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The Generation and Reactivity of Vinyl Carbocations

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The Generation and Reactivity of Vinyl Carbocations

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in Chemistry

by

Benjamin Wigman

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ABSTRACT OF THE DISSERTATION

The Generation and Reactivity of Vinyl Carbocations

by

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Doctor of Philosophy in Chemistry

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Professor Patrick G. Harran, Chair

This dissertation describes efforts to generate vinyl carbocation intermediates to leverage their high–reactivity, with a particular focus on subsequent C–H insertion reactions to forge new C–C bonds. These intermediates have historically been difficult to generate using catalytic regimes, but in doing so their reactivity can be controlled to give high-yielding methodologies. Additionally, efforts to search for new means to generate these intermediates often leads to discovery of novel reactivity. A variety of conditions have been developed to generate these intermediates that will be highlighted in five chapters of this thesis. An initial overview will be given to demonstrate how access to vinyl carbocations has steadily increased in the past decades, allowing for discovery of novel reactivity particularly highlighted by C–H functionalization.

Then, efforts of my colleagues and myself are partitioned into four main categories related to the generation of vinyl carbocations and their subsequent reactivity.

In the first chapter current state-of-the-art and previous methods of vinyl carbocation generation are reviewed to shed light on the massive amount of work already dedicated to producing these reactive intermediates. The second and third chapters cover the development of Brønsted basic conditions to generate these intermediates. These chapters detail the surprising discovery of utilizing lithium hexamethyl disilazide, a strong base, to generate vinyl carbocations that subsequently undergo C–H insertion reactions to yield olefinic products. These chapters will describe how these new basic conditions allowed for heteroatom containing substrates and additionally allowed for the use of much more easily accessible urea catalysts.

The fourth chapter describes electrochemical means to gain access to these intermediates primarily for nucleophilic fluorination to produce fluoro-olefins. This work was a direct result of the annoyance in needing to use strong Lewis acids; while still allowing fairly diverse substrates, these conditions drastically limited the types of reagents that could be utilized and overall limited the methodology. Instead, Lewis-acid free conditions utilizing electrodes to oxidize substrates to the vinyl carbocation intermediate were developed.

Finally, the fifth chapter details ongoing efforts to generate vinyl carbocations paired with chiral counterions to yield enantioselective C–H insertion reactions as well as the future outlook on other issues to tackle in developing new methodology. This work required small incremental discoveries in both catalyst and substrate design, and in all it took four PhD students almost two years to gain high levels of enantio- and regio- selectivity.

The dissertation of Benjamin Wigman is approved.

Neil Kamal Garg

Jose Alfonso Rodriguez

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Patrick G. Haran, Committee Chair

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2022

This dissertation is dedicated to my family.

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LIST OF ABBREVIATIONS

Ac = acetyl, acetate

AcOH = acetic acid

α = alpha

app. = apparent

aq. = aqueous

Ar = aryl

β = beta

br = broad

Bu = butyl

t-Bu = *tert*-butyl

°C = degrees Celsius

calcd = calculated

cat. = catalytic

Cl_{11} = $[CHB_{11}Cl_{11}]^-$

d = doublet

DC=direct current

dd = doublet of double

dr = diastereomeric ratio

δ = chemical shift

DCB = dichlorobenzene

DFB = difluorobenzene

DMF = dimethylformamide

DMSO = dimethylsulfoxide

equiv = equivalent

ESI = electrospray ionization

Et = ethyl

F_{15} = tris(pentafluorophenyl)borane

F_{20} = tetrakis(pentafluorophenyl)borate

g = gram(s)

h = hour(s)

HMDS = hexamethyldisilazane

HPLC = high performance liquid chromatography

HRMS = high resolution mass spectroscopy

Hz = Hertz

IR = infrared spectroscopy

i-Pr = isopropyl

J = coupling constant

L = liter

Li = lithium

LDA = lithium diisopropylamide

m = multiplet

m = meta

M = molar

m/z = mass to charge ratio

μ = micro

Me = methyl

MHz = megahertz

min = minutes

mol = mole(s)

MOM = methoxymethyl ether

mL= milli liter

mp = melting point

NMR = nuclear magnetic resonance

n-BuLi = *n*-butyl lithium

o = ortho

OTf = trifluoromethanesulfonate

OTs = *p*-toluenesulfonate

p = para

Ph = phenyl

pin = pinacolato

ppm = parts per million

Pr = propyl

q = quartet

rt = room temperature

s = singlet

t = triplet

TBAF = tetrabutyl ammonium fluoride

temp = temperature

TES = triethylsilyl

Tf = trifluoromethanesulfonyl

TFA = trifluoroacetic acid

THF = tetrahydrofuran

TIPS = triisopropylsilyl

TLC = thin layer chromatography

TMS = trimethylsilyl

Ts = *p*-toluenesulfonyl (tosyl)

UV = ultraviolet

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Firstly, I would like to thank my advisor Professor Hosea Nelson. Initially before visiting UCLA I didn't really know what graduate school to choose. However, simply after having lunch with Hosea on my visitation weekend my choice had become immediately obvious. Over the past five years there has never been a boring day in the lab, as Hosea ensures that we're always pushing to try new ideas, often times our own ideas. I never felt any of my tedious efforts were for nothing, and it made lab work feel much less like "work". Hosea has allowed for me the opportunity to make a hypothesis or think of a new idea, and test it in the lab with almost an endless supply of resources that any organic chemist in academia could need. I don't think this constant search for new discovery, with often times little precedent, is as prevalent in academic research as it should be. This experience has been invaluable to me and although hectic at times, I would not change any part of the journey so far. In addition to the opportunity he has given me in the lab, he has also spent many hours giving me advice in regards to practice talks, proposals, etc. Overall, he has been a highly supportive mentor.

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(2+2) and (2+1) reactions of vinyl carbocations over the past couple years and I hope one day these are published.

Overall, I have been able to meet many smart and motivated people throughout my time in graduate school. Graduate school is mostly a battle with oneself, but having nice people around makes it a million times better. Attending graduate school in West Los Angeles has been a great experience as well, I never thought that I would be so attached to going to the beach. If I were to go back and do it all over, I don't think I would change anything besides maybe eating a little more healthily.

Finally, I'd like to thank my family. My father inspired me to be a chemist; two times that really stick with me were learning how to clean up motor oil with the right solvent or making fire-crackers with Mg^{o} and $KMnO_4$. My mother allowed for me to focus on schoolwork much more than I am able to thank her for, and was always there to talk when things got tough. My identical twin was also great at supporting me throughout my PhD, and I always looked up to him as he was much more studious than I am. My older brother also served as a role model, I'm pretty sure he got a 5.0 GPA in high school, not totally sure how.

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- Department of Chemistry Outstanding Senior (Spring 2017)
- Outstanding Contribution to the Undergraduate Class (Spring 2017)

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2. **Chemocatalytic Amplification Probes Enable Transcriptionally-Regulated Au(I)-Catalysis in E. coli and Sensitive Detetion of SARS-CoV-2 RNA Fragments.** Green, S.A.; Wigman, B.; Nistanaki, S.K.; Montgomery, H.; Jones, C.G.; Nelson, H.M. *ChemRxiv* **2020**, https://doi.org/10.26434/chemrxiv.12915761.v2.

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4. **C–H Functionalization Reactions of Phenyl and Vinyl Carbocations Paired with Weakly Coordinating Anions.** Popov, S.; Shao, B.; Bagdasarian, A.L.; Wigman, B.; Nelson, H.M. *Syn. Lett.* **2020**, *31*, 1851–1856.

5. **Vinyl Carbocations Generated under Basic Conditions and their Intramolecular C–H Insertion Reactions.** Wigman, B.; Popov, S.; Bagdasarian, A. L.; Shao, B.; Benton, T.R.; Williams, C.G.; Fisher, S.P.; Lavallo, V.; Houk, K.N. *J. Am. Chem. Soc.* **2019**, *141,* 9140–9144.

CHAPTER ONE

Strategies to Generate Vinyl Carbocations

1.1 Abstract

Carbocations are one of the fundamental synthons in organic chemistry, acting as electrophiles. Many chemists refer/draw their electrophilic portion of a transformation in retrosynthesis as a cation, even though it may never carry a full positive charge, such as an aryl bromide in a palladium-catalyzed cross coupling reaction. These intermediates are widespread in synthetic organic chemistry, as well as in biological processes. Particularly well studied are alkyl or tricoordinated carbocations; this chapter will focus on the lesser-studied vinyl or dicoordinated carbocations. These latter intermediates are often regarded as higher-energy and thus have been challenging to generate. While many studies dating back to the 1960s do implicate vinyl carbocations, these methods of generation often rely on solvolysis and other harsh reaction conditions due to their high reactivity. Since the early methods of generation there have been tremendous amounts of effort made to produce these carbocations in much milder and tolerant fashions to yield novel reactivity. These efforts will be highlighted, particularly in the context of C–H insertion reactions.

1.2 Introduction

Carbocations have a rich history with a wide array of applications in synthetic organic chemistry that draw heavily from physical organic underpinnings.[1-3] A particular area of heated debate regarding these intermediates is that of the classical vs. non-classical carbocation debate of the 20th century.[4-7] This rich history and synthetic utility has culminated itself to be recognized

by the scientific community at large, and in 1994 the Nobel Prize in Chemistry was awarded to George Olah "for his contribution to carbocation chemistry".[8] Primarily this research and that of most focuses on sp^2 or tricoordinate carbenium ions (**1.1**, Figure 1.1); these stand in contrast to those of *sp* or dicoordinated carbenium ions (**1.2, 1.3).** The phenyl cation **1.3** will not be discussed in detail, but the principal remains the same for both vinyl and phenyl carbocations (dicoordinated).[9]

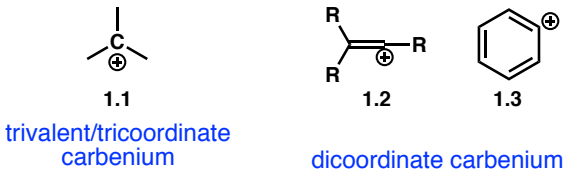

Figure 1.1 Different types of carbenium ions

Dicoordinated carbocations are often considered more reactive than tricoordinated carbocations due to their hybridization, including more *s*-character (sp^2 vs. *sp*).[10] This inherit destabilization perplexed chemists to the point that the existence of these intermediates wasn't feasible. One of the first examples that suggests otherwise is the solvolysis of vinyl bromides by Cseh, Grob, and Csapilla in 1964.[11] Initially solvolysis of a variety of vinyl bromides was performed, but the rate difference between the vinyl bromides with electron poor and electron donor groups was confounding (no reaction *vs.* reaction in this case) (Figure 1.2).

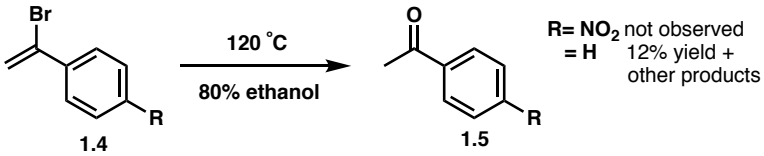

Figure 1.2 Solvolysis of vinyl bromides

The appended nitro group slowed down the rate of solvolysis to the ketone. They expected the vinyl bromide to serve as an electrophile in the rate-determining step of nucleophilic attack by solvent/water, but according to this trend it appeared that the rate-determining step actually relies on the ejection of the vinyl bromide to yield some type of carbocation. This carbocation is in turn

stabilized by the non-withdrawing group appended to the phenyl ring, a very early example of a Hammet-type analysis. This example serves as one of the first methods to generate vinyl carbocations, that of solvolyis of a leaving group. Many others have studied this type of reaction and done in-depth kinetic studies and even varied the leaving groups to also understand its effect.[12–14] Other leaving group examples include diazonium salts[15], iodonium salts[16], simple halides as seen above[17], and also triflates[18] and nonaflates[19]. These fundamental studies served as some of the testing grounds for the first means to generate vinyl carbocations, and a foundation for the rest of the field. I believe two key findings from these studies can be summarized in the following figure (Figure 1.3). The less linear a vinyl carbocation is, the higher in energy it is (see **1.6–1.8**). Additionally, appending electron donating groups or even substitutions around the vinyl cation (anything that donates electron density, see **1.9–1.11**) will lower the energy of the carbocation.[14,20]

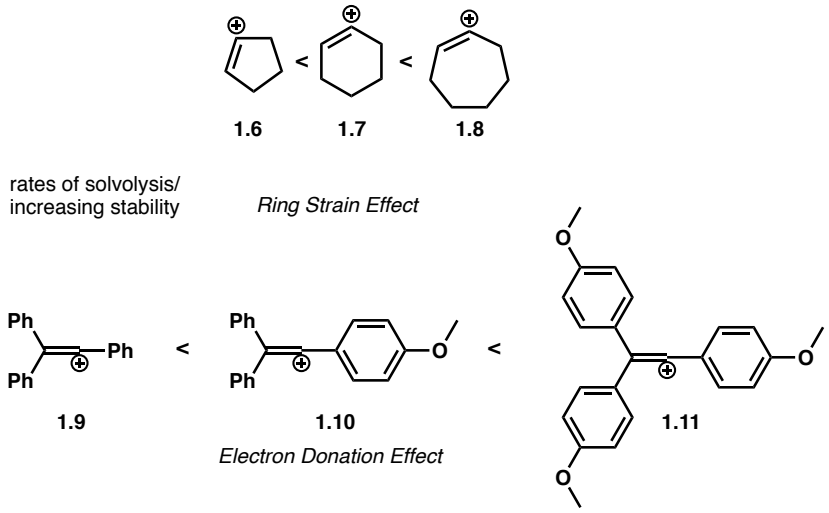

Figure 1.3 Relative Rates of Solvolysis: Dependent on Electronics and Ring Strain

With these initial studies it was at least known that these intermediates exist and what stabilizes them. This is an enormous contribution to the field, and with this many creative ways to generate vinyl carbocations have been discovered.

1.3 Non-thermolytic means to generate vinyl carbocations

I have chosen to separate thermolysis reactions to generate vinyl carbocations (section 1.2) into their own category; I think this is one of the divides between modern methods and early studies of vinyl carbocations. This section will focus on reactions where there is some catalyst or non-super stoichiometric reagent that is used to generate the vinyl carbocation, rather than simply heating in acid or solvent.

Likely the next contender for the most common way to generate vinyl carbocations is the activation/protonation of alkynes. This remains a constant area of research and new methodologies utilizing this strategy are still being published. One recent example demonstrating this is the activation of symmetric alkynes using chloroformates and stoichiometric Lewis acids. In this case, Metzger and coworkers propose the abstraction of a chloride from isopropyl chloroformate **1.12** (Figure 1.4) to yield an alkyl carbocation that subsequently can undergo nucleophilic attack by the alkyne **1.13** to yield vinyl carbocation **1.14**. This can undergo C–H insertion and reduction by triethyl silane to give the cyclopentane product **1.15**.[21] This set of conditions is quite powerful, as it is one of the first examples of high-yielding C–H insertion reactions of vinyl carbocations. These are observed in some solvolytic studies, but due to the presence of nucleophilic solvent, they are often only observed in trace amounts, even if the C–H insertion is intramolecular. Additionally this process is remarkable, as two C–C bonds are formed, including one intermolecularly.

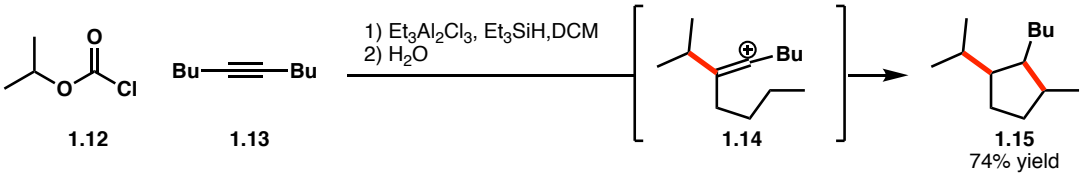

Figure 1.4 Activation of alkynes by Metzger and co-workers, 2006

Transition metals have been used to activate alkynes quite frequently. One key example that is very powerful is by Gaunt and coworkers.[22] Initially they reported the usage of a diaryliodonium triflate **1.16** (Figure **1.5**) to activate an alkyne (**1.17**); this is proposed to yield vinyl carbocation **1.18** that can subsequently be trapped in an intramolecular fashion to form a Friedel-Crafts product.

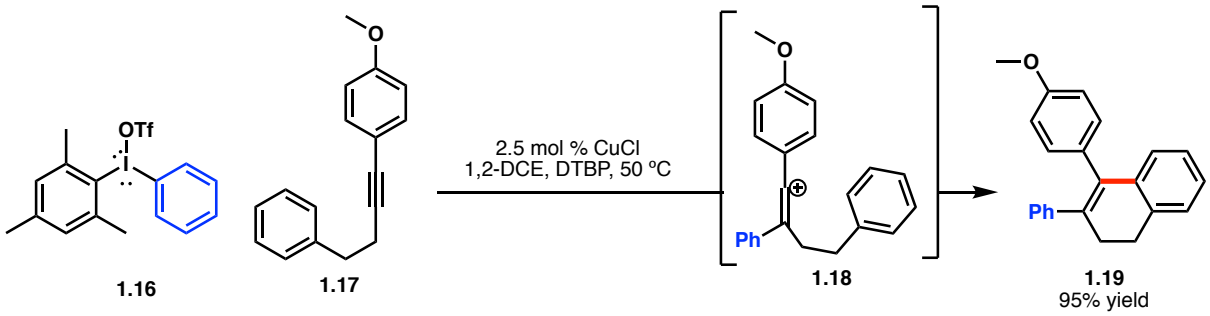

Figure 1.5 Copper activation of alkynes by Gaunt and co-workers, 2013

These reactions seem quite mild compared to the common use of strong Lewis acids, and their substrate scope demonstrates this. Oxazolidinones, N-Tosyl groups, chromanes, ketones, and morpholines are all tolerated in good yield. This was further extended to activate alkyl C–H bonds in 2014 by the same group through a similar proposed mechanism shown in Figure **1.6**. Again the diaryl iodonium triflate **1.16** can react with an alkyne (**1.20**), but in this case a tethered alkane is present that yields a cyclopentene product **1.21**.[23]

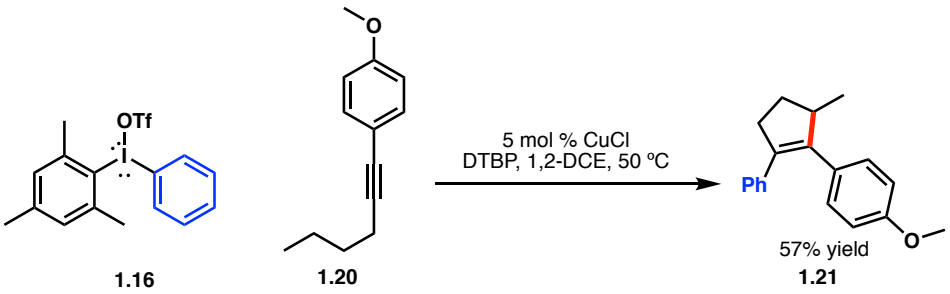

Figure 1.6 Copper activation of alkynes by Gaunt and co-workers followed by C–H insertion, 2014

One important aspect to note about this methodology is that typically activating alkynes in this fashion gives only trisubstituted olefinic products, but here two C–C bonds are being formed to yield a tetrasubstituted alkene. This usage of copper and high-valent iodonium salts has been utilized with alkynes to also generate vinyl carbocations that can subsequently be trapped by a variety of other nucleophiles.[24]

Another important example of vinyl cation generation using alkynes that highlights the a cascade reaction being employed with these intermediates is reported by Niggeman and coworkers.[25] Here (Figure 1.7) they employ an $Al(OTf)_3$ catalyst with Bu_4NPF_6 as an additive to promote the ionization of a benzylic alcohol **1.22** that is proposed to be subsequently attacked by alkyne **1.23** to yield a vinyl carbocation **1.24**. This is rather peculiar, as in this case they do not observe direct cyclization of the vinyl carbocation (**1.24**) onto the adjacent nucleophile, instead a bizarre 1,3-aryl shift is proposed to occur to yield the more stabilized allylic carbocation **1.25**; this undergoes cyclization to yield the final product **1.26**.

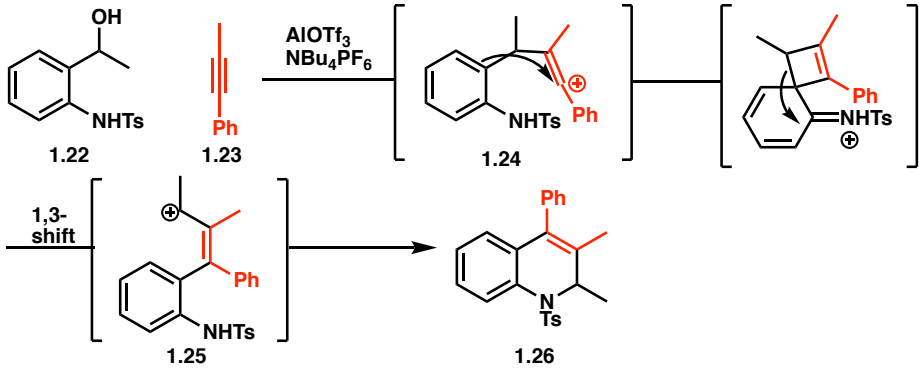

Figure 1.7 Alkyne activation and cascade cyclization by Niggeman and coworkers, 2017

Other metals have also been utilized to activate alkynes, particularly gold and silver.[26,27] In the case of gold, Au–NHC complexes have been observed by Das, Rasika-Dias and coworkers to cycloisomerize cycloctyne to bicyclooctene products. The proposed mechanism is shown in Figure 1.8, where the Au–NHC **1.27** is observed to bind to the alkyne **1.28** by X-ray

crystallography. This is then proposed to yield an Au-alkylidene complex **1.29**, a proposed resonance structure of the vinyl cation, that subsequently undergoes C–H insertion to give the cyclooctenyl products **1.30** after dissociation of the Au. Even more recently, Yu and coworkers have utilized cationic gold to promote cycloisomerization of linear diendiynes to access tricyclic products.[28]

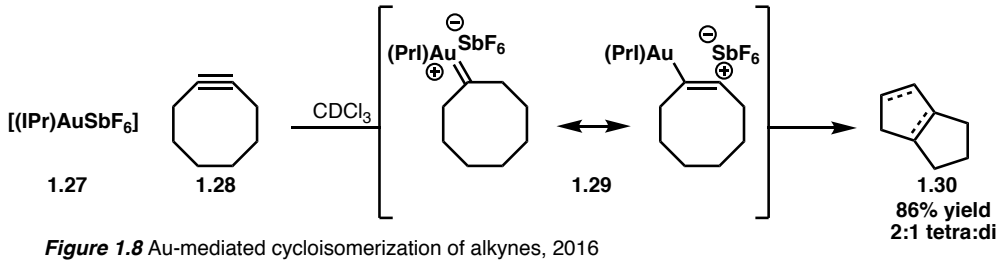

Figure 1.8 Au-mediated cycloisomerization of alkynes, 2016

Cationic silver also mediates these transformations, as demonstrated by Chen and co-workers.[26] Figure 1.9 shows the proposed reaction pathway for the reaction of alkyne **1.31** and olefin **1.32.** First the silver is proposed to bind to the alkyne and alkene, to yield alkyl carbocation **1.33** that can undergo alkyne addition to yield the silver alkylidene/vinyl carbocation **1.34/1.35,** which are proposed to be in equilibrium favoring the alkylylidene. This can subsequently undergo a C–H insertion with the cyclohexyl ring to yield product **1.36** after proto-demetallation.

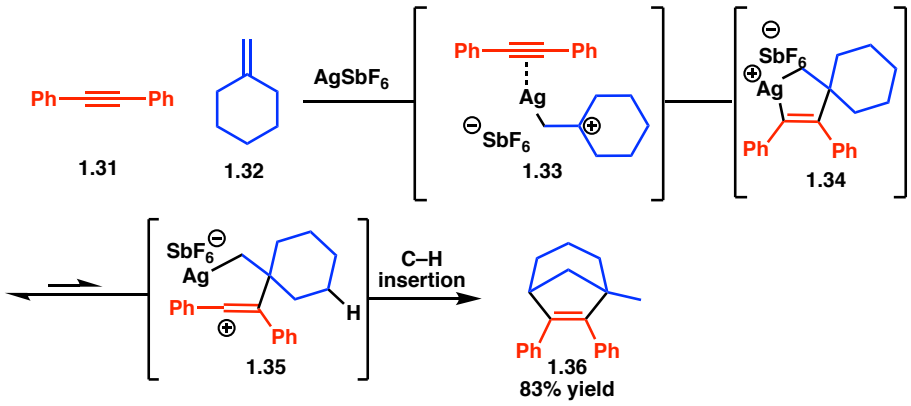

Figure 1.9 Alkyne activation and cascade cyclization by Chen and coworkers, 2018

Apart from transition metal activation of alkynes, one of the simplest ways to access vinyl carbocations is the protonation of alkynes. This type of generation dates back to the 1940's when acetylenic/alkynyl ethers were treated with aqueous/ethanolic solutions of acid by Jacobs and Searles at UCLA.[29] Their kinetic studies suggested the intermediacy of a carbocation produced after protonation of the alkynyl ether, yielding a vinyl carbocation. So, while this remains still a powerful way to generate vinyl carbocations, it dates back to one of the earliest methods to generate these intermediates. Now, non-aqueous acids such as trifluoromethanesulfonic acid or triflimide, can be used to prevent solvolytic reactions. Below in figure 1.10 is an example of triflimide used to protonate an alkene and activate an alkyne to promote a C–H insertion by Yamamoto and Jin and coworkers.[30] Here alkene **1.37** is proposed to be protonated and undergo nucleophilic attack by an alkyne of intermediate **1.38** to yield vinyl cation **1.39**. This is proposed to undergo a C–H functionalization, and it is posited to base promoted to give **1.41**.

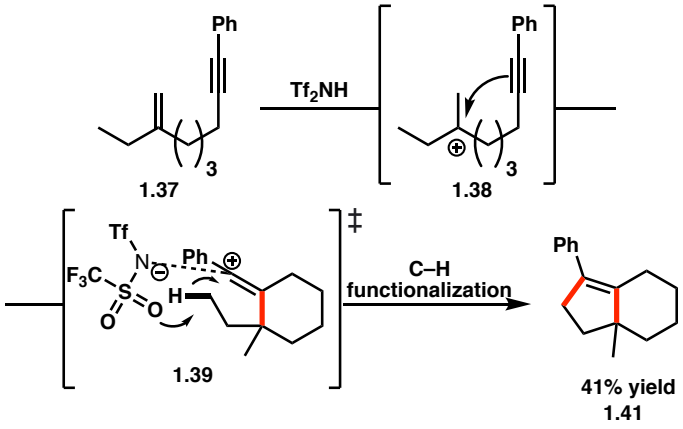

Figure 1.10 Alkyne activation by cascade 2010

An example of direct protonation is shown below (Figure 1.11), which I believe builds a lot of complexity from a simple substrate.[31] Here Chen and coworkers propose that alkyne **1.42** is directly protonated to give vinyl cation **1.43**. Instead of a concerted C–H insertion they propose a 1,5-hydride shift to yield alkyl carbocation **1.44** that can then undergo trapping by the

styrene to give benzylic carbocation **1.45**. Again, they propose a 1,5-hydride shift to give tertiary carbocation **1.46** that then is trapped by a Friedel-Crafts type reaction give the tricycle **1.47**.

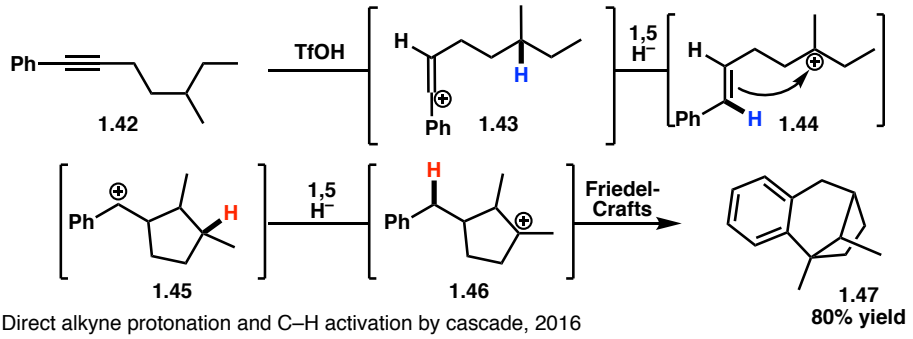

Figure 1.11 Direct alkyne protonation and C–H activation by cascade, 2016

This second 1,5-hydride shift is rather intriguing, as this apparently outcompetes E1 elimination. Their mechanistic proposal for this 1,5-hydride shift is a series of 1,2-hydride migrations to ultimately give carbocation **1.46**, that is indeed downhill in energy by 4.5 kcal/mol, according to calculations. These fairly modern examples demonstrate that by using common acids, complex cascade reactions that functionalize sp^3 C–H bonds can be promoted with vinyl carbocation intermediates.

Perhaps the next most common method to generate vinyl carbocations is that of leaving group abstraction. One example that we drew inspiration from initially in developing our work is by Brewer and coworkers in 2017 (Figure 1.12).[32] Here a β-hydroxy-α-diazo ketone (**1.48**) is activated by $SnCl_4$ to yield vinyldiazonium **1.49** that subsequently leaves to produce vinyl carbocation **1.50**. This undergoes a ring expansion, presumably to a lower energy non-α-keto cation, followed by a C–H insertion to yield **1.52**.

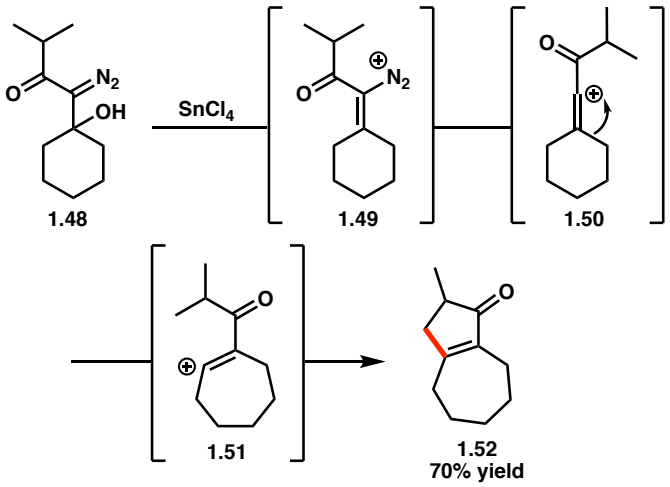

Figure 1.12 Leaving group abstraction and C–H activation by cascade 2017

An additional modern example incorporates weakly coordinating ions (WCA's) into their approach, very similar and reported shortly after our group published on Li^+ vinyl triflate abstraction (Figure **1.13**).[33] Here a lithium Lewis acid is used to promote the ionization of a vinyl triflate (**1.53**), that is subsequently trapped by solvent to produce a new C–C bond (**1.54**). While this is very similar to solvolysis, I chose to include this example as it is highly similar to our work and uses a catalyst to promote the cation formation.

