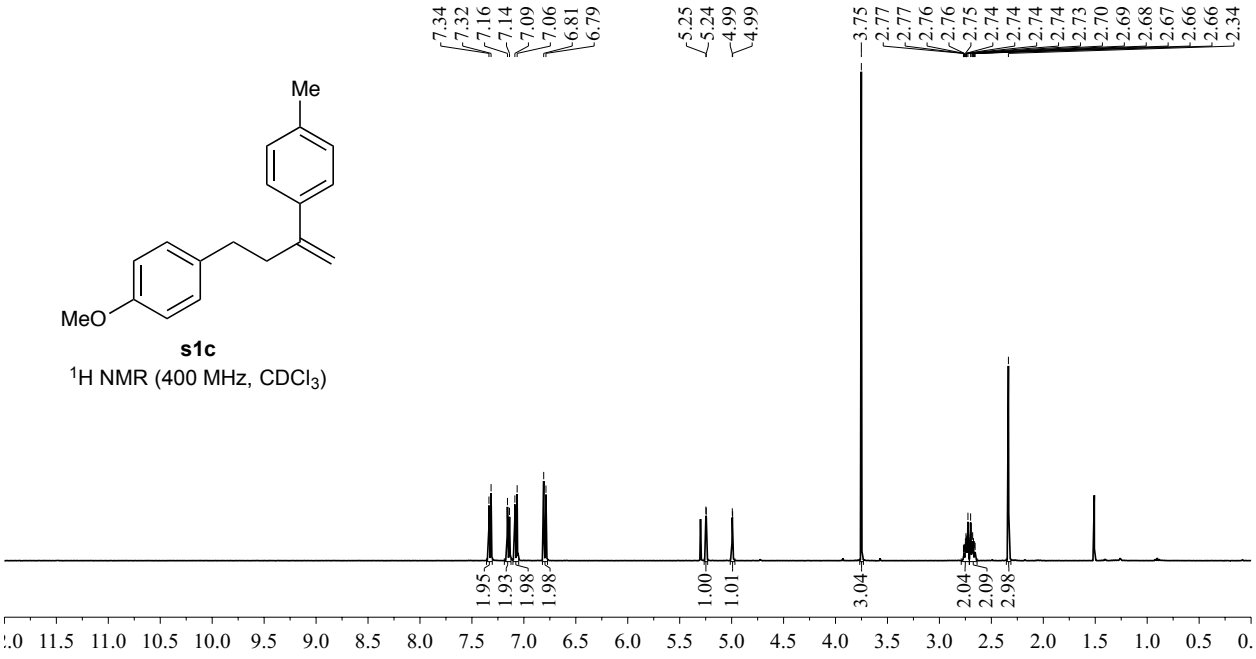

**s1b**

$^{1}$H NMR (400 MHz, $CDCl_3$)



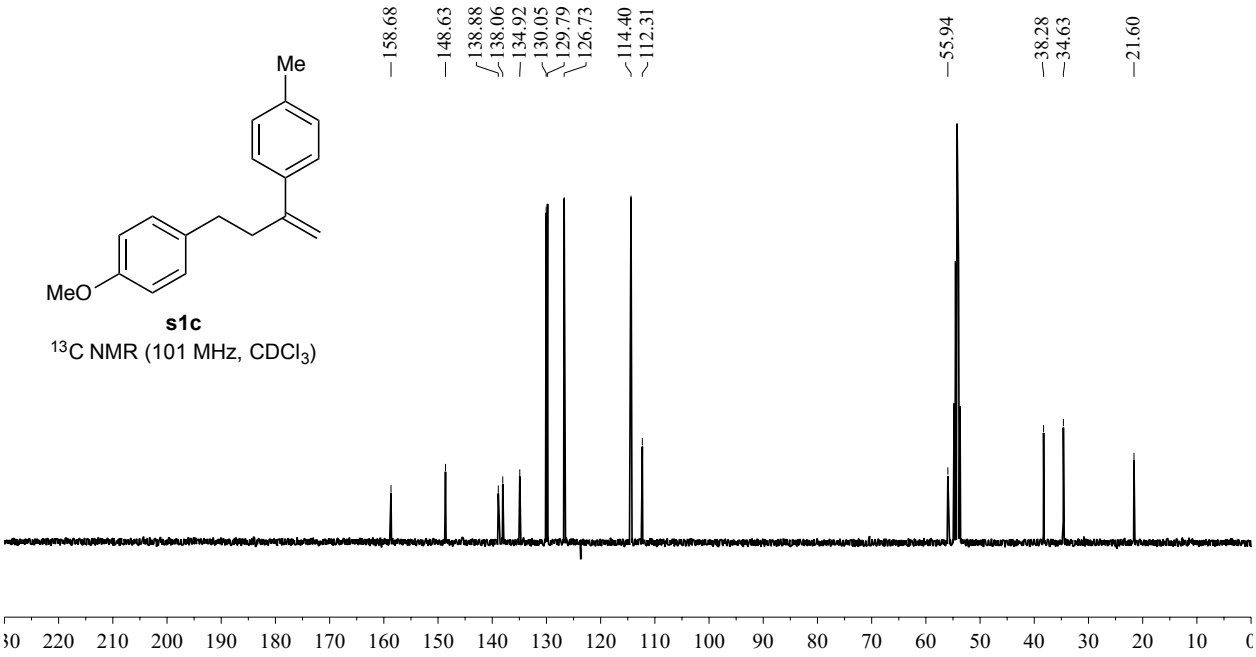

**s1b**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



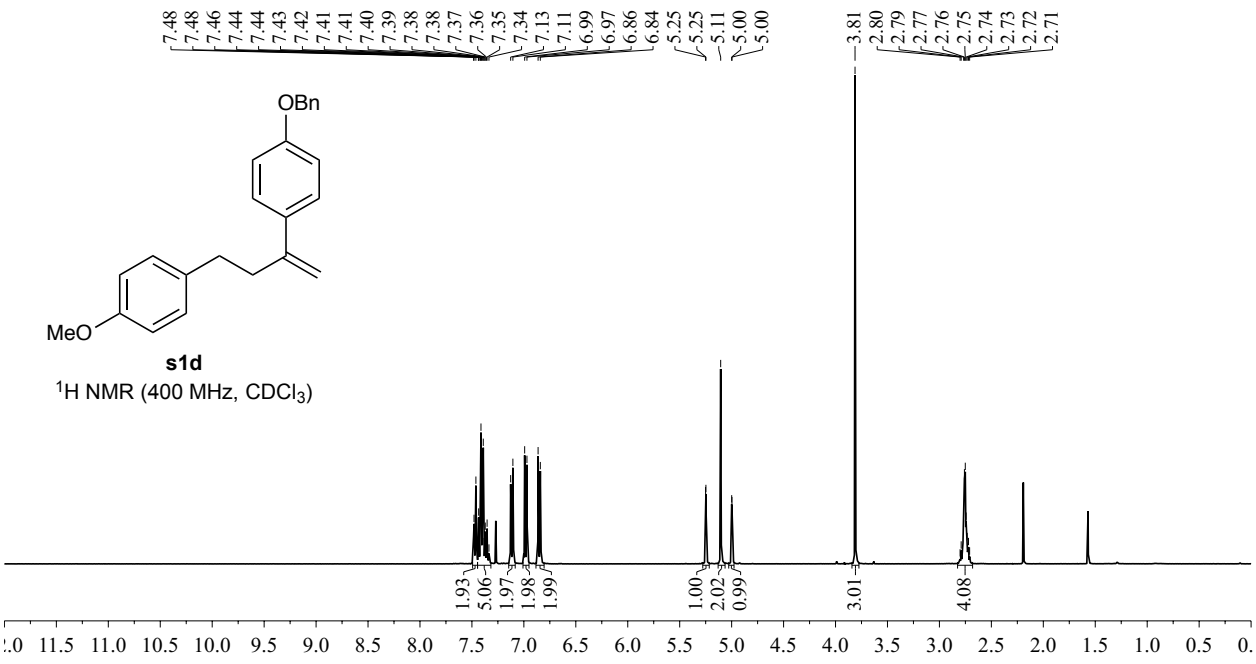

**s1c**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



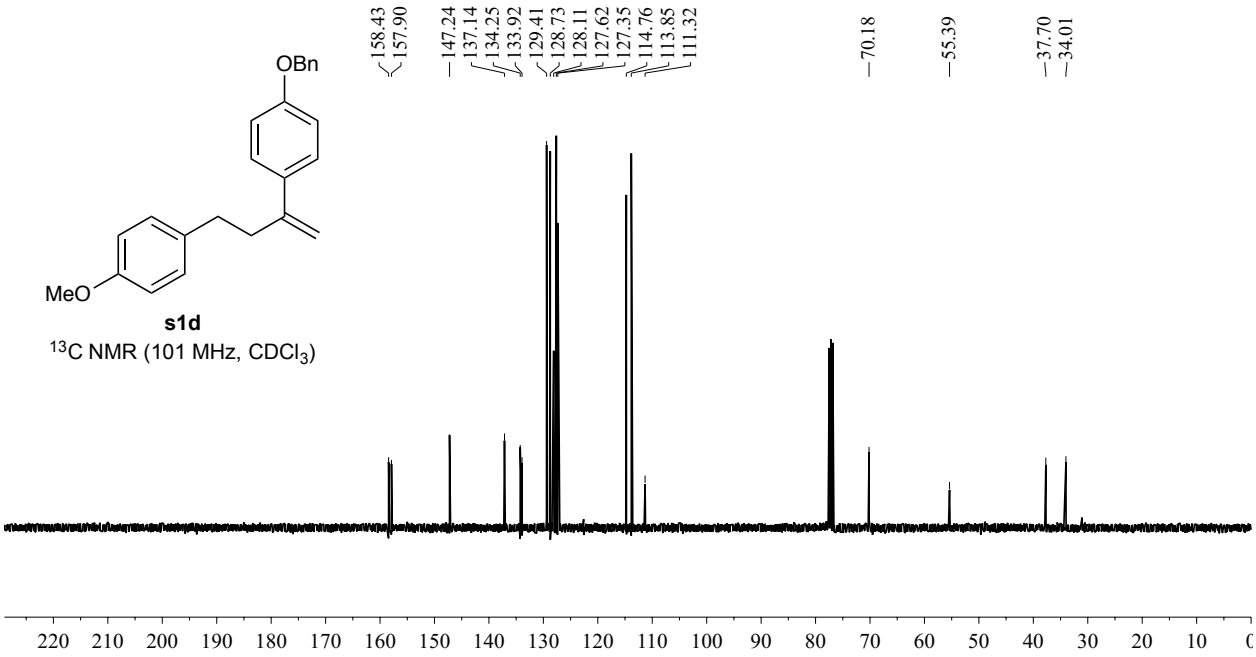

**s1c**

$^{13}$C NMR (101 MHz, $CDCl_3$)



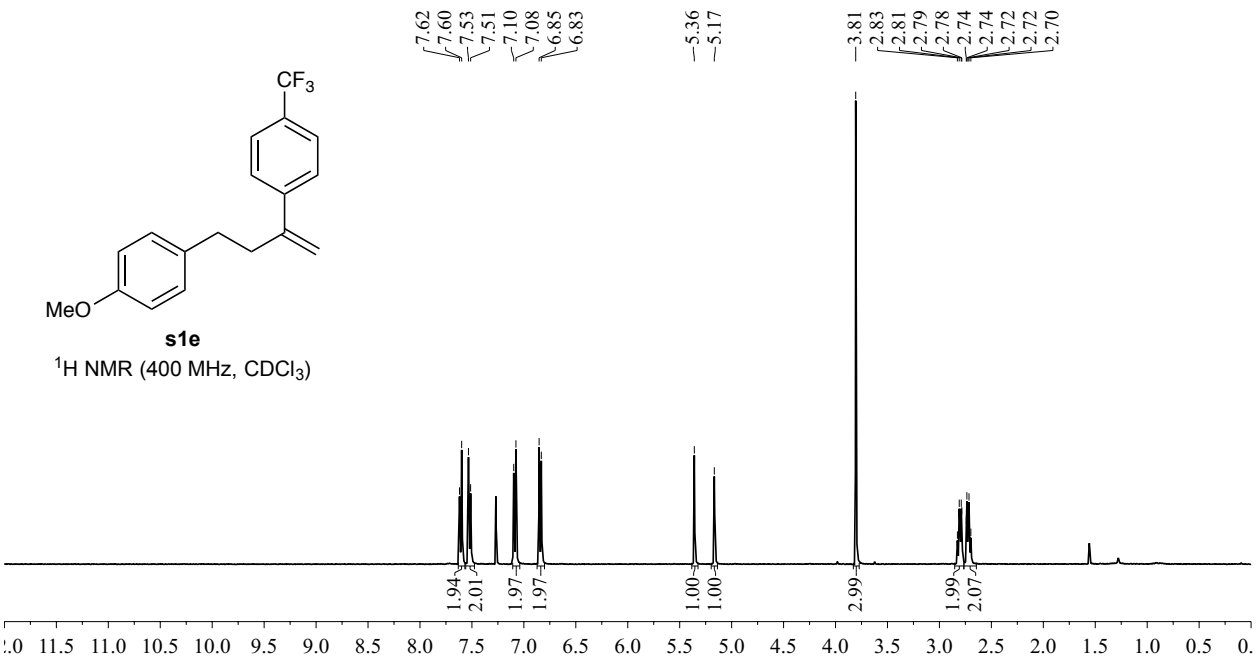

**s1d**

$^{1}$H NMR (400 MHz, $CDCl_3$)



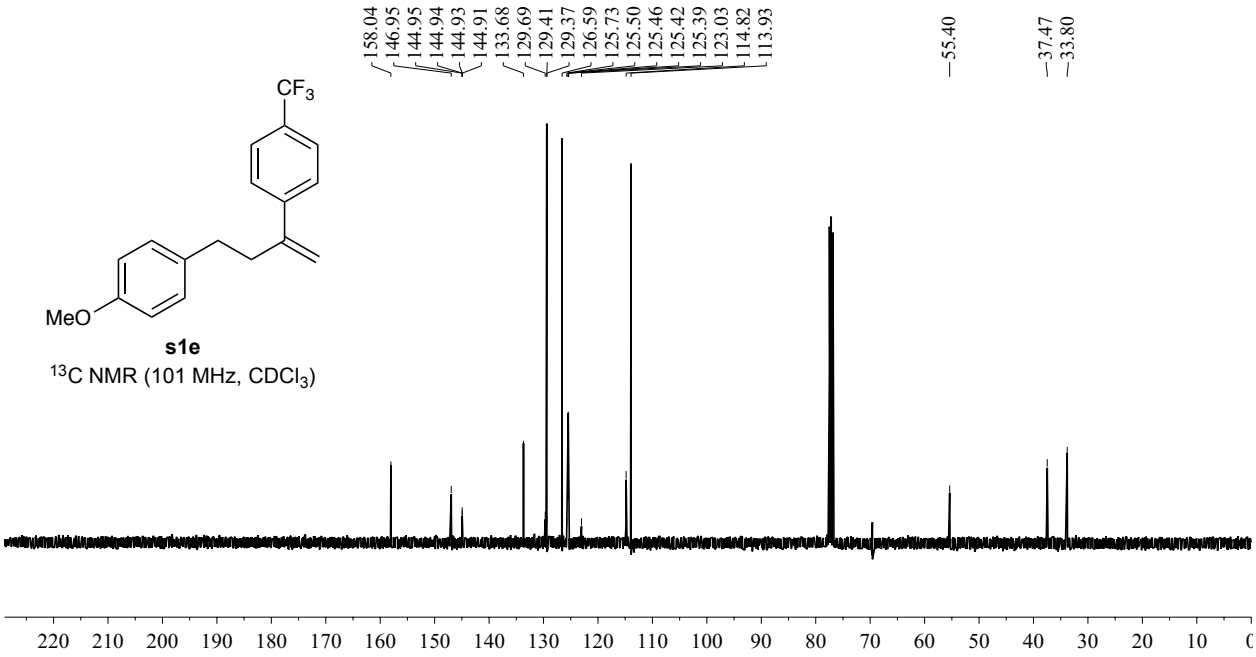

**s1d**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



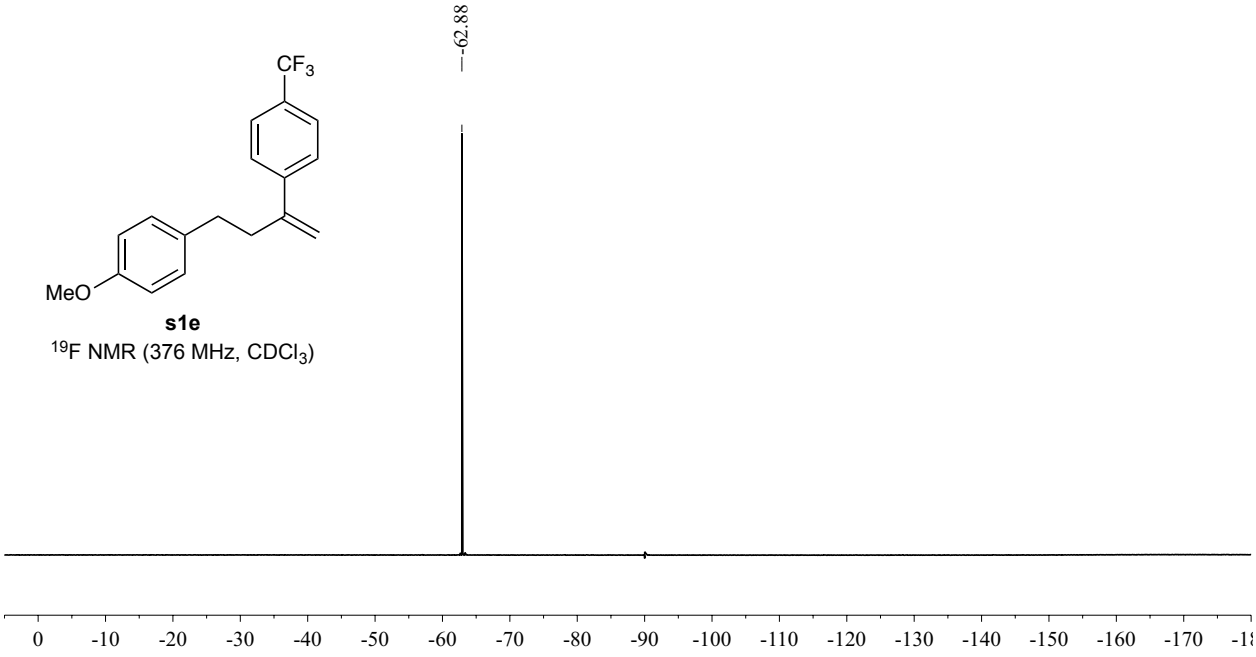

**s1e**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



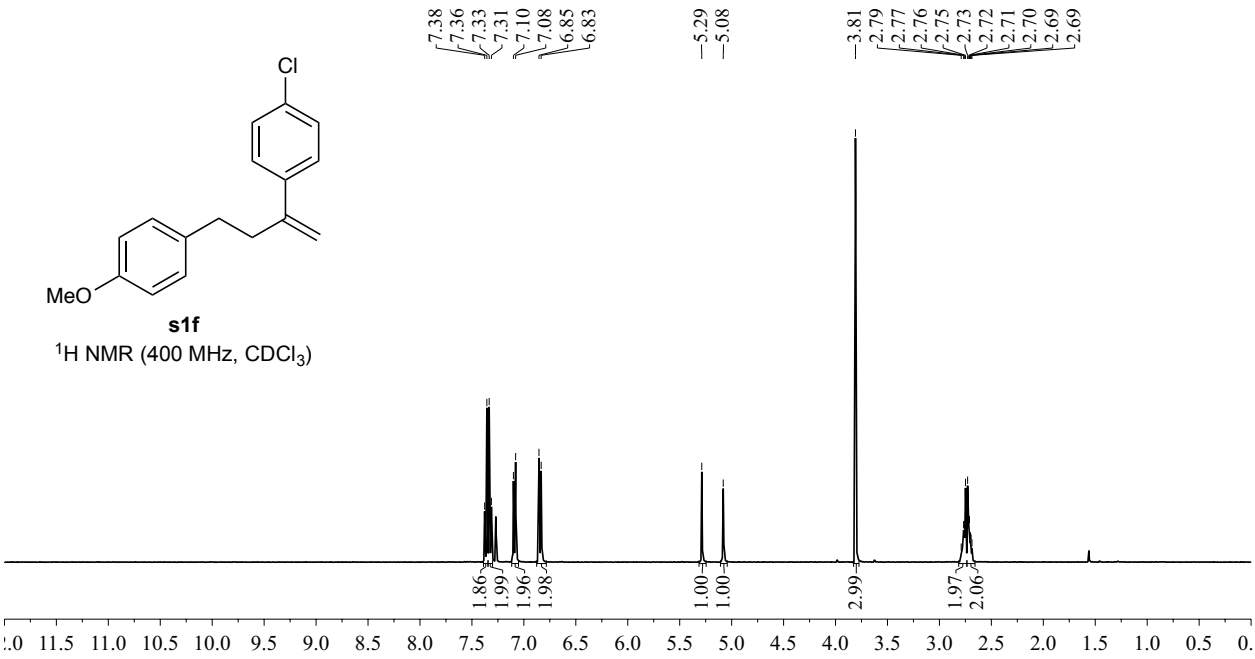

**s1e**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



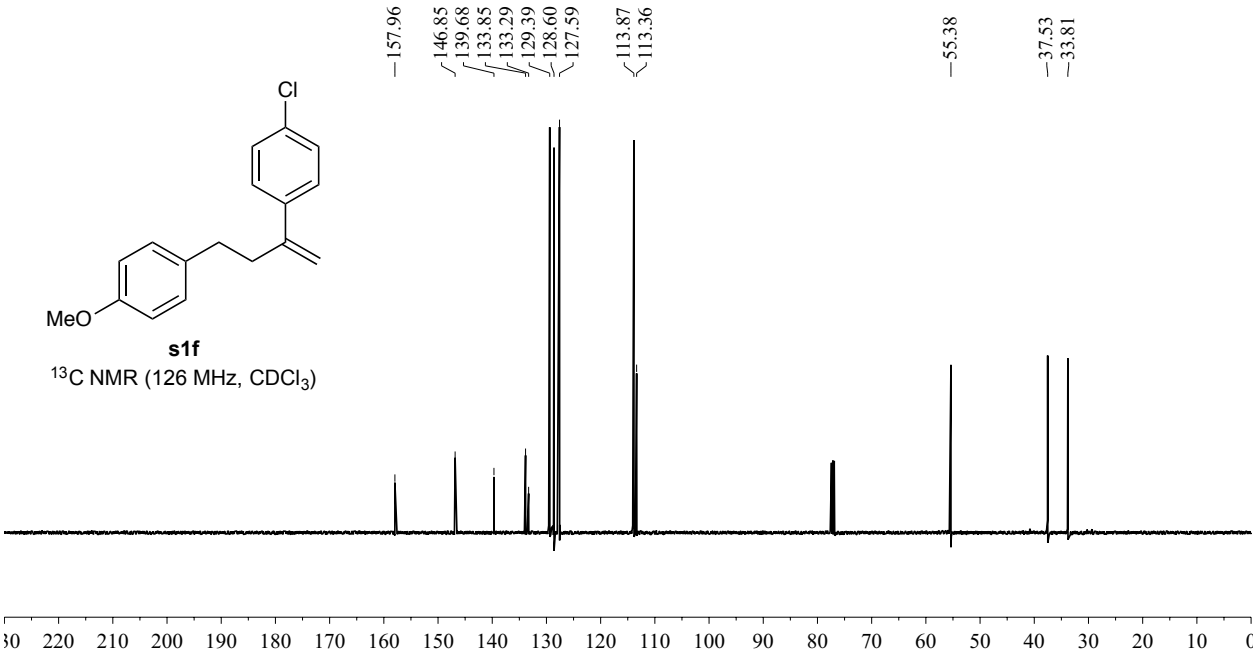

**s1e**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



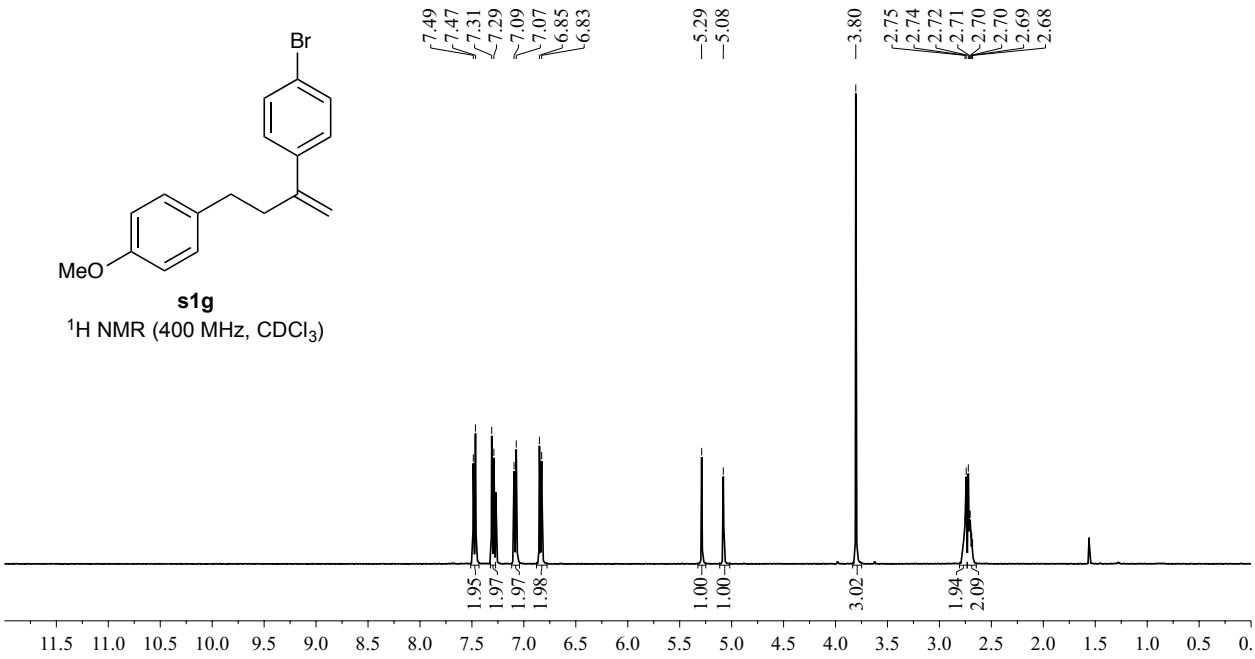

**s1f**

$^{1}$H NMR (400 MHz, $CDCl_3$)



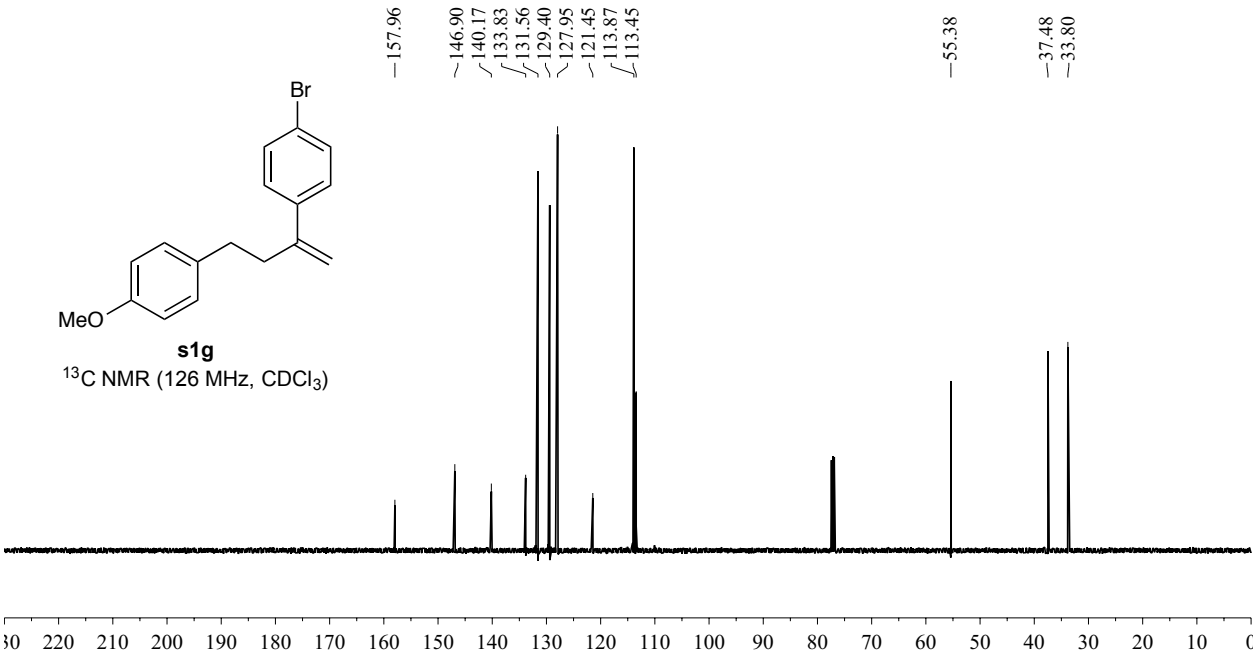

**s1f**

$^{13}$C NMR (126 MHz, $CDCl_3$)



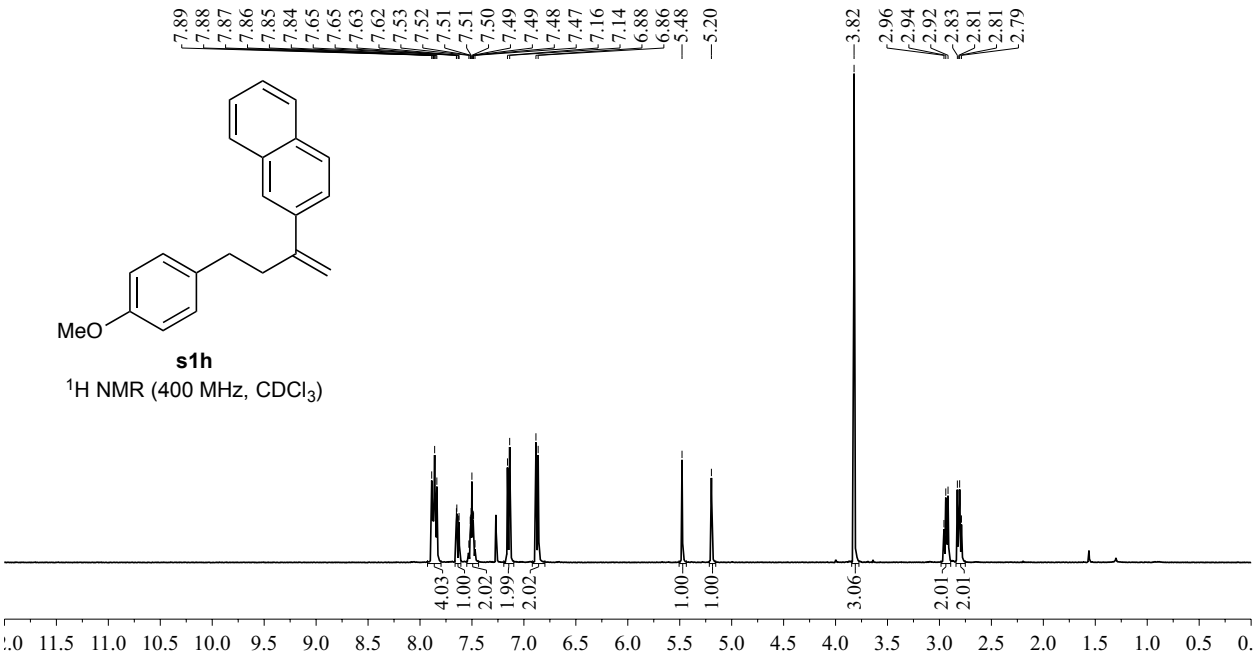

**s1g**

$^{1}$H NMR (400 MHz, $CDCl_3$)



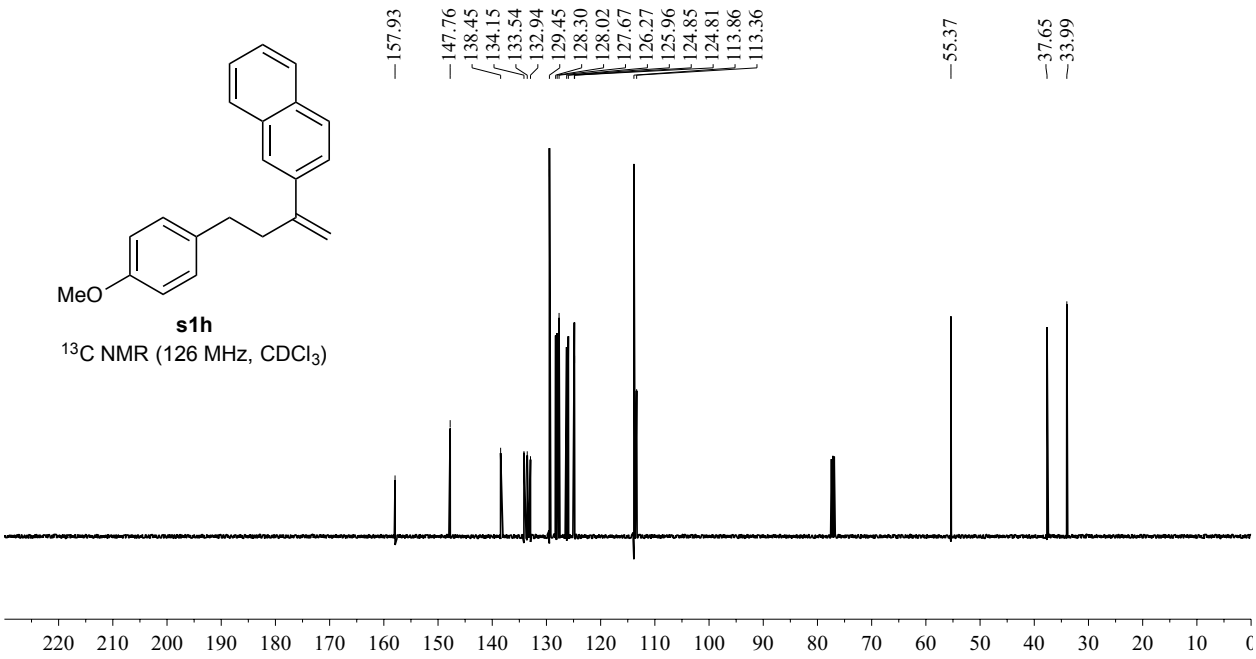

**s1g**

$^{13}$C NMR (126 MHz, $CDCl_3$)



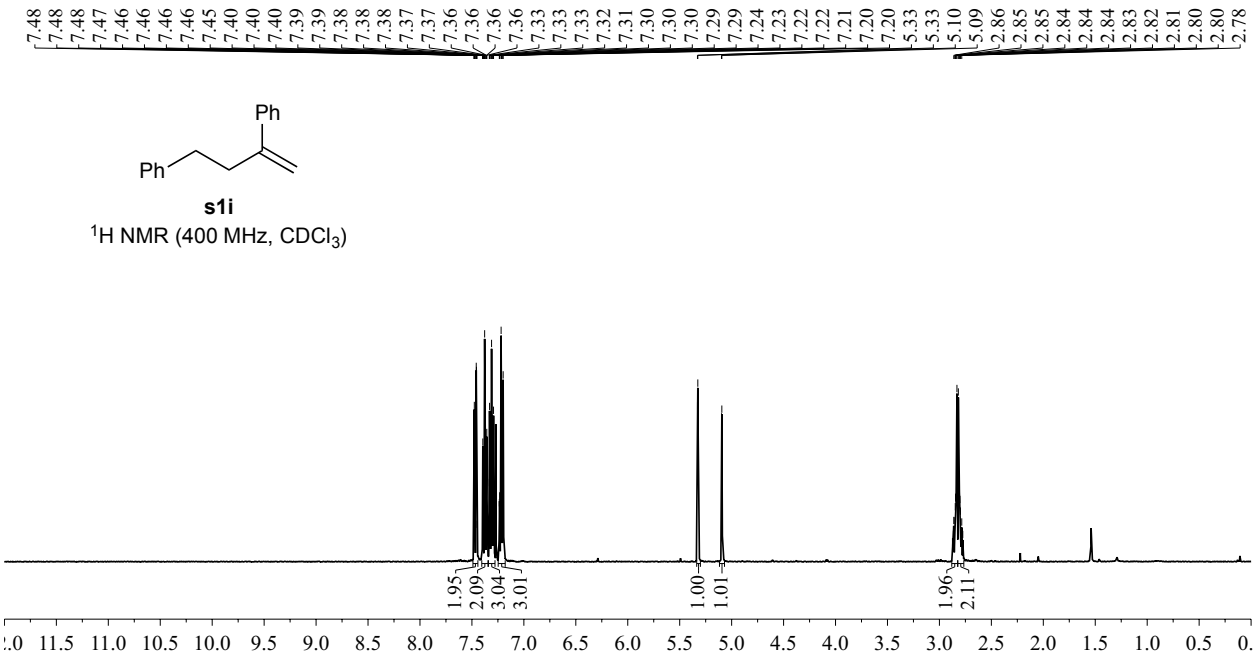

**s1h**

$^{1}$H NMR (400 MHz, $CDCl_3$)



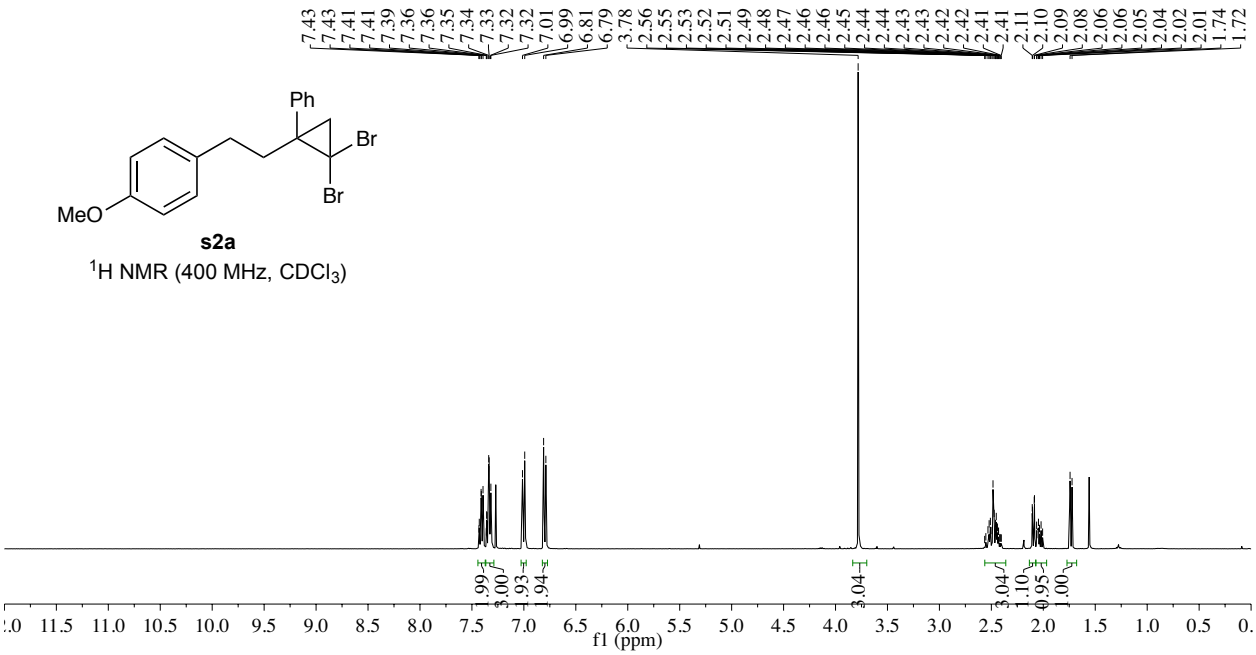

**s1h**

$^{13}$C NMR (126 MHz, $CDCl_3$)



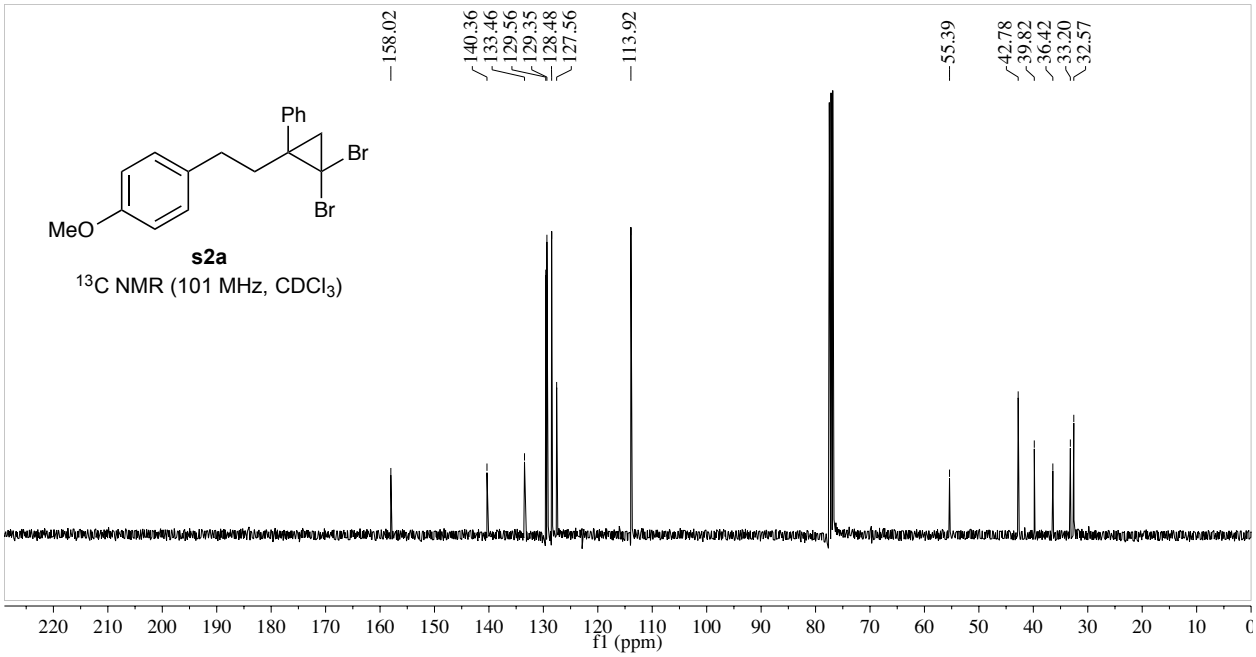

**s1i**

$^1$H NMR (400 MHz, $CDCl_3$)



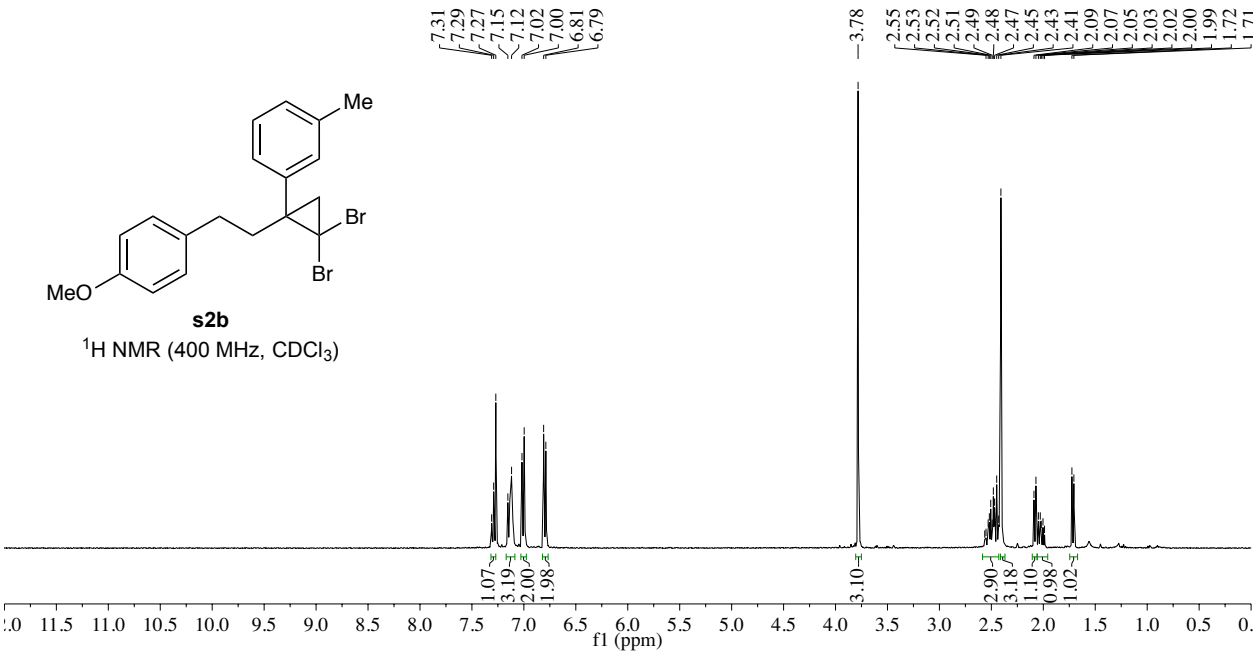

**s2a**

$^1$H NMR (400 MHz, $CDCl_3$)



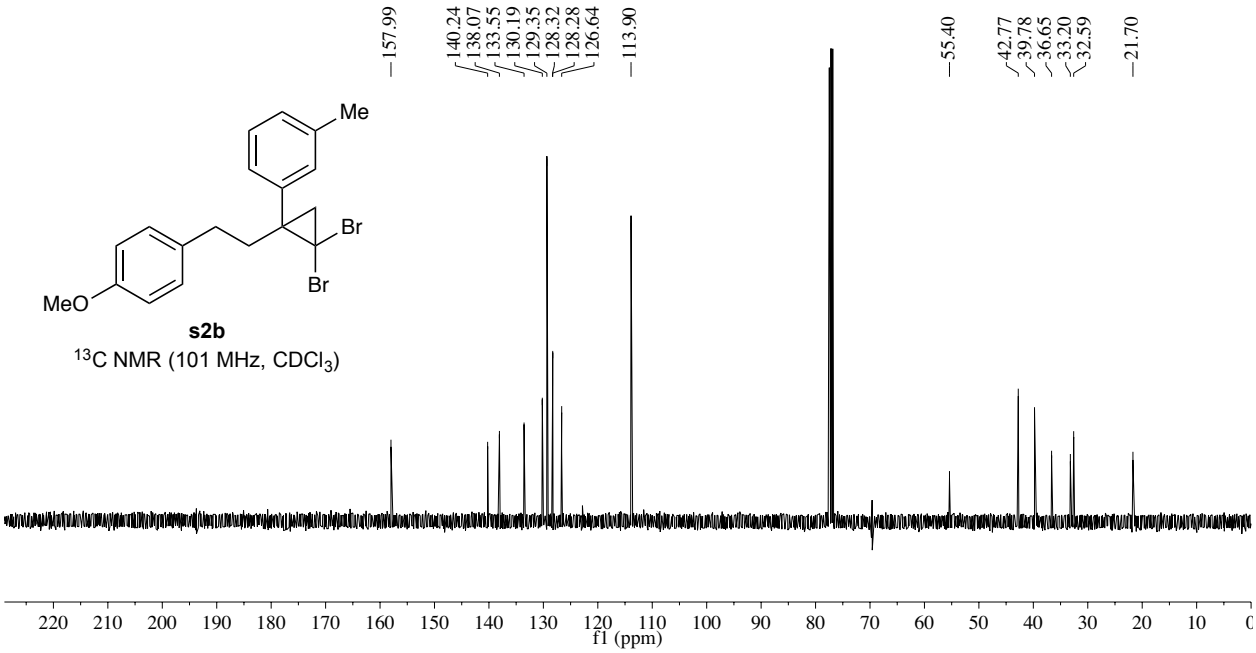

**s2a**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



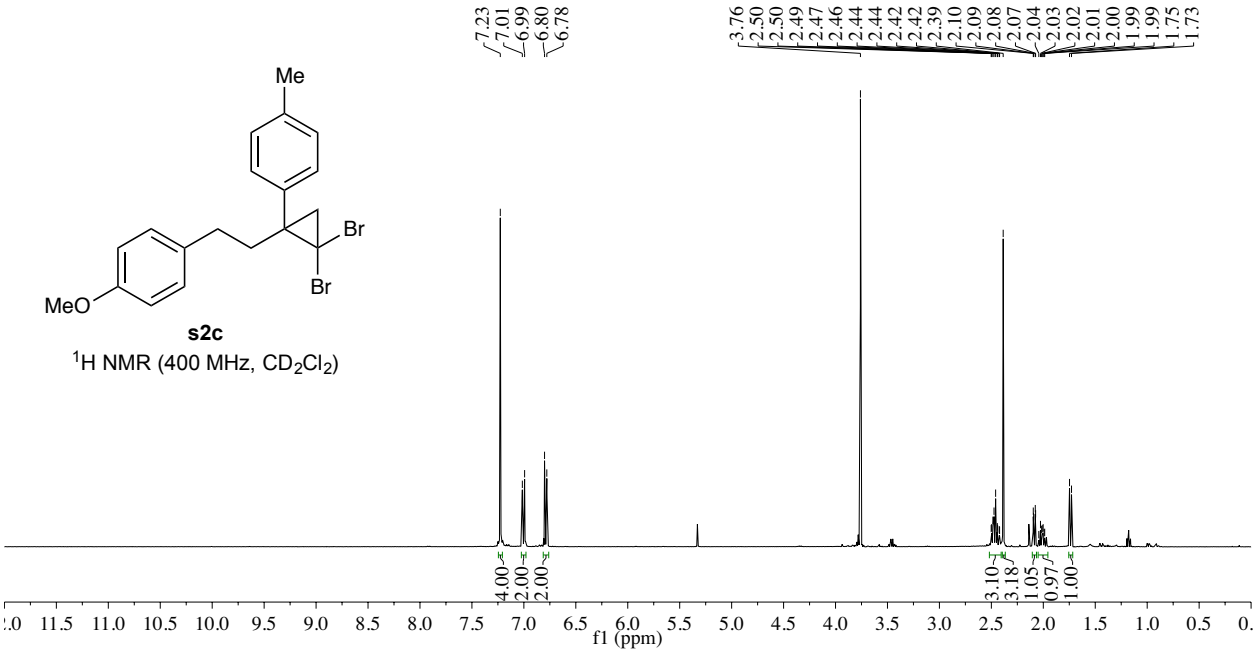

**s2b**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



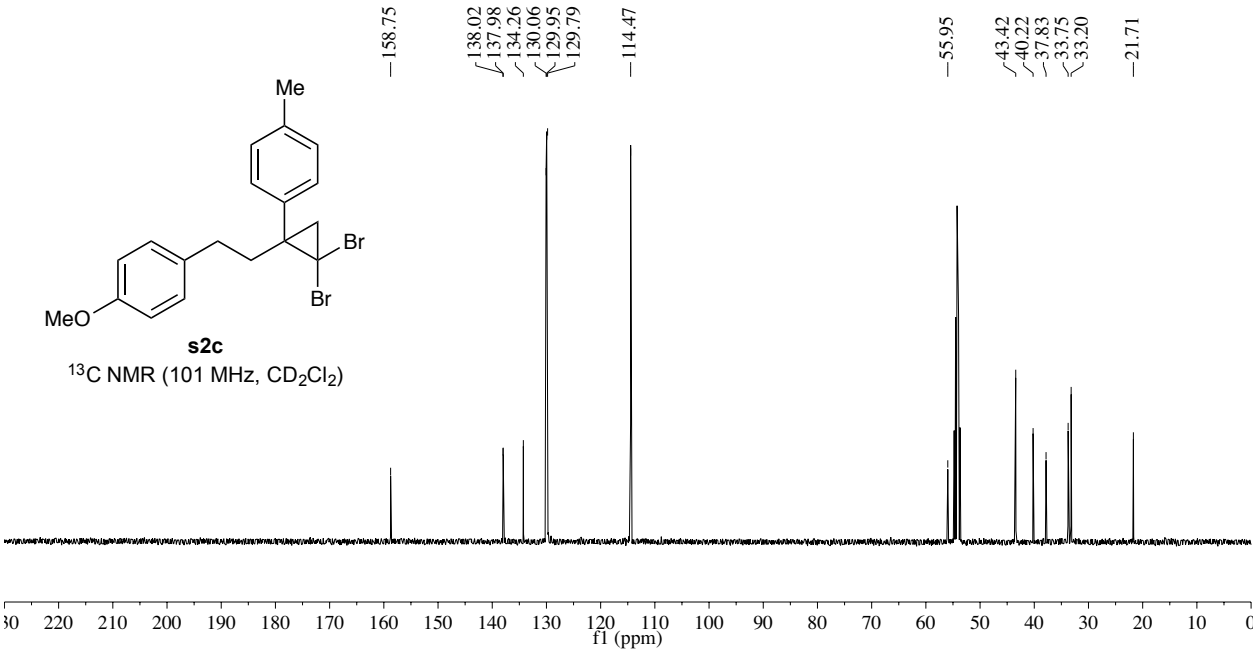

**s2b**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



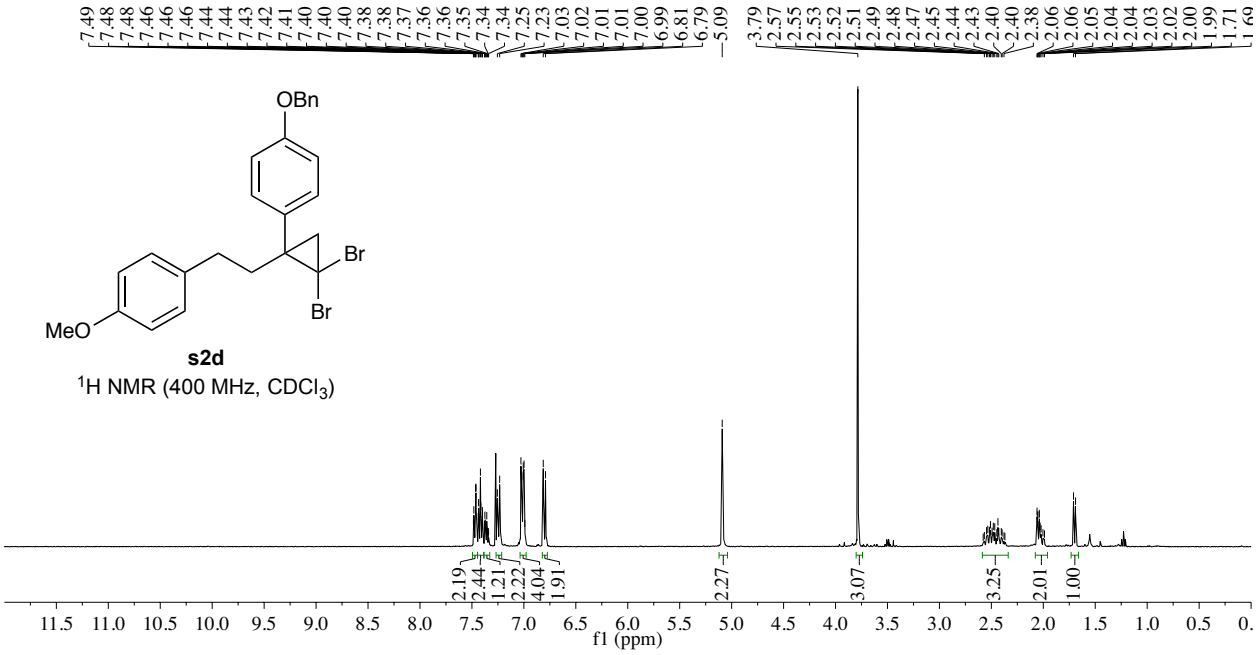

**s2c**

$^{1}H$ NMR (400 MHz, $CD_2Cl_2$)



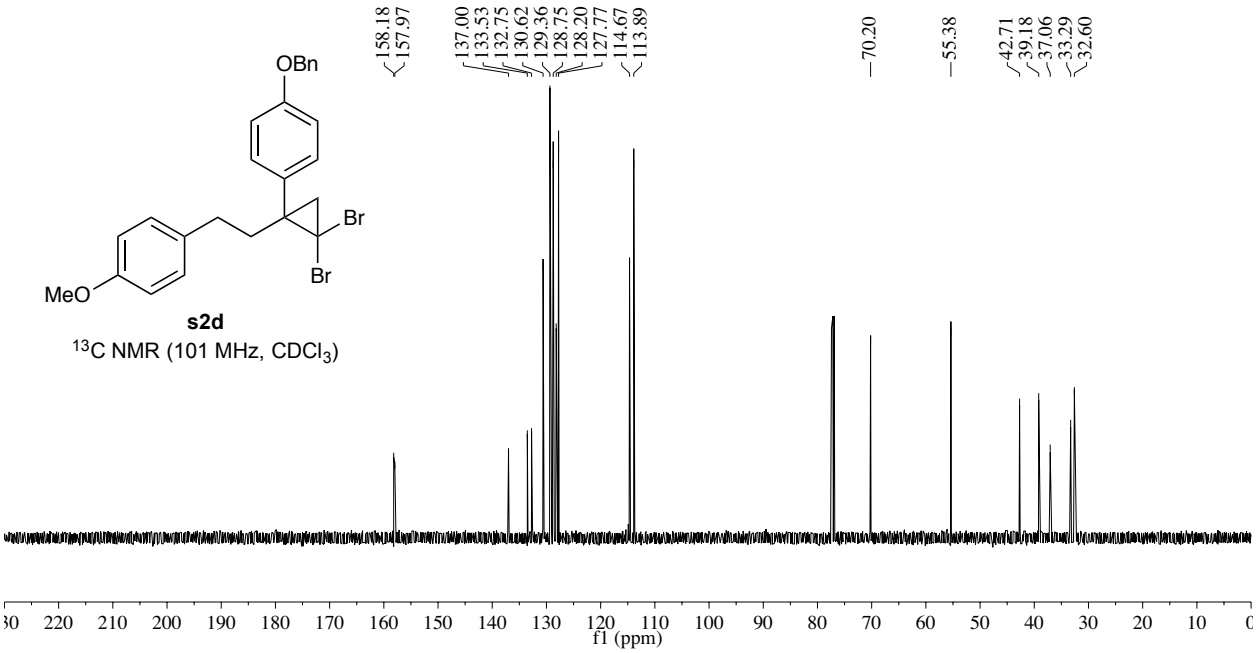

**s2c**

$^{13}C$ NMR (101 MHz, $CD_2Cl_2$)



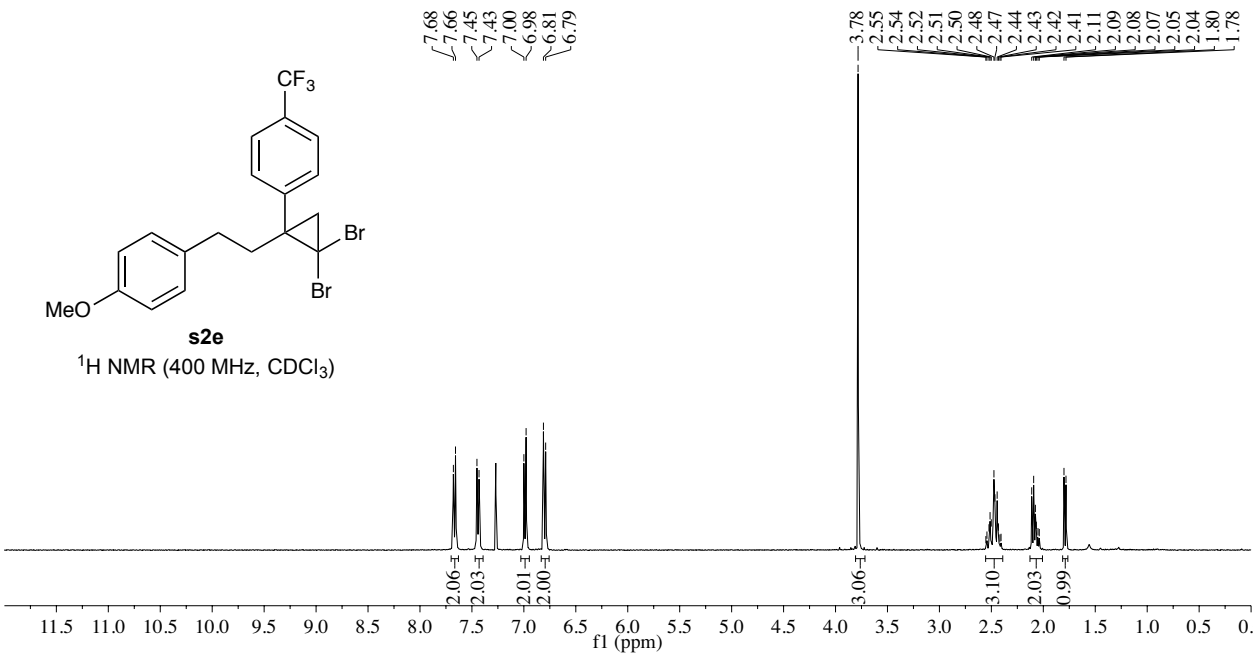

**s2d**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



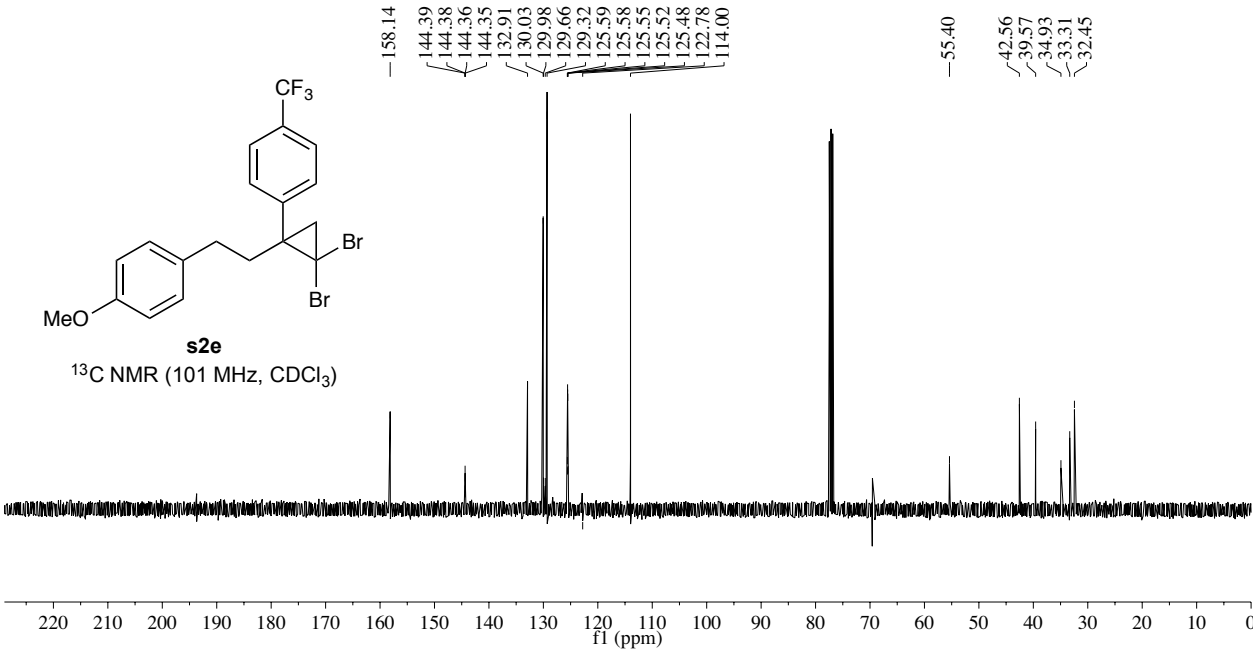

**s2d**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



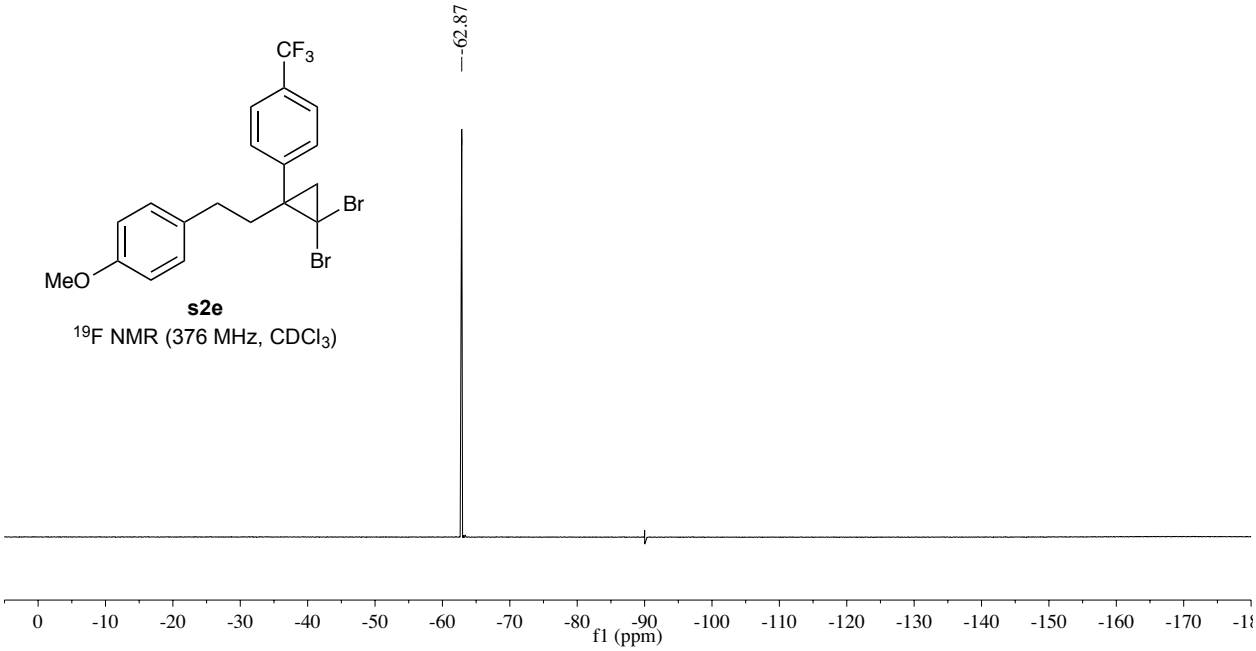

**s2e**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



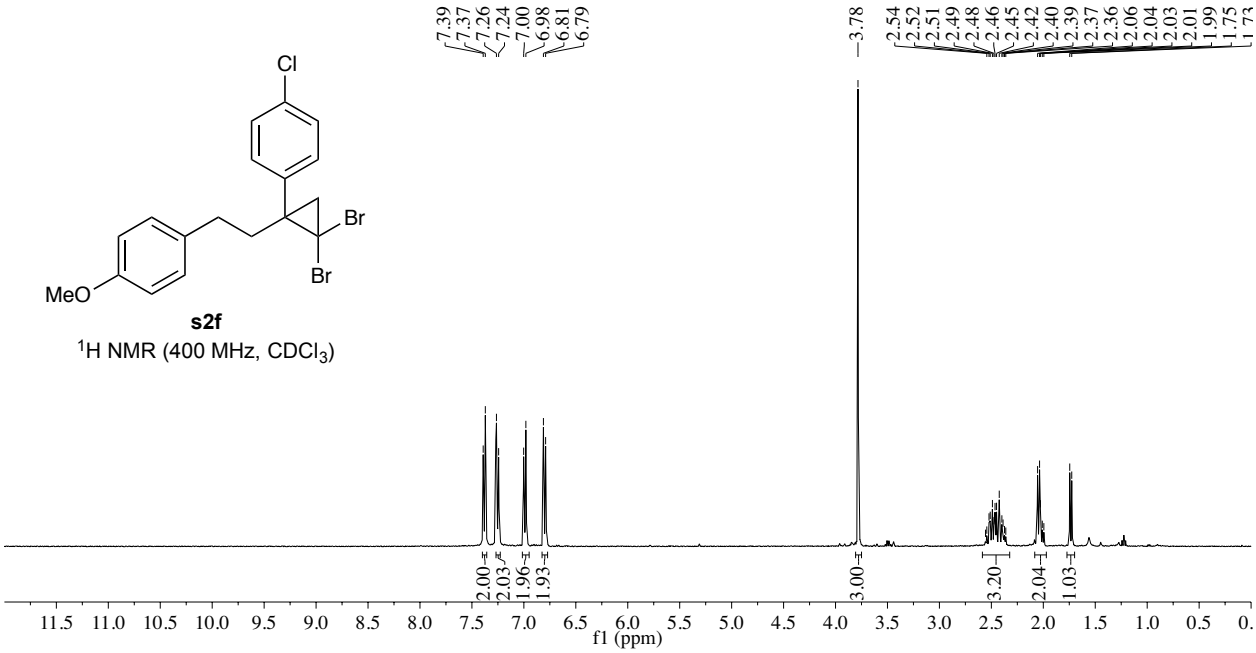

**s2e**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



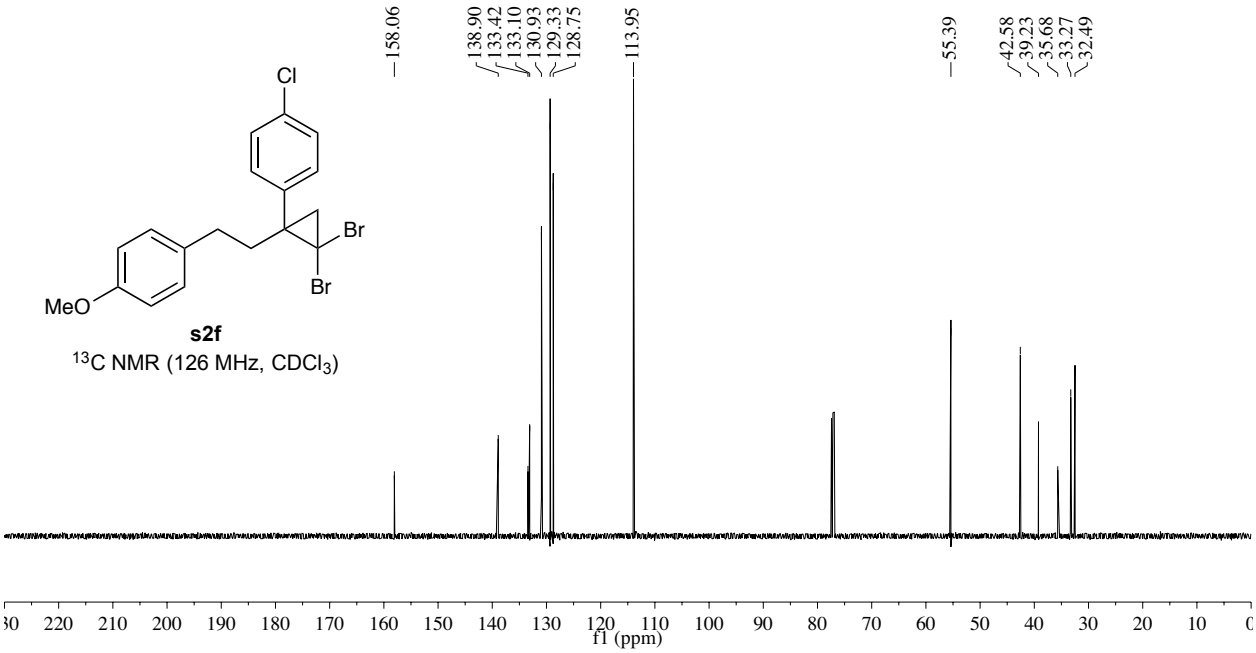

**s2e**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



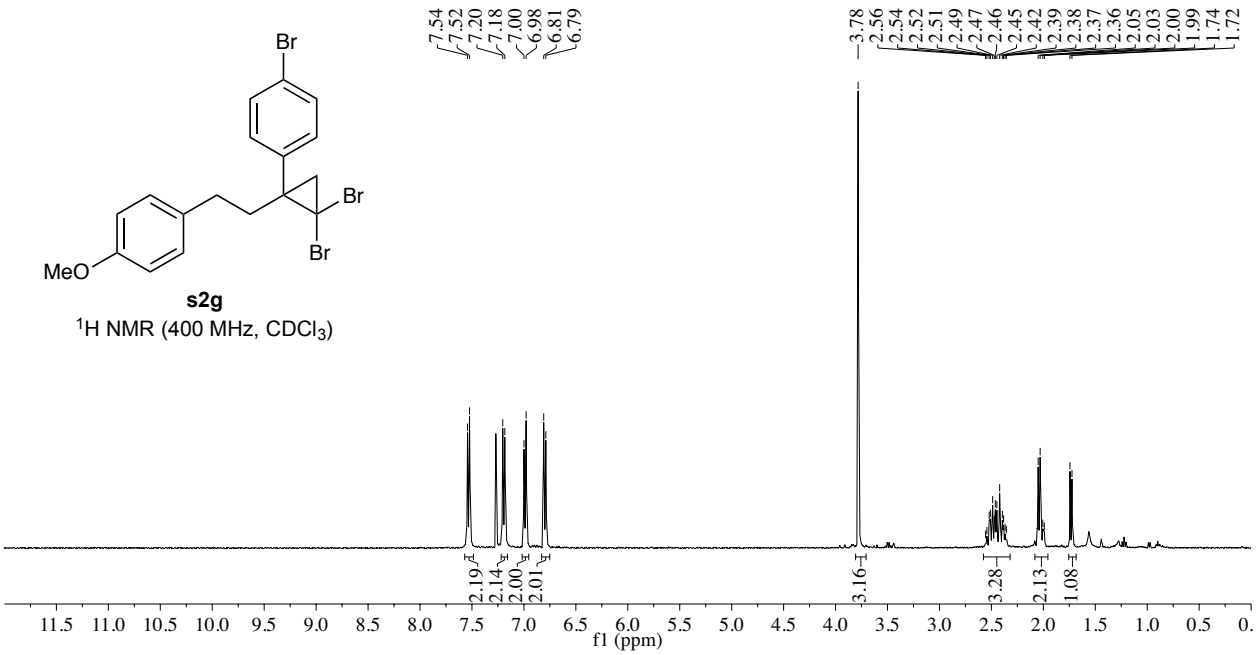

**s2f**

$^{1}$H NMR (400 MHz, $CDCl_3$)



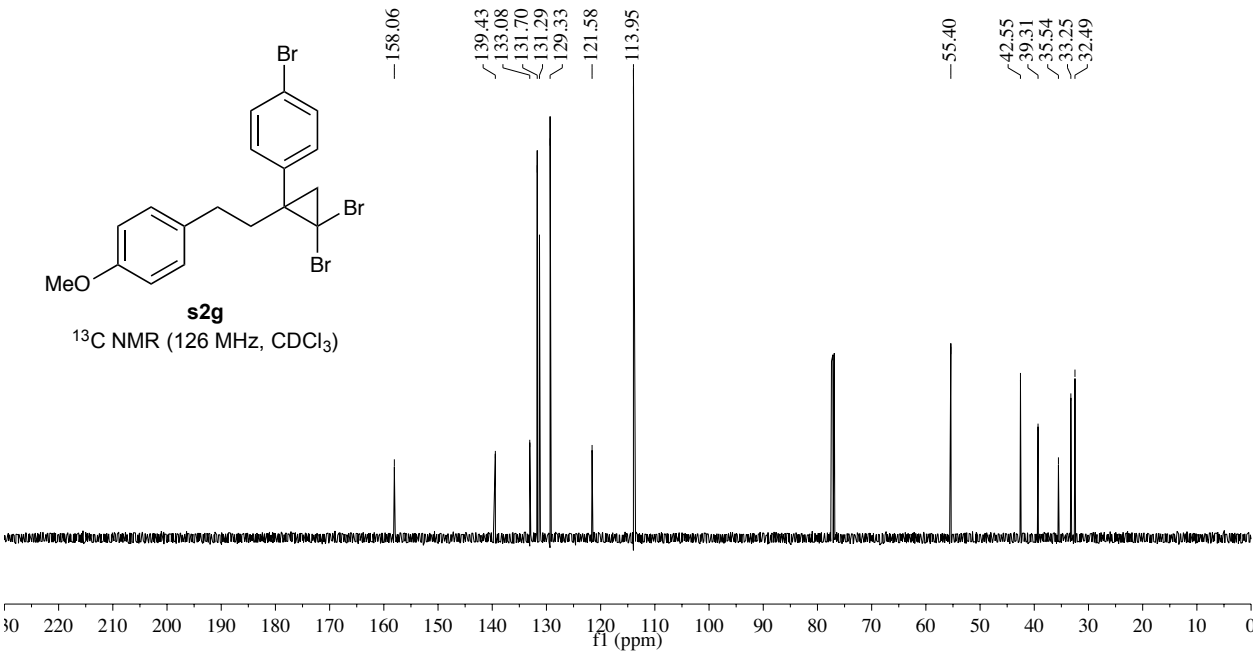

**s2f**

$^{13}$C NMR (126 MHz, $CDCl_3$)



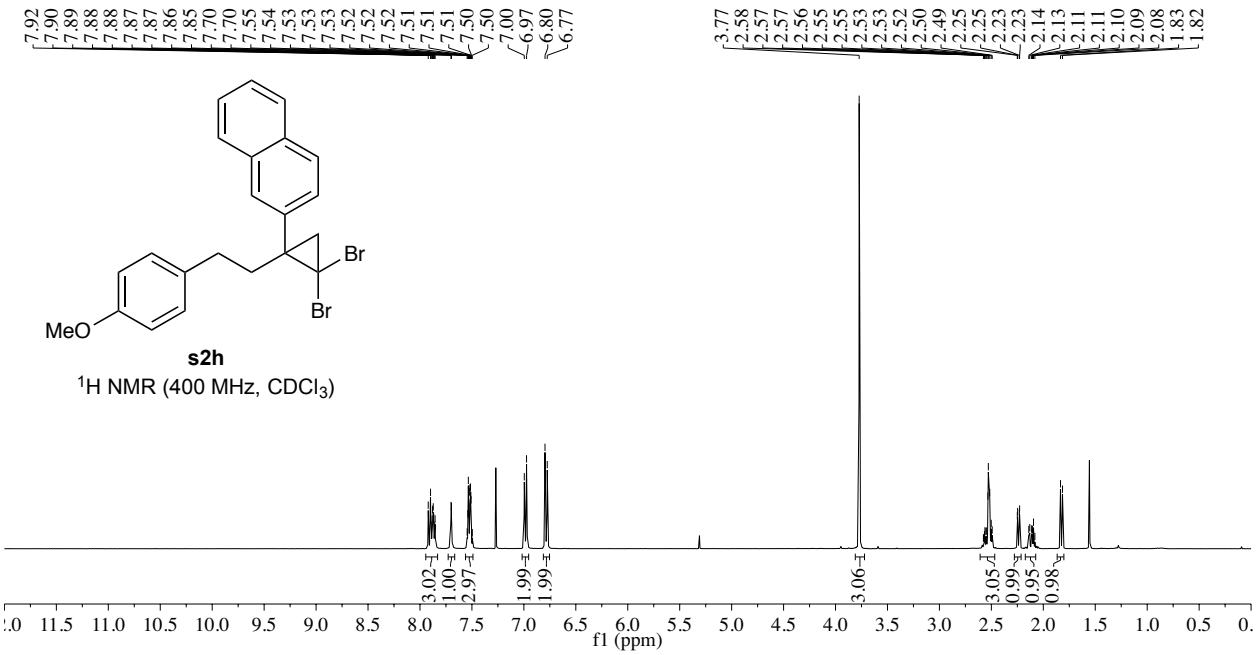

**s2g**

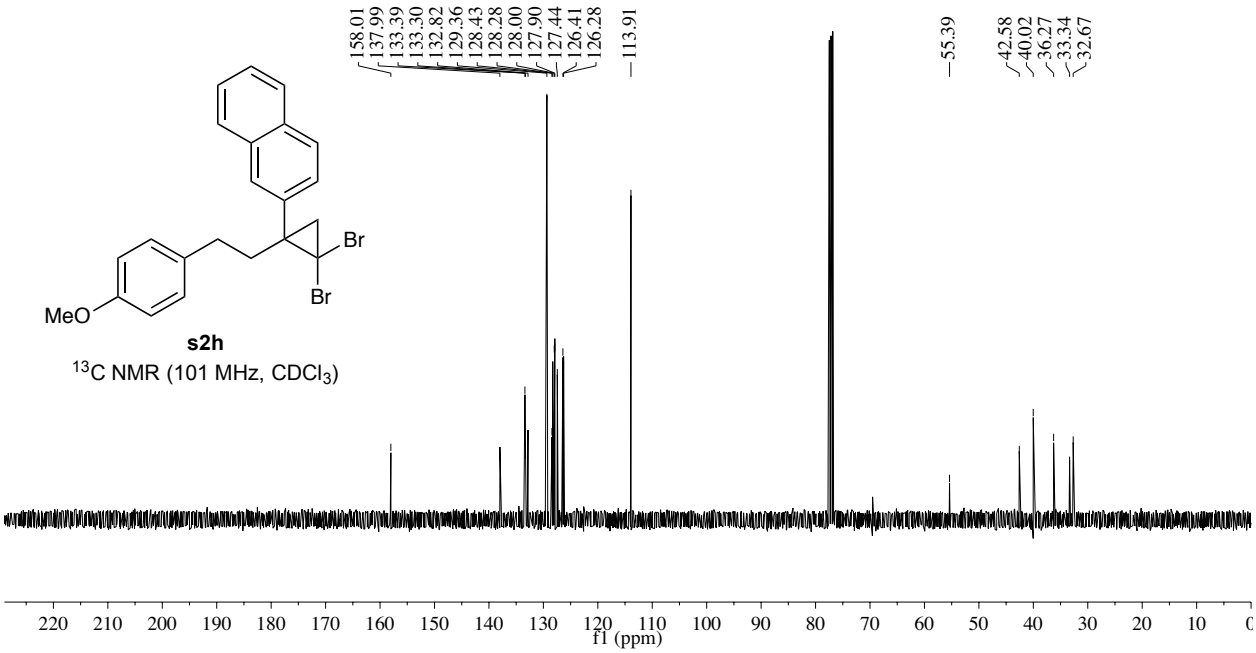
$^{1}$H NMR (400 MHz, $CDCl_3$)

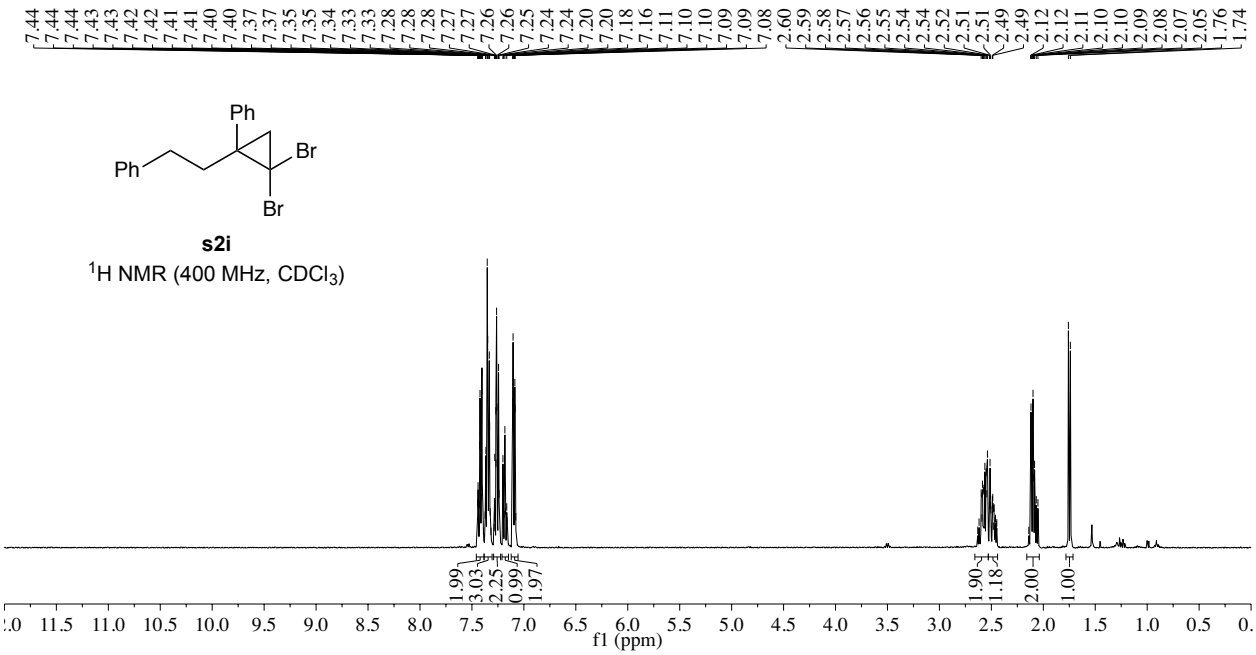


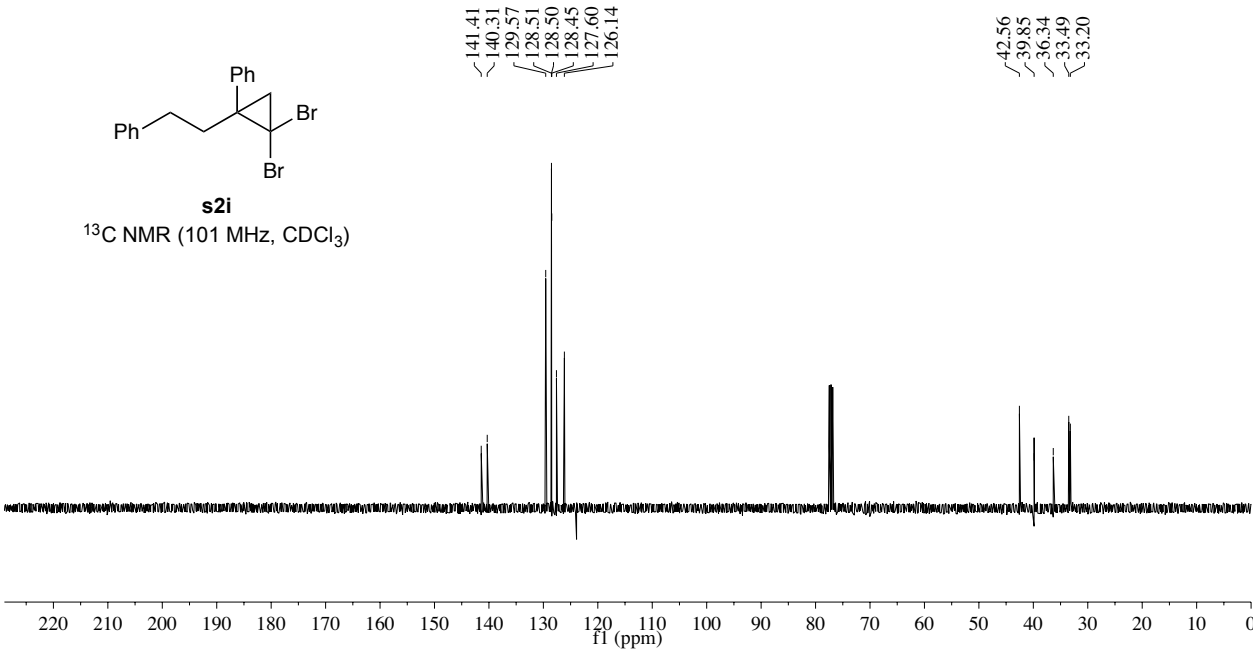

**s2g**

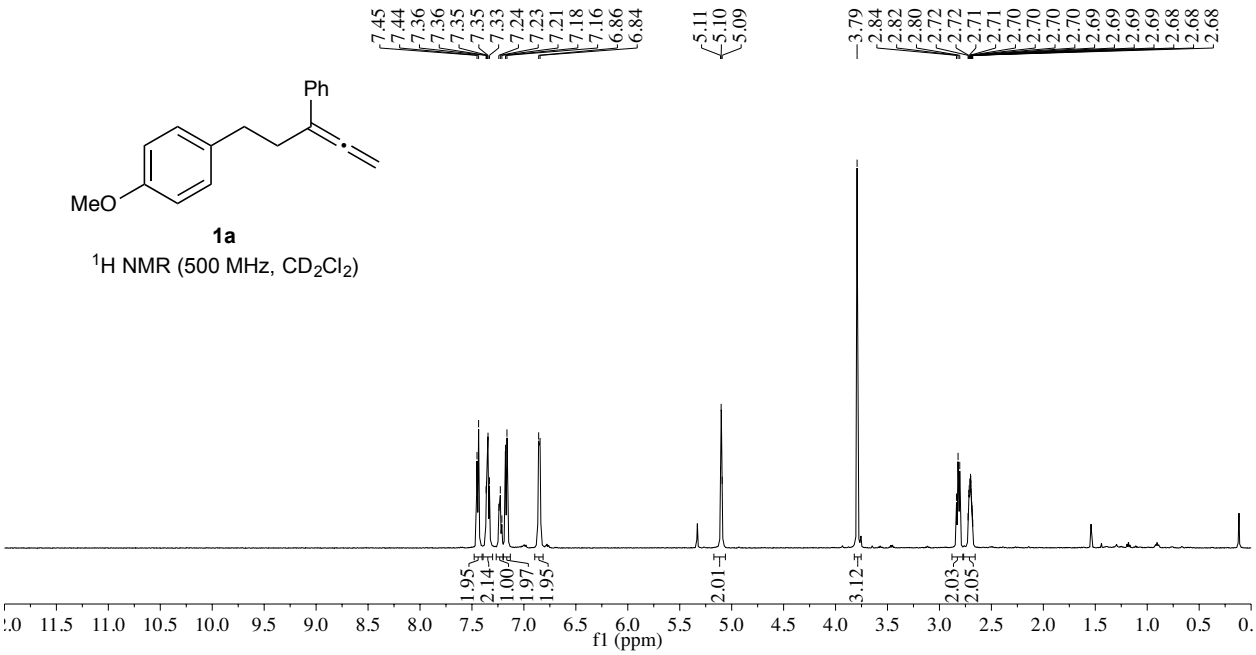
$^{13}$C NMR (126 MHz, $CDCl_3$)


Br
Br
MeO
s2h
1H NMR (400 MHz, CDCl3)
f1 (ppm)


Br
Br
MeO
s2h
13C NMR (101 MHz, CDCl3)
f1 (ppm)

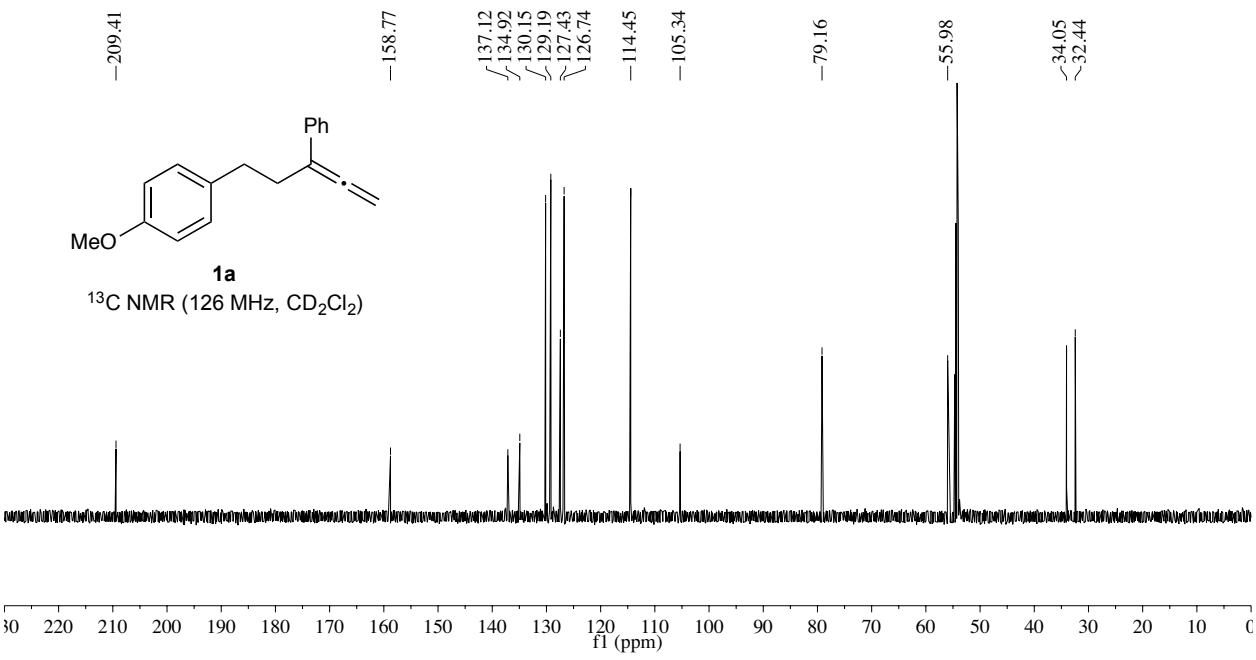

Ph
Br
Ph
Br
s2i
1H NMR (400 MHz, CDCl3)
1.99
3.03
2.25
0.99
1.97
1.90
1.18
2.00
1.00
f1 (ppm)


Ph
Br
Ph
Br
s2i
13C NMR (101 MHz, CDCl3)
141.41
140.31
129.57
128.51
128.50
128.45
127.60
126.14
42.56
39.85
36.34
33.49
33.20
f1 (ppm)



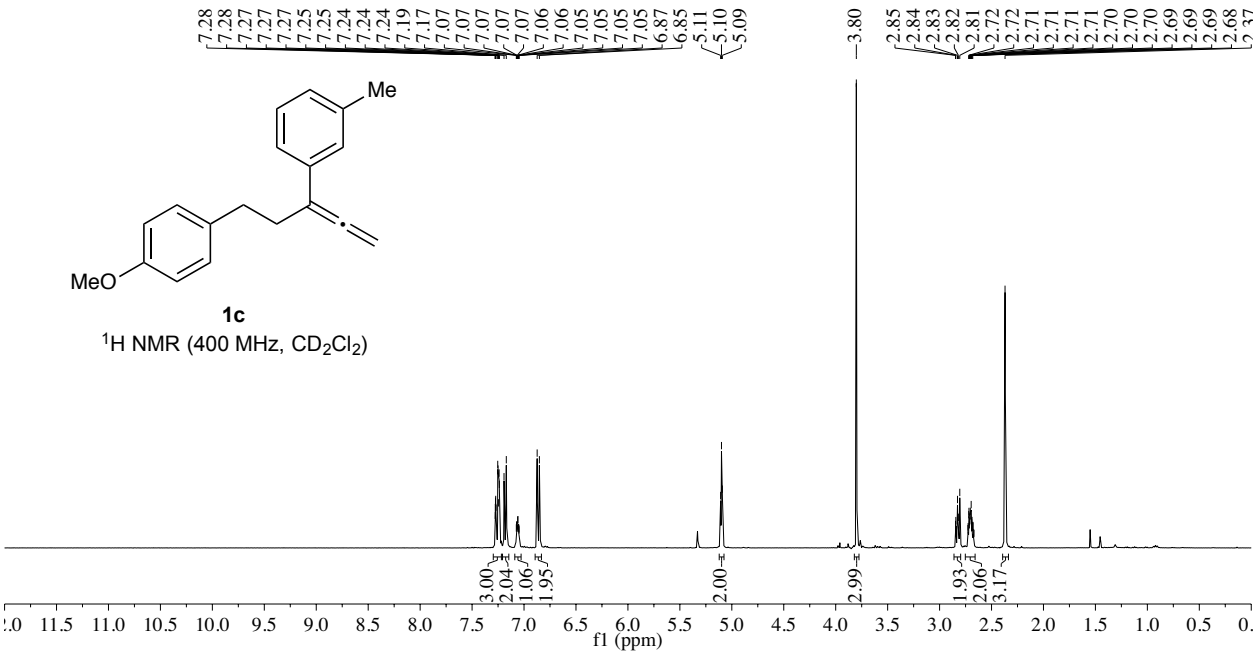

**1a**

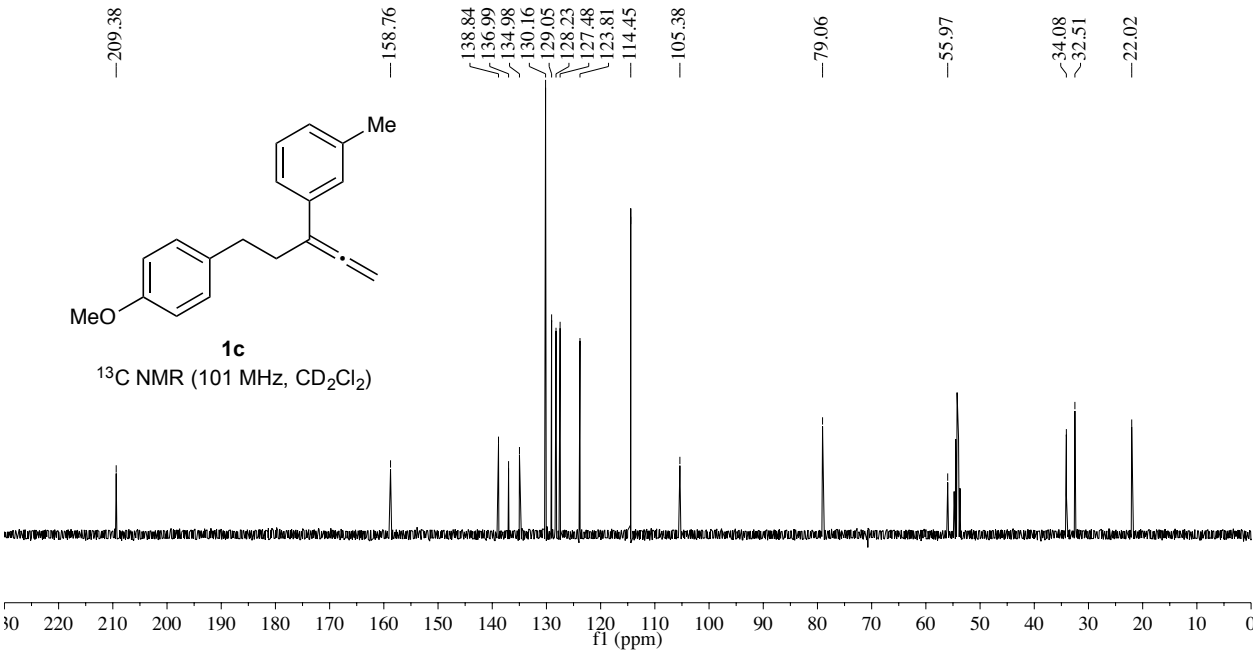
$^{1}$H NMR (500 MHz, $CD_2Cl_2$)

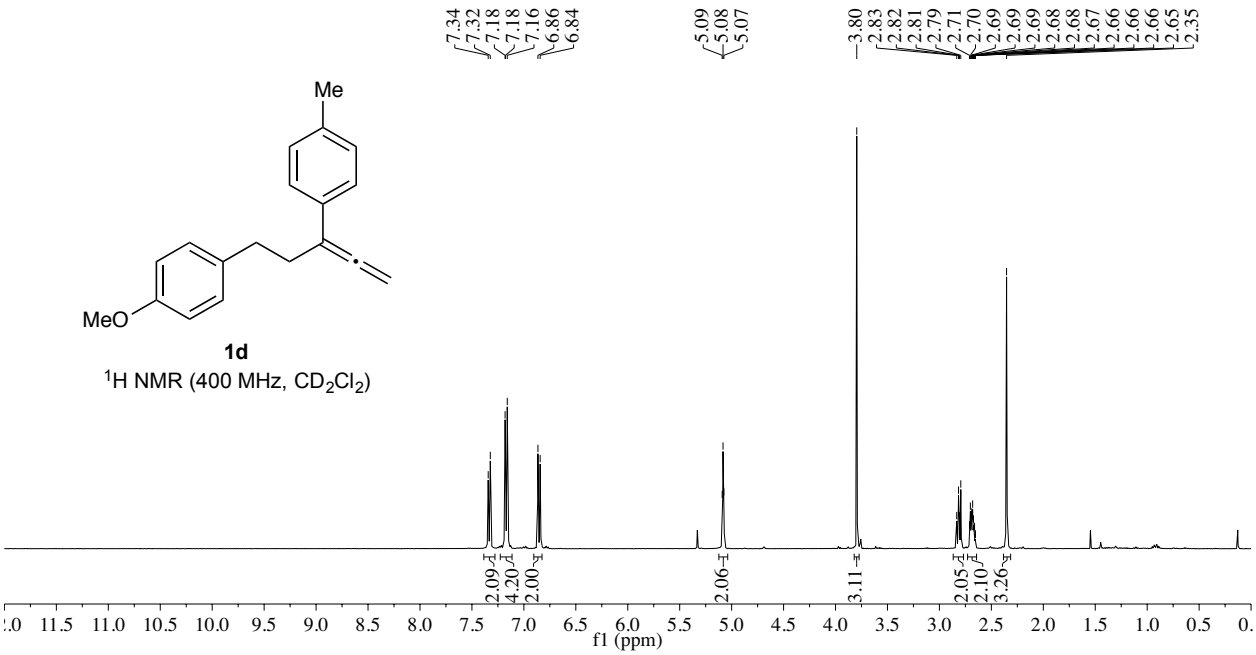


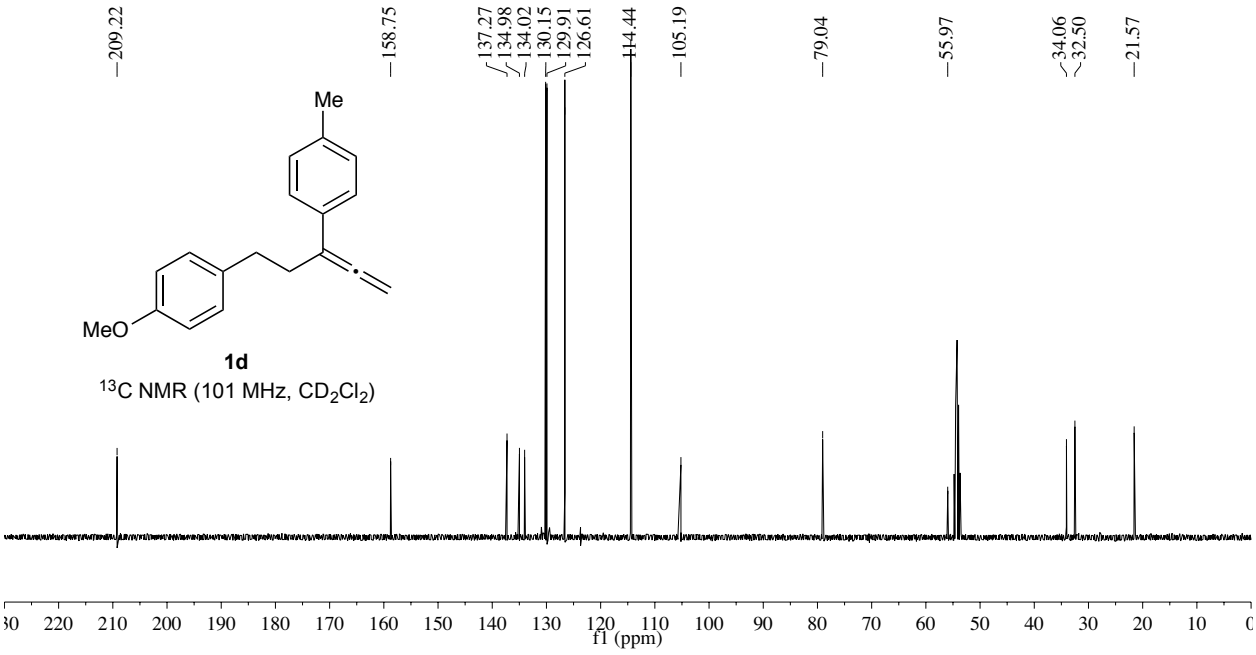

**1a**

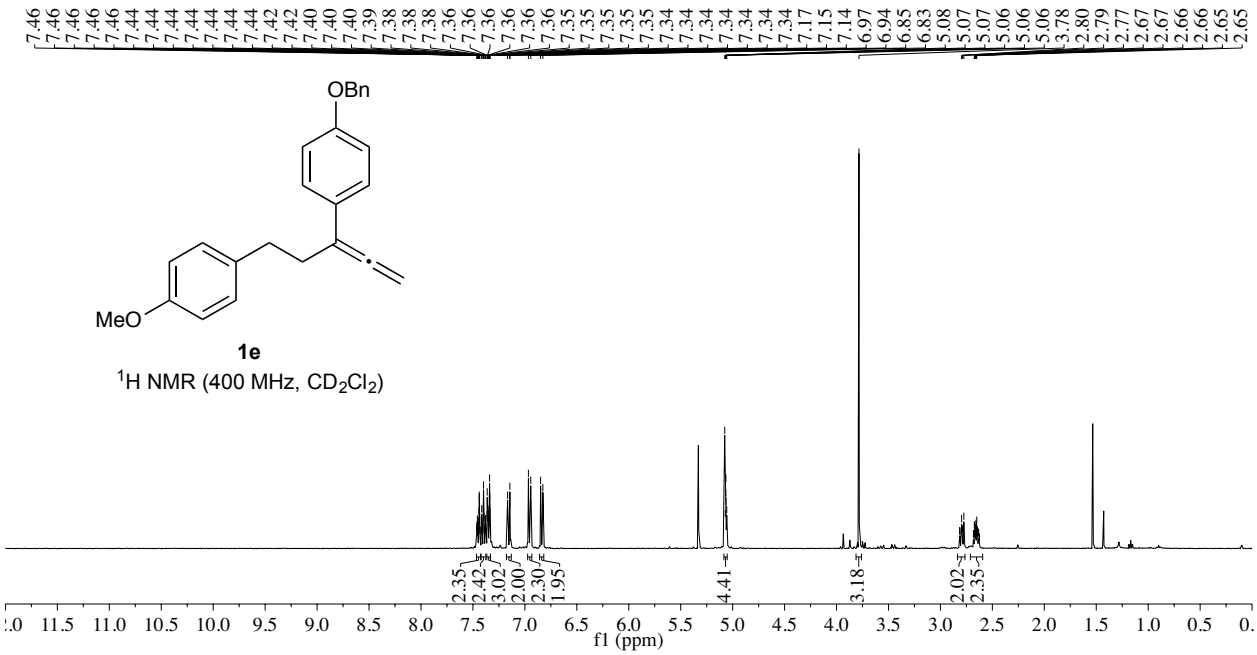
$^{13}$C NMR (126 MHz, $CD_2Cl_2$)

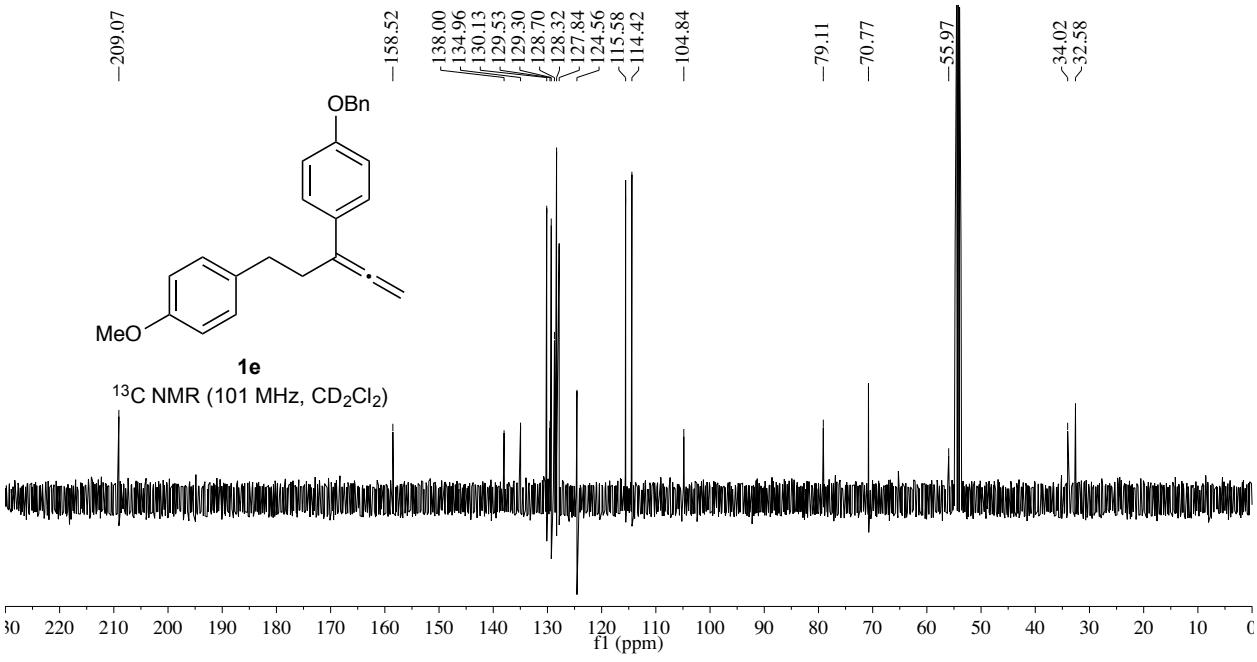

Me
MeO
1c
1H NMR (400 MHz, CD2Cl2)
f1 (ppm)

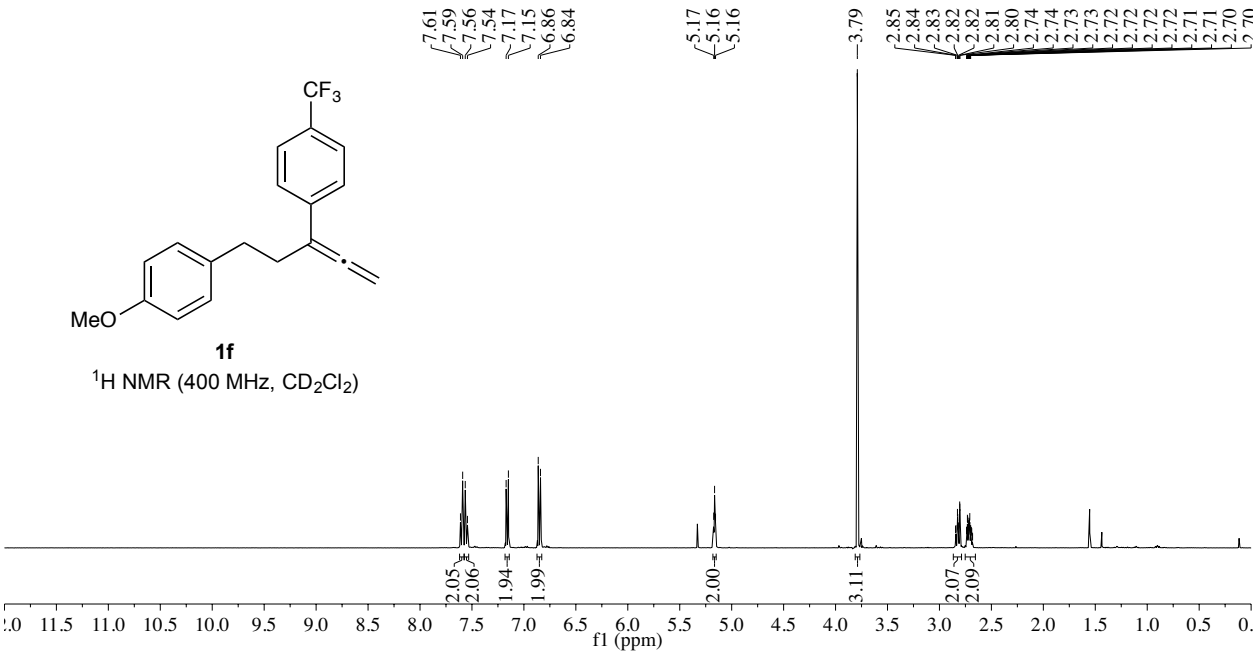

Me
MeO
1c
13C NMR (101 MHz, CD2Cl2)
f1 (ppm)


Me
MeO
1d
1H NMR (400 MHz, CD2Cl2)
f1 (ppm)


Me
MeO
1d
13C NMR (101 MHz, CD2Cl2)
f1 (ppm)

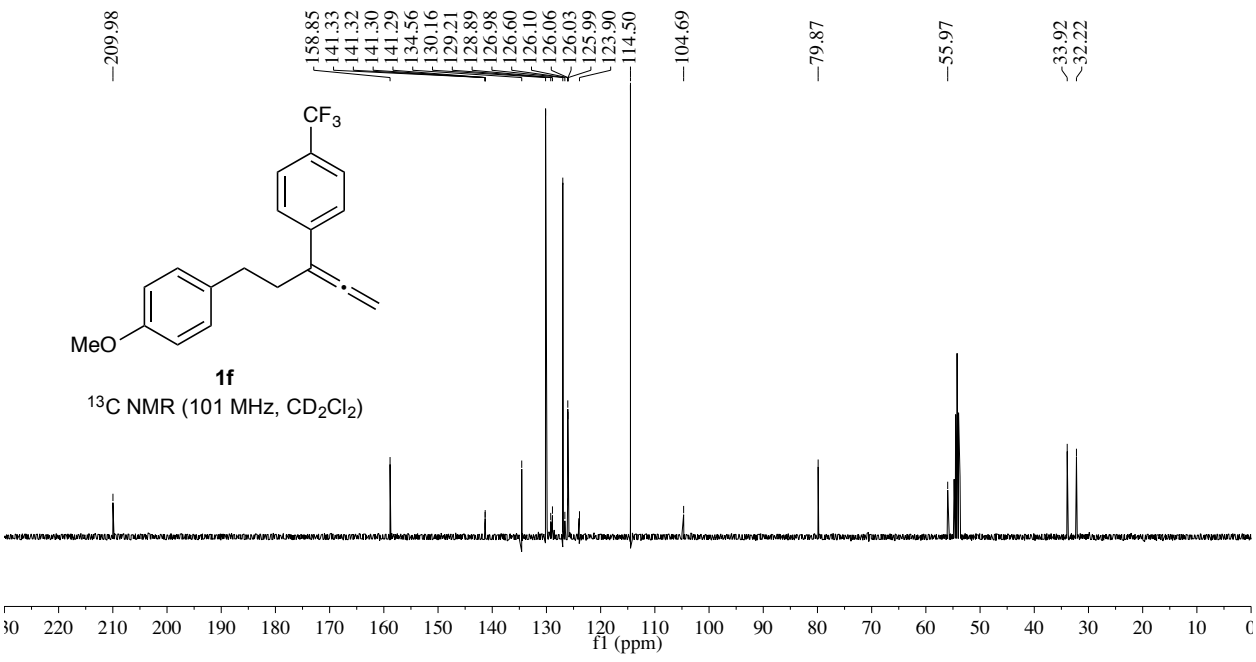

OBn
MeO
1e
1H NMR (400 MHz, CD2Cl2)
f1 (ppm)


OBn
MeO
1e
13C NMR (101 MHz, CD2Cl2)
f1 (ppm)



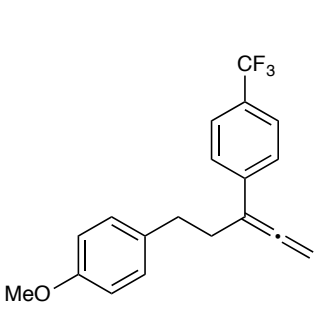

**1f**

$^{1}$H NMR (400 MHz, $CD_2Cl_2$)




**1f**

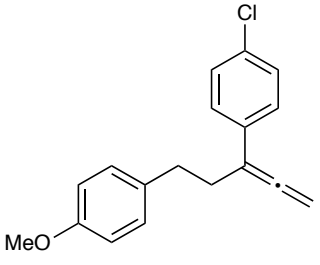
$^{13}$C NMR (101 MHz, $CD_2Cl_2$)




**1f**

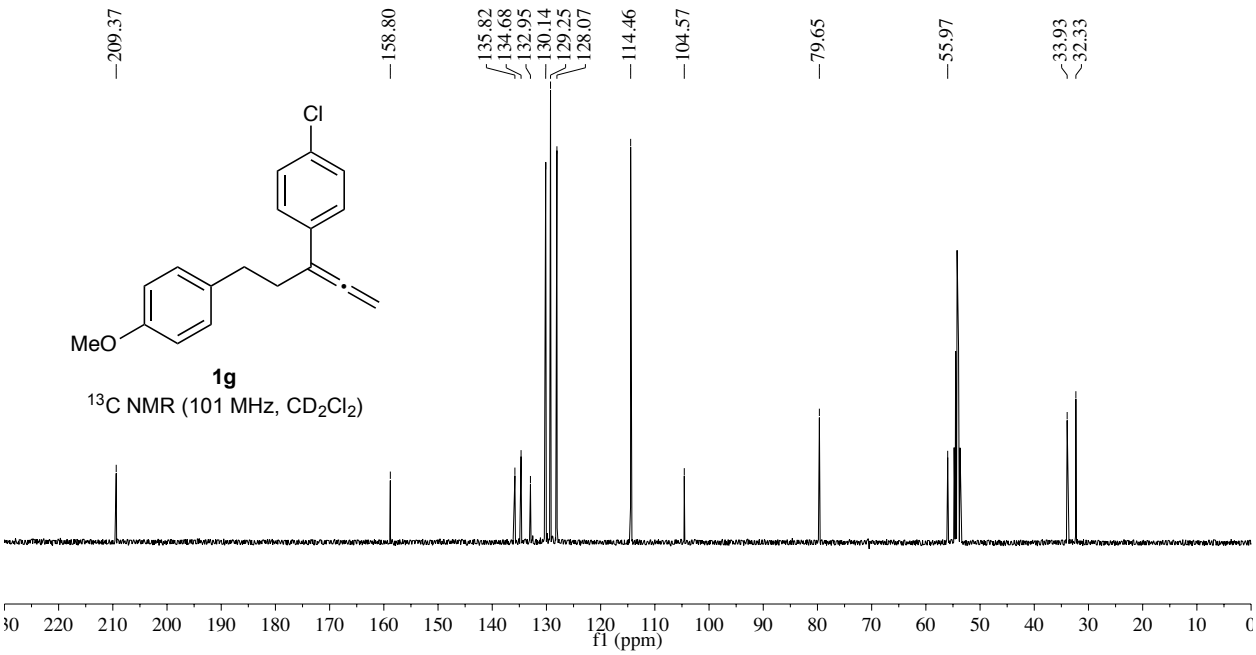
$^{19}F$ NMR (376 MHz, $CD_2Cl_2$)



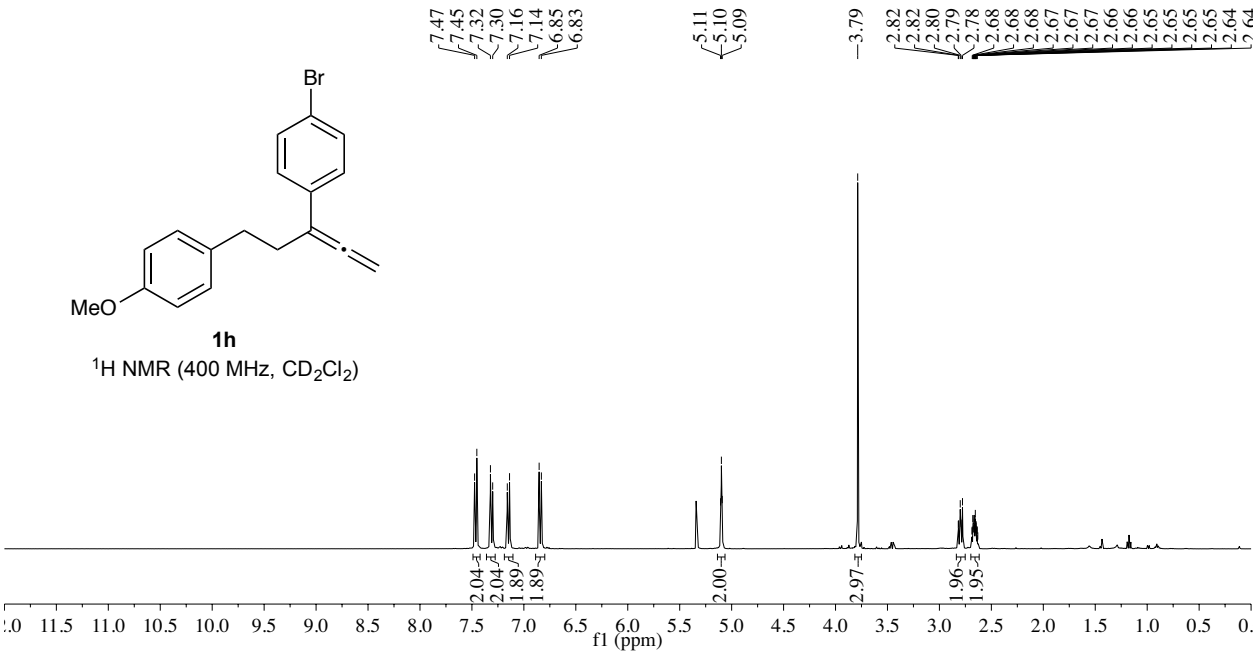

**1g**

$^{1}H$ NMR (400 MHz, $CD_2Cl_2$)



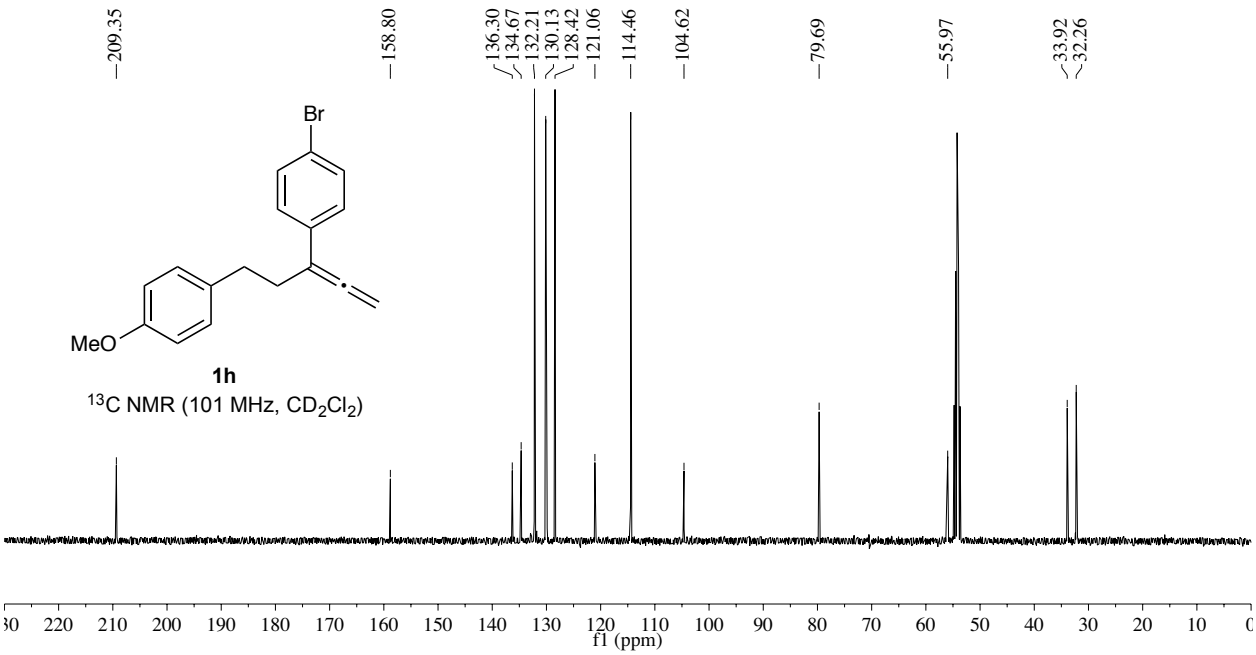

**1g**

$^{13}C$ NMR (101 MHz, $CD_2Cl_2$)



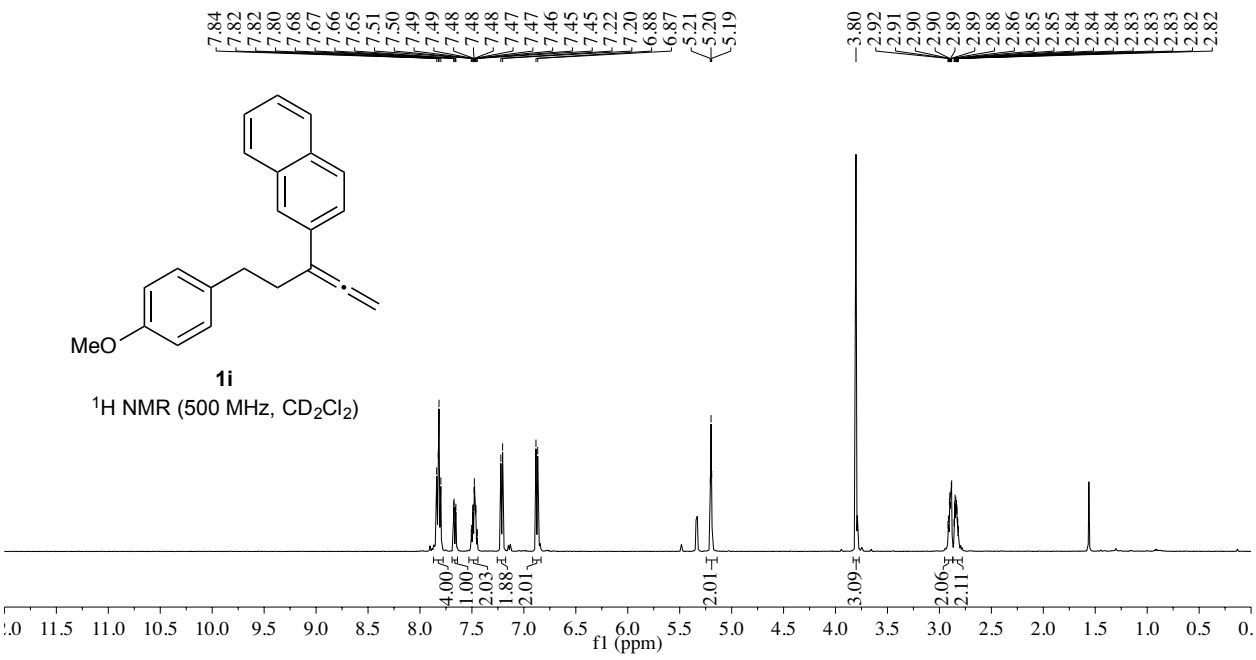

**1h**

$^{1}H$ NMR (400 MHz, $CD_2Cl_2$)



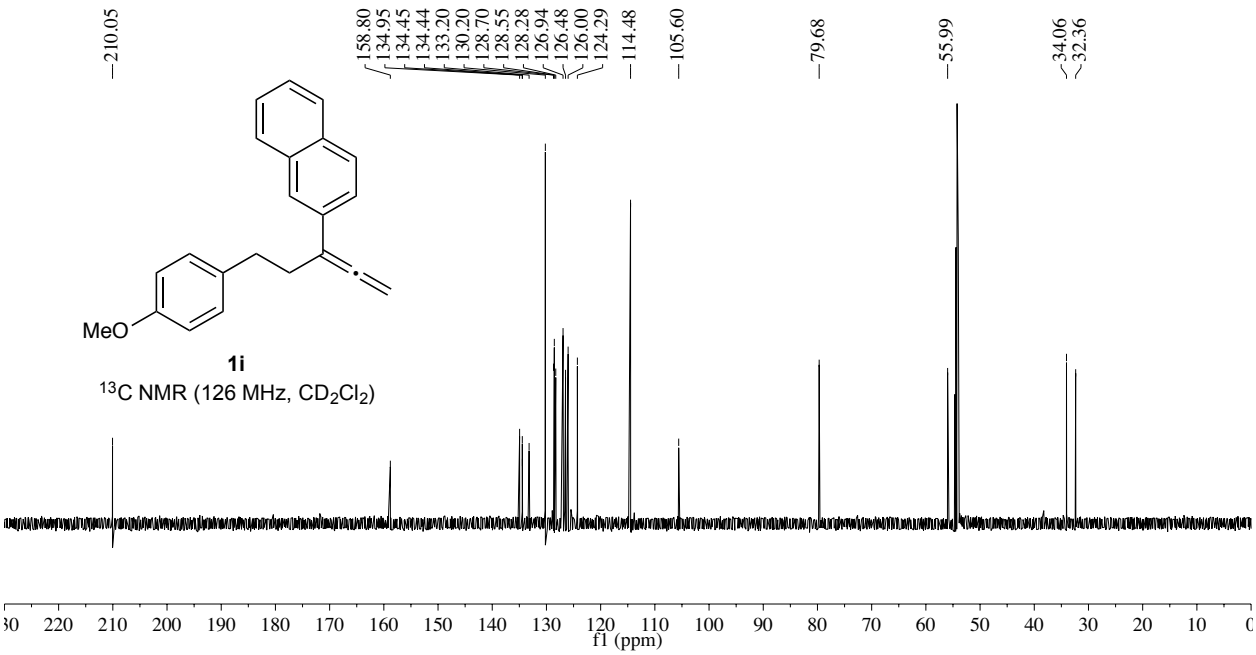

**1h**

$^{13}C$ NMR (101 MHz, $CD_2Cl_2$)



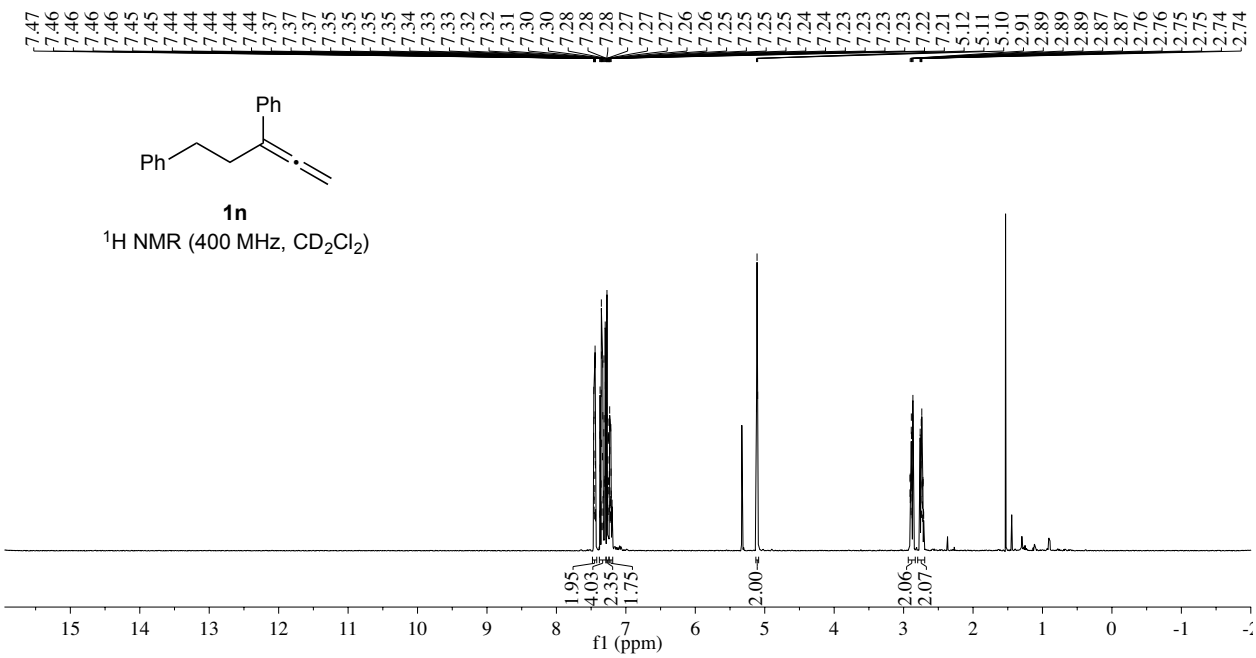

**1i**

$^{1}H$ NMR (500 MHz, $CD_2Cl_2$)



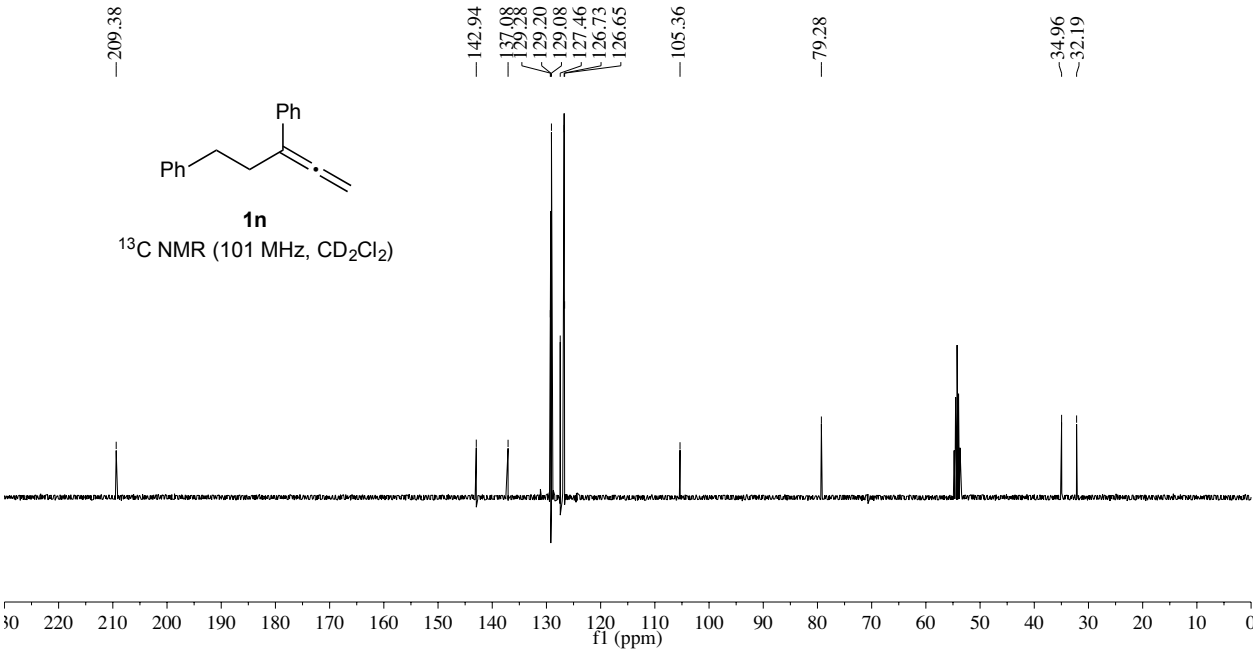

**1i**

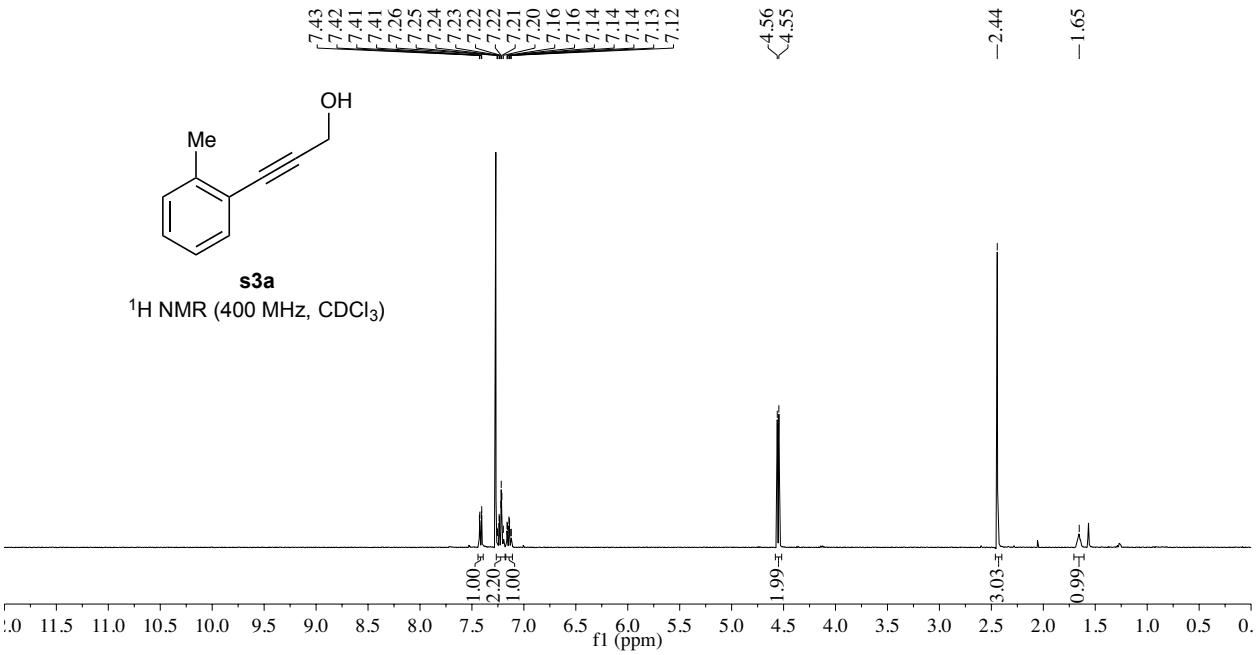
$^{13}$C NMR (126 MHz, $CD_2Cl_2$)

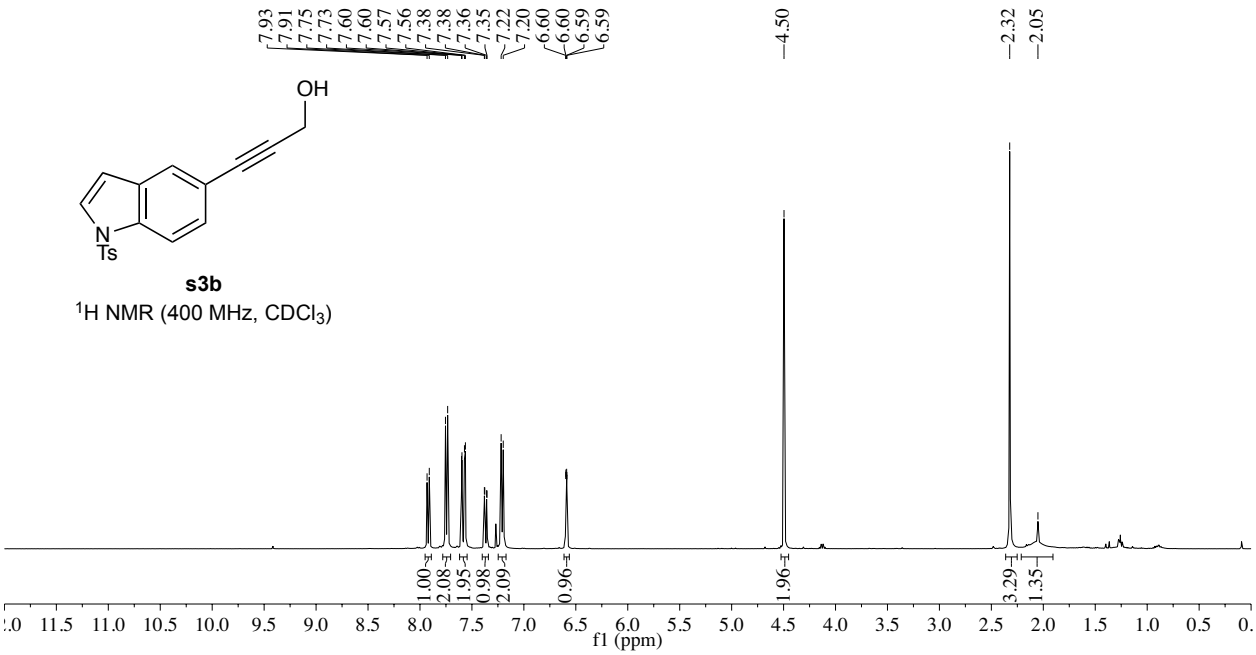



**1n**

$^{1}$H NMR (400 MHz, $CD_2Cl_2$)

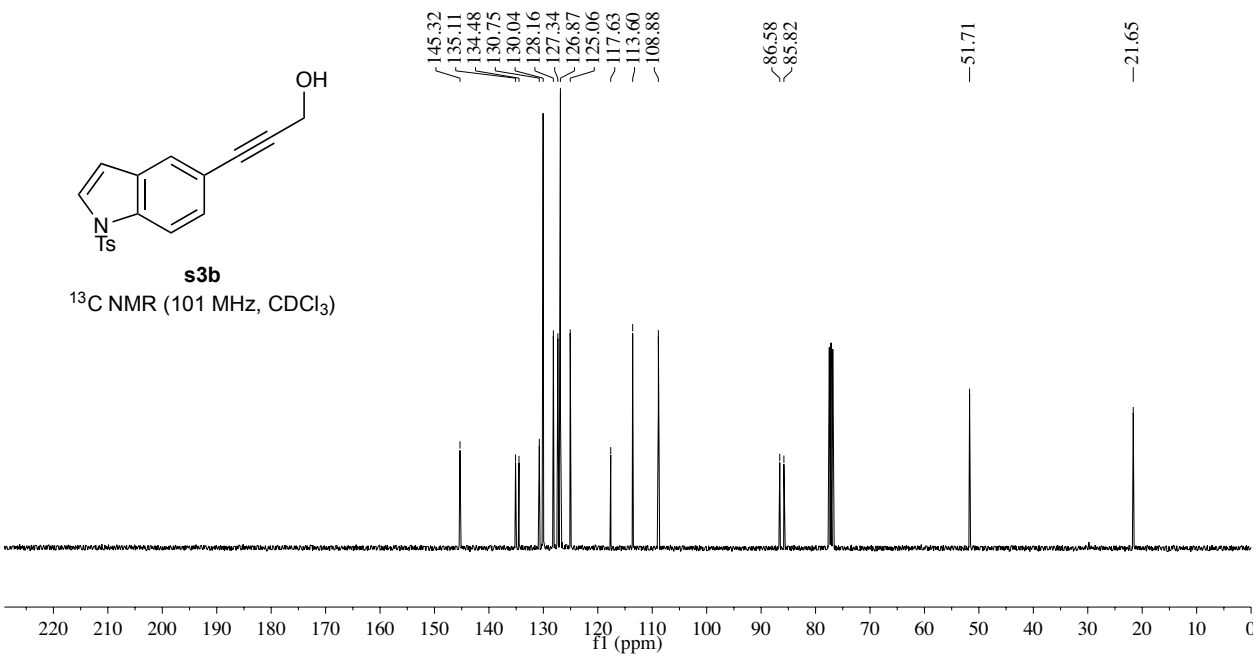

209.38
142.94
137.08
129.28
129.20
129.08
127.46
126.73
126.65
105.36
79.28
34.96
32.19
Ph
Ph
1n
13C NMR (101 MHz, CD2Cl2)
f1 (ppm)


7.43
7.42
7.41
7.41
7.26
7.25
7.24
7.23
7.22
7.22
7.21
7.20
7.16
7.16
7.14
7.14
7.14
7.13
7.12
4.56
4.55
2.44
1.65
OH
Me
s3a
1H NMR (400 MHz, CDCl3)
1.00
2.20
1.00
1.99
3.03
0.99
f1 (ppm)



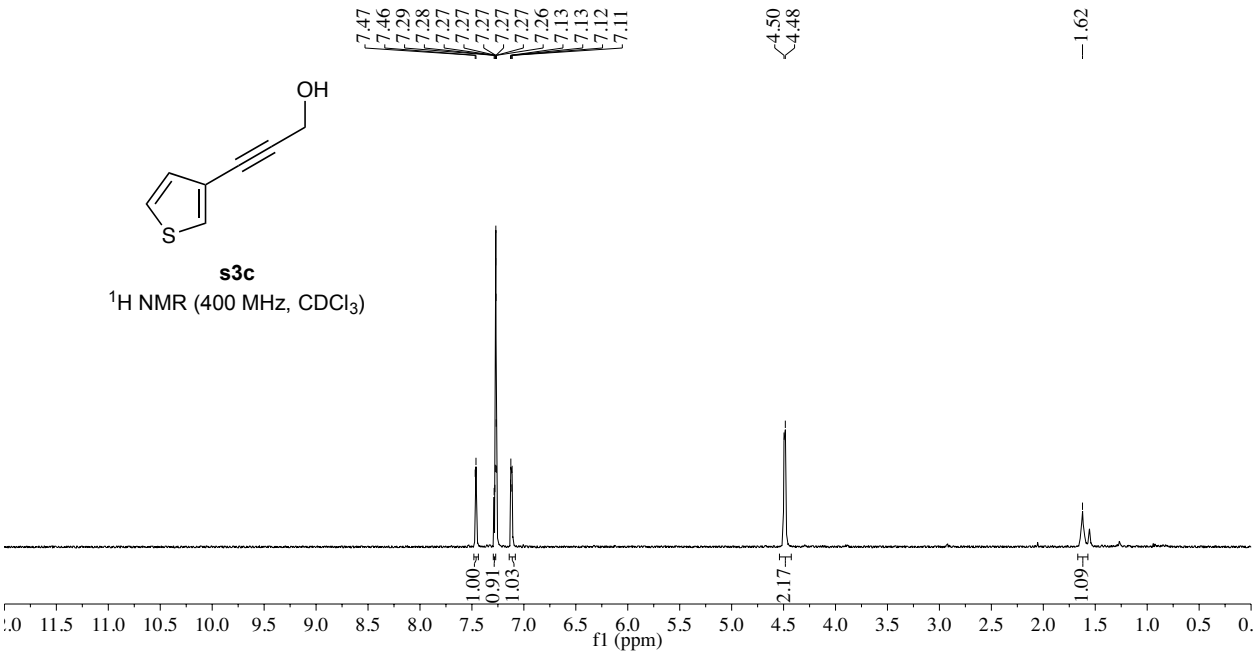

**s3b**

$^{1}$H NMR (400 MHz, $CDCl_3$)



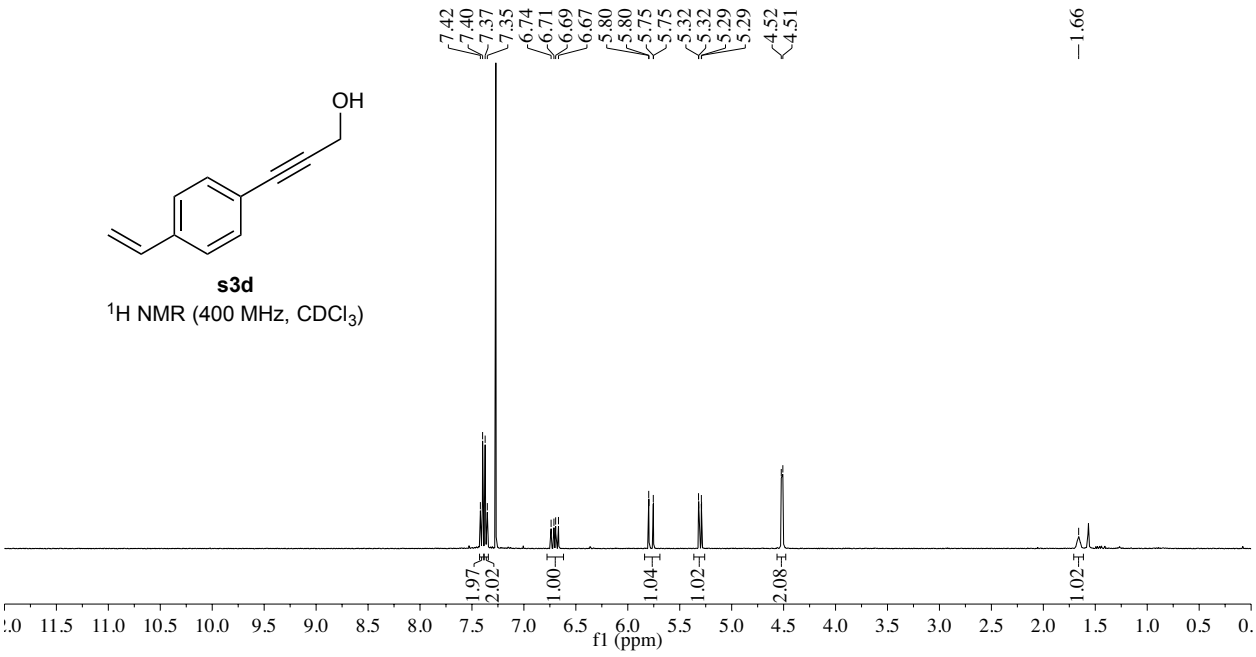

**s3b**

$^{13}$C NMR (101 MHz, $CDCl_3$)



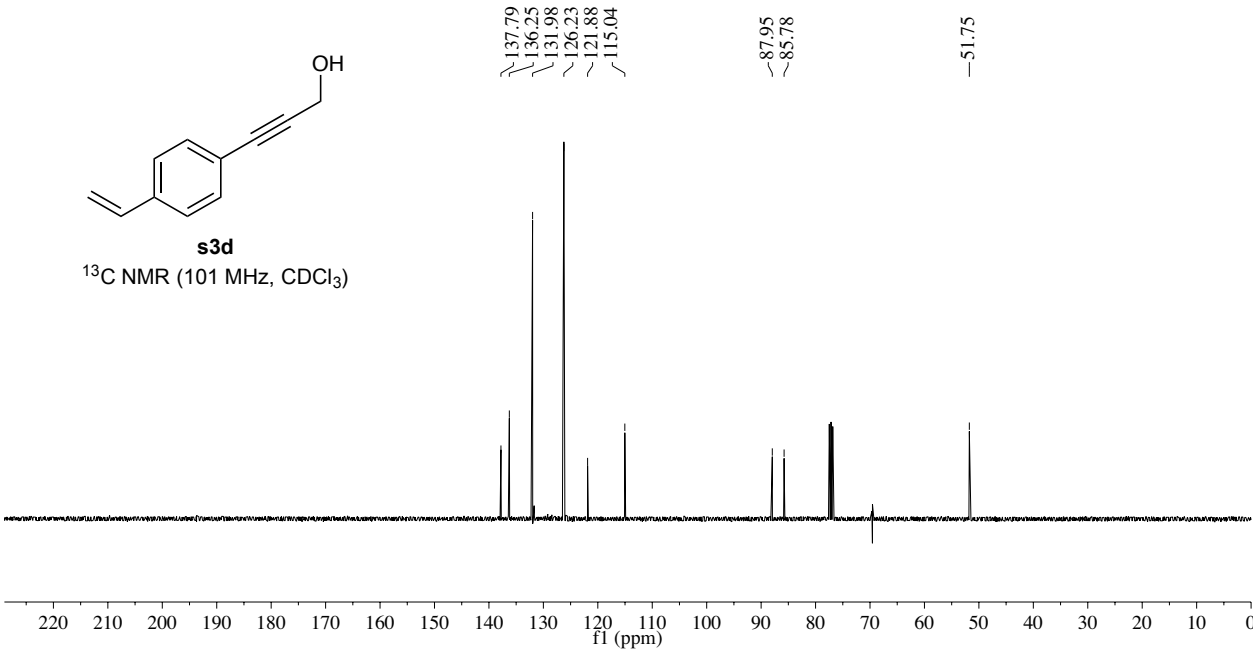

**s3c**

$^1$H NMR (400 MHz, $CDCl_3$)



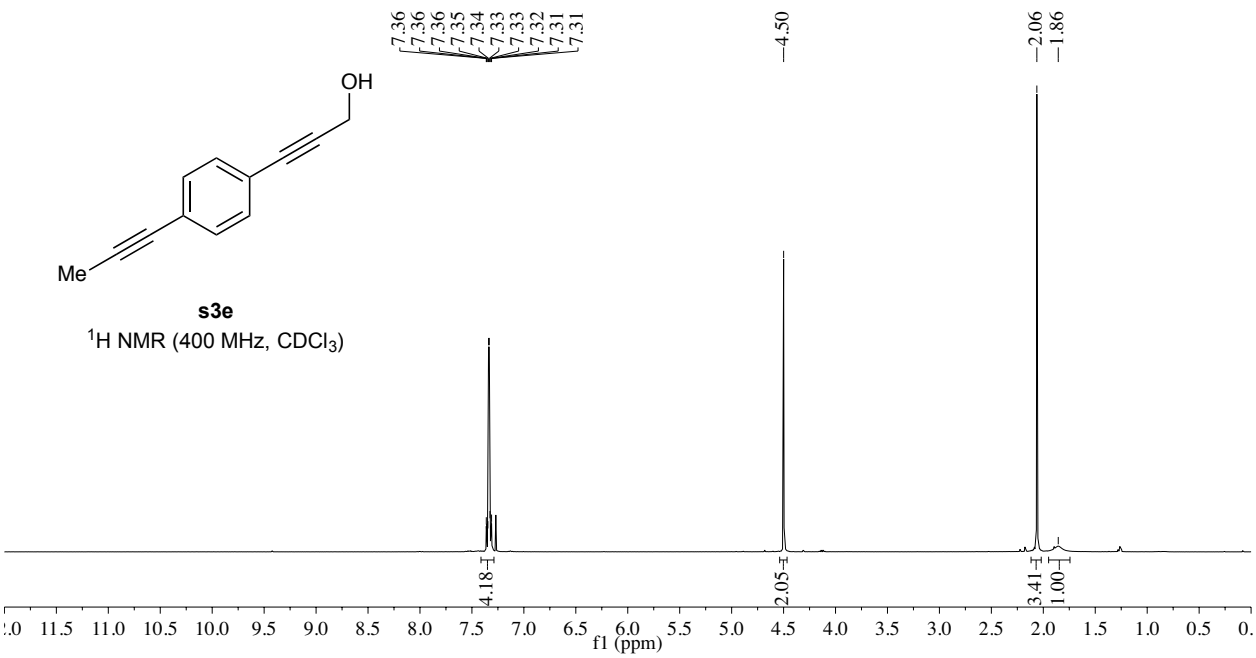

**s3d**

$^1$H NMR (400 MHz, $CDCl_3$)



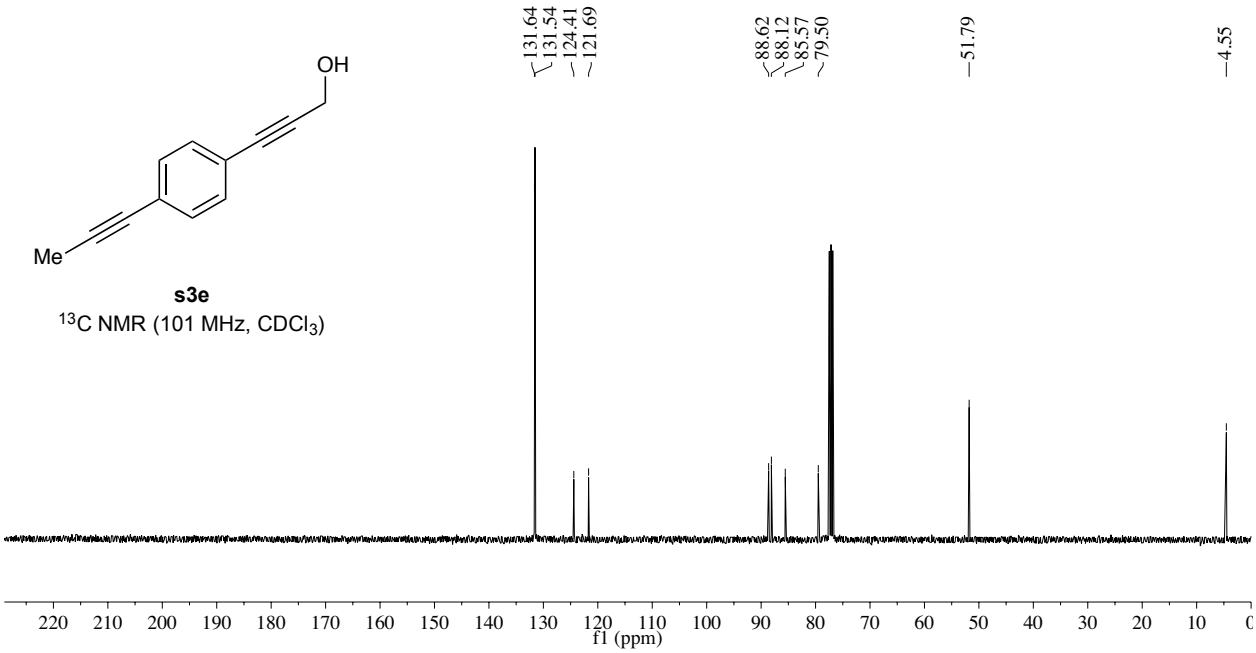

**s3d**

$^{13}$C NMR (101 MHz, $CDCl_3$)



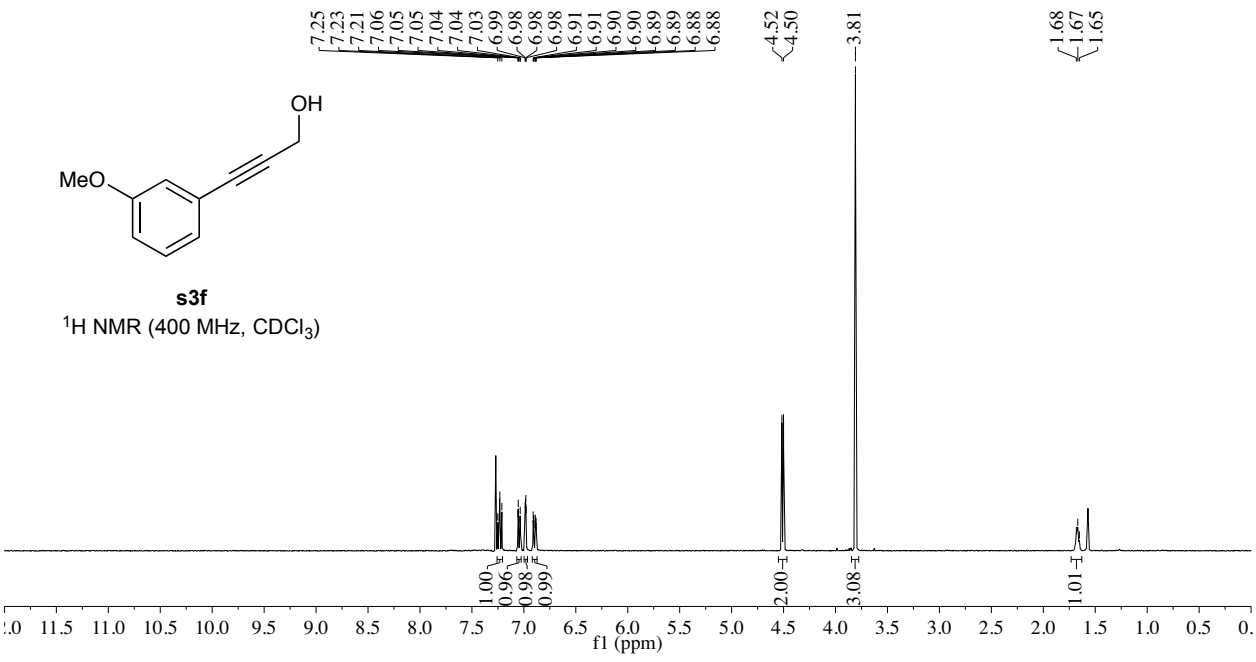

**s3e**

$^{1}$H NMR (400 MHz, $CDCl_3$)



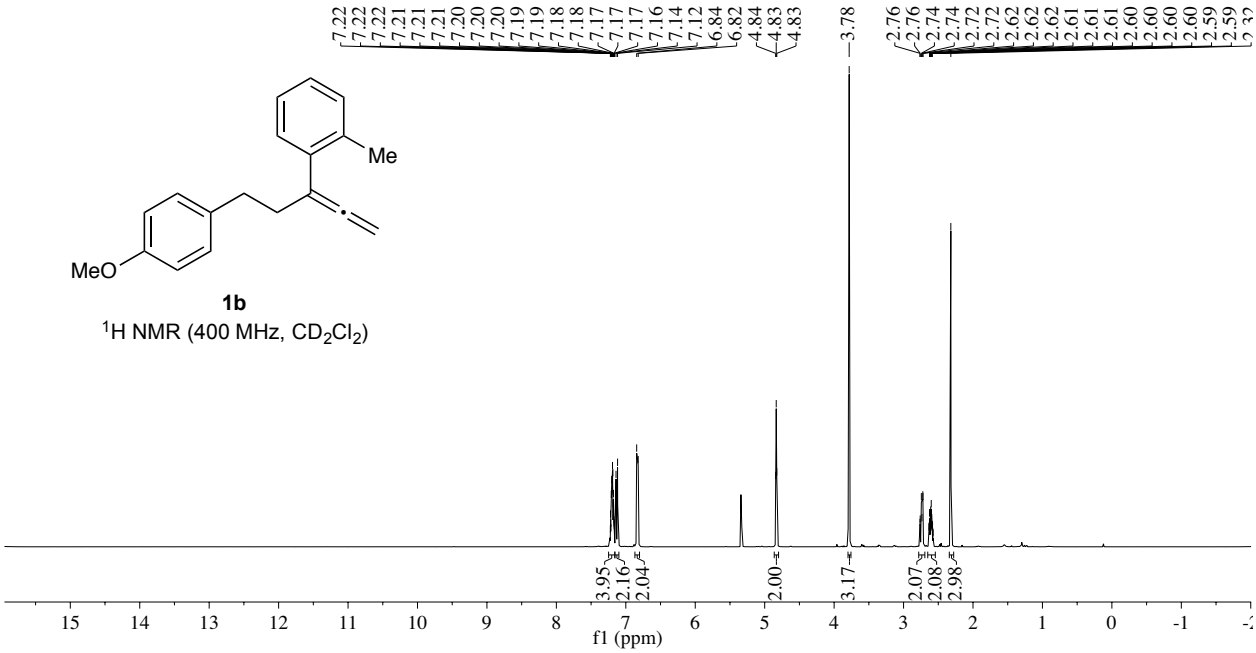

**s3e**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



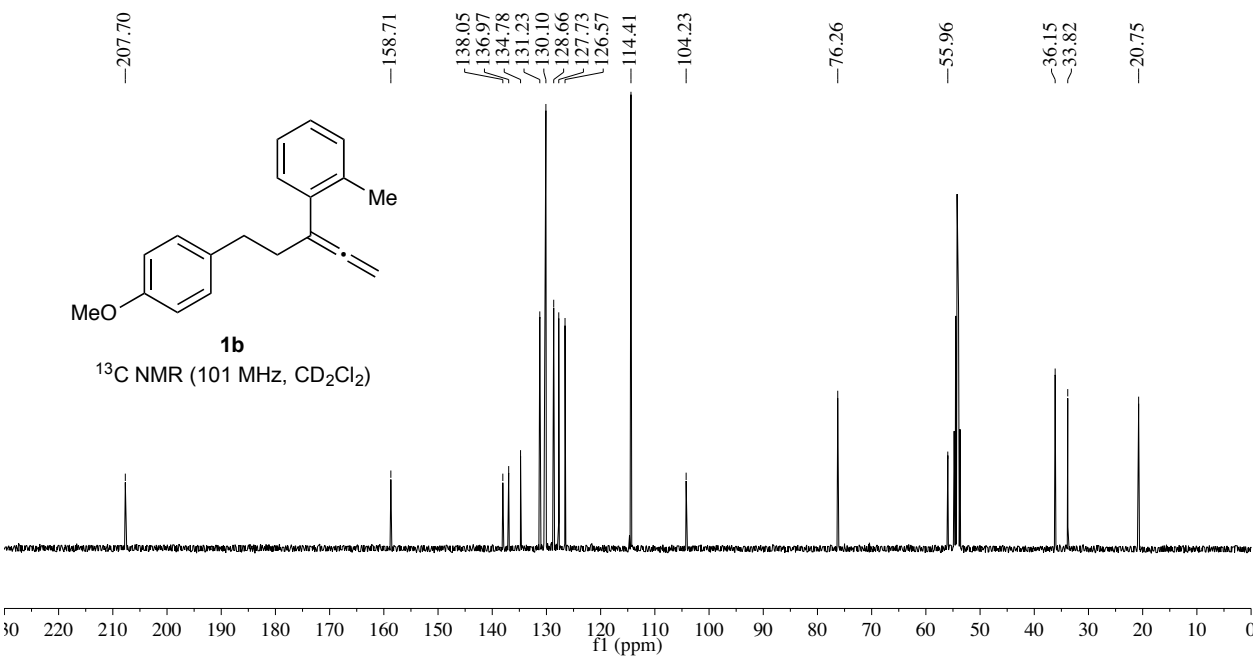

**s3f**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



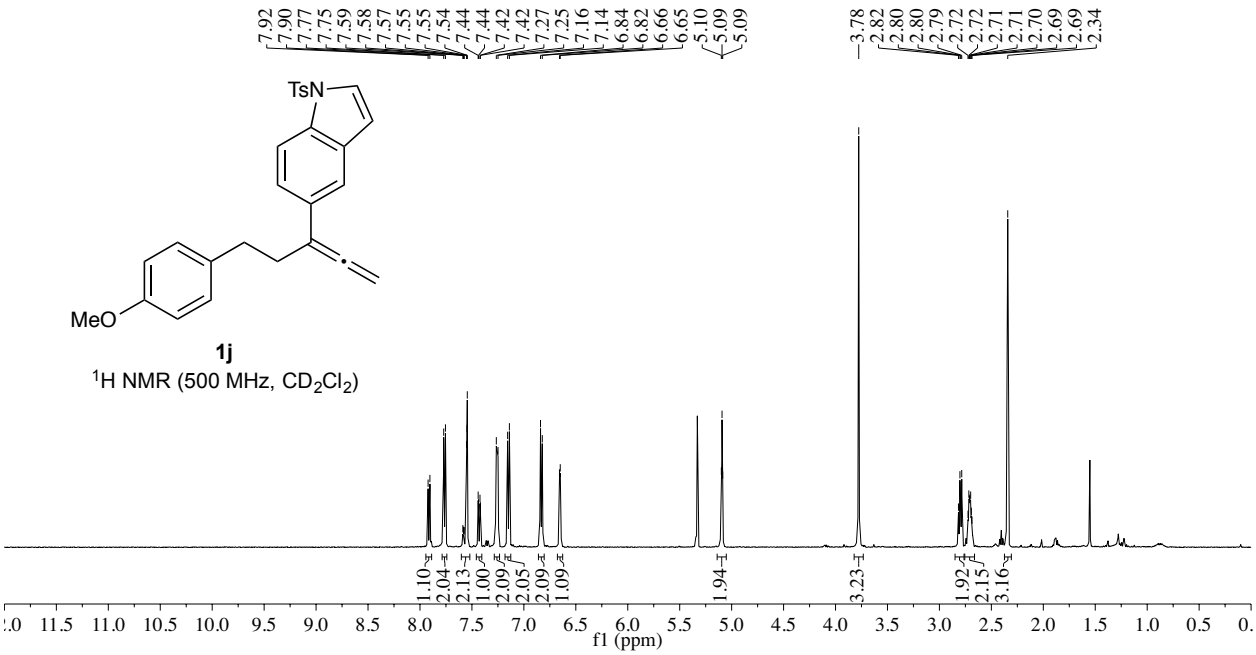

**1b**

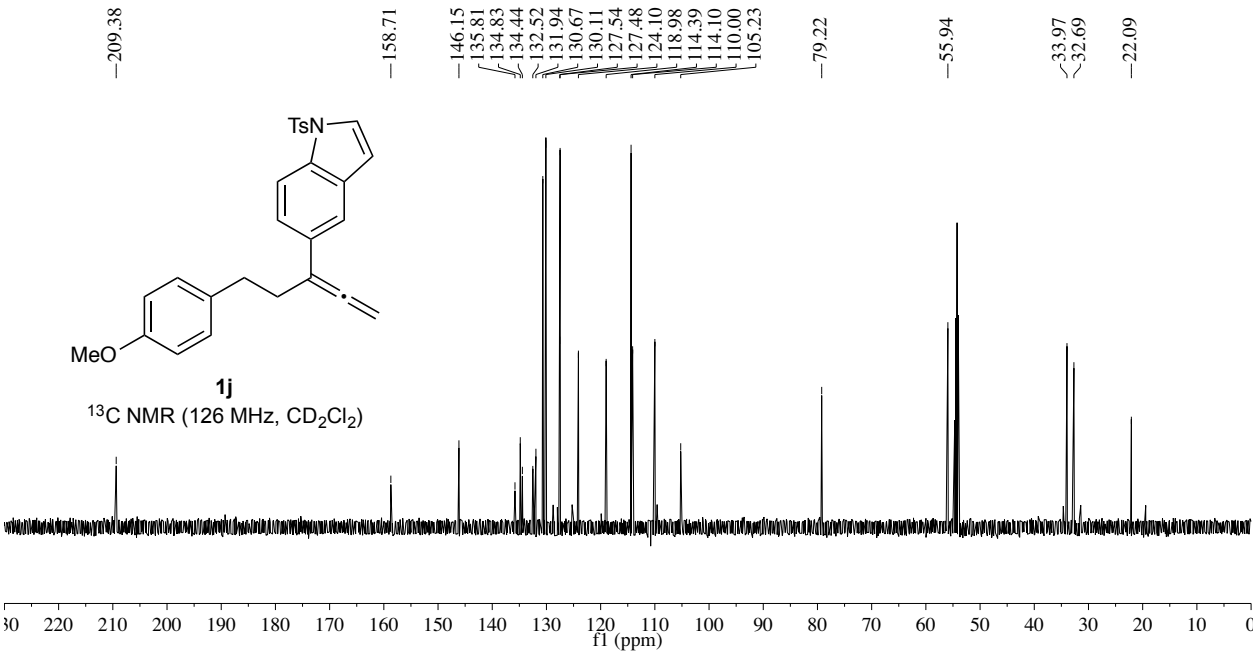
$^{1}$H NMR (400 MHz, $CD_2Cl_2$)

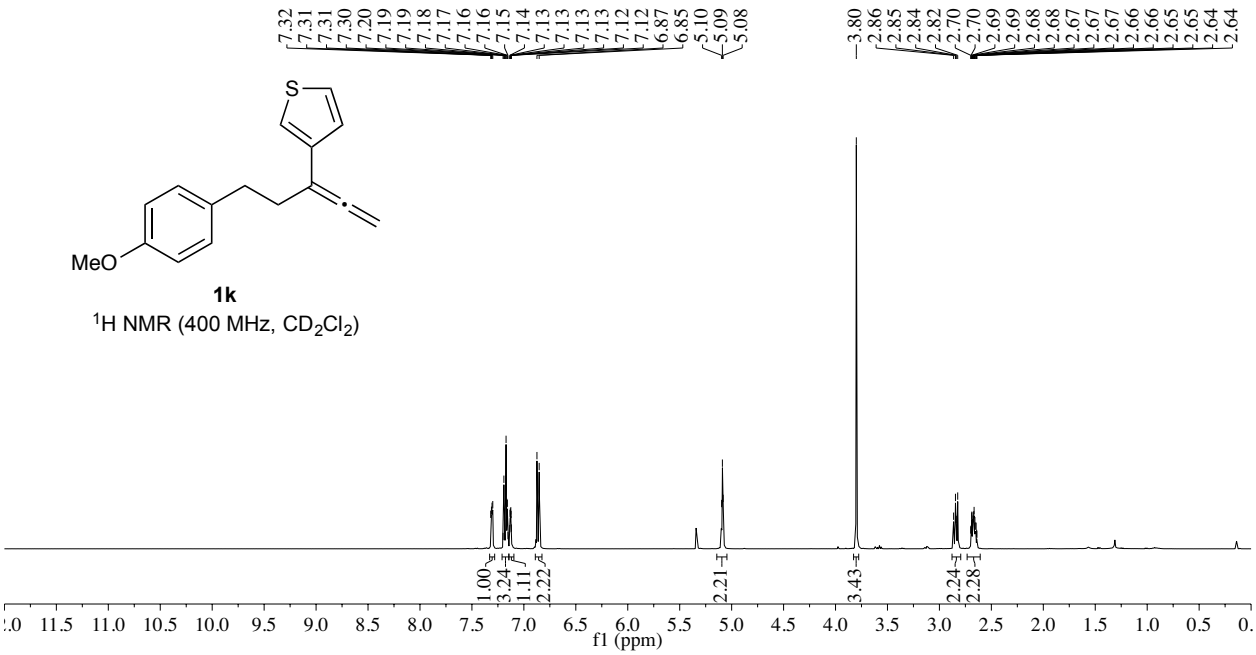



**1b**

$^{13}$C NMR (101 MHz, $CD_2Cl_2$)

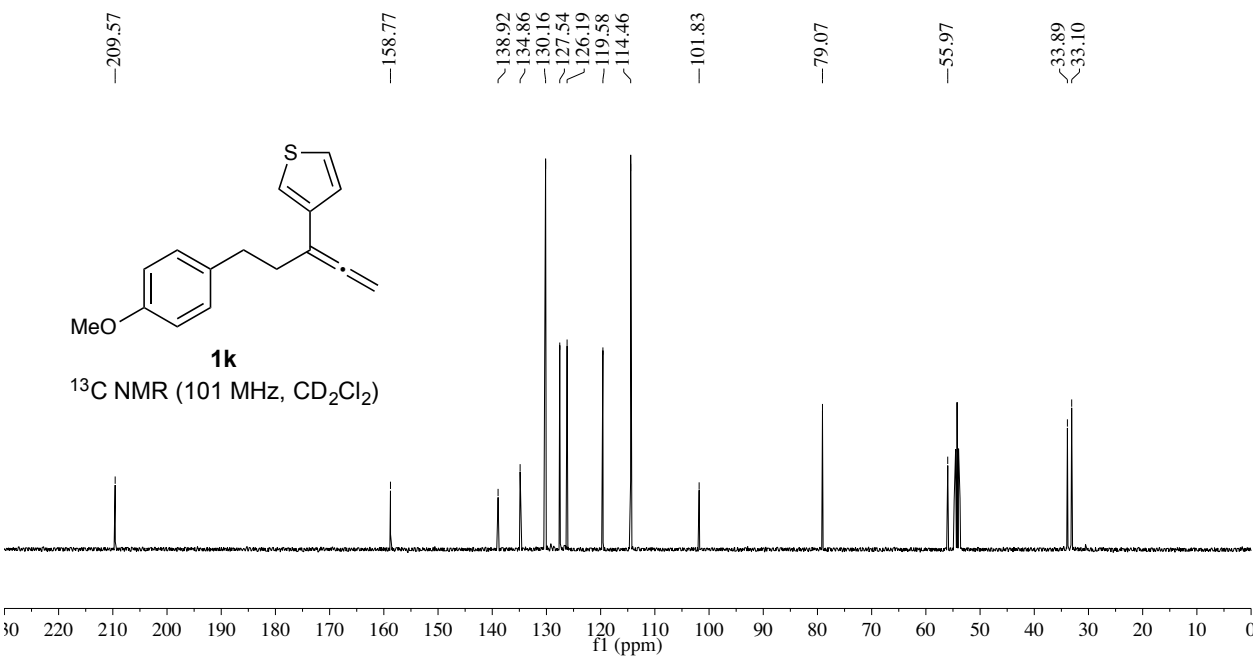

TsN
MeO
1j
1H NMR (500 MHz, CD2Cl2)
f1 (ppm)


TsN
MeO
1j
13C NMR (126 MHz, CD2Cl2)
f1 (ppm)



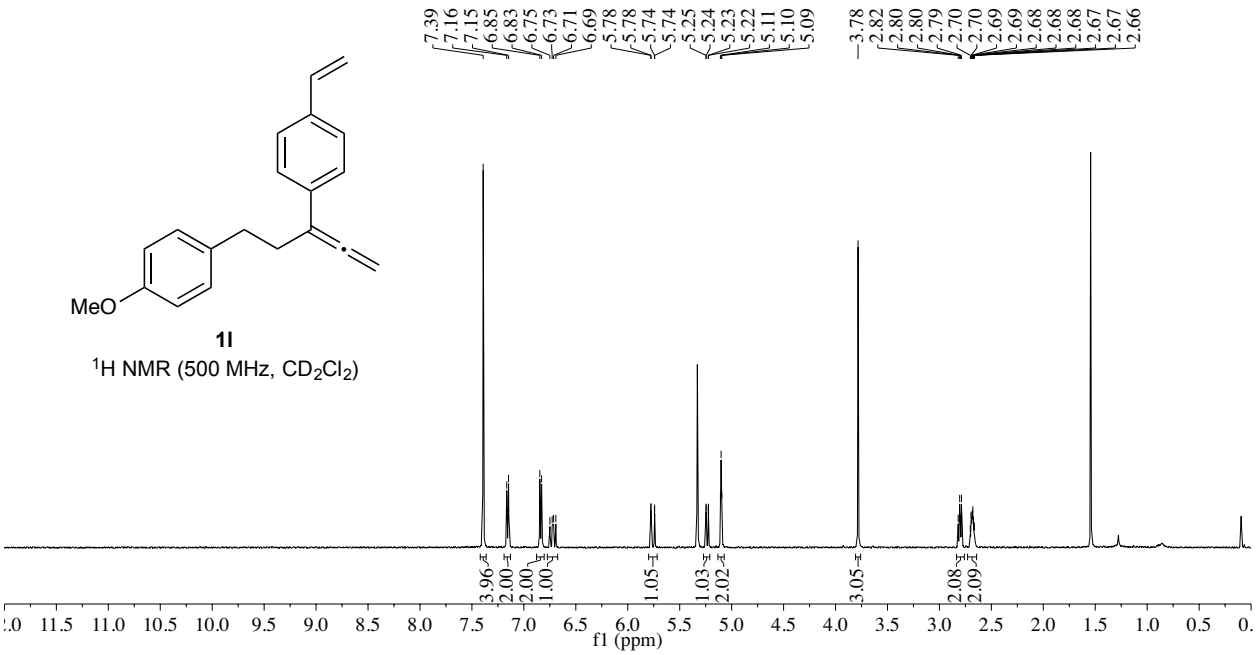

**1k**

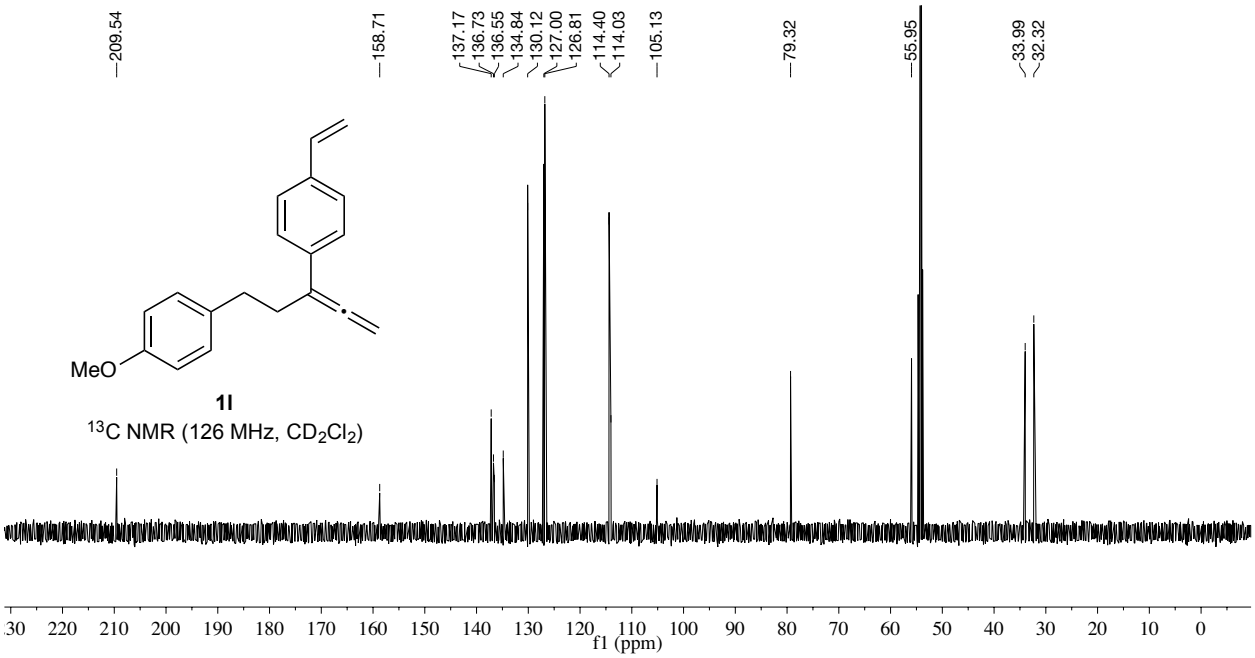
$^{1}H$ NMR (400 MHz, $CD_2Cl_2$)

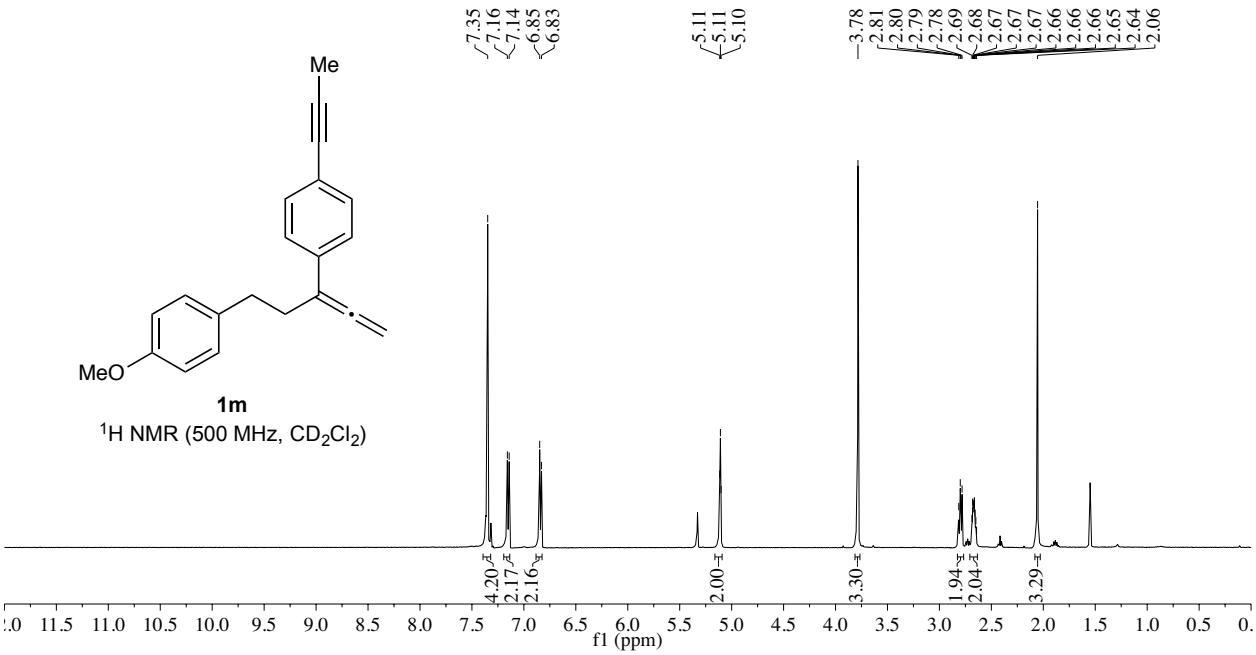



**1k**

$^{13}C$ NMR (101 MHz, $CD_2Cl_2$)

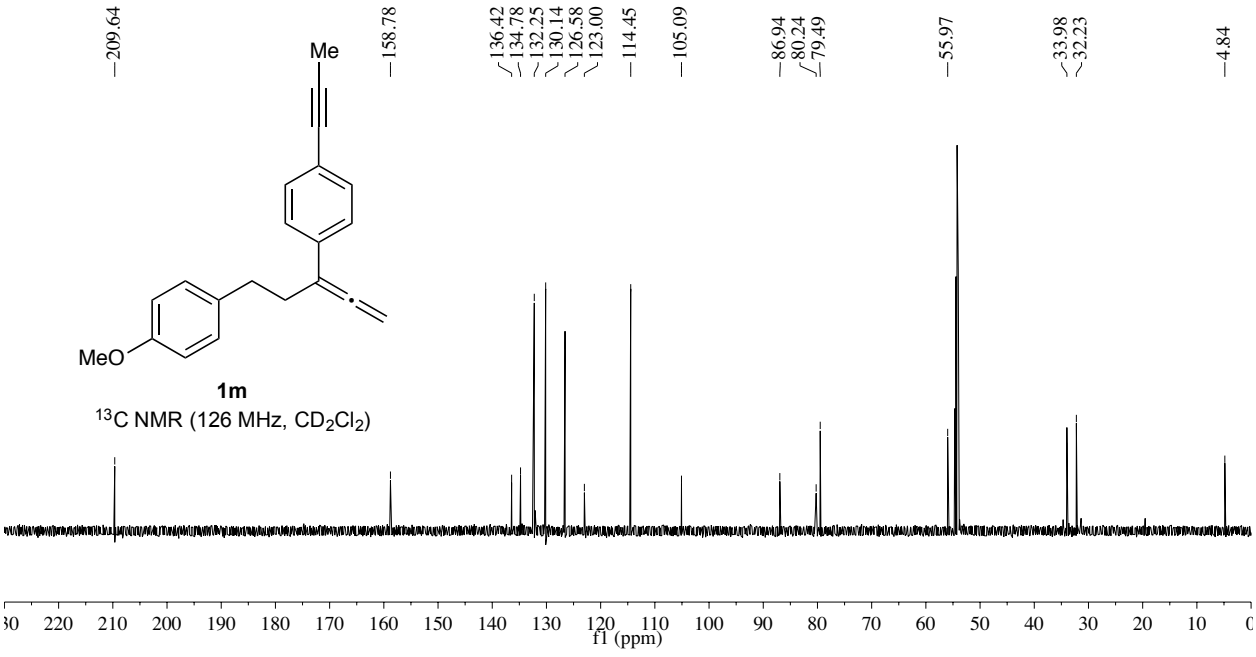

MeO
1I
$^1$H NMR (500 MHz, $CD_2Cl_2$)
f1 (ppm)


MeO
1I
$^{13}$C NMR (126 MHz, $CD_2Cl_2$)
f1 (ppm)



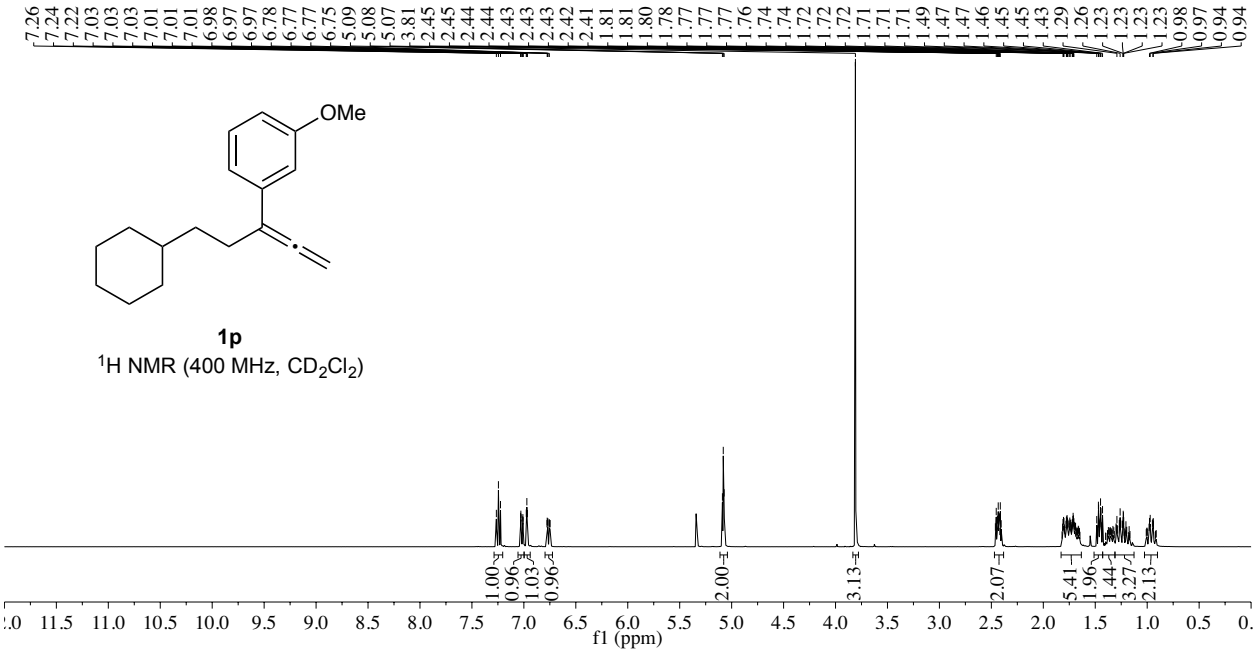

**1m**

$^{1}$H NMR (500 MHz, $CD_2Cl_2$)



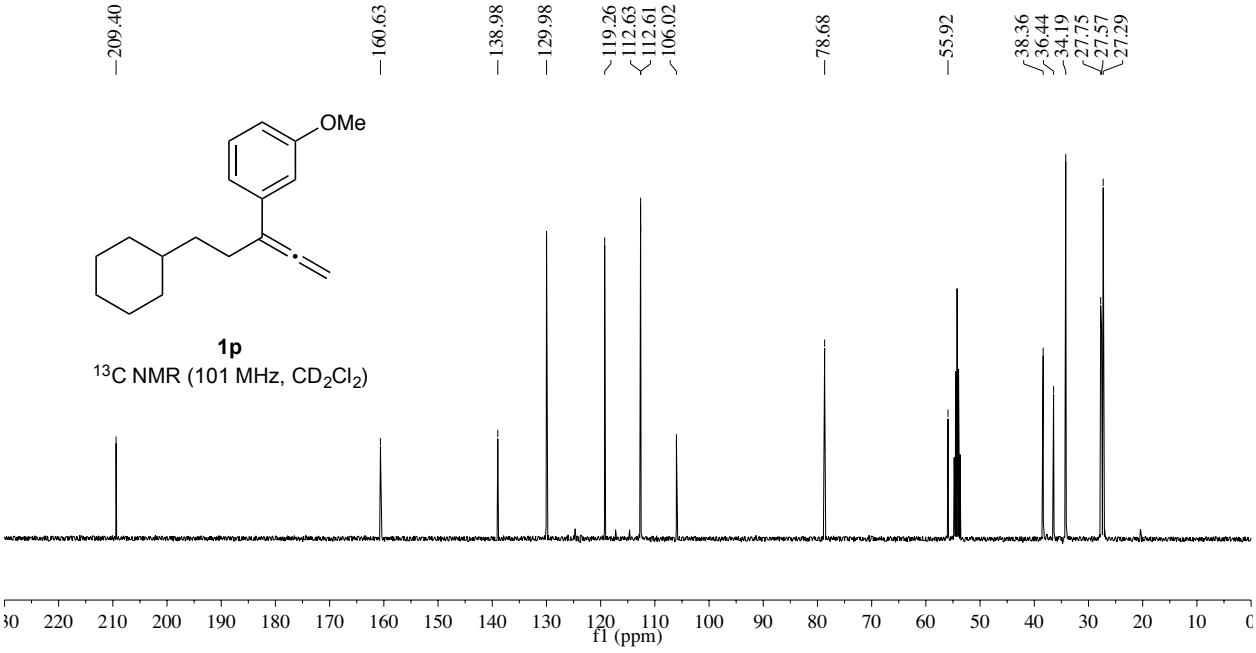

**1m**

$^{13}$C NMR (126 MHz, $CD_2Cl_2$)



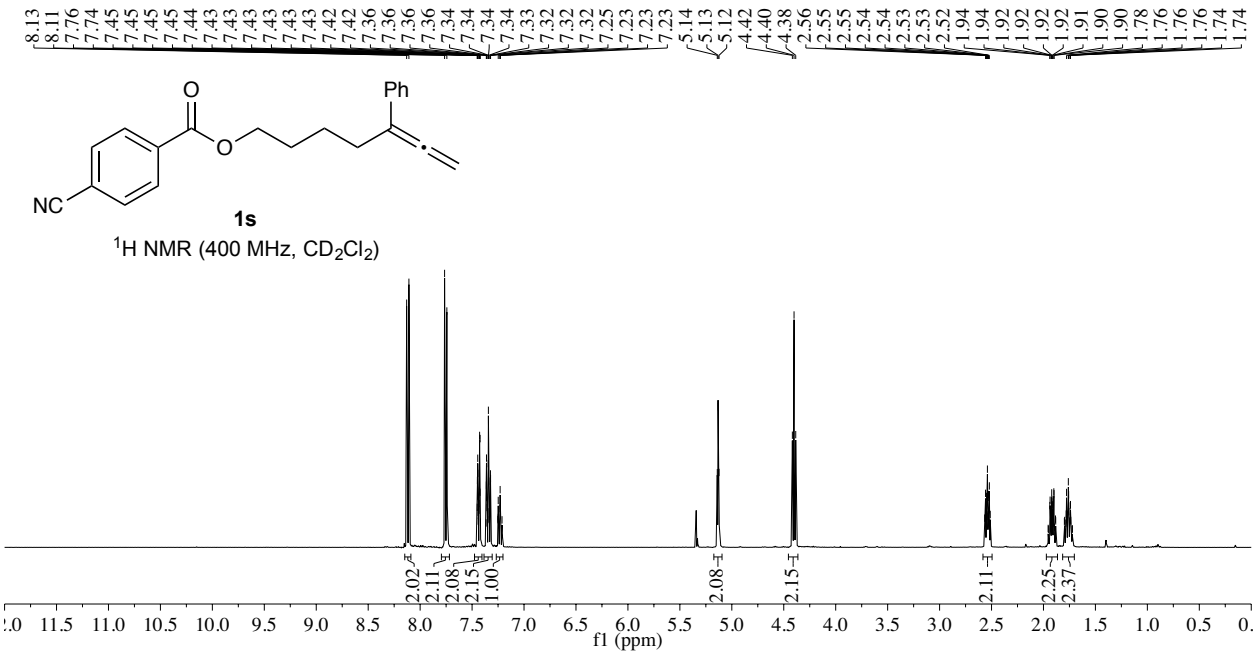

**1p**

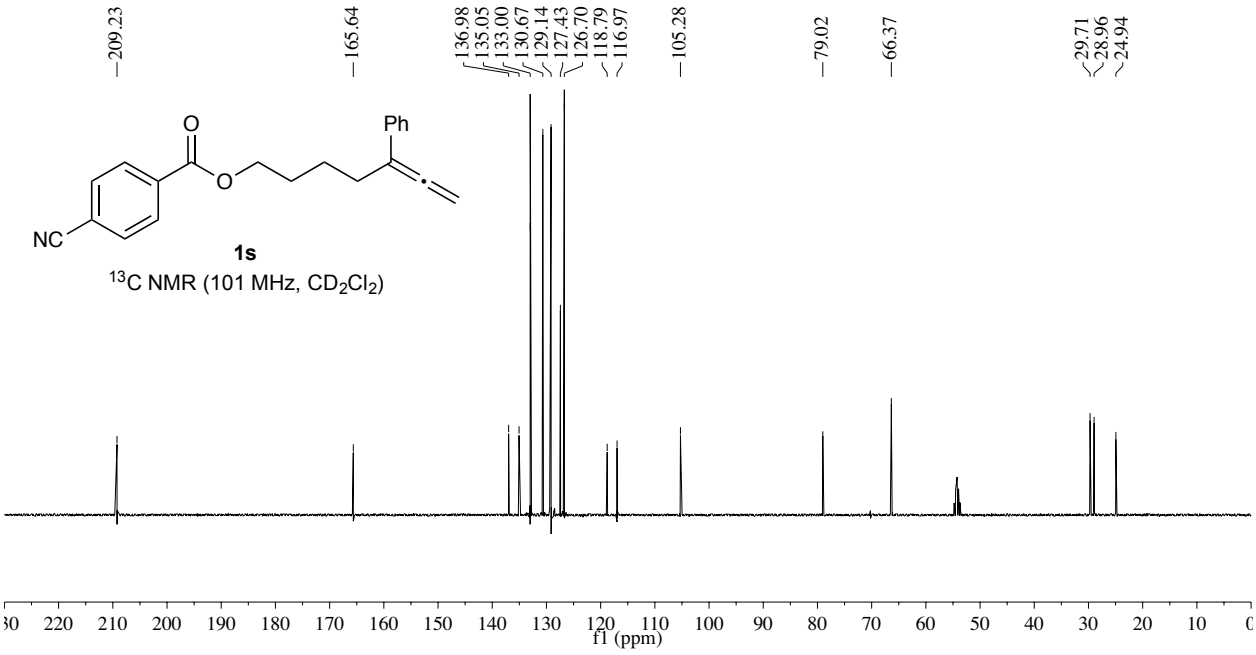
$^{1}$H NMR (400 MHz, $CD_2Cl_2$)

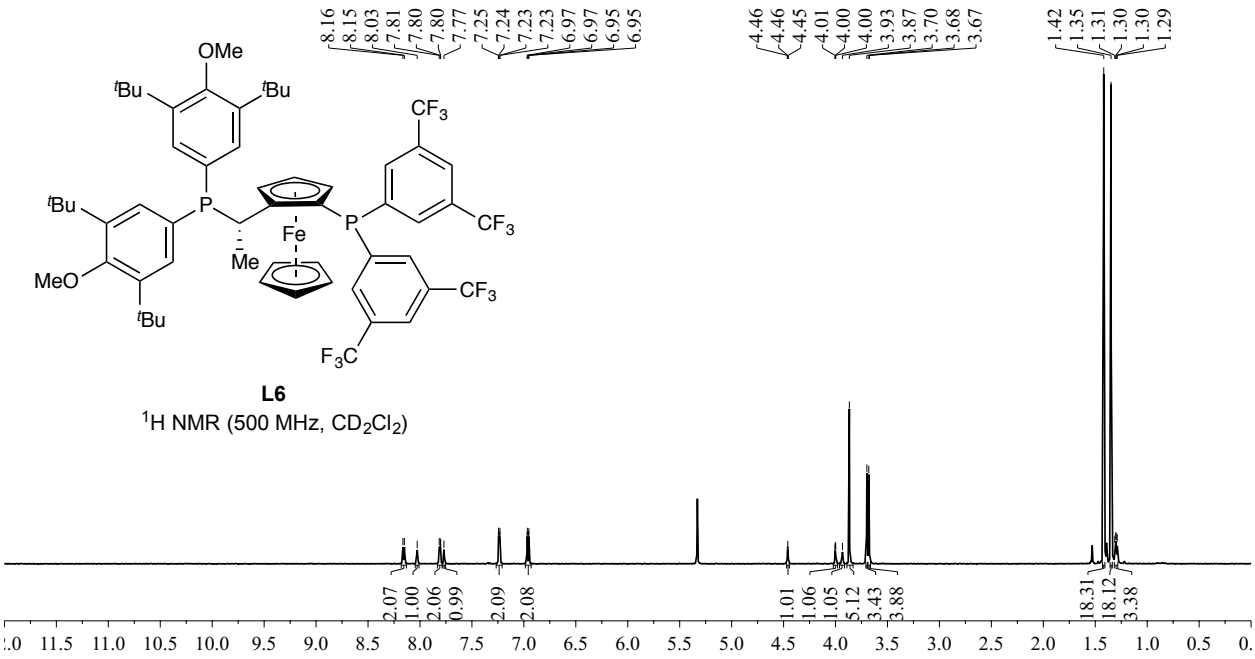



**1p**

$^{13}$C NMR (101 MHz, $CD_2Cl_2$)

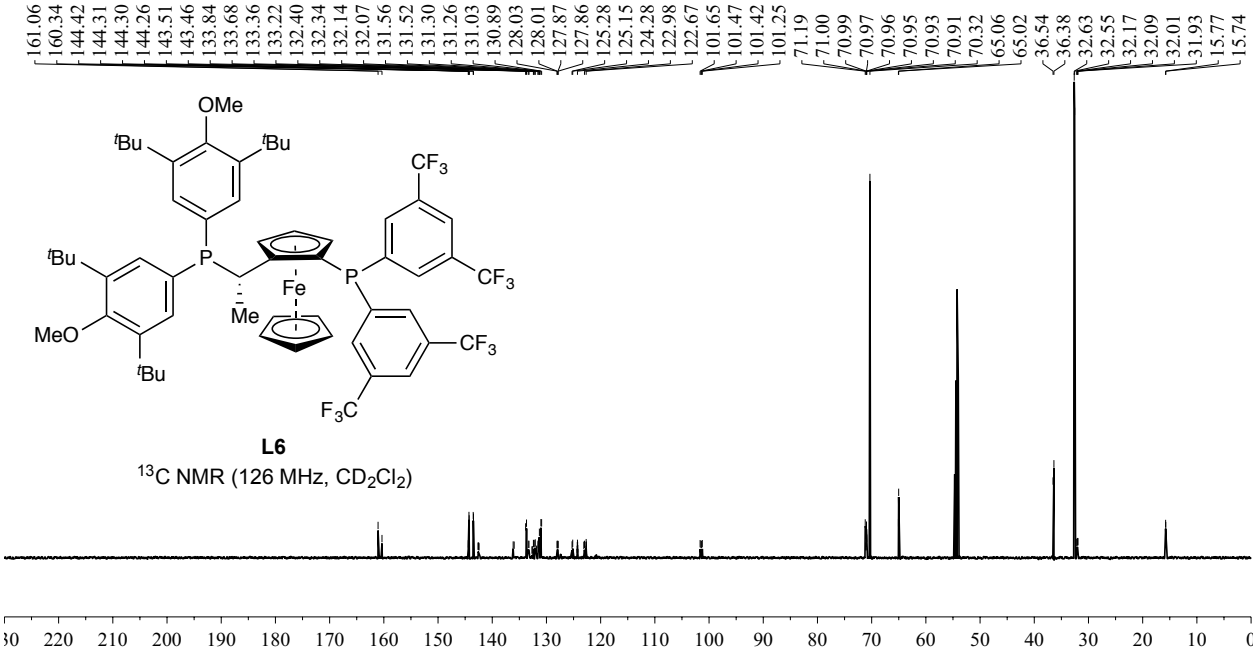

8.13 8.11 7.76 7.74 7.45 7.45 7.45 7.45 7.44 7.43 7.43 7.43 7.43 7.43 7.43 7.42 7.42 7.36 7.36 7.36 7.34 7.34 7.34 7.34 7.33 7.32 7.32 7.32 7.25 7.23 7.23 7.23 5.14 5.13 5.12 4.42 4.40 4.38 2.56 2.55 2.55 2.54 2.54 2.53 2.53 2.52 1.94 1.94 1.92 1.92 1.92 1.92 1.92 1.91 1.90 1.90 1.78 1.76 1.76 1.76 1.74 1.74
O
Ph
O
NC
1s
1H NMR (400 MHz, CD2Cl2)
2.02
2.11
2.08
2.15
1.00
2.08
2.15
2.11
2.25
2.37
f1 (ppm)


209.23
165.64
136.98
135.05
133.00
130.67
129.14
127.43
126.70
118.79
116.97
105.28
79.02
66.37
29.71
28.96
24.94
O
Ph
O
NC
1s
13C NMR (101 MHz, CD2Cl2)
f1 (ppm)



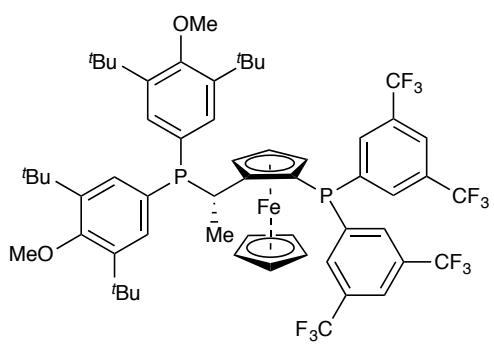

**L6**

$^{1}$H NMR (500 MHz, $CD_2Cl_2$)




**L6**

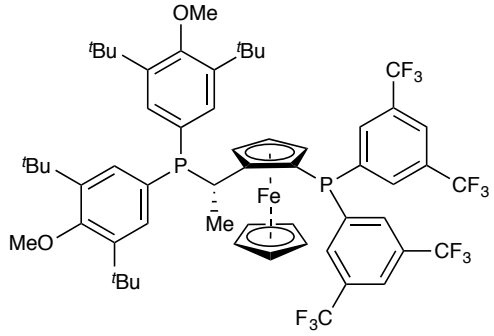
$^{13}$C NMR (126 MHz, $CD_2Cl_2$)




**L6**

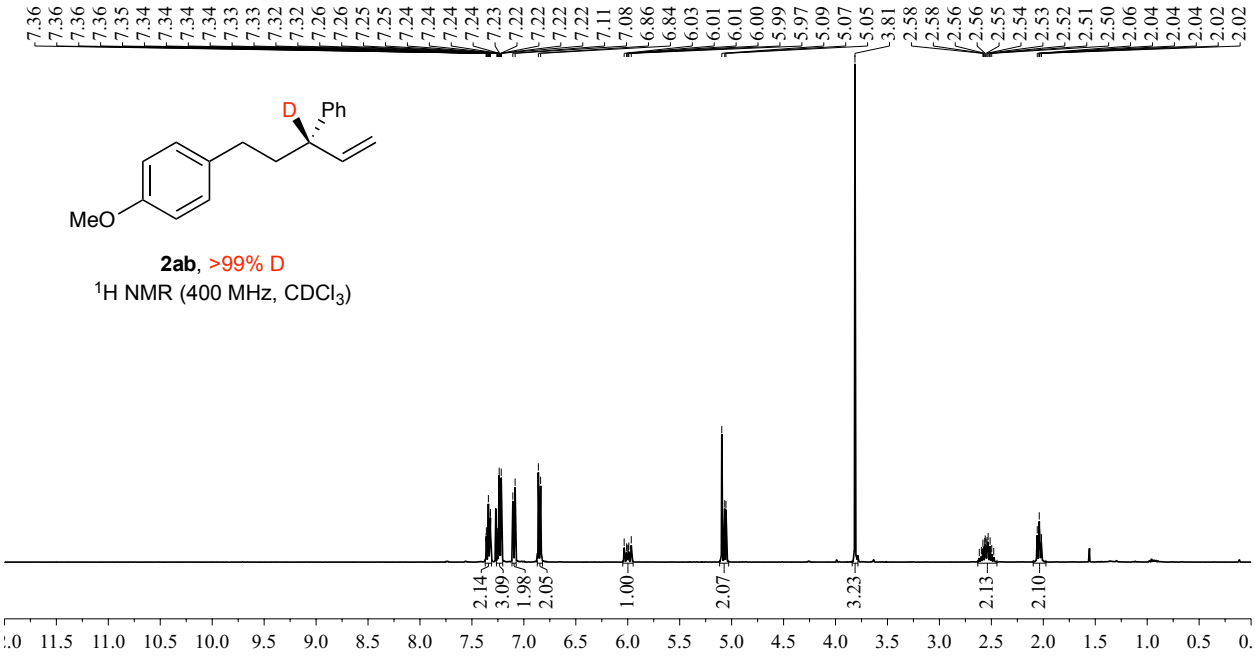
$^{31}P$ NMR (162 MHz, $CD_2Cl_2$)



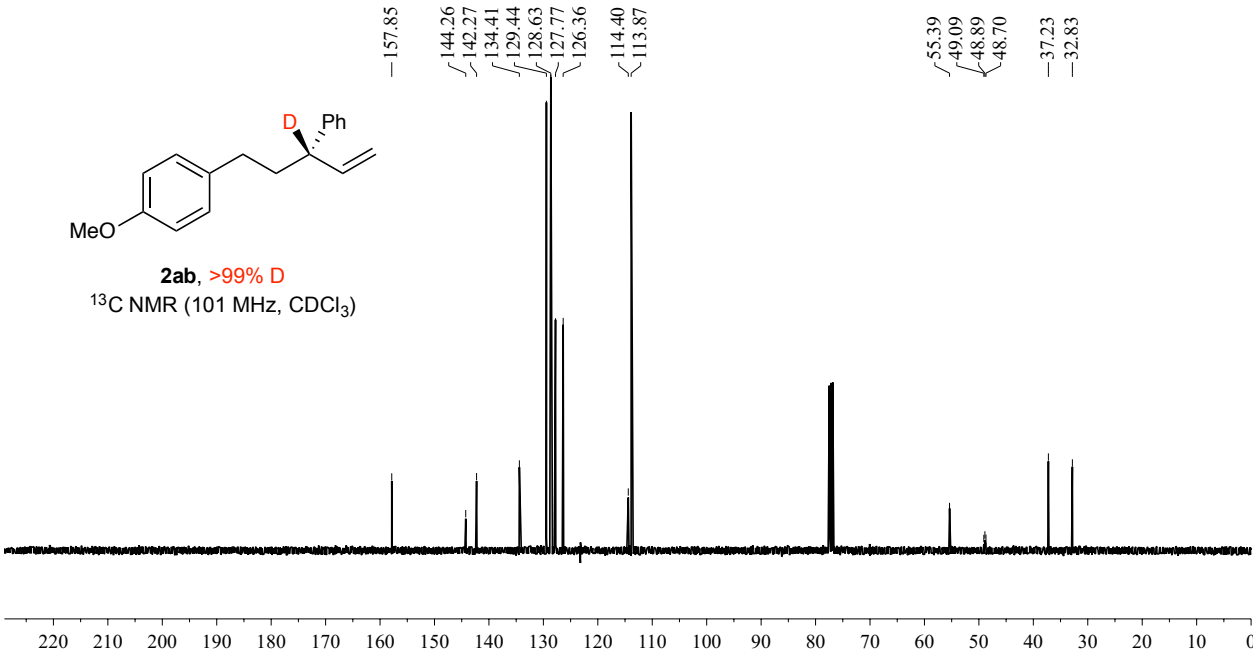

**L6**

$^{19}F$ NMR (376 MHz, $CD_2Cl_2$)



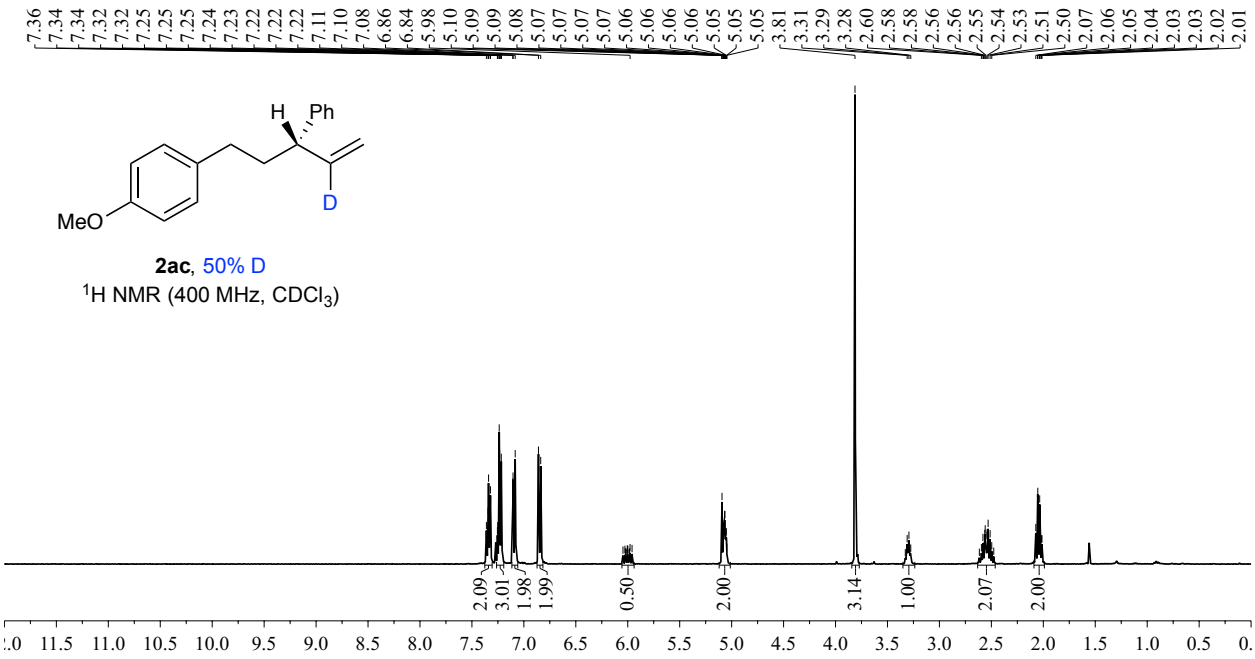

**2ab**, >99% D

$^{1}$H NMR (400 MHz, $CDCl_3$)



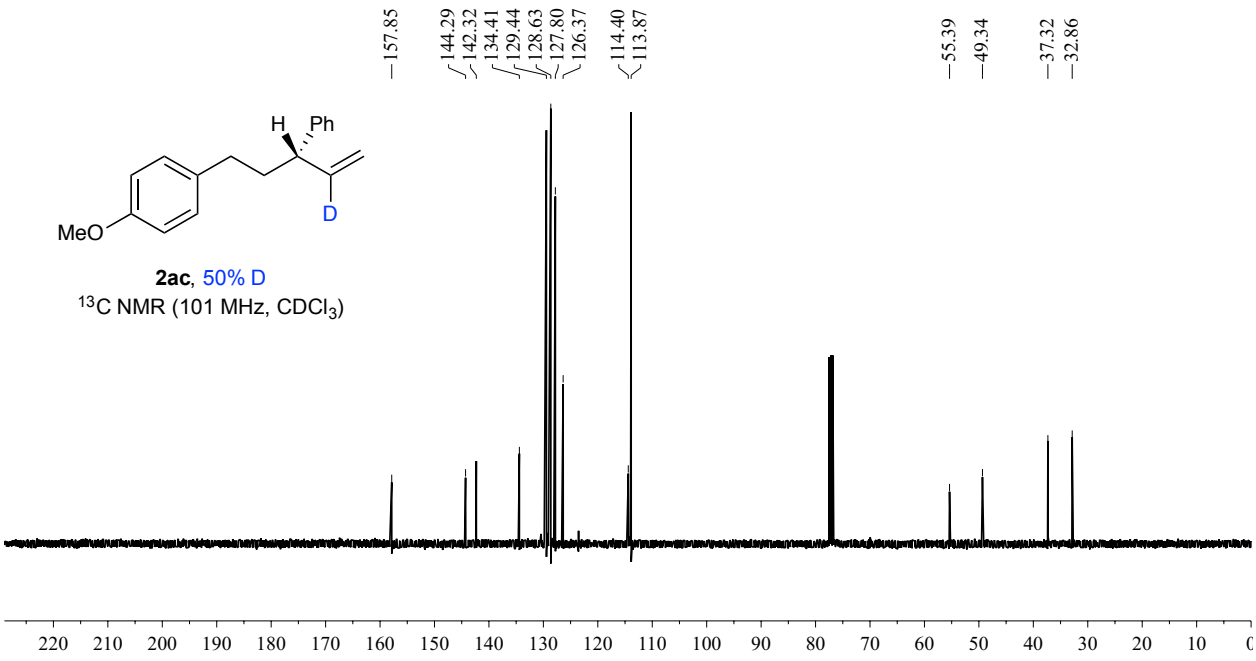

**2ab**, >99% D

$^{13}$C NMR (101 MHz, $CDCl_3$)




**2ac**, 50% D

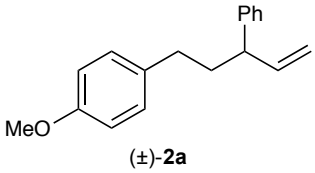
$^{1}$H NMR (400 MHz, $CDCl_3$)



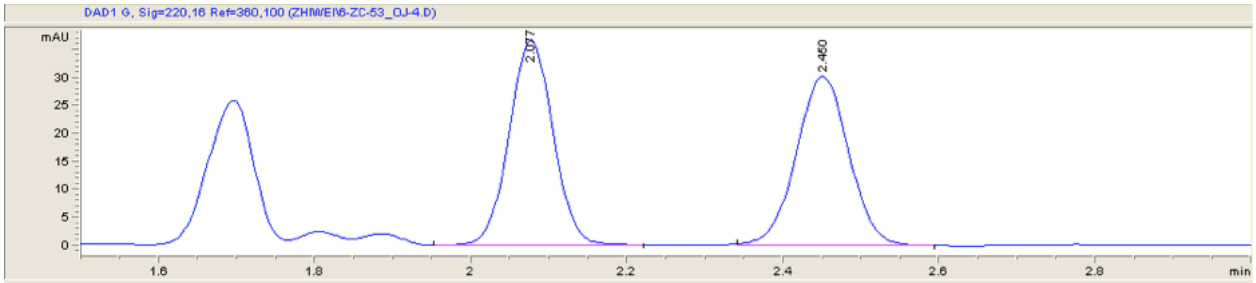

**2ac**, 50% D

$^{13}$C NMR (101 MHz, $CDCl_3$)

## 6. SFC Spectra




(±)-**2a**

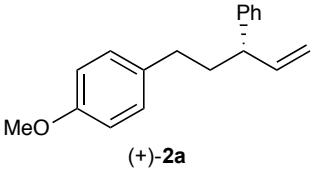



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.077 | 143.7 | 36.7 | 0.0617 | 50.463 | 0.938 |
| 2 | 2.45 | 141 | 30.2 | 0.0725 | 49.537 | 0.984 |

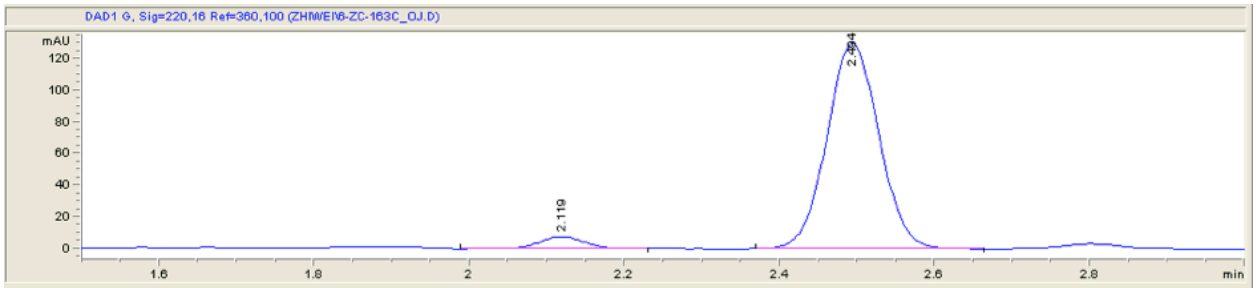
File Information

| | |
|---|---|
| LC-File | 6-ZC-53_OJ-4.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 12-Aug-16, 22:59:01 |

* peak at 1.7 min is residual internal alkene that was not completely separated from the product



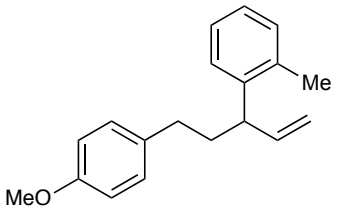

(+)-**2a**



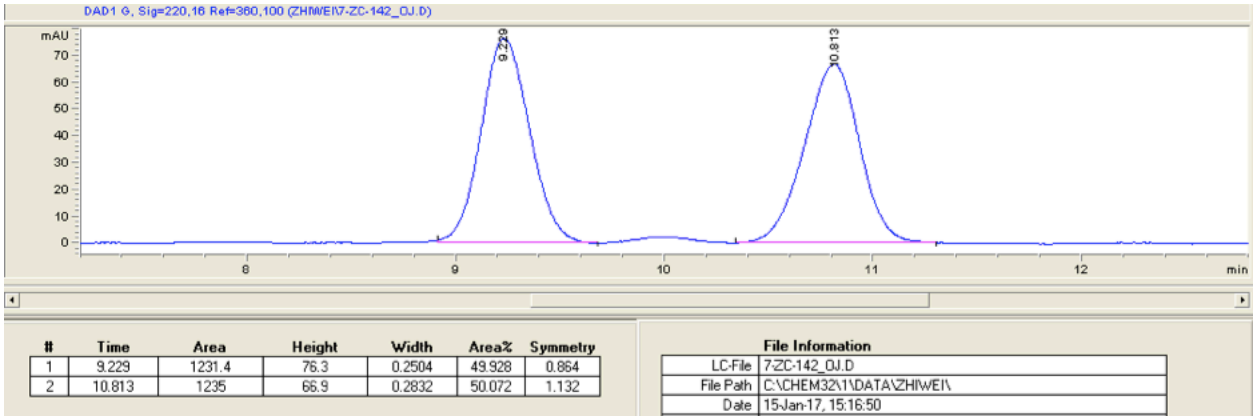

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.119 | 31.1 | 7.6 | 0.0635 | 4.887 | 0.914 |
| 2 | 2.494 | 604.4 | 129.4 | 0.0745 | 95.113 | 0.934 |

File Information

| | |
|---|---|
| LC-File | 6-ZC-163C_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 03-Oct-16, 12:01:54 |

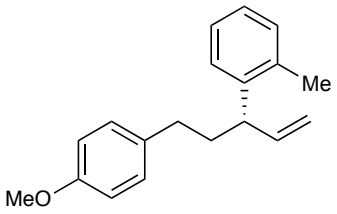



(±)-**2b**

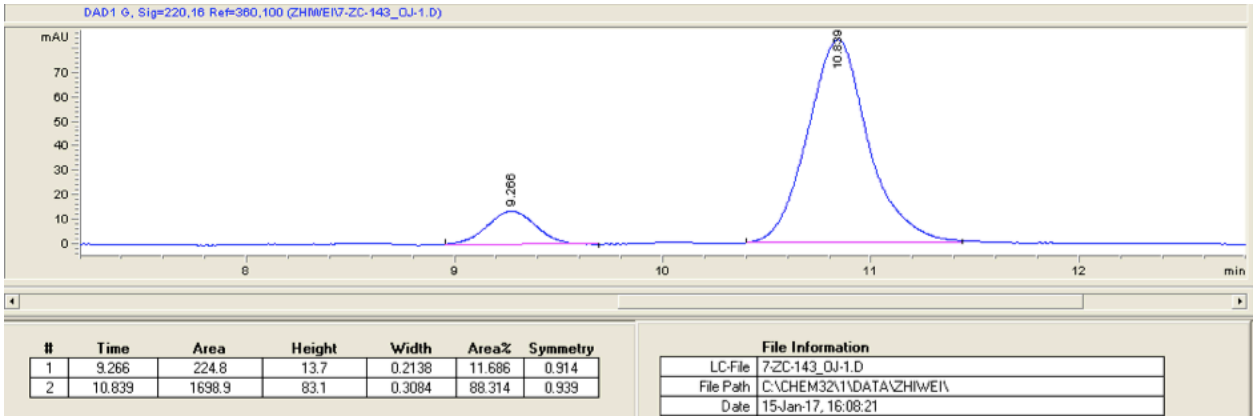



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.229 | 1231.4 | 76.3 | 0.2504 | 49.928 | 0.864 |
| 2 | 10.813 | 1235 | 66.9 | 0.2832 | 50.072 | 1.132 |

| File Information | |
|---|---|
| LC-File | 7-ZC-142_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 15-Jan-17, 15:16:50 |

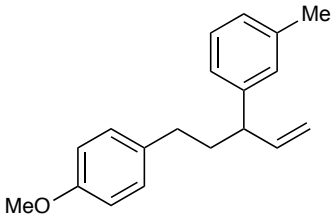



(+)-**2b**

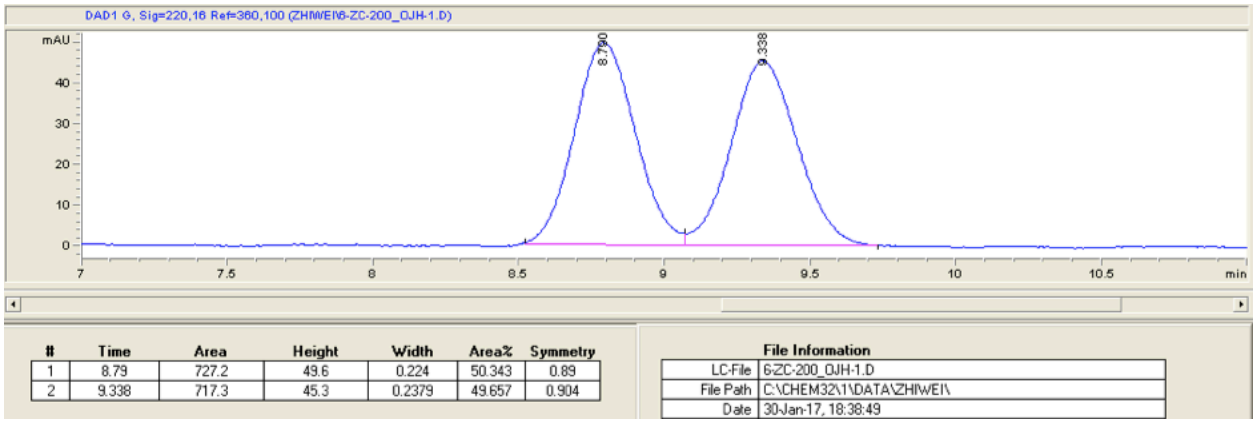



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.266 | 224.8 | 13.7 | 0.2138 | 11.686 | 0.914 |
| 2 | 10.839 | 1698.9 | 83.1 | 0.3084 | 88.314 | 0.939 |

| File Information | |
|---|---|
| LC-File | 7-ZC-143_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 15-Jan-17, 16:08:21 |

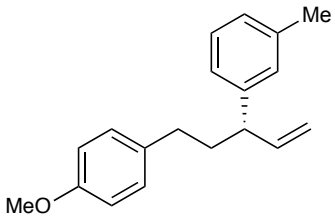



(±)-**2c**

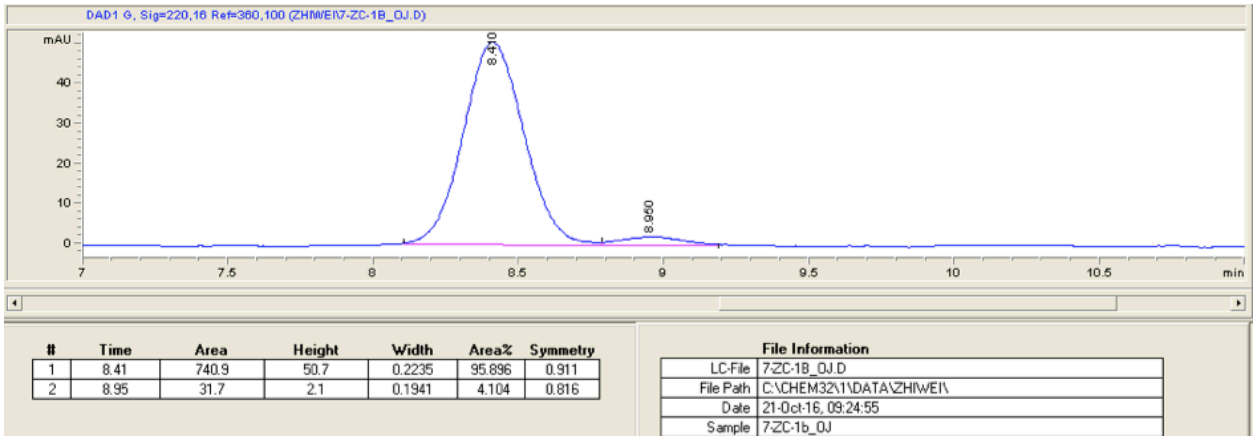



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.79 | 727.2 | 49.6 | 0.224 | 50.343 | 0.89 |
| 2 | 9.338 | 717.3 | 45.3 | 0.2379 | 49.657 | 0.904 |

| File Information | |
|---|---|
| LC-File | 6-ZC-200_OJH-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 18:38:49 |

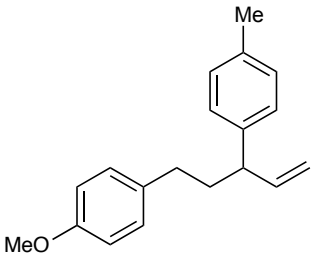



(+)-**2c**

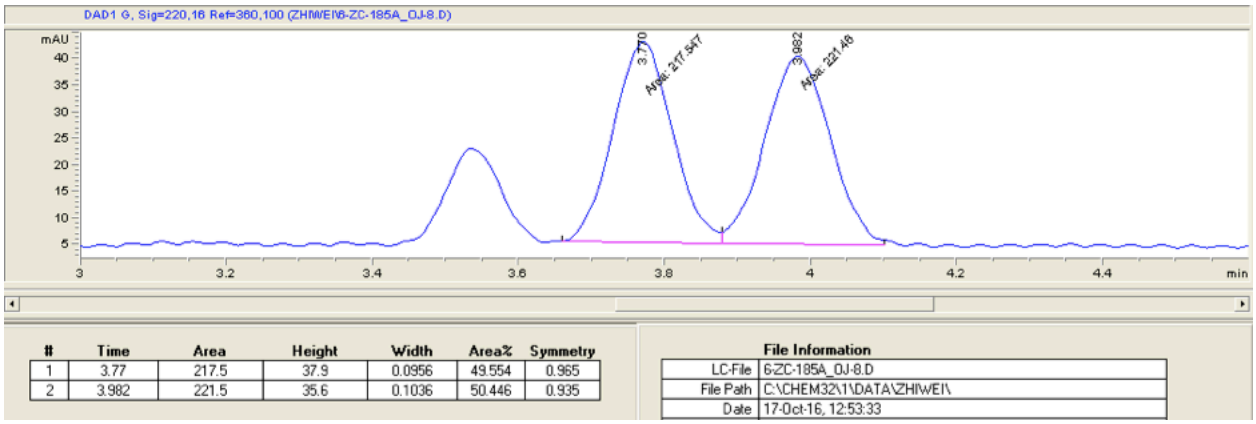



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.41 | 740.9 | 50.7 | 0.2235 | 95.896 | 0.911 |
| 2 | 8.95 | 31.7 | 2.1 | 0.1941 | 4.104 | 0.816 |

| File Information | |
|---|---|
| LC-File | 7-ZC-1B_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 21-Oct-16, 09:24:55 |
| Sample | 7-ZC-1b_OJ |



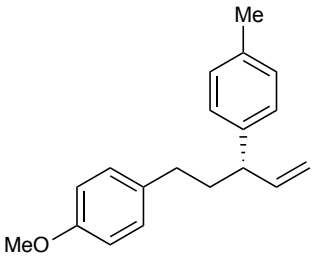

(±)-**2d**



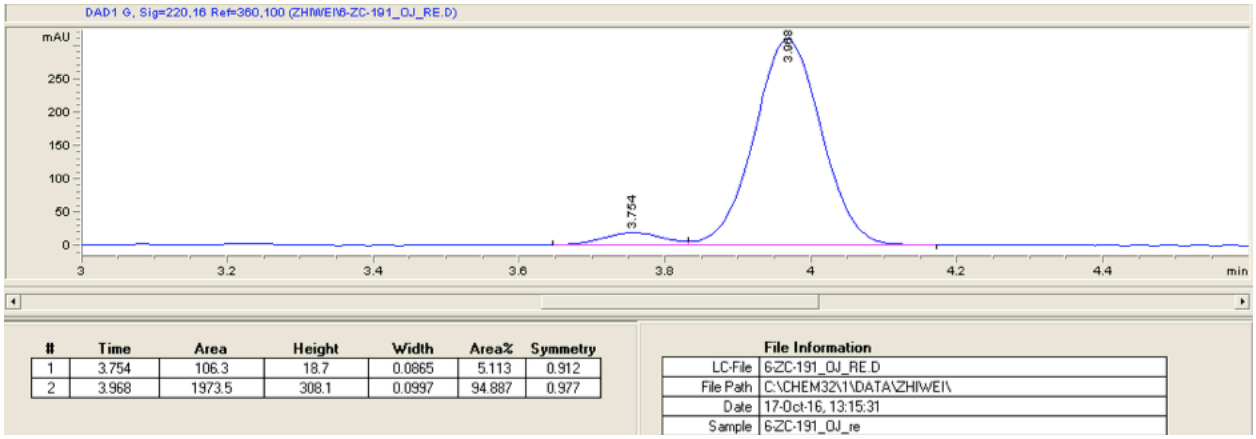

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.77 | 217.5 | 37.9 | 0.0956 | 49.554 | 0.965 |
| 2 | 3.982 | 221.5 | 35.6 | 0.1036 | 50.446 | 0.935 |

| File Information | |
|---|---|
| LC-File | 6-ZC-185A_OJ-8.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 17-Oct-16, 12:53:33 |

* peak at 3.5 min is residual internal alkene that was not completely separated from the product

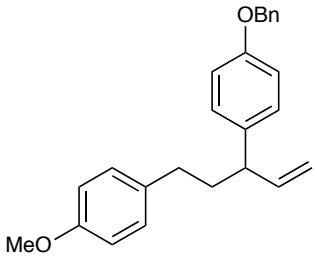



(+)-**2d**

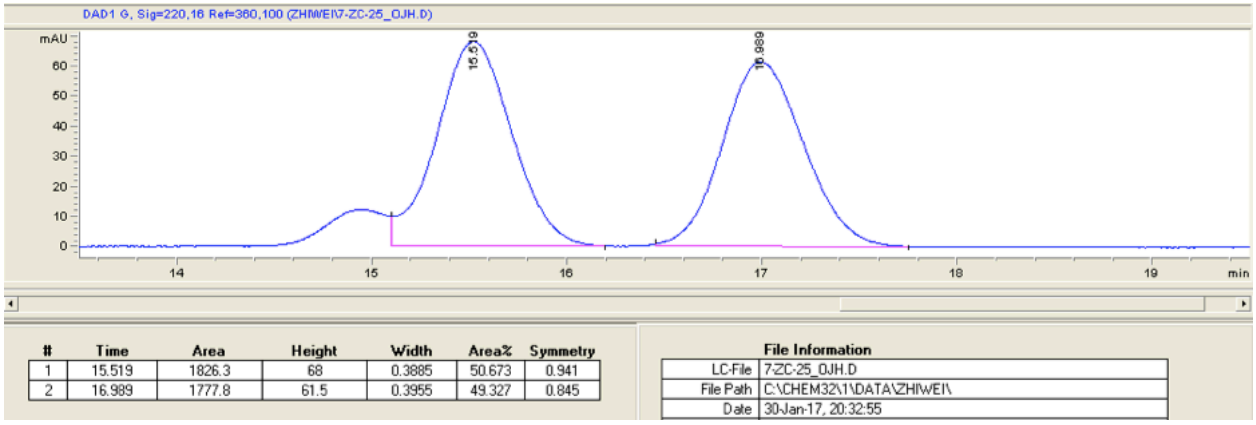



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.754 | 106.3 | 18.7 | 0.0865 | 5.113 | 0.912 |
| 2 | 3.968 | 1973.5 | 308.1 | 0.0997 | 94.887 | 0.977 |

| File Information | |
|---|---|
| LC-File | 6-ZC-191_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 17-Oct-16, 13:15:31 |
| Sample | 6-ZC-191_OJ_re |



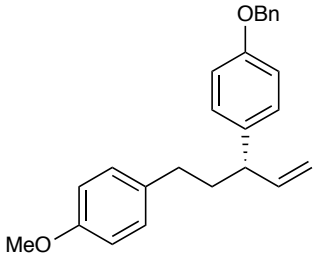

(±)-**2e**



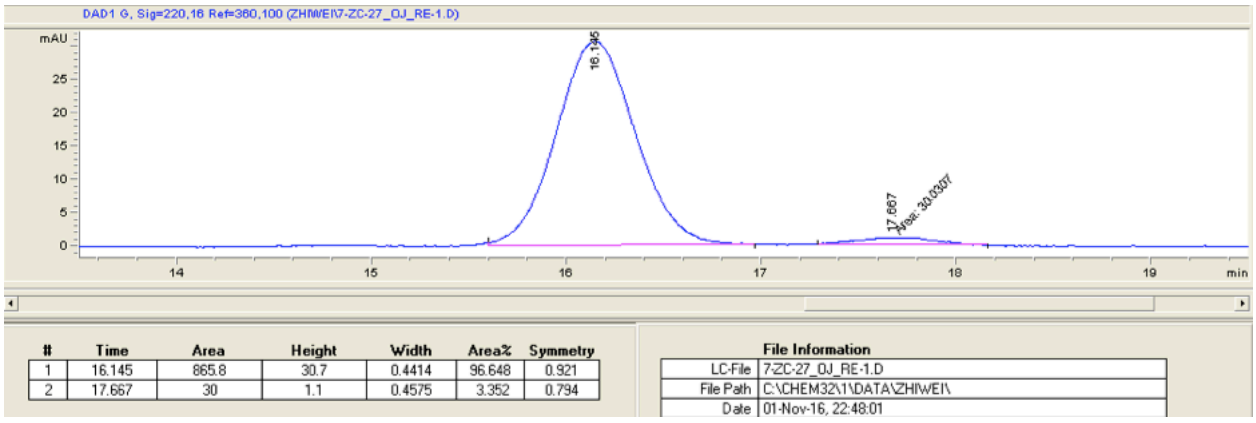

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.519 | 1826.3 | 68 | 0.3885 | 50.673 | 0.941 |
| 2 | 16.989 | 1777.8 | 61.5 | 0.3955 | 49.327 | 0.845 |

| File Information | |
|---|---|
| LC-File | 7-ZC-25_OJH.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 20:32:55 |

* peak at 14.9 min is residual internal alkene that was not completely separated from the product

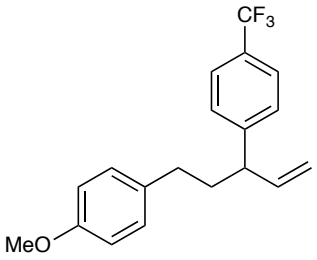



(+)-**2e**

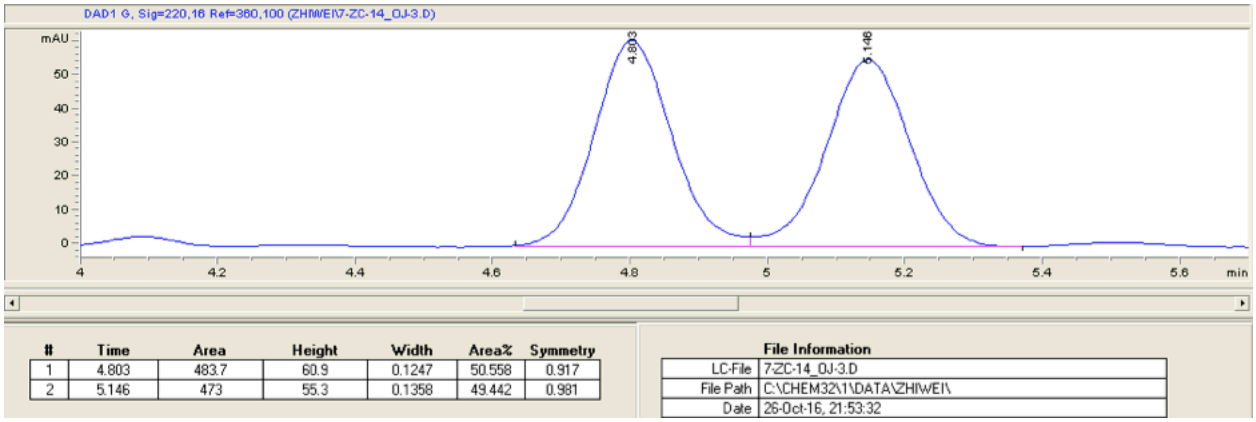



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 16.145 | 865.8 | 30.7 | 0.4414 | 96.648 | 0.921 |
| 2 | 17.667 | 30 | 1.1 | 0.4575 | 3.352 | 0.794 |

| File Information | |
|---|---|
| LC-File | 7-ZC-27_OJ_RE-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 01-Nov-16, 22:48:01 |

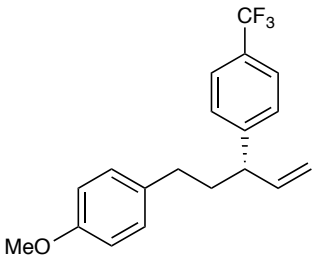



(±)-**2f**

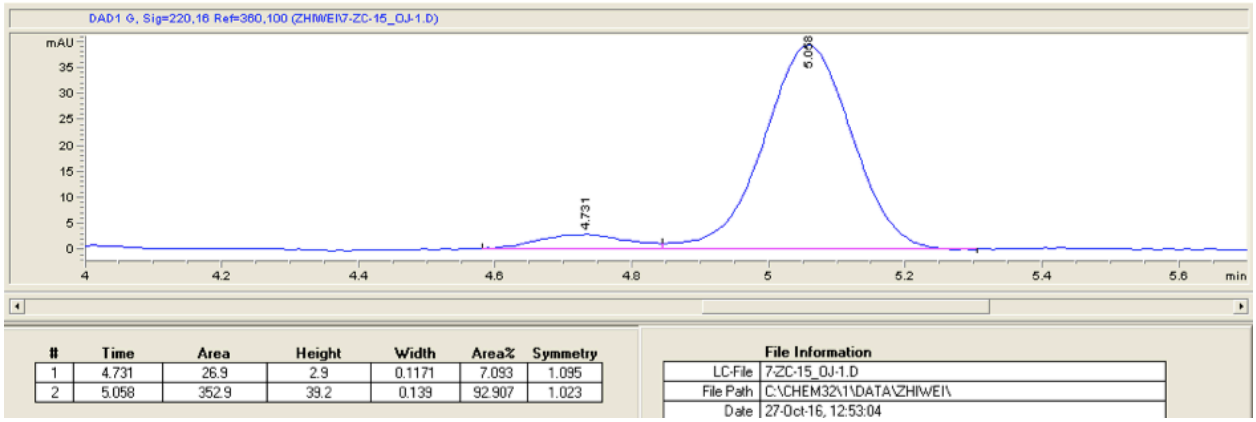



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.803 | 483.7 | 60.9 | 0.1247 | 50.558 | 0.917 |
| 2 | 5.146 | 473 | 55.3 | 0.1358 | 49.442 | 0.981 |

| File Information | |
|---|---|
| LC-File | 7-ZC-14_OJ-3.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 26-Oct-16, 21:53:32 |

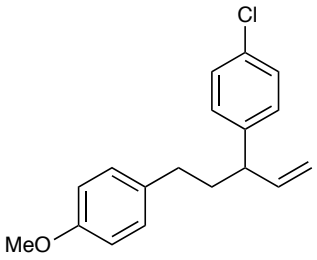



(+)-**2f**

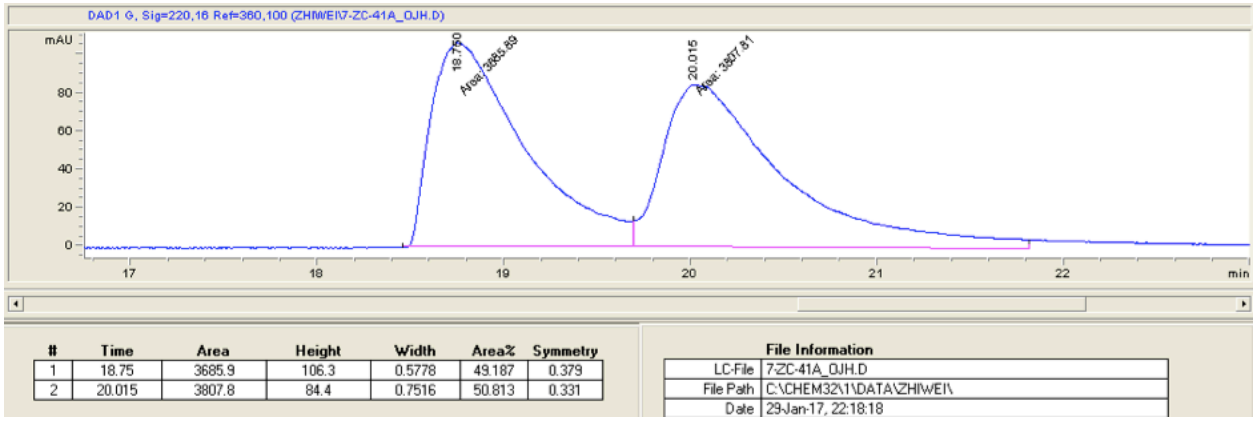



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.731 | 26.9 | 2.9 | 0.1171 | 7.093 | 1.095 |
| 2 | 5.058 | 352.9 | 39.2 | 0.139 | 92.907 | 1.023 |

| File Information | |
|---|---|
| LC-File | 7-ZC-15_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 27-Oct-16, 12:53:04 |

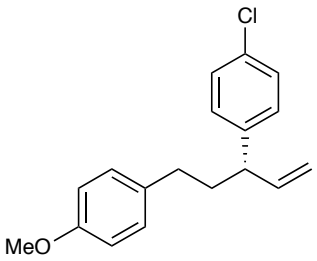



(±)-**2g**

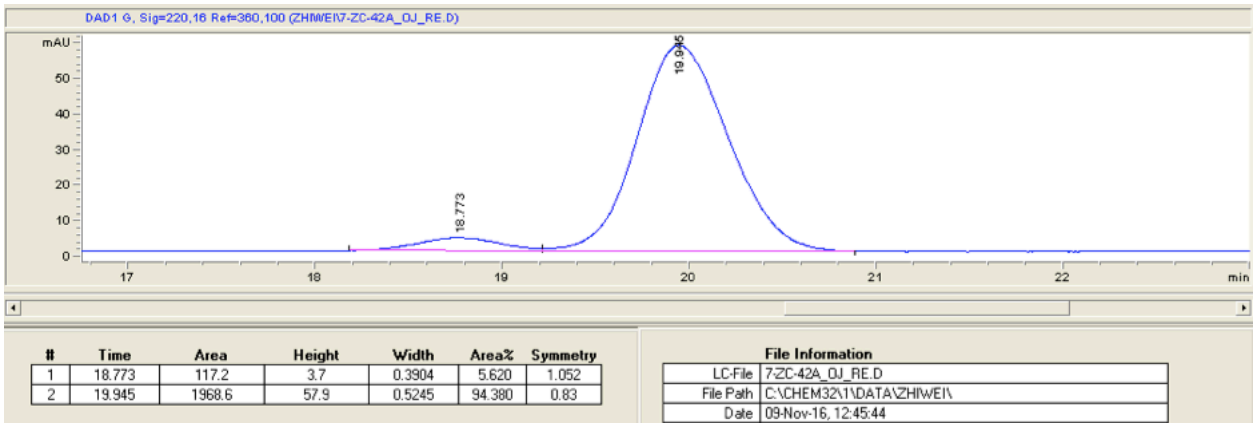



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 18.75 | 3685.9 | 106.3 | 0.5778 | 49.187 | 0.379 |
| 2 | 20.015 | 3807.8 | 84.4 | 0.7516 | 50.813 | 0.331 |

| File Information | |
|---|---|
| LC-File | 7-ZC-41A_OJH.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 29-Jan-17, 22:18:18 |

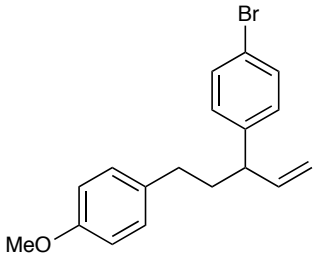



(+)-**2g**

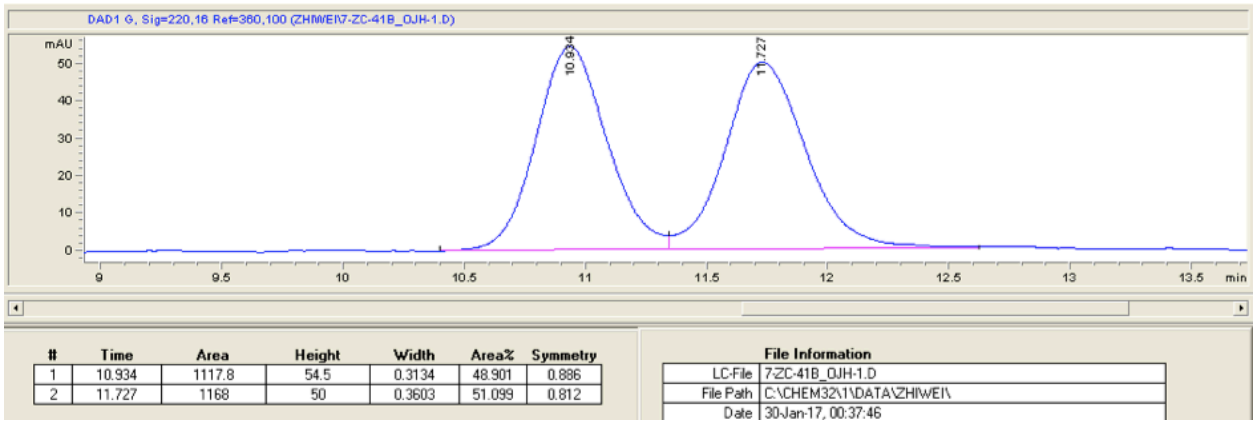



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 18.773 | 117.2 | 3.7 | 0.3904 | 5.620 | 1.052 |
| 2 | 19.945 | 1968.6 | 57.9 | 0.5245 | 94.380 | 0.83 |

| File Information | |
|---|---|
| LC-File | 7-ZC-42A_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 09-Nov-16, 12:45:44 |

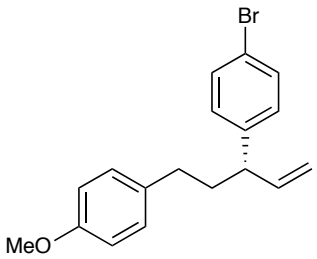



(±)-**2h**

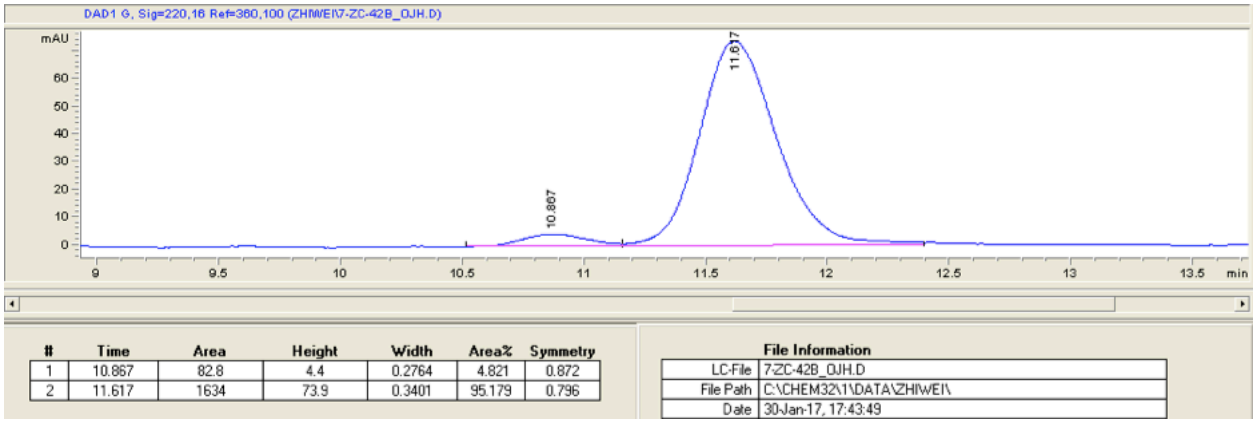



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.934 | 1117.8 | 54.5 | 0.3134 | 48.901 | 0.886 |
| 2 | 11.727 | 1168 | 50 | 0.3603 | 51.099 | 0.812 |

| File Information | |
|---|---|
| LC-File | 7-ZC-41B_OJH-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 00:37:46 |

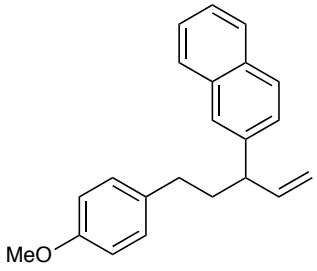



(+)-**2h**

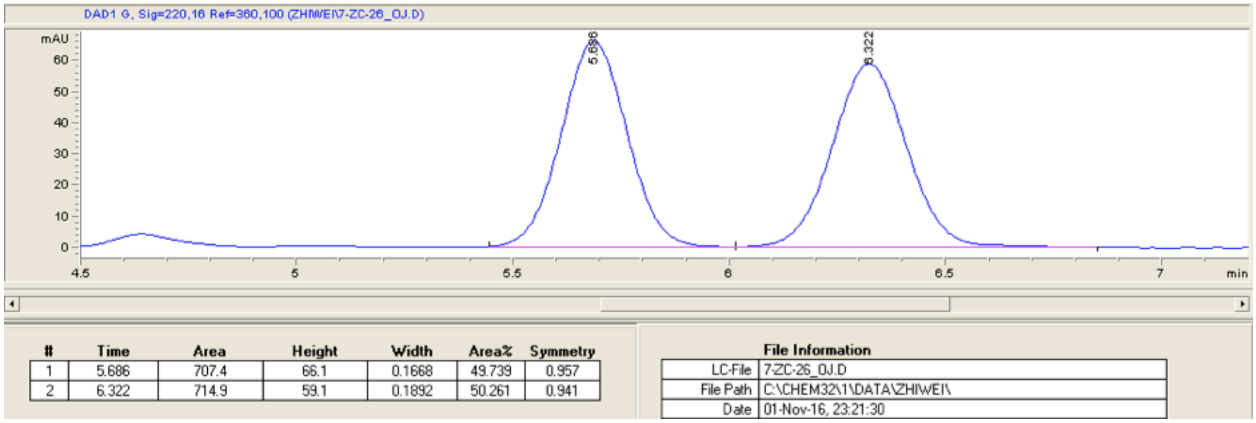



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.867 | 82.8 | 4.4 | 0.2764 | 4.821 | 0.872 |
| 2 | 11.617 | 1634 | 73.9 | 0.3401 | 95.179 | 0.796 |

| File Information | |
|---|---|
| LC-File | 7-ZC-42B_OJH.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 17:43:49 |

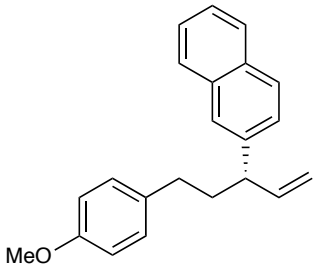



(±)-**2i**

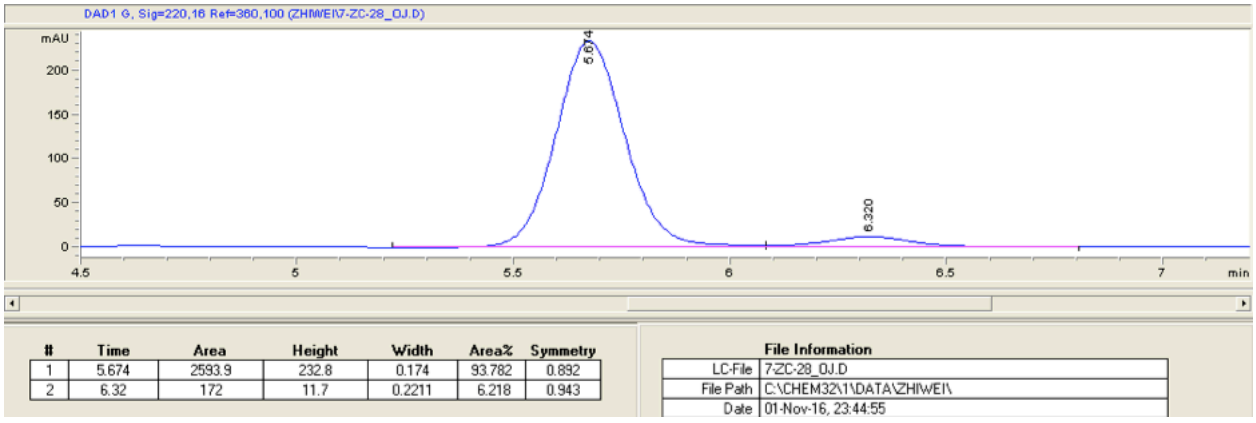



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.686 | 707.4 | 66.1 | 0.1668 | 49.739 | 0.957 |
| 2 | 6.322 | 714.9 | 59.1 | 0.1892 | 50.261 | 0.941 |

| File Information | |
|---|---|
| LC-File | 7-ZC-26_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 01-Nov-16, 23:21:30 |

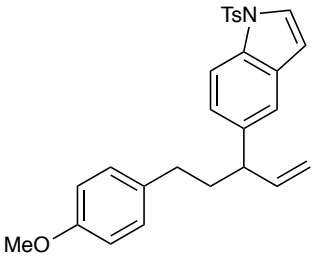



(+)-**2i**

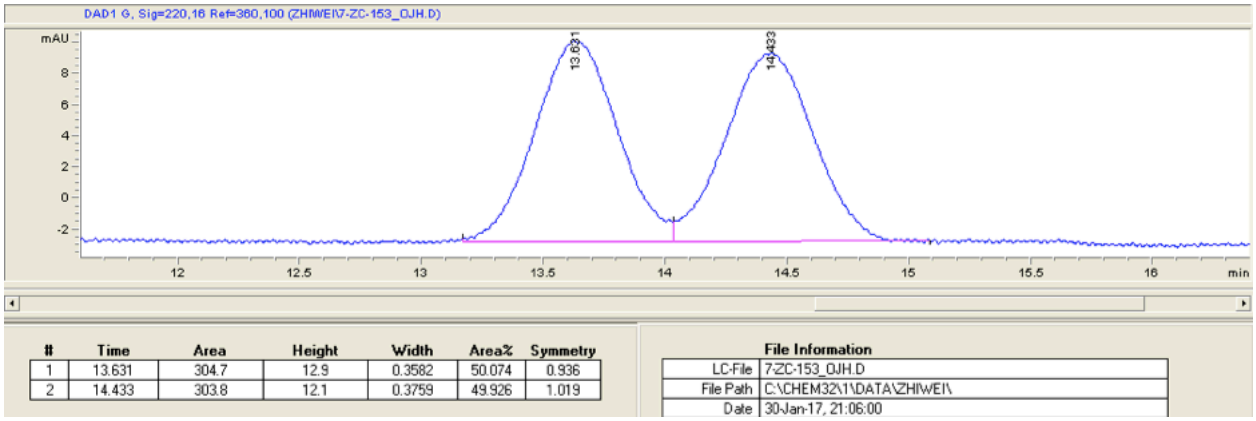



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.674 | 2593.9 | 232.8 | 0.174 | 93.782 | 0.892 |
| 2 | 6.32 | 172 | 11.7 | 0.2211 | 6.218 | 0.943 |

| File Information | |
|---|---|
| LC-File | 7-ZC-28_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 01-Nov-16, 23:44:55 |

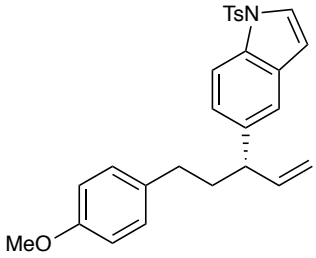



(±)-**2j**

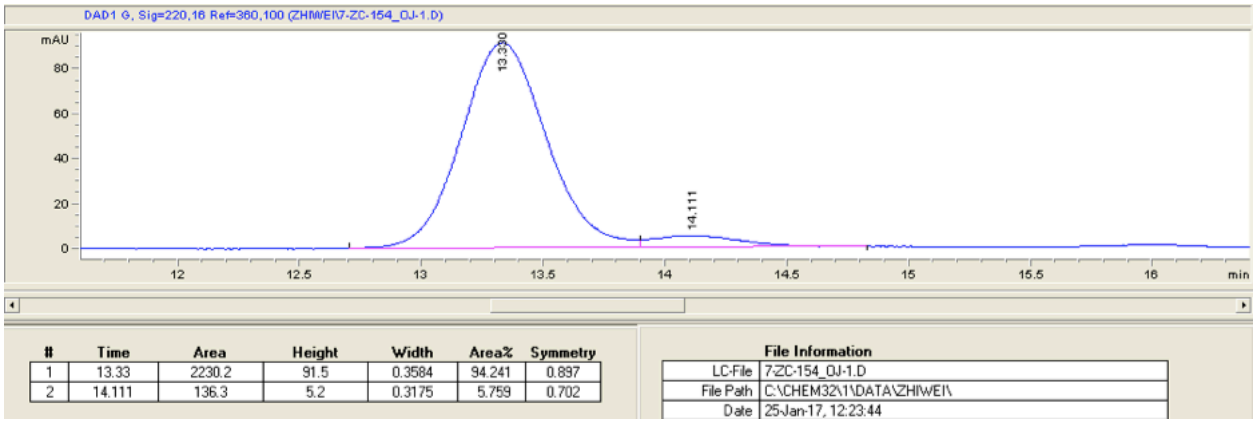



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.631 | 304.7 | 12.9 | 0.3582 | 50.074 | 0.936 |
| 2 | 14.433 | 303.8 | 12.1 | 0.3759 | 49.926 | 1.019 |

| File Information | |
|---|---|
| LC-File | 7-ZC-153_OJH.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 21:06:00 |

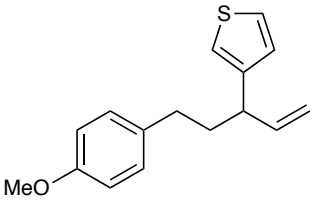



(+)-**2j**

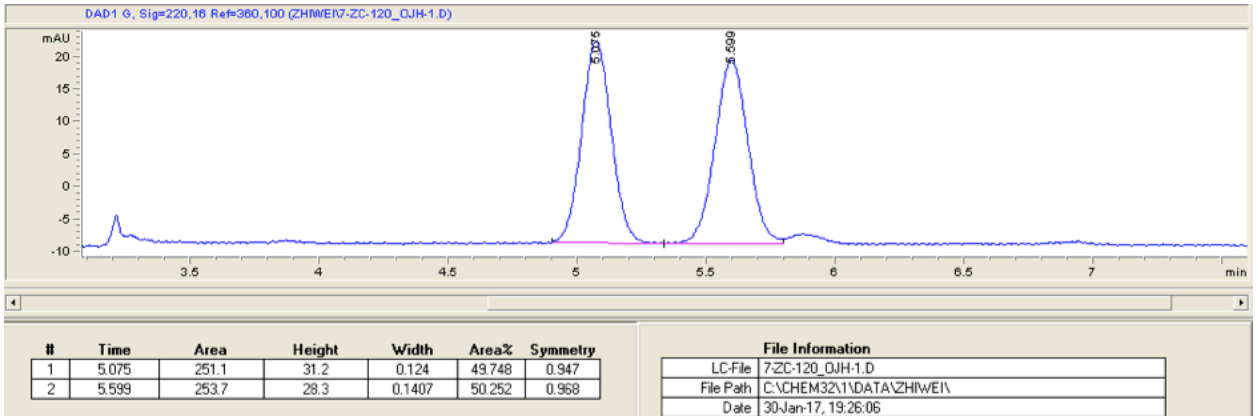



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.33 | 2230.2 | 91.5 | 0.3584 | 94.241 | 0.897 |
| 2 | 14.111 | 136.3 | 5.2 | 0.3175 | 5.759 | 0.702 |

| File Information | |
|---|---|
| LC-File | 7-ZC-154_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 25-Jan-17, 12:23:44 |



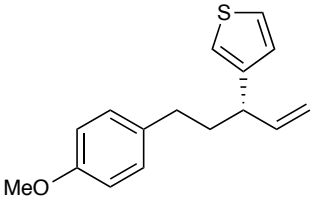

(±)-**2k**



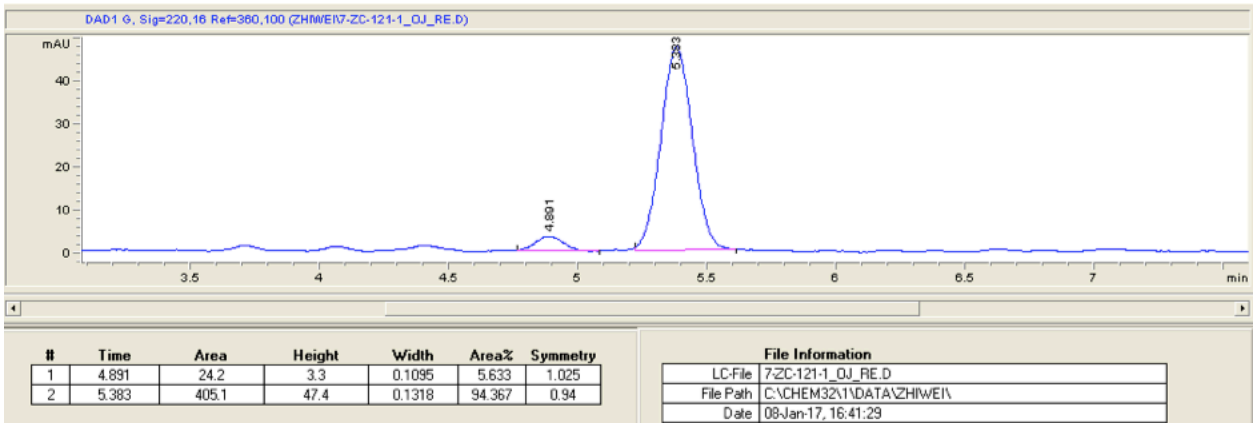

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.075 | 251.1 | 31.2 | 0.124 | 49.748 | 0.947 |
| 2 | 5.599 | 253.7 | 28.3 | 0.1407 | 50.252 | 0.968 |

| File Information | |
|---|---|
| LC-File | 7-ZC-120_OJH-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 19:26:06 |

* peak at 5.9 min is residual internal alkene that was not completely separated from the product

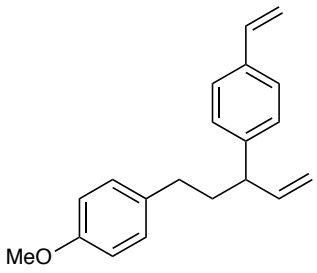



(+)-**2k**

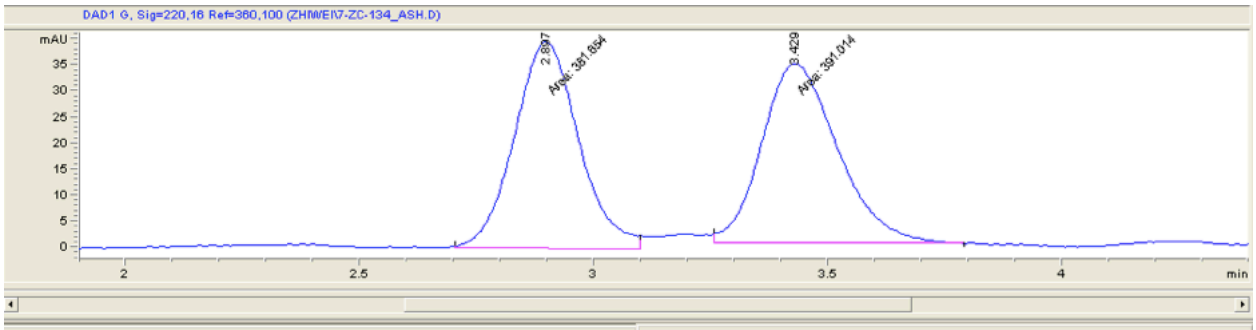



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.891 | 24.2 | 3.3 | 0.1095 | 5.633 | 1.025 |
| 2 | 5.383 | 405.1 | 47.4 | 0.1318 | 94.367 | 0.94 |

| File Information | |
|---|---|
| LC-File | 7-ZC-121-1_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 08-Jan-17, 16:41:29 |

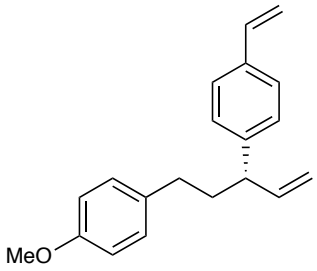



(±)-**2l**

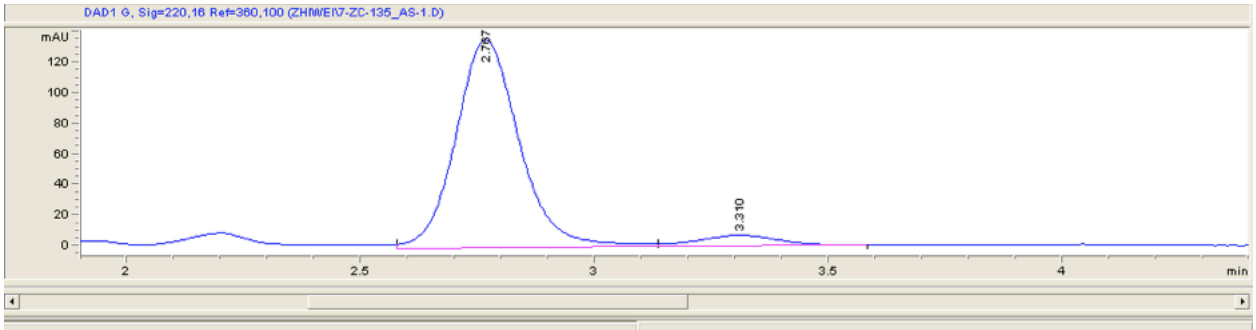



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.897 | 381.7 | 39.7 | 0.1603 | 49.394 | 0.892 |
| 2 | 3.429 | 391 | 34.5 | 0.1887 | 50.606 | 0.769 |

| File Information | |
|---|---|
| LC-File | 7-ZC-134_ASH.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 21:49:06 |

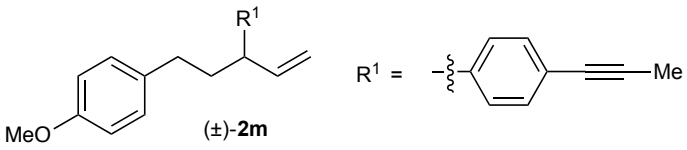


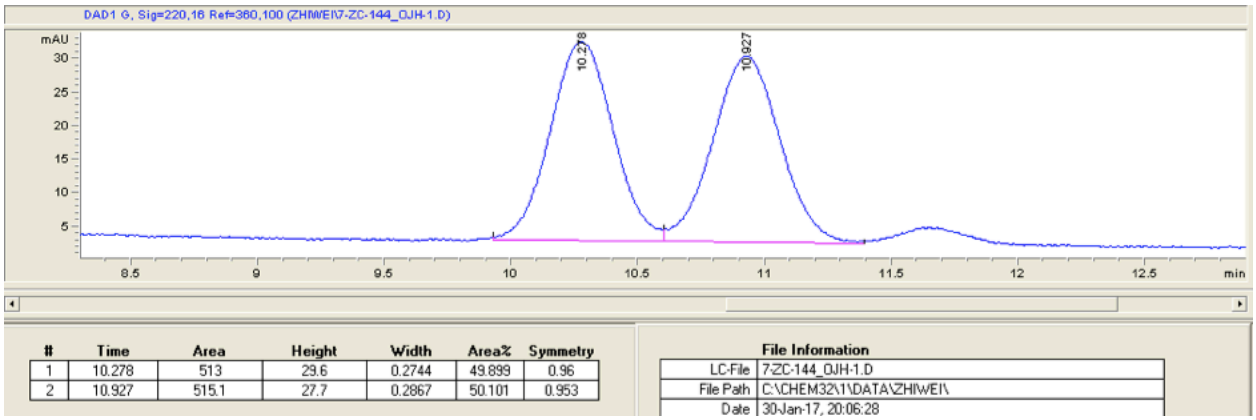

(+)-**2l**




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.767 | 1304.8 | 136.4 | 0.1476 | 93.190 | 0.834 |
| 2 | 3.31 | 95.4 | 7.5 | 0.188 | 6.810 | 0.964 |

| File Information | |
|---|---|
| LC-File | 7-ZC-135_AS-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 14-Jan-17, 14:09:29 |

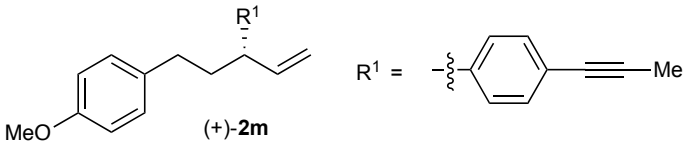


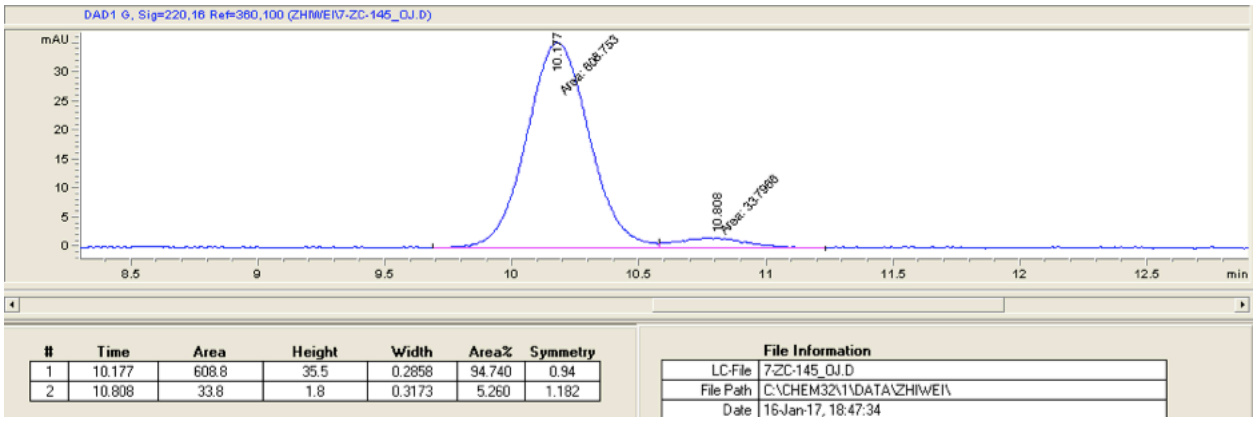




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.278 | 513 | 29.6 | 0.2744 | 49.899 | 0.96 |
| 2 | 10.927 | 515.1 | 27.7 | 0.2867 | 50.101 | 0.953 |

| File Information | |
|---|---|
| LC-File | 7-ZC-144_OJH-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jan-17, 20:06:28 |

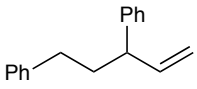
*peak at 11.7 min is residual internal alkene that was not completely separated from the product



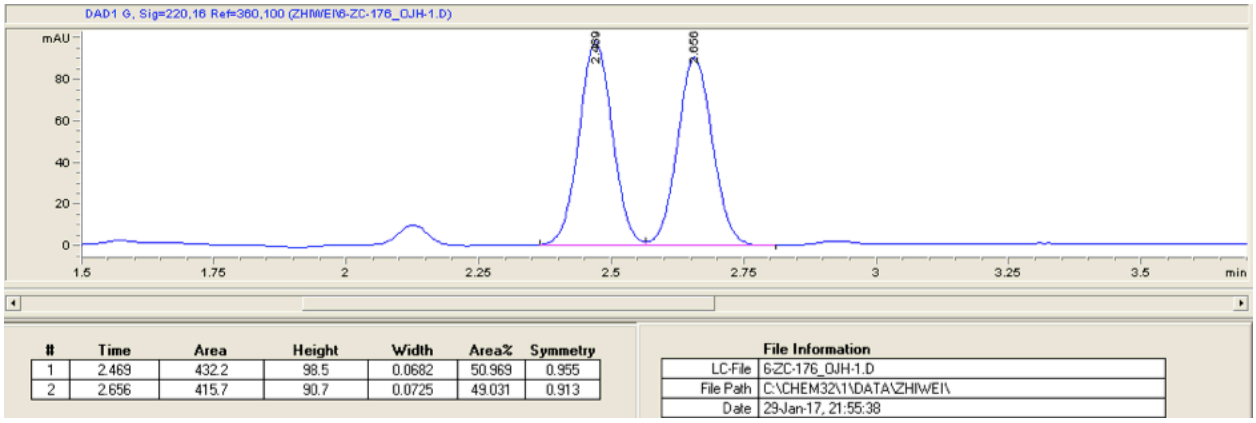




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.177 | 608.8 | 35.5 | 0.2858 | 94.740 | 0.94 |
| 2 | 10.808 | 33.8 | 1.8 | 0.3173 | 5.260 | 1.182 |

| File Information | |
|---|---|
| LC-File | 7-ZC-145_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 16-Jan-17, 18:47:34 |

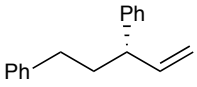



(±)-**2n**

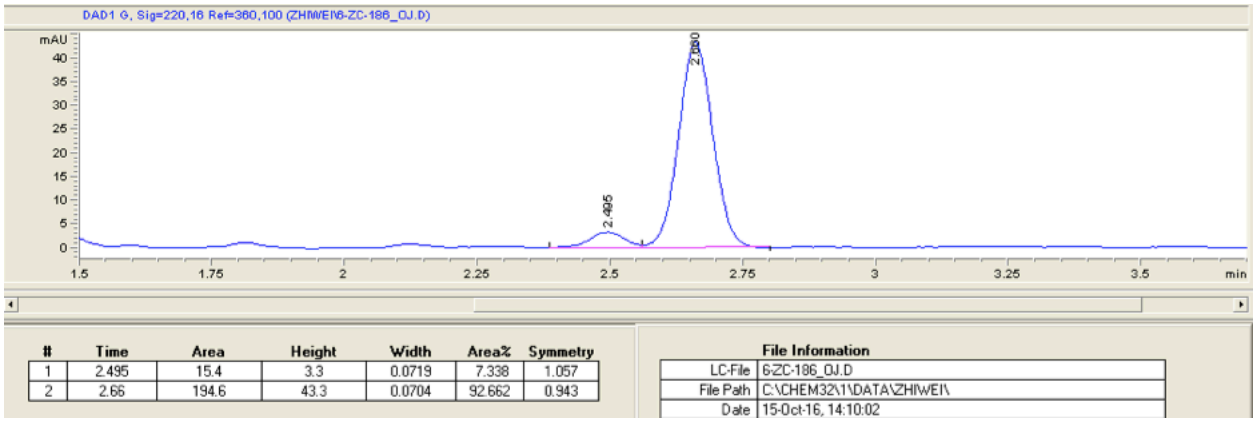



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.469 | 432.2 | 98.5 | 0.0682 | 50.969 | 0.955 |
| 2 | 2.656 | 415.7 | 90.7 | 0.0725 | 49.031 | 0.913 |

| File Information | |
|---|---|
| LC-File | 6-ZC-176_OJH-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 29-Jan-17, 21:55:38 |

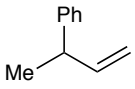



(+)-**2n**

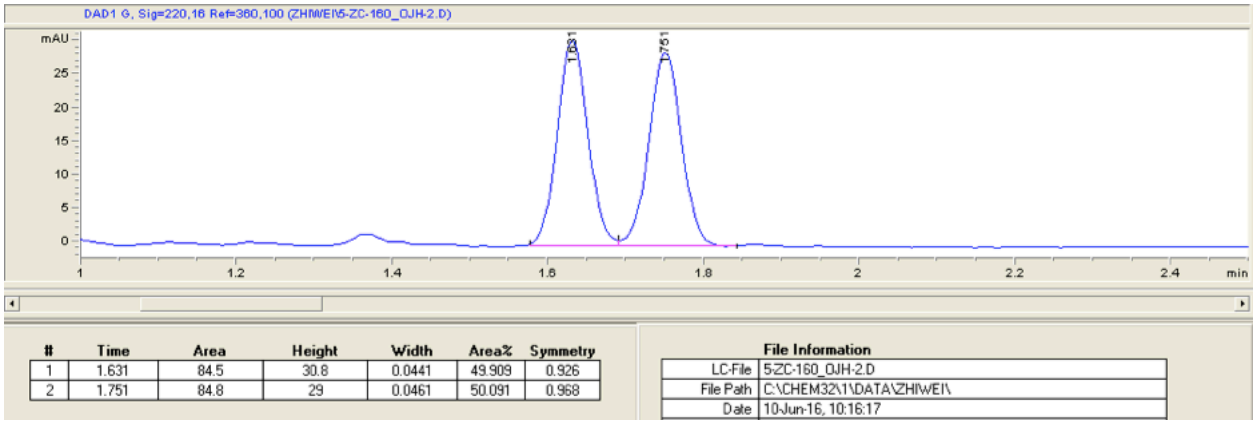



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.495 | 15.4 | 3.3 | 0.0719 | 7.338 | 1.057 |
| 2 | 2.66 | 194.6 | 43.3 | 0.0704 | 92.662 | 0.943 |

| File Information | |
|---|---|
| LC-File | 6-ZC-186_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 15-Oct-16, 14:10:02 |

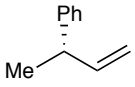



(±)-**2o**

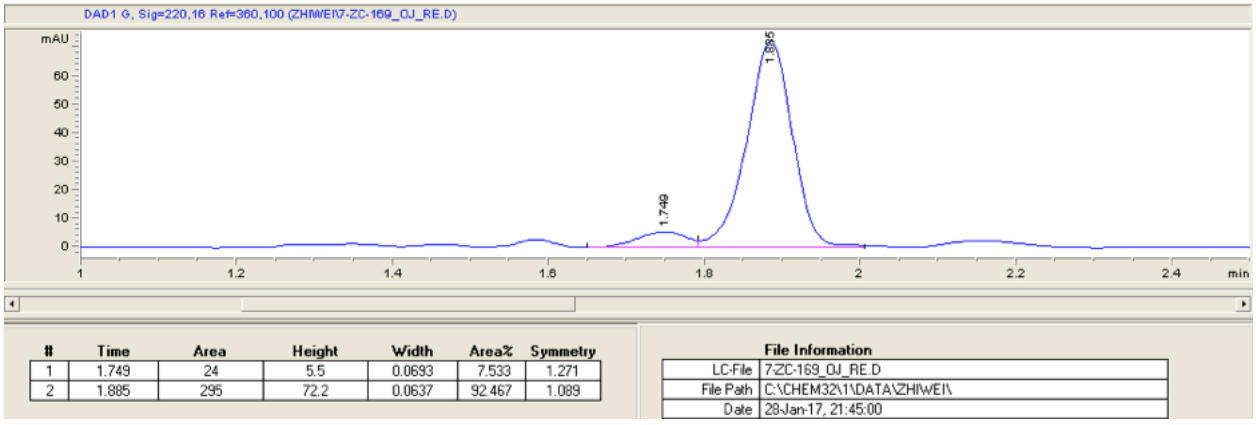



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 1.631 | 84.5 | 30.8 | 0.0441 | 49.909 | 0.926 |
| 2 | 1.751 | 84.8 | 29 | 0.0461 | 50.091 | 0.968 |

| File Information | |
|---|---|
| LC-File | 5-ZC-160_OJH-2.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 10-Jun-16, 10:16:17 |

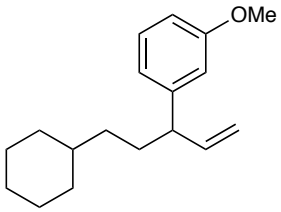



(+)-**2o**

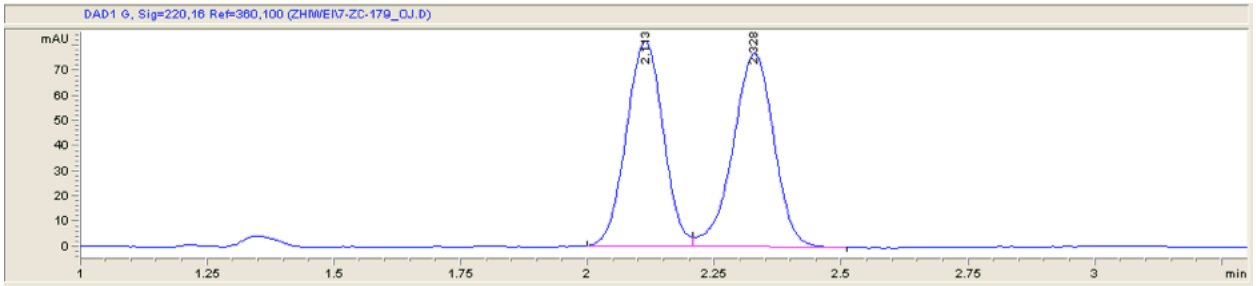



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 1.749 | 24 | 5.5 | 0.0693 | 7.533 | 1.271 |
| 2 | 1.885 | 295 | 72.2 | 0.0637 | 92.467 | 1.089 |

| File Information | |
|---|---|
| LC-File | 7-ZC-169_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 28-Jan-17, 21:45:00 |

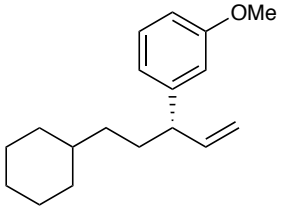



(±)-**2p**

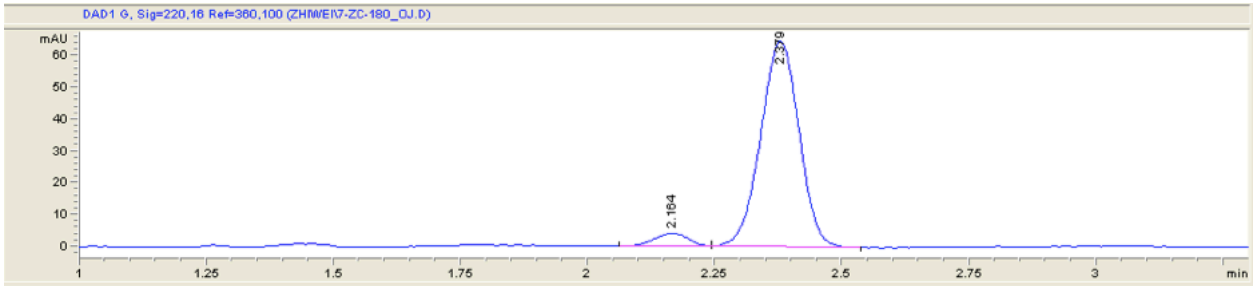



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.113 | 417.1 | 81.8 | 0.0805 | 49.027 | 1.013 |
| 2 | 2.328 | 433.7 | 77.3 | 0.0875 | 50.973 | 1.073 |

| File Information | |
|---|---|
| LC-File | 7-ZC-179_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 09-Feb-17, 09:52:21 |

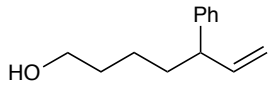



(+)-**2p**

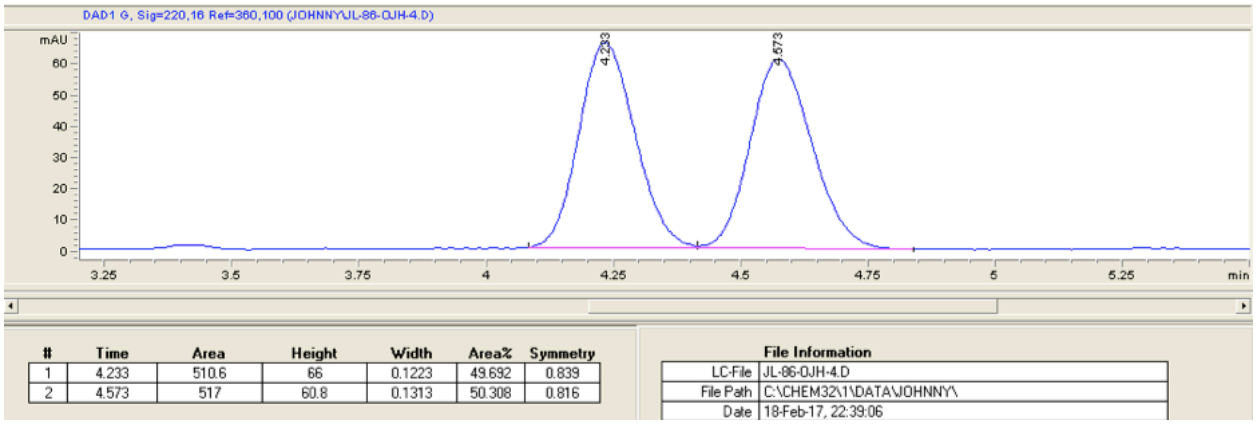



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.164 | 19.8 | 4.2 | 0.0757 | 5.503 | 1.041 |
| 2 | 2.379 | 340.4 | 64.7 | 0.0824 | 94.497 | 1.028 |

| File Information | |
|---|---|
| LC-File | 7-ZC-180_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 09-Feb-17, 10:09:23 |

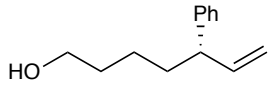



(±)-**2q**

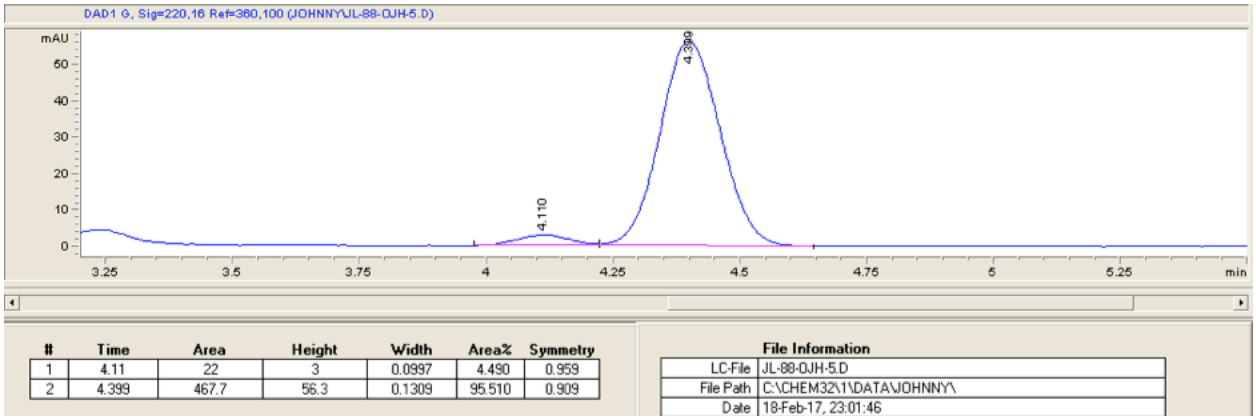



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.233 | 510.6 | 66 | 0.1223 | 49.692 | 0.839 |
| 2 | 4.573 | 517 | 60.8 | 0.1313 | 50.308 | 0.816 |

| File Information | |
|---|---|
| LC-File | JL-86-OJH-4.D |
| File Path | C:\CHEM32\1\DATA\JOHNNY\ |
| Date | 18-Feb-17, 22:39:06 |

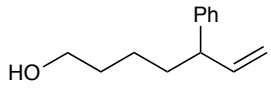



(+)-**2q**

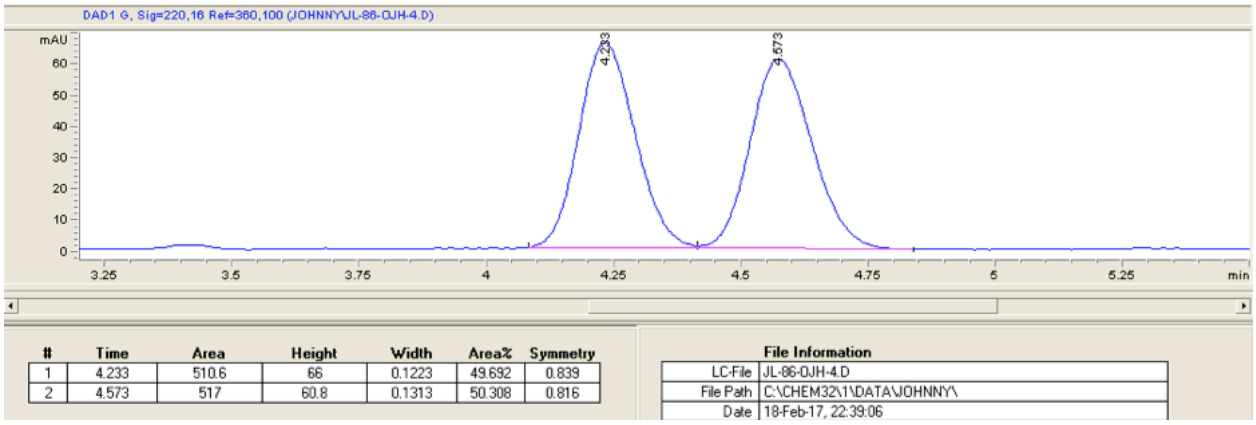



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.11 | 22 | 3 | 0.0997 | 4.490 | 0.959 |
| 2 | 4.399 | 467.7 | 56.3 | 0.1309 | 95.510 | 0.909 |

| File Information | |
|---|---|
| LC-File | JL-88-OJH-5.D |
| File Path | C:\CHEM32\1\DATA\JOHNNY\ |
| Date | 18-Feb-17, 23:01:46 |

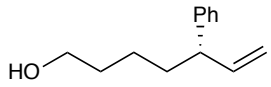



(±)-**2q**

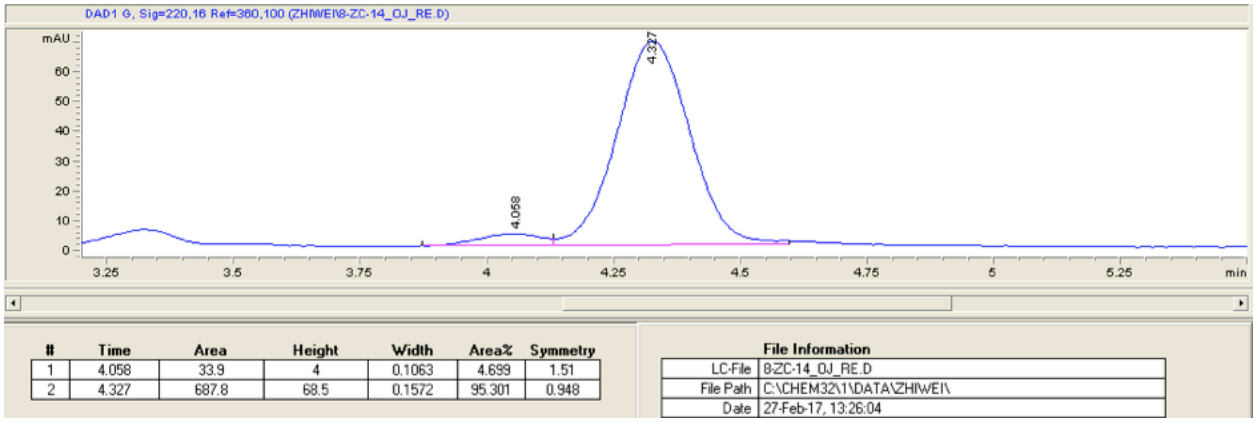



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.233 | 510.6 | 66 | 0.1223 | 49.692 | 0.839 |
| 2 | 4.573 | 517 | 60.8 | 0.1313 | 50.308 | 0.816 |

| File Information | |
|---|---|
| LC-File | JL-86-OJH-4.D |
| File Path | C:\CHEM32\1\DATA\JOHNNY\ |
| Date | 18-Feb-17, 22:39:06 |

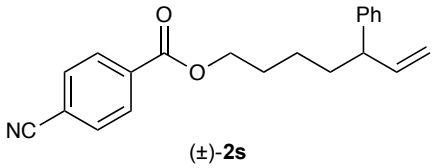



(+)-**2q** from (+)-**2r**

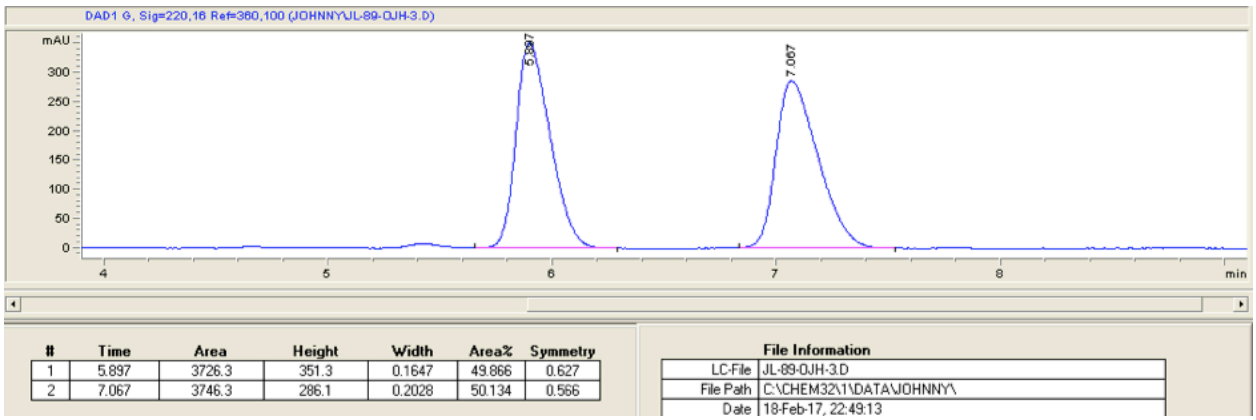



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.058 | 33.9 | 4 | 0.1063 | 4.699 | 1.51 |
| 2 | 4.327 | 687.8 | 68.5 | 0.1572 | 95.301 | 0.948 |

| File Information | |
|---|---|
| LC-File | 8-ZC-14_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 27-Feb-17, 13:26:04 |

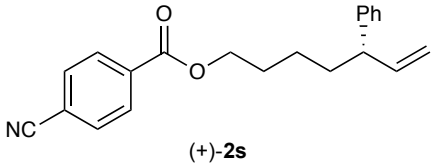



(±)-**2s**

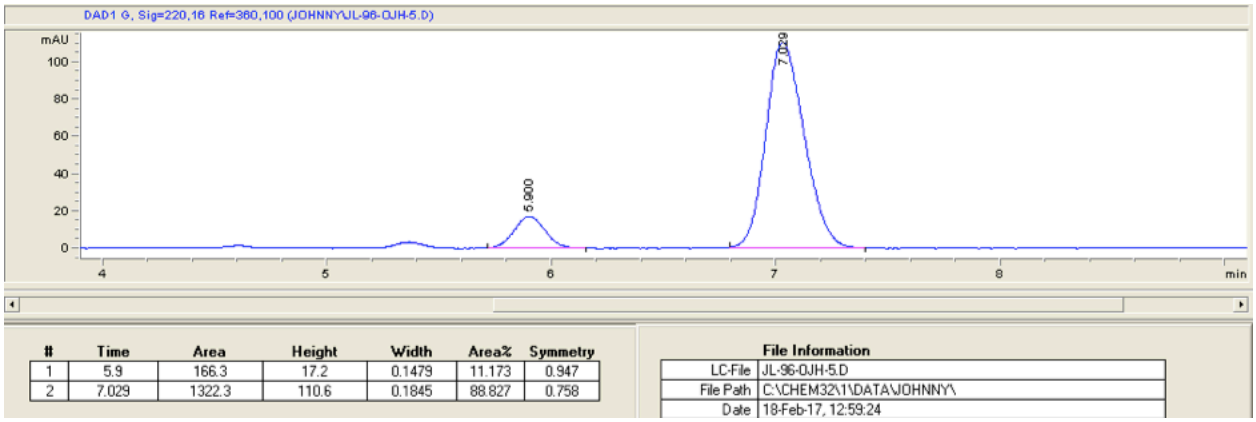



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.897 | 3726.3 | 351.3 | 0.1647 | 49.866 | 0.627 |
| 2 | 7.067 | 3746.3 | 286.1 | 0.2028 | 50.134 | 0.566 |

| File Information | |
|---|---|
| LC-File | JL-89-OJH-3.D |
| File Path | C:\CHEM32\1\DATA\JOHNNY\ |
| Date | 18-Feb-17, 22:49:13 |

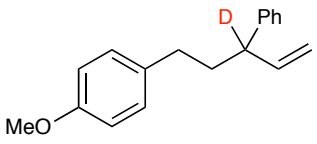



(+)-**2s**

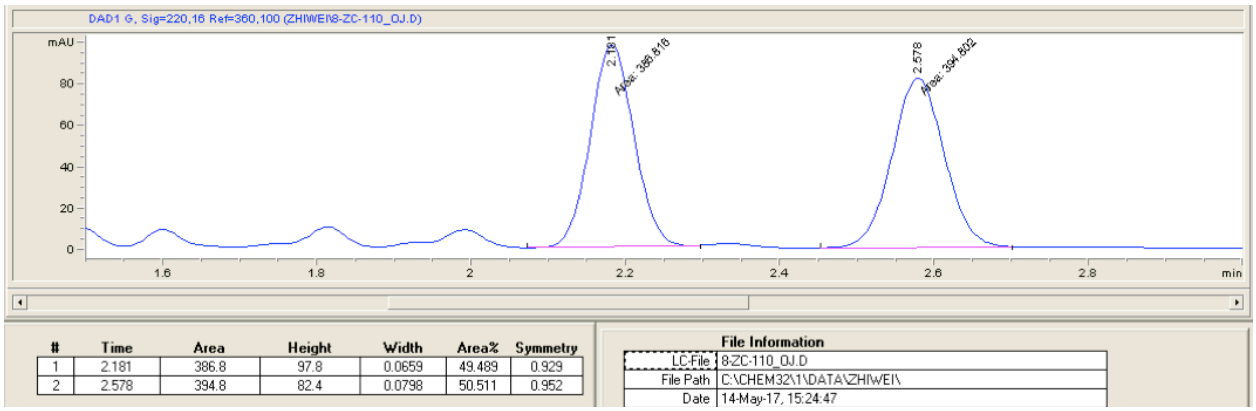



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.9 | 166.3 | 17.2 | 0.1479 | 11.173 | 0.947 |
| 2 | 7.029 | 1322.3 | 110.6 | 0.1845 | 88.827 | 0.758 |

| File Information | |
|---|---|
| LC-File | JL-96-OJH-5.D |
| File Path | C:\CHEM32\1\DATA\JOHNNY\ |
| Date | 18-Feb-17, 12:59:24 |

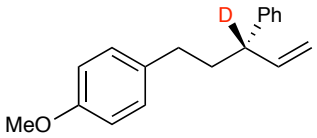



(±)-**2ab**

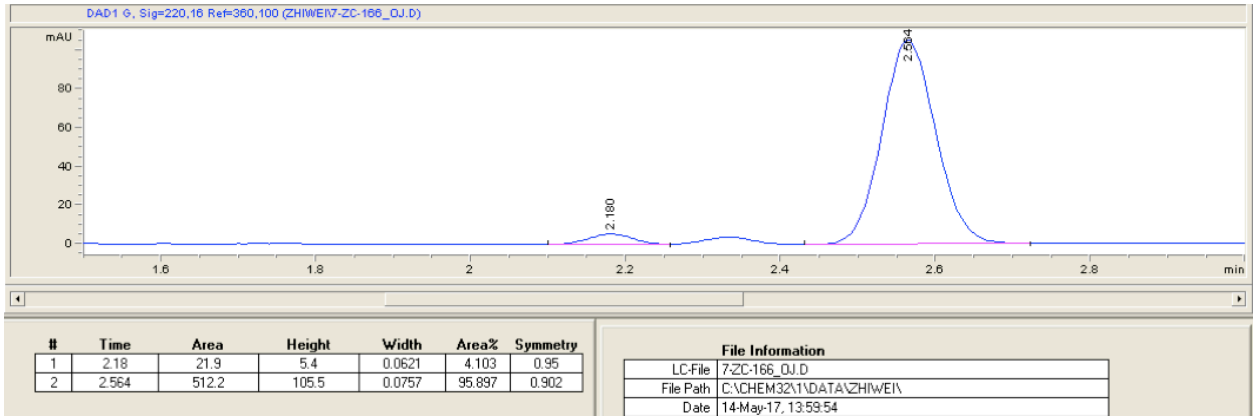



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.181 | 386.8 | 97.8 | 0.0659 | 49.489 | 0.929 |
| 2 | 2.578 | 394.8 | 82.4 | 0.0798 | 50.511 | 0.952 |

| File Information | |
|---|---|
| LC-File | 8-ZC-110_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 14-May-17, 15:24:47 |




(+)-**2ab**

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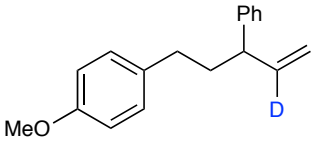
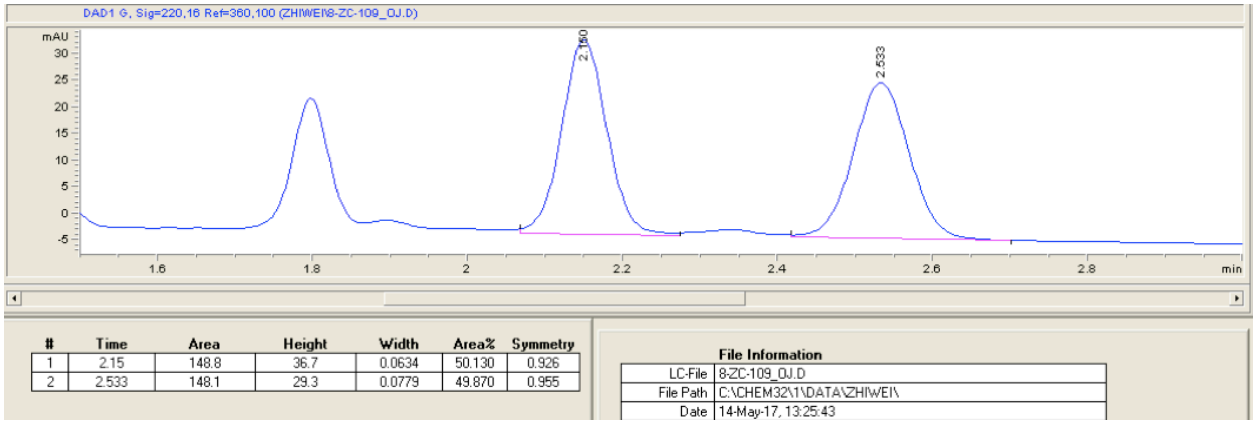



(±)-**2ac**

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| 2 | 2.533 | 148.1 | 29.3 | 0.0779 | 49.870 | 0.955 |

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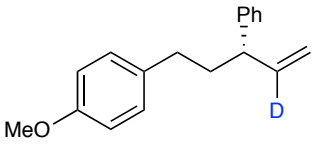
* peak at 1.8 min is residual internal alkene that was not completely separated from the product

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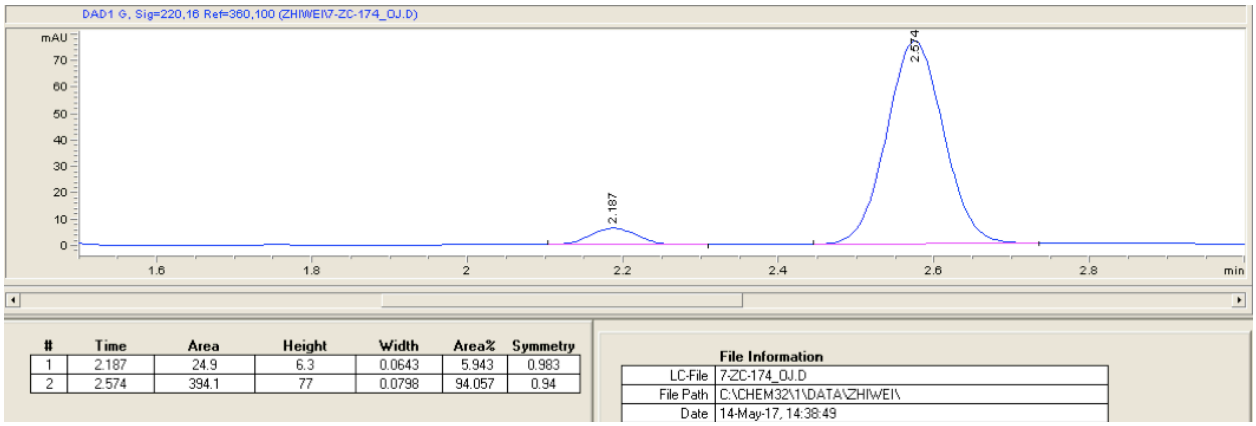


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## Appendix 2.1: Supporting Information for Chapter 2.1
## Diastereodivergent Construction of Bicyclic γ-Lactones via Enantioselective Ketone Hydroacylation

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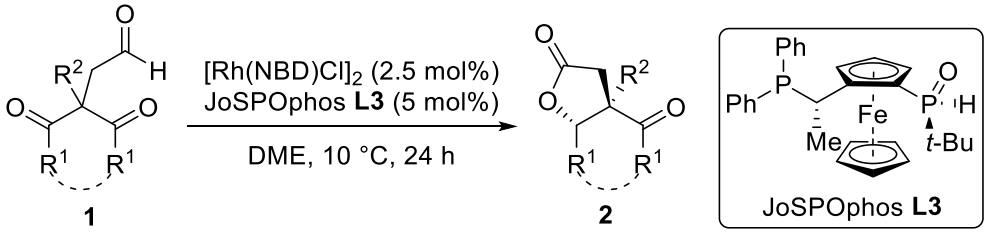
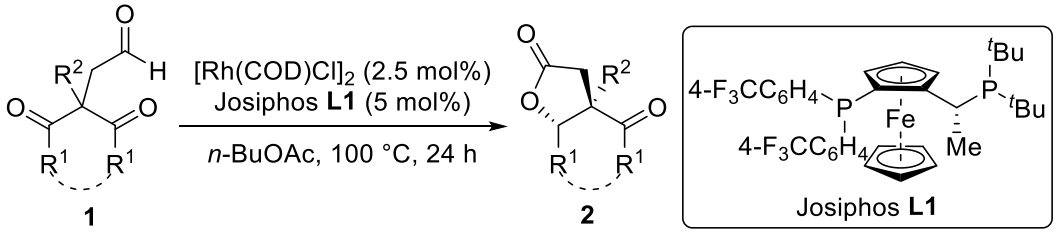
## 1. General Information

Commercially reagents were purchased from Sigma Aldrich, Strem, Acros Organics, TCI or Alfa Aesar and used without further purification. All experiments were performed in oven-dried or flame-dried glassware under an atmosphere of $N_2$. Tetrahydrofuran, 1,2-dichloroethane and toluene were purified using an Innovative Technologies Pure Solv system, degassed by three freeze-pump-thaw cycles, and stored over 3A MS within a $N_2$ filled glove box. Reactions were monitored either *via* gas chromatography using an Agilent Technologies 7890A GC system equipped with an Agilent Technologies 5975C inert XL EI/CI MSD or by analytical thin-layer chromatography on EMD Silica Gel 60 $F_{254}$ plates. Visualization of the developed plates was performed under UV light (254 nm) or using $KMnO_4$ or DNP stain. Purification and isolation of products were performed via silica gel chromatography (both column and preparative thin-layer chromatography). Column chromatography was performed with Silicycle Silia-P Flash Silica Gel using glass columns. $^1H$, $^{13}C$, $^{19}F$ NMR spectra and NOESY were recorded on a Bruker DRX-400 (400 MHz $^1H$, 100 MHz $^{13}C$, 376.5 MHz $^{19}F$) or CRYO-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$) spectrometer. $^1H$ NMR spectra were internally referenced to the residual solvent signal or TMS. $^{13}C$ NMR spectra were internally referenced to the residual solvent signal. Data for $^1H$ NMR are reported as follows: chemical shift (δ ppm, δ 7.26 for $CDCl_3$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for $^{13}C$ NMR are reported in terms of chemical shift (δ ppm, δ 77.16 for $CDCl_3$). Infrared spectra were obtained on a Thermo Scientific Nicolet iS5 FT-IR spectrometer equipped with an iD5 ATR accessory, and were reported in terms of frequency of absorption ($cm^{-1}$). Enantiomeric excesses for enantioselective reactions were determined by chiral SFC analysis using an Agilent Technologies HPLC (1200 series) system and Aurora A5 Fusion. High-resolution mass spectra (HRMS) were obtained on a micromass 70S-250 spectrometer (EI) or an ABI/Sciex QStar Mass Spectrometer (ESI), performed by the University of California, Irvine Mass Spectrometry Center. X-ray crystallography was performed by the University of California, Irvine, X-ray Crystallography Facility and the University of California, San Diego, X-ray Crystallography Facility.

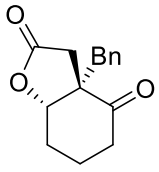
## 2. General Procedures for the *anti*-Diastereoselective Ketone Hydroacylation




**Method A:** In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and DME (0.40 mL) were added to a 1 dram vial containing $[Rh(NBD)Cl]_2$ (2.3 mg, 0.0050 mmol). After stirring for 20 min, **1** (0.20 mmol) was added. Then the reaction vessel was moved into a 10 ˚C low temperature thermostat bath, and the reaction mixture was stirred for 24 h. Upon completion, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture.



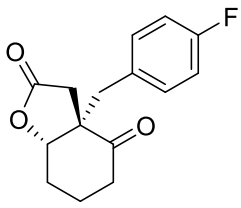

**Method B:** In a $N_2$-filled glovebox, Josiphos **L1** (3.4 mg, 0.0050 mmol) and *n*-BuOAc (0.20 mL) were added into a 1 dram vial containing $[Rh(COD)Cl]_2$ (1.2 mg, 0.0024 mmol). After stirring for 20 min, **1** (0.10 mmol) was added. Then the reaction mixture was stirred at 100 ˚C for 24 h. Upon completion, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture.



**2a**

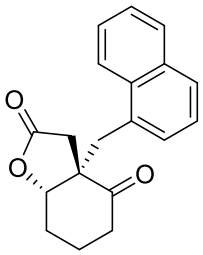
**(3a*R*,7a*S*)-3a-Benzylhexahydrobenzofuran-2,4-dione (2a)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (44.2 mg, 91% yield, *anti*:*syn* = 17:1, 99% *ee*, $[\alpha]^{24}_D$ = -61.9 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 3H), 7.04 – 7.00 (m, 2H), 4.21 – 4.12 (m, 1H), 3.51 (dd, *J* = 14.6, 1.9 Hz, 1H), 3.11 – 3.03 (m,

1H), 2.82 (d, $J$ = 14.6 Hz, 1H), 2.70 (dd, $J$ = 17.1, 2.3 Hz, 1H), 2.56 – 2.48 (m, 1H), 2.43 (d, $J$ = 17.1 Hz, 1H), 2.39 – 2.28 (m, 3H), 1.92 – 1.78 (m, 1H), **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 207.1, 174.5, 134.8, 129.4, 128.9, 127.5, 84.0, 59.9, 36.7, 35.5, 35.4, 22.0, 21.5. **IR** (ATR): 2958, 1781, 1714, 1177, 1043, 944, 731, 700 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 267.0992. **Chiral SFC**: 99% *ee*, 100 mm CHIRALCEL OJ-H, 3% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.3 min, $t_{R2}$ (major) = 2.9 min.



**2b**

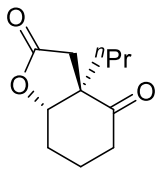
**(3a*R*,7a*S*)-3a-(4-Fluorobenzyl)hexahydrobenzofuran-2,4-dione (2b)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a white solid (43.5 mg, 83% yield, *anti*:*syn* = 12:1, 94% *ee*, $[\alpha]^{24}_D$ = +58.3 (*c* 0.81, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.02 – 6.87 (m, 4H), 4.12 (dd, $J$ = 11.4, 5.0 Hz, 1H), 3.41 (d, $J$ = 14.6 Hz, 1H), 3.04 – 2.89 (m, 1H), 2.77 (d, $J$ = 14.8 Hz, 1H), 2.66 (dd, $J$ = 17.1, 2.2 Hz, 1H), 2.48 (dd, $J$ = 15.5, 6.4 Hz, 1H), 2.39 – 2.17 (m, 4H), 1.90 – 1.72 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.0, 174.4, 162.3 (d, $J_{CF}$ = 246.6 Hz), 131.0 (d, $J_{CCCF}$ = 8.1 Hz), 130.6 (d, $J_{CCCCF}$ = 3.4 Hz), 116.0 (d, $J_{CCF}$ = 21.4 Hz), 83.9 (s), 59.9 (d, $J_{CCCCCF}$ = 1.1 Hz), 36.7, 35.5, 34.6, 22.0, 21.5. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.9. **IR** (ATR): 2924, 1788, 1716, 1510, 1218, 1178, 1042, 943, 838 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{15}FO_3NH_4$ $[M+NH_4]^+$ 280.1349, found 280.1345. **Chiral SFC**: 94% *ee*, 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 3.5 min, $t_{R2}$ (major) = 4.3 min.



**2c**

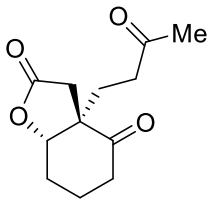
**(3a*R*,7a*S*)-3a-(Naphthalen-1-ylmethyl)hexahydrobenzofuran-2,4-dione (2c)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (30% ethyl acetate in hexanes) as a colorless oil (21.2 mg (from 0.10 mmol of starting material), 72% yield, *anti*:*syn* = 8:1, >99% *ee*, $[\alpha]^{24}_D$ = +18.2 (*c* 0.51, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H), 7.76 (d, $J$ = 8.2 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.36 (dd, $J$ = 8.2, 7.2 Hz, 1H), 7.12 (d, $J$ = 7.2 Hz, 1H), 4.14 (dd, $J$ = 12.4, 4.3 Hz, 1H), 3.71 (d, $J$ = 16.0 Hz, 1H), 3.60 (d, $J$ = 15.9 Hz, 1H), 3.07 – 2.97 (m, 1H), 2.78 (dd, $J$ = 17.2, 2.2 Hz, 1H), 2.53 – 2.40 (m, 2H), 2.39 – 2.28 (m, 3H), 1.91 – 1.78 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.8, 174.8, 134.1,

132.7, 131.1, 129.2, 128.3, 126.9, 126.4, 126.2, 125.4, 122.9, 84.5, 60.3, 36.8, 36.0, 30.6, 22.2, 21.7. **IR** (ATR): 1777, 1715, 1398, 1350, 1183, 1056, 946, 911, 807, 783 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{18}O_3NH_4$ $[M+NH_4]^+$ 312.1600, found 312.1595. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 20% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.5 min, $t_{R2}$ (major) = 6.8 min.



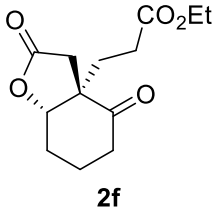
**2d**

**(3a*R*,7a*S*)-3a-Propylhexahydrobenzofuran-2,4-dione (2d)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (30% ethyl acetate in hexanes) as a colorless oil (31.4 mg, 80% yield, *anti*:*syn* = 8:1, >99% *ee*, $[\alpha]^{24}_D$ = +69.8 (*c* 0.93, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.62 (t, *J* = 3.3 Hz, 1H), 3.33 (d, *J* = 17.2 Hz, 1H), 2.57 – 2.39 (m, 2H), 2.27 – 2.16 (m, 2H), 2.11 – 1.92 (m, 3H), 1.85 – 1.75(m, 1H), 1.61 – 1.53 (m, 1H), 1.25 – 1.09 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.70, 174.93, 83.93, 59.33, 36.53, 36.09, 31.63, 22.05, 21.27, 17.10, 14.55. **IR** (ATR): 2960, 1783, 1716, 1218, 1174, 1040, 935 $cm^{-1}$. **HRMS** calculated for $C_{11}H_{16}O_3NH_4$ $[M+NH_4]^+$ 214.1443, found 214.1439. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.6 min, $t_{R2}$ (major) = 5.2 min.



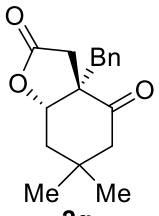
**2e**

**(3a*R*,7a*S*)-3a-(3-Oxobutyl)hexahydrobenzofuran-2,4-dione (2e)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a colorless oil (11.9 mg (from 0.10 mmol starting material), 53% yield, *anti*:*syn* = 6:1, >99% *ee*, $[\alpha]^{24}_D$ = +59.8 (*c* 0.45, $CHCl_3$)). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 4.04 (dd, *J* = 10.7, 5.7 Hz, 1H), 2.75 (dd, *J* = 17.0, 2.0 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.54 – 2.44 (m, 1H), 2.41 – 2.34 (m, 2H), 2.33 – 2.24 (m, 1H), 2.24 – 2.15 (m, 4H), 2.13 (s, 3H), 1.76 – 1.64 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 207.9, 206.4, 174.3, 83.6, 58.3, 37.5, 36.4, 36.1, 30.2, 22.5, 21.8, 20.9. **IR** (ATR): 2961, 1783, 1710, 1704, 1426, 1356, 1165, 1036, 939, 814 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{16}O_4NH_4$ $[M+NH_4]^+$ 242.1392, found 242.1388. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 6.9 min, $t_{R2}$ (minor) = 7.5 min.



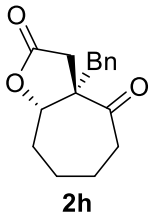
**2f**

**Ethyl 3-((3a*R*,7a*S*)-2,4-dioxohexahydrobenzofuran-3a(4*H*)-yl)propanoate (2f)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a colorless oil (41.4 mg, 82% yield, *anti*:*syn* = 8:1, >99% *ee*, $[\alpha]^{24}_{D}$ = +70.2 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.10 (q, *J* = 7.1 Hz, 2H), 4.03 (dd, *J* = 11.9, 4.5 Hz, 1H), 2.85 – 2.61 (m, 2H), 2.47 – 2.25 (m, 4H), 2.25 – 2.01 (m, 4H), 1.89 – 1.77 (m, 1H), 1.77 – 1.62 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.1, 174.0, 172.0, 83.6, 61.1, 58.6, 36.4, 35.8, 28.7, 24.4, 21.9, 21.0, 14.2. **IR** (ATR): 2961, 1785, 1726, 1716, 1176, 1032, 948, 920 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_5NH_4$ $[M+NH_4]^+$ 272.1498, found 272.1492. **Chiral SFC**: >99% *ee*, 100 mm CHIRALCEL AD-H, 5% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.5 min, $t_{R2}$ (major) = 4.8 min.



**2g**

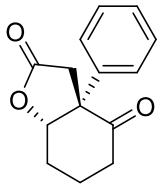
**(3a*R*,7a*S*)-3a-Benzyl-6,6-dimethylhexahydrobenzofuran-2,4-dione (2g)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a white solid (43.7 mg, 81% yield, *anti*:*syn* = 6:1, >99% *ee*, $[\alpha]^{24}_{D}$ = +78.1 (*c* 0.71, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 3H), 6.96 (dd, *J* = 7.6, 1.8 Hz, 2H), 4.25 (dd, *J* = 13.4, 3.9 Hz, 1H), 3.42 (dd, *J* = 14.8, 2.1 Hz, 1H), 2.99 (d, *J* = 14.8 Hz, 1H), 2.76 (d, *J* = 14.8 Hz, 1H), 2.66 (dd, *J* = 17.0, 2.3 Hz, 1H), 2.37 (d, *J* = 17.0 Hz, 1H), 2.29 – 2.18 (m, 2H), 2.04 (dd, *J* = 12.9, 3.2 Hz, 1H), 1.31 (s, 3H), 1.10 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.6, 174.9, 134.9, 129.3, 129.0, 127.6, 81.6, 59.7, 51.1, 35.8, 35.6, 35.4, 34.7, 32.8, 29.2. **IR** (ATR): 2922, 1781, 1703, 1119, 1044, 975, 739, 699 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{20}O_3NH_4$ $[M+NH_4]^+$ 290.1756, found 290.1746. **Chiral SFC**: >99% *ee*, 100 mm CHIRALCEL OJ-H, 0.1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 2.5 min, $t_{R2}$ (major) = 3.5 min.



**2h**

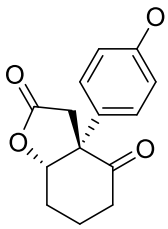
**(3a*R*,8a*S*)-3a-Benzylhexahydro-2*H*-cyclohepta[b]furan-2,4(3*H*)-dione (2h)**: The title compound was synthesized using **Method A** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a colorless oil (30.4 mg, 59% yield, *anti*:*syn* = 2:1, 98% *ee*, $[\alpha]^{24}_{D}$ = +41.8 (*c* 0.78, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 3H), 6.99 – 6.92 (m, 2H), 4.37 (dd, *J* = 11.8, 3.4 Hz,

1H), 3.55 (d, *J* = 14.5 Hz, 1H), 3.02 – 2.89 (m, 1H), 2.86 – 2.73 (m, 2H), 2.63 – 2.53 (m, 1H), 2.50 (d, *J* = 17.8 Hz, 1H), 2.40 – 2.31 (m, 1H), 2.29 – 2.10 (m, 3H), 2.03 – 1.93 (m, 1H), 1.69 – 1.59 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.9, 174.5, 134.7, 130.1, 128.9, 127.6, 82.6, 61.8, 44.1, 37.4, 35.4, 27.5, 25.7, 23.0. **IR** (ATR): 2923, 1779, 1694, 1223, 1194, 1003, 900, 757, 699 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_3NH_4$ $[M+NH_4]^+$ 276.1600, found 276.1597. **Chiral SFC**: 98% *ee*, 100 mm CHIRALCEL OJ-H, 0.3% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.2 min, $t_{R2}$ (major) = 5.0 min.



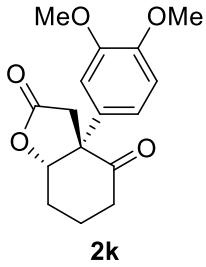
**2i**

**(3a*S*,7a*S*)-3a-Phenylhexahydrobenzofuran-2,4-dione (2i)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (18.6 mg, 81% yield, *anti*:*syn* = 10:1, 96% *ee*, $[\alpha]^{24}_D$ = -132.6 (*c* 0.92, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) *δ* 7.43 – 7.30 (m, 3H), 7.29 – 7.24 (m, 2H), 4.40 – 4.29 (m, 1H), 3.24 (dd, *J* = 16.7, 2.6 Hz, 1H), 2.60 – 2.42 (m, 3H), 2.42 – 2.28 (m, 2H), 2.02 – 1.94 (m, 1H), 1.78 – 1.64 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) *δ* 206.3, 174.1, 137.8, 130.0, 128.3, 127.2, 85.0, 64.2, 41.2, 37.8, 23.2, 22.2. **IR** (ATR): 2926, 1788, 1716, 1190, 1135, 1022, 944, 772, 707 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{14}O_3NH_4$ $[M+NH_4]^+$ 248.1287, found 248.1282. **Chiral SFC**: 96% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 4.0 min, $t_{R2}$ (minor) = 4.6 min.



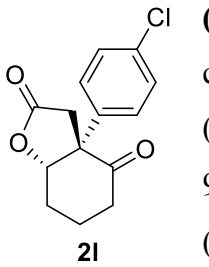
**2j**

**(3a*S*,7a*S*)-3a-(4-Methoxyphenyl)hexahydrobenzofuran-2,4-dione (2j)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a white solid (19.4 mg, 75% yield, *anti*:*syn* = 8:1, 95% *ee*, $[\alpha]^{24}_D$ = -101.3 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 9.0 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 4.32 (dd, *J* = 12.9, 4.0 Hz, 1H), 3.80 (s, 3H), 3.19 (d, *J* = 16.6 Hz, 1H), 2.57 – 2.39 (m, 3H), 2.37 – 2.26 (m, 2H), 2.02 – 1.94 (m, 1H), 1.75 – 1.62 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.5, 174.3, 159.3, 129.6, 128.5, 115.3, 85.0, 63.5, 55.5, 41.4, 37.6, 23.1, 22.2. **IR** (ATR): 2923, 1786, 1716, 1512, 1250, 1172, 1028, 932, 831 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_4NH_4$ $[M+NH_4]^+$ 278.1392, found 278.1390. **Chiral SFC**: 95% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 240 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 5.1 min, $t_{R2}$ (minor) = 5.9 min.



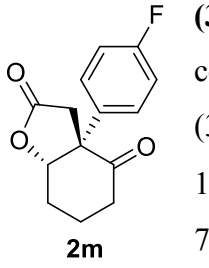
**2k**

**(3a*S*,7a*S*)-3a-(3,4-Dimethoxyphenyl)hexahydrobenzofuran-2,4-dione (2k)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a white solid (21.9 mg, 76% yield, *anti*:*syn* = 8:1, 97% *ee*, $[\alpha]^{24}_{D}$ = -129.3 (*c* 1.1, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.86 – 6.78 (m, 2H), 6.68 (s, 1H), 4.31 (dd, *J* = 12.9, 3.7 Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.19 (d, *J* = 16.6 Hz, 1H), 2.60 – 2.41 (m, 3H), 2.38 – 2.26 (m, 2H), 2.03 – 1.93 (m, 1H), 1.76 – 1.60 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.5, 174.3, 150.0, 148.9, 129.9, 119.7, 112.2, 110.0, 84.9, 63.7, 56.2, 56.0, 41.3, 37.7, 23.1, 22.0. **IR** (ATR): 2962, 1787, 1716, 1518, 1254, 1142, 1022, 940, 813, 766 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_5NH_4$ $[M+NH_4]^+$ 308.1498, found 308.1500. **Chiral SFC**: 97% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 9.7 min, $t_{R2}$ (minor) = 11.2 min.



**2l**

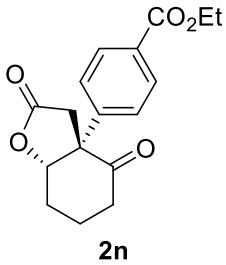
**(3a*S*,7a*S*)-3a-(4-Chlorophenyl)hexahydrobenzofuran-2,4-dione (2l)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (19.5 mg, 74% yield, *anti*:*syn* = 9:1, 94% *ee*, $[\alpha]^{24}_{D}$ = -130.8 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 4.33 (dd, *J* = 12.5, 4.4 Hz, 1H), 3.22 (d, *J* = 16.7 Hz, 1H), 2.52 – 2.29 (m, 5H), 2.05 – 1.95 (m, 1H), 1.78 – 1.64 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.8, 173.7, 136.2, 134.5, 130.2, 128.7, 84.7, 63.7, 41.1, 37.7, 23.1, 22.1. **IR** (ATR): 2921, 1788, 1716, 1165, 1051, 931, 823, 747 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{13}O_3ClNH_4$ $[M+NH_4]^+$ 282.0897, found 282.0897. **Chiral SFC**: 94% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 6.4 min, $t_{R2}$ (minor) = 7.4 min.



**2m**

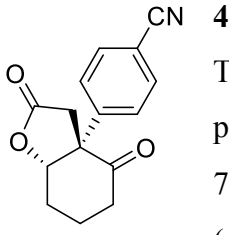
**(3a*S*,7a*S*)-3a-(4-Fluorophenyl)hexahydrobenzofuran-2,4-dione (2m)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a colorless oil (18.6 mg, 75% yield, *anti*:*syn* = 11:1, 94% *ee*, $[\alpha]^{24}_{D}$ = -120.5 (*c* 0.96, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 7.13 – 7.02 (m, 2H), 4.34 (dd, *J* = 12.7, 4.2 Hz, 1H), 3.21 (d,

$J$ = 16.7 Hz, 1H), 2.53 – 2.29 (m, 5H), 2.06 – 1.94 (m, 1H), 1.79 – 1.63 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.0, 173.9, 162.3 (d, $J_{CF}$ = 249.0 Hz), 133.5 (d, $J_{CCCCF}$ = 3.6 Hz), 129.1 (d, $J_{CCCF}$ = 8.0 Hz), 117.0 (d, $J_{CCF}$ = 21.4 Hz), 84.8, 63.6, 41.2, 37.7, 23.1, 22.1. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.5. **IR** (ATR): 2923, 1780, 1718, 1508, 1227, 1176, 1048, 933, 839, 810, 741 cm$^{-1}$. **HRMS** calculated for $C_{14}H_{13}O_3FNH_4$ $[M+NH_4]^+$ 266.1192, found 266.1183. **Chiral SFC**: 94% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 4.4 min, $t_{R2}$ (minor) = 4.8 min.



**2n**

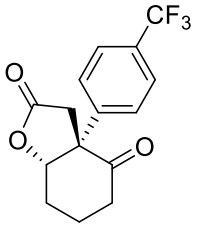
**Ethyl 4-((3a*S*,7a*S*)-2,4-dioxohexahydrobenzofuran-3a(4*H*)-yl)benzoate (2n)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a colorless oil (23.2 mg, 77% yield, *anti*:*syn* = 12:1, 95% *ee*, $[\alpha]^{24}_D$ = -128.1 (*c* 1.1, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, $J$ = 8.6 Hz, 2H), 7.35 (d, $J$ = 8.6 Hz, 2H), 4.41 – 4.33 (m, 3H), 3.26 (d, $J$ = 16.8 Hz, 1H), 2.50 – 2.31 (m, 5H), 2.04 – 1.94 (m, 1H), 1.78 – 1.64 (m, 1H), 1.38 (t, $J$ = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.6, 173.6, 165.9, 142.5, 131.2, 130.6, 127.3, 84.7, 64.2, 61.4, 40.9, 37.9, 23.2, 22.1, 14.4. **IR** (ATR): 2927, 1789, 1712, 1276, 1171, 1105, 1020, 933, 724 cm$^{-1}$. **HRMS** calculated for $C_{17}H_{18}O_5NH_4$ $[M+NH_4]^+$ 320.1498, found 320.1488. **Chiral SFC**: 95% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 13.8 min, $t_{R2}$ (minor) = 16.8 min.



**2o**

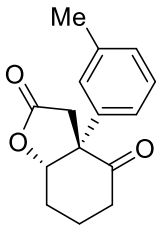
**4-((3a*S*,7a*S*)-2,4-Dioxohexahydrobenzofuran-3a(4*H*)-yl)benzonitrile (2o)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a colorless oil (18.9 mg, 74% yield, *anti*:*syn* = 11:1, 90% *ee*, $[\alpha]^{24}_D$ = -131.6 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, $J$ = 8.7 Hz, 2H), 7.41 (d, $J$ = 8.7 Hz, 2H), 4.37 (dd, $J$ = 11.8, 5.2 Hz, 1H), 3.27 (d, $J$ = 16.9 Hz, 1H), 2.46 – 2.30 (m, 5H), 2.06 – 1.96 (m, 1H), 1.81 – 1.66 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.9, 173.1, 142.8, 133.7, 128.2, 117.9, 112.7, 84.4, 64.2, 40.9, 38.0, 23.1, 22.1. **IR** (ATR): 2922, 2232, 1791, 1719, 1170, 1050, 934, 848, 826 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{13}NO_3NH_4$ $[M+NH_4]^+$ 273.1239, found 273.1238.

**Chiral SFC**: 90% *ee*, 250 mm CHIRALCEL IC, 15% *i*PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.7 min, $t_{R2}$ (major) = 10.5 min.



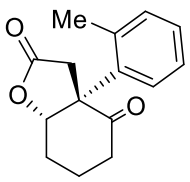
**2p**

**(3a*S*,7a*S*)-3a-(4-(Trifluoromethyl)phenyl)hexahydrobenzofuran-2,4-dione (2p)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a colorless oil (24.9 mg, 78% yield, *anti*:*syn* = 10:1, 92% *ee*, $[\alpha]^{24}_D$ = -95.0 (*c* 0.88, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.9 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 4.37 (dd, *J* = 11.3, 5.6 Hz, 1H), 3.27 (d, *J* = 16.8 Hz, 1H), 2.50 – 2.33 (m, 5H), 2.08 – 1.97 (m, 1H), 1.81 – 1.66 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.4, 173.4, 141.7, 130.8 (q, $J_{CCF}$ = 33.0 Hz), 127.8, 127.0 (q, $J_{CCCF}$ = 3.7 Hz), 123.8 (q, $J_{CF}$ = 272.3 Hz), 84.6, 64.1, 41.0, 37.9, 23.2, 22.2. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -63.4. **IR** (ATR): 2922, 1787, 1725, 1323, 1142, 1112, 1067, 936, 846, 708 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{13}O_3F_3NH_4$ $[M+NH_4]^+$ 316.1161, found 316.1146. **Chiral SFC**: 92% *ee*, 250 mm CHIRALCEL IC, 5% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 4.9 min, $t_{R2}$ (minor) = 6.1 min.



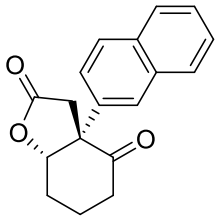
**2q**

**(3a*S*,7a*S*)-3a-(*m*-Tolyl)hexahydrobenzofuran-2,4-dione (2q)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a colorless oil (19.3 mg, 79% yield, *anti*:*syn* = 10:1, 94% *ee*, $[\alpha]^{24}_D$ = -150.2 (*c* 0.75, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 1H), 7.13 – 7.10 (m, 1H), 7.07 – 7.02 (m, 2H), 4.32 (dd, *J* = 12.9, 3.9 Hz, 1H), 3.21 (d, *J* = 16.7 Hz, 1H), 2.56 – 2.41 (m, 3H), 2.37 – 2.27 (m, 5H), 2.02 – 1.93 (m, 1H), 1.75 – 1.62 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 174.2, 139.9, 137.7, 129.8, 129.0, 127.7, 124.2, 85.0, 64.0, 41.2, 37.8, 23.2, 22.2, 21.7. **IR** (ATR): 2920, 1787, 1719, 1168, 1051, 934, 791, 729, 703 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 267.0989. **Chiral SFC**: 94% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 3.7 min, $t_{R2}$ (minor) = 4.5 min.



**2r**

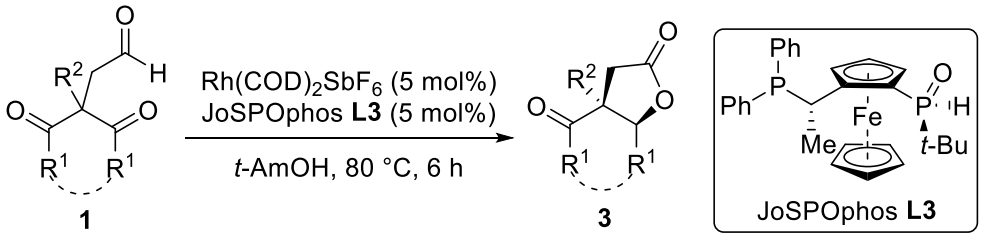
**(3a*S*,7a*S*)-3a-(*o*-Tolyl)hexahydrobenzofuran-2,4-dione (2r)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a colorless oil (16.3 mg, 67% yield, *anti*:*syn* = 6:1, 87% *ee*, $[\alpha]^{24}_{D}$ = -170.0 (*c* 0.60, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 1H), 7.25 – 7.17 (m, 3H), 4.19 (dd, *J* = 13.3, 3.8 Hz, 1H), 3.44 (d, *J* = 16.5 Hz, 1H), 2.76 (ddd, *J* = 25.6, 12.7, 5.1 Hz, 1H), 2.45 – 2.25 (m, 4H), 2.10 – 2.01 (m, 4H), 1.74 – 1.61 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.7, 174.3, 136.5, 135.9, 133.3, 128.6, 128.3, 126.7, 87.0, 65.3, 40.0, 38.2, 23.8, 23.7, 21.5. **IR** (ATR): 2922, 1788, 1717, 1169, 1049, 927, 768, 741 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 267.1003. **Chiral SFC**: 87% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 4.3 min, $t_{R2}$ (minor) = 6.4 min.



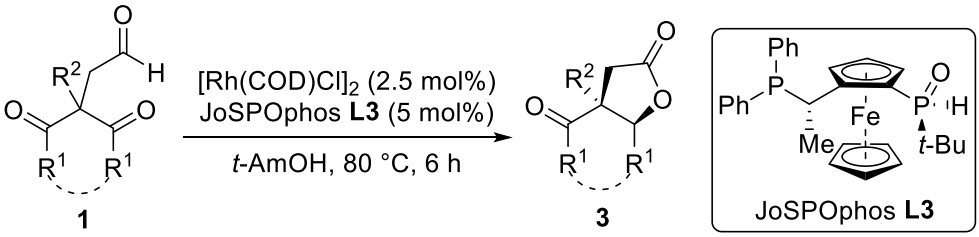
**2s**

**(3a*S*,7a*S*)-3a-(Naphthalen-2-yl)hexahydrobenzofuran-2,4-dione (2s)**: The title compound was synthesized using **Method B** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a colorless oil (19.0 mg, 68% yield, *anti*:*syn* = 9:1, 92% *ee*, $[\alpha]^{24}_{D}$ = -117.6 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.76 (m, 4H), 7.57 – 7.49 (m, 2H), 7.31 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.41 (dd, *J* = 13.0, 3.8 Hz, 1H), 3.31 (d, *J* = 16.7 Hz, 1H), 2.72 – 2.48 (m, 3H), 2.48 – 2.29 (m, 2H), 2.04 – 1.94 (m, 1H), 1.83 – 1.66 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 174.1, 135.0, 133.7, 132.7, 130.2, 128.3, 127.7, 127.1, 127.0, 126.7, 124.3, 85.0, 64.3, 41.2, 38.0, 23.3, 22.3. **IR** (ATR): 2923, 1788, 1719, 1174, 1051, 934, 822, 750, 726 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{16}O_3NH_4$ $[M+NH_4]^+$ 298.1443, found 298.1440. **Chiral SFC**: 92% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 10.3 min, $t_{R2}$ (minor) = 13.6 min.

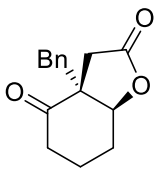
**3. General Procedures for the *syn*-Diastereoselective Ketone Hydroacylation**



**Method C:** In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and *t*-AmOH (1.0 mL) were added to a 1 dram vial containing $Rh(COD)_2SbF_6$ (5.6 mg, 0.010 mmol). After stirring for 20 min, **1** (0.20 mmol) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 1:1 ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture.

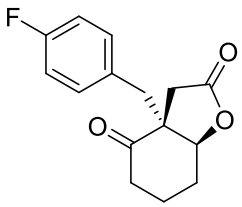



**Method D:** In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and *t*-AmOH (1.0 mL) were added to a 1 dram vial containing $[Rh(COD)Cl]_2$ (2.4 mg, 0.0049 mmol). After stirring for 20 min, **1** (0.20 mmol) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 1:1 ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture.



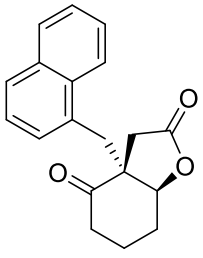
**3a**

**(3a*S*,7a*S*)-3a-Benzylhexahydrobenzofuran-2,4-dione (3a)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (47.8 mg, 98% yield, *syn*:*anti* = >20:1, 98% *ee*, $[\alpha]^{24}_D$ = -105.1 (*c* 1.5, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 3H), 7.04 (dd, J = 7.8, 1.5 Hz, 2H), 4.75 – 4.71 (m, 1H), 3.14 (d, *J* = 17.3 Hz, 1H), 3.07 (d, *J* = 13.8 Hz, 1H), 2.89 (d, *J* = 13.8 Hz, 1H), 2.50 – 2.34 (m, 3H), 2.22 – 2.14 (m, 1H), 2.04 – 1.80 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.1, 174.4, 134.9, 129.9, 129.0, 127.8, 83.8, 57.3, 40.5, 39.1, 36.9, 25.5, 19.8. **IR** (ATR): 2924, 1777, 1706, 1199, 1106, 954, 767, 700 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3NH_4$ $[M+NH_4]^+$ 262.1443, found 262.1445. **Chiral SFC**: 98% *ee*, 100 mm CHIRALCEL OJ-H, 3% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 3.6 min, $t_{R2}$ (major) = 6.3 min.



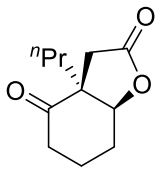
**3b**

**(3a*S*,7a*S*)-3a-(4-Fluorobenzyl)hexahydrobenzofuran-2,4-dione (3b)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (48.8 mg, 93% yield, *syn*:*anti* = >20:1, 97% *ee*, $[\alpha]^{24}_{D}$ = -95.7 (*c* 0.93, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.03 – 6.98 (m, 4H), 4.72 (t, *J* = 2.9 Hz, 1H), 3.12 (d, *J* = 17.3 Hz, 1H), 3.07 (d, *J* = 14.0 Hz, 1H), 2.89 (d, *J* = 14.0 Hz, 1H), 2.52 – 2.32 (m, 3H), 2.25 – 2.13 (m, 1H), 2.04 – 1.79 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.9, 174.2, 162.3 (d, $J_{CF}$ = 247.1 Hz), 131.4 (d, $J_{CCCF}$ = 8.0 Hz), 130.8 (d, $J_{CCCCF}$ = 3.5 Hz), 116.0 (d, $J_{CCF}$ = 21.4 Hz), 83.8, 57.3, 39.9, 39.1, 37.1, 25.8, 19.7. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.3. **IR** (ATR): 2933, 1778, 1707, 1508, 1220, 1200, 1158, 955, 825 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{15}FO_3NH_4$ $[M+NH_4]^+$ 280.1349, found 280.1348. **Chiral SFC**: 97% *ee*, 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.5 min, $t_{R2}$ (major) = 6.7 min.



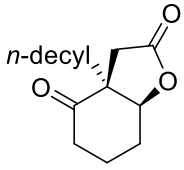
**3c**

**(3a*S*,7a*S*)-3a-(Naphthalen-1-ylmethyl)hexahydrobenzofuran-2,4-dione (3c)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (30% ethyl acetate in hexanes) as a yellow oil (29.3 mg (from 0.10 mmol starting material), 99% yield, *syn*:*anti* = >20:1, 96% *ee*, $[\alpha]^{24}_{D}$ = -119.4 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.88 (t, *J* = 7.7 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.59 – 7.50 (m, 2H), 7.46 – 7.42 (m, 1H), 7.25 (d, *J* = 7.0 Hz, 1H), 4.83 (s, 1H), 3.49 (d, *J* = 14.4 Hz, 1H), 3.37 (d, *J* = 14.5 Hz, 1H), 3.22 (d, *J* = 17.4 Hz, 1H), 2.49 (d, *J* = 16.1 Hz, 1H), 2.41 – 2.32 (m, 1H), 2.28 – 2.19 (m, 2H), 2.06 – 1.90 (m, 2H), 1.88 – 1.81 (m, 1H).**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 210.9, 174.4, 134.1, 132.5, 131.3, 129.3, 129.0, 128.8, 126.9, 126.3, 125.4, 123.5, 83.3, 57.4, 39.3, 37.0, 35.7, 25.3, 19.6. **IR** (ATR): 2946, 1779, 1706, 1201, 1108, 956, 910, 803, 780, 727 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{18}O_3Na$ $[M+Na]^+$ 317.1154, found 317.1153. **Chiral SFC**: 96% *ee*, 250 mm CHIRALCEL IC, 20% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 7.9 min, $t_{R2}$ (major) = 10.0 min.



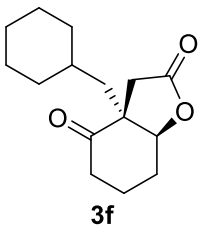
3d

**(3a*S*,7a*S*)-3a-Propylhexahydrobenzofuran-2,4-dione (3d)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (37.3 mg, 95% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -183.8 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 4.62 (s, 1H), 3.32 (d, *J* = 17.1 Hz, 1H), 2.54 – 2.39 (m, 2H), 2.26 – 2.17 (m, 2H), 2.10 – 1.92 (m, 3H), 1.84 – 1.74 (m, 1H), 1.61 – 1.52 (m, 1H), 1.26 – 1.08 (m, 2H), 0.97 – 0.83 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.9, 175.0, 85.9, 57.1, 38.5, 37.1, 36.9, 25.5, 20.7, 18.7, 14.4. **IR** (ATR): 2961, 1763, 1697, 1206, 1156, 1021, 952 $cm^{-1}$. **HRMS** calculated for $C_{11}H_{16}O_3NH_4$ $[M+NH_4]^+$ 214.1443, found 214.1432. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IA, 15% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.1 min, $t_{R2}$ (major) = 7.9 min.



3e

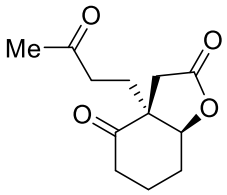
**(3a*S*,7a*S*)-3a-Decylhexahydrobenzofuran-2,4-dione (3e)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (30% ethyl acetate in hexanes) as a yellow oil (26.5 mg (from 0.10 mmol starting material), 90% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -118.8 (*c* 0.51, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.61 (s, 1H), 3.31 (d, *J* = 17.1 Hz, 1H), 2.54 – 2.38 (m, 2H), 2.26 – 2.14 (m, 2H), 2.10 – 2.00 (m, 1H), 1.99 – 1.91 (m, 2H), 1.84 – 1.74 (m, 1H), 1.63 – 1.53 (m, 1H), 1.32 – 1.04 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.9, 175.0, 85.9, 57.1, 38.5, 36.9, 34.9, 32.0, 29.8, 29.6, 29.6, 29.4, 25.5, 25.3, 22.8, 20.7, 14.2. **IR** (ATR): 2920, 2853, 1782, 1699, 1466, 1409, 1313, 1205, 1122, 947 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{30}O_3Na$ $[M+Na]^+$ 317.2093, found 317.2094. **Chiral SFC**: >99% *ee*, 100 mm CHIRALCEL OD-H, 1% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.2 min, $t_{R2}$ (major) = 12.4 min.



3f

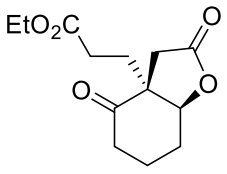
**(3a*S*,7a*S*)-3a-(Cyclohexylmethyl)hexahydrobenzofuran-2,4-dione (3f)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (30% ethyl acetate in hexanes) as a colorless oil (20.8 mg (from 0.10 mmol starting material), *syn*:*anti* = >20:1, 83% yield, >99% *ee*, $[\alpha]^{24}_{D}$ = -140.7 (*c* 0.94, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.55 (s, 1H), 3.43 (d, *J* = 17.0

Hz, 1H), 2.58 – 2.48 (m, 1H), 2.41 (d, *J* = 13.8 Hz, 1H), 2.25 – 2.14 (m, 2H), 2.13 – 2.02 (m, 1H), 2.01 – 1.90 (m, 2H), 1.89 – 1.81 (m, 1H), 1.71 – 1.57 (m, 4H), 1.56 – 1.49 (m, 1H), 1.48 – 1.41 (m, 1H), 1.26 – 1.02 (m, 4H), 0.93 – 0.80 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.2, 175.1, 86.8, 56.9, 42.6, 38.6, 37.9, 34.8, 34.5, 33.7, 26.1, 26.0, 26.0, 25.0, 21.5. **IR** (ATR): 2922, 2850, 1787, 1699, 1449, 1407, 1201, 1119, 988, 949 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{22}O_3Na$ $[M+Na]^+$ 273.1467, found 273.1464. **Chiral SFC**: >99% *ee*, 100 mm CHIRALCEL OD-H, 1% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 8.2 min, $t_{R2}$ (major) = 11.4 min.



**3g**

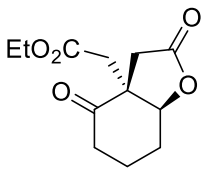
**(3a*S*,7a*S*)-3a-(3-Oxobutyl)hexahydrobenzofuran-2,4-dione (3g)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a colorless oil (16.2 mg (from 0.10 mmol starting material), 72% yield, *syn*:*anti* = >20:1, 83% *ee*, $[\alpha]^{24}_D$ = -152.6 (*c* 0.47, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.62 (t, *J* = 3.0 Hz, 1H), 3.28 (d, *J* = 17.0 Hz, 1H), 2.61 – 2.51 (m, 1H), 2.44 – 2.33 (m, 3H), 2.29 – 2.20 (m, 2H), 2.16 (d, *J* = 17.1 Hz, 1H), 2.12 – 2.03 (m, 4H), 1.99 – 1.91 (m, 2H), 1.85 – 1.77 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 210.2, 206.6, 174.4, 86.0, 56.1, 38.7, 38.5, 36.9, 30.2, 27.8, 25.2, 20.4. **IR** (ATR): 2922, 1769, 1722, 1704, 1266, 1202, 1160, 1031, 991, 947 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{16}O_4Na$ $[M+Na]^+$ 247.0946, found 247.0943. **Chiral SFC**: 83% *ee*, 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 3.1 min, $t_{R2}$ (major) = 3.6 min.



**3h**

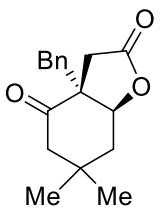
**Ethyl 3-((3a*S*,7a*S*)-2,4-dioxohexahydrobenzofuran-3a(4*H*)-yl)propanoate (3h)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a white solid (48.8 mg, 96% yield, *syn*:*anti* = >20:1, 98% *ee*, $[\alpha]^{24}_D$ = -139.4 (*c* 1.5, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.62 (t, *J* = 3.1 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.27 (d, *J* = 17.1 Hz, 1H), 2.63 – 2.48 (m, 1H), 2.45 – 2.38 (m, 1H), 2.29 – 2.00 (m, 6H), 2.00 – 1.85 (m, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.5, 174.3, 172.1, 85.8, 61.0, 56.1, 38.4, 36.6, 29.9, 29.2, 25.3, 20.4, 14.2. **IR** (ATR): 2937, 1787, 1726, 1708, 1200, 1178, 1029, 991, 952 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_5NH_4$ $[M+NH_4]^+$ 272.1498, found 272.1494.

**Chiral SFC**: 98% *ee*, 100 mm CHIRALCEL OJ-H, 1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 3.1 min, $t_{R2}$ (major) = 3.5 min.



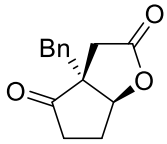
**3i**

**Ethyl 2-((3a*S*,7a*S*)-2,4-dioxohexahydrobenzofuran-3a(4*H*)-yl)acetate (3i)**: The title compound was synthesized using **Method C** and isolated via preparatory TLC (50% ethyl acetate in hexanes) as a colorless oil (12.2 mg (from 0.10 mmol starting material), 51% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_D$ = +128.1 (*c* 4.8, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.77 (dd, *J* = 7.7, 5.4 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.06 (d, *J* = 16.7 Hz, 1H), 2.86 (d, *J* = 17.9 Hz, 1H), 2.65 (d, *J* = 16.7 Hz, 1H), 2.62 – 2.53 (m, 1H), 2.50 – 2.43 (m, 1H), 2.40 (d, *J* = 17.8 Hz, 1H), 2.34 – 2.25 (m, 1H), 2.00 – 1.90 (m, 2H), 1.89 – 1.78 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 208.2, 173.5, 170.6, 84.0, 61.5, 52.2, 40.1, 37.6, 37.1, 28.6, 18.2, 14.2. **IR** (ATR): 2943, 1777, 1710, 1394, 1347, 1196, 1177, 1010, 979, 864 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{16}O_5NH_4$ $[M+NH_4]^+$ 258.1342, found 258.1336. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 6.0 min, $t_{R2}$ (major) = 8.2 min.



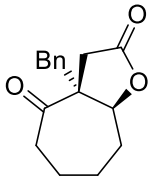
**3j**

**(3a*S*,7a*S*)-3a-Benzyl-6,6-dimethylhexahydrobenzofuran-2,4-dione (3j)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a white solid (50.1 mg, 92% yield, *syn*:*anti* = >20:1, 90% *ee*, $[\alpha]^{24}_D$ = -39.6 (*c* 0.88, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 3H), 7.08 (d, *J* = 6.8 Hz, 2H), 4.79 (t, *J* = 5.3 Hz, 1H), 3.23 (d, *J* = 13.7 Hz, 1H), 3.05 (d, *J* = 17.4 Hz, 1H), 2.83 (d, *J* = 13.7 Hz, 1H), 2.44 – 2.33 (m, 2H), 2.27 (d, *J* = 14.7 Hz, 1H), 2.01 (dd, *J* = 14.8, 4.8 Hz, 1H), 1.92 (dd, *J* = 14.8, 5.6 Hz, 1H), 0.95 (s, 3H), 0.76 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.0, 174.0, 135.2, 130.3, 128.8, 127.6, 82.8, 55.7, 51.1, 40.2, 39.0, 37.0, 34.1, 29.6, 28.9. **IR** (ATR): 2939, 1713, 1687, 1380, 1326, 1191, 1086, 940, 759, 703 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{20}O_3NH_4$ $[M+NH_4]^+$ 290.1756, found 290.1766. **Chiral SFC**: 90% *ee*, 100 mm CHIRALCEL OD-H, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 1.4 min, $t_{R2}$ (major) = 1.5 min.



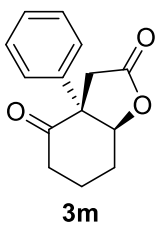

**3k**

**(3a*S*,6a*S*)-3a-benzyltetrahydro-2*H*-cyclopenta[b]furan-2,4(3*H*)-dione (3k)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (42.9 mg, 93% yield, *syn*:*anti* = >20:1, 95% *ee*, $[\alpha]^{24}_{D}$ = +10.6 (*c* 1.4, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 3H), 7.08 (dd, *J* = 7.7, 1.6 Hz, 2H), 5.02 (d, *J* = 4.6 Hz, 1H), 3.16 (d, *J* = 13.6 Hz, 1H), 2.78 (dd, *J* = 15.9, 2.2 Hz, 2H), 2.64 (d, *J* = 18.3 Hz, 1H), 2.44 – 2.31 (m, 1H), 2.25 – 2.11 (m, 2H), 1.53 – 1.41 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 219.4, 174.1, 135.2, 129.7, 129.1, 127.8, 85.6, 57.7, 39.4, 38.1, 35.1, 25.4. **IR** (ATR): 2950, 1772, 1746, 1192, 1164, 1022, 963, 744, 701 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{14}O_3NH_4$ $[M+NH_4]^+$ 248.1287, found 248.1293. **Chiral SFC**: 95% *ee*, 100 mm CHIRALCEL OJ-H, 0.1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 8.3 min, $t_{R2}$ (major) = 9.0 min.




**3l**

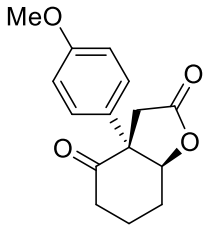
**(3a*S*,8a*S*)-3a-Benzylhexahydro-2*H*-cyclohepta[b]furan-2,4(3*H*)-dione (3l)**: The title compound was synthesized using **Method C** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (49.1 mg, 95% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -55.1 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 3H), 7.01 (dd, *J* = 7.4, 1.9 Hz, 2H), 4.57 (dd, *J* = 11.0, 1.8 Hz, 1H), 3.27 (d, *J* = 14.1 Hz, 1H), 2.98 (d, *J* = 14.0 Hz, 1H), 2.92 (dd, *J* = 18.4, 1.1 Hz, 1H), 2.74 – 2.65 (m, 1H), 2.53 – 2.46 (m, 1H), 2.42 (d, *J* = 18.4 Hz, 1H), 2.13 – 2.02 (m, 1H), 2.02 – 1.86 (m, 2H), 1.65 – 1.42 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.9, 174.5, 134.6, 129.9, 128.9, 127.8, 85.0, 61.4, 43.1, 41.2, 33.2, 32.9, 28.0, 26.1. **IR** (ATR): 2940, 1774, 1708, 1176, 1145, 999, 750, 701 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_3NH_4$ $[M+NH_4]^+$ 276.1600, found 276.1595. **Chiral SFC**: >99% *ee*, 100 mm CHIRALCEL OJ-H, 0.5% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.3 min, $t_{R2}$ (major) = 5.9 min.




**3m**

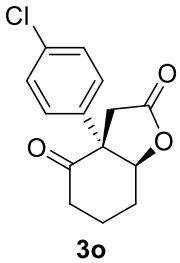
**(3a*R*,7a*S*)-3a-Phenylhexahydrobenzofuran-2,4-dione (3m)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (43.8 mg, 95% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -345 (*c* 1.5, $CHCl_3$)). **$^1$H NMR** (400 MHz, CDCl3) δ 7.42 – 7.30 (m, 3H), 7.25 – 7.20 (m, 2H), 5.39 (t, *J* = 2.7 Hz, 1H), 3.82 (d, *J* = 17.1 Hz, 1H), 2.51

(d, *J* = 17.1 Hz, 1H), 2.48 – 2.37 (m, 3H), 2.37 – 2.25 (m, 1H), 2.13 – 1.99 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.5, 174.0, 136.3, 129.6, 128.4, 126.3, 84.0, 60.3, 40.1, 38.6, 26.2, 21.4. **IR** (ATR): 2959, 1757, 1710, 1199, 1127, 954, 767, 700 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{14}O_3NH_4$ $[M+NH_4]^+$ 248.1287, found 248.1286. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 20% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.9 min, $t_{R2}$ (major) = 7.3 min.



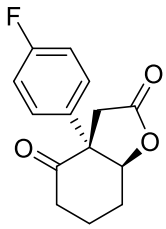
3n

**(3a*R*,7a*S*)-3a-(4-Methoxyphenyl)hexahydrobenzofuran-2,4-dione (3n)**: The title compound was synthesized using **Method D** and isolated by column chromatography (35% ethyl acetate in hexanes) as a white solid (48.8 g, 94% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_D$ = -359 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 5.33 (t, *J* = 2.6 Hz, 1H), 3.83 – 3.69 (m, 4H), 2.49 – 2.23 (m, 5H), 2.07 – 1.98 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.7, 174.1, 159.4, 128.1, 127.5, 114.9, 84.1, 59.6, 55.5, 40.1, 38.4, 26.1, 21.3. **IR** (ATR): 2936, 1785, 1709, 1512, 1252, 1184, 1029, 958, 829 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_4NH_4$ $[M+NH_4]^+$ 278.1392, found 278.1382. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.0 min, $t_{R2}$ (major) = 15.5 min.



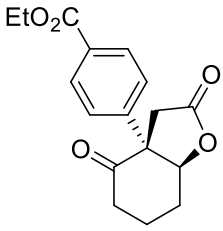
3o

**(3a*R*,7a*S*)-3a-(4-Chlorophenyl)hexahydrobenzofuran-2,4-dione (3o)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (50.2 mg, 95% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_D$ = -315 (*c* 1.1, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 5.34 (t, *J* = 2.7 Hz, 1H), 3.79 (d, *J* = 17.1 Hz, 1H), 2.51 – 2.21 (m, 5H), 2.10 – 2.01 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.1, 173.5, 134.7, 134.6, 129.8, 127.7, 83.7, 59.8, 40.0, 38.6, 26.1, 21.2. **IR** (ATR): 2918, 1784, 1711, 1190, 1126, 1104, 989, 957, 838, 697 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{13}O_3ClNH_4$ $[M+NH_4]^+$ 282.0897, found 282.0888. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 7.2 min, $t_{R2}$ (major) = 13.0 min.



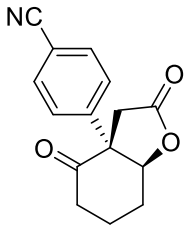
3p

**(3a*R*,7a*S*)-3a-(4-Fluorophenyl)hexahydrobenzofuran-2,4-dione (3p)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (45.5 mg, 92% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -317 (*c* 1.3, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.12 (m, 2H), 7.11 – 7.00 (m, 2H), 5.34 (t, *J* = 2.5 Hz, 1H), 3.77 (d, *J* = 17.1 Hz, 1H), 2.51 – 2.21 (m, 5H), 2.10 – 1.99 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.3, 173.7, 162.4 (d, $J_{CF}$ = 249.0 Hz), 132.1 (d, $J_{CCCCF}$ = 3.4 Hz), 128.2 (d, $J_{CCCF}$ = 8.2 Hz), 116.6 (d, $J_{CCF}$ = 21.6 Hz), 83.8, 59.6, 40.1, 38.5, 26.1, 21.2. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.4. **IR** (ATR): 2926, 1765, 1707, 1512, 1216, 1197, 1127, 1108, 958, 843, 817 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{13}O_3FNH_4$ $[M+NH_4]^+$ 266.1192, found 266.1197. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.2 min, $t_{R2}$ (major) = 8.3 min.



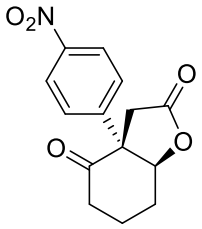
3q

**Ethyl 4-((3a*R*,7a*S*)-2,4-dioxohexahydrobenzofuran-3a(4*H*)-yl)benzoate (3q)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a white solid (57.4 mg, 95% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -297 (*c* 1.1, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 5.40 (t, *J* = 2.7 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.81 (d, *J* = 17.1 Hz, 1H), 2.55 – 2.23 (m, 5H), 2.14 – 2.00 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.9, 173.5, 165.8, 140.8, 130.7, 130.6, 126.4, 83.7, 61.4, 60.4, 39.9, 38.7, 26.2, 21.2, 14.4. **IR** (ATR): 2937, 1788, 1710, 1276, 1190, 1106, 958, 773, 709 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{18}O_5NH_4$ $[M+NH_4]^+$ 320.1498, found 320.1499. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 30% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.7 min, $t_{R2}$ (major) = 6.9 min.



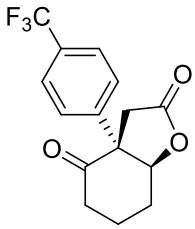
3r

**4-((3a*R*,7a*S*)-2,4-Dioxohexahydrobenzofuran-3a(4*H*)-yl)benzonitrile (3r)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a white solid (47.8 mg, 94% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -328 (*c* 1.1, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8 Hz, 2H), 7.37 (d, *J* = 8.8 Hz, 2H), 5.37 (t, *J* = 2.8 Hz, 1H), 3.79 (d, *J* = 17.1 Hz, 1H), 2.55 – 2.41 (m, 3H), 2.37 – 2.20 (m, 2H), 2.14 – 2.01 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 173.0, 141.2, 133.2, 127.3, 117.9, 112.6, 83.3, 60.2, 39.8, 38.8, 26.1, 21.0. **IR** (ATR): 2923, 2231, 1763, 1712, 1219, 1193, 1131, 994, 963, 841 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{13}NO_3NH_4$ $[M+NH_4]^+$ 273.1239, found 273.1246. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 20% *i*-PrOH, 3.0 mL/min, 240 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 7.6 min, $t_{R2}$ (major) = 10.6 min.



3s

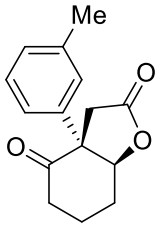
**(3a*R*,7a*S*)-3a-(4-Nitrophenyl)hexahydrobenzofuran-2,4-dione (3s)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (50% ethyl acetate in hexanes) as a yellow solid (50.4 mg, 92% yield, *syn*:*anti* = >20:1, 99% *ee*, $[\alpha]^{24}_{D}$ = -320 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 9.1 Hz, 2H), 7.44 (d, *J* = 9.1 Hz, 2H), 5.41 (t, *J* = 3.0 Hz, 1H), 3.82 (d, *J* = 17.0 Hz, 1H), 2.58 – 2.45 (m, 3H), 2.38 – 2.25 (m, 2H), 2.16 – 2.04 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.3, 172.8, 147.7, 143.1, 127.6, 124.6, 83.3, 60.2, 39.9, 38.9, 26.1, 21.0. **IR** (ATR): 3357, 2923, 1787, 1711, 1514, 1350, 1197, 1104, 957, 855, 707, 687 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{13}ClNO_5$ $[M+Cl]^-$ 310.0482, found 310.0481. **Chiral SFC**: 99% *ee*, 250 mm CHIRALCEL IC, 30% *i*-PrOH, 3.0 mL/min, 280 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.1 min, $t_{R2}$ (major) = 6.8 min.



3t

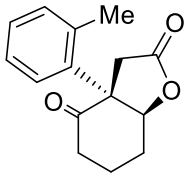
**(3a*R*,7a*S*)-3a-(4-(Trifluoromethyl)phenyl)hexahydrobenzofuran-2,4-dione (3t)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (55.2 mg, 93% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_{D}$ = -279 (*c* 1.5, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.8 Hz, 2H), 7.37 (d, *J* = 8.8 Hz, 2H), 5.40 (t, *J* = 2.8 Hz, 1H), 3.81 (d, *J* = 17.1 Hz, 1H), 2.55 – 2.41 (m, 3H), 2.41 – 2.23 (m, 2H), 2.16 – 2.00 (m,

2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.8, 173.3, 140.1, 130.8 (q, $J_{CCF}$ = 33.0 Hz), 126.9, 126.5 (q, $J_{CCCF}$ = 3.7 Hz), 123.7 (q, $J_{CF}$ = 272.3 Hz), 83.5, 60.2, 40.0, 38.8, 26.1, 21.1. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -63.3. **IR** (ATR): 2926, 1789, 1715, 1324, 1126, 1108, 1068, 962, 848, 699 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{13}O_3F_3NH_4$ $[M+NH_4]^+$ 316.1161, found 316.1162. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 10% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.5 min, $t_{R2}$ (major) = 7.3 min.



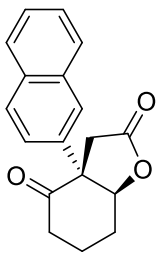
**3u**

**(3a*R*,7a*S*)-3a-(*m*-Tolyl)hexahydrobenzofuran-2,4-dione (3u)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a white solid (44.9 mg, 92% yield, *syn*:*anti* = >20:1, 98% *ee*, $[\alpha]^{24}_D$ = -325 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 1H), 7.15 – 7.11 (m, 1H), 7.05 – 6.98 (m, 2H), 5.38 (t, *J* = 2.7 Hz, 1H), 3.79 (d, *J* = 17.1 Hz, 1H), 2.49 (d, *J* = 17.1 Hz, 1H), 2.46 – 2.36 (m, 3H), 2.35 – 2.26 (m, 4H), 2.08 – 1.99 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.6, 174.1, 139.4, 136.1, 129.4, 129.2, 127.1, 123.1, 84.0, 60.2, 40.1, 38.6, 26.2, 21.6, 21.4. **IR** (ATR): 2927, 1787, 1710, 1200, 1106, 953, 786, 707, 696 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 297.0989. **Chiral SFC**: 98% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 6.7 min, $t_{R2}$ (major) = 10.0 min.



**3v**

**(3a*R*,7a*S*)-3a-(*o*-Tolyl)hexahydrobenzofuran-2,4-dione (3v)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (50% diethyl ether in hexanes) as a white solid (42.9 mg, 88% yield, *syn*:*anti* = >20:1, >99% *ee*, $[\alpha]^{24}_D$ = -163 (*c* 1.1, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.20 – 7.16 (m, 1H), 5.41 (t, *J* = 3.0 Hz, 1H), 3.89 (d, *J* = 17.0 Hz, 1H), 2.52 – 2.28 (m, 5H), 2.21 (s, 3H), 2.12 – 2.03 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.5, 174.2, 138.2, 134.2, 133.4, 128.6, 127.0, 126.2, 85.9, 61.3, 38.2, 37.7, 26.3, 23.8, 21.1. **IR** (ATR): 2932, 1768, 1708, 1206, 1125, 959, 770, 722 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 297.1002. **Chiral SFC**: >99% *ee*, 250 mm CHIRALCEL IC, 15% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.3 min, $t_{R2}$ (major) = 14.2 min.

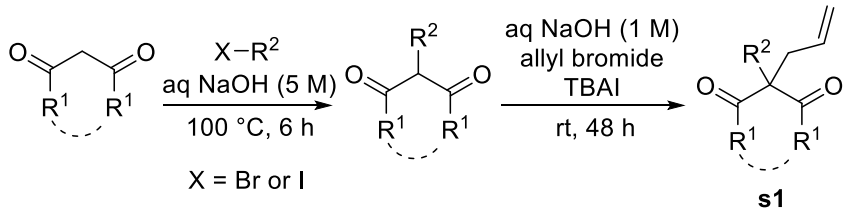


3w

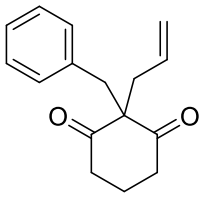
**(3a*R*,7a*S*)-3a-(Naphthalen-2-yl)hexahydrobenzofuran-2,4-dione (3w)**: The title compound was synthesized using **Method D** and isolated by preparatory TLC (35% ethyl acetate in hexanes) as a white solid (50.2 mg, 90% yield, *syn*:*anti* = >20:1, 98% *ee*, $[\alpha]^{24}_{D}$ = -251 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.89 – 7.79 (m, 3H), 7.69 (d, *J* = 1.8 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.30 (dd, *J* = 8.6, 2.0 Hz, 1H), 5.53 (t, *J* = 2.4 Hz, 1H), 3.90 (d, *J* = 17.1 Hz, 1H), 2.61 – 2.36 (m, 5H), 2.18 – 2.01 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.6, 174.0, 133.5, 133.3, 132.7, 129.6, 128.1, 127.8, 127.2, 127.1, 125.3, 123.8, 84.0, 60.4, 40.1, 38.7, 26.3, 21.4. **IR** (ATR): 2926, 1788, 1709, 1200, 1123, 1106, 954, 818, 750 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{16}O_3NH_4$ $[M+NH_4]^+$ 298.1443, found 298.1434. **Chiral SFC**: 98% *ee*, 250 mm CHIRALCEL IC, 30% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.8 min, $t_{R2}$ (major) = 7.9 min.

## 4. Substrate Preparation

### Preparation of Allylated 1,3-Diketones s1

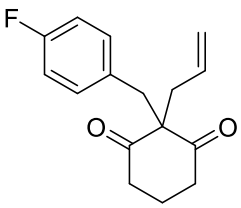



**Method E:** 1,3-Diketone (10 mmol) was dissolved in aqueous NaOH (5.0 M, 2.0 mL, 10 mmol) at 0 ˚C. Alkyl halide (20 mmol) was added to the resulting solution. The mixture was heated at 100 °C for 6 h. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated *in vacuo*. The alkylated product was used for next step without further purification. 2-Alkyl-2,3-dione (8.0 mmol) was dissolved in aqueous NaOH (1.0 M, 8.0 mL, 8.0 mmol) at 0 ˚C. Allyl bromide (1.4 mL, 1.9 g, 16 mmol) and TBAI (150 mg, 0.40 mmol) were added. The mixture was stirred vigorously at rt for 48 h. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated. The residue was purified by column chromatography to afford the allylated product (**s1**).[1]



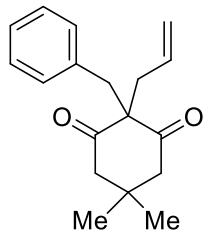
s1a

**2-Allyl-2-benzylcyclohexane-1,3-dione (s1a)**: The title compound was prepared using **Method E** from 1,3-cyclohexanedione and benzyl bromide, isolated by column chromatography (5% ethyl acetate in hexanes) as a colorless oil (1.98 g, 82% yield over 2 steps). (This compound is known[1]). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.14 (m, 3H), 7.02 – 6.95 (m, 2H), 5.58 – 5.45 (m, 1H), 5.16 – 4.88 (m, 2H), 3.09 (s, 2H), 2.64 (d, *J* = 7.5 Hz, 2H), 2.38 – 2.26 (m, 2H), 2.11 – 2.01 (m, 2H), 1.69 – 1.56 (m, 1H), 1.20 – 1.08 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 212.2, 136.6, 132.5, 130.0, 128.7, 127.2, 119.7, 69.4, 44.7, 43.0, 41.3, 15.6.



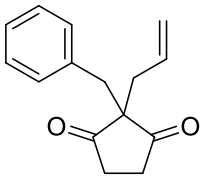
s1b

**2-Allyl-2-(4-fluorobenzyl)cyclohexane-1,3-dione (s1b)**: The title compound was prepared using **Method E** from 1,3-cyclohexanedione and 1-(bromomethyl)-4-fluorobenzene, isolated by column chromatography (5% ethyl acetate in hexanes) as a white solid (1.09g, 49% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.98 – 6.94 (m, 2H), 6.92 – 6.87 (m, 2H), 5.57 – 5.47 (m, 1H), 5.07 – 5.01 (m, 2H), 3.07 (s, 2H), 2.61 (d, *J* = 7.6 Hz, 2H), 2.39 – 2.31 (m, 2H), 2.14 – 2.06 (m, 2H), 1.72 – 1.63 (m, 1H), 1.23 – 1.13 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 212.0, 162.0 (d, *J* = 245.9 Hz, 1H), 132.5 (d, *J* = 3.4 Hz, 1H), 131.6 (d, *J* = 7.9 Hz, 3H), 132.3, 119.8, 115.5 (d, *J* = 21.1 Hz, 4H), 69.4 (d, *J* = 1.1 Hz, 1H). 43.3, 43.2, 41.2, 15.6. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -115.8. **IR** (ATR): 2960, 2884, 1719, 1691, 1505, 1216, 827 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{17}O_2FNH_4$ $[M+NH_4]^+$ 278.1556, found 278.1560.



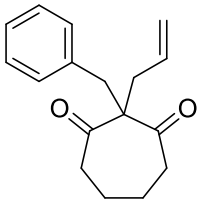
s1j

**2-Allyl-2-benzyl-5,5-dimethylcyclohexane-1,3-dione (s1j)**: The title compound was prepared using **Method E** from 5,5-dimethylcyclohexane-1,3-dione and benzyl bromide, isolated by column chromatography (5% ethyl acetate in hexanes) as a pale yellow solid (1.27 g, 59% yield over 2 steps). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.26 – 7.18 (m, 3H), 7.12 – 7.10 (m, 2H), 5.69 – 5.60 (m, 1H), 5.14 – 5.09 (m, 2H), 3.11 (d, *J* = 4.3 Hz, 2H), 2.59 – 2.57 (m, 2H), 2.48 – 2.44 (m, 2H), 2.33– 2.29 (m, 2H), 0.92 (d, *J* = 4.3 Hz, 3H), 0.57 (d, *J* = 4.3 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 209.9, 136.3, 132.7, 130.9, 128.2, 127.0, 119.7, 68.9, 53.2, 42.4, 40.9, 30.2, 29.0, 28.6. **IR** (ATR): 2951, 1717, 1686, 1425, 1330, 1078, 918, 756, 699 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{22}O_2$ $[M]^+$ 270.1620, found 270.1619.



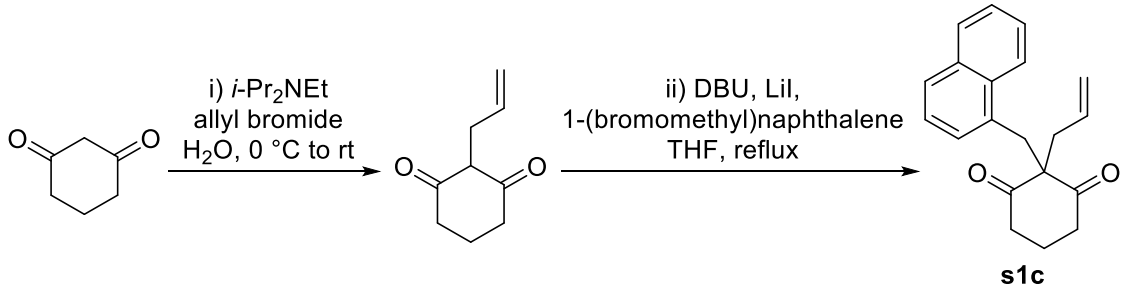
s1k

**2-Allyl-2-benzylcyclopentane-1,3-dione (s1k)**: The title compound was prepared using **Method E** from 1,3-cyclopentanedione and benzyl bromide, isolated by column chromatography (5% ethyl acetate in hexanes) as a white solid (0.83 g, 72% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.17 (m, 3H), 7.07 – 7.00 (m, 2H), 5.64 – 5.50 (m, 1H), 5.14 – 5.03 (m, 2H), 2.97 (s, 2H), 2.49 (d, *J* = 7.5 Hz, 2H), 2.39 (dd, *J* = 19.3, 6.9 Hz, 2H), 1.97 (dd, *J* = 19.2, 6.8 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 217.6, 135.6, 131.5, 129.8, 128.8, 127.4, 120.2, 63.3, 42.4, 40.4, 36.9. **IR** (ATR): 2908, 1719, 1410, 1184, 990, 936, 758, 704 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_2NH_4$ $[M+NH_4]^+$ 246.1494, found 246.1489.



s1l

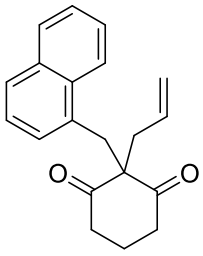
**2-Allyl-2-benzylcycloheptane-1,3-dione (s1l)** The title compound was prepared using **Method E** from 1,3-cycloheptanedione and benzyl bromide, isolated by column chromatography (5% ethyl acetate in hexanes) as a colorless oil (0.89 g, 40% yield over 2 steps). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.23 – 7.18 (m, 3H), 7.02 – 7.00 (m, 2H), 5.69 – 5.58 (m, 1H), 5.12 – 5.04 (m, 2H), 3.13 (s, 2H), 2.51 – 2.48 (m, 2H), 2.43 – 2.30 (m, 4H), 1.87 – 1.79 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 211.6, 136.2, 132.5, 130.3, 128.4, 127.0, 119.2, 70.1, 42.7, 37.8, 36.7, 28.0. **IR** (ATR): 2936, 2864, 1691, 1447, 1323, 1125, 917, 744, 700 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{20}O_2NH_4$ $[M+NH_4]^+$ 274.1807, found 274.1817.




s1c

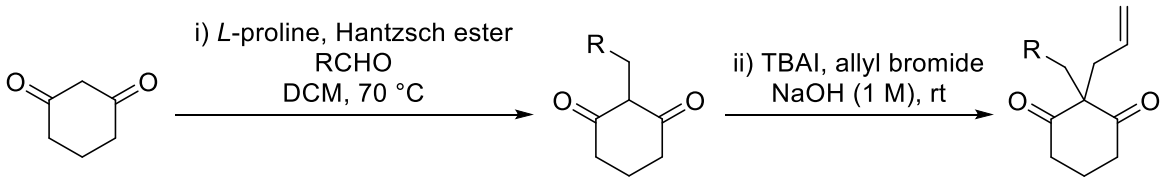
*i*-$Pr_2$NEt (2.9 mL, 16.4 mmol) was added dropwise to a solution of 1,3-cyclohexanedione (2.24 g, 20.0 mmol) in $H_2O$ (3.1 mL) at 0 ˚C. Allyl bromide (1.1 mL, 13.3 mmol) was added, and the solution was allowed to warm to rt. The reaction mixture was allowed to stir at rt overnight and acidified with concentrated HCl. The resulting mixture was extracted with ethyl acetate (3 × 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. 2-Allylcyclohexane-1,3-dione was obtained after purification by column chromatography (25%

ethyl acetate in hexanes) as a white solid (1.04 g, 51% yield). DBU (0.54 mL, 3.58 mmol) was added to a stirred suspension of 2-allylcyclohexane-1,3-dione (0.495 g, 3.25 mmol) and LiI (0.479 g, 3.58 mmol) in THF (6.8 mL). The resulting mixture was stirred at rt for 30 min. Then, 1-(bromomethyl)naphthalene (1.44 g, 6.50 mmol) was added, and the reaction mixture was stirred at reflux overnight. The reaction mixture was cooled to rt and quenched with saturated aqueous $NH_4Cl$ and extracted with ethyl acetate (3 × 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Pure 2-allyl-2-(naphthalen-1-ylmethyl)cyclohexane-1,3-dione (**s1c**) was obtained by column chromatography (10% ethyl acetate in hexanes) as a colorless oil (0.86 g, 85% yield).[2]



**s1c**

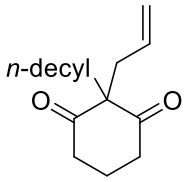
**2-Allyl-2-(naphthalen-1-ylmethyl)cyclohexane-1,3-dione (s1c)**: The title compound was isolated by column chromatography (10% ethyl acetate in hexanes) as a colorless oil (0.86 g, 43% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.6 Hz, 1H), 7.80 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.35 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.18 (dd, *J* = 7.1, 1.0 Hz, 1H), 5.58 – 5.46 (m, 1H), 5.10 – 4.99 (m, 2H), 3.59 (s, 2H), 2.83 (d, *J* = 7.5 Hz, 2H), 2.28 – 2.19 (m, 2H), 1.79 – 1.70 (m, 2H), 1.53 – 1.41 (m, 1H), 1.10 – 0.99 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 212.3, 133.9, 132.8, 132.7, 131.9, 128.7, 128.7, 128.1, 126.4, 125.9, 125.3, 124.4, 119.7, 69.2, 42.4, 41.4, 41.2, 15.4. **IR** (ATR): 2954, 1720, 1691, 1397, 1338, 1210, 1018, 992, 923, 803 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{20}O_2Na$ $[M+Na]^+$ 315.1361, found 315.1370.



**s1**

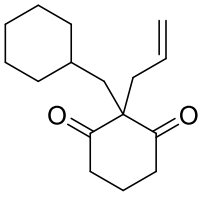
**Method F:** *L*-Proline (0.184 g, 1.6 mmol, 20 mol%) was added to a solution of 1,3-cyclohexanedione (0.897 g, 8.0 mmol), Hantzsch ester (2.03 g, 8.0 mmol), and the aldehyde (24.0 mmol) in dichloromethane (16 mL). The reaction mixture was stirred at 70 ˚C overnight and cooled to rt. The solvent was removed, and the residue was purified by column chromatography (25% ethyl acetate in hexanes) to afford the 2-alkylcyclohexane-1,3-dione.

TBAI (68.3 mg, 0.19 mmol, 5 mol%) was added to a solution of 2-alkylcyclohexane-1,3-dione (6.8 mmol) in aqueous NaOH (1.0 M, 6.8 mL, 6.8 mmol). Allyl bromide (1.2 mL, 13.6 mmol) was added, and the reaction mixture was stirred at rt for 48 h. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with ethyl acetate (3 × 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Pure allylated 1,3-cyclohexanedione was obtained by column chromatography.[1,3]



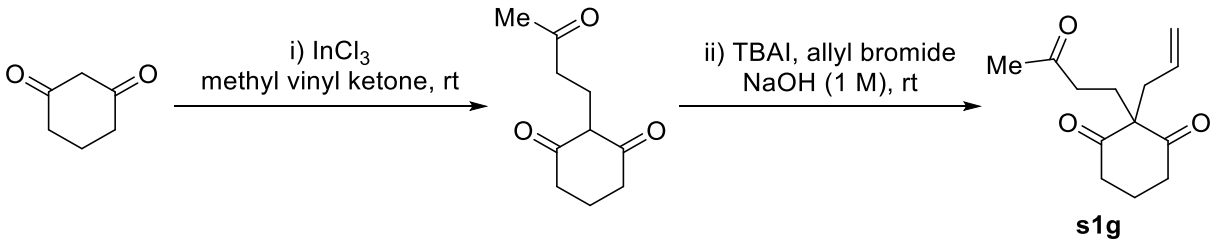
**s1e**

**2-Allyl-2-decylcyclohexane-1,3-dione (s1e)**: The title compound was prepared using **Method F** from 1,3-cyclohexanedione and *n*-decanal, isolated by column chromatography (10% ethyl acetate in hexanes) as a colorless oil (0.98 g, 43% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.37 – 5.25 (m, 1H), 4.78 – 4.71 (m, 2H), 2.41 – 2.25 (m, 4H), 2.22 (d, $J$ = 7.4 Hz, 2H), 1.73 – 1.64 (m, 2H), 1.53 – 1.46 (m, 2H), 1.04 – 0.93 (m, 14H), 0.88 – 0.76 (m, 2H), 0.62 (t, $J$ = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.0, 132.7, 118.4, 68.2, 40.2, 39.4, 36.5, 31.6, 29.7, 29.2, 29.2, 29.0, 28.9, 24.7, 22.3, 16.5, 13.8. **IR** (ATR): 2923, 2853, 1724, 1694, 1462, 1210, 1034, 919, 721 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{32}O_2NH_4$ $[M+NH_4]^+$ 310.2746, found 310.2749.