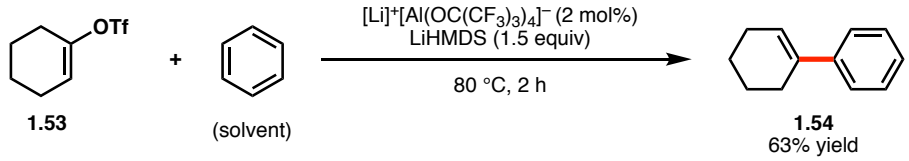

Figure 1.13 Lithium-aluminate promoted formation of vinyl carbocation, 2020

One other example of leaving group activation protonates a vinyl triazine that decomposes to a diazonium and subsequently produces the vinyl carbocation; this was work was performed in 1967 by Jones and Miller.[34] The above example in figure 1.13 and the work by Jones and Miller are the strategy that our lab traditionally utilizes. Initially we relied on the use of silylium Lewis acids paired with carborane WCA's to ionize vinyl triflates (**1.53)** that subsequently undergo intermolecular C–H insertion with alkanes to yield reduced products

(Figure 1.14).[35] This will be discussed in more detail in Chapter 2, but is shown here as the work performed by my previous colleagues is a large contribution to the field of vinyl carbocations and something that I based most of my PhD work on.

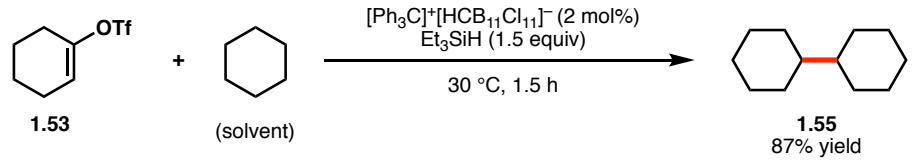

Figure 1.14 Silylium promoted vinyl carbocation formation and subsequent C–H insertion

The last two categories of vinyl carbocation generation to be discussed are the use of light and also radiolabelling. Light promoted vinyl carbocation formation does have some synthetic utility, and can produce fairly strained vinyl carbocations even at room temperature. The first example of this is a mechanistic study by Mayr and coworkers, where flash laser photolysis was used to ionize electron rich vinyl bromides (**1.56**) to the corresponding vinyl carbocation (**1.57**) (Figure 1.15).[36] This can subsequently react with a number of nucleophiles, of which the rate constant was also measured for each (**1.58**). Other examples of this include irradiating vinyl iodonium species that also yield vinyl carbocations; here cyclohexenyl and even cyclopentenyl vinyl carbocations can be generated.[37]

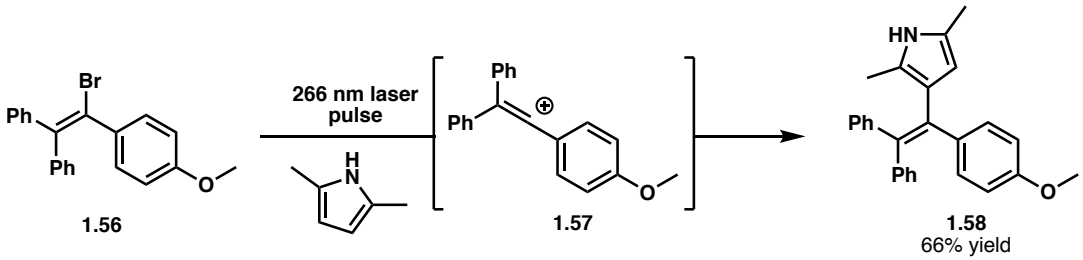

Figure 1.15 Flash laser promoted ionization of vinyl bromides to give vinyl carbocations, 2017

Finally radioactive decay to produce vinyl carbocations will be described. This is one of the most creative and fool-proof ways of generating these intermediates. While it may not be the most practical, it is a guarantee regardless of solvent, temperature, pressure or any other factor that may influence a typical reaction dealing with electrons. In this case Speranza and coworkers

prepared tritium labeled ethylene (**1.59**) that undergoes beta decay to helium and releases it to produce the ethenyl vinyl carbocation (**1.60**) (Figure 1.16).[38] This is likely the only solution phase study of the ethenyl vinyl carbocation, as it is quite unstable without any electron donor groups. It was shown to produce ethyl benzene upon storage in benzene/methanol.

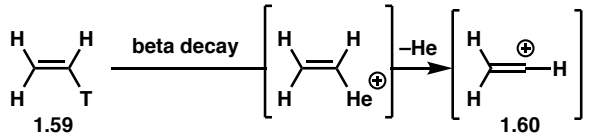

Figure 1.16 Proposed mechanism of beta decay, followed by heterolysis to give ethenyl carbocation, 1984

1.4 Conclusion

The methods mentioned above to generate vinyl carbocations can serve both synthetic and mechanistic purposes. Synthetic application is straightforward to envision why a method might be needed, but the mechanistic knowledge gained is equally invaluable. New ways to generate these intermediates have given us the ability to even crystallize vinyl carbocations and observe their fascinating linear geometry.[39,40] Generally the categories that have been covered include, solvolysis/thermolysis, leaving group abstraction, alkyne activation/protonation, photolysis, and radioactive decay. I hope that efforts to discover new ways to generate these intermediates continue, as each has its advantages and disadvantages.

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CHAPTER 2

Lithium-Weakly Coordinating Anion Lewis Acids Paired with Hexamethyldisilazide Brønsted Bases and their Usage to Generate Vinyl Carbocations

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2.1 Abstract

Here a novel Lewis acid system utilizing lithium paired with tetrakispentafluorophenyl borate in the presence of lithium hexamethyldisilazide (LiHMDS) is demonstrated to generate highly reactive vinyl carbocations from the corresponding vinyl triflate. These intermediates proceed to undergo facile C–H insertion reactions to forge C–C bonds and yield olefinic products. This surprising use of a Brønsted base in the presence of a Lewis acid has dramatically increased functional group tolerance compared to the previously utilized silylium Lewis acid conditions. Additionally, the reagents used are commercially available. Mechanistic studies are carried out to verify that a vinyl carbocation is present, and NMR experiments are performed to probe the Lewis acidity of the new catalytic system.

2.2 Introduction

Our group previously utilized silylium Lewis acids to generate both aryl and vinyl carbocations from the corresponding ortho-silyl aryl fluorides (**2.1**) and vinyl triflates (**2.2**) respectively (Figure 2.1).[1,2] Both of these reactions are quite powerful, as both promote the *inter*molecular C–H insertion reaction of highly reactive carbocations to forge new C–C bonds, all at or below 70 ºC.

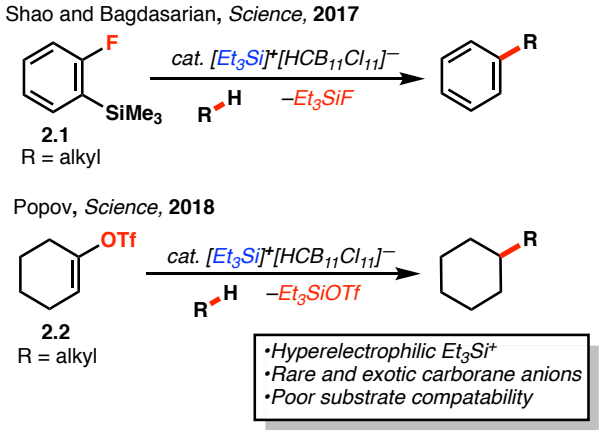


Figure 2.1 Our lab's previous means to generate dicoordinated carbocations

However, while this fundamental reactivity is powerful for the construction of new C–C bonds, it is drastically limited in scope. No heteroatoms were tolerated in the starting materials besides the triflate moiety itself, due to the hyperelectrophilic silylium. Generally, this can be perceived as a problem for the generation of most dicoordinated carbocations, as evidenced by several other literature reports.[3–5] We envisioned that a milder Lewis acid system could be utilized, that perhaps would lead to increased functional group tolerance. Reports by Michl and Uchiyama were inspiring as they utilized lithium salts to polymerize unactivated olefins (**2.3** transformed to **2.4**) at ambient temperatures and also abstract benzylic alcohols (**2.5**) to yield Friedel-Crafts products (**2.6**).[6–8] The latter transformation presumably took place in the presence of one equivalent of water (Figure 2.2).

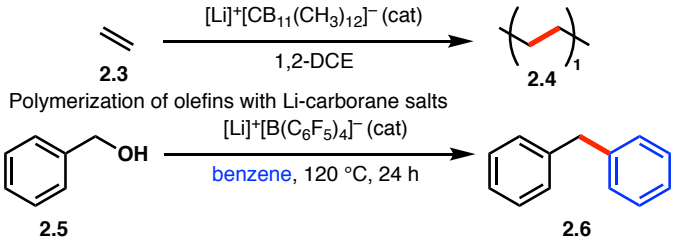


Figure 2.2 Literature applications of Li-WCA Lewis acids

2.3 LiHMDS Mediated C–H Insertion Reactions

With these previous examples it became clear that alkali and alkali earth metal cations paired with some weakly coordinating anion were good targets to investigate. The next piece that was required for screening new conditions was the substrate. From previous experience with vinyl carbocations in the group and literature evidence for linear precursors to undergo more facile ionization, a fairly linear, fast-reacting precursor was required to give the best chance for new discovery. Most screening prior to this endeavor had focused on the cyclohexenyl triflate (**2.2**), however, this yields a strained cyclohexenyl carbocation. I chose to screen conditions with the more linear cyclooctenyltriflate that was previously reported by our group to undergo nearly quantitative C–H insertion (**2.7** to **2.8**) in just under 15 minutes utilizing silylium as the Lewis acid (Figure 2.3).

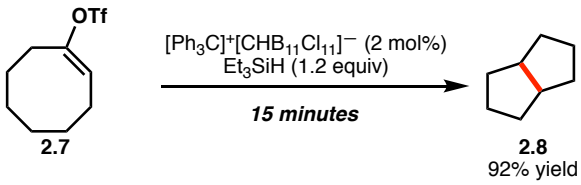


Figure 2.3 *Rapid C–H insertion of cyclooctenyl triflate*

With this in mind a variety of lithium, potassium, and magnesium salts were combined with catalytic amounts of $[Ph_3C]^+[HCB_{11}Cl_{11}]$ looking for consumption of the cyclooctenyl triflate. In most cases no consumption of this starting material was ever observed, even at elevated temperatures. However, when lithium hexamethyldisilazide was added, the starting

material was fully consumed in under one hour at room temperature (Figure 2.4). In this case a mixture of di-, tri-, and tetra- substituted olefins (**2.9**) was produced in nearly quantitative yield after some optimization (Table 2.1).

The proposed mechanism was very similar to the previous reports of C–H insertion, however in this case a strong Brønsted base is present which results in the production of the olefinic products. First it is proposed that the [Ph_3C][WCA] (**2.10**) undergoes nucleophilic attack by LiHMDS to produce the [Li][WCA] (**2.11**) that acts as the active Lewis acid. This can then abstract the vinyl triflate from (**2.7**) to yield a vinyl carbocation (**2.12**) paired with the WCA. A rapid transannular C–H insertion can occur to yield a mixture of alkyl carbocations (**2.13**); computations suggest a series of non-classical cations eventually yielding the tertiary carbocation that then undergoes deprotonation by LiHMDS to form the olefinic product (**2.9**) and also regenerates the active Lewis acid.

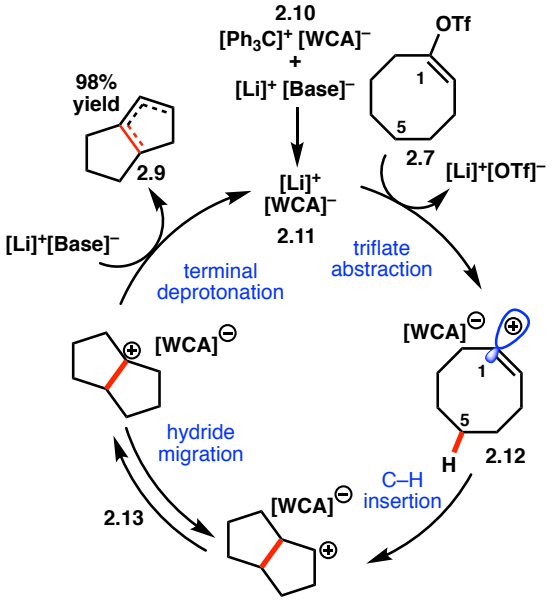


Figure 2.4 Proposed mechanism of transannular C–H insertion promoted by LiHMDS.

Additionally it was also surprising that the commercially available $[Ph_3C][B(C_6F_5)_4]$ outperformed the more exotic carborane salt (Table 2.1, entry 3). Further, the potassium and sodium salts did not promote the reaction, even at elevated temperatures.

entry	*cat.*	*catalyst loading*	*base (1.5 equiv)*	*solvent*	*yield*
1	$[Ph_3C]^+[CHB_{11}Cl_{11}]^-$	5 mol%	LiHMDS	*o*-DFB	90%
2	$[Ph_3C]^+[CHB_{11}Cl_{11}]^-$	5 mol%	LiHMDS	DCM	59%
3	$[Ph_3C]^+[B(C_6F_5)_4]^-$	5 mol%	LiHMDS	*o*-DFB	98%
4	none	0	LiHMDS	*o*-DFB	0%
5	$[Ph_3C]^+[B(C_6F_5)_4]^-$	5 mol%	NaHMDS	*o*-DFB	0%
6	$[Ph_3C]^+[B(C_6F_5)_4]^-$	5 mol%	KHMDS	*o*-DFB	0%
7	$[Li]^+[B(C_6F_5)_4]^-$	5 mol%	LiHMDS	*o*-DFB	84%

Table 2.1 Optimization table for transannular C–H insertion of cyclooctenyl triflate

In this case the differing reactivity was attributed to the cation Lewis acidity; this follows periodic trends, as you move farther down the periodic table the less Lewis acidic the cation is.[9] I was interested in validating this experimentally in our system. One popular way to compare Lewis acidities is known as the Gutmann-Beckett method.[10] A phosphine oxide is coordinated to a Lewis acid in a 1:1 fashion, and ^{31}P NMR gives a quantitative value to compare relative Lewis acidities. From this study (Figure 2.5) it was clear that the potassium salt was less Lewis acidic than that of the lithium salt. Furthermore it was demonstrated that in comparison to common lithium salts that I typically think the anion to be weakly coordinating, LiOTf and $LiBF_4$, LiHMDS is marginally more Lewis acidic. This data also shows the remarkable effect that when comparing the *in situ* generated lithium Lewis acid and the independently prepared $[Li][B(C_6F_5)_4]$, the LiHMDS only slightly decreases the Lewis acidity. Other relevant information is gained when comparing the carborane against the borate salt, it appears that $[Li][HCB_{11}Cl_{11}]$ is more Lewis acidic than $[Li][B(C_6F_5)_4]$. However, both of these Lewis acids pale in comparison to that of $[Et_3Si][B(C_6F_5)_4]$. These findings further bolstered the potential for these lithium Lewis acids to have functional group tolerance.

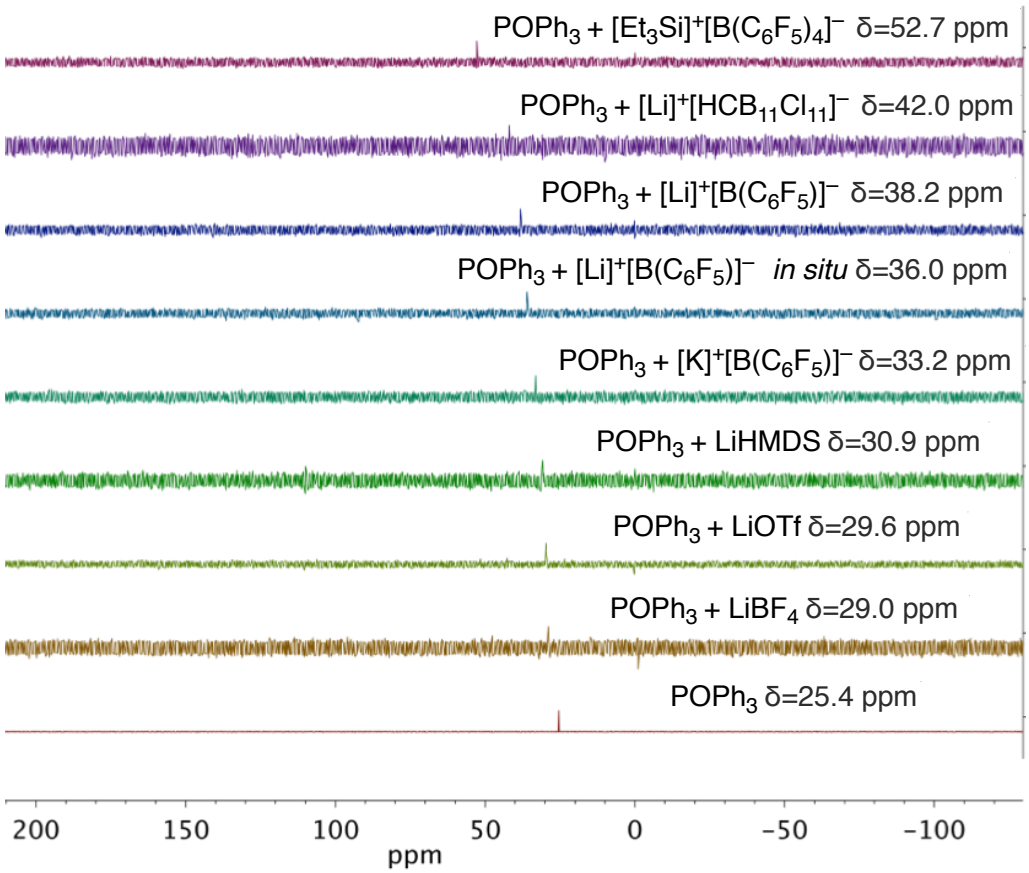


Figure 2.5 Gutmann-Beckett ^{31}P NMR spectra: further downfield indicates more Lewis acidity

With these results in hand, the primary goal became to see if these new conditions could tolerate Lewis basic heteroatoms. However, these new highly Brønsted basic conditions led to some issues with elimination of the vinyl carbocation intermediates. This is well documented in the literature and it occurs quite readily.[11] To combat this elimination a substrate class containing tetrasubstituted vinyl triflates was needed. We knew that the cyclooctenyl triflate could undergo high-yielding transannular C–H insertion without undergoing elimination, and so perhaps a tetrasubstituted vinyl triflate in a seven-membered ring may ionize and also prevent elimination (ring strain of the cyclooctyne or cycloheptyne preventing this). We had hoped making it benzo-fused and tetrasubstituted would provide enough electron donation to counteract the ring strain energy of the 7-membered vinyl carbocation; the benzosuberonyl triflate substrate class was

created accordingly (Figure 2.6). The general scheme of reactivity is shown starting from **2.14**; the alkylated benzosuberonyl triflate can undergo an annulation reaction to forge a new C–C bond. There were generally two sets of conditions that ended up being ideal: performing the reaction at room temperature in DCM (A) or at elevated temperature and more concentrated in cyclohexane (B).

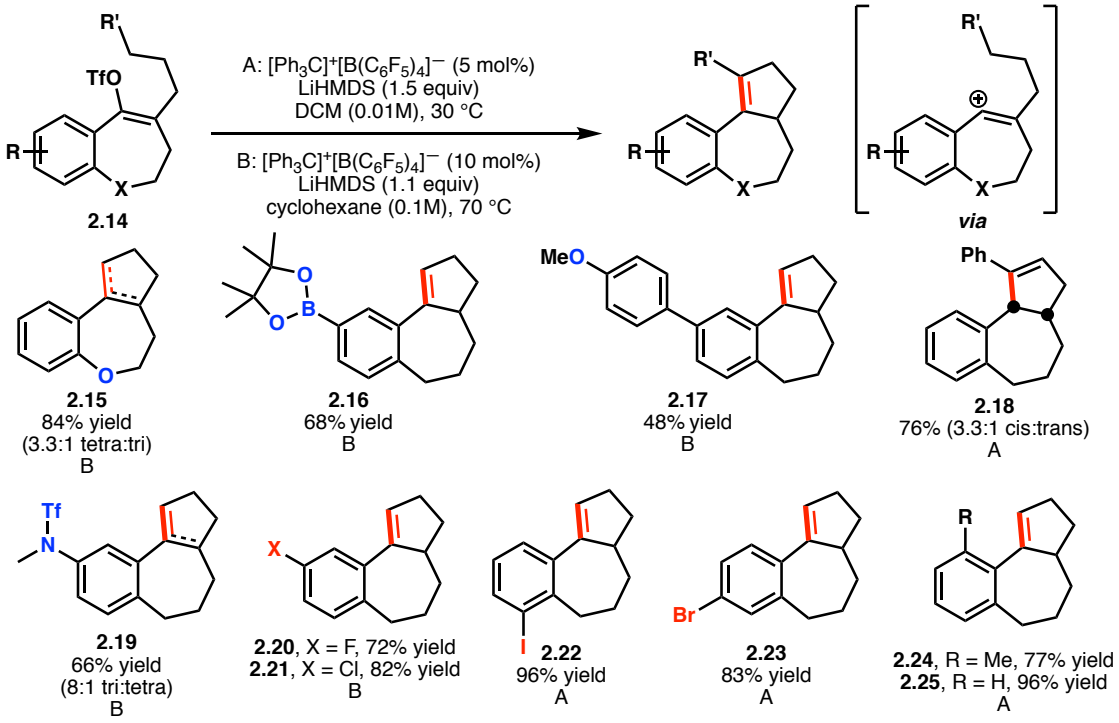


Figure 2.6 Alkylated benzosuberone triflate C–H annulation scope

Overall this substrate class gave highly selective product formation and primarily formed one or two olefin isomers. A benzoxapine (**2.15**), boronic ester (**2.16**), and extended anisole (**2.17**) were tolerated in moderate to good yield. In addition to activating 1º C–H bonds a benzylic C–H bond was functionalized to give **2.18**, a heavily protected nitrogen was tolerated (**2.19**), and several halogens that would typically react with transition metals were also tolerated (**2.20–2.23)**. Finally an electron rich ortho-methylated benzosuberone as well as the base benzeosuberonyl triflate under went rapid annulation (**2.24, 2.25**). Notably, **2.25** was produced

on a 1 mmol scale, and the olefin isomer ratio of the crude mixture was >20:1 with an isolated yield of 91%.

An additional class of cyclooctenyl triflate substrates was also produced, primarily by my selfless older colleagues Alex Bagdasarian and Brian Shao. Here the olefin isomers were more difficult to deal with. Purification of the styrenyl product was relatively easy using $AgNO_3$ impregnated silica gel, but isolation of the other olefins was rather troublesome (Figure 2.7). Particularly the isolation of the enol ether **2.27** from **2.26** was also difficult due to instability. The scope table below was able to show that even morpholines and thioethers can be tolerated (**2.28–2.29**).

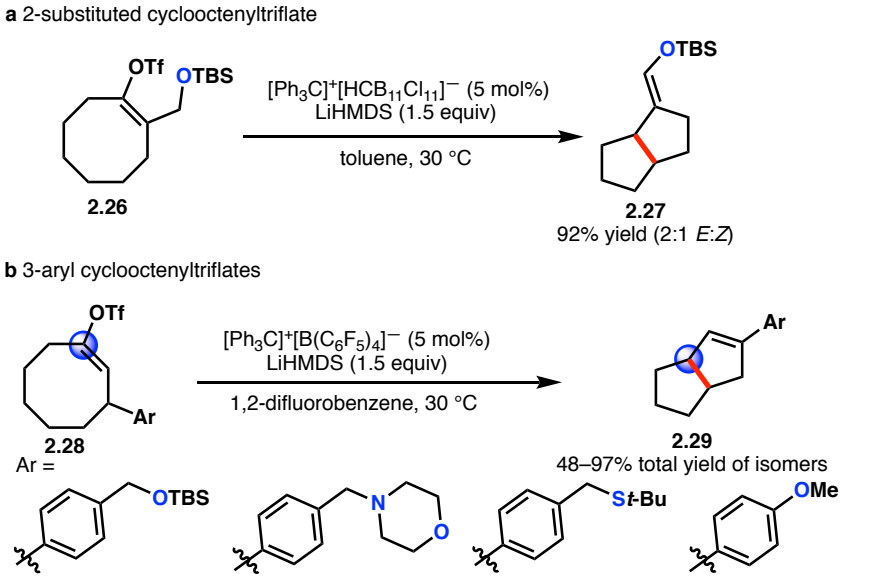


Figure 2.7 Cyclooctenyl triflate scope in the Li-WCA promoted C–H insertion reactions of vinyl cations

2.4 Mechanistic Studies

These Brønsted basic conditions were quite surprising, and even after demonstrating the substrate scope for this process I still had a lot of unanswered questions. Primarily what made LiHMDS so special? A brief lithium salt screen was able to give some insight into this, Figure 2.8, as more basic lithium salts (>26 pKa of LiHMDS) produced cyclooctyne.

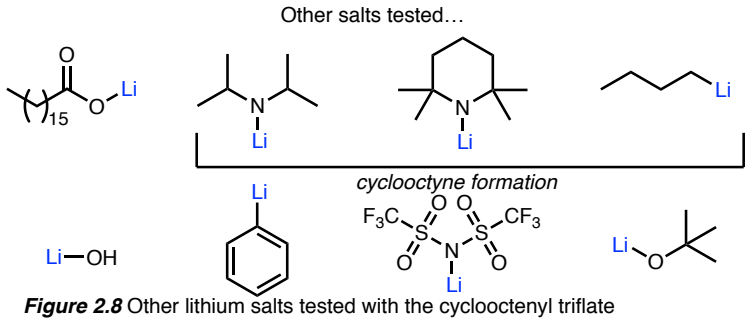


Figure 2.8 Other lithium salts tested with the cyclooctenyl triflate

The remainder of the lithium salts were either insoluble in arene/alkane solvents or already contained the Li–O bond that I hypothesized was driving the reaction to begin with.

One other broad remaining question was in regards to the mechanism. Under these basic conditions I wanted to validate that 1) a vinyl carbocation was still being generated 2) lithium was the active Lewis acid and 3) a concerted C–H insertion was the likely mechanism. To address the first question my colleague Stasik Popov utilized **2.30** as a mechanistic probe to see if any vinyl carbocation rearrangement would occur (Figure 2.9). Here the initial vinyl carbocation **2.31** would prefer to be more linear and have more electron donation from the aryl group, thus ring contracting to **2.32**. Indeed upon subjection of **2.30** to the reaction conditions in cyclohexane both the usual transannular C–H insertion product **2.33** and the rearrangement followed by C–H insertion product **2.34** were observed.

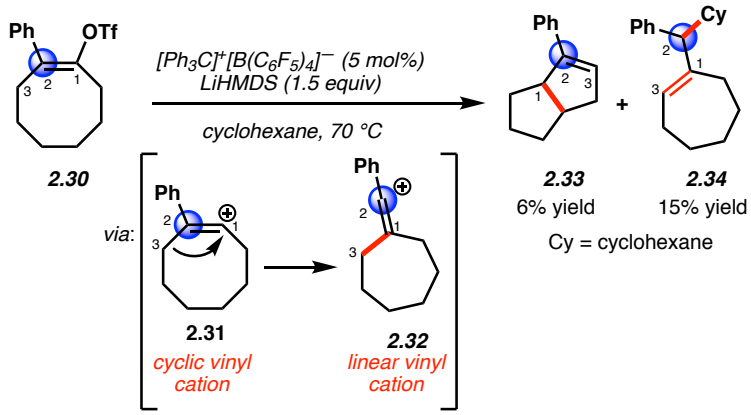


Figure 2.9 Ring contraction prone substrate to test for intermediate vinyl carbocation

The next mechanistic question was to validate that lithium is the active Lewis acid. This took two separate experiments. First, I wanted to verify by NMR that combining LiHMDS and $[Ph_3C][B(C_6F_5)_4]$ did produce $[Li][B(C_6F_5)_4]$. This reaction was observed to occur in C_6D_6 in a sealed NMR tube in less than one minute. The $[Li][B(C_6F_5)_4]$ was corroborated by ^{7}Li, ^{11}B, and ^{19}F spectroscopy. Additionally in this reaction the HMDS adduct of the trityl carbocation was observed, by only ^{1}H NMR, to be the para-adduct **2.35** (Figure 2.10).

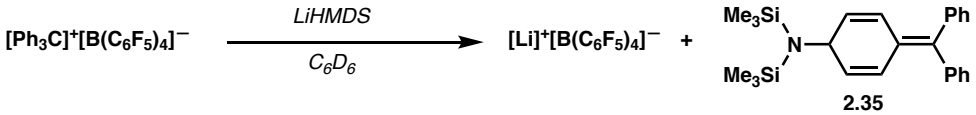


Figure 2.10 Reaction of LiHMDS and $[Ph_3C][B(C_6F_5)_4$

Additionally, the authentic lithium salt was prepared, and a stoichiometric amount was subjected to the benzosuberonyl vinyl triflate (Figure 2.11). Here the starting material was consumed and a fairly complex mixture was observed. However, one product was isolated that indicated new C–C bond formation (**2.36**). The proposed reasoning for the unsaturated product produced is due to the lack of base in the system. In this case we believe the only way to terminate the final alkyl carbocation is by some sort of intermolecular hydride transfer, which would yield a reduced rather than olefinic product. Additionally, LiOTf was observed by ^{19}F NMR validating that lithium is likely the abstraction reagent, and silylium from HMDS in solution is not the active Lewis acid.

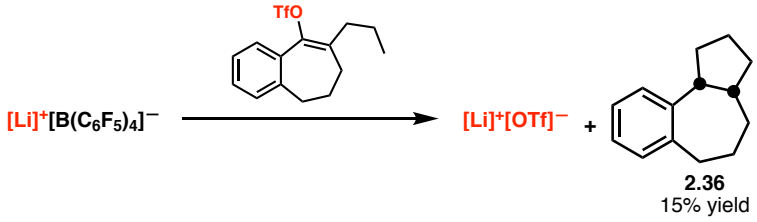


Figure 2.11 Stoichiometric catalyst production of unsaturated C–H insertion product and LiOTf

Finally to provide evidence for a concerted C–H insertion a substrate with an appended *tert*-butyl group (**2.37**, Figure 2.12) was prepared. Here the goal was to observe C–H

functionalization at the primary position; in this case it would produce a six membered ring (**2.38**). The production of a six-membered ring would rule out the possibility of a relatively facile 1,5-hydride transfer and only leave the highly unfavorable 1,6-hydride transfer as an alternative mechanism.[12–13] If the 1,6-hydride transfer did occur, an energetically disfavored primary carbocation would be produced, this would also likely undergo a rearrangement. In the end an 85% yield was obtained for the two styrenyl olefin isomers of **2.38**. No rearrangement products were detected in the crude ^{1}H NMR. Also interesting to note about this reaction was the temperature; at temperatures above –40ºC the other non-styrenyl olefin isomers were observed in a large amount (>25%). However, at –40ºC very small amounts were observed by ^{1}H NMR (<10%). In general temperature seemed to be the only controlling factor aside from the substrate in terms of alkene selectivity.

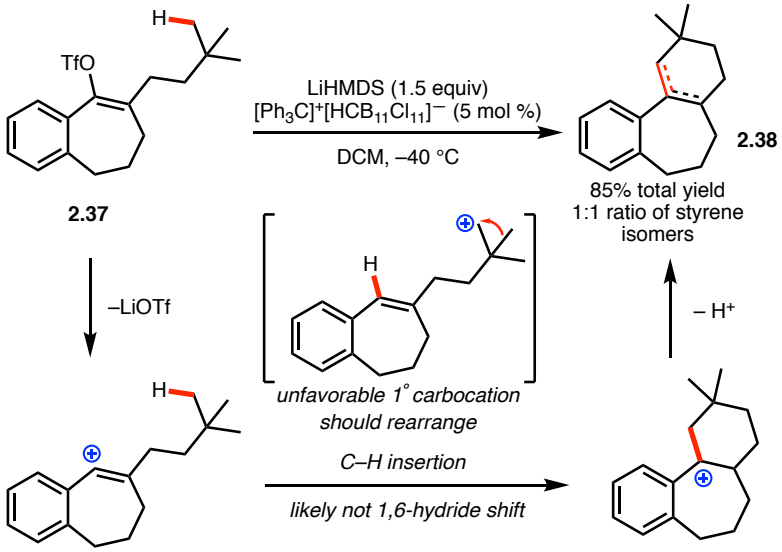


Figure 2.12 C–H insertion into primary C–H bond to form 6-membered ring as a mechanistic probe

2.5 Conclusion

In conclusion, the discovery of Brønsted basic but Lewis acidic conditions to heterolyze C–O bonds and yield vinyl carbocations was rather surprising. These highly reactive intermediates seemed unscathed by the strong amide base present in solution; intra-, and to some

extent inter-, molecular C–H insertion reactions were still possible, now giving olefinic products. Additionally these newfound conditions utilized commercially available reagents and tolerated previously incompatible morpholine, thioether, ether, amine, and boronic ester moieties. Mechanistic studies were performed to validate that the lithium Lewis acid was the active triflate abstraction agent and that a vinyl carbocation was likely being formed that subsequently undergoes a concerted C–H insertion process.

2.7 Experimental Section

2.7.1 Materials and Methods

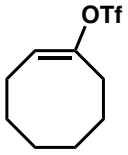
Unless otherwise stated, all reactions were performed in an MBraun glovebox under nitrogen atmosphere with ≤ 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and dried *in vacuo* before use. All liquid substrates were either dried over CaH_2 or filtered through dry neutral aluminum oxide. Solid substrates were dried over P_2O_5. All solvents were rigorously dried before use. Benzene, *o*-dichlorobenzene, and toluene were degassed and dried in a JC Meyer solvent system and stored inside a glovebox. Cyclohexane, fluorobenzene, and *n*-hexane were distilled over potassium. Chlorobenzene was distilled over sodium. *o*-Difluorobenzene was distilled over CaH_2. Pentane was distilled over sodium-potassium alloy. Chloroform was dried over CaH_2 and stored in a glovebox. Triethylsilane and triisopropylsilane were dried over sodium and stored inside a glovebox. *Closo*-Carborane catalysts were prepared according to literature procedure.[32] $[Li]^+[B(C_6F_5)_4]^-$ and $[K]^+[B(C_6F_5)_4]^-$ salts were synthesized according to literature procedure.[33] Hydrogen-bonding catalysts were prepared according to original or modified literature procedures.[34] Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. $AgNO_3$-Impregnated silica gel was prepared by mixing with a solution of $AgNO_3$ (150% v/w of 10% w/v solution in acetonitrile), removing solvent under reduced pressure, and drying at 120 °C. NMR spectra were recorded on a Bruker AV-300 (^1H, ^{19}F), Bruker AV-400 (^1H, ^{13}C, ^{19}F), Bruker DRX-500 (^1H), and Bruker AV-500 (^1H, ^{13}C). ^1H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^1H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz),

integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted otherwise. GC spectra were recorded on an Agilent 6850 series GC using an Agilent HP-1 (50 m, 0.32 mm ID, 0.25 mm DF) column. GCMS spectra were recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 mm DF) column interface at room temperature. IR Spectra were record on a Perkin Elmer 100 spectrometer and are reported in terms of frequency absorption (cm^{-1}). High resolution mass spectra (HR-MS) were recorded on a Waters (Micromass) GCT Premier spectrometer, a Waters (Micromass) LCT Premier, or an Agilent GC EI-MS, and are reported as follows: m/z (% relative intensity). Purification by preparative HPLC was done on an Agilent 1200 series instrument with a reverse phase Alltima C_{18} (5m, 25 cm length, 1 cm internal diameter) column.

2.7.2 Experimental Procedures for LiF_{20} Catalysis

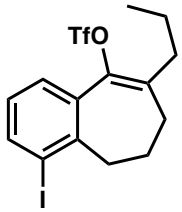
*Procedures and spectra for substrates in **Figure 2.6** are reported in the adapted article. Synthesis and spectra of substrates and products for **Figure 2.7** are reported in the adapated article.*

2.7.3 Preparation of Vinyl Triflate Substrates



(*E*)-Cyclooct-1-en-1-yl trifluoromethanesulfonate (2.7s). In a flame dried 250 mL round bottom flask, cyclooctanone (3.0 g, 23.8 mmol, 1.0 equiv) and freshly distilled 2-chloropyridine (3.0 g, 26.1 mmol, 1.1 equiv) were dissolved in anhydrous methylene chloride (90 mL). The

solution was cooled to 0 °C. Triflic anhydride (8.1 g, 28.5 mmol, 1.2 equiv) was added dropwise to the solution. After addition, the ice bath was removed and the reaction stirred for 16 hours. The reaction mixture was quenched with 0.5 M aqueous HCl (200 mL). The phases were separated and the aqueous layer was extracted with methylene chloride (2 x 100 mL). The combined organics were dried over magnesium sulfate, filtered and volatiles removed under reduced pressure to give the crude material as purple oil. The product was purified flash column chromatography (2% ether in hexanes) to give triflate **(2.7s)** as colorless oil (3.2 g, 51% yield). NMR data match those reported in literature.



4-iodo-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.22S).

In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (436 mg, 4.11 mmol, 3 equiv.) in anhydrous methylene chloride (14 mL). To this suspension was added corresponding ketone (450 mg, 1.37 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (426 mg, 1.51 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction wasn't done, triflic anhydride (426 mg, 1.51 mmol, 1.10 equiv.) and sodium carbonate (436 mg, 4.11 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (15 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as brown oil. The crude product was

purified by silica flash column chromatography (25% dichloromethane in hexanes) to give pure vinyl triflate **2.22S** as a yellow oil (298 mg, 47%).

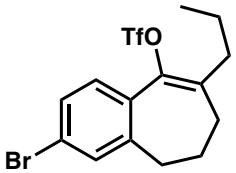
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.34 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 2.94 (t, *J* = 7.0 Hz, 2H), 2.56 – 2.28 (m, 2H), 2.19 (p, *J* = 7.2 Hz, 2H), 1.89 (t, *J* = 7.2 Hz, 2H), 1.65 – 1.55 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 139.8, 139.0, 136.6, 134.9, 127.6, 126.6, 118.3 (q, $^{1}J_{C–F}$ = 320.3 Hz), 100.5, 36.6, 34.1, 33.3, 28.2, 21.3, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.2.

FTIR (Neat film NaCl): 2963, 2936, 2865, 1551, 1452, 1411, 1278, 1245, 1115, 975, 859, 845, 787, 613.

HR-MS (EI-MS): Calculated for $C_{15}H_{16}F_3IO_3S$: 459.9817; measured: 459.9814.



3-bromo-8-propyl-6,7-dihydro-5H-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.23S). In a flame dried 100 mL roundbottom flask, sodium carbonate (628 mg, 5.90 mmol, 3.00 equiv.) was suspended in anhydrous methylene chloride (18 mL). To this suspension, corresponding ketone (0.556 g, 2.00 mmol, 1.00 equiv.) was added, and the reaction was cooled to 0 °C. Triflic anhydride (400 μL, 2.4 mmol, 1.20 equiv.) was added dropwise and the reaction was allowed to warm to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete additional triflic anhydride (400 μL, 2.4 mmol, 1.20 equiv.) and sodium carbonate (628 mg, 5.90 mmol, 3.00 equiv.) were added. Upon completion by TLC, the reaction was quenched with 50 mL of saturated aqueous sodium bicarbonate solution. The crude

product was then extracted with diethyl ether (3 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered, and then concentrated to give the crude compound. The crude product was purified by silica flash chromatography (100% hexanes to 1% ethyl acetate in hexanes) to give pure vinyl triflate **2.23S** as a white solid (628 mg, 77%).

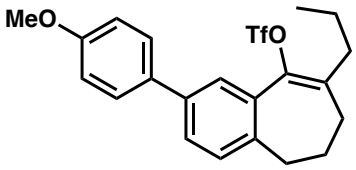
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 2H), 7.24 (d, *J* = 8.2 Hz, 1H), 2.66 (t, *J* = 7.2 Hz, 2H), 2.42 – 2.30 (m, 2H), 2.19 (p, *J* = 7.2 Hz, 2H), 1.92 (t, *J* = 7.2 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.01 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 138.7, 136.4, 132.8, 131.9, 129.4, 128.0, 123.0, 118.3 (q, $^{1}J_{C–F}$ = 320.1 Hz), 34.2, 34.1, 31.5, 28.1, 21.3, 14.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ –74.2.

FTIR (Neat film NaCl): 2962, 2937, 2867, 1663, 1589, 1477, 1409, 1205, 1138, 1085, 961, 858, 817, 607.

HR-MS (EI-MS): Calculated for $C_{15}H_{16}BrF_3O_3S$: 411.9956; measured: 411.9954.



2-(4-methoxyphenyl)-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.17S). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (188 mg, 1.77 mmol, 3 equiv.) in anhydrous methylene chloride (7 mL). To this suspension was added corresponding ketone (182 mg, 0.59 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (183 mg, 0.65 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic

anhydride (183 mg, 0.65 mmol, 1.10 equiv.) and sodium carbonate (188 mg, 1.77 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 10 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as brown oil. The crude product was purified by silica flash column chromatography (5% diethyl ether in hexanes) to give pure vinyl triflate **2.17S** as colorless oil (75 mg, 29%).

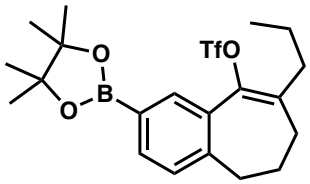
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 2.2 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.46 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 2.72 (t, *J* = 7.1 Hz, 2H), 2.41 (dd, *J* = 8.7, 6.9 Hz, 2H), 2.21 (p, *J* = 7.2 Hz, 2H), 1.97 (t, *J* = 7.2 Hz, 2H), 1.60 (sex, *J* = 8.0 Hz, 2H), 1.03 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 139.7, 139.3, 138.9, 135.7, 134.1, 133.0, 129.4, 127.9, 127.3, 124.78, 118.4 (q, $^{1}J_{C–F}$ = 320.3 Hz), 114.3, 55.3, 34.2, 34.1, 31.2, 28.2, 21.3, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.2.

FTIR (Neat film NaCl): 2961, 2937, 2868, 1610, 1520, 1489, 1410, 1246, 1210, 1140, 973, 826, 615.

HR-MS (EI-MS): Calculated for $C_{22}H_{23}F_3O_4S$: 440.1269; measured: 440.1273.



8-propyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.16S). In a flame dried 100 mL roundbottom flask was

suspended sodium carbonate (213 mg, 2.01 mmol, 3 equiv.) in anhydrous methylene chloride (7 mL). To this suspension was added corresponding ketone (220 mg, 0.67 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (208 mg, 0.74 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, an additional batch of triflic anhydride anhydride (208 mg, 0.74 mmol, 1.10 equiv.) and sodium carbonate (213 mg, 2.01 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 10 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as red oil. The crude product was purified by silica flash column chromatography (5% diethyl ether in hexanes) to give pure vinyl triflate **2.16S** as yellow oil (160 mg, 52%).

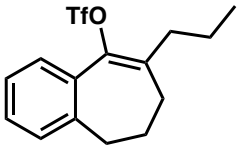
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.70 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 2.70 (t, *J* = 7.1 Hz, 2H), 2.48 – 2.30 (m, 2H), 2.19 (p, *J* = 7.2 Hz, 2H), 1.90 (t, *J* = 7.2 Hz, 2H), 1.58 (sex, *J* = 7.6 Hz, 2H), 1.34 (s, 12H), 1.01 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 139.6, 135.3, 135.3, 133.2, 133.0, 128.3, 118.3 (q, $^{1}J_{C–F}$ = 320.2 Hz), 83.9, 34.1, 33.9, 31.8, 28.0, 24.8, 21.3, 14.1. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.2.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.2.

HR-MS (EI-MS): Calculated for $C_{21}H_{28}BF_3O_3S$: 460.1703; Measured: 460.1712.



8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.25S). In a flame dried 100 mL round bottom flask was suspended sodium carbonate (563 mg, 5.31 mmol, 3 equiv.) in anhydrous methylene chloride (16 mL). To this suspension was added corresponding ketone (358 mg, 1.77 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (549 mg, 1.95 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (549 mg, 1.95 mmol, 1.10 equiv.) and sodium carbonate (563 mg, 5.31 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 30 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark red oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **2.25S** as yellow oil (540 mg, 91%).

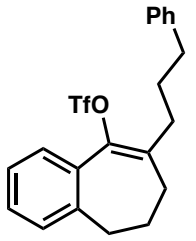
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 1H), 7.31 – 7.26 (m, 2H), 7.23 (dt, J = 4.6, 3.2 Hz, 1H), 2.70 (t, J = 7.1 Hz, 2H), 2.43 – 2.34 (m, 2H), 2.20 (p, J = 7.2 Hz, 2H), 1.93 (t, J = 7.2 Hz, 2H), 1.65 – 1.55 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.9, 139.6, 135.5, 133.8, 129.0, 128.9, 126.5, 126.2, 116.0 (q, $^{1}J_{C–F}$ = 258.0 Hz), 34.4, 34.1, 31.6, 28.1, 21.3, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.3.

FTIR (Neat film NaCl): 3069, 3027, 2937, 2864, 1455, 1411, 1208, 1140, 963, 857, 766, 678, 608.

HR-MS (EI-MS): Calculated for $C_{15}H_{17}F_3O_3S$: 334.0851; measured: 334.0866.



8-(3-phenylpropyl)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.18S). In a flame dried 100 mL round bottom flask was suspended sodium carbonate (857 mg, 8.08 mmol, 3 equiv.) in anhydrous methylene chloride (25 mL). To this suspension was added corresponding ketone (750 mg, 2.69 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (836 mg, 2.96 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (836 mg, 2.96 mmol, 1.10 equiv.) and sodium carbonate (857 mg, 8.08 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as a dark red oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **2.18S** as a yellow oil (880 mg, 80%).

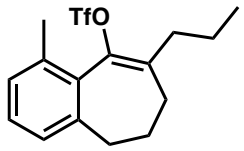
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 1H), 7.33 – 7.26 (m, 4H), 7.24 – 7.17 (m, 4H), 2.70 (dt, J = 13.8, 7.5 Hz, 4H), 2.52 – 2.40 (m, 2H), 2.19 (p, J = 7.1 Hz, 2H), 1.98 – 1.83 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 140.9, 139.7, 135.2, 133.7, 129.1, 128.9, 128.4 (2C), 126.5, 126.2, 125.9, 118.3 (q, $^1J_{C–F}$ = 320.3 Hz), 36.0, 34.4, 32.0, 31.6, 30.0, 28.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.2.

FTIR (Neat film NaCl): 3027, 2937, 2862, 1603, 1467, 1454, 1410, 1208, 1139, 996, 961, 854, 766, 699, 608, 514.

HR-MS (EI-MS): Calculated for $C_{21}H_{21}F_3O_3S$: 410.1164; measured: 410.1179.



1-methyl-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.24S).

In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (572 mg, 5.39 mmol, 3 equiv.) in anhydrous methylene chloride (15 mL). To this suspension was added ketone corresponding ketone (389 mg, 1.80 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (558 mg, 1.98 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (558 mg, 1.98 mmol, 1.10 equiv.) and sodium carbonate (572 mg, 5.39 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark brown oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **2.24S** as a yellow oil (437 mg, 70%).

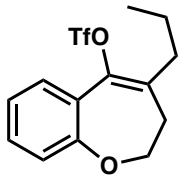
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 2.84 (td, *J* = 13.1, 7.8 Hz, 1H), 2.67 – 2.52 (m, 1H), 2.50 – 2.36 (m, 2H), 2.33 (s, 3H), 2.16 (tt, *J* = 13.0, 6.8 Hz, 1H), 2.07 – 1.93 (m, 2H), 1.85 – 1.54 (m, 3H), 1.03 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.2, 139.1, 136.7, 136.5, 132.1, 129.3, 128.7, 126.1, 118.2 (q, $^{1}J_{C-F}$ = 320.4 Hz), 33.3, 33.1, 31.5, 27.6, 21.2, 20.2, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ –75.0.

FTIR (Neat film NaCl): 2962, 2864, 1461, 1411, 1209, 1140, 963, 857, 829, 613.

HR-MS (EI-MS): Calculated for $C_{16}H_{29}F_3O_3S$: 348.1007; measured: 348.1001.



4-propyl-2,3-dihydrobenzo[*b*]oxepin-5-yl trifluoromethanesulfonate (2.15S). In a flame dried 100 mL roundbottom flask, sodium carbonate (1.37 g, 12.9 mmol, 3.00 equiv.) was suspended in anhydrous methylene chloride (40 mL). To this suspension, corresponding ketone (880 mg, 4.31 mmol, 1.00 equiv.) was added, and the reaction was cooled to 0 °C. Triflic anhydride (1.34 g, 4.74 mmol, 1.20 equiv.) was added dropwise and the reaction was allowed to warm to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete additional triflic anhydride (1.34 g, 4.74 mmol, 1.20 equiv.) and sodium carbonate (1.37 g, 12.9 mmol, 3.00 equiv.) was added. Upon completion by TLC, the reaction was quenched with 70 mL of aqueous sodium bicarbonate solution. The layers were separated and the crude product was then extracted out of the aqueous layer with diethyl ether (3 x 70 mL). The combined organic layers were dried over magnesium sulfate, filtered, and then concentrated to

give the crude compound. The crude was purified by silica flash chromatography (20% dichloromethane in hexanes) to give pure vinyl triflate **2.15S** as a yellow oil (510 mg, 31%).

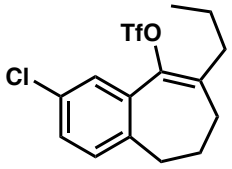
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 7.9 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 7.06 (d, J = 8.1 Hz, 1H), 4.50 (td, J = 6.2, 1.9 Hz, 2H), 2.40 (dtd, J = 12.6, 6.9, 6.2, 2.0 Hz, 4H), 1.64 – 1.57 (m, 2H), 1.01 (t, J = 7.4, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 139.0, 135.0, 130.3, 127.3, 126.1, 123.2, 122.0, 118.4 (q, $^1J_{C–F}$ = 320.2 Hz), 76.8, 34.3, 31.3, 20.8, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ –73.9.

FTIR (Neat film NaCl): 3073, 2965, 2936, 2877, 1603, 1574, 1487, 1447, 1412, 1284, 1244, 1204, 1139, 1114, 1008, 869, 854.

HR-MS (EI-MS): Calculated for $C_{14}H_{15}F_3O_4S$: 336.0643; measured: 336.0642.



2-Chloro-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.21S). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (255 mg, 2.40 mmol, 3 equiv.) in anhydrous methylene chloride (7.5 mL). To this suspension was added corresponding ketone (190 mg, 0.80 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (249 mg, 0.88 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not done, additional triflic anhydride (249 mg, 0.88 mmol, 1.10 equiv.) and sodium carbonate (255 mg, 2.40 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC,

the reaction was quenched with water (20 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as a brown oil. The crude product was purified by silica flash column chromatography (5% dichloromethane in hexanes) to give pure vinyl triflate **2.21S** as a yellow oil (140 mg, 47%).

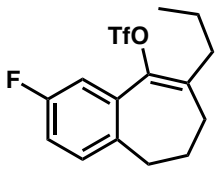
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 2.2 Hz, 1H), 7.24 (dd, J = 8.1, 2.2 Hz, 1H), 7.16 (d, J = 8.1 Hz, 1H), 2.66 (t, J = 7.2 Hz, 2H), 2.46 – 2.30 (m, 2H), 2.18 (p, J = 7.2 Hz, 2H), 1.93 (t, J = 7.2 Hz, 2H), 1.71 – 1.57 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.3, 138.3, 137.0, 135.4, 132.1, 130.3, 129.0, 126.5, 118.3 (q, $^{1}J_{C–F}$ = 320.2 Hz), 34.1, 34.0, 31.1, 28.0, 21.3, 14.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ –74.2.

FTIR (Neat film NaCl): 2963, 2937, 2867, 1592, 1410, 1204, 1138, 1003, 980, 862, 826, 607.

HR-MS (EI-MS): Calculated for $C_{15}H_{16}ClF_3O_3S$: 368.0461; measured: 368.0457.



2-fluoro-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.20S). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (296 mg, 2.79 mmol, 3 equiv.) in anhydrous methylene chloride (8 mL). To this suspension was added corresponding ketone (205 mg, 0.93 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (289 mg, 1.02 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (289 mg, 1.02 mmol, 1.10

equiv.) and sodium carbonate (296 mg, 2.79 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with methylene chloride (3 x 10 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark green oil. The crude product was purified by silica flash column chromatography (15% dichloromethane in hexanes) to give pure vinyl triflate **2.20S** as yellow oil (162 mg, 49%).

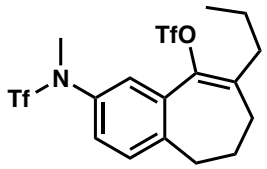
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 8.4, 5.6 Hz, 1H), 7.07 (dd, *J* = 9.4, 2.7 Hz, 1H), 6.98 (td, *J* = 8.4, 2.7 Hz, 1H), 2.66 (t, *J* = 7.1 Hz, 2H), 2.45 – 2.30 (m, 2H), 2.18 (p, *J* = 7.2 Hz, 2H), 1.93 (t, *J* = 7.2 Hz, 2H), 1.64 – 1.54 (m, 2H), 1.02 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2 (d, $^{1}J_{C–F}$ = 244.9 Hz), 138.6 (d, $^{4}J_{C–F}$ = 2.6 Hz), 136.9, 136.6 (d, $^{4}J_{C–F}$ = 3.3 Hz), 135.4 (d, $^{3}J_{C–F}$ = 7.8 Hz), 130.4 (d, $^{3}J_{C–F}$ = 8.0 Hz), 118.3 (q, $^{1}J_{C–F}$ = 320.1 Hz), 116.0 (d, $^{2}J_{C–F}$ = 21.2 Hz), 113.3 (d, $^{2}J_{C–F}$ = 22.7 Hz), 34.2, 34.1, 30.9, 28.1, 21.3, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.2, –116.2.

FTIR (Neat film NaCl): 2961, 2938, 2868, 1612, 1584, 1492, 1411, 1208, 1139, 988, 827, 650, 612.

HR-MS (EI-MS): Calculated for $C_{15}H_{16}F_4O_3S$: 352.0756; measured: 352.0754.



8-propyl-2-((1,1,1-trifluoro-*N*-methylmethyl)sulfonamido)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.19S).

In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (350 mg, 3.30 mmol, 3 equiv.) in anhydrous methylene chloride (10 mL). To this suspension was added corresponding ketone (400 mg, 1.10 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (342 mg, 1.21 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (342 mg, 1.21 mmol, 1.10 equiv.) and sodium carbonate (350 mg, 3.30 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with methylene chloride (3 x 15 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark brown oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **2.19S** as a white solid (363 mg, 67%).

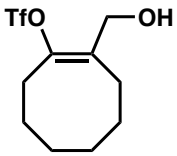
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.29 (d, J = 1.4 Hz, 2H), 3.44 (d, J = 1.1 Hz, 2H), 2.71 (t, J = 7.2 Hz, 2H), 2.50 – 2.35 (m, 2H), 2.22 (p, J = 7.2 Hz, 2H), 1.96 (t, J = 7.2 Hz, 2H), 1.71 – 1.56 (m, 2H), 1.03 (t, J = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 138.1, 137.6, 137.5, 135.26, 130.1, 128.1, 125.3, 120.4 (q, $^{2}J_{C–F}$ = 325.1 Hz), 118.3 (q, $^{2}J_{C–F}$ = 321.3 Hz), 40.5, 34.2, 34.1, 31.3, 28.1, 21.3, 14.2.

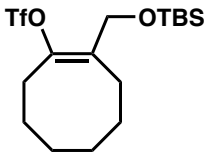
^{19}F NMR (376 MHz, $CDCl_3$) δ –73.5, –74.3.

FTIR (Neat film NaCl): 2928, 2869, 1492, 1455, 1395, 1209, 1128, 1071, 994, 930, 859, 834, 666, 606, 503.

HR-MS (EI-MS): Calculated for $C_{17}H_{19}F_6NO_5S_2$: 495.0609; Measured: 495.0608



(*Z*)-2-(hydroxymethyl)cyclooct-1-en-1-yl trifluoromethanesulfonate (2.26.1). Synthesized according to known procedures. Spectral data match those reported in the literature.[35]



(*Z*)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)cyclooct-1-en-1-yl trifluoromethanesulfonate (2.26S). In a 10 mL roundbottom flask, imidazole (809 mg, 11.9 mmol, 2.5 equiv.) and alcohol **2.26.1** (1.37 g, 4.75 mmol, 1 equiv.) were dissolved in anhydrous dimethylformamide (1.37 mL). TBSCl (860 mg, 5.70 mmol, 1.2 equiv.) was added and the reaction was stirred for 24h at room temperature. The reaction was diluted with water (10 mL) and the product was extracted out of the aqueous layer with diethyl ether (3 x 10 mL). The organics were washed with water (5 x 20 mL) followed by brine (1 x 20 mL), dried over magnesium sulfate, filtered and concentrated to give crude product as colorless oil. The crude was purified by silica flash column chromatography (100% hexanes to 5% ethyl acetate in hexanes) to give **2.26.S** as a colorless oil (1.29 g, 67%).

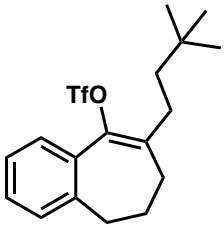
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.27 (s, 2H), 2.52 – 2.45 (m, 2H), 2.37 – 2.28 (m, 2H), 1.73 – 1.64 (m, 4H), 1.57 – 1.50 (m, 4H), 0.90 (s, 9H), 0.07 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 132.1, 118.4 (q, $^{1}J_{C–F}$ = 319.7 Hz), 59.5, 29.9, 29.2, 27.8, 27.1, 26.2, 25.8, 25.8, 18.3, –5.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ –74.9.

FTIR (Neat film NaCl): 2957, 2930, 2858, 1686, 1465, 1411, 1362, 1206, 1140, 1085, 918, 835, 615.

HRMS (GCT-CI): Calculated for [$C_{16}H_{29}F_3O_4SSi$ + H]: 403.1586; Measured: 403.1602.



8-(3,3-dimethylbutyl)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (2.37S). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (409 mg, 3.85 mmol, 3 equiv.) in anhydrous methylene chloride (10 mL). To this suspension was added ketone (314 mg, 1.28 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (399 mg, 1.41 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (399 mg, 1.41 mmol, 1.10 equiv.) and sodium carbonate (409 mg, 3.85 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark red oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **2.37S** as a white solid (430 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 1H), 7.30 – 7.26 (m, 2H), 7.24 – 7.20 (m, 1H), 2.69 (t, J = 7.2 Hz, 2H), 2.47 – 2.32 (m, 2H), 2.20 (p, J = 7.2 Hz, 2H), 1.92 (t, J = 7.2 Hz, 2H), 1.51 – 1.40 (m, 2H), 0.97 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.9, 139.3, 136.2, 133.8, 129.0, 128.9, 126.4, 118.3 (q, $^1J_{C–F}$ = 321.3 Hz), 41.9, 34.6, 31.7, 30.5, 29.2, 28.6, 27.9.

FTIR (Neat film NaCl): 2953, 2865, 1453, 1412, 1366, 1208, 1141, 1004, 964, 851, 802, 766, 608, 515.

HR-MS (EI-MS): Calculated for $C_{18}H_{23}F_3O_3S$: 376.1320; measured: 376.1320.

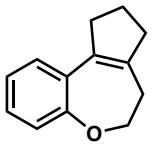
2.7.4 General Procedure for C–H Insertion Reactions

In this section, we outline the procedures used for the intramolecular C–H insertion reactions of benzosuberone derived vinyl triflates into tethered alkyl chains.

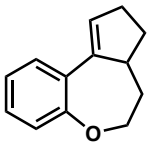
General Procedure A: In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[(C_6F_5)_4B]^-$ (0.05 equiv.) and this was dissolved in methylene chloride (enough to make a 0.0166 M solution with respect to vinyl triflate). Lithium hexamethyldisilazide (1.5 equiv.) was added along with a magnetic stirring bar to the solution. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate (1 equiv.) was added to the reaction and it was stirred at 30 °C. Upon completion, the reaction mixture was brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude product. The crude was then purified by silica flash column chromatography to give pure product.

General Procedure B: In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[(C_6F_5)_4B]^-$ (0.05 equiv.) and this was suspended in cyclohexane (enough to make a 0.1 M solution with respect to vinyl triflate). Lithium hexamethyldisilazide (1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate (1 equiv.) was added to the reaction and it was stirred at 70 °C. Upon completion, the reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and

concentrated to give crude product. The crude was then purified by silica flash column chromatography to give pure product.