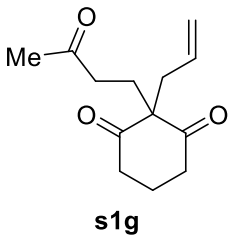


**s1f**

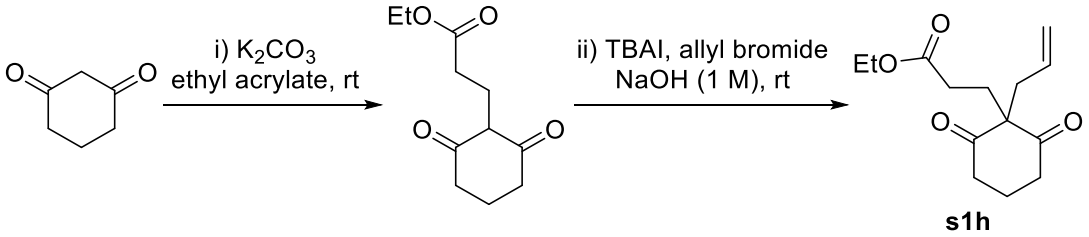
**2-Allyl-2-(cyclohexylmethyl)cyclohexane-1,3-dione (s1f)**: The title compound was prepared using **Method F** from 1,3-cyclohexanedione and cyclohexanecarbaldehyde, isolated by column chromatography (10% ethyl acetate in hexanes) as a yellow oil (0.69 g, 64% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.41 – 5.28 (m, 1H), 4.85 – 4.76 (m, 2H), 2.52 – 2.43 (m, 2H), 2.38 – 2.29 (m, 2H), 2.26 (d, $J$ = 7.4 Hz, 2H), 1.83 – 1.73 (m, 2H), 1.56 (d, $J$ = 6.1 Hz, 2H), 1.46 – 1.32 (m, 3H), 1.28 (d, $J$ = 11.7 Hz, 2H), 1.06 – 0.80 (m, 4H), 0.72 – 0.59 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.5, 132.6, 118.8, 67.3, 44.1, 42.1, 39.5, 34.3, 34.3, 26.0, 25.78, 16.7. **IR** (ATR): 2921, 2850, 1722, 1692, 1448, 1316, 1210, 1036, 988 cm$^{-1}$. **HRMS** calculated for $C_{16}H_{24}O_2Na$ $[M+Na]^+$ 271.1674, found 271.1674.



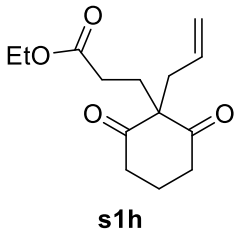

A flame-dried round-bottom flask was charged with 1,3-cyclohexanedione (1.12 g, 10.0 mmol) and $InCl_3$ (0.221 g, 1.0 mmol, 10 mol%). Methyl vinyl ketone (0.81 mL, 10.0 mmol) was added, and the reaction mixture was stirred at rt for 7 h. The reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with dichloromethane (3 × 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Pure 2-(3-oxobutyl)cyclohexane-1,3-dione was obtained by column chromatography (50% ethyl acetate in hexanes) as a white solid (0.751 g, 41% yield). TBAI (76 mg, 0.21 mmol, 5 mol%) was added to a solution of 2-(3-oxobutyl)cyclohexane-1,3-dione (0.751 g, 4.1 mmol) in aqueous NaOH (1.0 M, 4.1 mL, 4.1 mmol). Allyl bromide (0.71 mL, 8.2 mmol) was added, and the reaction mixture was stirred at rt for 48 h. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with dichloromethane (3 × 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Pure 2-allyl-2-(3-oxobutyl)cyclohexane-1,3-dione (**s1g**) was obtained by column chromatography (30% ethyl acetate in hexanes) as a colorless oil (0.65 g, 72% yield).[1,4]



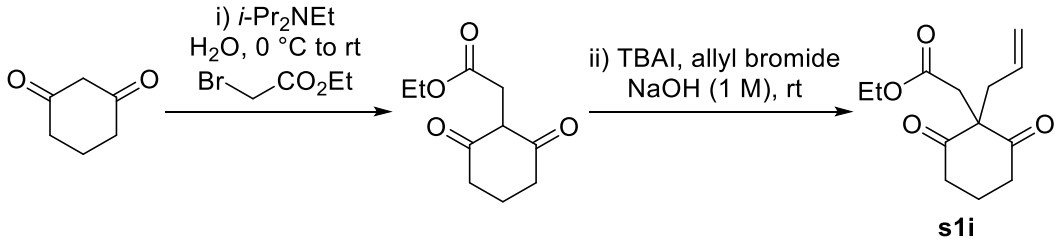

**2-Allyl-2-(3-oxobutyl)cyclohexane-1,3-dione (s1g)**: The title compound was isolated by column chromatography (30% ethyl acetate in hexanes) as a colorless oil (0.65 g, 30% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.54 – 5.42 (m, 1H), 5.02 – 4.95 (m, 2H), 2.64 – 2.47 (m, 4H), 2.42 (d, $J$ = 7.4 Hz, 2H), 2.28 – 2.23 (m, 2H), 2.03 (s, 3H), 1.99 – 1.93 (m, 2H), 1.93 – 1.86 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.7, 207.5, 132.1, 119.5, 67.7, 40.1, 38.9, 38.5, 29.9, 27.9, 17.0. **IR** (ATR): 2960, 1713, 1690, 1417, 1356, 1322, 1168, 1031, 996 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_3Na$ $[M+Na]^+$ 245.1154, found 245.1161.



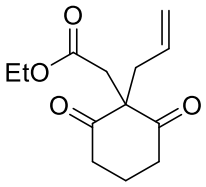

A vigorously stirred mixture of ethyl acrylate (2.2 g, 22 mmol) and 1,3-cyclohexanedione (2.24 g, 20 mmol) and $K_2CO_3$ (2.76 g, 20 mmol) is heated to 40 ˚C in a round bottom flask. After 12 h, HCl (2 M) was added to make the pH to neutral. The reaction mixture was extract with ethyl acetate (3 × 20 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (30% ethyl acetate in hexanes) to afford the alkylated product (1.25g, 30% yield). Allyl bromide (1.31 g, 10.8 mmol), TBAI (0.19 g, 0.54 mmol), 1,3-dione (1.15 g, 5.4 mmol) added to aqueous NaOH (1.0 M, 5.4 ml, 5.4 mmol). After 72 h organic layer was extracted by dichloromethane and washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (5% ethyl acetate in hexanes) to afford **s1h** as a colorless oil (0.92 g, 68% yield).[1,5]




**Ethyl 3-(1-allyl-2,6-dioxocyclohexyl)propanoate (s1h)**: The title compound was isolated by column chromatography (5% ethyl acetate in hexanes) as a colorless oil (0.89 g, 19% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.58 – 5.48 (m, 1H), 5.06 – 5.01 (m, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 2.67 – 2.53 (m, 4H), 2.48 (d, *J* = 7.3 Hz, 2H), 2.19 – 2.06 (m, 4H), 1.99 – 1.91 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.7, 172.9, 132.0, 119.8, 67.9, 60.7, 41.1, 39.2, 29.7, 29.1, 17.1, 14.3. **IR (ATR)**: 2979, 1723, 1692, 1443, 1177, 1026, 924, 734, 606 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{20}O_4H$ $[M+H]^+$: 253.1440, found 253.1441.

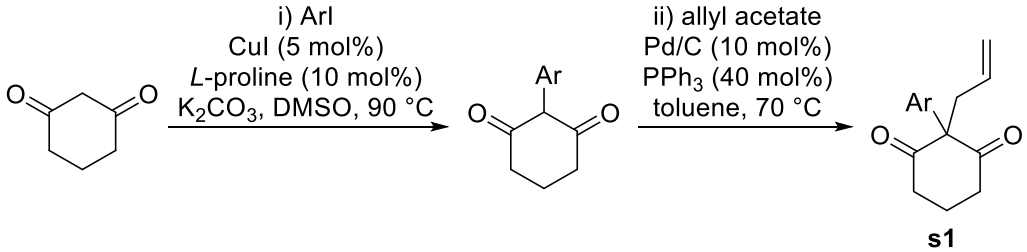


*i*-$Pr_2NEt$ (2.1 mL, 12.0 mmol) was added dropwise to a solution of 1,3-cyclohexanedione (1.68 g, 15.0 mmol) in $H_2O$ (2.3 mL) at 0 ˚C. Ethyl 2-bromoacetate (1.1 mL, 10.0 mmol) was added, and the solution was allowed to warm to rt. The reaction mixture was stirred at rt overnight and acidified with concentrated HCl. The resulting mixture was extracted with ethyl acetate (3 × 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Ethyl 2-(2,6-dioxocyclohexyl)acetate was obtained after purification by column chromatography (50% ethyl acetate in hexanes) as a yellow oil (1.16 g, 59% yield). TBAI (0.108 g, 0.29 mmol, 5 mol%) was added to a solution of ethyl 2-(2,6-dioxocyclohexyl)acetate (1.16 g, 5.9 mmol) in aqueous NaOH (1.0 M, 5.9 mL, 5.9 mmol). Allyl bromide (1.0 mL, 11.8 mmol) was added, and the reaction mixture was stirred at rt for 48 h. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with ethyl acetate (3 × 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Pure ethyl 2-(1-allyl-2,6-dioxocyclohexyl)acetate (**s1i**) was obtained by column chromatography (25% ethyl acetate in hexanes) as a yellow oil (0.45 g, 32% yield).[1,6]



**s1i**

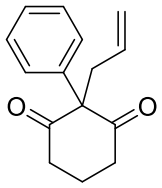
**Ethyl 2-(2,6-dioxo-1-(2-oxoethyl)cyclohexyl)acetate (s1i)**: The title compound was isolated by column chromatography (30% ethyl acetate in hexanes) as a yellow oil (0.45 g, 19% yield over two steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.39 – 5.27 (m, 1H), 4.94 – 4.83 (m, 2H), 3.81 (q, *J* = 7.1 Hz, 2H), 2.77 (s, 2H), 2.51 – 2.46 (m, 4H), 2.17 (d, *J* = 7.5 Hz, 2H), 1.93 – 1.84 (m, 2H), 0.99 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 208.8, 171.5, 130.8, 119.6, 64.6, 60.5, 40.7, 38.1, 37.5, 17.0, 13.7. **IR** (ATR): 2980, 1719, 1694, 1403, 1372, 1325, 1194, 1014, 925 cm$^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_4Na$ $[M+Na]^+$ 261.1103, found 261.1115.



**s1**

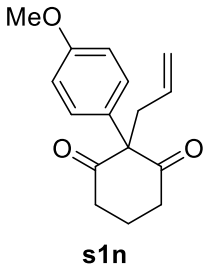
**Method G:** The aryl iodide (15 mmol) was added to a solution of CuI (143 mg, 5 mol%), *L*-proline (172 mg, 10 mol%), $K_2CO_3$ (8.28 g, 60 mmol) and 1,3-cyclohexanedione (5.00 g, 45

mmol) in anhydrous DMSO (60 ml). The reaction mixture was stirred at 90 ˚C for 48 h. Then the cooled solution was poured into aqueous HCl (1 N, 30 ml/mmol) and the organic layer was extracted with ethyl acetate (3 × 300 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude residue by column chromatography (ethyl acetate in hexanes) afforded the arylated 1,3-diketone. Pd/C (10 wt. %, 0.43 g, 0.40 mmol, 10 mol%), $Ph_3P$ (0.42 g, 1.6 mmol, 40 mol%), and allyl acetate (0.43 mL, 4.0 mmol) were added to a suspension of the arylated diketone (4.0 mmol) in toluene (24 mL). The reaction mixture was stirred at 70 ˚C overnight, filtered and concentrated *in vacuo*. The residue was purified by column chromatography afforded the product.[7]



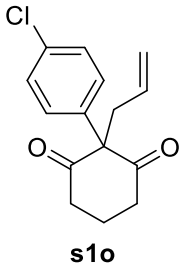
**s1m**

**2-Allyl-2-phenylcyclohexane-1,3-dione (s1m)**: The title compound was prepared using **Method G** and isolated by column chromatography (10% ethyl acetate in hexanes) as a yellow oil (0.78 g, 79% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 3H), 7.03 – 7.00 (m, 2H), 5.69 – 5.62 (m, 1H), 4.96 – 4.89 (m, 2H), 2.77 – 2.69 (m, 4H), 2.57– 2.50 (m, 2H), 1.88 – 1.86 (m, 1H), 1.74 – 1.70 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.3, 137.6, 134.5, 129.5, 128.0, 126.8, 118.4, 75.6, 39.4, 17.5. **IR** (ATR): 3077, 2959, 1727, 1697, 1493, 1217, 915, 759, 700 $cm^{-1}$. **HRMS** (ESI-TOF) calculated for $C_{15}H_{16}O_2NH_4$ $[M+NH_4]^+$ 246.1494, found 246.1492.



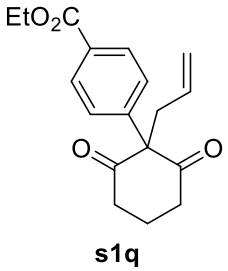
**s1n**

**2-Allyl-2-(4-methoxyphenyl)cyclohexane-1,3-dione (s1n)**: The title compound was prepared using **Method G** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.54 g, 49% yield over 2 steps). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.94 – 6.92 (m, 2H), 6.88 – 6.85 (m, 2H), 5.67 – 5.62 (m, 1H), 4.97 – 4.90 (m, 2H), 3.79 – 3.78 (m, 3H), 2.76 – 2.70 (m, 4H), 2.54 – 2.48 (m, 2H), 1.89 – 1.87 (m, 1H), 1.73 – 1.71 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 207.6, 159.2, 134.6, 129.4, 128.0, 118.4, 114.8, 74.8, 55.4, 39.3, 39.3, 17.4. **IR** (ATR): 2932, 2864, 1704, 1451, 1124, 994, 912, 613 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_3NH_4$ $[M+NH_4]^+$ 276.1600, found 276.1590.



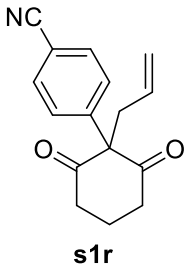
s1o

**2-Allyl-2-(4-chlorophenyl)cyclohexane-1,3-dione (s1o)**: The title compound was prepared using **Method G** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.55 g, 49% yield over 2 steps). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 2H), 6.96 – 6.94 (m, 2H), 5.68 – 5.50 (m, 1H), 4.97 – 4.75 (m, 2H), 2.76 – 2.60 (m, 4H), 2.56 – 2.50 (m, 2H), 1.91 – 1.83 (m, 1H), 1.76 –1.68 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 207.0, 136.0, 134.2, 134.0, 129.6, 128.2, 118.9, 74.7, 39.4, 17.3. **IR** (ATR): 2959, 1729, 1698, 1492, 1314, 1216, 1096, 915, 820, 716 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{15}ClO_2NH_4$ $[M+NH_4]^+$ 280.1104, found 280.1097.



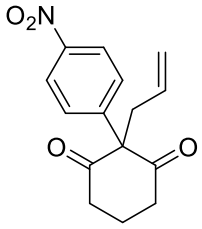
s1q

**Ethyl 4-(1-allyl-2,6-dioxocyclohexyl)benzoate (s1q)**: The title compound was prepared using **Method G** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.43 g, 36% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.06 – 7.04 (m, 2H), 5.63 – 5.53 (m, 1H), 4.87 – 4.81 (m, 2H), 4.32 – 4.27 (m, 2H), 2.70 – 2.62 (m, 4H), 2.54 – 2.47 (m, 2H), 1.84 – 1.79 (m, 1H), 1.72 – 1.65 (m, 1H), 1.32 (t, $J$ = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.6, 165.8, 142.1, 133.8, 130.5, 130.1, 126.8, 118.7, 75.3, 61.1, 39.3, 39.1, 17.2, 14.3. **IR** (ATR): 2979, 1715, 1698, 1607, 1275, 1106, 1020, 915, 852, 770, 714 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{20}O_4H$ $[M+H]^+$ 301.1440, found 301.1444.



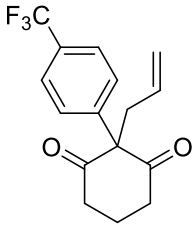
s1r

**4-(1-Allyl-2,6-dioxocyclohexyl)benzonitrile (s1r)**: The title compound was prepared using **Method G** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.42 g, 42% yield over 2 steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, $J$ = 8.5 Hz, 2H), 7.17 (d, $J$ = 8.5 Hz, 2H), 5.67–5.57 (m, 1H), 4.95 – 4.90 (m, 2H), 2.76 (d, $J$ = 7.1 Hz, 2H), 2.72 – 2.56 (m, 4H), 1.95 – 1.73 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.5, 142.6, 133.4, 133.1, 127.8, 119.5, 118.2, 112.2, 75.1, 39.6, 17.2. **IR** (ATR): 2970, 2230, 1724, 1694, 1500, 1426, 1316, 1266, 927, 840, 690, 566 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{15}NO_2$ $[M]^+$: 253.1103, found 253.1098.



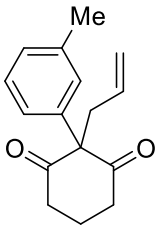
s1s

**2-Allyl-2-(4-nitrophenyl)cyclohexane-1,3-dione (s1s)**: The title compound was using **Method G** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.67 g, 59% yield over 2 steps). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 8.20 – 8.19 (m, 2H), 7.26 – 7.22 (m, 2H), 5.67 – 5.59 (m, 1H), 4.95 – 4.90 (m, 2H), 2.79 – 2.59 (m, 6H), 1.93 –1.88 (m, 1H), 1.84 – 1.77 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 206.5, 147.5, 144.5, 133.2, 128.1, 124.5, 119.6, 74.9, 39.7, 39.6, 17.2. **IR** (ATR): 2953, 1726, 1697, 1604, 1523, 1347, 1318, 1229, 1109, 914, 851, 715, 695 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{14}NO_4$ $[M-H]^-$ 272.0923, found 272.0917.



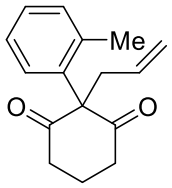
s1t

**2-Allyl-2-(4-(trifluoromethyl)phenyl)cyclohexane-1,3-dione (s1t)**: The title compound was using **Method G** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.60 g, 51% yield over 2 steps). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 5.71 – 5.54 (m, 1H), 5.00 – 4.82 (m, 2H), 2.81 – 2.64 (m, 4H), 2.62 –2.56 (m, 2H), 1.95 – 1.83 (m, 1H), 1.80 –1.74 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 206.8, 141.47, 133.7, 130.37 (d, *J* = 32.9 Hz), 127.4, 126.43 (q, *J* = 3.6 Hz), 126.4 (d, *J* = 3.7 Hz), 123.9 (d, *J* = 272.2 Hz), 119.2, 75.1, 39.6, 17.3. **$^{19}$F NMR** (376 MHz, CDCl3) δ -63.0. **IR** (ATR): 2965, 1731, 1699, 1618, 1325, 1167, 1117, 1069, 1017, 837, 605 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{15}F_3O_2$ $[M]^+$ 296.1024, found 296.1030.



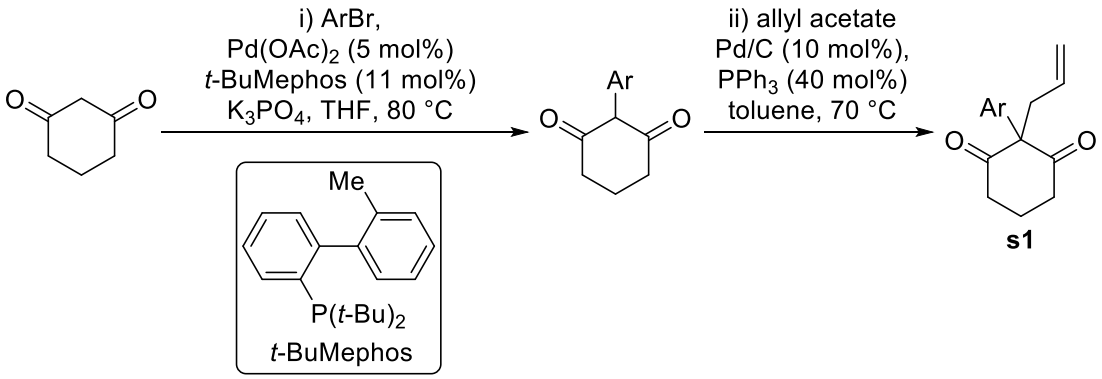
s1u

**2-Allyl-2-(*m*-tolyl)cyclohexane-1,3-dione (s1u)**: The title compound was using **Method G** and isolated by column chromatography (8% ethyl acetate in hexanes) as a yellow oil (0.81 g, 30% yield over 2 steps). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.34 –7.23 (m, 1H), 7.17 –7.11 (m, 1H), 6.90 –6.83 (m, 2H), 5.75 –5.62 (m, 1H), 5.04 – 4.93 (m, 2H), 2.84 – 2.73 (m, 4H), 2.62 – 2.53 (m, 2H), 2.37 (s, 3H), 1.99 – 1.89 (m, 1H), 1.82 – 1.70 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 207.4, 139.4, 137.6, 134.6, 129.4, 128.8, 127.3, 123.8, 118.3, 75.60, 39.5, 39.4, 21.7, 17.5. **IR** (ATR): 2955, 2864, 1727, 1697, 1426, 783, 705 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_2Na$ $[M+Na]^+$ 265.1205, found 265.1197.

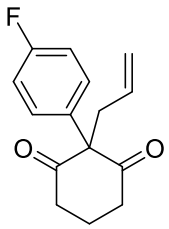



s1v

**2-Allyl-2-(*o*-tolyl)cyclohexane-1,3-dione (s1v)**: The title compound was using **Method G** and isolated by column chromatography (8% ethyl acetate in hexanes) as a yellow oil (0.29 g, 10% yield over 2 steps). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.22 – 7.14 (m, 3H), 6.92 – 6.88 (m, 1H), 5.73 – 5.61 (m, 1H), 4.88 – 4.82 (m, 2H), 2.90 – 2.80 (m, 4H), 2.66 – 2.58 (m, 2H), 2.15 (s, 3H), 1.99 – 1.89 (m, 1H), 1.74 – 1.62 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 207.4, 136.9, 136.5, 134.2, 132.7, 129.6, 127.9, 126.6, 117.9, 78.12, 39.4, 36.4, 21.2, 18.9. **IR** (ATR): 2926, 1727, 1696, 1201, 1019, 912, 756, 730 cm$^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_2Na$ $[M+Na]^+$ 265.1205, found 265.1199.

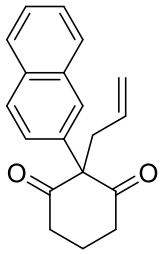



**Method H:** To a dry three-necked round-bottom flask was placed $Pd(OAc)_2$ (0.17 g, 0.75 mmol, 5 mol%), 2-di-tert-butylphosphino-2'-methylbiphenyl (0.52 g, 1.7 mmol, 11 mol%), 1,3-cyclohexanedione (2.02 g, 18 mmol), and $K_3PO_4$ (7.3 g, 35 mmol) under a $N_2$ atmosphere. The flask was flushed several times with $N_2$. THF (45 mL) and the aryl bromide (15 mmol) were added. The reaction mixture was stirred at 80 ˚C until TLC indicated complete consumption of the starting material. MeOH (75 mL) was added and the reaction mixture was stirred for 15 min, filtered and concentrated *in vacuo*. Purification of the crude residue by column chromatography (ethyl acetate in hexanes) afforded the arylated 1,3-diketone. Pd/C (10 wt. %, 0.43 g, 0.40 mmol, 10 mol%), $Ph_3P$ (0.42 g, 1.6 mmol, 40 mol%) followed by allyl acetate (0.43 mL, 4.0 mmol) were added to a suspension of the arylated 1,3-diketone (4.0 mmol) in toluene (24 mL). The reaction mixture was stirred at 70 ˚C overnight, then filtered and concentrated *in vacuo*. Purification by column chromatography afforded the desired product.[7]




s1p

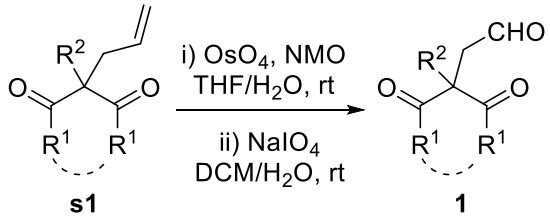
**2-allyl-2-(4-fluorophenyl)cyclohexane-1,3-dione (s1p)**: The title compound was prepared using **Method H** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.42 g, 42% yield over 2 steps). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.04 – 6.96 (m, 4H), 5.67 – 5.56 (m, 1H), 4.93 – 4.90 (m, 1H), 4.88 (t, *J* = 1.2 Hz, 1H), 2.74 – 2.66 (m, 4H), 2.56 – 2.49 (m, 2H), 1.89 – 2.49 (m, 1H), 1.76– 1.70 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.2, 162.3 (d, *J* = 248.3 Hz), 134.1, 133.3 (d, *J* = 3.5 Hz), 128.6 (d, *J* = 8.2 Hz), 118.7, 116.4 (d, *J* = 21.6 Hz), 74.7, 39.5, 39.3, 17.3. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.1. **IR** (ATR): 3076, 2959, 1728, 1697, 1507, 1232, 915, 833, 595 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{15}FO_2$ $[M]^+$ 246.1056, found 246.1052.




s1w

**2-Allyl-2-(naphthalen-2-yl)cyclohexane-1,3-dione (s1w)**: The title compound was prepared using **Method H** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.54 g, 48% yield over 2 steps). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 3H), 7.52 – 7.47 (m, 3H), 7.15 (dd, *J* = 8.6, 2.0 Hz, 1H), 5.76 – 5.65 (m, 1H), 4.99 – 4.90 (m, 2H), 2.87 – 2.84 (m, 2H), 2.83 – 2.74 (m, 2H), 2.62 – 2.55 (m, 2H), 1.94 – 1.84 (m, 1H), 1.79 – 1.68 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.4, 134.9, 134.4, 133.6, 132.6, 129.4, 128.2, 127.7, 126.8, 126.8, 126.2, 124.1, 118.6, 75.7, 39.5, 39.3, 17.5. **IR** (ATR): 3057, 2960, 1727, 1697, 1426, 1216, 913, 858, 818, 748 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{18}O_2$ $[M]^+$ 278.1307, found 278.1314.

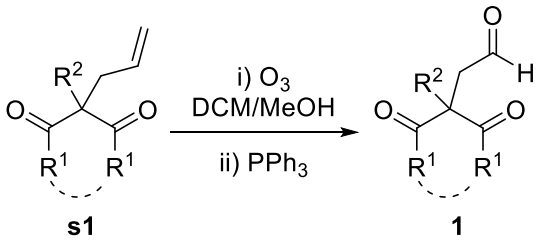
**Preparation of 4,4'-diketo aldehydes 1**




s1 1

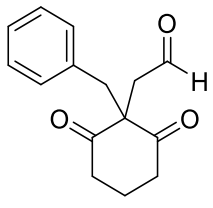
**Method I:** To a solution of **s1** (5 mmol) in THF (8 mL) and $H_2O$ (1.6 mL) was added osmium tetroxide (4% in water, 0.32 mL, 12.7 mg, 0.050 mmol). When the solution turned black, NMO (1.17g, 10 mmol) was added in portions to the reaction mixture. The black color faded and

stirring was continued overnight at rt. The crude mixture was filtered through a Celite pad. The filtrate was extracted with diethyl ether (3 × 40 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The solution of the crude residue dissolved in dichloromethane (4 mL) and $H_2O$ (3 mL) was added $NaIO_4$ (2.35 g, 11 mmol). The reaction mixture was stirred overnight at rt. The mixture was filtered through a Celite pad. The filtrate was extracted with dichloromethane (3 × 40 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography to afford the product **1**.[8]



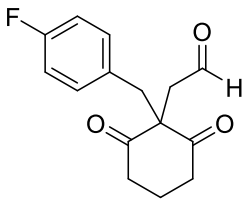
**s1** **1**

**Method J:** A two or three-neck round-bottom flask was added **s1** (1 equiv), indicator (Sudan III, 0.5 mg), solvent (dichloromethane/methanol = 2:1, 10 mL/mmol) and a stirring bar. The reaction mixture was cooled to -78 ˚C, then $O_3$ was bubbled through the reaction solution until the red color of reaction solution turns to purple/blue. The $O_3$ generator was turned off and $N_2$ was bubbled through the reaction solution for 30 min to remove the unreacted $O_3$. Triphenylphosphine (1.5 equiv) was added into the reaction solution. The resulted reaction solution was stirred in the dry ice bath for 1 h, then warmed up to room temperature and stirred for another 12 h. The solvent was removed by evaporation *in vacuo*. The residue was purified by column chromatography to afford the product **1**.



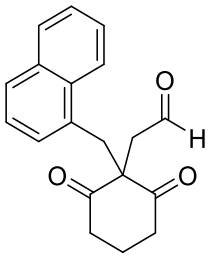
**1a**

**2-(1-Benzyl-2,6-dioxocyclohexyl)acetaldehyde (1a)**: The title compound was prepared using **Method I** and isolated by column chromatography (20% ethyl acetate in hexanes) as a white solid (0.89 g, 73% yield from 1.22 g of **s1a**). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 9.46 (s, 1H), 7.39 – 7.18 (m, 3H), 7.01 – 6.95 (m, 2H), 3.33 (s, 2H), 2.95 (s, 2H), 2.73 – 2.63 (m, 2H), 2.28 – 2.16 (m, 2H), 2.15 – 2.00 (m, 1H), 1.58 – 1.44 (m, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 210.8, 199.4, 135.0, 129.9, 128.9, 127.9, 64.3, 51.7, 44.7, 39.6, 16.7. **IR** (ATR): 1704, 1685, 1319, 1189, 1029, 943, 768, 698 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3NH_4$ $[M+NH_4]^+$ 262.1443, found 262.1440.



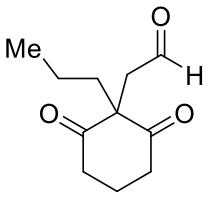
**1b**

**2-(1-(4-Fluorobenzyl)-2,6-dioxocyclohexyl)acetaldehyde (1b)**: The title compound was prepared using **Method I** and isolated by column chromatography (20% ethyl acetate in hexanes) as a white solid (0.59 g, 75% yield from 0.78 g of **s1b**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.00 – 6.86 (m, 4H), 3.27 (s, 2H), 2.90 (s, 2H), 2.72 – 2.63 (m, 2H), 2.29 – 2.16 (m, 2H), 2.15 – 2.01 (m, 1H), 1.58 – 1.48 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.6, 199.2, 162.3 (d, $J_{CF}$ = 247.0 Hz), 131.4 (d, $J_{CCCF}$ = 8.0 Hz), 130.7 (d, $J_{CCCCF}$ = 3.4 Hz), 115.8 (d, $J_{CCF}$ = 21.4 Hz), 64.2, 51.5, 43.5, 39.5, 16.8. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.2. **IR** (ATR): 1706, 1688, 1509, 1220, 1027, 941, 835, 766 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{15}FO_3NH_4$ $[M+NH_4]^+$ 280.1349, found 280.1344.



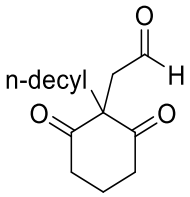
**1c**

**2-(1-(Naphthalen-1-ylmethyl)-2,6-dioxocyclohexyl)acetaldehyde (1c)**: The title compound was prepared using **Method I** and isolated by column chromatography (30% ethyl acetate in hexanes) as a colorless oil (0.37 g, 49% yield, from 0.75 g of **s1c**). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.82 (d, $J$ = 7.8 Hz, 2H), 7.76 (d, $J$ = 8.2 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.35 (t, $J$ = 7.6 Hz, 1H), 7.12 (d, $J$ = 7.0 Hz, 1H), 3.45 (s, 2H), 3.40 (s, 2H), 2.52 (d, $J$ = 16.7 Hz, 2H), 2.00 – 1.90 (m, 1H), 1.88 – 1.77 (m, 2H), 1.32 – 1.23 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 211.2, 199.4, 133.8, 132.0, 131.5, 128.9, 128.9, 128.5, 126.7, 126.0, 125.2, 123.7, 64.2, 52.3, 40.3, 39.8, 16.4. **IR** (ATR): 2920, 1705, 1685, 1378, 1320, 1189, 1099, 1029, 800 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{18}O_3Na$ $[M+Na]^+$ 317.1154, found 317.1151.



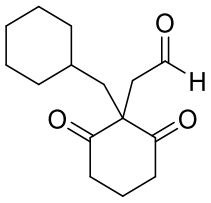
**1d**

**2-(2,6-Dioxo-1-propylcyclohexyl)acetaldehyde (1d)**: The title compound was prepared using **Method I** and isolated by column chromatography (20% ethyl acetate in hexanes) as a colorless oil (0.49g, 71% yield from 0.68 g of **s1d**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) $\delta$ 9.53 (s, 1H), 3.22 (s, 2H), 2.80 – 2.56 (m, 4H), 2.26 – 1.99 (m, 2H), 1.69 – 1.53 (m, 2H), 1.24 – 1.13 (m, 2H), 0.86 (t, $J$ = 7.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 209.4, 199.5, 64.4, 47.7, 39.0, 38.1, 18.1, 17.6, 14.3. **IR** (ATR): 2959, 1701, 1684, 1377, 1324, 1144, 1028 cm$^{-1}$. **HRMS** calculated for $C_{11}H_{16}O_3NH_4$ $[M+NH_4]^+$ 214.1443, found 214.1440.



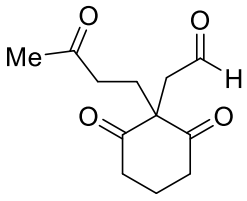
**1e**

**2-(1-Decyl-2,6-dioxocyclohexyl)acetaldehyde (1e)**: The title compound was prepared using **Method J** and isolated by column chromatography (30% ethyl acetate in hexanes) as a colorless oil (0.48 g, 49% yield from 0.98 g of **s1e**). **$^{1}$H NMR** (400 MHz, $CD_2Cl_2$) δ 9.53 (s, 1H), 3.18 (s, 2H), 2.75 – 2.59 (m, 4H), 2.13 – 2.03 (m, 2H), 1.67 – 1.60 (m, 2H), 1.32 – 1.20 (m, 14H), 1.18 – 1.08 (m, 2H), 0.89 (t, *J* = 6.7 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.4, 200.1, 65.0, 47.4, 38.3, 37.1, 32.3, 30.1, 29.9, 29.9, 29.7, 29.6, 24.8, 23.1, 17.9, 14.3. **IR** (ATR): 2923, 2853, 1694, 1457, 1379, 1325, 1208, 1096, 1027, 929 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{30}O_3Na$ $[M+Na]^+$ 317.2093, found 317.2092.



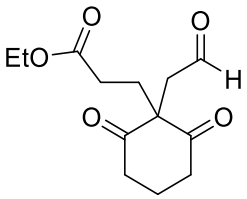
**1f**

**2-(1-(Cyclohexylmethyl)-2,6-dioxocyclohexyl)acetaldehyde (1f)**: The title compound was prepared using **Method J** and isolated by column chromatography (50% ethyl acetate in hexanes) as a yellow oil (0.27 g, 39% yield from 0.69 g of **s1f**). **$^{1}$H NMR** (400 MHz, $CD_2Cl_2$) δ 9.52 (s, 1H), 3.22 (s, 2H), 2.80 – 2.69 (m, 2H), 2.66 – 2.58 (m, 2H), 2.14 – 1.97 (m, 2H), 1.75 – 1.50 (m, 8H), 1.30 – 1.07 (m, 3H), 0.95 – 0.85 (m, 2H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 209.5, 200.0, 65.1, 47.8, 44.6, 38.3, 35.1, 34.0, 26.5, 26.3, 18.0. **IR** (ATR): 2921, 2850, 1708, 1694, 1448, 1313, 1091, 1028, 968 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{22}O_3Na$ $[M+Na]^+$ 273.1467, found 273.1463.



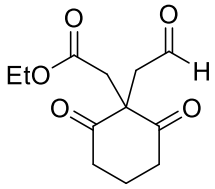
**1g**

**2-(2,6-Dioxo-1-(3-oxobutyl)cyclohexyl)acetaldehyde (1g)**: The title compound was prepared using **Method J** and isolated by column chromatography (50% ethyl acetate in hexanes) as a colorless oil (0.14 g, 63% yield from 0.22 g of **s1g**). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 9.49 (s, 1H), 3.16 (s, 2H), 2.77 – 2.69 (m, 2H), 2.67 – 2.61 (m, 2H), 2.39 (t, *J* = 6.9 Hz, 2H), 2.16 – 2.10 (m, 2H), 2.08 (s, 3H), 1.92 (t, *J* = 6.9 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.3, 206.3, 199.2, 62.5, 47.0, 37.7, 37.4, 23.0, 28.5, 17.2. **IR** (ATR): 2959, 1712, 1690, 1418, 1369, 1169, 1029, 912, 727 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{16}O_4Na$ $[M+Na]^+$ 247.0946, found 247.0951.



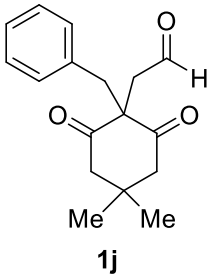

**1h**

**Ethyl 3-(2,6-dioxo-1-(2-oxoethyl)cyclohexyl)propanoate (1h)**: The title compound was prepared using **Method I** and isolated by column chromatography (50% ethyl acetate in hexanes) as a white solid (0.40 g, 49% yield from 0.81 g of **s1h**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.21 (s, 2H), 2.82 – 2.65 (m, 4H), 2.25 (t, *J* = 7.6 Hz, 2H), 2.22 – 2.10 (m, 2H), 1.99 (t, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.1, 199.2, 172.1, 62.9, 61.1, 47.2, 38.0, 30.4, 29.0, 17.5, 14.3. **IR** (ATR): 1719, 1709, 1687, 1377, 1194, 1026 cm$^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_5NH_4$ $[M+NH_4]^+$ 272.1498, found 272.1493.



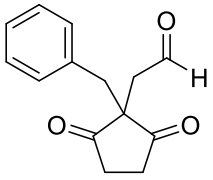

**1i**

**Ethyl 2-(2,6-dioxo-1-(2-oxoethyl)cyclohexyl)acetate (1i)**: The title compound was prepared using **Method J** and isolated by column chromatography (50% ethyl acetate in hexanes) as a yellow oil (0.18 g, 73% yield from 0.25 g of **s1i**). **$^1$H NMR** (499 MHz, $CDCl_3$) δ 9.49 (s, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 3.14 (s, 2H), 2.83 – 2.79 (m, 6H), 2.30 – 2.15 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.4, 198.5, 169.8, 61.4, 59.8, 50.2, 41.5, 38.2, 17.2, 14.0. **IR** (ATR): 2961, 1716, 1695, 1373, 1343, 1188, 1093, 1026, 955 cm$^{-1}$. **HRMS** calculated for $C_{12}H_{16}O_5Na$ $[M+Na]^+$ 263.0895, found 263.0894.



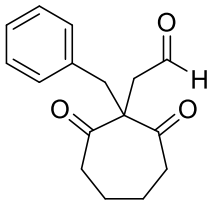

**1j**

**2-(1-Benzyl-4,4-dimethyl-2,6-dioxocyclohexyl)acetaldehyde (1j)**: The title compound was prepared using **Method I** and isolated by column chromatography (20% ethyl acetate in hexanes) as a white solid (0.73 g, 74% yield from 0.97 g of **s1j**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.32 – 7.26 (m, 3H), 7.00 – 6.93 (m, 2H), 3.06 (s, 2H), 2.96 – 2.84 (m, 4H), 2.55 (d, *J* = 15.1 Hz, 2H), 1.21 (s, 3H), 1.19 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.2, 197.8, 134.0, 130.0, 128.8, 128.0, 66.6, 51.4, 44.7, 44.4, 32.0, 31.3, 27.1. **IR** (ATR): 1713, 1687, 1381, 1192, 1086, 759, 704 cm$^{-1}$. **HRMS** calculated for $C_{17}H_{20}O_3NH_4$ $[M+NH_4]^+$ 290.1756, found 290.1760.



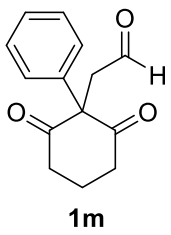
1k

**2-(1-Benzyl-2,5-dioxocyclopentyl)acetaldehyde (1k)**: The title compound was prepared using **Method I** and isolated by column chromatography (30% ethyl acetate in hexanes) as a yellow oil (0.49 g, 66% yield from 0.74 g of **s1k**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.30 – 7.24 (m, 3H), 7.06 – 7.00 (m, 2H), 3.29 (s, 2H), 2.85 (s, 2H), 2.82 – 2.66 (m, 2H), 2.04 – 1.88 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 217.1, 198.8, 134.0, 129.8, 128.9, 127.9, 57.5, 52.4, 42.2, 36.4. **IR** (ATR): 1717, 1706, 1412, 1200, 1003, 933, 754, 707 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{14}O_3NH_4$ $[M+ NH_4]^+$ 248.1287, found 248.1284.



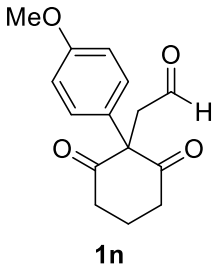
1l

**2-(1-Benzyl-2,7-dioxocycloheptyl)acetaldehyde (1l)**: The title compound was prepared using **Method J** and isolated by column chromatography (20% ethyl acetate in hexanes) as a yellow oil (0.40 g, 77% yield from 0.51 g of **s1l**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.60 (t, $J$ = 1.6 Hz, 1H), 7.26 – 7.20 (m, 3H), 7.02 – 6.98 (m, 2H), 3.28 (s, 2H), 2.73 (d, $J$ = 1.6 Hz, 2H), 2.71 – 2.63 (m, 2H), 2.60 – 2.52 (m, 2H), 1.98 – 1.89 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.1, 199.4, 135.3, 130.2, 128.8, 127.5, 68.4, 46.3, 42.0, 39.6, 27.1. **IR** (ATR): 1714, 1692, 1452, 1324, 1080, 974, 747, 701 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{19}O_3$ $[M+H]^+$ 259.1334, found 259.1341.



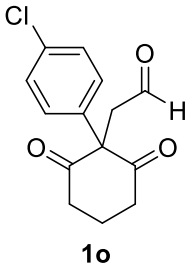
1m

**2-(2,6-Dioxo-1-phenylcyclohexyl)acetaldehyde (1m)**: The title compound was prepared using **Method I** and isolated by column chromatography (30% ethyl acetate in hexanes) as a white solid (0.58 g, 81% yield from 0.72 g of **s1m**). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 9.56 (s, 1H), 7.41 – 7.27 (m, 3H), 7.08 – 7.04 (m, 2H), 3.39 (s, 2H), 2.79 – 2.61 (m, 4H), 2.12 – 1.88 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 206.8, 198.7, 135.4, 129.9, 128.4, 126.6, 70.1, 51.6, 38.9, 17.4. **IR** (ATR): 1709, 1694, 1493, 1382, 1225, 1026, 760, 704 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{14}O_3NH_4$ $[M+NH_4]^+$ 248.1287, found 248.1284.



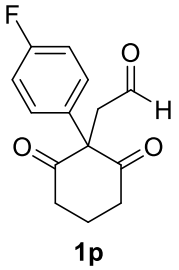
1n

**2-(1-(4-Methoxyphenyl)-2,6-dioxocyclohexyl)acetaldehyde (1n)**: The title compound was prepared using **Method I** and isolated by column chromatography (50% ethyl acetate in hexanes) as a white solid (0.37 g, 73% yield from 0.50 g of **s1n**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 6.96 (d, $J$ = 9.1 Hz, 2H), 6.86 (d, $J$ = 9.1 Hz, 2H), 3.78 (s, 3H), 3.35 (s, 2H), 2.77 – 2.60 (m, 4H), 2.09 – 1.98 (m, 1H), 1.98 – 1.87 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.0, 199.0, 159.6, 127.9, 126.9, 115.2, 69.3, 55.5, 51.5, 38.7, 17.4. **IR** (ATR): 1711, 1693, 1509, 1255, 1186, 1027, 824 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_4NH_4$ $[M+NH_4]^+$ 278.1392, found 278.1386.



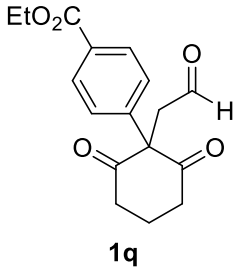
1o

**2-(1-(4-Chlorophenyl)-2,6-dioxocyclohexyl)acetaldehyde (1o)**: The title compound was prepared using **Method I** and isolated by column chromatography (30% ethyl acetate in hexanes) as a white solid (0.32 g, 65% yield from 0.49 g of **s1o**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.33 (d, $J$ = 8.9 Hz, 2H), 7.00 (d, $J$ = 8.9 Hz, 2H), 3.38 (s, 2H), 2.75 – 2.71 (m, 2H), 2.69 – 2.58 (m, 2H), 2.14 – 2.02 (m, 1H), 2.00 – 1.88 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.6, 198.5, 134.7, 133.7, 130.0, 128.1, 69.2, 51.7, 38.9, 17.3. **IR** (ATR): 1715, 1695, 1492, 1095, 1027, 1012, 817, 738 cm$^{-1}$. **HRMS** calculated for $C_{14}H_{13}O_3ClNH_4$ $[M+NH_4]^+$ 282.0897, found 282.0907.



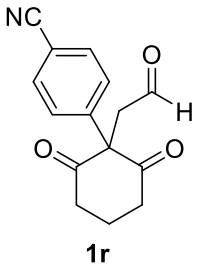
1p

**2-(1-(4-Fluorophenyl)-2,6-dioxocyclohexyl)acetaldehyde (1p)**: The title compound was prepared using **Method J** and isolated by column chromatography (1% acetone in dichloromethane) as a white solid (0.27 g, 70% yield from 0.39 g of **s1p**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.06 – 7.01 (m, 4H), 3.37 (s, 2H), 2.78 – 2.70 (m, 2H), 2.69 – 2.59 (m, 2H), 2.12 – 2.01 (m, 1H), 1.99 – 1.88 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.8, 198.6, 162.6 (d, $J_{CF}$ = 249.1 Hz), 130.9 (d, $J_{CCCCF}$ = 3.4 Hz), 128.5 (d, $J_{CCCF}$ = 8.2 Hz), 116.8 (d, $J_{CCF}$ = 21.6 Hz), 69.1, 51.8, 38.8, 17.3. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.7. **IR** (ATR): 1713, 1696, 1506, 1222, 1164, 1026, 825 cm$^{-1}$. **HRMS** calculated for $C_{14}H_{13}O_3FNH_4$ $[M+NH_4]^+$ 266.1192, found 266.1200.



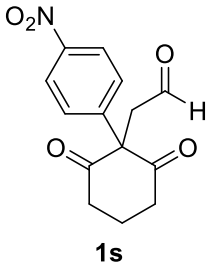
1q

**Ethyl 4-(2,6-dioxo-1-(2-oxoethyl)cyclohexyl)benzoate (1q)**: The title compound was prepared using **Method J** and isolated by column chromatography (2% acetone in dichloromethane) as a white solid (0.30 g, 75% yield from 0.40 g of **s1q**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.40 (s, 2H), 2.80 – 2.72 (m, 2H), 2.68 – 2.57 (m, 2H), 2.15 – 2.02 (m, 1H), 1.99 – 1.87 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 198.3, 165.8, 140.0, 130.9, 130.7, 126.7, 69.8, 61.4, 51.6, 39.0, 17.3, 14.4. **IR** (ATR): 1715, 1696, 1272, 1101, 1021, 767, 701 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{18}O_5NH_4$ $[M+NH_4]^+$ 320.1498, found 320.1503.



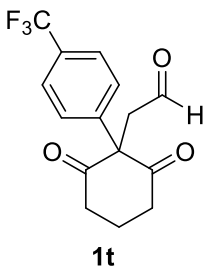
1r

**4-(2,6-Dioxo-1-(2-oxoethyl)cyclohexyl)benzonitrile (1r)**: The title compound was prepared using **Method J** and isolated by column chromatography (2% acetone in dichloromethane) as a white solid (0.32 g, 78% yield from 0.41 g of **s1r**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 3.41 (s, 2H), 2.84 – 2.76 (m, 2H), 2.66 – 2.56 (m, 2H), 2.19 – 2.06 (m, 1H), 1.99 – 1.89 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.2, 198.0, 140.5, 133.4, 127.6, 118.0, 112.7, 69.3, 51.9, 39.1, 17.2. **IR** (ATR): 2231, 1716, 1697, 1500, 1373, 1274, 1227, 1027, 930, 834 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{13}NO_3NH_4$ $[M+NH_4]^+$ 273.1239, found 273.1233.



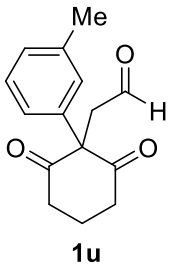
1s

**2-(1-(4-Nitrophenyl)-2,6-dioxocyclohexyl)acetaldehyde (1s)**: The title compound was prepared using **Method J** and isolated by column chromatography (5% acetone in dichloromethane) as a yellow solid (0.27 g, 41% yield from 0.66 g of **s1s**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.20 (d, *J* = 9.1 Hz, 2H), 7.29 (d, *J* = 9.1 Hz, 2H), 3.45 (s, 2H), 2.87 – 2.79 (m, 2H), 2.68 – 2.58 (m, 2H), 2.10 – 2.09 (m, 1H), 2.02 – 1.90 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.2, 197.9, 147.8, 142.3, 127.8, 124.8, 69.2, 52.0, 39.2, 17.2. **IR** (ATR): 1710, 1698, 1514, 1352, 1320, 1029, 843, 694 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{13}ClNO_5$ $[M+Cl]^-$ 310.0482, found 310.0482.



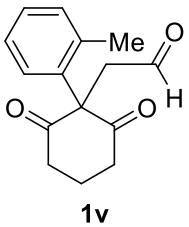
1t

**2-(2,6-Dioxo-1-(4-(trifluoromethyl)phenyl)cyclohexyl)acetaldehyde (1t)**: The title compound was prepared using **Method I** and isolated by column chromatography (30% ethyl acetate in hexanes) as a white solid (0.39 g, 70% yield from 0.56 g of **s1t**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.61 (d, $J$ = 8.3 Hz, 2H), 7.22 (d, $J$ = 8.3 Hz, 2H), 3.42 (s, 2H), 2.83 – 2.75 (m, 2H), 2.70 – 2.57 (m, 2H), 2.19 – 2.05 (m, 1H), 2.01 – 1.89 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 198.2), 139.3 (q, $J_{CCCCF}$ = 1.4 Hz), 130.9 (q, $J_{CCF}$ = 49.6 Hz), 127.2, 126.8 (q, $J_{CCCF}$ = 3.8 Hz), 123.8 (d, $J_{CF}$ = 272.3 Hz), 69.4, 51.8, 39.0, 17.3. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -63.1. **IR** (ATR): 1716, 1698, 1324, 1167, 1117, 1071, 1020, 835 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{13}O_3F_3NH_4$ $[M+NH_4]^+$ 316.1161, found 316.1173.



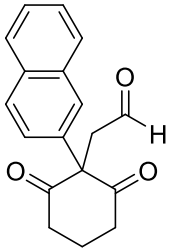
1u

**2-(2,6-Dioxo-1-(*m*-tolyl)cyclohexyl)acetaldehyde (1u)**: The title compound was prepared using **Method J** and isolated by column chromatography (20% ethyl acetate in hexanes) as a white solid (0.31 g, 78% yield from 0.40 g of **s1u**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.25 – 7.20 (m, 1H), 7.13 – 7.09 (m, 1H), 6.86 – 6.82 (m, 2H), 3.36 (s, 2H), 2.76 – 2.62 (m, 4H), 2.31 (s, 3H), 2.09 – 1.90 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.8, 198.8, 139.7, 135.3, 129.7, 129.1, 127.1, 123.6, 70.1, 51.5, 38.9, 21.6, 17.4. **IR** (ATR): 1711, 1693, 1380, 1275, 1024, 789, 702 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 267.0988.



1v

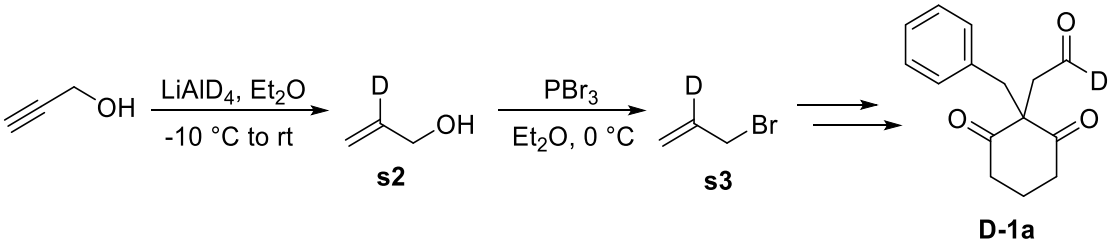
**2-(2,6-Dioxo-1-(*o*-tolyl)cyclohexyl)acetaldehyde (1v)**: The title compound was prepared using **Method J** and isolated by column chromatography (20% ethyl acetate in hexanes) as a white solid (0.22 g, 83% yield from 0.26 g of **s1v**). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 9.53 (t, $J$ = 1.4 Hz, 1H), 7.25 – 7.16 (m, 3H), 6.96 – 6.92 (m, 1H), 3.06 (d, $J$ = 1.4 Hz, 2H), 2.87 – 2.78 (m, 2H), 2.72 – 2.64 (m, 2H), 2.21 (s, 3H), 2.03 – 1.93 (m, 1H), 1.83 – 1.71 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.5, 198.8, 136.6, 135.2, 133.9, 128.6, 128.5, 127.4, 74.9, 45.6, 39.0, 21.1, 18.3. **IR** (ATR): 1717, 1696, 1309, 1021, 759, 727 cm$^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_3Na$ $[M+Na]^+$ 267.0997, found 267.0996.



1w

**2-(1-(Naphthalen-2-yl)-2,6-dioxocyclohexyl)acetaldehyde (1w)**: The title compound was prepared using **Method J** and isolated by column chromatography (1% acetone in dichloromethane) as a white solid (0.38 g, 70% yield from 0.54 g of **s1w**). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.90 – 7.72 (m, 3H), 7.57 – 7.45 (m, 3H), 7.19 (dd, *J* = 8.7, 2.1 Hz, 1H), 3.47 (s, 2H), 2.90 – 2.64 (m, 4H), 2.14 – 2.02 (m, 1H), 2.01 – 1.88 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.9, 198.7, 133.7, 132.7, 132.6, 129.8, 128.2, 127.7, 127.1, 127.0, 126.2, 123.6, 70.2, 51.5, 39.0, 17.4. **IR** (ATR): 2945, 1722, 1694, 1312, 1250, 1031, 956, 859, 815, 750 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{17}O_3$ $[M+H]^+$ 281.1178, found 281.1187.

**Preparation of D-1a**

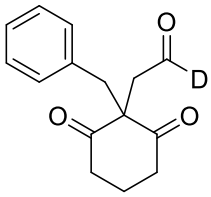


D-1a

A solution of $LiAlD_4$ (0.90 g, 21.4 mmol) in dry diethyl ether (70 mL) was cooled to -10 ˚C and a solution of propargyl alcohol (0.75 g, 13.4 mmol) in diethyl ether (33 mL) was added through an addition funnel over 30 min. The resulting solution was warmed to rt and stirred for 14 h. The mixture was cooled to 0 ˚C and was quenched slowly with $H_2O$ (4.0 mL). The solution was stirred for another 15 min and then aqueous NaOH (15 wt. %, 4.0 mL) and $H_2O$ (4.0 mL) were added. The white slurry was filtered through a short pad of Celite and was washed with diethyl ether (300 mL). The filtrate was concentrated *in vacuo* to give the crude allyl-2-*d* alcohol **s2** as a yellow oil.[9]

The crude allyl-2-*d* alcohol **s2** (0.75 g, 12.7 mmol) was added to a stirring solution of $PBr_3$ (0.60 mL, 1.73 g, 6.4 mmol) in diethyl ether (5 mL) dropwise at 0 ˚C. The resulting solution was stirred at 0 ˚C for 1 h and then carefully quenched by the addition of brine (3 mL). The layers were separated and the combined organic extracts were washed with a saturated aqueous $NaHCO_3$, brine and dried over $Na_2SO_4$. Excess solvent was removed via careful distillation (45-50 °C). The crude allyl-2-*d* bromide **s3** was obtained as colorless liquid (0.61 g, 37% yield over two steps).[9]

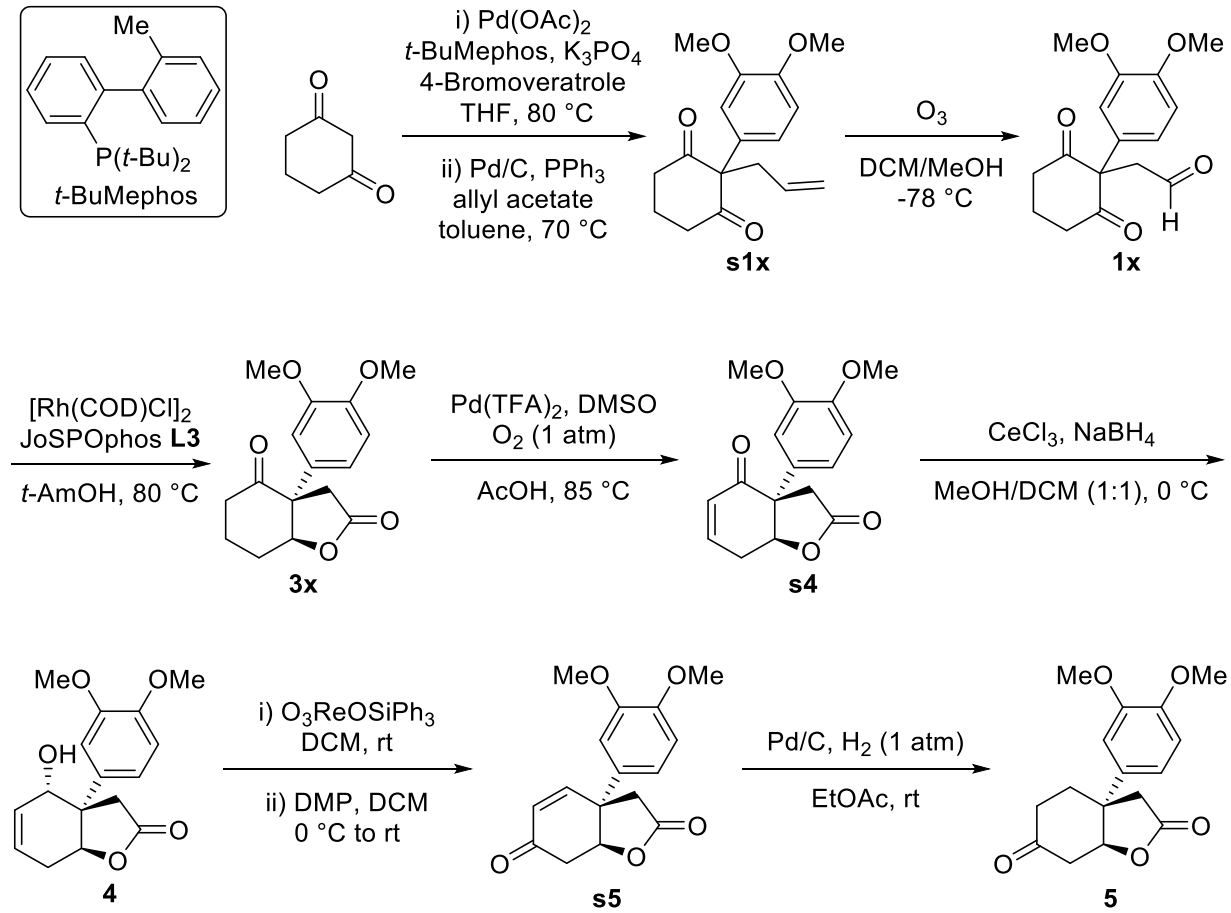
Deuterium labeled **D-1a** was synthesized from the crude allyl-2-*d* bromide **s3** and 2-benzyl-1,3-cyclohexanedione according to **Methods E** and **I** above.

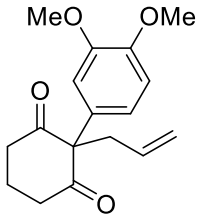


**D-1a**

**2-(1-Benzyl-2,6-dioxocyclohexyl)acetaldehyde-1-*d* (D-1a)**: The title compound was prepared according **Methods E** and **I**, and isolated by column chromatography (20% ethyl acetate in hexanes) as a white solid (0.37 g, 53% yield over two steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, **0.06H**), 7.33 – 7.26 (m, 3H), 6.98 (dd, *J* = 7.0, 2.3 Hz, 2H), 3.33 (s, 2H), 2.95 (s, 2H), 2.72 – 2.64 (m, 2H), 2.27 – 2.17 (m, 2H), 2.13 – 2.02 (m, 1H), 1.56 – 1.45 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.9, 199.3, 135.0, 129.9, 128.9, 127.9, 64.3, 51.6, 44.7, 39.7, 16.8. **HRMS** calculated for $C_{15}H_{15}DO_3NH_4$ $[M+NH_4]^+$ 263.1506, found 263.1502.

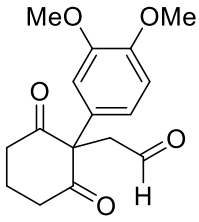
## 5. Formal Synthesis of (–)-Mesembrine





**s1x**

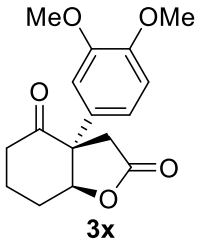
**2-allyl-2-(3,4-dimethoxyphenyl)cyclohexane-1,3-dione (s1x)**: To a dry three-necked round-bottom flask was added $Pd(OAc)_2$ (56 mg, 0.25 mmol, 5 mol%), 2-di-tert-butylphosphino-2'-methylbiphenyl (172 mg, 0.55 mmol, 11 mol%), 1,3-cyclohexanedione (672 mg, 6.0 mmol), and $K_3PO_4$ (2.46 g, 11.5 mmol) under a $N_2$ atmosphere. The flask was flushed several times with $N_2$. THF (15 mL) and 4-bromoveratrole (1.09 g, 5.0 mmol) were added. The reaction mixture was stirred at 80 ˚C until TLC indicated complete consumption of the starting material. MeOH (25 mL) was added and the reaction mixture was stirred for 15 min, filtered and concentrated *in vacuo*. Purification of the crude residue by column chromatography (30 % ethyl acetate in hexanes) afforded the arylated 1,3-diketone as a white solid (1.02 g, 82 % yield). Pd/C (10 wt. %, 0.43 g, 0.40 mmol, 10 mol%), $Ph_3P$ (0.42 g, 1.6 mmol, 40 mol%) followed by allyl acetate (0.40 g, 4.0 mmol) were added to a suspension of the arylated diketone (0.99 g, 4.0 mmol) in toluene (24 mL). The reaction mixture was stirred at 70 ˚C overnight, then filtered and concentrated *in vacuo*. Purification by column chromatography (40% ethyl acetate in hexanes) afforded the desired product **s1x** as a yellow oil (1.01 g, 88% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.78 (d, *J* = 8.3 Hz, 1H), 6.51 – 6.48 (m, 2H), 5.65– 5.56 (m, 1H), 4.94 – 4.87 (m, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 2.75 – 2.70 (m, 4H), 2.51 – 2.46 (m, 2H), 1.88 – 1.83 (m, 1H), 1.72-1.65 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 207.4, 149.6, 148.8, 134.5, 129.6, 119.2, 118.3, 111.6, 109.7, 74.9, 56.0, 55.9, 39.3, 39.2, 17.3. **IR** (ATR): 2957, 2836, 1725, 1696, 1515, 1463, 1256, 1240, 1150, 1023, 807, 767 cm$^{-1}$. **HRMS** calculated for $C_{17}H_{20}O_4NH_4$ $[M+NH_4]^+$: 306.1705, found 306.1696.



**1x**

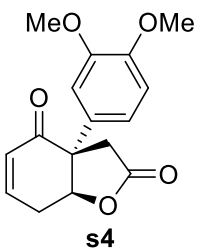
**2-(1-(3,4-Dimethoxyphenyl)-2,6-dioxocyclohexyl)acetaldehyde (1x)**: To a three-neck round-bottom flask equipped with a stir bar was added **s1x** (0.87 g, 3.0 mmol), indicator (Sudan III, 0.5 mg), and solvent (dichloromethane/methanol = 2:1, 30 mL) and a stirring bar. The reaction mixture was cooled to -78 ˚C, then $O_3$ was bubbled through the reaction solution until the red color of reaction solution turned to purple/blue. The $O_3$ generator was turned off and $N_2$ was bubbled through the reaction solution for 30 min to remove the unreacted $O_3$. Triphenylphosphine (1.18 g, 4.5 mmol) was added into the reaction solution. The resulted reaction solution was stirred in the dry ice bath for 1 h, then warmed up to room temperature and stirred for another 12 h. The solvent was removed by evaporation *in vacuo*. The residue was

purified by column chromatography (2% acetone in dichloromethane) to afford the product **1x** as a white solid (0.67 g, 77% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.58 – 6.53 (m, 2H), 3.86 (s, 3H), 3.82 (s, 3H), 3.38 (s, 2H), 2.78 – 2.64 (m, 4H), 2.11 – 2.01 (m, 1H), 2.00 – 1.89 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.0, 199.0, 150.0, 149.2, 127.2, 119.2, 112.0, 109.4, 69.5, 56.1, 56.0, 51.6, 38.8, 17.4. **IR** (ATR): 1703, 1690, 1512, 1240, 1155, 1020, 850, 815, 770 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{19}O_5$ $[M+H]^+$ 291.1232, found 291.1227.



**3x**

**(3a*R*,7a*S*)-3a-(3,4-Dimethoxyphenyl)hexahydrobenzofuran-2,4-dione (3x)**: In a $N_2$-filled glovebox, JoSPOphos **L3** (41.6 mg, 0.080 mmol) and *t*-AmOH (8.0 mL) were added to a 4 dram vial containing $[Rh(COD)Cl]_2$ (19.2 mg, 0.039 mmol). After stirring for 20 min, **1** (0.46 g, 1.6 mmol) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The compound **3x** was isolated by column chromatography (50% ethyl acetate in hexanes) as a white solid (0.42 g, 92% yield, *syn*:*anti* = >20:1, 97% *ee*). $[\alpha]^{24}_D$ = -131.1 (*c* 1.4, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.85 – 6.77 (m, 2H), 6.61 (d, *J* = 2.0 Hz, 1H), 5.34 (t, *J* = 2.5 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.76 (d, *J* = 17.1 Hz, 1H), 2.51 – 2.23 (m, 5H), 2.09 – 1.96 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.7, 174.0, 149.7, 149.1, 128.4, 118.2, 111.6, 109.8, 83.9, 59.8, 56.1, 56.0, 40.1, 38.4, 26.1, 21.3. **IR** (ATR): 2956, 1756, 1703, 1518, 1246, 1149, 1021, 961, 809, 765 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_5NH_4$ $[M+NH_4]^+$ 308.1498, found 308.1496. **Chiral SFC**: 97% *ee*, 250 mm CHIRALCEL IC, 20% *i*PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 8.0 min, $t_{R2}$ (major) = 10.5 min.

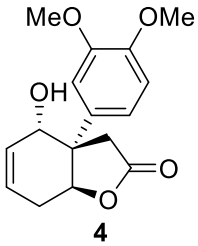


**s4**

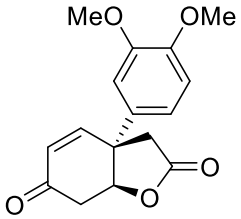
**(3a*R*,7a*S*)-3a-(3,4-Dimethoxyphenyl)-3,3a,7,7a-tetrahydrobenzofuran-2,4-dione (s4)**: A Schlenk tube was charged with lactone **3x** (145 mg, 0.50 mmol) and $Pd(TFA)_2$ (16.6 mg, 0.050 mmol, 10 mol%) and then purged with $O_2$. DMSO (7.1 μL, 20 mol%) was added followed by AcOH (2.5 mL). The resulting solution was stirred at 85 ˚C for 24 h under an atm of $O_2$ (balloon).

The reaction mixture was cooled to rt and neutralized carefully with saturated aqueous $NaHCO_3$. The reaction mixture was extracted with ethyl acetate (3 × 10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Enone **s4** was obtained by column chromatography (35% ethyl acetate in hexanes) as a white solid (103.7 mg, 72% yield).[10] $[\alpha]^{24}_D$ = -333.8 (*c* 0.32, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.89 – 6.83 (m, 1H), 6.82 – 6.72 (m, 3H), 6.20 (d, *J* = 10.1 Hz, 1H), 5.18 – 5.14 (m, 1H), 3.84 (s, 3H), 3.84 (s, 3H), 3.60 (d, *J* = 17.0 Hz, 1H), 3.09 – 2.90 (m, 2H), 2.83 (d, *J* = 17.0 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 195.9, 173.4, 149.6, 149.3, 144.6, 128.6, 128.3, 118.3, 111.5, 110.0, 81.5, 56.7, 56.2, 56.0, 40.3, 26.9. **IR** (ATR): 2956, 2936, 1775, 1701, 1516, 1455, 1241, 1203, 1145, 1023 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{16}O_5Na$ $[M+Na]^+$ 311.0895, found 311.0903.

**(3a*S*,4*S*,7a*S*)-3a-(3,4-Dimethoxyphenyl)-4-hydroxy-3a,4,7,7a-tetrahydrobenzofuran-2(3*H*)-one (4)**: To a solution of **s4** (93.4 mg, 0.32 mmol, 1.0 equiv) in MeOH (1.0 mL) and dichloromethane (1.0 mL) was added $CeCl_3$ (118.4 mg, 0.48 mmol). The resulting solution was stirred for 5 min at rt and cooled to 0 ˚C. $NaBH_4$ (13.3 mg, 0.35 mmol) was added, and the resulting solution was stirred at 0 ˚C for 30 min. The reaction was quenched with a few drops of 50% AcOH. The reaction mixture was diluted with saturated aqueous $NH_4Cl$, extracted with dichloromethane (3 × 10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The allylic alcohol **4** was obtained by column chromatography (50% ethyl acetate in hexanes) as a white solid (73.5 mg, 79% yield). $[\alpha]^{24}_D$ = +140 (*c* 0.38, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.86 – 6.83 (m, 1H), 6.70 – 6.66 (m, 2H), 5.86 – 5.75 (m, 2H), 4.84 (d, *J* = 6.4 Hz, 1H), 4.22 – 4.16 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.25 (d, *J* = 16.7 Hz, 1H), 2.91 (d, *J* = 16.7 Hz, 1H), 2.88 – 2.80 (m, 1H), 2.72 (d, *J* = 21.2 Hz, 1H), 1.30 (d, *J* = 10.9 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.0, 148.9, 148.8, 131.4, 129.4, 124.3, 120.6, 111.9, 111.2, 81.0, 69.2, 56.0, 55.9, 50.8, 41.4, 28.2. **IR** (ATR): 3474, 2857, 1754, 1522, 1261, 1237, 1155, 1019, 810, 733 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_5Na$ $[M+Na]^+$ 313.1052, found 313.1061.



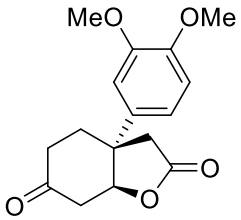
**4**



**s5**

**(3a*R*,7a*S*)-3a-(3,4-Dimethoxyphenyl)-3,3a,7,7a-tetrahydrobenzofuran-2,6-dione (s5)**: Under $N_2$ atmosphere, a 1-dram vial was charged **4** (29.0 mg, 0.10 mmol) and $O_3ReOSiPh_3$ (1.0 mg, 0.0020 mmol, 2.0 mol%). Dichloromethane (0.50 mL) was added, and the resulting solution was stirred overnight at rt. The reaction mixture was diluted with brine, extracted with dichloromethane (3 x 10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The unpurified isomeric allylic alcohol was dissolved in dry dichloromethane (10 mL), and the resulting solution was cooled to 0 ˚C. Dess-Martin periodinane (50.9 mg, 0.12 mmol) was added, and the resulting solution was warmed to room temperature and stirred for an additional 2 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$. The resulting mixture was stirred for 5 min, extracted with dichloromethane (3 x 10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The enone **s5** was purified by preparatory TLC (50% ethyl acetate in hexanes) and isolated as a white solid (18.9 mg, 65% yield).[11] $[\alpha]^{24}_D$ = +138 (*c* 0.31, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.93 – 6.83 (m, 3H), 6.69 (dd, *J* = 10.3, 2.2 Hz, 1H), 6.33 (d, *J* = 10.3 Hz, 1H), 4.96 (dd, *J* = 5.4, 2.9 Hz, 1H), 3.88 (s, 6H), 3.41 (d, *J* = 17.4 Hz, 1H), 2.91 (dd, *J* = 17.8, 2.8 Hz, 1H), 2.83 (d, *J* = 17.4 Hz, 1H), 2.69 (dd, *J* = 17.8, 3.3 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.2, 172.9, 149.8, 149.5, 148.0, 130.1, 128.7, 119.2, 111.8, 109.6, 83.5, 56.3, 56.2, 48.3, 42.7, 37.0. **IR** (ATR): 2924, 1771, 1683, 1520, 1243, 1208, 1160, 1144, 1016, 975 cm$^{-1}$. **HRMS** calculated for $C_{16}H_{16}O_5Na$ $[M+Na]^+$ 311.0895, found 311.0884.

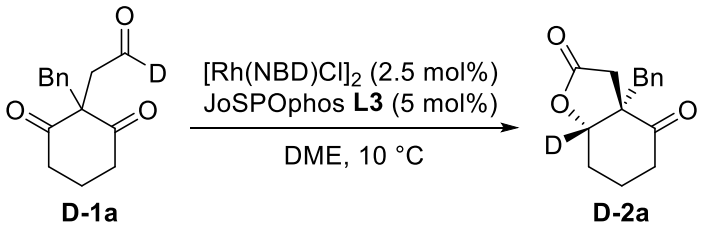
**(3a*S*,7a*S*)-3a-(3,4-Dimethoxyphenyl)hexahydrobenzofuran-2,6-dione (5)**: To a solution of **s5** (12.6 mg, 0.044 mmol) in ethyl acetate (0.25 mL) was added Pd/C (10 wt. %, 4.7 mg). The resulting solution was stirred for 3 h under an atmosphere of $H_2$ (balloon) at rt. The reaction mixture was filtered and concentrated *in vacuo*. The isomeric lactone **5** was purified by preparatory TLC (50% ethyl acetate in hexanes) and isolated as a white solid (6.4 mg, 51% yield). $[\alpha]^{24}_D$ = -46.5 (*c* 0.20, $CHCl_3$). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.88 (d, *J* = 8.4 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.73 (d, *J* = 2.2 Hz, 1H), 5.26 (dd, *J* = 4.9, 2.8 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.02 – 2.95 (m, 2H), 2.90 – 2.84 (m, 2H), 2.34 – 2.22 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 206.4, 174.1, 149.8, 148.8, 134.0, 117.9, 111.5, 109.3, 82.6, 56.3, 56.1, 45.2, 45.1, 42.0, 36.3, 33.6. **IR** (ATR): 2919, 1774, 1720, 1520, 1414, 1252, 1148, 1022, 952,



**5**

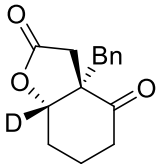
728 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}O_5Na$ $[M+Na]^+$ 313.1052, found 313.1058. (The racemic compound is known[12])

**6. Deuterium labeling experiments**



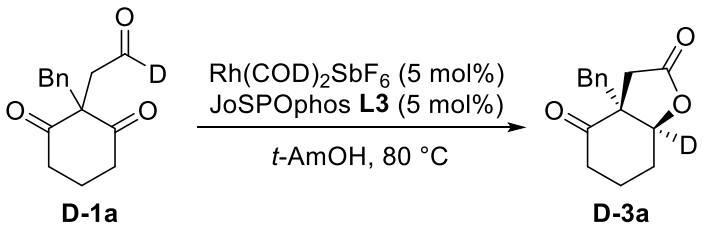
**D-1a** **D-2a**

In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and DME (0.40 mL) were added to a 1- dram vial containing $[Rh(NBD)Cl]_2$ (2.3 mg, 0.0050 mmol). After stirring for 20 min, **D-1a** (49.0 mg, 0.20 mmol) was added. Then the reaction vessel was moved into a 10 ˚C low temperature thermostat bath, and the reaction mixture was stirred for 24 h. Upon completion, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford the product **D-2a** (46.6 mg, 95% yield).



**D-2a**

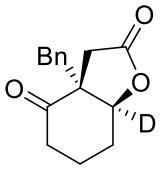
**(3a*R*,7a*S*)-3a-Benzylhexahydrobenzofuran-2,4-dione-7a-*d* (D-2a)**: **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.19 (m, 3H), 6.97 (dd, *J* = 7.6, 1.8 Hz, 2H), 4.15 – 4.08 (m, **0.06H**), 3.46 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.10 – 2.95 (m, 1H), 2.78 (d, *J* = 14.6 Hz, 1H), 2.66 (dd, *J* = 17.1, 2.3 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.39 (d, *J* = 17.1 Hz, 1H), 2.35 – 2.23 (m, 3H), 1.88 – 1.72 (m, 1H**). $^{13}$C NMR** (101 MHz, $CDCl_3$) δ 207.2, 174.6, 134.9, 129.5, 129.0, 127.6, 83.7 (q), 59.9, 36.8, 35.5, 35.4, 22.0, 21.6.



**D-1a** **D-3a**

In a $N_2$-filled glovebox, JoSPOphos (5.2 mg, 0.010 mmol) and *t*-AmOH (1.0 mL) were added to a 1 dram vial containing $Rh(COD)_2SbF_6$ (5.6 mg, 0.010 mmol). After stirring for 20 min, **D-1a**

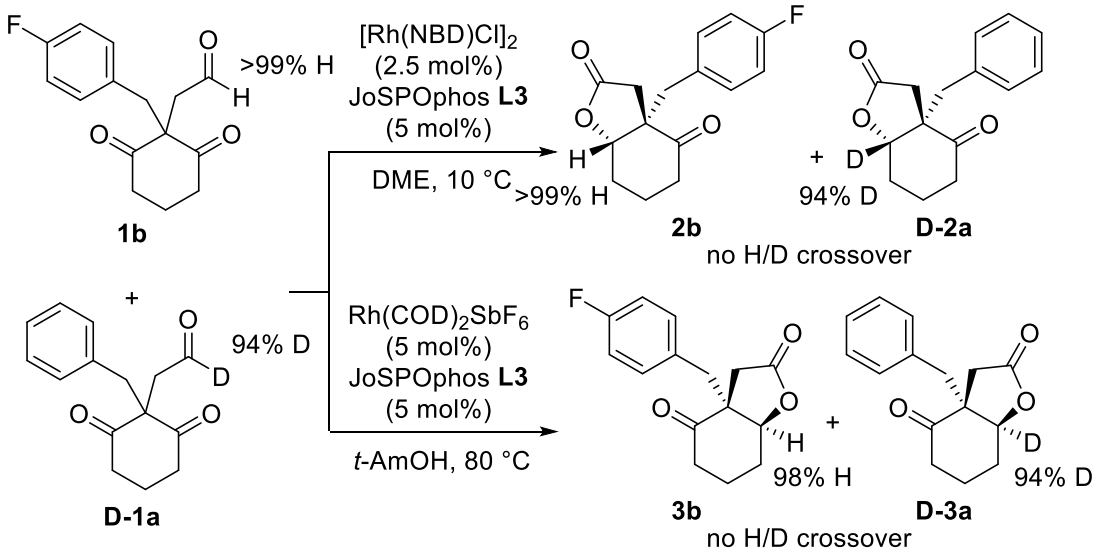
(49.0 mg, 0.20 mmol) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford the product **D-3a** (46.0 mg, 94% yield).



**D-3a**

**(3a*S*,7a*S*)-3a-Benzylhexahydrobenzofuran-2,4-dione-7a-*d* (D-3a)**: **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 3H), 7.05 (dd, *J* = 7.8, 1.5 Hz, 2H), 4.74 (t, *J* = 3.4 Hz, **0.06H**), 3.15 (d, *J* = 17.4 Hz, 1H), 3.09 (d, *J* = 13.8 Hz, 1H), 2.89 (d, *J* = 13.8 Hz, 1H), 2.51 – 2.35 (m, 3H), 2.23 – 2.13 (m, 1H), 2.05 – 1.80 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.1, 174.4, 135.0, 130.0, 129.0, 127.8, 83.5 (q), 57.2, 40.6, 39.1, 37.0, 25.5, 19.7.

**7. H/D Crossover Experiment**



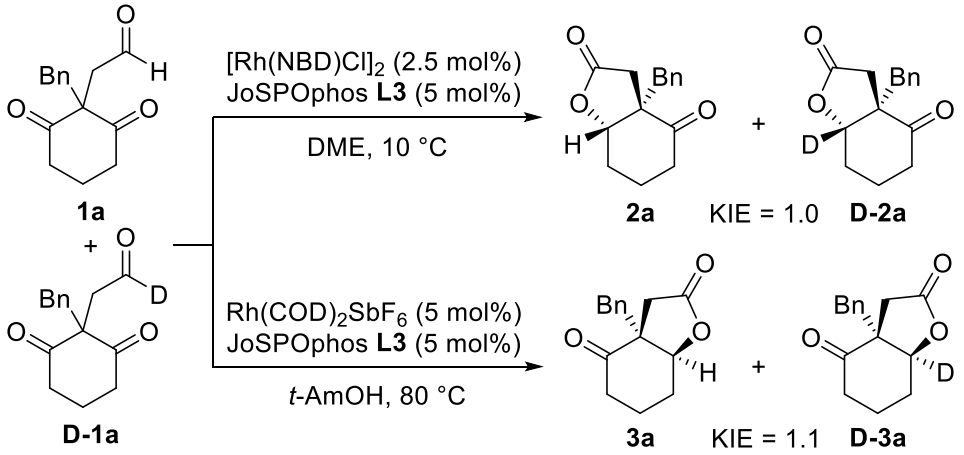

In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and DME (0.40 mL) were added to a 1- dram vial containing $[Rh(NBD)Cl]_2$ (2.3 mg, 0.0050 mmol). After stirring for 20 min, **1b** (26.2 mg, 0.10 mmol) and **D-1a** (24.5 mg, 0.10 mmol) were added. Then the reaction vessel was moved into a 10 ˚C low temperature thermostat bath, and the reaction mixture was stirred for 24 h. Upon completion, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The crude reaction

mixture was analyzed by GC-MS in comparison with the standard samples of **2b** and **D-2a**. Purification of the crude reaction mixture by preparatory TLC (35% ethyl acetate in hexanes) afforded a mixture of **2b** and **D-2a** (44.6 mg, about 88% yield).

In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and *t*-AmOH (1.0 mL) were added to a 1 dram vial containing $Rh(COD)_2SbF_6$ (5.6 mg, 0.010 mmol). After stirring for 20 min, **1b** (26.2 mg, 0.10 mmol) and **D-1a** (24.5 mg, 0.10 mmol) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The crude reaction mixture was analyzed by GC-MS in comparison with the standard samples of **3b** and **D-3a**. Purification of the crude reaction mixture by preparatory TLC (35% ethyl acetate in hexanes) afforded a mixture of **3b** and **D-3a** (46.0 mg, about 91% yield).

In both *anti* and *syn* cases, no H/D crossover was observed. These results suggest that Rh-hydride insertion is intramolecular, rather than intermolecular process.

**8. Kinetic Isotope Effect Experiments**




In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and DME (0.40 mL) were added to a 1 dram vial containing $[Rh(NBD)Cl]_2$ (2.3 mg, 0.0050 mmol). After stirring for 20 min, **1a** (22.9 mg, 0.094 mmol) and **D-1a** (26.1 mg, 0.106 mmol) were added. Then the reaction vessel was moved into a 10 ˚C low temperature thermostat bath, and the reaction mixture was stirred for 1 h. Upon completion, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue

was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford the mixture of **2a** and **D-2a** (9.2 mg, 19% yield). The ratio (1.0 : 1.0) of **2a** and **D-2a** was determined by $^1$H NMR.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 3H), 6.97 (dd, *J* = 7.5, 1.8 Hz, 2H), 4.11 (dd, *J* = 9.3, 7.2 Hz, **0.49H**), 3.46 (dd, *J* = 14.6, 2.1 Hz, 1H), 3.08 – 2.94 (m, 1H), 2.78 (d, *J* = 14.6 Hz, 1H), 2.66 (dd, *J* = 17.1, 2.3 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.39 (d, *J* = 17.1 Hz, 1H), 2.34 – 2.24 (m, 3H), 1.87 – 1.75 (m, 1H).

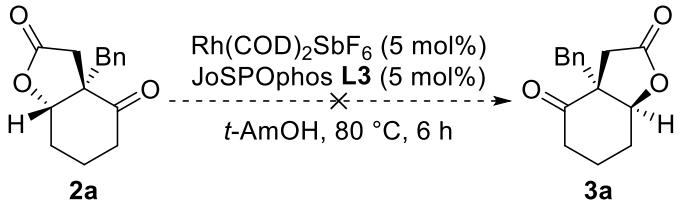
Recovered unreacted **1a** and **D-1a** (35.2 mg, 72% yield, **1a** : **D-1a** = 1.0 : 1.0): **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, **0.50H**), 7.32 – 7.24 (m, 3H), 7.01 – 6.95 (m, 2H), 3.33 (d, *J* = 2.1 Hz, 2H), 2.95 (s, 2H), 2.72 – 2.64 (m, 2H), 2.27 – 2.17 (m, 2H), 2.14 – 2.02 (m, 1H), 1.55 – 1.45 (m, 1H).

In a $N_2$-filled glovebox, JoSPOphos **L3** (5.2 mg, 0.010 mmol) and *t*-AmOH (1.0 mL) were added to a 1 dram vial containing $Rh(COD)_2SbF_6$ (5.6 mg, 0.010 mmol). After stirring for 20 min, **1a** (22.9 mg, 0.094 mmol) and **D-1a** (26.1 mg, 0.106 mmol) were added. Then the reaction mixture was heated at 80 ˚C for 10 min. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford the mixture of **3a** and **D-3a** (5.9 mg, 12% yield). The ratio (1.1 : 1.0) of **3a** and **D-3a** was determined by $^1$H NMR.

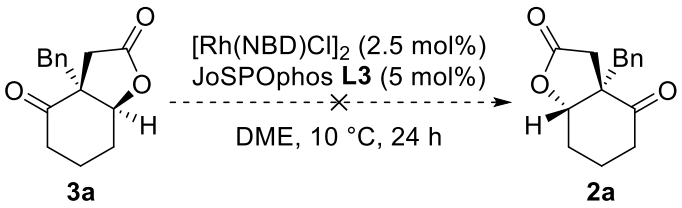
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 3H), 7.05 (dd, *J* = 7.8, 1.6 Hz, 2H), 4.74 (t, *J* = 3.4 Hz, **0.53H**), 3.15 (d, *J* = 17.4 Hz, 1H), 3.09 (d, *J* = 13.8 Hz, 1H), 2.89 (dd, *J* = 13.8, 1.4 Hz, 1H), 2.51 – 2.35 (m, 3H), 2.24 – 2.16 (m, 1H), 2.04 – 1.81 (m, 3H).

Recovered unreacted **1a** and **D-1a** (39.6 mg, 81% yield, **1a** : **D-1a** = 1.0 : 1.0): **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, **0.49H**), 7.32 – 7.23 (m, 3H), 7.01 – 6.94 (m, 2H), 3.33 (d, *J* = 2.1 Hz, 2H), 2.95 (s, 2H), 2.68 (ddd, *J* = 16.7, 6.0, 4.4 Hz, 2H), 2.27 – 2.17 (m, 2H), 2.13 – 2.01 (m, 1H), 1.55 – 1.46 (m, 1H).

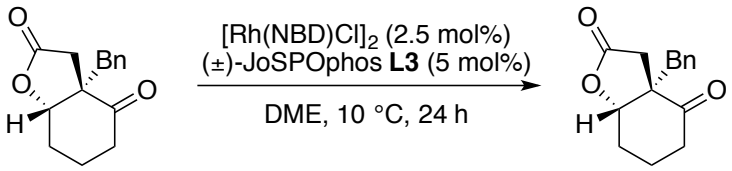
**9. Study on the Interconversion of *anti* and *syn* Diastereomers**




In a $N_2$-filled glovebox, JoSPOphos **L3** (2.6 mg, 0.0050 mmol) and *t*-AmOH (0.50 mL) were added to a 1 dram vial containing $Rh(COD)_2SbF_6$ (2.8 mg, 0.0050 mmol). After stirring for 20 min, **2a** (24.4 mg, 0.10 mmol) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by prep TLC (35% ethyl acetate in hexanes) to afford recovered **2a** (23.6 mg, 97% yield). No **3a** was observed.

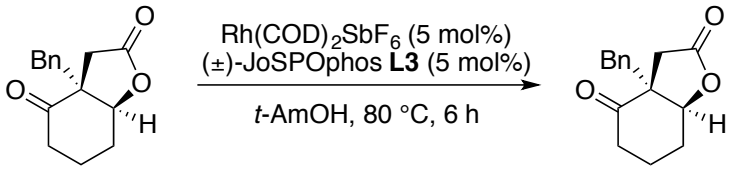



In a $N_2$-filled glovebox, JoSPOphos **L3** (2.6 mg, 0.0050 mmol) and DME (0.20 mL) were added to a 1 dram vial containing $[Rh(NBD)Cl]_2$ (1.1 mg, 0.0024 mmol). After stirring for 20 min, **3a** (24.4 mg, 0.10 mmol) was added. Then the reaction vessel was moved into a 10 ˚C low temperature thermostat bath, and the reaction mixture was stirred for 24 h. The reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford recovered **3a** (23.9 mg, 98% yield). No **2a** was observed.




**2a**, 99% *ee* **2a**, 99% *ee*

In a $N_2$-filled glovebox, (±)-JoSPOphos **L3** (2.6 mg, 0.0050 mmol) and DME (0.20 mL) were added to a 1 dram vial containing $[Rh(NBD)Cl]_2$ (1.1 mg, 0.0024 mmol). After stirring for 20 min, **2a** (24.4 mg, 0.10 mmol, 99% *ee*) was added. Then the reaction vessel was moved into a 10 ˚C low temperature thermostat bath, and the reaction mixture was stirred for 24 h. The reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford recovered **2a** (23.8 mg, 98% yield, 99% *ee*).

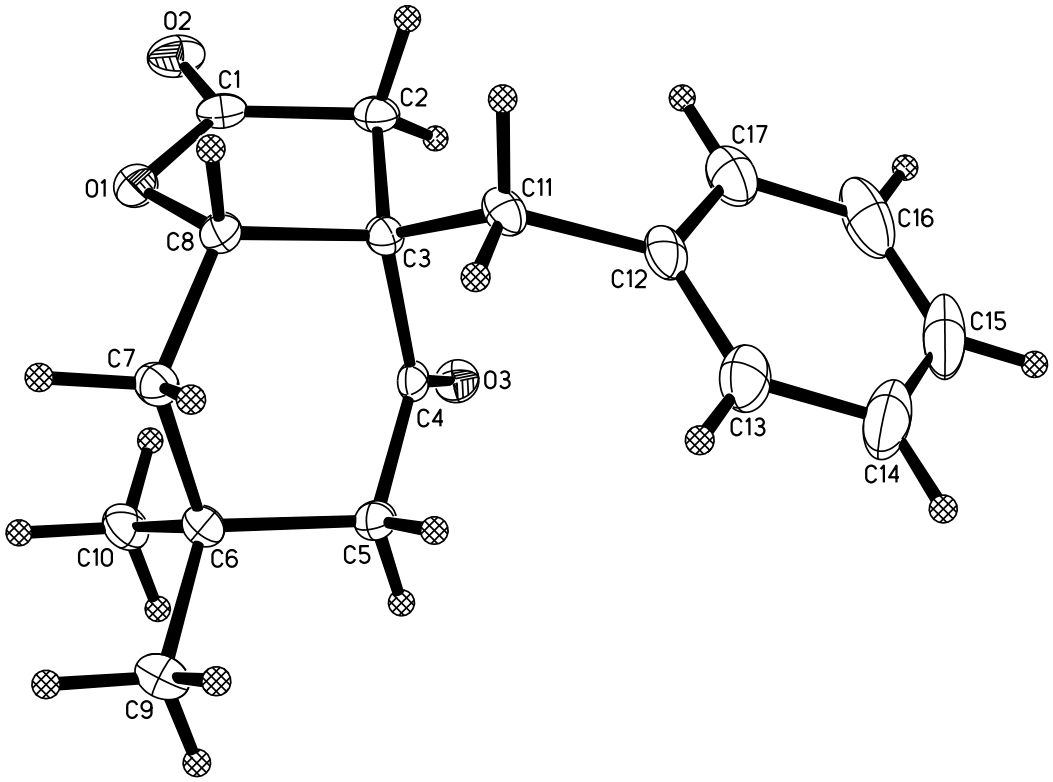



**3a**, 98% *ee* **3a**, 98% *ee*

In a $N_2$-filled glovebox, (±)-JoSPOphos **L3** (2.6 mg, 0.0050 mmol) and *t*-AmOH (0.50 mL) were added to a 1 dram vial containing $Rh(COD)_2SbF_6$ (2.8 mg, 0.0050 mmol). After stirring for 20 min, **3a** (24.4 mg, 0.10 mmol, 98% *ee*) was added. Then the reaction mixture was heated at 80 ˚C for 6 h. After cooling to rt, the reaction mixture was filtered through a short silica gel pad and washed with 50% ethyl acetate in hexanes. The filtrate was concentrated *in vacuo*. The residue was purified by preparatory TLC (35% ethyl acetate in hexanes) to afford recovered **3a** (23.4 mg, 96% yield, 98% *ee*).

**10. X-Ray Crystallographic Data**

**X-ray Crystallography Data for 2g (CCDC 1483272)**




X-ray Data Collection, Structure Solution and Refinement for vmd24 (**2g**).

A colorless crystal was mounted in a cryoloop and transferred to a Bruker MICROSTAR rotating-anode diffractometer. The APEX2[1] program package was used to determine the unit-cell parameters and for data collection. The raw frame data was processed using SAINT[2] and SADABS[3] to yield the reflection data file. Subsequent calculations were carried out using the SHELXTL[4] program. The diffraction symmetry was *mmm* and the systematic absences were consistent with the orthorhombic space group $P2_12_12_1$ which was later determined to be correct.

The structure was solved by direct methods and refined on $F^2$ by full-matrix least-squares techniques. The analytical scattering factors[5] for neutral atoms were used throughout the analysis. Hydrogen atoms were included using a riding model.

At convergence, wR2 = 0.0844 and Goof = 1.100 for 183 variables refined against 2665 data (0.83Å), R1 = 0.0327 for those 2599 data with $I > 2.0\sigma(I)$. The absolute structure was assigned by refinement of the Flack parameter[6] which supported the synthetic method employed.

References.


1. APEX2 Version 2014.11-0, Bruker AXS, Inc.; Madison, WI 2014.
2. SAINT Version 8.34a, Bruker AXS, Inc.; Madison, WI 2013.
3. Sheldrick, G. M. SADABS, Version 2014/5, Bruker AXS, Inc.; Madison, WI 2014.
4. Sheldrick, G. M. SHELXTL, Version 2014/7, Bruker AXS, Inc.; Madison, WI 2014.
5. International Tables for Crystallography 1992, Vol. C., Dordrecht: Kluwer Academic Publishers.
6. Parsons, S., Flack, H. D., Wagner, T. Acta Cryst. B69, 249-259, 2013.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Definitions:

$wR2 = [\Sigma[w(F_o^2-F_c^2)^2] / \Sigma[w(F_o^2)^2] ]^{1/2}$

$R1 = \Sigma||F_o|-|F_c|| / \Sigma|F_o|$

$Goof = S = [\Sigma[w(F_o^2-F_c^2)^2] / (n-p)]^{1/2}$ where n is the number of reflections and p is the total number of parameters refined.

The thermal ellipsoid plot is shown at the 50% probability level.

**Table A2.1.1.** Crystal data and structure refinement for vmd24.

| | | |
|---|---|---|
| Identification code | vmd24 (Xuesong Wu) | |
| Empirical formula | $C_{17}\ H_{20}\ O_3$ | |
| Formula weight | 272.33 | |
| Temperature | 100(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 5.81920(10) Å | α= 90°. |
| | b = 8.5684(2) Å | β= 90°. |
| | c = 29.2539(5) Å | γ= 90°. |
| Volume | 1458.64(5) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.240 $Mg/m^3$ | |

| | |
|---|---|
| Absorption coefficient | 0.673 $mm^{-1}$ |
| F(000) | 584 |
| Crystal color | colorless |
| Crystal size | 0.130 x 0.120 x 0.100 $mm^3$ |
| Theta range for data collection | 3.021 to 68.189° |
| Index ranges | $-6 \le h \le 6$, $-10 \le k \le 8$, $-35 \le l \le 34$ |
| Reflections collected | 13289 |
| Independent reflections | 2665 [R(int) = 0.0427] |
| Completeness to theta = 67.679° | 99.9 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.8643 and 0.6565 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 2665 / 0 / 183 |
| Goodness-of-fit on $F^2$ | 1.100 |
| Final R indices [I>2sigma(I) = 2599 data] | R1 = 0.0327, wR2 = 0.0837 |
| R indices (all data, ? Å) | R1 = 0.0337, wR2 = 0.0844 |
| Absolute structure parameter | -0.01(9) |
| Largest diff. peak and hole | 0.189 and -0.197 e.$Å^{-3}$ |

**Table A2.1.2** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for vmd24 (**2g**). U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 7107(2) | 5073(2) | 4805(1) | 18(1) |
| O(2) | 3830(2) | 6247(2) | 5002(1) | 24(1) |
| O(3) | 4589(2) | 4797(2) | 3635(1) | 18(1) |
| C(1) | 5399(3) | 6104(2) | 4736(1) | 17(1) |
| C(2) | 5770(3) | 6983(2) | 4294(1) | 16(1) |
| C(3) | 7641(3) | 6047(2) | 4052(1) | 14(1) |
| C(4) | 6590(3) | 4763(2) | 3750(1) | 13(1) |
| C(5) | 8184(3) | 3463(2) | 3623(1) | 16(1) |
| C(6) | 9022(3) | 2599(2) | 4058(1) | 15(1) |
| C(7) | 10205(3) | 3796(2) | 4372(1) | 16(1) |
| C(8) | 8911(3) | 5305(2) | 4462(1) | 14(1) |

| | | | | |
|---|---|---|---|---|
| C(9) | 10802(4) | 1371(2) | 3915(1) | 20(1) |
| C(10) | 7005(4) | 1791(2) | 4294(1) | 20(1) |
| C(11) | 9358(3) | 7026(2) | 3765(1) | 16(1) |
| C(12) | 8510(3) | 7470(2) | 3293(1) | 19(1) |
| C(13) | 9629(4) | 6864(3) | 2910(1) | 29(1) |
| C(14) | 8853(5) | 7206(3) | 2472(1) | 40(1) |
| C(15) | 6985(5) | 8162(3) | 2410(1) | 42(1) |
| C(16) | 5860(5) | 8790(3) | 2788(1) | 40(1) |
| C(17) | 6623(4) | 8436(3) | 3229(1) | 28(1) |

**Table A2.1.3.** Bond lengths [Å] and angles [°] for vmd24 (**2g**).

| | |
|---|---|
| O(1)-C(1) | 1.345(2) |
| O(1)-C(8) | 1.466(2) |
| O(2)-C(1) | 1.205(2) |
| O(3)-C(4) | 1.212(2) |
| C(1)-C(2) | 1.511(3) |
| C(2)-C(3) | 1.527(2) |
| C(3)-C(4) | 1.537(2) |
| C(3)-C(8) | 1.547(2) |
| C(3)-C(11) | 1.550(2) |
| C(4)-C(5) | 1.497(2) |
| C(5)-C(6) | 1.552(2) |
| C(6)-C(10) | 1.527(3) |
| C(6)-C(9) | 1.534(3) |
| C(6)-C(7) | 1.539(2) |
| C(7)-C(8) | 1.519(2) |
| C(11)-C(12) | 1.516(2) |
| C(12)-C(17) | 1.387(3) |
| C(12)-C(13) | 1.396(3) |
| C(13)-C(14) | 1.388(3) |

| | |
|---|---|
| C(14)-C(15) | 1.373(4) |
| C(15)-C(16) | 1.394(4) |
| C(16)-C(17) | 1.396(3) |

| | |
|---|---|
| C(1)-O(1)-C(8) | 109.70(14) |
| O(2)-C(1)-O(1) | 121.97(18) |
| O(2)-C(1)-C(2) | 127.52(19) |
| O(1)-C(1)-C(2) | 110.51(15) |
| C(1)-C(2)-C(3) | 103.76(14) |
| C(2)-C(3)-C(4) | 111.04(15) |
| C(2)-C(3)-C(8) | 101.26(14) |
| C(4)-C(3)-C(8) | 109.98(14) |
| C(2)-C(3)-C(11) | 115.23(15) |
| C(4)-C(3)-C(11) | 109.50(14) |
| C(8)-C(3)-C(11) | 109.51(14) |
| O(3)-C(4)-C(5) | 122.94(16) |
| O(3)-C(4)-C(3) | 121.63(16) |
| C(5)-C(4)-C(3) | 115.41(15) |
| C(4)-C(5)-C(6) | 110.22(15) |
| C(10)-C(6)-C(9) | 109.36(15) |
| C(10)-C(6)-C(7) | 112.09(15) |
| C(9)-C(6)-C(7) | 108.55(15) |
| C(10)-C(6)-C(5) | 110.18(16) |
| C(9)-C(6)-C(5) | 108.38(15) |
| C(7)-C(6)-C(5) | 108.19(15) |
| C(8)-C(7)-C(6) | 116.72(15) |
| O(1)-C(8)-C(7) | 111.02(14) |
| O(1)-C(8)-C(3) | 104.19(14) |
| C(7)-C(8)-C(3) | 116.82(15) |
| C(12)-C(11)-C(3) | 114.74(15) |
| C(17)-C(12)-C(13) | 118.90(19) |

| | |
|---|---|
| C(17)-C(12)-C(11) | 121.97(18) |
| C(13)-C(12)-C(11) | 119.12(19) |
| C(14)-C(13)-C(12) | 120.6(2) |
| C(15)-C(14)-C(13) | 120.4(2) |
| C(14)-C(15)-C(16) | 119.7(2) |
| C(15)-C(16)-C(17) | 120.0(2) |
| C(12)-C(17)-C(16) | 120.3(2) |

**Table A2.1.4.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for vmd24 (**2g**). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 22(1) | 18(1) | 15(1) | -1(1) | 3(1) | 1(1) |
| O(2) | 23(1) | 23(1) | 25(1) | -7(1) | 7(1) | -2(1) |
| O(3) | 17(1) | 19(1) | 18(1) | -1(1) | -2(1) | -2(1) |
| C(1) | 17(1) | 15(1) | 20(1) | -6(1) | 0(1) | -2(1) |
| C(2) | 16(1) | 14(1) | 19(1) | -4(1) | -3(1) | 0(1) |
| C(3) | 15(1) | 12(1) | 14(1) | 1(1) | -2(1) | 1(1) |
| C(4) | 16(1) | 13(1) | 10(1) | 3(1) | 1(1) | -3(1) |
| C(5) | 19(1) | 14(1) | 14(1) | -1(1) | 0(1) | -2(1) |
| C(6) | 17(1) | 12(1) | 17(1) | 1(1) | 0(1) | -1(1) |
| C(7) | 16(1) | 14(1) | 17(1) | 0(1) | -2(1) | 2(1) |
| C(8) | 15(1) | 14(1) | 14(1) | -1(1) | -1(1) | -1(1) |
| C(9) | 21(1) | 14(1) | 25(1) | -1(1) | 0(1) | 2(1) |
| C(10) | 23(1) | 14(1) | 23(1) | 2(1) | 1(1) | -2(1) |
| C(11) | 15(1) | 13(1) | 20(1) | 3(1) | -3(1) | -3(1) |
| C(12) | 21(1) | 16(1) | 21(1) | 5(1) | -3(1) | -8(1) |
| C(13) | 31(1) | 30(1) | 25(1) | 7(1) | 5(1) | -5(1) |
| C(14) | 52(2) | 47(2) | 21(1) | 9(1) | 3(1) | -13(1) |
| C(15) | 52(2) | 47(2) | 26(1) | 18(1) | -11(1) | -22(1) |
| C(16) | 35(1) | 35(1) | 48(1) | 21(1) | -18(1) | -4(1) |
| C(17) | 29(1) | 23(1) | 31(1) | 6(1) | -8(1) | -2(1) |

**Table A2.1.5.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for vmd24 (**2g**).

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2A) | 6284 | 8065 | 4354 | 19 |
| H(2B) | 4343 | 7013 | 4110 | 19 |
| H(5A) | 9521 | 3890 | 3455 | 19 |
| H(5B) | 7379 | 2720 | 3419 | 19 |
| H(7A) | 10509 | 3287 | 4669 | 19 |
| H(7B) | 11711 | 4065 | 4236 | 19 |
| H(8) | 10027 | 6088 | 4584 | 17 |
| H(9A) | 12104 | 1889 | 3766 | 30 |
| H(9B) | 10095 | 633 | 3701 | 30 |
| H(9C) | 11343 | 809 | 4186 | 30 |
| H(10A) | 7560 | 1230 | 4564 | 30 |
| H(10B) | 6290 | 1052 | 4082 | 30 |
| H(10C) | 5870 | 2574 | 4387 | 30 |
| H(11A) | 9721 | 7994 | 3936 | 19 |
| H(11B) | 10803 | 6427 | 3733 | 19 |
| H(13) | 10934 | 6211 | 2949 | 34 |
| H(14) | 9619 | 6777 | 2215 | 48 |
| H(15) | 6460 | 8394 | 2110 | 50 |
| H(16) | 4575 | 9459 | 2747 | 47 |
| H(17) | 5847 | 8858 | 3486 | 33 |

**Table A2.1.6.** Torsion angles [°] for vmd24 (**2g**).

| | |
|---|---|
| C(8)-O(1)-C(1)-O(2) | -172.49(17) |
| C(8)-O(1)-C(1)-C(2) | 7.89(19) |
| O(2)-C(1)-C(2)-C(3) | -166.21(18) |
| O(1)-C(1)-C(2)-C(3) | 13.4(2) |
| C(1)-C(2)-C(3)-C(4) | 89.51(16) |

| | |
|---|---|
| C(1)-C(2)-C(3)-C(8) | -27.22(18) |
| C(1)-C(2)-C(3)-C(11) | -145.28(15) |
| C(2)-C(3)-C(4)-O(3) | 17.9(2) |
| C(8)-C(3)-C(4)-O(3) | 129.16(18) |
| C(11)-C(3)-C(4)-O(3) | -110.46(18) |
| C(2)-C(3)-C(4)-C(5) | -160.42(15) |
| C(8)-C(3)-C(4)-C(5) | -49.2(2) |
| C(11)-C(3)-C(4)-C(5) | 71.21(18) |
| O(3)-C(4)-C(5)-C(6) | -116.69(19) |
| C(3)-C(4)-C(5)-C(6) | 61.6(2) |
| C(4)-C(5)-C(6)-C(10) | 65.10(19) |
| C(4)-C(5)-C(6)-C(9) | -175.28(15) |
| C(4)-C(5)-C(6)-C(7) | -57.76(19) |
| C(10)-C(6)-C(7)-C(8) | -72.9(2) |
| C(9)-C(6)-C(7)-C(8) | 166.17(15) |
| C(5)-C(6)-C(7)-C(8) | 48.8(2) |
| C(1)-O(1)-C(8)-C(7) | -152.28(15) |
| C(1)-O(1)-C(8)-C(3) | -25.71(17) |
| C(6)-C(7)-C(8)-O(1) | 78.72(19) |
| C(6)-C(7)-C(8)-C(3) | -40.5(2) |
| C(2)-C(3)-C(8)-O(1) | 32.09(16) |
| C(4)-C(3)-C(8)-O(1) | -85.42(16) |
| C(11)-C(3)-C(8)-O(1) | 154.21(14) |
| C(2)-C(3)-C(8)-C(7) | 154.94(16) |
| C(4)-C(3)-C(8)-C(7) | 37.4(2) |
| C(11)-C(3)-C(8)-C(7) | -82.94(19) |
| C(2)-C(3)-C(11)-C(12) | -81.7(2) |
| C(4)-C(3)-C(11)-C(12) | 44.3(2) |
| C(8)-C(3)-C(11)-C(12) | 164.94(16) |
| C(3)-C(11)-C(12)-C(17) | 64.1(2) |
| C(3)-C(11)-C(12)-C(13) | -114.5(2) |
| C(17)-C(12)-C(13)-C(14) | -0.8(3) |
| C(11)-C(12)-C(13)-C(14) | 177.9(2) |
| C(12)-C(13)-C(14)-C(15) | 0.7(4) |
| C(13)-C(14)-C(15)-C(16) | -0.1(4) |
| C(14)-C(15)-C(16)-C(17) | -0.5(4) |

| | |
|---|---|
| C(13)-C(12)-C(17)-C(16) | 0.1(3) |
| C(11)-C(12)-C(17)-C(16) | -178.5(2) |
| C(15)-C(16)-C(17)-C(12) | 0.5(4) |

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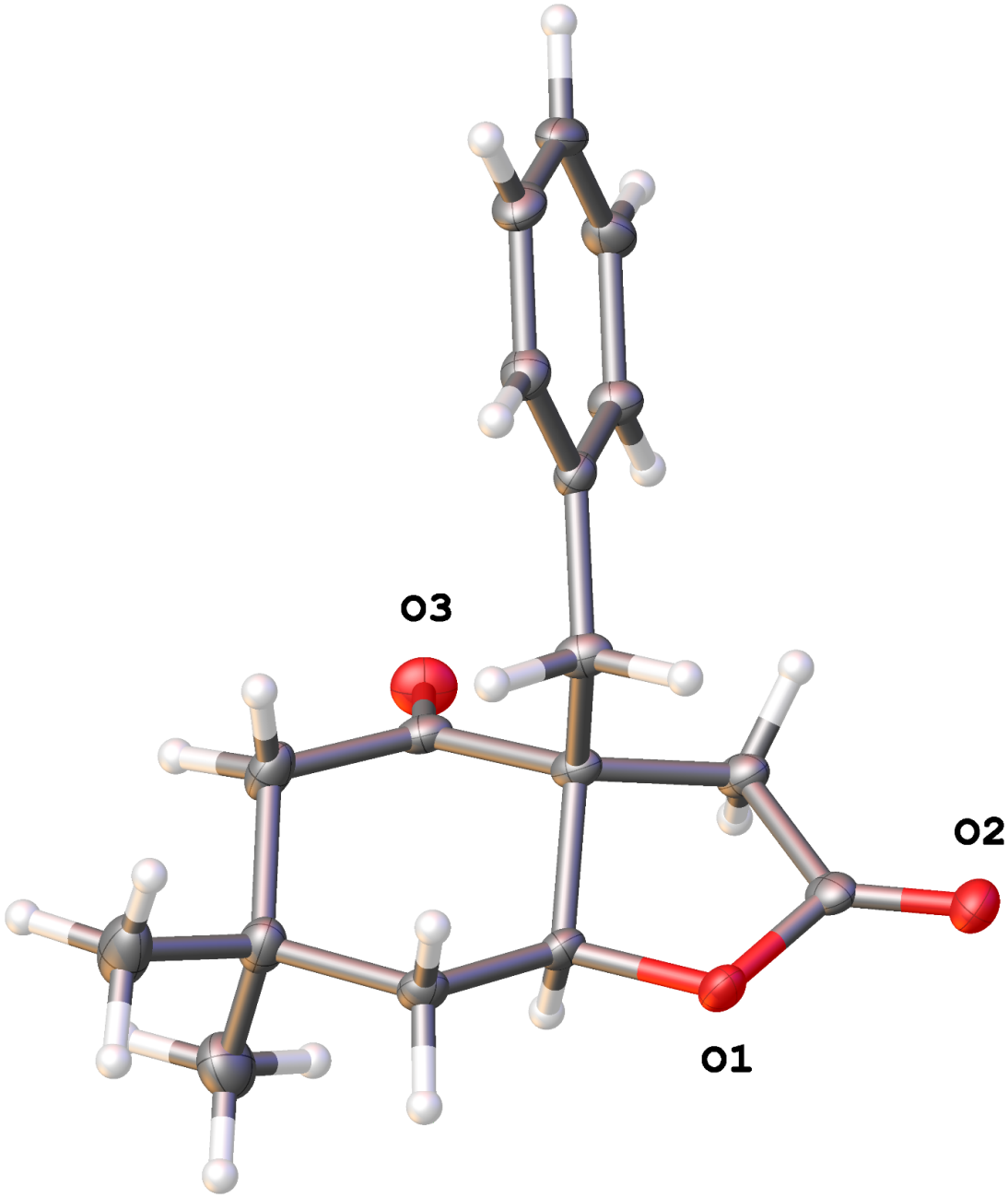
**X-ray Crystallography Data for 3j (CCDC 1483273)**



The single crystal X-ray diffraction studies were carried out on a Bruker SMART Platinum 135 CCD diffractometer equipped with Cu $K_a$ radiation ($\lambda$ = 1.5478). Crystals of the subject compound were used as received.

A 0.20 x 0.180 x 0.125 mm colorless block was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 125(2) K using $\phi$ and $\varpi$ scans. Crystal-to-detector distance was 45 mm using variable exposure time (1.5, and 3s) depending on $\theta$ with a scan width of 1.5°. Data collection was 99.9% complete to 67.50° in $\theta$. A total of 11781 reflections were collected covering the indices, -13<=h<=12, -7<=k<=7, -14<=l<=14. 2719 reflections were found to be symmetry independent, with a $R_{int}$ of 0.0437. Indexing and unit cell refinement indicated a **Primitive**, **Monoclinic** lattice. The space group was found to be $\boldsymbol{P2_1}$. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized in Table A2.1.7.

Notes: Absolute structure parameter -0.02(7)

**Table A2.1.7.** Crystal data and structure refinement for UCI_XW176-1 (**3j**).

| | | |
|---|---|---|
| Report date | 2016-05-20 | |
| Identification code | uci_xw176-1 | |
| Empirical formula | C17 H20 O3 | |
| Molecular formula | C17 H20 O3 | |
| Formula weight | 272.33 | |
| Temperature | 125.0 K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Monoclinic | |
| Space group | P 1 21 1 | |
| Unit cell dimensions | a = 10.7939(2) Å | $\alpha$= 90°. |
| | b = 6.10190(10) Å | $\beta$= 109.9660(10)°. |

| | |
|---|---|
| | c = 11.6030(3) Å γ= 90°. |
| Volume | 718.28(3) $Å^3$ |
| Z | 2 |
| Density (calculated) | 1.259 $Mg/m^3$ |
| Absorption coefficient | 0.683 $mm^{-1}$ |
| F(000) | 292 |
| Crystal size | 0.2 x 0.18 x 0.125 $mm^3$ |
| Crystal color, habit | colorless block |
| Theta range for data collection | 4.053 to 70.309°. |
| Index ranges | -13<=h<=12, -7<=k<=7, -14<=l<=14 |
| Reflections collected | 11781 |
| Independent reflections | 2719 [R(int) = 0.0437] |
| Completeness to theta = 67.500° | 99.9 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.5220 and 0.4092 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 2719 / 1 / 184 |
| Goodness-of-fit on $F^2$ | 1.047 |
| Final R indices [I>2sigma(I)] | R1 = 0.0261, wR2 = 0.0639 |
| R indices (all data) | R1 = 0.0270, wR2 = 0.0646 |
| Absolute structure parameter | -0.02(7) |
| Extinction coefficient | 0.0054(10) |
| Largest diff. peak and hole | 0.159 and -0.140 $e.Å^{-3}$ |

**Table A2.1.8.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for UCI_XW176-1 (**3j**). U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 723(1) | 3094(2) | 5602(1) | 20(1) |
| O(2) | 668(1) | 3899(2) | 3708(1) | 23(1) |
| O(3) | 3597(1) | 8085(2) | 7892(1) | 25(1) |
| C(1) | 1119(2) | 4262(3) | 4790(2) | 18(1) |
| C(2) | 2188(2) | 5883(3) | 5475(2) | 19(1) |

| | | | | |
|---|---|---|---|---|
| C(3) | 2725(2) | 4797(3) | 6737(2) | 16(1) |
| C(4) | 3321(2) | 6164(3) | 7893(2) | 18(1) |
| C(5) | 3492(2) | 4873(3) | 9053(2) | 23(1) |
| C(6) | 2220(2) | 3704(3) | 9084(2) | 23(1) |
| C(7) | 1516(2) | 2474(3) | 7866(2) | 18(1) |
| C(8) | 1400(1) | 4002(3) | 6816(1) | 16(1) |
| C(9) | 2613(2) | 2031(4) | 10128(2) | 35(1) |
| C(10) | 1303(2) | 5428(4) | 9326(2) | 33(1) |
| C(11) | 3663(2) | 2893(3) | 6714(2) | 18(1) |
| C(12) | 5055(2) | 3541(3) | 6805(1) | 16(1) |
| C(13) | 5412(2) | 5599(3) | 6506(2) | 19(1) |
| C(14) | 6705(2) | 6034(3) | 6584(2) | 22(1) |
| C(15) | 7661(2) | 4420(3) | 6965(2) | 23(1) |
| C(16) | 7323(2) | 2381(3) | 7281(2) | 23(1) |
| C(17) | 6034(2) | 1944(3) | 7204(2) | 20(1) |

**Table A2.1.9.** Bond lengths [Å] and angles [°] for UCI_XW176-1 (**3j**).

| | | | |
|---|---|---|---|
| O(1)-C(1) | 1.362(2) | C(6)-C(9) | 1.530(3) |
| O(1)-C(8) | 1.4565(19) | C(6)-C(10) | 1.534(3) |
| O(2)-C(1) | 1.202(2) | C(7)-H(7A) | 0.9900 |
| O(3)-C(4) | 1.209(2) | C(7)-H(7B) | 0.9900 |
| C(1)-C(2) | 1.521(2) | C(7)-C(8) | 1.504(2) |
| C(2)-H(2A) | 0.9900 | C(8)-H(8) | 1.0000 |
| C(2)-H(2B) | 0.9900 | C(9)-H(9A) | 0.9800 |
| C(2)-C(3) | 1.530(2) | C(9)-H(9B) | 0.9800 |
| C(3)-C(4) | 1.523(2) | C(9)-H(9C) | 0.9800 |
| C(3)-C(8) | 1.543(2) | C(10)-H(10A) | 0.9800 |
| C(3)-C(11) | 1.548(2) | C(10)-H(10B) | 0.9800 |
| C(4)-C(5) | 1.516(2) | C(10)-H(10C) | 0.9800 |
| C(5)-H(5A) | 0.9900 | C(11)-H(11A) | 0.9900 |
| C(5)-H(5B) | 0.9900 | C(11)-H(11B) | 0.9900 |
| C(5)-C(6) | 1.559(2) | C(11)-C(12) | 1.522(2) |
| C(6)-C(7) | 1.550(2) | C(12)-C(13) | 1.392(2) |

| | | | |
|---|---|---|---|
| C(12)-C(17) | 1.395(2) | C(7)-C(6)-C(5) | 111.22(14) |
| C(13)-H(13) | 0.9500 | C(9)-C(6)-C(5) | 108.38(14) |
| C(13)-C(14) | 1.393(2) | C(9)-C(6)-C(7) | 108.42(15) |
| C(14)-H(14) | 0.9500 | C(9)-C(6)-C(10) | 109.50(16) |
| C(14)-C(15) | 1.385(3) | C(10)-C(6)-C(5) | 108.60(16) |
| C(15)-H(15) | 0.9500 | C(10)-C(6)-C(7) | 110.67(14) |
| C(15)-C(16) | 1.381(3) | C(6)-C(7)-H(7A) | 110.0 |
| C(16)-H(16) | 0.9500 | C(6)-C(7)-H(7B) | 110.0 |
| C(16)-C(17) | 1.390(2) | H(7A)-C(7)-H(7B) | 108.4 |
| C(17)-H(17) | 0.9500 | C(8)-C(7)-C(6) | 108.51(14) |
| | | C(8)-C(7)-H(7A) | 110.0 |
| C(1)-O(1)-C(8) | 107.34(13) | C(8)-C(7)-H(7B) | 110.0 |
| O(1)-C(1)-C(2) | 109.86(13) | O(1)-C(8)-C(3) | 103.37(12) |
| O(2)-C(1)-O(1) | 121.02(16) | O(1)-C(8)-C(7) | 115.03(14) |
| O(2)-C(1)-C(2) | 129.07(16) | O(1)-C(8)-H(8) | 107.7 |
| C(1)-C(2)-H(2A) | 111.6 | C(3)-C(8)-H(8) | 107.7 |
| C(1)-C(2)-H(2B) | 111.6 | C(7)-C(8)-C(3) | 114.85(13) |
| C(1)-C(2)-C(3) | 100.98(13) | C(7)-C(8)-H(8) | 107.7 |
| H(2A)-C(2)-H(2B) | 109.4 | C(6)-C(9)-H(9A) | 109.5 |
| C(3)-C(2)-H(2A) | 111.6 | C(6)-C(9)-H(9B) | 109.5 |
| C(3)-C(2)-H(2B) | 111.6 | C(6)-C(9)-H(9C) | 109.5 |
| C(2)-C(3)-C(8) | 97.89(12) | H(9A)-C(9)-H(9B) | 109.5 |
| C(2)-C(3)-C(11) | 110.16(13) | H(9A)-C(9)-H(9C) | 109.5 |
| C(4)-C(3)-C(2) | 120.90(14) | H(9B)-C(9)-H(9C) | 109.5 |
| C(4)-C(3)-C(8) | 104.00(13) | C(6)-C(10)-H(10A) | 109.5 |
| C(4)-C(3)-C(11) | 110.15(13) | C(6)-C(10)-H(10B) | 109.5 |
| C(8)-C(3)-C(11) | 112.99(13) | C(6)-C(10)-H(10C) | 109.5 |
| O(3)-C(4)-C(3) | 124.08(16) | H(10A)-C(10)-H(10B) | 109.5 |
| O(3)-C(4)-C(5) | 123.33(16) | H(10A)-C(10)-H(10C) | 109.5 |
| C(5)-C(4)-C(3) | 112.56(14) | H(10B)-C(10)-H(10C) | 109.5 |
| C(4)-C(5)-H(5A) | 108.6 | C(3)-C(11)-H(11A) | 108.3 |
| C(4)-C(5)-H(5B) | 108.6 | C(3)-C(11)-H(11B) | 108.3 |
| C(4)-C(5)-C(6) | 114.64(14) | H(11A)-C(11)-H(11B) | 107.4 |
| H(5A)-C(5)-H(5B) | 107.6 | C(12)-C(11)-C(3) | 116.13(14) |
| C(6)-C(5)-H(5A) | 108.6 | C(12)-C(11)-H(11A) | 108.3 |
| C(6)-C(5)-H(5B) | 108.6 | C(12)-C(11)-H(11B) | 108.3 |

| | | | |
|---|---|---|---|
| C(13)-C(12)-C(11) | 124.57(14) | C(14)-C(15)-H(15) | 120.3 |
| C(13)-C(12)-C(17) | 118.06(15) | C(16)-C(15)-C(14) | 119.34(15) |
| C(17)-C(12)-C(11) | 117.36(15) | C(16)-C(15)-H(15) | 120.3 |
| C(12)-C(13)-H(13) | 119.6 | C(15)-C(16)-H(16) | 119.8 |
| C(12)-C(13)-C(14) | 120.80(16) | C(15)-C(16)-C(17) | 120.36(16) |
| C(14)-C(13)-H(13) | 119.6 | C(17)-C(16)-H(16) | 119.8 |
| C(13)-C(14)-H(14) | 119.8 | C(12)-C(17)-H(17) | 119.5 |
| C(15)-C(14)-C(13) | 120.41(17) | C(16)-C(17)-C(12) | 121.02(17) |
| C(15)-C(14)-H(14) | 119.8 | C(16)-C(17)-H(17) | 119.5 |

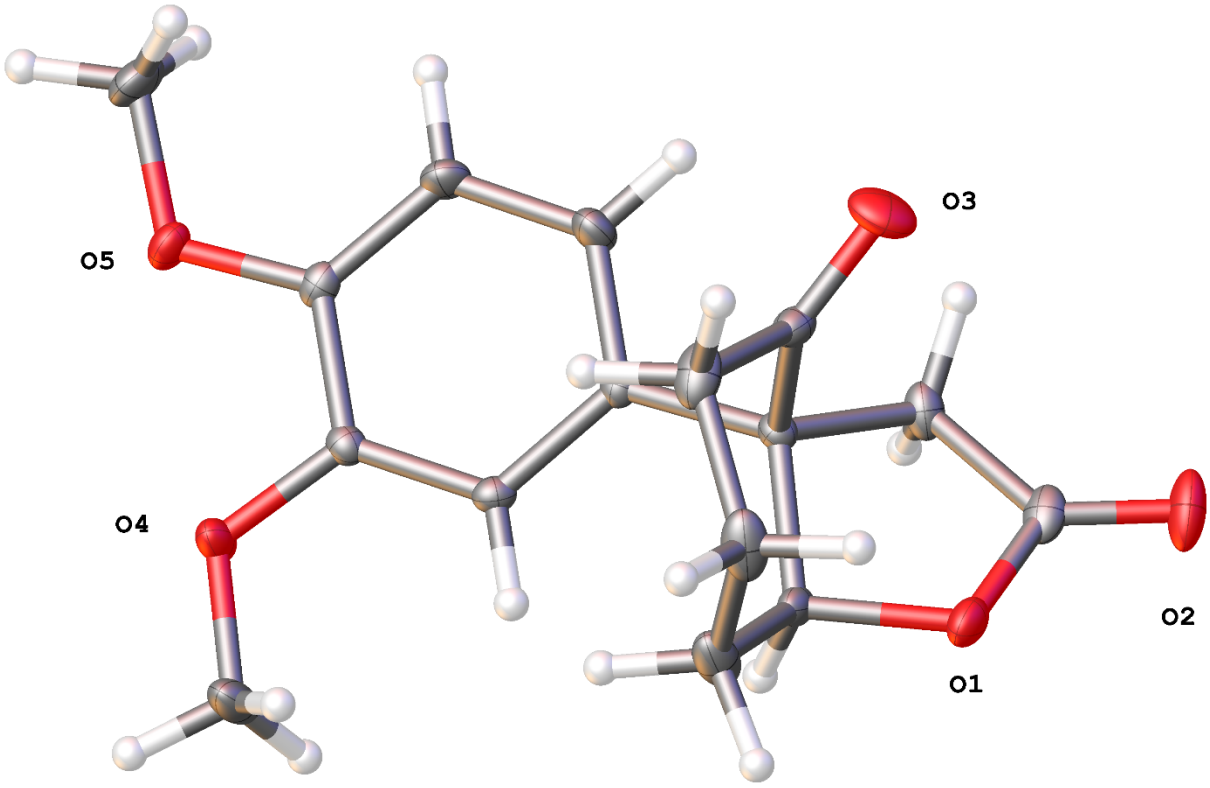
**Table A2.1.10.** Anisotropic displacement parameters ($Å^2 \times 10^3$) for UCI_XW176-1 (**3j**). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 15(1) | 25(1) | 16(1) | 1(1) | 2(1) | -4(1) |
| O(2) | 19(1) | 29(1) | 18(1) | 1(1) | 3(1) | 2(1) |
| O(3) | 27(1) | 15(1) | 32(1) | -1(1) | 11(1) | -4(1) |
| C(1) | 13(1) | 21(1) | 20(1) | 4(1) | 4(1) | 4(1) |
| C(2) | 14(1) | 20(1) | 21(1) | 5(1) | 4(1) | 0(1) |
| C(3) | 12(1) | 15(1) | 19(1) | 3(1) | 4(1) | 0(1) |
| C(4) | 11(1) | 18(1) | 24(1) | 1(1) | 5(1) | 0(1) |
| C(5) | 22(1) | 22(1) | 19(1) | 1(1) | -1(1) | -6(1) |
| C(6) | 22(1) | 26(1) | 17(1) | 2(1) | 4(1) | -5(1) |
| C(7) | 15(1) | 20(1) | 20(1) | 1(1) | 5(1) | -4(1) |
| C(8) | 12(1) | 19(1) | 16(1) | -1(1) | 2(1) | -2(1) |
| C(9) | 36(1) | 40(1) | 22(1) | 7(1) | 4(1) | -14(1) |
| C(10) | 35(1) | 39(1) | 26(1) | -6(1) | 13(1) | -3(1) |
| C(11) | 15(1) | 14(1) | 26(1) | 2(1) | 6(1) | 0(1) |
| C(12) | 14(1) | 18(1) | 14(1) | -1(1) | 3(1) | 0(1) |
| C(13) | 16(1) | 18(1) | 23(1) | 1(1) | 6(1) | 1(1) |
| C(14) | 21(1) | 24(1) | 22(1) | -1(1) | 10(1) | -6(1) |
| C(15) | 13(1) | 35(1) | 21(1) | -6(1) | 8(1) | -2(1) |
| C(16) | 16(1) | 31(1) | 22(1) | 0(1) | 4(1) | 7(1) |
| C(17) | 20(1) | 20(1) | 19(1) | 1(1) | 5(1) | 4(1) |

**Table A2.1.11.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for UCI_XW176-1 (**3j**).

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2A) | 1816 | 7351 | 5522 | 23 |
| H(2B) | 2875 | 6013 | 5092 | 23 |
| H(5A) | 3806 | 5880 | 9762 | 27 |
| H(5B) | 4185 | 3754 | 9151 | 27 |
| H(7A) | 2029 | 1159 | 7809 | 22 |
| H(7B) | 629 | 1996 | 7836 | 22 |
| H(8) | 896 | 5322 | 6915 | 20 |
| H(9A) | 3174 | 903 | 9959 | 52 |
| H(9B) | 1819 | 1345 | 10194 | 52 |
| H(9C) | 3097 | 2772 | 10900 | 52 |
| H(10A) | 1755 | 6154 | 10111 | 49 |
| H(10B) | 502 | 4712 | 9356 | 49 |
| H(10C) | 1068 | 6518 | 8666 | 49 |
| H(11A) | 3723 | 1889 | 7401 | 22 |
| H(11B) | 3262 | 2062 | 5943 | 22 |
| H(13) | 4766 | 6721 | 6245 | 23 |
| H(14) | 6932 | 7446 | 6375 | 26 |
| H(15) | 8540 | 4713 | 7008 | 27 |
| H(16) | 7976 | 1271 | 7552 | 28 |
| H(17) | 5816 | 535 | 7427 | 24 |

**X-ray Crystallography Data for 3x (CCDC 1483274)**




The single crystal X-ray diffraction studies were carried out on a Bruker SMART Platinum 135 CCD diffractometer equipped with Cu $K_a$ radiation ($\lambda = 1.5478$). Crystals of the subject compound were used as received.

A 0.20 x 0.200 x 0.165 mm colorless block was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 125(2) K using $\phi$ and $\varpi$ scans. Crystal-to-detector distance was 45 mm using variable exposure time (1.5, and 3s) depending on $\theta$ with a scan width of 1.5°. Data collection was 99.9% complete to 67.50° in $\theta$. A total of 23800 reflections were collected covering the indices,-8<=h<=8, -9<=k<=9, -32<=l<=32. 2642 reflections were found to be symmetry independent, with a $R_{int}$ of 0.0420. Indexing and unit cell refinement indicated a **Primitive**, **Orthorhombic** lattice. The space group was found to be $\boldsymbol{P2_12_12_1}$. The data were integrated using the Bruker SAINT software program and scaled using

the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized in Table A2.1.12.

Notes: Absolute structure parameter 0.05(5)

**Table A2.1.12.** Crystal data and structure refinement for UCI_XW131 (**3x**).

| | | |
|---|---|---|
| Report date | 2016-05-20 | |
| Identification code | uci_xw131 | |
| Empirical formula | C16 H18 O5 | |
| Molecular formula | C16 H18 O5 | |
| Formula weight | 290.30 | |
| Temperature | 125.0 K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 6.6302(2) Å | $\alpha$= 90°. |
| | b = 7.9041(2) Å | $\beta$= 90°. |
| | c = 26.5947(8) Å | $\gamma$ = 90°. |
| Volume | 1393.72(7) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.384 $Mg/m^3$ | |
| Absorption coefficient | 0.852 $mm^{-1}$ | |
| F(000) | 616 | |
| Crystal size | 0.2 x 0.2 x 0.165 $mm^3$ | |
| Crystal color, habit | colourless block | |
| Theta range for data collection | 3.323 to 70.035°. | |
| Index ranges | -8<=h<=8, -9<=k<=9, -32<=l<=32 | |
| Reflections collected | 23800 | |
| Independent reflections | 2642 [R(int) = 0.0420] | |

| | |
|---|---|
| Completeness to theta = 67.500° | 99.9 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.5220 and 0.4444 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 2642 / 0 / 192 |
| Goodness-of-fit on $F^2$ | 1.084 |
| Final R indices [I>2sigma(I)] | R1 = 0.0281, wR2 = 0.0721 |
| R indices (all data) | R1 = 0.0284, wR2 = 0.0725 |
| Absolute structure parameter | 0.05(5) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.204 and -0.188 e.$Å^{-3}$ |

**Table A2.1.13.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for UCI_XW131 (**3x**). U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 6616(2) | 3042(2) | 6983(1) | 20(1) |
| O(2) | 7880(2) | 641(2) | 6677(1) | 30(1) |
| O(3) | 11316(2) | 4581(2) | 6492(1) | 29(1) |
| O(4) | 4090(2) | 10171(2) | 5817(1) | 20(1) |
| O(5) | 6753(2) | 10758(2) | 5131(1) | 18(1) |
| C(1) | 7467(3) | 2105(2) | 6613(1) | 19(1) |
| C(2) | 7766(3) | 3204(2) | 6155(1) | 18(1) |
| C(3) | 7752(2) | 4984(2) | 6379(1) | 12(1) |
| C(4) | 9825(2) | 5361(2) | 6619(1) | 15(1) |
| C(5) | 9857(3) | 6698(2) | 7017(1) | 23(1) |
| C(6) | 8421(3) | 6180(2) | 7445(1) | 25(1) |
| C(7) | 6293(3) | 5953(2) | 7244(1) | 24(1) |
| C(8) | 6181(2) | 4755(2) | 6800(1) | 15(1) |
| C(9) | 7344(2) | 6427(2) | 6011(1) | 12(1) |
| C(10) | 5723(2) | 7549(2) | 6070(1) | 13(1) |
| C(11) | 5557(2) | 8971(2) | 5770(1) | 13(1) |
| C(12) | 7004(2) | 9298(2) | 5396(1) | 13(1) |

| | | | | |
|---|---|---|---|---|
| C(13) | 8552(3) | 8147(2) | 5320(1) | 18(1) |
| C(14) | 8724(3) | 6726(2) | 5629(1) | 18(1) |
| C(15) | 2672(3) | 9966(3) | 6218(1) | 27(1) |
| C(16) | 8324(3) | 11202(2) | 4788(1) | 25(1) |

**Table A2.1.14.** Bond lengths [Å] and angles [°] for UCI_XW131 (**3x**).

| | | | |
|---|---|---|---|
| O(1)-C(1) | 1.354(2) | C(9)-C(14) | 1.387(2) |
| O(1)-C(8) | 1.4679(19) | C(10)-H(10) | 0.9500 |
| O(2)-C(1) | 1.202(2) | C(10)-C(11) | 1.382(2) |
| O(3)-C(4) | 1.213(2) | C(11)-C(12) | 1.407(2) |
| O(4)-C(11) | 1.364(2) | C(12)-C(13) | 1.386(2) |
| O(4)-C(15) | 1.430(2) | C(13)-H(13) | 0.9500 |
| O(5)-C(12) | 1.361(2) | C(13)-C(14) | 1.396(2) |
| O(5)-C(16) | 1.429(2) | C(14)-H(14) | 0.9500 |
| C(1)-C(2) | 1.510(2) | C(15)-H(15A) | 0.9800 |
| C(2)-H(2A) | 0.9900 | C(15)-H(15B) | 0.9800 |
| C(2)-H(2B) | 0.9900 | C(15)-H(15C) | 0.9800 |
| C(2)-C(3) | 1.529(2) | C(16)-H(16A) | 0.9800 |
| C(3)-C(4) | 1.544(2) | C(16)-H(16B) | 0.9800 |
| C(3)-C(8) | 1.539(2) | C(16)-H(16C) | 0.9800 |
| C(3)-C(9) | 1.528(2) | | |
| C(4)-C(5) | 1.497(2) | C(1)-O(1)-C(8) | 110.20(13) |
| C(5)-H(5A) | 0.9900 | C(11)-O(4)-C(15) | 117.30(13) |
| C(5)-H(5B) | 0.9900 | C(12)-O(5)-C(16) | 116.67(14) |
| C(5)-C(6) | 1.539(3) | O(1)-C(1)-C(2) | 109.08(14) |
| C(6)-H(6A) | 0.9900 | O(2)-C(1)-O(1) | 121.20(17) |
| C(6)-H(6B) | 0.9900 | O(2)-C(1)-C(2) | 129.72(18) |
| C(6)-C(7) | 1.519(3) | C(1)-C(2)-H(2A) | 111.3 |
| C(7)-H(7A) | 0.9900 | C(1)-C(2)-H(2B) | 111.3 |
| C(7)-H(7B) | 0.9900 | C(1)-C(2)-C(3) | 102.30(13) |
| C(7)-C(8) | 1.515(2) | H(2A)-C(2)-H(2B) | 109.2 |
| C(8)-H(8) | 1.0000 | C(3)-C(2)-H(2A) | 111.3 |
| C(9)-C(10) | 1.402(2) | C(3)-C(2)-H(2B) | 111.3 |

| | | | |
|---|---|---|---|
| C(2)-C(3)-C(4) | 109.49(14) | C(7)-C(8)-H(8) | 109.5 |
| C(2)-C(3)-C(8) | 100.36(13) | C(10)-C(9)-C(3) | 122.46(14) |
| C(8)-C(3)-C(4) | 108.93(13) | C(14)-C(9)-C(3) | 118.66(14) |
| C(9)-C(3)-C(2) | 115.98(12) | C(14)-C(9)-C(10) | 118.66(14) |
| C(9)-C(3)-C(4) | 106.17(13) | C(9)-C(10)-H(10) | 119.6 |
| C(9)-C(3)-C(8) | 115.71(13) | C(11)-C(10)-C(9) | 120.74(14) |
| O(3)-C(4)-C(3) | 120.80(15) | C(11)-C(10)-H(10) | 119.6 |
| O(3)-C(4)-C(5) | 122.99(16) | O(4)-C(11)-C(10) | 124.67(14) |
| C(5)-C(4)-C(3) | 116.20(14) | O(4)-C(11)-C(12) | 115.06(14) |
| C(4)-C(5)-H(5A) | 109.9 | C(10)-C(11)-C(12) | 120.23(15) |
| C(4)-C(5)-H(5B) | 109.9 | O(5)-C(12)-C(11) | 115.98(14) |
| C(4)-C(5)-C(6) | 109.00(15) | O(5)-C(12)-C(13) | 124.94(15) |
| H(5A)-C(5)-H(5B) | 108.3 | C(13)-C(12)-C(11) | 119.08(15) |
| C(6)-C(5)-H(5A) | 109.9 | C(12)-C(13)-H(13) | 119.9 |
| C(6)-C(5)-H(5B) | 109.9 | C(12)-C(13)-C(14) | 120.26(15) |
| C(5)-C(6)-H(6A) | 109.6 | C(14)-C(13)-H(13) | 119.9 |
| C(5)-C(6)-H(6B) | 109.6 | C(9)-C(14)-C(13) | 120.91(15) |
| H(6A)-C(6)-H(6B) | 108.1 | C(9)-C(14)-H(14) | 119.5 |
| C(7)-C(6)-C(5) | 110.27(14) | C(13)-C(14)-H(14) | 119.5 |
| C(7)-C(6)-H(6A) | 109.6 | O(4)-C(15)-H(15A) | 109.5 |
| C(7)-C(6)-H(6B) | 109.6 | O(4)-C(15)-H(15B) | 109.5 |
| C(6)-C(7)-H(7A) | 108.9 | O(4)-C(15)-H(15C) | 109.5 |
| C(6)-C(7)-H(7B) | 108.9 | H(15A)-C(15)-H(15B) | 109.5 |
| H(7A)-C(7)-H(7B) | 107.8 | H(15A)-C(15)-H(15C) | 109.5 |
| C(8)-C(7)-C(6) | 113.15(15) | H(15B)-C(15)-H(15C) | 109.5 |
| C(8)-C(7)-H(7A) | 108.9 | O(5)-C(16)-H(16A) | 109.5 |
| C(8)-C(7)-H(7B) | 108.9 | O(5)-C(16)-H(16B) | 109.5 |
| O(1)-C(8)-C(3) | 102.50(13) | O(5)-C(16)-H(16C) | 109.5 |
| O(1)-C(8)-C(7) | 107.97(13) | H(16A)-C(16)-H(16B) | 109.5 |
| O(1)-C(8)-H(8) | 109.5 | H(16A)-C(16)-H(16C) | 109.5 |
| C(3)-C(8)-H(8) | 109.5 | H(16B)-C(16)-H(16C) | 109.5 |
| C(7)-C(8)-C(3) | 117.39(14) | | |

**Table A2.1.15.** Anisotropic displacement parameters ($Å^2 \times 10^3$) for UCI_XW131 (**3x**). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 19(1) | 16(1) | 24(1) | 9(1) | 0(1) | 0(1) |
| O(2) | 41(1) | 12(1) | 36(1) | 3(1) | -15(1) | 0(1) |
| O(3) | 13(1) | 40(1) | 34(1) | -1(1) | 0(1) | 6(1) |
| O(4) | 20(1) | 19(1) | 21(1) | 8(1) | 7(1) | 8(1) |
| O(5) | 24(1) | 14(1) | 16(1) | 4(1) | 4(1) | -1(1) |
| C(1) | 19(1) | 14(1) | 24(1) | 0(1) | -9(1) | -4(1) |
| C(2) | 23(1) | 14(1) | 18(1) | -1(1) | -5(1) | 3(1) |
| C(3) | 11(1) | 13(1) | 13(1) | -1(1) | -1(1) | 1(1) |
| C(4) | 12(1) | 16(1) | 17(1) | 5(1) | -1(1) | -2(1) |
| C(5) | 28(1) | 16(1) | 25(1) | 1(1) | -11(1) | -4(1) |
| C(6) | 42(1) | 19(1) | 14(1) | -2(1) | -6(1) | 7(1) |
| C(7) | 32(1) | 24(1) | 15(1) | 4(1) | 6(1) | 12(1) |
| C(8) | 13(1) | 14(1) | 19(1) | 7(1) | 1(1) | 2(1) |
| C(9) | 14(1) | 12(1) | 12(1) | 0(1) | -2(1) | -1(1) |
| C(10) | 11(1) | 15(1) | 11(1) | 0(1) | 0(1) | -1(1) |
| C(11) | 12(1) | 13(1) | 14(1) | -1(1) | -1(1) | 0(1) |
| C(12) | 17(1) | 12(1) | 11(1) | -1(1) | -2(1) | -2(1) |
| C(13) | 18(1) | 21(1) | 14(1) | 2(1) | 5(1) | 1(1) |
| C(14) | 18(1) | 18(1) | 18(1) | 0(1) | 4(1) | 6(1) |
| C(15) | 24(1) | 29(1) | 28(1) | 10(1) | 12(1) | 13(1) |
| C(16) | 28(1) | 24(1) | 24(1) | 9(1) | 6(1) | -6(1) |

**Table A2.1.16.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for UCI_XW131 (**3x**).

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2A) | 6655 | 3053 | 5910 | 22 |
| H(2B) | 9066 | 2956 | 5987 | 22 |
| H(5A) | 9425 | 7795 | 6873 | 28 |
| H(5B) | 11244 | 6831 | 7150 | 28 |
| H(6A) | 8891 | 5107 | 7597 | 30 |
| H(6B) | 8425 | 7061 | 7709 | 30 |
| H(7A) | 5422 | 5515 | 7517 | 28 |
| H(7B) | 5757 | 7070 | 7141 | 28 |
| H(8) | 4794 | 4788 | 6652 | 18 |
| H(10) | 4727 | 7329 | 6318 | 15 |
| H(13) | 9500 | 8325 | 5058 | 21 |
| H(14) | 9800 | 5952 | 5577 | 22 |
| H(15A) | 1836 | 8966 | 6154 | 41 |
| H(15B) | 1811 | 10971 | 6239 | 41 |
| H(15C) | 3398 | 9819 | 6536 | 41 |
| H(16A) | 8356 | 10384 | 4511 | 38 |
| H(16B) | 9622 | 11191 | 4964 | 38 |
| H(16C) | 8071 | 12337 | 4653 | 38 |

## 11. DFT Computations

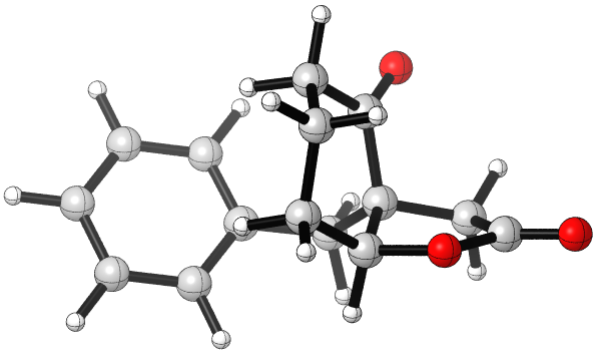
### a. Computational Details

The energetic difference between *syn* **3a** and *anti* **2a** was studied using a multi-level procedure in which the conformational freedom was first explored using OPLS-2005 force field[13] and then the best conformers inside 6 kcal/mol were re-optimized using TPSSh-D3/def2-TZVP[14,15] in gas-phase (Figure S1). The conformational freedom search was performed using systematic torsional sampling in Maestro 2015[16] with the following settings: Torsion sampling options "Intermediate"; maximum number of steps "2000"; steps per rotatable bond "10"; energy window for saving structures "5 kcal/mol". For DFT computations, we used Turbomole 7.0 program package.[17] The atom-pairwise dispersion correction by Grimme was used with BJ-damping.[18] The computations were further sped-up using multipole-acccelerated resolution-of-

idendity approximation for the Coulomb part with the corresponding auxiliary basis set.(cite MARI-J and aux-basis).[19,20] Also fine integration grid *m4* was used throughout computations.

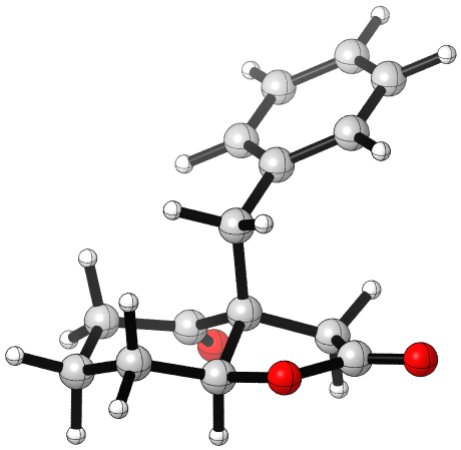
For the lowest conformer for both **3a** and **2a**, the vibrational frequencies were computed using harmonic approximation and these were further used to compute the chemical potential (c.p.) using standard rigid-rotor harmonic-oscillator approximation. The Gibbs free energies where then calculated using G = E(0) + c.p. Pictures of the computed structures were generated using Cylview.[21]

*syn* **3a**
**E =** –807.3213984112
**c.p. =** 616.80



ΔG=0.0 kcal/mol

*anti* **2a**
**E =** –807.3121299829
**c.p.** = 617.03



ΔG=5.8 kcal/mol

**Figure A2.1.1.** The relative energies and geometries of the lowest-energy conformers for **3a** and **2a** based on TPSSh-D3/def2-TZVP.

**b. Cartesian coordinates**

The Cartesian coordinates, relative, absolute energies (in *Hartrees*) and the chemical potentials (in kJ/mol) of the lowest energy structures for *syn* **3a** and *anti* **2a** at TPSSh-D3/def2-TZVP level are given below.

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| | | | |
|---|---|---|---|
| C | -0.2183129 | 1.9617615 | 0.7864555 |
| C | -0.8452586 | 1.2944226 | 2.0118339 |
| C | 1.1055986 | 1.3582093 | 0.3848281 |
| C | -0.9790639 | -0.2048794 | 1.7709593 |
| C | 0.3747151 | -0.8461162 | 1.5308144 |
| C | 1.3021538 | -0.1688168 | 0.4950735 |
| C | 2.6876508 | -0.4595859 | 1.0825934 |
| C | 2.4450631 | -0.6169505 | 2.5676322 |
| H | 3.4140494 | 0.3241699 | 0.8769475 |

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| | | | |
|---|---|---|---|
| C | -2.3325400 | 0.0034723 | -1.2644277 |
| C | -1.9171908 | -0.0834163 | -2.7540627 |
| C | -1.4372812 | 0.9299536 | -0.4478320 |
| C | -0.4051100 | -0.2727825 | -2.9816557 |
| C | 0.2730035 | 0.7959906 | -2.1626636 |
| C | 0.0409700 | 0.6519249 | -0.6415947 |
| C | 1.0485101 | 1.6861140 | -0.1593126 |
| C | 2.1928559 | 1.4883115 | -1.1470545 |
| H | 1.3940773 | 1.5638630 | 0.8642140 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| H | 3.0879838 | -1.4055488 | 0.7032501 | H | 0.6474229 | 2.6986462 | -0.2671348 |
| O | 1.1113727 | -0.8005810 | 2.7826718 | O | 1.7051561 | 0.8888284 | -2.2882958 |
| O | 2.0018125 | 2.0360050 | -0.0745203 | O | -1.8671343 | 1.8412840 | 0.2243946 |
| O | 3.2390052 | -0.6014685 | 3.4653861 | O | 3.3522555 | 1.7589321 | -1.0245180 |
| H | -0.0682009 | 3.0347350 | 0.9142919 | H | -2.2858668 | -0.9954223 | -0.8183105 |
| H | -0.8873535 | 1.8223568 | -0.0731379 | H | -3.3596288 | 0.3565891 | -1.1707974 |
| H | -1.8251044 | 1.7354060 | 2.2080083 | H | -2.2242132 | 0.8433663 | -3.2484744 |
| H | -0.2293722 | 1.4732839 | 2.8972627 | H | -2.4727189 | -0.8931078 | -3.2313302 |
| H | -1.6088969 | -0.3885224 | 0.8959151 | H | -0.1726870 | -0.1515017 | -4.0418130 |
| H | -1.4467147 | -0.7015181 | 2.6244604 | H | -0.0722046 | -1.2687414 | -2.6825454 |
| H | 0.2538811 | -1.9043784 | 1.2736897 | H | -0.1340909 | 1.7692644 | -2.4731837 |
| C | 1.1838867 | -0.7726839 | -0.9322153 | C | 0.4393560 | -0.7651379 | -0.1372355 |
| H | 1.4038846 | -1.8408037 | -0.8443782 | C | 0.5050138 | -0.8617671 | 1.3654120 |
| H | 1.9780155 | -0.3190476 | -1.5298981 | H | 1.4178036 | -1.0074843 | -0.5604600 |
| C | -0.1422725 | -0.5842070 | -1.6216728 | H | -0.2612078 | -1.5067183 | -0.5228444 |
| C | -1.1526109 | -1.5412513 | -1.5058749 | C | 1.7374297 | -0.8411017 | 2.0207313 |
| C | -0.3924833 | 0.5598337 | -2.3839520 | C | -0.6580483 | -0.9534863 | 2.1331800 |
| C | -1.6287958 | 0.7546195 | -2.9907015 | C | -0.5917614 | -1.0171583 | 3.5199696 |
| C | -2.3904510 | -1.3506332 | -2.1110701 | C | 0.6427085 | -0.9918200 | 4.1624789 |
| C | -2.6341371 | -0.1976630 | -2.8510341 | C | 1.8082659 | -0.9050902 | 3.4087966 |
| H | -3.5965200 | -0.0482262 | -3.3260474 | H | 2.6498691 | -0.7726842 | 1.4370727 |
| H | -1.8044993 | 1.6481941 | -3.5784317 | H | 0.6948407 | -1.0417663 | 5.2437179 |
| H | -0.9663889 | -2.4482342 | -0.9395242 | H | 2.7744173 | -0.8873797 | 3.8995096 |
| H | -3.1618190 | -2.1053822 | -2.0102581 | H | -1.6272865 | -0.9739592 | 1.6465192 |
| H | 0.3891829 | 1.3035009 | -2.4993573 | H | -1.5049855 | -1.0860151 | 4.0995504 |

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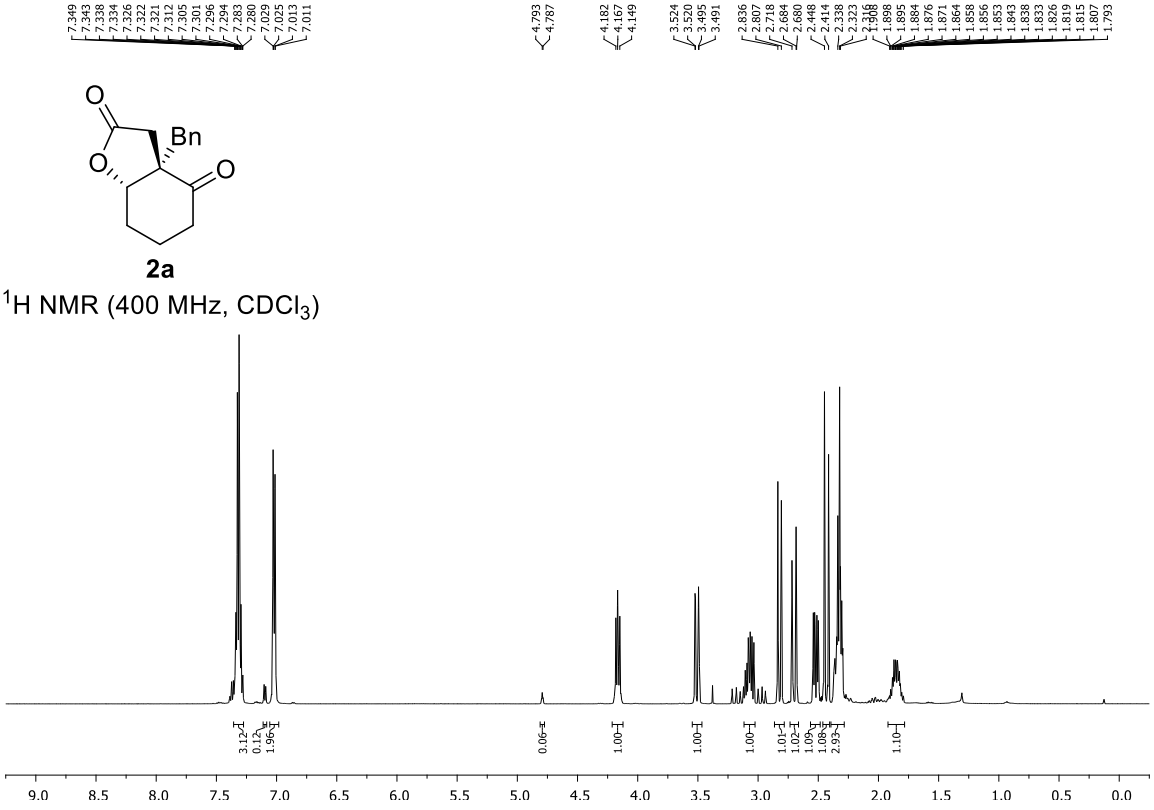
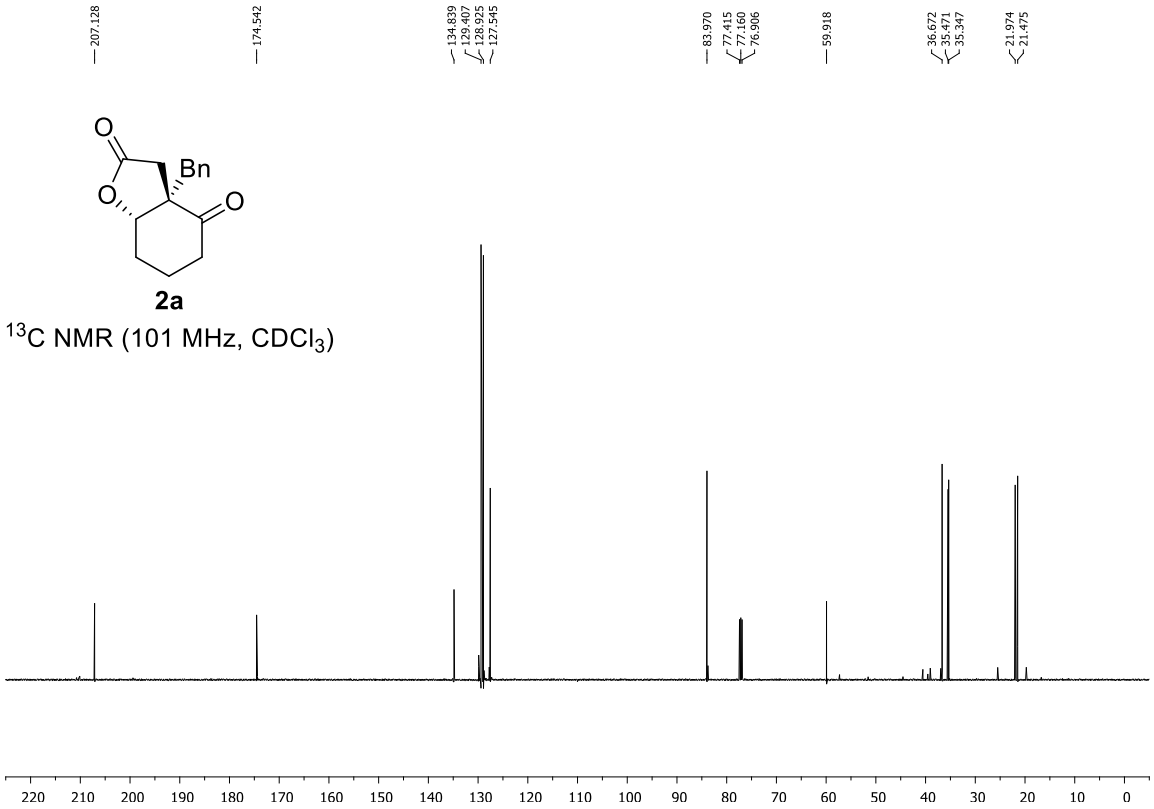
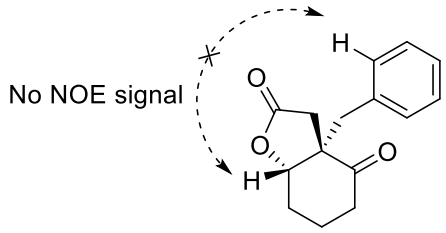
## 13. NMR Spectra

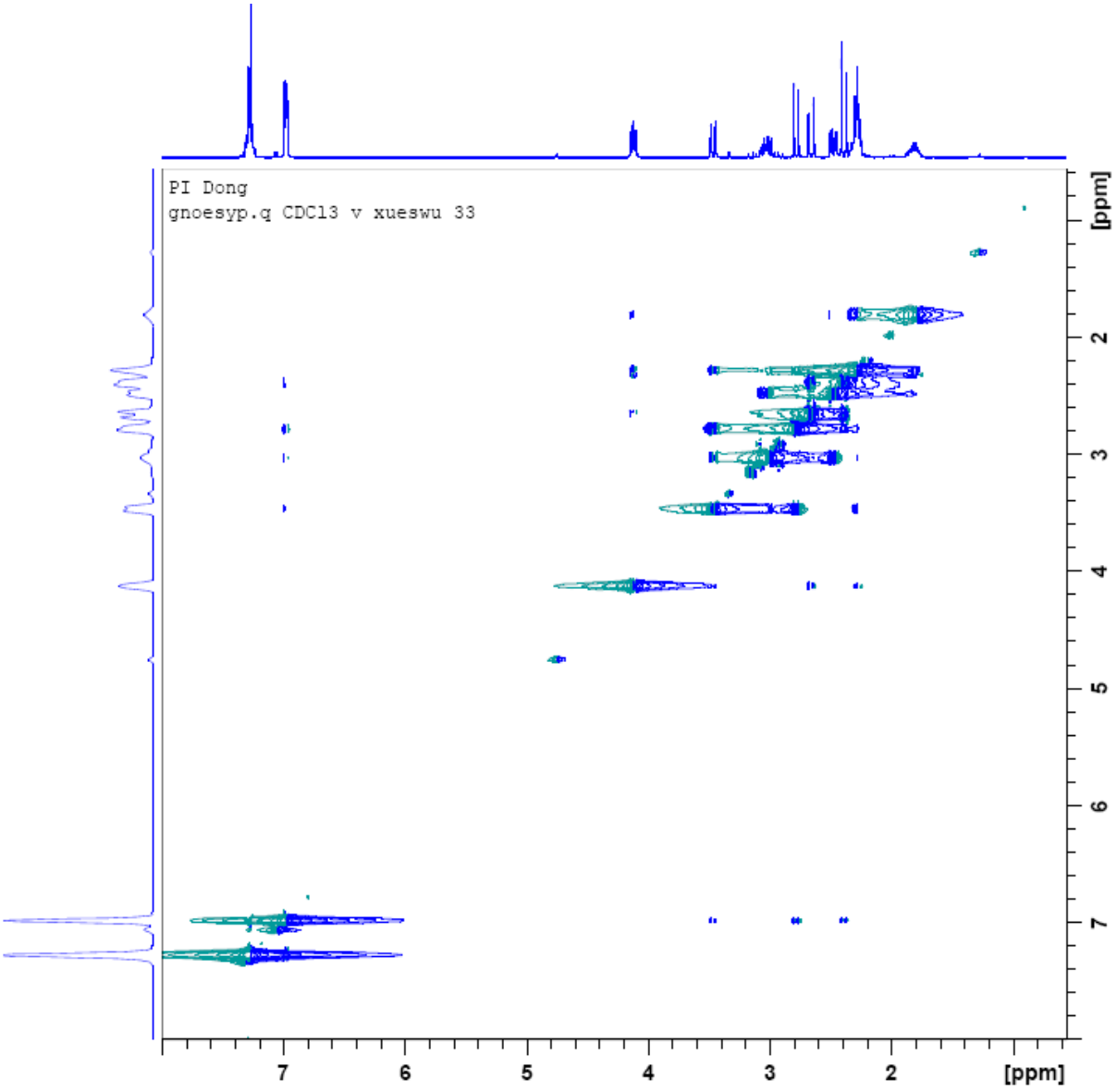


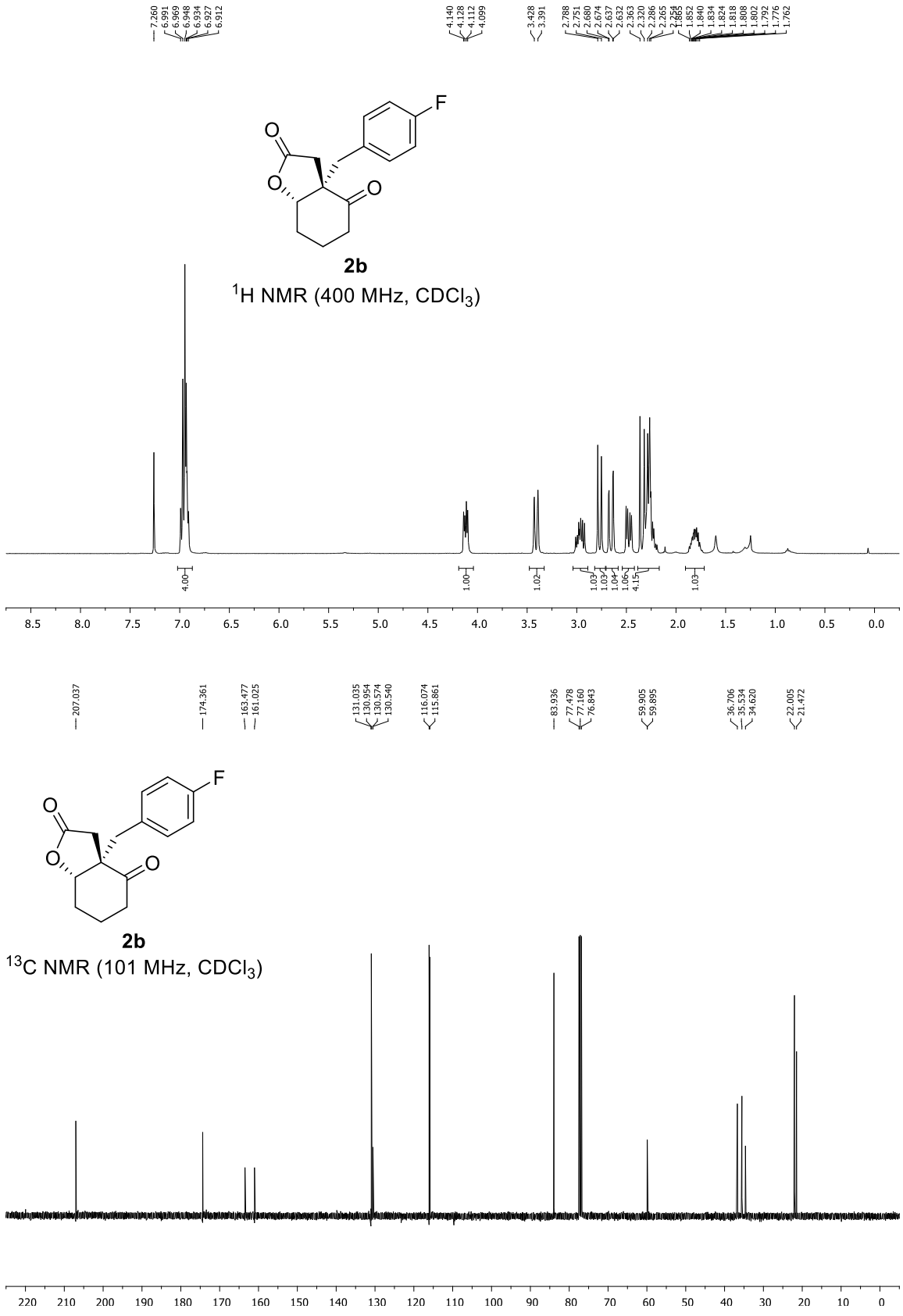



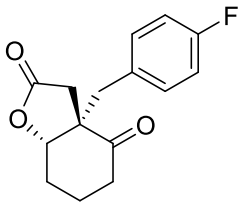

No NOE signal
H
O
O
O
H

**2a**

NOESY

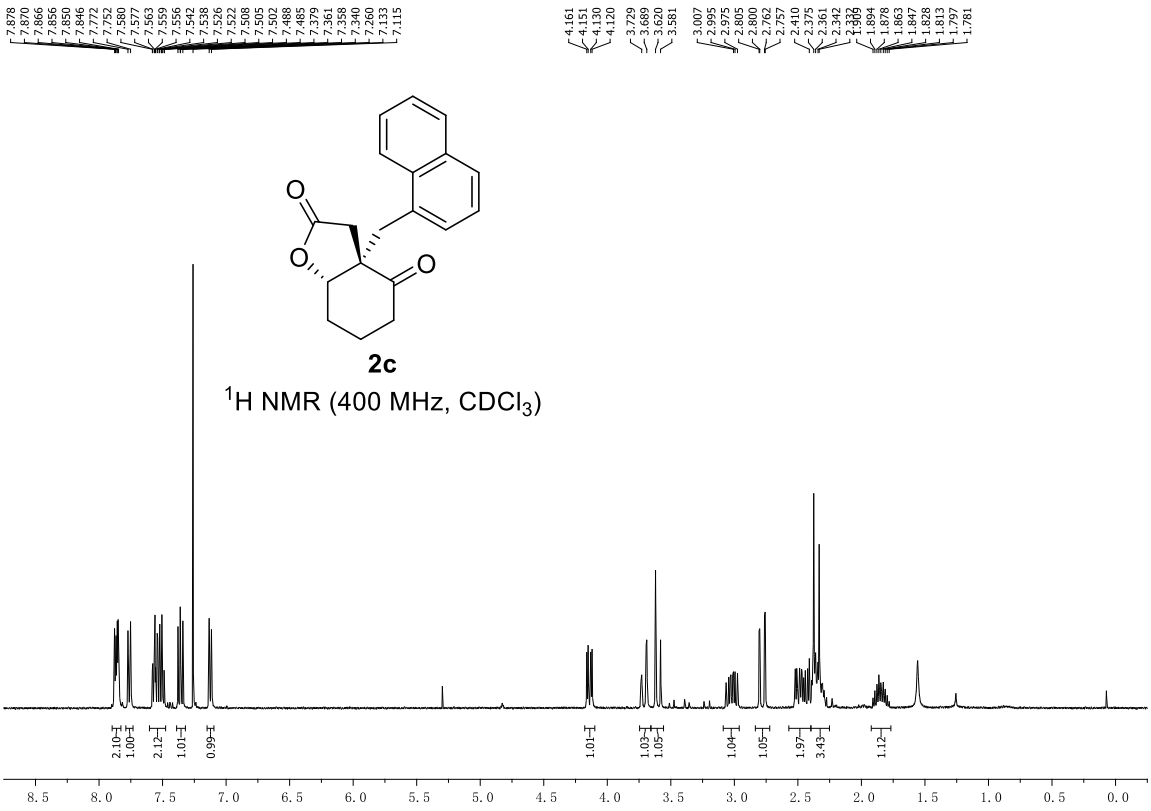

PI Dong
gnoesyp.q CDCl3 v xueswu 33
[ppm]
7
6
5
4
3
2
[ppm]

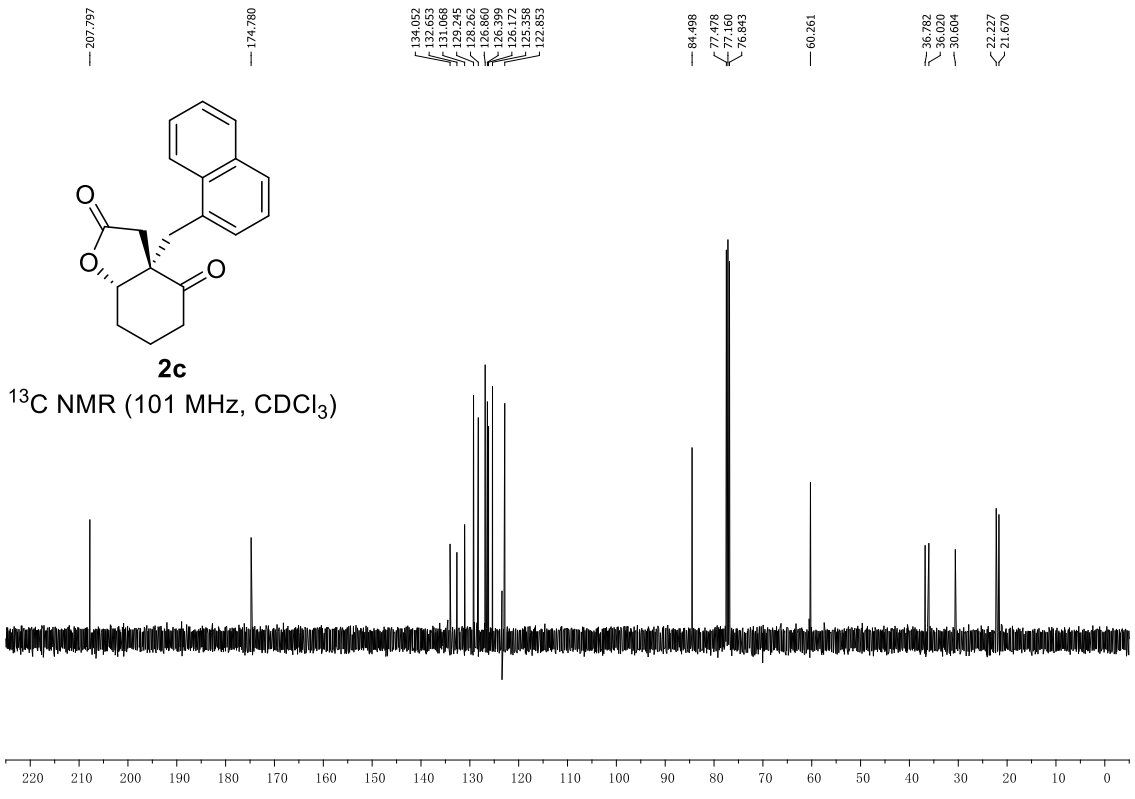

7.260
6.991
6.969
6.948
6.934
6.927
6.912
4.140
4.128
4.112
4.099
3.428
3.391
2.788
2.751
2.680
2.674
2.637
2.632
2.363
2.320
2.286
2.265
2.254
1.885
1.852
1.840
1.834
1.824
1.818
1.808
1.800
1.802
1.792
1.776
1.762
F
O
O
O
2b
1H NMR (400 MHz, CDCl3)
4.00
1.00
1.02
1.03
1.03
1.04
1.06
4.15
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
207.037
174.361
163.477
161.025
131.035
130.954
130.574
130.540
116.074
115.861
83.936
77.478
77.160
76.843
59.905
59.895
36.706
35.534
34.620
22.005
21.472
F
O
O
O
2b
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

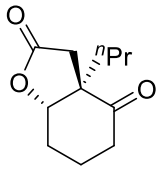



**2b**

$^{19}F$ NMR (376 MHz, $CDCl_3$)

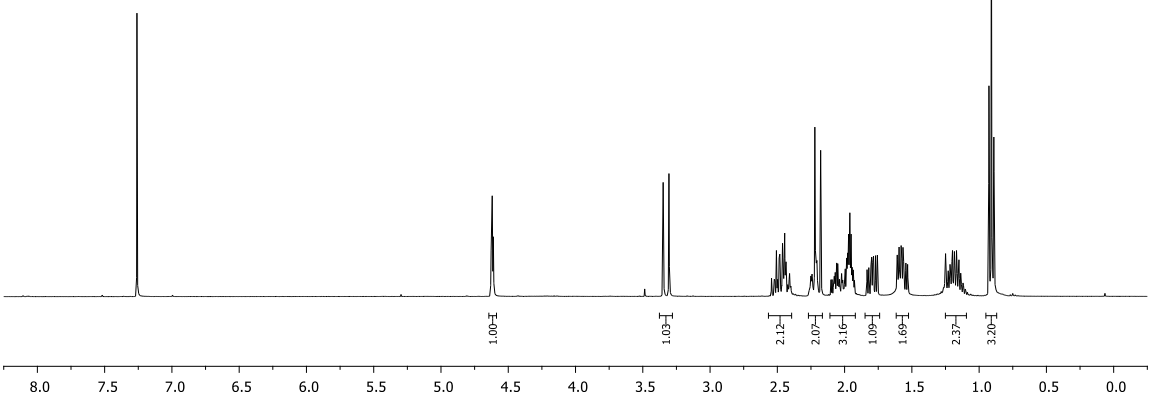

7.878
7.870
7.866
7.856
7.850
7.846
7.772
7.752
7.580
7.577
7.563
7.559
7.556
7.542
7.538
7.526
7.522
7.508
7.505
7.502
7.488
7.485
7.379
7.361
7.358
7.340
7.260
7.133
7.115
4.161
4.151
4.130
4.120
3.729
3.689
3.620
3.581
3.007
2.995
2.975
2.805
2.800
2.762
2.757
2.410
2.375
2.361
2.342
1.909
1.894
1.878
1.863
1.847
1.828
1.813
1.797
1.781
O
O
O
2c
1H NMR (400 MHz, CDCl3)
2.10
1.00
2.12
1.01
0.99
1.01
1.03
1.05
1.04
1.05
1.97
3.43
1.12
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

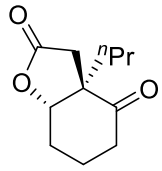

207.797
174.780
134.052
132.653
131.068
129.245
128.262
126.860
126.399
126.172
125.358
122.853
84.498
77.478
77.160
76.843
60.261
36.782
36.020
30.604
22.227
21.670
O
O
O
2c
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



**2d**

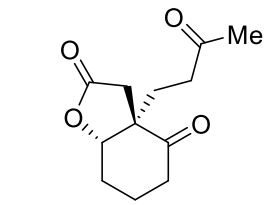
$^{1}$H NMR (400 MHz, $CDCl_3$)





**2d**

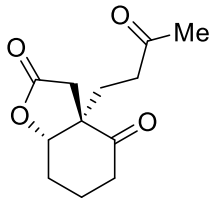
$^{13}$C NMR (101 MHz, $CDCl_3$)




**2e**

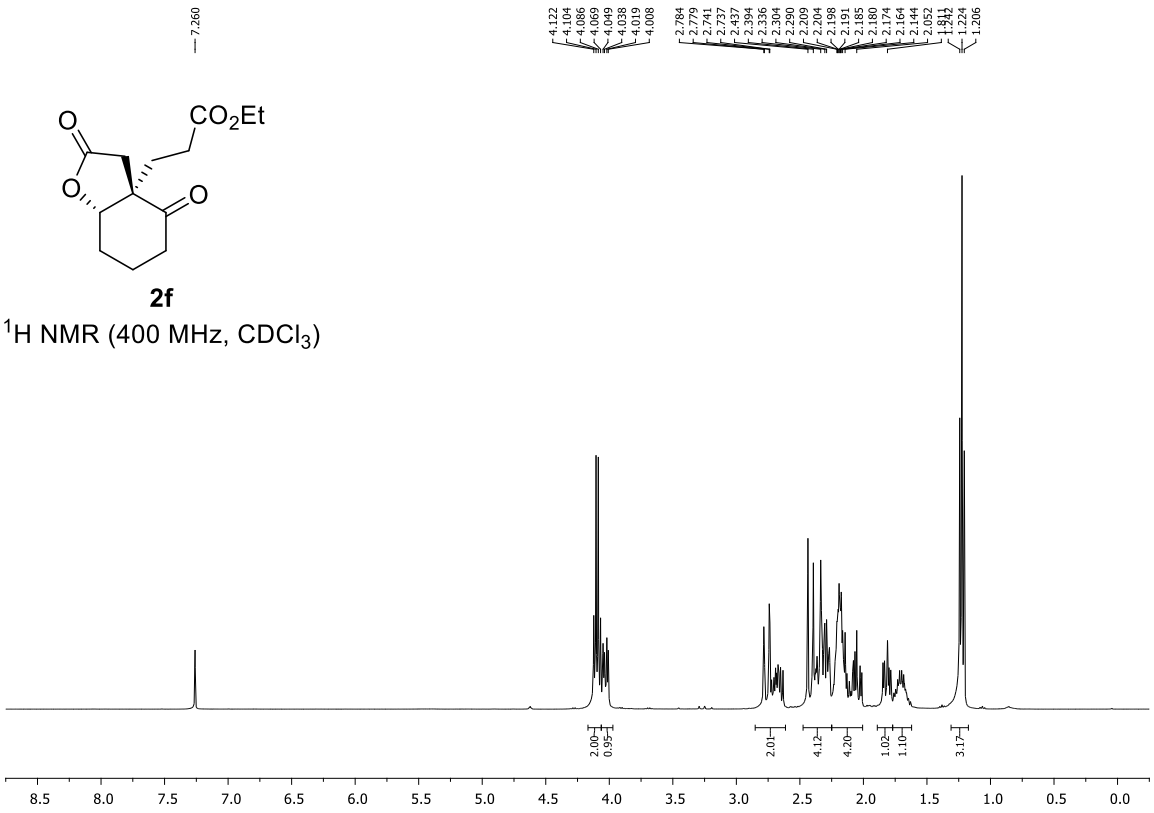
$^{1}$H NMR (500 MHz, $CDCl_3$)



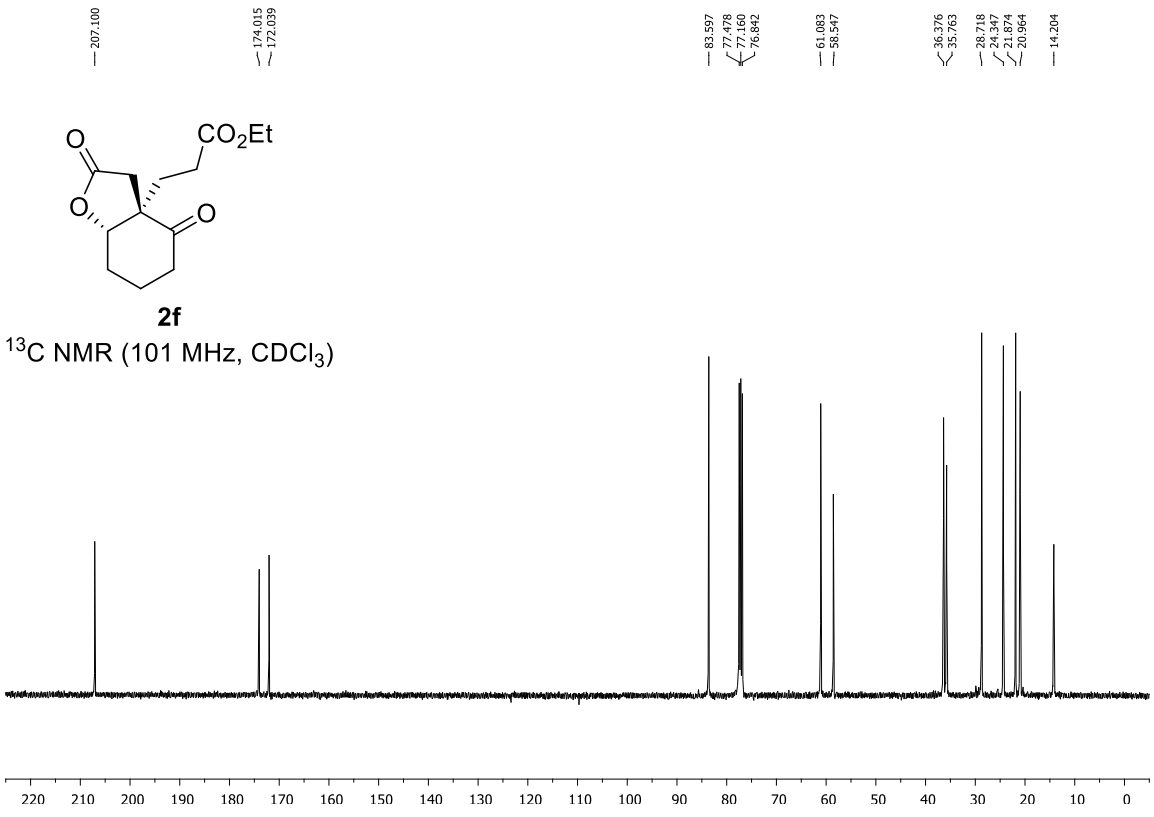

**2e**

$^{13}$C NMR (126 MHz, $CDCl_3$)



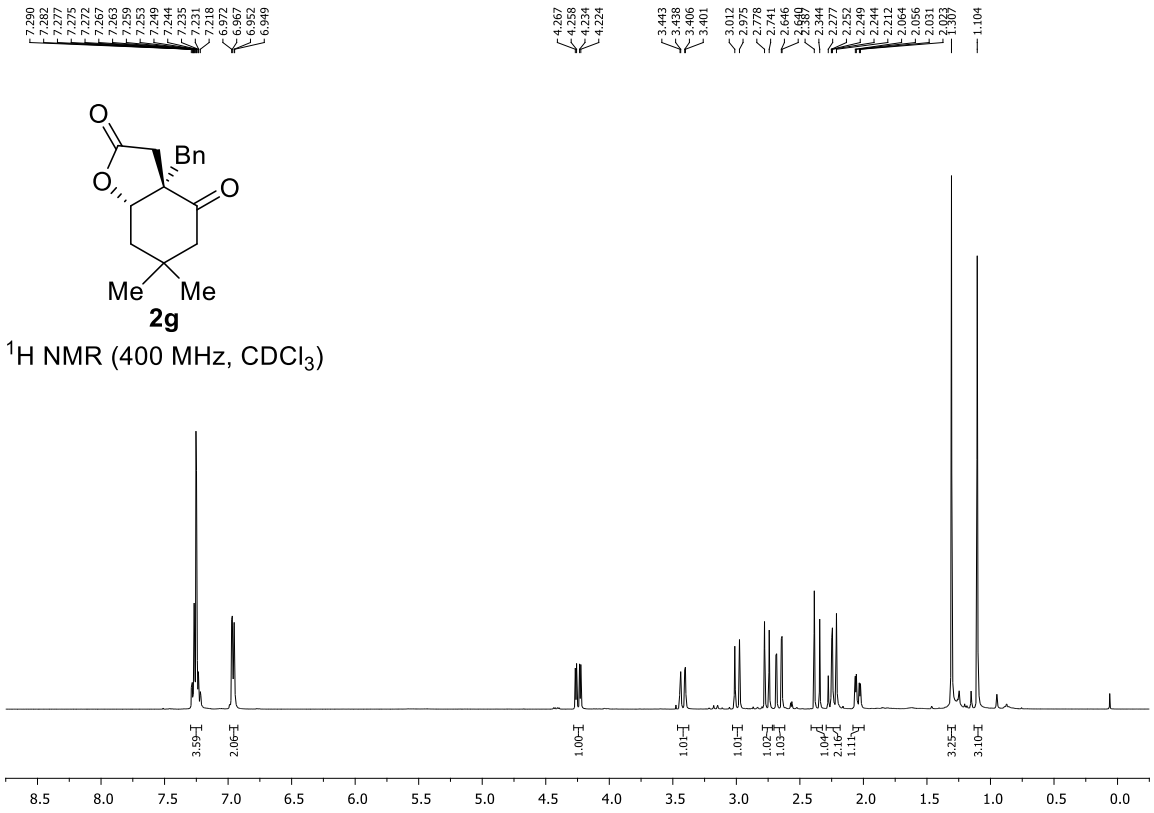

**2f**

$^{1}$H NMR (400 MHz, $CDCl_3$)



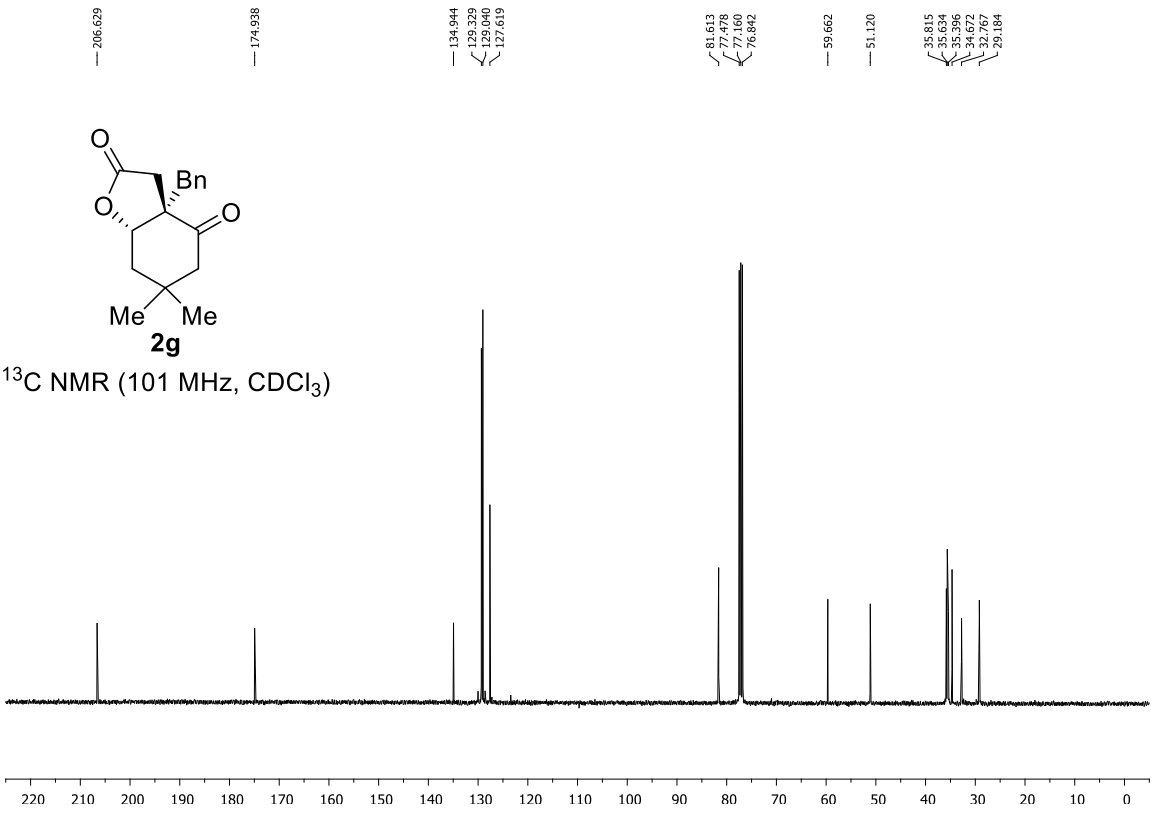

**2f**

$^{13}$C NMR (101 MHz, $CDCl_3$)



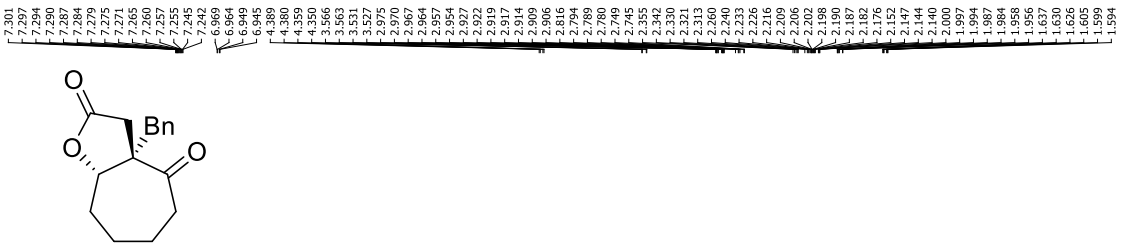

**2g**

$^1$H NMR (400 MHz, $CDCl_3$)




**2g**

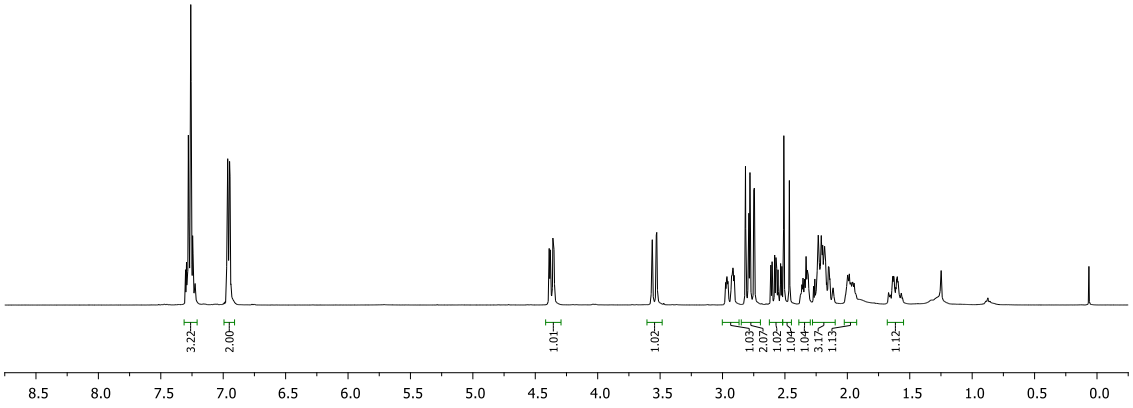
$^{13}$C NMR (101 MHz, $CDCl_3$)

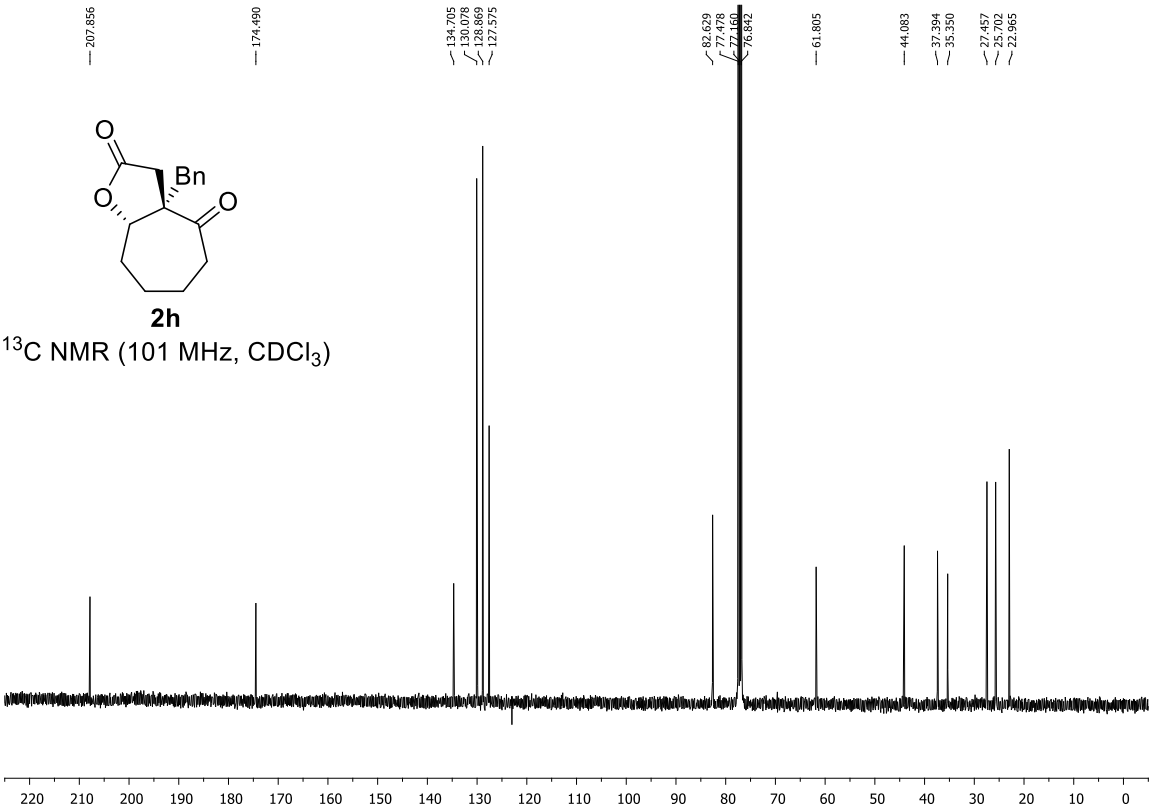




**2h**

$^{1}$H NMR (400 MHz, $CDCl_3$)

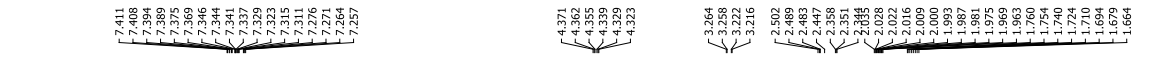


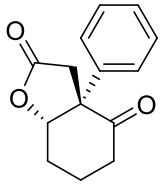




**2h**

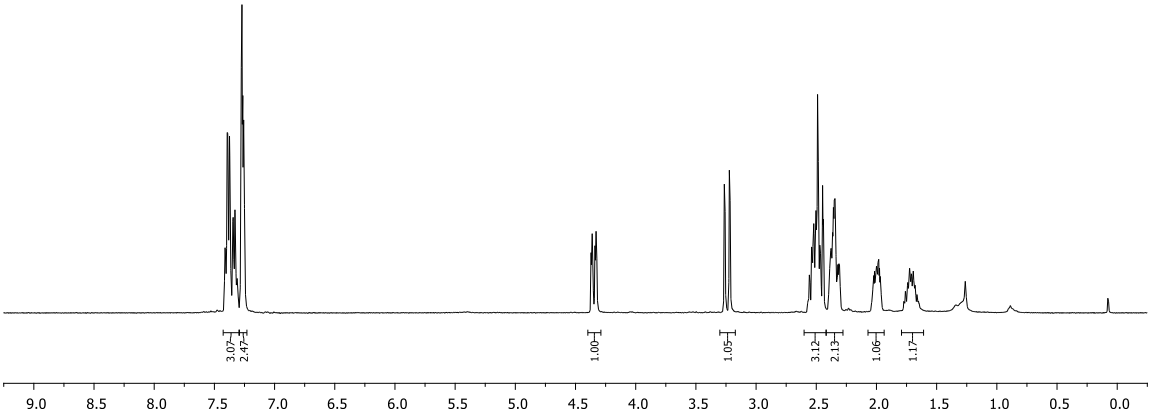
$^{13}$C NMR (101 MHz, $CDCl_3$)

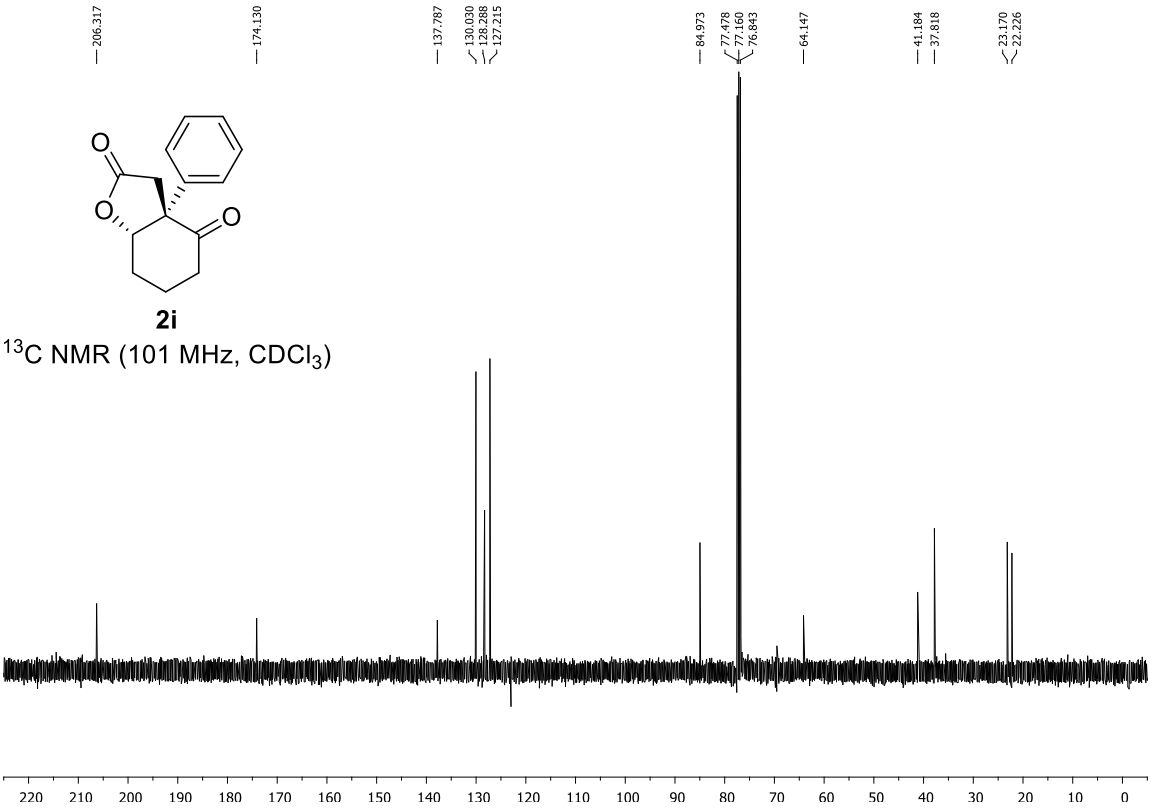


**2i**

$^{1}$H NMR (400 MHz, $CDCl_3$)

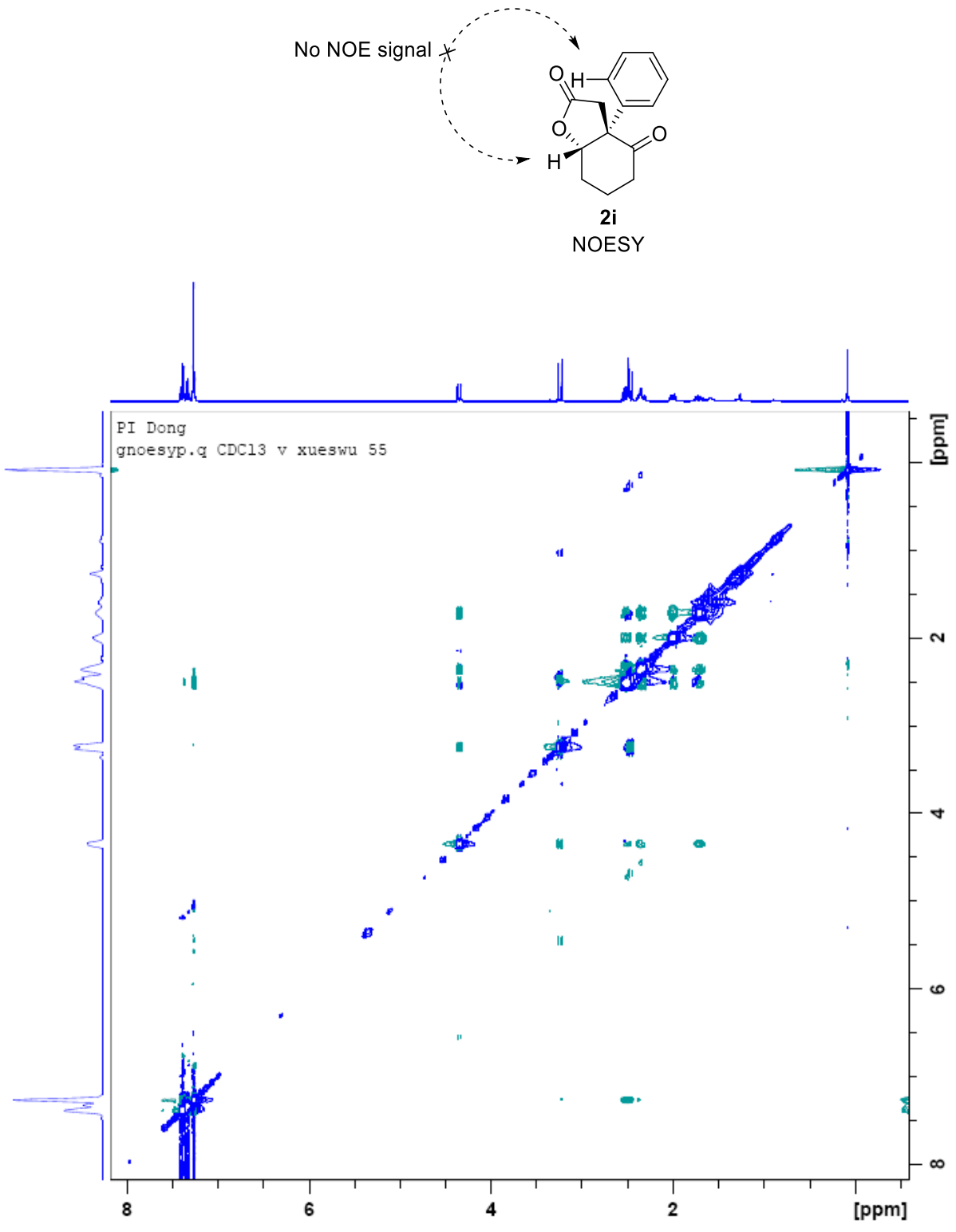


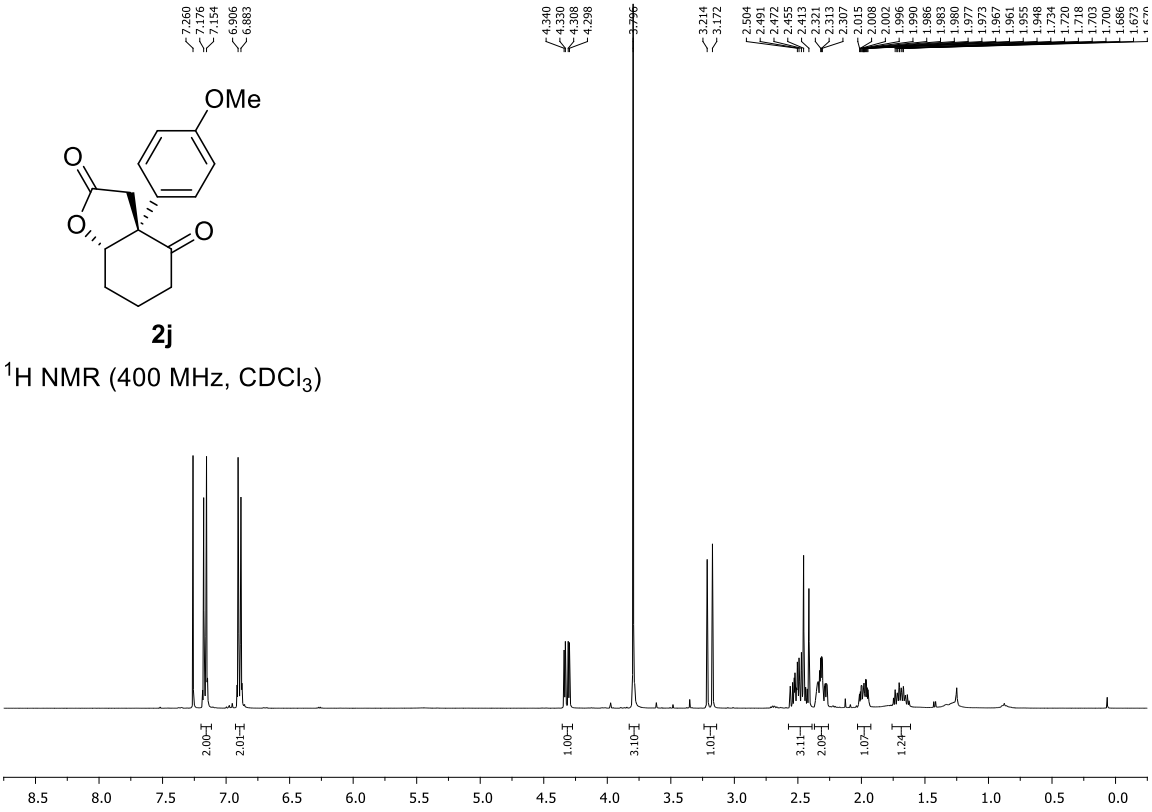



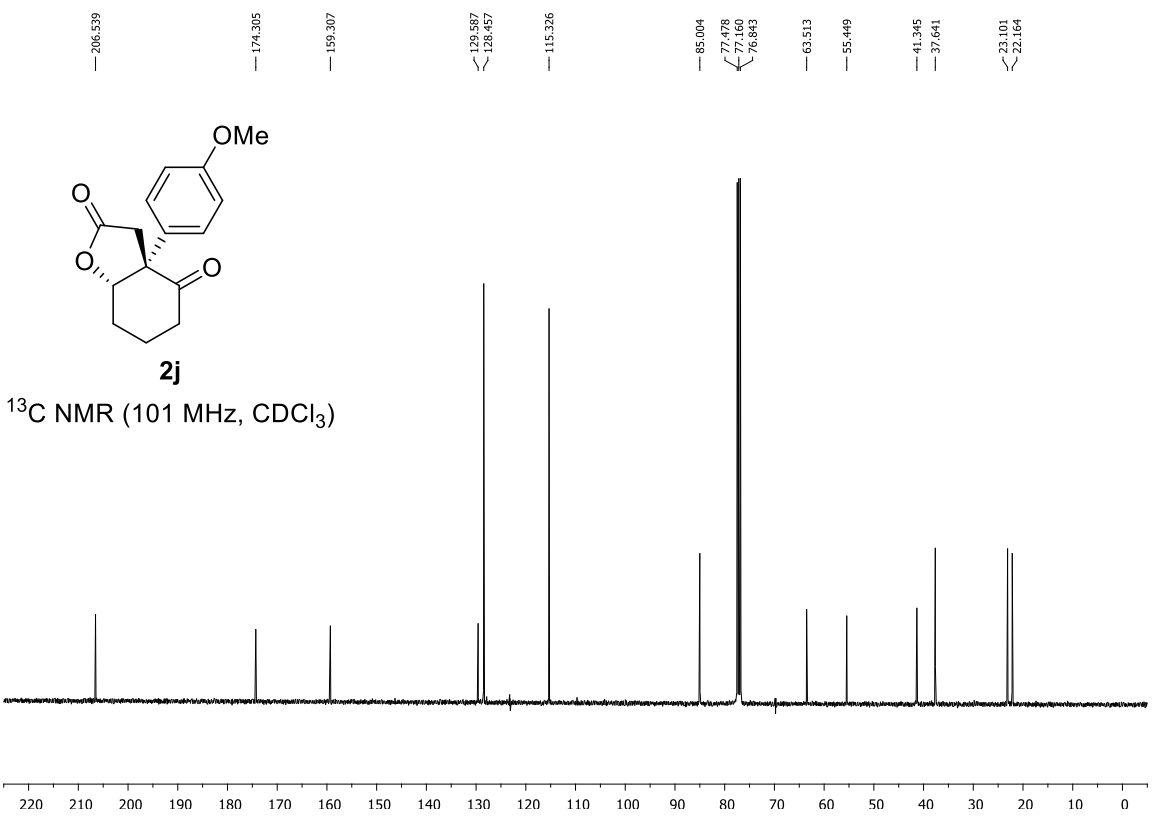


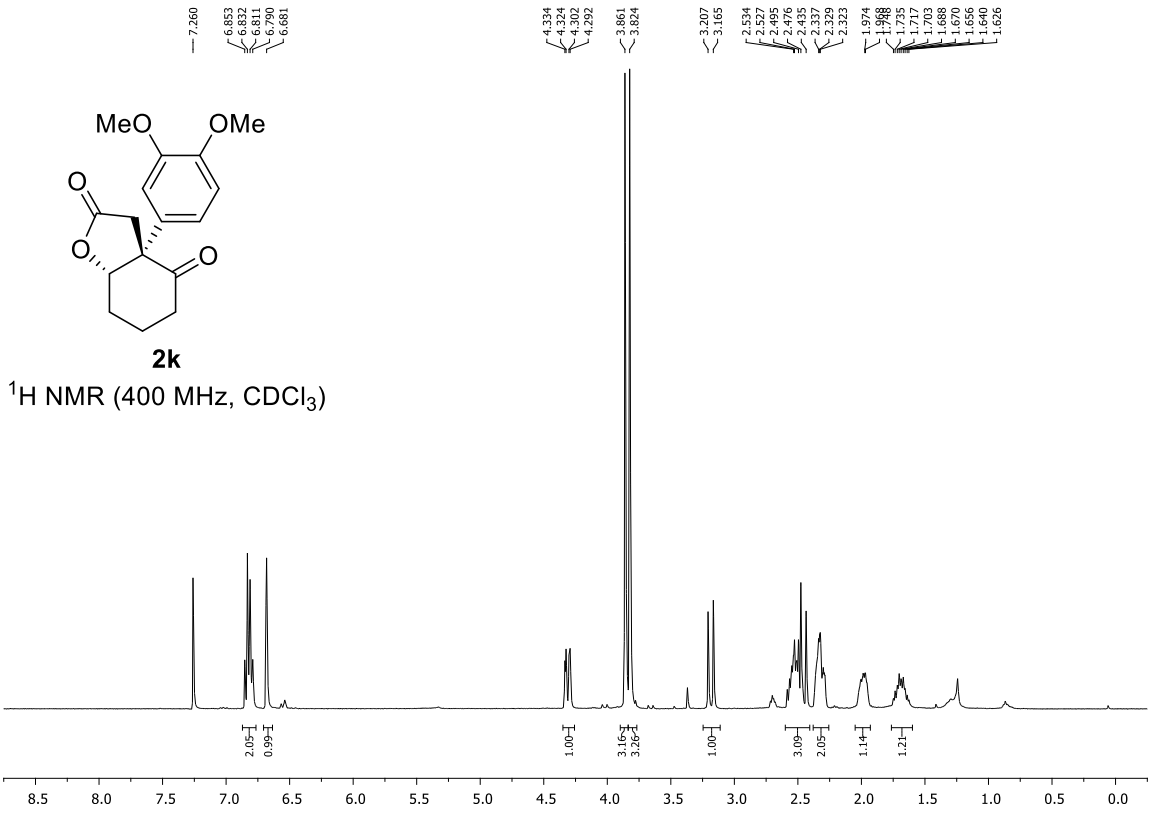

**2i**

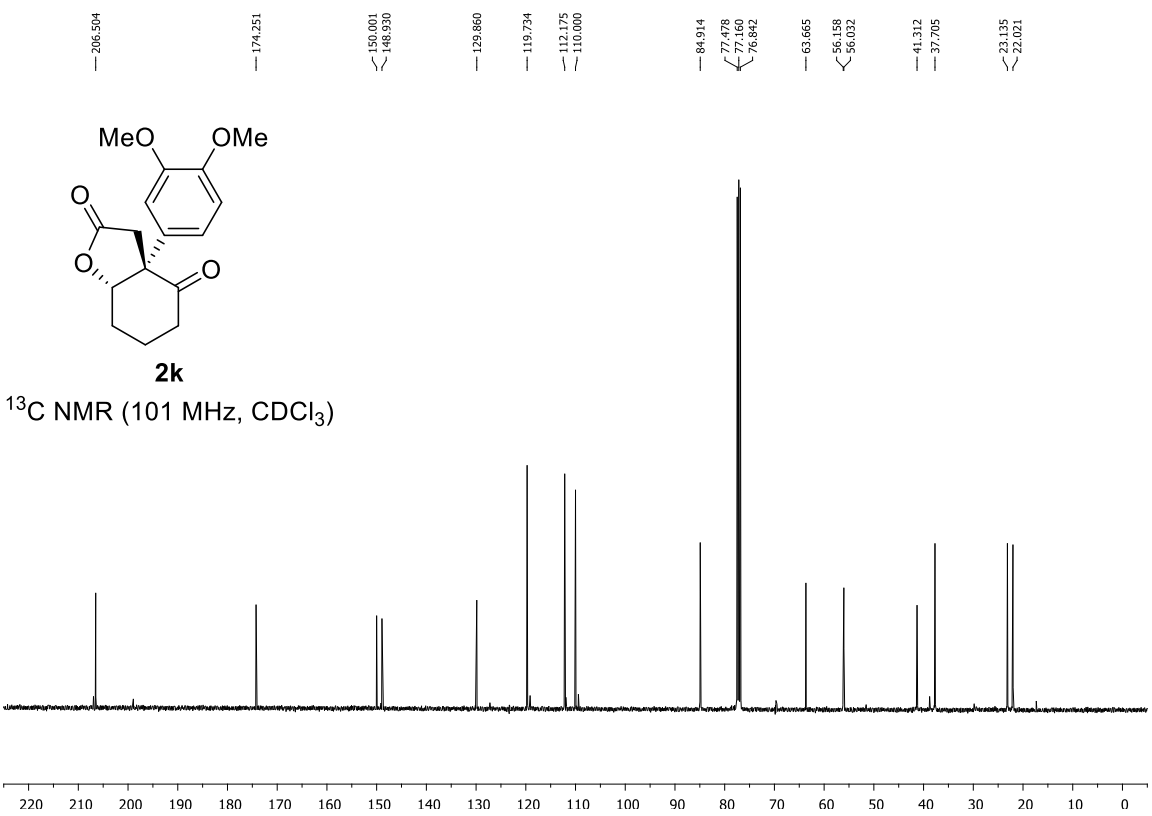
$^{13}$C NMR (101 MHz, $CDCl_3$)

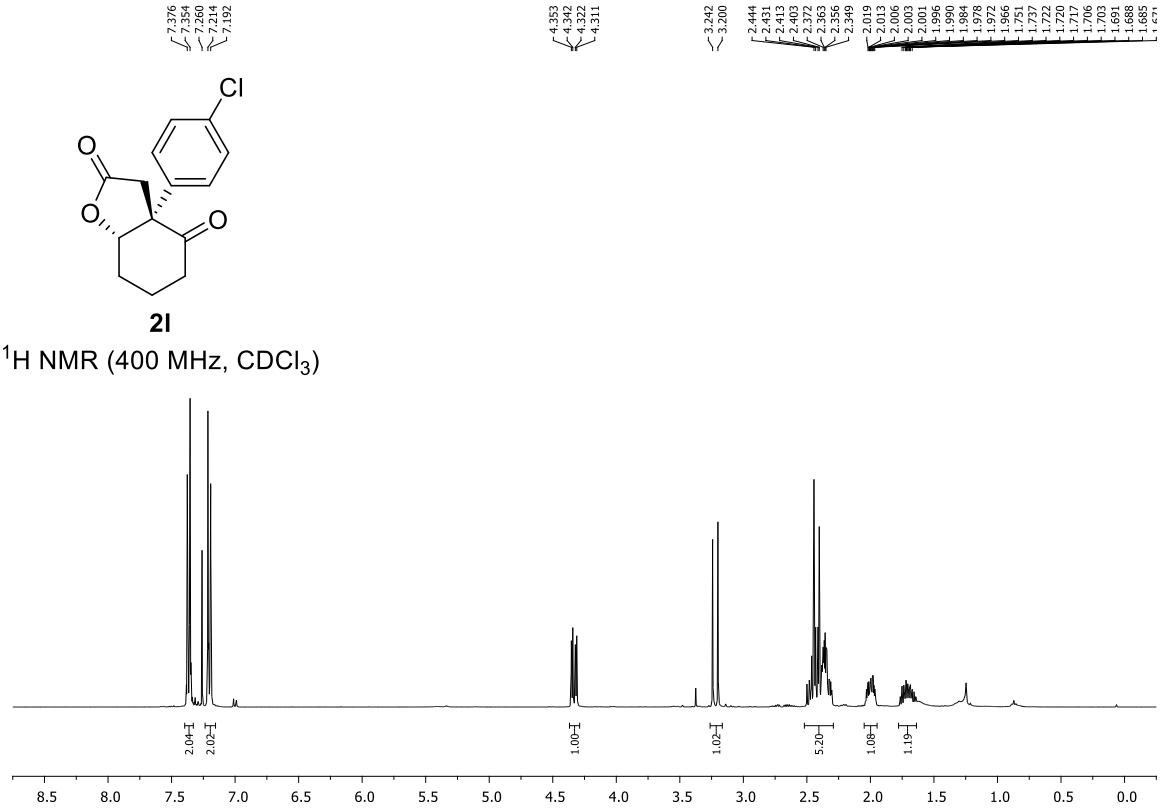

No NOE signal
O
H
O
O
H
O
2i
NOESY
PI Dong
gnoesyp.q CDCl3 v xueswu 55
[ppm]
8
6
4
2
[ppm]


OMe
O
O
O
2j
1H NMR (400 MHz, CDCl3)


OMe
O
O
O
2j
13C NMR (101 MHz, CDCl3)

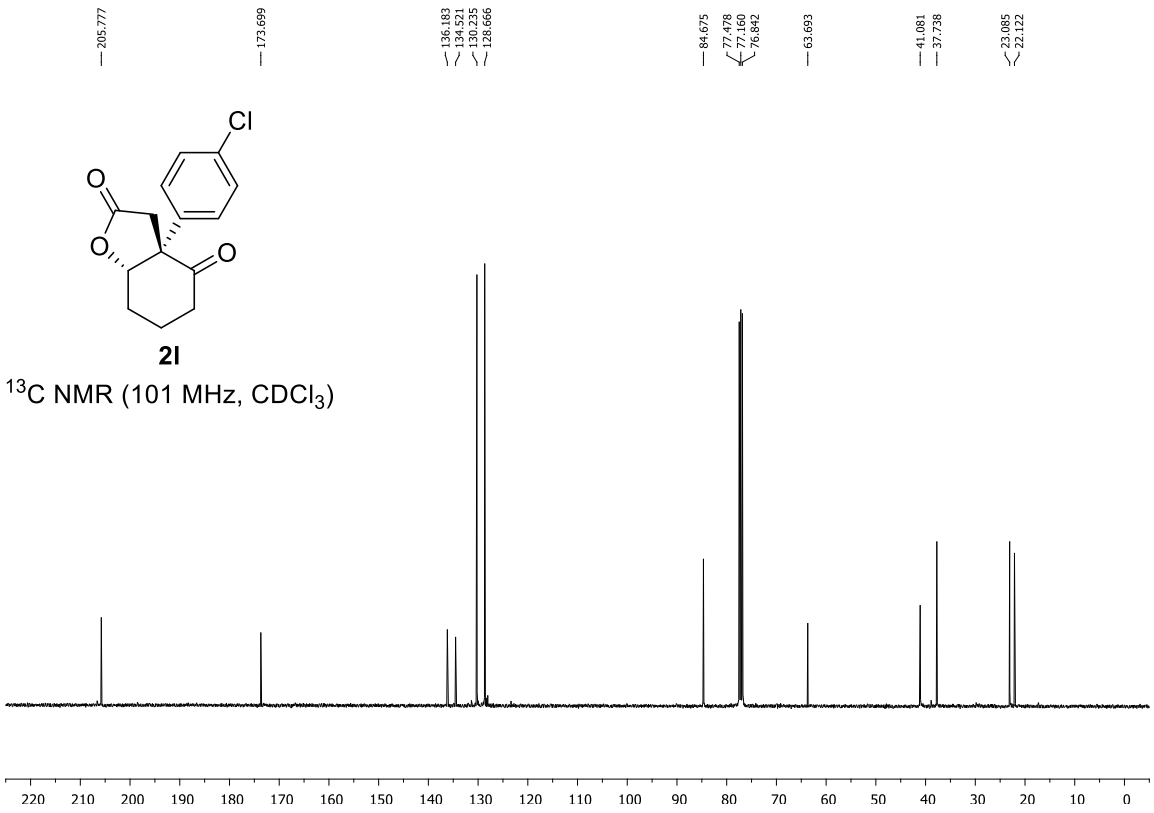

MeO
OMe
O
O
O
2k
1H NMR (400 MHz, CDCl3)


MeO
OMe
O
O
O
2k
13C NMR (101 MHz, CDCl3)



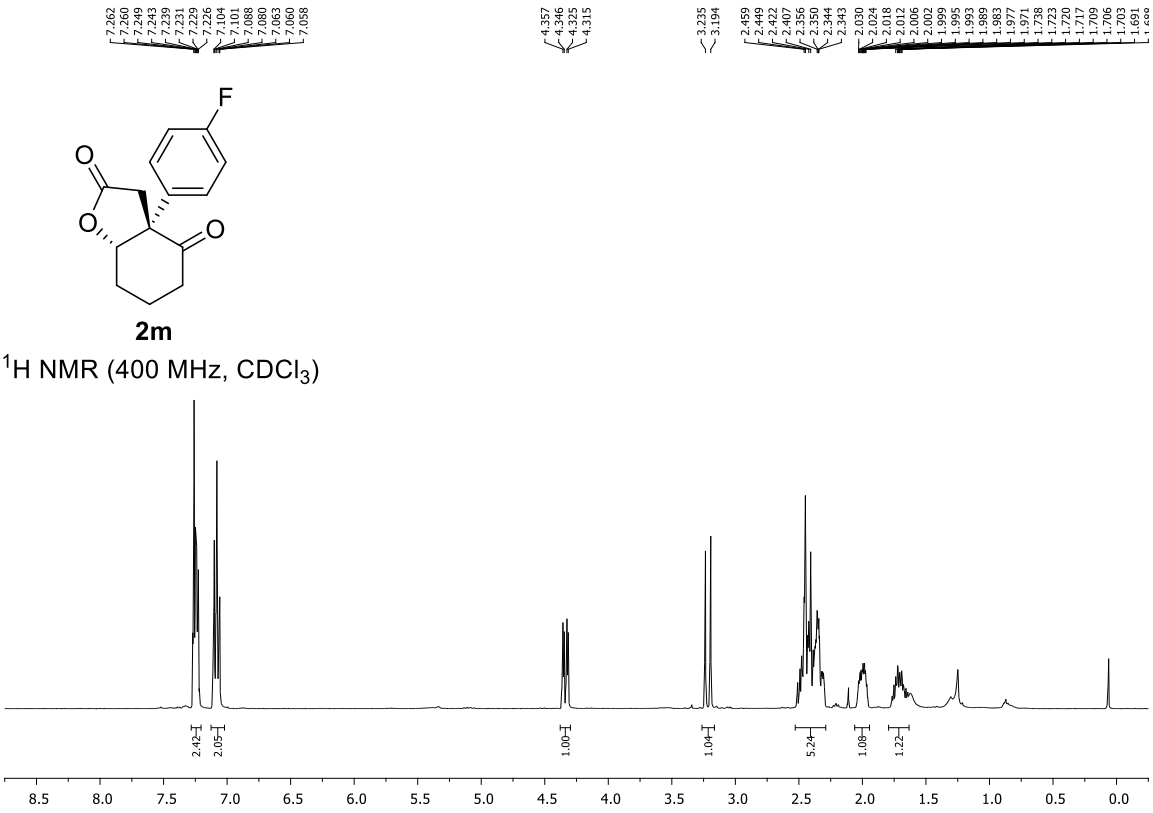

**2l**

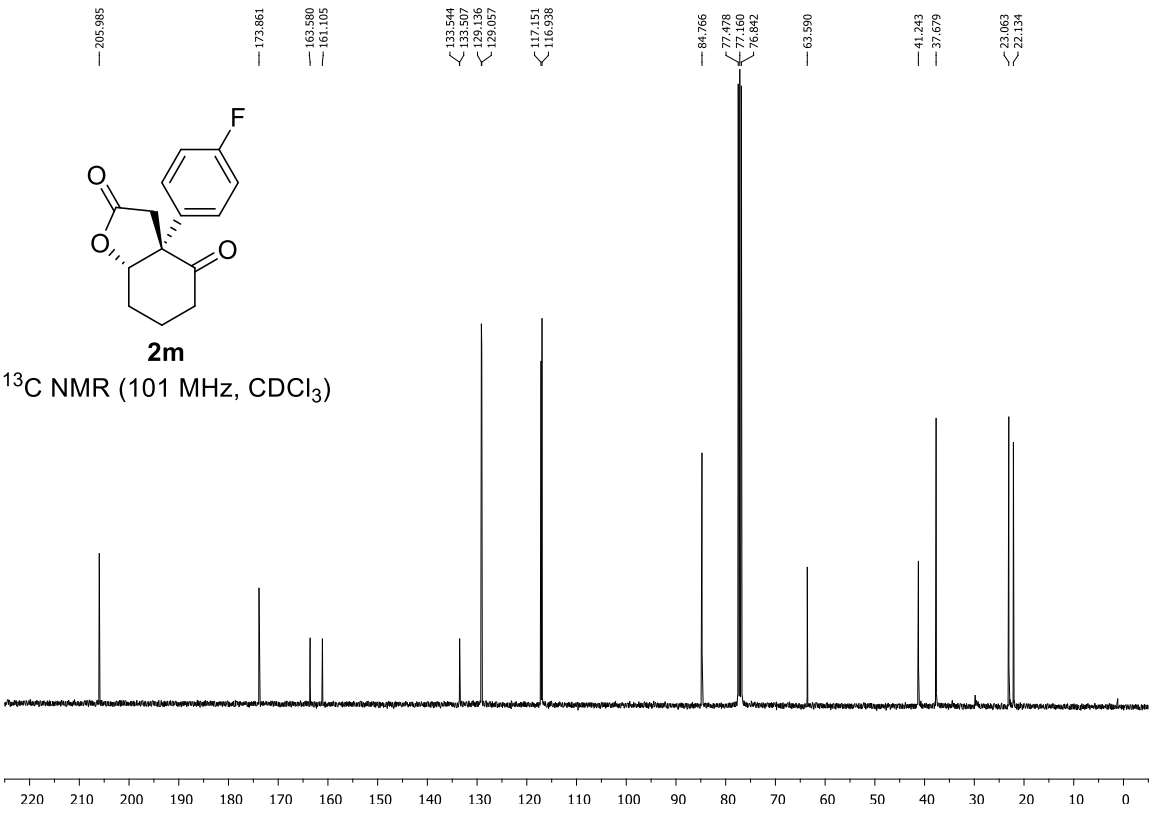
$^{1}$H NMR (400 MHz, $CDCl_3$)

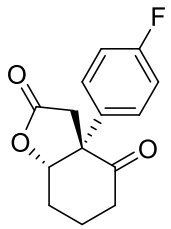



**2l**

$^{13}$C NMR (101 MHz, $CDCl_3$)

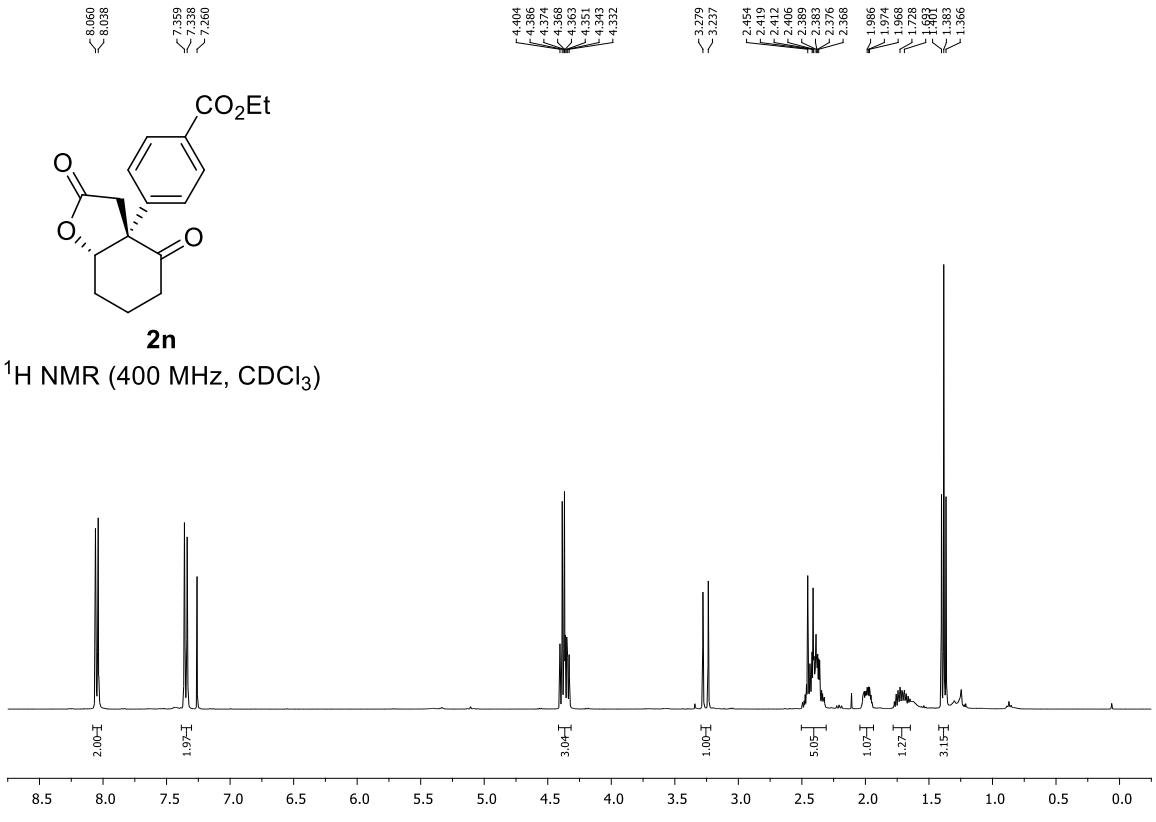

F
O
O
O
2m
1H NMR (400 MHz, CDCl3)


F
O
O
O
2m
13C NMR (101 MHz, CDCl3)



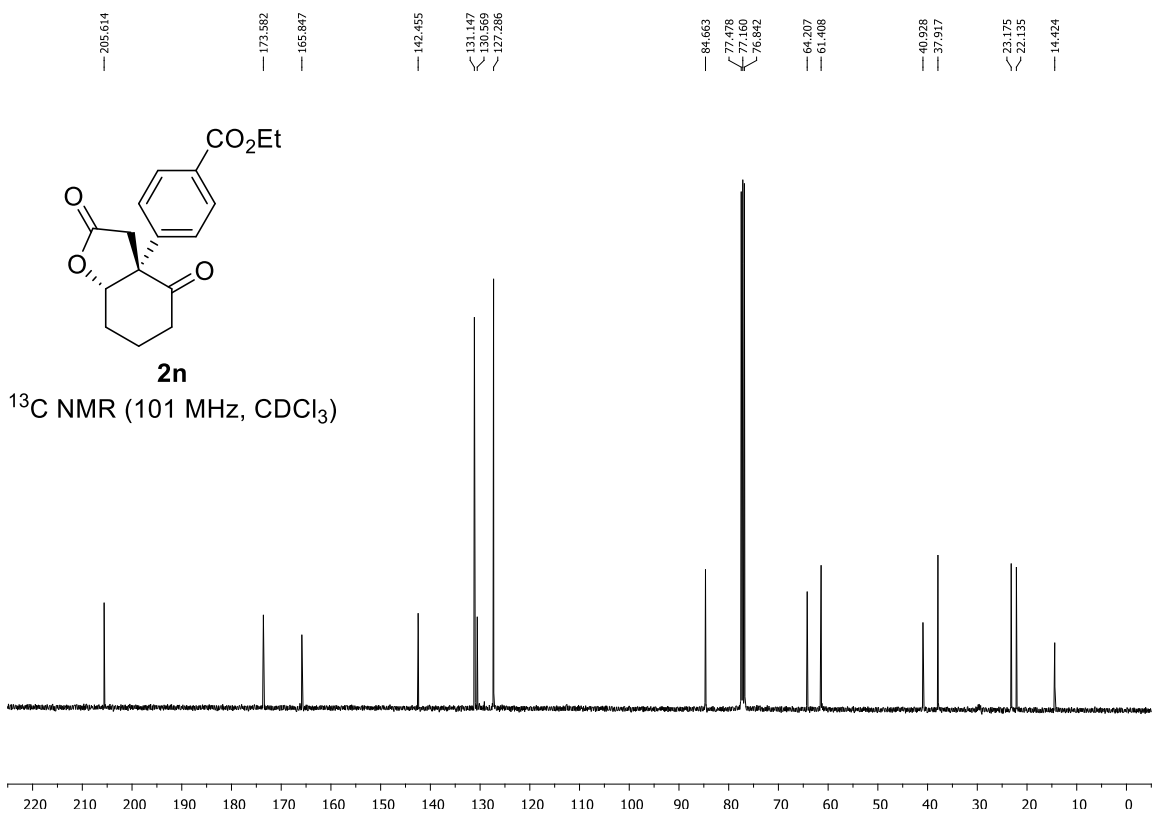

**2m**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



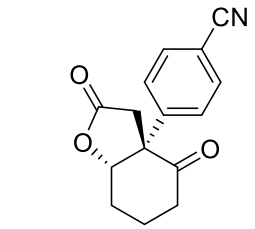

**2n**

$^{1}$H NMR (400 MHz, $CDCl_3$)




**2n**

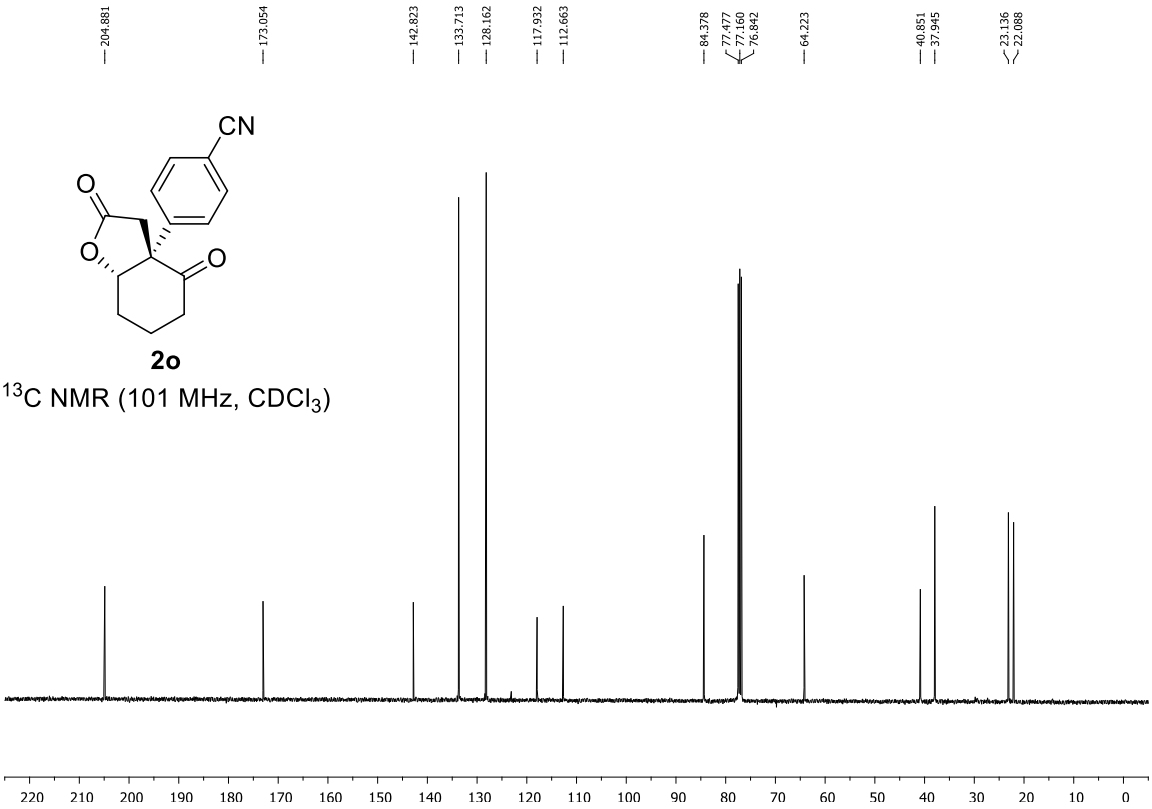
$^{13}$C NMR (101 MHz, $CDCl_3$)




**2o**

$^{1}$H NMR (400 MHz, $CDCl_3$)



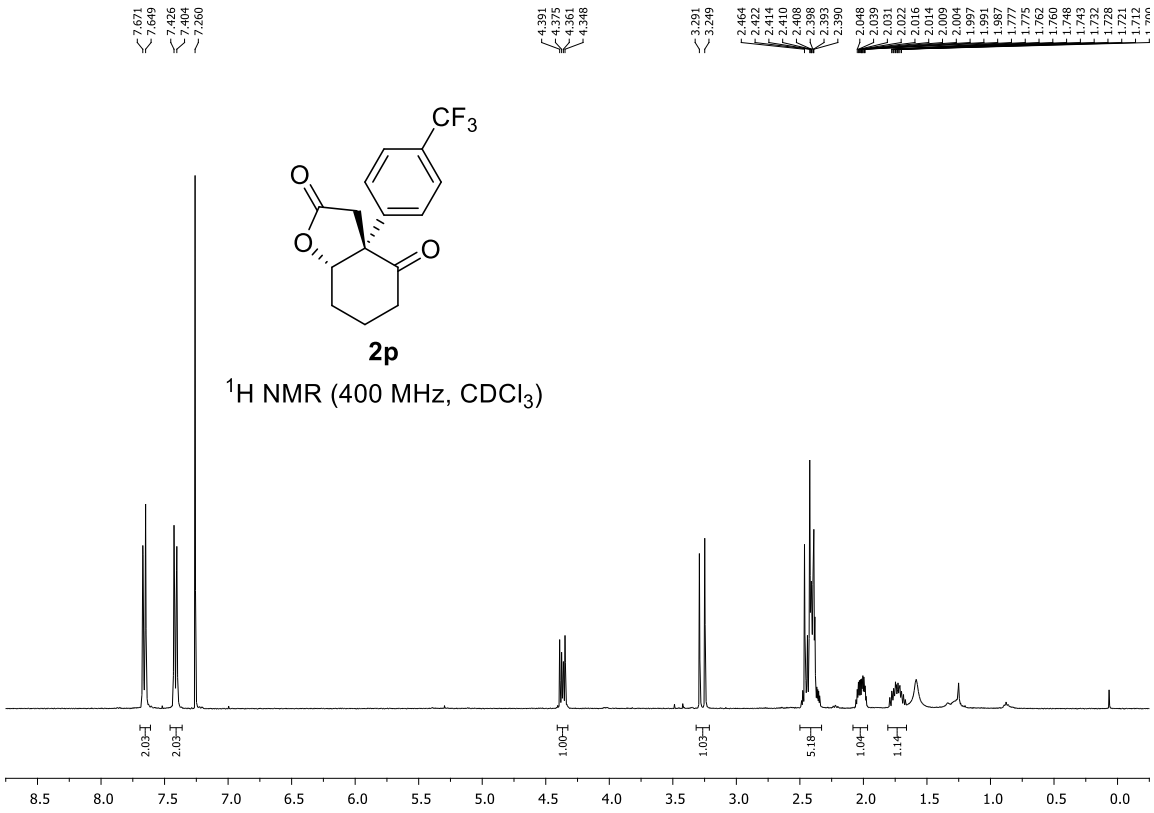







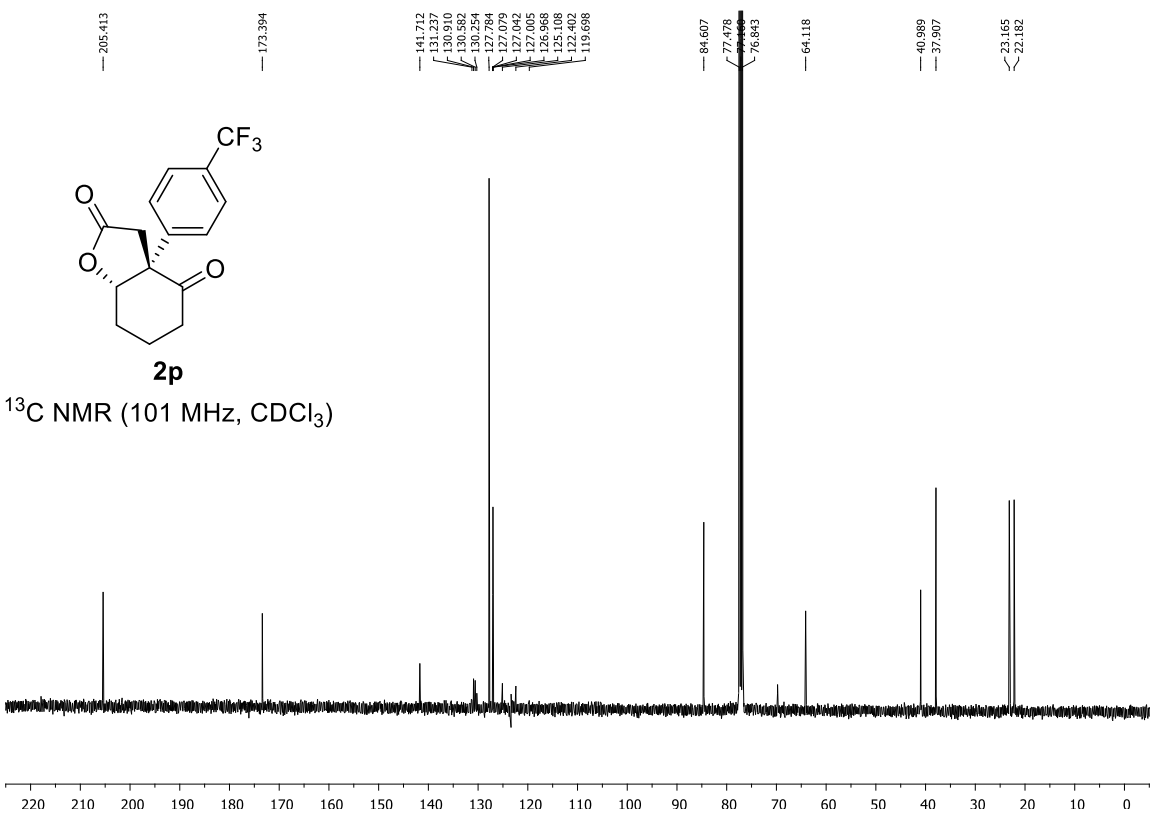
**2o**

$^{13}$C NMR (101 MHz, $CDCl_3$)



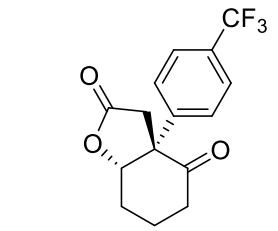

**2p**

$^{1}$H NMR (400 MHz, $CDCl_3$)



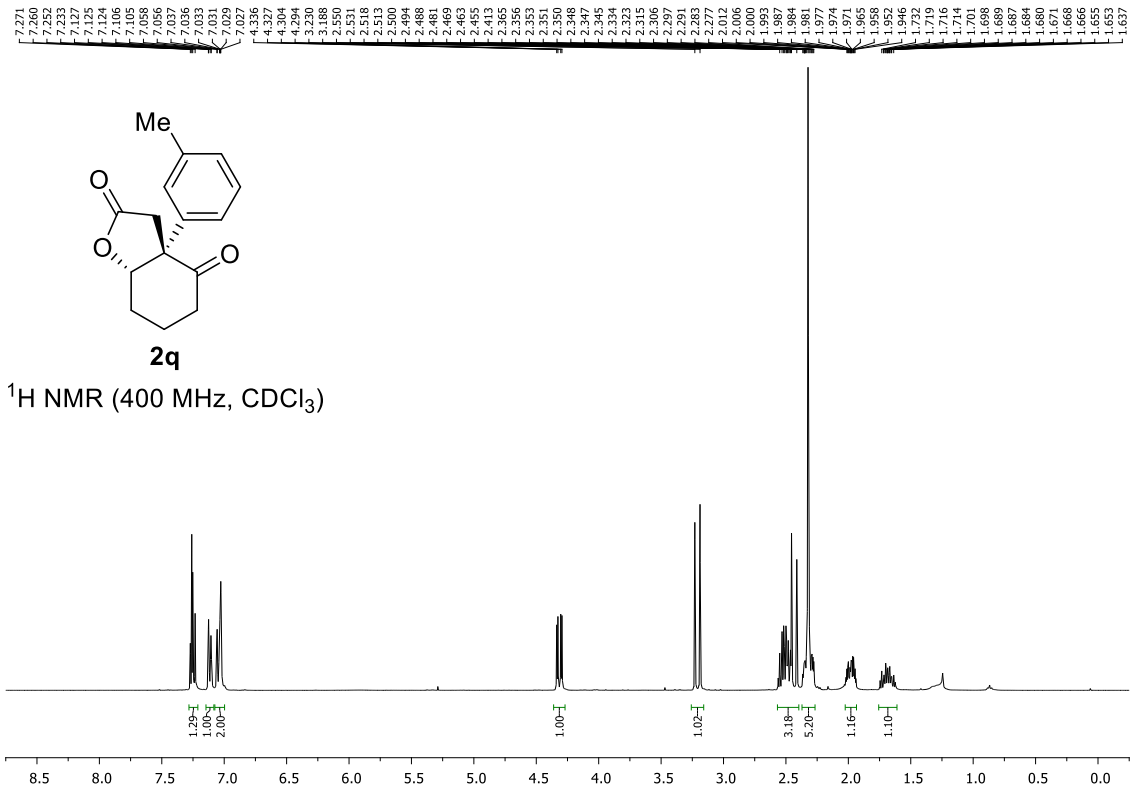

**2p**

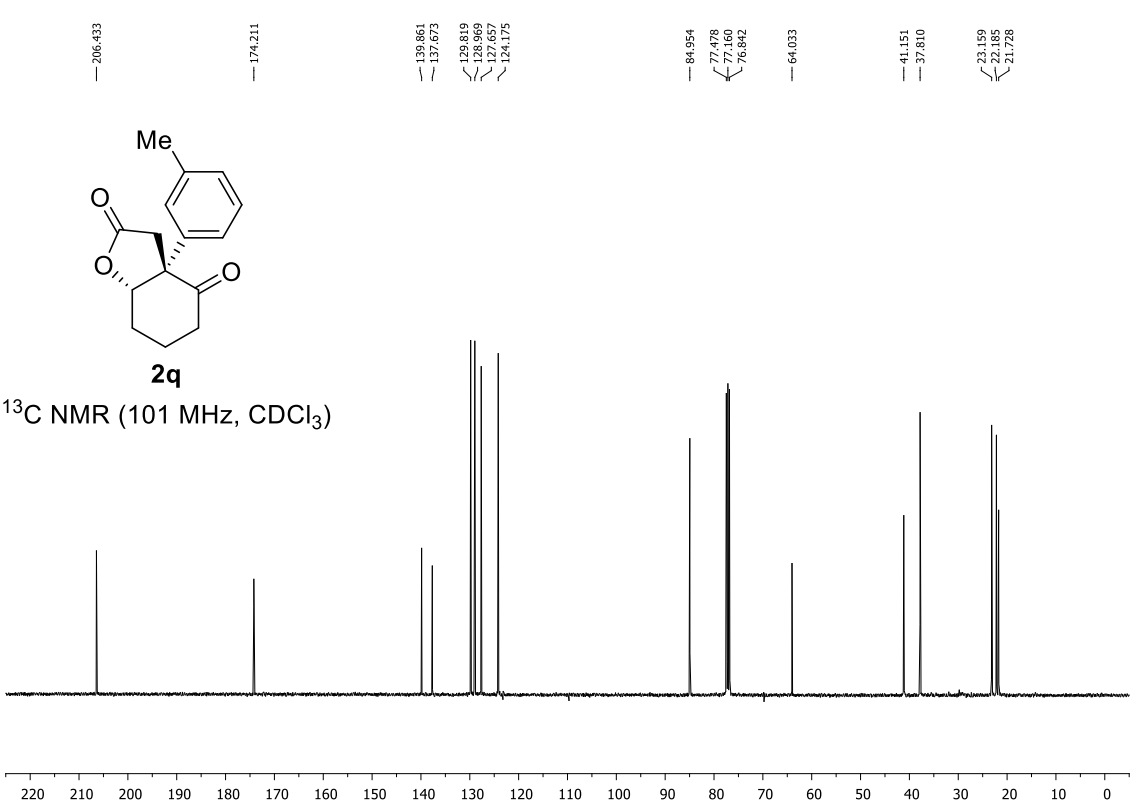
$^{13}$C NMR (101 MHz, $CDCl_3$)

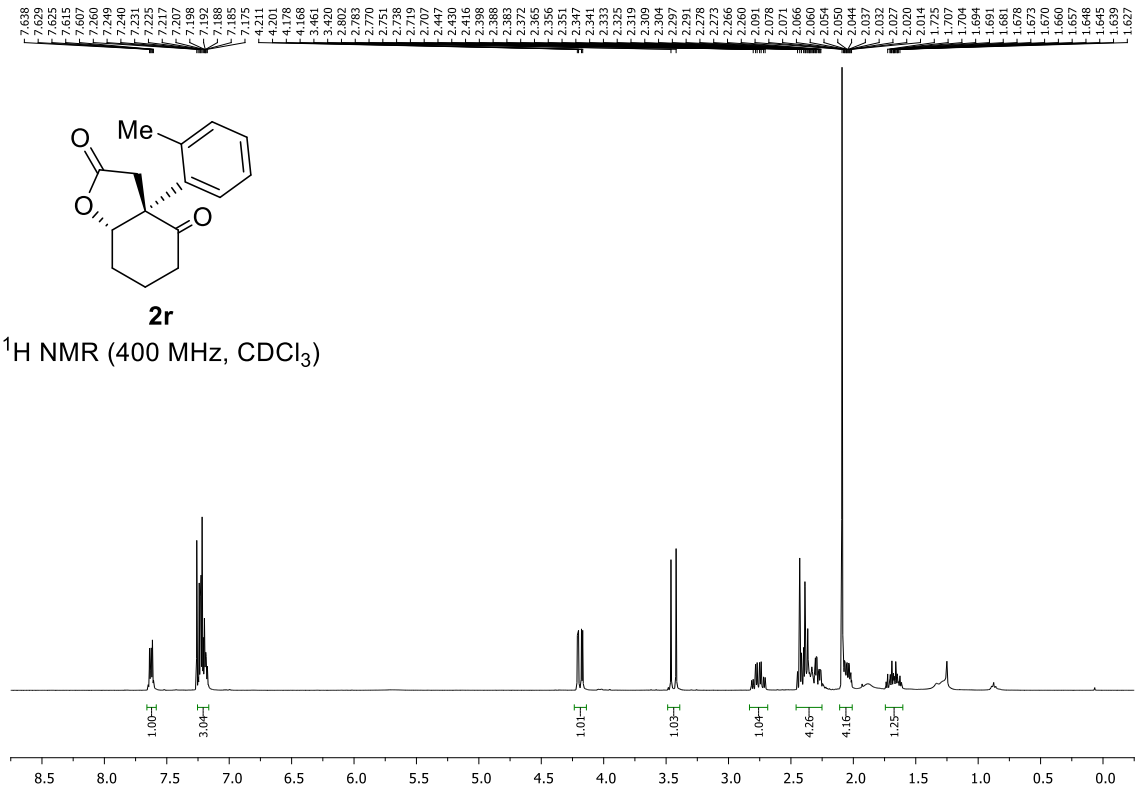



**2p**

$^{19}F$ NMR (376 MHz, $CDCl_3$)

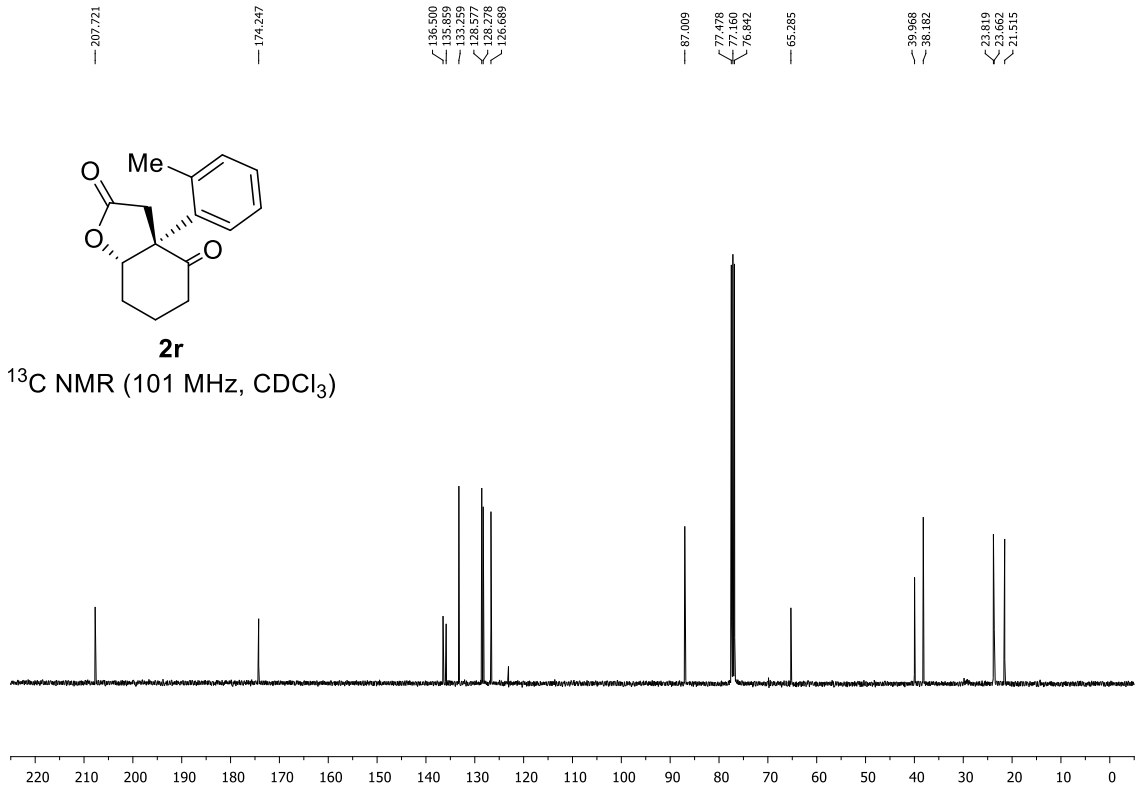

Me
O
O
O
2q
1H NMR (400 MHz, CDCl3)


Me
O
O
O
2q
13C NMR (101 MHz, CDCl3)



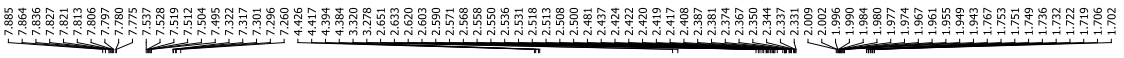

**2r**

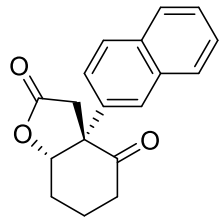
$^{1}$H NMR (400 MHz, $CDCl_3$)




**2r**

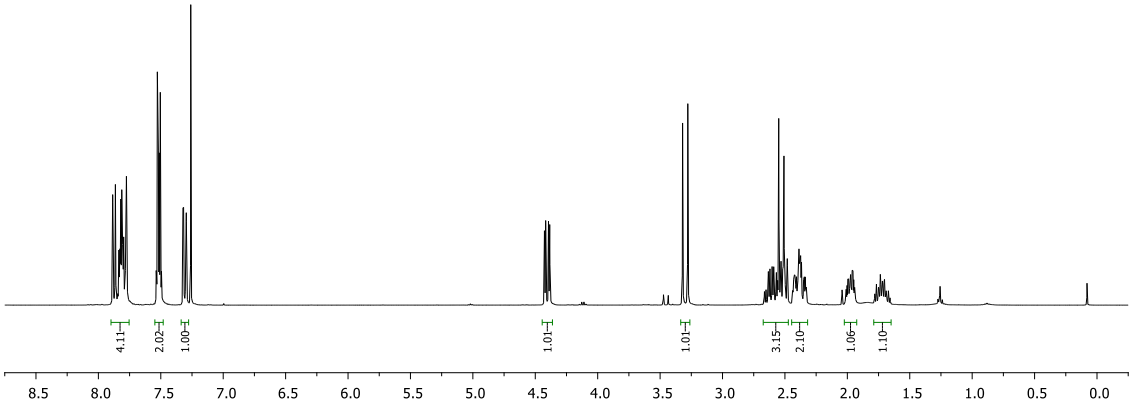
$^{13}$C NMR (101 MHz, $CDCl_3$)

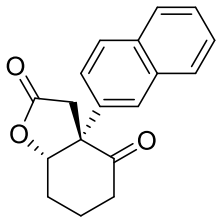




**2s**

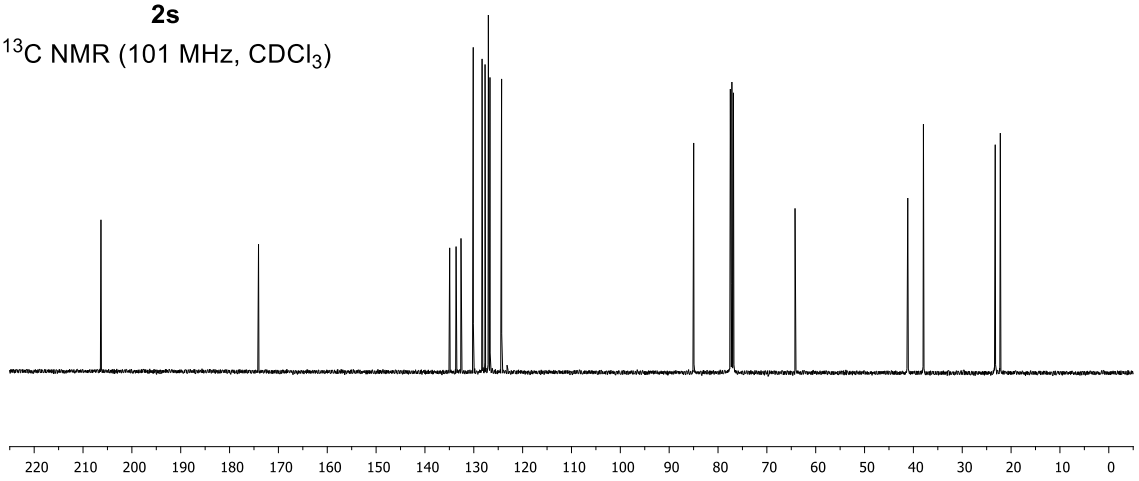
$^{1}H$ NMR (400 MHz, $CDCl_3$)





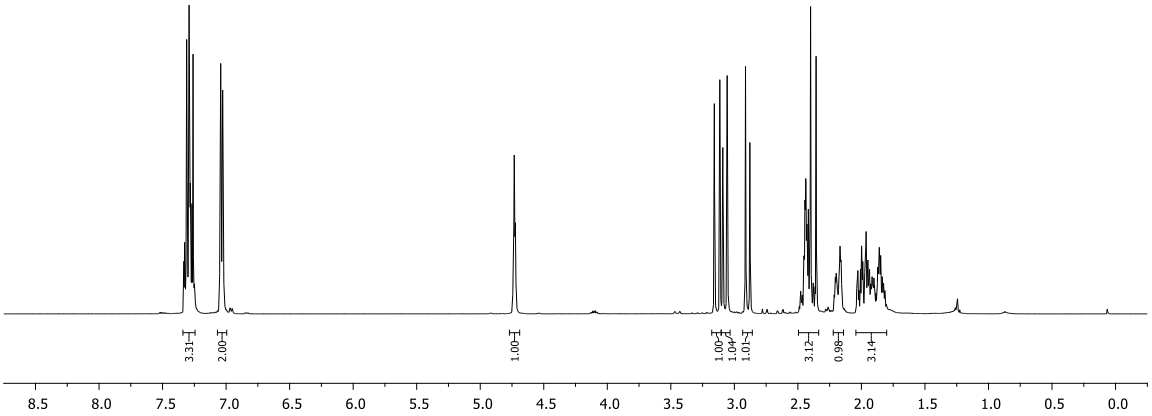
**2s**

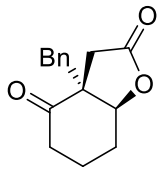
$^{13}C$ NMR (101 MHz, $CDCl_3$)



**3a**

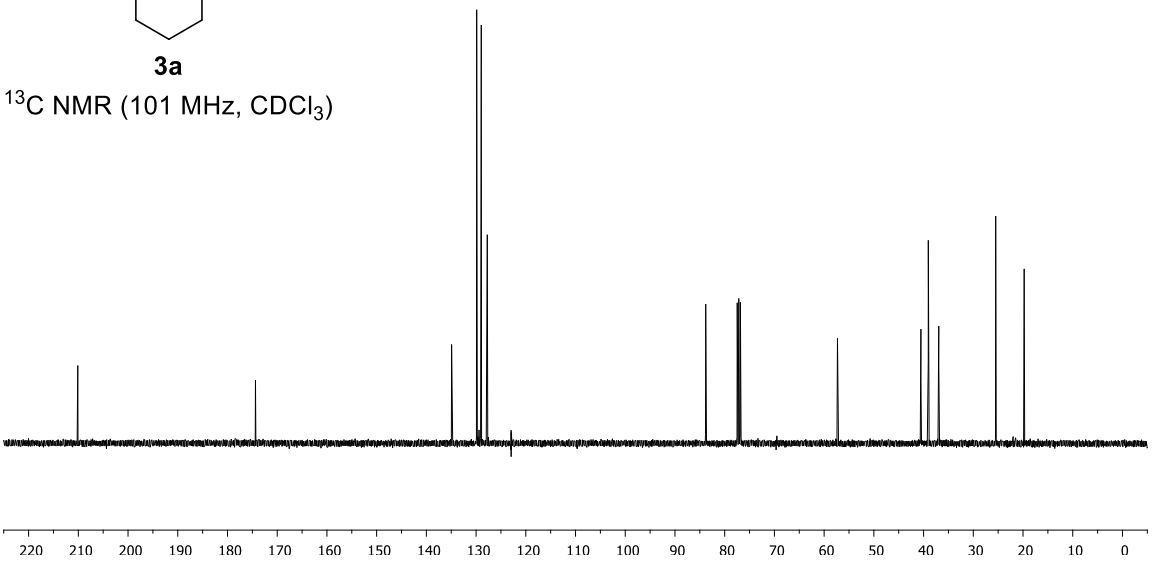
$^{1}H$ NMR (400 MHz, $CDCl_3$)

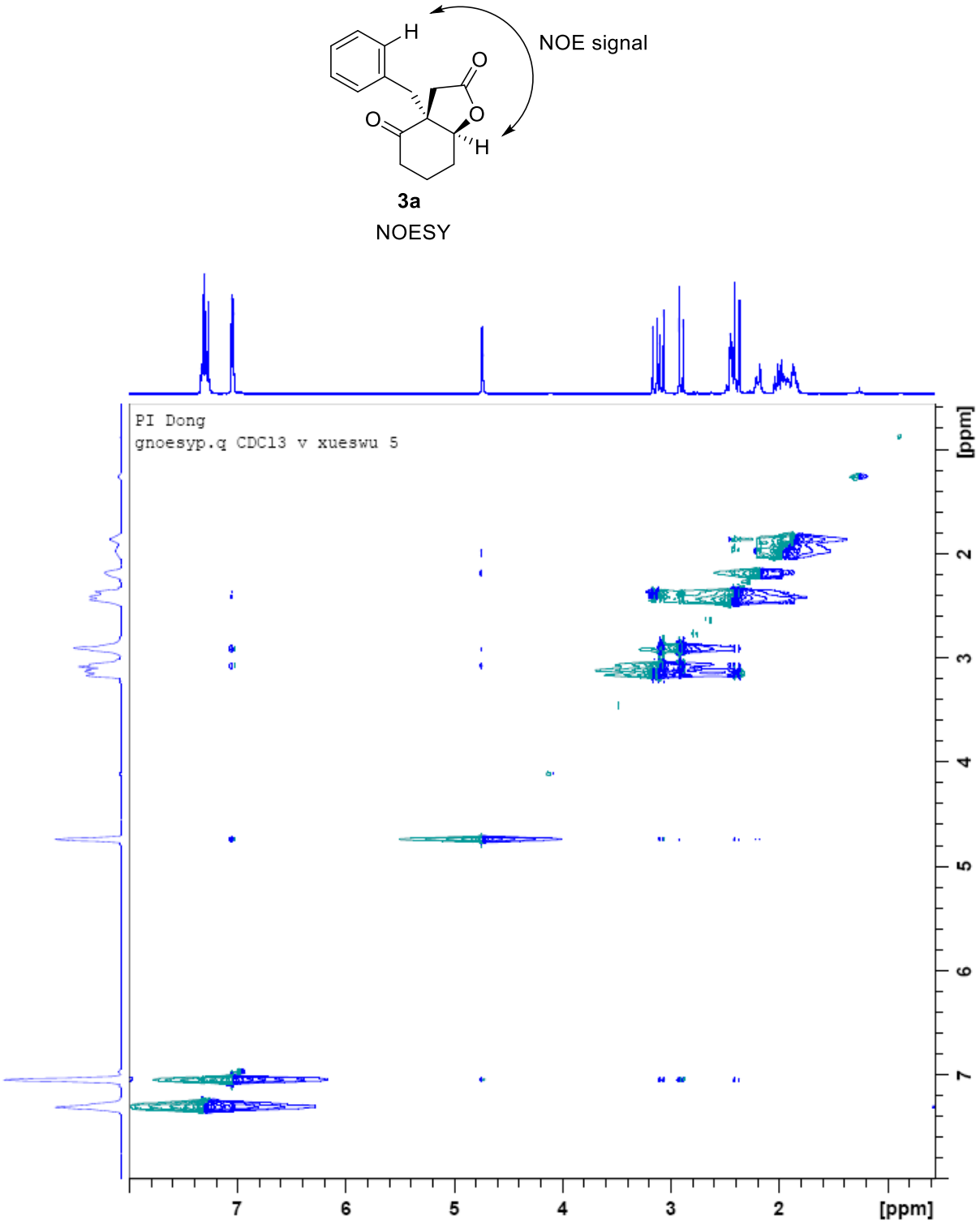


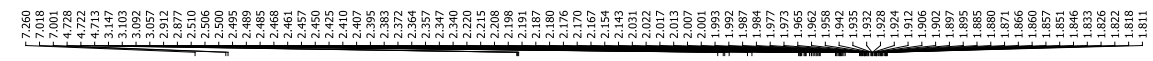


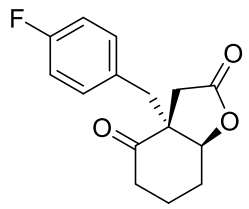
**3a**

$^{13}C$ NMR (101 MHz, $CDCl_3$)



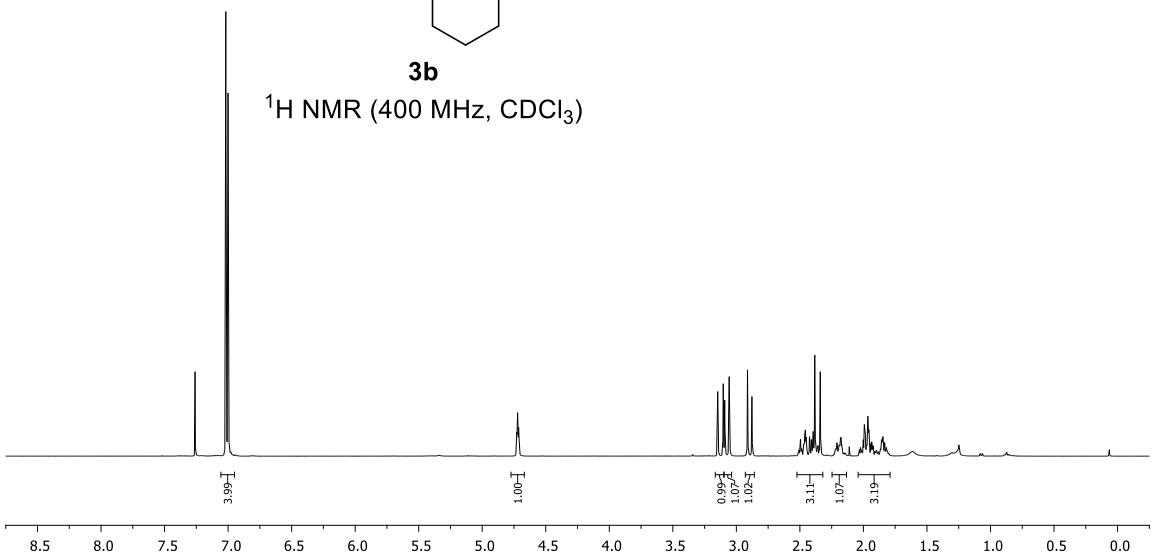

H
O
O
O
H
NOE signal
3a
NOESY
PI Dong
gnoesyp.q CDCl3 v xueswu 5
[ppm]
7
6
5
4
3
2
[ppm]

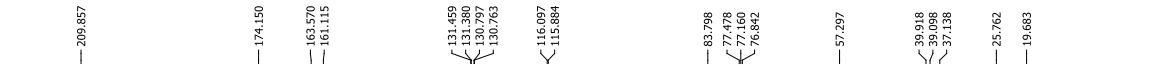


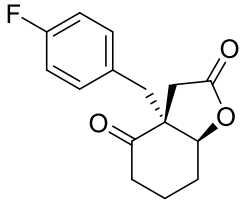


**3b**

$^{1}$H NMR (400 MHz, $CDCl_3$)

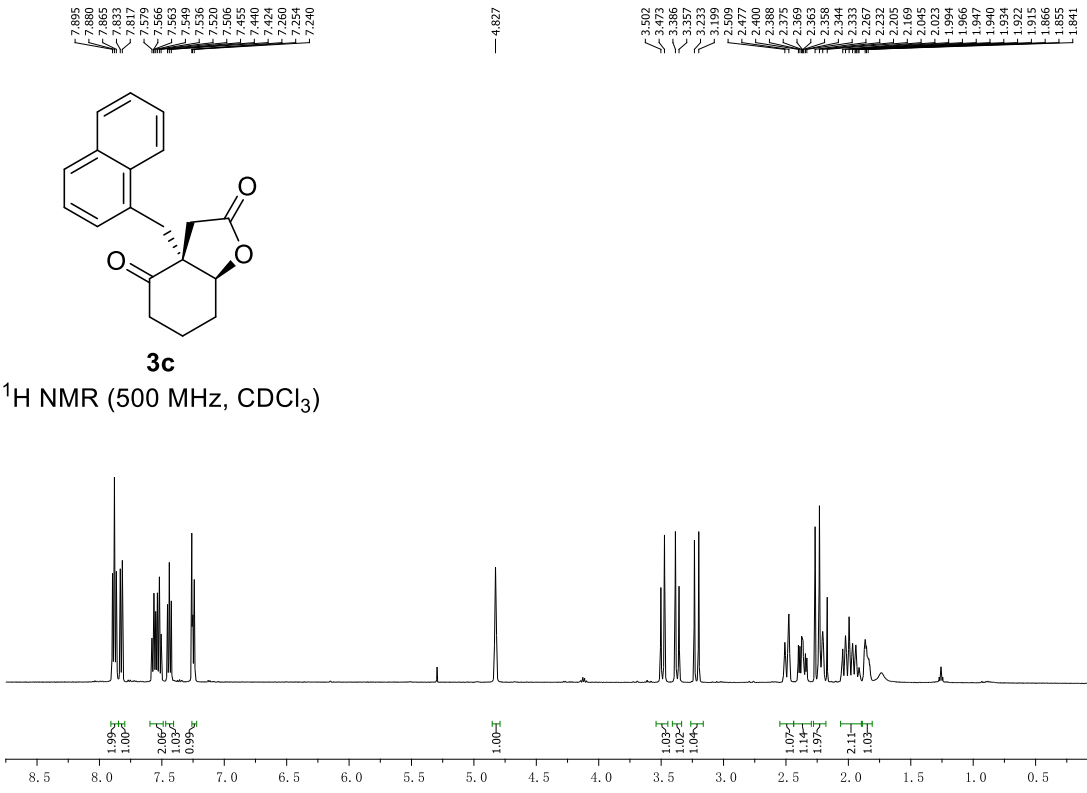






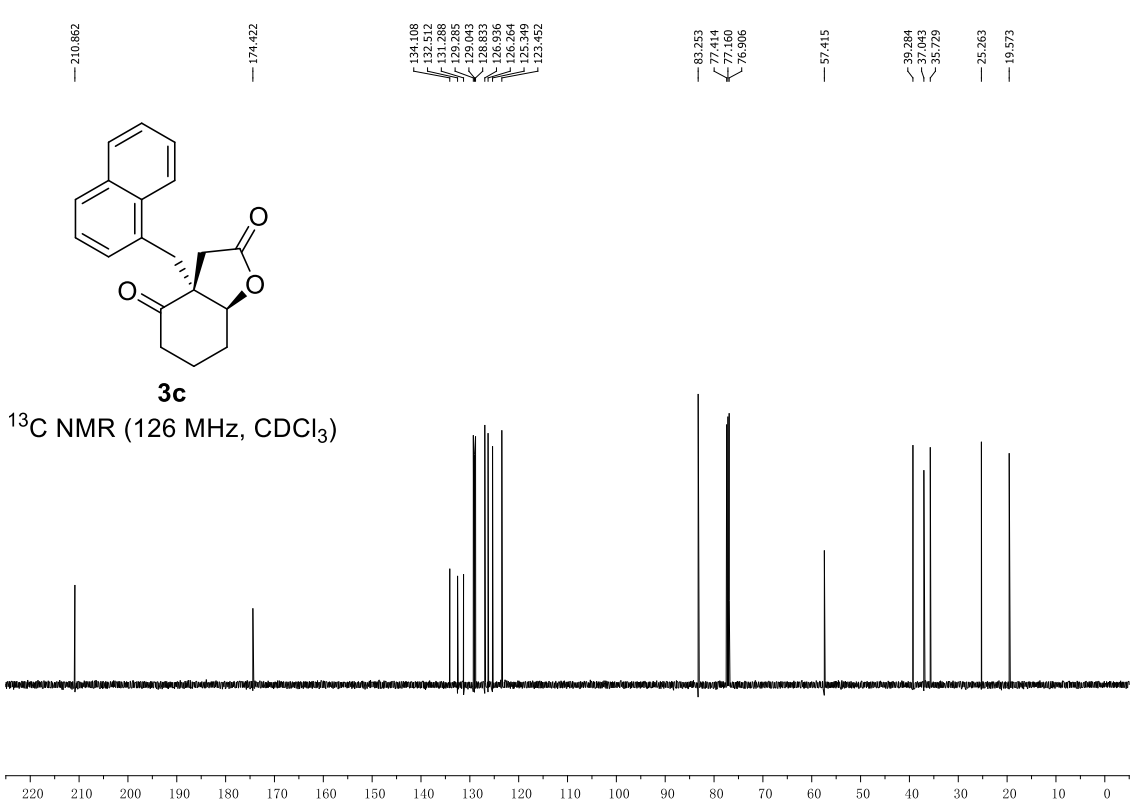
**3b**

$^{13}$C NMR (101 MHz, $CDCl_3$)



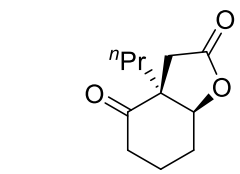

**3c**

$^{1}$H NMR (500 MHz, $CDCl_3$)




**3c**

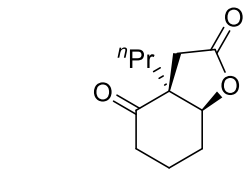
$^{13}$C NMR (126 MHz, $CDCl_3$)



**3d**

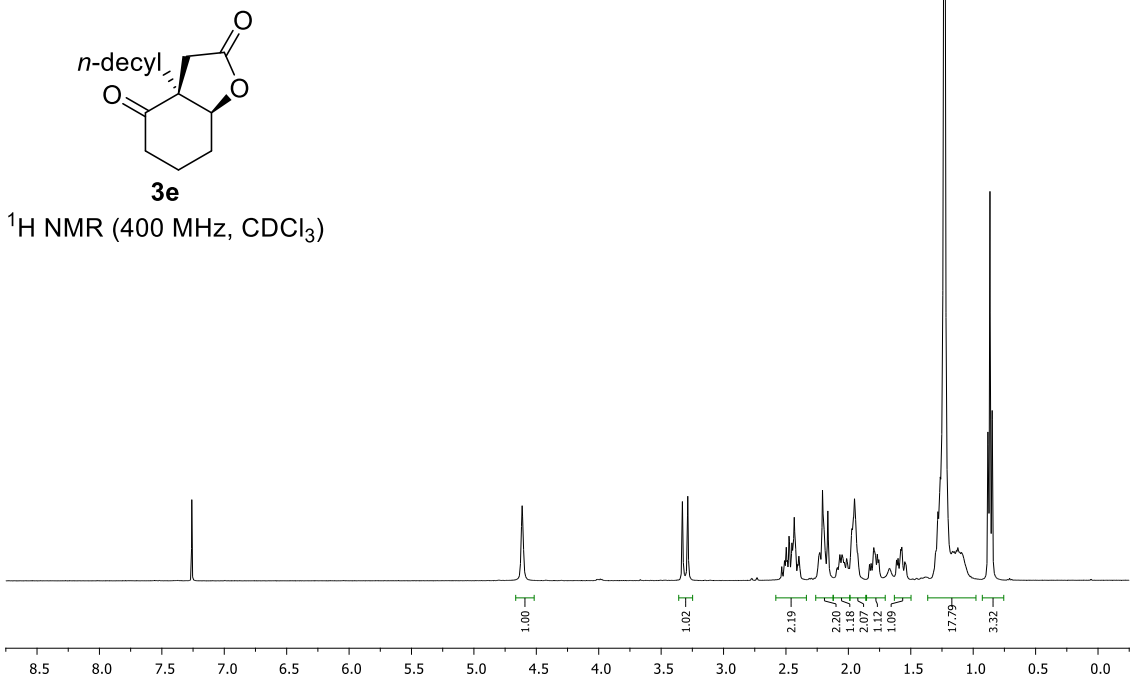
$^1$H NMR (400 MHz, $CDCl_3$)



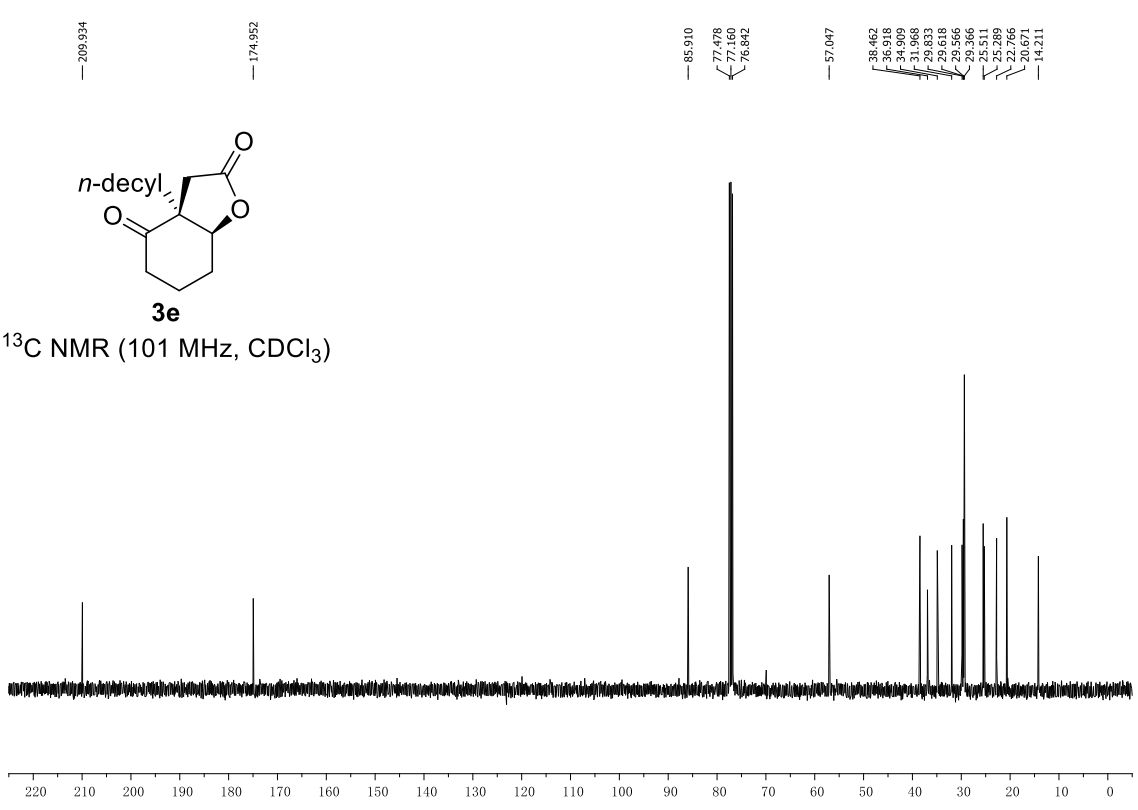
**3d**

$^{13}$C NMR (101 MHz, $CDCl_3$)



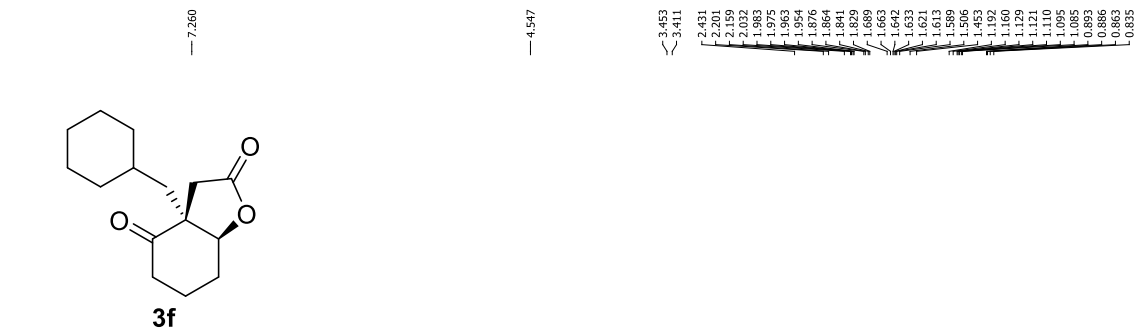

**3e**

$^{1}$H NMR (400 MHz, $CDCl_3$)



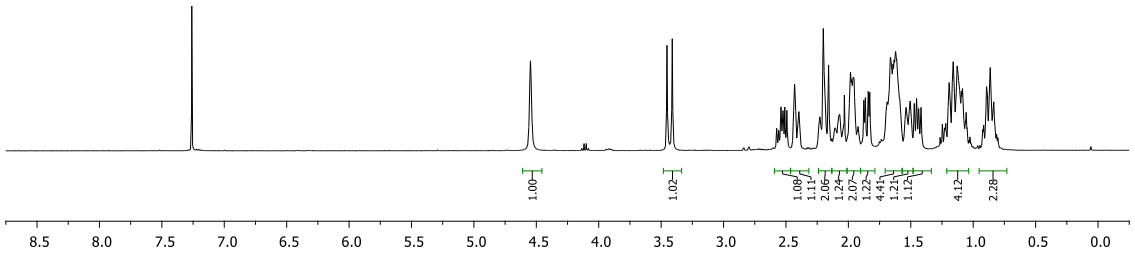

**3e**

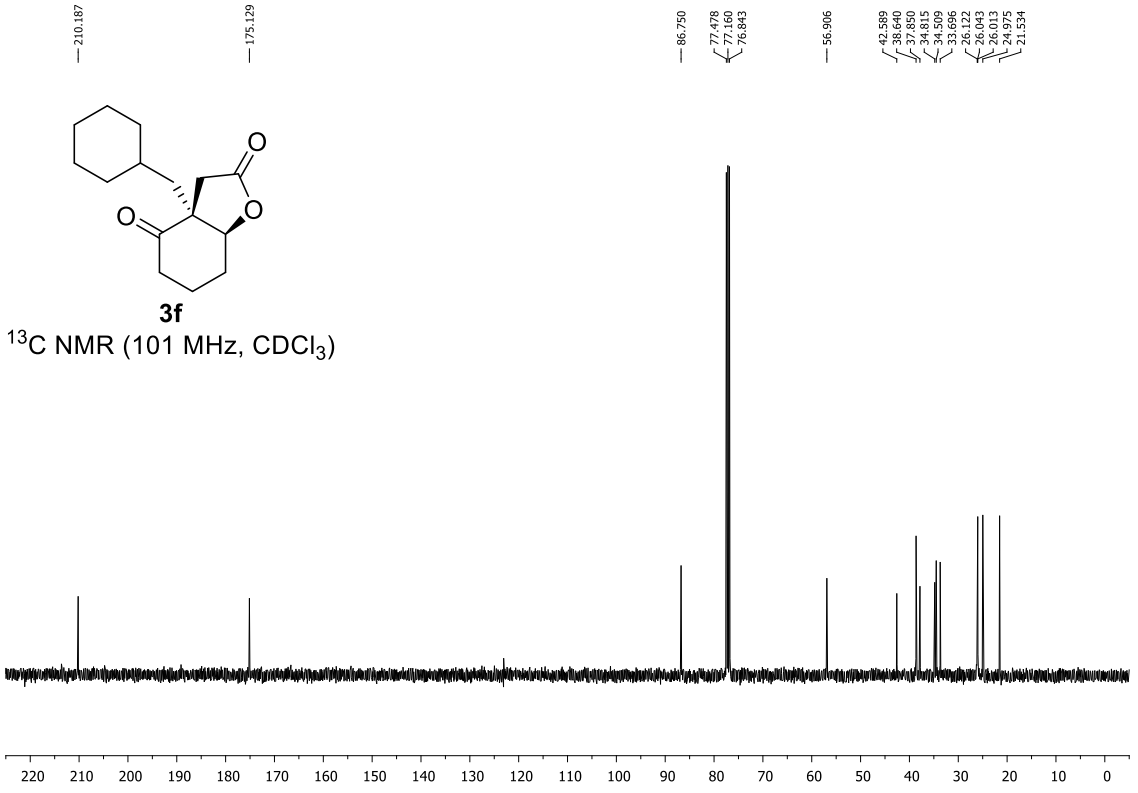
$^{13}$C NMR (101 MHz, $CDCl_3$)



**3f**

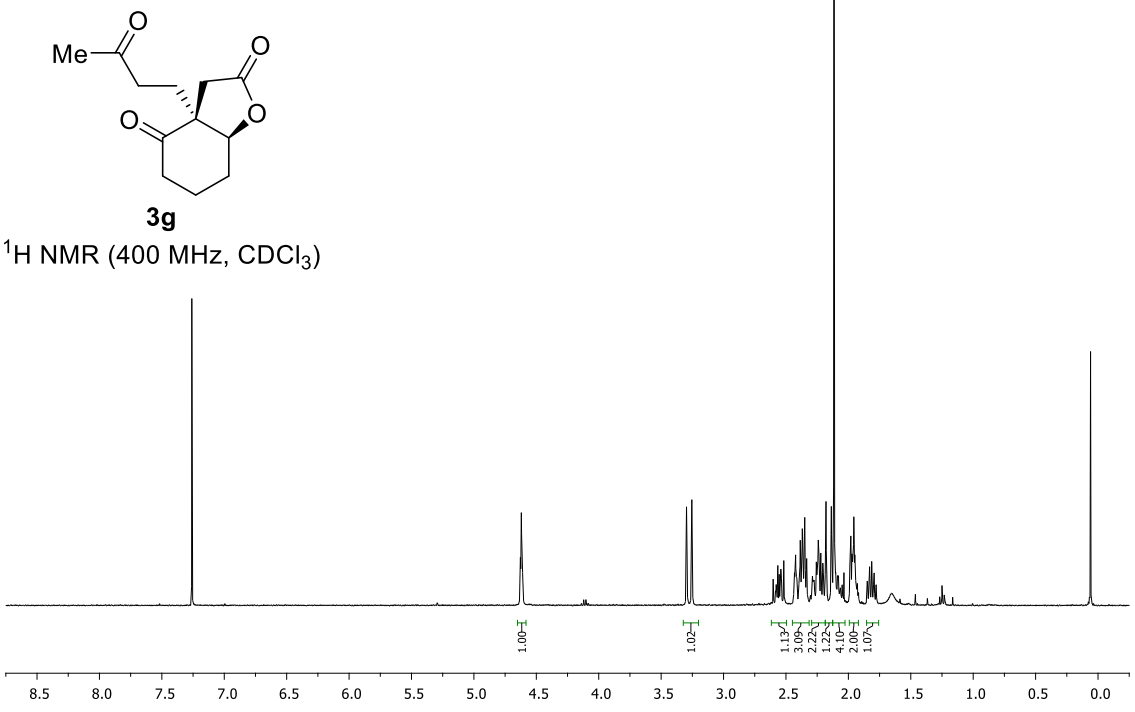
$^{1}$H NMR (400 MHz, $CDCl_3$)





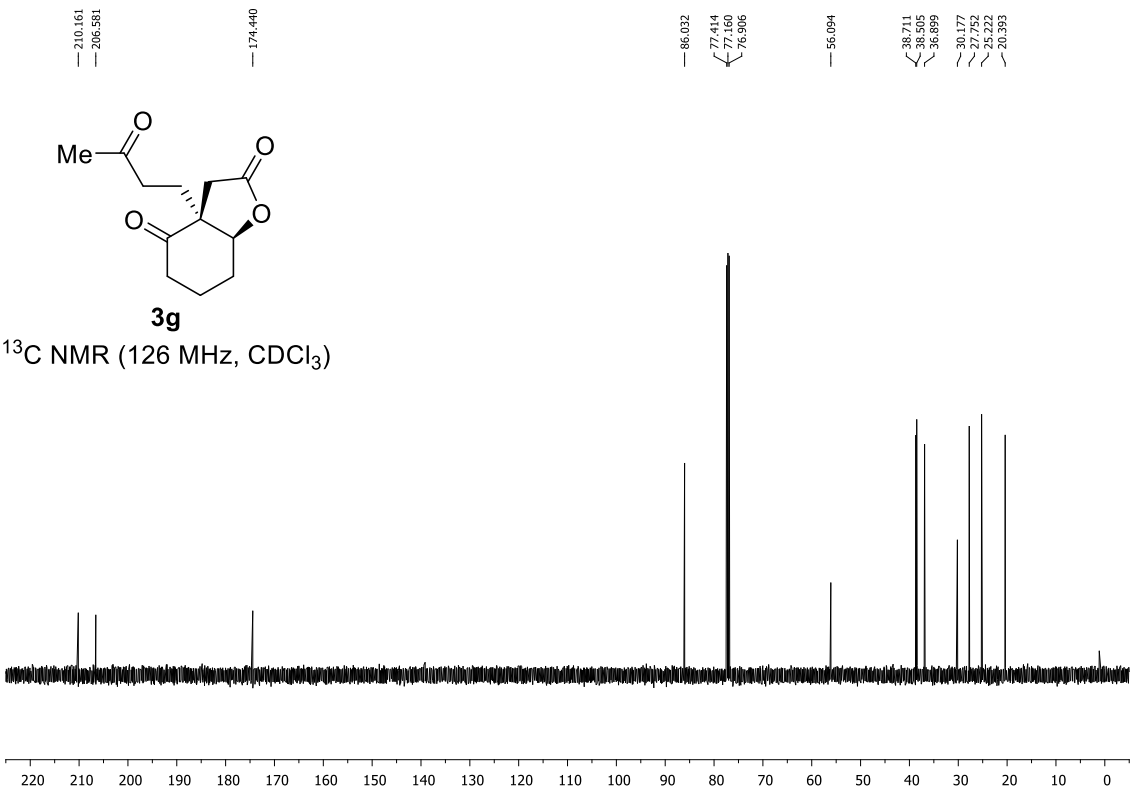
**3f**

$^{13}$C NMR (101 MHz, $CDCl_3$)



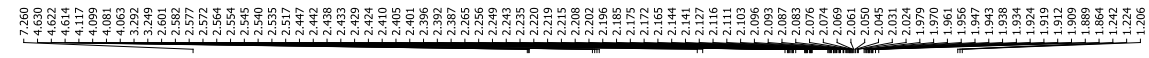

**3g**

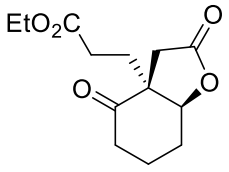
$^{1}$H NMR (400 MHz, $CDCl_3$)




**3g**

$^{13}$C NMR (126 MHz, $CDCl_3$)

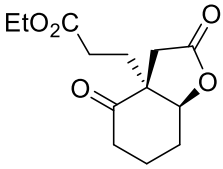




**3h**

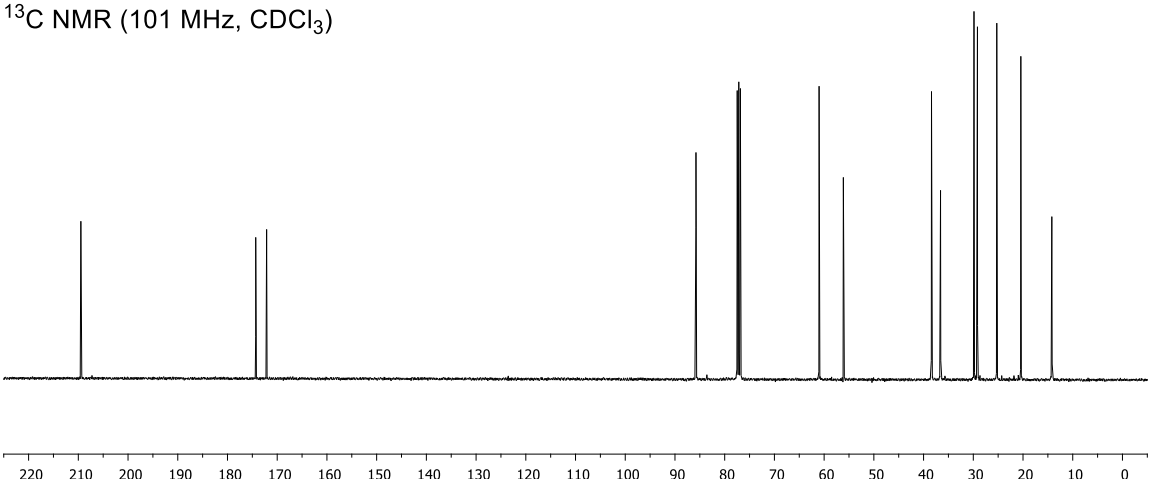
$^{1}$H NMR (400 MHz, $CDCl_3$)

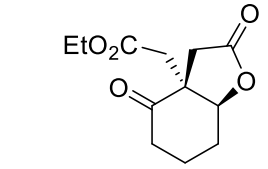




**3h**

$^{13}$C NMR (101 MHz, $CDCl_3$)

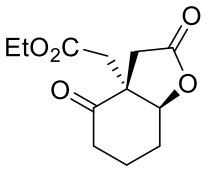




**3i**

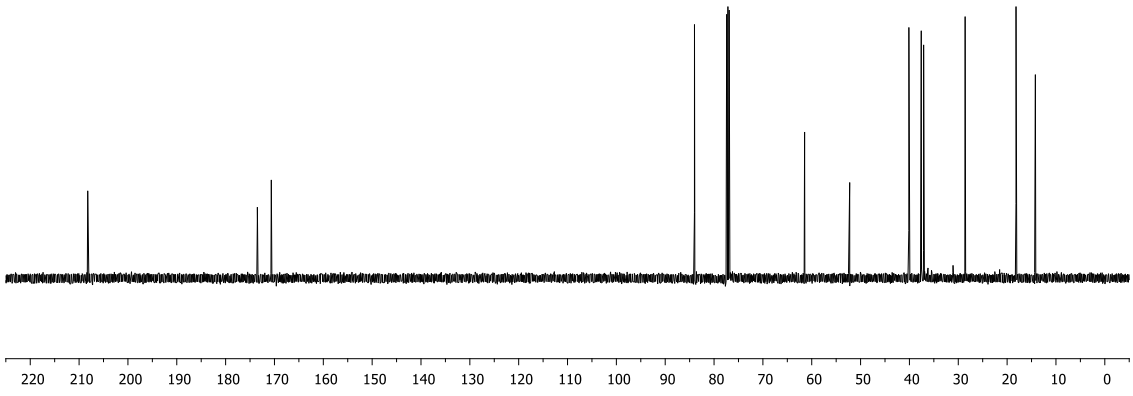
$^{1}$H NMR (400 MHz, $CDCl_3$)

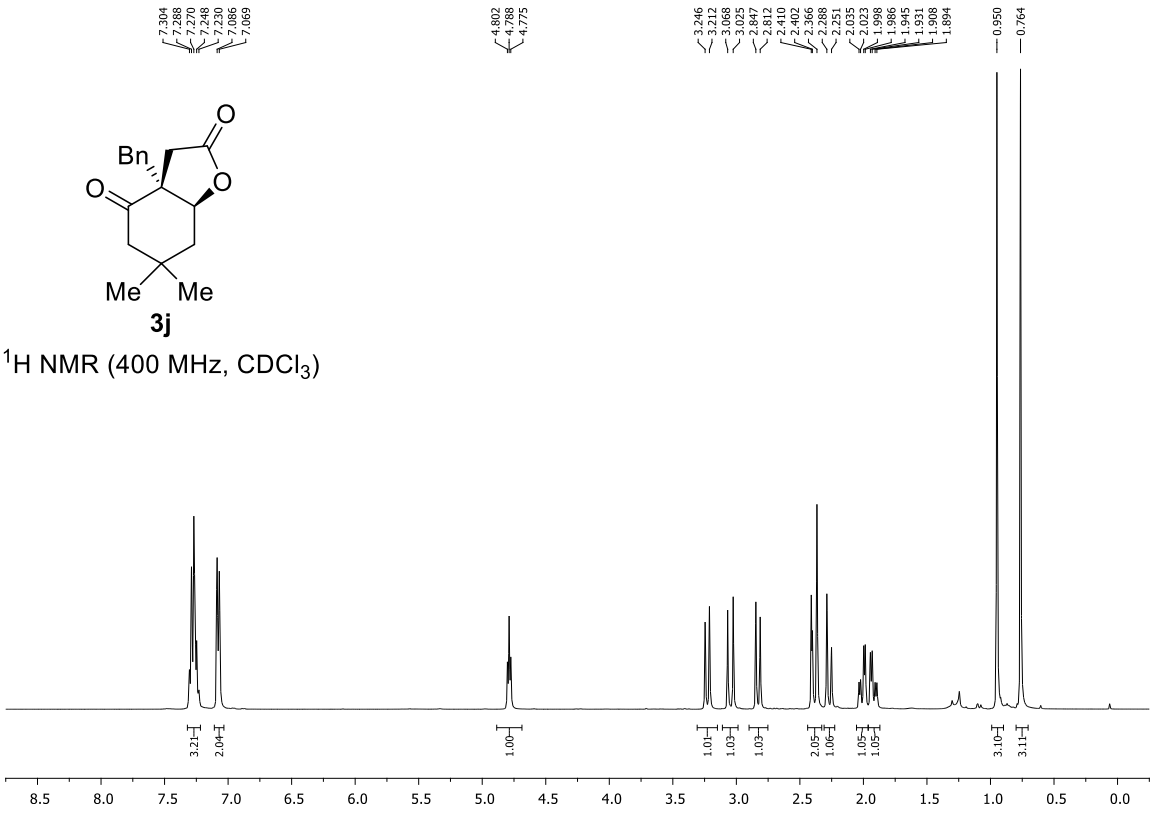




**3i**

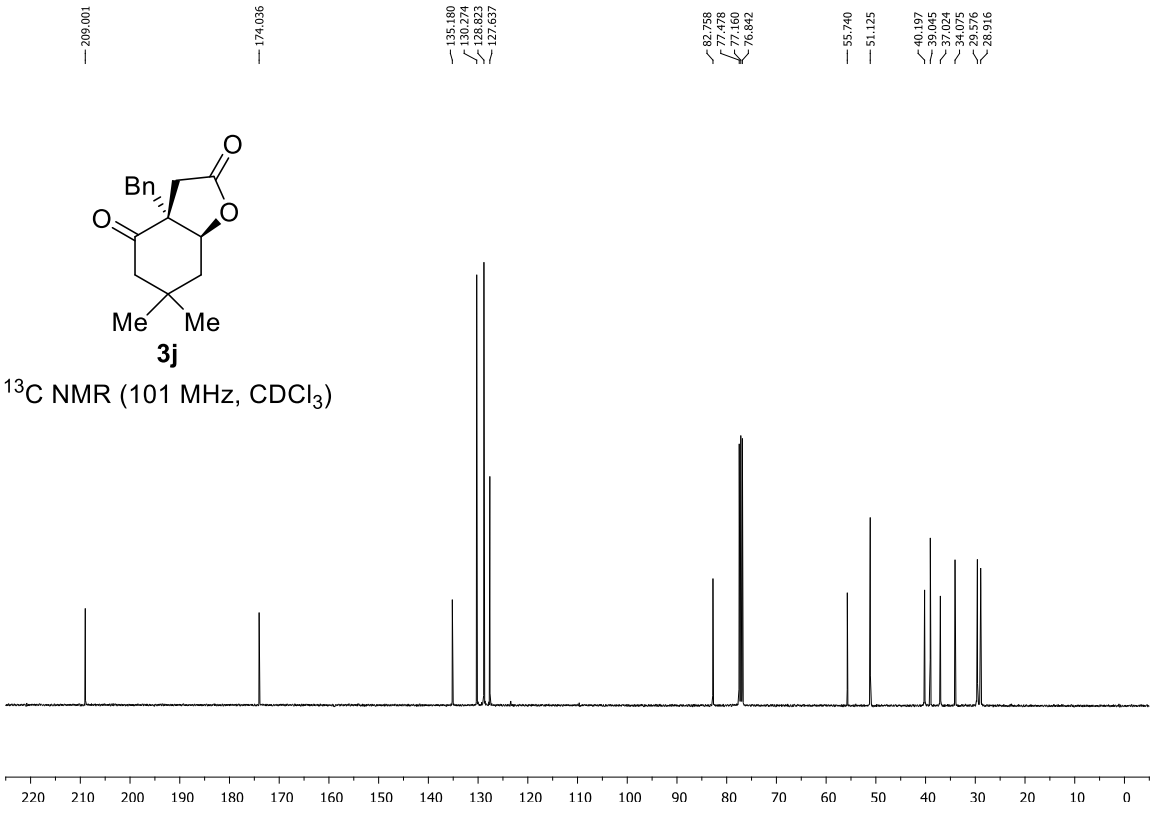
$^{13}$C NMR (126 MHz, $CDCl_3$)






**3j**

$^{1}$H NMR (400 MHz, $CDCl_3$)




**3j**

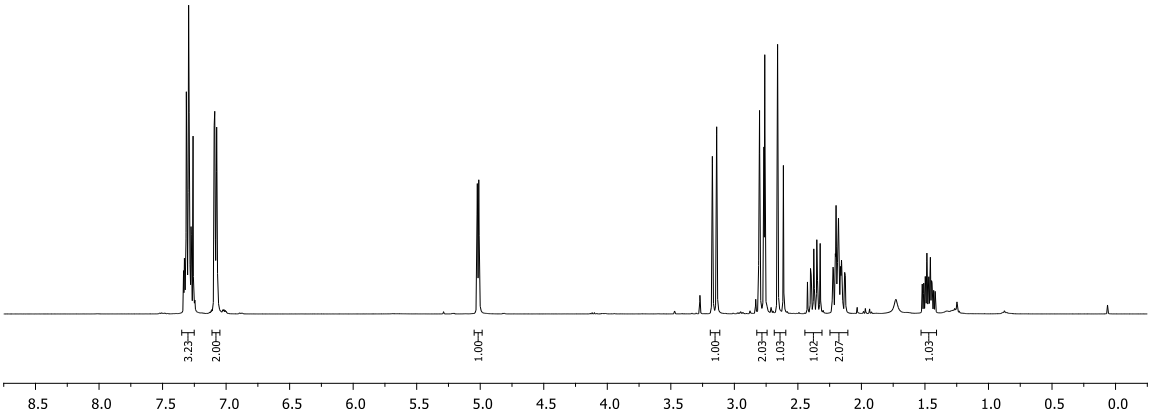
$^{13}$C NMR (101 MHz, $CDCl_3$)



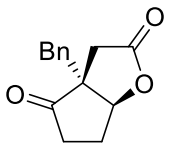


**3k**

$^{1}$H NMR (400 MHz, $CDCl_3$)

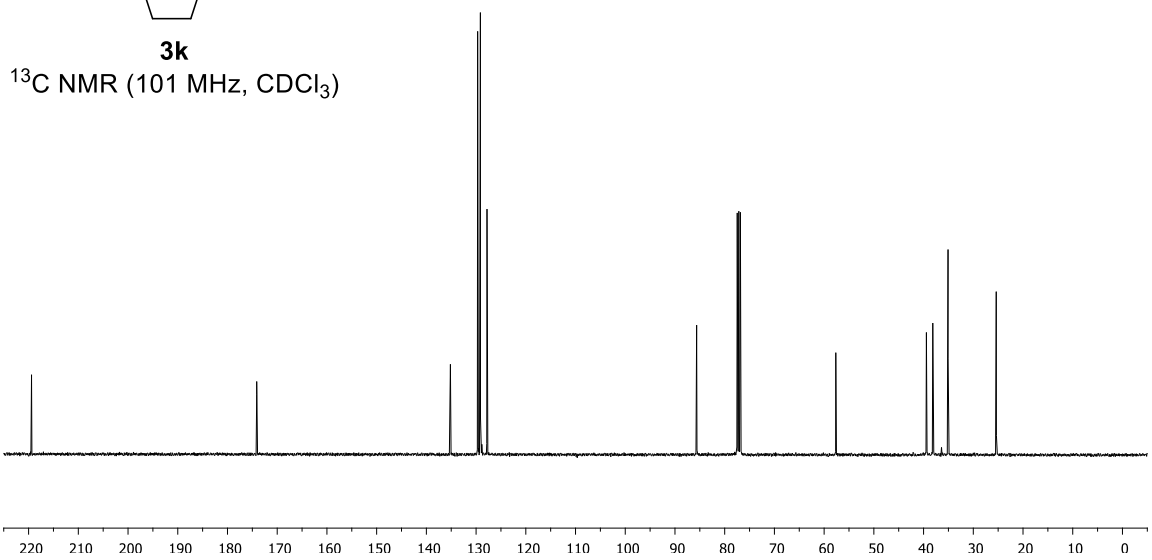


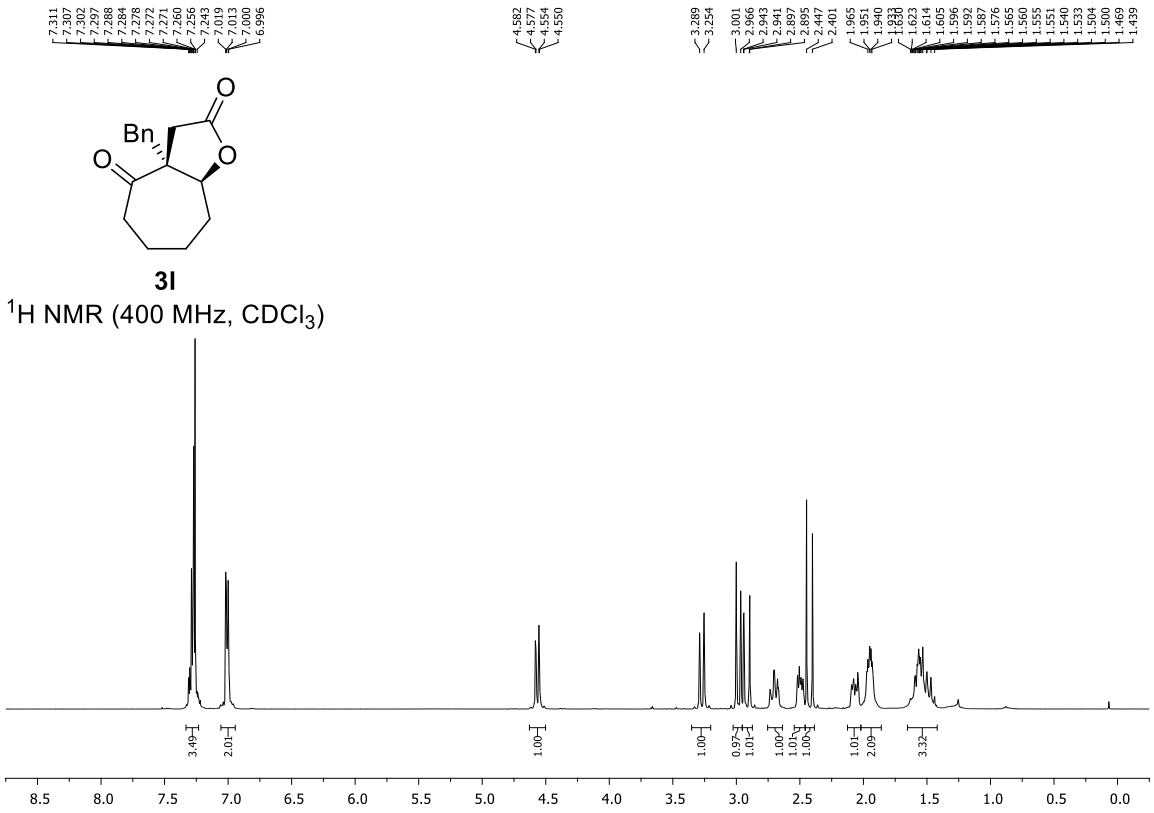





**3k**

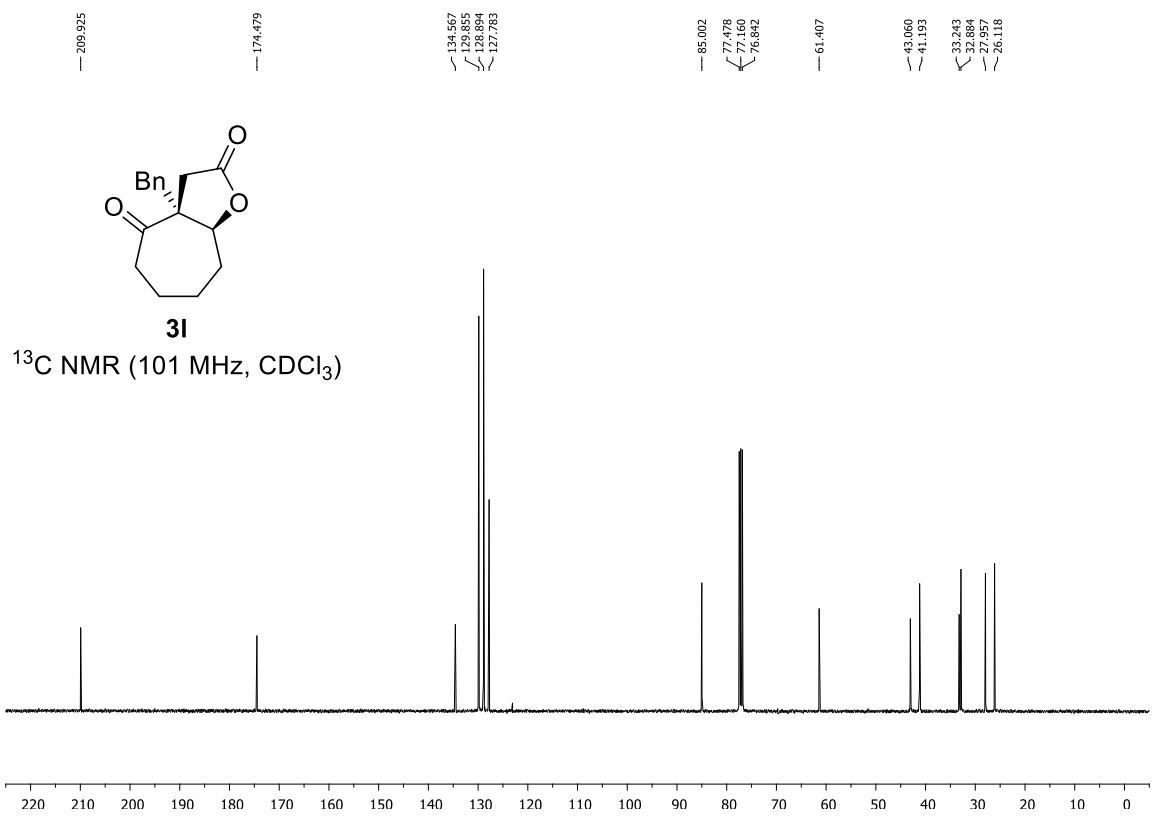
$^{13}$C NMR (101 MHz, $CDCl_3$)





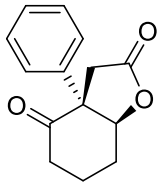

**3l**

$^{1}$H NMR (400 MHz, $CDCl_3$)



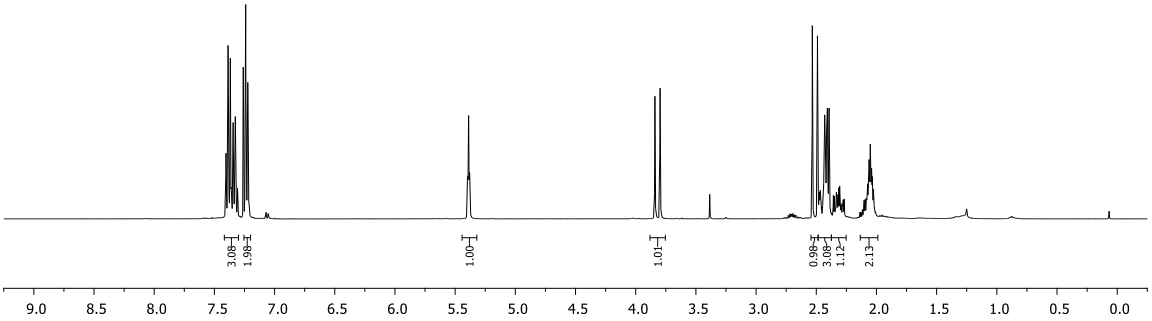

**3l**

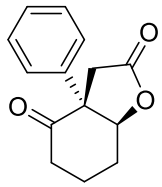
$^{13}$C NMR (101 MHz, $CDCl_3$)



**3m**

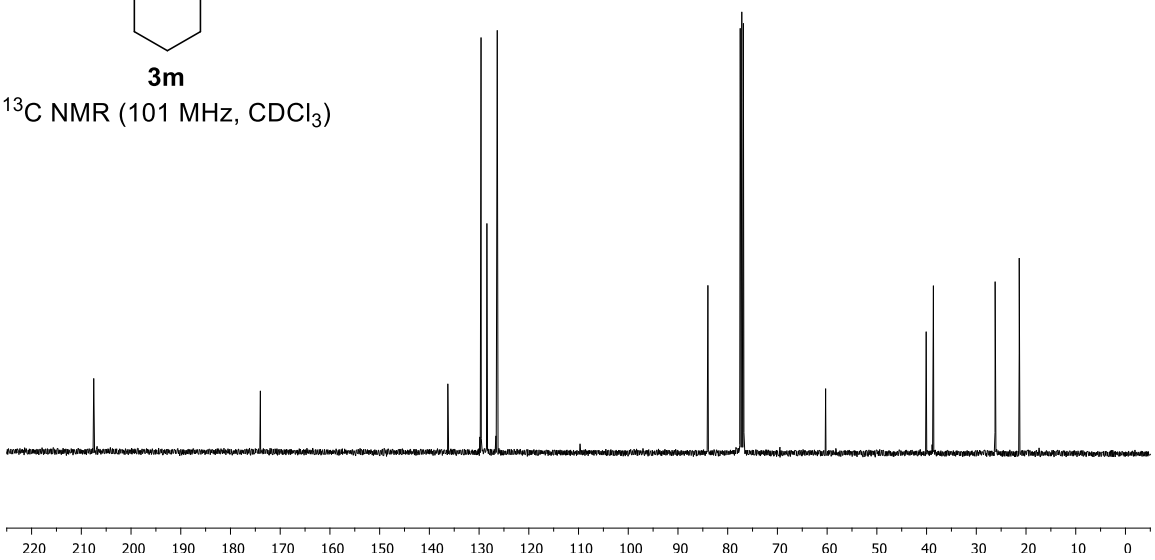
$^{1}H$ NMR (400 MHz, $CDCl_3$)

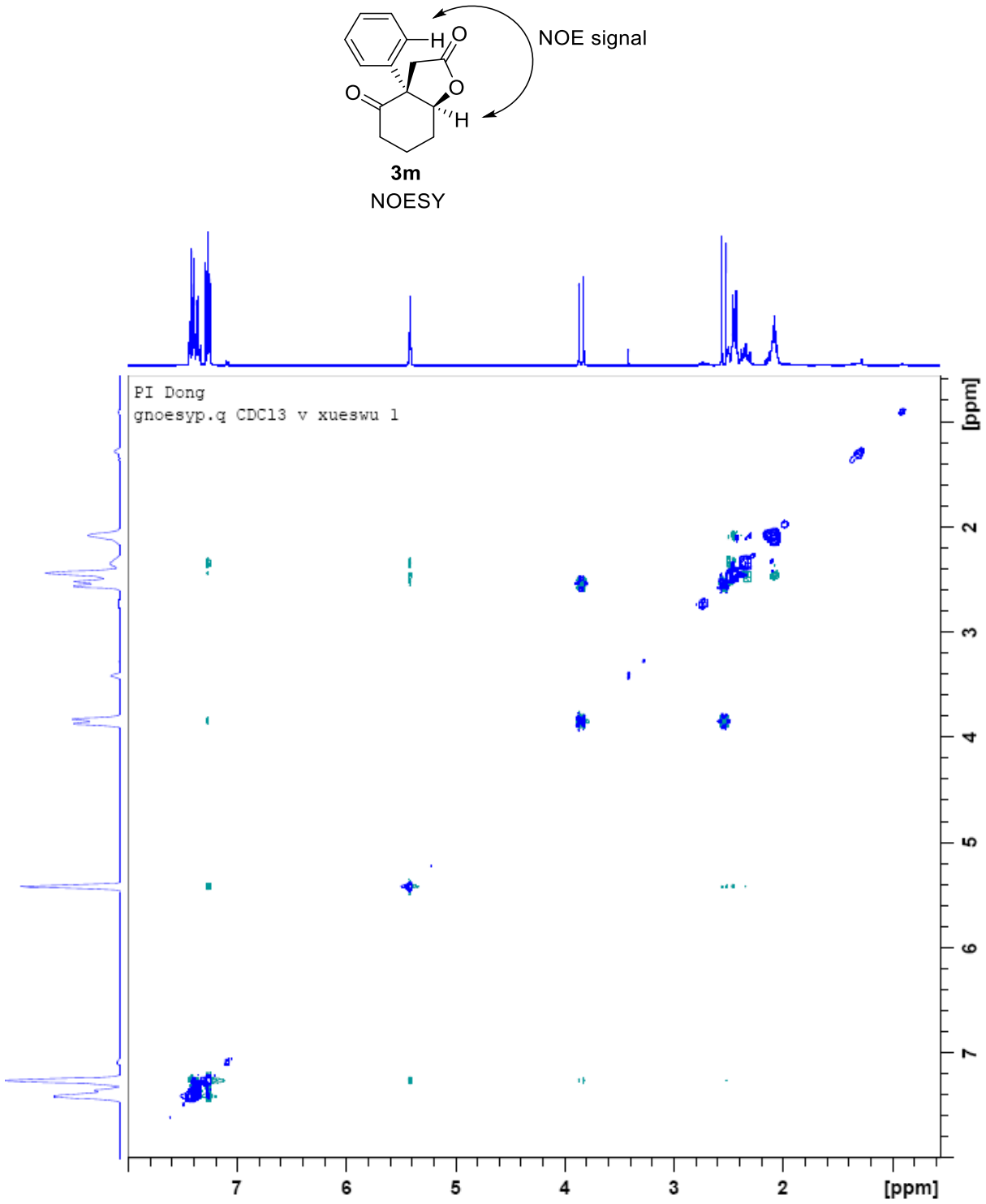


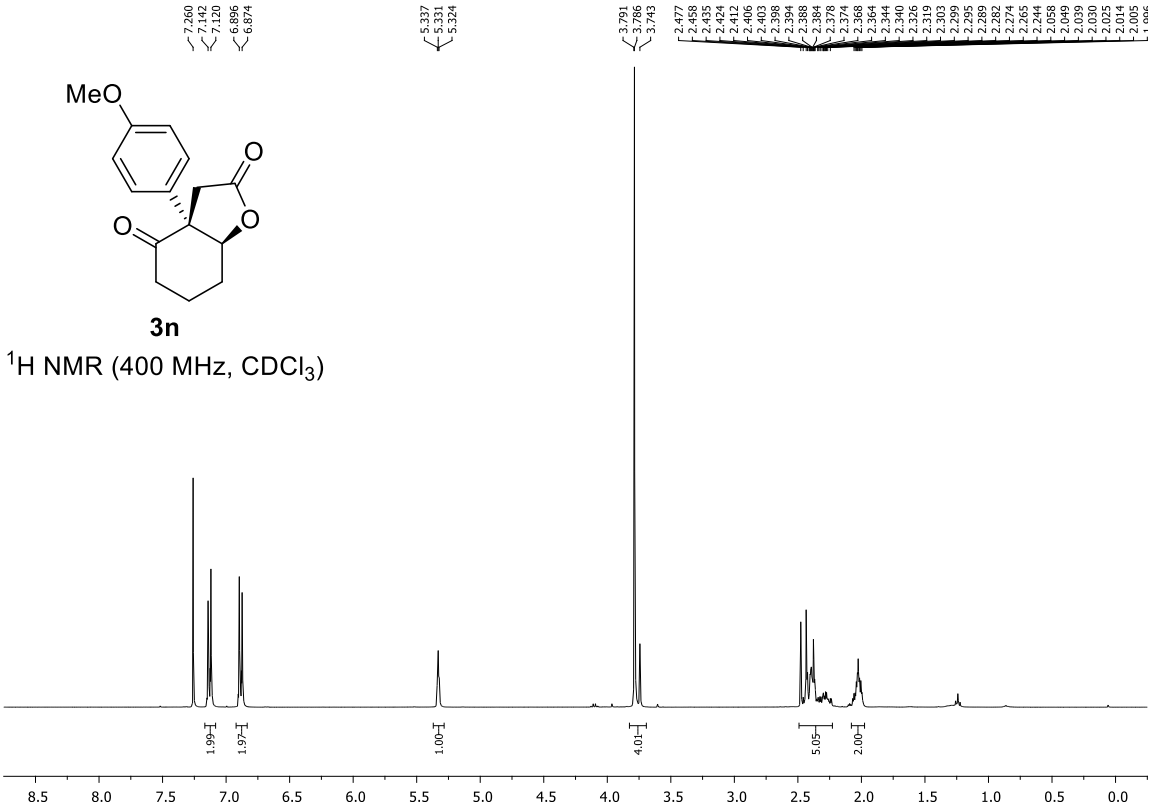


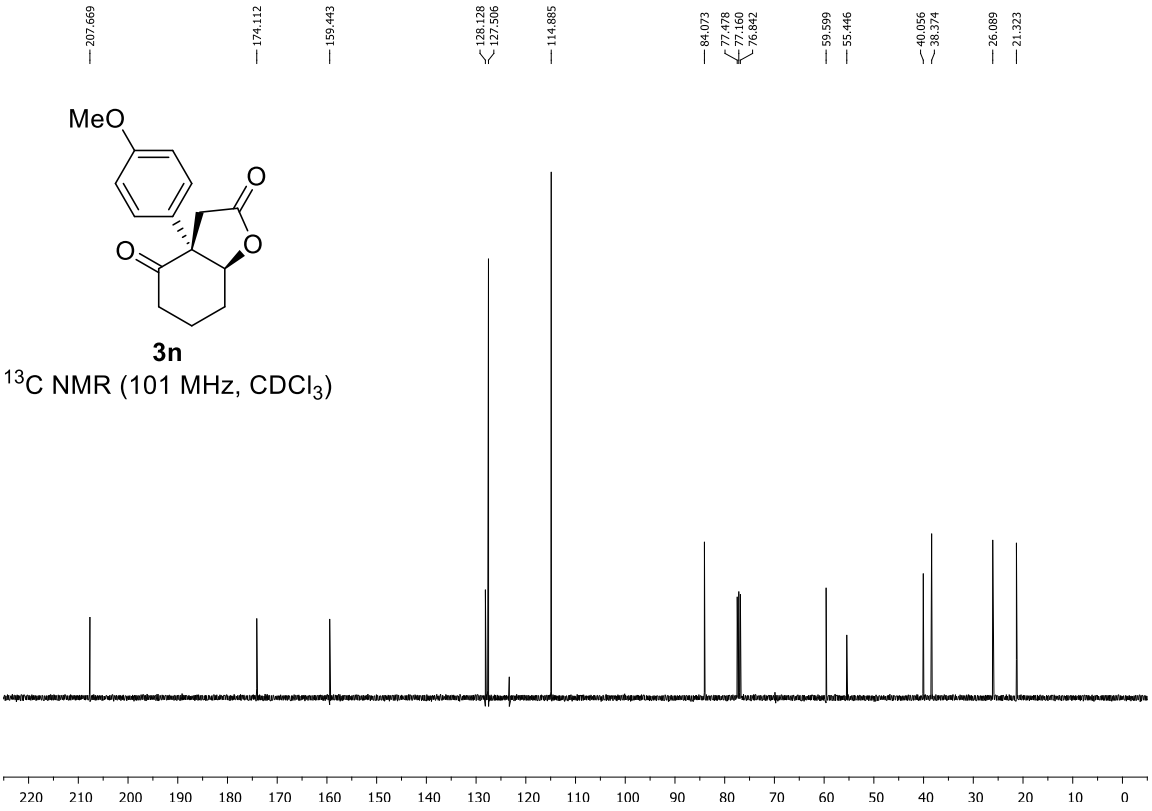
**3m**

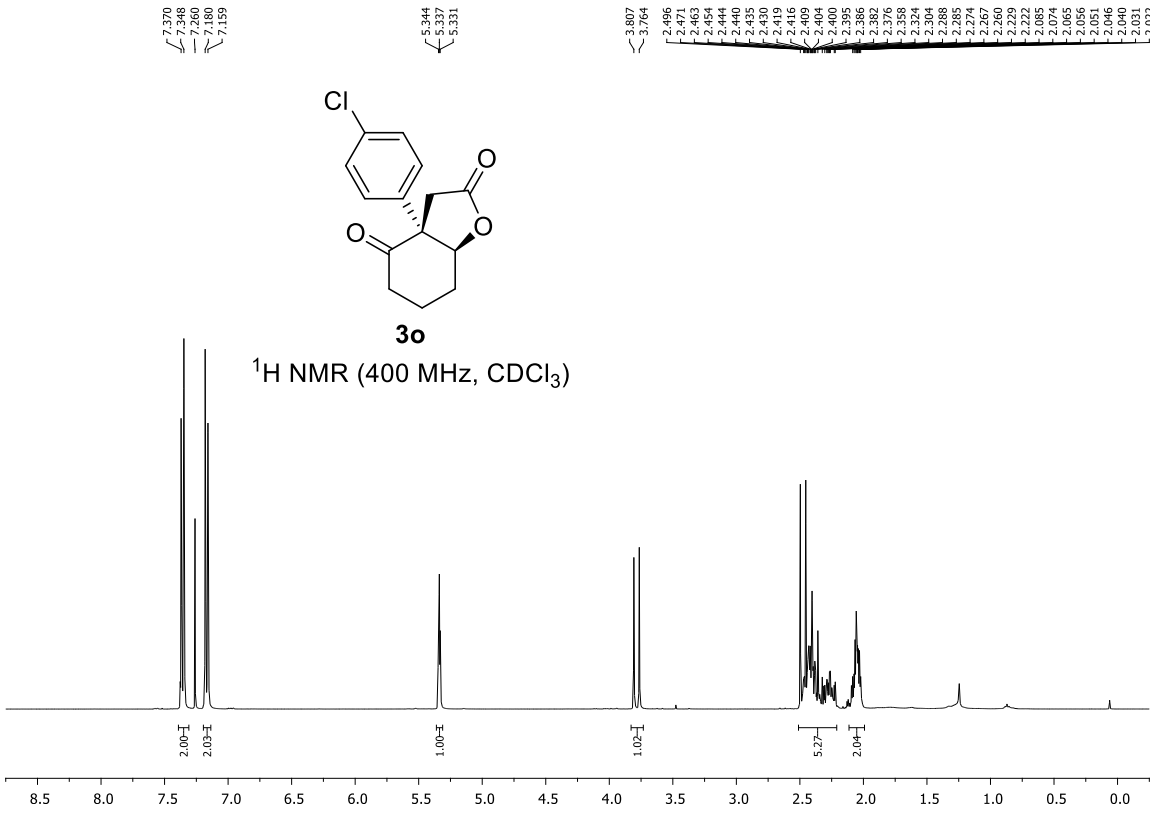
$^{13}C$ NMR (101 MHz, $CDCl_3$)




NOE signal
3m
NOESY
PI Dong
gnoesyp.q CDCl3 v xueswu 1
[ppm]
7
6
5
4
3
2
[ppm]

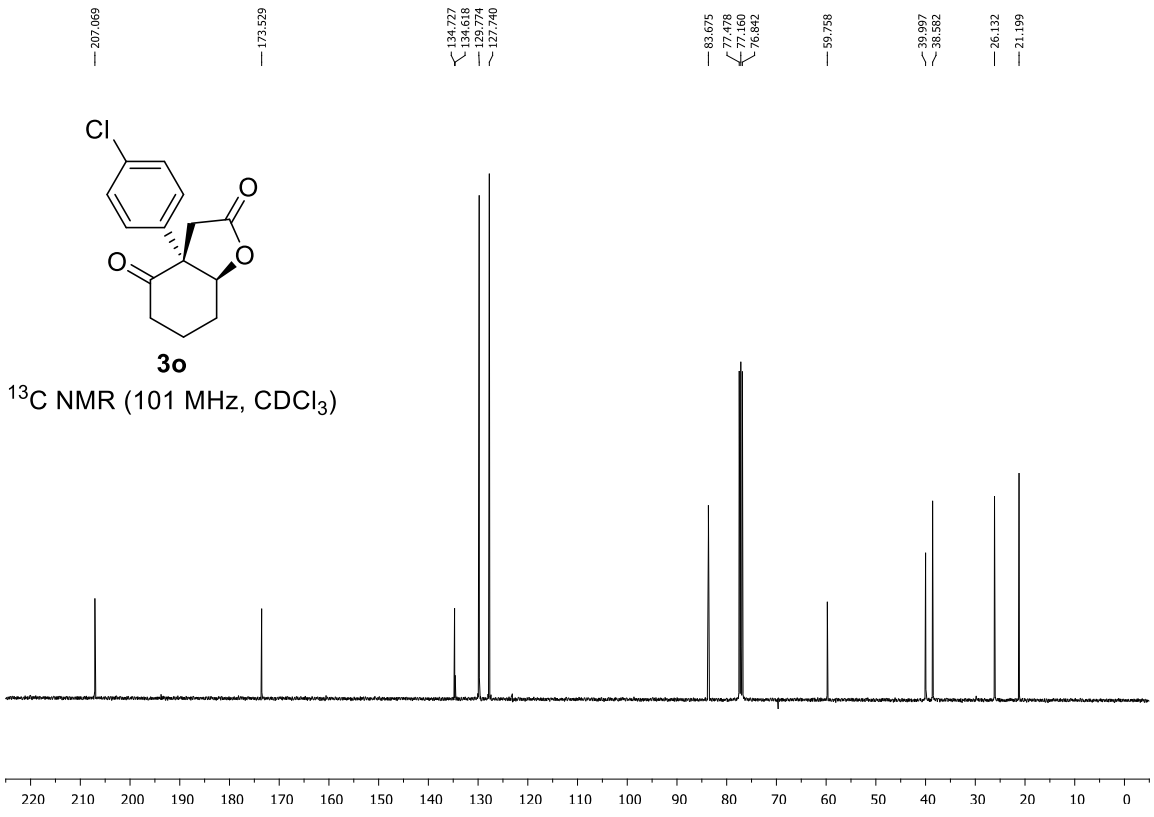

MeO
O
O
O
3n
$^1$H NMR (400 MHz, $CDCl_3$)


MeO
O
O
O
3n
$^{13}$C NMR (101 MHz, $CDCl_3$)



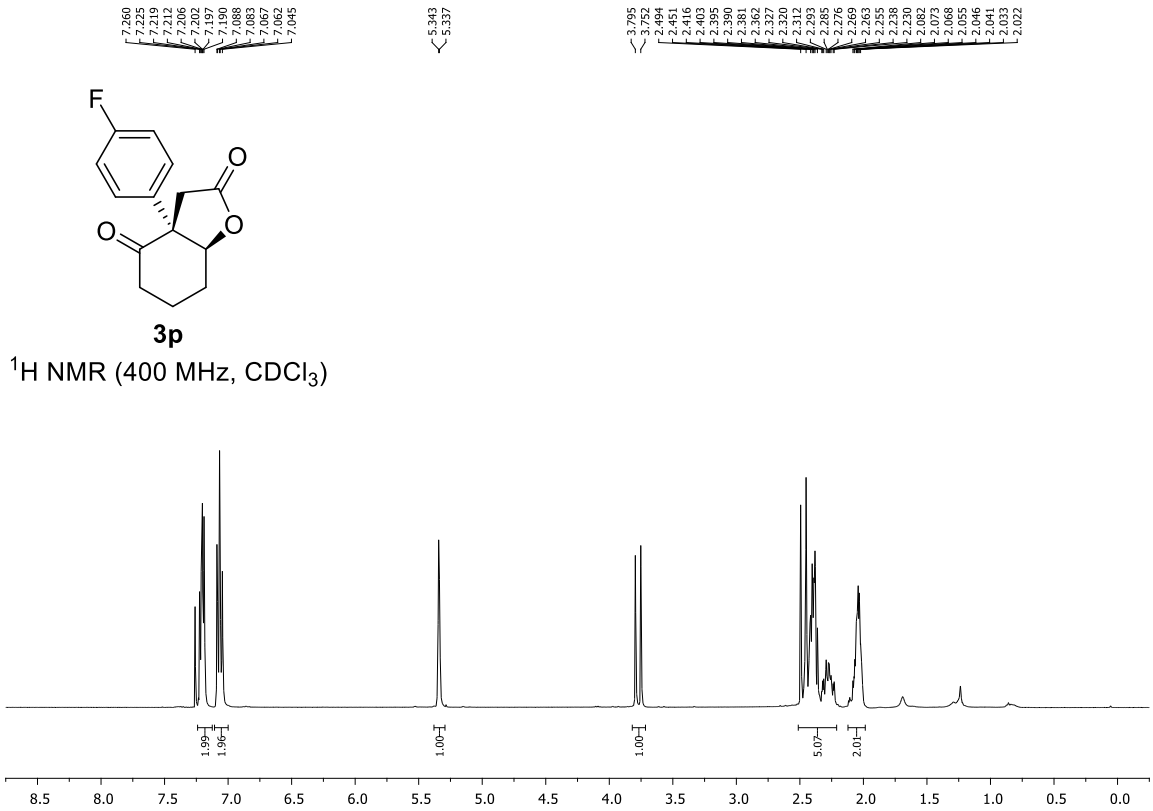

**3o**

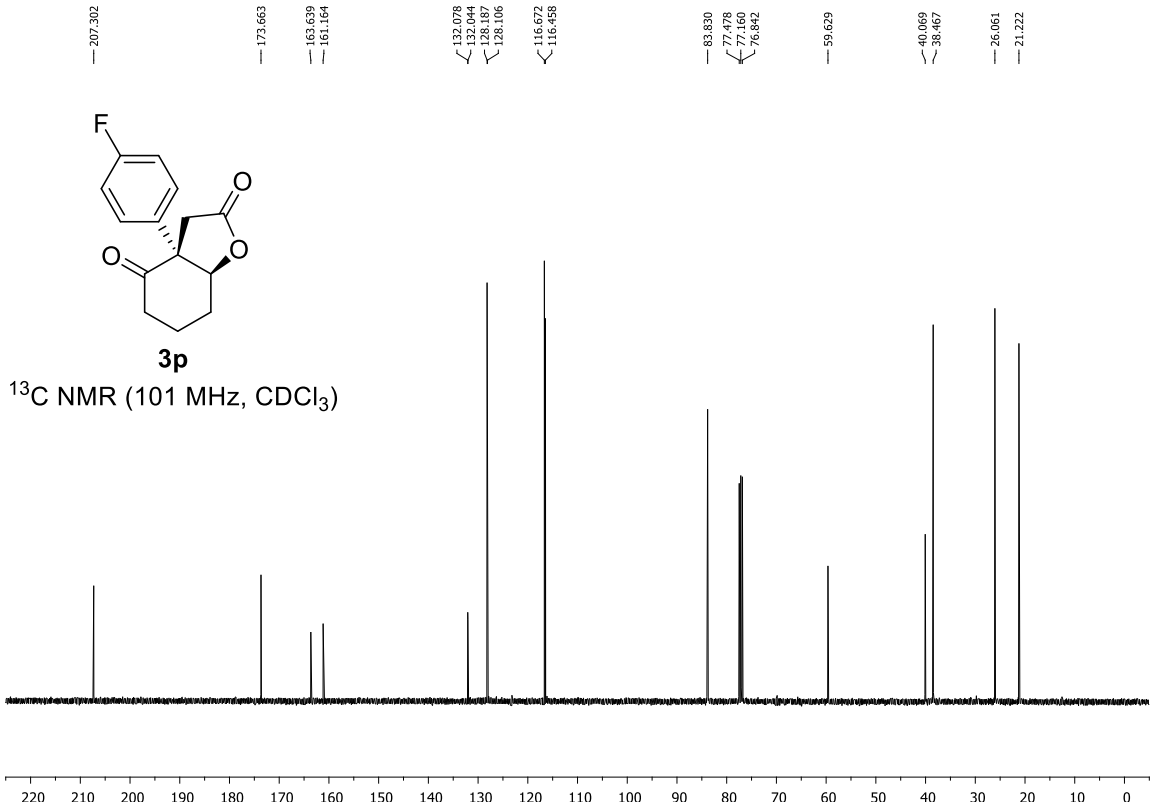
$^{1}$H NMR (400 MHz, $CDCl_3$)

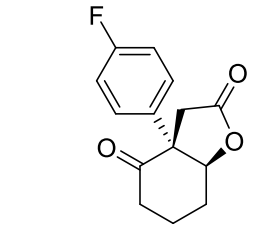



**3o**

$^{13}$C NMR (101 MHz, $CDCl_3$)

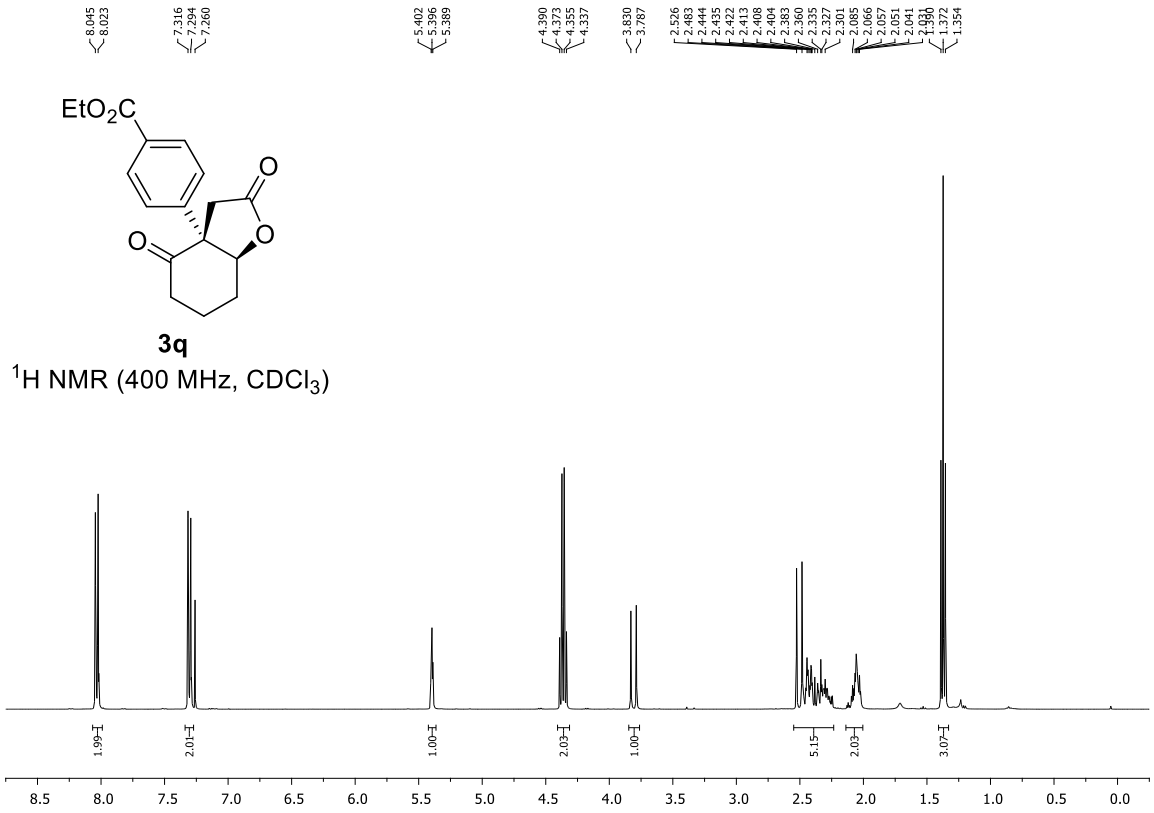

7.260
7.225
7.219
7.212
7.206
7.202
7.197
7.190
7.088
7.083
7.067
7.062
7.045
5.343
5.337
3.795
3.752
2.494
2.451
2.416
2.403
2.395
2.390
2.381
2.362
2.327
2.320
2.312
2.293
2.285
2.276
2.269
2.263
2.255
2.238
2.230
2.082
2.073
2.068
2.055
2.046
2.041
2.033
2.022
F
O
O
O
3p
1H NMR (400 MHz, CDCl3)
1.99
1.96
1.00
1.00
5.07
2.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


207.302
173.663
163.639
161.164
132.078
132.044
128.187
128.106
116.672
116.458
83.830
77.478
77.160
76.842
59.629
40.069
38.467
26.061
21.222
F
O
O
O
3p
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



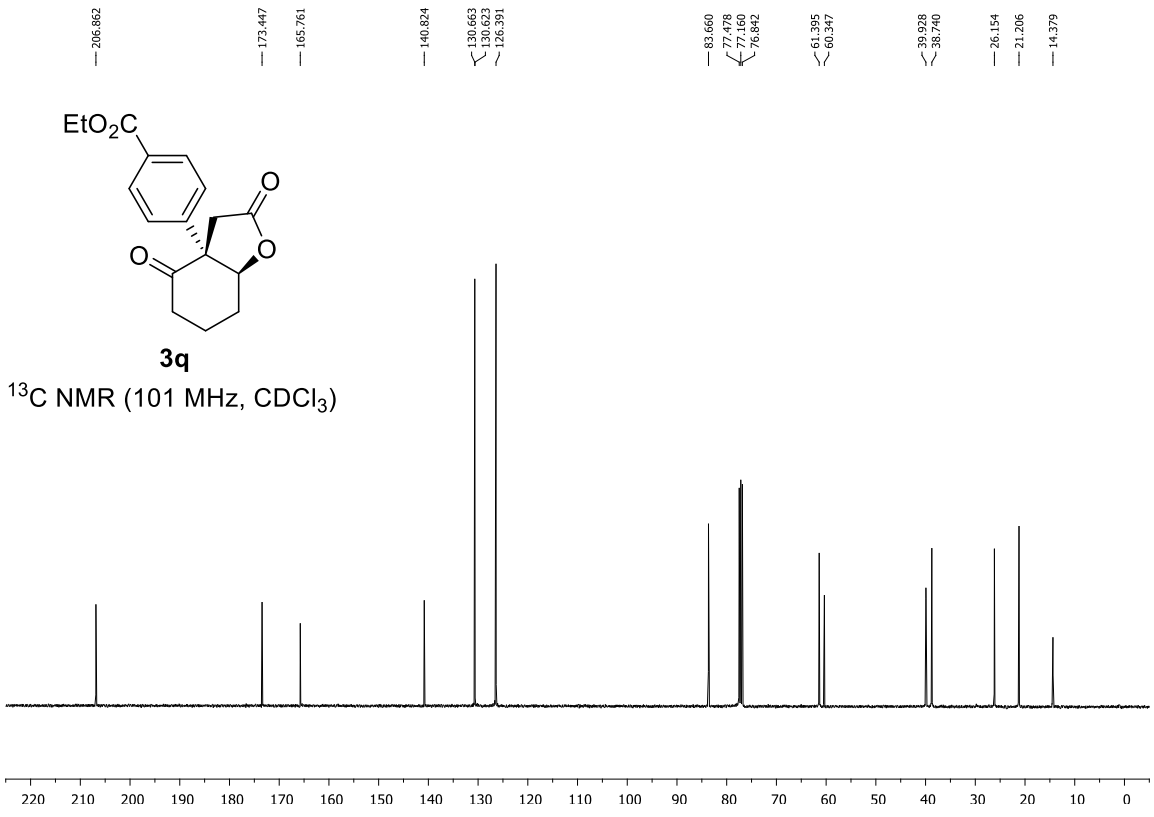

**3p**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



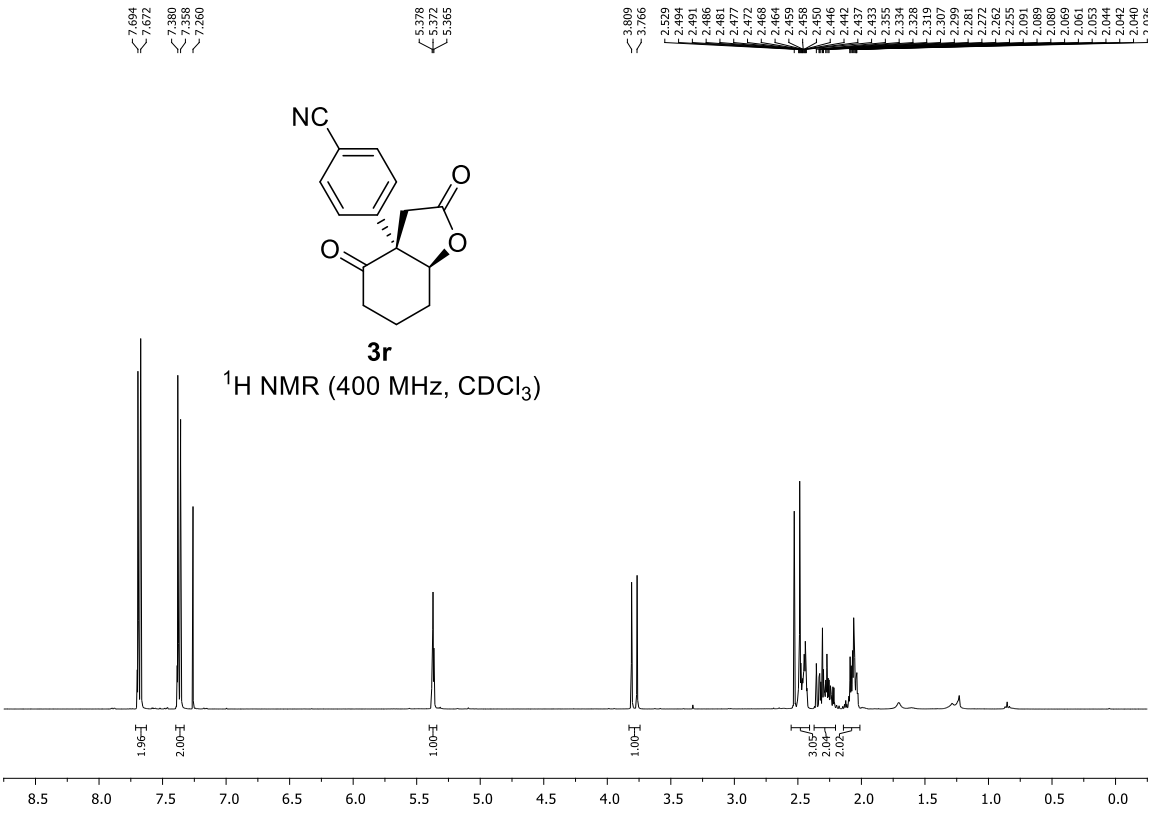

**3q**

$^{1}$H NMR (400 MHz, $CDCl_3$)



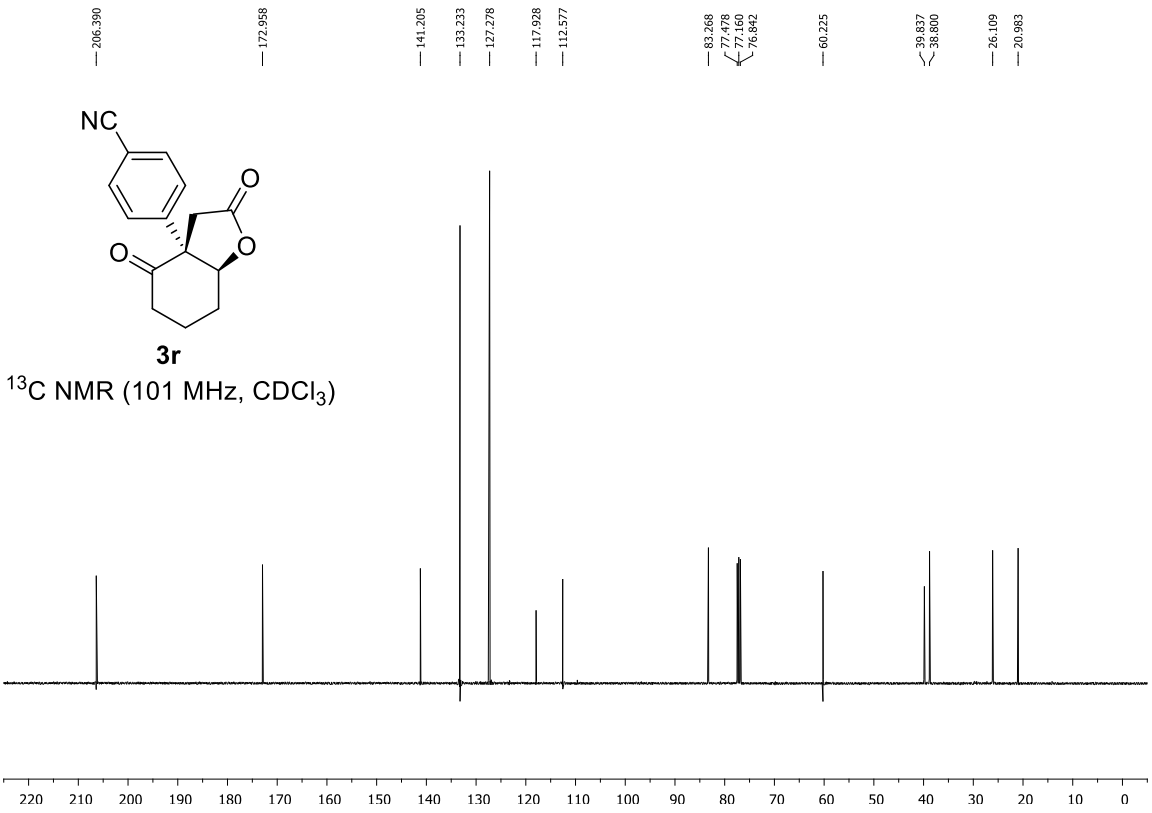

**3q**

$^{13}$C NMR (101 MHz, $CDCl_3$)



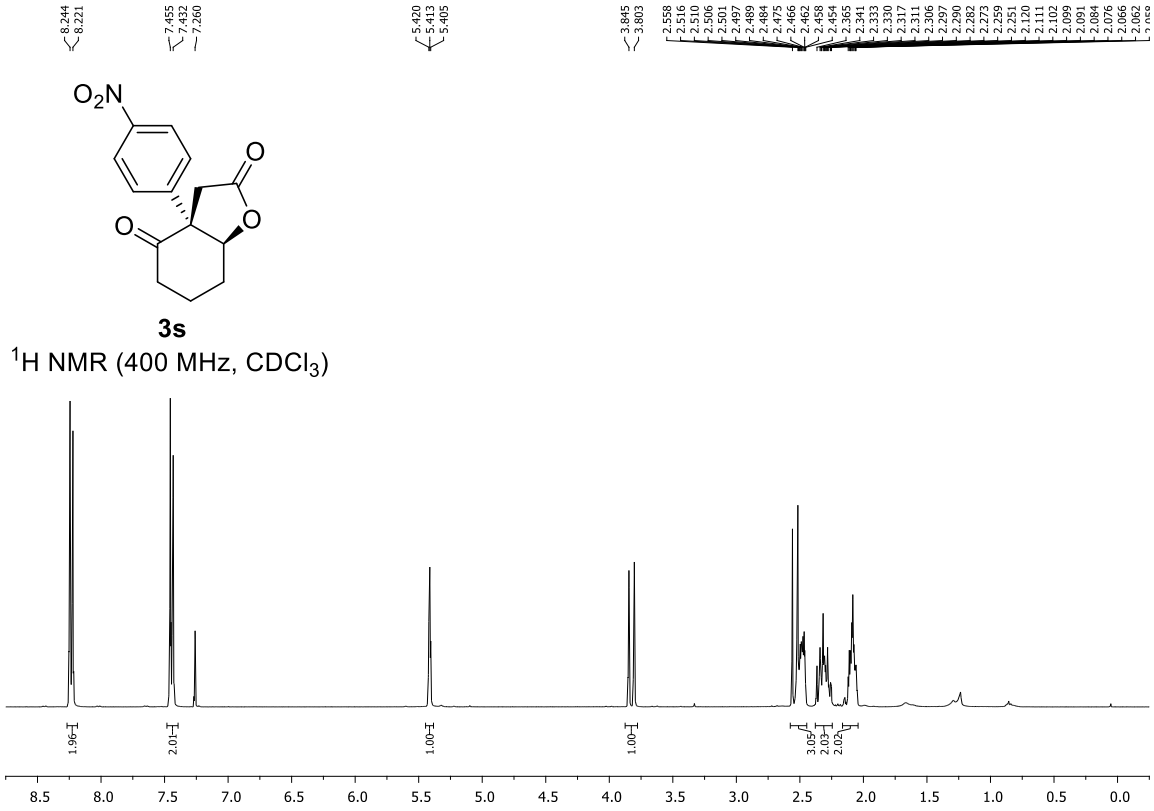

**3r**

$^{1}$H NMR (400 MHz, $CDCl_3$)



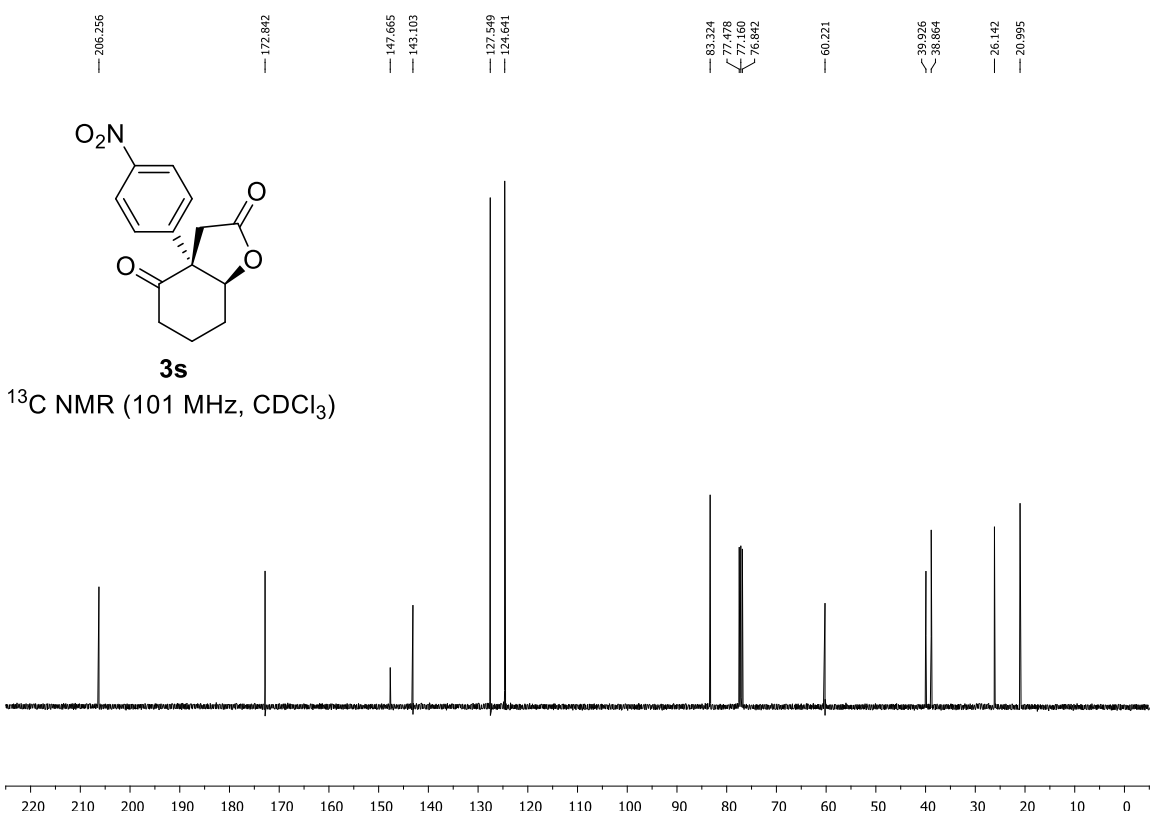

**3r**

$^{13}$C NMR (101 MHz, $CDCl_3$)



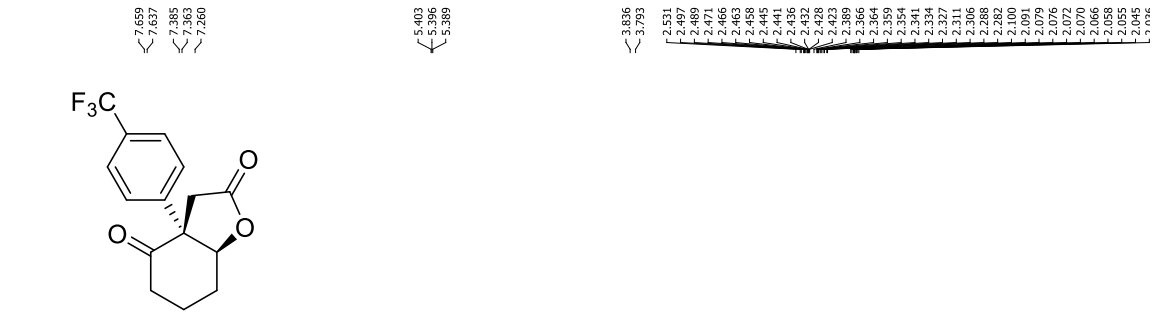

**3s**

$^{1}$H NMR (400 MHz, $CDCl_3$)



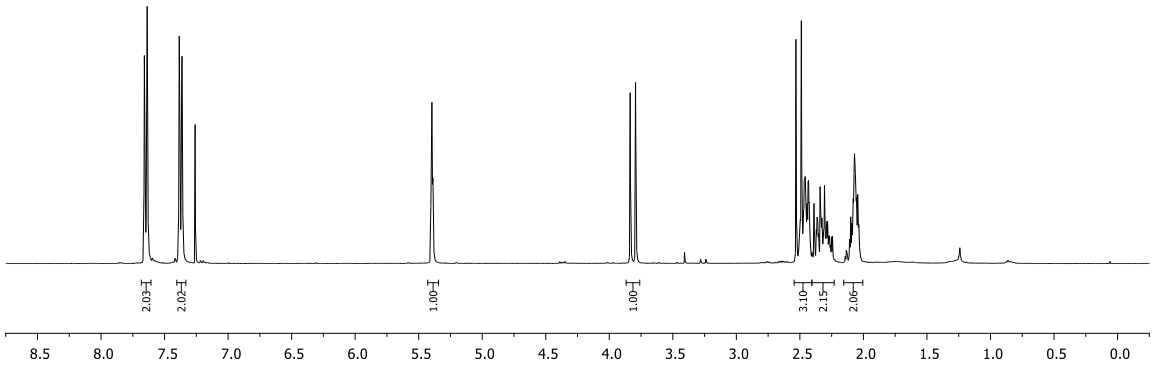

**3s**

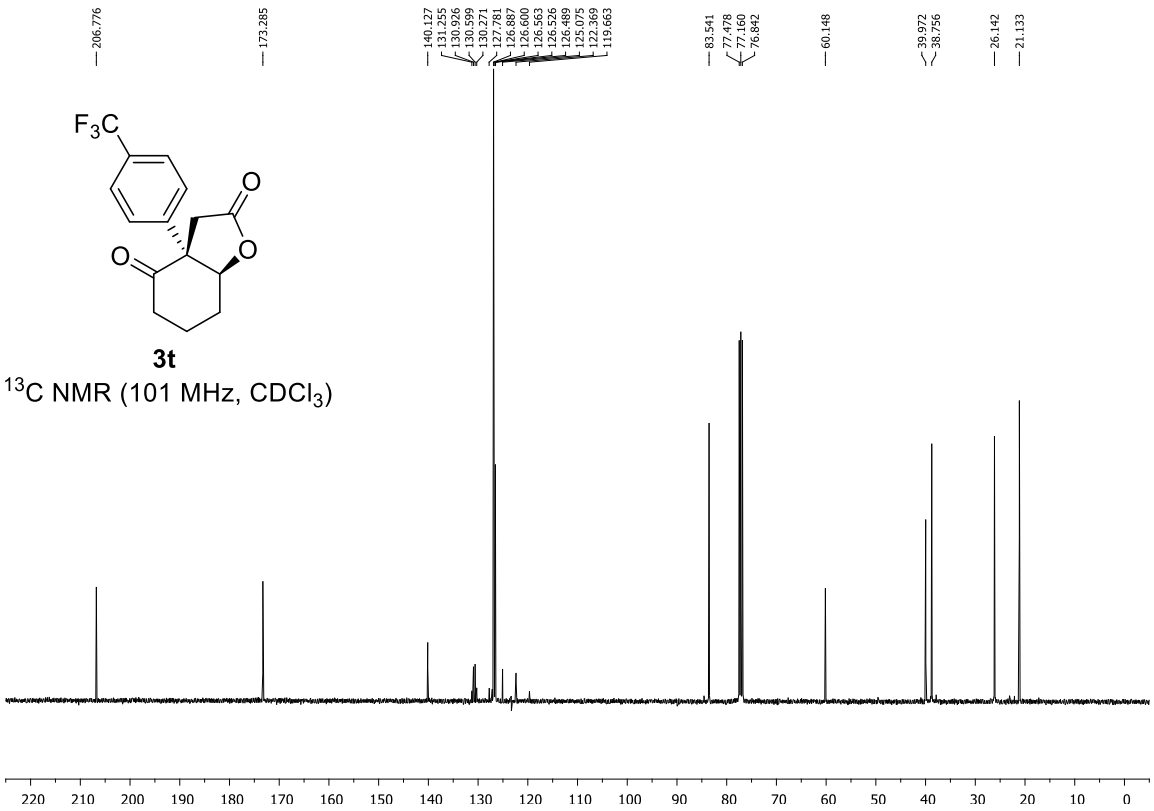
$^{13}$C NMR (101 MHz, $CDCl_3$)



**3t**

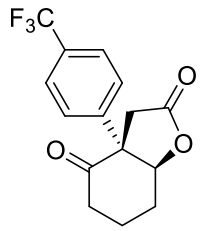
$^1$H NMR (400 MHz, $CDCl_3$)





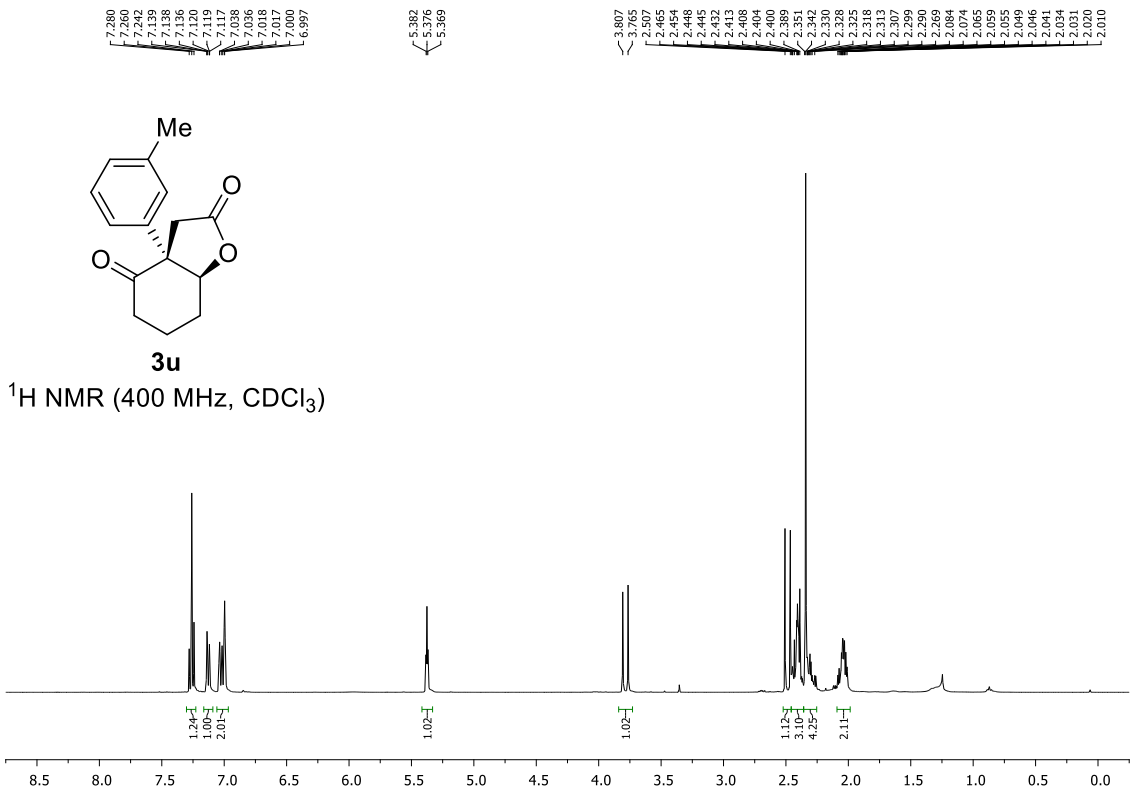
**3t**

$^{13}$C NMR (101 MHz, $CDCl_3$)



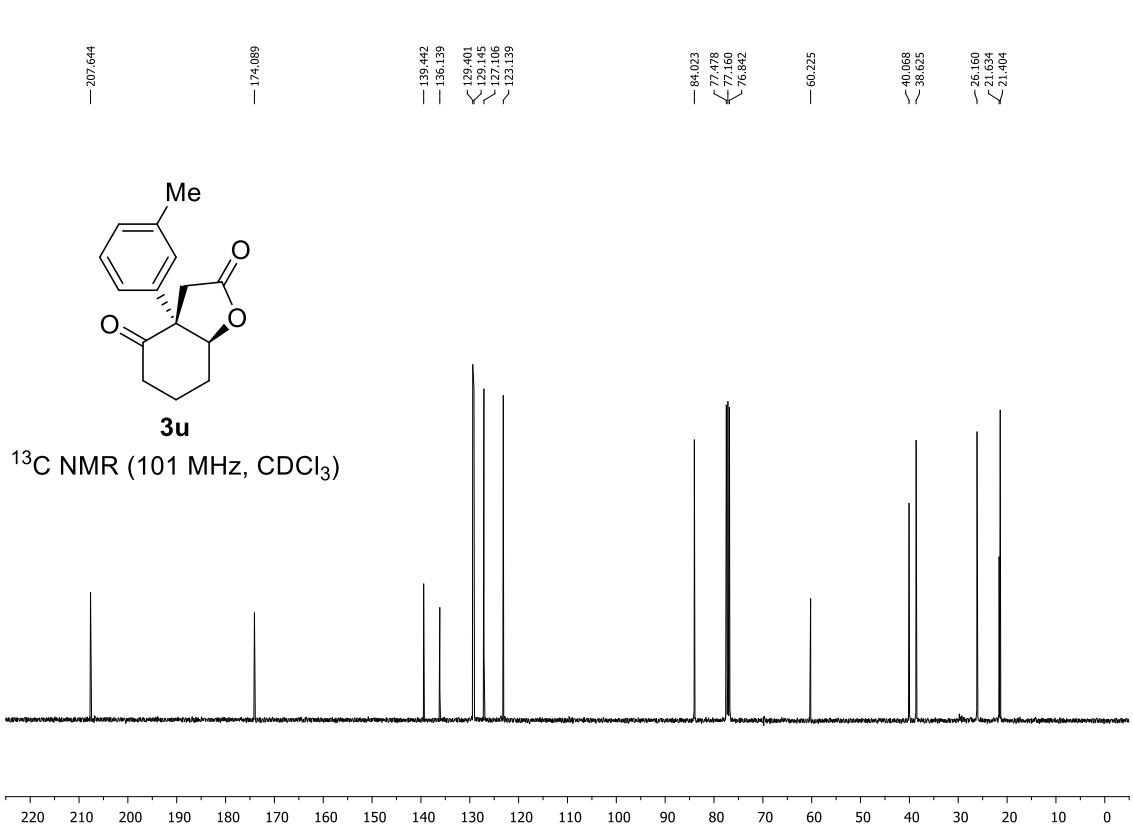

**3t**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



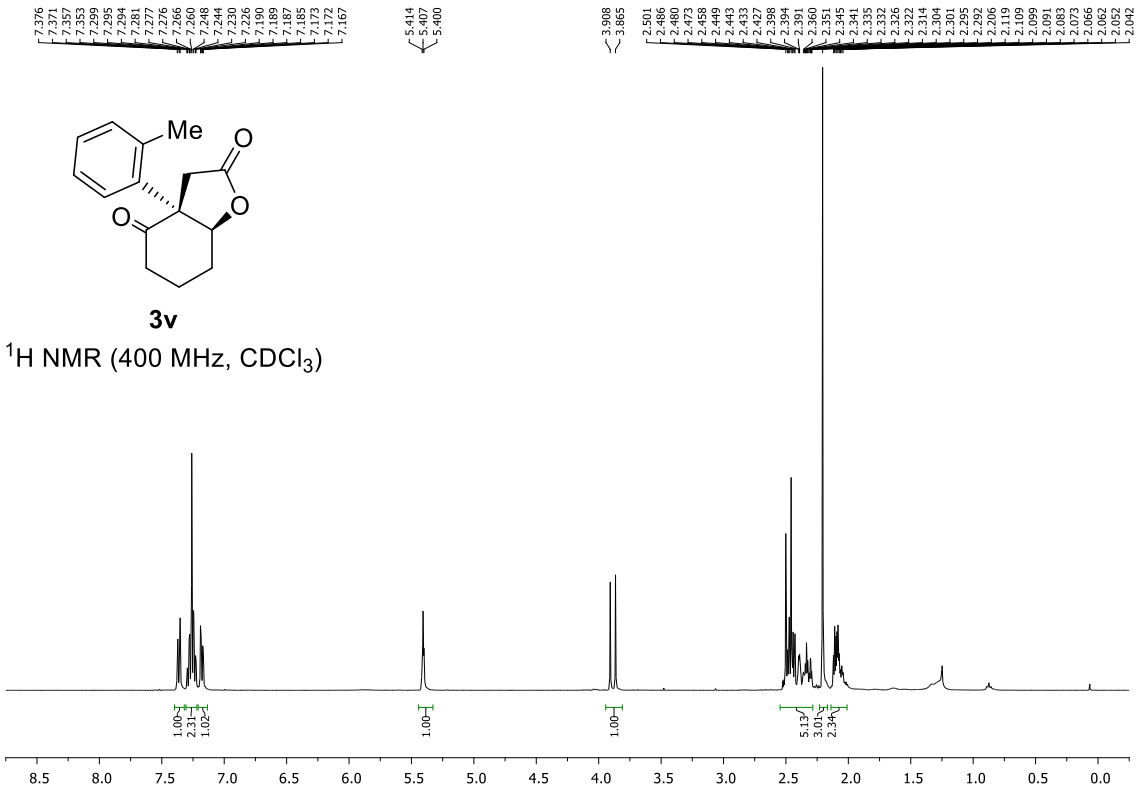

**3u**

$^{1}$H NMR (400 MHz, $CDCl_3$)



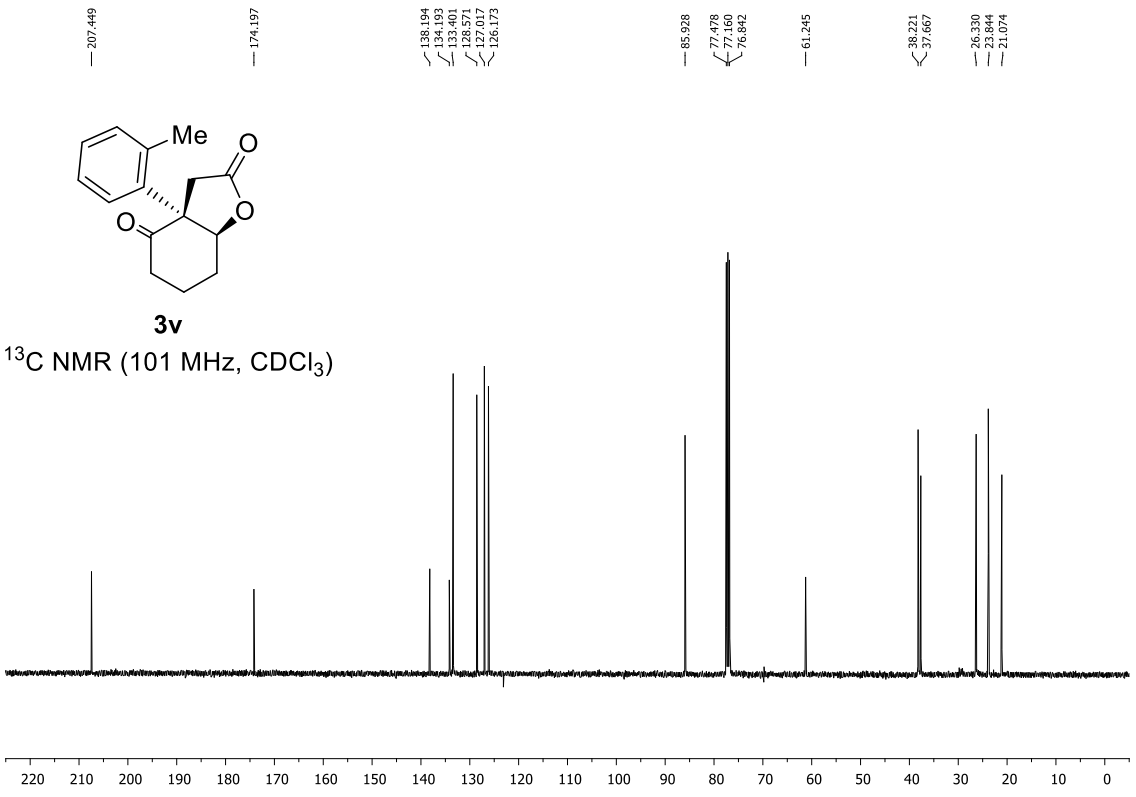

**3u**

$^{13}$C NMR (101 MHz, $CDCl_3$)



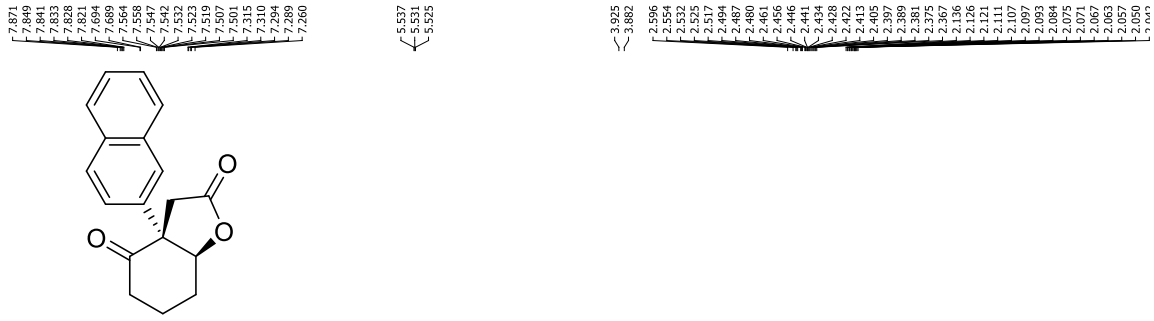

**3v**

$^{1}$H NMR (400 MHz, $CDCl_3$)



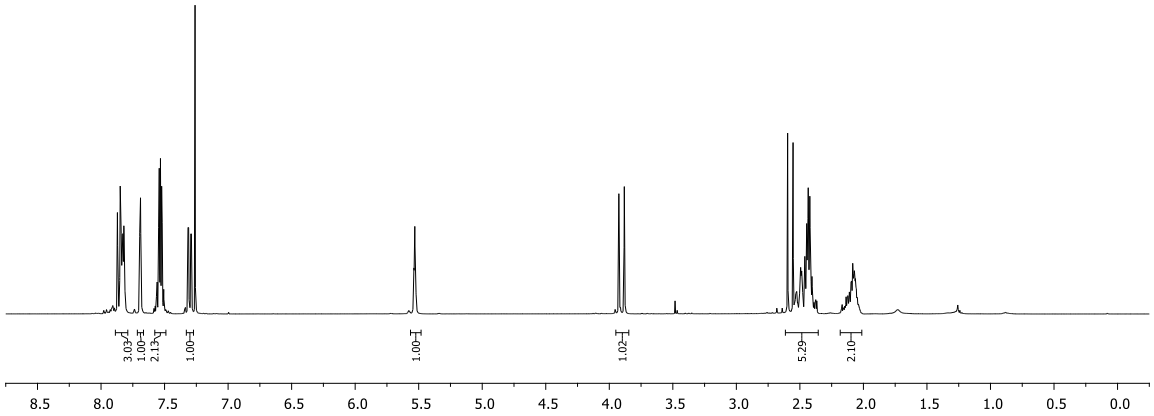

**3v**

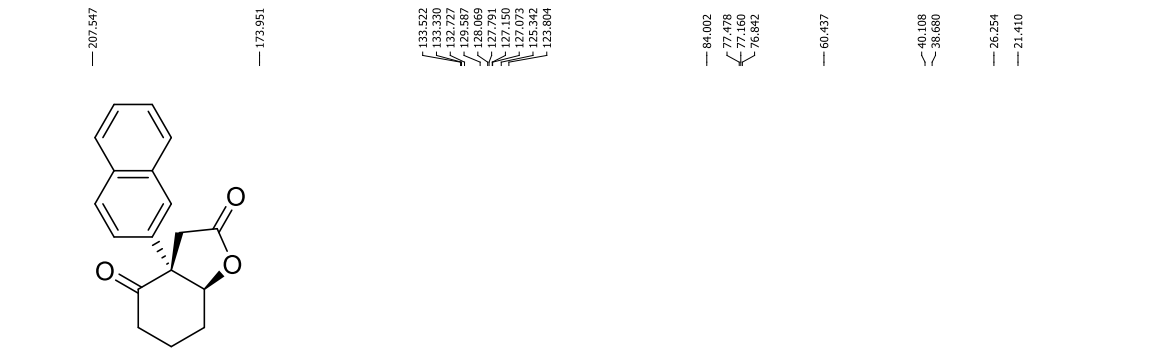
$^{13}$C NMR (101 MHz, $CDCl_3$)



**3w**

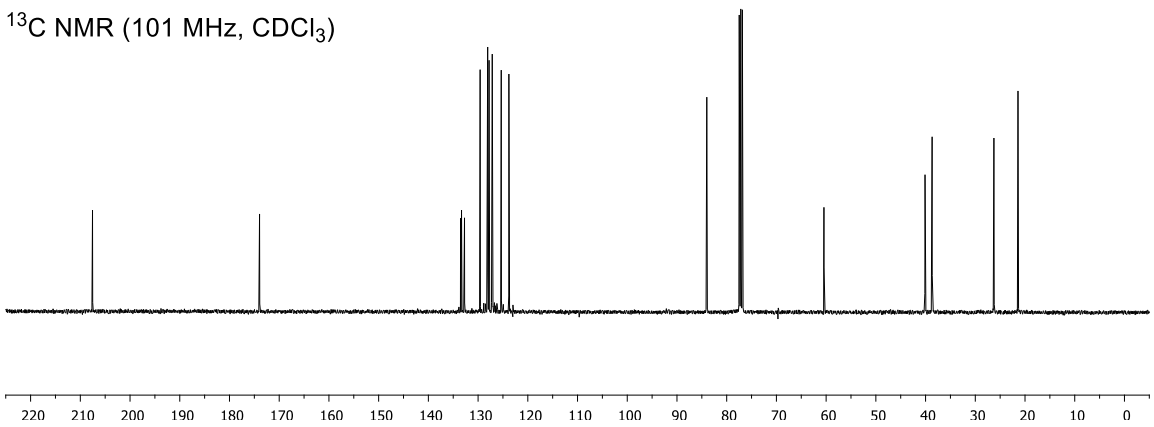
$^1$H NMR (400 MHz, $CDCl_3$)