3.17a



3.17b

7,8,9,10-tetrahydro-6*H*-benzo[*b*]cyclopenta[*d*]oxepine (2.15). Synthesized according to a modified version of general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (4.6 mg, 0.005 mmol, 0.10 equiv.) and this was suspended in cyclohexane (0.5 mL). Lithium hexamethyldisilazide (5.02 mg, 0.028 mmol, 0.6 equiv.) was added along with a magnetic stirring bar to the suspension. Vinyl triflate **2.15** (16.8 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was heated to 70 °C for 60 minutes. The reaction mixture was cooled to room temperature and then another batch of LiHMDS (4.30 mg, 0.022 mmol, 0.5 equiv.) was added and the reaction was heated to 70 °C for an additional hour. The reaction was then cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **2.15a** as brown oil (66% NMR yield.). The crude was then purified by silica column chromatography on silver nitrate treated silica (2% ethyl acetate in hexanes) to give product **2.15a** as colorless oil. The remaining material was further purified *via* silica flash column chromatography on silver nitrate impregnated silica (10% benzene in hexanes) to give the minor trisubstituted isomer **2.15b** as colorless oil.

Characterization of 2.15a

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.10 (td, *J* = 7.6, 1.7 Hz, 1H), 7.02 (td, *J* = 7.5, 1.5 Hz, 1H), 6.97 (dd, *J* = 7.9, 1.5 Hz, 1H), 4.21 (t, *J* = 5.2 Hz, 2H), 2.96 – 2.76 (m, 2H), 2.65 (br s, 2H), 2.61 – 2.57 (m, 2H), 1.95 (p, *J* = 7.4 Hz, 2H).

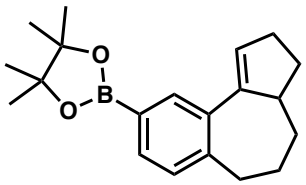
^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 140.7, 131.3, 128.9, 127.2, 127.0, 122.6, 120.1, 69.5, 39.9, 36.9, 34.7, 21.6.

FTIR (Neat film NaCl): 3062, 3023, 2950, 2885, 2807, 1640, 1599, 1489, 1218, 1123, 1064, 986, 755 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{13}H_{14}O$: 186.1045; measured: 186.1041.

Characterization of 2.15b

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.14 (ddd, *J* = 8.0, 7.3, 1.8 Hz, 1H), 6.97 (td, *J* = 7.5, 1.3 Hz, 1H), 6.94 (dd, *J* = 8.0, 1.3 Hz, 1H), 5.92 – 5.89 (br q, *J* = 2.5 Hz, 1H), 4.25 (ddd, *J* = 12.2, 7.1, 3.8 Hz, 1H), 3.97 (ddd, *J* = 12.2, 7.5, 3.6 Hz, 1H), 3.02 (dddd, *J* = 8.4, 4.2, 2.8, 1.5 Hz, 1H), 2.63 – 2.52 (m, 1H), 2.44 – 2.36 (m, 1H), 2.33 – 2.23 (m, 1H), 2.20 – 2.13 (m, 1H), 1.81 – 1.68 (m, 2H).



2-(2,3,3a,4,5,6-hexahydrobenzo[*e*]azulen-9-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.16). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.25 mL). Lithium hexamethyldisilazide (4.6 mg, 0.033

mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.16** (11.5 mg, 0.025 mmol, 1 equiv.) was added to the reaction and it was subsequently stirred for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. The reaction was quenched with saturated aqueous ammonium chloride and extracted with diethyl ether. The combined organics were filtered through a pad of silica gel and concentrated to give crude tricyclic compound **2.16** as a yellow oil (68% NMR yield). The crude was then purified by flash silver nitrate impregnated silica gel chromatography (2% ethyl acetate in hexanes) to give pure product **2.16** as a colorless oil.

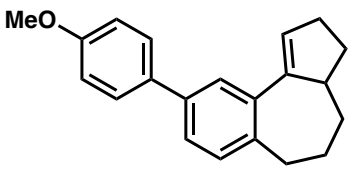
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 1H), 5.79 (s, 1H), 2.84 (dd, *J* = 14.6, 7.8 Hz, 1H), 2.71 – 2.60 (m, 2H), 2.54 (dt, *J* = 16.9, 8.3 Hz, 1H), 2.39 – 2.29 (m, 1H), 2.28 – 2.16 (m, 1H), 2.05 – 1.87 (m, 2H), 1.65 – 1.58 (m, 1H), 1.55 – 1.52 (m, 2H), 1.33 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 144.4, 138.7, 135.0, 133.4, 128.8, 127.7, 83.6, 47.1, 37.5, 37.2, 32.7, 31.3, 26.8, 24.9, 24.8. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 31.6.

FTIR (Neat film NaCl): 2969, 2925, 2852, 1602, 1360, 1260, 1146, 798, 689 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{20}H_{27}BO_2$: 310.2104; measured: 310.2101.



9-(4-methoxyphenyl)-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (2.17). Synthesized according to general procedure 3.8.2.2.1B. In a

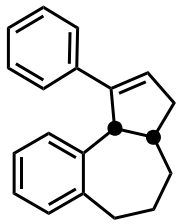
well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (4.3 mg, 0.0047 mmol, 0.10 equiv.) and this was suspended in cyclohexane (0.47 mL). Lithium hexamethyldisilazide (8.65 mg, 0.052 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. Vinyl triflate **2.17** (20.7 mg, 0.047 mmol, 1 equiv.) was added to the reaction and it was heated to 70 °C for 10 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **2.17**as brown oil (48% NMR yield, 44% solated yield on 0.1 mmol scale). The crude was then purified by silica column chromatography on silver nitrate treated silica (5% ethyl acetate in hexanes) to give product **2.17** as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 2H), 7.47 (d, *J* = 2.1 Hz, 1H), 7.32 (dd, *J* = 7.8, 2.1 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.00 – 6.90 (m, 2H), 5.81 (t, *J* = 2.0 Hz, 1H), 3.85 (s, 3H), 2.93 – 2.83 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.77 – 2.64 (m, 2H), 2.63 – 2.53 (m, 1H), 2.44 – 2.34 (m, 1H), 2.32 – 2.23 m, 1H), 2.07 – 1.89 (m, 2H), 1.71 – 1.56 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 149.9, 139.4, 138.4, 133.6, 129.8, 128.0, 127.7, 126.9, 125.0, 114.1, 55.3, 47.1, 37.4, 36.6, 32.7, 31.3, 27.0.

FTIR (Neat film NaCl): 3035, 2924, 2848, 1609, 1518, 1486, 1441, 1247, 1177, 1030, 817 cm^{-1}.

HR-MS (GCT-LIFDI): Calculated for $C_{21}H_{27}O$: 290.1671; Measured: 290.1678.



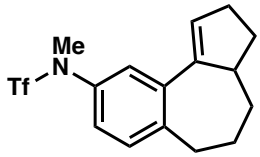
1-phenyl-3,3a,4,5,6,10b-hexahydrobenzo[*e*]azulene (2.18). Synthesized according to general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (5.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C and then cooled to –40 °C. Vinyl triflate **2.18** (20.5 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at –40 °C for 30 minutes. The reaction mixture was warmed to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **2.18** as a yellow oil (61% NMR yield). The crude was purified first by flash silica gel column chromatography (hexanes) to give product **2.18** as a mixture of diastereomers. This mixture was further purified by HPLC to give the major *cis*-ring fused product **2.18** as a white solid. Assignment of the major *cis* product was determined by key cross peaks in ^{1}H NOESY experiments. HSQC and ^{1}H COSY experiments led to the assignment of the tertiary allylic benzylic proton to be at 4.50 ppm and the other tertiary proton to be at 2.09 ppm. Further, the two diastereotopic CH_2 benzylic protons on the seven membered ring were assigned to be at 3.15 ppm and 2.79 ppm. The allylic benzylic proton showed key NOE interactions with the other ring tertiary CH proton as well as one of the diastereotopic benzylic protons at 3.15 ppm. The other diasteretopic benzylic proton at 2.79 ppm showed an NOE with the neighboring aromatic CH doublet at 6.5 ppm. These NOE interactions lead to the assignment of the product as the *cis* fused product.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.0 Hz, 3H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.12 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.00 (td, *J* = 7.3, 1.4 Hz, 1H), 6.88 (dd, *J* = 8.2, 6.9 Hz, 1H),

6.22 (q, J = 2.4 Hz, 1H), 4.50 (d, J = 9.2 Hz, 1H), 3.15 (t, J = 13.6 Hz, 1H), 2.79 (dd, J = 14.0, 6.4 Hz, 1H), 2.71 – 2.63 (m, 1H), 2.25 – 2.17 (m, 2H), 2.14 – 2.04 (m, 2H), 1.86 (qd, J = 12.9, 4.0 Hz, 1H), 1.46 – 1.37 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 143.2, 142.7, 137.4, 130.2, 129.0, 128.2, 126.6, 126.5, 125.9, 125.7, 125.4, 54.1, 46.8, 39.8, 37.7, 35.4, 28.0.

FTIR (Neat film NaCl): 3029, 2918, 2848, 1598, 1493, 1444, 1259, 1155, 1074, 1039, 1019, 797, 752, 693, 613 cm^{-1}.



1,1,1-trifluoro-*N*-(2,3,3a,4,5,6-hexahydrobenzo[*e*]azulen-9-yl)-*N*-methylmethanesulfonamide (2.19). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.7 mg, 0.003 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.3 mL). Lithium hexamethyldisilazide (6.8 mg, 0.045 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.19**(12.4 mg, 0.03 mmol, 1.0 equiv.) was added to the reaction and it was subsequently heated to 70 °C for 3 hours. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **2.19** as a yellow oil (51% NMR yield). The crude was then purified by silver impregnated silica flash column chromatography (1% ethyl acetate in hexanes) to give pure product **2.19** as a colorless oil.

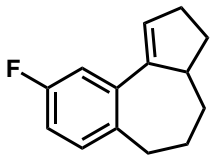
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, J = 2.1 Hz, 1H), 7.14 – 7.05 (m, 2H), 5.85 – 5.69 (m, 1H), 3.45 (s, 3H), 2.86 (dd, J = 14.7, 8.0 Hz, 1H), 2.72 – 2.66 (m, 1H), 2.66 – 2.49 (m, 2H), 2.41 – 2.34 (m, 1H), 2.31 – 2.20 (m, 1H), 2.03 – 1.95 (m, 1H), 1.94 – 1.86 (m, 1H), 1.67 – 1.60 (m, 1H), 1.57 – 1.52 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.5, 141.9, 140.7, 136.9, 130.5, 129.1, 127.3, 125.4, 120.5 (q, $^{1}J_{C–F}$ = 324.7 Hz), 46.9, 40.7, 37.1, 36.5, 32.6, 31.3, 26.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ –73.3.

FTIR (Neat film NaCl): 3042, 2924, 2850, 1489, 1392, 1227, 1188, 1127, 1072, 920, 821, 621, 588 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{16}H_{18}F_3NO_2S$: 345.1013; measured: 345.1006.



9-Fluoro-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (2.20). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.7 mg, 0.003 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.3 mL). Lithium hexamethyldisilazide (5.5 mg, 0.033 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.20** (10.6 mg, 0.03 mmol, 1.0 equiv.) was added to the reaction and it was subsequently heated to 70 °C for 10 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **2.20** as a yellow oil

(72% NMR yield). The crude was then purified by silica flash column chromatography (hexanes) to give pure product **2.20** as a colorless oil.

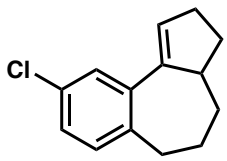
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (dd, *J* = 8.3, 5.9 Hz, 1H), 6.96 (dd, *J* = 9.9, 2.8 Hz, 1H), 6.79 (td, *J* = 8.4, 2.8 Hz, 1H), 5.77 (q, *J* = 2.2 Hz, 1H), 2.81 (dd, *J* = 14.6, 8.4 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.63 – 2.49 (m, 2H), 2.41 – 2.32 (m, 1H), 2.25 (dddd, *J* = 12.6, 9.5, 8.6, 7.3 Hz, 1H), 2.06 – 1.94 (m, 1H), 1.90 (dtdd, *J* = 10.3, 5.1, 3.5, 2.0 Hz, 1H), 1.62 (ddt, *J* = 12.5, 8.7, 3.7 Hz, 1H), 1.57 – 1.50 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 161.08 (d, *J* = 243.1 Hz), 148.94 (d, *J* = 1.8 Hz), 140.82 (d, *J* = 7.6 Hz), 136.56, 130.59 (d, *J* = 8.1 Hz), 128.59, 114.99 (d, *J* = 21.1 Hz), 112.95 (d, *J* = 20.5 Hz), 46.86, 36.97, 35.97, 32.69, 31.19, 26.87.

^{19}F NMR (282 MHz, $CDCl_3$) δ –118.7.

FTIR (Neat film NaCl): 3036, 2919, 2848, 1607, 1582, 1488, 1443, 1419, 1351, 1266, 1162, 1104, 847, 811, 754, 713 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{15}F$: 202.1158; measured: 202.1154.



9-Chloro-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (2.21). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.25 mL). Lithium hexamethyldisilazide (4.6 mg, 0.033 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.21** (9.2 mg, 0.025 mmol, 1 equiv.) was added to the reaction

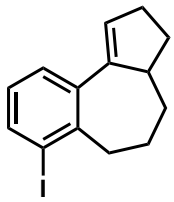
and it was subsequently heated to 70 °C for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **2.21** as a yellow oil (82% NMR yield). The crude was then purified by silica flash column chromatography (hexanes) to give pure product **2.21** as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 2.3 Hz, 1H), 7.07 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 2.81 (dd, *J* = 14.9, 8.6 Hz, 1H), 2.70 – 2.64 (m, 1H), 2.63 – 2.50 (m, 2H), 2.41 – 2.32 (m, 1H), 2.24 (dddd, *J* = 12.7, 9.6, 8.7, 7.4 Hz, 1H), 2.04 – 1.95 (m, 1H), 1.92 – 1.86 (m, 1H), 1.62 (ddt, *J* = 12.4, 8.6, 3.6 Hz, 1H), 1.58 – 1.48 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 140.8, 139.3, 131.2, 130.6, 128.7, 128.2, 126.4, 46.9, 37.1, 36.2, 32.6, 31.2, 26.7.

FTIR (Neat film NaCl): 3040, 2920, 2849, 1591, 1560, 1478, 1442, 1402, 1094, 884, 813, 691 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{15}Cl$: 218.0862; measured: 218.0855.



7-iodo-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (2.22). Synthesized according to general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (9.2 mg, 0.010 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (5.0 mL). Lithium hexamethyldisilazide (50.2 mg, 0.30 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the solution. Vinyl triflate **2.22** (92.1 mg, 0.20 mmol, 1

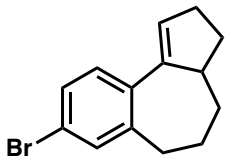
equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude product as brown oil (96% NMR yield). The crude was then purified by silica flash column chromatography (hexanes) to give product **2.22** as a colorless oil (55.9 mg, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 7.4 Hz, 1H), 6.77 (t, *J* = 7.7 Hz, 1H), 5.75 (br s, 1H), 3.23 (dd, *J* = 14.6, 9.1 Hz, 1H), 2.71 (ddd, *J* = 15.1, 9.5, 2.0 Hz, 1H), 2.65 (br s, 1H), 2.60 – 2.51 (m, 1H), 2.40 – 2.33 (m, 1H), 2.24 – 2.16 (m, 1H), 1.99 – 1.82 (m, 2H), 1.65 – 1.58 (m, 1H), 1.57 – 1.48 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 143.0, 140.5, 138.1, 128.8, 128.1, 127.4, 102.1, 46.8, 40.6, 36.0, 32.9, 31.1, 25.6.

FTIR (Neat film NaCl): 3048, 2917, 2846, 1549, 1444, 1423, 1347, 1169, 834, 778, 731, 686, 651 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{15}I$: 310.0219; measured: 310.0214.



8-bromo-2,3,3a,4,5,6-hexahydrobenzo[e]azulene (2.23). Synthesized according to general procedure 3.8.2.2.1A. In a well-kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.). This was suspended in methylene chloride (3.2 mL) and stirred for 5 minutes at 30 °C. Vinyl triflate **2.23**(20.7 mg, 0.05 mmol, 1.0 equiv.) was added to the reaction and the reaction was stirred for 15 minutes. The reaction was brought outside the

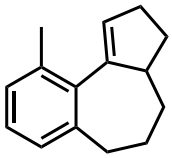
glovebox and was passed through a pad of silica with diethyl ether and concentrated to give crude tricyclic compound **2.23** as a yellow oil (77% NMR yield). The crude was then purified by silica flash chromatography (hexanes) to give pure product **2.23** as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.22 (m, 2H), 7.11 (d, *J* = 7.9 Hz, 1H), 5.75 (q, *J* = 2.1 Hz, 1H), 2.84 – 2.73 (dd, *J* = 14.2, 8.0 Hz, 1H), 2.69 – 2.46 (m, 3H), 2.39 – 2.30 (m, 1H), 2.28 – 2.18 (m, 1H), 1.99 – 1.83 (m, 2H), 1.62 (ddt, *J* = 12.8, 8.5, 3.7 Hz, 1H), 1.57 – 1.47 (d, *J* = 13.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 143.0, 138.0, 132.0, 130.1, 128.7, 128.3, 120.3, 46.9, 37.1, 36.6, 32.6, 31.3, 26.6.

FTIR (Neat film NaCl): 3040, 2917, 2846, 1584, 1479, 1441, 1087, 882, 822, 805, 677, 528 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{15}Br$: 264.0337; measured: 264.0335.



10-methyl-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (2.24). Synthesized according to general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (3.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.24** (17.4 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed

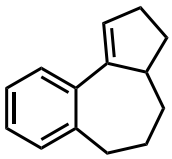
through silica and concentrated to give crude tricyclic compound **2.24** as a yellow oil (77% NMR yield, 60% isolated yield on 0.1 mmol scale). The crude was then purified by flash silver impregnated silica gel column chromatography (hexanes) to give pure product **2.24** as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (d, J = 7.5 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 7.3 Hz, 1H), 5.55 (s, 1H), 2.72 – 2.62 (m, 2H), 2.63 – 2.57 (m, 1H), 2.46 – 2.34 (m, 2H), 2.22 – 2.14 (m, 1H), 1.97 – 1.83 (m, 2H), 1.76 – 1.55 (m, 3H), 1.51 – 1.35 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.7, 142.1, 139.1, 135.4, 128.5, 127.8, 126.3, 126.1, 47.1, 37.4, 37.0, 33.0, 31.3, 27.0, 21.0.

FTIR (Neat film NaCl): 3061.21, 3038.21, 3014.47, 2918.18, 2847.38, 1579.33, 1461.65, 1441.41, 1477.77, 1348.43, 1290.94, 1260.12, 1096.13, 1034.94, 961.28, 818.33, 772.70, 742.88 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{15}H_{18}$: 198.1409; measured: 198.1403.



2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (2.25). Synthesized according to a modified general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.9 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (5.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.25** (16.7 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was cooled to room temperature

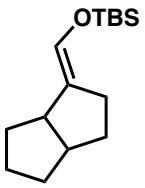
and brought outside the glovebox. It was quenched by addition of diethyl ether and pass through silica and concentrated to give crude tricyclic compound **2.25** as a yellow oil (96% NMR yield, 90% isolated yield on 0.2 mmol scale). The crude was then purified by silica flash column chromatography (hexanes) to give pure product **2.25** as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.24 (m, 1H), 7.16 – 7.10 (m, 2H), 7.10 – 7.06 (m, 1H), 5.74 (q, *J* = 2.2 Hz, 1H), 2.90 – 2.79 (m, 1H), 2.74 – 2.60 (m, 2H), 2.59 – 2.49 (m, 1H), 2.41 – 2.30 (m, 1H), 2.29 – 2.20 (m, 1H), 2.05 – 1.83 (m, 1H), 1.67 – 1.51 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.8, 140.9, 139.1, 129.3, 128.5, 127.5, 126.8, 125.9, 47.0, 37.3, 36.9, 32.7, 31.2, 26.9.

FTIR (Neat film NaCl): 3015, 2917, 2848, 1483, 1448, 1350, 873, 755, 734, 529 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{16}$: 184.1252; measured: 184.1249.



(*E/Z*)-*tert*-butyl((hexahydropentalen-1(2*H*)-ylidene)methoxy)dimethylsilane (2.27E and 2.27Z). In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[CHB_{11}Cl_{11}]^-$ (7.6 mg, 0.010 mmol, 0.05 equiv.) and this was dissolved in toluene (0.4 mL). Lithium hexamethyldisilazide (50.1 mg, 0.30 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the solution. The solution was stirred for 4 minutes at 30 °C. Vinyl triflate **2.26** (80.4 mg, 0.20 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 12 hours. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and filtered. The supernatant was concentrated to give crude product as orange oil (60% NMR yield of major olefin isomer **2.27E**,

32% minor olefin isomer **2.27Z**). The crude was then purified by silica flash column chromatography (1% ethyl acetate in hexanes**)** to give the major (*E*)–isomer **2.27E** as colorless oil. Assignment of the major isomer was based on key cross peaks in ^{1}H NOESY experiments. Through HSQC and COSY experiments it was determined that the proton at 2.86 ppm was the tertiary allylic ring fusion proton and that the CH_2 protons adjacent to that CH showed up at 1.46 and 1.33. There were key NOEs present between the olefinic proton at 6.25 and the tertiary allylic proton at 2.86 as well as one of the protons on the aforementioned CH_2 leading to the assignment of the (*E*)–isomer.

The minor (*Z*)–isomer was found to be unstable on SiO2, so the crude reaction mixture could be purified by flash column chromatography on triethylamine treated silica gel (0.1:99.9 NEt_3:hexanes) to give pure **2.27Z** as colorless oil. The olefin geometry of this isomer was assigned based on key cross peaks in ^{1}H NOESY experiments. There were key NOEs present between the olefinic proton and the protons on the allylic methylene carbon. This lead to assignment of the minor compound as the (*Z*)–isomer.

Characterization of 2.27E

^{1}H NMR (500 MHz, C_6D_6) δ 6.25 (q, *J* = 2.2 Hz, 1H), 2.90 – 2.83 (m, 1H), 2.50 (dddd, *J* = 8.0, 6.9, 2.3, 1.2 Hz, 2H), 2.41 (qt, *J* = 8.4, 5.1 Hz, 1H), 1.84 – 1.70 (m, 2H), 1.69 – 1.54 (m, 2H), 1.53 – 1.41 (m, 2H), 1.36 – 1.29 (m, 1H), 1.28 – 1.22 (m, 1H), 0.98 (s, 9H), 0.08 (d, *J* = 1.1 Hz, 6H).

^{13}C NMR (126 MHz, C_6D_6) δ 132.2, 130.3, 45.5, 44.6, 35.8, 33.5, 32.2, 27.9, 27.0, 26.0, 18.5, –5.2, –5.1.

FTIR (Neat film NaCl): 2929, 2858, 1679, 1463, 1890, 1362, 1253, 1173, 1137, 834, 777, 671 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{15}H_{28}OSi$: 252.1909; measured: 252.1898.

Characterization of 2.27Z

^{1}H NMR (500 MHz, C_6D_6) δ 6.19 (br s, 1H), 3.27 – 3.20 (m, 1H), 2.48 – 2.37 (m, 1H), 2.25 – 2.17 (m, 1H), 2.16 – 2.09 (m, 1H), 2.08 – 2.02 (m, 1H), 1.71 – 1.62 (m, 3H), 1.62 – 1.55 (m, 1H), 1.47 – 1.41 (m, 1H), 1.40 – 1.33 (m, 1H), 1.26 – 1.15 (m, 1H), 0.95 (s, 9H), 0.04 (s, 6H).

^{13}C NMR (126 MHz, C_6D_6) δ 130.8, 129.8, 44.5, 44.4, 34.2, 33.6, 32.8, 29.2, 27.7, 25.9, 18.4, –5.1, –5.2.

FTIR (Neat film NaCl): 2931, 2859, 1682, 1472, 1463, 1449, 1406, 1389, 1362, 1252, 1189, 1172, 1129, 852, 837, 779 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{15}H_{28}OSi$: 252.1909; measured: 252.1912.

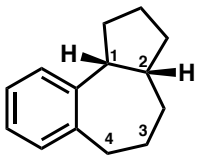
2.7.5 Mechanistic Studies

This section describes the experiments in ***2.9, 2.10, 2.11, and 2.12***

Stoichiometric LiF_{20} Experiment

In a In a well-kept glovebox, (H_2O, $O_2 \leq 0.5$ ppm), a J. Young tube was charged with $[Li]^+[B(C_6F_5)_4]^-$ (18.1 mg, 0.0026 mmol, 1.05 equiv.) and suspended in dry $CDCl_3$ (0.5 mL). Vinyl triflate **2.25** (8.3 mg, 0.025 mmol, 1.0 equiv.) was added to the reaction and the reaction was shaken by hand for 10 minutes. At this point, ^{1}H and ^{19}F NMR spectra were acquired indicating incomplete reaction. The reaction was shaken by hand for an additional 80 minutes and another ^{1}H and ^{19}F NMR spectra were acquired. At this point, full consumption of starting material was observed. The reaction was poured into D_2O (0.8 mL) and the layers were separated. The aqueous layer was analyzed by ^{19}F NMR and LiOTf was observed. The organic

layer had many products, but HRMS data was suggestive that intermolecular hydride transfer was occurring to quench the incipient cations resulting in insertion products with varying degrees of unsaturation. One such product was **2.25** which was identified in 15% NMR yield from the crude reaction mixture.



(Preparation of authentic sample of reduced product)

(3a*R*,10b*R*)-1,2,3,3a,4,5,6,10b-octahydrobenzo[*e*]azulene (2.25). In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.0030 mmol, 0.02 equiv.) and this was suspended in cyclohexane (1.5 mL). Triethylsilane (36 μL, 0.225 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **2.25** (16.7 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was passed through a plug of silica with hexanes in the glovebox. The resulting solution was brought outside of the glovebox and concentrated to give crude tricyclic compound **2.25** in 76% NMR yield. The crude was then purified by silica flash column chromatography (hexanes) to give pure product **2.25** as a colorless oil. Assignment of the major *cis*-diastereomer was done using 2D NMR experiments: ^{13}C–^{1}H HSQC, ^{1}H–^{1}H COSY and ^{1}H–^{1}H NOESY. Three key NOE interactions were observed. The interaction between the protons on C1 and C2, the interaction between the proton on C1 with one of the protons on C4, and lastly, the proton of C2 with the protons on C3.

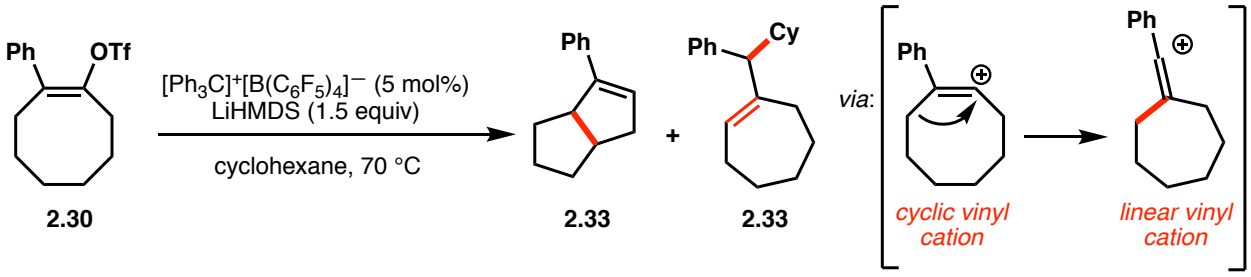
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.17 (m, 2H), 7.16 – 7.12 (m, 1H), 7.08 – 7.04 (m, 1H), 3.50 – 3.25 (m, 1H), 2.84 (ddd, *J* = 13.4, 11.3, 7.2 Hz, 1H), 2.62 (ddd, *J* = 13.4, 6.7, 2.6 Hz, 1H), 2.20 – 2.04 (m, 2H), 1.99 – 1.91 (m, 1H), 1.91 – 1.84 (m, 1H), 1.83 – 1.77 (m, 1H), 1.72 – 1.64 (m, 1H), 1.62 – 1.56 (m, 1H), 1.54 – 1.48 (m, 1H), 1.49 – 1.42 (m, 1H), 1.16 – 1.02 (m, 1H), 1.02 – 0.87 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 139.7, 128.3, 126.1, 126.0, 125.9, 44.6, 40.3, 34.7, 32.1, 31.1, 28.6, 25.4, 25.2.

FTIR (Neat film NaCl): 3063, 3016, 2926, 2855, 1685, 1487, 1451, 1378, 1258, 1047, 764, 751, 714 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{18}$: 186.1408; measured: 186.1414.

Vinyl Cation Rearrangment Experiment



1-(cyclohexyl(phenyl)methyl)cyclohept-1-ene and **6-phenyl-1,2,3,3a,4,6a-hexahydropentalene (2.33 and 2.34).** Synthesized according to general procedure B. In a well-kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.). This was suspended in cyclohexane (0.5 mL) and stirred for 5 minutes at 30 °C. Vinyl triflate **2.30** (16.7 mg, 0.05 mmol, 1.0 equiv.) was added to the reaction and the reaction was stirred for

5 minutes at 70 °C. The reaction was cooled to room temperature and brought outside the glovebox and was passed through a pad of silica with diethyl ether and concentrated to give crude bicyclic compound **2.33** and ring contracted cyclohexylated product **2.34** as yellow solid (6% NMR yield of transannular product **2.33**, 15% NMR yield of cyclohexylated product **2.34**). The crude was then purified by silica flash chromatography (hexanes) to give pure cyclohexylated product **2.33** as a white solid. The transannular insertion product was further purified by preparative reverse phase HPLC (10% water in acetonitrile) to give bicycle **2.34** as a colorless oil.

Characterization of bicycle 2.33:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.39 (m, 2H), 7.31 (t, *J* = 7.7 Hz, 3H), 7.24 – 7.16 (m, 1H), 6.01 (q, *J* = 2.1 Hz, 1H), 3.66 – 3.39 (m, 1H), 2.98 – 2.65 (m, 2H), 2.17 (dd, *J* = 17.3, 2.9 Hz, 1H), 1.97 – 1.78 (m, 2H), 1.54 – 1.44 (m, 3H), 1.42 – 1.35 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.1, 136.5, 128.2, 126.6, 126.2, 125.1, 50.4, 41.2, 40.5, 35.6, 32.2, 26.0.

FTIR (Neat film NaCl): 3064, 2957, 2925, 2854, 1719, 1681, 1449, 1261, 1178, 1020, 911, 798, 699 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{16}$: 184.1252; measured: 184.1244.

Characterization of cyclohexyl adduct 2.34:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.23 (m, 2H), 7.20 – 7.12 (m, 3H), 5.75 (t, *J* = 6.6 Hz, 1H), 2.18 – 1.93 (m, 4H), 1.90 – 1.72 (m, 3H), 1.67 – 1.56 (m, 4H), 1.52 – 1.42 (m, 2H), 1.39 – 1.24 (m, 3H), 1.22 – 1.10 (m, 2H), 1.07 – 0.98 (m, 1H), 0.93 – 0.84 (m, 1H), 0.75 – 0.63 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 143.2, 128.5, 127.9, 126.8, 125.6, 62.4, 37.6, 32.6, 32.4, 31.7, 30.1, 28.3, 27.0, 26.7, 26.6, 26.5, 26.4.

FTIR (Neat film NaCl): 3082, 3059, 3024, 2919, 2849, 1599, 1495, 1448, 1309, 1262, 1180, 1031, 833, 700, 622 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{20}H_{28}$: 268.2191; measured: 268.2188.

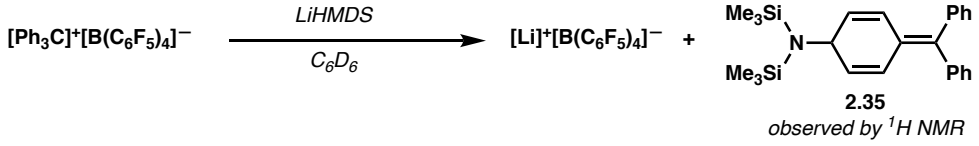
Gutmann-Beckett Lewis Acidity Experiments

^{31}P NMR spectra were all acquired according to the following general procedure.

In a well kept glovebox, (H_2O, $O_2 \leq 0.5$ ppm), a dram vial was charged with triphenylphosphine oxide (2.8 mg, 0.01 mmol, 1.0 equiv). To this was added the corresponding lithium salt/Lewis acid (0.01 mmol, 1.0 equiv) followed by dry benzene (0.5 mL). The solution was stirred for 5 minutes at 30 °C and then transferred with a pipette to a J. Young tube, sealed, and removed from the glove box. A ^{31}P NMR spectrum was acquired after first referencing to an external standard of triphenylphosphine oxide in C_6D_6 (0.01 mmol in 0.5 mL C_6D_6).

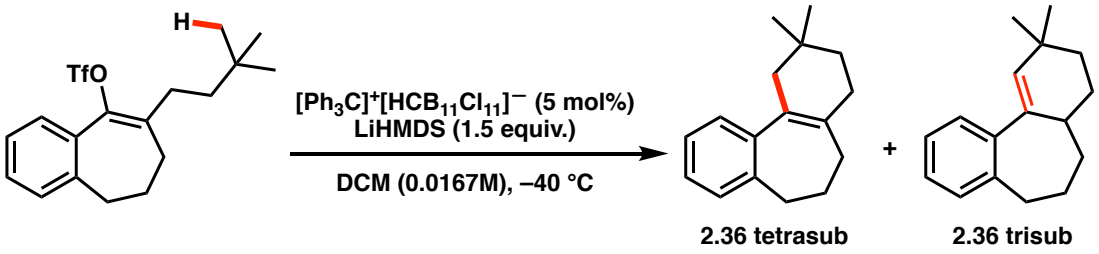
***In Situ* Preparation of Lithium Tetrakis(pentaflurophenyl)borate**

In a well kept glovebox, (H_2O, $O_2 \leq 0.5$ ppm), a dram vial was charged with triphenylcarbenium tetrakis(pentafluorophenyl)borate (9.2 mg, 0.010 mmol, 1.0 equiv) followed by lithium hexamethyldisilazide (1.8 mg, 0.011 mmol, 1.1 equiv). To this was added dry C_6D_6 (0.5 mL) and the mixture was stirred at 30°C for 5 minutes. The solution was transferred with a pipette to a J. Young tube, sealed, and removed from the glove box. ^{19}F and ^{11}B NMR spectra matched those reported in the literature for $[Li]^+[B(C_6F_5)_4]^-$. ^{7}Li NMR was corroborated with an authentic sample of $[Li]^+[B(C_6F_5)_4]^-$. See later attached spectrum of **2.35**.



2.35

observed by ^{1}H NMR



2,2-dimethyl-2,3,4,5,6,7-hexahydro-dibenzo[*a*,*c*][7]annulene (mixture of olefin isomers 2.36 trisub and 2.36 tetrasub). Synthesized according to general procedure A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[CHB_{11}Cl_{11}]^-$ (1.9 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (3.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C and then cooled to –40 °C. Vinyl triflate **2.35** (18.8 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at –40 °C for 30 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compounds **2.36** as a yellow oil (41% NMR yield of **2.36 trisub,** 44% NMR yield of **2.36 tetrasub**). The crude was then purified by flash silver impregnated silica gel column chromatography (hexanes) to give pure tetra-substituted olefin product **2.36 trisub** as a colorless oil and tri-substituted product **2.36 tetrasub** as a colorless solid.

Characterization data of tetrasubstituted olefin isomer 2.36 trisub:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (td, *J* = 7.3, 1.6 Hz, 1H), 7.19 – 7.13 (m, 2H), 7.11 (td, *J* = 7.2, 1.6 Hz, 1H), 2.52 (t, *J* = 7.1 Hz, 2H), 2.34 – 2.23 (m, 2H), 2.14 (br s, 2H), 2.08 (p, *J* = 7.1 Hz, 2H), 1.81 (t, *J* = 7.2 Hz, 2H), 1.47 (t, *J* = 6.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 140.2, 133.4, 129.5, 128.4, 125.9, 125.8, 125.7, 43.0, 35.9, 33.6, 32.3, 30.6, 29.4, 29.0, 28.2.

FTIR (Neat film NaCl): 3060, 3014, 2924, 2854, 2830, 1449, 1363, 1229, 806, 758.

HR-MS (EI-MS): Calculated for $C_{17}H_{22}$: 226.1722; measured: 226.1716.

Characterization data of trisubstituted olefin isomer 2.36 tetrasub:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 – 7.09 (m, 3H), 7.06 – 7.04 (m, 1H), 5.41 (s, 1H), 2.75 – 2.64 (m, 2H), 2.14 – 2.07 (m, 1H), 1.99 – 1.94 (m, 1H), 1.85 (tdd, *J* = 13.0, 5.4, 3.0 Hz, 1H), 1.79 – 1.71 (m, 2H), 1.65 (td, *J* = 13.2, 2.9 Hz, 1H), 1.61 – 1.55 (m, 1H), 1.52 – 1.47 (m, 1H), 1.46 – 1.40 (m, 1H), 1.06 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 141.8, 140.6, 136.5, 128.6, 128.4, 126.5, 126.0, 37.4, 37.3, 36.2, 32.9, 32.4, 31.3, 28.9, 28.0, 27.6.

FTIR (Neat film NaCl): 2954, 2924, 2856, 1485, 1449, 1381, 1090, 880, 802, 737 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{17}H_{22}$: 226.1722; measured: 226.1718.

2.8 Spectra Relevant to Chapter Two:

Lithium-Weakly Coordinating Anion Lewis Acids Paired with Hexamethyldisilazide Brønsted Bases and their Usage to Generate Vinyl Carbocations

Benjamin Wigman, Stasik Popov, Alex L. Bagdasarian, Brian Shao, Tyler R. Benton, Chloé G. Williams, Steven P. Fisher, Vincent Lavallo, K. N. Houk, and Hosea M. Nelson *J. Am. Chem. Soc.* **2019**, *141*, 9140–9144.

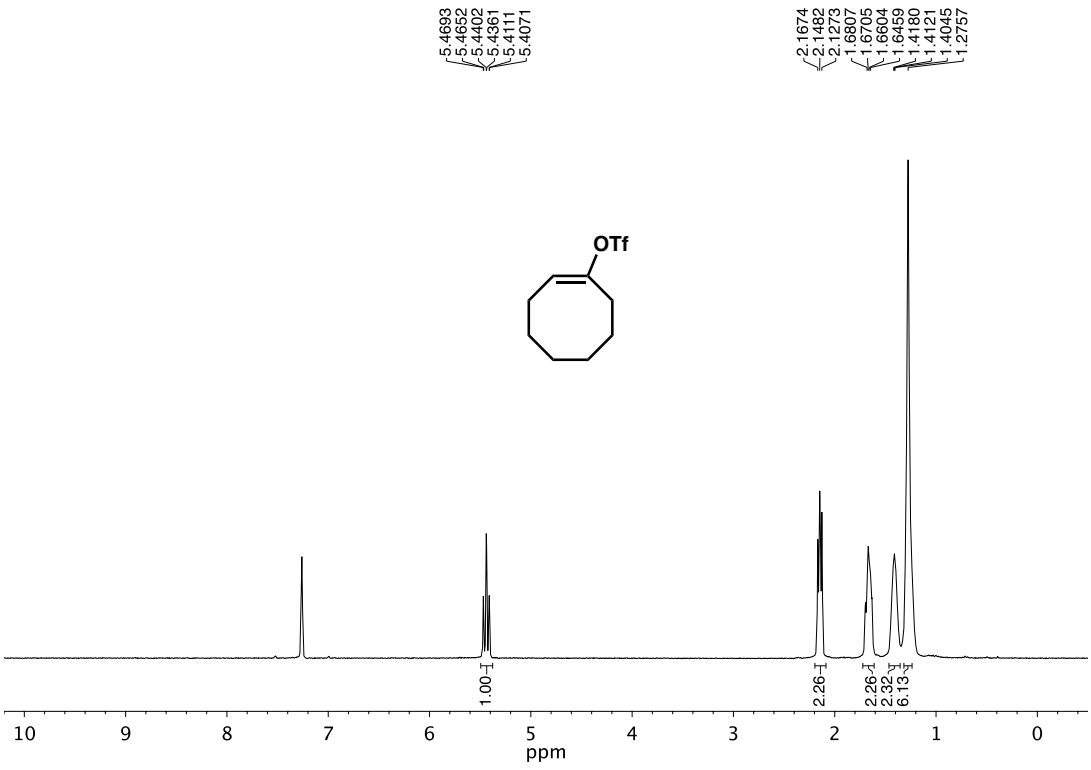


Figure 2.13 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.7**.

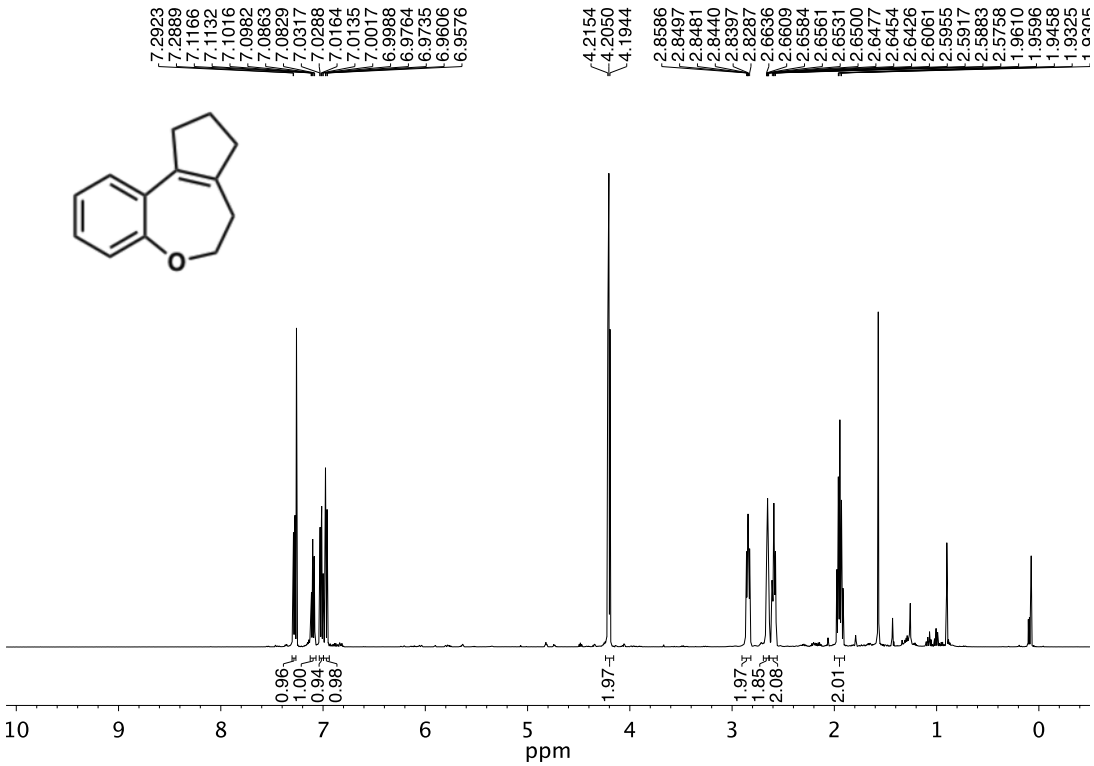


Figure 2.14 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.15**.

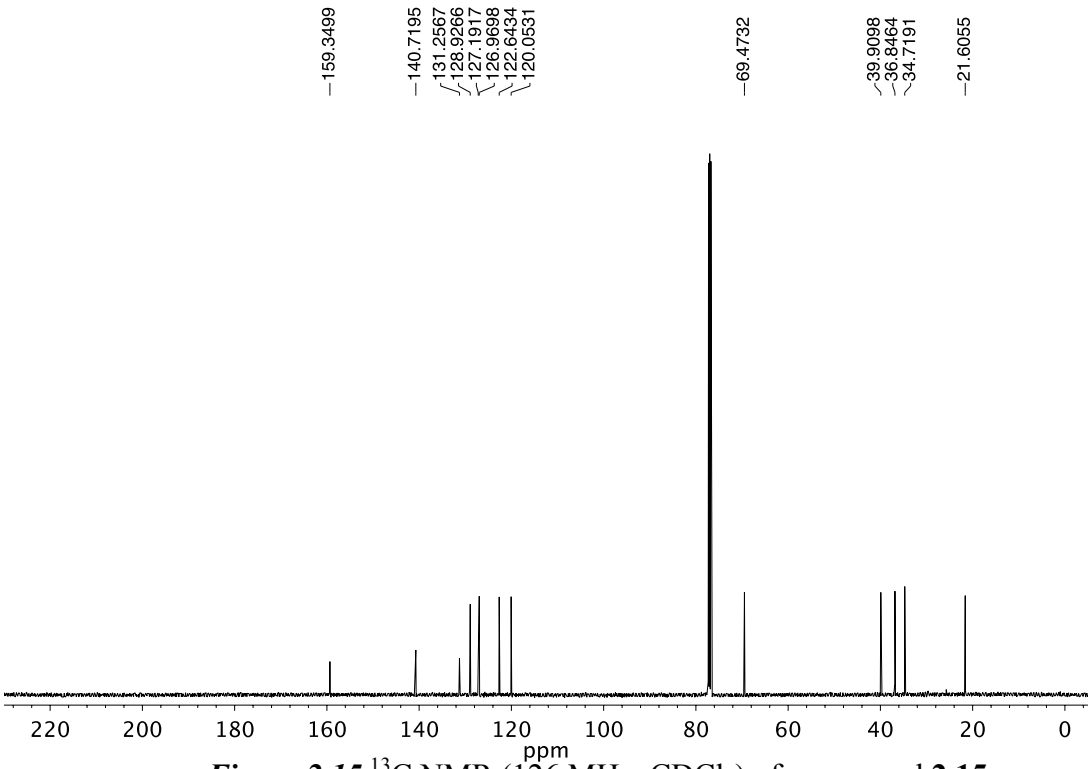


Figure 2.15 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.15**.

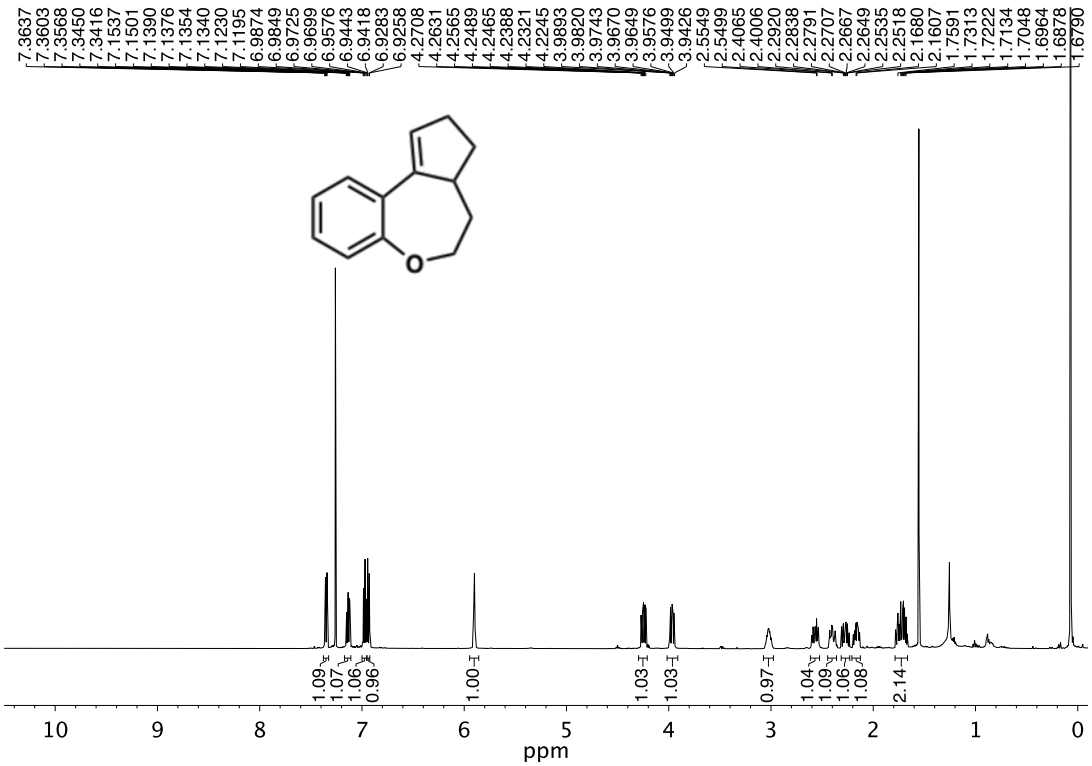


Figure 2.16 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.15b**

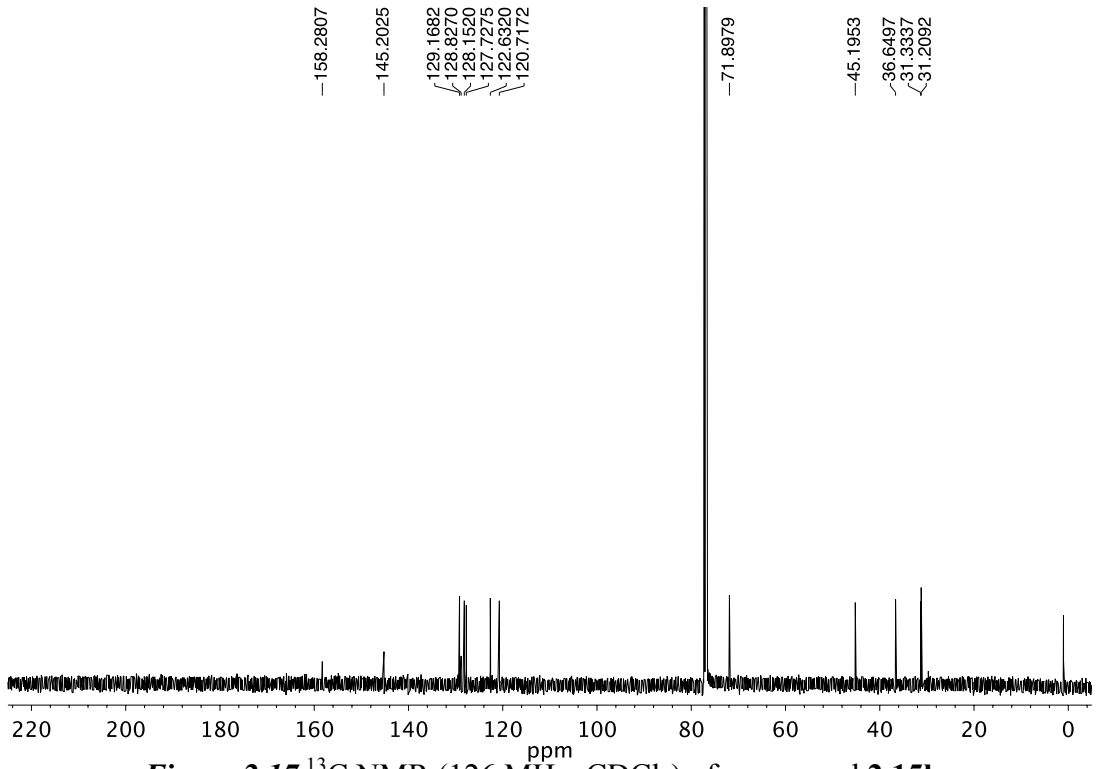


Figure 2.17 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.15b**.

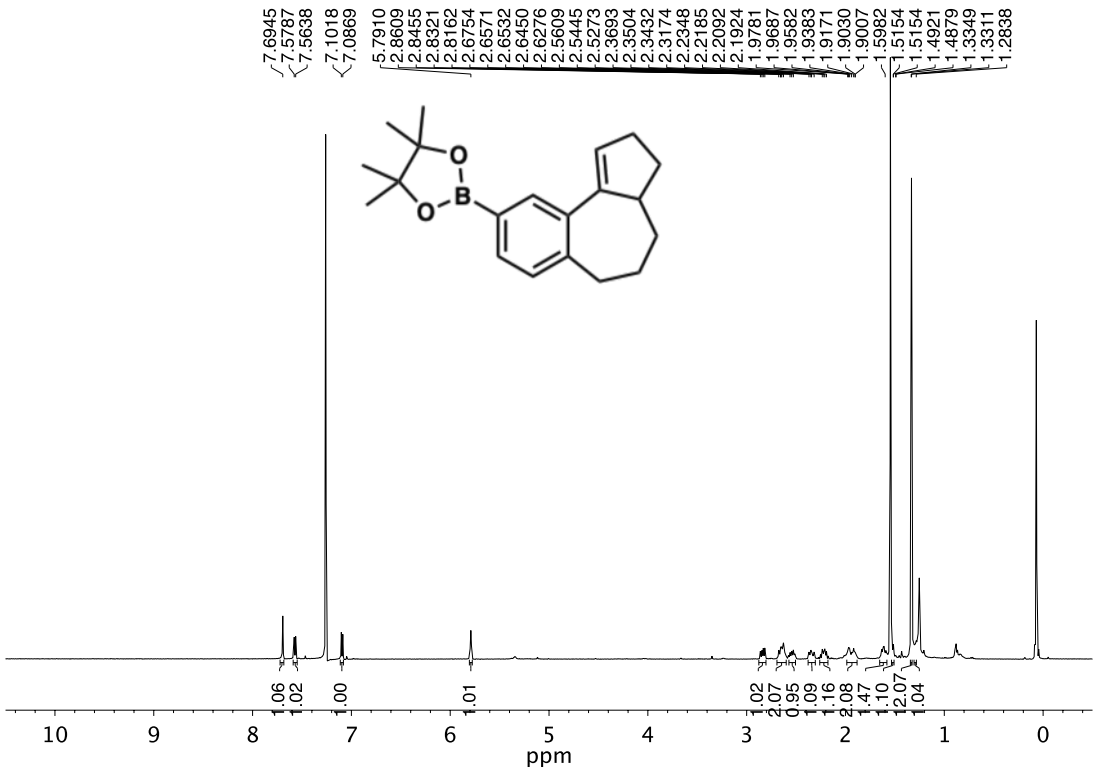


Figure 2.18 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.16**

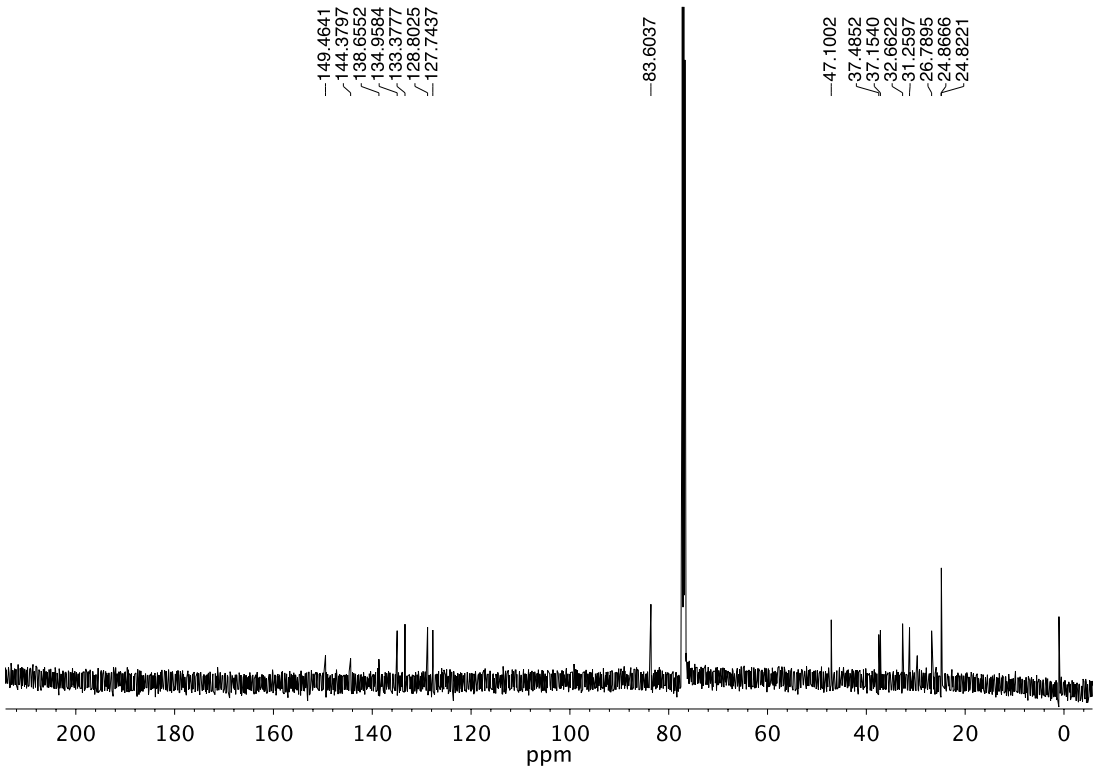


Figure 2.19 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.16**

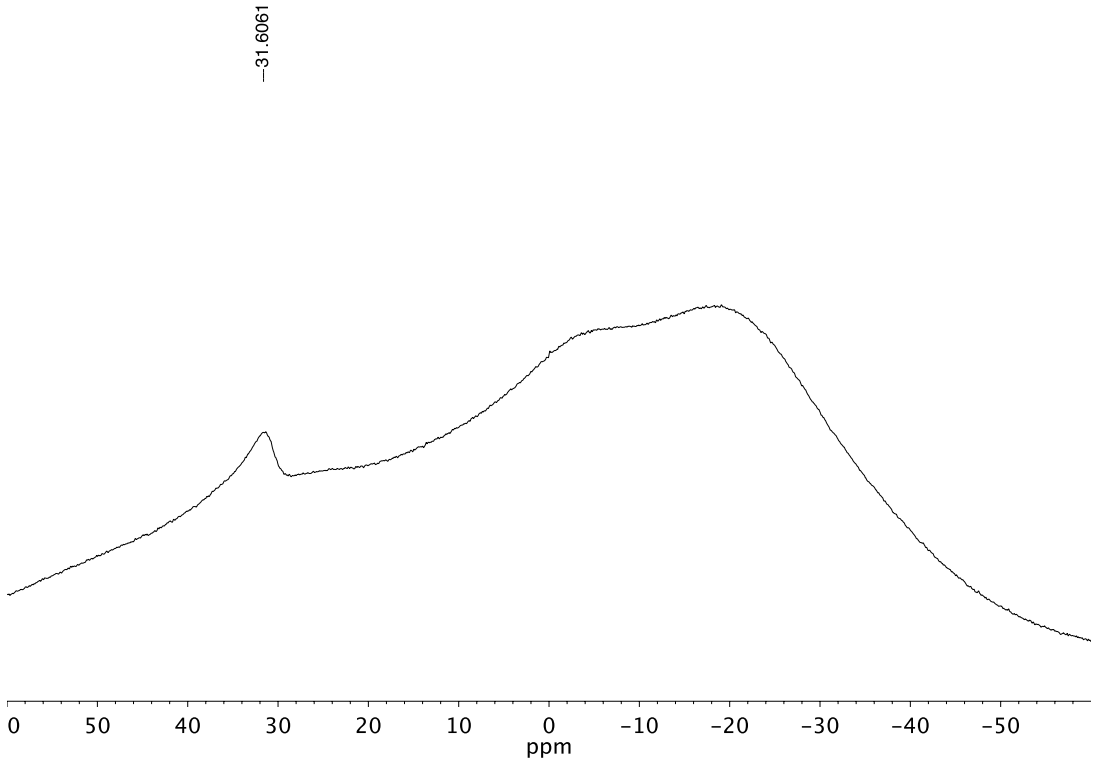


Figure 2.20 ^{11}B NMR (128 MHz, $CDCl_3$) of compound **2.16**

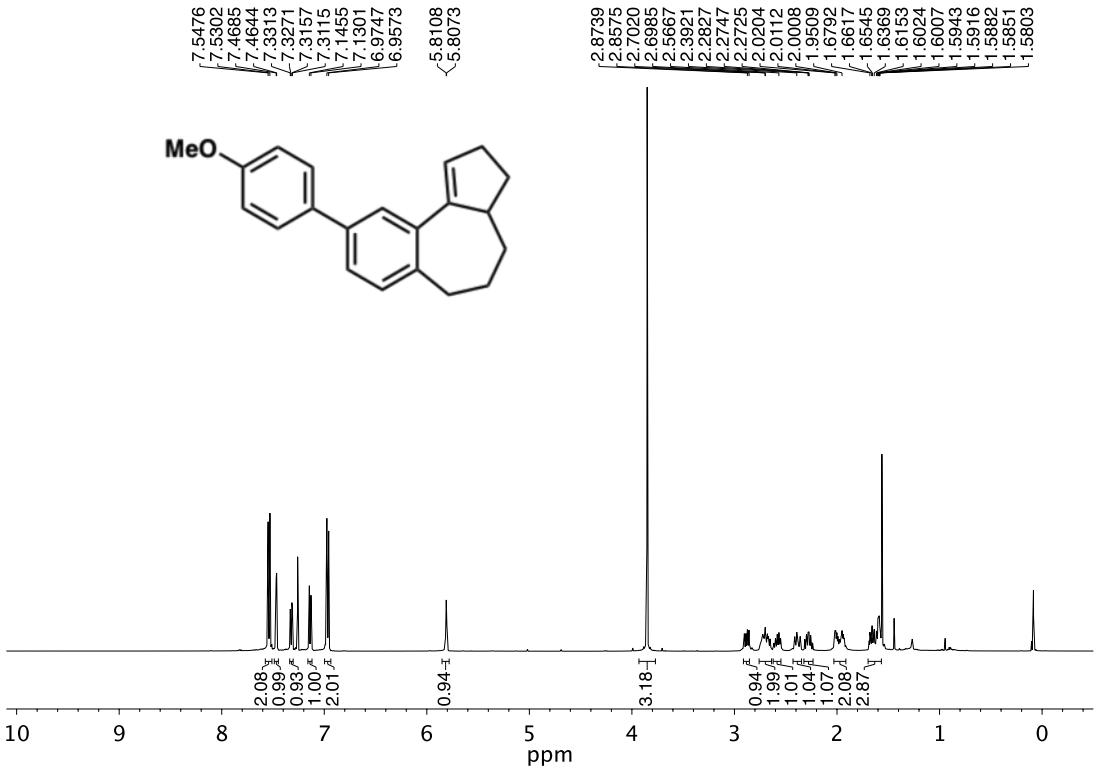


Figure 2.21 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.17**.