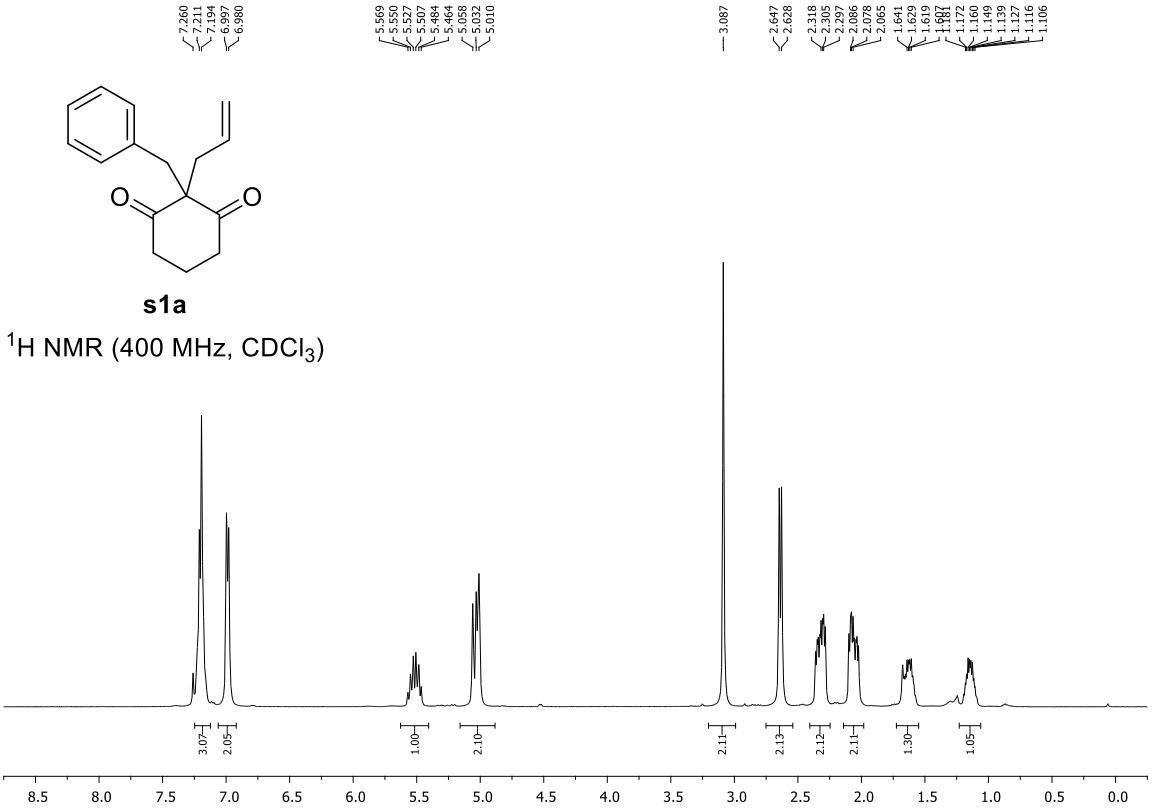




**3w**

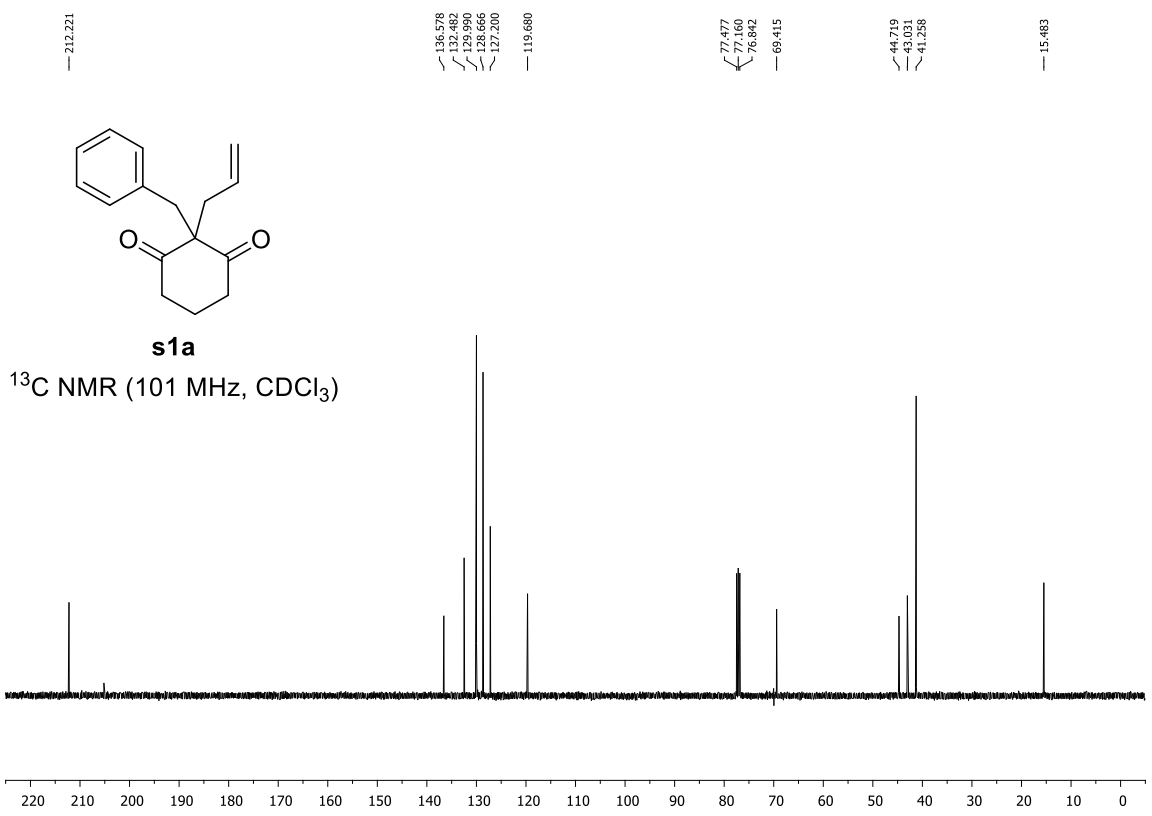
$^{13}$C NMR (101 MHz, $CDCl_3$)





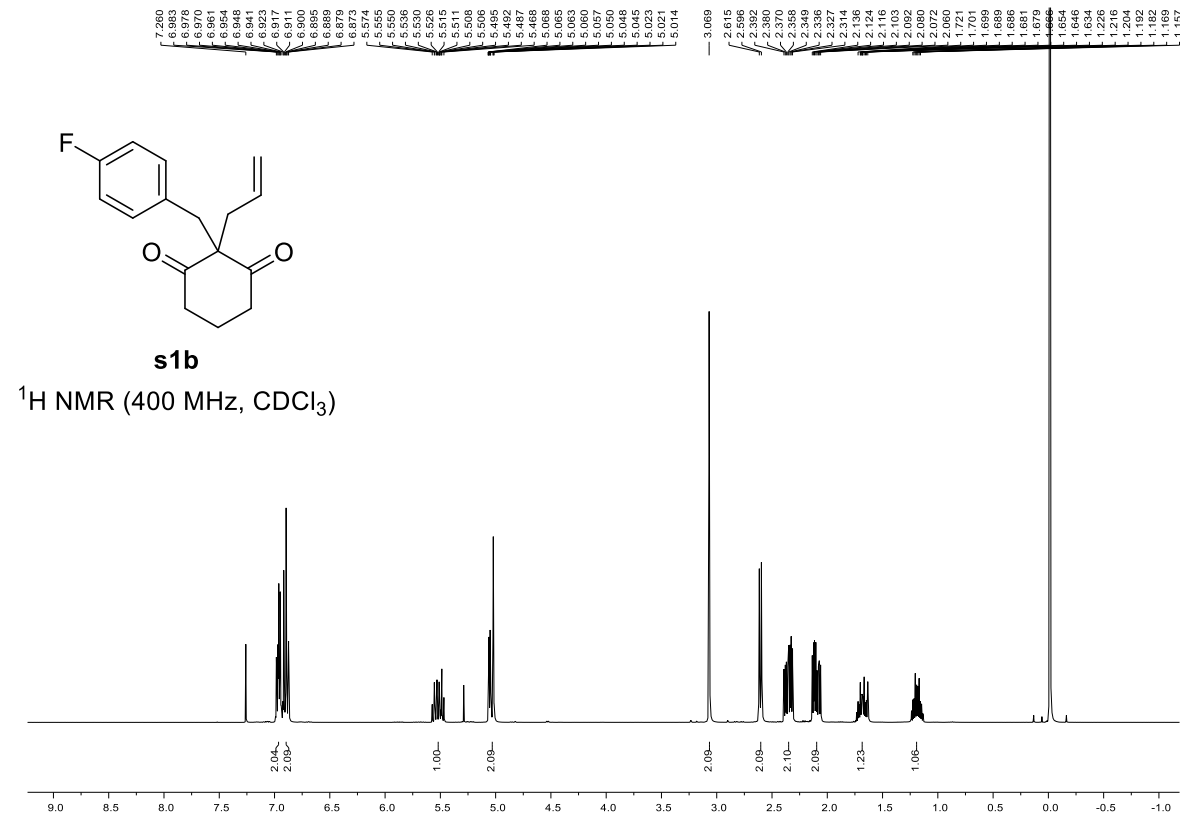

**s1a**

$^{1}$H NMR (400 MHz, $CDCl_3$)



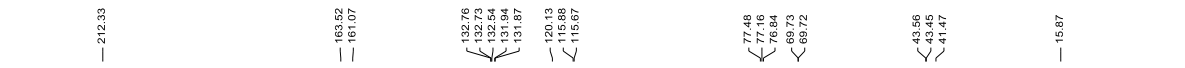

**s1a**

$^{13}$C NMR (101 MHz, $CDCl_3$)



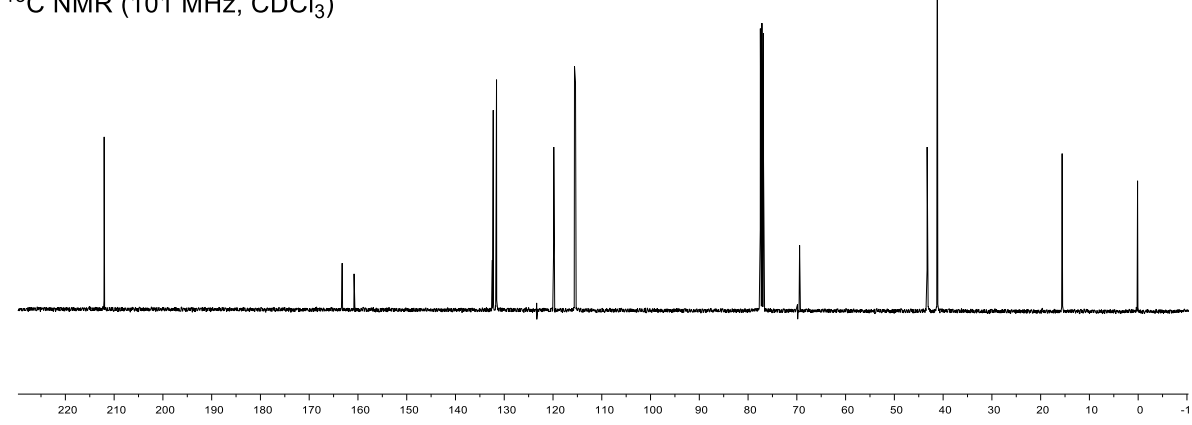

**s1b**

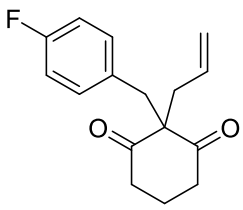
$^{1}$H NMR (400 MHz, $CDCl_3$)




**s1b**

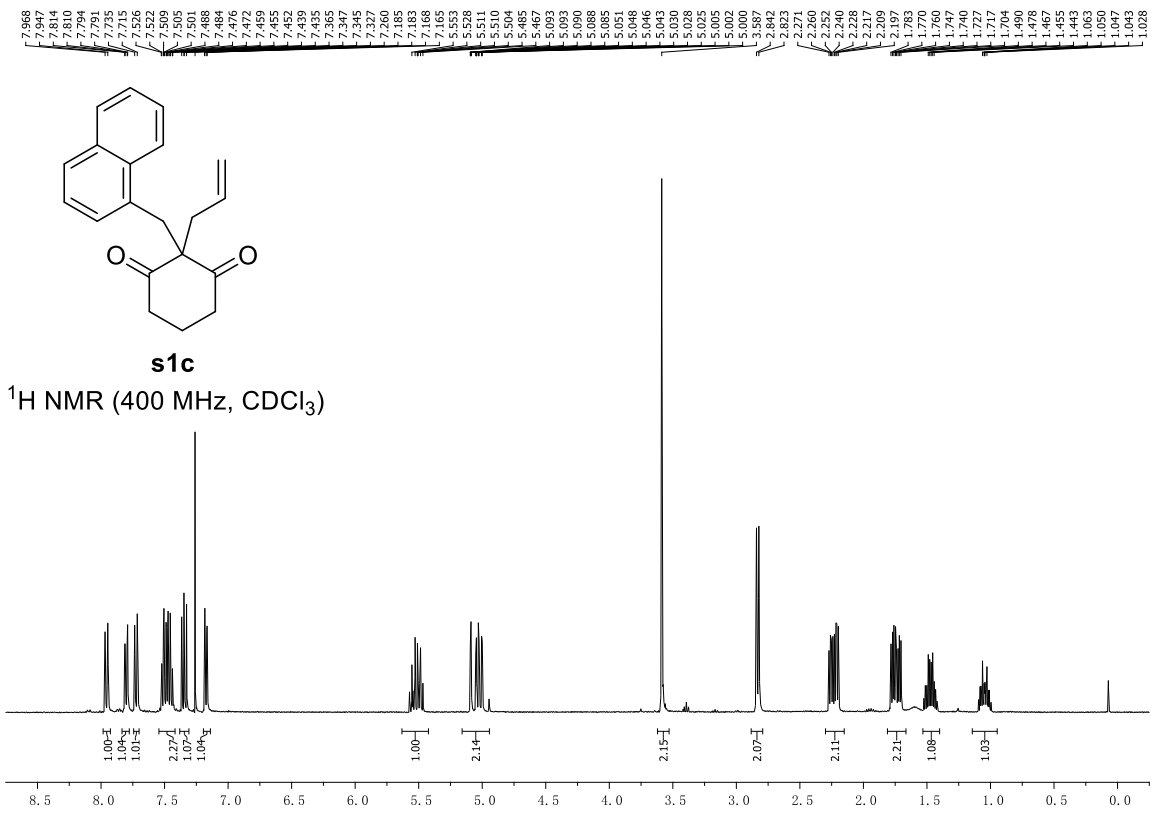
$^{13}$C NMR (101 MHz, $CDCl_3$)





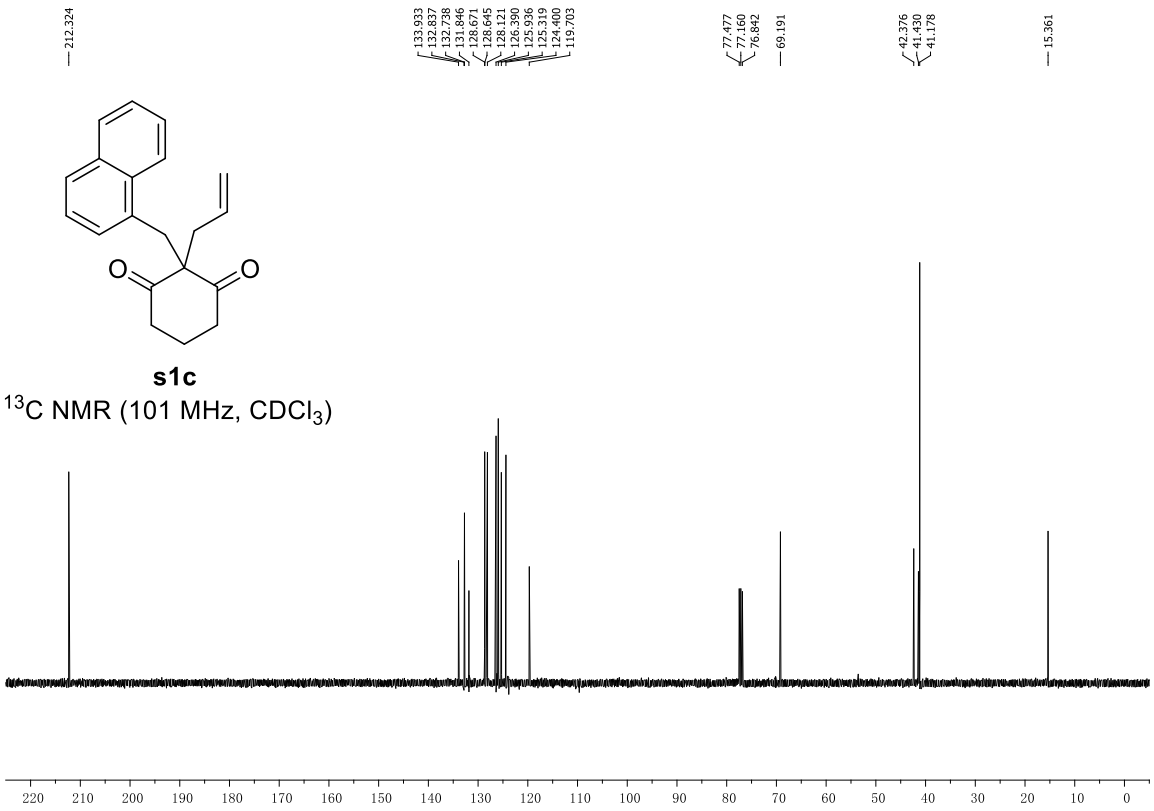

**s1b**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



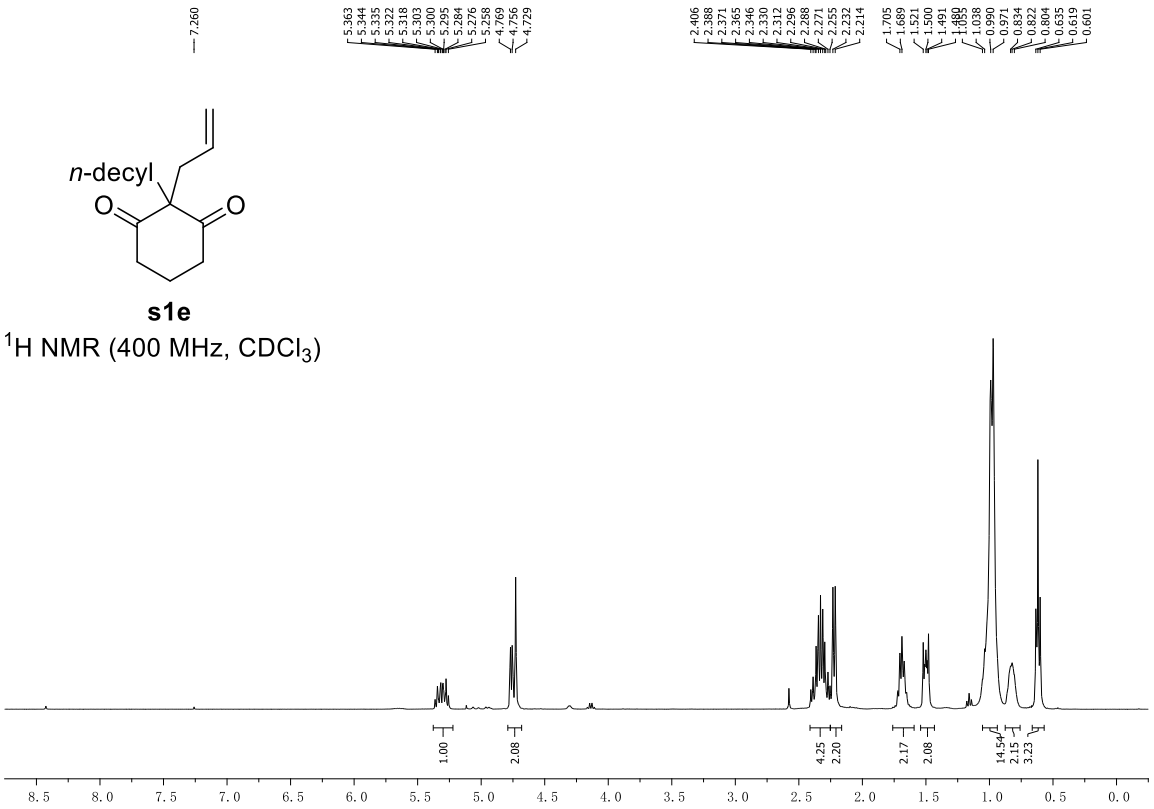
**s1c**

$^{1}$H NMR (400 MHz, $CDCl_3$)



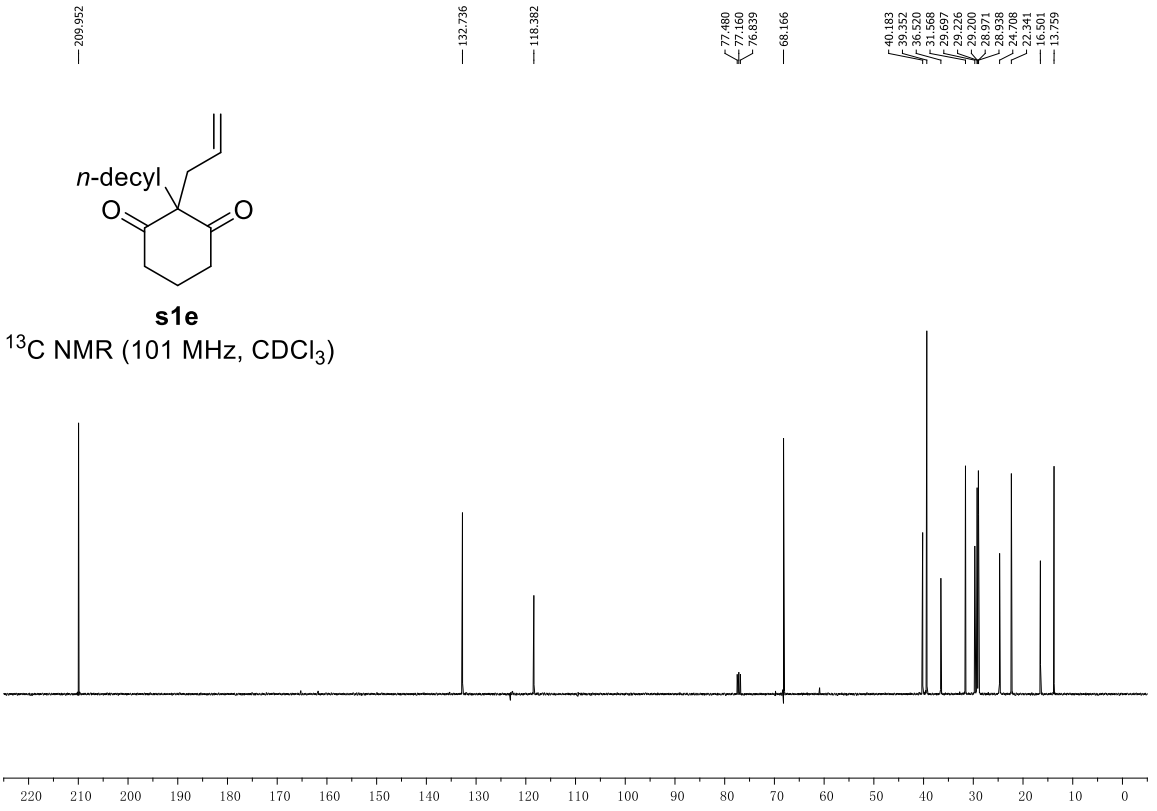
**s1c**

$^{13}$C NMR (101 MHz, $CDCl_3$)



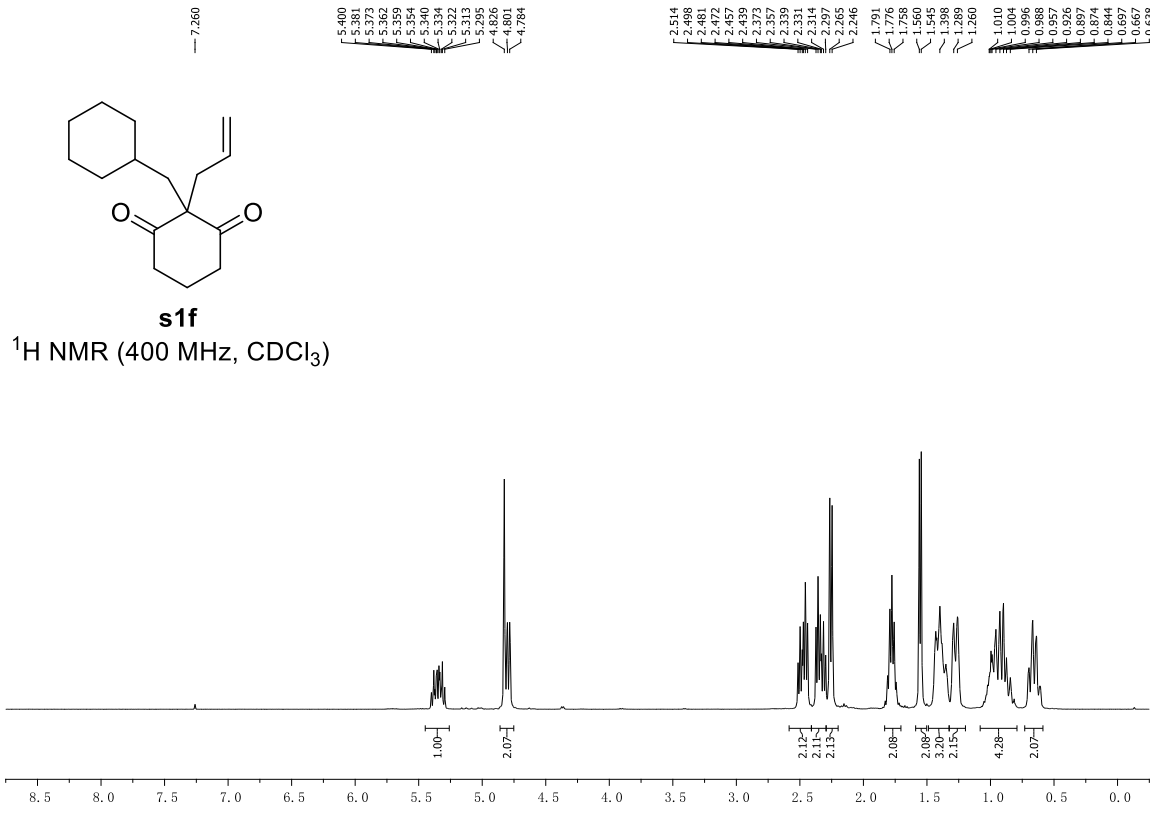

**s1e**

$^{1}$H NMR (400 MHz, $CDCl_3$)



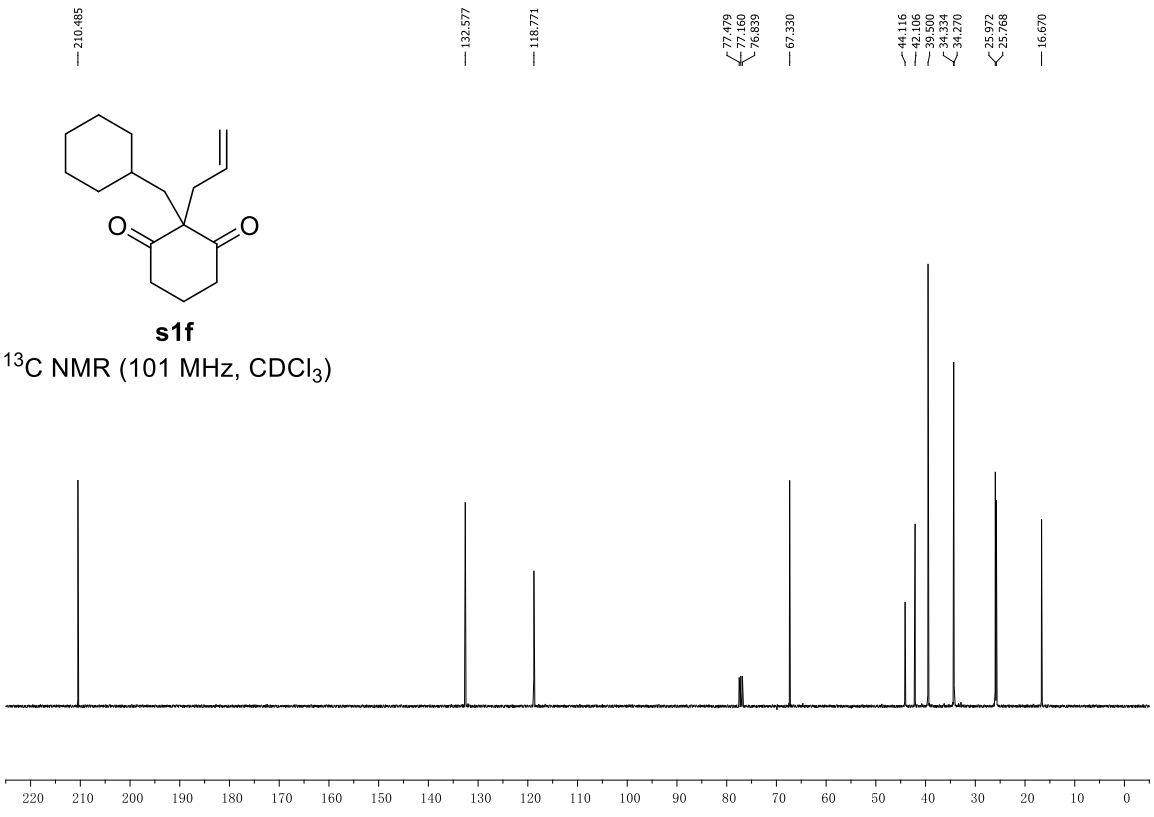

**s1e**

$^{13}$C NMR (101 MHz, $CDCl_3$)



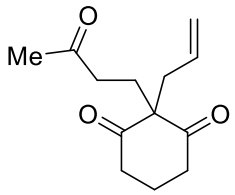

**s1f**

$^{1}$H NMR (400 MHz, $CDCl_3$)




**s1f**

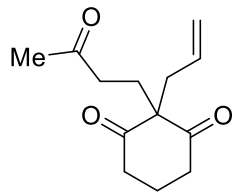
$^{13}$C NMR (101 MHz, $CDCl_3$)




**s1g**

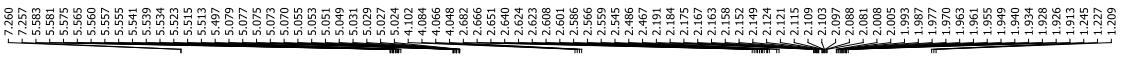
$^{1}$H NMR (400 MHz, $CDCl_3$)

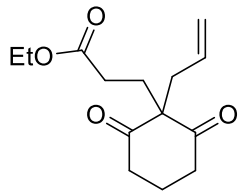



**s1g**

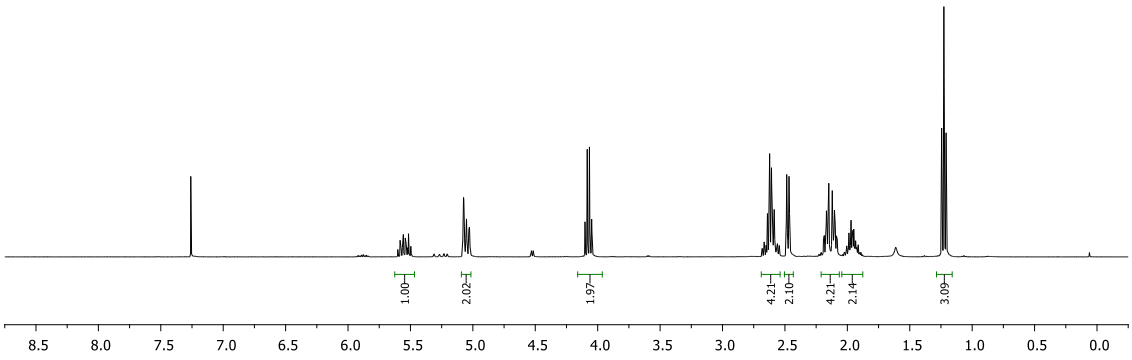
$^{13}$C NMR (101 MHz, $CDCl_3$)

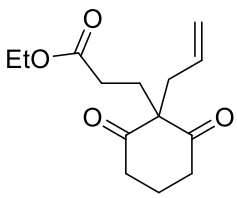




**s1h**

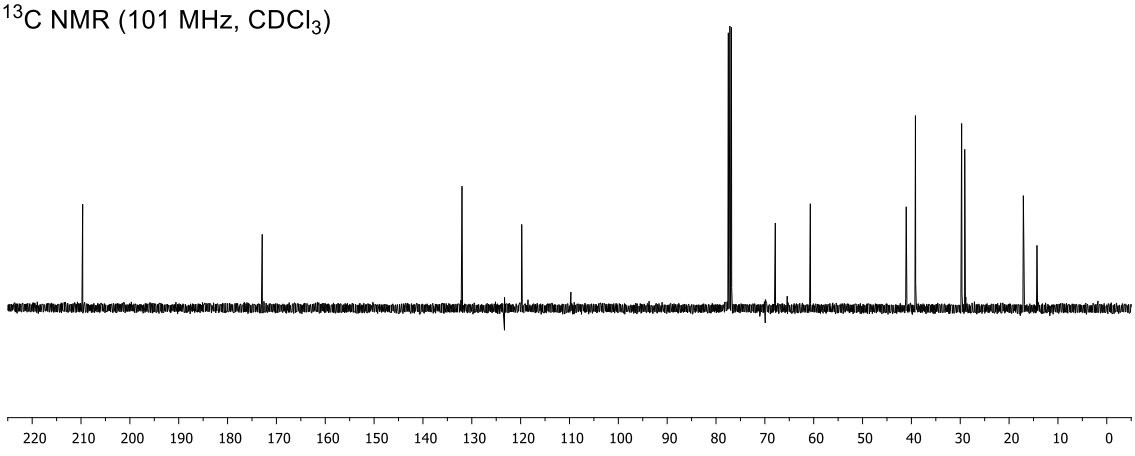
$^{1}$H NMR (400 MHz, $CDCl_3$)

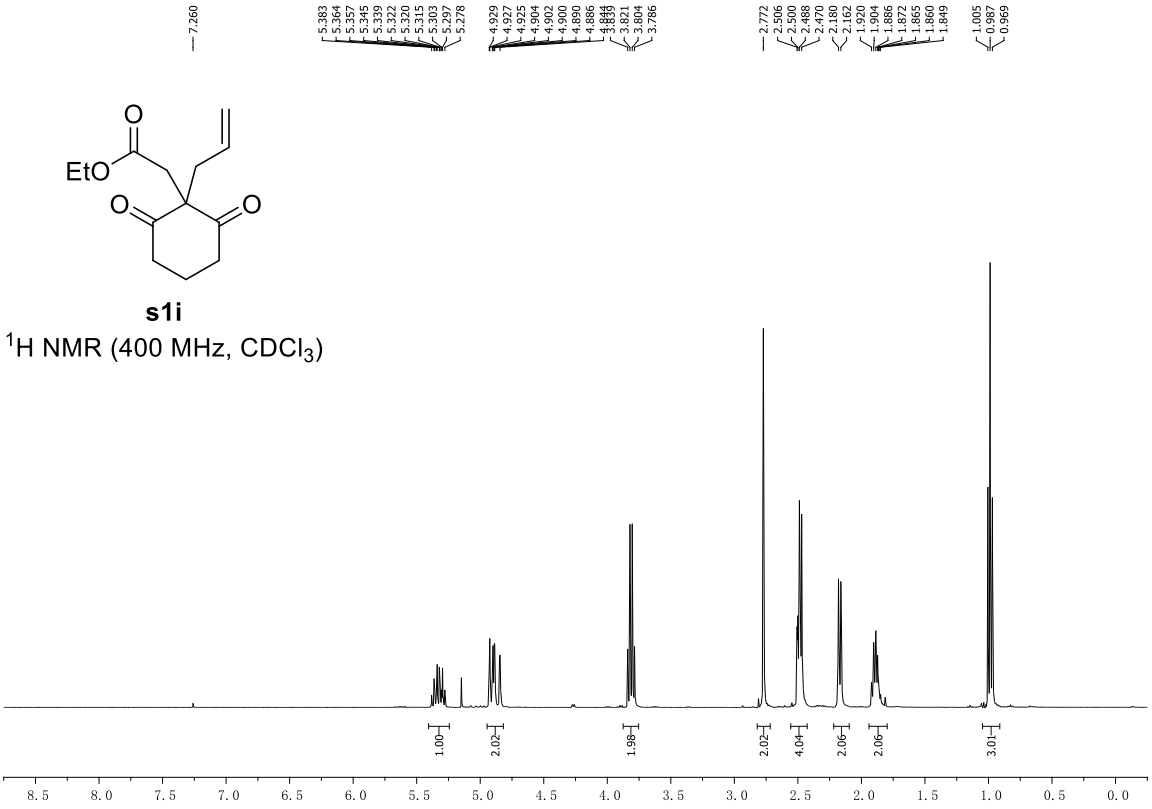


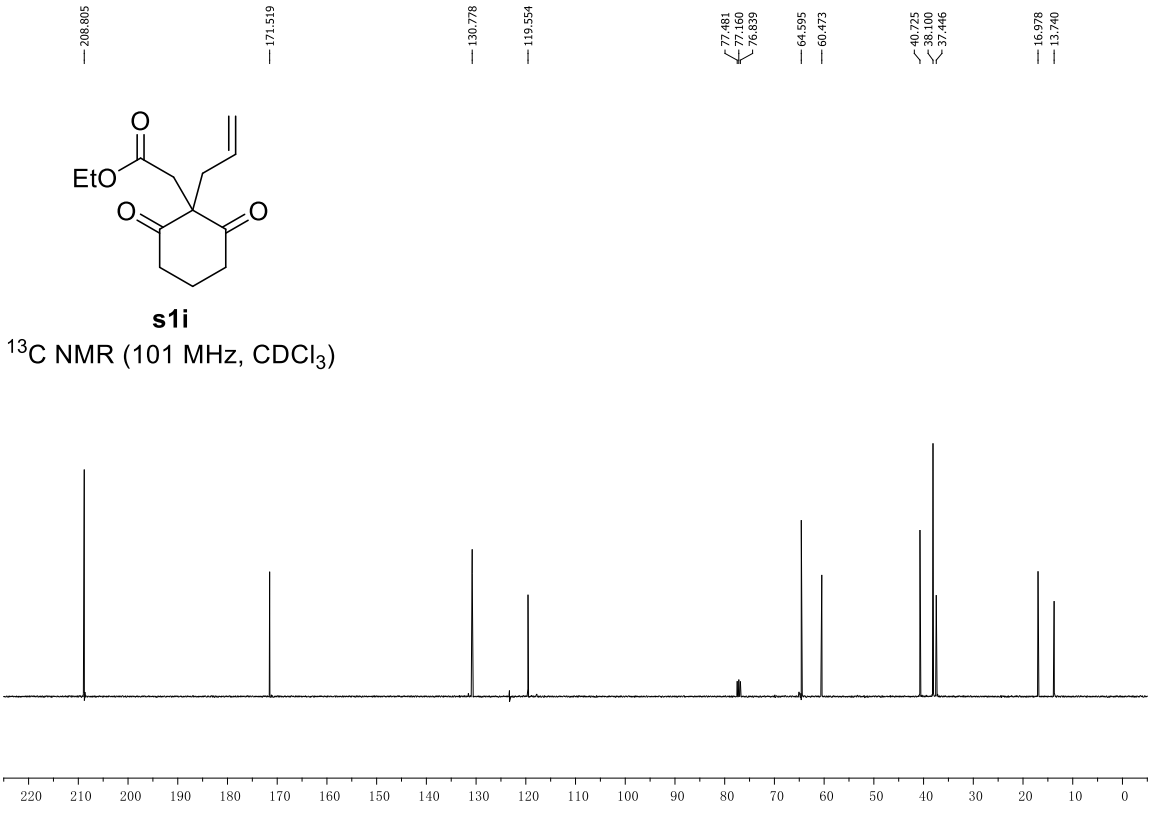


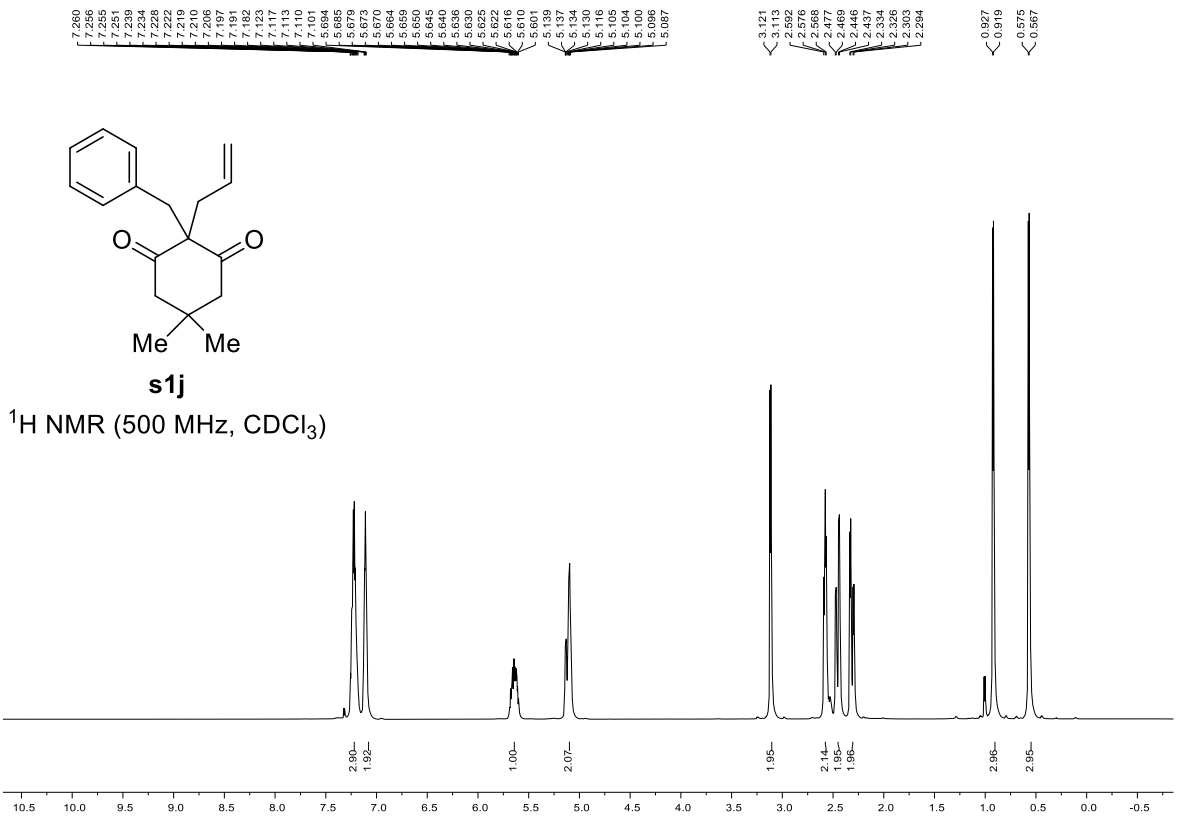
**s1h**

$^{13}$C NMR (101 MHz, $CDCl_3$)



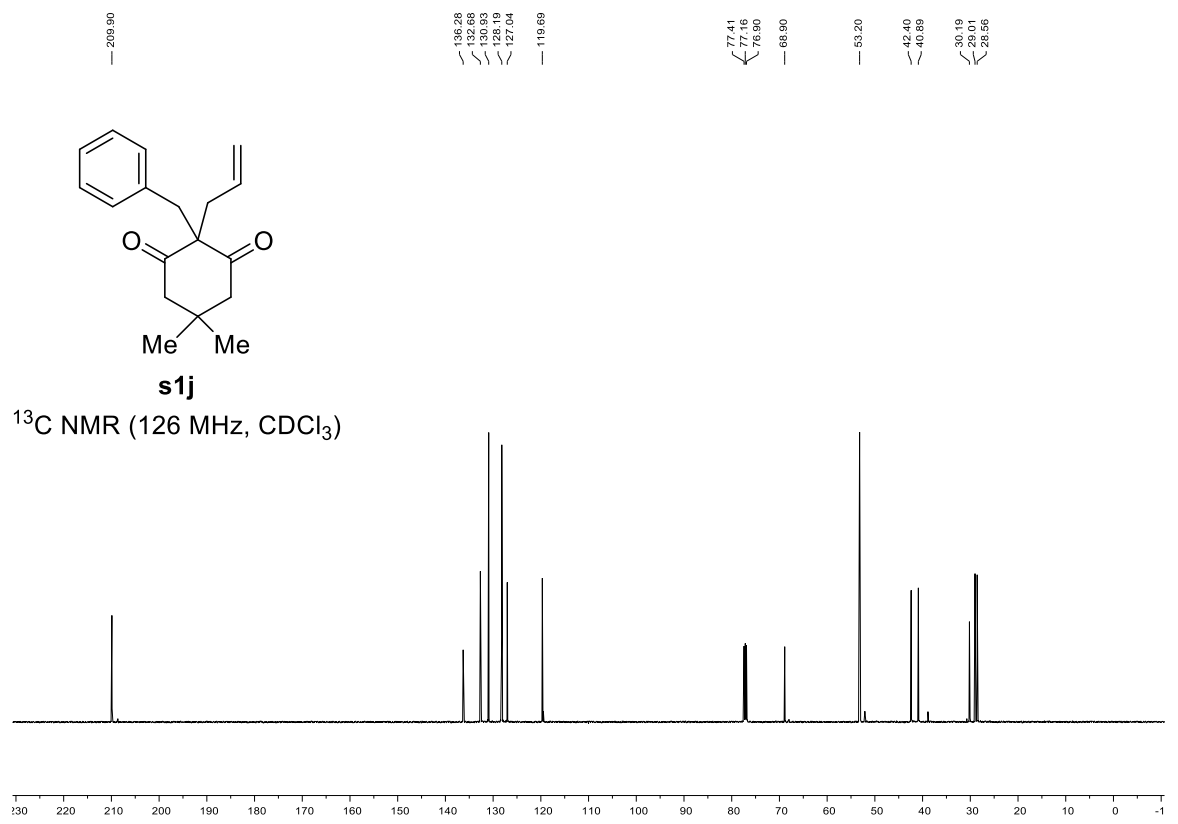

7.260
5.383
5.364
5.357
5.345
5.339
5.322
5.320
5.315
5.303
5.297
5.278
4.929
4.927
4.925
4.904
4.902
4.900
4.890
4.886
3.844
3.821
3.804
3.786
2.772
2.506
2.500
2.488
2.470
2.180
2.162
1.920
1.904
1.886
1.872
1.865
1.860
1.849
1.005
0.987
0.969
EtO
O
O
O
s1i
1H NMR (400 MHz, CDCl3)
1.00
2.02
1.98
2.02
4.04
2.06
2.06
3.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


208.805
171.519
130.778
119.554
77.481
77.160
76.839
64.595
60.473
40.725
38.100
37.446
16.978
13.740
EtO
O
O
O
s1i
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



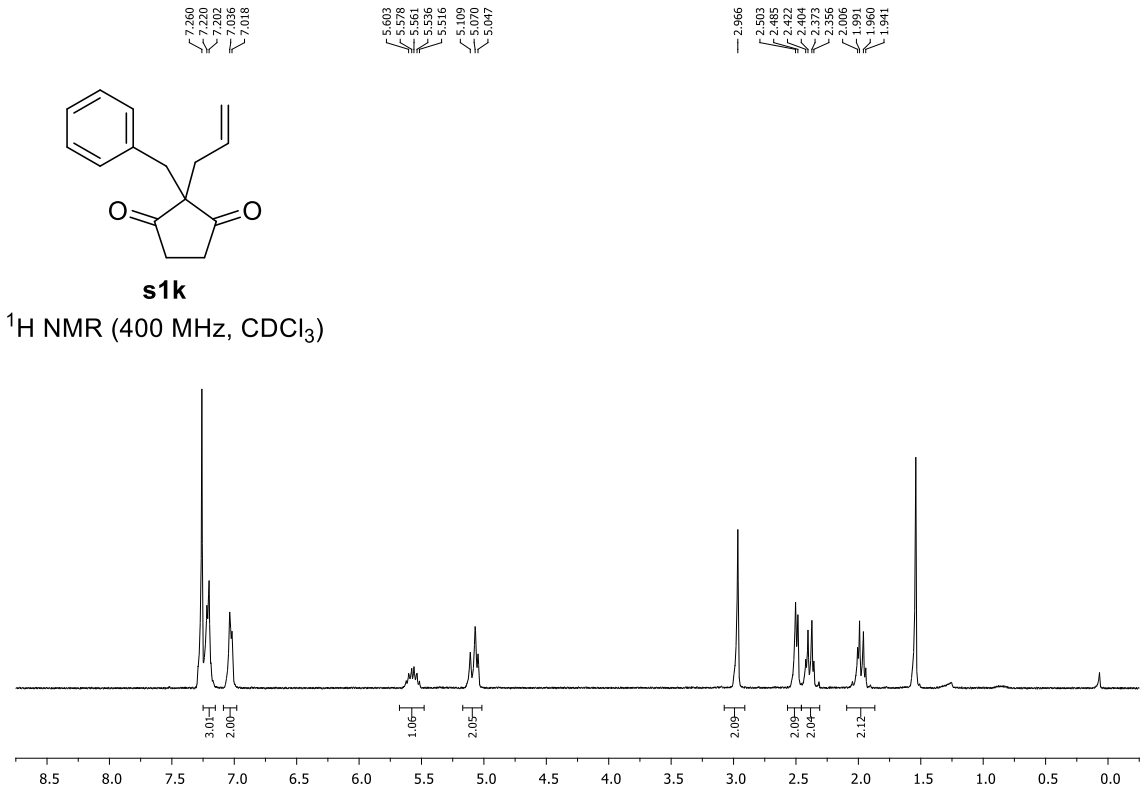

**s1j**

$^{1}$H NMR (500 MHz, $CDCl_3$)



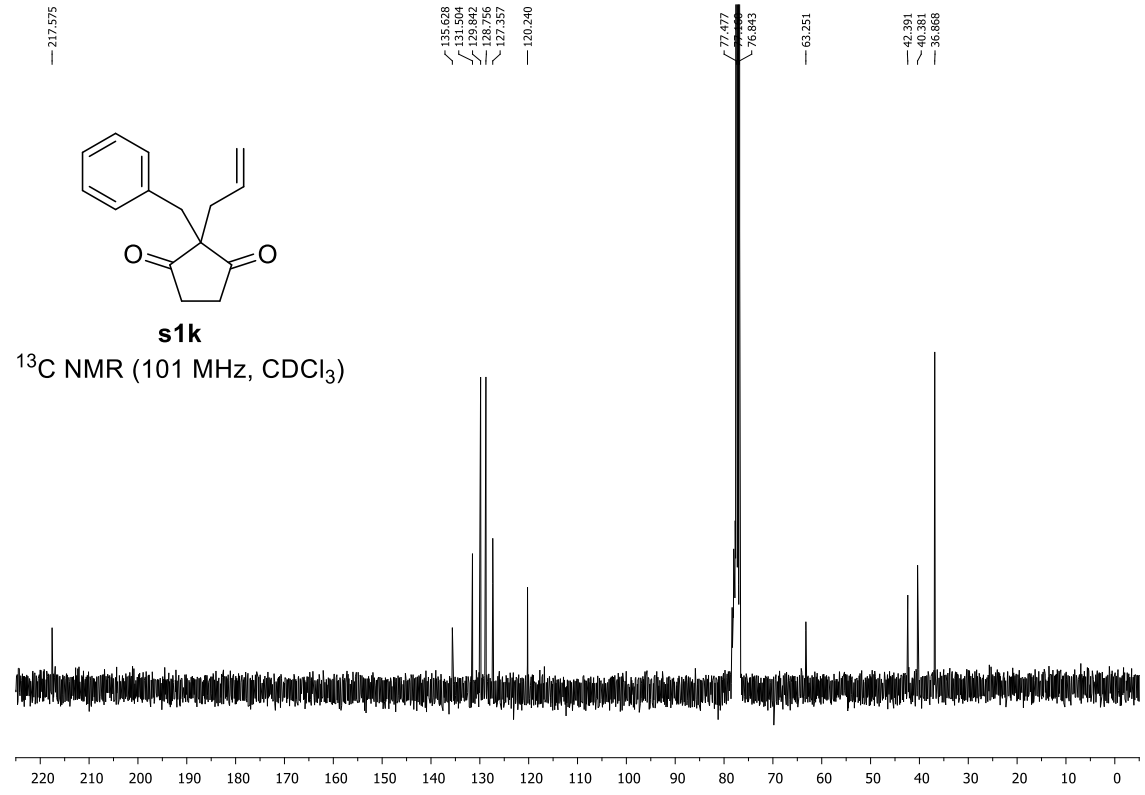

**s1j**

$^{13}$C NMR (126 MHz, $CDCl_3$)



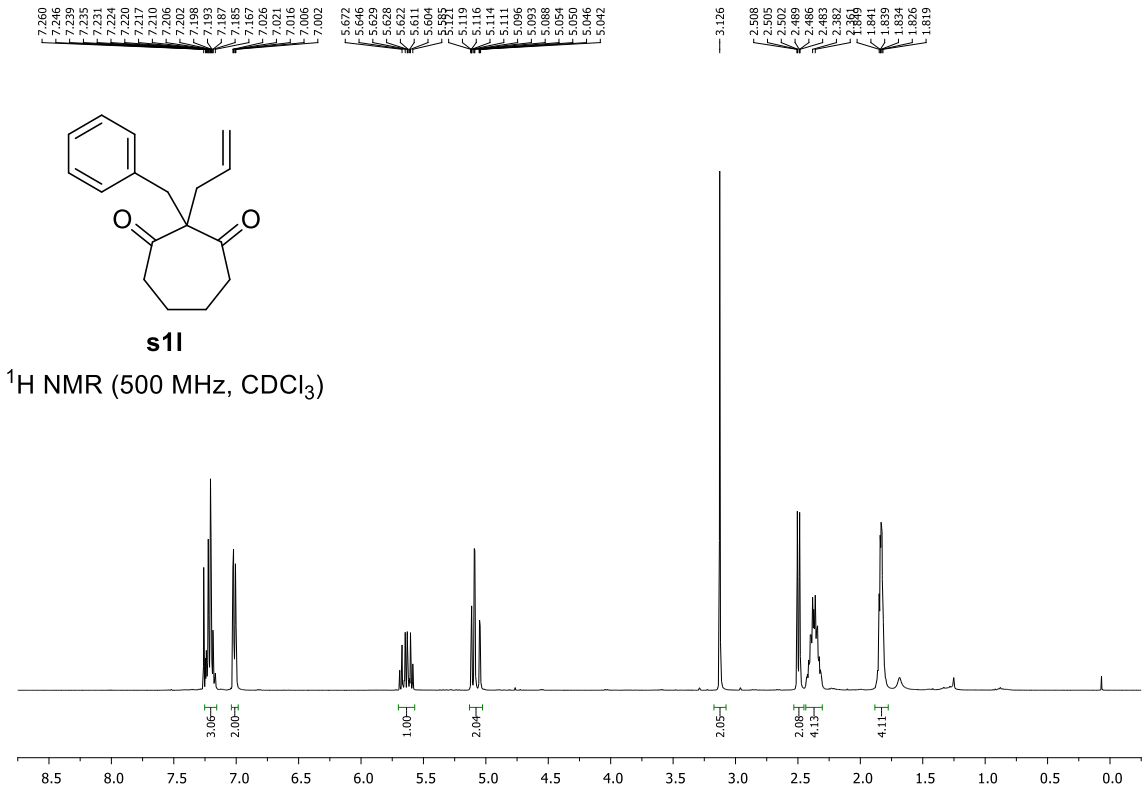

**s1k**

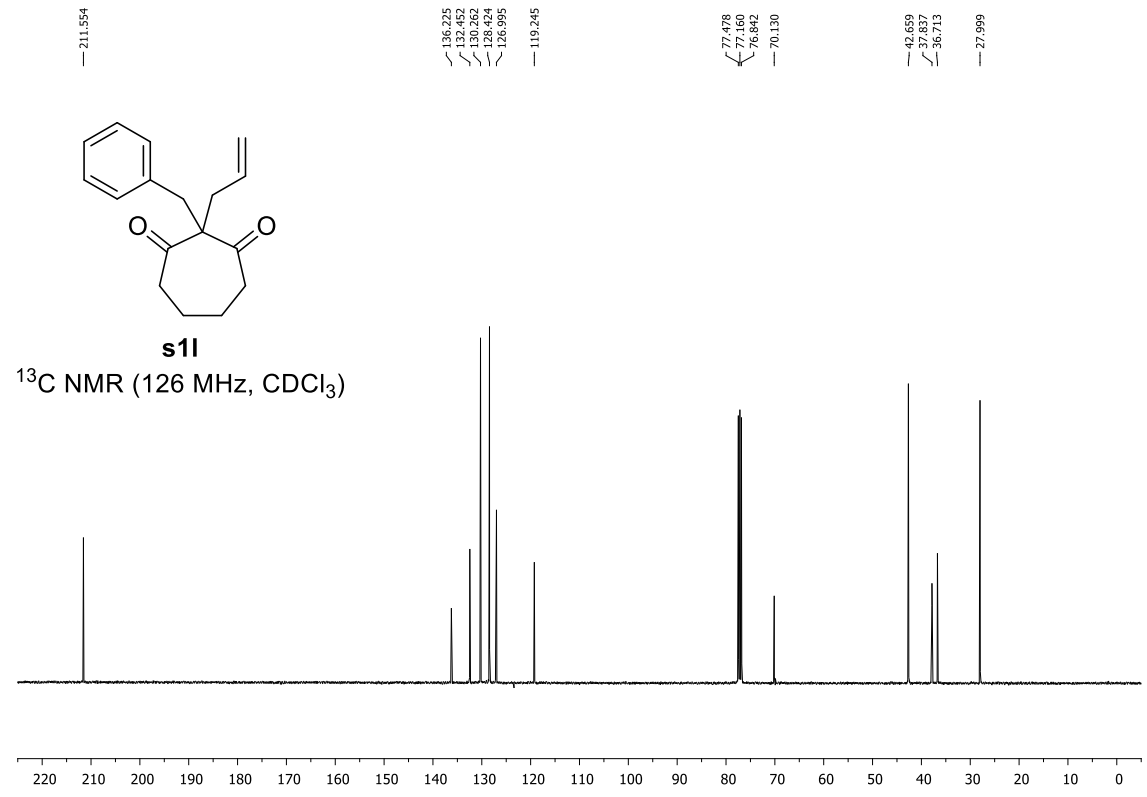
$^{1}$H NMR (400 MHz, $CDCl_3$)

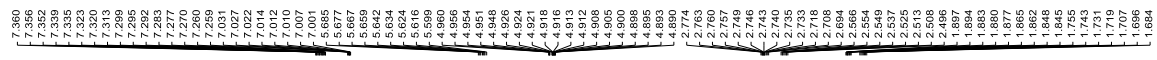


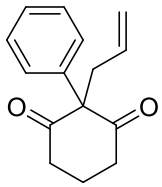

**s1k**

$^{13}$C NMR (101 MHz, $CDCl_3$)


7.260
7.246
7.239
7.235
7.231
7.224
7.220
7.217
7.210
7.206
7.202
7.198
7.193
7.187
7.185
7.167
7.026
7.021
7.016
7.006
7.002
5.672
5.646
5.629
5.628
5.622
5.611
5.604
5.585
5.121
5.119
5.116
5.114
5.111
5.096
5.093
5.088
5.054
5.050
5.046
5.042
3.126
2.508
2.505
2.502
2.498
2.486
2.483
2.382
2.361
1.849
1.841
1.839
1.834
1.826
1.819
O
O
s1l
1H NMR (500 MHz, CDCl3)
3.06
2.00
1.00
2.04
2.05
2.08
4.13
4.11
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


211.554
136.225
132.452
130.262
128.424
126.995
119.245
77.478
77.160
76.842
70.130
42.659
37.837
36.713
27.999
O
O
s1l
13C NMR (126 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

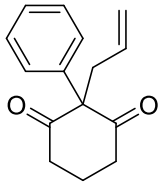




**s1m**

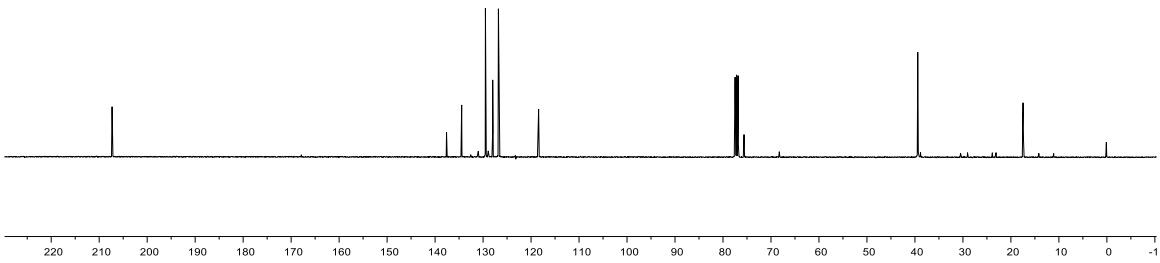
$^{1}H$ NMR (400 MHz, $CDCl_3$)

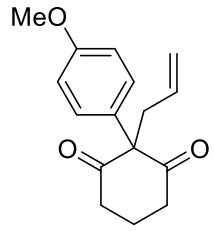




**s1m**

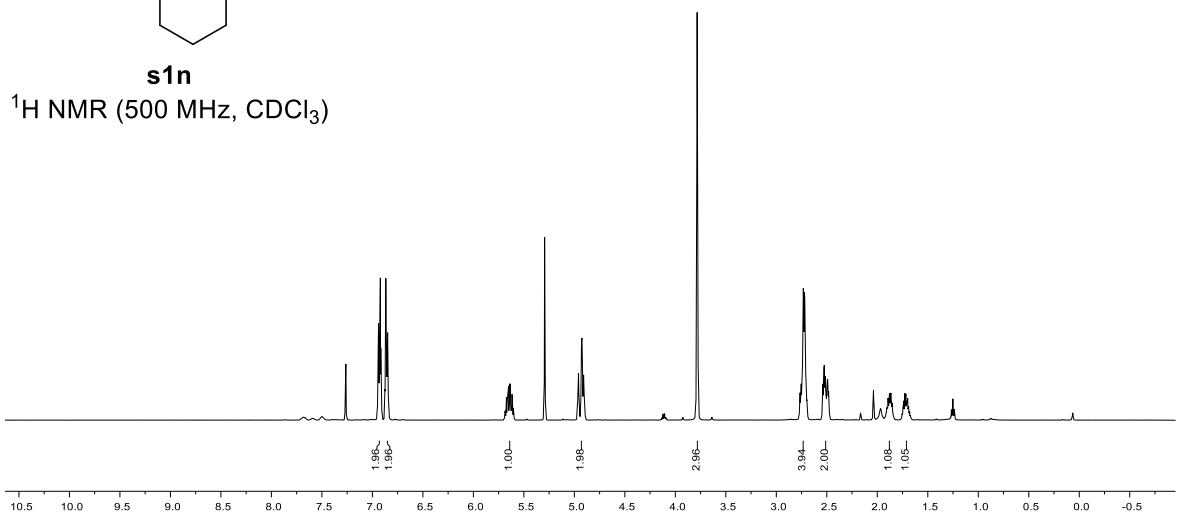
$^{13}C$ NMR (101 MHz, $CDCl_3$)

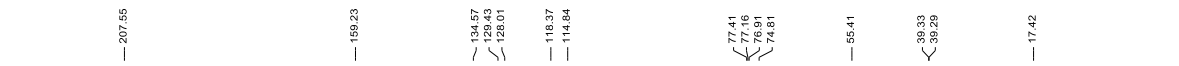


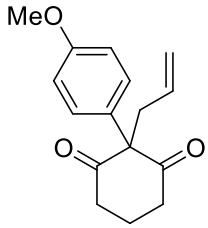


**s1n**

$^{1}$H NMR (500 MHz, $CDCl_3$)

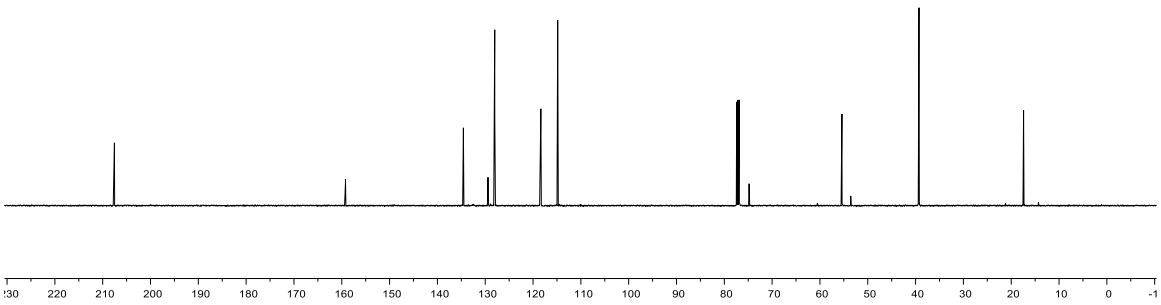


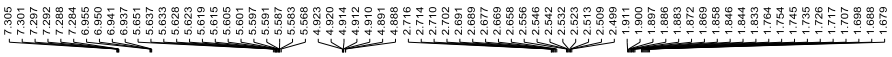


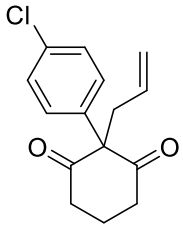


**s1n**

$^{13}$C NMR (126 MHz, $CDCl_3$)

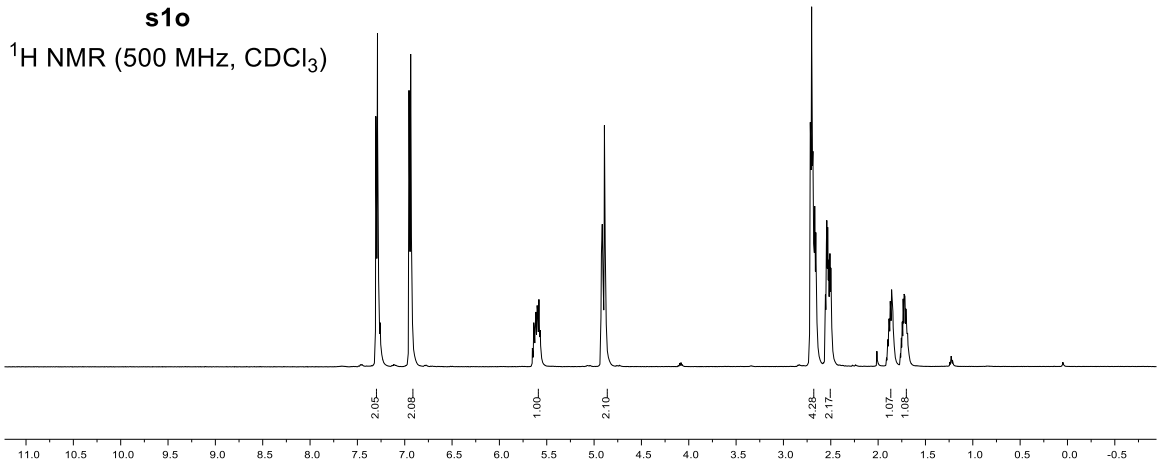




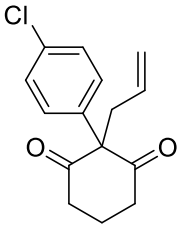




**s1o**

$^{1}$H NMR (500 MHz, $CDCl_3$)

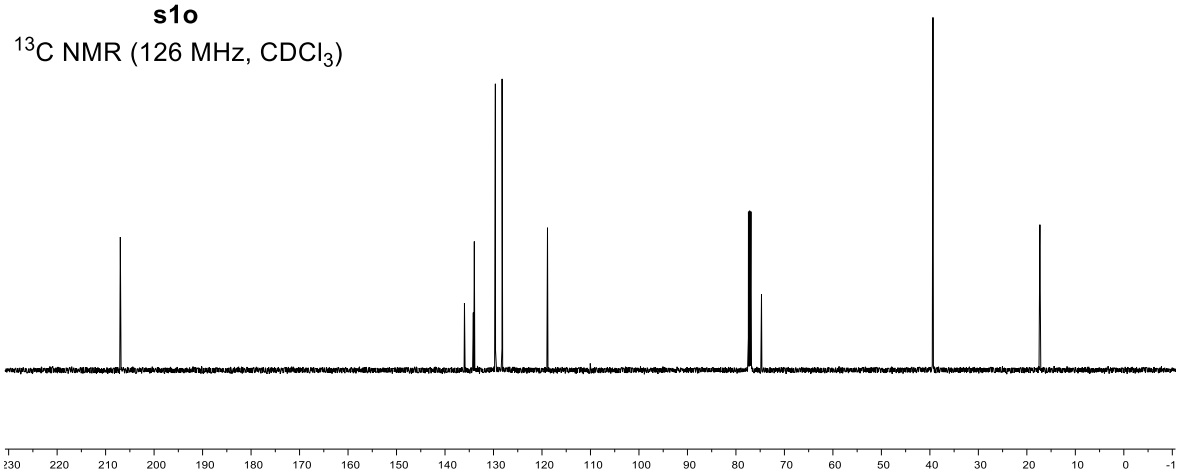


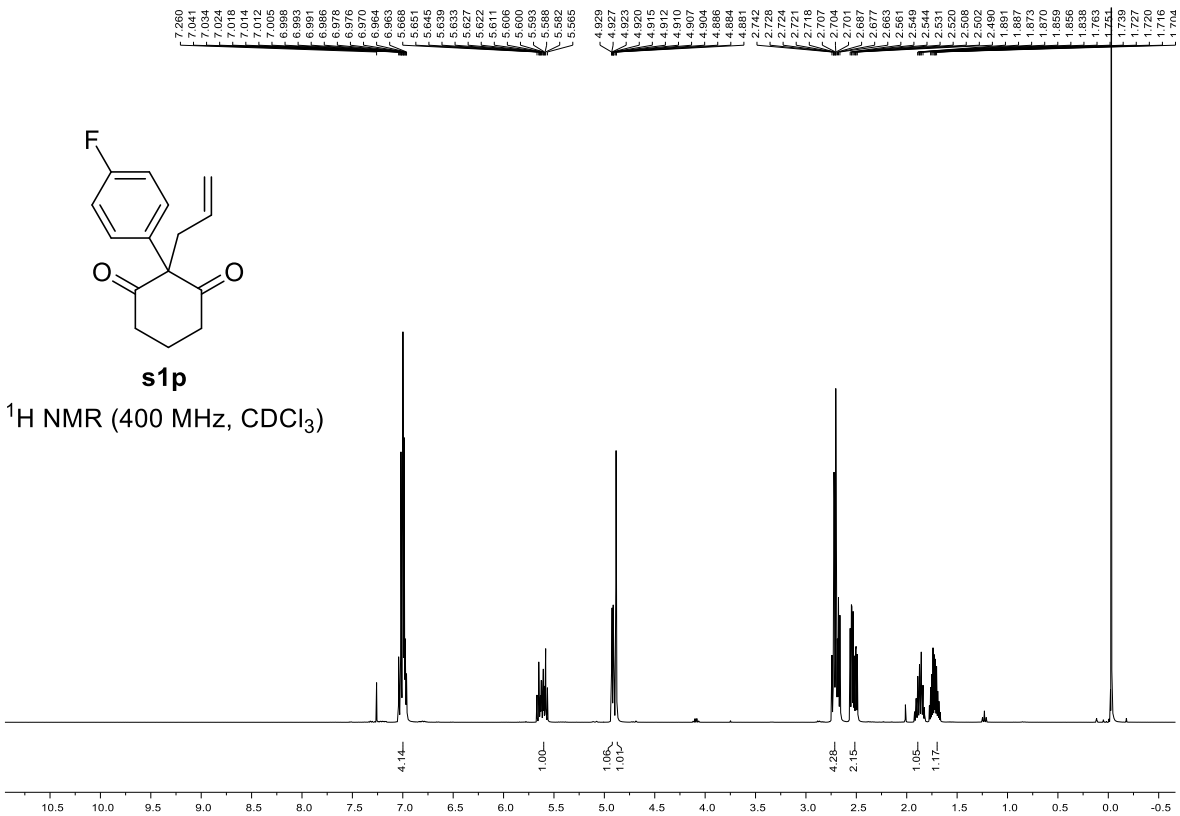


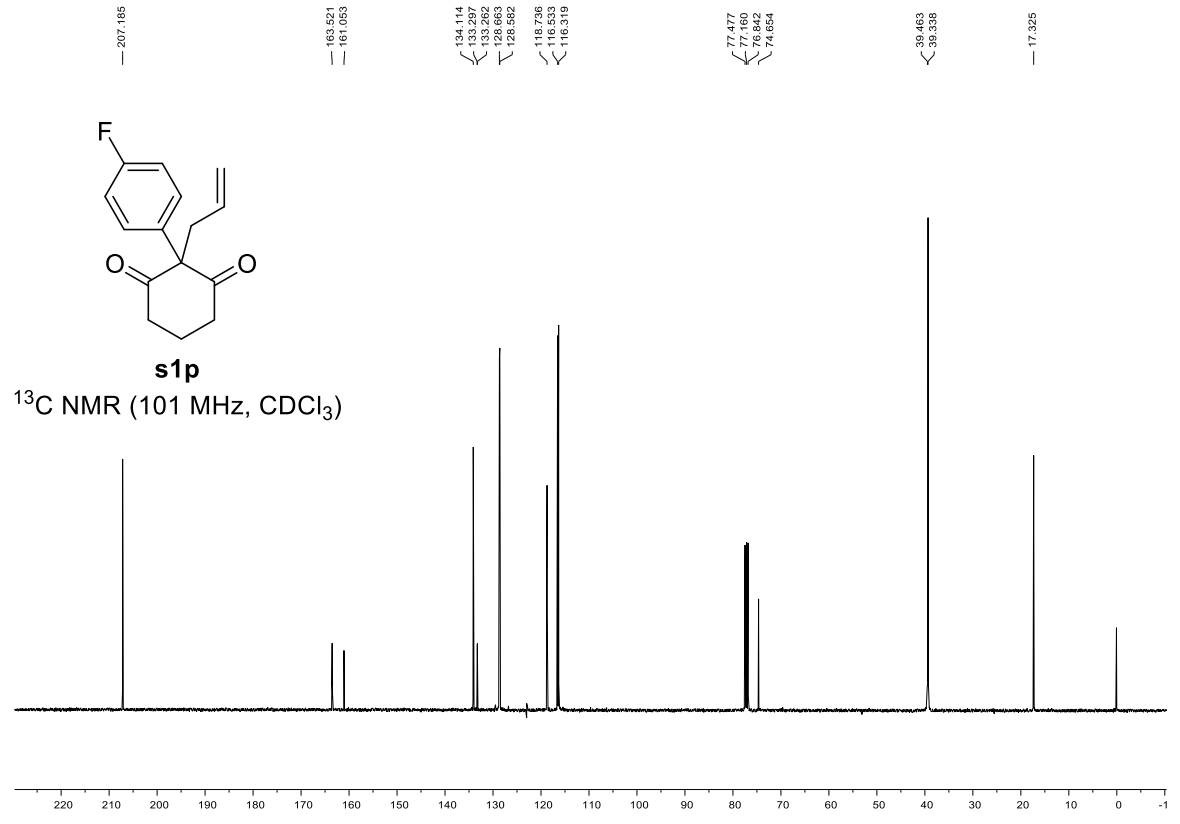


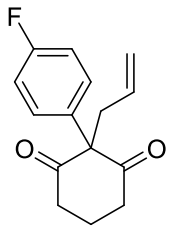

**s1o**

$^{13}$C NMR (126 MHz, $CDCl_3$)



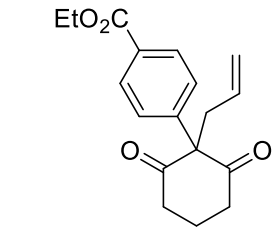

F
O
O
s1p
1H NMR (400 MHz, CDCl3)
7.260
7.044
7.041
7.034
7.024
7.018
7.014
7.012
7.005
6.998
6.993
6.991
6.986
6.978
6.976
6.970
6.964
6.963
6.956
5.651
5.645
5.639
5.633
5.627
5.622
5.611
5.606
5.600
5.593
5.588
5.582
5.565
4.929
4.927
4.923
4.920
4.915
4.912
4.910
4.907
4.904
4.886
4.884
4.881
2.742
2.728
2.724
2.721
2.718
2.707
2.704
2.701
2.687
2.677
2.663
2.561
2.549
2.544
2.531
2.520
2.508
2.502
2.490
1.891
1.887
1.873
1.870
1.859
1.856
1.838
1.763
1.751
1.739
1.727
1.720
1.716
1.704
4.14
1.00
1.06
1.01
4.28
2.15
1.05
1.17
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


207.185
163.521
161.053
134.114
133.997
133.262
128.663
128.582
118.736
116.533
116.319
77.477
77.160
76.842
74.654
39.463
39.338
17.325
F
O
O
s1p
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1




**s1p**

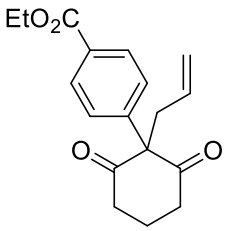
$^{19}F$ NMR (376 MHz, $CDCl_3$)



**s1q**

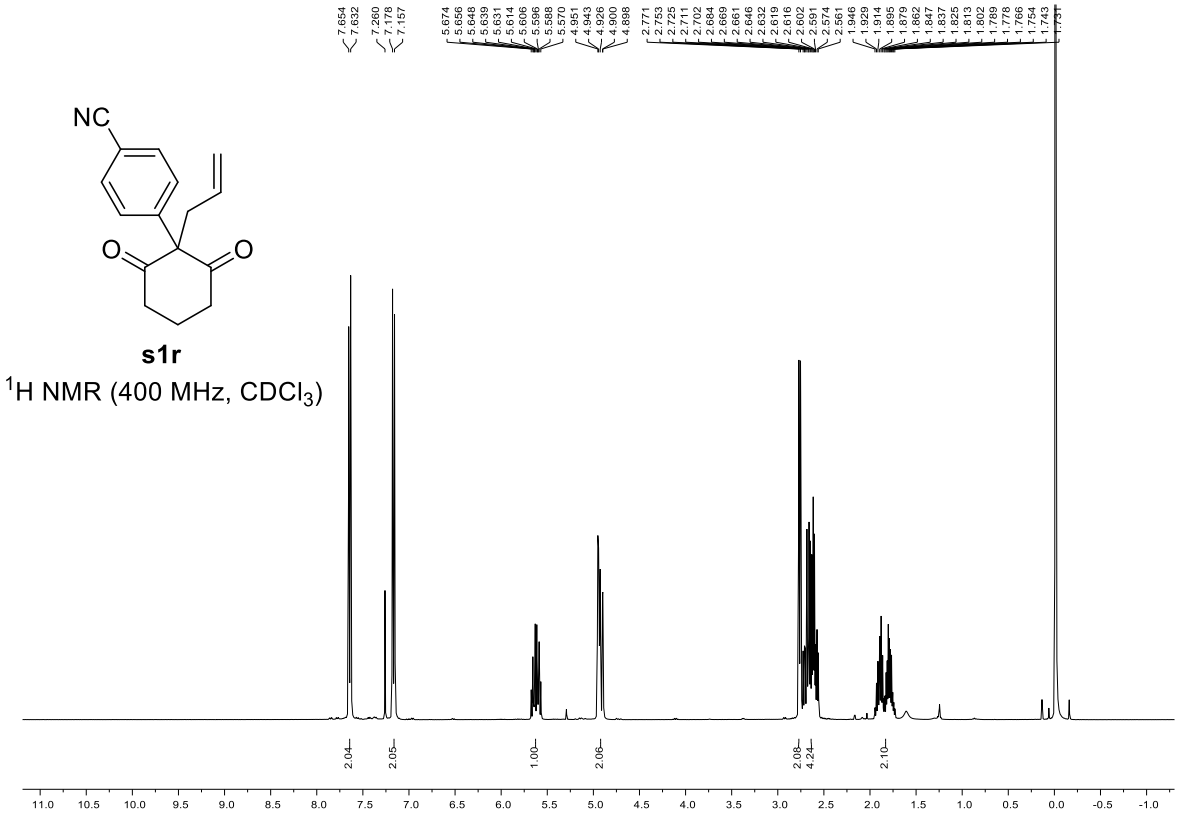
$^1$H NMR (400 MHz, $CDCl_3$)





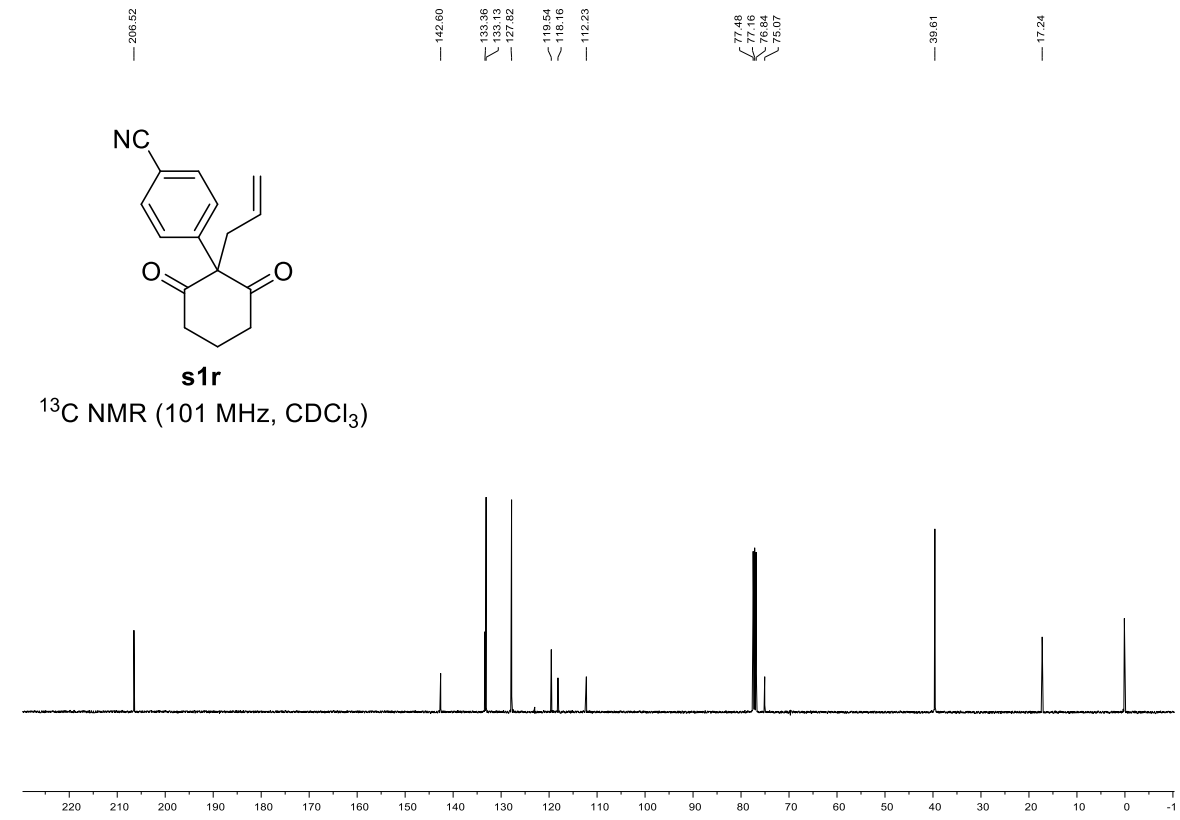
**s1q**

$^{13}$C NMR (101 MHz, $CDCl_3$)



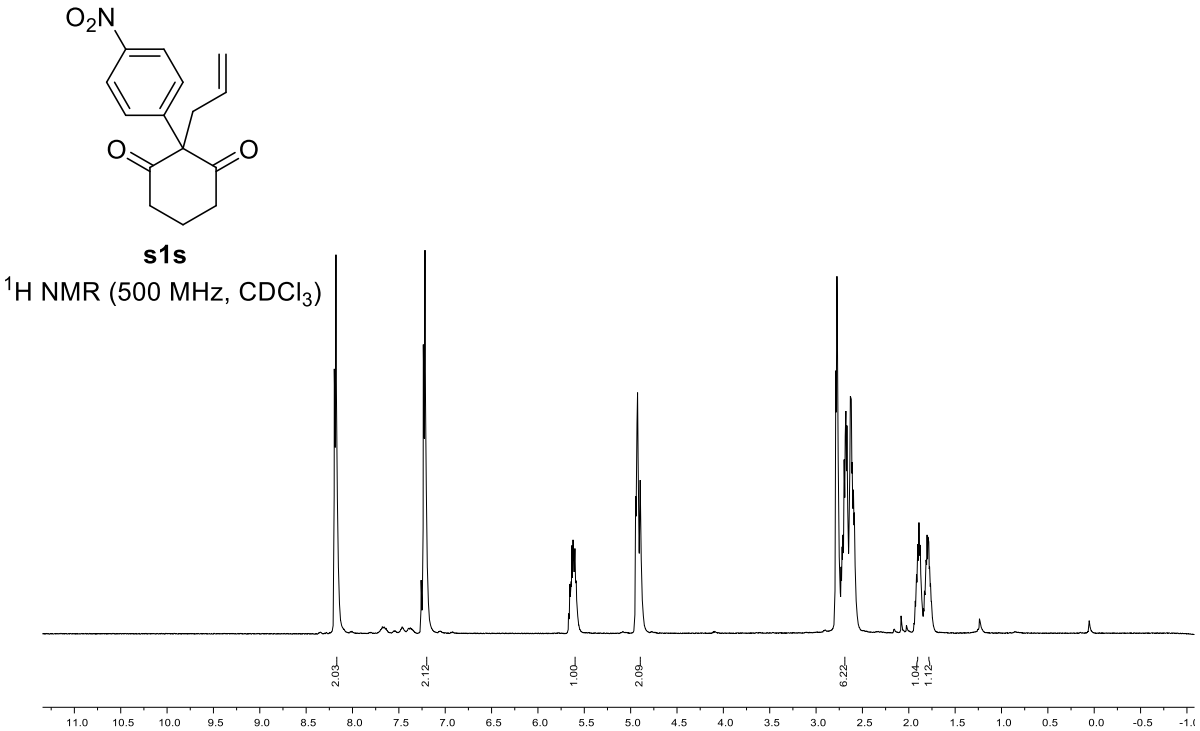

**s1r**

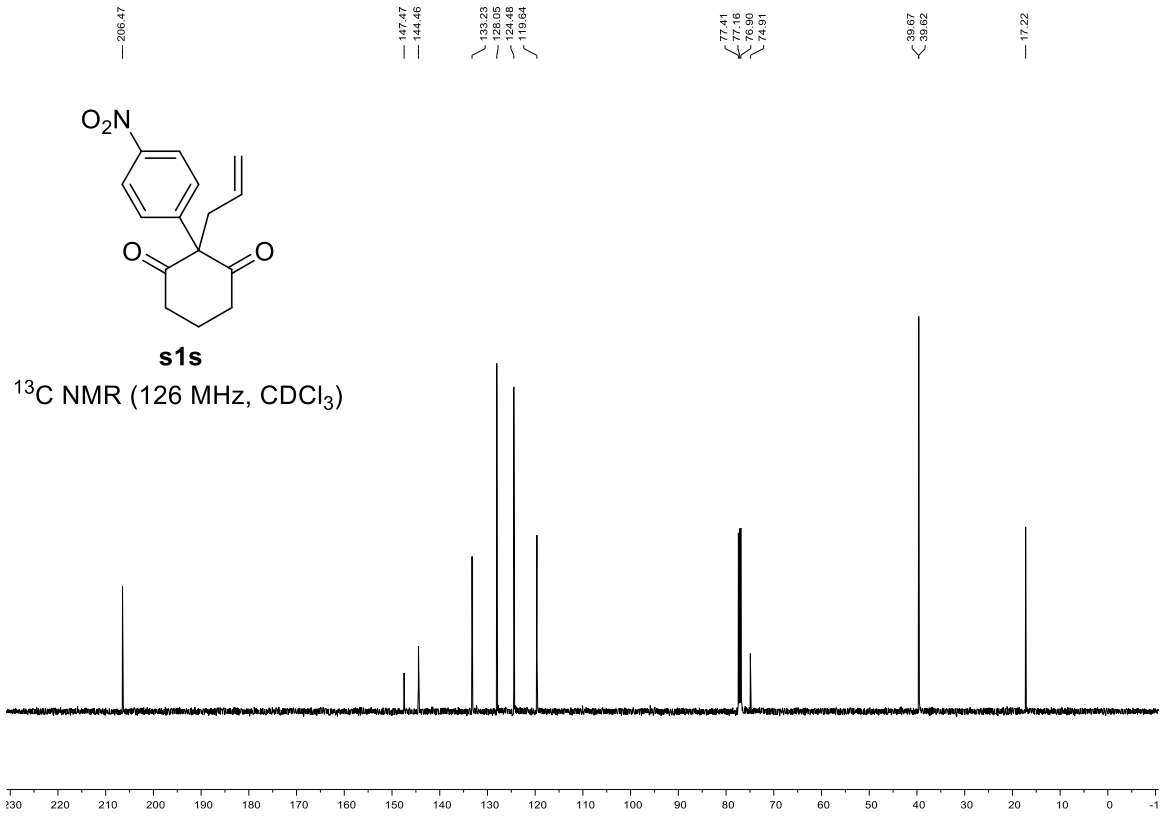
$^{1}$H NMR (400 MHz, $CDCl_3$)

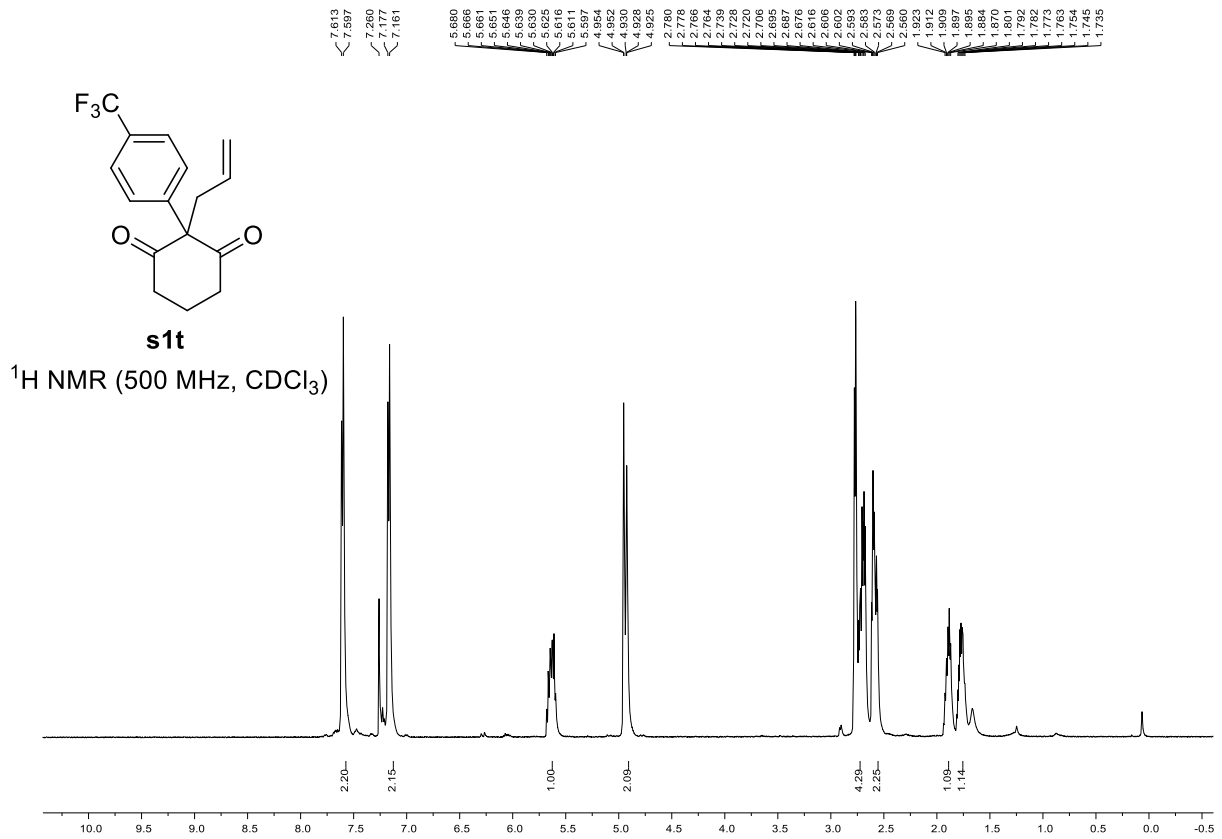


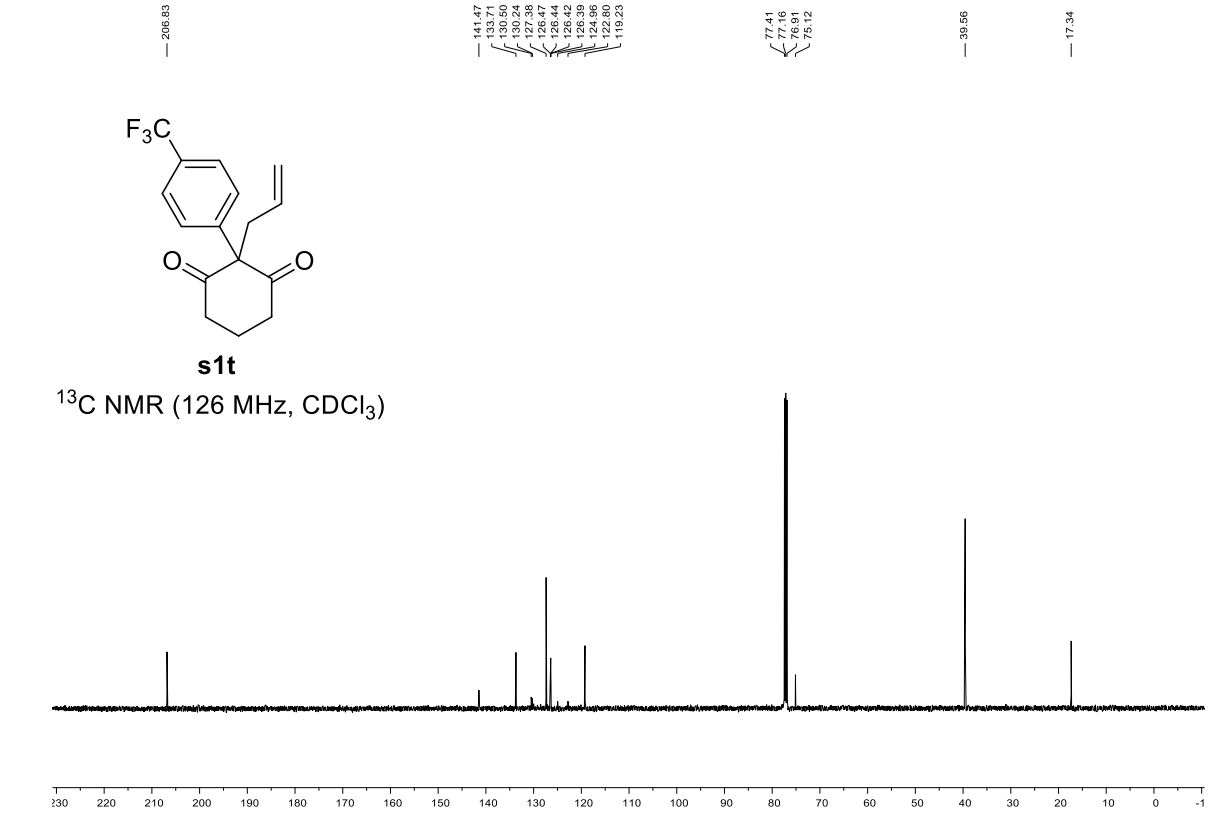

**s1r**

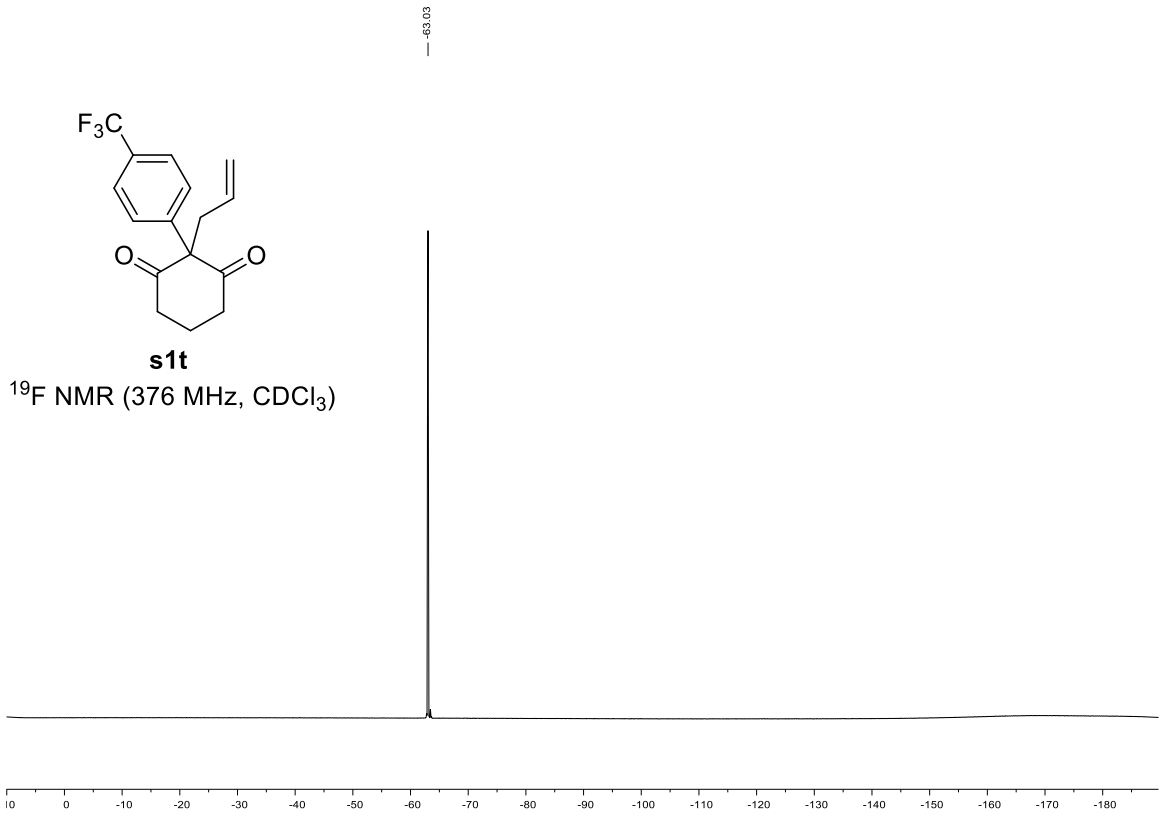
$^{13}$C NMR (101 MHz, $CDCl_3$)


O2N
O
O
s1s
1H NMR (500 MHz, CDCl3)
2.03
2.12
1.00
2.09
6.22
1.04
1.12


O2N
O
O
s1s
13C NMR (126 MHz, CDCl3)
206.47
147.47
144.46
133.23
128.05
124.48
119.64
77.41
77.16
76.90
74.91
39.67
39.62
17.22

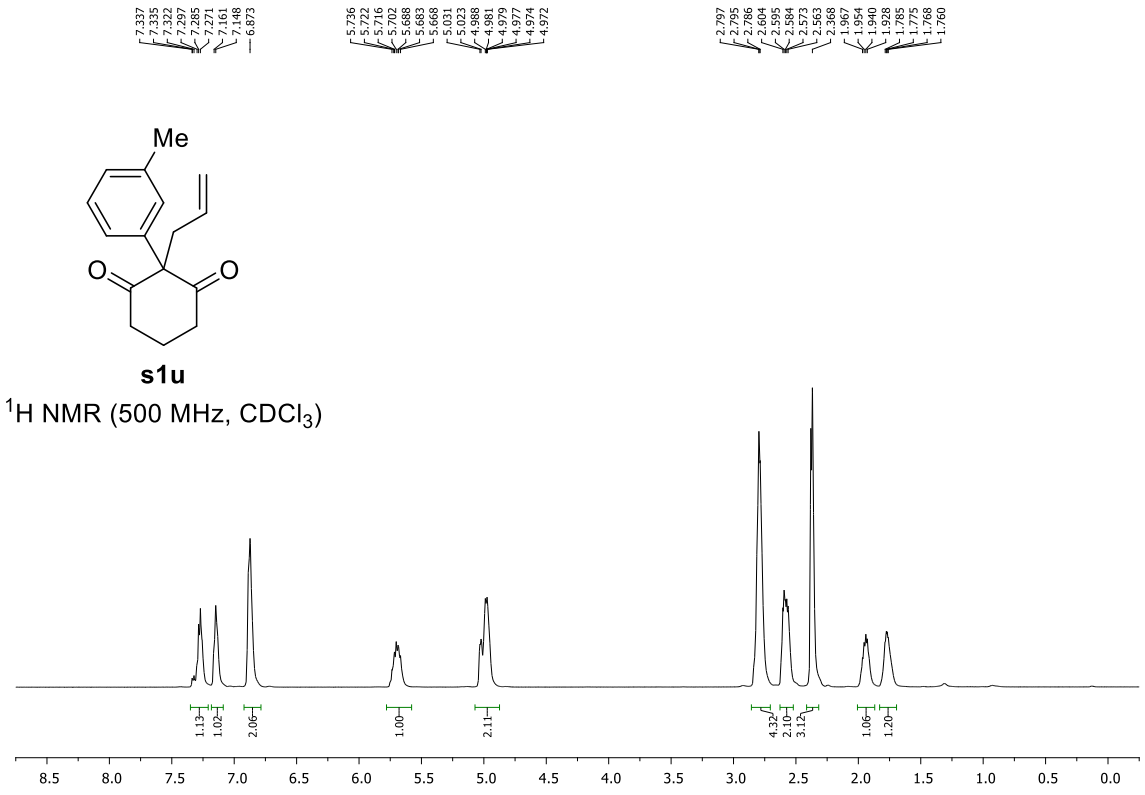

F3C
O
O
s1t
1H NMR (500 MHz, CDCl3)

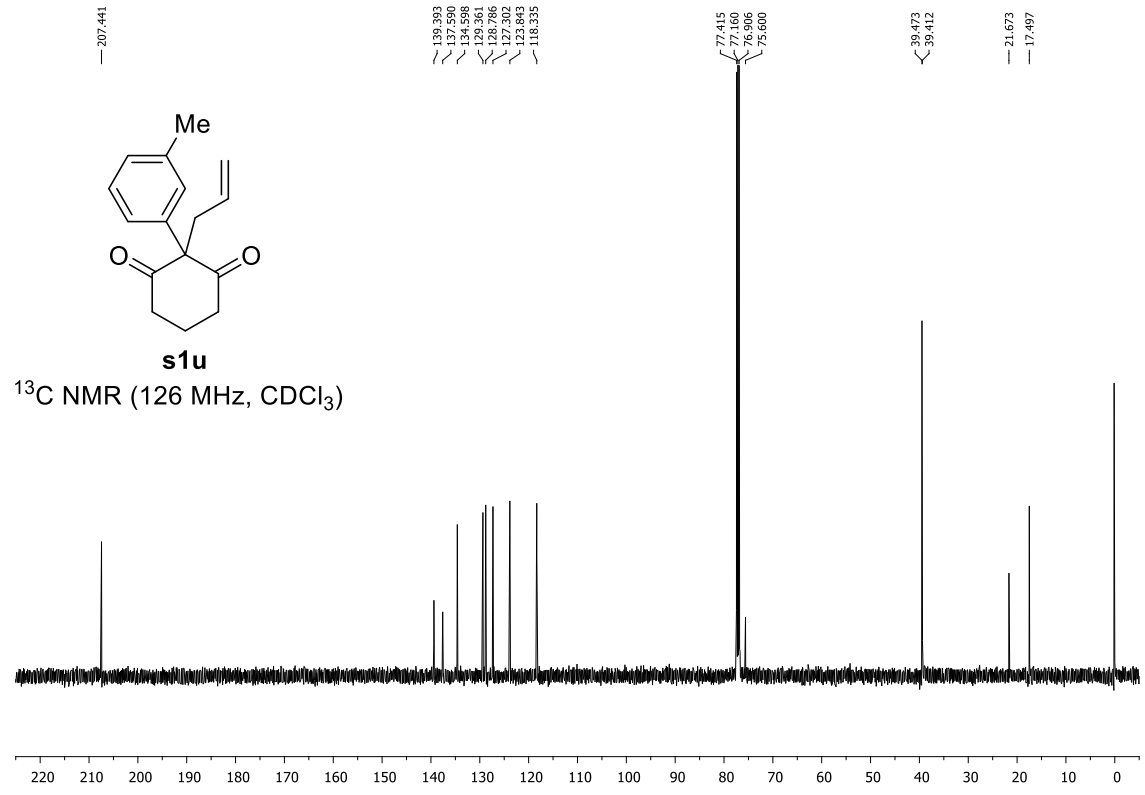

F3C
O
O
s1t
13C NMR (126 MHz, CDCl3)

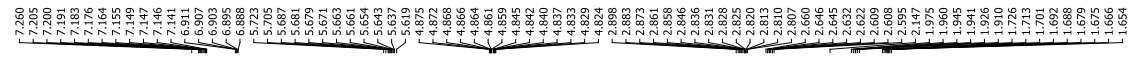


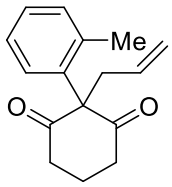

**s1t**

$^{19}$F NMR (376 MHz, $CDCl_3$)


7.337
7.335
7.322
7.297
7.285
7.271
7.161
7.148
6.873
5.736
5.722
5.716
5.702
5.688
5.683
5.668
5.031
5.023
4.988
4.981
4.979
4.977
4.974
4.972
2.797
2.795
2.786
2.604
2.595
2.584
2.573
2.563
2.368
1.967
1.954
1.940
1.928
1.785
1.775
1.768
1.760
Me
O
O
s1u
1H NMR (500 MHz, CDCl3)
1.13
1.02
2.06
1.00
2.11
4.32
2.10
3.12
1.06
1.20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


207.441
139.393
137.590
134.598
129.361
128.786
127.302
123.843
118.335
77.415
77.160
76.906
75.600
39.473
39.412
21.673
17.497
Me
O
O
s1u
13C NMR (126 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

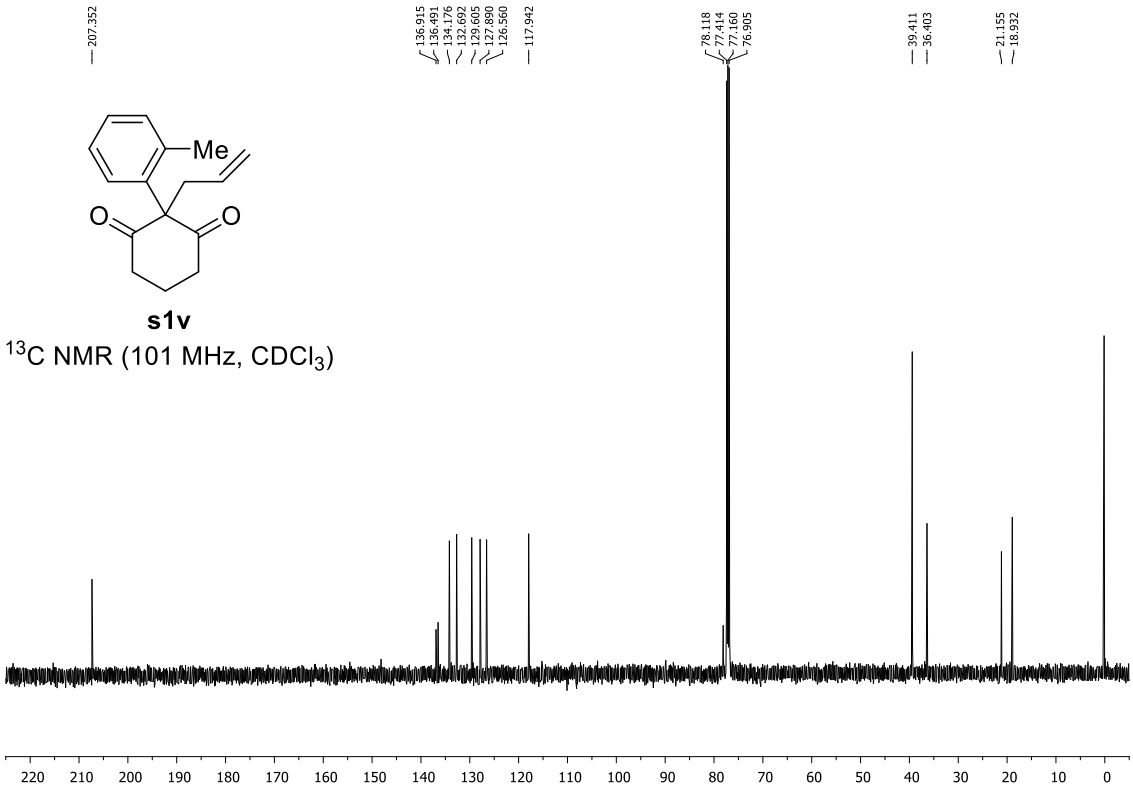





**s1v**

$^{1}$H NMR (400 MHz, $CDCl_3$)

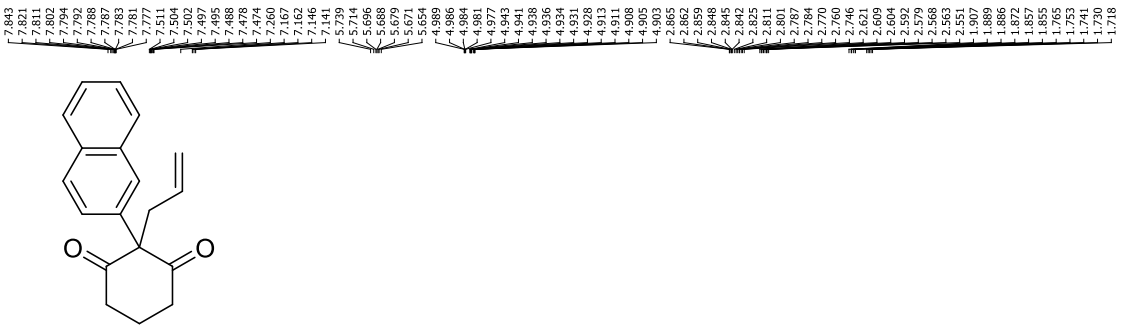




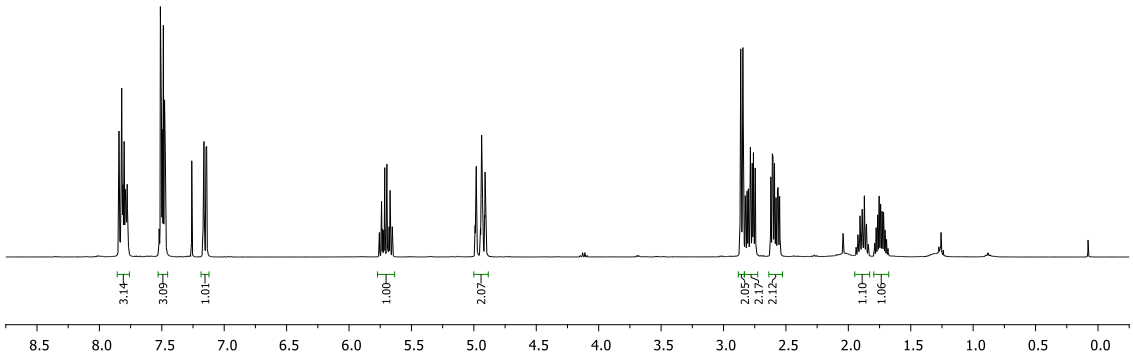

**s1v**

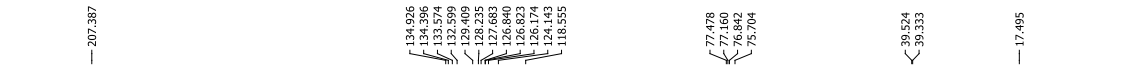
$^{13}$C NMR (101 MHz, $CDCl_3$)

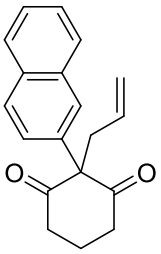


**s1w**

$^{1}$H NMR (400 MHz, $CDCl_3$)

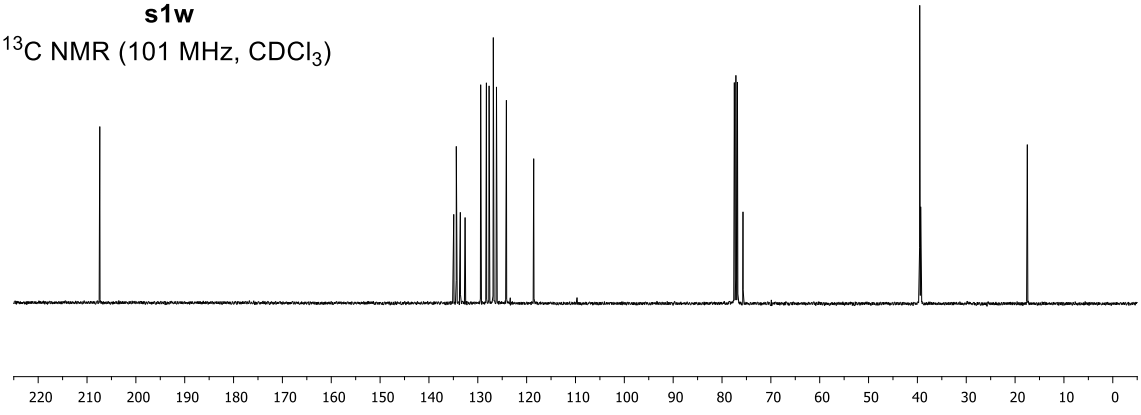


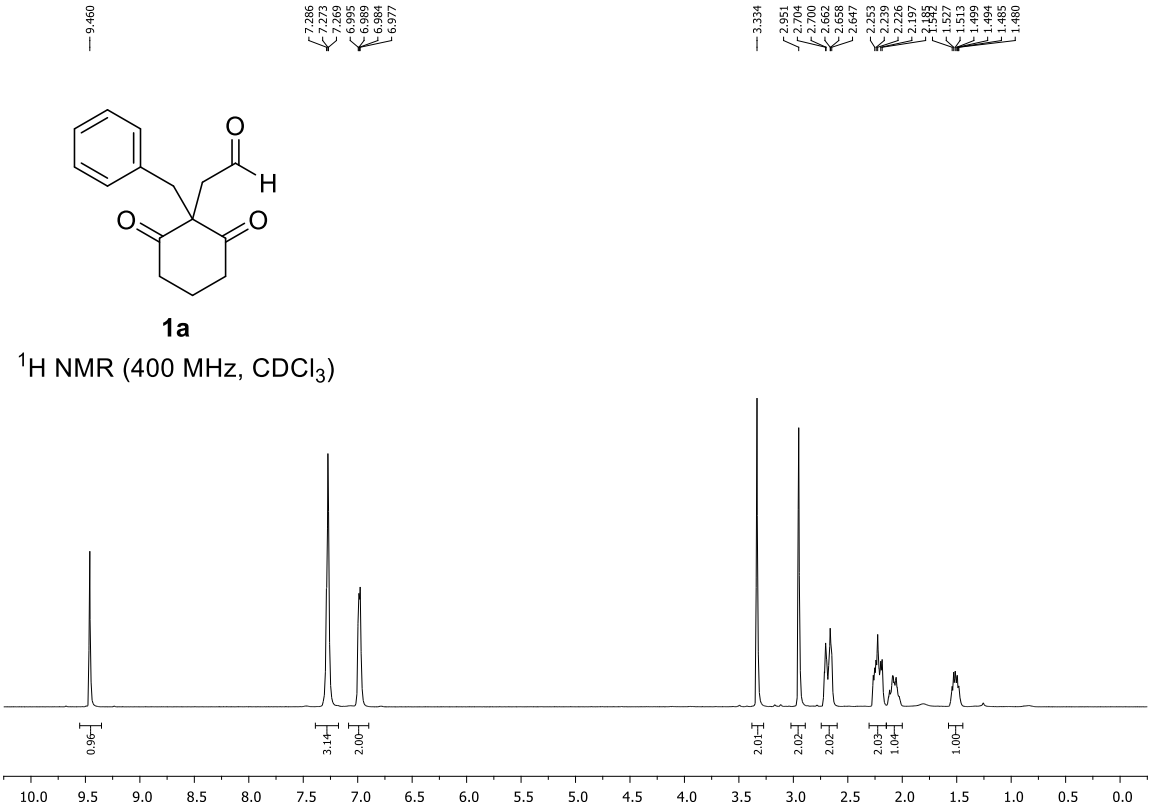




**s1w**

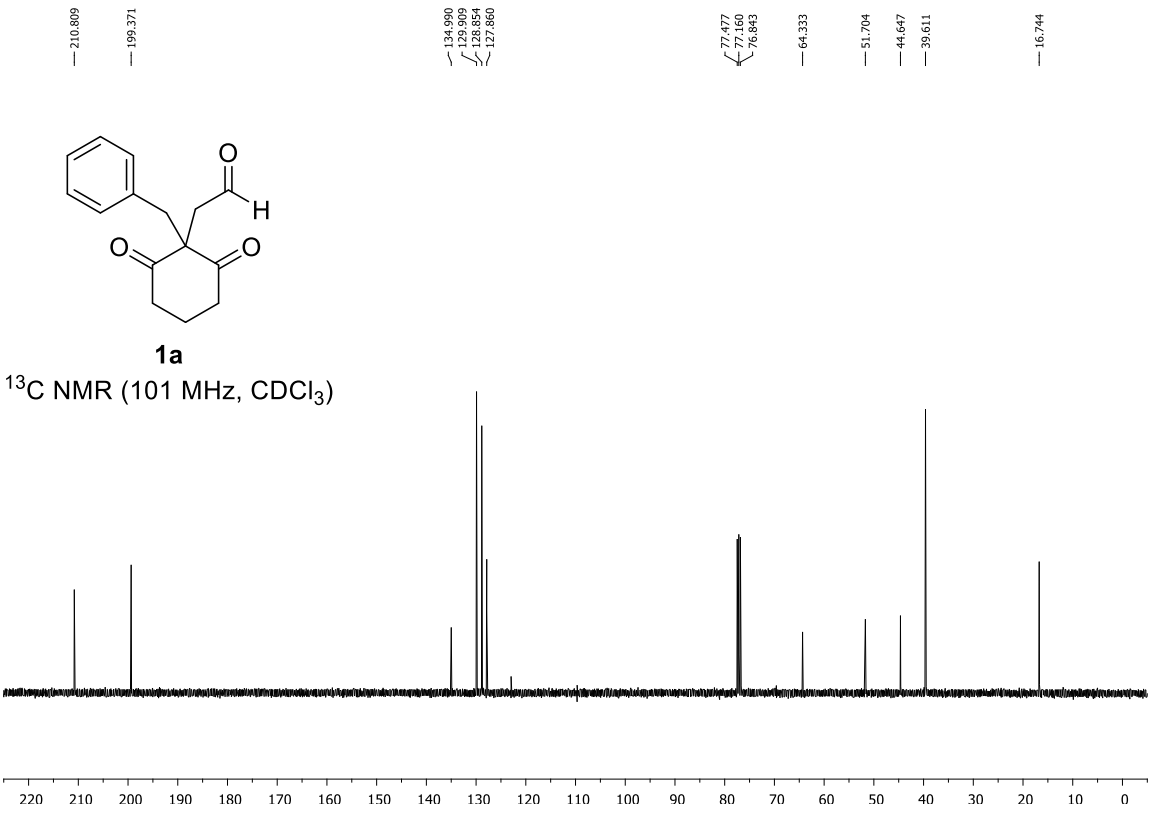
$^{13}$C NMR (101 MHz, $CDCl_3$)





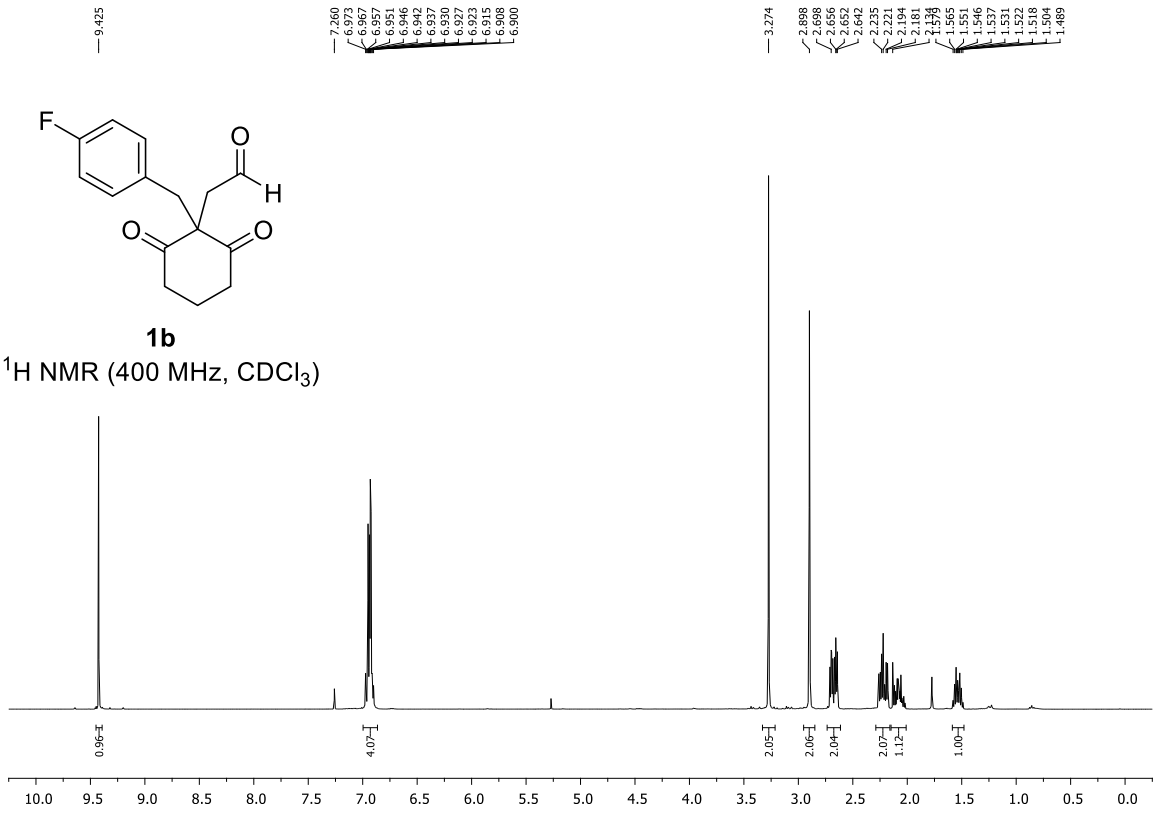

**1a**

$^{1}$H NMR (400 MHz, $CDCl_3$)



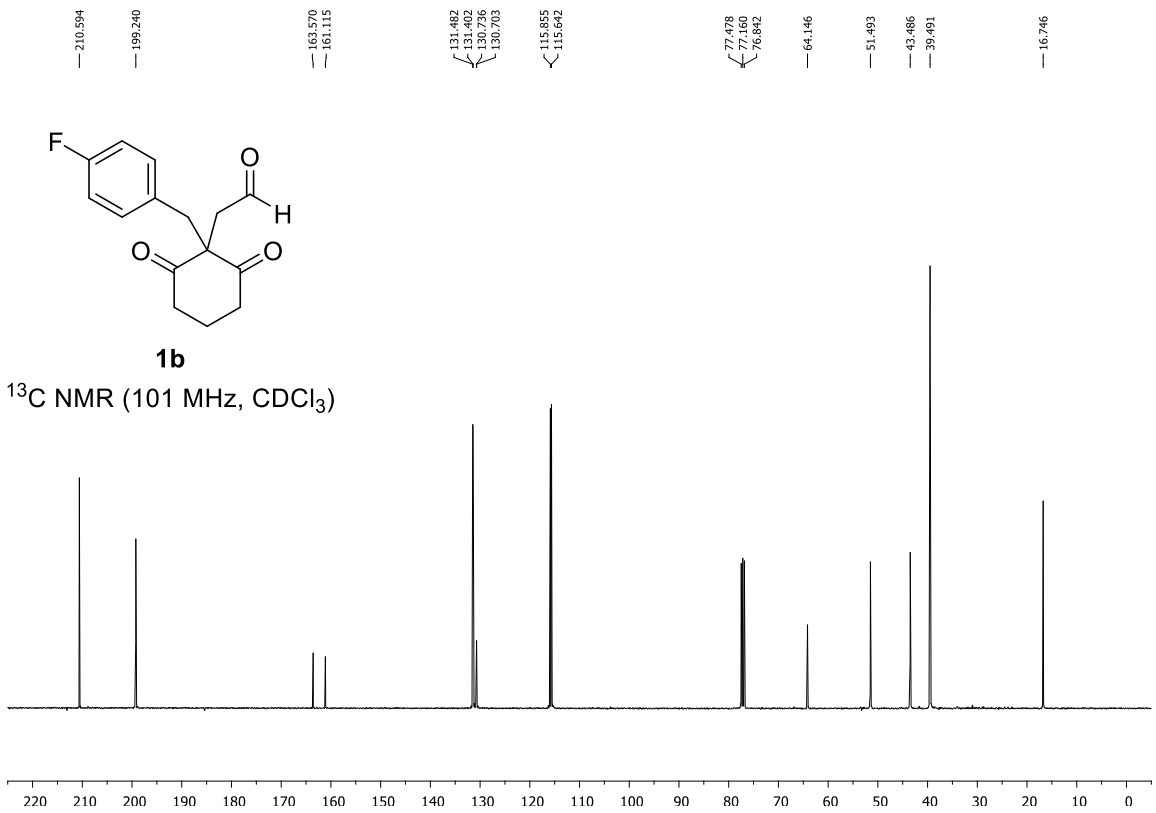

**1a**

$^{13}$C NMR (101 MHz, $CDCl_3$)



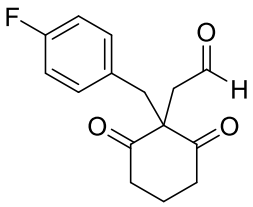

**1b**

$^{1}$H NMR (400 MHz, $CDCl_3$)



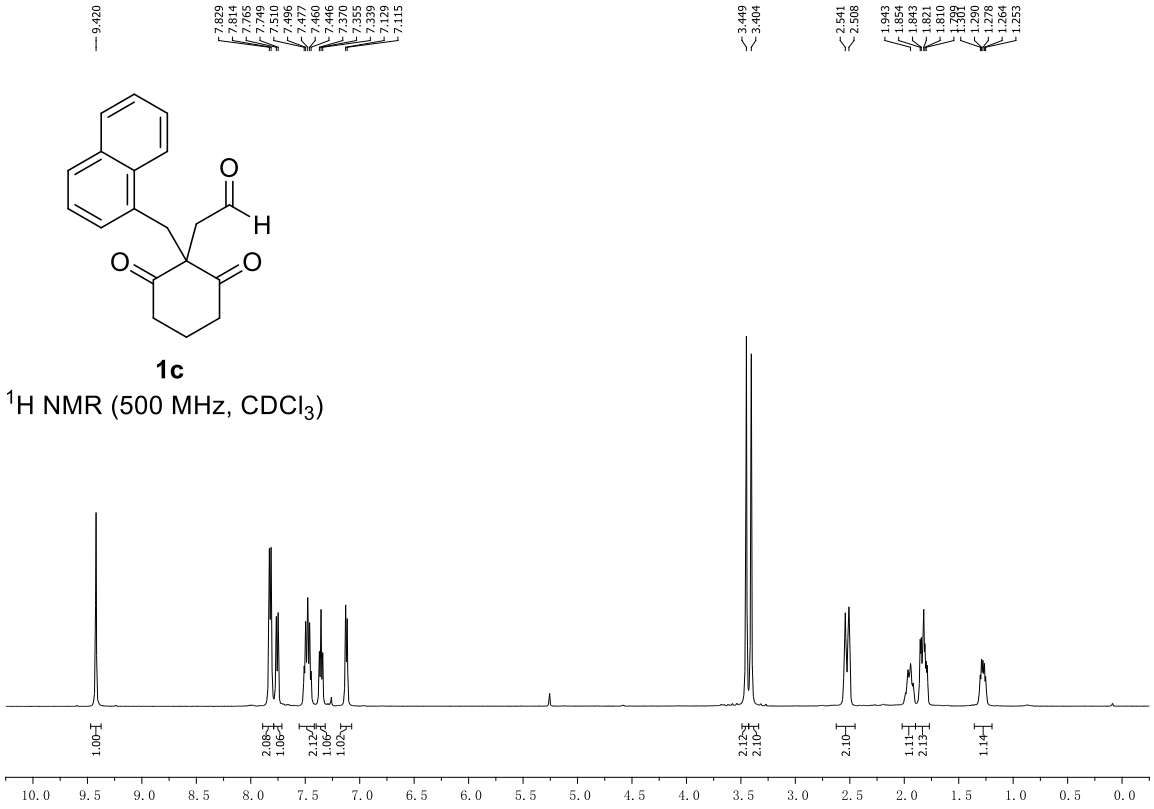

**1b**

$^{13}$C NMR (101 MHz, $CDCl_3$)



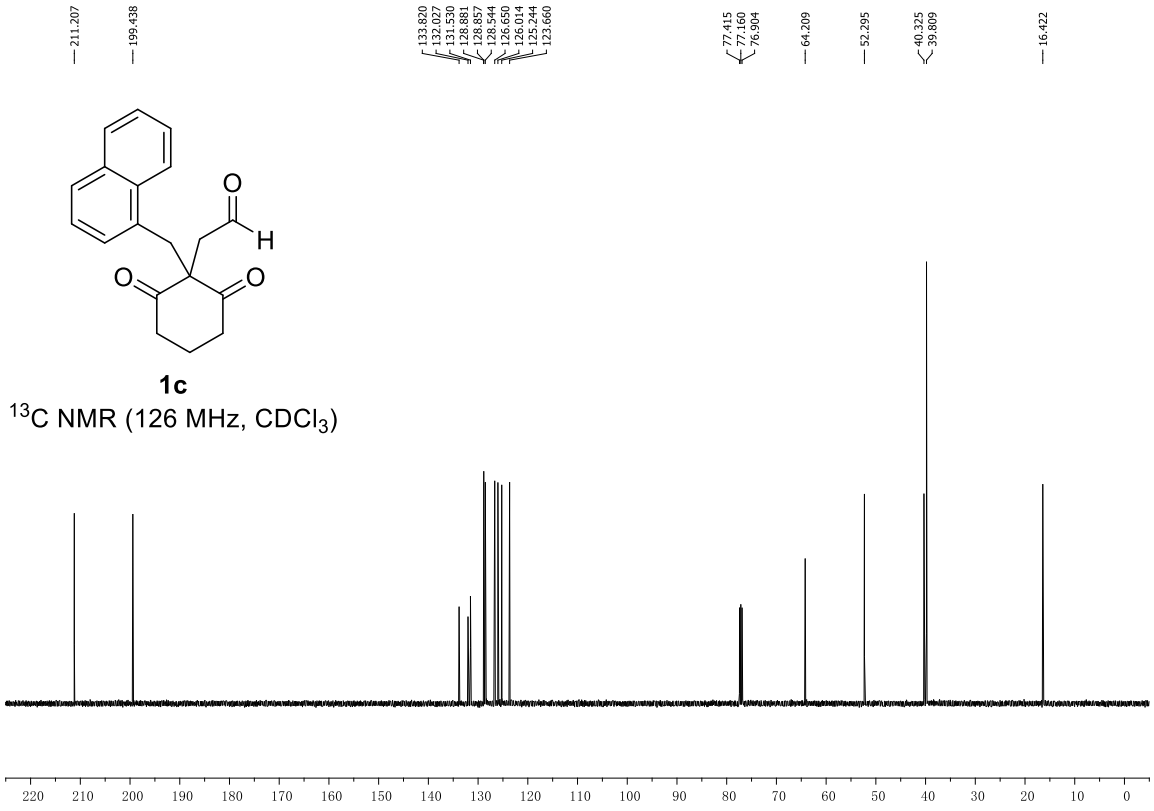

**1b**

$^{19}F$ NMR (376 MHz, $CDCl_3$)



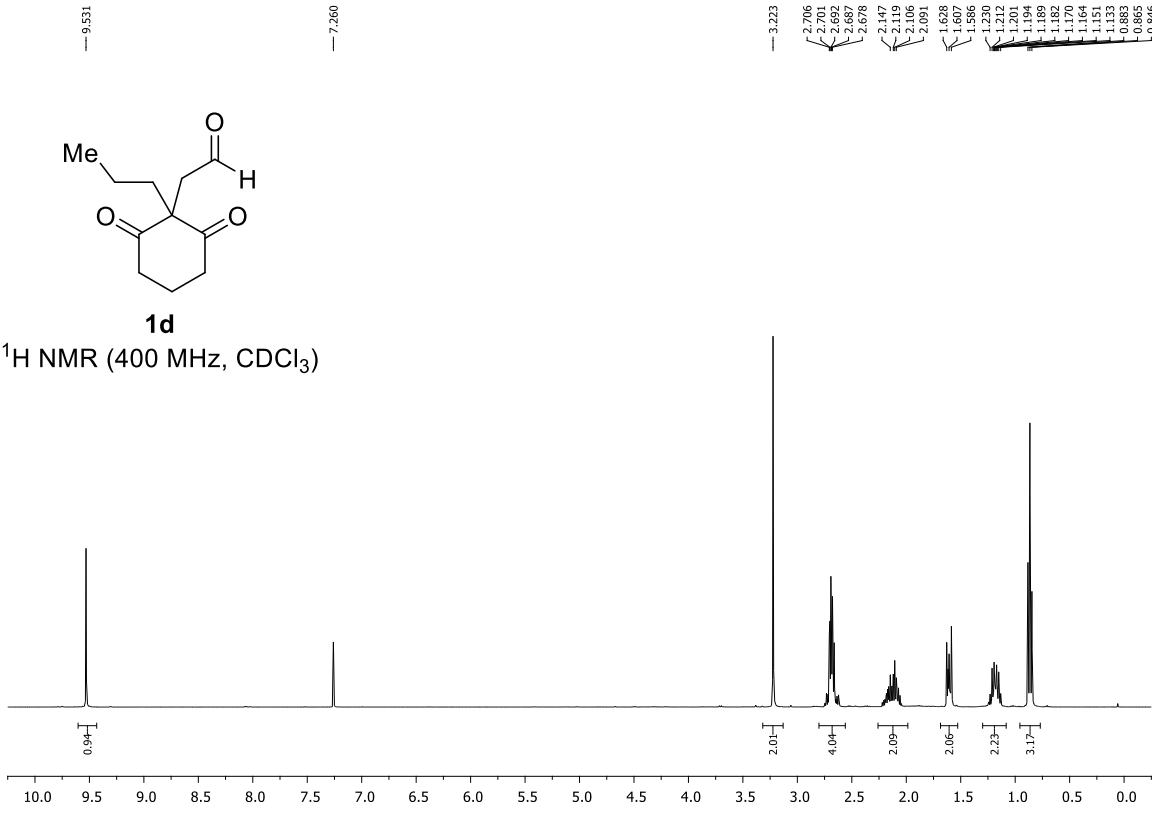

**1c**

$^{1}$H NMR (500 MHz, $CDCl_3$)



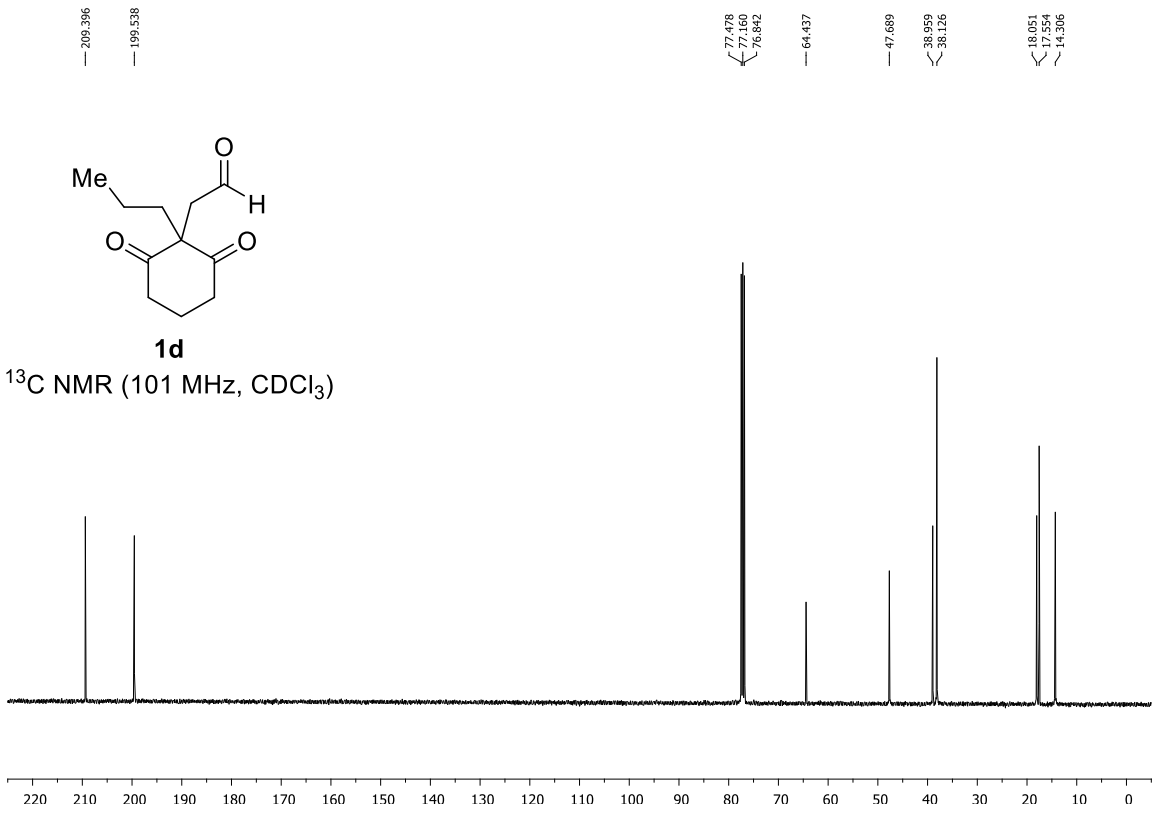

**1c**

$^{13}$C NMR (126 MHz, $CDCl_3$)



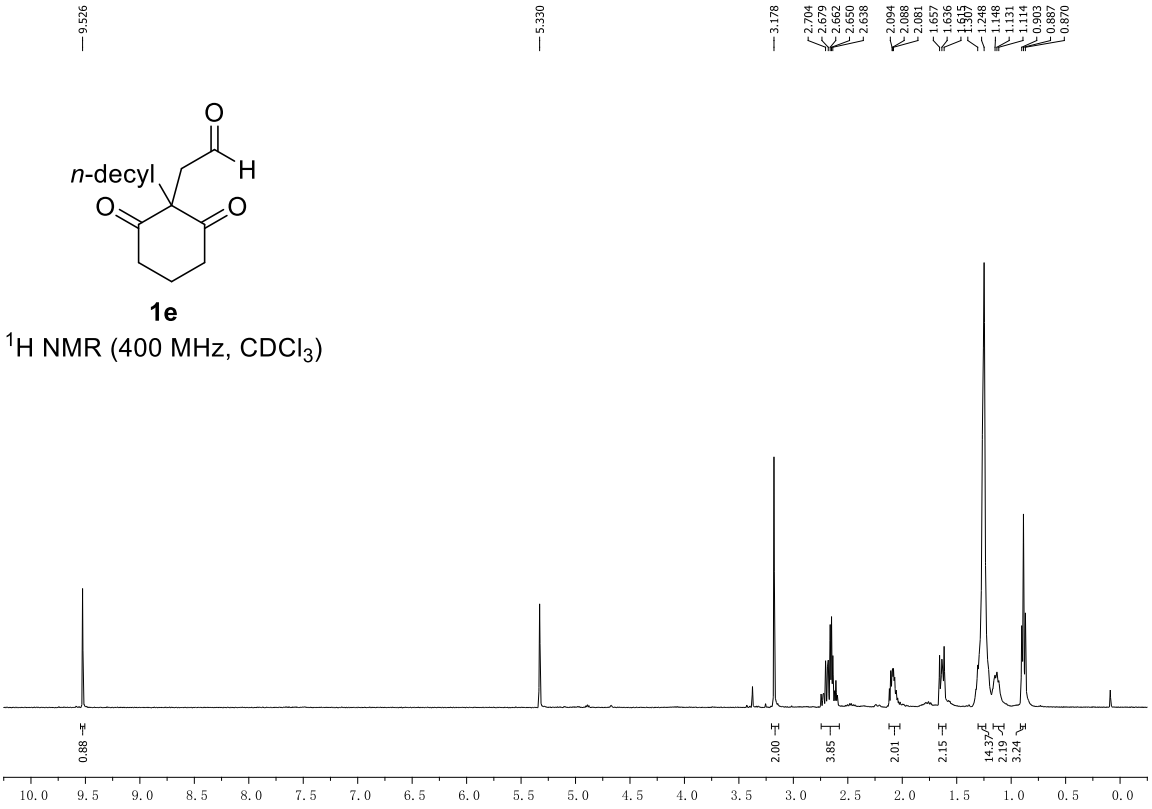

**1d**

$^{1}$H NMR (400 MHz, $CDCl_3$)



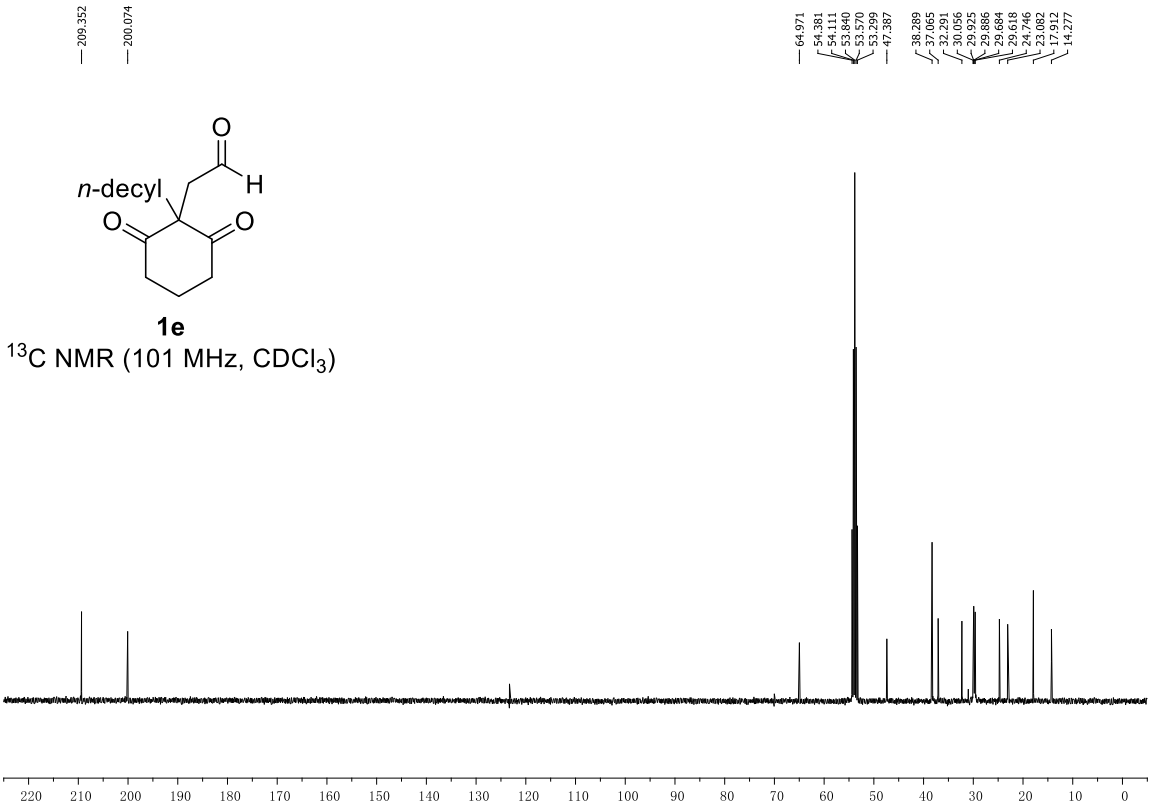

**1d**

$^{13}$C NMR (101 MHz, $CDCl_3$)



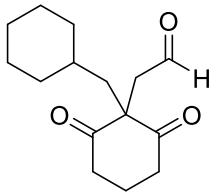

**1e**

$^{1}$H NMR (400 MHz, $CDCl_3$)




**1e**

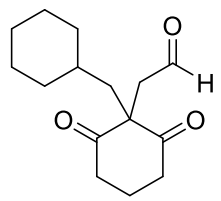
$^{13}$C NMR (101 MHz, $CDCl_3$)



**1f**

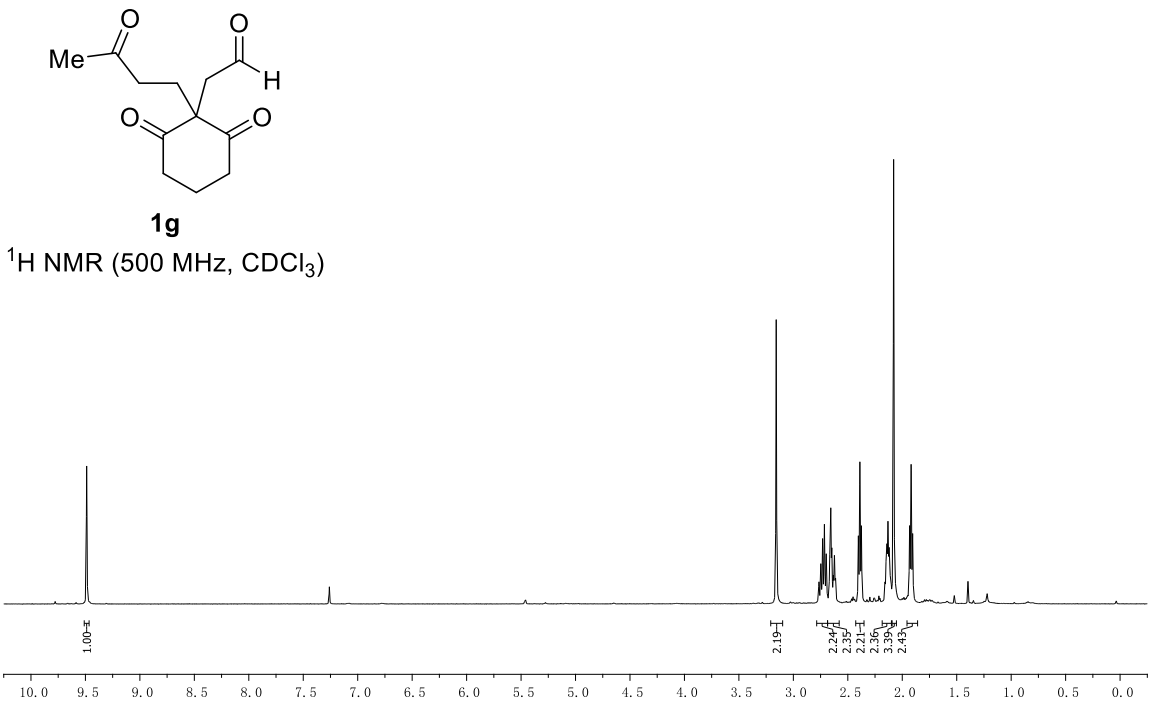
$^{1}$H NMR (400 MHz, $CDCl_3$)





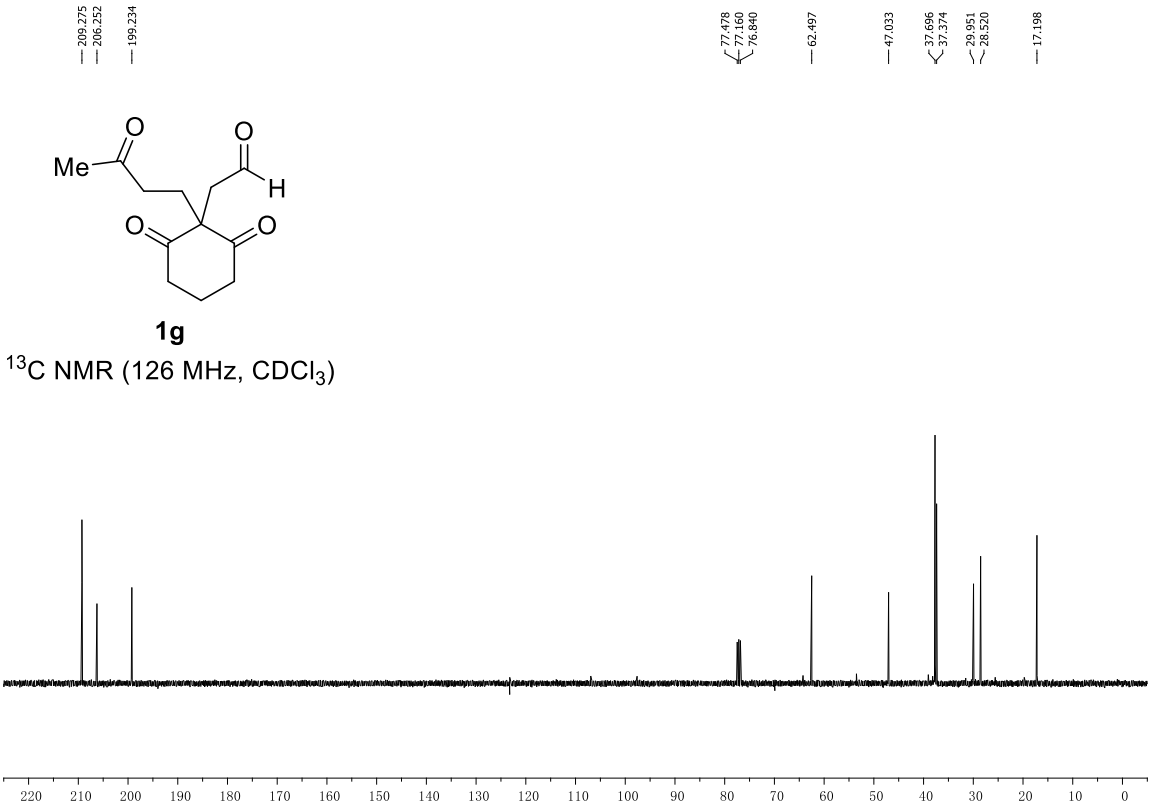
**1f**

$^{13}$C NMR (101 MHz, $CDCl_3$)



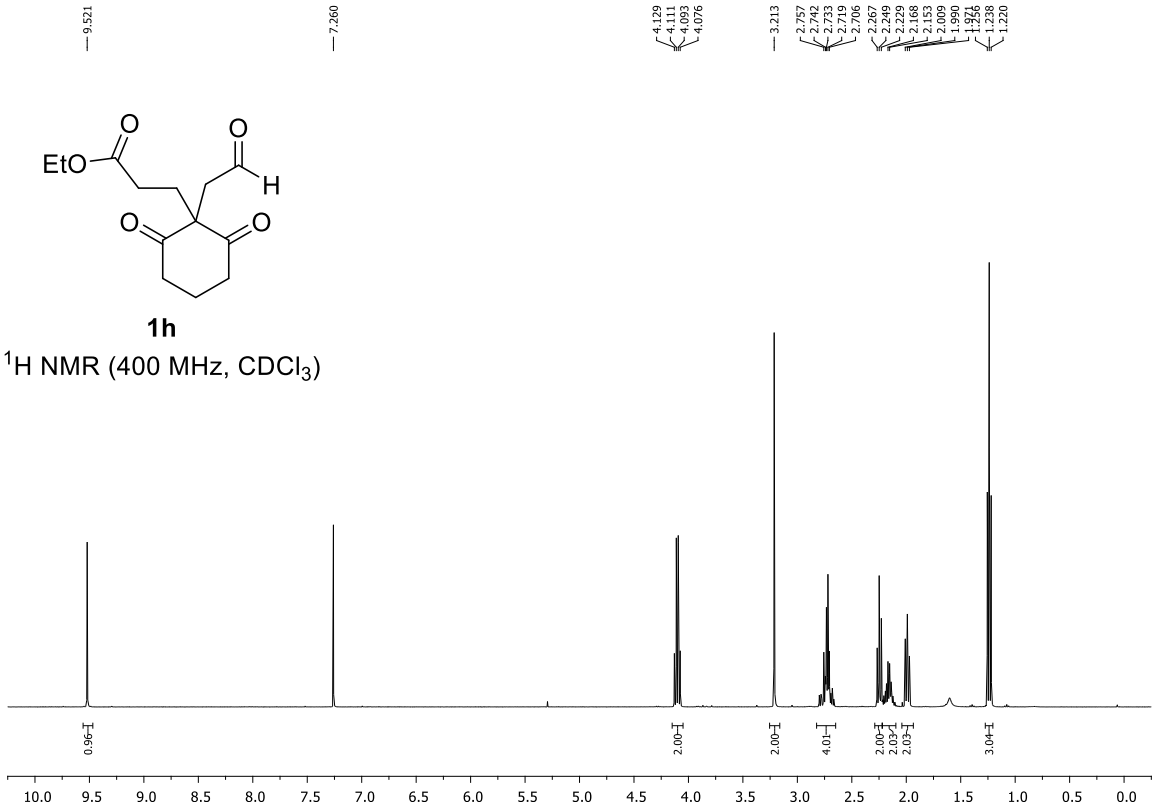

**1g**

$^{1}$H NMR (500 MHz, $CDCl_3$)



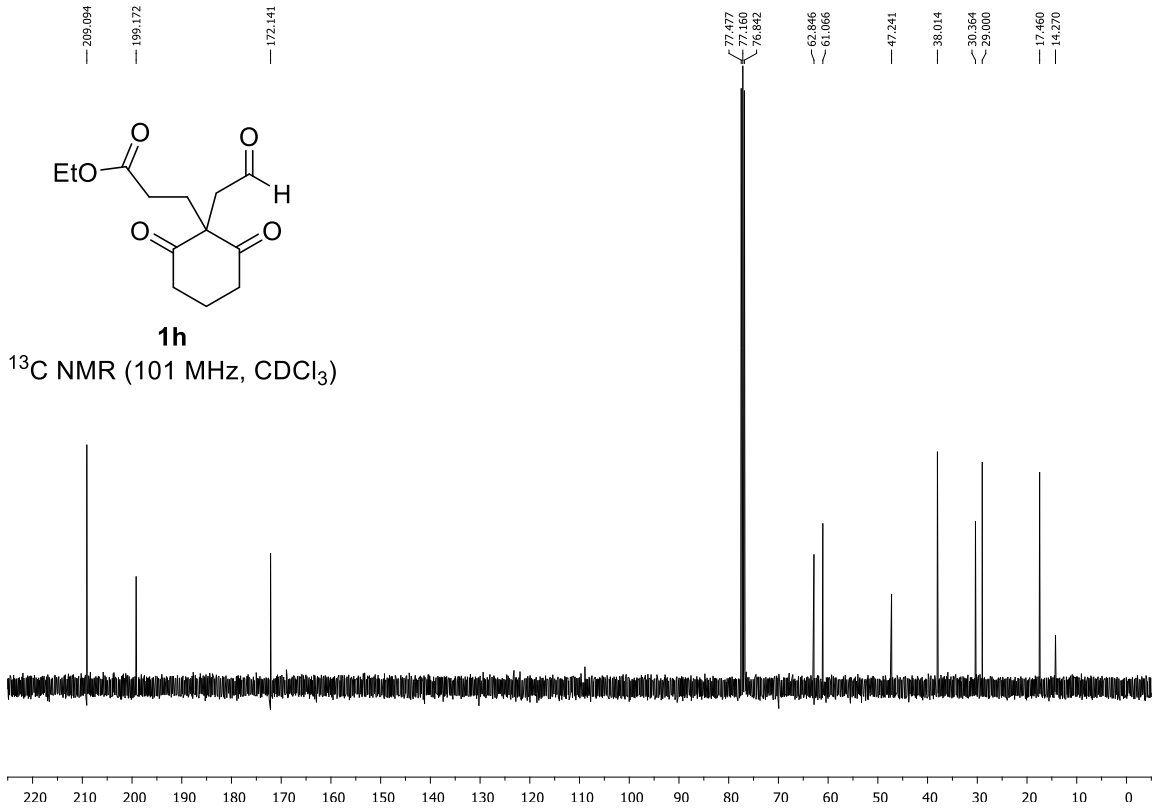

**1g**

$^{13}$C NMR (126 MHz, $CDCl_3$)



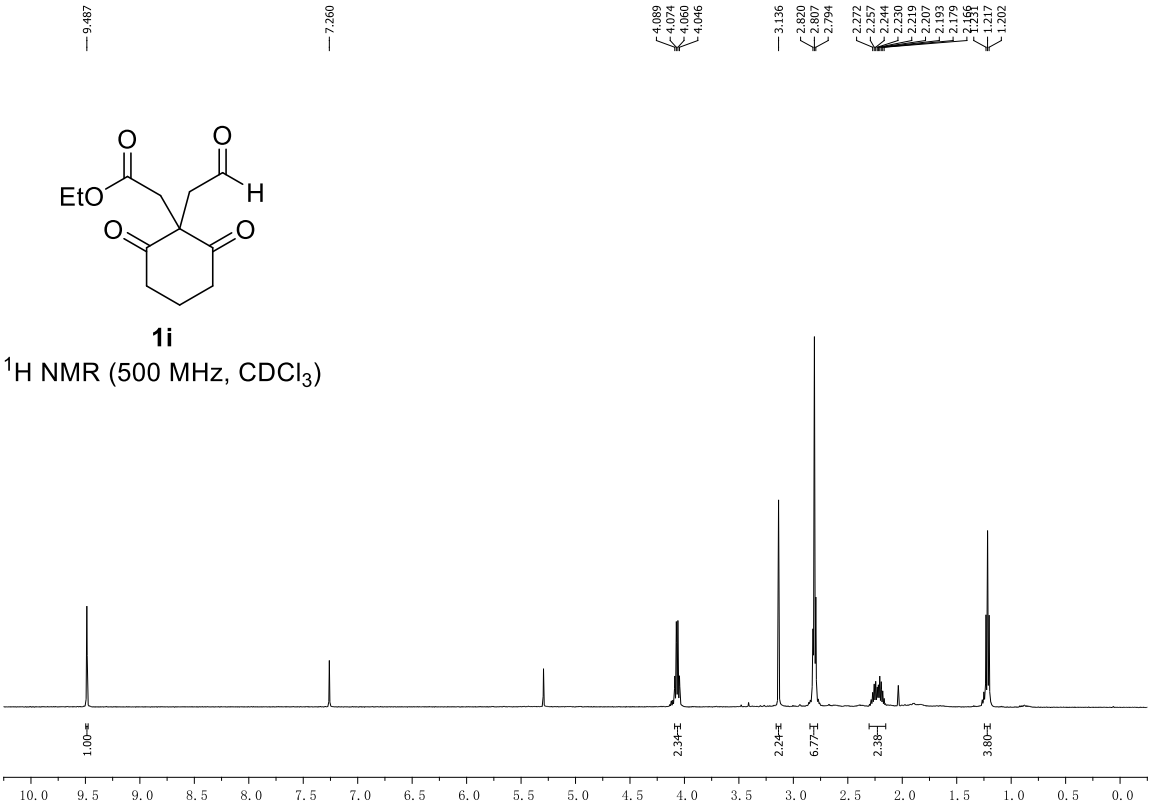

**1h**

$^{1}$H NMR (400 MHz, $CDCl_3$)



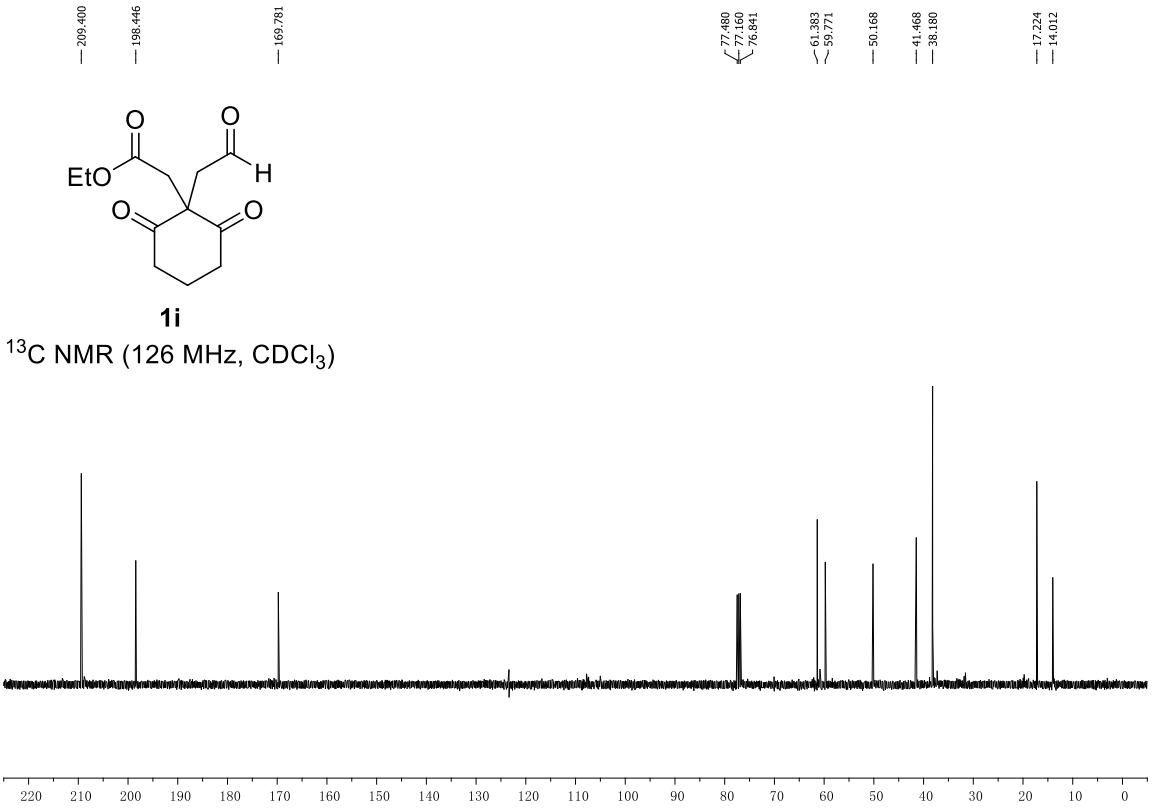

**1h**

$^{13}$C NMR (101 MHz, $CDCl_3$)



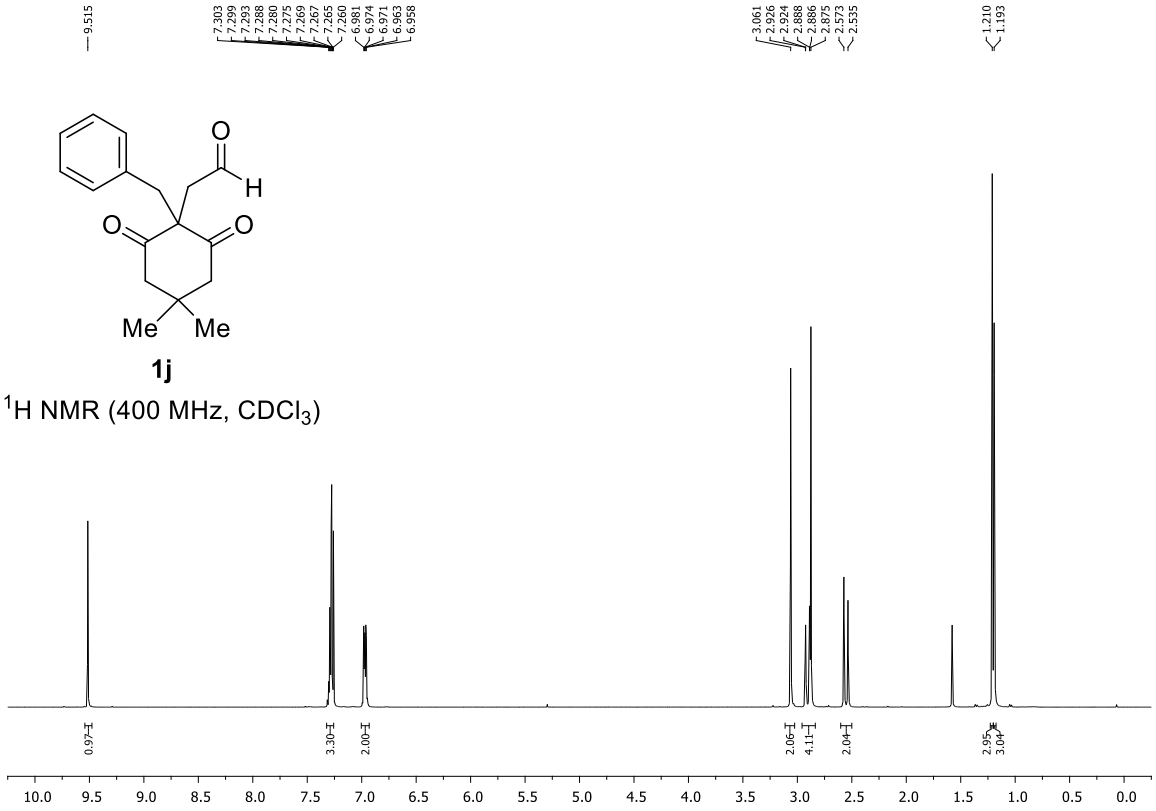

**1i**

$^{1}$H NMR (500 MHz, $CDCl_3$)



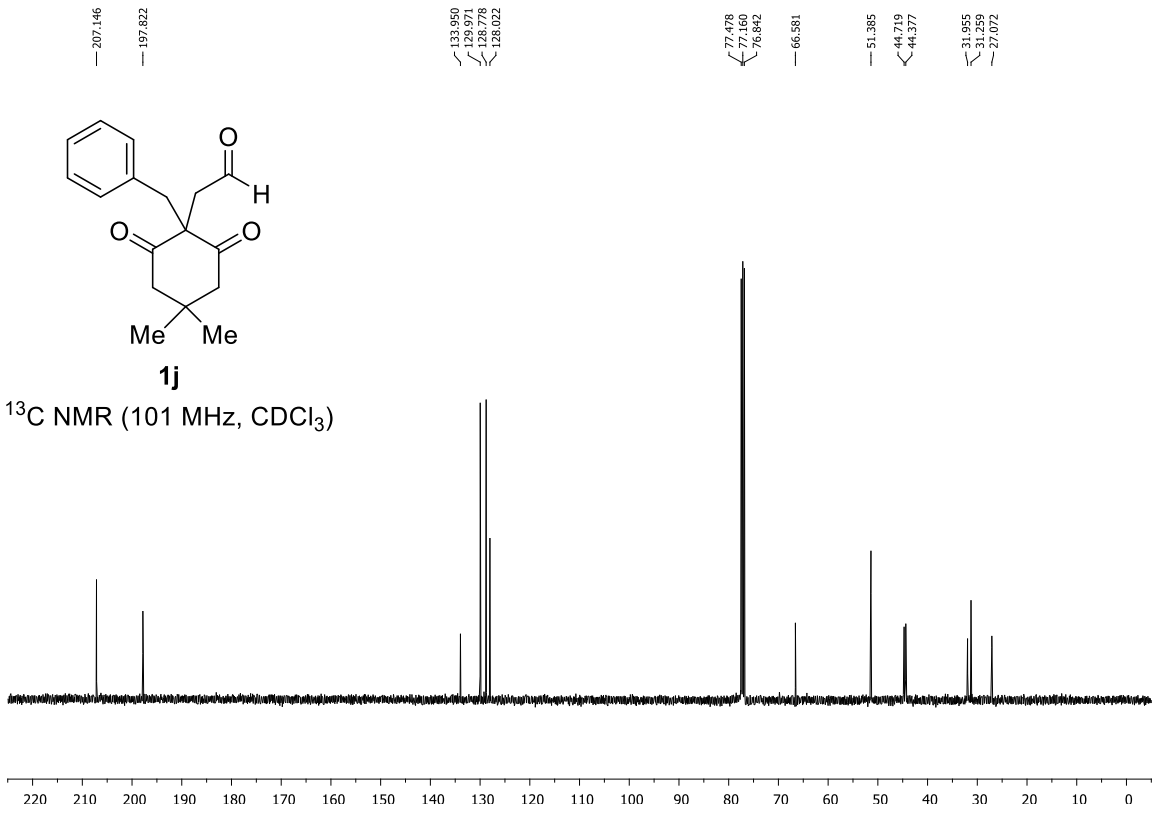

**1i**

$^{13}$C NMR (126 MHz, $CDCl_3$)



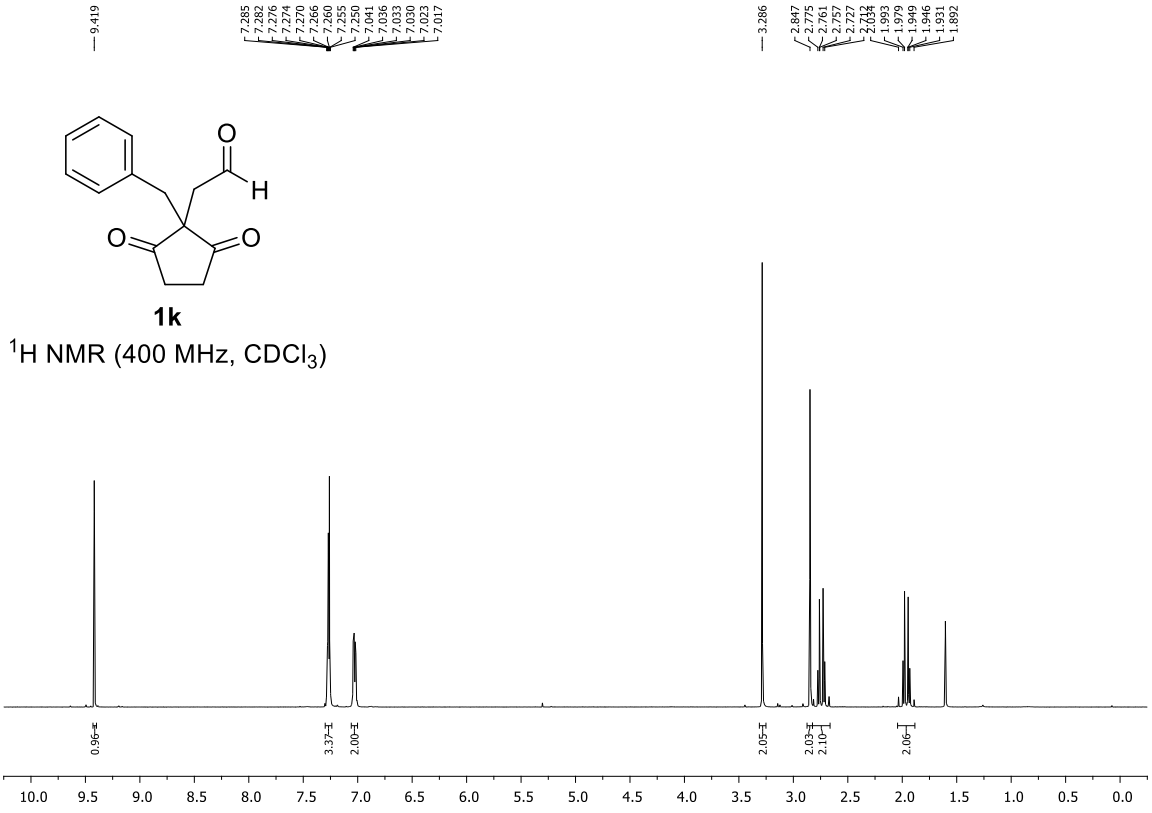

**1j**

$^{1}$H NMR (400 MHz, $CDCl_3$)



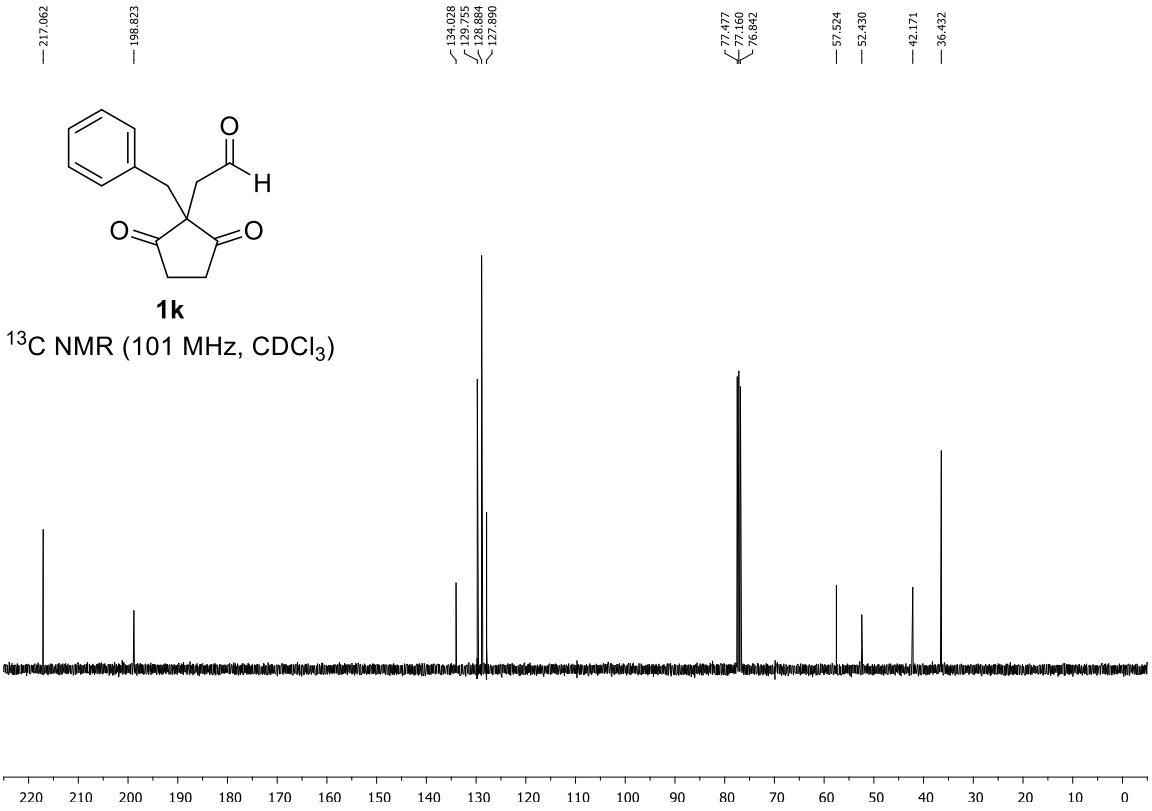

**1j**

$^{13}$C NMR (101 MHz, $CDCl_3$)



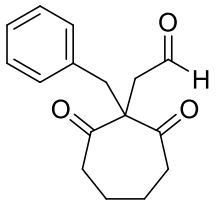

**1k**

$^{1}$H NMR (400 MHz, $CDCl_3$)



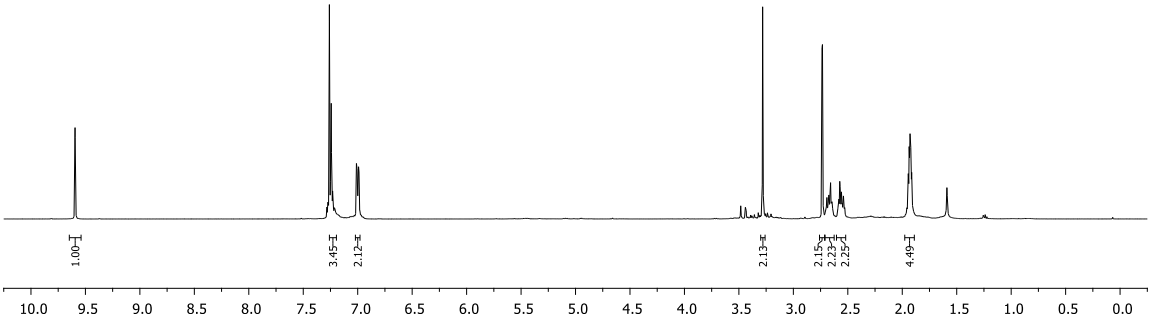

**1k**

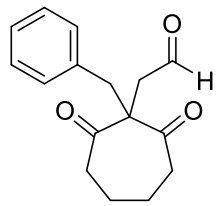
$^{13}$C NMR (101 MHz, $CDCl_3$)



**1l**

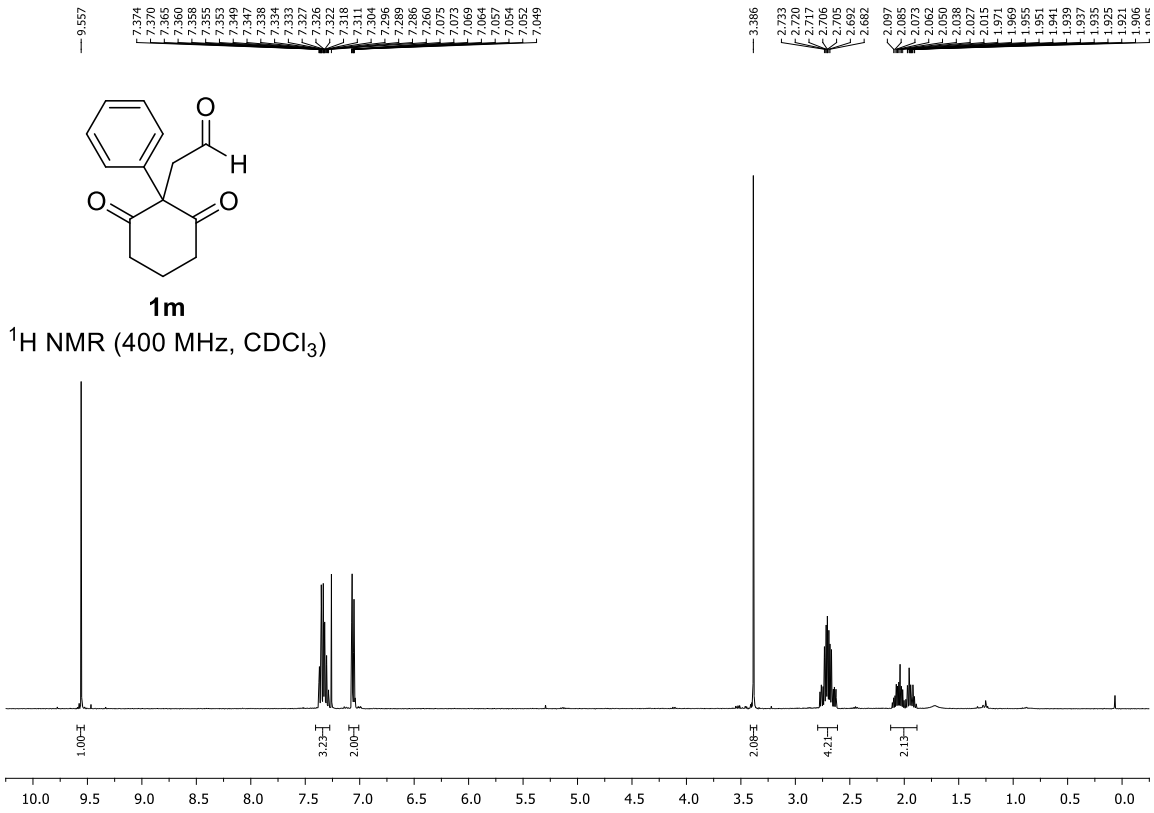
$^{1}$H NMR (400 MHz, $CDCl_3$)





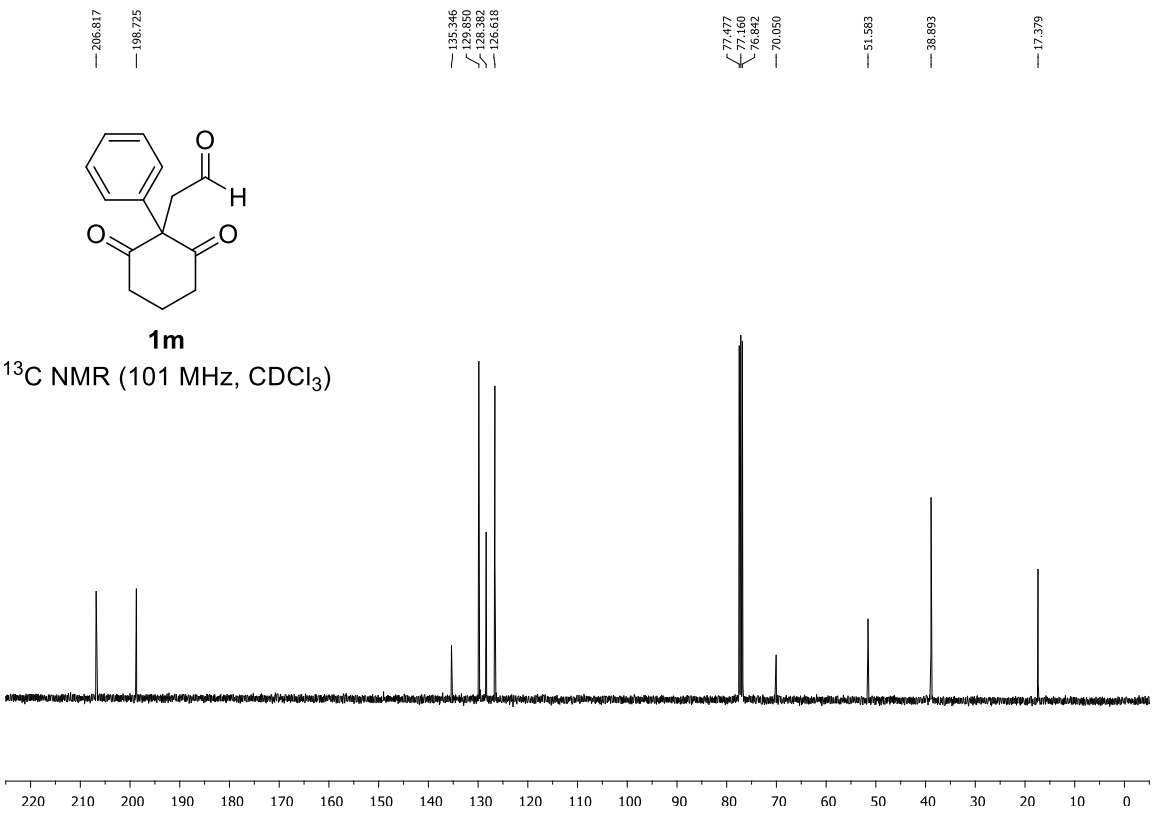
**1l**

$^{13}$C NMR (101 MHz, $CDCl_3$)



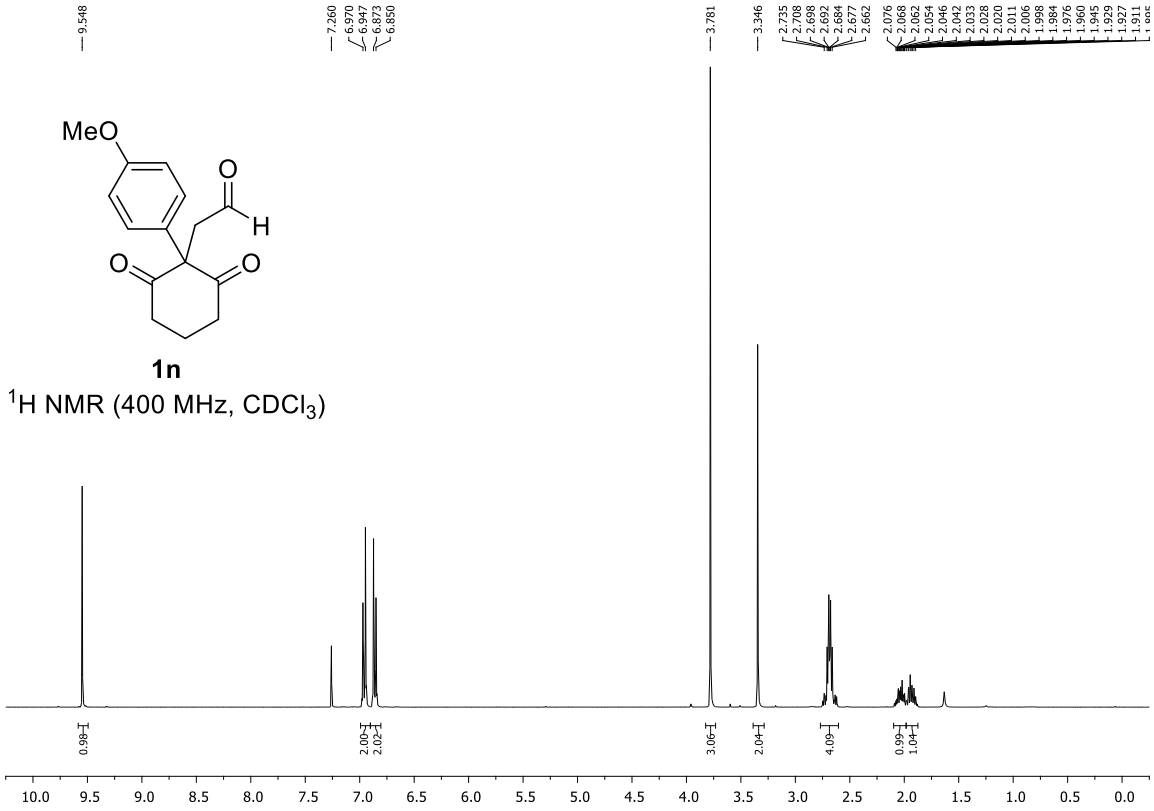

**1m**

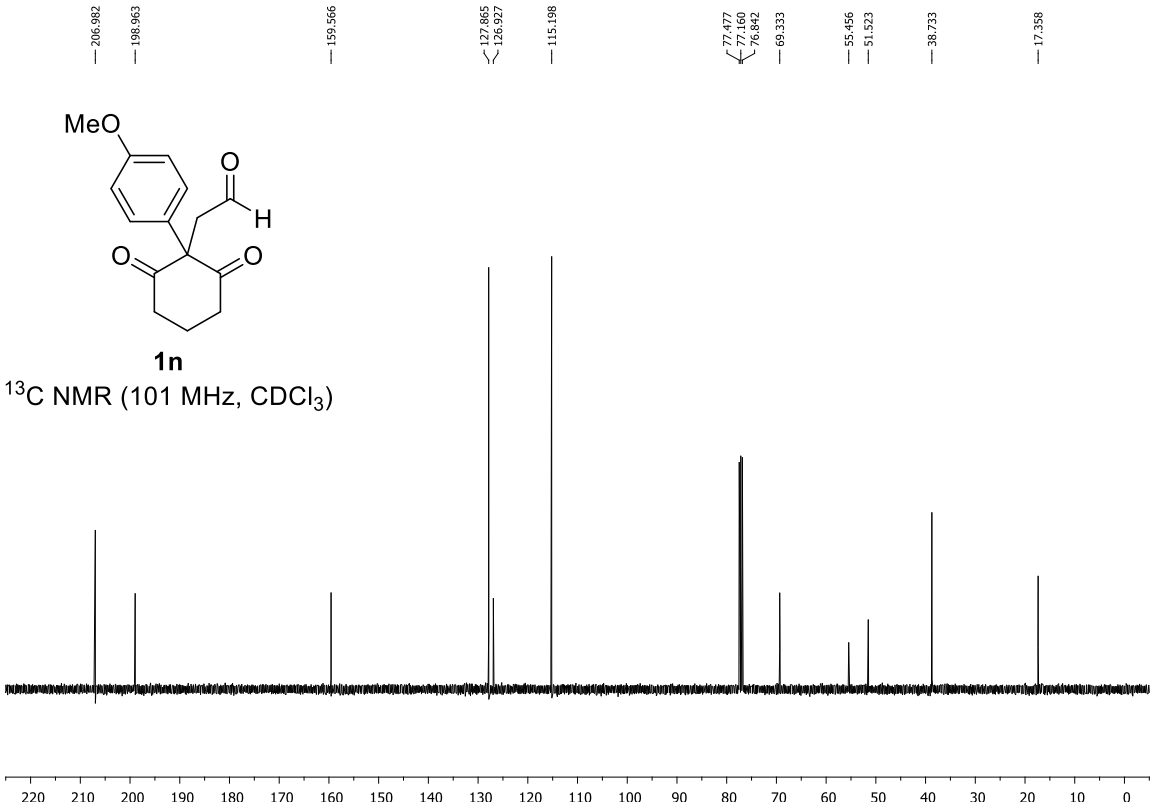
$^{1}$H NMR (400 MHz, $CDCl_3$)

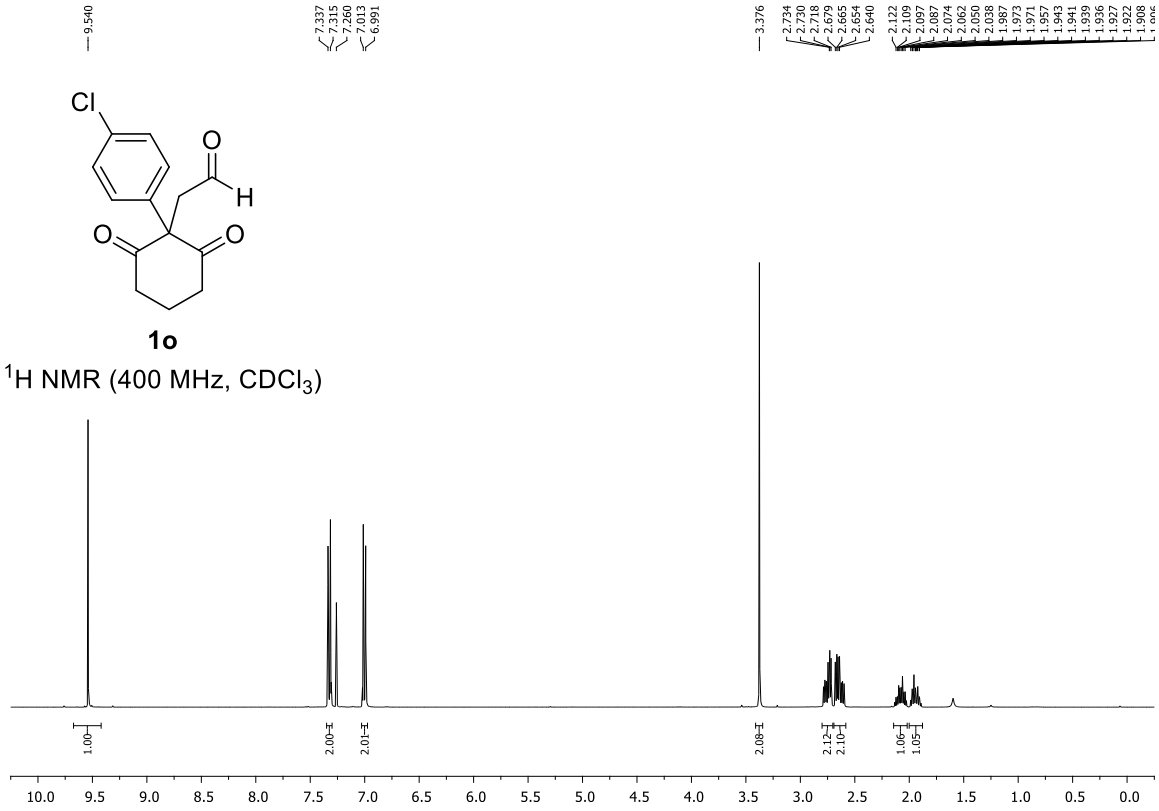



**1m**

$^{13}$C NMR (101 MHz, $CDCl_3$)

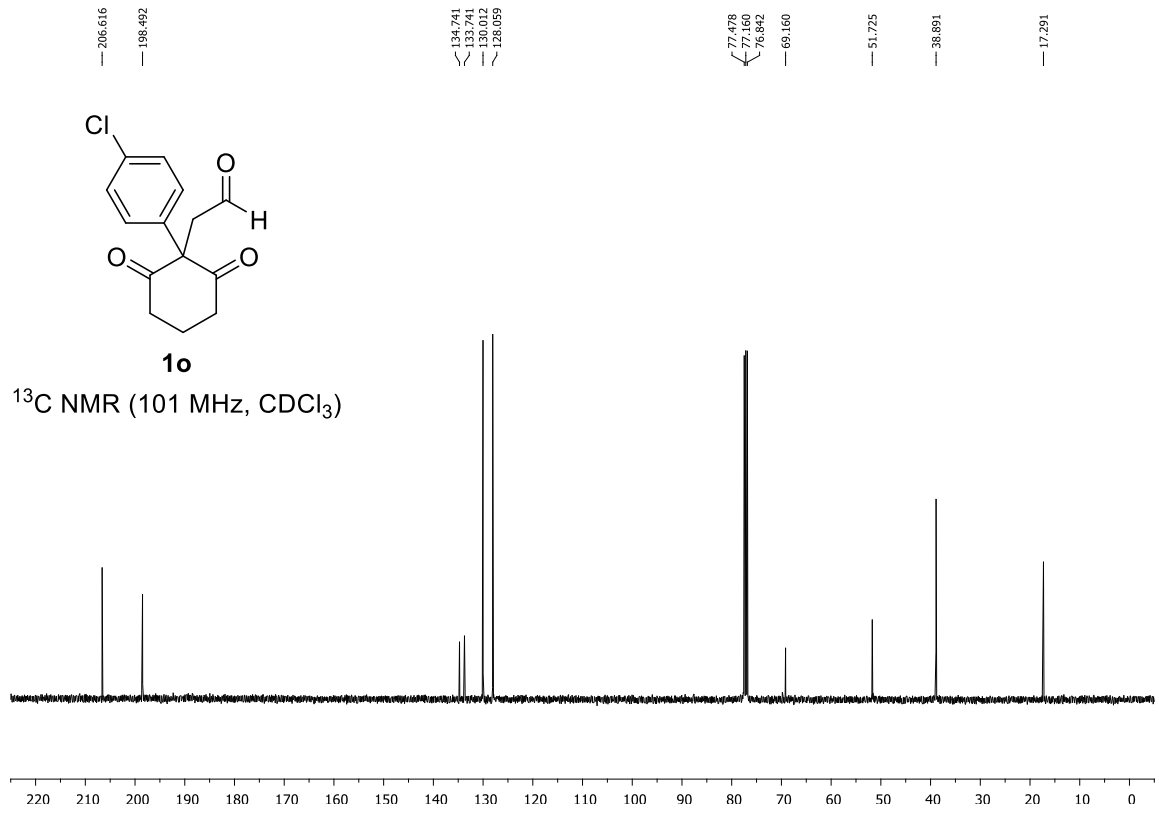

MeO
O
H
O
O
1n
1H NMR (400 MHz, CDCl3)


MeO
O
H
O
O
1n
13C NMR (101 MHz, CDCl3)



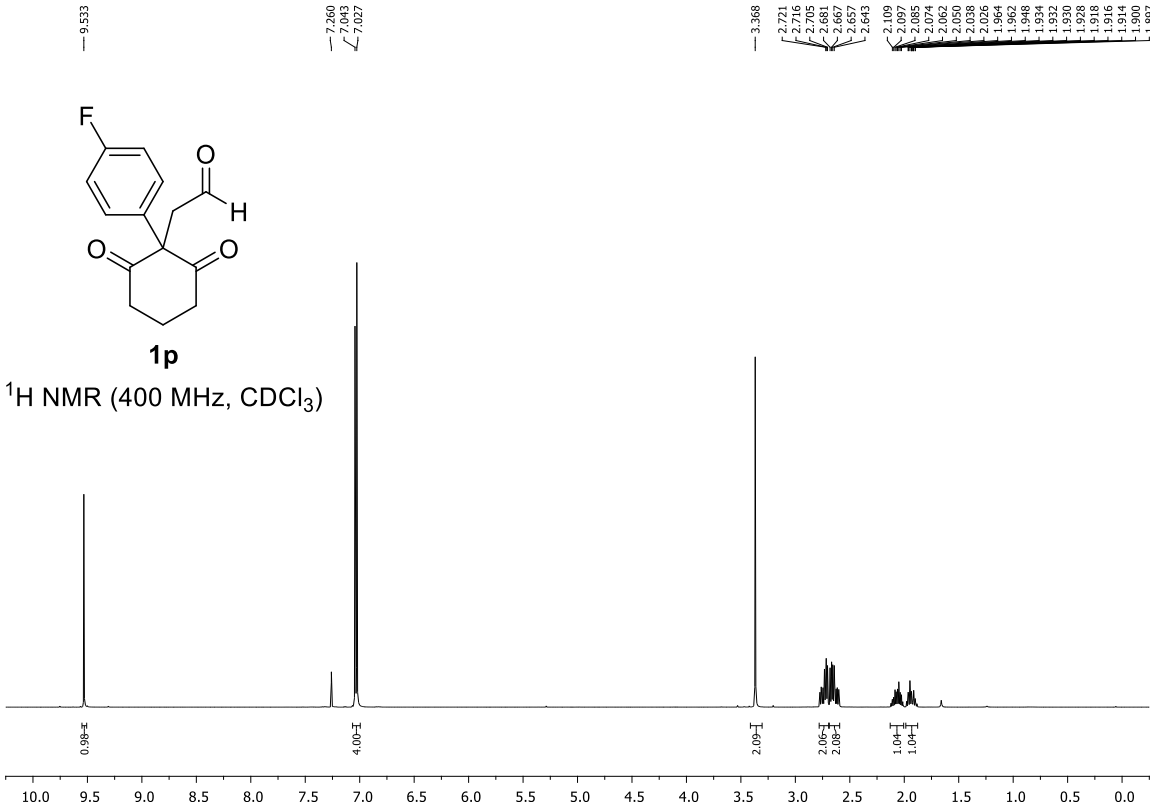

**1o**

$^{1}$H NMR (400 MHz, $CDCl_3$)



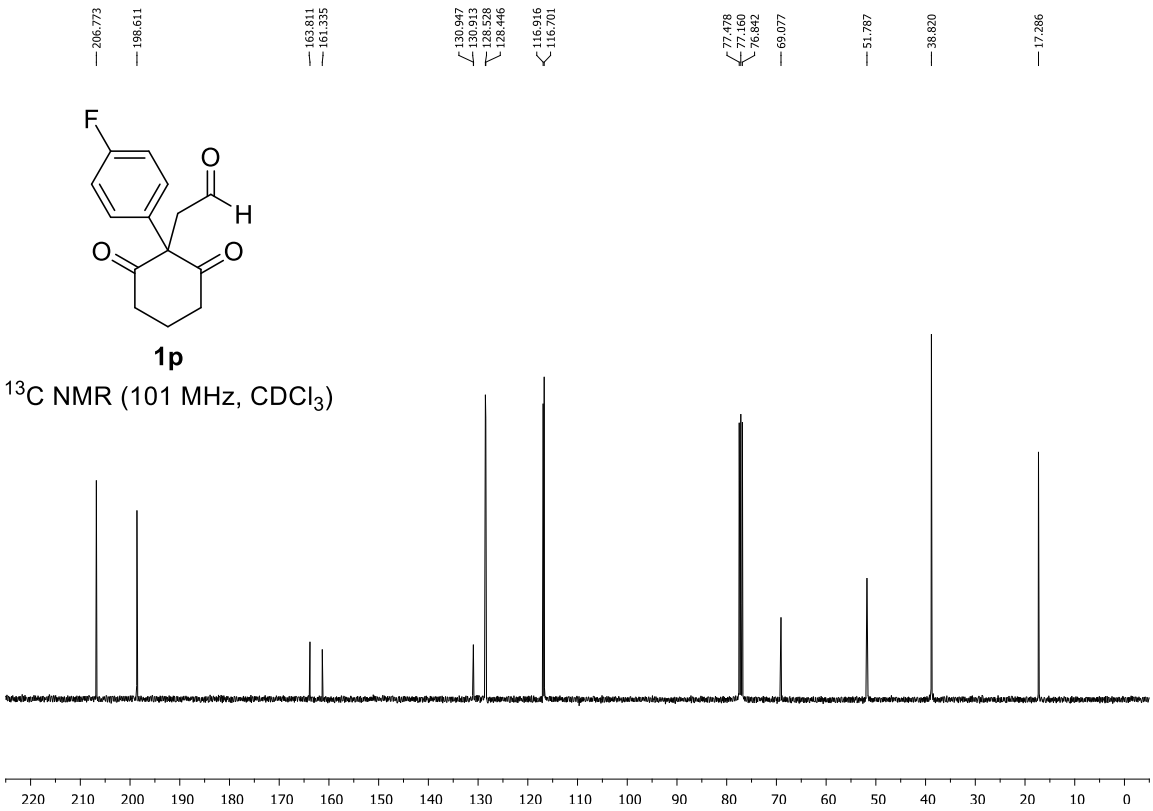

**1o**

$^{13}$C NMR (101 MHz, $CDCl_3$)



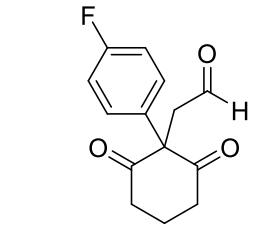

**1p**

$^{1}$H NMR (400 MHz, $CDCl_3$)



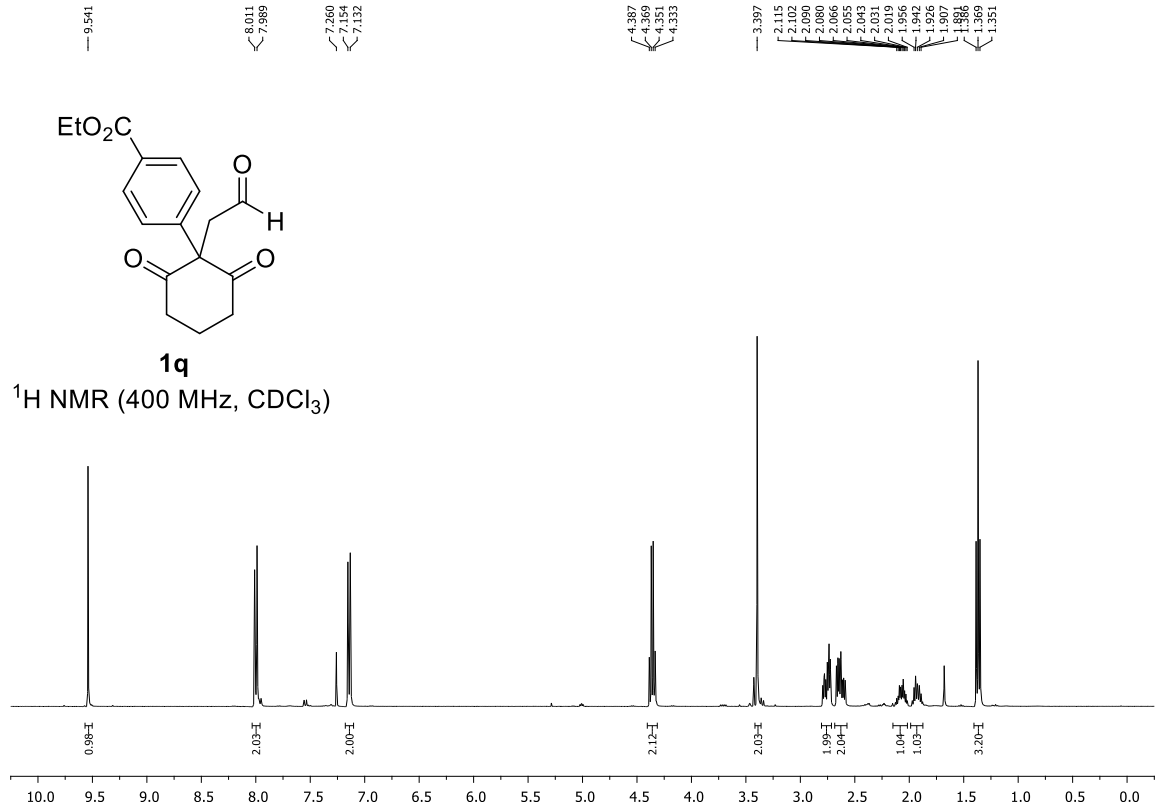

**1p**

$^{13}$C NMR (101 MHz, $CDCl_3$)



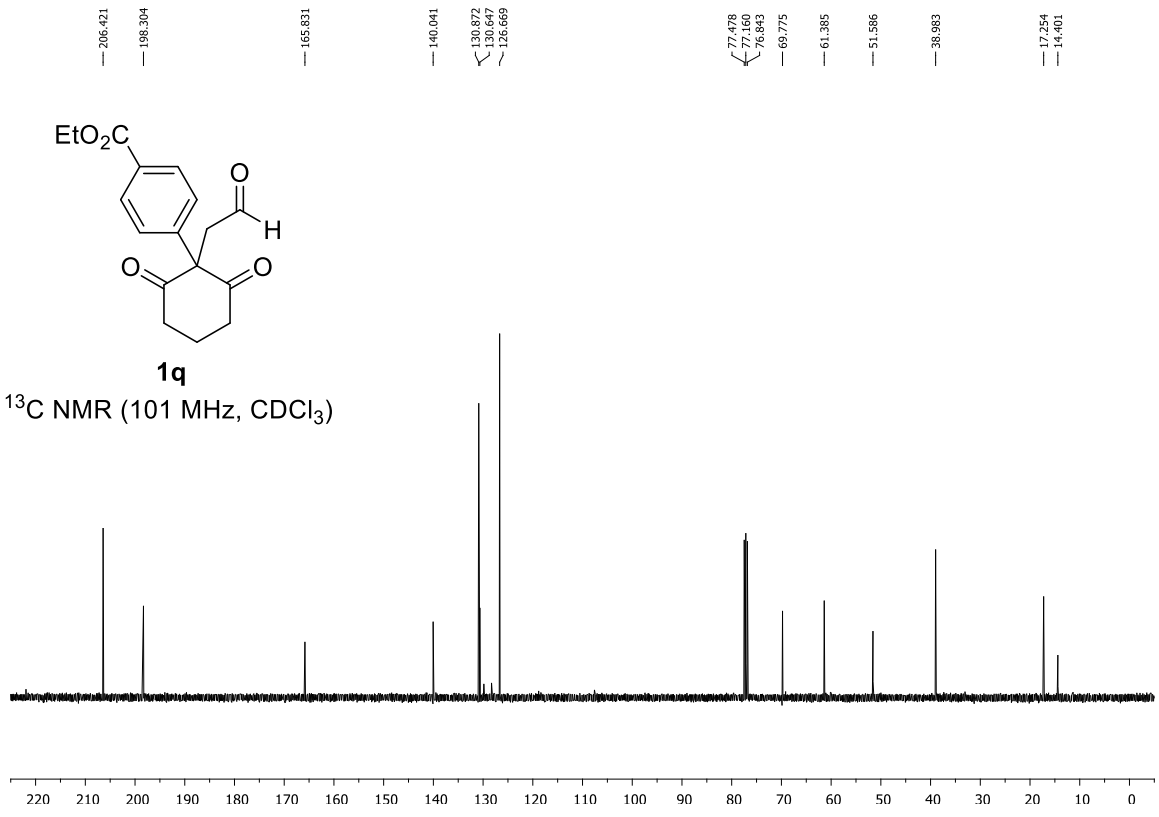

**1p**

$^{19}$F NMR (376 MHz, $CDCl_3$)



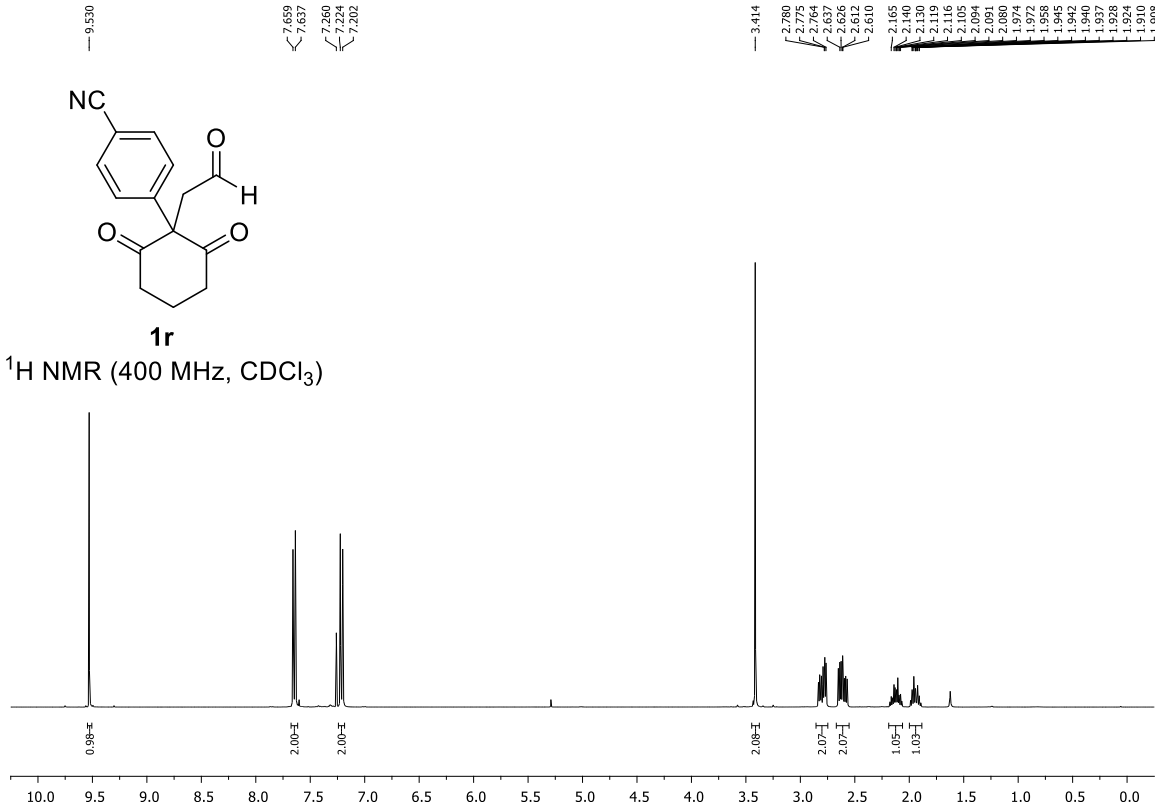

**1q**

$^{1}$H NMR (400 MHz, $CDCl_3$)



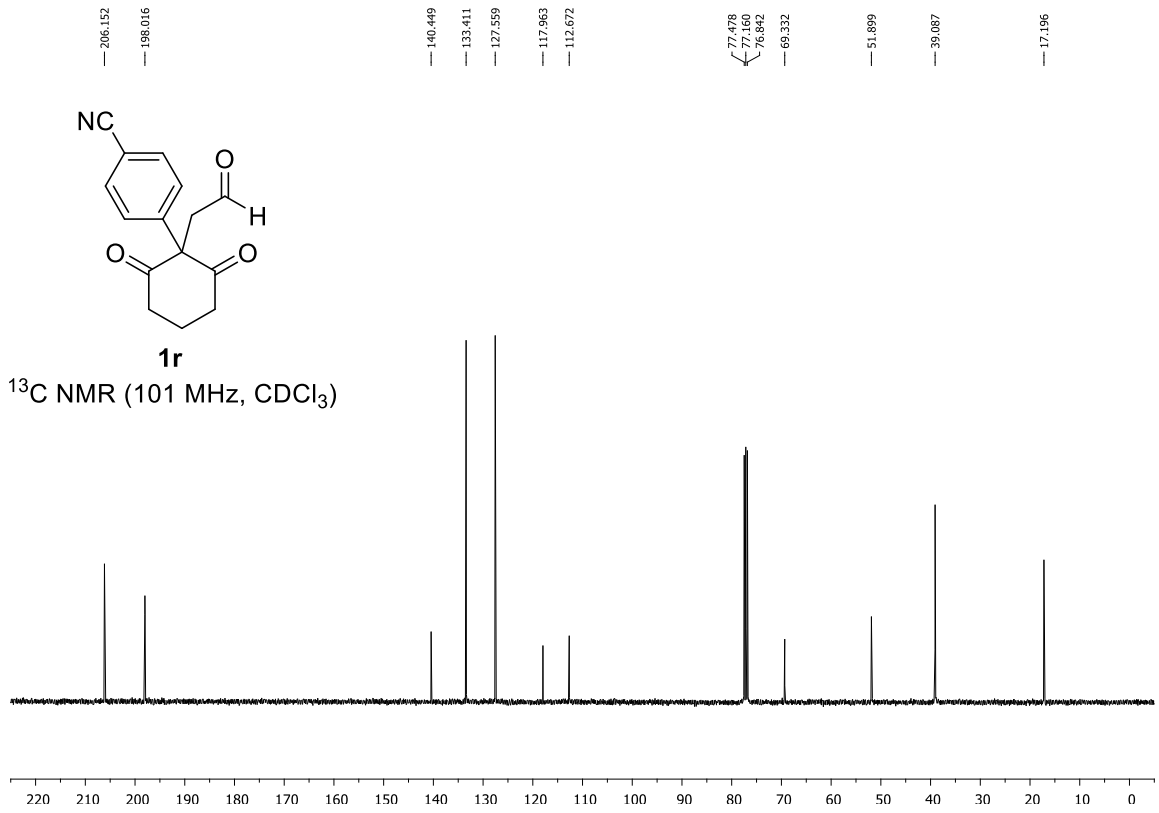

**1q**

$^{13}$C NMR (101 MHz, $CDCl_3$)



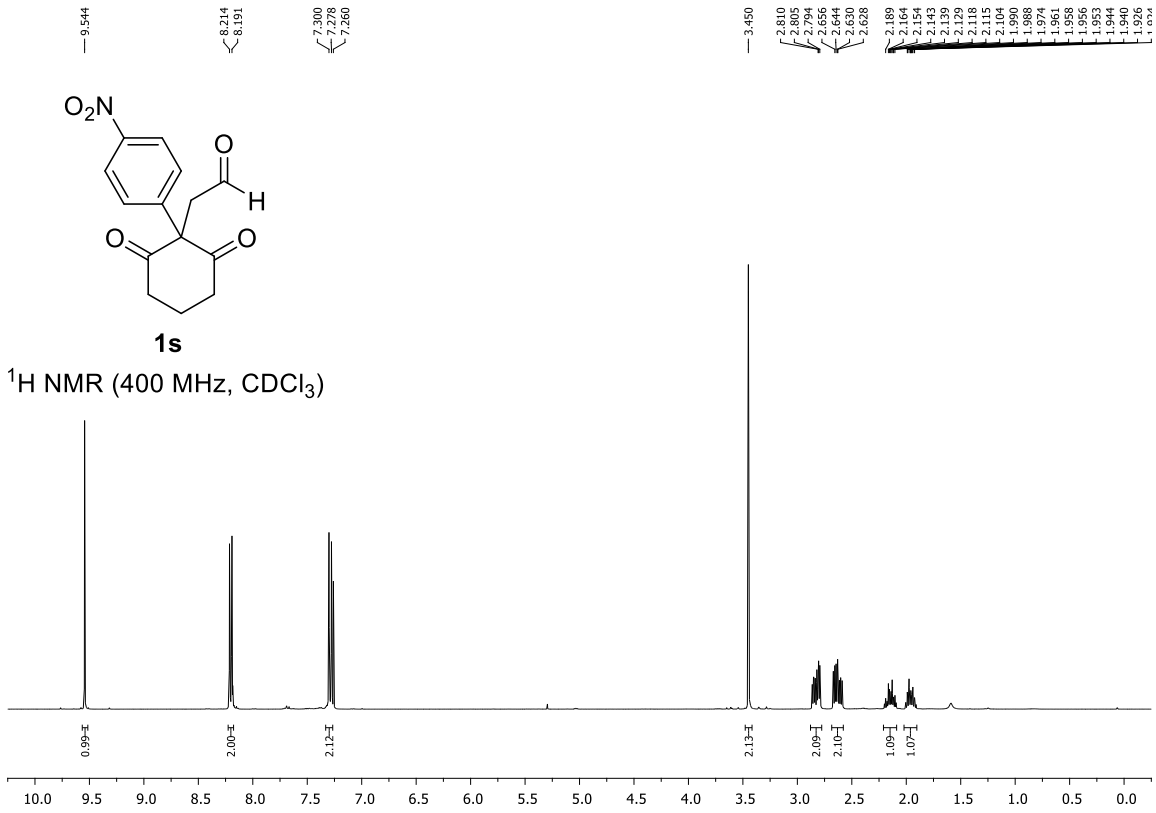

**1r**

$^{1}$H NMR (400 MHz, $CDCl_3$)



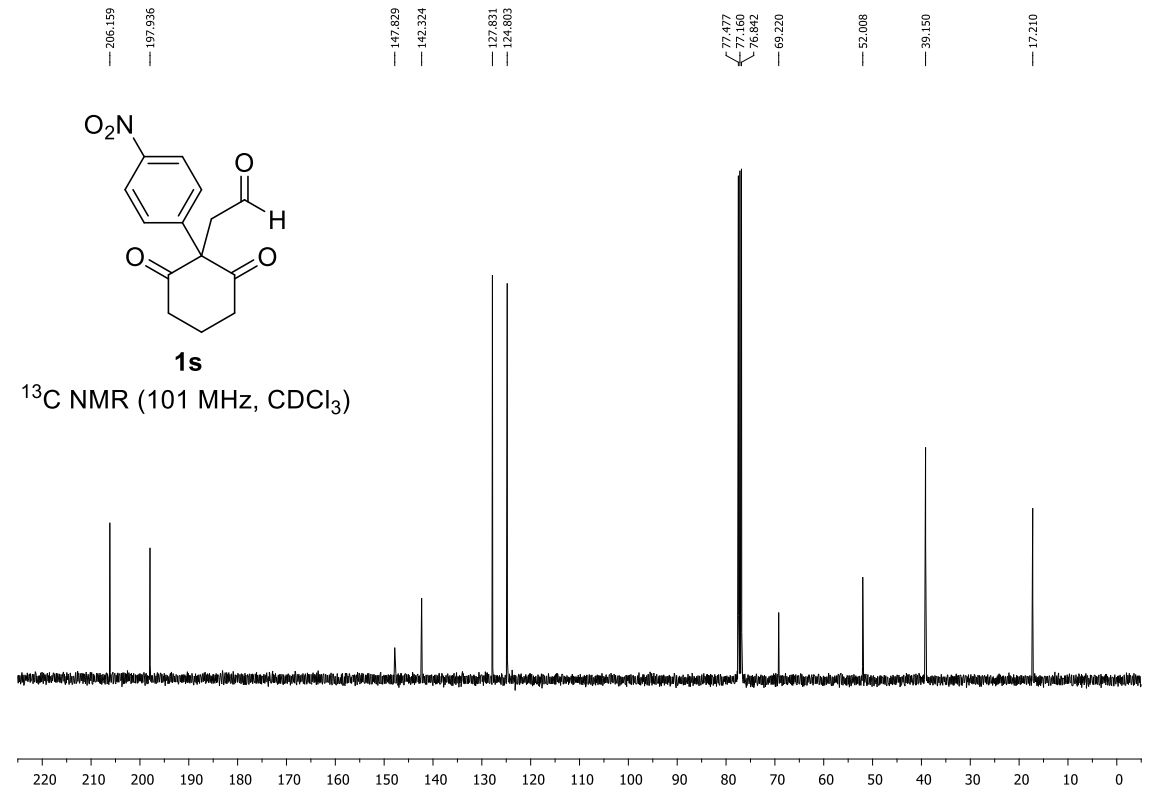

**1r**

$^{13}$C NMR (101 MHz, $CDCl_3$)



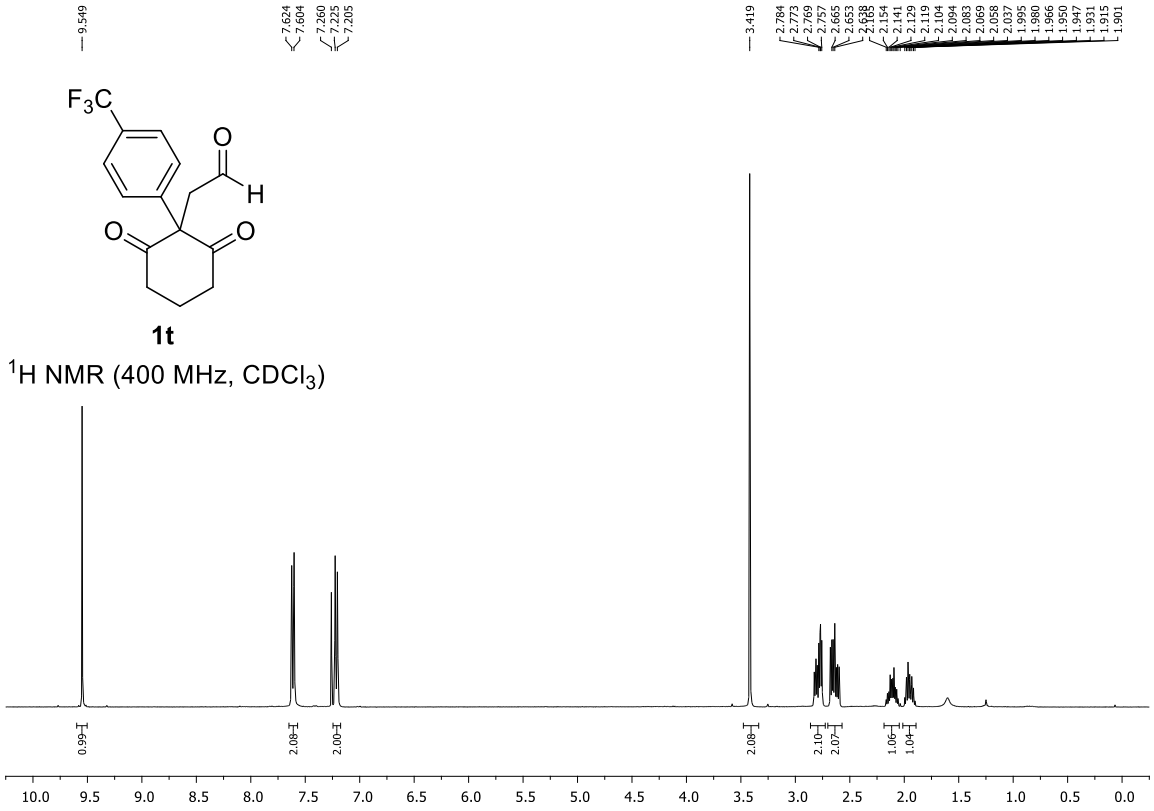

**1s**

$^{1}$H NMR (400 MHz, $CDCl_3$)



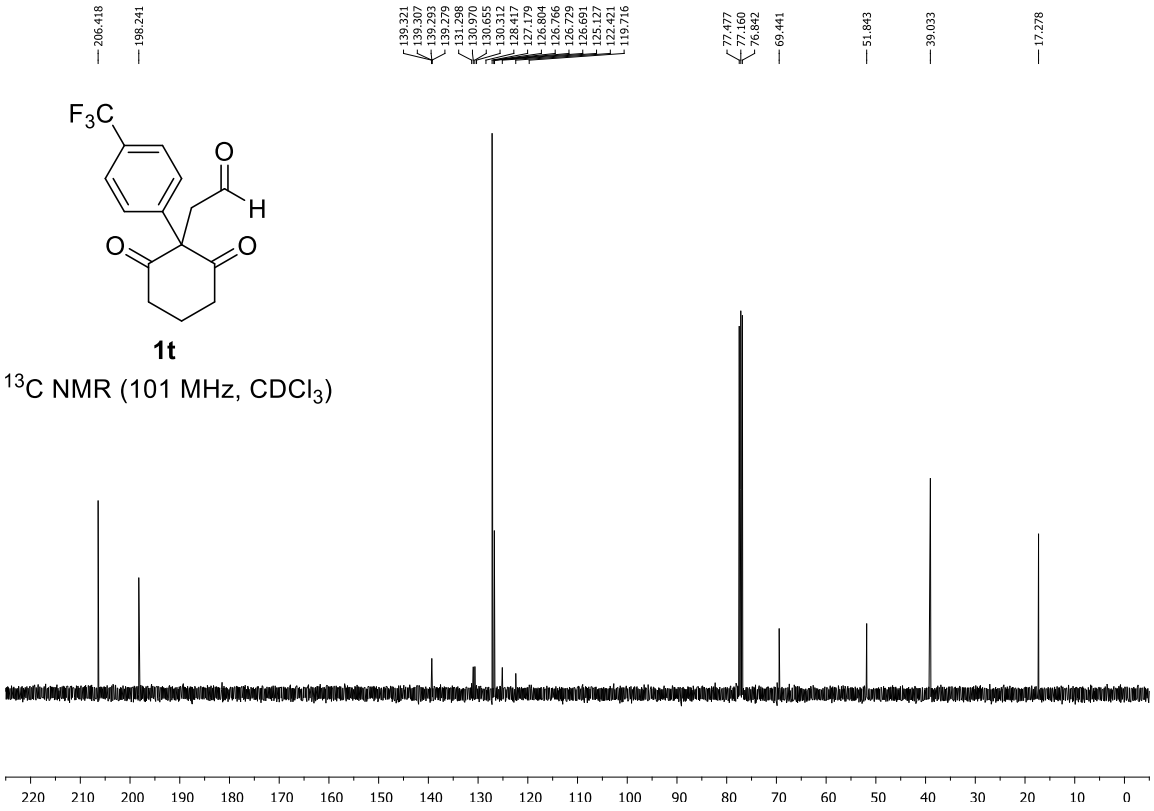

**1s**

$^{13}$C NMR (101 MHz, $CDCl_3$)



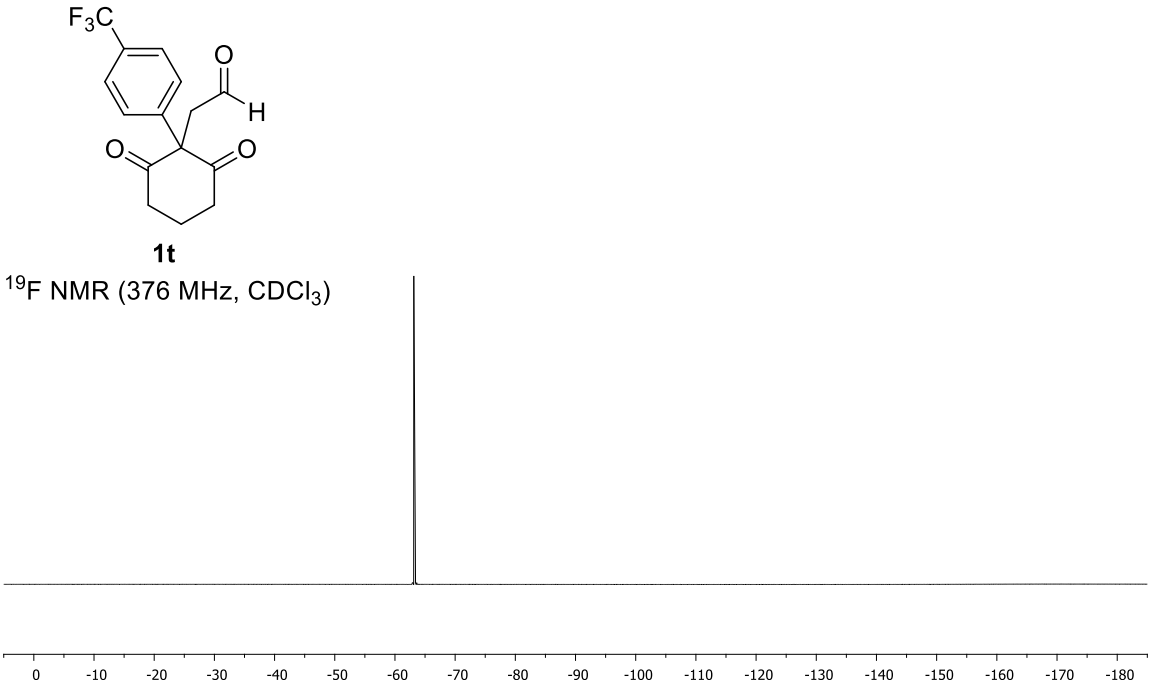

**1t**

$^{1}$H NMR (400 MHz, $CDCl_3$)



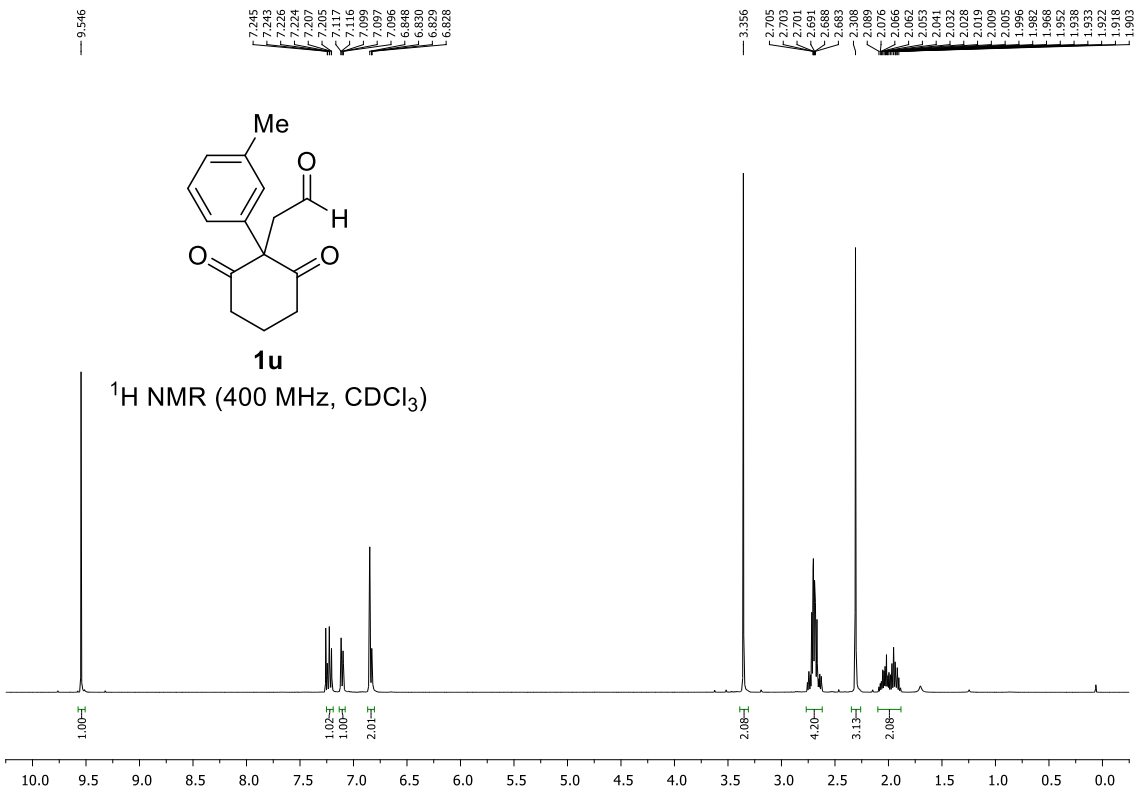

**1t**

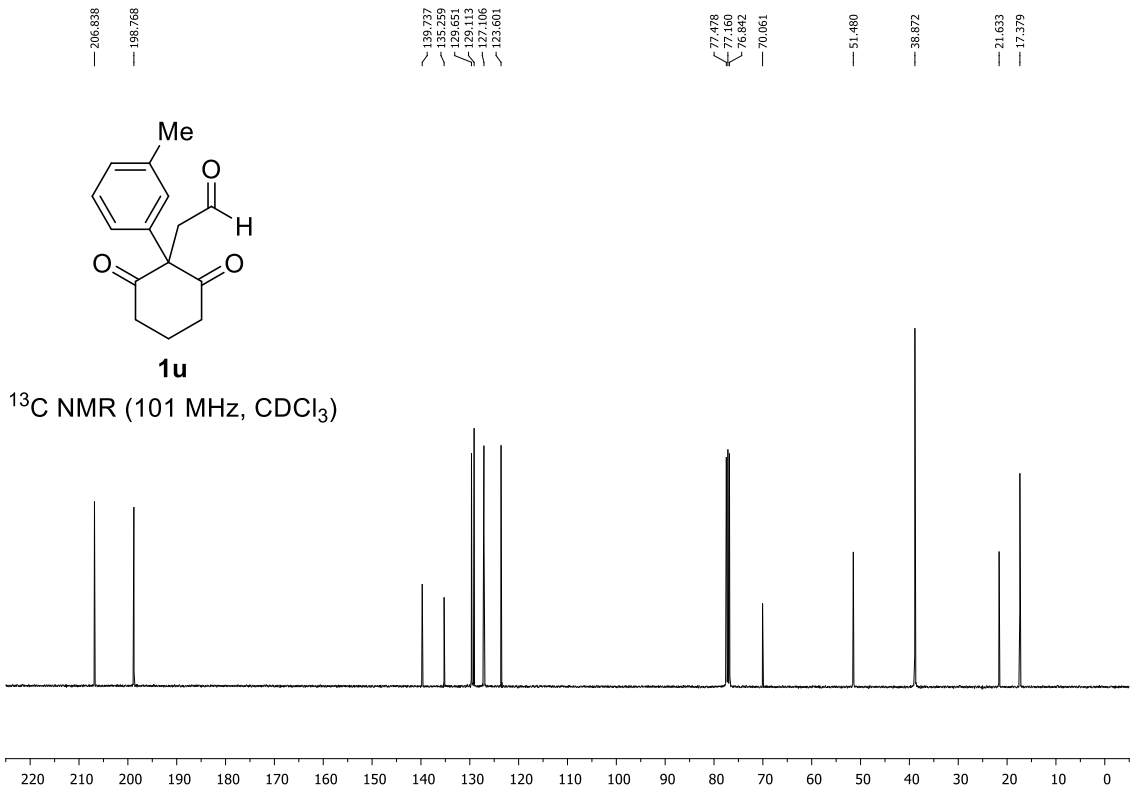
$^{13}$C NMR (101 MHz, $CDCl_3$)

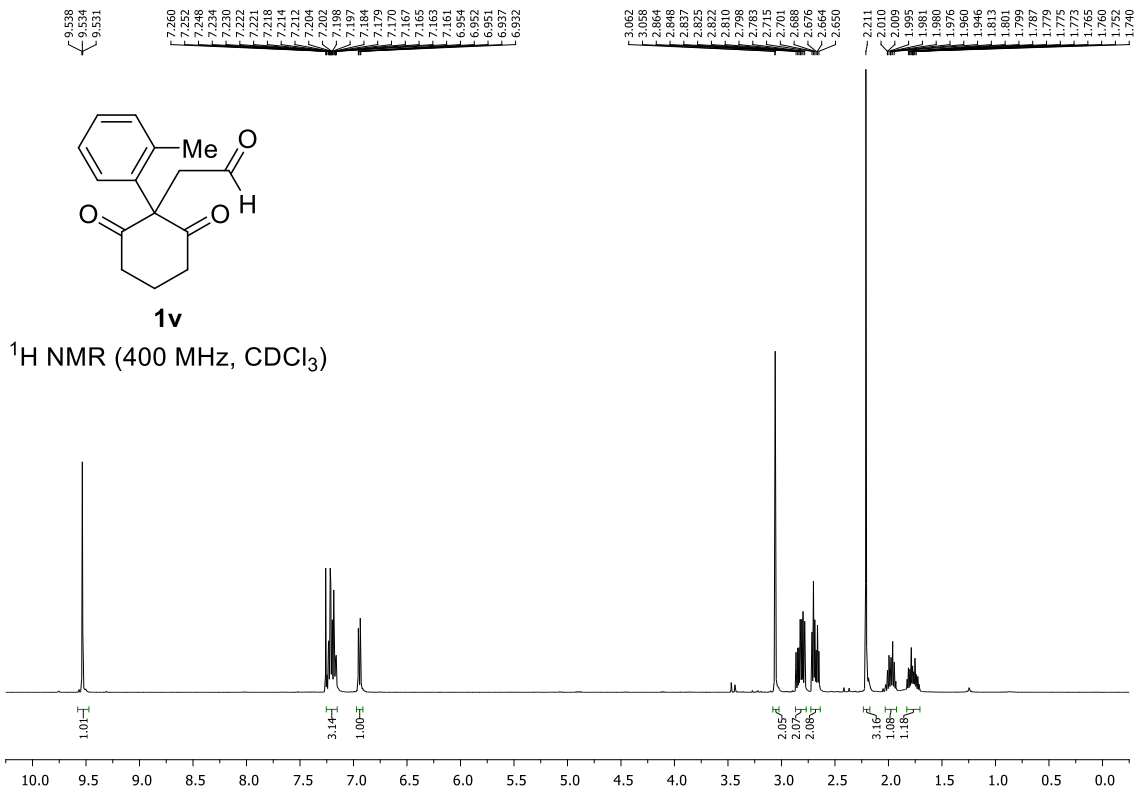



**1t**

$^{19}F$ NMR (376 MHz, $CDCl_3$)

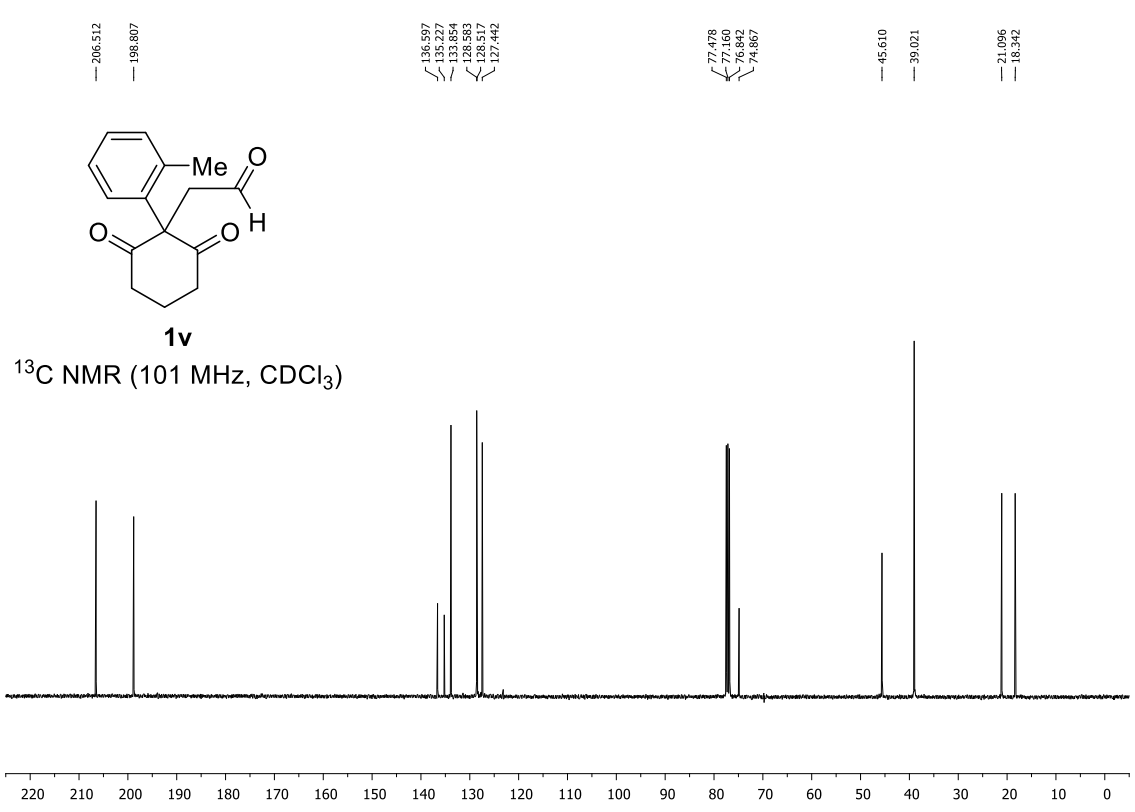

9.546
7.245
7.243
7.226
7.224
7.207
7.205
7.117
7.116
7.099
7.097
7.096
6.848
6.830
6.829
6.828
3.356
2.705
2.703
2.701
2.691
2.688
2.683
2.308
2.089
2.076
2.066
2.062
2.053
2.041
2.032
2.028
2.019
2.009
2.005
1.996
1.982
1.968
1.952
1.938
1.933
1.922
1.918
1.903
Me
O
H
O
O
1u
1H NMR (400 MHz, CDCl3)
1.00
1.02
1.00
2.01
2.08
4.20
3.13
2.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


206.838
198.768
139.737
135.259
129.651
129.113
127.106
123.601
77.478
77.160
76.842
70.061
51.480
38.872
21.633
17.379
Me
O
H
O
O
1u
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



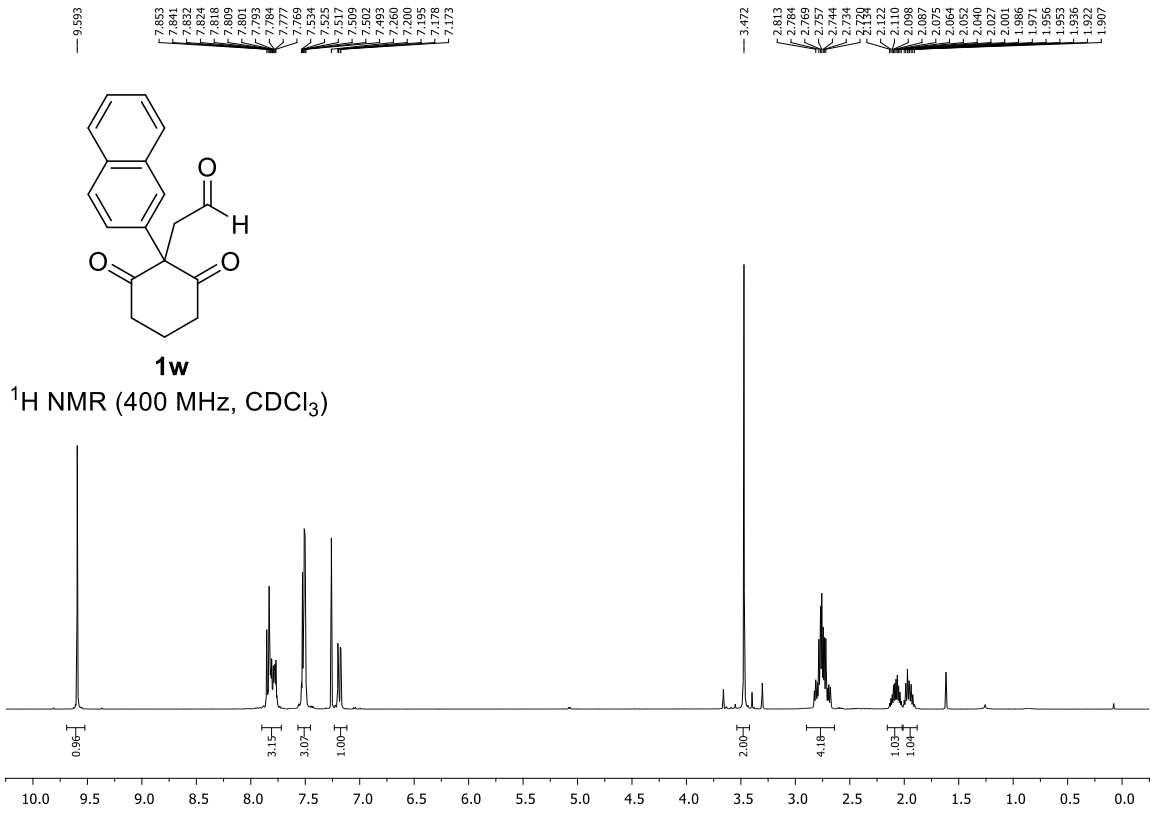

**1v**

$^{1}$H NMR (400 MHz, $CDCl_3$)



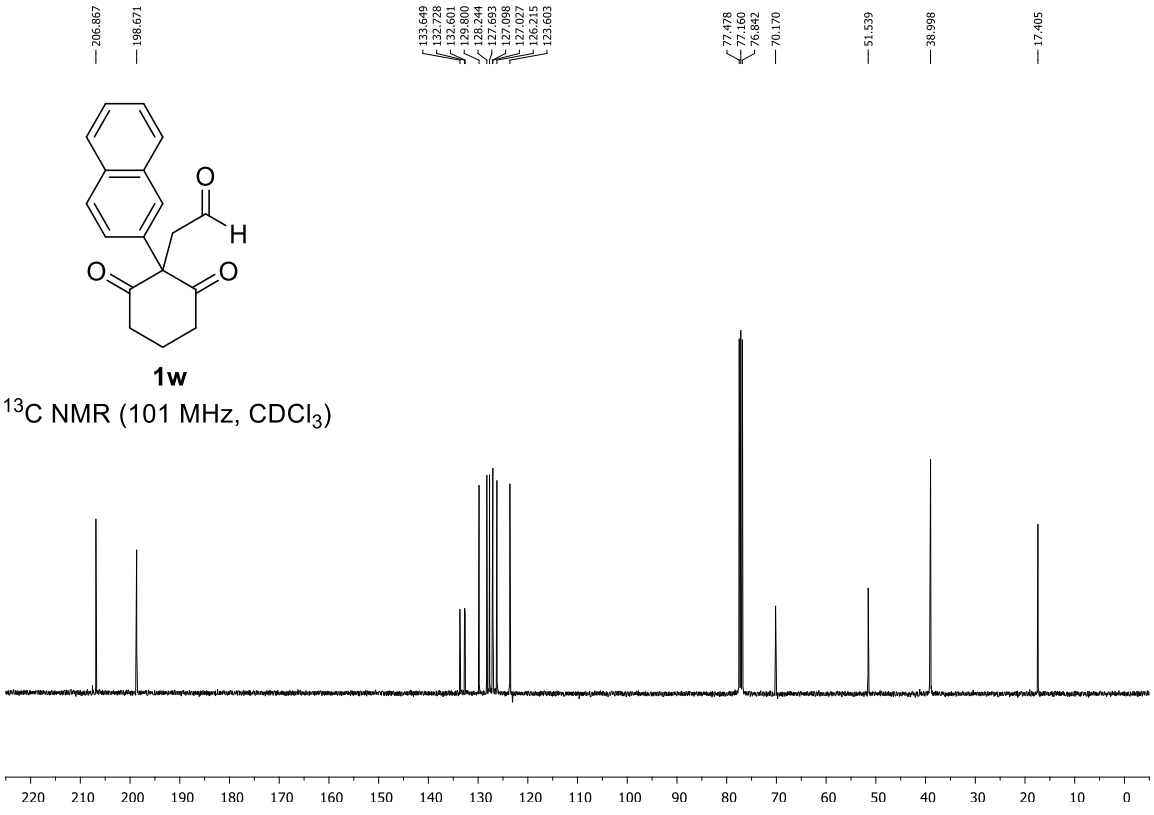

**1v**

$^{13}$C NMR (101 MHz, $CDCl_3$)



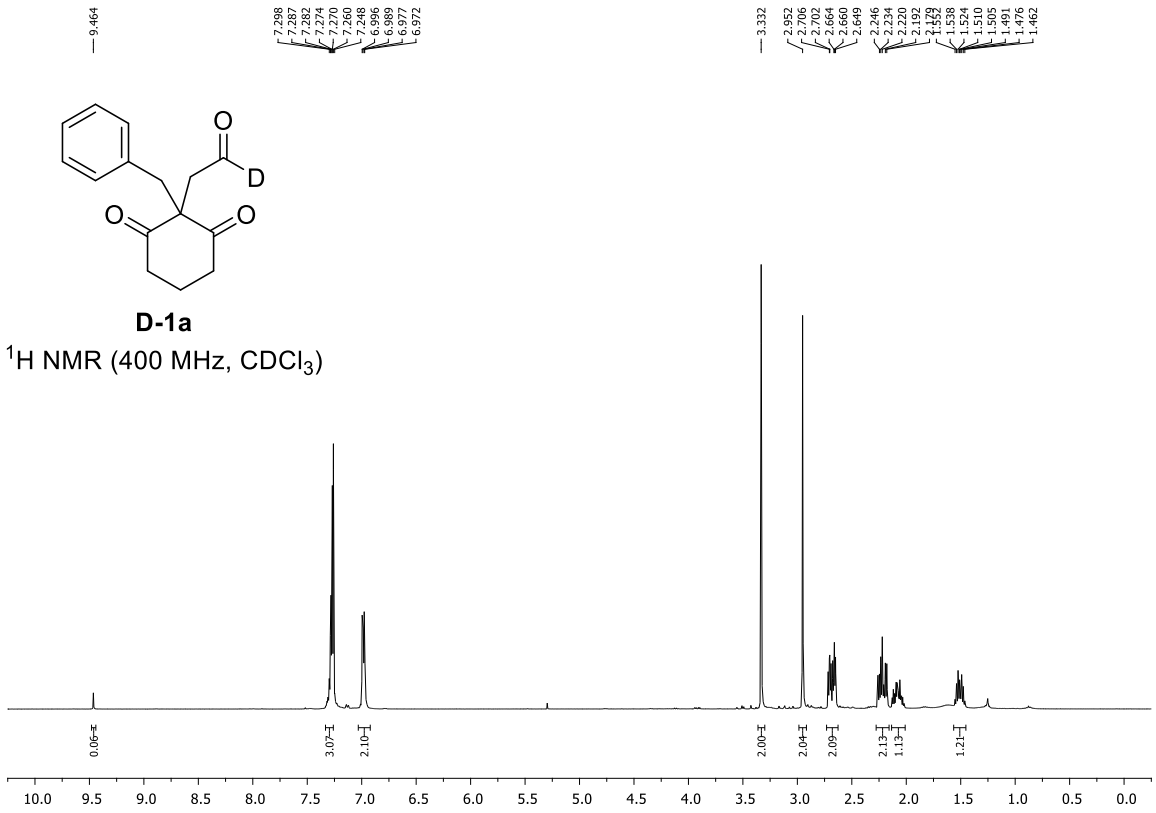
**1w**

$^{1}$H NMR (400 MHz, $CDCl_3$)



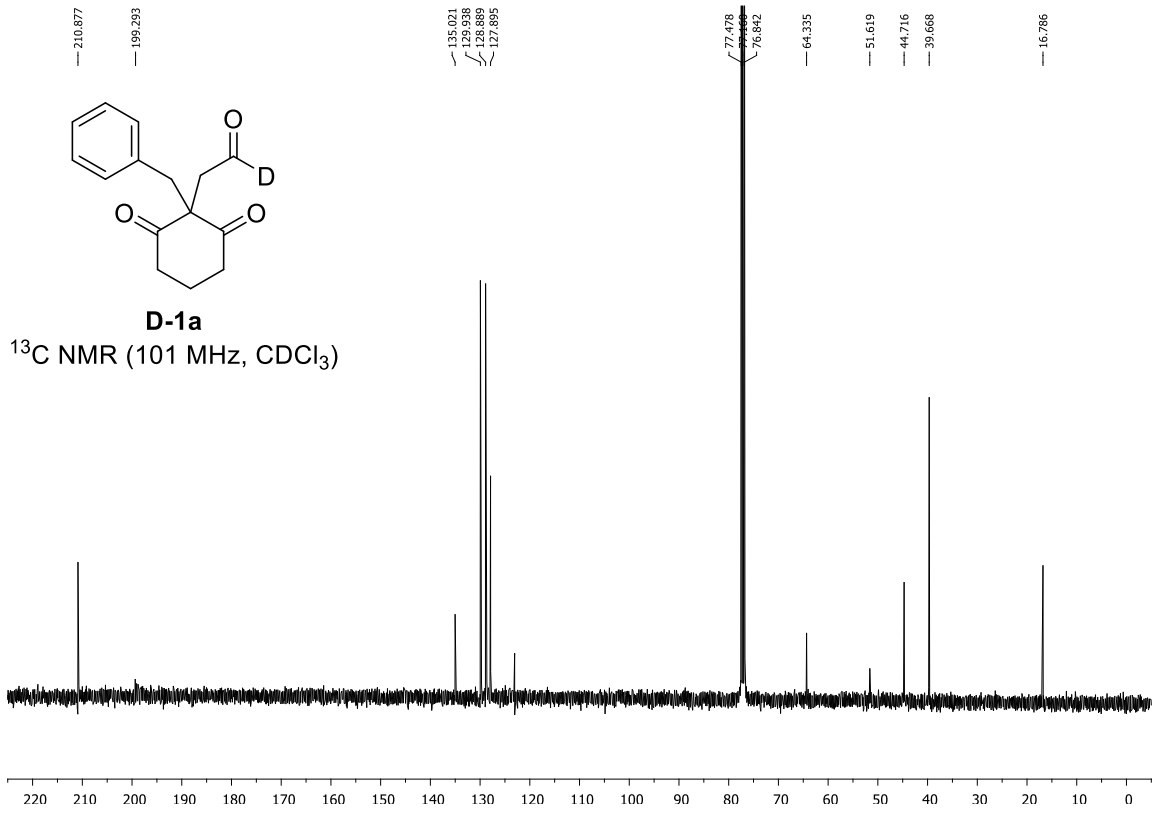
**1w**

$^{13}$C NMR (101 MHz, $CDCl_3$)



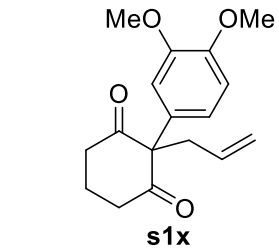

**D-1a**

$^{1}$H NMR (400 MHz, $CDCl_3$)




**D-1a**

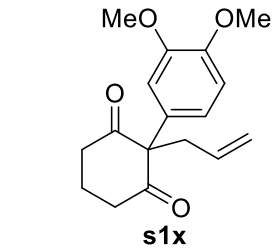
$^{13}$C NMR (101 MHz, $CDCl_3$)




**s1x**

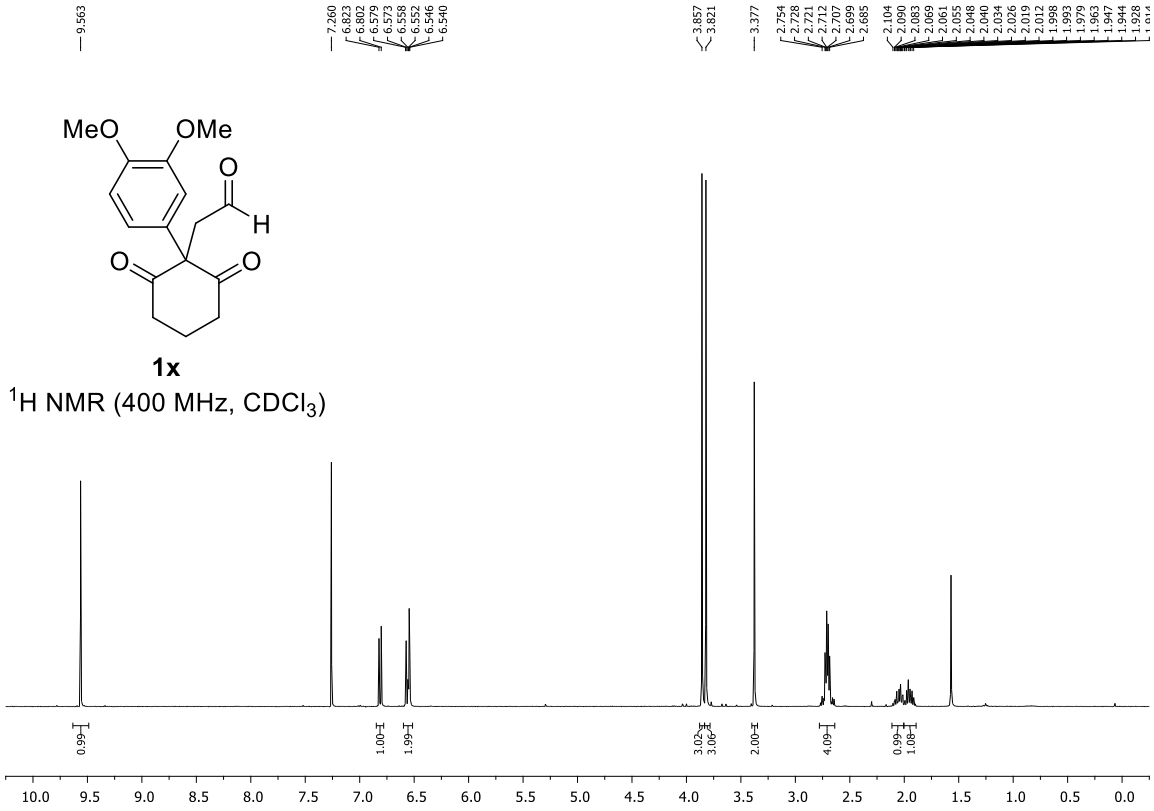
$^{1}$H NMR (500 MHz, $CDCl_3$)



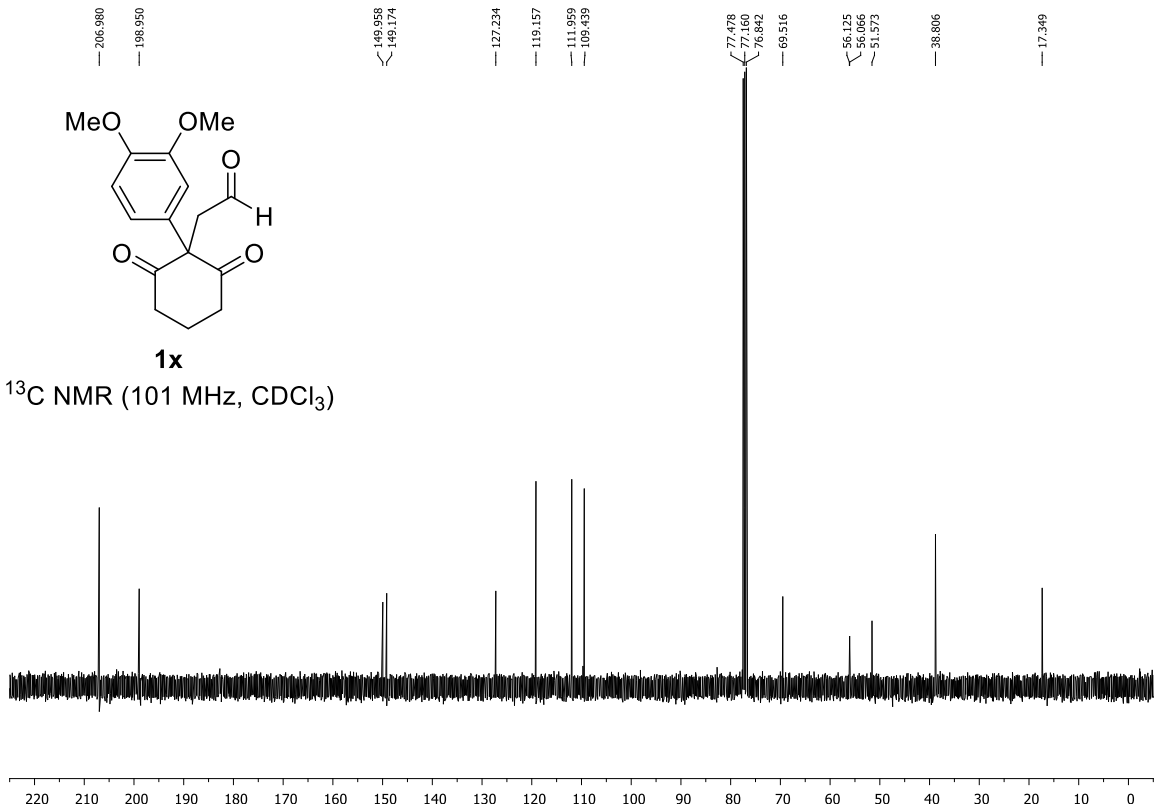

**s1x**

$^{13}$C NMR (126 MHz, $CDCl_3$)



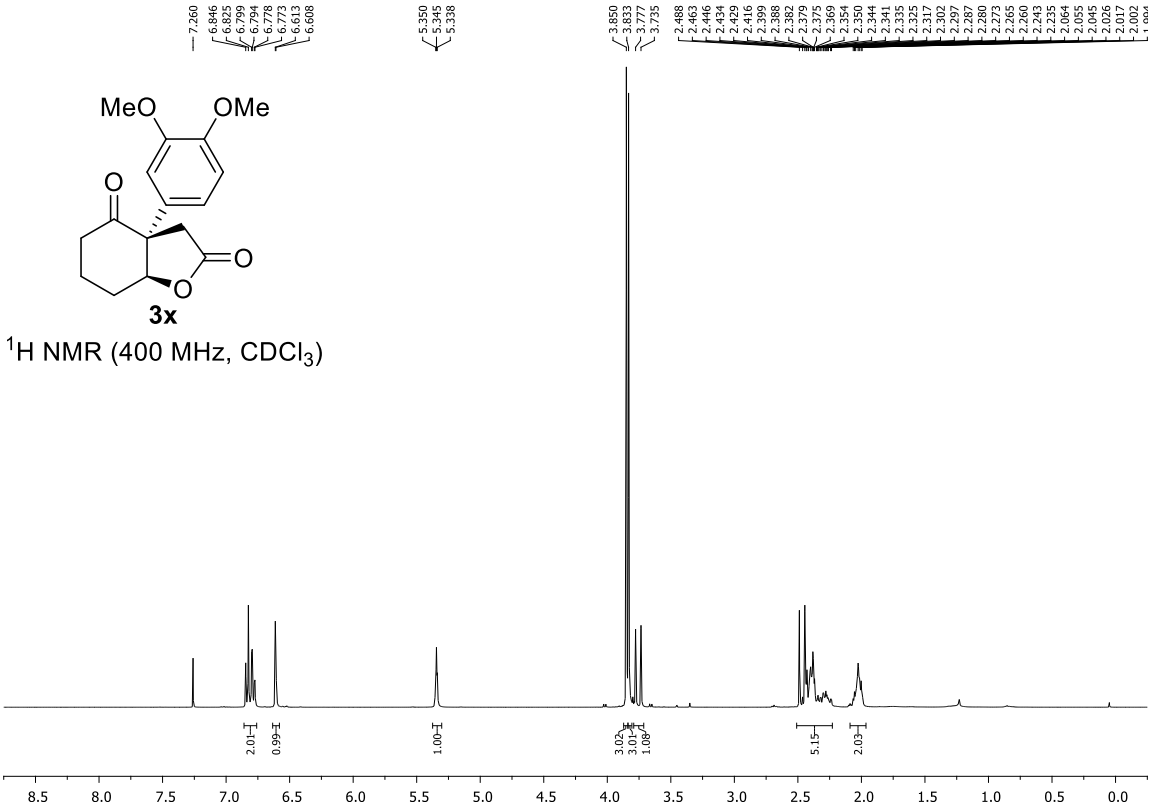

**1x**

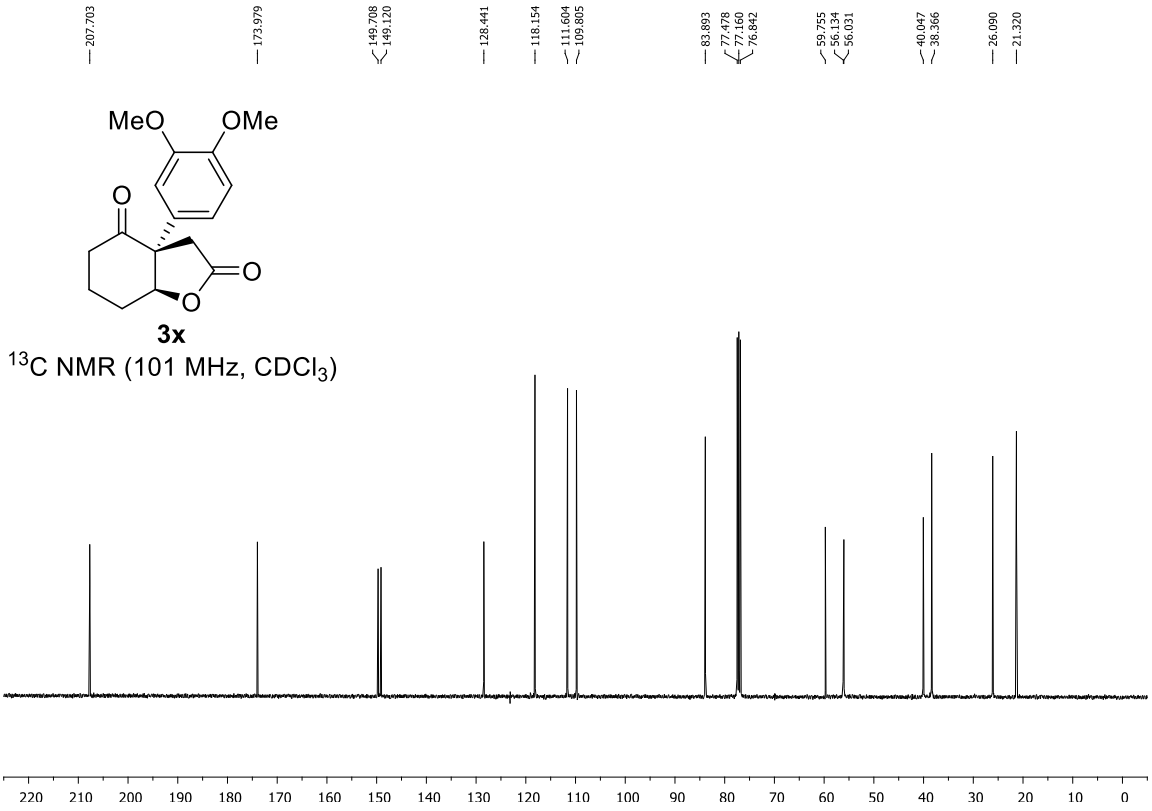
$^{1}$H NMR (400 MHz, $CDCl_3$)

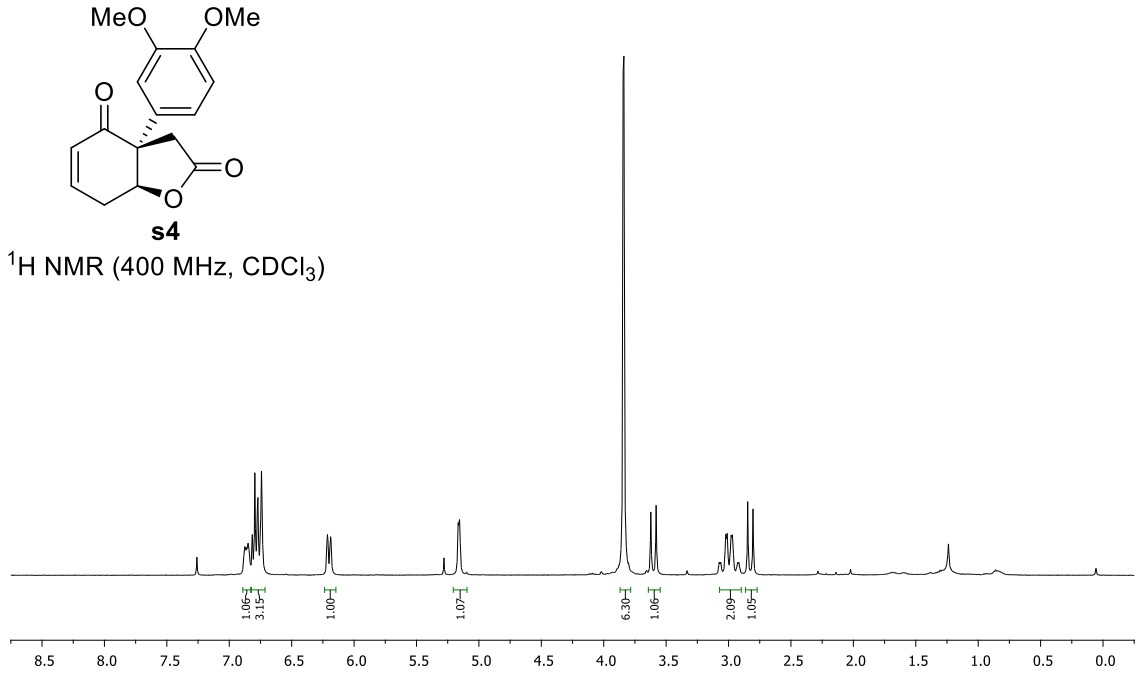



**1x**

$^{13}$C NMR (101 MHz, $CDCl_3$)

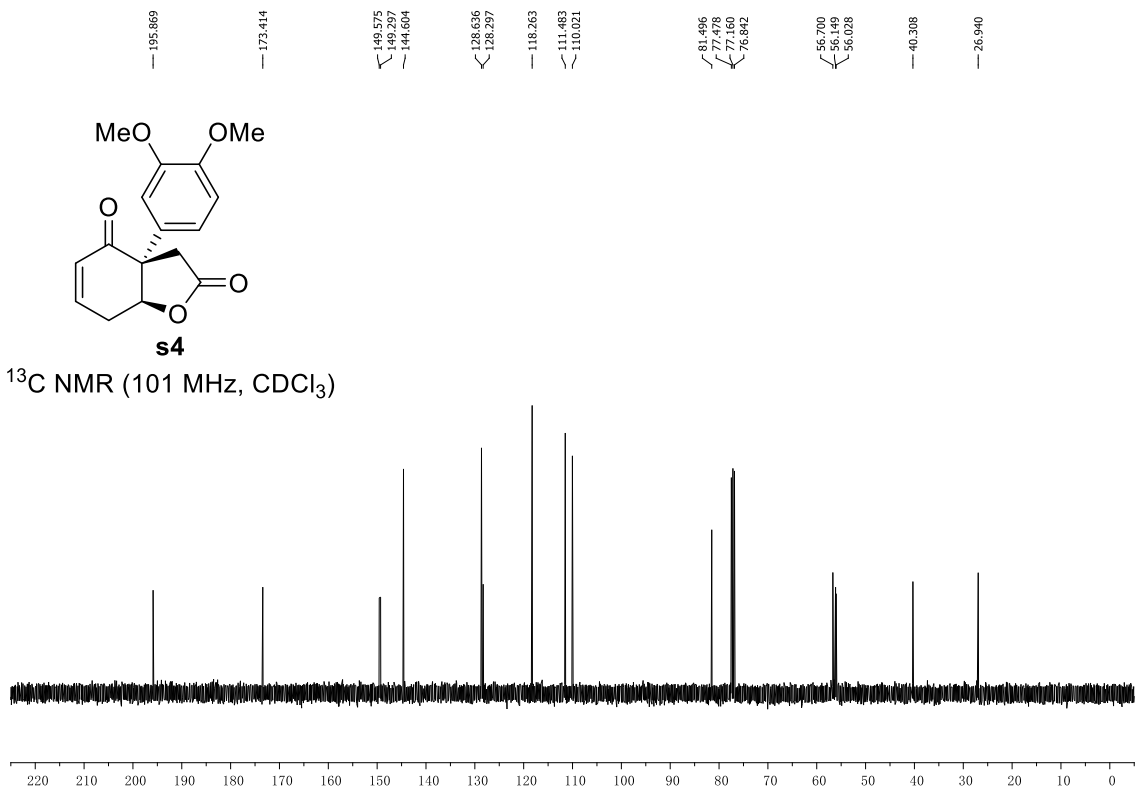

MeO
OMe
O
O
O
3x
$^1$H NMR (400 MHz, $CDCl_3$)


MeO
OMe
O
O
O
3x
$^{13}$C NMR (101 MHz, $CDCl_3$)



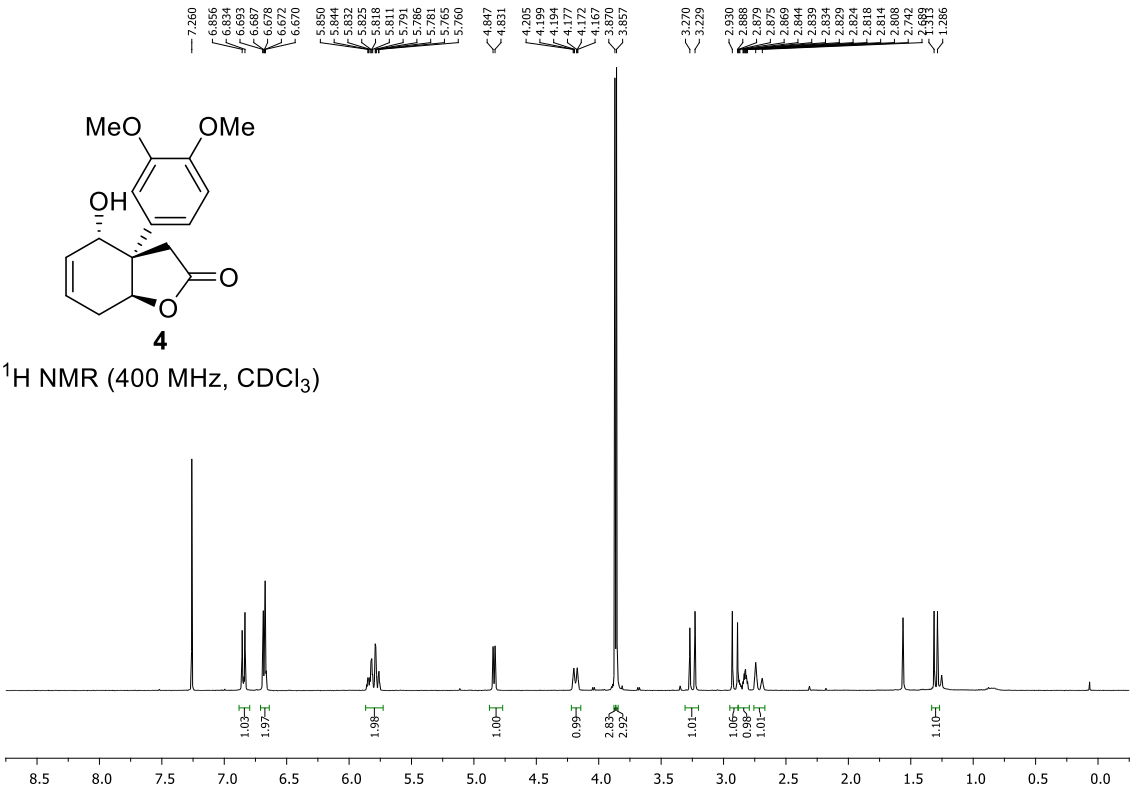

**s4**

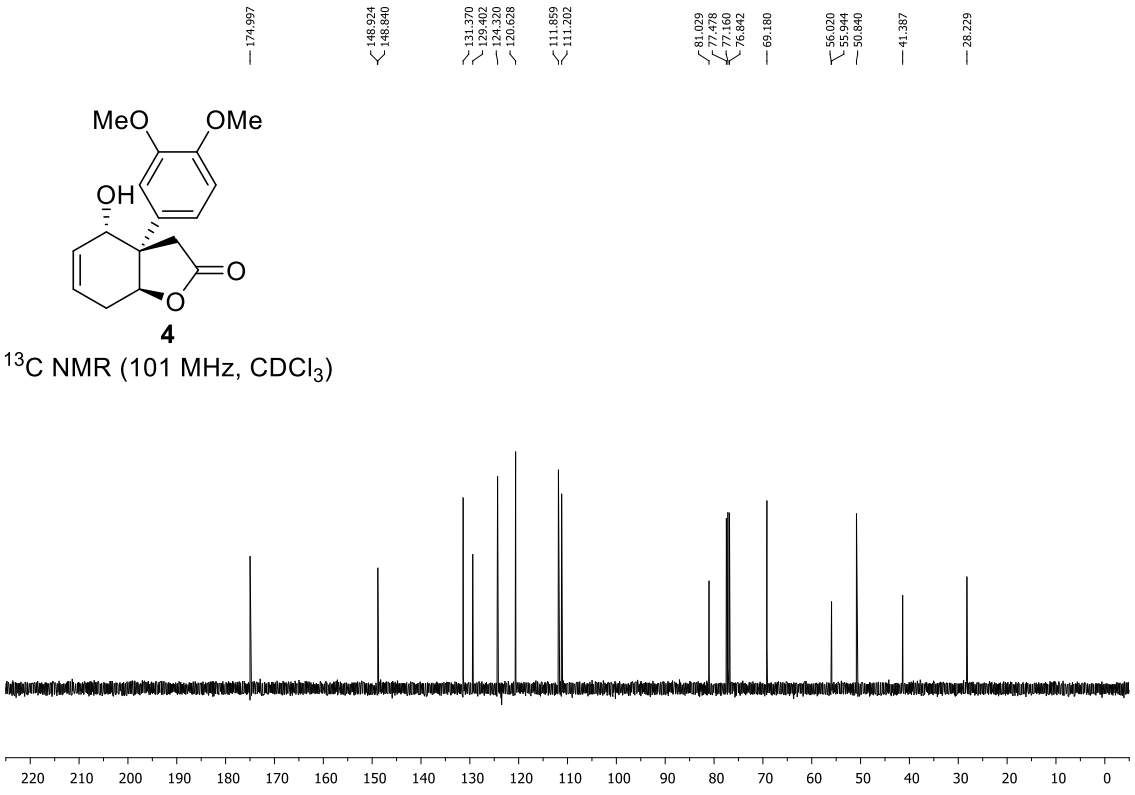
$^{1}$H NMR (400 MHz, $CDCl_3$)

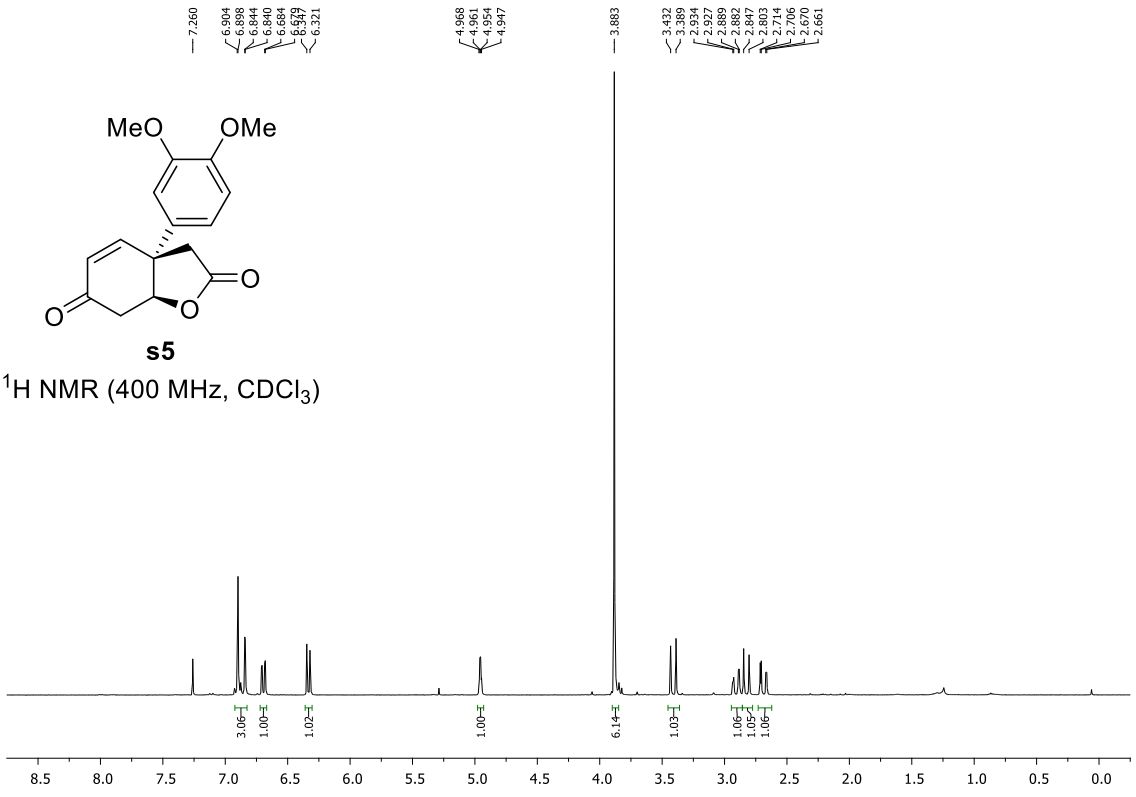



**s4**

$^{13}$C NMR (101 MHz, $CDCl_3$)

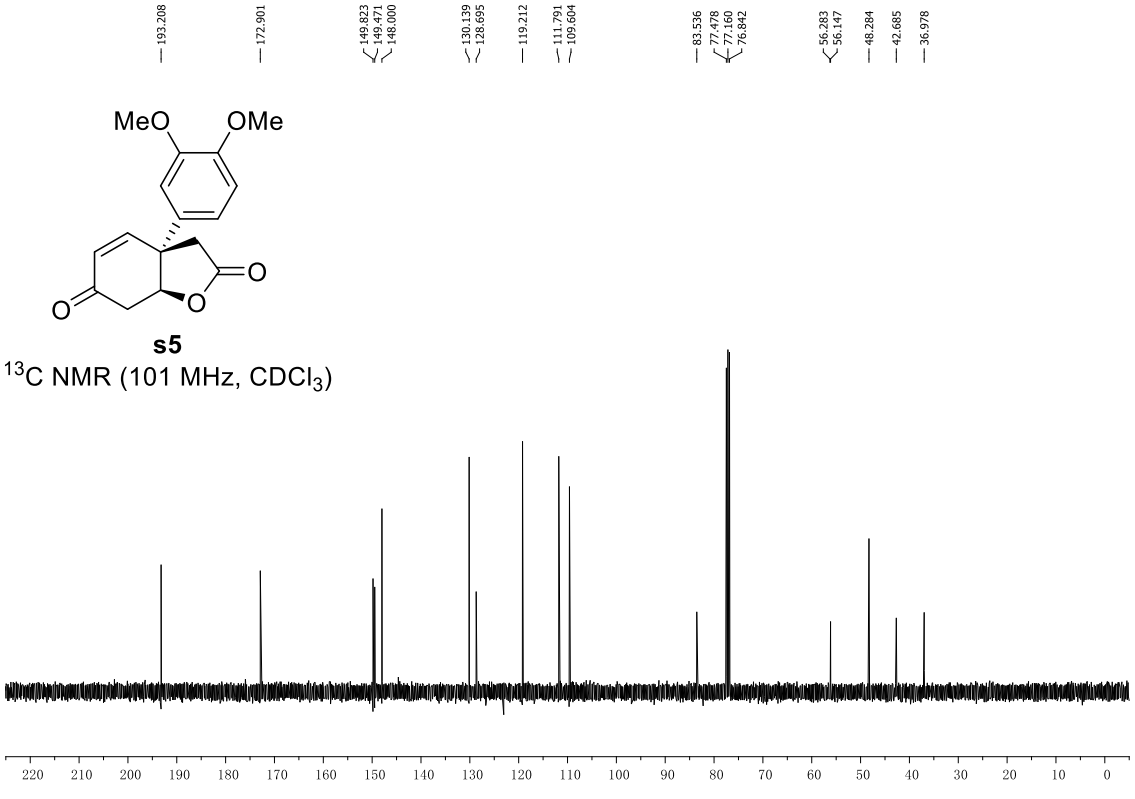

MeO
OMe
OH
O
O
4
1H NMR (400 MHz, CDCl3)


MeO
OMe
OH
O
O
4
13C NMR (101 MHz, CDCl3)



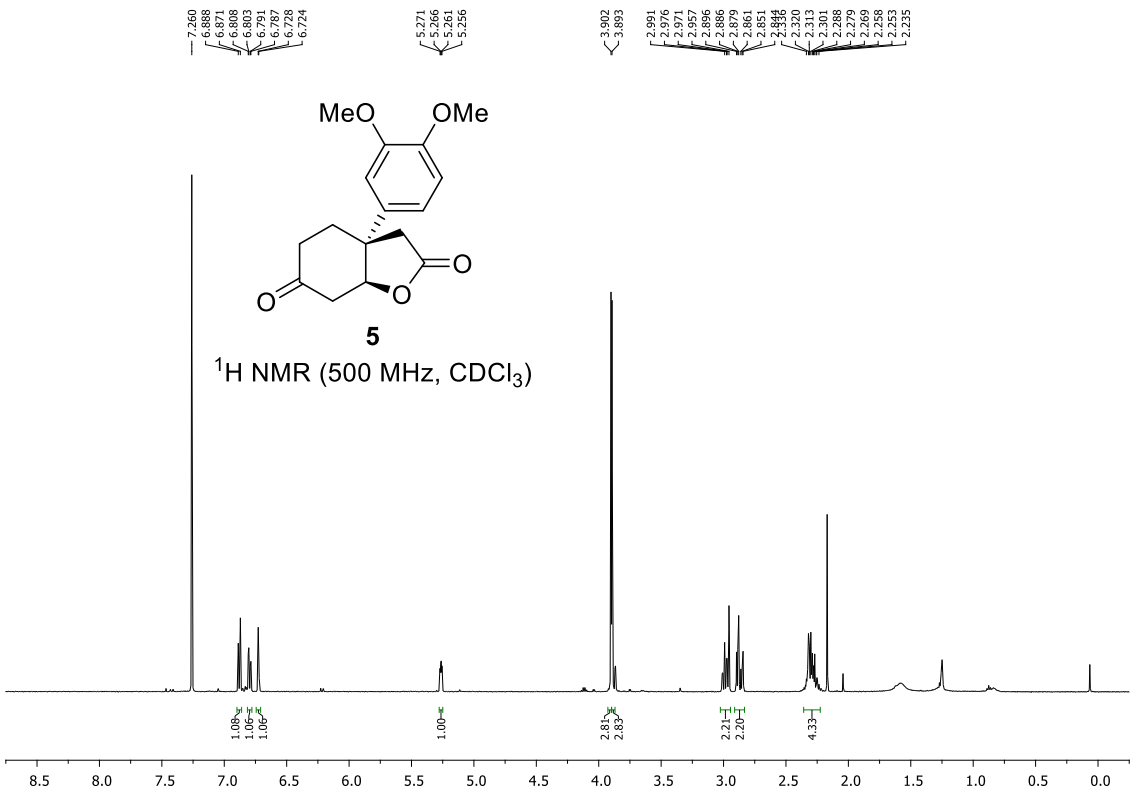

**s5**

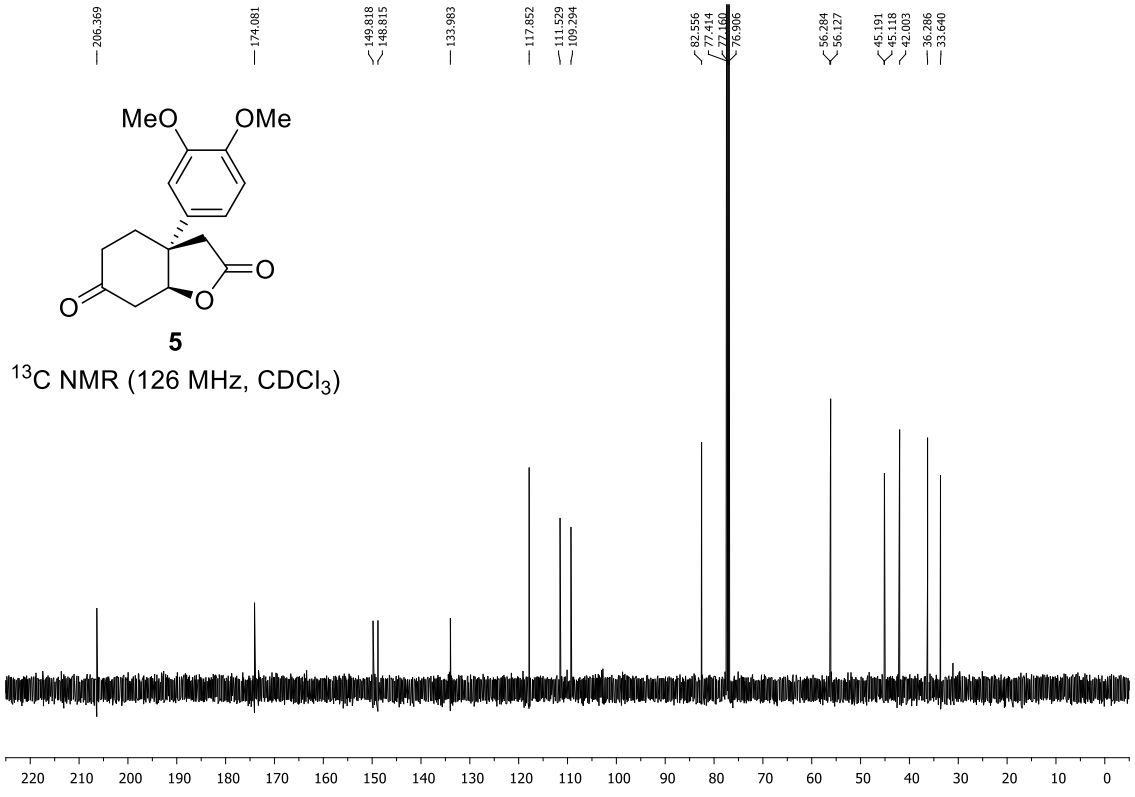
$^{1}$H NMR (400 MHz, $CDCl_3$)

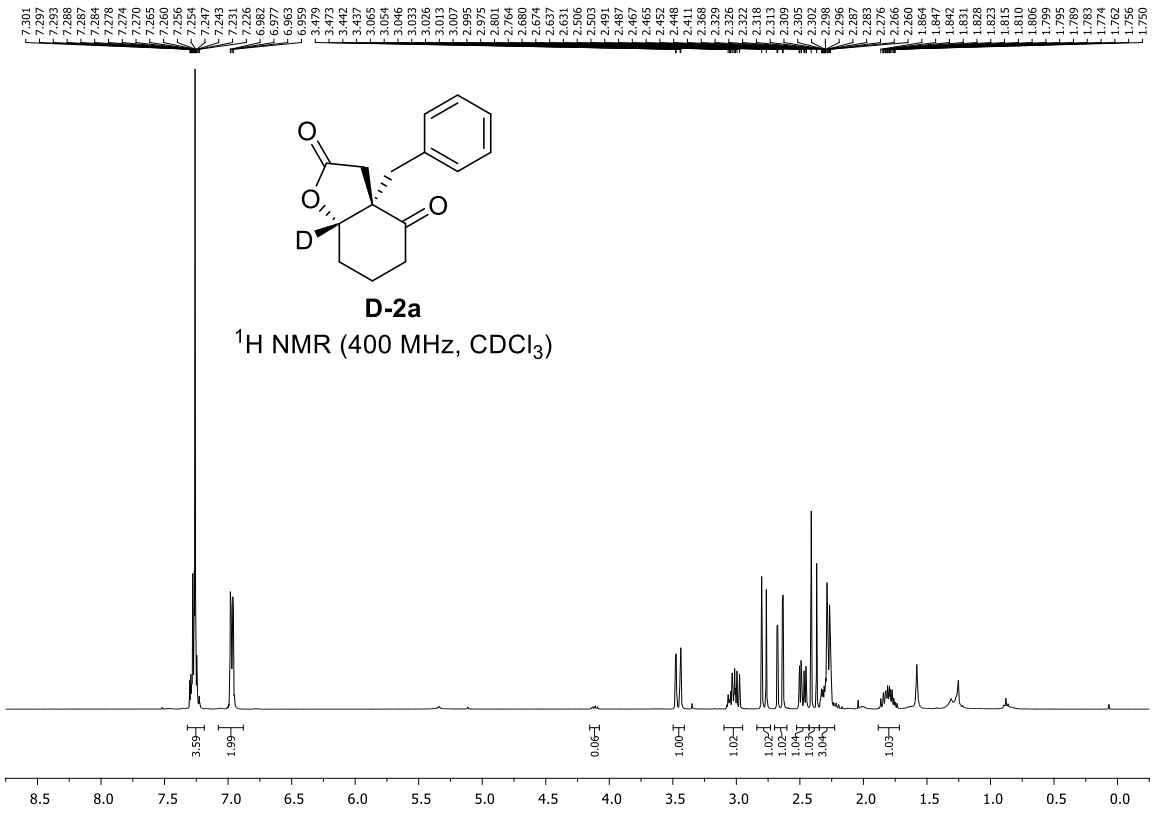



**s5**

$^{13}$C NMR (101 MHz, $CDCl_3$)

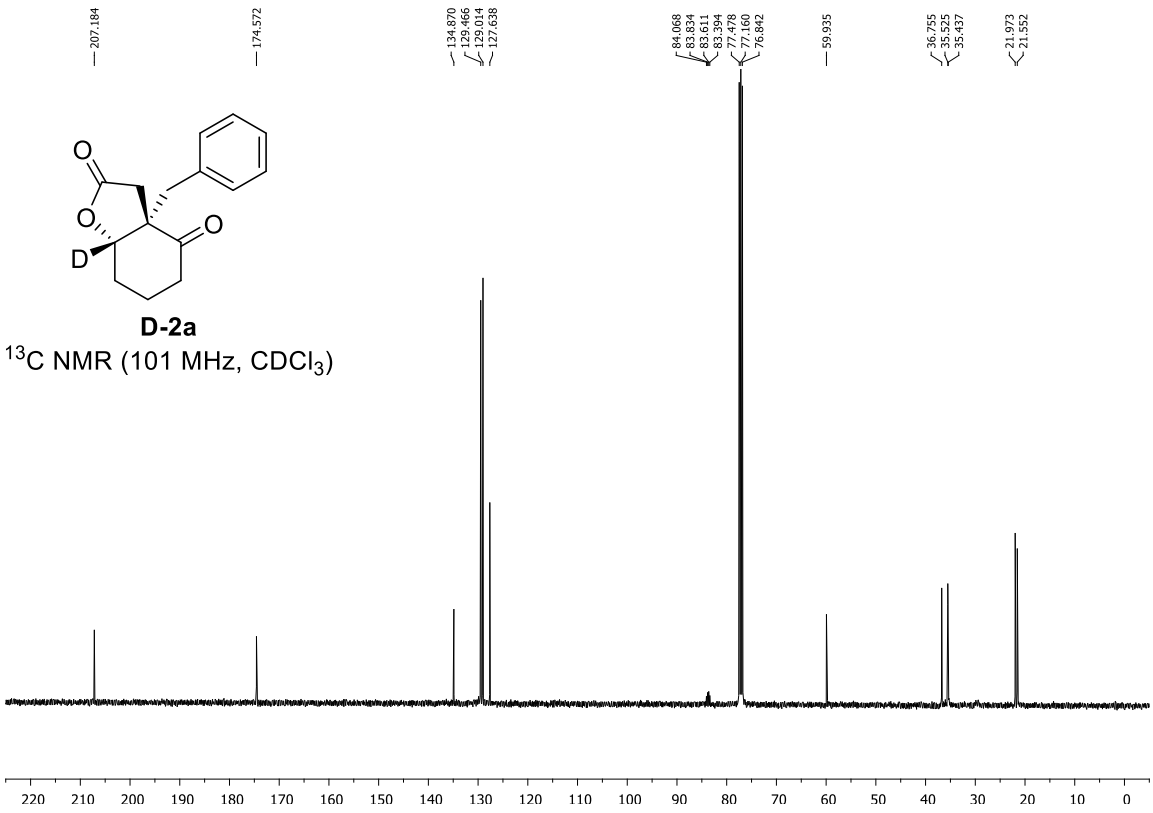

MeO
OMe
O
O
O
5
1H NMR (500 MHz, CDCl3)


MeO
OMe
O
O
O
5
13C NMR (126 MHz, CDCl3)



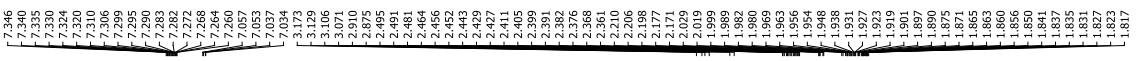

**D-2a**

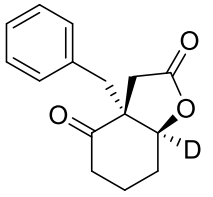
$^{1}$H NMR (400 MHz, $CDCl_3$)




**D-2a**

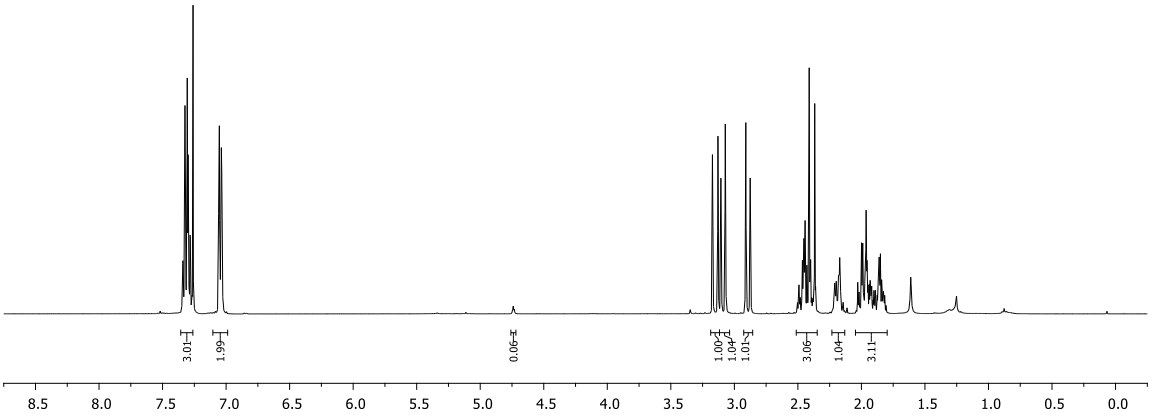
$^{13}$C NMR (101 MHz, $CDCl_3$)

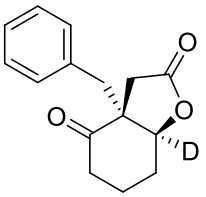




**D-3a**

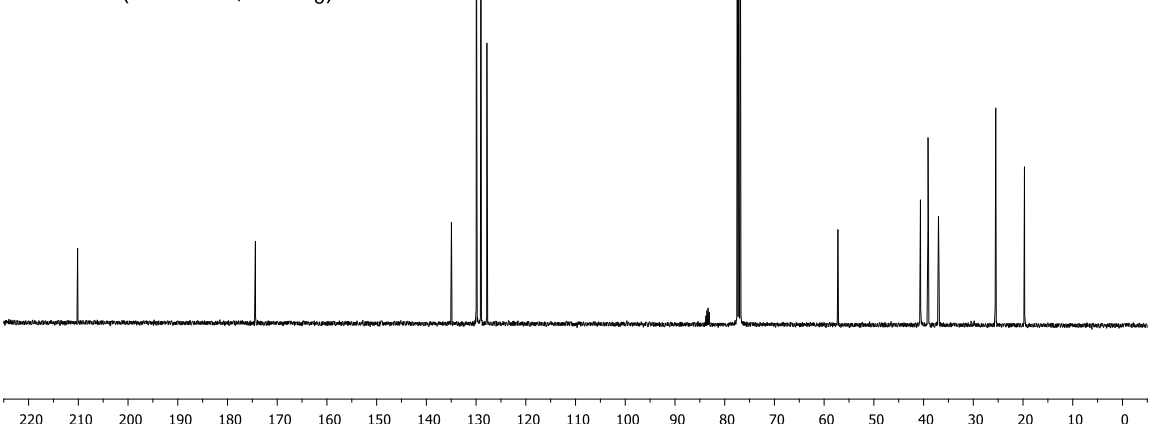
$^{1}$H NMR (400 MHz, $CDCl_3$)

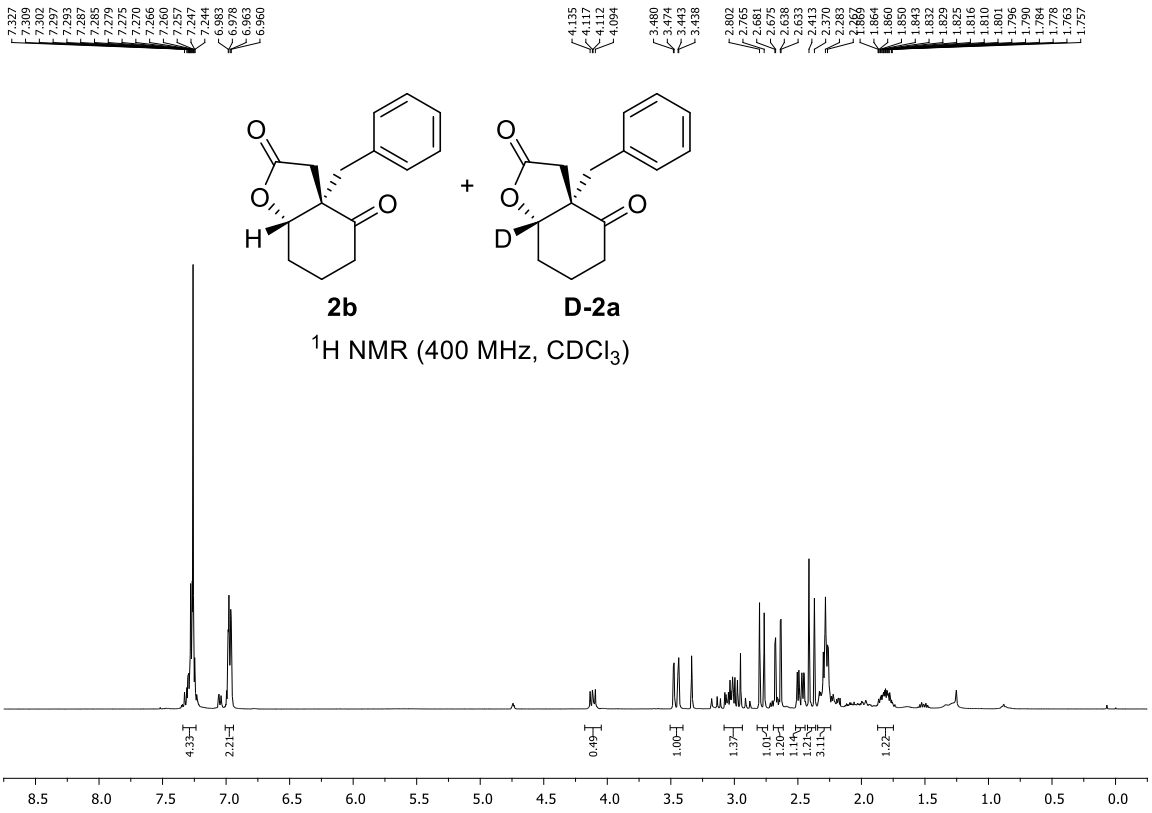


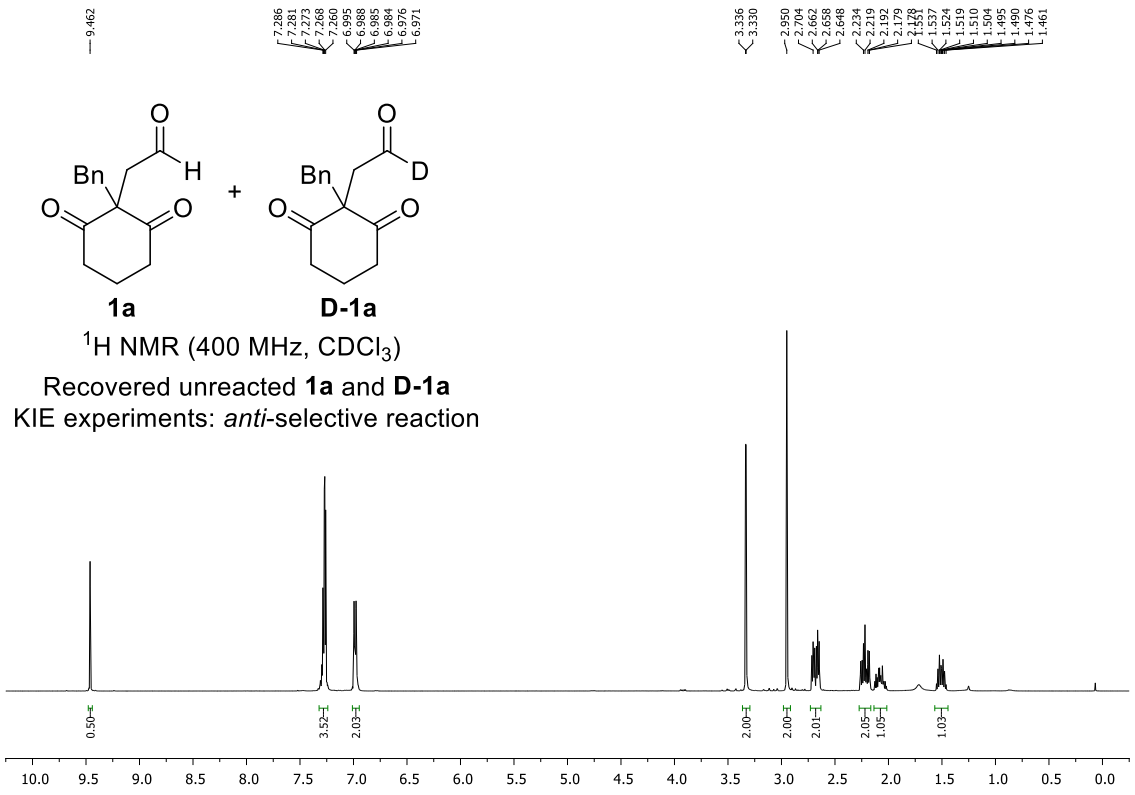


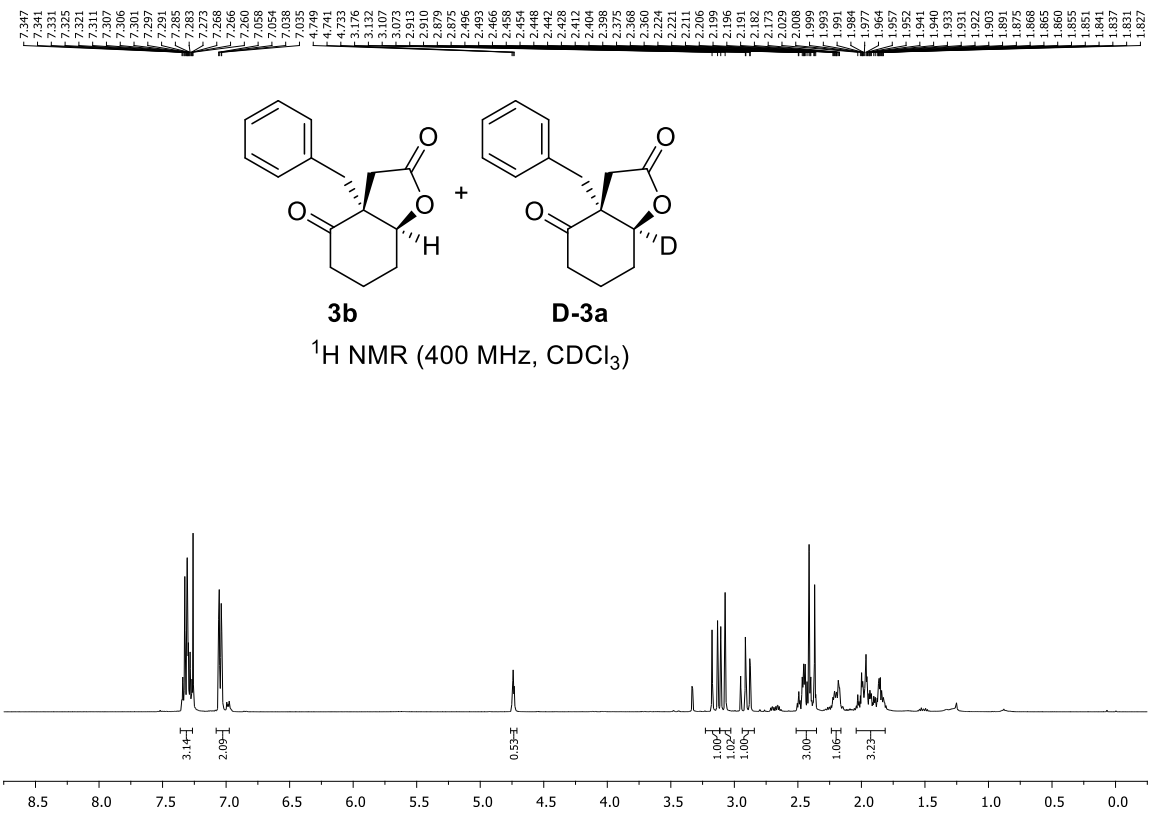
**D-3a**

$^{13}$C NMR (101 MHz, $CDCl_3$)




2b
D-2a
1H NMR (400 MHz, CDCl3)

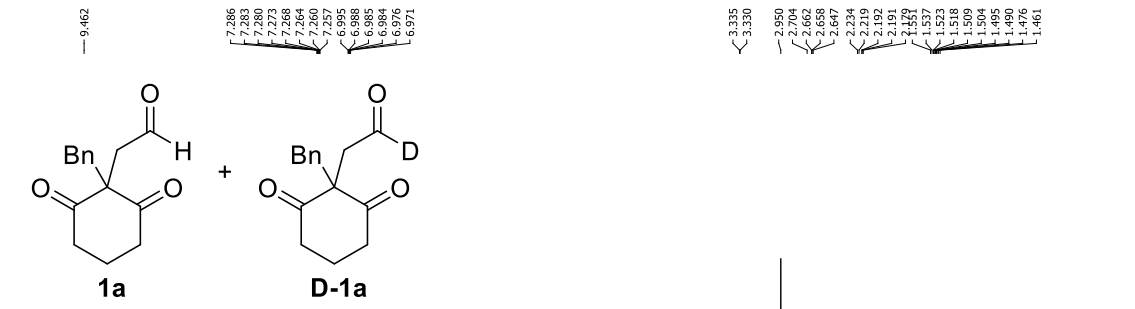

1a
D-1a
1H NMR (400 MHz, CDCl3)
Recovered unreacted 1a and D-1a
KIE experiments: anti-selective reaction



**3b** **D-3a**

$^1$H NMR (400 MHz, $CDCl_3$)



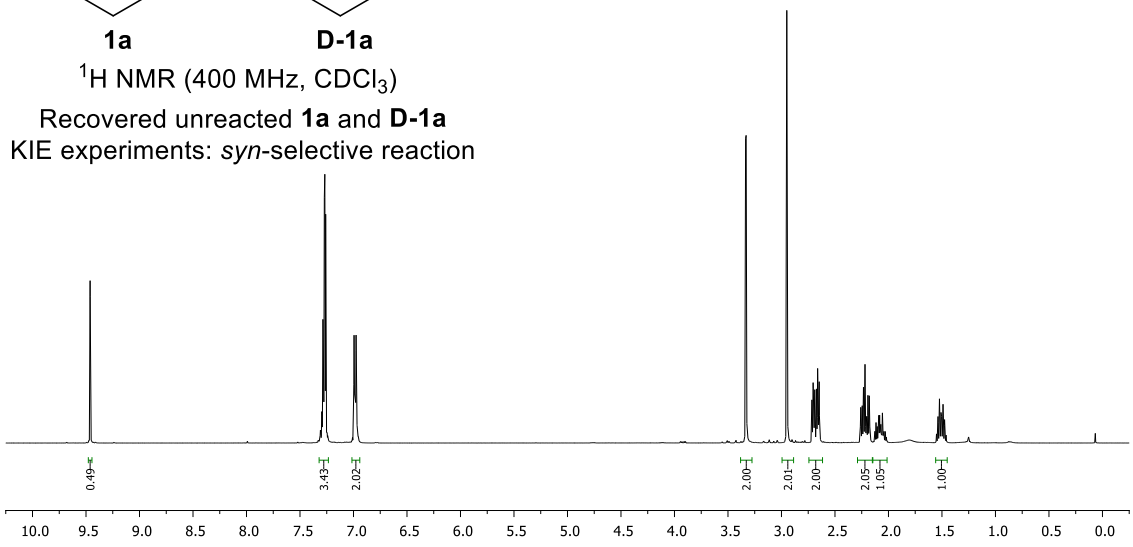


**1a** **D-1a**

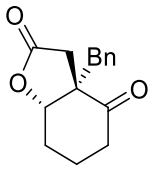
$^1$H NMR (400 MHz, $CDCl_3$)

Recovered unreacted **1a** and **D-1a**

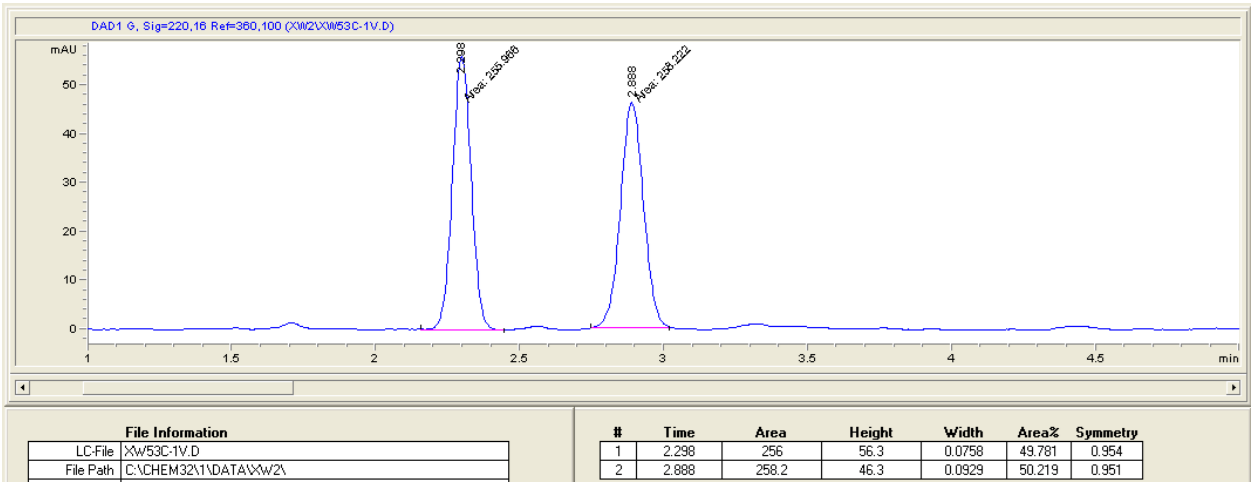
KIE experiments: *syn*-selective reaction



## 14. SFC Spectra

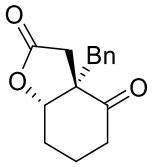



***rac*-2a**

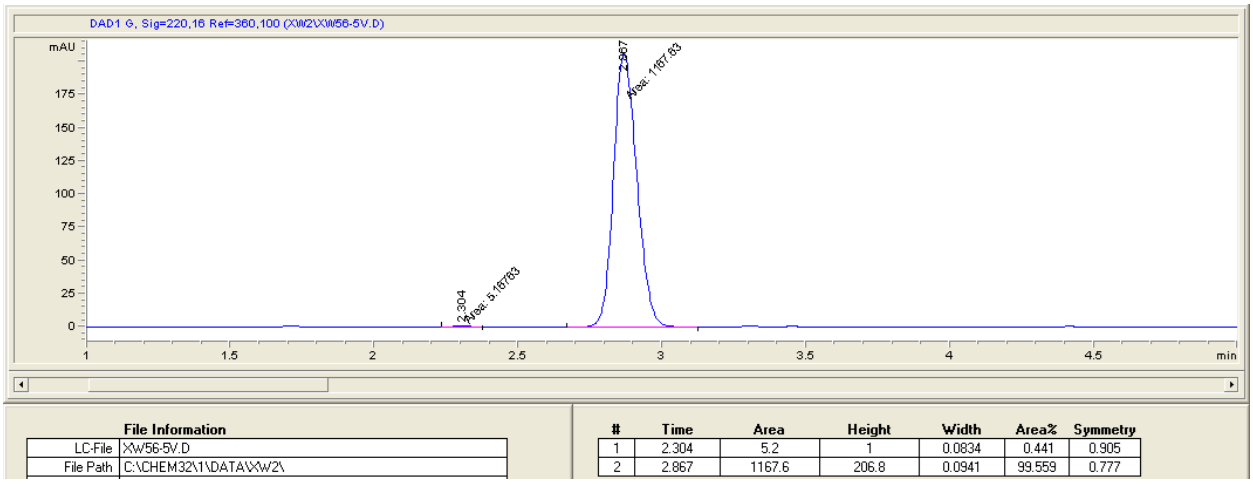



| File Information | |
|---|---|
| LC-File | XW53C-1V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.298 | 256 | 56.3 | 0.0758 | 49.781 | 0.954 |
| 2 | 2.888 | 258.2 | 46.3 | 0.0929 | 50.219 | 0.951 |

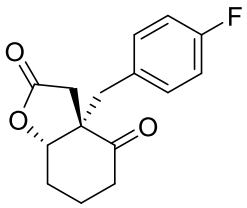



**2a**

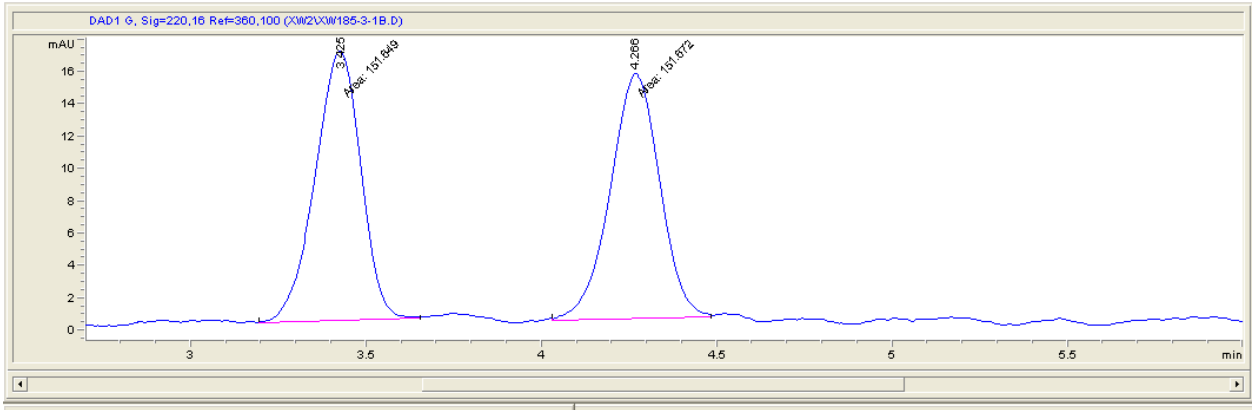



| File Information | |
|---|---|
| LC-File | XW56-5V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.304 | 5.2 | 1 | 0.0834 | 0.441 | 0.905 |
| 2 | 2.867 | 1167.6 | 206.8 | 0.0941 | 99.559 | 0.777 |

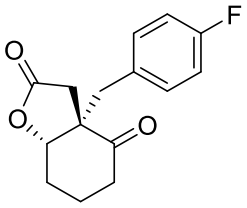


***rac*-2b**

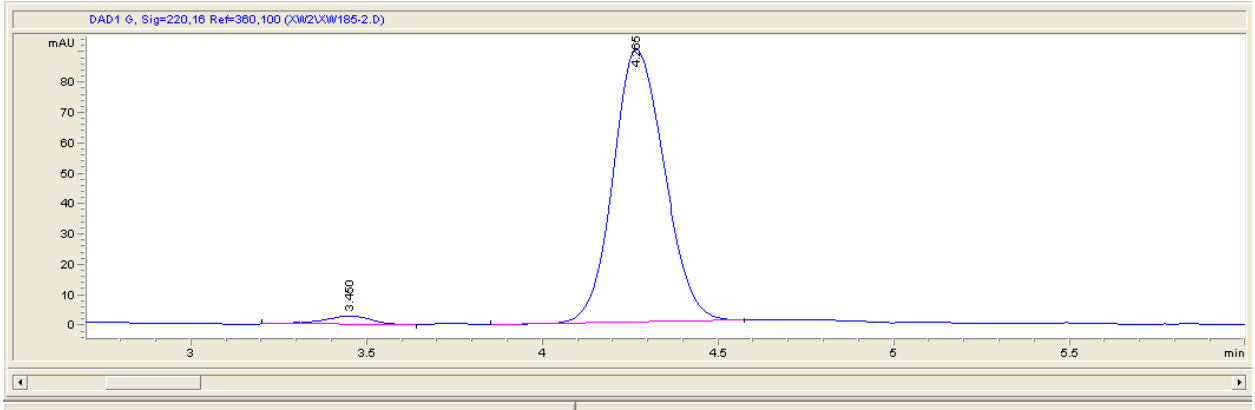



| File Information | |
|---|---|
| LC-File | XW185-3-1B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.425 | 151.6 | 16.7 | 0.1513 | 49.996 | 1.168 |
| 2 | 4.266 | 151.7 | 15.2 | 0.1664 | 50.004 | 1.005 |

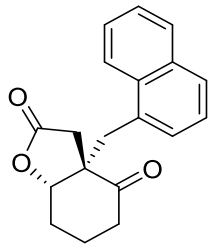


**2b**

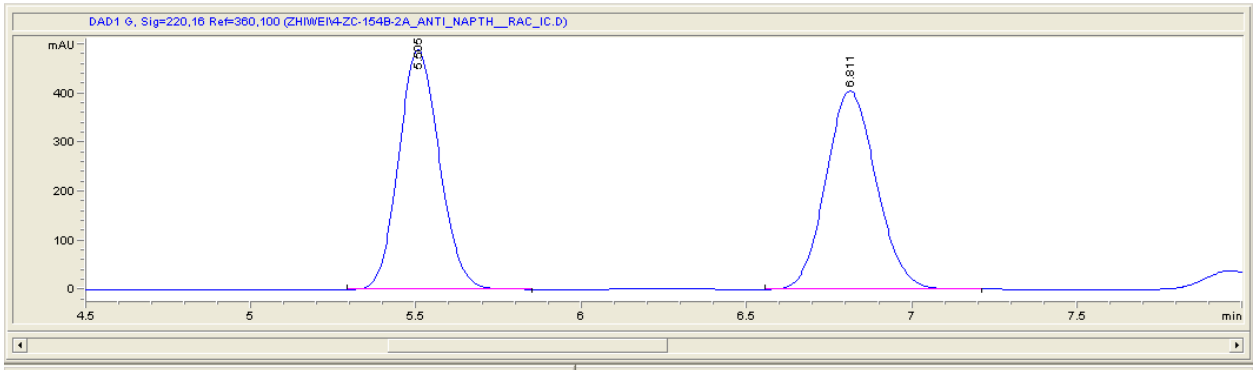



| File Information | |
|---|---|
| LC-File | XW185-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.45 | 29.3 | 2.9 | 0.1293 | 3.107 | 1.422 |
| 2 | 4.265 | 915 | 89.8 | 0.1589 | 96.893 | 0.802 |

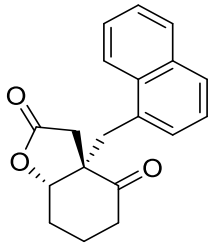


***rac*-2c**

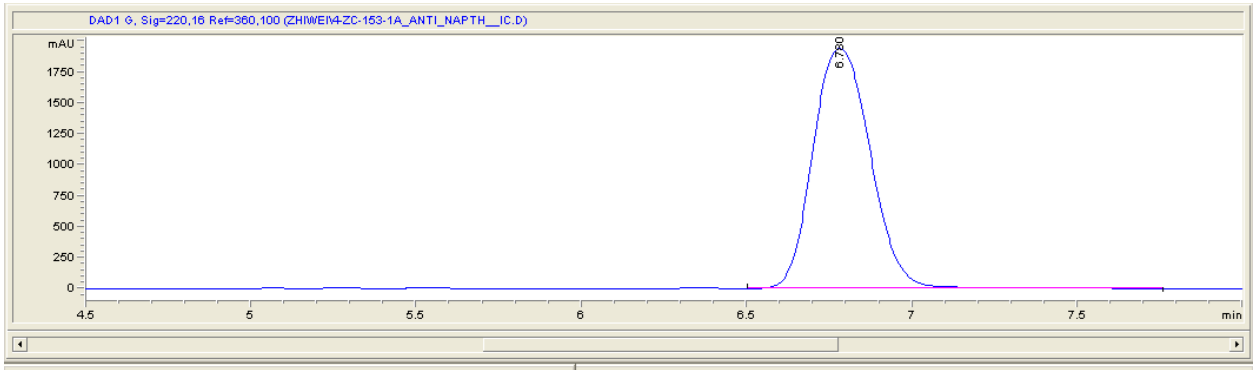



| File Information | |
|---|---|
| LC-File | 4-ZC-154B-2A_ANTI_NAPTH__RAC_IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.505 | 4185.6 | 489.1 | 0.1338 | 49.372 | 0.877 |
| 2 | 6.811 | 4292.1 | 404.8 | 0.1657 | 50.628 | 0.882 |

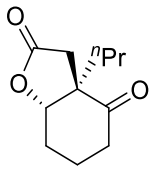


**2c**

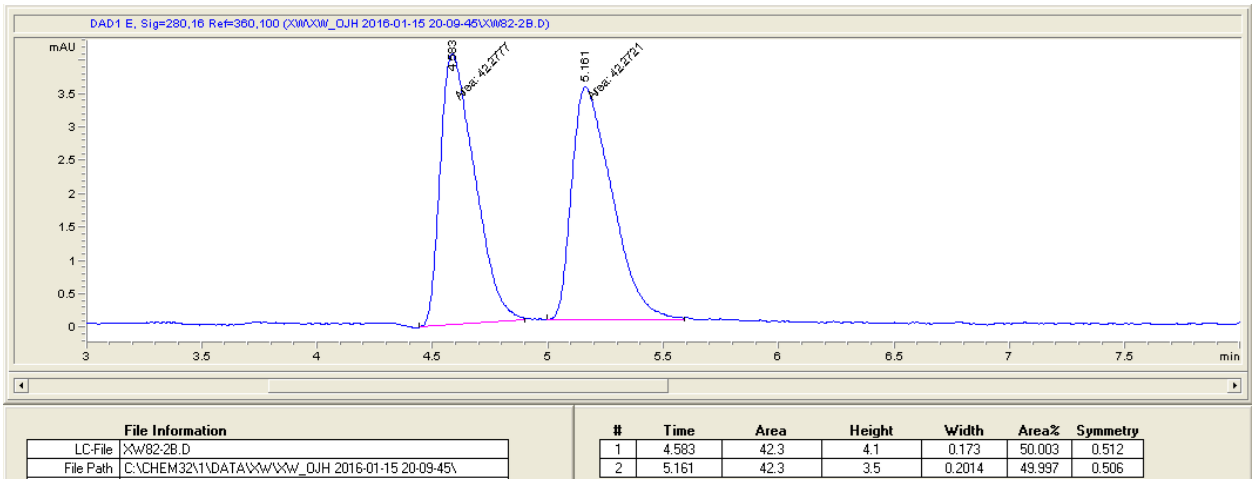



| File Information | |
|---|---|
| LC-File | 4-ZC-153-1A_ANTI_NAPTH__IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.78 | 23499 | 1937.7 | 0.1935 | 100.000 | 0.822 |

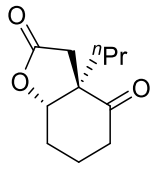



***rac*-2d**

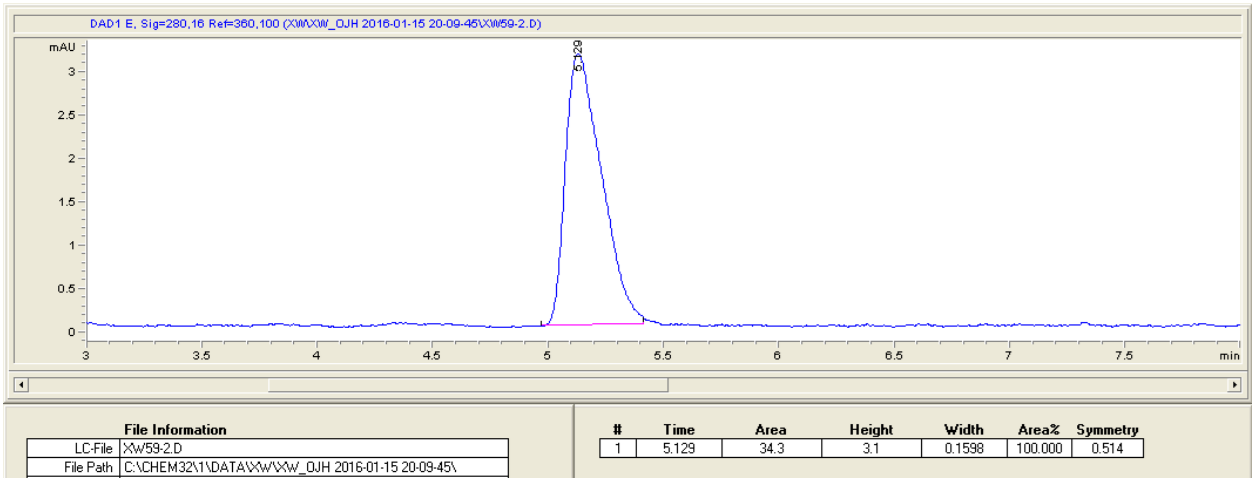



| File Information | |
|---|---|
| LC-File | XW82-2B.D |
| File Path | C:\CHEM32\1\DATA\XW\XW_OJH 2016-01-15 20-09-45\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.583 | 42.3 | 4.1 | 0.173 | 50.003 | 0.512 |
| 2 | 5.161 | 42.3 | 3.5 | 0.2014 | 49.997 | 0.506 |

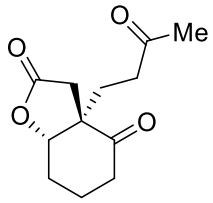



**2d**

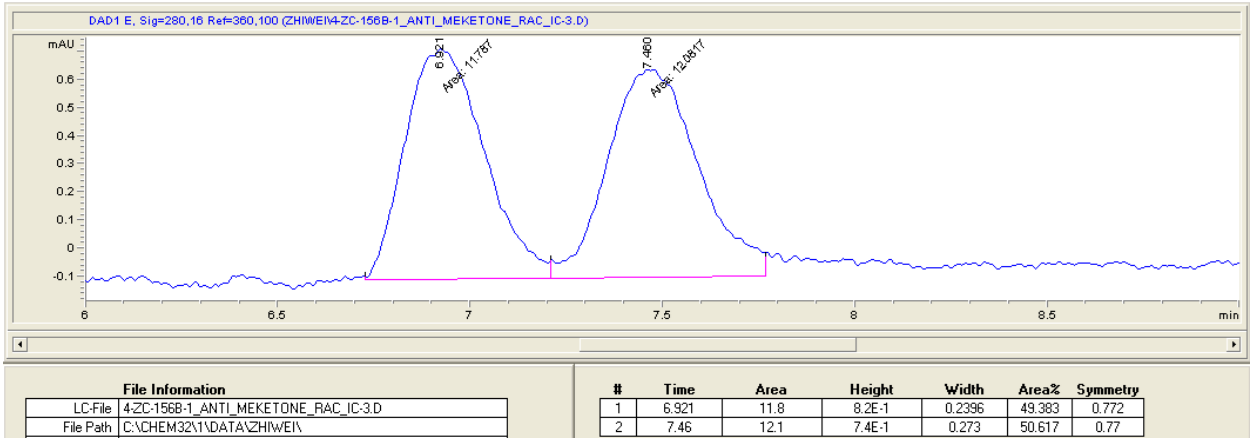



| File Information | |
|---|---|
| LC-File | XW59-2.D |
| File Path | C:\CHEM32\1\DATA\XW\XW_OJH 2016-01-15 20-09-45\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.129 | 34.3 | 3.1 | 0.1598 | 100.000 | 0.514 |

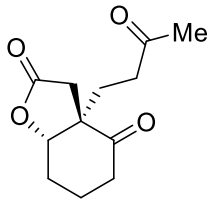


***rac*-2e**

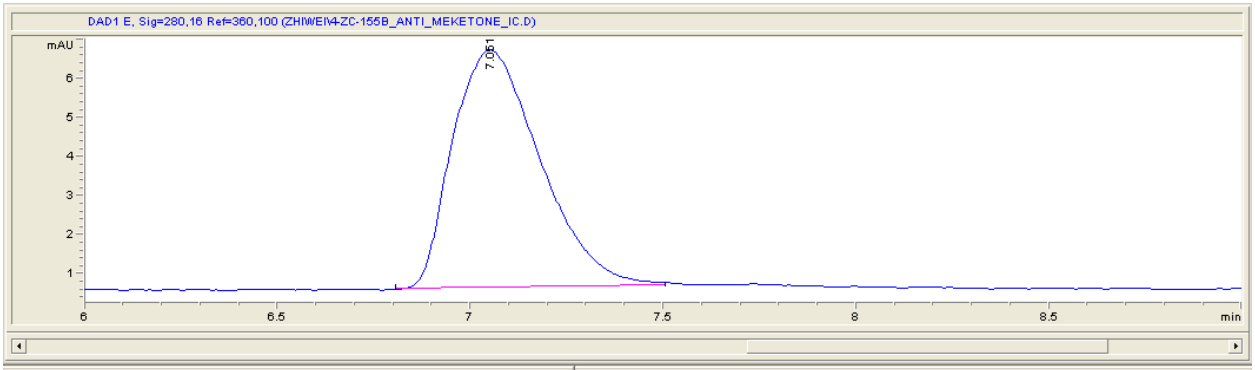



| File Information | |
|---|---|
| LC-File | 4-ZC-156B-1_ANTI_MEKETONE_RAC_IC-3.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.921 | 11.8 | 8.2E-1 | 0.2396 | 49.383 | 0.772 |
| 2 | 7.46 | 12.1 | 7.4E-1 | 0.273 | 50.617 | 0.77 |

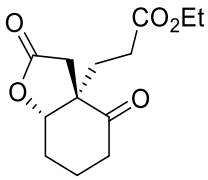


**2e**

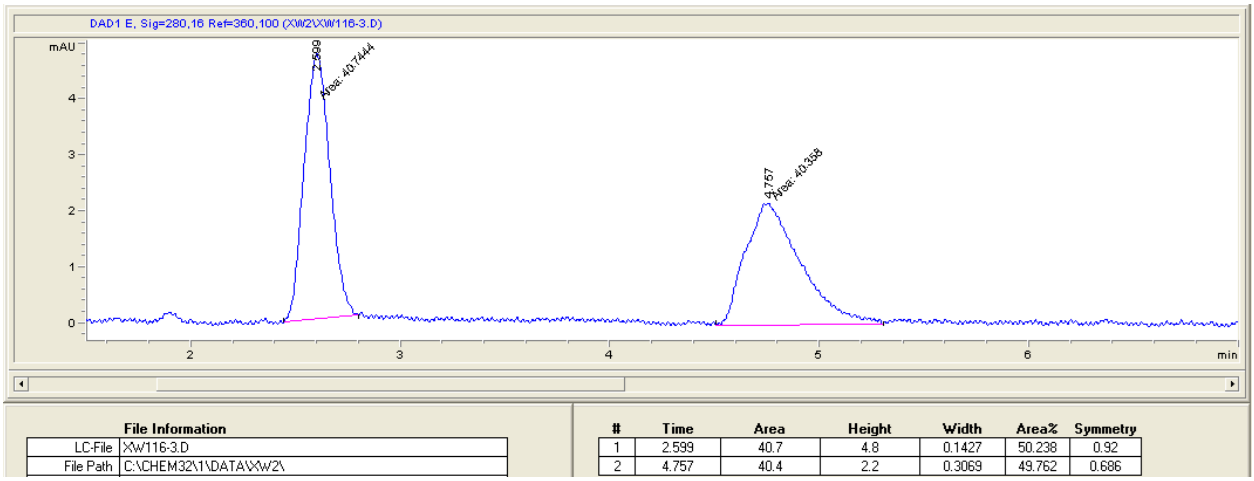



| File Information | |
|---|---|
| LC-File | 4-ZC-155B_ANTI_MEKETONE_IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.051 | 96.2 | 6.1 | 0.2519 | 100.000 | 0.698 |

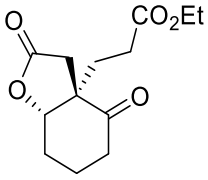


***rac*-2f**

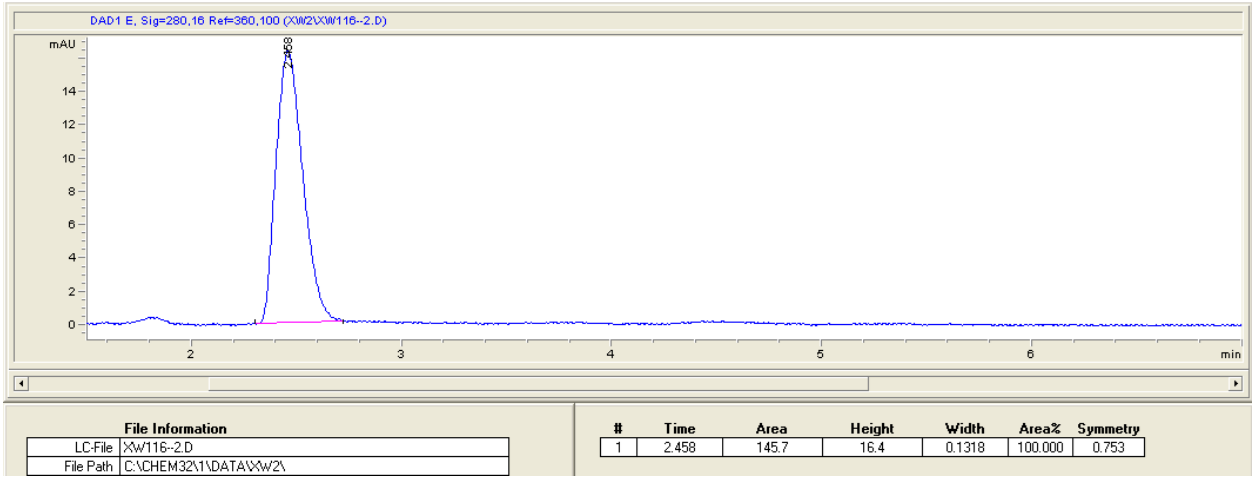



| File Information | |
|---|---|
| LC-File | XW116-3.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.599 | 40.7 | 4.8 | 0.1427 | 50.238 | 0.92 |
| 2 | 4.757 | 40.4 | 2.2 | 0.3069 | 49.762 | 0.686 |

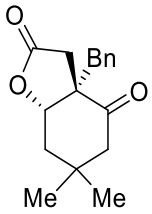


**2f**

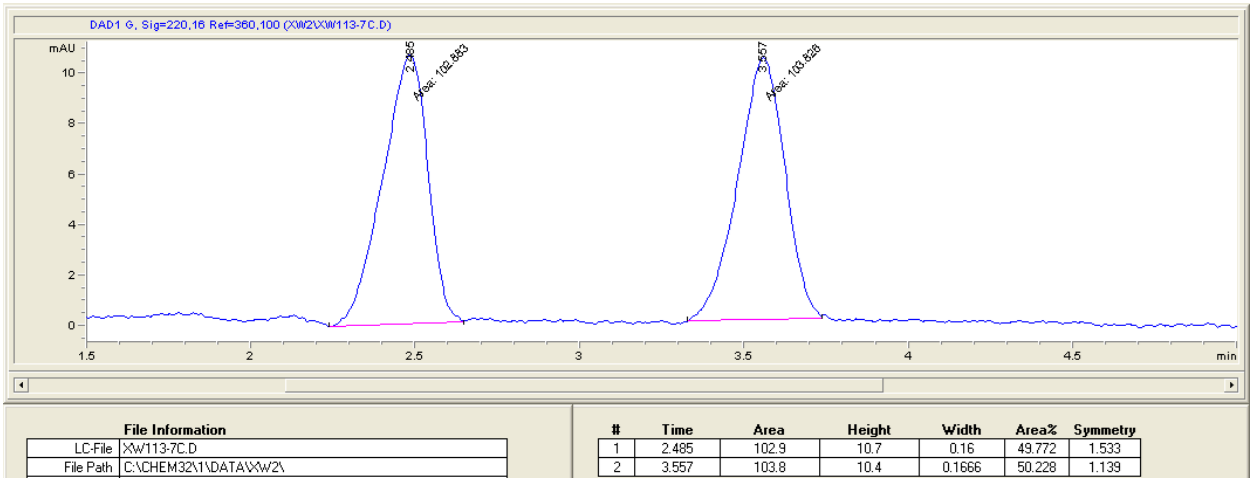



| File Information | |
|---|---|
| LC-File | XW116--2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.458 | 145.7 | 16.4 | 0.1318 | 100.000 | 0.753 |

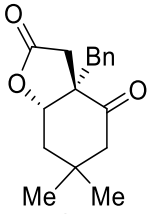



***rac*-2g**

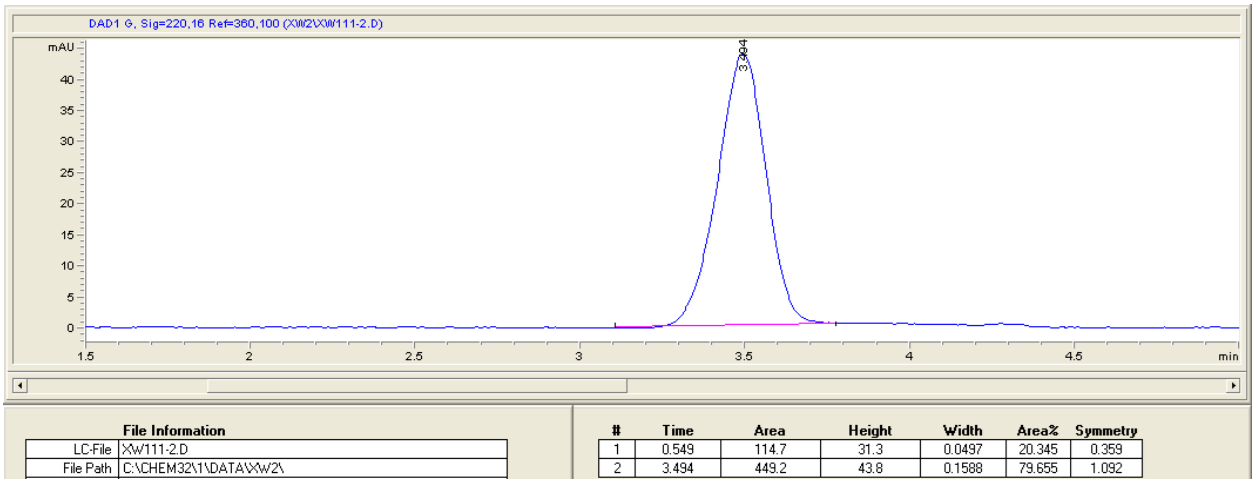



| File Information | |
|---|---|
| LC-File | XW113-7C.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.485 | 102.9 | 10.7 | 0.16 | 49.772 | 1.533 |
| 2 | 3.557 | 103.8 | 10.4 | 0.1666 | 50.228 | 1.139 |

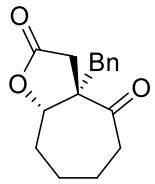



**2g**

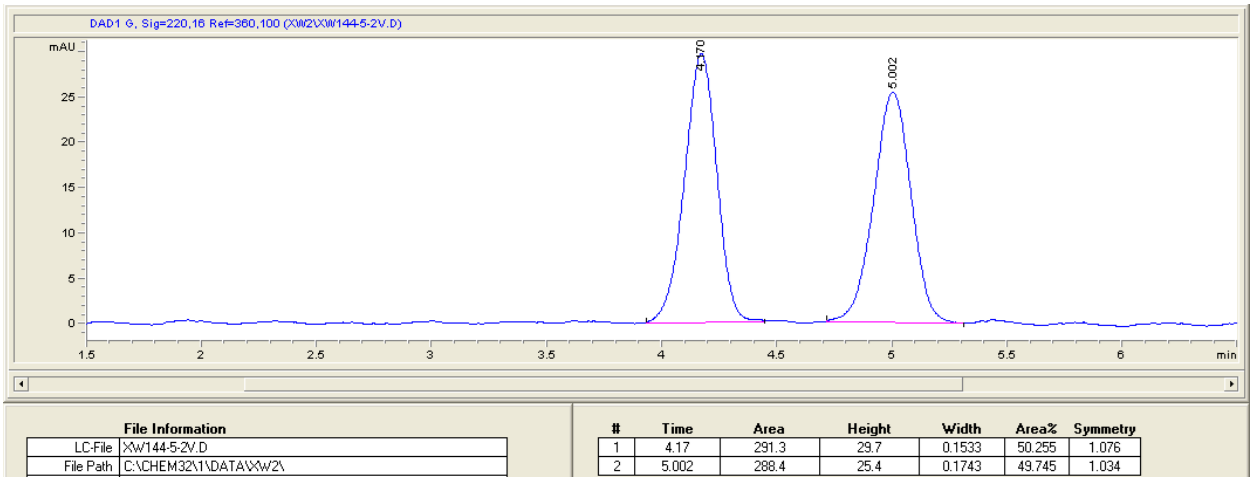



| File Information | |
|---|---|
| LC-File | XW111-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 0.549 | 114.7 | 31.3 | 0.0497 | 20.345 | 0.359 |
| 2 | 3.494 | 449.2 | 43.8 | 0.1588 | 79.655 | 1.092 |

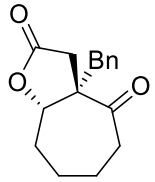



***rac*-2h**

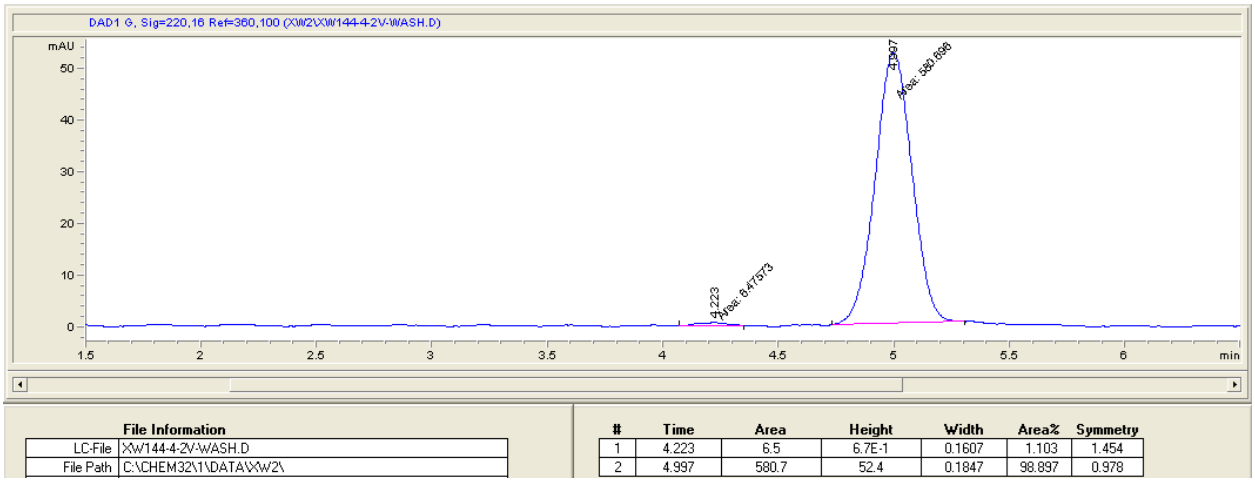



| File Information | |
|---|---|
| LC-File | XW144-5-2V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.17 | 291.3 | 29.7 | 0.1533 | 50.255 | 1.076 |
| 2 | 5.002 | 288.4 | 25.4 | 0.1743 | 49.745 | 1.034 |

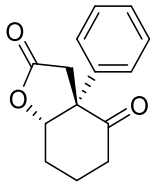



**2h**

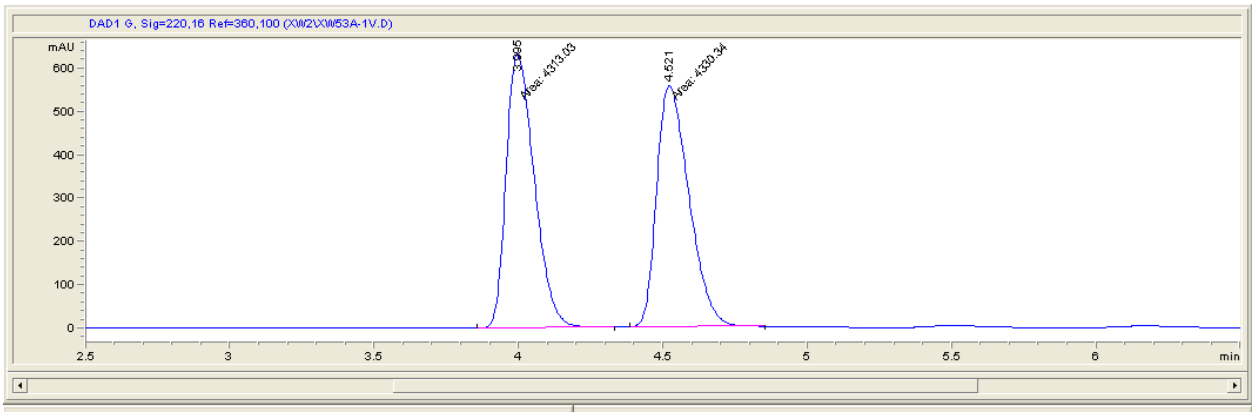



| File Information | |
|---|---|
| LC-File | XW144-4-2V-WASH.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.223 | 6.5 | 6.7E-1 | 0.1607 | 1.103 | 1.454 |
| 2 | 4.997 | 580.7 | 52.4 | 0.1847 | 98.897 | 0.978 |

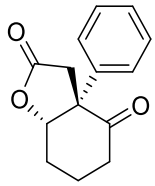


***rac*-2i**

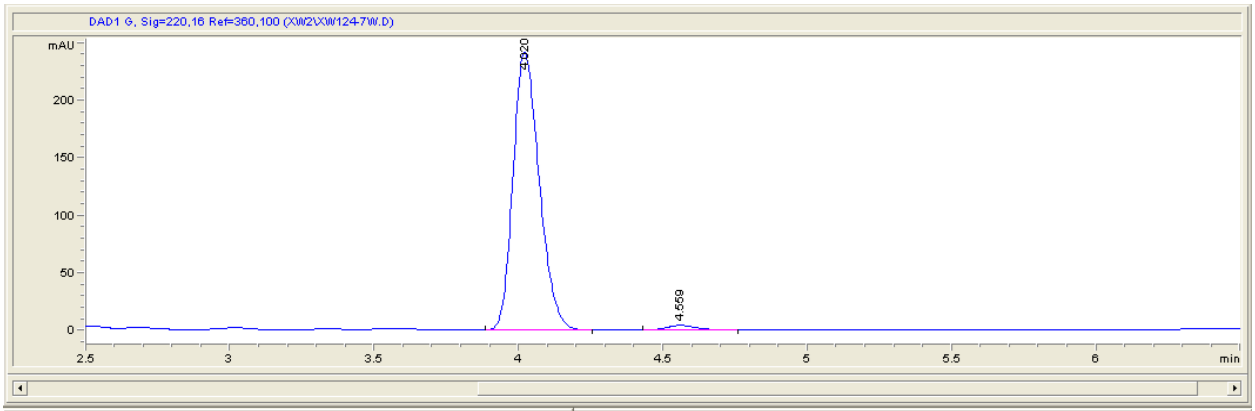



| File Information | |
|---|---|
| LC-File | XW53A-1V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.995 | 4313 | 633.7 | 0.1134 | 49.900 | 0.648 |
| 2 | 4.521 | 4330.3 | 556 | 0.1298 | 50.100 | 0.619 |

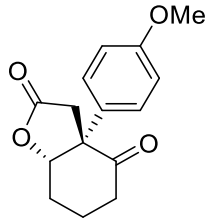


**2i**

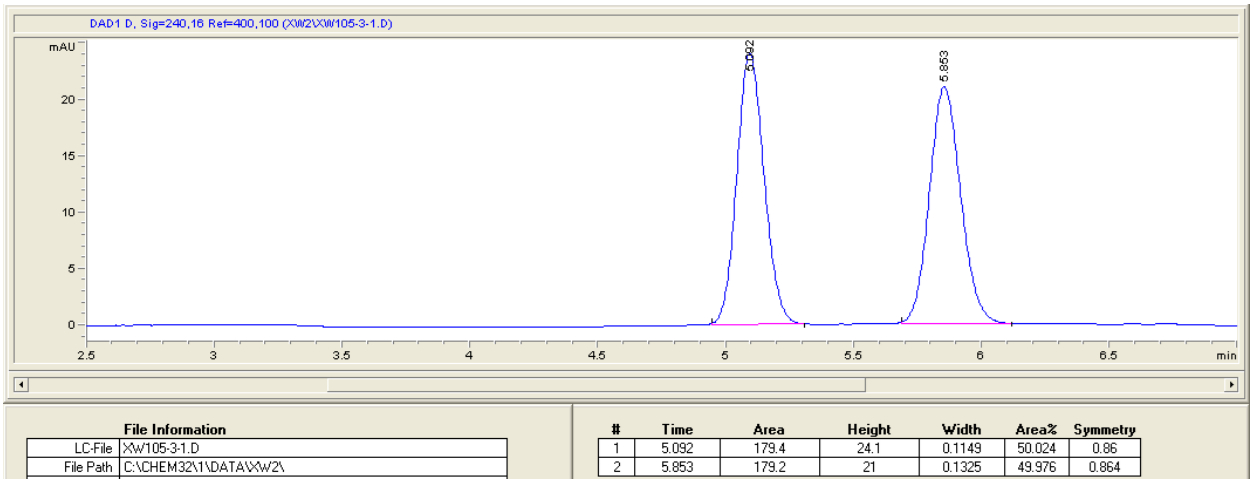



| File Information | |
|---|---|
| LC-File | XW124-7W.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.02 | 1524.5 | 241.8 | 0.0975 | 98.203 | 0.744 |
| 2 | 4.559 | 27.9 | 3.9 | 0.1088 | 1.797 | 0.78 |

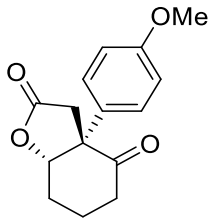



***rac*-2j**

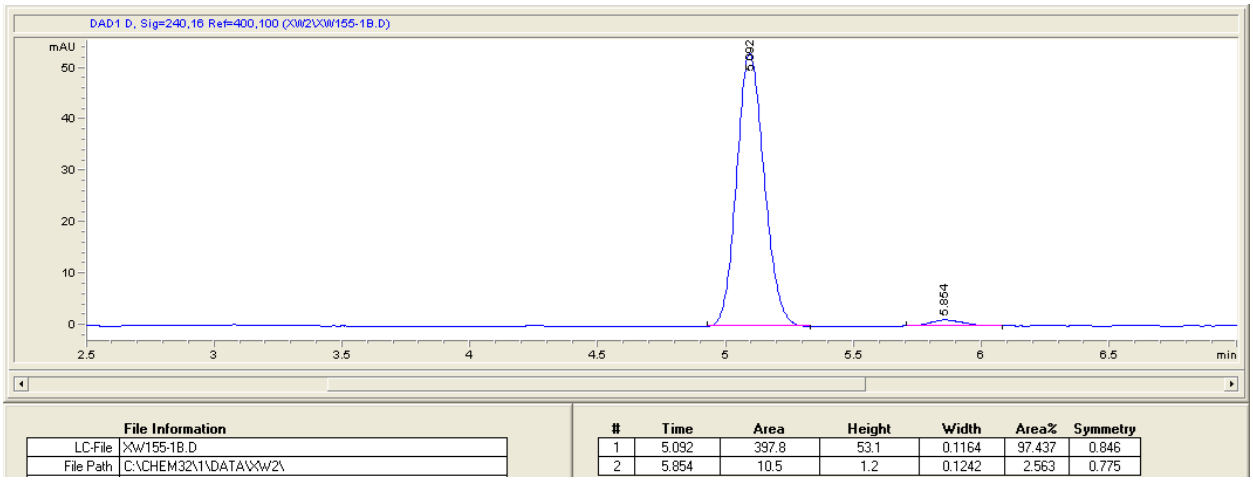



| File Information | |
|---|---|
| LC-File | XW105-3-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.092 | 179.4 | 24.1 | 0.1149 | 50.024 | 0.86 |
| 2 | 5.853 | 179.2 | 21 | 0.1325 | 49.976 | 0.864 |

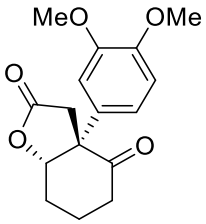



**2j**

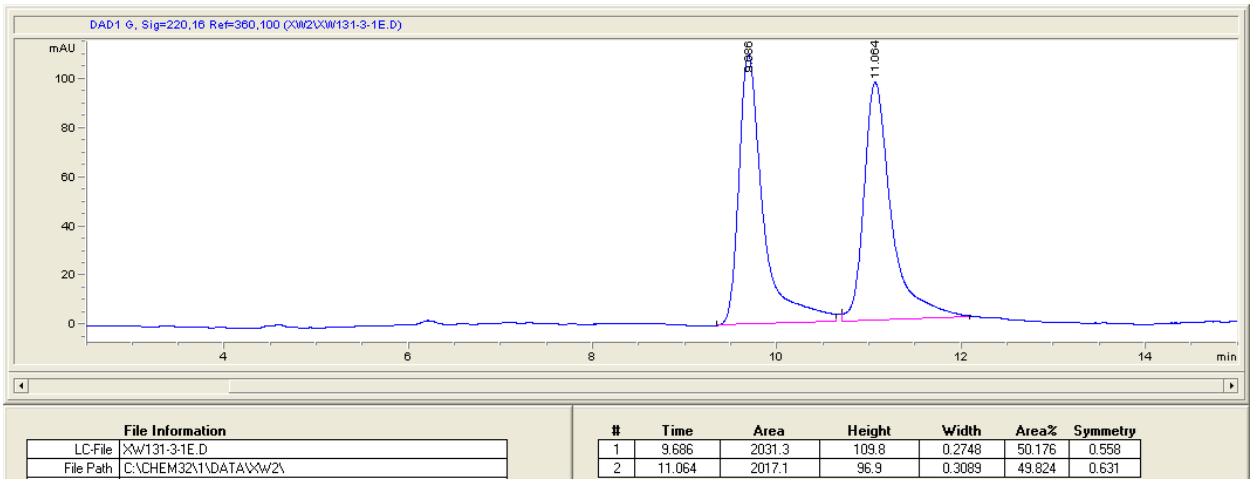



| File Information | |
|---|---|
| LC-File | XW155-1B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.092 | 397.8 | 53.1 | 0.1164 | 97.437 | 0.846 |
| 2 | 5.854 | 10.5 | 1.2 | 0.1242 | 2.563 | 0.775 |

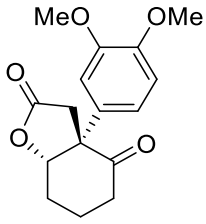



***rac*-2k**

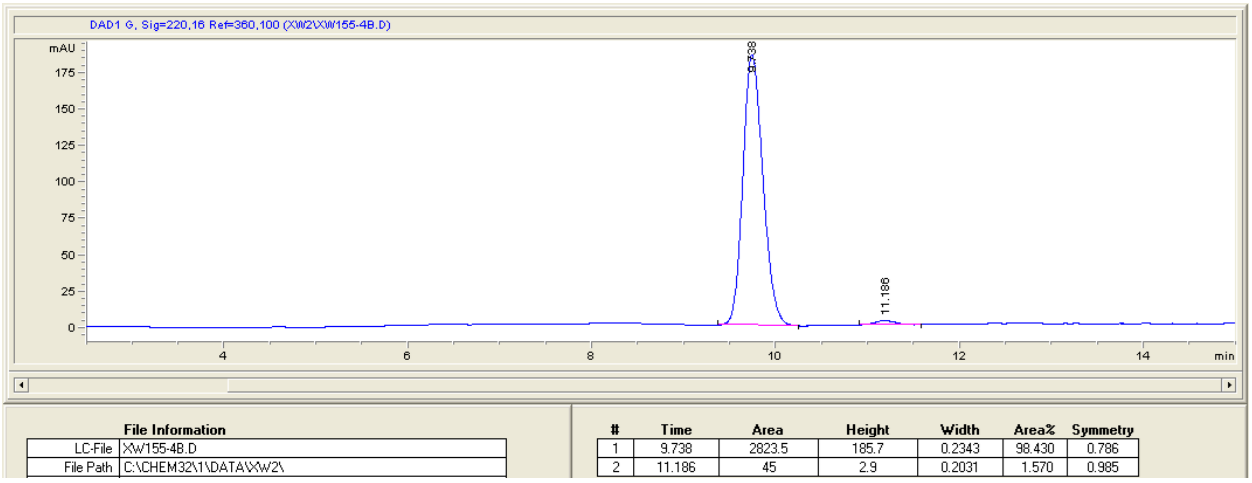



| File Information | |
|---|---|
| LC-File | XW131-3-1E.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.686 | 2031.3 | 109.8 | 0.2748 | 50.176 | 0.558 |
| 2 | 11.064 | 2017.1 | 96.9 | 0.3089 | 49.824 | 0.631 |

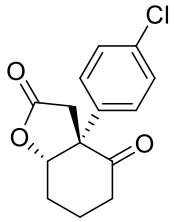



**2k**

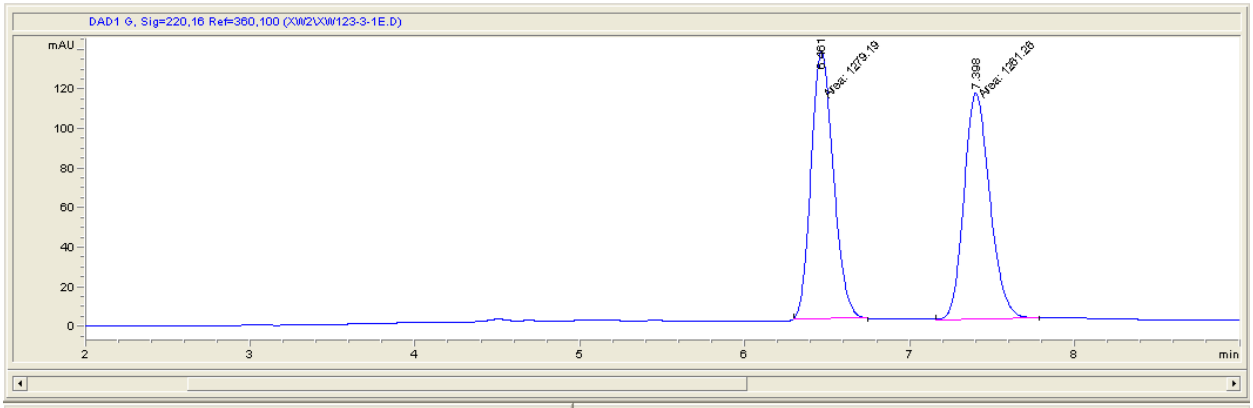



| File Information | |
|---|---|
| LC-File | XW155-4B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.738 | 2823.5 | 185.7 | 0.2343 | 98.430 | 0.786 |
| 2 | 11.186 | 45 | 2.9 | 0.2031 | 1.570 | 0.985 |

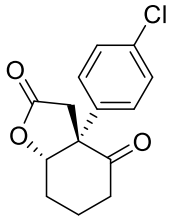


***rac*-2l**

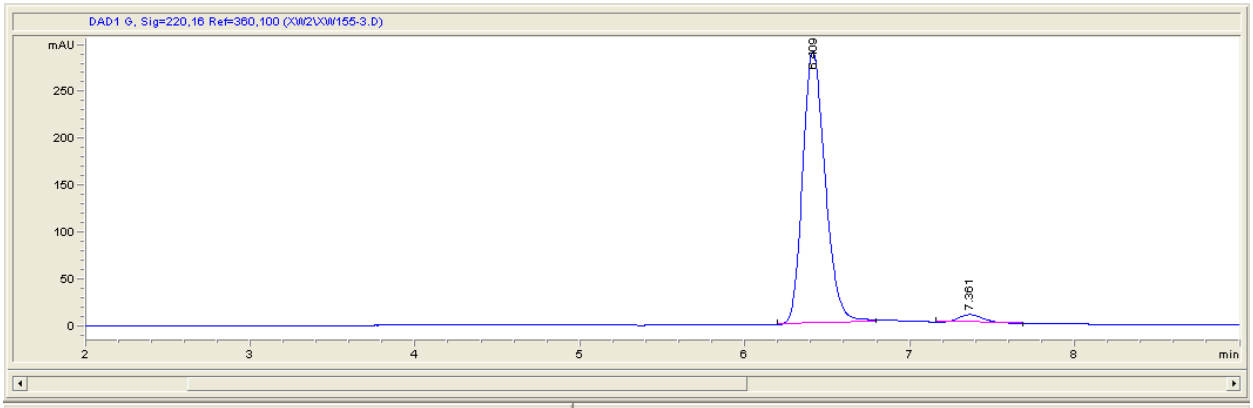



| File Information | |
|---|---|
| LC-File | XW123-3-1E.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.461 | 1279.2 | 135.5 | 0.1573 | 50.353 | 0.819 |
| 2 | 7.398 | 1261.3 | 114.7 | 0.1833 | 49.647 | 0.813 |

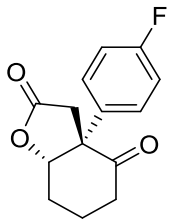


**2l**

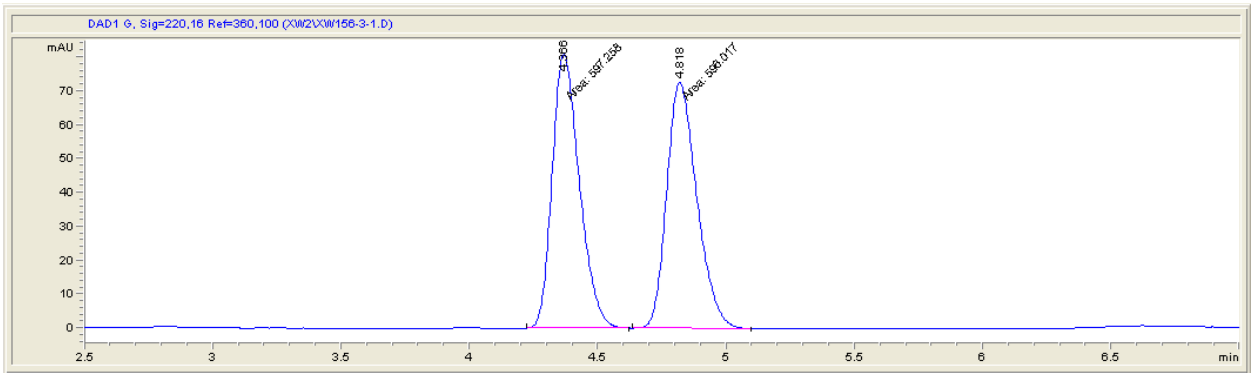



| File Information | |
|---|---|
| LC-File | XW155-3.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.409 | 2767.5 | 290.3 | 0.1472 | 96.860 | 0.76 |
| 2 | 7.361 | 89.7 | 8.5 | 0.1675 | 3.140 | 0.792 |

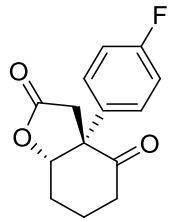


***rac*-2m**

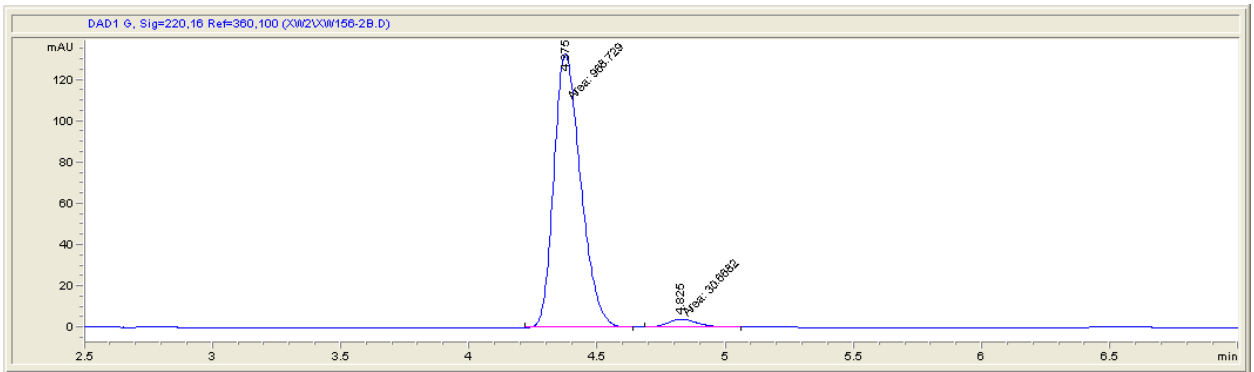



| File Information | |
|---|---|
| LC-File | XW156-3-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.366 | 597.3 | 81 | 0.123 | 50.052 | 0.727 |
| 2 | 4.818 | 596 | 72.6 | 0.1369 | 49.948 | 0.734 |

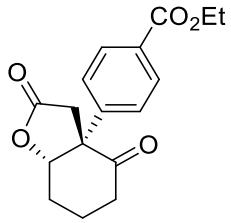


**2m**

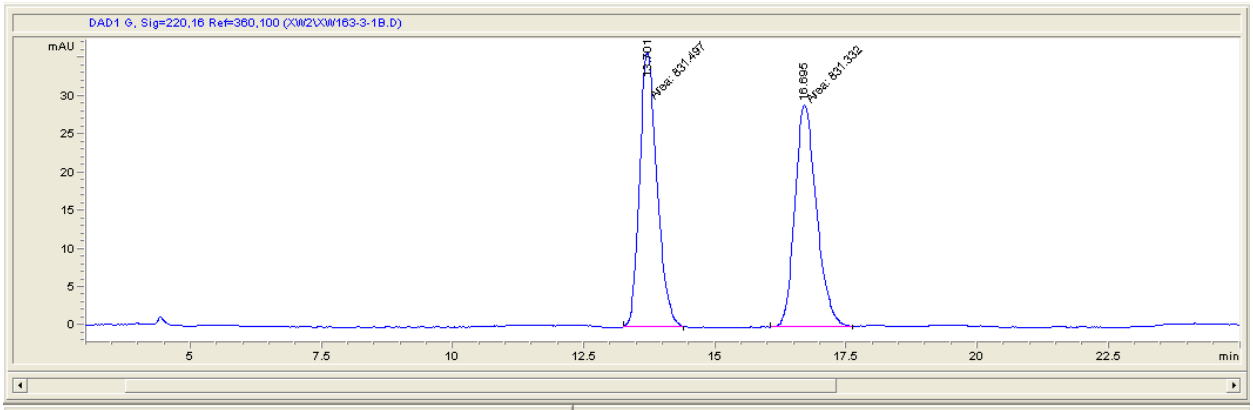



| File Information | |
|---|---|
| LC-File | XW156-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.375 | 968.7 | 132.9 | 0.1215 | 96.931 | 0.727 |
| 2 | 4.825 | 30.7 | 3.9 | 0.131 | 3.069 | 0.76 |

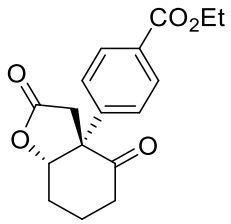


***rac*-2n**

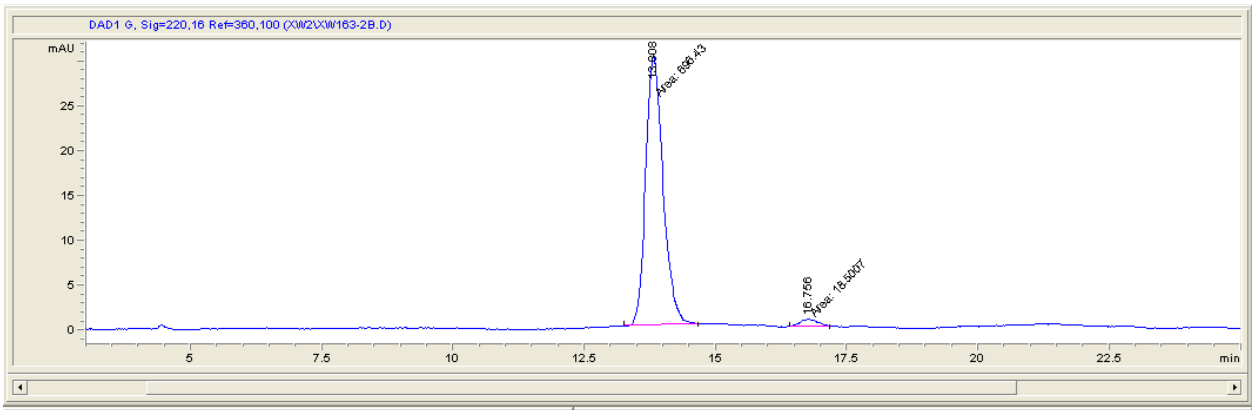



| File Information | |
|---|---|
| LC-File | XW163-3-1B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.701 | 831.5 | 35.9 | 0.3865 | 50.005 | 0.763 |
| 2 | 16.695 | 831.3 | 29 | 0.4781 | 49.995 | 0.758 |

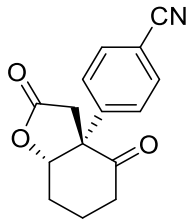


**2n**

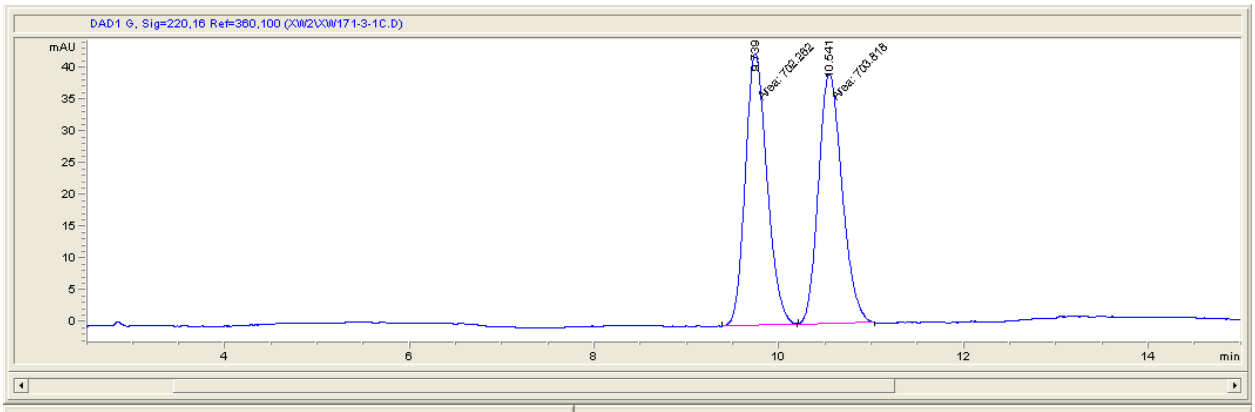



| File Information | |
|---|---|
| LC-File | XW163-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.808 | 696.4 | 30.1 | 0.385 | 97.412 | 0.762 |
| 2 | 16.756 | 18.5 | 7.8E-1 | 0.3972 | 2.588 | 0.882 |

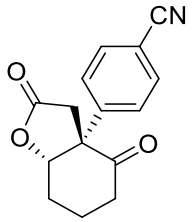



***rac*-2o**

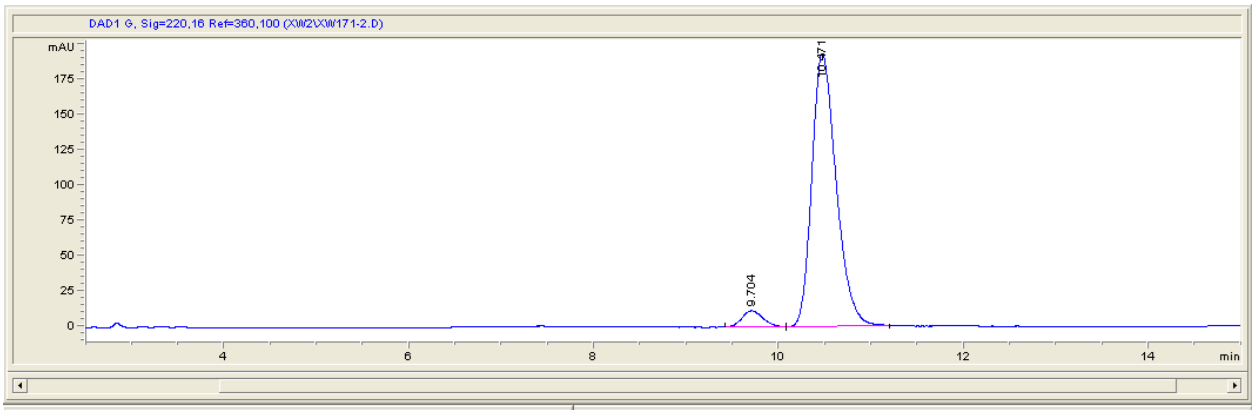



| File Information | |
|---|---|
| LC-File | XW171-3-1C.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.739 | 702.3 | 42.8 | 0.2733 | 49.945 | 0.803 |
| 2 | 10.541 | 703.8 | 39.4 | 0.2979 | 50.055 | 0.807 |

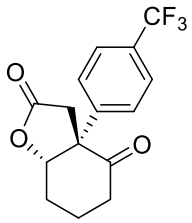



**2o**

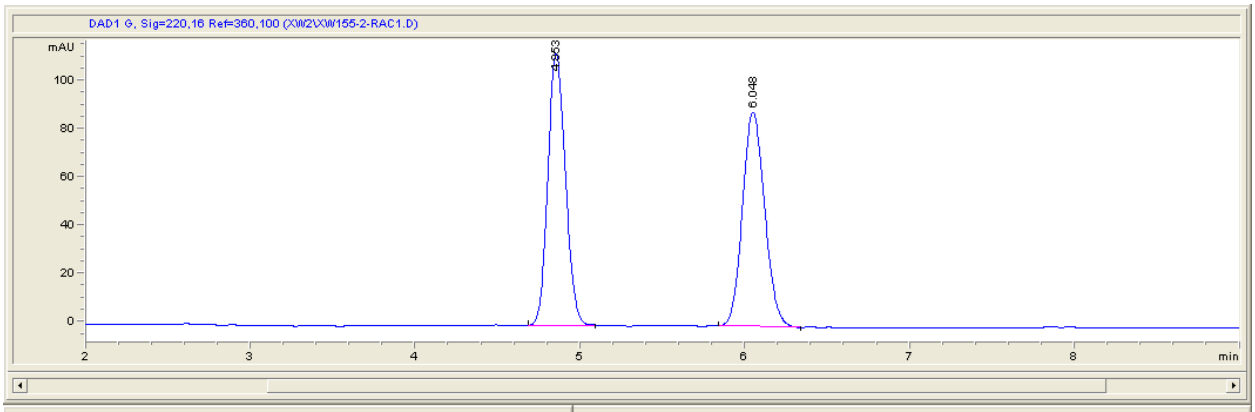



| File Information | |
|---|---|
| LC-File | XW171-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.704 | 181.3 | 11.5 | 0.2394 | 4.869 | 0.807 |
| 2 | 10.471 | 3542.4 | 193.2 | 0.2789 | 95.131 | 0.715 |

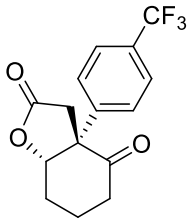


***rac*-2p**

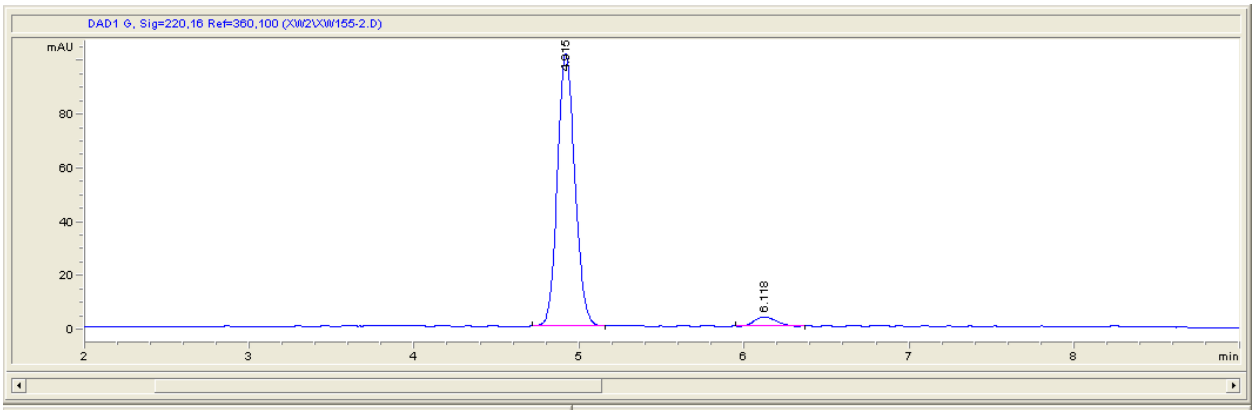



| File Information | |
|---|---|
| LC-File | XW155-2-RAC1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.853 | 837.5 | 112.9 | 0.1156 | 50.041 | 0.842 |
| 2 | 6.048 | 836.2 | 89 | 0.1476 | 49.959 | 0.868 |

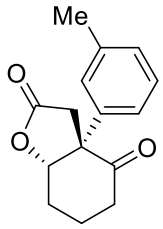


**2p**

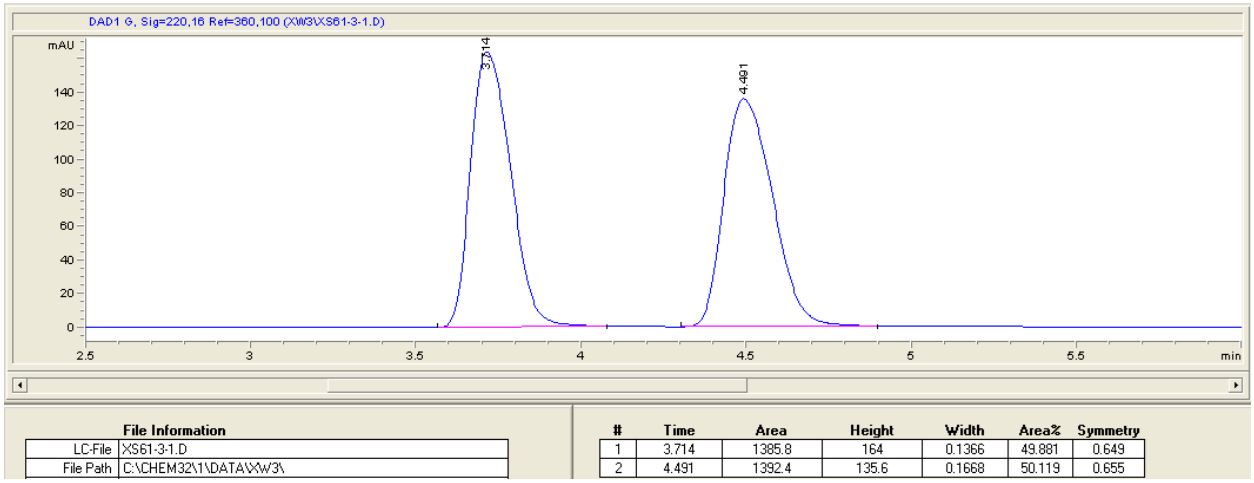



| File Information | |
|---|---|
| LC-File | XW155-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.915 | 747.9 | 101.4 | 0.1151 | 95.986 | 0.856 |
| 2 | 6.118 | 31.3 | 3.4 | 0.1439 | 4.014 | 0.794 |

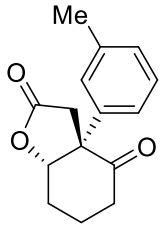



***rac*-2q**

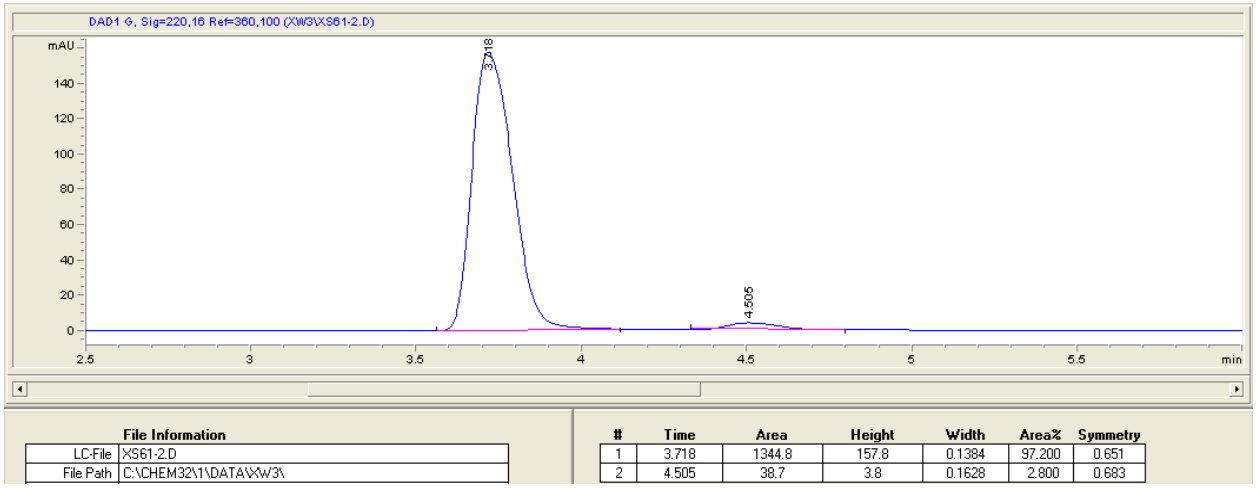



| File Information | |
|---|---|
| LC-File | XS61-3-1.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.714 | 1385.8 | 164 | 0.1366 | 49.881 | 0.649 |
| 2 | 4.491 | 1392.4 | 135.6 | 0.1668 | 50.119 | 0.655 |

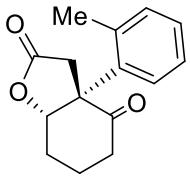



**2q**

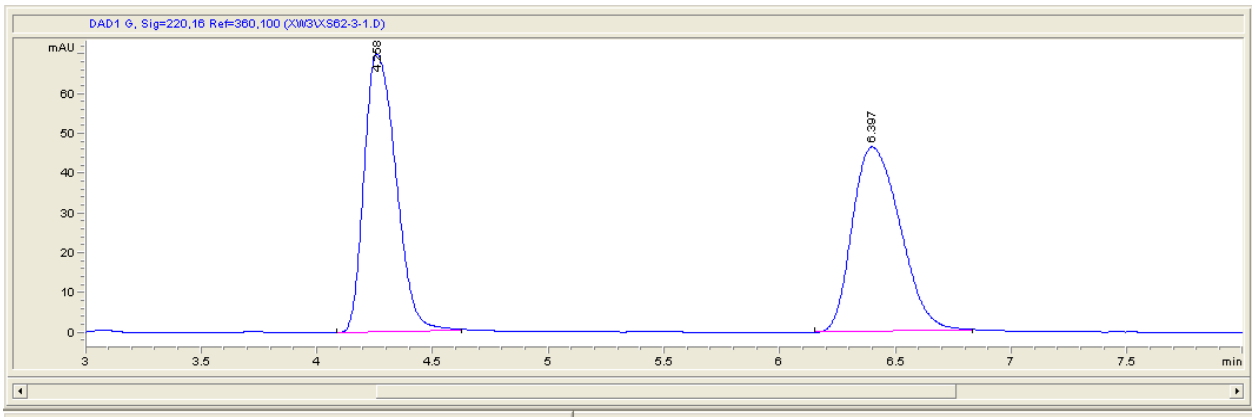



| File Information | |
|---|---|
| LC-File | XS61-2.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.718 | 1344.8 | 157.8 | 0.1384 | 97.200 | 0.651 |
| 2 | 4.505 | 38.7 | 3.8 | 0.1628 | 2.800 | 0.683 |

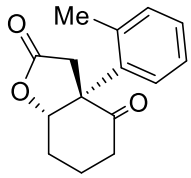



***rac*-2r**

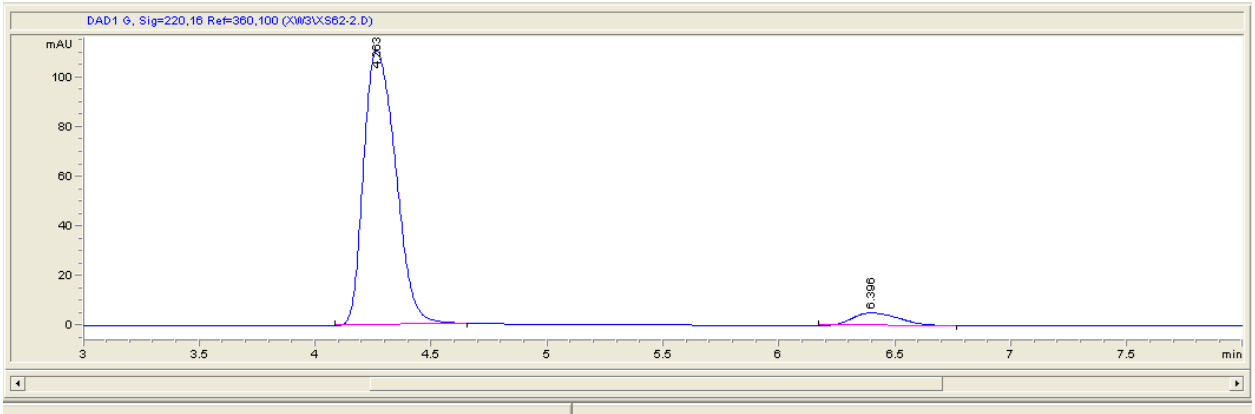



| File Information | |
|---|---|
| LC-File | XS62-3-1.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.258 | 672.4 | 69.9 | 0.1562 | 50.035 | 0.652 |
| 2 | 6.397 | 671.4 | 46.5 | 0.2336 | 49.965 | 0.672 |

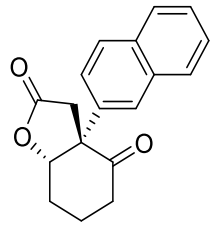



**2r**

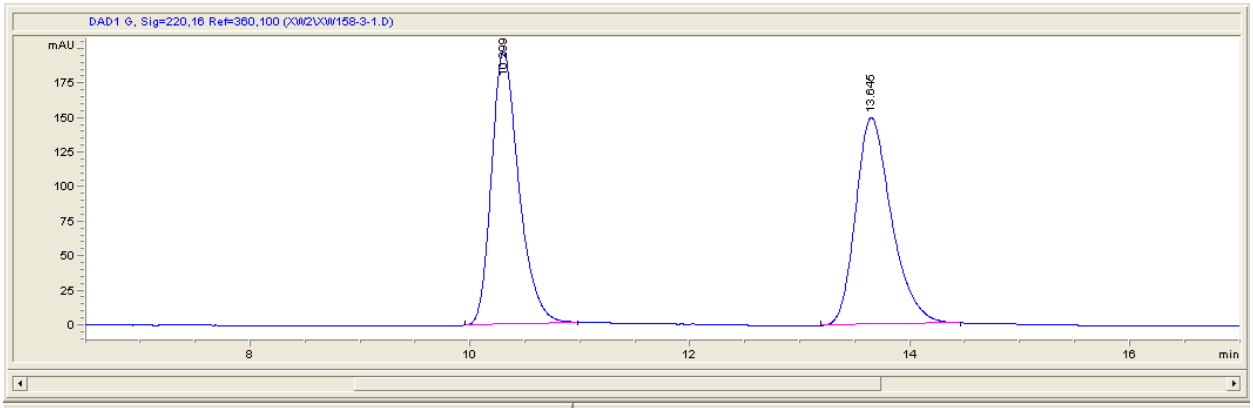



| File Information | |
|---|---|
| LC-File | XS62-2.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.263 | 1063 | 110.5 | 0.1562 | 93.634 | 0.648 |
| 2 | 6.396 | 72.3 | 5.1 | 0.2016 | 6.366 | 0.668 |

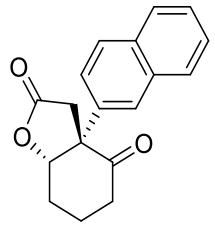


***rac*-2s**

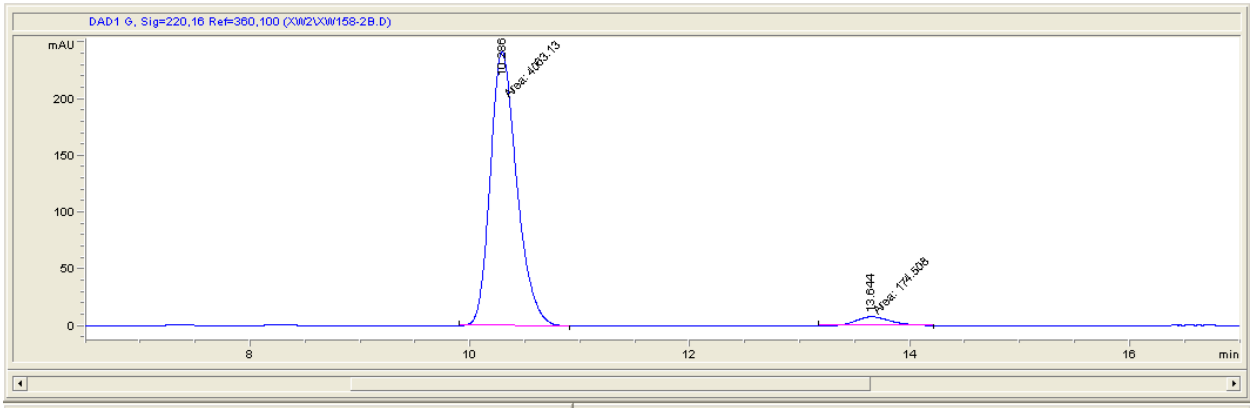



| File Information | |
|---|---|
| LC-File | XW158-3-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.299 | 3426.5 | 197.4 | 0.2645 | 50.060 | 0.72 |
| 2 | 13.645 | 3418.2 | 150 | 0.3469 | 49.940 | 0.716 |

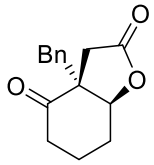


**2s**

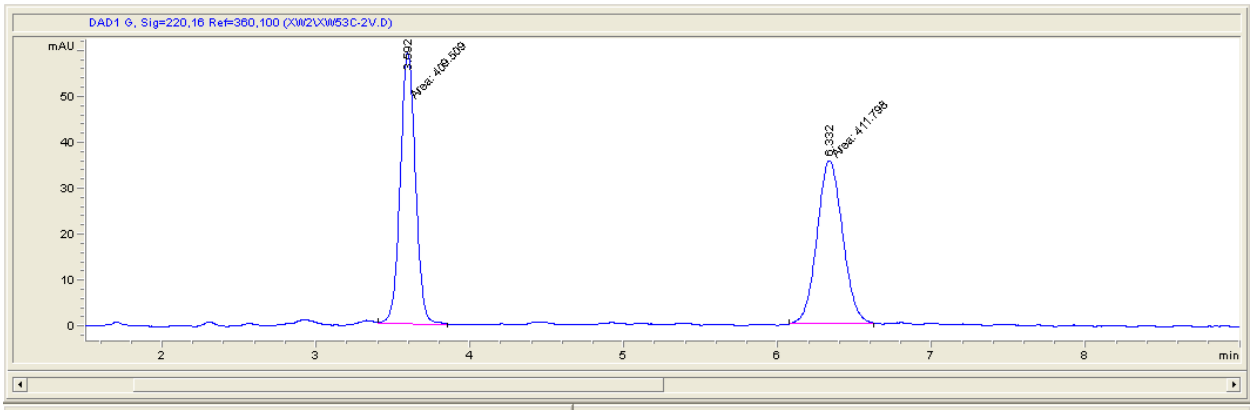



| File Information | |
|---|---|
| LC-File | XW158-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.286 | 4063.1 | 241.6 | 0.2803 | 95.882 | 0.758 |
| 2 | 13.644 | 174.5 | 7.8 | 0.3721 | 4.118 | 0.784 |

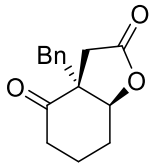



***rac*-3a**

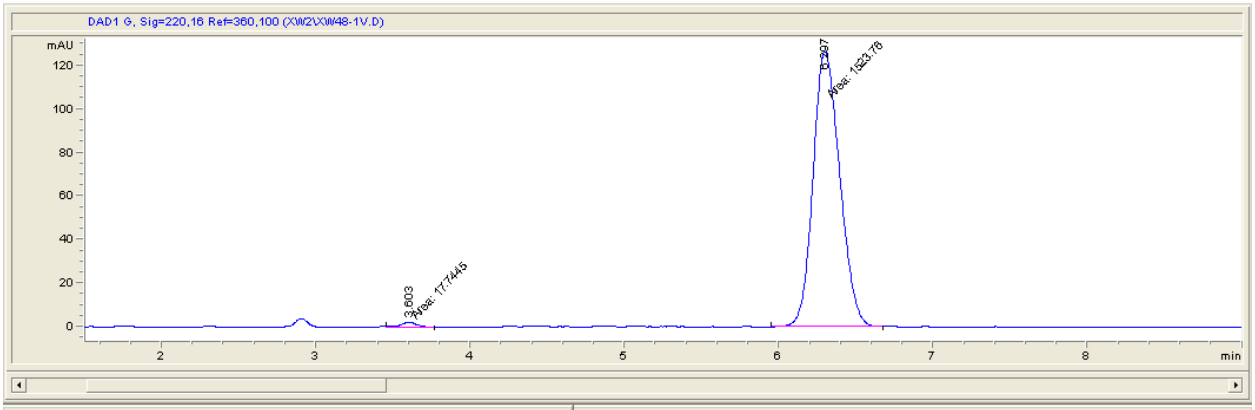



| File Information | |
|---|---|
| LC-File | XW53C-2V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.592 | 409.5 | 59.2 | 0.1152 | 49.861 | 0.925 |
| 2 | 6.332 | 411.8 | 35.6 | 0.193 | 50.139 | 0.909 |

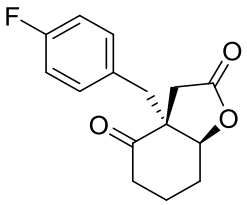



**3a**

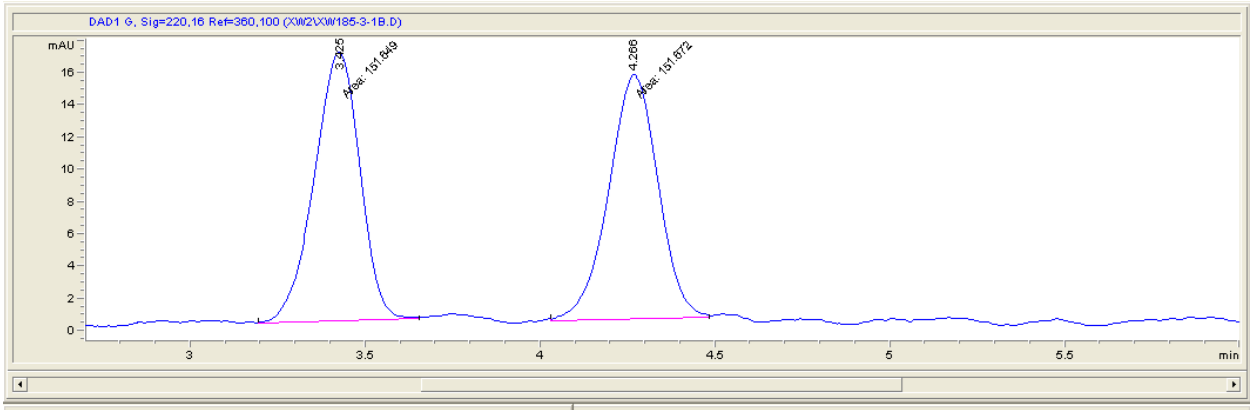



| File Information | |
|---|---|
| LC-File | XW48-1V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.603 | 17.7 | 2.3 | 0.1285 | 1.151 | 1.096 |
| 2 | 6.297 | 1523.8 | 126.4 | 0.201 | 98.849 | 0.782 |

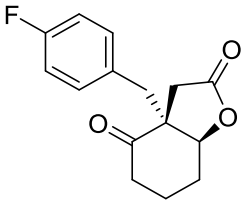


***rac*-3b**

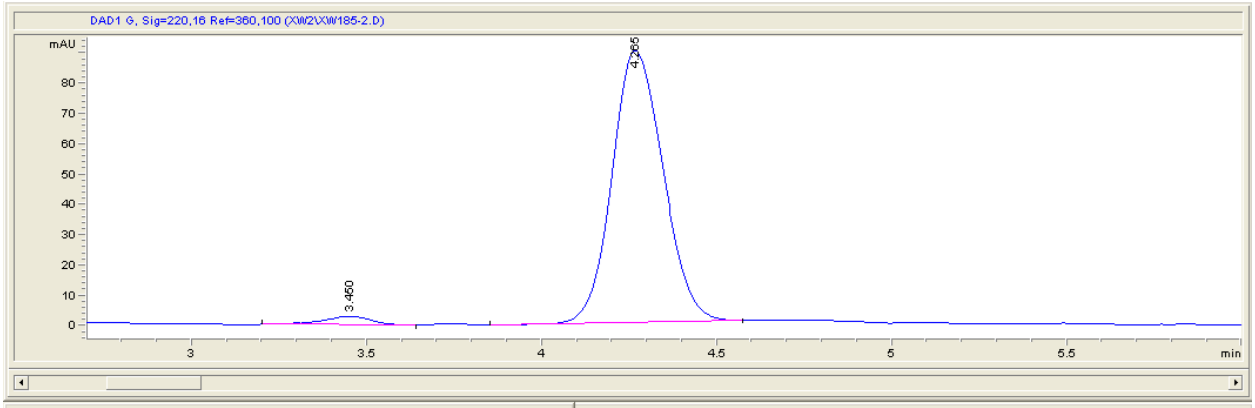



| File Information | |
|---|---|
| LC-File | XW185-3-1B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.425 | 151.6 | 16.7 | 0.1513 | 49.996 | 1.168 |
| 2 | 4.266 | 151.7 | 15.2 | 0.1664 | 50.004 | 1.005 |

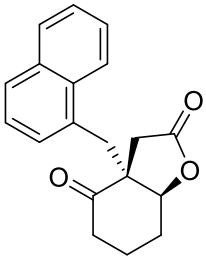


**3b**

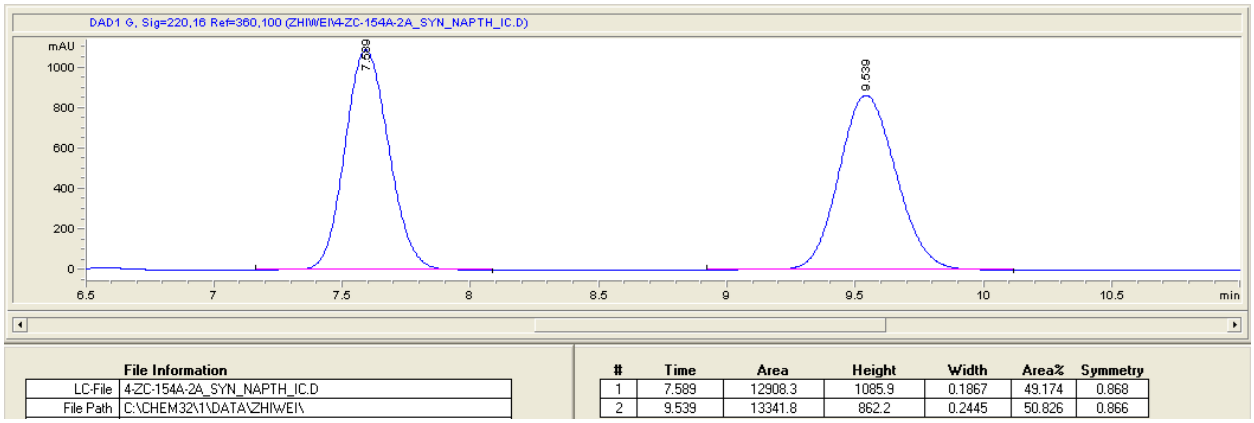



| File Information | |
|---|---|
| LC-File | XW185-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.45 | 29.3 | 2.9 | 0.1293 | 3.107 | 1.422 |
| 2 | 4.265 | 915 | 89.8 | 0.1589 | 96.893 | 0.802 |

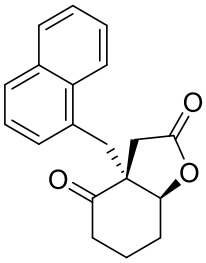


***rac*-3c**

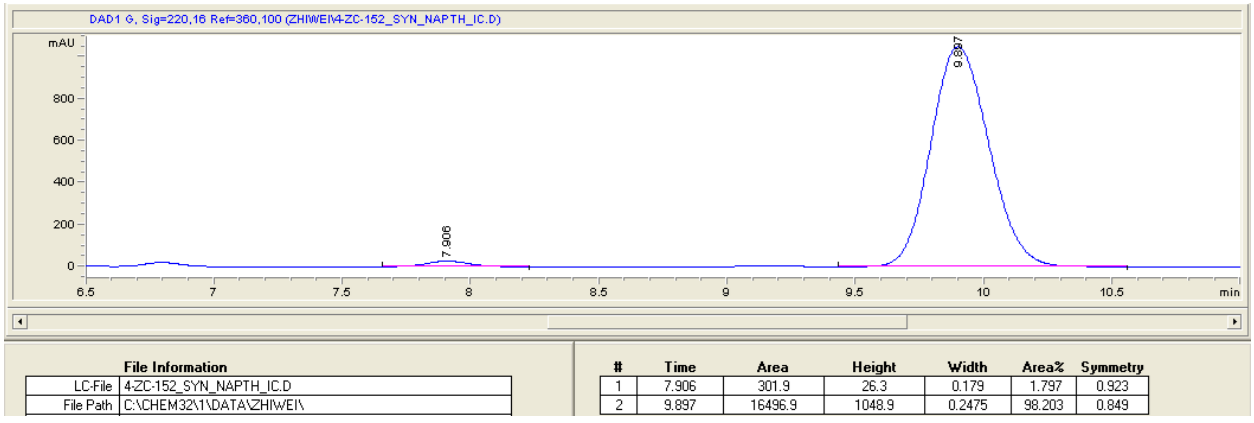



| File Information | |
|---|---|
| LC-File | 4-ZC-154A-2A_SYN_NAPTH_IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.589 | 12908.3 | 1085.9 | 0.1867 | 49.174 | 0.868 |
| 2 | 9.539 | 13341.8 | 862.2 | 0.2445 | 50.826 | 0.866 |

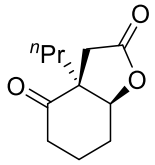


**3c**

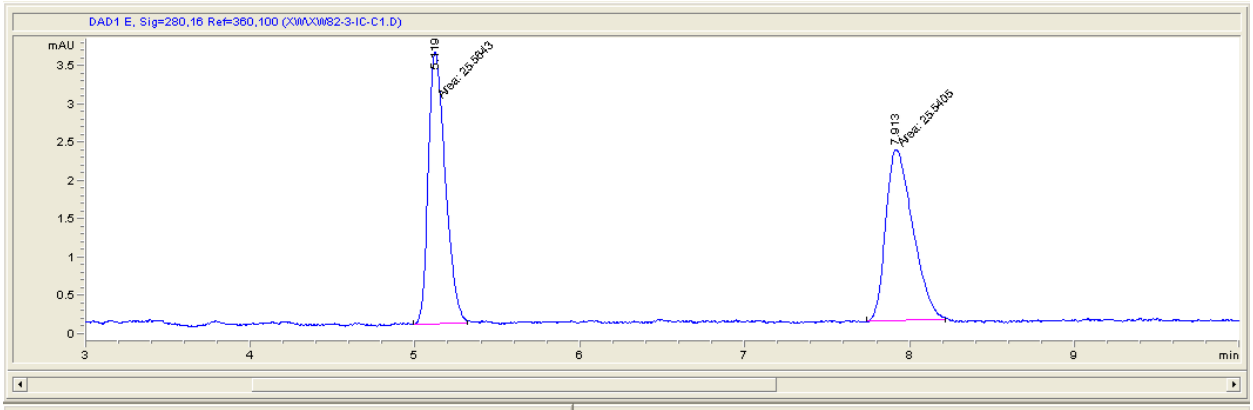



| File Information | |
|---|---|
| LC-File | 4-ZC-152_SYN_NAPTH_IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.906 | 301.9 | 26.3 | 0.179 | 1.797 | 0.923 |
| 2 | 9.897 | 16496.9 | 1048.9 | 0.2475 | 98.203 | 0.849 |

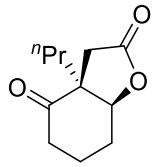


***rac*-3d**

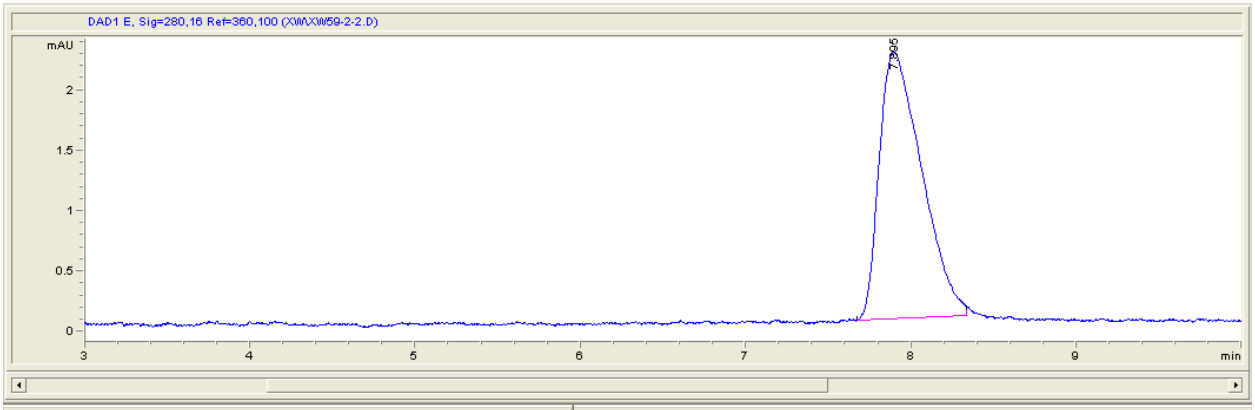



| File Information | |
|---|---|
| LC-File | XW82-3-IC-C1.D |
| File Path | C:\CHEM32\1\DATA\XW\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.119 | 25.6 | 3.6 | 0.1198 | 50.023 | 0.652 |
| 2 | 7.913 | 25.5 | 2.2 | 0.1908 | 49.977 | 0.585 |

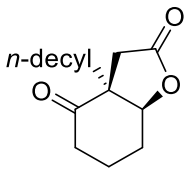


**3d**

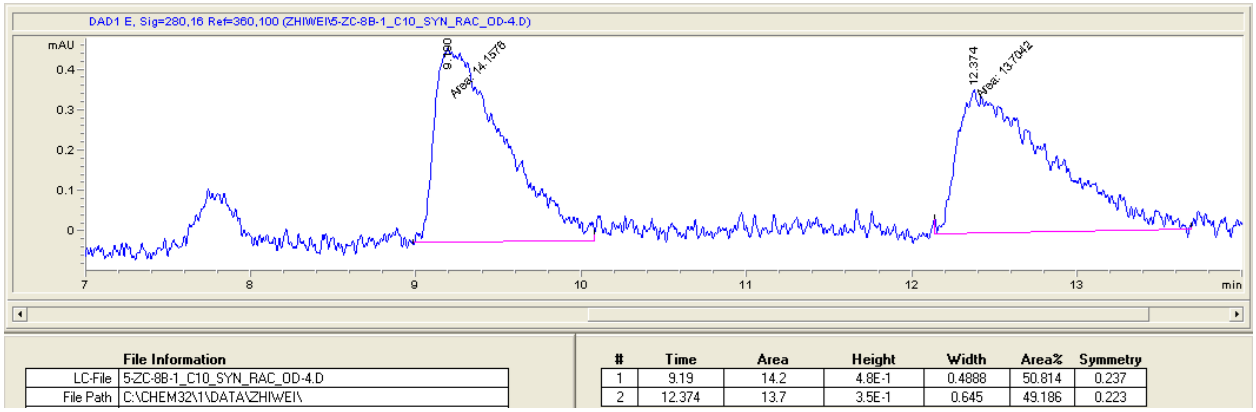



| File Information | |
|---|---|
| LC-File | XW59-2-2.D |
| File Path | C:\CHEM32\1\DATA\XW\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.895 | 39.5 | 2.2 | 0.2147 | 100.000 | 0.509 |

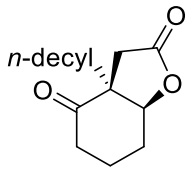



***rac*-3e**

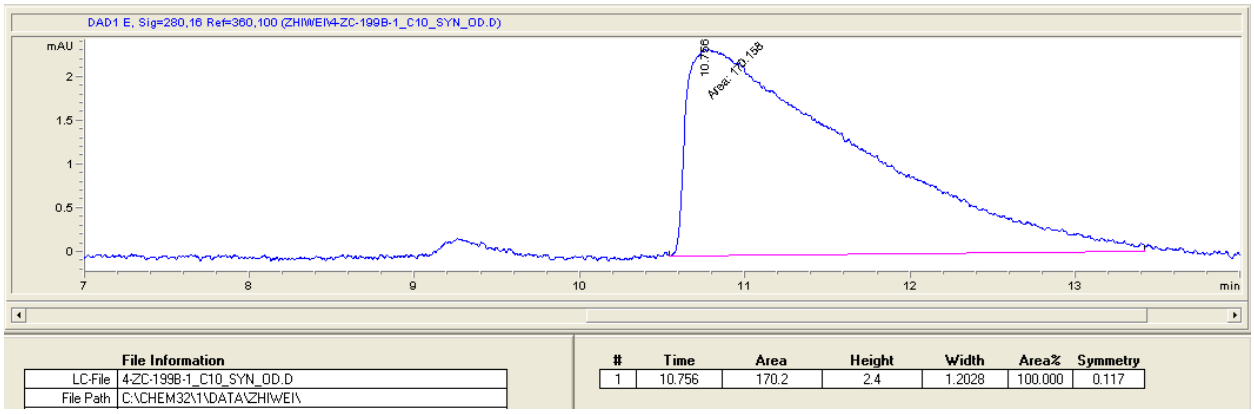



| File Information | |
|---|---|
| LC-File | 5-ZC-8B-1_C10_SYN_RAC_OD-4.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.19 | 14.2 | 4.8E-1 | 0.4888 | 50.814 | 0.237 |
| 2 | 12.374 | 13.7 | 3.5E-1 | 0.645 | 49.186 | 0.223 |

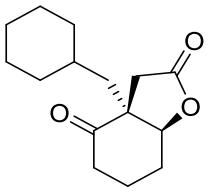



**3e**

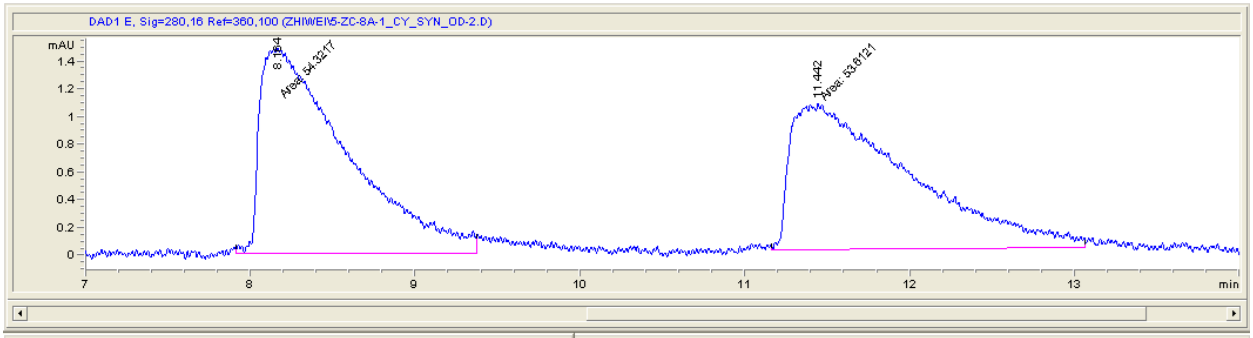



| File Information | |
|---|---|
| LC-File | 4-ZC-199B-1_C10_SYN_OD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.756 | 170.2 | 2.4 | 1.2028 | 100.000 | 0.117 |

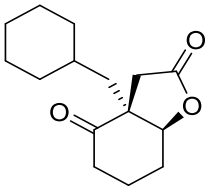


***rac*-3f**

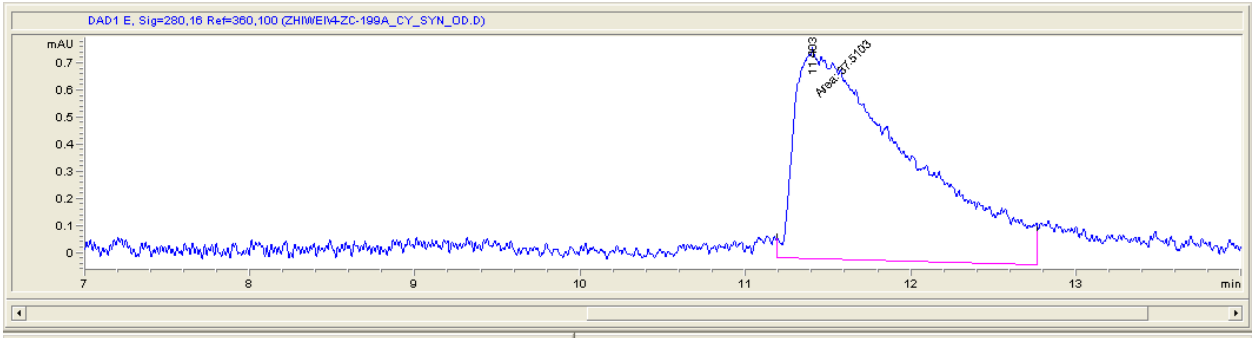



| File Information | |
|---|---|
| LC-File | 5-ZC-8A-1_CY_SYN_OD-2.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.164 | 54.3 | 1.5 | 0.6114 | 50.329 | 0.251 |
| 2 | 11.442 | 53.6 | 1.1 | 0.8432 | 49.671 | 0.286 |

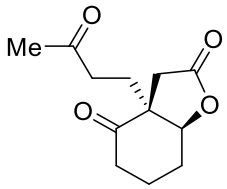


**3f**

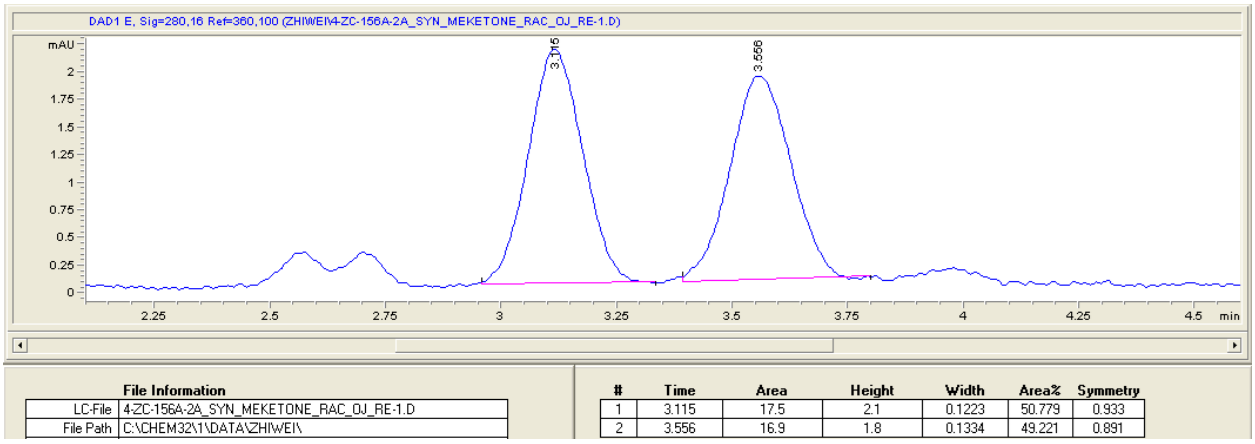



| File Information | |
|---|---|
| LC-File | 4-ZC-199A_CY_SYN_OD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 11.403 | 37.5 | 7.8E-1 | 0.7984 | 100.000 | 0.185 |

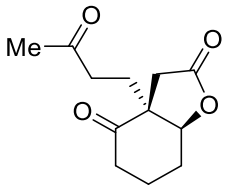


***rac*-3g**

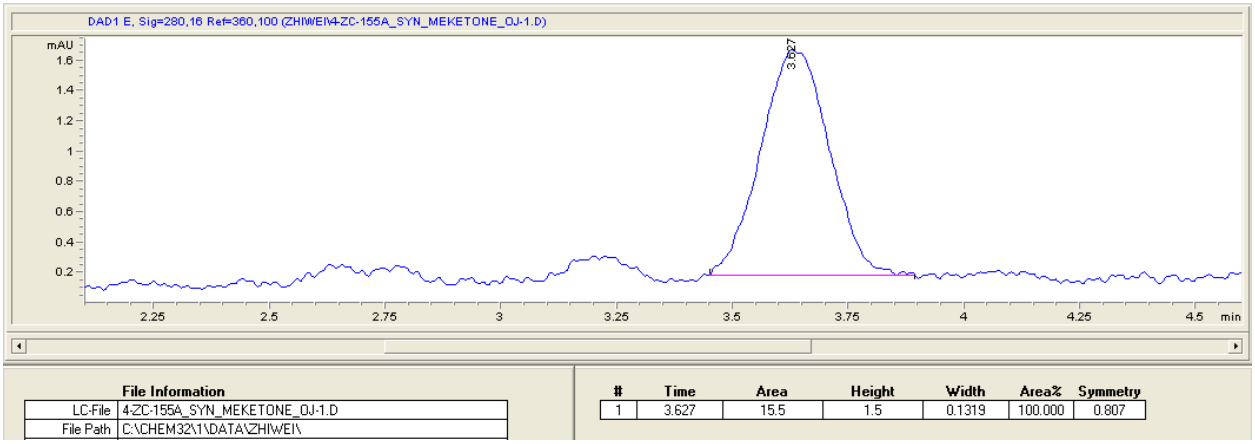



| File Information | |
|---|---|
| LC-File | 4-ZC-156A-2A_SYN_MEKETONE_RAC_OJ_RE-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.115 | 17.5 | 2.1 | 0.1223 | 50.779 | 0.933 |
| 2 | 3.556 | 16.9 | 1.8 | 0.1334 | 49.221 | 0.891 |

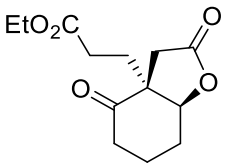


**3g**

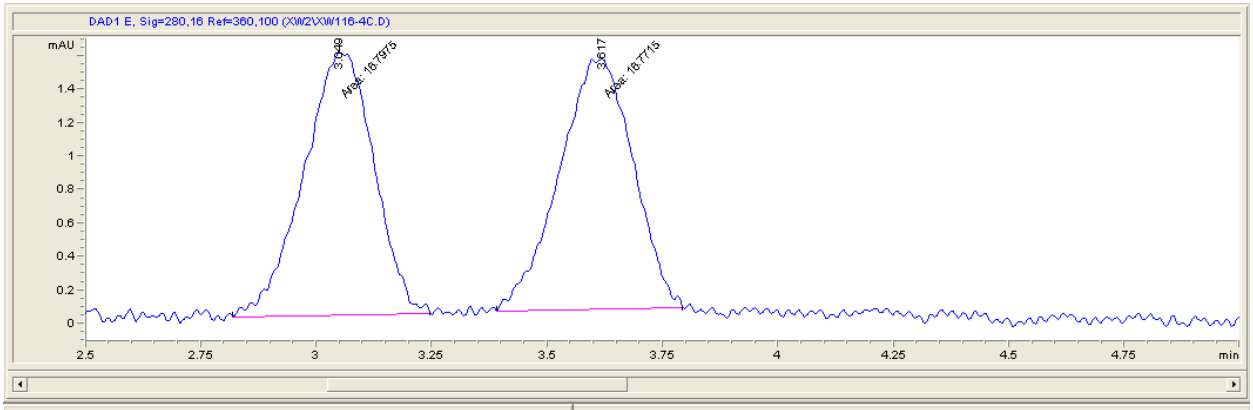



| File Information | |
|---|---|
| LC-File | 4-ZC-155A_SYN_MEKETONE_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.627 | 15.5 | 1.5 | 0.1319 | 100.000 | 0.807 |

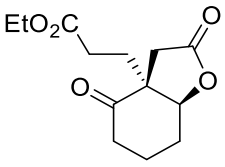


***rac*-3h**

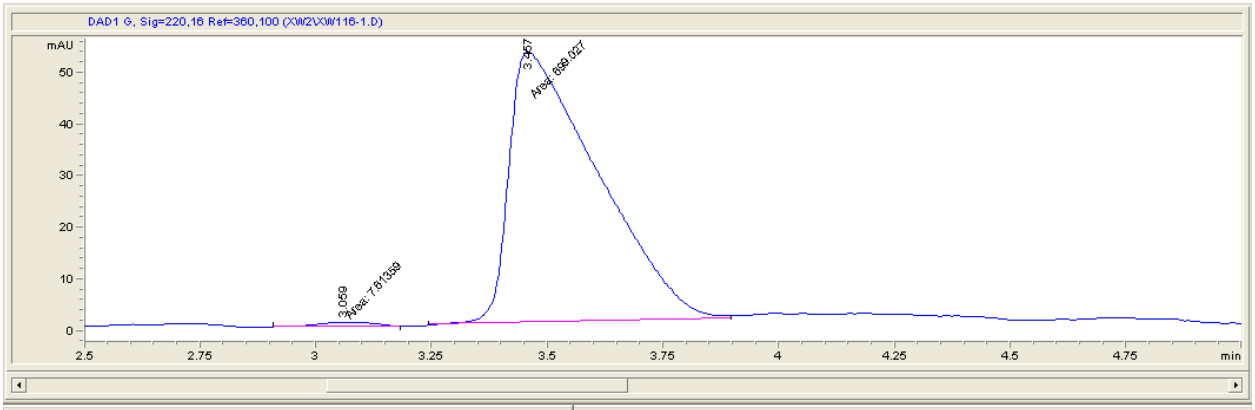



| File Information | |
|---|---|
| LC-File | XW116-4C.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.049 | 16.8 | 1.6 | 0.1769 | 50.039 | 1.019 |
| 2 | 3.617 | 16.8 | 1.5 | 0.186 | 49.961 | 1.281 |

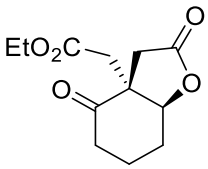


**3h**

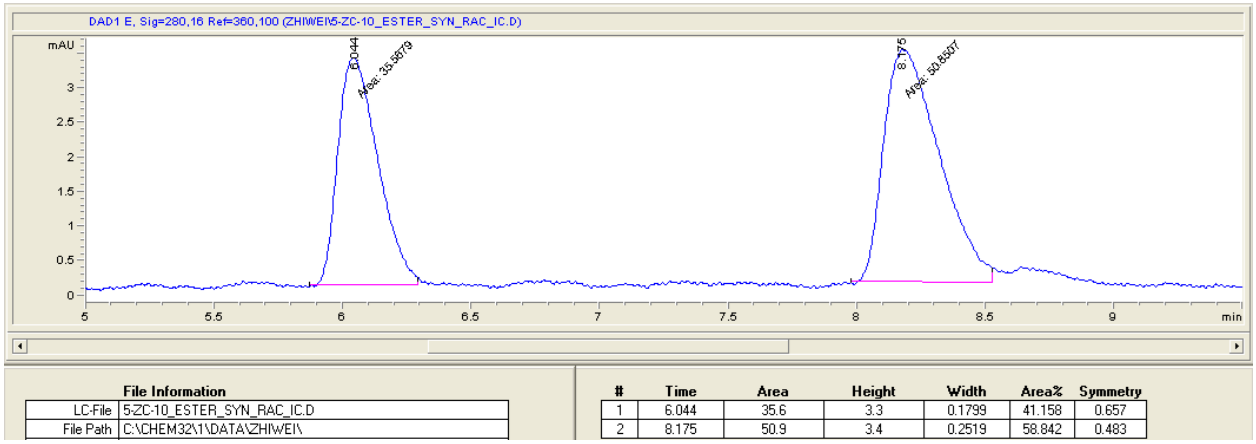



| File Information | |
|---|---|
| LC-File | XW116-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 3.059 | 7.6 | 8.8E-1 | 0.145 | 1.077 | 0.879 |
| 2 | 3.457 | 699 | 52.5 | 0.2221 | 98.923 | 0.27 |

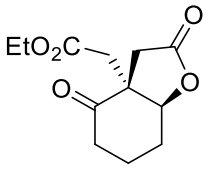


***rac*-3i**

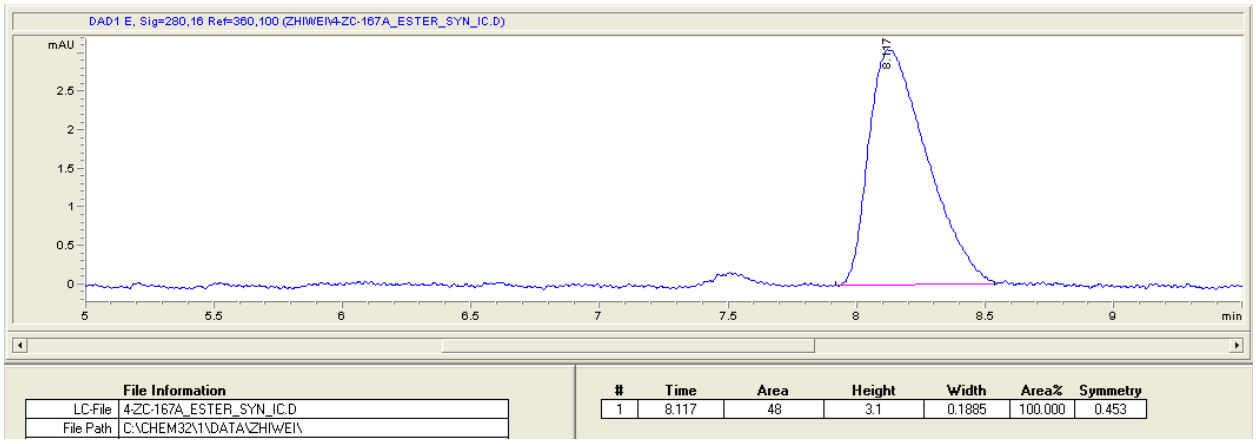



| File Information | |
|---|---|
| LC-File | 5-ZC-10_ESTER_SYN_RAC_IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.044 | 35.6 | 3.3 | 0.1799 | 41.158 | 0.657 |
| 2 | 8.175 | 50.9 | 3.4 | 0.2519 | 58.842 | 0.483 |

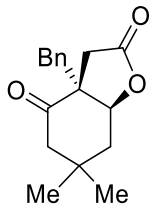


**3i**

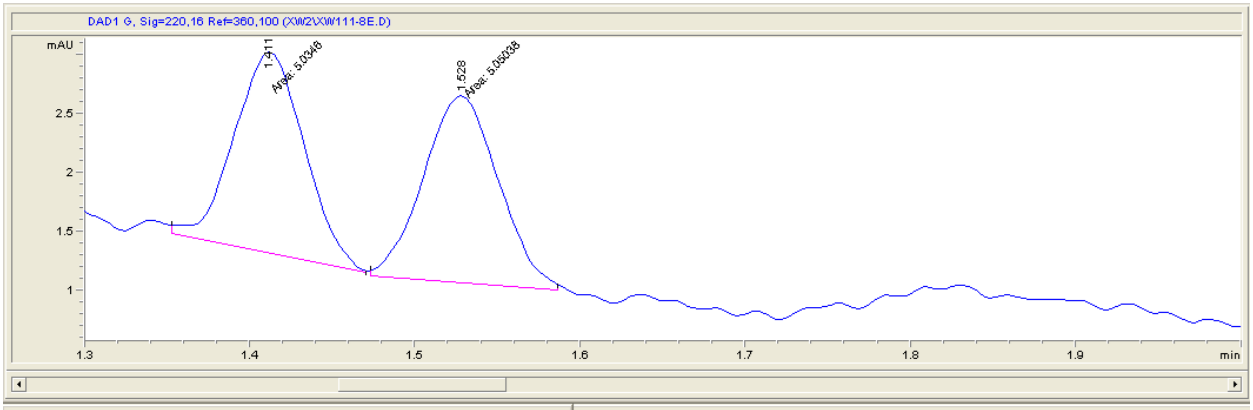



| File Information | |
|---|---|
| LC-File | 4-ZC-167A_ESTER_SYN_IC.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.117 | 48 | 3.1 | 0.1885 | 100.000 | 0.453 |

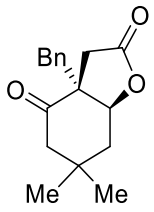



***rac*-3j**

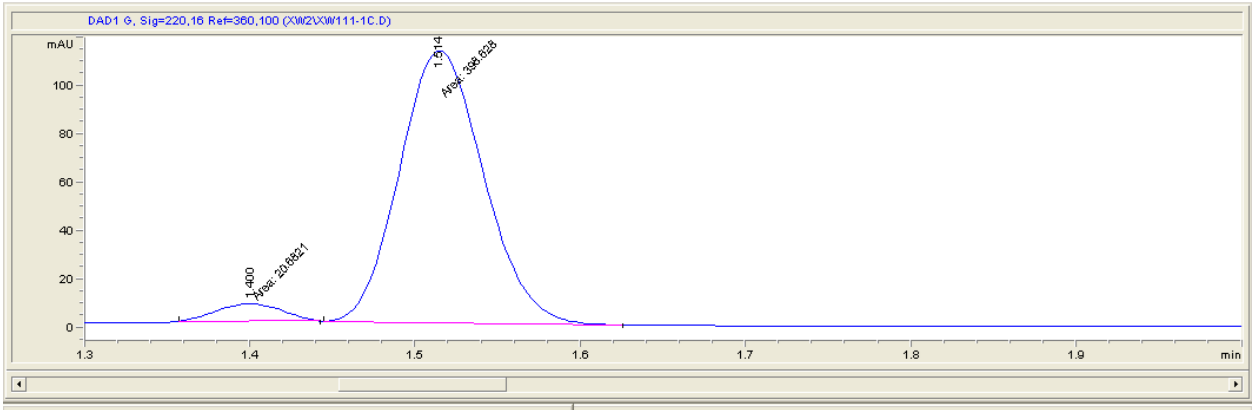



| File Information | |
|---|---|
| LC-File | XW111-8E.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 1.411 | 5 | 1.7 | 0.0491 | 49.922 | 0.959 |
| 2 | 1.528 | 5.1 | 1.6 | 0.0529 | 50.078 | 0.971 |

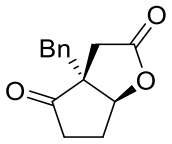



**3j**

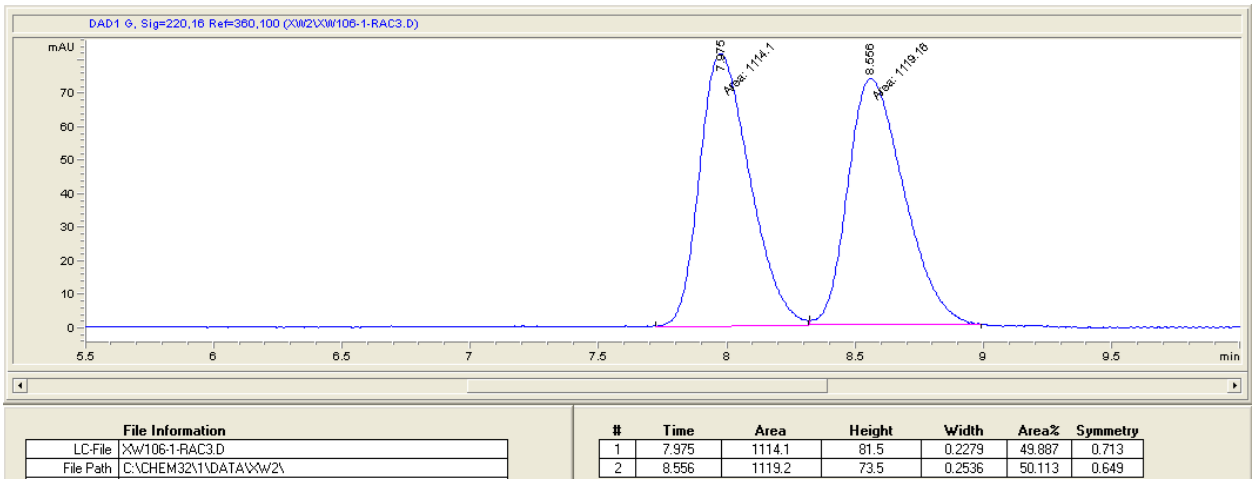



| File Information | |
|---|---|
| LC-File | XW111-1C.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 1.4 | 20.7 | 7.5 | 0.0459 | 4.932 | 1.009 |
| 2 | 1.514 | 398.6 | 112.8 | 0.0589 | 95.068 | 0.866 |

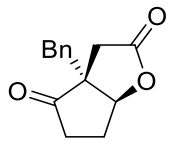



***rac*-3k**

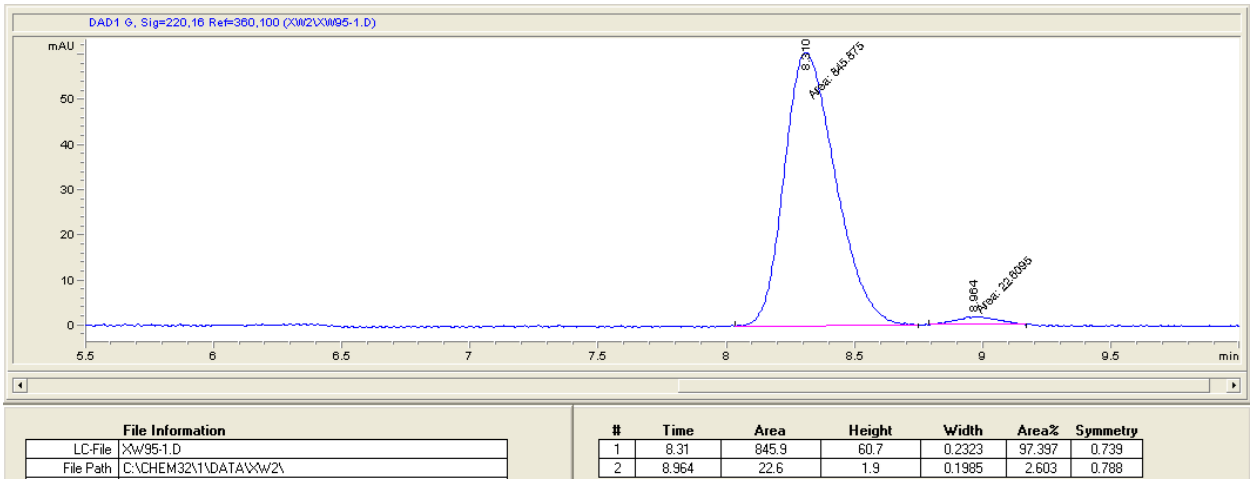



| File Information | |
|---|---|
| LC-File | XW106-1-RAC3.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.975 | 1114.1 | 81.5 | 0.2279 | 49.887 | 0.713 |
| 2 | 8.556 | 1119.2 | 73.5 | 0.2536 | 50.113 | 0.649 |

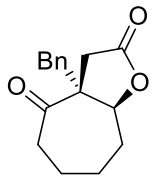



**3k**

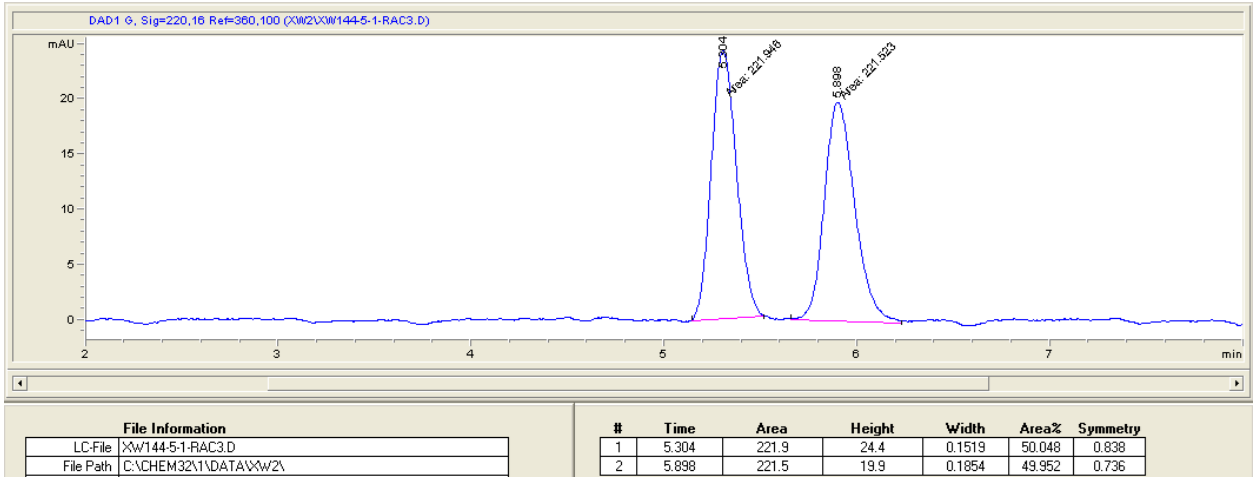



| File Information | |
|---|---|
| LC-File | XW95-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.31 | 845.9 | 60.7 | 0.2323 | 97.397 | 0.739 |
| 2 | 8.964 | 22.6 | 1.9 | 0.1985 | 2.603 | 0.788 |

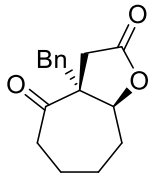


***rac*-3l**

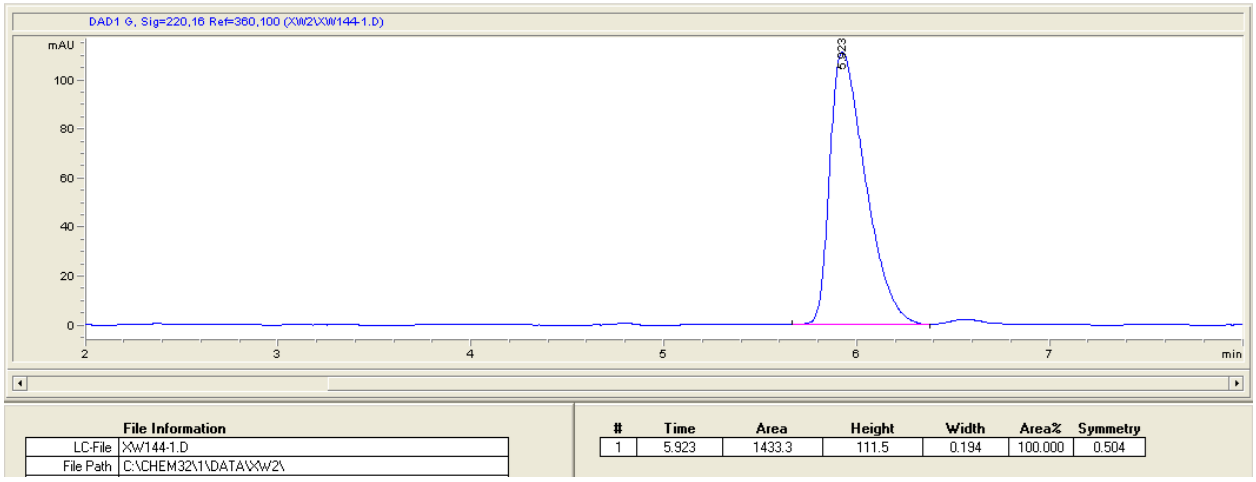



| File Information | |
|---|---|
| LC-File | XW144-5-1-RAC3.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.304 | 221.9 | 24.4 | 0.1519 | 50.048 | 0.838 |
| 2 | 5.898 | 221.5 | 19.9 | 0.1854 | 49.952 | 0.736 |

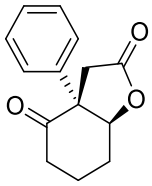


**3l**

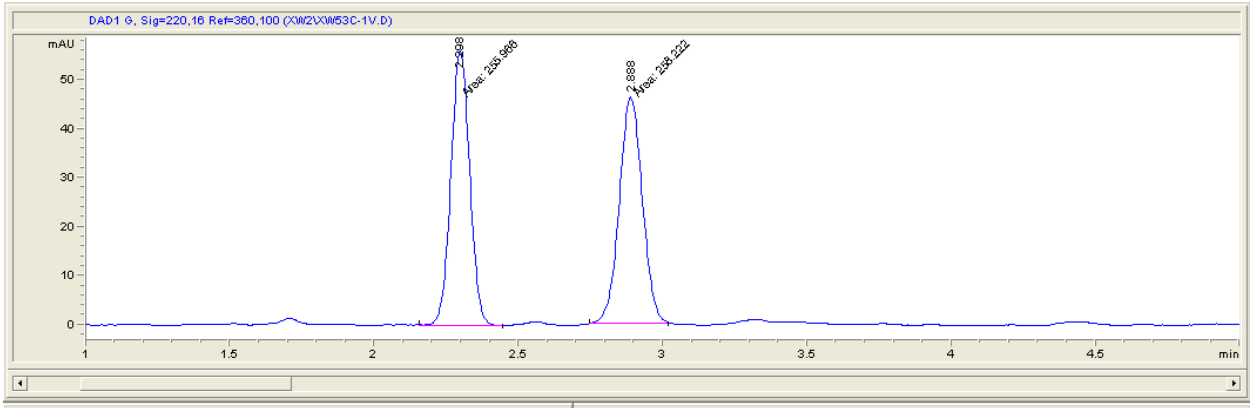



| File Information | |
|---|---|
| LC-File | XW144-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.923 | 1433.3 | 111.5 | 0.194 | 100.000 | 0.504 |

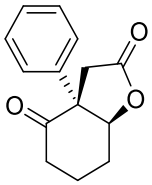


***rac*-3m**

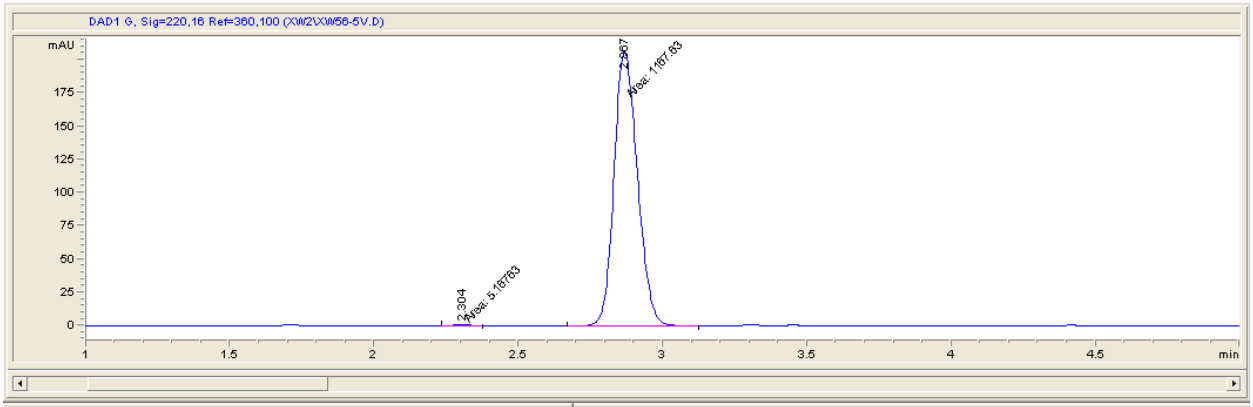



| File Information | |
|---|---|
| LC-File | XW53C-1V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.298 | 256 | 56.3 | 0.0758 | 49.781 | 0.954 |
| 2 | 2.888 | 258.2 | 46.3 | 0.0929 | 50.219 | 0.951 |

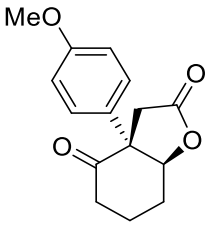


**3m**

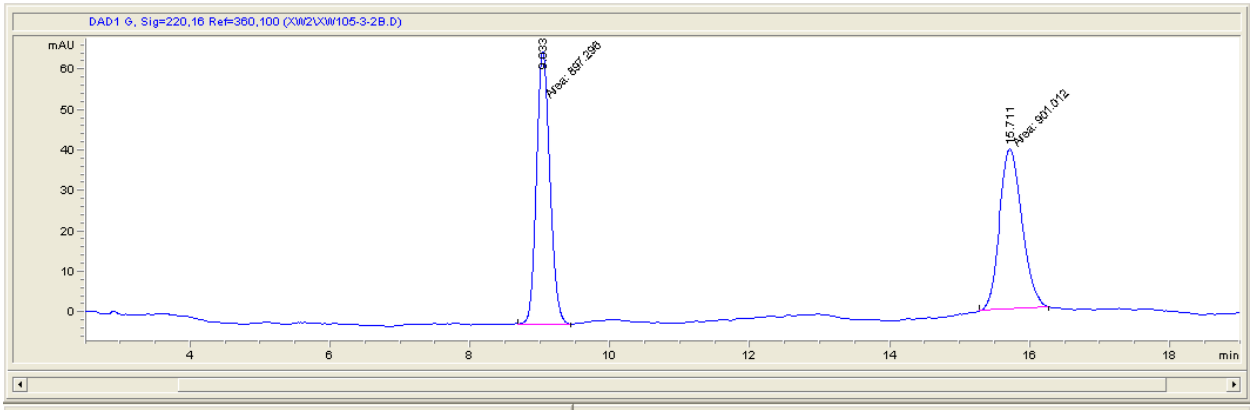



| File Information | |
|---|---|
| LC-File | XW56-5V.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 2.304 | 5.2 | 1 | 0.0834 | 0.441 | 0.905 |
| 2 | 2.867 | 1167.6 | 206.8 | 0.0941 | 99.559 | 0.777 |

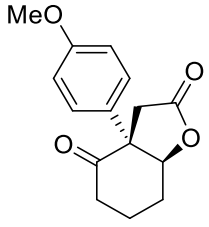



***rac*-3n**

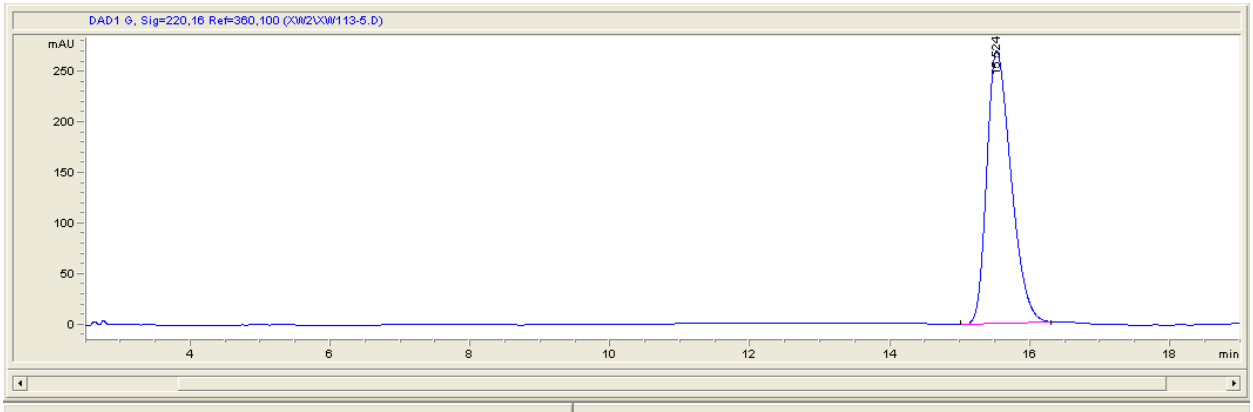



| File Information | |
|---|---|
| LC-File | XW105-3-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.033 | 897.3 | 67.5 | 0.2217 | 49.897 | 0.857 |
| 2 | 15.711 | 901 | 39.6 | 0.3793 | 50.103 | 0.844 |

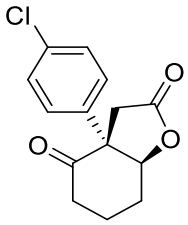



**3n**

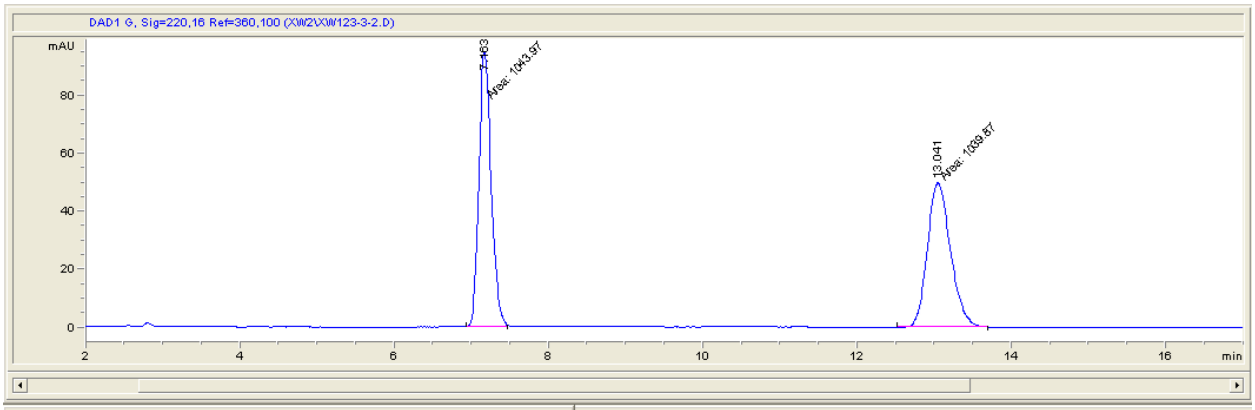



| File Information | |
|---|---|
| LC-File | XW113-5.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.524 | 6492.2 | 270.2 | 0.3633 | 100.000 | 0.651 |

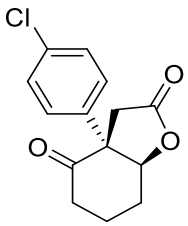


***rac*-3o**

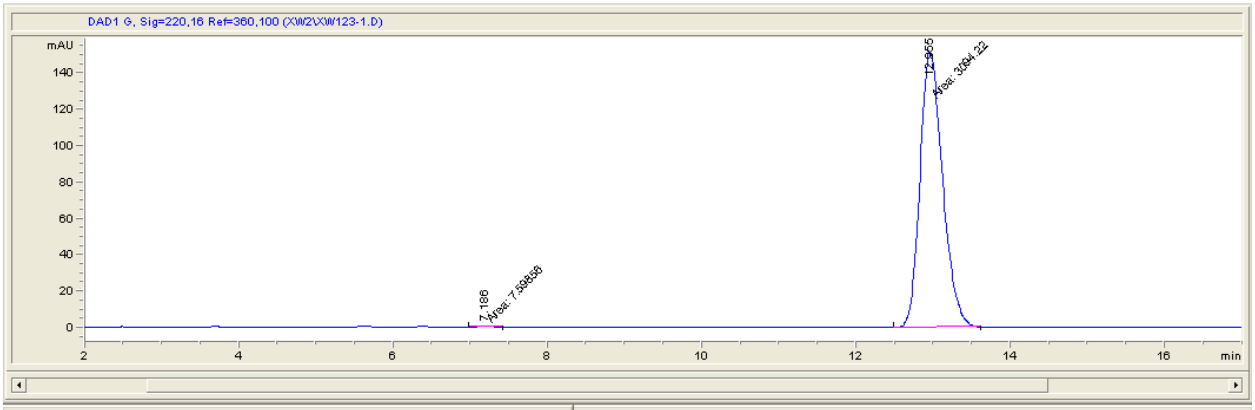



| File Information | |
|---|---|
| LC-File | XW123-3-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.163 | 1044 | 94.5 | 0.1841 | 50.098 | 0.795 |
| 2 | 13.041 | 1039.9 | 49.9 | 0.3473 | 49.902 | 0.811 |

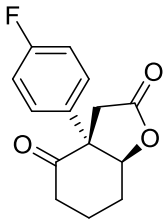


**3o**

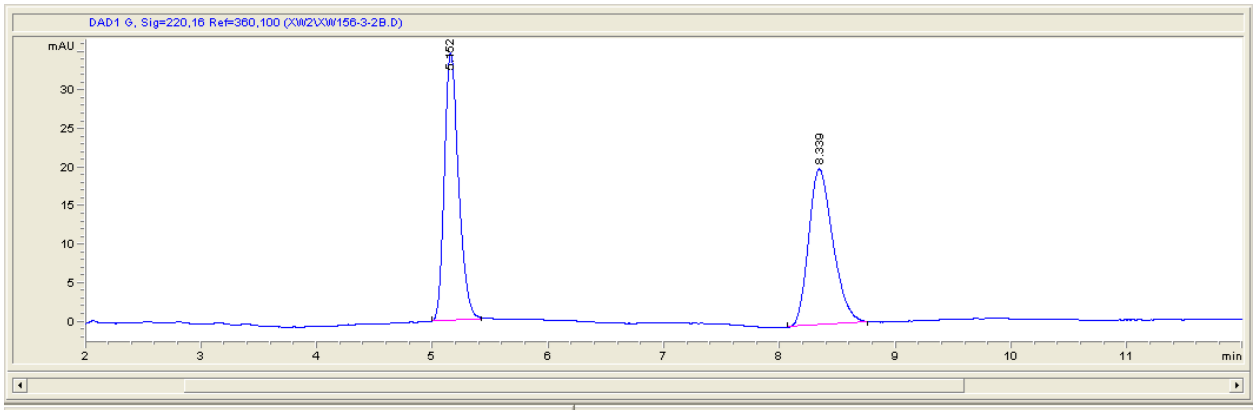



| File Information | |
|---|---|
| LC-File | XW123-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.186 | 7.6 | 7.2E-1 | 0.1758 | 0.245 | 0.915 |
| 2 | 12.955 | 3094.2 | 151.6 | 0.3403 | 99.755 | 0.764 |

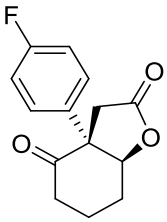


***rac*-3p**

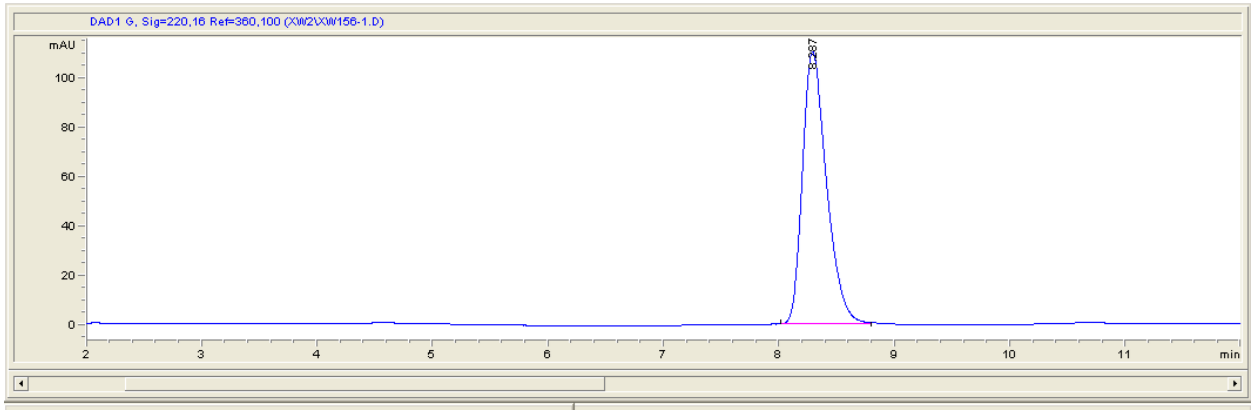



| File Information | |
|---|---|
| LC-File | XW156-3-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.152 | 297.6 | 34.8 | 0.1308 | 49.888 | 0.717 |
| 2 | 8.339 | 299 | 20.4 | 0.2244 | 50.112 | 0.736 |

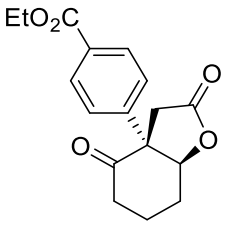


**3p**

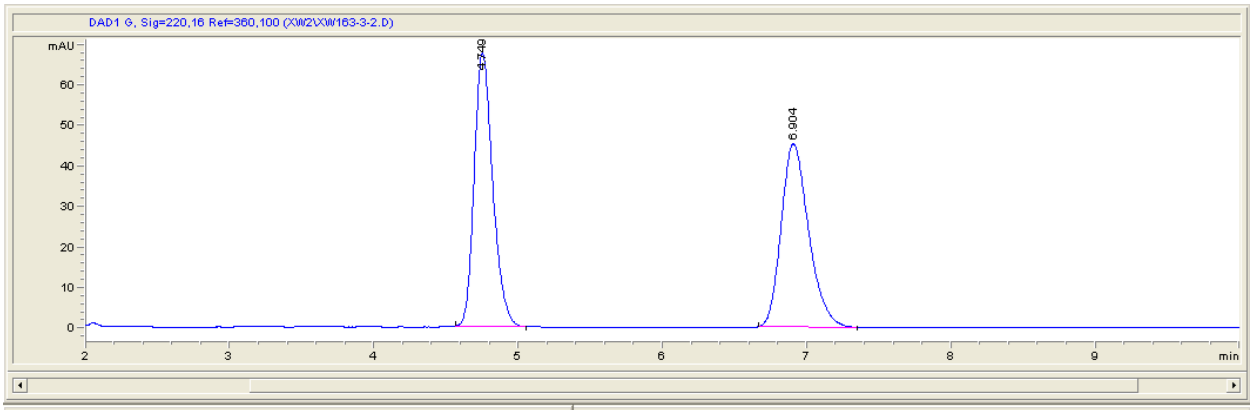



| File Information | |
|---|---|
| LC-File | XW156-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.287 | 1598.4 | 110.5 | 0.2228 | 100.000 | 0.665 |

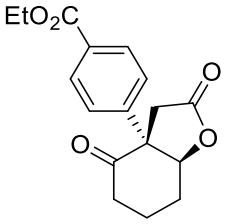


***rac*-3q**

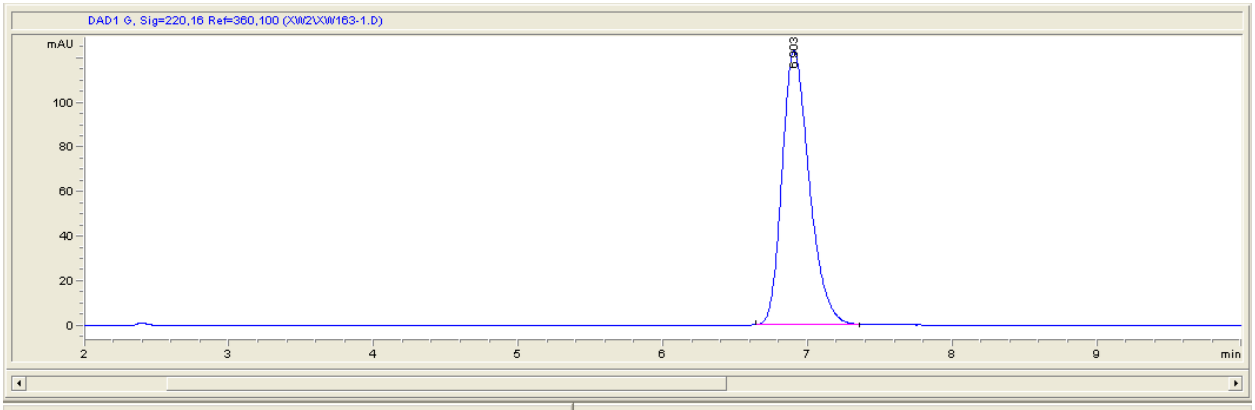



| File Information | |
|---|---|
| LC-File | XW163-3-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.749 | 604.3 | 67.8 | 0.1371 | 50.079 | 0.76 |
| 2 | 6.904 | 602.4 | 45.3 | 0.203 | 49.921 | 0.751 |

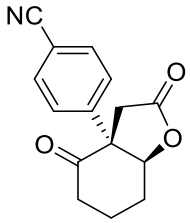


**3q**

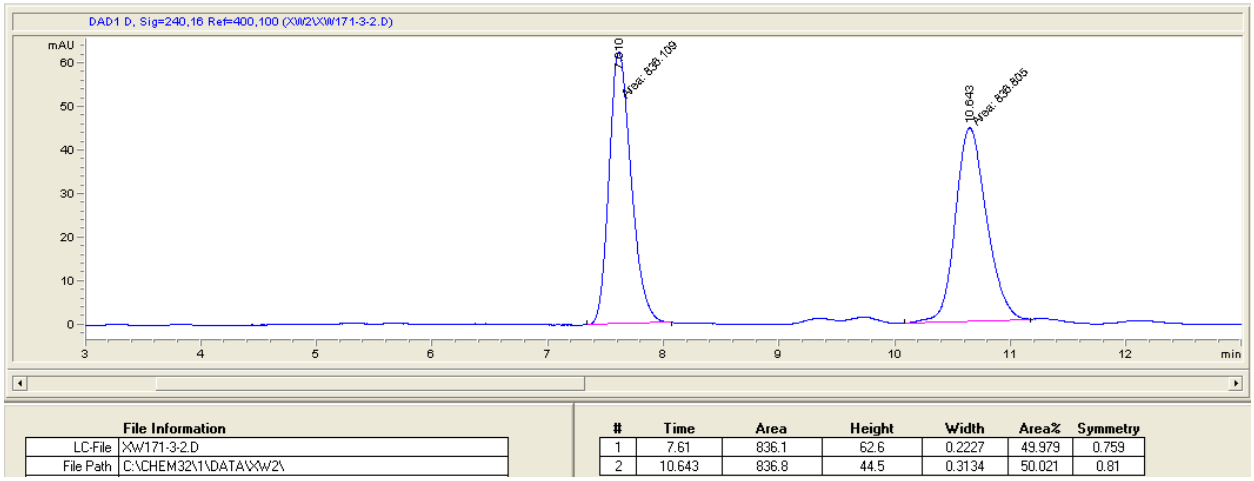



| File Information | |
|---|---|
| LC-File | XW163-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.903 | 1610 | 123 | 0.1997 | 100.000 | 0.728 |

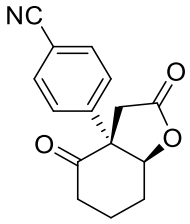


***rac*-3r**

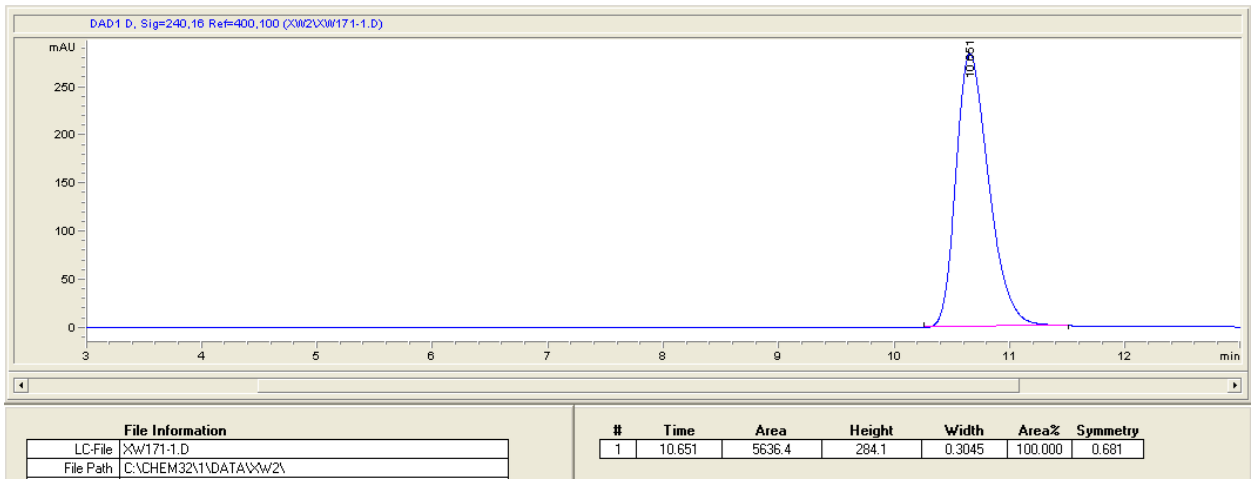



| File Information | |
|---|---|
| LC-File | XW171-3-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.61 | 836.1 | 62.6 | 0.2227 | 49.979 | 0.759 |
| 2 | 10.643 | 836.8 | 44.5 | 0.3134 | 50.021 | 0.81 |

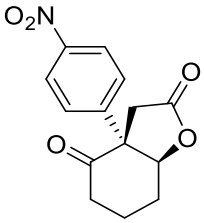


**3r**

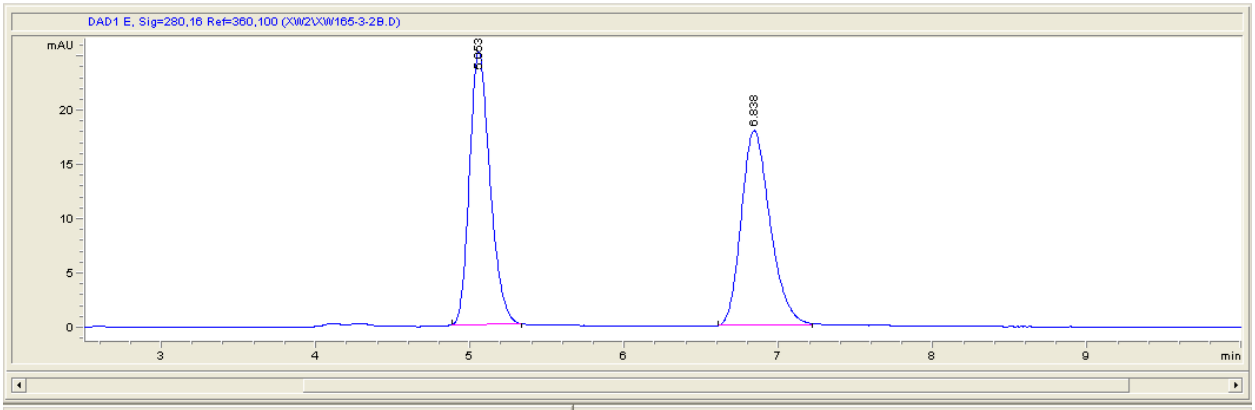



| File Information | |
|---|---|
| LC-File | XW171-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.651 | 5636.4 | 284.1 | 0.3045 | 100.000 | 0.681 |

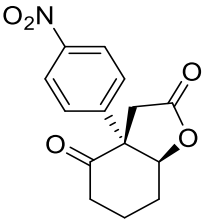


***rac*-3s**

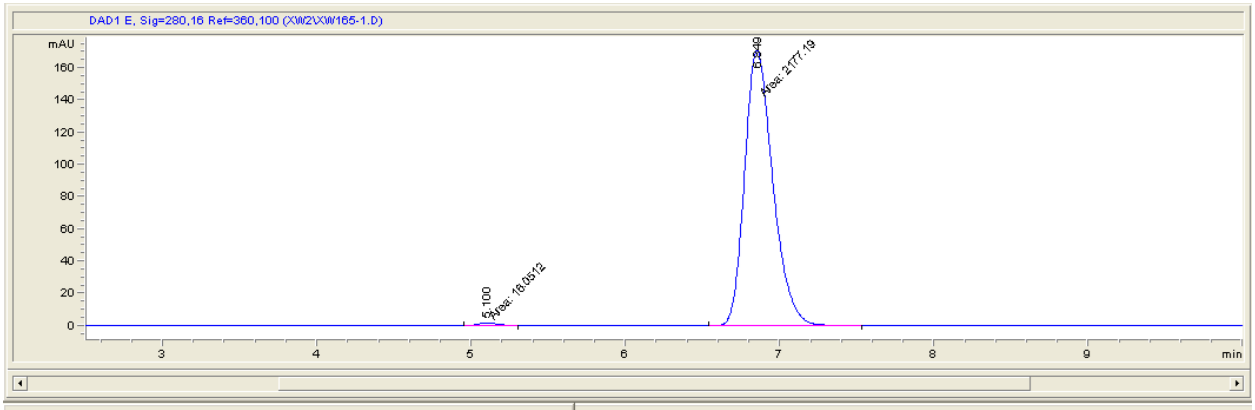



| File Information | |
|---|---|
| LC-File | XW165-3-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.053 | 234.5 | 25.2 | 0.1424 | 49.995 | 0.753 |
| 2 | 6.838 | 234.5 | 18 | 0.1992 | 50.005 | 0.755 |

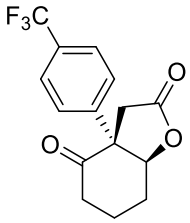


**3s**

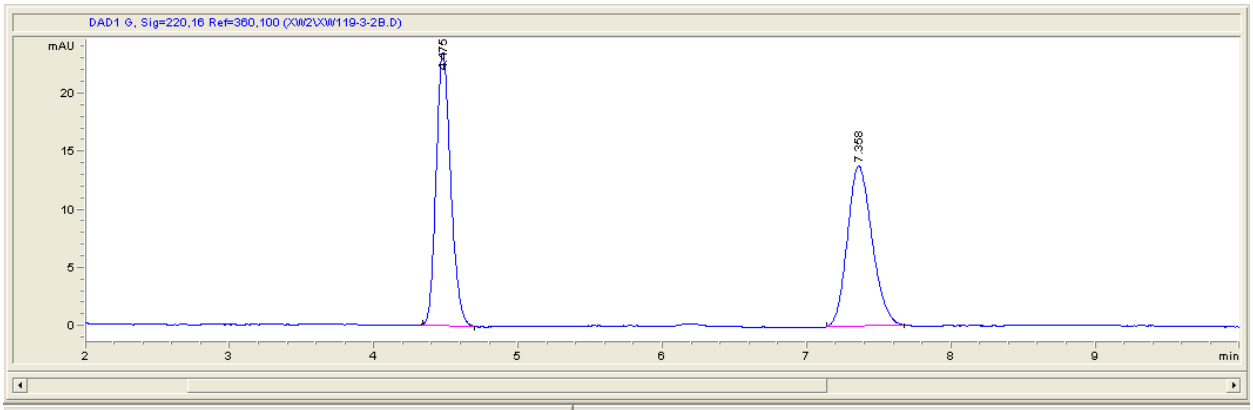



| File Information | |
|---|---|
| LC-File | XW165-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.1 | 16.1 | 1.8 | 0.1493 | 0.732 | 0.781 |
| 2 | 6.849 | 2177.2 | 170.9 | 0.2123 | 99.268 | 0.75 |

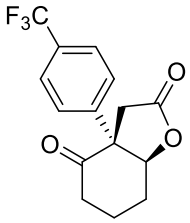


***rac*-3t**

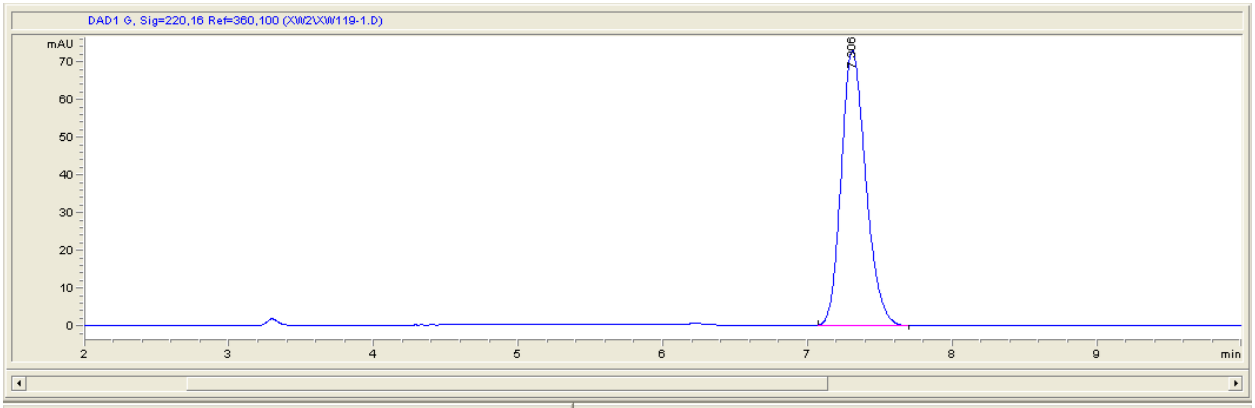



| File Information | |
|---|---|
| LC-File | XW119-3-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.475 | 165.8 | 23.5 | 0.1072 | 49.958 | 0.787 |
| 2 | 7.358 | 166.1 | 13.8 | 0.1861 | 50.042 | 0.8 |

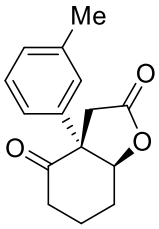


**3t**

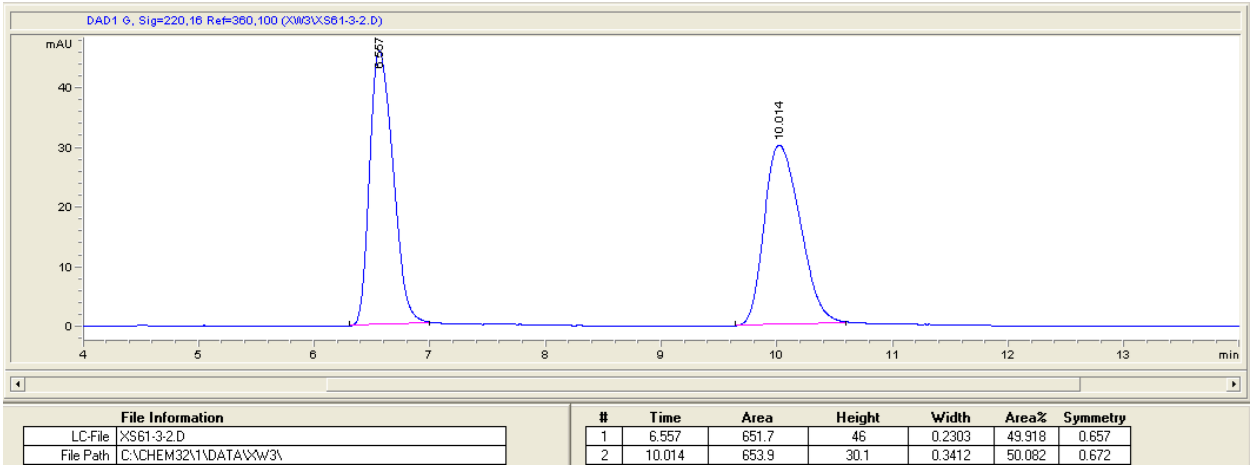



| File Information | |
|---|---|
| LC-File | XW119-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.306 | 863.3 | 73 | 0.182 | 100.000 | 0.785 |

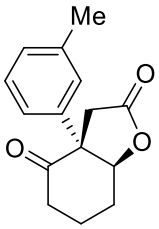



***rac*-3u**

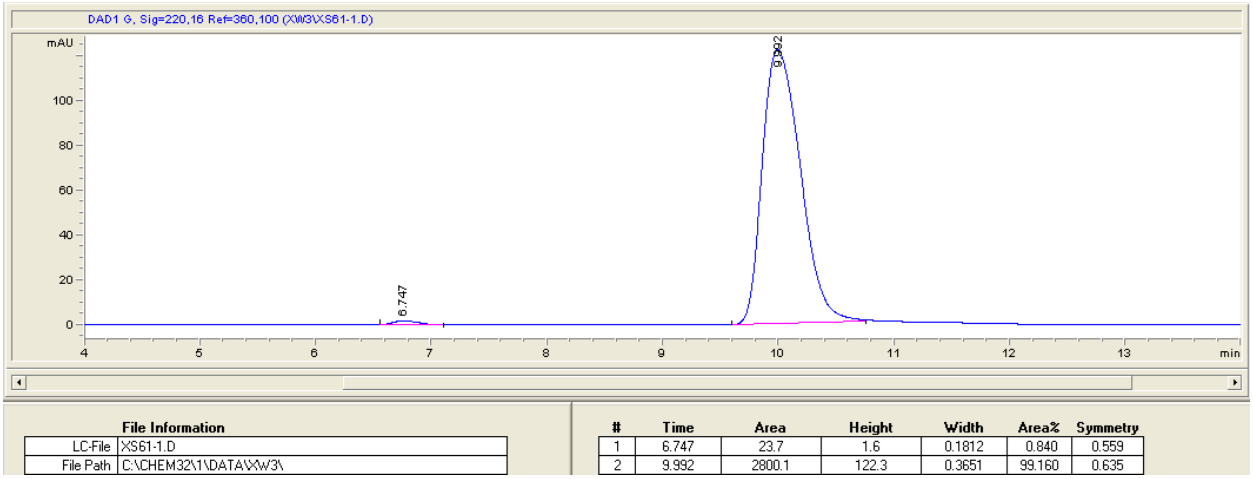



| File Information | |
|---|---|
| LC-File | XS61-3-2.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.557 | 651.7 | 46 | 0.2303 | 49.918 | 0.657 |
| 2 | 10.014 | 653.9 | 30.1 | 0.3412 | 50.082 | 0.672 |

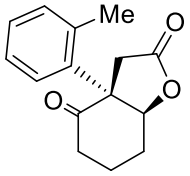



**3u**

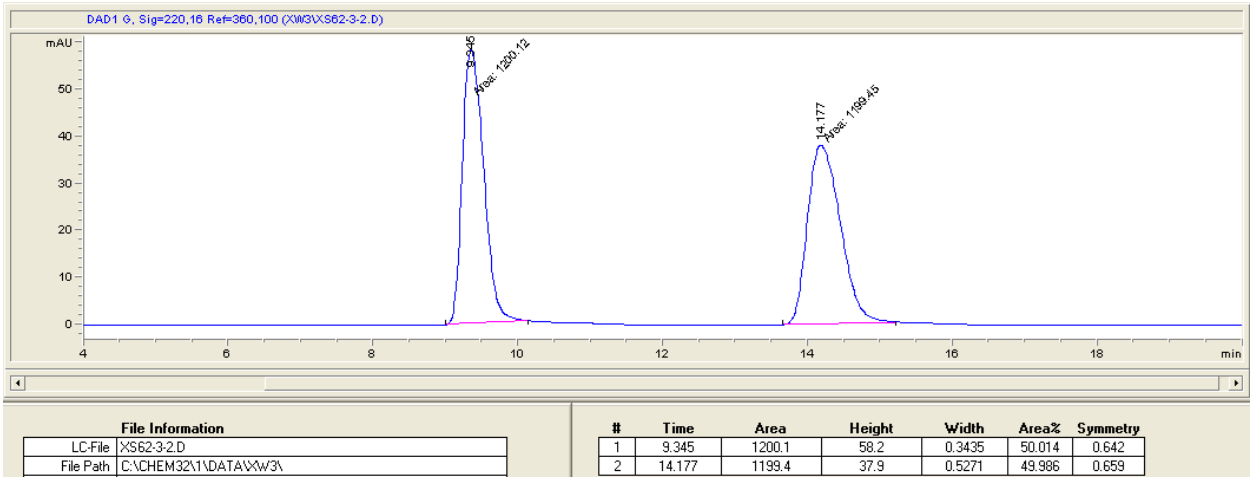



| File Information | |
|---|---|
| LC-File | XS61-1.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.747 | 23.7 | 1.6 | 0.1812 | 0.840 | 0.559 |
| 2 | 9.992 | 2800.1 | 122.3 | 0.3651 | 99.160 | 0.635 |

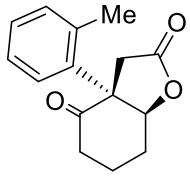



***rac*-3v**

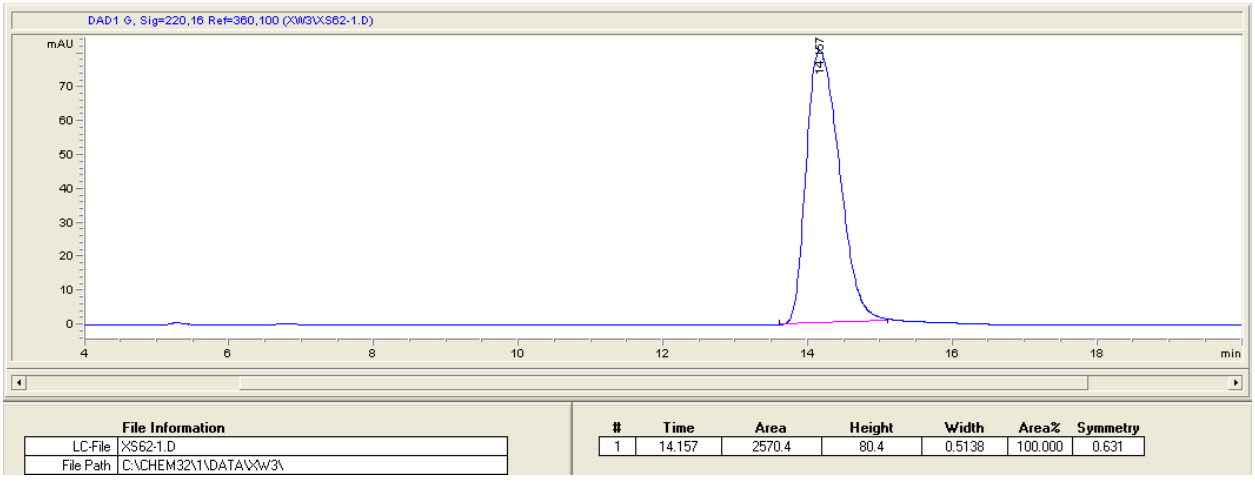



| File Information | |
|---|---|
| LC-File | XS62-3-2.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.345 | 1200.1 | 58.2 | 0.3435 | 50.014 | 0.642 |
| 2 | 14.177 | 1199.4 | 37.9 | 0.5271 | 49.986 | 0.659 |

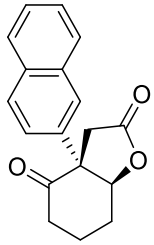



**3v**

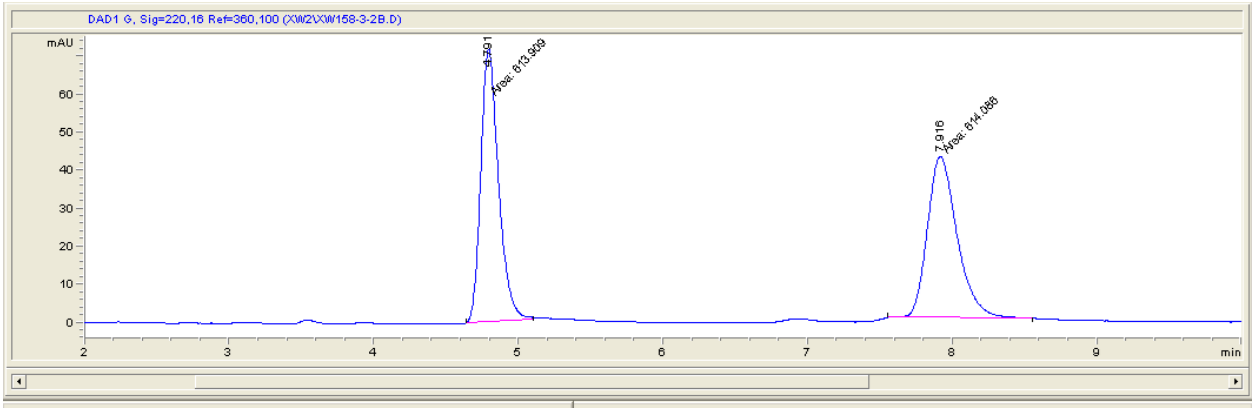



| File Information | |
|---|---|
| LC-File | XS62-1.D |
| File Path | C:\CHEM32\1\DATA\XW3\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 14.157 | 2570.4 | 80.4 | 0.5138 | 100.000 | 0.631 |

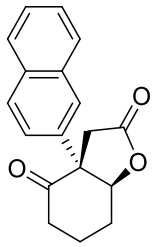


***rac*-3w**

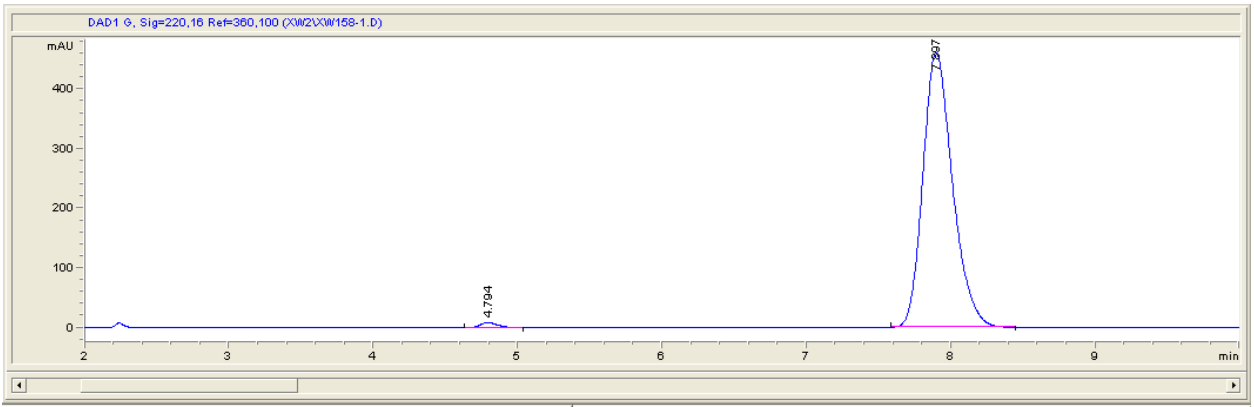



| File Information | |
|---|---|
| LC-File | XW158-3-2B.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.791 | 613.9 | 71.7 | 0.1427 | 49.993 | 0.742 |
| 2 | 7.916 | 614.1 | 42.4 | 0.2411 | 50.007 | 0.753 |

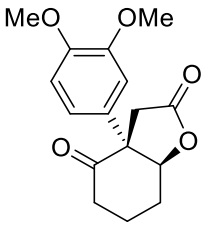


**3w**

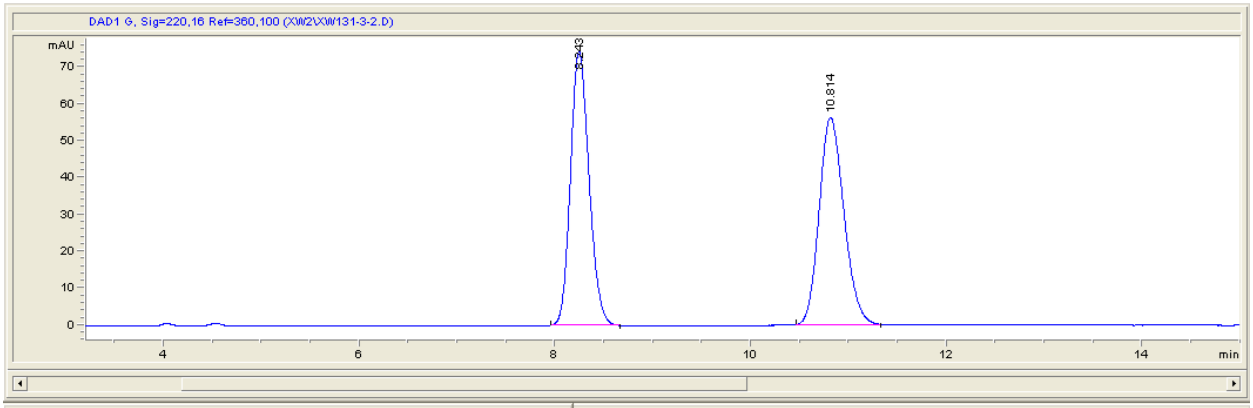



| File Information | |
|---|---|
| LC-File | XW158-1.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.794 | 75.4 | 8.9 | 0.1311 | 1.132 | 0.739 |
| 2 | 7.897 | 6588.9 | 461.1 | 0.2187 | 98.868 | 0.762 |

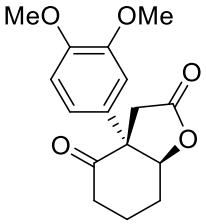



***rac*-3x**

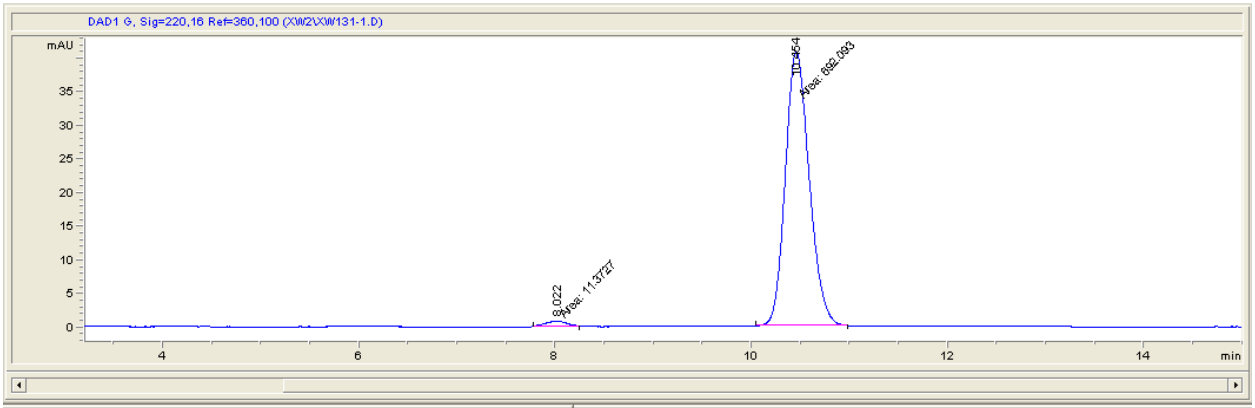



| File Information | |
|---|---|
| LC-File | XW131-3-2.D |
| File Path | C:\CHEM32\1\DATA\XW2\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.243 | 981.5 | 74.3 | 0.2041 | 49.712 | 0.815 |
| 2 | 10.814 | 992.8 | 56.2 | 0.273 | 50.288 | 0.812 |




**3x**

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| 2 | 10.454 | 692.1 | 40.8 | 0.2829 | 98.383 | 0.806 |

## Appendix 2.2: Supporting Information for Chapter 2.2
## Rhodium-Catalyzed Enantioselective Cycloisomerization to Cyclohexenes Bearing Quaternary Carbon Centers

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## 1. General Considerations

All experiments were performed in oven-dried or flame-dried glassware under an atmosphere of $N_2$. Tetrahydrofuran, dichloromethane, toluene, and diethyl ether were purified using an Innovative Technologies Pure Solv system, degassed by three freeze-pump-thaw cycles, and stored over 3A MS within a $N_2$ filled glove box. The molarity of organolithium reagents was determined by titration with *iso*-propanol/1,10-phenanthroline. Reactions were monitored either *via* gas chromatography using an Agilent Technologies 7890A GC system equipped with an Agilent Technologies 5975C inert XL EI/CI MSD or by analytical thin-layer chromatography on EMD Silica Gel 60 $F_{254}$ plates. Visualization of the developed plates was performed under UV light (254 nm) or using either $KMnO_4$ or *p*-anisaldehyde stain. Column chromatography was performed with Silicycle Silia-P Flash Silica Gel using glass columns. Automated column chromatography was performed using either a Biotage SP1 or Teledyne Isco CombiFlash Rf 200 purification system. $^1H$, $^2D$ and $^{13}C$ spectra were recorded on a Bruker DRX-400 (400 MHz $^1H$, 100 MHz $^{13}C$, 376.5 MHz $^{19}F$), GN-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$) or CRYO-500 (500 MHz $^1H$, 125.7 MHz $^{13}C$) spectrometer. $^1H$ NMR spectra were internally referenced to the residual solvent signal or TMS. $^{13}C$ NMR spectra were internally referenced to the residual solvent signal. Data for $^1H$ NMR are reported as follows: chemical shift (δ ppm, δ 7.27 for $CDCl_3$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for $^{13}C$ NMR are reported in terms of chemical shift (δ ppm, δ 77.16 for $CDCl_3$). Infrared spectra were obtained on a Thermo Scientific Nicolet iS5 FT-IR spectrometer equipped with an iD5 ATR accessory. Enantiomeric excesses for stereoselective reactions were determined by chiral SFC analysis using an Agilent Technologies HPLC (1200 series) system and Aurora A5 Fusion. High resolution mass spectrometry (HRMS) was performed by the University of California, Irvine Mass Spectrometry Center. X-ray crystallography was performed by the University of California, Irvine, X-ray Crystallography Facility. $[(coe)_2RhCl]_2$ was prepared by the reported procedure.[1] NaBArF was purchased from Matrix Scientific. (*R*)- and (*S*)-Ph-SDP and (*S*)-Xyl-SDP were purchased from Strem Chemical, Inc.

## 2. Rh-Catalyzed Cycloisomerization of α,α-Bisallylaldehydes 1

### Representative procedure for Rh-catalyzed cycloisomerization

In a $N_2$-filled glove box, a 1-dram vial was charged with the indicated amount of $[(coe)_2RhCl]_2$, bisphosphine ligand, and 1,2-dichloroethane (0.2 M). The solution was stirred at rt for 30 min. Next, NaBArF was added, and the mixture was stirred for additional 5 min prior to addition of the α,α-bisallylaldehyde **1a**. The vial was then sealed with a Teflon-lined screw cap, and the reaction mixture was stirred for the indicated reaction time. Reaction progress and chemoselectivity were determined from analysis of the GC-FID chromatogram or $^1$H NMR spectrum of the reaction mixture. The cycloisomerization products were isolated by preparative TLC. The enantiomeric excess was determined by chiral SFC analysis of the corresponding alcohol (Procedure A) or benzoyl ester (Procedure B).

For the reactions of **1a**, **1c**, **1e-f**, **1i** and **1j**, 1.25 mol% $[(coe)_2RhCl]_2$, 2.75 mol% (*R*)-DTBM-SDP, 3 mol% NaBArF, and DCE (0.2 M) were used, and the reactions were performed at 40 °C for 6-12 h.

For the reaction of **1b**, 1 mol% $[(coe)_2RhCl]_2$, 2.2 mol% (*R*)-DTBM-SDP, 2.5 mol% NaBArF, and DCE (0.2 M) were used, and the reactions were performed at rt for 2 h.

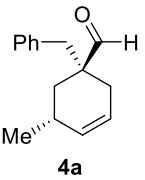
For the reaction of **1d** and **1g**, 1 mol% $[(coe)_2RhCl]_2$, 2.2 mol% (*R*)-DTBM-SDP, 2.5 mol% NaBArF, and DCE (0.2 M) were used, and the reactions were performed at 40 $^oC$ for 4 h.

For reactions of **1k-1s**, 2.5 mol% $[(coe)_2RhCl]_2$, 5.5 mol% (*R*)- or (*S*)-Ph-SDP ligand, 6 mol% NaBArF, and DCE (0.2 M) were used, and the reactions were performed at 40 $^oC$ for 18 h. For **1r**, (*S*)-Tol-SDP was used as the ligand.

**Procedure A, conversion to the corresponding alcohol:** Cyclohexenecarbaldehyde **4** (1 equiv) was dissolved in ethanol (0.1 M), and $NaBH_4$ (3 equiv) was added to the solution in one portion. The solution was stirred at rt for 1 h. EtOAc (20 ml) and aqueous HCl (1 N, 1 ml) were added to the solution, and the mixture was washed with water and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The pure alcohol **4-OH** was obtained by preparative TLC (eluting with 25% EtOAc in hexanes) and submitted to chiral SFC analysis.

**Procedure B, conversion to the corresponding benzoyl ester:** Alcohol **4-OH** (1 equiv) was dissolved in DCM (0.1 M). Pyridine (2 equiv) and benzoyl chloride (1.5 equiv) were added to the solution sequentially. The solution was stirred at rt for 3 h. EtOAc (20 ml), and the mixture was washed with water and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The pure ester **4-ester** was obtained by preparative TLC (eluting with 5% EtOAc in hexanes) and submitted to chiral SFC analysis.

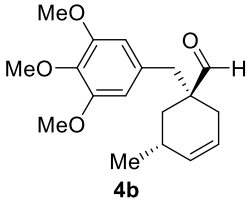
**(*1S*,*5R*)-1-Benzyl-5-methylcyclohex-3-ene-1-carbaldehyde (4a)**



**4a**

Using (*R*)-DTBM-SDP as the ligand, product **4a** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (20.3 mg, 92%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.31 – 7.20 (m, 3H), 7.10 – 7.05 (m, 2H), 5.62 (ddt, *J* = 9.8, 4.8, 2.2 Hz, 1H), 5.51 – 5.43 (m, 1H), 2.84 (d, *J* = 13.5 Hz, 1H), 2.68 (d, *J* = 13.5 Hz, 1H), 2.32 – 2.21 (m, 1H), 2.17 – 2.08 (m, 2H), 1.98 (dq, *J* = 17.7, 2.7 Hz, 1H), 1.20 – 1.11 (m, 1H), 0.99 (d, *J* = 6.7 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.28, 136.00, 133.50, 130.38, 128.34, 126.81, 124.05, 50.16, 44.13, 37.71, 30.11, 28.34, 21.69. **IR** (ATR): 3024, 2955, 2924, 2868, 2837, 1722, 1495, 1453, 755, 717, 700 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{18}O_3NH_4$ $[M + NH_4]^+$: 232.1701, found: 232.1691. $[\alpha]_D^{25.6}$ –2.13 (*c* 0.750, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** 95% *ee*, 250 mm CHIRALCEL IC, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 10.03 min, $t_{R2}$ (minor) = 12.33 min.

**(*1S*,*5R*)-5-Methyl-1-(3,4,5-trimethoxybenzyl)cyclohex-3-ene-1-carbaldehyde (4b)**

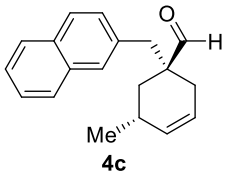


**4b**

Using (*R*)-DTBM-SDP as the ligand, product **4b** was obtained as the major product and isolated by preparative TLC (eluting with 20% EtOAc in hexanes) as a colorless oil (27.8 mg, 91%, <5% isomerized cyclohexenecarbaldehyde **7b** included). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 6.27 (s, 2H), 5.64 (ddt, *J* = 9.8, 4.9, 2.2 Hz, 1H), 5.49 (ddd, *J* = 10.1, 3.0, 1.6 Hz, 1H), 3.83 (d, *J* = 2.3 Hz, 10H), 2.82 (d, *J* = 13.6 Hz, 1H), 2.60 (d, *J* = 13.6 Hz, 1H), 2.29 (ddd, *J* = 17.6, 5.2, 1.9 Hz, 1H), 2.19 – 2.10 (m, 2H), 1.99 (dq, *J* = 17.6, 2.8 Hz, 1H), 1.23 – 1.11 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.6, 153.0, 137.0, 133.6, 131.7, 124.0, 107.4, 107.4, 61.0, 56.3, 50.1, 44.8, 38.1, 30.4, 28.3, 21.7. **IR** (ATR): 2927, 2838, 2360,

1723, 1589, 1507, 1456, 1421, 1334, 1240, 1125, 1009, 835 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{18}H_{24}O_4Na$ $[M + Na]^+$: 327.1572, found: 327.1563. $[\alpha]_D^{25.9}$ –4.3 (*c* 1.05, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** 98% *ee*, 100 mm CHIRALCEL AD-H, 4% *i*PrOH, 3 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 15.53 min, $t_{R2}$ (minor) = 17.42 min.

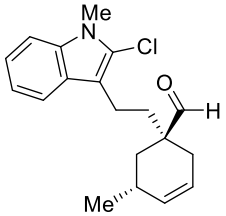
**(*1S*,*5R*)-5-methyl-1-(naphthalen-2-ylmethyl)cyclohex-3-ene-1-carbaldehyde** (**4c**)



**4c**

Using (*R*)-DTBM-SDP as the ligand, product **4c** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (20.9 mg, 79%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.84 – 7.74 (m, 4H), 7.56 – 7.54 (m, 1H), 7.51 – 7.43 (m, 2H), 7.21 (dd, *J* = 8.4, 1.8 Hz, 1H), 5.62 (ddt, *J* = 9.8, 4.8, 2.2 Hz, 1H), 5.50 – 5.44 (m, 1H), 3.01 (d, *J* = 13.5 Hz, 1H), 2.85 (d, *J* = 13.5 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.23 – 2.16 (m, 1H), 2.14 (dt, *J* = 12.4, 4.4 Hz, 1H), 2.05 (ddt, *J* = 17.6, 4.3, 2.5 Hz, 1H), 1.21 (dd, *J* = 12.6, 10.7 Hz, 1H), 0.99 (d, *J* = 6.7 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 133.6, 133.5, 133.4, 132.4, 128.9, 128.7, 127.9, 127.7, 126.3, 125.8, 124.0, 50.3, 44.3, 37.8, 30.3, 28.4, 21.7. **IR** (ATR): 3054, 3019,2955, 2925, 2870, 2849, 1721, 1599, 1507, 1454, 1264, 1073, 1017, 907, 857, 820, 730 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{19}H_{20}ONa$ $[M + Na]^+$: 287.1412, found: 287.1421. $[\alpha]_D^{24}$ –22.2 (*c* 1.135, $CDCl_3$). **SFC analysis (of the corresponding alcohol):** 96% *ee*, 100 mm CHIRALCEL AD-H, 8% *i*PrOH, 3 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 7.42 min, $t_{R2}$ (minor) = 8.72 min.

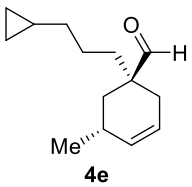
**(*1S*,*5R*)-1-(2-(2-chloro-1-methyl-1*H*-indol-3-yl)ethyl)-5-methylcyclohex-3-ene-1-carbaldehyde** (**4d**) Using (*R*)-DTBM-SDP as the ligand, product **4d** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a yellow oil (26.5 mg, 84%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.47 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.22 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.13 (ddd, *J* = 8.0, 6.7, 1.4 Hz, 1H), 5.71 (ddt, *J* = 9.8, 4.9, 2.3 Hz, 1H), 5.53 (ddt, *J* = 10.0, 3.3, 1.6 Hz, 1H), 3.71 (s, 3H), 2.80 – 2.55 (m, 3H), 2.19 – 1.98 (m, 4H), 1.88 (ddd, *J* = 14.1, 11.8, 5.3 Hz, 2H), 1.71 (ddd, *J* = 14.0, 11.9, 5.3 Hz, 2H), 1.27 – 1.16 (m, 3H), 1.02 (d, *J* = 6.7 Hz, 3H).**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.5,



**4d**

135.8, 133.5, 126.3, 124.2, 123.5, 121.9, 119.8, 118.1, 110.7, 109.3, 49.5, 37.8, 30.0, 29.9, 29.9, 29.7, 28.2, 21.8, 18.6. **IR** (ATR): 3056, 3018, 2952, 2925, 2870, 1723, 1612, 1493, 1470, 1455, 1426, 1348, 1328, 1304, 1264, 1188, 1089, 1038, 1020, 993, 737, 691 $cm^{-1}$. **HRMS** (CI-TOF) *m* / *z* calcd for $C_{19}H_{22}OClN$ $[M]^+$: 315.1390, found: 315.1399. $[\alpha]_D^{25.8}$ –22.7 (*c* 1.325, $CDCl_3$). **SFC analysis (of the corresponding alcohol):** 97% *ee*, 100 mm CHIRALCEL AD-H, 7% *i*PrOH, 3 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 10.52 min, $t_{R2}$ (minor) = 9.24 min.

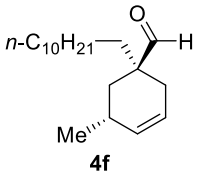
**(*1S*,*5R*)-1-(3-cyclopropylpropyl)-5-methylcyclohex-3-ene-1-carbaldehyde** (**4e**)



**4e**

Using (*R*)-DTBM-SDP as the ligand, product **4e** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (16.1 mg, 78%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 5.66 (ddt, *J* = 9.9, 5.0, 2.3 Hz, 1H), 5.48 (ddq, *J* = 10.0, 3.2, 1.5 Hz, 1H), 2.49 – 2.37 (m, 1H), 2.17 – 2.07 (m, 1H), 2.08 – 2.00 (m, 1H), 1.86 (ddt, *J* = 17.8, 4.8, 2.6 Hz, 1H), 1.63 – 1.55 (m, 1H), 1.55 – 1.49 (m, 1H), 1.46 – 1.39 (m, 1H), 1.39 – 1.34 (m, 1H), 1.34 – 1.20 (m, 3H), 1.19 – 1.07 (m, 3H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.68 – 0.57 (m, 1H), 0.43 – 0.36 (m, 2H), 0.01 – -0.05 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.1, 133.4, 124.3, 49.5, 38.0, 37.7, 35.4, 29.9, 28.3, 23.7, 21.8, 10.8, 4.6, 4.5. **IR** (ATR): 3075, 3018, 3001, 2954, 2927, 2870, 2846, 2688, 1725, 1456, 1013, 820, 716, 679 $cm^{-1}$. **HRMS** (CI-TOF) *m* / *z* calcd for $C_{14}H_{22}ONH_4$ $[M + NH_4]^+$: 224.2014, found: 224.2011. $[\alpha]_D^{25.1}$ –21.6 (*c* 0.805, $CHCl_3$). **SFC analysis (of the corresponding benzoic ester after $NaBH_4$ reduction):** 93% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 5.63 min, $t_{R2}$ (minor) = 6.10 min.

**(*1S*,*5R*)-5-Methyl-1-undecylcyclohex-3-ene-1-carbaldehyde** (**4f**)

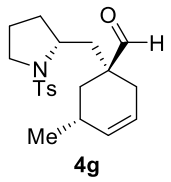


**4f**

Using (*R*)-DTBM-SDP as the ligand, product **4g** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (20.5 mg, 74%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 5.65 (ddd, *J* = 9.9, 5.0, 2.4 Hz, 1H), 5.48 (ddd, *J* = 10.0, 3.0, 1.5 Hz, 1H), 2.49 – 2.33 (m, 1H), 2.09 (ddt, *J* = 6.8, 4.6, 2.2 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.84 (ddt, *J* = 17.8, 4.6, 2.5 Hz, 1H), 1.55 – 1.45 (m, 1H), 1.41 – 1.33 (m, 1H), 1.26 (m, 18H), 1.11 (dd, *J* = 12.9,

11.0 Hz, 1H), 0.99 (d, $J$ = 6.8 Hz, 3H), 0.93 – 0.84 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.1, 133.4, 124.3, 49.5, 38.0, 32.1, 30.4, 29.9, $29.7_8$, $29.7_7$, $29.7_5$, $29.6_9$, $29.5_7$, $29.4_9$, 28.3,23.6, 22.8, 21.8, 14.3, 0.2. **IR** (ATR): 3019, 2954, 2923, 2852, 2690, 1726, 1456, 915, 718, 682 cm$^{-1}$. **HRMS** (CI-TOF) $m$ / $z$ calcd for $C_{19}H_{34}ONH_4$ $[M + NH_4]^+$: 296.2953, found: 296.2965. $[\alpha]_D^{26.0}$ – 7.6 ($c$ 1.0, $CHCl_3$). **SFC analysis (of the corresponding benzoic ester after $NaBH_4$ reduction):** 93% *ee*, 250 mm CHIRALCEL IC, 2% *i*PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 9.27 min, $t_{R2}$ (minor) = 10.09 min.

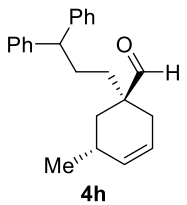
**(*1S*,*5R*)-5-methyl-1-(((*R*)-1-tosylpyrrolidin-2-yl)methyl)cyclohex-3-ene-1-carbaldehyde** (**4g**)



**4g**

Using (*R*)-DTBM-SDP as the ligand, product **4g** was obtained as the major product and isolated by preparative TLC (eluting with 25% EtOAc in hexanes) as a colorless oil (30.7 mg, 85%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.68 (d, $J$ = 8.2 Hz, 2H), 7.33 (d, $J$ = 8.3 Hz, 2H), 5.67 (dd, $J$ = 9.9, 5.2 Hz, 1H), 5.49 (d, $J$ = 10.2 Hz, 1H), 3.55 (ddd, $J$ = 13.8, 7.0, 3.3 Hz, 1H), 3.39 – 3.30 (m, 1H), 3.11 (dt, $J$ = 10.6, 6.9 Hz, 1H), 2.52 (dd, $J$ = 18.3, 2.3 Hz, 1H), 2.43 (s, 3H), 2.23 (dd, $J$ = 14.3, 2.5 Hz, 1H), 2.06 (d, $J$ = 14.2 Hz, 3H), 1.78 (dd, $J$ = 12.0, 8.0 Hz, 1H), 1.72 (dd, $J$ = 14.5, 7.4 Hz, 1H), 1.58 – 1.49 (m, 1H), 1.44 – 1.27 (m, 2H), 1.17 (dd, $J$ = 14.2, 12.9 Hz, 1H), 0.98 (d, $J$ = 6.4 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.9, 143.7, 134.3, 133.4, 129.9, 127.7, 123.8, 56.3, 49.1, 48.8,45.9, 38.6, 33.3, 30.0, 28.0, 24.4, 21.70, 21.68. **IR** (ATR): 2954, 1722, 1597, 1453, 1340, 1157, 1090, 815, 730, 662 cm$^{-1}$. **HRMS** (ESI-TOF) $m$ / $z$ calcd for $C_{20}H_{27}NO_3SNa$ $[M + Na]^+$: 384.1609, found: 384.1613. $[\alpha]_D^{25.1}$ –89.1 ($c$ 0.800, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** >20:1 *dr*, 100 mm CHIRALCEL AD-H, 5% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 19.46 min, $t_{R2}$ (major) = 21.13 min.

**(*1S*,*5R*)-1-(3,3-diphenylpropyl)-5-methylcyclohex-3-ene-1-carbaldehyde** (**4h**)

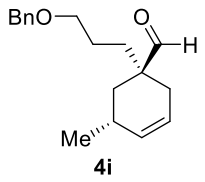


**4h**

Using (*R*)-DTBM-SDP as the ligand, product **4h** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (42.6 mg, 71%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 7.37 – 7.11 (m, 10 H), 5.63 (ddt, $J$ = 9.9, 4.9, 2.4 Hz, 1H), 5.47 (dq, $J$ = 10.1, 1.4 Hz, 1H), 3.79 (t, $J$ = 7.8 Hz, 1H), 2.51 – 2.37 (m, 1H), 2.13 – 1.87 (m, 5H), 1.83 (ddt, $J$ = 17.8, 4.7, 2.7 Hz, 1H), 1.51 (ddd, $J$ = 13.8, 12.2, 4.3 Hz, 1H), 1.37 (ddd, $J$ = 14.0, 12.6, 5.0 Hz,

1H), 1.12 (s, 1H), 0.96 (d, $J$ = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.7, 144.6$_0$, 144.5$_6$, 133.4, 128.7, 127.8$_5$, 127.8$_1$, 126.4, 124.1, 51.9, 49.3, 37.9, 36.1, 29.8, 29.5, 28.2, 21.7. **IR** (ATR): 3024, 2925, 1722, 1599, 1493, 1450, 801, 765, 747, 735, 698 cm$^{-1}$. **HRMS** (ESI-TOF) $m$ / $z$ calcd for $C_{23}H_{26}ONH_4$ $[M + Na]^+$: 336.2327, found: 336.2335. $[\alpha]_D^{26.6}$ –12.7 ($c$ 0.700, $CDCl_3$). **SFC analysis (of the corresponding alcohol):** 88% *ee*, 100 mm CHIRALCEL AD-H, 6% *i*PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 9.95 min, $t_{R2}$ (minor) = 8.38 min.

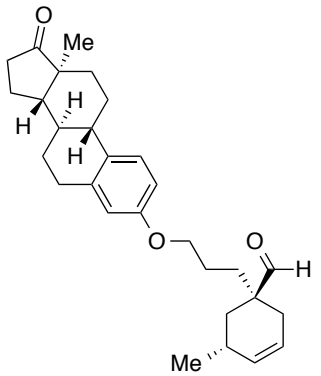
**(*1S*,5*R*)-1-(3-(Benzyloxy)propyl)-5-methylcyclohex-3-ene-1-carbaldehyde (4i)**



**4i**

Using (*R*)-DTBM-SDP as the ligand, product **4i** was obtained as the major product and isolated by preparative TLC (eluting with 10% EtOAc in hexanes) as a colorless oil (20.4 mg, 75%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.39 – 7.27 (m, 5H), 5.65 (ddd, $J$ = 9.8, 5.0, 2.4 Hz, 1H), 5.49 (d, $J$ = 10.1 Hz, 1H), 4.48 (s, 2H), 3.46 – 3.39 (m, 2H), 2.42 (ddd, $J$ = 17.7, 5.0, 1.7 Hz, 1H), 2.09 (ddd, $J$ = 8.9, 4.3, 2.2 Hz, 1H), 2.06 – 1.96 (m, 1H), 1.86 (ddd, $J$ = 17.7, 5.2, 3.2 Hz, 1H), 1.63 – 1.54 (m, 2H), 1.53 – 1.42 (m, 2H), 1.13 (dd, $J$ = 13.0, 11.3 Hz, 1H), 0.99 (d, $J$ = 6.9 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.8, 138.6, 133.5, 128.6, 127.82, 127.79, 124.2, 73.1, 70.5, 49.1, 38.0, 34.3, 29.9, 28.3, 24.1, 21.8. **IR** (ATR): 3019, 2925, 2853, 1724, 1454, 1361, 1203, 1097, 734, 697 cm$^{-1}$. **HRMS** (CI-TOF) $m$ / $z$ calcd for $C_{18}H_{24}O_2H$ $[M + H]^+$: 273.1855, found: 273.1866. $[\alpha]_D^{25.2}$ –65.4 ($c$ 0.0933, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** 90% *ee*, 100 mm CHIRALCEL IC, 5% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 13.04 min, $t_{R2}$ (minor) = 14.77 min.

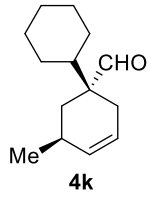
**(1*S*,5*R*)-5-Methyl-1-(3-(((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)propyl)cyclohex-3-ene-1-carbaldehyde (4j)** Using (*R*)-DTBM-SDP as the ligand, product **4j** was obtained as the major product and isolated by preparative TLC (eluting with 25% EtOAc in hexanes) as a white solid (37.1 mg, 85%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.19 (d, $J$ = 8.6 Hz, 1H), 6.69 (d, $J$ = 8.6 Hz, 1H), 6.62 (s, 1H), 5.66 (s, 1H), 5.51 (d,



**4j**

$J$ = 9.4 Hz, 1H), 3.89 (d, $J$ = 5.3 Hz, 2H), 2.89 (d, $J$ = 4.4 Hz, 2H), 2.55 – 2.37 (m, 3H), 2.26 (s, 1H), 2.19 – 2.10 (m, 2H), 2.10 – 1.98 (m, 4H), 1.93 (dd, $J$ = 30.2, 13.7 Hz, 3H), 1.71 (d, $J$ = 9.1 Hz, 2H), 1.68 – 1.57 (m, 5H), 1.54 – 1.38 (m, 5H), 1.17 (t, $J$ = 11.9 Hz, 1H), 1.00 (d, $J$ = 6.7 Hz, 3H), 0.92 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 221.1, 205.8, 157.1, 138.0, 133.5, 132.3, 126.5, 124.1, 114.8, 112.3, 68.0, 50.6, 49.1, 48.2, 44.2, 38.6, 38.0, 36.1, 34.2, 31.8, $29.9_2$, $29.8_5$, 28.3, 26.8, 26.1, 23.8, 21.8, 14.1. **IR** (ATR): 2929, 2873, 1731, 1611, 1573, 1497, 1255, 1056, 1005, 721 cm$^{-1}$. **HRMS** (CI-TOF) $m$ / $z$ calcd for $C_{29}H_{38}O_3Na$ $[M + Na]^+$: 457.2719, found: 457.2729. $[\alpha]_D^{25}$ +99.0 ($c$ 0.487, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** >20:1 *dr*, 100 mm CHIRALCEL IC, 20% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 20.06 min, $t_{R2}$ (major) = 21.59 min.

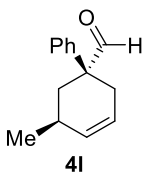
**(1*R*,5*S*)-5-Methyl-[1,1'-bi(cyclohexan)]-3-ene-1-carbaldehyde (4k)**



**4k**

Using (*S*)-Ph-SDP as the ligand, product **4k** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (14.1 mg, 68%). **4k**:**6k**=3:1. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.45 (s, 1H), 5.66 (ddt, $J$ = 9.9, 5.0, 2.4 Hz, 1H), 5.45 (ddq, $J$ = 10.0, 3.2, 1.6 Hz, 1H), 2.38 – 2.30 (m, 1H), 2.04 (ddqt, $J$ = 11.4, 9.1, 4.6, 2.3 Hz, 1H), 1.96 (ddt, $J$ = 13.0, 5.5, 1.7 Hz, 1H), 1.92 – 1.85 (m, 1H), 1.84 – 1.71 (m, 3H), 1.67 (dtt, $J$ = 10.8, 3.2, 1.5 Hz, 1H), 1.61 – 1.54 (m, 1H), 1.46 (tt, $J$ = 12.1, 3.1 Hz, 1H), 1.30 – 1.00 (m, 6H), 0.99 (d, $J$ = 6.9 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 206.8, 133.1, 124.8, 52.4, 43.8, 35.4, 28.3, 27.9, 27.0, 26.9, 26.7, 26.6, 26.6, 21.8. **IR** (ATR): 3018, 2924, 2852, 2693, 1724, 1450, 1008, 912, 846, 805, 716, 695 cm$^{-1}$. **HRMS** (CI-TOF) $m$ / $z$ calcd for $C_{14}H_{22}ONH_4$ $[M + NH_4]^+$: 224.2014, found: 224.2017. $[\alpha]_D^{25.2}$ +49.4 ($c$ 0.575, $CHCl_3$). **SFC analysis (of the corresponding benzoic ester after $NaBH_4$ reduction):** >99% *ee*, 100 mm CHIRALCEL AD-H, 5% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 5.49 min, $t_{R2}$ (minor) = 5.05 min.

**(*1R*,*3S*)-3-Methyl-3,6-dihydro-[1,1'-biphenyl]-1(2H)-carbaldehyde (4l)**

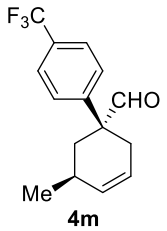


**4l**

Using (*S*)-Ph-SDP as the ligand (0.5 mmol scale reaction), product **4l** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (68.9 mg, 68%). **4l**:**6l**:**8l**=6:2:1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.43 – 7.35 (m, 2H), 7.33 – 7.27 (m, 3H), 5.75 (ddt, $J$ = 9.9,

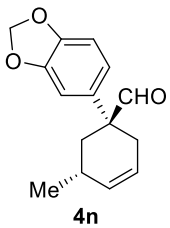
4.9, 2.3 Hz, 1H), 5.56 (ddq, *J* = 10.0, 2.9, 1.4 Hz, 1H), 2.88 (ddtd, *J* = 17.5, 5.2, 2.2, 1.5 Hz, 1H), 2.57 (dddd, *J* = 13.1, 5.4, 2.3, 1.2 Hz, 1H), 2.33 – 2.22 (m, 1H), 2.23 – 2.14 (m, 1H), 1.62 (dd, *J* = 13.1, 11.2 Hz, 1H), 1.10 (d, *J* = 6.9 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.7, 140.3, 132.9, 129.1, 127.6, 126.8, 124.3, 53.7, 36.1, 31.6, 28.6, 21.8. **IR** (ATR): 3021, 2995, 2925, 2870, 2700, 1723, 1493, 1446, 1140, 827, 757, 715, 697, 676 $cm^{-1}$. $[\alpha]_D^{26.1}$ +244.8 (*c* 0.750, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** >99% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 4.80 min, $t_{R2}$ (minor) = 5.70 min.

**(*1R*,*3S*)-3-Methyl-4'-(trifluoromethyl)-3,6-dihydro-[1,1'-biphenyl]-1(2H)-carbaldehyde** (**4m**) Using (*S*)-Ph-SDP as the ligand, product **4m** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (17.4 mg, 65%). **4m**:**6m**:**8m**=6:2:1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 7.64 (dt, *J* = 8.2, 0.7 Hz, 2H), 7.43 (dt, *J* = 7.7, 0.9 Hz, 2H), 5.75 (ddt, *J* = 9.9, 4.9, 2.3 Hz, 1H), 5.58 (ddq, *J* = 10.0, 2.9, 1.4 Hz, 1H), 2.94 – 2.85 (m, 1H), 2.58 (dddd, *J* = 13.0, 5.5, 2.3, 1.2 Hz, 1H), 2.29 (dtt, *J* = 9.3, 5.4, 2.2 Hz, 1H), 2.24 – 2.16 (m, 1H), 1.63 (dd, *J* = 13.0, 11.2 Hz, 1H), 1.11 (d, *J* = 6.9 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.3, 144.5, 133.1, 127.2, 126.0 (q, *J* = 3.8 Hz), 123.8, 53.8, 36.3, 31.6, 28.5, 21.7. **IR** (ATR): 2959, 1726, 1324, 1166, 1122, 1069, 1016, 833, 715, 605 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{15}F_3O$ $[M]^+$: 268.1075, found: 268.1073. $[\alpha]_D^{25}$ +72.4 (*c* 0.396, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** 98% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 3.92 min, $t_{R2}$ (minor) = 4.85 min.



**4m**

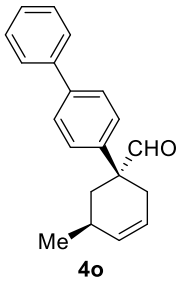
**(*1S*,*5R*)-1-(Benzo[d][1,3]dioxol-5-yl)-5-methylcyclohex-3-ene-1-carbaldehyde** (**4n**) Using (*R*)-Ph-SDP as the ligand, product **7i** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (15.4 mg, 63%). **4n**:**6n**:**8n**=6:2:1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 6.82 – 6.77 (m, 2H), 6.73 (dd, *J* = 8.1, 1.9 Hz, 1H), 5.95 (s, 2H), 5.72 (ddt, *J* = 9.9, 5.0, 2.4 Hz, 1H), 5.53 (ddd, *J* = 9.8, 3.1, 1.8 Hz, 1H), 2.85 – 2.77 (m, 1H), 2.49 (dddd, *J* = 13.1, 5.5, 2.3, 1.2 Hz, 1H), 2.29 – 2.16 (m, 1H), 2.16 – 2.07 (m, 1H), 1.53 (dd, *J* = 13.0, 11.2 Hz, 1H), 1.08 (d, *J* = 7.0 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.1,



**4n**

148.3, 146.9, 133.9, 132.7, 124.1, 120.0, 108.5, 107.2, 101.2, 53.2, 36.2, 31.6, 28.5, 21.6. **IR** (ATR): 3020, 2955, 1720, 1505, 1485, 1239, 1126, 1038, 934, 809, 712 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{16}O_3Na$ $[M+Na]^+$: 267.0997, found: 267.0990. $[\alpha]_D^{25}$ –96.1 (*c* 0.627, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** >99% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 15.24 min, $t_{R2}$ (minor) = 18.03 min.

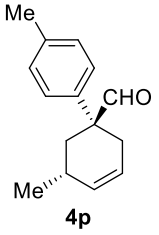
**(*1R*,*3S*)-3-methyl-3,6-dihydro-[1,1':4',1''-terphenyl]-1(2H)-carbaldehyde** (**4o**)



**4o**

Using (*S*)-Ph-SDP as the ligand, product **4o** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (18.0 mg, 65%). **4o**:**6o**:**8o**=6:2:1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.64 – 7.56 (m, 4H), 7.49 – 7.42 (m, 2H), 7.41 – 7.33 (m, 3H), 5.77 (ddt, *J* = 9.8, 4.8, 2.3 Hz, 1H), 5.58 (dq, *J* = 10.0, 1.6 Hz, 1H), 2.97 – 2.87 (m, 1H), 2.67 – 2.57 (m, 1H), 2.30 (ddt, *J* = 9.4, 4.4, 2.4 Hz, 1H), 2.23 (ddt, *J* = 16.8, 4.2, 2.1 Hz, 1H), 1.65 (dd, *J* = 13.1, 11.1 Hz, 1H), 1.12 (d, *J* = 6.9 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.6, 140.6, 140.50, 139.23, 133.0, 129.0, 127.8, 127.6, 127.2, 124.2, 53.5, 36.3, 31.6, 28.6, 21.81. **IR** (ATR): 3391, 3016, 2952, 2869, 1486, 1041, 829, 765, 732, 696 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{20}H_{20}ONa$ $[M+Na]^+$: 299.1412, found: 299.1409. $[\alpha]_D^{25}$ –0.76 (*c* 0.567, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** 98% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 10.22 min, $t_{R2}$ (minor) = 9.22 min.

**(1*S*,3*R*)-3,4'-Dimethyl-3,6-dihydro-[1,1'-biphenyl]-1(2*H*)-carbaldehyde (4p)**

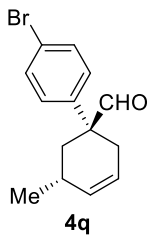


**4p**

Using (*R*)-Ph-SDP as the ligand, product **4q** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (11.6 mg, 54%). **4p**:**6p**:**8p**=3:1:1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.19 (s, 4H), 5.75 (ddt, *J* = 9.9, 5.0, 2.3 Hz, 1H), 5.59 – 5.51 (m, 1H), 2.92 – 2.80 (m, 1H), 2.55 (dddd, *J* = 13.1, 5.5, 2.2, 1.2 Hz, 1H), 2.35 (s, 4H), 2.21 – 2.10(m, 1H), 1.64 – 1.53 (m, 2H), 1.10 (d, *J* = 7.0 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.8, 137.4, 137.3, 133.0, 129.9, 126.7, 124.4, 53.4, 36.2, 28.6, 21.9, 21.2. **IR** (ATR): 3021, 2955, 2923, 1723, 1513, 1455, 1020, 810, 720, 710 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{18}ONa$

[M+Na]$^+$: 237.1255, found: 237.1250. $[\alpha]_D^{25}$ –115.4 (*c* 0.367, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** >99% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 7.18 min, $t_{R2}$ (major) = 8.26 min.

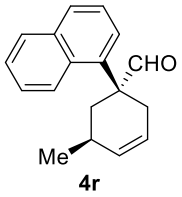
**(1*S*,3*R*)-4'-Bromo-3-methyl-3,6-dihydro-[1,1'-biphenyl]-1(2H)-carbaldehyde** (**4q**)



**4q**

Using (*R*)-Ph-SDP as the ligand, product **4r** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (17.8 mg, 63%). **4q**:**6q**:**8q**=3:1:1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 5.74 (dddd, *J* = 16.9, 10.3, 8.1, 6.7 Hz, 2H), 5.18 – 4.98 (m, 4H), 4.34 – 4.18 (m, 2H), 2.54 (dd, *J* = 13.6, 6.7 Hz, 2H), 2.19 (dd, *J* = 13.6, 8.1 Hz, 2H), 1.89 – 1.72 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 200.4, 139.4, 133.1, 132.2, 128.6, 124.0, 121.9, 53.4, 36.2, 31.6, 28.6, 21.8. **IR** (ATR): 2956, 2870, 1724, 1491, 1265, 1078, 1008, 817, 720, 694 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{14}H_{15}BrONa$ [M+Na]$^+$: 301.0204, found: 301.0159. $[\alpha]_D^{25}$ –105.7 (*c* 0.613, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** >99% *ee*, 100 mm CHIRALCEL AD-H, 3% *i*PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.29 min, $t_{R2}$ (major) = 10.75 min.

**(*1R*,*5S*)-5-Methyl-1-(naphthalen-1-yl)cyclohex-3-ene-1-carbaldehyde** (**4r**)

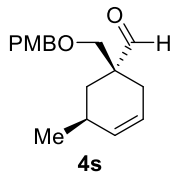


**4r**

Using (*S*)-Tol-SDP as the ligand (0.2 mmol scale), product **4r** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (17.8 mg, 35%). **4r**:**6r**=1:1.5. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.64 – 7.56 (m, 4H), 7.49 – 7.42 (m, 2H), 7.41 – 7.33 (m, 3H), 5.77 (ddt, *J* = 9.8, 4.8, 2.3 Hz, 1H), 5.58 (dq, *J* = 10.0, 1.6 Hz, 1H), 2.97 – 2.87 (m, 1H), 2.67 – 2.57 (m, 1H), 2.30 (ddt, *J* = 9.4, 4.4, 2.4 Hz, 1H), 2.23 (ddt, *J* = 16.8, 4.2, 2.1 Hz, 1H), 1.65 (dd, *J* = 13.1, 11.1 Hz, 1H), 1.12 (d, *J* = 6.9 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 202.4, 137.6, 134.8, 132.5, 131.8, 129.5, 129.2, 126.3, 125.6, 125.3, 124.5, 124.5, 54.2, 37.0, 32.2, 28.2, 21.8. **IR** (ATR): 3049, 3020, 2955, 2926, 2870, 2698, 1723, 1599, 1510, 1400, 1028, 1024, 907, 799, 775, 730, 712 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{18}H_{18}ONa$ [M+Na]$^+$: 273.1255, found: 273.1245. $[\alpha]_D^{24}$ +229.4 (*c* 0.755, $CDCl_3$). **SFC analysis (of the corresponding alcohol):**

96% *ee*, 100 mm CHIRALCEL AD-H, 7% *i*PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 7.17 min, $t_{R2}$ (minor) = 7.90 min.

**(*1R*,*5S*)-1-(((4-Methoxybenzyl)oxy)methyl)-5-methylcyclohex-3-ene-1-carbaldehyde (4s)**



**4s**

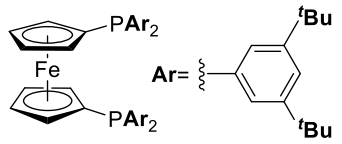
Using (*S*)-Ph-SDP as the ligand, product **4s** was obtained as the major product and isolated by preparative TLC (eluting with 5% EtOAc in hexanes) as a colorless oil (9.9 mg, 36%). **4s**:**8s**=1:1.8. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.66 (ddt, *J* = 9.9, 4.9, 2.3 Hz, 1H), 5.55 – 5.46 (m, 1H), 4.40 (d, *J* = 2.6 Hz, 2H), 3.82 (s, 4H), 3.48 (d, *J* = 9.0 Hz, 1H), 3.38 – 3.31 (m, 1H), 2.59 – 2.48 (m, 1H), 2.20 – 2.06 (m, 2H), 1.92 (dq, *J* = 18.0, 3.0 Hz, 1H), 1.16 – 1.06 (m, 1H), 0.99 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.7, 159.4, 133.6, 130.1, 129.5, 129.3, 123.8, 123.1, 113.9, 75.5, 73.2, 55.4, 50.5, 34.5, 28.4, 27.5, 21.7. **IR** (ATR): 3018, 2954, 2924, 2850, 2695, 1729, 1611, 1586, 1512, 1455, 1302, 1245, 1172, 1086, 1033, 818, 755, 719, 686 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{17}H_{22}O_3Na$ $[M+Na]^+$: 297.1467, found: 297.1466. $[\alpha]_D^{24.4}$ +12.2 (*c* 0.495, $CHCl_3$). **SFC analysis (of the corresponding alcohol):** 71% *ee*, 100 mm CHIRALCEL AD-H, 7% *i*PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 6.48 min, $t_{R2}$ (minor) = 7.11 min.

## 3. Preparation of Ligands and Substrates

1,1-Bis(diarylphosphino)ferrocenes (DTB-DPPF, DTBM-DPPF and DTMS-DPPF) were synthesized by a modified procedure (DTB=3,5-(di-*t*-butyl)phenyl, DTBM=3,5-(di-*t*-butyl)-4-methoxyphenyl, DTMS=3,5-bis(trimethylsilyl)phenyl)).[2]

***Representative procedure for DTB-DPPF***: An oven dried round-bottom flask was charged with magnesium turnings (84 mg, 3.5 mmol, 1.1 equiv), an iodine crystal, THF (3 ml), and a magnetic stir bar. A reflux condenser was attached to the flask and the top was sealed with a septum. 3,5-Di(*t*-butyl)bromobenzene (861 mg, 3.2 mmol, 8.0 equiv) was added dropwise to the reaction mixture via syringe at rt. Once all of the aryl bromide was added, the mixture was brought to reflux (73 °C). After 2 h, the reaction mixture was cooled to rt. 1,1'-

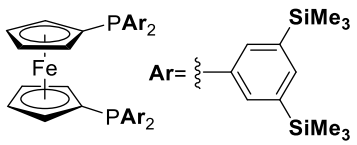
bis(dichlorophosphino)ferrocene (154 mg, 0.4 mmol, 1 equiv) was added to the Grignard solution. After stirring for 12 h, the reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 times). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The pure ligand was obtained by recrystallization from hexanes to afford the 1,1'-bis(di(3,5-*t*-butylphenyl)phosphino)ferrocene as a yellow solid (77.2 mg, 19% yield).




DTB-DPPF

**1,1'-Bis(bis(3,5-di-*tert*-butylphenylphosphino)ferrocene (DTB-DPPF)**

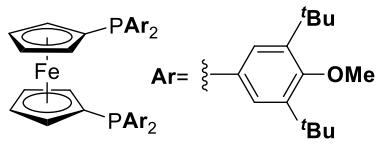
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 (s, 4H), 7.25 (dd, *J* = 9.9, 2.6 Hz, 8H), 4.28 (s, 4H), 4.05 (s, 4H), 1.26 (s, 72H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ $150.4_4$, $150.3_8$, 128.2, 128.1, 122.9, 73.6, 73.5, 72.7, 35.1, 31.6. **$^{31}$P NMR** (162 MHz, $CDCl_3$) δ -14.2. **MS** (ESI-TOF) *m* / *z* calcd for $C_{66}H_{93}FeP_2$ $[M+H]^+$: 1003.6, found: 1003.5.




DTMS-DPPF

**1,1'-Bis(bis(3,5-di-(trimethylsilyl)phenylphosphino)ferrocene (DTMS-DPPF)**

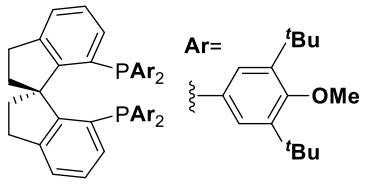
The tile compound was isolated as a yellow solid (160.8 mg, 36% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.61 (s, 4H), 7.52 (d, *J* = 7.5 Hz, 8H), 4.23 (s, 4H), 4.01 (s, 4H), 0.22 (s, 72H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 139.3, 139.2, $139.1_4$, $139.1_1$, 138.4, 73.5, 73.4, 72.3, -1.0. **$^{31}$P NMR** (162 MHz, $CDCl_3$) δ -17.2. **MS** (ESI-TOF) *m* / *z* calcd for $C_{58}H_{93}FeP_2Si_8$ $[M+H]^+$: 1131.4,found: 1131.4.




DTBM-DPPF

**1,1'-Bis(bis(3,5-di-*tert*-butyl-4-methoxyphenylphosphino)ferrocene, DTBM-DPPF**

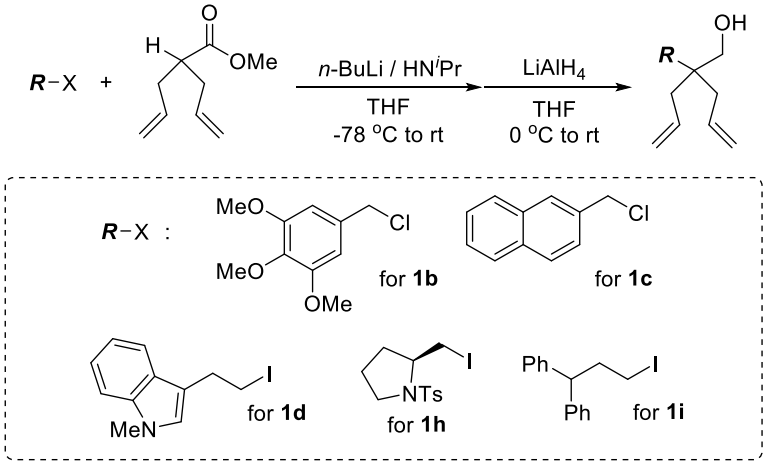
1,1'-Bis(dichlorophosphino)ferrocene (230 mg, 0.595 mmol, 1 equiv), 1-bromo-3,5-di(*t*-butyl)-4-methoxybenzene (887 mg, 2.98 mmol, 5 equiv), Mg turnings (79 mg, 3.27 mmol, 6 equiv) was used. The title compound was isolated by recrystallization as an orange solid (371 mg, 55% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 11.0 Hz, 8H), 4.66 (s, 4H), 4.33 (s, 4H), 3.68 (s, 12H), 1.37 (s, 72H). **$^{31}$P NMR** (162 MHz, $CDCl_3$) δ -12.0. **MS** (ESI-TOF) *m* / *z* calcd for $C_{70}H_{101}FeO_4P_2$ $[M+H]^+$: 1123.7, found: 1123.6.




(*R*)-DTBM-SDP

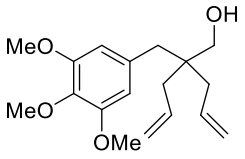
(*R*)-DTBM-SDP was synthesized by modified procedure reported by Zhou[3] using (*R*)-spinol triflate (410 mg, >99% *ee*) and bis(3,5-*t*-butyl-4-methoxyphenyl)phosphine oxide. Pure (*R*)-DTBM-SDP (455 mg) was obtained as a white solid. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.32 (m, 2H), 7.29 – 7.24 (m, 2H), 7.21 – 7.18 (m, 2H), 7.17 – 7.12 (m, 4H), 7.03 – 6.92 (m, 4H), 3.72 – 3.67 (m, 6H), 3.64 (s, 6H), 2.86 (dt, *J* = 17.5, 9.3 Hz, 2H), 2.52 (dd, *J* = 16.2, 8.7 Hz, 2H), 1.89 (dd, *J* = 12.8, 7.9 Hz, 2H), 1.50 (s, 2H), 1.39 – 1.30 (m, 36H), 1.17 – 1.04 (m, 36H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 162.6, 161.0, 150.7, 145.1, 144.0, 133.6, 133.4, 132.3, 132.0, 127.7, 64.8, 64.3, 38.3, 36.1, 35.9, 32.0, 31.9, 31.8, 30.5. **$^{31}$P NMR** (162 MHz, $CDCl_3$) δ -11.7. **MS** (ESI-TOF) *m* / *z* calcd for $C_{77}H_{10}O_4P_2Na$ $[M+Na]^+$: 1179.7, found: 1179.7. $[\alpha]_D^{26.8}$ +111 (*c* 0.355, $CHCl_3$).

Substrates **1a**, **1f**, **1k** and **1n-r** are known compounds and were prepared by reported procedures.




***Representative procedure for a-alkylation and reduction of ester (1b-OH)***

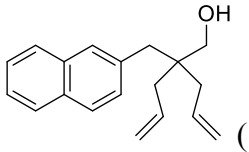
Methyl 2-allyl-4-pentenoate was prepared by a sequence involving bisallylation of Meldrum's acid, methanolysis by NaOMe/MeOH and decarboxylation. To a THF solution of diisopropylamine (0.84 mL, 6.0 mmol) was added dropwise *n*-BuLi (3.8 mL, 1.6 M solution in hexanes, 6.0 mmol) at 0 °C, and the solution was stirred for 20 min at 0 °C. The solution was cooled to –78 °C, and methyl 2-allyl-4-pentenoate (617 mg, 4.0 mmol) was then added dropwise to the solution. The solution was stirred for 30 min at –78 °C. A solution of 3,4,5-trimethoxybenzyl chloride (1.03 mg, 4.75 mmol) in THF was added dropwise to the solution. The mixture was warmed to rt and stirred overnight. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution and extracted with EtOAc. The organic layer was washed with aqueous 1N HCl and $H_2O$ three times, dried over $MgSO_4$, and concentrated *in vacuo*. The alkylated bisallylester was used without further purification. For reduction of the alkylated bisallylester, $LiAlH_4$ (455 mg, 12.0 mmol, 3.0 equiv) was added carefully to the THF solution of the α,α-bisallyl ester at 0 °C. The slurry was stirred for 4 h. The reaction mixture was quenched using the Fieser method and the solution was dried with $MgSO_4$, filtered, and concentrated. The pure alcohol **1b-OH** was obtained after column chromatography (3:1 hexanes:EtOAc) as a yellow oil (630 mg, 51% over two steps).



(**1b-OH**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.47 (s, 2H), 6.04 – 5.86 (m, 2H), 5.21 – 5.07 (m, 4H), 3.84 (s, 9H), 3.41 (s, 2H), 2.59 (s, 2H), 2.09 (dt, *J* = 7.5, 1.3 Hz, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 152.9, 134.8, 134.0, 118.1, 107.8, 67.1, 61.0, 56.2, 42.3, 41.0, 38.9. **IR** (ATR): 3481 (br), 3073, 2934, 2836, 1637, 1588, 1507, 1456, 1421, 1323, 1238, 1123, 1002, 912, 835, 781, 734, 699 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{18}H_{26}O_4Na$ $[M+Na]^+$: 329.1729, found: 329.1721.

In the synthesis of **1c-OH**, the representative α-alkylation and $LiAlH_4$ reduction procedure were applied. For the alkylation of bisallyl ester, methyl 2-allyl-4-pentenoate ester (617 mg, 4 mmol), diisopropylamine (0.84 mL, 6.0 mmol), *n*-BuLi (3.8 mL, 1.6 M solution in hexanes, 6.0 mmol), 2-naphthylmethyl chloride (1.06 g, 6.0 mmol) were used. For reduction of the ester, $LiAlH_4$ (174 mg, 2.02 mmol, 3.0 equiv) and THF (20.0 mL, 0.2 M) were used. The pure alcohol **1c-OH** was obtained by column chromatography (5:1 hexanes:EtOAc) as a yellow oil (410 mg, 39% over two steps).

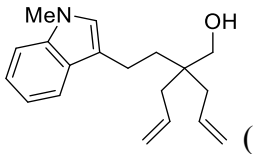


(**1c-OH**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.86 – 7.75 (m, 3H), 7.71 – 7.66 (m, 1H), 7.50 – 7.42 (m, 2H), 7.40 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.07 – 5.94 (m, 2H), 5.20 – 5.11 (m, 4H), 3.44 (s, 2H), 2.84 (s, 2H), 2.13 (dd, *J* = 7.4, 1.2 Hz, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 136.1, 134.9, 133.5, 132.3, 129.4, 129.2, 127.8, 127.7, 127.6, 126.1, 125.6, 118.3, 67.1, 42.7, 40.8, 39.0. **IR** (ATR): 3434 (br), 3056, 2975, 2922, 1637, 1600, 1507, 1439, 1414, 1350, 1323, 1265, 1018, 995, 751, 735 $cm^{-1}$. **HRMS** (CI-TOF) *m* / *z* calcd for $C_{19}H_{22}O$ $[M]^+$: 266.1671, found: 266.1674.

In the synthesis of **1d-OH**, the representative α-alkylation and $LiAlH_4$ reduction procedures were applied. For the alkylation of bisallyl ester, methyl 2-allyl-4-pentenoate ester (594 mg, 3.85 mmol), diisopropylamine (0.84 mL, 6.0 mmol), *n*-BuLi (3.3 mL, 1.6 M solution in hexanes, 5.25 mmol), 3-(2-iodoethyl)-1-methyl-1H-indole (1.0 g, 3.5 mmol) were used. Hexamethylphosphoramide (1.2 mL, 7 mmol) was added to the reaction mixture along with

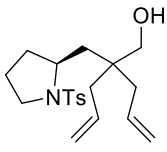
iodoalkane addition. For reduction of the ester, $LiAlH_4$ (400 mg, 10.5 mmol, 3.0 equiv) and THF (20.0 mL, 0.175 M) were used. The pure alcohol **1d-OH** was obtained by column chromatography (5:1 hexanes:EtOAc) as a yellow oil (372 mg, 38% over two steps).




(**1d-OH**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.29 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.22 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.11 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 6.84 (d, *J* = 0.9 Hz, 1H), 5.94 (ddt, *J* = 17.6, 10.1, 7.5 Hz, 2H), 5.24 – 5.08 (m, 4H), 3.75 (s, 3H), 3.53 (s, 2H), 2.82 – 2.69 (m, 2H), 2.20 (ddt, *J* = 7.5, 2.4, 1.2 Hz, 4H), 1.75 – 1.63 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.2, 134.9, 127.9, 125.9, 121.6, 119.1, 118.7, 117.9, 115.6, 109.3, 67.6, 60.6, 41.3, 39.1, 34.8, 32.7, 18.8. **IR** (ATR): 3404 (br), 3071, 2919, 1637, 1614, 1483, 1471, 1375, 1325, 1246, 1029, 1011, 997, 911, 736 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{19}H_{25}ON$ $[M]^+$: 283.1936, found: 283.1930.

In the synthesis of **1h-OH**, the representative α-alkylation and $LiAlH_4$ reduction procedures were applied. For the alkylation of bisallyl ester, methyl 2-allylpent-4-enoate (142 mg, 0.92 mmol, 1.0 equiv), *n*-BuLi (1.6 M in hexanes, 0.75 mL, 1.2 mmol, 1.3 equiv), isopropylamine (0.18 mL, 1.3 mmol, 1.4 equiv) (*S*)-2-(iodomethyl)-1-tosylpyrrolidine (335 mg, 0.92 mmol, 1.0 equiv) were used. The alkylated bisallyl ester was obtained by column chromatography (3:1 hexanes:EtOAc) as a yellow oil (220 mg, 61% yield). For reduction of the ester, the alkylated bisallyl ester (220 mg, 0.56 mmol, 1.0 equiv), $LiAlH_4$ (53.4 mg, 1.4 mmol, 2.5 equiv) and THF (1.4 mL, 0.4 M) were used. The pure alcohol **1h-OH** was obtained by column chromatography (3:1 hexanes:EtOAc) as a colorless oil (131 mg, 64%).

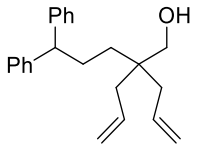



(**1h-OH**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.93 – 5.75 (m, 2H), 5.09 (dt, *J* = 9.8, 5.6 Hz, 4H), 3.87 – 3.76 (m, 1H), 3.62 (d, *J* = 11.9 Hz, 1H), 3.44 (d, *J* =

11.9 Hz, 1H), 3.36 (ddd, $J$ = 11.4, 7.1, 4.4 Hz, 1H), 3.10 (dt, $J$ = 10.3, 7.3 Hz, 1H), 2.67 (s, 1H), 2.42 (s, 3H), 2.21 – 2.06 (m, 2H), 1.98 (dd, $J$ = 9.2, 5.0 Hz, 3H), 1.86 – 1.74 (m, 1H), 1.62 – 1.44 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.7, 134.6, 134.4, 134.1, 129.9, 127.6, 118.22, 118.15, 66.9, 56.7, 48.4, 42.4, 41.0, 39.6, 38.3, 33.7, 24.4, 21.7. **IR** (ATR): 3534, 3072, 2922, 1597, 1334, 1154, 1090, 1049, 912, 815, 663 cm$^{-1}$. **HRMS** (ESI-TOF) $m$ / $z$ calcd for $C_{20}H_{29}NO_3SNa$ $[M+Na]^+$: 386.1766, found: 386.1752. $[\alpha]_D^{24}$ –83.0 ($c$ 1.08, $CHCl_3$).

In the synthesis of **1i-OH**, the representative α-alkylation and $LiAlH_4$ reduction procedures were applied. For alkylation of bisallyl ester, methyl 2-allyl-4-pentenoate ester (555 mg, 3.6 mmol), diisopropylamine (0.76 mL, 5.4 mmol), *n*-BuLi (3.3 mL, 1.6 M solution in hexanes, 5.25 mmol), (3-iodopropane-1,1-diyl)dibenzene (1.0 g, 3.5 mmol) were used. Hexamethylphosphoramide (1.25 mL, 7.2 mmol) was added to the reaction mixture along with iodoalkane addition. For reduction of the ester, $LiAlH_4$ (379 mg, 10.0 mmol, 2.9 equiv) and THF (20.0 mL, 0.2 M) were used. The pure alcohol **1i-OH** was obtained by column chromatography (5:1 hexanes:EtOAc) as a yellow oil (667.8 mg, 60% over two steps).



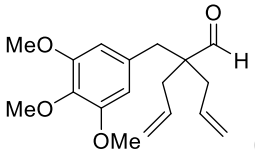

(**1i-OH**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.24 (m, 8H), 7.24 – 7.15 (m, 2H), 5.78 (ddt, $J$ = 17.5, 10.2, 7.4 Hz, 2H), 5.16 – 4.96 (m, 4H), 3.82 (t, $J$ = 7.7 Hz, 1H), 3.39 (s, 2H), 2.15 – 1.97(m, 6H), 1.32 – 1.17 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.1, 134.7, 128.6, 127.9, 126.3, 117.7, 67.4, 52.3, 41.0, 39.0, 32.2, 29.3. **IR** (ATR): 3398 (br), 3061, 3025, 2929, 1637, 1599, 1493, 1450, 1031, 997, 912, 765, 734, 698 cm$^{-1}$. **HRMS** (ESI-TOF) $m$ / $z$ calcd for $C_{23}H_{28}ONH_4$ $[M+NH_4]^+$: 338.2484, found: 338.2497.

***Representative Swern oxidation procedure for the synthesis of 1b***

DMSO (426 μL, 6.0 mmol, 3.1 equiv) was added dropwise to a DCM (10 mL) solution of oxalyl chloride (240 μL, 2.8 mmol, 1.45 equiv) at –78 °C in an acetone/dry ice bath, and then stirred for 30 min. A solution of alcohol **1b-OH** (590 mg, 1.93 mmol, 1 equiv) in DCM (2 mL) was added dropwise at –78 °C and stirred for 30 min. Triethylamine (1.4 mL, 10.0 mmol, 5.2 equiv) was

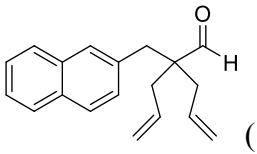
added dropwise at –78 °C. The reaction mixture was then warmed to rt and stirred for an additional 30 min. The reaction was quenched with water and extracted with DCM. The organic layer was washed with water, dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The pure aldehyde **1b** was obtained by column chromatography as a yellow oil (516 mg, 88%).



(**1b**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 6.32 (s, 2H), 5.78 (ddt, *J* = 16.9, 10.4, 7.3 Hz, 2H), 5.21 – 5.10 (m, 4H), 3.83 (s, 3H), 3.82 (s, 6H), 2.81 (s, 2H), 2.45 – 2.20 (m, 5H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.1, 153.0, 136.9, 132.9, 132.9, 132.2, 123.0, 119.3, 107.5, 61.0, 56.2, 53.1, 40.0, 36.8. **IR** (ATR): 2937, 2837, 1722, 1588, 1507, 1456, 1421, 1335, 1239, 1123, 1006, 917 $cm^{-1}$. **HRMS** (CI-TOF) *m* / *z* calcd for $C_{18}H_{24}O_4Na$ $[M+Na]^+$: 327.1572, found: 327.1576.

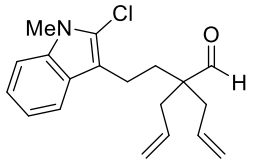
For the synthesis of 2-allyl-2-(naphthalen-2-ylmethyl)pent-4-enal (**1c**), the representative Swern oxidation protocol was applied. Alcohol **1c-OH** (370 mg, 1.4 mmol), oxalyl chloride (174 μL, 2.02 mmol, 1.46 equiv), DMSO (310 μL, 4.36 mmol, 3.1 equiv), triethylamine (1.0 mL, 7.12 mmol, 5.1 equiv) and DCM (8.0 mL, 0.17 M) were used. The pure aldehyde **1c** was obtained after column chromatography as a yellow oil (277 mg, 75%).



(**1c**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.84 – 7.73 (m, 3H), 7.65 – 7.56 (m, 1H), 7.51 – 7.42 (m, 2H), 7.24 (dd, *J* = 8.4, 1.8 Hz, 1H), 5.83 (ddt, *J* = 17.4, 10.3, 7.3 Hz, 2H), 5.23 – 5.10 (m, 4H), 3.05 (s, 2H), 2.35 (qdt, *J* = 14.5, 7.4, 1.3 Hz, 4H).**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.1, 134.2, 133.4, 132.9, 132.4, 129.1, 128.6, 128.0, 127.7, 126.3, 125.8, 123.0, 119.4, 53.2, 39.9, 36.9. **IR** (ATR): 3058, 2916, 1723, 1639, 1508, 1439, 917, 853, 820, 785, 751 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{19}H_{20}ONa$ $[M+Na]^+$: 287.1412, found: 287.1408.

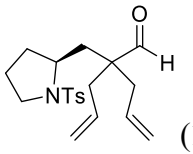
For the synthesis of 2-allyl-2-(2-(2-chloro-1-methyl-1H-indol-3-yl)ethyl)pent-4-enal (**1d**), the representative Swern oxidation procedure was applied. Alcohol **1d-OH** (400 mg, 1.411 mmol), oxalyl chloride (182 μL, 2.17 mmol), DMSO (301 μL, 4.23 mmol), triethylamine (1.0 mL, 7.06 mmol) and DCM (10 mL, 0.14 M) were used. The pure aldehyde **1d** was obtained by column chromatography as an off-white solid (281 mg, 63%).




(**1d**)

**$^1$H NMR** (499 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.49 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.26 (d, *J* = 7.1 Hz, 1H), 7.22 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.16 – 7.10 (m, 1H), 5.79 (ddt, *J* = 17.4, 10.1, 7.4 Hz, 2H), 5.26 – 5.13 (m, 4H), 3.72 (s, 3H), 2.76 – 2.60 (m, 2H), 2.41 (ddd, *J* = 7.4, 2.9, 1.4 Hz, 4H), 1.92 – 1.74 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.8, 135.8, 132.8, 126.3, 123.5, 121.9, 119.8, 119.1, 118.2, 110.7, 109.3, 52.3, 36.5, 32.8, 30.0, 18.7. **IR** (ATR): 3058, 2930, 2798, 1715, 1466, 1326, 991, 925, 910, 740 $cm^{-1}$. **HRMS** (CI-TOF) *m* / *z* calcd for $C_{19}H_{22}OClN$ $[M]^+$: 315.1390, found: 315.1395.

For the synthesis of (*S*)-2-allyl-2-((1-tosylpyrrolidin-2-yl)methyl)pent-4-enal (**1h**), representative Swern oxidation procedure was applied. Alcohol **1h-OH** (131 mg, 0.36 mmol, 1.0 equiv), oxalyl chloride (42 μL, 0.49 mmol, 1.4 equiv), DMSO (77 μL, 1.1 mmol, 3.1 equiv), triethylamine (0.25 mL, 1.8 mmol, 5.0 equiv) and DCM (0.20 mL) were used. The pure aldehyde **1h** was obtained after column chromatography as a yellow oil (116 mg, 89%).

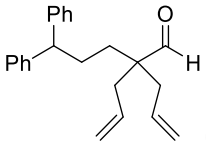



(**1h**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.83 (ddt, *J* = 14.8, 10.5, 7.3 Hz, 1H), 5.76 – 5.62 (m, 1H), 5.21 – 5.06 (m, 4H), 3.71 – 3.60 (m, 1H), 3.30 (dt, *J* = 11.2, 6.7 Hz, 1H), 3.25 – 3.14 (m, 1H), 2.50 – 2.37 (m, 5H), 2.37 – 2.27 (m, 2H), 2.22 (dd, *J* = 14.7, 4.4 Hz, 1H), 1.80 – 1.65 (m, 2H), 1.51 – 1.28 (m, 3H). **$^{13}$C NMR** (101

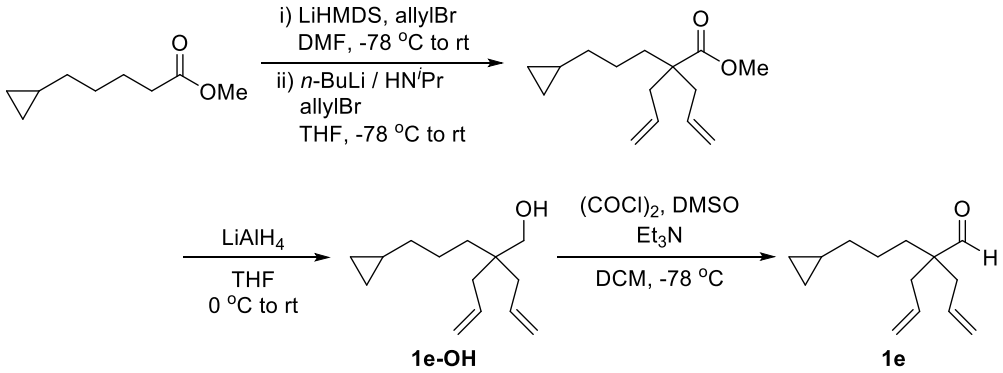
MHz, $CDCl_3$) δ 206.2, 143.7, 134.6, 132.6, 132.5, 129.9, 127.7, 119.4, 119.3, 57.1, 51.7, 48.4, 40.9, 36.9, 36.3, 32.6, 24.3, 21.7. **IR** (ATR): 2976, 1721, 1448, 1341, 1156, 1090, 990, 917, 816, 663 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{20}H_{27}NO_3SClCH_3OH$ $[M+Cl^-+MeOH]^-$: 428.1662, found: 428.1661. $[\alpha]_D^{24}$ –108 (*c* 0.920, $CHCl_3$).

For the synthesis of 2-allyl-2-(3,3-diphenylpropyl)pent-4-enal (**1i**), the representative Swern oxidation protocol was applied. Alcohol **1i-OH** (620 mg, 1.935 mmol), oxalyl chloride (216 μL, 2.52 mmol), DMSO (412 μL, 5.80 mmol), triethylamine (1.36 mL, 9.67 mmol) and DCM (12.9 mL, 0.15 M) were used. The pure aldehyde **1i** was obtained after column chromatography as a yellow oil (573 mg, 93%).



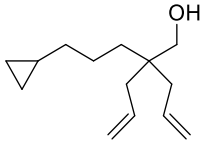

(**1i**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.32 – 7.25 (m, 5H), 7.24 – 7.15 (m, 6H), 5.61 (ddt, *J* = 17.1, 9.6, 7.4 Hz, 2H), 5.15 – 4.99 (m, 4H), 3.81 (t, *J* = 7.7 Hz, 1H), 2.27 (dq, *J* = 7.4, 1.1 Hz, 4H), 2.03 – 1.90 (m, 2H), 1.54 – 1.43 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.0, 144.6, 132.7, 128.7, 127.9, 126.5, 118.8, 52.2, 52.0, 36.5, 31.2, 29.7. **IR** (ATR): 3062, 2934, 1722, 1493, 1450, 995, 916, 747, 734, 699 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{23}H_{26}ONH_4$ $[M+NH_4]^+$: 336.2327, found: 336.2330.




Methyl 5-cyclopropylpentanoate was prepared from cyclopropanation of methyl 6-heptenoate using $ZnEt_2/CH_2I_2$. For the first allylation, methyl 5-cyclopropylpentanoate (1.1 g, 6.46 mmol) was added dropwise to a DMF (12 mL) solution of LiHMDS (2.16 g, 12.92 mmol) at –78 °C by

using a flask cooled in an acetone/dry ice bath. The reaction mixture was stirred for 30 min. Allyl bromide (1.12 mL, 12.92 mmol) was added to the mixture and the reaction was stirred for 4 h. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution and extracted with EtOAc three times. The organic layer was separated and washed with $H_2O$ three times, dried over $MgSO_4$, and concentrated *in vacuo*. The monoallylated ester (1.28 g, 94%) was used without further purification. For the second allylation, to a THF solution of diisopropylamine (1.4 mL, 10.0 mmol) was added dropwise *n*-BuLi (1.6 M solution in hexane, 6.2 mL, 10.0 mmol) at 0 °C, and the solution was stirred for 20 min at 0 °C. The solution was cooled to –78 °C by using a flask cooled in an acetone/dry ice bath, and monoallylated ester (1.2 g, 5.71 mmol) was then added dropwise to the solution. The solution was stirred for 30 min at –78 °C. HMPA (2.0 mL, 2 equiv) and allyl bromide (1.0 mL, 11.4 mmol) were added dropwise to the solution and the mixture was warmed to rt and stirred overnight. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution and EtOAc was added to the mixture. The organic layer was washed with 1N HCl (aq), and $H_2O$ for three times, dried over $MgSO_4$, and concentrated *in vacuo*. The bisallylated ester (1.38 g) was used without further purification. For the reduction of bisallylated ester, the representative $LiAlH_4$ reduction procedure was applied. α,α-Bisallyl ester (1.3 g, 5.19 mmol), $LiAlH_4$ (591 mg, 15.58 mmol, 3.0 equiv) and THF (30 mL, 0.173 M) were used. The pure alcohol **1e-OH** was obtained after column chromatography as a colorless oil (0.822 mg, 76%).

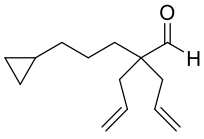



**(1e-OH)**

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.86 (ddt, *J* = 17.0, 10.2, 7.5 Hz, 2H), 5.17 – 5.02 (m, 4H), 3.41 (s, 2H), 2.07 (ddd, *J* = 7.5, 2.2, 1.1 Hz, 4H), 1.42 – 1.34 (m, 2H), 1.30 – 1.23 (m, 2H), 1.18 (q, *J* = 7.1 Hz, 2H), 0.76 – 0.59 (m, 1H), 0.47 – 0.33 (m, 2H), 0.10 – -0.08 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 135.0, 117.6, 67.7, 41.0, 39.1, 35.7, 33.6, 23.1, 11.0, 4.6. **IR (ATR)**: 3363 (br), 3074, 3001, 2977, 2929, 1638, 1441, 1040, 1014, 995, 910, 820, 732 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{14}H_{22}ONH_4$ $[M+NH_4]^+$: 226.2171, found: 226.2173.

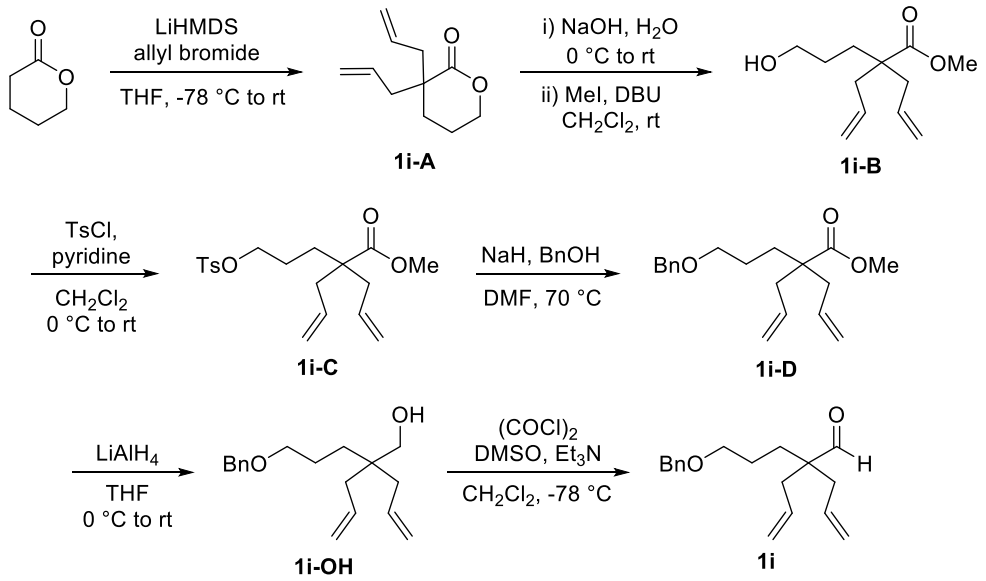
For the synthesis of 2-allyl-2-(3-cyclopropylpropyl)pent-4-enal (**1e**), representative Swern oxidation protocol was applied. Alcohol **1e-OH** (760 mg, 3.65 mmol), oxalyl chloride (407 μL),

DMSO (777 μL), triethylamine (2.56 mL) and DCM (20 mL) were used. The pure aldehyde **1e** was obtained after column chromatography as a colorless oil (692 mg, 92%).



**(1e)**

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 5.81 – 5.59 (m, 2H), 5.10 (dtd, *J* = 13.2, 2.4, 1.1 Hz, 4H), 2.29 (dt, *J* = 7.4, 1.2 Hz, 4H), 1.61 – 1.46 (m, 2H), 1.38 – 1.26 (m, 2H), 1.25 – 1.11(m, 2H), 0.64 (ddt, *J* = 9.6, 7.8, 3.0 Hz, 1H), 0.47 – 0.33 (m, 2H), 0.07 – -0.07 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 133.0, 118.7, 52.2, 36.6, 35.3, 32.5, 23.7, 10.8, 4.6. **IR** (ATR): 3076, 2929, 2849, 1725, 1640, 1442, 1014, 994, 915, 821 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{14}H_{22}ONH_4$ $[M+NH_4]^+$: 224.2014, found: 224.2007.




**3,3-diallyltetrahydro-2*H*-pyran-2-one** (**1i-A**): LiHMDS (4.18 g, 25.0 mmol, 2.5 equiv) was dissolved in THF (25 mL) under $N_2$ atmosphere. The solution was cooled to –78 °C, and δ-valerolactone (0.93 mL, 10.0 mmol, 1.0 equiv) was added over 10 min. The solution was allowed to stir for 15 min. Then, allyl bromide (2.2 mL, 25.0 mmol, 2.5 equiv) was added over 20 min. The reaction mixture was allowed to warm to rt overnight. The reaction mixture was quenched with 1 M HCl and extracted with EtOAc (3 x 15 mL). The organic layers were

combined, washed with brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. The pure bisallyl lactone **1i-A** was obtained by column chromatography (1:10 EtOAc:hexanes) as a colorless oil (1.73 g, 96% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.74 (dddd, *J* = 16.9, 10.3, 8.1, 6.7 Hz, 2H), 5.18 – 4.98 (m, 4H), 4.34 – 4.18 (m, 2H), 2.54 (dd, *J* = 13.6, 6.7 Hz, 2H), 2.19 (dd, *J* = 13.6, 8.1 Hz, 2H), 1.89 – 1.72 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.2, 133.4, 119.4, 70.4, 46.0, 43.9, 28.7, 21.2. **IR** (ATR): 3077, 2938, 1720, 1639, 1440, 1142, 1085, 996, 977, 916 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{11}H_{16}O_2H$ $[M+H]^+$: 181.1228, found: 181.1228.

**Methyl 2-allyl-2-(3-hydroxypropyl)pent-4-enoate** (**1i-B**): Compound **1i-A** (1.70 g, 9.4 mmol, 1.0 equiv) was mixed with $H_2O$ (5.0 mL), and the mixture was cooled to 0 °C. Then, a solution of NaOH (0.452 g, 11.3 mmol, 1.2 equiv) in 10 mL of $H_2O$ was added dropwise. The reaction mixture was warmed to rt and stirred for 4 h. The reaction mixture was cooled to 0 °C and acidified with conc. HCl. The reaction mixture was extracted with DCM (3 x 15 mL). The combined organic layers were dried with $Na_2SO_4$ and concentrated *in vacuo* to afford the hydroxy acid as a white solid. The hydroxy acid was dissolved in 9.6 mL of DCM. To this solution was added DBU (1.4 mL, 9.4 mmol, 1.0 equiv), followed by MeI (0.59 mL, 9.4 mmol, 1.0 equiv). The reaction mixture was stirred at rt for 2 h. The reaction mixture was quenched with 1 M HCl and extracted with DCM (3 x 15 mL). The combined organic layers were dried with $Na_2SO_4$ and concentrated *in vacuo*. The pure ester **1i-B** was obtained by column chromatography (1:3 EtOAc:hexanes) as a yellow oil (1.70 g, 84% yield over two steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.77 – 5.61 (m, 2H), 5.13 – 5.02 (m, 4H), 3.68 (d, *J* = 2.8 Hz, 3H), 3.61 (t, *J* = 6.4 Hz, 2H), 2.38 – 2.30 (m, 4H), 1.68 – 1.56 (m, 2H), 1.56 – 1.45 (m, 2H), 1.43 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 176.6, 133.5, 118.3, 62.7, 51.6, 49.1, 38.8, 31.1, 27.3. **IR** (ATR): 3365, 3077, 2949, 1729, 1640, 1450, 1212, 1055, 994, 915 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{12}H_{20}O_3H$ $[M+H]^+$: 213.1491, found: 213.1494.

**Methyl 2-allyl-2-(3-(tosyloxy)propyl)pent-4-enoate** (**1i-C**): To a solution of **1i-B** (1.31 g, 6.2 mmol, 1.0 equiv) in DCM (5.0 mL) and pyridine (3.0 mL) at 0 °C was added *p*-TsCl (1.30 g, 6.8 mmol, 1.1 equiv). The reaction mixture was allowed to stir overnight, slowly warming to rt. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with DCM (3 x 15 mL). The combined organic layers were washed with 1 M HCl, brine, dried with $Na_2SO_4$, and

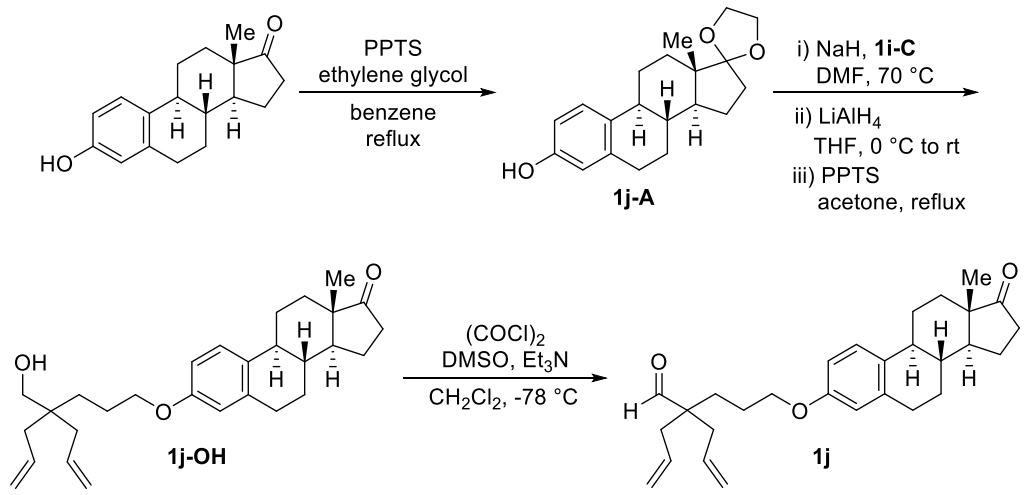
concentrated *in vacuo*. The pure tosylate **1i-C** was obtained by column chromatography (1:3 EtOAc:hexanes) as a colorless oil (1.93 g, 85% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.65 (ddt, *J* = 17.8, 10.5, 7.4 Hz, 2H), 5.10 – 5.00 (m, 4H), 4.00 (t, *J* = 5.9 Hz, 2H), 3.66 (s, 3H), 2.46 (s, 3H), 2.30 (dd, *J* = 7.4, 0.8 Hz, 4H), 1.63 – 1.50 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.9, 144.8, 133.23, 133.19, 129.9, 127.9, 118.6, 70.7, 51.8, 48.9, 38.9, 30.7, 23.9, 21.7. **IR** (ATR): 2951, 1727, 1450, 1358, 1188, 1175, 917, 814, 735, 662 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{19}H_{26}O_5SNa$ $[M+Na]^+$: 389.1399, found: 389.1395.

**Methyl 2-allyl-2-(3-(benzyloxy)propyl)pent-4-enoate** (**1i-D**): To a suspension of NaH (60% w/w, 42.6 mg, 1.06 mmol, 1.06 equiv) in DMF (2.0 mL) was added benzyl alcohol (0.11 mL, 1.06 mmol, 1.06 equiv). The mixture was stirred at 70 °C for 15 min. Then, **1i-C** was added as a solution in DMF (3.0 mL). The reaction mixture was stirred at 70 °C for 5 h. The reaction mixture was cooled to rt, quenched with saturated aqueous $NH_4Cl$. The mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with $H_2O$, brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. The pure benzyl ether **1i-D** was obtained by column chromatography (1:10 EtOAc:hexanes) as a colorless oil (272 mg, 90% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.29 (m, 5H), 5.78 (ddd, *J* = 25.0, 14.4, 7.4 Hz, 2H), 5.20 – 5.09 (m, 4H), 4.55 (s, 2H), 3.72 (s, 3H), 3.50 (t, *J* = 6.3 Hz, 2H), 2.42 (d, *J* = 7.4 Hz, 4H), 1.76 – 1.55 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 176.4, 138.6, 133.7, 128.4, 127.61, 127.56, 118.3, 72.8, 70.5, 51.6, 49.2, 38.9, 31.6, 24.5. **IR** (ATR): 2949, 2856, 1728, 1453, 1197, 1101, 994, 915, 734, 697 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{19}H_{26}O_3H$ $[M+H]^+$: 303.1960, found: 303.1964.

**2-Allyl-2-(3-(benzyloxy)propyl)pent-4-en-1-ol** (**1i-OH**): Compound **1i-D** (272 mg, 0.90 mmol, 1.0 equiv) was dissolved in THF (2.0 mL) and cooled to 0 °C. $LiAlH_4$ (41.8 mg, 1.1 mmol, 2.5 equiv) was added slowly to the stirring ester solution. The reaction was warmed to rt and allowed to stir at rt for 4 h. The reaction mixture was quenched using the Fieser method, and the solution was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The pure alcohol **1i-OH** was obtained by column chromatography (1:3 EtOAc:hexanes) as a colorless oil (207 mg, 84% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.29 (m, 5H), 5.90 (ddt, *J* = 15.0, 10.3, 7.5 Hz, 2H), 5.22 – 5.07 (m, 4H), 4.56 (s, 2H), 3.51 (t, *J* = 6.5 Hz, 2H), 3.42 (s, 2H), 2.30 (s, 1H), 2.14 – 2.01

(m, 4H), 1.74 – 1.59 (m, 2H), 1.43 – 1.31 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.5, 134.7, 128.5, 127.8, 127.7, 117.6, 73.1, 71.1, 66.9, 40.7, 38.8, 30.1, 23.4. **IR** (ATR): 3419, 2923, 2858, 1453, 1360, 1096, 1043, 956, 911, 734 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{18}H_{26}O_2Na$ $[M+Na]^+$: 297.1830, found: 297.1824.

**2-Allyl-2-(3-(benzyloxy)propyl)pent-4-enal** (**1i**): Oxalyl chloride (94 μL, 1.1 mmol, 1.4 equiv) was dissolved in DCM (1.0 mL) and cooled to –78 °C. DMSO (0.17 mL, 2.4 mmol, 3.0 equiv) was added, and the solution was allowed to stir for 30 min at –78 °C. Then, a solution of alcohol **1i-OH** (222 mg, 0.81 mmol, 1.0 equiv) in DCM (2.2 mL) was added, and the reaction mixture was allowed to stir for 30 min at –78 °C. $Et_3N$ (0.57 mL, 4.1 mmol, 5.0 equiv) was added. The reaction mixture was warmed to rt and allowed to stir for 30 min. The reaction mixture was quenched with $H_2O$ and extracted with DCM (3 x 10 mL). The combined organic layers were washed with $H_2O$, dried with $Na_2SO_4$, and concentrated *in vacuo*. The pure aldehyde **1i** was obtained by column chromatography (1:10 EtOAc:hexanes) as a colorless oil (166 mg, 75% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.43-7.31 (m, 5H), 5.74 (dddd, *J* = 16.9, 10.3, 8.1, 6.7 Hz, 2H), 5.18 – 4.98 (m, 4H), 4.34 – 4.18 (m, 2H), 2.54 (dd, *J* = 13.6, 6.7 Hz, 2H), 2.19 (dd, *J* = 13.6, 8.1 Hz, 2H), 1.89 – 1.72 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.9, 138.6, 132.8, 128.5, 127.68, 127.66, 118.8, 73.0, 70.4, 51.8, 36.6, 29.1, 24.0. **IR** (ATR): 2924, 2855, 1723, 1453, 1360, 1100, 994, 915, 734, 697 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{18}H_{24}O_2H$ $[M+H]^+$: 273.1855, found: 273.1857.

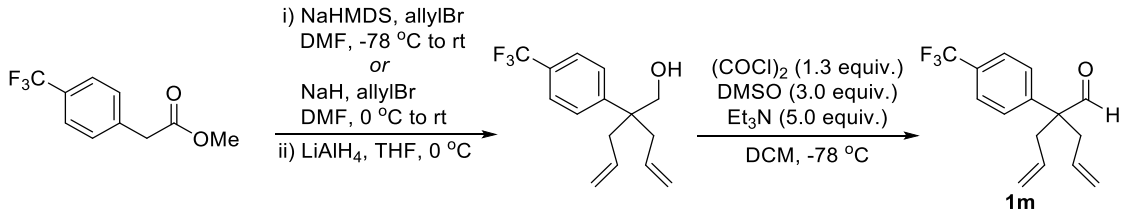


**(8*R*,9*S*,13*S*,14*S*)-13-Methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolan]-3-ol** (**1j-A**): To a solution of estrone (541 mg, 2.0 mmol, 1.0 equiv) in benzene (20 mL) was added ethylene glycol (0.56 mL, 10.0 mmol, 5.0 equiv) and PPTS (151 mg, 0.60 mmol, 0.30 equiv). The reaction mixture was stirred and heated at reflux with a Dean-Stark apparatus for 5 h. The reaction mixture was cooled to rt and concentrated *in vacuo*. The pure was dissolved in ether and washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was concentrated *in vacuo* to afford acetal **1j-A** as a white solid (593 mg, 94% yield). $^1$H NMR data matched with literature reported values.[5] **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.5 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 1.9 Hz, 1H), 5.42 (s, 1H), 3.97 (ddd, *J* = 11.9, 8.6, 4.5 Hz, 4H), 2.83 (dd, *J* = 20.6, 10.6 Hz, 2H), 2.32 (dd, *J* = 13.3, 2.7 Hz, 1H), 2.22 (dd, *J* = 14.5, 6.8 Hz, 1H), 2.08 (dd, *J* = 15.1, 10.2 Hz, 1H), 1.88 (dt, *J* = 9.3, 7.8 Hz, 2H), 1.79 (td, *J* = 12.6, 3.9 Hz, 2H), 1.70 – 1.60 (m, 1H), 1.59 – 1.23 (m, 6H), 0.91 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 153.6, 138.4, 132.8, 126.7, 119.8, 115.5, 112.9, 65.4, 64.8, 49.5, 46.4, 43.7, 39.2, 34.4, 30.9, 29.8, 27.1, 26.3, 22.5, 14.5.

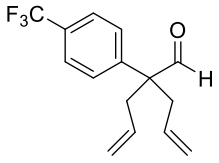
**(8*R*,9*S*,13*S*,14*S*)-3-((4-allyl-4-(hydroxymethyl)hept-6-en-1-yl)oxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one** (**1j-OH**): To a suspension of NaH (60% w/w, 80.0 mg, 2.0 mmol, 1.1 equiv) in DMF (1.0 mL) was added a solution of **1j-A** (590 mg, 1.9 mmol, 1.0 equiv) in DMF (3 mL). The mixture was stirred at 70 °C for 30 min. Then, tosylate **1i-C** was added as a solution in DMF (6.0 mL). The reaction mixture was stirred at 70 °C for 10 h. The reaction mixture was cooled to rt, quenched with saturated aqueous $NH_4Cl$, and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with $H_2O$, brine, dried with $Na_2SO_4$, and concentrated *in vacuo* to afford the methyl ester as a yellow oil, which was used without further purification. $LiAlH_4$ (178 mg, 4.7 mmol, 2.5 equiv) was slowly added to a solution of the methyl ester in THF (5.0 mL) at 0 °C. The reaction mixture was allowed to stir overnight. The reaction mixture was quenched using the Fieser method, and the solution was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The alcohol was used without further purification. PPTS (142 mg, 0.56 mmol, 0.30 equiv) was added to a solution of alcohol in acetone (8 mL) and $H_2O$ (2.0 mL). The reaction mixture was stirred and heated at reflux for 4 h. The reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was dissolved in ether and washed with saturated aqueous $NaHCO_3$ and brine. The

combined organic layers were dried with $Na_2SO_4$, and concentrated *in vacuo*. The pure alcohol **1j-OH** was obtained by column chromatography (1:3 EtOAc:hexanes) as a white solid (632 mg, 77% yield over three steps). **$^1$H NMR** (499 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.5 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 6.64 (s, 1H), 5.87 (td, *J* = 17.6, 7.5 Hz, 2H), 5.16 – 4.99 (m, 4H), 3.91 (t, *J* = 6.4 Hz, 2H), 3.44 (s, 2H), 2.89 (d, *J* = 5.1 Hz, 2H), 2.51 (dd, *J* = 18.9, 8.8 Hz, 1H), 2.40 (d, *J* = 10.3 Hz, 1H), 2.26 (d, *J* = 9.8 Hz, 1H), 2.19 – 1.88 (m, 9H), 1.84 – 1.73 (m, 2H), 1.71 (s, 1H), 1.67 – 1.33 (m, 9H), 0.92 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 221.1, 157.1, 137.9, 134.7, 132.2, 126.5, 117.9, 114.7, 112.2, 68.6, 67.3, 50.6, 48.2, 44.2, 40.8, 39.0, 38.6, 36.1, 31.8, 30.0, 29.8, 26.7, 26.1, 23.2, 21.8, 14.0. **IR** (ATR): 3541, 2930, 2864, 1721, 1501, 1470, 1235, 1052, 907, 874 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{29}H_{40}O_3Na$ $[M+Na]^+$: 459.2875, found: 459.2882. $[\alpha]_D^{24}$ +97.6 (*c* 0.420, $CHCl_3$).

**2-Allyl-2-(3-(((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)propyl)pent-4-enal** (**1j**): Oxalyl chloride (78 μL, 0.91 mmol, 1.3 equiv) was dissolved in DCM (0.80 mL) and cooled to –78 °C. DMSO (0.15 mL, 2.1 mmol, 3.0 equiv) was added, and the solution was allowed to stir for 30 min at –78 °C. Then, a solution of alcohol **1j-OH** (306 mg, 0.70 mmol, 1.0 equiv) in DCM (2.0 mL) was added, and the reaction mixture was allowed to stir for 30 min at –78 °C. $Et_3N$ (0.49 mL, 3.5 mmol, 5.0 equiv) was added. The reaction mixture was warmed to rt and allowed to stir at rt for 30 min. The reaction mixture was quenched with $H_2O$ and extracted with DCM (3 x 10 mL). The combined organic layers were washed with $H_2O$, dried with $Na_2SO_4$, and concentrated *in vacuo*. The pure aldehyde **1j** was obtained by column chromatography (1:3 EtOAc:hexanes) as a white solid (307 mg, 99% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.19 (d, *J* = 8.6 Hz, 1H), 6.69 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.62 (d, *J* = 2.6 Hz, 1H), 5.71 (ddt, *J* = 20.9, 9.5, 7.4 Hz, 2H), 5.18 – 5.05 (m, 4H), 3.90 (dd, *J* = 5.4, 3.3 Hz, 2H), 2.97 – 2.79 (m, 2H), 2.50 (dd, *J* = 18.7, 8.5 Hz, 1H), 2.39 (dd, *J* = 9.3, 3.9 Hz, 1H), 2.32 (d, *J* = 7.4 Hz, 4H), 2.22 (dd, *J* = 13.4, 9.3 Hz, 1H), 2.16 – 1.90 (m, 4H), 1.67 (dd, *J* = 12.4, 3.3 Hz, 4H), 1.63 – 1.36 (m, 6H), 0.91 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 220.9, 205.8, 157.0, 137.8, 132.7, 132.2, 126.4, 118.9, 114.6, 112.2, 67.9, 51.8, 50.5, 48.10, 44.08, 38.5, 36.7, 36.0, 31.7, 29.8, 28.9, 26.7, 26.1, 23.6, 21.7, 14.0. **IR** (ATR): 2928, 2888, 1729, 1709, 1497, 1280, 1256, 1061, 943, 864 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{29}H_{38}O_3Na$ $[M + Na]^+$: 457.2719, found: 457.2733. $[\alpha]_D^{24}$ +87.9 (*c* 0.347, $CHCl_3$).



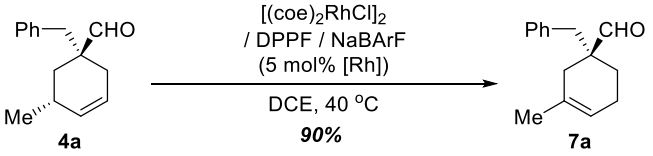

Sodium bis(trimethylsilyl)amide (NaHMDS) solution (6.5 mL, 2.0 M solution in THF, 12.5 mmol, 2.5 equiv) was added to THF solution of methyl 4-(α,α,α-trifluoromethyl)phenylacetate (1.1 g, 5.0 mmol, 1 equiv) in an acetone/dry ice bath at –78 °C. The solution was stirred for 30 min. Then, allyl bromide (1.1 mL, 12.5 mmol, 2.5 equiv) was added dropwise to the reaction mixture. The solution was warmed to rt and stirred for 4 h. The reaction mixture was quenched with aqueous $NH_4Cl$ solution and aqueous 2 M HCl solution, and the aqueous layer extracted with EtOAc three times. The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated. The α,α-bisallylester was used without further purification. $LiAlH_4$ (473 mg, 12.5 mmol, 2.5 equiv) was added slowly to a stirring solution of the crude ester (1.3 g, 5 mmol, 1 equiv) in 25 mL THF at 0 °C using an ice bath. After addition of $LiAlH_4$, the ice bath was removed and the reaction mixture was allowed to stir at rt for 4 h. The reaction mixture was quenched using the Fieser method and the solution was dried with $MgSO_4$, filtered, and concentrated. For oxidation, the representative Swern oxidation protocol was applied. Alcohol **1m-OH**, oxalyl chloride (371 μL), DMSO (710 μL), triethylamine (2.3 mL) and DCM (20 mL) were used. The pure aldehyde **1m** was obtained after column chromatography as a colorless oil (796 mg, 59.4% over three steps).



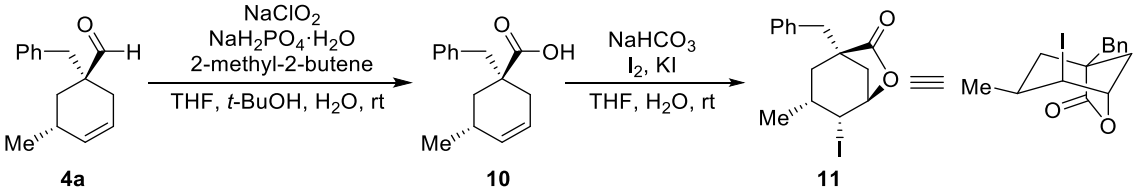

(**1m**)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.72 – 7.60 (m, 2H), 7.43 – 7.32 (m, 2H), 5.54 (ddt, *J* = 17.1, 9.7, 7.3 Hz, 2H), 5.18 – 5.01 (m, 5H), 2.74 (ddt, *J* = 7.1, 3.3, 1.2 Hz, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 201.4, 132.1, 128.3, 125.9 (q, *J* = 3.8 Hz), 119.8, 57.1, 37.2. **IR** (ATR): 3081, 2982, 1725, 1326, 1167, 1122, 1071, 1016, 920, 834 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{15}OF_3NH_4$ $[M+NH_4]^+$: 286.1419, found: 286.1407.

## 4. Elaboration of Cyclohexenecarbaldehydes



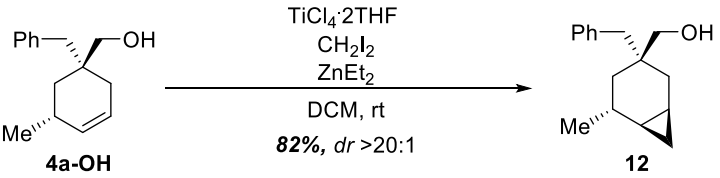

In a 1 dram vial, $[(coe)_2RhCl]_2$ (1.8 mg, 0.0025 mmol, 2.5 mol%) and DPPF (3.0 mg, 0.0055 mmol, 5.5 mol%) were dissolved in DCE (500 mL, 0.2 M), and the solution was stirred at rt for 30 min. NaBArF (5.3 mg, 0.06 mmol, 6 mol%) was added to the solution and the mixture was stirred for 5 min. To the solution was added aldehyde **4a** (21.4 mg, 0.1 mmol), and the reaction mixture was stirred at 40 °C for 12 h. Completion of the reaction was judged by GC-MS. Aldehyde **7a** was isolated by preparative TLC (20:1 hexanes:EtOAc, 19.2 mg, 90%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.33 – 7.18 (m, 5H), 7.11 – 7.04 (m, 2H), 5.38 (d, *J* = 1.5 Hz, 1H), 2.87 (d, *J* = 13.6 Hz, 1H), 2.75 (d, *J* = 13.6 Hz, 1H), 2.19 – 2.09 (m, 1H), 2.09 – 1.97 (m, 2H), 1.91 (dddd, *J* = 13.2, 6.1, 4.2, 1.6 Hz, 2H), 1.68 (dd, *J* = 2.4, 1.4 Hz, 3H), 1.59 – 1.42 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 206.4, 136.5, 131.9, 130.4, 128.4, 126.7, 120.8, 49.8, 42.3, 34.4, 27.5, 23.9, 22.5. **IR** (ATR): 3028, 2916, 2849, 2707, 1722, 1603, 1453, 1442, 1029, 981, 914, 867, 833, 805, 751, 730, 700 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{18}ONa$ $[M+Na]^+$: 237.1255, found: 237.1254. $[\alpha]_D^{26.9}$ +59.5 (*c* 0.565, $CHCl_3$).




Aldehyde **4a** (18.3 mg, 0.086 mmol, 1.0 equiv) was dissolved in THF (0.17 mL), *t*-BuOH (0.17 mL), and $H_2O$ (0.34 mL). 2-Methyl-2-butene (45 μL, 0.42 mmol, 4.9 equiv), $NaH_2PO_4$•$H_2O$ (58.0 mg, 0.42 mmol, 4.9 equiv), and $NaClO_2$ (38.0 mg, 0.42 mmol, 4.9 equiv) were added sequentially. The reaction mixture was allowed to stir at rt for 2 h. The reaction mixture was poured into brine and extracted with EtOAc (5 x 5 mL). The combined organic layers were dried with $Na_2SO_4$ and concentrated *in vacuo*. The pure carboxylic acid **10** was obtained by preparative TLC (1:20 MeOH:DCM) as a yellow oil (15.4 mg, 78% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.29 (dq, *J* = 9.6, 1.9 Hz, 3H), 7.19 – 7.10 (m, 2H), 5.65 – 5.56 (m, 1H), 5.50 (d, *J* =

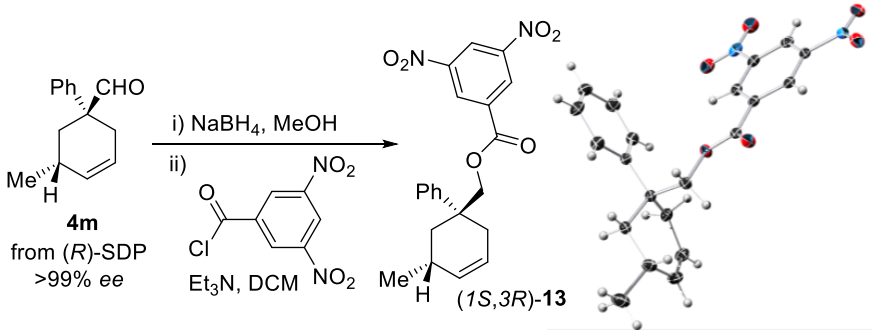
10.0 Hz, 1H), 3.01 (d, *J* = 13.2 Hz, 1H), 2.82 (d, *J* = 13.2 Hz, 1H), 2.44 (dd, *J* = 17.5, 3.8 Hz, 1H), 2.40 – 2.29 (m, 1H), 2.28 – 2.20 (m, 1H), 2.02 – 1.88 (m, 1H), 1.22 – 1.10 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 182.4, 136.7, 133.0, 130.2, 128.3, 127.0, 124.5, 47.9, 47.3, 40.2, 32.3, 28.7, 21.8. **IR** (ATR): 3026, 2953, 1697, 1453, 1243, 770, 738, 722, 700, 683 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{17}O_2$ $[M–H]^-$: 229.1228, found: 229.1225.

$NaHCO_3$ (16.9 mg, 0.20 mmol, 3.0 equiv) was added to a solution of acid **10** (15.4 mg, 0.067 mmol, 1.0 equiv) in THF (0.15 mL) and $H_2O$ (0.15 mL). The reaction mixture was allowed to stir at rt for 5 min. KI (14.5 mg, 0.087 mmol, 1.3 equiv) and $I_2$ (22.1 mg, 0.087 mmol, 1.3 equiv) were added sequentially. The reaction mixture was allowed to stir in the dark at rt for 4 h. The reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ until the solution turned colorless and extracted with ether (3 x 5 mL). The combined organic layers were dried with $Na_2SO_4$ and concentrated *in vacuo*. The pure lactone **11** was obtained by preparative TLC (1:10 EtOAc:hexanes) as a white solid (15.1 mg, 63% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 11.3, 4.4 Hz, 2H), 7.25 (d, *J* = 7.4 Hz, 1H), 7.19 – 7.13 (m, 2H), 4.81 (dd, *J* = 5.9, 4.2 Hz, 1H), 4.51 (t, *J* = 4.3 Hz, 1H), 3.06 (d, *J* = 13.8 Hz, 1H), 2.76 (d, *J* = 13.9 Hz, 1H), 2.57 (d, *J* = 12.2 Hz, 1H), 2.14 (dd, *J* = 12.2, 6.1 Hz, 1H), 1.60 – 1.51 (m, 2H), 1.20 (t, *J* = 12.0 Hz, 1H), 1.03 (d, *J* = 6.2 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 179.2, 136.4, 130.3, 128.7, 127.1, 79.1, 47.4, 40.3, 38.19, 38.18, 37.6, 30.2, 23.9. **IR** (ATR): 2984, 2908, 1773, 1455, 1314, 1141, 1095, 1038, 950, 903 cm$^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{15}H_{17}O_2INa$ $[M+Na]^+$: 379.0171, found: 379.0163. $[\alpha]_D^{25}$ +5.7 (*c* 0.247, $CHCl_3$).

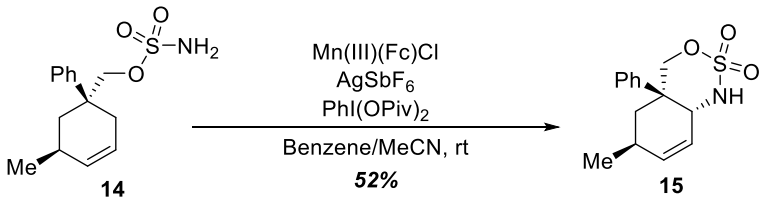



Alcohol **4a-OH** (19.0 mg, 0.088 mmol), $TiCl_4$•2THF (2.9 mg, 0.0088 mmol, 10 mol%) and $CH_2I_2$ (21 μL, 0.254 mmol, 3 equiv) were dissolved in DCM, the mixture was cooled to 0 °C. $ZnEt_2$ (1.5 M solution in toluene, 117 μL, 0.176 mmol, 2 equiv) were added dropwise to the solution. The mixture was stirred at rt for 6 h. The reaction was quenched with aqueous $NH_4Cl$ solution, then the mixture was diluted with EtOAc, and washed with $H_2O$ and brine. The

collecting organic layer was dried over $MgSO_4$, concentrated *in vacuo*. The pure alcohol **12** was obtained by preparative TLC (15.7 mg, 82%) as a colorless oil. Diastereomeric ratio was determined by $^1H$ and $^{13}C$ NMR. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 5H), 3.28 (d, $J$ = 1.5 Hz, 2H), 2.75 (s, 2H), 1.84 (dd, $J$ = 14.4, 7.0 Hz, 1H), 1.46 (dd, $J$ = 12.6, 2.5 Hz, 1H), 1.22 – 1.12 (m, 4H), 1.13 – 1.03 (m, 1H), 0.88 (tdd, $J$ = 11.5, 5.3, 3.6 Hz, 1H), 0.84 – 0.71 (m, 2H), 0.55 (tdd, $J$ = 8.4, 5.8, 4.2 Hz, 1H), 0.01 (q, $J$ = 4.4 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.7, 130.6, 128.0, 126.0, 68.7, 44.7, 40.5, 40.1, 30.1, 29.7, 22.6, 17.3, 14.5, 7.8. **IR** (ATR): 3377 (br), 3060, 3025, 2989, 2948, 2922, 2866, 1601, 1495, 1453, 1041, 1025, 814, 782, 749, 734, 701 $cm^{-1}$. **HRMS** (ESI-TOF) $m$ / $z$ calcd for $C_{16}H_{22}ONa$ $[M+Na]^+$: 253.1568, found: 253.1562. $[\alpha]_D^{25.3}$ –23.0 ($c$ 0.685, $CHCl_3$).



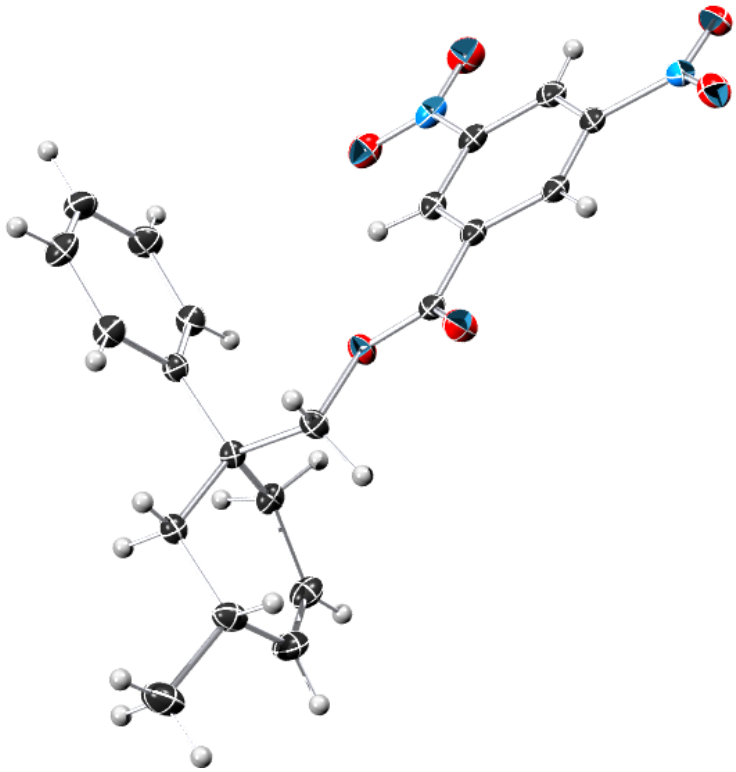

3,5-Dinitrobenzoyl chloride was dissolved in DCM, and **4m-OH** (15.9 mg, 0.075 mmol, >99% *ee*) and triethylamine (0.15 mmol) were added to the solution. The mixture was stirred at rt for 2 h. After the reaction, the mixture was diluted with dichloromethane, and washed with saturated aqueous $NaHCO_3$ and brine. The combined organic layers was dried over $MgSO_4$ and concentrated *in vacuo*. The pure ester **9** was obtained by preparative TLC (25 mg, 84%). The chemical structure was unambiguously determined by single crystal X-ray diffraction. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.17 (t, $J$ = 2.1 Hz, 1H), 8.92 (d, $J$ = 2.2 Hz, 2H), 7.53 – 7.45 (m, 2H), 7.45 – 7.36 (m, 2H), 7.31 – 7.22 (m, 4H), 5.74 (ddd, $J$ = 9.1, 4.6, 2.3 Hz, 1H), 5.68 (d, $J$ = 10.2 Hz, 1H), 4.67 (d, $J$ = 10.8 Hz, 1H), 4.57 (d, $J$ = 10.8 Hz, 1H), 2.60 – 2.50 (m, 1H), 2.52 – 2.36 (m, 2H), 1.11 (d, $J$ = 6.7 Hz, 4H). **HRMS** (ESI-TOF) $m$ / $z$ calcd for $C_{21}H_{20}O_6N_2Cl$ $[M+Cl]^+$: 431.1010, found: 431.1021.




Sulfamate **14** was prepared by the reported procedure for sulfamylation.[6] **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.46 – 7.34 (m, 5H), 5.75 – 5.59 (m, 2H), 4.46 (d, *J* = 9.7 Hz, 1H), 4.34 (br, 1H), 4.24 (d, *J* = 8.5 Hz, 2H), 2.45 – 2.32 (m, 4H), 1.54 – 1.41 (m, 1H), 1.17 – 1.01 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.9, 132.8, 128.6, 126.9, 126.1, 123.5, 75.3, 40.3, 37.3, 33.8, 27.9, 21.7. **IR** (ATR): 3379 (br), 3285 (br), 3022, 2956, 2926, 2871, 2854, 1656, 1601, 1553, 1497, 1453, 1446, 1361, 1179, 974, 918, 824, 756, 698 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{14}H_{19}O_3SNNa$ $[M + Na]^+$: 304.0983, found: 304.0971. $[\alpha]_D^{24.1}$ –28.2 (*c* 0.330, $CHCl_3$).

In 1 dram vial, manganese(III) phthalocyanine chloride (4.3 mg, 0.007 mmol, 10 mol%) and $AgSbF_6$ (19.0 mg, 0.007 mmol, 10 mol%) were dissolved in benzene/MeCN (180/20 μL). Sulfamate **14** (20.0 mg, 0.071 mmol) and $PhI(OPiv)_2$ (57.6 mg, 0.014 mmol, 2 equiv) were added to the mixture, and the mixture was stirred for 24 h at rt at which full conversion of **14** was observed by TLC analysis. The pure cyclic sulfamate **15** was obtained by preparative TLC (3:1 hexanes:EtOAc, 10.2 mg, 52% yield) as a white solid. Diastereomeric ratio was determined by $^1$H and $^{13}$C NMR analysis. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.49 – 7.38 (m, 4H), 7.36 – 7.29 (m, 1H), 5.99 (dt, *J* = 10.2, 2.7 Hz, 1H), 5.82 (dtd, *J* = 10.2, 2.5, 0.9 Hz, 1H), 4.98 (d, *J* = 12.2 Hz, 1H), 4.78 (dd, *J* = 12.2, 1.7 Hz, 1H), 4.59 – 4.52 (m, 1H), 2.40 – 2.31 (m, 1H), 2.00 (dd, *J* = 14.6, 6.2 Hz, 1H), 1.76 (dd, *J* = 14.6, 8.5 Hz, 2H), 0.87 (d, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.2, 135.0, 129.3, 127.8, 126.6, 125.3, 74.4, 58.9, 39.0, 38.1, 28.1, 21.2. **IR** (ATR): 3275, 3029, 2958, 2927, 2855, 1418, 1392, 1361, 1183, 1006, 953, 917, 751, 698, 666 $cm^{-1}$. **HRMS** (ESI-TOF) *m* / *z* calcd for $C_{14}H_{17}O_3SNNa$ $[M+Na]^+$: 302.0827, found: 302.0819. $[\alpha]_D^{25.1}$ –92.9 (*c* 0.435, $CHCl_3$).

**5. X-ray Crystallographic Data for 13**



X-ray Data Collection, Structure Solution and Refinement for vmd21.

A colorless crystal of approximate dimensions 0.148 x 0.382 x 0.436 mm was mounted on a glass fiber and transferred to a Bruker SMART APEX II diffractometer. The APEX2[1] program package was used to determine the unit-cell parameters and for data collection (15 sec/frame scan time for a sphere of diffraction data). The raw frame data was processed using SAINT[2] and SADABS[3] to yield the reflection data file. Subsequent calculations were carried out using the SHELXTL[4] program. The diffraction symmetry was *mmm* and the systematic absences were consistent with the orthorhombic space group $P2_12_12_1$ that was later determined to be correct.

The structure was solved by direct methods and refined on $F^2$ by full-matrix least-squares techniques. The analytical scattering factors[5] for neutral atoms were used throughout the analysis. Hydrogen atoms were located from a difference-Fourier map and refined (x,y,z and $U_{iso}$).

At convergence, wR2 = 0.0760 and Goof = 1.032 for 342 variables refined against 4704 data (0.74Å), R1 = 0.0304 for those 4396 data with $I > 2.0\sigma(I)$. The absolute structure was assigned by the synthetic method used and was confirmed by refinement of the Flack parameter[6].

References.


1. APEX2 Version 2014.11-0, Bruker AXS, Inc.; Madison, WI 2014.
2. SAINT Version 8.34a, Bruker AXS, Inc.; Madison, WI 2013.
3. Sheldrick, G. M. SADABS, Version 2014/5, Bruker AXS, Inc.; Madison, WI 2014.
4. Sheldrick, G. M. SHELXTL, Version 2014/7, Bruker AXS, Inc.; Madison, WI 2014.
5. International Tables for Crystallography 1992, Vol. C., Dordrecht: Kluwer Academic Publishers.
6. Parsons, S., Flack, H. D., Wagner, T. Acta Cryst. B69, 249-259, 2013.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Definitions:

$wR2 = [\Sigma[w(F_o^2-F_c^2)^2] / \Sigma[w(F_o^2)^2] ]^{1/2}$

$R1 = \Sigma||F_o|-|F_c|| / \Sigma|F_o|$

$Goof = S = [\Sigma[w(F_o^2-F_c^2)^2] / (n-p)]^{1/2}$ where n is the number of reflections and p is the total number of parameters refined.

The thermal ellipsoid plot is shown at the 50% probability level.

**Table A2.2.1.** Crystal data and structure refinement for vmd21.

| | |
|---|---|
| Identification code | vmd21 |
| Empirical formula | $C_{21}\ H_{20}\ N_2\ O_6$ |
| Formula weight | 396.39 |
| Temperature | 133(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Orthorhombic |
| Space group | $P2_12_12_1$ |

| | | |
|---|---|---|
| Unit cell dimensions | a = 5.8695(3) Å | α= 90°. |
| | b = 9.7673(5) Å | β= 90°. |
| | c = 33.5180(18) Å | γ= 90°. |
| Volume | 1921.56(17) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.370 $Mg/m^3$ | |
| Absorption coefficient | 0.102 $mm^{-1}$ | |
| F(000) | 832 | |
| Crystal color | colorless | |
| Crystal size | 0.436 x 0.382 x 0.148 $mm^3$ | |
| Theta range for data collection | 2.172 to 28.801° | |
| Index ranges | $-7 \le h \le 7, -13 \le k \le 13, -44 \le l \le 44$ | |
| Reflections collected | 23122 | |
| Independent reflections | 4704 [R(int) = 0.0256] | |
| Completeness to theta = 25.500° | 99.9 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.8621 and 0.8197 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 4704 / 0 / 342 | |
| Goodness-of-fit on $F^2$ | 1.032 | |
| Final R indices [I>2sigma(I) = 4396 data] | R1 = 0.0304, wR2 = 0.0742 | |
| R indices (all data, 0.74Å) | R1 = 0.0334, wR2 = 0.0760 | |
| Absolute structure parameter | -0.2(3) | |
| Largest diff. peak and hole | 0.228 and -0.165 $e.Å^{-3}$ | |

**Table A2.2.2.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$ x $10^3$) for vmd21. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 668(2) | 9264(1) | 957(1) | 18(1) |
| O(2) | 3623(2) | 8488(1) | 594(1) | 23(1) |
| O(3) | -5546(2) | 11628(1) | 314(1) | 27(1) |
| O(4) | -5851(2) | 11621(1) | -331(1) | 32(1) |
| O(5) | -333(2) | 9166(1) | -1133(1) | 28(1) |
| O(6) | 2732(2) | 8405(1) | -848(1) | 27(1) |
| N(1) | -4878(2) | 11311(1) | -20(1) | 22(1) |
| N(2) | 848(3) | 8944(1) | -838(1) | 21(1) |
| C(1) | 511(3) | 9480(2) | 1672(1) | 16(1) |
| C(2) | -1704(3) | 8648(2) | 1712(1) | 19(1) |
| C(3) | -1319(3) | 7232(2) | 1879(1) | 24(1) |
| C(4) | 573(3) | 6846(2) | 2062(1) | 24(1) |
| C(5) | 2570(3) | 7770(2) | 2131(1) | 21(1) |
| C(6) | 1916(3) | 9266(2) | 2056(1) | 18(1) |
| C(7) | 48(3) | 11006(2) | 1596(1) | 17(1) |
| C(8) | 1703(3) | 11990(2) | 1674(1) | 22(1) |
| C(9) | 1336(3) | 13365(2) | 1584(1) | 26(1) |
| C(10) | -677(3) | 13785(2) | 1411(1) | 26(1) |
| C(11) | -2339(3) | 12819(2) | 1327(1) | 25(1) |
| C(12) | -1969(3) | 11447(2) | 1419(1) | 21(1) |
| C(13) | 3571(4) | 7593(2) | 2548(1) | 33(1) |
| C(14) | 1910(3) | 8936(2) | 1320(1) | 17(1) |
| C(15) | 1741(3) | 8984(2) | 618(1) | 17(1) |
| C(16) | 351(3) | 9374(2) | 263(1) | 17(1) |
| C(17) | -1652(3) | 10132(2) | 295(1) | 18(1) |
| C(18) | -2780(3) | 10489(2) | -51(1) | 19(1) |

| | | | | |
|---|---|---|---|---|
| C(19) | -2035(3) | 10115(2) | -429(1) | 20(1) |
| C(20) | -47(3) | 9360(2) | -446(1) | 18(1) |
| C(21) | 1163(3) | 8982(2) | -110(1) | 17(1) |

**Table A2.2.3.** Bond lengths [Å] and angles [°] for vmd21.

| | |
|---|---|
| O(1)-C(15) | 1.3264(18) |
| O(1)-C(14) | 1.4540(18) |
| O(2)-C(15) | 1.209(2) |
| O(3)-N(1) | 1.2253(19) |
| O(4)-N(1) | 1.2271(19) |
| O(5)-N(2) | 1.2259(18) |
| O(6)-N(2) | 1.2256(19) |
| N(1)-C(18) | 1.474(2) |
| N(2)-C(20) | 1.472(2) |
| C(1)-C(14) | 1.532(2) |
| C(1)-C(7) | 1.536(2) |
| C(1)-C(2) | 1.540(2) |
| C(1)-C(6) | 1.543(2) |
| C(2)-C(3) | 1.508(2) |
| C(3)-C(4) | 1.325(3) |
| C(4)-C(5) | 1.497(3) |
| C(5)-C(13) | 1.528(2) |
| C(5)-C(6) | 1.531(2) |
| C(7)-C(8) | 1.392(2) |
| C(7)-C(12) | 1.392(2) |
| C(8)-C(9) | 1.393(2) |
| C(9)-C(10) | 1.379(3) |
| C(10)-C(11) | 1.386(3) |
| C(11)-C(12) | 1.392(2) |
| C(15)-C(16) | 1.493(2) |

| | |
|---|---|
| C(16)-C(21) | 1.391(2) |
| C(16)-C(17) | 1.393(2) |
| C(17)-C(18) | 1.383(2) |
| C(18)-C(19) | 1.387(2) |
| C(19)-C(20) | 1.382(2) |
| C(20)-C(21) | 1.382(2) |
| C(15)-O(1)-C(14) | 115.64(12) |
| O(3)-N(1)-O(4) | 124.38(15) |
| O(3)-N(1)-C(18) | 118.11(14) |
| O(4)-N(1)-C(18) | 117.50(14) |
| O(6)-N(2)-O(5) | 124.30(14) |
| O(6)-N(2)-C(20) | 117.72(13) |
| O(5)-N(2)-C(20) | 117.98(14) |
| C(14)-C(1)-C(7) | 107.65(12) |
| C(14)-C(1)-C(2) | 109.69(12) |
| C(7)-C(1)-C(2) | 112.19(13) |
| C(14)-C(1)-C(6) | 108.01(12) |
| C(7)-C(1)-C(6) | 111.42(12) |
| C(2)-C(1)-C(6) | 107.81(13) |
| C(3)-C(2)-C(1) | 113.00(14) |
| C(4)-C(3)-C(2) | 123.95(16) |
| C(3)-C(4)-C(5) | 123.77(16) |
| C(4)-C(5)-C(13) | 111.93(15) |
| C(4)-C(5)-C(6) | 110.75(14) |
| C(13)-C(5)-C(6) | 110.75(15) |
| C(5)-C(6)-C(1) | 113.57(13) |
| C(8)-C(7)-C(12) | 117.39(15) |
| C(8)-C(7)-C(1) | 121.01(14) |
| C(12)-C(7)-C(1) | 121.44(14) |
| C(7)-C(8)-C(9) | 121.15(17) |
| C(10)-C(9)-C(8) | 120.69(17) |

| | |
|---|---|
| C(9)-C(10)-C(11) | 119.09(16) |
| C(10)-C(11)-C(12) | 120.04(17) |
| C(11)-C(12)-C(7) | 121.64(16) |
| O(1)-C(14)-C(1) | 107.43(12) |
| O(2)-C(15)-O(1) | 125.01(14) |
| O(2)-C(15)-C(16) | 123.24(14) |
| O(1)-C(15)-C(16) | 111.75(13) |
| C(21)-C(16)-C(17) | 120.34(15) |
| C(21)-C(16)-C(15) | 117.31(14) |
| C(17)-C(16)-C(15) | 122.32(14) |
| C(18)-C(17)-C(16) | 118.21(15) |
| C(17)-C(18)-C(19) | 123.31(15) |
| C(17)-C(18)-N(1) | 118.45(15) |
| C(19)-C(18)-N(1) | 118.23(14) |
| C(20)-C(19)-C(18) | 116.38(15) |
| C(21)-C(20)-C(19) | 122.87(15) |
| C(21)-C(20)-N(2) | 118.12(15) |
| C(19)-C(20)-N(2) | 119.01(14) |
| C(20)-C(21)-C(16) | 118.88(15) |

**Table A2.2.4.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for vmd21. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 16(1) | 23(1) | 15(1) | -1(1) | 0(1) | 3(1) |
| O(2) | 23(1) | 25(1) | 21(1) | 2(1) | 2(1) | 9(1) |
| O(3) | 22(1) | 24(1) | 36(1) | -2(1) | 4(1) | 5(1) |
| O(4) | 26(1) | 30(1) | 39(1) | 2(1) | -11(1) | 6(1) |
| O(5) | 40(1) | 27(1) | 17(1) | 2(1) | -3(1) | -3(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| O(6) | 30(1) | 28(1) | 22(1) | 0(1) | 6(1) | 3(1) |
| N(1) | 17(1) | 16(1) | 34(1) | 0(1) | -3(1) | 0(1) |
| N(2) | 30(1) | 16(1) | 17(1) | 1(1) | 2(1) | -4(1) |
| C(1) | 13(1) | 17(1) | 17(1) | -1(1) | 0(1) | 2(1) |
| C(2) | 15(1) | 19(1) | 24(1) | -2(1) | 2(1) | 1(1) |
| C(3) | 21(1) | 18(1) | 31(1) | 1(1) | 6(1) | -2(1) |
| C(4) | 26(1) | 19(1) | 28(1) | 5(1) | 6(1) | 1(1) |
| C(5) | 20(1) | 24(1) | 20(1) | 4(1) | 1(1) | 5(1) |
| C(6) | 18(1) | 21(1) | 17(1) | -1(1) | -1(1) | 1(1) |
| C(7) | 18(1) | 18(1) | 16(1) | -2(1) | 2(1) | 1(1) |
| C(8) | 19(1) | 21(1) | 27(1) | 0(1) | -2(1) | 0(1) |
| C(9) | 27(1) | 18(1) | 34(1) | -1(1) | 0(1) | -5(1) |
| C(10) | 33(1) | 18(1) | 26(1) | 3(1) | 2(1) | 4(1) |
| C(11) | 24(1) | 25(1) | 26(1) | 3(1) | -3(1) | 6(1) |
| C(12) | 19(1) | 21(1) | 23(1) | -1(1) | -2(1) | 0(1) |
| C(13) | 37(1) | 38(1) | 24(1) | 8(1) | -4(1) | 5(1) |
| C(14) | 16(1) | 21(1) | 16(1) | 0(1) | -1(1) | 2(1) |
| C(15) | 20(1) | 13(1) | 18(1) | 0(1) | 2(1) | 0(1) |
| C(16) | 18(1) | 13(1) | 19(1) | 0(1) | 0(1) | -2(1) |
| C(17) | 18(1) | 16(1) | 21(1) | -1(1) | 2(1) | -1(1) |
| C(18) | 16(1) | 14(1) | 27(1) | 0(1) | -1(1) | 0(1) |
| C(19) | 21(1) | 16(1) | 22(1) | 2(1) | -4(1) | -3(1) |
| C(20) | 24(1) | 14(1) | 17(1) | 0(1) | 2(1) | -4(1) |
| C(21) | 19(1) | 12(1) | 21(1) | 0(1) | 2(1) | -1(1) |

**Table A2.2.5.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$ x $10^3$) for vmd21.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2A) | -2760(40) | 9160(20) | 1885(6) | 24(5) |
| H(2B) | -2410(40) | 8560(20) | 1446(6) | 24(5) |
| H(3A) | -2590(40) | 6610(20) | 1846(6) | 29(5) |
| H(4A) | 690(40) | 5930(20) | 2146(6) | 34(6) |
| H(5A) | 3760(40) | 7490(20) | 1943(6) | 24(5) |
| H(6A) | 3280(30) | 9810(20) | 2051(5) | 18(4) |
| H(6B) | 970(30) | 9590(20) | 2283(5) | 19(5) |
| H(8A) | 3120(40) | 11740(20) | 1787(6) | 29(5) |
| H(9A) | 2390(40) | 13970(20) | 1646(6) | 35(6) |
| H(10A) | -960(40) | 14750(20) | 1350(6) | 35(6) |
| H(11A) | -3710(40) | 13090(20) | 1215(6) | 27(5) |
| H(12A) | -3150(40) | 10860(20) | 1363(6) | 33(6) |
| H(13A) | 4940(50) | 8200(20) | 2588(7) | 40(6) |
| H(13B) | 2480(40) | 7830(20) | 2749(6) | 32(6) |
| H(13C) | 4060(40) | 6630(20) | 2588(6) | 36(6) |
| H(14A) | 3410(30) | 9375(17) | 1308(5) | 12(4) |
| H(14B) | 2070(30) | 7915(18) | 1323(5) | 13(4) |
| H(17A) | -2170(40) | 10450(20) | 546(6) | 31(6) |
| H(19A) | -2770(40) | 10400(20) | -651(6) | 21(5) |
| H(21A) | 2540(30) | 8468(18) | -133(5) | 13(4) |

**Table A2.2.6.** Torsion angles [°] for vmd21.

| | |
|---|---|
| C(14)-C(1)-C(2)-C(3) | 73.56(17) |
| C(7)-C(1)-C(2)-C(3) | -166.85(13) |
| C(6)-C(1)-C(2)-C(3) | -43.81(18) |
| C(1)-C(2)-C(3)-C(4) | 15.8(2) |
| C(2)-C(3)-C(4)-C(5) | 0.5(3) |
| C(3)-C(4)-C(5)-C(13) | 137.95(19) |
| C(3)-C(4)-C(5)-C(6) | 13.8(2) |
| C(4)-C(5)-C(6)-C(1) | -45.01(19) |
| C(13)-C(5)-C(6)-C(1) | -169.80(14) |
| C(14)-C(1)-C(6)-C(5) | -57.92(17) |
| C(7)-C(1)-C(6)-C(5) | -175.95(14) |
| C(2)-C(1)-C(6)-C(5) | 60.54(17) |
| C(14)-C(1)-C(7)-C(8) | -79.75(17) |
| C(2)-C(1)-C(7)-C(8) | 159.48(15) |
| C(6)-C(1)-C(7)-C(8) | 38.5(2) |
| C(14)-C(1)-C(7)-C(12) | 95.42(17) |
| C(2)-C(1)-C(7)-C(12) | -25.4(2) |
| C(6)-C(1)-C(7)-C(12) | -146.33(15) |
| C(12)-C(7)-C(8)-C(9) | 1.0(2) |
| C(1)-C(7)-C(8)-C(9) | 176.31(16) |
| C(7)-C(8)-C(9)-C(10) | -0.7(3) |
| C(8)-C(9)-C(10)-C(11) | 0.1(3) |
| C(9)-C(10)-C(11)-C(12) | 0.2(3) |
| C(10)-C(11)-C(12)-C(7) | 0.1(3) |
| C(8)-C(7)-C(12)-C(11) | -0.7(2) |
| C(1)-C(7)-C(12)-C(11) | -176.04(15) |
| C(15)-O(1)-C(14)-C(1) | 173.70(12) |
| C(7)-C(1)-C(14)-O(1) | -54.16(15) |
| C(2)-C(1)-C(14)-O(1) | 68.17(15) |

| | |
|---|---|
| C(6)-C(1)-C(14)-O(1) | -174.59(12) |
| C(14)-O(1)-C(15)-O(2) | 0.1(2) |
| C(14)-O(1)-C(15)-C(16) | -179.13(12) |
| O(2)-C(15)-C(16)-C(21) | 8.3(2) |
| O(1)-C(15)-C(16)-C(21) | -172.37(13) |
| O(2)-C(15)-C(16)-C(17) | -169.94(15) |
| O(1)-C(15)-C(16)-C(17) | 9.3(2) |
| C(21)-C(16)-C(17)-C(18) | -0.6(2) |
| C(15)-C(16)-C(17)-C(18) | 177.62(14) |
| C(16)-C(17)-C(18)-C(19) | 0.9(2) |
| C(16)-C(17)-C(18)-N(1) | -178.92(13) |
| O(3)-N(1)-C(18)-C(17) | -0.9(2) |
| O(4)-N(1)-C(18)-C(17) | 179.80(15) |
| O(3)-N(1)-C(18)-C(19) | 179.24(15) |
| O(4)-N(1)-C(18)-C(19) | 0.0(2) |
| C(17)-C(18)-C(19)-C(20) | -0.6(2) |
| N(1)-C(18)-C(19)-C(20) | 179.19(14) |
| C(18)-C(19)-C(20)-C(21) | 0.1(2) |
| C(18)-C(19)-C(20)-N(2) | -179.31(14) |
| O(6)-N(2)-C(20)-C(21) | -7.1(2) |
| O(5)-N(2)-C(20)-C(21) | 173.24(14) |
| O(6)-N(2)-C(20)-C(19) | 172.33(14) |
| O(5)-N(2)-C(20)-C(19) | -7.3(2) |
| C(19)-C(20)-C(21)-C(16) | 0.2(2) |
| N(2)-C(20)-C(21)-C(16) | 179.55(13) |
| C(17)-C(16)-C(21)-C(20) | 0.1(2) |
| C(15)-C(16)-C(21)-C(20) | -178.20(13) |

## 6. References


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4. Park, J.-W.; Kou, K. G. M.; Kim, D. K.; Dong, V. M. *Chem. Sci.* **2015**, *6*, 4479.
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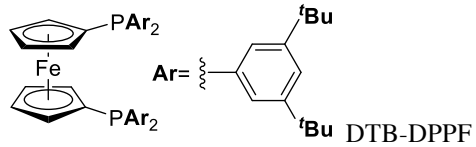
6. Paradine, S. M.; Griffin, J. R.; Zhao, J.; Petronico, A. L.; Miller S. M.; White, M. C. *Nature Chem.* **2015**, *7*, 987.


## 7. NMR Spectra

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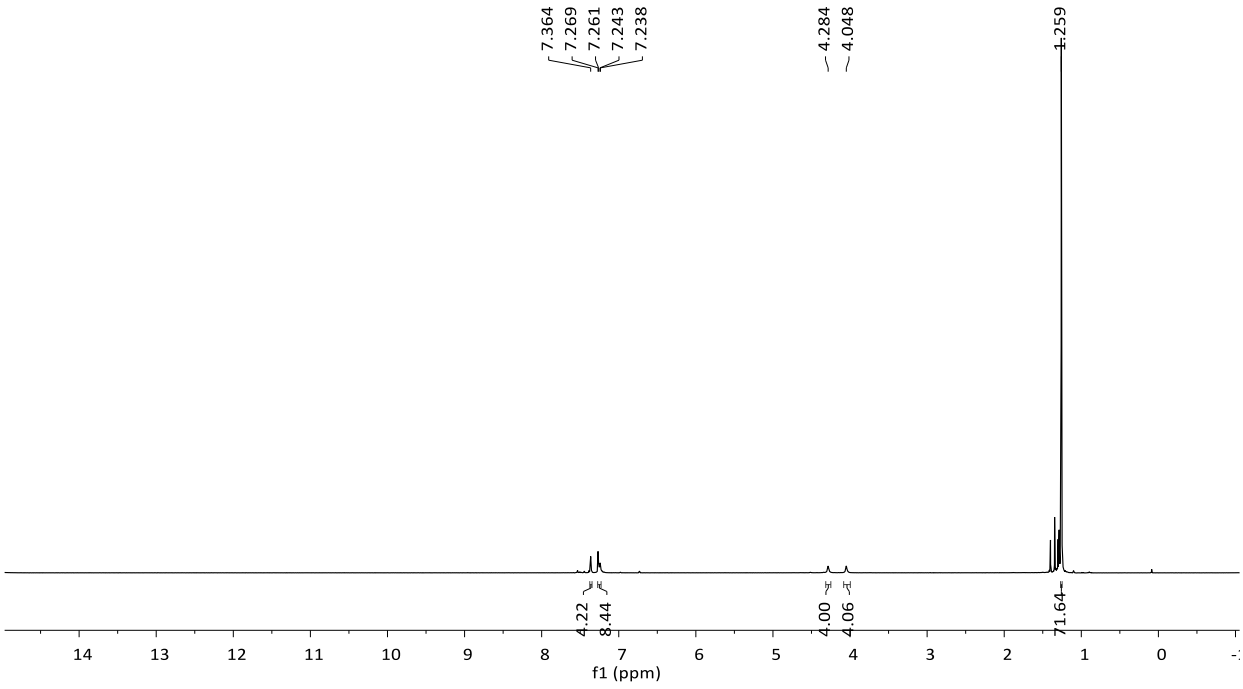

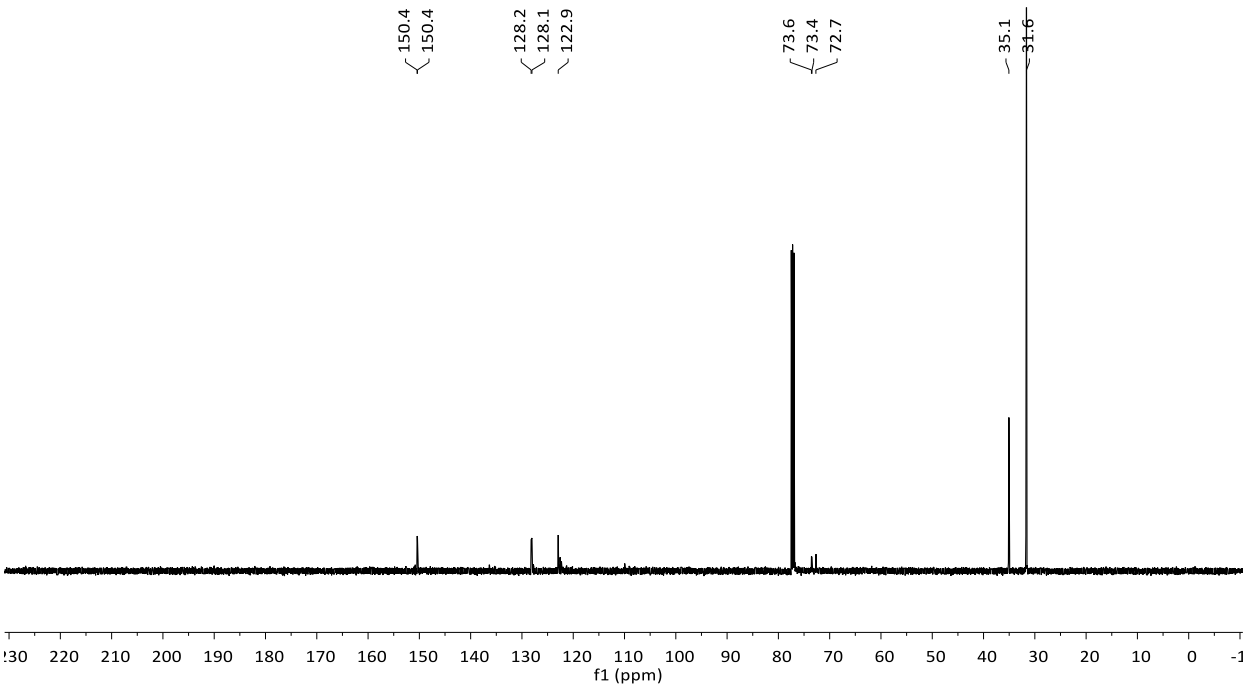
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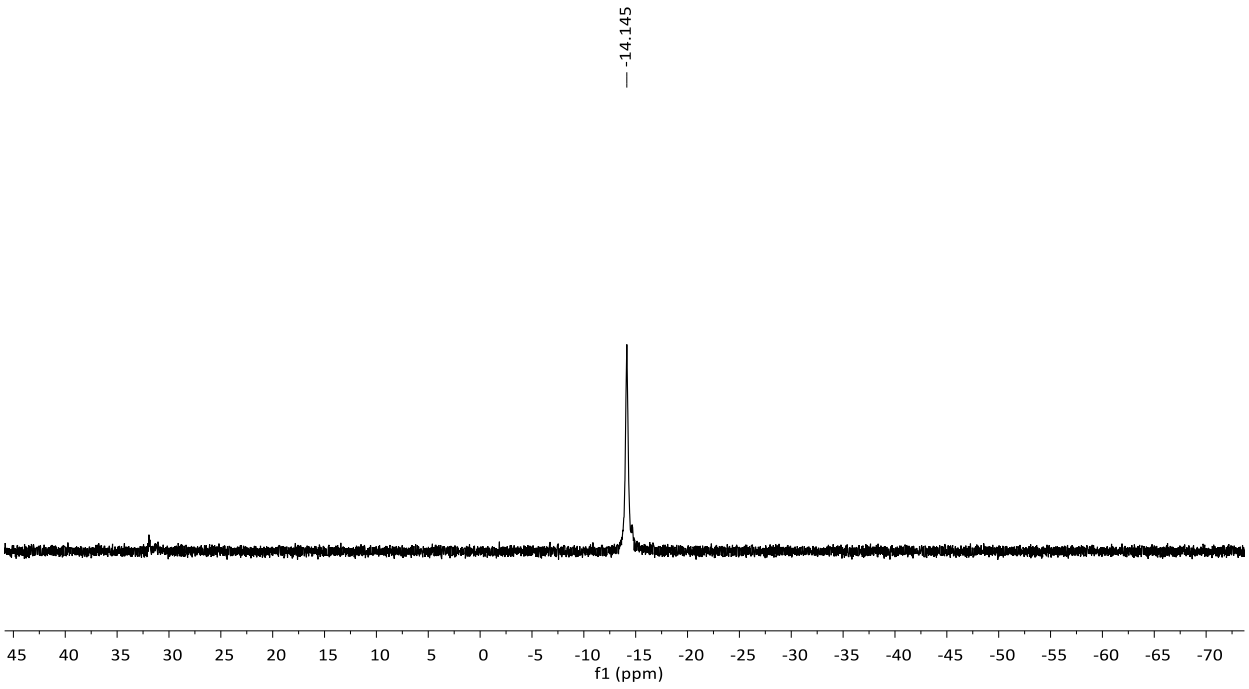
128.1
122.9
73.6
73.4
72.7
35.1
31.6
f1 (ppm)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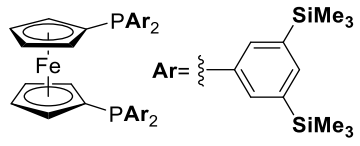
f1 (ppm)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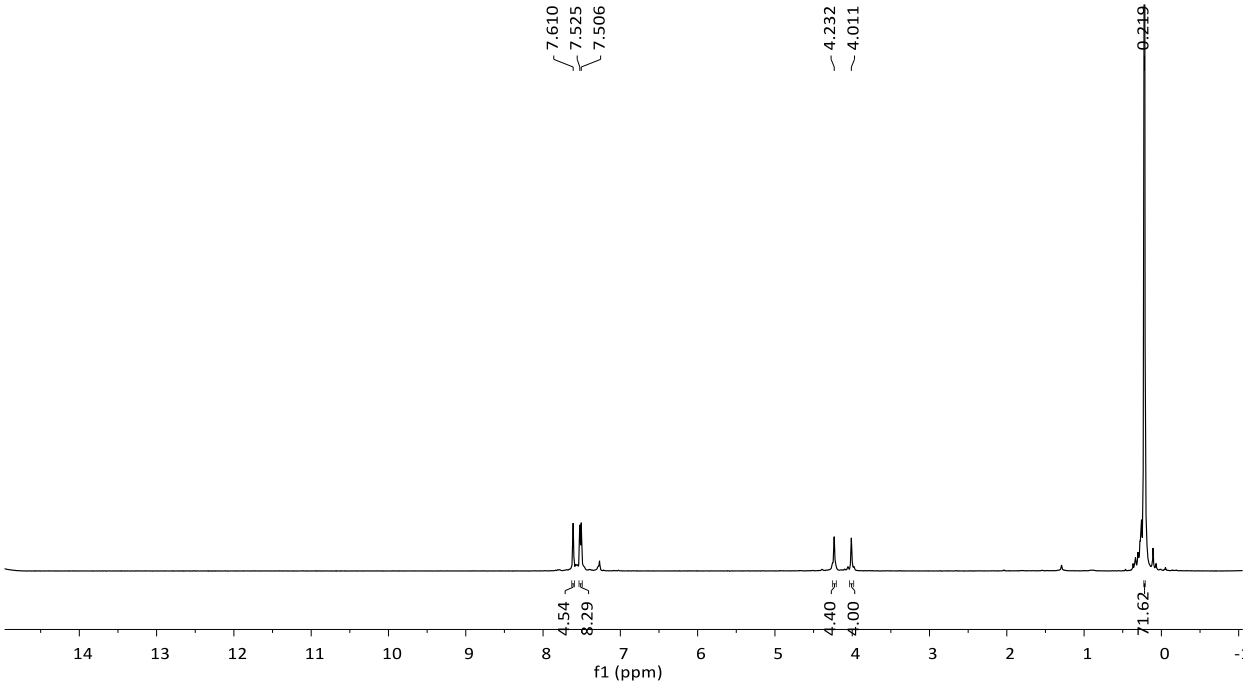
Fe
PAr2
Ar=
SiMe3
SiMe3

DTMS-DPPF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4.011
0.219
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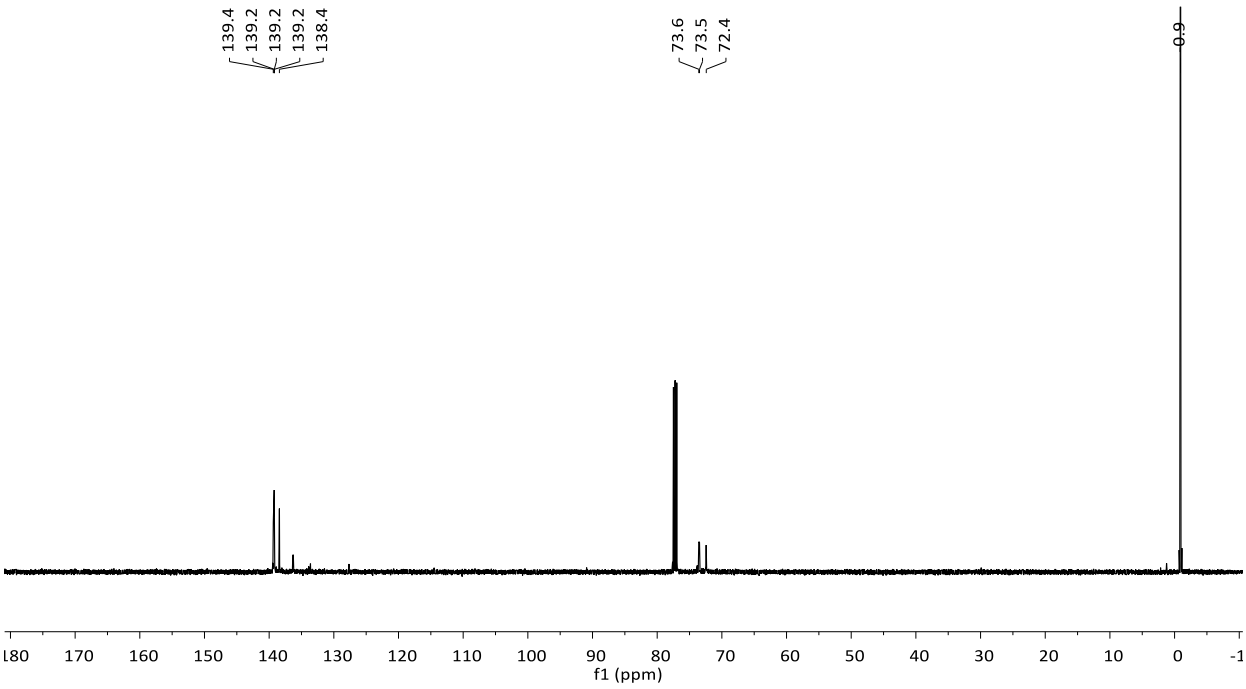
8.29
4.40
4.00
71.62
f1 (ppm)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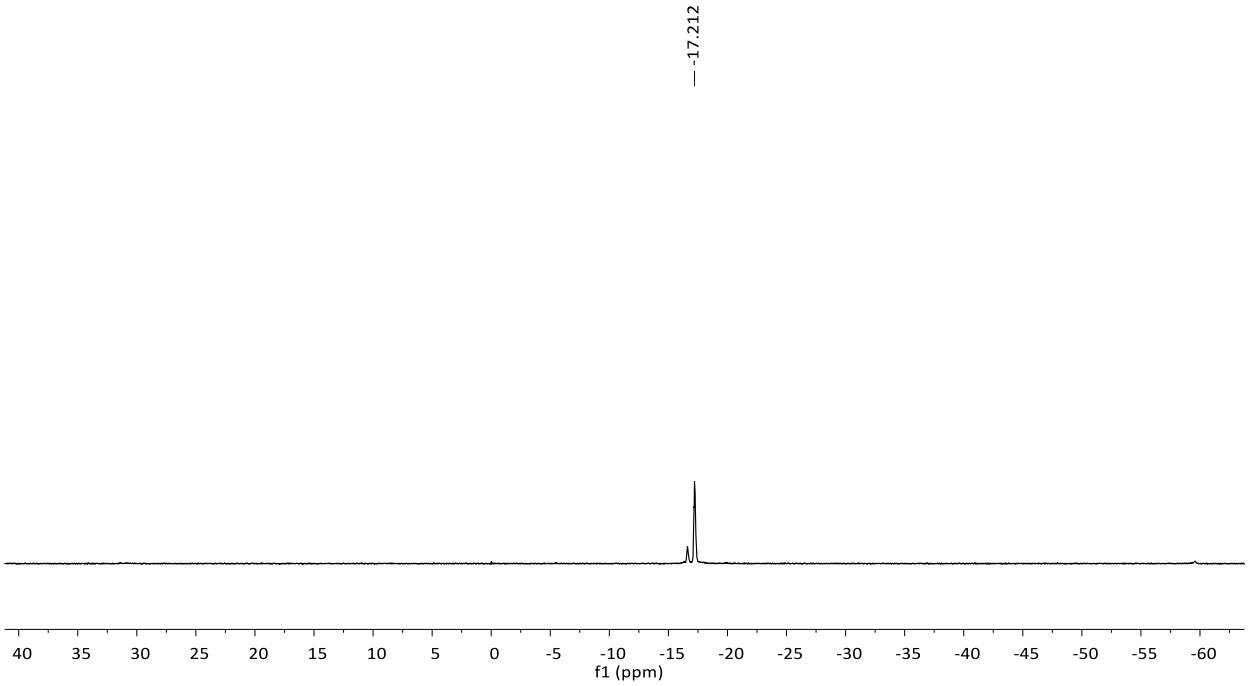
139.2
139.2
138.4
73.6
73.5
72.4
0.9
f1 (ppm)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35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
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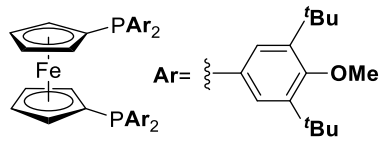
-40
-45
-50
-55
-60
f1 (ppm)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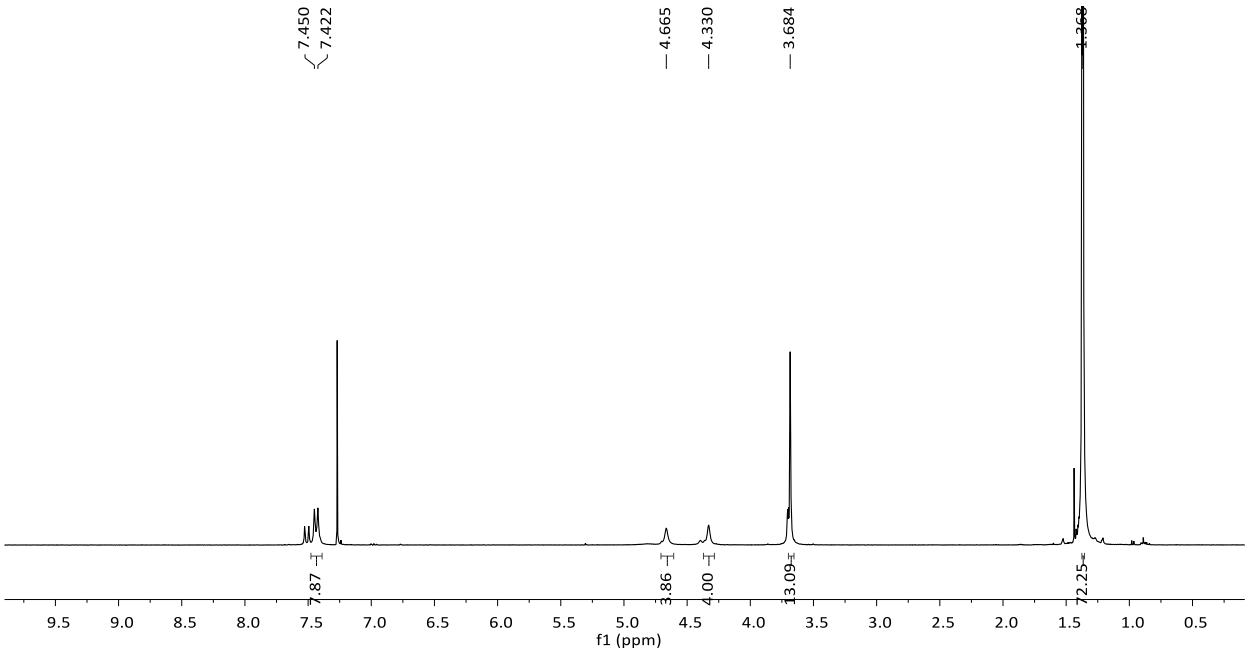
Fe
PAr2
Ar=
tBu
OMe
tBu

DTBM-DPPF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4.665
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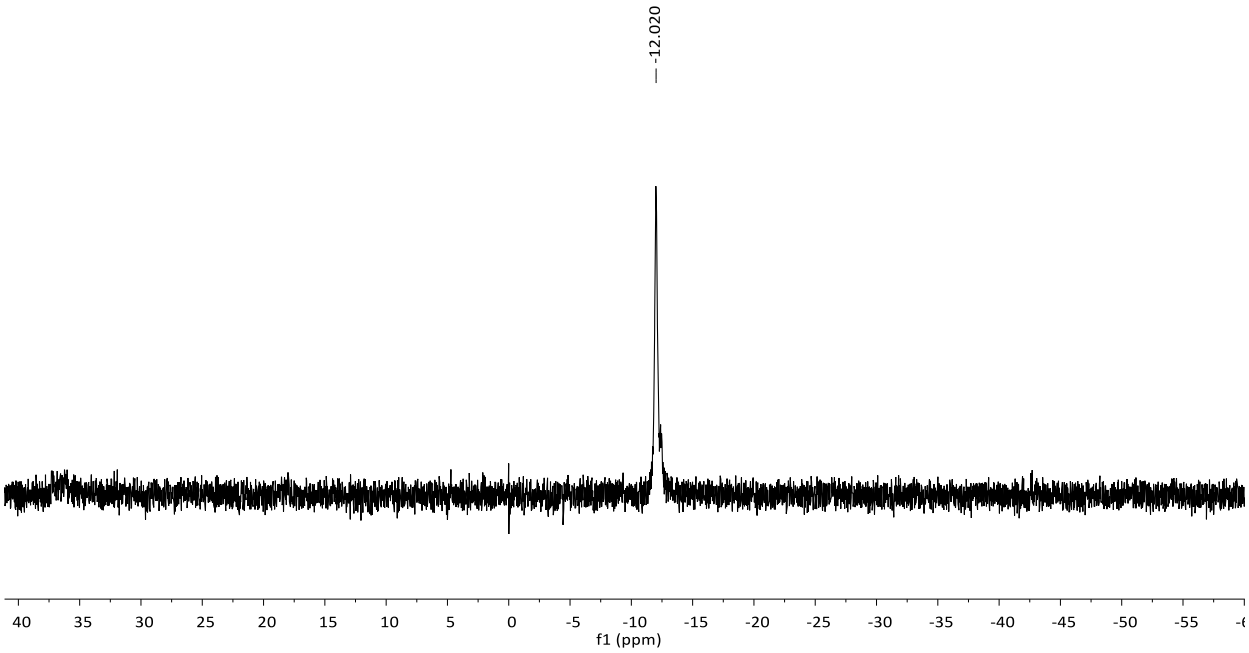
3.684
1.368
7.87
3.86
4.00
13.09
72.25
f1 (ppm)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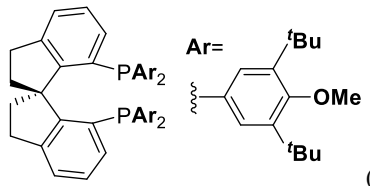
f1 (ppm)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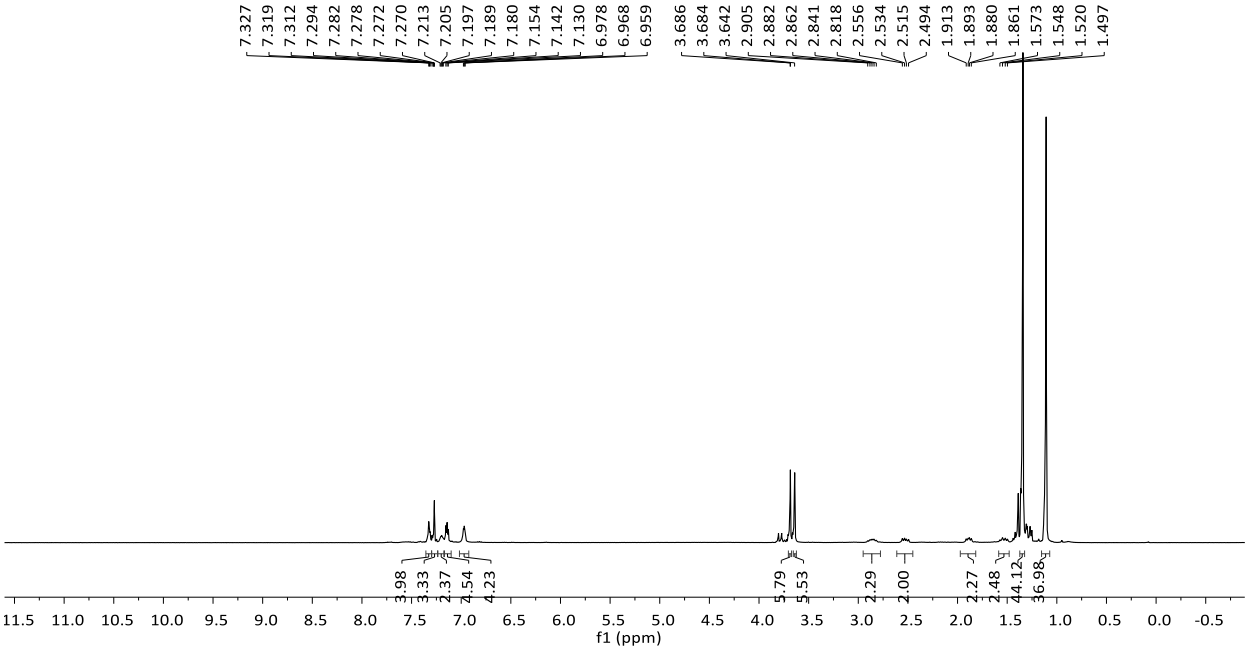
PAr2
Ar=
tBu
OMe
tBu

(*R*)-DTBM-SDP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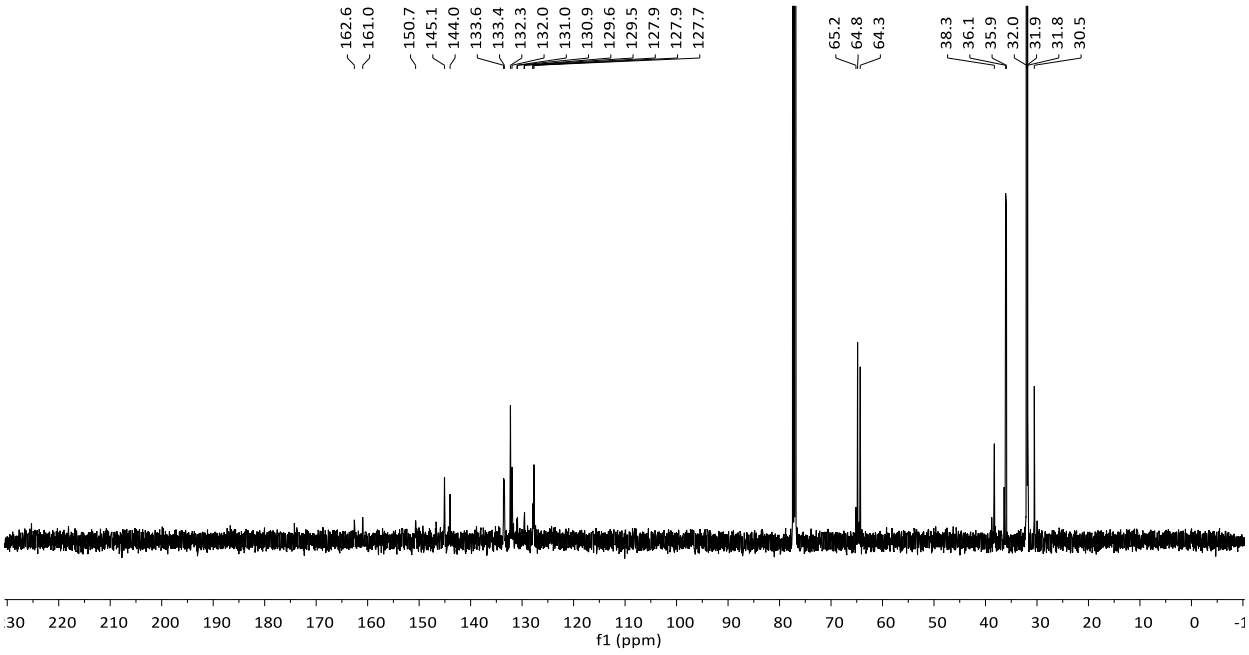
3.686 3.684 3.642 2.905 2.882 2.862 2.841 2.818 2.556 2.534 2.515 2.494
1.913 1.893 1.880 1.861 1.573 1.548 1.520 1.497
3.98 3.33 2.37 4.54 4.23 5.79 5.53 2.29 2.00 2.27 2.48 44.12 36.98
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


162.6 161.0 150.7 145.1 144.0 133.6 133.4 132.3 132.0 131.0 130.9 129.6 129.5 127.9 127.9 127.7
65.2 64.8 64.3
38.3 36.1 35.9 32.0 31.9 31.8 30.5
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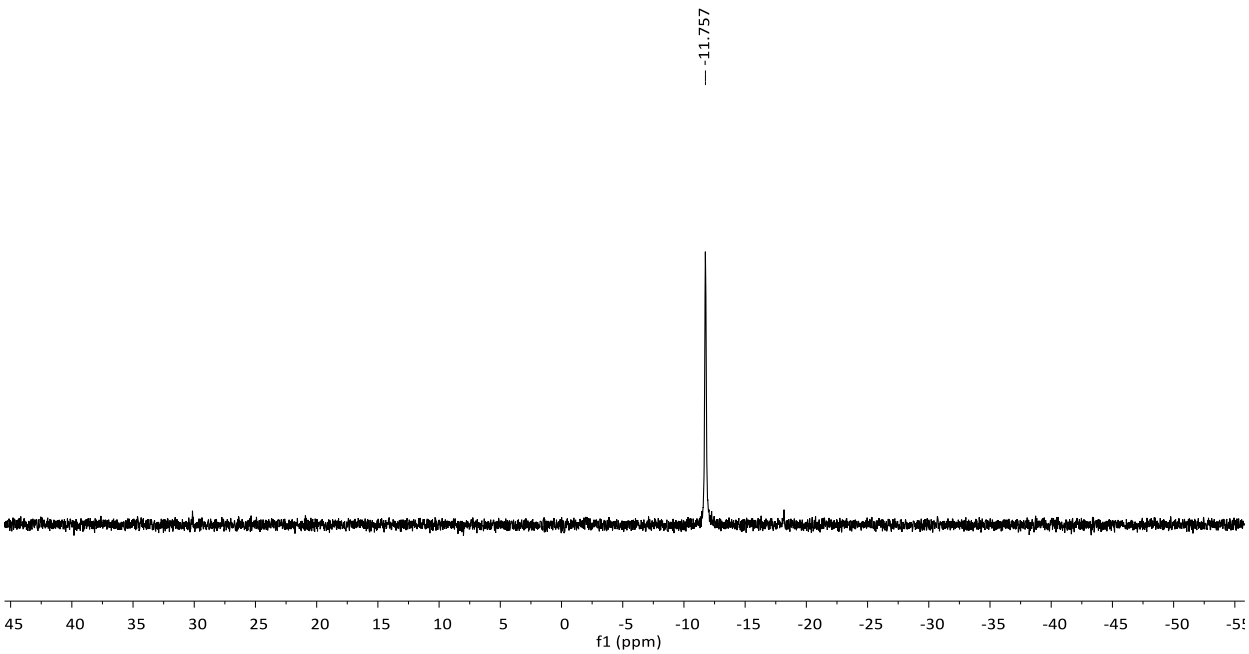
f1 (ppm)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35
30
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15
10
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0
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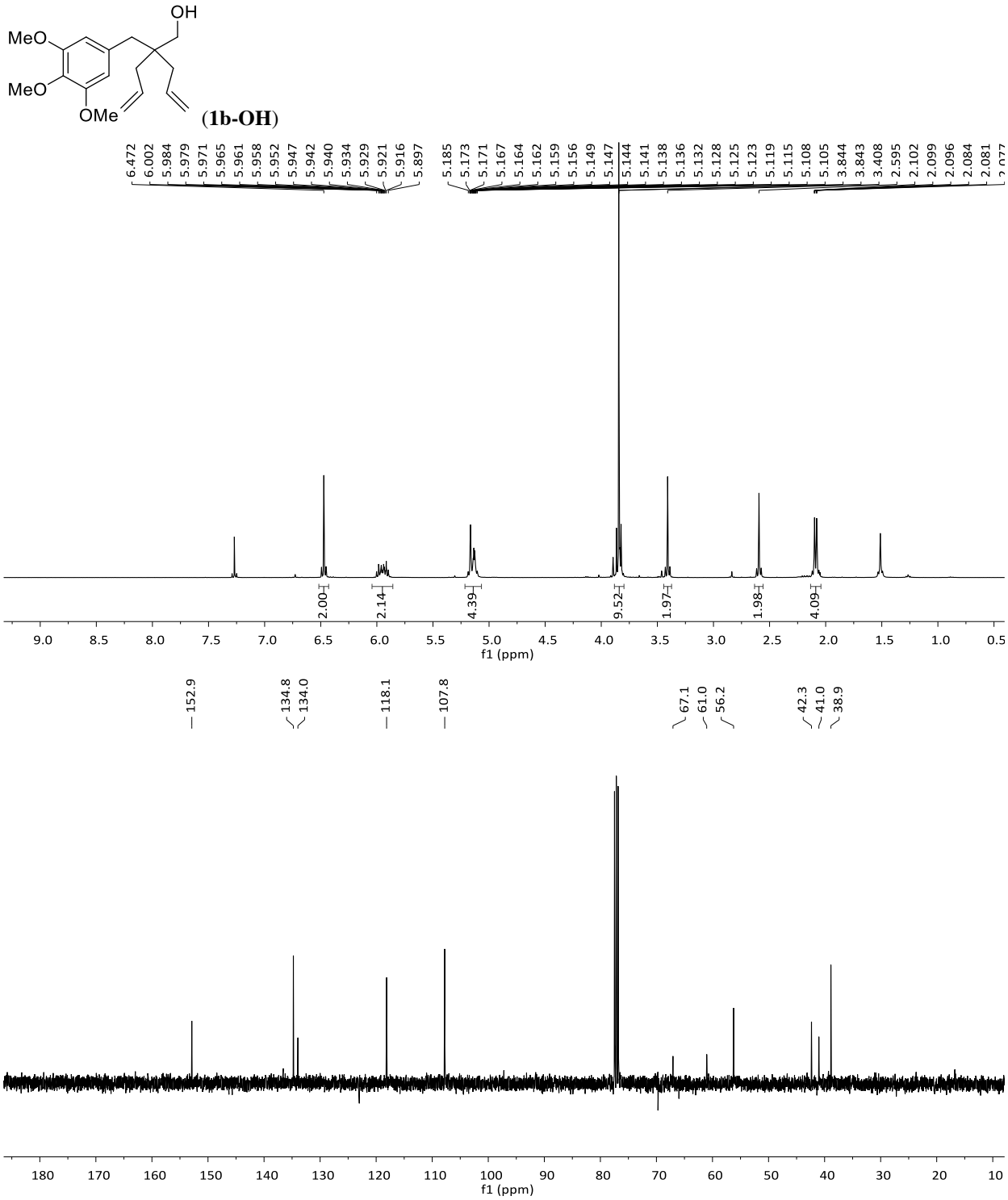
-10
-15
-20
-25
-30
-35
-40
-45
-50
f1 (ppm)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MeO
MeO
OMe
(1b-OH)
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5.979
5.971
5.965
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5.958
5.952
5.947
5.942
5.940
5.934
5.929
5.921
5.916
5.897
5.185
5.173
5.171
5.167
5.164
5.162
5.159
5.156
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5.147
5.144
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5.132
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5.125
5.123
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5.115
5.108
5.105
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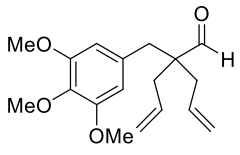
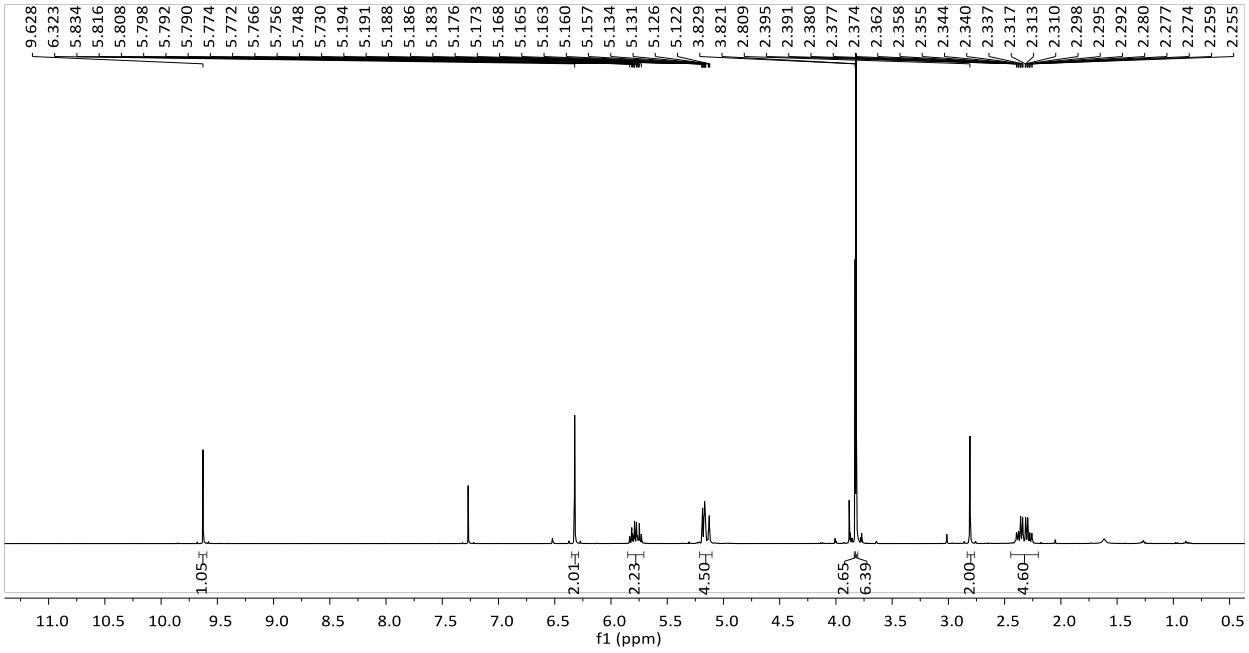
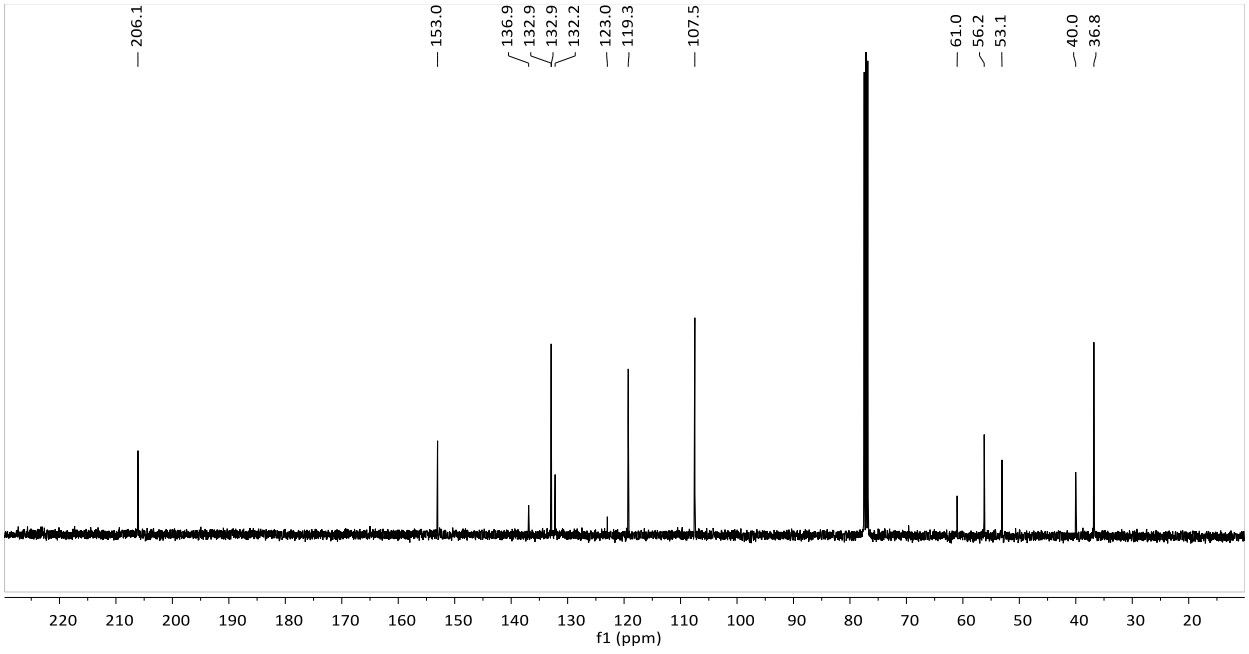
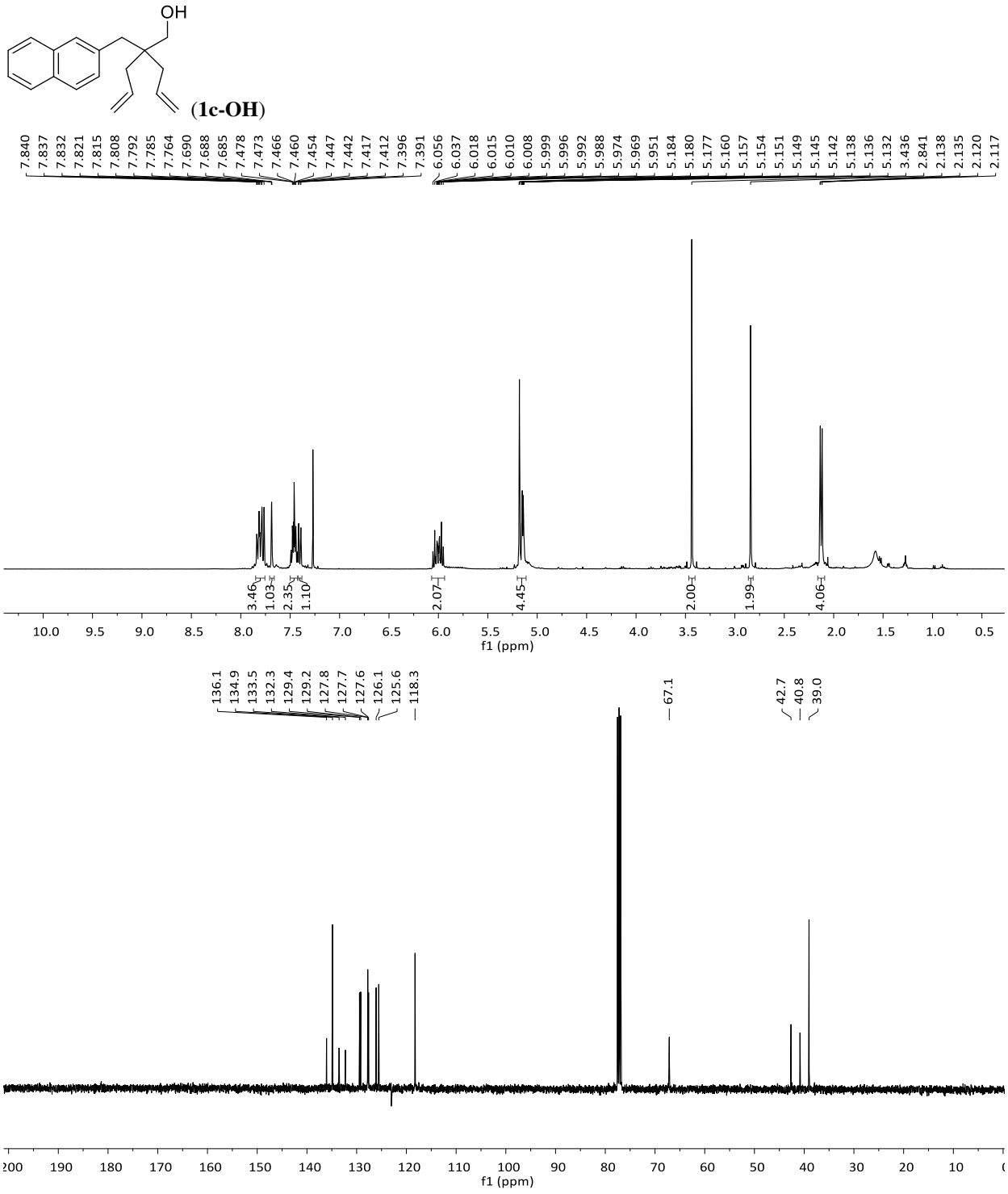
2.14
4.39
9.52
1.97
1.98
4.09
f1 (ppm)
152.9
134.8
134.0
118.1
107.8
67.1
61.0
56.2
42.3
41.0
38.9
f1 (ppm)

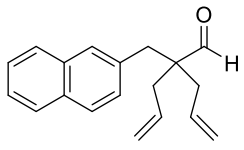

MeO
MeO
OMe
O
H

(**1b**)

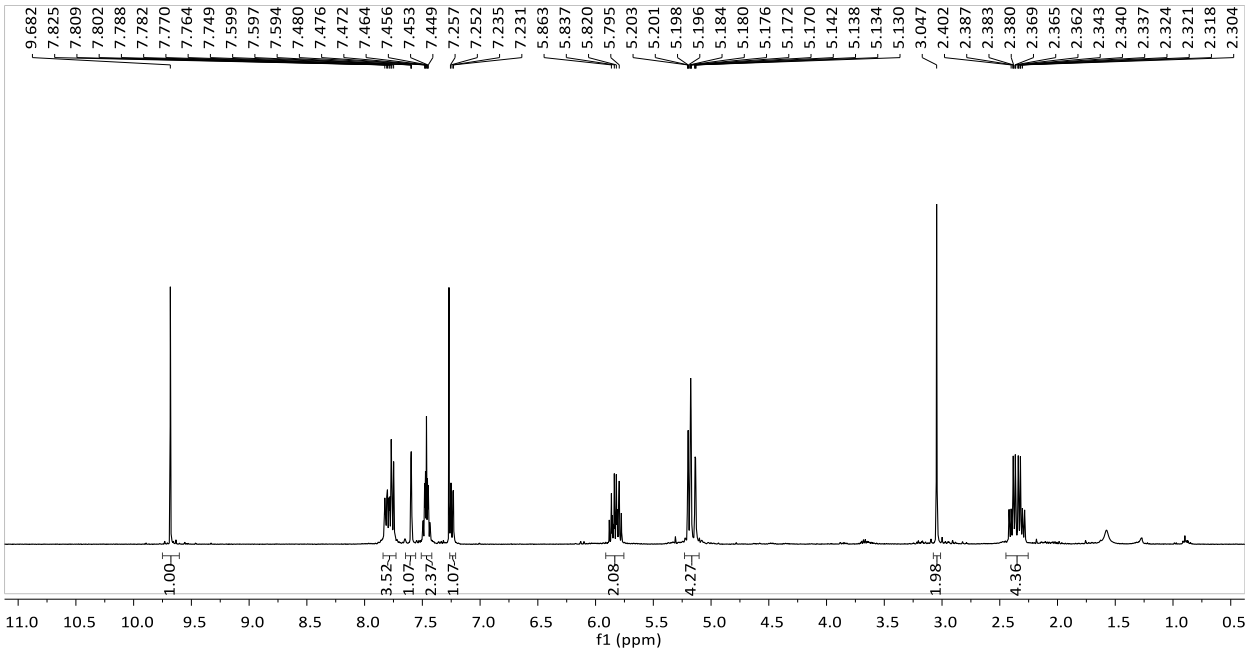

9.628
6.323
5.834
5.816
5.808
5.798
5.792
5.790
5.774
5.772
5.766
5.756
5.748
5.730
5.194
5.191
5.188
5.186
5.183
5.176
5.173
5.168
5.165
5.163
5.160
5.157
5.134
5.131
5.126
5.122
3.829
3.821
2.809
2.395
2.391
2.380
2.377
2.374
2.362
2.358
2.355
2.344
2.340
2.337
2.317
2.313
2.310
2.298
2.295
2.292
2.280
2.277
2.274
2.259
2.255
1.05
2.01
2.23
4.50
2.65
6.39
2.00
4.60
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

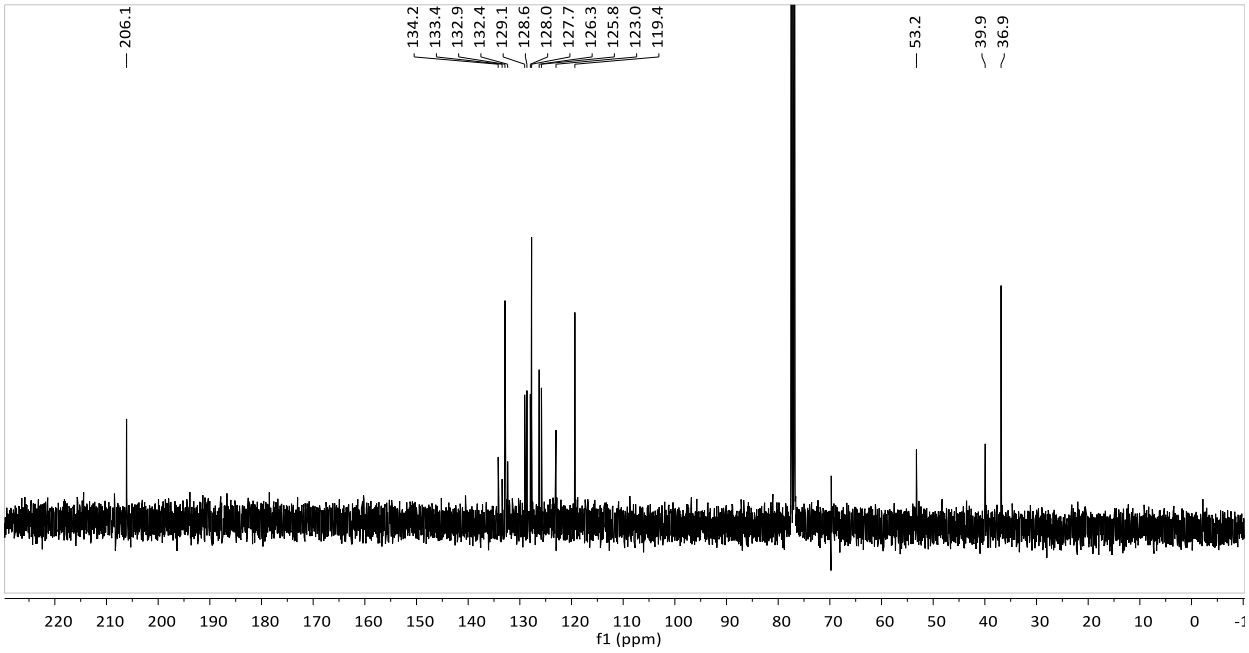

206.1
153.0
136.9
132.9
132.9
132.2
123.0
119.3
107.5
61.0
56.2
53.1
40.0
36.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

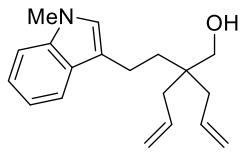

OH
(1c-OH)
7.840 7.837 7.832 7.821 7.815 7.808 7.792 7.785 7.764 7.690 7.688 7.685 7.478 7.473 7.466 7.460 7.454 7.447 7.442 7.417 7.412 7.396 7.391
6.056 6.037 6.018 6.015 6.010 6.008 5.999 5.996 5.992 5.988 5.974 5.969 5.951 5.184 5.180 5.177 5.160 5.157 5.154 5.151 5.149 5.145 5.142 5.138 5.136 5.132 3.436 2.841 2.138 2.135 2.120 2.117
3.46 1.03 2.35 1.10 2.07 4.45 2.00 1.99 4.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
136.1 134.9 133.5 132.3 129.4 129.2 127.8 127.7 127.6 126.1 125.6 118.3
67.1
42.7 40.8 39.0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
H

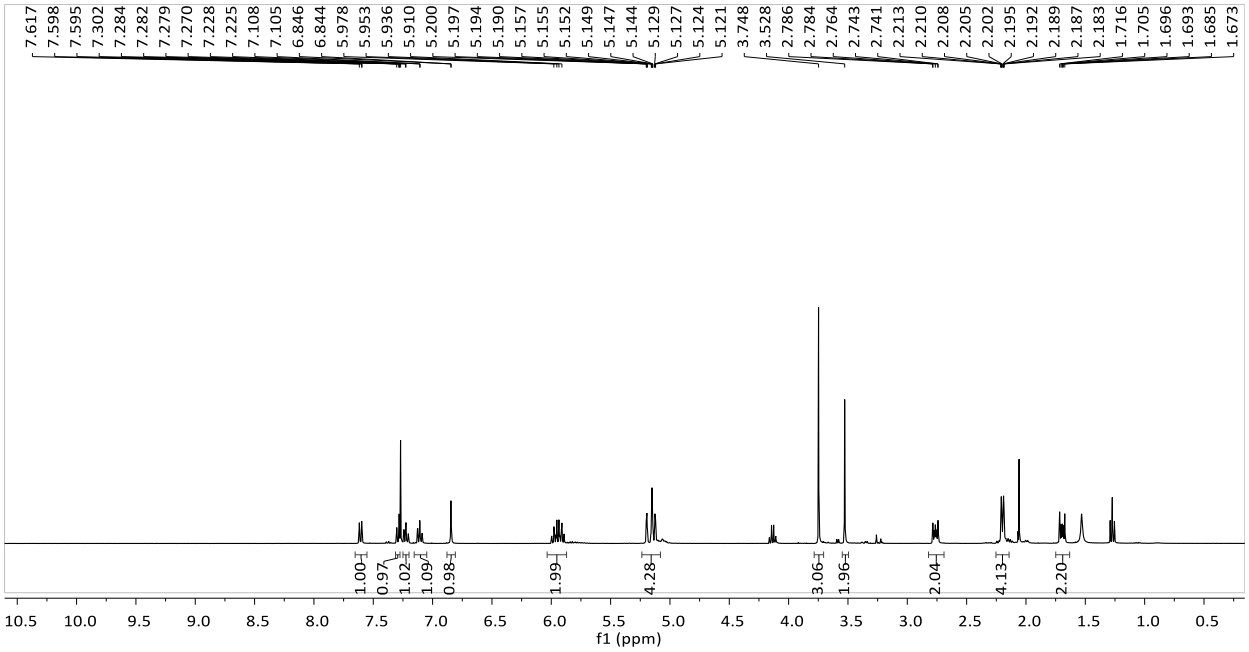
(**1c**)

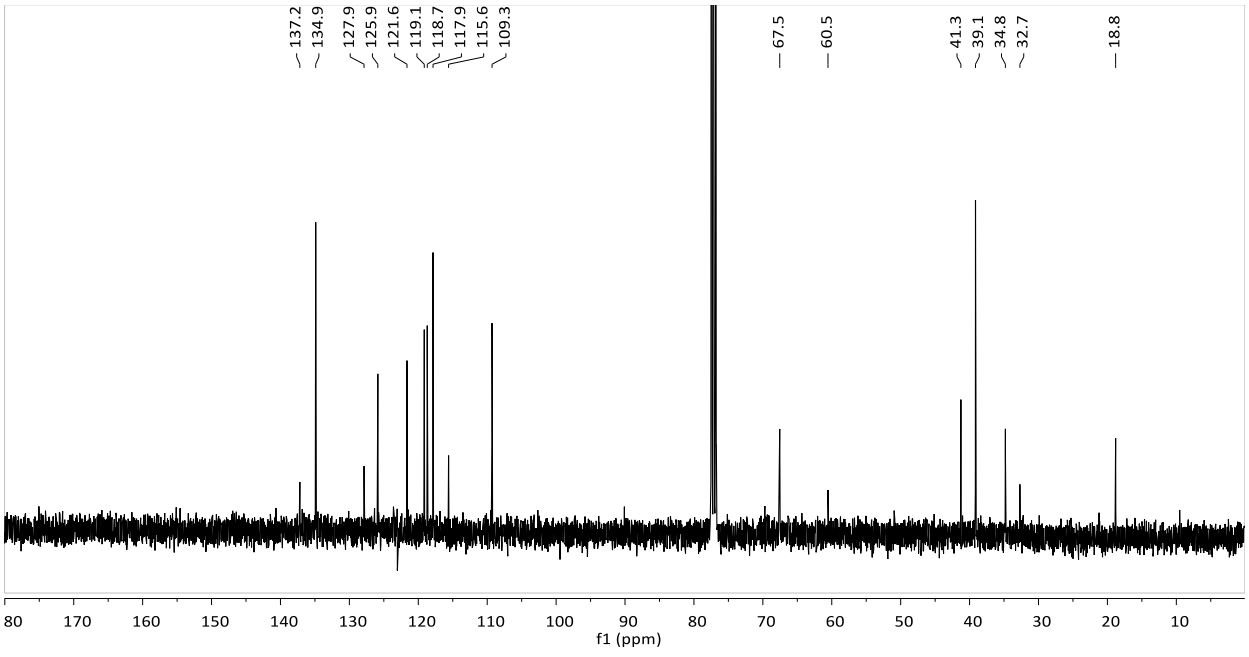

9.682
7.825
7.809
7.802
7.788
7.782
7.770
7.764
7.749
7.599
7.597
7.594
7.480
7.476
7.472
7.464
7.456
7.453
7.449
7.257
7.252
7.235
7.231
5.863
5.837
5.820
5.795
5.203
5.201
5.198
5.196
5.184
5.180
5.176
5.172
5.170
5.142
5.138
5.134
5.130
3.047
2.402
2.387
2.383
2.380
2.369
2.365
2.362
2.343
2.340
2.337
2.324
2.321
2.318
2.304
1.00
3.52
1.07
2.37
1.07
2.08
4.27
1.98
4.36
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

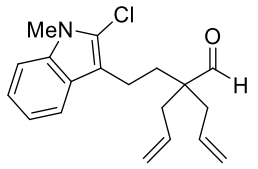

206.1
134.2
133.4
132.9
132.4
129.1
128.6
128.0
127.7
126.3
125.8
123.0
119.4
53.2
39.9
36.9
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MeN
OH

(**1d-OH**)


7.617
7.598
7.595
7.302
7.284
7.282
7.279
7.270
7.228
7.225
7.108
7.105
6.846
6.844
5.978
5.953
5.936
5.910
5.200
5.197
5.194
5.190
5.157
5.155
5.152
5.149
5.147
5.144
5.129
5.127
5.124
5.121
3.748
3.528
2.786
2.784
2.764
2.743
2.741
2.213
2.210
2.208
2.205
2.202
2.195
2.192
2.189
2.187
2.183
1.716
1.705
1.696
1.693
1.685
1.673
1.00
0.97
1.02
1.09
0.98
1.99
4.28
3.06
1.96
2.04
4.13
2.20
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


137.2
134.9
127.9
125.9
121.6
119.1
118.7
117.9
115.6
109.3
67.5
60.5
41.3
39.1
34.8
32.7
18.8
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


MeN
Cl
O
H

(**1d**)


9.567
7.497
7.483
7.481
7.479
7.270
7.258
7.256
7.254
7.241
7.239
7.227
7.225
7.133
7.130
5.813
5.793
5.779
5.759
5.220
5.217
5.214
5.192
5.190
5.186
5.183
5.180
5.172
5.170
5.168
5.166
3.719
2.703
2.693
2.687
2.685
2.678
2.668
2.426
2.424
2.421
2.417
2.415
2.412
2.409
2.406
2.403
2.400
2.397
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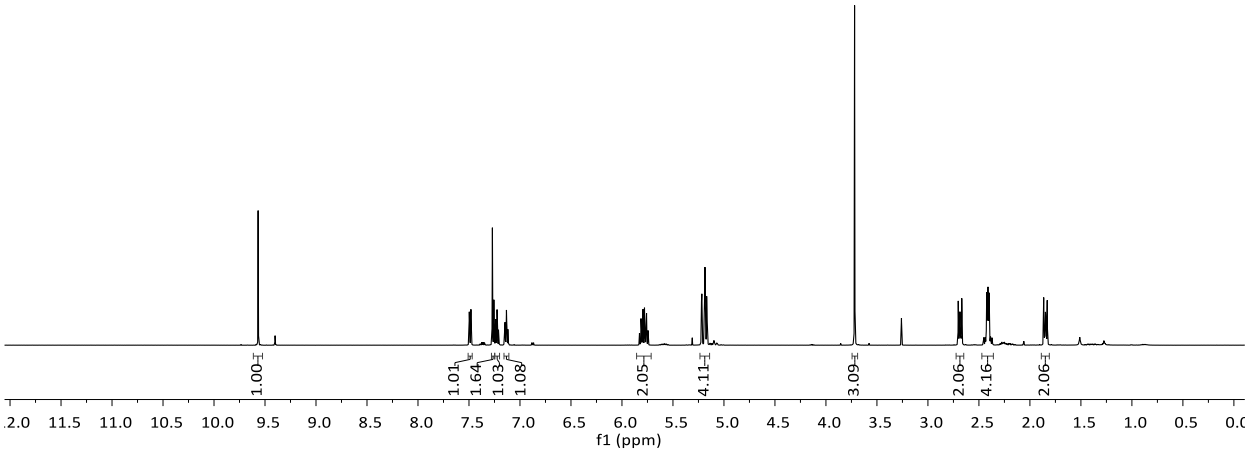
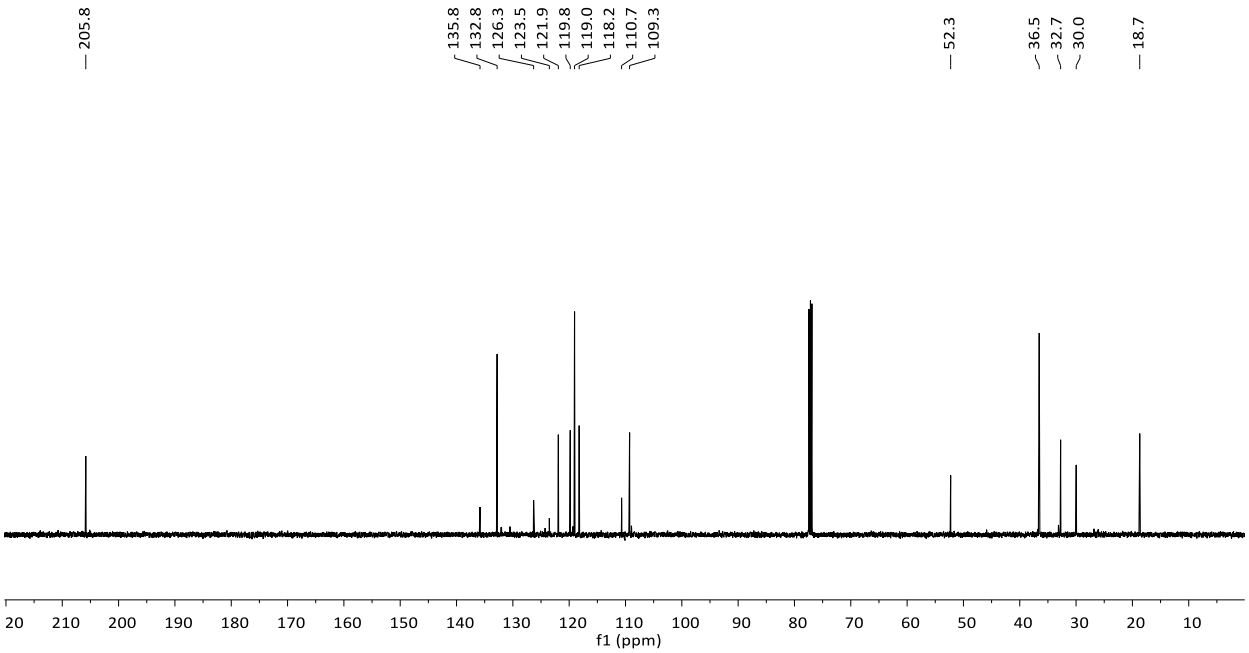
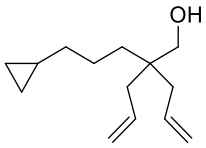
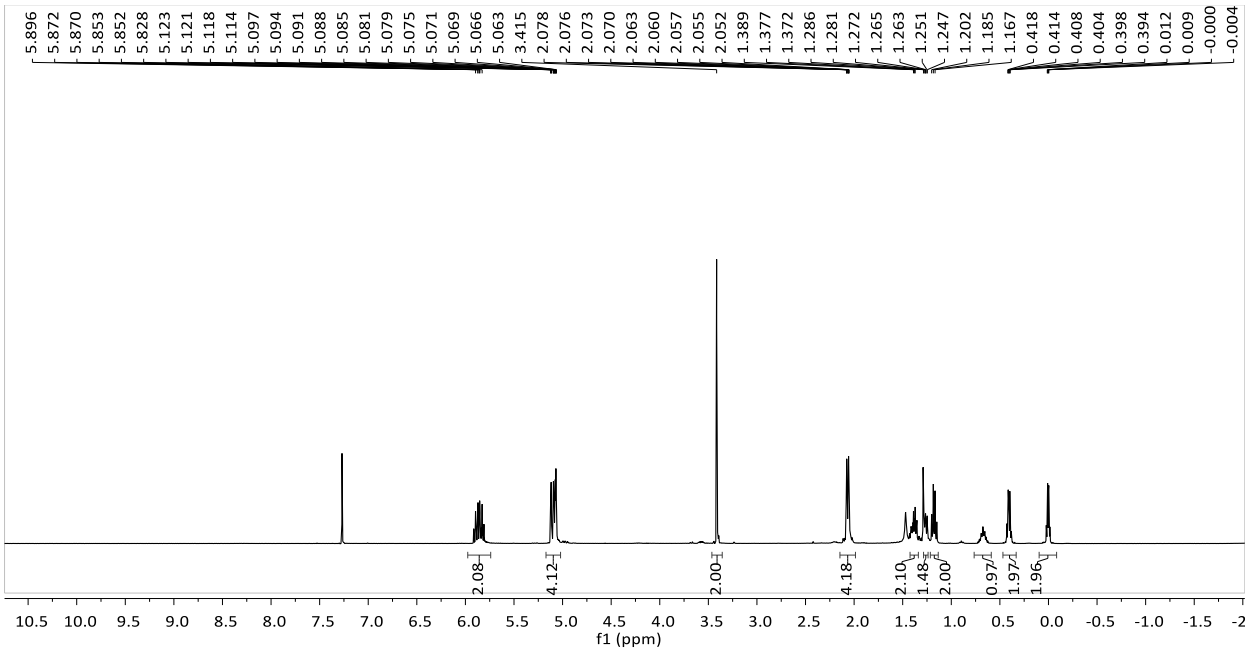
1.855
1.848
1.846
1.840
1.830

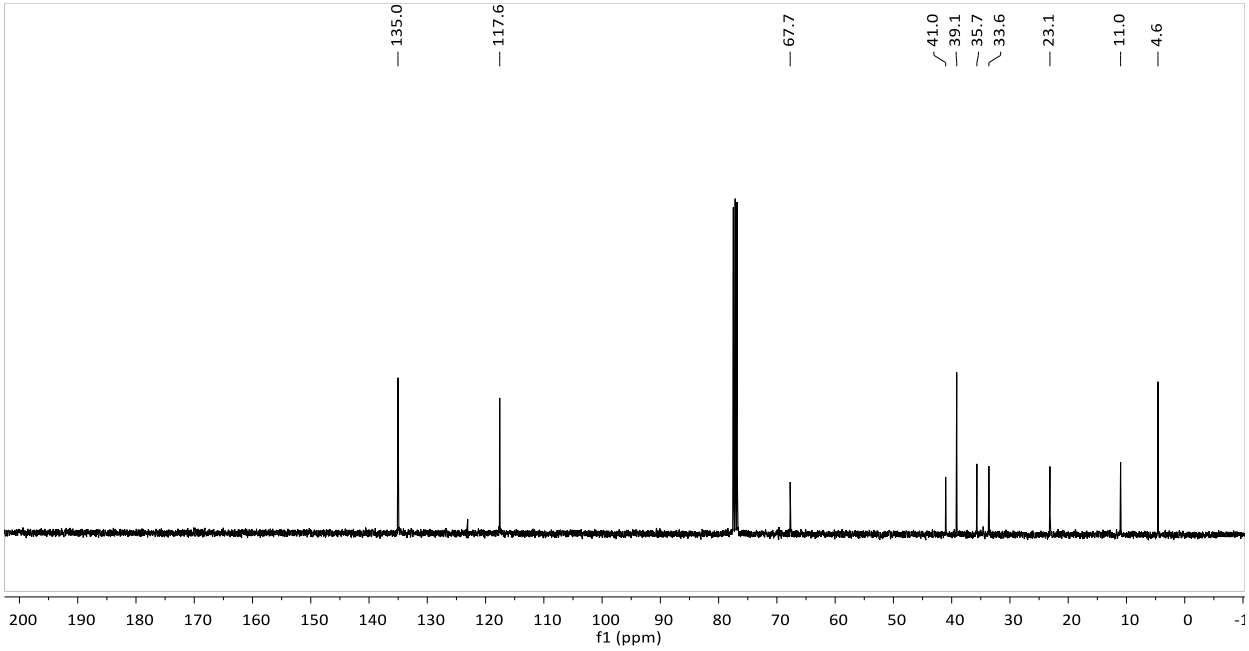

1.00
1.01
1.64
1.03
1.08
2.05
4.11
3.09
2.06
4.16
2.06
f1 (ppm)

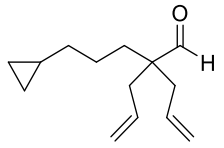

205.8
135.8
132.8
126.3
123.5
121.9
119.8
119.0
118.2
110.7
109.3
52.3
36.5
32.7
30.0
18.7
f1 (ppm)


OH

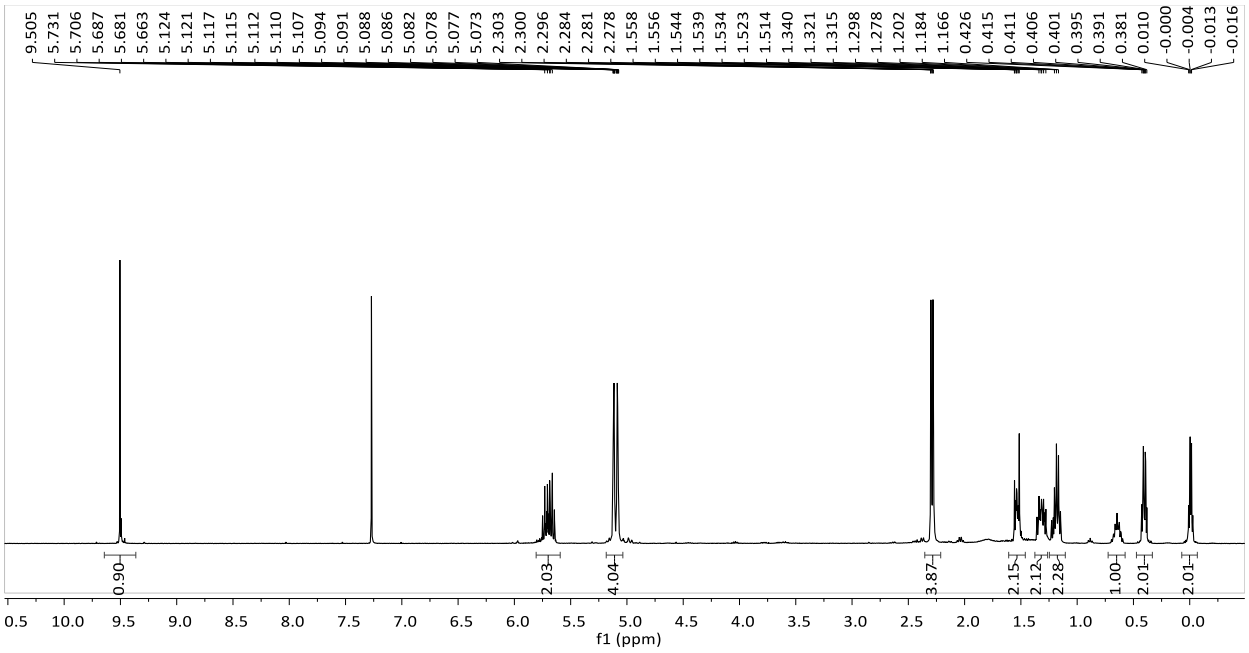
(**1e-OH**)

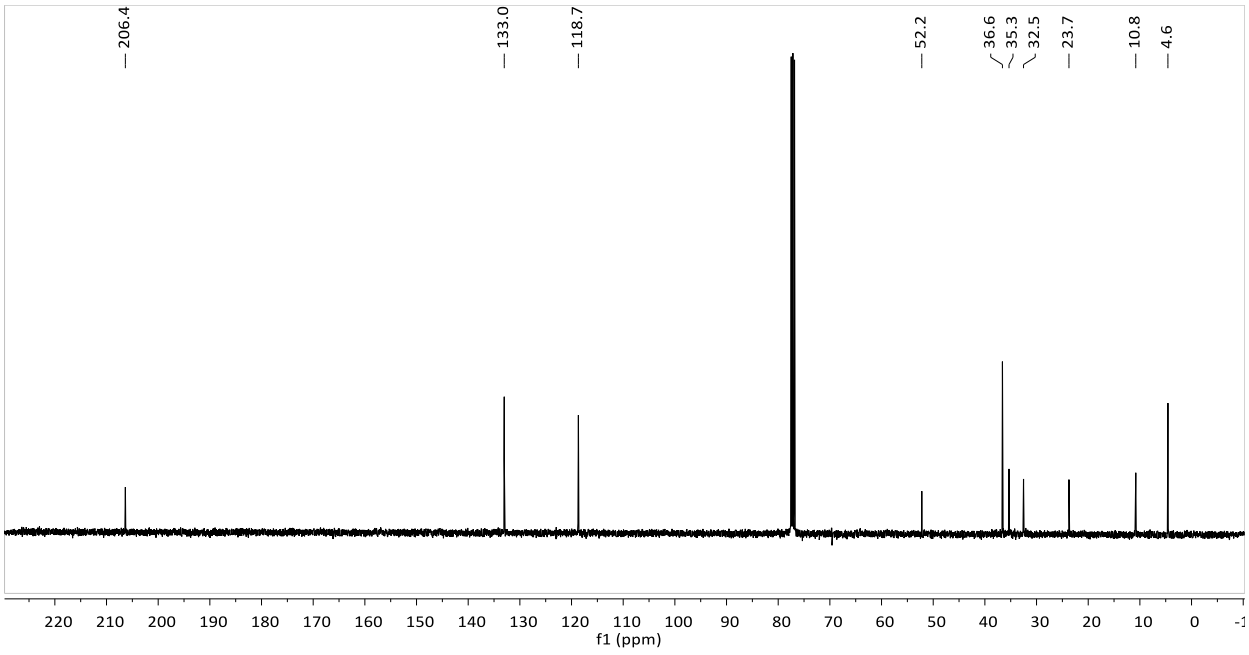

5.896
5.872
5.870
5.853
5.852
5.828
5.123
5.121
5.118
5.114
5.097
5.094
5.091
5.088
5.085
5.081
5.079
5.075
5.071
5.069
5.066
5.063
3.415
2.078
2.076
2.073
2.070
2.063
2.060
2.057
2.055
2.052
1.389
1.377
1.372
1.286
1.281
1.272
1.265
1.263
1.251
1.247
1.202
1.185
1.167
0.418
0.414
0.408
0.404
0.398
0.394
0.012
0.009
-0.000
-0.004
2.08
4.12
2.00
4.18
2.10
1.48
2.00
0.97
1.97
1.96
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2
f1 (ppm)

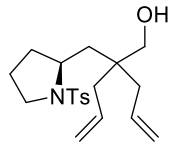

135.0
117.6
67.7
41.0
39.1
35.7
33.6
23.1
11.0
4.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
H

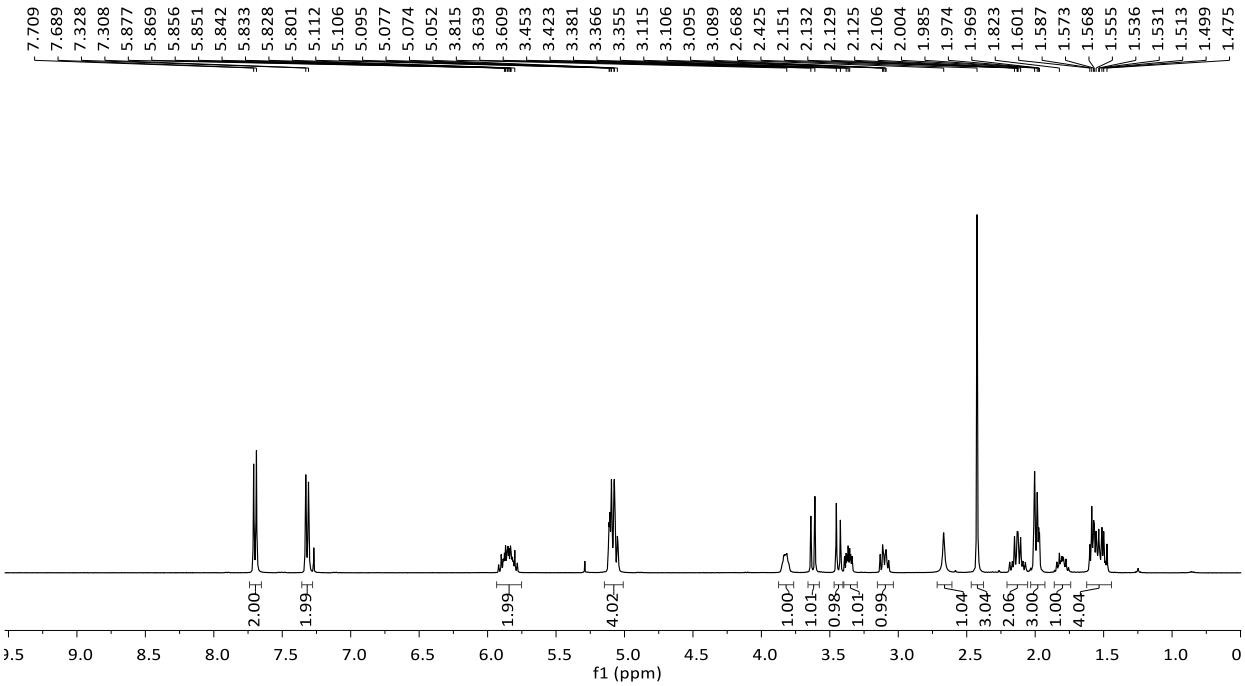
(**1e**)


9.505
5.731
5.706
5.687
5.681
5.663
5.124
5.121
5.117
5.115
5.112
5.110
5.107
5.094
5.091
5.088
5.086
5.082
5.078
5.077
5.073
2.303
2.300
2.296
2.284
2.281
2.278
1.558
1.556
1.544
1.539
1.534
1.523
1.514
1.340
1.321
1.315
1.298
1.278
1.202
1.184
1.166
0.426
0.415
0.411
0.406
0.401
0.395
0.391
0.381
0.010
-0.000
-0.004
-0.013
-0.016
0.90
2.03
4.04
3.87
2.15
2.12
2.28
1.00
2.01
2.01
f1 (ppm)


206.4
133.0
118.7
52.2
36.6
35.3
32.5
23.7
10.8
4.6
f1 (ppm)


OH
NTs

(**1g-OH**)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7.689
7.328
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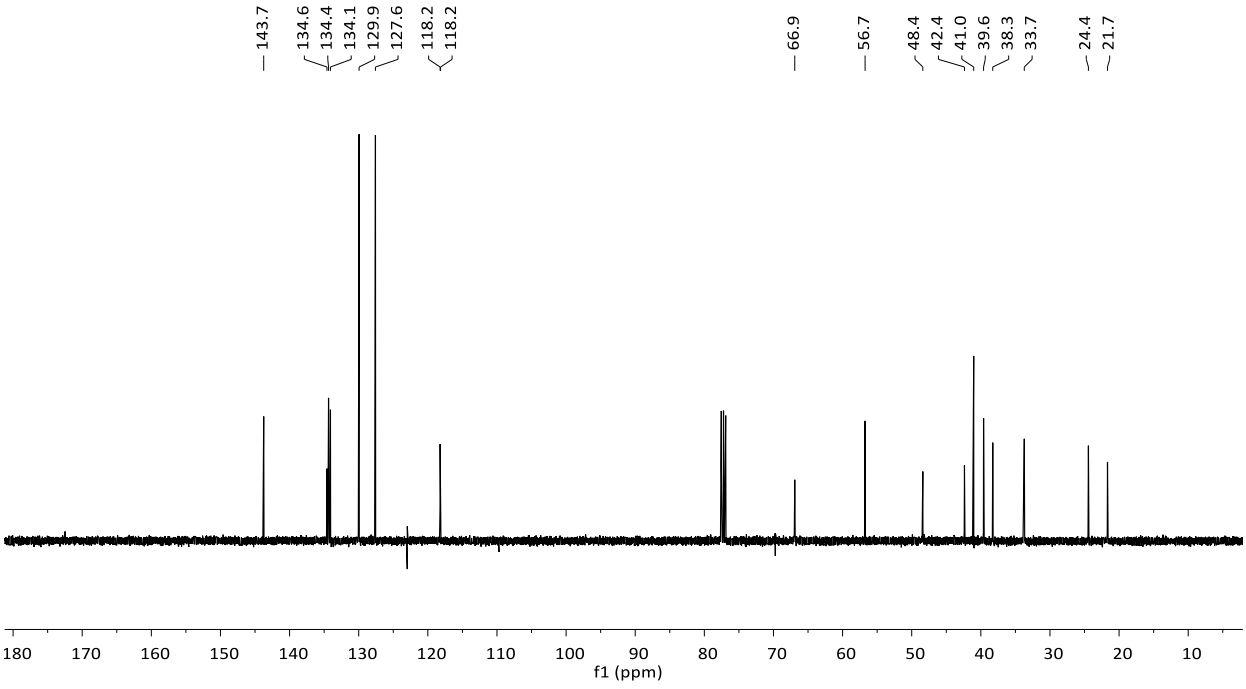
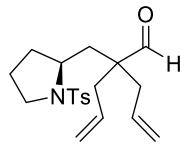
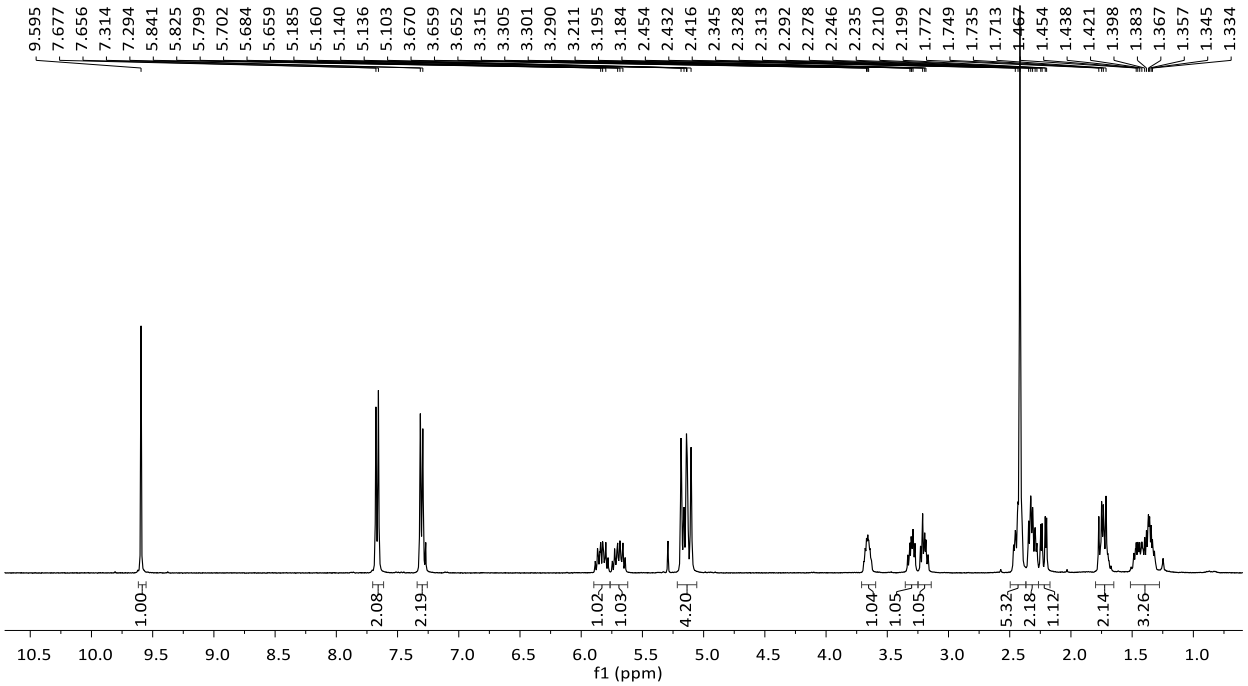
5.877
5.869
5.856
5.851
5.842
5.833
5.828
5.801
5.112
5.106
5.095
5.077
5.074
5.052
3.815
3.639
3.609
3.453
3.423
3.381
3.366
3.355
3.115
3.106
3.095
3.089
2.668
2.425
2.151
2.132
2.129
2.125
2.106
2.004
1.985
1.974
1.969
1.823
1.601
1.587
1.573
1.568
1.555
1.536
1.531
1.513
1.499
1.475
2.00
1.99
1.99
4.02
1.00
1.01
0.98
1.01
0.99
1.04
3.04
2.06
3.00
1.00
4.04
f1 (ppm)


143.7
134.6
134.4
134.1
129.9
127.6
118.2
118.2
66.9
56.7
48.4
42.4
41.0
39.6
38.3
33.7
24.4
21.7
f1 (ppm)


O
H
NTs

(**1g**)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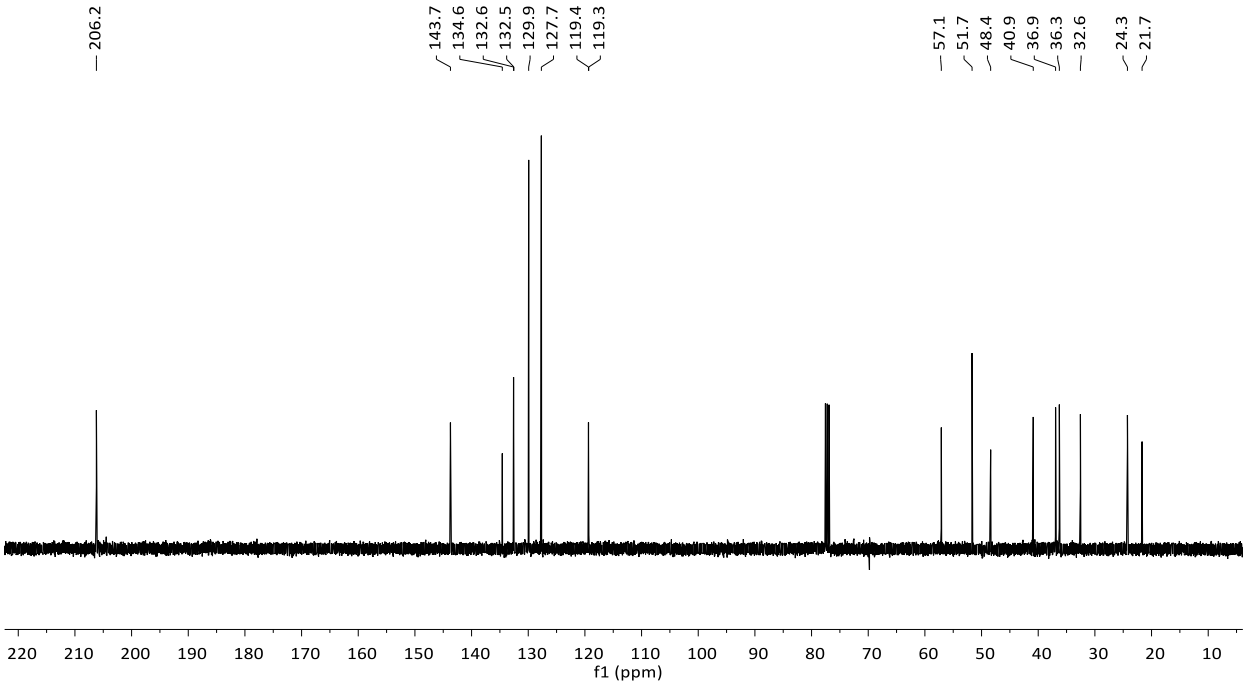
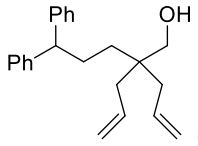
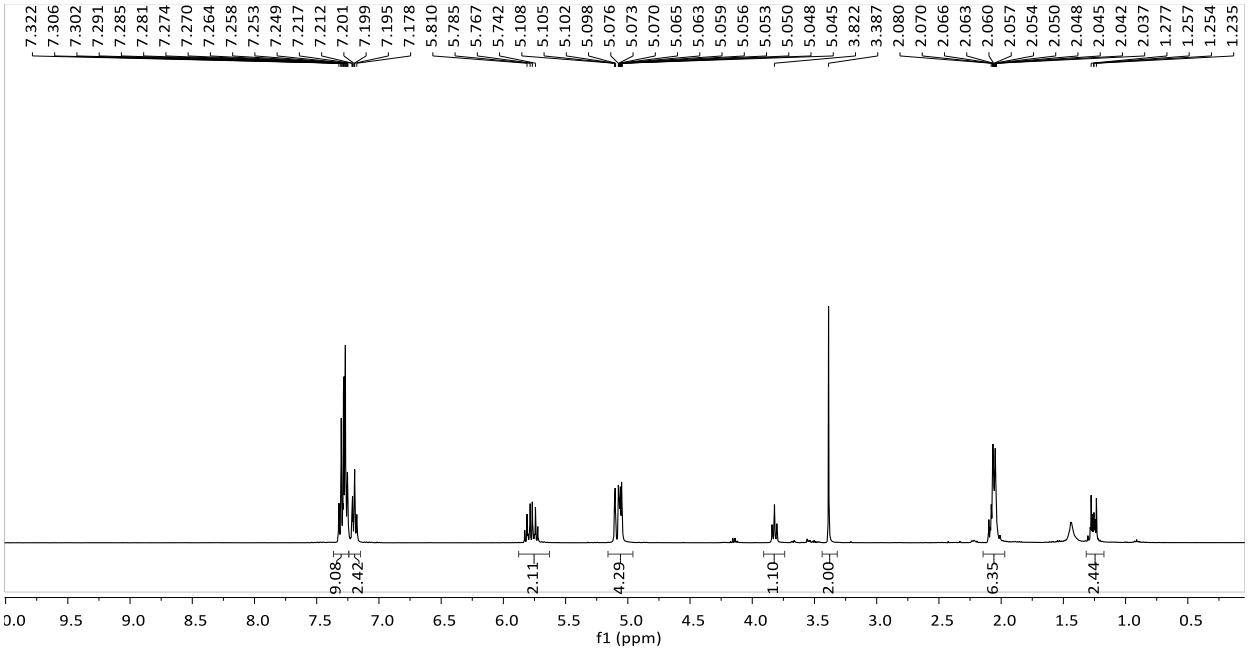
7.677
7.656
7.314
7.294
5.841
5.825
5.799
5.702
5.684
5.659
5.185
5.160
5.140
5.136
5.103
3.670
3.659
3.652
3.315
3.305
3.301
3.290
3.211
3.195
3.184
2.454
2.432
2.416
2.345
2.328
2.313
2.292
2.278
2.246
2.235
2.210
2.199
1.772
1.749
1.735
1.713
1.467
1.454
1.438
1.421
1.398
1.383
1.367
1.357
1.345
1.334
1.00
2.08
2.19
1.02
1.03
4.20
1.04
1.05
1.05
5.32
2.18
1.12
2.14
3.26
f1 (ppm)


206.2
143.7
134.6
132.6
132.5
129.9
127.7
119.4
119.3
57.1
51.7
48.4
40.9
36.9
36.3
32.6
24.3
21.7
f1 (ppm)


Ph
OH
Ph

(**1h-OH**)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7.306
7.302
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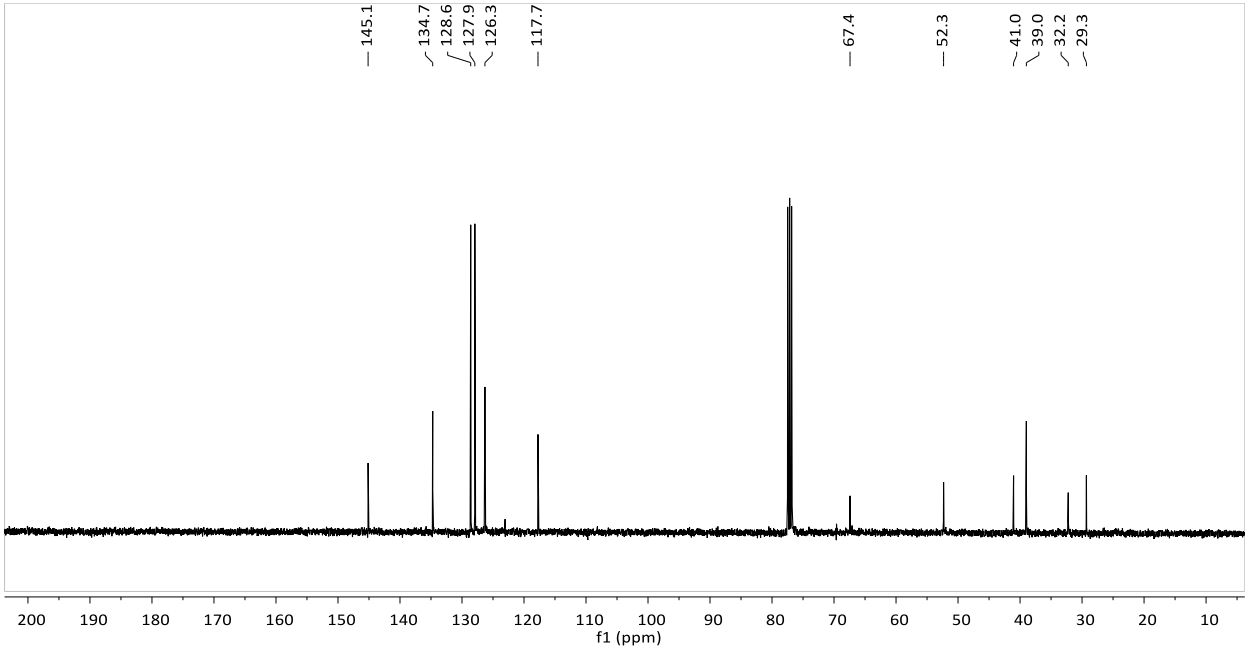
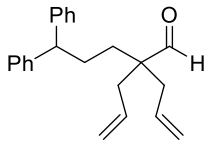
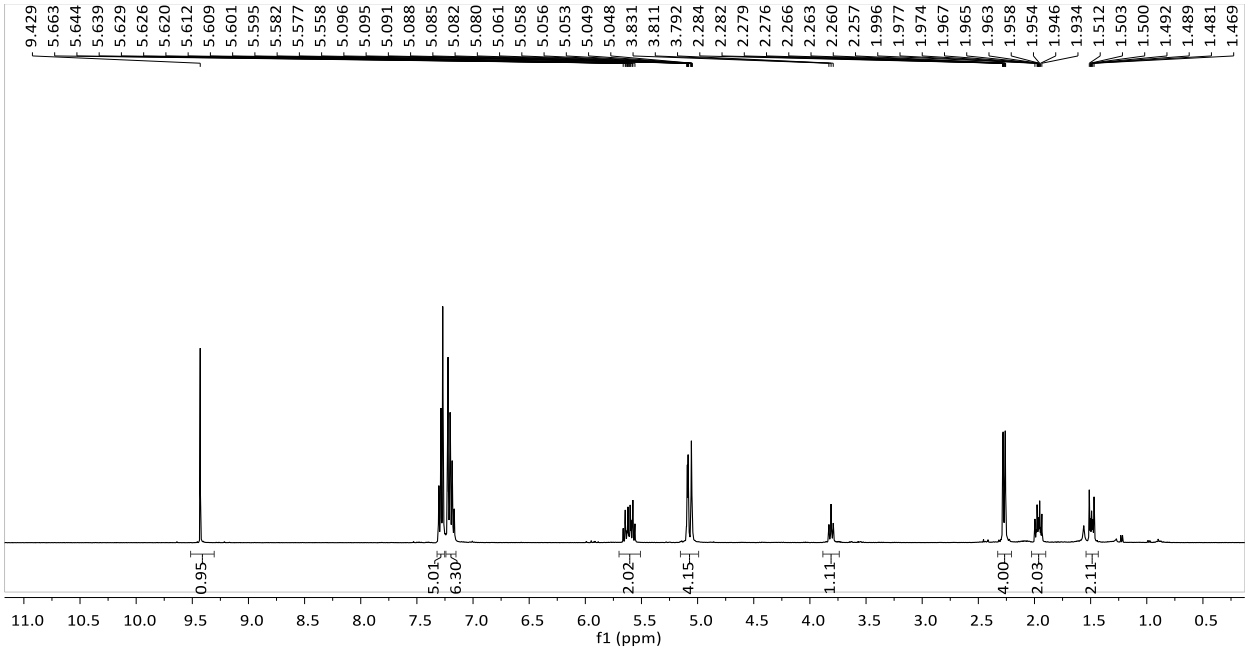
7.285
7.281
7.274
7.270
7.264
7.258
7.253
7.249
7.217
7.212
7.201
7.199
7.195
7.178
5.810
5.785
5.767
5.742
5.108
5.105
5.102
5.098
5.076
5.073
5.070
5.065
5.063
5.059
5.056
5.053
5.050
5.048
5.045
3.822
3.387
2.080
2.070
2.066
2.063
2.060
2.057
2.054
2.050
2.048
2.045
2.042
2.037
1.277
1.257
1.254
1.235
9.08
2.42
2.11
4.29
1.10
2.00
6.35
2.44
f1 (ppm)


145.1
134.7
128.6
127.9
126.3
117.7
67.4
52.3
41.0
39.0
32.2
29.3
f1 (ppm)


Ph
O
Ph
H

(**1h**)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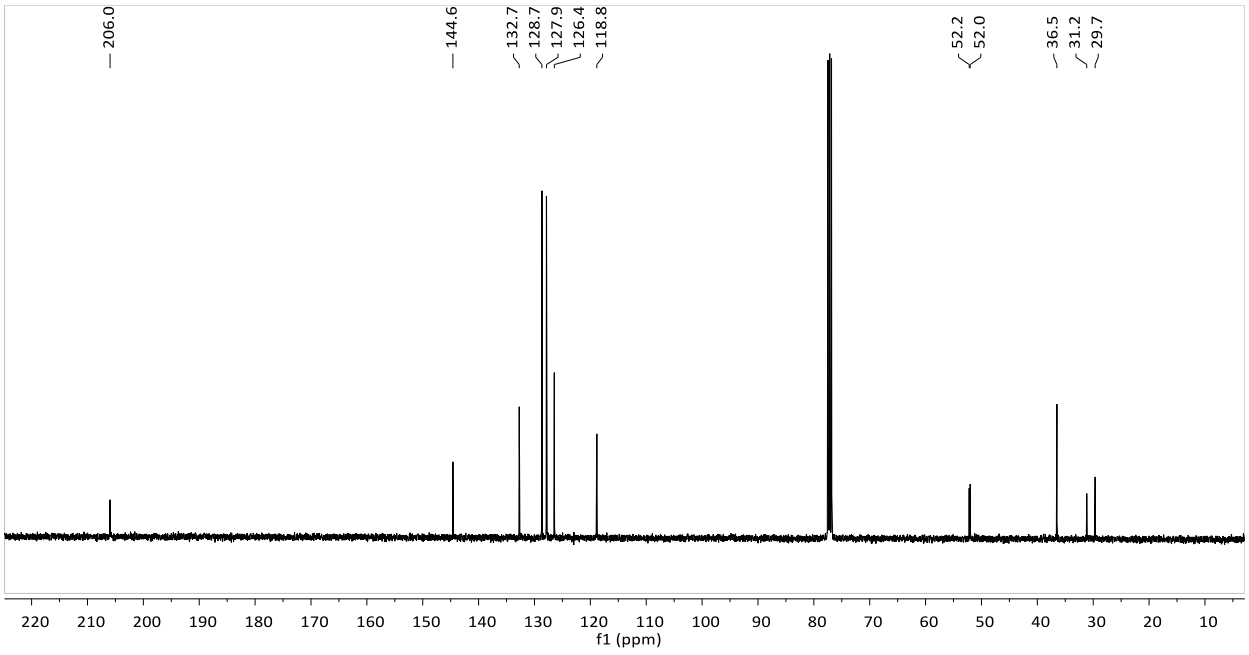
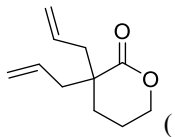
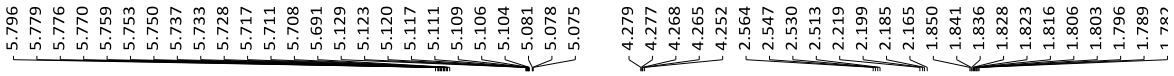
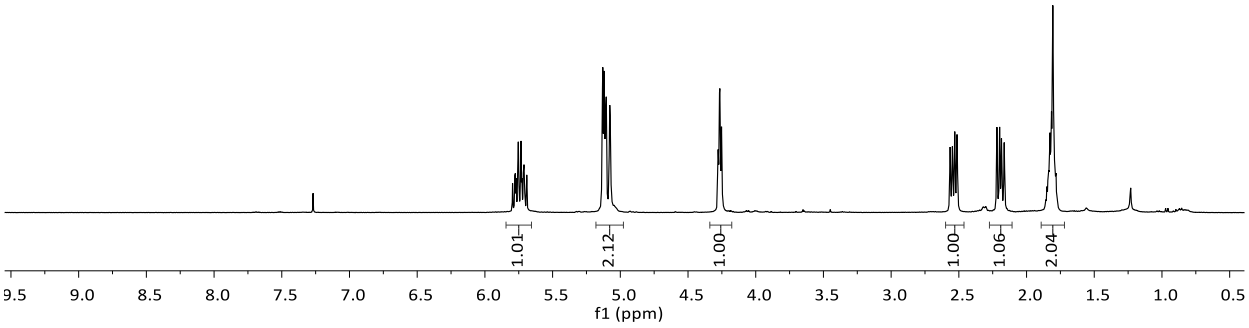
5.663
5.644
5.639
5.629
5.626
5.620
5.612
5.609
5.601
5.595
5.582
5.577
5.558
5.096
5.095
5.091
5.088
5.085
5.082
5.080
5.061
5.058
5.056
5.053
5.049
5.048
3.831
3.811
3.792
2.284
2.282
2.279
2.276
2.266
2.263
2.260
2.257
1.996
1.977
1.974
1.967
1.965
1.963
1.958
1.954
1.946
1.934
1.512
1.503
1.500
1.492
1.489
1.481
1.469
0.95
5.01
6.30
2.02
4.15
1.11
4.00
2.03
2.11
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

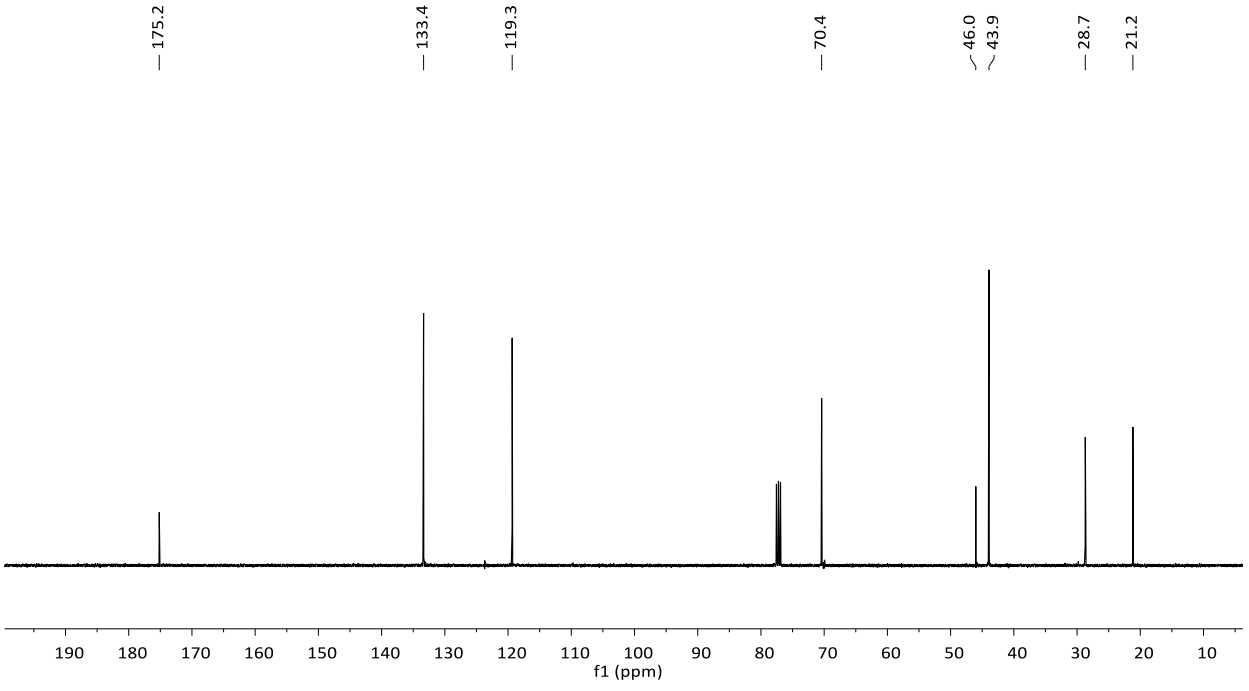

206.0
144.6
132.7
128.7
127.9
126.4
118.8
52.2
52.0
36.5
31.2
29.7
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

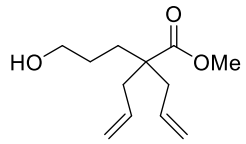


( **1i - A**)

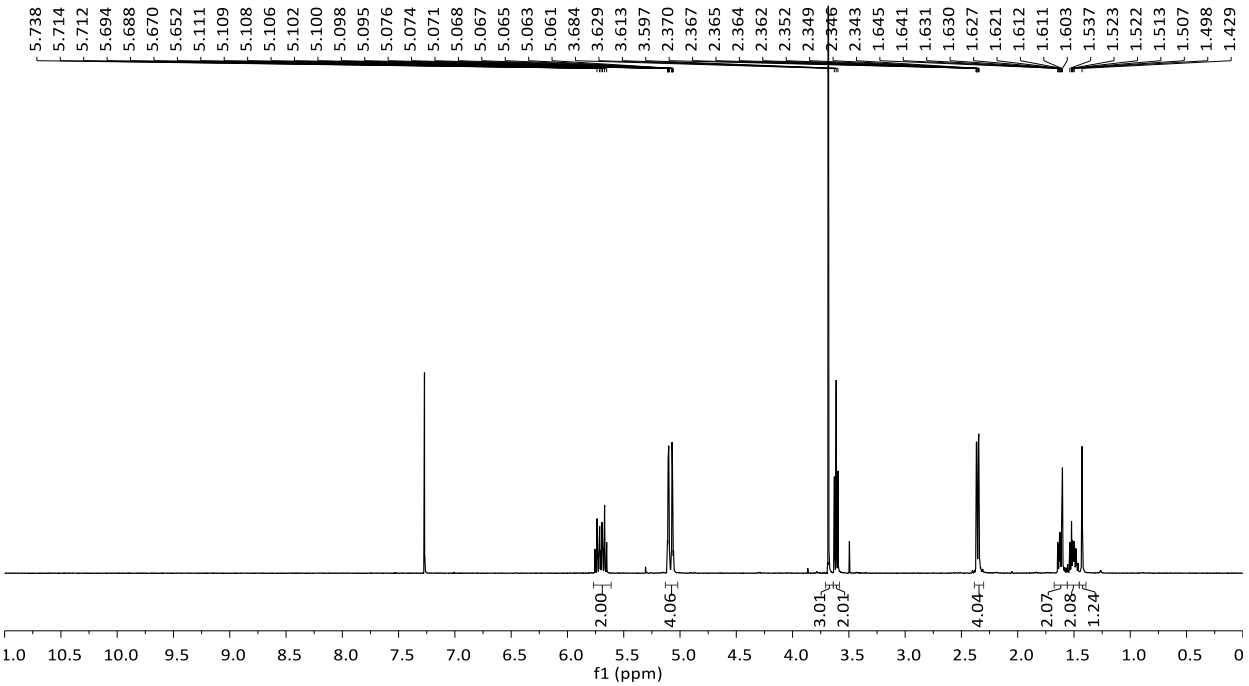

5.796
5.779
5.776
5.770
5.759
5.753
5.750
5.737
5.733
5.728
5.717
5.711
5.708
5.691
5.129
5.123
5.120
5.117
5.111
5.109
5.106
5.104
5.081
5.078
5.075
4.279
4.277
4.268
4.265
4.252
2.564
2.547
2.530
2.513
2.219
2.199
2.185
2.165
1.850
1.841
1.836
1.828
1.823
1.816
1.806
1.803
1.796
1.789


1.01
2.12
1.00
1.00
1.06
2.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


175.2
133.4
119.3
70.4
46.0
43.9
28.7
21.2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O
HO
OMe

( **1i - B**)


5.738
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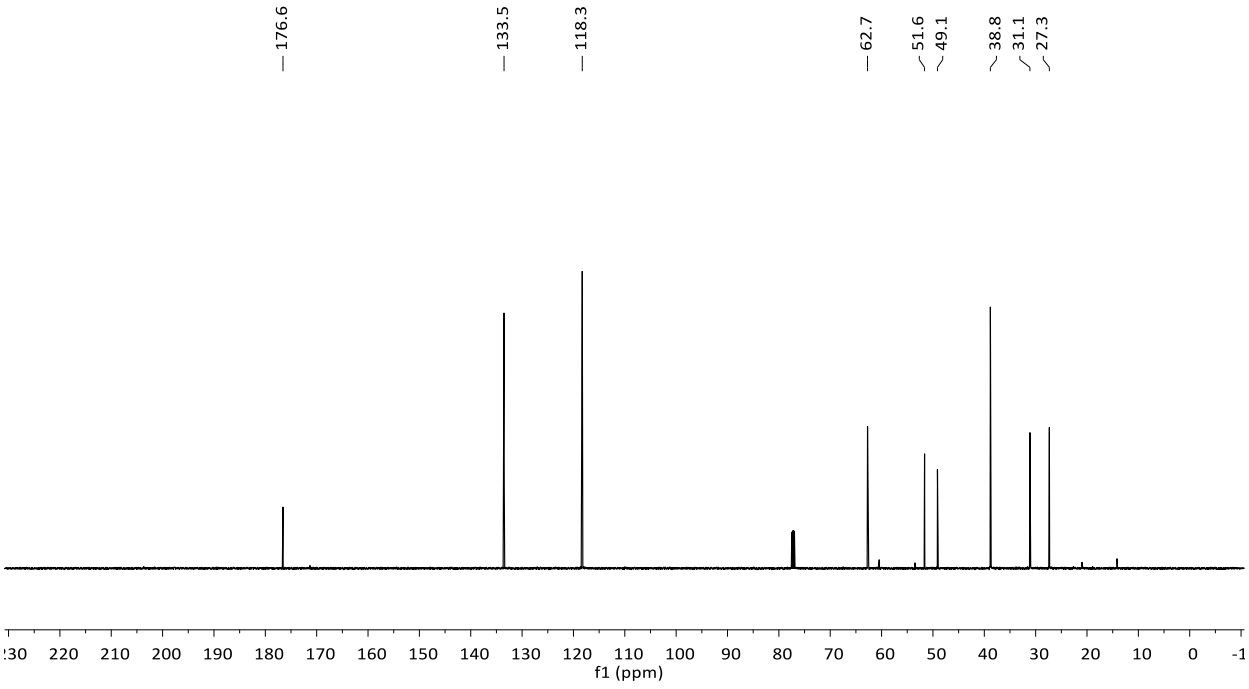
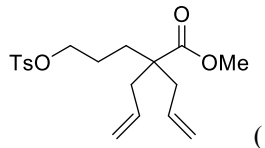
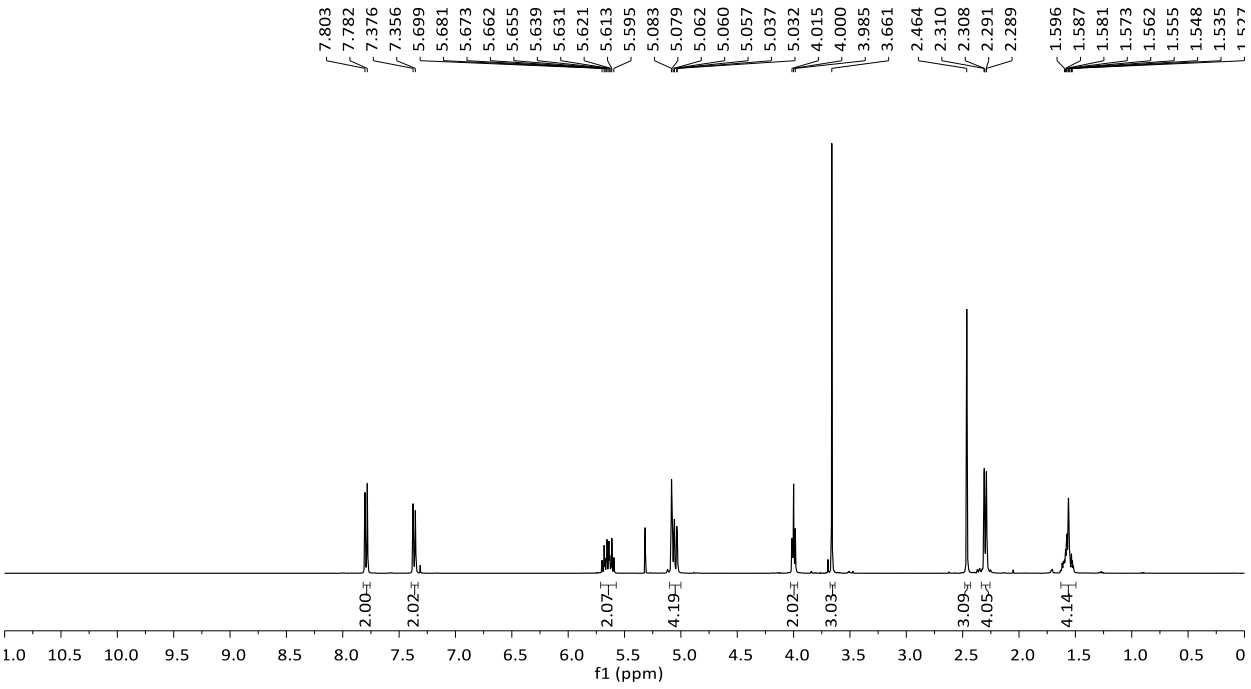
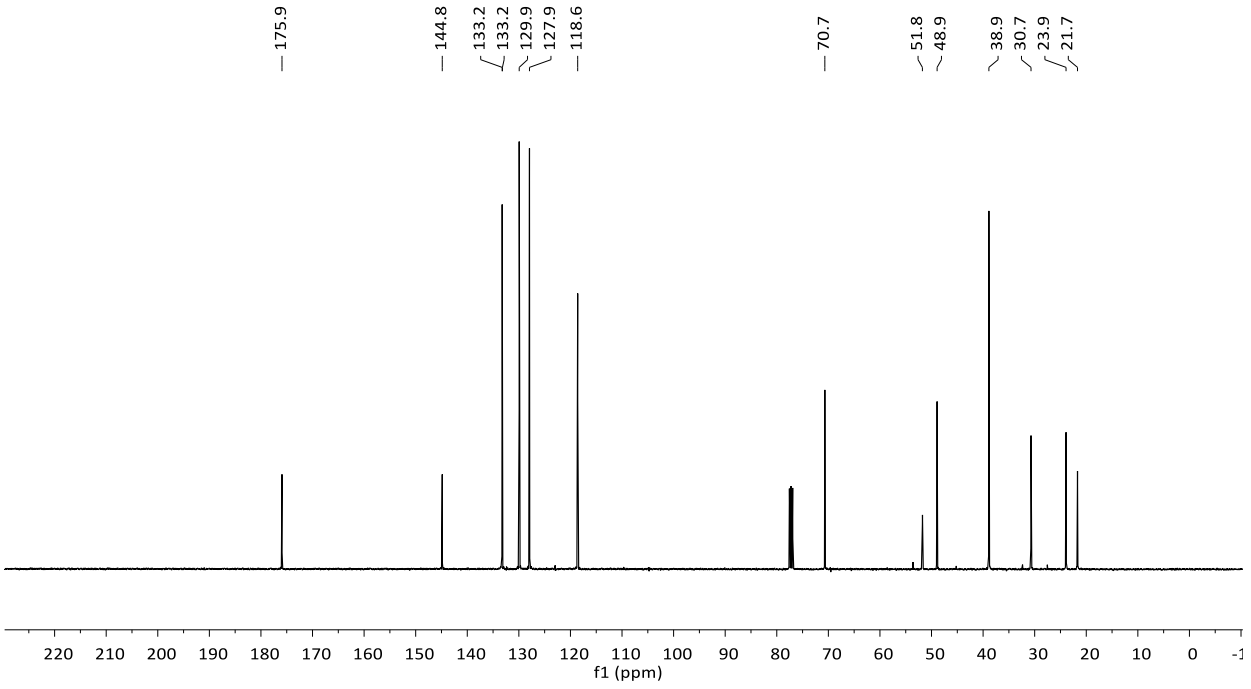
5.712
5.694
5.688
5.670
5.652
5.111
5.109
5.108
5.106
5.102
5.100
5.098
5.095
5.076
5.074
5.071
5.068
5.067
5.065
5.063
5.061
3.684
3.629
3.613
3.597
2.370
2.367
2.365
2.364
2.362
2.352
2.349
2.346
2.343
1.645
1.641
1.631
1.630
1.627
1.621
1.612
1.611
1.603
1.537
1.523
1.522
1.513
1.507
1.498
1.429
2.00
4.06
3.01
2.01
4.04
2.07
2.08
1.24
f1 (ppm)

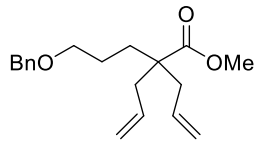

176.6
133.5
118.3
62.7
51.6
49.1
38.8
31.1
27.3
f1 (ppm)


O
TsO
OMe

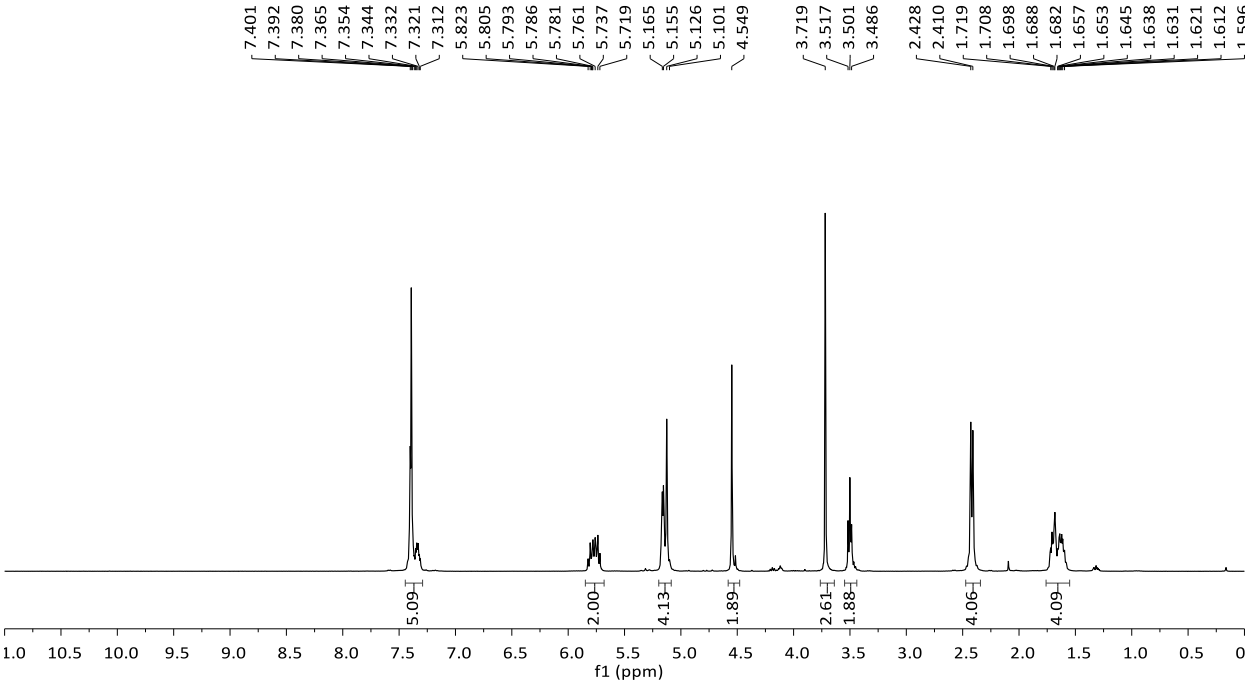
( **1i - C**)

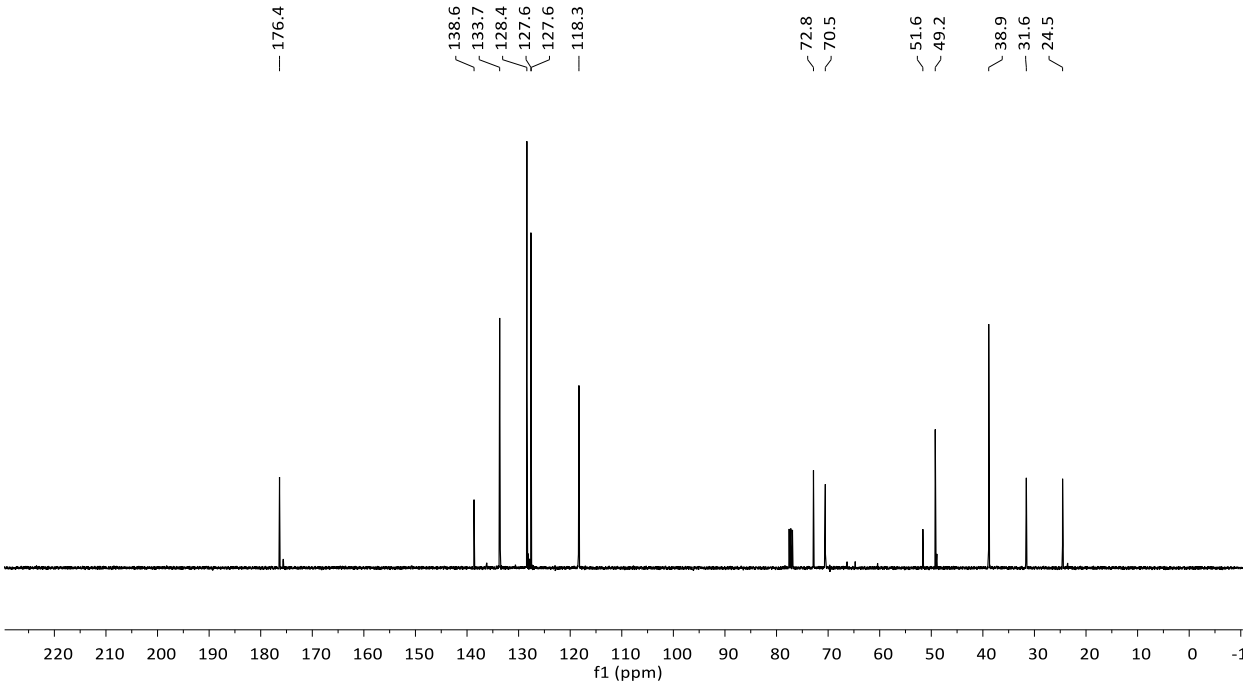

7.803
7.782
7.376
7.356
5.699
5.681
5.673
5.662
5.655
5.639
5.631
5.621
5.613
5.595
5.083
5.079
5.062
5.060
5.057
5.037
5.032
4.015
4.000
3.985
3.661
2.464
2.310
2.308
2.291
2.289
1.596
1.587
1.581
1.573
1.562
1.555
1.548
1.535
2.00
2.02
2.07
4.19
2.02
3.03
3.09
4.05
4.14
f1 (ppm)

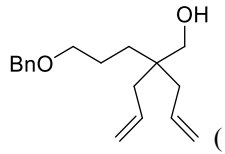

175.9
144.8
133.2
133.2
129.9
127.9
118.6
70.7
51.8
48.9
38.9
30.7
23.9
21.7
f1 (ppm)


O
BnO
OMe

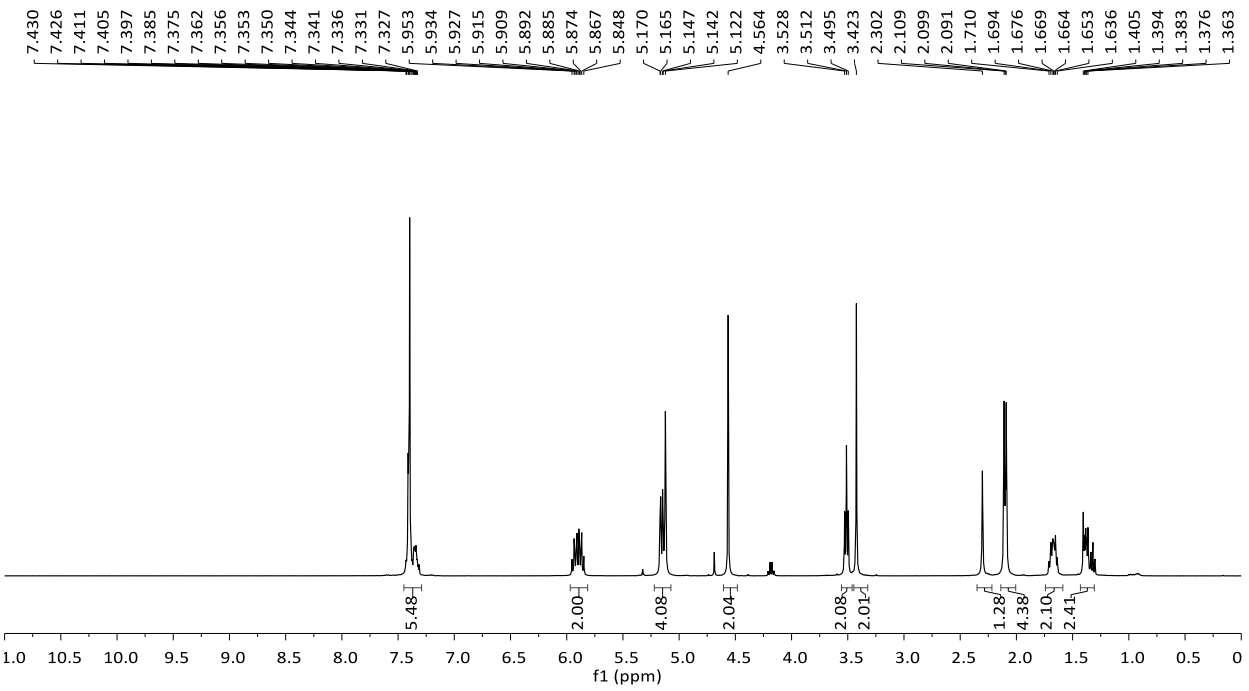
**( 1i - D)**


7.401
7.392
7.380
7.365
7.354
7.344
7.332
7.321
7.312
5.823
5.805
5.793
5.786
5.781
5.761
5.737
5.719
5.165
5.155
5.126
5.101
4.549
3.719
3.517
3.501
3.486
2.428
2.410
1.719
1.708
1.698
1.688
1.682
1.657
1.653
1.645
1.638
1.631
1.621
1.612
5.09
2.00
4.13
1.89
2.61
1.88
4.06
4.09
f1 (ppm)


176.4
138.6
133.7
128.4
127.6
127.6
118.3
72.8
70.5
51.6
49.2
38.9
31.6
24.5
f1 (ppm)


OH
BnO

**( 1i - OH)**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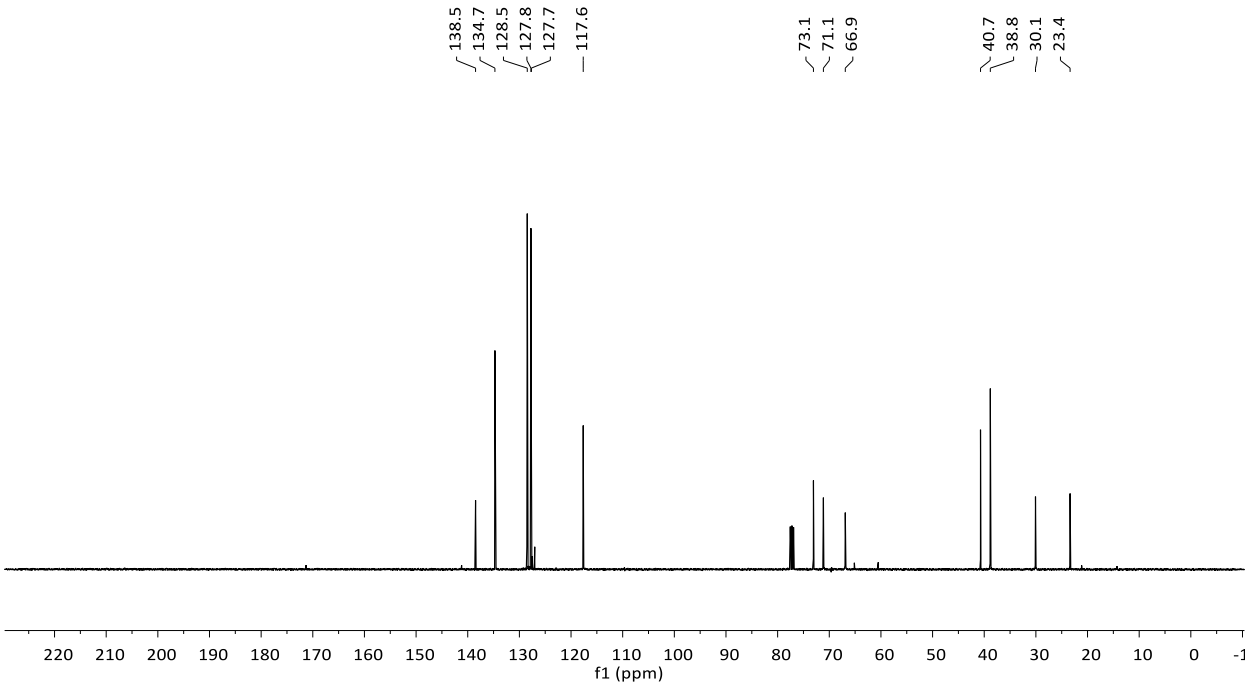
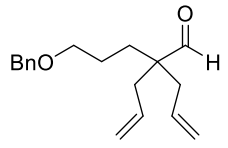
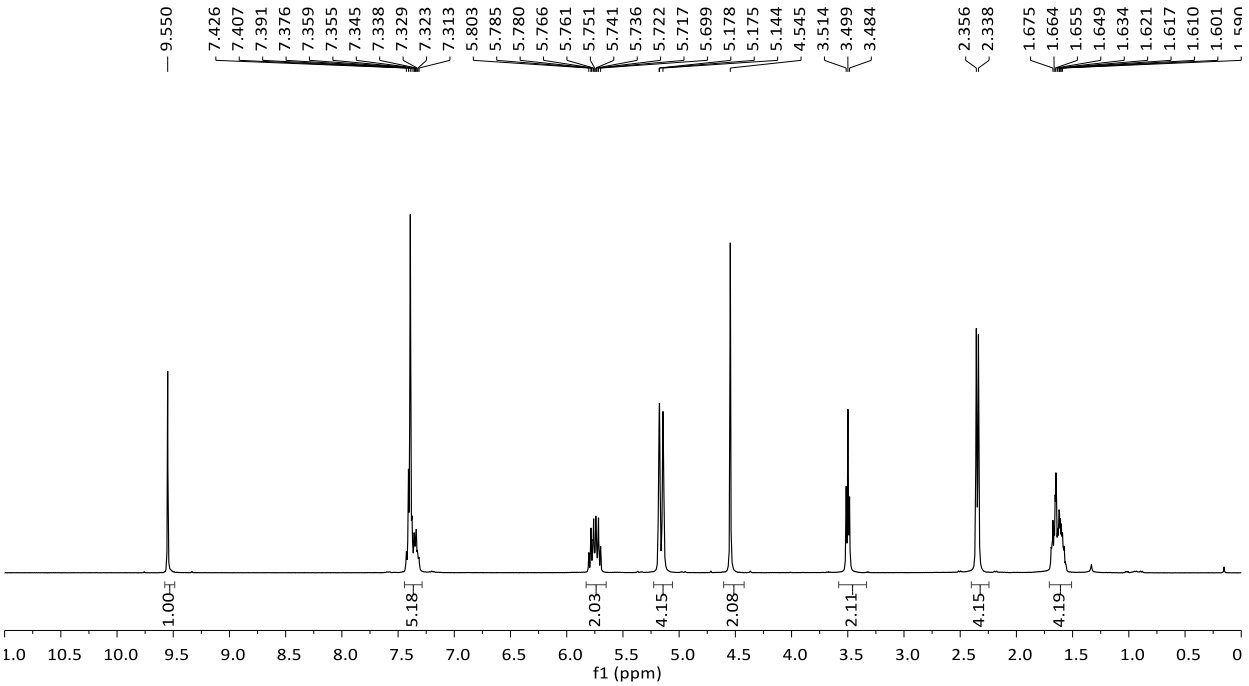
7.411
7.405
7.397
7.385
7.375
7.362
7.356
7.353
7.350
7.344
7.341
7.336
7.331
7.327
5.953
5.934
5.927
5.915
5.909
5.892
5.885
5.874
5.867
5.848
5.170
5.165
5.147
5.142
5.122
4.564
3.528
3.512
3.495
3.423
2.302
2.109
2.099
2.091
1.710
1.694
1.676
1.669
1.664
1.653
1.636
1.405
1.394
1.383
1.376
1.363
5.48
2.00
4.08
2.04
2.08
2.01
1.28
4.38
2.10
2.41
f1 (ppm)


138.5
134.7
128.5
127.8
127.7
117.6
73.1
71.1
66.9
40.7
38.8
30.1
23.4
f1 (ppm)


O
BnO
H

(**1i**)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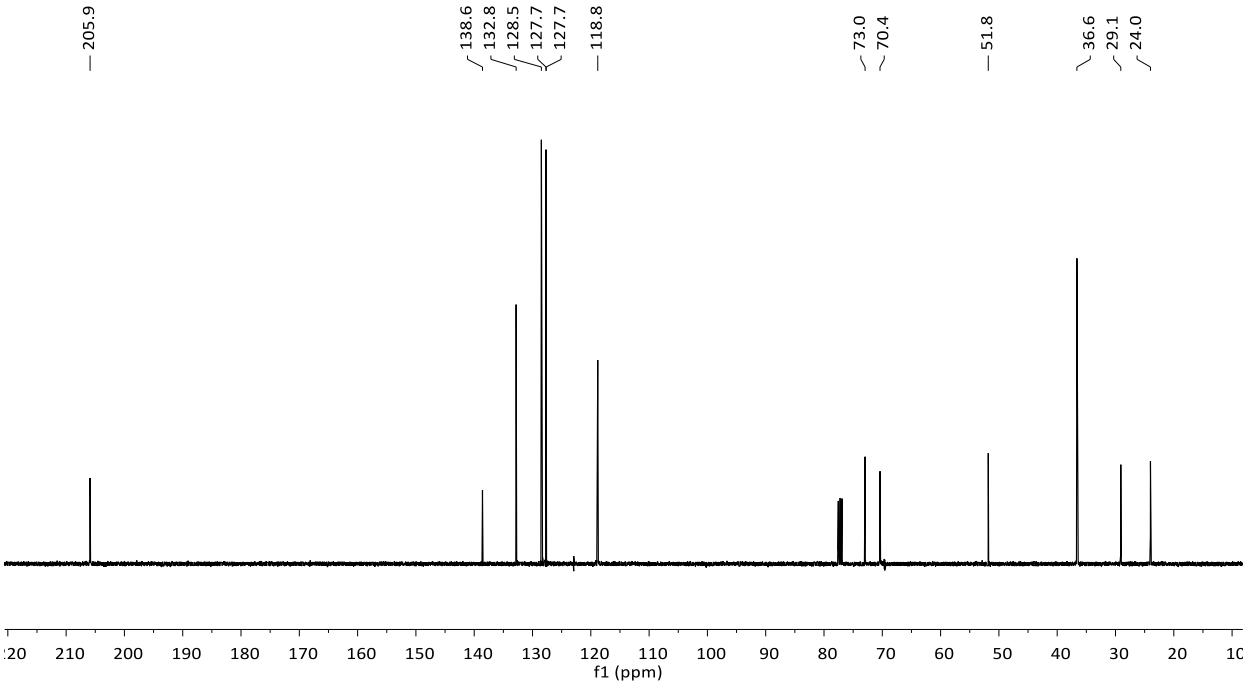
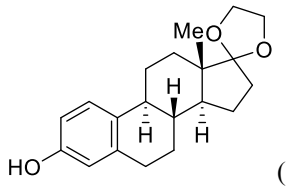
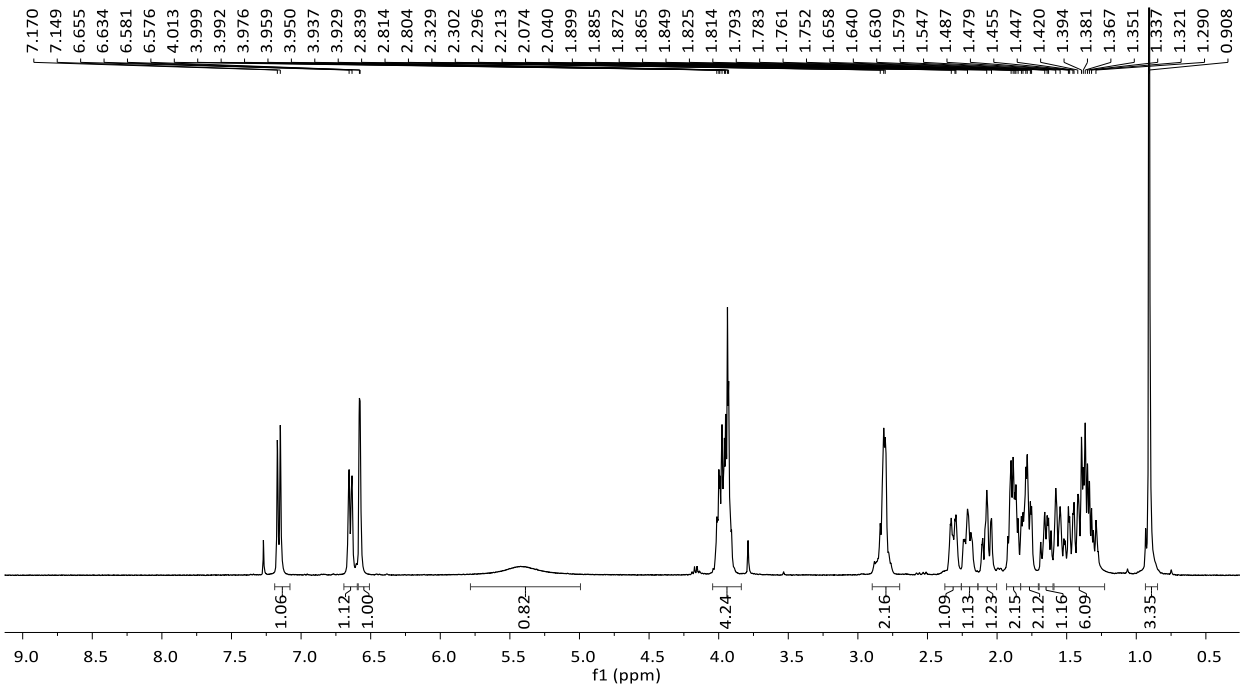
7.407
7.391
7.376
7.359
7.355
7.345
7.338
7.329
7.323
7.313
5.803
5.785
5.780
5.766
5.761
5.751
5.741
5.736
5.722
5.717
5.699
5.178
5.175
5.144
4.545
3.514
3.499
3.484
2.356
2.338
1.675
1.664
1.655
1.649
1.634
1.621
1.617
1.610
1.601
1.590
1.00
5.18
2.03
4.15
2.08
2.11
4.15
4.19
f1 (ppm)


205.9
138.6
132.8
128.5
127.7
127.7
118.8
73.0
70.4
51.8
36.6
29.1
24.0
f1 (ppm)


MeO
O
H
H
H
HO

( **1j - A**)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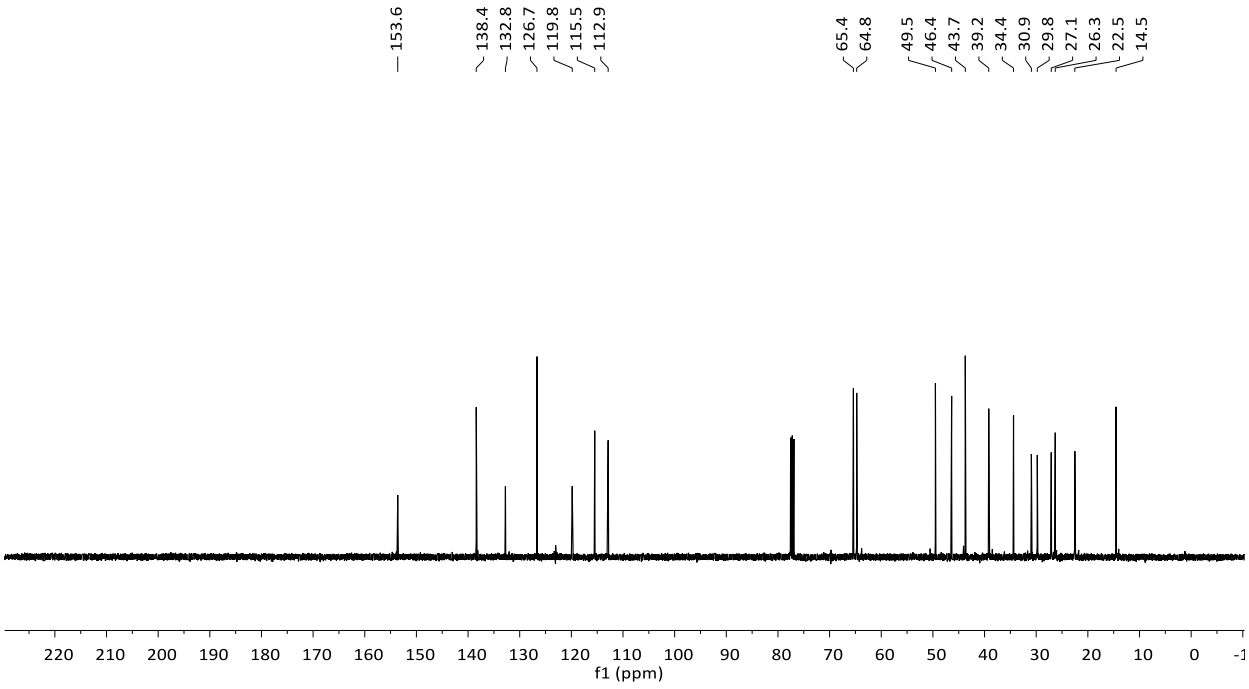
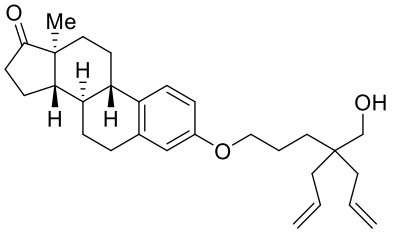
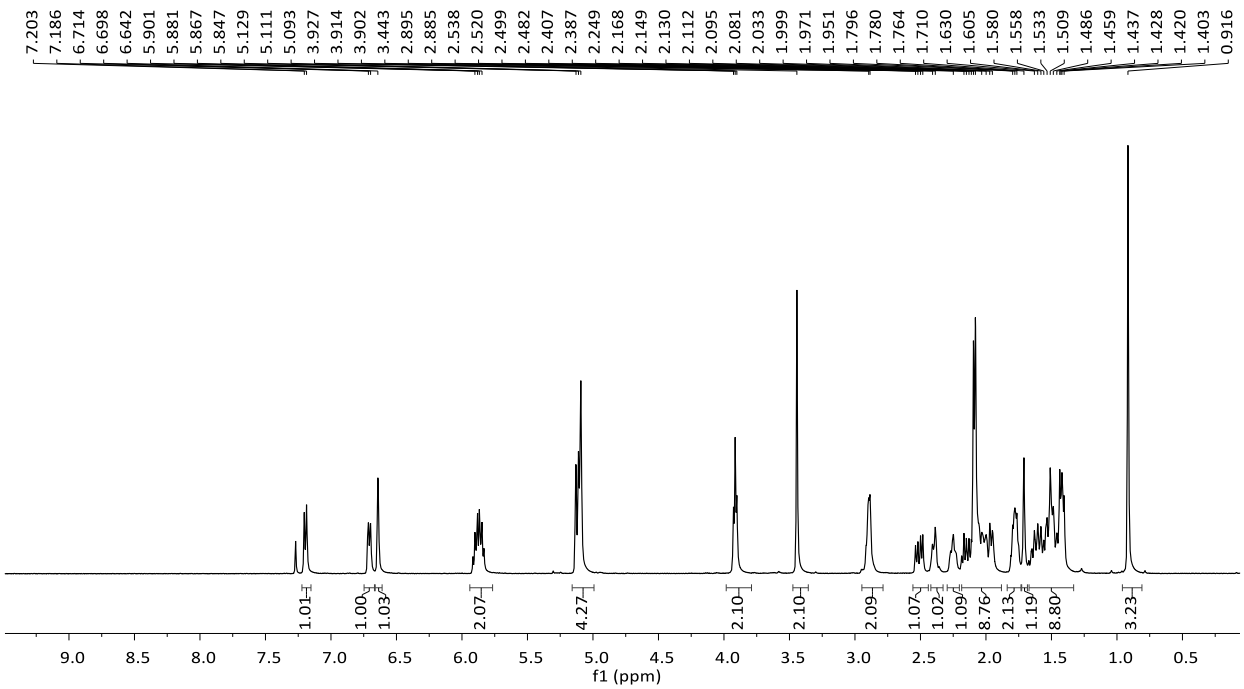
7.149
6.655
6.634
6.581
6.576
4.013
3.999
3.992
3.976
3.959
3.950
3.937
3.929
2.839
2.814
2.804
2.329
2.302
2.296
2.213
2.074
2.040
1.899
1.885
1.872
1.865
1.849
1.825
1.814
1.793
1.783
1.761
1.752
1.658
1.640
1.630
1.579
1.547
1.487
1.479
1.455
1.447
1.420
1.394
1.381
1.367
1.351
1.337
1.321
1.290
0.908
1.06
1.12
1.00
0.82
4.24
2.16
1.09
1.13
1.23
2.15
2.12
1.16
6.09
3.35
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