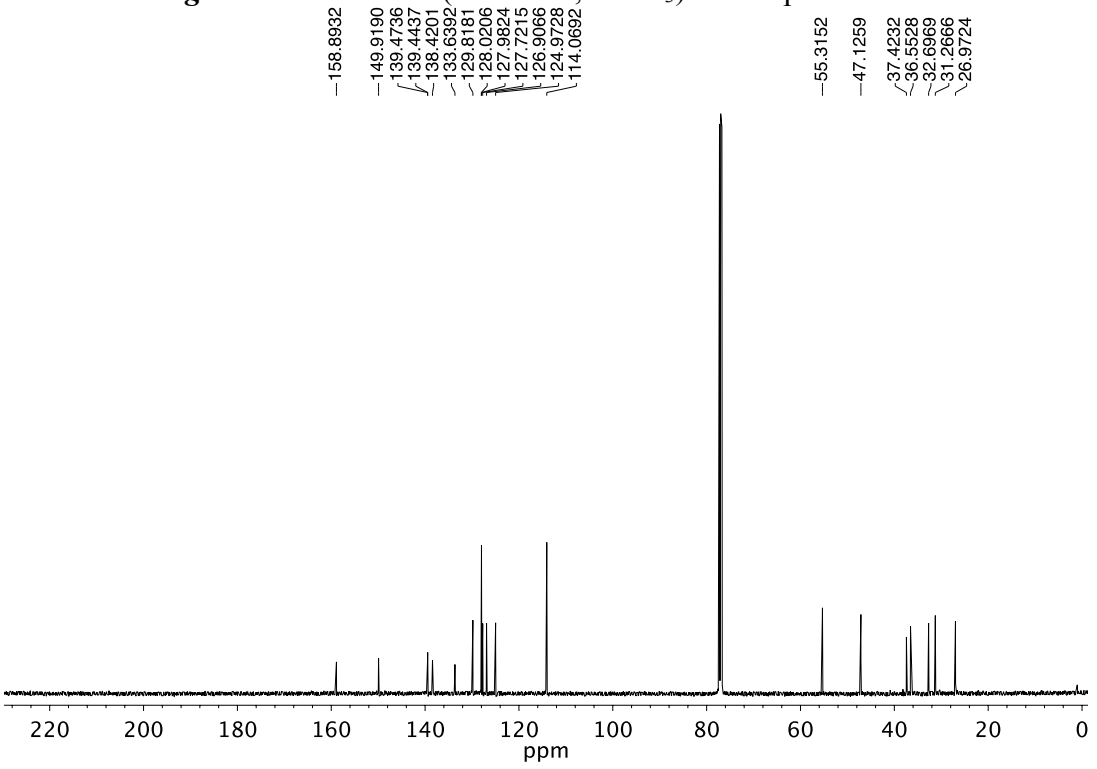


Figure 2.22 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.17**.

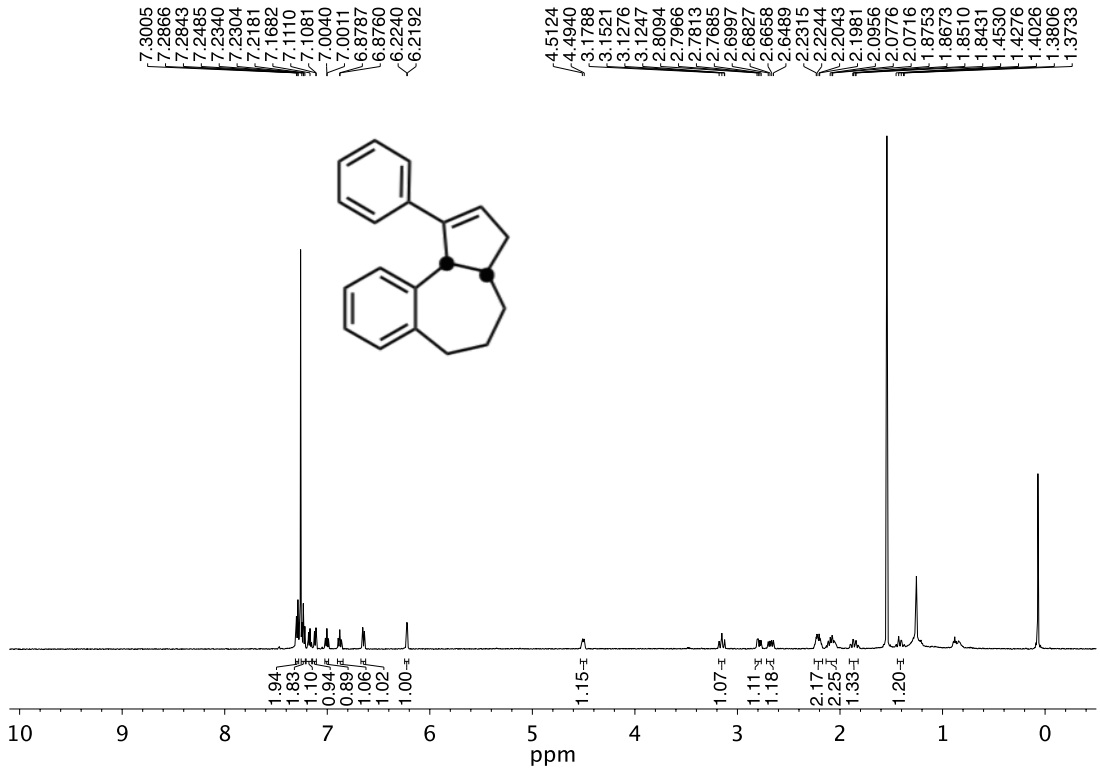


Figure 2.23 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.17**.

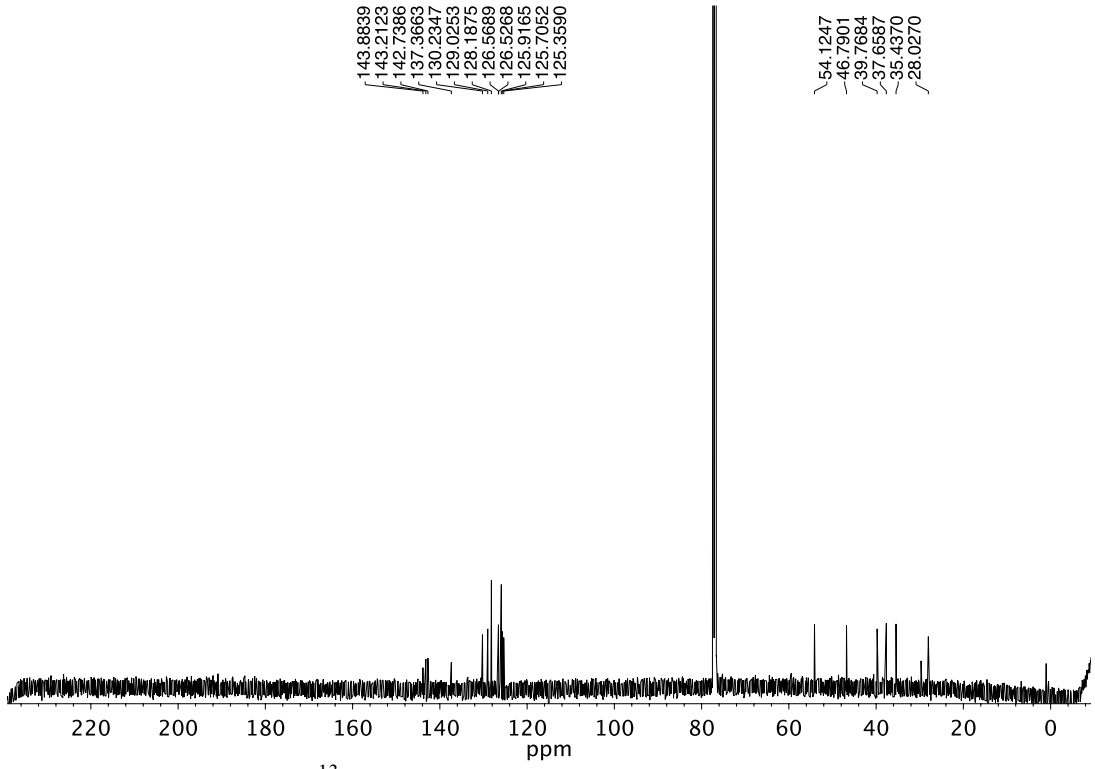


Figure 2.24 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.17.**

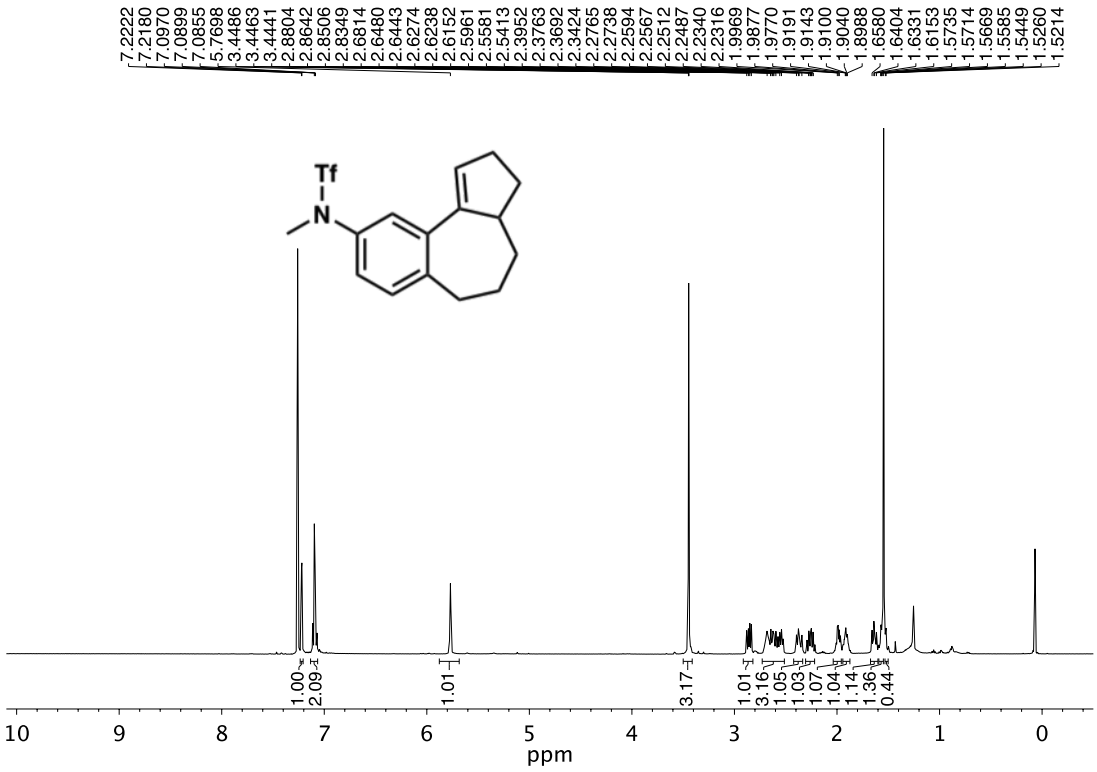


Figure 2.25 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.19**.

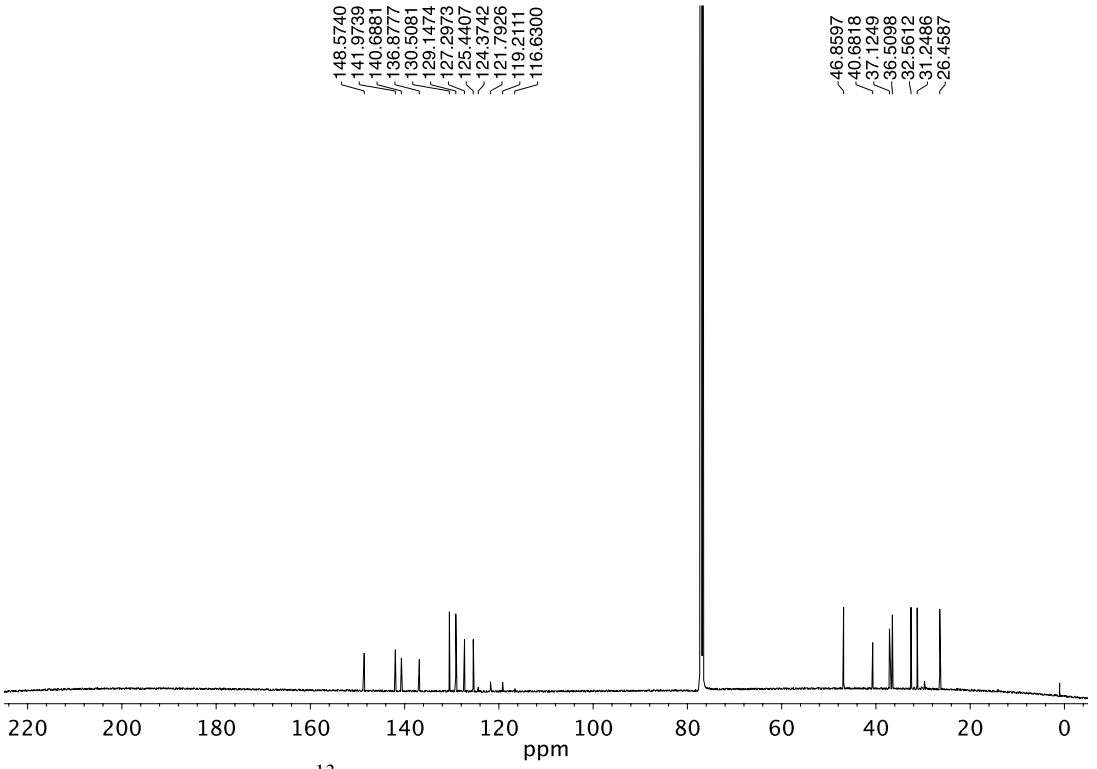


Figure 2.26 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.19**.

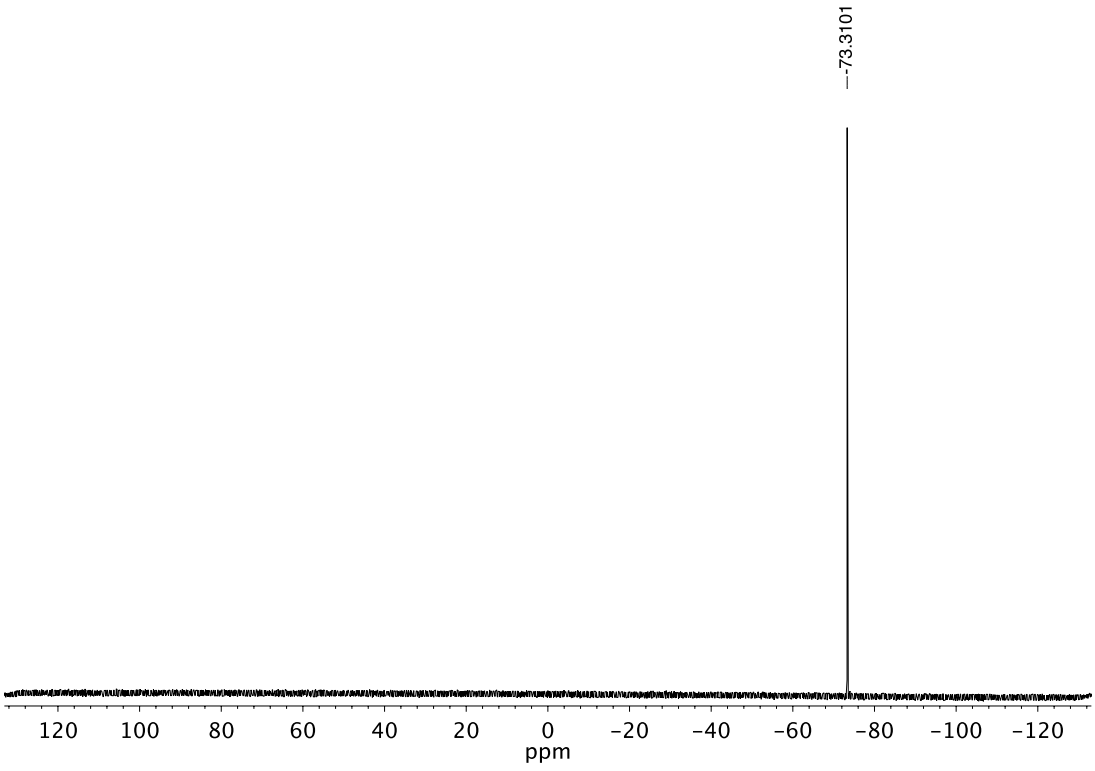


Figure 2.27 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **2.19**.

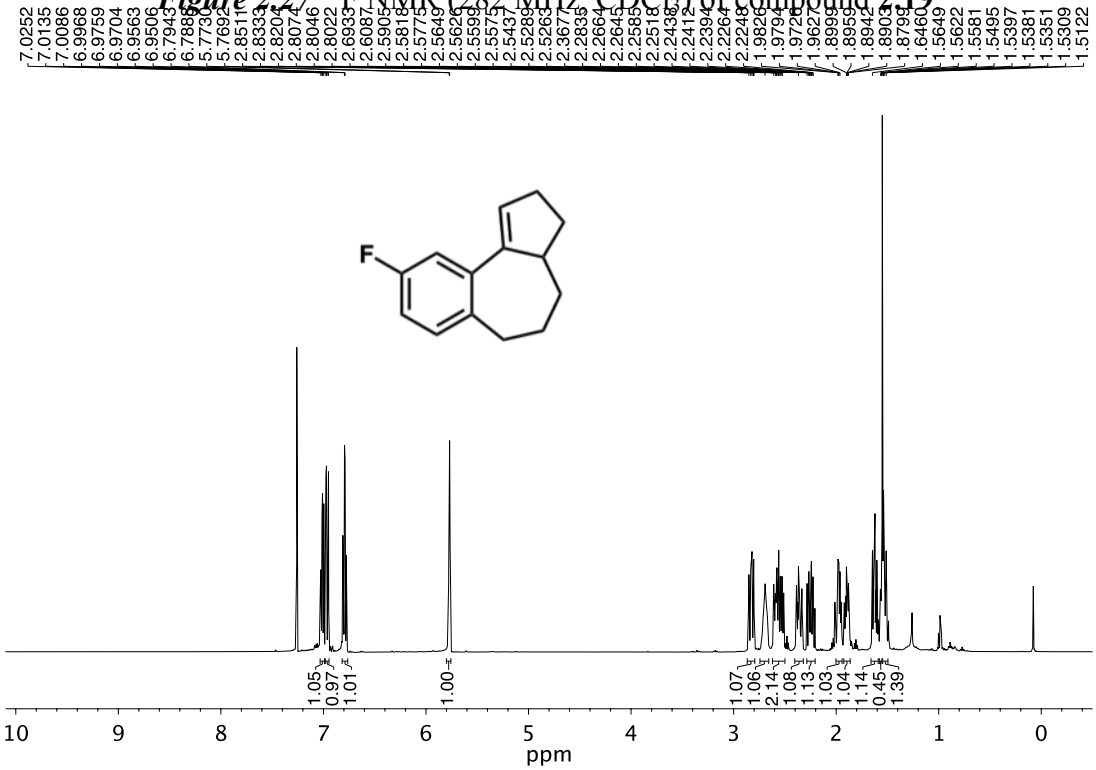


Figure 2.28 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.20**.

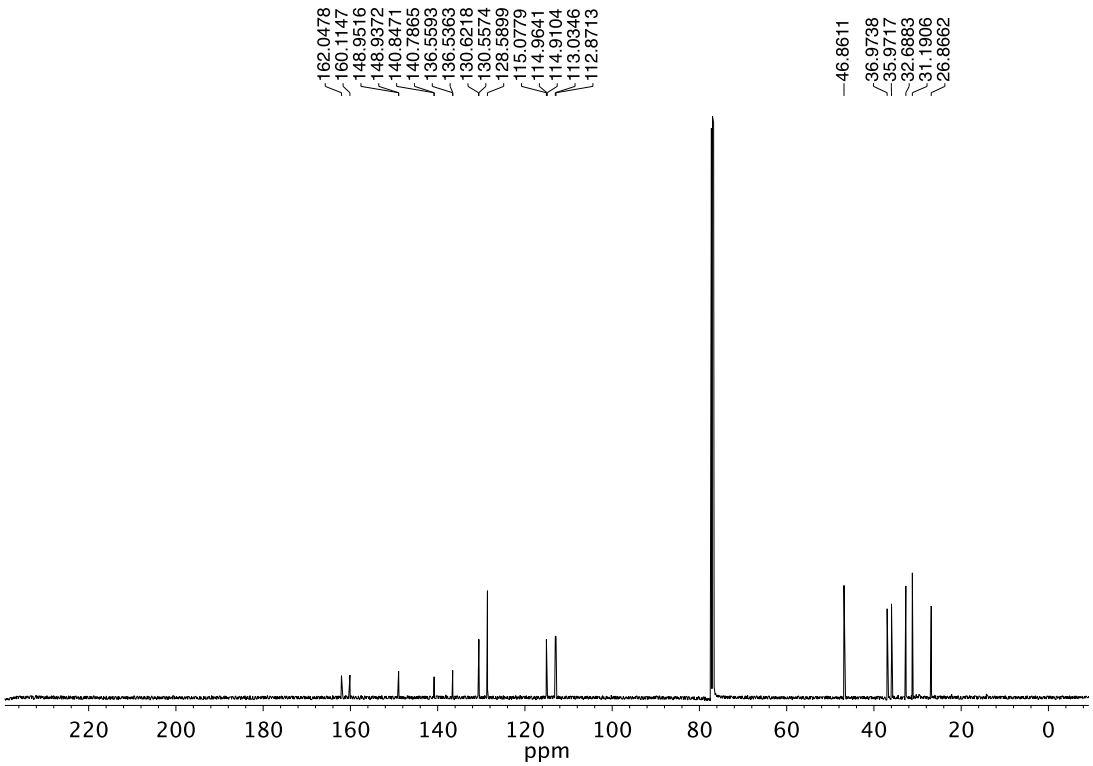


Figure 2.29 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.20**.

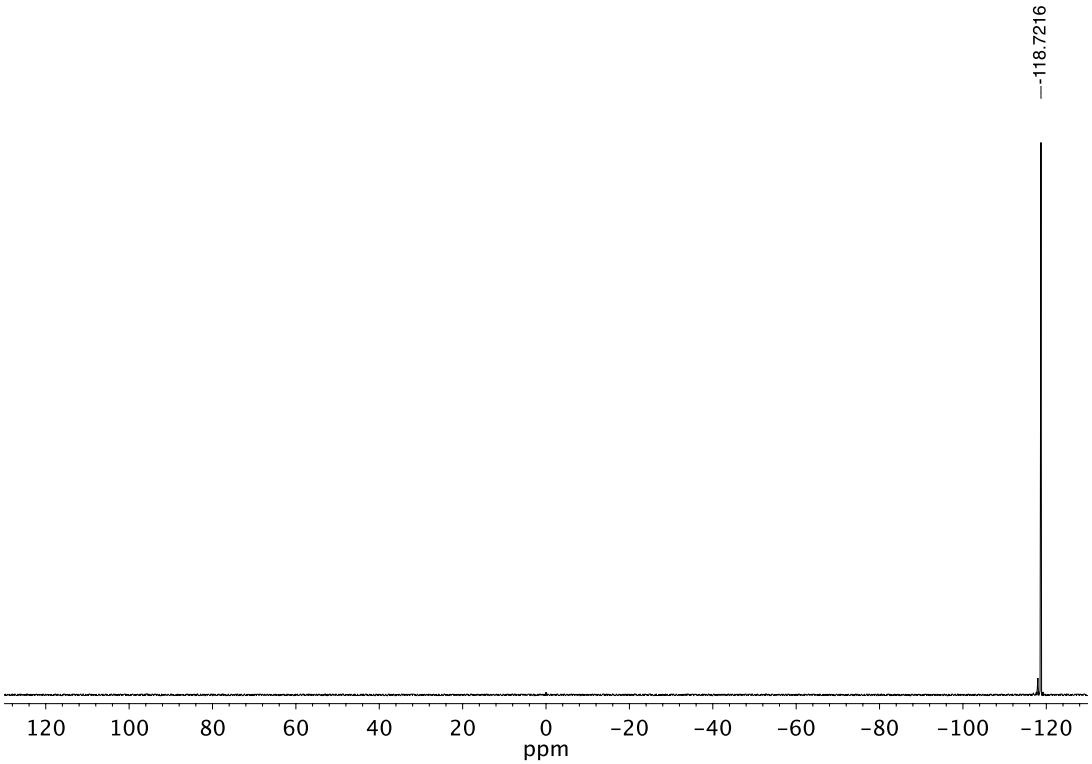


Figure 2.30 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **2.20**.

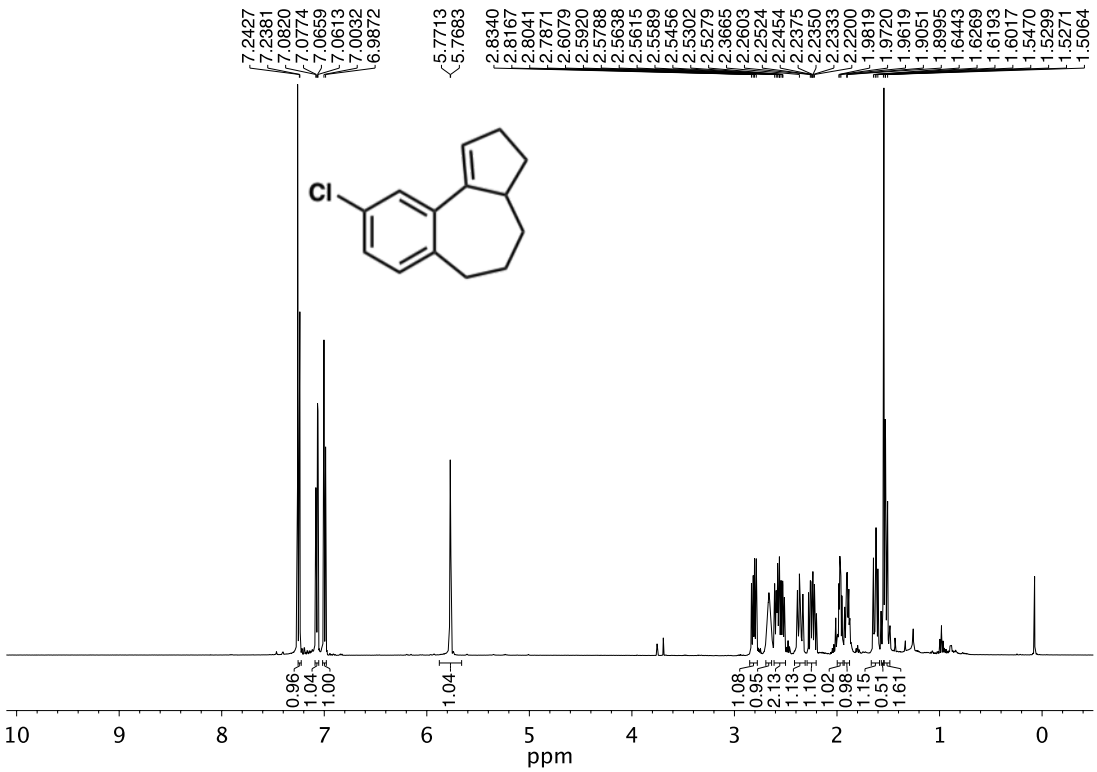


Figure 2.31 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.21**.

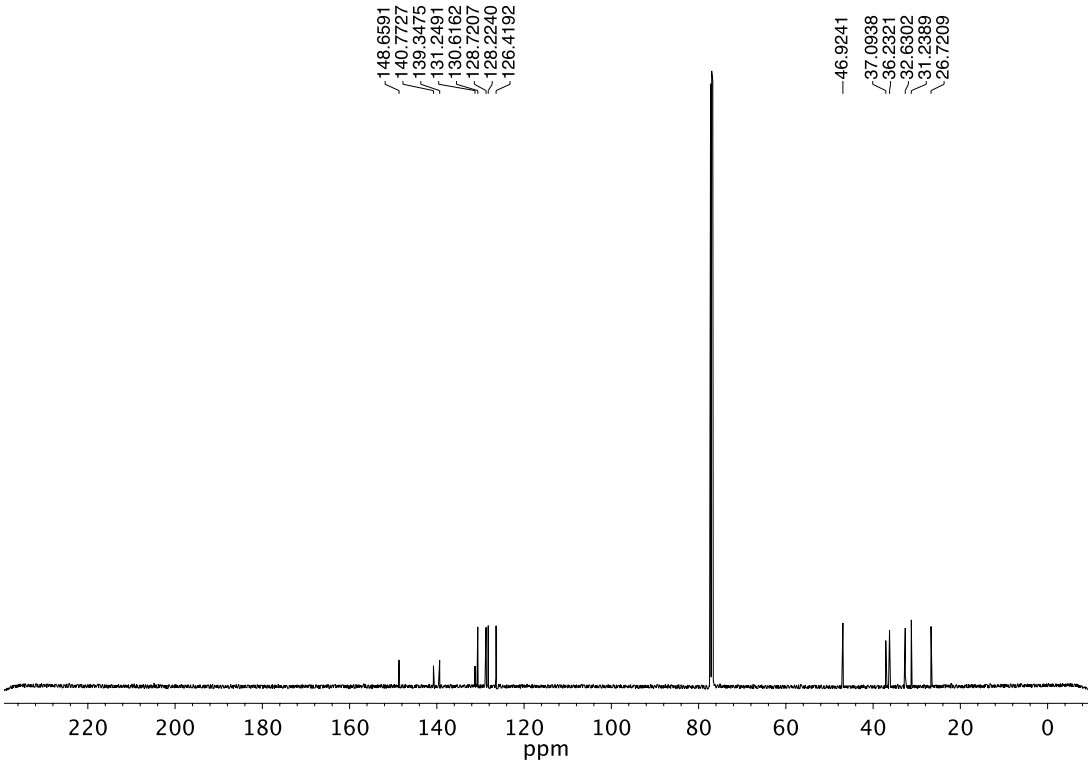


Figure 2.32 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.21**.