153.6
138.4
132.8
126.7
119.8
115.5
112.9
65.4
64.8
49.5
46.4
43.7
39.2
34.4
30.9
29.8
27.1
26.3
22.5
14.5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
Me
H
H
H
OH
O

**( 1j - OH)**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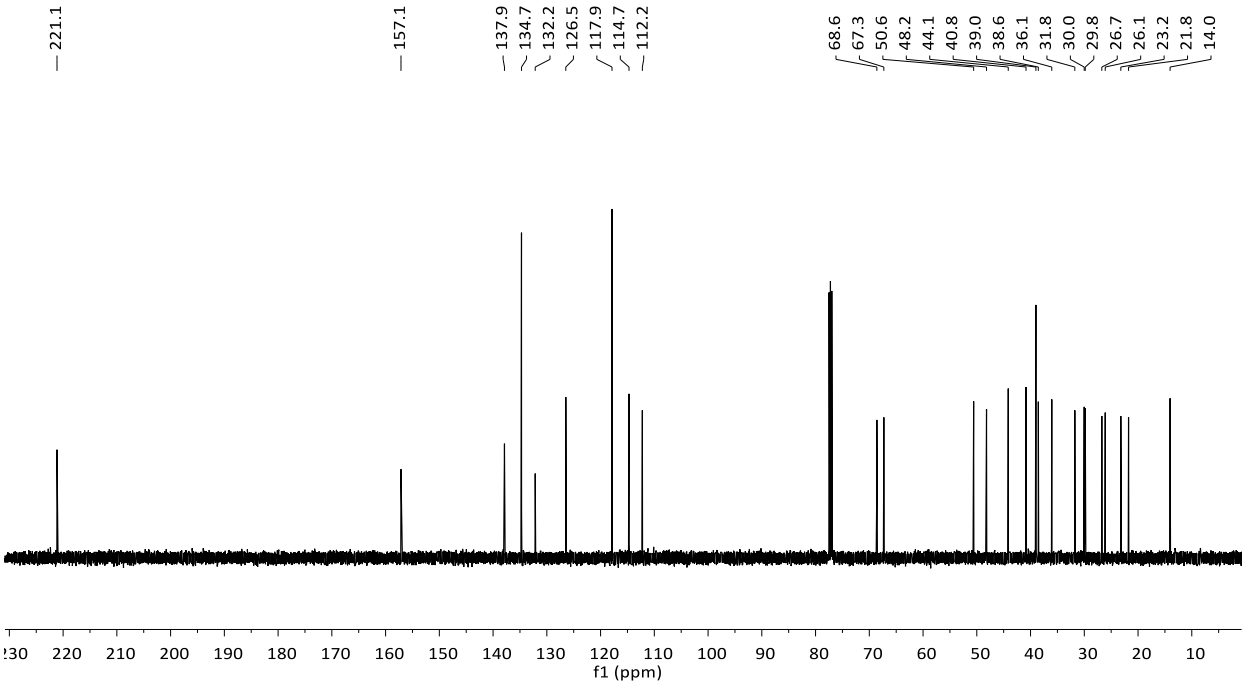
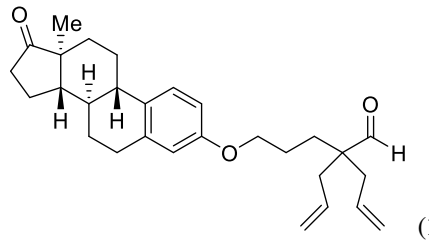
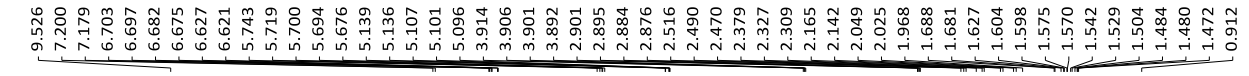
7.186
6.714
6.698
6.642
5.901
5.881
5.867
5.847
5.129
5.111
5.093
3.927
3.914
3.902
3.443
2.895
2.885
2.538
2.520
2.499
2.482
2.407
2.387
2.249
2.168
2.149
2.130
2.112
2.095
2.081
2.033
1.999
1.971
1.951
1.796
1.780
1.764
1.710
1.630
1.605
1.580
1.558
1.533
1.509
1.486
1.459
1.437
1.428
1.420
1.403
0.916
1.01
1.00
1.03
2.07
4.27
2.10
2.10
2.09
1.07
1.02
1.09
8.76
2.13
1.19
8.80
3.23
f1 (ppm)


221.1
157.1
137.9
134.7
132.2
126.5
117.9
114.7
112.2
68.6
67.3
50.6
48.2
44.1
40.8
39.0
38.6
36.1
31.8
30.0
29.8
26.7
26.1
23.2
21.8
14.0
f1 (ppm)


O
Me
H
H
H
O
O
H

(**1j**)


9.526
7.200
7.179
6.703
6.697
6.682
6.675
6.627
6.621
5.743
5.719
5.700
5.694
5.676
5.139
5.136
5.107
5.101
5.096
3.914
3.906
3.901
3.892
2.901
2.895
2.884
2.876
2.516
2.490
2.470
2.379
2.327
2.309
2.165
2.142
2.049
2.025
1.968
1.688
1.681
1.627
1.604
1.598
1.575
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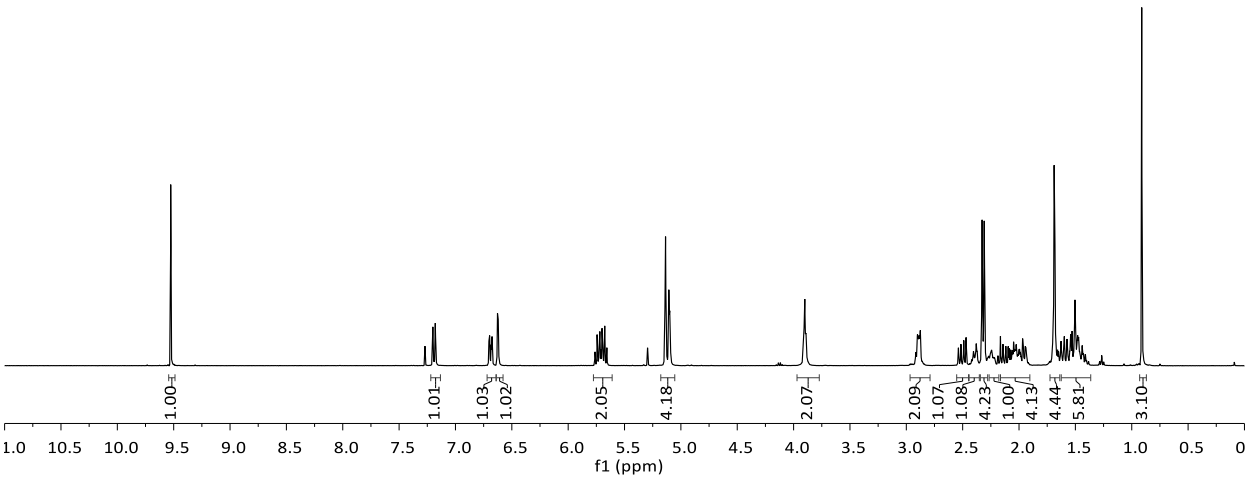
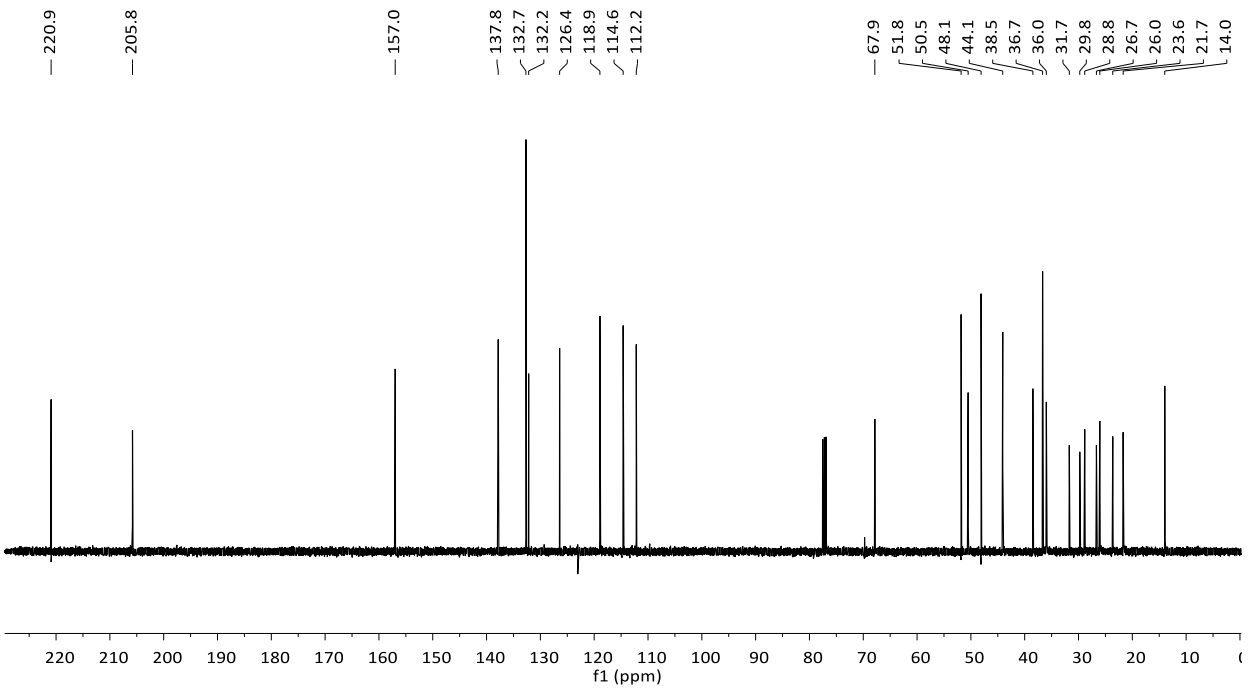
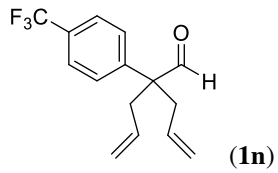
1.529
1.504
1.484
1.480
1.472
0.912

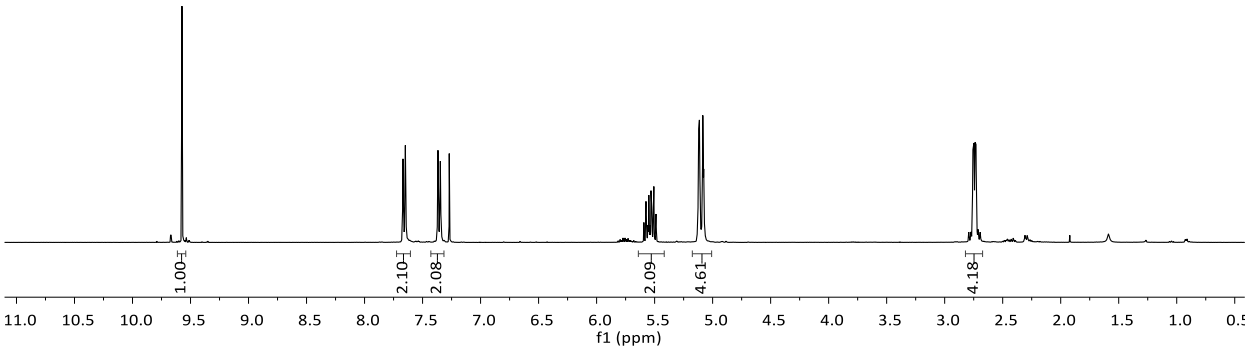

1.00
1.01
1.03
1.02
2.05
4.18
2.07
2.09
1.07
1.08
4.23
1.00
4.13
4.44
5.81
3.10
f1 (ppm)

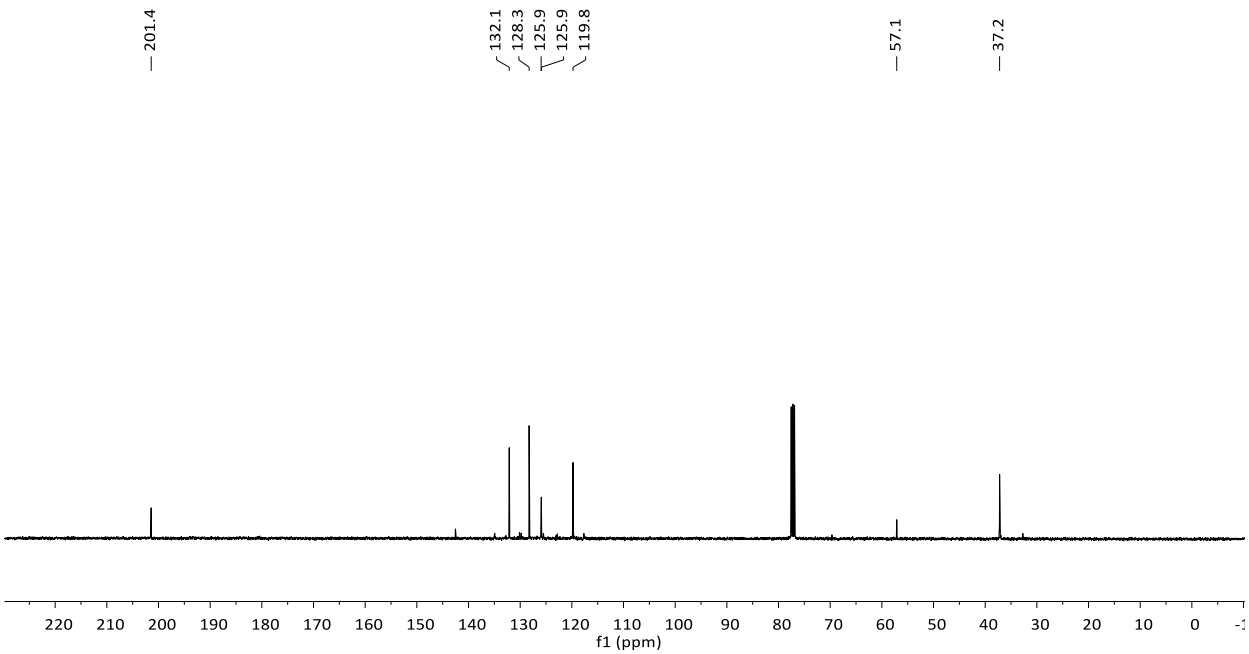

220.9
205.8
157.0
137.8
132.7
132.2
126.4
118.9
114.6
112.2
67.9
51.8
50.5
48.1
44.1
38.5
36.7
36.0
31.7
29.8
28.8
26.7
26.0
23.6
21.7
14.0
f1 (ppm)

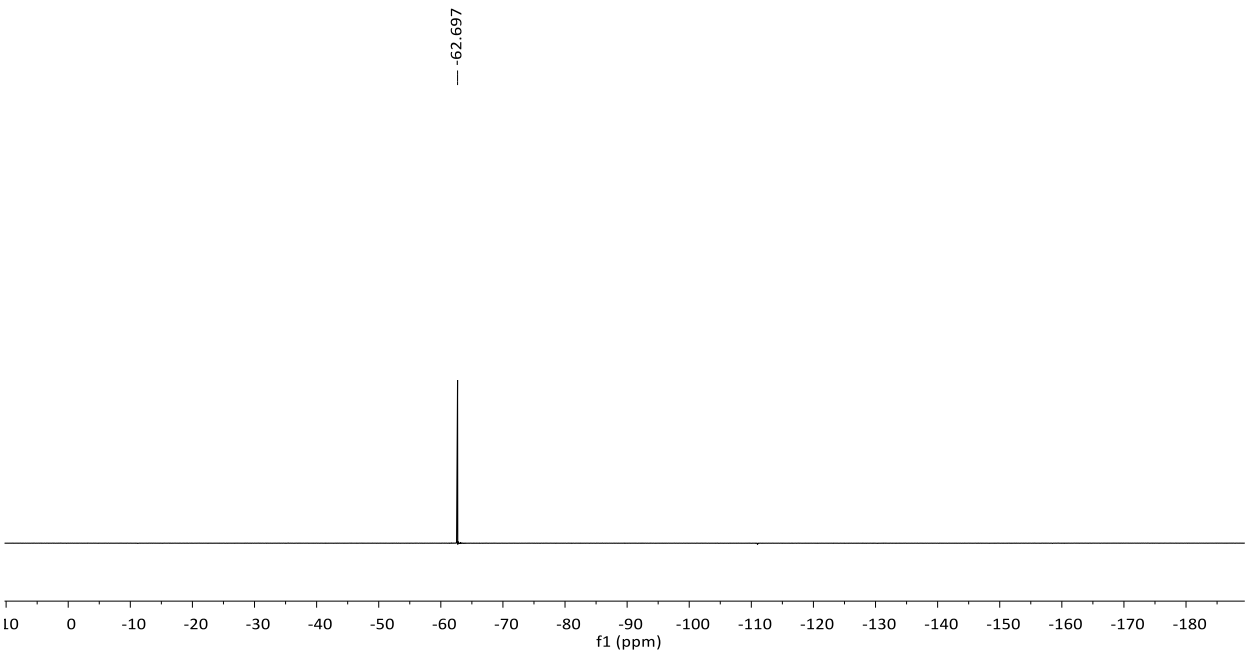

F3C
O
H

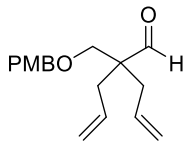
(**1n**)


9.574
7.669
7.649
7.647
7.369
7.367
7.364
7.347
7.345
5.575
5.568
5.556
5.550
5.531
5.525
5.513
5.507
5.488
5.124
5.120
5.116
5.114
5.111
5.109
5.090
5.087
5.085
5.081
5.077
2.760
2.757
2.754
2.751
2.748
2.745
2.741
2.738
2.735
2.733
2.730

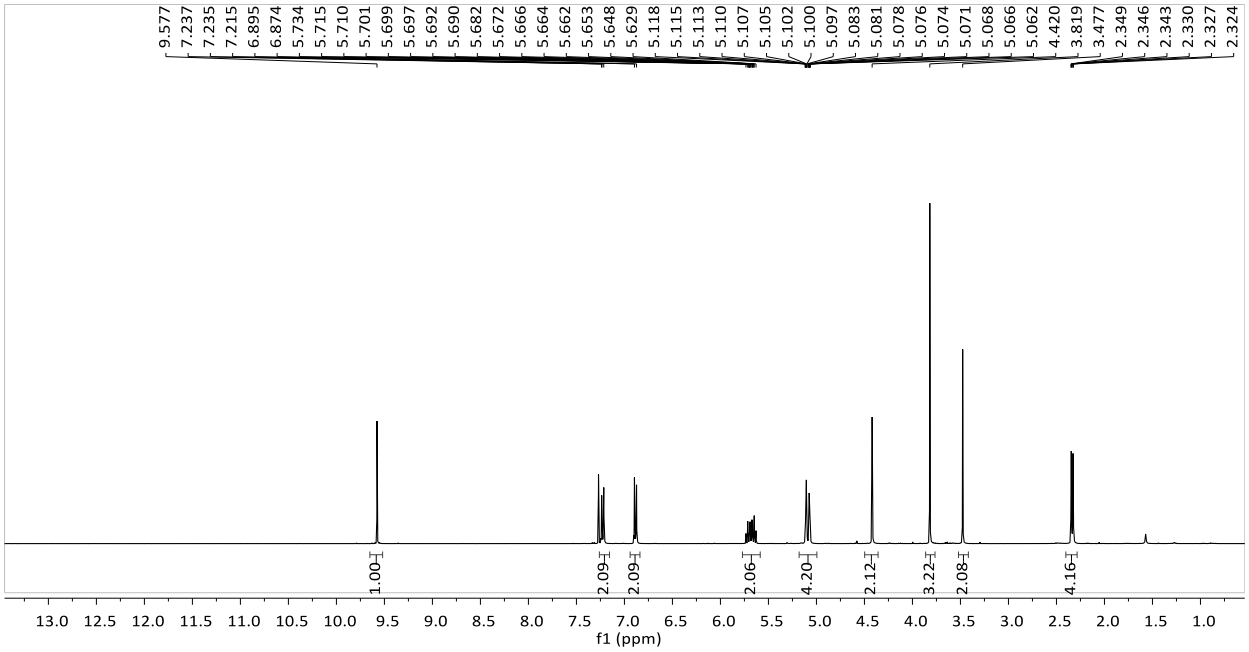

1.00
2.10
2.08
2.09
4.61
4.18
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


201.4
132.1
128.3
125.9
125.9
119.8
57.1
37.2
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-62.697
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)


O
PMBO
H

(**1s**)


9.577
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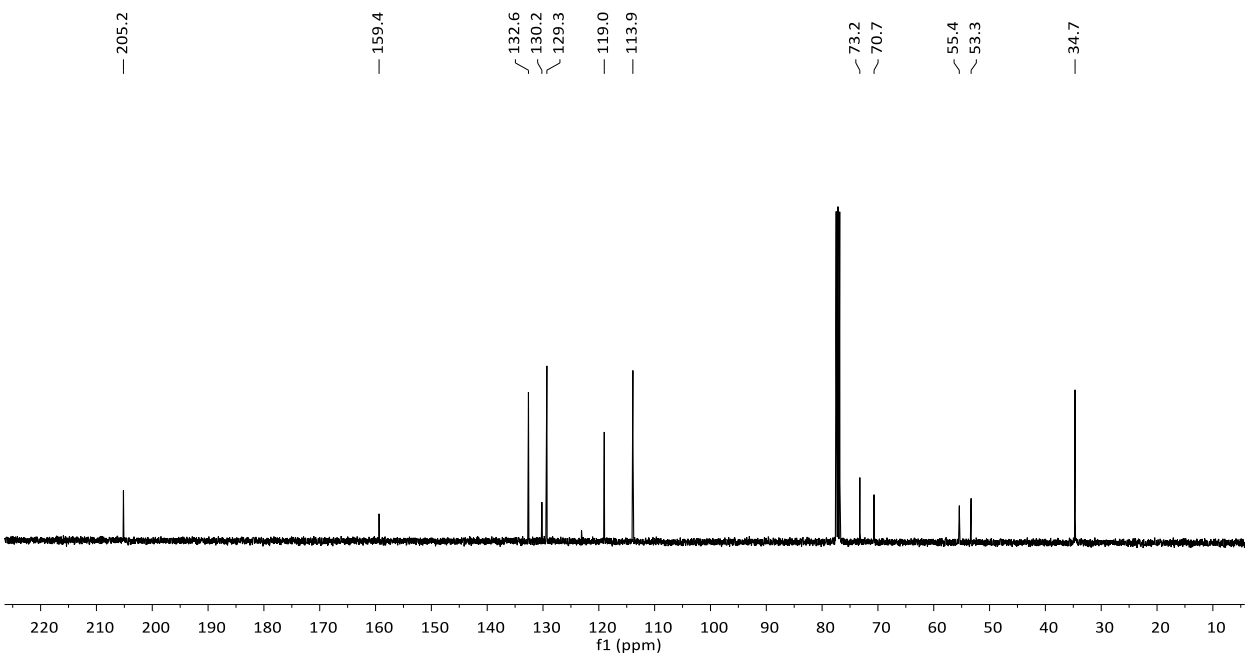
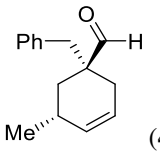
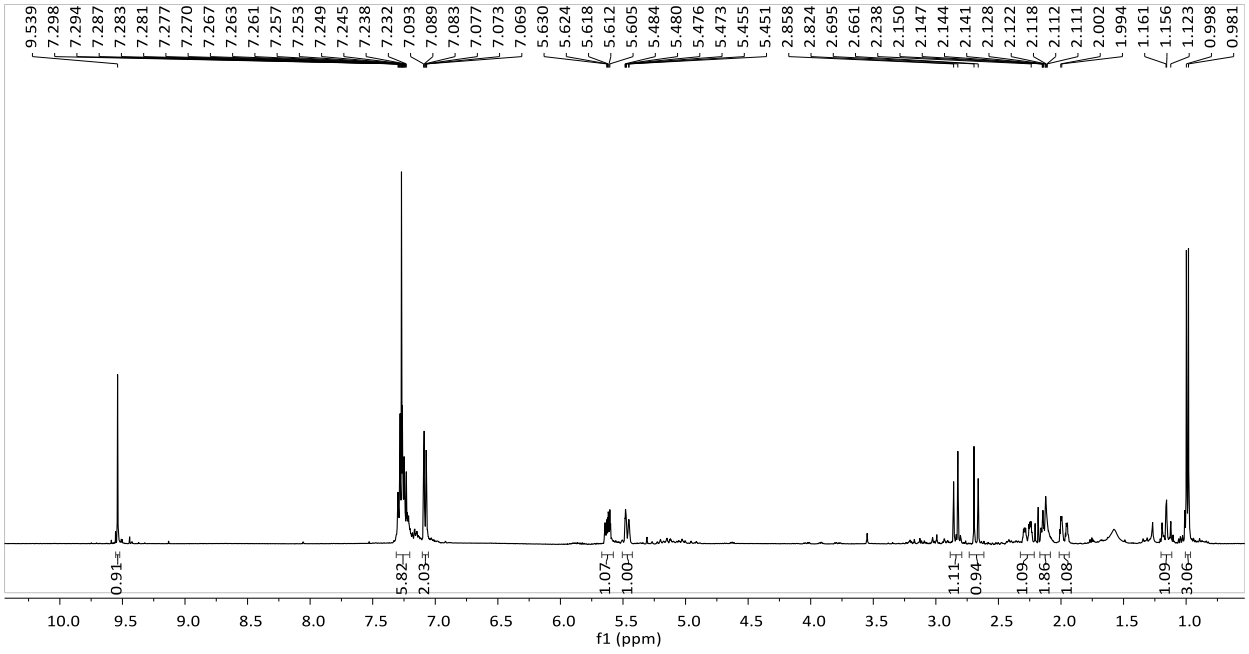
7.235
7.215
6.895
6.874
5.734
5.715
5.710
5.701
5.699
5.697
5.692
5.690
5.682
5.672
5.666
5.664
5.662
5.653
5.648
5.629
5.118
5.115
5.113
5.110
5.107
5.105
5.102
5.100
5.097
5.083
5.081
5.078
5.076
5.074
5.071
5.068
5.066
5.062
4.420
3.819
3.477
2.349
2.346
2.343
2.330
2.327
2.324
1.00
2.09
2.09
2.06
4.20
2.12
3.22
2.08
4.16
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)


205.2
159.4
132.6
130.2
129.3
119.0
113.9
73.2
70.7
55.4
53.3
34.7
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
Ph
H
Me

(**4a**)


9.539
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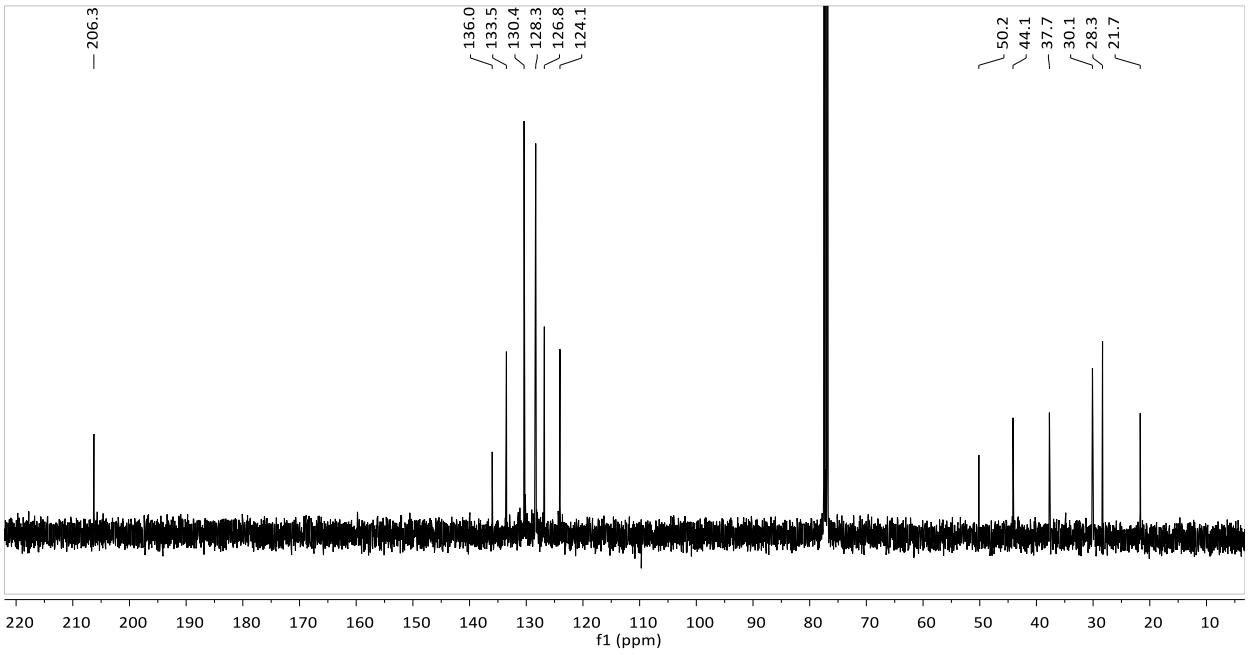
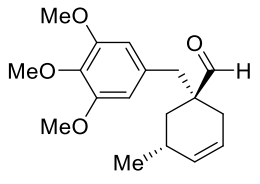
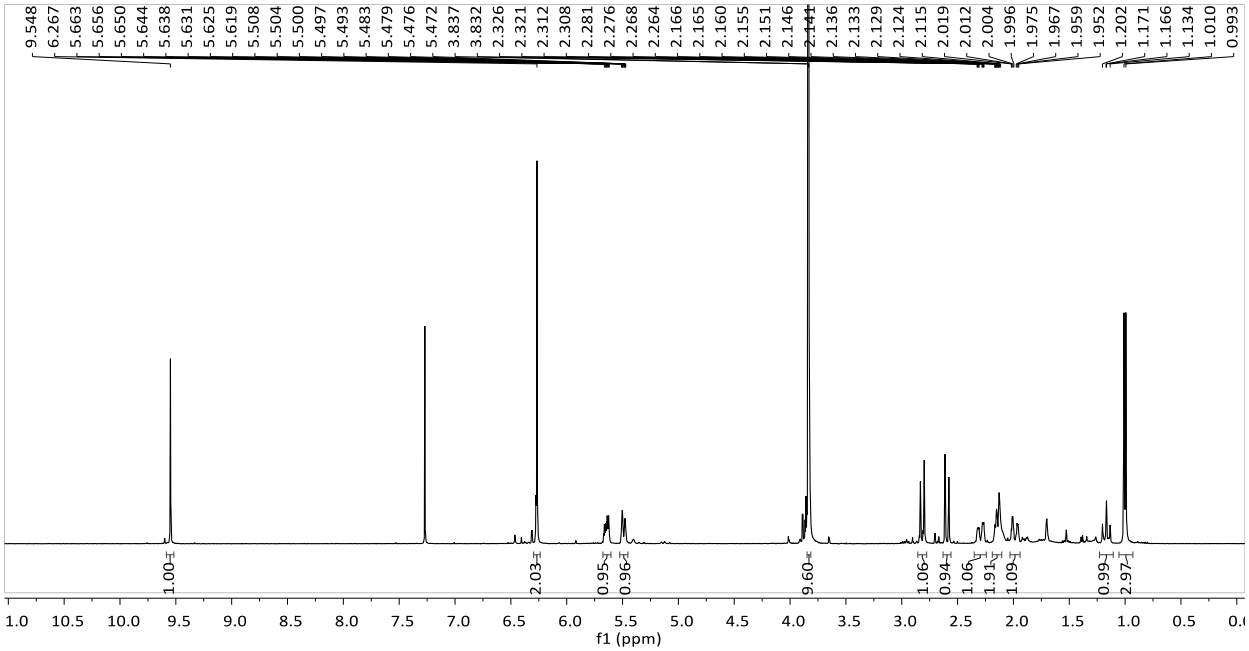
7.294
7.287
7.283
7.281
7.277
7.270
7.267
7.263
7.261
7.257
7.253
7.249
7.245
7.238
7.232
7.093
7.089
7.083
7.077
7.073
7.069
5.630
5.624
5.618
5.612
5.605
5.484
5.480
5.476
5.473
5.455
5.451
2.858
2.824
2.695
2.661
2.238
2.150
2.147
2.144
2.141
2.128
2.122
2.118
2.112
2.111
2.002
1.994
1.161
1.156
1.123
0.998
0.981
0.91
5.82
2.03
1.07
1.00
1.11
0.94
1.09
1.86
1.08
1.09
3.06
f1 (ppm)


206.3
136.0
133.5
130.4
128.3
126.8
124.1
50.2
44.1
37.7
30.1
28.3
21.7
f1 (ppm)


MeO
MeO
MeO
O
H
Me

(**4b**)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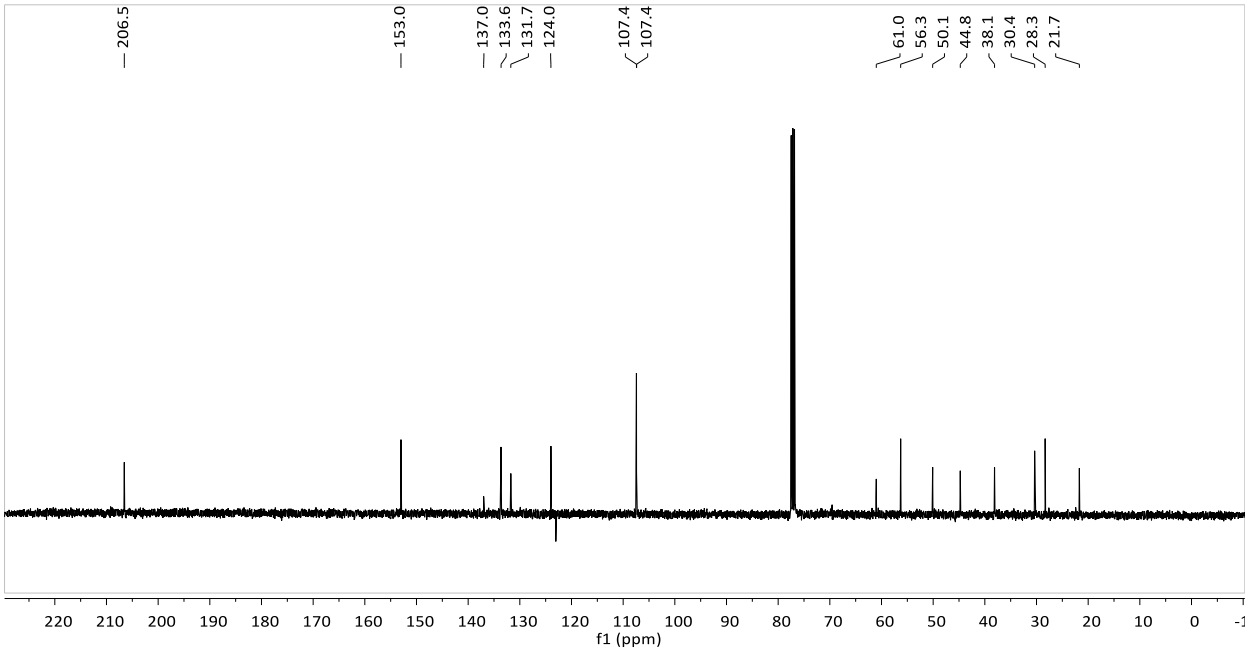
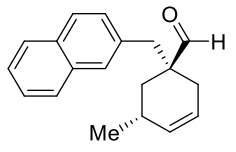
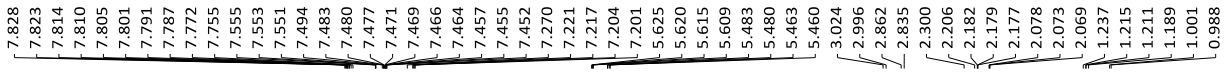
6.267
5.663
5.656
5.650
5.644
5.638
5.631
5.625
5.619
5.508
5.504
5.500
5.497
5.493
5.483
5.479
5.476
5.472
3.837
3.832
2.326
2.321
2.312
2.308
2.281
2.276
2.268
2.264
2.166
2.165
2.160
2.155
2.151
2.146
2.141
2.136
2.133
2.129
2.124
2.115
2.019
2.012
2.004
1.996
1.975
1.967
1.959
1.952
1.202
1.171
1.166
1.134
1.010
0.993
1.00
2.03
0.95
0.96
9.60
1.06
0.94
1.06
1.91
1.09
0.99
2.97
f1 (ppm)


206.5
153.0
137.0
133.6
131.7
124.0
107.4
107.4
61.0
56.3
50.1
44.8
38.1
30.4
28.3
21.7
f1 (ppm)


O
H
Me

(**4c**)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7.823
7.814
7.810
7.805
7.801
7.791
7.787
7.772
7.755
7.555
7.553
7.551
7.494
7.483
7.480
7.477
7.471
7.469
7.466
7.464
7.457
7.455
7.452
7.270
7.221
7.217
7.204
7.201
5.625
5.620
5.615
5.609
5.483
5.480
5.463
5.460
3.024
2.996
2.862
2.835
2.300
2.206
2.182
2.179
2.177
2.078
2.073
2.069
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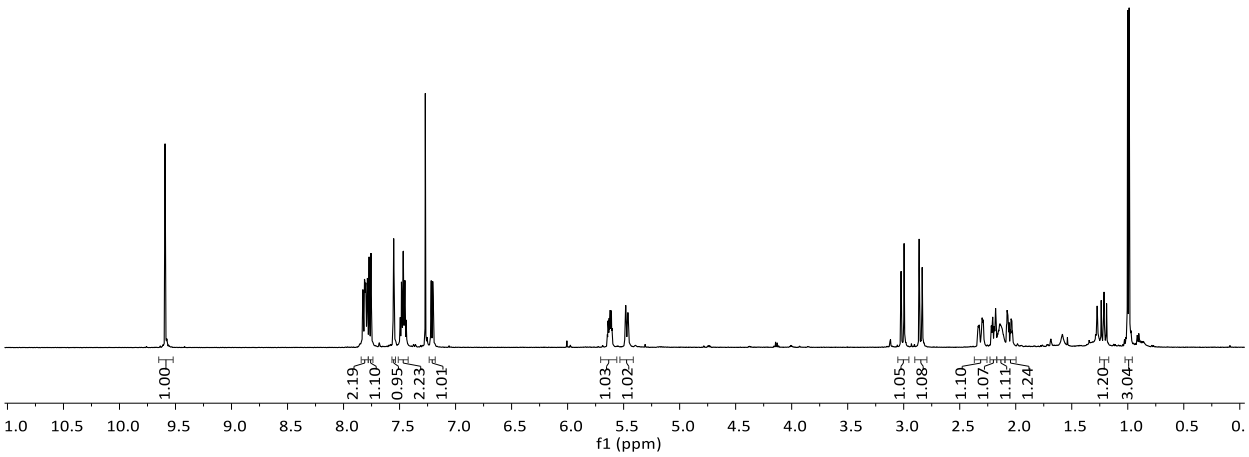
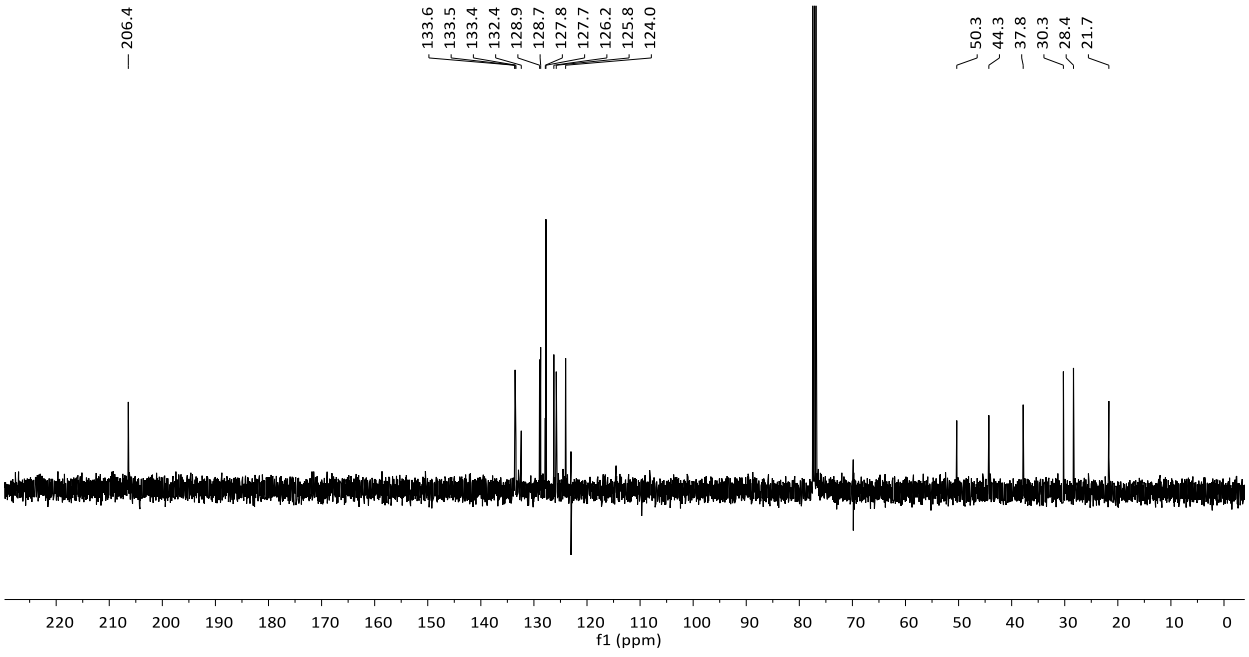
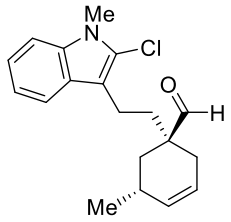
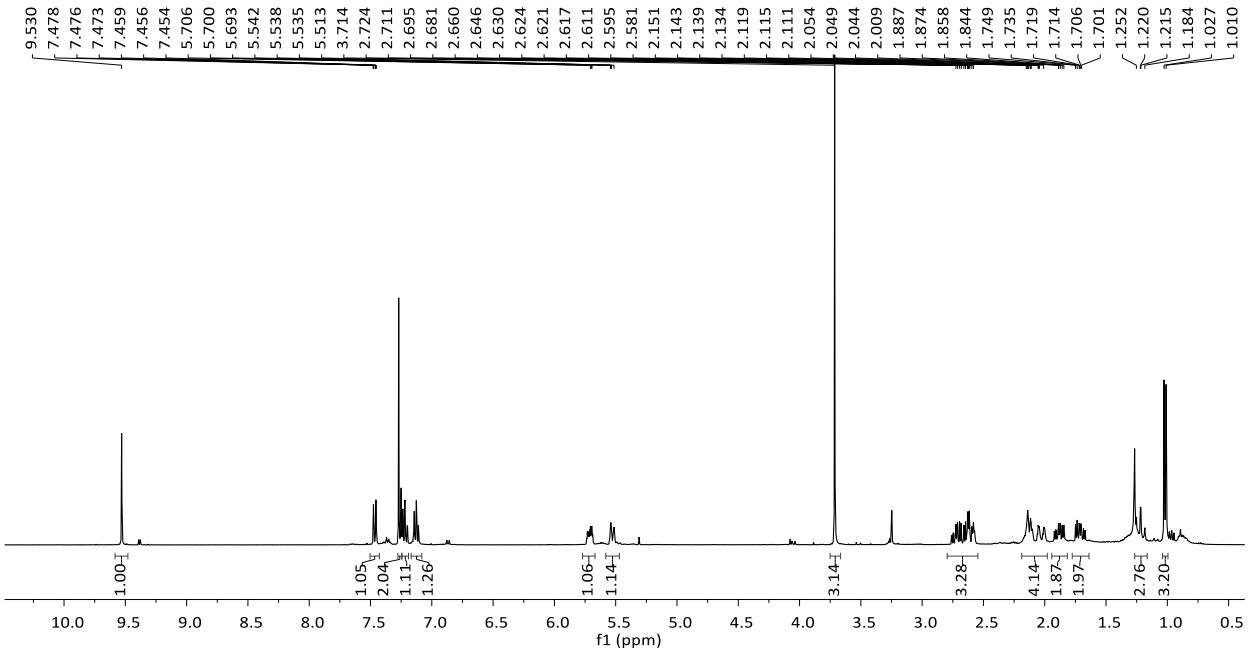
1.215
1.211
1.189
1.001
0.988


1.00
2.19
1.10
0.95
2.23
1.01
1.03
1.02
1.05
1.08
1.10
1.07
1.11
1.24
1.20
3.04
f1 (ppm)


206.4
133.6
133.5
133.4
132.4
128.9
128.7
127.8
127.7
126.2
125.8
124.0
50.3
44.3
37.8
30.3
28.4
21.7
f1 (ppm)


Me
N
Cl
O
H
Me

(**4d**)


9.530
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7.473
7.459
7.456
7.454
5.706
5.700
5.693
5.542
5.538
5.535
5.513
3.714
2.724
2.711
2.695
2.681
2.660
2.646
2.630
2.624
2.621
2.617
2.611
2.595
2.581
2.151
2.143
2.139
2.134
2.119
2.115
2.111
2.054
2.049
2.044
2.009
1.887
1.874
1.858
1.844
1.749
1.735
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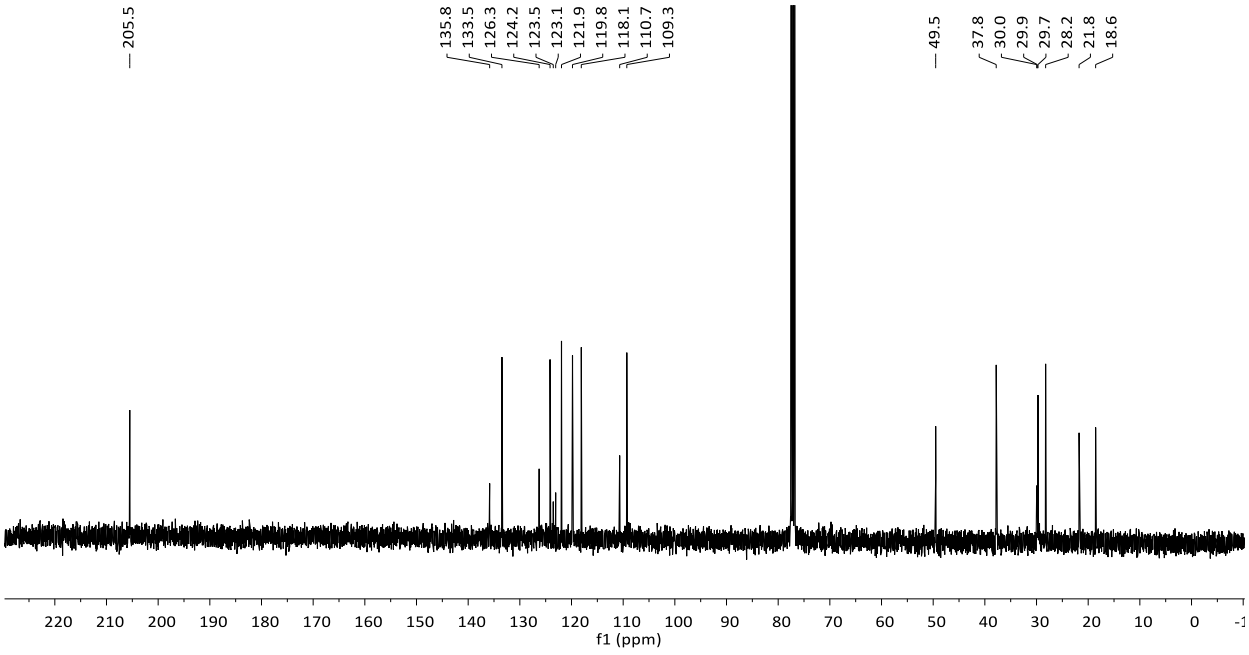
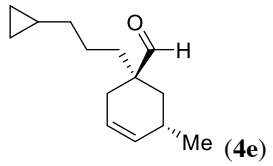
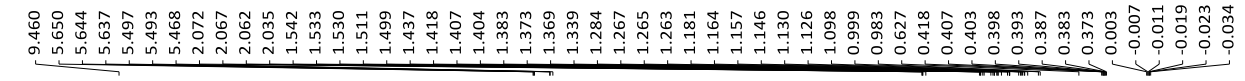
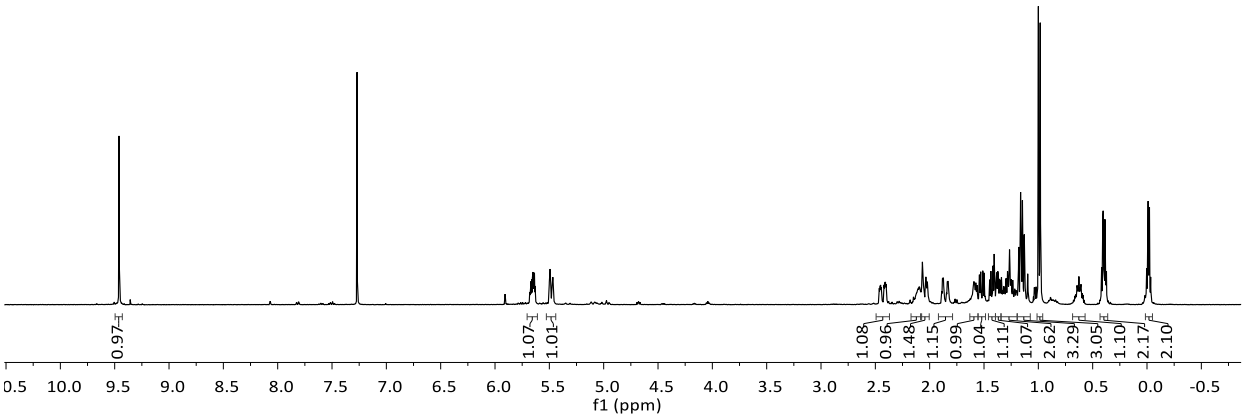
1.714
1.706
1.701
1.252
1.220
1.215
1.184
1.027
1.010
1.00
1.05
2.04
1.11
1.26
1.06
1.14
3.14
3.28
4.14
1.87
1.97
2.76
3.20
f1 (ppm)

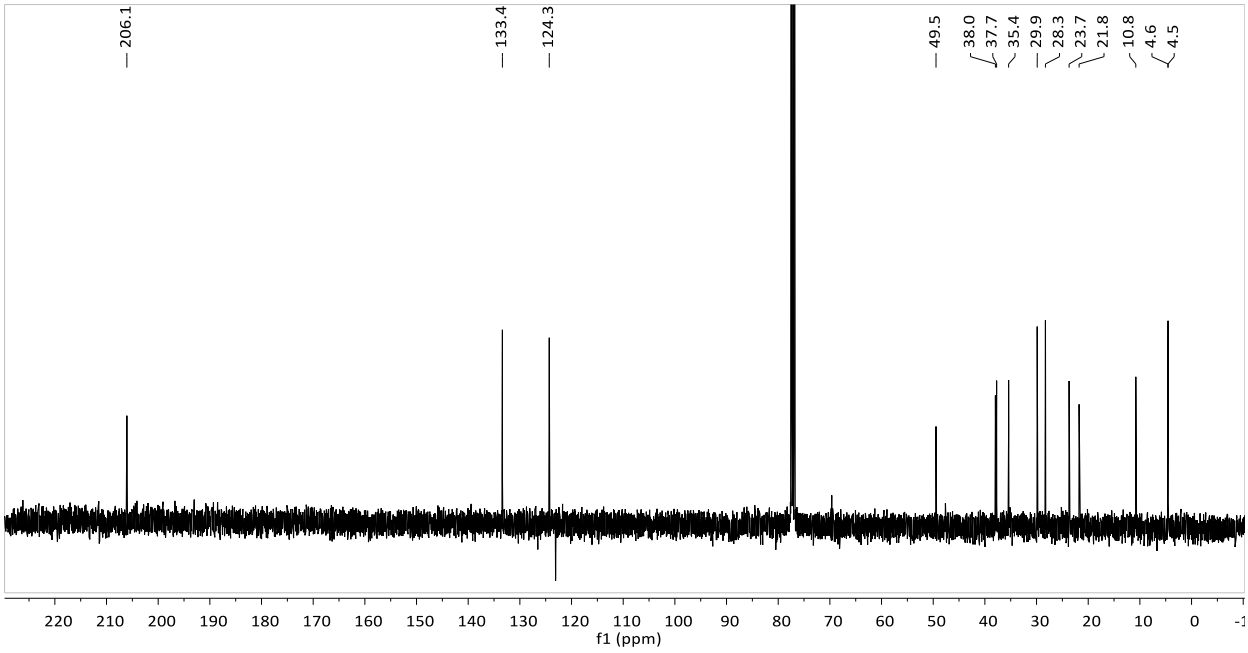

205.5
135.8
133.5
126.3
124.2
123.5
123.1
121.9
119.8
118.1
110.7
109.3
49.5
37.8
30.0
29.9
29.7
28.2
21.8
18.6
f1 (ppm)

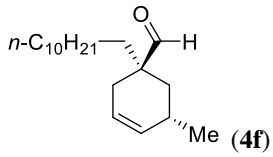

O
H
Me

(**4e**)

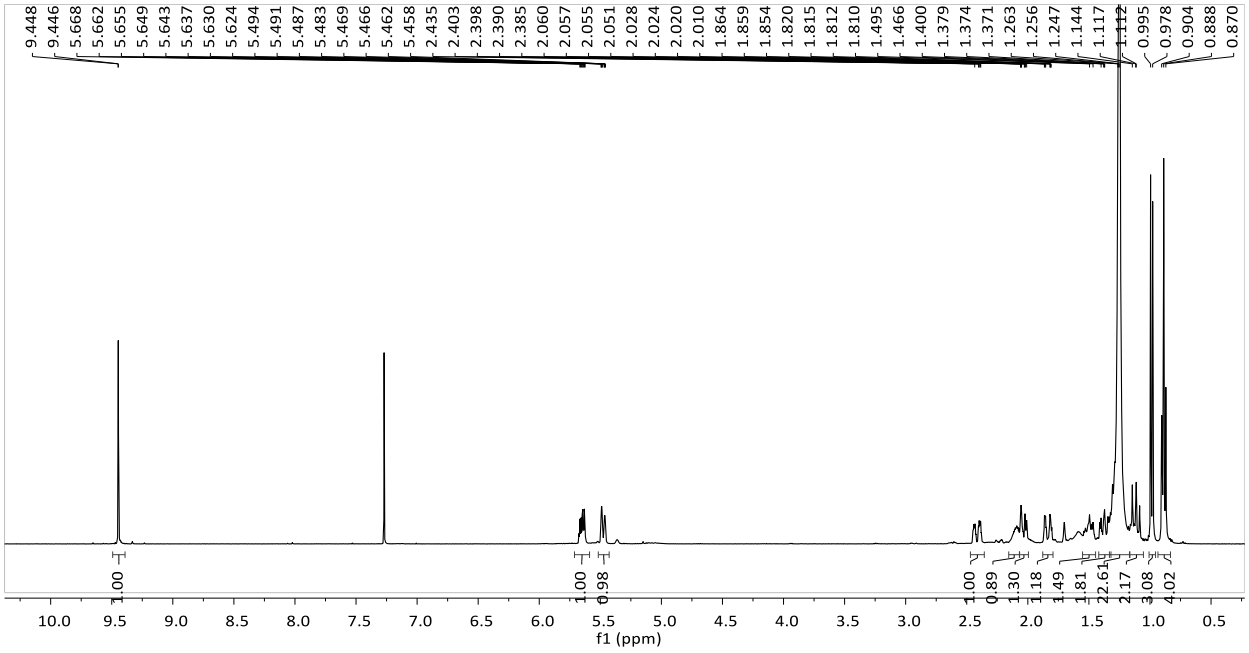

9.460
5.650
5.644
5.637
5.497
5.493
5.468
2.072
2.067
2.062
2.035
1.542
1.533
1.530
1.511
1.499
1.437
1.418
1.407
1.404
1.383
1.373
1.369
1.339
1.284
1.267
1.265
1.263
1.181
1.164
1.157
1.146
1.130
1.126
1.098
0.999
0.983
0.627
0.418
0.407
0.403
0.398
0.393
0.387
0.383
0.373
0.003
-0.007
-0.011
-0.019
-0.023
-0.034

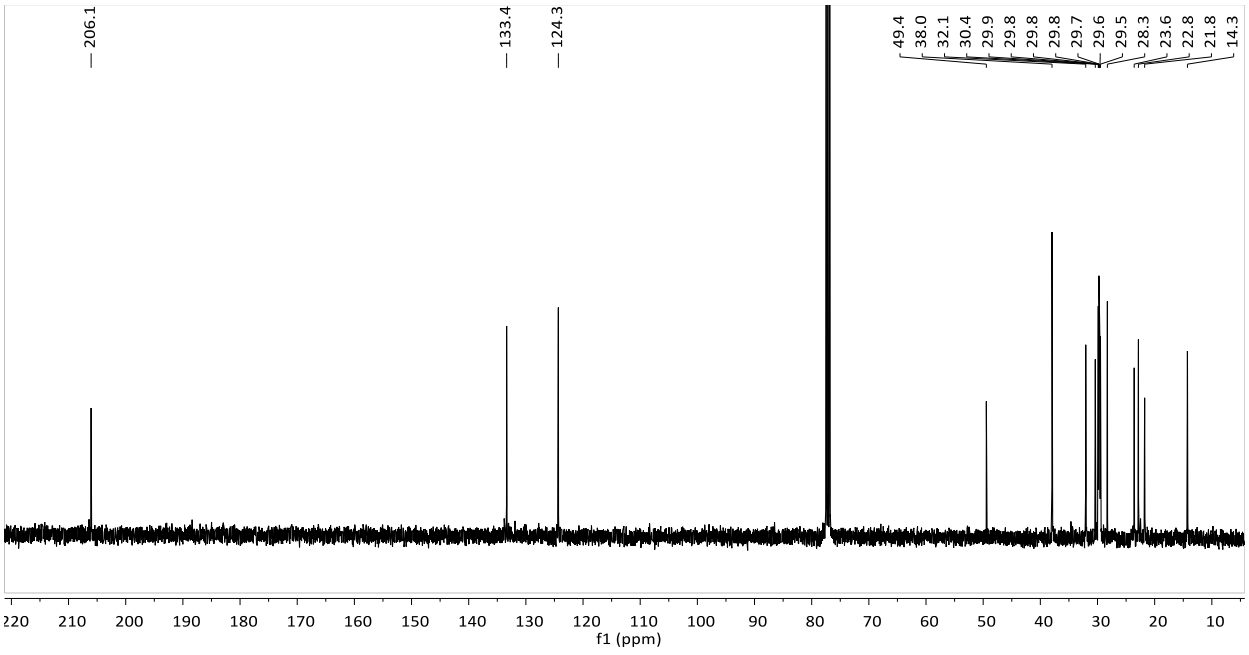

0.97
1.07
1.01
1.08
0.96
1.48
1.15
0.99
1.04
1.11
1.07
2.62
3.29
3.05
1.10
2.17
2.10
f1 (ppm)

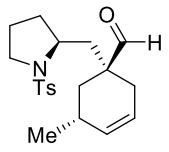

206.1
133.4
124.3
49.5
38.0
37.7
35.4
29.9
28.3
23.7
21.8
10.8
4.6
4.5
f1 (ppm)


O
H
n-C10H21
Me

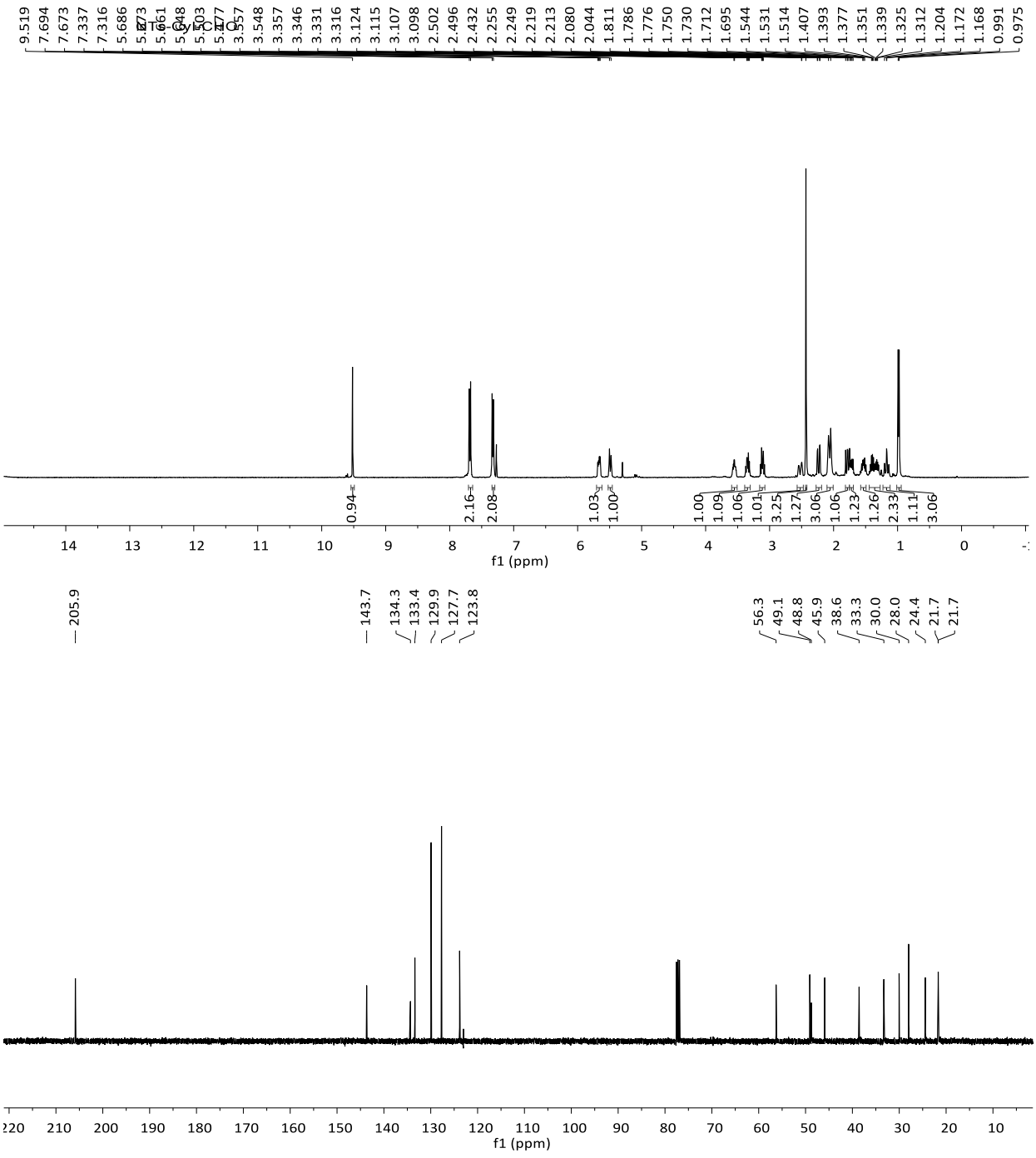
(**4f**)

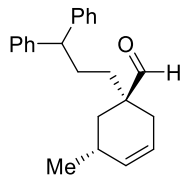

9.448 9.446 5.668 5.662 5.655 5.649 5.643 5.637 5.630 5.624 5.494 5.491 5.487 5.483 5.469 5.466 5.462 5.458 2.435 2.403 2.398 2.390 2.385 2.060 2.057 2.055 2.051 2.028 2.024 2.020 2.010 1.864 1.859 1.854 1.820 1.815 1.812 1.810 1.495 1.466 1.400 1.379 1.374 1.371 1.263 1.256 1.247 1.144 1.117 1.112 0.995 0.978 0.904 0.888 0.870
1.00 1.00 0.98 1.00 0.89 1.30 1.18 1.49 1.81 22.61 2.17 3.08 4.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


206.1 133.4 124.3
49.4 38.0 32.1 30.4 29.9 29.8 29.8 29.8 29.7 29.6 29.5 28.3 23.6 22.8 21.8 14.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

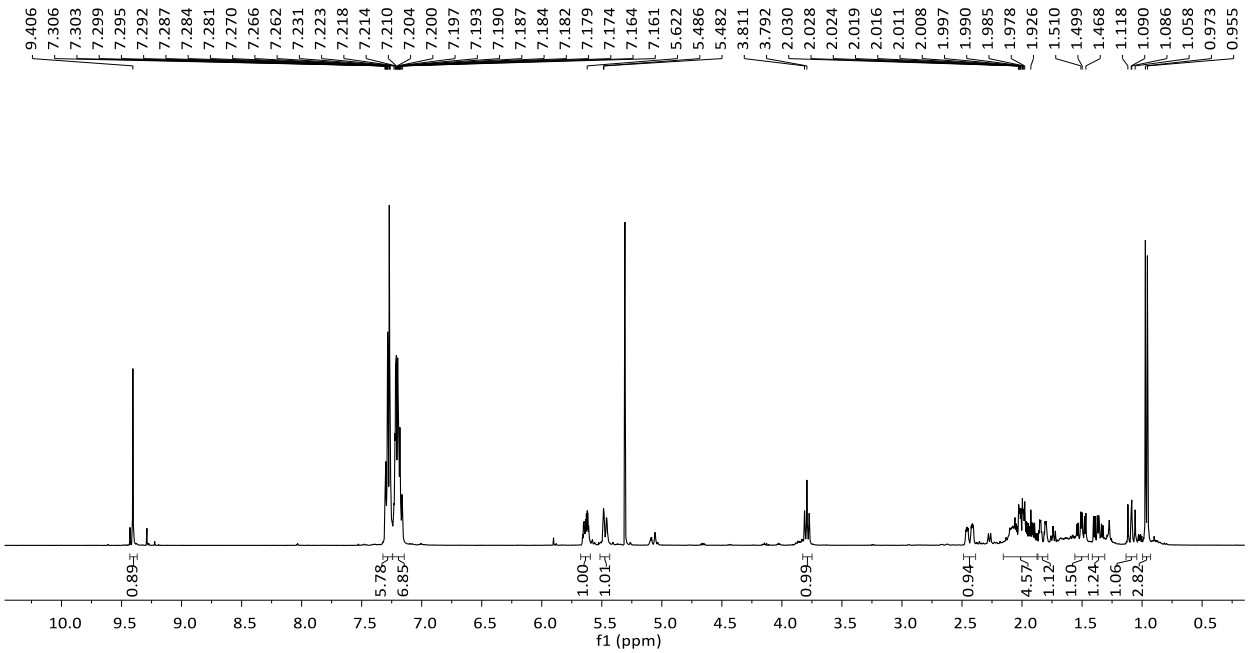

O
H
N
Ts
Me

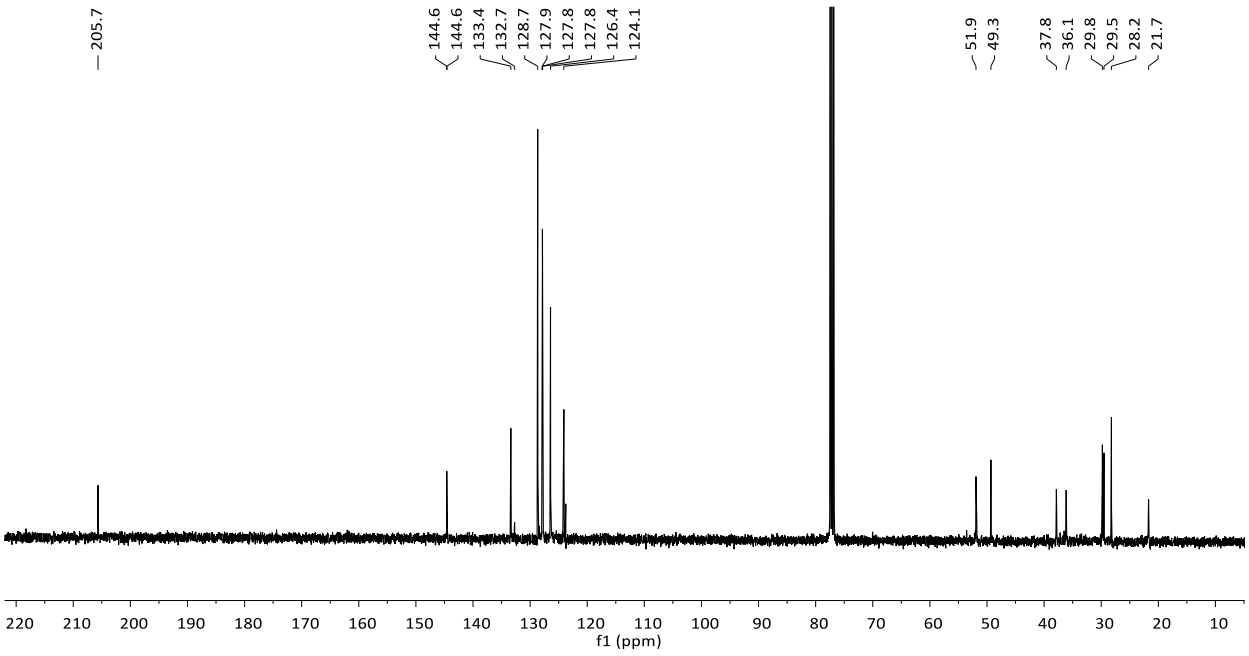
(**4g**)

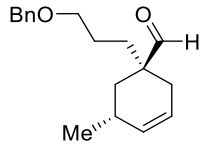

9.519
7.694
7.673
7.337
7.316
5.686
5.661
5.548
5.503
5.477
3.557
3.548
3.357
3.346
3.331
3.316
3.124
3.115
3.107
3.098
2.502
2.496
2.432
2.255
2.249
2.219
2.213
2.080
2.044
1.811
1.786
1.776
1.750
1.730
1.712
1.695
1.544
1.531
1.514
1.407
1.393
1.377
1.351
1.339
1.325
1.312
1.204
1.172
1.168
0.991
0.975
0.94
2.16
2.08
1.03
1.00
1.00
1.09
1.06
1.01
3.25
1.27
3.06
1.06
1.23
1.26
2.33
1.11
3.06
f1 (ppm)
205.9
143.7
134.3
133.4
129.9
127.7
123.8
56.3
49.1
48.8
45.9
38.6
33.3
30.0
28.0
24.4
21.7
21.7
f1 (ppm)


Ph
Ph
O
H
Me

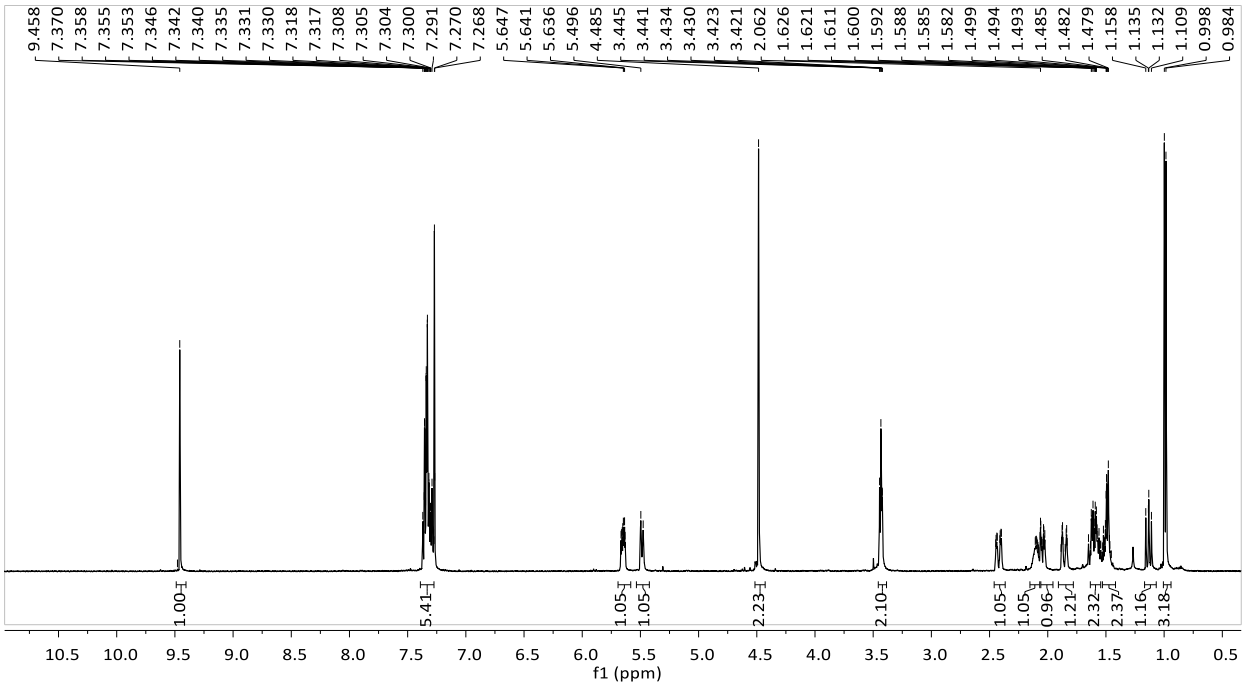
(**4h**)

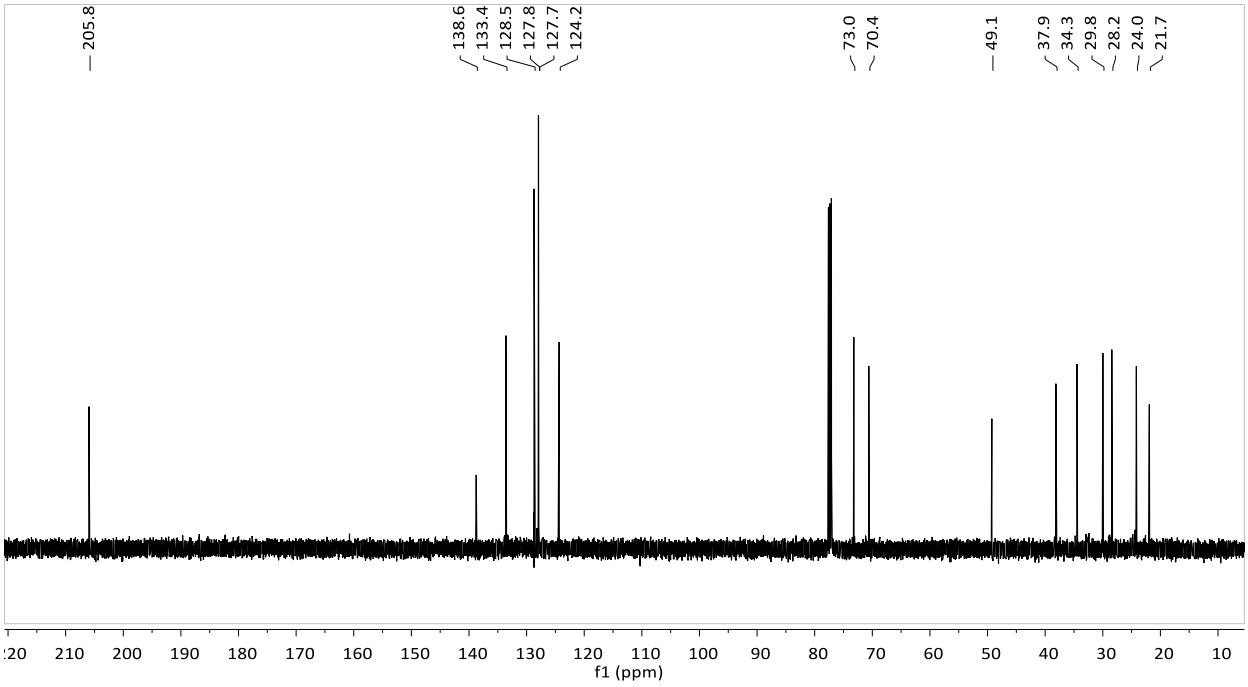

9.406
7.306
7.303
7.299
7.295
7.292
7.287
7.284
7.281
7.270
7.266
7.262
7.231
7.223
7.218
7.214
7.210
7.204
7.200
7.197
7.193
7.190
7.187
7.184
7.182
7.179
7.174
7.164
7.161
5.622
5.486
5.482
3.811
3.792
2.030
2.028
2.024
2.019
2.016
2.011
2.008
1.997
1.990
1.985
1.978
1.926
1.510
1.499
1.468
1.118
1.090
1.086
1.058
0.973
0.955
0.89
5.78
6.85
1.00
1.01
0.99
0.94
4.57
1.12
1.50
1.24
1.06
2.82
f1 (ppm)

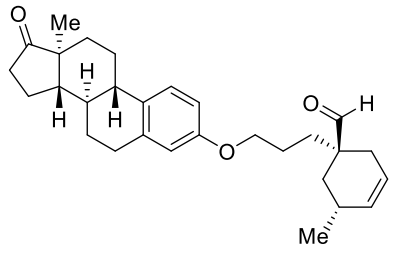

205.7
144.6
144.6
133.4
132.7
128.7
127.9
127.8
127.8
126.4
124.1
51.9
49.3
37.8
36.1
29.8
29.5
28.2
21.7
f1 (ppm)


BnO
O
H
Me

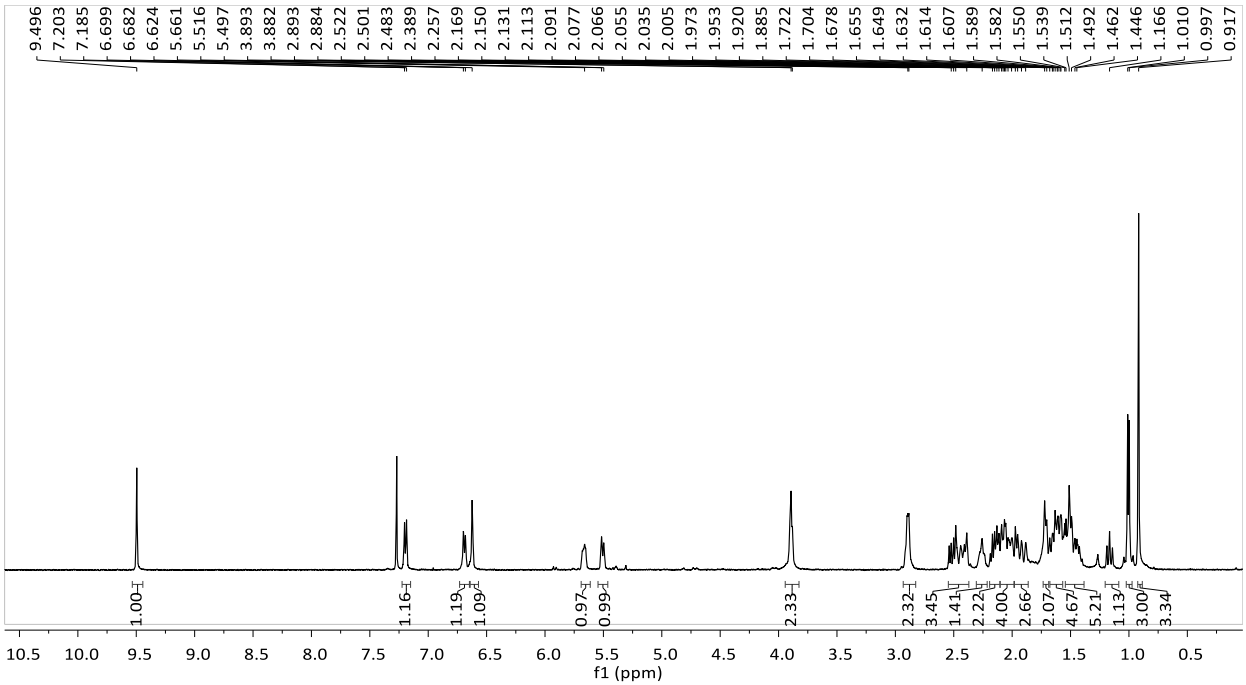
(**4i**)

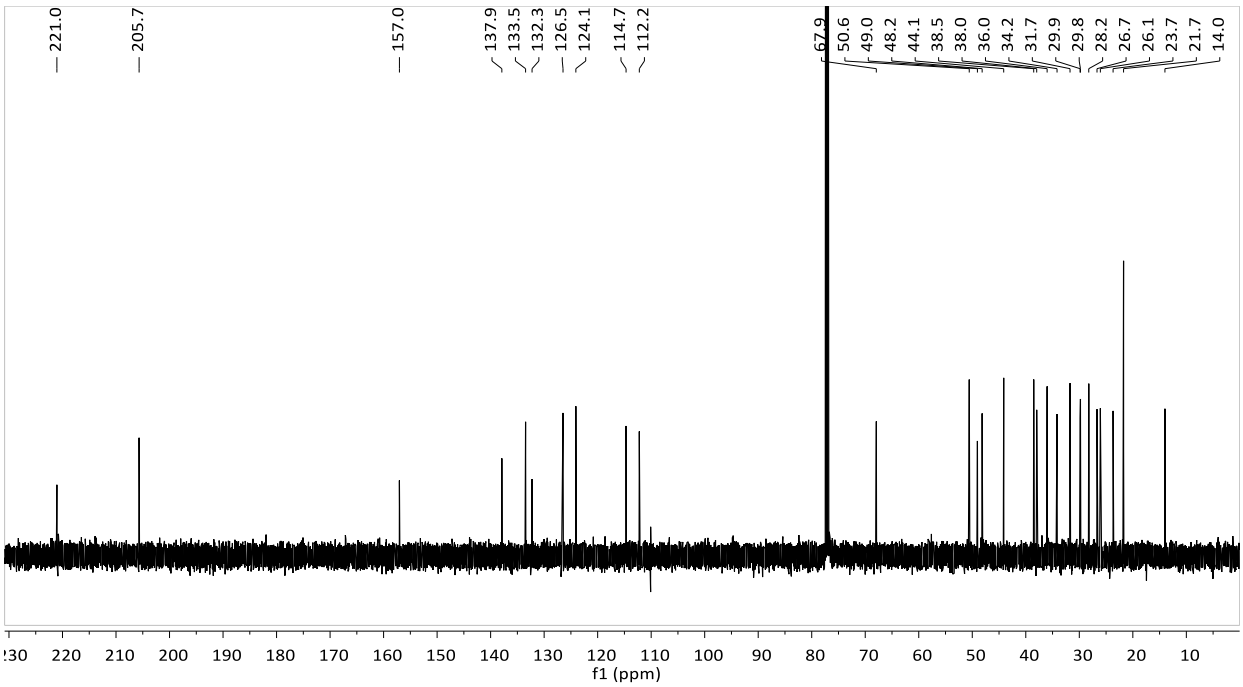

9.458
7.370
7.358
7.355
7.353
7.346
7.342
7.340
7.335
7.331
7.330
7.318
7.317
7.308
7.305
7.304
7.300
7.291
7.270
7.268
5.647
5.641
5.636
5.496
4.485
3.445
3.441
3.434
3.430
3.423
3.421
2.062
1.626
1.621
1.611
1.600
1.592
1.588
1.585
1.582
1.499
1.494
1.493
1.485
1.482
1.479
1.158
1.135
1.132
1.109
0.998
0.984
1.00
5.41
1.05
1.05
2.23
2.10
1.05
1.05
0.96
1.21
2.32
2.37
1.16
3.18
f1 (ppm)

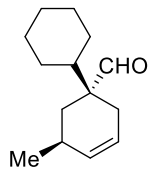

205.8
138.6
133.4
128.5
127.8
127.7
124.2
73.0
70.4
49.1
37.9
34.3
29.8
28.2
24.0
21.7
f1 (ppm)


O
Me
H
H
H
O
O
H
Me

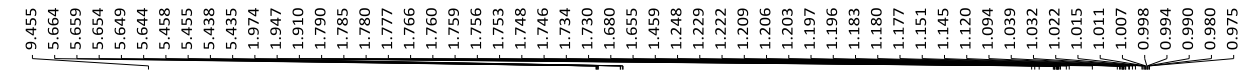
(**4j**)

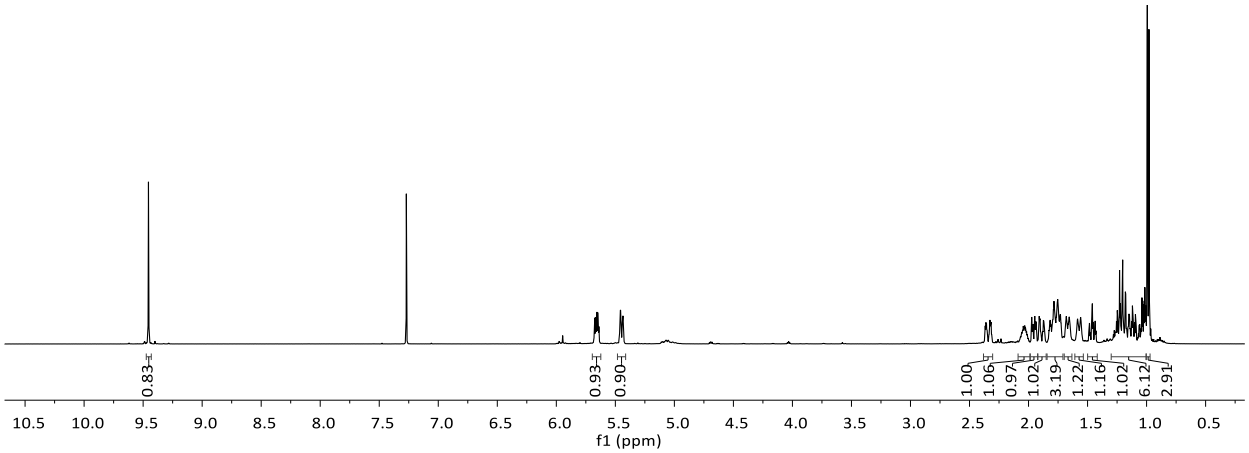

9.496
7.203
7.185
6.699
6.682
6.624
6.661
5.516
5.497
3.893
3.882
2.893
2.884
2.522
2.501
2.483
2.389
2.257
2.169
2.150
2.131
2.113
2.091
2.077
2.066
2.055
2.035
2.005
1.973
1.953
1.920
1.885
1.722
1.704
1.678
1.655
1.649
1.632
1.614
1.607
1.589
1.582
1.550
1.539
1.512
1.492
1.462
1.446
1.166
1.010
0.997
0.917
1.00
1.16
1.19
1.09
0.97
0.99
2.33
2.32
3.45
1.41
2.22
4.00
2.66
2.07
4.67
5.21
1.13
3.00
3.34
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

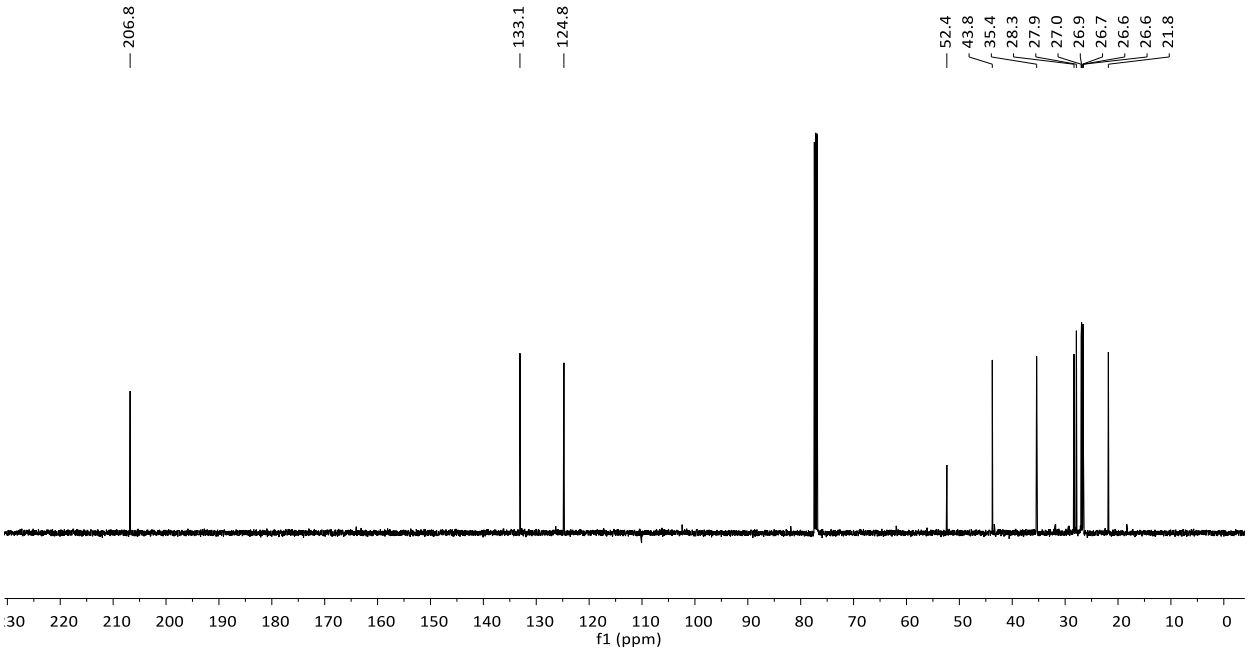

221.0
205.7
157.0
137.9
133.5
132.3
126.5
124.1
114.7
112.2
67.9
50.6
49.0
48.2
44.1
38.5
38.0
36.0
34.2
31.7
29.9
29.8
28.2
26.7
26.1
23.7
21.7
14.0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

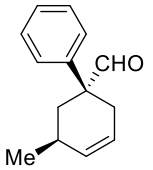

CHO
Me

(**4k**)

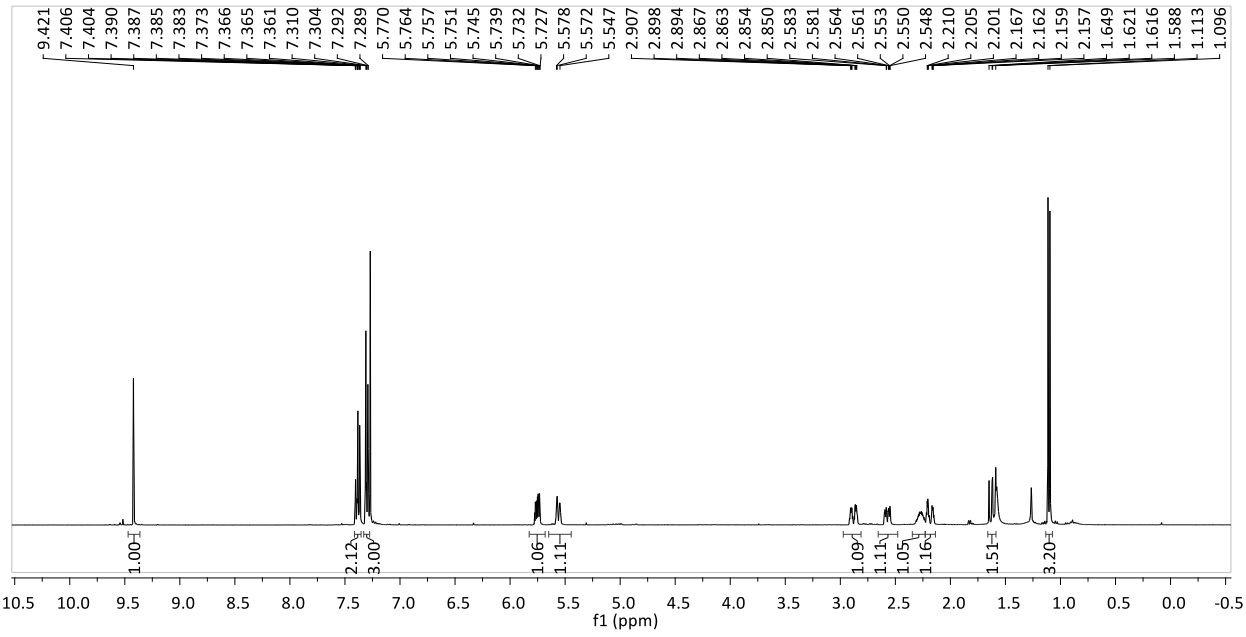

9.455
5.664
5.659
5.654
5.649
5.644
5.458
5.455
5.438
5.435
1.974
1.947
1.910
1.790
1.785
1.780
1.777
1.766
1.760
1.759
1.756
1.753
1.748
1.746
1.734
1.730
1.680
1.655
1.459
1.248
1.229
1.222
1.209
1.206
1.203
1.197
1.196
1.183
1.180
1.177
1.151
1.145
1.120
1.094
1.039
1.032
1.022
1.015
1.011
1.007
0.998
0.994
0.990
0.980
0.975

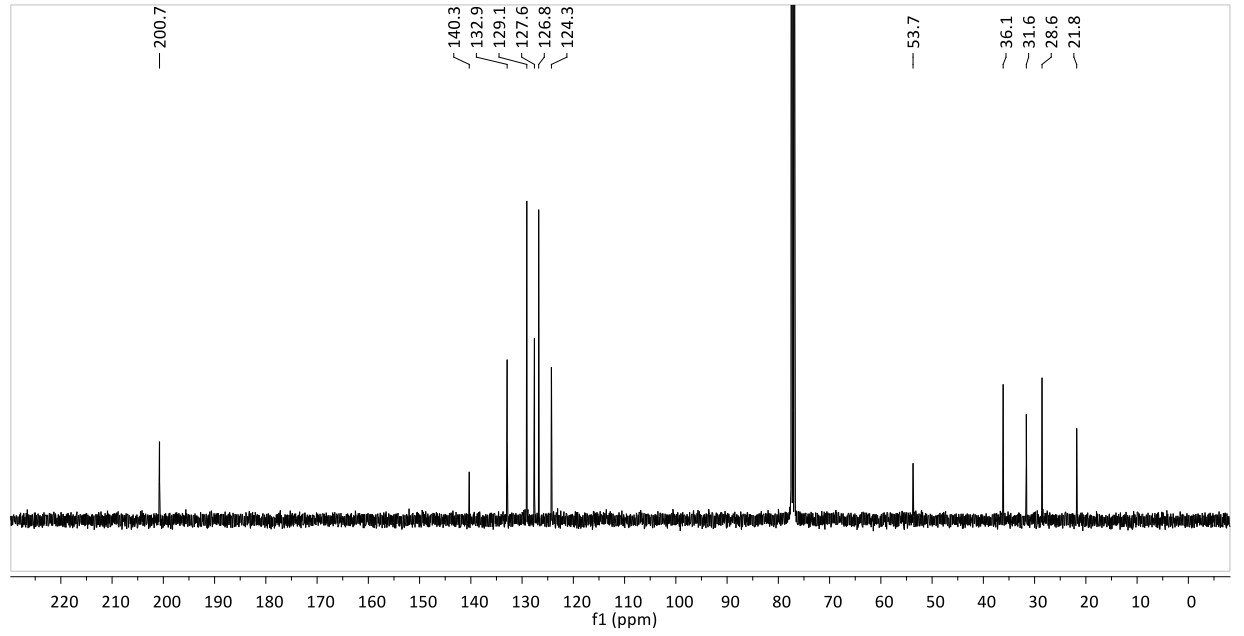

0.83
0.93
0.90
1.00
1.06
0.97
1.02
3.19
1.22
1.16
1.02
6.12
2.91
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


206.8
133.1
124.8
52.4
43.8
35.4
28.3
27.9
27.0
26.9
26.7
26.6
26.6
21.8
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

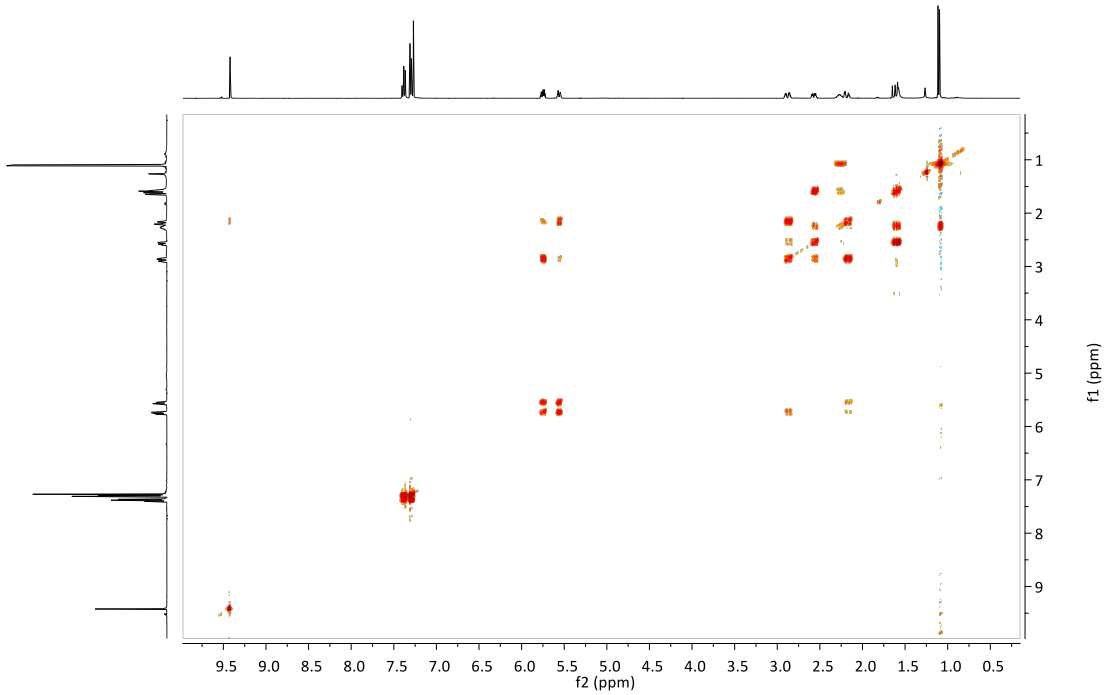

CHO
Me

( **4l** )

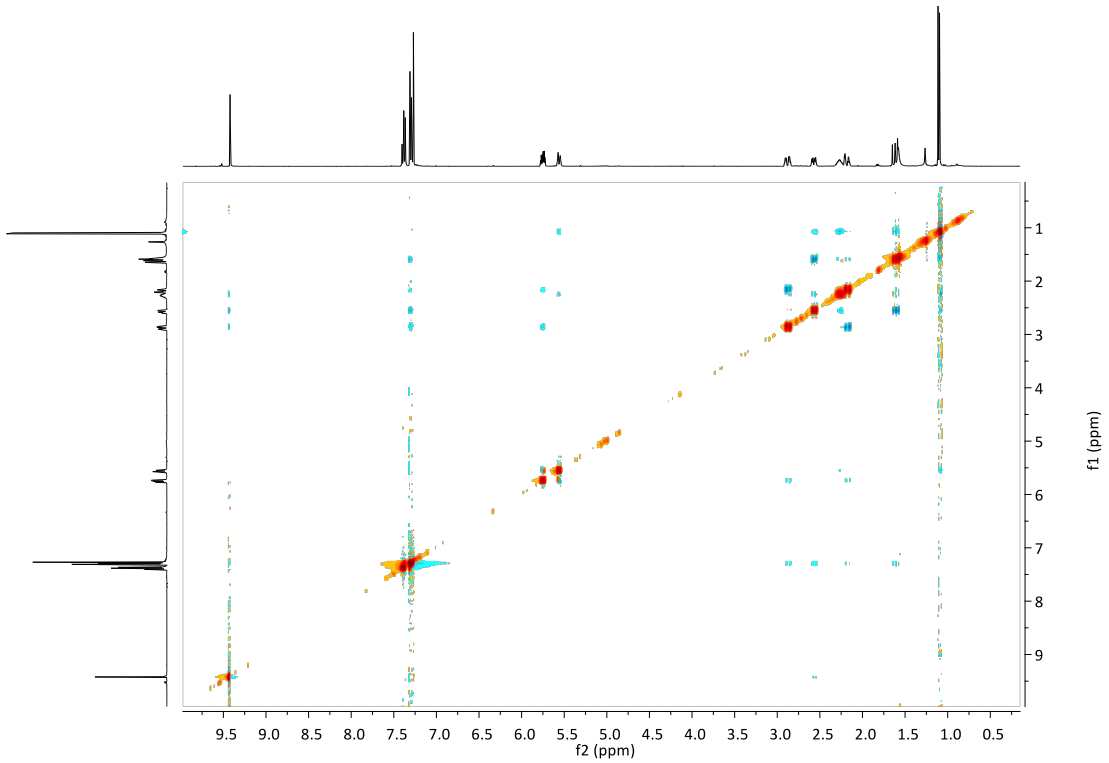

9.421
7.406
7.404
7.390
7.387
7.385
7.383
7.373
7.366
7.365
7.361
7.310
7.304
7.292
7.289
5.770
5.764
5.757
5.751
5.745
5.739
5.732
5.727
5.578
5.572
5.547
2.907
2.898
2.894
2.867
2.863
2.854
2.850
2.583
2.581
2.564
2.561
2.553
2.550
2.548
2.210
2.205
2.201
2.167
2.162
2.159
2.157
1.649
1.621
1.616
1.588
1.113
1.096
1.00
2.12
3.00
1.06
1.11
1.09
1.11
1.05
1.16
1.51
3.20
f1 (ppm)

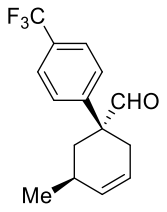

200.7
140.3
132.9
129.1
127.6
126.8
124.3
53.7
36.1
31.6
28.6
21.8
f1 (ppm)

COSY spectrum of **4l**

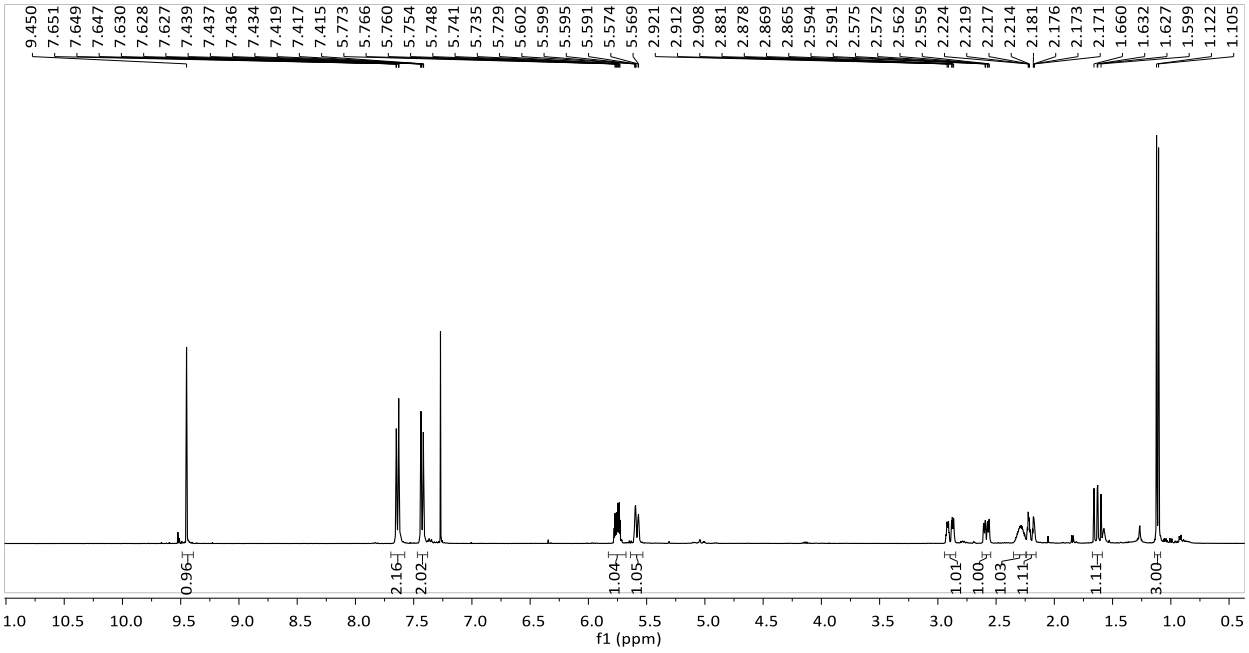


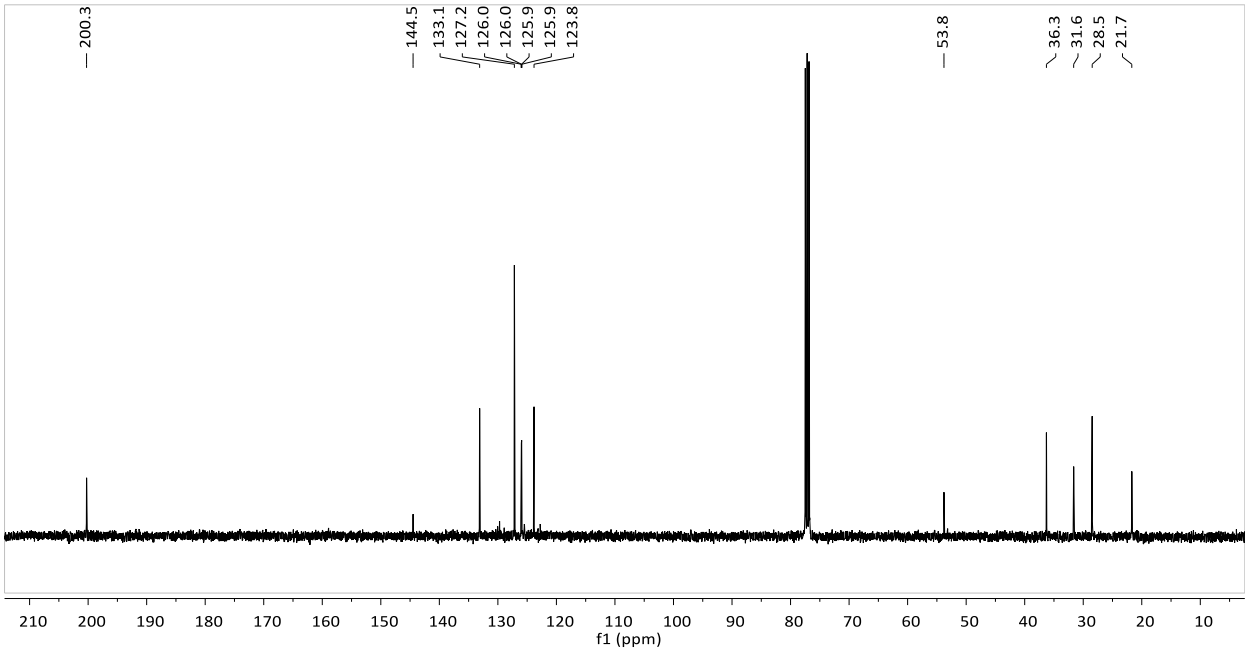

NOESY spectrum of **4l**

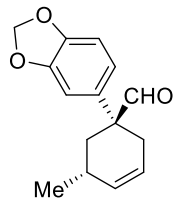



F3C
CHO
Me

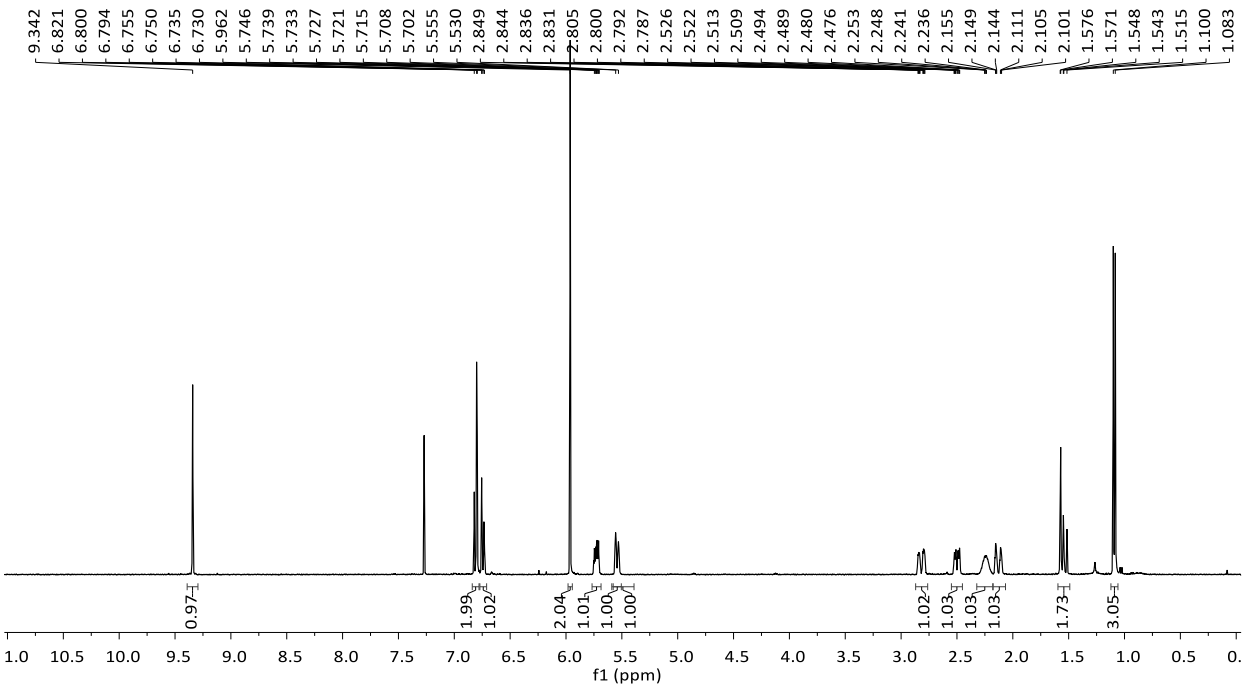
(**4m**)

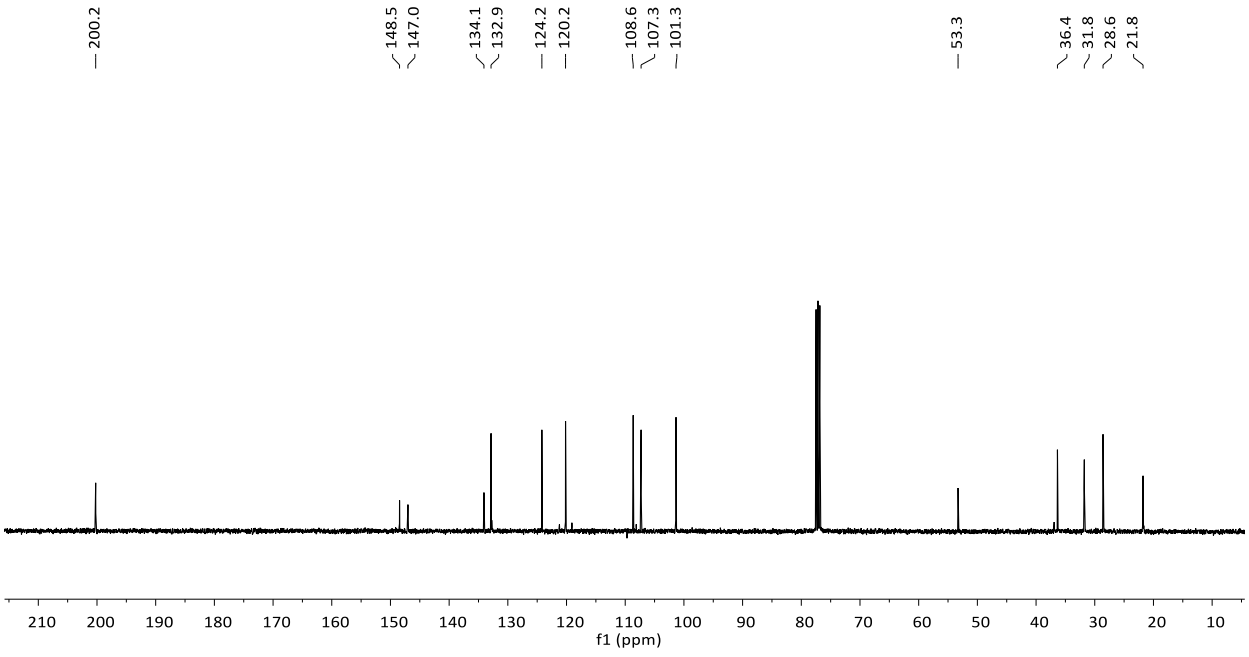

9.450
7.651
7.649
7.647
7.630
7.628
7.627
7.439
7.437
7.436
7.434
7.419
7.417
7.415
5.773
5.766
5.760
5.754
5.748
5.741
5.735
5.729
5.602
5.599
5.595
5.591
5.574
5.569
2.921
2.912
2.908
2.881
2.878
2.869
2.865
2.594
2.591
2.575
2.572
2.562
2.559
2.224
2.219
2.217
2.214
2.181
2.176
2.173
2.171
1.660
1.632
1.627
1.599
1.122
1.105
0.96
2.16
2.02
1.04
1.05
1.01
1.00
1.03
1.11
1.11
3.00
f1 (ppm)

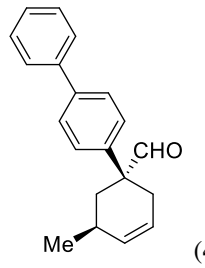

200.3
144.5
133.1
127.2
126.0
126.0
125.9
125.9
123.8
53.8
36.3
31.6
28.5
21.7
f1 (ppm)


O
O
CHO
Me

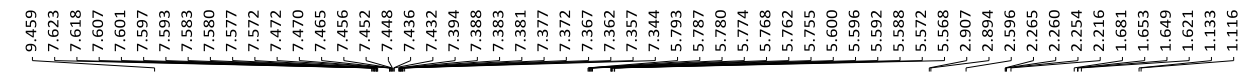
(**4n**)

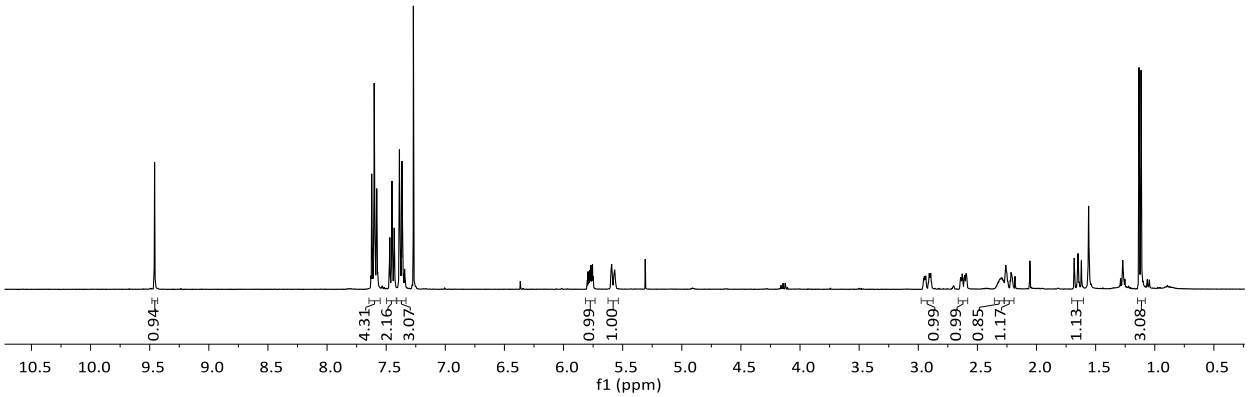

9.342
6.821
6.800
6.794
6.755
6.750
6.735
6.730
5.962
5.746
5.739
5.733
5.727
5.721
5.715
5.708
5.702
5.555
5.530
2.849
2.844
2.836
2.831
2.805
2.800
2.792
2.787
2.526
2.522
2.513
2.509
2.494
2.489
2.480
2.476
2.253
2.248
2.241
2.236
2.155
2.149
2.144
2.111
2.105
2.101
1.576
1.571
1.548
1.543
1.515
1.100
1.083
0.97
1.99
1.02
2.04
1.01
1.00
1.00
1.02
1.03
1.03
1.03
1.73
3.05
f1 (ppm)

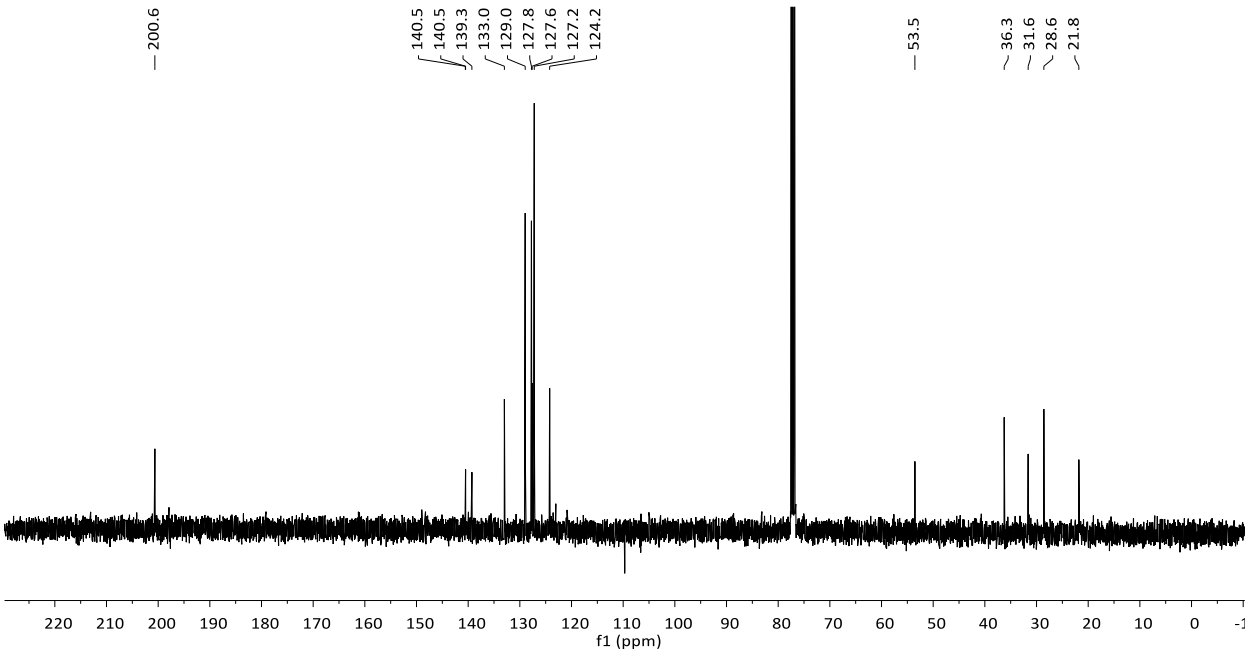

200.2
148.5
147.0
134.1
132.9
124.2
120.2
108.6
107.3
101.3
53.3
36.4
31.8
28.6
21.8
f1 (ppm)

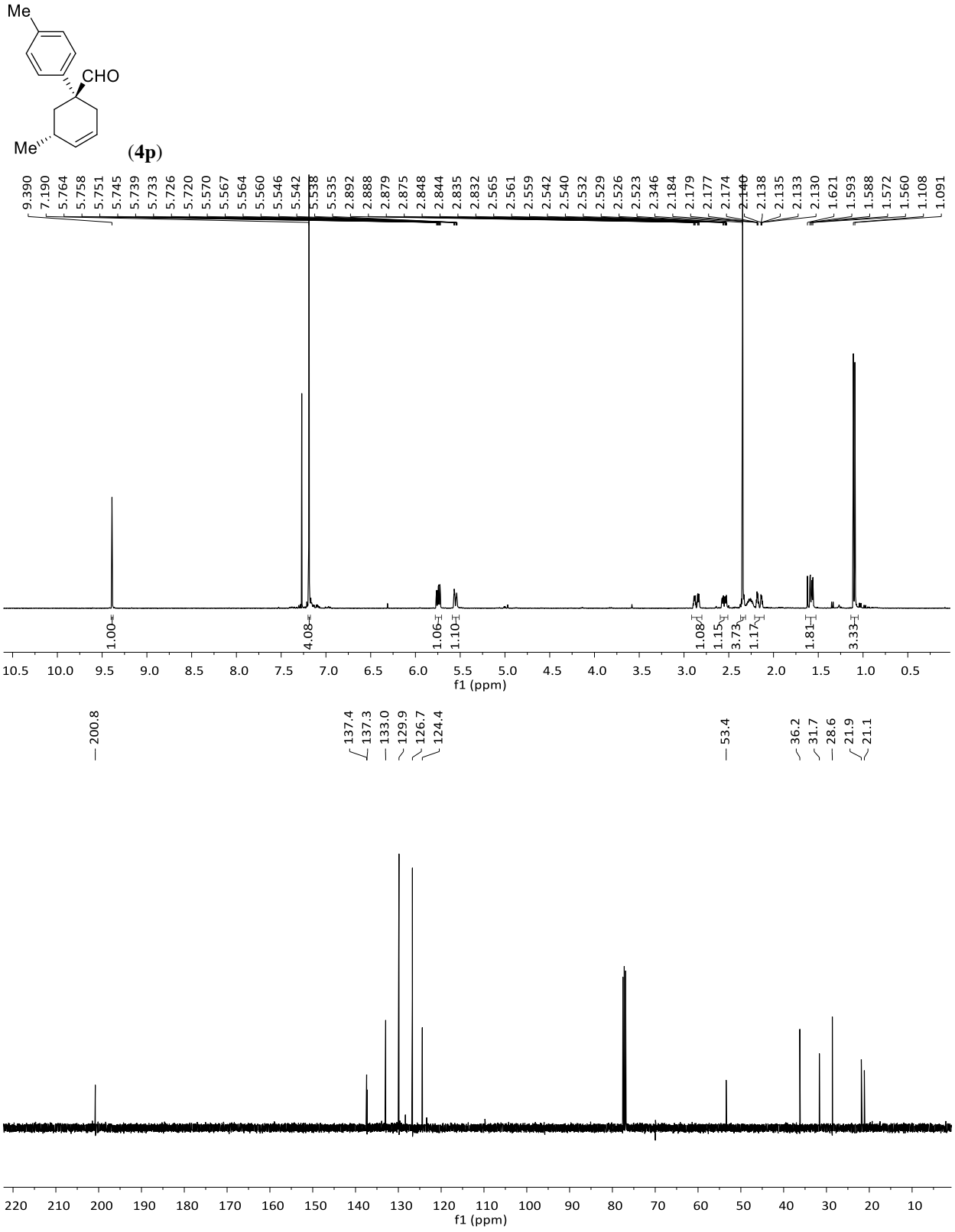

CHO
Me

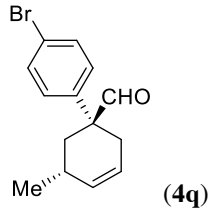
(**4o**)


9.459
7.623
7.618
7.607
7.601
7.597
7.593
7.583
7.580
7.577
7.572
7.472
7.470
7.465
7.456
7.452
7.448
7.436
7.432
7.394
7.388
7.383
7.381
7.377
7.372
7.367
7.362
7.357
7.344
5.793
5.787
5.780
5.774
5.768
5.762
5.755
5.600
5.596
5.592
5.588
5.572
5.568
2.907
2.894
2.596
2.265
2.260
2.254
2.216
1.681
1.653
1.649
1.621
1.133
1.116

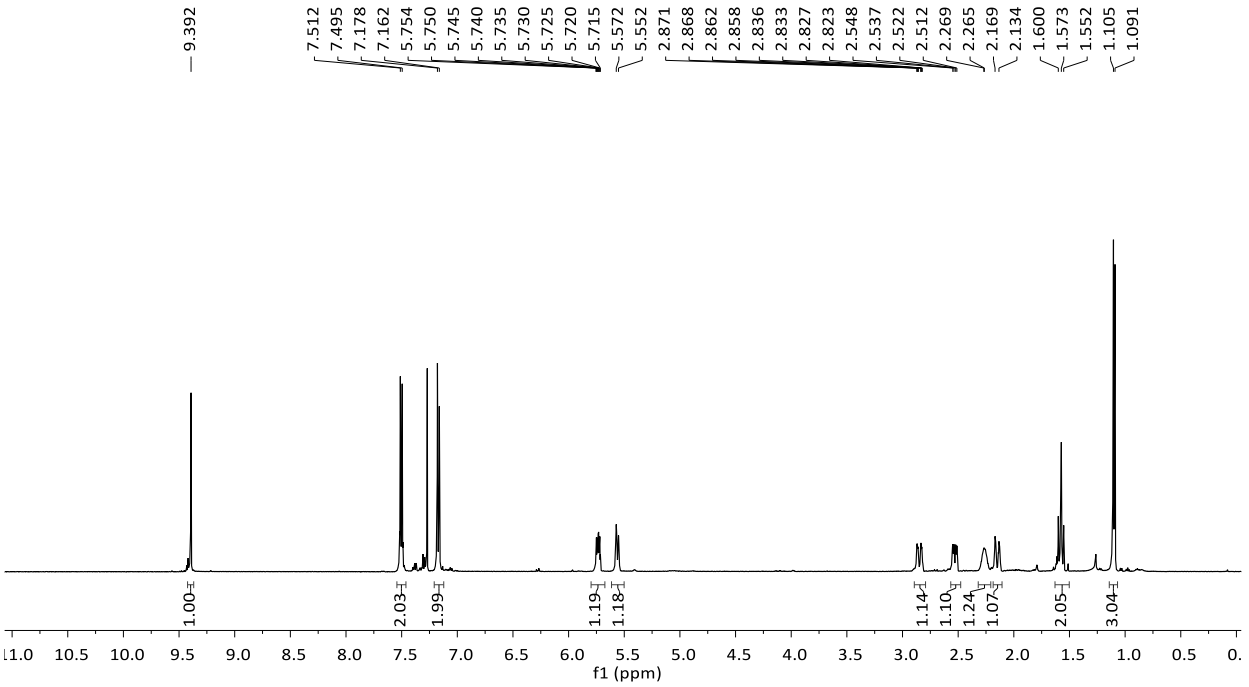

0.94
4.31
2.16
3.07
0.99
1.00
0.99
0.99
0.85
1.17
1.13
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

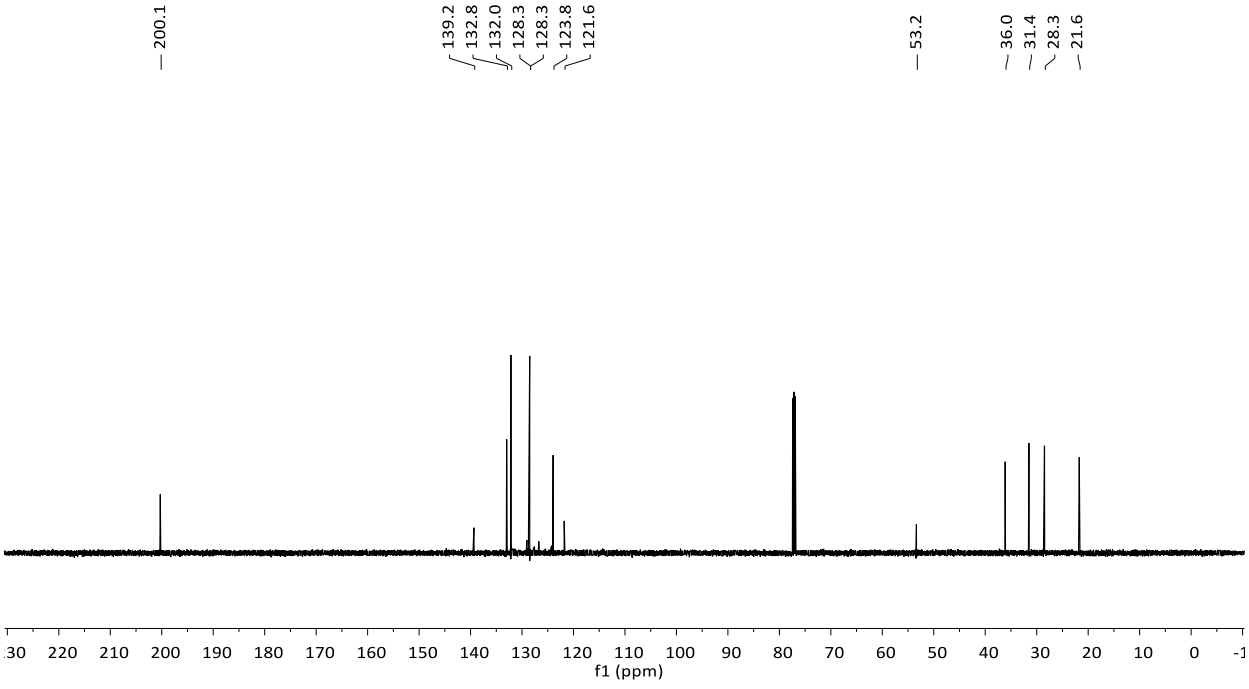

200.6
140.5
140.5
139.3
133.0
129.0
127.8
127.6
127.2
124.2
53.5
36.3
31.6
28.6
21.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

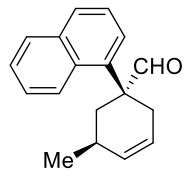

Me
CHO
Me
(4p)
9.390
7.190
5.764
5.758
5.751
5.745
5.739
5.733
5.726
5.720
5.570
5.567
5.564
5.560
5.546
5.542
5.538
5.535
2.892
2.888
2.879
2.875
2.848
2.844
2.835
2.832
2.565
2.561
2.559
2.542
2.540
2.532
2.529
2.526
2.523
2.346
2.184
2.179
2.177
2.174
2.140
2.138
2.135
2.133
2.130
1.621
1.593
1.588
1.572
1.560
1.108
1.091
1.00
4.08
1.06
1.10
1.08
1.15
3.73
1.17
1.81
3.33
f1 (ppm)
200.8
137.4
137.3
133.0
129.9
126.7
124.4
53.4
36.2
31.7
28.6
21.9
21.1
f1 (ppm)


Br
CHO
Me

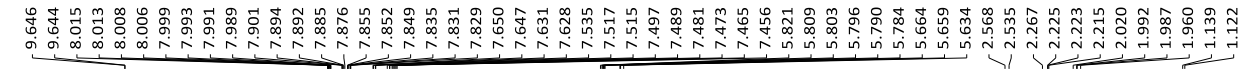
(**4q**)

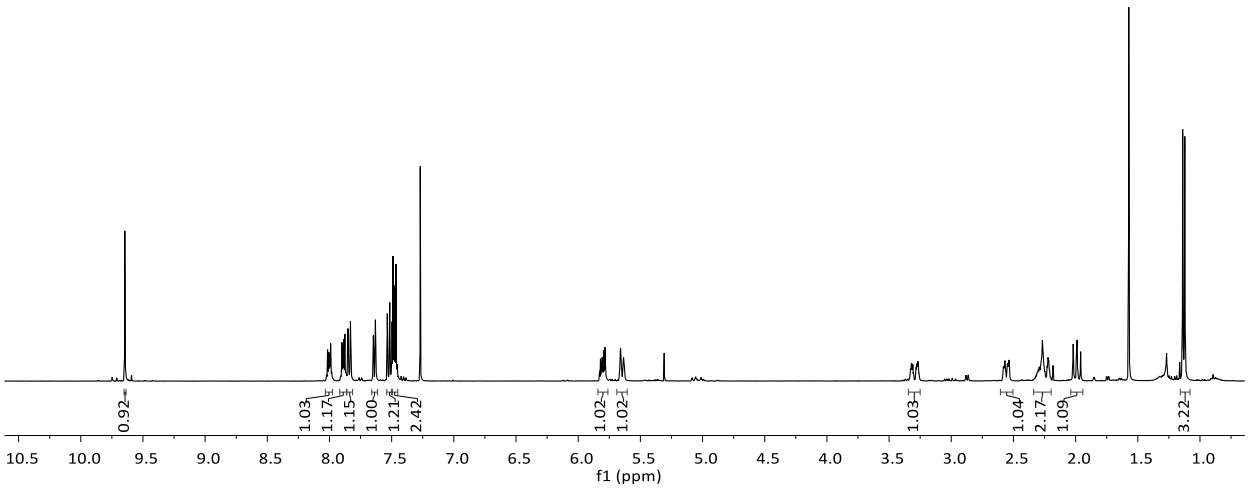

9.392
7.512
7.495
7.178
7.162
5.754
5.750
5.745
5.740
5.735
5.730
5.725
5.720
5.715
5.572
5.552
2.871
2.868
2.862
2.858
2.836
2.833
2.827
2.823
2.548
2.537
2.522
2.512
2.269
2.265
2.169
2.134
1.600
1.573
1.552
1.105
1.091
1.00
2.03
1.99
1.19
1.18
1.14
1.10
1.24
1.07
2.05
3.04
f1 (ppm)

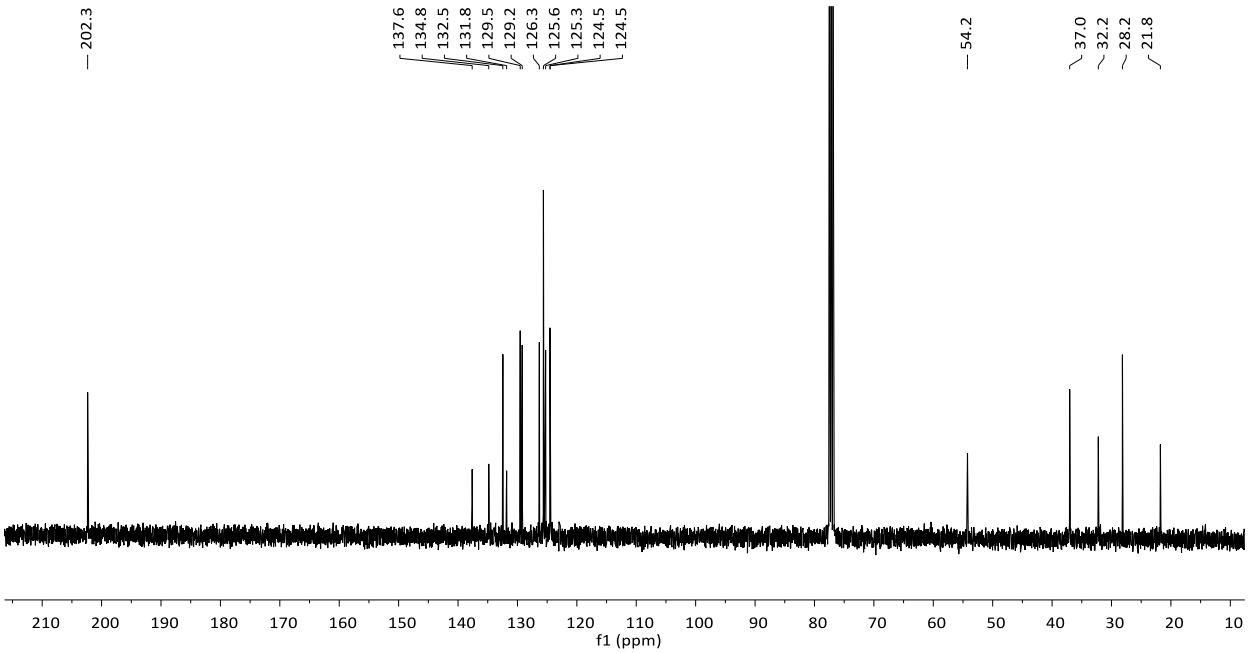

200.1
139.2
132.8
132.0
128.3
128.3
123.8
121.6
53.2
36.0
31.4
28.3
21.6
f1 (ppm)

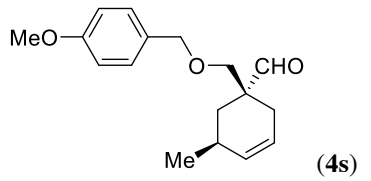

CHO
Me

(**4r**)

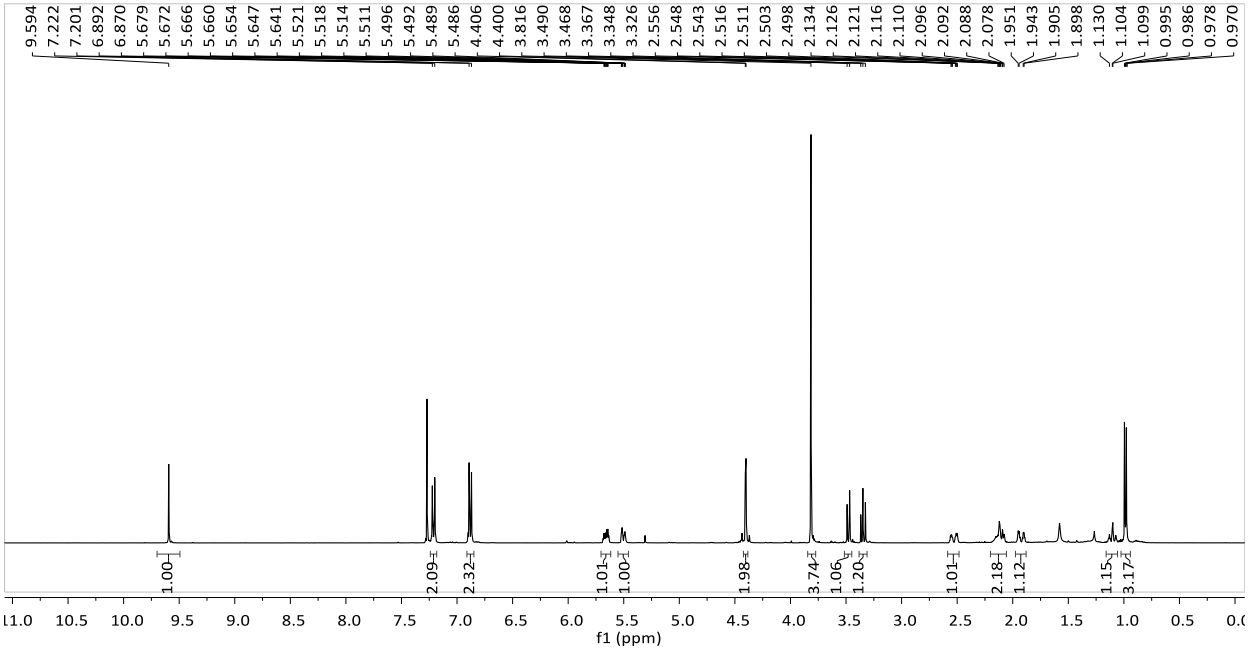

9.646
9.644
8.015
8.013
8.008
8.006
7.999
7.993
7.991
7.989
7.901
7.894
7.892
7.885
7.876
7.855
7.852
7.849
7.835
7.831
7.829
7.650
7.647
7.631
7.628
7.535
7.517
7.515
7.497
7.489
7.481
7.473
7.465
7.456
5.821
5.809
5.803
5.796
5.790
5.784
5.664
5.659
5.634
2.568
2.535
2.267
2.225
2.223
2.215
2.020
1.992
1.987
1.960
1.139
1.122

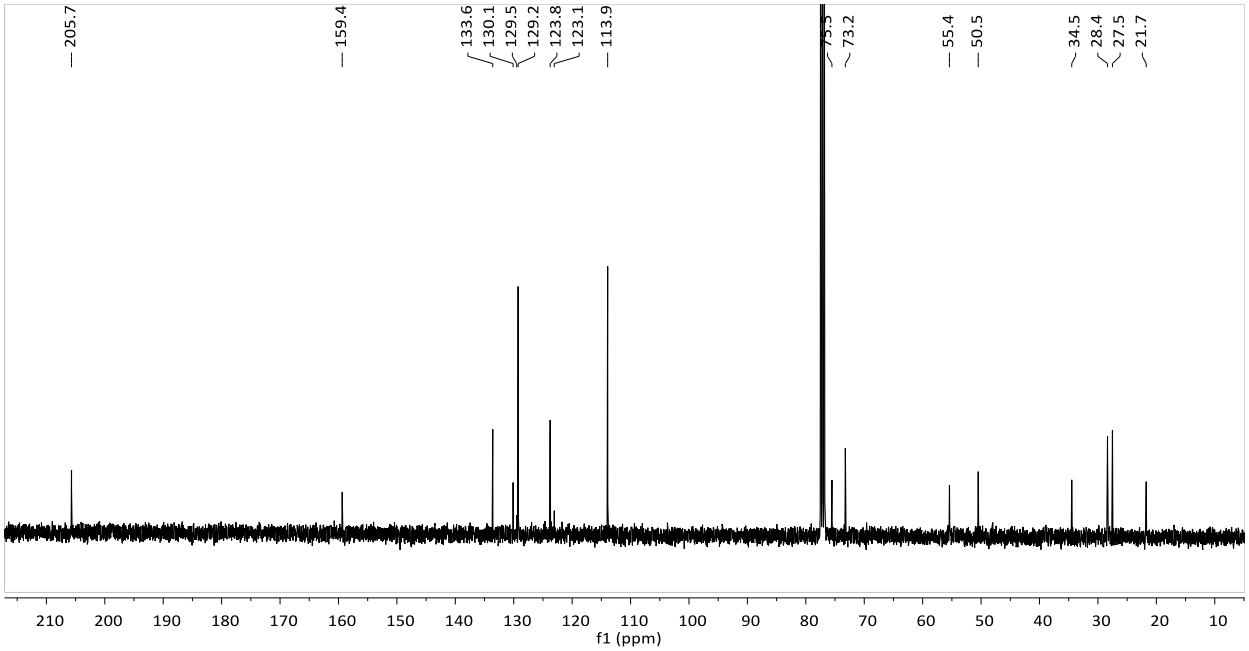

0.92
1.03
1.17
1.15
1.00
1.21
2.42
1.02
1.02
1.03
1.04
2.17
1.09
3.22
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

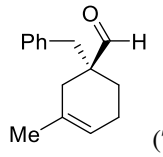

202.3
137.6
134.8
132.5
131.8
129.5
129.2
126.3
125.6
125.3
124.5
124.5
54.2
37.0
32.2
28.2
21.8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


MeO
O
CHO
Me

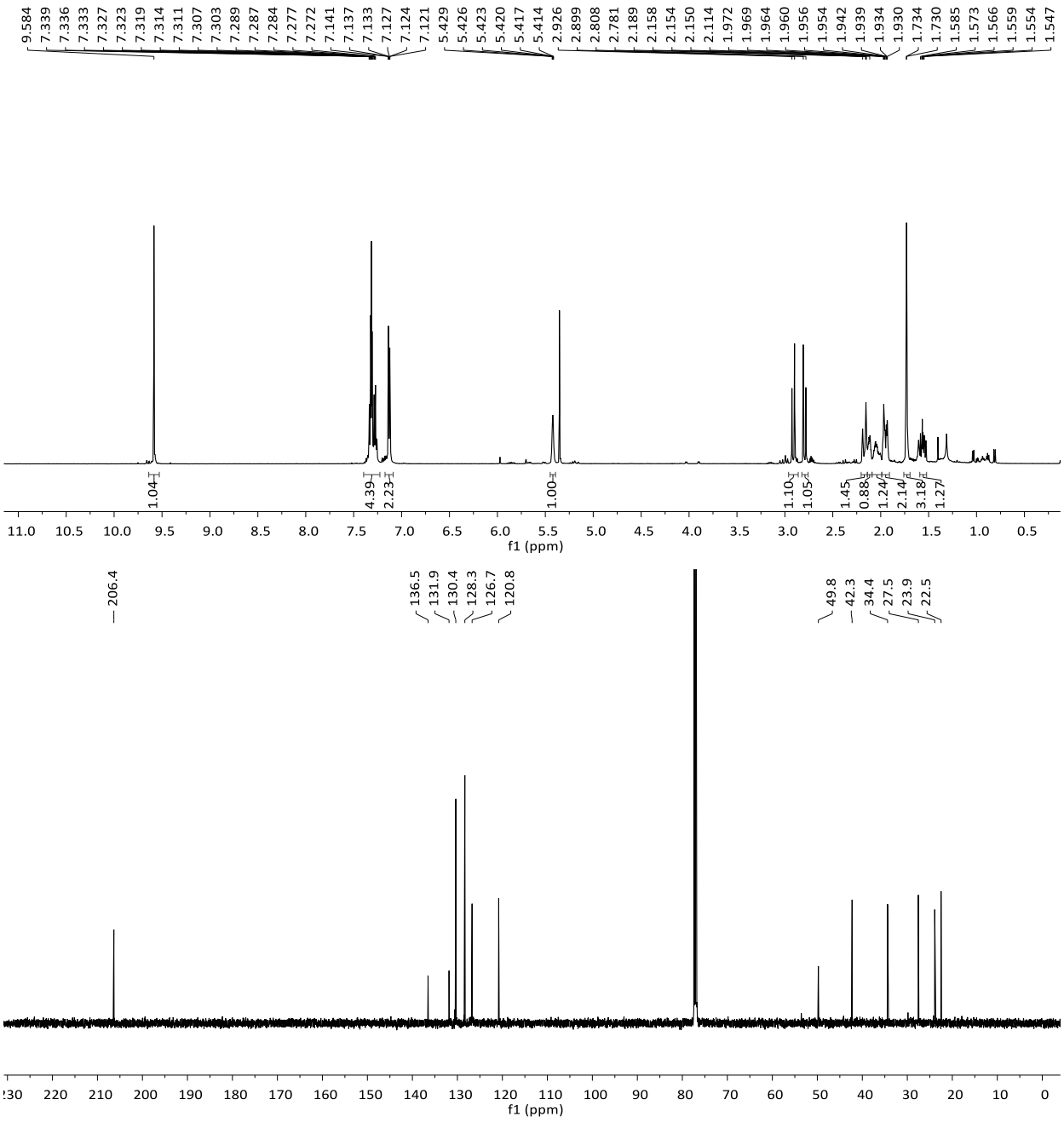
(**4s**)

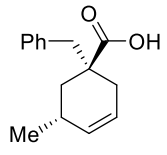

9.594
7.222
7.201
6.892
6.870
5.679
5.672
5.666
5.660
5.654
5.647
5.641
5.521
5.518
5.514
5.511
5.496
5.492
5.489
5.486
4.406
4.400
3.816
3.490
3.468
3.367
3.348
3.326
2.556
2.548
2.543
2.516
2.511
2.503
2.498
2.134
2.126
2.121
2.116
2.110
2.096
2.092
2.088
2.078
1.951
1.943
1.905
1.898
1.130
1.104
1.099
0.995
0.986
0.978
0.970
1.00
2.09
2.32
1.01
1.00
1.98
3.74
1.06
1.20
1.01
2.18
1.12
1.15
3.17
f1 (ppm)


205.7
159.4
133.6
130.1
129.5
129.2
123.8
123.1
113.9
73.5
73.2
55.4
50.5
34.5
28.4
27.5
21.7
f1 (ppm)

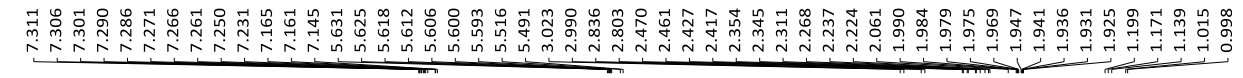

O
Ph
H
Me

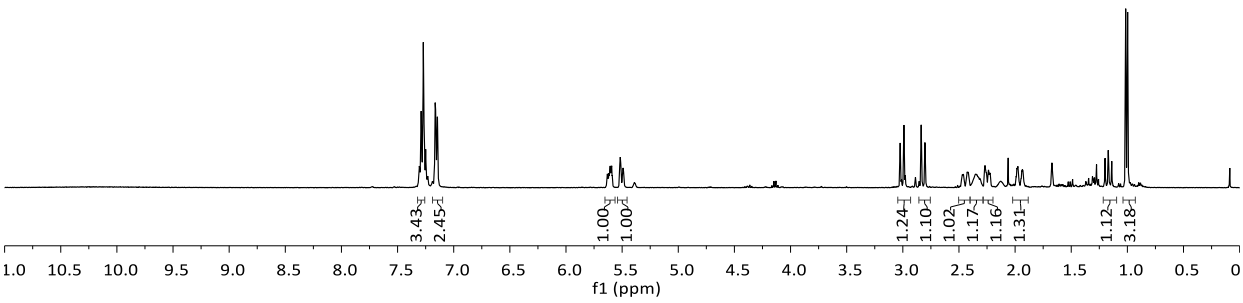
(**7a**)

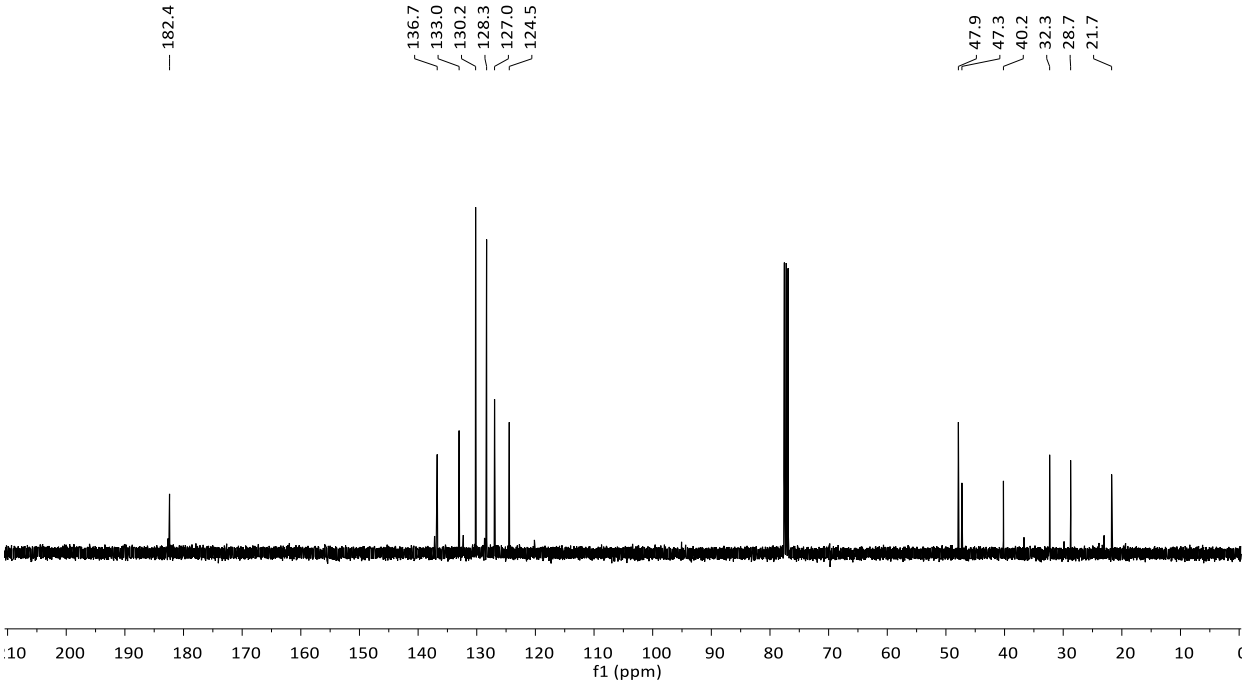

9.584
7.339
7.336
7.333
7.327
7.323
7.319
7.314
7.311
7.307
7.303
7.289
7.287
7.284
7.277
7.272
7.141
7.137
7.133
7.127
7.124
7.121
5.429
5.426
5.423
5.420
5.417
5.414
2.926
2.899
2.808
2.781
2.189
2.158
2.154
2.150
2.114
1.972
1.969
1.964
1.960
1.956
1.954
1.942
1.939
1.934
1.930
1.734
1.730
1.585
1.573
1.566
1.559
1.554
1.547
1.04
4.39
2.23
1.00
1.10
1.05
1.45
0.88
1.24
2.14
3.18
1.27
f1 (ppm)
206.4
136.5
131.9
130.4
128.3
126.7
120.8
49.8
42.3
34.4
27.5
23.9
22.5
f1 (ppm)

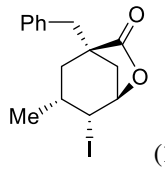

O
Ph
OH
Me

(**10**)

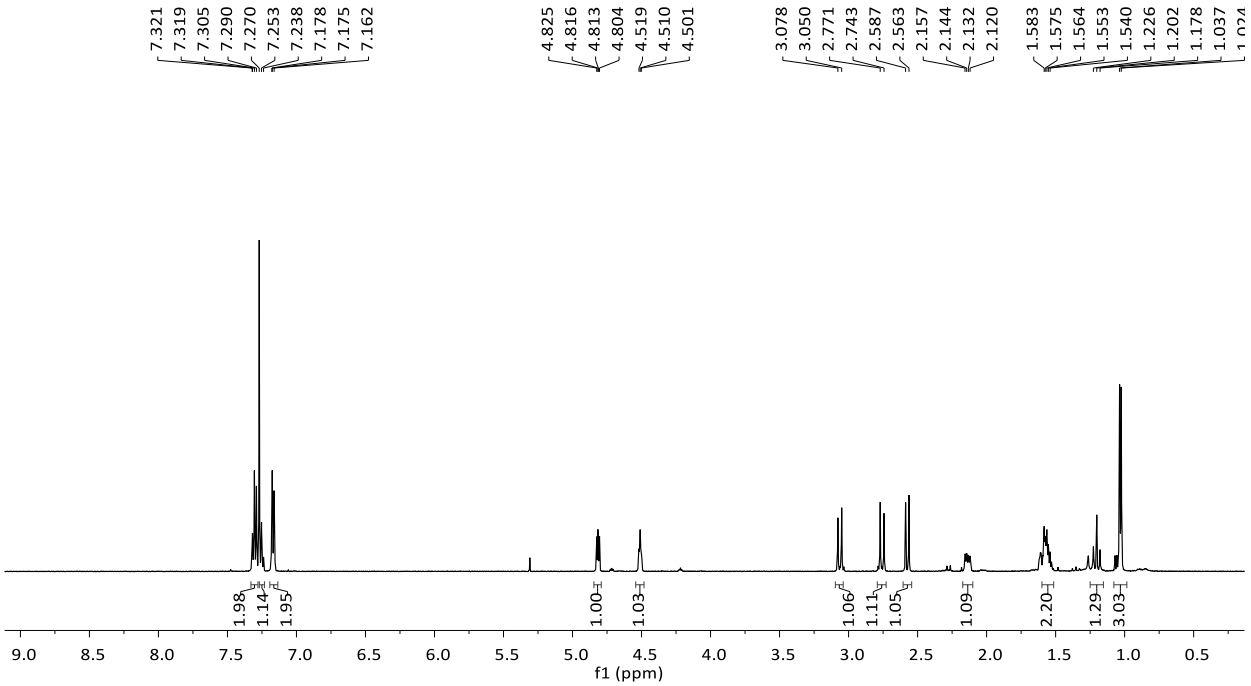

7.311
7.306
7.301
7.290
7.286
7.271
7.266
7.261
7.250
7.231
7.165
7.161
7.145
5.631
5.625
5.618
5.612
5.606
5.600
5.593
5.516
5.491
3.023
2.990
2.836
2.803
2.470
2.461
2.427
2.417
2.354
2.345
2.311
2.268
2.237
2.224
2.061
1.990
1.984
1.979
1.975
1.969
1.947
1.941
1.936
1.931
1.925
1.199
1.171
1.139
1.015
0.998

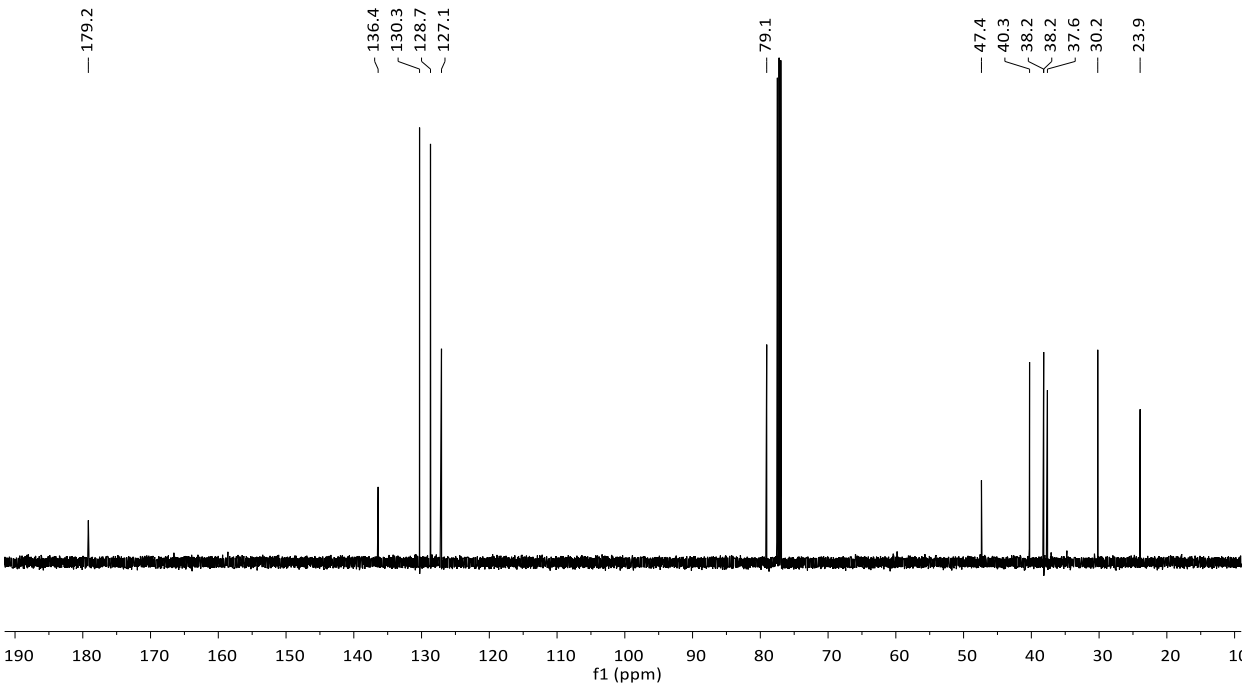

3.43
2.45
1.00
1.00
1.24
1.10
1.02
1.17
1.16
1.31
1.12
3.18
f1 (ppm)

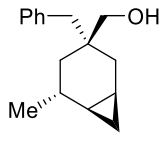

182.4
136.7
133.0
130.2
128.3
127.0
124.5
47.9
47.3
40.2
32.3
28.7
21.7
f1 (ppm)


Ph
O
O
Me
I

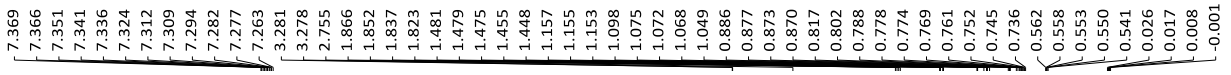
(**11**)

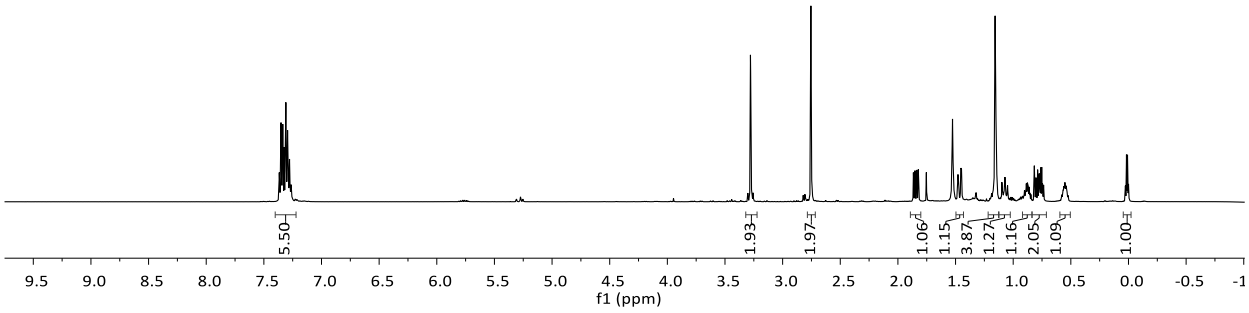

7.321
7.319
7.305
7.290
7.270
7.253
7.238
7.178
7.175
7.162
4.825
4.816
4.813
4.804
4.519
4.510
4.501
3.078
3.050
2.771
2.743
2.587
2.563
2.157
2.144
2.132
2.120
1.583
1.575
1.564
1.553
1.540
1.226
1.202
1.178
1.037
1.98
1.14
1.95
1.00
1.03
1.06
1.11
1.05
1.09
2.20
1.29
3.03
f1 (ppm)

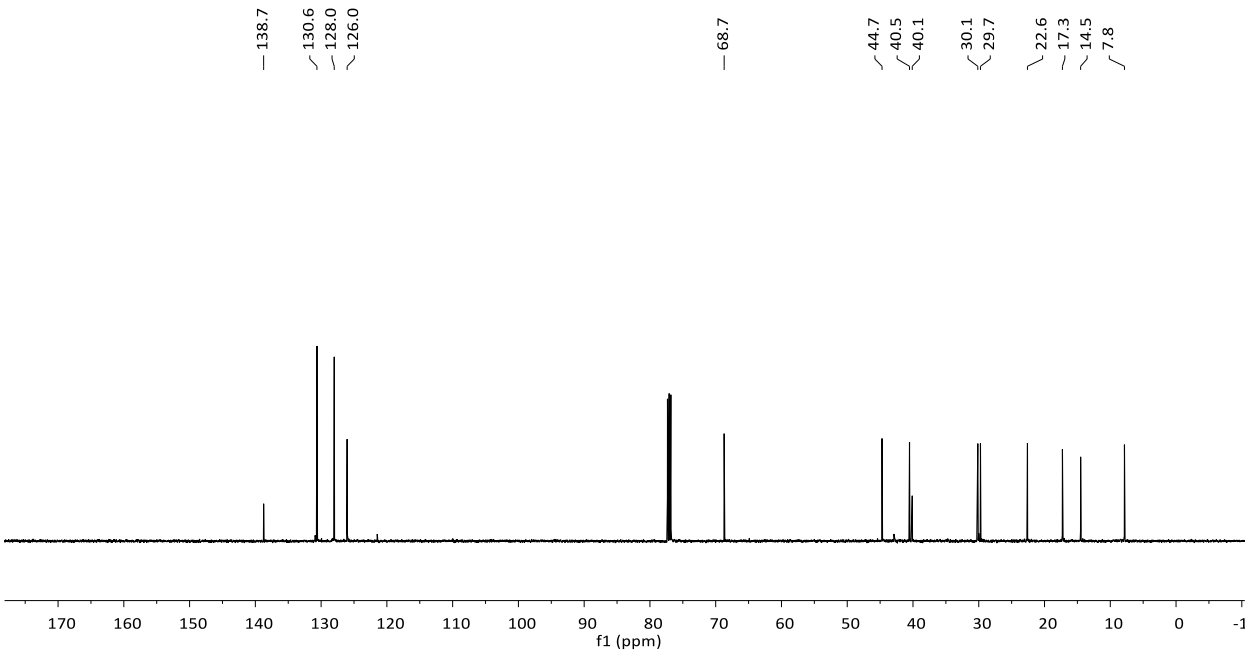

179.2
136.4
130.3
128.7
127.1
79.1
47.4
40.3
38.2
38.2
37.6
30.2
23.9
f1 (ppm)

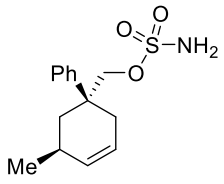

Ph
OH
Me

(**12**)

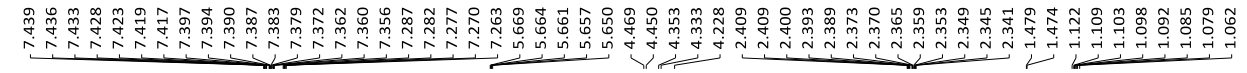

7.369
7.366
7.351
7.341
7.336
7.324
7.312
7.309
7.294
7.282
7.277
7.263
3.281
3.278
2.755
1.866
1.852
1.837
1.823
1.481
1.479
1.475
1.455
1.448
1.157
1.155
1.153
1.098
1.075
1.072
1.068
1.049
0.886
0.877
0.873
0.870
0.817
0.802
0.788
0.778
0.774
0.769
0.761
0.752
0.745
0.736
0.562
0.558
0.553
0.550
0.541
0.026
0.017
0.008
-0.001

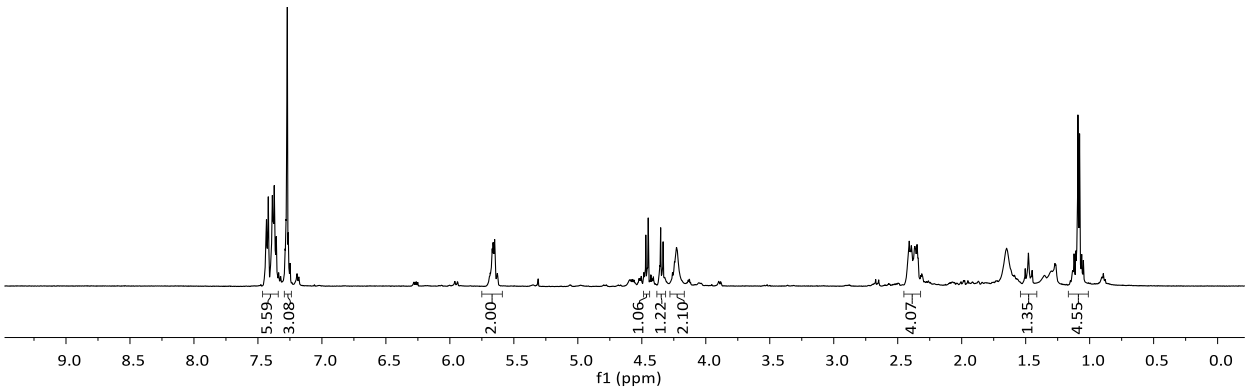

5.50
1.93
1.97
1.06
1.15
3.87
1.27
1.16
2.05
1.09
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

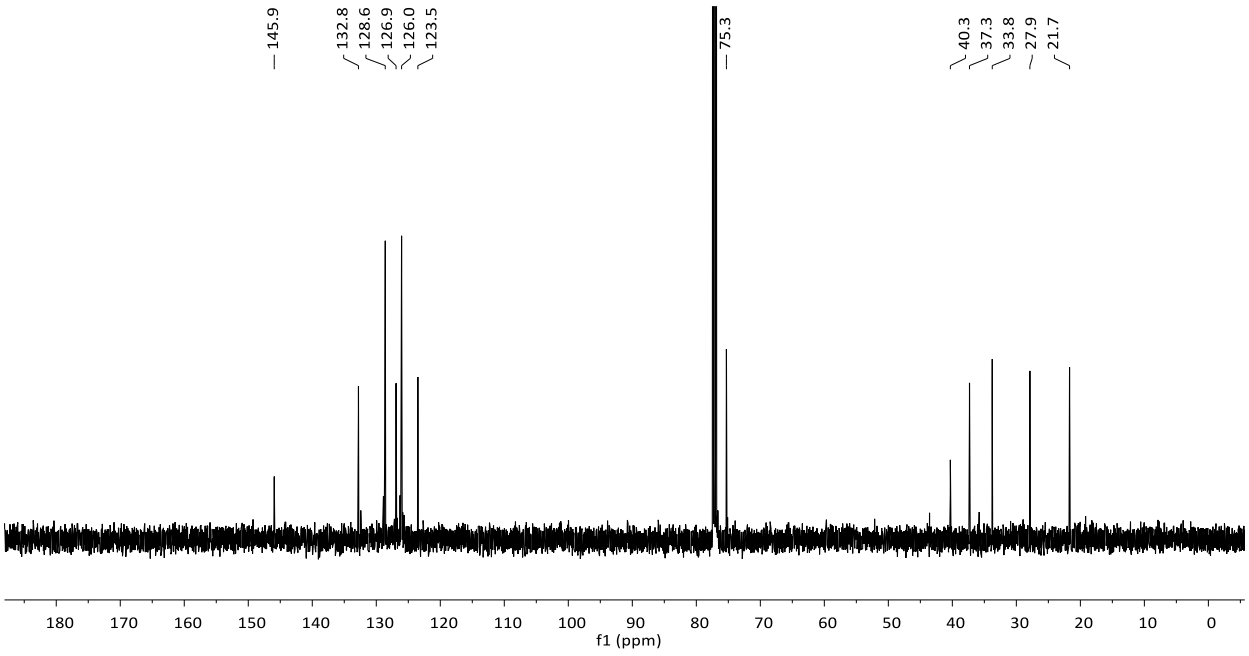

138.7
130.6
128.0
126.0
68.7
44.7
40.5
40.1
30.1
29.7
22.6
17.3
14.5
7.8
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

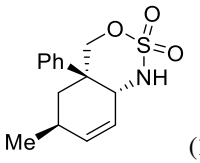

O
O
S
NH2
Ph
O
Me

(**14**)

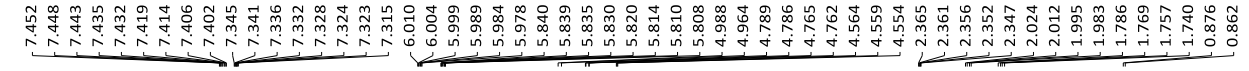

7.439
7.436
7.433
7.428
7.423
7.419
7.417
7.397
7.394
7.390
7.387
7.383
7.379
7.372
7.362
7.360
7.356
7.287
7.282
7.277
7.270
7.263
5.669
5.664
5.661
5.657
5.650
4.469
4.450
4.353
4.333
4.228
2.409
2.409
2.400
2.393
2.389
2.373
2.370
2.365
2.359
2.353
2.349
2.345
2.341
1.479
1.474
1.122
1.109
1.103
1.098
1.092
1.085
1.079
1.062

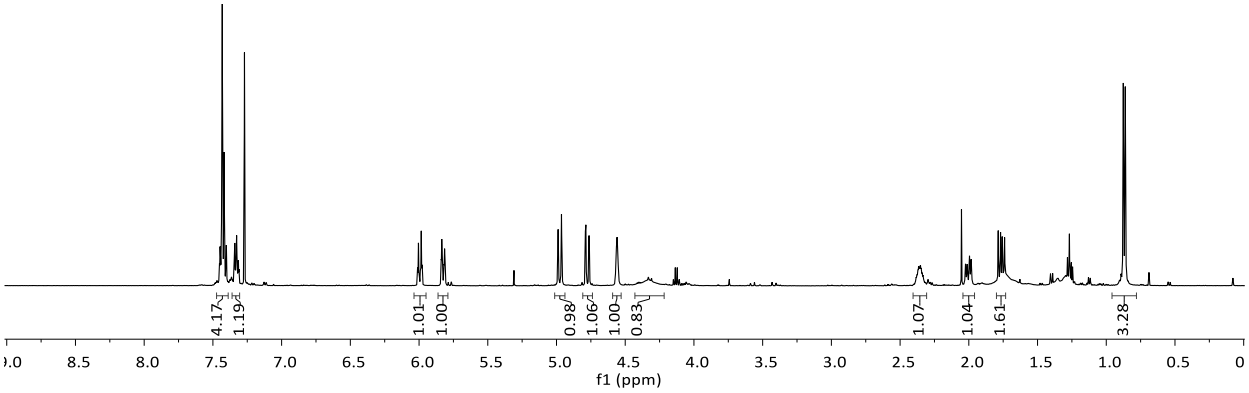

5.59
3.08
2.00
1.06
1.22
2.10
4.07
1.35
4.55
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

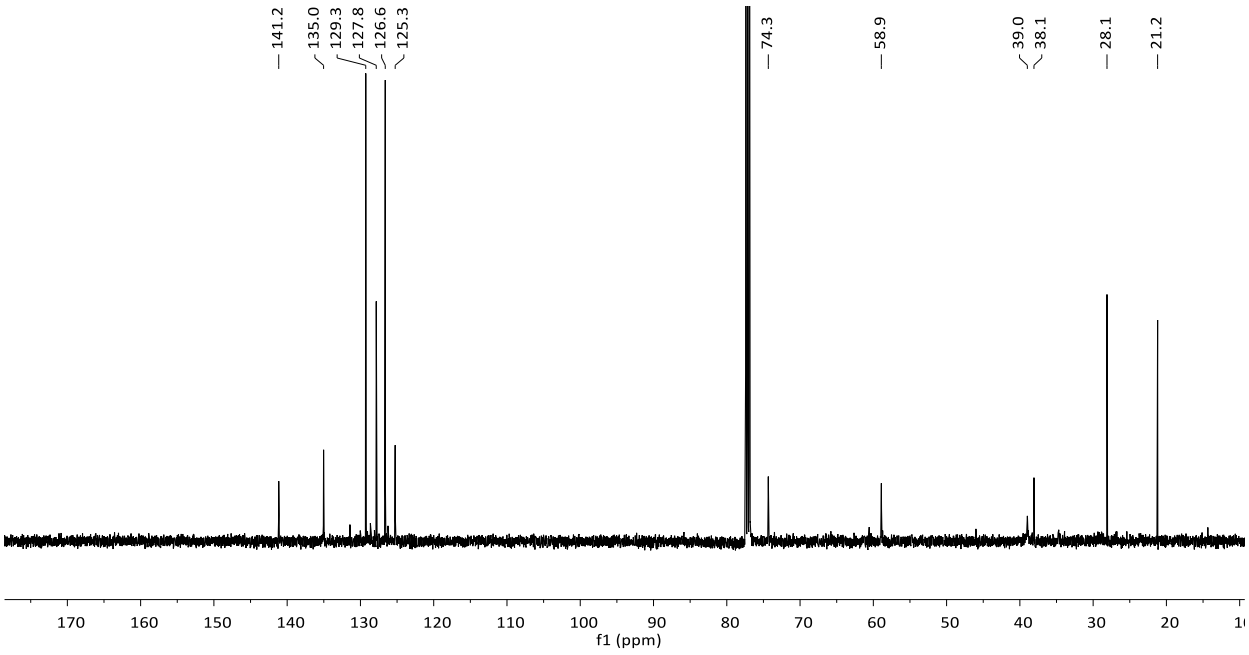

145.9
132.8
128.6
126.9
126.0
123.5
75.3
40.3
37.3
33.8
27.9
21.7
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
S
O
Ph
NH
Me

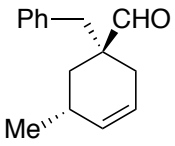
(**15**)


7.452
7.448
7.443
7.435
7.432
7.419
7.414
7.406
7.402
7.345
7.341
7.336
7.332
7.328
7.324
7.323
7.315
6.010
6.004
5.999
5.989
5.984
5.978
5.840
5.839
5.835
5.830
5.820
5.814
5.810
5.808
4.988
4.964
4.789
4.786
4.765
4.762
4.564
4.559
4.554
2.365
2.361
2.356
2.352
2.347
2.024
2.012
1.995
1.983
1.786
1.769
1.757
1.740
0.876
0.862

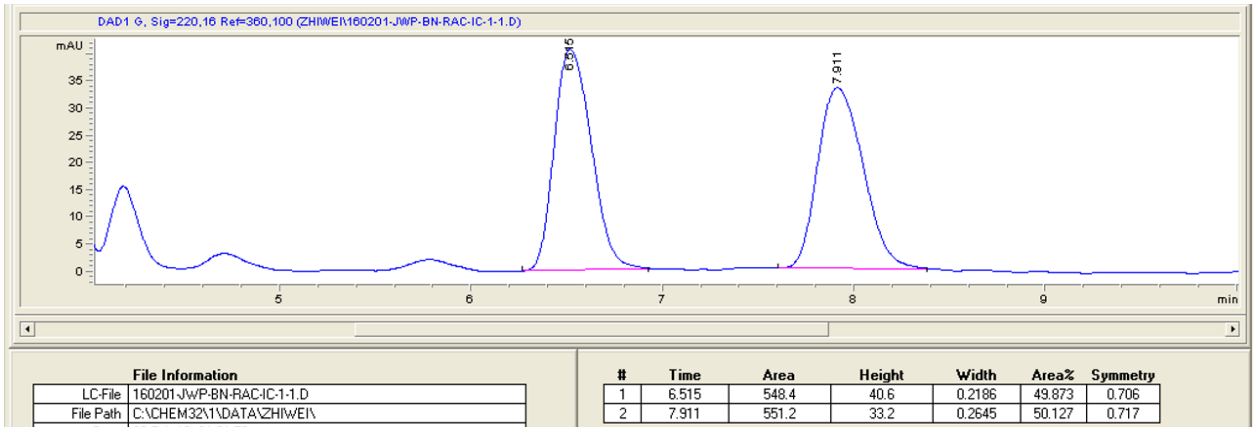

4.17
1.19
1.01
1.00
0.98
1.06
1.00
0.83
1.07
1.04
1.61
3.28
f1 (ppm)


141.2
135.0
129.3
127.8
126.6
125.3
74.3
58.9
39.0
38.1
28.1
21.2
f1 (ppm)

## 8. Chiral SFC Analysis

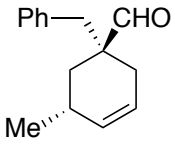



(±)-**4a**

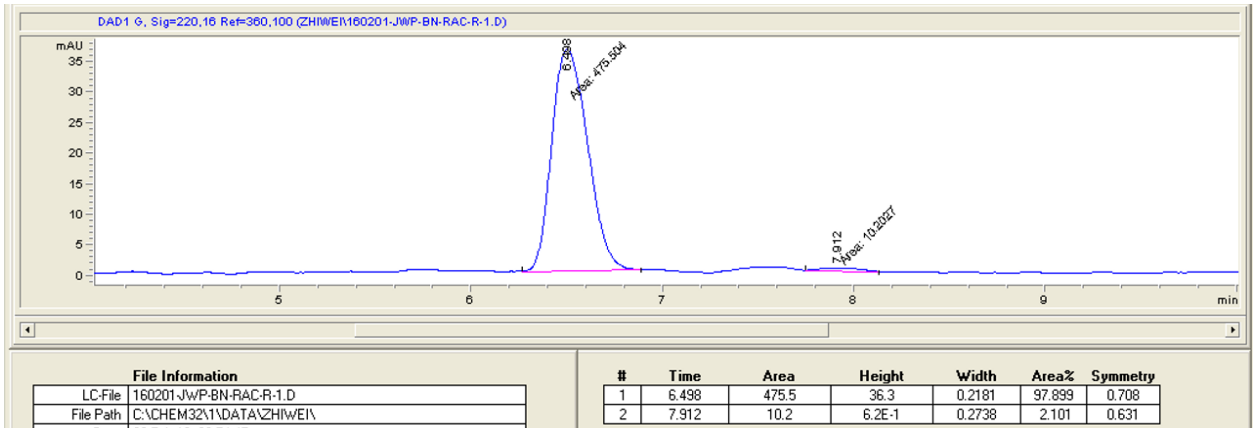



| File Information | |
|---|---|
| LC-File | 160201JWP-BN-RAC-IC-1-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.515 | 548.4 | 40.6 | 0.2186 | 49.873 | 0.706 |
| 2 | 7.911 | 551.2 | 33.2 | 0.2645 | 50.127 | 0.717 |

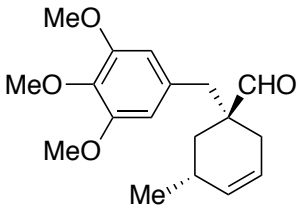



(+)-**4a**

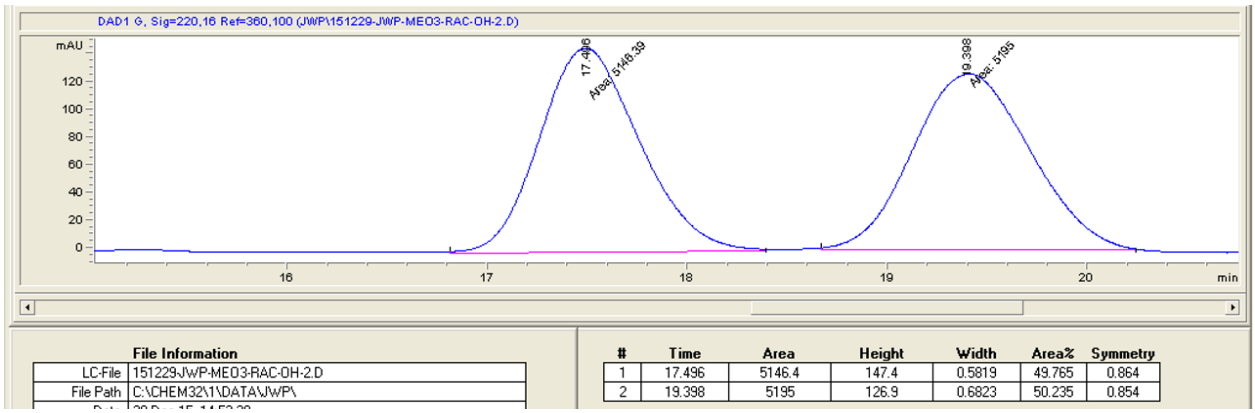



| File Information | |
|---|---|
| LC-File | 160201JWP-BN-RAC-R-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.498 | 475.5 | 36.3 | 0.2181 | 97.899 | 0.708 |
| 2 | 7.912 | 10.2 | 6.2E-1 | 0.2738 | 2.101 | 0.631 |



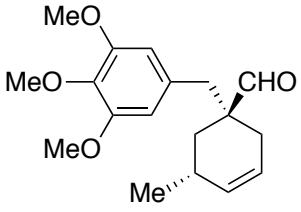

(±)-**4b**



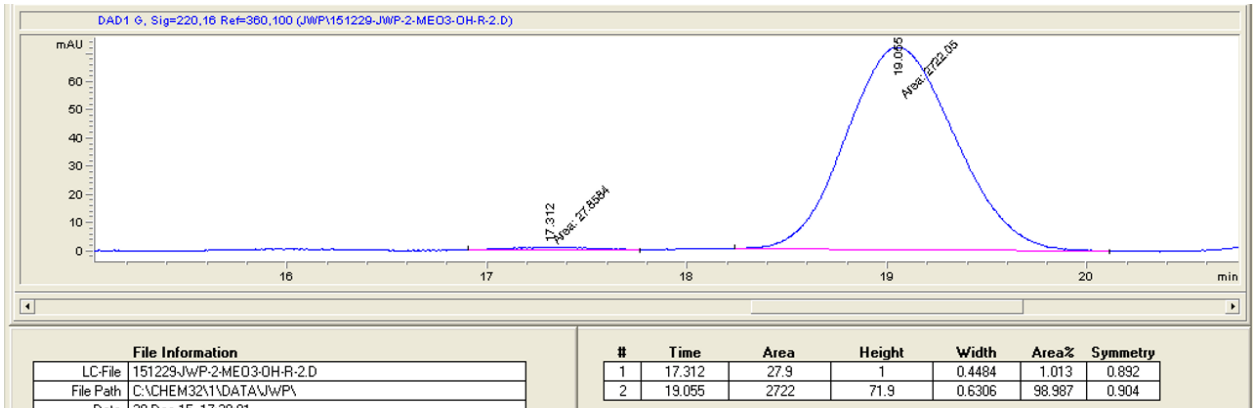

**File Information**

| | |
|---|---|
| LC-File | 151229-JWP-MEO3-RAC-OH-2.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 17.496 | 5146.4 | 147.4 | 0.5819 | 49.765 | 0.864 |
| 2 | 19.398 | 5195 | 126.9 | 0.6823 | 50.235 | 0.854 |



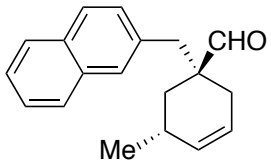

(–)-**4b**



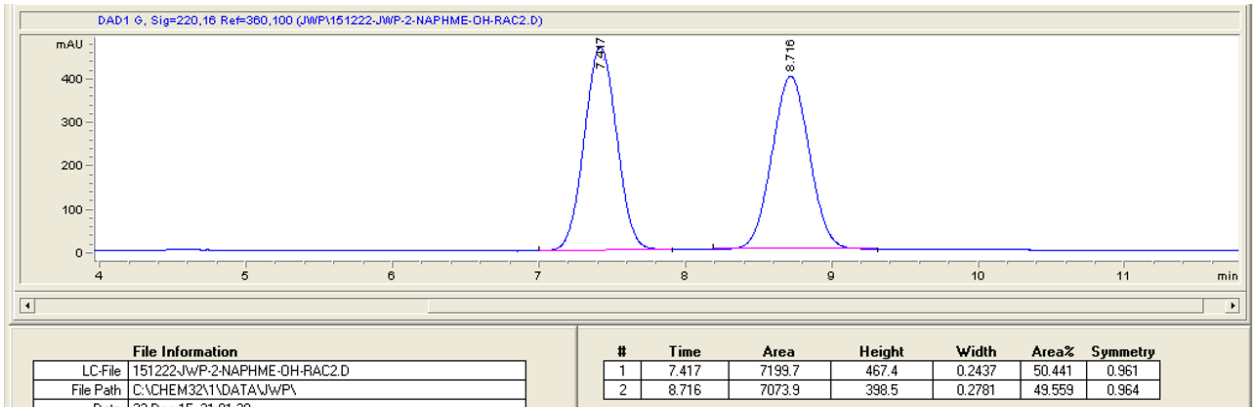

**File Information**

| | |
|---|---|
| LC-File | 151229-JWP-2-MEO3-OH-R-2.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 17.312 | 27.9 | 1 | 0.4484 | 1.013 | 0.892 |
| 2 | 19.055 | 2722 | 71.9 | 0.6306 | 98.987 | 0.904 |

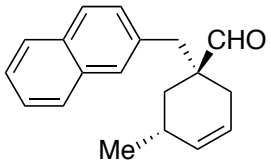



(±)-**4c**

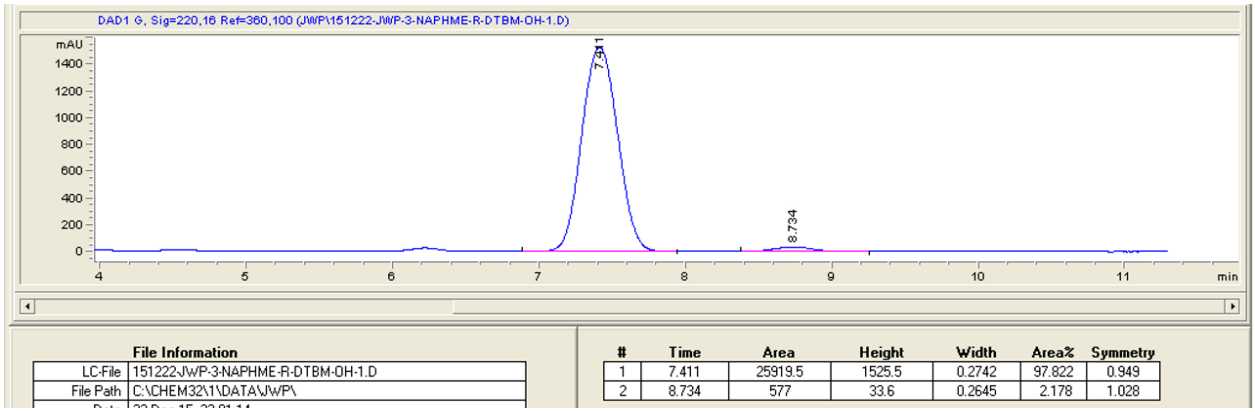



| File Information | |
|---|---|
| LC-File | 151222-JWP-2-NAPHME-OH-RAC2.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.417 | 7199.7 | 467.4 | 0.2437 | 50.441 | 0.961 |
| 2 | 8.716 | 7073.9 | 398.5 | 0.2781 | 49.559 | 0.964 |

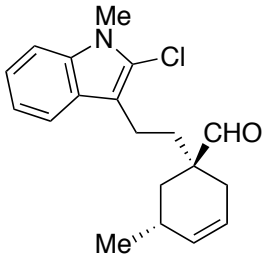



(+)-**4c**

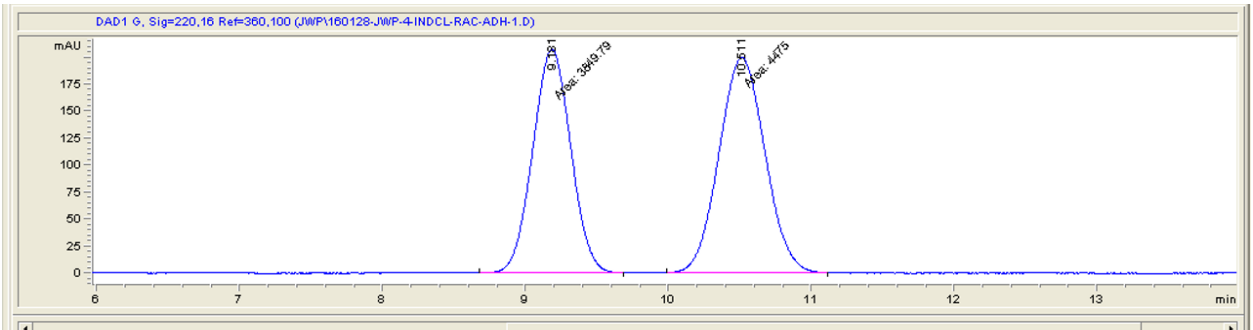



| File Information | |
|---|---|
| LC-File | 151222-JWP-3-NAPHME-R-DTBM-OH-1.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.411 | 25919.5 | 1525.5 | 0.2742 | 97.822 | 0.949 |
| 2 | 8.734 | 577 | 33.6 | 0.2645 | 2.178 | 1.028 |

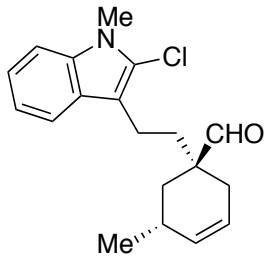



(±)-**4d**

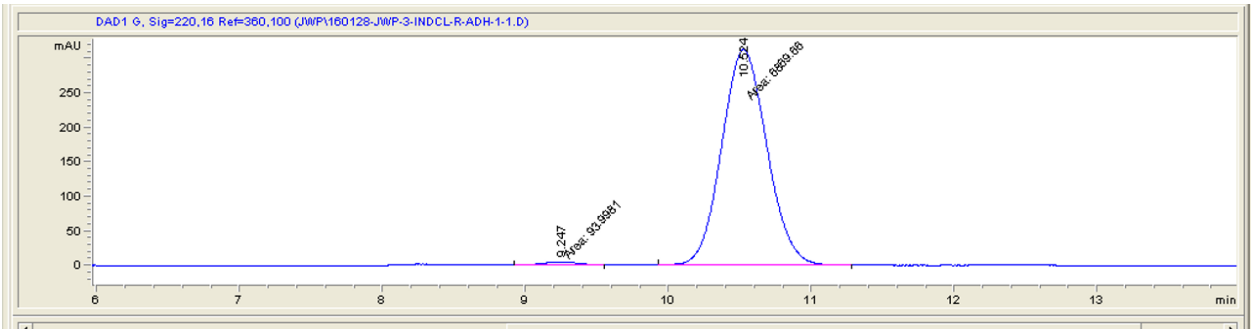



| File Information | |
|---|---|
| LC-File | 160128-JWP-4-INDCL-RAC-ADH-1.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.181 | 3849.8 | 207.3 | 0.3095 | 46.245 | 0.992 |
| 2 | 10.511 | 4475 | 200 | 0.373 | 53.755 | 0.964 |

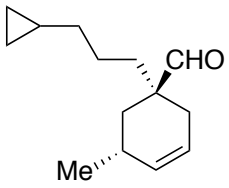



(+)-**4d**

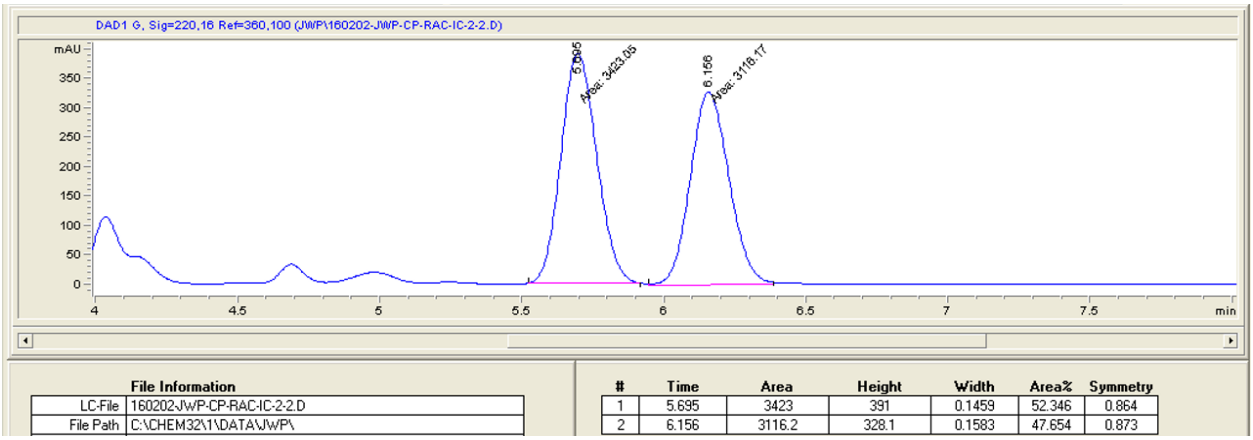



| File Information | |
|---|---|
| LC-File | 160128-JWP-3-INDCL-R-ADH-1-1.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.247 | 94 | 5 | 0.3114 | 1.350 | 1.172 |
| 2 | 10.524 | 6869.7 | 312.5 | 0.3664 | 98.650 | 0.922 |

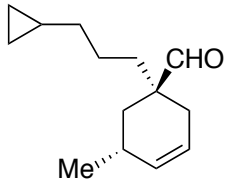



(±)-**4e**

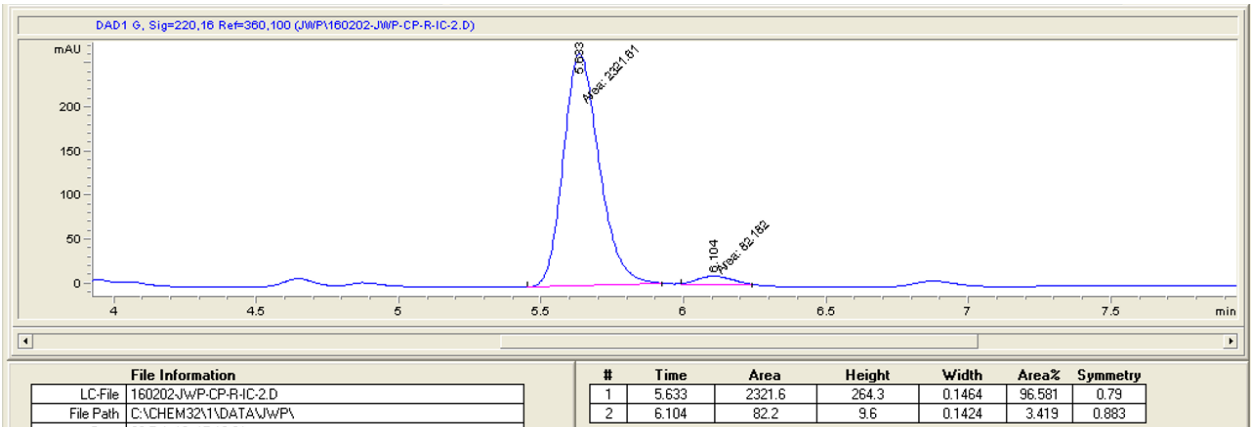



| File Information | |
|---|---|
| LC-File | 160202-JWP-CP-RAC-IC-2-2.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.695 | 3423 | 391 | 0.1459 | 52.346 | 0.864 |
| 2 | 6.156 | 3116.2 | 328.1 | 0.1583 | 47.654 | 0.873 |

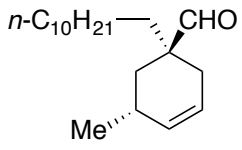



(+)-**4e**

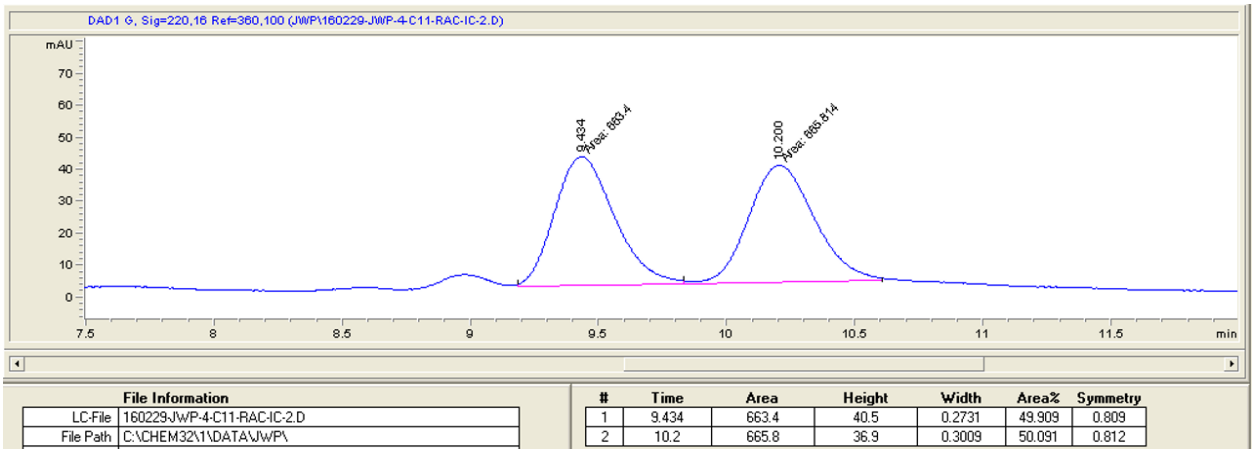



| File Information | |
|---|---|
| LC-File | 160202-JWP-CP-R-IC-2.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.633 | 2321.6 | 264.3 | 0.1464 | 96.581 | 0.79 |
| 2 | 6.104 | 82.2 | 9.6 | 0.1424 | 3.419 | 0.883 |

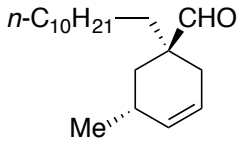



(±)-**4f**

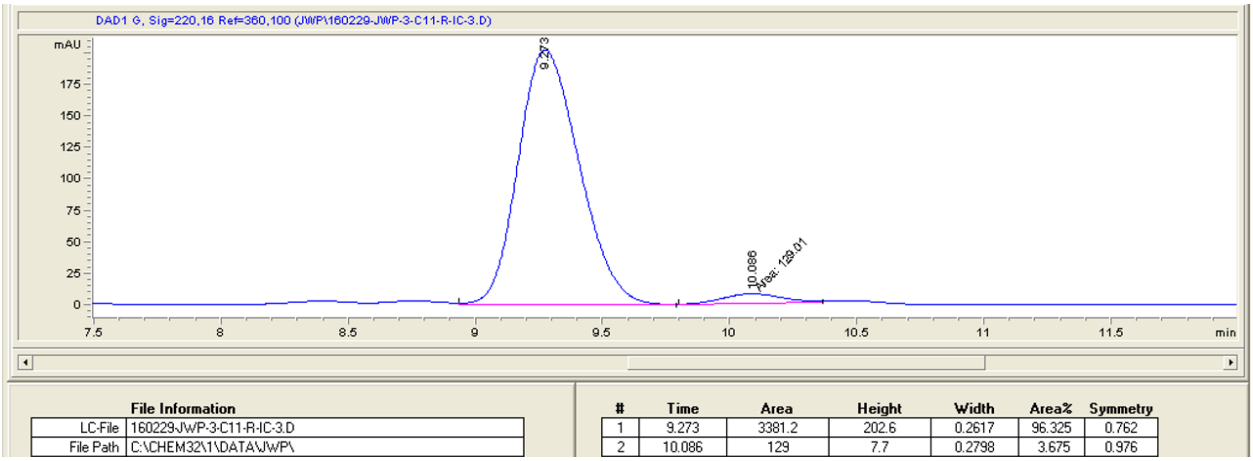



| File Information | |
|---|---|
| LC-File | 160229-JWP-4-C11-RAC-IC-2.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.434 | 663.4 | 40.5 | 0.2731 | 49.909 | 0.809 |
| 2 | 10.2 | 665.8 | 36.9 | 0.3009 | 50.091 | 0.812 |

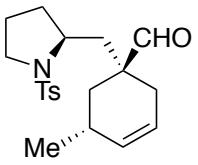



(+)-**4f**

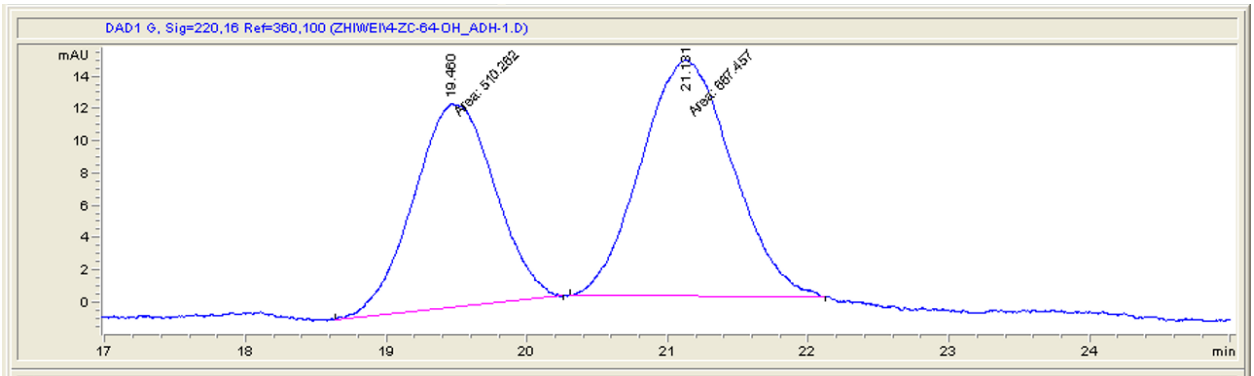



| File Information | |
|---|---|
| LC-File | 160229-JWP-3-C11-R-IC-3.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.273 | 3381.2 | 202.6 | 0.2617 | 96.325 | 0.762 |
| 2 | 10.086 | 129 | 7.7 | 0.2798 | 3.675 | 0.976 |

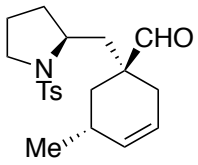



(±)-**4g**

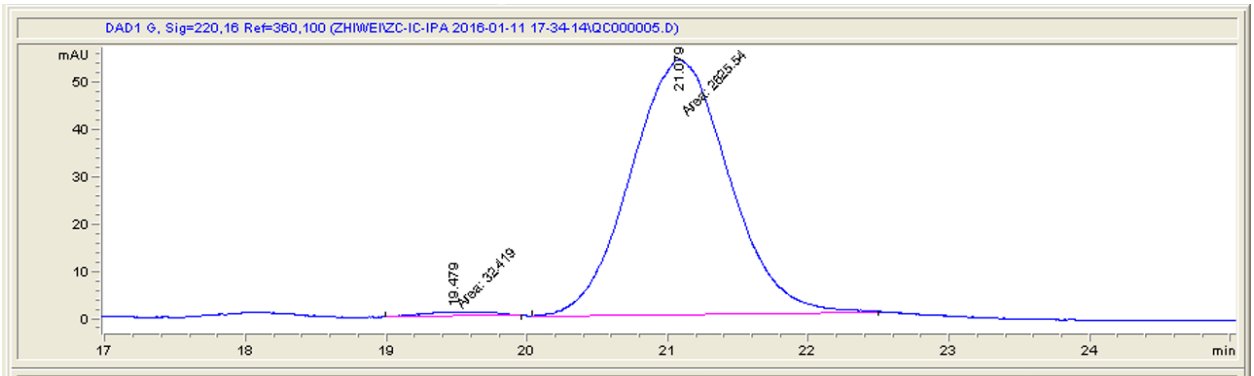



| File Information | |
|---|---|
| LC-File | 4-ZC-64-OH_ADH-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 19.46 | 510.3 | 12.7 | 0.6713 | 43.326 | 0.886 |
| 2 | 21.131 | 667.5 | 14.7 | 0.7557 | 56.674 | 0.968 |

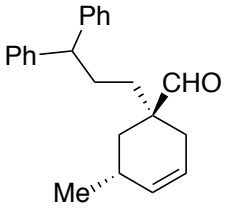



(+)-**4g**

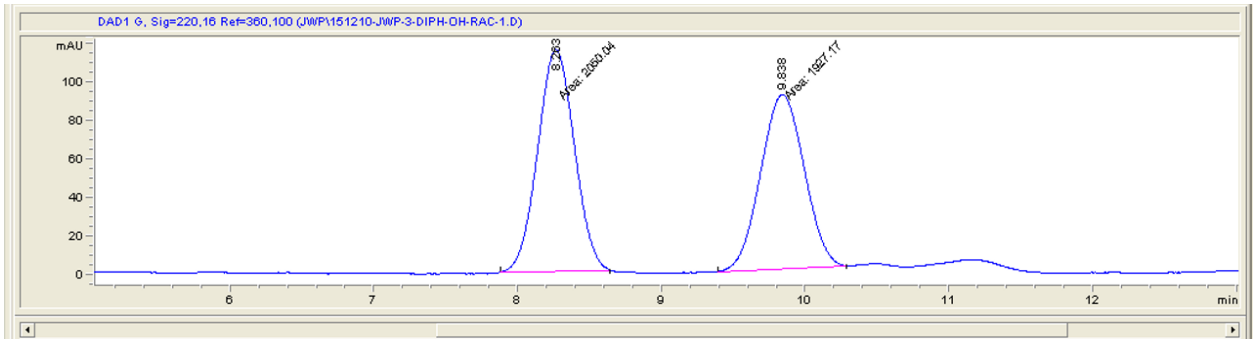



| File Information | |
|---|---|
| LC-File | QC000005.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ZC-IC-IPA 2016-01-11 17-34-14\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 19.479 | 32.4 | 9.3E-1 | 0.5791 | 1.220 | 0.795 |
| 2 | 21.079 | 2625.5 | 54.1 | 0.8095 | 98.780 | 0.955 |

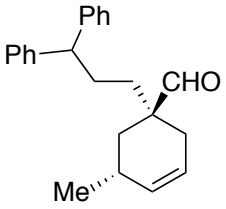



(±)-**4h**

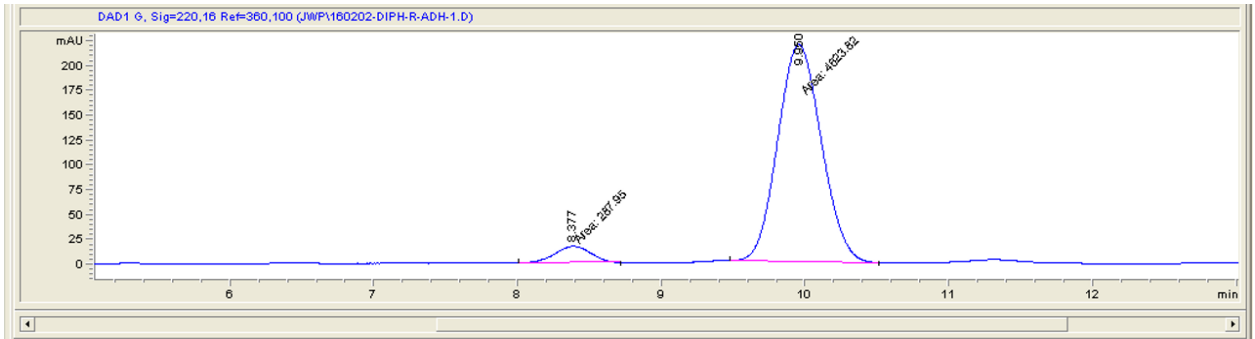



| File Information | |
|---|---|
| LC-File | 151210-JWP-3-DIPH-OH-RAC-1.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.263 | 2050 | 115.3 | 0.2963 | 51.545 | 0.957 |
| 2 | 9.838 | 1927.2 | 90.9 | 0.3532 | 48.455 | 0.968 |

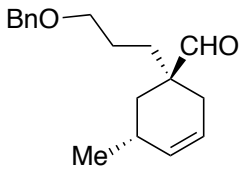



(+)-**4h**

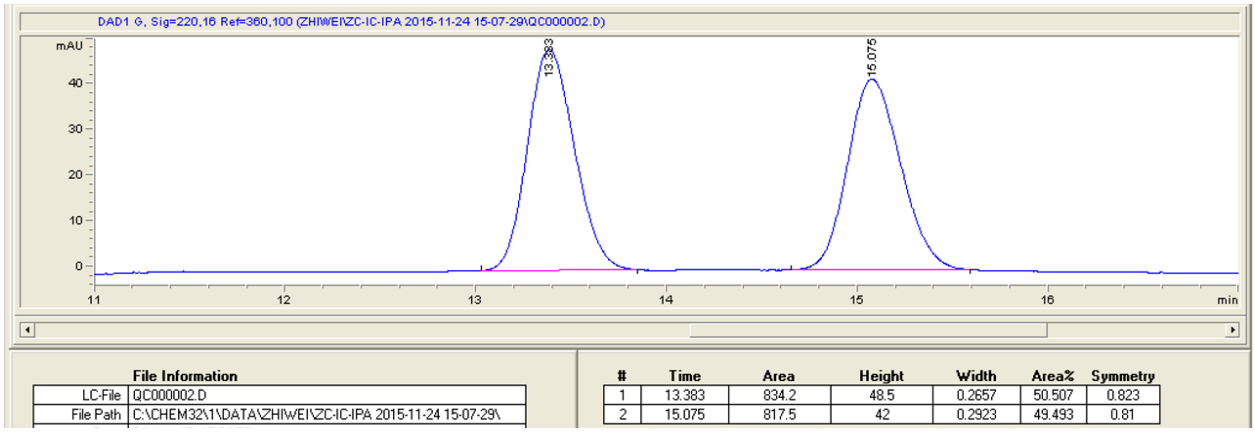



| File Information | |
|---|---|
| LC-File | 160202-DIPH-R-ADH-1.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.377 | 287.9 | 16.5 | 0.2916 | 5.862 | 0.945 |
| 2 | 9.95 | 4623.8 | 218.8 | 0.3522 | 94.138 | 0.877 |

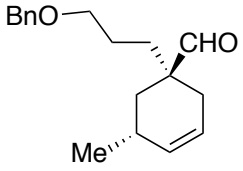



(±)-**4i**

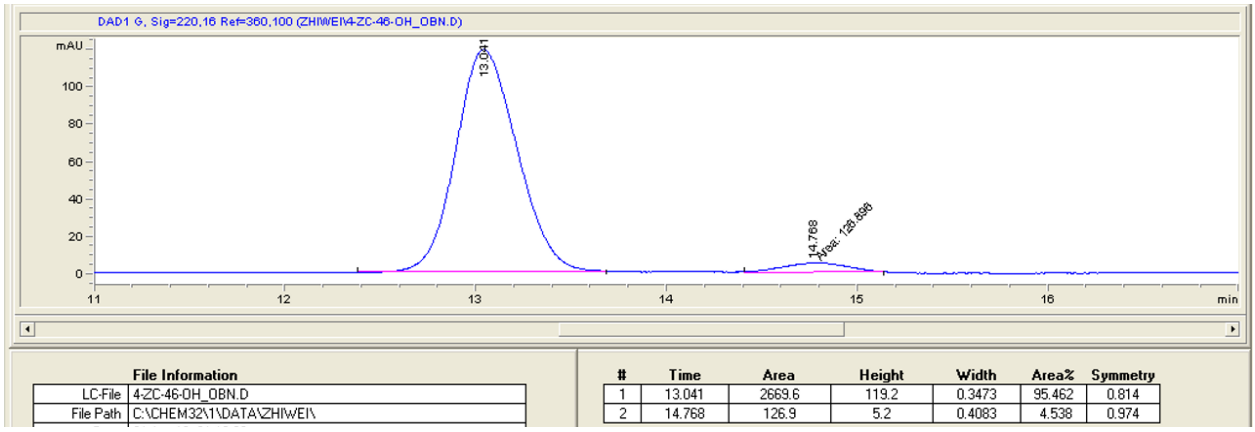



| File Information | |
|---|---|
| LC-File | QC000002.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ZC-IC-IPA 2015-11-24 15-07-29\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.383 | 834.2 | 48.5 | 0.2657 | 50.507 | 0.823 |
| 2 | 15.075 | 817.5 | 42 | 0.2923 | 49.493 | 0.81 |

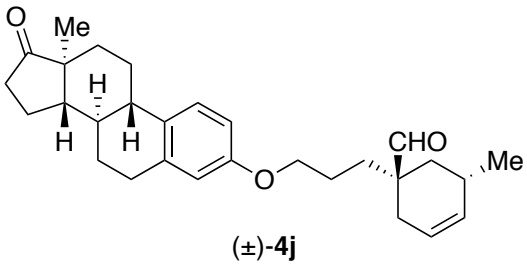



(+)-**4i**

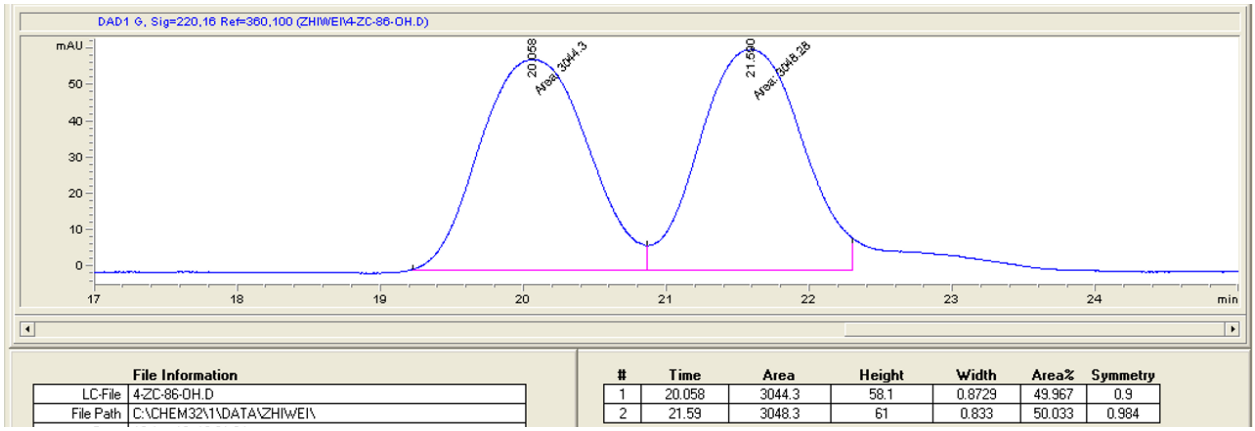



| File Information | |
|---|---|
| LC-File | 4-ZC-46-OH_OBN.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.041 | 2669.6 | 119.2 | 0.3473 | 95.462 | 0.814 |
| 2 | 14.768 | 126.9 | 5.2 | 0.4083 | 4.538 | 0.974 |

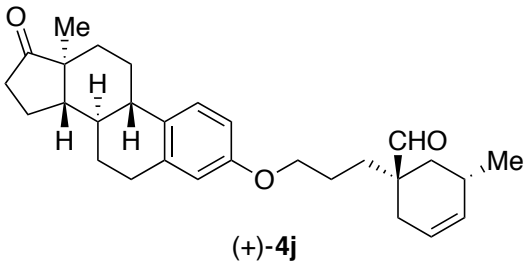


(±)-**4j**

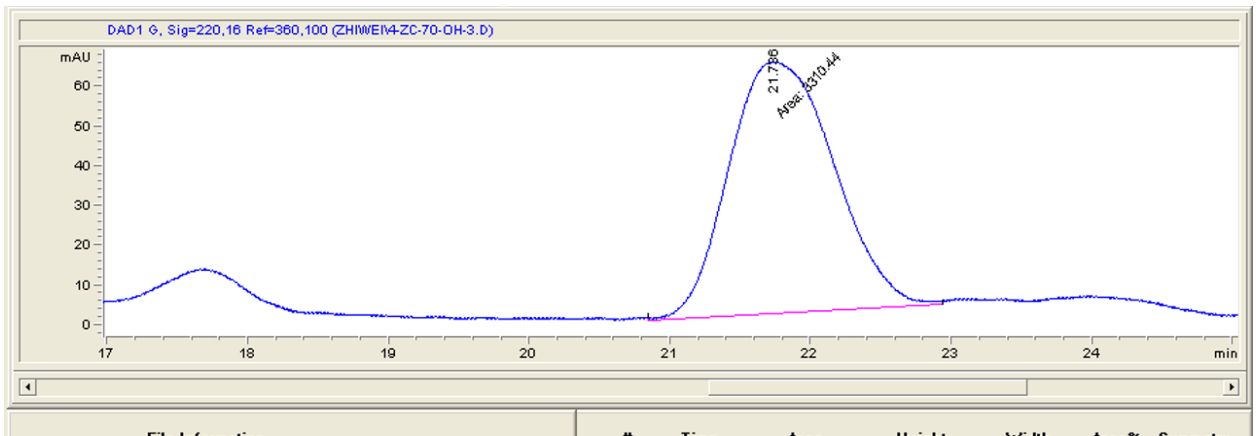



| File Information | |
|---|---|
| LC-File | 4-ZC-86-OH.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 20.058 | 3044.3 | 58.1 | 0.8729 | 49.967 | 0.9 |
| 2 | 21.59 | 3048.3 | 61 | 0.833 | 50.033 | 0.984 |

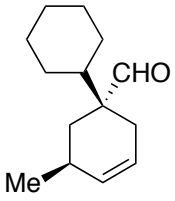


(+)-**4j**

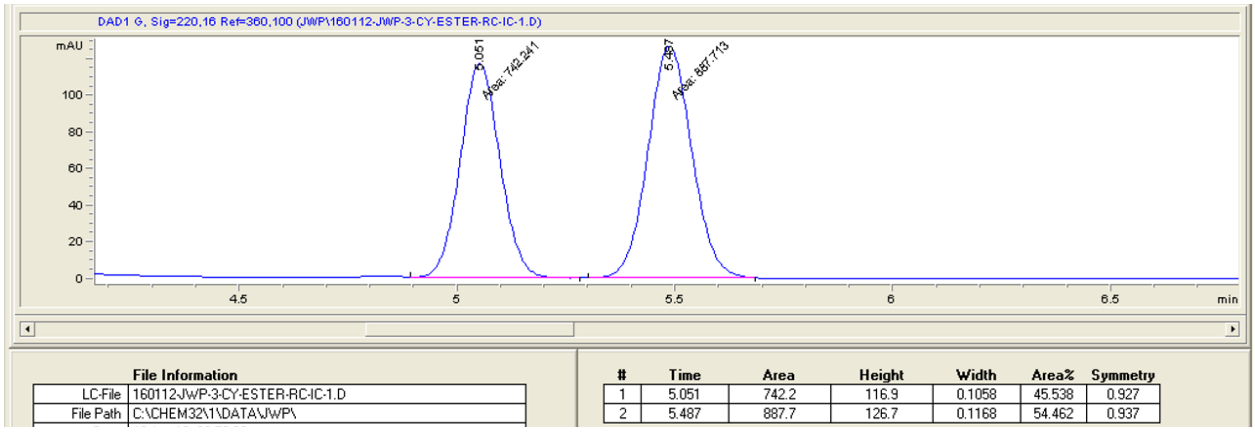


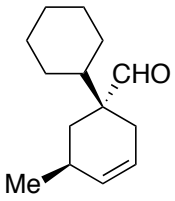

| File Information | |
|---|---|
| LC-File | 4-ZC-70-OH-3.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 21.736 | 3310.4 | 63.5 | 0.8684 | 100.000 | 0.751 |

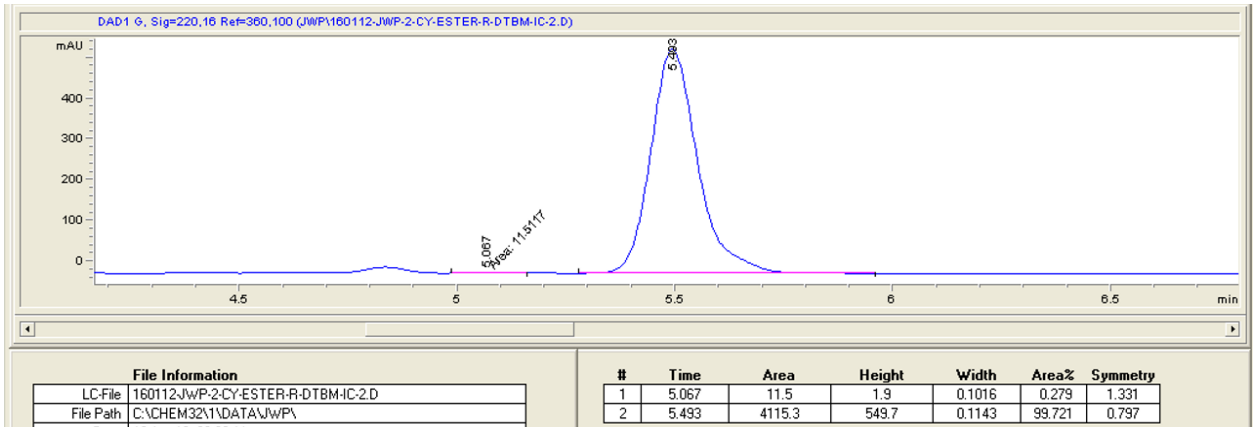

CHO
Me

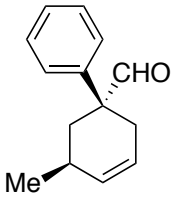
(±)-**4k**


DAD1 G, Sig=220,16 Ref=360,100 (JWP\160112-JWP-3-CY-ESTER-RC-IC-1.D)
mAU
5.051
Area: 742.241
5.487
Area: 887.713
min
File Information
LC-File 160112-JWP-3-CY-ESTER-RC-IC-1.D
File Path C:\CHEM32\1\DATA\JWP\
# Time Area Height Width Area% Symmetry
1 5.051 742.2 116.9 0.1058 45.538 0.927
2 5.487 887.7 126.7 0.1168 54.462 0.937

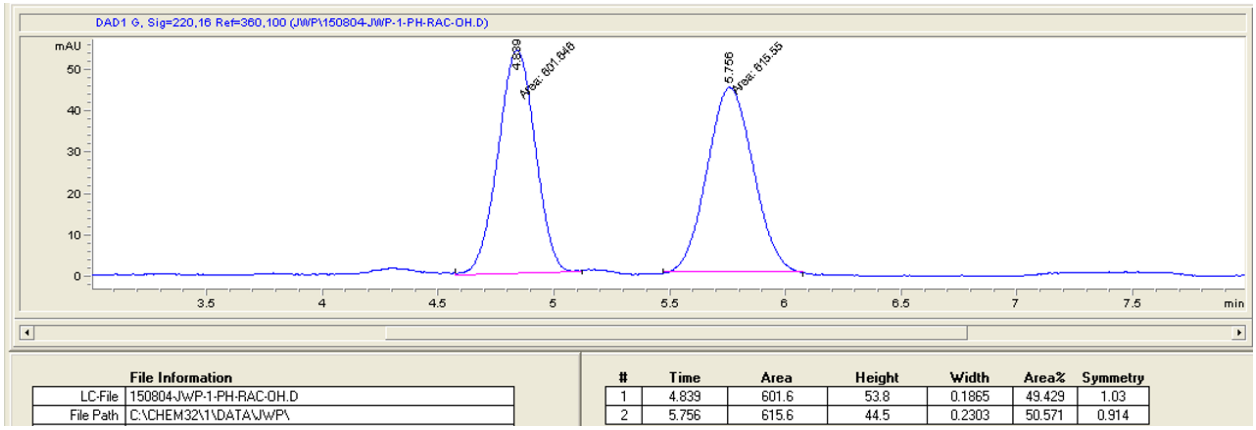

CHO
Me

(–)-**4k**


DAD1 G, Sig=220,16 Ref=360,100 (JWP\160112-JWP-2-CY-ESTER-R-DTBM-IC-2.D)
mAU
5.493
5.067
Area: 11.5117
min
File Information
LC-File 160112-JWP-2-CY-ESTER-R-DTBM-IC-2.D
File Path C:\CHEM32\1\DATA\JWP\
# Time Area Height Width Area% Symmetry
1 5.067 11.5 1.9 0.1016 0.279 1.331
2 5.493 4115.3 549.7 0.1143 99.721 0.797

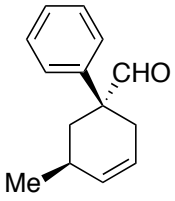



(±)-**4l**

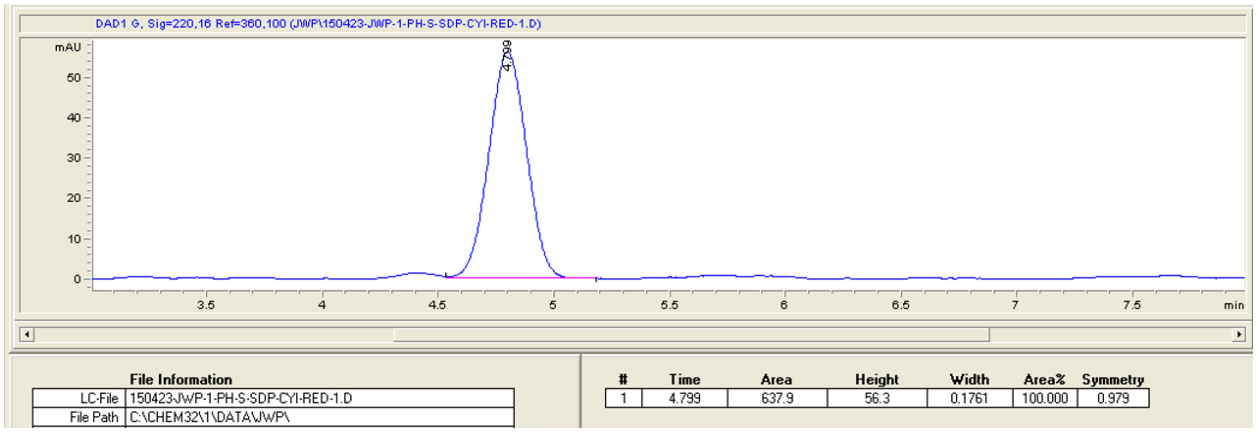



| File Information | |
|---|---|
| LC-File | 150804-JWP-1-PH-RAC-OH.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.839 | 601.6 | 53.8 | 0.1865 | 49.429 | 1.03 |
| 2 | 5.756 | 615.6 | 44.5 | 0.2303 | 50.571 | 0.914 |

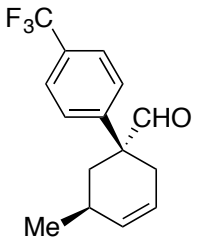



(–)-**4l**

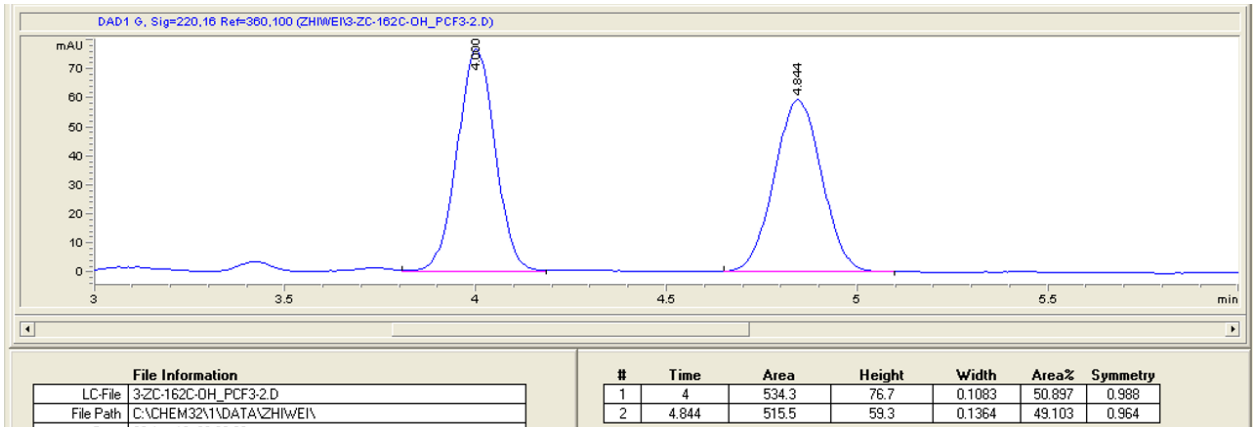



| File Information | |
|---|---|
| LC-File | 150423-JWP-1-PH-S-SDP-CYI-RED-1.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.799 | 637.9 | 56.3 | 0.1761 | 100.000 | 0.979 |




(±)-**4m**

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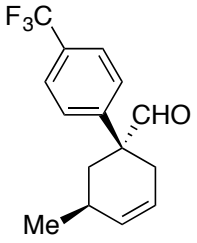


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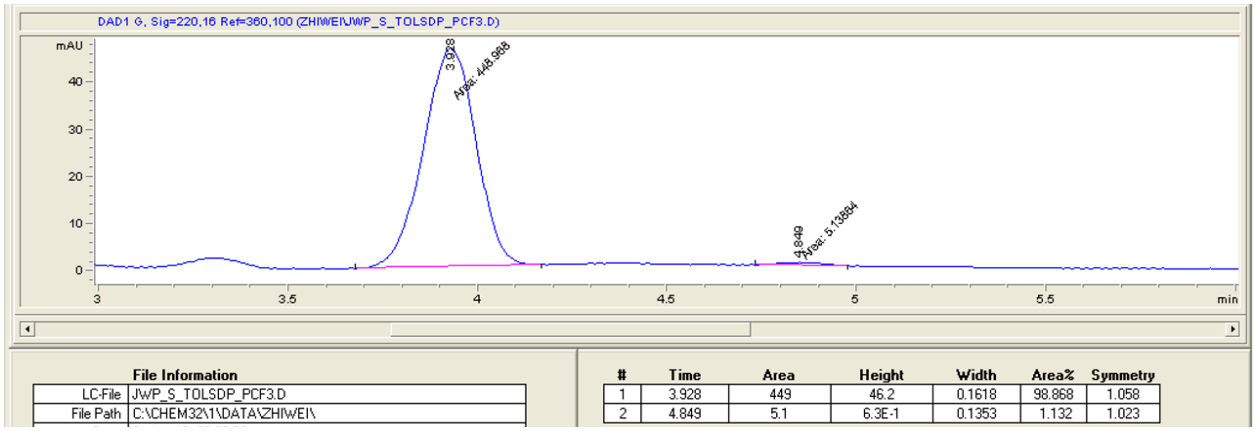


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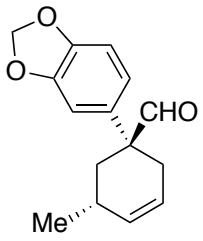


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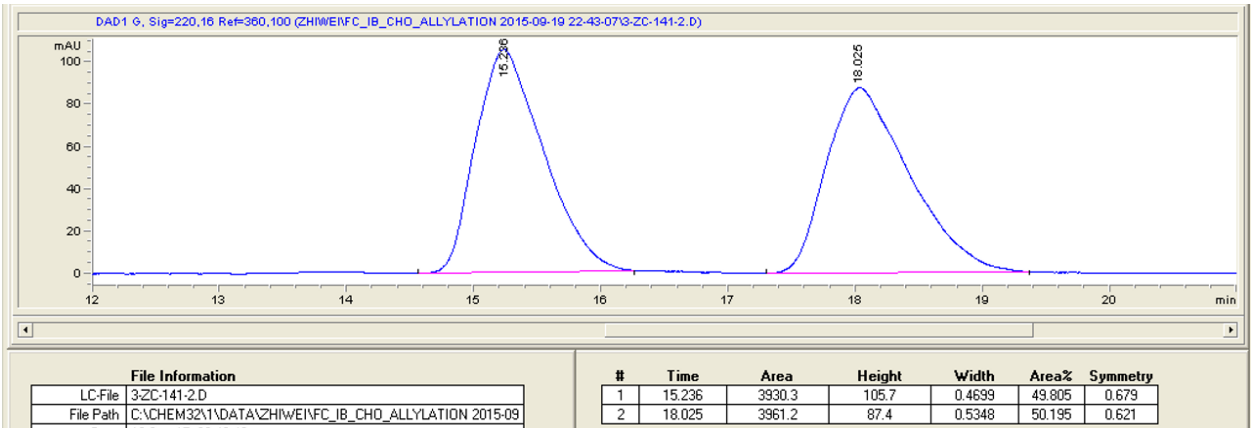


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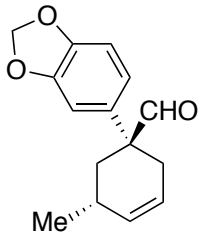


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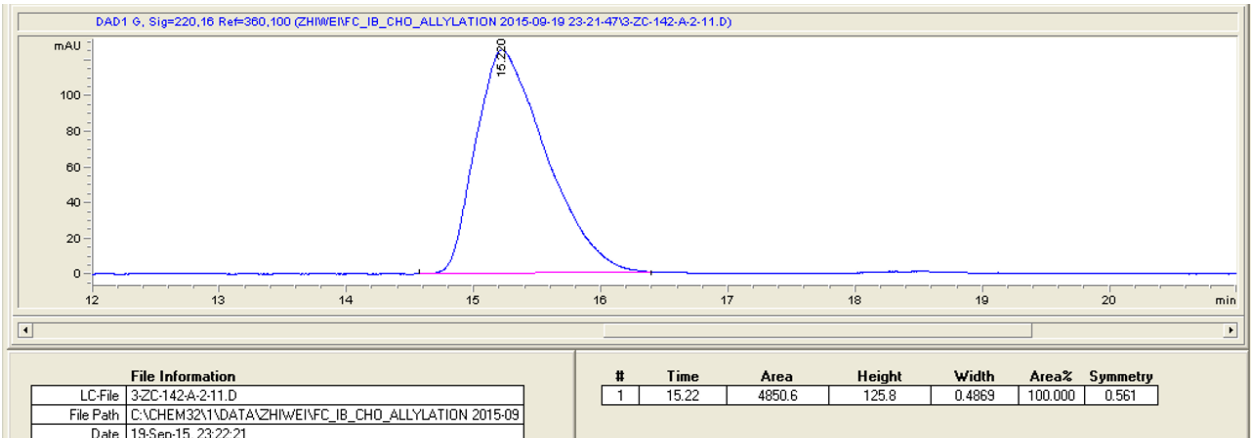


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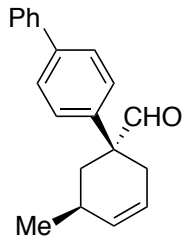


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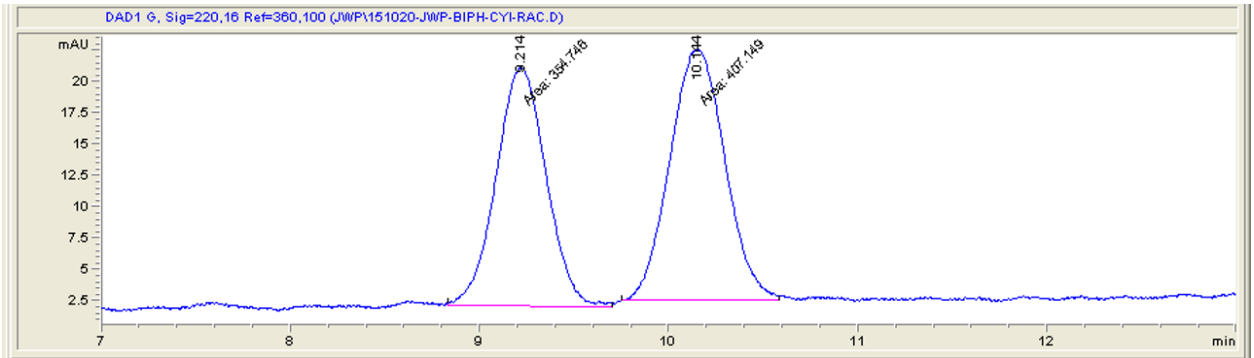


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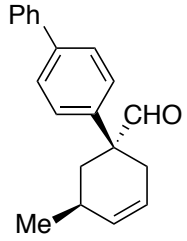


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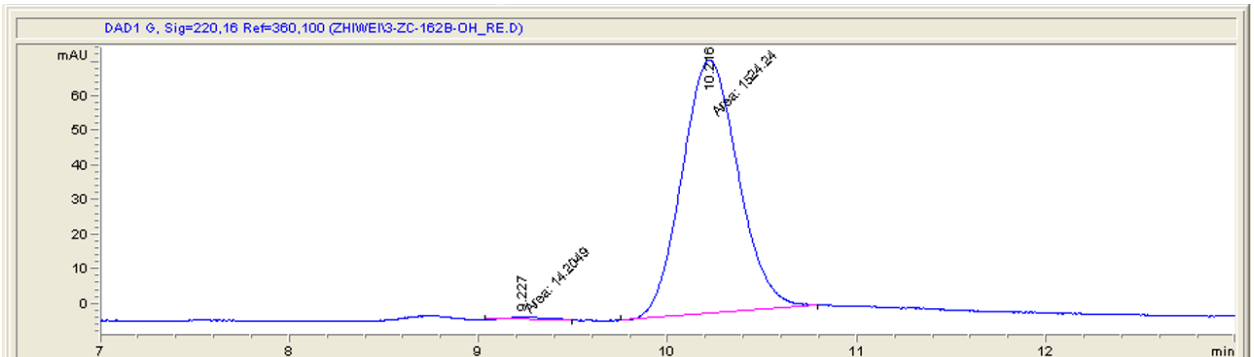


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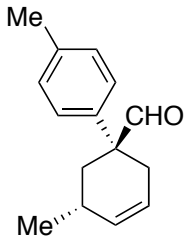
| 2 | 10.216 | 1524.2 | 73.5 | 0.3454 | 99.077 | 0.903 |

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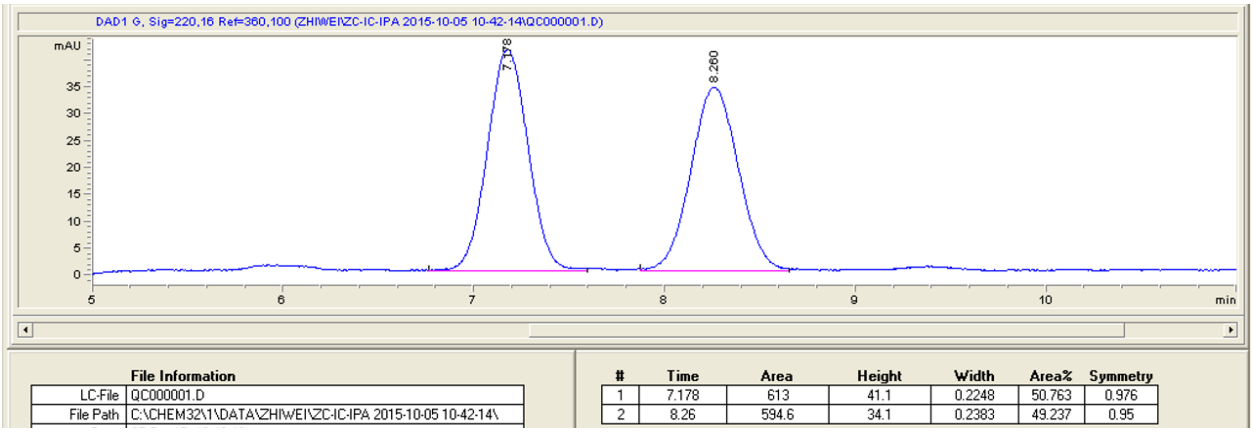


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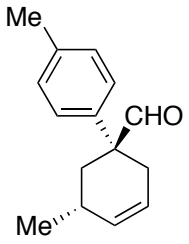
| 2 | 8.26 | 594.6 | 34.1 | 0.2383 | 49.237 | 0.95 |

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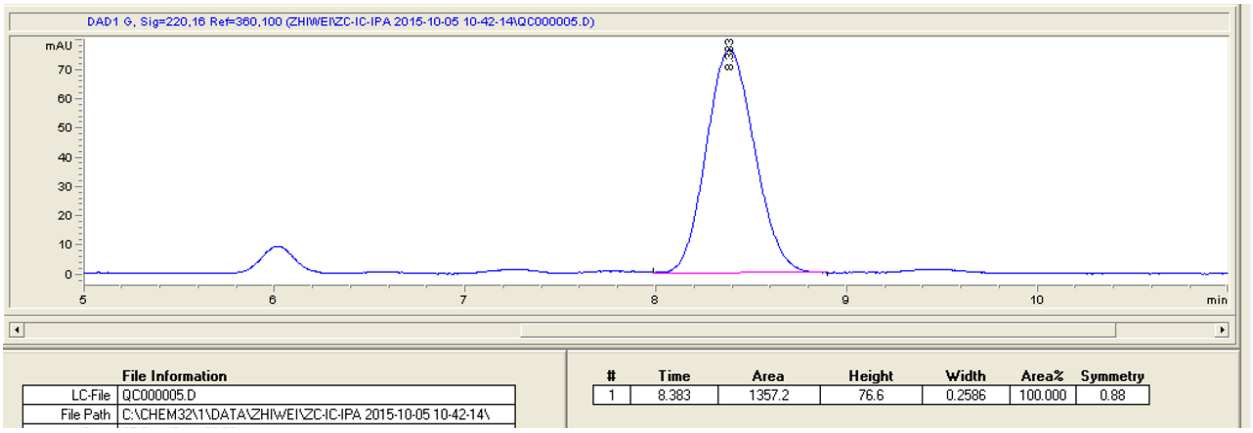


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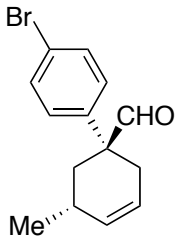
Br
CHO
Me

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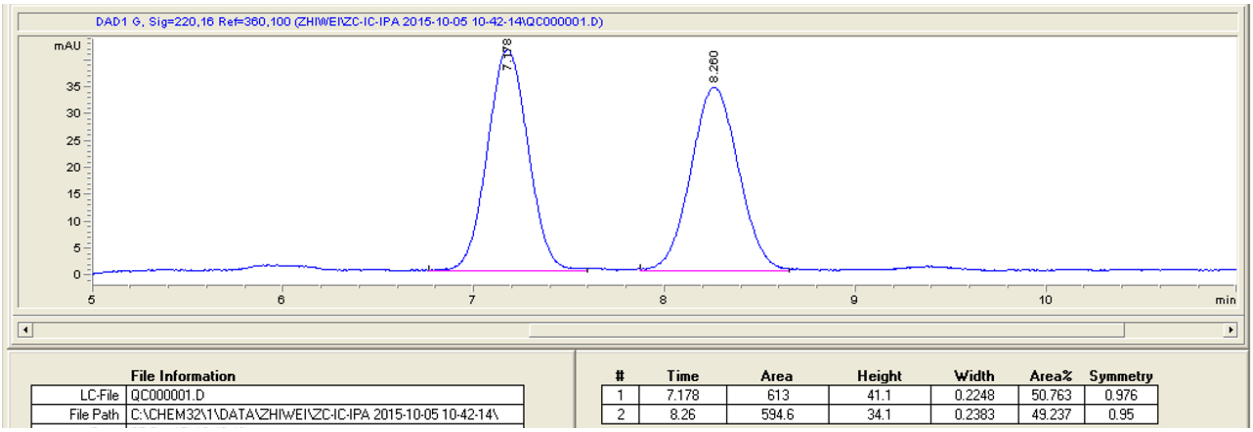
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8.260
min
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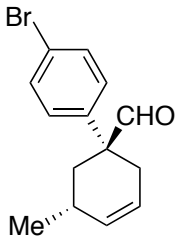
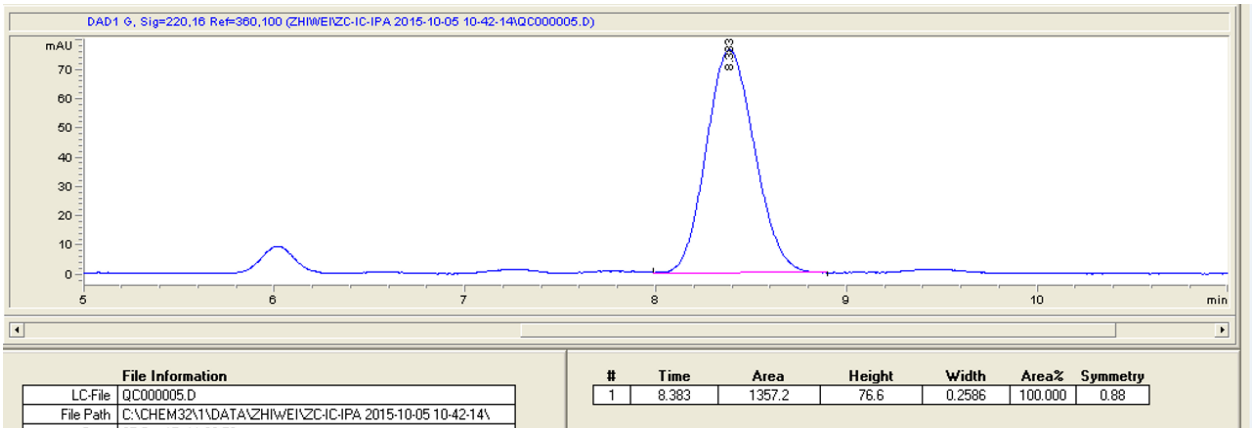
2 8.26 594.6 34.1 0.2383 49.237 0.95


Br
CHO
Me

(–)-**4p**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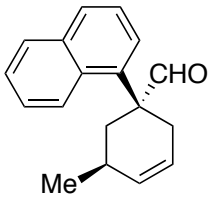


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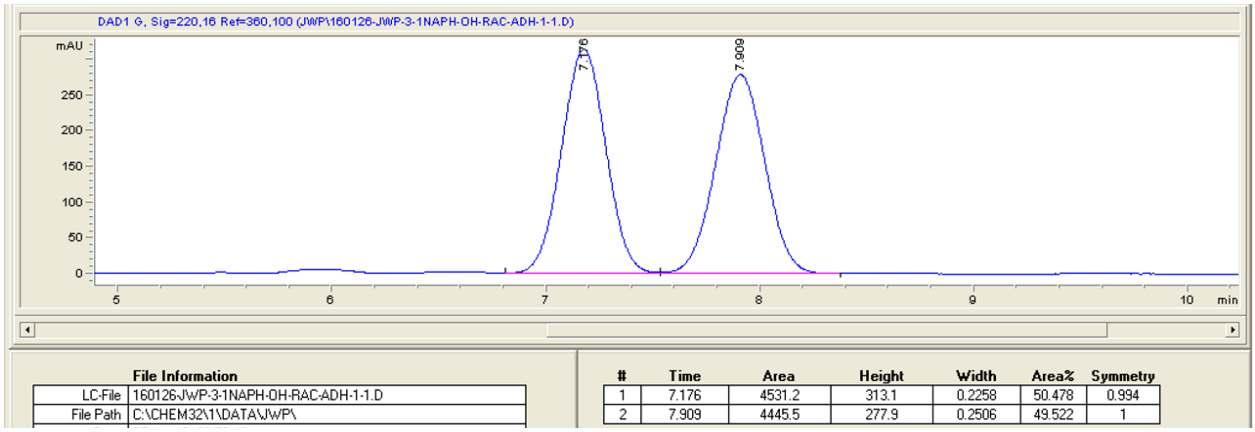


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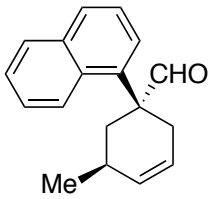
| 2 | 7.909 | 4445.5 | 277.9 | 0.2506 | 49.522 | 1 |

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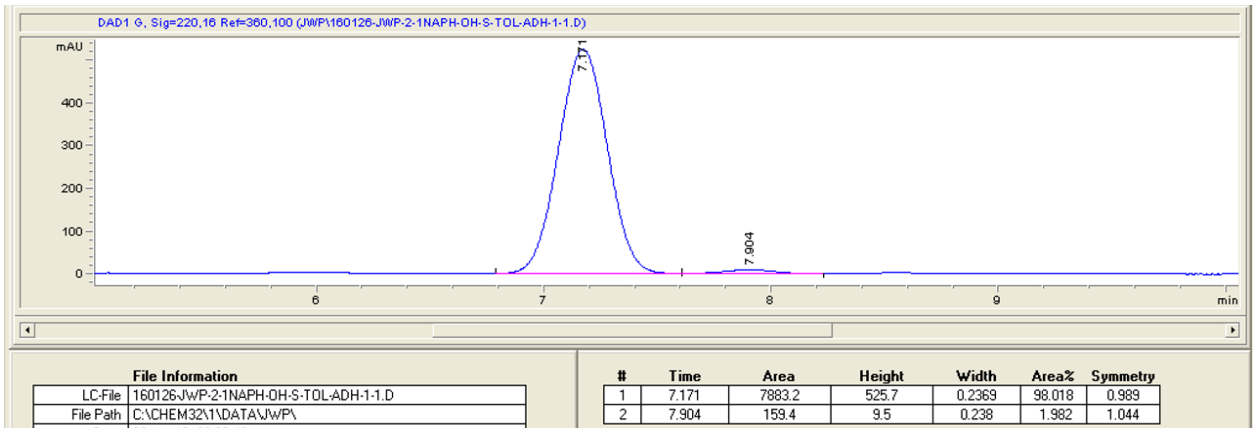


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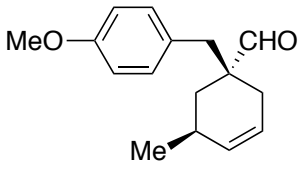
| 1 | 7.171 | 7883.2 | 525.7 | 0.2369 | 98.018 | 0.989 |
| 2 | 7.904 | 159.4 | 9.5 | 0.238 | 1.982 | 1.044 |

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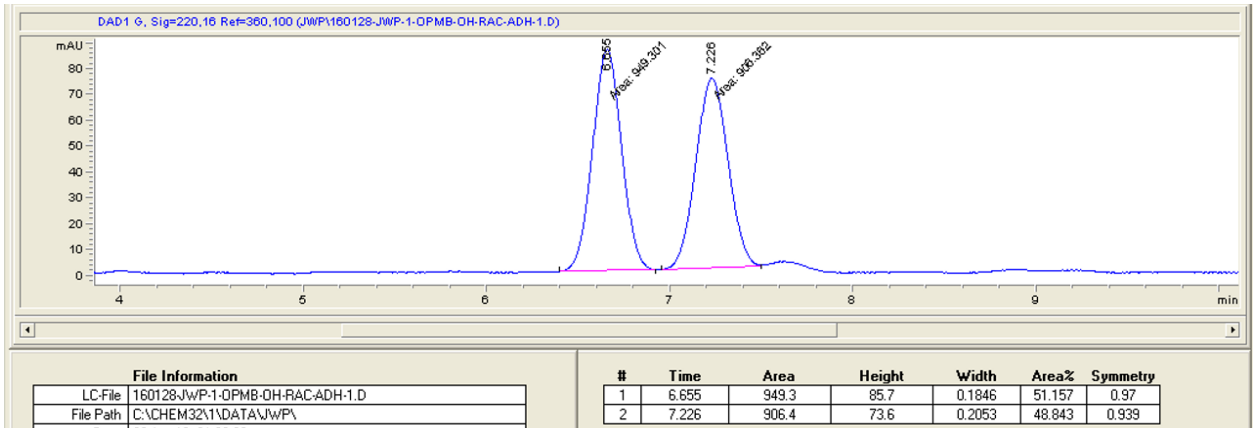


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|---|---|
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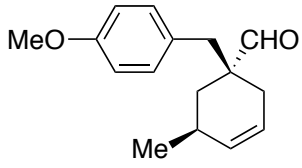
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.655 | 949.3 | 85.7 | 0.1846 | 51.157 | 0.97 |
| 2 | 7.226 | 906.4 | 73.6 | 0.2053 | 48.843 | 0.939 |

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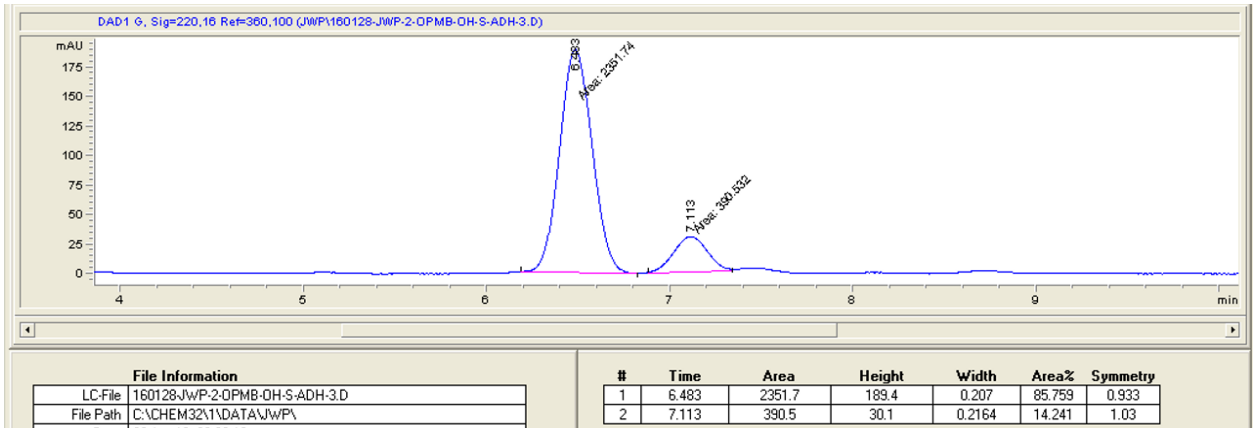


| File Information | |
|---|---|
| LC-File | 160128-JWP-2-OPMB-OH-S-ADH-3.D |
| File Path | C:\CHEM32\1\DATA\JWP\ |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.483 | 2351.7 | 189.4 | 0.207 | 85.759 | 0.933 |
| 2 | 7.113 | 390.5 | 30.1 | 0.2164 | 14.241 | 1.03 |

## Appendix 2.3: Supporting Information for Chapter 2.3
## Dynamic Kinetic Resolution of Aldehydes by Hydroacylation

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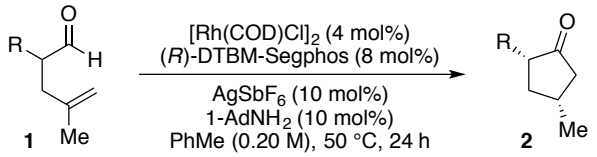
## 1. General Information

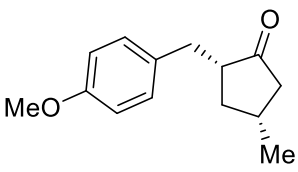
Commercially reagents were purchased from Sigma Aldrich, Strem, Acros Organics, TCI or Alfa Aesar and used without further purification. All experiments were performed in oven-dried or flame-dried glassware under an atmosphere of $N_2$. Tetrahydrofuran, diethyl ether, toluene, and dichloromethane were purified using an Innovative Technologies Pure Solv system, degassed by three freeze-pump-thaw cycles, and stored over 3A MS within a $N_2$ filled glove box. Reactions were monitored either via gas chromatography using an Agilent Technologies 7890A GC system equipped with an Agilent Technologies 5975C inert XL EI/CI MSD or by analytical thin-layer chromatography on EMD Silica Gel 60 F254 plates. Visualization of the developed plates was performed under UV light (254 nm) or using KMnO4 stain. Purification and isolation of products were performed via silica gel chromatography (both column and preparative thin-layer chromatography). Column chromatography was performed with Silicycle Silia-P Flash Silica Gel using glass columns. $^{1}H$, $^{13}C$, $^{19}F$, and $^{31}P$ NMR spectra were recorded on a Bruker DRX-400 (400 MHz $^{1}H$, 100 MHz $^{13}C$, 376.5 MHz $^{19}F$, 162 MHz $^{31}P$), GN-500 (500 MHz $^{1}H$, 125.7 MHz $^{13}C$, 202 MHz $^{31}P$), or CRYO-500 (500 MHz $^{1}H$, 125.7 MHz $^{13}C$) spectrometer. $^{1}H$ NMR spectra were internally referenced to the residual solvent signal or TMS. $^{13}C$ NMR spectra were internally referenced to the residual solvent signal. Data for $^{1}H$ NMR are reported as follows: chemical shift (δ ppm, δ 7.27 for $CDCl_3$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for $^{13}C$ NMR are reported in terms of chemical shift (δ ppm, δ 77.16 for $CDCl_3$). Infrared spectra were obtained on a Thermo Scientific Nicolet iS5 FT-IR spectrometer equipped with an iD5 ATR accessory, and were reported in terms of frequency of absorption ($cm^{-1}$). Enantiomeric excesses for enantioselective reactions were determined by chiral SFC analysis using an Agilent Technologies HPLC (1200 series) system and Aurora A5 Fusion. High-resolution mass spectra (HRMS) were obtained on a micromass 70S-250 spectrometer (EI) or an ABI/Sciex QStar Mass Spectrometer (ESI), performed by the University of California, Irvine Mass Spectrometry Center. X-ray crystallography was performed by the X-ray Crystallography Facility of the University of California, San Diego.

## 2. General Procedures for the Dynamic Kinetic Resolution

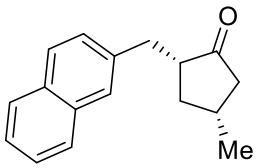



**Method A:** In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol, 4 mol%), (*R*)-DTBM-Segphos (10.7 mg, 0.0080 mmol, 8 mol%), and toluene (0.50 mL, 0.20 M) were added to a 1 dram vial equipped with a magnetic stir bar. The solution was stirred at 30 °C for 10 min. $AgSbF_6$ (3.4 mg, 0.010 mmol, 10 mol%), was added, and the resulting mixture was stirred at 30 °C for 30 min. Aldehyde **1** (0.10 mmol, 1.0 equiv) and 1-$AdNH_2$ (1.5 mg, 0.010 mmol, 10 mol%) were added. The vial was then sealed with a Teflon-lined screw cap and stirred at 50 °C for 24 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The ketone **2** was purified using preparative thin-layer chromatography.

**(2*R*,4*R*)-2-(4-methoxybenzyl)-4-methylcyclopentan-1-one (2a)**: The title compound was

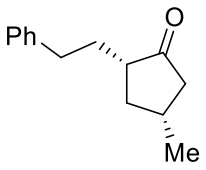



synthesized according to Method A and isolated by preparatory TLC (5% EtOAc in hexanes) as a white solid (20.5 mg, 94% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = +151 (*c* 0.52, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.11 (dd, *J* = 13.8, 4.0 Hz, 1H), 2.56 – 2.45 (m, 2H), 2.40 (dtd, *J* = 12.4, 8.1, 4.1 Hz, 1H), 2.21 – 2.03 (m, 2H), 1.71 (dd, *J* = 18.4, 11.3 Hz, 1H), 1.21 – 1.11 (m, 1H), 1.10 (d, *J* = 6.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 219.8, 158.2, 132.2, 129.9, 114.0, 55.4, 53.1, 47.0, 38.3, 34.8, 29.7, 20.4. **IR** (ATR): 2952, 2934, 1721, 1610, 1319, 1181, 1037, 711 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{18}O_2Na$ $[M+Na]^+$ 241.1205, found 241.1204. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 6.1 min, $t_{R2}$ (minor) = 8.3 min.

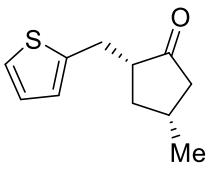



**(2*R*,4*R*)-4-methyl-2-(naphthalen-2-ylmethyl)cyclopentan-1-one (2b)**: The title compound was synthesized according to Method A and isolated by prep TLC (5% EtOAc in hexanes) as a white solid (21.9 mg, 94%

yield, >20:1 *dr*, 93% *ee*, $[\alpha]^{24}_D$ = +206 (*c* 0.93, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.73 (m, 3H), 7.62 (s, 1H), 7.50 – 7.40 (m, 2H), 7.31 (dd, *J* = 8.4, 1.4 Hz, 1H),3.36 (dd, *J* = 13.8, 4.1 Hz, 1H), 2.72 (dd, *J* = 13.8, 9.5 Hz, 1H), 2.54 (ddd, *J* = 12.6, 9.1, 6.4 Hz, 2H),2.21 – 2.05 (m, 2H), 1.76 (dd, *J* = 18.6, 11.3 Hz, 1H), 1.21 (q, *J* = 11.7 Hz, 1H), 1.10 (d, *J* = 6.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 219.6, 137.8, 133.7, 132.3, 128.2, 127.8, 127.59, 127.55, 127.2, 126.1, 125.5, 52.9, 46.9, 38.4, 35.9, 29.7, 20.3. **IR** (ATR): 2953, 1734, 1507, 1153, 775 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{18}ONa$ $[M+Na]^+$ 261.1255, found 261.1255. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 0.5% *i*-PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 9.2 min, $t_{R2}$ (minor) = 11.5 min.

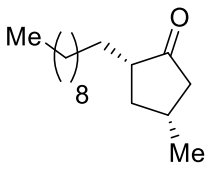



**(2*S*,4*R*)-4-methyl-2-phenethylcyclopentan-1-one (2c)**: The title compound was synthesized according to Method A and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (20.7 mg, 86% yield, >20:1 *dr*, 93% *ee*, $[\alpha]^{24}_D$ = +114 (*c* 0.41, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.25 (m, 2H), 7.19 (dd, *J* = 10.2, 4.3 Hz, 3H), 2.79 – 2.69 (m, 1H), 2.69 – 2.58 (m, 1H), 2.46(dd, *J* = 18.3, 7.4 Hz, 1H), 2.41 – 2.30 (m, 1H), 2.22 – 2.05 (m, 3H), 1.76 (dd, *J* = 18.4, 11.6 Hz, 1H), 1.65 – 1.51 (m, 1H), 1.23 – 1.10 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 220.8, 141.8, 128.6, 128.5, 126.1, 50.3, 47.0, 38.8, 33.8, 31.6, 29.8, 20.5. **IR** (ATR): 2951, 2924, 1733, 1603, 1454, 906 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{18}ONa$ $[M+Na]^+$ 225.1255, found 225.1250. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 0% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 7.8 min, $t_{R2}$ (major) = 8.6 min.

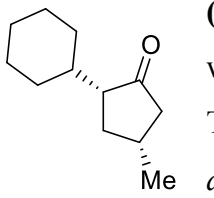



**(2*R*,4*R*)-4-methyl-2-(thiophen-2-ylmethyl)cyclopentan-1-one (2d)**: The title compound was synthesized according to Method A and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (18.3 mg, 94% yield, >20:1 *dr*, 93% *ee*, $[\alpha]^{24}_D$ = +173 (*c* 0.58, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.92 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.82 – 6.77 (m, 1H), 3.34 (dd, *J* = 15.0, 4.0 Hz, 1H), 2.84 (dd, *J* = 15.0, 8.9 Hz, 1H), 2.56 – 2.40 (m, 2H), 2.34 – 2.24 (m, 1H), 2.21 – 2.07 (m, 1H), 1.74 (dd, *J* = 18.5, 11.5 Hz, 1H), 1.26 – 1.16 (m, 1H), 1.12 (d, *J* = 6.5 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 219.1, 142.4, 126.9, 125.5, 123.7, 52.9, 46.9, 38.2, 29.8, 29.6, 20.3. **IR** (ATR): 2953, 1736, 1455, 1437, 1245, 1154, 849 $cm^{-1}$. **HRMS** calculated

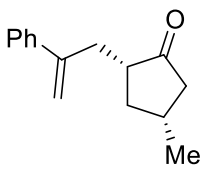
for $C_{11}H_{14}OSNa$ $[M+Na]^+$ 217.0663, found 217.0658. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C,nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 5.1 min, $t_{R2}$ (minor) = 6.2 min.




**(2*S*,4*R*)-2-decyl-4-methylcyclopentan-1-one (2e)**: The title compound was synthesized according to Method A at 60 °C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (15.4 mg, 65% yield, >20:1 *dr*, 96% *ee*, $[\alpha]^{24}_D$ = +99 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 2.46 (dd, *J* = 18.4, 7.4 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.13 (qd, *J* = 12.4, 6.4 Hz, 2H), 1.76 (ddd, *J* = 24.5, 14.9, 8.1 Hz, 2H), 1.26 (s, 17H), 1.12 (dd, *J* = 11.6, 9.3 Hz, 4H), 0.89 (t, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 221.3, 51.1, 47.0, 38.8, 32.1, 29.9, 29.84, 29.75, 29.7, 29.6, 29.5, 27.7, 22.8, 20.5, 14.3. **IR** (ATR): 2953, 2922, 2852, 1739, 1456, 1155, 720 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{30}ONa$ $[M+Na]^+$ 261.2194, found 261.2184. **Chiral SFC** (of the corresponding tertiary alcohol after treatment with PhMgBr): 100 mm CHIRALPAK AD-H, 2% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 10.5 min, $t_{R2}$ (major) = 12.0 min.

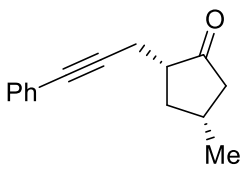



**(2*R*,4*R*)-2-cyclohexyl-4-methylcyclopentan-1-one (2f)**: The title compound was synthesized according to Method A at 60 °C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (11.4 mg, 63% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = +80 (*c* 0.94, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 2.50 – 2.36 (m, 1H), 2.18 – 1.99 (m, 3H), 1.86 – 1.56 (m, 6H), 1.47 – 1.36 (m, 1H), 1.35 – 1.19 (m, 3H), 1.18 – 1.00 (m, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 220.8, 56.6, 48.2, 37.5, 34.4, 31.9, 29.7, 28.9, 26.7, 26.52, 26.48, 20.4. **IR** (ATR): 2922, 2851, 1733, 1449, 1152, 1076, 892 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{20}OH$ $[M+H]^+$ 181.1592, found 181.1598. **Chiral SFC** (of the corresponding tertiary alcohol after treatment with PhMgBr): 100 mm CHIRALPAK AD-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 14.2 min, $t_{R2}$ (major) = 18.2 min.



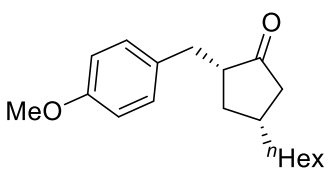

**(2*R*,4*R*)-4-methyl-2-(2-phenylallyl)cyclopentan-1-one (2g)**: The title compound was synthesized according to Method A and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (16.5 mg, 69% yield, >20:1 *dr*,

94% *ee*, $[\alpha]^{24}_D$ = +85 (*c* 0.67, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.31 – 7.24 (m, 1H), 5.28 (s, 1H), 5.09 (s, 1H), 3.34 – 3.20 (m, 1H), 2.45 (dd, *J* = 18.3, 7.2 Hz, 1H), 2.31 – 2.10 (m, 3H), 2.04 (ddt, *J* = 18.1, 12.2, 6.2 Hz, 1H), 1.74 (dd, *J* = 18.4, 11.5 Hz, 1H), 1.16 – 0.99 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 220.2, 146.8, 140.4, 128.5, 127.8, 126.4, 113.8, 49.7, 46.8, 38.7, 36.2, 29.6, 20.4. **IR** (ATR): 2953, 1734, 1627, 1494, 1454, 1155 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{18}ONa$ $[M+Na]^+$ 237.1255, found 237.1256. **Chiral SFC**: 250 mm CHIRALPAK AD, 1% *i*-PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.4 min, $t_{R2}$ (major) = 10.4 min.

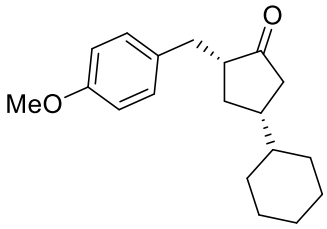



**(2*R*,4*R*)-4-methyl-2-(3-phenylprop-2-yn-1-yl)cyclopentan-1-one (2h)**: The title compound was synthesized according to Method A at 60 °C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (14.5 mg, 68% yield, 11:1 *dr*, 95% *ee*, $[\alpha]^{24}_D$ = +212 (*c* 0.81, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 5.0 Hz, 2H), 7.28 (dd, *J* = 4.5, 2.3 Hz, 3H), 2.80 (dd, *J* = 16.8, 3.3 Hz, 1H), 2.63 – 2.36 (m, 4H), 2.21 (dt, *J* = 18.1, 5.9 Hz, 1H), 1.78 (dd, *J* = 18.4, 11.6 Hz, 1H), 1.49 (q, *J* = 15.1 Hz, 1H), 1.19 (d, *J* = 6.4 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.5, 131.7, 128.3, 127.9, 123.8, 87.5, 81.9, 49.8, 46.9, 37.8, 29.6, 20.4, 19.7. **IR** (ATR): 2954, 1738, 1498, 1455, 1339, 1156, 911 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}ONa$ $[M+Na]^+$ 235.1099, found 235.1092. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 1% *i*-PrOH, 3.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 4.4 min, $t_{R2}$ (minor) = 5.3 min.

**(2*R*,4*R*)-4-hexyl-2-(4-methoxybenzyl)cyclopentan-1-one (2i)**: The title compound was synthesized according to Method A and isolated by prep TLC (5% EtOAc in hexanes) as a yellow oil (18.9 mg, 66% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = +82 (*c* 1.2, $CHCl_3$)). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.11 (dd, *J* = 13.9, 3.7 Hz, 1H), 2.49 (dd, *J* = 14.3, 9.3 Hz, 2H), 2.38 (d, *J* = 9.1 Hz, 1H), 2.23 – 2.12 (m, 1H), 2.06 – 1.92 (m, 1H), 1.72 (dd, *J* = 18.5, 11.6 Hz, 1H), 1.38 (s, 2H), 1.27 (s, 8H), 1.14 (q, *J* = 12.1 Hz, 1H), 0.88 (t, *J* = 6.3 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 219.7, 158.1, 132.2, 129.9, 113.9, 55.4, 52.6, 45.6, 36.3, 36.0, 35.0, 34.8, 31.9, 29.5, 27.9, 22.8, 14.2. **IR** (ATR): 2954, 2922, 2853, 1737, 1611, 1512, 1464, 1245, 1176, 1036 $cm^{-1}$. **HRMS** calculated

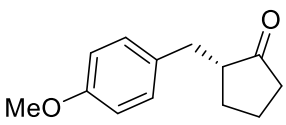


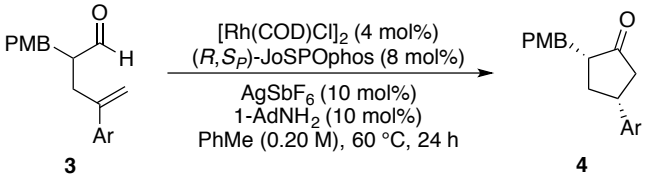
for $C_{19}H_{28}O_2Na$ $[M+Na]^+$ 311.1987, found 311.1980. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 2% *i*-PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 6.2 min, $t_{R2}$ (minor) = 11.9 min.



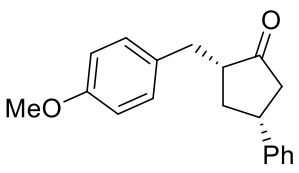

**(2*R*,4*R*)-4-cyclohexyl-2-(4-methoxybenzyl)cyclopentan-1-one (2j)**: The title compound was synthesized according to Method A at 60 °C using (*R*,$S_p$)-JoSPOphos and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (25.5 mg, 89% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = +46 (*c* 0.39, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.12 (dd, *J* = 13.9, 4.0 Hz, 1H), 2.48 (dt, *J* = 21.9, 11.0 Hz, 2H), 2.41 – 2.27 (m, 1H), 2.24 – 2.12 (m, 1H), 1.83 – 1.59 (m, 7H), 1.28 – 1.05 (m, 5H), 1.00 – 0.79 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 219.6, 158.1, 132.2, 129.9, 114.0, 55.4, 52.7, 43.7, 43.6, 40.9, 34.8, 34.1, 32.0, 31.0, 26.6, 26.3, 26.2. **IR** (ATR): 2921, 2849, 1735, 1611, 1511, 1448, 1245, 1176, 1035, 831 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{26}O_2H$ $[M+H]^+$ 287.2011, found 287.1998. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 2% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 11.9 min, $t_{R2}$ (minor) = 19.3 min.

**(*R*)-2-(4-methoxybenzyl)cyclopentan-1-one (2k)**: The title compound was synthesized according to Method A and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (10.6 mg, 52% yield, 82% *ee*, $[\alpha]^{24}_D$ = +107 (*c* 0.48, $CHCl_3$)). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.07 (dd, *J* = 14.0, 3.7 Hz, 1H), 2.53 (dd, *J* = 13.9, 9.3 Hz, 1H), 2.38 – 2.26 (m, 2H), 2.16 – 2.04 (m, 2H), 1.95 (d, *J* = 6.5 Hz, 1H), 1.79 – 1.67 (m, 1H), 1.57 (dd, *J* = 15.5, 7.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 220.5, 158.2, 132.1, 130.0, 114.0, 55.4, 51.3, 38.4, 34.8, 29.2, 20.7. **IR** (ATR): 2957, 1734, 1610, 1510, 1243, 1177 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{16}O_2Na$ $[M+Na]^+$ 227.1048, found 227.1042. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 6.4 min, $t_{R2}$ (minor) = 7.8 min.

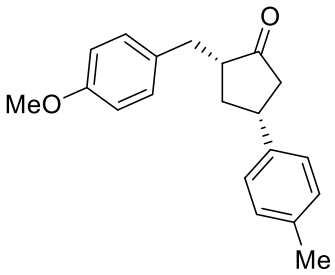




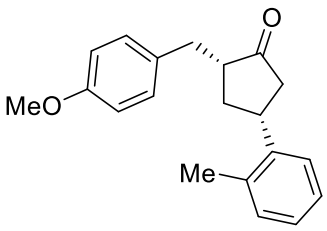

**Method B:** In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol, 4 mol%), (*R*,$S_P$)-JoSPOphos (4.4 mg, 0.0080 mmol, 8 mol%), and toluene (0.50 mL, 0.20 M) were added to a 1 dram vial equipped with a magnetic stir bar. The solution was stirred at 30 °C for 10 min. $AgSbF_6$ (3.4 mg, 0.010 mmol, 10 mol%), was added, and the resulting mixture was stirred at 30 °C for 30 min. Aldehyde **3** (0.10 mmol, 1.0 equiv) and 1-$AdNH_2$ (1.5 mg, 0.010 mmol, 10 mol%) were added. The vial was then sealed with a Teflon-lined screw cap and stirred at 60 °C for 24 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The ketone **4** was purified using preparative thin-layer chromatography.



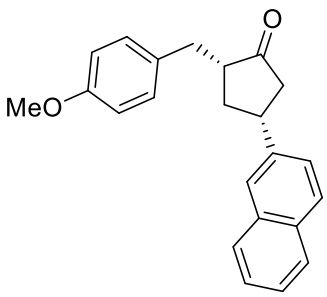

**(2*R*,4*R*)-2-(4-methoxybenzyl)-4-phenylcyclopentan-1-one (4a)**: The title compound was synthesized according to Method B and isolated by prep TLC (5% EtOAc in hexanes) as a white solid (21.3 mg, 76% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = +60.3 (*c* 1.0, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 – 7.18 (m, 3H), 7.11 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 3.35 – 3.23 (m, 1H), 3.19 (dd, *J* = 13.1, 3.2 Hz, 1H), 2.79 (dd, *J* = 19.0, 7.1 Hz, 1H), 2.67 – 2.51 (m, 2H), 2.46 (ddd, *J* = 12.9, 7.7, 2.2 Hz, 1H), 2.30(dd, *J* = 18.5, 12.2 Hz, 1H), 1.69 (q, *J* = 12.1 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.2, 158.3, 143.0, 131.9, 130.0, 128.8, 126.84, 126.83, 114.1, 55.4, 53.0, 45.9, 40.1, 37.7, 34.8. **IR** (ATR): 2921, 1724, 1608, 1510, 1441, 1242, 1028, 811, 758, 699 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{20}O_2Na$ $[M+Na]^+$ 303.1361, found 303.1375. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 8% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ = 7.6 min, $t_{R2}$ = 9.2 min, $t_{R3}$ (major) = 10.7 min, $t_{R4}$ (minor) = 12.0 min.



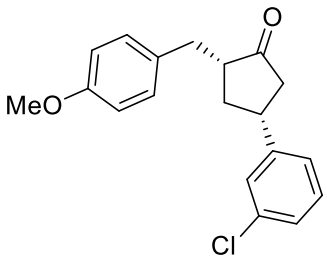

**(2*R*,4*R*)-2-(4-methoxybenzyl)-4-(p-tolyl)cyclopentan-1-one (4b)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a white solid (26.5 mg, 90% yield, >20:1 *dr*, 95% *ee*, $[\alpha]^{24}_{D}$ = +67.8 (*c* 1.6, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 15.5, 8.3 Hz, 6H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.27 (dt, *J* = 11.9, 6.3 Hz, 1H), 3.18 (dt, *J* = 11.2, 5.7 Hz, 1H), 2.77 (dd, *J* = 18.5, 7.5 Hz, 1H), 2.67 – 2.51 (m, 2H), 2.44 (dt, *J* = 11.9, 3.8 Hz, 1H), 2.34 (s, 3H), 2.28 (dd, *J* = 18.5, 12.2 Hz, 1H), 1.66 (q, *J* = 12.0 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.3, 158.2, 140.0, 136.4, 131.9, 130.0, 129.4, 126.7, 114.0, 55.4, 53.0, 46.0, 39.7, 37.8, 34.8, 21.1. **IR** (ATR): 2923, 1721, 1608, 1510, 1440, 1242, 1170, 1031, 828, 811 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{22}O_2Na$ $[M+Na]^+$ 317.1518, found 317.1511. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ = 6.9 min, $t_{R2}$ = 9.5 min, $t_{R3}$ (major) = 10.7 min, $t_{R4}$ (minor) = 12.2 min.



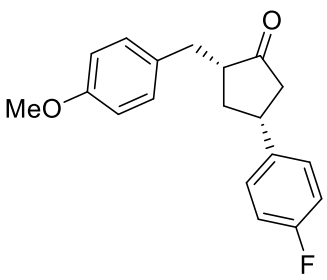

**(2*R*,4*R*)-2-(4-methoxybenzyl)-4-(*o*-tolyl)cyclopentan-1-one (4c)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (22.5 mg, 80% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_{D}$ = +44.3 (*c* 1.4, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.80 (s, 3H), 3.54 – 3.40 (m, 1H), 3.21 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.75 (dd, *J* = 18.5, 7.3 Hz, 1H), 2.68 – 2.53 (m, 2H), 2.41 – 2.31 (m, 4H), 2.26 (dd, *J* = 18.5, 12.2 Hz, 1H), 1.72 (q, *J* = 12.1 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.3, 158.2, 140.8, 136.1, 131.9, 130.7, 130.0, 126.58, 126.56, 124.9, 114.0, 55.4, 52.9, 45.6, 36.7, 36.3, 34.9, 19.8. **IR** (ATR): 2931, 1736, 1611, 1511, 1441, 1243, 1176, 1033, 835, 755 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{22}O_2Na$ $[M+Na]^+$ 317.1518, found 317.1514. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ = 6.3 min, $t_{R2}$ = 6.6 min, $t_{R3}$ (major) = 8.3 min, $t_{R4}$ (minor) = 12.5 min.




**(2*R*,4*R*)-2-(4-methoxybenzyl)-4-(naphthalen-2-yl)cyclopentan-1-one (4d)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (29.1 mg, 88% yield, >20:1 *dr*, 96% *ee*, $[\alpha]^{24}_{D}$ = +65.0 (*c* 1.8, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.81 (t, *J* = 7.9 Hz, 3H), 7.64 (s, 1H), 7.52 – 7.42 (m, 2H), 7.34 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.54 – 3.37 (m, 1H), 3.29 – 3.14 (m, 1H), 2.87 (dd, *J* = 18.9, 7.2 Hz, 1H), 2.72 – 2.59 (m, 2H), 2.59 – 2.48 (m, 1H), 2.41 (dd, *J* = 18.5, 12.2 Hz, 1H), 1.79 (q, *J* = 11.8 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.1, 158.3, 140.4, 133.6, 132.5, 131.9, 130.0, 128.5, 127.8, 127.7, 126.4, 125.8, 125.4, 125.0, 114.1, 55.4, 53.0, 45.9, 40.2, 37.6, 34.8. **IR** (ATR): 2930, 1736, 1610, 1511, 1300, 1243, 1177, 1033, 853, 817 $cm^{-1}$. **HRMS** calculated for $C_{23}H_{22}O_2Na$ $[M+Na]^+$ 353.1518, found 353.1534. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 7% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ = 29.5 min, $t_{R2}$ = 49.4 min, $t_{R3}$ (major) = 56.5 min, $t_{R4}$ (minor) = 64.8 min.

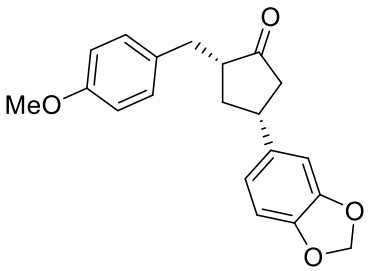


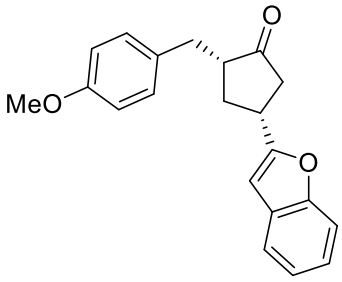

**(2*R*,4*R*)-4-(3-chlorophenyl)-2-(4-methoxybenzyl)cyclopentan-1-one (4e)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (23.9 mg, 77% yield, >20:1 *dr*, 94% *ee*, $[\alpha]^{24}_{D}$ = +93.7 (*c* 1.4, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.17 (m, 3H), 7.09 (t, *J* = 7.8 Hz, 3H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.32 – 3.14 (m, 2H), 2.78 (dd, *J* = 18.5, 7.4 Hz, 1H), 2.58 (ddt, *J* = 12.4, 9.0, 6.3 Hz, 2H), 2.49 – 2.39 (m, 1H), 2.25 (dd, *J* = 18.5, 12.2 Hz, 1H), 1.65 (q, *J* = 12.0 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 217.3, 158.3, 145.1, 134.6, 131.7, 130.02, 129.96, 127.1, 127.0, 125.1, 114.1, 55.4, 52.8, 45.7, 39.8, 37.4, 34.7. **IR** (ATR): 2931, 1737, 1597, 1511, 1243, 1176, 1033, 832, 784, 692 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{19}ClO_2Na$ $[M+Na]^+$ 337.0971, found 337.0977. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 7% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ = 5.2 min, $t_{R2}$ = 6.0 min, $t_{R3}$ (major) = 6.3 min, $t_{R4}$ (minor) = 7.3 min.



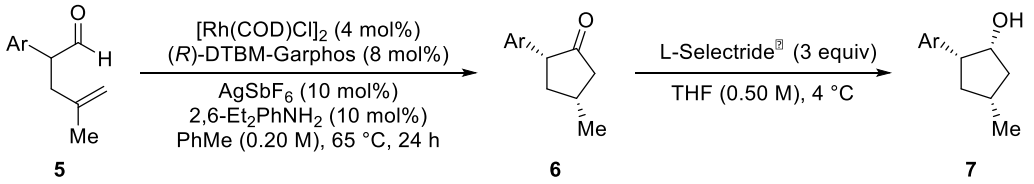

**(2*R*,4*R*)-4-(4-fluorophenyl)-2-(4-methoxybenzyl)cyclopentan-1-one (4f)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (27.2 mg, 91% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_{D}$ = +86.7 (*c* 1.6, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 7.00 (t, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.27 (ddd, *J* = 18.9, 12.5, 6.6 Hz, 1H), 3.21 – 3.11 (m, 1H), 2.78 (dd, *J* = 18.7, 7.5 Hz, 1H), 2.67 – 2.50 (m, 2H), 2.43 (dt, *J* = 10.7, 5.4 Hz, 1H), 2.24 (dd, *J* = 18.5, 12.2 Hz, 1H), 1.69 – 1.57 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 217.8, 161.7 (d, *J* = 244.9 Hz), 158.3, 138.64 (d, *J* = 3.1 Hz), 131.7, 130.0, 128.3 (d, *J* = 7.8 Hz), 115.5 (d, *J* = 21.2 Hz), 114.1, 55.4, 52.9, 46.1, 39.4, 37.7, 34.7. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -116.5. **IR** (ATR): 2919, 1737, 1609, 1510, 1243, 1221, 1177, 1149, 1033, 865 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{19}FO_2Na$ $[M+Na]^+$ 321.1267, found 321.1258. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 2% *i*-PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ = 10.2 min, $t_{R2}$ = 11.3 min, $t_{R3}$ (major) = 12.6 min, $t_{R4}$ (minor) = 15.9 min.

**(2*R*,4*R*)-4-(benzo[*d*][1,3]dioxol-5-yl)-2-(4-methoxybenzyl)cyclopentan-1-one (4g)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (10% EtOAc in hexanes) as a yellow solid (27.0 mg, 83% yield, >20:1 *dr*, 96% *ee*, $[\alpha]^{24}_{D}$ = +94.7 (*c* 1.5, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.71 – 6.62 (m, 2H), 5.93 (s, 2H), 3.79 (s, 3H), 3.20 (ddd, *J* = 16.7, 12.8, 5.0 Hz, 2H), 2.74 (dd, *J* = 18.4, 7.6 Hz, 1H), 2.65 – 2.47 (m, 2H), 2.45 – 2.34 (m, 1H), 2.21 (dd, *J* = 18.5, 12.2 Hz, 1H), 1.62 (q, *J* = 12.1 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.0, 158.2, 148.0, 146.4, 136.9, 131.8, 130.0, 119.8, 114.0, 108.4, 107.2, 101.1, 55.4, 52.9, 46.2, 39.8, 37.8, 34.7. **IR** (ATR): 2925, 1717, 1511, 1439, 1239, 1177, 1030, 935, 836, 806 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{20}O_4Na$ $[M+Na]^+$ 347.1259, found 347.1270. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 5% *i*-PrOH, 2.5 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 8.6 min, $t_{R2}$ (minor) = 10.4 min.



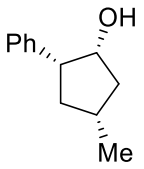


**(2*R*,4*R*)-4-(benzofuran-2-yl)-2-(4-methoxybenzyl)cyclopentan-1-one (4h)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a yellow solid (17.1 mg, 53% yield, >20:1 *dr*, 74% *ee*, $[\alpha]^{24}_{D}$ = +134.6 (*c* 0.97, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 1H), 7.44 – 7.39 (m, 1H), 7.27 – 7.16 (m, 2H), 7.13 – 7.07 (m, 2H), 6.87 – 6.80 (m, 2H), 6.43 (s, 1H), 3.80 (s, 3H), 3.54 – 3.40 (m, 1H), 3.26 – 3.15 (m, 1H), 2.83 (dd, *J* = 18.6, 7.9 Hz, 1H), 2.64 – 2.42 (m, 4H), 1.91 – 1.79 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 216.9, 159.4, 158.3, 154.9, 131.6, 130.0, 128.5, 123.9, 122.9, 120.7, 114.1, 111.0, 101.7, 55.4, 52.3, 43.4, 34.9, 34.8, 34.1. **IR** (ATR): 2930, 1724, 1608, 1510, 1453, 1245, 1176, 1031, 805, 738 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{20}O_3Na$ $[M+Na]^+$ 343.1310, found 343.1303. **Chiral SFC**: 100 mm CHIRALCEL OJ-H, 10% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 15.3 min, $t_{R2}$ (major) = 22.9 min.

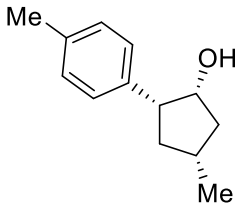



**Method C:** In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol, 4 mol%), (*R*)-DTBM-Garphos (10.7 mg, 0.0080 mmol, 8 mol%), and toluene (0.50 mL, 0.20 M) were added to a 1 dram vial equipped with a magnetic stir bar. The solution was stirred at 30 °C for 10 min. $AgSbF_6$ (3.4 mg, 0.010 mmol, 10 mol%), was added, and the resulting mixture was stirred at 30 °C for 30 min. Aldehyde **5** (0.10 mmol, 1.0 equiv) and 2,6-$Et_2PhNH_2$ (1.6 mL, 0.010 mmol, 10 mol%) were added. The vial was then sealed with a Teflon-lined screw cap and stirred at 65 °C for 24 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The hydroacylation yield and diastereoselectivity were determined by $^1$H NMR analysis of the unpurified reaction mixture using triphenylmethane as an internal standard. The crude ketone **6** was dissolved in THF (0.50 M) and cooled to 4 °C. L-Selectride® (3 equiv, 1.0 M in THF) was added dropwise, and the resulting mixture was allowed to stirred at 4 °C for 16 h. The reaction mixture was quenched with 2 M aqueous NaOH and 30% aqueous $H_2O_2$, and the resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were

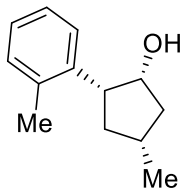
washed with brine, dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The alcohol **7** was purified using preparative thin-layer chromatography.



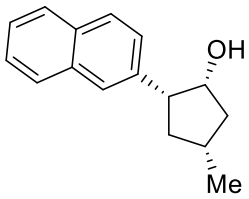

**(1*R*,2*R*,4*R*)-4-methyl-2-phenylcyclopentan-1-ol (7a)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (12.7 mg, 76% yield over 2 steps, >20:1:1:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = –25.1 (*c* 0.60, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.32(m, 2H), 7.32 – 7.28 (m, 2H), 7.28 – 7.23 (m, 1H), 4.30 (dd, *J* = 7.5, 3.2 Hz, 1H), 3.16 – 3.02 (m, 1H), 2.43 – 2.26 (m, 1H), 2.21 – 2.09 (m, 1H), 2.05 (dt, *J* = 18.1, 6.3 Hz, 1H), 1.87 – 1.72 (m, 1H), 1.41 (ddd, *J* = 14.2, 7.2, 2.1 Hz, 1H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.10 (d, *J* = 5.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.9, 128.8, 128.7, 126.8, 75.8, 52.7, 42.7, 36.9, 32.3, 21.8. **IR** (ATR): 3426, 2952, 2868, 1683, 1449, 1215, 1030, 1004, 754, 698 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{16}ONa$ $[M+Na]^+$ 199.1099, found 199.1092. **Chiral SFC**: 250 mm CHIRALPAK AD, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 6.2 min, $t_{R2}$ = 6.7 min, $t_{R3}$ (major) = 7.5 min, $t_{R4}$ = 9.2 min.



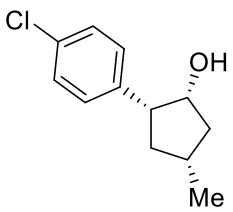

**(1*R*,2*R*,4*R*)-4-methyl-2-(*p*-tolyl)cyclopentan-1-ol (7b)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (12.5 mg, 65% yield over 2 steps, >20:1:1:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = –22.0 (*c* 0.68, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 4.28 (t, *J* = 4.5 Hz, 1H), 3.12 – 3.01 (m, 1H), 2.39 – 2.30 (m, 4H), 2.19 – 2.06 (m, 1H), 2.02 (dt, *J* = 12.5, 6.3 Hz, 1H), 1.78 (dd, *J* = 23.2, 12.0 Hz, 1H), 1.40 (ddd, *J* = 14.2, 7.3, 1.9 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.12 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 136.7, 136.4, 129.4, 128.6, 75.8, 52.3, 42.6, 37.0, 32.3, 21.8, 21.1. **IR** (ATR): 3449, 2951, 2926, 2868, 1515, 1455, 1129, 1103, 1002, 815 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}ONa$ $[M+Na]^+$ 213.1255, found 213.1255. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 3% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.5 min, $t_{R2}$ (major) = 7.5 min.




**(1*R*,2*R*,4*R*)-4-methyl-2-(*o*-tolyl)cyclopentan-1-ol (7c)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (9.3 mg, 48% yield over 2 steps, >20:1:1:1 *dr*, 95% *ee*, $[\alpha]^{24}_{D}$ = –33.0 (*c* 0.53, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.2 Hz, 1H), 7.25 – 7.13 (m, 3H), 4.37 – 4.31 (m, 1H), 3.31 – 3.17 (m, 1H), 2.44 – 2.31 (m, 4H), 2.08 (dt, *J* = 16.9, 8.6 Hz, 1H), 1.91 (dd, *J* = 13.6, 5.6 Hz, 2H), 1.39 (ddd, *J* = 14.2, 7.9, 2.2 Hz, 1H), 1.20 (d, *J* = 6.6 Hz, 3H), 1.04 – 0.88 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.3, 136.8, 130.6, 128.2, 126.8, 126.1, 73.2, 49.1, 43.0, 37.1, 32.2, 21.4, 19.9. **IR** (ATR):3439, 2951, 2927, 2868, 1489, 1457, 1130, 1004, 755, 726 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}ONa$ $[M+Na]^+$ 213.1255, found 213.1255. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 2% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 5.4 min, $t_{R2}$ (major) = 6.5 min.

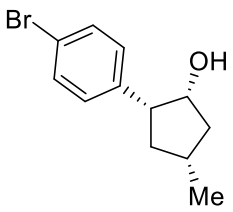



**(1*R*,2*R*,4*R*)-4-methyl-2-(naphthalen-2-yl)cyclopentan-1-ol (7d)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a yellow solid (11.5 mg, 51% yield over 2 steps, >20:1:1:1 *dr*, 97% *ee*, $[\alpha]^{24}_{D}$ = –29.7 (*c* 0.75, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 3H), 7.75 (s, 1H), 7.47 (ddd, *J* = 16.9, 11.6, 6.6 Hz, 3H), 4.41 (t, *J* = 4.6 Hz, 1H), 3.32 – 3.21 (m, 1H), 2.47 – 2.34 (m, 1H), 2.26 – 2.07 (m, 2H), 1.95 (dd, *J* = 22.9, 11.6 Hz, 1H), 1.46 (ddd, *J* = 14.3, 7.0, 1.9 Hz, 1H), 1.24 (d, *J* = 6.4 Hz, 3H), 1.14 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.4, 133.7, 132.6, 128.2, 127.8, 127.7, 127.4, 127.1, 126.3, 125.7, 75.8, 52.8, 42.8, 36.9, 32.4, 21.8. **IR** (ATR): 3466, 2950, 2925, 2865, 1507, 1454, 1190, 1129, 1002, 829, 745 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}ONa$ $[M+Na]^+$ 249.1255, found 249.1255. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 3% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 18.4 min, $t_{R2}$ (major) = 20.7 min.

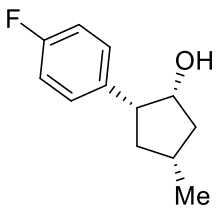



**(1*R*,2*R*,4*R*)-2-(4-chlorophenyl)-4-methylcyclopentan-1-ol (7e)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (12.7 mg, 57% yield over 2 steps, >20:1:1:1 *dr*, 99% *ee*, $[\alpha]^{24}_{D}$ = –40.9 (*c* 0.30, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 4.32 – 4.25 (m,

1H), 3.09 – 2.98 (m, 1H), 2.42 – 2.29 (m, 1H), 2.12 (dtd, *J* = 13.6, 10.3, 6.8 Hz, 1H), 2.02 (dt, *J* = 12.5, 6.2 Hz, 1H), 1.75 (dd, *J* = 23.2, 11.9 Hz, 1H), 1.39 (ddd, *J* = 14.3, 7.2, 2.1 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.05 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.5, 132.6, 130.1, 128.7, 75.7, 52.0, 42.9, 37.1, 32.3, 21.7. **IR** (ATR): 3437, 2952, 2927, 2868, 1492, 1129, 1090, 1002, 831, 721 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{15}ClO$ $[M]^+$ 210.0811, found 210.0817. **Chiral SFC**: 250 mm CHIRALPAK AD, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 9.6 min, $t_{R2}$ = 10.4 min, $t_{R3}$ (major) = 11.5 min, $t_{R4}$ = 12.0 min.

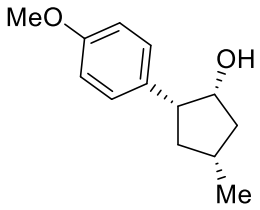



**(1*R*,2*R*,4*R*)-2-(4-bromophenyl)-4-methylcyclopentan-1-ol (7f)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (14.2 mg, 57% yield over 2 steps, >20:1:1:1 *dr*, 98% *ee*, $[\alpha]^{24}_D$ = –27.7 (*c* 0.33, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.14 (m, 2H), 4.29 (t, *J* = 4.5 Hz, 1H), 3.08 – 2.96 (m, 1H), 2.42 – 2.29 (m, 1H), 2.19 – 2.06 (m, 1H), 2.06 – 1.96 (m, 1H), 1.81 – 1.67 (m, 1H), 1.39 (ddd, *J* = 14.3, 7.2, 2.1 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.03 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.0, 131.7, 130.5, 120.6, 75.7, 52.1, 42.9, 37.1, 32.3, 21.7. **IR** (ATR): 3440, 2951, 2926, 2868, 1489, 1129, 1072, 1009, 818, 795 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{15}BrO$ $[M]^+$ 254.0306, found 254.0297. **Chiral SFC**: 250 mm CHIRALPAK AD, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 12.9 min, $t_{R2}$ (major) = 16.1 min.

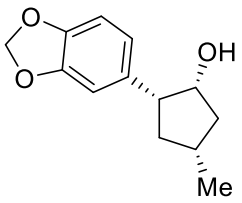



**(1*R*,2*R*,4*R*)-2-(4-fluorophenyl)-4-methylcyclopentan-1-ol (7g)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (11.5 mg, 56% yield over 2 steps, >20:1:1:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = –18.3 (*c* 0.26, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 7.0, 3.8 Hz, 2H), 7.07 – 6.99 (m, 2H), 4.28 (t, *J* = 4.5 Hz, 1H), 3.12 – 2.98 (m, 1H), 2.40 – 2.28 (m, 1H), 2.12 (dtd, *J* = 13.3, 10.0, 6.8 Hz, 1H), 2.02 (dt, *J* = 12.4, 6.3 Hz, 1H), 1.75 (dd, *J* = 22.9, 12.2 Hz, 1H), 1.39 (ddd, *J* = 14.4, 7.2, 2.1 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.05 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 161.9 (d, *J* = 244.7 Hz), 135.5 (d, *J* = 3.2 Hz), 130.1 (d, *J* = 7.8 Hz), 115.4 (d, *J* = 21.0 Hz), 75.7, 51.9, 42.8, 37.3, 32.3, 21.8. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -116.8. **IR** (ATR): 3469, 2955, 2929, 2871, 1598, 1509,

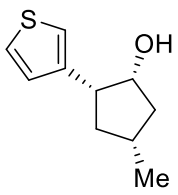
1222, 1157, 1004, 832 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{15}FO$ $[M]^+$ 194.1107, found 194.1110. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 2% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 4.6 min, $t_{R2}$ (major) = 5.8 min.




**(1*R*,2*R*,4*R*)-2-(4-methoxyphenyl)-4-methylcyclopentan-1-ol (7h)**: The title compound was synthesized according to Method C and isolated by prep TLC (10% EtOAc in hexanes) as a colorless oil (10.4 mg, 50% yield over 2 steps, >20:1:1:1 *dr*, 99% *ee*, $[\alpha]^{24}_D$ = –39.1 (*c* 0.51, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.17 (m, 2H), 6.93 – 6.85 (m, 2H), 4.28 – 4.21 (m, 1H), 3.81 (s, 3H), 3.10 – 2.98 (m, 1H), 2.39 – 2.28 (m, 1H), 2.11 (ddt, *J* = 10.2, 9.5, 6.7 Hz, 1H), 2.01 (dt, *J* = 12.4, 6.4 Hz, 1H), 1.81 – 1.68 (m, 1H), 1.39 (ddd, *J* = 14.2, 7.3, 2.1 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.12 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.6, 131.7, 129.7, 114.1, 75.8, 55.4, 51.8, 42.6, 37.2, 32.3, 21.8. **IR** (ATR): 3450, 2951, 2868, 1611, 1512, 1245, 1178, 1033, 1002, 830 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_2Na$ $[M+Na]^+$ 229.1205, found 229.1204. **Chiral SFC**: 250 mm CHIRALPAK AD, 5% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 10.2 min, $t_{R2}$ = 11.3 min, $t_{R3}$ (major) = 12.4 min, $t_{R4}$ = 14.2 min.



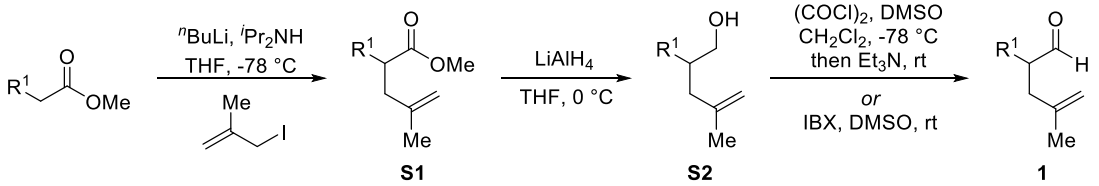

**(1*R*,2*R*,4*R*)-2-(benzo[*d*][1,3]dioxol-5-yl)-4-methylcyclopentan-1-ol (7i)**: The title compound was synthesized according to Method C and isolated by preparatory TLC (10% EtOAc in hexanes) as a colorless oil (11.3 mg, 51% yield over 2 steps, >20:1:1:1 *dr*, 99% *ee*, $[\alpha]^{24}_D$ = –40.9 (*c* 0.58, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.82 – 6.76 (m, 2H), 6.74 (ddd, *J* = 8.0, 1.6, 0.6 Hz, 1H), 5.95 (s, 2H), 4.28 – 4.16 (m, 1H), 3.07 – 2.94 (m, 1H), 2.38 – 2.24 (m, 1H), 2.16 – 2.03 (m, 1H), 1.99 (dt, *J* = 12.4, 6.4 Hz, 1H), 1.77 – 1.64 (m, 1H), 1.38 (ddd, *J* = 14.2, 7.2, 2.0 Hz, 1H), 1.17 (d, *J* = 6.6 Hz, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.0, 146.4, 133.6, 121.5, 109.2, 108.4, 101.1, 75.8, 52.3, 42.6, 37.2, 32.2, 21.8. **IR** (ATR): 3557, 2951, 2868, 1503, 1489, 1440, 1250, 1229, 1037, 932 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{16}O_3Na$ $[M+Na]^+$ 243.0997, found 243.1000. **Chiral SFC**: 250 mm CHIRALPAK AD, 10% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 7.0 min, $t_{R2}$ = 7.9 min, $t_{R3}$ (major) = 11.6 min, $t_{R4}$ = 14.4 min.

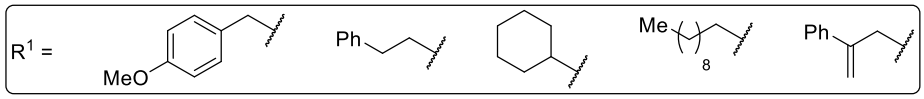


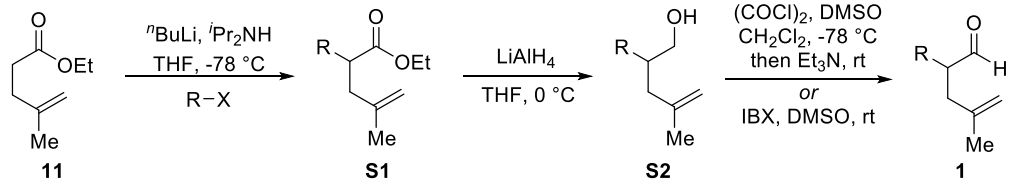
**(1*R*,2*R*,4*R*)-4-methyl-2-(thiophen-3-yl)cyclopentan-1-ol (7j)**: The title compound was synthesized according to Method B and isolated by preparatory TLC (5% EtOAc in hexanes) as a colorless oil (9.3 mg, 51% yield, >20:1:1:1 *dr*, >99% *ee*, $[\alpha]^{24}_{D}$ = –26.1 (*c* 0.52, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.04 (d, *J* = 4.9 Hz, 1H), 4.27 (t, *J* = 4.4 Hz, 1H), 3.21 – 3.07 (m, 1H), 2.37 – 2.22 (m, 1H), 2.19 – 2.01 (m, 2H), 1.79 – 1.65 (m, 1H), 1.40 (ddd, *J* = 14.3, 6.5, 2.0 Hz, 1H), 1.19 (s, 1H), 1.17 (d, *J* = 6.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.1, 128.2, 126.0, 121.7, 75.3, 48.5, 42.5, 38.0, 32.2, 21.9. **IR** (ATR): 3440, 2951, 2926, 2867, 1455, 1128, 1002, 833, 778, 683 $cm^{-1}$. **HRMS** calculated for $C_{10}H_{14}OSNa$ $[M+Na]^+$ 205.0663, found 205.0658. **Chiral SFC**: 250 mm CHIRALPAK AD, 2% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 14.0 min, $t_{R2}$ (major) = 18.9 min.

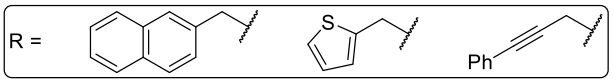
## 3. Preparation of Substrates

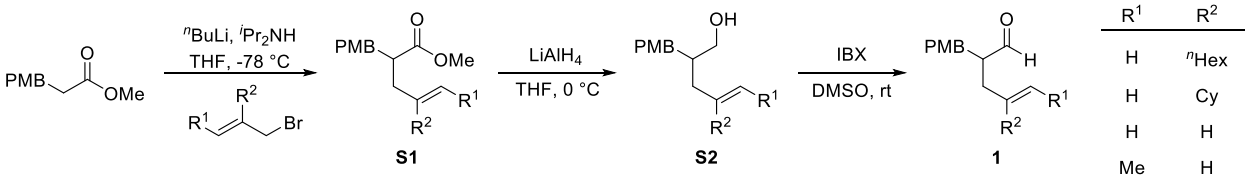
### *Preparation of Aldehydes 1*




| R$^1$ | R$^2$ |
|---|---|
| H | $^n$Hex |
| H | Cy |
| H | H |
| Me | H |

***Preparation of methallyl iodide***

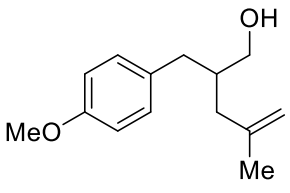
To a round bottom flask was added NaI (1.5 equiv) and acetone (1 M). Then, methallyl chloride (1.0 equiv) was added dropwise, and the resulting mixture was allowed to stir at rt for 3 h. The reaction was quenched with $H_2O$ and extracted with pentanes. The combined organic layers were washed with 10% aqueous $Na_2S_2O_3$, dried with anhydrous $MgSO_4$, and concentrated *in vacuo* below rt. The crude methallyl iodide was used without further purification.

***General Procedure for the Ester Alkylation***

To an oven-dried round bottom flask was added $^{i}Pr_2NH$ (1.2 equiv) and THF (0.5 M), and the resulting solution was cooled to -78 °C. Then, $^{n}$BuLi (1.1 equiv, 2.5 M in THF) was added dropwise, and the resulting mixture was stirred for 45 min. A solution of the ester (1 equiv) in THF (0.5 M) was added dropwise, and the resulting mixture was stirred for 1 h. The appropriate alkyl halide (1.2 equiv) was added, and the reaction mixture was stirred until full consumption of the ester was observed by GC-MS. The reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The alkylated ester was used without further purification.

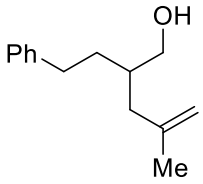
***General Procedure for the Reduction with $LiAlH_4$***

The crude alkylated ester was dissolved in THF (0.50 M), and the resulting solution was cooled to 0 °C. $LiAlH_4$ (1.5 equiv) was added portionwise, and the resulting mixture was allowed to stir for 30 min. The reaction was quenched using the Fieser method, filtered through celite, and concentrated *in vacuo*. The residue was purified by column chromatography to afford the pure alcohol **S2**.

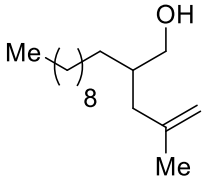



**2-(4-methoxybenzyl)-4-methylpent-4-en-1-ol (S2a)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 3-(4-methoxyphenyl)propanoate (3.9 g, 20 mmol, 1 equiv), $^{i}Pr_2NH$ (3.4 mL, 24 mmol, 1.2 equiv), $^{n}$BuLi (8.8 mL, 22 mmol, 1.1 equiv, 2.5 M in THF),methallyl iodide (4.4 g,

24 mmol, 1.2 equiv), and THF (80 mL, 0.25 M). Crude **S1a** (1 equiv) was reduced to **S2a** using $LiAlH_4$ (1.1 g, 30 mmol, 1.5 equiv) and THF (40 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2a** as a clear oil (2.27 g, 51% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.81 (s, 1H), 4.78 (s, 1H), 3.80 (s, 3H), 3.58 – 3.47 (m, 2H), 2.58 (d, *J* = 6.8 Hz, 2H), 2.13 (dd, *J* = 13.3, 7.9 Hz, 1H), 2.02 (dt, *J* = 12.6, 5.7 Hz, 2H), 1.74 (s, 3H), 1.43 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 144.7, 132.7, 130.2, 113.9, 112.3, 65.2, 55.4, 40.6, 40.4, 36.9, 22.4. **IR** (ATR): 3368, 2923, 2853, 1511, 1244, 887 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{20}O_2Na$ $[M+Na]^+$ 243.1361, found 243.1360.

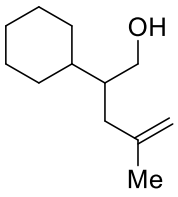



**4-methyl-2-phenethylpent-4-en-1-ol (S2c)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 4-phenylbutanoate (2.0 g, 11.2 mmol, 1 equiv), $^i$Pr$_2$NH (1.9 mL, 13.4 mmol, 1.2 equiv), $^n$BuLi (4.9 mL, 12.3 mmol, 1.1 equiv, 2.5 M in THF), methallyl iodide (2.4 g, 13.4 mmol, 1.2 equiv), and THF (45 mL, 0.25 M). Crude **S1c** (1 equiv) was reduced to **S2c** using $LiAlH_4$ (637 mg, 16.8 mmol, 1.5 equiv) and THF (22 mL, 0.51 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2c** as a colorless oil (1.30 g, 57% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.16 (m, 3H), 4.83 – 4.78 (m, 1H), 4.78 – 4.73 (m, 1H), 3.61 (s, 2H), 2.73 – 2.62 (m, 2H), 2.16 – 2.06 (m, 2H), 1.81 – 1.59 (m, 6H), 1.34 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.8, 142.6, 128.5, 125.9, 112.2, 65.8, 40.7, 38.0, 33.4, 33.0, 22.4. **IR** (ATR): 3335, 2920, 1648, 1453, 1029, 667 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{20}ONa$ $[M+Na]^+$ 227.1412, found 227.1412.

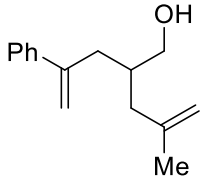



**2-(2-methylallyl)dodecan-1-ol (S2e)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl dodecanoate (2.1 g, 8.5 mmol, 1 equiv), $^i$Pr$_2$NH (1.4 mL, 10.2 mmol, 1.2 equiv), $^n$BuLi (3.7 mL, 9.4 mmol, 1.1 equiv, 2.5 M in THF), methallyl iodide (1.9 g, 10.2 mmol, 1.2 equiv), and THF (34 mL, 0.25 M). Crude **S1e** (1 equiv) was reduced to **S2e** using $LiAlH_4$ (484 mg, 12.8 mmol, 1.5 equiv) and THF (17 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2e** as a colorless oil (1.48 g, 72% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.78 (s, 1H), 4.74 (s, 1H),

3.55 (dd, $J$ = 5.3, 2.3 Hz, 2H), 2.10 – 2.00 (m, 2H), 1.74 (s, 3H), 1.73 – 1.56 (m, 2H), 1.27 (s, 18H), 0.89 (t, $J$ = 6.7 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.2, 111.9, 66.1, 40.9, 38.5, 32.1, 31.3, 30.1, 29.80, 29.77, 29.5, 27.1, 22.8, 22.4, 14.3. **IR** (ATR): 3343, 2921, 2852, 1455, 1375, 886 cm$^{-1}$. **HRMS** calculated for $C_{16}H_{32}O$ $[M]^+$ 240.2453, found 240.2458.

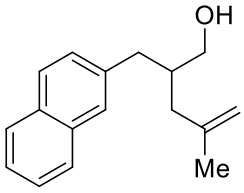



**2-cyclohexyl-4-methylpent-4-en-1-ol (S2f)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-cyclohexylacetate (1.5 g, 9.7 mmol, 1 equiv), $^{i}Pr_2NH$ (1.6 mL, 11.7 mmol, 1.2 equiv), $^{n}$BuLi (4.3 mL, 10.7 mmol, 1.1 equiv, 2.5 M in THF), methallyl iodide (2.1 g, 11.7 mmol, 1.2 equiv), and THF (39 mL, 0.25 M). Crude **S1f** (1 equiv) was reduced to **S2f** using $LiAlH_4$ (552 mg, 14.6 mmol, 1.5 equiv) and THF (19 mL, 0.51 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2f** as a colorless oil (1.25 g, 71% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.78 (s, 1H), 4.75 (s, 1H), 3.65 – 3.53 (m, 2H), 2.07 (ddd, $J$ = 23.0, 13.8, 7.4 Hz, 2H), 1.74 (s, 4H), 1.67 (d, $J$ = 10.3 Hz, 3H), 1.61 – 1.55 (m, 1H), 1.45 (d, $J$ = 11.8 Hz, 2H), 1.32 – 1.16 (m, 3H), 1.08 (dt, $J$ = 24.3, 12.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.8, 111.9, 64.1, 43.8, 39.0, 37.9, 30.2, 30.1, 27.0, 26.91, 26.87, 22.3. **IR** (ATR): 3335, 2910, 2850, 1647, 1447, 1069 cm$^{-1}$. **HRMS** calculated for $C_{12}H_{22}OH$ $[M+H]^+$ 183.1749, found 183.1753.

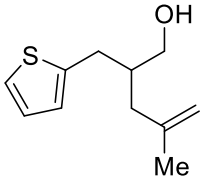



**4-methyl-2-(2-phenylallyl)pent-4-en-1-ol (S2g)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 4-phenylpent-4-enoate[1] (1.6 g, 8.3 mmol, 1 equiv), $^{i}Pr_2NH$ (1.4 mL, 10.0 mmol, 1.2 equiv), $^{n}$BuLi (3.6 mL, 9.1 mmol, 1.1 equiv, 2.5 M in THF), methallyl iodide (1.8 g, 10.0 mmol, 1.2 equiv), and THF (33 mL, 0.25 M). Crude **S1g** (1 equiv) was reduced to **S2g** using $LiAlH_4$ (472 mg, 12.5 mmol, 1.5 equiv) and THF (17 mL, 0.49 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2g** as a yellow oil (1.23 g, 68% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H), 7.38 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 5.32 (d, $J$ = 1.7 Hz, 1H), 5.12 (m, 1H), 4.83 – 4.77 (m, 1H), 4.77 – 4.70 (m, 1H), 3.54 (d, $J$ = 5.0 Hz, 2H), 2.55 (dd, $J$ = 4.8, 3.5 Hz, 2H), 2.16 – 2.01 (m, 2H), 1.88 – 1.75 (m, 1H), 1.63 (dd, $J$ = 1.4, 0.9 Hz, 3H), 1.45 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 147.5, 144.7, 141.1, 128.5, 127.6, 126.4, 114.4, 112.3, 65.6, 40.5, 37.7,

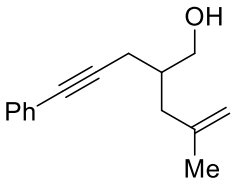
36.7, 22.3. **IR** (ATR): 3391, 2930, 1682, 1446, 1027 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{20}O$ $[M]^+$ 216.1514, found 216.1507.



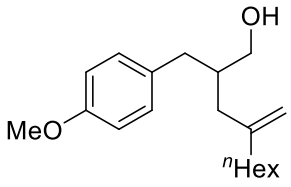

**4-methyl-2-(naphthalen-2-ylmethyl)pent-4-en-1-ol (S2b)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from ethyl 4-methylpent-4-enoate[2] (**11**) (1.7 g, 12 mmol, 1 equiv), $^{i}Pr_2NH$ (2.0 mL, 14.4 mmol, 1.2 equiv), $^{n}BuLi$ (5.3 mL, 13.2 mmol, 1.1 equiv, 2.5 M in THF), 2-(bromomethyl)naphthalene (3.2 g, 14.4 mmol, 1.2 equiv), and THF (48 mL, 0.25 M). Crude **S1b** (1 equiv) was reduced to **S2b** using $LiAlH_4$ (683 mg, 18 mmol, 1.5 equiv) and THF (24 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2b** as a yellow oil (1.64 g, 57% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 16.1, 7.8 Hz, 3H), 7.64 (s, 1H), 7.51 – 7.42 (m, 2H), 7.36 (dd, *J* = 8.3, 1.4 Hz, 1H), 4.84 (s, 1H), 4.82 (s, 1H), 3.63 – 3.53 (m, 2H), 2.88 – 2.75 (m, 2H), 2.27 – 2.04 (m, 3H), 1.76 (s, 3H), 1.46 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.6, 138.3, 133.7, 132.2, 128.1, 127.9, 127.7, 127.6, 126.1, 125.4, 112.4, 65.1, 62.9, 40.4, 37.9, 29.9, 22.4. **IR** (ATR): 3355, 2923, 1600, 1444, 1077 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{20}ONa$ $[M+Na]^+$ 263.1412, found 263.1418.



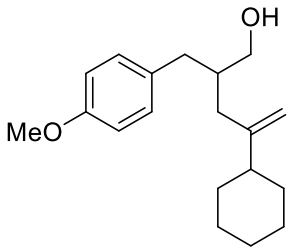

**4-methyl-2-(thiophen-2-ylmethyl)pent-4-en-1-ol (S2d)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from ethyl 4-methylpent-4-enoate[2] (**11**) (3.5 g, 25 mmol, 1 equiv), $^{i}Pr_2NH$ (4.2 mL, 30 mmol, 1.2 equiv), $^{n}BuLi$ (11 mL, 27.5 mmol, 1.1 equiv, 2.5 M in THF), 2-(bromomethyl)thiophene[3] (5.3 g, 30 mmol, 1.2 equiv), and THF (100 mL, 0.25 M). Crude **S1d** (1 equiv) was reduced to **S2d** using $LiAlH_4$ (1.4 g, 38 mmol, 1.5 equiv) and THF (50 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2d** as a yellow oil (3.73 g, 76% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 5.1 Hz, 1H), 6.94 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.82 (d, *J* = 3.4 Hz, 1H), 4.83 (s, 1H), 4.79 (s, 1H), 3.58 (d, *J* = 4.6 Hz, 2H), 2.95 – 2.79 (m, 2H), 2.18 – 1.99 (m, 3H), 1.75 (s, 3H), 1.43 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.3, 143.2, 126.9, 125.6, 123.6, 112.5, 64.9, 40.7, 40.0, 31.5, 22.4. **IR** (ATR): 3341, 2919, 1648, 1439, 1032, 888 $cm^{-1}$. **HRMS** calculated for $C_{11}H_{16}OSNa$ $[M+Na]^+$ 219.0820, found 219.0814.



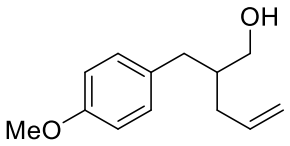

**4-methyl-2-(3-phenylprop-2-yn-1-yl)pent-4-en-1-ol (S2h)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from ethyl 4-methylpent-4-enoate[2] (**11**) (2.6 g, 18 mmol, 1 equiv), $^{i}Pr_2NH$ (3.1 mL, 21.6 mmol, 1.2 equiv), $^{n}BuLi$ (7.9 mL, 19.8 mmol, 1.1 equiv, 2.5 M in THF), (3-bromoprop-1-yn-1-yl)benzene[4] (4.2 g, 21.6 mmol, 1.2 equiv), and THF (72 mL, 0.25 M). Crude **S1h** (1 equiv) was reduced to **S2h** using $LiAlH_4$ (1.0 g, 27 mmol, 1.5 equiv) and THF (36 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2h** as a yellow oil (2.57 g, 67% yield). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.33 – 7.26 (m, 3H), 4.84 (s, 1H), 4.81 (s, 1H), 3.79 – 3.67 (m, 2H), 2.55 (dd, *J* = 17.0, 5.3 Hz, 1H), 2.46 (dd, *J* = 17.0, 6.6 Hz, 1H), 2.25 – 2.13 (m, 2H), 2.11 – 1.99 (m, 1H), 1.81 (s, 1H), 1.78 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.7, 131.7, 128.4, 127.8, 123.9, 112.6, 88.1, 82.3, 65.4, 39.5, 38.0, 22.4, 21.1. **IR** (ATR): 3334, 2928, 1649, 1489, 1069, 945 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{18}ONa$ $[M+Na]^+$ 237.1255, found 237.1243.



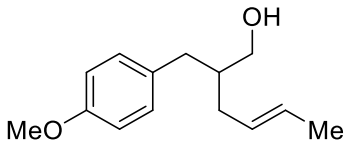

**2-(4-methoxybenzyl)-4-methylenedecan-1-ol (S2i)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 3-(4-methoxyphenyl)propanoate (971 mg, 5.0 mmol, 1 equiv), $^{i}Pr_2NH$ (0.85 mL, 6.0 mmol, 1.2 equiv), $^{n}BuLi$ (2.2 mL, 5.5 mmol, 1.1 equiv, 2.5 M in THF), 2-(bromomethyl)oct-1-ene[5] (1.2 g, 6.0 mmol, 1.2 equiv), and THF (20 mL, 0.25 M). Crude **S1i** (1 equiv) was reduced to **S2i** using $LiAlH_4$ (285 mg, 7.5 mmol, 1.5 equiv) and THF (10 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2i** as a yellow oil (717 mg, 49% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 4.81 (s, 1H), 4.80 (s, 1H), 3.80 (s, 3H), 3.53 (s, 2H), 2.58 (t, *J* = 11.3 Hz, 2H), 2.16 – 1.91 (m, 5H), 1.35 (s, 3H), 1.27 (s, 6H), 0.89 (t, *J* = 6.4 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.0, 148.8, 132.7, 130.2, 113.9, 111.0, 65.3, 55.4, 40.7, 38.5, 37.0, 35.8, 31.9, 29.2, 27.7, 22.8, 14.2. **IR** (ATR): 3351, 2925, 2855, 1612, 1511, 1441, 1244, 1176, 1035, 890 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{30}O_2Na$ $[M+Na]^+$ 313.2144, found 313.2131.




**4-cyclohexyl-2-(4-methoxybenzyl)pent-4-en-1-ol (S2j)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 3-(4-methoxyphenyl)propanoate (311 mg, 1.6 mmol, 1 equiv), $^{i}Pr_2NH$ (0.27 mL, 1.9 mmol, 1.2 equiv), $^{n}$BuLi (0.70 mL, 1.8 mmol, 1.1 equiv, 2.5 M in THF), (3-bromoprop-1-en-2-yl)cyclohexane[6] (488 mg, 2.4 mmol, 1.5 equiv), and THF (6.4 mL, 0.25 M). Crude **S1j** (1 equiv) was reduced to **S2j** using $LiAlH_4$ (91.1 mg, 2.4 mmol, 1.5 equiv) and THF (3.2 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2j** as a colorless oil (239 mg, 52% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.11 (d, $J$ = 8.6 Hz, 2H), 6.84 (d, $J$ = 8.6 Hz, 2H), 4.83 (s, 1H), 4.79 (s, 1H), 3.80 (s, 3H), 3.57 – 3.48 (m, 2H), 2.63 – 2.52 (m, 2H), 2.15 – 2.03 (m, 2H), 2.03 – 1.93 (m, 1H), 1.86 – 1.64 (m, 6H), 1.34 (s, 1H), 1.29 – 1.02 (m, 5H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 154.0, 132.8, 130.2, 113.9, 109.0, 65.3, 55.4, 43.6, 41.1, 37.8, 37.0, 32.8, 32.5, 27.0, 26.9, 26.5. **IR** (ATR): 3357, 2922, 2850, 1611, 1511, 1447, 1244, 1176, 1034, 885 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{28}O_2Na$ $[M+Na]^+$ 311.1987, found 311.1990.



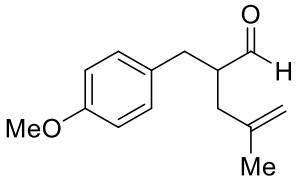

**2-(4-methoxybenzyl)pent-4-en-1-ol (S2k)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 3-(4-methoxyphenyl)propanoate (1.9 g, 9.8 mmol, 1 equiv), $^{i}Pr_2NH$ (1.7 mL, 11.8 mmol, 1.2 equiv), $^{n}$BuLi (4.3 mL, 10.8 mmol, 1.1 equiv, 2.5 M in THF), allyl bromide (1.0 mL, 11.8 mmol, 1.2 equiv), and THF (39 mL, 0.25 M). Crude **S1k** (1 equiv) was reduced to **S2k** using $LiAlH_4$ (558 mg, 14.7 mmol, 1.5 equiv) and THF (20 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2k** as a colorless oil (1.76 g, 87% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.11 (d, $J$ = 8.5 Hz, 2H), 6.84 (d, $J$ = 8.5 Hz, 2H), 5.84 (ddt, $J$ = 17.2, 10.2, 7.1 Hz, 1H), 5.12 – 5.04 (m, 2H), 3.80 (s, 3H), 3.59 – 3.51 (m, 2H), 2.60 (dd, $J$ = 7.2, 2.5 Hz, 2H), 2.13 (t, $J$ = 6.9 Hz, 2H), 1.93 – 1.84 (m, 1H), 1.31 (s, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.0, 137.1, 132.6, 130.2, 116.7, 113.9, 64.9, 55.4, 42.7, 36.5, 35.6. **IR** (ATR): 3353, 2913, 1510, 1243, 1176 cm$^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_2Na$ $[M+Na]^+$ 229.1205, found 229.1203.




**(*E*)-2-(4-methoxybenzyl)hex-4-en-1-ol (S2l)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 3-(4-methoxyphenyl)propanoate (1.2 g, 6.0 mmol, 1 equiv), $^{i}Pr_2NH$ (1.0 mL, 7.2 mmol, 1.2 equiv), $^{n}BuLi$ (2.6 mL, 6.6 mmol, 1.1 equiv, 2.5 M in THF), crotyl bromide (1.2 g, 9.0 mmol, 1.5 equiv), and THF (24 mL, 0.25 M). Crude **S1l** (1 equiv) was reduced to **S2l** using $LiAlH_4$ (342 mg, 9.0 mmol, 1.5 equiv) and THF (12 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2l** as a light yellow oil (613 mg, 46% yield). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.54 – 5.40 (m, 2H), 3.80 (s, 3H), 3.54 (dd, *J* = 5.0, 2.6 Hz, 2H), 2.57 (d, *J* = 7.2 Hz, 2H), 2.09 – 2.01 (m, 2H), 1.89 – 1.77 (m, 1H), 1.68 (d, *J* = 4.8 Hz, 3H), 1.29 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 132.8, 130.2, 129.3, 127.2, 113.9, 65.1, 55.4, 43.0, 36.6, 34.4, 18.1. **IR** (ATR): 3358, 2915, 1611, 1511, 1244, 1177, 1034, 967 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{20}O_2Na$ $[M+Na]^+$ 243.1361, found 243.1369.

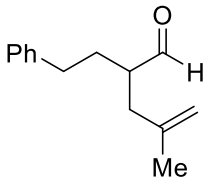
***General Procedure for Swern Oxidation of Alcohols S2***

To an oven-dried round bottom flask was added oxalyl chloride (1.3 equiv) and $CH_2Cl_2$ (0.60 M). The mixture was cooled -78 °C, and DMSO (3 equiv) was added. The resulting mixture was stirred for 30 min. Alcohol **S2** (1 equiv) was added as a solution in $CH_2Cl_2$ (0.60 M), and the resulting mixture was stirred for 30 min. $Et_3N$ (5 equiv) was added, and the resulting mixture was allowed to warm to rt and stirred for 30 min. The reaction mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford aldehyde **1**.

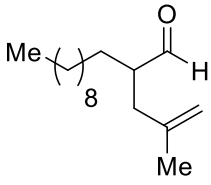



**2-(4-methoxybenzyl)-4-methylpent-4-enal (1a)**: The title compound was prepared following the general procedure for Swern oxidation using **S2a** (2.3 g, 10.3 mmol, 1 equiv), oxalyl chloride (1.1 mL, 13.3 mmol, 1.3 equiv), DMSO (2.2 mL, 31 mmol, 3 equiv), $Et_3N$ (7.2 mL, 51.5 mmol, 5 equiv), and $CH_2Cl_2$ (34.3 mL, 0.30 M). The crude material was purified by column

chromatography (5% EtOAc in hexanes) to afford **1a** as a colorless oil (2.0 g, 88% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.6 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.84 (d, *J* = 1.4 Hz, 1H), 4.75 (d, *J* = 0.5 Hz, 1H), 3.79 (s, 3H), 2.90 (dd, *J* = 13.4, 7.4 Hz, 1H), 2.79 (dddd, *J* = 13.4, 7.0, 6.2, 2.5 Hz, 1H), 2.71 (dd, *J* = 13.4, 6.0 Hz, 1H), 2.39 (dd, *J* = 14.8, 7.7 Hz, 1H), 2.15 (dd, *J* = 14.8, 6.2 Hz, 1H), 1.73 (d, *J* = 0.9 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.6, 158.4, 142.3, 130.8, 130.1, 114.1, 113.0, 55.4, 51.5, 37.2, 34.3, 22.6. **IR** (ATR): 2932, 2835, 1724, 1338, 1245, 907 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{18}O_2Na$ $[M+Na]^+$ 241.1205, found 241.1195.

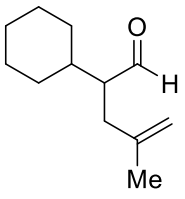



**4-methyl-2-phenethylpent-4-enal (1c)**: The title compound was prepared following the general procedure for Swern oxidation using **S2c** (1.2 g, 6.1 mmol, 1 equiv), oxalyl chloride (0.68 mL, 8.0 mmol, 1.3 equiv), DMSO (1.3 mL, 18.3 mmol, 3 equiv), $Et_3N$ (4.3 mL, 30.6 mmol, 5 equiv), and $CH_2Cl_2$ (20.4 mL, 0.30 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1c** as a light yellow oil (1.07 g, 87% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 2.7 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.20 (dd, *J* = 14.1, 7.3 Hz, 3H), 4.82 (s, 1H), 4.73 (s, 1H), 2.75 – 2.57 (m, 2H), 2.57 – 2.47 (m, 1H), 2.42 (dd, *J* = 14.3, 7.6 Hz, 1H), 2.19 (dd, *J* = 14.3, 6.9 Hz, 1H), 2.03 – 1.90 (m, 1H), 1.82 – 1.72 (m, 1H), 1.69 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.7, 142.2, 141.5, 128.62, 128.56, 126.3, 113.1, 49.1, 37.5, 33.3, 30.5, 22.5. **IR** (ATR): 2927, 1727, 1651, 1495, 1454, 892 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{18}ONa$ $[M+Na]^+$ 225.1255, found 225.1250.

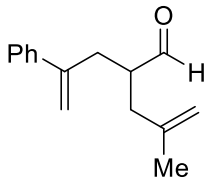



**2-(2-methylallyl)dodecanal (1e)**: The title compound was prepared following the general procedure for Swern oxidation using **S2e** (1.5 g, 6.1 mmol, 1 equiv), oxalyl chloride (0.68 mL, 7.9 mmol, 1.3 equiv), DMSO (1.3 mL, 18.2 mmol, 3 equiv), $Et_3N$ (4.2 mL, 30.3 mmol, 5 equiv), and $CH_2Cl_2$ (20 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **1e** as a light yellow oil (1.38 g, 95% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.57 (d, *J* = 3.1 Hz, 1H), 4.80 (s, 1H), 4.72 (s, 1H), 2.45 (ddd, *J* = 11.1, 7.2, 3.1 Hz, 1H), 2.37 (dd, *J* = 14.4, 7.9 Hz, 1H), 2.13 (dd, *J* = 14.3, 6.3 Hz, 1H), 1.72 (s, 3H), 1.26 (s, 18H), 0.89 (t, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.2, 142.6, 112.7, 49.9, 37.5, 32.0, 29.8, 29.72, 29.70, 29.6, 29.5,

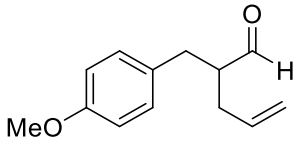
29.1, 27.1, 22.8, 22.6, 14.2. **IR** (ATR): 2922, 2853, 1726, 1456, 1054, 891 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{30}ONH_4$ $[M+NH_4]^+$ 256.2640, found 256.2633.




**2-cyclohexyl-4-methylpent-4-enal (1f)**: The title compound was prepared following the general procedure for Swern oxidation using **S2f** (1.2 g, 6.6 mmol, 1 equiv), oxalyl chloride (0.73 mL, 8.5 mmol, 1.3 equiv), DMSO (1.4 mL, 19.7 mmol, 3 equiv), $Et_3N$ (4.6 mL, 32.8 mmol, 5 equiv), and $CH_2Cl_2$ (22 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **1f** as a light yellow oil (1.13 g, 95% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.60 (d, *J* = 3.5 Hz, 1H), 4.77 (s, 1H), 4.69 (s, 1H), 2.40 (dd, *J* = 13.9, 9.6 Hz, 1H), 2.31 (dt, *J* = 9.4, 3.9 Hz, 1H), 2.21 (dd, *J* = 14.0, 4.1 Hz, 1H), 1.81 – 1.59 (m, 9H), 1.32 – 1.18 (m, 2H), 1.18 – 1.03 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.6, 143.2, 112.4, 55.4, 38.7, 34.7, 30.6, 30.5, 26.60, 26.55, 26.4, 22.7. **IR** (ATR): 2923, 2852, 2705, 1724, 889 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{20}O$ $[M]^+$ 180.1514, found 180.1521.




**4-methyl-2-(2-phenylallyl)pent-4-enal (1g)**: The title compound was prepared following the general procedure for Swern oxidation using **S2g** (1.2 g, 5.5 mmol, 1 equiv), oxalyl chloride (0.61 mL, 7.1 mmol, 1.3 equiv), DMSO (1.2 mL, 16.4 mmol, 3 equiv), $Et_3N$ (3.8 mL, 27.4 mmol, 5 equiv), and $CH_2Cl_2$ (18 mL, 0.30 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1g** as a light yellow oil (911 mg, 78% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.61 (d, *J* = 2.5 Hz, 1H), 7.42 – 7.28 (m, 5H), 5.34 (s, 1H), 5.12 (d, *J* = 1.0 Hz, 1H), 4.82 (s, 1H), 4.71 (s, 1H), 2.86 (dd, *J* = 14.2, 7.5 Hz, 1H), 2.61 (ddd, *J* = 14.1, 10.1, 4.4 Hz, 2H), 2.36 (dd, *J* = 14.4, 7.5 Hz, 1H), 2.18 (dd, *J* = 14.4, 6.1 Hz, 1H), 1.64 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.5, 145.6, 142.2, 140.5, 128.6, 127.9, 126.4, 115.2, 113.3, 47.6, 37.3, 35.0, 22.5. **IR** (ATR): 2934, 1723, 1627, 1443, 1376, 1302 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{18}ONH_4$ $[M+NH_4]^+$ 232.1701, found 232.1703.

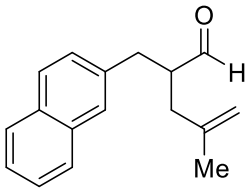



**2-(4-methoxybenzyl)pent-4-enal (1k)**: The title compound was prepared following the general procedure for Swern oxidation using **S2k** (1.04 g, 5.0 mmol, 1 equiv), oxalyl chloride (0.56 mL, 6.5 mmol,

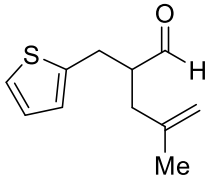
1.3 equiv), DMSO (1.1 mL, 15.1 mmol, 3 equiv), $Et_3N$ (3.5 mL, 25 mmol, 5 equiv), and $CH_2Cl_2$ (17 mL, 0.30 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1k** as a colorless oil (929 mg, 91% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.83 – 5.71 (m, 1H), 5.12 – 5.06 (m, 2H), 3.79 (s, 3H), 2.95 (dd, *J* = 13.1, 6.2 Hz, 1H), 2.75 – 2.66 (m, 2H), 2.46 – 2.35 (m, 1H), 2.28 (dd, *J* = 13.2, 7.4 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.4, 158.4, 134.9, 130.7, 130.1, 117.7, 114.1, 55.4, 53.1, 33.8, 32.8. **IR** (ATR): 2913, 2835, 1723, 1511, 1244 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{16}O_2Na$ $[M+Na]^+$ 227.1048, found 227.1044.

***General Procedure for Oxidation of Alcohols with IBX***

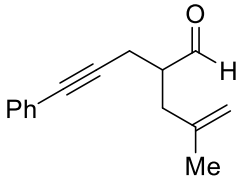
To a round bottom flask was added alcohol **S2** (1 equiv) and DMSO (0.25 M). IBX[7] (1.1–1.2 equiv) was added, and the resulting mixture was stirred at rt for 2 h. The reaction was quenched with $H_2O$ and filtered. The filtrate was extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford aldehyde **1**.



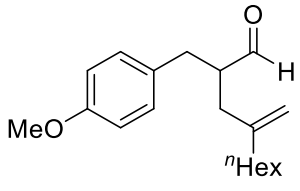

**4-methyl-2-(naphthalen-2-ylmethyl)pent-4-enal (1b)**: The title compound was prepared following the general oxidation procedure with IBX using **S2b** (889 mg, 3.7 mmol, 1 equiv), IBX (1.2 g, 4.4 mmol, 1.2 equiv), and DMSO (15 mL, 0.25 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1b** as a colorless oil (758 mg, 86% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.72 (d, *J* = 2.4 Hz, 1H), 7.85 – 7.75 (m, 3H), 7.63 (s, 1H), 7.51 – 7.41 (m, 2H), 7.31 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.87 (s, 1H), 4.78 (s, 1H), 3.14 (td, *J* = 9.9, 3.7 Hz, 1H), 3.00 – 2.88 (m, 2H), 2.49 – 2.40 (m, 1H), 2.21 (dd, *J* = 14.8, 5.7 Hz, 1H), 1.74 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 204.4, 142.2, 136.4, 133.7, 132.4, 128.4, 127.8, 127.66, 127.65, 127.5, 126.3, 125.7, 113.2, 51.2, 37.3, 35.3, 22.6. **IR** (ATR): 2932, 1723, 1599, 1507, 891 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{18}ONa$ $[M+Na]^+$ 261.1255, found 261.1258.




**4-methyl-2-(thiophen-2-ylmethyl)pent-4-enal (1d)**: The title compound was prepared following the general oxidation procedure with IBX using **S2d** (766 mg, 3.9 mmol, 1 equiv), IBX (1.31 g, 4.7 mmol, 1.2 equiv), and DMSO (16 mL, 0.25 M). The residue was purified by column chromatography (5% EtOAc in hexanes) to afford **1d** as a colorless oil (705 mg, 93% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.71 (d, *J* = 2.1 Hz, 1H), 7.15 (d, *J* = 5.1 Hz, 1H), 6.92 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.81 (d, *J* = 3.3 Hz, 1H), 4.88 (s, 1H), 4.78 (s, 1H), 3.19 (dd, *J* = 15.1, 7.7 Hz, 1H), 3.01 (dd, *J* = 15.1, 5.8 Hz, 1H), 2.85 (qd, *J* = 7.7, 2.1 Hz, 1H), 2.43 (dd, *J* = 14.7, 7.6 Hz, 1H), 2.22 (dd, *J* = 14.7, 7.1 Hz, 1H), 1.75 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 203.8, 141.9, 141.2, 127.1, 126.0, 124.1, 113.5, 51.3, 37.1, 28.9, 22.5. **IR** (ATR): 3074, 2915, 1723, 1438, 893 $cm^{-1}$. **HRMS** calculated for $C_{11}H_{14}OSNa$ $[M+Na]^+$ 217.0663, found 217.0669.

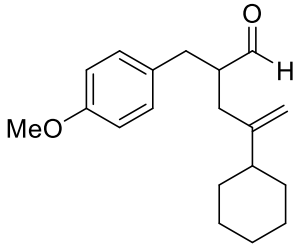



**4-methyl-2-(3-phenylprop-2-yn-1-yl)pent-4-enal (1h)**: The title compound was prepared following the general oxidation procedure with IBX using **S2h** (310 mg, 1.5 mmol, 1 equiv), IBX (508 mg, 1.8 mmol, 1.2 equiv), and DMSO (6 mL, 0.25 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1h** as a yellow oil (258 mg, 81% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.81 (d, *J* = 1.6 Hz, 1H), 7.39 (ddd, *J* = 7.0, 4.9, 3.5 Hz, 2H), 7.32 – 7.27 (m, 3H), 4.91 – 4.87 (m, 1H), 4.85 – 4.81 (m, 1H), 2.75 (dddd, *J* = 7.9, 7.2, 5.1, 1.6 Hz, 1H), 2.71 – 2.64 (m, 2H), 2.54 (dd, *J* = 14.4, 6.5 Hz, 1H), 2.39 (dd, *J* = 14.6, 7.3 Hz,1H), 1.79 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 203.3, 141.7, 131.7, 128.4, 128.1, 123.5, 113.6, 86.3, 82.9, 48.5, 36.6, 22.5, 19.0. **IR** (ATR): 3076, 2932, 1726, 1650, 1598, 1375, 1069 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}ONa$ $[M+Na]^+$ 235.1099, found 235.1105.

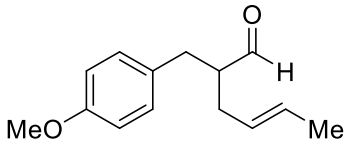



**2-(4-methoxybenzyl)-4-methylenedecanal (1i)**: The title compound was prepared following the general oxidation procedure with IBX using **S2i** (500 mg, 1.7 mmol, 1 equiv), IBX (560 mg, 2.0 mmol, 1.1 equiv), and DMSO (7 mL, 0.25 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1i** as a light yellow oil (229 mg, 46% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.65 (d, *J* = 2.4 Hz, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 4.84 (s, 1H), 4.76 (s, 1H), 3.79 (s, 3H), 2.90 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.78 (s, 1H),

2.71 (dd, *J* = 13.7, 5.9 Hz, 1H), 2.38 (dd, *J* = 14.8, 8.2 Hz, 1H), 2.14 (dd, *J* = 14.8, 5.9 Hz, 1H), 1.99 (t, *J* = 7.4 Hz, 2H), 1.38 (s, 2H), 1.27 (s, 6H), 0.89 (t, *J* = 6.3 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 204.7, 158.4, 146.4, 130.8, 130.1, 114.1, 111.7, 55.4, 51.6, 36.1, 35.4, 34.4, 31.9, 29.1, 27.7, 22.7, 14.2. **IR** (ATR): 2927, 2855, 1725, 1612, 1512, 1442, 1246, 1177, 1036, 895 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{28}O_2Na$ $[M+Na]^+$ 311.1987, found 311.1985.



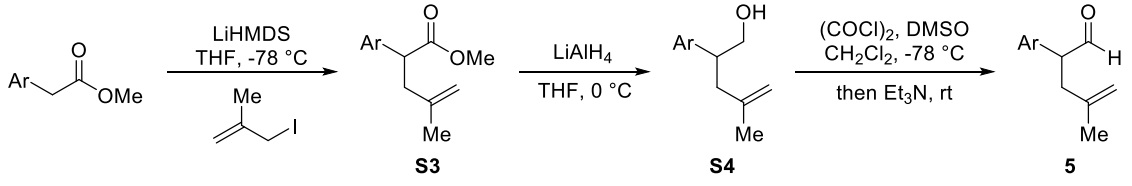

**4-cyclohexyl-2-(4-methoxybenzyl)pent-4-enal (1j)**: The title compound was prepared following the general oxidation procedure with IBX using **S2j** (238 mg, 0.83 mmol, 1 equiv),IBX (254 mg, 0.91 mmol, 1.1 equiv), and DMSO (3.3 mL, 0.25 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1j** as a colorless oil (165 mg, 70% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.64 (d, *J* = 2.6 Hz,1H), 7.08 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.85 (s, 1H), 4.74 (s, 1H), 3.79 (s, 3H), 2.89 (dd, *J* = 13.3, 7.5 Hz, 1H), 2.80 (tdd, *J* = 13.5, 7.1, 2.6 Hz, 1H), 2.72 (dd, *J* = 13.3, 5.9 Hz, 1H), 2.41 (dd, *J* = 15.3, 7.9 Hz, 1H), 2.16 (dd, *J* = 15.3, 6.0 Hz, 1H), 1.83 – 1.64 (m, 6H), 1.32 – 1.06 (m, 5H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.9, 158.4, 151.7, 130.8, 130.1, 114.1, 109.7, 55.4, 51.8, 44.2, 34.6, 34.5, 32.52, 32.48, 26.87, 26.85, 26.4. **IR** (ATR): 2924, 2851, 1724, 1612,1512, 1446, 1245, 1177, 1035, 887 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{26}O_2Na$ $[M+Na]^+$ 309.1830, found 309.1817.

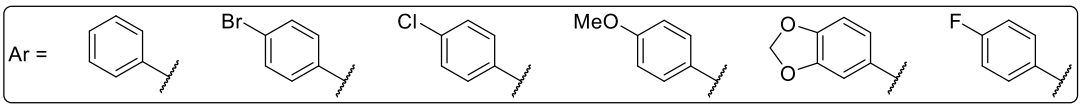


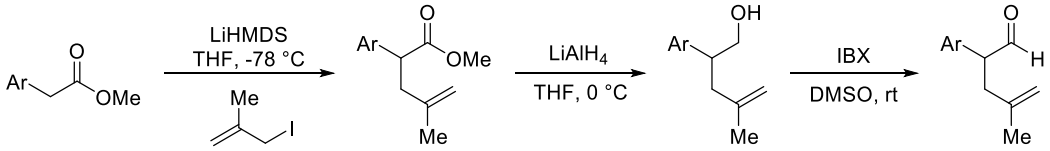

**(*E*)-2-(4-methoxybenzyl)hex-4-enal (1l)**: The title compound was prepared following the general oxidation procedure with IBX using **S2l** (613 mg, 2.8 mmol, 1 equiv), IBX (856 mg, 3.1 mmol, 1.1 equiv), and DMSO (12 mL, 0.25 M). The crude material was purified by column chromatography (5% EtOAc in hexanes) to afford **1l** as a colorless oil (340 mg, 56% yield, 10:1 *E*:*Z*). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.68 (d, *J* = 2.1 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.51 (dq, *J* = 13.8, 6.3 Hz, 1H), 5.37 (dtd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 3.79 (s, 3H), 2.93 (dd, *J* = 13.8, 7.0 Hz, 1H), 2.74 – 2.58 (m, 2H), 2.32 (dt, *J* = 14.2, 7.0 Hz, 1H), 2.26 – 2.16 (m, 1H), 1.66 (dd, *J* = 6.3, 1.3 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.8, 158.3, 131.0, 130.1, 128.4, 127.2, 114.1, 55.4, 53.6, 33.8, 31.8, 18.1. **IR** (ATR): 2916, 2836, 1723, 1612,

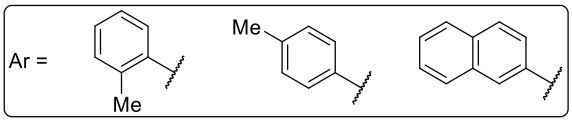
1512, 1441, 1244, 1177, 1034, 967 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{18}O_2Na$ $[M+Na]^+$ 241.1205, found 241.1220.

***Preparation of Aldehydes 5***



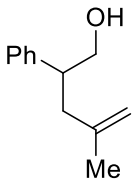

***General Procedure for Ester Alkylation***

To an oven-dried round bottom flask was added the appropriate ester and THF (0.25 M), and the resulting solution was cooled to -78 °C. Then, LiHMDS (1.1 equiv, 1.0 M in THF) was added dropwise, and the resulting mixture was stirred for 1 h. A solution of the methallyl iodide (1.2 equiv) was added dropwise, and the resulting mixture was stirred for 1 h. The reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The alkylated ester **S3** was used without further purification.

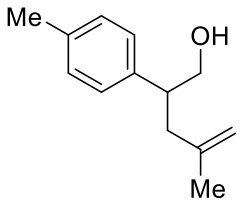
***General Procedure for Ester Reduction***

The crude alkylated ester **S3** was dissolved in THF (0.25 M), and the resulting solution was cooled to 0 °C. $LiAlH_4$ (1.5 equiv) was added portionwise, and the resulting mixture was stirred

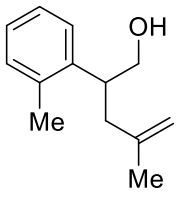
for 30 min. The reaction was quenched using the Fieser method, filtered through celite, and concentrated *in vacuo*. The residue was purified by column chromatography to afford alcohol **S4**.



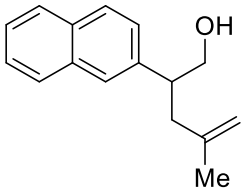

**4-methyl-2-phenylpent-4-en-1-ol (S4a)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-phenylacetate (3.0 g, 20 mmol, 1 equiv), LiHMDS (1.0 M in THF, 22 mL, 22 mmol, 1.1 equiv), methallyl iodide (4.4 g, 24 mmol, 1.2 equiv), and THF (80 mL, 0.25 M). Crude **S3a** (1 equiv) was reduced to **S4a** using $LiAlH_4$ (1.1 g, 30 mmol, 1.5 equiv) and THF (40 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4a** as a colorless oil (2.33 g, 66% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 9.7, 5.5 Hz, 2H), 7.28 – 7.19 (m, 3H), 4.73 (s, 1H), 4.68 (s, 1H), 3.76(ddd, *J* = 18.3, 10.9, 6.6 Hz, 2H), 3.10 – 2.98 (m, 1H), 2.48 (dd, *J* = 14.1, 7.3 Hz, 1H), 2.35(dd, *J* = 14.1, 7.9 Hz, 1H), 1.72 (s, 3H), 1.51 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.5, 142.3, 128.7, 128.1, 126.9, 112.5, 67.4, 46.4, 40.9, 22.5. **IR** (ATR): 3355, 3073, 2928, 1649, 1494, 1452, 1066, 1030, 886, 756 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{16}ONH_4$ $[M+NH_4]^+$ 194.1545, found 194.1537.



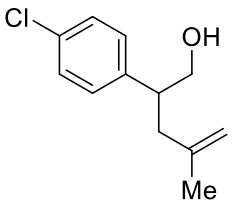

**4-methyl-2-(*p*-tolyl)pent-4-en-1-ol (S4b)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(*p*-tolyl)acetate (1.6 g, 10 mmol, 1 equiv), LiHMDS (1.0 M in THF, 11 mL, 11 mmol, 1.1 equiv), methallyl iodide (2.2 g, 12 mmol, 1.2 equiv), and THF (40 mL, 0.25 M). Crude **S3b** (1 equiv) was reduced to **S4b** using LiAlH4 (569 mg, 15 mmol, 1.5 equiv) and THF (20 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4b** as a colorless oil (1.42 g, 75% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.18 – 7.09 (m, 4H), 4.75 – 4.71 (m, 1H), 4.68 (dd, *J* = 2.0, 0.9 Hz, 1H), 3.77 (dd, *J* = 10.8, 5.6 Hz, 1H), 3.70 (dd, *J* = 10.8, 7.6 Hz, 1H), 3.01 (qd, *J* = 7.6, 5.7 Hz, 1H), 2.46 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.38 – 2.28 (m, 4H), 1.72 (s, 3H), 1.42 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.7, 139.1, 136.4, 129.5, 128.0, 112.4, 67.5, 45.9, 40.9, 22.5, 21.2. **IR** (ATR): 3356, 2922, 1650, 1514, 1445, 1374, 1066, 1034, 885, 811 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}ONa$ $[M+Na]^+$ 213.1255, found 213.1245.



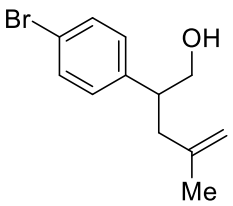

**4-methyl-2-(*o*-tolyl)pent-4-en-1-ol (S4c)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(*o*-tolyl)acetate (1.6 g, 10 mmol, 1 equiv), LiHMDS (1.0 M in THF, 11 mL, 11 mmol, 1.1 equiv), methallyl iodide (2.2 g, 12 mmol, 1.2 equiv), and THF (40 mL, 0.25 M). Crude **S3c** (1 equiv) was reduced to **S4c** using LiAlH4 (569 mg, 15 mmol, 1.5 equiv) and THF (20 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4c** as a colorless oil (1.15 g, 61% yield). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 3H), 7.16 – 7.09 (m, 1H), 4.76 – 4.72 (m, 1H), 4.70 (dd, *J* = 2.0, 0.9 Hz, 1H), 3.77 (qd, *J* = 10.9, 6.5 Hz, 2H), 3.45 – 3.32 (m, 1H), 2.50 – 2.42 (m, 1H), 2.39 (s, 3H), 2.33 (dd, *J* = 14.1, 7.3 Hz, 1H), 1.74 (s, 3H), 1.45 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.9, 140.5, 136.8, 130.8, 126.49, 126.45, 126.1, 112.4, 67.0, 41.0, 40.9, 22.6, 19.9. **IR** (ATR): 3353, 3072, 2936, 1648, 1461, 1374, 1033, 886, 757, 726 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}ONH_4$ $[M+ NH_4]^+$ 208.1701, found 208.1694.



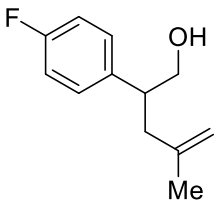

**4-methyl-2-(naphthalen-2-yl)pent-4-en-1-ol (S4d)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(naphthalen-2-yl)acetate (2.0 g, 10 mmol, 1 equiv), LiHMDS (1.0 M in THF, 11 mL, 11 mmol, 1.1 equiv), methallyl iodide (2.2 g, 12 mmol, 1.2 equiv), and THF (40 mL, 0.25 M). Crude **S3d** (1 equiv) was reduced to **S4d** using LiAlH4 (569 mg, 15 mmol, 1.5 equiv) and THF (20 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4d** as a yellow oil (962 mg, 43% yield). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 3H), 7.69(s, 1H), 7.47 (dqd, *J* = 8.4, 6.8, 1.6 Hz, 2H), 7.39 (dd, *J* = 8.5, 1.7 Hz, 1H), 4.75 – 4.64 (m, 2H), 3.85 (qd, *J* = 10.9, 6.6 Hz, 2H), 3.30 – 3.14 (m, 1H), 2.56 (dd, *J* = 14.1, 7.2 Hz, 1H), 2.46 (dd, *J* = 14.1, 8.0 Hz, 1H), 1.75 (s, 3H), 1.41 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.5, 139.7, 133.7, 132.7, 128.5, 127.8, 127.0, 126.2, 126.1, 125.7, 112.7, 67.4, 46.6, 40.8, 22.6. **IR** (ATR): 3352, 2929, 1648, 1442, 1373, 1061, 1027, 887, 854, 815, 745 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{18}ONa$ $[M+Na]^+$ 249.1255, found 249.1257.



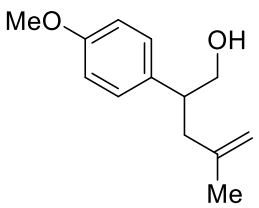

**2-(4-chlorophenyl)-4-methylpent-4-en-1-ol (S4e)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(4-chlorophenyl)acetate (1.43 g, 7.8 mmol, 1 equiv), LiHMDS (1.0 M in THF, 8.5 mL, 8.5 mmol, 1.1 equiv), methallyl iodide (1.70 g, 9.3 mmol, 1.2 equiv), and THF (31 mL, 0.25 M). Crude **S3e** (1 equiv) was reduced to **S4e** using $LiAlH_4$ (442 mg, 11.6 mmol, 1.5 equiv) and THF (15.5 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4e** as a colorless oil (1.31 g, 80% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.19 – 7.13 (m, 2H), 4.75 – 4.68 (m, 1H), 4.65 (dd, *J* = 2.0, 0.9 Hz, 1H), 3.77 (dd, *J* = 10.9, 5.6 Hz, 1H), 3.70 (dd, *J* = 10.9, 7.4 Hz, 1H), 3.09 – 2.94 (m, 1H), 2.46 (dd, *J* = 14.1, 7.0 Hz, 1H), 2.36 – 2.24 (m, 1H), 1.70 (s, 3H), 1.46 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.1, 140.8, 132.6, 129.5,128.8, 112.8, 67.3, 45.8, 40.7, 22.5. **IR** (ATR): 3342, 2931, 1649, 1491, 1444, 1091, 1035, 1014, 889, 821 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{15}ClONH_4$ $[M+NH_4]^+$ 228.1155, found 228.1146.



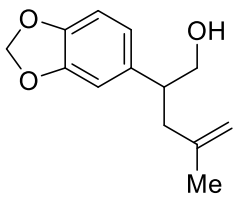

**2-(4-bromophenyl)-4-methylpent-4-en-1-ol (S4f)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(4-bromophenyl)acetate (1.83 g, 8.0 mmol, 1 equiv), LiHMDS (1.0 M in THF, 8.8 mL, 8.8 mmol, 1.1 equiv), methallyl iodide (1.75 g, 9.6 mmol, 1.2 equiv), and THF (32 mL, 0.25 M). Crude **S3f** (1 equiv) was reduced to **S4f** using $LiAlH_4$ (455 mg, 12.0 mmol, 1.5 equiv) and THF (16 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4f** as a colorless oil (1.74 g, 85% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 2H), 7.14 – 7.07 (m, 2H), 4.72 (d, *J* = 1.5 Hz, 1H), 4.65 (dd, *J* = 1.9, 0.9 Hz, 1H), 3.77 (dd, *J* = 10.9, 5.6 Hz, 1H), 3.69 (dd, *J* = 10.9, 7.3 Hz, 1H), 3.07 – 2.91 (m, 1H), 2.46 (dd, *J* = 14.1, 7.0 Hz, 1H), 2.30 (dd, *J* = 14.1, 8.3 Hz, 1H), 1.70 (s, 3H), 1.45 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.1, 141.4, 131.8, 129.9, 120.6, 112.8, 67.2, 45.9, 40.7, 22.5. **IR** (ATR): 3345, 2930, 1649, 1444, 1487, 1374,1073, 1009, 889, 817 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{15}BrONH_4$ $[M+NH_4]^+$ 272.0650, found 272.0645.



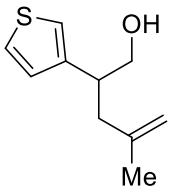

**2-(4-fluorophenyl)-4-methylpent-4-en-1-ol (S4g)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(4-fluorophenyl)acetate (1.27 g, 7.6 mmol, 1 equiv), LiHMDS (1.0 M in THF, 8.3 mL, 8.3 mmol, 1.1 equiv), methallyl iodide (1.65 g, 9.1 mmol, 1.2 equiv), and THF (30 mL, 0.25 M). Crude **S3g** (1 equiv) was reduced to **S4g** using $LiAlH_4$ (429 mg, 11.3 mmol, 1.5 equiv) and THF (15.2 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4g** as a colorless oil (1.29 g, 88% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 2H), 7.06 – 6.96 (m, 2H), 4.76 – 4.69 (m, 1H), 4.65 (dd, *J* = 2.0, 0.9 Hz, 1H), 3.77 (dd, *J* = 10.8, 5.6 Hz, 1H), 3.69 (dd, *J* = 10.8, 7.4 Hz, 1H), 3.09 – 2.94 (m, 1H), 2.46 (dd, *J* = 14.1, 7.0 Hz, 1H), 2.36 – 2.25 (m, 1H), 1.70 (s, 3H), 1.44 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 244.6 Hz), 143.3, 137.9 (d, *J* = 3.2 Hz), 129.5 (d, *J* = 7.8 Hz), 115.5 (d, *J* = 21.1 Hz), 112.7, 67.4, 45.7, 41.0, 22.5. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -116.6. **IR** (ATR): 3353, 2930, 1650, 1508, 1445, 1221, 1159, 1028, 889, 830 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{15}FONH_4$ $[M+NH_4]^+$ 212.1451, found 212.1455.




**2-(4-methoxyphenyl)-4-methylpent-4-en-1-ol (S4h)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(4-methoxyphenyl)acetate (1.33 g, 7.4 mmol, 1 equiv), LiHMDS (1.0 M in THF, 8.1 mL, 8.1 mmol, 1.1 equiv), methallyl iodide (1.61 g, 8.9 mmol, 1.2 equiv), and THF (30 mL, 0.25 M). Crude **S3h** (1 equiv) was reduced to **S4h** using $LiAlH_4$ (421 mg, 11.1 mmol, 1.5 equiv) and THF (14.8 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4h** as a colorless oil (1.29 g, 84% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.72 (s, 1H), 4.67 (s, 1H), 3.80 (s, 3H), 3.70 (dd, *J* = 24.8, 17.2 Hz, 2H), 3.06 – 2.93 (m, 1H), 2.44 (dd, *J* = 14.0, 7.1 Hz, 1H), 2.31 (dd, *J* = 14.1, 8.1 Hz, 1H), 1.71(s, 3H), 1.37 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.6, 143.7, 134.1, 129.0, 114.2, 112.5, 67.6, 55.4, 45.6, 41.0, 22.5. **IR** (ATR): 3377, 2932, 1611, 1511, 1442, 1245, 1178, 1033, 887, 827 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{18}O_2NH_4$ $[M+NH_4]^+$ 224.1651, found 224.1665.



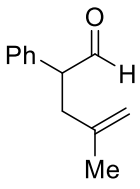

**2-(benzo[*d*][1,3]dioxol-5-yl)-4-methylpent-4-en-1-ol (S4i)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(benzo[*d*][1,3]dioxol-5-yl)acetate (1.04 g, 5.4 mmol, 1 equiv), LiHMDS (1.0 M in THF, 5.9 mL, 5.9 mmol, 1.1 equiv), methallyl iodide (1.17 g, 6.4 mmol, 1.2 equiv), and THF (21 mL, 0.25 M). Crude **S3i** (1 equiv) was reduced to **S4i** using $LiAlH_4$ (305 mg, 8.0 mmol, 1.5 equiv) and THF (10.8 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4i** as a colorless oil (942 mg, 80% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.75 (dd, *J* = 15.4, 4.8 Hz, 2H), 6.68 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.94 (d, *J* = 0.5 Hz, 2H), 4.73 (d, *J* = 1.5 Hz, 1H), 4.67 (dd, *J* = 2.0, 0.9 Hz, 1H), 3.74 (dd, *J* = 10.8, 5.5 Hz, 1H), 3.65 (dd, *J* = 10.8, 7.7 Hz, 1H), 2.96 (qd, *J* = 7.6, 5.6 Hz, 1H), 2.41 (dd, *J* = 14.1, 7.0 Hz, 1H), 2.27 (dd, *J* = 14.1, 8.2 Hz, 1H), 1.70 (s, 3H), 1.48 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.0, 146.4, 143.4, 136.0,121.3, 112.6, 108.5, 108.1, 101.0, 67.5, 46.2, 41.0, 22.5. **IR** (ATR): 3362, 2894, 1504, 1486, 1439, 1243, 1036, 935, 888, 808 cm$^{-1}$. **HRMS** calculated for $C_{13}H_{16}O_3NH_4$ $[M+NH_4]^+$ 238.1443, found 238.1442.



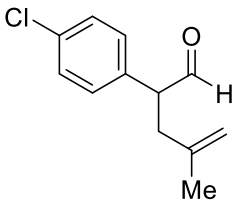

**4-methyl-2-(thiophen-3-yl)pent-4-en-1-ol (S4j)**: The title compound was prepared using the general procedures for ester alkylation and ester reduction starting from methyl 2-(thiophen-3-yl)acetate (1.08 g, 6.4 mmol, 1 equiv), LiHMDS (1.0 M in THF, 7.0 mL, 7.0 mmol, 1.1 equiv), methallyl iodide (1.39 g, 7.6 mmol, 1.2 equiv), and THF (25 mL, 0.25 M). Crude **S3j** (1 equiv) was reduced to **S4j** using $LiAlH_4$ (363 mg, 9.6 mmol, 1.5 equiv) and THF (12.8 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S4j** as a colorless oil (1.11 g, 96% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 4.9, 2.9 Hz, 1H), 7.06 (dd, *J* = 2.9, 0.9 Hz, 1H), 7.01 (dd, *J* = 5.0, 1.3 Hz, 1H), 4.76 (d, *J* = 1.4 Hz, 1H), 4.70 (d, *J* = 1.0 Hz, 1H), 3.77 (dd, *J* = 10.8, 5.3 Hz, 1H), 3.68 (dd, *J* = 10.8, 7.1 Hz, 1H), 3.18 (qd, *J* = 7.4, 5.4 Hz, 1H), 2.45 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.34 (dd, *J* = 14.0, 7.7 Hz, 1H), 1.72 (s, 3H), 1.56 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.5, 143.1, 127.0, 126.0, 121.3, 112.5, 66.9, 41.8, 40.8, 22.4. **IR** (ATR): 3361, 2929, 1647, 1444, 1374, 1064, 1027, 888, 775, 648 cm$^{-1}$. **HRMS** calculated for $C_{10}H_{14}OSNH_4$ $[M+NH_4]^+$ 200.1109, found 200.1109.

***General Procedure for Swern Oxidation of Alcohols***

To an oven-dried round bottom flask was added oxalyl chloride (1.3 equiv) and $CH_2Cl_2$ (0.60 M). The mixture was cooled to -78 °C, and DMSO (3 equiv) was added. The resulting mixture was stirred for 30 min. Alcohol **S4** (1 equiv) was added as a solution in $CH_2Cl_2$ (0.60 M), and the resulting mixture was stirred for 30 min. $Et_3N$ (5 equiv) was added, and the resulting mixture was allowed to warm to rt and stirred for 30 min. The reaction mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford aldehyde **5**.

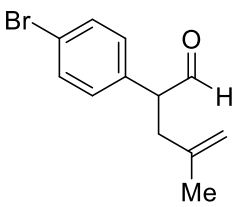



**4-methyl-2-phenylpent-4-enal (5a)**: The title compound was prepared following the general procedure for Swern oxidation using **S4a** (2.27 g, 13.0 mmol, 1 equiv), oxalyl chloride (1.4 mL, 16.9 mmol, 1.3 equiv), DMSO(2.8 mL, 39 mmol, 3 equiv), $Et_3N$ (9.1 mL, 65 mmol, 5 equiv), and $CH_2Cl_2$ (43 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5a** as a colorless oil (1.93 g, 85% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.69 (d, $J$ = 2.2 Hz, 1H), 7.41 – 7.34(m, 2H), 7.33 – 7.28 (m, 1H), 7.24 – 7.20 (m, 2H), 4.78 – 4.72 (m, 1H), 4.69 – 4.61 (m, 1H), 3.76 (td, $J$ = 7.5, 2.1 Hz, 1H), 2.87 (dd, $J$ = 14.8, 7.2 Hz, 1H), 2.46 (dd, $J$ = 14.9, 7.7 Hz, 1H), 1.72 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.4, 142.1, 136.1, 129.2, 128.9, 127.8, 113.0, 57.3, 37.8, 22.8. **IR** (ATR): 2936, 2714, 1720, 1650, 1492, 1453, 1076, 891, 755, 698 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{14}ONa$ $[M+Na]^+$ 197.0942, found 197.0946.

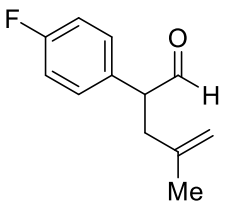



**2-(4-chlorophenyl)-4-methylpent-4-enal (5e)**: The title compound was prepared following the general procedure for Swern oxidation using **S4e** (1.27 g, 6.0 mmol, 1 equiv), oxalyl chloride (0.67 mL, 7.8 mmol, 1.3 equiv), DMSO (1.3 mL, 18 mmol, 3 equiv), $Et_3N$ (4.2 mL, 30 mmol, 5 equiv), and $CH_2Cl_2$ (20 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5e** as a light yellow oil (539 mg, 43% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.66 (d, $J$ = 2.0 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.18 – 7.10 (m, 2H), 4.76 (d, $J$ = 1.4 Hz, 1H), 4.65 (s, 1H), 3.79 – 3.68 (m, 1H), 2.83 (dd, $J$ = 14.8, 6.9 Hz, 1H), 2.43 (ddd, $J$ = 14.8, 8.2, 0.8 Hz, 1H), 1.70 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 199.8, 141.7, 134.6, 133.8, 130.2,

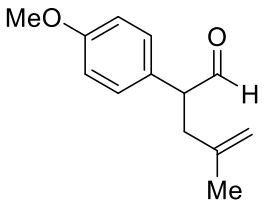
129.3, 113.3, 56.6, 37.8, 22.7. **IR** (ATR): 2936, 1722, 1650, 1491, 1445, 1376, 1093, 1014, 893, 820 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{13}ClONH_4$ $[M+NH_4]^+$ 226.0999, found 226.0988.



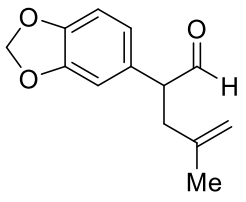

**2-(4-bromophenyl)-4-methylpent-4-enal (5f)**: The title compound was prepared following the general procedure for Swern oxidation using **S4f** (1.70 g, 6.7 mmol, 1 equiv), oxalyl chloride (0.74 mL, 8.7 mmol, 1.3 equiv), DMSO (1.4 mL, 20 mmol, 3 equiv), $Et_3N$ (4.6 mL, 33 mmol, 5 equiv), and $CH_2Cl_2$ (22 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5f** as a light yellow oil (1.15 g, 68% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.0 Hz, 1H), 7.55 – 7.44 (m, 2H), 7.13 – 7.02 (m, 2H), 4.76 (s, 1H),4.65 (s, 1H), 3.77 – 3.67 (m, 1H), 2.83 (dd, *J* = 14.8, 6.9 Hz, 1H), 2.43 (dd, *J* = 14.8, 8.2 Hz, 1H),1.70 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 199.7, 141.6, 135.1, 132.3, 130.6, 121.9, 113.4, 56.7, 37.8, 22.7. **IR** (ATR): 2936, 2819, 2719, 1721, 1650, 1488, 1073, 1010, 892, 816 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{13}BrONH_4$ $[M+NH_4]^+$ 270.0493, found 270.0505.



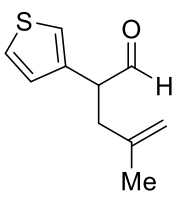

**2-(4-fluorophenyl)-4-methylpent-4-enal (5g)**: The title compound was prepared following the general procedure for Swern oxidation using **S4g** (1.29 g, 6.6 mmol, 1 equiv), oxalyl chloride (0.74 mL, 8.6 mmol, 1.3 equiv), DMSO (1.4 mL, 20 mmol, 3 equiv), $Et_3N$ (4.6 mL, 33 mmol, 5 equiv), and $CH_2Cl_2$ (22 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5g** as a colorless oil (1.13 g, 89% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.67 (d, *J* = 2.1 Hz, 1H), 7.21 – 7.15 (m, 2H), 7.10 – 7.03 (m, 2H), 4.76 (d, *J* = 1.4 Hz, 1H), 4.67 – 4.61 (m, 1H), 3.79 – 3.70 (m, 1H), 2.84 (dd, *J* = 14.8, 7.0 Hz, 1H), 2.42 (ddd, *J* = 14.8, 8.1, 0.8 Hz, 1H), 1.70 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.1 (d, *J* = 0.9 Hz), 162.4 (d, *J* = 246.5 Hz), 141.8, 131.8 (d, *J* = 3.3 Hz), 130.4 (d, *J* = 8.1 Hz), 116.1 (d, *J* = 21.4 Hz), 113.2, 56.5, 37.9, 22.7. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.9. **IR** (ATR): 2938, 2722, 1722, 1650, 1508, 1445, 1223, 1160, 893, 831 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{13}FONH_4$ $[M+NH_4]^+$ 210.1294, found 210.1291.




**2-(4-methoxyphenyl)-4-methylpent-4-enal (5h)**: The title compound was prepared following the general procedure for Swern oxidation using **S4h** (1.24 g, 6.0 mmol, 1 equiv), oxalyl chloride (0.67 mL, 7.8 mmol, 1.3 equiv), DMSO (1.3 mL, 18 mmol, 3 equiv), $Et_3N$ (4.2 mL, 30 mmol, 5 equiv), and $CH_2Cl_2$ (20 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5h** as a light yellow oil (432 mg, 35% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.64 (d, *J* = 2.2 Hz, 1H), 7.17 – 7.09 (m, 2H), 6.94 – 6.87 (m, 2H), 4.78 – 4.72 (m, 1H), 4.69 – 4.63 (m, 1H), 3.81 (s, 3H), 3.70 (td, *J* = 7.6, 2.2 Hz, 1H), 2.82 (dd, *J* = 14.8, 7.1 Hz, 1H), 2.46 – 2.36 (m, 1H), 1.71 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.4, 159.2, 142.3, 129.9, 127.9, 114.6, 112.9, 56.5, 55.4, 37.8, 22.8. **IR** (ATR): 2936, 2836, 1720, 1609, 1511, 1248, 1178, 1032, 891, 827 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{16}O_2NH_4$ $[M+NH_4]^+$ 222.1494, found 222.1496.




**2-(benzo[*d*][1,3]dioxol-5-yl)-4-methylpent-4-enal (5i)**: The title compound was prepared following the general procedure for Swern oxidation using **S4i** (903 mg, 4.1 mmol, 1 equiv), oxalyl chloride (0.46 mL, 5.3 mmol, 1.3 equiv), DMSO (0.87 mL, 12.3 mmol, 3 equiv), $Et_3N$ (2.9 mL, 20.5 mmol, 5 equiv), and $CH_2Cl_2$ (13.7 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5i** as a light yellow oil (303 mg, 34% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 2.1 Hz, 1H), 6.81 (dd, *J* = 7.8, 0.5 Hz, 1H), 6.71 – 6.65 (m, 2H), 5.97 (s, 2H), 4.76 (d, *J* = 1.4 Hz, 1H), 4.67 (d, *J* = 0.5 Hz, 1H), 3.70 – 3.62(m, 1H), 2.80 (dd, *J* = 15.1, 6.8 Hz, 1H), 2.40 (dd, *J* = 14.8, 8.0 Hz, 1H), 1.71 (d, *J* = 0.4 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.1, 148.4, 147.3, 142.1, 129.7, 122.3, 113.0, 109.0, 108.9, 101.3, 56.9, 37.8, 22.7. **IR** (ATR): 2898, 1721, 1504, 1485, 1441, 1244, 1037, 934, 895, 808 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{14}O_3NH_4$ $[M+NH_4]^+$ 236.1287, found 236.1287.

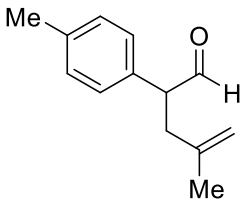



**4-methyl-2-(thiophen-3-yl)pent-4-enal (5j)**: The title compound was prepared following the general procedure for Swern oxidation using **S4j** (1.07 g, 5.9 mmol, 1 equiv), oxalyl chloride (0.65 mL, 7.6 mmol, 1.3 equiv), DMSO (1.2 mL, 17.5 mmol, 3 equiv), $Et_3N$ (4.1 mL, 29.2 mmol, 5 equiv), and $CH_2Cl_2$ (19.5 mL, 0.30 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to

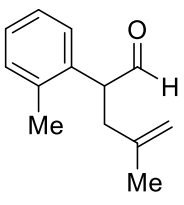
afford **5j** as a light yellow oil (777 mg, 74% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.61 (d, *J* = 2.5 Hz, 1H), 7.36 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.14 (d, *J* = 2.2 Hz, 1H), 6.99 (d, *J* = 4.9 Hz, 1H), 4.79 (s, 1H), 4.71 (s, 1H), 3.89 (td, *J* = 7.4, 2.2 Hz, 1H), 2.82 (dd, *J* = 14.6, 7.6 Hz, 1H), 2.48 (dd, *J* = 14.7, 7.2 Hz, 1H), 1.73 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 199.7, 142.0, 136.3, 127.4, 126.6, 122.9, 113.0, 52.5, 37.7, 22.7. **IR** (ATR): 2936, 2818, 2718, 1723, 1650, 1376, 1076, 892, 777, 642 $cm^{-1}$. **HRMS** calculated for $C_{10}H_{12}SONH_4$ $[M+NH_4]^+$ 198.0953, found 198.0947.

***General Procedure for Oxidation of Alcohols with IBX***

To a round bottom flask was added alcohol **S4** (1 equiv) and DMSO (0.25 M). IBX[7] (1.1 equiv) was added, and the resulting mixture was stirred at rt for 2 h. The reaction mixture was quenched with $H_2O$ and filtered. The filtrate was extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford aldehyde **5**.

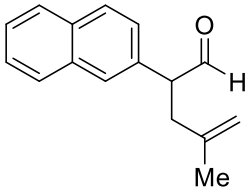



**4-methyl-2-(*p*-tolyl)pent-4-enal (5b)**: The title compound was prepared following the general oxidation procedure with IBX using **S4b** (380 mg, 2.0 mmol, 1 equiv), IBX (616 mg, 2.2 mmol, 1.1 equiv), and DMSO (8 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5b** as a colorless oil (311 mg, 83% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.2 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.76 (d, *J* = 1.7 Hz, 1H), 4.67 (d, *J* = 0.5 Hz, 1H), 3.72 (td, *J* = 7.5, 2.2 Hz, 1H), 2.84 (dd, *J* = 14.8, 7.1 Hz, 1H), 2.44 (dd, *J* = 14.8, 7.9 Hz, 1H), 2.35 (s, 3H), 1.71 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.5, 142.3, 137.5, 133.0, 129.9, 128.8, 112.9, 56.9, 37.7, 22.8, 21.2. **IR** (ATR): 2921, 2716, 1721, 1650, 1513, 1445, 1376, 1021, 890, 810 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{16}O$ $[M]^+$ 188.1201, found 188.1208.



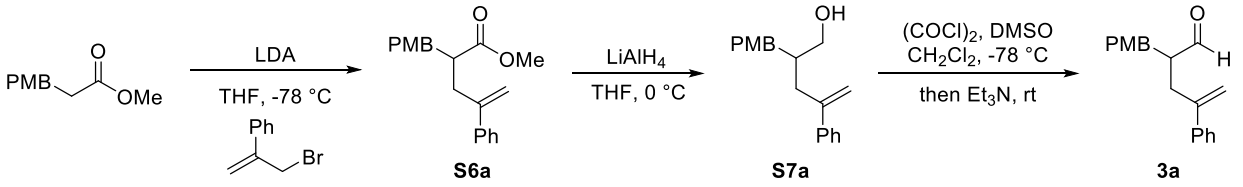

**4-methyl-2-(*o*-tolyl)pent-4-enal (5c)**: The title compound was prepared following the general oxidation procedure with IBX using **S4c** (380 mg, 2.0 mmol, 1 equiv), IBX (616 mg, 2.2 mmol, 1.1 equiv), and DMSO (8 mL,0.25 M). The crude material was purified by column chromatography (3% EtOAc in

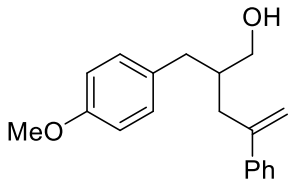
hexanes) to afford **5c** as a colorless oil (346 mg, 92% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 2.1 Hz, 1H), 7.26 – 7.19 (m, 3H), 7.14 – 7.10 (m, 1H), 4.80 – 4.73 (m, 1H), 4.69 (dd, *J* = 1.7, 0.8 Hz, 1H), 4.01 (td, *J* = 7.3, 2.1 Hz, 1H), 2.89 (dd, *J* = 14.7, 7.5 Hz, 1H), 2.47 – 2.34 (m, 4H), 1.73 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.2, 142.4, 137.2, 134.7, 131.1, 128.0, 127.6, 126.7, 112.8, 53.4, 37.5, 22.9, 20.0. **IR** (ATR): 2935, 2717, 1720, 1650, 1490, 1445,1377, 891, 755, 724 cm$^{-1}$. **HRMS** calculated for $C_{13}H_{16}ONa$ $[M+Na]^+$ 211.1099, found 211.1106.




**4-methyl-2-(naphthalen-2-yl)pent-4-enal (5d)**: The title compound was prepared following the general oxidation procedure with IBX using **S4d** (453 mg, 2.0 mmol, 1 equiv), IBX (616 mg, 2.2 mmol, 1.1 equiv), and DMSO (8 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **5d** as a colorless oil (212.6 mg, 47% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.76 (d, *J* = 2.1 Hz, 1H), 7.89 – 7.80 (m, 3H), 7.70 (s, 1H), 7.54 – 7.46 (m, 2H), 7.34 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.77 (s, 1H), 4.71 (s, 1H), 3.94 (td, *J* = 7.6, 2.1 Hz, 1H), 2.96 (dd, *J* = 15.0, 6.9 Hz, 1H), 2.58 (dd, *J* = 14.9, 7.9 Hz, 1H), 1.75 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 200.3, 142.1, 133.7, 133.5, 132.9, 129.0, 128.0, 127.89, 127.86, 126.6, 126.3, 113.1, 57.5, 37.8, 22.8. **IR** (ATR): 2935, 2716, 1720, 1650, 1507, 1441, 891, 857, 816, 746 cm$^{-1}$. **HRMS** calculated for $C_{16}H_{16}ONa$ $[M+Na]^+$ 247.1099, found 247.1096.

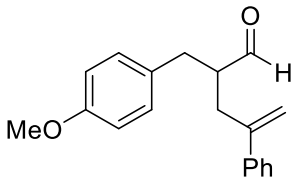
***Preparation of Aldehyde 3a***




**2-(4-methoxybenzyl)-4-phenylpent-4-en-1-ol (S7a)**: To an oven-dried round bottom flask was added $^i$Pr$_2$NH (2.1 mL, 15 mmol, 1.3 equiv) and THF (25 mL), and the resulting solution was cooled to -78 °C. Then, $^n$BuLi (5.8 mL, 14.4 mmol, 1.2 equiv, 2.5 M in THF) was added dropwise, and the resulting mixture was stirred for 1 h. A solution of methyl 3-(4-methoxyphenyl)propanoate (2.33 g, 12 mmol, 1.0 equiv) in THF (10 mL) was added dropwise, and the resulting mixture was stirred for 1 h. Next, (3-bromoprop-1-en-2-yl)benzene[8] (3.55 g, 18

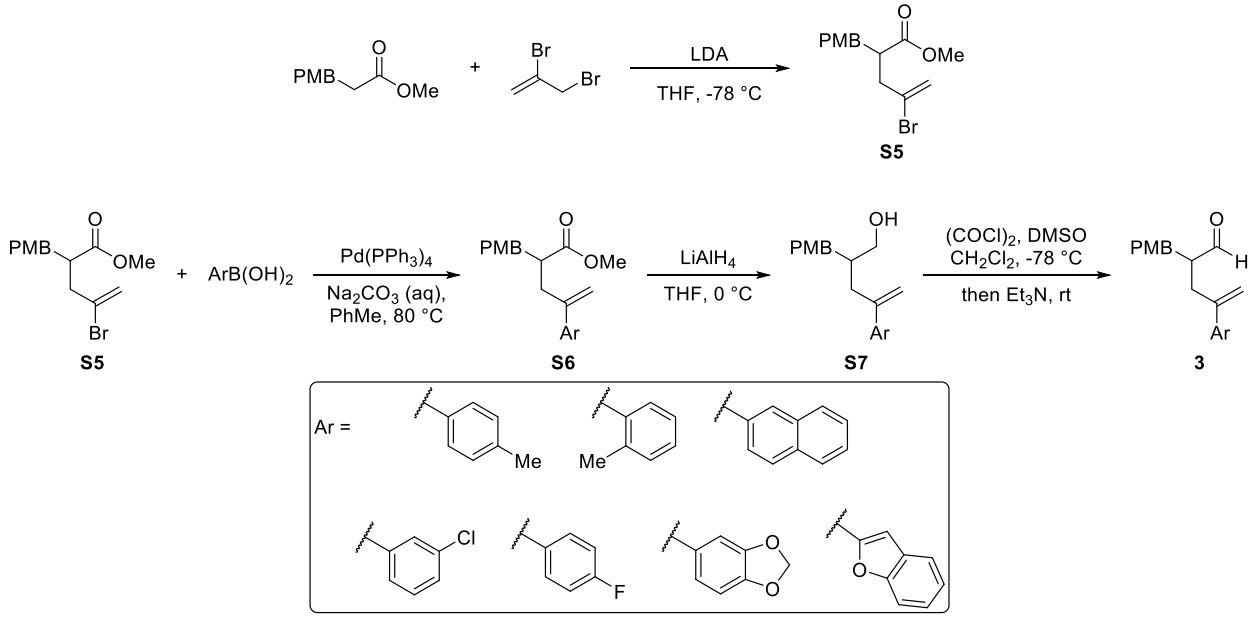
mmol, 1.5 equiv) was added, and the reaction mixture was stirred for 3 h. The reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The ester **S6a** was used without further purification. Crude **S6a** was dissolved in THF (24 mL, 0.50 M), and the solution was cooled to 0 °C. $LiAlH_4$ (683 mg, 18 mmol, 1.5 equiv) was added portionwise, and the resulting mixture was stirred at 0 °C for 30 min. The reaction was quenched using the Fieser method, filtered through celite, and concentrated *in vacuo*. The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7a** as a colorless oil (1.74 g, 52% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 5H), 7.06 – 7.00 (m, 2H), 6.85 – 6.79 (m, 2H), 5.34 (d, *J* = 1.6 Hz, 1H), 5.13 (d, *J* = 1.4 Hz, 1H), 3.80 (s, 3H), 3.57 – 3.45 (m, 2H), 2.66 – 2.51 (m, 4H), 1.93 – 1.81 (m, 1H), 1.27 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 147.4, 140.9, 132.6, 130.2, 128.5, 127.6, 126.4, 114.4, 113.9, 64.7, 55.4, 41.1, 37.2, 36.7. **IR** (ATR): 3360, 2930, 1611, 1511, 1442, 1300, 1244, 1177, 1027, 897, 779 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{22}O_2Na$ $[M+Na]^+$ 305.1518, found 305.1505.

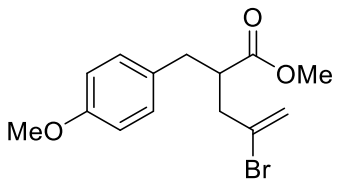



**2-(4-methoxybenzyl)-4-phenylpent-4-enal (3a)**: To an oven-dried round bottom flask was added oxalyl chloride (1.1 mL, 12.4 mmol, 2 equiv) and $CH_2Cl_2$ (14 mL). The mixture was cooled to -78 °C, and DMSO (1.3 mL, 18.6 mmol, 3 equiv) was added. The resulting mixture was stirred for 10 min. Alcohol **S7a** (1.7 g, 6.2 mmol, 1.0 equiv) was added dropwise as a solution in $CH_2Cl_2$ (14 mL), and the resulting mixture was stirred for 15 min. $Et_3N$ (5.2 mL, 37.2 mmol, 6 equiv) was added, and the resulting mixture was allowed to warm to rt and stirred for 10 min. The reaction mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude material was purified by column chromatography (50% $CH_2Cl_2$ in hexanes) to afford **3a** as a light yellow oil (1.27 g, 73% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.67 (d, *J* = 2.0 Hz, 1H), 7.36 – 7.28 (m, 5H), 7.05 – 6.97 (m, 2H), 6.84 – 6.79(m, 2H), 5.36 (d, *J* = 1.2 Hz, 1H), 5.13 (d, *J* = 1.2 Hz, 1H), 3.79 (s, 3H), 2.90 (ddd, *J* = 9.2, 3.6, 1.6 Hz, 2H), 2.78 – 2.68 (m, 2H), 2.66 – 2.58 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.3, 158.4, 145.6, 140.4, 130.6, 130.2, 128.6, 127.9, 126.4, 115.2, 114.1, 55.4, 51.7, 34.8, 34.2. **IR** (ATR):

2933, 2835, 1723, 1611, 1511, 1245, 1178, 1034, 901, 779, 704 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{20}O_2Na$ $[M+Na]^+$ 303.1361, found 303.1367.

***Preparation of Aldehydes 3b-h***



**methyl 4-bromo-2-(4-methoxybenzyl)pent-4-enoate (S5):** To an oven-dried round bottom flask was added $^{i}Pr_2NH$ (3.4 mL, 24 mmol, 1.2 equiv) and THF (60 mL, 0.33 M), and the resulting solution was cooled to -78 °C. Then, $^{n}$BuLi (8.8 mL, 22 mmol, 1.1 equiv, 2.5 M in THF) was added dropwise, and the resulting mixture was stirred for 45 min. A solution of methyl 3-(4-methoxyphenyl)propanoate (3.88 g, 20 mmol, 1 equiv) in THF (10 mL) was added dropwise, and the resulting mixture was allowed to stir for 1 h. Next, 2,3-dibromoprop-1-ene (5.33 g, 1.2 equiv, 90 wt%) was added, and the reaction mixture was stirred for 2 h. The reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (3% EtOAc in hexanes) to afford **S5** as a colorless oil (4.74 g, 75% yield). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, $J$ = 8.5 Hz, 2H), 6.83 (d, $J$ = 8.6 Hz, 2H), 5.64 (s, 1H), 5.47 (d, $J$ = 1.5 Hz, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 3.12 – 3.01 (m, 1H), 2.92 – 2.73 (m, 3H), 2.55 (dd, $J$ = 14.6, 6.0 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 174.8, 158.5, 131.2, 130.5, 130.0, 119.1, 114.0, 55.4, 51.8, 46.4, 43.4, 36.8.

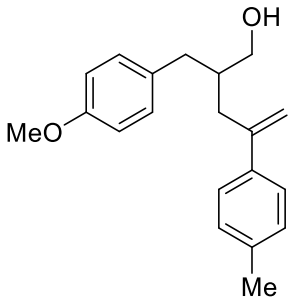
**IR** (ATR): 2951, 1733, 1628, 1612, 1512, 1435, 1246, 1176, 1034, 893 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{17}BrO_3Na$ $[M+Na]^+$ 335.0259, found 335.0275.

***General Procedure for Suzuki Cross-coupling***

To a round bottom flask was charged $Pd(PPh_3)_4$ (1 mol%), the appropriate arylboronic acid (1.2 equiv), **S5** (1 equiv), $Na_2CO_3$ (3.0 equiv, 2 M in $H_2O$), and PhMe (0.20 M). The resulting mixture was stirred at 80 °C overnight. The reaction was cooled to rt and quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The ester **S6** was used without further purification.

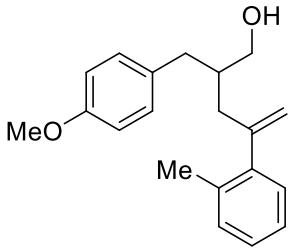
***General Procedure for Ester Reduction***

The crude ester **S6** was dissolved in THF (0.50 M), and the resulting solution was cooled to 0 °C. $LiAlH_4$ (1.5 equiv) was added portionwise, and the resulting mixture was stirred for 30 min. The reaction was quenched using the Fieser method, filtered through celite, and concentrated *in vacuo*. The residue was purified by column chromatography to afford alcohol **S7**.

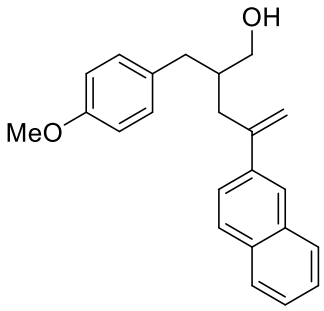



**2-(4-methoxybenzyl)-4-(*p*-tolyl)pent-4-en-1-ol (S7b)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), *p*-tolylboronic acid (490 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6b** (1 equiv) was reduced to **S7b** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7b** as a colorless oil (787 mg, 89% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.32 (s, 1H), 5.09 (s, 1H), 3.81 (s, 3H), 3.51 (s, 2H), 2.61 (dd, *J* = 7.2, 2.9 Hz, 2H), 2.56 (d, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.95 – 1.81 (m, 1H), 1.28 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 147.2, 137.9, 137.4, 132.6, 130.2, 129.2, 126.3, 113.9, 113.6, 64.7, 55.4, 41.1, 37.3, 36.8, 21.2. **IR** (ATR):

3369, 2920, 1611, 1510, 1442, 1244, 1177, 1031, 894, 825 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{24}O_2H$ $[M+H]^+$ 297.1855, found 297.1856.

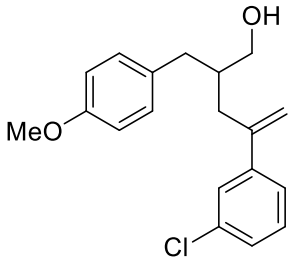



**2-(4-methoxybenzyl)-4-(*o*-tolyl)pent-4-en-1-ol (S7c)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), *o*-tolylboronic acid (490 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6c** (1 equiv) was reduced to **S7c** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7c** as a colorless oil (821 mg, 92% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 7.13 (m, 3H), 7.11 (d, *J* = 6.7 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 5.27 (d, *J* = 1.0 Hz, 1H), 5.01 (d, *J* = 2.0 Hz, 1H), 3.79 (s, 3H), 3.57 – 3.45 (m, 2H), 2.66 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.59 – 2.48 (m, 2H), 2.40 (dd, *J* =14.4, 6.6 Hz, 1H), 2.29 (s, 3H), 1.84 – 1.73 (m, 1H), 1.22 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 148.6, 142.4, 135.0, 132.5, 130.5, 130.1, 128.6, 127.1, 125.7, 116.2, 113.9, 64.7, 55.4, 40.8, 39.2, 36.5, 20.1. **IR** (ATR): 3367, 2926, 1611, 1511, 1441, 1243, 1177, 1032, 903, 732 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{24}O_2Na$ $[M+Na]^+$ 319.1674, found 319.1664.

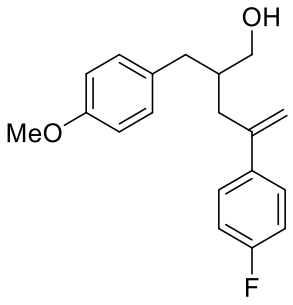



**2-(4-methoxybenzyl)-4-(naphthalen-2-yl)pent-4-en-1-ol (S7d)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), 2-naphthylboronic acid (619 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6d** (1 equiv) was reduced to **S7d** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7d** as a white solid (851 mg, 85% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.73 (m, 3H), 7.66 (s, 1H), 7.54 – 7.49 (m, 1H), 7.49 – 7.43 (m, 2H), 7.08 – 7.02 (m, 2H), 6.87 – 6.80 (m, 2H), 5.50 (d, *J* = 1.5 Hz, 1H), 5.24 (d, *J* = 1.2 Hz, 1H), 3.82 (s, 3H), 3.56 (d, *J* = 4.6 Hz, 2H), 2.75 – 2.56 (m, 4H), 1.93 (tt, *J* = 7.6, 4.2 Hz, 1H), 1.34 (s, 1H). **$^{13}$C NMR** (101 MHz,

$CDCl_3$) δ 158.1, 147.1, 137.9, 133.5, 133.0, 132.6, 130.3, 128.3, 128.0, 127.6, 126.2, 126.0, 125.1, 124.8, 114.9, 113.9, 64.8, 55.4, 41.3, 37.0, 36.9. **IR** (ATR): 3306, 2931, 1610, 1509,1243, 1023, 886, 828, 809, 751 $cm^{-1}$. **HRMS** calculated for $C_{23}H_{24}O_2Na$ $[M+Na]^+$ 355.1674, found 355.1680.

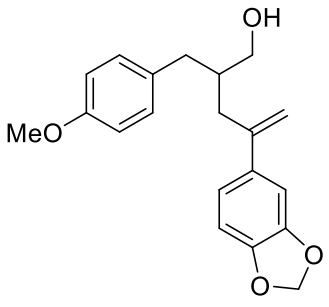



**4-(3-chlorophenyl)-2-(4-methoxybenzyl)pent-4-en-1-ol (S7e)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), 3-chlorophenylboronic acid (563 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6e** (1 equiv) was reduced to **S7e** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7e** as a colorless oil (732 mg, 77% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 3H), 7.17 (dd, *J* = 4.5, 1.9 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 5.34 (s, 1H), 5.16 (s, 1H), 3.80 (s, 3H), 3.56 – 3.47 (m, 2H), 2.64 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.60 – 2.45 (m, 3H), 1.90 – 1.78 (m, 1H), 1.27 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.1, 146.2, 142.8, 134.5, 132.4, 130.2,129.7, 127.7, 126.6, 124.6, 115.4, 114.0, 64.6, 55.4, 41.0, 36.9, 36.7. **IR** (ATR): 3359, 2929, 1511, 1441, 1299, 1244, 1177, 1031, 804, 789 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{21}ClO_2Na$ $[M+Na]^+$ 339.1128, found 339.1129.

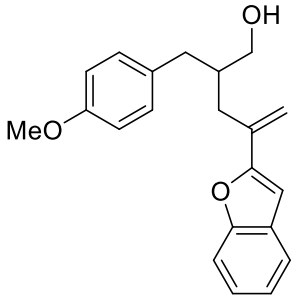



**4-(4-fluorophenyl)-2-(4-methoxybenzyl)pent-4-en-1-ol (S7f)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), 4-fluorophenylboronic acid (504 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6f**(1 equiv) was reduced to **S7f** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7f** as a colorless oil (808 mg, 90% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.21 (m, 2H), 7.00(dd, *J* = 16.8, 8.5 Hz, 4H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.28 (s, 1H), 5.11 (s, 1H), 3.80 (s, 3H), 3.56 –

3.42 (m, 2H), 2.67 – 2.45 (m, 4H), 1.89 – 1.75 (m, 1H), 1.35 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 162.4 (d, *J* = 246.3 Hz), 158.1, 146.3, 136.9 (d, *J* = 3.3 Hz), 132.5, 130.2, 128.0 (d, *J* = 7.9 Hz), 115.3 (d, *J* = 21.3 Hz), 114.3 (d, *J* = 1.2 Hz), 113.9, 64.6, 55.4, 41.1, 37.3, 36.7. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -115.3. **IR** (ATR): 3344, 2929, 1601, 1508, 1244, 1177, 1030, 898, 839, 806 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{21}FO_2Na$ $[M+Na]^+$ 323.1423, found 323.1409.




**4-(benzo[*d*][1,3]dioxol-5-yl)-2-(4-methoxybenzyl)pent-4-en-1-ol (S7g)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), 3,4-(methylenedioxy)phenylboronic acid (597 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$(34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6g** (1 equiv) was reduced to **S7g** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S7g** as a yellow oil (880 mg, 90% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.07 – 7.01 (m, 2H), 6.85 – 6.76 (m, 4H), 6.74 (dd, *J* = 8.1, 0.5 Hz, 1H), 5.96 (dd, *J* = 1.4, 0.5 Hz, 1H), 5.95 (dd, *J* = 1.4, 0.4 Hz, 1H), 5.24 (d, *J* = 1.6 Hz, 1H), 5.04 (d, *J* = 1.1 Hz, 1H), 3.80 (s, 3H), 3.56 – 3.43 (m, 2H), 2.65 – 2.55 (m, 2H), 2.55 – 2.42 (m, 2H), 1.93 – 1.80 (m, 1H), 1.42 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 147.8, 147.1, 146.8, 135.1, 132.6, 130.2, 119.9, 113.9, 113.4, 108.2, 107.0, 101.1, 64.6, 55.4, 41.1, 37.4, 36.7. **IR** (ATR): 3375, 2915, 1610, 1511, 1488, 1440, 1231, 1177, 1034, 935, 807 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{22}O_4H$ $[M+H]^+$ 327.1596, found 327.1599.

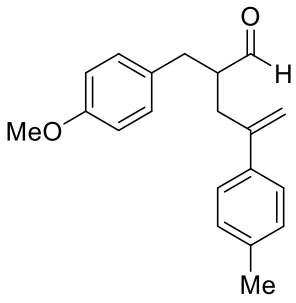



**4-(benzofuran-2-yl)-2-(4-methoxybenzyl)pent-4-en-1-ol (S7h)**: The title compound was prepared following the general procedures for Suzuki cross-coupling and ester reduction using **S5** (940 mg, 3.0 mmol, 1 equiv), 2-benzofuranylboronic acid (583 mg, 3.6 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (34.7 mg, 0.030 mmol, 1 mol%), $Na_2CO_3$ (4.5 mL, 9.0 mmol, 3.0 equiv, 2 M in $H_2O$), and PhMe (15 mL, 0.20 M). Crude **S6h** (1 equiv) was reduced to **S7h** using $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 equiv) and THF (6.0 mL, 0.50 M). The crude material was purified by column chromatography (10% EtOAc in hexanes) to

afford **S7h** as a yellow oil (379 mg, 39% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.48 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.44 (s, 1H), 5.87 (s, 1H), 5.21 (s, 1H), 3.77 (s, 3H), 3.59 – 3.48 (m, 2H), 2.65 (qd, *J* = 13.6, 7.2 Hz, 2H), 2.53 (dd, *J* = 14.2, 8.1 Hz, 1H), 2.42 (dd, *J* = 14.2, 5.9 Hz, 1H), 2.09 – 1.99 (m, 1H), 1.47 (s, 1H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 158.2, 156.4, 154.8, 136.3, 132.6, 130.3, 129.1, 124.7, 122.8, 121.1, 114.3, 113.8, 110.9, 103.2, 64.2, 55.3, 42.5, 36.8, 34.8. **IR** (ATR): 3387, 2930, 1611, 1511, 1452, 1244, 1176, 1031, 804, 743 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{22}O_3Na$ $[M+Na]^+$ 345.1467, found 345.1482.

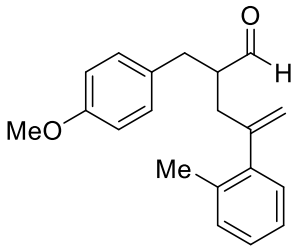
***General Procedure for Swern Oxidation of Alcohols S7***

To an oven-dried round bottom flask was added oxalyl chloride (1.3 equiv) and $CH_2Cl_2$ (0.50 M). The mixture was cooled to -78 °C, and DMSO (3 equiv) was added. The resulting mixture was stirred for 30 min. Alcohol **S7** (1 equiv) was added as a solution in $CH_2Cl_2$ (0.50 M), and the resulting mixture was stirred for 30 min. $Et_3N$ (5 equiv) was added, and the resulting mixture was allowed to warm to rt and stirred for 30 min. The reaction mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography to afford aldehyde **3**.

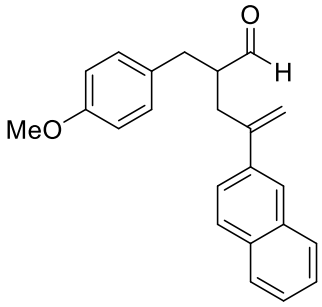



**2-(4-methoxybenzyl)-4-(*p*-tolyl)pent-4-enal (3b)**: The title compound was prepared following the general procedure for Swern oxidation using **S7b** (754 mg, 2.5 mmol, 1 equiv), oxalyl chloride (0.28 mL, 3.3 mmol, 1.3 equiv), DMSO (0.54 mL, 7.6 mmol, 3 equiv), $Et_3N$ (1.8 mL, 12.7 mmol, 5 equiv), and $CH_2Cl_2$ (10.2 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3b** as a light yellow oil (611 mg, 82% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.67 (d, *J* = 1.6 Hz, 1H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 5.33 (s, 1H), 5.08 (s, 1H), 3.79 (s, 3H), 2.93 – 2.82 (m, 2H), 2.77 – 2.67 (m, 2H), 2.60 (dd, *J* = 14.4, 5.7 Hz, 1H), 2.36 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.4, 158.4, 145.4, 137.7, 137.4, 130.7, 130.2, 129.3, 126.3, 114.4, 114.1, 55.4, 51.7, 34.8, 34.2,

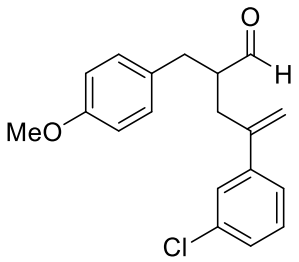
21.2. **IR** (ATR): 2919, 2834, 1723, 1611, 1511, 1442, 1245, 1177, 1034, 825 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{22}O_2NH_4$ $[M+ NH_4]^+$ 312.1964, found 312.1973.



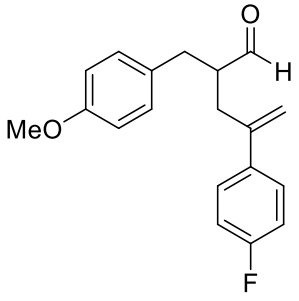

**2-(4-methoxybenzyl)-4-(*o*-tolyl)pent-4-enal (3c)**: The title compound was prepared following the general procedure for Swern oxidation using **S7c** (763 mg, 2.6 mmol, 1 equiv), oxalyl chloride (0.29 mL, 3.3 mmol, 1.3 equiv), DMSO (0.55 mL, 7.7 mmol, 3 equiv), $Et_3N$ (1.8 mL, 12.9 mmol, 5 equiv), and $CH_2Cl_2$ (10.3 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3c** as a colorless oil (713 mg, 94% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 2.3 Hz, 1H), 7.21 – 7.12 (m, 3H), 7.06 (d, *J* = 7.2 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.83 – 6.76 (m, 2H), 5.26 (d, *J* = 1.5 Hz, 1H), 5.01 (d, *J* = 1.6 Hz, 1H), 3.79 (s, 3H), 2.88 (dd, *J* = 14.1, 7.7 Hz, 1H), 2.81 – 2.71 (m, 2H), 2.70 – 2.60 (m, 1H), 2.49 (dd, *J* = 14.7, 5.9 Hz, 1H), 2.26 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.3, 158.4, 146.9, 141.6, 135.1, 130.54, 130.48, 130.1, 128.7, 127.4, 125.8, 116.8, 114.1, 55.4, 51.5, 36.8, 34.4, 20.0. **IR** (ATR): 2931, 2835, 1724, 1611, 1512, 1245, 1178, 1034, 769, 732 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{22}O_2Na$ $[M+ Na]^+$ 317.1518, found 317.1513.



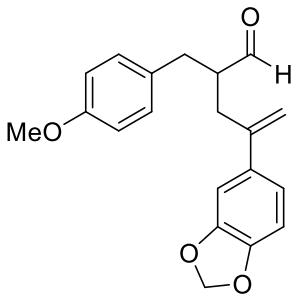

**2-(4-methoxybenzyl)-4-(naphthalen-2-yl)pent-4-enal (3d)**: The title compound was prepared following the general procedure for Swern oxidation using **S7d** (807 mg, 2.4 mmol, 1 equiv), oxalyl chloride (0.27 mL, 3.2 mmol, 1.3 equiv), DMSO(0.52 mL, 7.3 mmol, 3 equiv), $Et_3N$ (1.7 mL, 12.1 mmol, 5 equiv), and $CH_2Cl_2$ (9.7 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3d** as a white solid (685 mg, 85% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.72 (d, *J* = 1.5 Hz, 1H), 7.86 – 7.70 (m, 3H), 7.63 (s, 1H), 7.53 – 7.43 (m, 3H), 7.04(d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.51 (s, 1H), 5.24 (s, 1H), 3.81 (s, 3H), 3.05 – 2.87 (m, 2H), 2.83 – 2.68 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.2, 158.4, 145.4, 137.4, 133.5, 133.1, 130.6, 130.2, 128.32, 128.27, 127.7, 126.4, 126.2, 125.1, 124.7, 115.7, 114.1, 55.4, 51.8, 34.6, 34.3. **IR** (ATR): 2929, 2834, 1717, 1611, 1511, 1245, 1177, 1031, 828, 816, 754 $cm^{-1}$. **HRMS** calculated for $C_{23}H_{22}O_2Na$ $[M+ Na]^+$ 353.1518, found 353.1518.



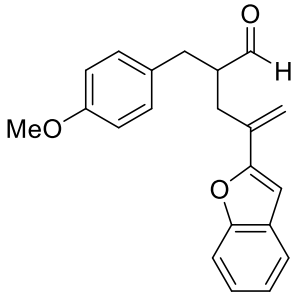

**4-(3-chlorophenyl)-2-(4-methoxybenzyl)pent-4-enal (3e)**: The title compound was prepared following the general procedure for Swern oxidation using **S7e** (732 mg, 2.3 mmol, 1 equiv), oxalyl chloride (0.26 mL, 3.0 mmol, 1.3 equiv), DMSO (0.49 mL, 6.9 mmol, 3 equiv), $Et_3N$ (1.6 mL, 11.6 mmol, 5 equiv), and $CH_2Cl_2$ (9.2 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3e** as a light yellow oil (710 mg, 98% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.68 (d, *J* = 1.9 Hz, 1H), 7.26 – 7.22 (m, 3H), 7.15 (dt, *J* = 6.4, 2.1 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.85 – 6.81 (m, 2H), 5.36 (d, *J* = 0.5 Hz, 1H), 5.16 (d, *J* = 1.1 Hz, 1H), 3.80 (s, 3H), 2.96 – 2.82 (m, 2H), 2.74 – 2.65 (m, 2H), 2.61 – 2.54 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 203.9, 158.5, 144.5, 142.3, 134.6, 130.3, 130.2, 129.9, 128.0, 126.6, 124.6, 116.2, 114.2, 55.4, 51.6, 34.4, 34.2. **IR** (ATR): 2933, 2834, 1723, 1611, 1511, 1300, 1245, 1178, 1034, 790 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{19}ClO_2Na$ [M+ Na]$^+$ 337.0971, found 337.0987.




**4-(4-fluorophenyl)-2-(4-methoxybenzyl)pent-4-enal (3f)**: The title compound was prepared following the general procedure for Swern oxidation using **S7f** (773 mg, 2.6 mmol, 1 equiv), oxalyl chloride (0.29 mL, 3.0 mmol, 1.3 equiv), DMSO (0.55 mL, 7.7 mmol, 3 equiv), $Et_3N$ (1.8 mL, 12.9 mmol, 5 equiv), and $CH_2Cl_2$ (10.3 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3f** as a colorless oil (721 mg, 94% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.67 (d, *J* = 2.0 Hz, 1H), 7.26 – 7.21 (m, 2H), 7.00 (dd, *J* = 8.5, 8.0 Hz, 4H), 6.82 (d, *J* = 8.3 Hz, 2H), 5.29 (s, 1H), 5.11 (s, 1H), 3.79 (s, 3H), 2.94 – 2.82 (m, 2H), 2.74 – 2.64 (m, 2H), 2.58 (dd, *J* = 14.5, 4.9 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.1, 162.6 (d, *J* = 246.9 Hz), 158.5, 144.6, 136.4 (d, *J* = 3.3 Hz), 130.4, 130.2, 128.0 (d, *J* = 8.0 Hz), 115.5 (d, *J* = 21.4 Hz), 115.1 (d, *J* = 1.2 Hz), 114.1, 55.4, 51.7, 34.8, 34.2. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.8. **IR** (ATR): 2934, 2835, 1723, 1611, 1508, 1245, 1178, 1161, 1034, 839 cm$^{-1}$. **HRMS** calculated for $C_{19}H_{19}FO_2Na$ [M+ Na]$^+$ 321.1267, found 321.1264.

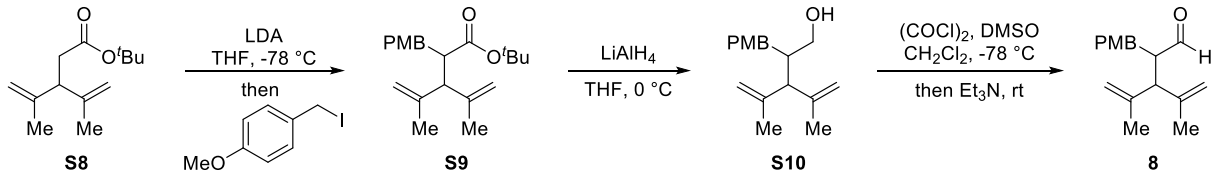


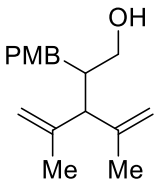
**4-(benzo[*d*][1,3]dioxol-5-yl)-2-(4-methoxybenzyl)pent-4-enal (3g)**: The title compound was prepared following the general procedure for Swern oxidation using **S7g** (756 mg, 2.3 mmol, 1 equiv), oxalyl chloride (0.26 mL, 3.0 mmol, 1.3 equiv), DMSO (0.49 mL, 6.9 mmol, 3 equiv), $Et_3N$ (1.6 mL, 11.6 mmol, 5 equiv), and $CH_2Cl_2$ (9.3 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3g** as a colorless oil (595 mg, 79% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 1.9 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.85 – 6.78 (m, 3H), 6.75 (d, *J* = 1.0 Hz, 2H), 5.98 – 5.93 (m, 2H), 5.25 (s, 1H), 5.04 (s, 1H), 3.79 (s, 3H), 2.86 (ddd, *J* = 21.6, 15.3, 8.3 Hz, 2H), 2.75 – 2.66 (m, 2H), 2.55 (dd, *J* = 14.3, 5.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.2, 158.4, 148.0, 147.4, 145.1, 134.6, 130.6, 130.2, 119.9, 114.3, 114.1, 108.3, 107.0, 101.3, 55.4, 51.7, 35.0, 34.2. **IR** (ATR): 2906, 2835, 1722, 1611, 1512, 1440, 1231, 1178, 1035, 809 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{20}O_4Na$ $[M+ Na]^+$ 347.1259, found 347.1263.



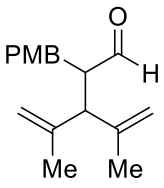
**4-(benzofuran-2-yl)-2-(4-methoxybenzyl)pent-4-enal (3h)**: The title compound was prepared following the general procedure for Swern oxidation using **S7h** (379 mg, 1.2 mmol, 1 equiv), oxalyl chloride (0.13 mL, 1.5 mmol, 1.3 equiv), DMSO (0.25 mL, 3.5 mmol, 3 equiv), $Et_3N$ (0.82 mL, 5.9 mmol, 5 equiv), and $CH_2Cl_2$ (4.8 mL, 0.25 M). The crude material was purified by column chromatography (3% EtOAc in hexanes) to afford **3h** as a yellow oil (297 mg, 79% yield). **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 9.70 (d, *J* = 1.9 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 7.7 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.43 (s, 1H), 5.87 (s, 1H), 5.21 (s, 1H), 3.76 (s, 3H), 2.93 (ddd, *J* = 20.4, 14.0, 7.0 Hz, 2H), 2.79 (ddd, *J* = 19.5, 13.9, 7.0 Hz, 2H), 2.53 (dd, *J* = 14.3, 5.2 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CD_2Cl_2$) δ 203.6, 158.6, 155.7, 154.8, 134.9, 130.5, 130.2, 128.9, 124.9, 122.9, 121.2, 114.9, 114.1, 111.0, 103.1, 55.3, 52.6, 34.5, 32.0. **IR** (ATR): 2933, 2834, 1723, 1611, 1511, 1452, 1245, 1176, 1034, 806, 743 $cm^{-1}$. **HRMS** calculated for $C_{21}H_{20}O_3Na$ $[M+ Na]^+$ 343.1310, found 343.1302.

***Preparation of Aldehyde 8***



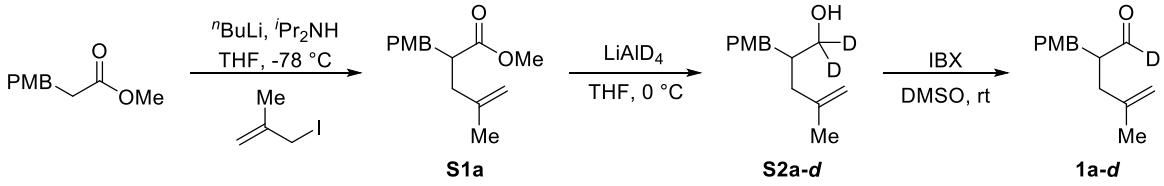



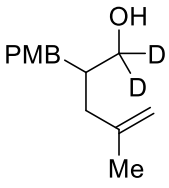

**2-(4-methoxybenzyl)-4-methyl-3-(prop-1-en-2-yl)pent-4-en-1-ol (S10)**: To an oven-dried round bottom flask was added $^i$Pr$_2$NH (3.5 mL, 25 mmol, 1.3 equiv) and THF (47 mL, 0.33 M), and the resulting solution was cooled to -78 °C. Then, $^n$BuLi (9.6 mL, 24 mmol, 1.2 equiv, 2.5 M in THF) was added dropwise, and the resulting mixture was stirred for 1 hr. A solution of ester **S8**[9] (4.21 g, 20 mmol, 1.0 equiv) in THF (10 mL) was added dropwise, and the resulting mixture was stirred for 1 h. Then, 4-methoxybenzyl iodide[10] (7.44 g, 30 mmol, 1.5 equiv) was added, and the reaction mixture was stirred for 3 h. The reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The ester **S9** was used without further purification. Crude **S9** was dissolved in THF (40 mL, 0.50 M), and the solution was cooled to 0 °C. $LiAlH_4$ (1.1 g, 30 mmol, 1.5 equiv) was added portionwise, and the resulting mixture was stirred at 60 °C for 12 h. The reaction was cooled to rt and quenched using the Fieser method. The resulting mixture was filtered through celite and concentrated *in vacuo*. The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S10** as a colorless oil (3.16 g, 61% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.14 (d, $J$ = 8.5 Hz, 2H), 6.84 (d, $J$ = 8.5 Hz, 2H), 5.02 (s, 1H), 4.95 (s, 1H), 4.90 (s, 1H), 4.87 (s, 1H), 3.80 (s, 3H), 3.55 (dd, $J$ = 11.3, 3.7 Hz, 1H), 3.48 (dd, $J$ = 11.3, 3.1 Hz, 1H), 2.81 (dd, $J$ = 13.9, 3.1 Hz, 1H), 2.72 (d, $J$ = 11.4 Hz, 1H), 2.47 (dd, $J$ = 13.8, 10.5 Hz, 1H), 2.04 (ddd, $J$ = 14.3, 7.2, 3.4 Hz, 1H), 1.76 (s, 3H), 1.69 (s, 3H), 1.39 (s, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.0, 145.7, 144.5, 133.1, 130.2, 113.9, 112.8, 112.3, 61.8, 56.3, 55.4, 41.8, 34.0, 21.8, 20.2. **IR** (ATR): 3411, 2936, 1611, 1510, 1442, 1244, 1177, 1035, 890, 808 cm$^{-1}$. **HRMS** calculated for $C_{17}H_{24}O_2Na$ $[M+Na]^+$ 283.1674, found 283.1687.



**2-(4-methoxybenzyl)-4-methyl-3-(prop-1-en-2-yl)pent-4-enal (8)**: To an oven-dried round bottom flask was added oxalyl chloride (1.0 mL, 11.5 mmol, 1.3 equiv) and $CH_2Cl_2$ (18 mL, 0.50 M). The mixture was cooled to -78 °C, and DMSO (1.9 mL, 26.5 mmol, 3 equiv) was added. The resulting mixture was stirred for 30 min. Alcohol **S10** (2.30 g, 8.83 mmol, 1.0 equiv) was added as a solution in $CH_2Cl_2$ (18 mL, 0.50 M), and the resulting mixture was stirred for 30 min. $Et_3N$ (6.2 mL, 44.2 mmol, 5 equiv) was added, and the resulting mixture was allowed to warm to rt and stirred for 30 min. The reaction mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (5% EtOAc in hexanes) to afford **8** as a colorless oil (1.71 g, 75% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.50 (d, *J* = 3.1 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.05 (s, 1H), 4.97 (s, 1H), 4.91 (s, 1H), 4.80 (s, 1H), 3.78 (s, 3H), 3.01 – 2.92 (m, 2H), 2.89 – 2.82 (m, 1H), 2.70 (dd, *J* = 14.4, 8.7 Hz, 1H), 1.71 (s, 3H), 1.67 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.5, 158.3, 143.7, 142.6, 130.7, 130.1, 114.4, 114.1, 113.6, 55.4, 55.1, 53.2, 34.0, 21.6, 19.9. **IR** (ATR): 2938, 2835, 1727, 1612, 1512, 1245, 1178, 1035, 896, 827 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{22}O_2Na$ $[M+Na]^+$ 281.1518, found 281.1515.

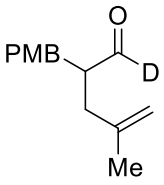
***Preparation of Aldehyde 1a-d***



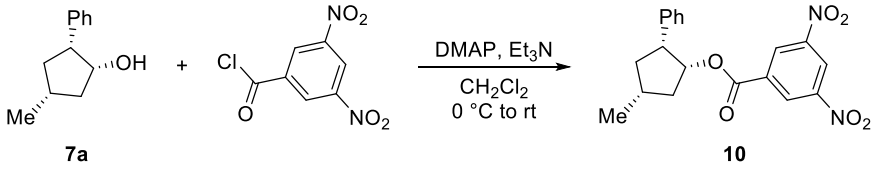
**2-(4-methoxybenzyl)-4-methylpent-4-en-1,1-$d_2$-1-ol (S2a-*d*)**: To an oven-dried round bottom flask was added $^i$Pr$_2$NH (0.85 mL, 6.0 mmol, 1.2 equiv) and THF (10 mL, 0.33 M), and the resulting solution was cooled to -78 °C. Then, $^n$BuLi (2.2 mL, 5.5 mmol, 1.1 equiv, 2.5 M in THF) was added dropwise, and the resulting mixture was allowed to stir for 45 min. A solution of methyl 3-(4-methoxyphenyl)propanoate (971 mg, 5.0 mmol, 1.0 equiv) in THF (5 mL) was added dropwise, and the resulting mixture was allowed to stir for 1 h. Then, methallyl iodide (1.1 g, 6.0 mmol, 1.2 equiv) was added, and the reaction mixture was allowed to stir for 2 h. The reaction was

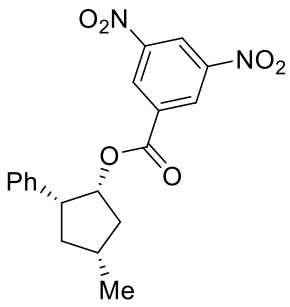
quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The ester **S1a** was used without further purification. Crude **S1a** was dissolved in THF (10 mL, 0.50 M), and the solution was cooled to 0 °C. $LiAlD_4$ (315 mg, 7.5 mmol, 1.5 equiv) was added portionwise, and the resulting mixture was stirred for 1 h. The reaction was quenched using the Fieser method. The resulting mixture was filtered through celite and concentrated *in vacuo*. The crude material was purified by column chromatography (10% EtOAc in hexanes) to afford **S2a-*d*** as a colorless oil (478 mg, 43% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.81 (s, 1H), 4.78 (s, 1H), 3.80 (s, 3H), 2.58 (d, *J* = 6.8 Hz, 2H), 2.17 – 2.07 (m, 1H), 2.00 (ddd, *J* = 21.2, 13.9, 6.6 Hz, 2H), 1.73 (s, 3H), 1.37 (s, 1H). **$^{13}$C NMR** (151 MHz, $CDCl_3$) δ 158.0, 144.7, 132.7, 130.2, 113.9, 112.2, 65.1 – 63.7 (m), 55.4, 40.3, 40.3, 36.8, 22.4. **IR** (ATR): 3369, 2914, 1611, 1511, 1442, 1244, 1177, 1035, 888, 829 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{18}D_2O_2Na$ $[M+Na]^+$ 245.1487, found 245.1489.




**2-(4-methoxybenzyl)-4-methylpent-4-enal-1-*d* (1a-*d*)**: To a round bottom flask was added alcohol **S2a-*d*** (453 mg, 2.0 mmol, 1.0 equiv) and DMSO (8 mL, 0.25 M). IBX[7] (628 mg, 2.2 mmol, 1.1 equiv) was added, and the resulting mixture was stirred overnight at rt. The reaction mixture was quenched with $H_2O$ (32 mL) and extracted with $CH_2Cl_2$ (3 x 10 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (5% EtOAc in hexanes) to afford **1a-*d*** as a colorless oil (365 mg, 82% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 4.84 (s, 1H), 4.75 (s, 1H), 3.79 (s, 3H), 2.90 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.79 (dt, *J* = 13.9, 6.9 Hz, 1H), 2.71 (dd, *J* = 13.7, 6.1 Hz, 1H), 2.39 (dd, *J* = 14.8, 8.0 Hz, 1H), 2.15 (dd, *J* = 14.9, 6.3 Hz, 1H), 1.73 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.8 – 203.8 (m), 158.4, 142.3, 130.7, 130.1, 114.1, 113.0, 55.4, 51.4 – 51.2 (m), 37.2, 34.3, 22.6. **IR** (ATR): 2935, 2836, 1710, 1612, 1512, 1442, 1244, 1178, 1034, 830 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{17}DO_2Na$ $[M+Na]^+$ 242.1267, found 242.1273.

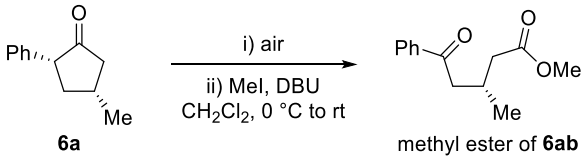
## 4. Esterification of 7a

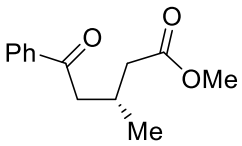



**(1*R*,2*R*,4*R*)-4-methyl-2-phenylcyclopentyl 3,5-dinitrobenzoate (10)**: Alcohol **7a** (20.8 mg, 0.12 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (0.24 mL, 0.50 M) in a 1 dram vial equipped with a magnetic stir bar. $Et_3N$ (33 mL, 0.24 mmol, 2.0 equiv) and DMAP (1.4 mg, 0.012 mmol, 10 mol%) were added. The resulting solution was cooled to 0 °C, and 3,5-dinitrobenzoyl chloride (40.8 mg, 0.18 mmol, 1.5 equiv) was added. The vial was then sealed with a Teflon-lined screw cap and stirred overnight. The reaction mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3 x 5 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. The title compound was isolated by preparative thin-layer chromatography (30% EtOAc in hexanes) as a yellow solid (37.3 mg, 85% yield, $[\alpha]^{24}_D$ = –112.2 (*c* 0.56, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.12 (t, *J* = 2.1 Hz, 1H), 8.78 (d, *J* = 2.1 Hz, 2H), 7.31 (dd, *J* = 12.6, 7.2 Hz, 4H), 7.15 (t, *J* = 7.1 Hz, 1H), 5.63 (td, *J* = 6.4, 3.6 Hz, 1H), 3.51 – 3.38 (m, 1H), 2.72 – 2.55 (m, 1H), 2.35 – 2.16 (m, 2H), 2.01 – 1.89 (m, 1H), 1.59 (ddd, *J* = 14.4, 8.3, 3.5 Hz, 1H), 1.32 – 1.11 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 162.0, 148.6, 139.0, 134.4, 129.2, 128.5, 128.4, 126.9, 122.1, 81.0, 50.3, 41.6, 38.5, 32.4, 21.0. **IR** (ATR): 3113, 2956, 1715, 1630, 1546, 1460, 1344, 1287, 1174, 754 $cm^{-1}$.

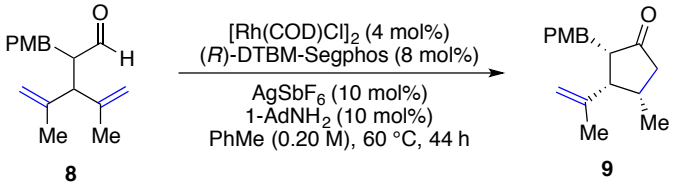
## 5. Oxidative Decomposition of 6a

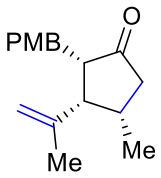



**methyl (*R*)-3-methyl-5-oxo-5-phenylpentanoate**: Ketone **6a** (12.0 mg, 0.069 mmol, 1.0 equiv) was allowed to stand in a 1 dram vial opened to air until full consumption of **6a** was observed by $^{1}$H NMR (ca. 2 weeks). Then, $CH_2Cl_2$ (0.20 mL) and DBU (15 mL, 0.10 mmol, 1.5 equiv) was added to the crude material. The resulting mixture was cooled to 0 °C, and MeI (8.6 mL, 0.14 mmol, 2.0 equiv) was added. The vial was then sealed with a Teflon-lined screw cap and stirred overnight. The reaction mixture was concentrated *in vacuo*. The title compound was isolated by preparative thin-layer chromatography (5% EtOAc in hexanes) as a colorless oil (4.5 mg, 30% yield, $[\alpha]^{24}_{D}$ = +3.7 (*c* 0.30, $CHCl_3$)). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 3.68 (s, 3H), 3.11 (dd, *J* = 16.2, 5.9 Hz, 1H), 2.85 (dd, *J* = 16.3, 7.5 Hz, 1H), 2.69 (dq, *J* = 13.5, 6.7 Hz, 1H), 2.45 (dd, *J* = 15.3, 6.6 Hz, 1H), 2.33 (dd, *J* = 15.3, 7.0 Hz, 1H), 1.06 (d, *J* = 6.7 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 199.4, 173.2, 137.2, 133.2, 128.8, 128.3, 51.6, 45.0, 41.1, 27.0, 20.3. **IR** (ATR): 2954, 1732, 1682, 1448, 1368, 1211, 1159, 1002, 753, 690 cm$^{-1}$. **HRMS** calculated for $C_{13}H_{16}O_3Na$ $[M+Na]^+$ 243.0997, found 243.0996.

## 6. Hydroacylation of Aldehyde 8

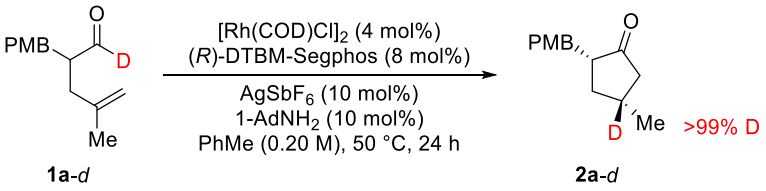


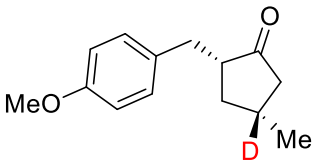

**(2*S*,3*R*,4*S*)-2-(4-methoxybenzyl)-4-methyl-3-(prop-1-en-2-yl)cyclopentan-1-one (9)**: In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol, 4 mol%), (*R*)-DTBM-Segphos (10.7 mg, 0.0080 mmol, 8 mol%), and toluene (0.50 mL, 0.20 M) were added to a 1 dram vial equipped with a magnetic stir bar. The solution was stirred at 30 °C for 10 min. $AgSbF_6$ (3.4 mg, 0.010 mmol, 10 mol%), was added, and the resulting mixture was stirred 30 °C for 30 min. Aldehyde **8** (25.8 mg, 0.10 mmol, 1.0 equiv) and 1-$AdNH_2$ (1.5 mg, 0.010 mmol, 10 mol%) were added. The vial was then sealed with

a Teflon-lined screw cap and stirred at 60 °C for 44 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The title compound was isolated by preparative thin-layer chromatography (5% EtOAc in hexanes) as a colorless oil (13.7 mg, 53% yield, >20:1:1:1 *dr*, >99% *ee*, $[\alpha]^{24}_D$ = +74.3 (*c* 0.56, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.09 – 7.01 (m, 2H), 6.81 – 6.74 (m, 2H), 4.93 (dq, *J* = 2.9, 1.4 Hz, 1H), 4.83 (dd, *J* = 1.5, 0.6 Hz, 1H), 3.78 (s, 3H), 2.92 (dd, *J* = 14.1, 4.5 Hz, 1H), 2.72 (dd, *J* = 14.1, 5.5 Hz, 1H), 2.56 – 2.45 (m, 1H), 2.45 – 2.35 (m, 1H), 2.08 – 1.91 (m, 2H), 1.68 – 1.54 (m, 4H), 0.97 (d, *J* = 6.1 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.3, 158.1, 142.8, 131.4, 131.0, 115.1, 113.6, 57.2, 55.33, 55.26, 46.6, 32.9, 32.3, 17.88, 17.76. **IR** (ATR): 2954, 2915, 1738, 1611, 1511, 1441, 1244, 1177, 1035, 893 cm$^{-1}$. **HRMS** calculated for $C_{17}H_{22}O_2Na$ $[M+Na]^+$ 281.1518, found 281.1507. **Chiral SFC**: 250 mm CHIRALPAK IC, 3% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (minor) = 13.6 min, $t_{R2}$ (major) = 14.8 min.

## 7. Deuterium Labeling Experiment



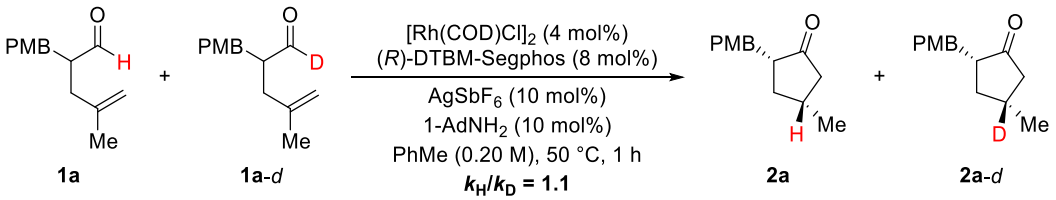

**1a**-*d* **2a**-*d*




**(2*R*,4*R*)-2-(4-methoxybenzyl)-4-methylcyclopentan-1-one-4-*d* (2a-*d*)**: In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol, 4 mol%), (*R*)-DTBM-Segphos (10.7 mg, 0.0080 mmol, 8 mol%), and toluene (0.50 mL, 0.20 M) were added to a 1 dram vial equipped with a magnetic stir bar. The solution was stirred at 30 °C for 10 min. $AgSbF_6$ (3.4 mg, 0.010 mmol, 10 mol%), was added, and the resulting mixture was stirred 30 °C for 30 min. Aldehyde **1a**-*d* (21.9 mg, 0.10 mmol, 1.0 equiv) and 1-$AdNH_2$ (1.5 mg, 0.010 mmol, 10 mol%) were added. The vial was then sealed with a Teflon-lined screw cap and stirred at 50 °C for 24 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The title compound was isolated by preparative thin-layer chromatography (5% EtOAc in hexanes) as

a white solid (18.2 mg, 83% yield, >20:1 *dr*, >99% *ee*, $[\alpha]^{24}_{D}$ = +71.2 (*c* 0.78, $CHCl_3$)). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.11 (dd, *J* = 13.8, 3.9 Hz, 1H), 2.56 – 2.44 (m, 2H), 2.44 – 2.35 (m, 1H), 2.20 – 2.10 (m, 1H), 1.71 (d, *J* = 18.5 Hz, 1H), 1.15 (t, *J* = 12.4 Hz, 1H), 1.09 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 219.9, 158.1, 132.2, 129.9, 114.0, 55.4, 53.1, 46.9, 38.2, 34.8, 29.3 (t, *J* = 19.6 Hz), 20.2. **IR** (ATR): 2953, 2867, 1736, 1611, 1511, 1455, 1243, 1177, 1034, 818 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{17}DO_2Na$ $[M+Na]^+$ 242.1267, found 242.1278. **Chiral SFC**: 100 mm CHIRALPAK AD-H, 1% *i*-PrOH, 2.0 mL/min, 220 nm, 44 °C, nozzle pressure = 200 bar $CO_2$, $t_{R1}$ (major) = 5.8 min, $t_{R2}$ (minor) = 7.9 min.

## 8. Kinetic Isotope Effect Experiment

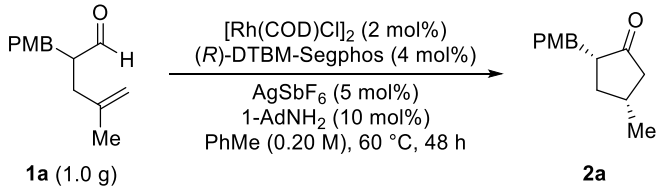



In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (2.0 mg, 0.0040 mmol), (*R*)-DTBM-Segphos (10.7 mg, 0.0080 mmol), and toluene (0.25 mL) were added to a 1 dram vial equipped with a magnetic stir bar. The solution was stirred at 30 °C for 10 min. $AgSbF_6$ (3.4 mg, 0.010 mmol) was added, and the resulting mixture was stirred 30 °C for 30 min. Aldehydes **1a** (11.0 mg, 0.050 mmol) and **1a**-*d* (11.0 mg, 0.050 mmol) were added as a solution in toluene (0.25 mL). Then, 1-$AdNH_2$(1.5 mg, 0.010 mmol) was added. The vial was then sealed with a Teflon-lined screw cap and stirred at 50 °C for 1 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The crude mixture was purified by preparative thin-layer chromatography (5% EtOAc in hexanes) to afford a mixture of **2a** and **2a**-*d* (3.9 mg, 18% yield). The ratio (1.1:1.0) of **2a** and **2a**-*d* was determined by $^1$H NMR.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.11 (dd, *J* = 13.7, 3.9 Hz, 1H), 2.55 – 2.45 (m, 2H), 2.44 – 2.35 (m, 1H), 2.16 (d, *J* = 12.1 Hz, 1H), 2.12 – 2.03 (m, **0.54H**), 1.77 – 1.66 (m, 1H), 1.22 – 1.12 (m, 1H), 1.10 (d, *J* = 6.3 Hz, 3H).

Recovered unreacted **1a** and **1a**-*d* (19.3 mg, 88% yield): **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.5 Hz, **0.43H**), 7.09 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.84 (s, 1H), 4.75 (s, 1H), 3.79 (s, 3H), 2.90 (dd, *J* = 13.4, 7.4 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.71(dd, *J* = 13.4, 6.0 Hz, 1H), 2.39 (dd, *J* = 14.8, 7.9 Hz, 1H), 2.15 (dd, *J* = 14.7, 6.2 Hz, 1H), 1.72 (s, 3H).

## 9. Gram-scale Dynamic Kinetic Resolution of 1a

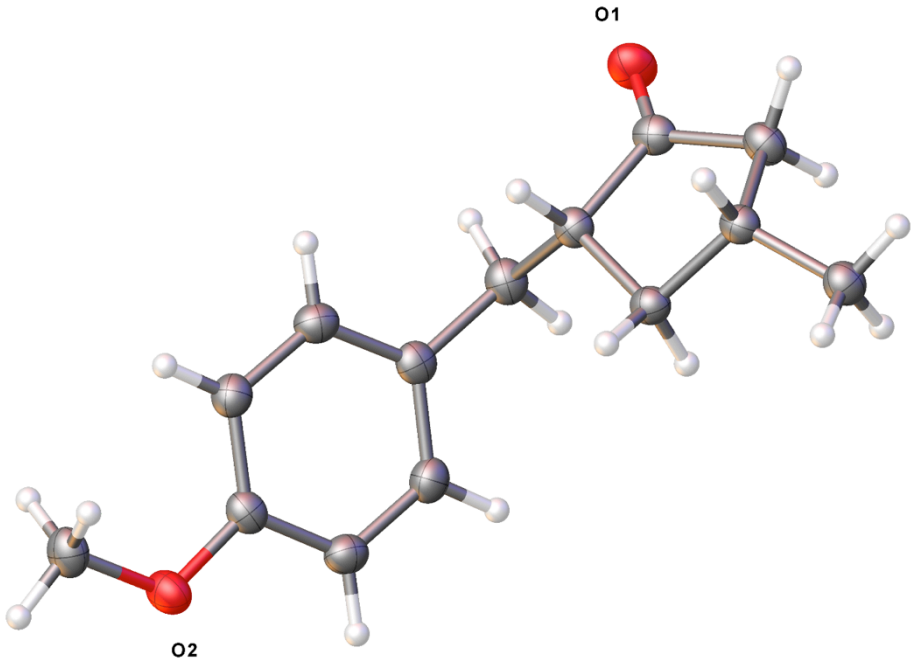



**1a** (1.0 g) **2a**

In a $N_2$-filled glovebox, $[Rh(COD)Cl]_2$ (45.2 mg, 0.092 mmol, 2 mol%), (*R*)-DTBM-Segphos (216 mg, 0.183 mmol, 4 mol%), and toluene (23 mL, 0.20 M) were added to an oven-dried round bottom flask equipped with a magnetic stir bar. The solution was stirred at 30 °C for 15 min. $AgSbF_6$ (78.7 mg, 0.229 mmol, 5 mol%) was added, and the resulting mixture was stirred 30 °C for 30 min. Aldehyde **1a** (1.0 g, 4.58 mmol, 1.0 equiv) and 1-$AdNH_2$ (69.3 mg, 0.458 mmol, 10 mol%) were added sequentially. The flask was then sealed with a rubber septum and removed from the glovebox. A $N_2$-filled balloon was attached, and the reaction was stirred at 60 °C for 48 h. The reaction mixture was cooled to rt, filtered through celite, and concentrated *in vacuo*. The diastereoselectivity was determined by $^1$H NMR analysis of the unpurified reaction mixture. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to afford **2a** as a light yellow solid (891 mg, 89% yield, >20:1 *dr*, >99% *ee*). The $^1$H NMR data matched those for **2a** obtained by following general Method A (page 569). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.11 (dd, *J* = 13.8, 4.0 Hz, 1H), 2.56 – 2.45 (m, 2H), 2.40 (dtd, *J* = 12.4, 8.1, 4.1 Hz, 1H), 2.21 – 2.03 (m, 2H), 1.71 (dd, *J* = 18.4, 11.3 Hz, 1H), 1.21 – 1.11 (m, 1H), 1.10 (d, *J* = 6.3 Hz, 3H).

## 10. X-ray Crystallographic Data

***X-ray Crystallographic Data for 2a* (CCDC 1869120)**




The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX-II CCD diffractometer equipped with Cu $K_a$ radiation (l = 1.5478). A 0.153 x 0.067 x 0.042 mm piece of a colorless block was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using f and v scans. Crystal-to-detector distance was 40 mm using variable exposure time (5s-20s) depending on q with a scan width of 2.0°. Data collection was 99.0% complete to 68.00° in *q*. A total of 12765 reflections were collected covering the indices, -5<=h<=6, -11<=k<=11, -14<=l<=14. 2136 reflections were found to be symmetry independent, with a $R_{int}$ of 0.0286. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be $P2_1$. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained

relative to their parent atom using the appropriate HFIX command in SHELXL-2014. The absolute stereochemistry of the molecule was established by anomalous dispersion using the Parson's method with a Flack parameter of 0.022(64). Crystallographic data are summarized in Table A2.3.1.

**Table A2.3.1.** Crystal data and structure refinement for UCI_Dong_11-ZC-4.

| | | |
|---|---|---|
| Report date | 2018-06-27 | |
| Identification code | 11-ZC-4 | |
| Empirical formula | C14 H18 O2 | |
| Molecular formula | C14 H18 O2 | |
| Formula weight | 218.28 | |
| Temperature | 100.0 K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Monoclinic | |
| Space group | P 1 21 1 | |
| Unit cell dimensions | a = 5.1826(3) Å | α= 90°. |
| | b = 9.6599(5) Å | β= 93.160(2)°. |
| | c = 11.8510(6) Å | γ = 90°. |
| Volume | 592.40(5) $Å^3$ | |
| Z | 2 | |
| Density (calculated) | 1.224 $Mg/m^3$ | |
| Absorption coefficient | 0.634 $mm^{-1}$ | |
| F(000) | 236 | |
| Crystal size | 0.153 x 0.067 x 0.042 $mm^3$ | |
| Crystal color, habit | Colorless Block | |
| Theta range for data collection | 3.735 to 68.149°. | |

| | |
|---|---|
| Index ranges | -5<=h<=6, -11<=k<=11, -14<=l<=14 |
| Reflections collected | 12765 |
| Independent reflections | 2136 [R(int) = 0.0286, R(sigma) = 0.0187] |
| Completeness to theta = 68.000° | 99.0 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.3200 and 0.2284 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 2136 / 1 / 147 |
| Goodness-of-fit on $F^2$ | 1.043 |
| Final R indices [I>2sigma(I)] | R1 = 0.0264, wR2 = 0.0670 |
| R indices (all data) | R1 = 0.0272, wR2 = 0.0674 |
| Absolute structure parameter | 0.02(6) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.114 and -0.130 e.$Å^{-3}$ |

**Table A2.3.2.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for UCI_Dong_11-ZC-4. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 10292(3) | 2748(1) | 5621(1) | 32(1) |
| O(2) | 976(3) | 6936(1) | 10207(1) | 31(1) |
| C(1) | 8554(3) | 3506(2) | 5284(2) | 25(1) |
| C(2) | 7910(4) | 3901(2) | 4069(2) | 27(1) |

| | | | | |
|---|---|---|---|---|
| C(3) | 5249(3) | 4593(2) | 4073(1) | 24(1) |
| C(4) | 5314(4) | 5292(2) | 5244(1) | 24(1) |
| C(5) | 6663(3) | 4229(2) | 6033(1) | 23(1) |
| C(6) | 7990(4) | 4765(2) | 7133(2) | 28(1) |
| C(7) | 6116(4) | 5325(2) | 7949(1) | 24(1) |
| C(8) | 4598(3) | 4437(2) | 8553(2) | 27(1) |
| C(9) | 2833(4) | 4918(2) | 9306(2) | 26(1) |
| C(10) | 2584(3) | 6336(2) | 9469(1) | 25(1) |
| C(11) | 4082(4) | 7246(2) | 8871(2) | 28(1) |
| C(12) | 5821(4) | 6744(2) | 8123(2) | 27(1) |
| C(13) | 4690(4) | 5572(2) | 3088(2) | 28(1) |
| C(14) | -674(4) | 6038(2) | 10795(2) | 31(1) |

**Table A2.3.3.** Bond lengths [Å] and angles [°] for UCI_Dong_11-ZC-4.

| | | | |
|---|---|---|---|
| O(1)-C(1) | 1.212(2) | C(2)-C(3)-C(4) | 102.64(14) |
| O(2)-C(10) | 1.370(2) | C(13)-C(3)-C(2) | 113.76(15) |
| O(2)-C(14) | 1.426(2) | C(13)-C(3)-C(4) | 114.42(15) |
| C(1)-C(2) | 1.509(3) | C(5)-C(4)-C(3) | 104.03(14) |
| C(1)-C(5) | 1.526(2) | C(1)-C(5)-C(4) | 103.81(14) |
| C(2)-C(3) | 1.533(3) | C(1)-C(5)-C(6) | 112.14(14) |
| C(3)-C(4) | 1.542(2) | C(4)-C(5)-C(6) | 117.49(15) |
| C(3)-C(13) | 1.518(3) | C(7)-C(6)-C(5) | 113.12(14) |
| C(4)-C(5) | 1.530(2) | C(8)-C(7)-C(6) | 120.79(16) |
| C(5)-C(6) | 1.531(2) | C(8)-C(7)-C(12) | 117.44(17) |

| | | | |
|---|---|---|---|
| C(6)-C(7) | 1.509(2) | C(12)-C(7)-C(6) | 121.77(17) |
| C(7)-C(8) | 1.389(3) | C(7)-C(8)-C(9) | 122.31(17) |
| C(7)-C(12) | 1.395(3) | C(10)-C(9)-C(8) | 119.19(17) |
| C(8)-C(9) | 1.392(3) | O(2)-C(10)-C(9) | 124.77(16) |
| C(9)-C(10) | 1.390(3) | O(2)-C(10)-C(11) | 115.73(15) |
| C(10)-C(11) | 1.392(3) | C(9)-C(10)-C(11) | 119.49(16) |
| C(11)-C(12) | 1.386(3) | C(12)-C(11)-C(10) | 120.34(17) |

| | |
|---|---|
| C(11)-C(12)-C(7) | 121.23(17) |
| C(10)-O(2)-C(14) | 117.18(14) |
| O(1)-C(1)-C(2) | 126.03(18) |
| O(1)-C(1)-C(5) | 125.09(17) |
| C(2)-C(1)-C(5) | 108.87(15) |
| C(1)-C(2)-C(3) | 105.00(15) |

**Table A2.3.4.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for UCI_Dong_11-ZC-4. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 26(1) | 36(1) | 35(1) | 0(1) | 1(1) | 8(1) |
| O(2) | 28(1) | 32(1) | 34(1) | -5(1) | 8(1) | -1(1) |
| C(1) | 18(1) | 25(1) | 31(1) | -2(1) | 2(1) | -2(1) |
| C(2) | 23(1) | 31(1) | 28(1) | -3(1) | 3(1) | 1(1) |
| C(3) | 21(1) | 24(1) | 26(1) | -1(1) | 2(1) | -1(1) |
| C(4) | 22(1) | 23(1) | 26(1) | -1(1) | 2(1) | 1(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(5) | 19(1) | 26(1) | 25(1) | 0(1) | 2(1) | -1(1) |
| C(6) | 22(1) | 34(1) | 26(1) | 0(1) | -1(1) | -1(1) |
| C(7) | 22(1) | 29(1) | 21(1) | 0(1) | -4(1) | 0(1) |
| C(8) | 26(1) | 25(1) | 29(1) | -1(1) | -2(1) | 0(1) |
| C(9) | 24(1) | 28(1) | 26(1) | 1(1) | 0(1) | -3(1) |
| C(10) | 20(1) | 31(1) | 23(1) | -2(1) | -1(1) | 1(1) |
| C(11) | 29(1) | 24(1) | 29(1) | 0(1) | -1(1) | 2(1) |
| C(12) | 26(1) | 30(1) | 25(1) | 4(1) | 0(1) | -2(1) |
| C(13) | 27(1) | 31(1) | 26(1) | -1(1) | 1(1) | 1(1) |
| C(14) | 24(1) | 40(1) | 29(1) | 1(1) | 5(1) | 1(1) |

**Table A2.3.5.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for UCI_Dong_11-ZC-4.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2A) | 7845 | 3070 | 3579 | 32 |
| H(2B) | 9213 | 4551 | 3795 | 32 |
| H(3) | 3895 | 3855 | 4049 | 28 |
| H(4A) | 6300 | 6169 | 5242 | 28 |
| H(4B) | 3543 | 5486 | 5476 | 28 |
| H(5) | 5341 | 3532 | 6237 | 28 |
| H(6A) | 8994 | 4002 | 7502 | 33 |
| H(6B) | 9221 | 5506 | 6952 | 33 |

| | | | | |
|---|---|---|---|---|
| H(8) | 4770 | 3467 | 8449 | 32 |
| H(9) | 1813 | 4286 | 9703 | 31 |
| H(11) | 3912 | 8216 | 8976 | 33 |
| H(12) | 6831 | 7377 | 7721 | 32 |
| H(13A) | 2989 | 5998 | 3155 | 42 |
| H(13B) | 4706 | 5055 | 2377 | 42 |
| H(13C) | 6016 | 6296 | 3096 | 42 |
| H(14A) | -1835 | 5550 | 10249 | 46 |
| H(14B) | -1696 | 6584 | 11306 | 46 |
| H(14C) | 377 | 5364 | 11234 | 46 |

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***X-ray Crystallographic Data for 4a*** **(CCDC 1869122)**

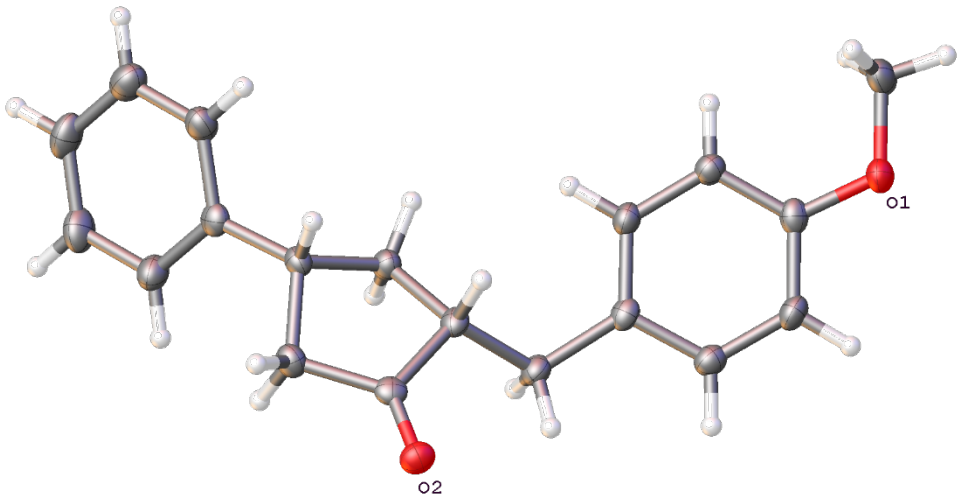



**Table A2.3.6.** Crystal data and structure refinement for UCIDong_16b_0m_a.

| | |
|---|---|
| Identification code | ucidong_16b_0m_a |
| Empirical formula | C19 H20 O2 |
| Formula weight | 280.35 |
| Temperature | 100.0 K |
| Wavelength | 1.54178 Å |
| Crystal system | Monoclinic |
| Space group | P 21 |

| | | |
|---|---|---|
| Unit cell dimensions | a = 7.7848(5) Å | α= 90°. |
| | b = 6.8098(4) Å | β= 91.804(3)°. |
| | c = 14.0541(7) Å | γ = 90°. |
| Volume | 744.68(7) $Å^3$ | |
| Z | 2 | |
| Density (calculated) | 1.250 $Mg/m^3$ | |
| Absorption coefficient | 0.626 $mm^{-1}$ | |
| F(000) | 300 | |
| Crystal size | 0.30 x 0.29 x 0.28 $mm^3$ | |
| Theta range for data collection | 3.146 to 68.286°. | |
| Index ranges | -9<=h<=9, -8<=k<=8, -16<=l<=16 | |
| Reflections collected | 8800 | |
| Independent reflections | 2712 [R(int) = 0.0327] | |
| Completeness to theta = 67.679° | 99.8 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.3201 and 0.2289 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 2712 / 1 / 191 | |
| Goodness-of-fit on $F^2$ | 1.091 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0315, wR2 = 0.0768 | |
| R indices (all data) | R1 = 0.0318, wR2 = 0.0771 | |
| Absolute structure parameter | 0.01(6) | |
| Extinction coefficient | n/a | |
| Largest diff. peak and hole | 0.240 and -0.153 e.$Å^{-3}$ | |

**Table A2.3.7.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for UCIDong_16b_0m_a. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 574(2) | 7987(2) | 1024(1) | 30(1) |
| O(2) | 3074(2) | 117(2) | 5242(1) | 29(1) |
| C(1) | 1350(3) | 9883(3) | 982(1) | 34(1) |
| C(2) | 716(2) | 7020(3) | 1878(1) | 25(1) |
| C(3) | 1543(2) | 7758(3) | 2694(1) | 25(1) |
| C(4) | 1644(2) | 6612(3) | 3519(1) | 26(1) |
| C(5) | 942(2) | 4738(3) | 3553(1) | 24(1) |
| C(6) | 72(2) | 4054(3) | 2732(1) | 27(1) |
| C(7) | -42(2) | 5160(3) | 1909(1) | 29(1) |

| | | | | |
|---|---|---|---|---|
| C(8) | 1072(2) | 3421(3) | 4423(1) | 25(1) |
| C(9) | 2688(2) | 3650(2) | 5067(1) | 23(1) |
| C(10) | 3158(2) | 1748(3) | 5592(1) | 23(1) |
| C(11) | 3762(2) | 2233(3) | 6598(1) | 27(1) |
| C(12) | 4100(2) | 4442(2) | 6577(1) | 23(1) |
| C(13) | 2675(2) | 5166(3) | 5871(1) | 25(1) |
| C(14) | 4165(2) | 5543(2) | 7513(1) | 24(1) |
| C(15) | 5160(2) | 7241(3) | 7592(1) | 31(1) |
| C(16) | 5219(3) | 8340(3) | 8425(1) | 36(1) |
| C(17) | 4280(3) | 7758(3) | 9198(1) | 36(1) |
| C(18) | 3286(3) | 6079(3) | 9130(1) | 36(1) |
| C(19) | 3230(2) | 4970(3) | 8296(1) | 31(1) |

**Table A2.3.8.** Bond lengths [Å] and angles [°] for UCIDong_16b_0m_a.

| | |
|---|---|
| O(1)-C(1) | 1.428(2) |
| O(1)-C(2) | 1.370(2) |
| O(2)-C(10) | 1.215(2) |
| C(1)-H(1A) | 0.9800 |
| C(1)-H(1B) | 0.9800 |
| C(1)-H(1C) | 0.9800 |
| C(2)-C(3) | 1.392(2) |
| C(2)-C(7) | 1.399(3) |
| C(3)-H(3) | 0.9500 |
| C(3)-C(4) | 1.398(2) |
| C(4)-H(4) | 0.9500 |
| C(4)-C(5) | 1.389(3) |
| C(5)-C(6) | 1.399(2) |
| C(5)-C(8) | 1.518(2) |
| C(6)-H(6) | 0.9500 |
| C(6)-C(7) | 1.381(3) |
| C(7)-H(7) | 0.9500 |
| C(8)-H(8B) | 0.9900 |
| C(8)-H(8A) | 0.9900 |

| | |
|---|---|
| C(8)-C(9) | 1.534(2) |
| C(9)-H(9) | 1.0000 |
| C(9)-C(10) | 1.529(2) |
| C(9)-C(13) | 1.531(2) |
| C(10)-C(11) | 1.513(2) |
| C(11)-H(11A) | 0.9900 |
| C(11)-H(11B) | 0.9900 |
| C(11)-C(12) | 1.528(2) |
| C(12)-H(12) | 1.0000 |
| C(12)-C(13) | 1.545(2) |
| C(12)-C(14) | 1.514(2) |
| C(13)-H(13A) | 0.9900 |
| C(13)-H(13B) | 0.9900 |
| C(14)-C(15) | 1.394(3) |
| C(14)-C(19) | 1.394(3) |
| C(15)-H(15) | 0.9500 |
| C(15)-C(16) | 1.389(3) |
| C(16)-H(16) | 0.9500 |
| C(16)-C(17) | 1.386(3) |
| C(17)-H(17) | 0.9500 |
| C(17)-C(18) | 1.382(3) |
| C(18)-H(18) | 0.9500 |
| C(18)-C(19) | 1.394(3) |
| C(19)-H(19) | 0.9500 |

| | |
|---|---|
| C(2)-O(1)-C(1) | 116.63(13) |
| O(1)-C(1)-H(1A) | 109.5 |
| O(1)-C(1)-H(1B) | 109.5 |
| O(1)-C(1)-H(1C) | 109.5 |
| H(1A)-C(1)-H(1B) | 109.5 |
| H(1A)-C(1)-H(1C) | 109.5 |
| H(1B)-C(1)-H(1C) | 109.5 |
| O(1)-C(2)-C(3) | 124.83(16) |
| O(1)-C(2)-C(7) | 116.10(15) |
| C(3)-C(2)-C(7) | 119.07(15) |
| C(2)-C(3)-H(3) | 120.2 |

| | |
|---|---|
| C(2)-C(3)-C(4) | 119.65(16) |
| C(4)-C(3)-H(3) | 120.2 |
| C(3)-C(4)-H(4) | 119.0 |
| C(5)-C(4)-C(3) | 121.96(15) |
| C(5)-C(4)-H(4) | 119.0 |
| C(4)-C(5)-C(6) | 117.28(16) |
| C(4)-C(5)-C(8) | 123.63(15) |
| C(6)-C(5)-C(8) | 119.09(16) |
| C(5)-C(6)-H(6) | 119.1 |
| C(7)-C(6)-C(5) | 121.72(17) |
| C(7)-C(6)-H(6) | 119.1 |
| C(2)-C(7)-H(7) | 119.9 |
| C(6)-C(7)-C(2) | 120.27(16) |
| C(6)-C(7)-H(7) | 119.9 |
| C(5)-C(8)-H(8B) | 108.1 |
| C(5)-C(8)-H(8A) | 108.1 |
| C(5)-C(8)-C(9) | 116.63(14) |
| H(8B)-C(8)-H(8A) | 107.3 |
| C(9)-C(8)-H(8B) | 108.1 |
| C(9)-C(8)-H(8A) | 108.1 |
| C(8)-C(9)-H(9) | 107.5 |
| C(10)-C(9)-C(8) | 112.19(14) |
| C(10)-C(9)-H(9) | 107.5 |
| C(10)-C(9)-C(13) | 102.83(13) |
| C(13)-C(9)-C(8) | 118.64(14) |
| C(13)-C(9)-H(9) | 107.5 |
| O(2)-C(10)-C(9) | 124.77(15) |
| O(2)-C(10)-C(11) | 126.05(16) |
| C(11)-C(10)-C(9) | 109.18(14) |
| C(10)-C(11)-H(11A) | 110.9 |
| C(10)-C(11)-H(11B) | 110.9 |
| C(10)-C(11)-C(12) | 104.20(14) |
| H(11A)-C(11)-H(11B) | 108.9 |
| C(12)-C(11)-H(11A) | 110.9 |
| C(12)-C(11)-H(11B) | 110.9 |
| C(11)-C(12)-H(12) | 107.5 |

| | |
|---|---|
| C(11)-C(12)-C(13) | 101.89(14) |
| C(13)-C(12)-H(12) | 107.5 |
| C(14)-C(12)-C(11) | 118.12(14) |
| C(14)-C(12)-H(12) | 107.5 |
| C(14)-C(12)-C(13) | 113.77(14) |
| C(9)-C(13)-C(12) | 103.72(13) |
| C(9)-C(13)-H(13A) | 111.0 |
| C(9)-C(13)-H(13B) | 111.0 |
| C(12)-C(13)-H(13A) | 111.0 |
| C(12)-C(13)-H(13B) | 111.0 |
| H(13A)-C(13)-H(13B) | 109.0 |
| C(15)-C(14)-C(12) | 118.86(15) |
| C(19)-C(14)-C(12) | 122.94(15) |
| C(19)-C(14)-C(15) | 118.17(17) |
| C(14)-C(15)-H(15) | 119.4 |
| C(16)-C(15)-C(14) | 121.13(18) |
| C(16)-C(15)-H(15) | 119.4 |
| C(15)-C(16)-H(16) | 119.9 |
| C(17)-C(16)-C(15) | 120.15(19) |
| C(17)-C(16)-H(16) | 119.9 |
| C(16)-C(17)-H(17) | 120.3 |
| C(18)-C(17)-C(16) | 119.39(18) |
| C(18)-C(17)-H(17) | 120.3 |
| C(17)-C(18)-H(18) | 119.7 |
| C(17)-C(18)-C(19) | 120.57(18) |
| C(19)-C(18)-H(18) | 119.7 |
| C(14)-C(19)-C(18) | 120.59(18) |
| C(14)-C(19)-H(19) | 119.7 |
| C(18)-C(19)-H(19) | 119.7 |

---

Symmetry transformations used to generate equivalent atoms:

**Table A2.3.9.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for UCIDong_16b_0m_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}]$

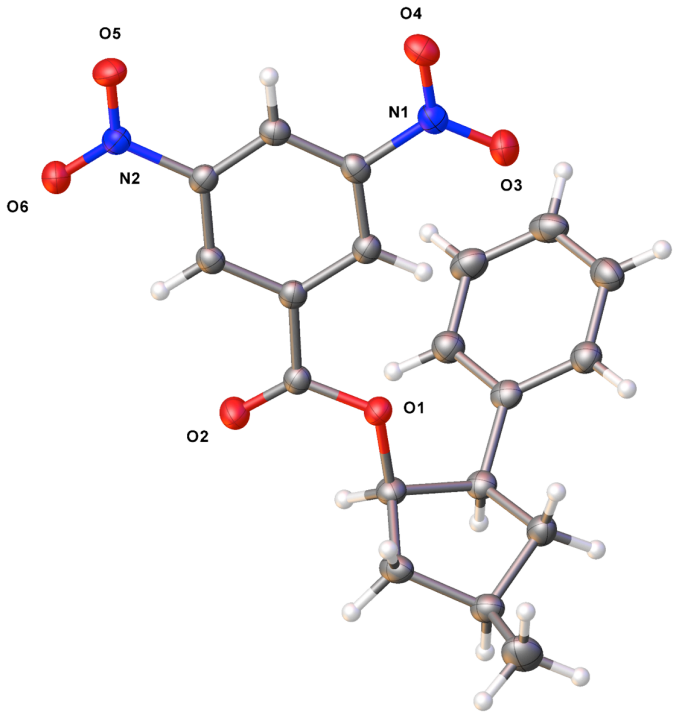
| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 37(1) | 32(1) | 20(1) | 1(1) | -2(1) | -1(1) |
| O(2) | 32(1) | 22(1) | 32(1) | -4(1) | 3(1) | 0(1) |
| C(1) | 44(1) | 33(1) | 24(1) | 2(1) | 1(1) | -2(1) |
| C(2) | 24(1) | 30(1) | 21(1) | 0(1) | 2(1) | 5(1) |
| C(3) | 26(1) | 25(1) | 25(1) | -2(1) | 0(1) | -2(1) |
| C(4) | 26(1) | 29(1) | 22(1) | -3(1) | -2(1) | -2(1) |
| C(5) | 21(1) | 27(1) | 23(1) | -2(1) | 0(1) | 1(1) |
| C(6) | 28(1) | 26(1) | 26(1) | -3(1) | 0(1) | -3(1) |
| C(7) | 31(1) | 32(1) | 23(1) | -5(1) | -4(1) | -2(1) |
| C(8) | 25(1) | 26(1) | 25(1) | 0(1) | -1(1) | -3(1) |
| C(9) | 23(1) | 24(1) | 23(1) | 0(1) | 1(1) | -1(1) |
| C(10) | 19(1) | 25(1) | 27(1) | 0(1) | 5(1) | 0(1) |
| C(11) | 30(1) | 24(1) | 25(1) | 3(1) | 1(1) | 2(1) |
| C(12) | 23(1) | 25(1) | 22(1) | 1(1) | 1(1) | -1(1) |
| C(13) | 28(1) | 23(1) | 25(1) | -1(1) | -1(1) | 1(1) |
| C(14) | 23(1) | 26(1) | 24(1) | 1(1) | -3(1) | 4(1) |
| C(15) | 37(1) | 28(1) | 28(1) | 3(1) | -1(1) | 0(1) |
| C(16) | 44(1) | 29(1) | 36(1) | -5(1) | -5(1) | -1(1) |
| C(17) | 38(1) | 41(1) | 30(1) | -11(1) | -6(1) | 9(1) |
| C(18) | 34(1) | 51(1) | 24(1) | -3(1) | 4(1) | 5(1) |
| C(19) | 28(1) | 38(1) | 26(1) | -1(1) | 0(1) | -4(1) |

**Table A2.3.10.** Hydrogen coordinates ( $x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for UCIDong_16b_0m_a.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 1155 | 10438 | 344 | 50 |
| H(1B) | 2588 | 9766 | 1118 | 50 |

| | | | | |
|---|---|---|---|---|
| H(1C) | 840 | 10746 | 1454 | 50 |
| H(3) | 2037 | 9034 | 2691 | 31 |
| H(4) | 2209 | 7129 | 4073 | 31 |
| H(6) | -454 | 2796 | 2741 | 32 |
| H(7) | -639 | 4656 | 1362 | 34 |
| H(8B) | 1007 | 2040 | 4206 | 30 |
| H(8A) | 56 | 3668 | 4812 | 30 |
| H(9) | 3663 | 3985 | 4650 | 28 |
| H(11A) | 4824 | 1502 | 6775 | 32 |
| H(11B) | 2867 | 1910 | 7058 | 32 |
| H(12) | 5228 | 4648 | 6269 | 28 |
| H(13A) | 1545 | 5194 | 6176 | 30 |
| H(13B) | 2937 | 6496 | 5631 | 30 |
| H(15) | 5809 | 7654 | 7066 | 37 |
| H(16) | 5904 | 9493 | 8465 | 44 |
| H(17) | 4319 | 8506 | 9768 | 44 |
| H(18) | 2636 | 5677 | 9656 | 43 |
| H(19) | 2549 | 3813 | 8261 | 37 |

***X-ray Crystallographic Data for 10*** **(CCDC 1869121)**



The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX-II CCD diffractometer equipped with Cu $K_a$ radiation (l = 1.5478). Crystals of the subject compound were grown by dissolving approximately 1mg of sample in 350μL of Dichloromethane, which was then vapor diffused with Pentane over 2 days. A 0.357 x 0.046 x 0.023 mm piece of a colorless needle was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using f and v scans. Crystal-to-detector distance was 40 mm using variable exposure time (5s-20s) depending on q with a scan width of 2.0°. Data collection was 99.5% complete to 68.00° in *q*. A total of 25579 reflections were collected covering the indices, -12<=h<=12, -5<=k<=6, -19<=l<=19. 3089 reflections were found to be symmetry independent, with a $R_{int}$ of 0.0376. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be $P2_1$. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure. All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. The absolute stereochemistry of the molecule was established by anomalous dispersion using the Parson's method with a Flack parameter of 0.010(52). Crystallographic data are summarized in Table A2.3.11.

**Table A2.3.11.** Crystal data and structure refinement for UCI_Dong_ZC-11-16a.

| | |
|---|---|
| Report date | 2018-06-14 |
| Identification code | ZC-11-16a |
| Empirical formula | C19 H18 N2 O6 |
| Molecular formula | C19 H18 N2 O6 |
| Formula weight | 370.35 |
| Temperature | 100.0 K |
| Wavelength | 1.54178 Å |
| Crystal system | Monoclinic |

| | | |
|---|---|---|
| Space group | P 1 21 1 | |
| Unit cell dimensions | a = 10.1670(3) Å | α= 90°. |
| | b = 5.5064(2) Å | β= 104.9590(10)°. |
| | c = 16.0224(5) Å | γ = 90°. |
| Volume | 866.59(5) $Å^3$ | |
| Z | 2 | |
| Density (calculated) | 1.419 $Mg/m^3$ | |
| Absorption coefficient | 0.898 $mm^{-1}$ | |
| F(000) | 388 | |
| Crystal size | 0.357 x 0.046 x 0.023 $mm^3$ | |
| Crystal color, habit | Colorless Needle | |
| Theta range for data collection | 2.855 to 68.272°. | |
| Index ranges | -12<=h<=12, -5<=k<=6, -19<=l<=19 | |
| Reflections collected | 25579 | |
| Independent reflections | 3089 [R(int) = 0.0376, R(sigma) = 0.0204] | |
| Completeness to theta = 68.000° | 99.5 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.3200 and 0.2206 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 3089 / 1 / 245 | |
| Goodness-of-fit on $F^2$ | 1.050 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0246, wR2 = 0.0649 | |
| R indices (all data) | R1 = 0.0251, wR2 = 0.0654 | |
| Absolute structure parameter | 0.01(5) | |
| Extinction coefficient | n/a | |

Largest diff. peak and hole 0.131 and -0.141 e.Å$^{-3}$

**Table A2.3.12.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters (Å$^2$x $10^3$) for UCI_Dong_ZC-11-16a. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 2372(1) | 3438(2) | 7378(1) | 22(1) |
| O(2) | 1314(1) | 261(3) | 6598(1) | 29(1) |
| O(3) | 4531(1) | 9475(2) | 5962(1) | 32(1) |
| O(4) | 3988(1) | 9739(2) | 4567(1) | 29(1) |
| O(5) | 1174(1) | 3543(3) | 2846(1) | 30(1) |
| O(6) | 566(1) | 463(3) | 3500(1) | 29(1) |
| N(1) | 3921(1) | 8765(3) | 5244(1) | 24(1) |
| N(2) | 1080(1) | 2469(3) | 3497(1) | 23(1) |
| C(1) | 2327(2) | 2226(3) | 8184(1) | 23(1) |
| C(2) | 1143(2) | 3249(4) | 8510(1) | 27(1) |
| C(3) | 1780(2) | 4412(4) | 9392(1) | 27(1) |
| C(4) | 3204(2) | 5122(4) | 9323(1) | 27(1) |
| C(5) | 3635(2) | 2929(3) | 8874(1) | 22(1) |
| C(6) | 4895(2) | 3171(3) | 8540(1) | 24(1) |
| C(7) | 5231(2) | 1316(4) | 8041(1) | 28(1) |
| C(8) | 6378(2) | 1473(4) | 7728(1) | 32(1) |
| C(9) | 7217(2) | 3494(4) | 7908(1) | 32(1) |
| C(10) | 6900(2) | 5347(4) | 8403(1) | 32(1) |

| | | | | |
|---|---|---|---|---|
| C(11) | 5746(2) | 5183(4) | 8719(1) | 27(1) |
| C(12) | 960(2) | 6497(5) | 9617(2) | 40(1) |
| C(13) | 1853(2) | 2217(3) | 6649(1) | 21(1) |
| C(14) | 2050(2) | 3547(3) | 5874(1) | 21(1) |
| C(15) | 2866(2) | 5603(3) | 5939(1) | 22(1) |
| C(16) | 3038(2) | 6624(3) | 5184(1) | 22(1) |
| C(17) | 2440(2) | 5701(3) | 4371(1) | 22(1) |
| C(18) | 1654(2) | 3641(3) | 4339(1) | 22(1) |
| C(19) | 1440(2) | 2552(3) | 5069(1) | 22(1) |

**Table A2.3.13.** Bond lengths [Å] and angles [°] for UCI_Dong_ZC-11-16a.

| | | | |
|---|---|---|---|
| O(1)-C(1) | 1.4655(19) | C(4)-C(5) | 1.526(3) |
| O(1)-C(13) | 1.333(2) | C(5)-C(6) | 1.517(2) |
| O(2)-C(13) | 1.202(2) | C(6)-C(7) | 1.393(3) |
| O(3)-N(1) | 1.2223(19) | C(6)-C(11) | 1.389(3) |
| O(4)-N(1) | 1.2277(19) | C(7)-C(8) | 1.386(3) |
| O(5)-N(2) | 1.2252(19) | C(8)-C(9) | 1.387(3) |
| O(6)-N(2) | 1.223(2) | C(9)-C(10) | 1.380(3) |
| N(1)-C(16) | 1.470(2) | C(10)-C(11) | 1.395(2) |
| N(2)-C(18) | 1.472(2) | C(13)-C(14) | 1.499(2) |
| C(1)-C(2) | 1.537(2) | C(14)-C(15) | 1.391(3) |
| C(1)-C(5) | 1.544(2) | C(14)-C(19) | 1.391(2) |
| C(2)-C(3) | 1.535(2) | C(15)-C(16) | 1.385(2) |

| | | | |
|---|---|---|---|
| C(3)-C(4) | 1.532(2) | C(16)-C(17) | 1.384(2) |
| C(3)-C(12) | 1.516(3) | C(17)-C(18) | 1.381(3) |
| C(18)-C(19) | 1.381(2) | C(10)-C(9)-C(8) | 119.39(17) |
| | | C(9)-C(10)-C(11) | 120.23(19) |
| C(13)-O(1)-C(1) | 116.58(14) | C(6)-C(11)-C(10) | 120.93(18) |
| O(3)-N(1)-O(4) | 124.18(15) | O(1)-C(13)-C(14) | 111.86(14) |
| O(3)-N(1)-C(16) | 118.09(14) | O(2)-C(13)-O(1) | 125.55(16) |
| O(4)-N(1)-C(16) | 117.74(14) | O(2)-C(13)-C(14) | 122.57(15) |
| O(5)-N(2)-C(18) | 118.00(15) | C(15)-C(14)-C(13) | 122.67(14) |
| O(6)-N(2)-O(5) | 124.47(15) | C(15)-C(14)-C(19) | 120.35(15) |
| O(6)-N(2)-C(18) | 117.52(14) | C(19)-C(14)-C(13) | 116.87(15) |
| O(1)-C(1)-C(2) | 109.75(14) | C(16)-C(15)-C(14) | 118.14(15) |
| O(1)-C(1)-C(5) | 107.44(13) | C(15)-C(16)-N(1) | 118.77(15) |
| C(2)-C(1)-C(5) | 105.66(14) | C(17)-C(16)-N(1) | 117.91(15) |
| C(3)-C(2)-C(1) | 106.56(13) | C(17)-C(16)-C(15) | 123.30(16) |
| C(4)-C(3)-C(2) | 102.78(13) | C(18)-C(17)-C(16) | 116.50(15) |
| C(12)-C(3)-C(2) | 114.05(15) | C(17)-C(18)-N(2) | 118.89(14) |
| C(12)-C(3)-C(4) | 114.36(17) | C(17)-C(18)-C(19) | 122.76(15) |
| C(5)-C(4)-C(3) | 102.93(15) | C(19)-C(18)-N(2) | 118.26(15) |
| C(4)-C(5)-C(1) | 103.71(13) | C(18)-C(19)-C(14) | 118.93(16) |
| C(6)-C(5)-C(1) | 114.80(13) | | |
| C(6)-C(5)-C(4) | 117.89(15) | | |
| C(7)-C(6)-C(5) | 119.54(16) | | |
| C(11)-C(6)-C(5) | 122.37(16) | | |

| | |
|---|---|
| C(11)-C(6)-C(7) | 118.09(16) |
| C(8)-C(7)-C(6) | 121.08(18) |
| C(7)-C(8)-C(9) | 120.27(18) |

**Table A2.3.14.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for UCI_Dong_ZC-11-16a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 24(1) | 24(1) | 18(1) | 0(1) | 4(1) | -3(1) |
| O(2) | 34(1) | 28(1) | 25(1) | -1(1) | 7(1) | -9(1) |
| O(3) | 34(1) | 31(1) | 33(1) | -7(1) | 8(1) | -9(1) |
| O(4) | 28(1) | 27(1) | 34(1) | 5(1) | 11(1) | -2(1) |
| O(5) | 30(1) | 41(1) | 21(1) | 1(1) | 9(1) | -5(1) |
| O(6) | 29(1) | 31(1) | 27(1) | -5(1) | 7(1) | -7(1) |
| N(1) | 22(1) | 22(1) | 29(1) | -1(1) | 8(1) | 0(1) |
| N(2) | 20(1) | 29(1) | 22(1) | -3(1) | 6(1) | -1(1) |
| C(1) | 25(1) | 24(1) | 20(1) | 3(1) | 5(1) | -1(1) |
| C(2) | 21(1) | 37(1) | 24(1) | 4(1) | 6(1) | -1(1) |
| C(3) | 23(1) | 35(1) | 24(1) | 1(1) | 8(1) | 1(1) |
| C(4) | 23(1) | 34(1) | 25(1) | -6(1) | 6(1) | -2(1) |
| C(5) | 22(1) | 26(1) | 19(1) | 3(1) | 4(1) | 2(1) |
| C(6) | 22(1) | 29(1) | 19(1) | 3(1) | 3(1) | 3(1) |
| C(7) | 26(1) | 30(1) | 28(1) | -1(1) | 7(1) | 1(1) |
| C(8) | 29(1) | 41(1) | 28(1) | -2(1) | 10(1) | 7(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(9) | 23(1) | 48(1) | 28(1) | 5(1) | 9(1) | 4(1) |
| C(10) | 25(1) | 39(1) | 30(1) | 2(1) | 5(1) | -4(1) |
| C(11) | 26(1) | 31(1) | 23(1) | -1(1) | 5(1) | 0(1) |
| C(12) | 32(1) | 44(1) | 48(1) | -5(1) | 19(1) | 2(1) |
| C(13) | 18(1) | 23(1) | 21(1) | -2(1) | 4(1) | 1(1) |
| C(14) | 18(1) | 22(1) | 22(1) | -2(1) | 6(1) | 2(1) |
| C(15) | 19(1) | 24(1) | 22(1) | -2(1) | 4(1) | 2(1) |
| C(16) | 17(1) | 21(1) | 28(1) | 0(1) | 7(1) | 2(1) |
| C(17) | 19(1) | 23(1) | 24(1) | 2(1) | 7(1) | 3(1) |
| C(18) | 18(1) | 26(1) | 21(1) | -2(1) | 4(1) | 3(1) |
| C(19) | 18(1) | 23(1) | 25(1) | 0(1) | 6(1) | 0(1) |

**Table A2.3.15.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$ x $10^3$) for UCI_Dong_ZC-11-16a.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1) | 2250 | 424 | 8107 | 28 |
| H(2A) | 633 | 4477 | 8101 | 33 |
| H(2B) | 510 | 1933 | 8568 | 33 |
| H(3) | 1876 | 3134 | 9847 | 33 |
| H(4A) | 3175 | 6614 | 8973 | 33 |
| H(4B) | 3832 | 5382 | 9901 | 33 |
| H(5) | 3821 | 1583 | 9308 | 27 |

| | | | | |
|---|---|---|---|---|
| H(7) | 4665 | -78 | 7913 | 34 |
| H(8) | 6590 | 189 | 7388 | 39 |
| H(9) | 8002 | 3604 | 7692 | 39 |
| H(10) | 7469 | 6739 | 8529 | 38 |
| H(11) | 5539 | 6466 | 9060 | 32 |
| H(12A) | 867 | 7777 | 9181 | 59 |
| H(12B) | 1428 | 7149 | 10185 | 59 |
| H(12C) | 55 | 5912 | 9630 | 59 |
| H(15) | 3293 | 6287 | 6486 | 26 |
| H(17) | 2565 | 6445 | 3862 | 26 |
| H(19) | 884 | 1145 | 5022 | 26 |

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## 11. References


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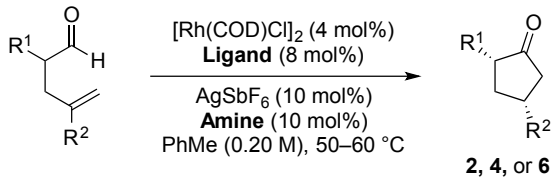
## 12. Ligand and Amine Combinations for Various Aldehydes



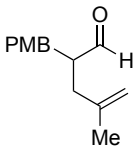
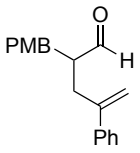
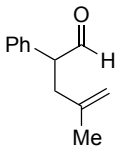
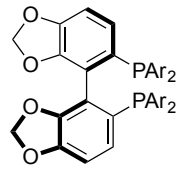
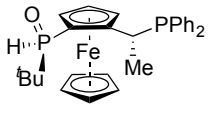
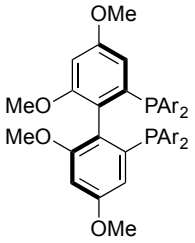
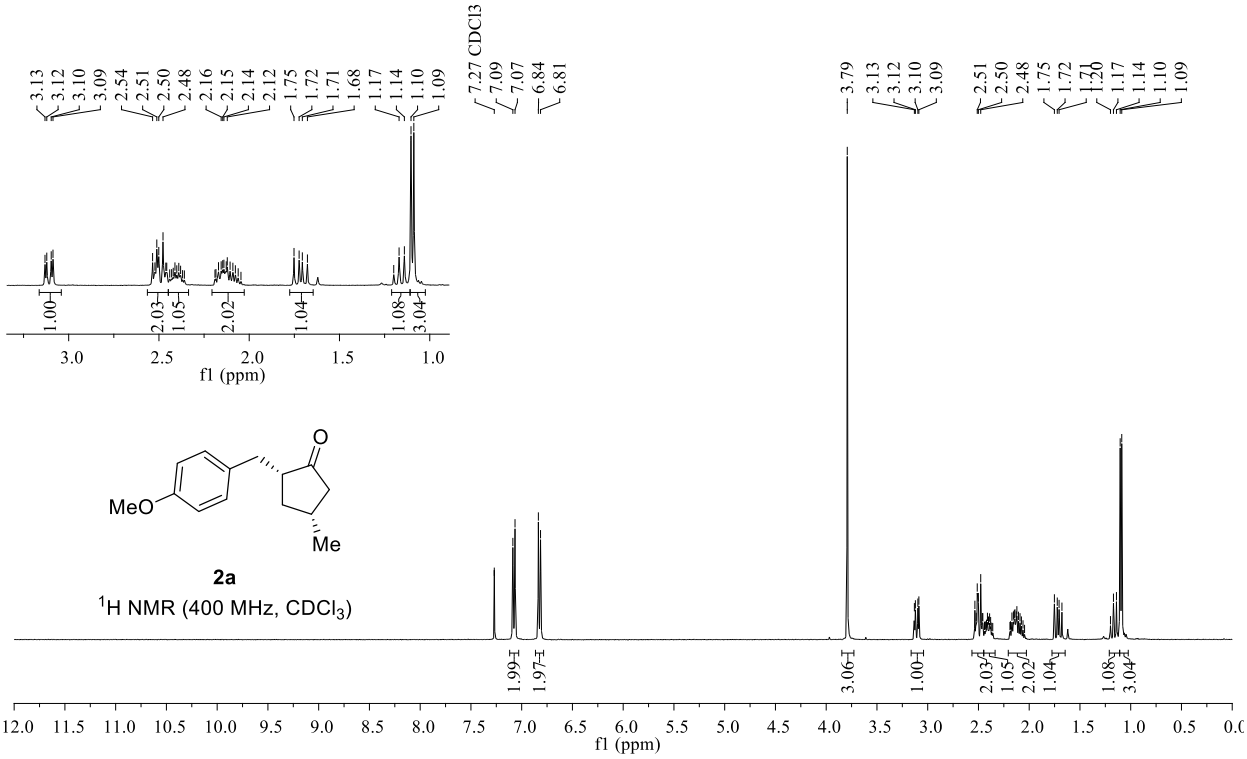
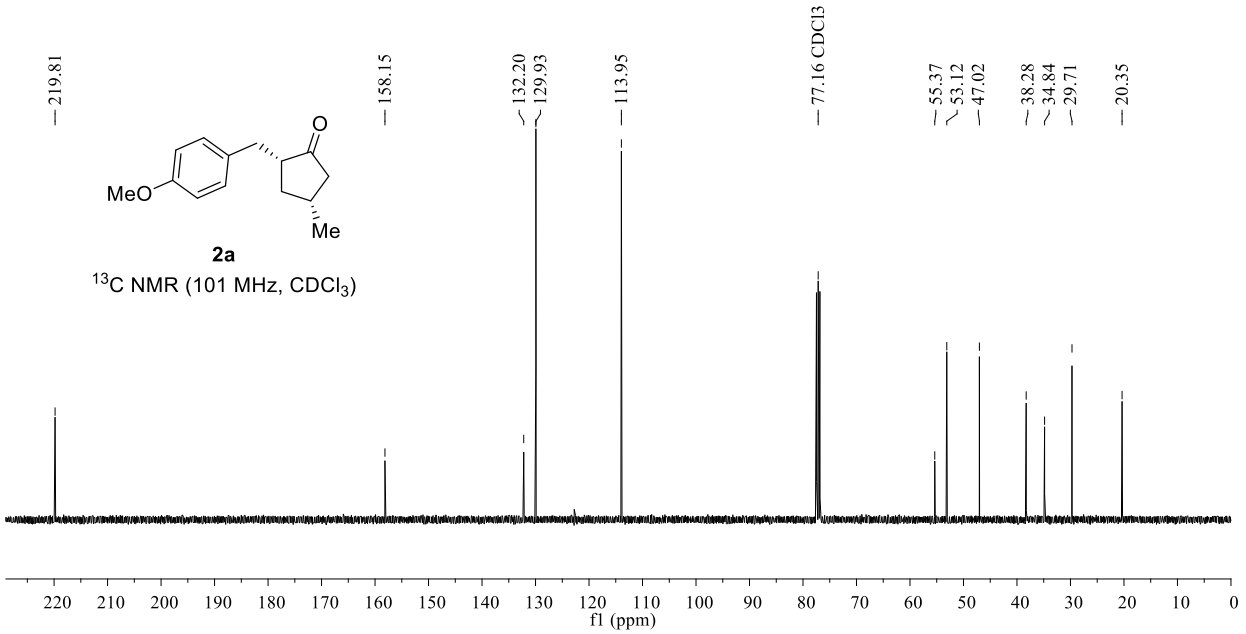
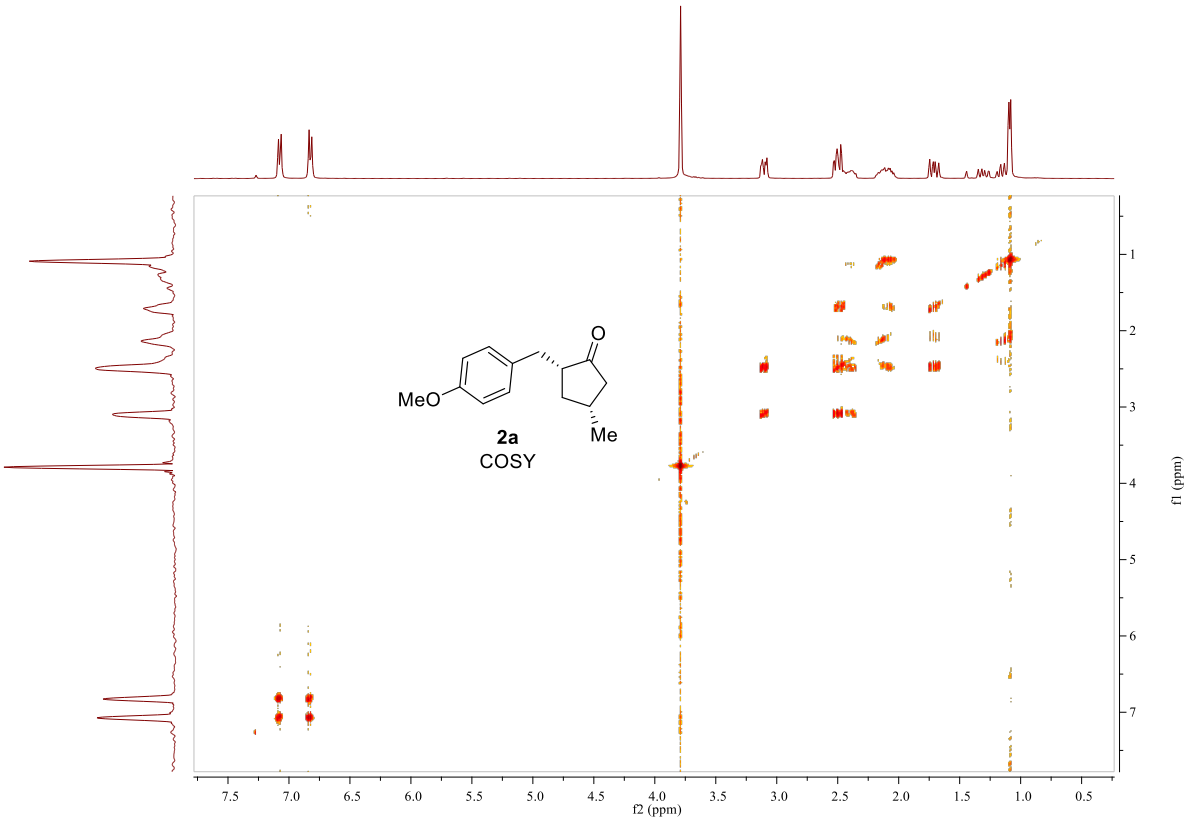

| |  α–alkyl aldehyde with alkyl olefin (**1a**) |  α–alkyl aldehyde with styrenyl olefin (**3a**) |  α–aryl aldehyde with alkyl olefin (**5a**) |
|---|---|---|---|
|  (Ar = 3,5-$^t$Bu$_2$-4-OMePh) DTBM-Segphos (**L3**)/ 1-AdNH$_2$ (**A5**) | **2a**, 94% >20:1 *dr*, >99% *ee* | **4a**, <10% *dr* ND, *ee* ND | **6a**, 24% >20:1 *dr*, >99% *ee* |
|  JoSPOphos (**L4**)/ 1-AdNH$_2$ (**A5**) | **2a**, 78% >20:1 *dr*, >99% *ee* | **4a**, 76% >20:1 *dr*, >99% *ee* | **6a**, 54% 10:1 *dr*, 87% *ee* |
|  (Ar = 3,5-$^t$Bu$_2$-4-OMePh) DTBM-Garphos (**L5**)/ 2,6-Et$_2$PhNH$_2$ (**A8**) | **2a**, 83% >20:1 *dr*, 93% *ee* | **4a**, <10% *dr* ND, *ee* ND | **6a**, 87% >20:1 *dr*, >99% *ee* |

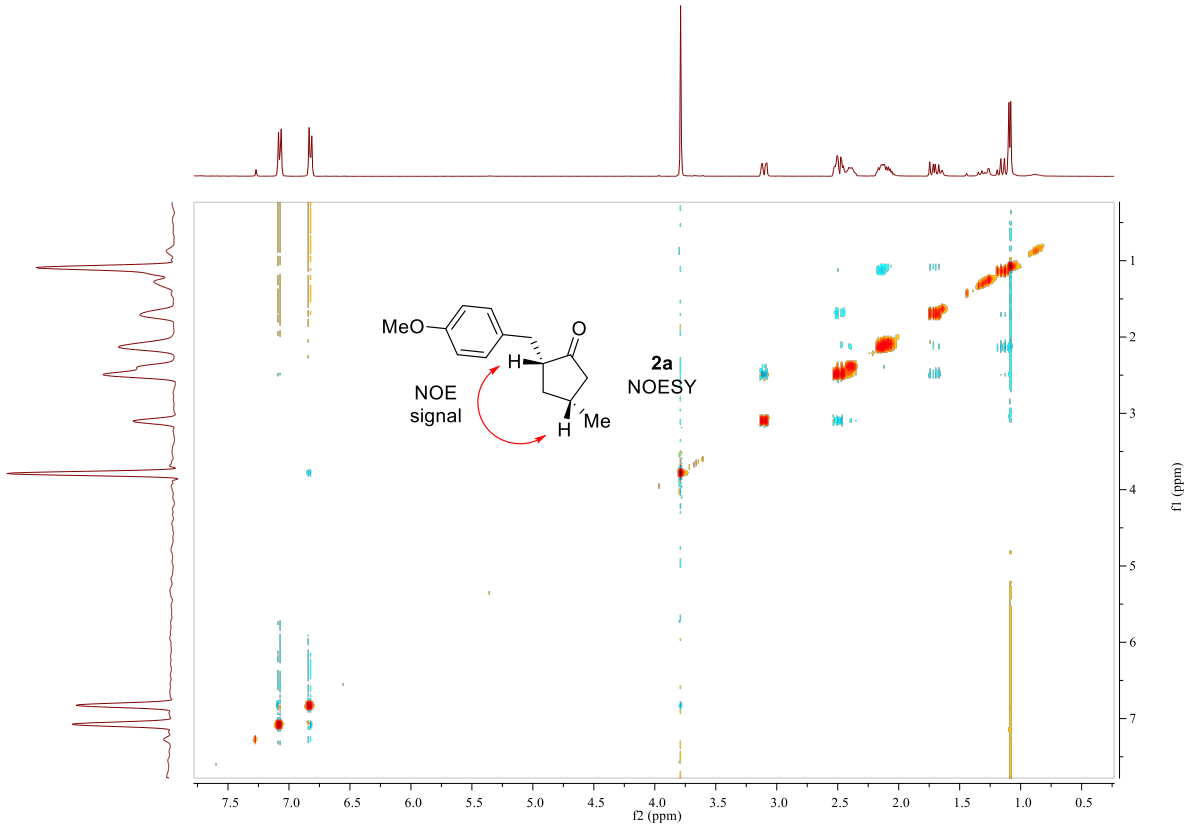
**Figure A2.3.1.** Empirical trend for optimal amine and ligand.

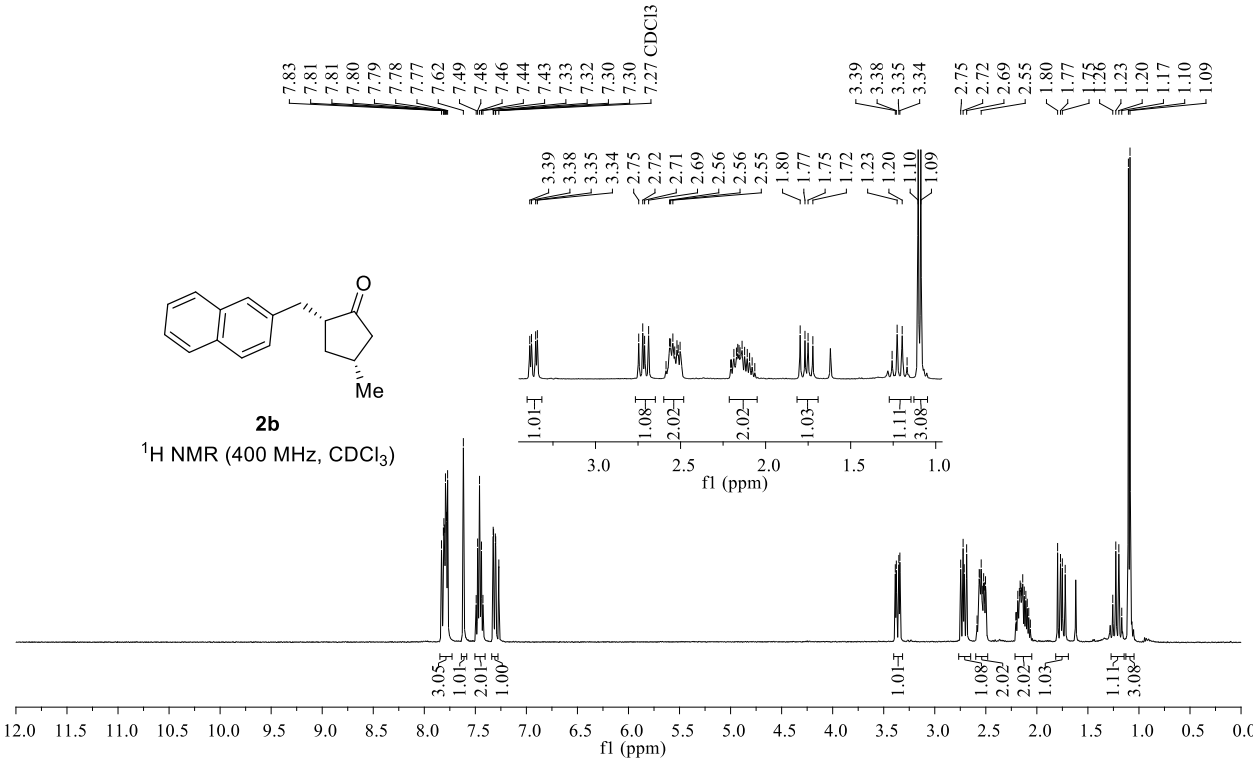
## 13. NMR Spectra

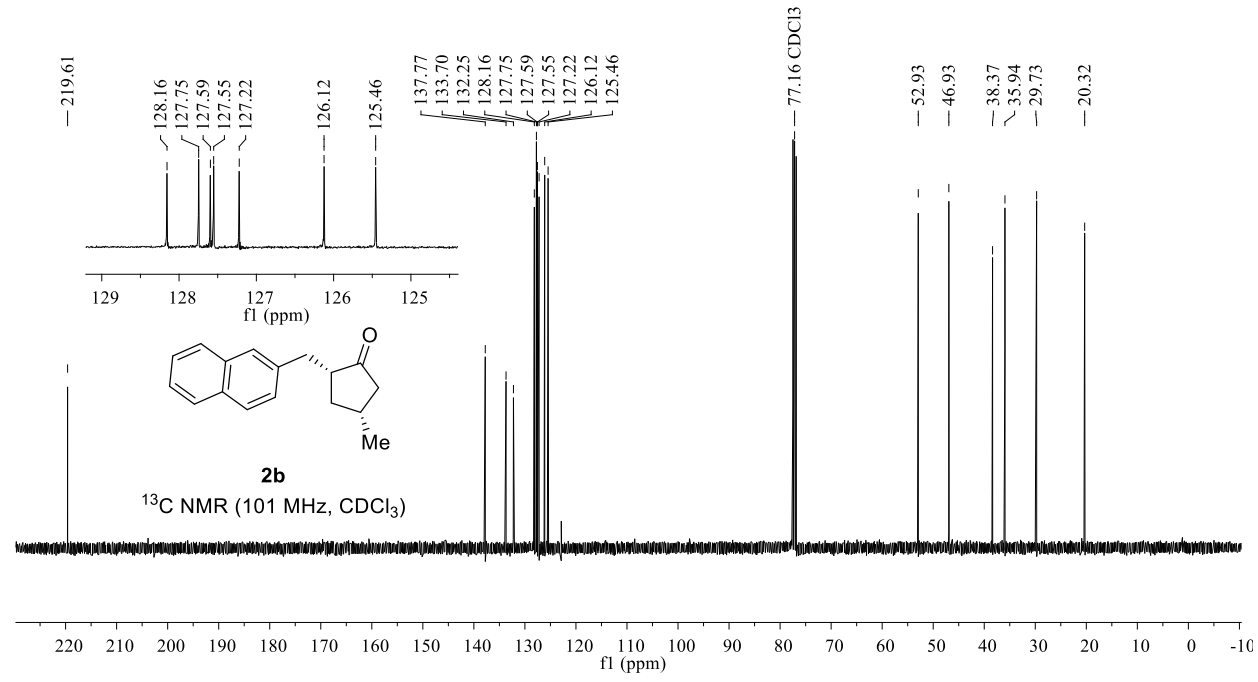


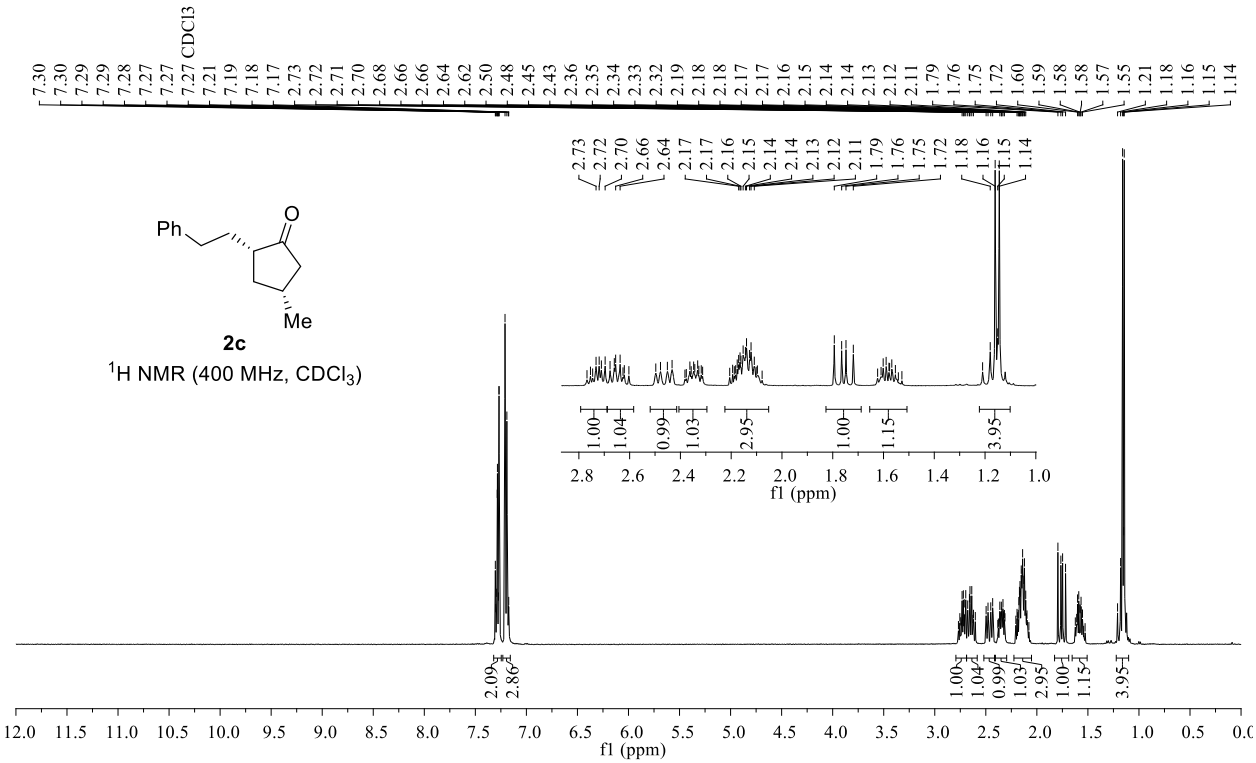



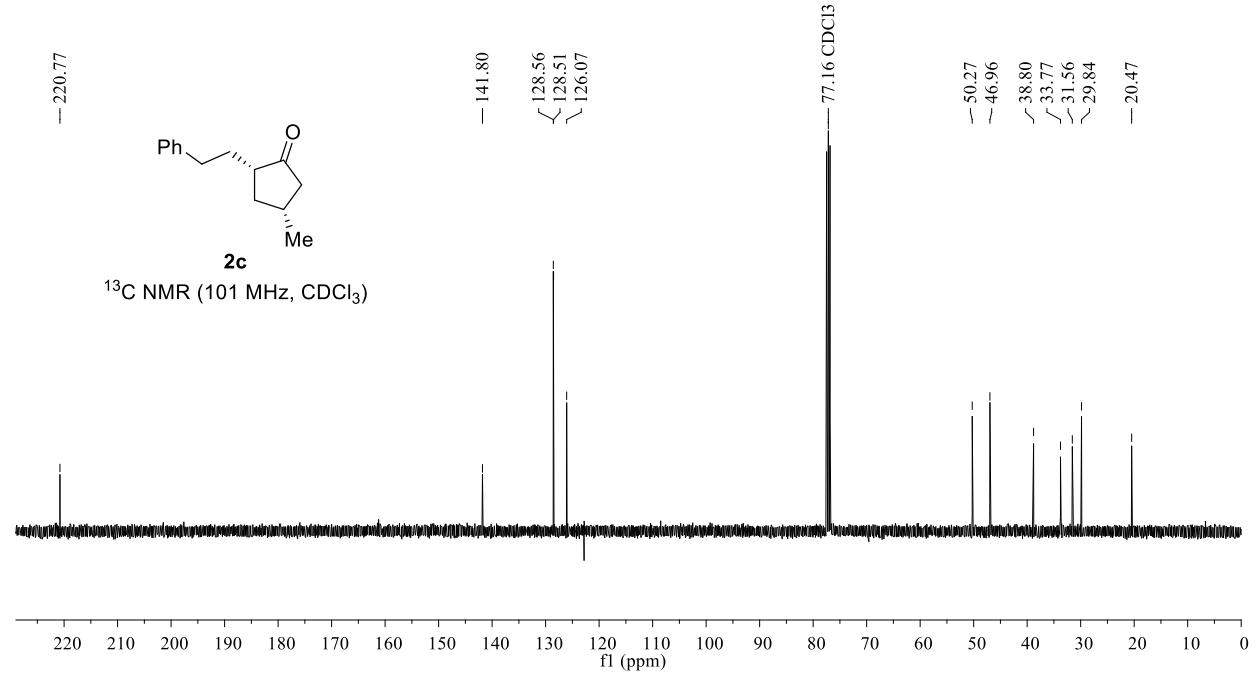

MeO
O
Me
2a
COSY
f2 (ppm)
f1 (ppm)

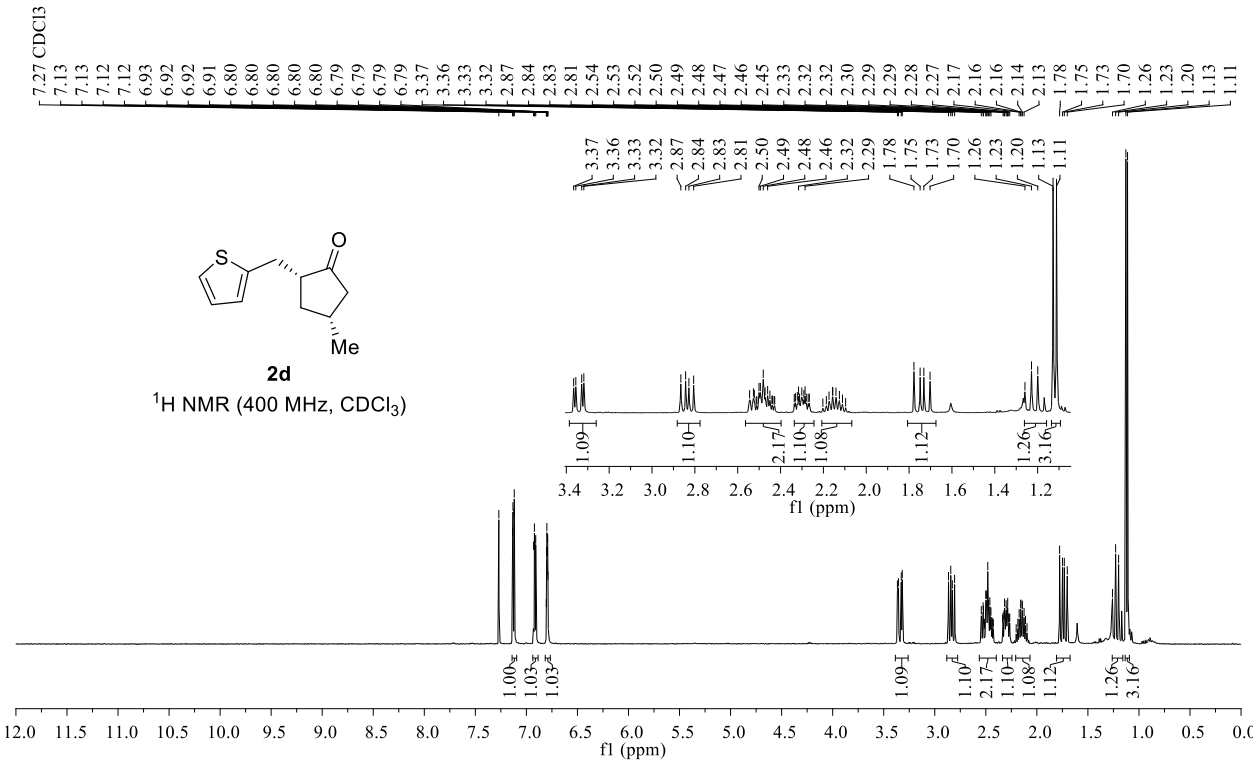

MeO
O
H
H
Me
NOE
signal
2a
NOESY
f2 (ppm)
f1 (ppm)

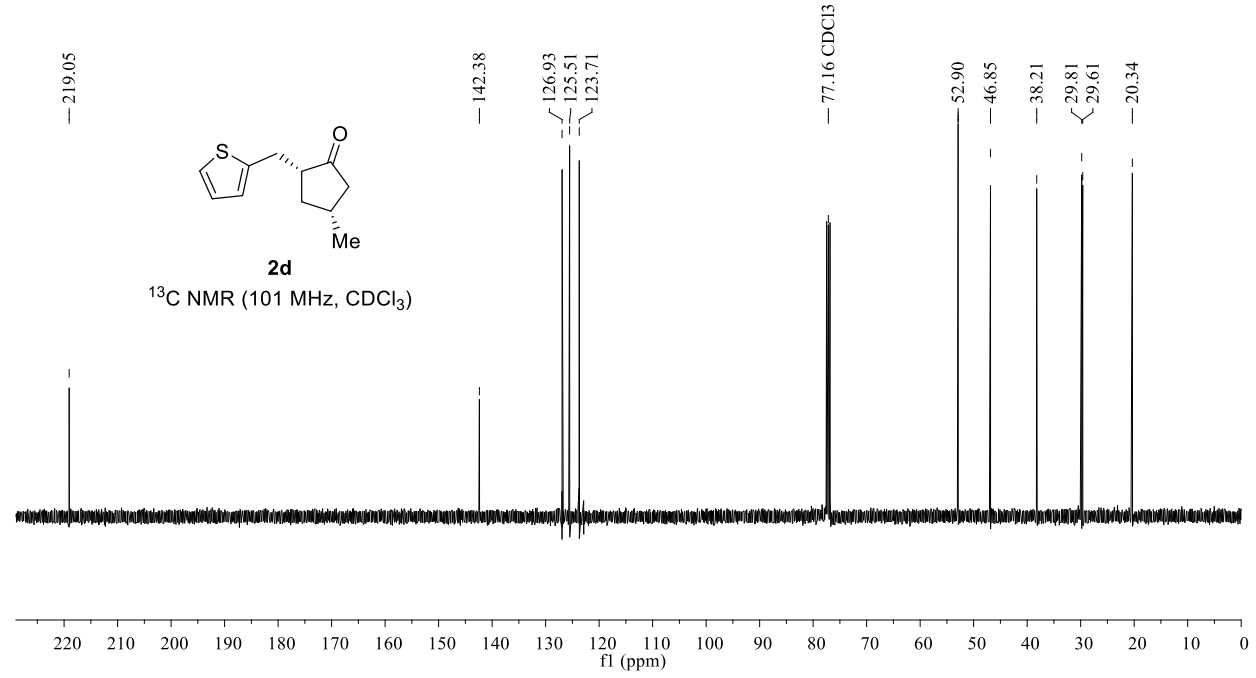

7.83
7.81
7.81
7.80
7.79
7.78
7.77
7.62
7.49
7.48
7.46
7.44
7.43
7.33
7.32
7.30
7.27 CDCl3
3.39
3.38
3.35
3.34
2.75
2.72
2.69
2.55
1.80
1.77
1.23
1.20
1.17
1.10
1.09
O
Me
2b
1H NMR (400 MHz, CDCl3)
3.05
1.01
2.01
1.00
1.01
1.08
2.02
2.02
1.03
1.11
3.08
f1 (ppm)

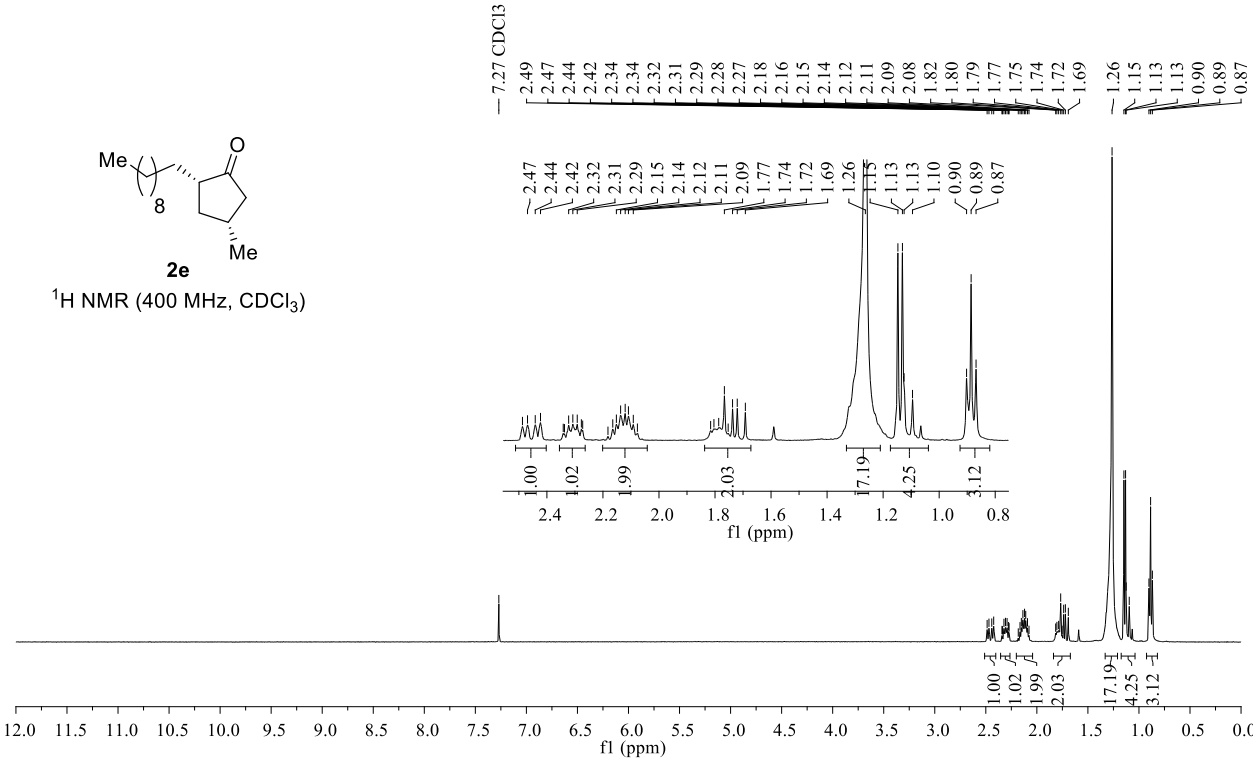

219.61
128.16
127.75
127.59
127.55
127.22
126.12
125.46
137.77
133.70
132.25
128.16
127.75
127.59
127.55
127.22
126.12
125.46
77.16 CDCl3
52.93
46.93
38.37
35.94
29.73
20.32
f1 (ppm)
O
Me
2b
13C NMR (101 MHz, CDCl3)
f1 (ppm)

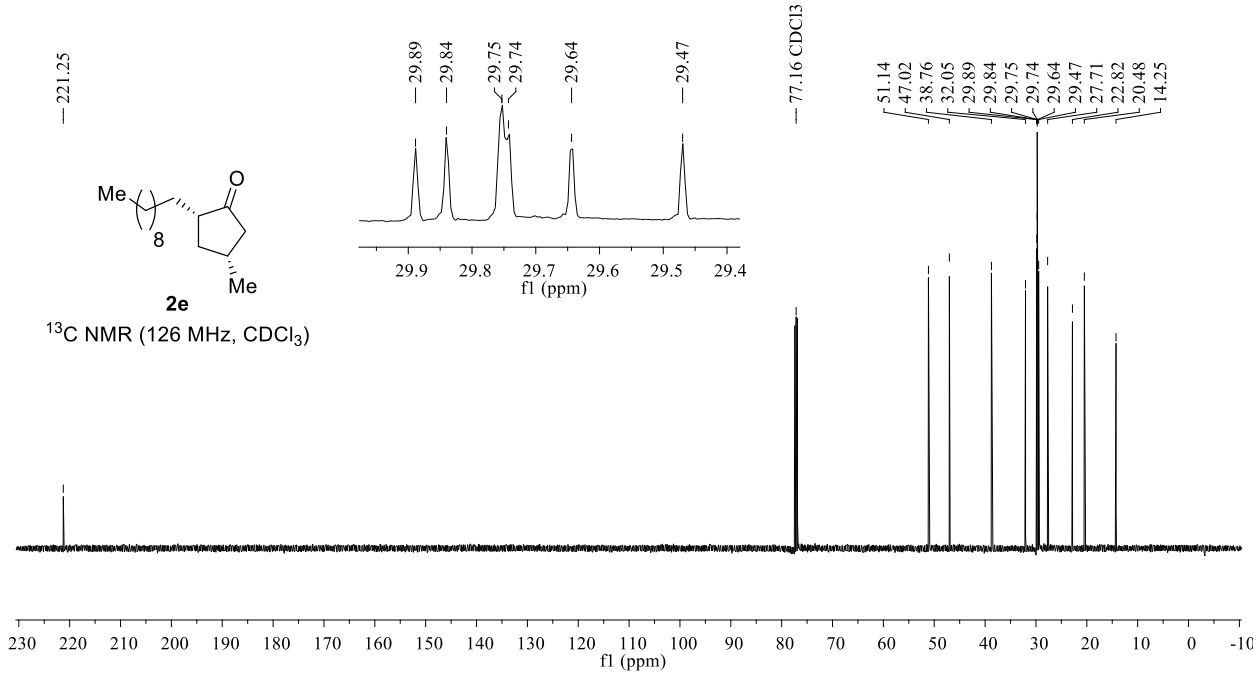

Ph
O
Me
2c
1H NMR (400 MHz, CDCl3)
f1 (ppm)

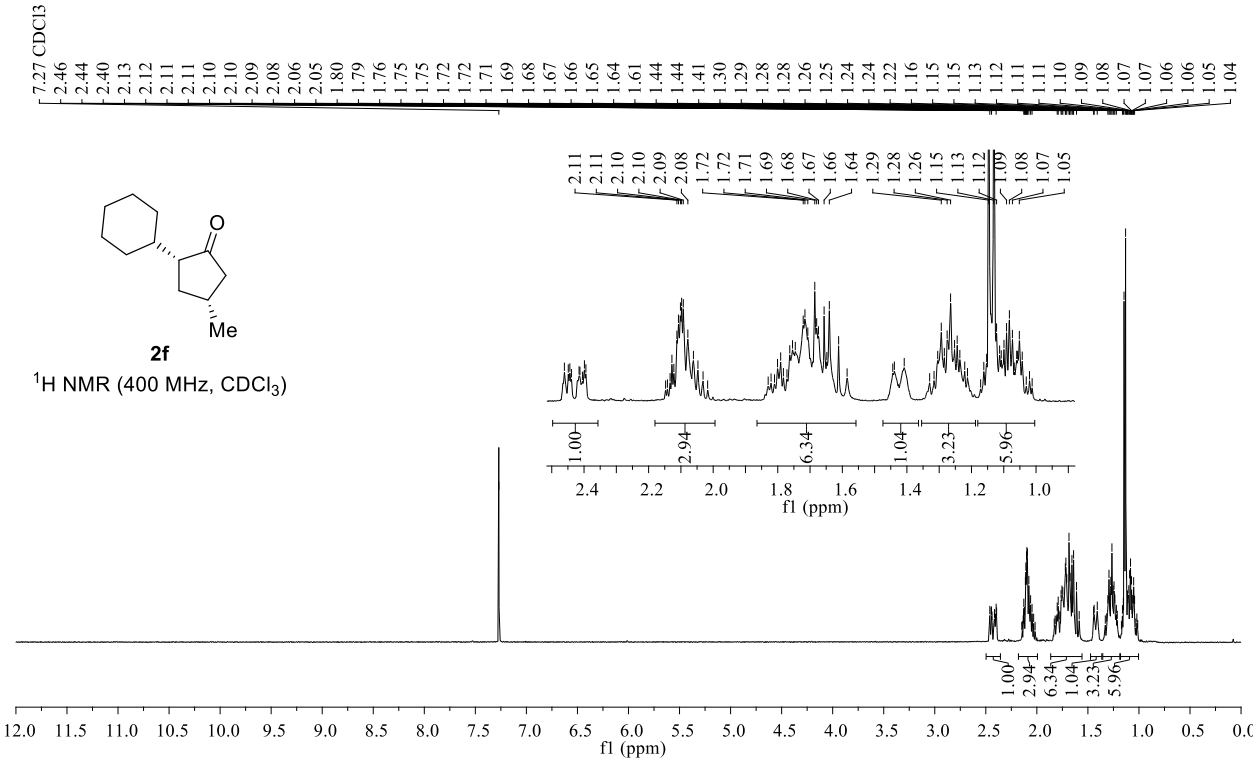

Ph
O
Me
2c
13C NMR (101 MHz, CDCl3)
f1 (ppm)

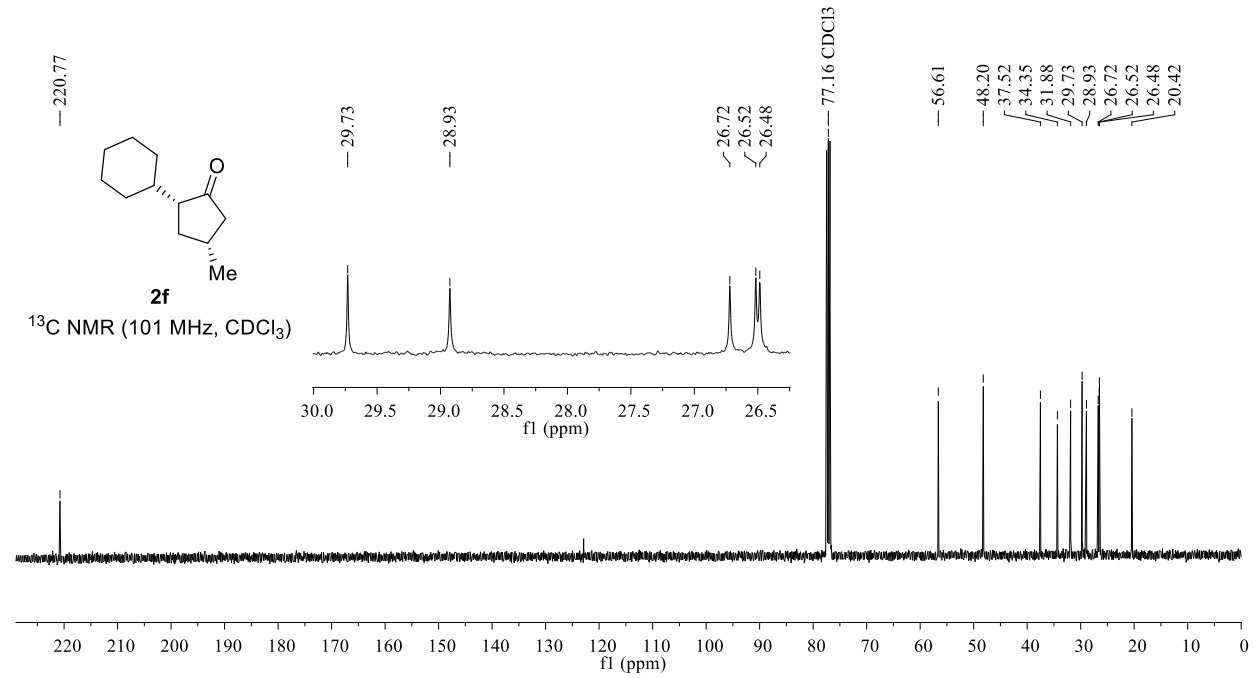

7.27 CDCl3
7.13
7.13
7.12
7.12
6.93
6.92
6.92
6.91
6.80
6.80
6.80
6.80
6.80
6.79
6.79
6.79
6.79
3.37
3.36
3.33
3.32
2.87
2.84
2.83
2.81
2.54
2.53
2.52
2.50
2.49
2.48
2.47
2.46
2.45
2.33
2.32
2.32
2.30
2.29
2.29
2.28
2.27
2.17
2.16
2.16
2.14
2.13
1.78
1.75
1.73
1.70
1.26
1.23
1.20
1.13
1.11
S
O
Me
2d
1H NMR (400 MHz, CDCl3)
1.09
1.10
2.17
1.10
1.08
1.12
1.26
3.16
3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
1.00
1.03
1.03
1.09
1.10
2.17
1.10
1.08
1.12
1.26
3.16
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

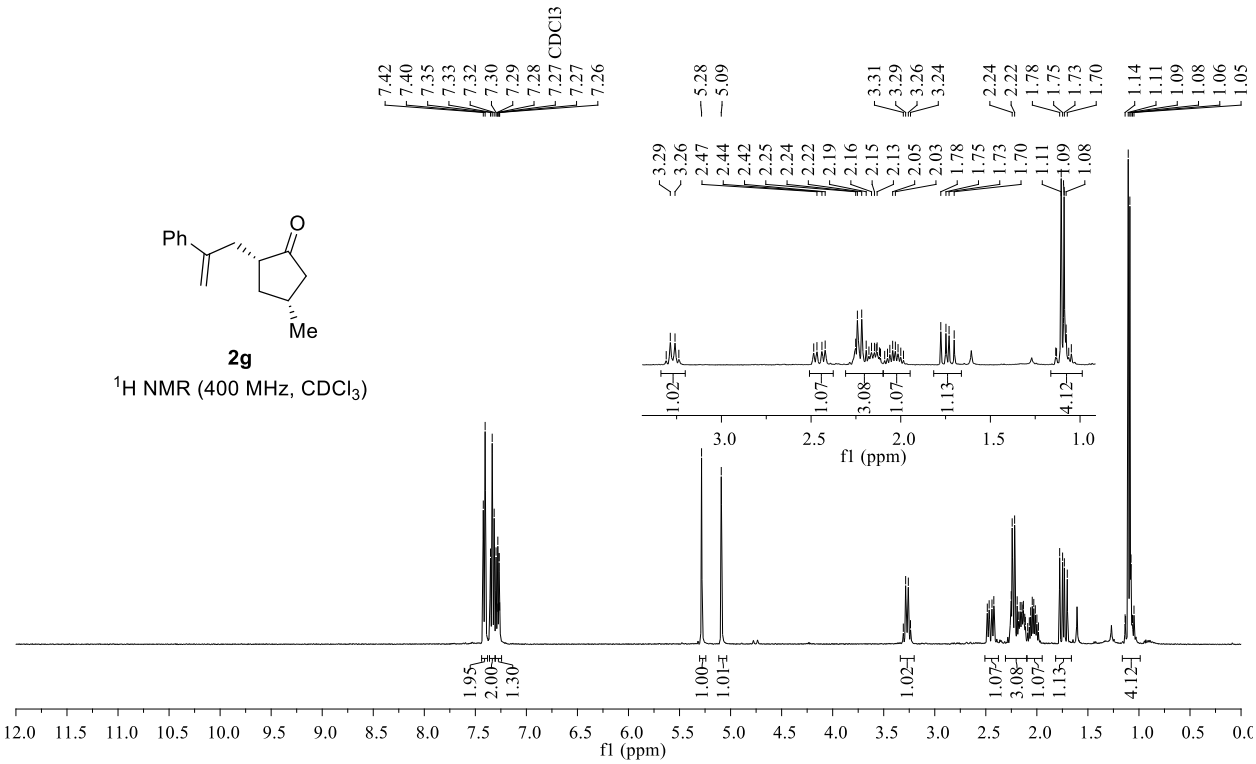

219.05
142.38
126.93
125.51
123.71
77.16 CDCl3
52.90
46.85
38.21
29.81
29.61
20.34
S
O
Me
2d
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

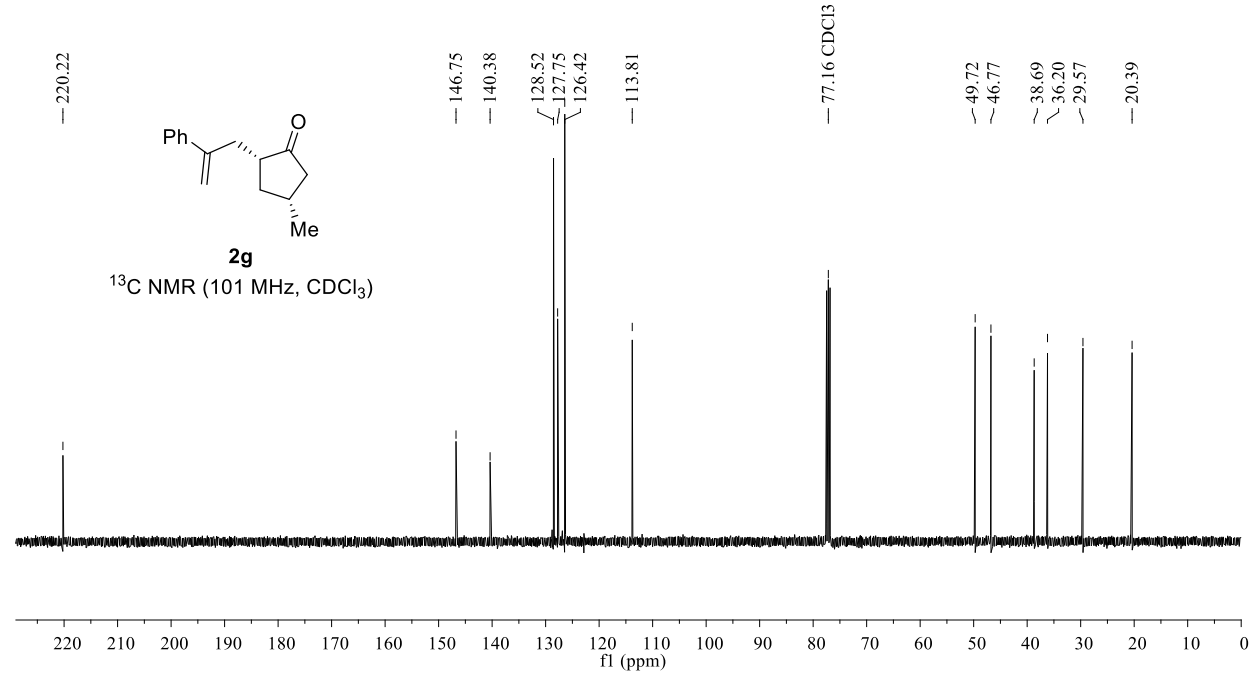

Me
O
8
Me
2e
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
f1 (ppm)

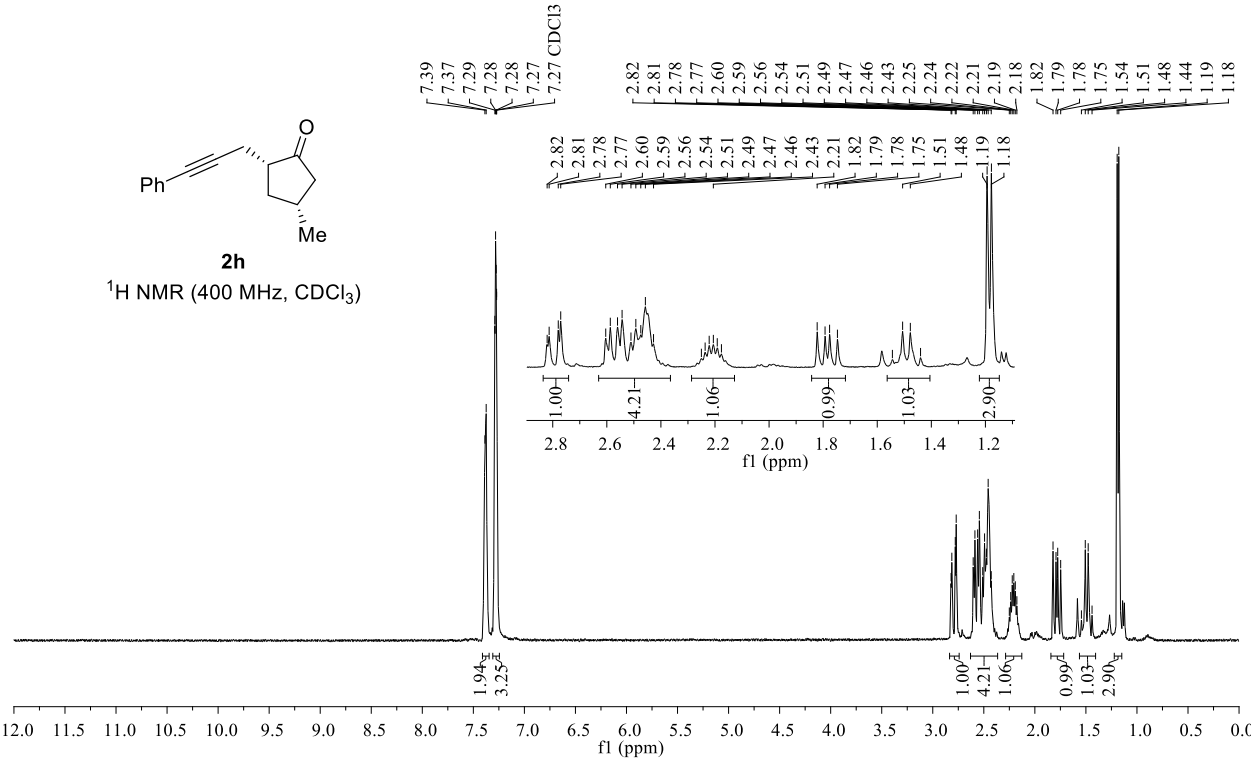

221.25
77.16 CDCl3
Me
O
8
Me
2e
13C NMR (126 MHz, CDCl3)
f1 (ppm)

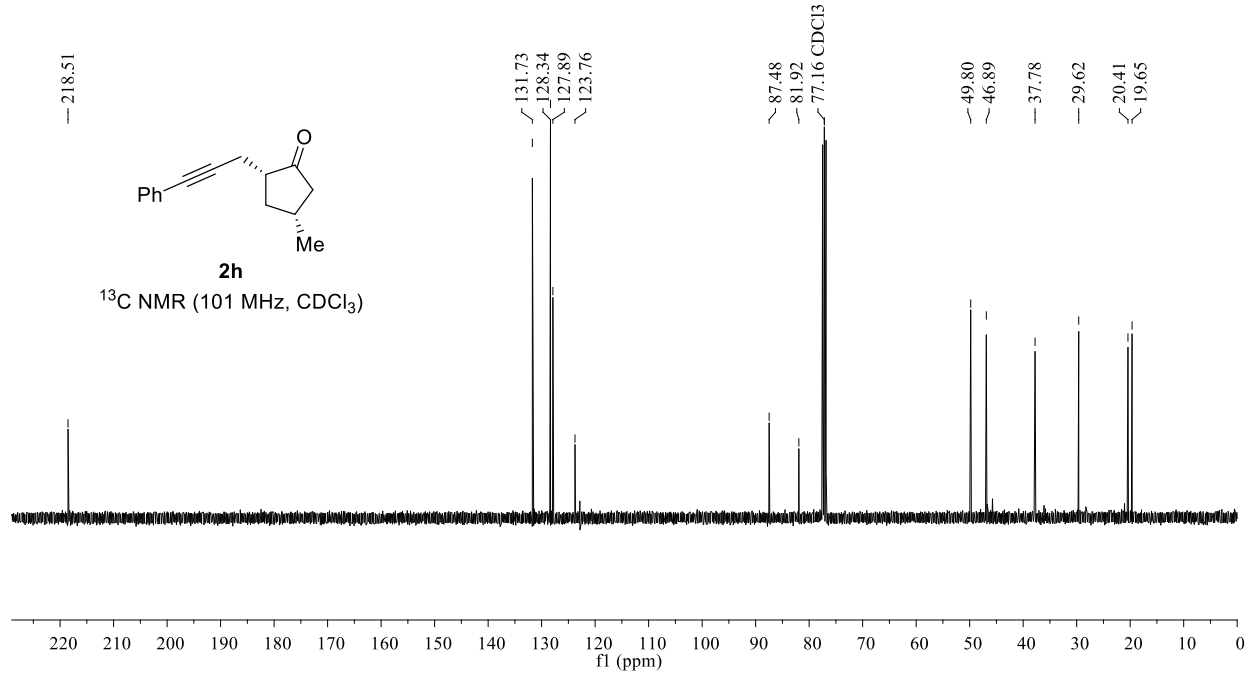

7.27 CDCl3
O
Me
2f
1H NMR (400 MHz, CDCl3)
f1 (ppm)

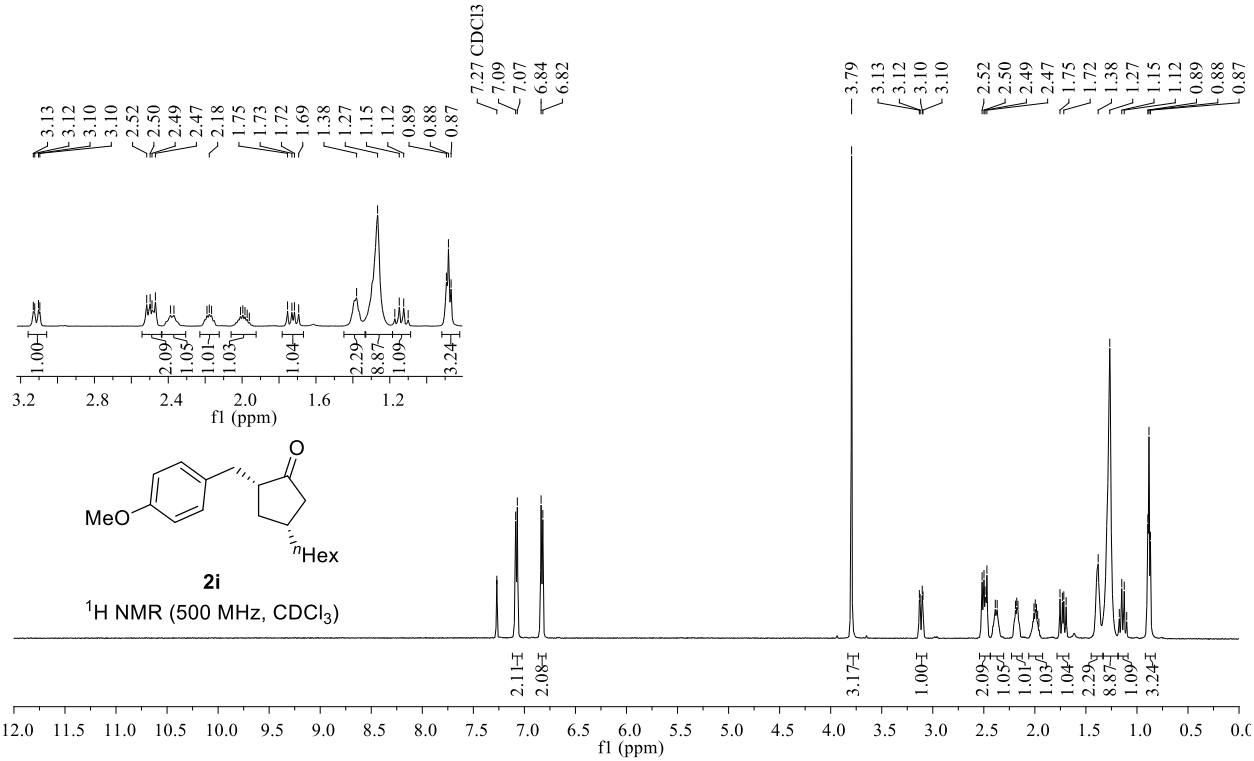

220.77
77.16 CDCl3
56.61
48.20
37.52
34.35
31.88
29.73
28.93
26.72
26.52
26.48
20.42
O
Me
2f
13C NMR (101 MHz, CDCl3)
f1 (ppm)

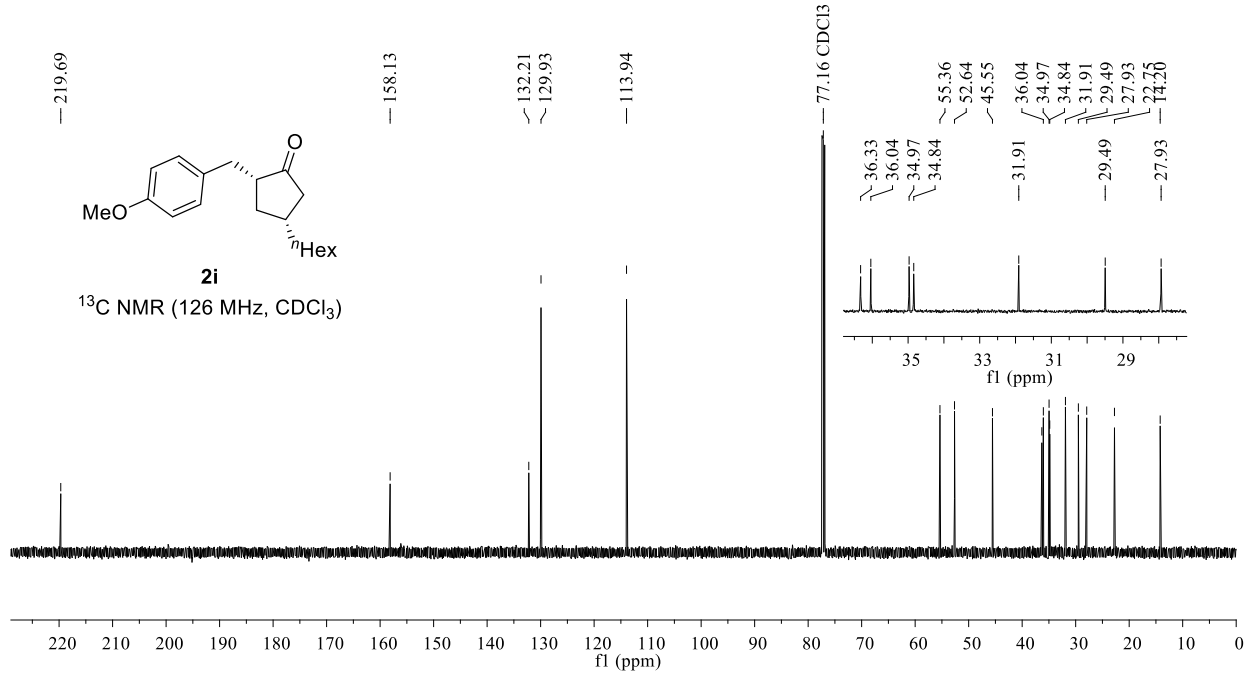

Ph
O
Me
2g
$^{1}$H NMR (400 MHz, $CDCl_3$)
f1 (ppm)

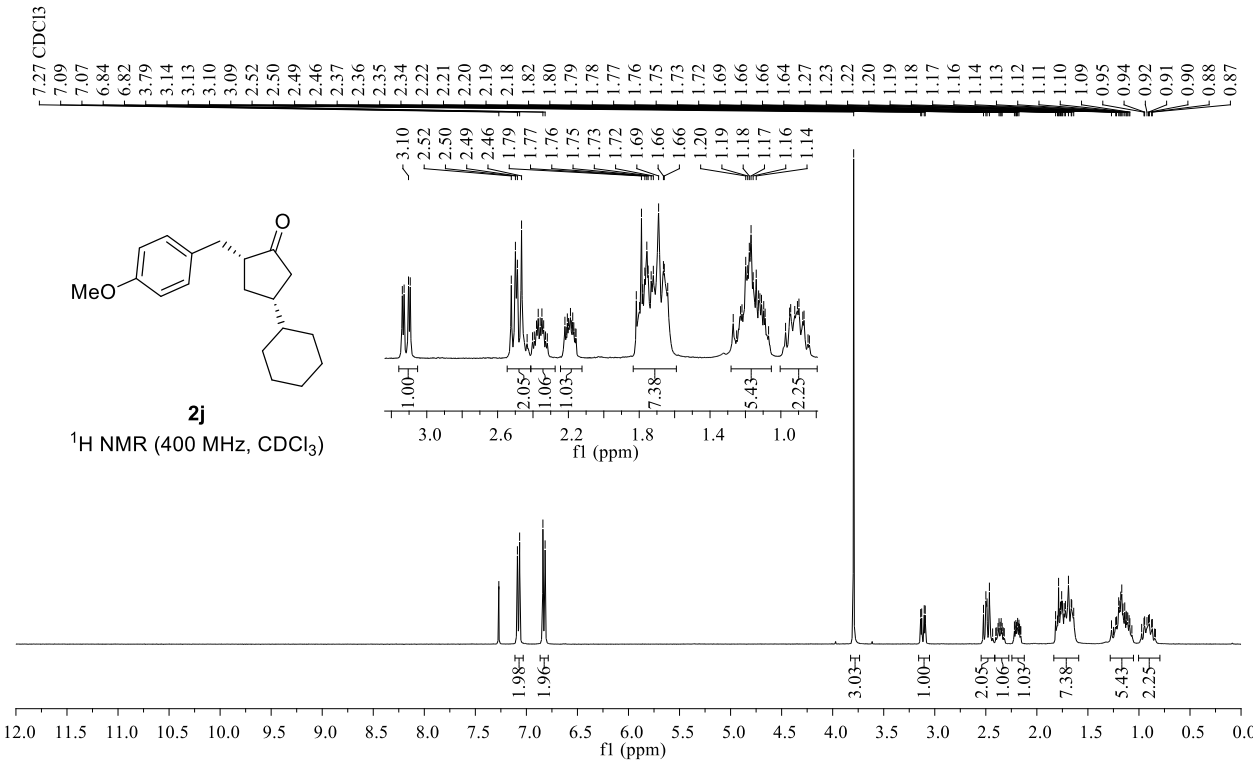

Ph
O
Me
2g
$^{13}$C NMR (101 MHz, $CDCl_3$)
f1 (ppm)

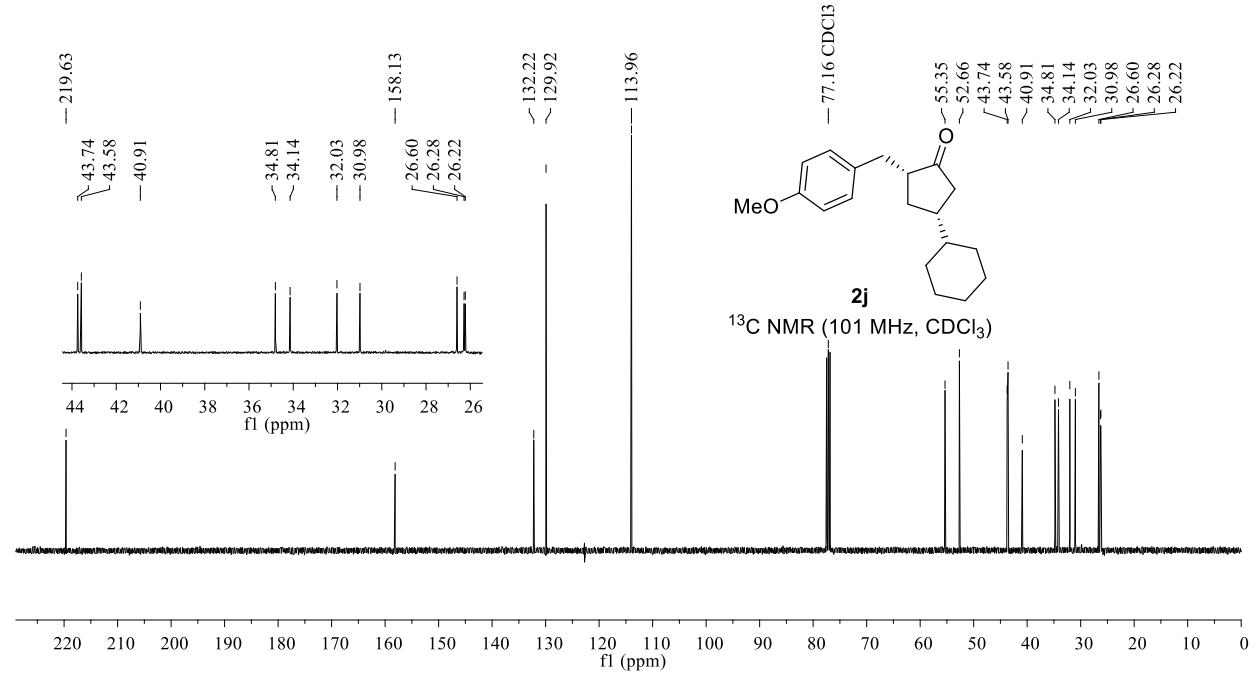

Ph
O
Me
2h
$^1$H NMR (400 MHz, $CDCl_3$)
f1 (ppm)

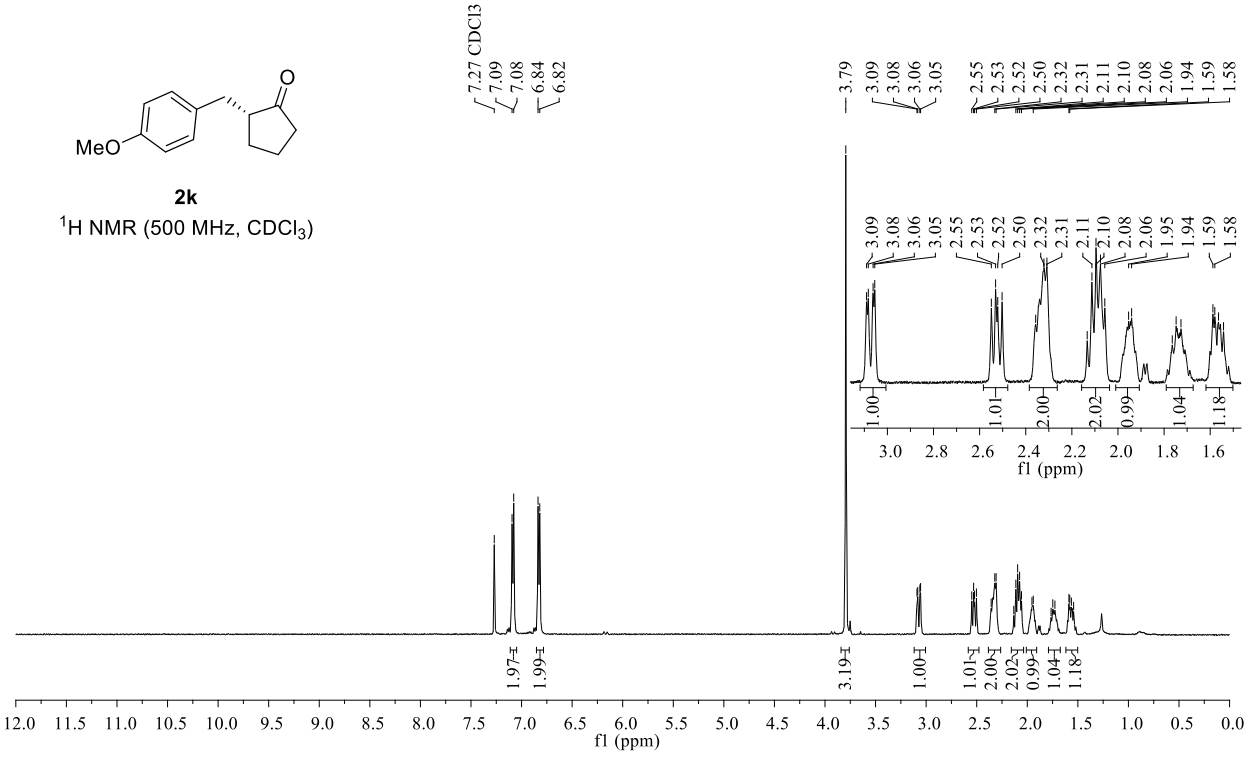

Ph
O
Me
2h
$^{13}$C NMR (101 MHz, $CDCl_3$)
f1 (ppm)

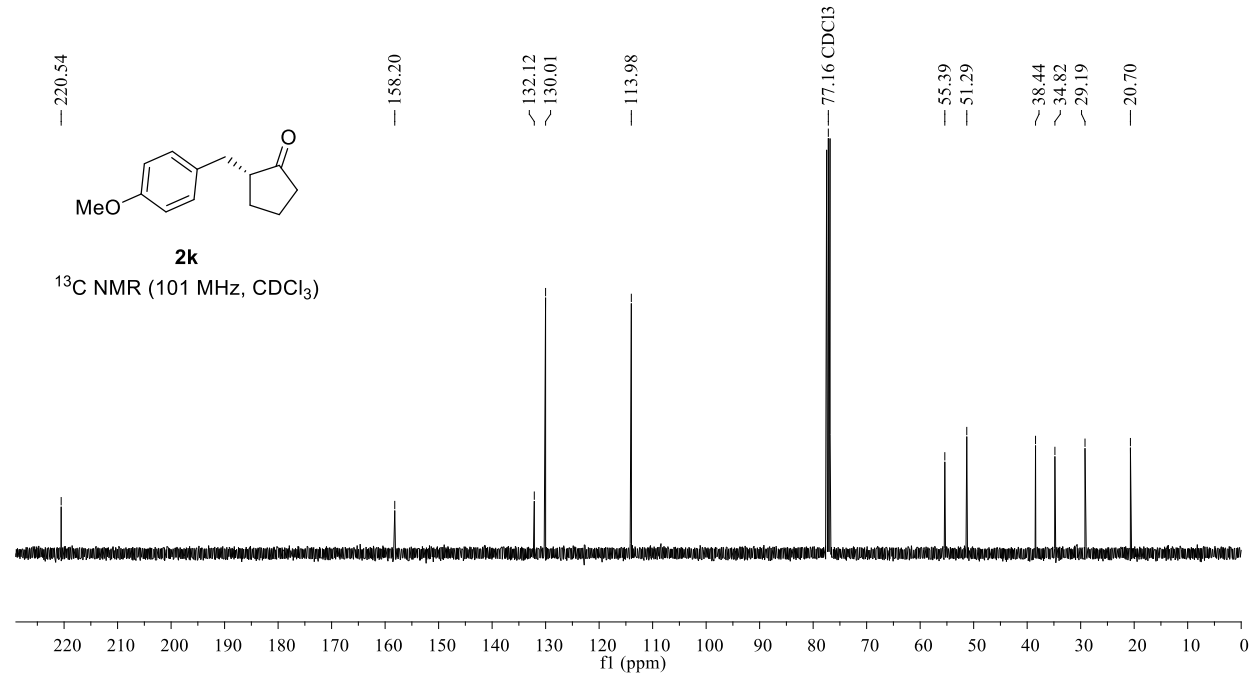

7.27 CDCl3
7.09
7.07
6.84
6.82
3.79
3.13
3.12
3.10
2.52
2.50
2.49
2.47
1.75
1.72
1.38
1.27
1.15
1.12
0.89
0.88
0.87
MeO
nHex
O
2i
1H NMR (500 MHz, CDCl3)
f1 (ppm)

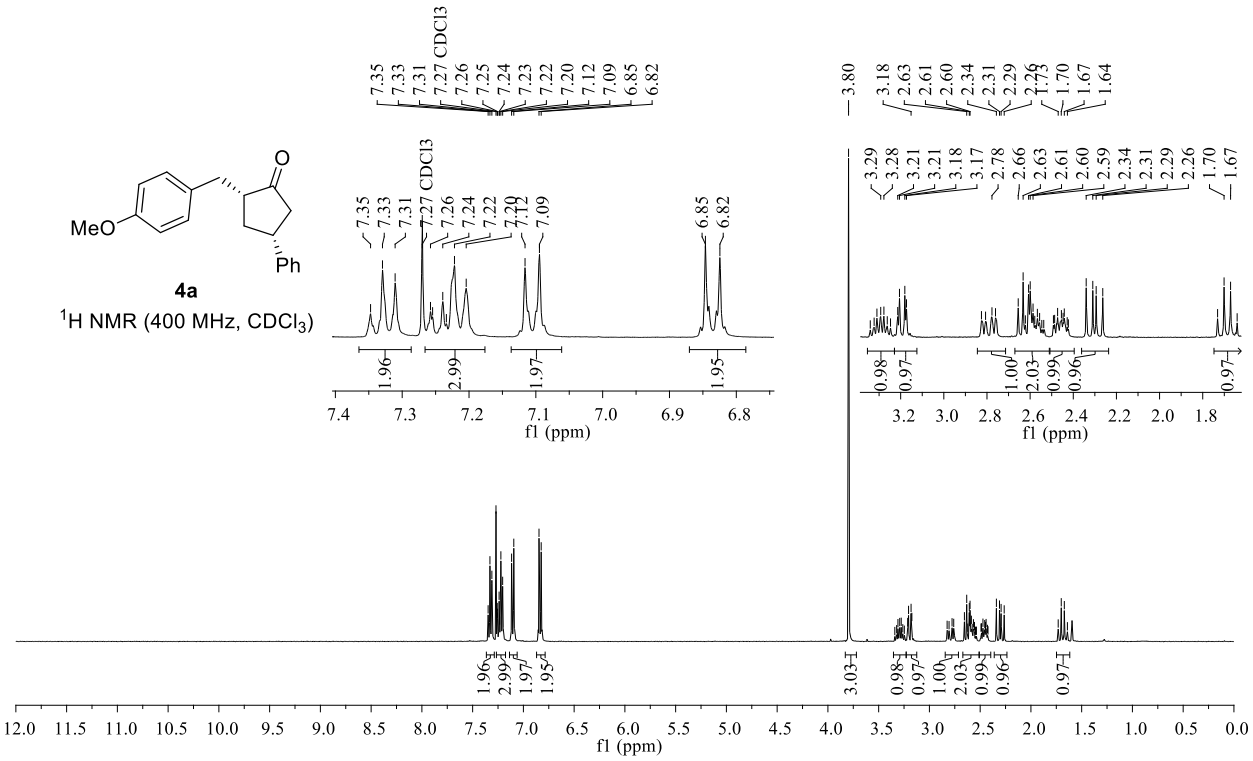

219.69
158.13
132.21
129.93
113.94
77.16 CDCl3
55.36
52.64
45.55
36.04
34.97
34.84
31.91
29.49
27.93
22.75
14.20
MeO
nHex
O
2i
13C NMR (126 MHz, CDCl3)
f1 (ppm)

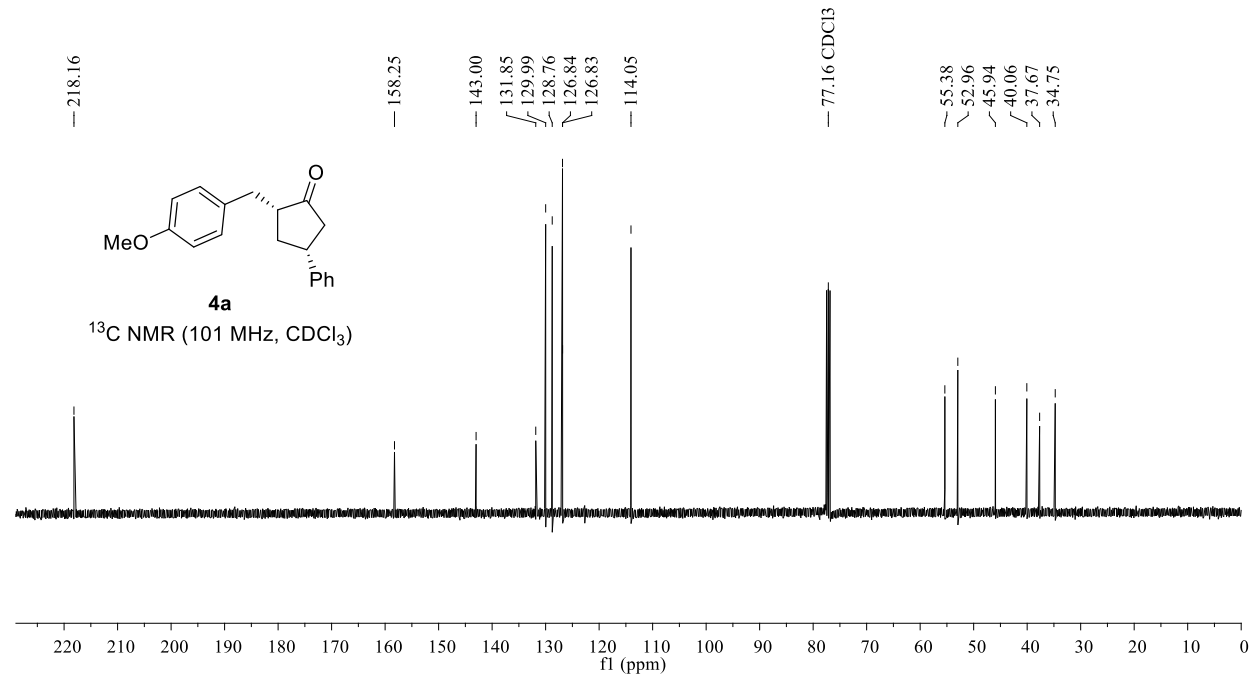

MeO
O
2j
$^1$H NMR (400 MHz, $CDCl_3$)
f1 (ppm)

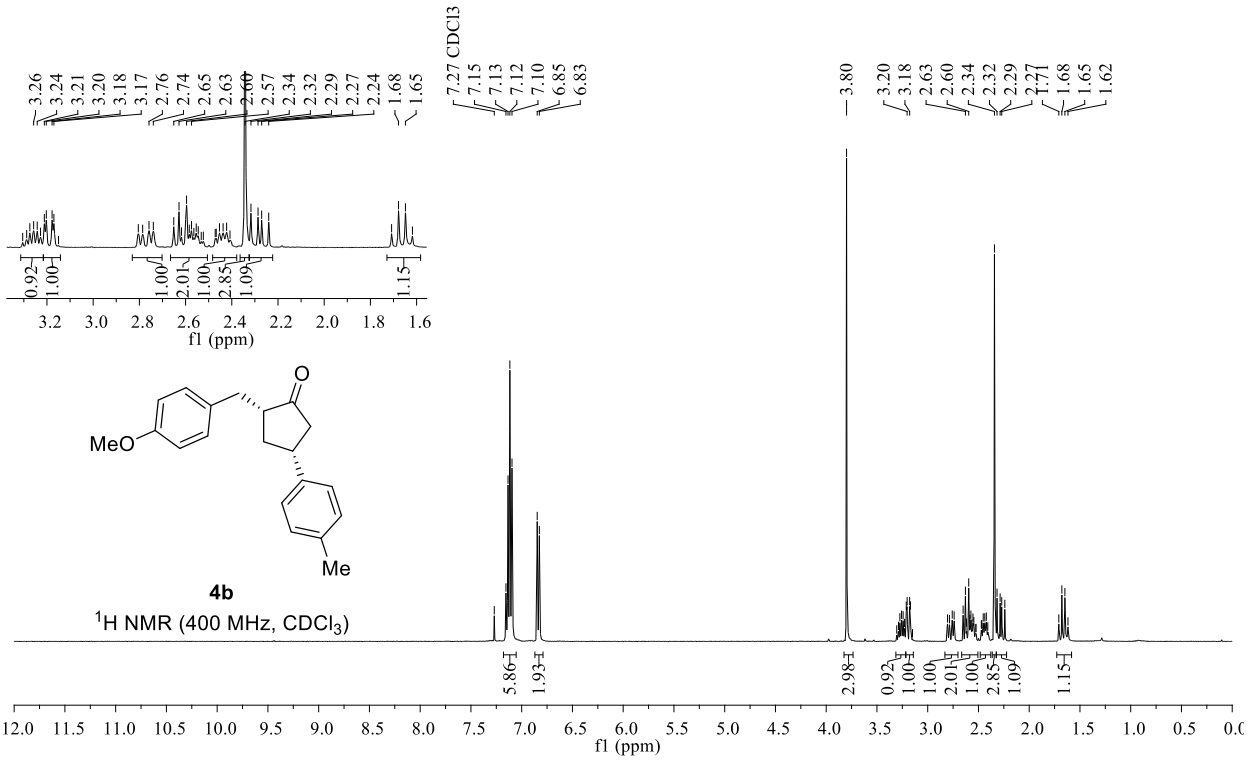

MeO
O
2j
$^{13}$C NMR (101 MHz, $CDCl_3$)
f1 (ppm)

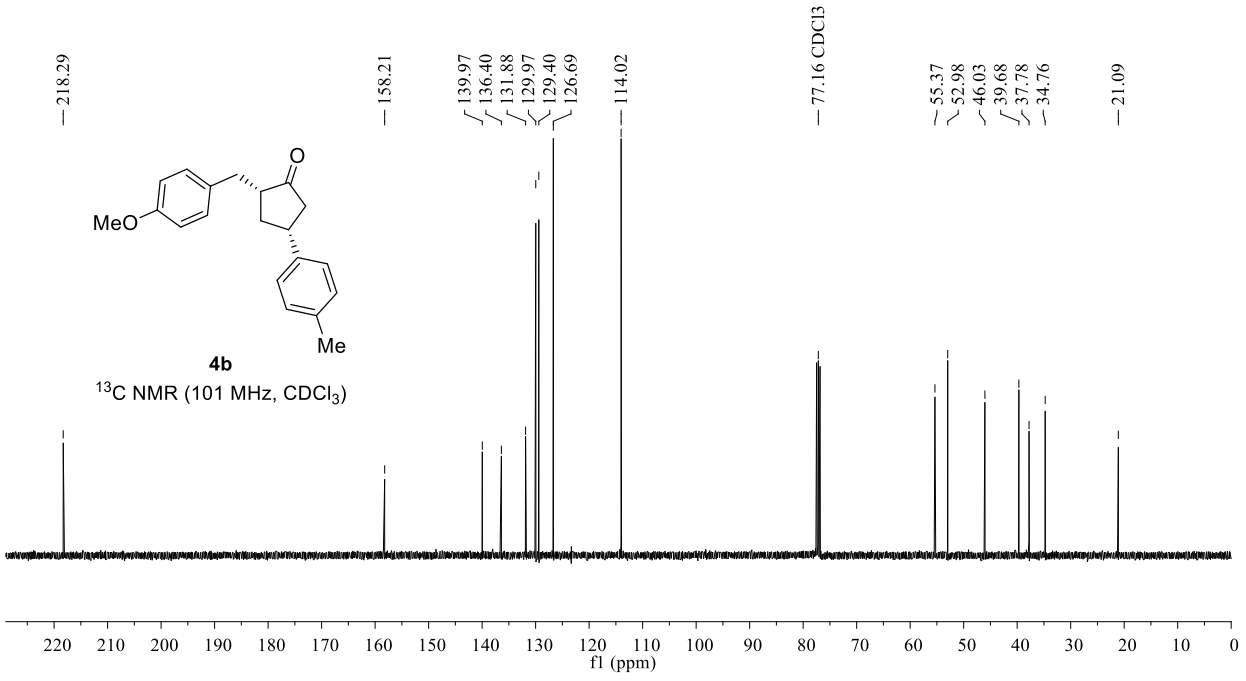

MeO
O
2k
$^1$H NMR (500 MHz, $CDCl_3$)
7.27 CDCl3
7.09
7.08
6.84
6.82
3.79
3.09
3.08
3.06
3.05
2.55
2.53
2.52
2.50
2.32
2.31
2.11
2.10
2.08
2.06
1.95
1.94
1.59
1.58
1.00
1.01
2.00
2.02
0.99
1.04
1.18
1.97
1.99
3.19
1.00
1.01
2.00
2.02
0.99
1.04
1.18
fl (ppm)

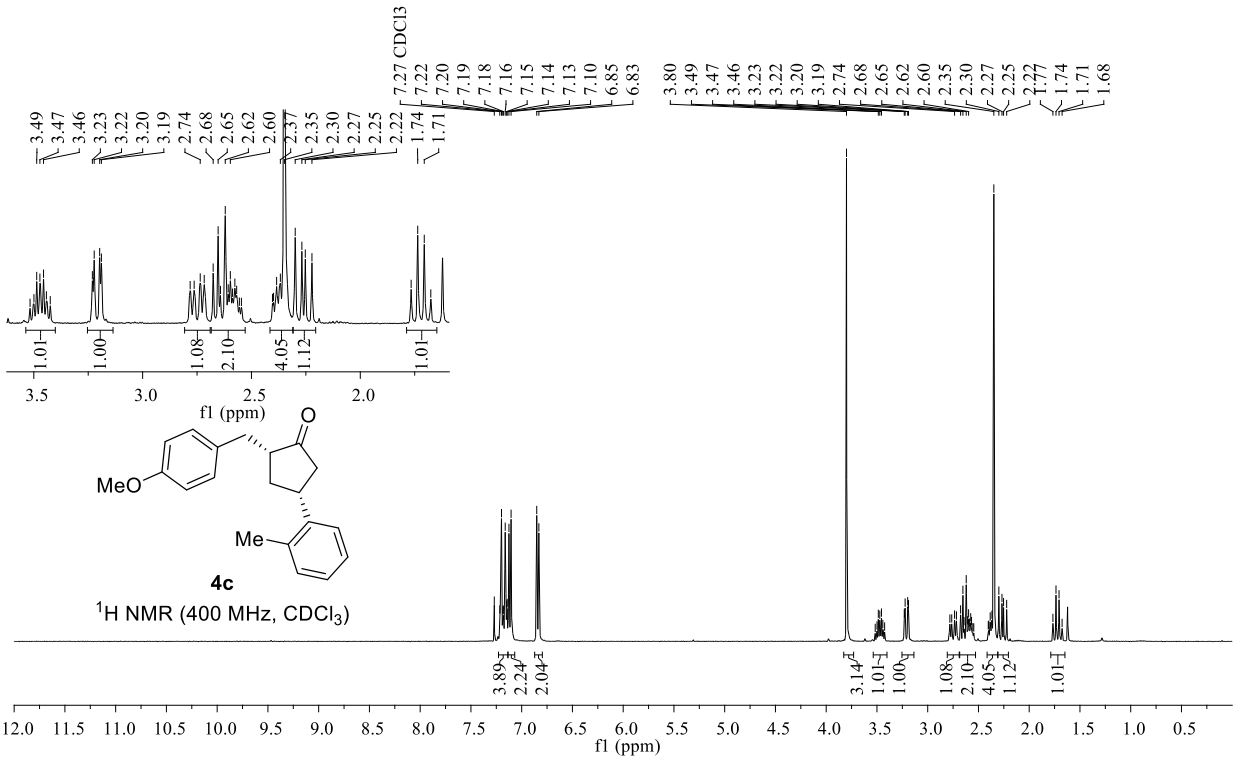

MeO
O
2k
$^{13}$C NMR (101 MHz, $CDCl_3$)
220.54
158.20
132.12
130.01
113.98
77.16 CDCl3
55.39
51.29
38.44
34.82
29.19
20.70
fl (ppm)

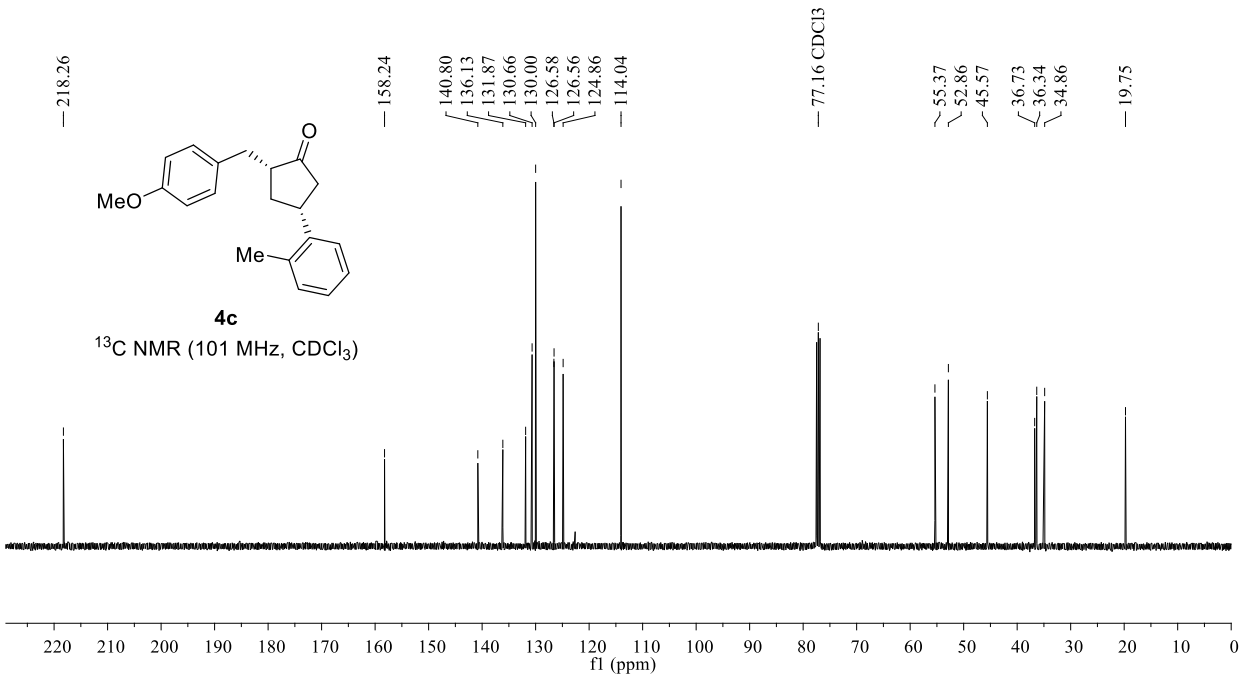

MeO
O
Ph
4a
$^1$H NMR (400 MHz, $CDCl_3$)
fl (ppm)

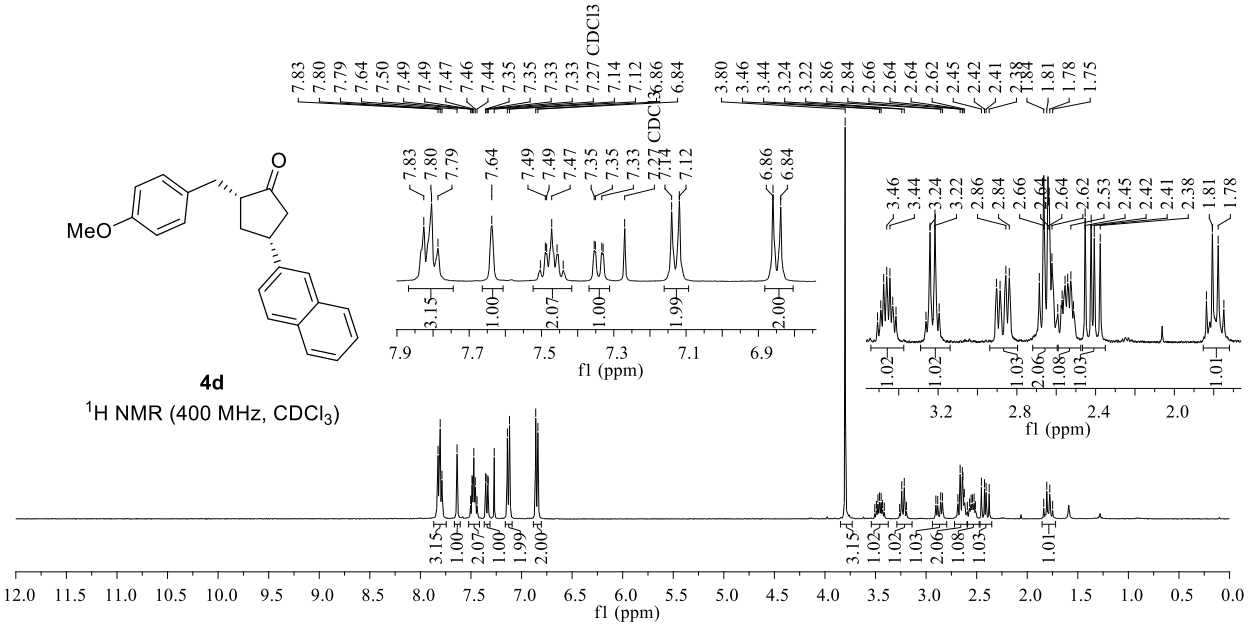

MeO
O
Ph
4a
$^{13}$C NMR (101 MHz, $CDCl_3$)
fl (ppm)

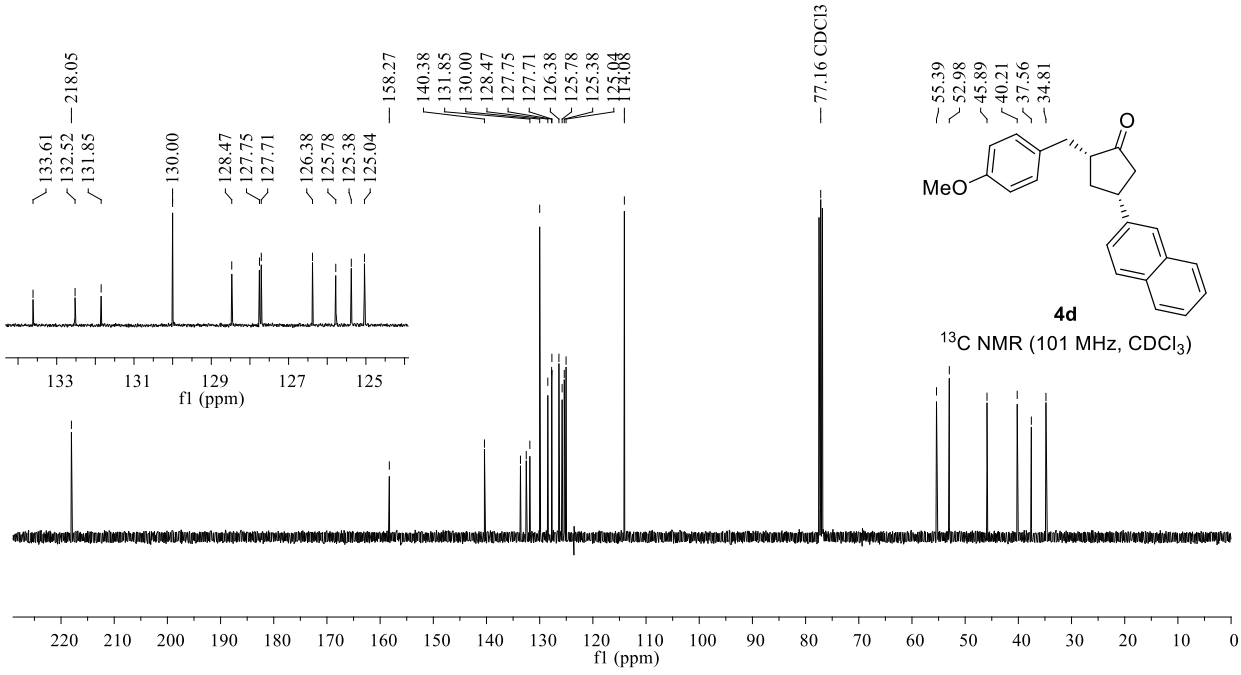

7.27 CDCl3
3.80
MeO
Me
4b
1H NMR (400 MHz, CDCl3)
f1 (ppm)

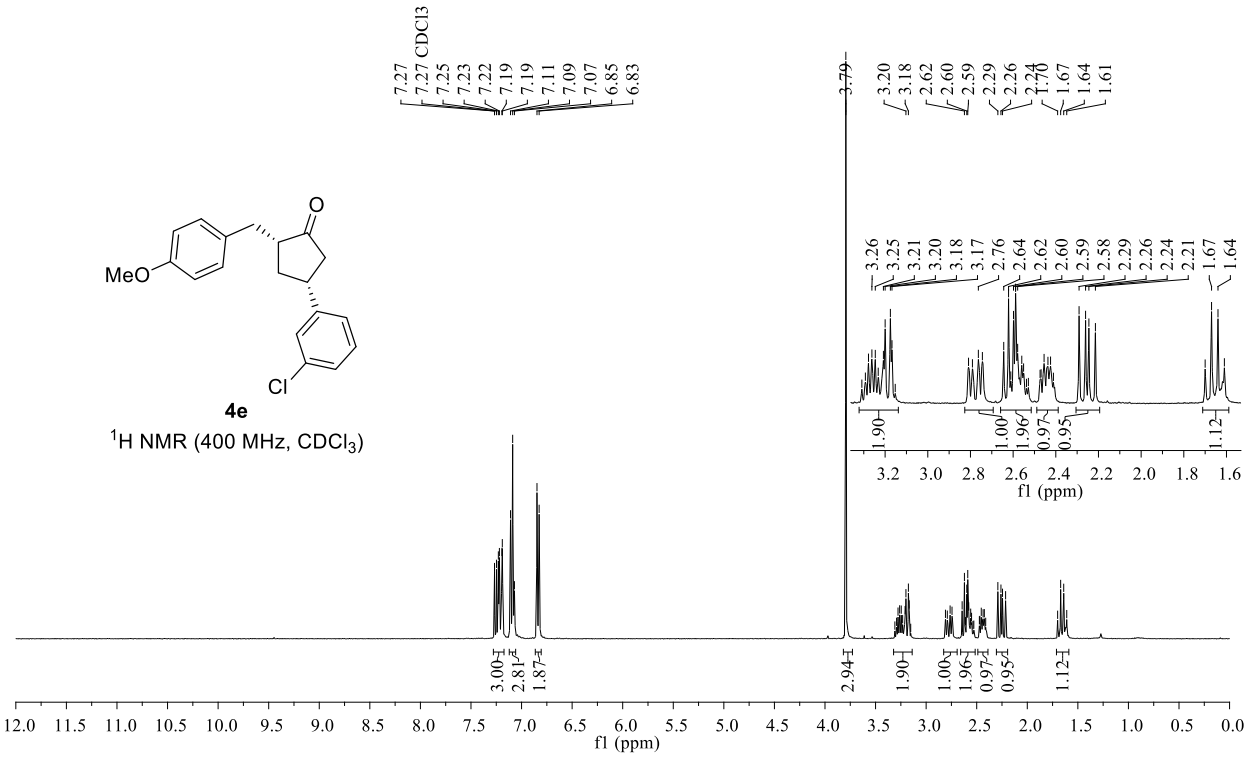

218.29
158.21
139.97
136.40
131.88
129.97
129.40
126.69
114.02
77.16 CDCl3
55.37
52.98
46.03
39.68
37.78
34.76
21.09
MeO
Me
4b
13C NMR (101 MHz, CDCl3)
f1 (ppm)

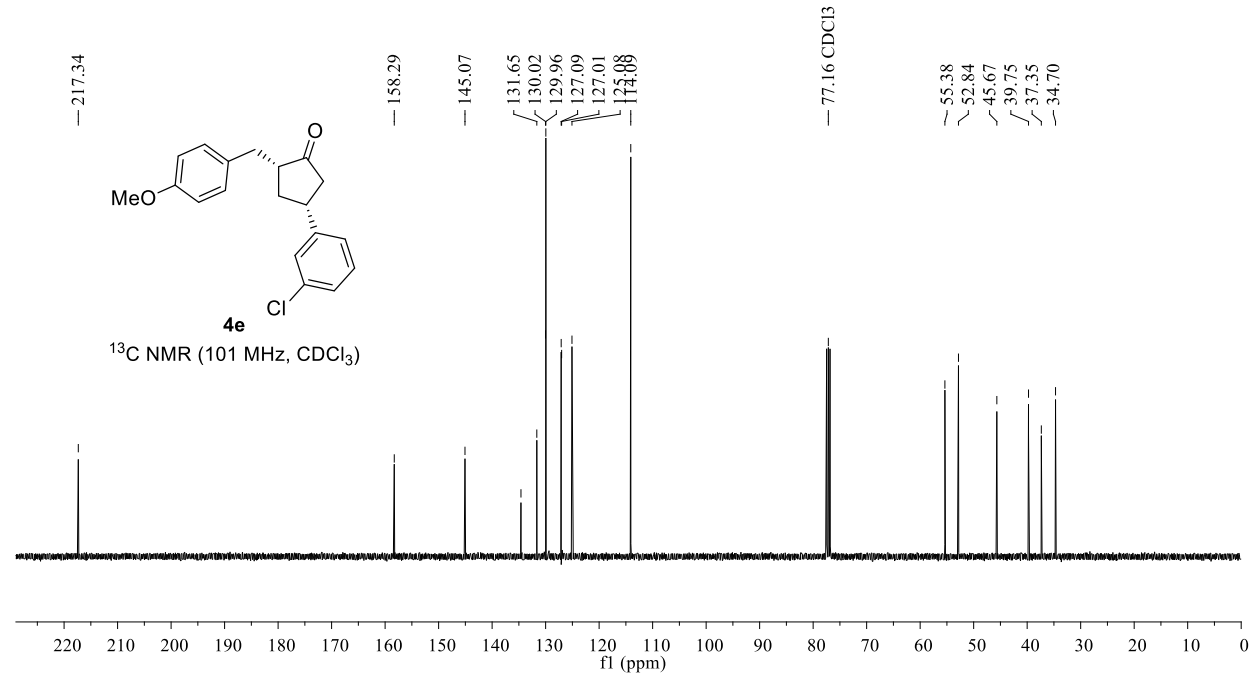

7.27 CDCl3
3.80
3.49
3.47
3.46
3.23
3.22
3.20
3.19
2.74
2.68
2.65
2.62
2.60
2.37
2.35
2.30
2.27
2.25
2.22
1.74
1.71
1.68
1.01
1.00
1.08
2.10
4.05
1.12
1.01
f1 (ppm)
MeO
O
Me
4c
1H NMR (400 MHz, CDCl3)
3.89
2.24
2.04
3.14
1.01
1.00
1.08
2.10
4.05
1.12
1.01
f1 (ppm)

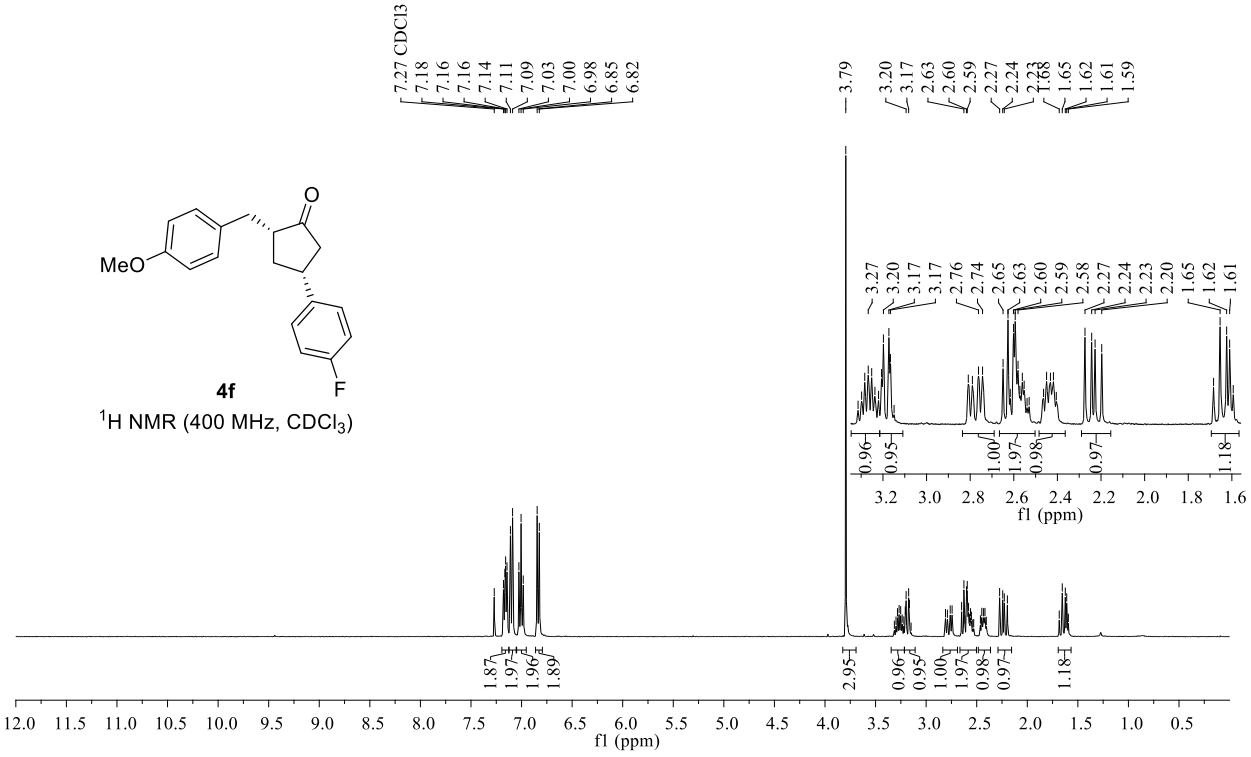

218.26
158.24
140.80
136.13
131.87
130.66
130.00
126.58
126.56
124.86
114.04
77.16 CDCl3
55.37
52.86
45.57
36.73
36.34
34.86
19.75
MeO
O
Me
4c
13C NMR (101 MHz, CDCl3)
f1 (ppm)

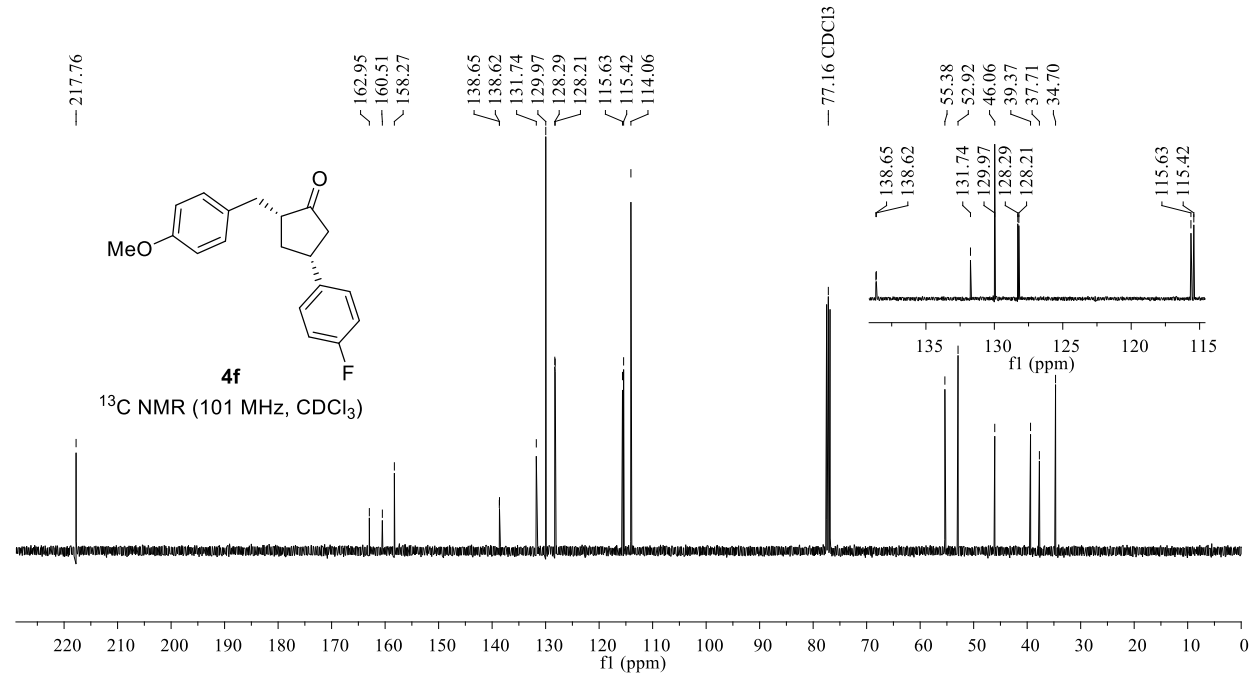

MeO
O
4d
$^1$H NMR (400 MHz, $CDCl_3$)
f1 (ppm)

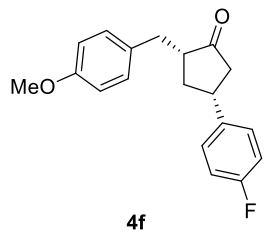

MeO
O
4d
$^{13}$C NMR (101 MHz, $CDCl_3$)
f1 (ppm)


MeO
Cl
O
4e
$^1$H NMR (400 MHz, CDCl$_3$)
fl (ppm)


MeO
Cl
O
4e
$^{13}$C NMR (101 MHz, CDCl$_3$)
77.16 CDCl3
fl (ppm)


7.27 CDCl3
7.18
7.16
7.16
7.14
7.11
7.09
7.03
7.00
6.98
6.85
6.82
3.79
3.20
3.17
2.63
2.60
2.59
2.27
2.24
2.23
1.68
1.65
1.62
1.61
1.59
O
MeO
F
4f
1H NMR (400 MHz, CDCl3)
3.27
3.20
3.17
3.17
2.76
2.74
2.65
2.63
2.60
2.59
2.58
2.27
2.24
2.23
2.20
1.65
1.62
1.61
0.96
0.95
1.00
1.97
0.98
0.97
1.18
3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)
1.87
1.97
1.96
1.89
2.95
0.96
0.95
1.00
1.97
0.98
0.97
1.18
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

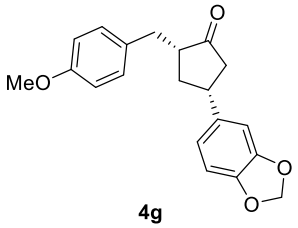

217.76
162.95
160.51
158.27
138.65
138.62
131.74
129.97
128.29
128.21
115.63
115.42
114.06
77.16 CDCl3
55.38
52.92
46.06
39.37
37.71
34.70
138.65
138.62
131.74
129.97
128.29
128.21
115.63
115.42
135 130 125 120 115
f1 (ppm)
O
MeO
F
4f
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)




**4f**

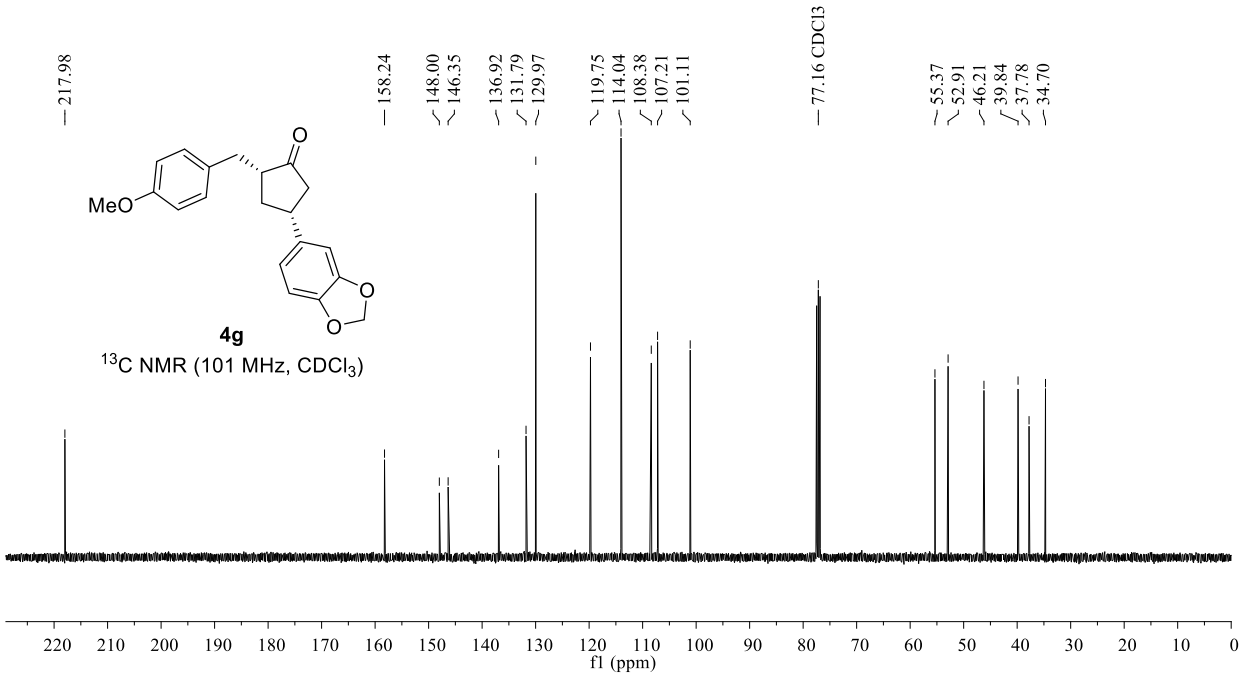
$^{19}$F NMR (376 MHz, $CDCl_3$)

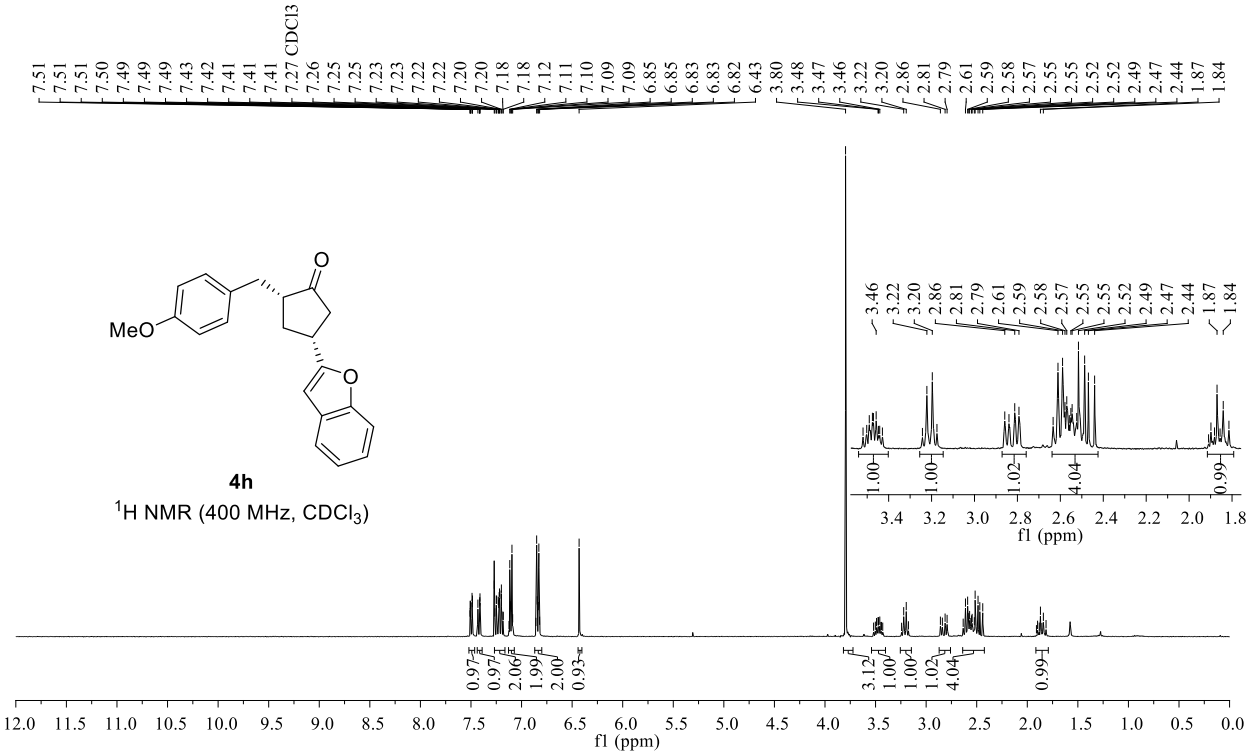


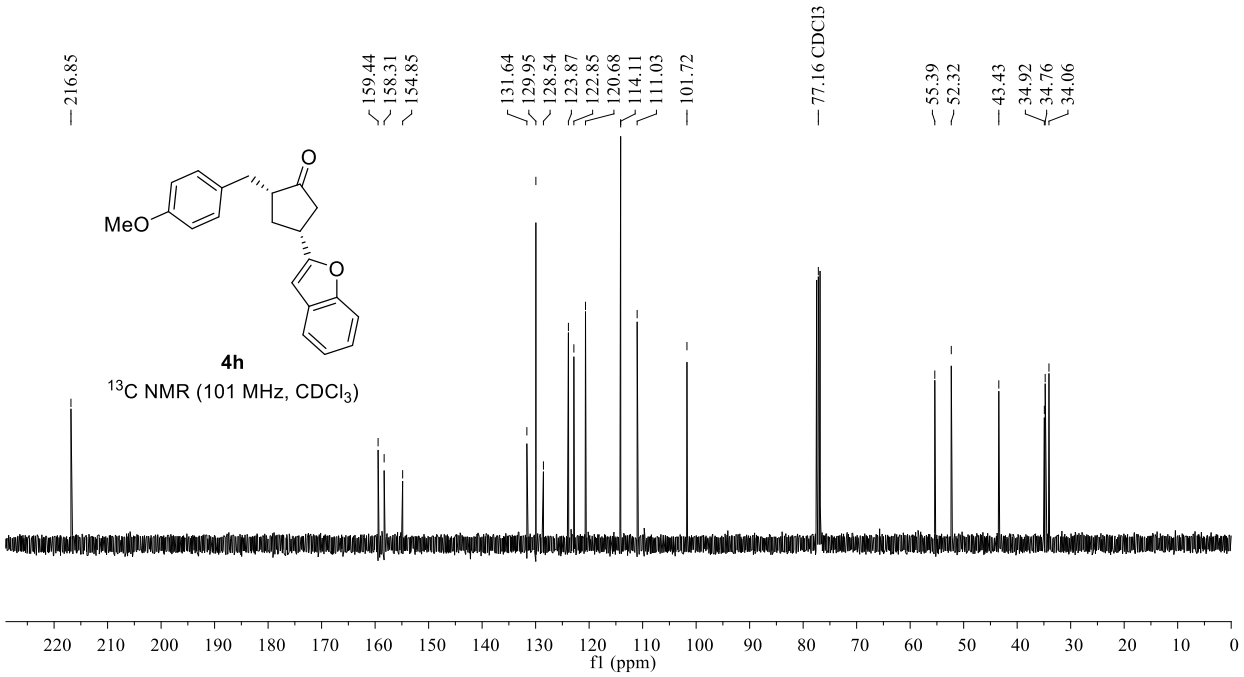



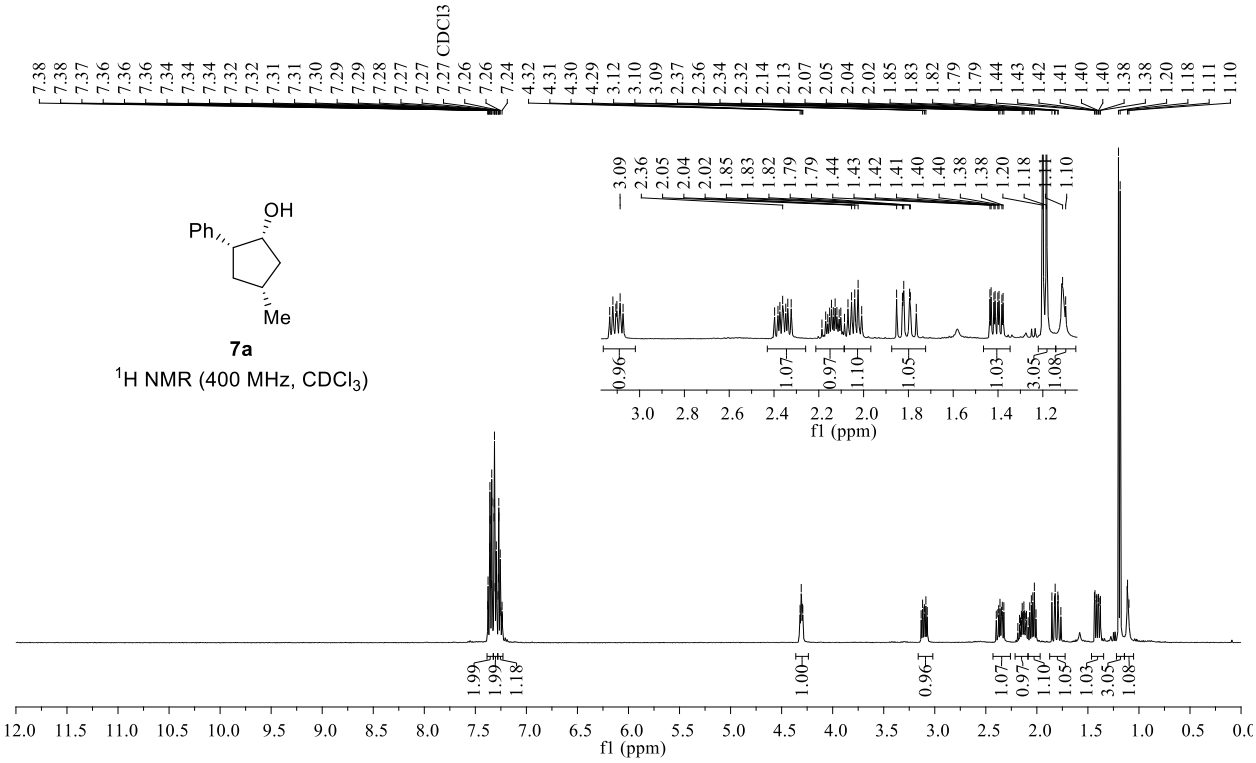

**4g**

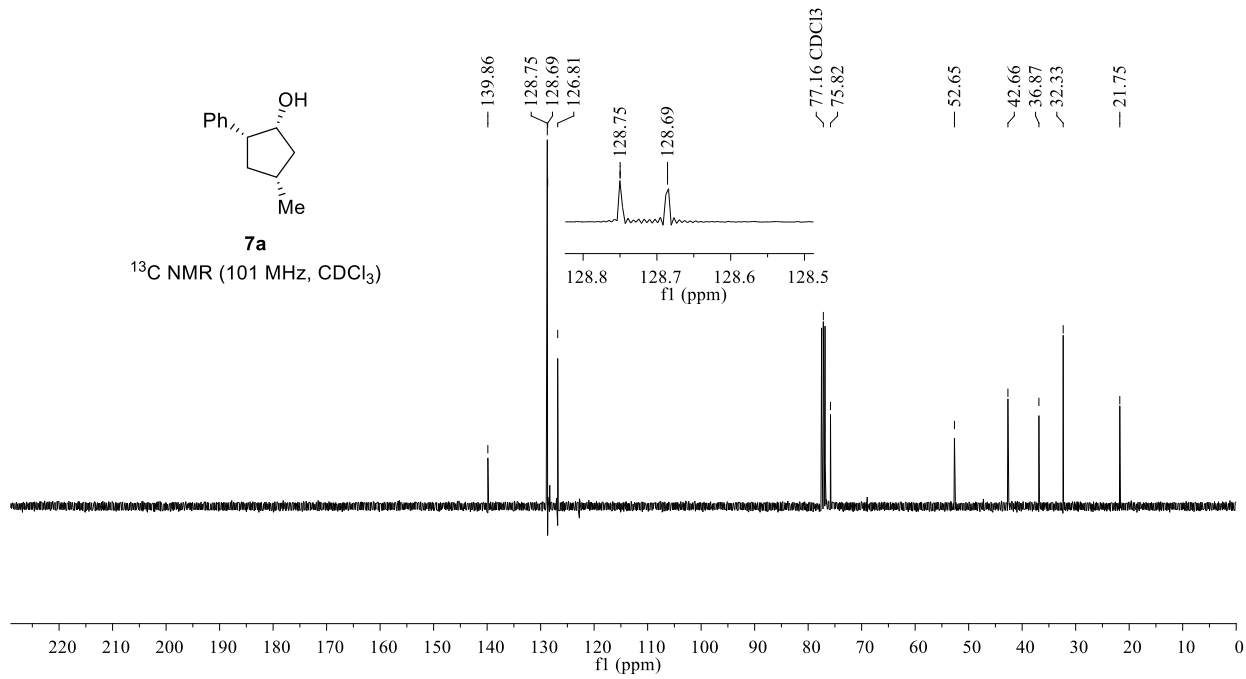
$^{1}$H NMR (400 MHz, $CDCl_3$)

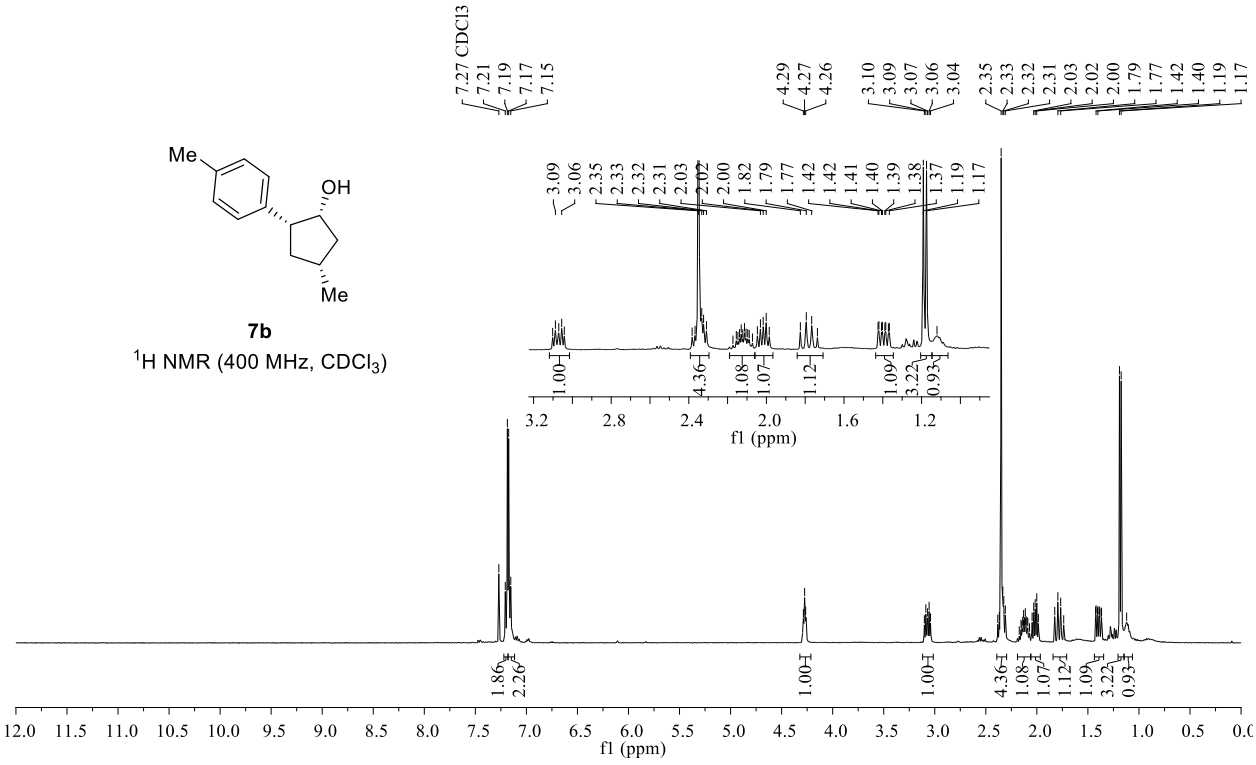

217.98
158.24
148.00
146.35
136.92
131.79
129.97
119.75
114.04
108.38
107.21
101.11
77.16 CDCl3
55.37
52.91
46.21
39.84
37.78
34.70
MeO
O
O
O
4g
13C NMR (101 MHz, CDCl3)
f1 (ppm)

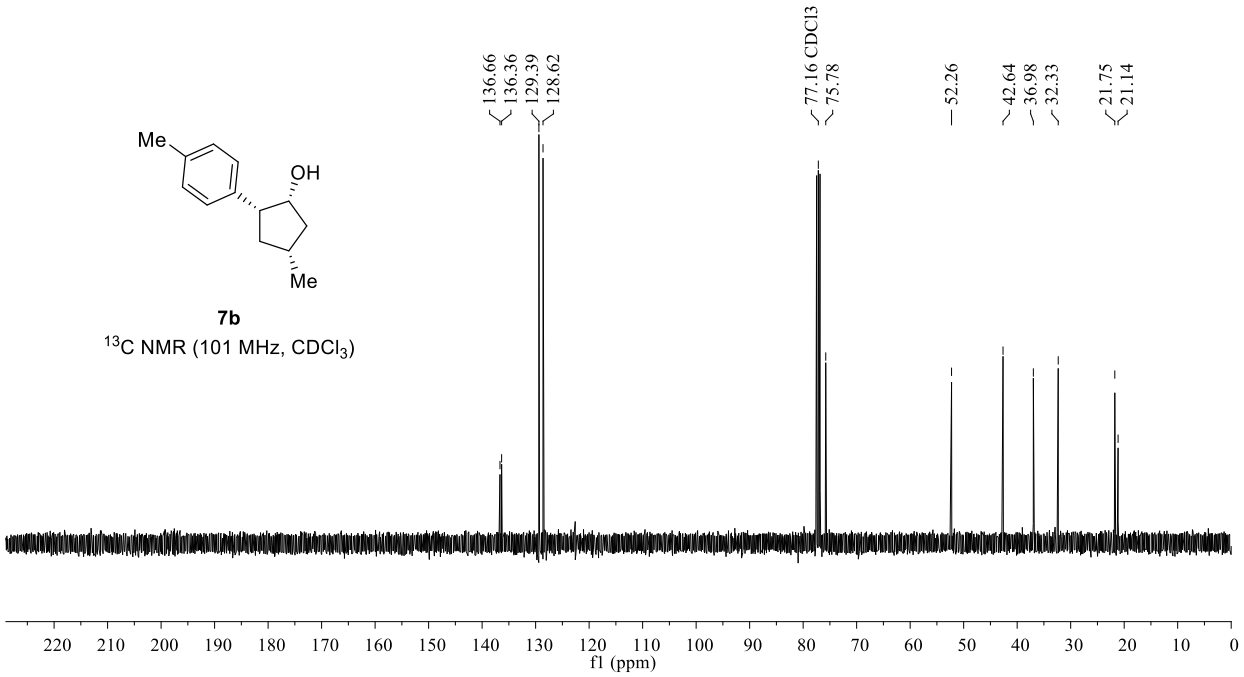

7.51
7.27 CDCl3
6.85
6.83
6.82
6.43
3.80
3.48
3.47
3.46
3.22
3.20
2.86
2.81
2.79
2.61
2.59
2.58
2.57
2.55
2.52
2.49
2.47
2.44
1.87
1.84
MeO
O
O
4h
1H NMR (400 MHz, CDCl3)
0.97
0.97
2.06
1.99
2.00
0.93
3.12
1.00
1.00
1.02
4.04
0.99
f1 (ppm)


216.85
159.44
158.31
154.85
131.64
129.95
128.54
123.87
122.85
120.68
114.11
111.03
101.72
77.16 CDCl3
55.39
52.32
43.43
34.92
34.76
34.06
MeO
O
O
4h
13C NMR (101 MHz, CDCl3)
f1 (ppm)


7.38
7.38
7.37
7.36
7.36
7.36
7.34
7.34
7.34
7.32
7.32
7.31
7.31
7.30
7.29
7.29
7.28
7.27
7.27
7.27 CDCl3
7.26
7.26
7.24
4.32
4.31
4.30
4.29
3.12
3.10
3.09
2.37
2.36
2.34
2.32
2.14
2.13
2.07
2.05
2.04
2.02
1.85
1.83
1.82
1.79
1.79
1.44
1.43
1.42
1.41
1.40
1.40
1.38
1.38
1.20
1.18
1.11
1.10
OH
Ph
Me
7a
1H NMR (400 MHz, CDCl3)
f1 (ppm)

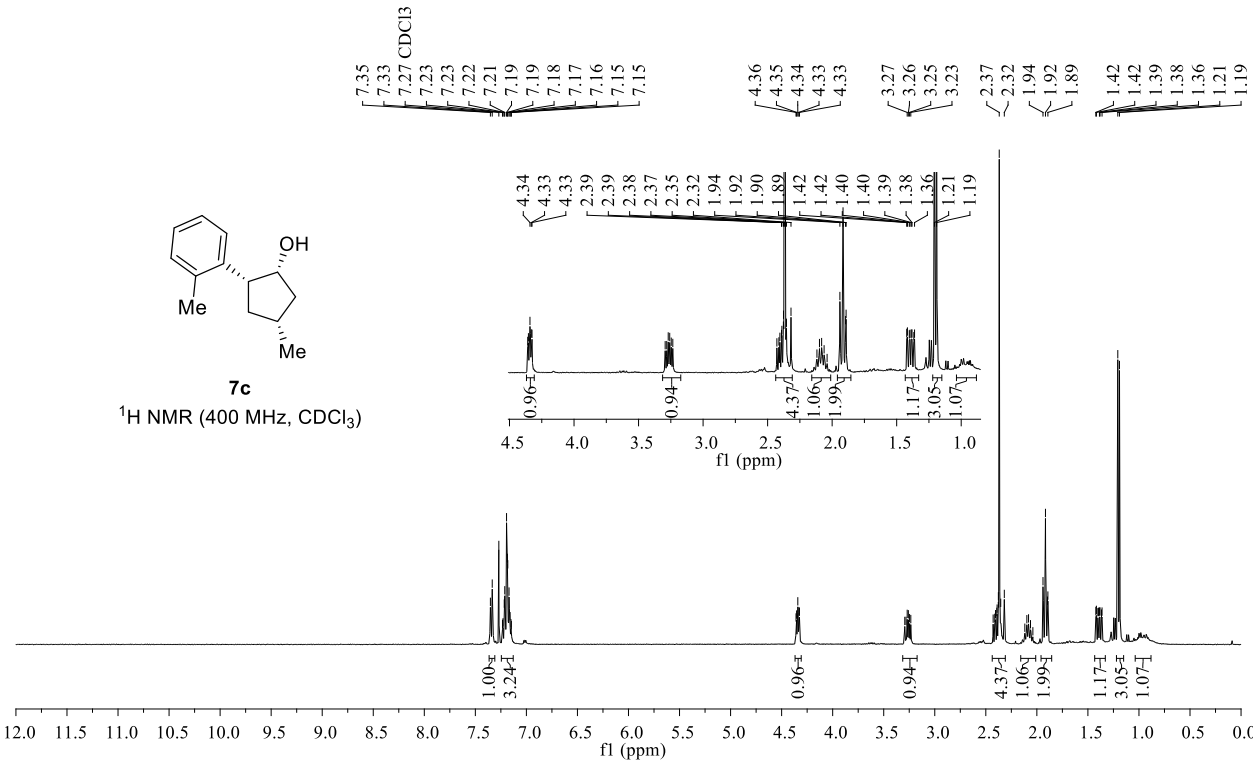

OH
Ph
Me
7a
13C NMR (101 MHz, CDCl3)
139.86
128.75
128.69
126.81
77.16 CDCl3
75.82
52.65
42.66
36.87
32.33
21.75
128.8
128.7
128.6
128.5
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Me
OH
Me
7b
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
7.21
7.19
7.17
7.15
4.29
4.27
4.26
3.10
3.09
3.07
3.06
3.04
2.35
2.33
2.32
2.31
2.03
2.02
2.00
1.79
1.77
1.42
1.40
1.19
1.17
3.2
2.8
2.4
2.0
1.6
1.2
f1 (ppm)
1.86
2.26
1.00
1.00
4.36
1.08
1.07
1.12
1.09
3.22
0.93
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



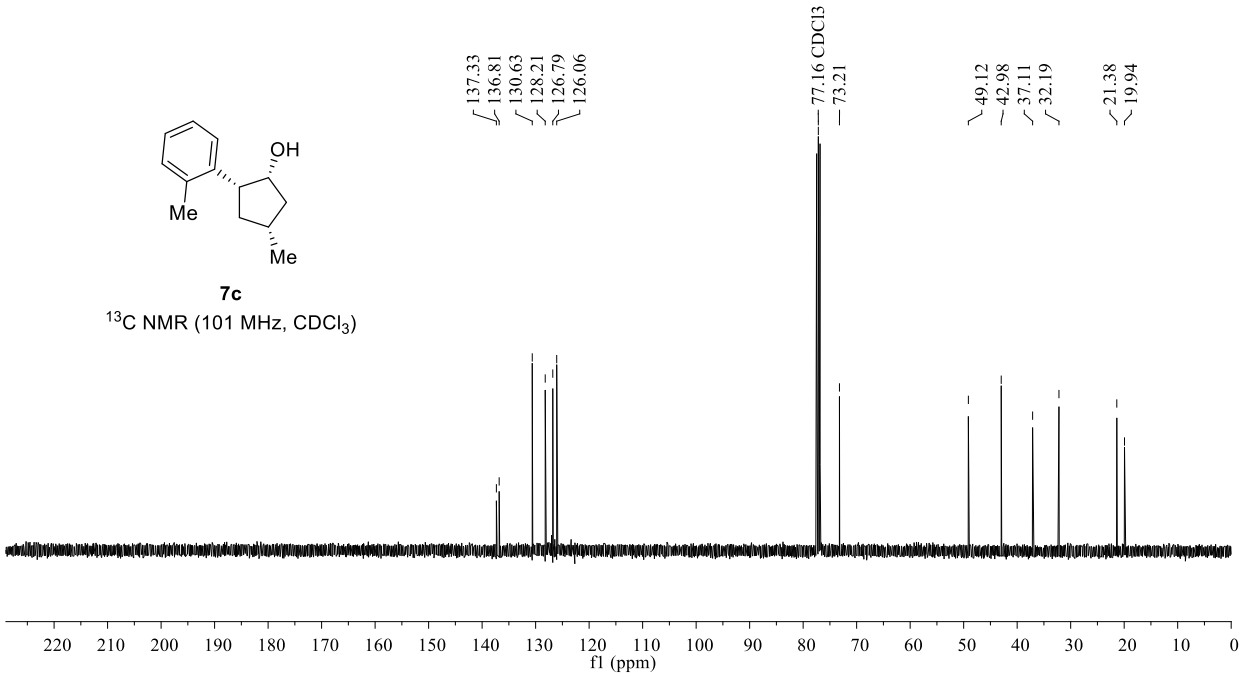

**7b**

$^{13}$C NMR (101 MHz, $CDCl_3$)



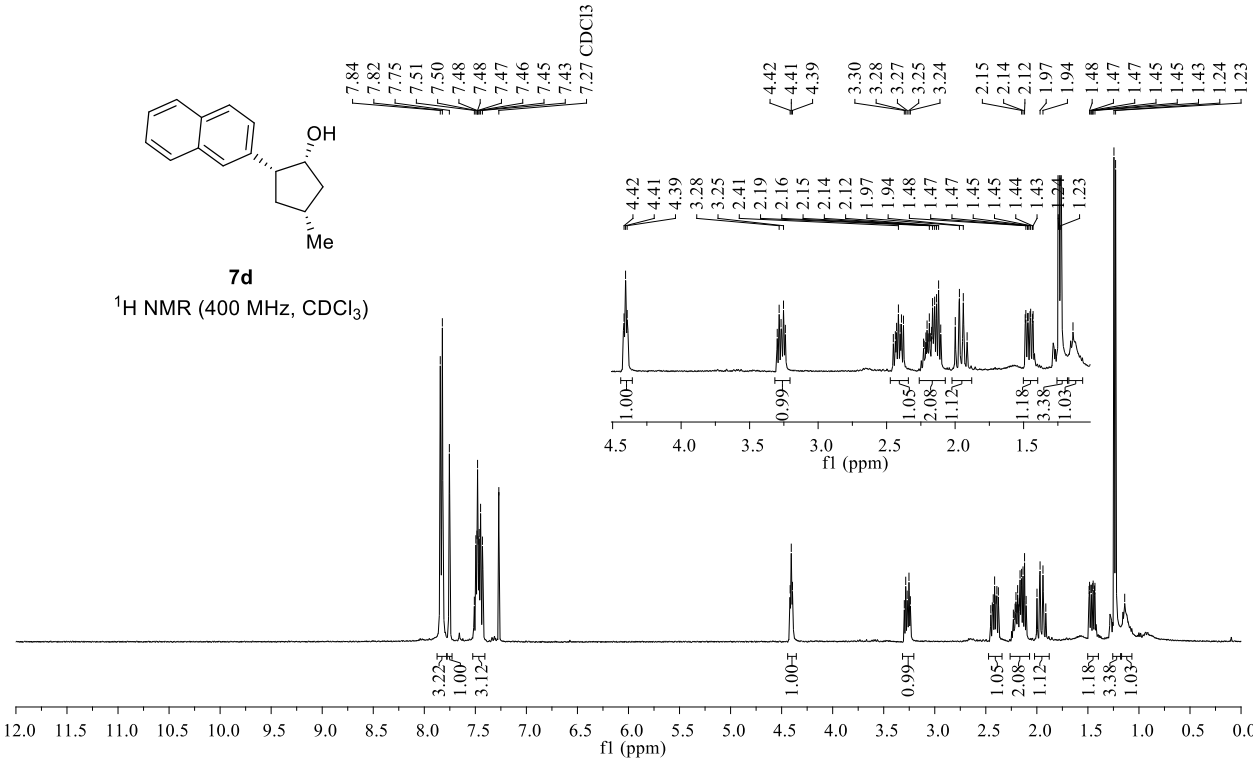

**7c**

$^{1}$H NMR (400 MHz, $CDCl_3$)



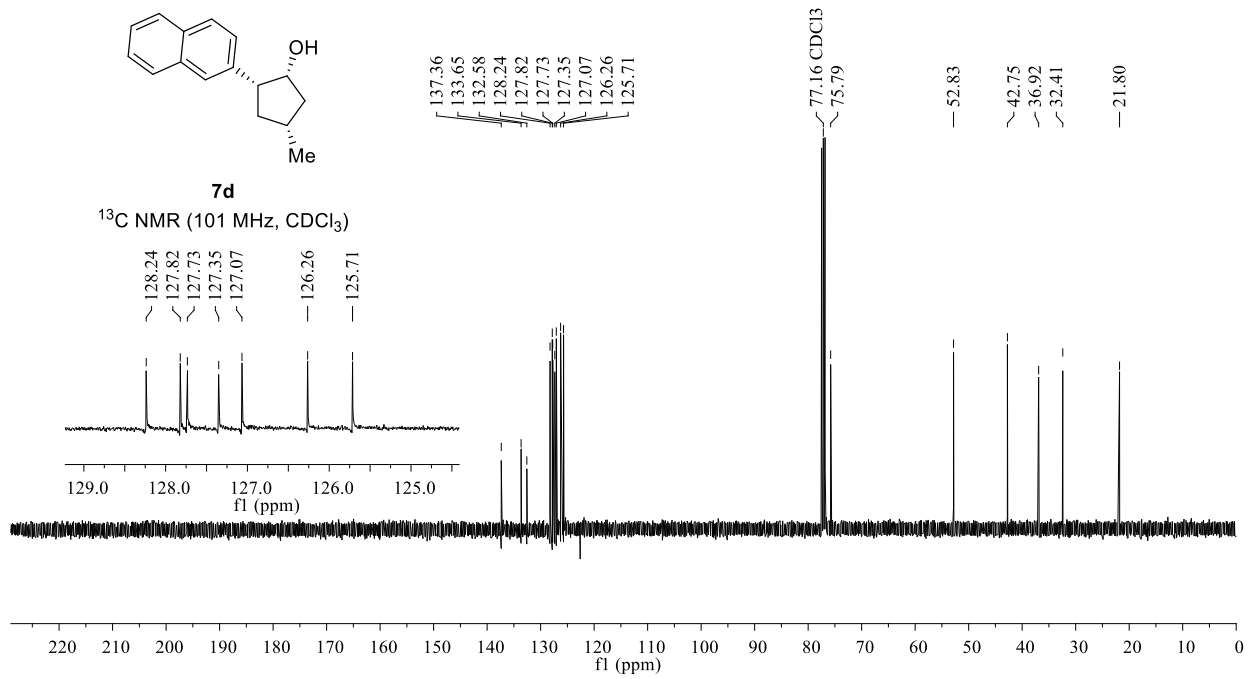

**7c**

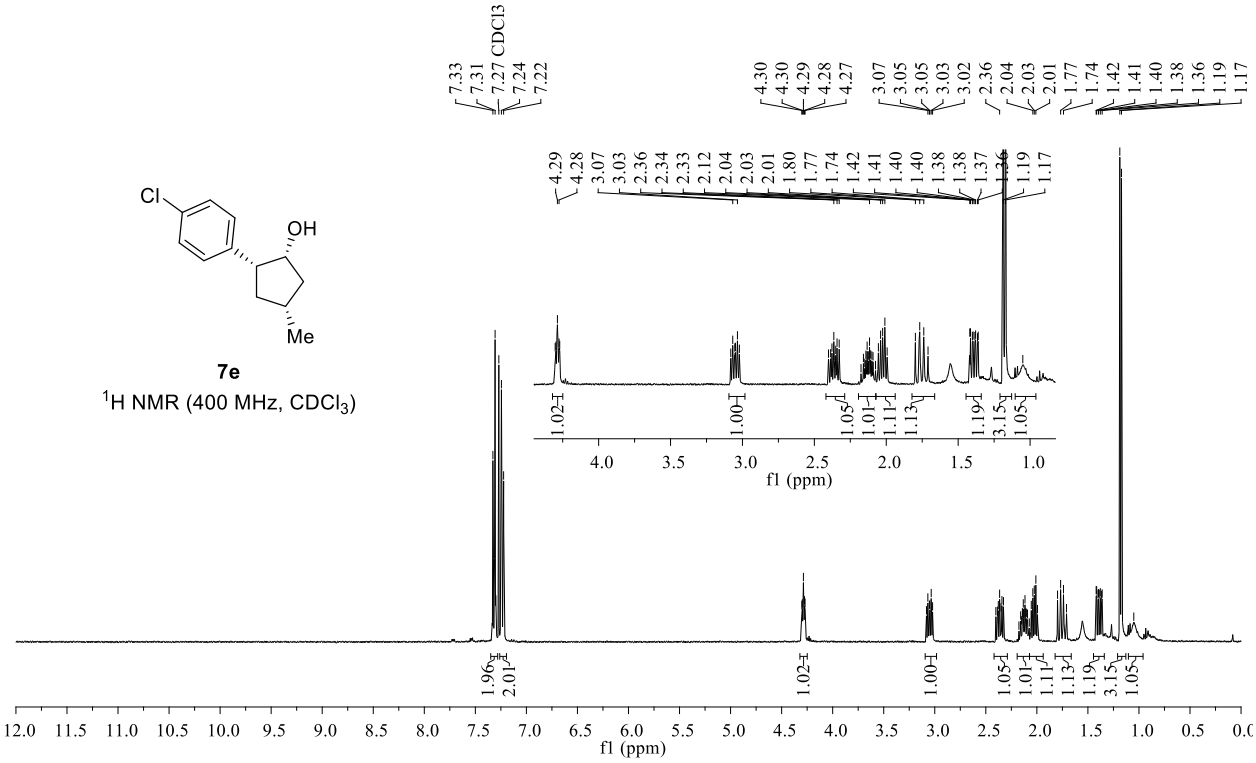
$^{13}$C NMR (101 MHz, $CDCl_3$)

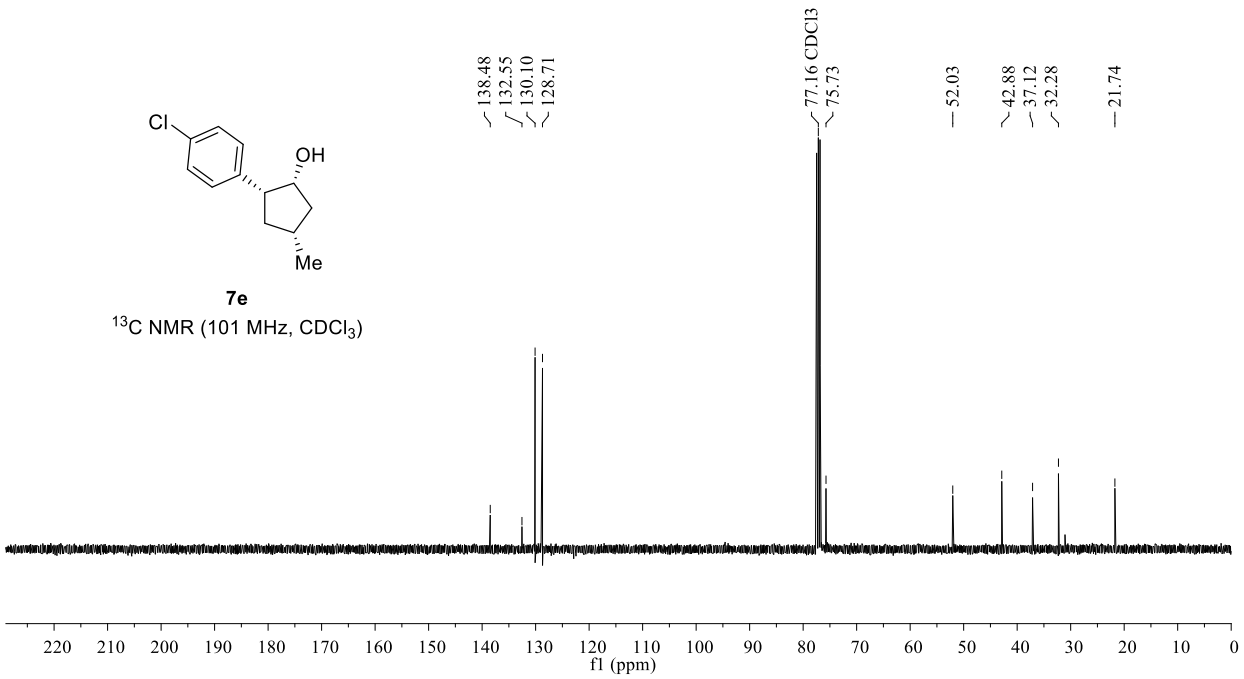



**7d**

$^{1}$H NMR (400 MHz, $CDCl_3$)

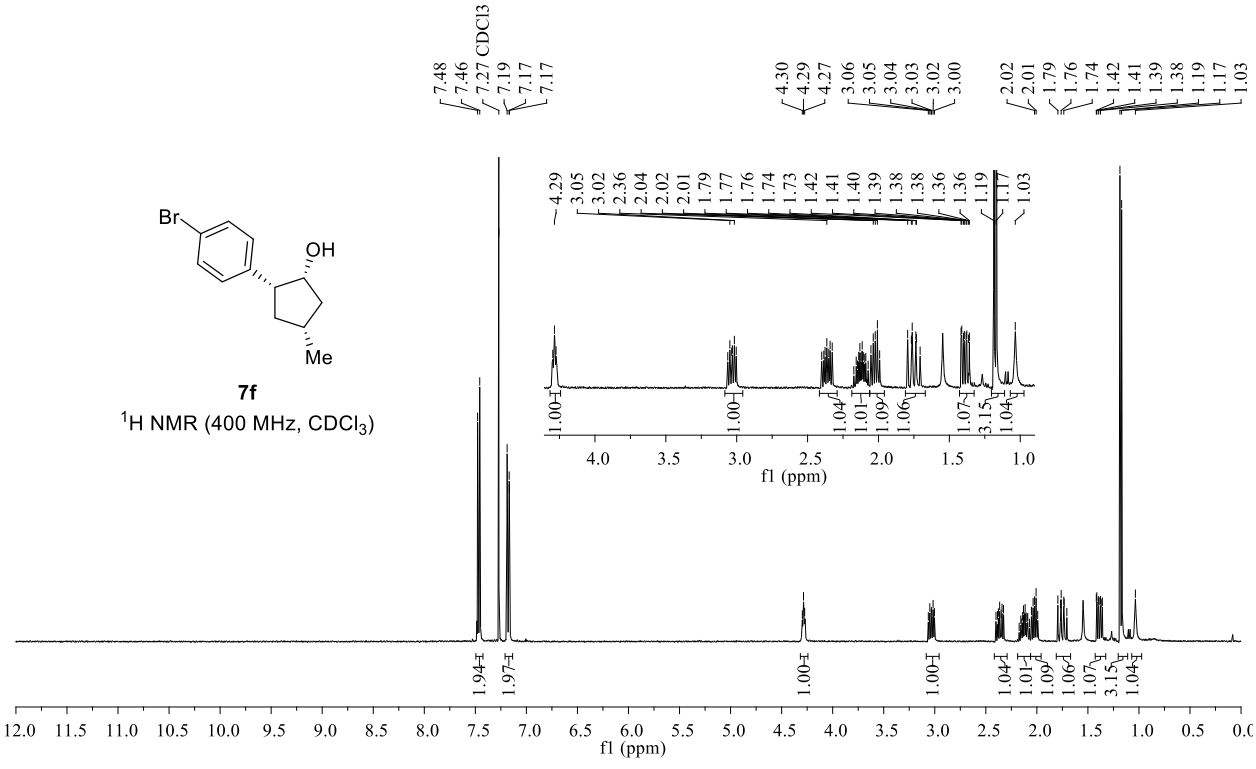

OH
Me
7d
$^{13}$C NMR (101 MHz, CDCl$_3$)
137.36
133.65
132.58
128.24
127.82
127.73
127.35
127.07
126.26
125.71
77.16 CDCl3
75.79
52.83
42.75
36.92
32.41
21.80
f1 (ppm)


Cl
OH
Me
7e
$^{1}$H NMR (400 MHz, CDCl$_3$)
7.33
7.31
7.27 CDCl3
7.24
7.22
4.30
4.29
4.28
4.27
3.07
3.05
3.03
3.02
2.36
2.04
2.03
2.01
1.77
1.74
1.42
1.41
1.40
1.38
1.36
1.19
1.17
1.02
1.00
1.05
1.01
1.11
1.13
1.19
3.15
1.05
f1 (ppm)



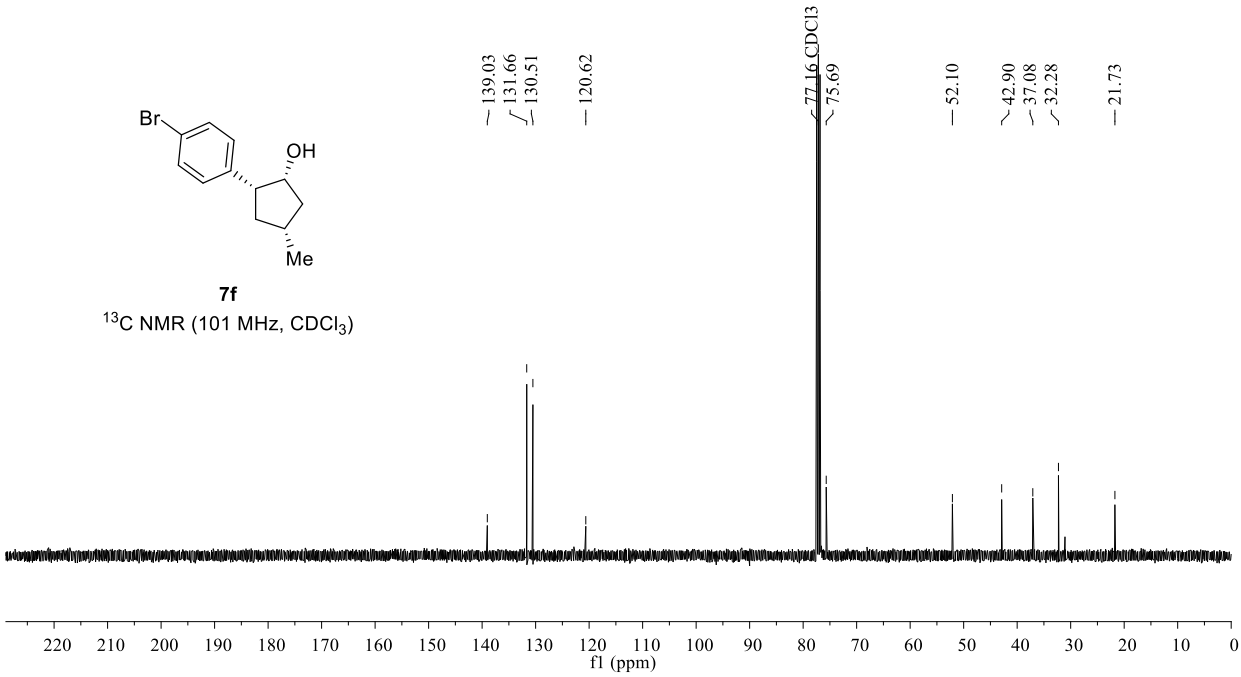

**7e**

$^{13}$C NMR (101 MHz, $CDCl_3$)



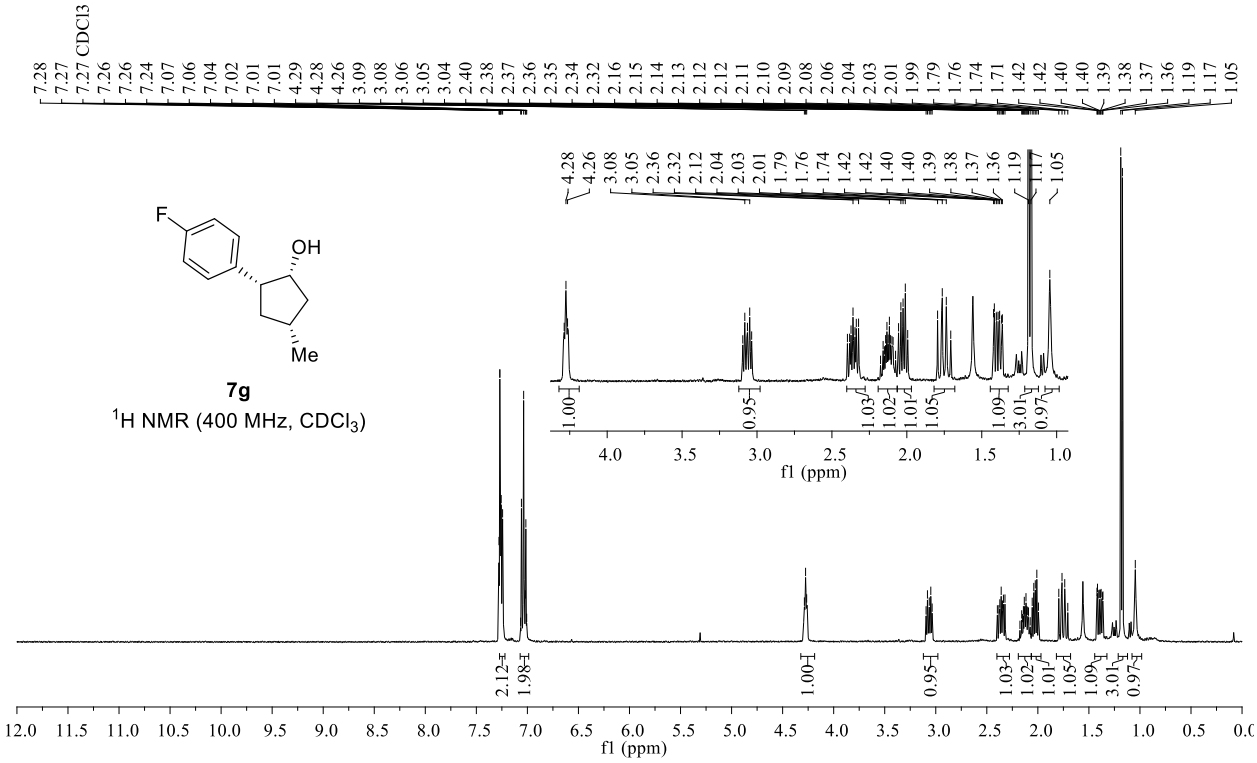

**7f**

$^{1}$H NMR (400 MHz, $CDCl_3$)



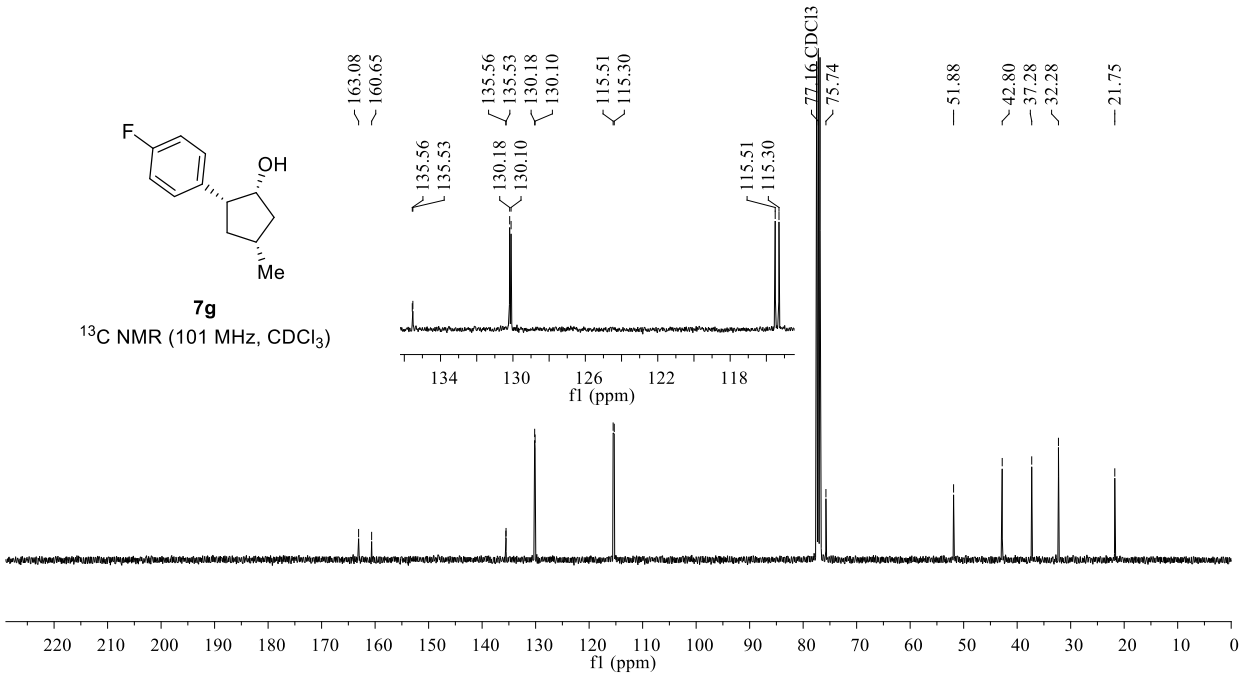

**7f**

$^{13}$C NMR (101 MHz, $CDCl_3$)



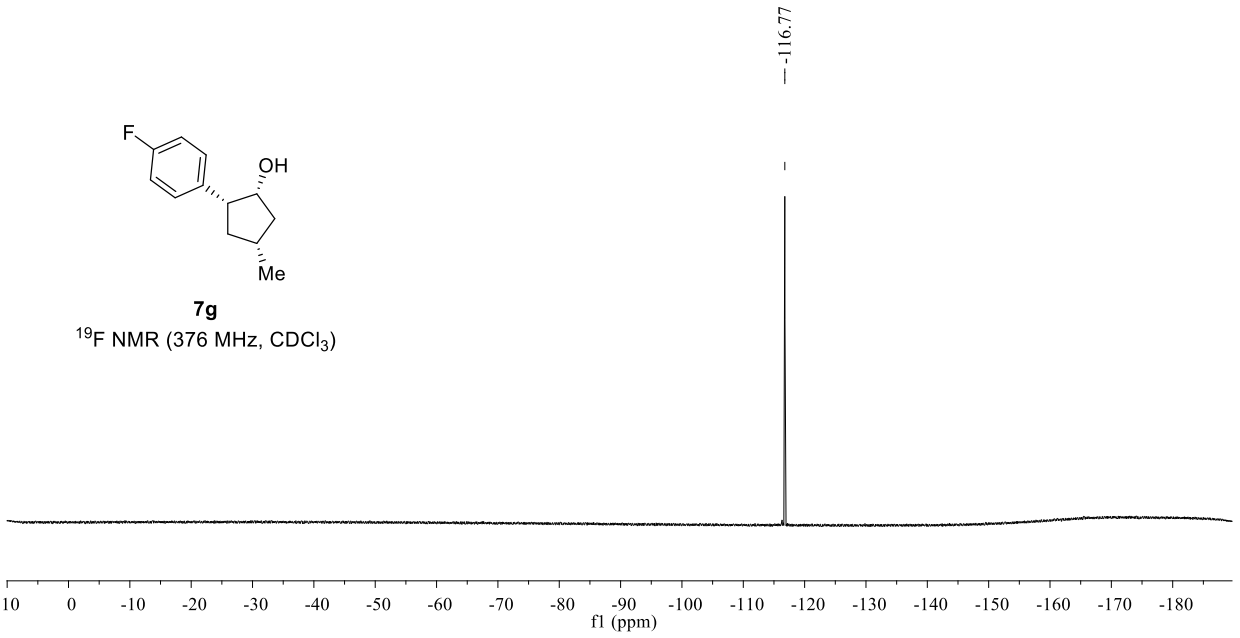

**7g**

$^{1}$H NMR (400 MHz, $CDCl_3$)



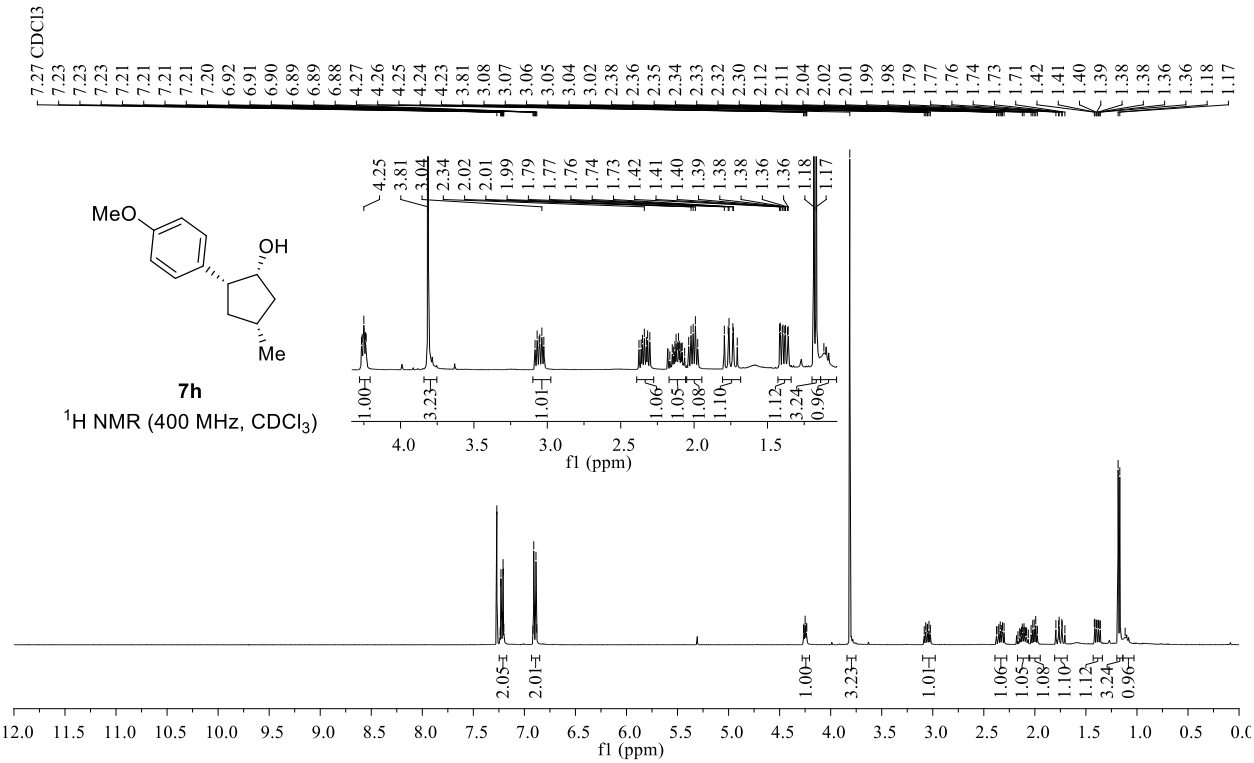

**7g**

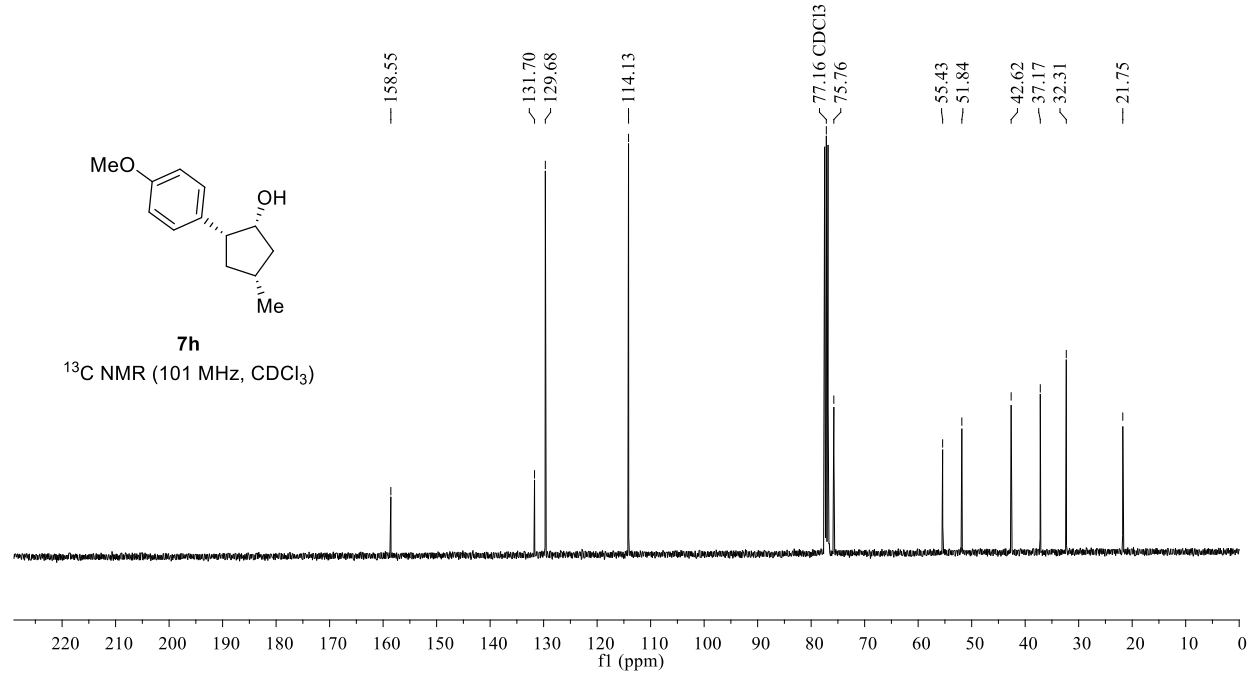
$^{13}C$ NMR (101 MHz, $CDCl_3$)

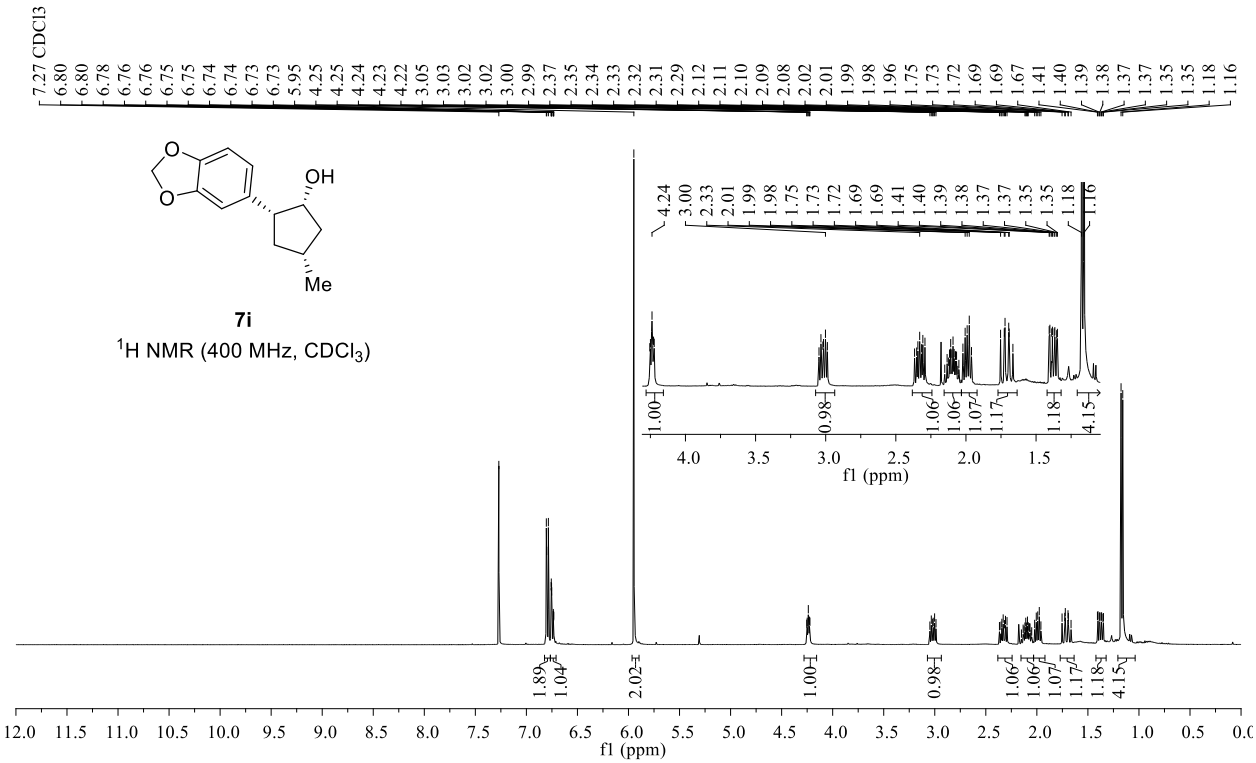


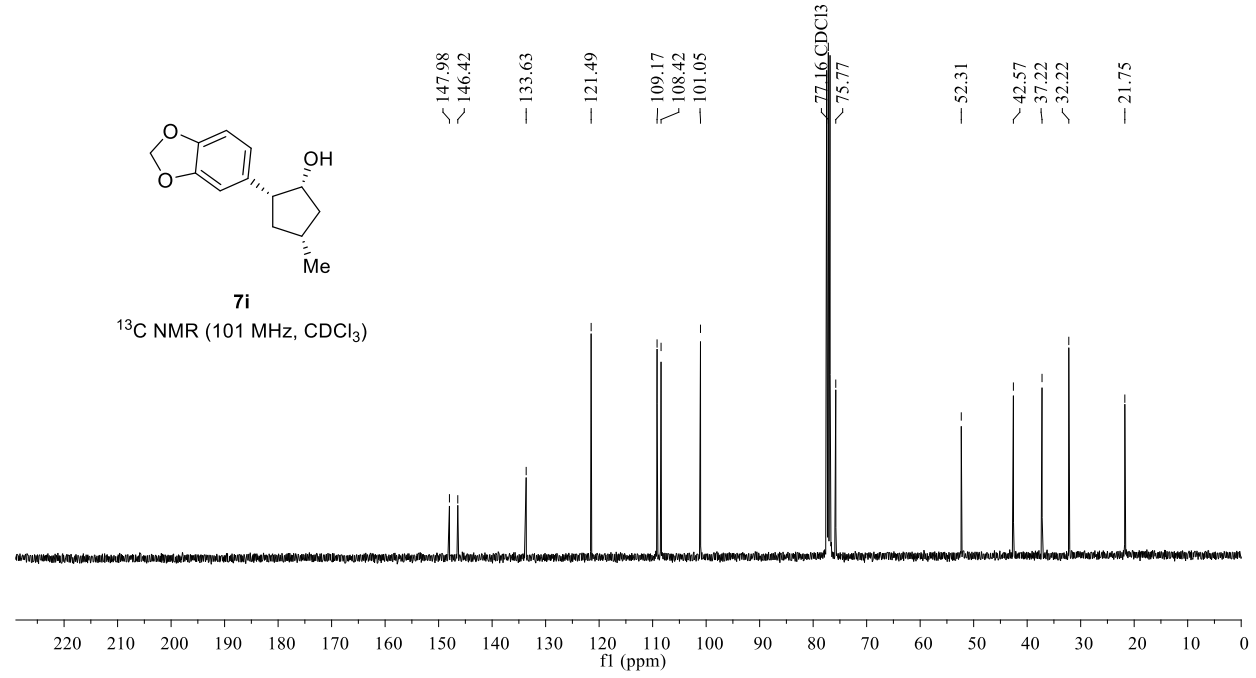

**7g**

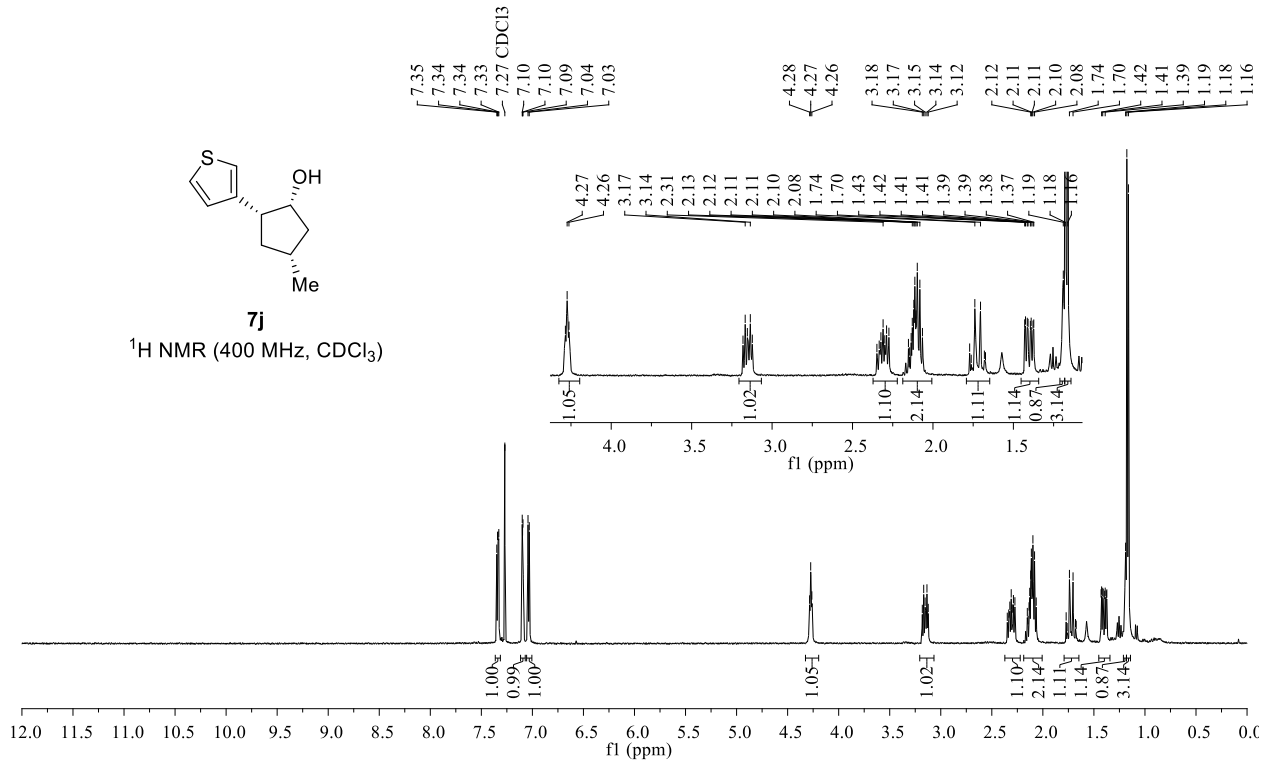
$^{19}F$ NMR (376 MHz, $CDCl_3$)

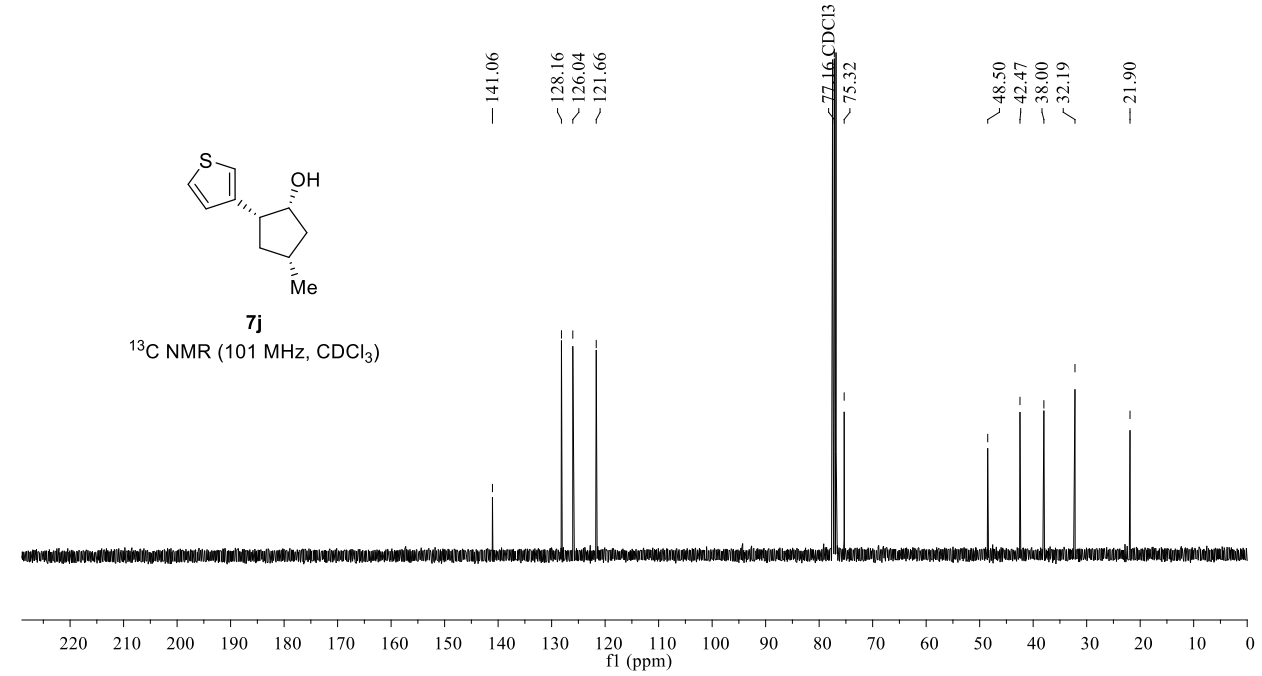

MeO
OH
Me
7h
1H NMR (400 MHz, CDCl3)
fl (ppm)

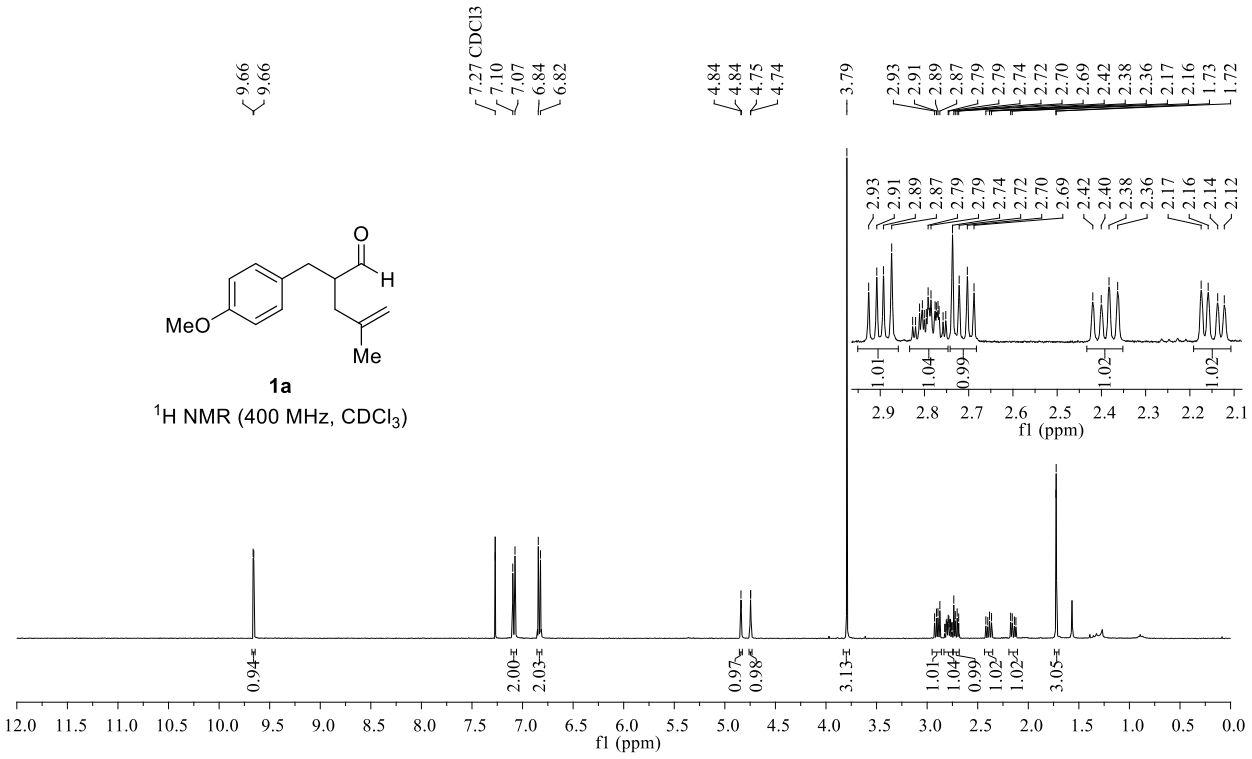

MeO
OH
Me
7h
13C NMR (101 MHz, CDCl3)
fl (ppm)

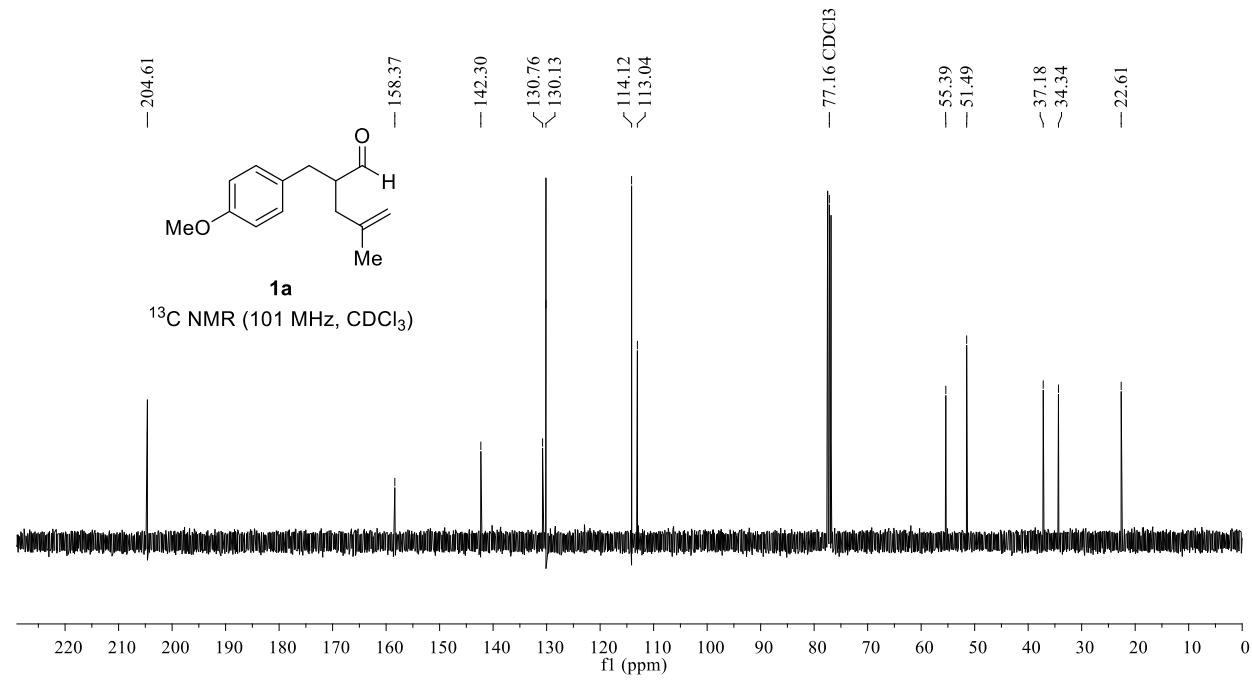

7.27 CDCl3
6.80 6.80 6.78 6.76 6.76 6.75 6.75 6.74 6.74 6.73 6.73 5.95 4.25 4.25 4.24 4.23 4.22 3.05 3.03 3.02 3.02 3.00 2.99 2.37 2.35 2.34 2.33 2.32 2.31 2.29 2.12 2.11 2.10 2.09 2.08 2.02 2.01 1.99 1.98 1.96 1.75 1.73 1.72 1.69 1.67 1.41 1.40 1.39 1.38 1.37 1.37 1.35 1.35 1.18 1.16
O
O
OH
Me
7i
1H NMR (400 MHz, CDCl3)
4.24 3.00 2.33 2.01 1.99 1.98 1.75 1.73 1.72 1.69 1.69 1.41 1.40 1.39 1.38 1.37 1.37 1.35 1.35 1.18 1.16
1.00 0.98 1.06 1.06 1.07 1.17 1.18 4.15
4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)
1.89 1.04 2.02 1.00 0.98 1.06 1.06 1.07 1.17 1.18 4.15
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

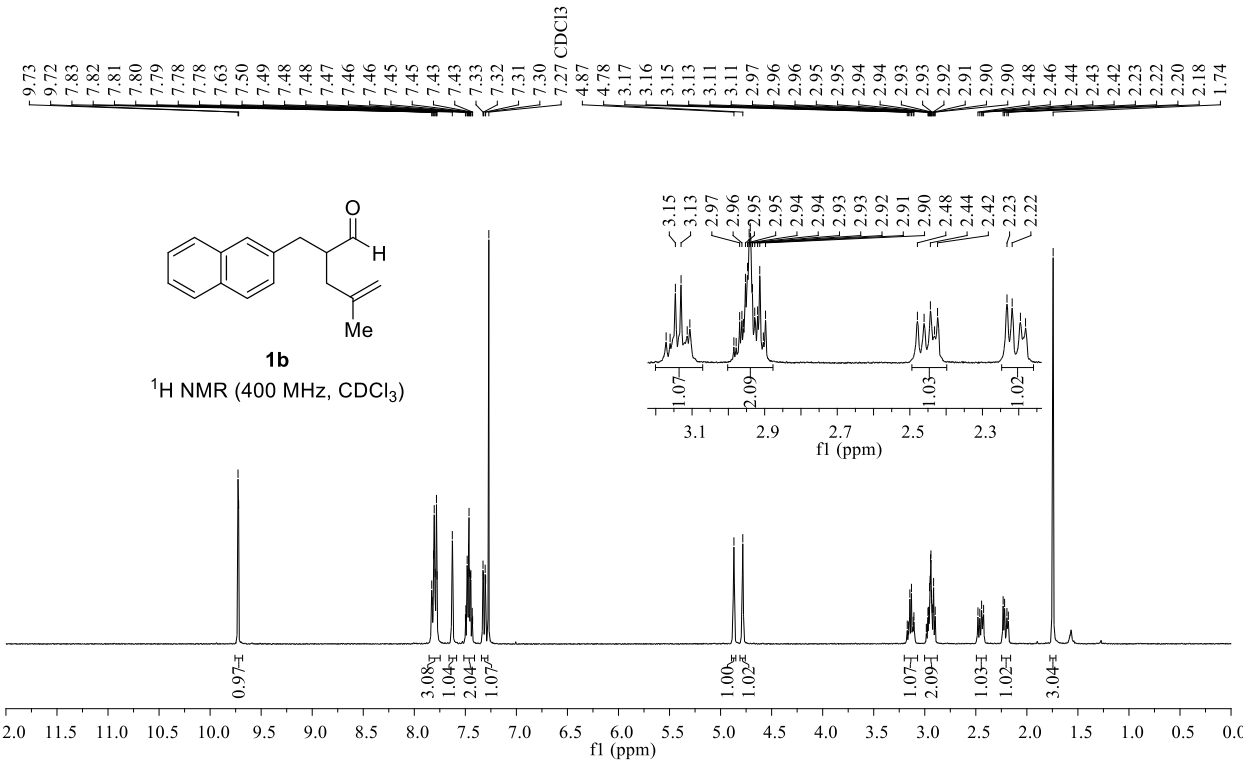

147.98
146.42
133.63
121.49
109.17
108.42
101.05
77.16 CDCl3
75.77
52.31
42.57
37.22
32.22
21.75
O
O
OH
Me
7i
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

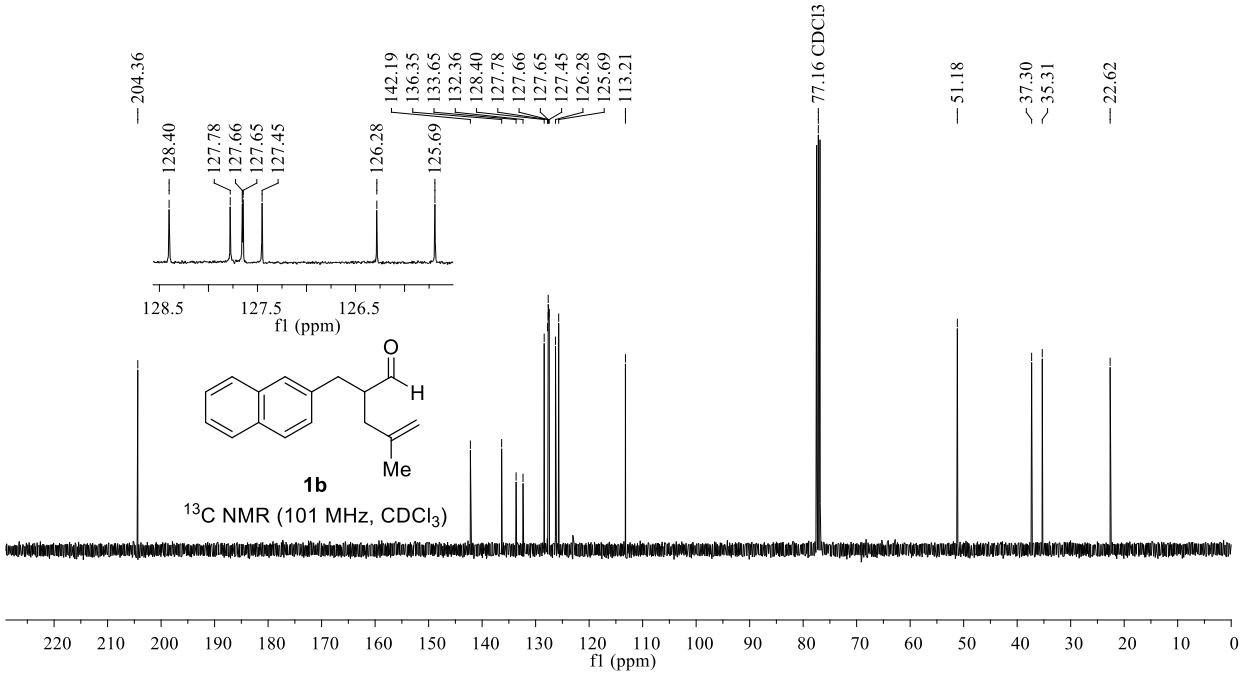

7.35
7.34
7.34
7.33
7.27 CDCl3
7.10
7.10
7.09
7.04
7.03
4.28
4.27
4.26
3.18
3.17
3.15
3.14
3.12
2.12
2.11
2.11
2.10
2.08
1.74
1.70
1.42
1.41
1.39
1.19
1.18
1.16
S
OH
Me
7j
1H NMR (400 MHz, CDCl3)
1.00
0.99
1.00
1.05
1.02
1.10
2.14
1.11
1.14
0.87
3.14
f1 (ppm)

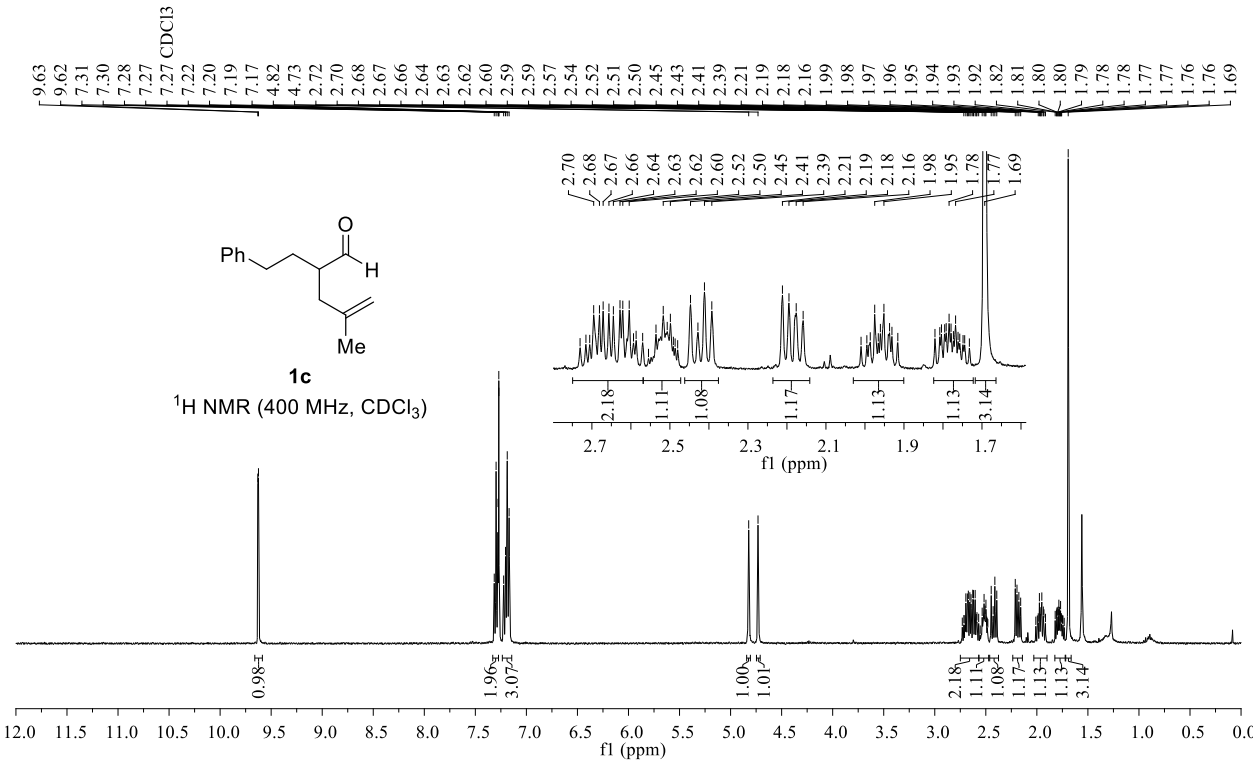

141.06
128.16
126.04
121.66
77.16 CDCl3
75.32
48.50
42.47
38.00
32.19
21.90
S
OH
Me
7j
13C NMR (101 MHz, CDCl3)
f1 (ppm)

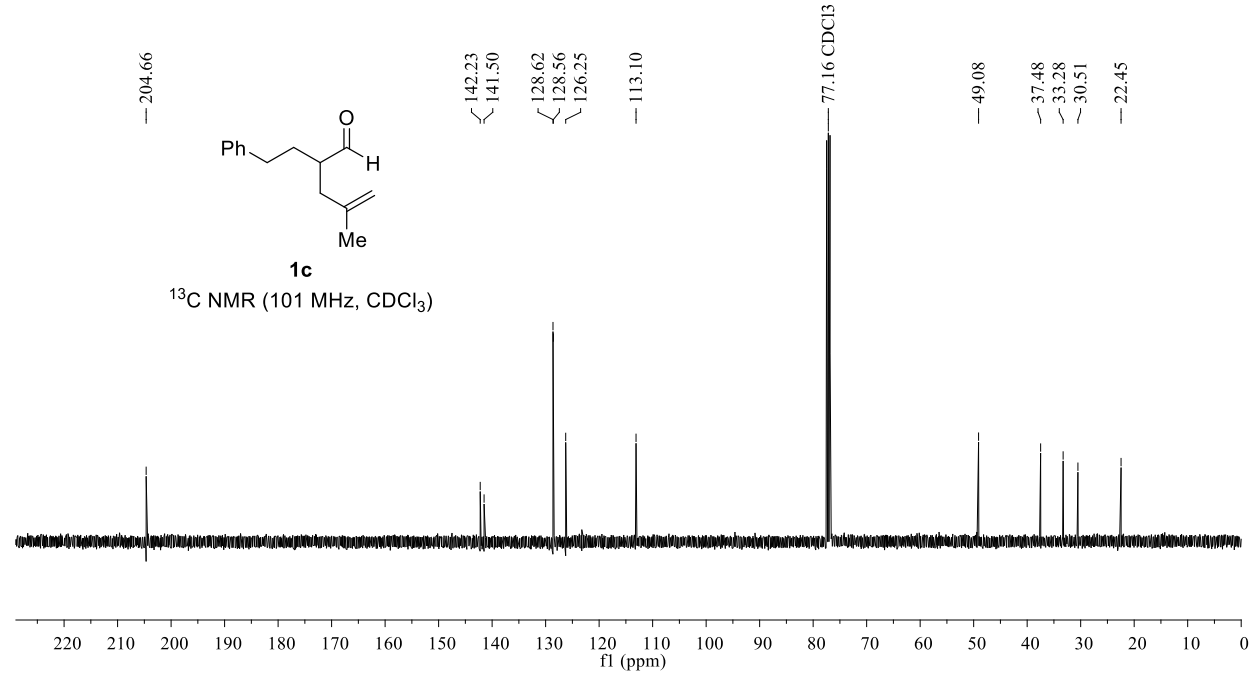

9.66
9.66
7.27 CDCl3
7.10
7.07
6.84
6.82
4.84
4.84
4.75
4.74
3.79
2.93
2.91
2.89
2.87
2.79
2.79
2.74
2.72
2.70
2.69
2.42
2.38
2.36
2.17
2.16
1.73
1.72
2.40
2.14
2.12
O
H
MeO
Me
1a
1H NMR (400 MHz, CDCl3)
1.01
1.04
0.99
1.02
1.02
0.94
2.00
2.03
0.97
0.98
3.13
1.01
1.04
0.99
1.02
1.02
3.05
fl (ppm)

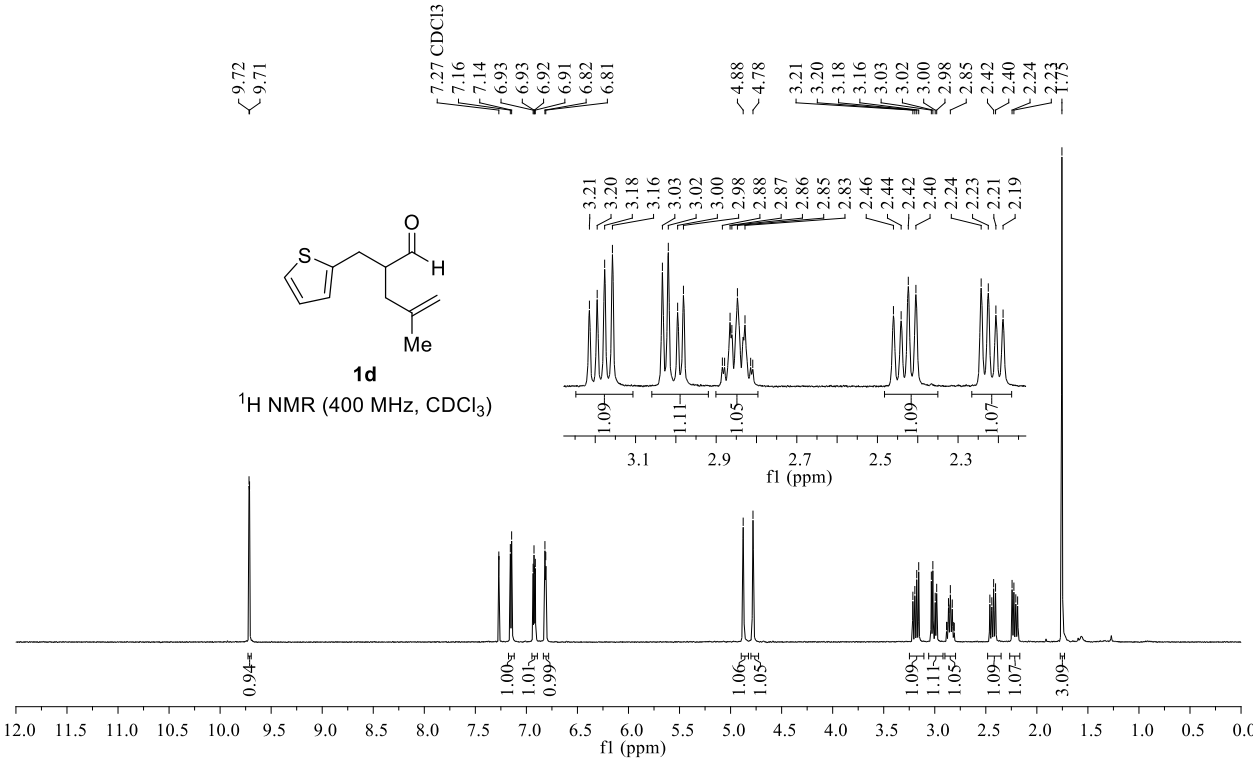

204.61
158.37
142.30
130.76
130.13
114.12
113.04
77.16 CDCl3
55.39
51.49
37.18
34.34
22.61
O
H
MeO
Me
1a
13C NMR (101 MHz, CDCl3)
fl (ppm)

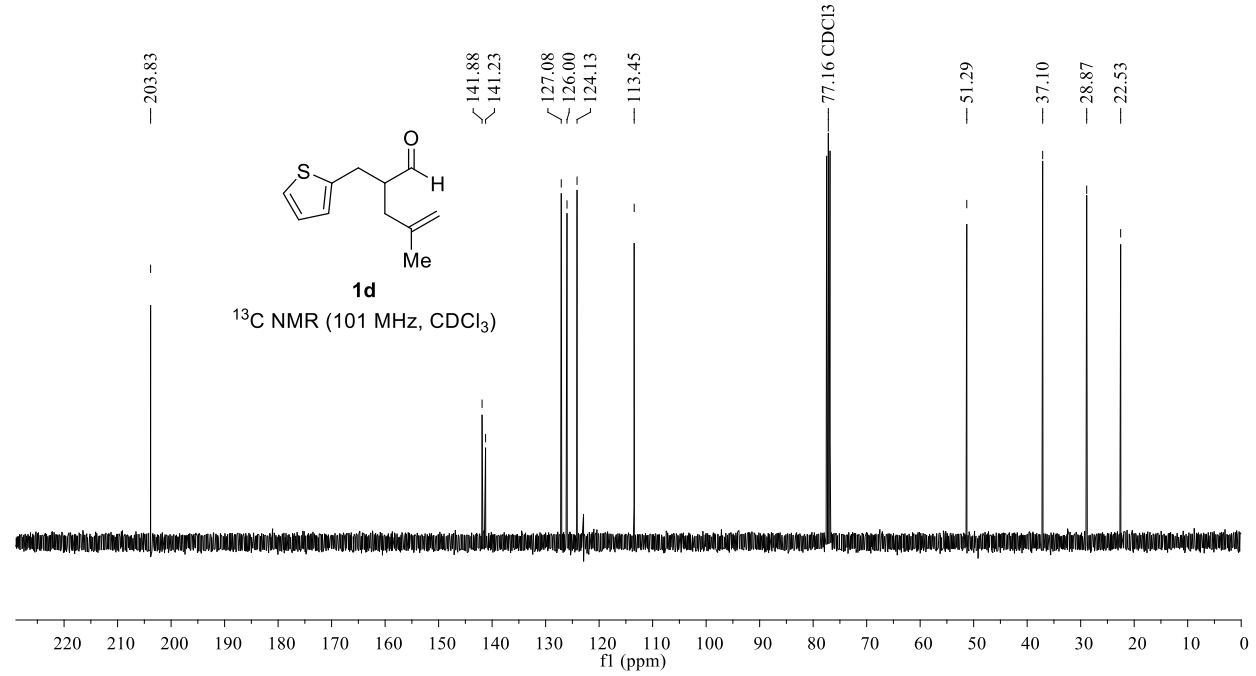

9.73 9.72 7.83 7.82 7.81 7.80 7.79 7.78 7.78 7.63 7.50 7.49 7.48 7.48 7.47 7.46 7.46 7.45 7.45 7.43 7.43 7.33 7.32 7.31 7.30 7.27 CDCl3 4.87 4.78 3.17 3.16 3.15 3.13 3.11 3.11 2.97 2.96 2.96 2.95 2.95 2.94 2.94 2.93 2.93 2.92 2.91 2.90 2.90 2.48 2.46 2.44 2.43 2.42 2.23 2.22 2.20 2.18 1.74
O
H
Me
1b
1H NMR (400 MHz, CDCl3)
3.15 3.13 2.97 2.96 2.95 2.95 2.94 2.94 2.93 2.93 2.92 2.91 2.90 2.48 2.44 2.42 2.23 2.22
1.07 2.09 1.03 1.02
3.1 2.9 2.7 2.5 2.3
f1 (ppm)
0.97 3.08 1.04 2.04 1.07 1.00 1.02 1.07 2.09 1.03 1.02 3.04
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

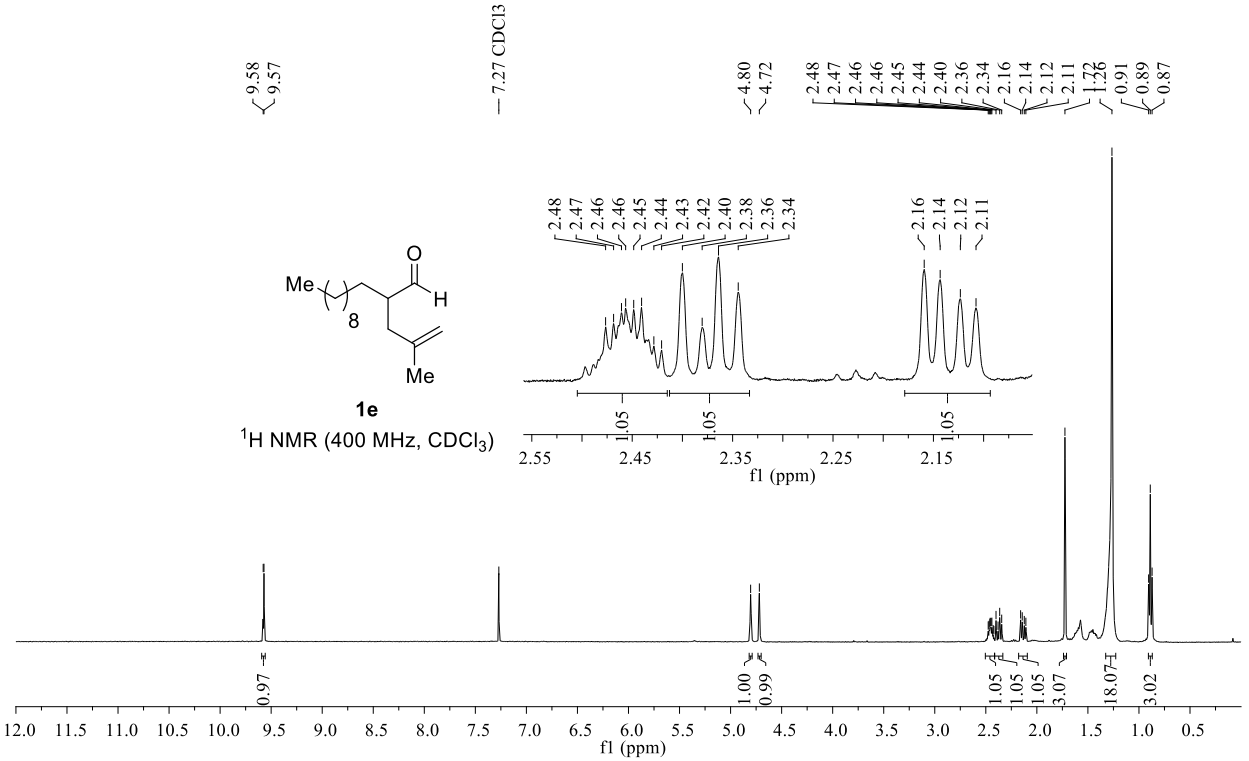

204.36 128.40 127.78 127.66 127.65 127.45 126.28 125.69 142.19 136.35 133.65 132.36 128.40 127.78 127.66 127.65 127.45 126.28 125.69 113.21 77.16 CDCl3 51.18 37.30 35.31 22.62
128.5 127.5 126.5
f1 (ppm)
O
H
Me
1b
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

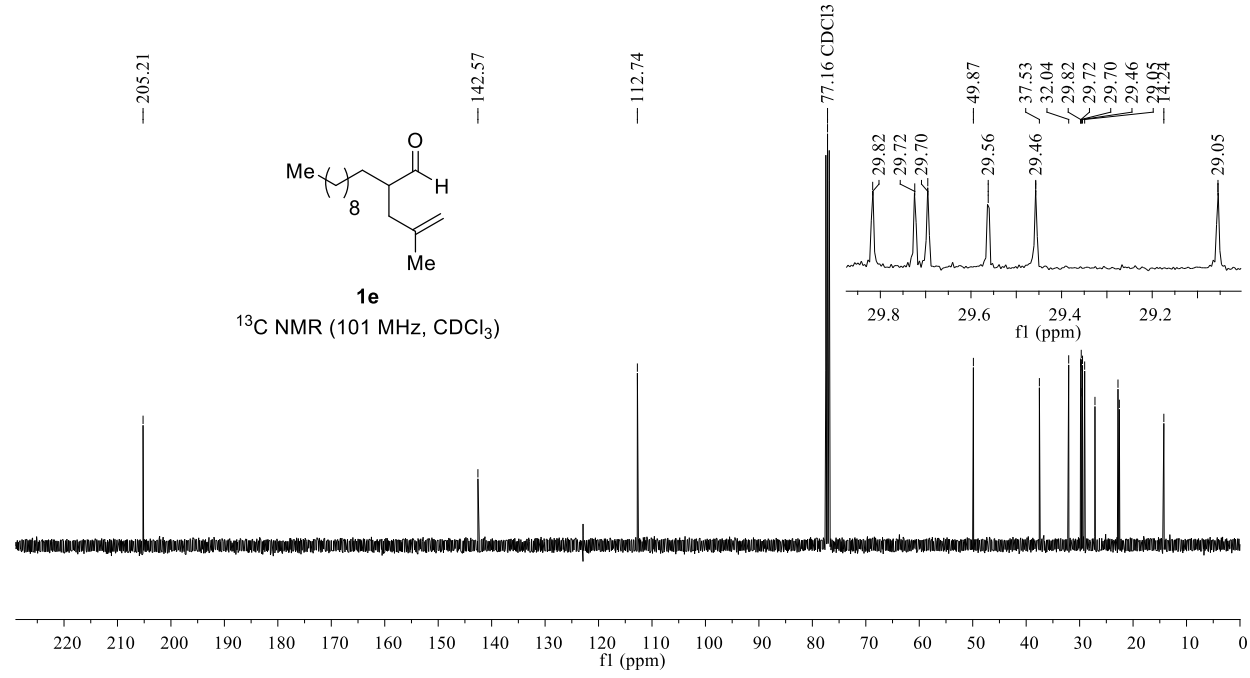

9.63 9.62 7.31 7.30 7.28 7.27 7.27 CDCl3 7.22 7.20 7.19 7.17 4.82 4.73 2.72 2.70 2.68 2.67 2.66 2.64 2.63 2.62 2.60 2.59 2.59 2.57 2.54 2.52 2.51 2.50 2.45 2.43 2.41 2.39 2.21 2.19 2.18 2.16 1.99 1.98 1.97 1.96 1.95 1.94 1.93 1.92 1.82 1.81 1.80 1.80 1.79 1.78 1.78 1.77 1.77 1.76 1.76 1.69
2.70 2.68 2.67 2.66 2.64 2.63 2.62 2.60 2.52 2.50 2.45 2.41 2.39 2.21 2.19 2.18 2.16 1.98 1.95 1.78 1.77 1.69
2.18 1.11 1.08 1.17 1.13 1.13 3.14
2.7 2.5 2.3 2.1 1.9 1.7
f1 (ppm)
Ph
O
H
Me
1c
$^1$H NMR (400 MHz, $CDCl_3$)
0.98 1.96 3.07 1.00 1.01 2.18 1.11 1.08 1.17 1.13 1.13 3.14
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

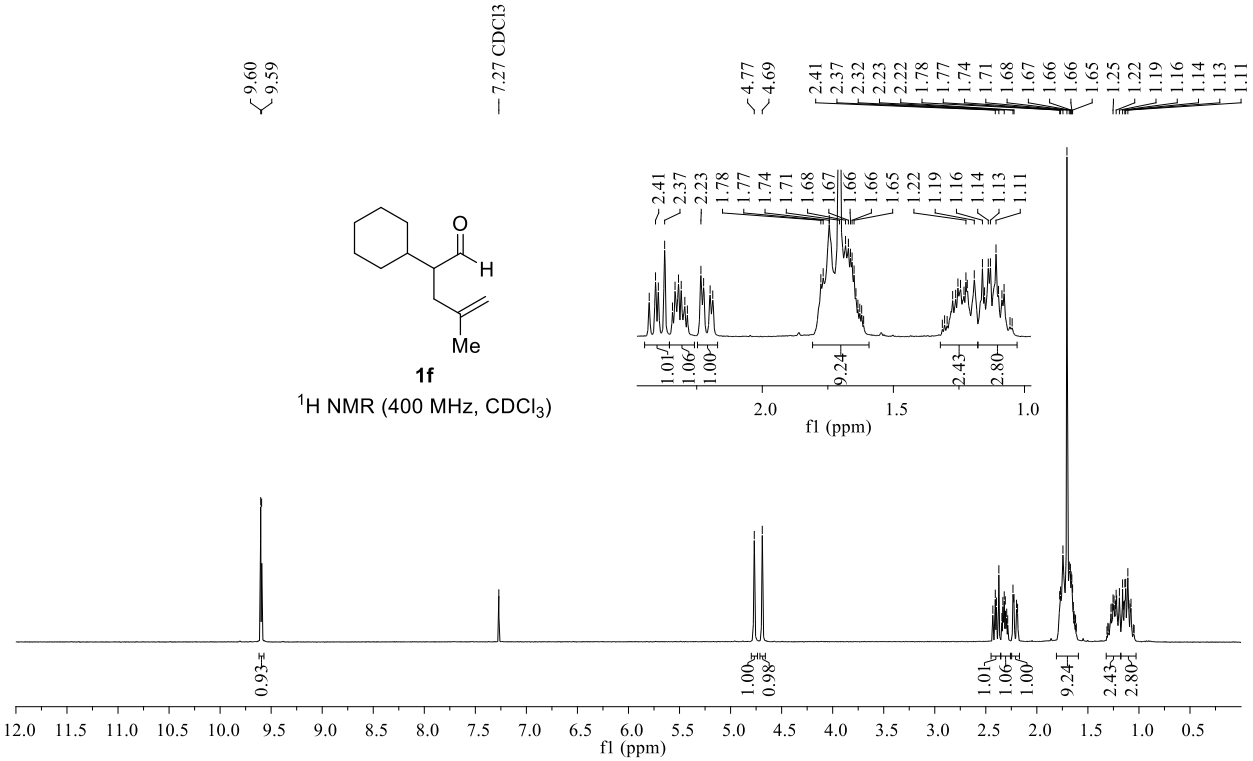

204.66
142.23 141.50 128.62 128.56 126.25 113.10 77.16 CDCl3 49.08 37.48 33.28 30.51 22.45
Ph
O
H
Me
1c
$^{13}$C NMR (101 MHz, $CDCl_3$)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

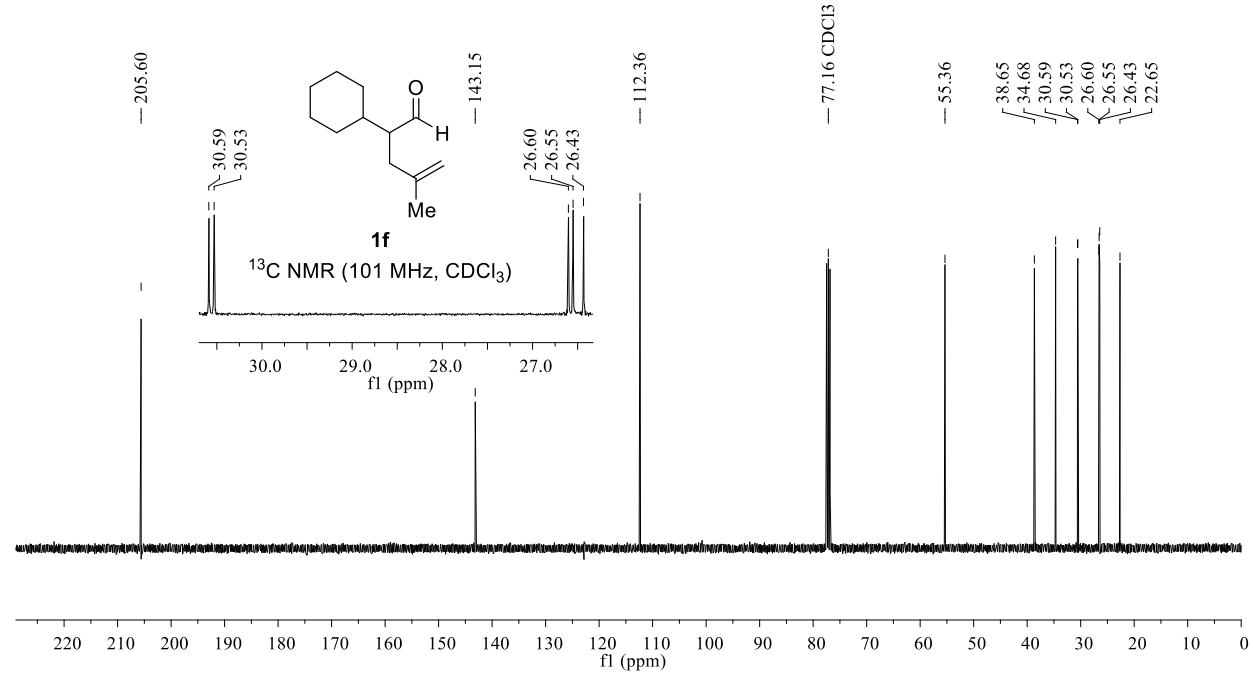

9.72
9.71
7.27 CDCl3
7.16
7.14
6.93
6.93
6.92
6.91
6.82
6.81
4.88
4.78
3.21
3.20
3.18
3.16
3.03
3.02
3.00
2.98
2.85
2.42
2.40
2.24
2.23
1.75
O
S
H
Me
1d
1H NMR (400 MHz, CDCl3)
0.94
1.00
1.01
0.99
1.06
1.05
1.09
1.11
1.05
1.09
1.07
3.09
f1 (ppm)

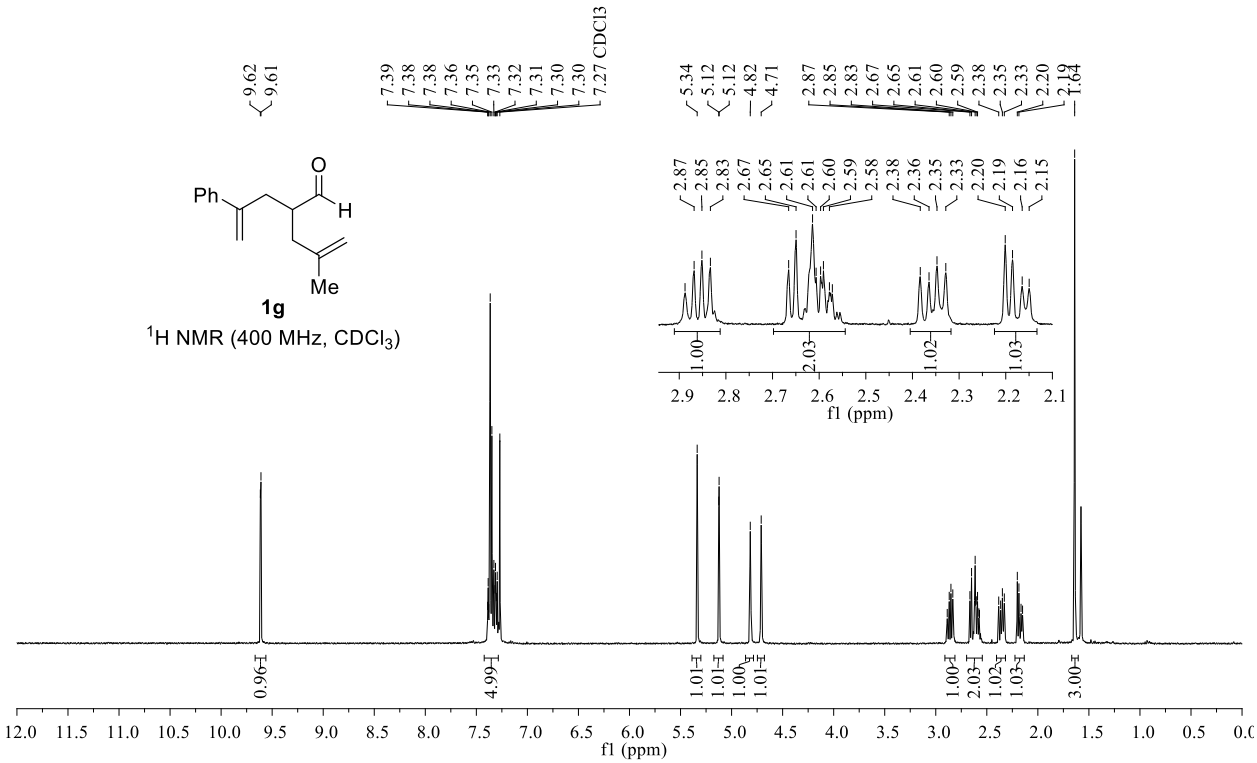

203.83
141.88
141.23
127.08
126.00
124.13
113.45
77.16 CDCl3
51.29
37.10
28.87
22.53
O
S
H
Me
1d
13C NMR (101 MHz, CDCl3)
f1 (ppm)

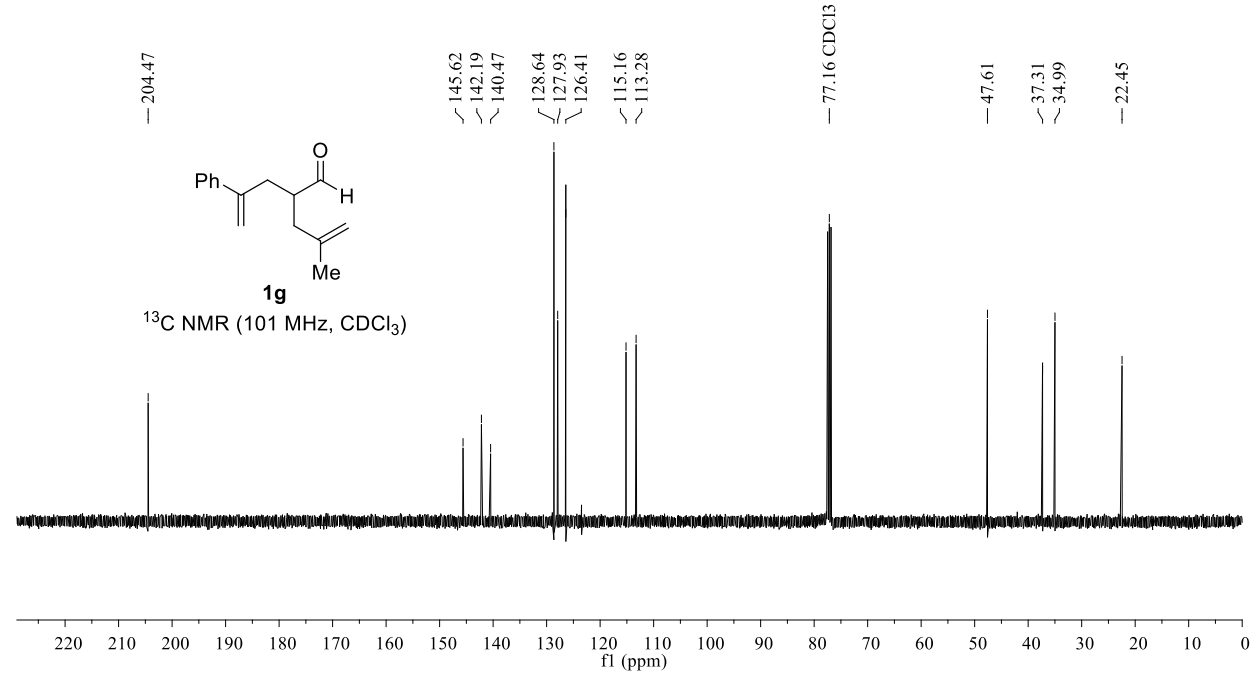

9.58
9.57
7.27 CDCl3
4.80
4.72
2.48
2.47
2.46
2.46
2.45
2.44
2.40
2.36
2.34
2.16
2.14
2.12
2.11
1.72
1.26
0.91
0.89
0.87
Me
8
O
H
Me
1e
1H NMR (400 MHz, CDCl3)
1.05
1.05
1.05
2.55
2.45
2.35
2.25
2.15
f1 (ppm)
0.97
1.00
0.99
1.05
1.05
1.05
3.07
18.07
3.02
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

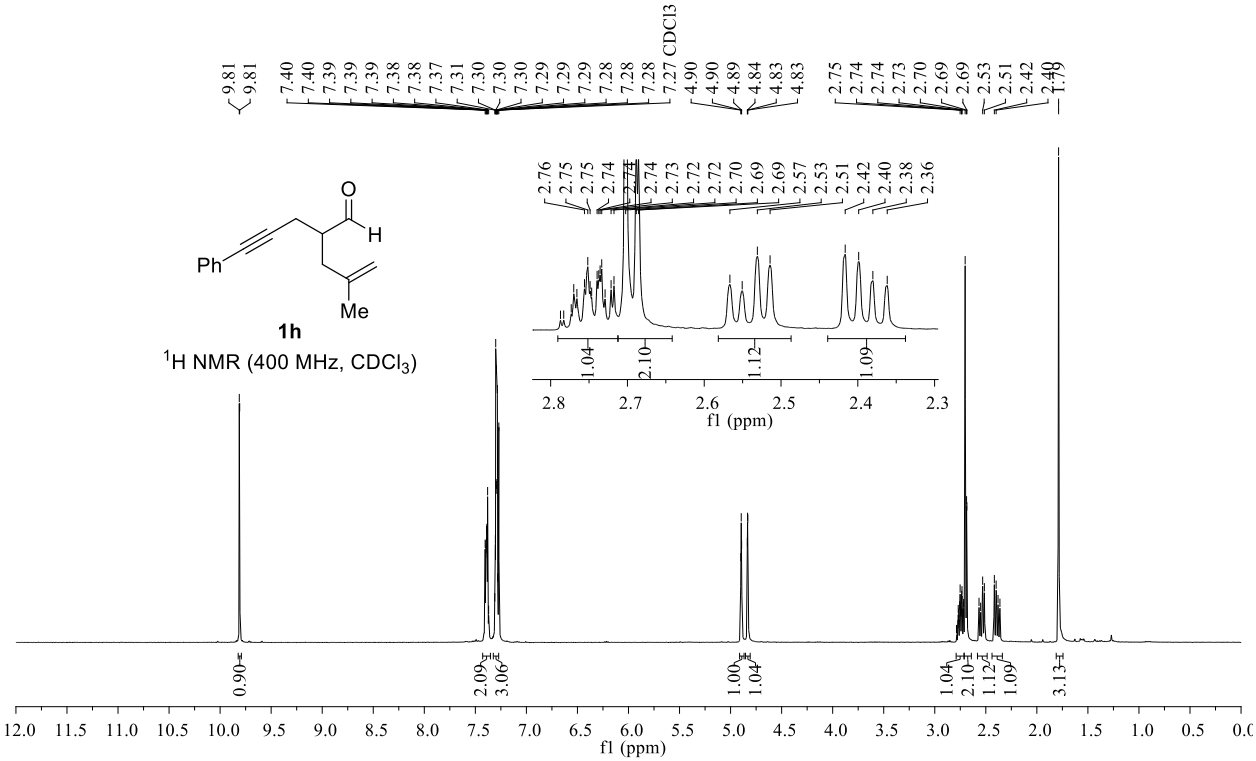

205.21
142.57
112.74
77.16 CDCl3
49.87
37.53
32.04
29.82
29.72
29.70
29.46
29.05
14.24
Me
8
O
H
Me
1e
13C NMR (101 MHz, CDCl3)
29.8
29.6
29.4
29.2
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

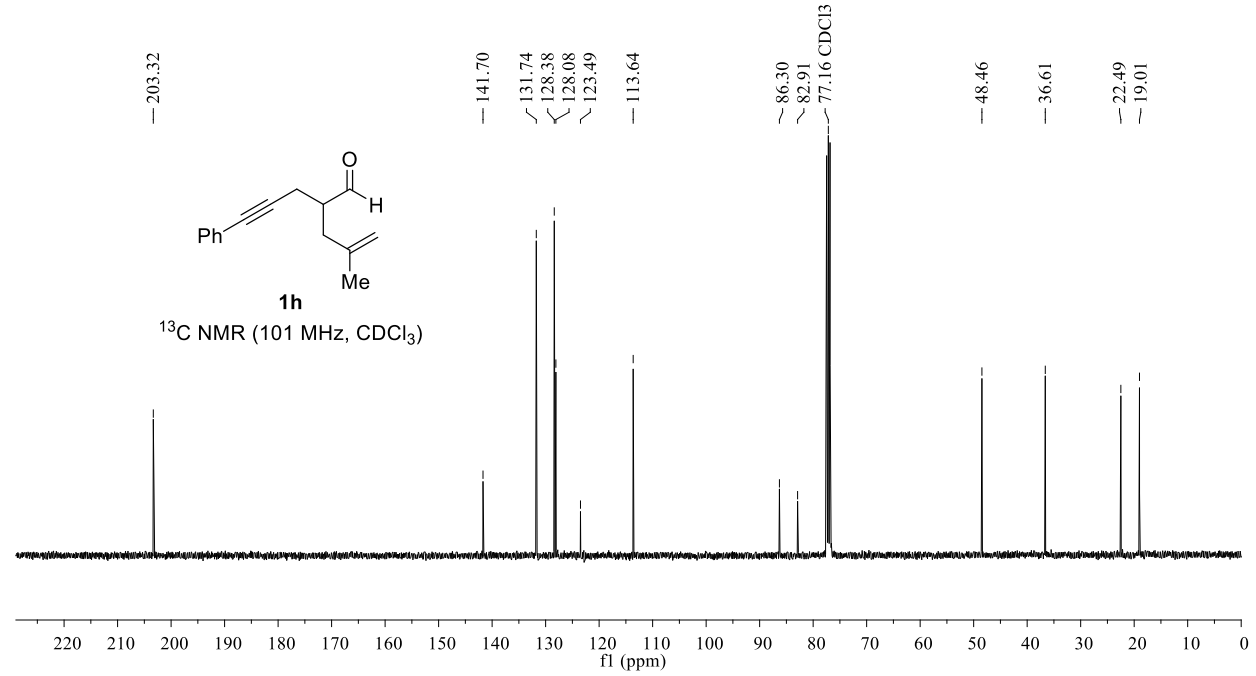

9.60
9.59
7.27 CDCl3
4.77
4.69
2.41
2.37
2.32
2.23
2.22
1.78
1.77
1.74
1.71
1.68
1.67
1.66
1.65
1.25
1.22
1.19
1.16
1.14
1.13
1.11
O
H
Me
1f
1H NMR (400 MHz, CDCl3)
1.01
1.06
1.00
9.24
2.43
2.80
f1 (ppm)
0.93
1.00
0.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

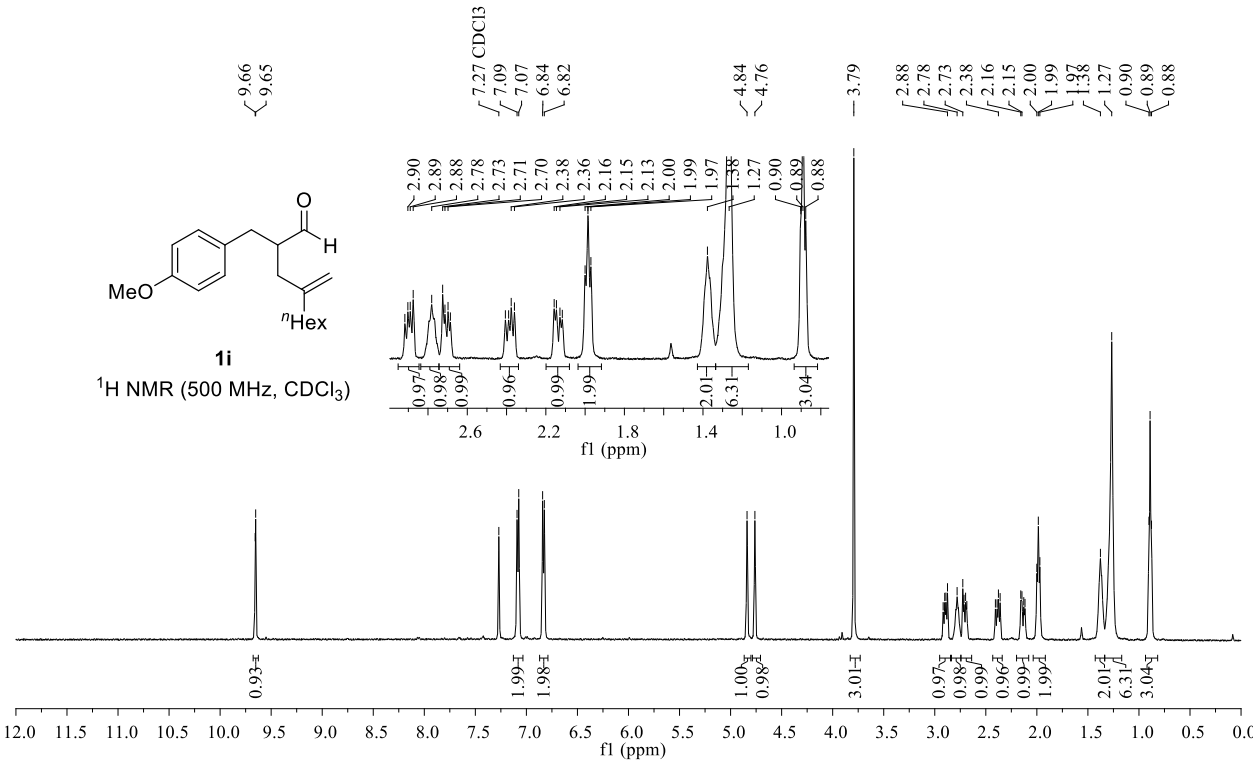

205.60
143.15
112.36
77.16 CDCl3
55.36
38.65
34.68
30.59
30.53
26.60
26.55
26.43
22.65
30.59
30.53
26.60
26.55
26.43
O
H
Me
1f
13C NMR (101 MHz, CDCl3)
30.0 29.0 28.0 27.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

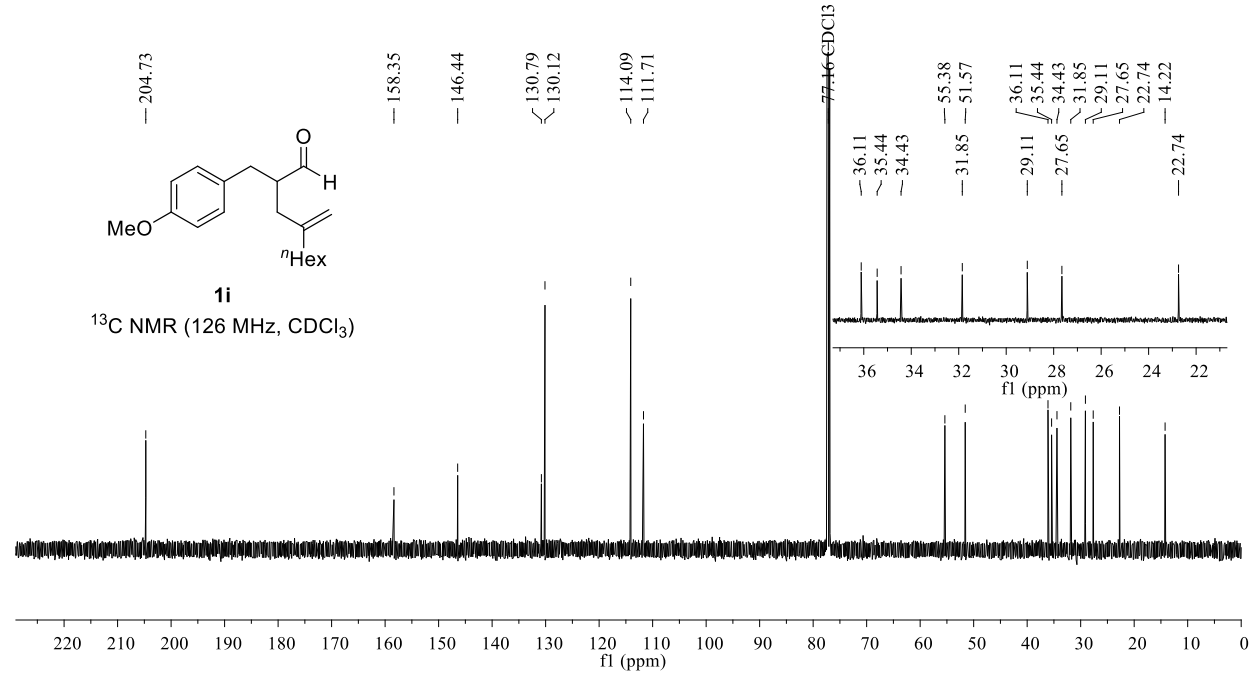

9.62
9.61
7.39
7.38
7.38
7.36
7.35
7.33
7.32
7.31
7.30
7.30
7.27 CDCl3
5.34
5.12
5.12
4.82
4.71
2.87
2.85
2.83
2.67
2.65
2.61
2.60
2.59
2.38
2.35
2.33
2.20
2.19
1.64
O
H
Ph
Me
1g
1H NMR (400 MHz, CDCl3)
2.87
2.85
2.83
2.67
2.65
2.61
2.61
2.60
2.59
2.58
2.38
2.36
2.35
2.33
2.20
2.19
2.16
2.15
1.00
2.03
1.02
1.03
2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1
f1 (ppm)
0.96
4.99
1.01
1.01
1.00
1.01
1.00
2.03
1.02
1.03
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

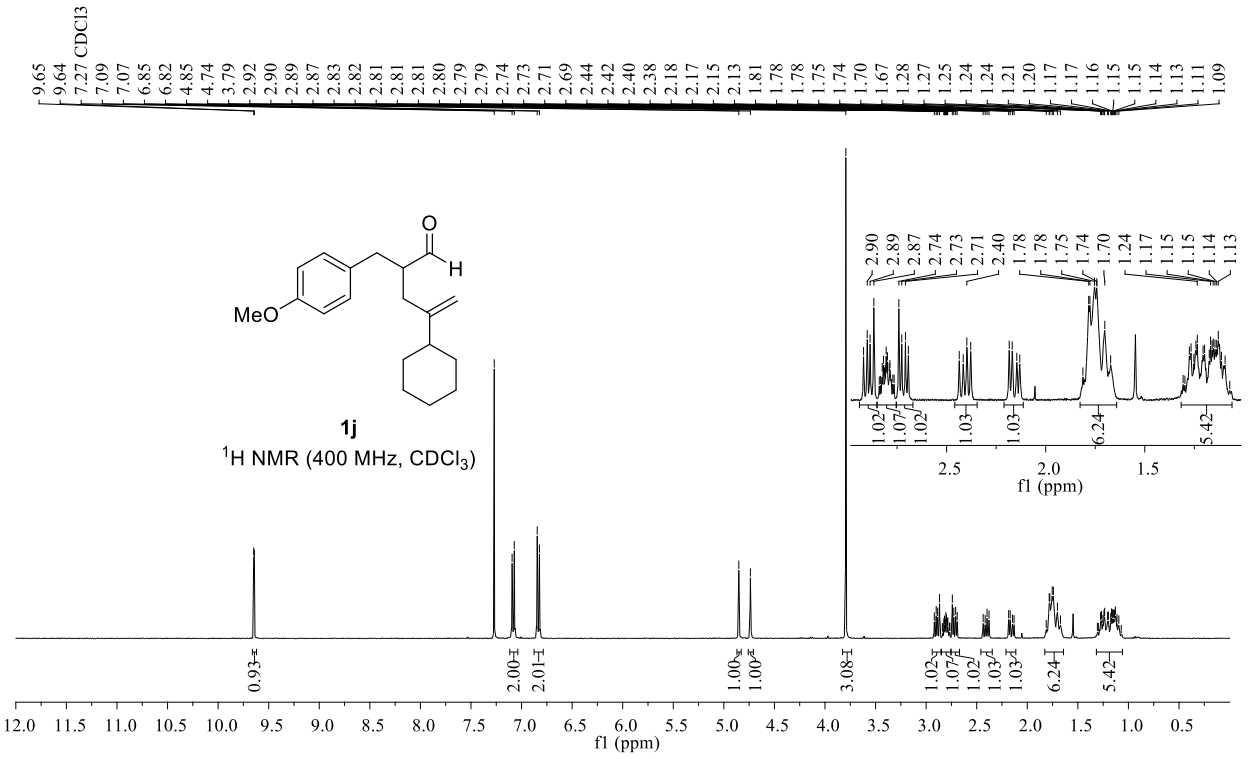

204.47
145.62
142.19
140.47
128.64
127.93
126.41
115.16
113.28
77.16 CDCl3
47.61
37.31
34.99
22.45
O
H
Ph
Me
1g
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

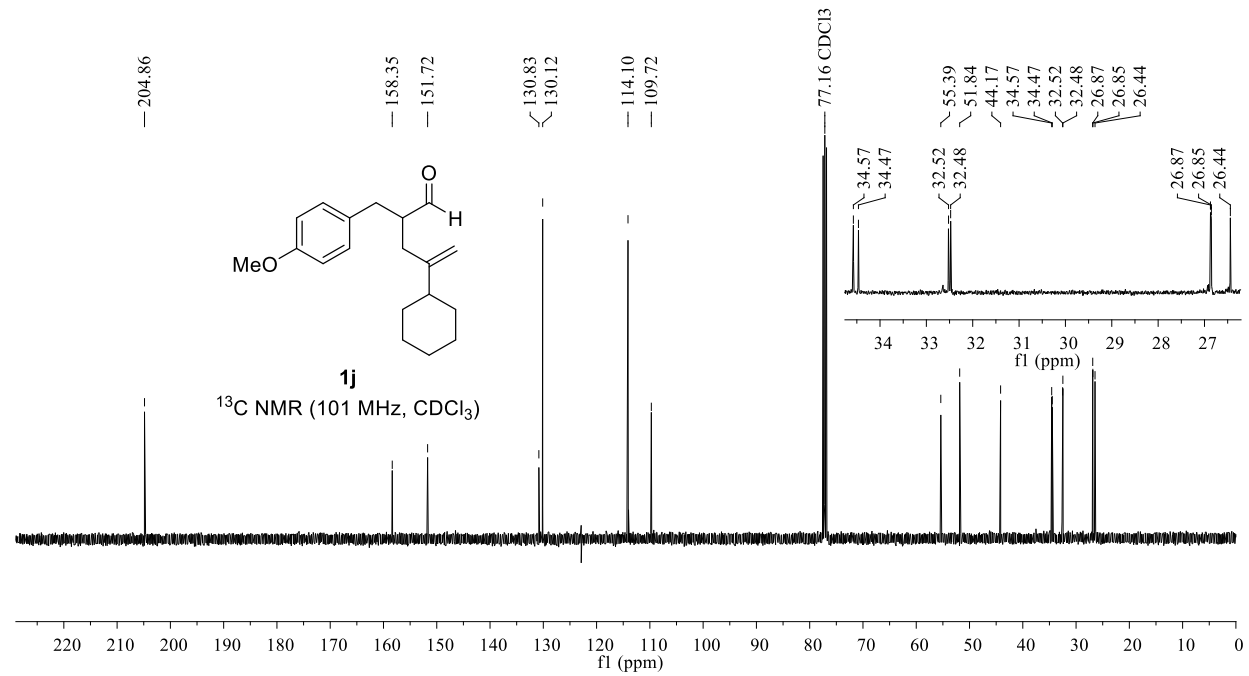

9.81
9.81
7.40
7.40
7.39
7.39
7.39
7.38
7.38
7.37
7.31
7.30
7.30
7.30
7.29
7.29
7.29
7.28
7.28
7.28
7.27 CDCl3
4.90
4.90
4.89
4.84
4.83
4.83
2.75
2.74
2.74
2.73
2.70
2.69
2.69
2.53
2.51
2.42
2.40
1.79
O
H
Ph
Me
1h
1H NMR (400 MHz, CDCl3)
2.76
2.75
2.75
2.74
2.74
2.74
2.73
2.72
2.72
2.70
2.69
2.69
2.57
2.53
2.51
2.42
2.40
2.38
2.36
1.04
2.10
1.12
1.09
2.8
2.7
2.6
2.5
2.4
2.3
f1 (ppm)
0.90
2.09
3.06
1.00
1.04
1.04
2.10
1.12
1.09
3.13
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

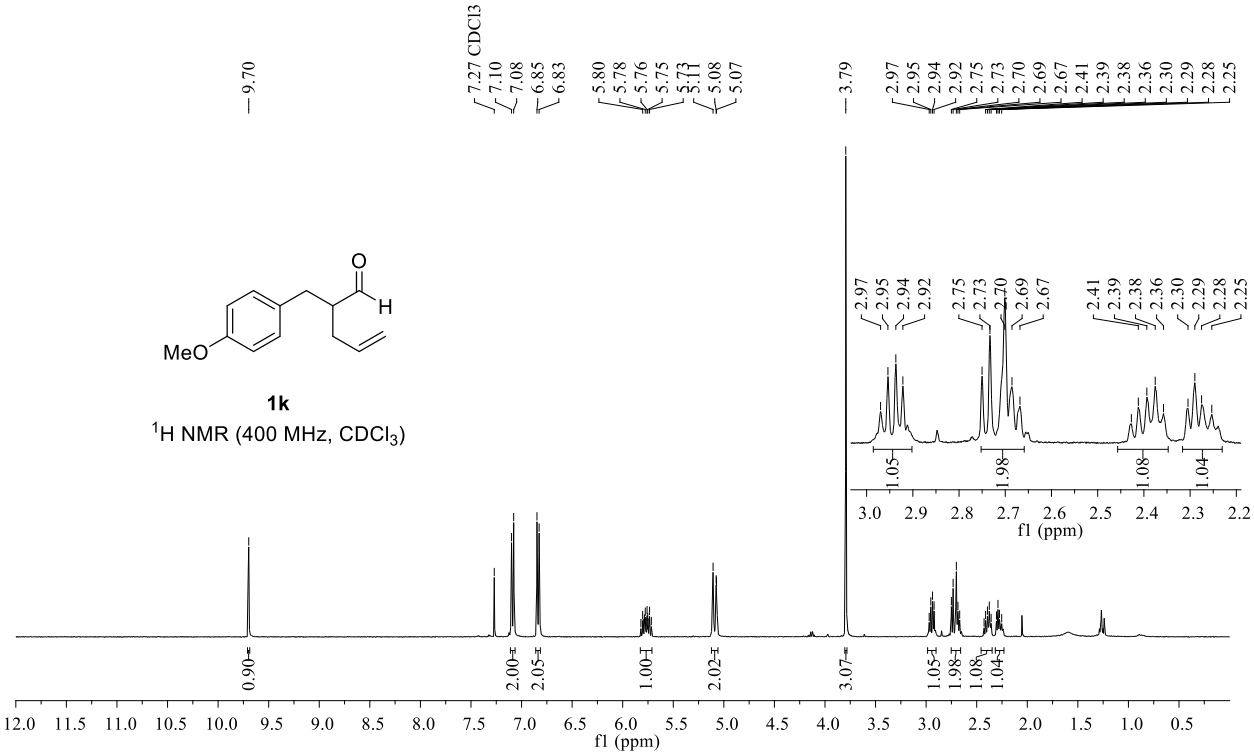

203.32
141.70
131.74
128.38
128.08
123.49
113.64
86.30
82.91
77.16 CDCl3
48.46
36.61
22.49
19.01
O
H
Ph
Me
1h
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

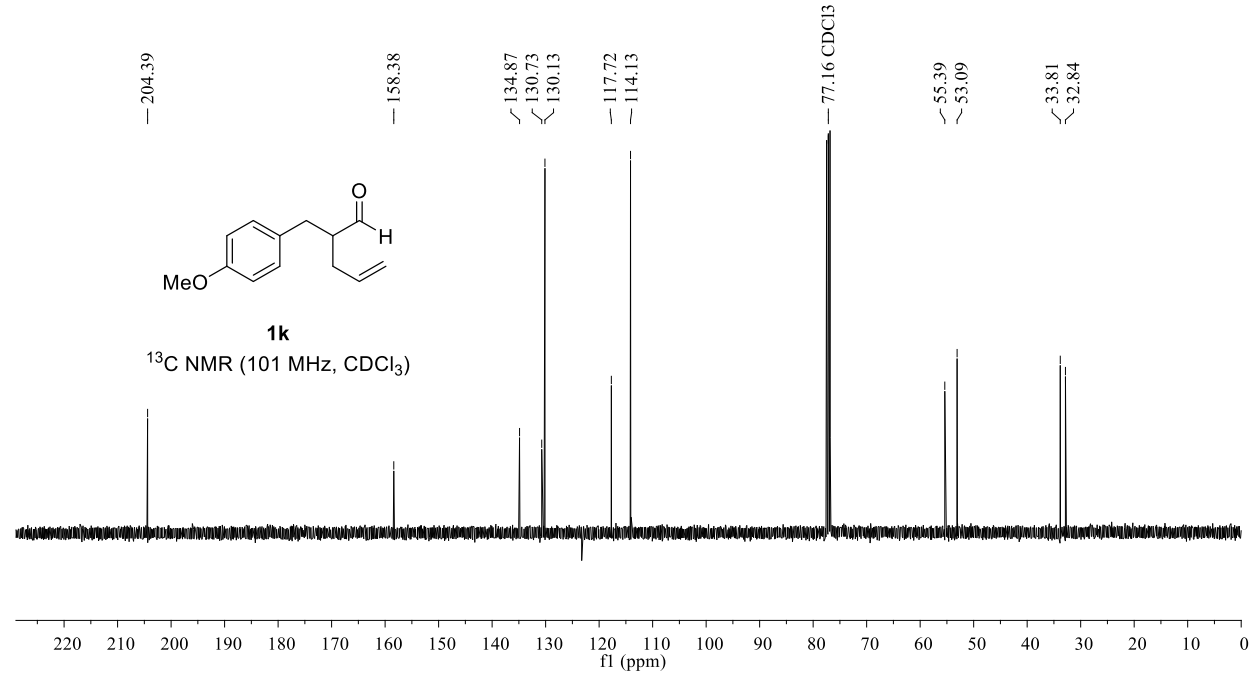

9.66
9.65
7.27 CDCl3
7.09
7.07
6.84
6.82
4.84
4.76
3.79
2.88
2.78
2.73
2.38
2.16
2.15
2.00
1.99
1.97
1.38
1.27
0.90
0.89
0.88
O
H
MeO
nHex
1i
1H NMR (500 MHz, CDCl3)
f1 (ppm)

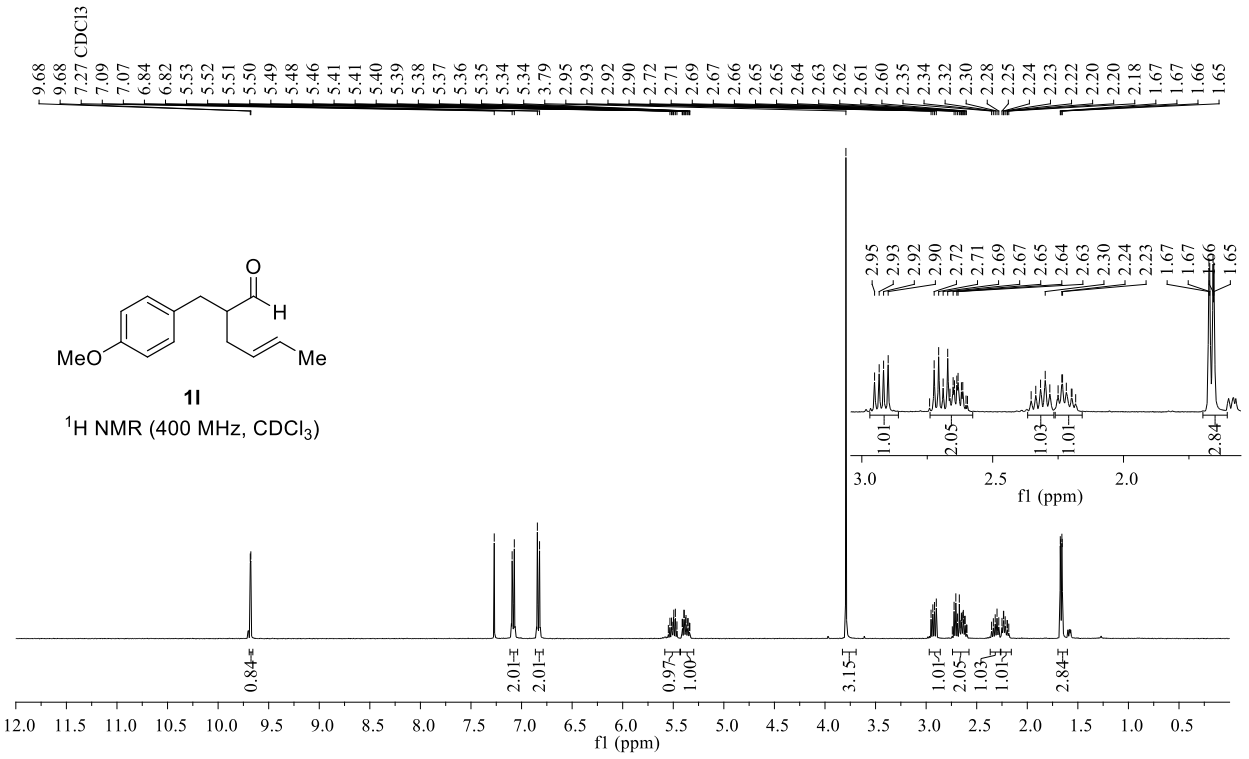

204.73
158.35
146.44
130.79
130.12
114.09
111.71
77.16 CDCl3
55.38
51.57
36.11
35.44
34.43
31.85
29.11
27.65
22.74
14.22
O
H
MeO
nHex
1i
13C NMR (126 MHz, CDCl3)
f1 (ppm)

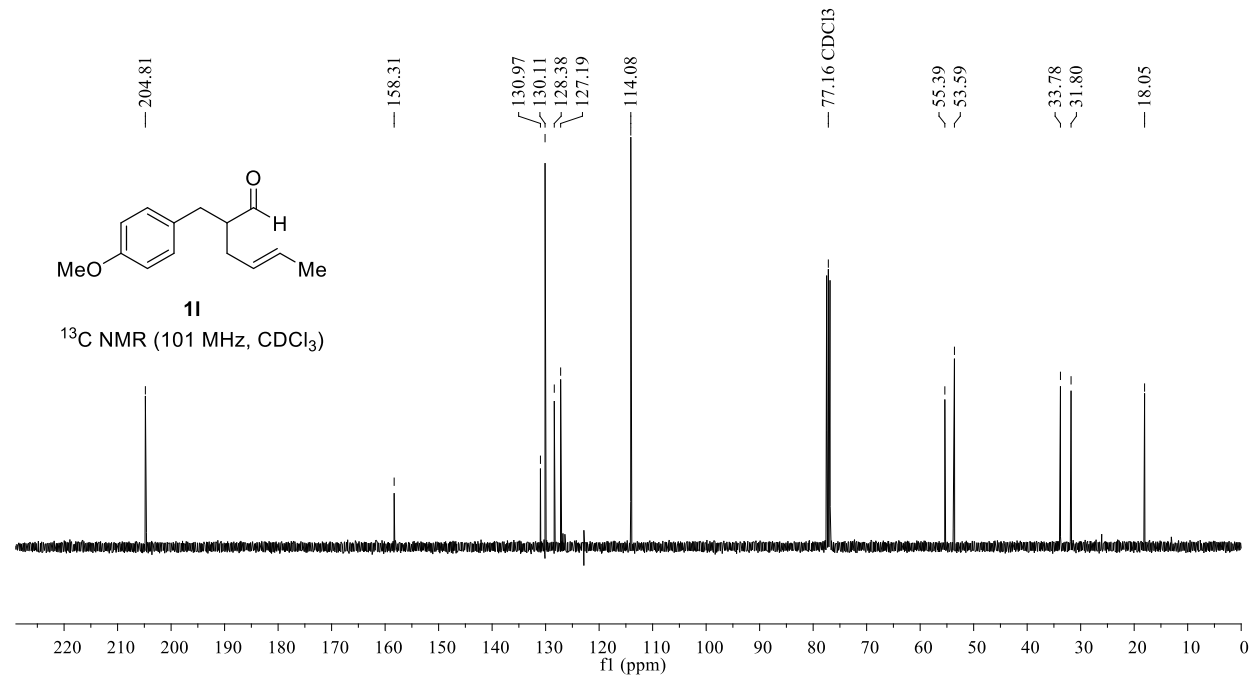

9.65 9.64 7.27 CDCl3 7.09 7.07 6.85 6.82 4.85 4.74 3.79 2.92 2.90 2.89 2.87 2.83 2.82 2.81 2.81 2.81 2.80 2.79 2.79 2.74 2.73 2.71 2.69 2.44 2.42 2.40 2.38 2.18 2.17 2.15 2.13 1.81 1.78 1.78 1.75 1.74 1.70 1.67 1.28 1.27 1.25 1.24 1.24 1.21 1.20 1.17 1.17 1.16 1.15 1.15 1.14 1.13 1.11 1.09
O
H
MeO
1j
1H NMR (400 MHz, CDCl3)
2.90 2.89 2.87 2.74 2.73 2.71 2.40 1.78 1.78 1.75 1.74 1.70 1.24 1.17 1.15 1.15 1.14 1.13
1.02 1.07 1.02 1.03 1.03 6.24 5.42
2.5 2.0 1.5
f1 (ppm)
0.93 2.00 2.01 1.00 1.00 3.08 1.02 1.07 1.02 1.03 1.03 6.24 5.42
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

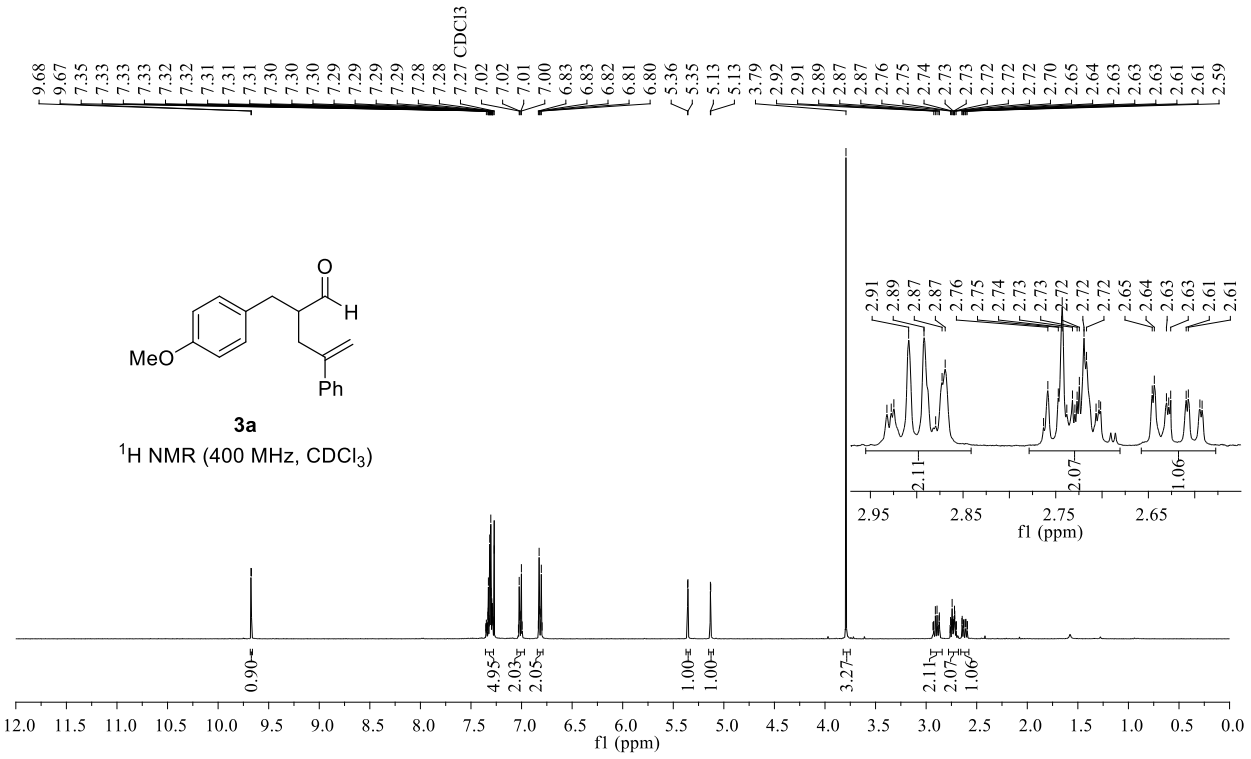

204.86
158.35
151.72
130.83
130.12
114.10
109.72
77.16 CDCl3
55.39
51.84
44.17
34.57
34.47
32.52
32.48
26.87
26.85
26.44
O
H
MeO
1j
13C NMR (101 MHz, CDCl3)
34.57 34.47 32.52 32.48 26.87 26.85 26.44
34 33 32 31 30 29 28 27
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

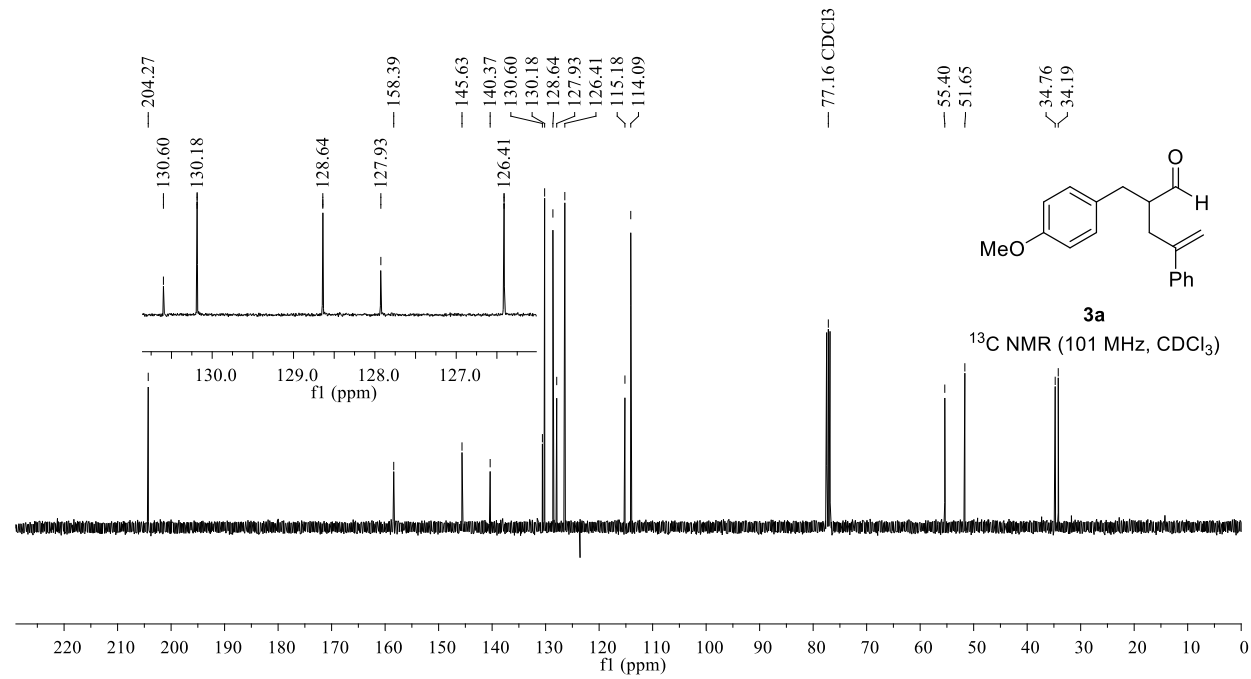

9.70
7.27 CDCl3
7.10
7.08
6.85
6.83
5.80
5.78
5.76
5.75
5.11
5.08
5.07
3.79
2.97
2.95
2.94
2.92
2.75
2.73
2.70
2.69
2.67
2.41
2.39
2.38
2.36
2.30
2.29
2.28
2.25
O
H
MeO
1k
1H NMR (400 MHz, CDCl3)
1.05
1.98
1.08
1.04
0.90
2.00
2.05
1.00
2.02
3.07
1.05
1.98
1.08
1.04
f1 (ppm)

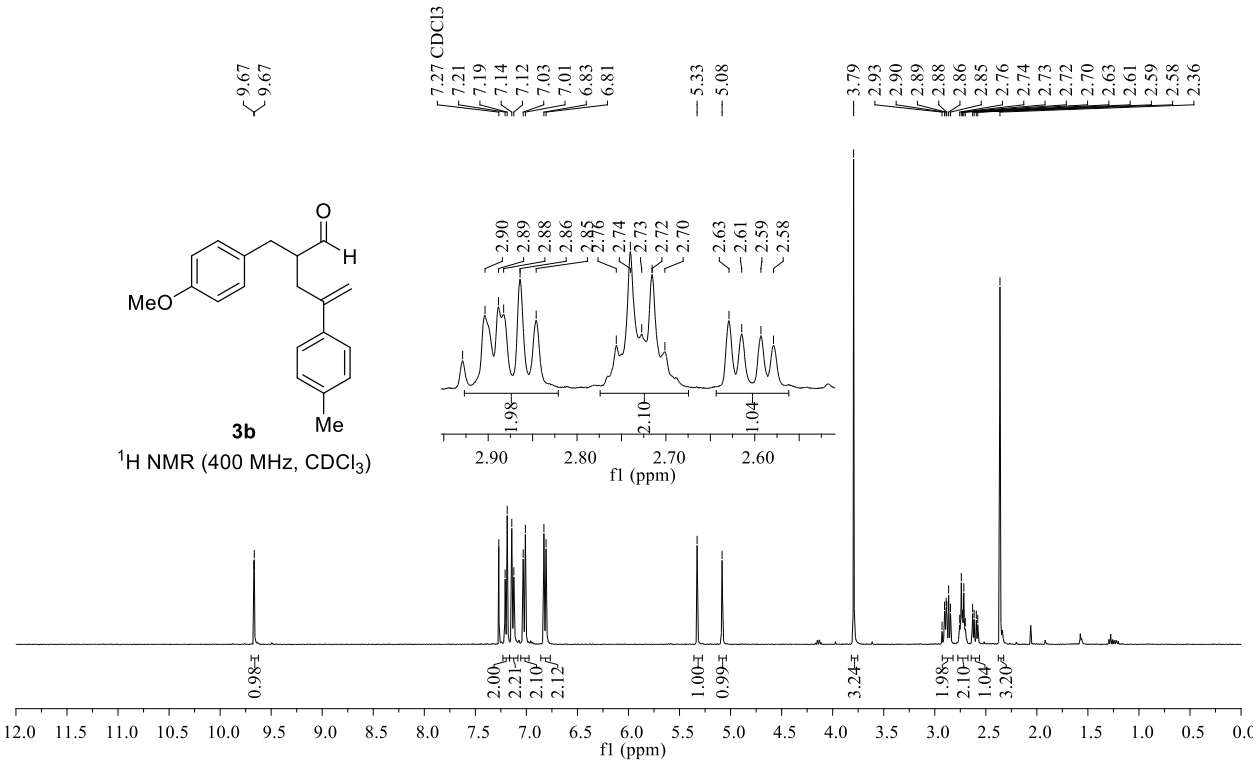

204.39
158.38
134.87
130.73
130.13
117.72
114.13
77.16 CDCl3
55.39
53.09
33.81
32.84
O
H
MeO
1k
13C NMR (101 MHz, CDCl3)
f1 (ppm)

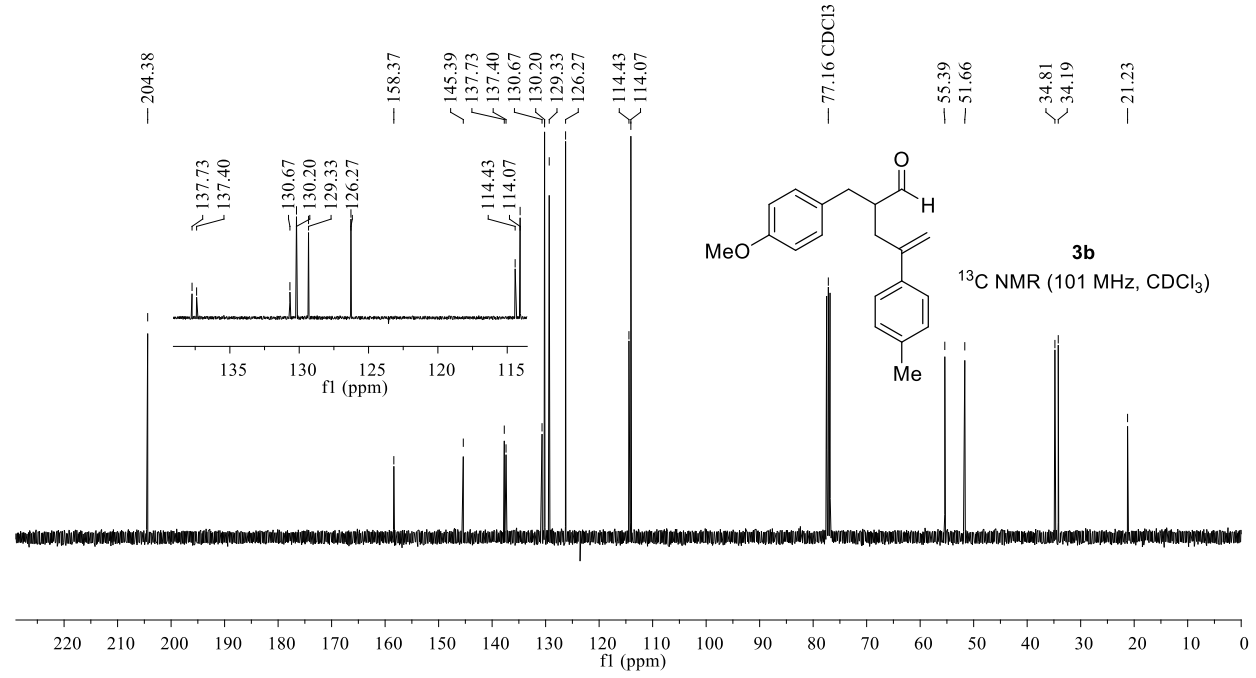

MeO
Me
O
H
1l
1H NMR (400 MHz, CDCl3)
fl (ppm)

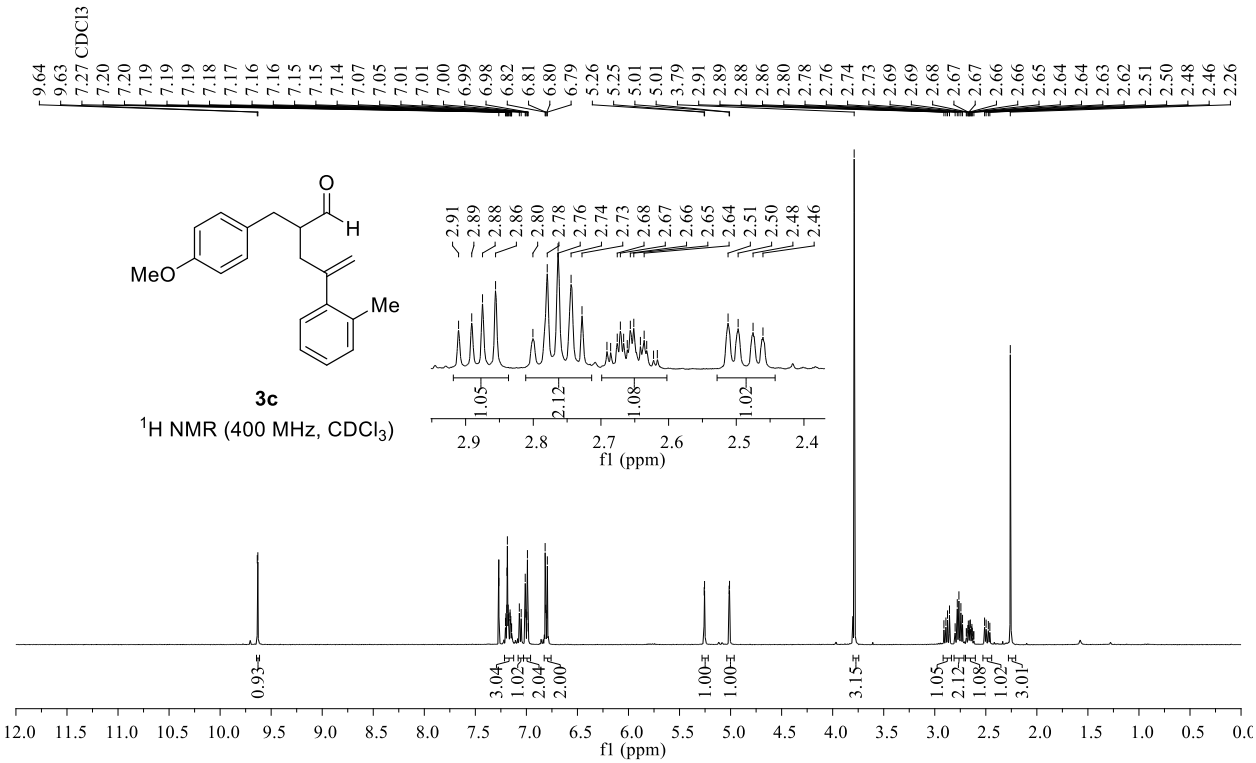

MeO
Me
O
H
1l
13C NMR (101 MHz, CDCl3)
fl (ppm)

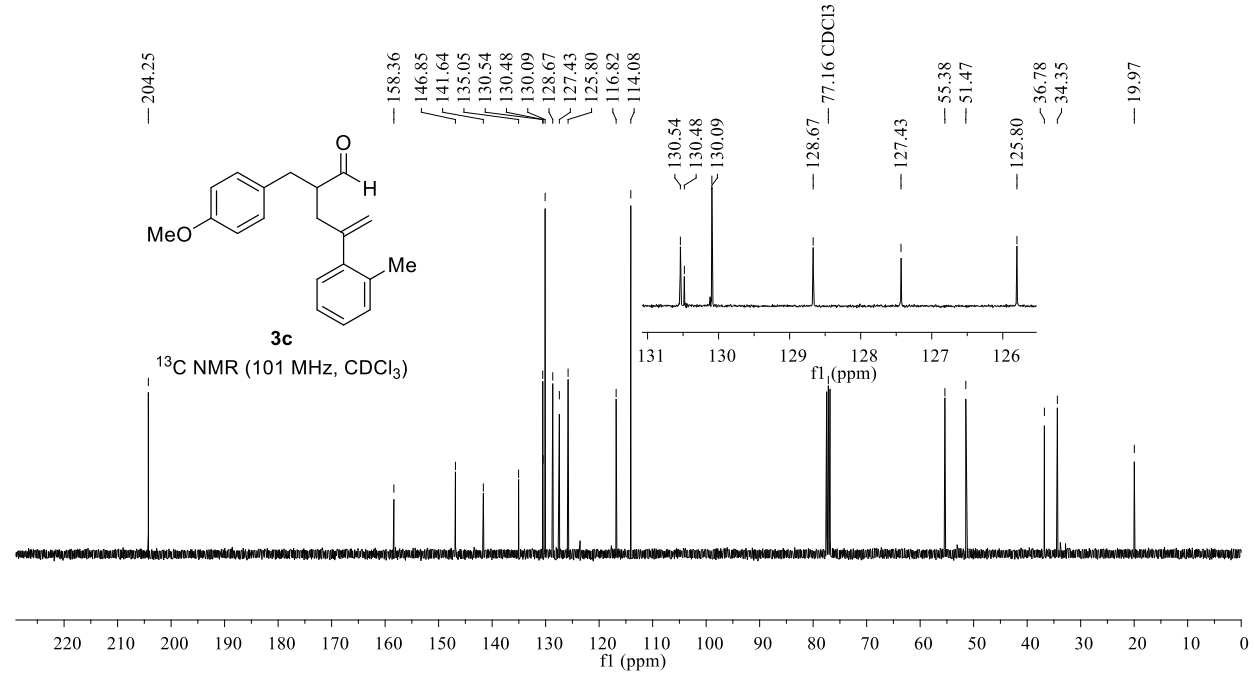

MeO
O
H
Ph
3a
1H NMR (400 MHz, CDCl3)
fl (ppm)

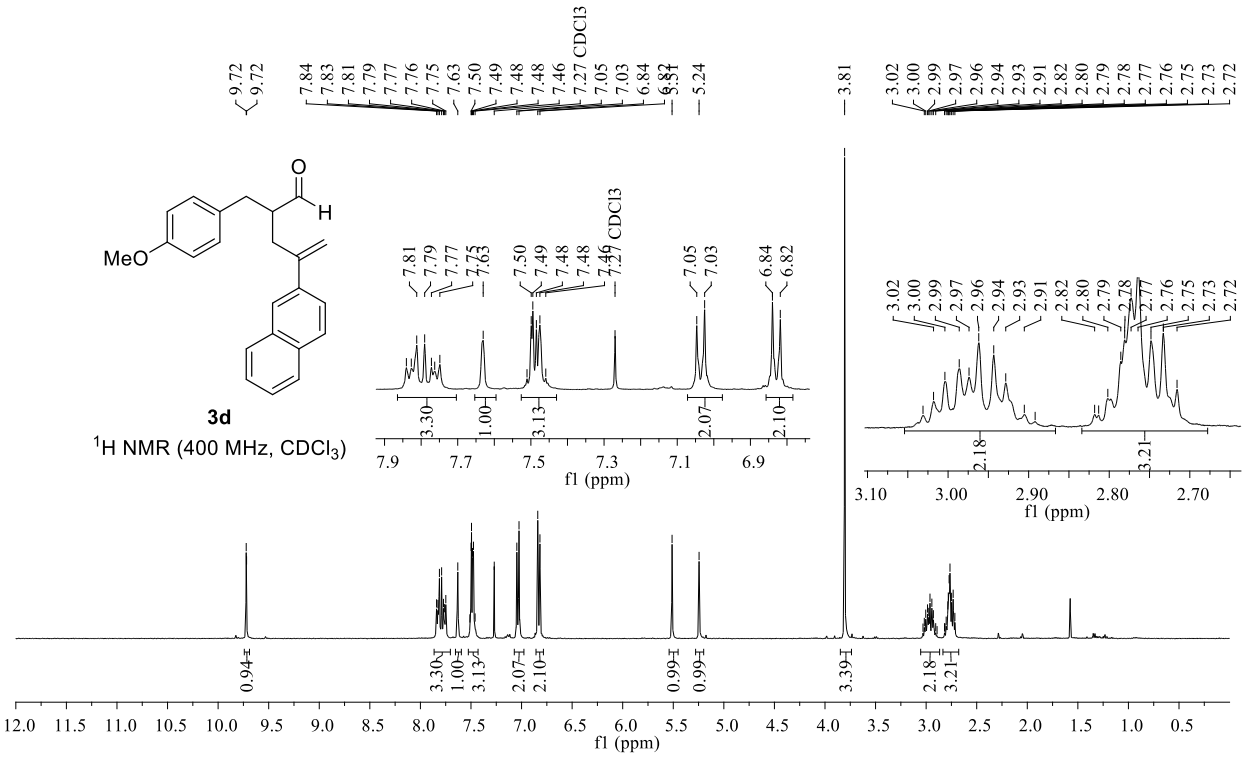

MeO
O
H
Ph
3a
13C NMR (101 MHz, CDCl3)
fl (ppm)

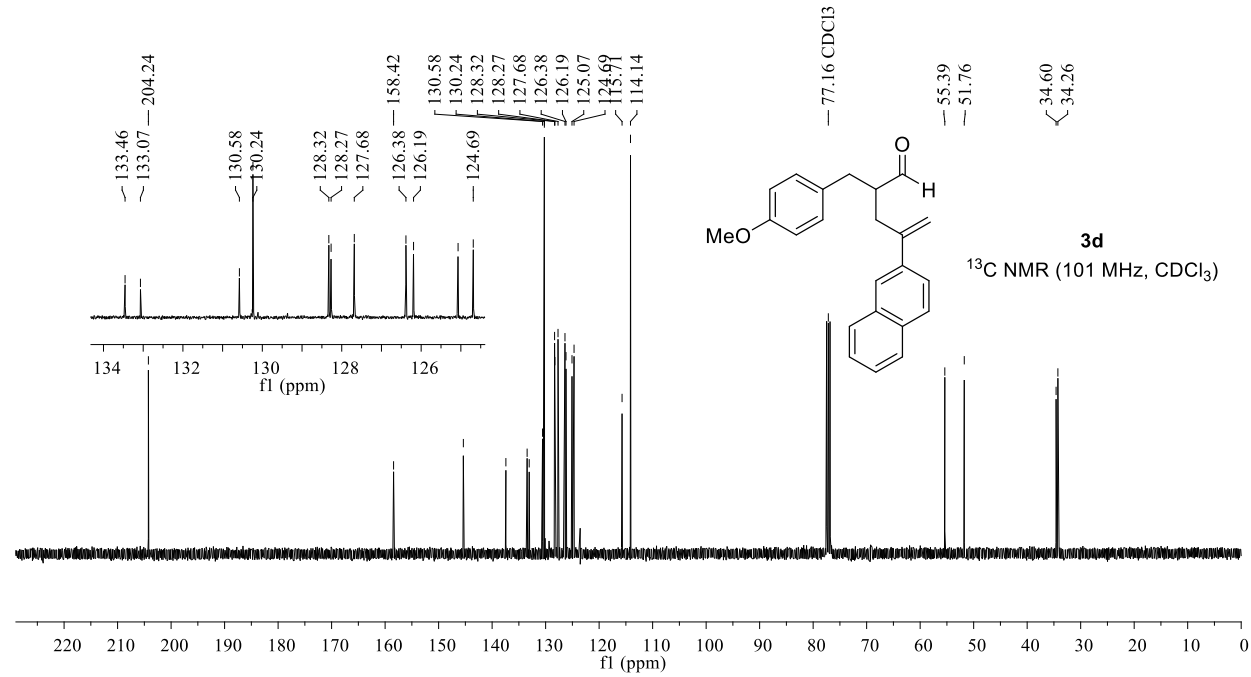

9.67
9.67
7.27 CDCl3
7.21
7.19
7.14
7.12
7.03
7.01
6.83
6.81
5.33
5.08
3.79
2.93
2.90
2.89
2.88
2.86
2.85
2.76
2.74
2.73
2.72
2.70
2.63
2.61
2.59
2.58
2.36
O
H
MeO
Me
3b
1H NMR (400 MHz, CDCl3)
1.98
2.10
1.04
2.90
2.80
2.70
2.60
f1 (ppm)
0.98
2.00
2.21
2.10
2.12
1.00
0.99
3.24
1.98
2.10
1.04
3.20
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