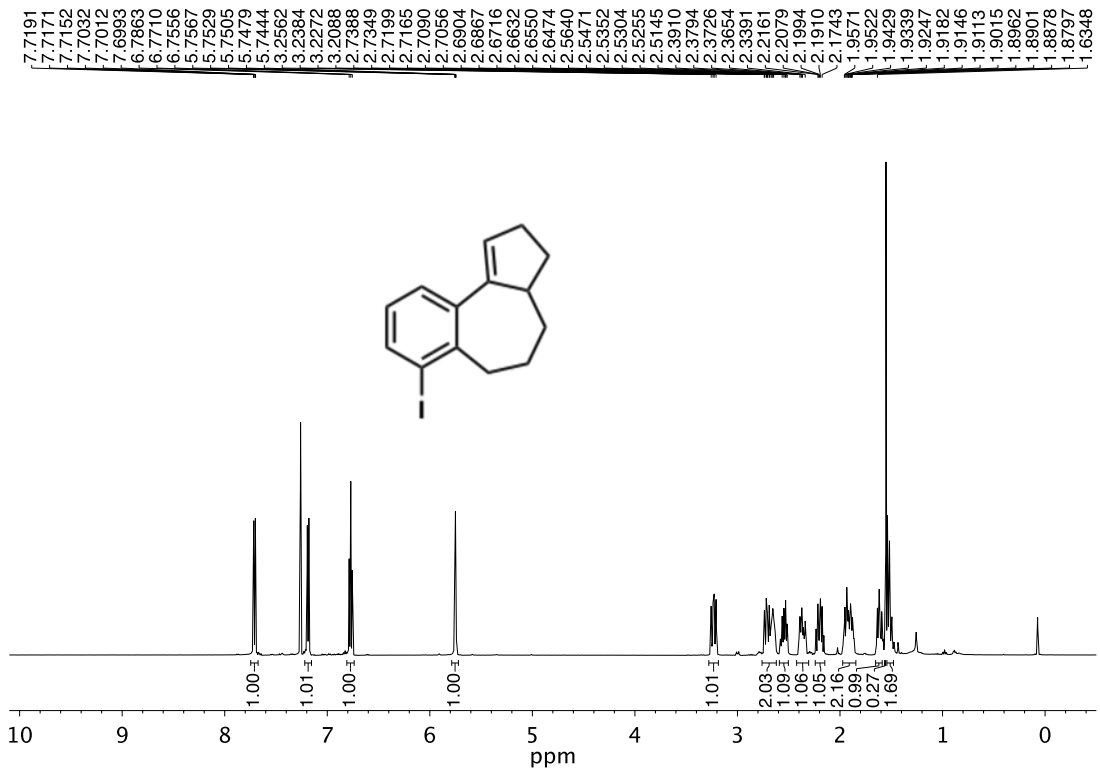


Figure 2.33 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.22**.

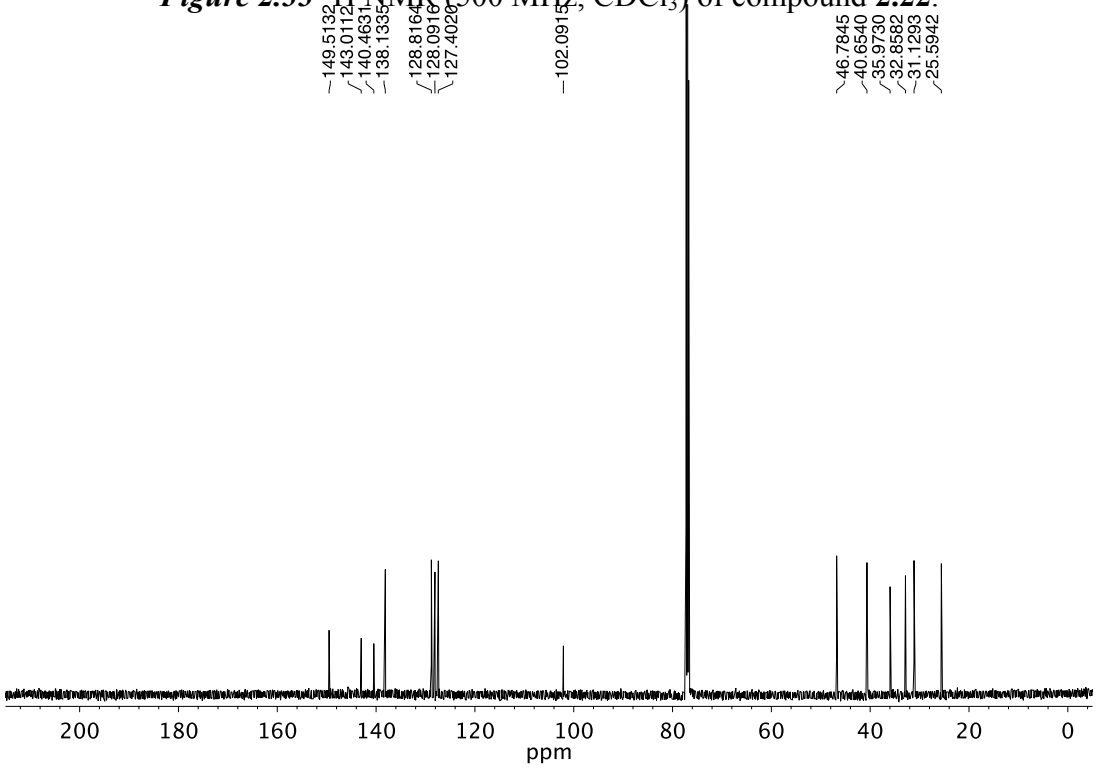


Figure 2.34 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.22**.

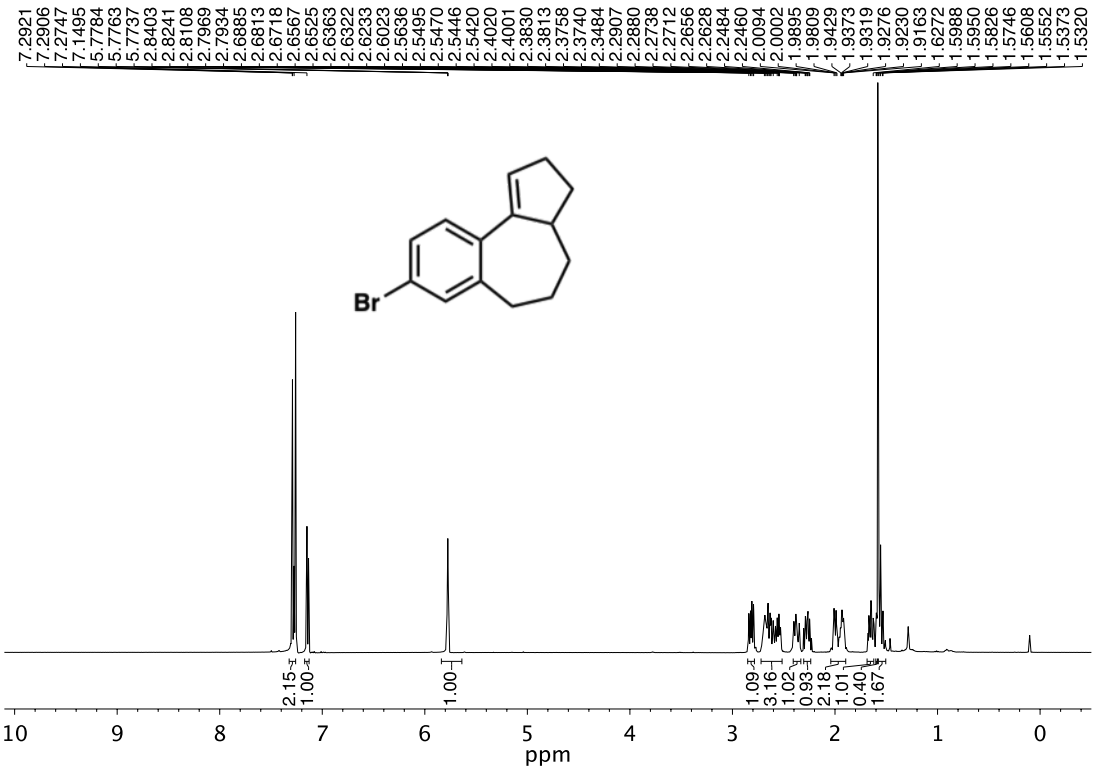


Figure 2.35 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.23**.

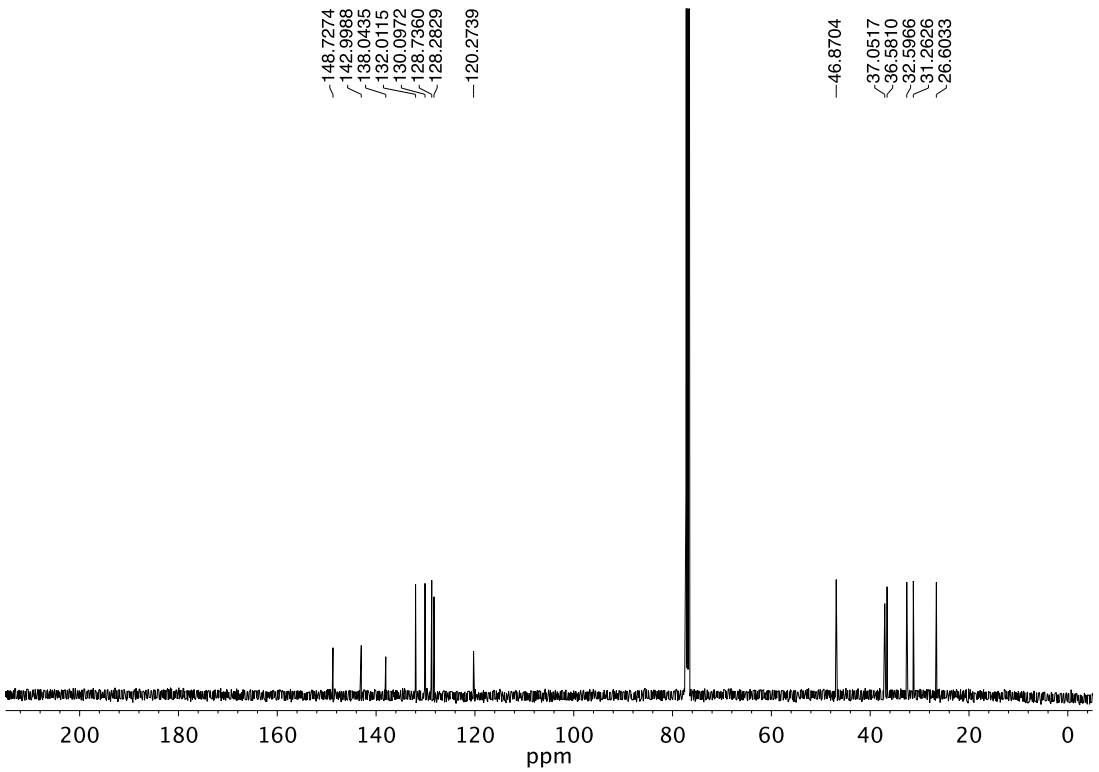


Figure 2.36 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.23**.

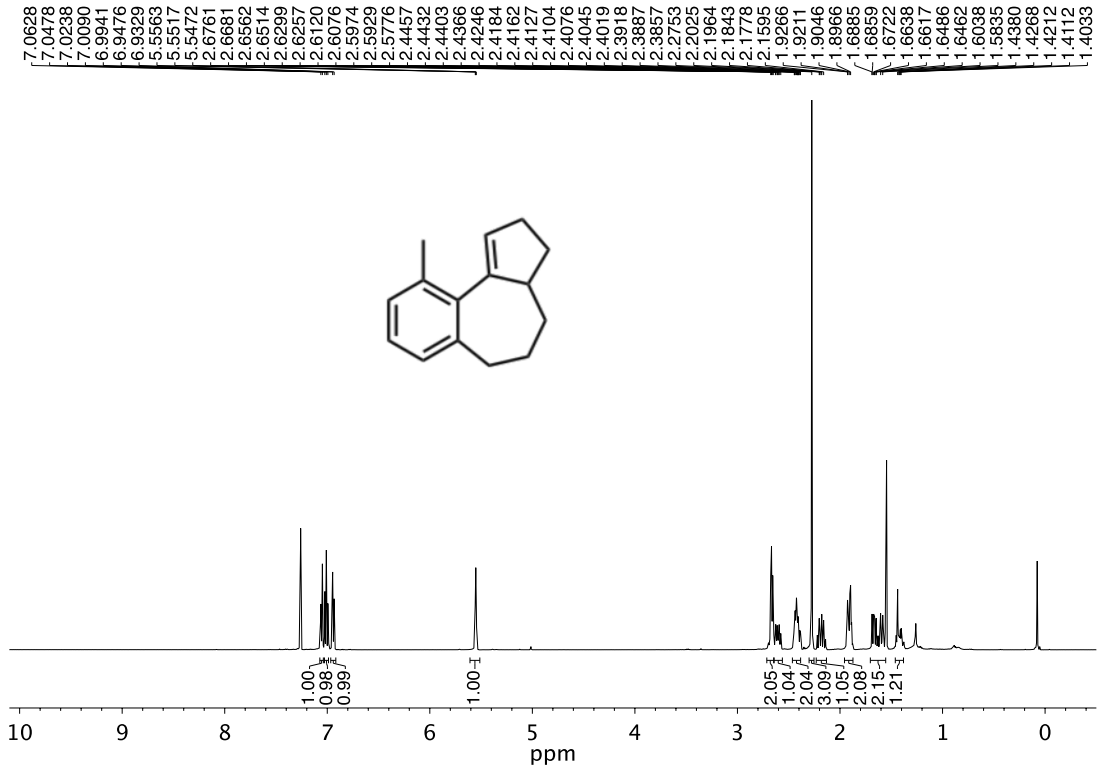


Figure 2.37 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.24**.

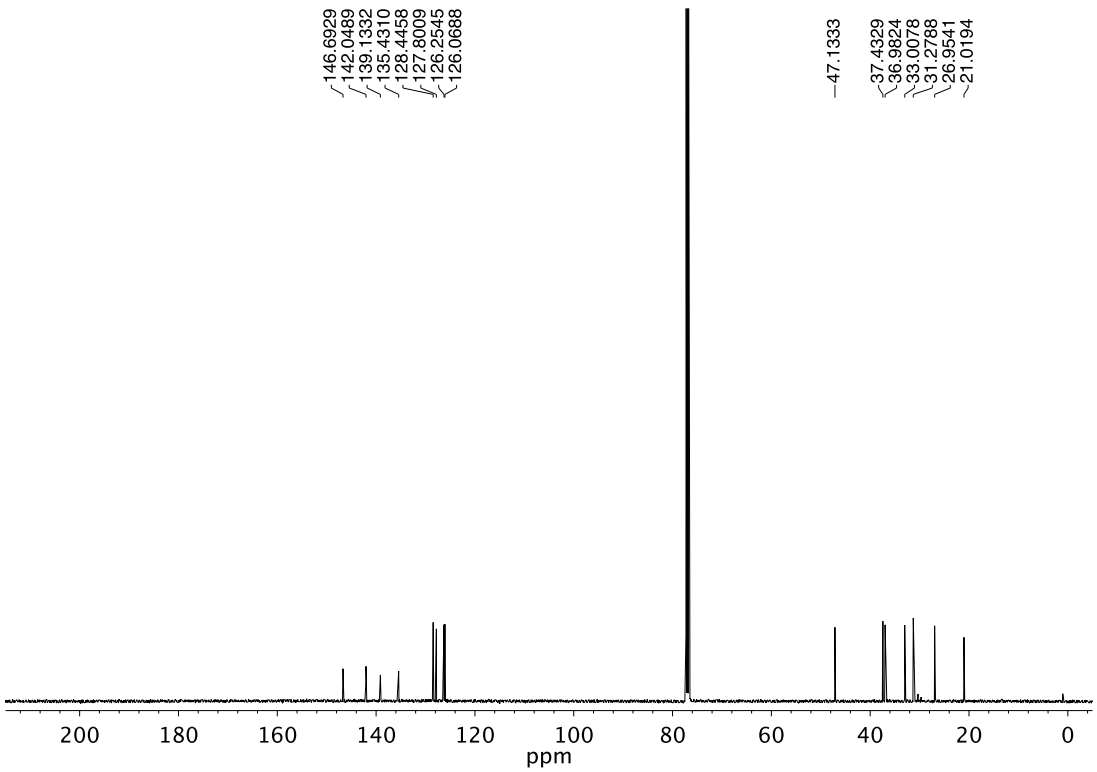


Figure 2.38 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.24**.

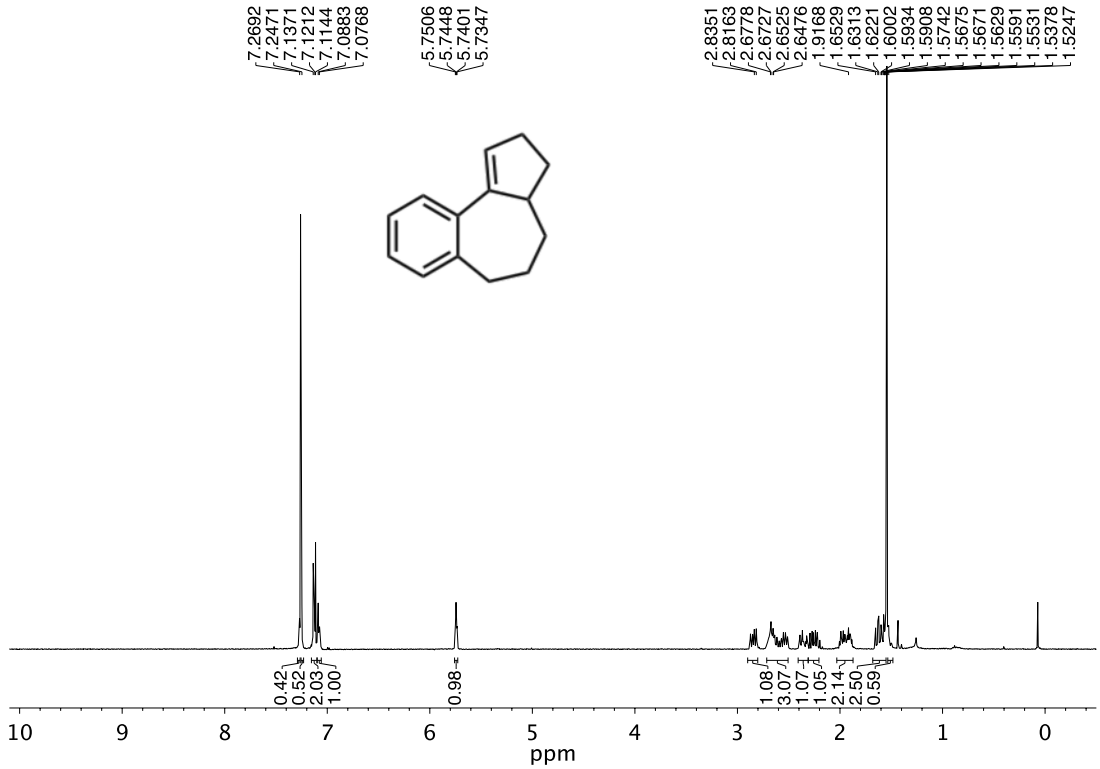


Figure 2.39 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.25**.

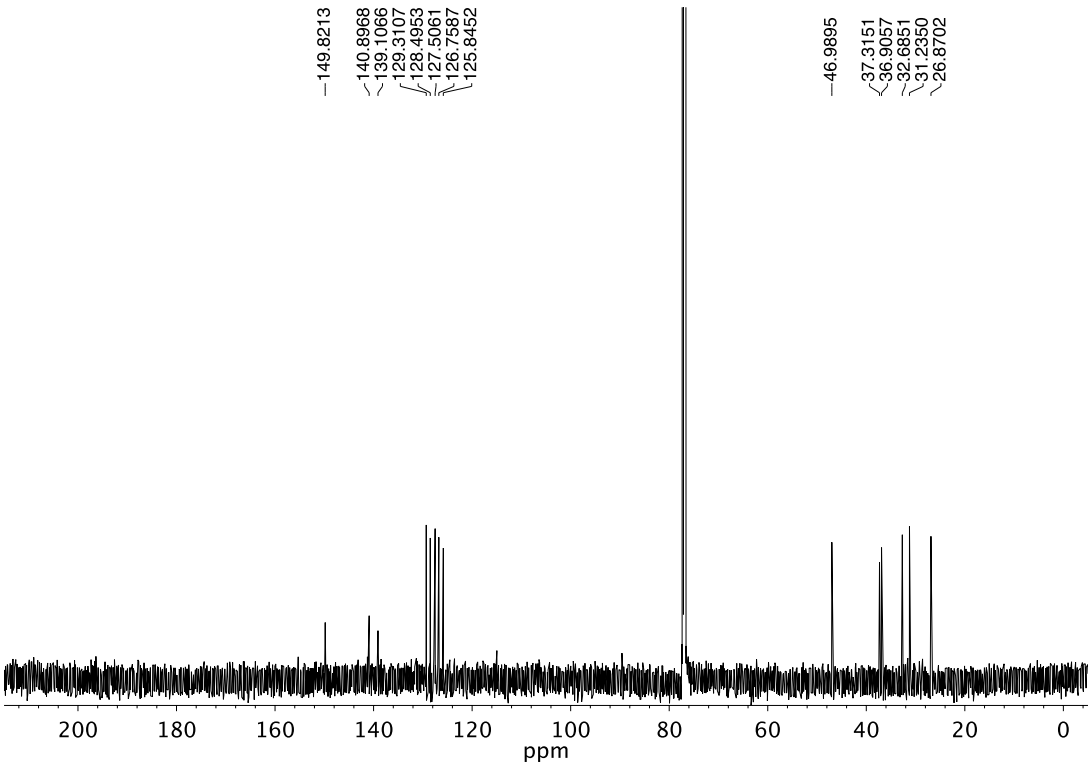


Figure 2.40 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.25**.

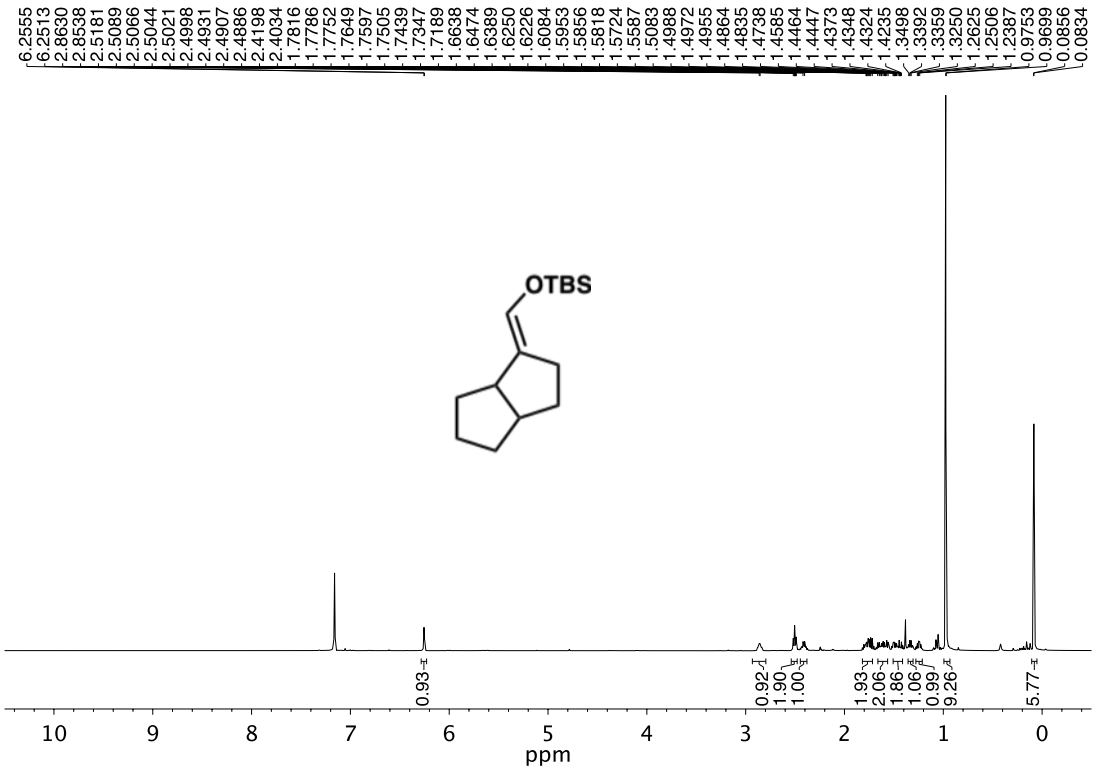


Figure 2.41 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.27E**

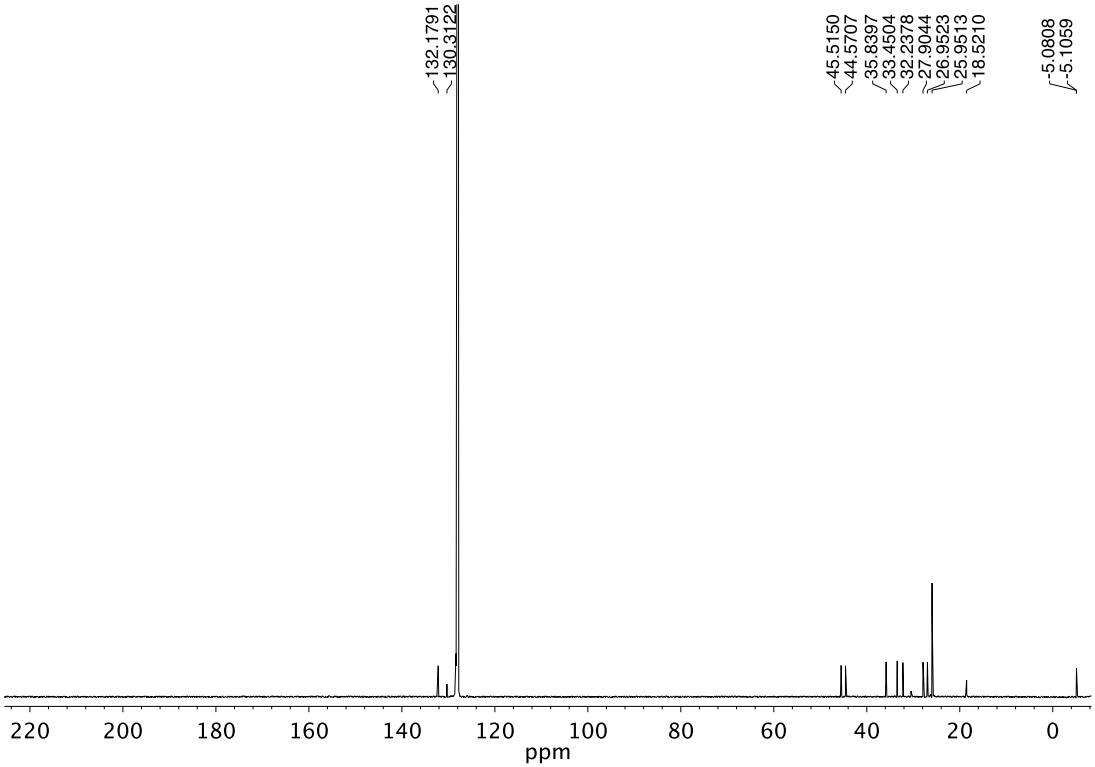


Figure 2.42 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.27E**.

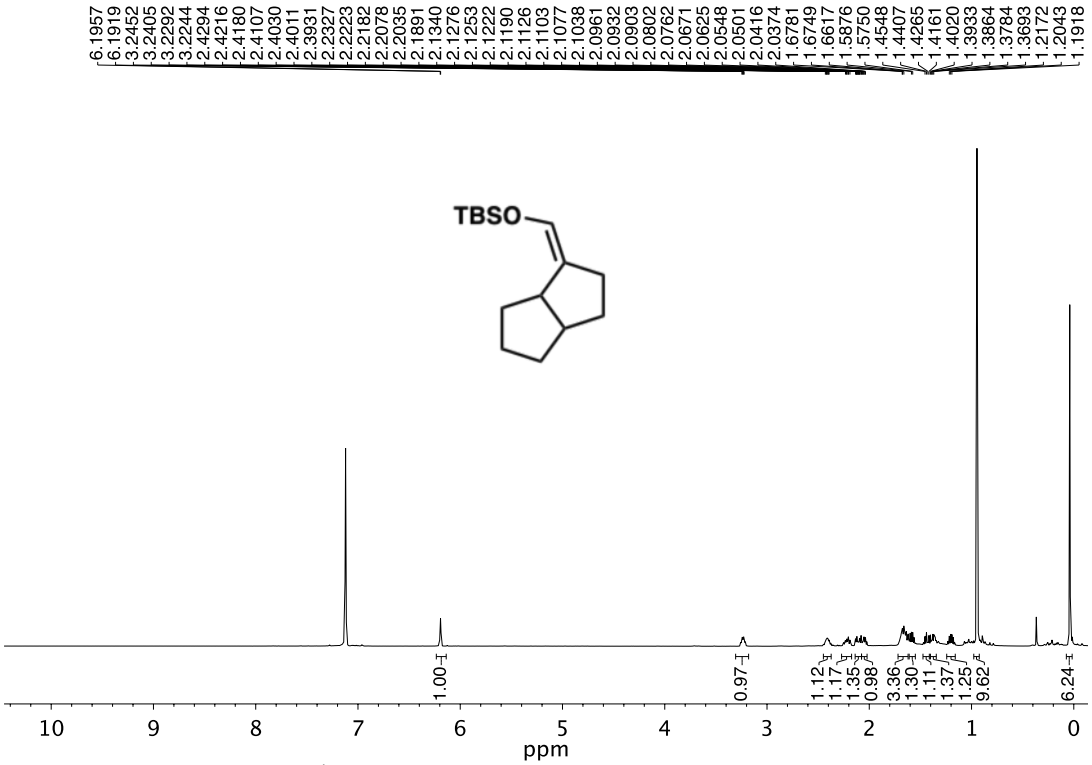


Figure 2.43 ^{1}H NMR (500 MHz, C_6D_6) of compound **2.27Z**.