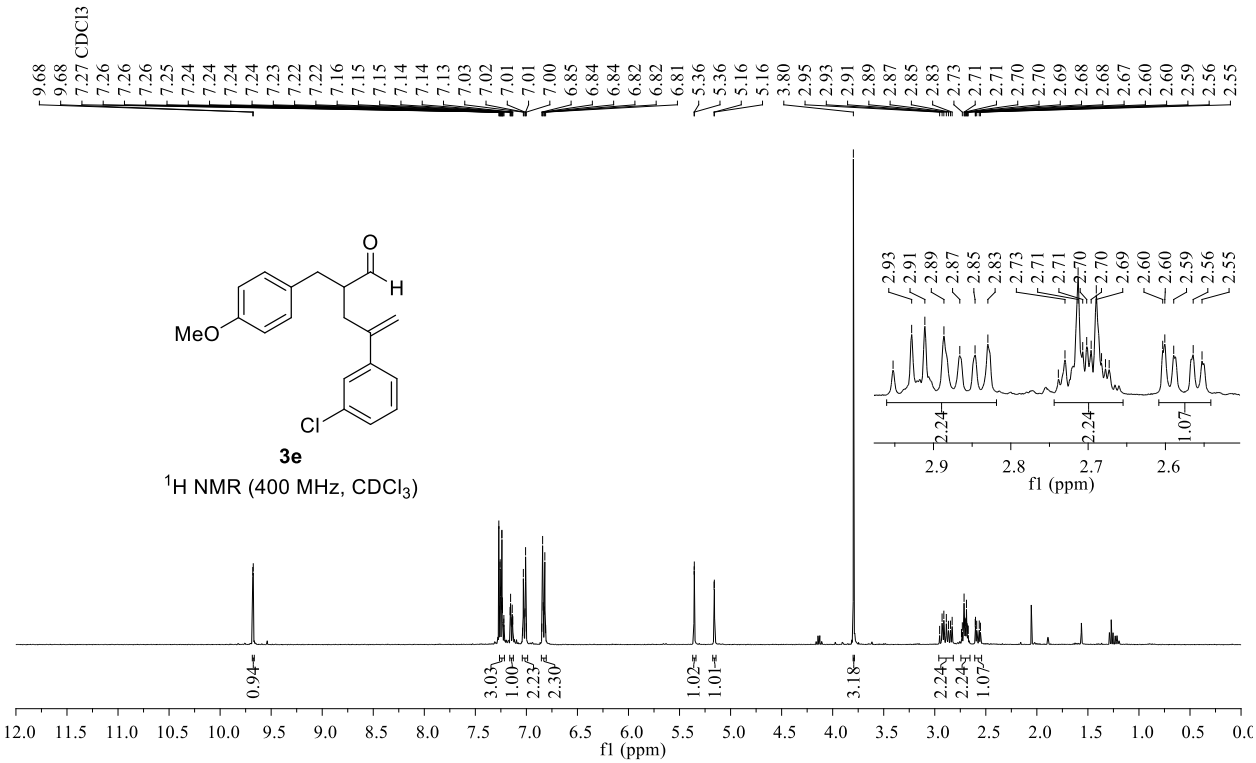

204.38
158.37
145.39
137.73
137.40
130.67
130.20
129.33
126.27
114.43
114.07
77.16 CDCl3
55.39
51.66
34.81
34.19
21.23
137.73
137.40
130.67
130.20
129.33
126.27
114.43
114.07
135
130
125
120
115
f1 (ppm)
O
H
MeO
Me
3b
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

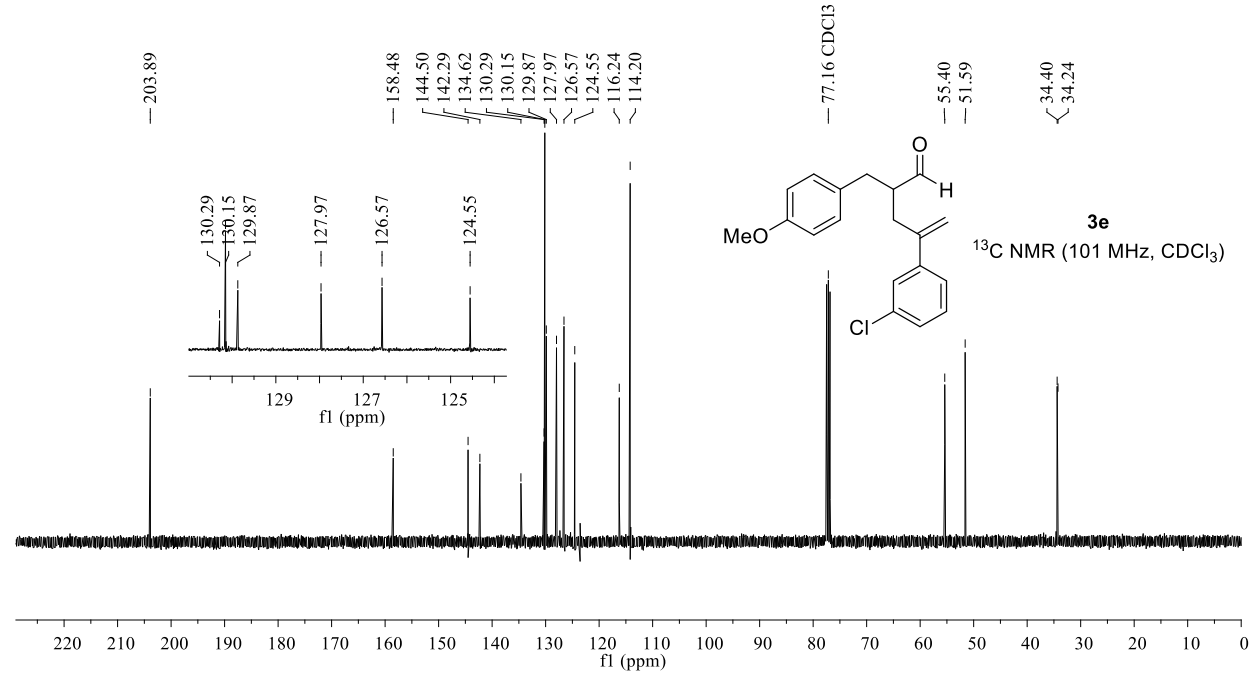

9.64 9.63 7.27 CDCl3 7.20 7.20 7.19 7.19 7.19 7.18 7.17 7.16 7.16 7.15 7.15 7.14 7.07 7.05 7.01 7.01 7.00 6.99 6.98 6.82 6.81 6.80 6.79 5.26 5.25 5.01 5.01 3.79 2.91 2.89 2.88 2.86 2.80 2.78 2.76 2.74 2.73 2.69 2.69 2.68 2.67 2.67 2.66 2.66 2.65 2.64 2.64 2.63 2.62 2.51 2.50 2.48 2.46 2.26
O
H
MeO
Me
3c
1H NMR (400 MHz, CDCl3)
2.91 2.89 2.88 2.86 2.80 2.78 2.76 2.74 2.73 2.68 2.67 2.66 2.65 2.64 2.51 2.50 2.48 2.46
1.05 2.12 1.08 1.02
2.9 2.8 2.7 2.6 2.5 2.4
f1 (ppm)
0.93 3.04 1.02 2.04 2.00 1.00 1.00 3.15 1.05 2.12 1.08 1.02 3.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

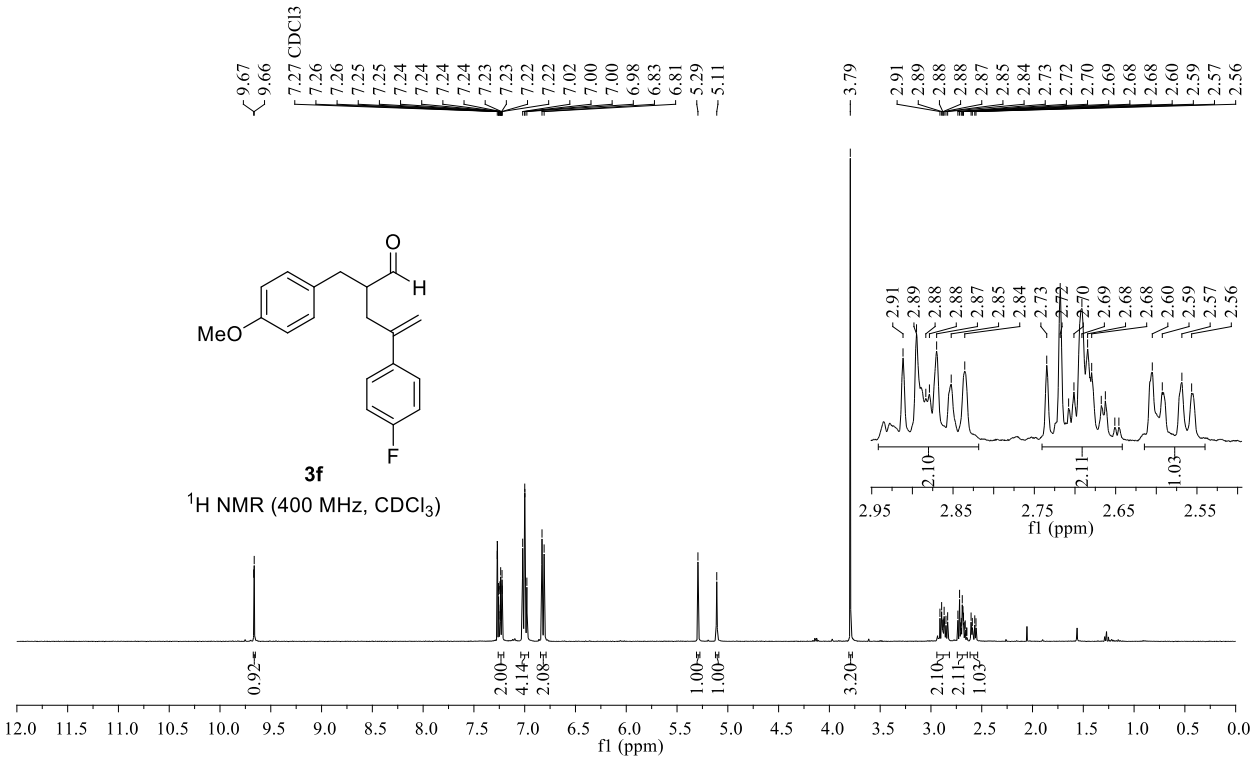

204.25 158.36 146.85 141.64 135.05 130.54 130.48 130.09 128.67 127.43 125.80 116.82 114.08 77.16 CDCl3 55.38 51.47 36.78 34.35 19.97
O
H
MeO
Me
3c
13C NMR (101 MHz, CDCl3)
130.54 130.48 130.09 128.67 127.43 125.80
131 130 129 128 127 126
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

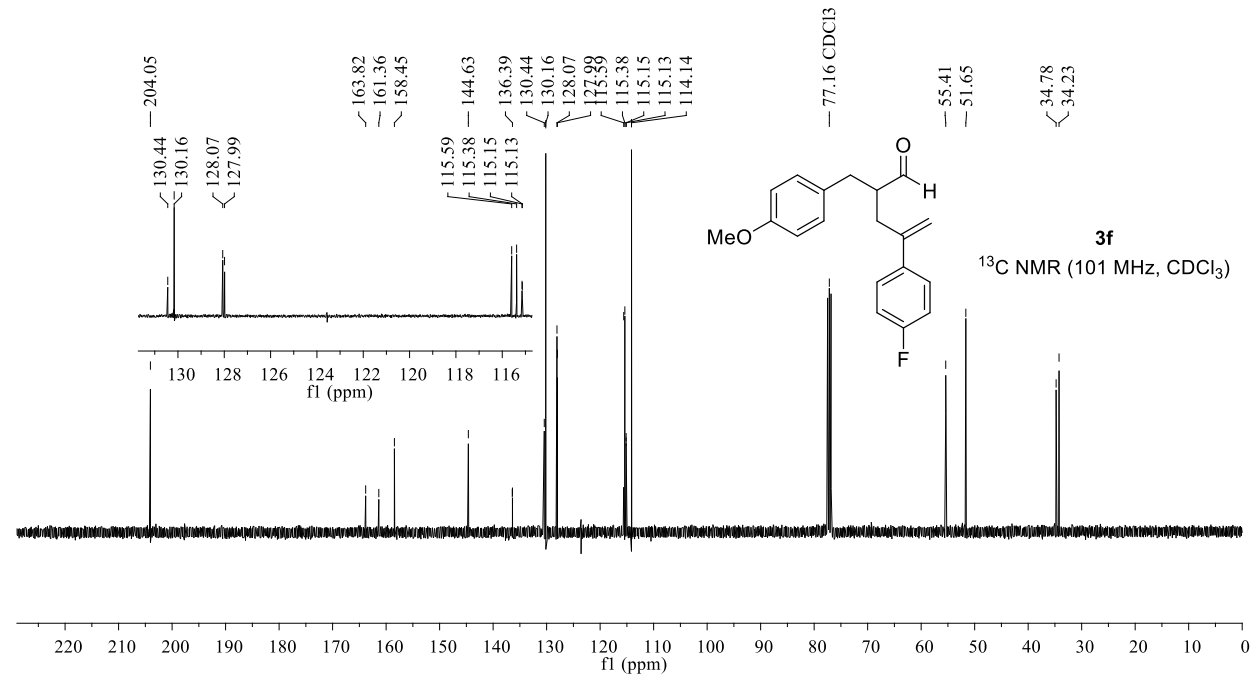

3d
$^1$H NMR (400 MHz, CDCl$_3$)
MeO
O
H
CDCl3
fl (ppm)

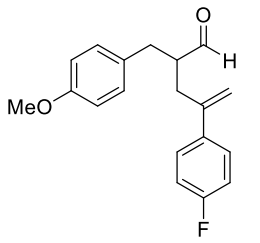

3d
$^{13}$C NMR (101 MHz, CDCl$_3$)
MeO
O
H
CDCl3
fl (ppm)


3e
$^1$H NMR (400 MHz, $CDCl_3$)
f1 (ppm)


3e
$^{13}$C NMR (101 MHz, $CDCl_3$)
f1 (ppm)


9.67
9.66
7.27 CDCl3
7.26
7.26
7.25
7.25
7.24
7.24
7.24
7.24
7.23
7.23
7.22
7.22
7.02
7.00
7.00
6.98
6.83
6.81
5.29
5.11
3.79
2.91
2.89
2.88
2.88
2.87
2.85
2.84
2.73
2.72
2.70
2.69
2.68
2.68
2.60
2.59
2.57
2.56
O
H
MeO
F
3f
1H NMR (400 MHz, CDCl3)
2.10
2.11
1.03
2.95
2.85
2.75
2.65
2.55
f1 (ppm)
0.92
2.00
4.14
2.08
1.00
1.00
3.20
2.10
2.11
1.03
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

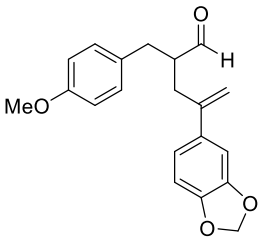

204.05
130.44
130.16
128.07
127.99
163.82
161.36
158.45
144.63
136.39
130.44
130.16
128.07
127.99
115.59
115.38
115.38
115.15
115.13
115.13
114.14
77.16 CDCl3
55.41
51.65
34.78
34.23
O
H
MeO
F
3f
13C NMR (101 MHz, CDCl3)
130
128
126
124
122
120
118
116
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)




**3f**

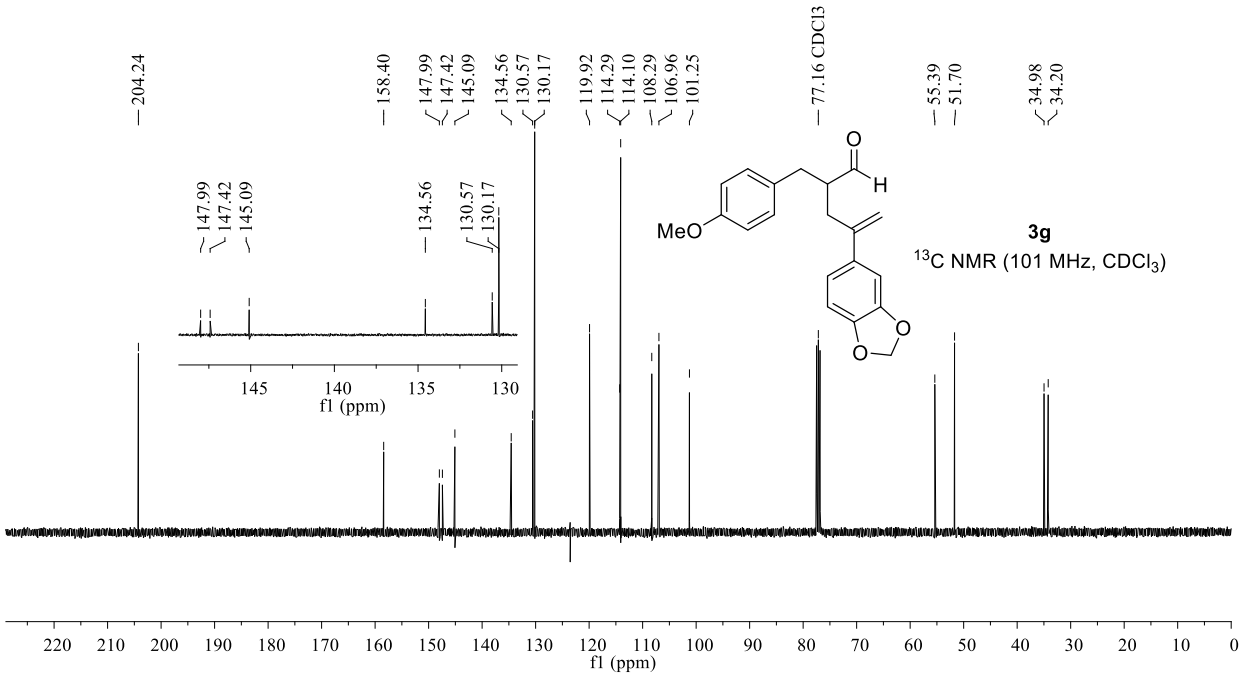
$^{19}$F NMR (376 MHz, $CDCl_3$)

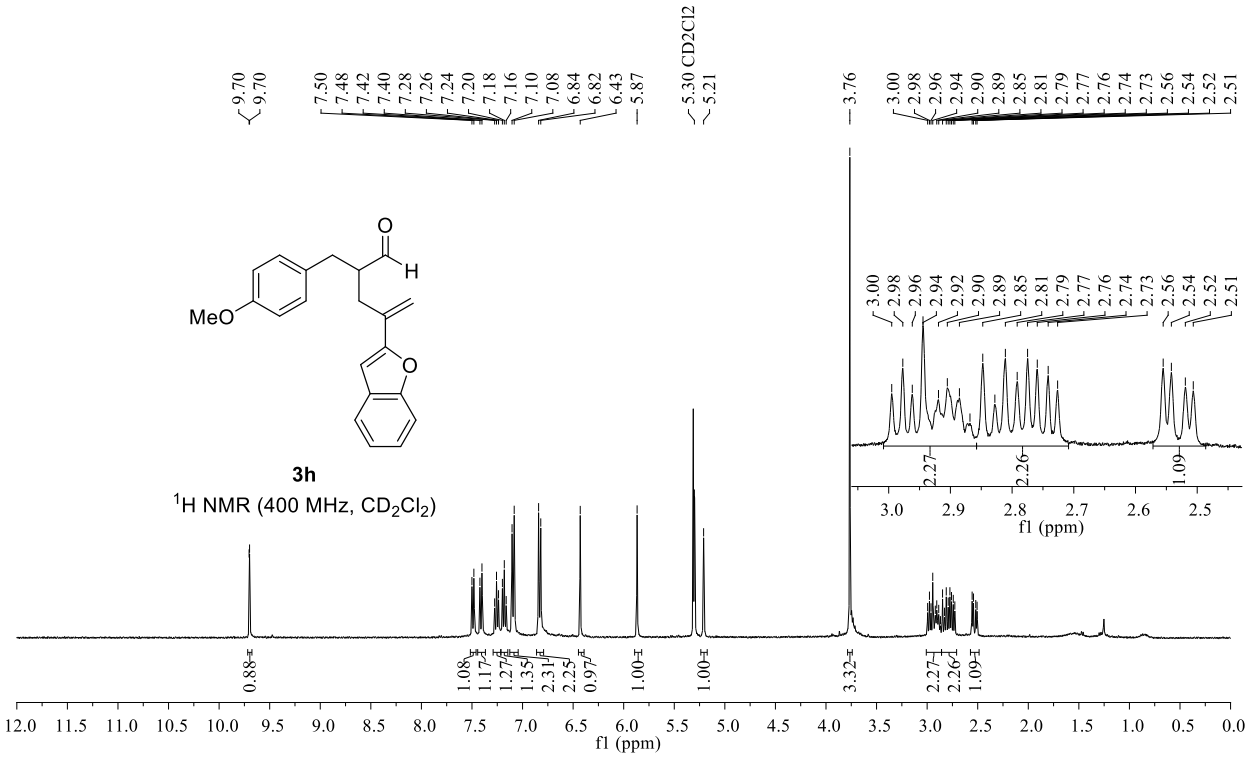


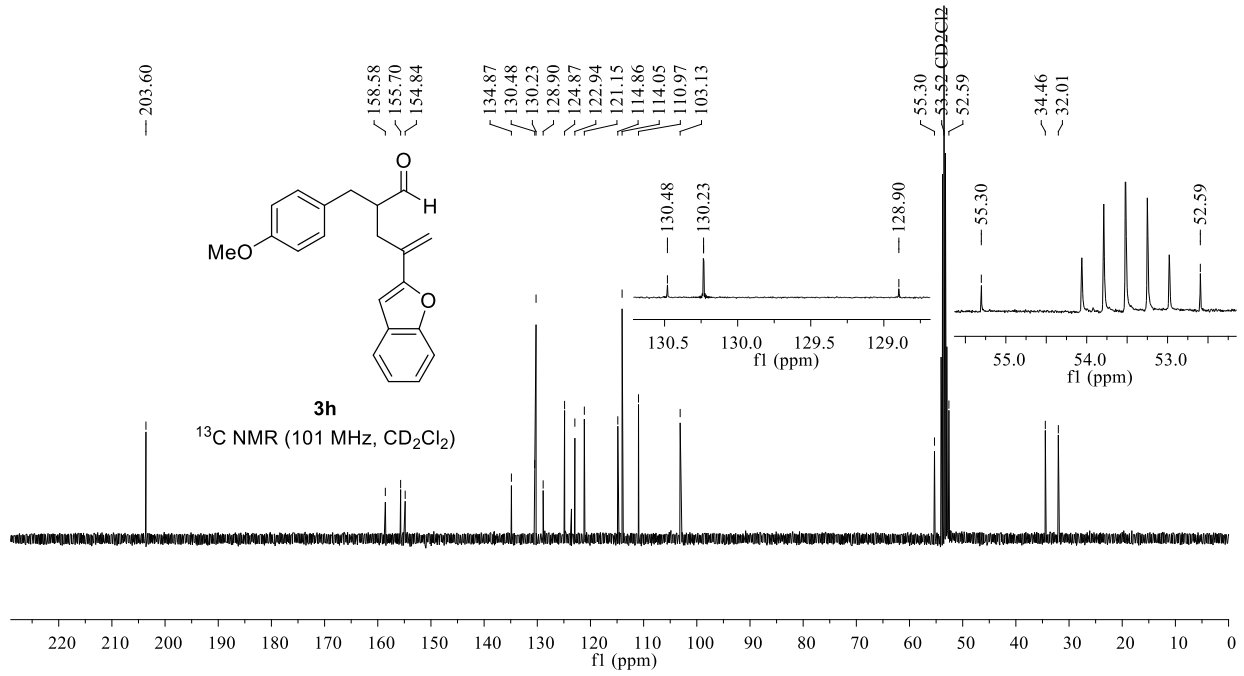



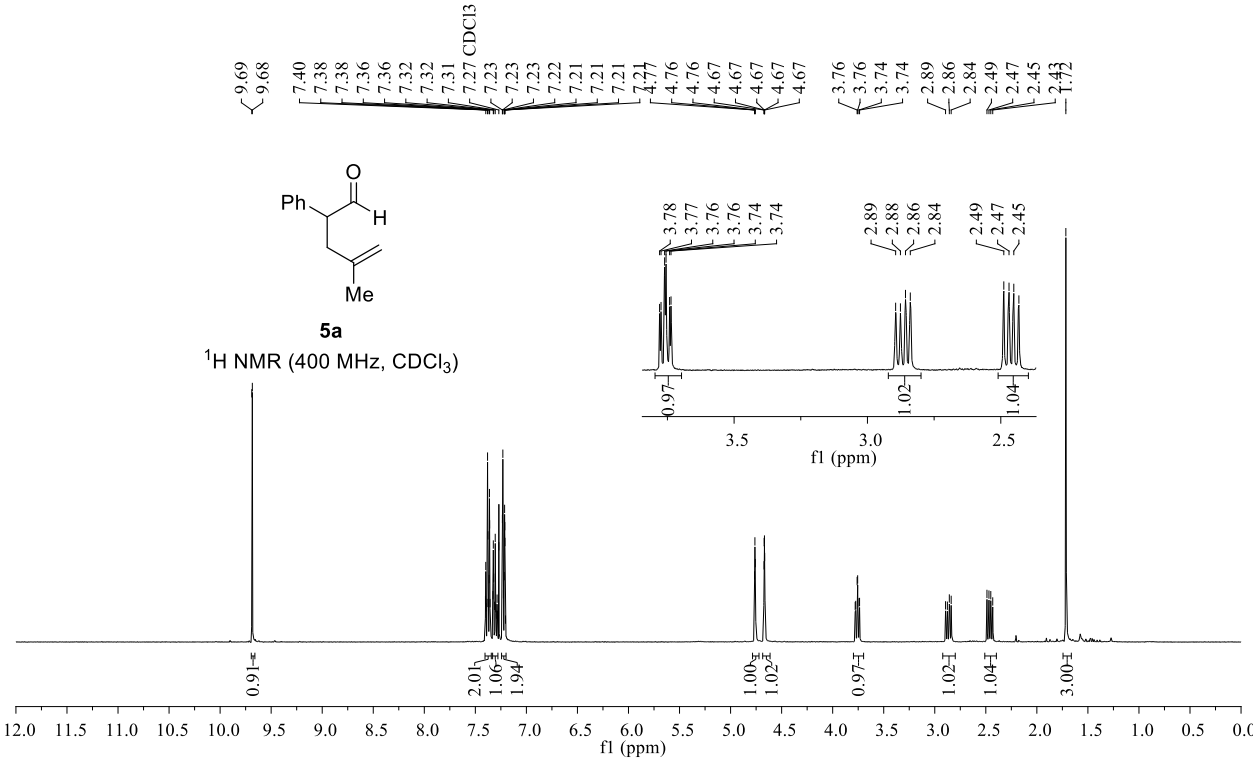

**3g**

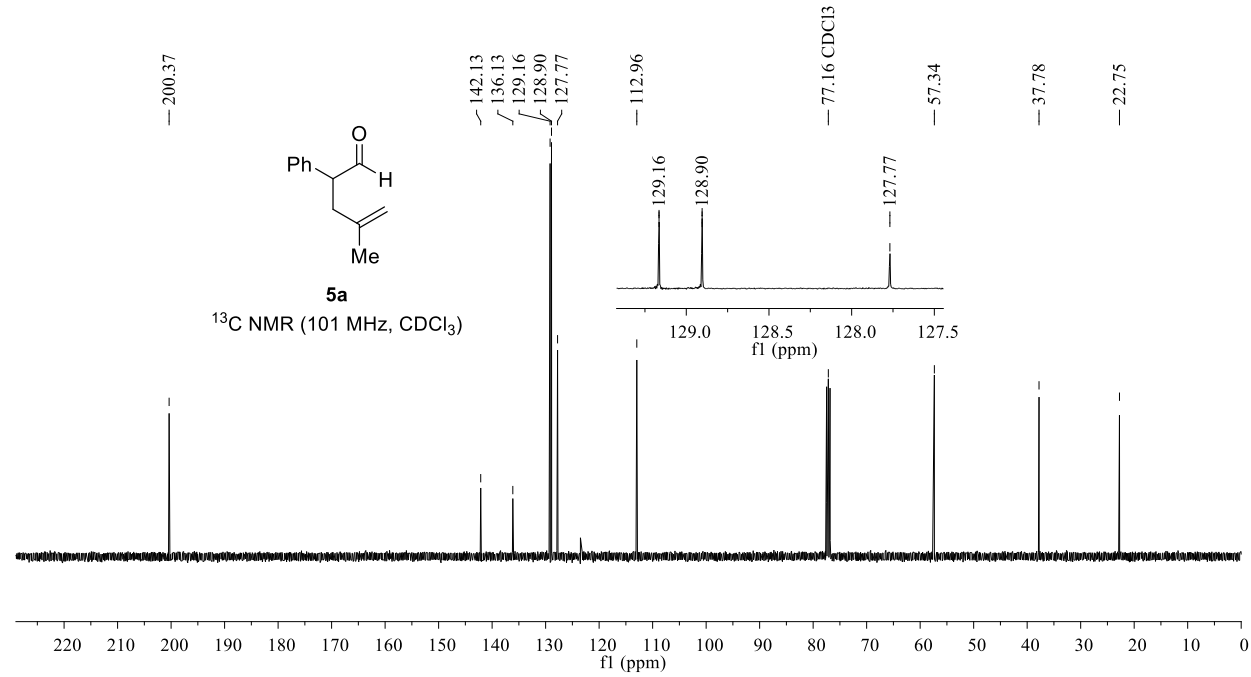
$^{1}$H NMR (400 MHz, $CDCl_3$)

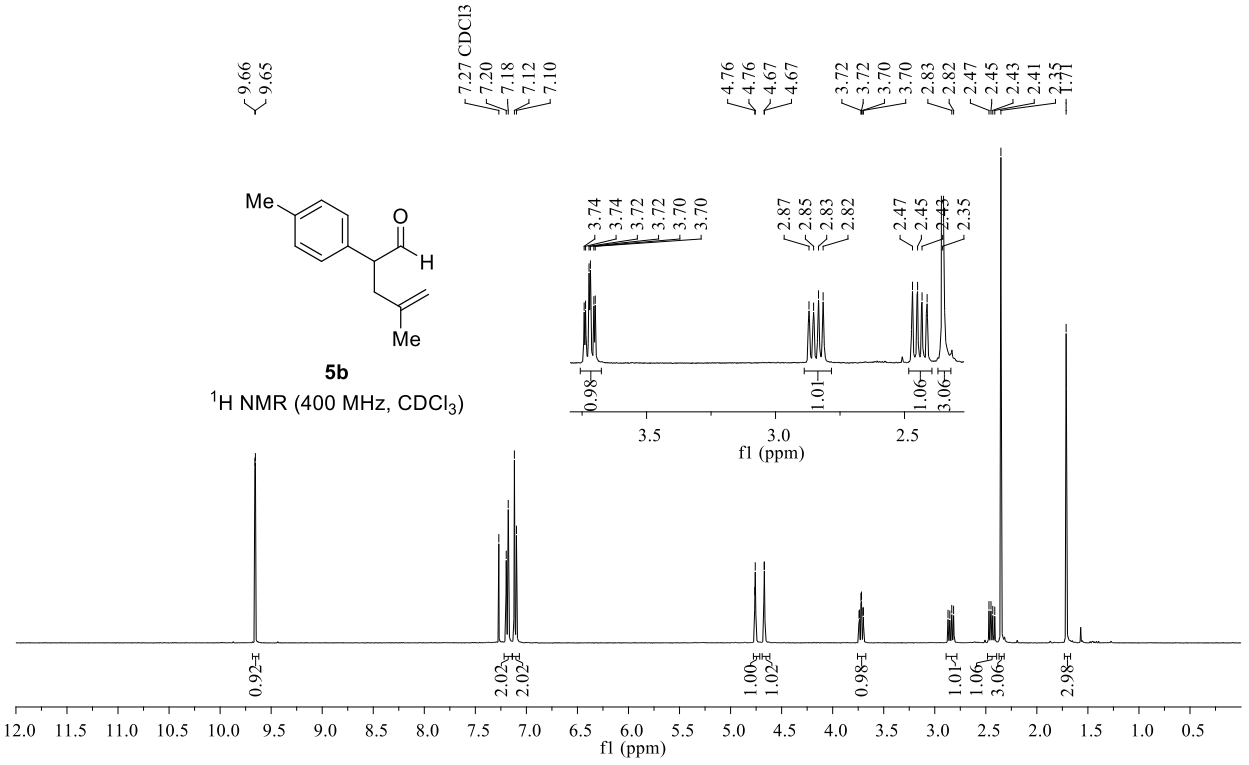

204.24
158.40
147.99
147.42
145.09
134.56
130.57
130.17
119.92
114.29
114.10
108.29
106.96
101.25
77.16 CDCl3
55.39
51.70
34.98
34.20
MeO
O
H
O
O
3g
13C NMR (101 MHz, CDCl3)
fl (ppm)

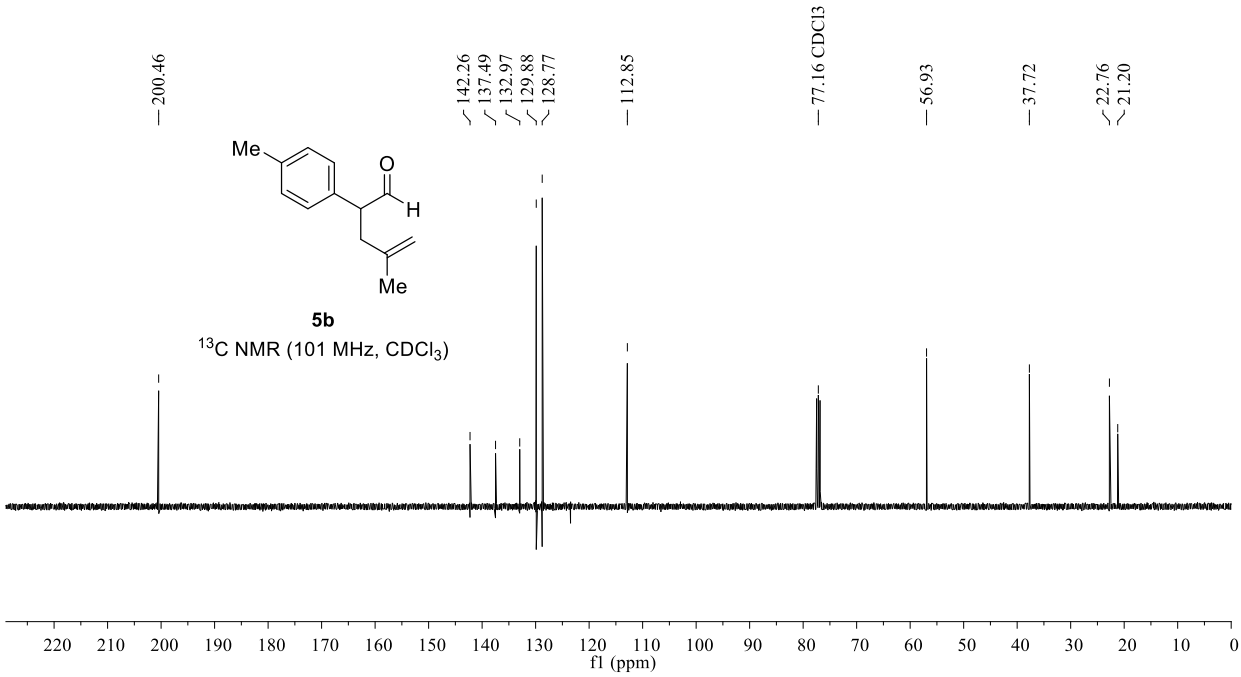

9.70
7.50
7.48
7.42
7.40
7.28
7.26
7.24
7.20
7.18
7.16
7.10
7.08
6.84
6.82
6.43
5.87
5.30 CD2Cl2
5.21
3.76
3.00
2.98
2.96
2.94
2.92
2.90
2.89
2.85
2.81
2.79
2.77
2.76
2.74
2.73
2.56
2.54
2.52
2.51
MeO
O
H
O
3h
1H NMR (400 MHz, CD2Cl2)
0.88
1.08
1.17
1.27
1.35
2.31
2.25
0.97
1.00
1.00
3.32
2.27
2.26
1.09
fl (ppm)

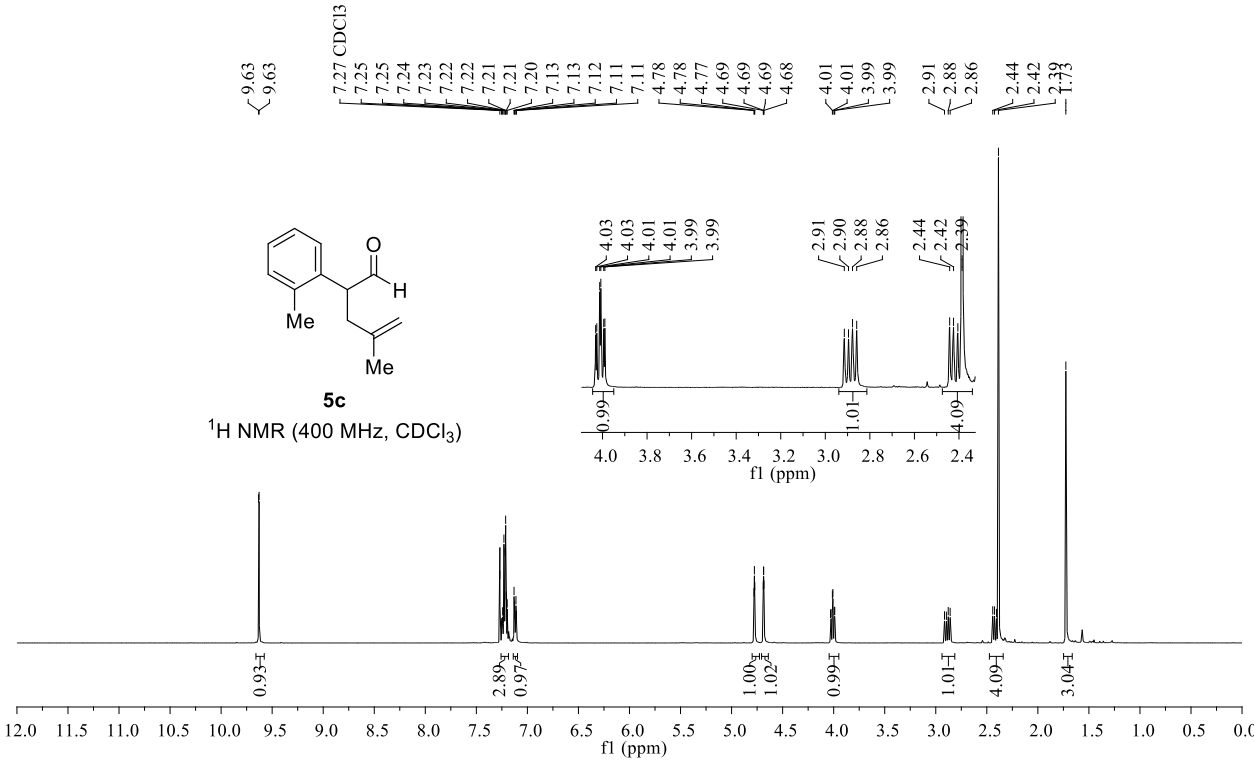

203.60
158.58
155.70
154.84
134.87
130.48
130.23
128.90
124.87
122.94
121.15
114.86
114.05
110.97
103.13
55.30
53.52 CD2Cl2
52.59
34.46
32.01
MeO
O
H
O
3h
13C NMR (101 MHz, CD2Cl2)
fl (ppm)

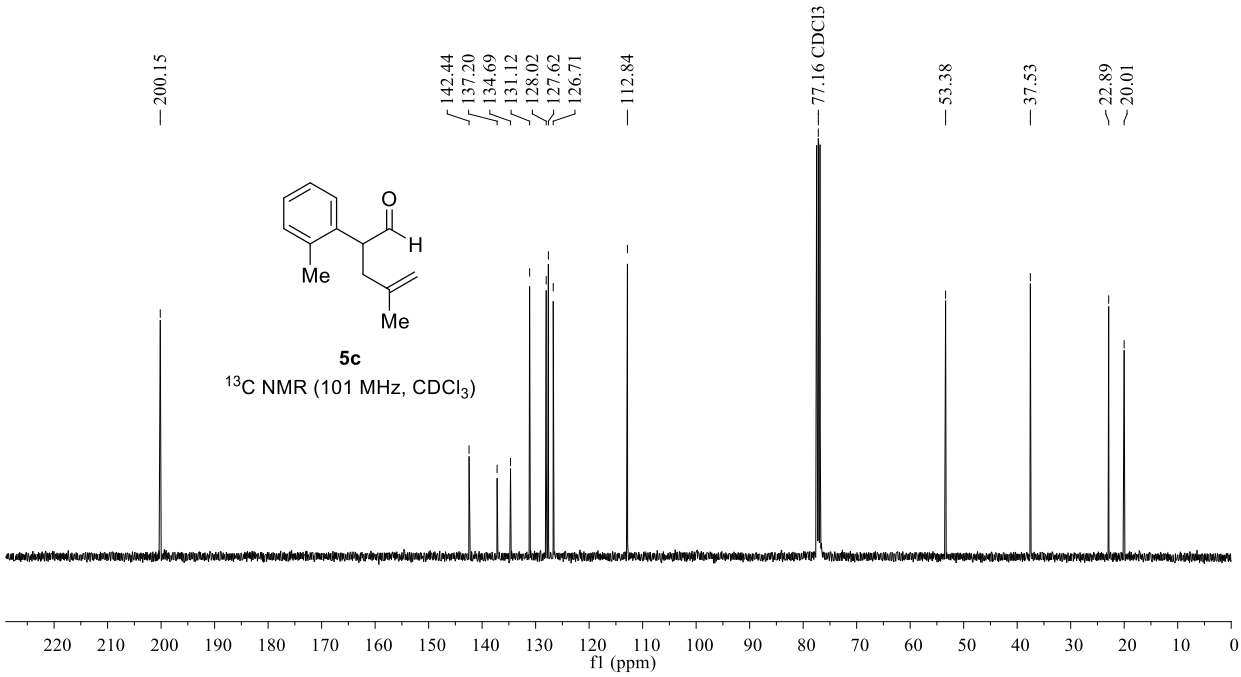

9.69
9.68
7.40
7.38
7.38
7.36
7.36
7.32
7.32
7.31
7.27 CDCl3
7.23
7.23
7.23
7.22
7.21
7.21
7.21
4.76
4.76
4.67
4.67
4.67
4.67
3.76
3.76
3.74
3.74
2.89
2.86
2.84
2.49
2.47
2.45
Ph
O
H
Me
5a
1H NMR (400 MHz, CDCl3)
fl (ppm)


200.37
142.13
136.13
129.16
128.90
127.77
112.96
77.16 CDCl3
57.34
37.78
22.75
O
Ph
H
Me
5a
13C NMR (101 MHz, CDCl3)
129.16
128.90
127.77
129.0
128.5
128.0
127.5
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.66
9.65
7.27 CDCl3
7.20
7.18
7.12
7.10
4.76
4.76
4.67
4.67
3.72
3.72
3.70
3.70
2.83
2.82
2.47
2.45
2.43
2.41
2.35
1.71
Me
O
H
Me
5b
1H NMR (400 MHz, CDCl3)
3.74
3.74
3.72
3.72
3.70
3.70
2.87
2.85
2.83
2.82
2.47
2.45
2.43
2.35
0.98
1.01
1.06
3.06
3.5
3.0
2.5
f1 (ppm)
0.92
2.02
2.02
1.00
1.02
0.98
1.01
1.06
3.06
2.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

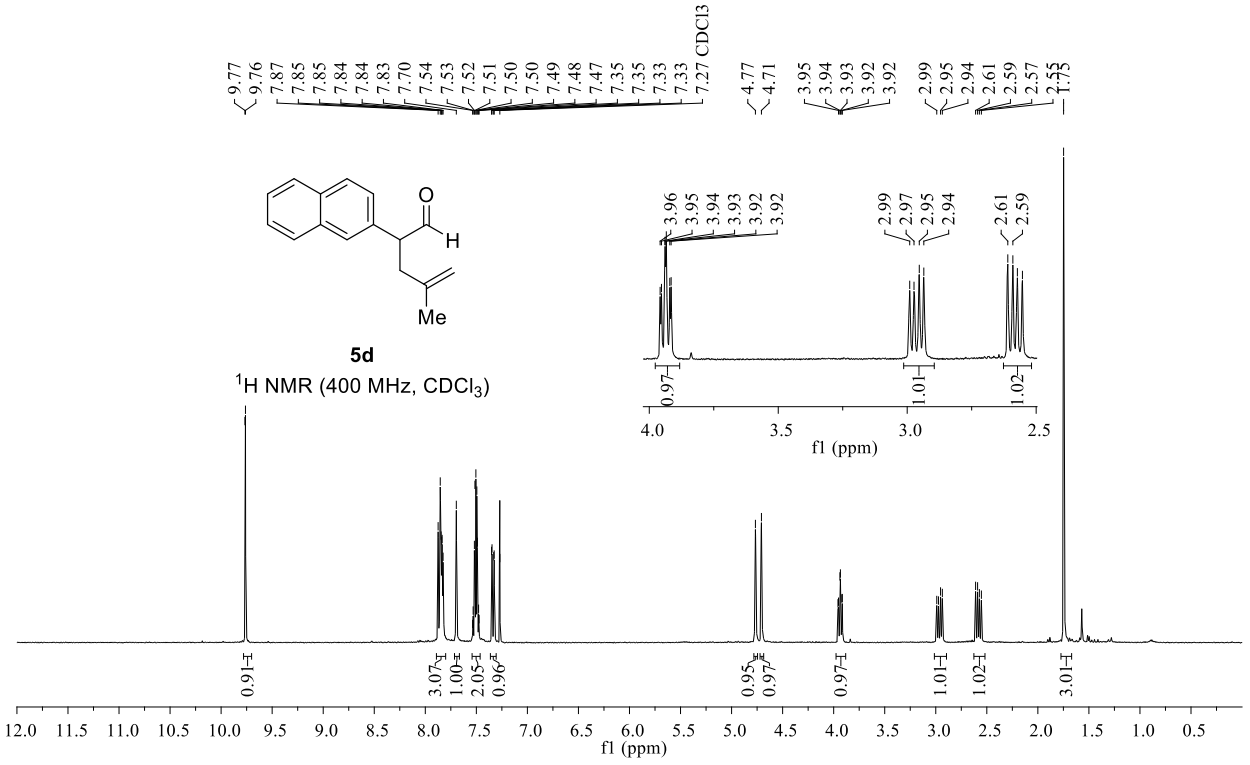

200.46
142.26
137.49
132.97
129.88
128.77
112.85
77.16 CDCl3
56.93
37.72
22.76
21.20
Me
O
H
Me
5b
13C NMR (101 MHz, CDCl3)
f1 (ppm)


9.63
9.63
7.27 CDCl3
4.78
4.77
4.69
4.68
4.01
3.99
2.91
2.88
2.86
2.44
2.42
2.39
1.73
Me
O
H
Me
5c
1H NMR (400 MHz, CDCl3)
0.99
1.01
4.09
0.93
2.89
0.97
1.00
1.02
0.99
1.01
4.09
3.04
f1 (ppm)



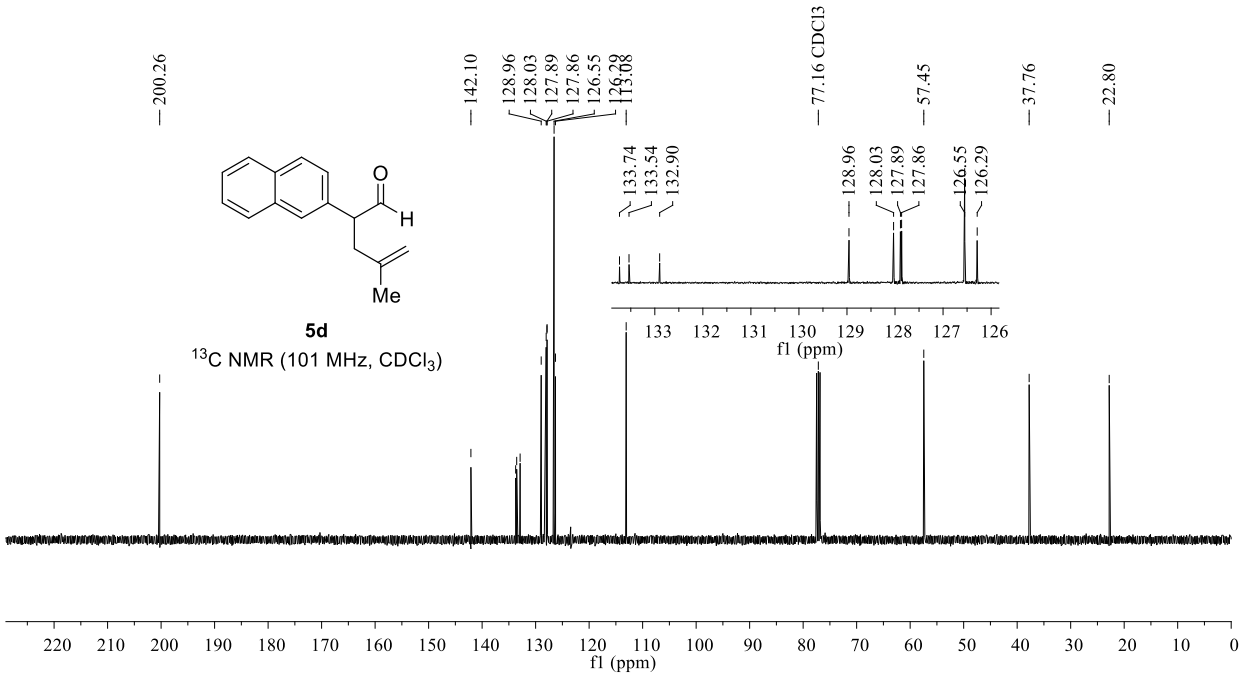

**5c**

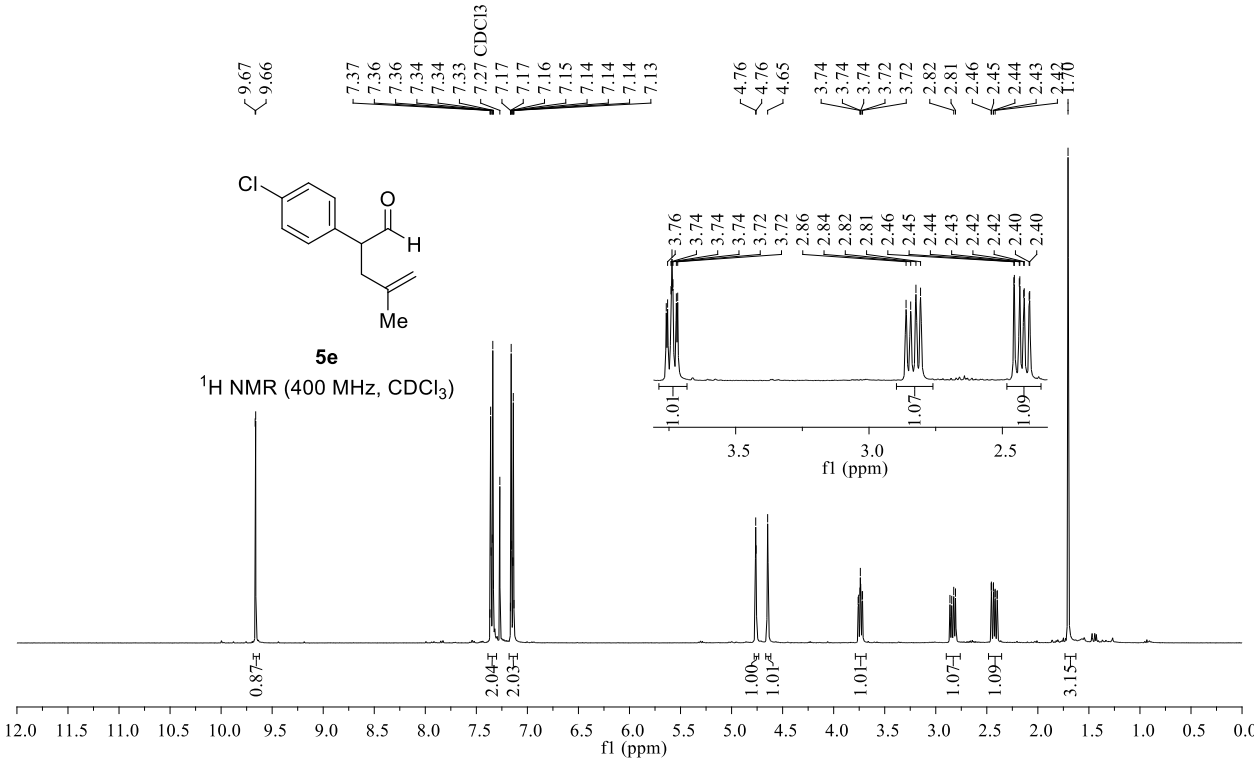
$^{13}$C NMR (101 MHz, $CDCl_3$)

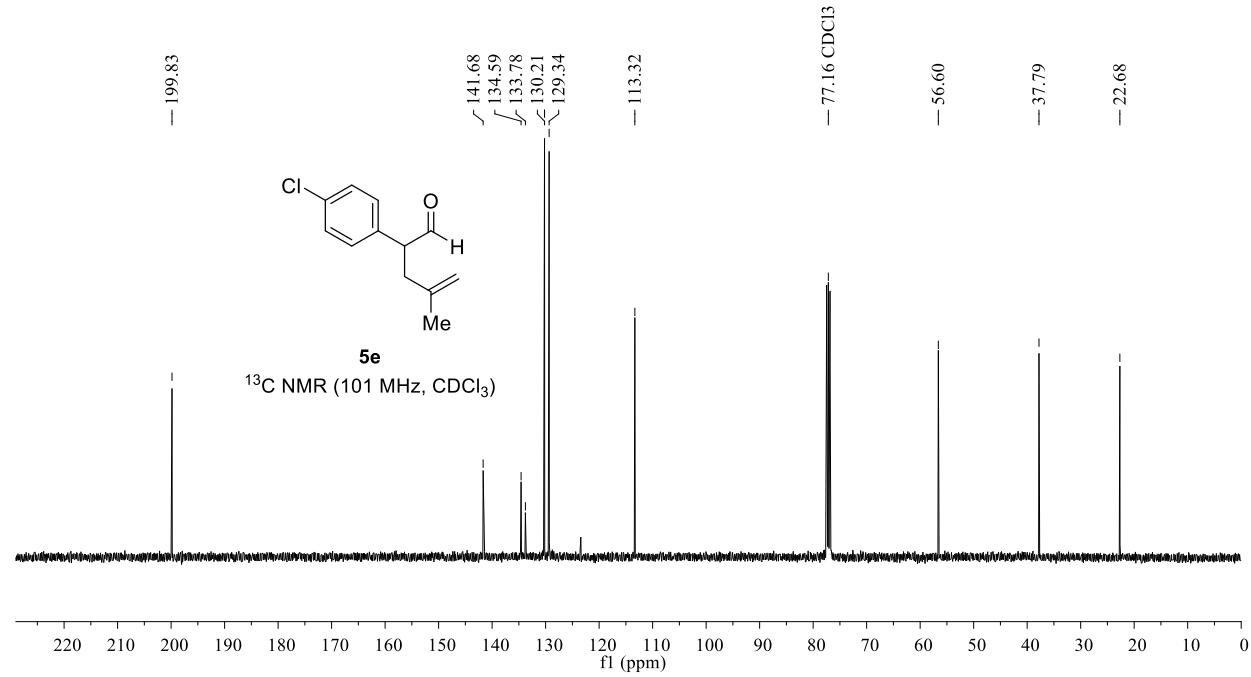


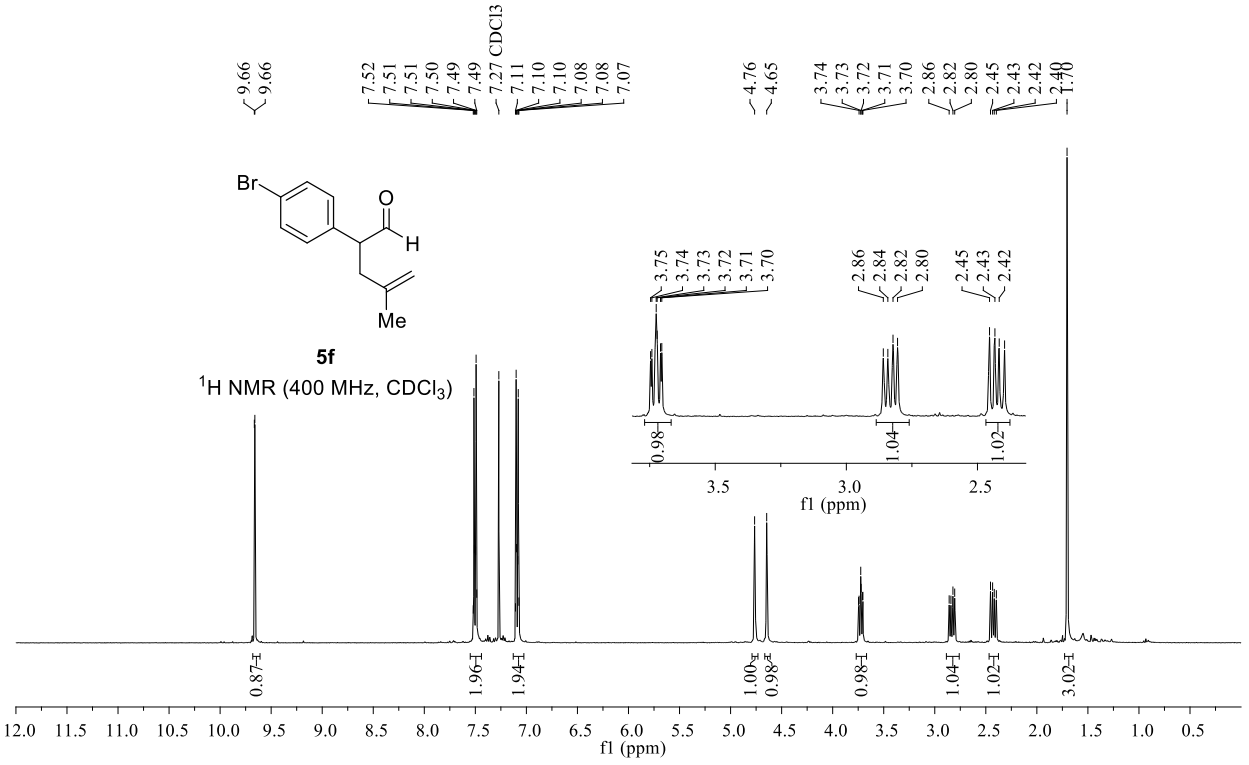

**5d**

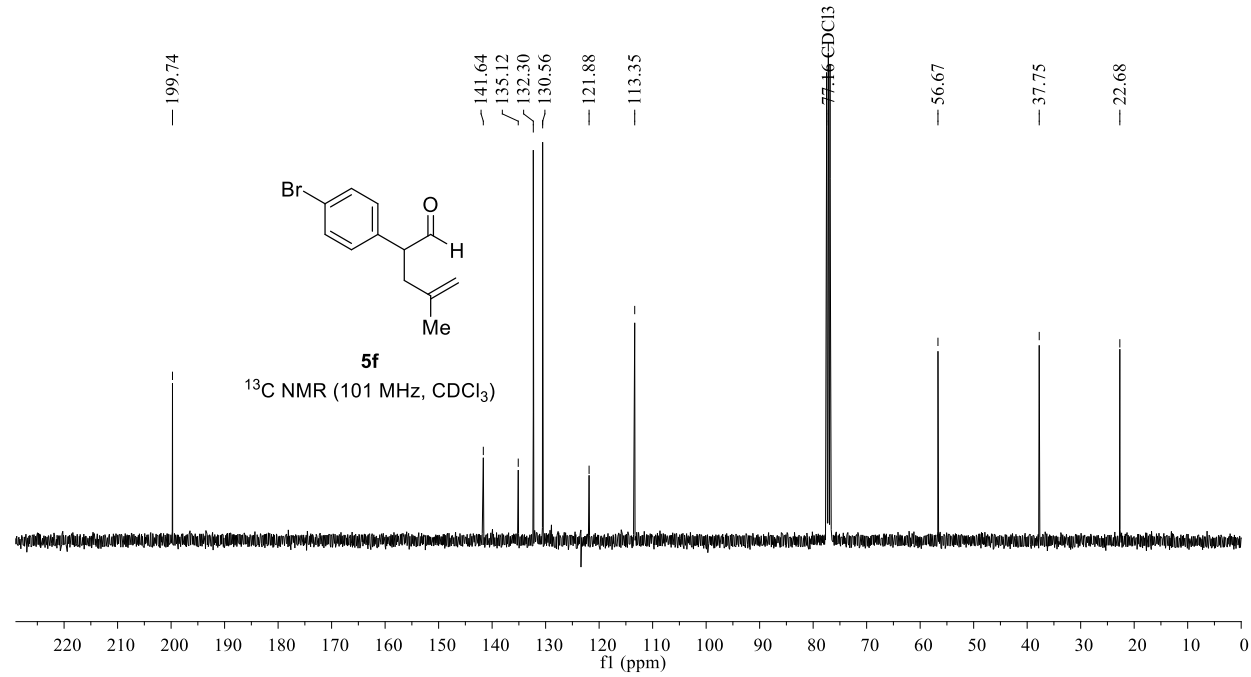
$^{1}$H NMR (400 MHz, $CDCl_3$)

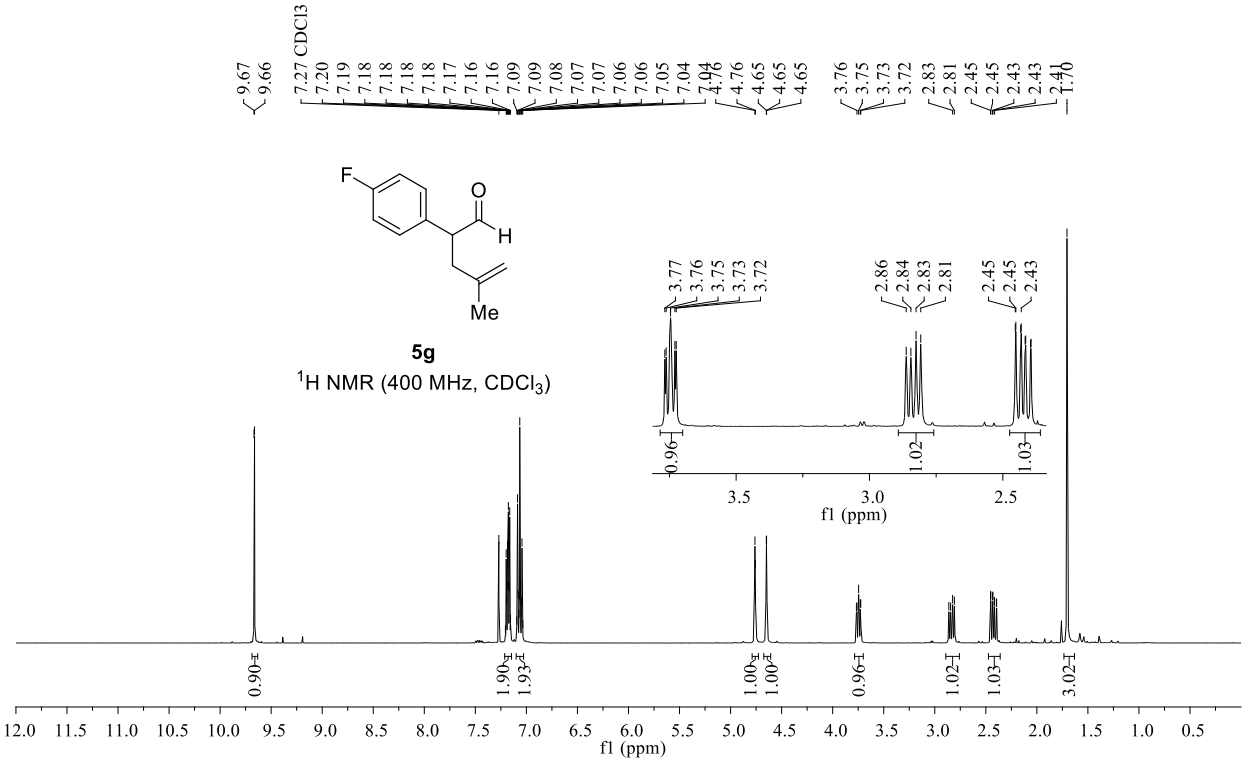

200.26
142.10
128.96
128.03
127.89
127.86
126.55
126.29
115.08
77.16 CDCl3
57.45
37.76
22.80
133.74
133.54
132.90
O
H
Me
5d
13C NMR (101 MHz, CDCl3)
fl (ppm)

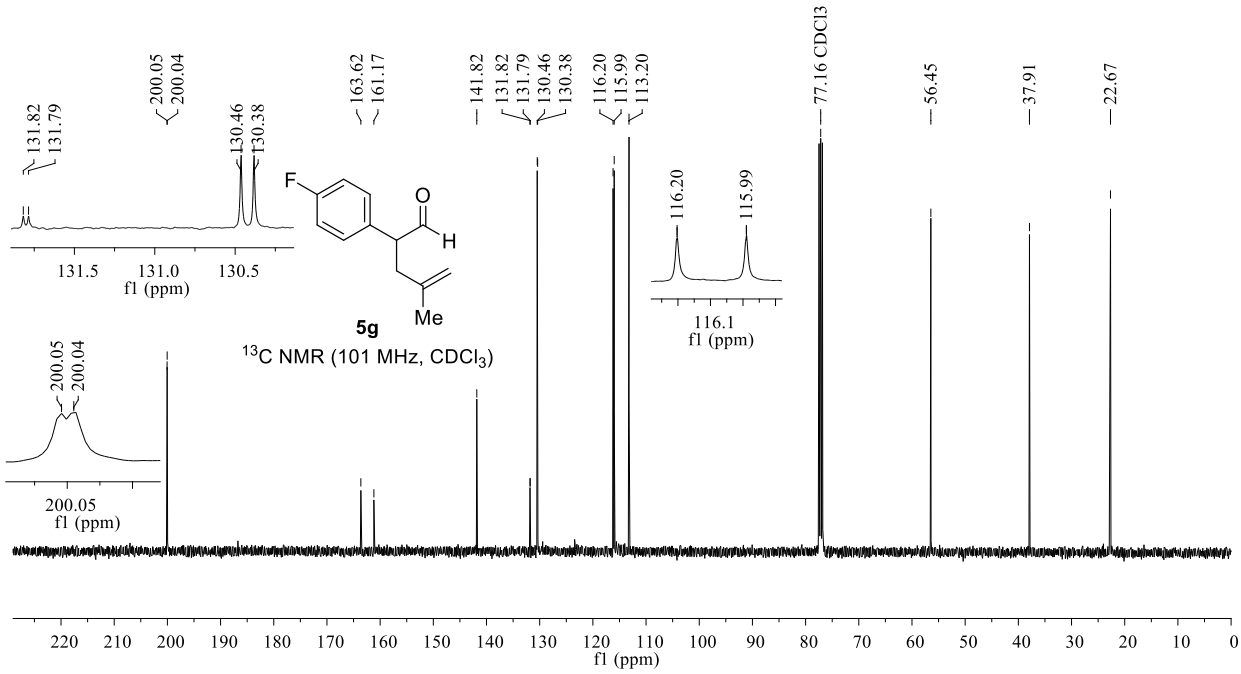

9.67
9.66
7.37
7.36
7.36
7.34
7.34
7.33
7.27 CDCl3
7.17
7.17
7.16
7.15
7.14
7.14
7.14
7.13
4.76
4.76
4.65
3.74
3.74
3.74
3.72
3.72
2.82
2.81
2.46
2.45
2.44
2.43
2.42
1.70
Cl
O
H
Me
5e
1H NMR (400 MHz, CDCl3)
0.87
2.04
2.03
1.00
1.01
1.01
1.07
1.09
3.15
fl (ppm)

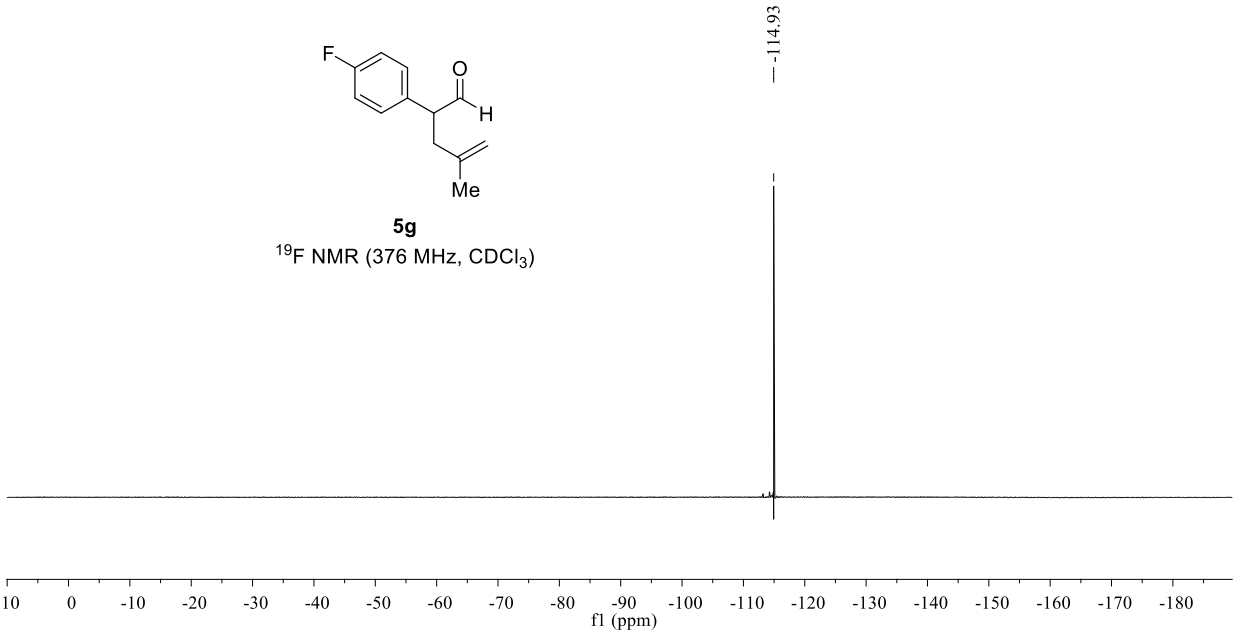

199.83
141.68
134.59
133.78
130.21
129.34
113.32
77.16 CDCl3
56.60
37.79
22.68
Cl
O
H
Me
5e
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

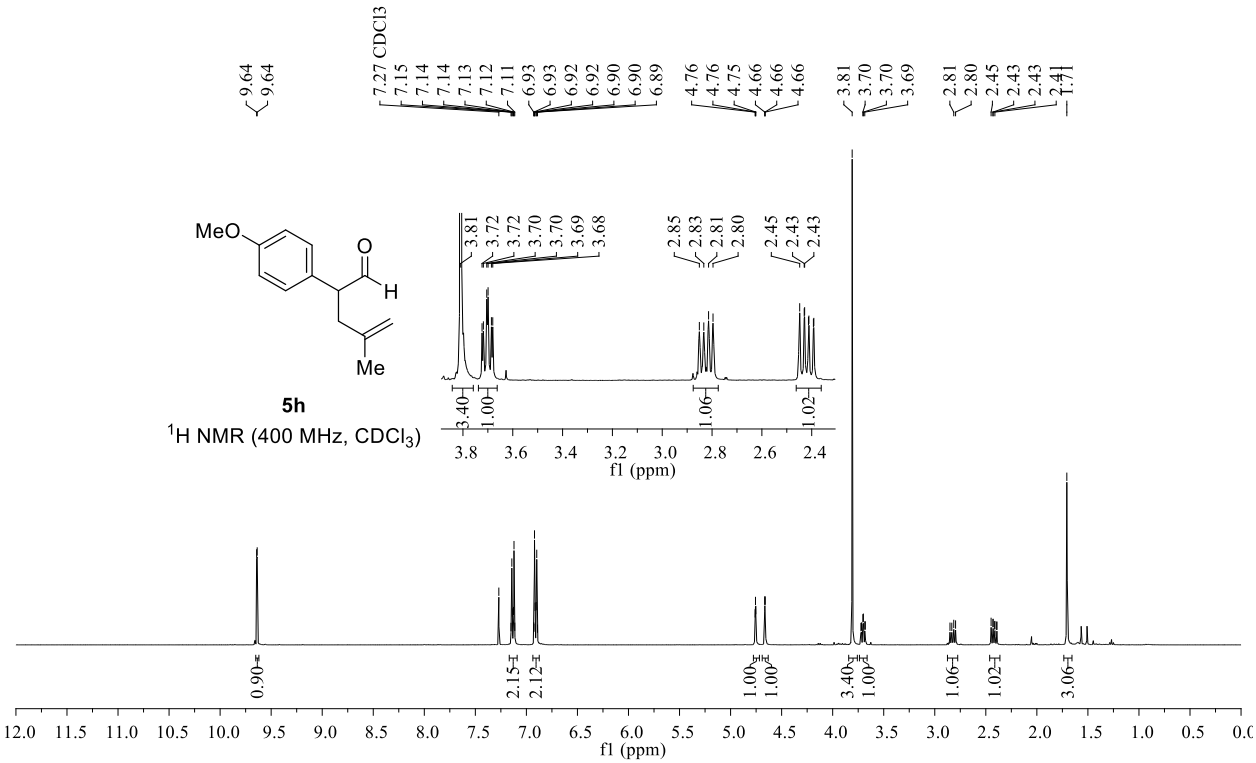

9.66
9.66
7.52
7.51
7.51
7.50
7.49
7.49
7.27 CDCl3
7.11
7.10
7.10
7.08
7.08
7.07
4.76
4.65
3.74
3.73
3.72
3.71
3.70
2.86
2.82
2.80
2.45
2.43
2.42
1.70
Br
O
H
Me
5f
1H NMR (400 MHz, CDCl3)
3.75
3.74
3.73
3.72
3.71
3.70
2.86
2.84
2.82
2.80
2.45
2.43
2.42
0.98
1.04
1.02
3.5
3.0
2.5
f1 (ppm)
0.87
1.96
1.94
1.00
0.98
0.98
1.04
1.02
3.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

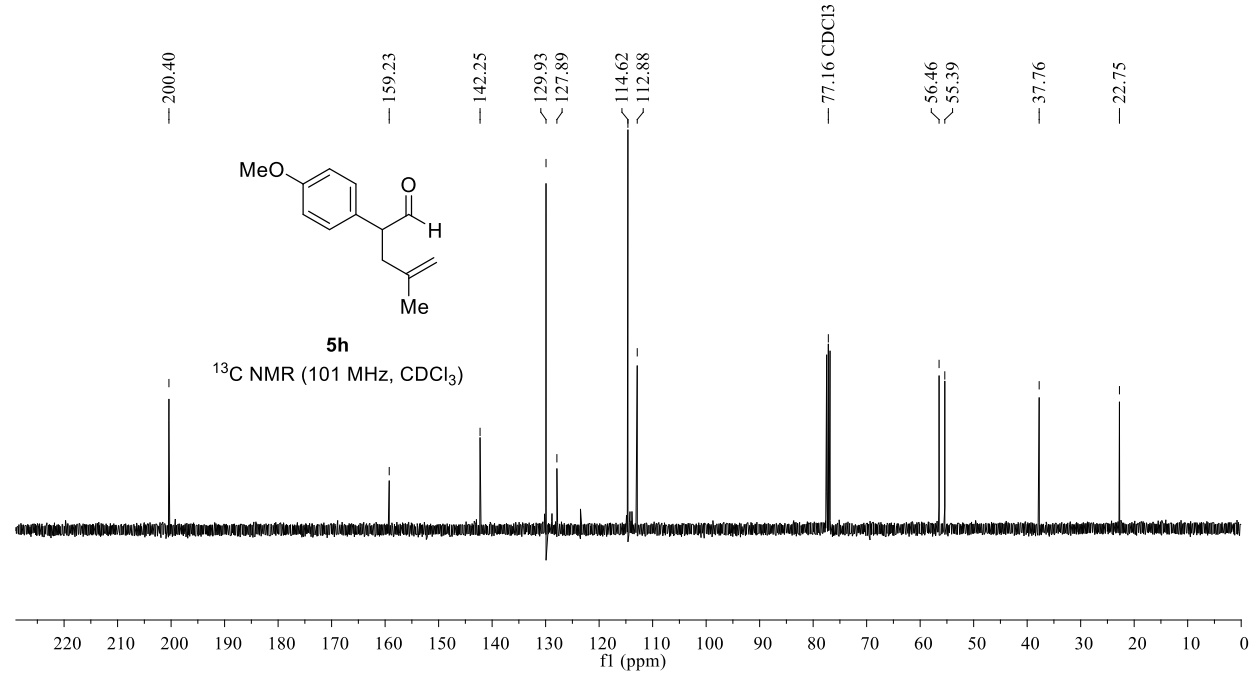

199.74
141.64
135.12
132.30
130.56
121.88
113.35
77.16 CDCl3
56.67
37.75
22.68
Br
O
H
Me
5f
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

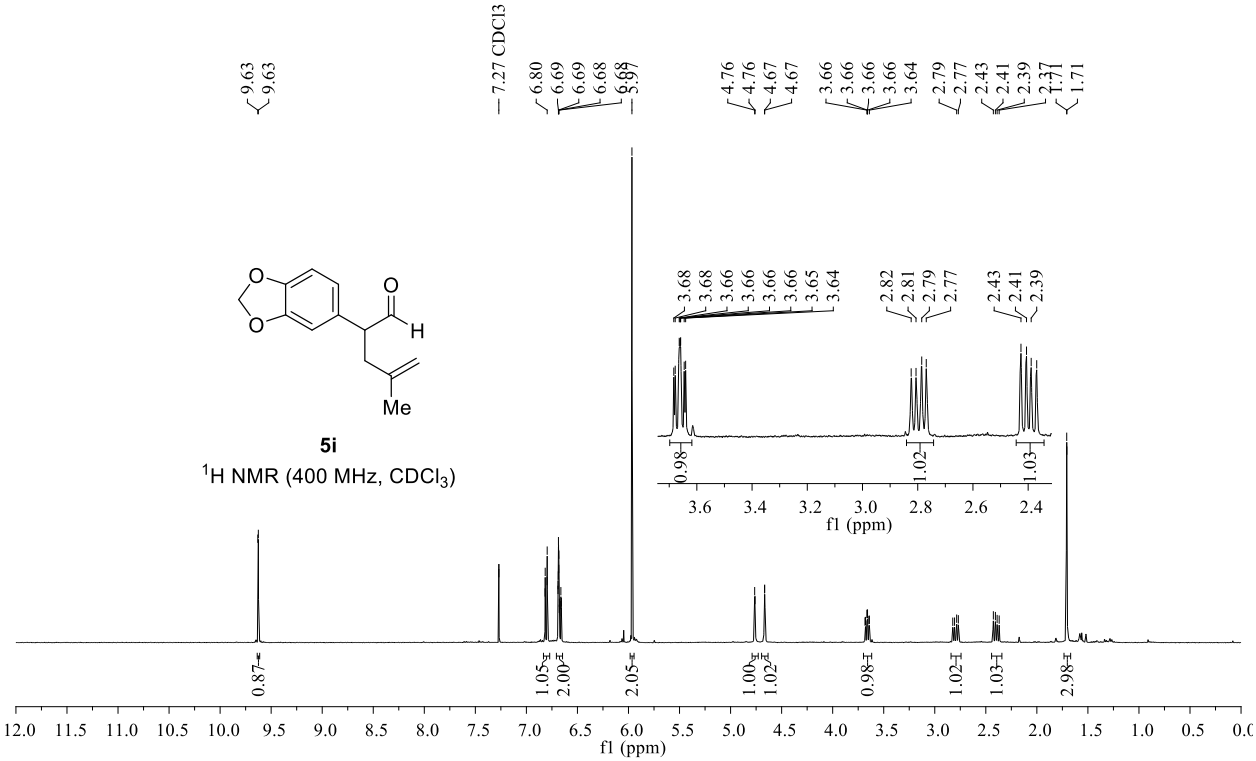

9.67
9.66
7.27 CDCl3
7.20
7.19
7.18
7.18
7.18
7.18
7.17
7.16
7.16
7.09
7.09
7.08
7.07
7.07
7.06
7.06
7.05
7.04
4.76
4.65
4.65
4.65
3.76
3.75
3.73
3.72
2.83
2.81
2.45
2.43
2.43
1.70
F
O
H
Me
5g
1H NMR (400 MHz, CDCl3)
3.77
3.76
3.75
3.73
3.72
2.86
2.84
2.83
2.81
2.45
2.45
2.43
0.96
1.02
1.03
3.5
3.0
2.5
f1 (ppm)
0.90
1.90
1.93
1.00
1.00
0.96
1.02
1.03
3.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

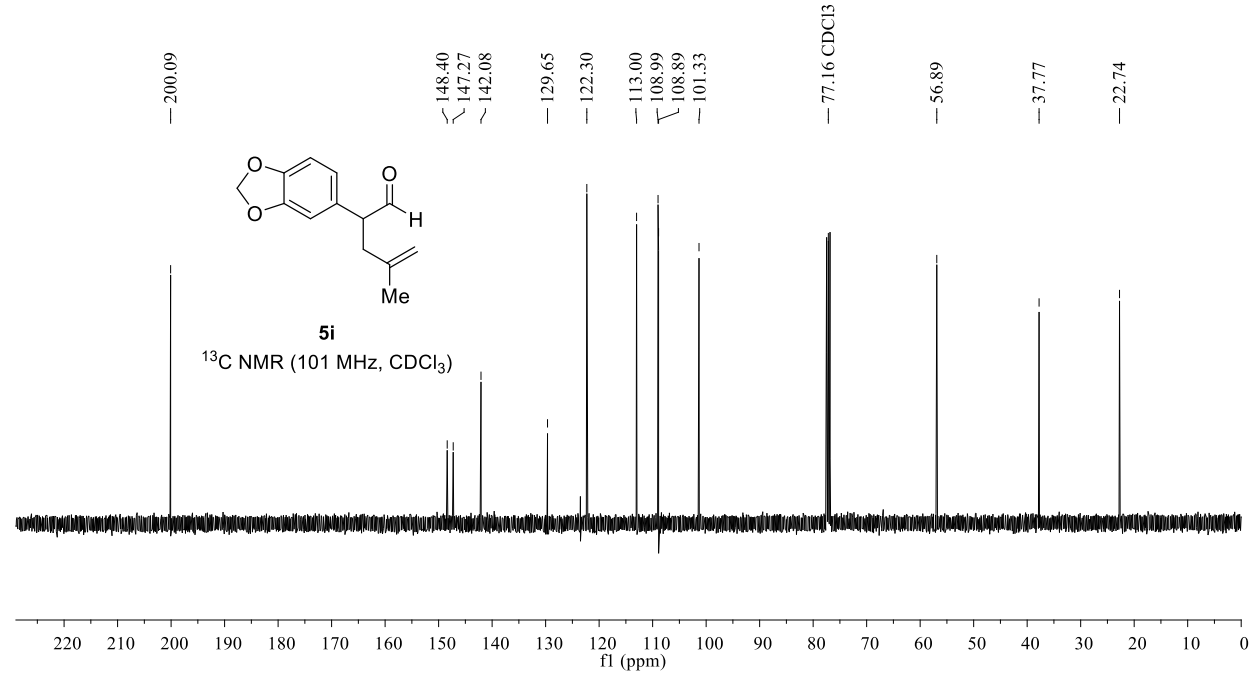

131.82
131.79
200.05
200.04
130.46
130.38
163.62
161.17
141.82
131.82
131.79
130.46
130.38
116.20
115.99
113.20
77.16 CDCl3
56.45
37.91
22.67
F
O
H
Me
5g
13C NMR (101 MHz, CDCl3)
131.5
131.0
130.5
f1 (ppm)
116.20
115.99
116.1
f1 (ppm)
200.05
200.04
200.05
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

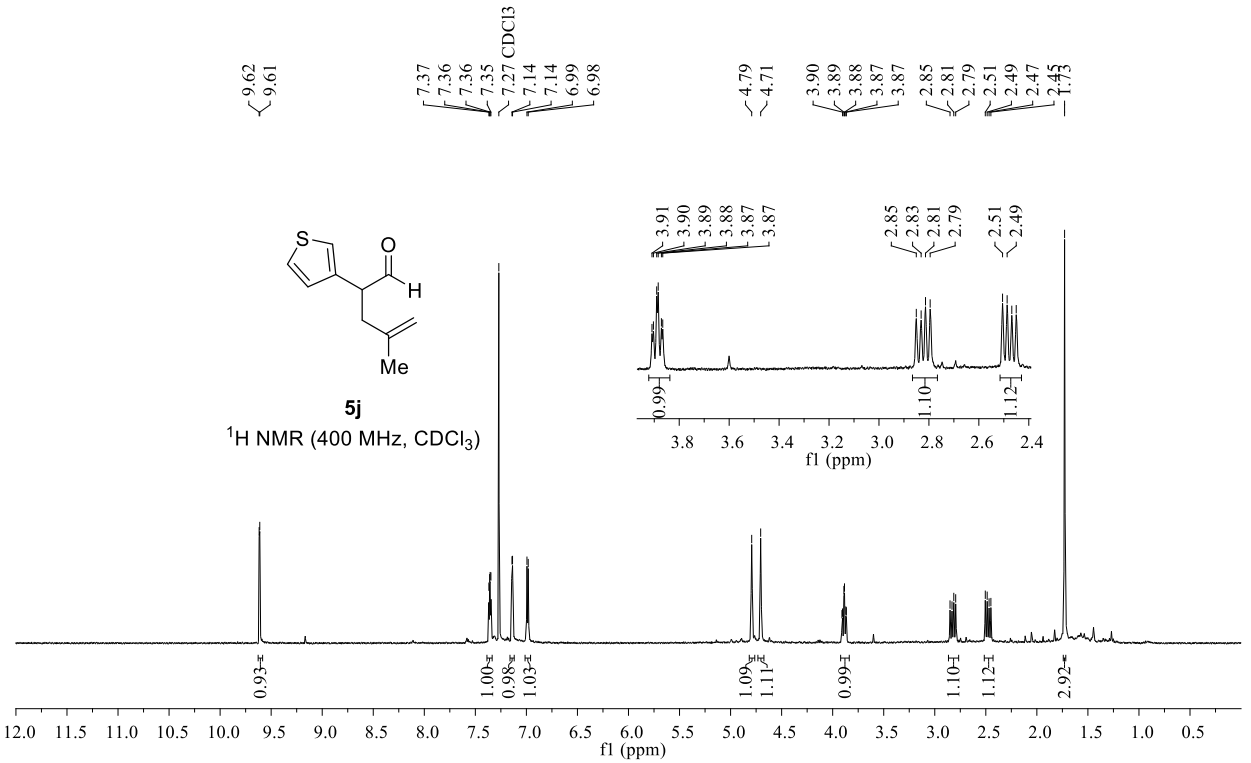

F
O
H
Me
5g
19F NMR (376 MHz, CDCl3)
-114.93
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)

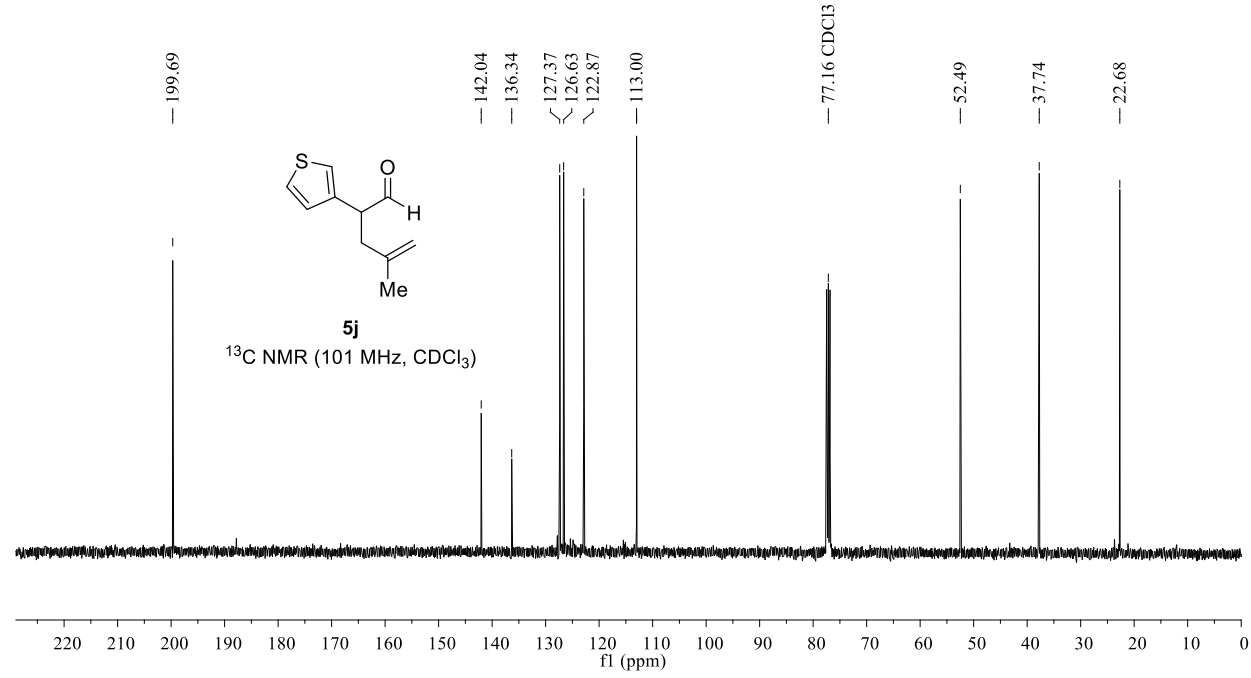

MeO
O
H
Me
5h
1H NMR (400 MHz, CDCl3)
f1 (ppm)

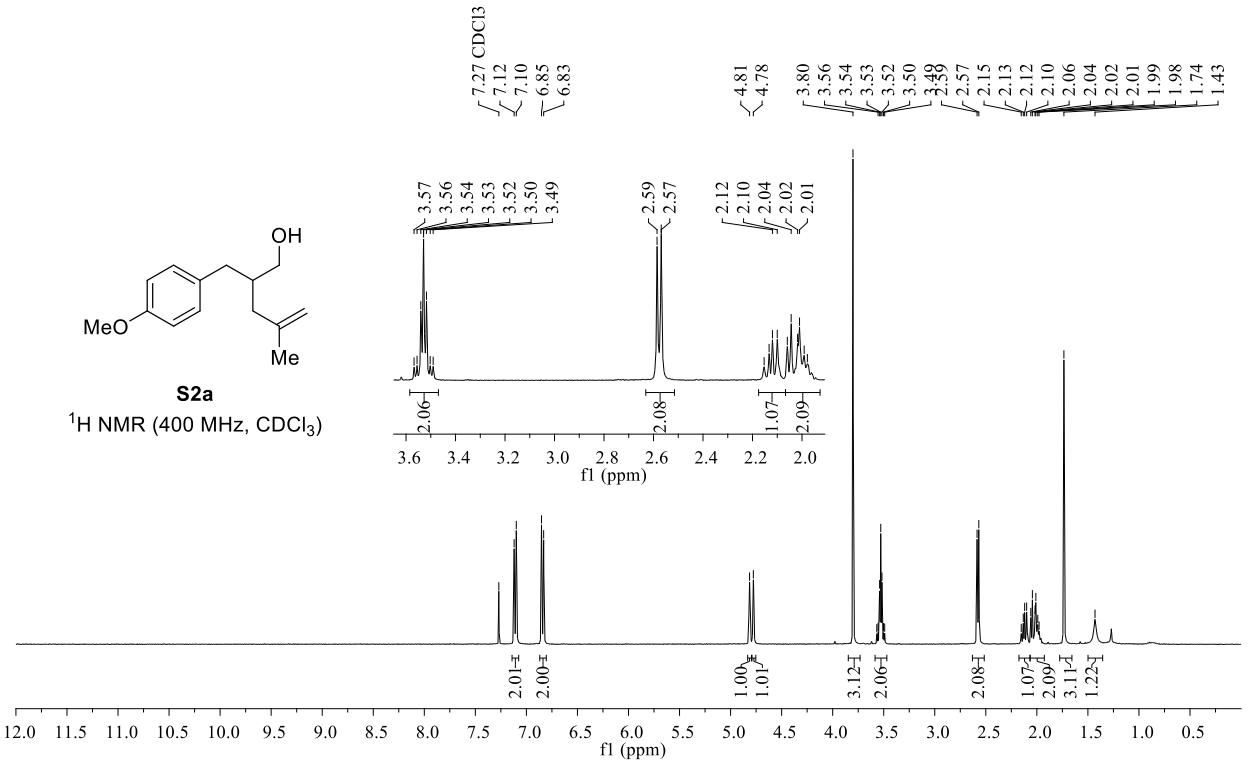

MeO
O
H
Me
5h
13C NMR (101 MHz, CDCl3)
f1 (ppm)

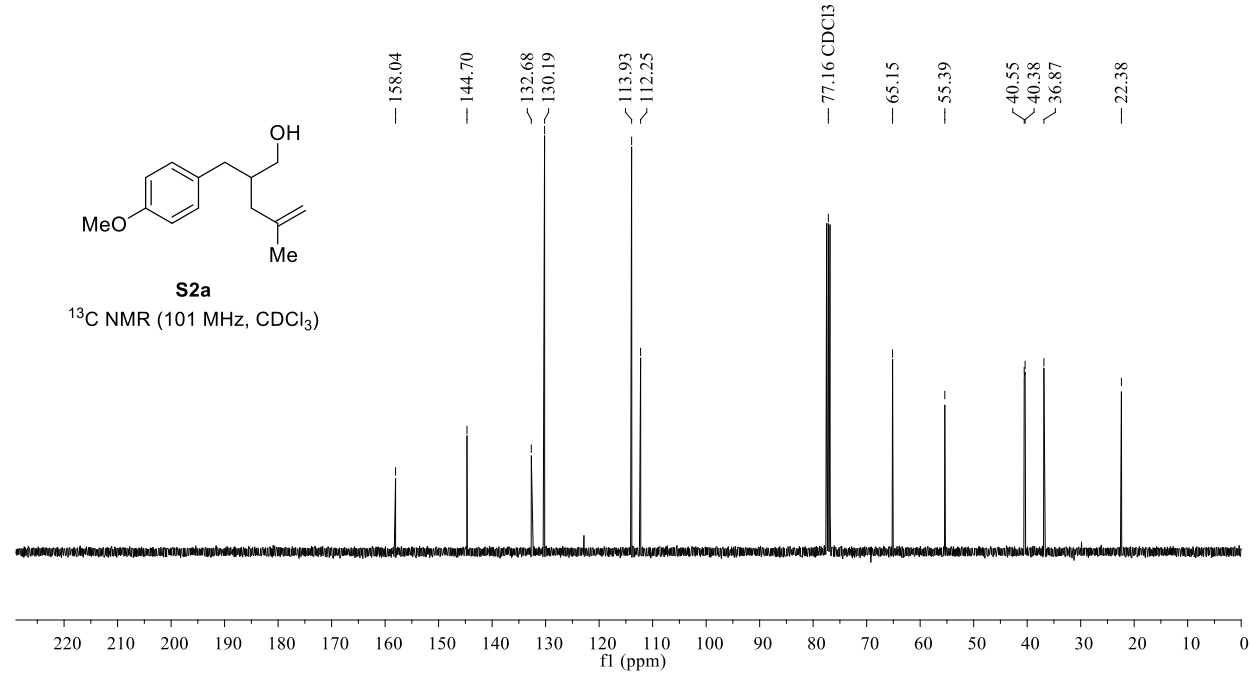

9.63
9.63
7.27 CDCl3
6.80
6.69
6.69
6.68
6.68
5.99
4.76
4.76
4.67
4.67
3.66
3.66
3.66
3.66
3.64
2.79
2.77
2.43
2.41
2.39
1.71
1.71
O
O
O
H
Me
5i
1H NMR (400 MHz, CDCl3)
0.87
1.05
2.00
2.05
1.00
1.02
0.98
1.02
1.03
2.98
f1 (ppm)

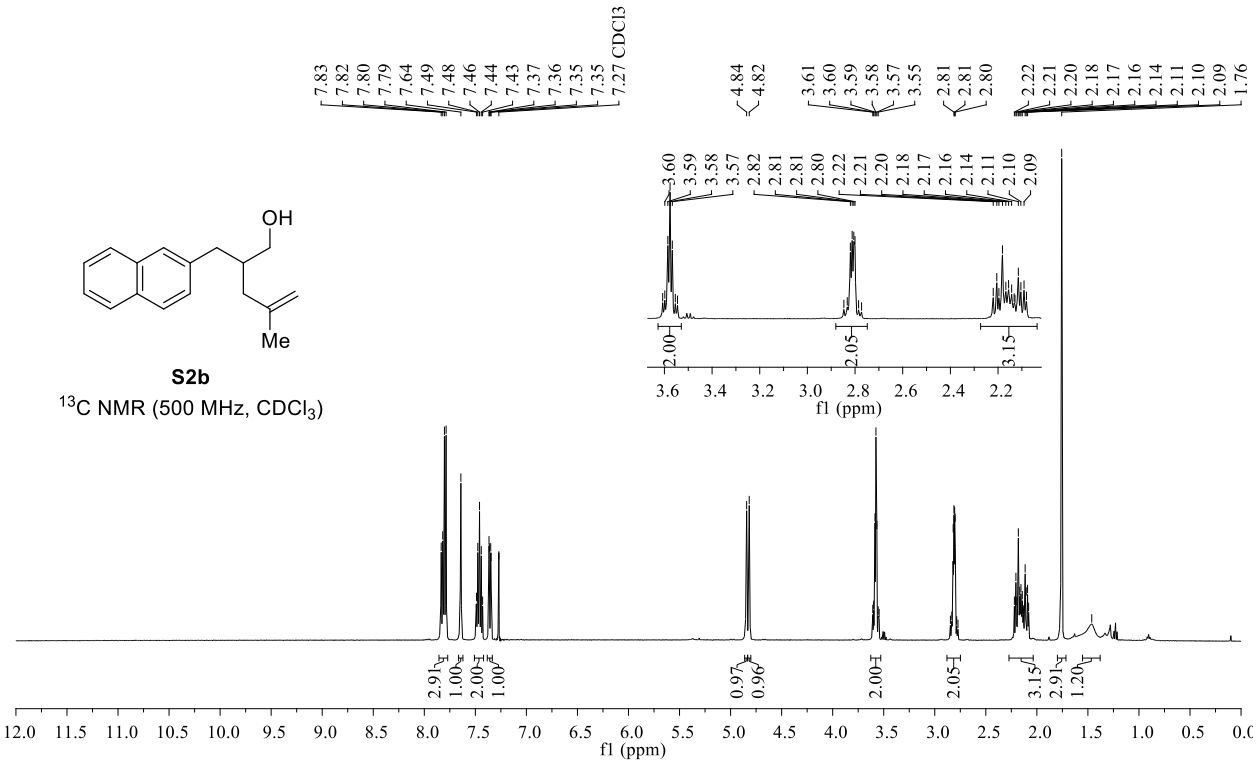

200.09
148.40
147.27
142.08
129.65
122.30
113.00
108.99
108.89
101.33
77.16 CDCl3
56.89
37.77
22.74
O
O
O
H
Me
5i
13C NMR (101 MHz, CDCl3)
f1 (ppm)

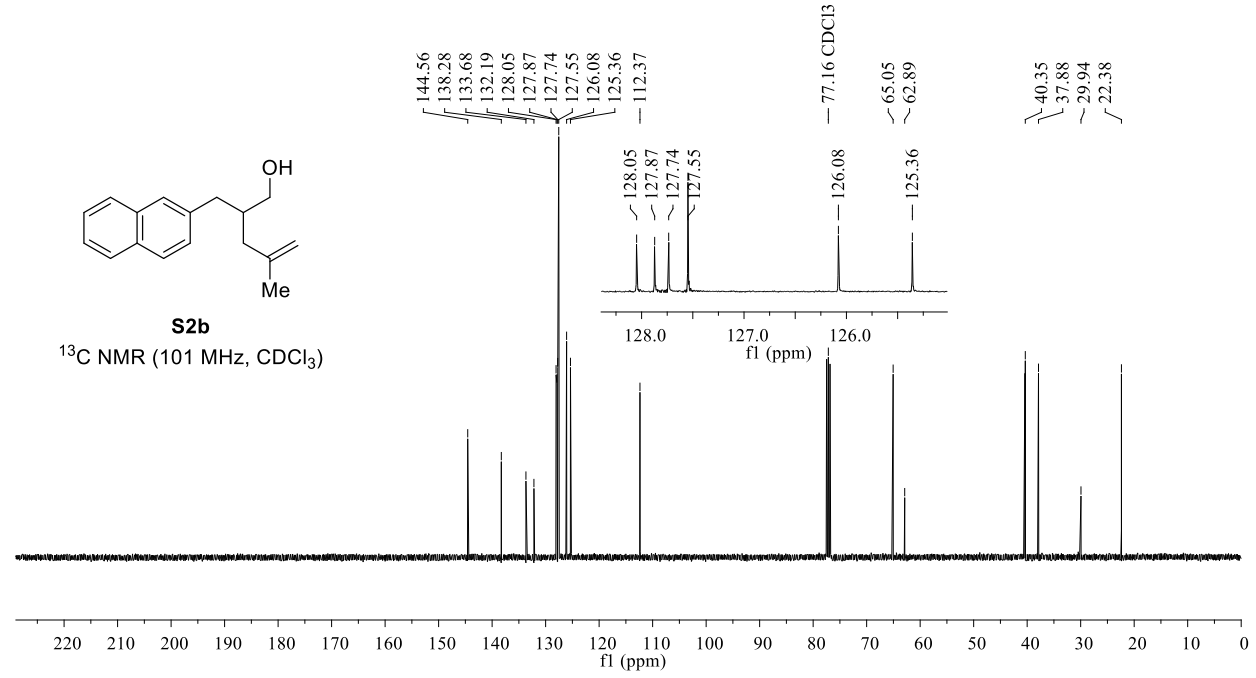

9.62
9.61
7.37
7.36
7.36
7.35
7.27 CDCl3
7.14
7.14
6.99
6.98
4.79
4.71
3.90
3.89
3.88
3.87
3.87
2.85
2.81
2.79
2.51
2.49
2.47
2.45
1.73
S
O
H
Me
5j
1H NMR (400 MHz, CDCl3)
0.93
1.00
0.98
1.03
1.09
1.11
0.99
1.10
1.12
2.92
f1 (ppm)

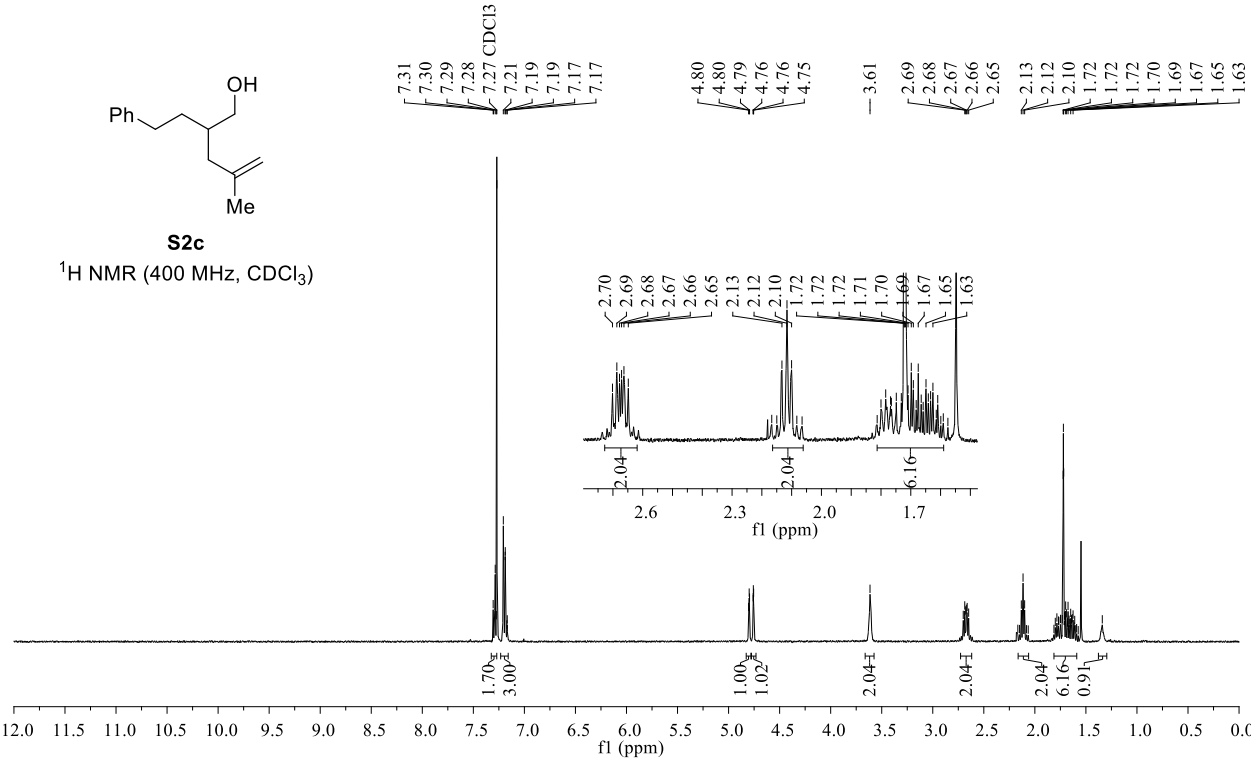

199.69
142.04
136.34
127.37
126.63
122.87
113.00
77.16 CDCl3
52.49
37.74
22.68
S
O
H
Me
5j
13C NMR (101 MHz, CDCl3)
f1 (ppm)

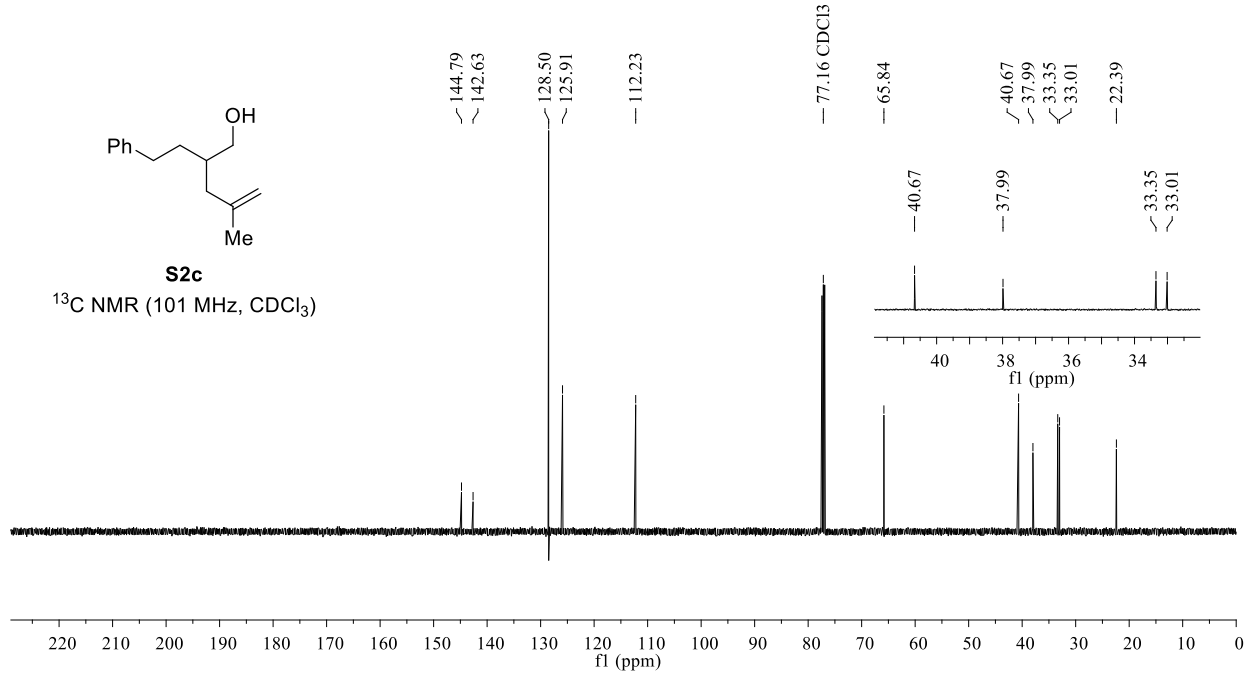

OH
MeO
Me
S2a
1H NMR (400 MHz, CDCl3)
f1 (ppm)

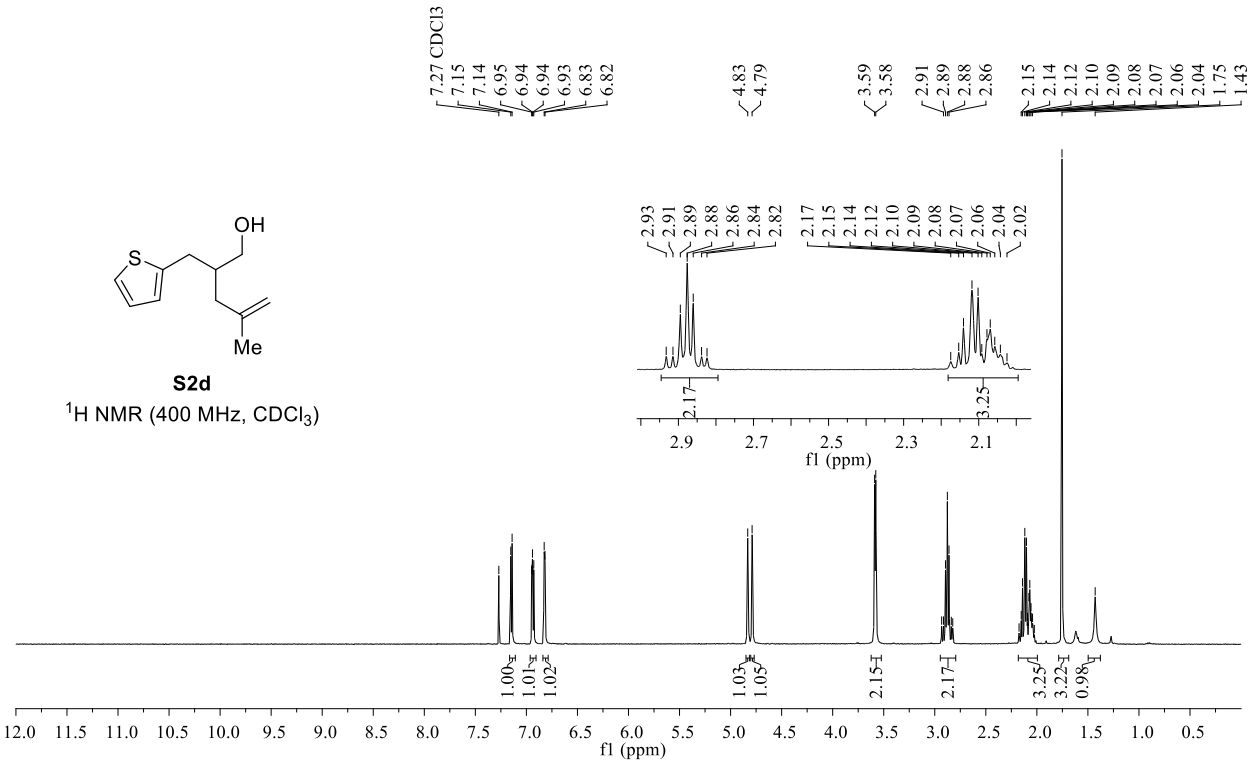

OH
MeO
Me
S2a
13C NMR (101 MHz, CDCl3)
f1 (ppm)

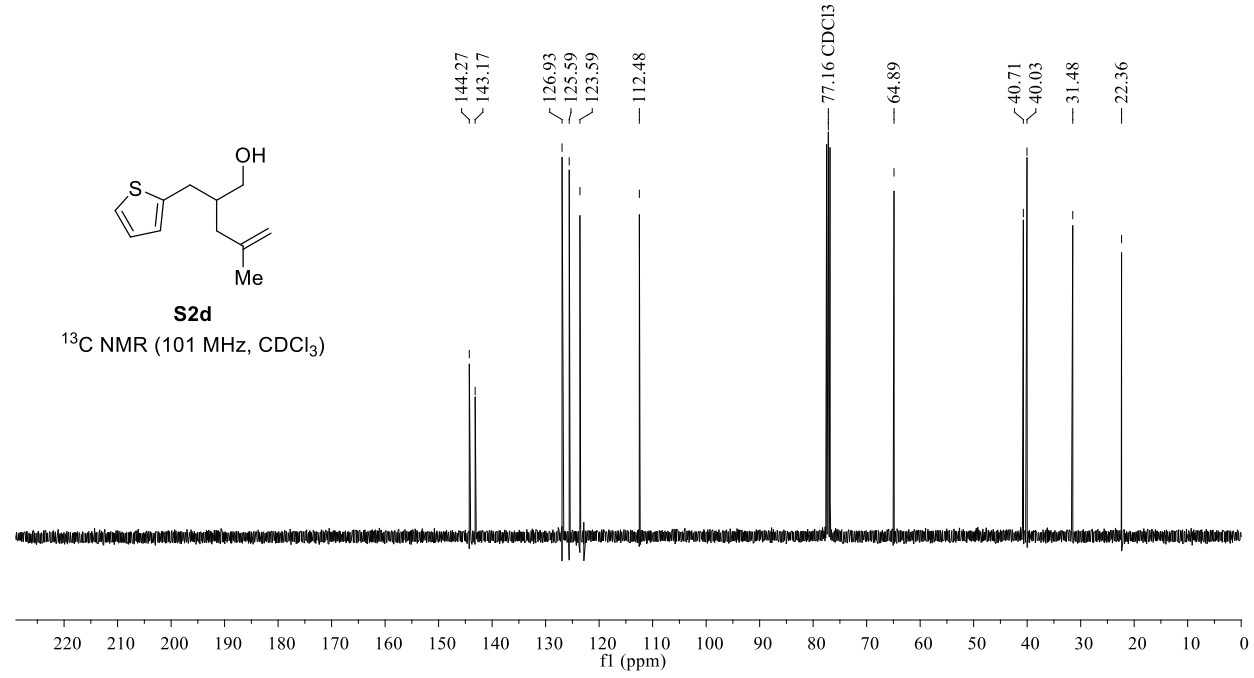

OH
Me
S2b
13C NMR (500 MHz, CDCl3)
f1 (ppm)

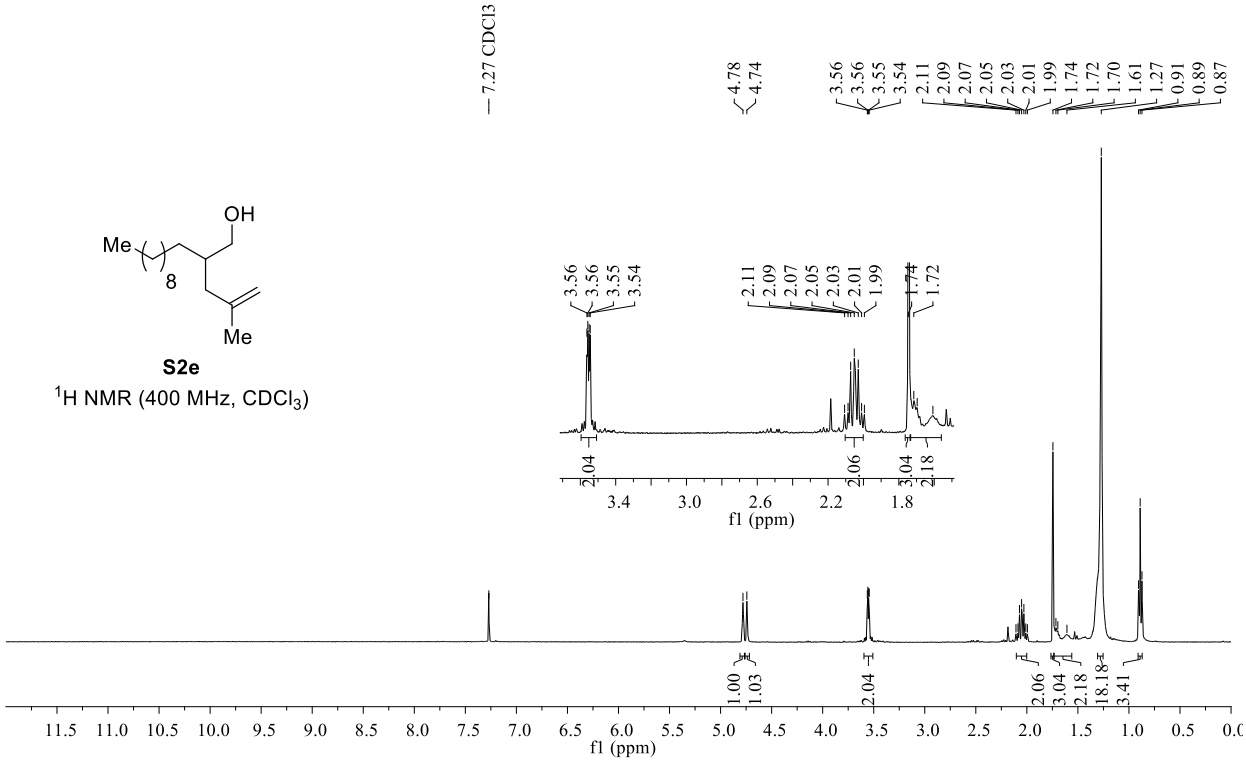

OH
Me
S2b
13C NMR (101 MHz, CDCl3)
f1 (ppm)

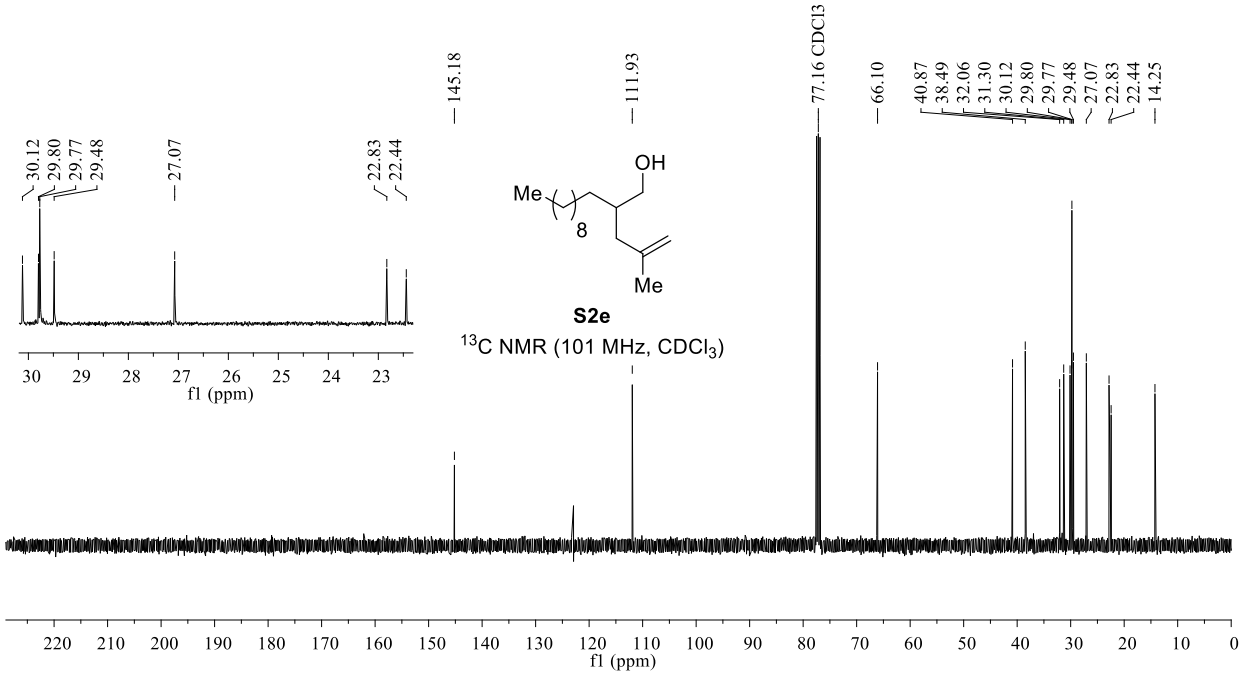

OH
Ph
Me
S2c
1H NMR (400 MHz, CDCl3)
7.31
7.30
7.29
7.28
7.27 CDCl3
7.21
7.19
7.19
7.17
7.17
4.80
4.80
4.79
4.76
4.76
4.75
3.61
2.69
2.68
2.67
2.66
2.65
2.13
2.12
2.10
1.72
1.72
1.72
1.70
1.69
1.67
1.65
1.63
2.04
2.04
6.16
2.6
2.3
2.0
1.7
f1 (ppm)
1.70
3.00
1.00
1.02
2.04
2.04
2.04
6.16
0.91
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

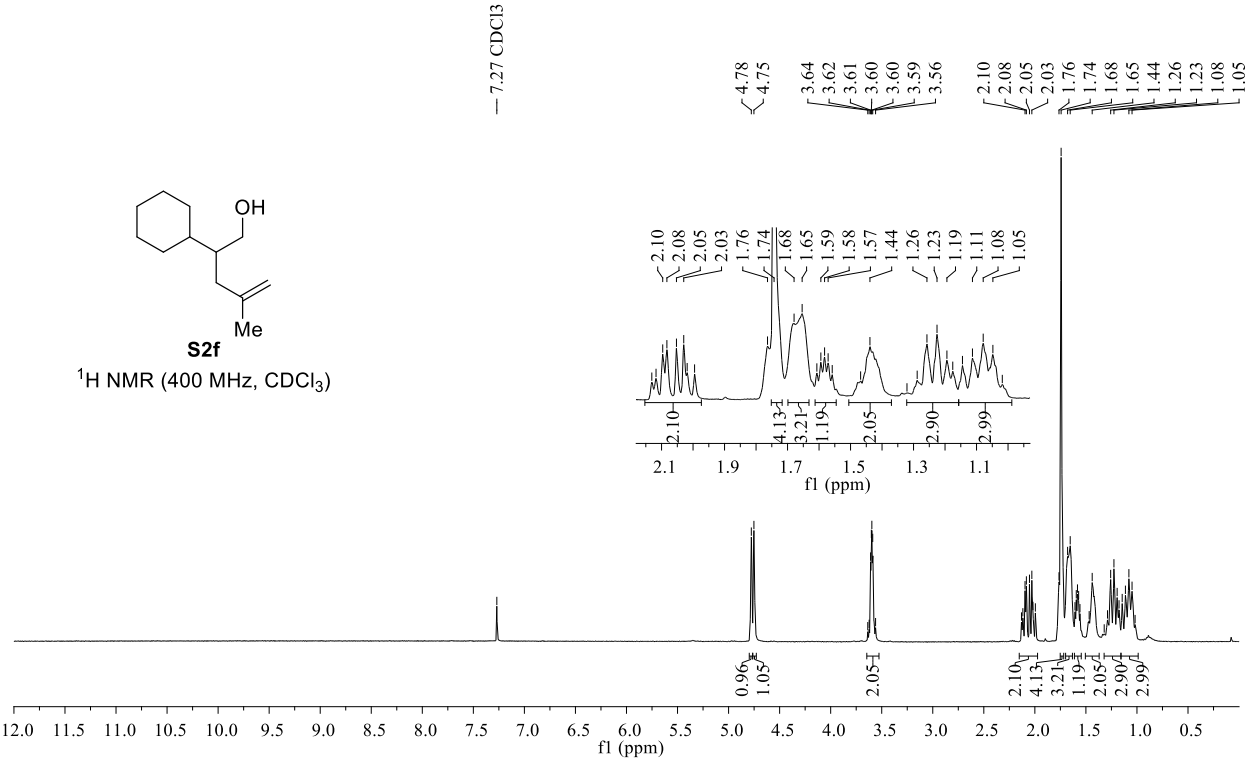

OH
Ph
Me
S2c
13C NMR (101 MHz, CDCl3)
144.79
142.63
128.50
125.91
112.23
77.16 CDCl3
65.84
40.67
37.99
33.35
33.01
22.39
40.67
37.99
33.35
33.01
40
38
36
34
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

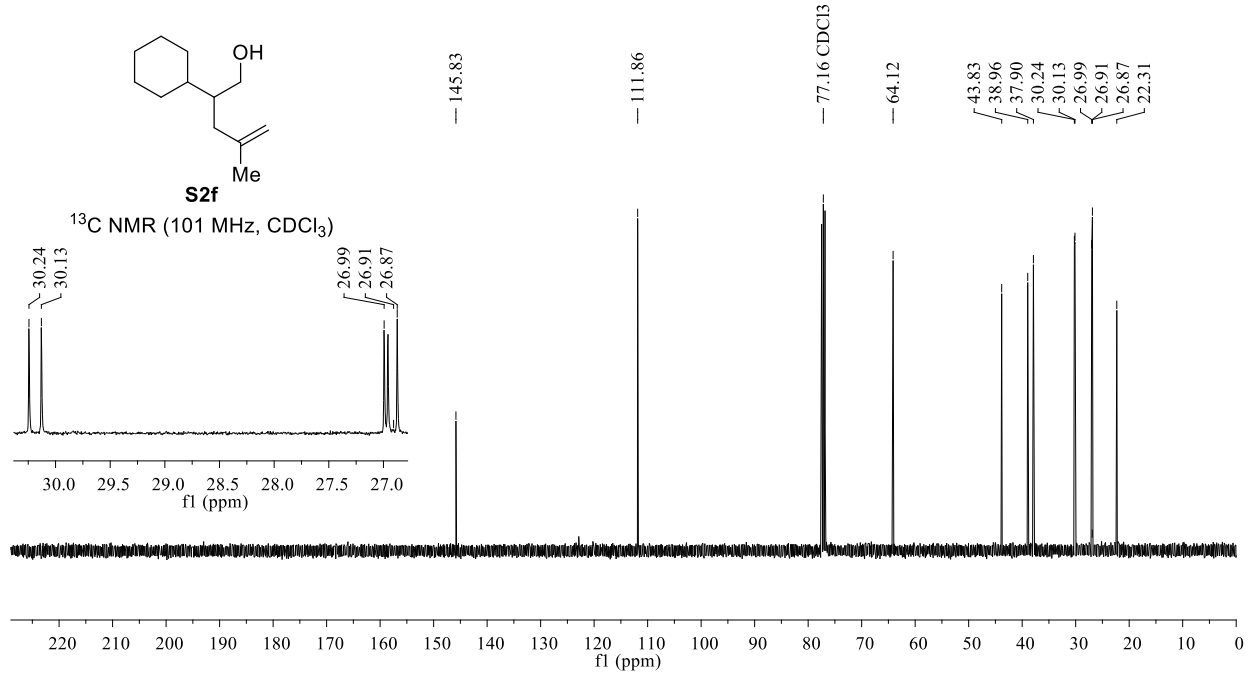

7.27 CDCl3
7.15
7.14
6.95
6.94
6.94
6.93
6.83
6.82
4.83
4.79
3.59
3.58
2.91
2.89
2.88
2.86
2.15
2.14
2.12
2.10
2.09
2.08
2.07
2.06
2.04
1.75
1.43
2.93
2.91
2.89
2.88
2.86
2.84
2.82
2.17
2.15
2.14
2.12
2.10
2.09
2.08
2.07
2.06
2.04
2.02
2.17
3.25
2.9
2.7
2.5
2.3
2.1
f1 (ppm)
OH
S
Me
S2d
1H NMR (400 MHz, CDCl3)
1.00
1.01
1.02
1.03
1.05
2.15
2.17
3.25
3.22
0.98
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

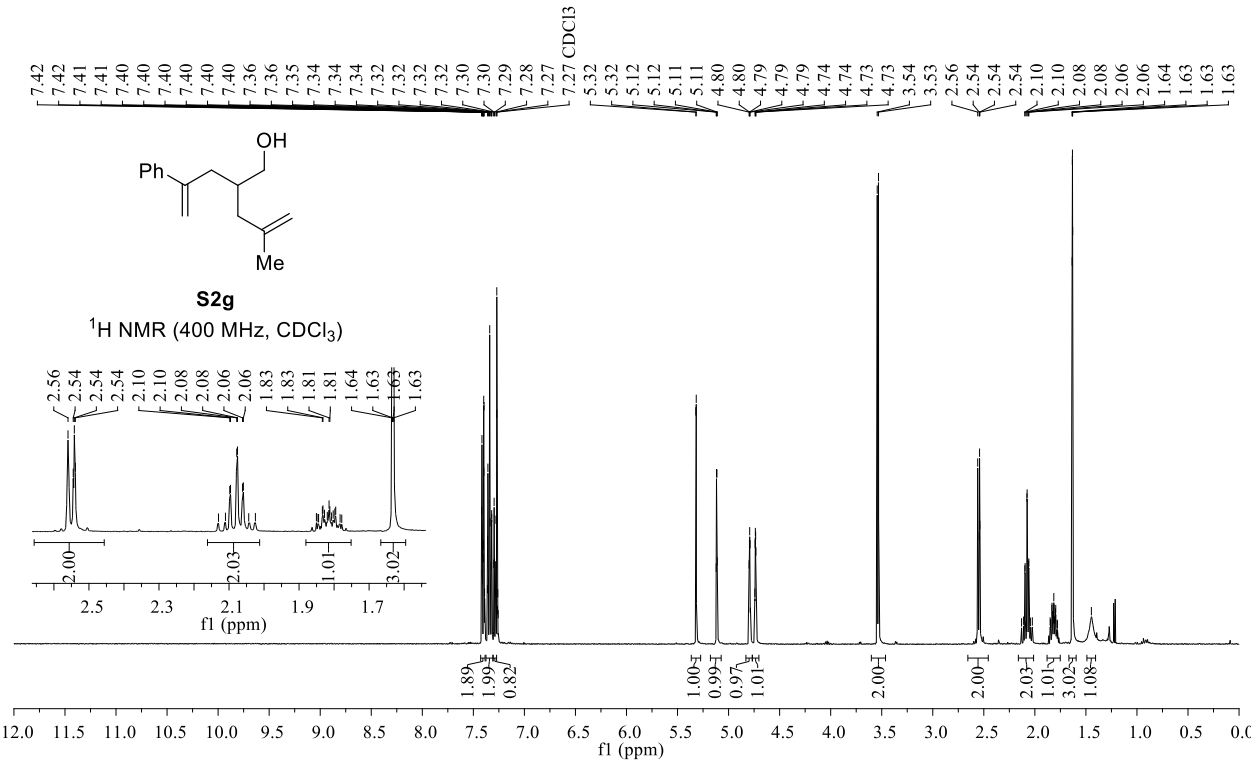

144.27
143.17
126.93
125.59
123.59
112.48
77.16 CDCl3
64.89
40.71
40.03
31.48
22.36
OH
S
Me
S2d
13C NMR (101 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

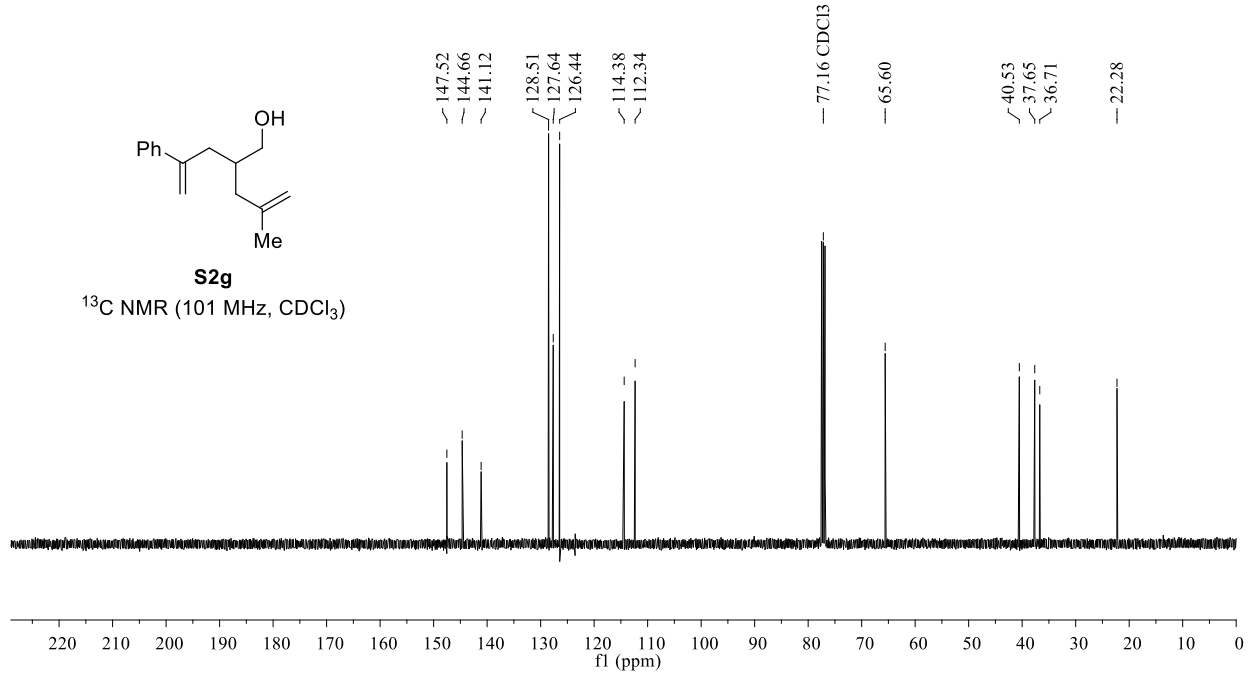

7.27 CDCl3
4.78
4.74
3.56
3.56
3.55
3.54
2.11
2.09
2.07
2.05
2.03
2.01
1.99
1.74
1.72
1.70
1.61
1.27
0.91
0.89
0.87
OH
Me
8
Me
S2e
1H NMR (400 MHz, CDCl3)
2.04
2.06
3.04
2.18
f1 (ppm)
1.00
1.03
2.04
2.06
3.04
2.18
18.18
3.41
f1 (ppm)

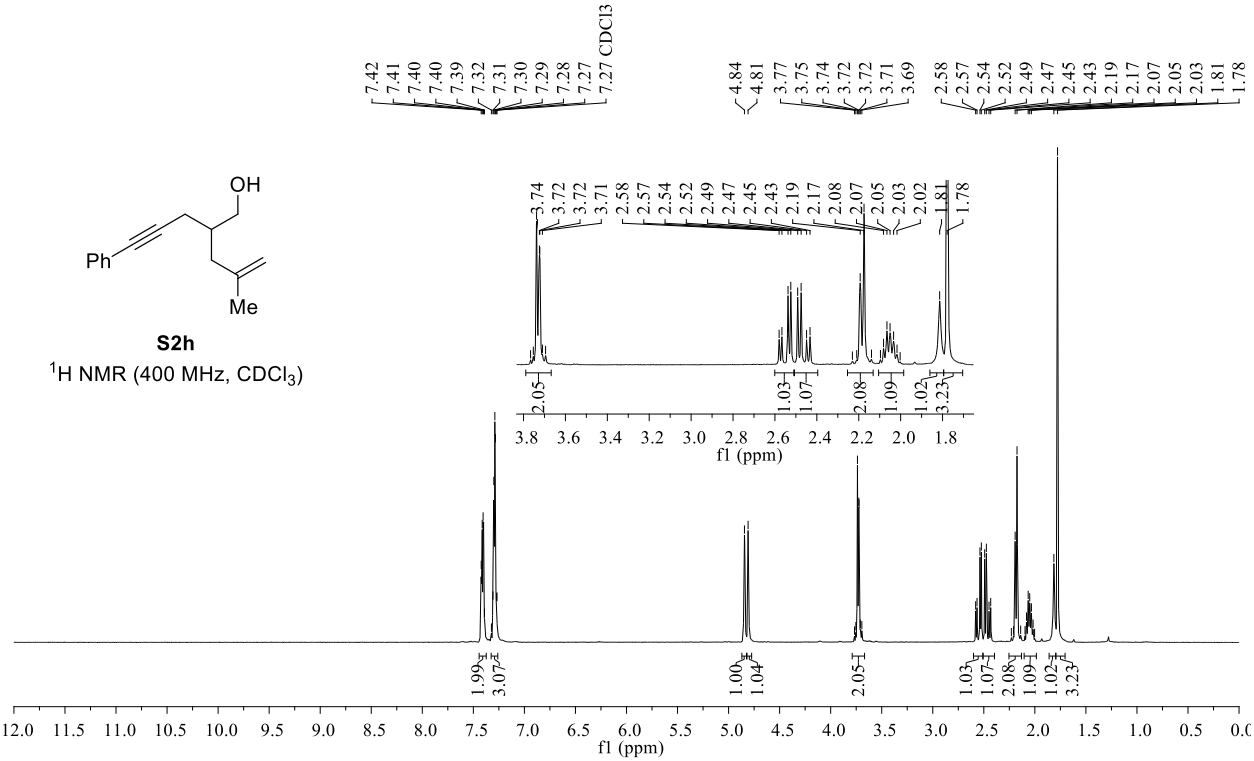

145.18
111.93
77.16 CDCl3
66.10
40.87
38.49
32.06
31.30
30.12
29.80
29.77
29.48
27.07
22.83
22.44
14.25
30.12
29.80
29.77
29.48
27.07
22.83
22.44
OH
Me
8
Me
S2e
13C NMR (101 MHz, CDCl3)
f1 (ppm)
f1 (ppm)

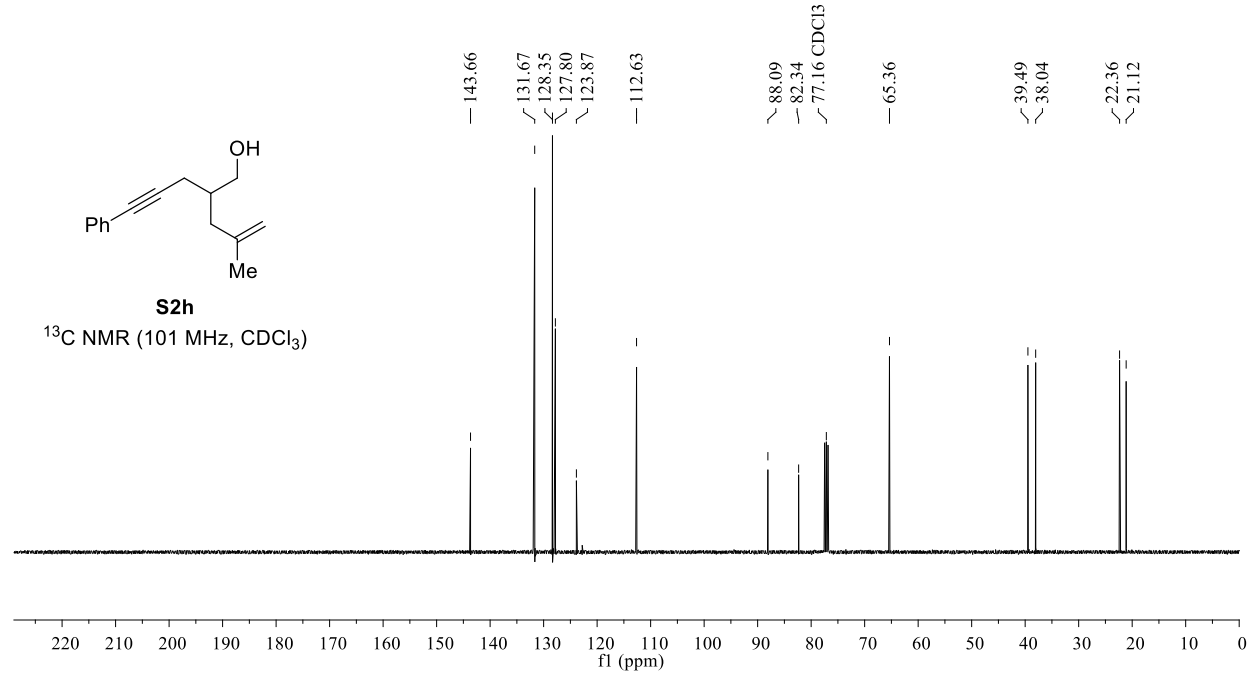

OH
Me
S2f
$^1$H NMR (400 MHz, $CDCl_3$)
7.27 CDCl3
4.78
4.75
3.64
3.62
3.61
3.60
3.60
3.59
3.56
2.10
2.08
2.05
2.03
1.76
1.74
1.68
1.65
1.44
1.26
1.23
1.08
1.05
0.96
1.05
2.05
2.10
4.13
3.21
1.19
2.05
2.90
2.99
f1 (ppm)

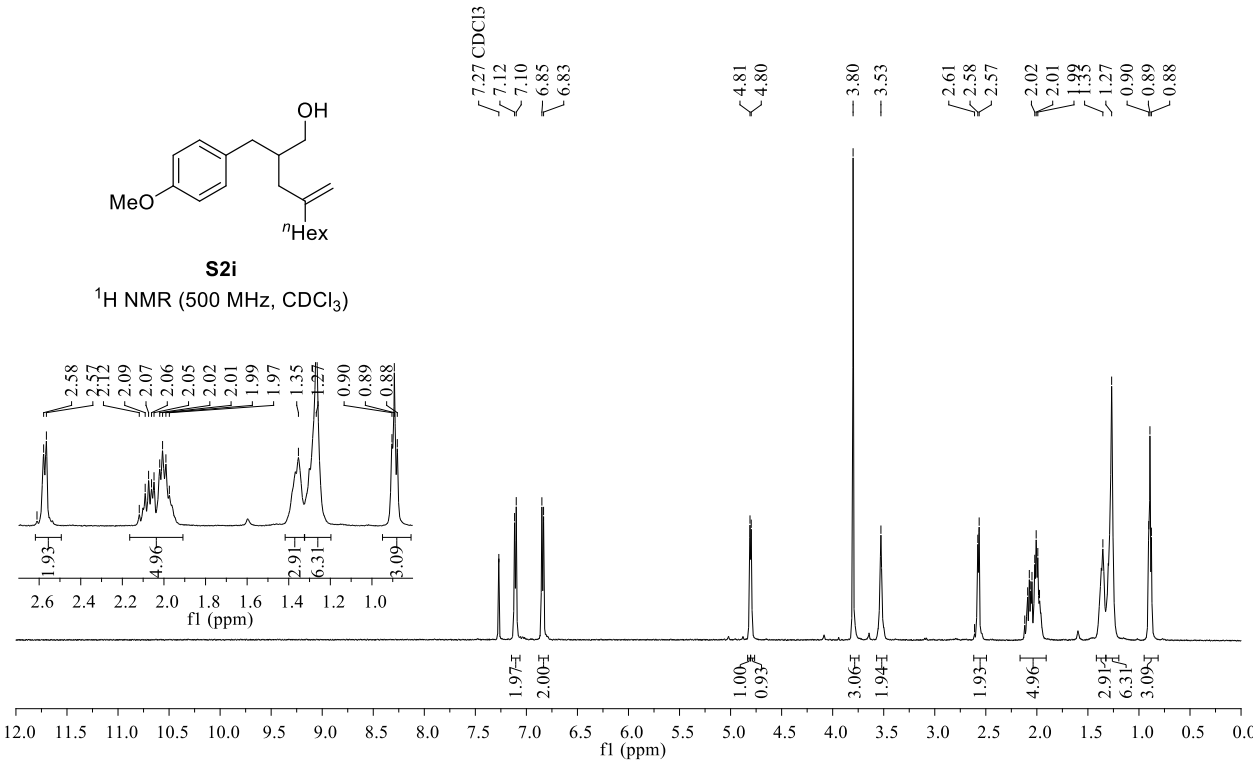

OH
Me
S2f
$^{13}$C NMR (101 MHz, $CDCl_3$)
145.83
111.86
77.16 CDCl3
64.12
43.83
38.96
37.90
30.24
30.13
26.99
26.91
26.87
22.31
f1 (ppm)

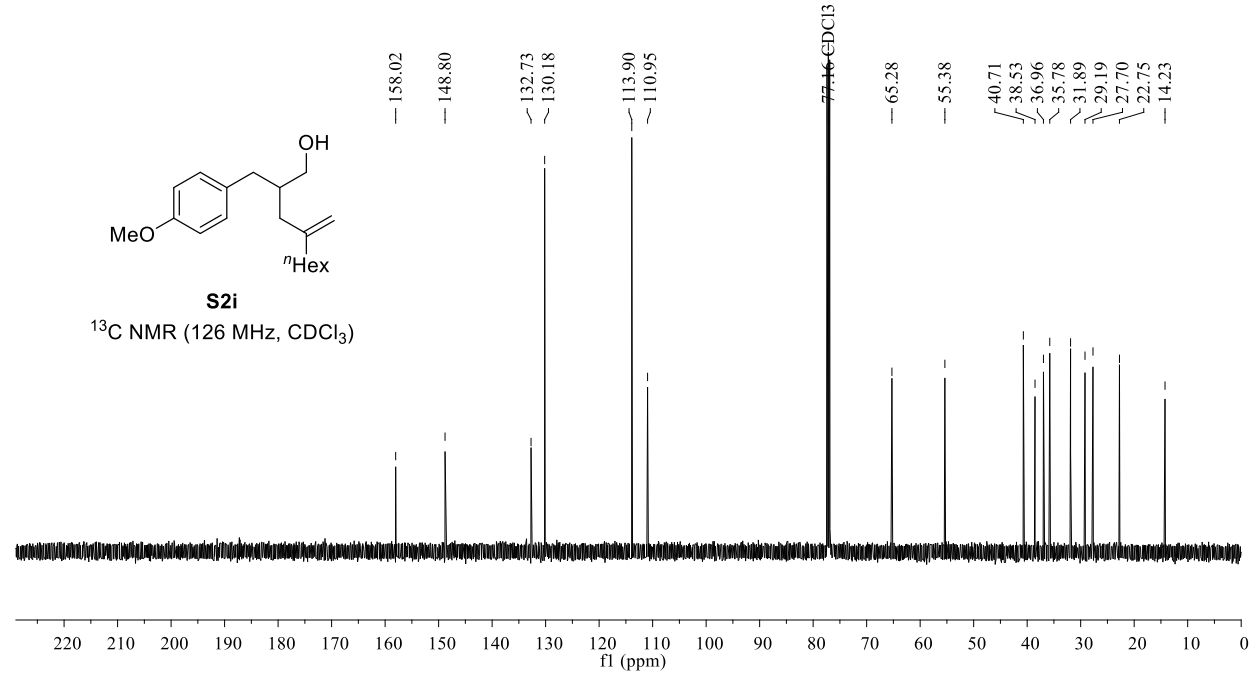

OH
Ph
Me
S2g
1H NMR (400 MHz, CDCl3)
CDCl3
fl (ppm)

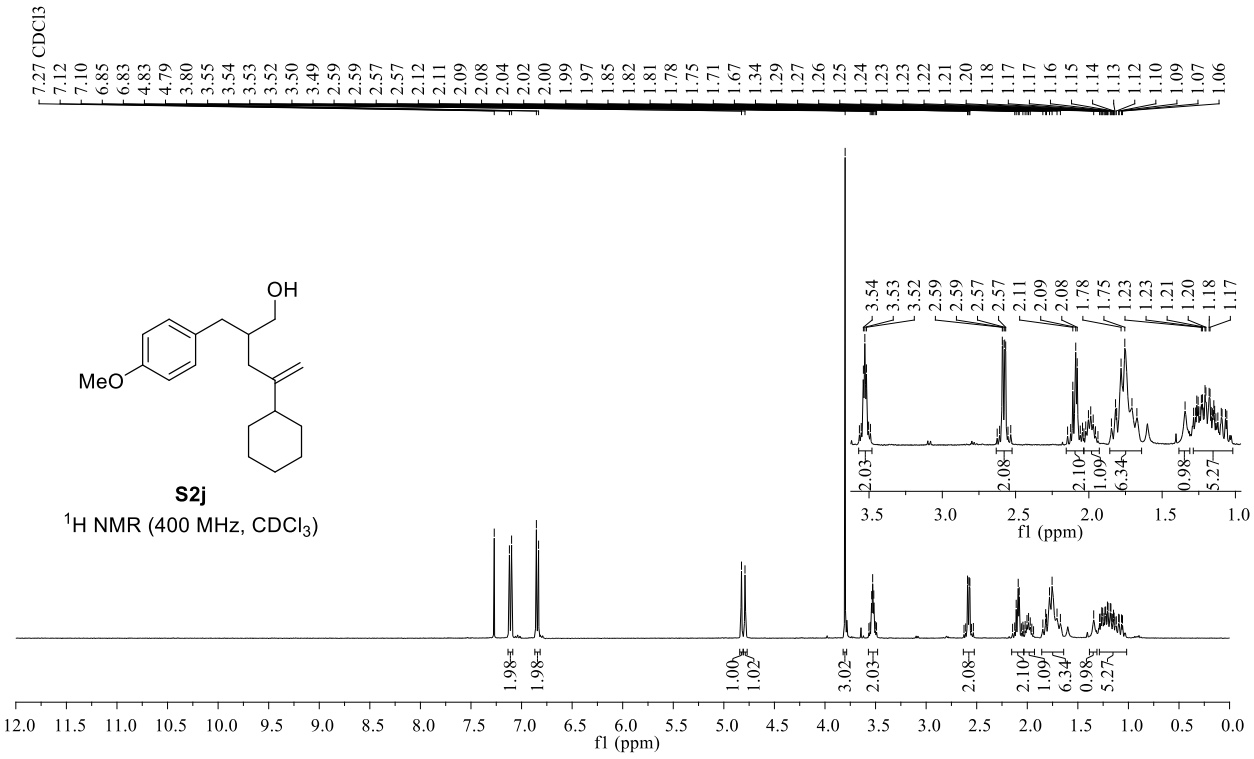

OH
Ph
Me
S2g
13C NMR (101 MHz, CDCl3)
77.16 CDCl3
fl (ppm)

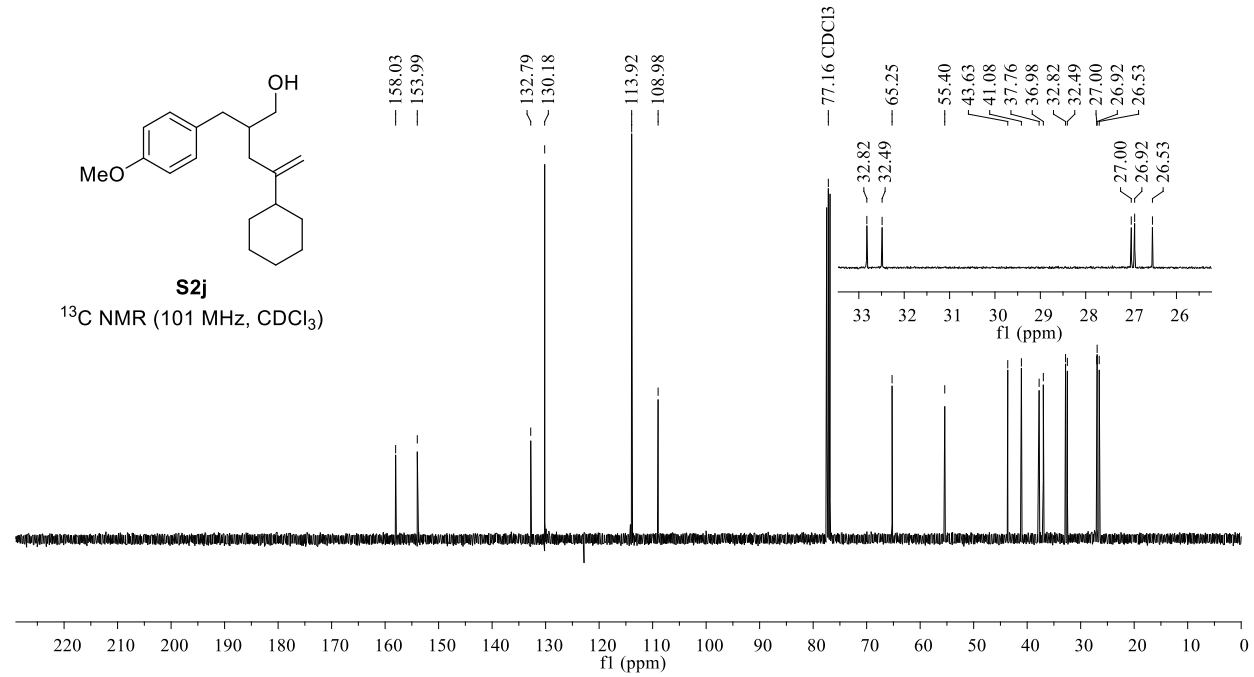

OH
Ph
Me
S2h
1H NMR (400 MHz, CDCl3)
f1 (ppm)

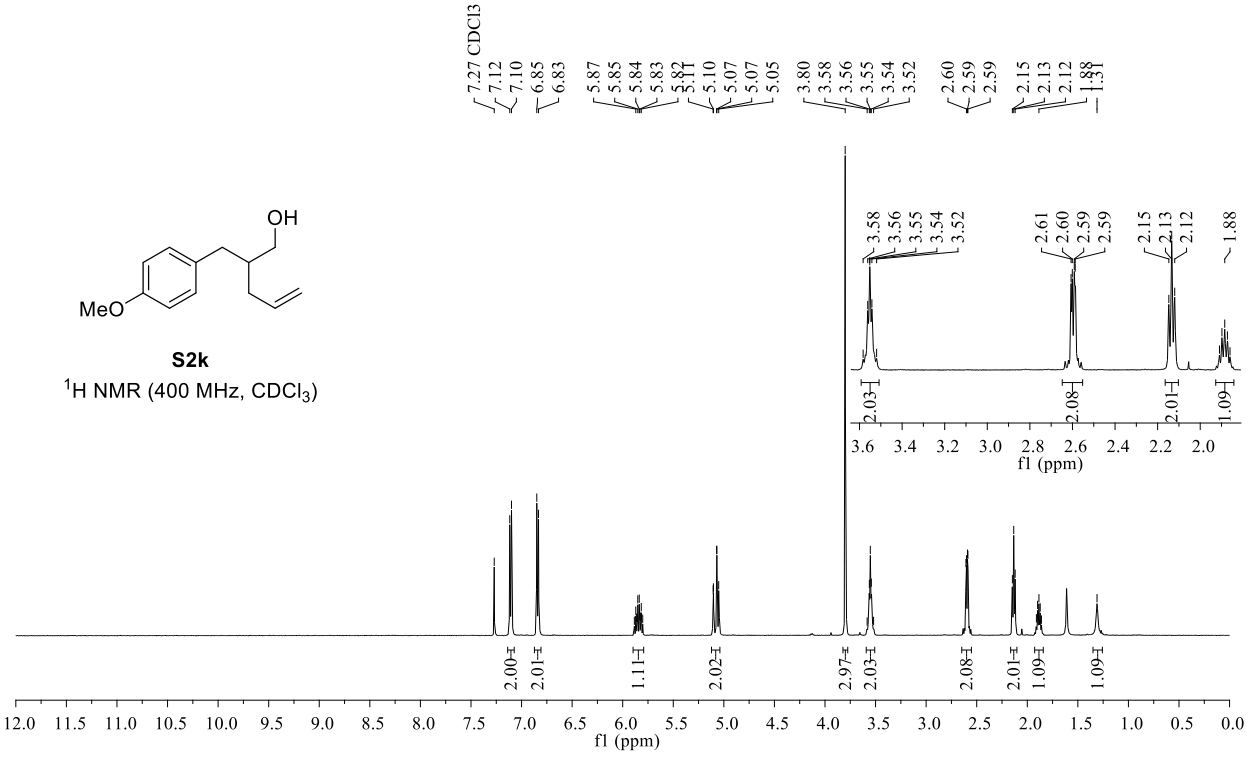

OH
Ph
Me
S2h
13C NMR (101 MHz, CDCl3)
f1 (ppm)


OH
MeO
nHex
S2i
1H NMR (500 MHz, CDCl3)
7.27 CDCl3
7.12
7.10
6.85
6.83
4.81
4.80
3.80
3.53
2.61
2.58
2.57
2.02
2.01
1.35
1.27
0.90
0.89
0.88
1.97
2.00
1.00
0.93
3.06
1.94
1.93
4.96
2.91
6.31
3.09
f1 (ppm)


OH
MeO
nHex
S2i
13C NMR (126 MHz, CDCl3)
158.02
148.80
132.73
130.18
113.90
110.95
77.16 CDCl3
65.28
55.38
40.71
38.53
36.96
35.78
31.89
29.19
27.70
22.75
14.23
f1 (ppm)


OH
MeO
S2j
1H NMR (400 MHz, CDCl3)
fl (ppm)


OH
MeO
S2j
13C NMR (101 MHz, CDCl3)
fl (ppm)


OH
MeO
S2k
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
7.12
7.10
6.85
6.83
5.87
5.85
5.84
5.83
5.82
5.11
5.10
5.07
5.07
5.05
3.80
3.58
3.56
3.55
3.54
3.52
2.60
2.59
2.59
2.15
2.13
2.12
1.88
1.31
2.00
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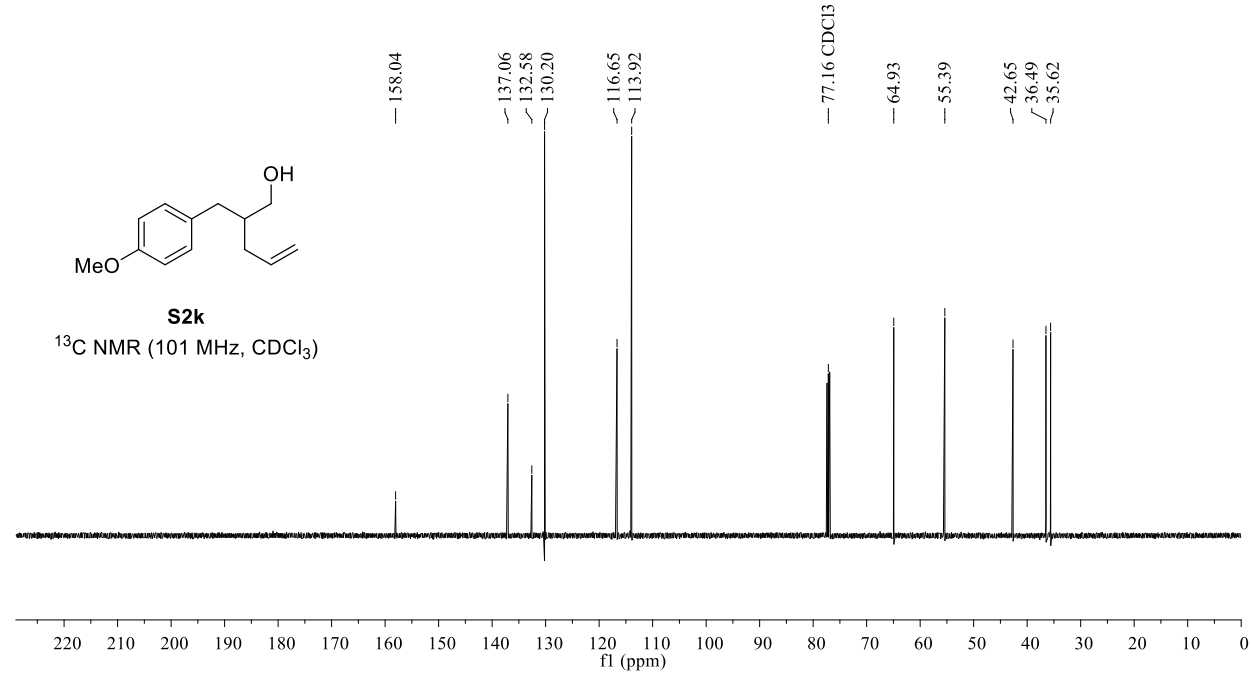
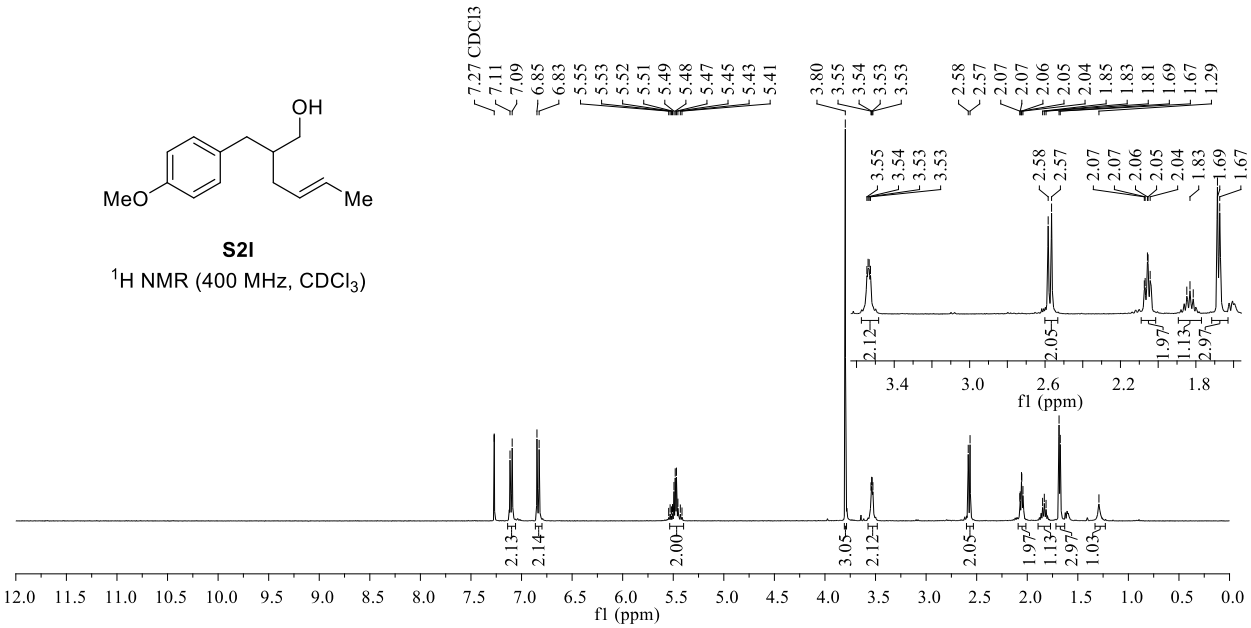
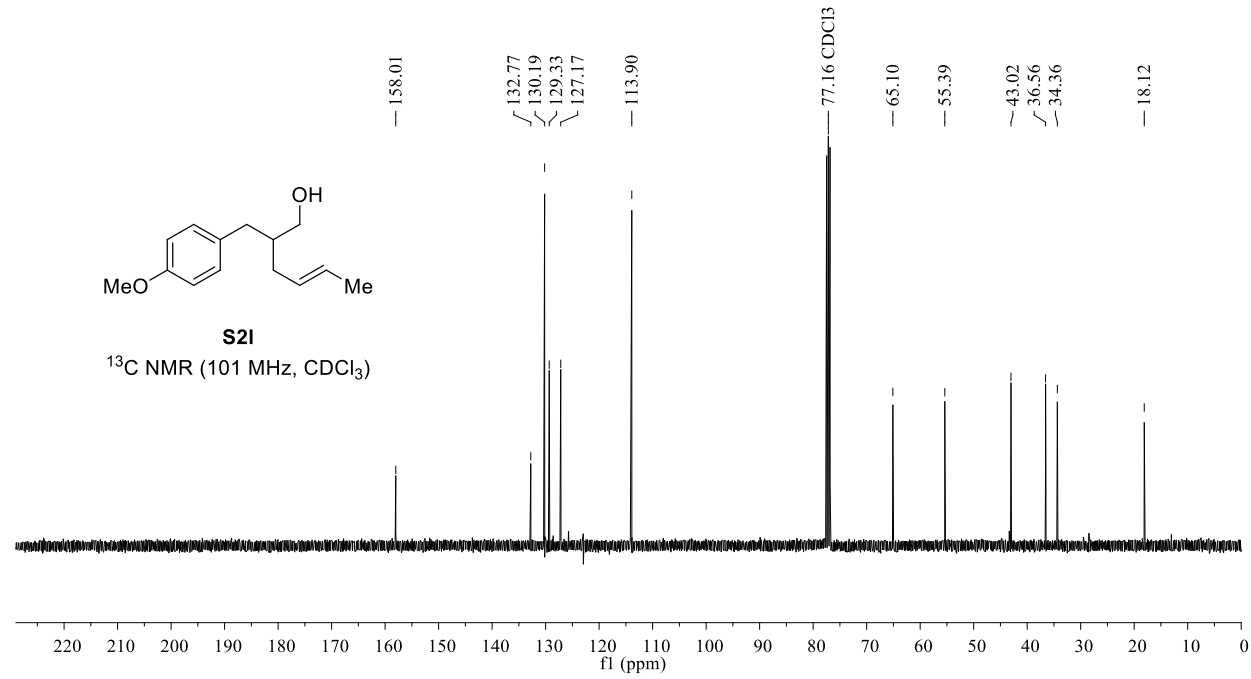
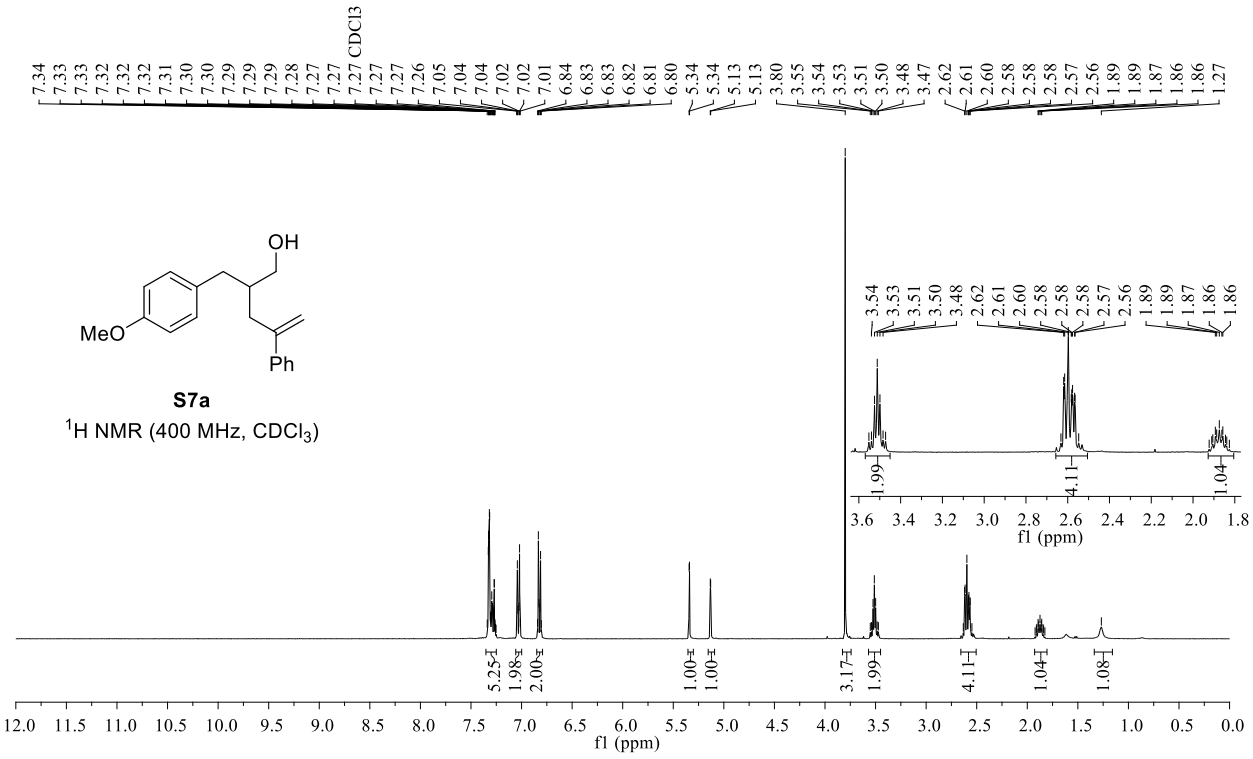
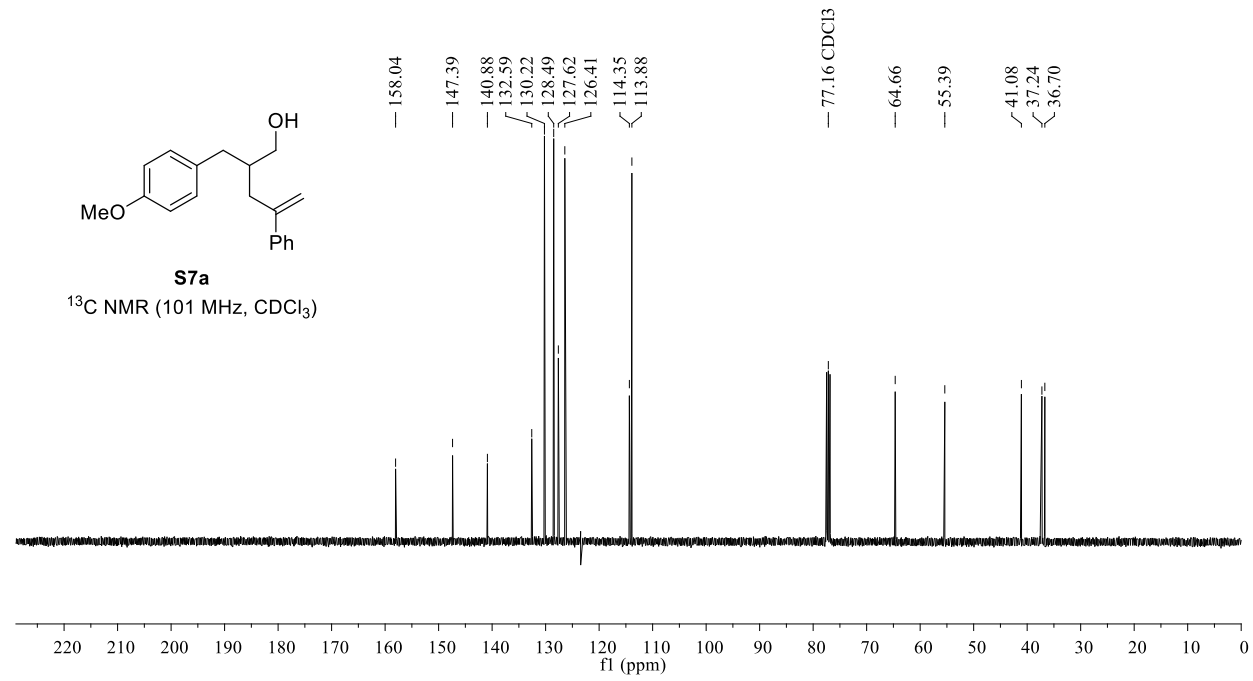
1.11
2.02
2.97
2.03
2.08
2.01
1.09
1.09
fl (ppm)

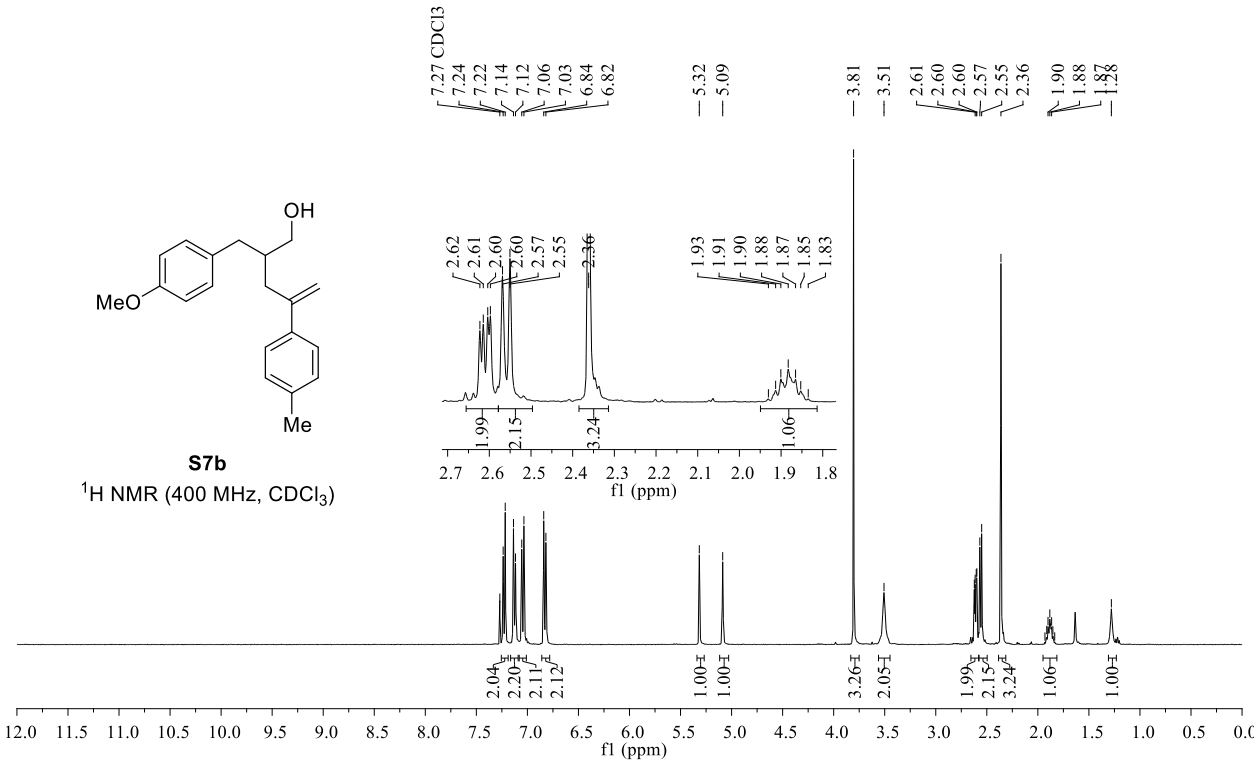

OH
MeO
S2k
13C NMR (101 MHz, CDCl3)
158.04
137.06
132.58
130.20
116.65
113.92
77.16 CDCl3
64.93
55.39
42.65
36.49
35.62
fl (ppm)

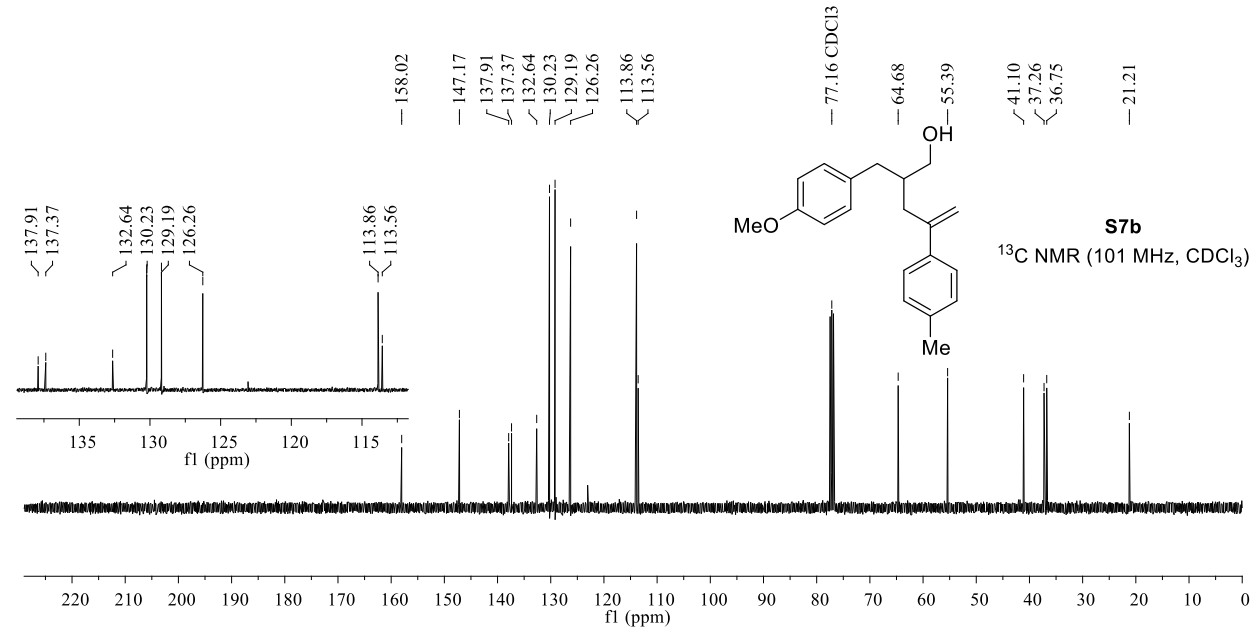

OH
MeO
Me
S2I
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
7.11
7.09
6.85
6.83
5.55
5.53
5.52
5.51
5.49
5.48
5.47
5.45
5.43
5.41
3.80
3.55
3.54
3.53
3.53
2.58
2.57
2.07
2.07
2.06
2.05
2.04
1.85
1.83
1.81
1.69
1.67
1.29
2.13
2.14
2.00
3.05
2.12
2.05
1.97
1.13
2.97
1.03
fl (ppm)

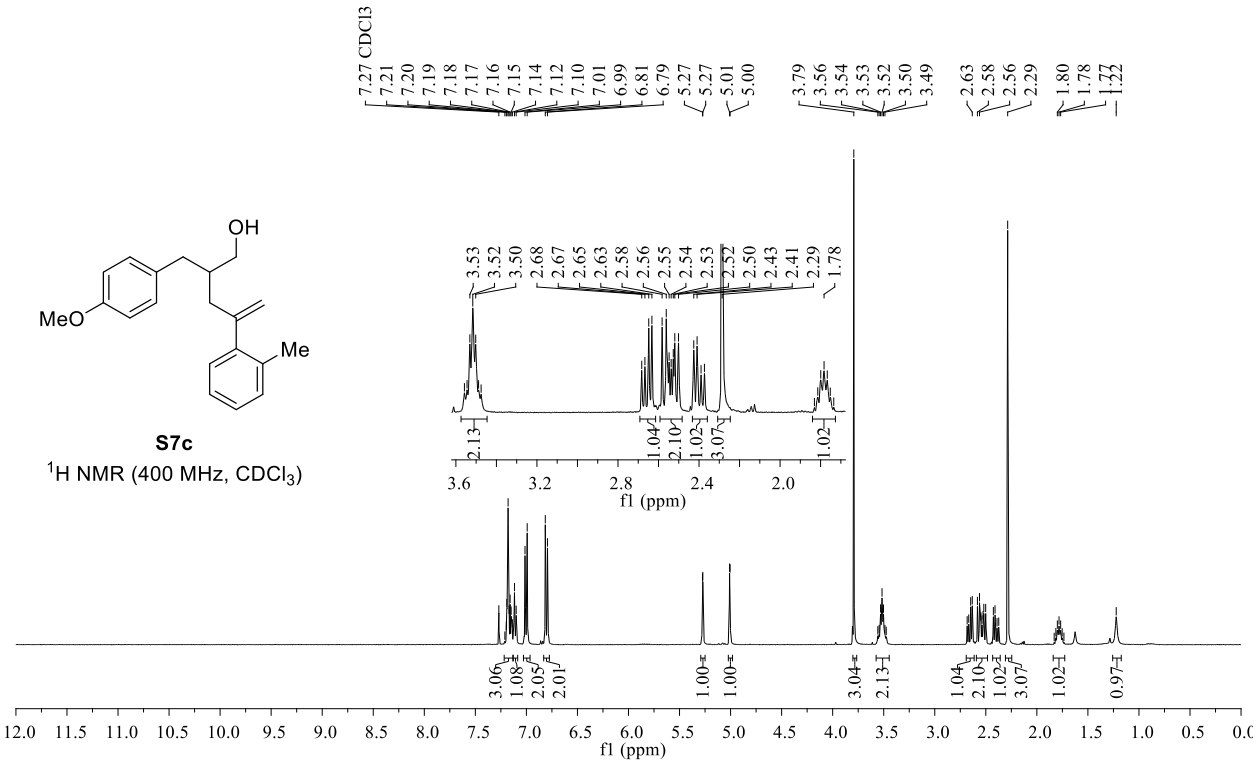

OH
MeO
Me
S2I
13C NMR (101 MHz, CDCl3)
158.01
132.77
130.19
129.33
127.17
113.90
77.16 CDCl3
65.10
55.39
43.02
36.56
34.36
18.12
fl (ppm)

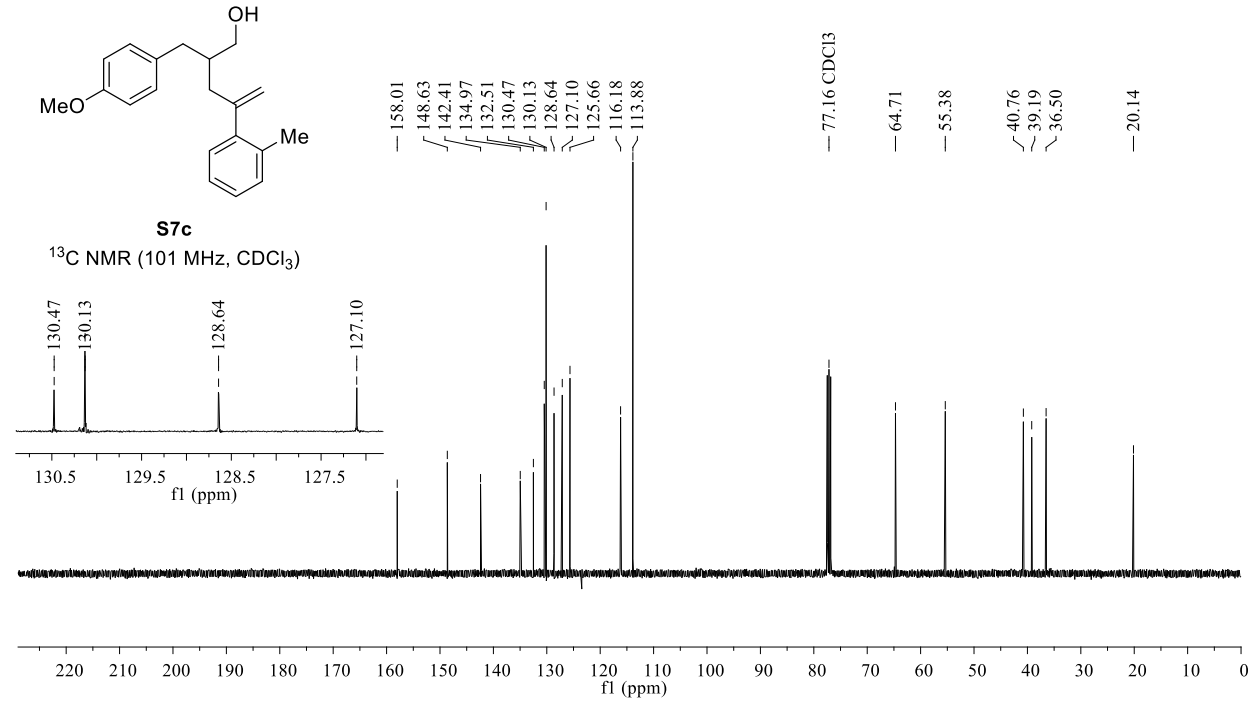

7.34 7.33 7.33 7.32 7.32 7.32 7.31 7.30 7.30 7.29 7.29 7.29 7.28 7.27 7.27 7.27 CDCl3 7.27 7.27 7.26 7.05 7.04 7.04 7.02 7.02 7.01 6.84 6.83 6.83 6.82 6.81 6.80 5.34 5.34 5.13 5.13 3.80 3.55 3.54 3.53 3.51 3.50 3.48 3.47 2.62 2.61 2.60 2.58 2.58 2.58 2.58 2.57 2.56 1.89 1.89 1.87 1.86 1.86 1.27
OH
MeO
Ph
S7a
1H NMR (400 MHz, CDCl3)
3.54 3.53 3.51 3.50 3.48 2.62 2.61 2.60 2.58 2.58 2.58 2.57 2.56 1.89 1.89 1.87 1.86 1.86
1.99 4.11 1.04
3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8
f1 (ppm)
5.25 1.98 2.00 1.00 1.00 3.17 1.99 4.11 1.04 1.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

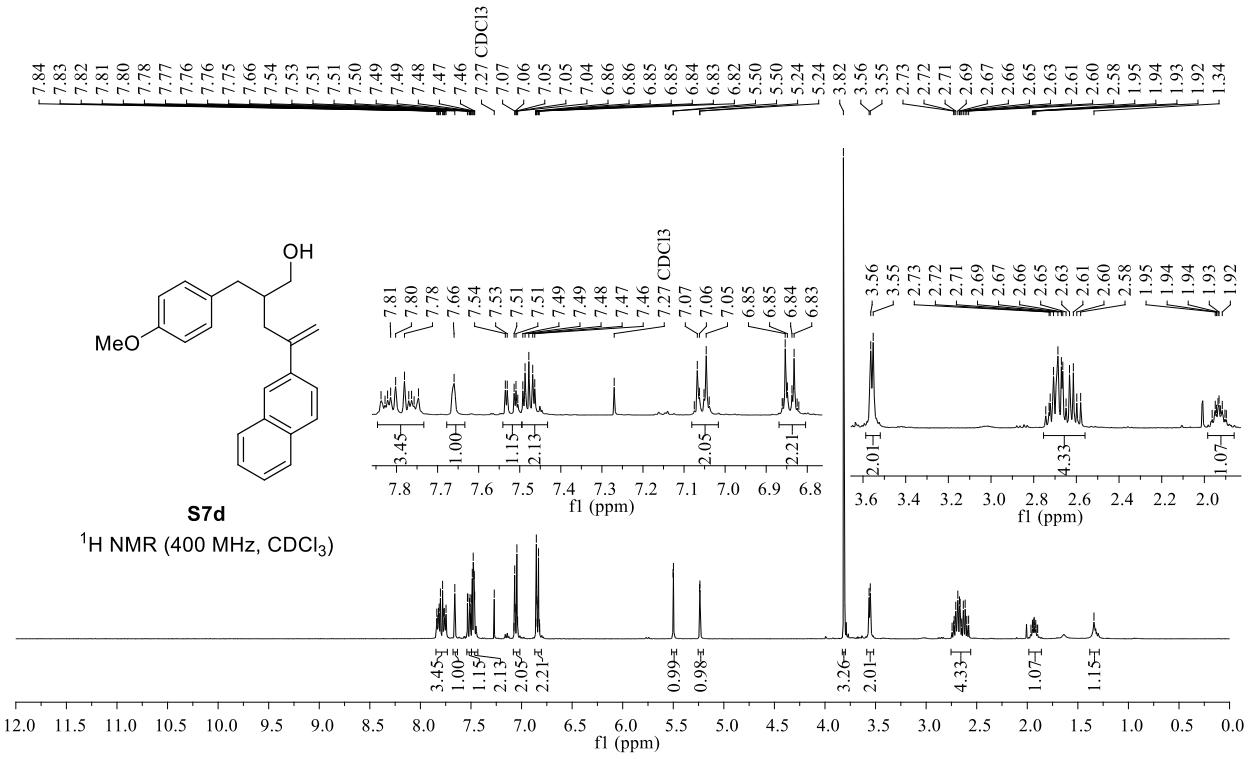

158.04 147.39 140.88 132.59 130.22 128.49 127.62 126.41 114.35 113.88 77.16 CDCl3 64.66 55.39 41.08 37.24 36.70
OH
MeO
Ph
S7a
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

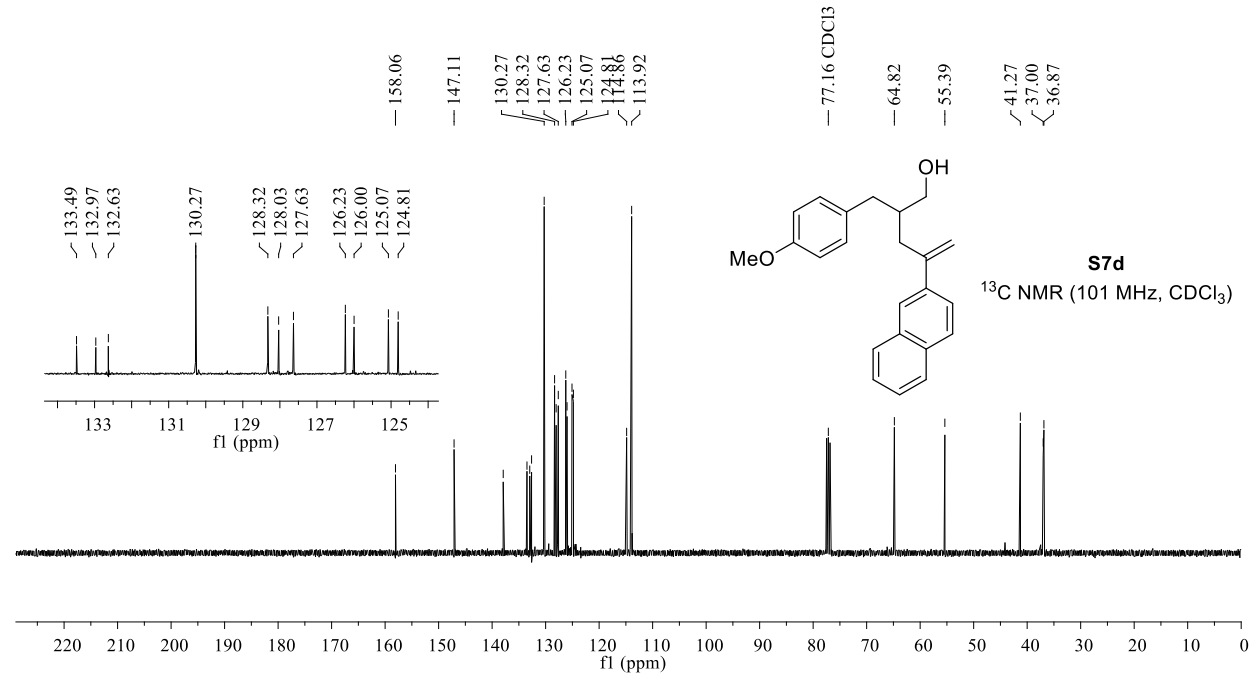

OH
MeO
Me
S7b
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
7.24
7.22
7.14
7.12
7.06
7.03
6.84
6.82
5.32
5.09
3.81
3.51
2.61
2.60
2.60
2.57
2.55
2.36
1.90
1.88
1.87
1.28
2.62
2.61
2.60
2.60
2.57
2.55
2.36
1.93
1.91
1.90
1.88
1.87
1.85
1.83
1.99
2.15
3.24
1.06
2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8
f1 (ppm)
2.04
2.20
2.11
2.12
1.00
1.00
3.26
2.05
1.99
2.15
3.24
1.06
1.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

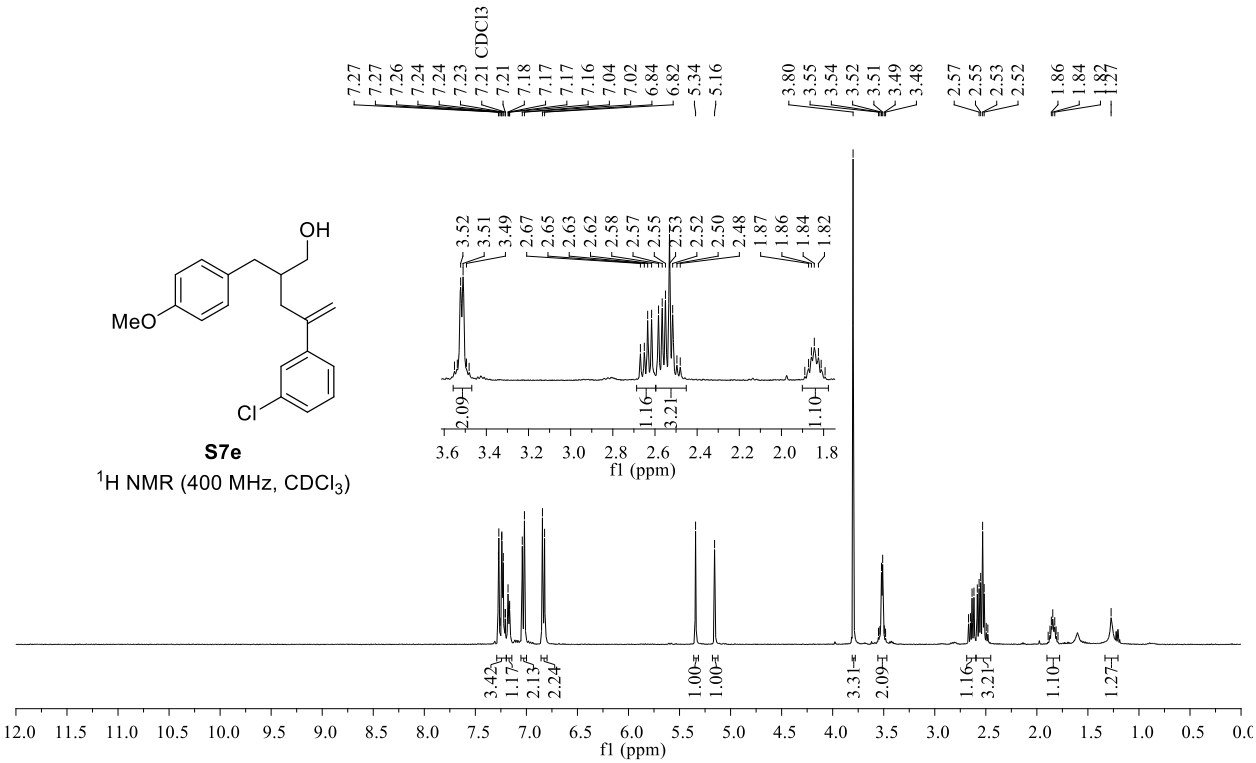

158.02
147.17
137.91
137.37
132.64
130.23
129.19
126.26
113.86
113.56
77.16 CDCl3
64.68
55.39
41.10
37.26
36.75
21.21
137.91
137.37
132.64
130.23
129.19
126.26
113.86
113.56
135 130 125 120 115
f1 (ppm)
OH
MeO
Me
S7b
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

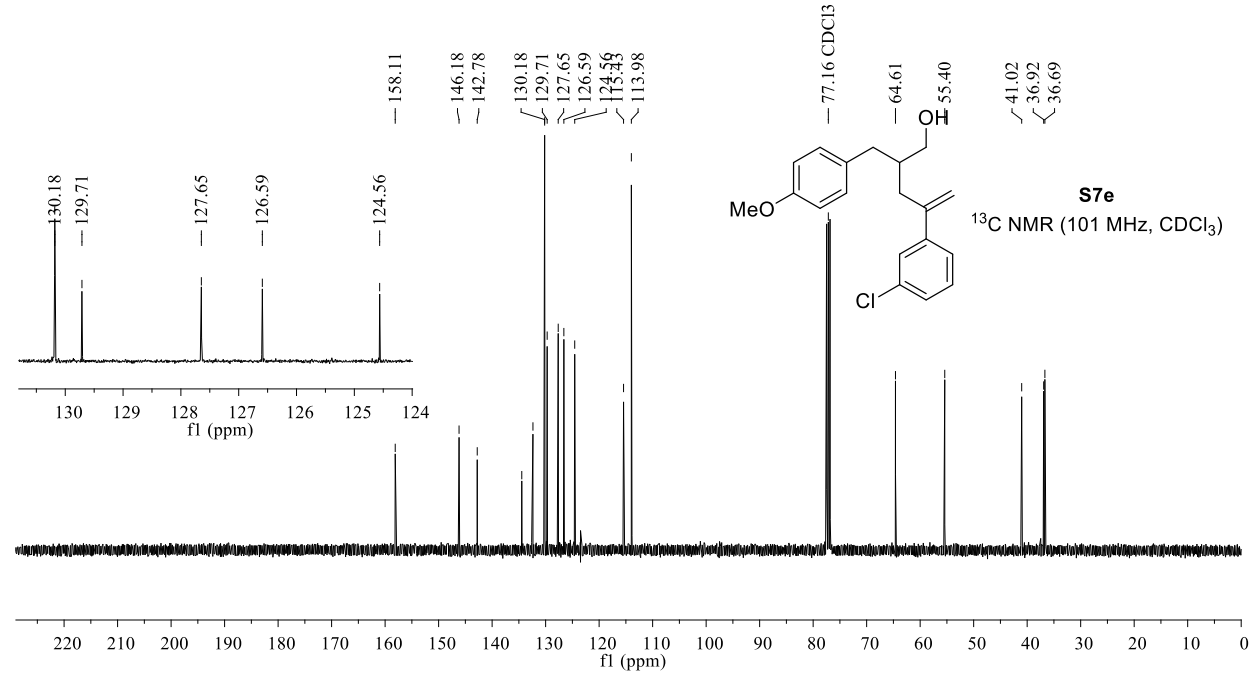

OH
MeO
Me
S7c
1H NMR (400 MHz, CDCl3)
f1 (ppm)

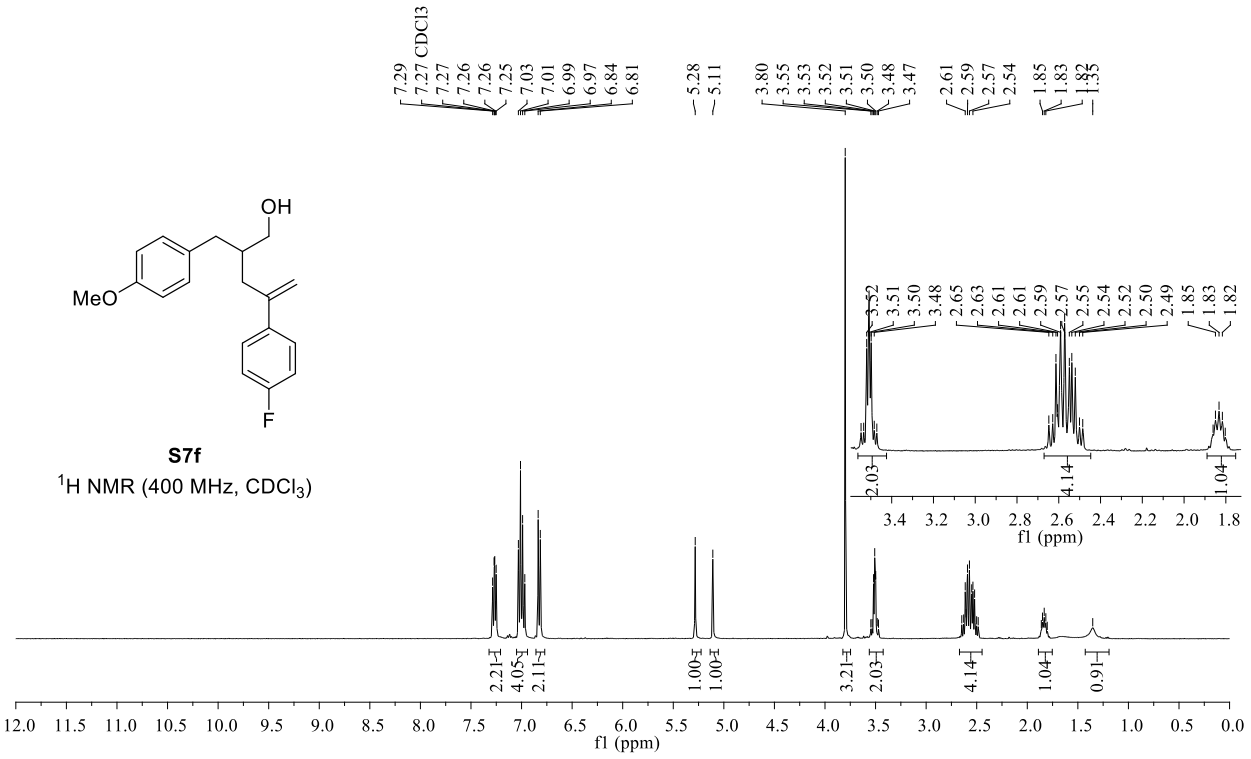

OH
MeO
Me
S7c
13C NMR (101 MHz, CDCl3)
f1 (ppm)

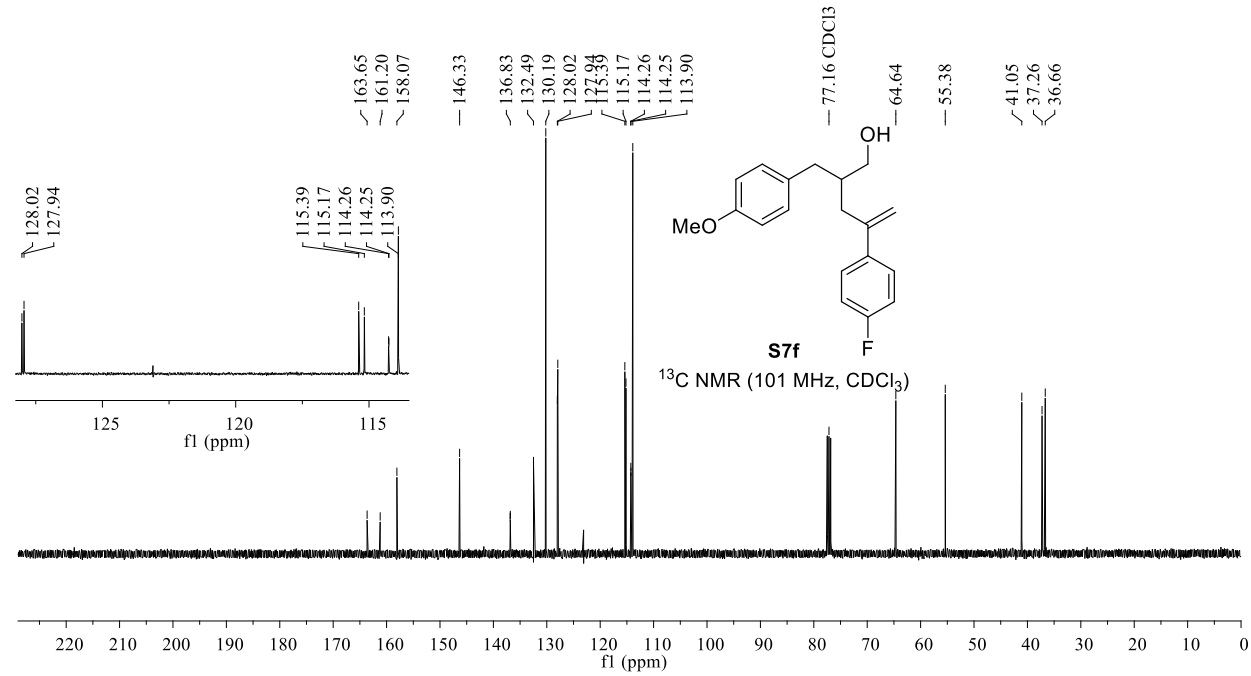

OH
MeO
S7d
1H NMR (400 MHz, CDCl3)
fl (ppm)

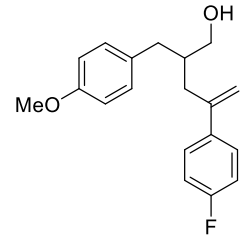

OH
MeO
S7d
13C NMR (101 MHz, CDCl3)
fl (ppm)


OH
MeO
Cl
S7e
1H NMR (400 MHz, CDCl3)
f1 (ppm)


OH
MeO
Cl
S7e
13C NMR (101 MHz, CDCl3)
f1 (ppm)


7.29
7.27 CDCl3
7.27
7.26
7.26
7.25
7.03
7.01
6.99
6.97
6.84
6.81
5.28
5.11
3.80
3.55
3.53
3.52
3.51
3.50
3.48
3.47
2.61
2.59
2.57
2.54
1.85
1.83
1.82
1.35
OH
MeO
F
S7f
1H NMR (400 MHz, CDCl3)
2.21
4.05
2.11
1.00
1.00
3.21
2.03
4.14
1.04
0.91
f1 (ppm)

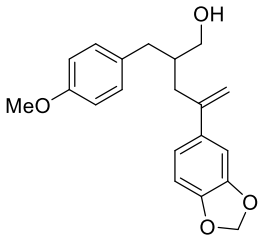

163.65
161.20
158.07
146.33
136.83
132.49
130.19
128.02
127.94
115.39
115.17
114.26
114.25
113.90
77.16 CDCl3
64.64
55.38
41.05
37.26
36.66
OH
MeO
F
S7f
13C NMR (101 MHz, CDCl3)
f1 (ppm)




**S7f**

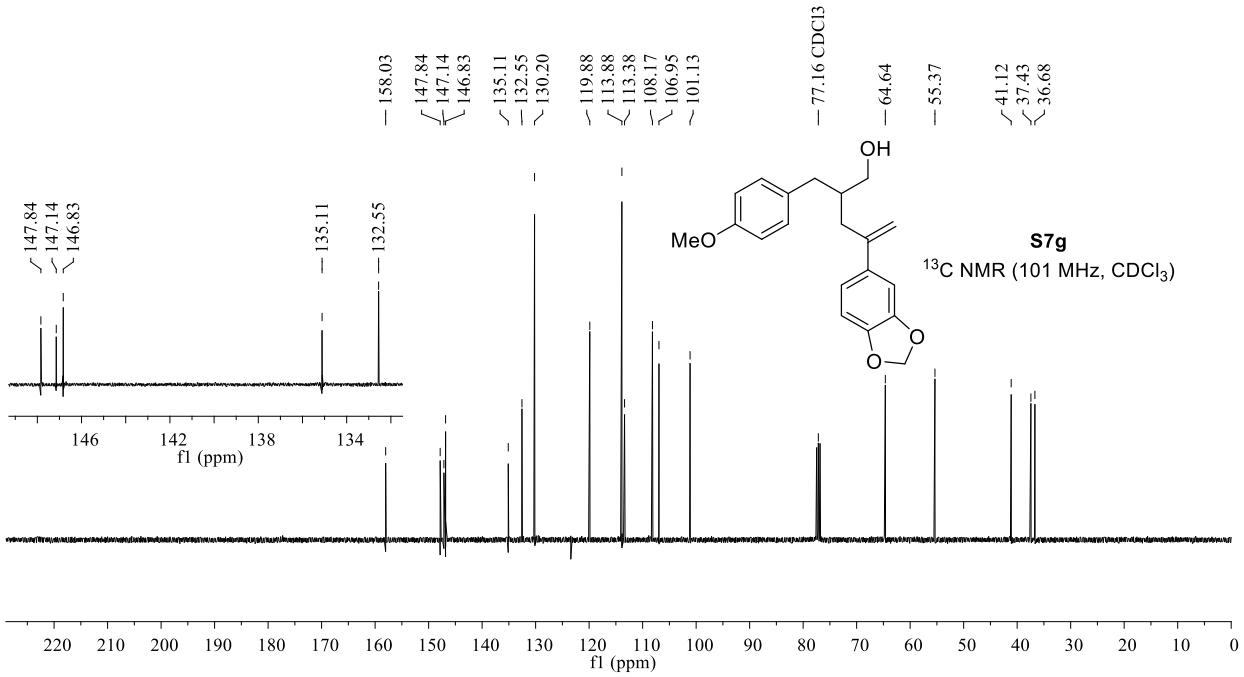
$^{19}$F NMR (376 MHz, $CDCl_3$)

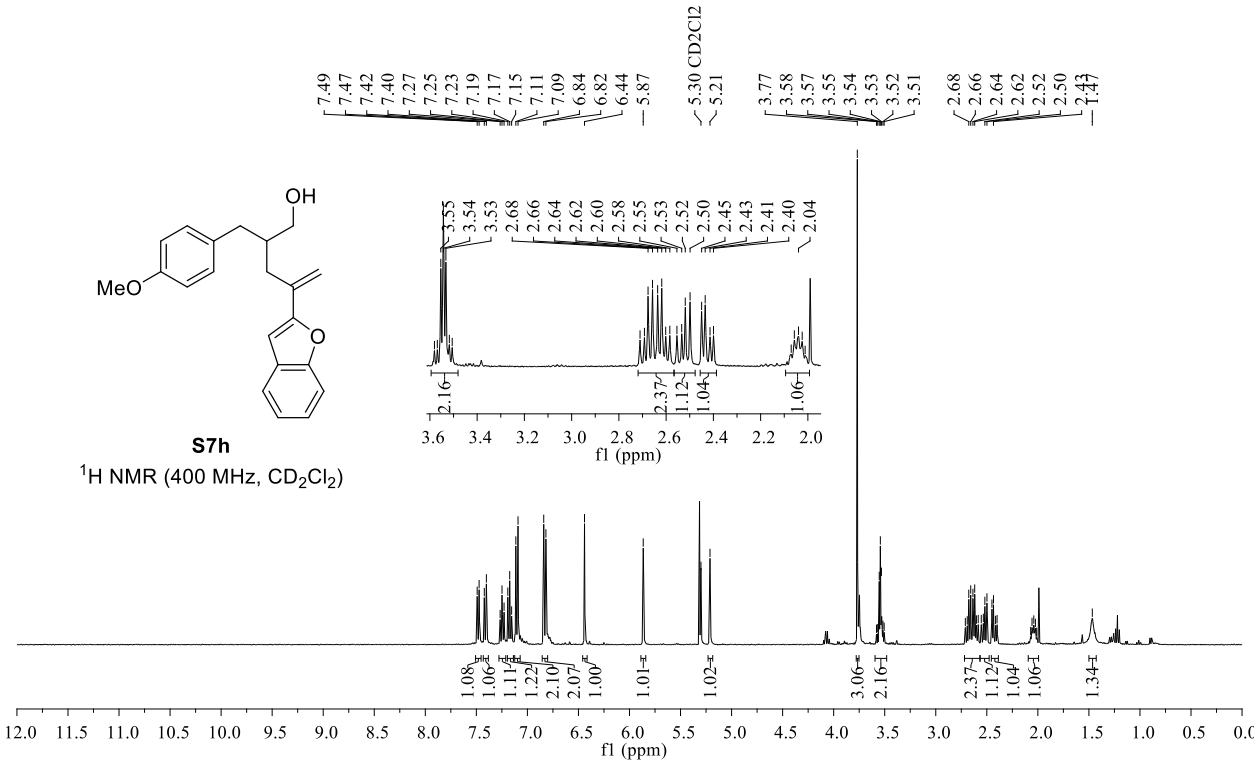


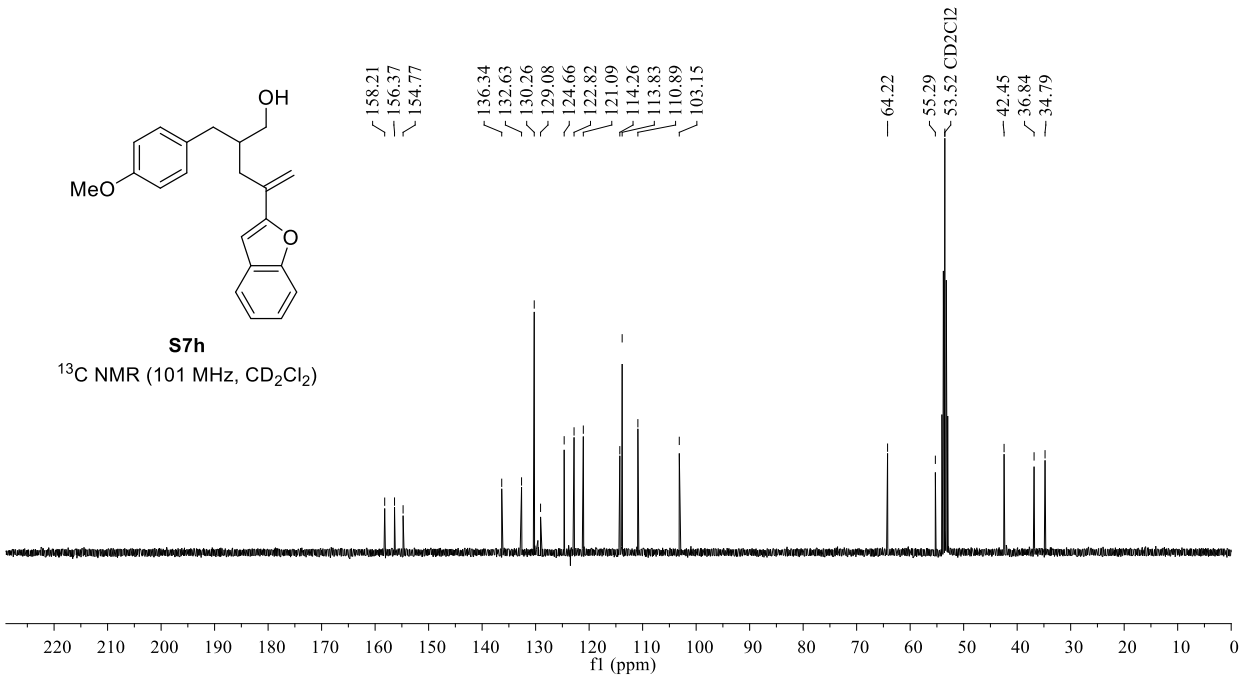




**S7g**

$^{1}$H NMR (400 MHz, $CDCl_3$)

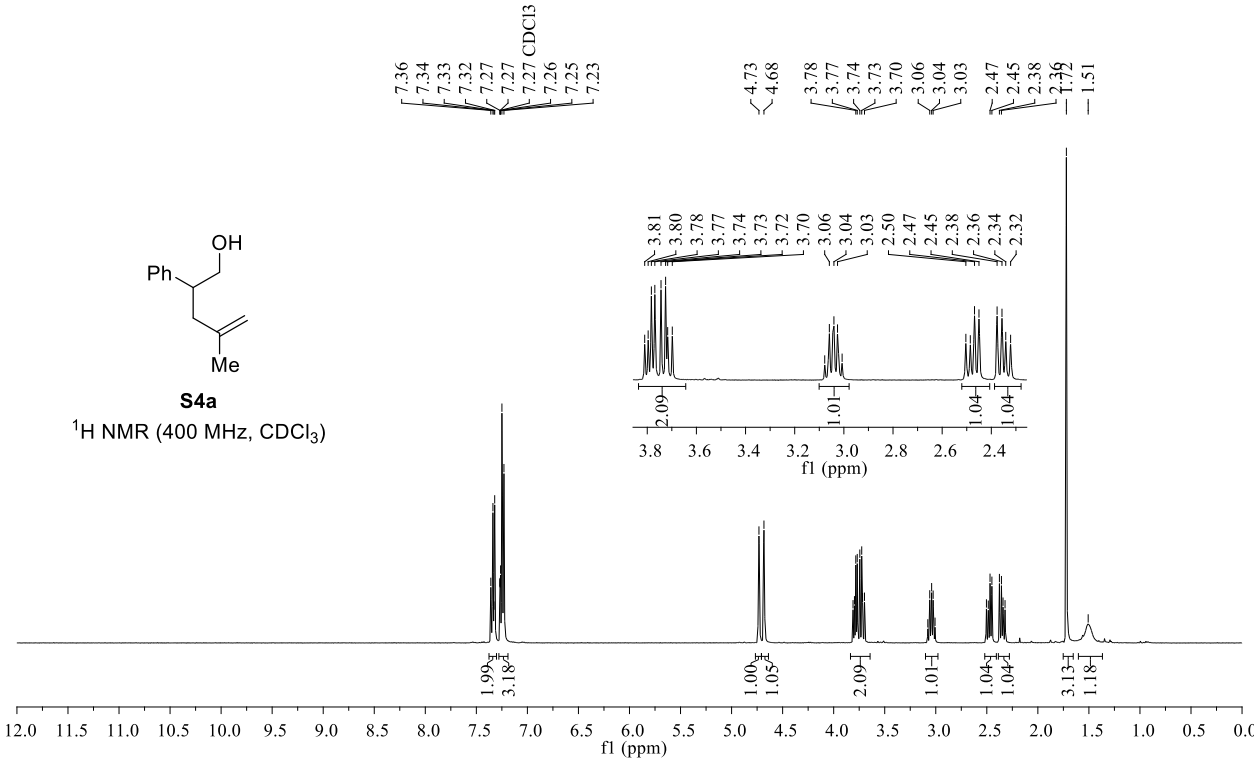

158.03
147.84
147.14
146.83
135.11
132.55
130.20
119.88
113.88
113.38
108.17
106.95
101.13
77.16 CDCl3
64.64
55.37
41.12
37.43
36.68
OH
MeO
O
O
S7g
13C NMR (101 MHz, CDCl3)
fl (ppm)


7.49
7.47
7.42
7.40
7.27
7.25
7.23
7.19
7.17
7.15
7.11
7.09
6.84
6.82
6.44
5.87
5.30 CD2Cl2
5.21
3.77
3.58
3.57
3.55
3.54
3.53
3.52
3.51
2.68
2.66
2.64
2.62
2.52
2.50
1.47
OH
MeO
O
S7h
1H NMR (400 MHz, CD2Cl2)
fl (ppm)



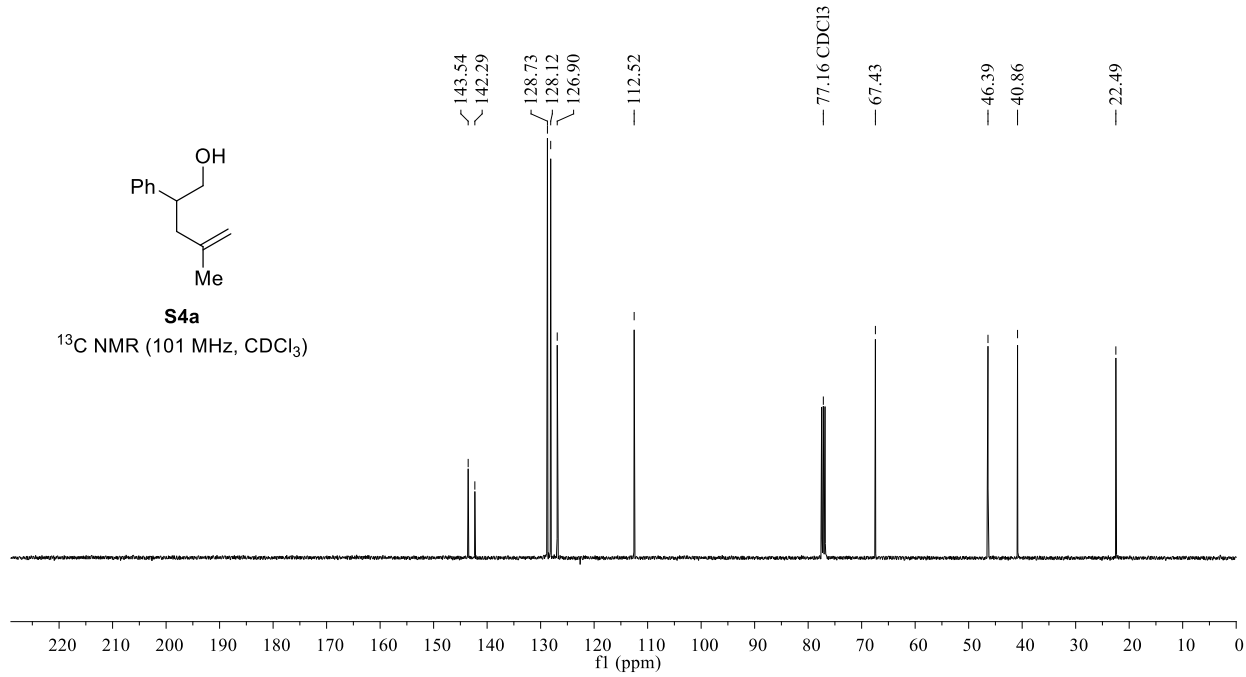

**S7h**

$^{13}C$ NMR (101 MHz, $CD_2Cl_2$)



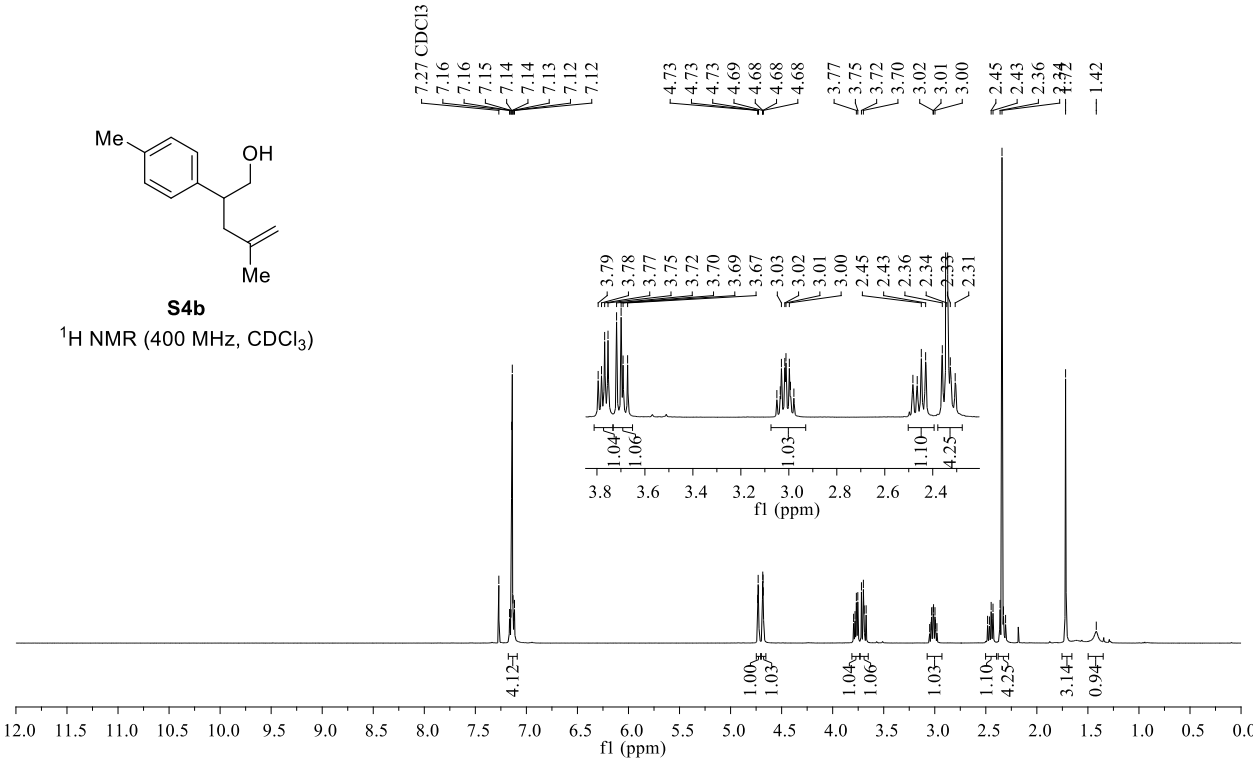

**S4a**

$^{1}H$ NMR (400 MHz, $CDCl_3$)



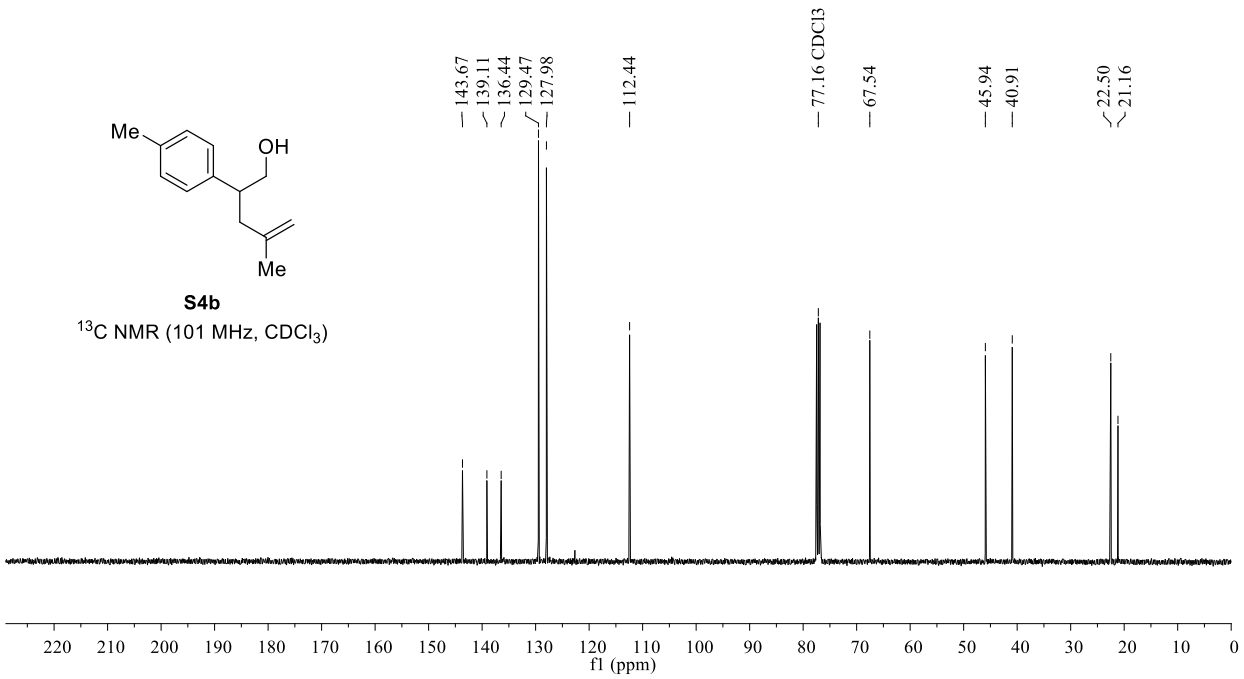

**S4a**

$^{13}$C NMR (101 MHz, $CDCl_3$)



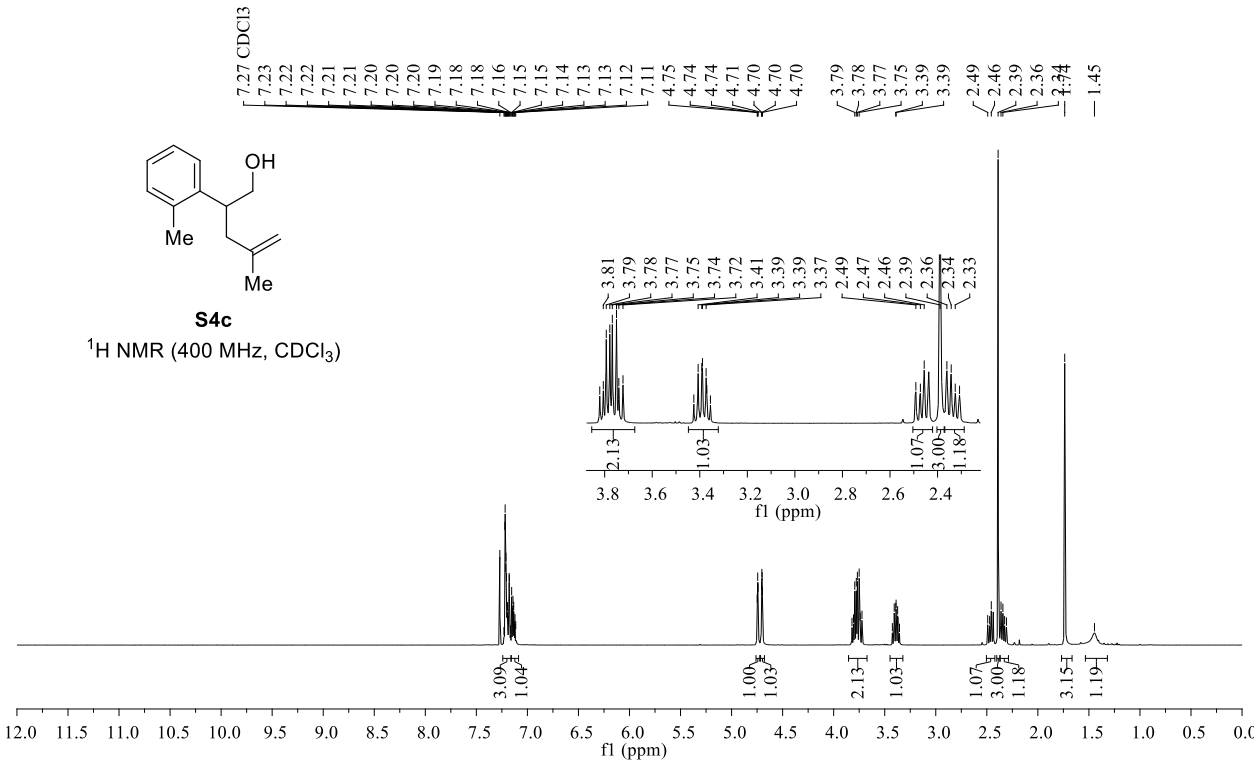

**S4b**

$^{1}$H NMR (400 MHz, $CDCl_3$)



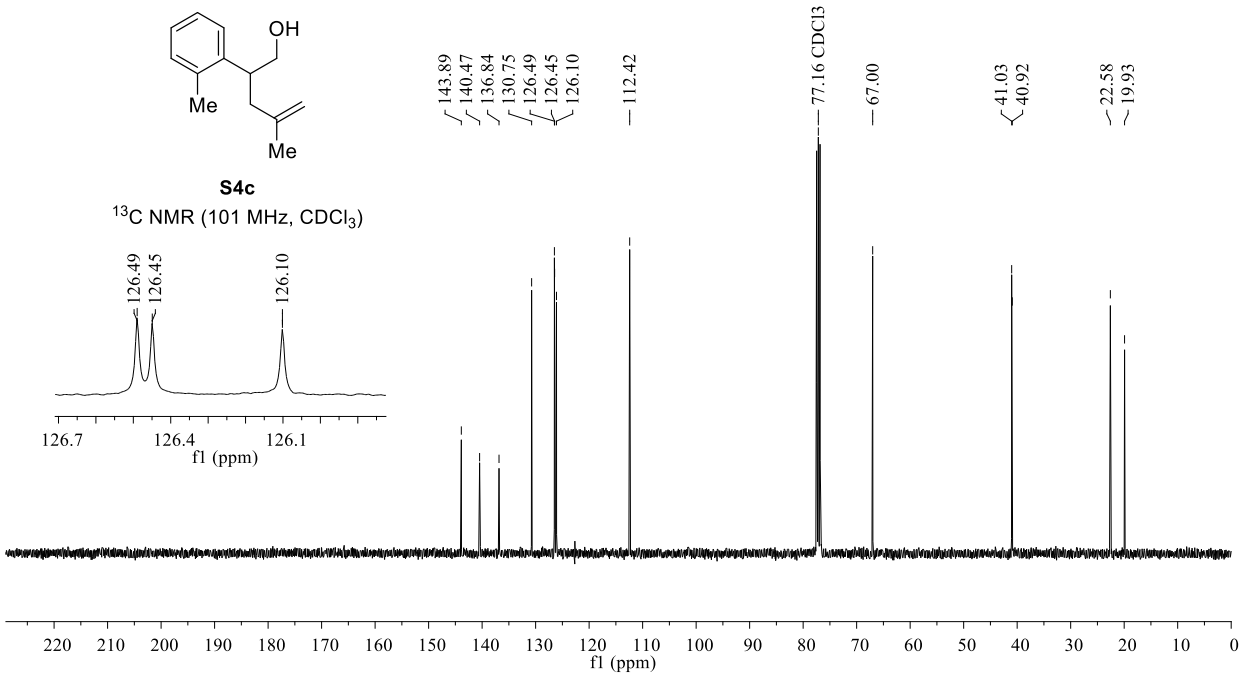

**S4b**

$^{13}$C NMR (101 MHz, $CDCl_3$)



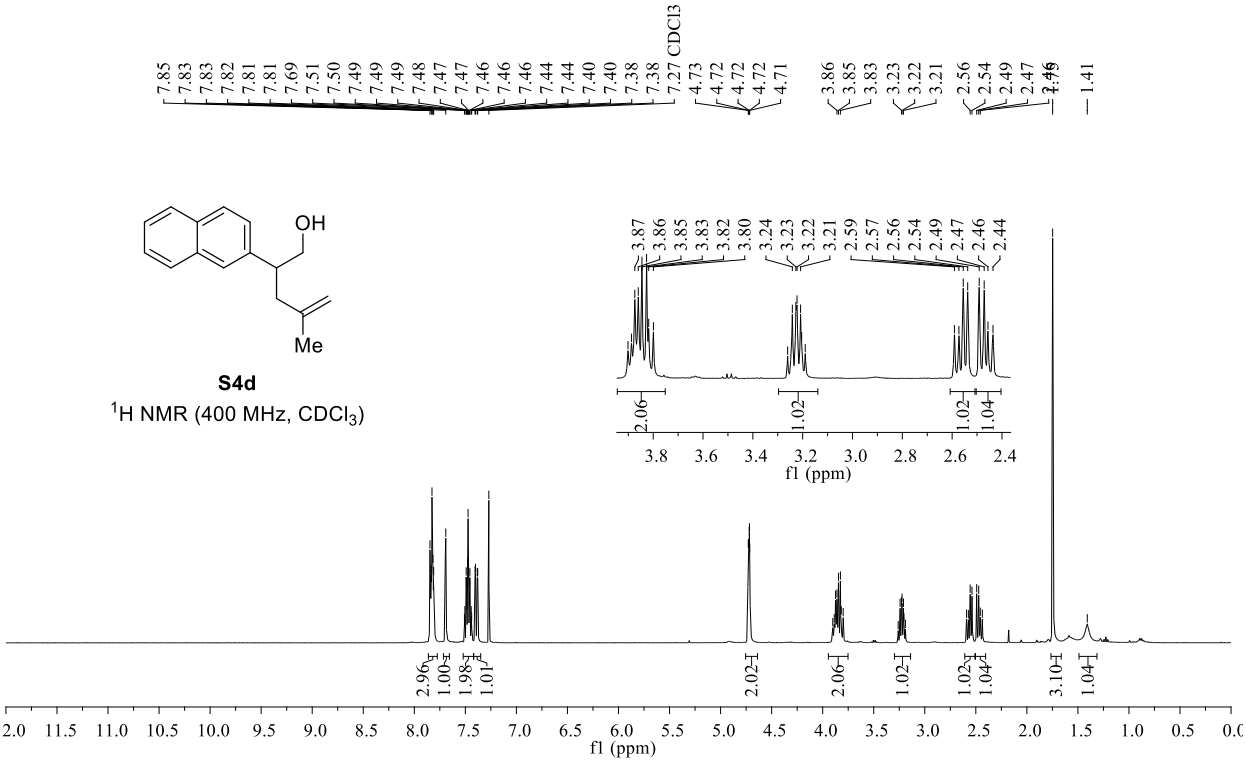

**S4c**

$^{1}$H NMR (400 MHz, $CDCl_3$)



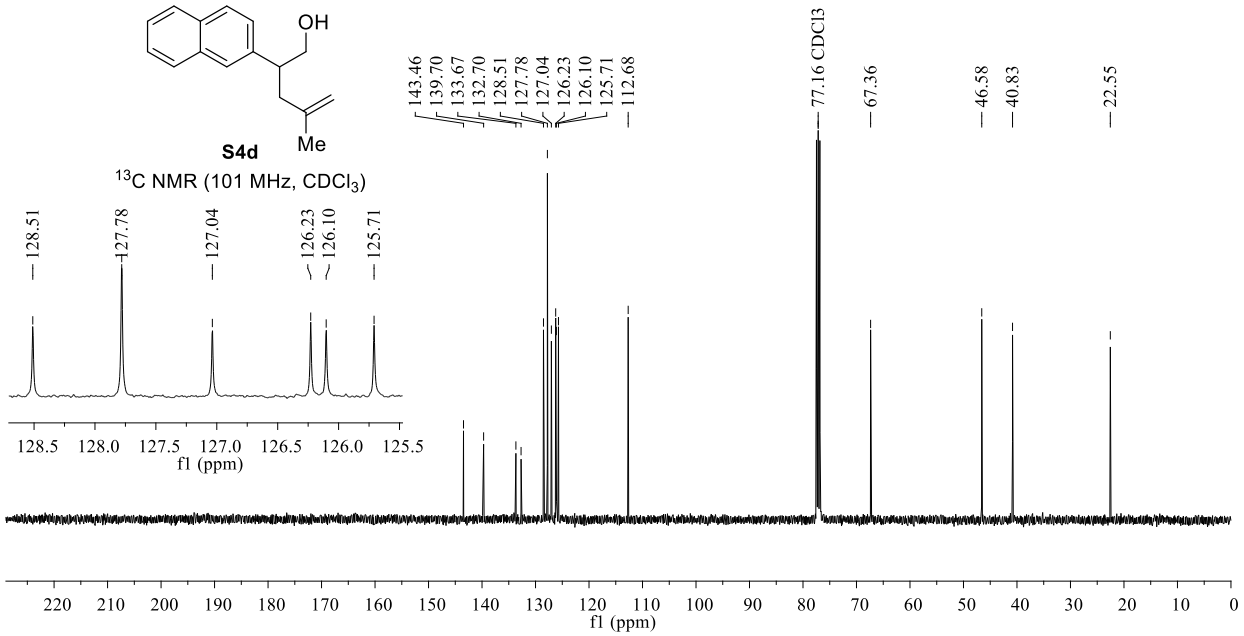

**S4c**

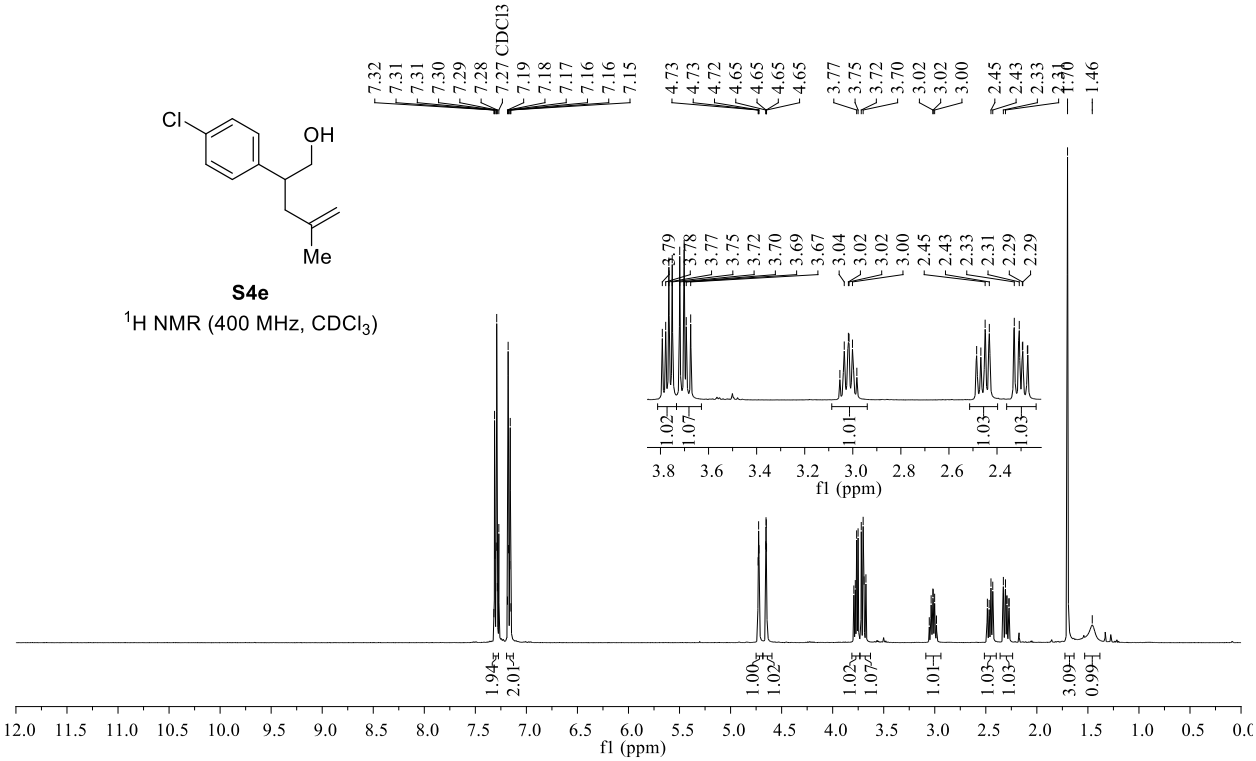
$^{13}$C NMR (101 MHz, $CDCl_3$)

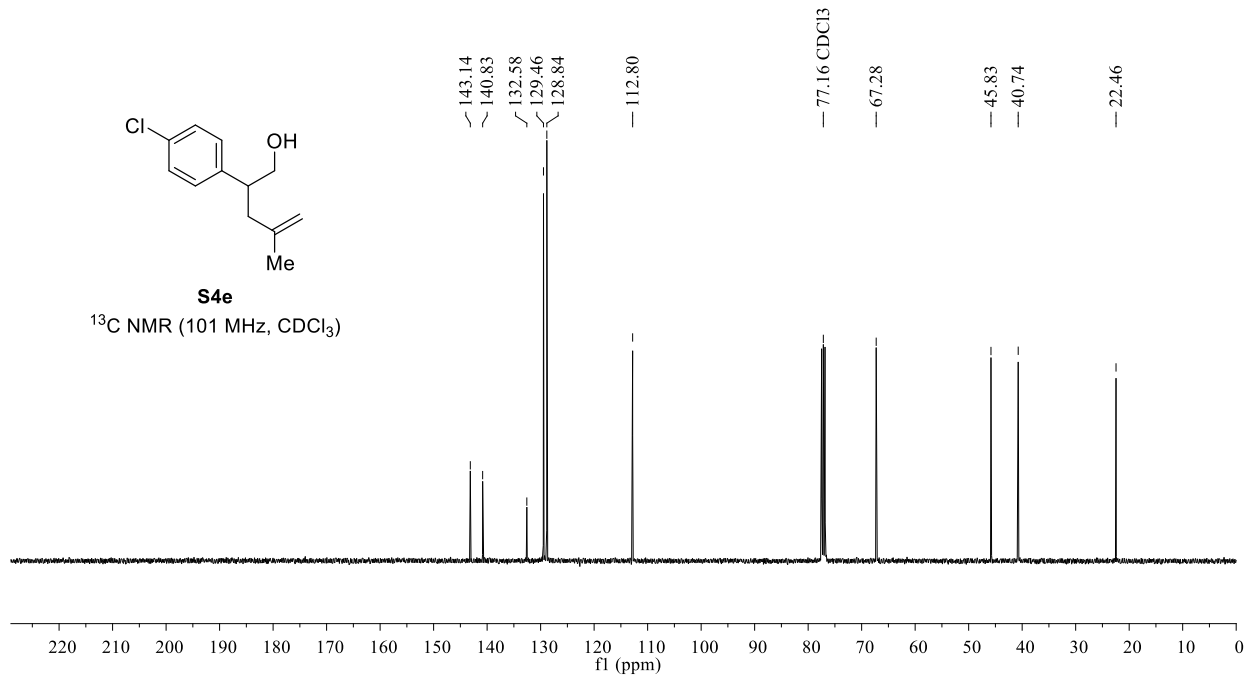



**S4d**

$^{1}$H NMR (400 MHz, $CDCl_3$)

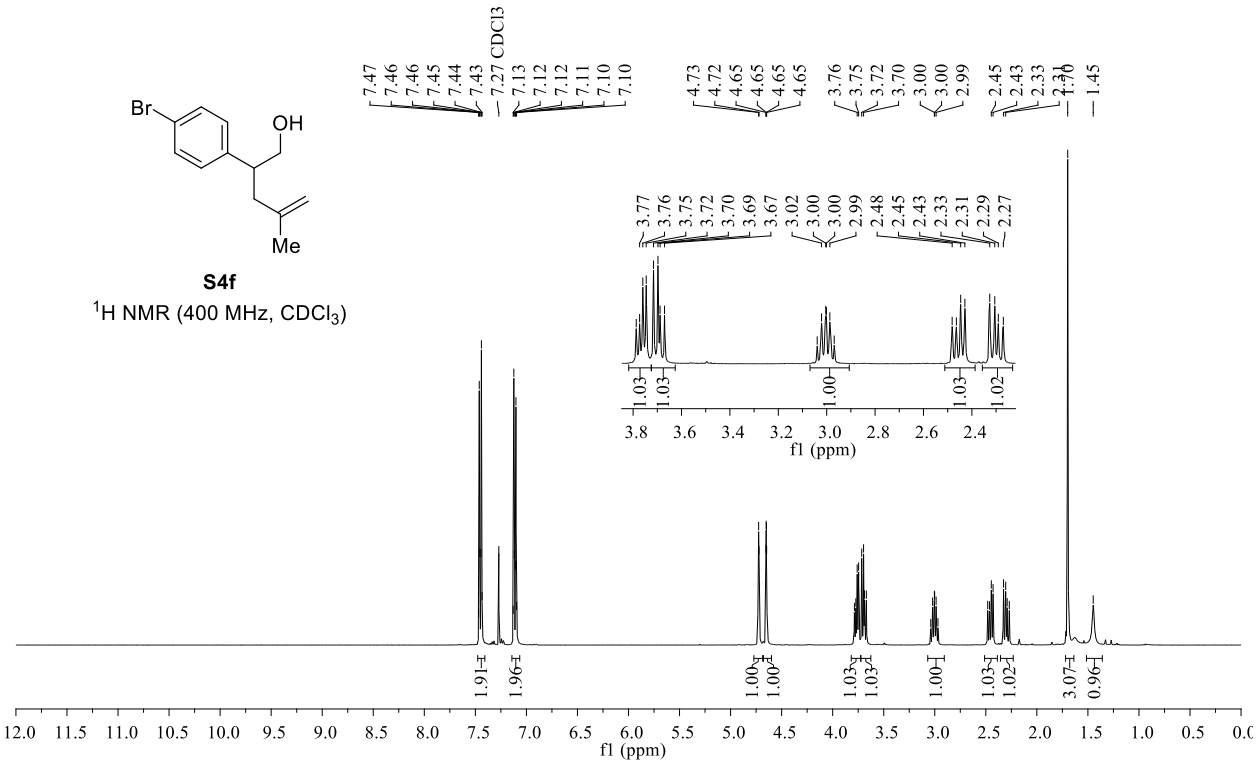

OH
Me
S4d
$^{13}$C NMR (101 MHz, CDCl$_3$)
143.46
139.70
133.67
132.70
128.51
127.78
127.04
126.23
126.10
125.71
112.68
77.16 CDCl3
67.36
46.58
40.83
22.55
fl (ppm)


Cl
OH
Me
S4e
$^{1}$H NMR (400 MHz, CDCl$_3$)
7.27 CDCl3
1.46
fl (ppm)



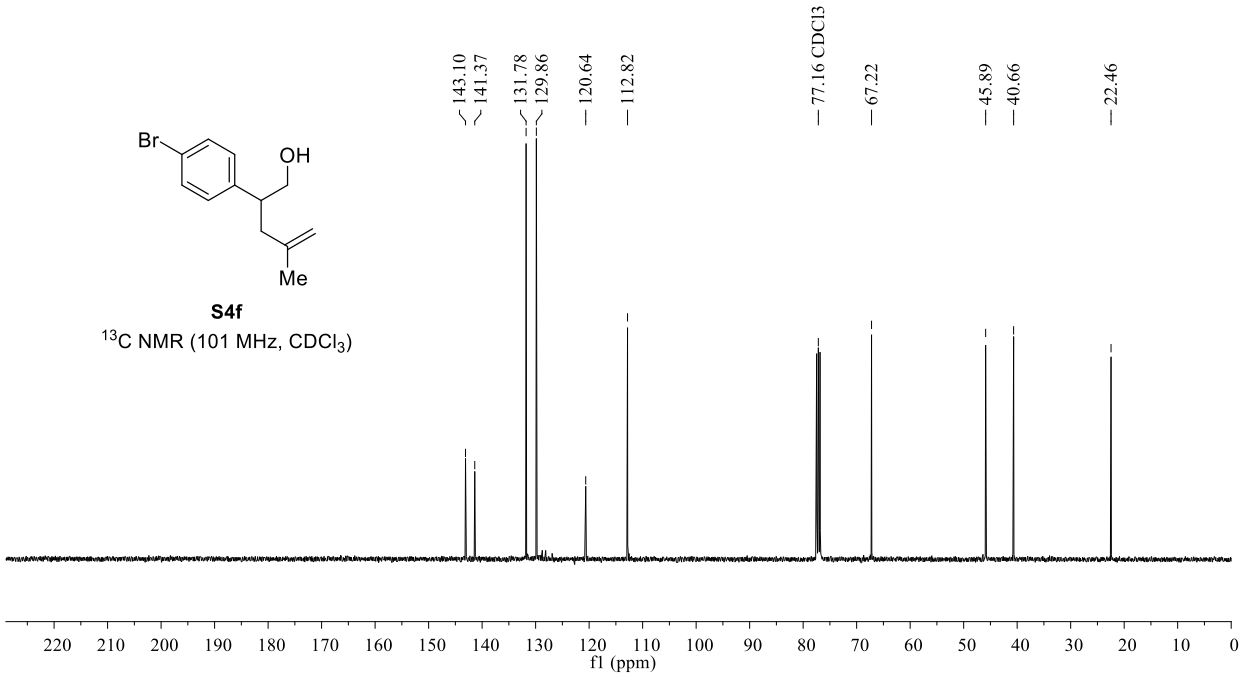

**S4e**

$^{13}$C NMR (101 MHz, $CDCl_3$)



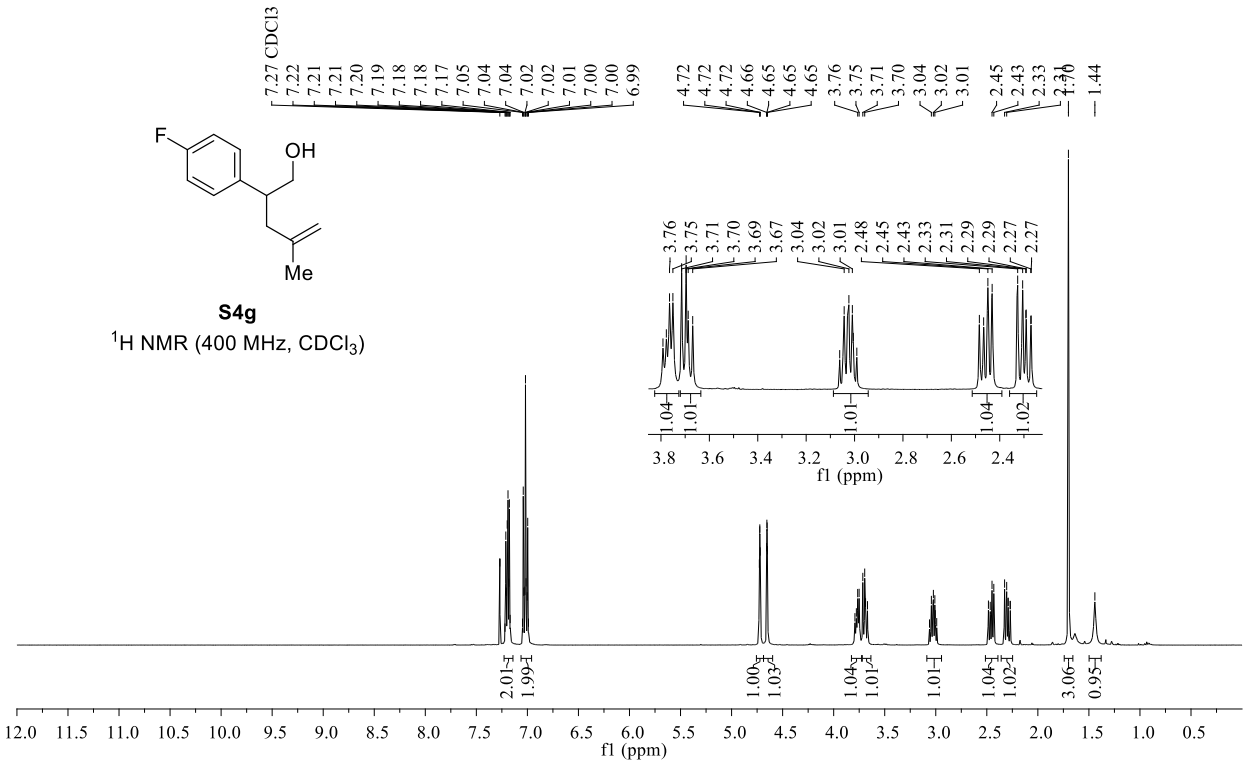

**S4f**

$^{1}$H NMR (400 MHz, $CDCl_3$)



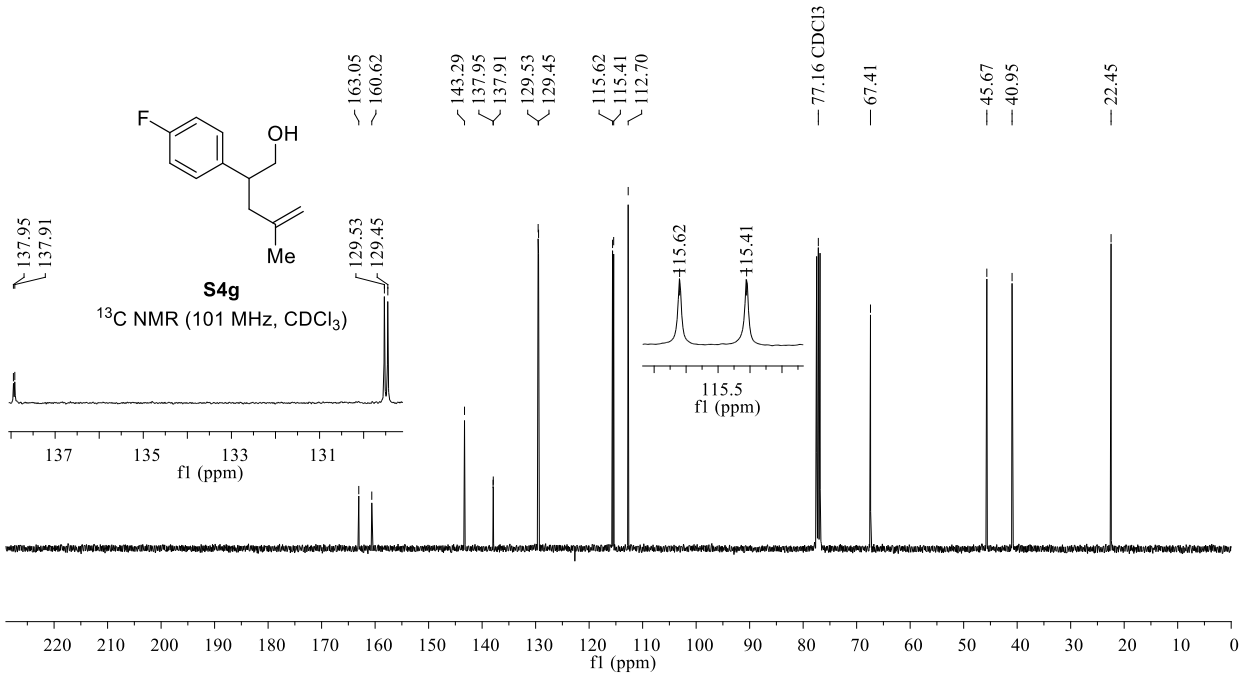

**S4f**

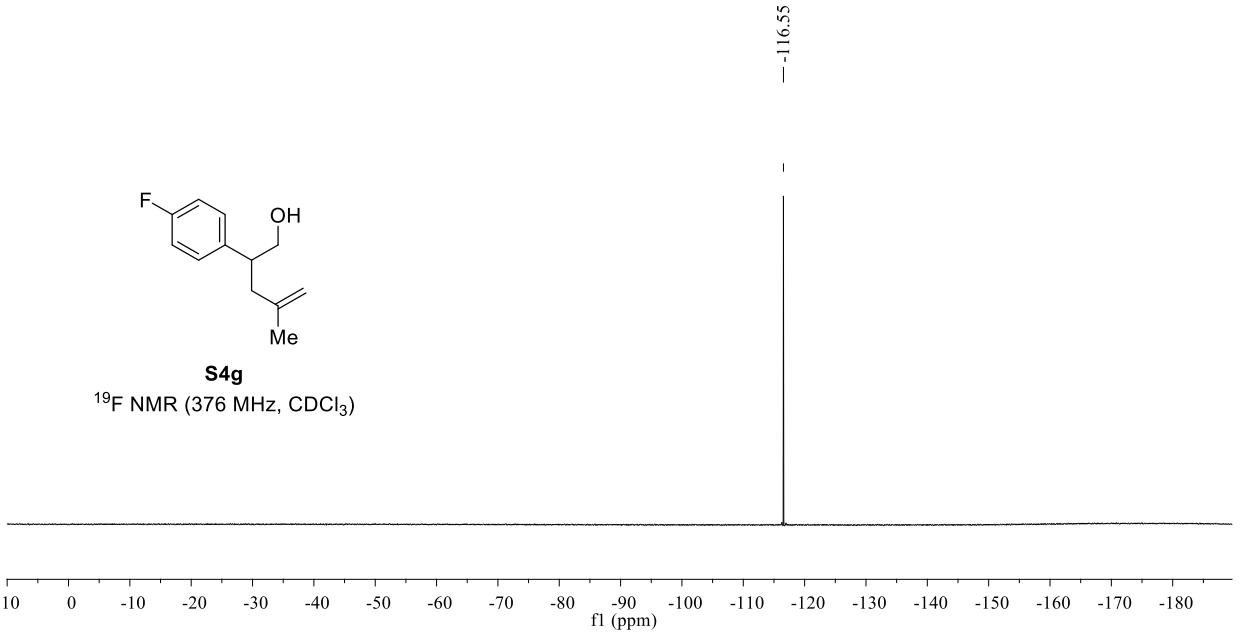
$^{13}$C NMR (101 MHz, $CDCl_3$)

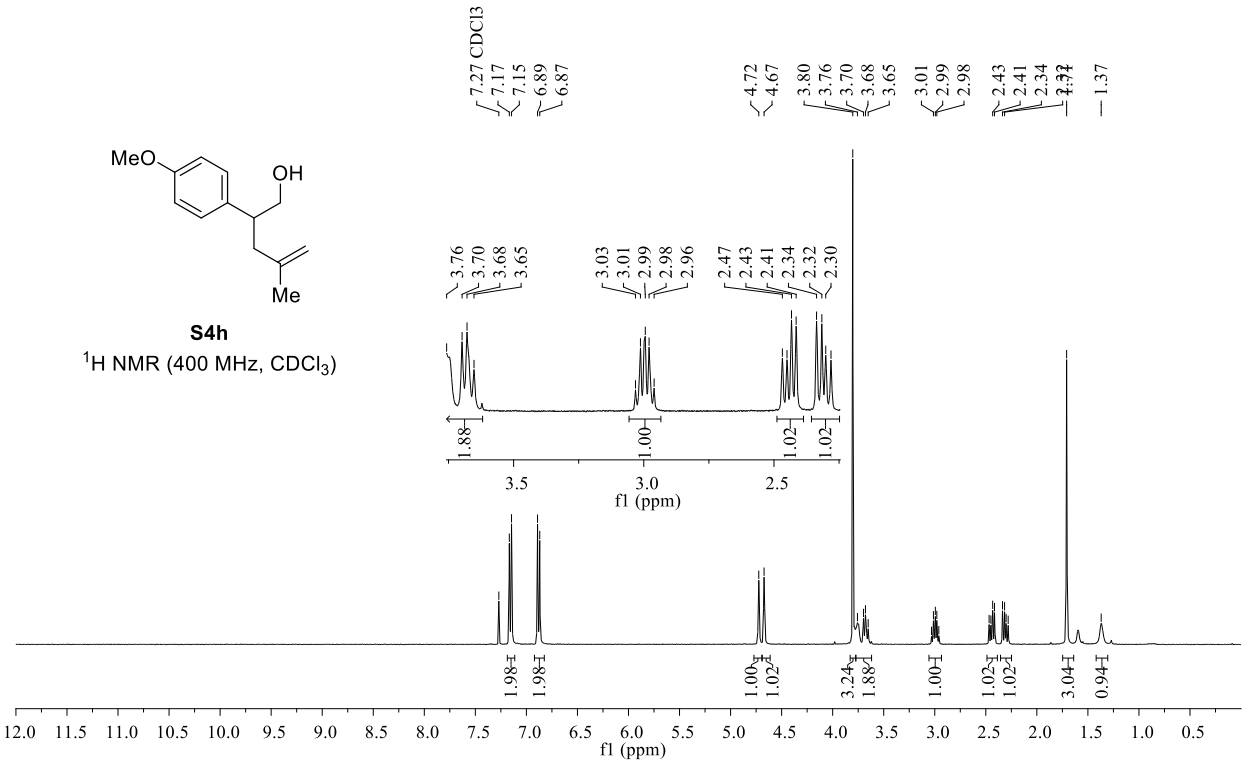



**S4g**

$^{1}$H NMR (400 MHz, $CDCl_3$)

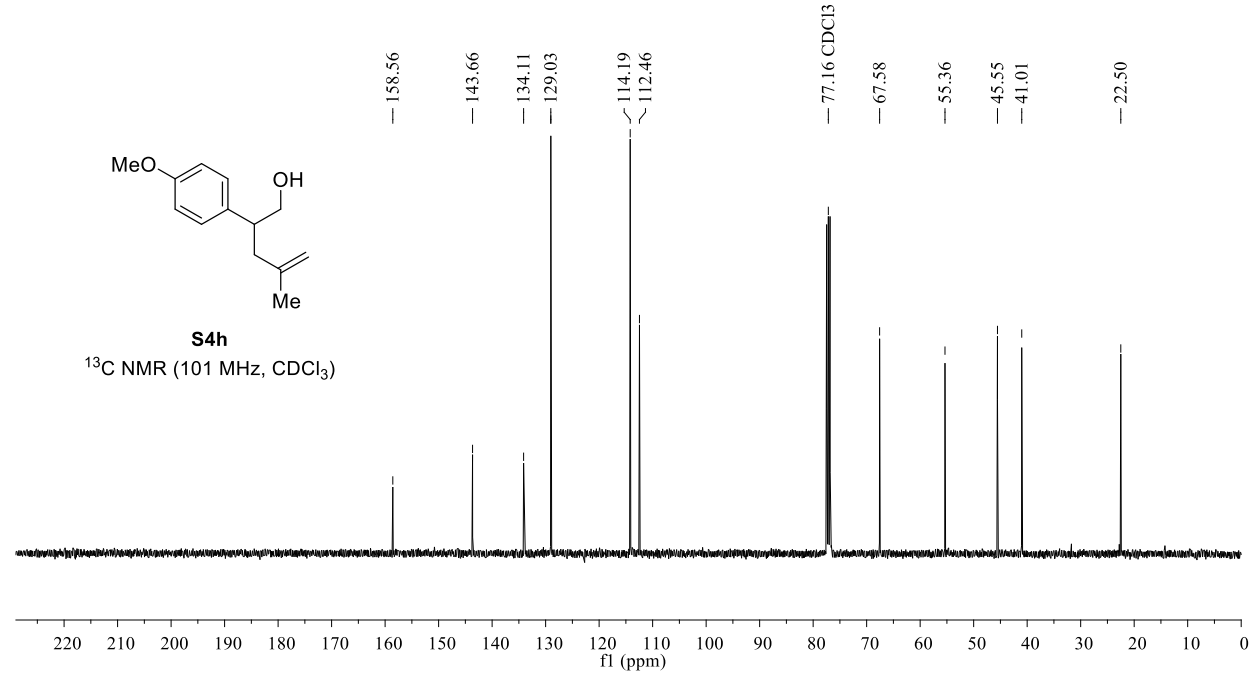

F
OH
Me
S4g
$^{13}$C NMR (101 MHz, CDCl$_3$)
163.05
160.62
143.29
137.95
137.91
129.53
129.45
115.62
115.41
112.70
77.16 CDCl3
67.41
45.67
40.95
22.45
137.95
137.91
129.53
129.45
115.62
115.41
137
135
133
131
f1 (ppm)
115.5
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-116.55
F
OH
Me
S4g
$^{19}$F NMR (376 MHz, CDCl$_3$)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)



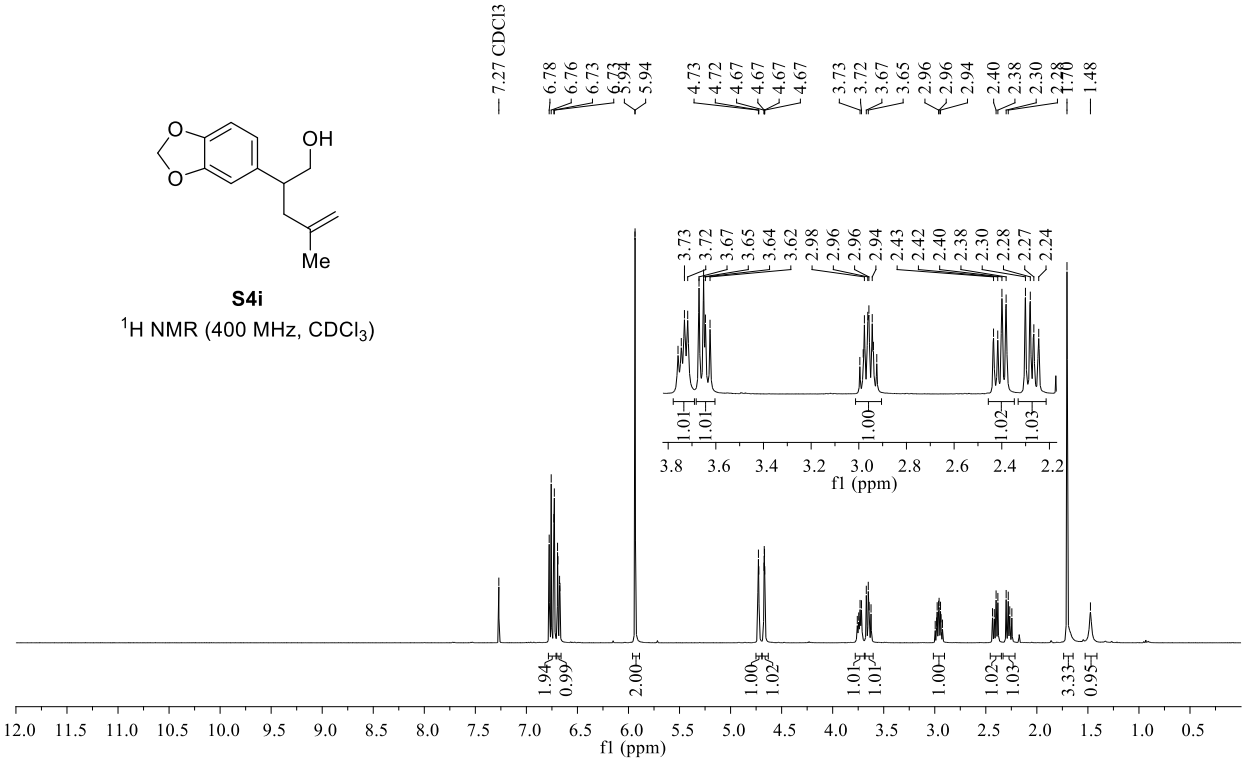

**S4h**

$^{1}$H NMR (400 MHz, $CDCl_3$)



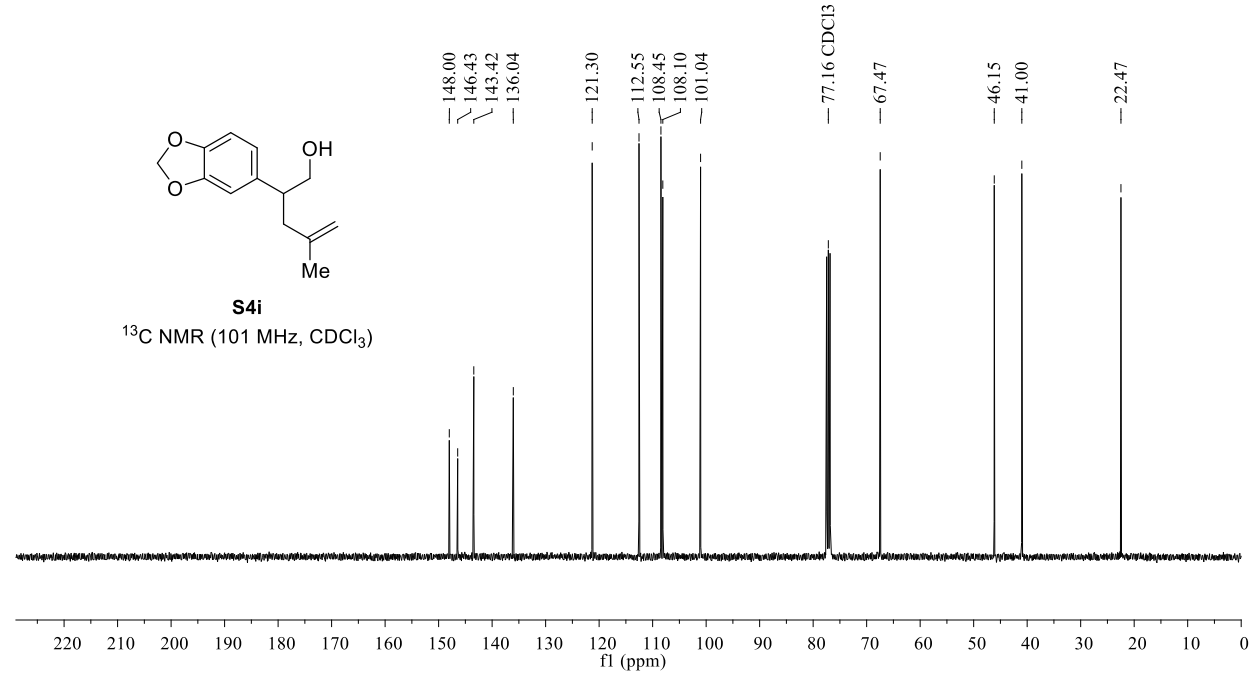

**S4h**

$^{13}$C NMR (101 MHz, $CDCl_3$)



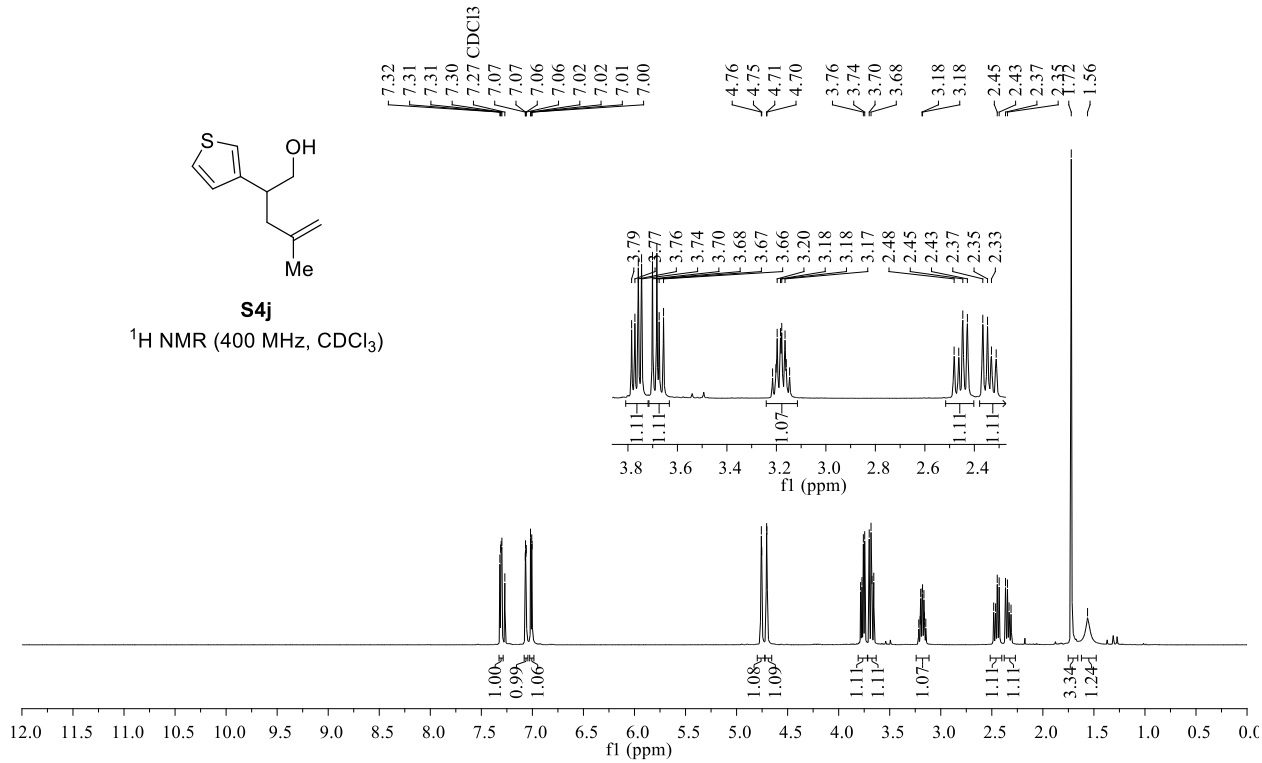

**S4i**

$^{1}$H NMR (400 MHz, $CDCl_3$)



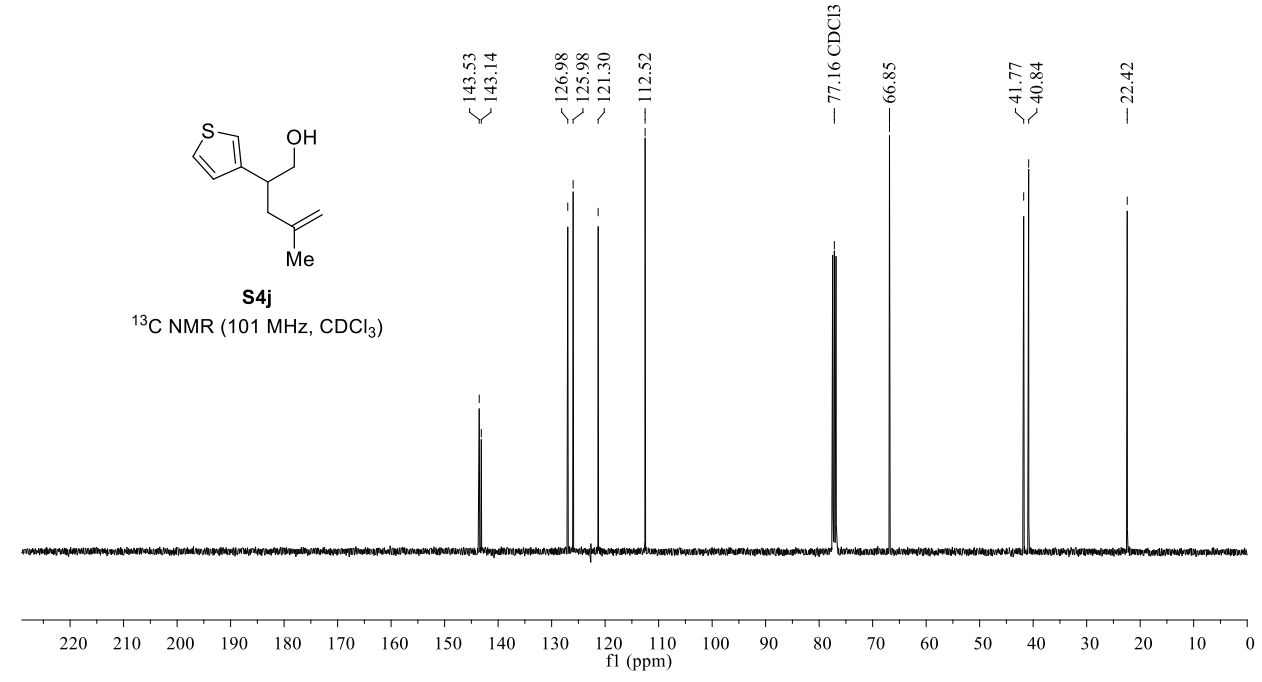

**S4i**

$^{13}$C NMR (101 MHz, $CDCl_3$)



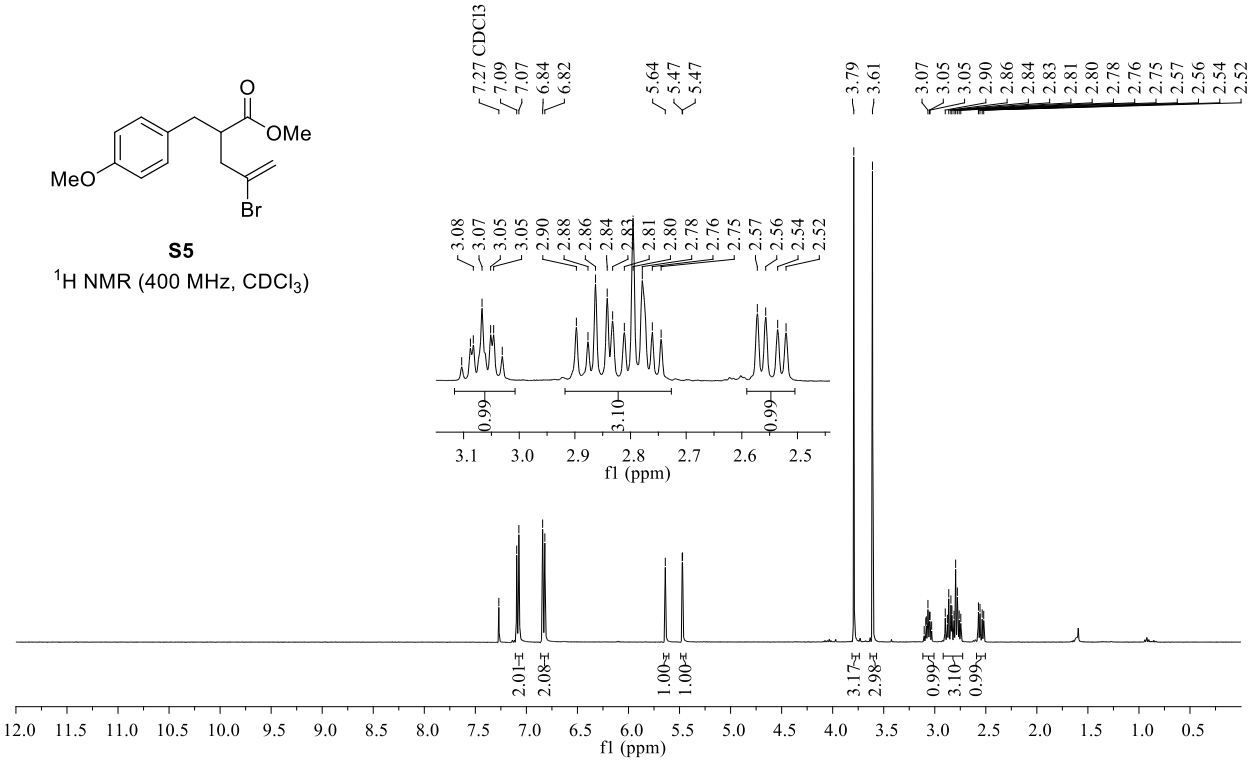

**S4j**

$^{1}$H NMR (400 MHz, $CDCl_3$)



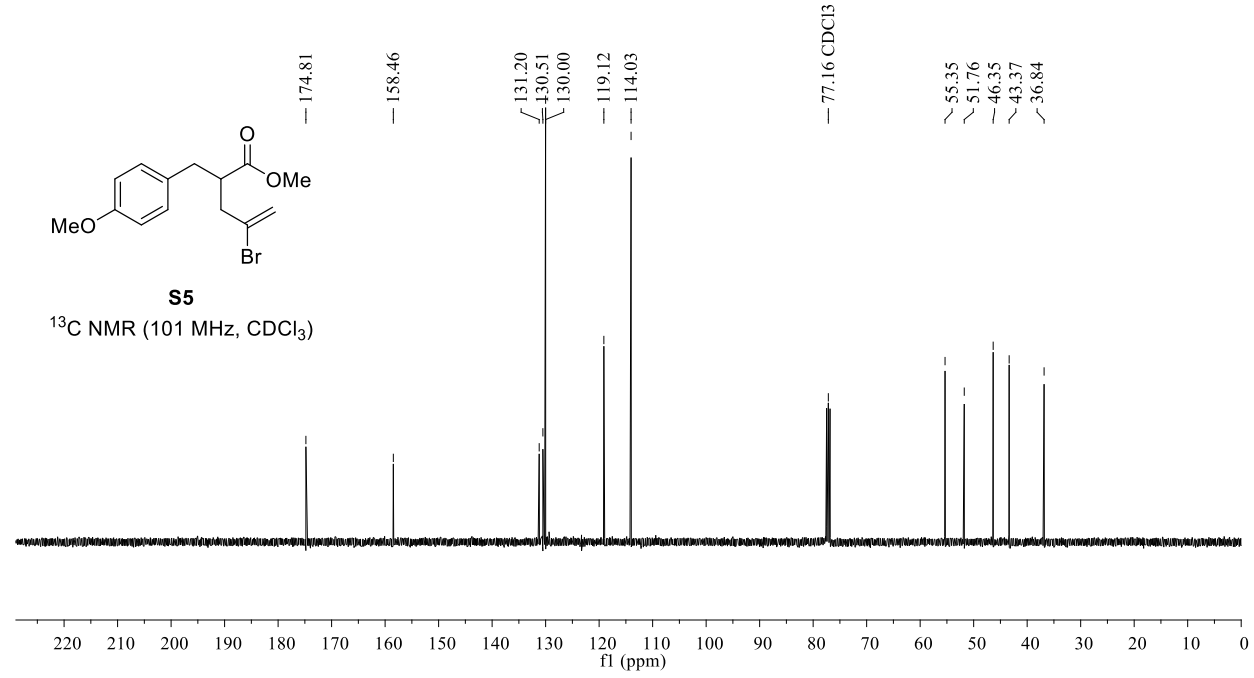

**S4j**

$^{13}$C NMR (101 MHz, $CDCl_3$)



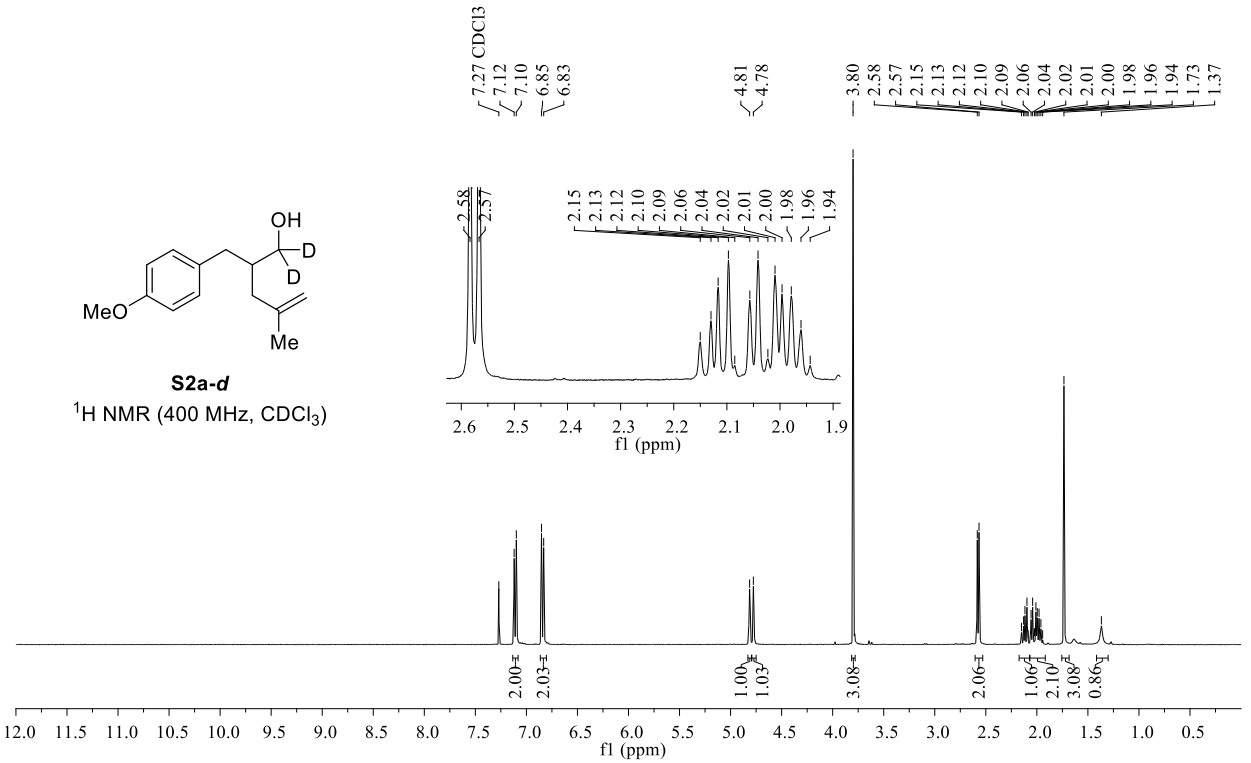

**S5**

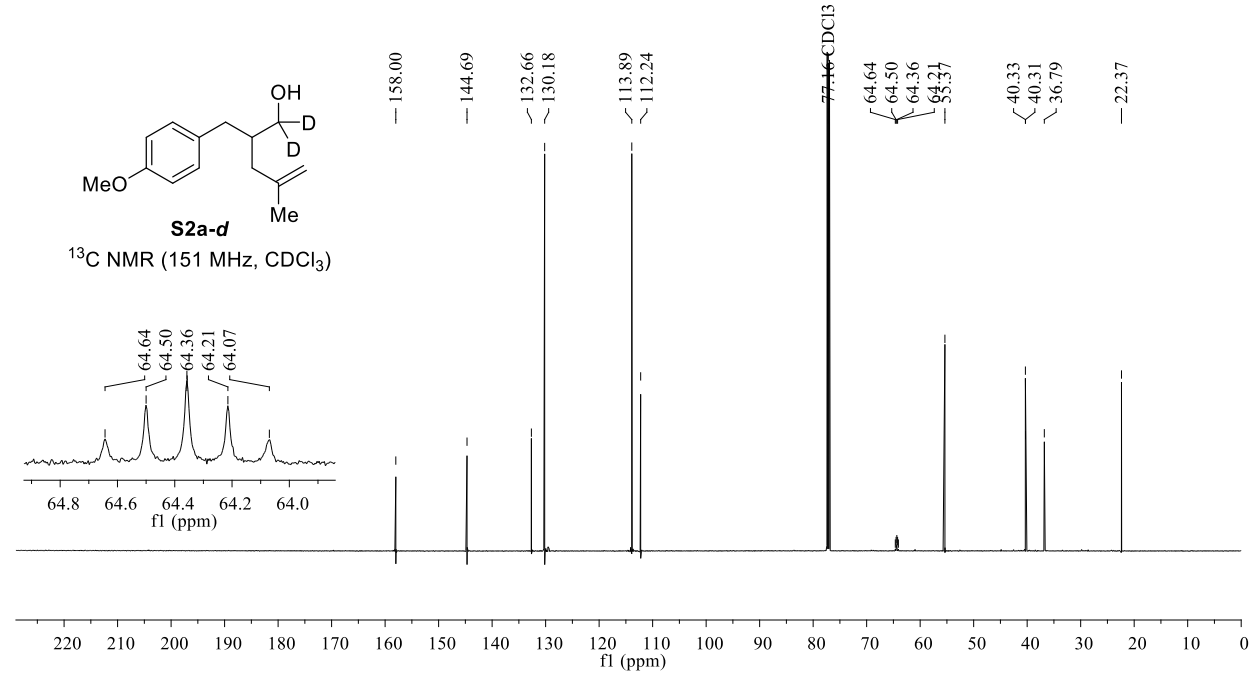
$^{1}$H NMR (400 MHz, $CDCl_3$)

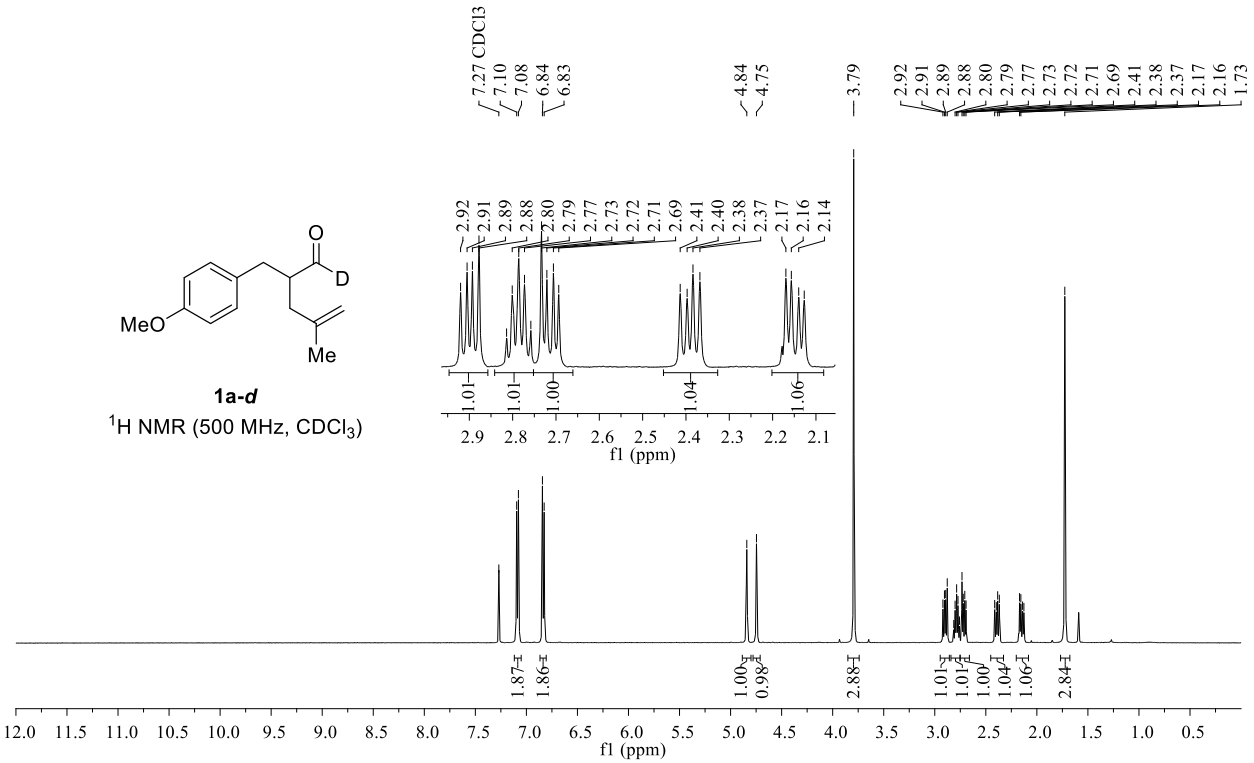


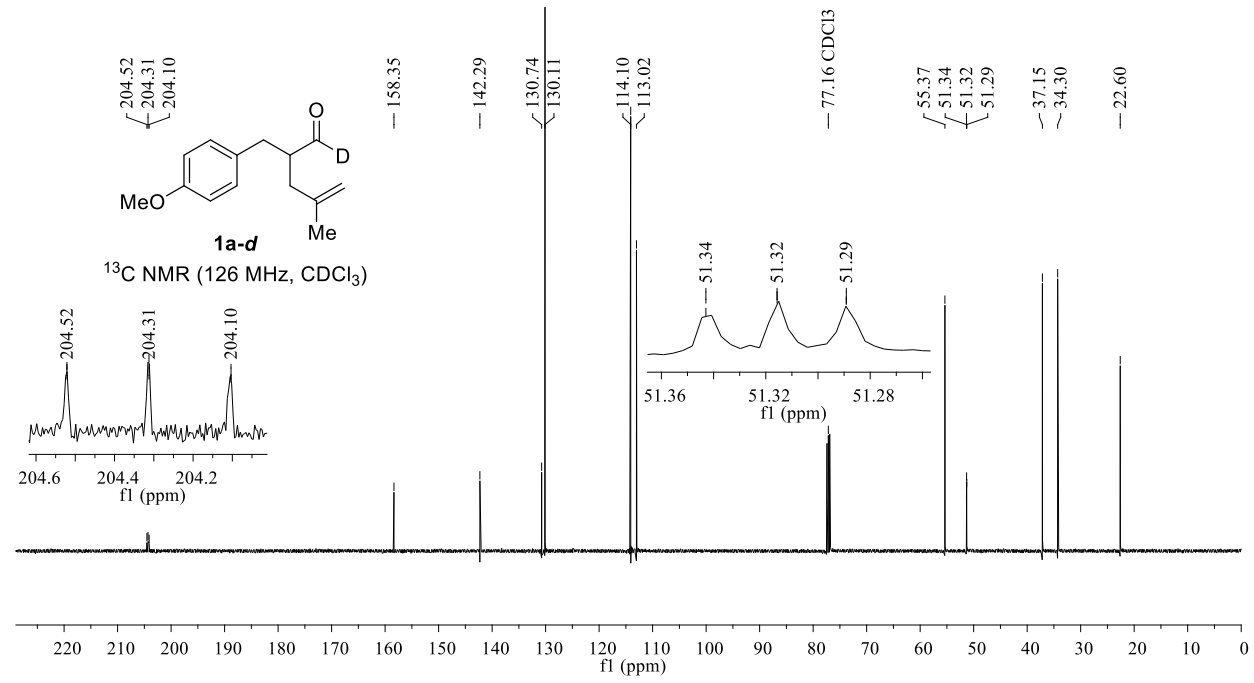

**S5**

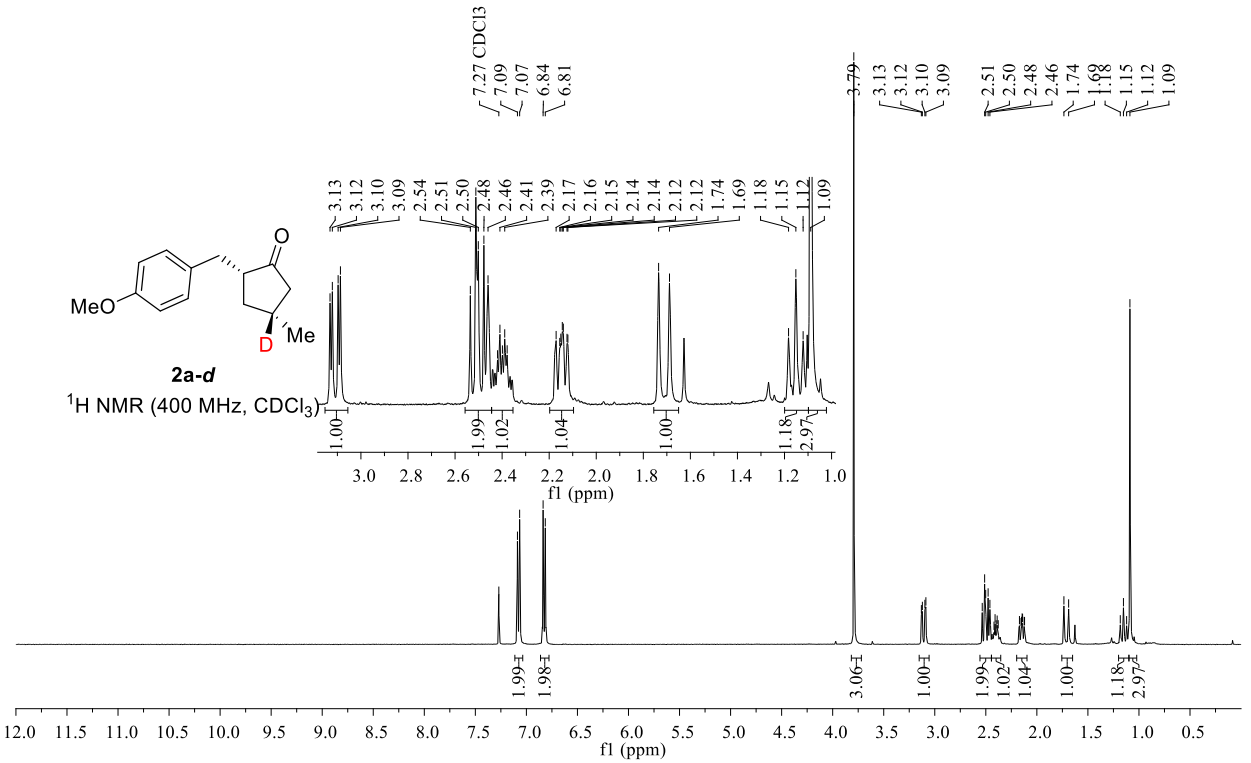
$^{13}$C NMR (101 MHz, $CDCl_3$)

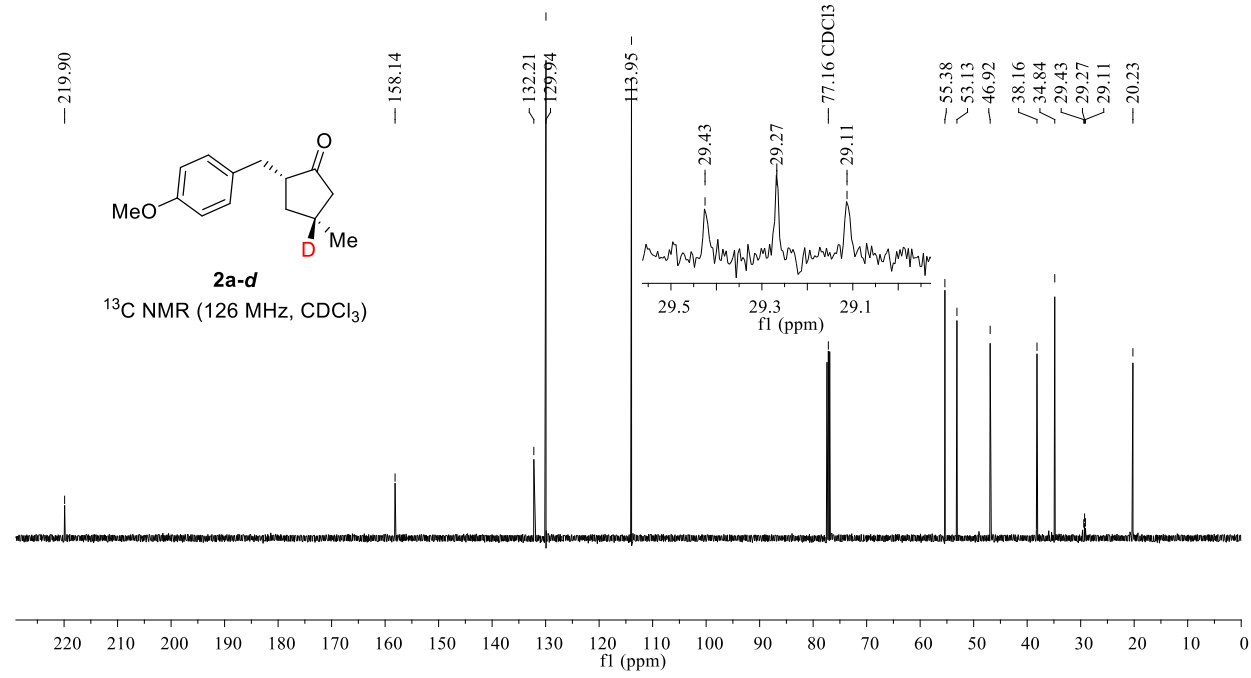

OH
D
D
MeO
Me
S2a-d
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
7.12
7.10
6.85
6.83
4.81
4.78
3.80
2.58
2.57
2.15
2.13
2.12
2.10
2.09
2.06
2.04
2.02
2.01
2.00
1.98
1.96
1.94
1.73
1.37
2.00
2.03
1.00
1.03
3.08
2.06
1.06
2.10
3.08
0.86
f1 (ppm)

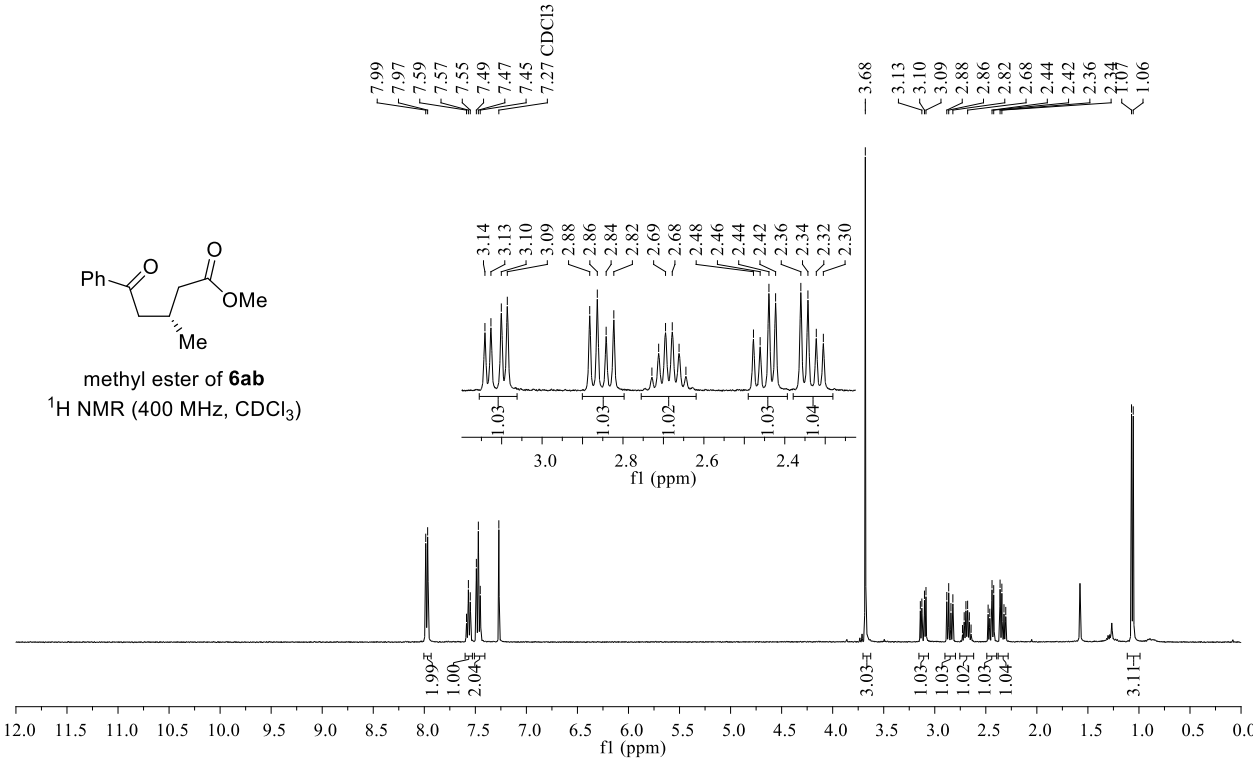

OH
D
D
MeO
Me
S2a-d
13C NMR (151 MHz, CDCl3)
158.00
144.69
132.66
130.18
113.89
112.24
77.16 CDCl3
64.64
64.50
64.36
64.21
64.07
55.37
40.33
40.31
36.79
22.37
f1 (ppm)

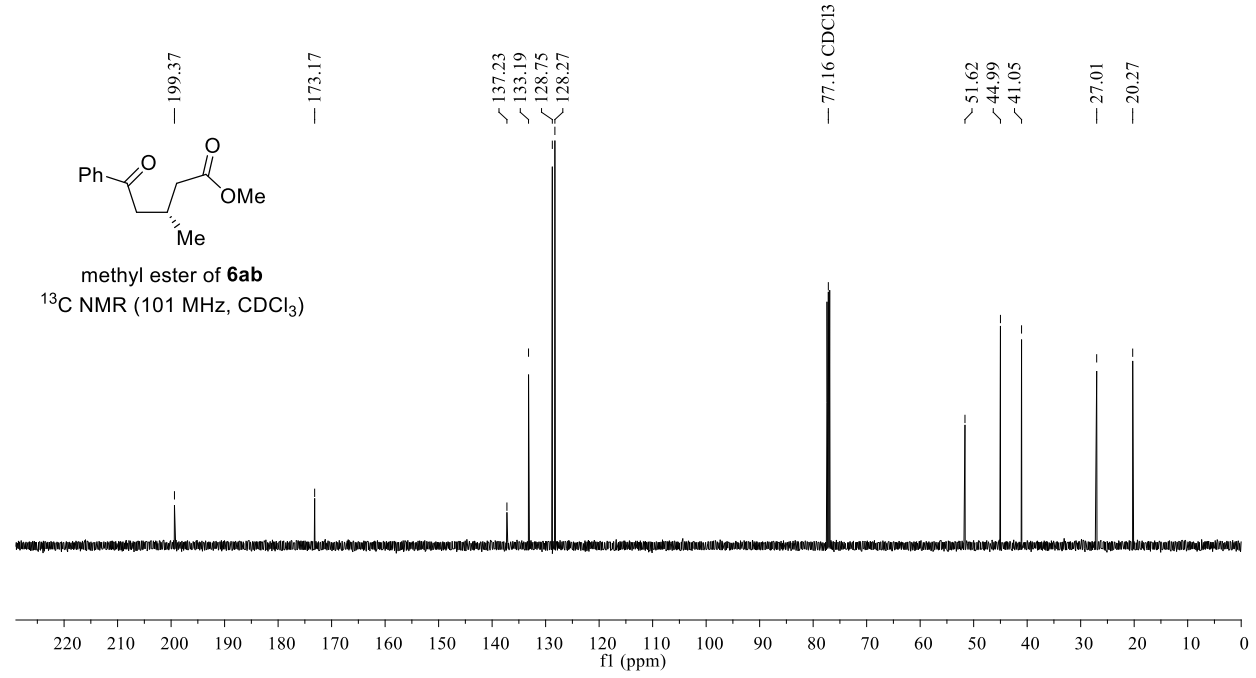

7.27 CDCl3
7.10
7.08
6.84
6.83
4.84
4.75
3.79
2.92
2.91
2.89
2.88
2.80
2.79
2.77
2.73
2.72
2.71
2.69
2.41
2.40
2.38
2.37
2.17
2.16
2.14
1.01
1.01
1.00
1.04
1.06
f1 (ppm)
1.87
1.86
1.00
0.98
2.88
1.01
1.01
1.00
1.04
1.06
2.84
f1 (ppm)
MeO
O
D
Me
1a-d
1H NMR (500 MHz, CDCl3)

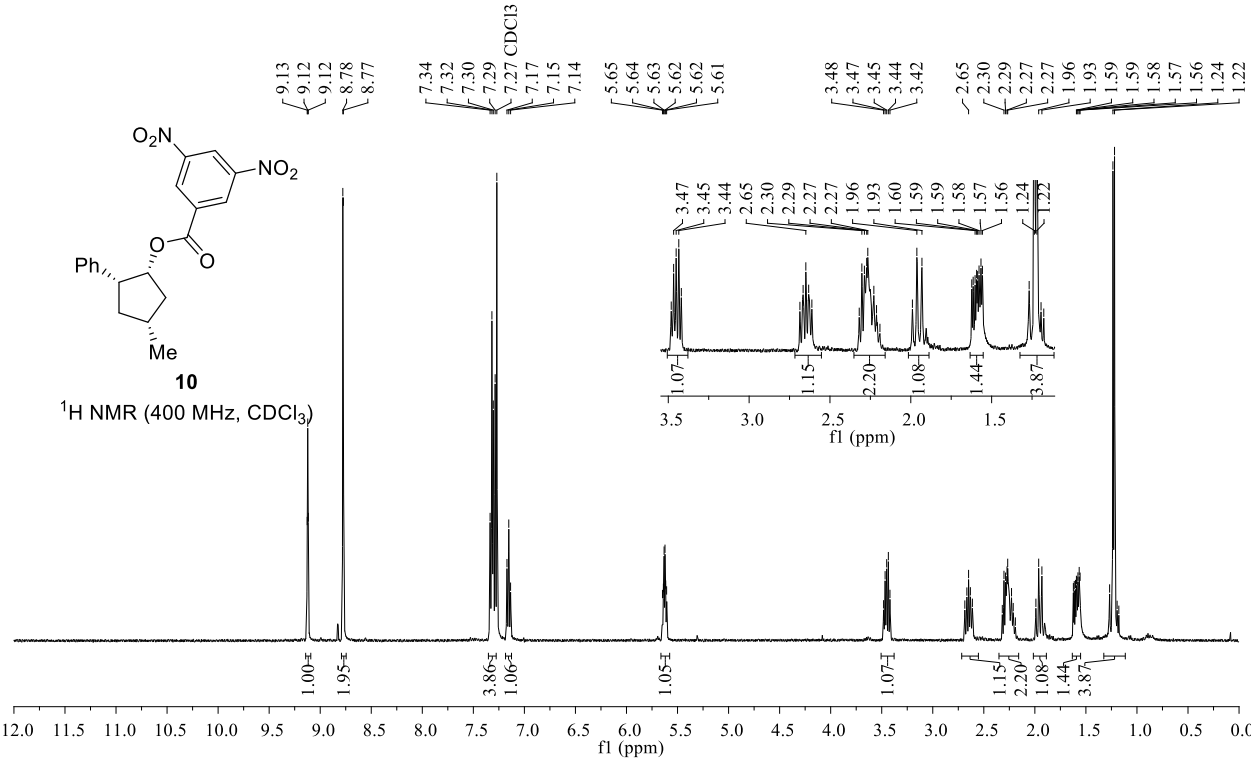

204.52
204.31
204.10
158.35
142.29
130.74
130.11
114.10
113.02
77.16 CDCl3
55.37
51.34
51.32
51.29
37.15
34.30
22.60
204.6
204.4
204.2
f1 (ppm)
51.36
51.32
51.28
f1 (ppm)
f1 (ppm)
MeO
O
D
Me
1a-d
13C NMR (126 MHz, CDCl3)

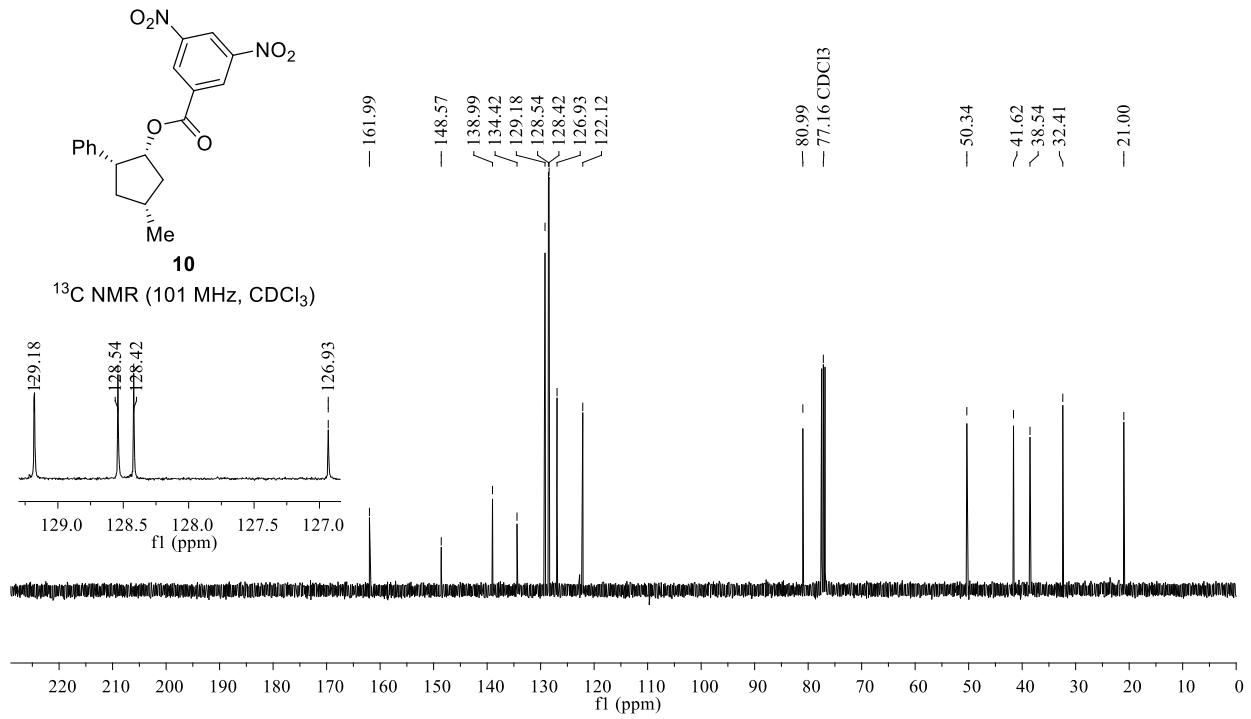

MeO
O
D
Me
2a-d
1H NMR (400 MHz, CDCl3)
f1 (ppm)

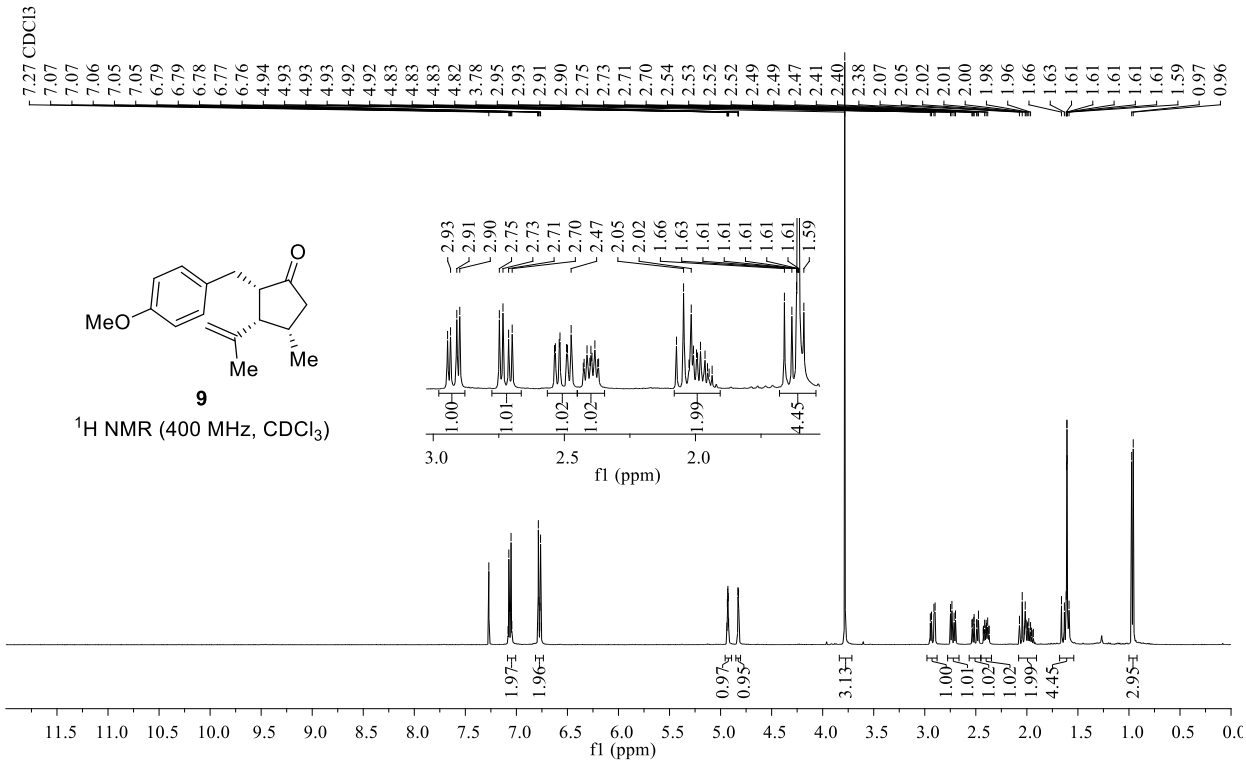

MeO
O
D
Me
2a-d
13C NMR (126 MHz, CDCl3)
f1 (ppm)

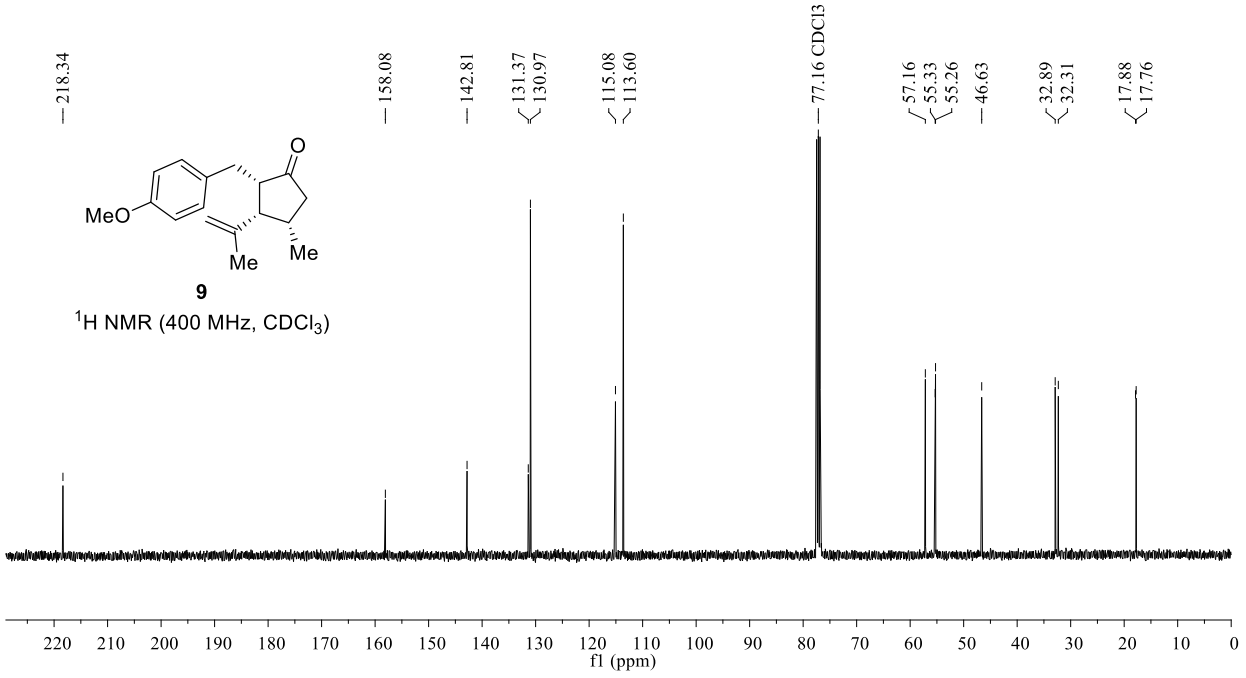

7.99
7.97
7.59
7.57
7.55
7.49
7.47
7.45
7.27 CDCl3
3.68
3.13
3.10
3.09
2.88
2.86
2.82
2.68
2.44
2.42
2.36
1.07
1.06
3.14
3.13
3.10
3.09
2.88
2.86
2.84
2.82
2.69
2.68
2.48
2.46
2.44
2.42
2.36
2.34
2.32
2.30
1.03
1.03
1.02
1.03
1.04
3.0
2.8
2.6
2.4
f1 (ppm)
Ph
O
O
OMe
Me
methyl ester of 6ab
1H NMR (400 MHz, CDCl3)
1.99
1.00
2.04
3.03
1.03
1.03
1.02
1.03
1.04
3.11
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

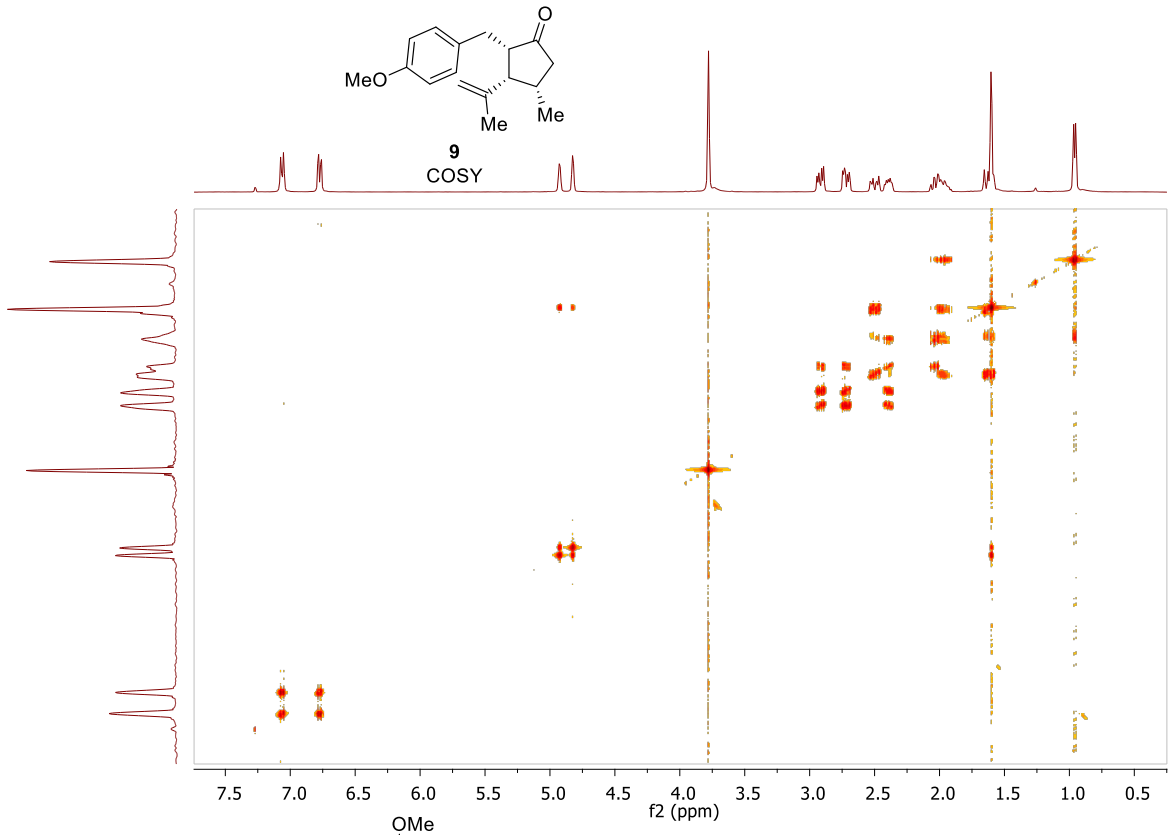

199.37
173.17
137.23
133.19
128.75
128.27
77.16 CDCl3
51.62
44.99
41.05
27.01
20.27
Ph
O
O
OMe
Me
methyl ester of 6ab
13C NMR (101 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

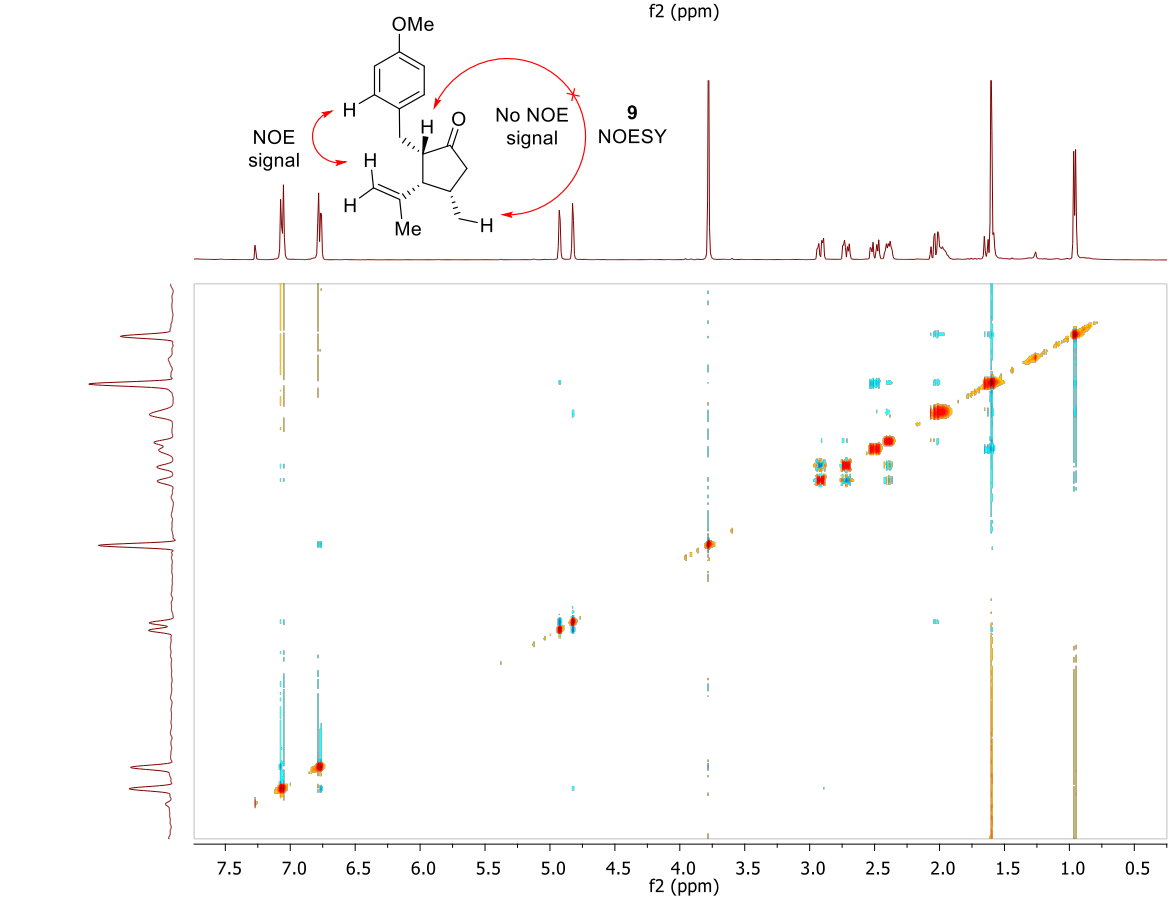

9.13
9.12
9.12
8.78
8.77
7.34
7.32
7.30
7.29
7.27 CDCl3
7.17
7.15
7.14
5.65
5.64
5.63
5.62
5.62
5.61
3.48
3.47
3.45
3.44
3.42
2.65
2.30
2.29
2.27
2.27
1.96
1.93
1.59
1.59
1.58
1.57
1.56
1.24
1.22
O2N
NO2
O
O
Ph
Me
10
1H NMR (400 MHz, CDCl3)
1.00
1.95
3.86
1.06
1.05
1.07
1.15
2.20
1.08
1.44
3.87
f1 (ppm)

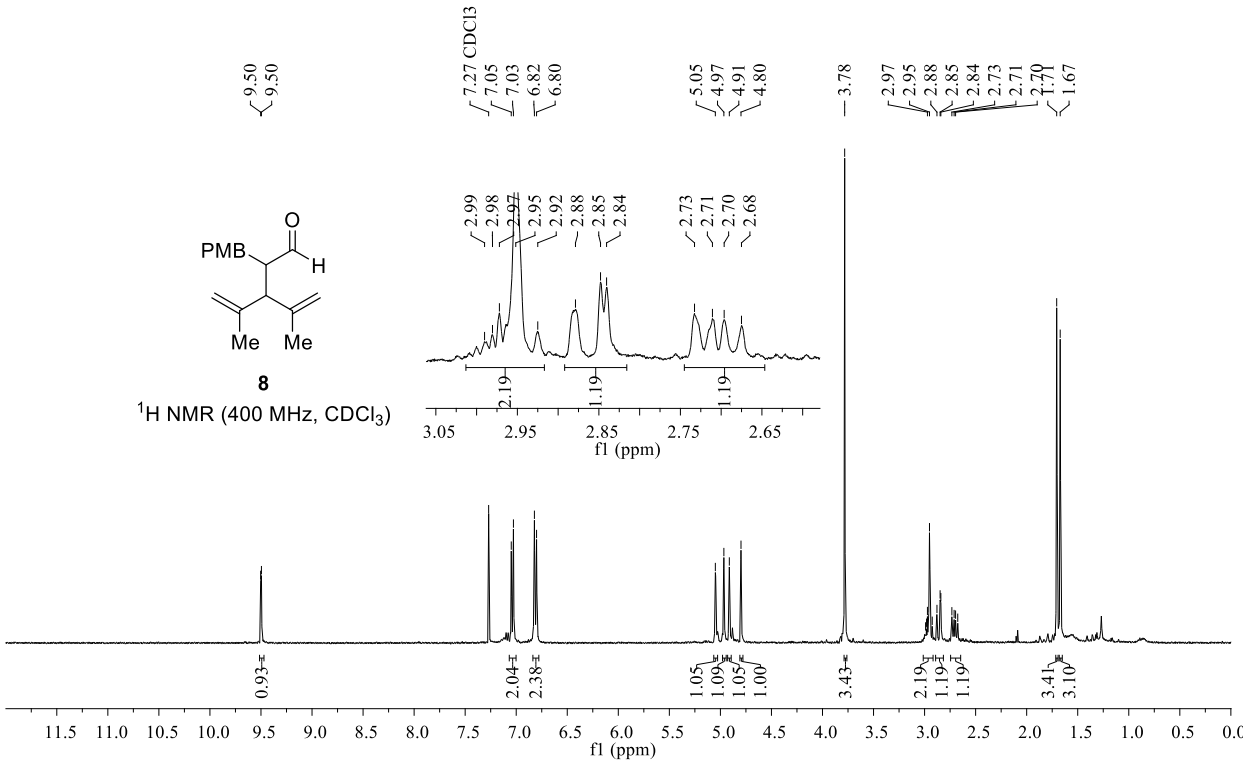

O2N
NO2
O
O
Ph
Me
10
13C NMR (101 MHz, CDCl3)
161.99
148.57
138.99
134.42
129.18
128.54
128.42
126.93
122.12
80.99
77.16 CDCl3
50.34
41.62
38.54
32.41
21.00
f1 (ppm)

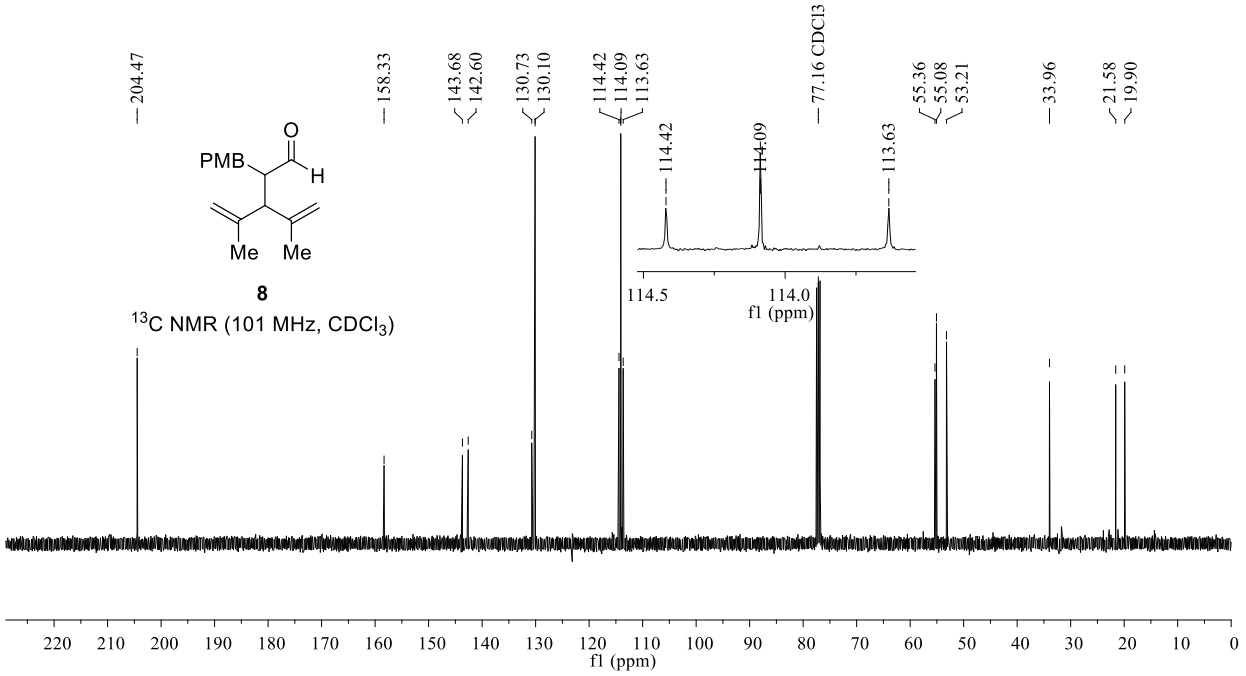

MeO
Me
Me
O
9
$^1$H NMR (400 MHz, $CDCl_3$)
fl (ppm)

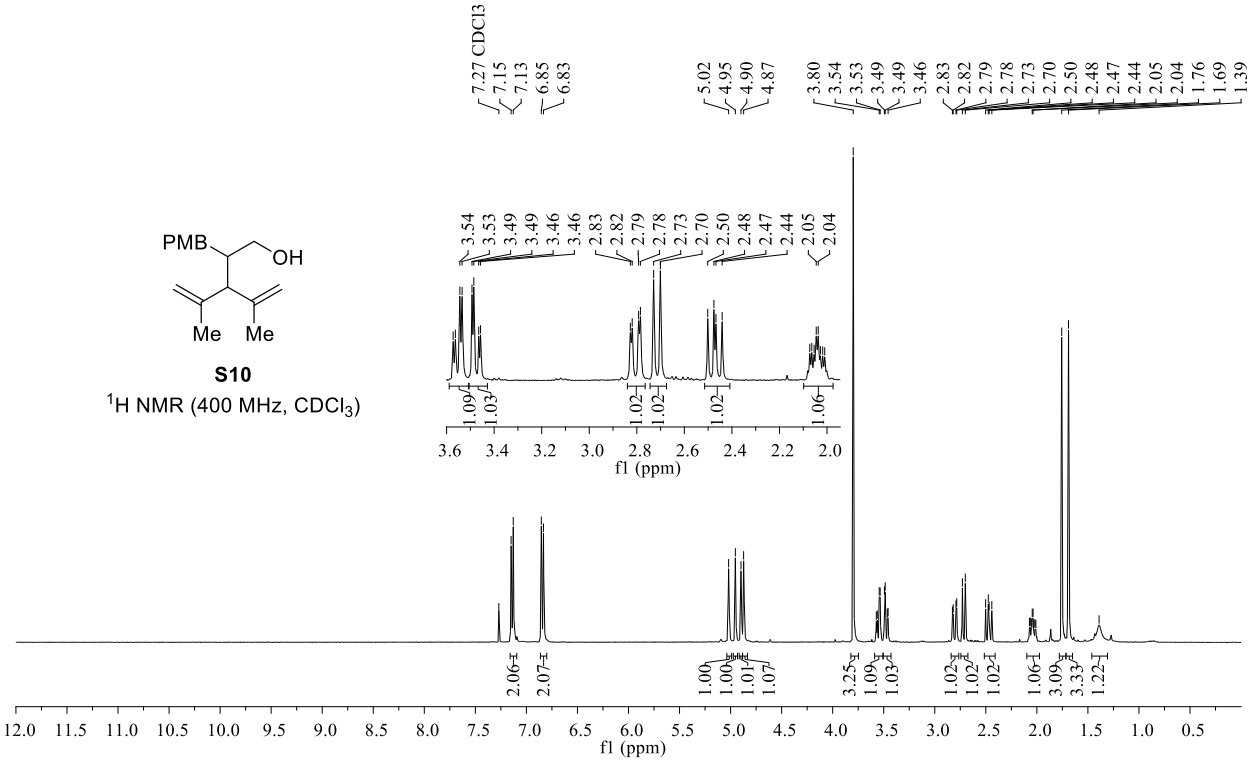

MeO
Me
Me
O
9
$^1$H NMR (400 MHz, $CDCl_3$)
fl (ppm)

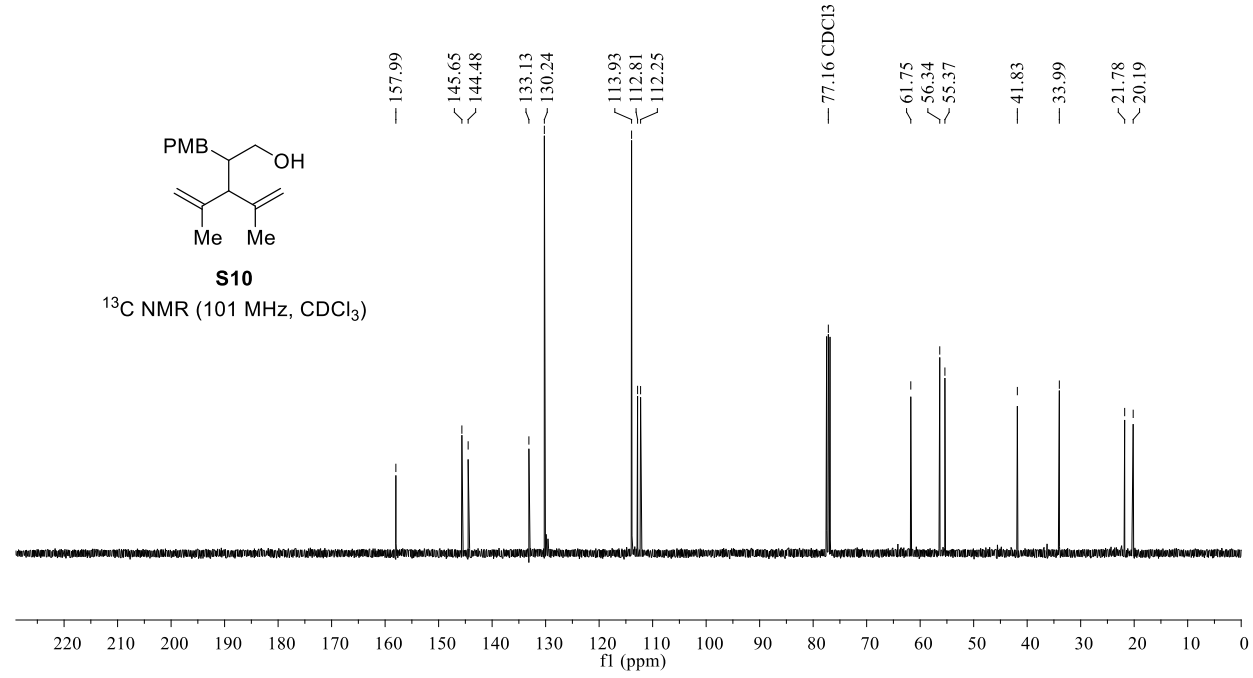

MeO
O
Me
Me
9
COSY
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)


OMe
H
H
O
H
H
Me
H
NOE
signal
No NOE
signal
9
NOESY
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)

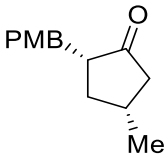

9.50
9.50
7.27 CDCl3
7.05
7.03
6.82
6.80
5.05
4.97
4.91
4.80
3.78
2.97
2.95
2.88
2.85
2.84
2.73
2.71
2.70
1.71
1.67
PMB
O
H
Me
Me
8
1H NMR (400 MHz, CDCl3)
2.99
2.98
2.97
2.95
2.92
2.88
2.85
2.84
2.73
2.71
2.70
2.68
2.19
1.19
1.19
3.05
2.95
2.85
2.75
2.65
f1 (ppm)
0.93
2.04
2.38
1.05
1.09
1.05
1.00
3.43
2.19
1.19
1.19
3.41
3.10
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


204.47
158.33
143.68
142.60
130.73
130.10
114.42
114.09
113.63
77.16 CDCl3
55.36
55.08
53.21
33.96
21.58
19.90
PMB
O
H
Me
Me
8
13C NMR (101 MHz, CDCl3)
114.42
114.09
113.63
114.5
114.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

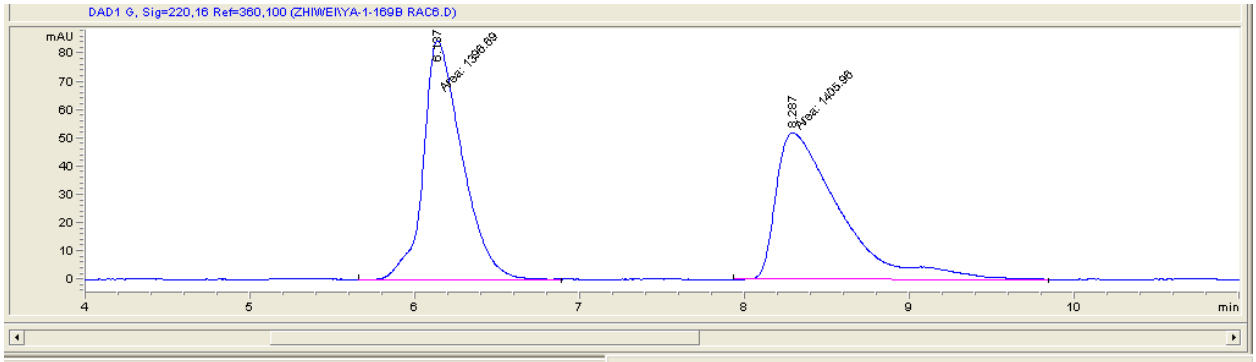

PMB
OH
Me
Me
S10
1H NMR (400 MHz, CDCl3)
7.27 CDCl3
7.15
7.13
6.85
6.83
5.02
4.95
4.90
4.87
3.80
3.54
3.53
3.49
3.49
3.46
2.83
2.82
2.79
2.78
2.73
2.70
2.50
2.48
2.47
2.44
2.05
2.04
1.76
1.69
1.39
f1 (ppm)


PMB
OH
Me
Me
S10
13C NMR (101 MHz, CDCl3)
157.99
145.65
144.48
133.13
130.24
113.93
112.81
112.25
77.16 CDCl3
61.75
56.34
55.37
41.83
33.99
21.78
20.19
f1 (ppm)

## 14. SFC Spectra




(±)-**2a**




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.137 | 1396.7 | 84.7 | 0.2749 | 49.835 | 0.596 |
| 2 | 8.287 | 1406 | 51.8 | 0.4521 | 50.165 | 0.333 |

| File Information | |
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| LC-File | YA-1-169B RAC6.D |
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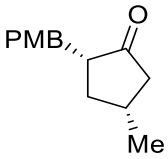
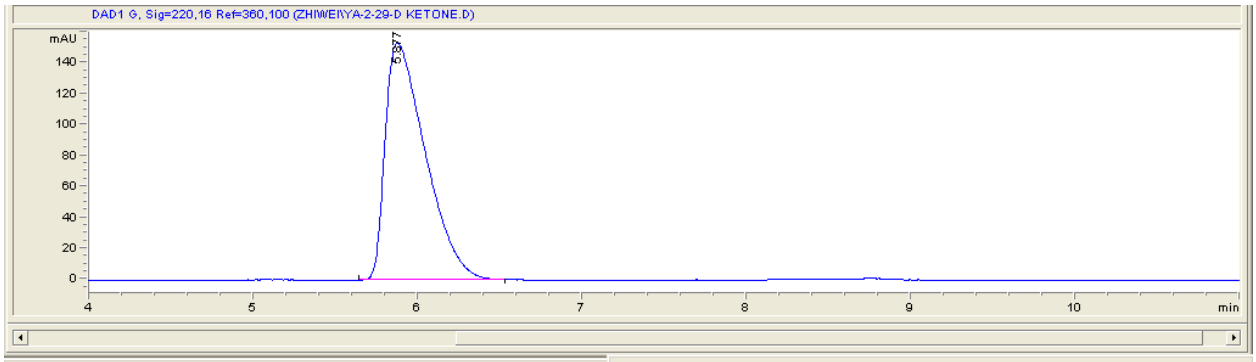
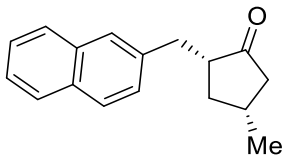



(+)-**2a**

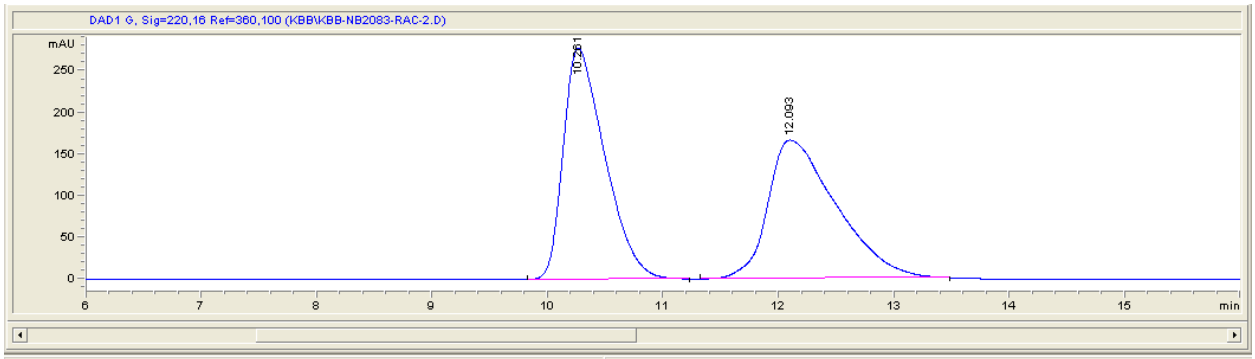



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.877 | 2625 | 153.5 | 0.2546 | 100.000 | 0.409 |

| File Information | |
|---|---|
| LC-File | YA-2-29-D KETONE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

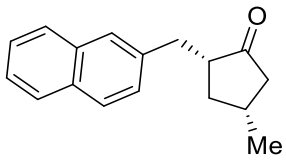



(±)-**2b**

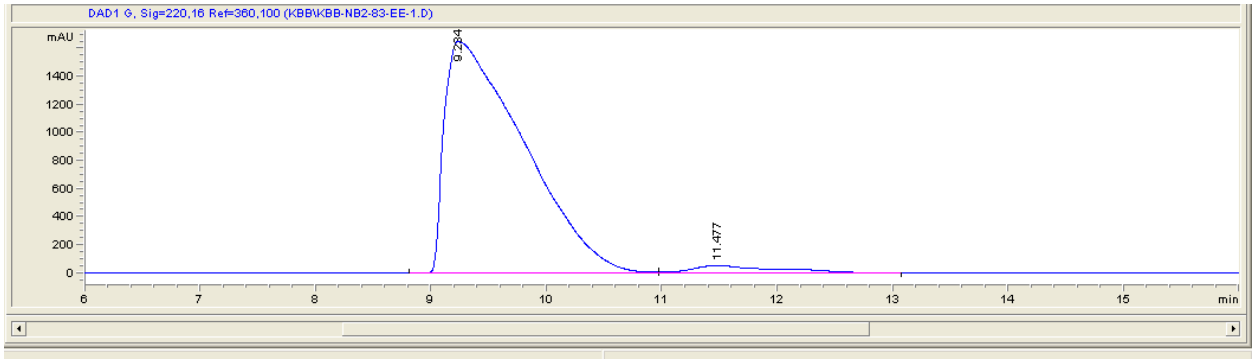



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.261 | 6941.6 | 277.5 | 0.3558 | 50.179 | 0.534 |
| 2 | 12.093 | 6892.1 | 166.4 | 0.5433 | 49.821 | 0.454 |

| File Information | |
|---|---|
| LC-File | KBB-NB2083-RAC-2.D |
| File Path | C:\CHEM32\1\DATA\KBB\ |

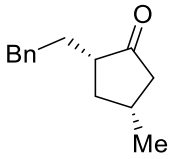



(+)-**2b**

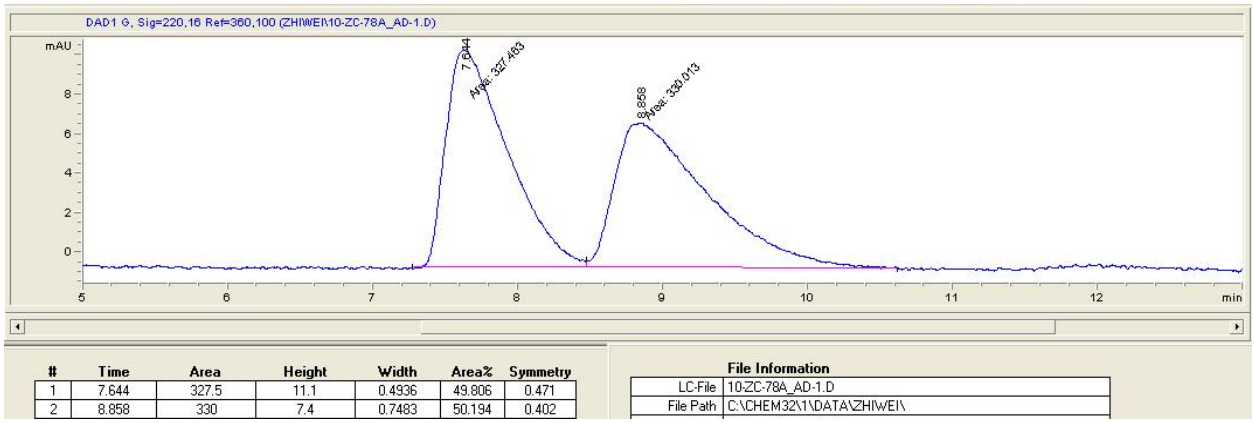



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.234 | 78823.5 | 1652.9 | 0.6134 | 96.567 | 0.202 |
| 2 | 11.477 | 2802.4 | 53.1 | 0.6358 | 3.433 | 0.388 |

| File Information | |
|---|---|
| LC-File | KBB-NB2-83-EE-1.D |
| File Path | C:\CHEM32\1\DATA\KBB\ |

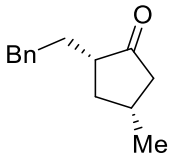



(±)-**2c**

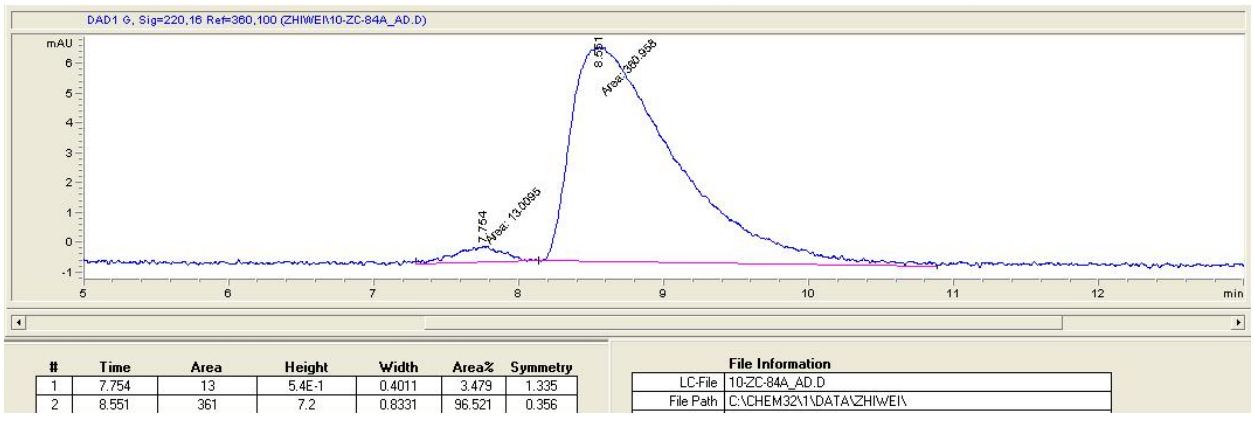



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.644 | 327.5 | 11.1 | 0.4936 | 49.806 | 0.471 |
| 2 | 8.858 | 330 | 7.4 | 0.7483 | 50.194 | 0.402 |

| File Information | |
|---|---|
| LC-File | 10-ZC-78A_AD-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

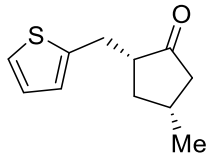



(+)-**2c**

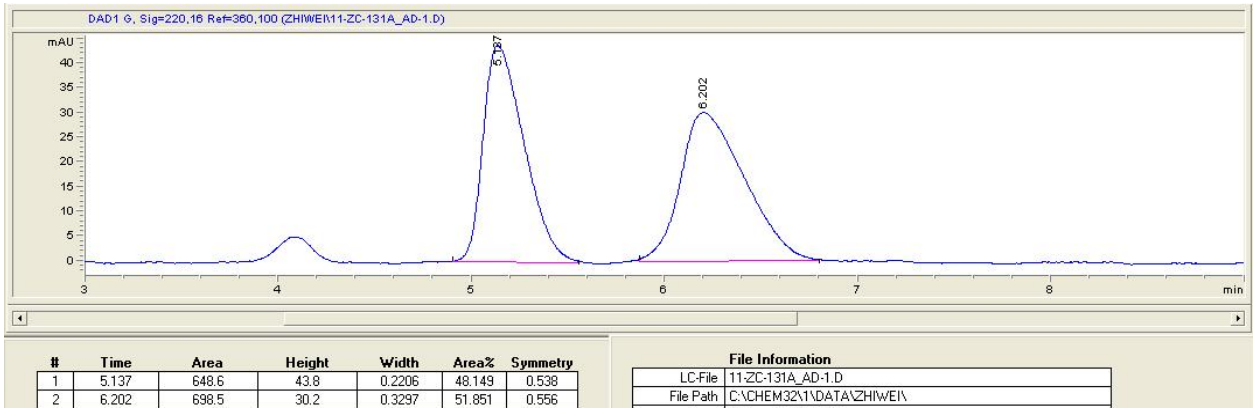



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.754 | 13 | 5.4E-1 | 0.4011 | 3.479 | 1.335 |
| 2 | 8.551 | 361 | 7.2 | 0.8331 | 96.521 | 0.356 |

| File Information | |
|---|---|
| LC-File | 10-ZC-84A_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |



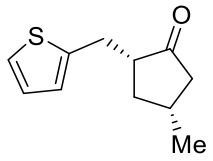

(±)-**2d**



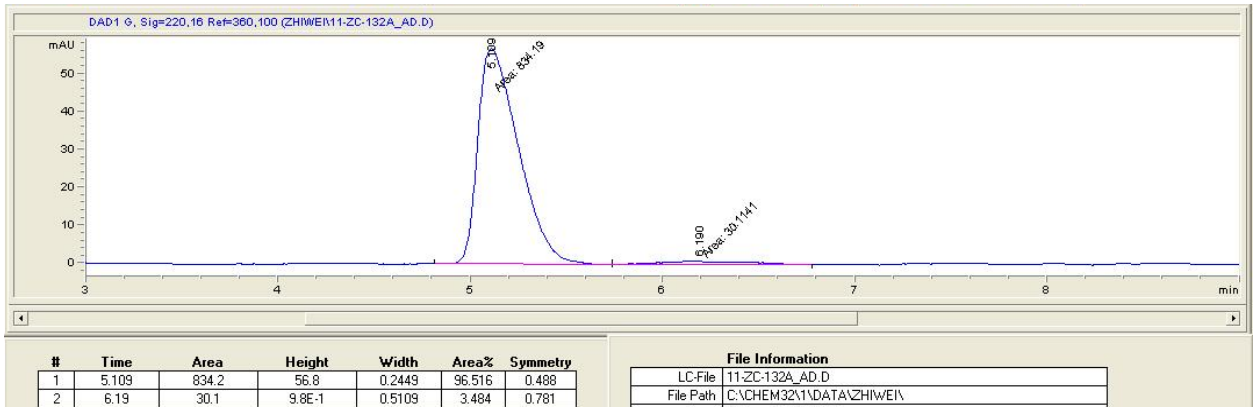

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.137 | 648.6 | 43.8 | 0.2206 | 48.149 | 0.538 |
| 2 | 6.202 | 698.5 | 30.2 | 0.3297 | 51.851 | 0.556 |

| File Information | |
|---|---|
| LC-File | 11-ZC-131A_AD-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

* the peak at 4.1 min correspond to the *trans* diastereomer that was not separated from the product

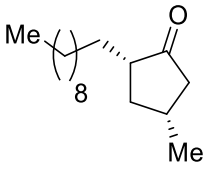



(+)-**2d**

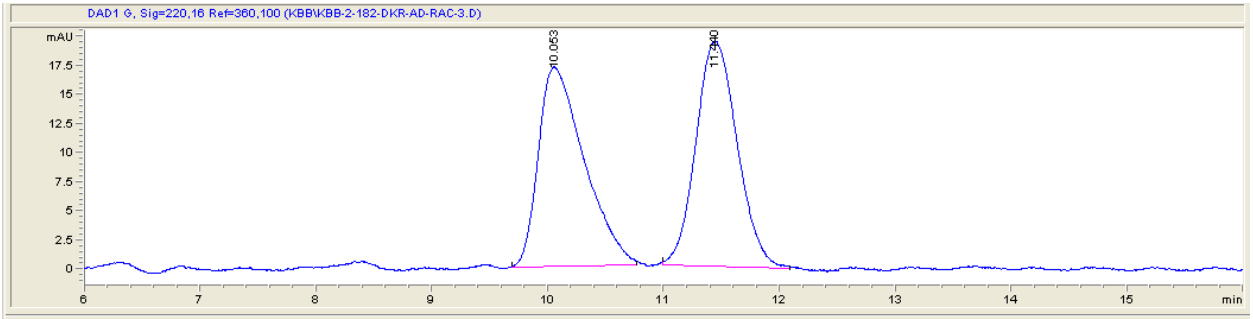



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.109 | 834.2 | 56.8 | 0.2449 | 96.516 | 0.488 |
| 2 | 6.19 | 30.1 | 9.8E-1 | 0.5109 | 3.484 | 0.781 |

| File Information | |
|---|---|
| LC-File | 11-ZC-132A_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

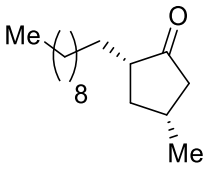



(±)-**2e**

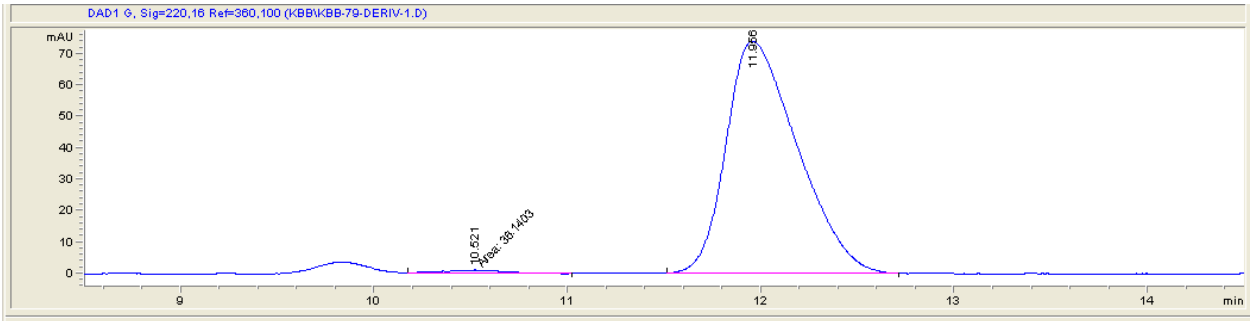



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.053 | 474.3 | 17.2 | 0.343 | 49.645 | 0.504 |
| 2 | 11.44 | 481 | 19.3 | 0.3142 | 50.355 | 0.82 |

| File Information | |
|---|---|
| LC-File | KBB-2-182-DKR-AD-RAC-3.D |
| File Path | C:\CHEM32\1\DATA\KBB\ |

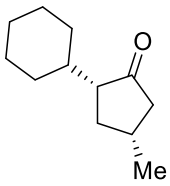



(+)-**2e**

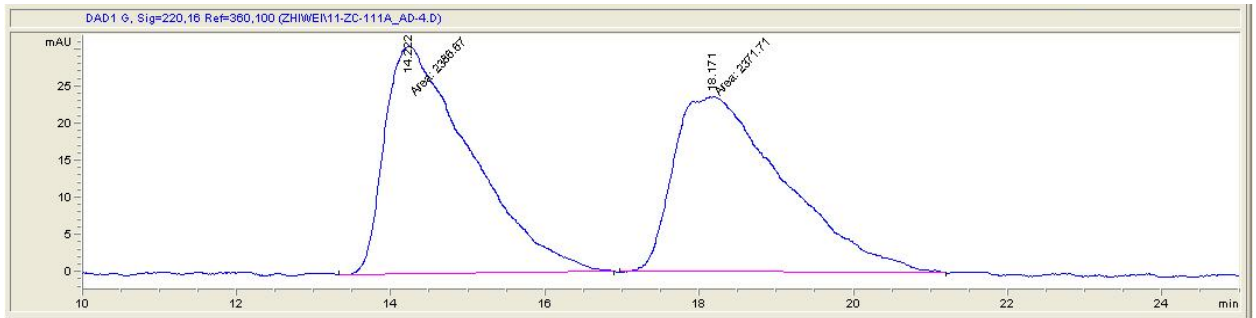



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.521 | 36.1 | 1.3 | 0.4568 | 1.864 | 0.995 |
| 2 | 11.956 | 1902.7 | 74 | 0.3619 | 98.136 | 0.579 |

| File Information | |
|---|---|
| LC-File | KBB-79-DERIV-1.D |
| File Path | C:\CHEM32\1\DATA\KBB\ |

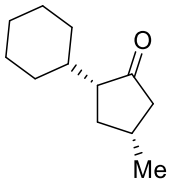



(±)-**2f**

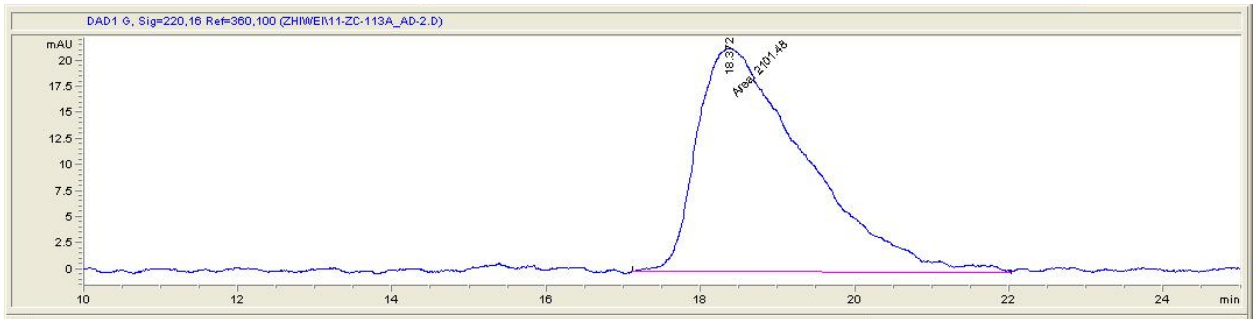



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 14.222 | 2386.7 | 30.7 | 1.294 | 50.157 | 0.374 |
| 2 | 18.171 | 2371.7 | 23.7 | 1.6693 | 49.843 | 0.526 |

| File Information | |
|---|---|
| LC-File | 11-ZC-111A_AD-4.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

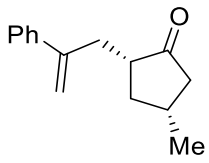



(+)-**2f**

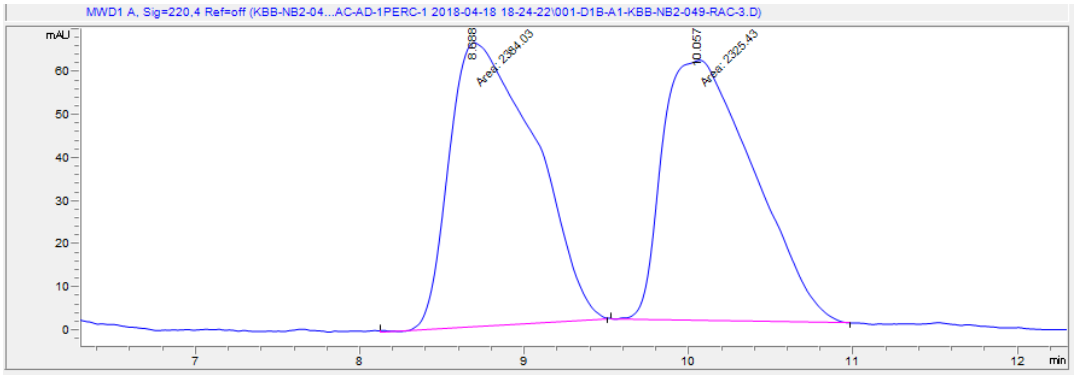



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 18.372 | 2101.5 | 21.5 | 1.6324 | 100.000 | 0.417 |

| File Information | |
|---|---|
| LC-File | 11-ZC-113A_AD-2.D |

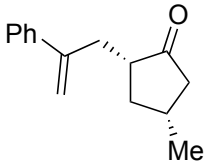



(±)-**2g**

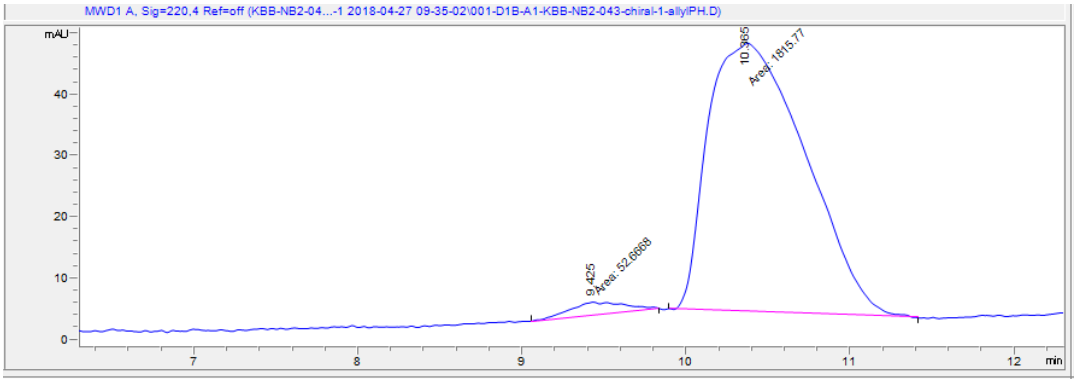



| File Information | |
|---|---|
| LC-File | 001-D1B-A1-KBB-NB2-049-RAC-3.D |
| File Path | C:\Chem32\1\Data\KBB-NB2-049-RAC-AD-1PERC-1 |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 8.688 | MM | 2384 | 65.9 | 0.6028 | 50.622 | 0.413 |
| 2 | 10.057 | MM | 2325.4 | 60.3 | 0.6424 | 49.378 | 0.653 |

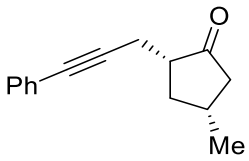



(+)-**2g**

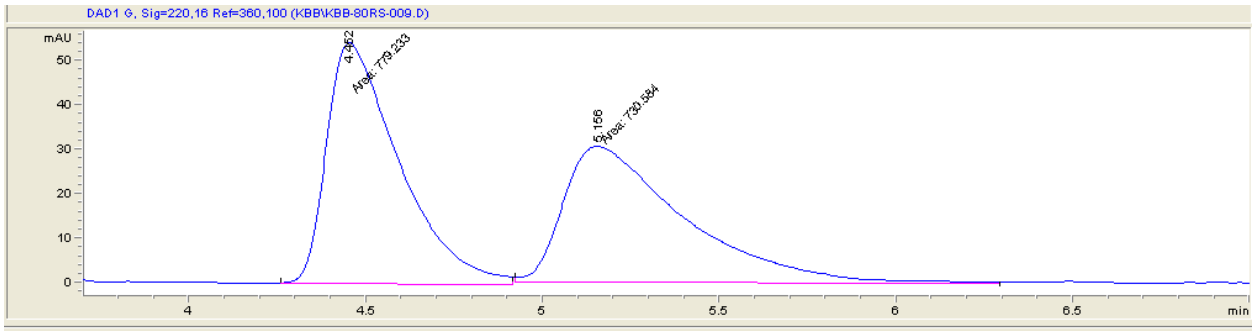



| File Information | |
|---|---|
| LC-File | 001-D1B-A1-KBB-NB2-043-chiral-1-allylPH.D |
| File Path | C:\Chem32\1\Data\KBB-NB2-043-allylPH-chiral-AD-1 |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 9.425 | MM | 52.7 | 2.2 | 0.394 | 2.819 | 0.837 |
| 2 | 10.365 | MM | 1815.8 | 44 | 0.6879 | 97.181 | 0.657 |

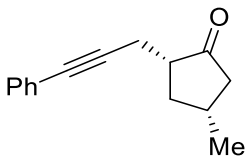



(±)-**2h**

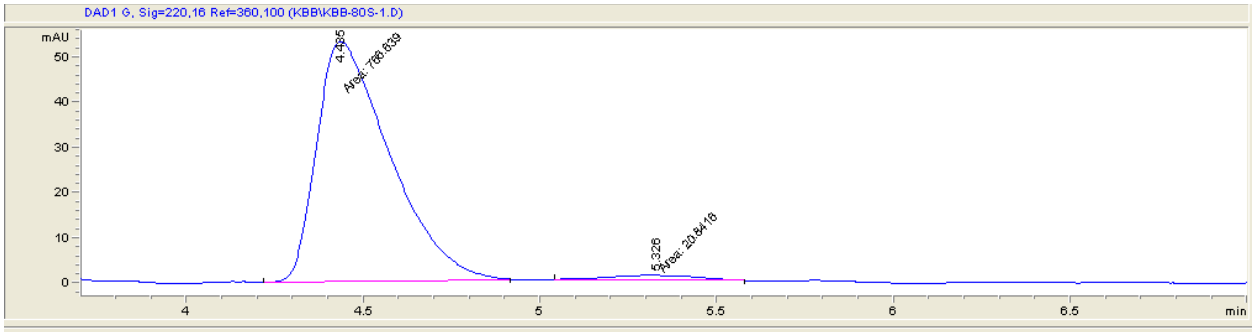



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.452 | 779.2 | 54.5 | 0.2384 | 51.611 | 0.446 |
| 2 | 5.156 | 730.6 | 30.6 | 0.3981 | 48.389 | 0.393 |

| File Information | |
|---|---|
| LC-File | KBB-80RS-009.D |
| File Path | C:\CHEM32\1\DATA\KBB\ |

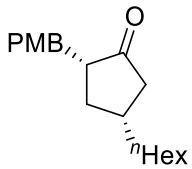



(+)-**2h**

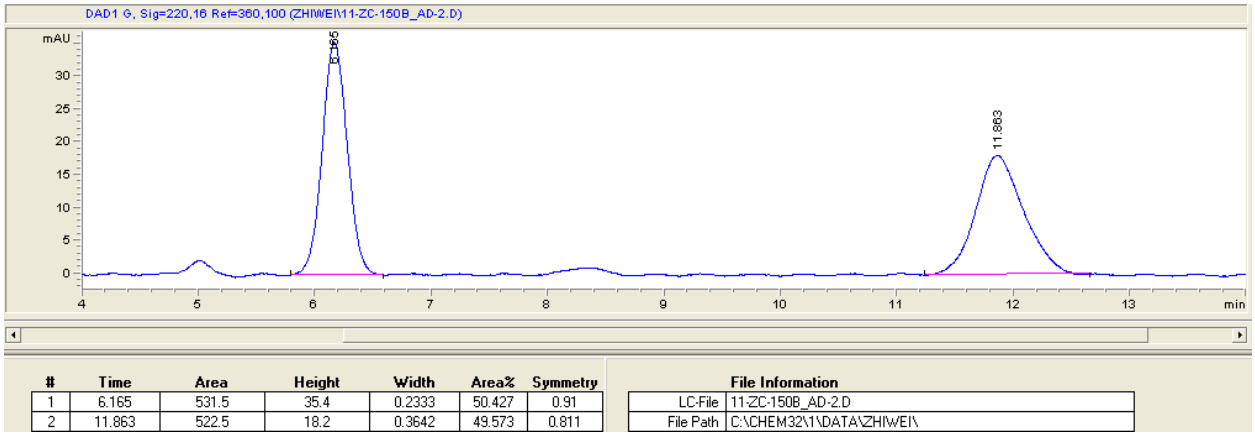



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.435 | 766.6 | 53.2 | 0.2403 | 97.353 | 0.475 |
| 2 | 5.326 | 20.8 | 1.2 | 0.2984 | 2.647 | 1.297 |

| File Information | |
|---|---|
| LC-File | KBB-80S-1.D |
| File Path | C:\CHEM32\1\DATA\KBB\ |

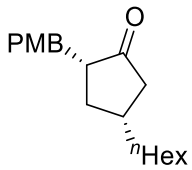



(±)-**2i**

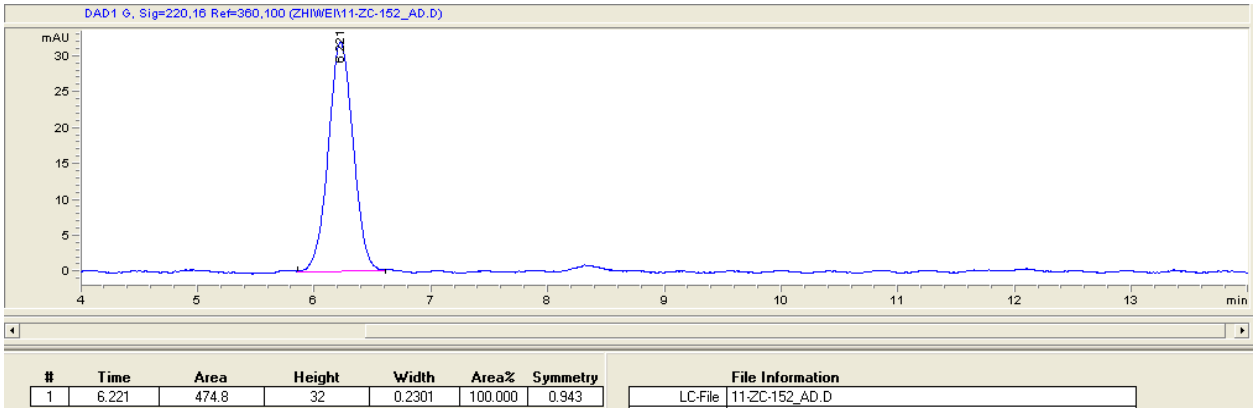



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.165 | 531.5 | 35.4 | 0.2333 | 50.427 | 0.91 |
| 2 | 11.863 | 522.5 | 18.2 | 0.3642 | 49.573 | 0.811 |

| File Information | |
|---|---|
| LC-File | 11-ZC-150B_AD-2.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

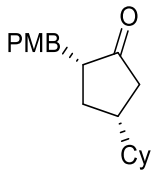



(+)-**2i**

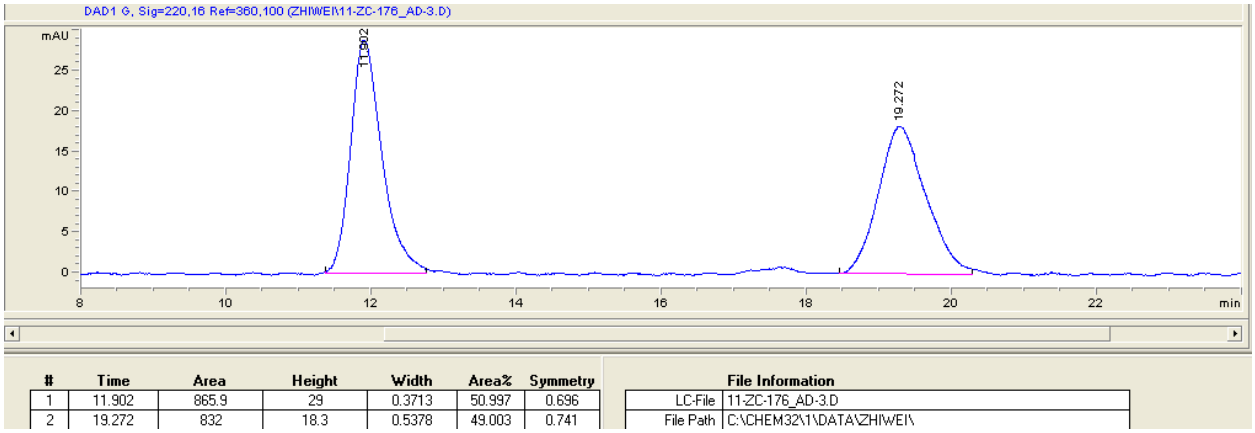



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.221 | 474.8 | 32 | 0.2301 | 100.000 | 0.943 |

| File Information | |
|---|---|
| LC-File | 11-ZC-152_AD.D |

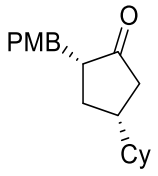



(±)-**2j**

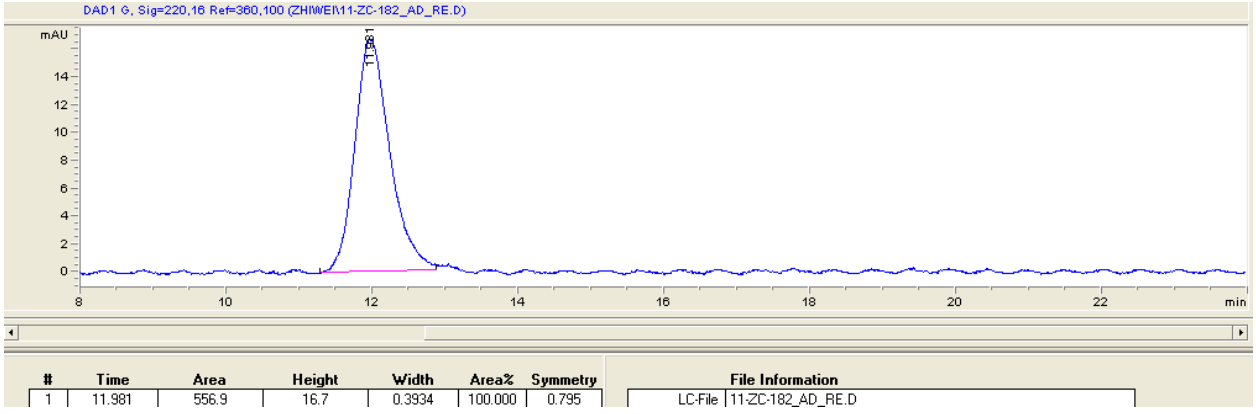



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 11.902 | 865.9 | 29 | 0.3713 | 50.997 | 0.696 |
| 2 | 19.272 | 832 | 18.3 | 0.5378 | 49.003 | 0.741 |

| File Information | |
|---|---|
| LC-File | 11-ZC-176_AD-3.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

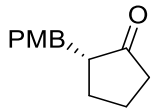



(+)-**2j**

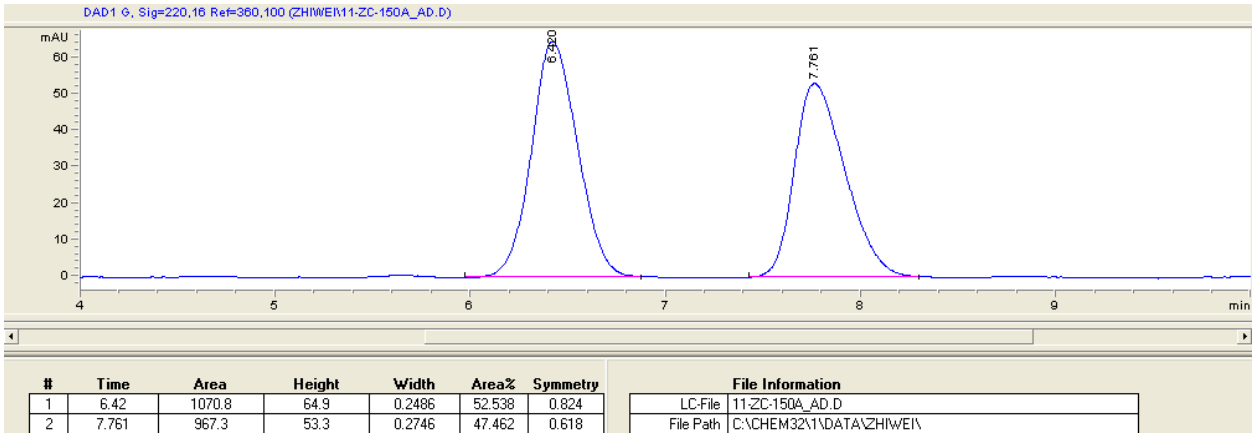



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 11.981 | 556.9 | 16.7 | 0.3934 | 100.000 | 0.795 |

| File Information | |
|---|---|
| LC-File | 11-ZC-182_AD_RE.D |

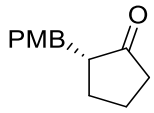



(±)-**2k**

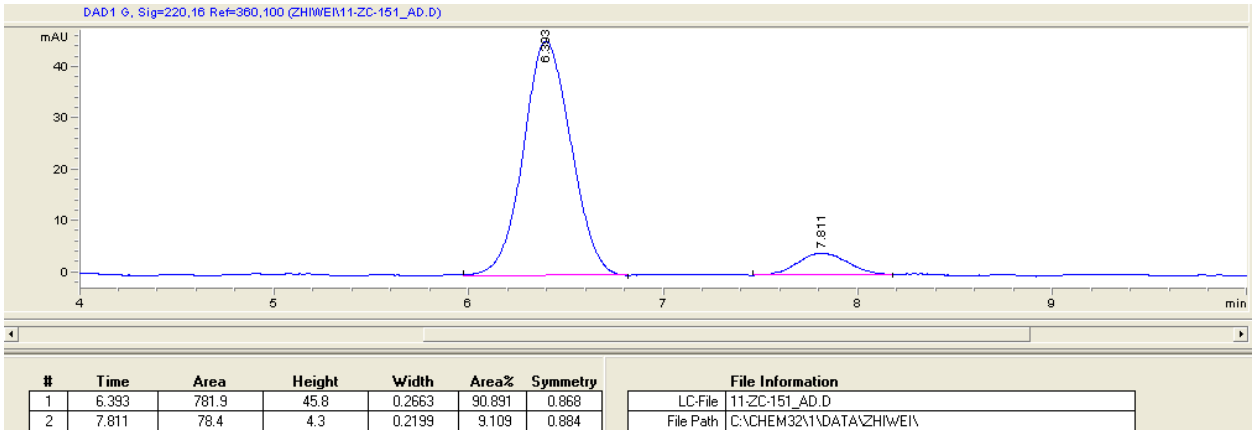



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.42 | 1070.8 | 64.9 | 0.2486 | 52.538 | 0.824 |
| 2 | 7.761 | 967.3 | 53.3 | 0.2746 | 47.462 | 0.618 |

| File Information | |
|---|---|
| LC-File | 11-ZC-150A_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

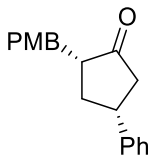



(+)-**2k**

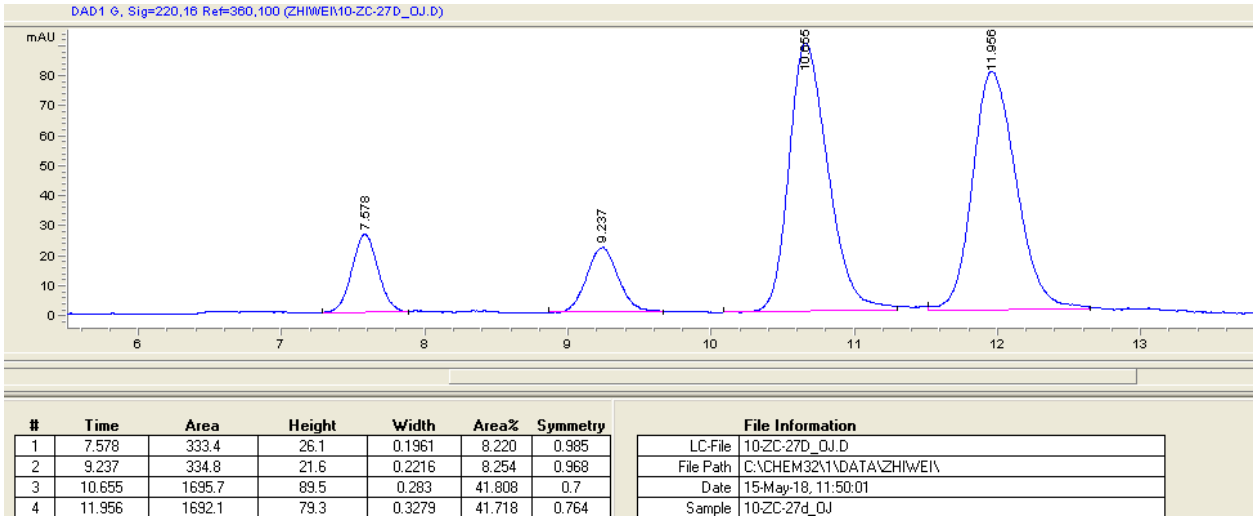



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.393 | 781.9 | 45.8 | 0.2663 | 90.891 | 0.868 |
| 2 | 7.811 | 78.4 | 4.3 | 0.2199 | 9.109 | 0.884 |

| File Information | |
|---|---|
| LC-File | 11-ZC-151_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |



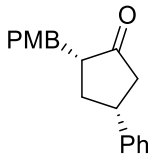

(±)-**4a**



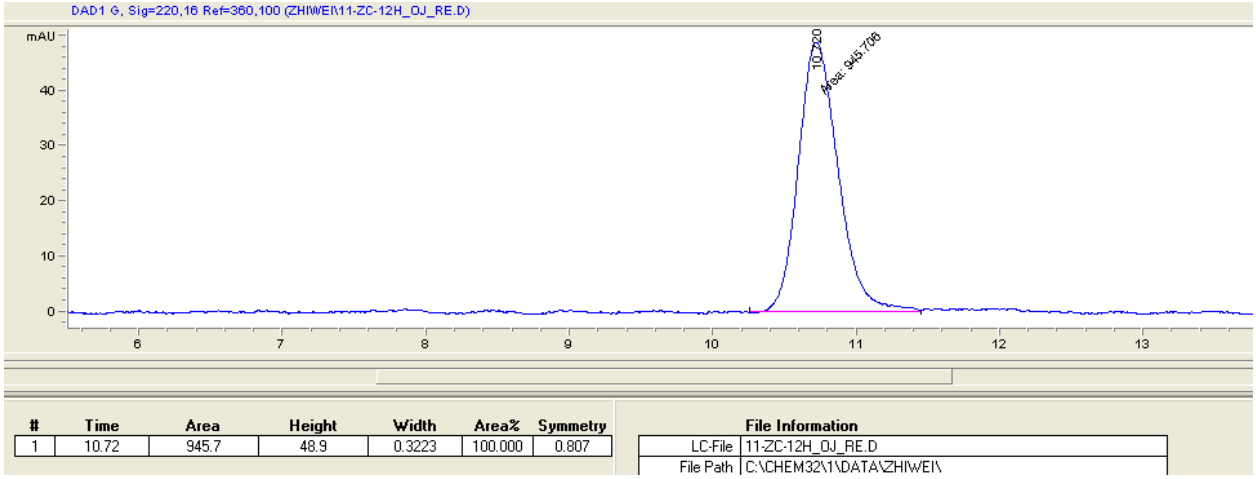

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.578 | 333.4 | 26.1 | 0.1961 | 8.220 | 0.985 |
| 2 | 9.237 | 334.8 | 21.6 | 0.2216 | 8.254 | 0.968 |
| 3 | 10.655 | 1695.7 | 89.5 | 0.283 | 41.808 | 0.7 |
| 4 | 11.956 | 1692.1 | 79.3 | 0.3279 | 41.718 | 0.764 |

| File Information | |
|---|---|
| LC-File | 10-ZC-27D_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 15-May-18, 11:50:01 |
| Sample | 10-ZC-27d_OJ |

* peaks at 7.6 and 9.2 min correspond to the *trans* diastereomer that was not separated from the product

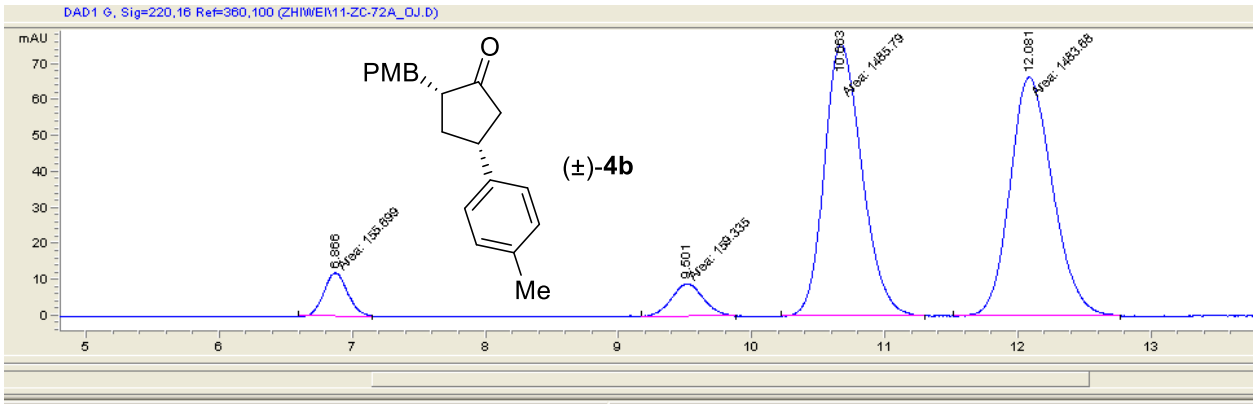



(+)-**4a**




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.72 | 945.7 | 48.9 | 0.3223 | 100.000 | 0.807 |

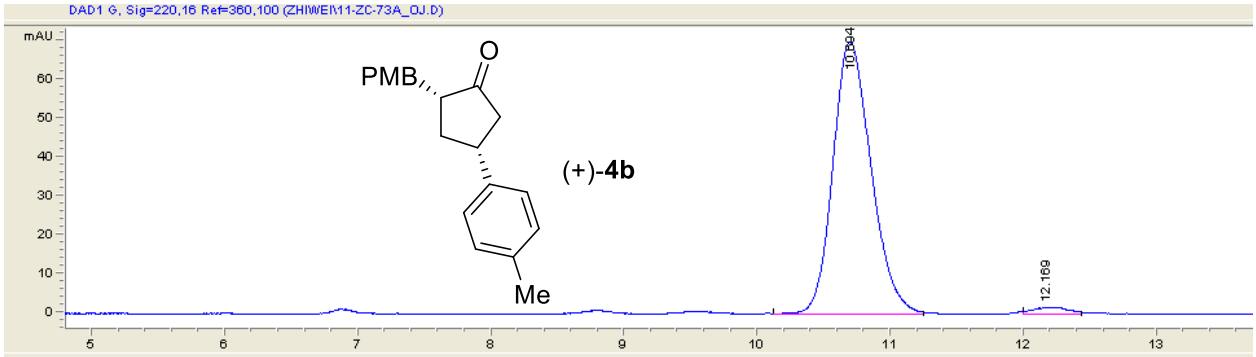
| File Information | |
|---|---|
| LC-File | 11-ZC-12H_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.866 | 155.7 | 12.2 | 0.2124 | 4.740 | 0.856 |
| 2 | 9.501 | 159.3 | 9.3 | 0.2861 | 4.851 | 0.87 |
| 3 | 10.663 | 1485.8 | 75.7 | 0.3273 | 45.236 | 0.737 |
| 4 | 12.081 | 1483.7 | 66.5 | 0.3716 | 45.172 | 0.797 |

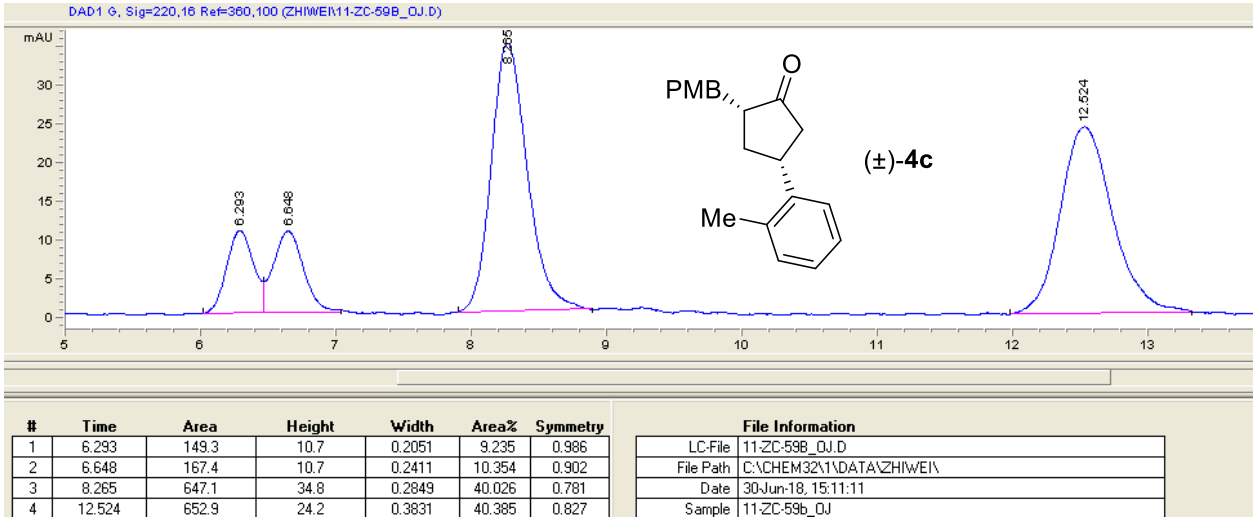
| File Information | |
|---|---|
| LC-File | 11-ZC-72A_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 13-Jul-18, 14:50:32 |
| Sample | 11-ZC-72a_OJ |

* peaks at 6.9 and 9.5 min correspond to the *trans* diastereomer that was not separated from the product




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.694 | 1407.2 | 70.3 | 0.2885 | 97.518 | 0.765 |
| 2 | 12.169 | 35.8 | 1.9 | 0.2239 | 2.482 | 0.612 |

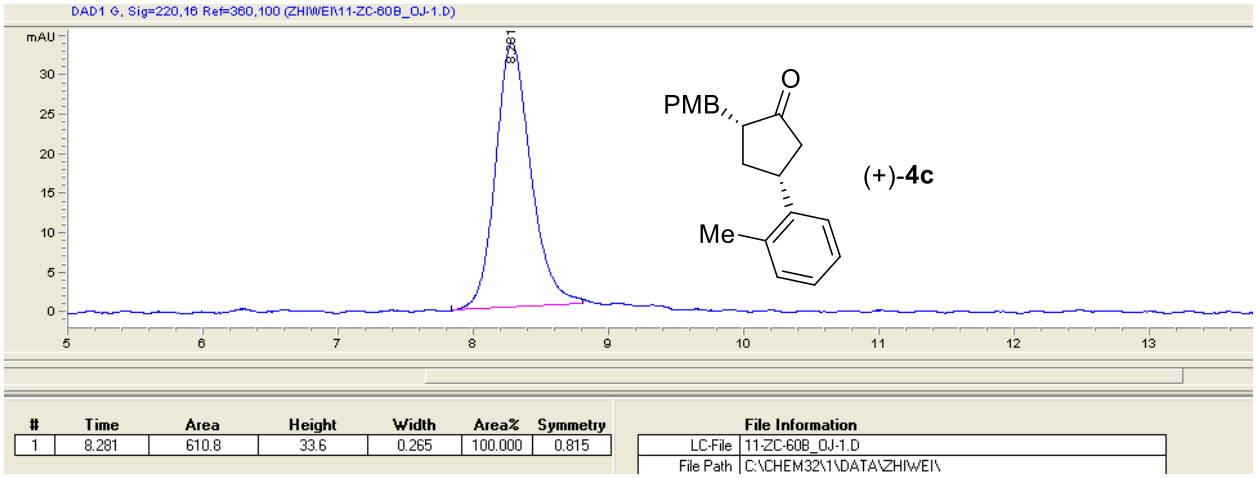
| File Information | |
|---|---|
| LC-File | 11-ZC-73A_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.293 | 149.3 | 10.7 | 0.2051 | 9.235 | 0.986 |
| 2 | 6.648 | 167.4 | 10.7 | 0.2411 | 10.354 | 0.902 |
| 3 | 8.265 | 647.1 | 34.8 | 0.2849 | 40.026 | 0.781 |
| 4 | 12.524 | 652.9 | 24.2 | 0.3831 | 40.385 | 0.827 |

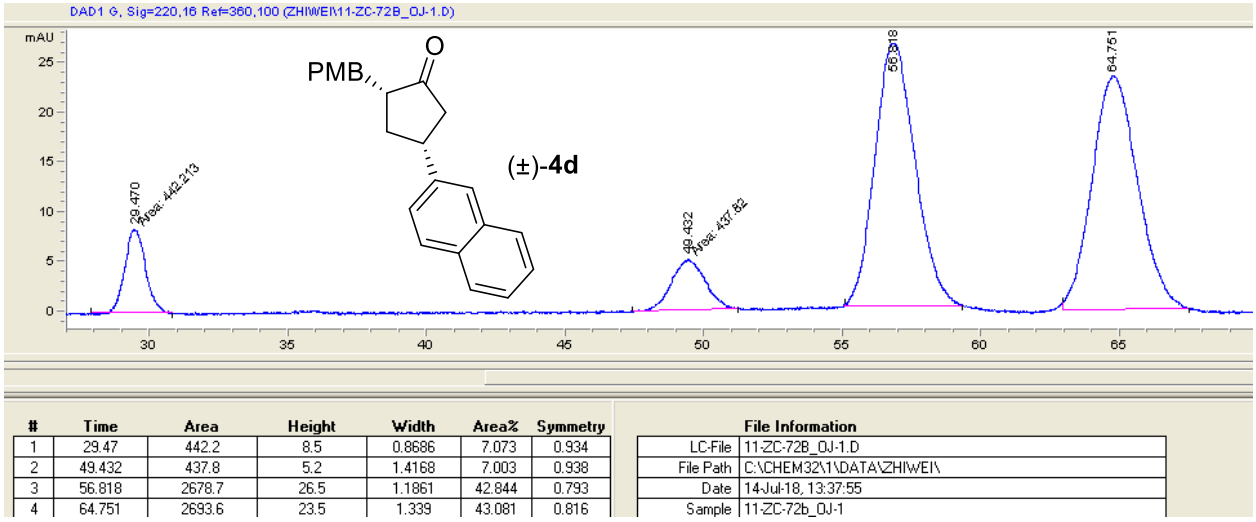
| File Information | |
|---|---|
| LC-File | 11-ZC-59B_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jun-18, 15:11:11 |
| Sample | 11-ZC-59b_OJ |

* peaks at 6.3 and 6.6 min correspond to the *trans* diastereomer that was not separated from the product




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.281 | 610.8 | 33.6 | 0.265 | 100.000 | 0.815 |

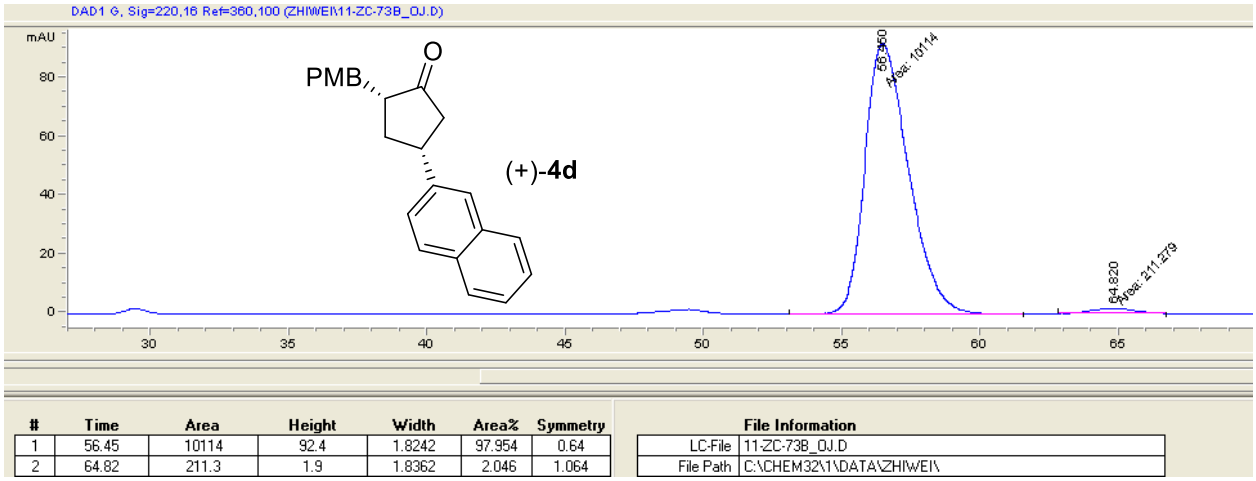
| File Information | |
|---|---|
| LC-File | 11-ZC-60B_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 29.47 | 442.2 | 8.5 | 0.8686 | 7.073 | 0.934 |
| 2 | 49.432 | 437.8 | 5.2 | 1.4168 | 7.003 | 0.938 |
| 3 | 56.818 | 2678.7 | 26.5 | 1.1861 | 42.844 | 0.793 |
| 4 | 64.751 | 2693.6 | 23.5 | 1.339 | 43.081 | 0.816 |

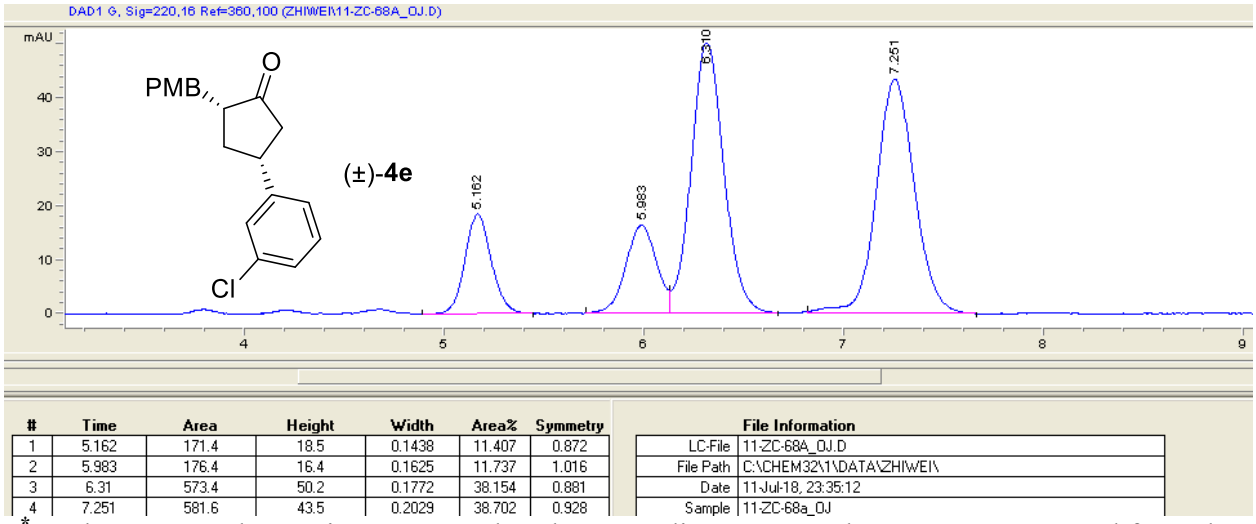
| File Information | |
|---|---|
| LC-File | 11-ZC-72B_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 14-Jul-18, 13:37:55 |
| Sample | 11-ZC-72b_OJ-1 |

* peaks at 29.5 and 49.4 min correspond to the *trans* diastereomer that was not separated from the product




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 56.45 | 10114 | 92.4 | 1.8242 | 97.954 | 0.64 |
| 2 | 64.82 | 211.3 | 1.9 | 1.8362 | 2.046 | 1.064 |

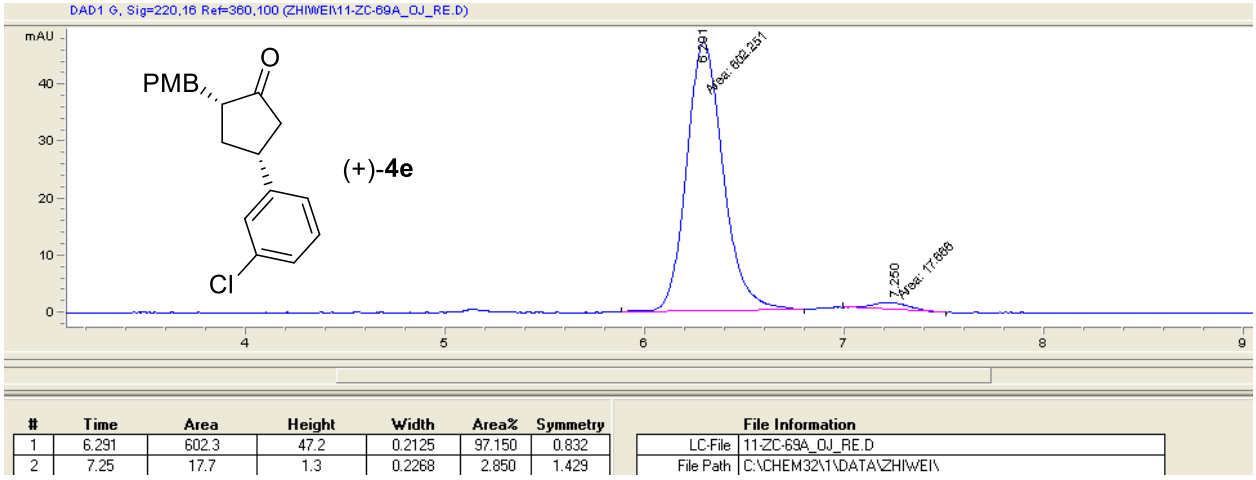
| File Information | |
|---|---|
| LC-File | 11-ZC-73B_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.162 | 171.4 | 18.5 | 0.1438 | 11.407 | 0.872 |
| 2 | 5.983 | 176.4 | 16.4 | 0.1625 | 11.737 | 1.016 |
| 3 | 6.31 | 573.4 | 50.2 | 0.1772 | 38.154 | 0.881 |
| 4 | 7.251 | 581.6 | 43.5 | 0.2029 | 38.702 | 0.928 |

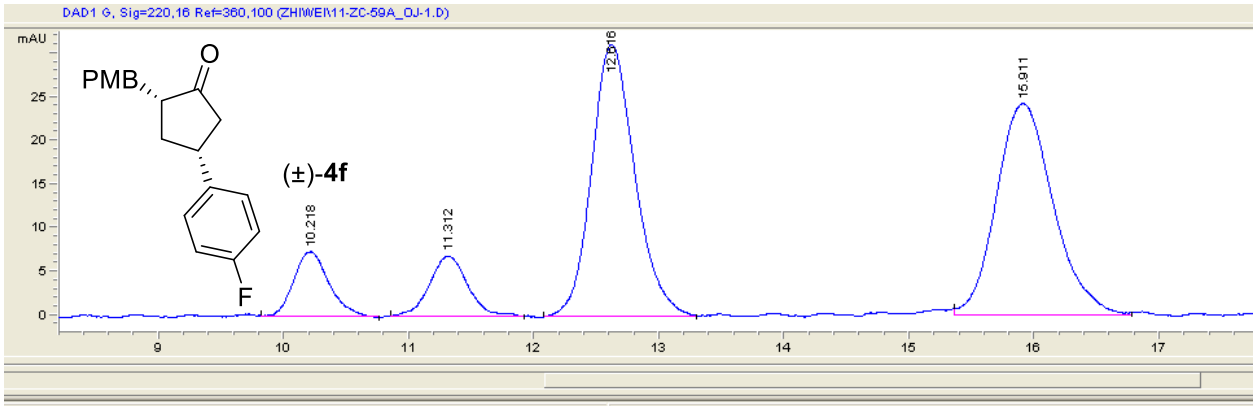
| File Information | |
|---|---|
| LC-File | 11-ZC-68A_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 11-Jul-18, 23:35:12 |
| Sample | 11-ZC-68a_OJ |

* peaks at 5.2 and 6.0 min correspond to the *trans* diastereomer that was not separated from the product




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.291 | 602.3 | 47.2 | 0.2125 | 97.150 | 0.832 |
| 2 | 7.25 | 17.7 | 1.3 | 0.2268 | 2.850 | 1.429 |

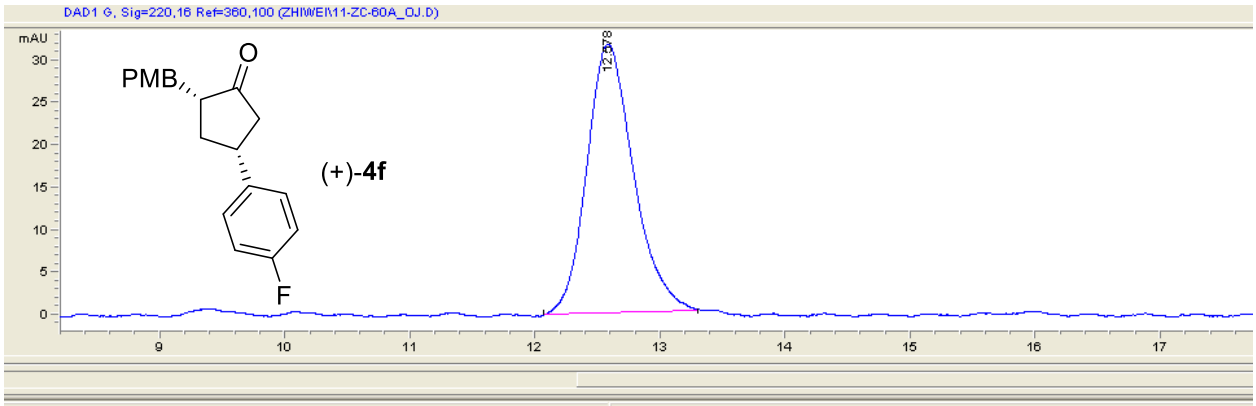
| File Information | |
|---|---|
| LC-File | 11-ZC-69A_OJ_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.218 | 148.3 | 7.5 | 0.2377 | 8.149 | 0.955 |
| 2 | 11.312 | 152.8 | 7 | 0.2714 | 8.392 | 0.949 |
| 3 | 12.616 | 752.5 | 31.2 | 0.3454 | 41.338 | 0.811 |
| 4 | 15.911 | 766.7 | 24.3 | 0.3787 | 42.121 | 0.876 |

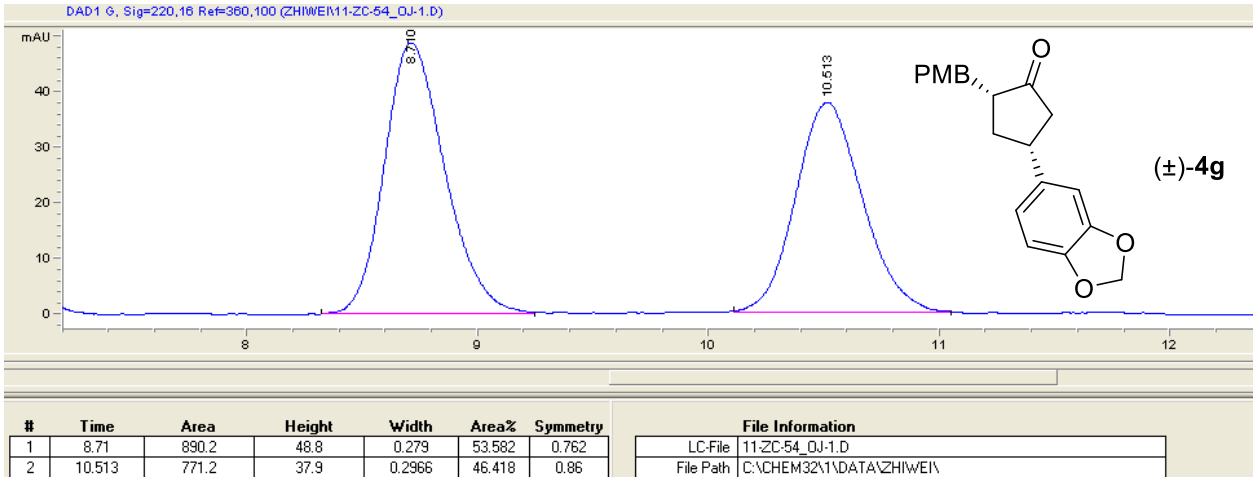
| File Information | |
|---|---|
| LC-File | 11-ZC-59A_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |
| Date | 30-Jun-18, 14:15:53 |
| Sample | 11-ZC-59a_OJ-1 |

* peaks at 10.2 and 11.3 min correspond to the *trans* diastereomer that was not separated from the product



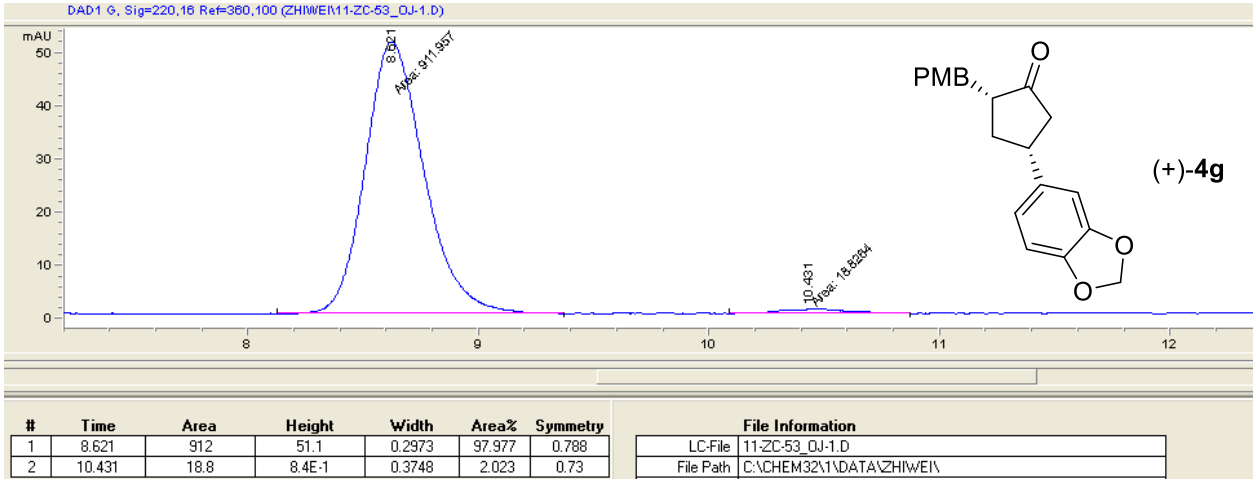

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 12.578 | 828.9 | 31.8 | 0.3322 | 100.000 | 0.81 |

| File Information | |
|---|---|
| LC-File | 11-ZC-60A_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |



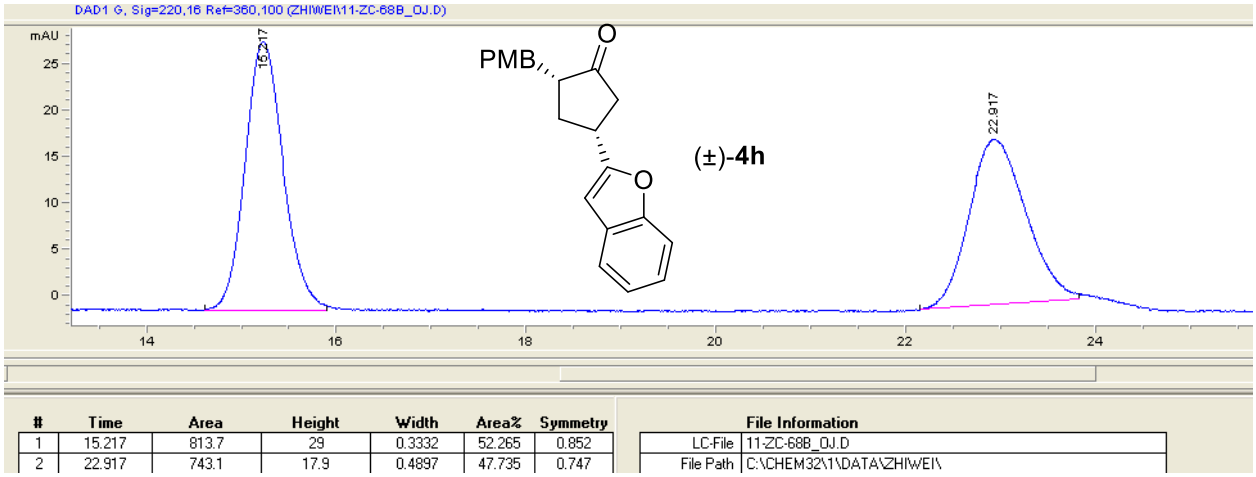

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.71 | 890.2 | 48.8 | 0.279 | 53.582 | 0.762 |
| 2 | 10.513 | 771.2 | 37.9 | 0.2966 | 46.418 | 0.86 |

| File Information | |
|---|---|
| LC-File | 11-ZC-54_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |



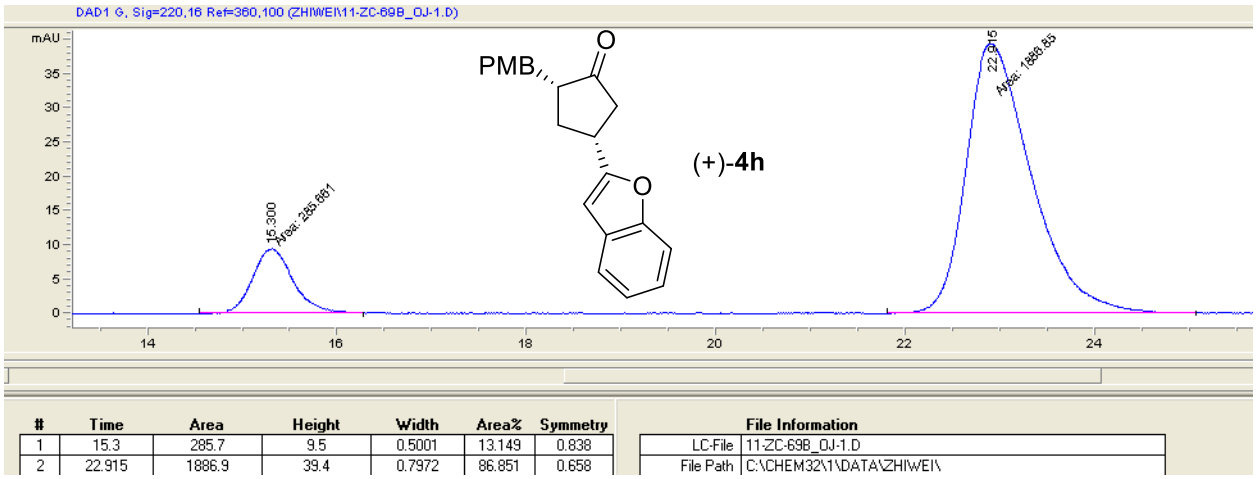

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.621 | 912 | 51.1 | 0.2973 | 97.977 | 0.788 |
| 2 | 10.431 | 18.8 | 8.4E-1 | 0.3748 | 2.023 | 0.73 |

| File Information | |
|---|---|
| LC-File | 11-ZC-53_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |



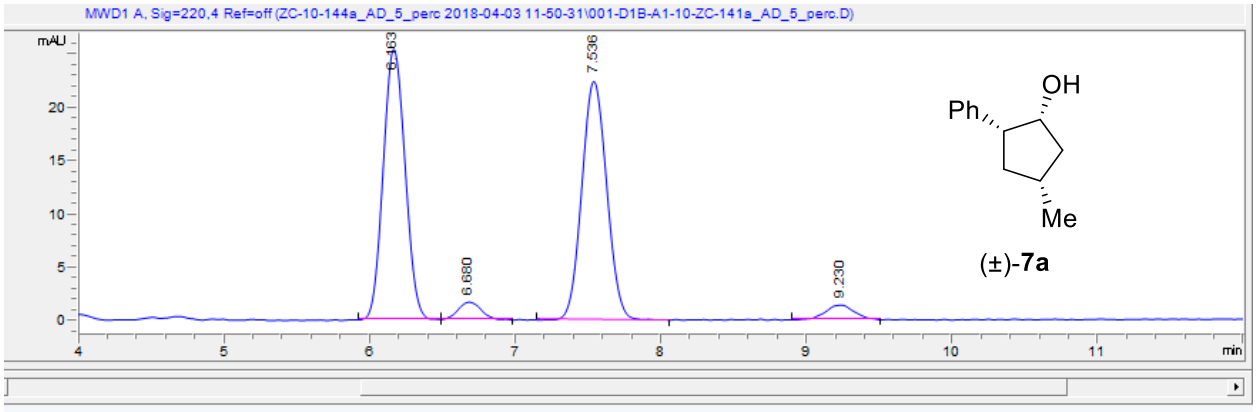

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.217 | 813.7 | 29 | 0.3332 | 52.265 | 0.852 |
| 2 | 22.917 | 743.1 | 17.9 | 0.4897 | 47.735 | 0.747 |

| File Information | |
|---|---|
| LC-File | 11-ZC-68B_OJ.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.3 | 285.7 | 9.5 | 0.5001 | 13.149 | 0.838 |
| 2 | 22.915 | 1886.9 | 39.4 | 0.7972 | 86.851 | 0.658 |

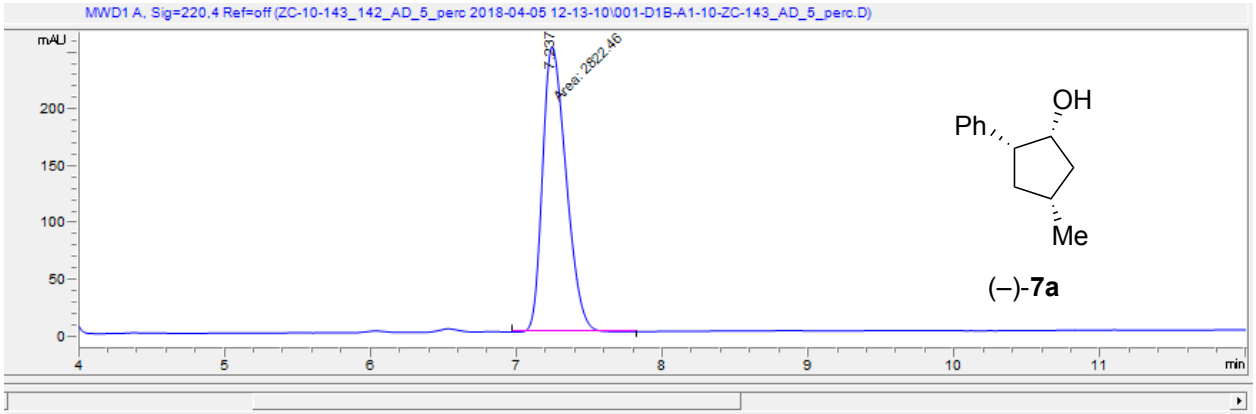
| File Information | |
|---|---|
| LC-File | 11-ZC-69B_OJ-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| File Information | |
|---|---|
| LC-File | 001-D1B-A1-10-ZC-141a_AD_5_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-144a_AD_5_perc 2018-0 |
| Date | 03-Apr-18, 11:51:27 |
| Sample | 10-ZC-141a_AD_5_perc |

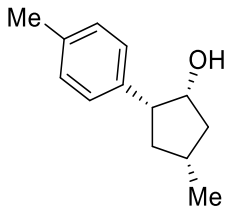
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 6.163 | BV | 267.6 | 25.6 | 0.166 | 46.514 | 0.896 |
| 2 | 6.68 | VB | 19.2 | 1.7 | 0.1803 | 3.339 | 0.886 |
| 3 | 7.536 | BB | 268.7 | 22.6 | 0.189 | 46.713 | 0.907 |
| 4 | 9.23 | BB | 19.8 | 1.4 | 0.2069 | 3.434 | 1.089 |

* peaks at 6.7 and 9.2 min correspond to another diastereomer that was not separated from the product

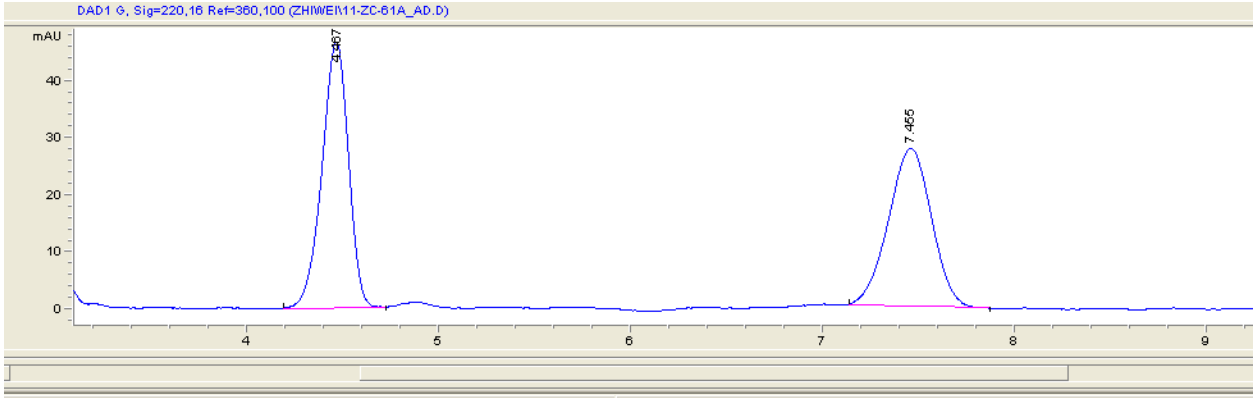



| File Information | |
|---|---|
| LC-File | 001-D1B-A1-10-ZC-143_AD_5_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-143_142_AD_5_perc 201 |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 7.237 | MM | 2822.5 | 251.1 | 0.1874 | 100.000 | 0.665 |

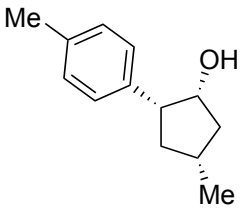



(±)-**7b**

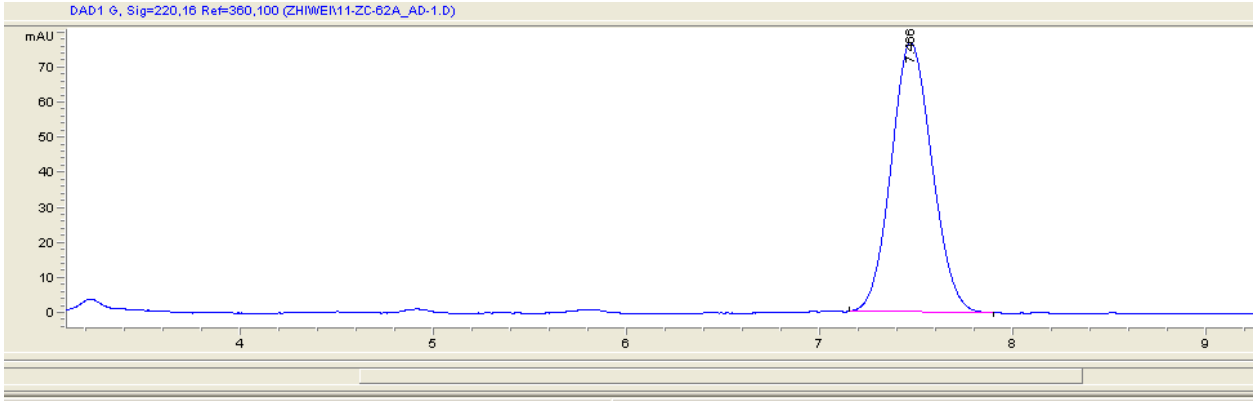



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.467 | 451.5 | 46.7 | 0.1497 | 51.057 | 1.154 |
| 2 | 7.455 | 432.8 | 27.7 | 0.2326 | 48.943 | 1.04 |

| File Information | |
|---|---|
| LC-File | 11-ZC-61A_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

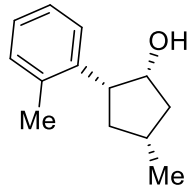



(–)-**7b**

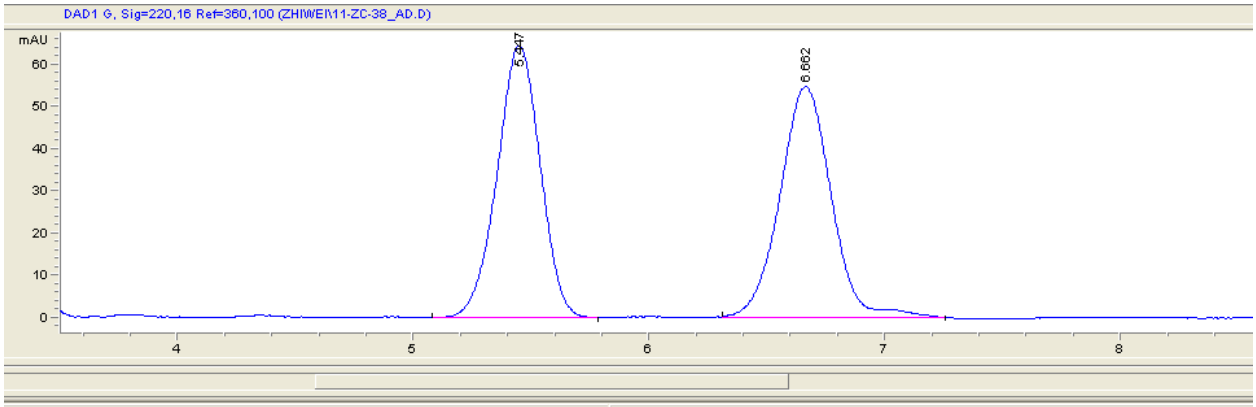



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.466 | 1134.9 | 77.1 | 0.2267 | 100.000 | 0.884 |

| File Information | |
|---|---|
| LC-File | 11-ZC-62A_AD-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

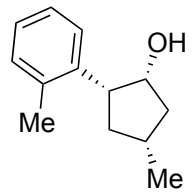



(±)-**7c**

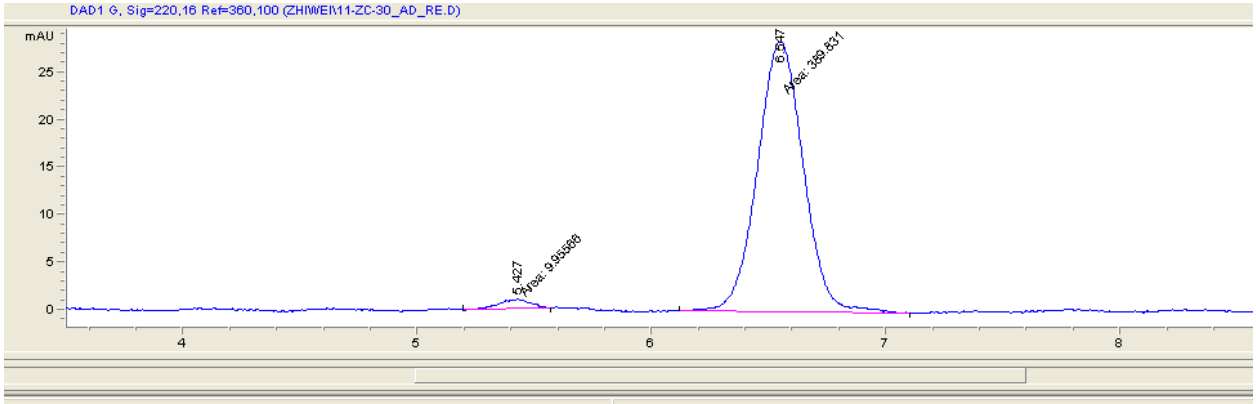



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.447 | 822.3 | 64.6 | 0.1886 | 49.559 | 1.04 |
| 2 | 6.662 | 836.9 | 54.9 | 0.2309 | 50.441 | 0.934 |

| File Information | |
|---|---|
| LC-File | 11-ZC-38_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

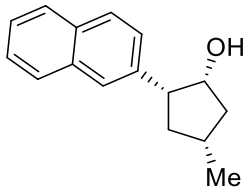



(–)-**7c**

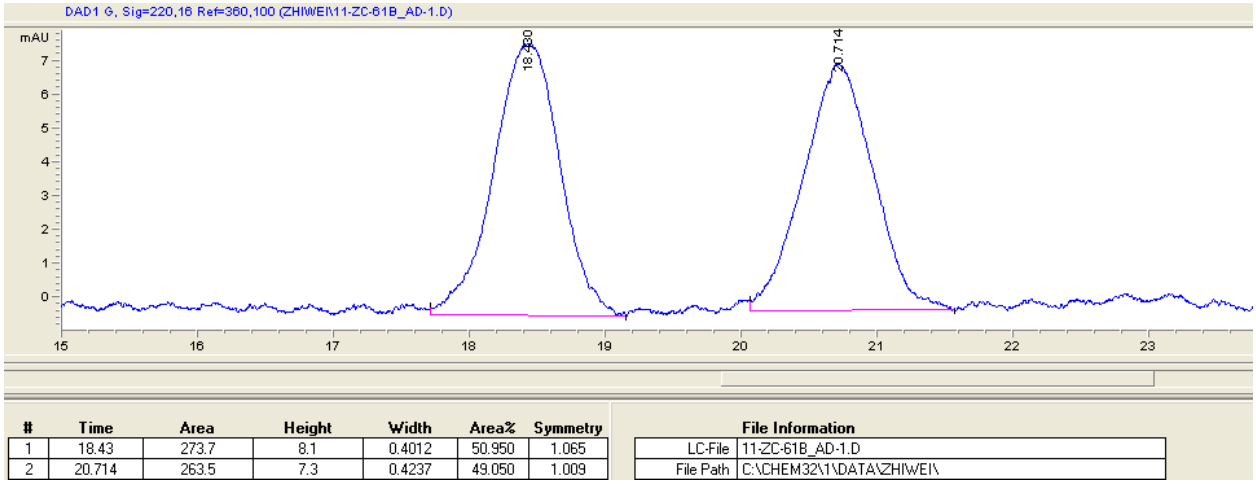



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.427 | 10 | 1 | 0.1647 | 2.490 | 1.472 |
| 2 | 6.547 | 389.8 | 28.4 | 0.2284 | 97.510 | 0.945 |

| File Information | |
|---|---|
| LC-File | 11-ZC-30_AD_RE.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

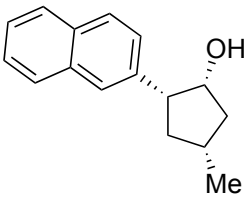



(±)-**7d**

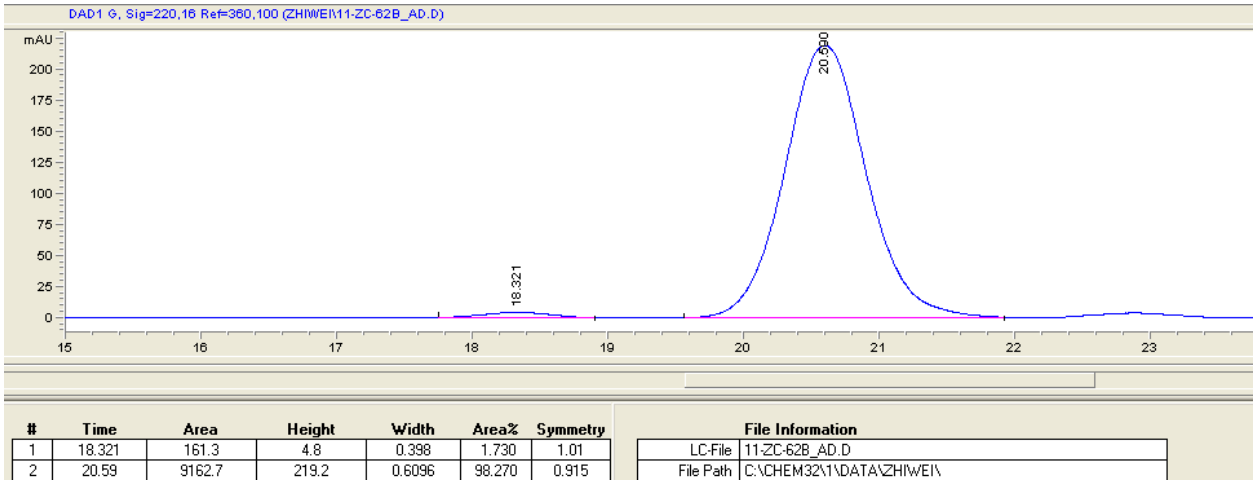



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 18.43 | 273.7 | 8.1 | 0.4012 | 50.950 | 1.065 |
| 2 | 20.714 | 263.5 | 7.3 | 0.4237 | 49.050 | 1.009 |

| File Information | |
|---|---|
| LC-File | 11-ZC-61B_AD-1.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

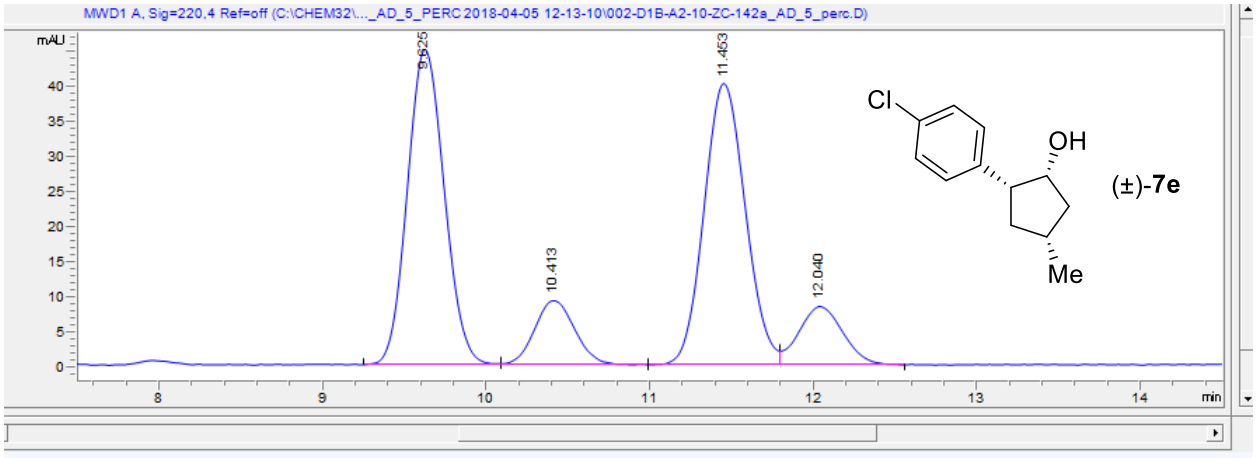



(–)-**7d**




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 18.321 | 161.3 | 4.8 | 0.398 | 1.730 | 1.01 |
| 2 | 20.59 | 9162.7 | 219.2 | 0.6096 | 98.270 | 0.915 |

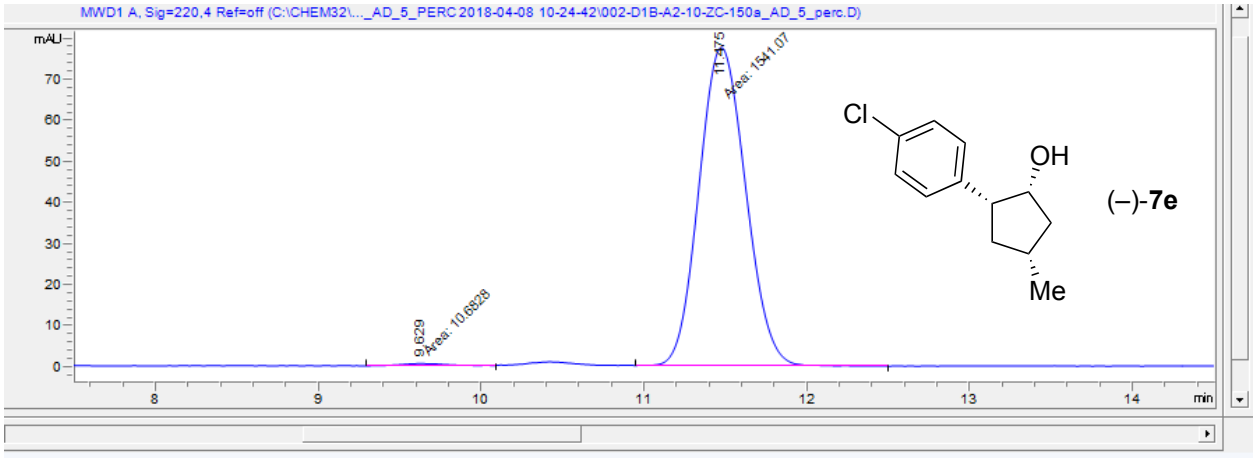
| File Information | |
|---|---|
| LC-File | 11-ZC-62B_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| File Information | |
|---|---|
| LC-File | 002-D1B-A2-10-ZC-142a_AD_5_perc.D |
| File Path | C:\CHEM32\1\DATA\ZC-10-143_142_AD_5_PERC 2018 |
| Date | 05-Apr-18, 12:34:52 |
| Sample | 10-ZC-142a_AD_5_perc |

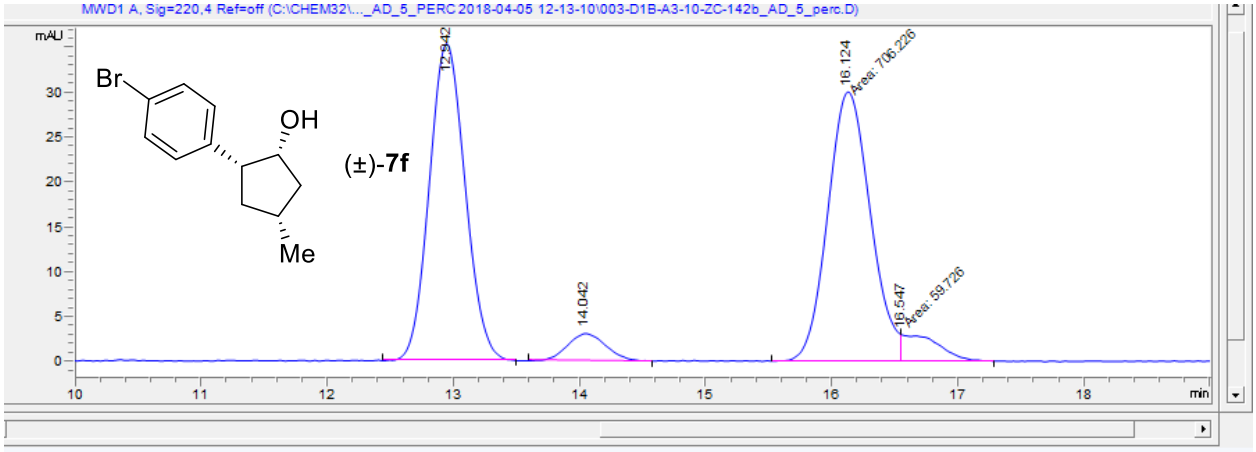
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 9.625 | BV | 706.1 | 45 | 0.2472 | 40.981 | 0.88 |
| 2 | 10.413 | VV R | 156.3 | 9.1 | 0.2597 | 9.074 | 0.875 |
| 3 | 11.453 | BV | 705 | 40.1 | 0.2749 | 40.918 | 0.884 |
| 4 | 12.04 | VV R | 155.5 | 8.3 | 0.2902 | 9.027 | 0.879 |

* peaks at 10.4 and 12.0 min correspond to another diastereomer that was not separated from the product




| File Information | |
|---|---|
| LC-File | 002-D1B-A2-10-ZC-150a_AD_5_perc.D |
| File Path | C:\CHEM32\1\DATA\ZC-10-150A_151_AD_5_PERC 201 |
| Date | 08-Apr-18, 10:56:33 |

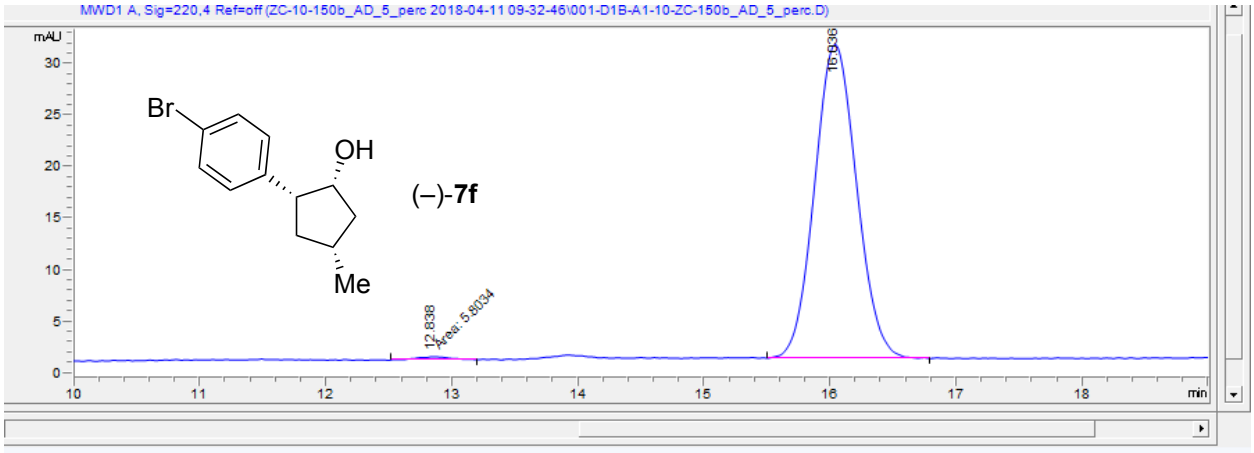
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 9.629 | MM | 10.7 | 5.5E-1 | 0.3234 | 0.688 | 0.879 |
| 2 | 11.475 | MM | 1541.1 | 77.4 | 0.3316 | 99.312 | 0.89 |




| File Information | |
|---|---|
| LC-File | 003-D1B-A3-10-ZC-142b_AD_5_perc.D |
| File Path | C:\CHEM32\1\DATA\ZC-10-143_142_AD_5_PERC 2018 |
| Date | 05-Apr-18, 12:55:41 |
| Sample | 10-ZC-142b_AD_5_perc |

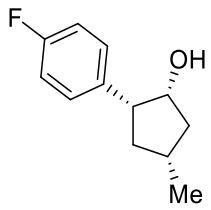
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 12.942 | VB | 698.2 | 35.3 | 0.309 | 45.661 | 0.9 |
| 2 | 14.042 | BB | 65 | 3 | 0.2728 | 4.249 | 0.878 |
| 3 | 16.124 | MM | 706.2 | 30 | 0.3928 | 46.185 | 0.893 |
| 4 | 16.547 | MM | 59.7 | 3 | 0.2428 | 3.906 | 0 |

* peaks at 14.0 and 16.5 min correspond to another diastereomer that was not separated from the product

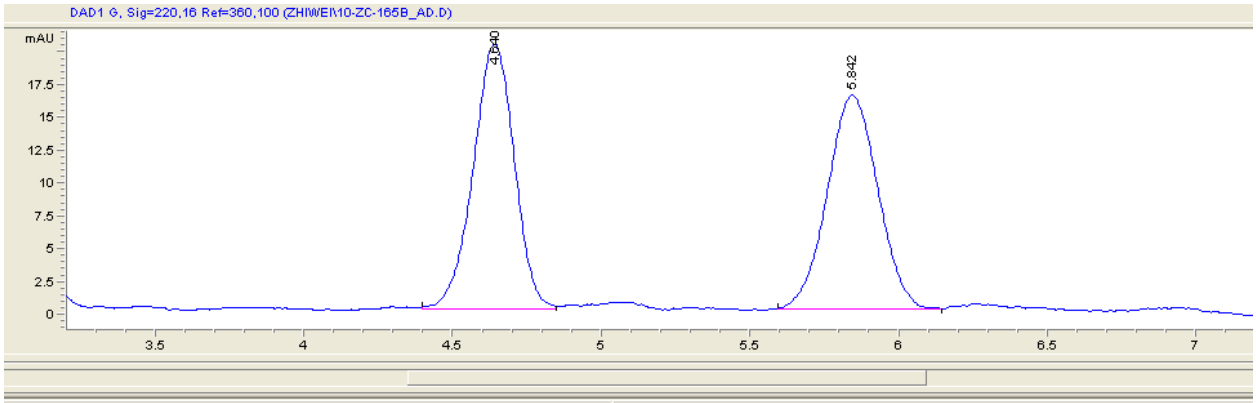



| File Information | |
|---|---|
| LC-File | 001-D1B-A1-10-ZC-150b_AD_5_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-150b_AD_5_perc 2018-04-1 |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 12.838 | MM | 5.8 | 3E-1 | 0.3228 | 0.818 | 0.755 |
| 2 | 16.036 | BV R | 703.7 | 30.4 | 0.3582 | 99.182 | 0.921 |

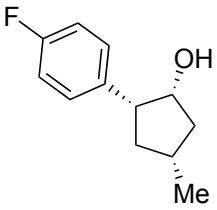



(±)-**7g**

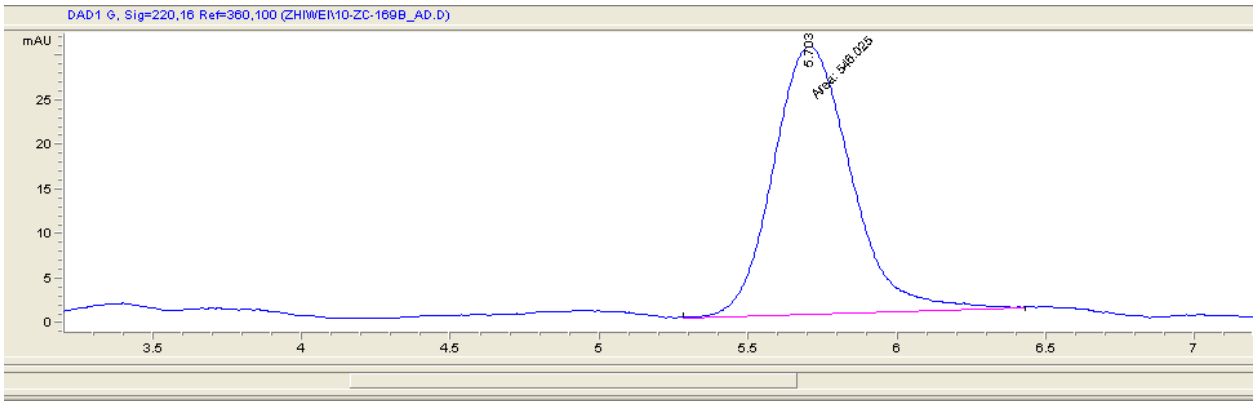



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.64 | 196.8 | 20.3 | 0.1503 | 50.357 | 1.076 |
| 2 | 5.842 | 194 | 16.4 | 0.1802 | 49.643 | 0.949 |

| File Information | |
|---|---|
| LC-File | 10-ZC-165B_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |

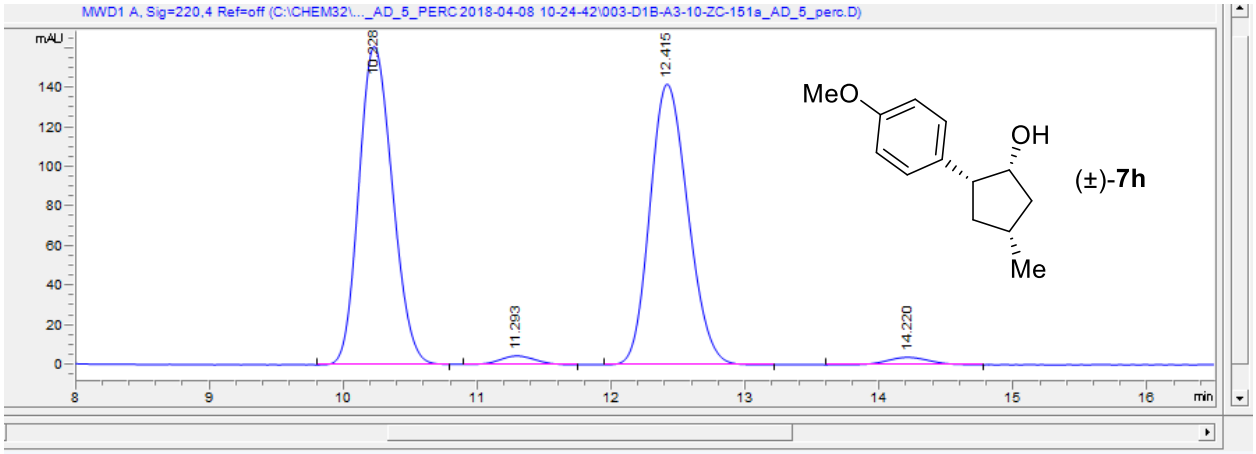



(–)-**7g**




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.703 | 546 | 30.1 | 0.3028 | 100.000 | 0.82 |

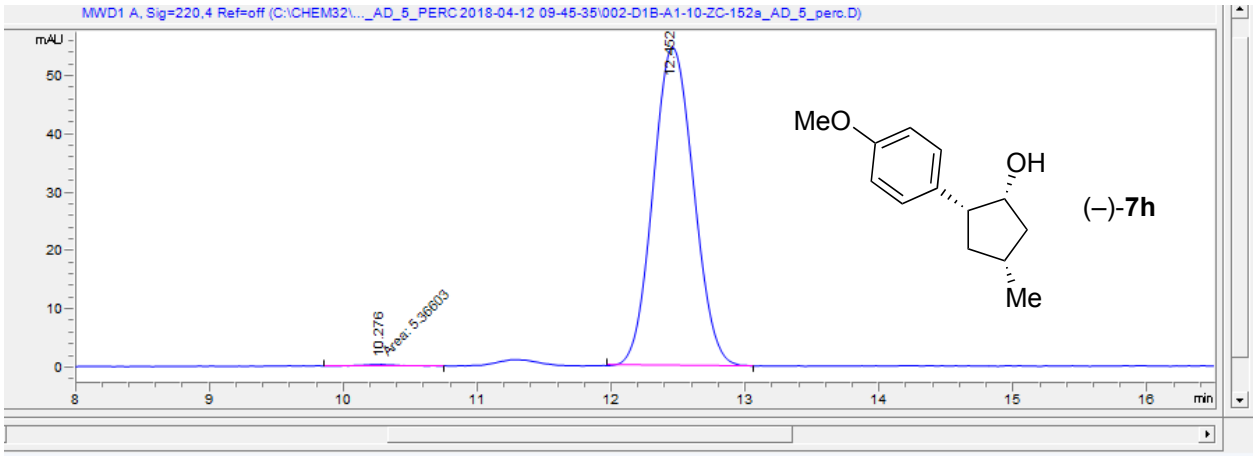
| File Information | |
|---|---|
| LC-File | 10-ZC-169B_AD.D |
| File Path | C:\CHEM32\1\DATA\ZHIWEI\ |




| File Information | |
|---|---|
| LC-File | 003-D1B-A3-10-ZC-151a_AD_5_perc.D |
| File Path | C:\CHEM32\1\DATA\ZC-10-150A_151_AD_5_PERC 201 |
| Date | 08-Apr-18, 11:27:26 |
| Sample | 10-ZC-151a_AD_5_perc |

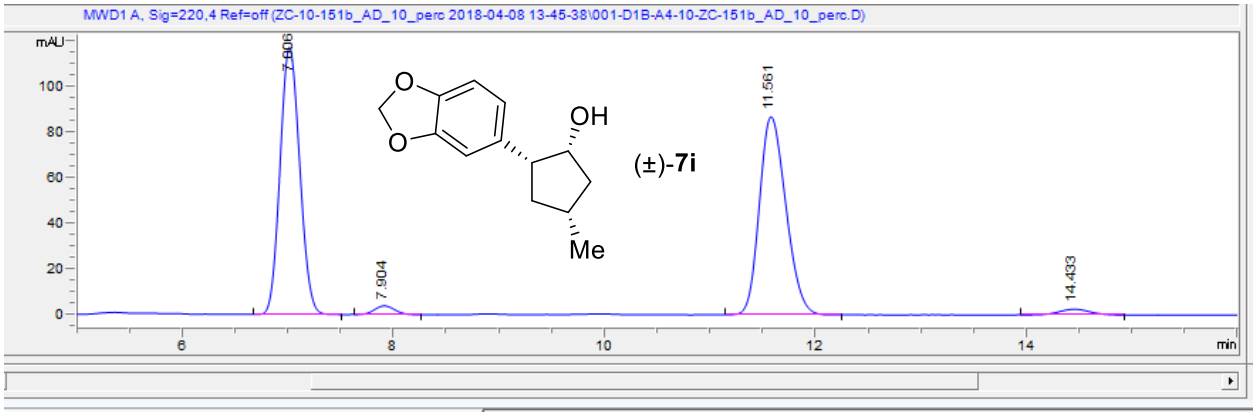
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 10.228 | BB | 2787.3 | 160.4 | 0.2747 | 48.523 | 0.811 |
| 2 | 11.293 | BB | 79.5 | 4.3 | 0.2695 | 1.384 | 0.895 |
| 3 | 12.415 | BV R | 2793 | 141.5 | 0.3063 | 48.622 | 0.8 |
| 4 | 14.22 | BB | 84.5 | 3.7 | 0.3152 | 1.471 | 1.013 |

* peaks at 11.3 and 14.2 min correspond to another diastereomer that was not separated from the product




| File Information | |
|---|---|
| LC-File | 002-D1B-A1-10-ZC-152a_AD_5_perc.D |
| File Path | C:\CHEM32\1\DATA\ZC-10-152A_AD_5_PERC 2018-04 |

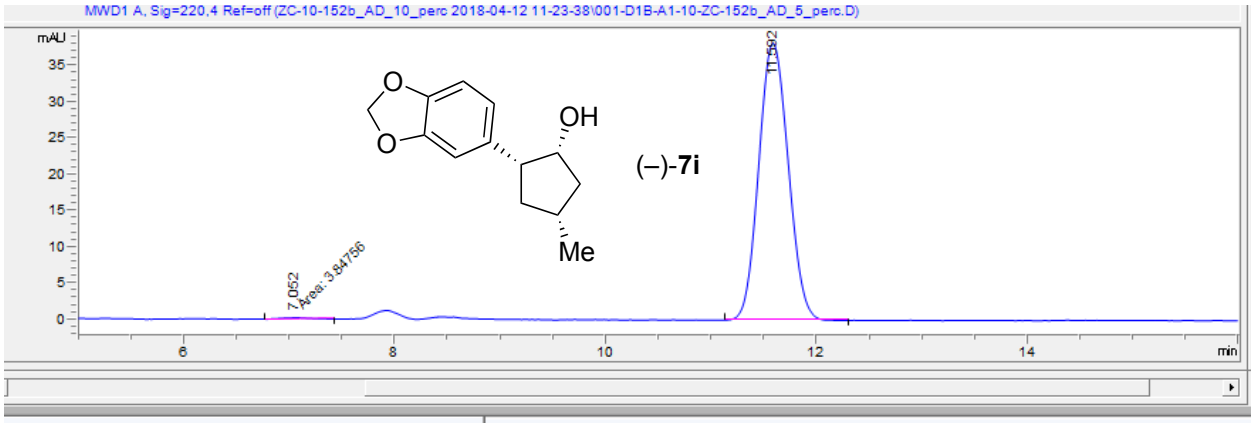
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 10.276 | MM | 5.4 | 2.8E-1 | 0.3155 | 0.465 | 1.099 |
| 2 | 12.452 | BB | 1147.9 | 54.5 | 0.3339 | 99.535 | 0.896 |




| File Information | |
|---|---|
| LC-File | 001-D1B-A4-10-ZC-151b_AD_10_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-151b_AD_10_perc 2018- |
| Date | 08-Apr-18, 13:46:38 |
| Sample | 10-ZC-151b_AD_10_perc |

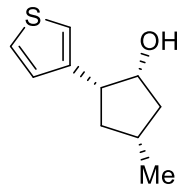
| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 7.006 | BB | 1509.6 | 117.1 | 0.2044 | 48.359 | 0.879 |
| 2 | 7.904 | BB | 51.4 | 3.8 | 0.2121 | 1.648 | 0.902 |
| 3 | 11.561 | BB | 1509.3 | 86.8 | 0.2728 | 48.349 | 0.755 |
| 4 | 14.433 | BB | 51.3 | 2.5 | 0.3042 | 1.645 | 0.978 |

* peaks at 7.9 and 14.4 min correspond to another diastereomer that was not separated from the product

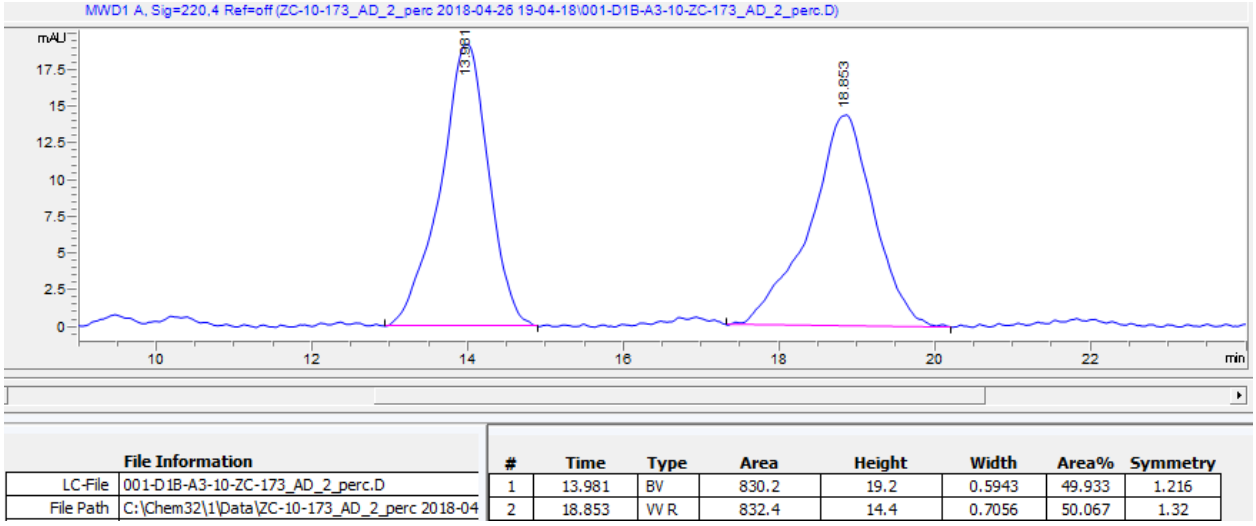



| File Information | |
|---|---|
| LC-File | 001-D1B-A1-10-ZC-152b_AD_5_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-152b_AD_10_perc 2018- |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 7.052 | MM | 3.8 | 2.3E-1 | 0.2848 | 0.516 | 0.976 |
| 2 | 11.592 | BB | 741.7 | 38.1 | 0.3113 | 99.484 | 0.886 |

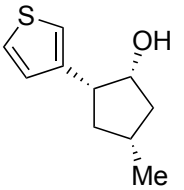



(±)-**7j**

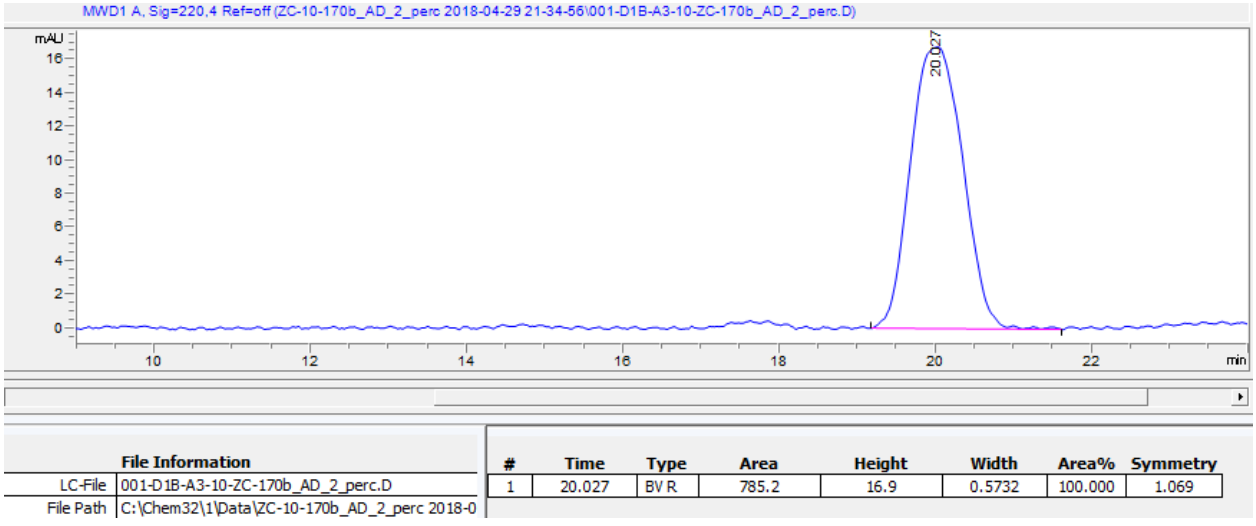



| File Information | |
|---|---|
| LC-File | 001-D1B-A3-10-ZC-173_AD_2_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-173_AD_2_perc 2018-04 |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 13.981 | BV | 830.2 | 19.2 | 0.5943 | 49.933 | 1.216 |
| 2 | 18.853 | VV R | 832.4 | 14.4 | 0.7056 | 50.067 | 1.32 |

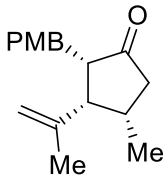



(–)-**7j**

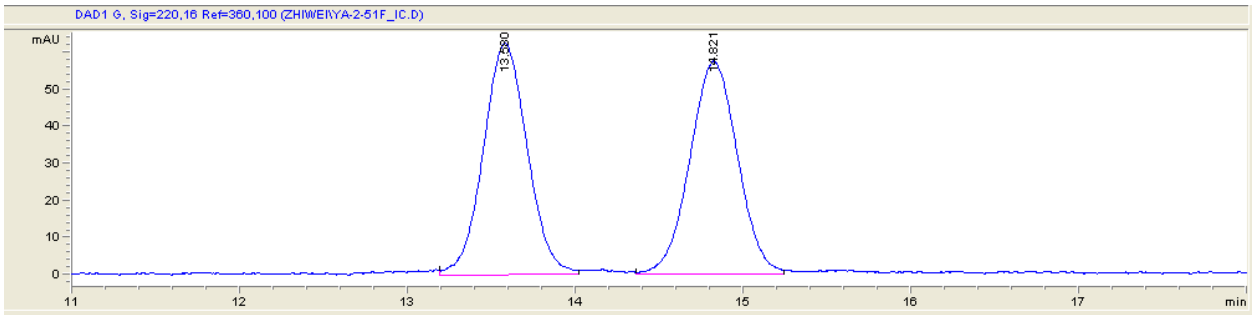



| File Information | |
|---|---|
| LC-File | 001-D1B-A3-10-ZC-170b_AD_2_perc.D |
| File Path | C:\Chem32\1\Data\ZC-10-170b_AD_2_perc 2018-0 |

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|---|
| 1 | 20.027 | BV R | 785.2 | 16.9 | 0.5732 | 100.000 | 1.069 |




(±)-**9**




| # | Time | Area | Height | Width | Area% | Symmetry |
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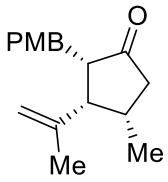
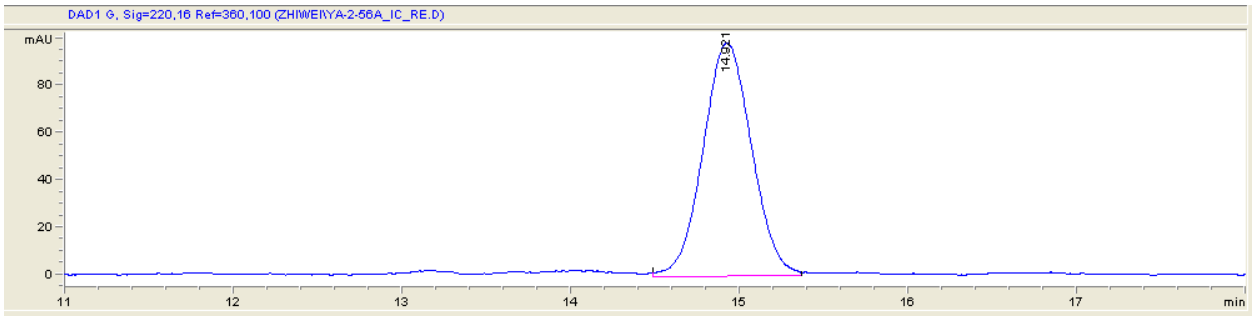



(+)-**9**

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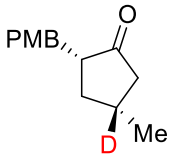
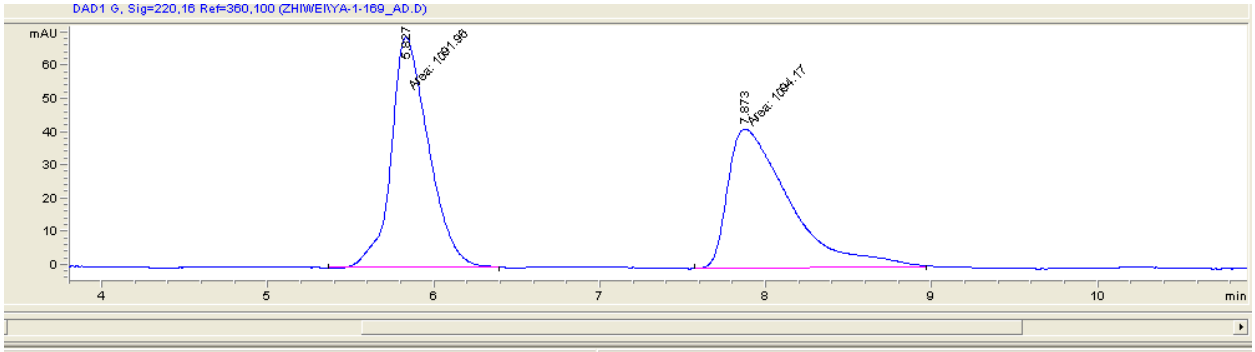



(±)-**2a**-*d*

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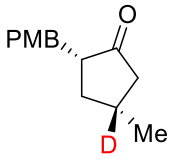


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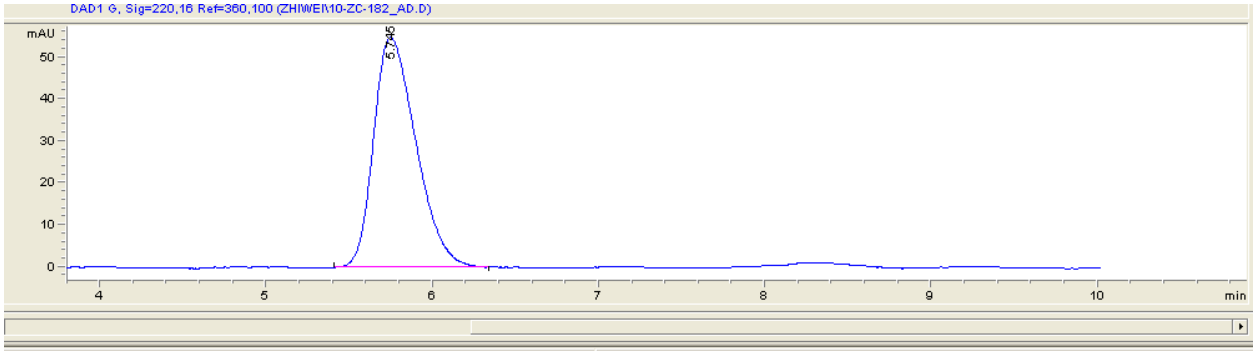


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## Appendix 3.1: Supporting Information for Chapter 3.1
## Cyclic Ketone Synthesis from Cyclopropanes

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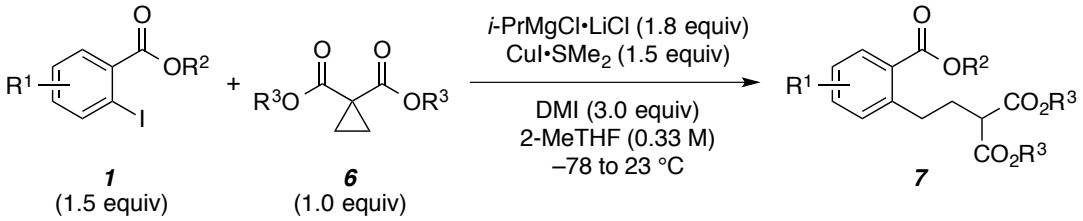
## 1. General Information

All reactions were carried out in heat gun-dried screw-cap vials with Teflon septa equipped with Teflon stir bars under a nitrogen atmosphere unless otherwise noted. Thin-layer chromatography (TLC) was conducted with EMD silica gel 60 F254 pre-coated plates and visualized using UV light (254 nm) or stained with $KMnO_4$. Flash column chromatography was performed with pre-packed RediSep silica gel Standard or Gold columns on a CombiFlash ISCO system using *i*-PrOAc in heptane (0−50% gradient) as eluent. Reported yields correspond to isolated material. All new compounds were characterized by $^1$H NMR, $^{13}$C NMR, IR, and HRMS. $^1$H and $^{13}$C Nuclear Magnetic Resonance spectra were recorded on a Bruker 300 or Bruker 500 MHz instrument at ambient temperature. All $^1$H NMR spectra were measured in parts per million (ppm) relative to the residual chloroform signal in deuterated solvent, unless otherwise stated. Data for $^1$H NMR were reported in ppm relative to residual chloroform (δ 7.26 ppm) as follows: chemical shift, multiplicity (br = broad signal, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet), coupling constants, and integration. All $^{13}$C NMR spectra are reported in ppm relative to residual chloroform (δ 77.16 ppm) or THF (δ 67.57 ppm), and were obtained with complete $^1$H decoupling unless otherwise stated. All $^{19}$F NMR spectra were obtained on a Bruker 300 MHz instrument at ambient temperature, with complete $^1$H decoupling. When the reported spectra contain diastereomers, terms such as “major” and “minor” were used to indicate peaks respectively. IR spectra were recorded on a Bruker Alpha Platinum-ATR spectrometer and are reported in frequency of absorption ($cm^{-1}$). HRMS data was obtained on a LTQ Orbitrap Discovery (Thermo Fisher Scientific) at Genentech, Inc. High-resolution mass spectrometry (HRMS) data was acquired on a Thermo Scientific Orbitrap Fusion mass spectrometer. HPLC analyses were performed on an Agilent 1260 Infinity HPLC system with a UV detector at 220, 254, and 280 nm using a Waters SL XBRIDGE column. All reagents and solvents were purchased from commercial suppliers and used without further purification. Anhydrous solvents were utilized if available, but no effort was undertaken to further increase the purity of commercially available solvents. 5-Phenyl iodoaryl ester SI-**1bb**,[1] iodoindole ester SI-**1bm**,[2] phenyl cyclopropyl diester **12**,[3] lactone-fused cyclopropane **13**,[4] and nitrile ester cyclopropane **17**[5] were prepared according to literature procedures. Diisopropyl cyclopropane-1,1-dicarboxylate (SI-**6ac**), and di-*tert*-butyl cyclopropane-1,1-dicarboxylate (SI-**6ad**),

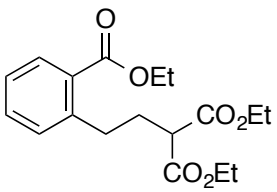
cyclopropane-1,1-dicarbonitrile (**16**) were prepared by modifications of a literature procedure from the corresponding activated methylene compounds.[6]

## 2. General Procedure for the Homoconjugate Addition



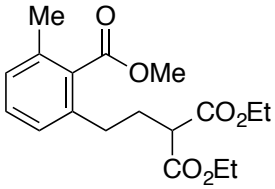

In a heat-gun dried 2-dram vial was added 2-iodoester **1** (0.90 mmol, 1.5 equiv) and anhydrous 2-MeTHF (0.60 mL). The solution was cooled to –78 °C, and *i*-PrMgCl·LiCl (0.83 mL, 1.1 mmol, 1.8 equiv, 1.3 M in THF) was added. The resulting mixture was stirred at –78 °C for 30 min. $CuI{\cdot}SMe_2$ (228 mg, 0.90 mmol, 1.5 equiv) was added as a suspension in anhydrous 2-MeTHF (1.2 mL), followed by DMI (0.20 mL, 1.8 mmol, 3.0 equiv) and diethyl 1,1-cyclopropane dicarboxylate **6** (0.11 mL, 0.6 mmol, 1 equiv). The resulting mixture was allowed to stir overnight, slowly warming to ambient temperature. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with *i*-PrOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography ($SiO_2$) to afford the triester.

## 3. Characterization Data for Triesters 7



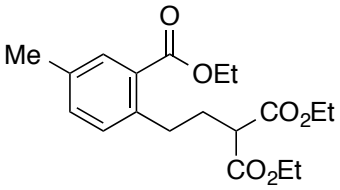
**Diethyl 2-(2-(ethoxycarbonyl)phenethyl)malonate (7aa):** The title compound was synthesized according to the general procedure (0.20 mmol of cyclopropane starting material **6a** and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (53.1 mg, 79% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.43 (td, *J* = 7.3, 1.5 Hz, 1H), 7.31 – 7.23 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.20 (q, *J* = 6.9 Hz, 4H), 3.40 (t, *J* = 7.5 Hz, 1H), 3.09 – 2.94 (m, 2H), 2.32 – 2.13 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.5, 167.5, 142.7, 132.1, 131.3, 130.9, 130.0, 126.4, 61.5, 61.0, 51.9, 32.1, 30.5, 14.4, 14.2. **IR** (ATR): 2981, 1716, 1447, 1367, 1250,

1149, 1131, 1081, 1037, 754 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}O_6H$ $[M+H]^+$ 337.1646, found 337.1647.




**Diethyl 2-(2-(methoxycarbonyl)-3-methylphenethyl)malonate (7ba):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1ba**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (200.1 mg, 99% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.6 Hz, 1H), 7.06 (dd, *J* = 7.6, 2.4 Hz, 2H), 4.19 (q, *J* = 6.9 Hz, 4H), 3.91 (s, 3H), 3.35 (t, *J* = 7.3 Hz, 1H), 2.70 – 2.58 (m, 2H), 2.30 (s, 3H), 2.24 – 2.11 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 170.3, 169.2, 137.9, 135.2, 133.8, 129.6, 128.2, 127.0, 61.4, 52.0, 51.6, 31.5, 30.4, 19.8, 14.1. **IR** (ATR): 2982, 2953, 1725, 1596, 1464, 1369, 1265, 1218, 1146, 1074 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}O_6NH_4$ $[M+NH_4]^+$ 354.1911, found 354.1913.

**Diethyl 2-(2-(2-(methoxycarbonyl)-[1,1'-biphenyl]-3-yl)ethyl)malonate (7bb):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bb**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (236.6 mg, 99% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.43 – 7.30 (m, 6H), 7.28 – 7.21 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 4H), 3.56 (s, 3H), 3.40 (t, *J* = 7.3 Hz, 1H), 2.79 – 2.68 (m, 2H), 2.23 (dt, *J* = 10.7, 7.7 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 170.0, 169.2, 140.9, 140.5, 138.5, 133.2, 129.7, 128.6, 128.33, 128.29,127.9, 127.5, 61.5, 51.9, 51.6, 31.4, 30.4, 14.2. **IR** (ATR): 2981, 2953, 1720, 1435, 1369, 1266, 1198, 1138, 1080, 1043 $cm^{-1}$. **HRMS** calculated for $C_{23}H_{26}O_6NH_4$ $[M+NH_4]^+$ 416.2068, found 416.2070.

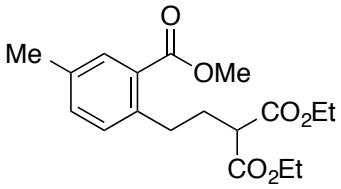




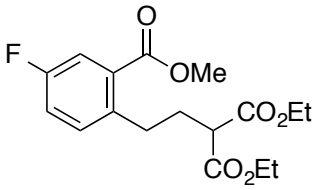


**Diethyl 2-(2-(ethoxycarbonyl)-4-methylphenethyl)malonate (7ae):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1ae**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (203.4 mg, 97% yield). **$^1$H NMR** (300 MHz,

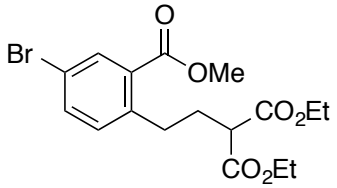
$CDCl_3$) δ 7.68 (d, *J* = 2.0 Hz, 1H), 7.24 – 7.17 (m, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.18 (q, *J* = 6.7 Hz, 4H), 3.37 (t, *J* = 7.5 Hz, 1H), 3.02 – 2.88 (m, 2H), 2.32 (s, 3H), 2.26 – 2.12 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.4, 167.6, 139.5, 135.9, 132.7, 131.2, 131.1, 129.7, 61.3, 60.8, 51.8, 31.6, 30.5,20.8, 14.3, 14.1. **IR** (ATR): 2981, 2937, 1716, 1500, 1447, 1367, 1265, 1138, 1022, 863 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{26}O_6H$ $[M+H]^+$ 351.1802, found 351.1803.



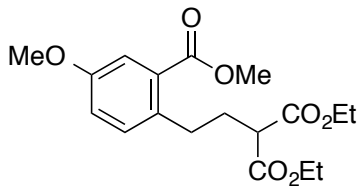

**Diethyl 2-(2-(methoxycarbonyl)-4-methylphenethyl)malonate (7bc):** (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bc**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (190.2 mg, 94% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.22 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 4.24 – 4.12 (m, 4H), 3.86 (s, 3H), 3.37 (t, *J* = 7.5 Hz, 1H), 3.00 – 2.91 (m, 2H), 2.32 (s, 3H), 2.25 – 2.12 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.4,167.9, 139.7, 135.9, 132.9, 131.3, 131.2, 129.3, 61.3, 51.9, 51.8, 31.6, 30.5, 20.8, 14.1. **IR** (ATR):2981, 2949, 1723, 1460, 1369, 1259, 1177, 1148, 1067, 761, 701 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}O_6H$ $[M+H]^+$ 337.1646, found 337.1648.



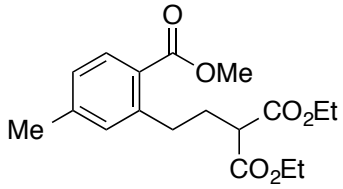

**Diethyl 2-(4-fluoro-2-(methoxycarbonyl)phenethyl)malonate (7bd):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bd**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (193.5 mg, 95% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 9.5, 2.8 Hz, 1H), 7.23 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.12 (td, *J* = 8.2, 2.8 Hz, 1H), 4.19 (q, *J* = 7.1, 6.6 Hz, 4H), 3.88 (s, 3H), 3.37 (t, *J* = 7.4 Hz, 1H), 3.02 – 2.92 (m, 2H), 2.23 – 2.11 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.4, 166.6 (d, *J* = 2.7 Hz), 160.9 (d, *J* = 245.7 Hz), 138.8 (d, *J* = 3.5 Hz), 132.9 (d, *J* = 7.5 Hz), 130.9 (d, *J* = 7.1 Hz), 119.2 (d, *J* = 20.8 Hz), 117.6 (d, *J* = 23.2 Hz), 61.5, 52.3, 51.8, 31.3, 30.5, 14.2. **$^{19}$F NMR** (282 MHz, $CDCl_3$) δ -116.0. **IR** (ATR): 2982, 2955, 1724, 1582, 1497, 1437, 1266, 1208, 1182, 1148, 1071 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{21}FO_6H$ $[M+H]^+$ 341.1395, found 341.1398.



**Diethyl 2-(4-bromo-2-(methoxycarbonyl)phenethyl)malonate (7be):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1be**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (236.3 mg, 98% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.3 Hz, 1H), 7.53 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 4.19 (q, *J* = 7.2, 6.6 Hz, 4H), 3.88 (s, 3H), 3.37 (t, *J* = 7.4 Hz, 1H), 3.02 – 2.90 (m, 2H), 2.25 – 2.10 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.3, 166.4, 141.9, 135.1, 133.8, 132.9, 131.2, 120.0, 61.5, 52.3, 51.7, 31.5, 30.3, 14.2. **IR** (ATR): 2981, 1722, 1480, 1391, 1215, 1190, 1138, 1080, 1041, 967 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{21}BrO_6H$ $[M+H]^+$ 403.0574, found 403.0576.

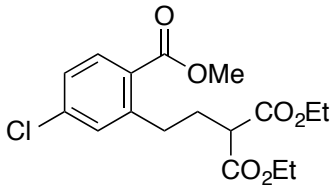


**Diethyl 2-(4-methoxy-2-(methoxycarbonyl)phenethyl)malonate (7bf):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bf**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a yellow oil (209.9 mg, 99% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.40 (d, *J* = 2.9 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.5, 2.9 Hz, 1H), 4.18 (qd, *J* = 7.1, 0.8 Hz, 4H), 3.87 (s, 3H), 3.79 (s, 3H), 3.36 (t, *J* = 7.5 Hz, 1H), 2.99 – 2.86 (m, 2H), 2.22 – 2.08 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.4, 167.6, 157.8, 134.8, 132.4, 130.3, 118.4, 115.5, 61.3, 55.5, 52.1, 51.8, 31.2, 30.6, 14.1. **IR** (ATR): 2981, 2953, 1720, 1609, 1501, 1435, 1280, 1219, 1076, 1039 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}O_7H$ $[M+H]^+$ 353.1595, found 353.1595.



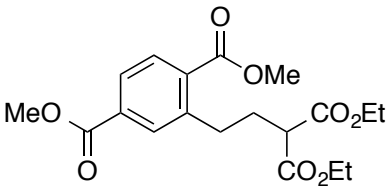
**Diethyl 2-(2-(methoxycarbonyl)-5-methylphenethyl)malonate (7bh):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bh**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (199.9 mg, 99% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.6 Hz, 1H), 7.03 (d, *J* = 7.1 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 4H),3.83 (s, 3H), 3.38 (t, *J* = 7.5 Hz, 1H), 3.03 – 2.92 (m, 2H), 2.32 (s, 3H), 2.24 – 2.12 (m, 2H), 1.25 (t, *J* = 7.1

Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.3, 167.6, 143.0, 142.6, 132.0, 131.1, 127.0, 126.4, 61.3, 51.8, 51.7, 32.0, 30.4, 21.3, 14.1. **IR** (ATR): 2981, 2953, 1717, 1612, 1435, 1262, 1136, 1083, 1025, 813 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}O_6H$ $[M+H]^+$ 337.1646, found 337.1647.

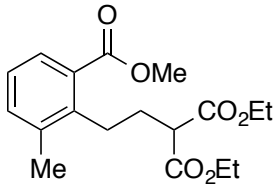



**Diethyl 2-(5-chloro-2-(methoxycarbonyl)phenethyl)malonate (7bi):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bi**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (182.8 mg, 85% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 1H), 7.29 – 7.22 (m, 2H), 4.21 (q, *J* = 7.1 Hz, 4H), 3.89 (s, 3H),3.39 (t, *J* = 7.4 Hz, 1H), 3.06 – 2.95 (m, 2H), 2.26 – 2.15 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.3, 166.9, 145.1, 138.4, 132.6, 131.3, 127.9, 126.7, 61.6, 52.2, 51.8, 32.0, 30.2, 14.2. **IR** (ATR): 2982, 2954, 1720, 1593, 1564, 1435, 1251, 1149, 1024, 779 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{21}ClO_6H$ $[M+H]^+$ 357.1099, found 357.1100.

**Dimethyl 2-(4-ethoxy-3-(ethoxycarbonyl)-4-oxobutyl)terephthalate (7bj):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bj**) and isolated by column chromatography ($SiO_2$, 20% *i*-PrOAc in heptane) as a colorless oil (216.0 mg, 95% yield).

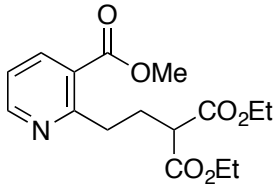



**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.92 – 7.90 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 4H), 3.92 (s, 3H), 3.90 (s, 3H), 3.38 (t, *J* = 7.4 Hz, 1H), 3.09 – 2.97 (m, 2H), 2.29 – 2.15 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.3, 167.2, 166.3, 142.8, 133.6, 133.1, 132.2, 130.9, 127.4, 61.5, 52.43, 52.35, 51.8, 31.9, 30.3, 14.2. **IR** (ATR): 2981, 2954, 1719, 1435, 1369, 1251, 1192, 1112, 1023, 754 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{24}O_8H$ $[M+H]^+$ 381.1544, found 381.1545.



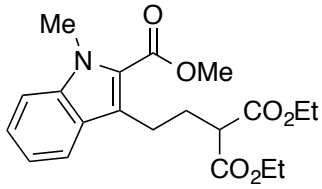

**Diethyl 2-(2-(methoxycarbonyl)-6-methylphenethyl)malonate (7bk):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bk**) and isolated by column chromatography ($SiO_2$, 0–30% *i*-PrOAc

in heptane) as a colorless oil (148.4 mg, 74% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.24 (d, *J* = 7.9 Hz, 1H), 7.15 (dd, *J* = 7.7, 7.7 Hz, 1H), 4.22 (qd, *J* = 7.1, 1.2 Hz, 4H), 3.88 (s, 3H), 3.49 (dd, *J* = 7.4, 7.4 Hz, 1H), 3.02 – 2.89 (m, 2H), 2.39 (s, 3H), 2.20 – 2.07 (m, 2H), 1.28 (dd, *J* = 7.1, 7.1 Hz, 6H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 169.3, 168.6, 140.4, 137.7, 134.0, 130.6, 128.2, 125.9, 61.3, 52.2, 28.9, 28.0, 20.0, 19.6, 14.1. **IR** 2981, 2954, 2375, 1719, 1686, 1459, 1438, 1369, 1266, 1250, 1220, 1188, 1174, 1151, 1130, 1094, 1078, 1049, 1022, 975, 910, 861, 811, 759, 643, 592, 460 $cm^{-1}$. **HRMS** calculated for $C_{18}H_{24}O_6H$ $[M+H]^+$ 351.1802, found 351.1804.




**Diethyl 2-(2-(3-(methoxycarbonyl)pyridin-2-yl)ethyl)malonate (7bl):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bl**) and isolated by column chromatography ($SiO_2$, 50% *i*-PrOAc in heptane) as a yellow oil (109.6 mg, 57% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 8.65 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.17 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.22 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.25 – 4.15 (m, 4H), 3.92 (s, 3H), 3.48 (t, *J* = 7.5 Hz, 1H), 3.30 – 3.18 (m, 2H), 2.43 – 2.31 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.5, 166.9, 161.8, 152.1, 138.7, 125.6, 121.3, 61.4, 52.5, 51.9, 34.4, 28.3, 14.2. **IR** (ATR): 2982, 2954, 1722, 1569, 1432, 1262, 1132, 1084, 1029, 774 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{21}NO_6H$ $[M+H]^+$ 324.1442, found 324.1440.

**Diethyl 2-(2-(2-(methoxycarbonyl)-1-methyl-1H-indol-3-yl)ethyl)malonate (7bm):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bm**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a yellow oil (163.7 mg, 73% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.16 (ddd, *J* = 8.0, 4.9, 3.0 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 4H), 4.01 (s, 3H), 3.96 (s, 3H), 3.43 (t, *J* = 7.3 Hz, 1H), 3.23 – 3.12 (m, 2H), 2.36 – 2.20 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.5, 163.2, 138.9, 126.6, 125.5, 124.9, 123.7, 120.8, 120.1, 110.2, 61.4, 51.8, 51.6, 32.2, 30.0, 23.3, 14.2. **IR** (ATR): 2981, 2951, 1746, 1728, 1529, 1440, 1367, 1241, 1102, 969, 740 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{25}NO_6H$ $[M+H]^+$ 376.1755, found 376.1754.

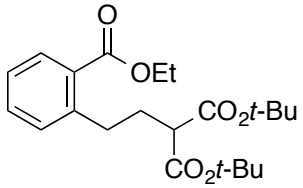


**Diethyl 2-(2-(2-(methoxycarbonyl)benzo[b]thiophen-3-yl)ethyl)malonate (7bn):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **6a** and iodoester partner SI-**1bn**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a red solid (204.8 mg, 90% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 1H), 7.87 – 7.80 (m, 1H), 7.52 – 7.41 (m, 2H), 4.22 (q, *J* = 7.2, 6.6 Hz, 4H), 3.93 (s, 3H), 3.50 (t, *J* = 7.3 Hz, 1H), 3.45 – 3.34 (m, 2H), 2.34 – 2.19 (m, 2H), 1.27 (d, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.4, 163.5, 144.2, 140.8, 139.4, 127.4, 127.3, 124.8, 123.9, 122.8, 61.6, 52.3, 51.9, 28.8, 25.1, 14.2. **IR** (ATR): 3017, 2917, 2849, 1713, 1531, 1445, 1231, 1194, 1029, 738 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{22}SO_6H$ $[M+H]^+$ 379.1210, found 379.1217.

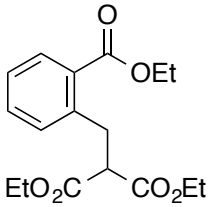
**Dimethyl 2-(2-(ethoxycarbonyl)phenethyl)malonate (7ab):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane SI-**6ab** and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a yellow oil (166.5 mg, 90% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.95 – 7.86 (m, 1H), 7.47 – 7.38 (m, 1H), 7.30 – 7.23 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 6H), 3.45 (t, *J* = 7.5 Hz, 1H), 3.07 – 2.96 (m, 2H), 2.32 – 2.17 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.8, 167.4, 142.5, 132.0, 131.2, 130.9, 129.9, 126.4, 60.9, 52.5, 51.5, 32.0, 30.6, 14.4. **IR** (ATR): 2954, 1733, 1715, 1435, 1251, 1150, 1131, 1082, 755, 710 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{20}O_6H$ $[M+H]^+$ 309.1333, found 309.1332.

**Diisopropyl 2-(2-(ethoxycarbonyl)phenethyl)malonate (7ac):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material SI-**6ac** and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (170.5 mg, 78% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.42 (td, *J* = 7.4, 1.5 Hz, 1H), 7.25 (ddd, *J* = 8.5, 4.0, 1.8 Hz, 2H), 5.06 (sept, *J* = 6.3 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.33 (t, *J* = 7.5 Hz, 1H), 3.07 – 2.95 (m, 2H), 2.27 – 2.13 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.3 Hz, 12H). **$^{13}$C NMR** (75 MHz,

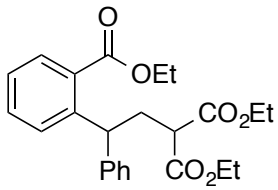
$CDCl_3$) δ 168.9, 167.4, 142.7, 132.0, 131.2, 130.8, 130.0, 126.3, 68.8, 60.9, 52.2, 32.0, 30.3,21.7, 21.6, 14.3. **IR** (ATR): 2981, 2937, 1717, 1453, 1366, 1250, 1100, 1017, 755, 710 $cm^{-1}$. **HRMS** calculated for $C_{20}H_{28}O_6H$ $[M+H]^+$ 365.1959, found 365.1960.




**Di-*tert*-butyl 2-(2-(ethoxycarbonyl)phenethyl)malonate (7ad):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material SI-**6ad** and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (110.0 mg, 47% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 1H), 7.41 (td, *J* = 7.5, 1.5 Hz, 1H), 7.29 – 7.24 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.19 (t, *J* = 7.5 Hz, 1H), 3.05 – 2.95 (m, 2H), 2.13 (q, *J* = 7.7 Hz, 2H), 1.47 (s, 18H), 1.39 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 168.9, 167.6, 143.0, 132.0, 131.3, 130.9, 130.1, 126.3, 81.5, 61.0, 53.9, 32.1, 30.5, 28.1, 14.5. **IR** (ATR): 2978, 2934, 1718, 1455, 1367, 1249, 1129, 1081, 849, 743 $cm^{-1}$. **HRMS** calculated for $C_{22}H_{32}O_6Na$ $[M+Na]^+$ 415.2091, found 415.2094.



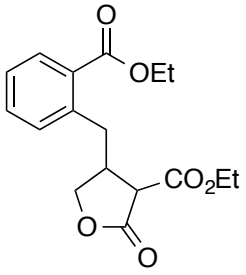

**Diethyl 2-(2-(ethoxycarbonyl)benzyl)malonate (19):** The title compound was synthesized according to the general procedure (0.60 mmol of diethyl 2-methylenemalonate (**11**) and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a colorless oil (140.6 mg, 73% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.40 (td, *J* = 7.5, 1.6 Hz, 1H), 7.33 – 7.23 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.14 (qd, *J* = 7.1, 2.4 Hz, 4H), 3.89 (t, *J* = 7.7 Hz, 1H), 3.55 (d, *J* = 7.7 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.1, 167.2, 139.6, 132.14, 132.06, 131.2, 129.9, 127.1, 61.4, 61.1, 53.3, 33.8, 14.3, 14.1. **IR** (ATR): 2982, 1713, 1447, 1367, 1294, 1256, 1151, 1134, 855, 753 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{22}O_6H$ $[M+H]^+$ 323.1489, found 323.1490.



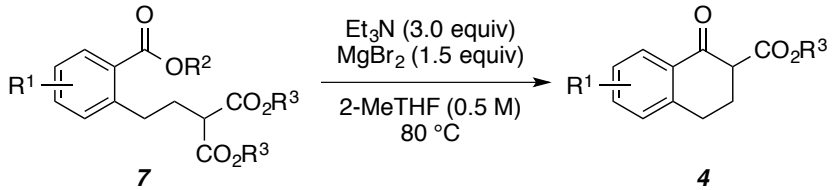

**Diethyl 2-(2-(2-(ethoxycarbonyl)phenyl)-2-phenylethyl)malonate (20):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **12** and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 0–30% *i*-

PrOAc in heptane) as a colorless oil (161.1 mg, 65% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.3 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.32 – 7.20 (m, 5H), 7.21 – 7.13 (m, 1H), 5.12 (dd, *J* = 8.0, 8.0 Hz, 1H), 4.31 (qd, *J* = 7.1, 2.2 Hz, 2H), 4.23 – 4.02 (m, 4H), 3.26 (dd, *J* = 7.3, 7.3 Hz, 1H), 2.71 (ddd, *J* = 13.9, 7.7, 7.7 Hz, 1H), 2.61 (ddd, *J* = 13.9, 8.1, 7.2 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.23 (q, *J* = 7.0 Hz, 6H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 169.4, 169.2, 167.8, 144.1, 143.4, 131.7, 131.1, 130.3, 128.4, 128.2, 128.1, 126.4, 126.2, 61.4, 61.4, 61.0, 50.4, 42.6, 34.7, 14.2, 14.0, 14.0. **IR** 2981, 2938, 2906, 2873, 2373, 2258, 2163, 1718, 1686, 1599, 1453, 1466, 1458, 1447, 1389, 1367, 1262, 1224, 1150, 1133, 1093, 1074, 1044, 1023, 910, 860, 787, 729, 700, 648, 591, 562, 478 $cm^{-1}$. **HRMS** calculated for $C_{24}H_{28}O_6H$ $[M+H]^+$ 413.1959, found 413.1965.

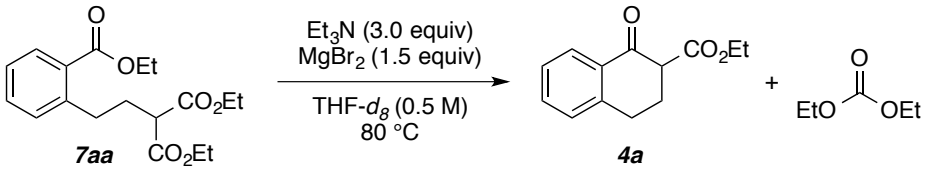
**Ethyl 4-(2-(ethoxycarbonyl)benzyl)-2-oxotetrahydrofuran-3-carboxylate (21):** The title compound was synthesized according to the general procedure (0.60 mmol of cyclopropane starting material **13** and iodoester partner **1a**) and isolated by column chromatography ($SiO_2$, 0–50% *i*-PrOAc in heptane) as a colorless oil (180.1 mg, 94% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.46 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H), 7.32 (ddd, *J* = 7.6, 7.6, 1.3 Hz, 1H), 7.22 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.52 – 4.44 (m, 1H), 4.36 (qd, *J* = 7.1, 0.9 Hz, 2H), 4.10 – 3.96 (m, 3H), 3.44 – 3.35 (m, 2H), 3.34 – 3.27 (m, 1H), 3.23 – 3.14 (m, 1H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 172.1, 167.3, 166.9, 139.5, 132.3, 131.5, 131.4, 129.6, 127.2, 71.6, 61.9, 61.1, 52.1, 41.7, 35.9, 14.3, 13.9. **IR** (ATR) 2982, 2934, 2908, 2873, 1778, 1733, 1710, 1601, 1576, 1447, 1368, 1347, 1258, 1244, 1208, 1139, 1083, 1015, 932, 855, 799, 712, 693, 665, 638, 598, 552, 519, 479 $cm^{-1}$. **HRMS** calculated for $C_{17}H_{20}O_6H$ $[M+H]^+$ 321.1333, found 321.1337.




## 4. General Procedure for the Annulation



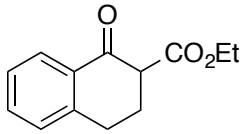
In a 2-dram vial was added triester (0.20 mmol, 1.0 equiv), $MgBr_2$ (55.8 mg, 0.30 mmol, 1.5 equiv), 2-MeTHF (0.40 mL, 0.50 M), and $Et_3N$ (84.5 mL, 0.60 mmol, 3.0 equiv). The resulting mixture was stirred at 80 °C for 4 h. The reaction mixture was quenched with 2 M HCl and extracted with *i*-PrOAc (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography ($SiO_2$) to afford the β-ketoester.




**Deuterated Solvent $^{13}$C NMR Experiment for the Observation of Diethyl Carbonate**

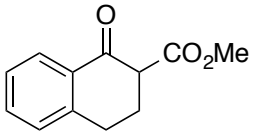
To a 2 dram vial was added $MgBr_2$ (55.8 mg, 0.30 mmol, 1.5 equiv), stir bar, triester **7aa**, $Et_3N$ (84.5 mL, 0.60 mmol, 3.0 equiv), and THF-$d_8$ (0.40 mL, 0.50 M). The resulting mixture was stirred at 80 °C for 5 h. The reaction mixture was transferred to an NMR tube and analyzed by $^{13}$C NMR. The crude spectrum was compared to the spectrum of an authentic sample of diethyl carbonate in THF-$d_8$.

## 5. Characterization Data for β-Ketoesters 4

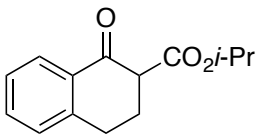



**Ethyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4a):** The title compound was synthesized according to the general procedure (from 0.30 mmol of starting material **7aa**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (59.3 mg, 91% yield, 2:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.48 (s, 1H), 7.80 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.38 – 7.26 (m, 2H), 7.16 (ddd, *J* = 7.3, 1.7, 0.8 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.78 – 2.83 (m, 2H), 2.63 – 2.51 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 8.04 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.48 (td, *J* = 7.5, 1.5 Hz, 1H), 7.25 (td, *J* = 6.7, 6.2, 3.2 Hz, 2H), 4.26 – 4.19(m, 2H), 3.59 (dd, *J* = 10.3, 4.8 Hz, 1H), 3.02 (dt, *J* = 9.7, 5.3 Hz, 2H), 2.52 – 2.43 (m, 1H), 2.41 – 2.28 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.4, 172.9, 170.3, 165.1, 143.8, 139.5, 134.0, 131.9, 130.6, 130.2, 128.9, 127.9,

127.5, 127.0, 126.7, 124.4, 97.2, 61.4, 60.7, 54.7, 27.9, 27.8, 26.5, 20.7, 14.5, 14.3. **IR** (ATR): 2980, 2935, 1737, 1686, 1643, 1617, 1569, 1296, 1156, 1022 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{14}O_3H$ $[M+H]^+$ 219.1016, found 219.1013.

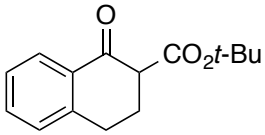



**Methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4b):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7ab**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (32.0 mg, 78% yield, 1.5:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.40 (s, 1H), 7.80 (dd, *J* = 7.0, 2.2 Hz, 1H), 7.38 – 7.26 (m, 2H), 7.22 – 7.11 (m, 1H), 3.82 (s, 3H), 2.80 (dd, *J* = 8.9, 6.5 Hz, 2H), 2.64 – 2.54 (m, 2H). Minor peaks corresponding to the keto tautomer observed at δ 8.04(dd, *J* = 7.9, 1.5 Hz, 1H), 7.49 (td, *J* = 7.5, 1.5 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.20 – 7.12 (m, 1H), 3.77 (s, 3H), 3.62 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.02 (dt, *J* = 10.0, 5.2 Hz, 2H), 2.48 (ddd, *J* = 10.2, 8.1, 4.3 Hz, 1H), 2.42 – 2.28 (m, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.2, 173.2, 170.7, 165.2, 143.8, 139.5, 134.0, 131.8, 130.7, 130.1, 128.9, 127.9, 127.5, 127.0, 126.7, 124.5, 96.9, 54.6, 52.4, 51.7, 27.9, 27.7, 26.5, 20.7. **IR** (ATR): 2951, 2847, 1742, 1684, 1645, 1618, 1568, 1438, 1360, 1263, 1084 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{12}O_3H$ $[M+H]^+$ 205.0859, found 205.0855.

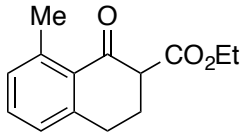



**Isopropyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4c):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7ac**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (31.6 mg, 68% yield, 3:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.57 (s, 1H), 7.90 – 7.74 (m, 1H), 7.39 – 7.27 (m, 2H), 7.23 – 7.10 (m, 1H), 5.18 (sept, *J* = 6.2 Hz, 1H), 2.82 (dd, *J* = 8.9, 6.5 Hz, 2H), 2.63 – 2.53 (m, 2H), 1.34 (d, *J* = 6.2 Hz, 6H). Minor peaks corresponding to the keto tautomer observed at δ 8.06 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.50 (td, *J* = 7.5, 1.5 Hz, 1H), 7.27 (td, *J* = 6.9, 6.1, 3.3 Hz, 2H), 5.16 – 5.08 (m, 1H), 3.57 (dd, *J* = 10.4, 4.8 Hz, 1H), 3.22 – 2.95 (m, 2H), 2.52 – 2.43 (m, 1H), 2.42 – 2.29 (m, 1H), 1.29 (d, *J* = 6.3 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.5, 172.5, 169.9, 165.0, 143.7, 139.5, 133.9, 132.0, 130.5, 130.3, 128.9, 127.8, 127.5, 127.0, 126.7, 124.4, 97.5, 68.9, 68.1, 54.9, 27.9, 27.8, 26.5, 22.1, 21.9, 20.7. **IR** (ATR):

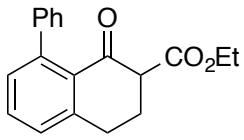
2980, 2936, 1734, 1687, 1641, 1615, 1570, 1382, 1266, 1103, 1082 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{16}O_3H$ $[M+H]^+$ 233.1172, found 233.1170.



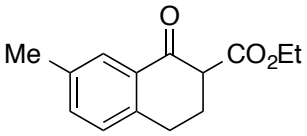

***tert*-Butyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4d):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7ad**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (36.3 mg, 74% yield, 2:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.62 (s, 1H), 7.78 (dd, *J* = 7.2, 1.9 Hz, 1H), 7.35 – 7.21 (m, 3H), 2.78 (dd, *J* = 8.9, 6.6 Hz, 2H), 2.51 (dd, *J* = 8.8, 6.3 Hz, 2H), 1.55 (s, 9H). Minor peaks corresponding to the keto tautomer observed at δ 8.04 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.19 – 7.11 (m, 2H), 3.49 (dd, *J* = 9.8, 4.8 Hz, 1H), 3.24 – 2.91 (m, 2H), 2.46 – 2.38 (m, 1H), 2.38 – 2.20 (m, 1H), 1.48 (s, 9H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.9, 172.7, 169.6, 164.6, 143.7, 139.4, 133.8, 132.2, 130.5, 130.3, 128.9, 127.7, 127.4, 126.9, 126.6, 124.3, 98.5, 81.9, 81.4, 55.5, 28.5, 28.2, 28.0, 27.7, 26.6, 21.1. **IR** (ATR): 2980, 2936, 1734, 1687, 1641, 1615, 1570, 1382, 1266, 1103, 1082 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{18}O_3Na$ $[M+Na]^+$ 269.1148, found 269.1147.



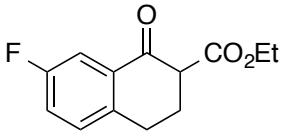

**Ethyl 8-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4e):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7ba**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (43.6 mg, 94% yield, 1:2 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 3.4 Hz, 1H), 7.09 (d, *J* = 3.9 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.60 (dd, *J* = 10.6, 5.0 Hz, 1H), 3.04 (dt, *J* = 10.3, 5.2 Hz, 2H), 2.64 (s, 3H), 2.58 – 2.41 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H). Minor peaks corresponding to the enol tautomer observed at δ 13.03 (s, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.08 – 6.97 (m, 2H), 4.33 – 4.27 (m, 2H), 2.74 (dd, *J* = 8.9, 5.9 Hz, 2H), 2.64 (s, 3H), 2.39 – 2.26 (m, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 195.2, 173.2, 170.7, 168.8, 144.8, 142.1, 141.4, 138.0, 132.8, 130.8, 130.7, 130.6, 130.0, 128.8, 126.9, 125.5, 98.2, 61.3, 60.6, 56.4, 29.8, 28.9, 26.2, 23.3, 23.0, 20.7, 14.5, 14.3. **IR** (ATR): 2978, 2932, 1736, 1677, 1634, 1593, 1563, 1309, 956, 774 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{16}O_3H$ $[M+H]^+$ 233.1172, found 233.1171.



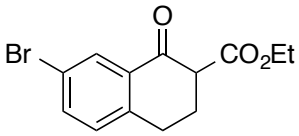

**Ethyl 1-oxo-8-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4f):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bb**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (10.4 mg, 18% yield, 1:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.34 (s, 1H), 7.51 – 7.12 (m, 8H),4.26 (q, *J* = 7.0 Hz, 2H), 2.82 (dd, *J* = 8.8, 5.8 Hz, 2H), 2.58 (dd, *J* = 8.8, 5.8 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 7.73 – 6.51 (m, 8H), 4.24 – 4.16 (m, 2H), 3.59 (dd, *J* = 9.1, 5.1 Hz, 1H), 3.24 – 3.10 (m, 1H), 3.09 – 2.94 (m, 1H), 2.50 (dd, *J* = 8.9, 4.9 Hz, 1H), 2.45 – 2.29 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.8, 172.8, 170.3, 167.0, 144.6, 144.4, 143.2, 142.4, 141.9, 141.4, 132.3, 130.9, 130.7, 130.6, 129.7, 128.6, 128.4, 128.18, 128.17, 128.0, 127.6, 127.0,126.8, 126.6, 98.6, 61.4, 60.6, 55.8, 29.7, 28.4, 26.6, 20.7, 14.5, 14.3. **IR** (ATR): 3057, 2981, 2929, 1735, 1687, 1634, 1609, 1259, 1232, 938, 757 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{18}O_3H$ $[M+H]^+$ 295.1329, found 295.1310.




**Ethyl 7-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4g):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7ae**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (35.0 mg, 75% yield, 1:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.52 (s, 1H), 7.68 – 7.57 (m, 1H), 7.14 (d, *J* = 7.7 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.77 (dd, *J* = 8.9, 6.5 Hz, 2H), 2.63 – 2.51 (m, 2H), 2.37 (s,3H), 1.36 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 7.92 – 7.82 (m, 1H), 7.31 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 4.30 – 4.17 (m, 2H), 3.58 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.07 – 2.91 (m, 2H), 2.52 – 2.41 (m, 1H), 2.37 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.6, 172.9,170.4, 165.4, 140.9, 136.7, 136.6, 136.2, 135.0, 131.7, 131.3, 130.0, 128.8, 127.9, 127.4, 124.9, 97.1, 61.3, 60.6, 54.8, 27.5, 27.4, 26.7, 21.2, 21.0, 20.8, 14.5, 14.3. **IR** (ATR): 2980, 2930, 1738,1685, 1642, 1597, 1573, 1269, 1215, 1086, 814 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{16}O_3H$ $[M+H]^+$ 233.1172, found 233.1171.

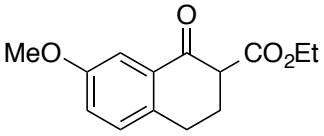



**Ethyl 7-fluoro-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4h):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bd**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a white solid (39.7 mg, 84% yield, 4:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.42 (s, 1H), 7.49 (dd, *J* = 9.5, 2.7 Hz, 1H), 7.13 (dd, *J* = 8.3, 5.4 Hz, 1H), 7.01 (td, *J* = 8.4, 2.7 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.84 – 2.72 (m, 2H), 2.67 – 2.53 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 7.71 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.28 – 7.17 (m, 2H), 4.27 – 4.20 (m, 2H), 3.59 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.00 (dt, *J* = 13.8, 5.2 Hz, 2H), 2.53 – 2.43 (m, 1H), 2.37 (ddt, *J* = 8.8, 6.2, 4.7 Hz, 1H), 1.30 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 192.4 (d, *J* = 1.5 Hz), 172.7, 170.0, 163.9 (d, *J* = 2.4 Hz), 161.7 (d, *J* = 246.7 Hz), 161.9 (d, *J* = 243.9 Hz), 139.5 (d, *J* = 3.0 Hz), 134.9 (d, *J* = 3.3 Hz), 133.5 (d, *J* = 6.3 Hz), 131.9 (d, *J* = 7.9 Hz), 130.8 (d, *J* = 7.0 Hz), 128.8 (d, *J* = 7.6 Hz), 121.4 (d, *J* = 22.2 Hz), 117.1 (d, *J* = 21.6 Hz), 113.7 (d, *J* = 22.1 Hz), 111.4 (d, *J* = 23.5 Hz), 98.0, 61.5, 60.9, 54.3, 27.1, 27.0, 26.6, 20.8, 14.4, 14.3. **$^{19}$F NMR** (282 MHz, $CDCl_3$) δ -114.62 (keto), -115.82 (enol). **IR** (ATR): 2927, 2852, 1644, 1604, 1573, 1493, 1278, 1219, 972, 811 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{13}FO_3H$ $[M+H]^+$ 237.0921, found 237.0919.

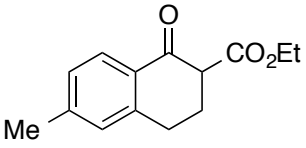



**Ethyl 7-bromo-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4i):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7be**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a white solid (53.8 mg, 91% yield, 17:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.42 (s, 1H), 7.92 (d, *J* = 2.1 Hz, 1H), 7.42 (d, *J* = 2.2 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.76 (dd, *J* = 8.9, 6.7 Hz, 2H), 2.62 – 2.50 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 8.17 (d, *J* = 2.2 Hz, 1H), 7.60 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 4.29 – 4.21 (m, 2H), 3.59 (dd, *J* = 9.9, 4.7 Hz, 1H), 3.11 – 2.98 (m, 1H), 2.93 (ddd, *J* = 16.7, 9.0, 4.5 Hz, 1H), 2.49 (dq, *J* = 9.4, 4.7 Hz, 1H), 2.36 (ddt, *J* = 11.1, 6.3, 3.2 Hz, 1H), 1.36 – 1.30 (m, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 192.1, 172.6, 169.9, 163.6, 142.4, 138.1, 136.7, 133.2, 132.0, 130.7, 130.6, 129.1, 127.4, 121.0, 120.4, 98.0, 61.6, 60.9, 54.2,

32.0, 27.4, 22.8, 20.5, 14.4, 14.2. **IR** (ATR): 2940, 2853, 1615, 1586, 1556, 1475, 1349, 1271, 1025, 814 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{13}BrO_3H$ $[M+H]^+$ 297.0121, found 297.0121.

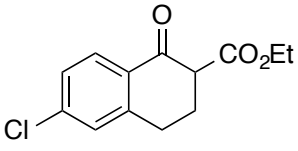



**Ethyl 7-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4j):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bf**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (44.9 mg, 80% yield, 1:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.53 (s, 1H), 7.35 (d, *J* = 2.8 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.88 (dd, *J* = 8.3, 2.8 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 2.74 (dd, *J* = 9.0, 6.4 Hz, 2H), 2.68 – 2.50 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 7.52 (d, *J* = 2.8 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 4.27 – 4.19 (m, 2H), 3.83 (s, 3H), 3.57 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.06 – 2.84 (m, 2H), 2.51 – 2.41 (m, 1H), 2.40 – 2.28 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.3, 172.9, 170.4, 165.0, 158.6, 158.5, 136.4, 132.6, 131.7, 131.0, 130.1, 128.4, 122.4, 117.0, 109.6, 108.9, 97.4, 61.3, 60.7, 55.6, 55.5, 54.5, 27.00, 26.95, 26.8, 21.0, 14.4, 14.3. **IR** (ATR): 2935, 1737, 1683, 1644, 1596, 1570, 1497, 1219, 1026, 811 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{16}O_4H$ $[M+H]^+$ 249.1121, found 249.1121.

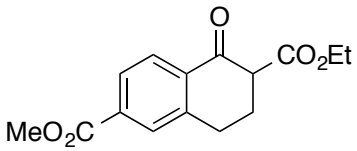



**Ethyl 6-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4k):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bh**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (38.0 mg, 82% yield, 3:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.51 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 7.00 (s, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.84 – 2.73 (m, 2H), 2.62 – 2.53 (m, 2H), 2.37 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.12 – 7.15 (m, 2H), 4.27 – 4.21 (m, 2H),3.58 (dd, *J* = 10.3, 4.8 Hz, 1H), 2.98 (dt, *J* = 9.7, 5.3 Hz, 2H), 2.54 – 2.40 (m, 2H), 2.39 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 193.0, 172.9, 170.5, 165.5, 144.9, 143.8, 141.0, 139.6, 129.6, 129.3, 128.3, 128.0, 128.0, 127.5, 127.4, 124.4, 96.3, 61.3, 60.5, 54.7, 28.0, 27.7, 26.6, 21.8, 21.6, 20.8, 14.5, 14.3. **IR** (ATR): 2979, 2906, 1737, 1682, 1640, 1610,

1561, 1268, 1208, 1090, 1022 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{16}O_3H$ $[M+H]^+$ 233.1172, found 233.1172.

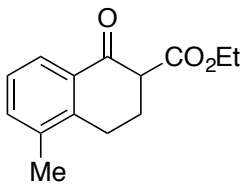



**Ethyl 6-chloro-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4l):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bi**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (49.0 mg, 97% yield, 4:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.46 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.25 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.19 – 7.15 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.79 (dd, *J* = 8.8, 6.7 Hz, 2H), 2.58 (dd, *J* = 8.9, 6.7 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 7.99 (d, *J* = 8.4 Hz, 1H), 7.30 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.28 – 7.23 (m, 1H), 4.28 – 4.22 (m, 2H), 3.59 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.05 (dt, *J* = 17.1, 5.4 Hz, 1H), 2.97 (ddd, *J* = 17.1, 9.3, 4.7 Hz, 1H), 2.50 (ddt, *J* = 14.1, 9.5, 4.4 Hz, 1H), 2.36 (ddt, *J* = 13.5, 6.2, 4.6 Hz, 1H), 1.30 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 192.3, 172.7, 170.0, 164.2, 145.3, 141.2, 140.3, 136.4, 130.4, 129.5, 128.8, 128.7, 127.63,127.60, 126.9, 125.8, 97.3, 61.5, 60.8, 54.4, 27.8, 27.6, 26.3, 20.5, 14.4, 14.3. **IR** (ATR): 2980, 2850, 1739, 1689, 1644, 1615, 1592, 1559, 1262, 1195, 1022 $cm^{-1}$. **HRMS** calculated for $C_{13}H_{13}ClO_3H$ $[M+H]^+$ 253.0626, found 253.0624.

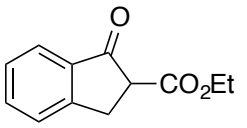



**2-Ethyl 6-methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylate (4m):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bj**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a white solid (53.7 mg, 97% yield, 4:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.41 (s, 1H), 7.98 – 7.89 (m, 1H), 7.85 (s, 1H), 7.87 – 7.79 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 3H), 2.85 (dd, *J* = 9.0, 6.6 Hz, 2H), 2.59 (dd, *J* = 8.8, 6.4 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the keto tautomer observed at δ 8.09 (d, *J* = 8.6 Hz, 1H), 7.92 (d, *J* = 1.7 Hz, 2H), 4.26 – 4.20 (m, 2H), 3.94 (s, 3H), 3.63 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.07 (dq, *J* = 8.8, 5.2, 4.8 Hz, 2H), 2.54 – 2.45 (m, 1H), 2.43 – 2.33 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) of the enol and keto tautomers, δ 192.8, 172.6, 169.9, 166.8, 166.3, 163.7, 143.6, 139.3, 134.9, 134.5, 134.2, 131.5, 130.3, 128.5, 128.0, 127.9, 127.7, 124.4, 99.1, 61.5, 60.9, 54.6,

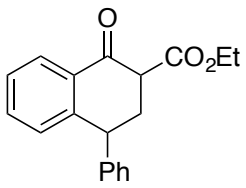
52.6, 52.3, 27.7, 27.6, 26.3, 20.6, 14.4, 14.3. **IR** (ATR): 2947, 2923, 2852, 1714, 1637, 1603, 1561, 1258, 1024, 786 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{16}O_5H$ $[M+H]^+$ 277.1071, found 277.1070.



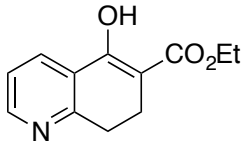

**Ethyl 5-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4n):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bk**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a colorless oil (45.8 mg, 99% yield, 1:1.5 enol:keto). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.27 – 7.15 (m, 1H), 4.28 – 4.21 (m, 2H), 3.58 (dd, *J* = 10.7, 4.6 Hz, 1H), 3.00 (ddd, *J* = 17.4, 5.2, 5.2 Hz, 1H), 2.82 (ddd, *J* = 17.4, 9.6, 4.9 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.41 – 2.34 (m, 1H), 2.31 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). Minor peaks corresponding to the enol tautomer observed at δ 12.46 (s, 1H), 7.69 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.27 – 7.15 (m, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.75 (dd, *J* = 8.8, 6.9 Hz, 2H), 2.56 (dd, *J* = 8.8, 6.8 Hz, 2H), 2.30 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 193.6, 172.7, 170.2, 165.3, 141.9, 137.7, 136.4, 135.2, 134.9, 132.4, 132.0, 130.0, 126.4, 125.9, 125.6, 122.3, 96.4, 61.2, 60.5, 53.9, 25.5, 24.8, 23.8, 20.1, 19.4, 19.4, 14.4, 14.2. **IR** 3070, 2970, 2953, 2871, 2851, 1736, 1686, 1649, 1617, 1595, 1580, 1464, 1398, 1376, 1348, 1323, 1275, 1220, 1201, 1140, 1095, 1077, 1032, 934, 903, 827, 796, 764, 740, 592, 580, 544, 528 $cm^{-1}$. **HRMS** calculated for $C_{14}H_{16}O_3H$ $[M+H]^+$ 233.1172, found 233.1174.



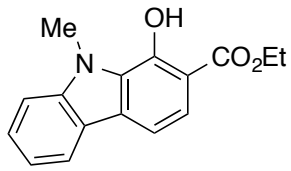

**Ethyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **19**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a yellow oil (36.6 mg, 90% yield, <1:20 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.4, 1.3 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.43 – 7.36 (m, 1H), 4.31 – 4.19 (m, 2H), 3.71 (dd, *J* = 8.3, 4.1 Hz, 1H), 3.62 – 3.48 (m, 1H), 3.37 (dd, *J* = 17.3, 8.3 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 199.6, 169.2, 153.7, 135.5, 135.4, 127.9, 126.7, 124.8, 61.8, 53.5, 30.4, 14.3. **IR** (ATR): 2981, 2934, 1737, 1709, 1572, 1255, 1150, 1091, 1007, 760 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{12}O_3H$ $[M+H]^+$ 205.0859, found 205.0857.




**Ethyl 1-oxo-4-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4o):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **20**) and isolated by column chromatography ($SiO_2$, 50% *i*-PrOAc in heptane) as a white solid (52.5 mg, 89% yield, >20:1 enol:keto). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 12.48 (s, 1H), 7.89 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.38 – 7.15 (m, 7H), 6.86 (ddd, *J* = 7.7, 1.2, 1.2 Hz, 1H), 4.34 – 4.19 (m, 2H), 4.15 (dd, *J* = 10.5, 6.6 Hz, 1H), 2.94 (dd, *J* = 15.7, 6.7 Hz, 1H), 2.83 (dd, *J* = 15.7, 10.5 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 172.6, 164.6, 143.3, 141.6, 130.7, 130.1, 128.6, 128.5, 127.7, 126.8, 126.8, 124.4, 95.9, 60.6, 44.1, 29.1, 14.2. **IR** 3060, 3025, 2981, 2972, 2928, 2902, 2852, 1734, 1717, 1698, 1684, 1647, 1617, 1568, 1541, 1521, 1507, 1496, 1489, 1473, 1454, 1400, 1378, 1345, 1321, 1268, 1241, 1181, 1137, 1082, 1025, 969, 953, 932, 914, 823,766, 749, 701, 527, 614, 588, 563, 505, 458, 419 $cm^{-1}$. **HRMS** calculated for $C_{19}H_{18}O_3H$ $[M+H]^+$ 295.1329, found 295.1332.

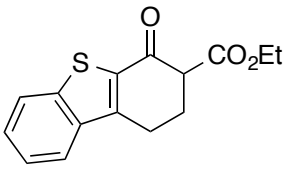



**Ethyl 5-oxo-5,6,7,8-tetrahydroquinoline-6-carboxylate (4p):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bl**) and isolated by column chromatography ($SiO_2$, 50% *i*-PrOAc in heptane) as a white solid (20.0 mg, 46% yield, >20:1 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 12.39 (s, 1H), 8.49 (dd, *J* = 5.0, 1.8 Hz, 1H), 8.04 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.23 (dd, *J* = 7.8, 4.9 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.03 (dd, *J* = 8.9, 7.0 Hz, 2H), 2.70 (dd, *J* = 8.8, 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 172.6, 163.3, 159.5, 150.5, 131.6, 126.0, 122.0, 97.9, 61.0, 30.6, 20.1, 14.4. **IR** (ATR): 2922, 2853, 1736, 1647, 1621, 1563, 1270, 1207, 751, 723 $cm^{-1}$. **HRMS** calculated for $C_{12}H_{13}NO_3H$ $[M+H]^+$ 220.0968, found 220.0965.



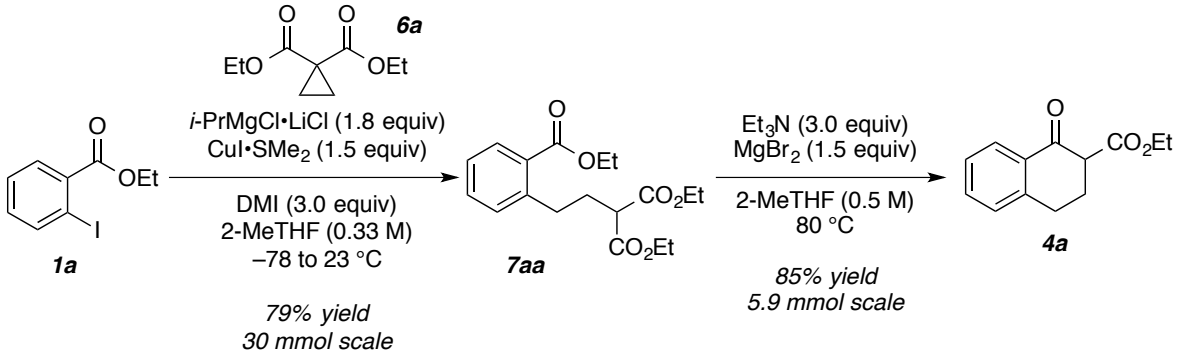

**Ethyl 1-hydroxy-9-methyl-9H-carbazole-2-carboxylate (23):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bm**) and isolated by column chromatography ($SiO_2$, 15% *i*-PrOAc in heptane) as a yellow solid (31.7 mg, 59% yield). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 11.79 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.59 – 7.49 (m, 2H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.26 (ddd, *J* = 8.0, 5.7,

1.0 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 4.26 (s, 3H), 1.48 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 171.8, 151.1, 142.5, 128.8, 128.7, 127.1, 122.4, 121.1, 119.7, 119.4, 111.0, 109.3, 108.2, 61.4, 32.2, 14.4. **IR** (ATR): 2922, 1660, 1632, 1461, 1370, 1310, 1105, 787, 716 $cm^{-1}$. **HRMS** calculated for $C_{16}H_{15}NO_3H$ $[M+H]^+$ 270.1125, found 270.1124.




**Ethyl 4-oxo-1,2,3,4-tetrahydrodibenzo[b,d]thiophene-3-carboxylate (4q):** The title compound was synthesized according to the general procedure (from 0.20 mmol of starting material **7bn**) and isolated by column chromatography ($SiO_2$, 10% *i*-PrOAc in heptane) as a yellow oil (39.8 mg, 72% yield, <1:20 enol:keto). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 7.3 Hz, 1H), 7.51 (ddd, *J* = 8.1, 7.1, 1.5 Hz, 1H), 7.44 (td, *J* = 7.5, 1.3 Hz, 1H), 4.33 – 4.18 (m, 2H), 3.71 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.24 (ddd, *J* = 17.5, 6.5, 4.9 Hz, 1H), 3.05 (ddd, *J* = 17.4, 8.0, 5.0 Hz, 1H), 2.79 – 2.61 (m, 1H), 2.52 (ddt, *J* = 13.7, 6.4, 4.9 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 188.3, 169.8, 147.8, 143.0, 138.0, 135.3, 128.5, 125.0, 124.0, 123.6, 61.6, 54.2, 27.3, 22.6, 14.3. **IR** (ATR): 2979, 2936, 1729, 1660, 1526, 1382, 1218, 1148, 1008, 756 $cm^{-1}$. **HRMS** calculated for $C_{15}H_{14}SO_3H$ $[M+H]^+$ 275.0736, found 275.0716.

## 6. Gram-scale Synthesis of 4a




In a heat-gun dried 500 mL round-bottom flask was added ethyl 2-iodobenzoate (**1a**) (12.81 g, 45 mmol, 1.5 equiv) and anhydrous 2-MeTHF (30 mL). The solution was cooled to –78 °C, and *i*-PrMgCl·LiCl (42 mL, 1.1 mmol, 1.8 equiv, 1.3 M in THF) was added. The resulting mixture was stirred at –78 °C for 30 min. CuI·$SMe_2$ (11.14 g, 11.4 mmol, 1.5 equiv) was added as a suspension in anhydrous 2-MeTHF (60 mL), followed by DMI (9.9 mL, 90 mmol, 3.0 equiv) and

diethyl 1,1-cyclopropane dicarboxylate (**6a**) (5.59 g, 5.30 mL, 30 mmol, 1 equiv). The resulting mixture was allowed to stir overnight (19.5 h), slowly warming to ambient temperature. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with *i*-PrOAc (2 × 60 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography ($SiO_2$, 0–20% *i*-PrOAc in heptane) to afford the triester **7aa** (8.01 g, 23.8 mmol, 79% yield) as a tan oil.

In a 60 mL scintillation vial was added triester **7aa** (2.0 g, 5.94 mmol, 1.0 equiv), $MgBr_2$ (1.66 g, 8.92 mmol, 1.5 equiv), 2-MeTHF (12 mL, 0.50 M), and $Et_3N$ (2.51 mL, 17.84 mmol, 3.0 equiv). The resulting mixture was stirred at 80 °C for 1 h. The reaction mixture was quenched with 2 M HCl (9 mL) and extracted with *i*-PrOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography ($SiO_2$, 0–20% *i*-PrOAc in heptane) to afford the β-ketoester **4a** (1.10 g, 5.04 mmol, 85% yield) as a pale tan oil.

## 7. References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2. Buchgraber, P.; Domostoj, M. M.; Scheiper, B.; Wirtz, C.; Mynott, R.; Rust, J.; Fürstner, A. *Tetrahedron* **2009**, *65*, 6519.
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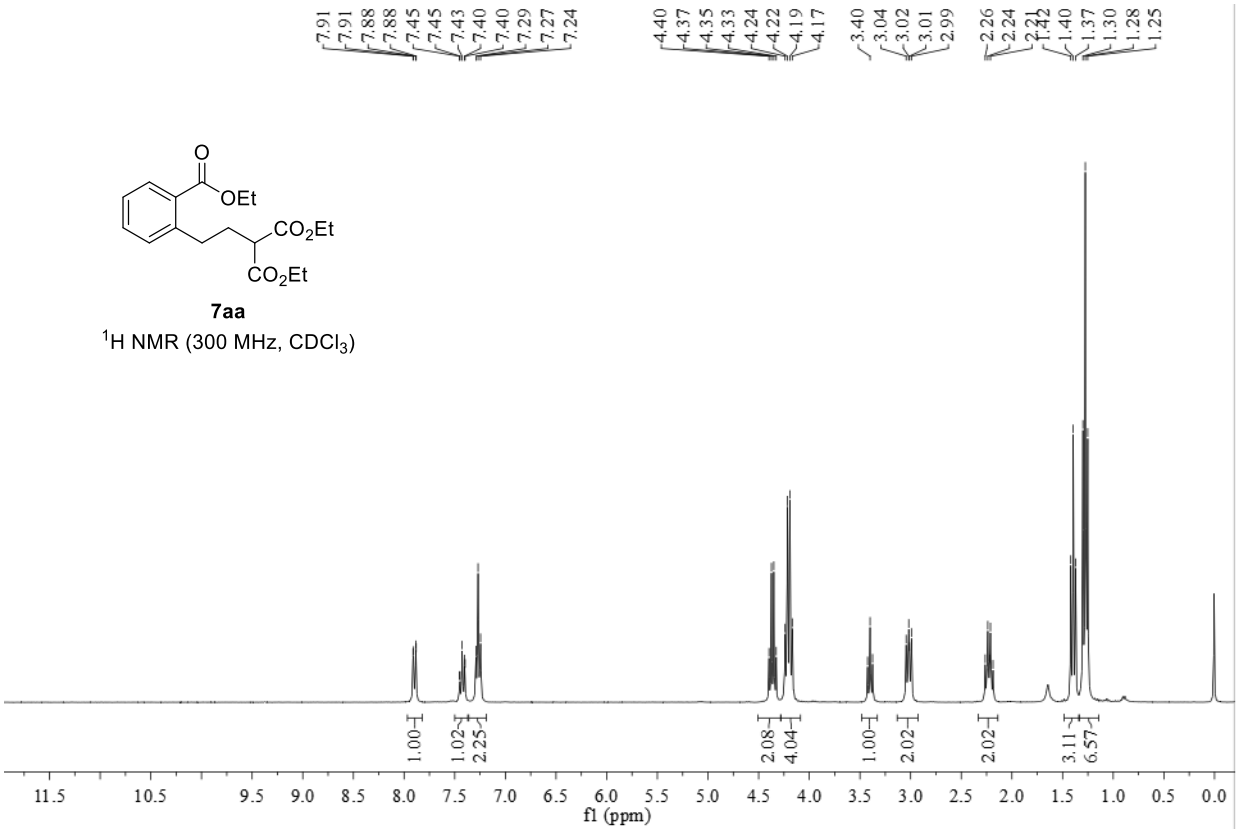
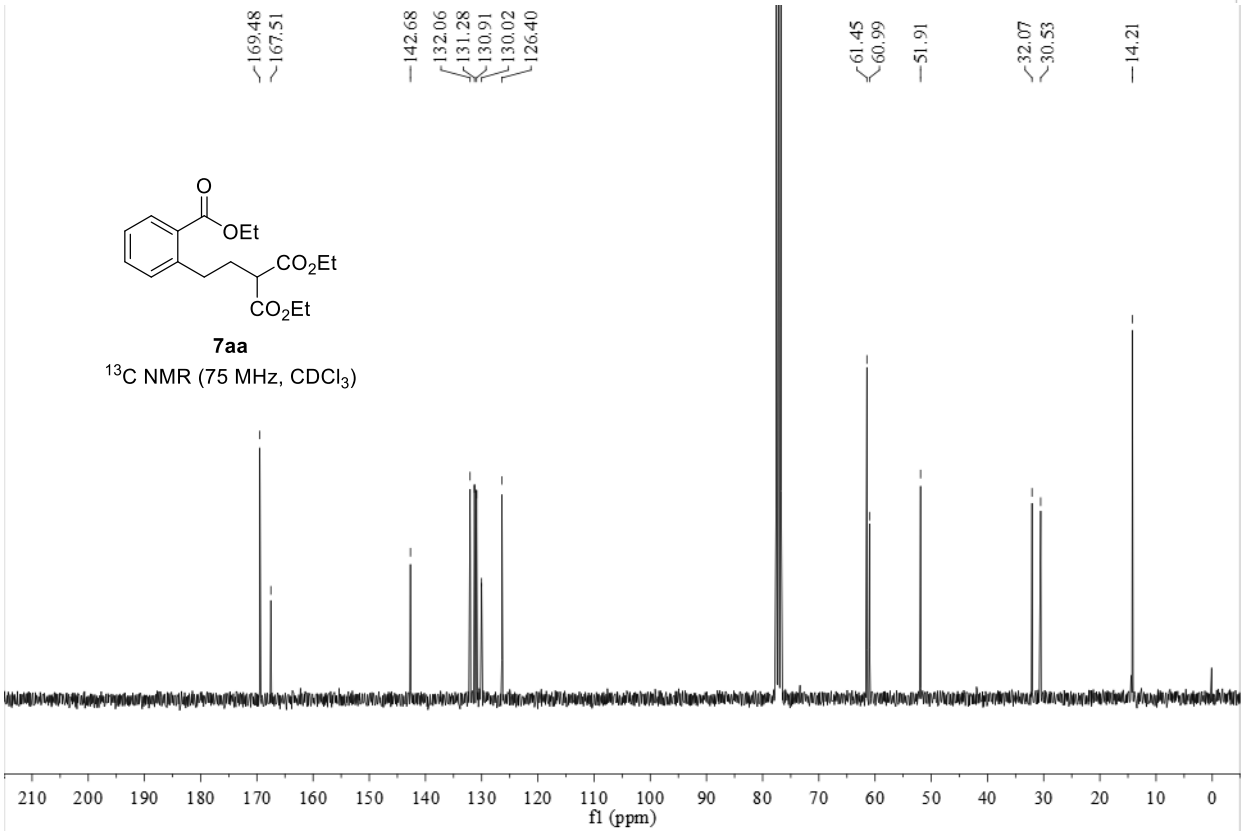
## 8. NMR Spectra




**7aa**

$^{1}$H NMR (300 MHz, $CDCl_3$)

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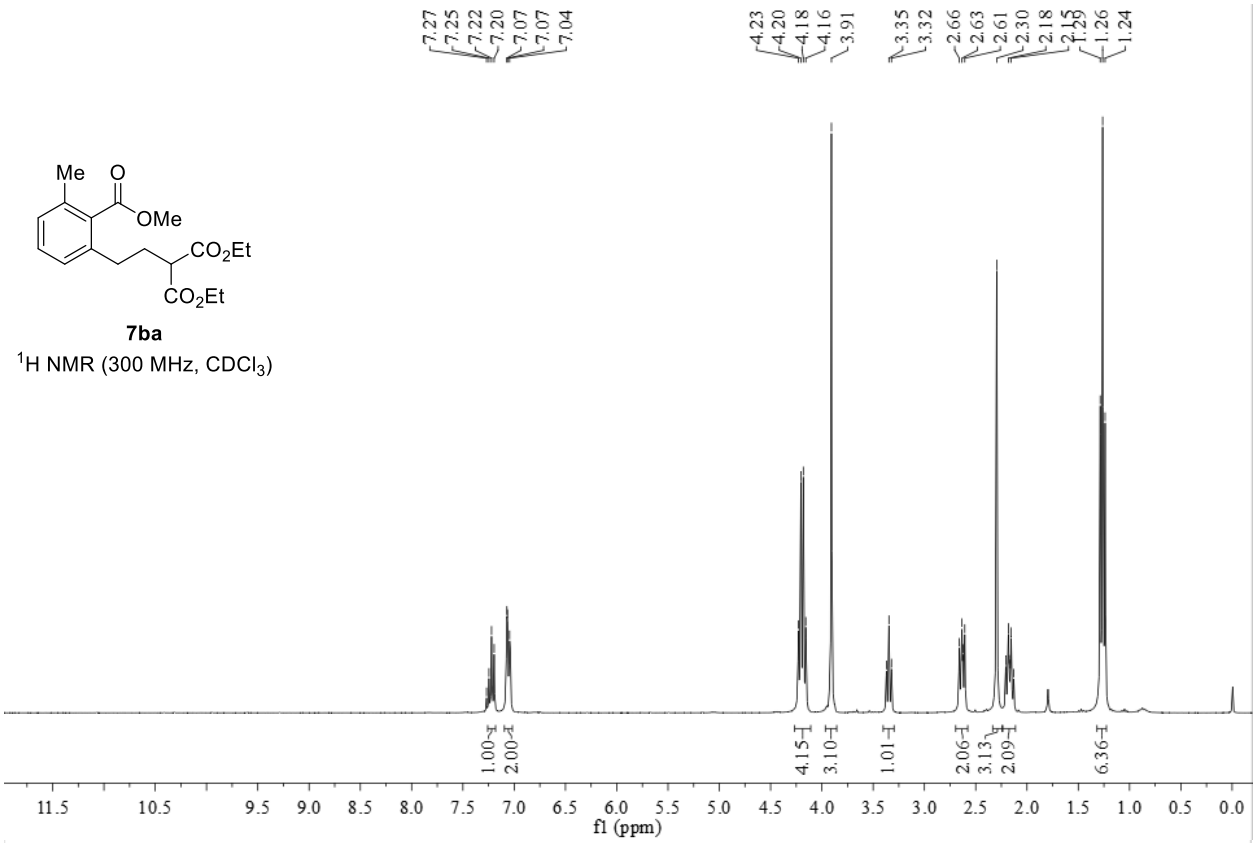


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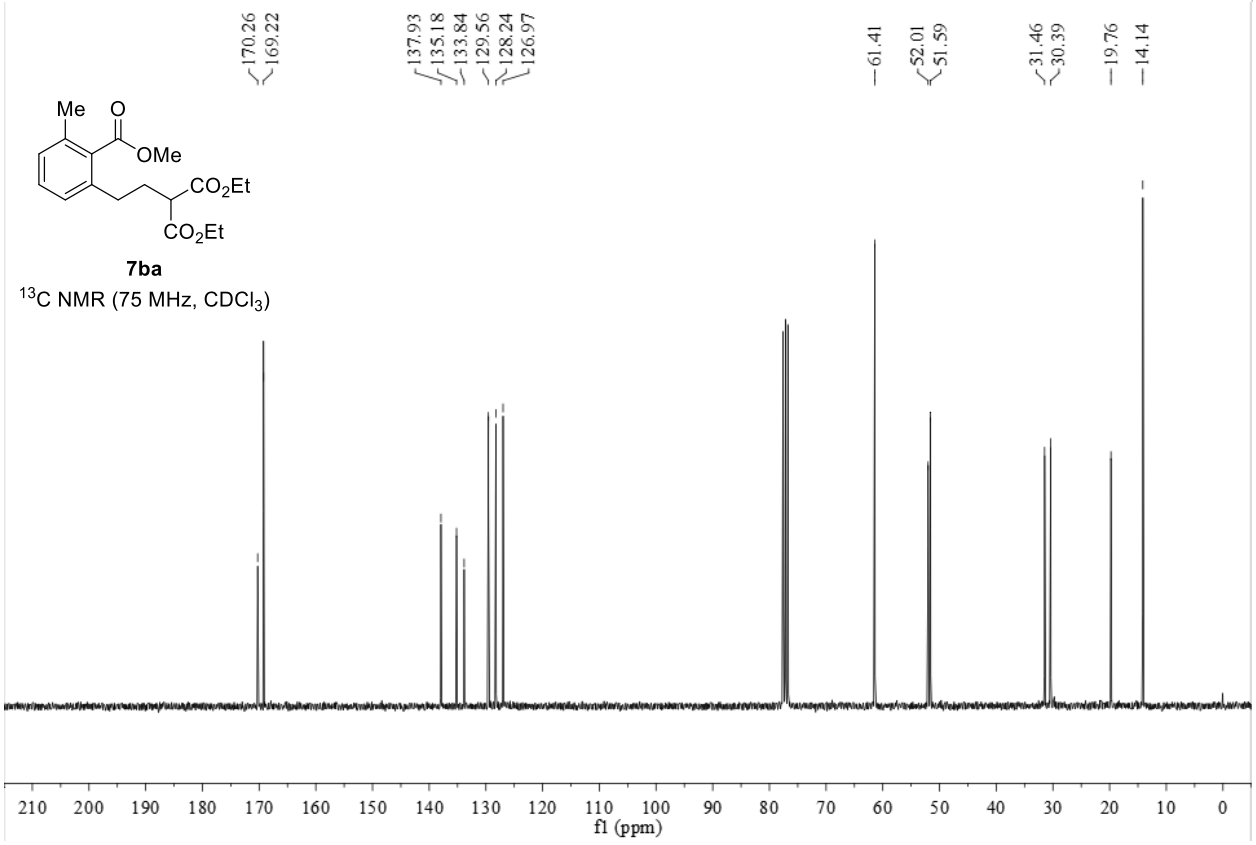


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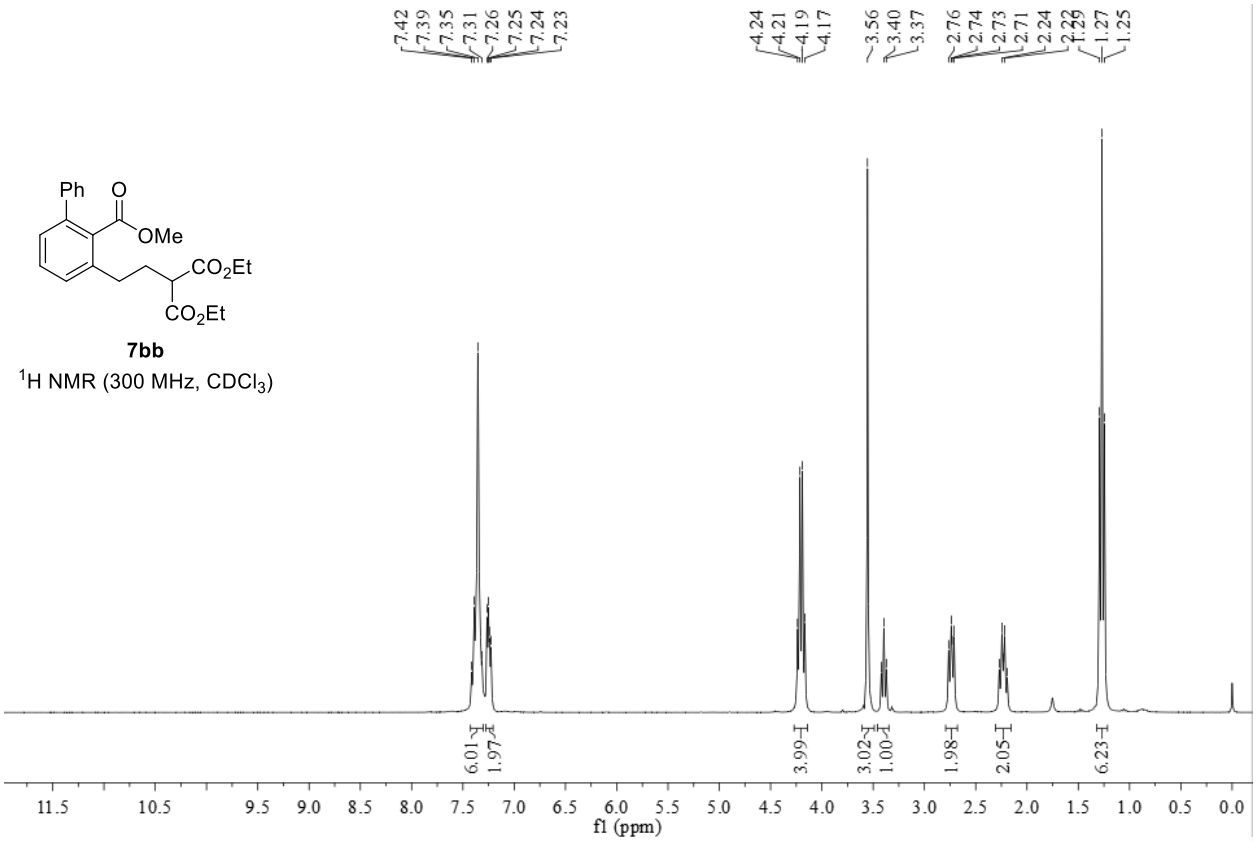


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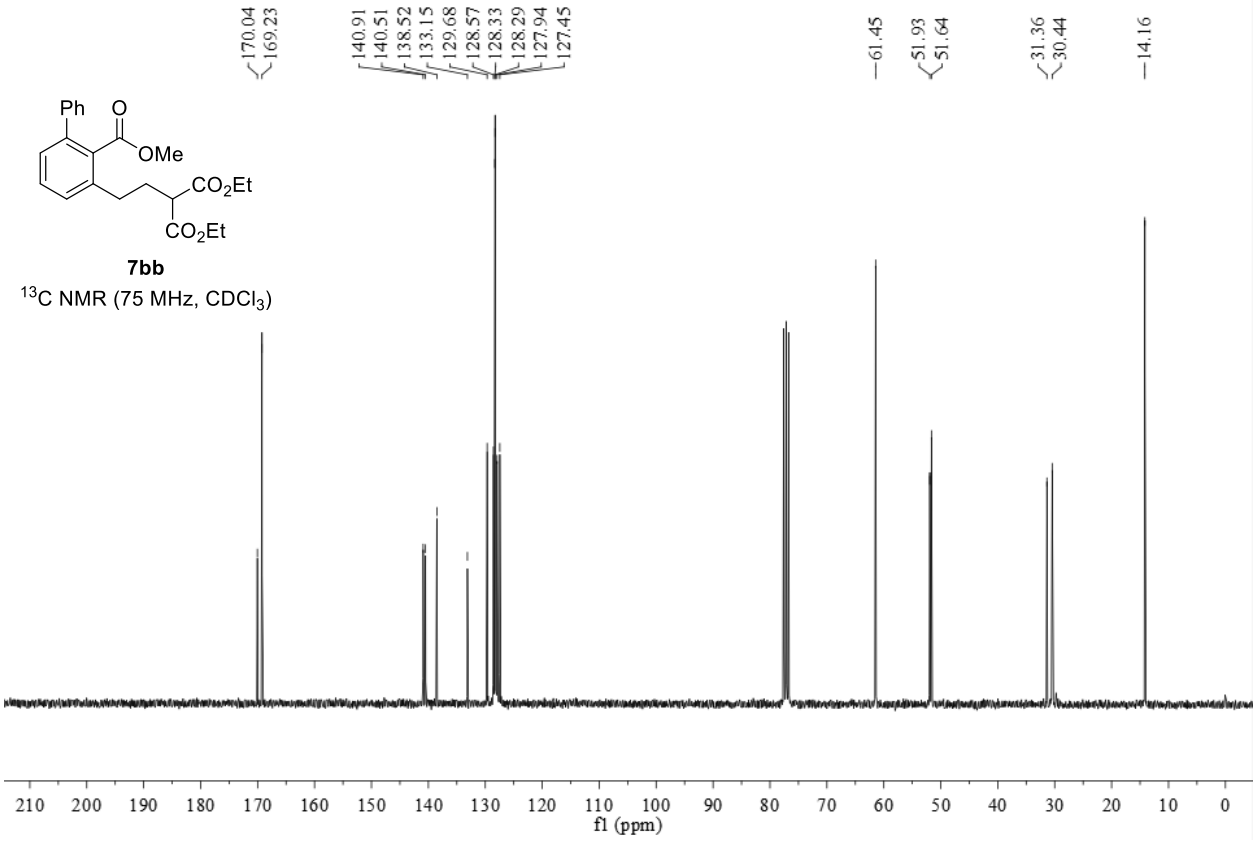


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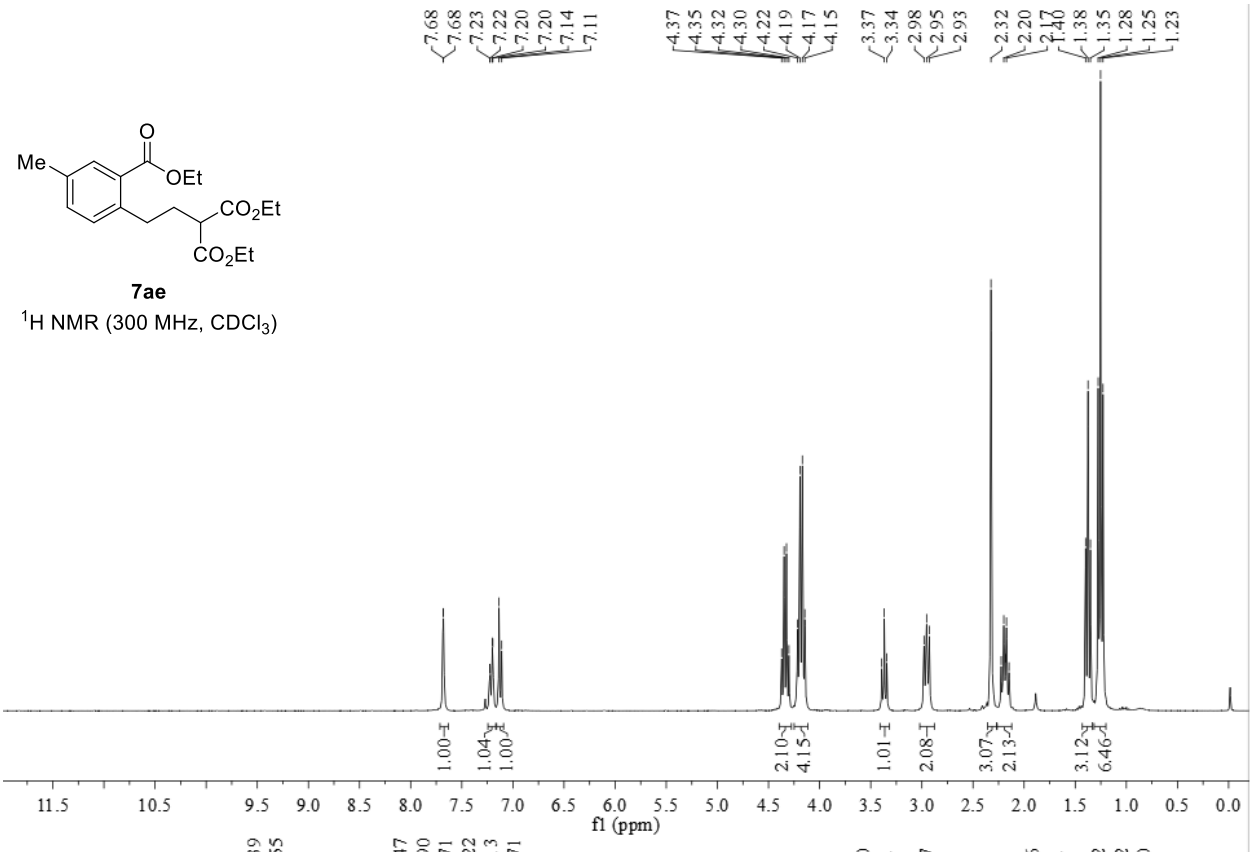
$^{13}$C NMR (75 MHz, $CDCl_3$)

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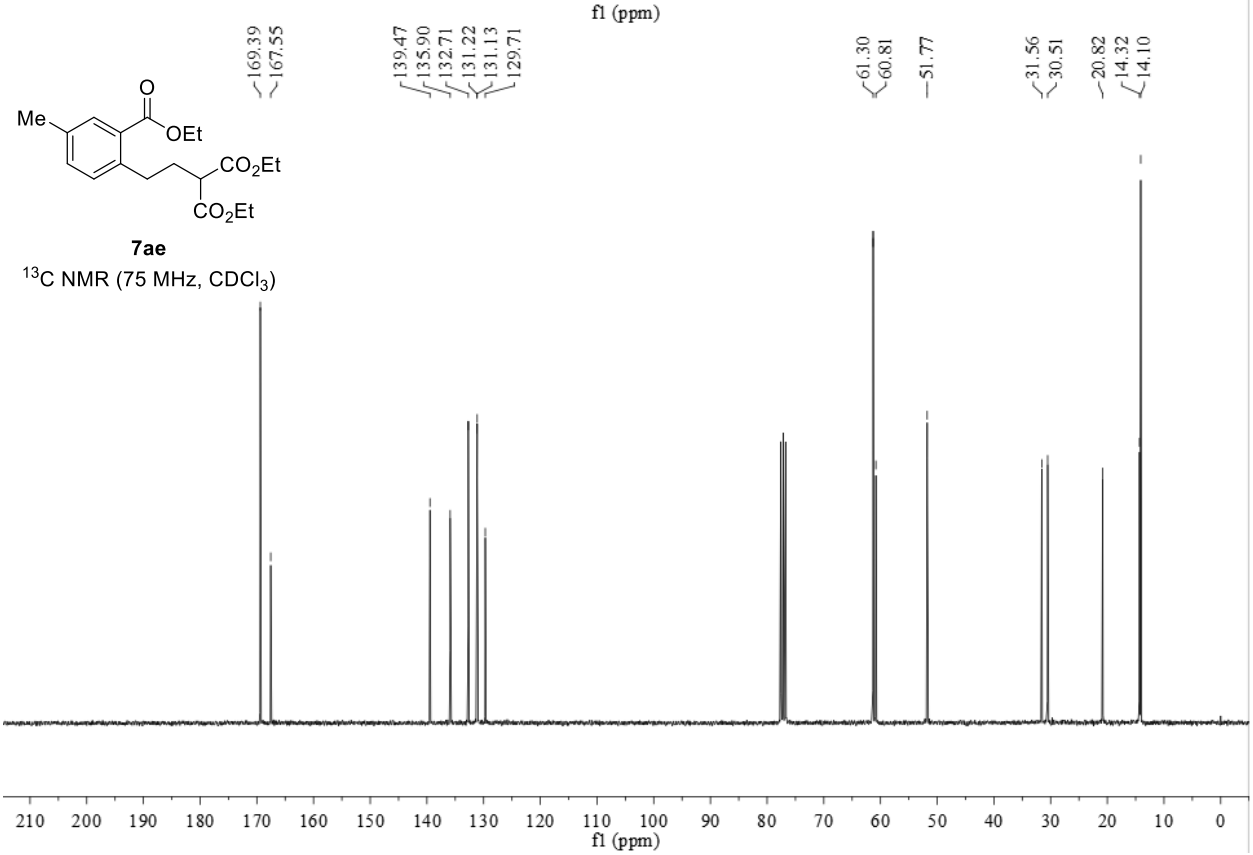


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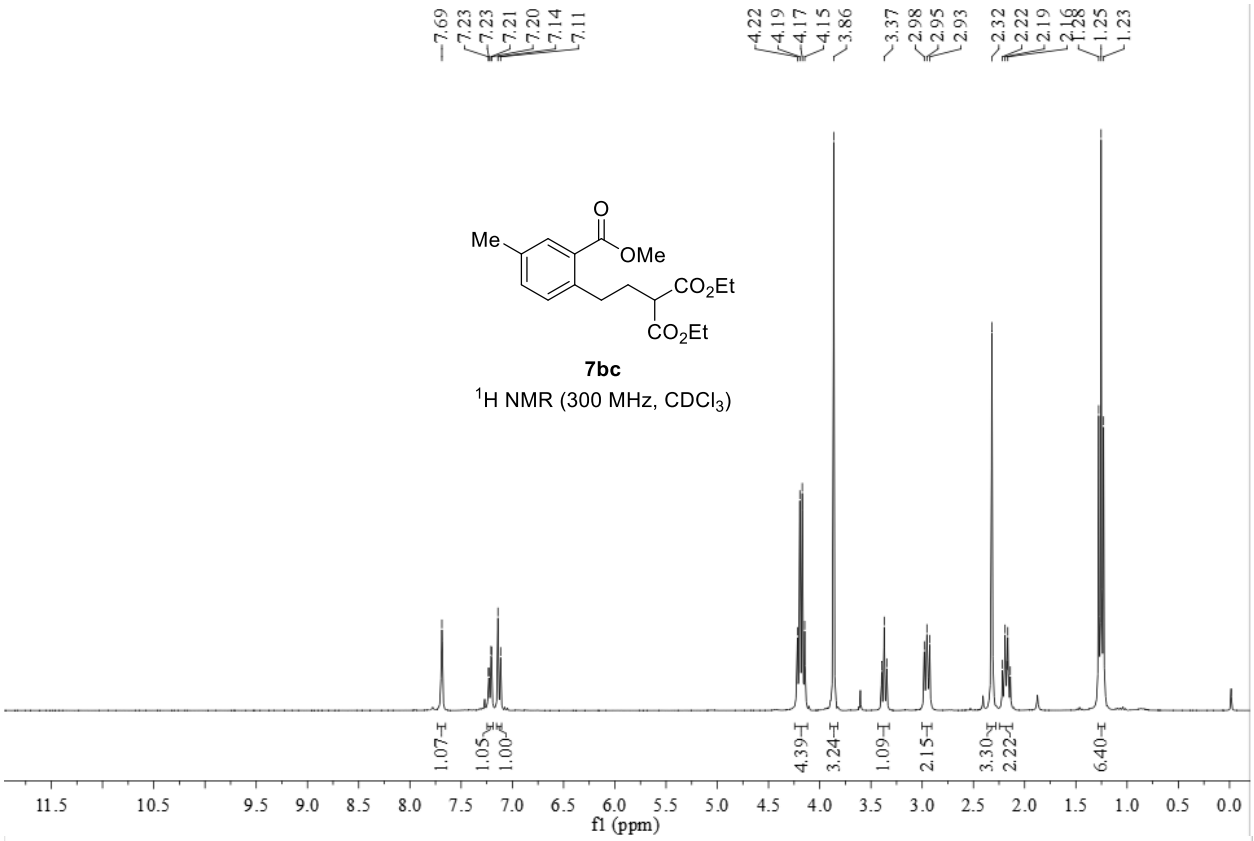


**7bc**

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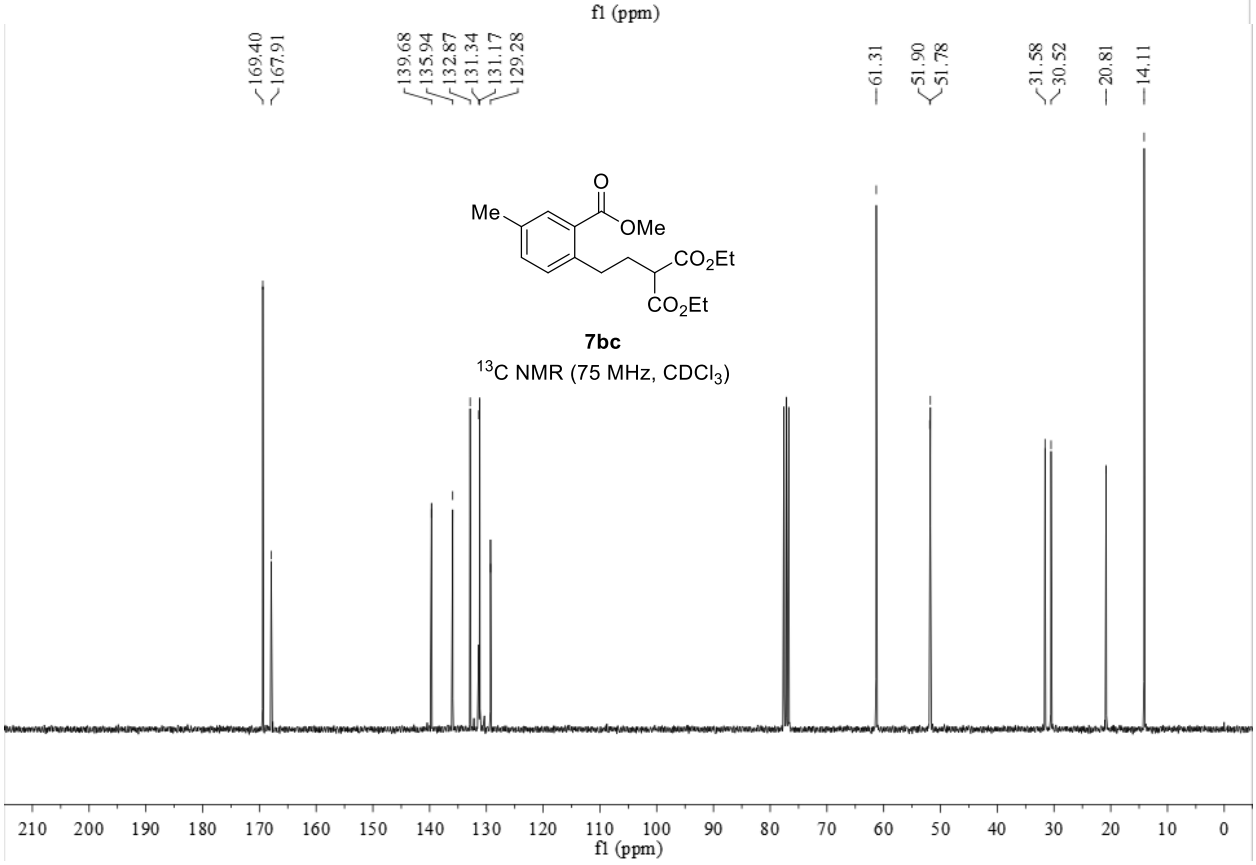
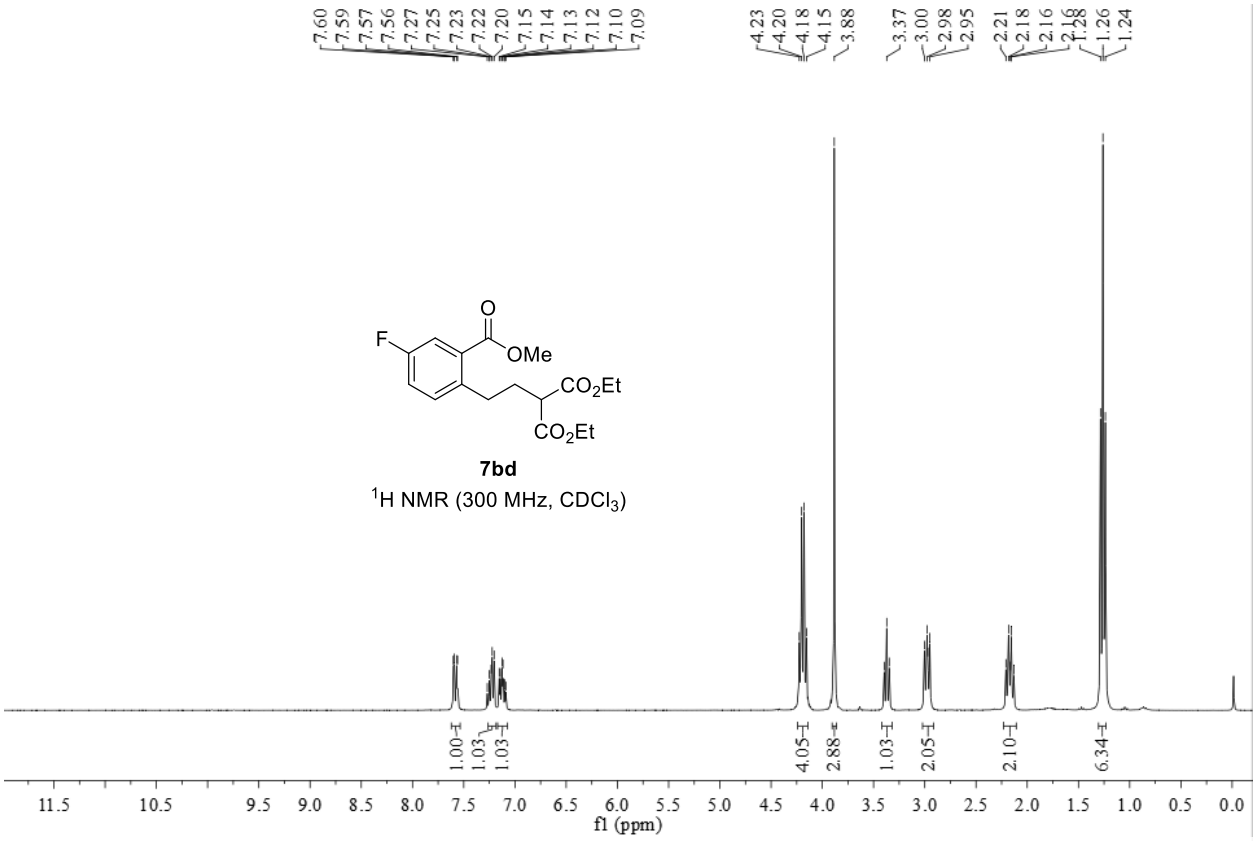



**7bc**

$^{13}$C NMR (75 MHz, $CDCl_3$)

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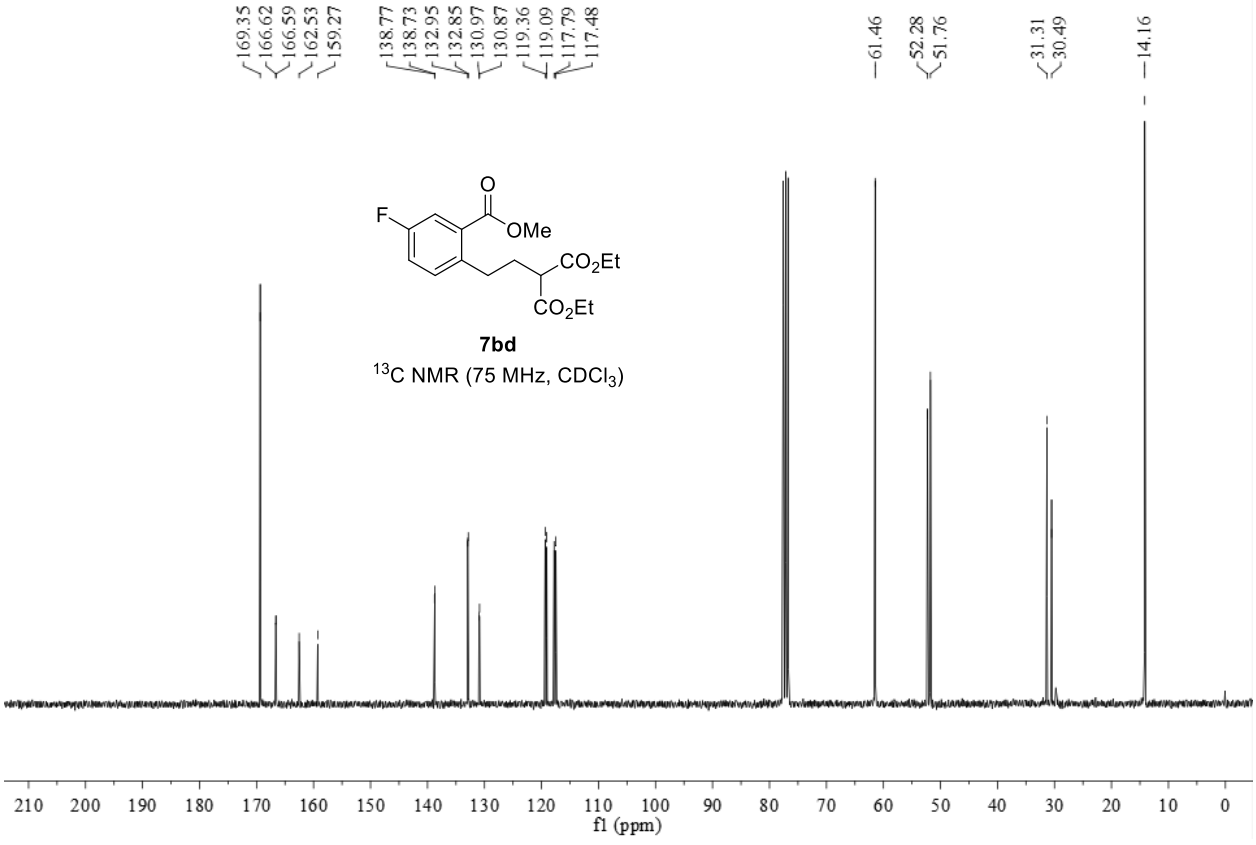
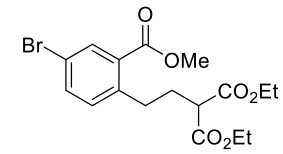



**7bd**

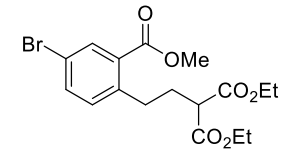
$^{13}$C NMR (75 MHz, $CDCl_3$)




**7be**

$^{1}$H NMR (300 MHz, $CDCl_3$)




**7be**

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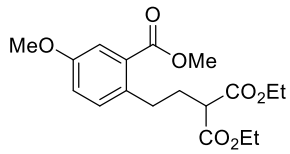


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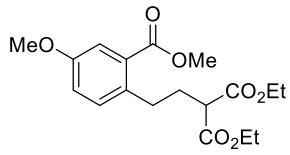


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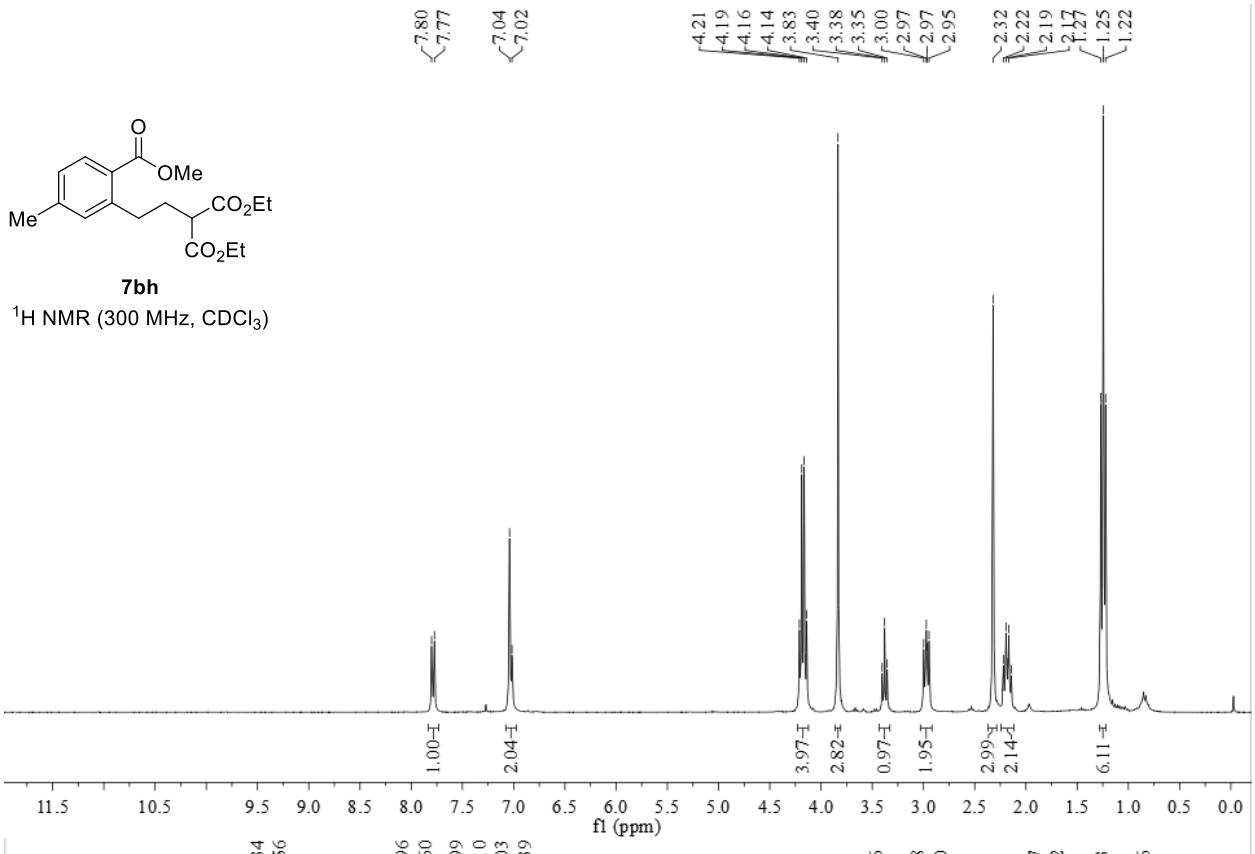


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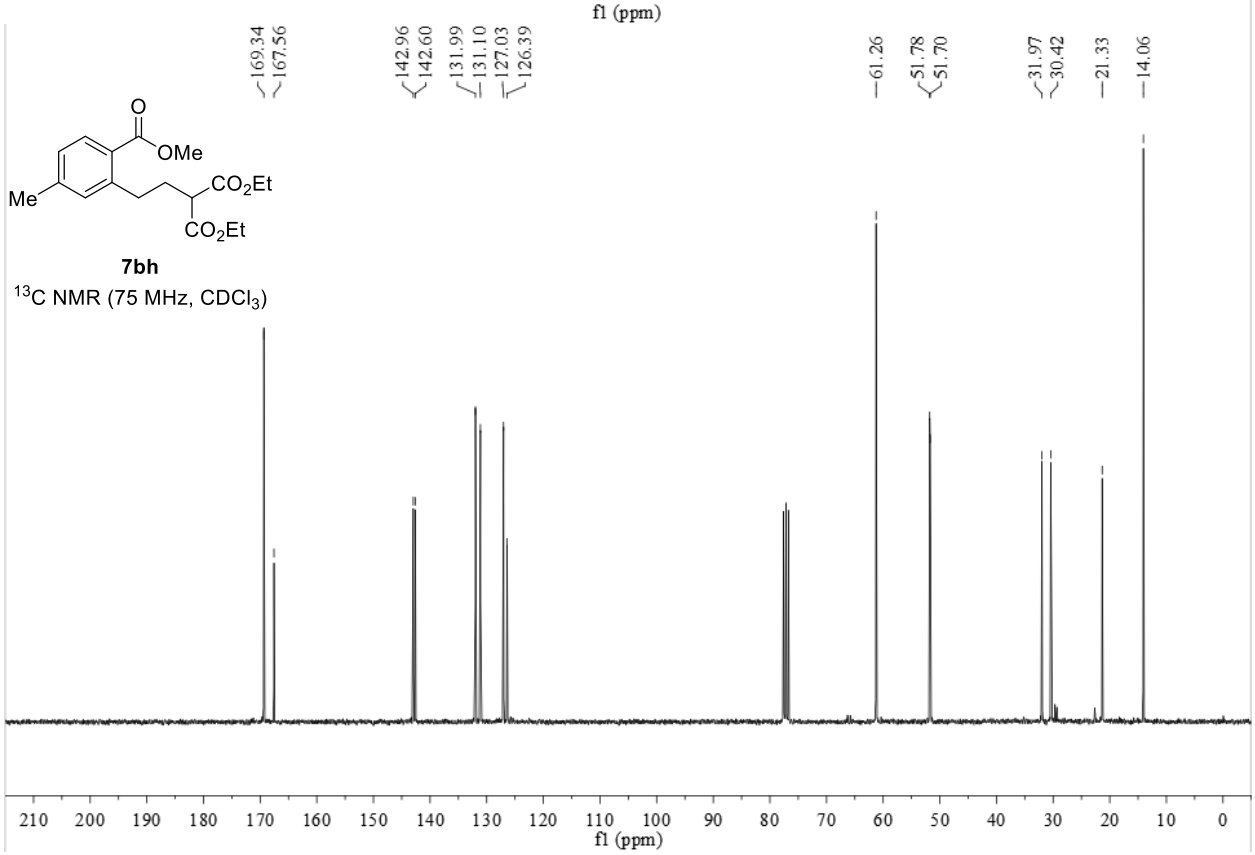


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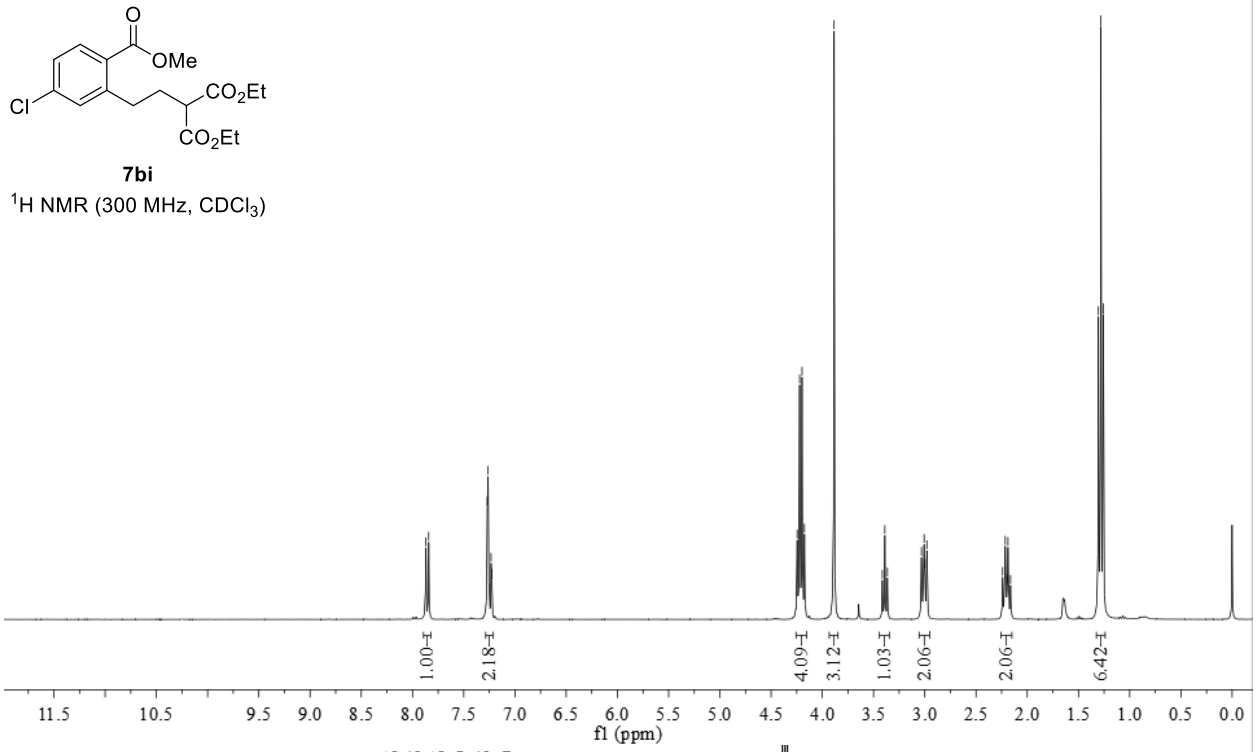
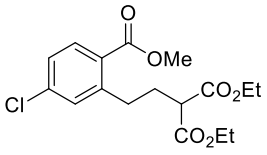



**7bi**

$^{1}$H NMR (300 MHz, $CDCl_3$)

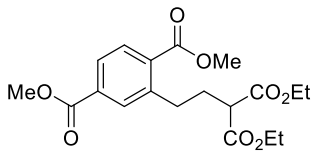






**7bi**

$^{13}$C NMR (75 MHz, $CDCl_3$)




**7bj**

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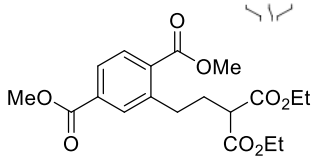


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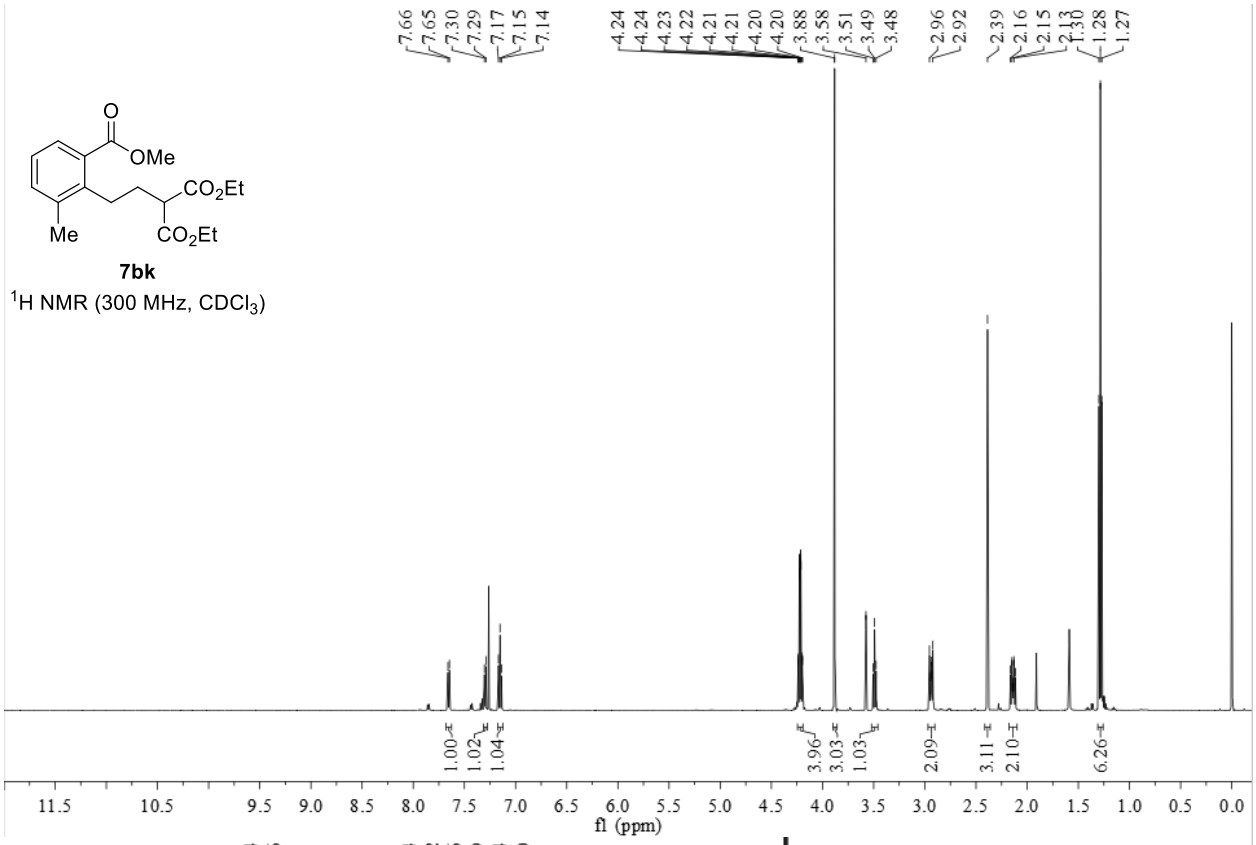
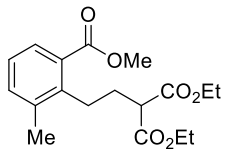



**7bk**

$^{1}$H NMR (300 MHz, $CDCl_3$)

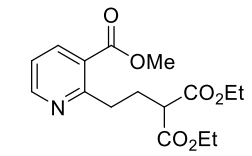






**7bk**

$^{13}$C NMR (75 MHz, $CDCl_3$)




**7bl**

$^{1}$H NMR (300 MHz, $CDCl_3$)

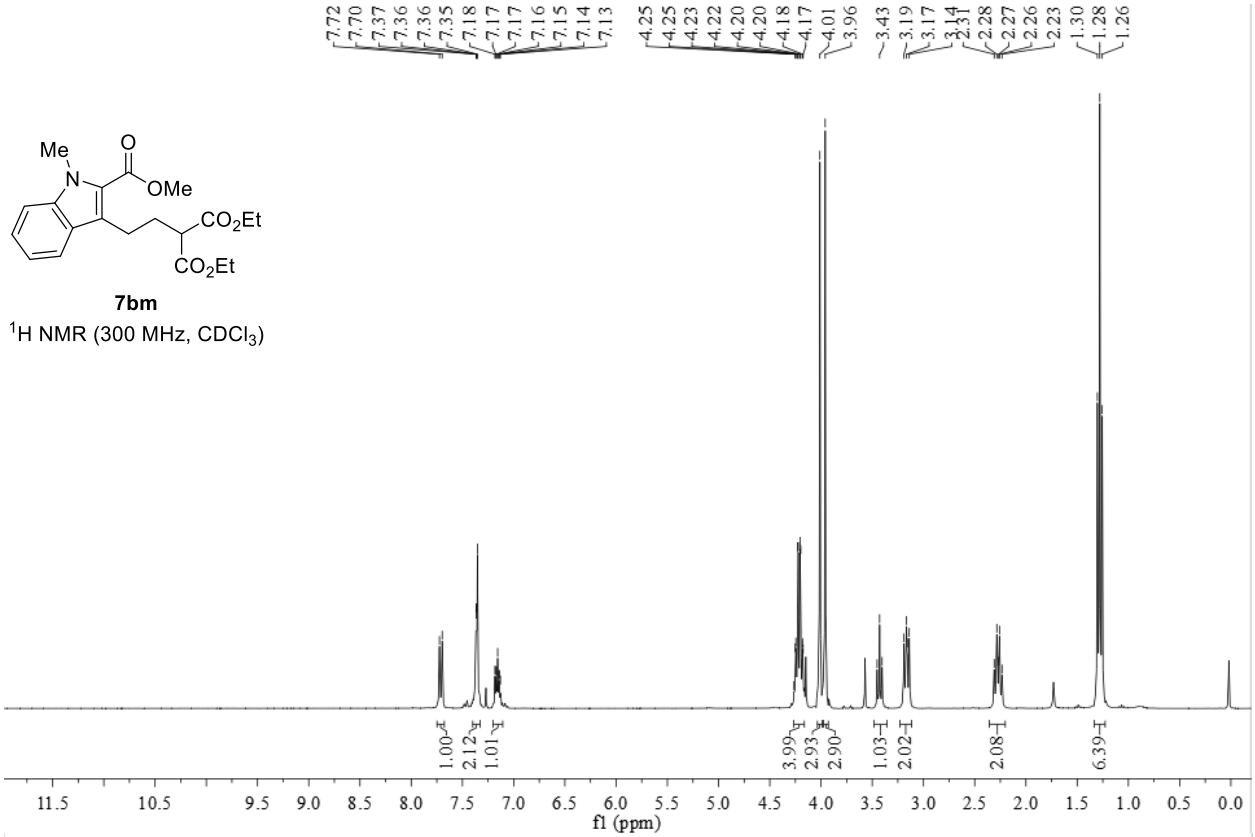






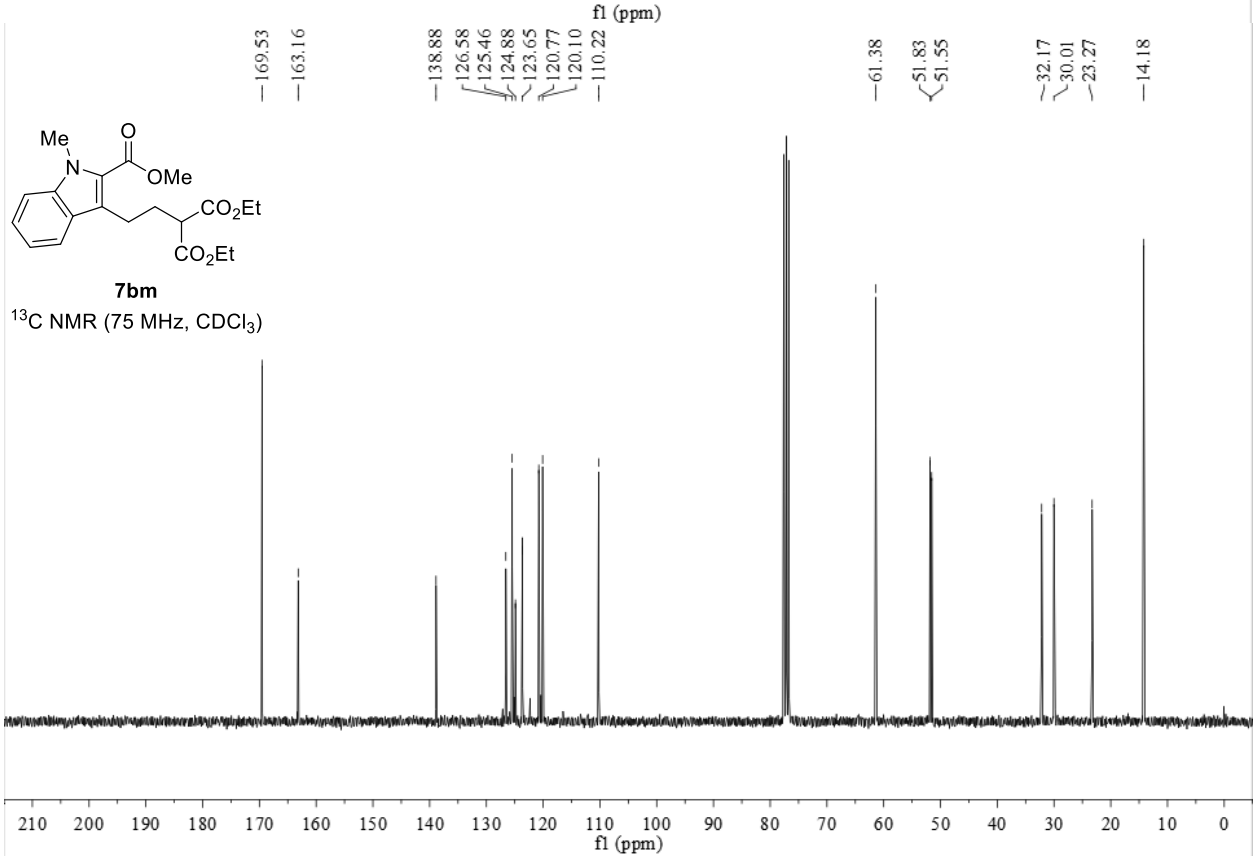
**7bl**

$^{13}$C NMR (75 MHz, $CDCl_3$)




**7bm**

$^{1}$H NMR (300 MHz, $CDCl_3$)




**7bm**

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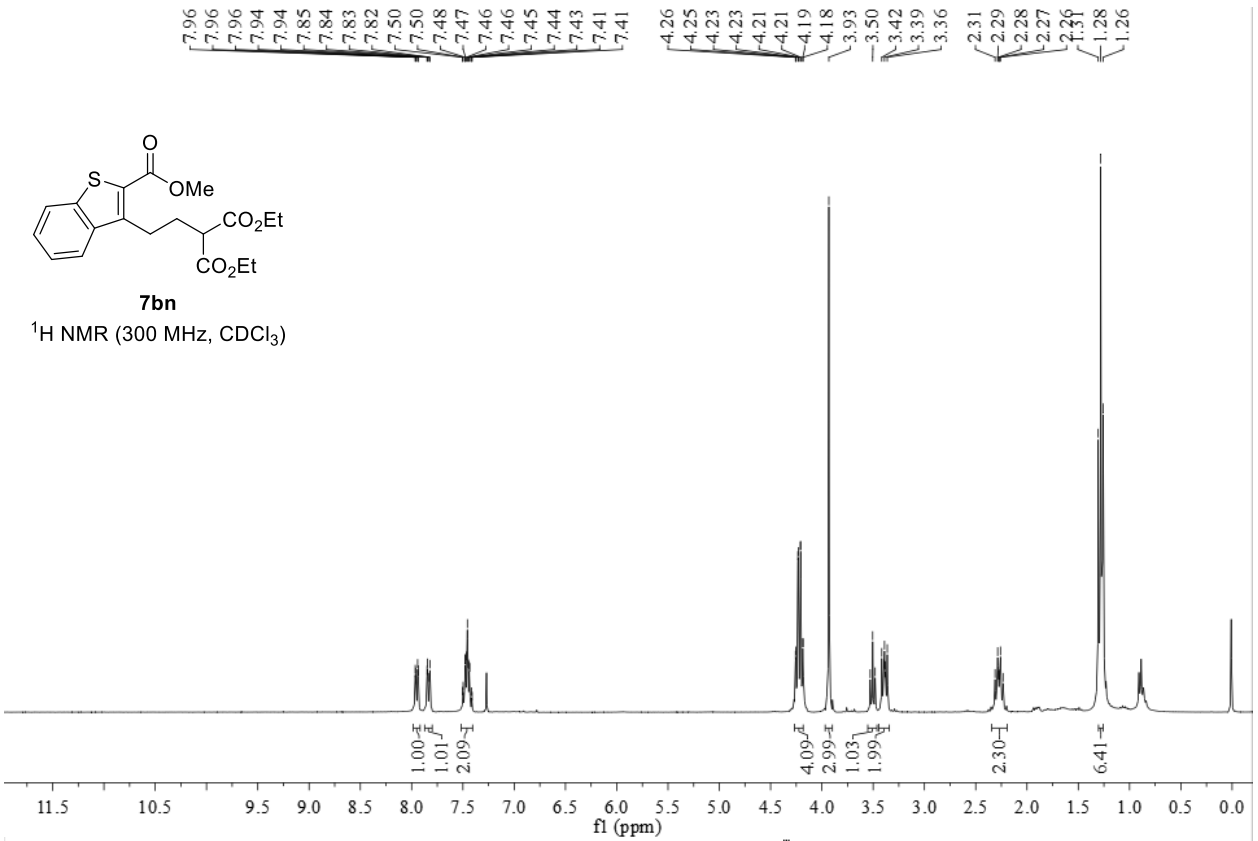


**7bn**

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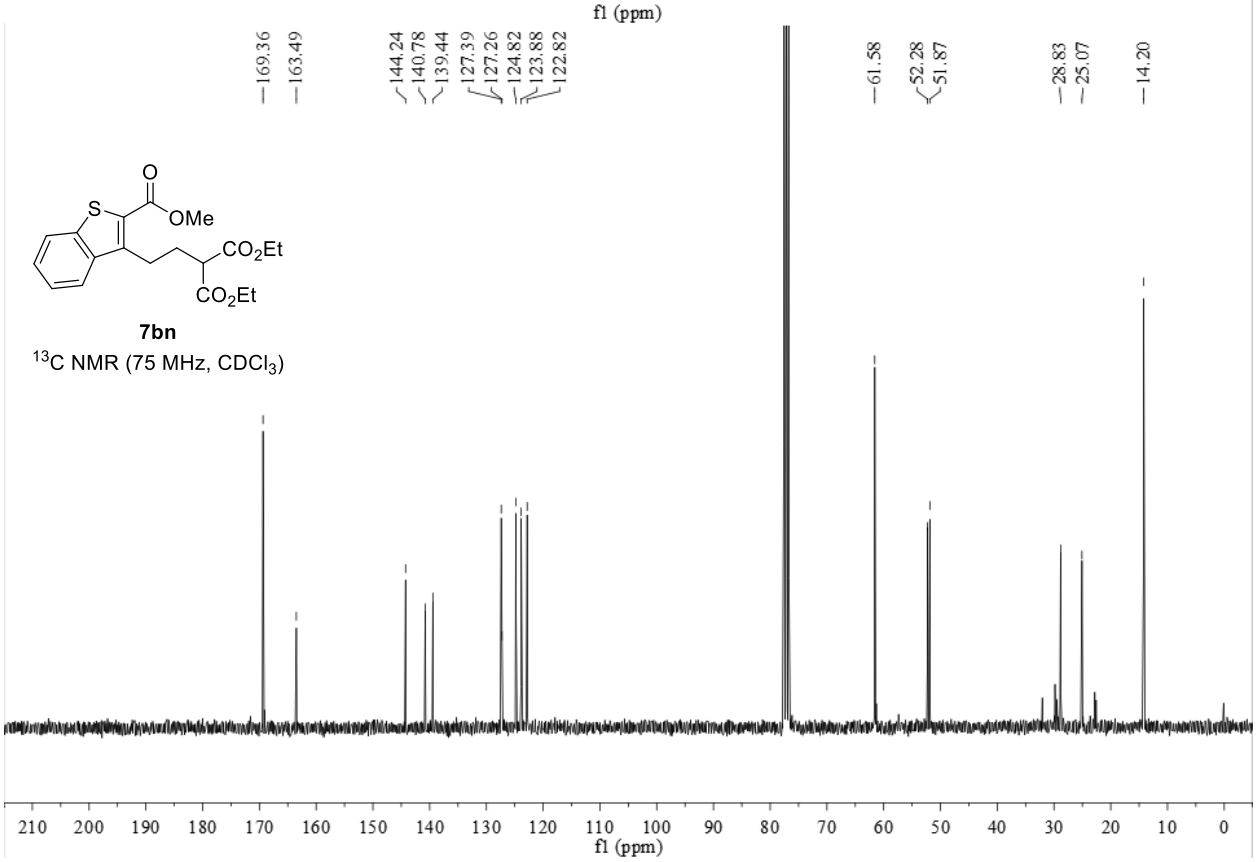


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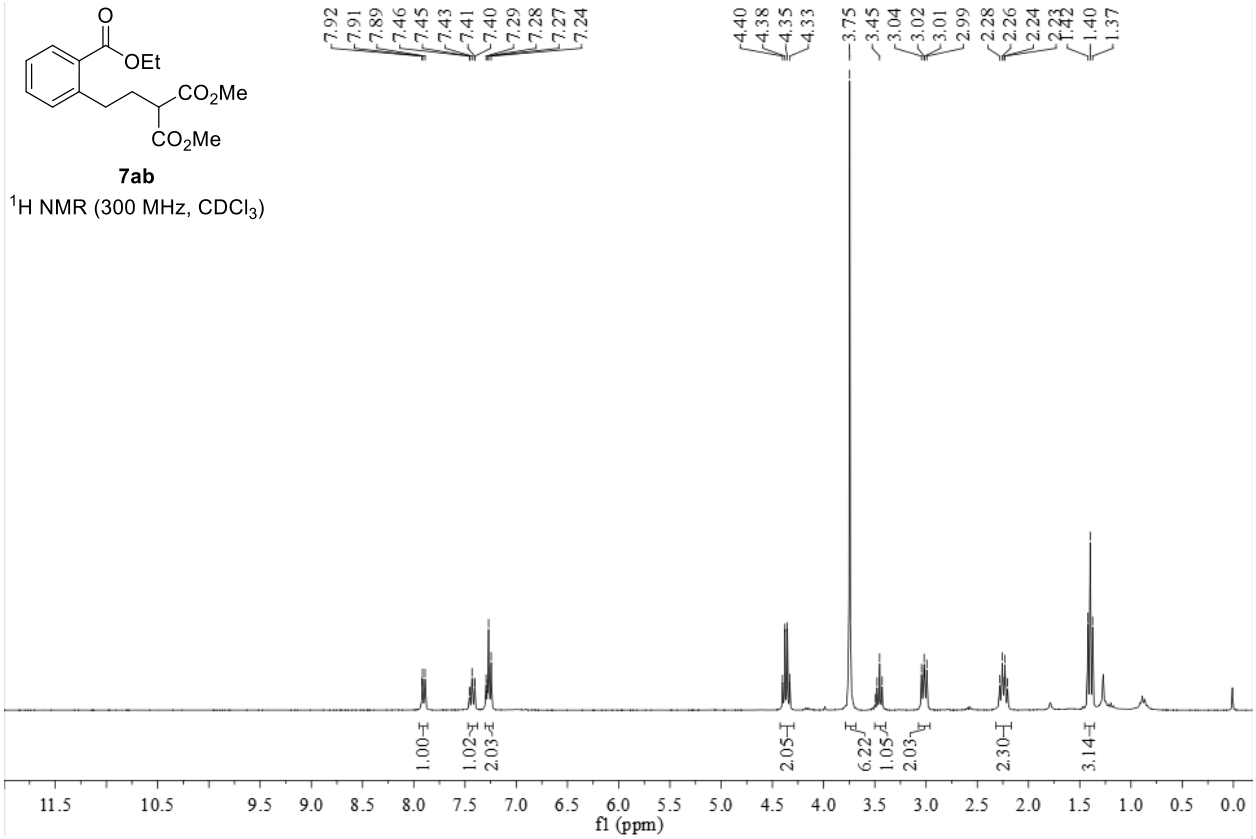


**7ab**

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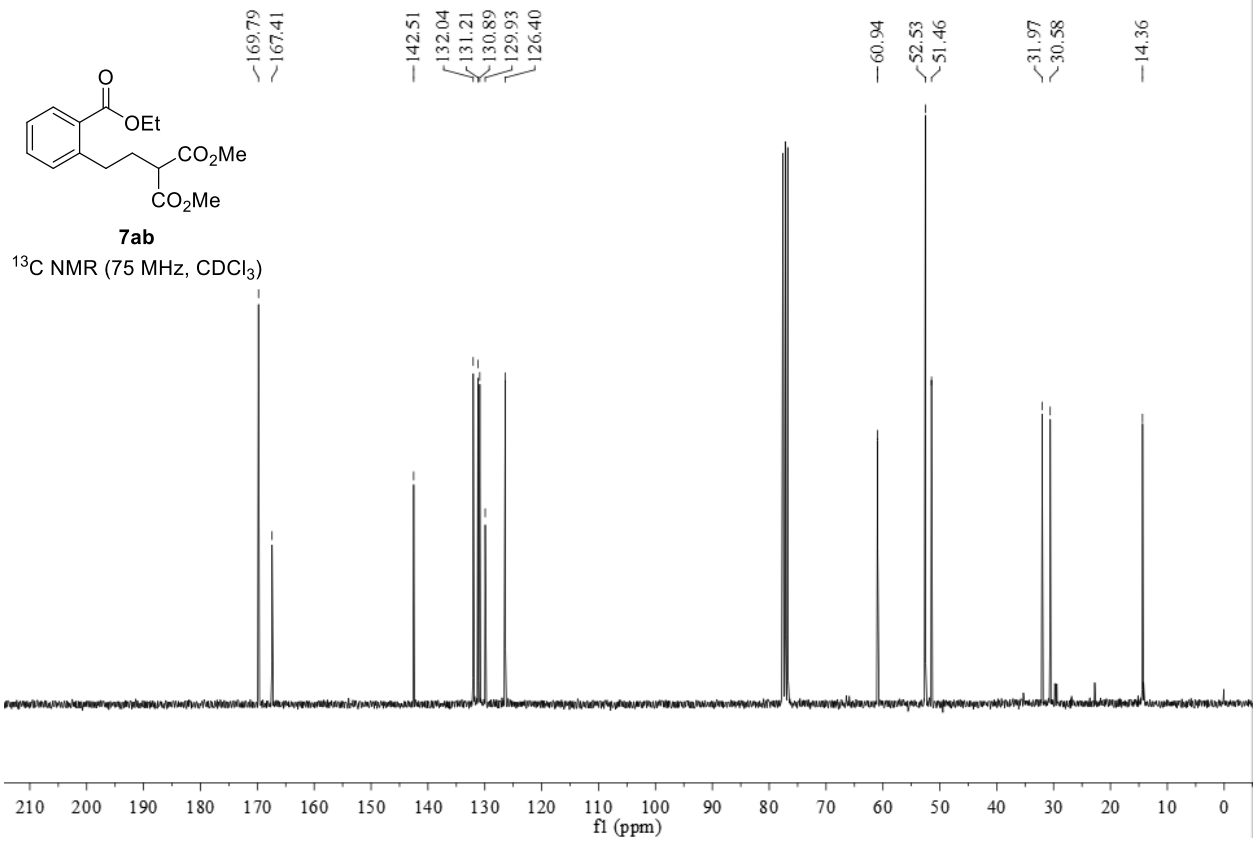
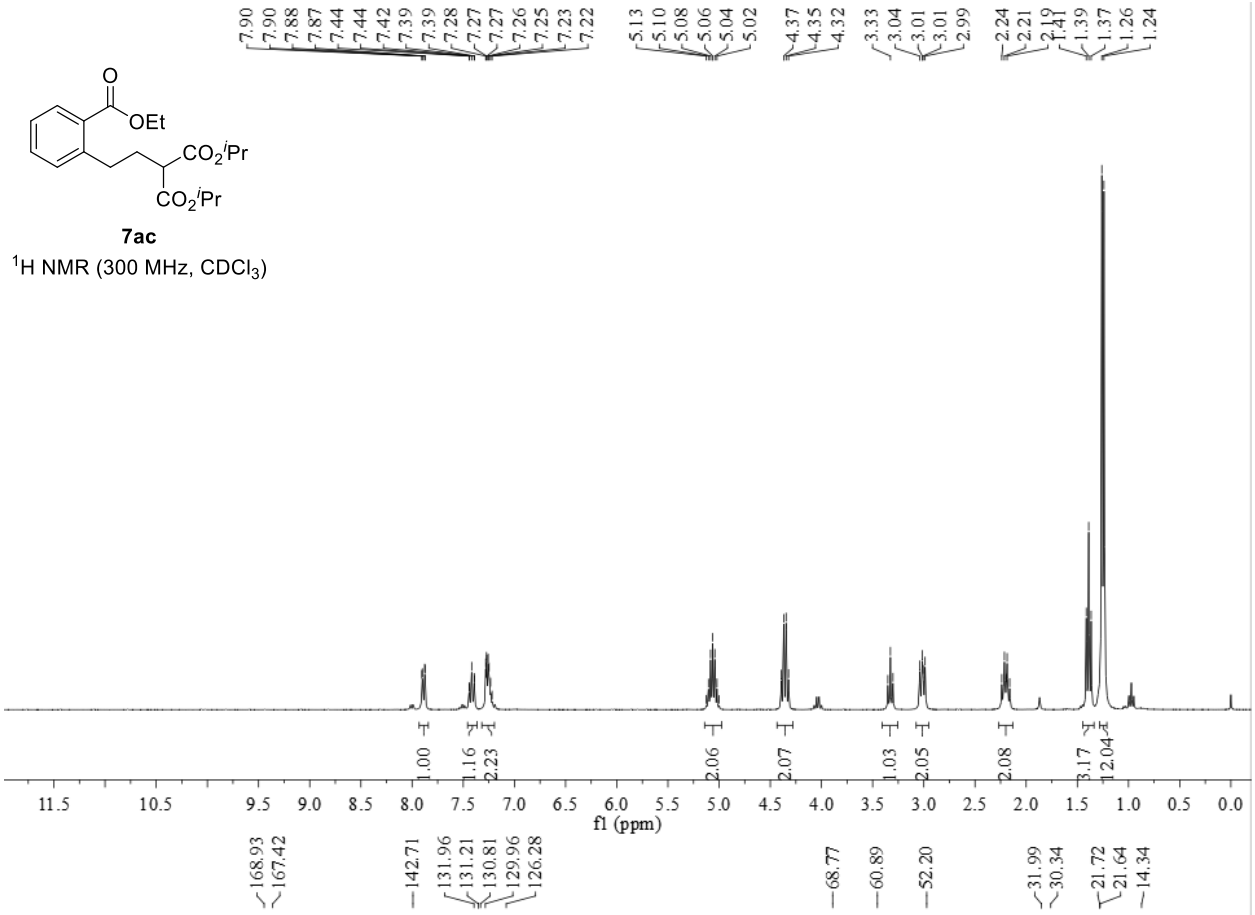



**7ab**

$^{13}$C NMR (75 MHz, $CDCl_3$)




**7ac**

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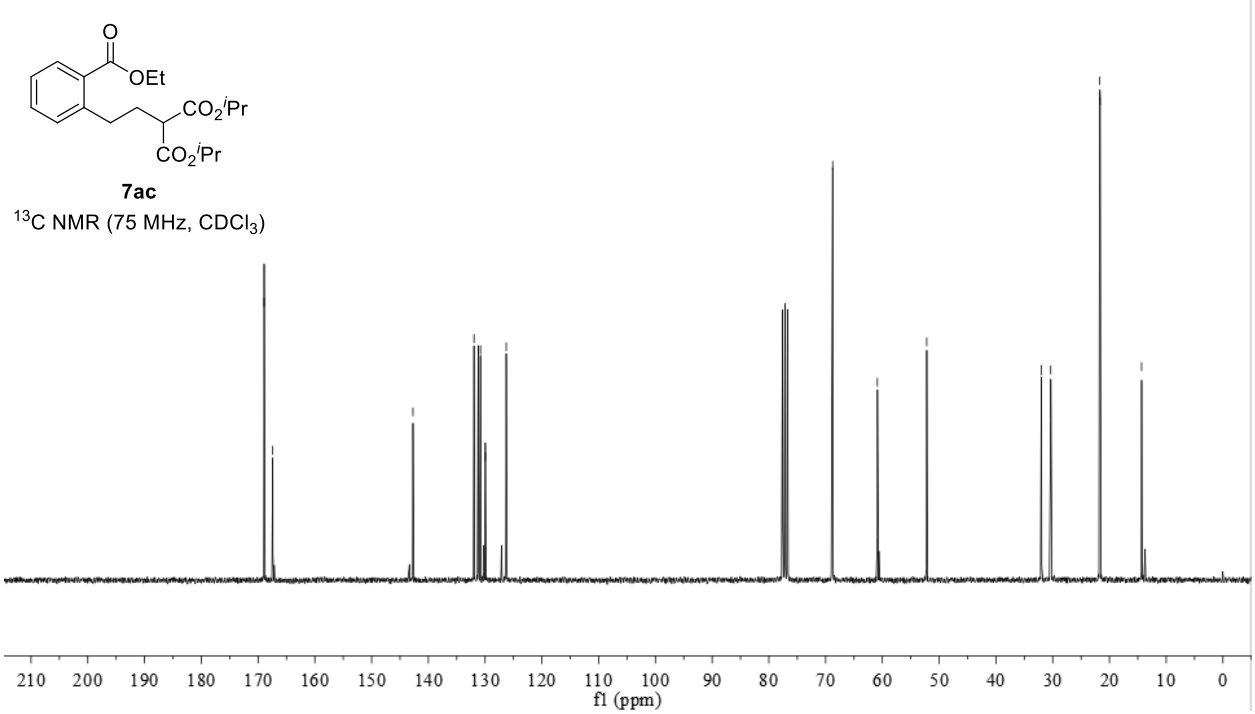


**7ac**

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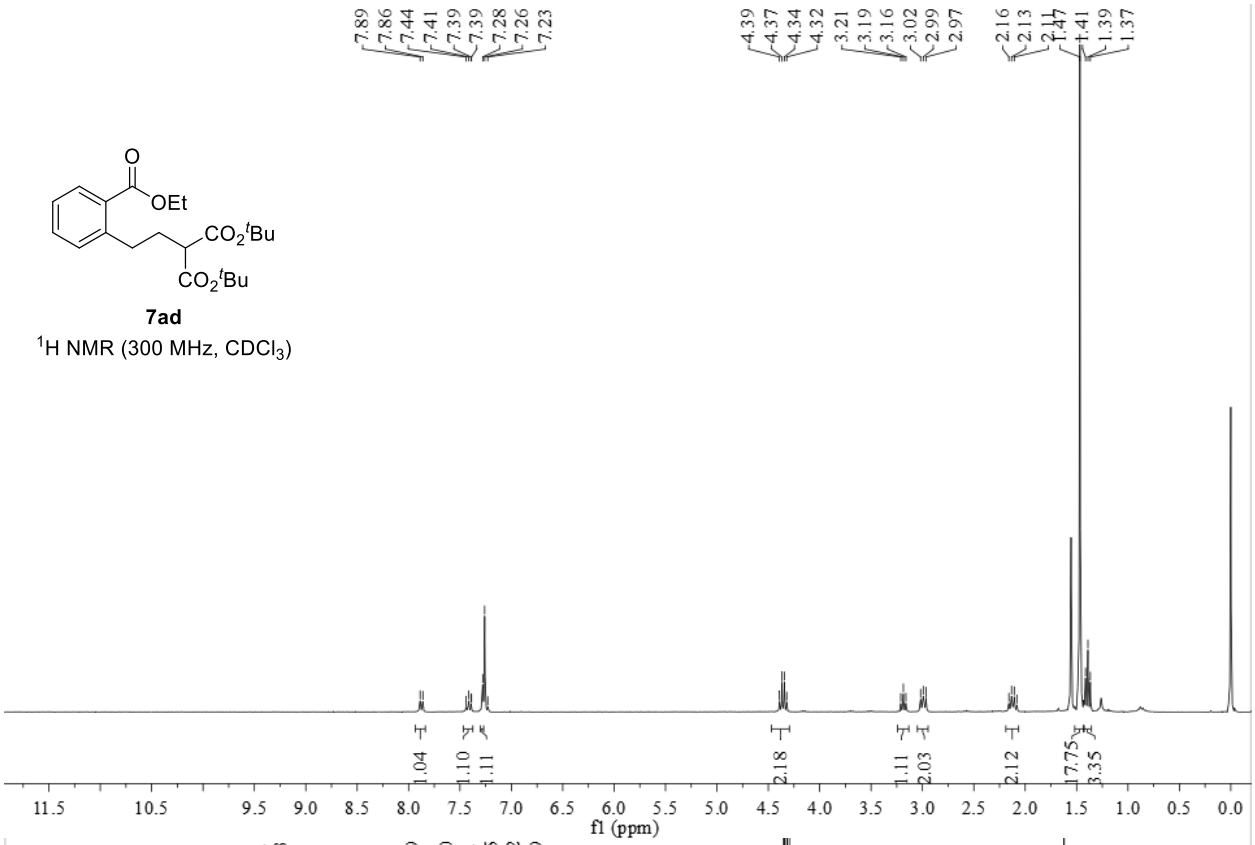
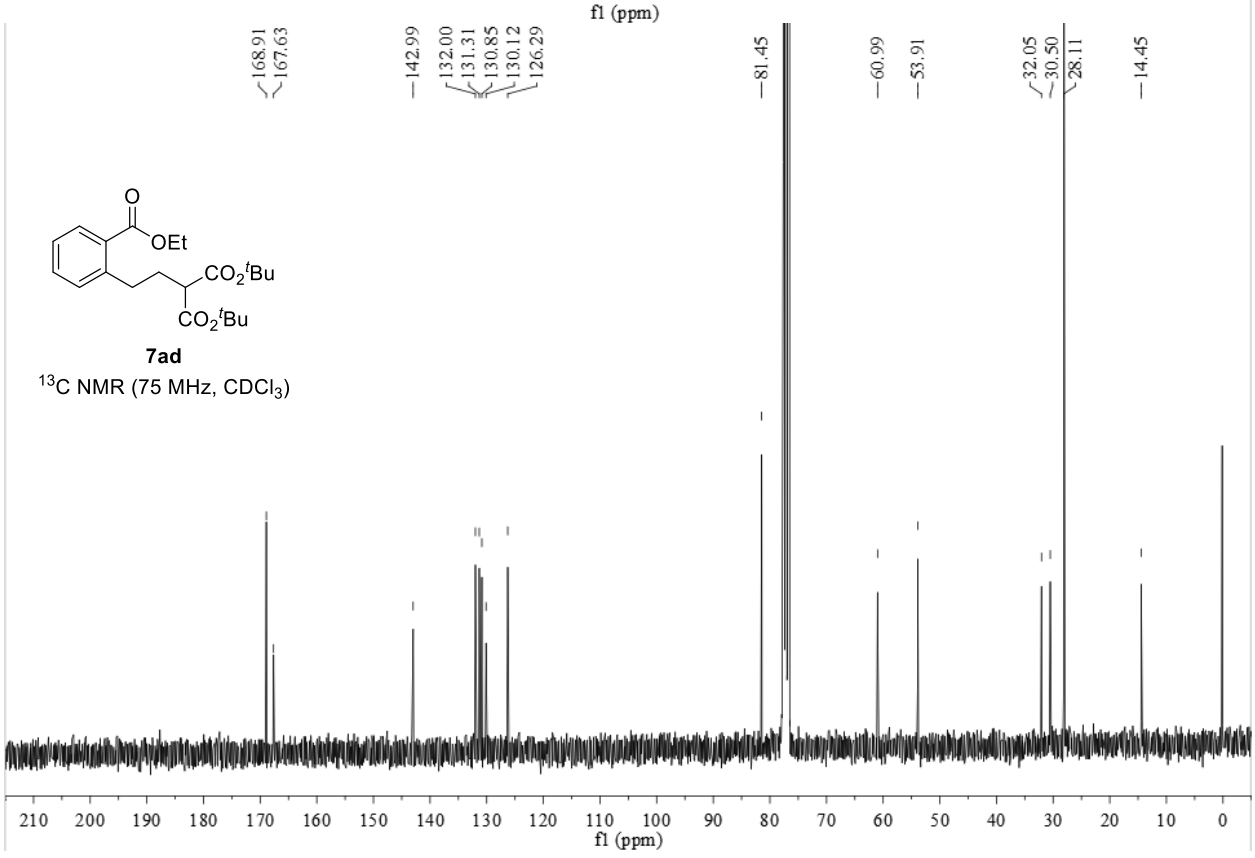


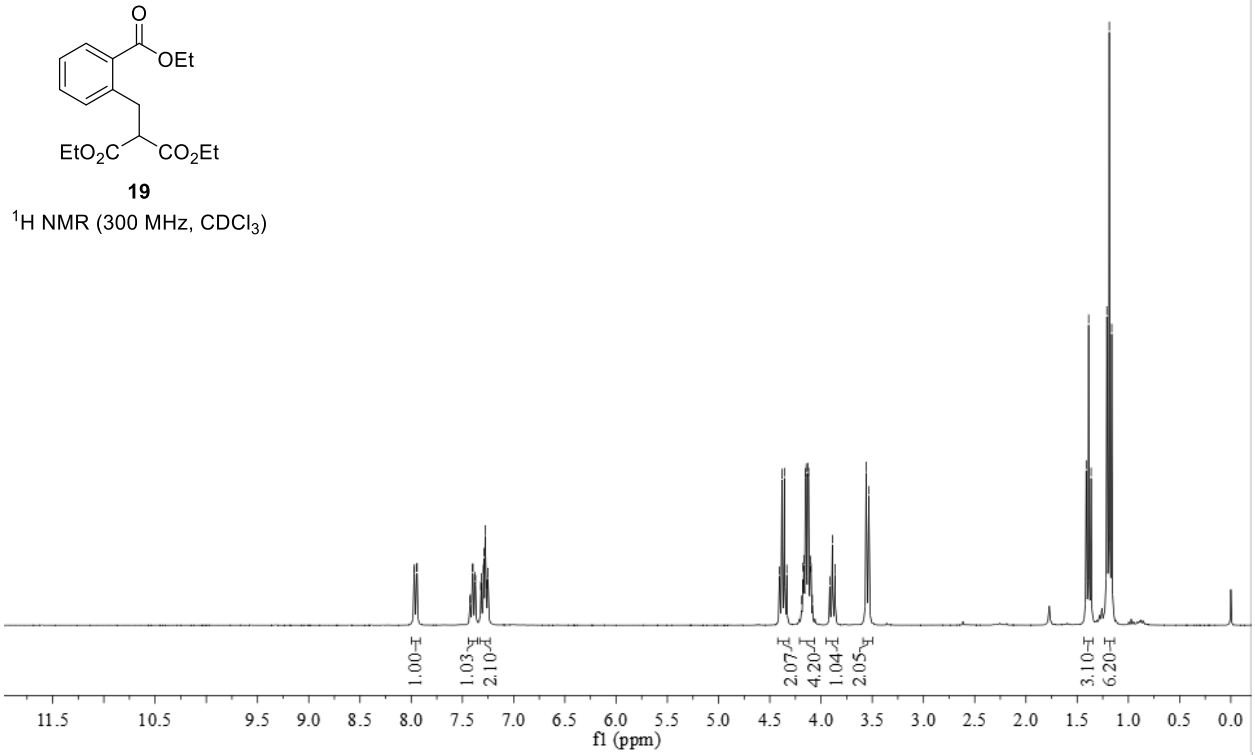

**7ad**

$^{1}$H NMR (300 MHz, $CDCl_3$)




**7ad**

$^{13}$C NMR (75 MHz, $CDCl_3$)

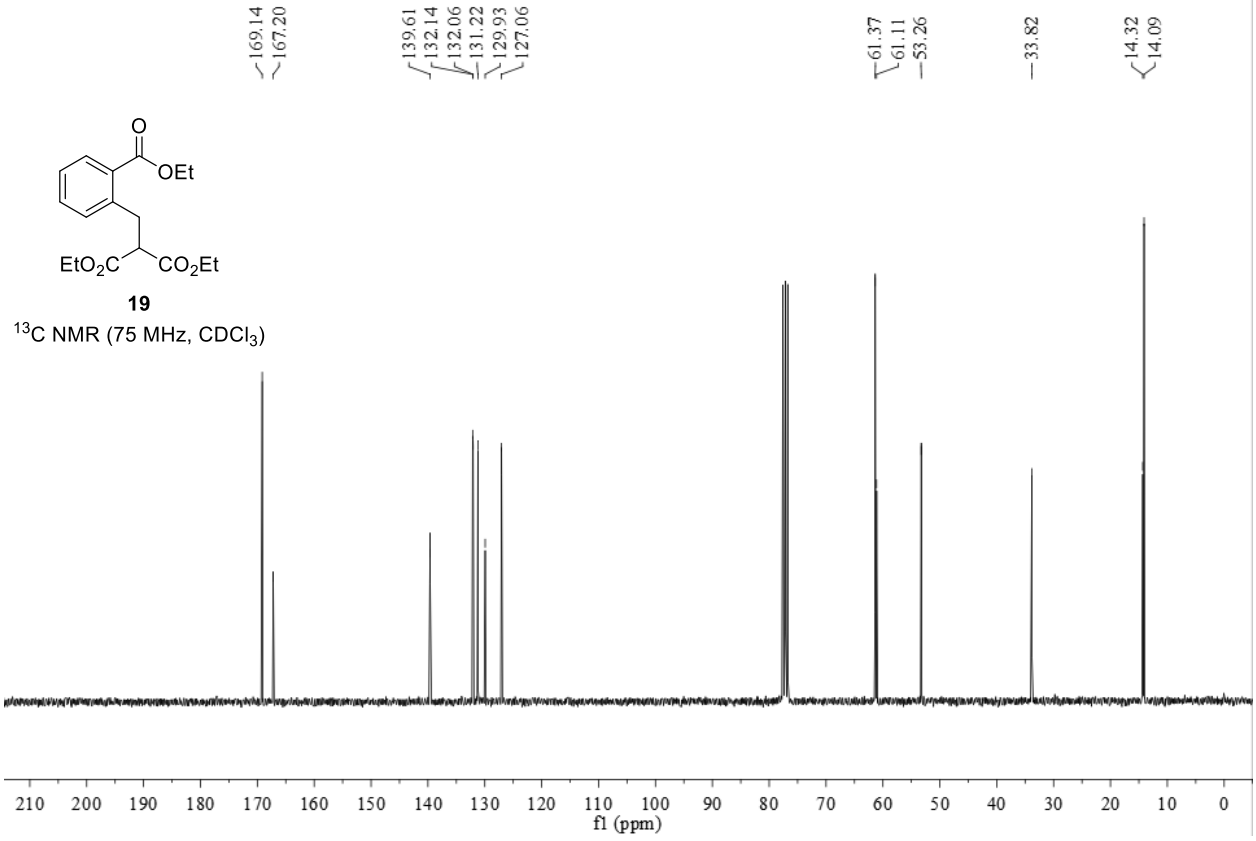






**19**

$^{1}$H NMR (300 MHz, $CDCl_3$)

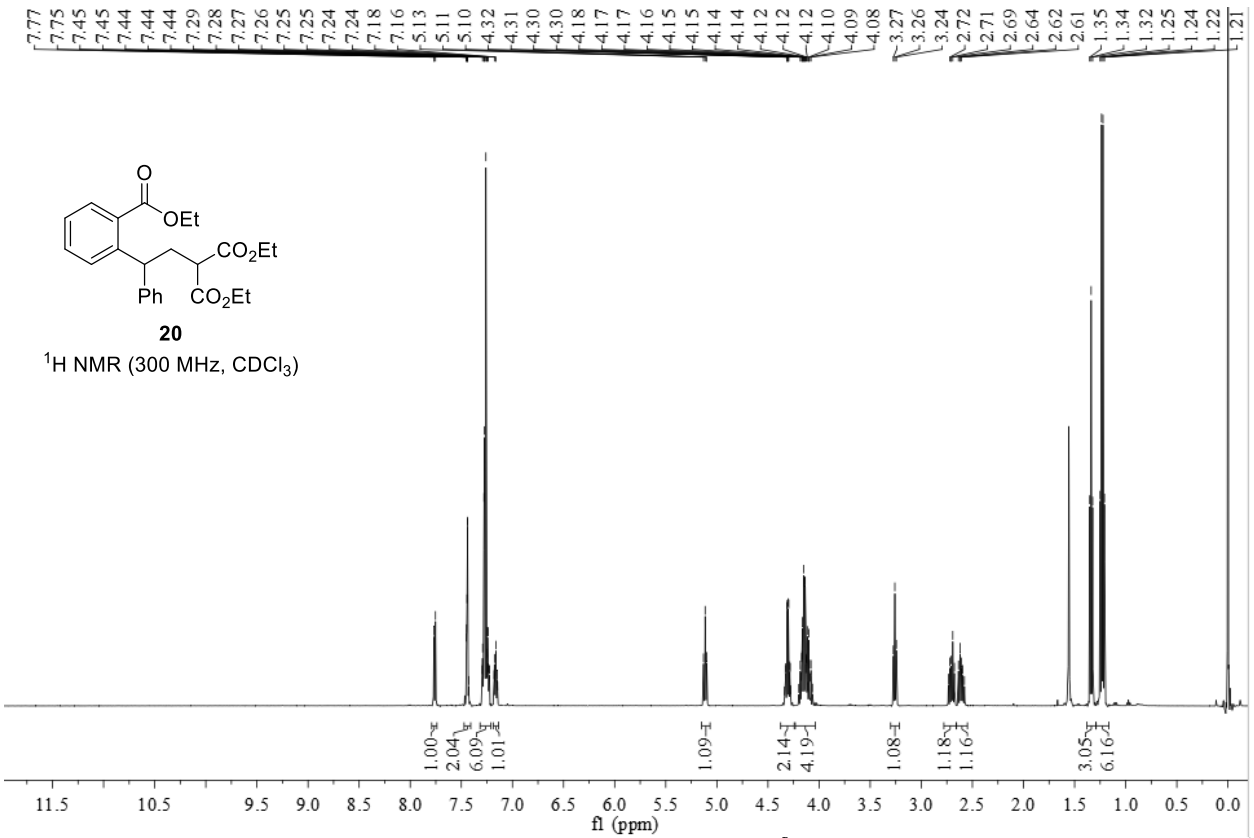






**19**

$^{13}$C NMR (75 MHz, $CDCl_3$)

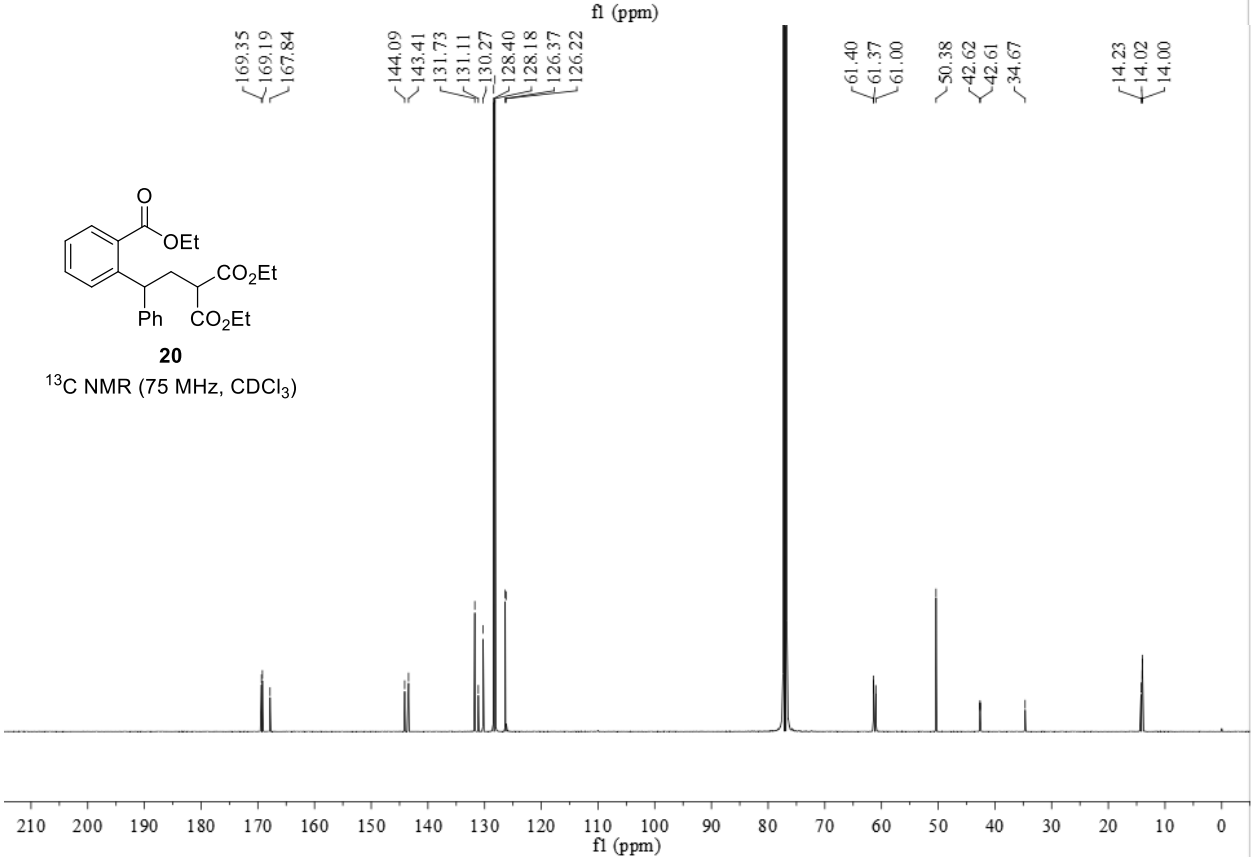






**20**

$^{1}$H NMR (300 MHz, $CDCl_3$)







**20**

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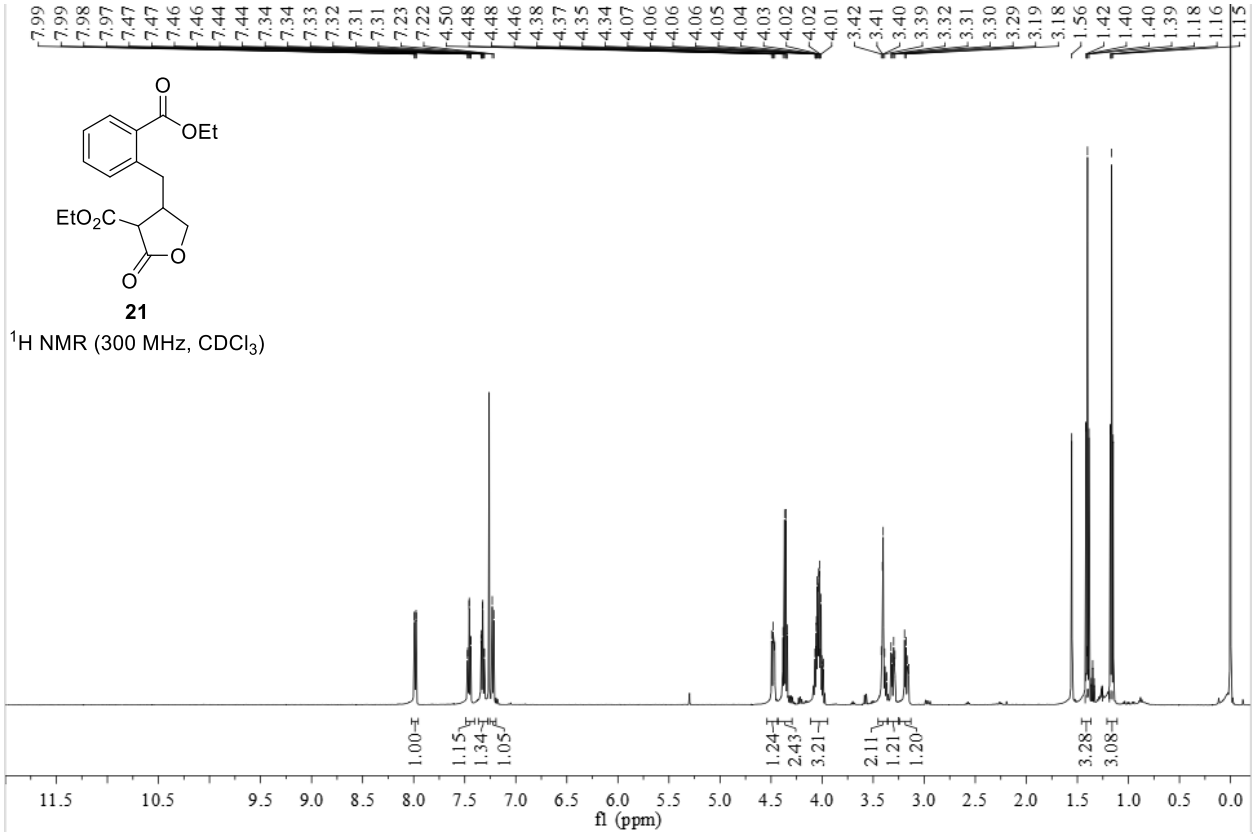
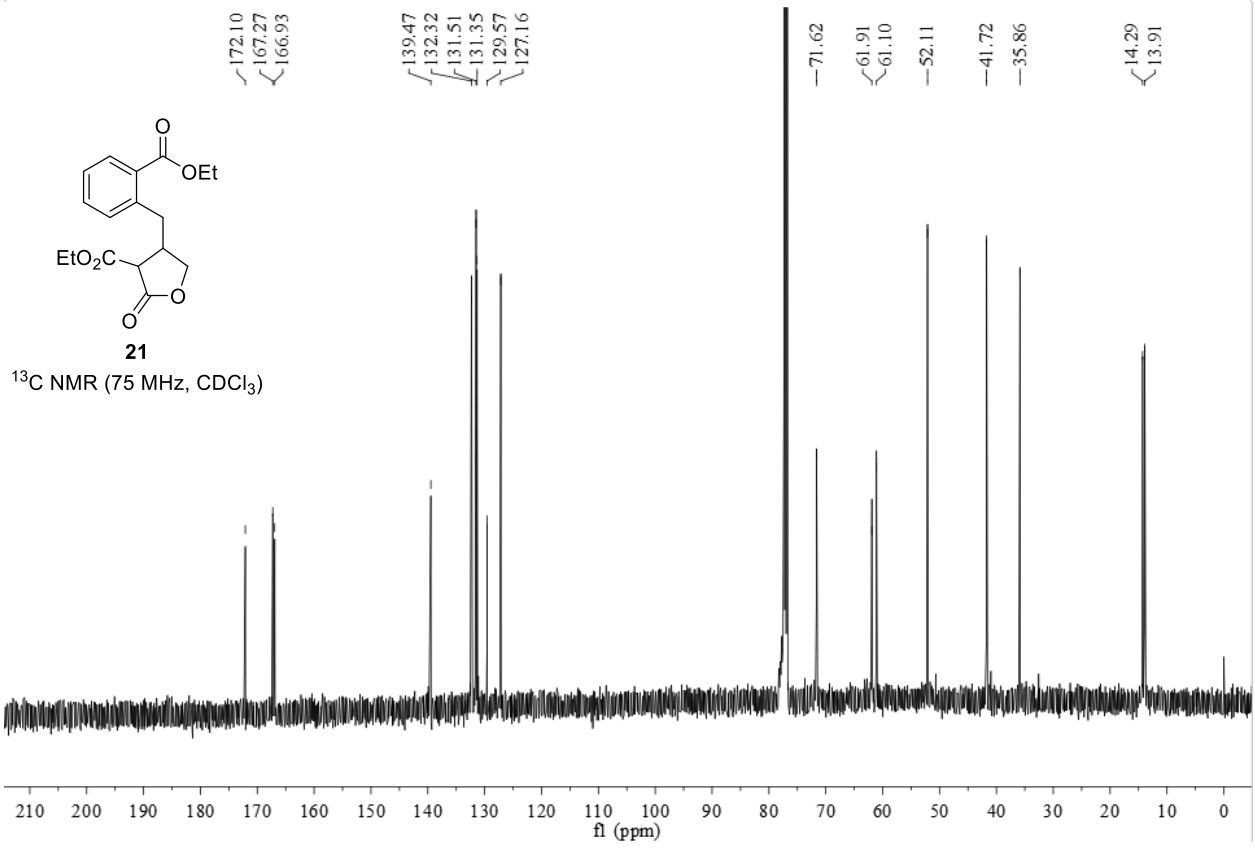



**21**

$^{1}$H NMR (300 MHz, $CDCl_3$)




**21**

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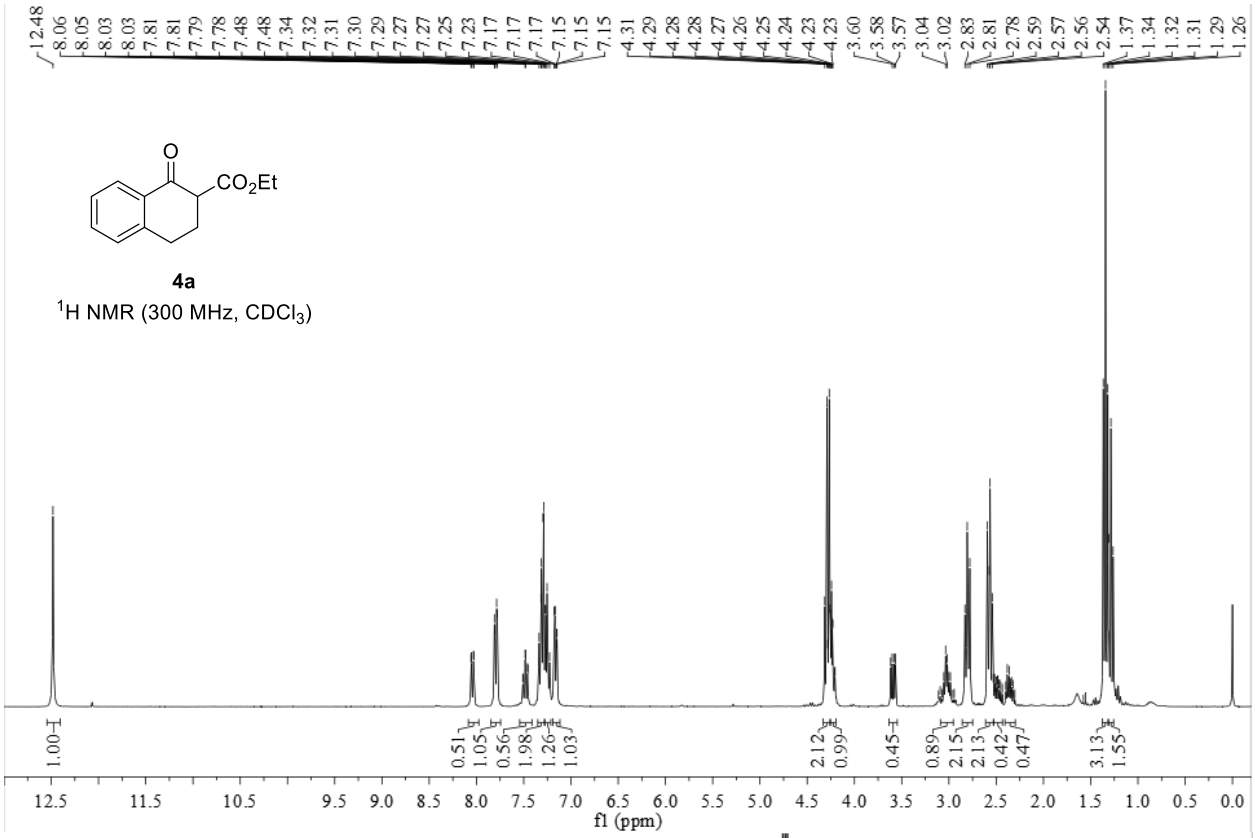
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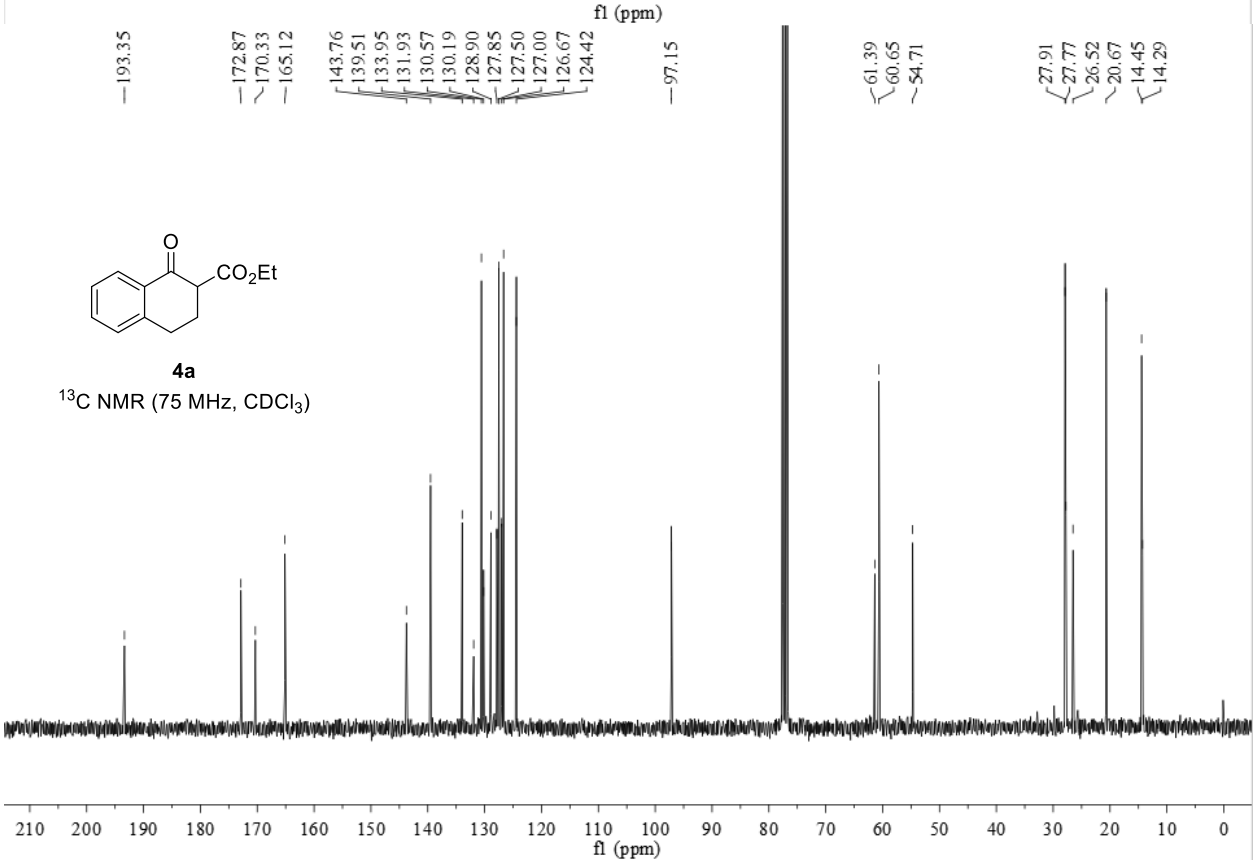
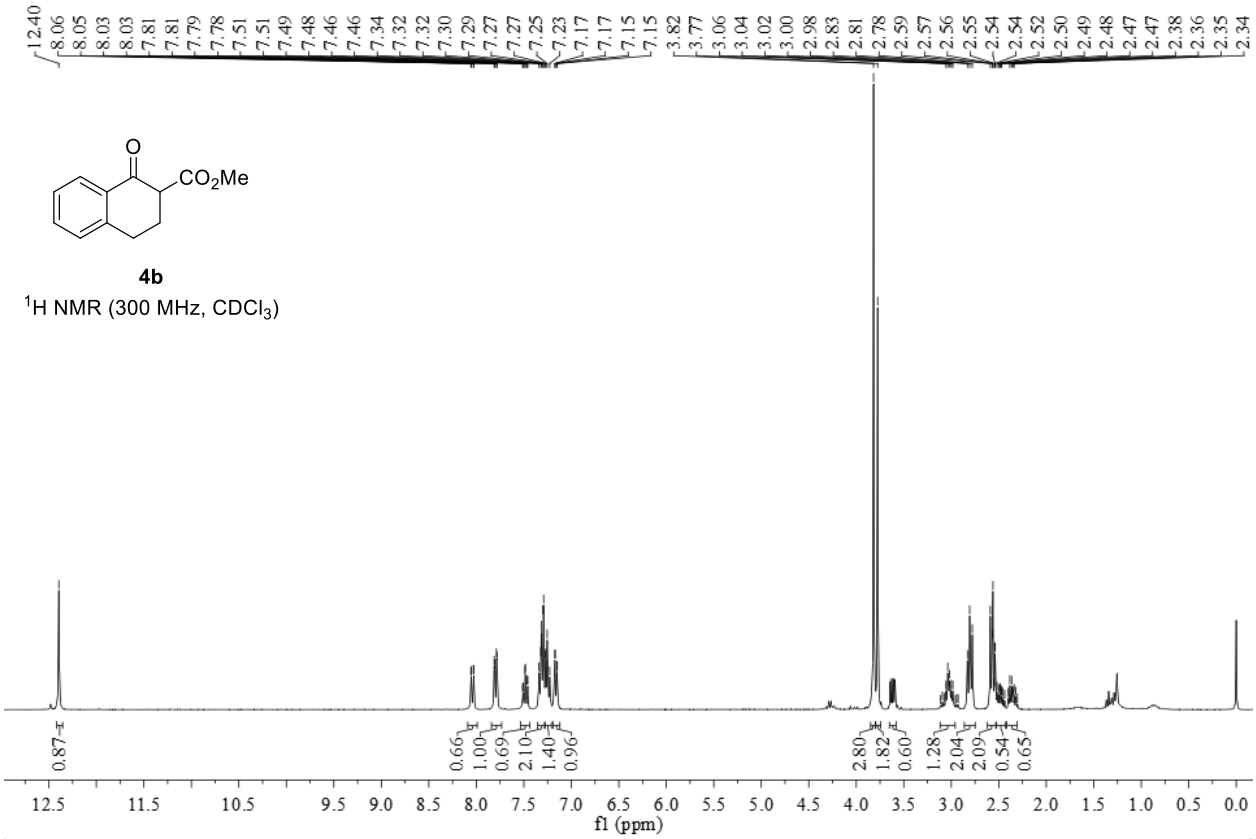
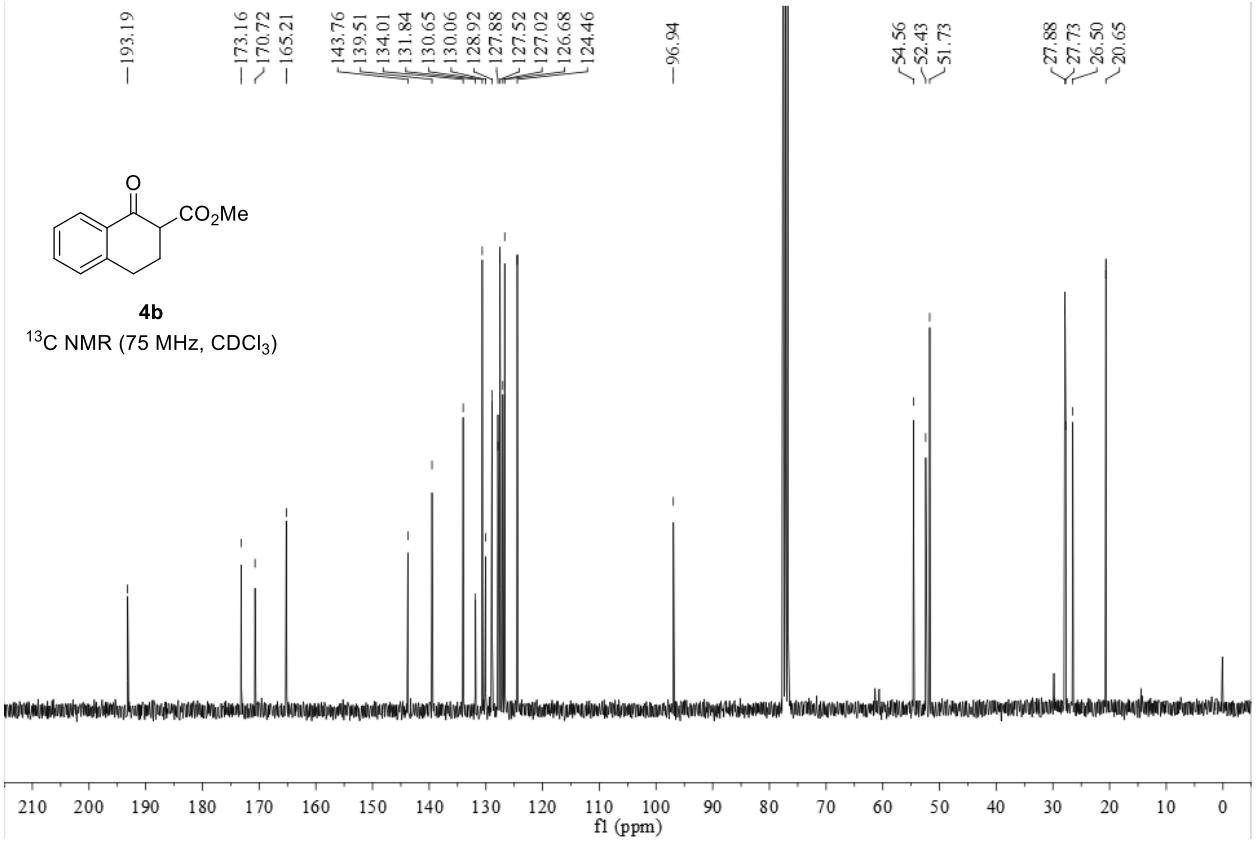
4.24
4.23
4.23
3.60
3.58
3.57
3.04
3.02
2.83
2.81
2.78
2.59
2.57
2.56
2.54
1.37
1.34
1.32
1.31
1.29
1.26
O
CO2Et
4a
1H NMR (300 MHz, CDCl3)
1.00
0.51
1.05
0.56
1.98
1.26
1.03
2.12
0.99
0.45
0.89
2.15
2.13
0.42
0.47
3.13
1.55
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


193.35
172.87
170.33
165.12
143.76
139.51
133.95
131.93
130.57
130.19
128.90
127.85
127.50
127.00
126.67
124.42
97.15
61.39
60.65
54.71
27.91
27.77
26.52
20.67
14.45
14.29
O
CO2Et
4a
13C NMR (75 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



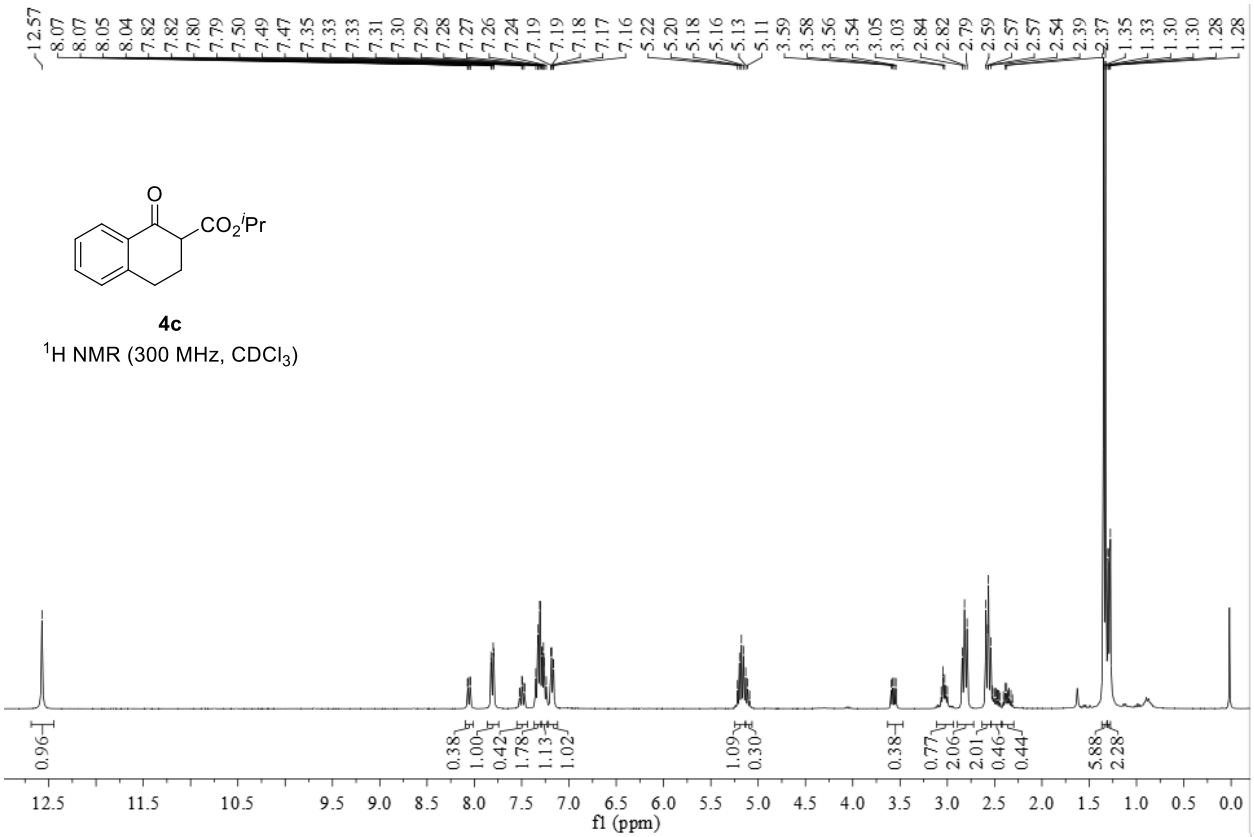

**4b**

$^{1}$H NMR (300 MHz, $CDCl_3$)



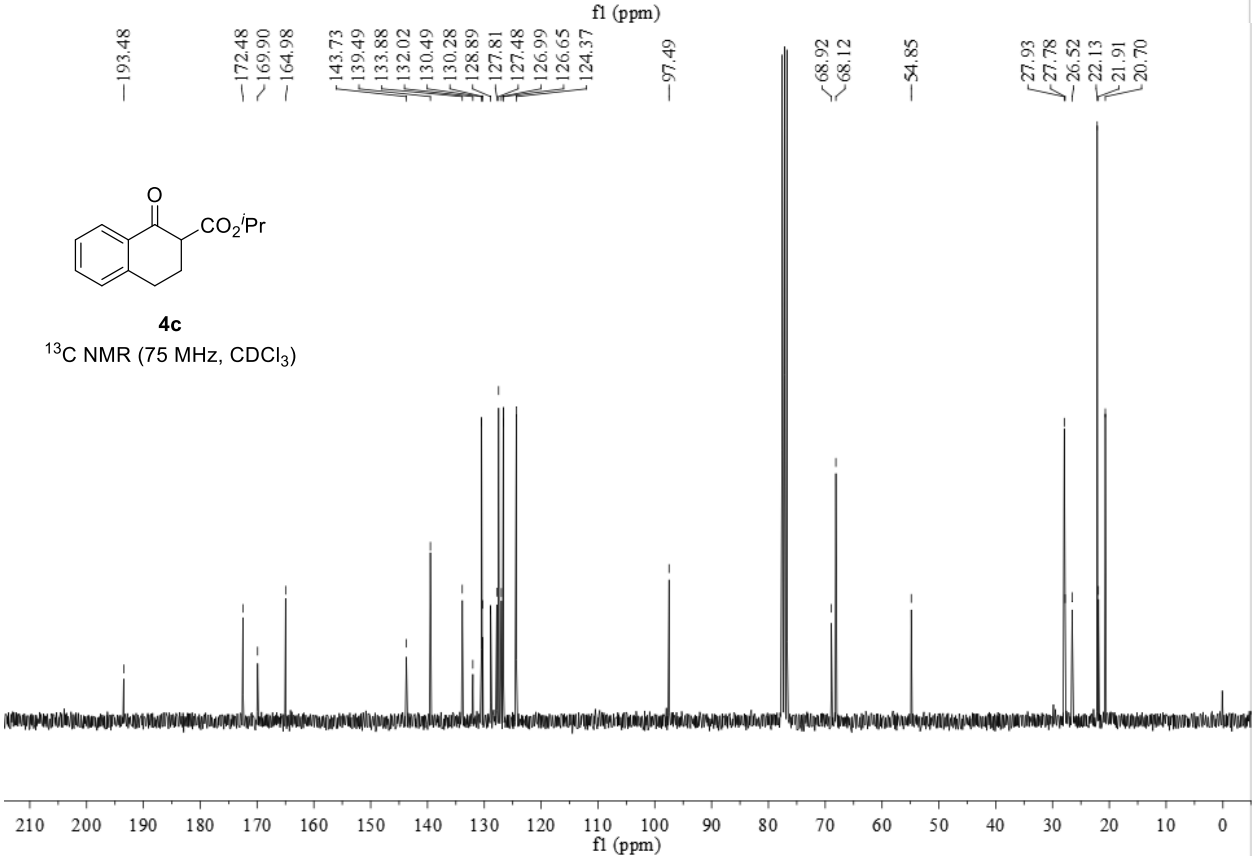

**4b**

$^{13}$C NMR (75 MHz, $CDCl_3$)



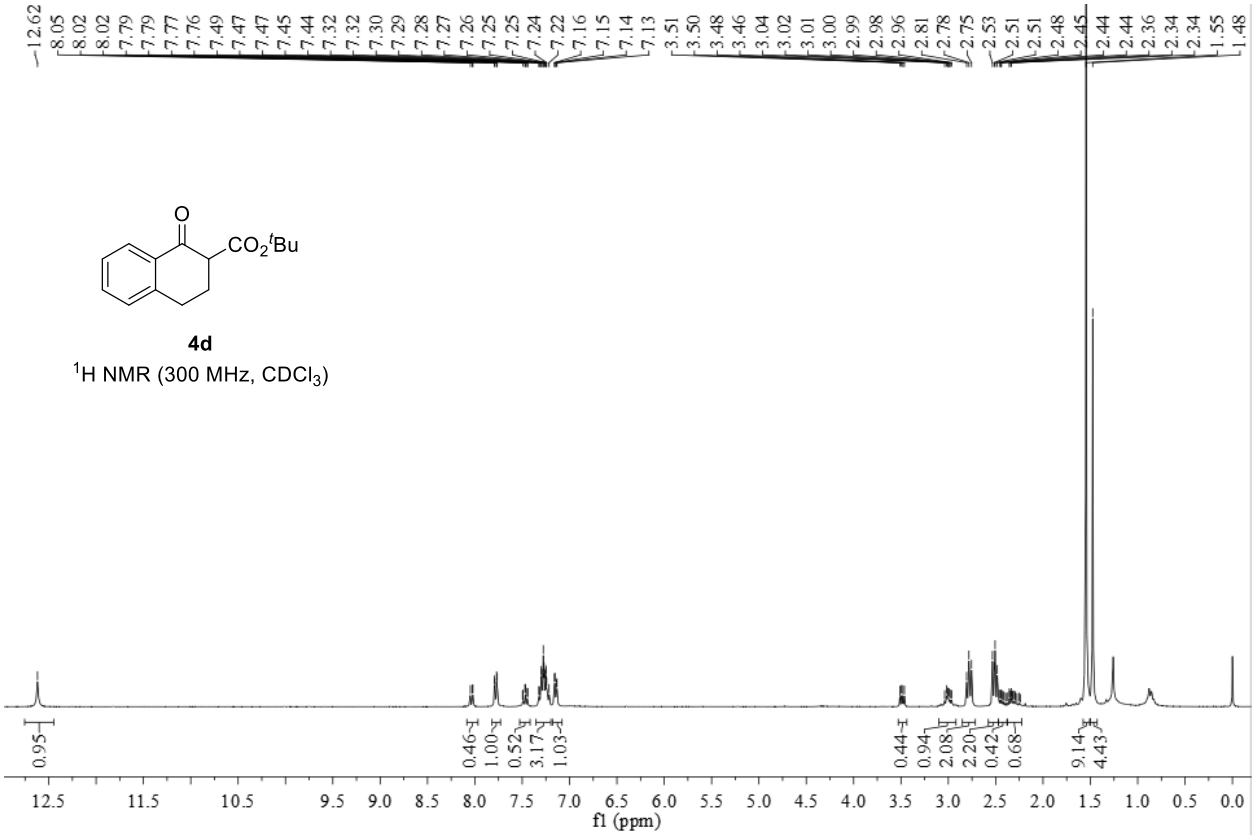

**4c**

$^{1}$H NMR (300 MHz, $CDCl_3$)



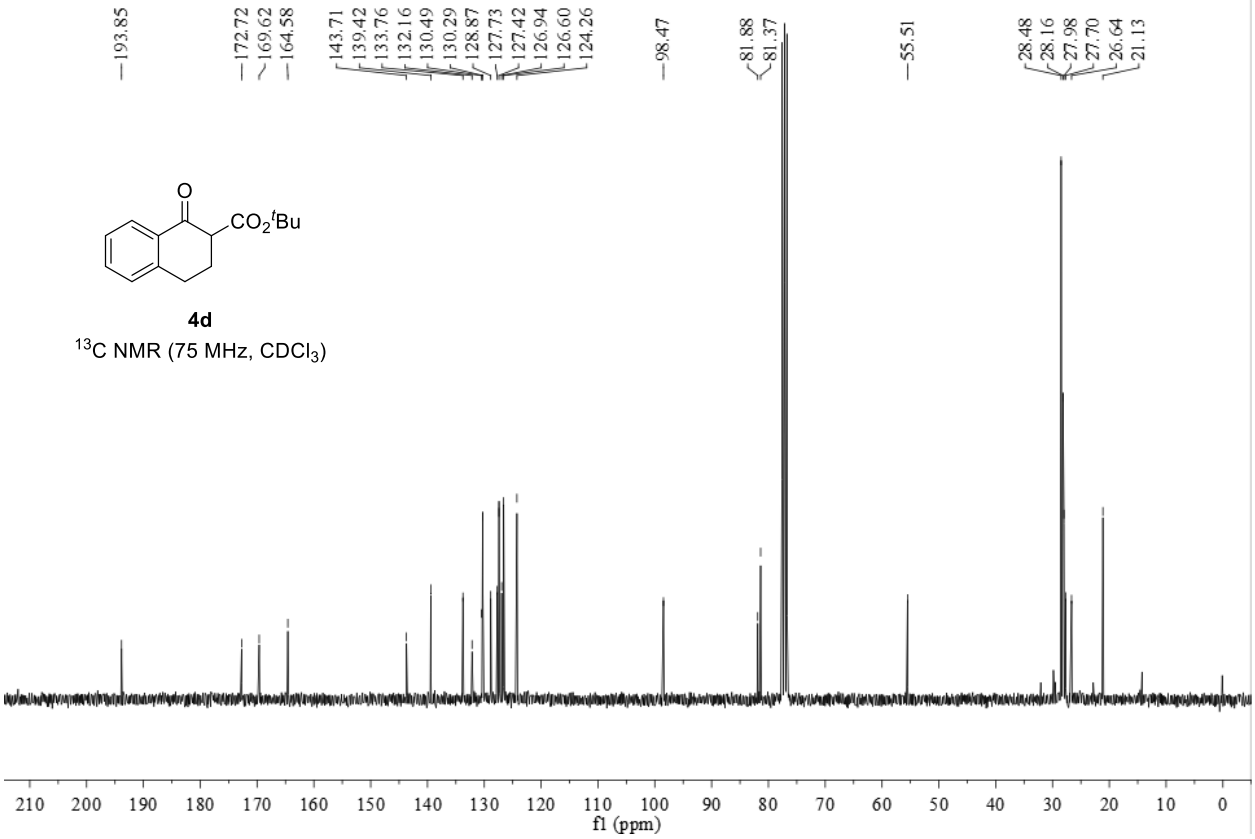

**4c**

$^{13}$C NMR (75 MHz, $CDCl_3$)



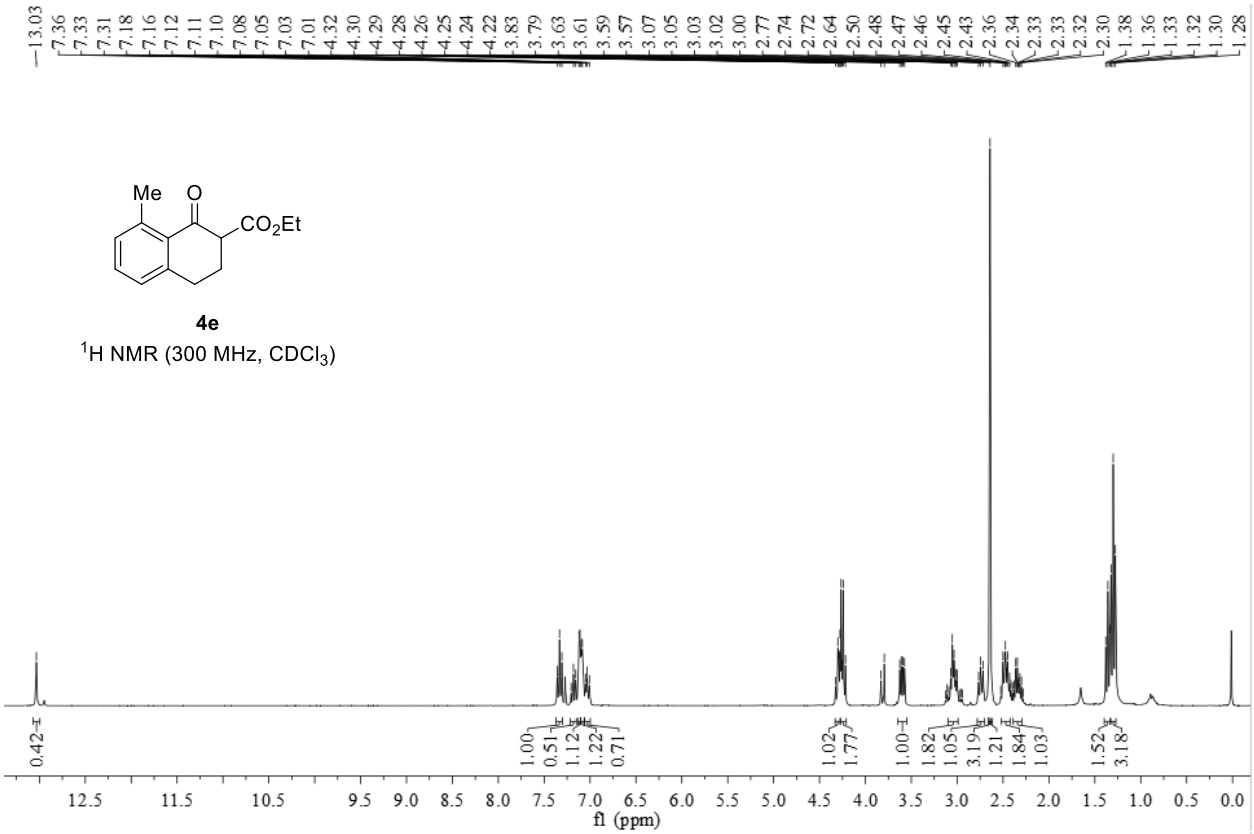

**4d**

$^{1}$H NMR (300 MHz, $CDCl_3$)



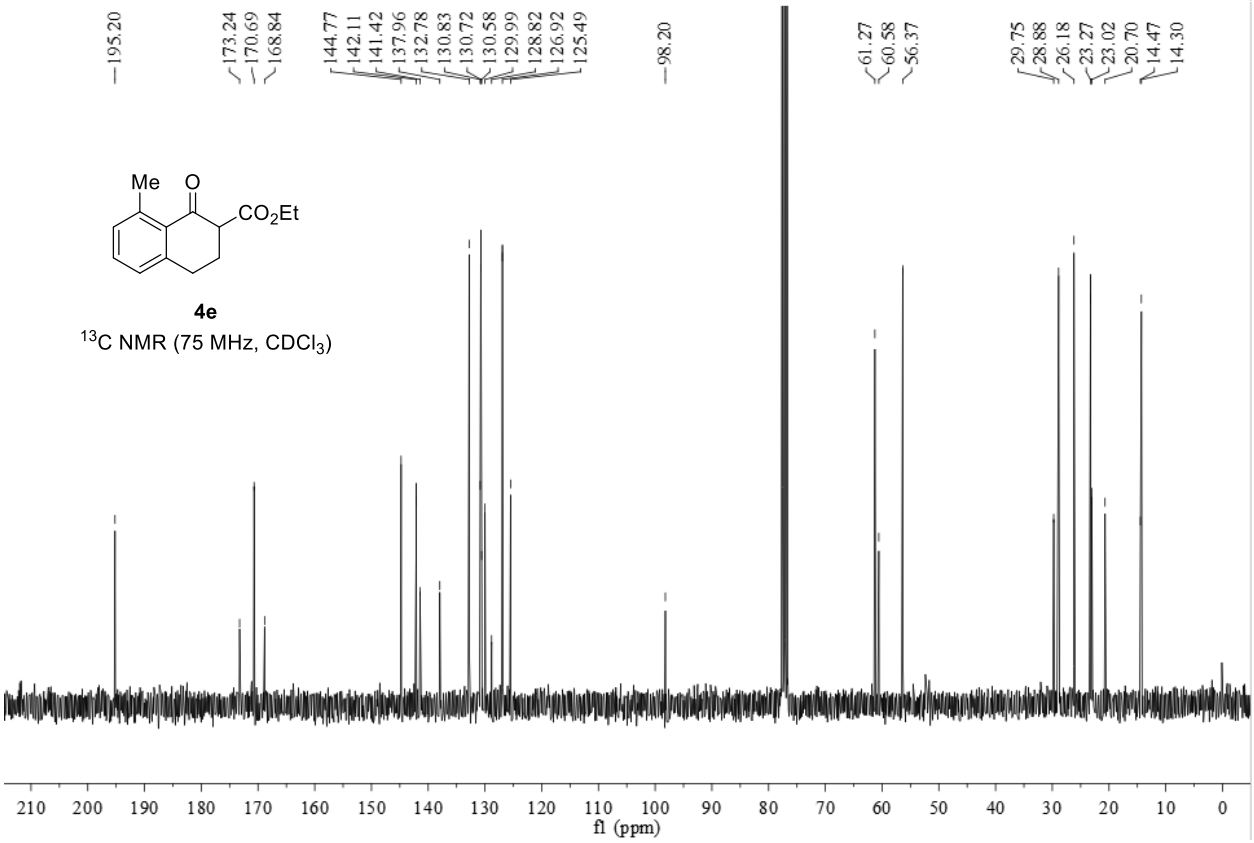

**4d**

$^{13}$C NMR (75 MHz, $CDCl_3$)



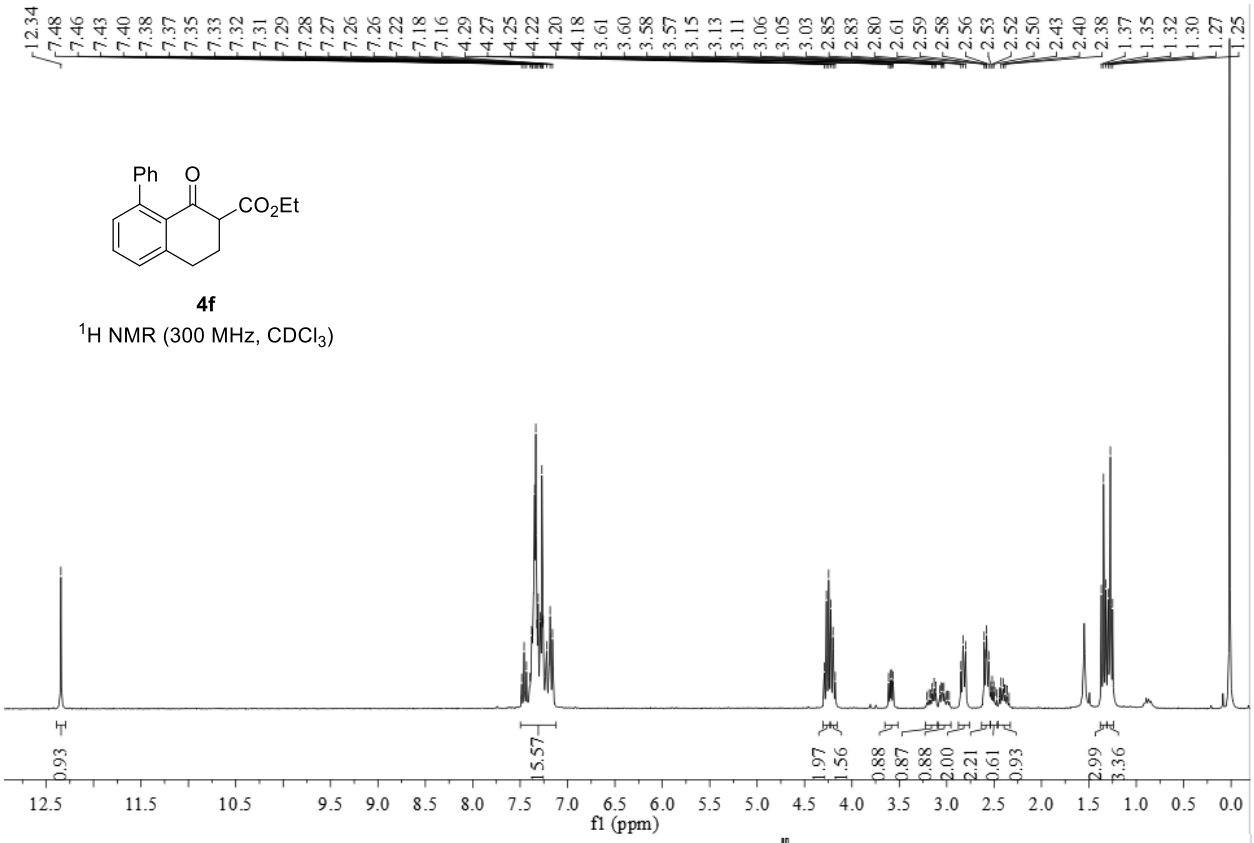

**4e**

$^{1}$H NMR (300 MHz, $CDCl_3$)



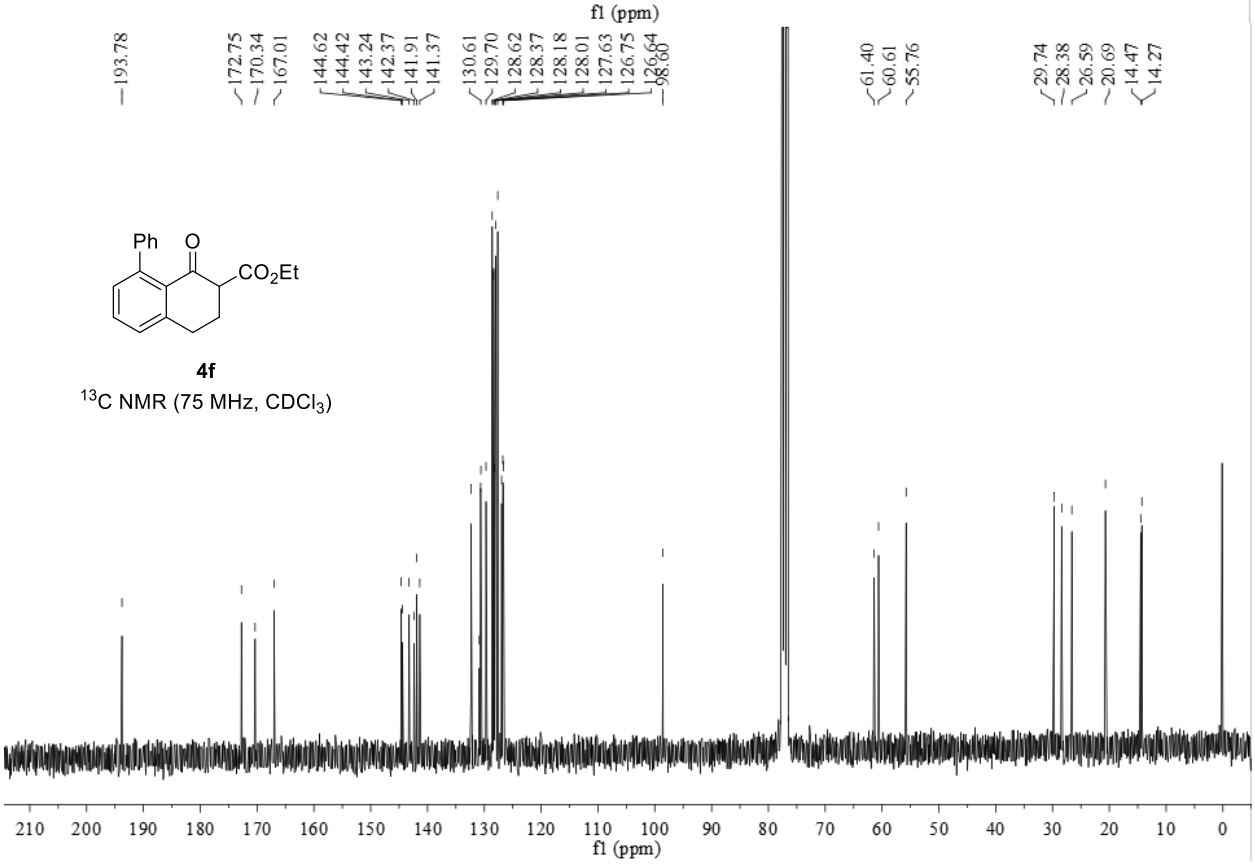

**4e**

$^{13}$C NMR (75 MHz, $CDCl_3$)



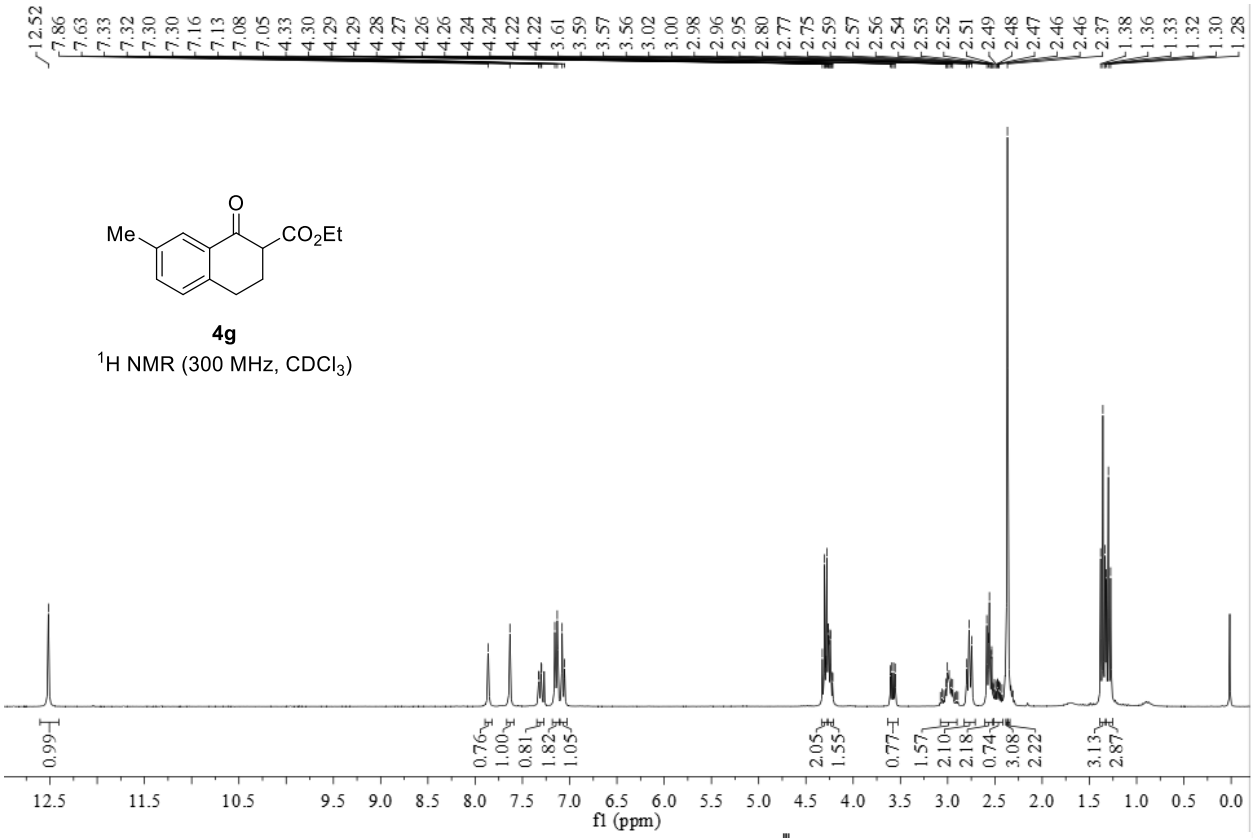

**4f**

$^{1}$H NMR (300 MHz, $CDCl_3$)



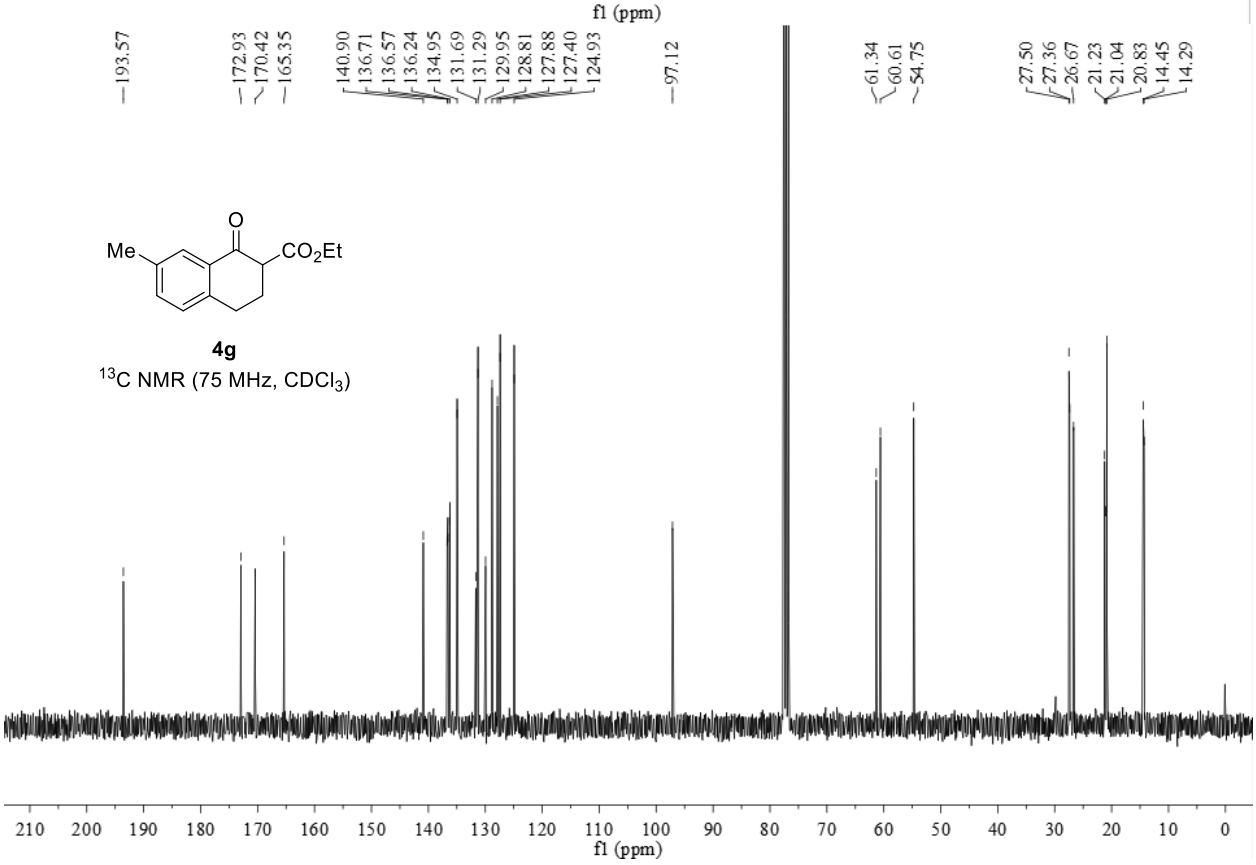

**4f**

$^{13}$C NMR (75 MHz, $CDCl_3$)



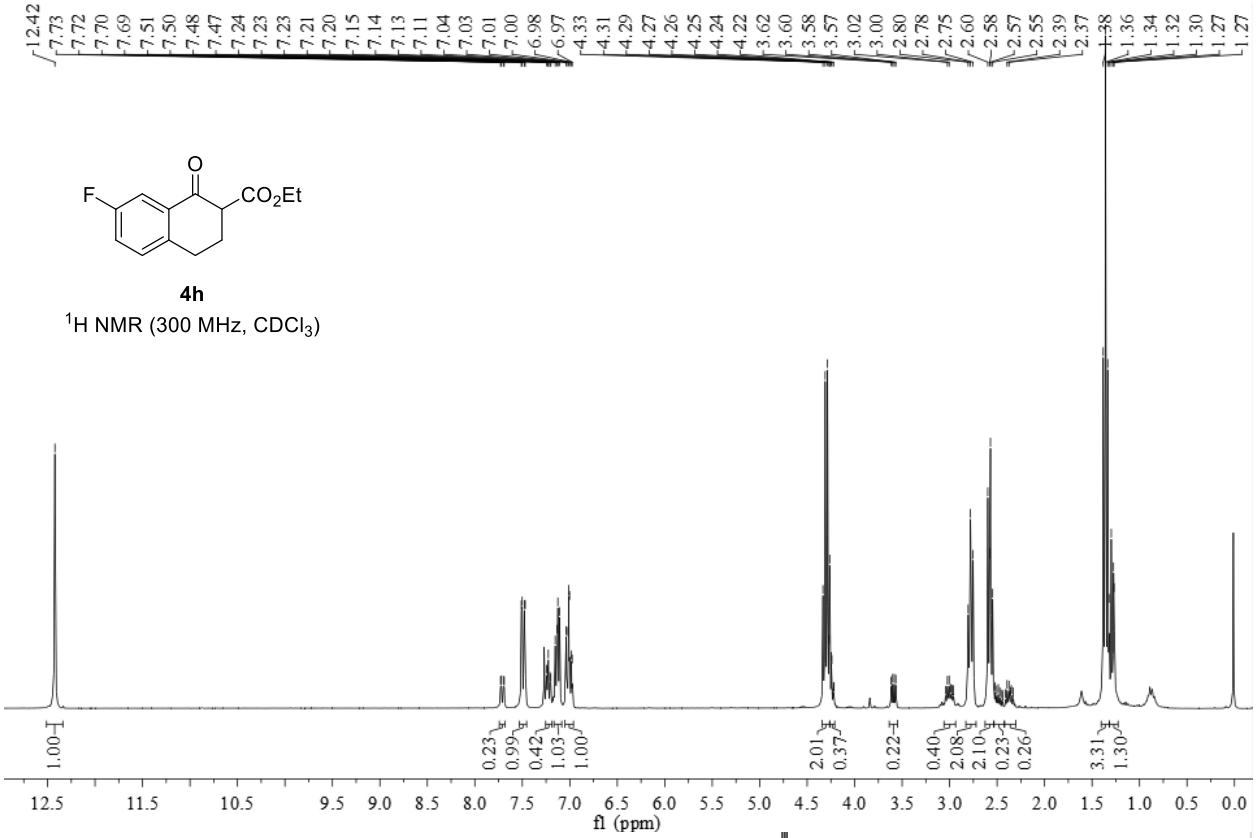

**4g**

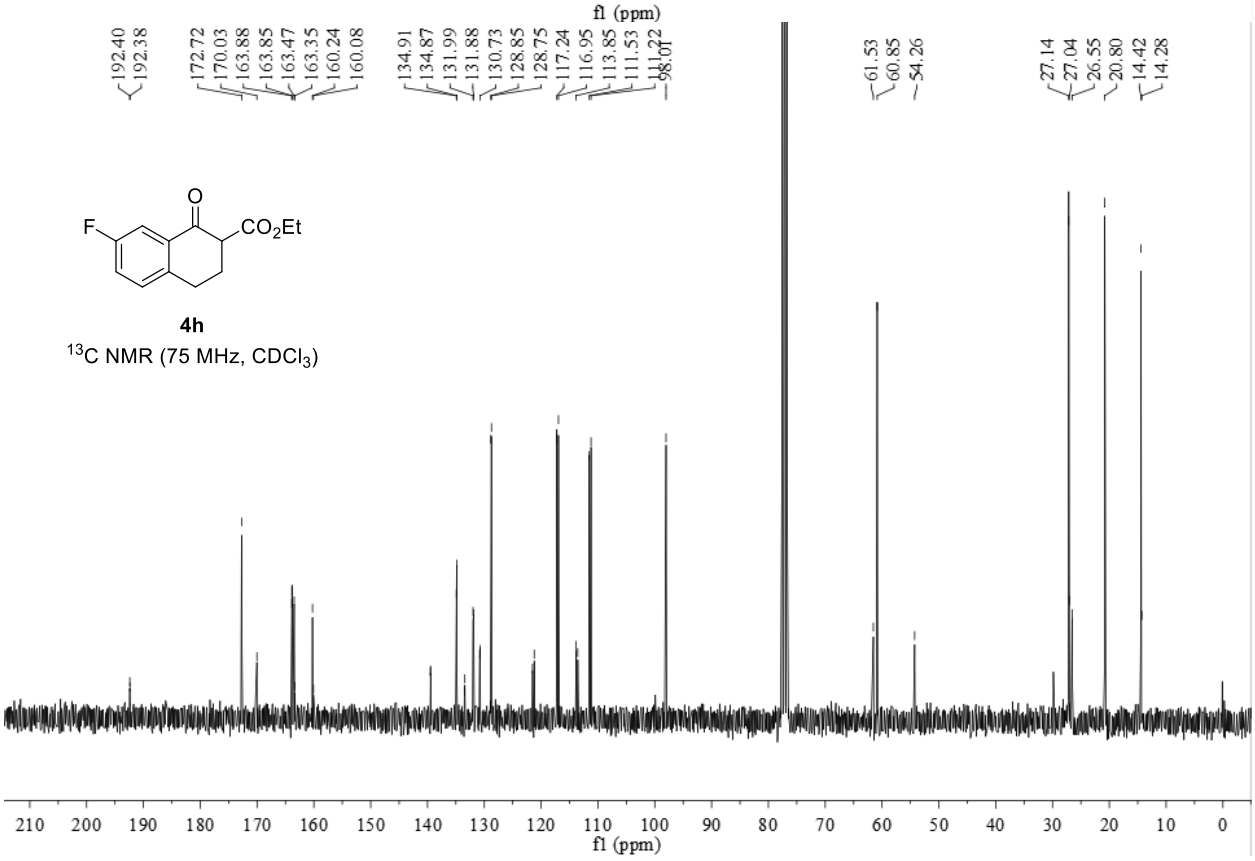
$^{1}$H NMR (300 MHz, $CDCl_3$)

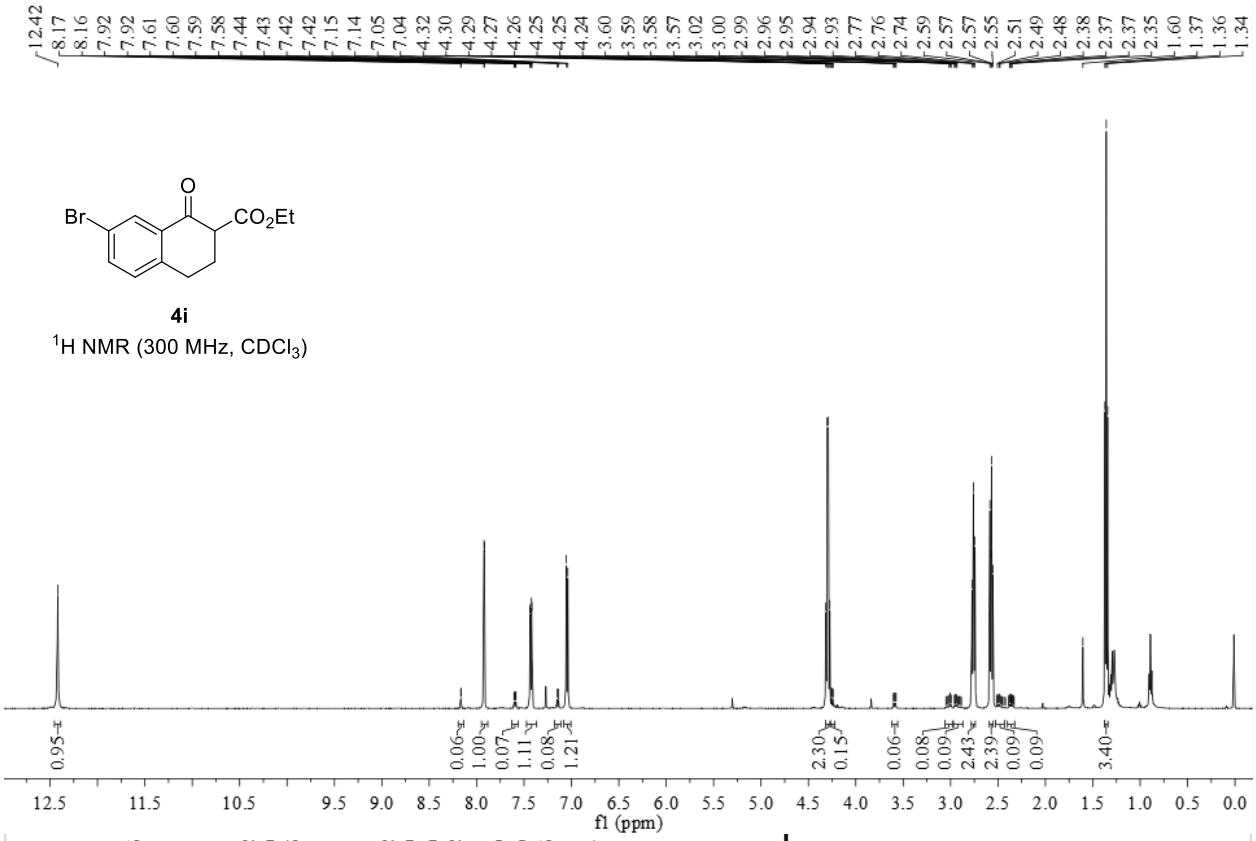



**4g**

$^{13}$C NMR (75 MHz, $CDCl_3$)

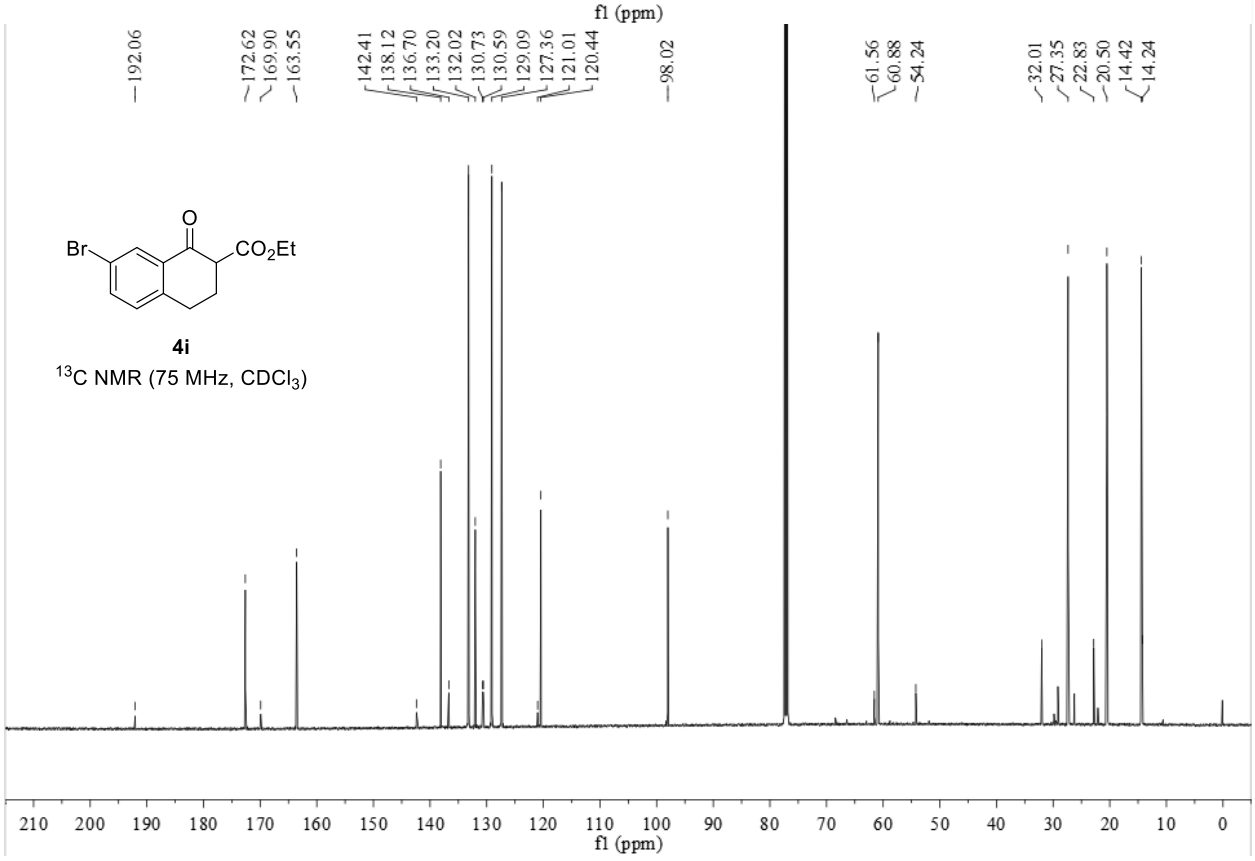

12.42
7.73
7.72
7.70
7.69
7.51
7.50
7.48
7.47
7.24
7.23
7.23
7.21
7.20
7.15
7.14
7.13
7.11
7.04
7.03
7.01
7.00
6.98
6.97
4.33
4.31
4.29
4.27
4.26
4.25
4.24
4.22
3.62
3.60
3.58
3.57
3.02
3.00
2.80
2.78
2.75
2.60
2.58
2.57
2.55
2.39
2.37
1.38
1.36
1.34
1.32
1.30
1.27
1.27
O
F
CO2Et
4h
1H NMR (300 MHz, CDCl3)
1.00
0.23
0.99
0.42
1.03
1.00
2.01
0.37
0.22
0.40
2.08
2.10
0.23
0.26
3.31
1.30
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


192.40
192.38
172.72
170.03
163.88
163.85
163.47
163.35
160.24
160.08
134.91
134.87
131.99
131.88
130.73
128.85
128.75
117.24
116.95
113.85
111.53
111.22
98.01
61.53
60.85
54.26
27.14
27.04
26.55
20.80
14.42
14.28
O
F
CO2Et
4h
13C NMR (75 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



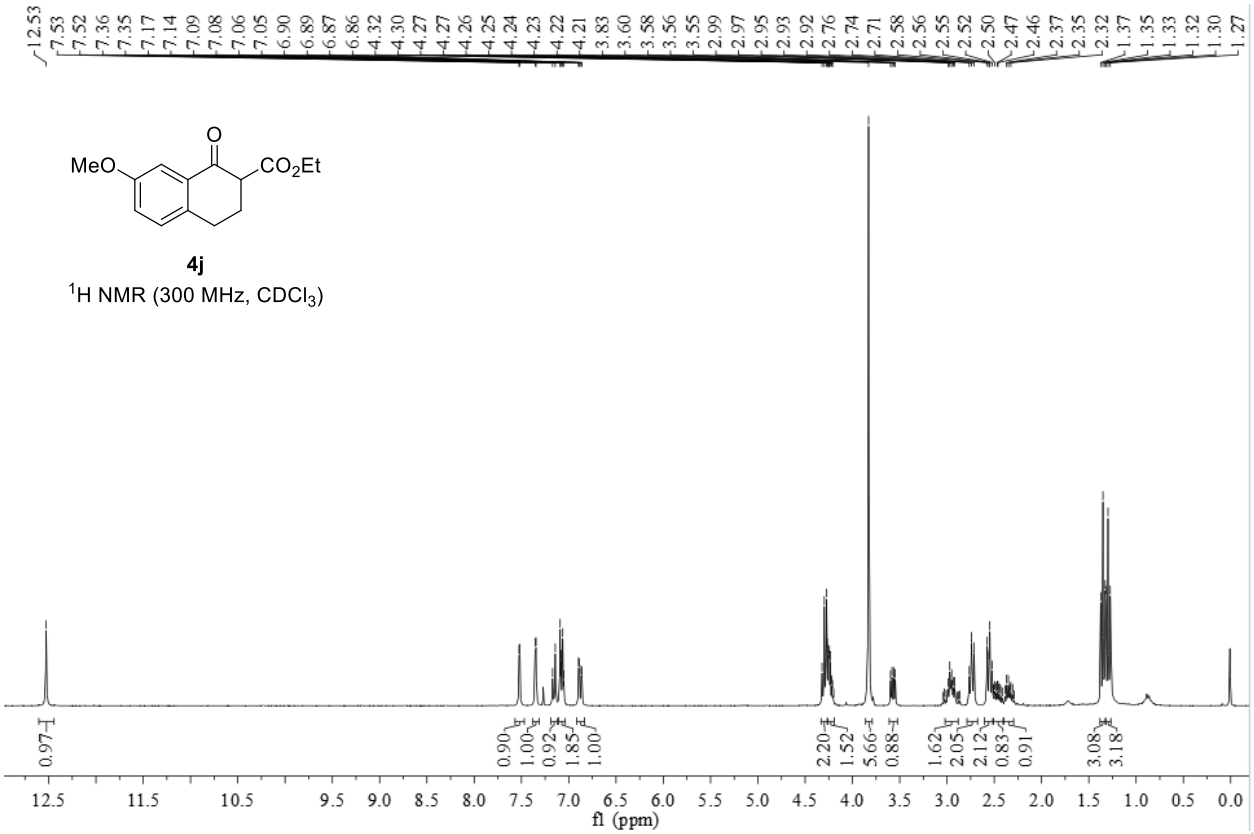

**4i**

$^{1}$H NMR (300 MHz, $CDCl_3$)



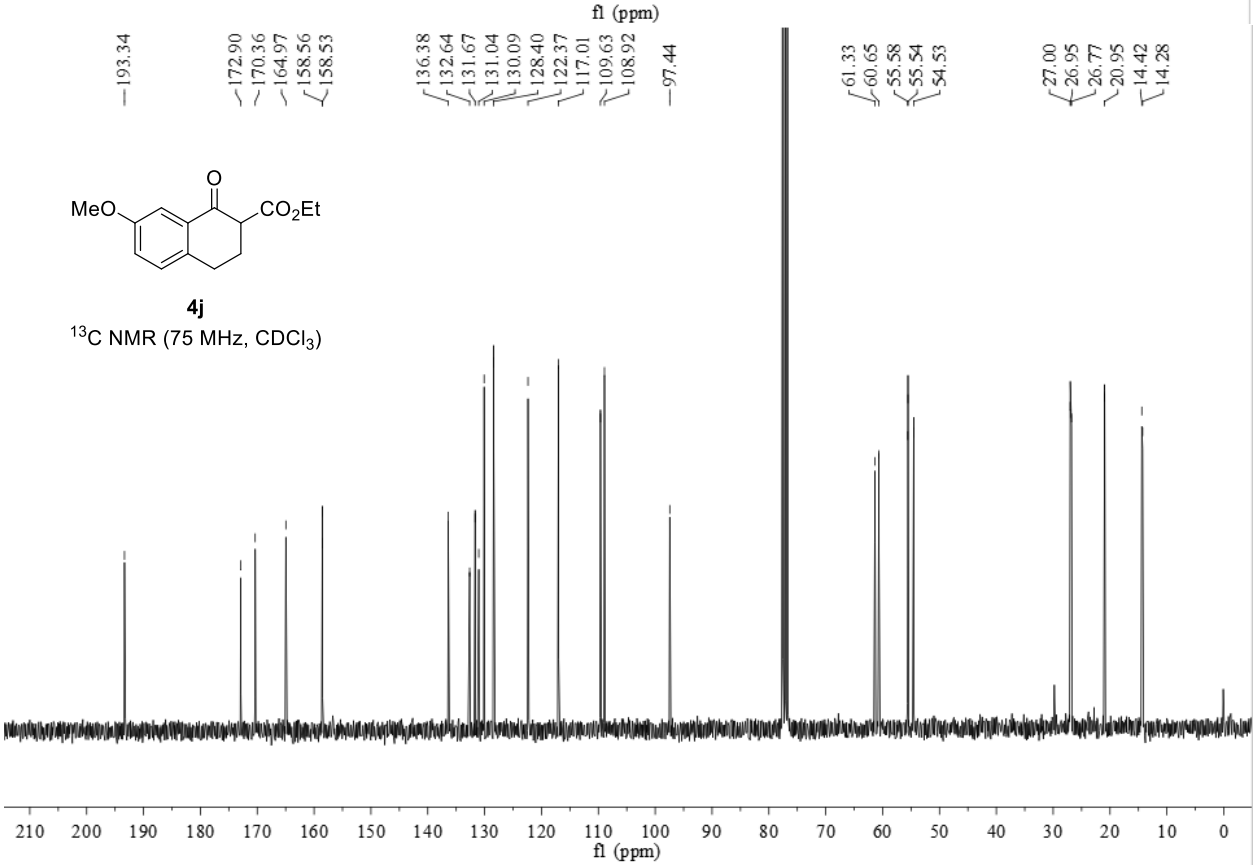

**4i**

$^{13}$C NMR (75 MHz, $CDCl_3$)



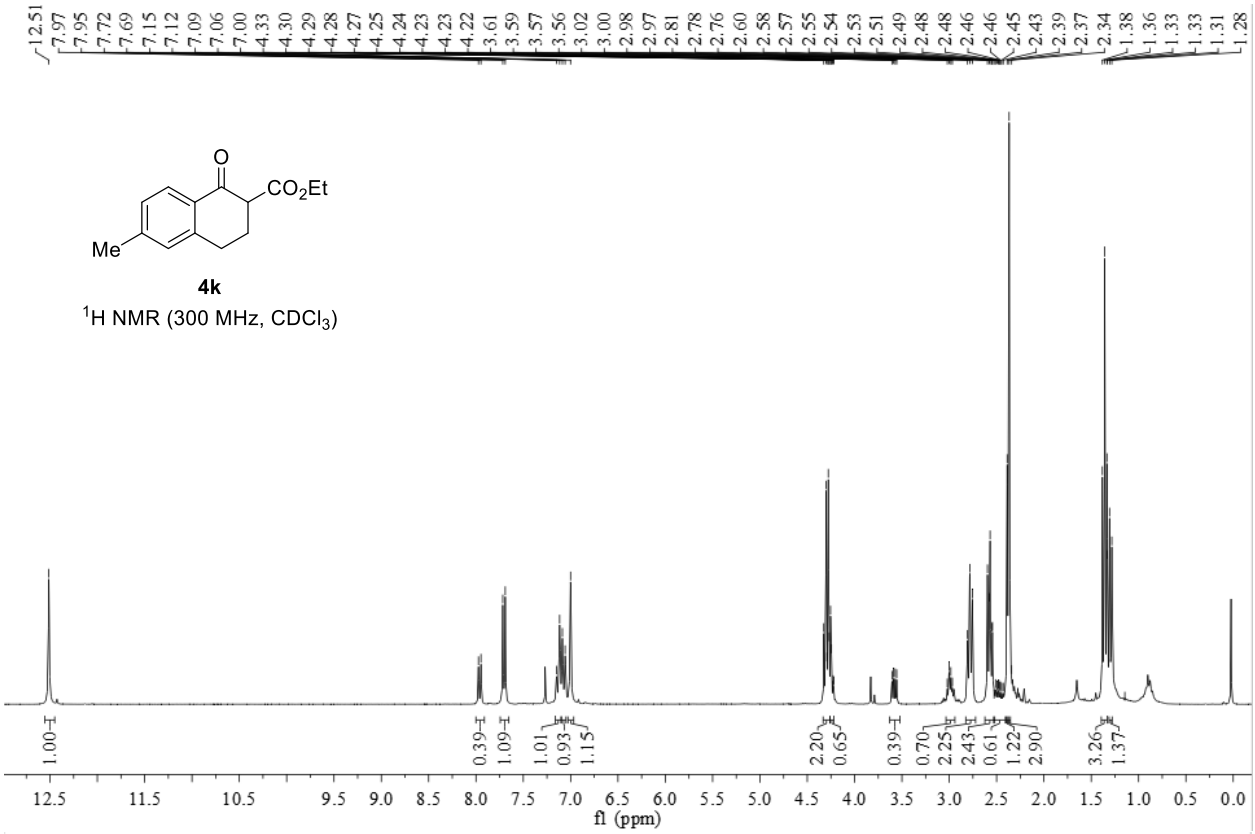

**4j**

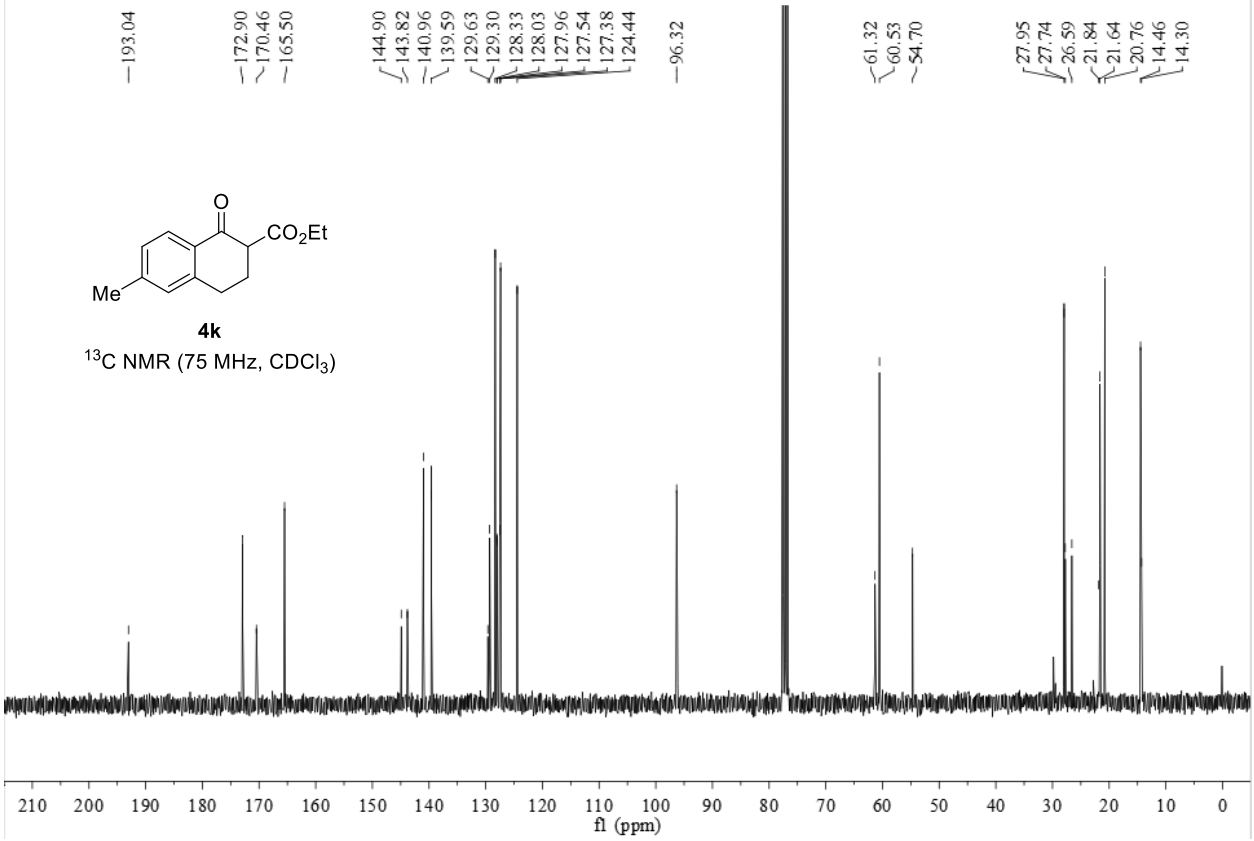
$^{1}$H NMR (300 MHz, $CDCl_3$)

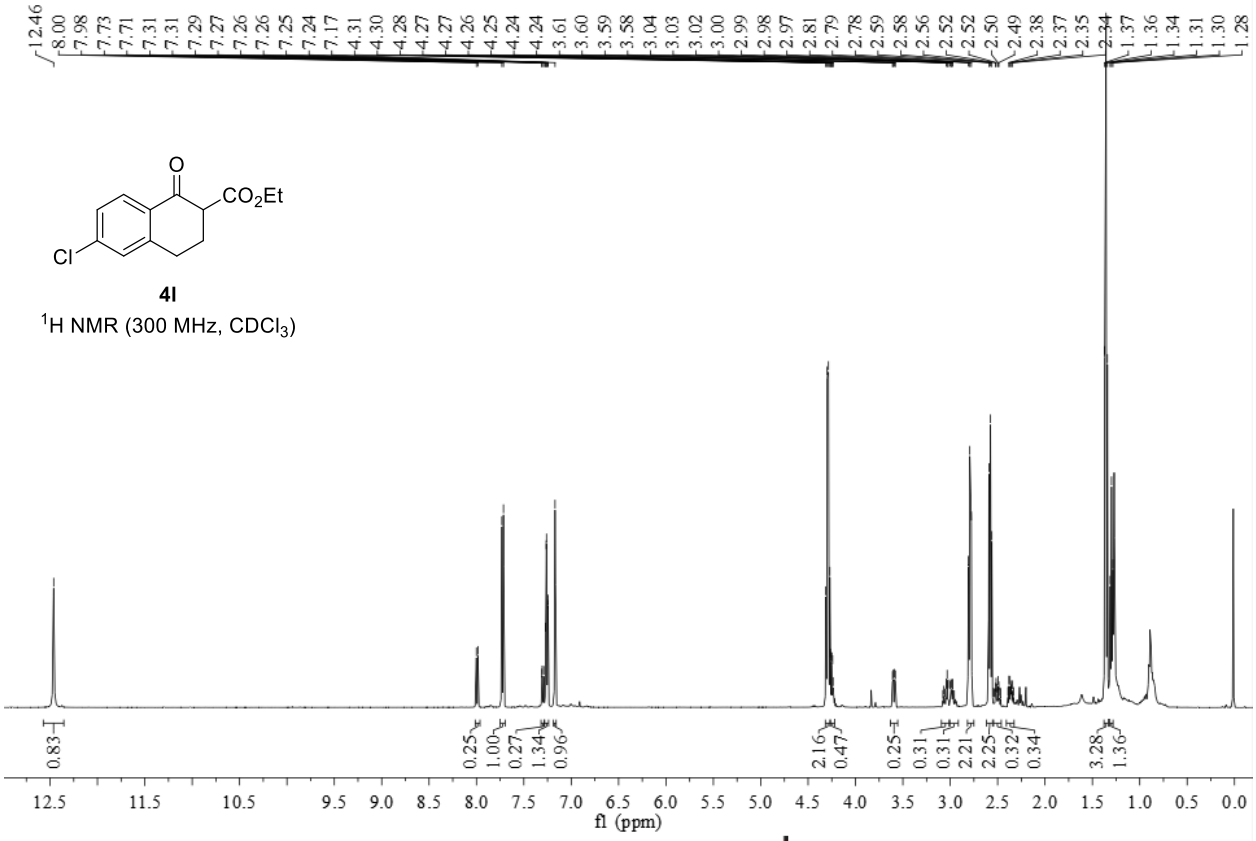


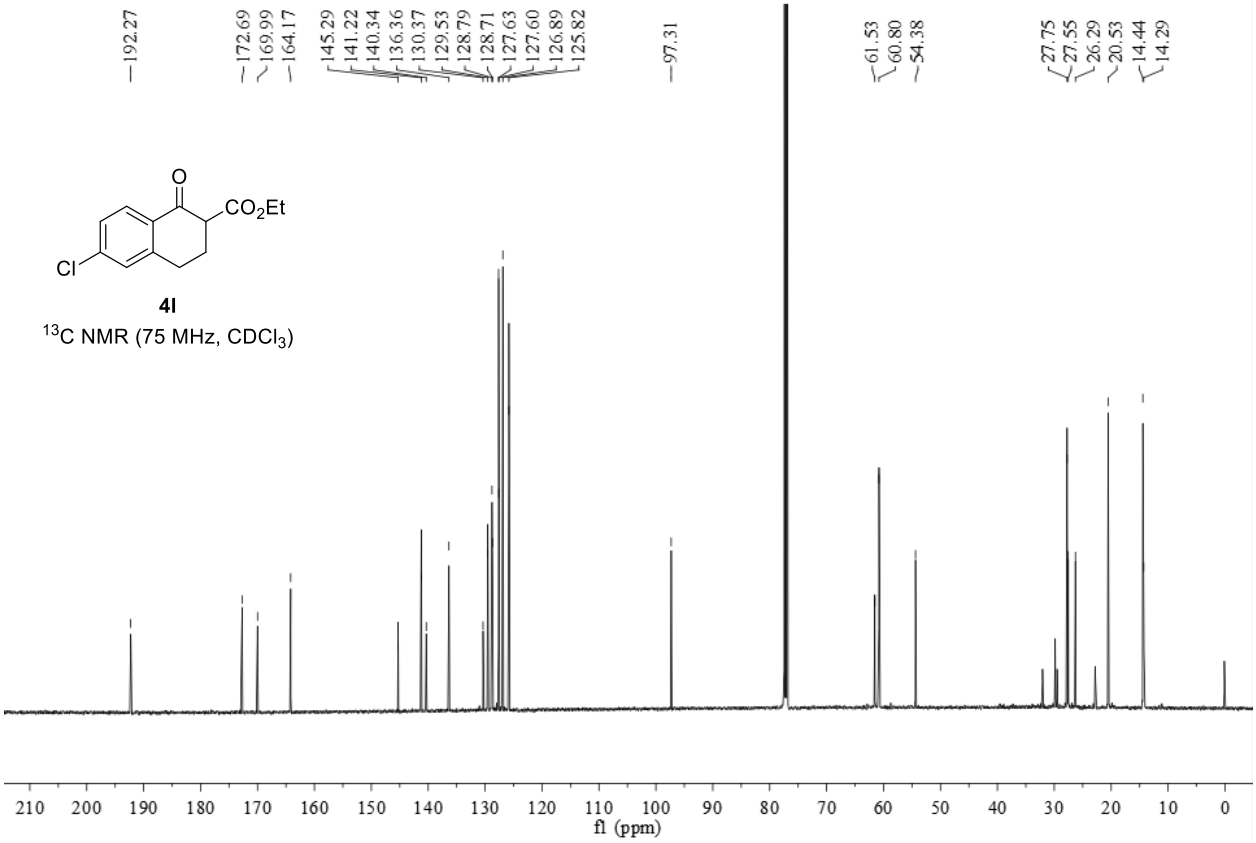

**4j**

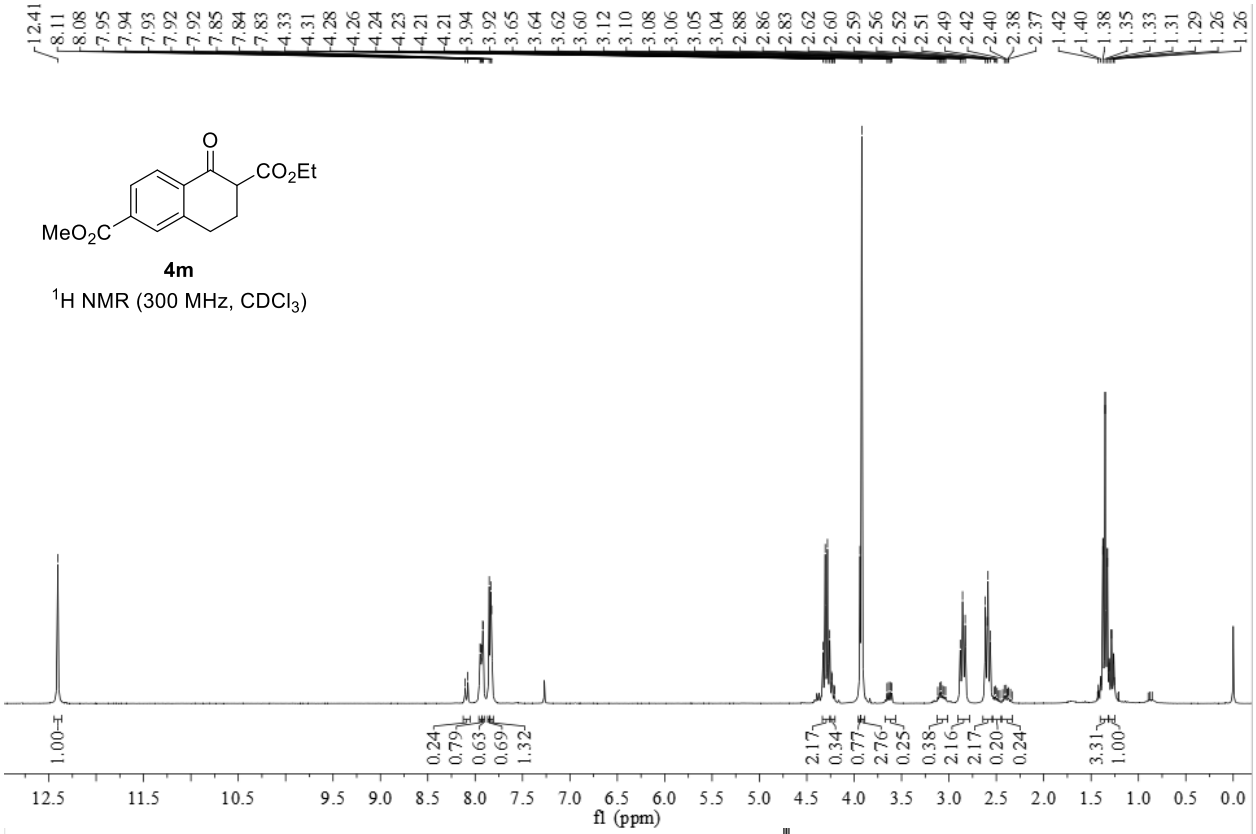
$^{13}$C NMR (75 MHz, $CDCl_3$)

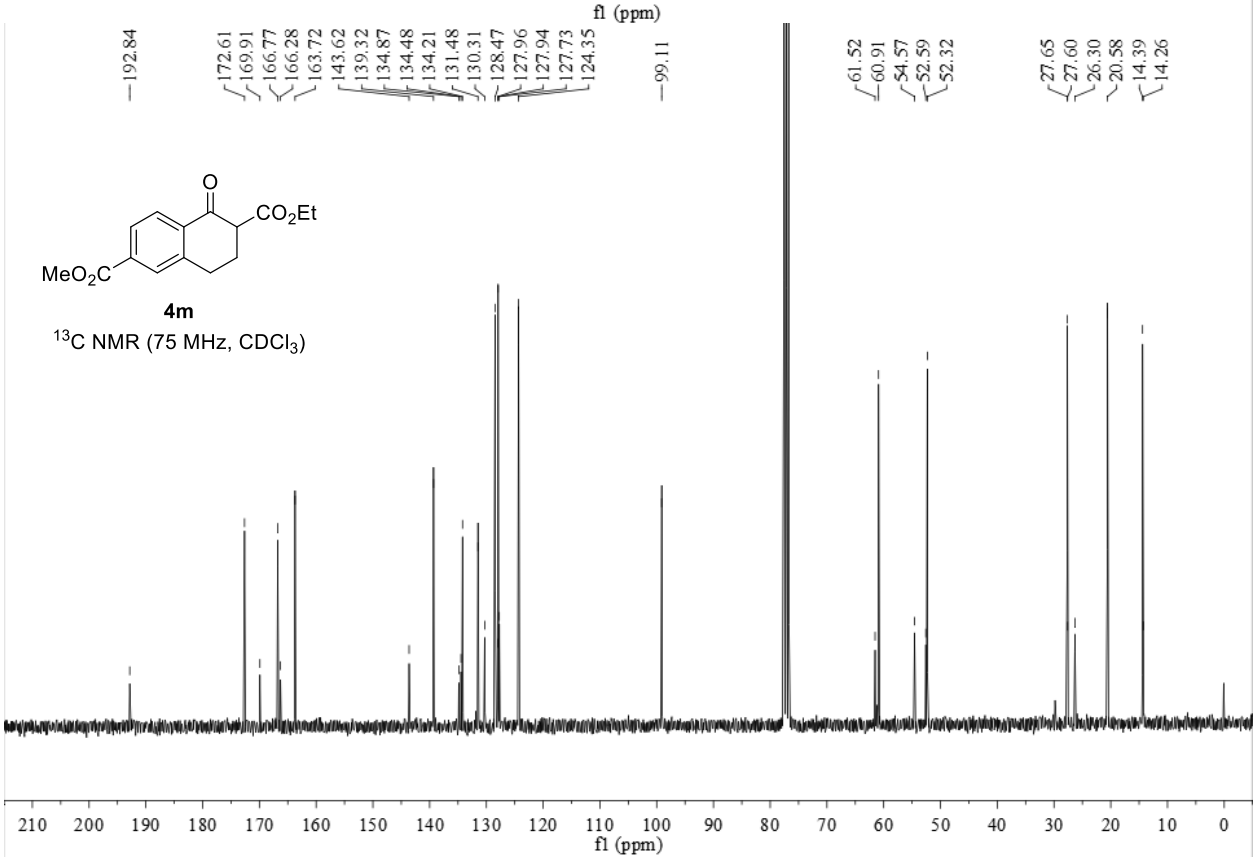

12.51
7.97
7.95
7.72
7.69
7.15
7.12
7.09
7.06
7.00
4.33
4.30
4.29
4.28
4.27
4.25
4.24
4.23
4.23
4.22
3.61
3.59
3.57
3.56
3.02
3.00
2.98
2.97
2.81
2.78
2.76
2.60
2.58
2.57
2.55
2.54
2.53
2.51
2.49
2.48
2.48
2.46
2.46
2.45
2.43
2.39
2.37
2.34
1.38
1.36
1.33
1.33
1.31
1.28
O
CO2Et
Me
4k
1H NMR (300 MHz, CDCl3)
1.00
0.39
1.09
1.01
0.93
1.15
2.20
0.65
0.39
0.70
2.25
2.43
0.61
1.22
2.90
3.26
1.37
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

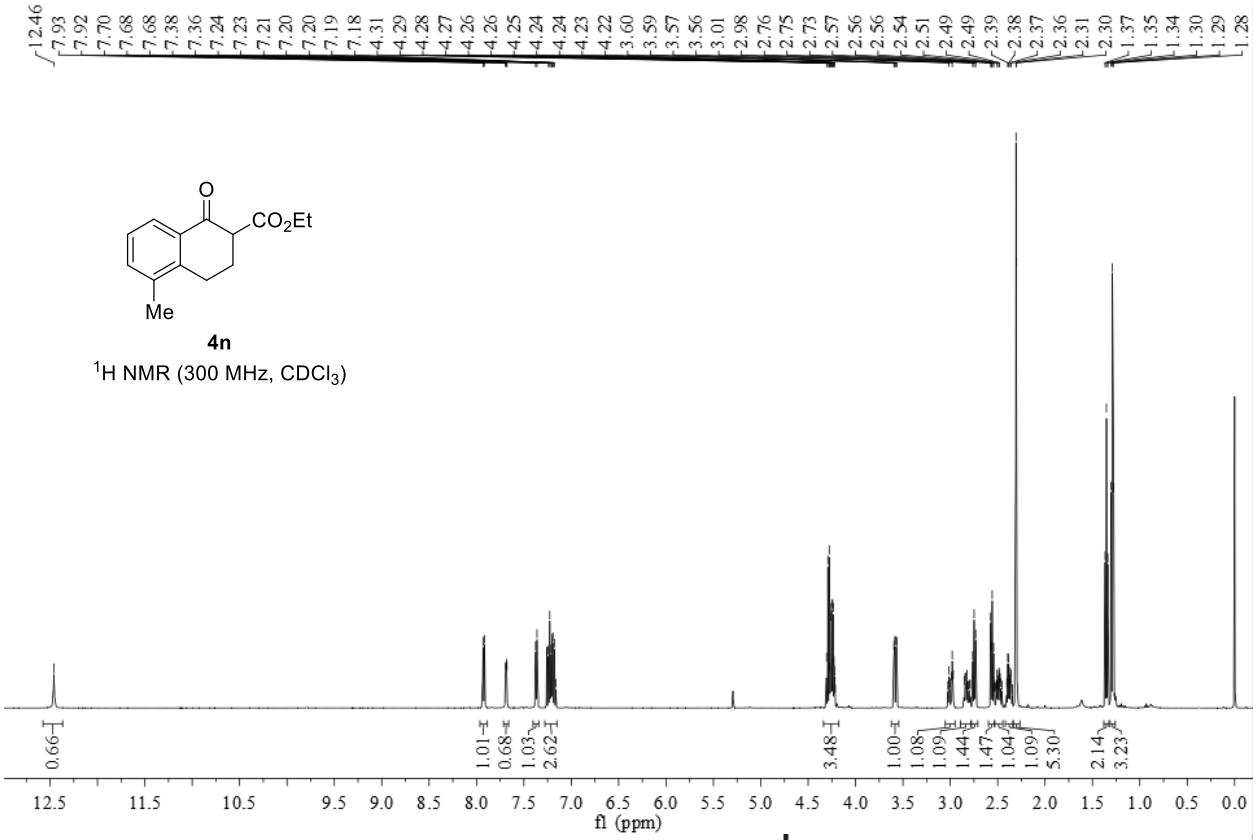

193.04
172.90
170.46
165.50
144.90
143.82
140.96
139.59
129.63
129.30
128.33
128.03
127.96
127.54
127.38
124.44
96.32
61.32
60.53
54.70
27.95
27.74
26.59
21.84
21.64
20.76
14.46
14.30
O
CO2Et
Me
4k
13C NMR (75 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


12.46
8.00
7.98
7.73
7.71
7.31
7.31
7.29
7.27
7.26
7.26
7.25
7.24
7.17
4.31
4.30
4.28
4.27
4.27
4.26
4.25
4.24
4.24
3.61
3.60
3.59
3.58
3.04
3.03
3.02
3.00
2.99
2.98
2.97
2.81
2.79
2.78
2.59
2.58
2.56
2.52
2.52
2.50
2.49
2.38
2.37
2.35
2.34
1.37
1.36
1.34
1.31
1.30
1.28
O
CO2Et
Cl
4l
1H NMR (300 MHz, CDCl3)
0.83
0.25
1.00
0.27
1.34
0.96
2.16
0.47
0.25
0.31
0.31
2.21
2.25
0.32
0.34
3.28
1.36
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


192.27
172.69
169.99
164.17
145.29
141.22
140.34
136.36
130.37
129.53
128.79
128.71
127.63
127.60
126.89
125.82
97.31
61.53
60.80
54.38
27.75
27.55
26.29
20.53
14.44
14.29
O
CO2Et
Cl
4l
13C NMR (75 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

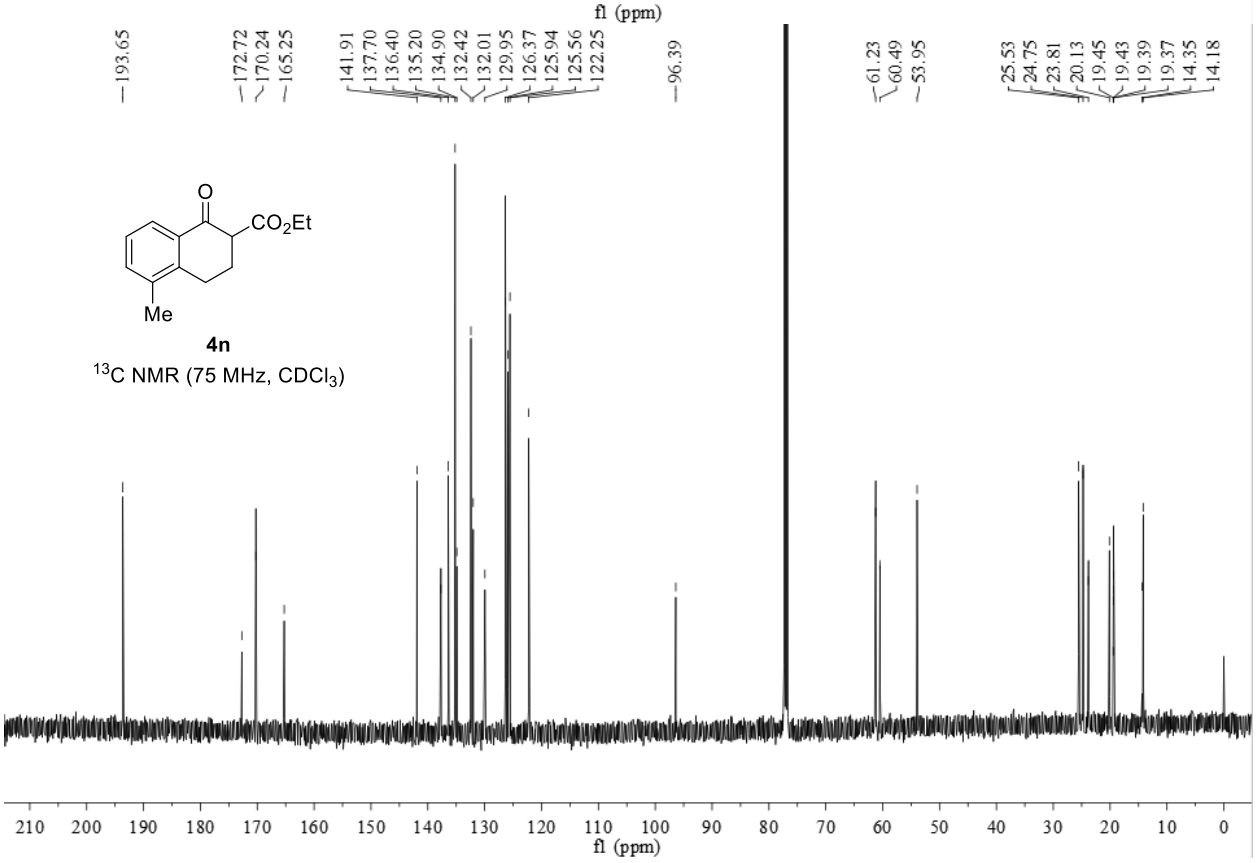

12.41
8.11
8.08
7.95
7.94
7.93
7.92
7.92
7.85
7.84
7.83
4.33
4.31
4.28
4.26
4.24
4.23
4.21
4.21
3.94
3.92
3.65
3.64
3.62
3.60
3.12
3.10
3.08
3.06
3.05
3.04
2.88
2.86
2.83
2.62
2.60
2.59
2.56
2.52
2.51
2.49
2.42
2.40
2.38
2.37
1.42
1.40
1.38
1.35
1.33
1.31
1.29
1.26
1.26
O
CO2Et
MeO2C
4m
1H NMR (300 MHz, CDCl3)
1.00
0.24
0.79
0.63
0.69
1.32
2.17
0.34
0.77
2.76
0.25
0.38
2.16
2.17
0.20
0.24
3.31
1.00
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


192.84
172.61
169.91
166.77
166.28
163.72
143.62
139.32
134.87
134.48
134.21
131.48
130.31
128.47
127.96
127.94
127.73
124.35
99.11
61.52
60.91
54.57
52.59
52.32
27.65
27.60
26.30
20.58
14.39
14.26
O
CO2Et
MeO2C
4m
13C NMR (75 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



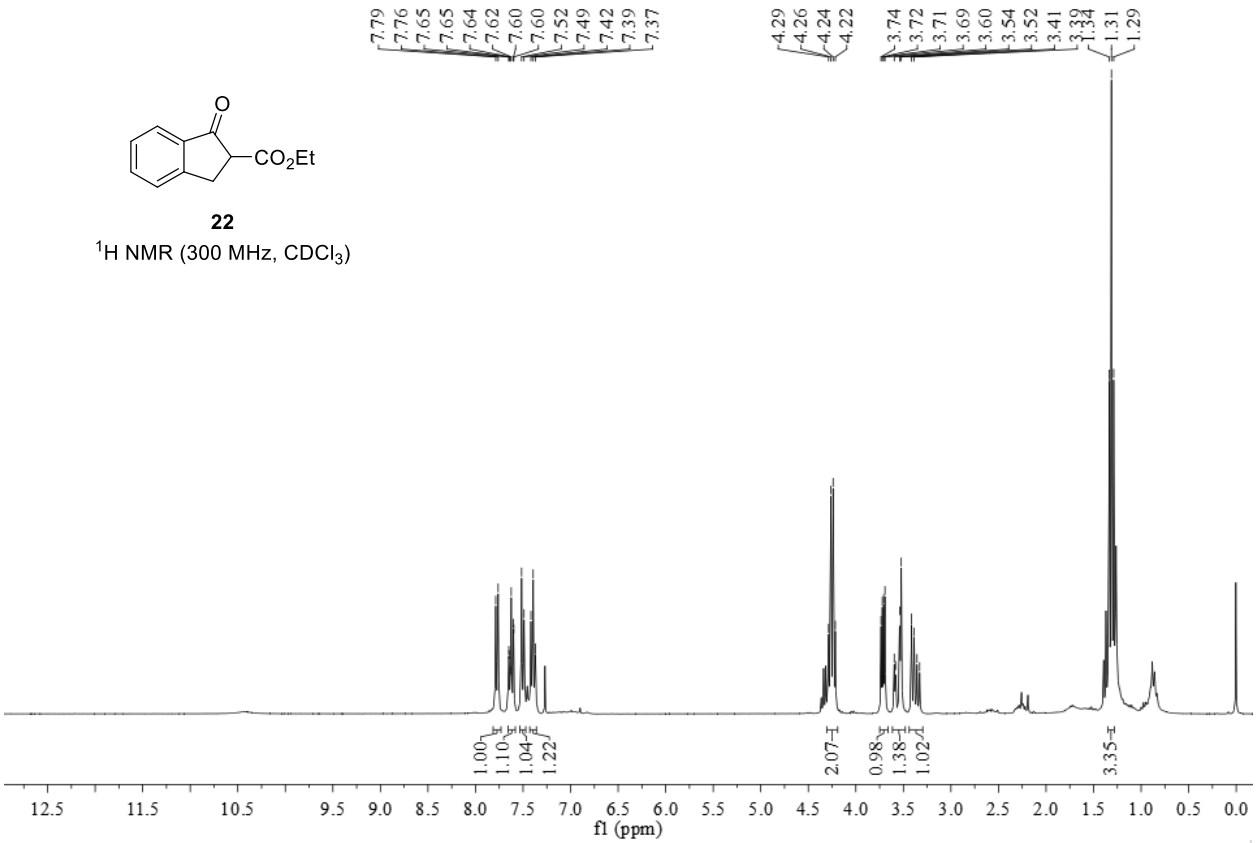

**4n**

$^{1}$H NMR (300 MHz, $CDCl_3$)



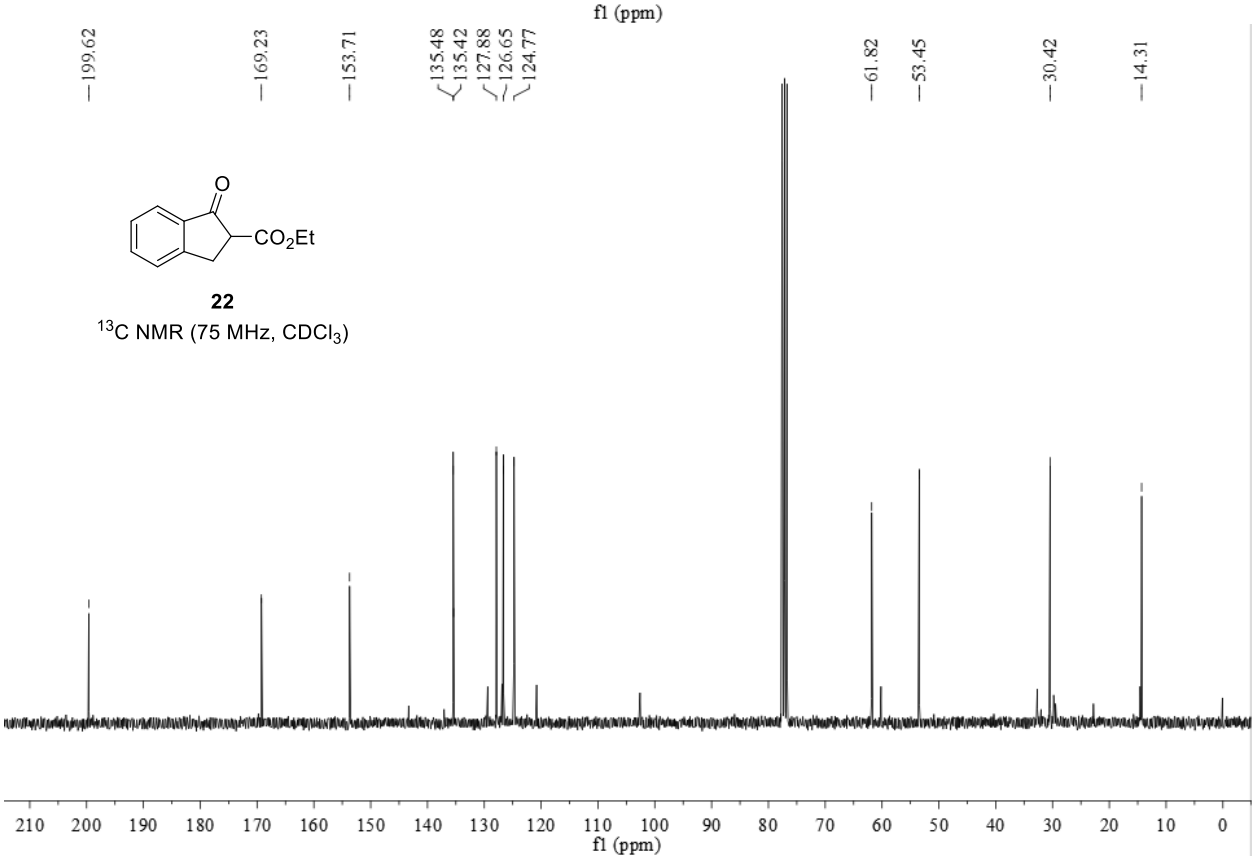

**4n**

$^{13}$C NMR (75 MHz, $CDCl_3$)



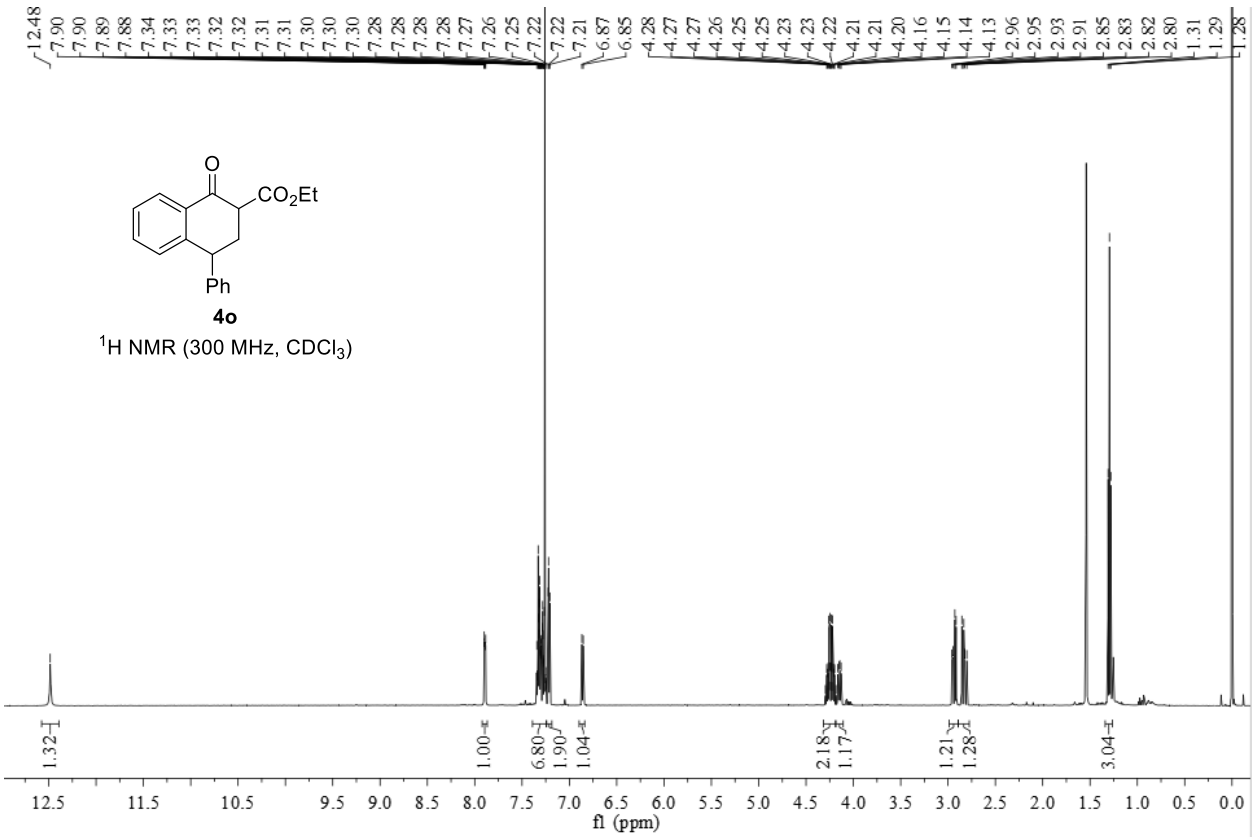

**22**

$^{1}$H NMR (300 MHz, $CDCl_3$)



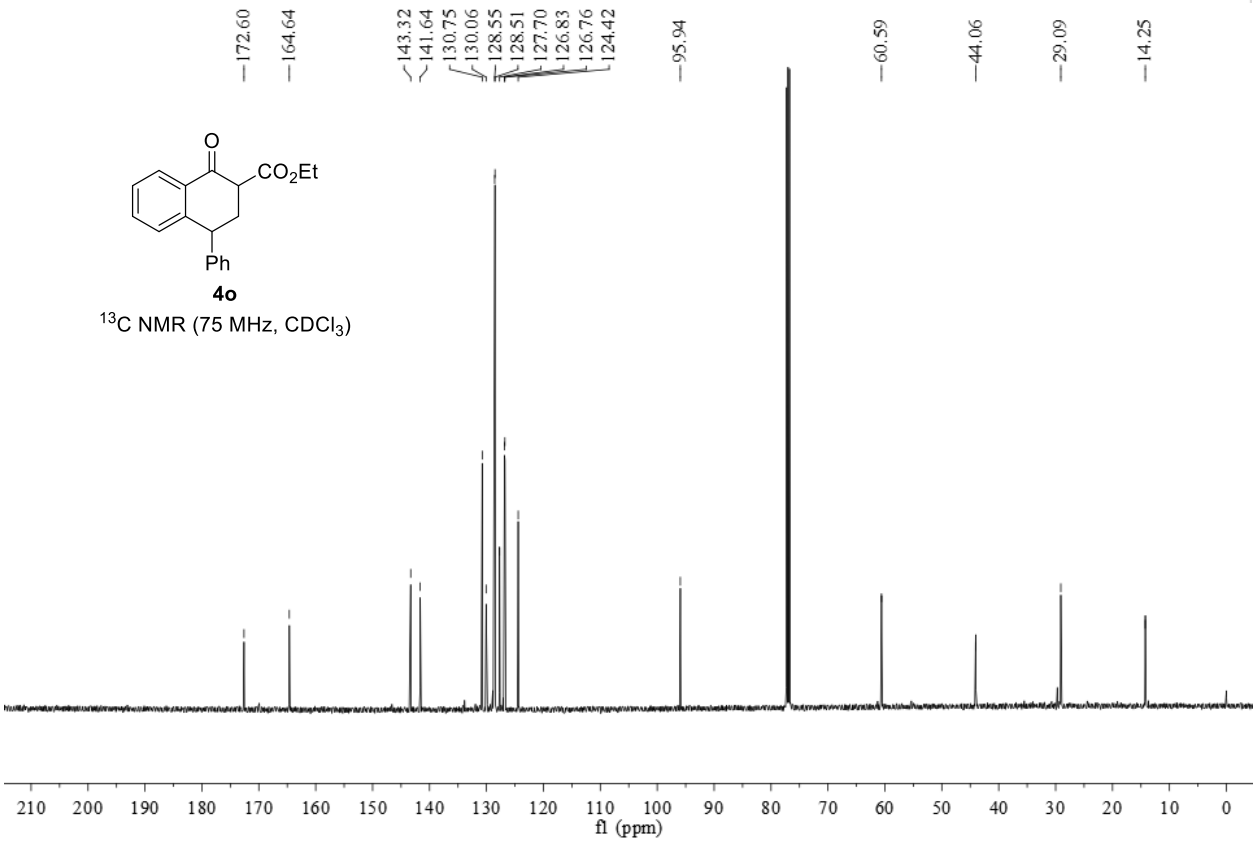

**22**

$^{13}$C NMR (75 MHz, $CDCl_3$)



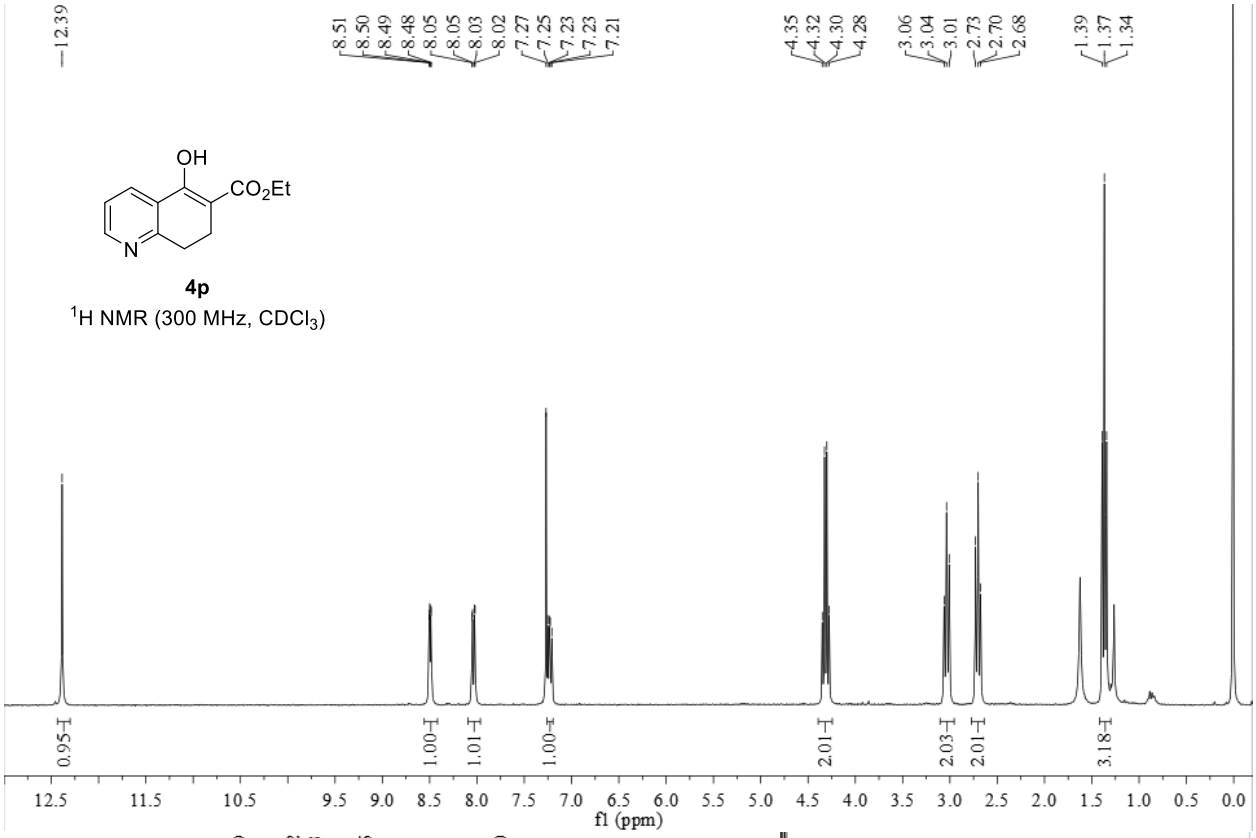

**4o**

$^{1}$H NMR (300 MHz, $CDCl_3$)



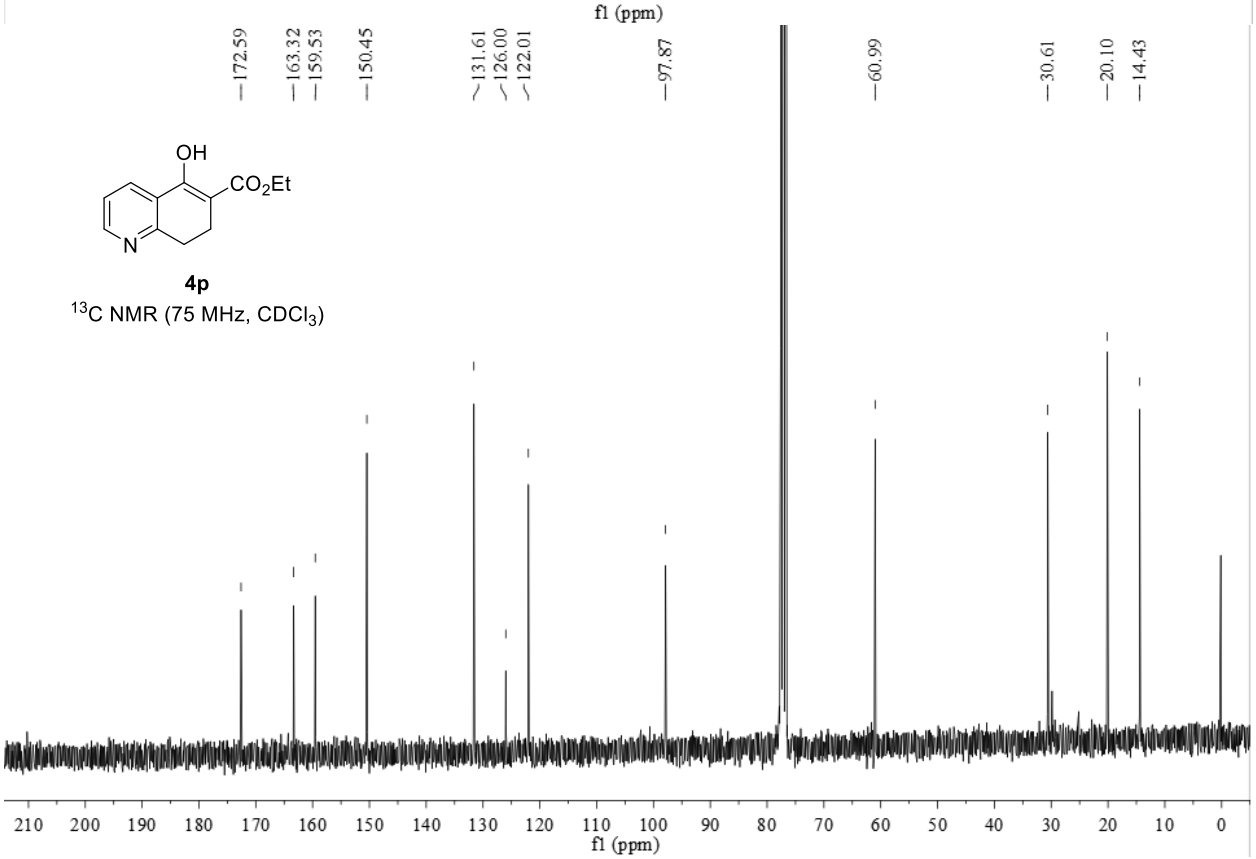

**4o**

$^{13}$C NMR (75 MHz, $CDCl_3$)



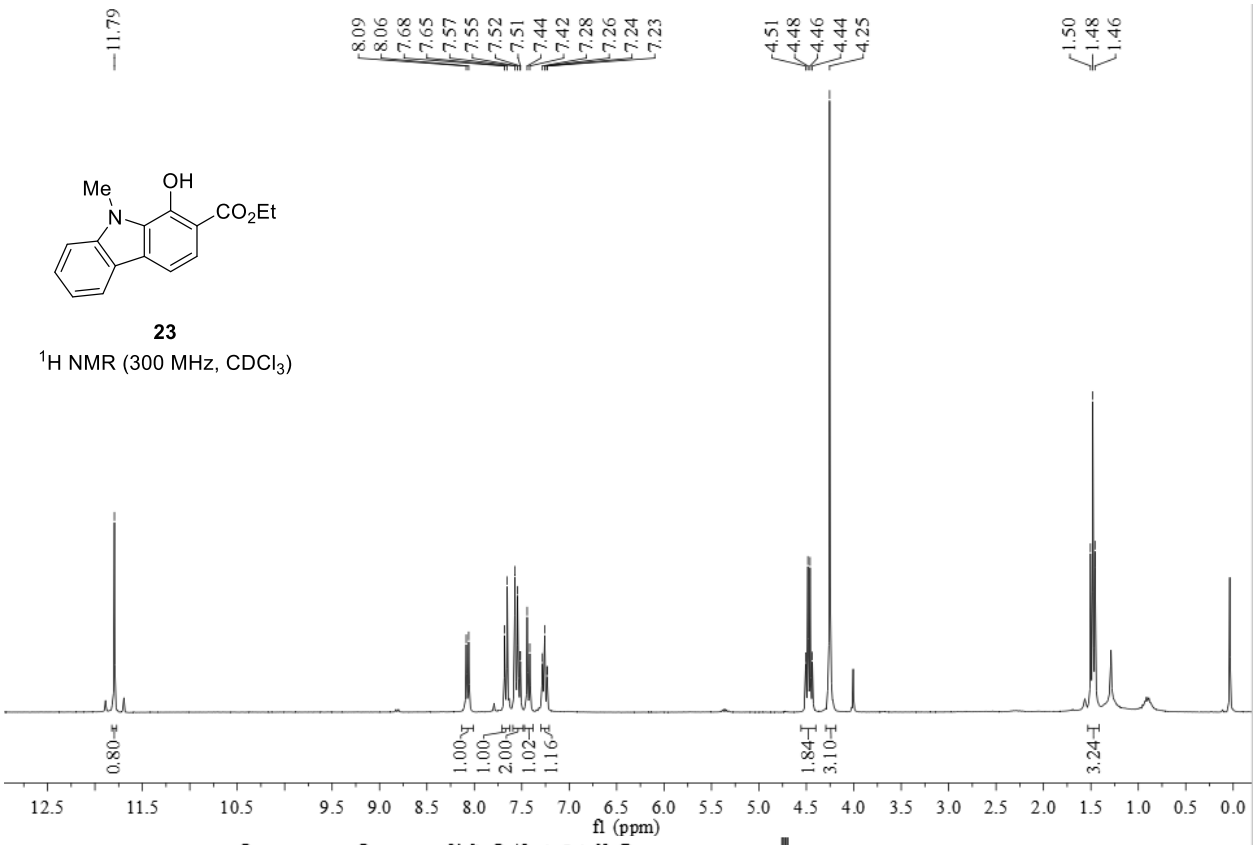

**4p**

$^{1}$H NMR (300 MHz, $CDCl_3$)



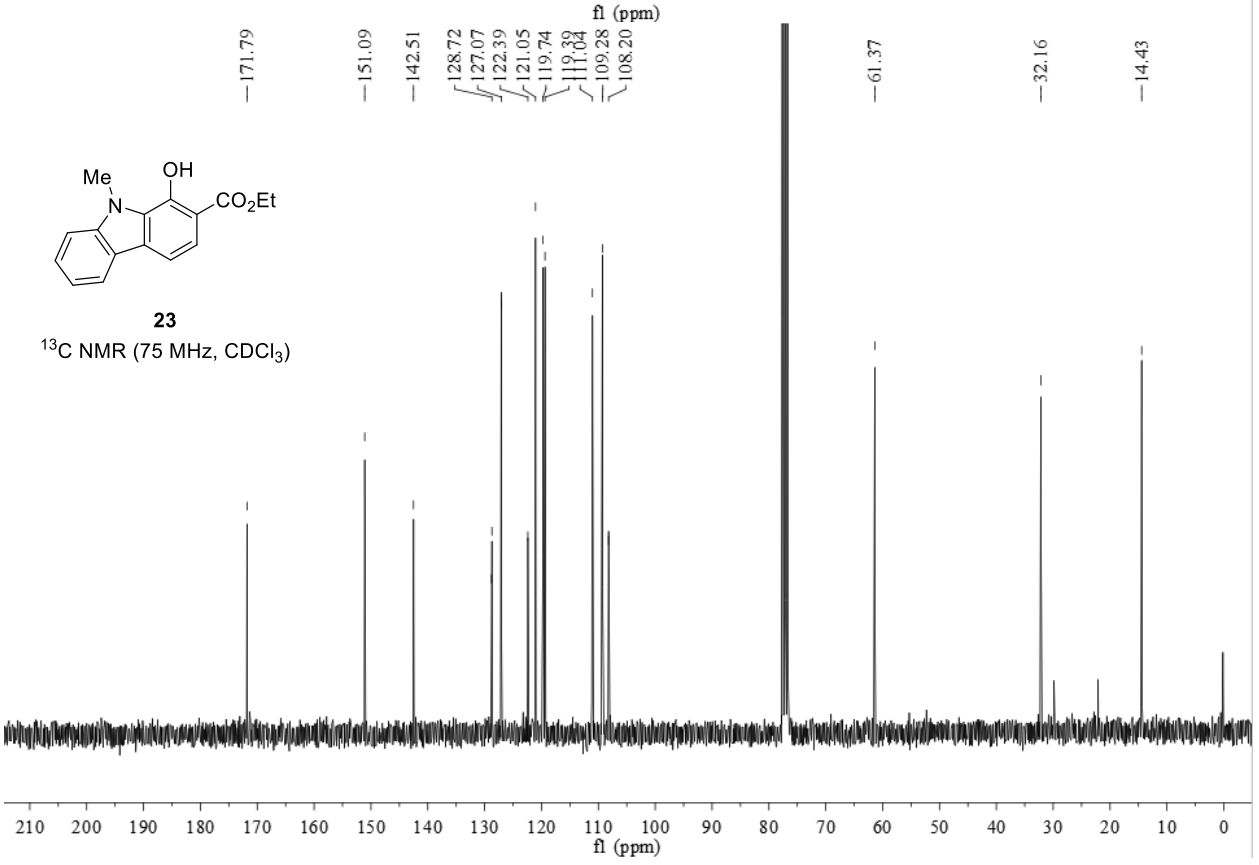

**4p**

$^{13}$C NMR (75 MHz, $CDCl_3$)



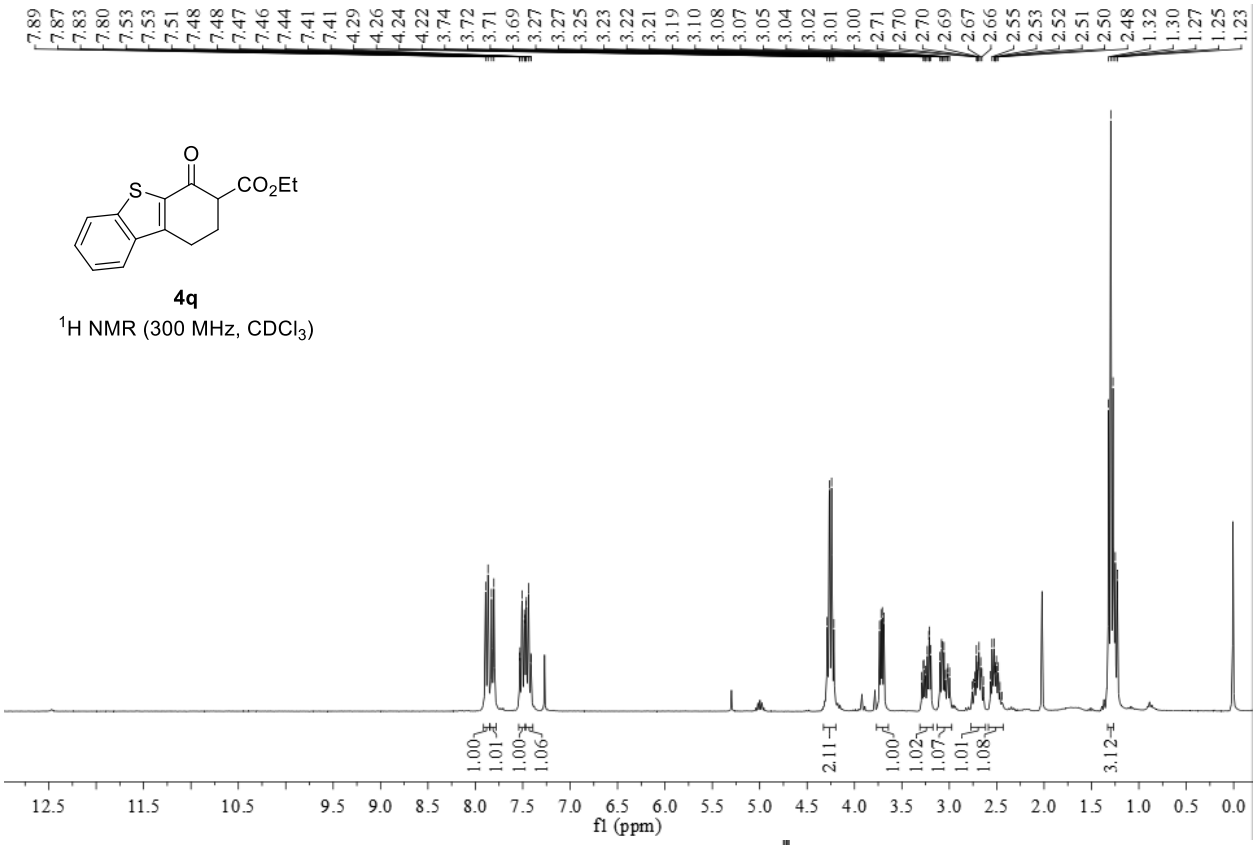

**23**

$^{1}$H NMR (300 MHz, $CDCl_3$)



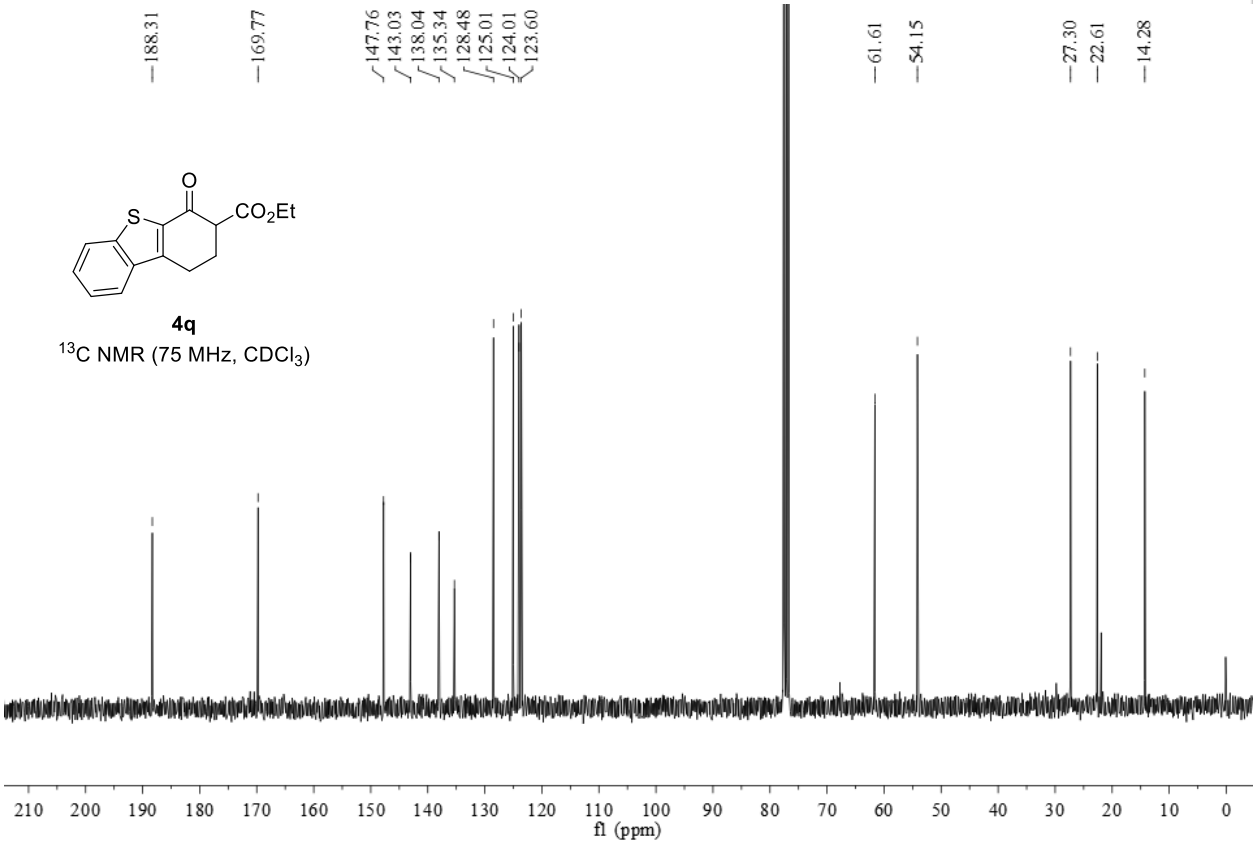

**23**

$^{13}$C NMR (75 MHz, $CDCl_3$)




**4q**

$^{1}$H NMR (300 MHz, $CDCl_3$)




**4q**

$^{13}$C NMR (75 MHz, $CDCl_3$)