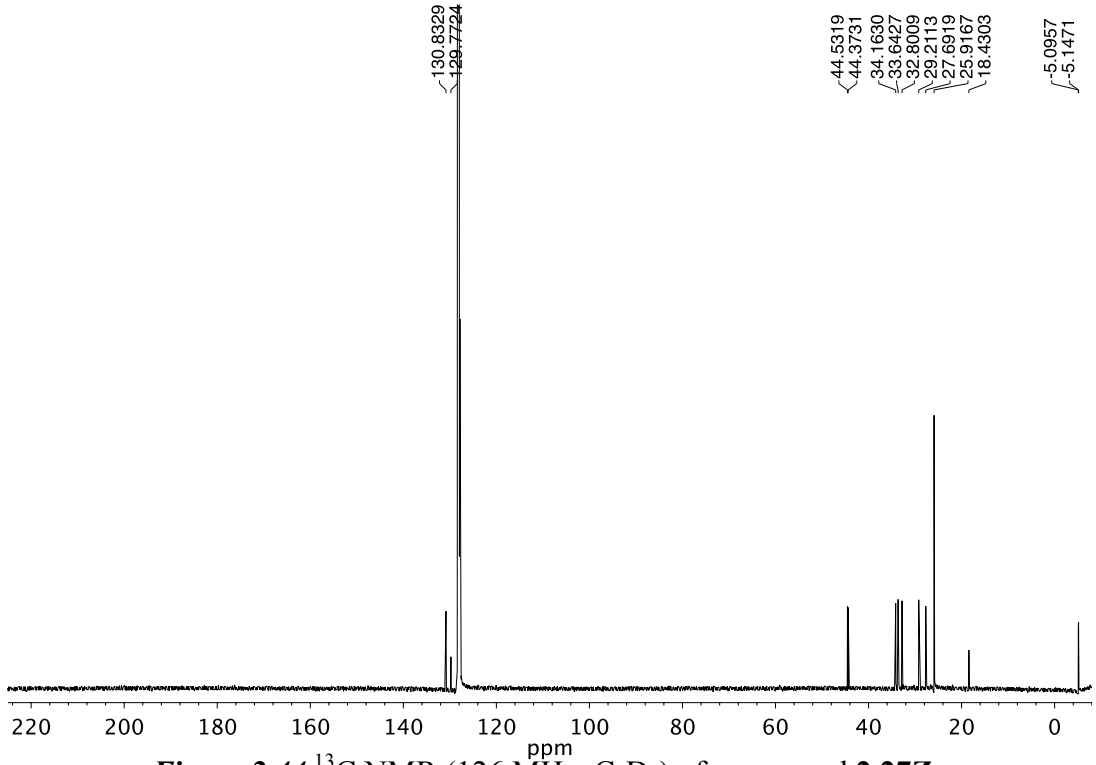


Figure 2.44 ^{13}C NMR (126 MHz, C_6D_6) of compound **2.27Z**.

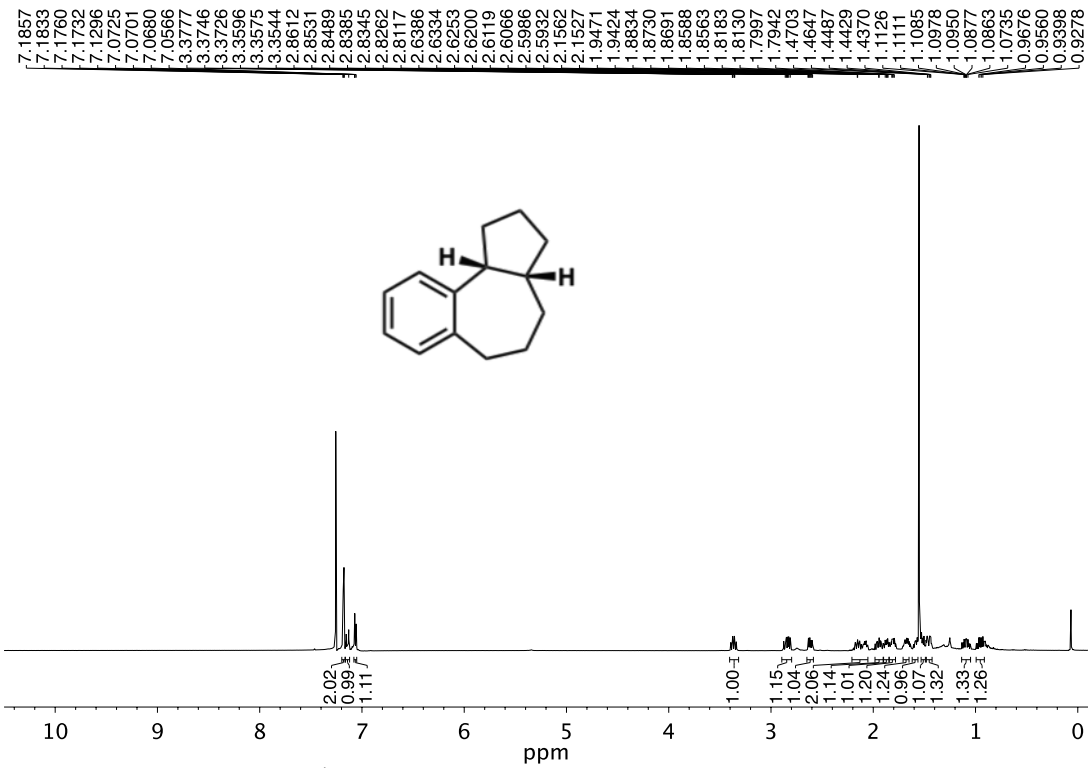


Figure 2.45 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.34**.

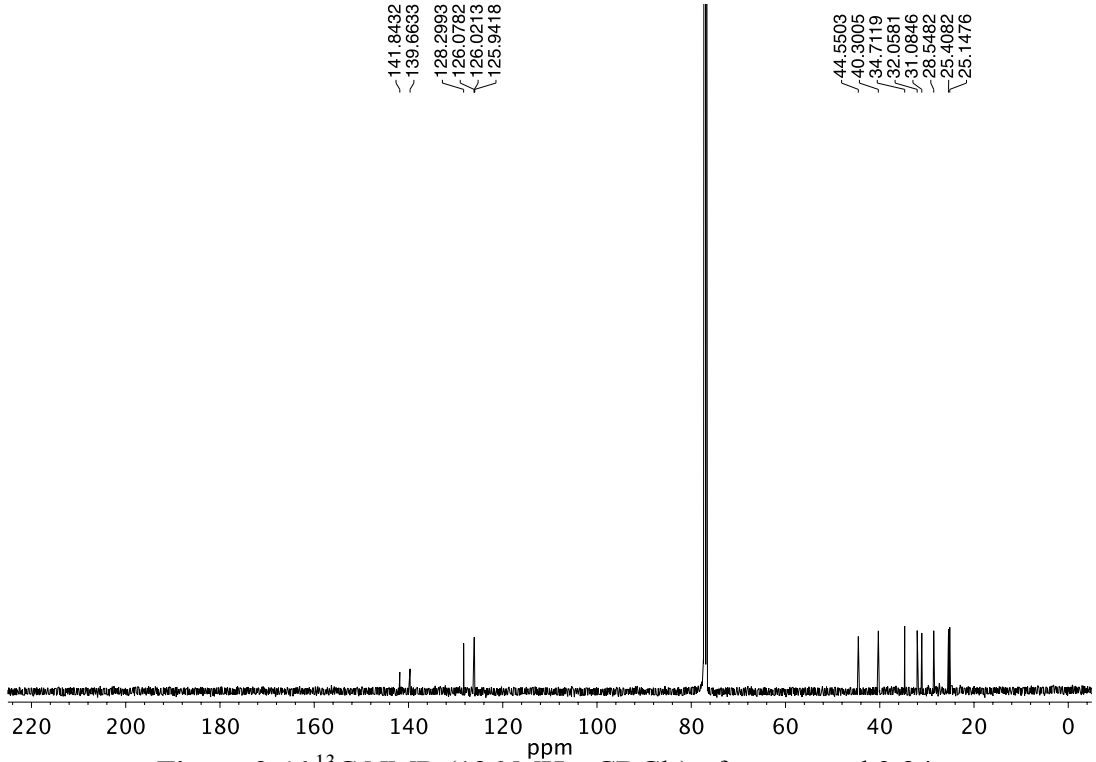


Figure 2.46 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.34**.

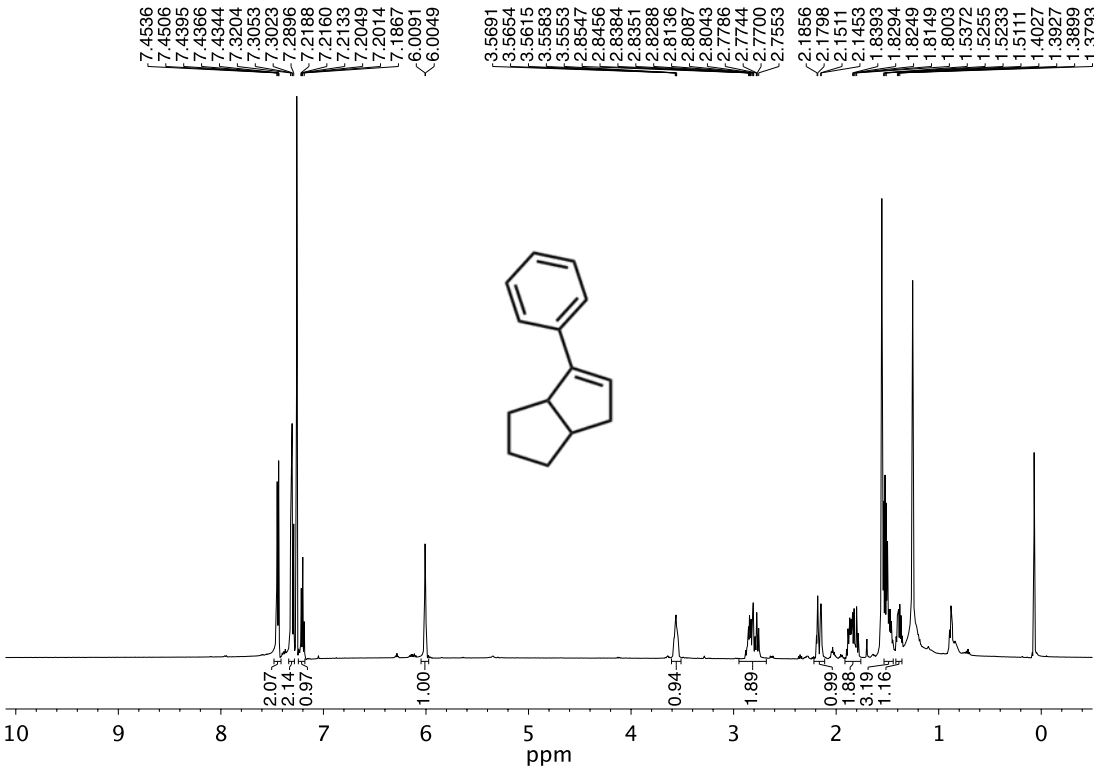


Figure 2.47 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.33**.

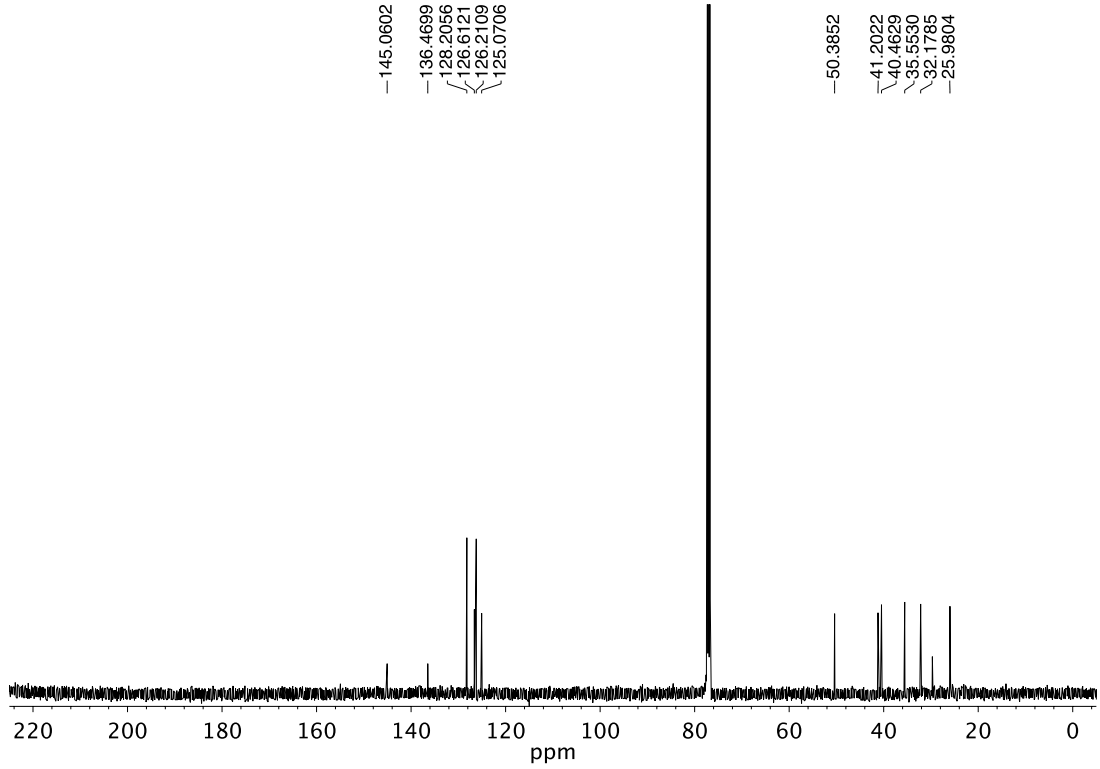


Figure 2.48 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.33**.

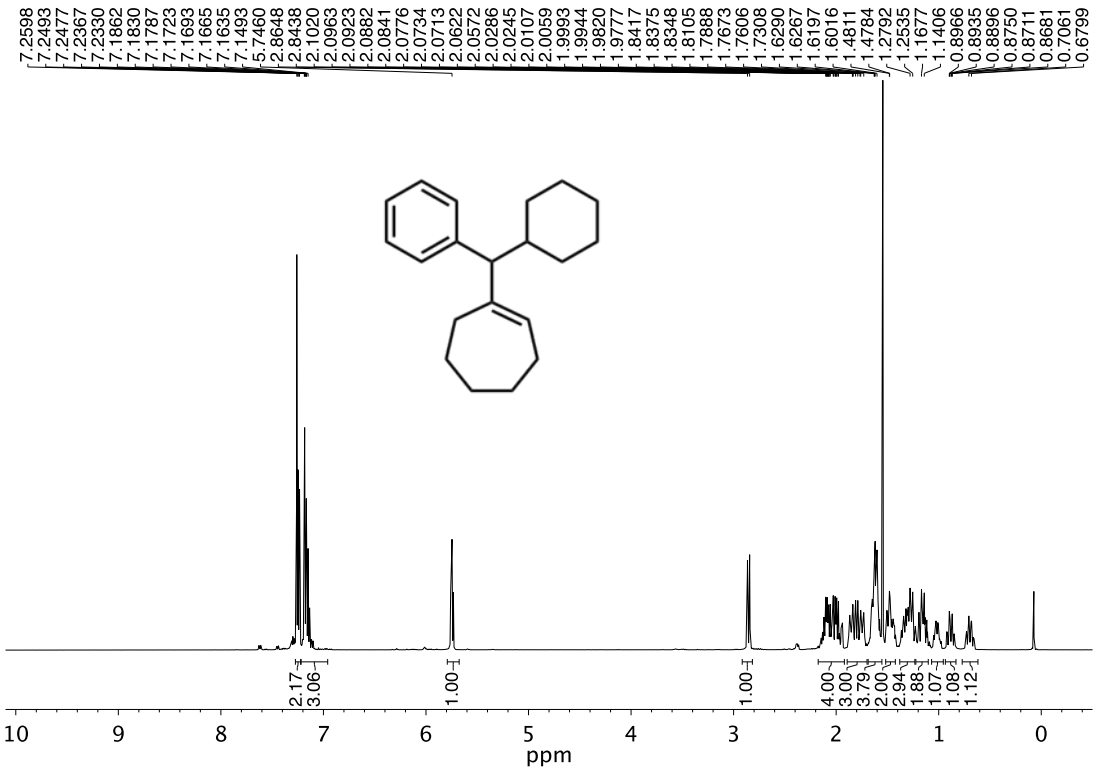


Figure 2.49 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.34**.

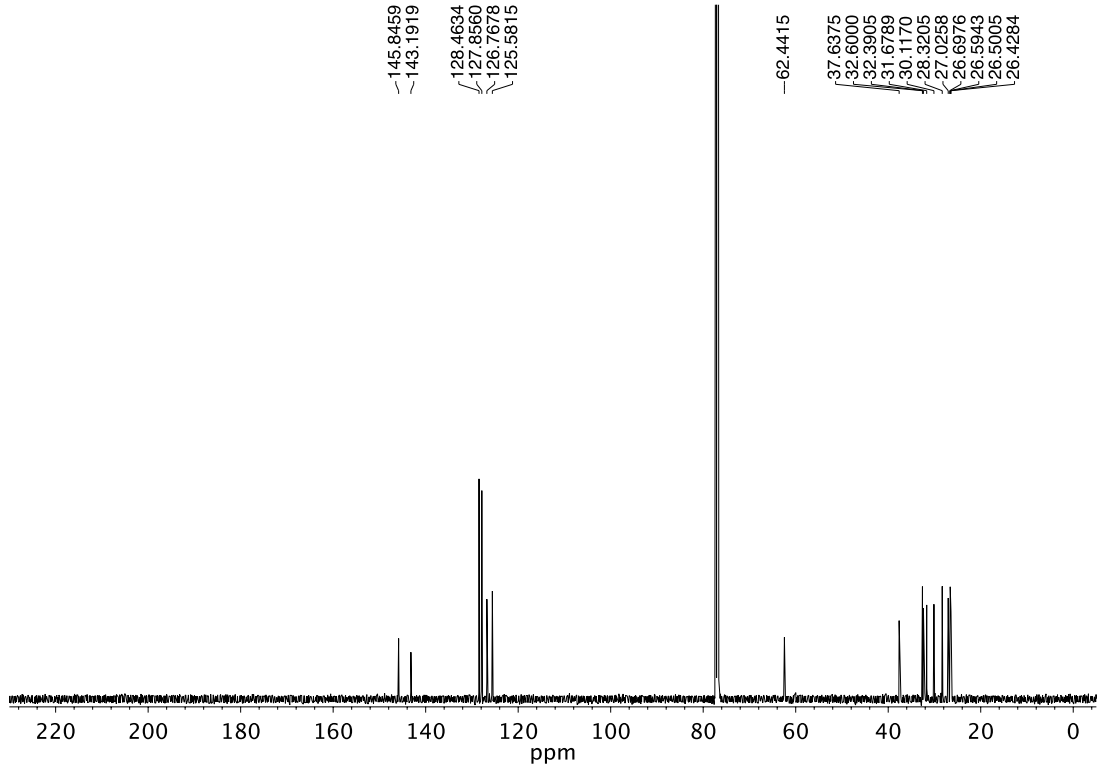


Figure 2.50 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.34**.

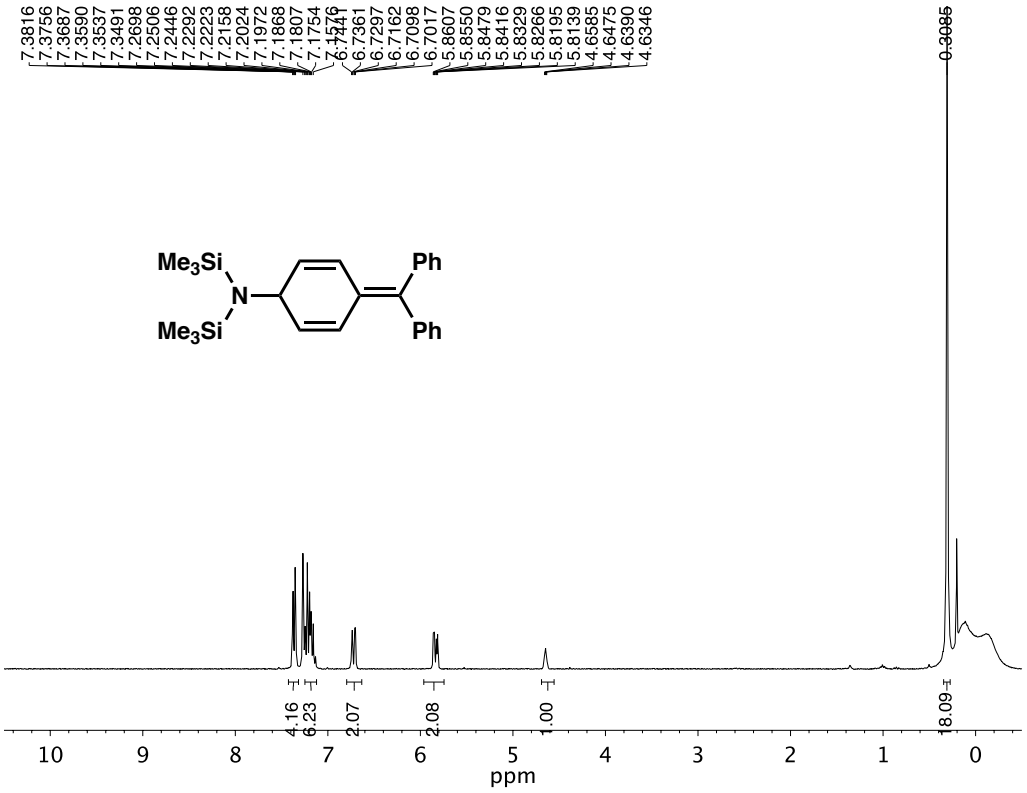


Figure 2.51 ^{1}H NMR (500 MHz, C_6D_6) of compound **2.35**.

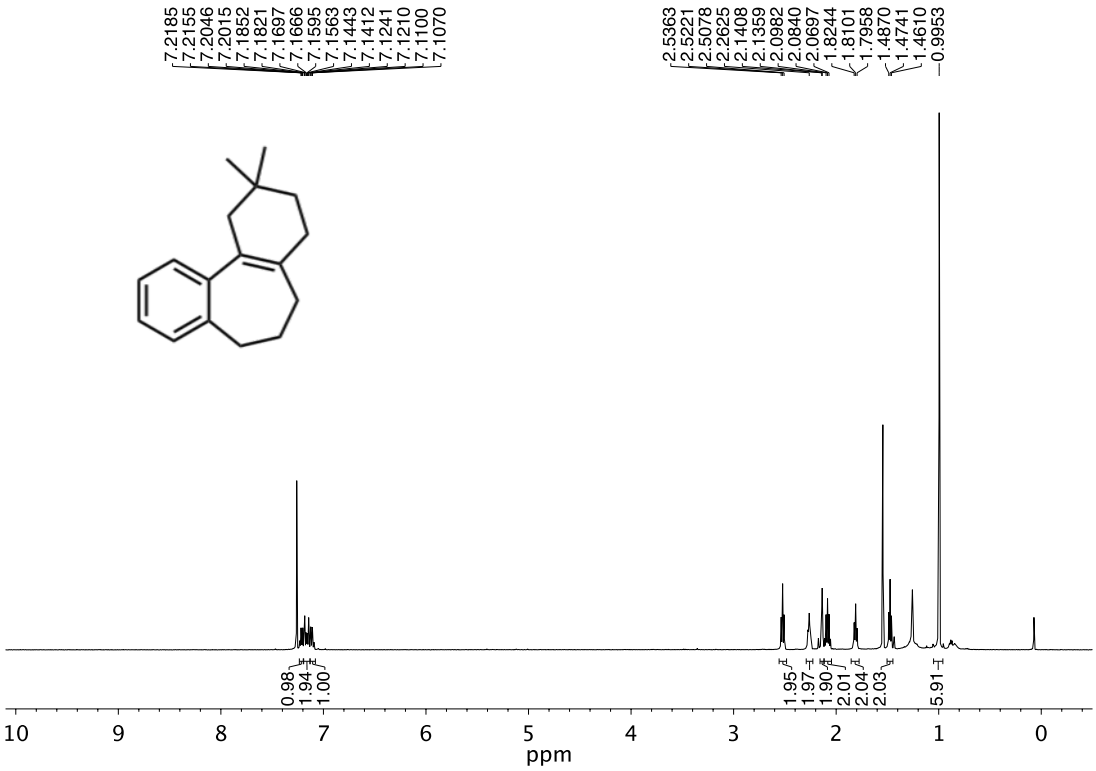


Figure 2.52 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.37.1**

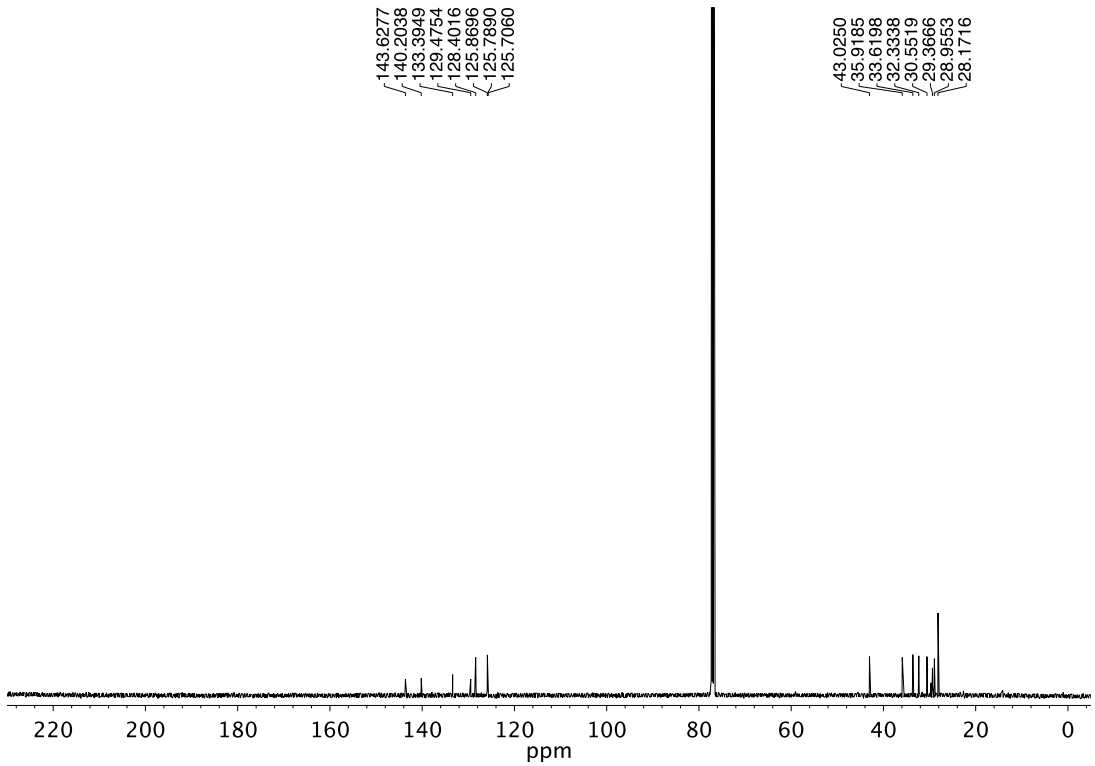


Figure 2.53 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.37.1**

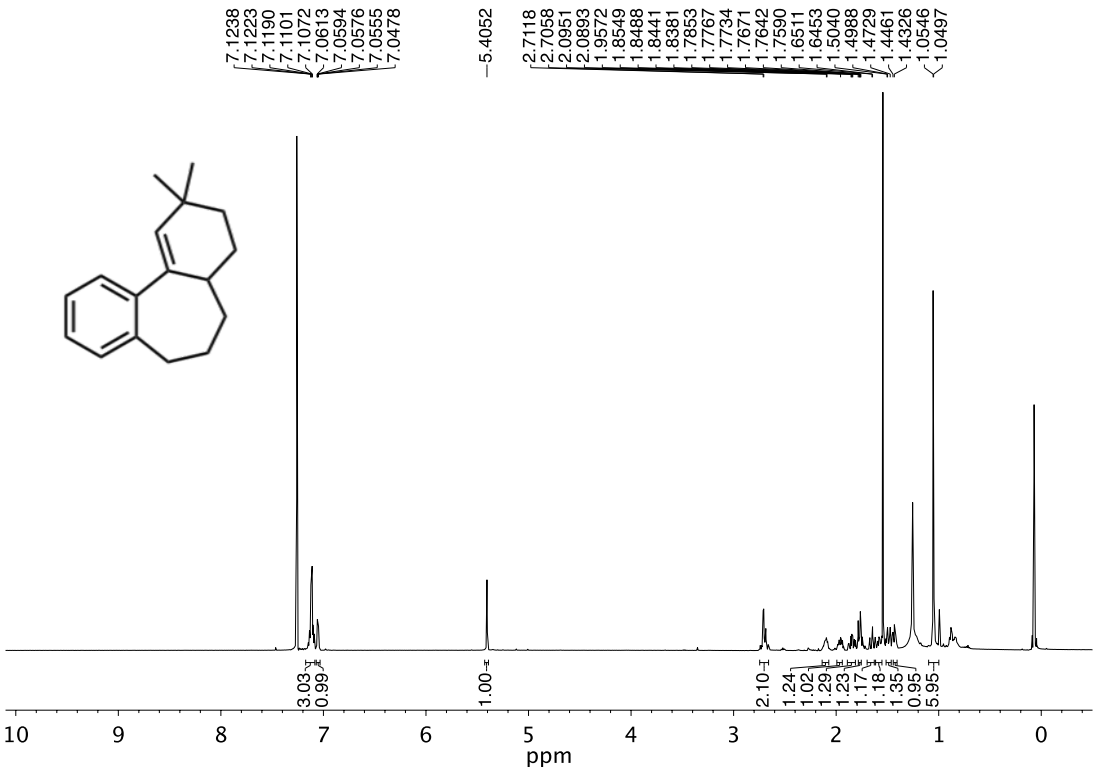


Figure 2.54 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **2.37.2**

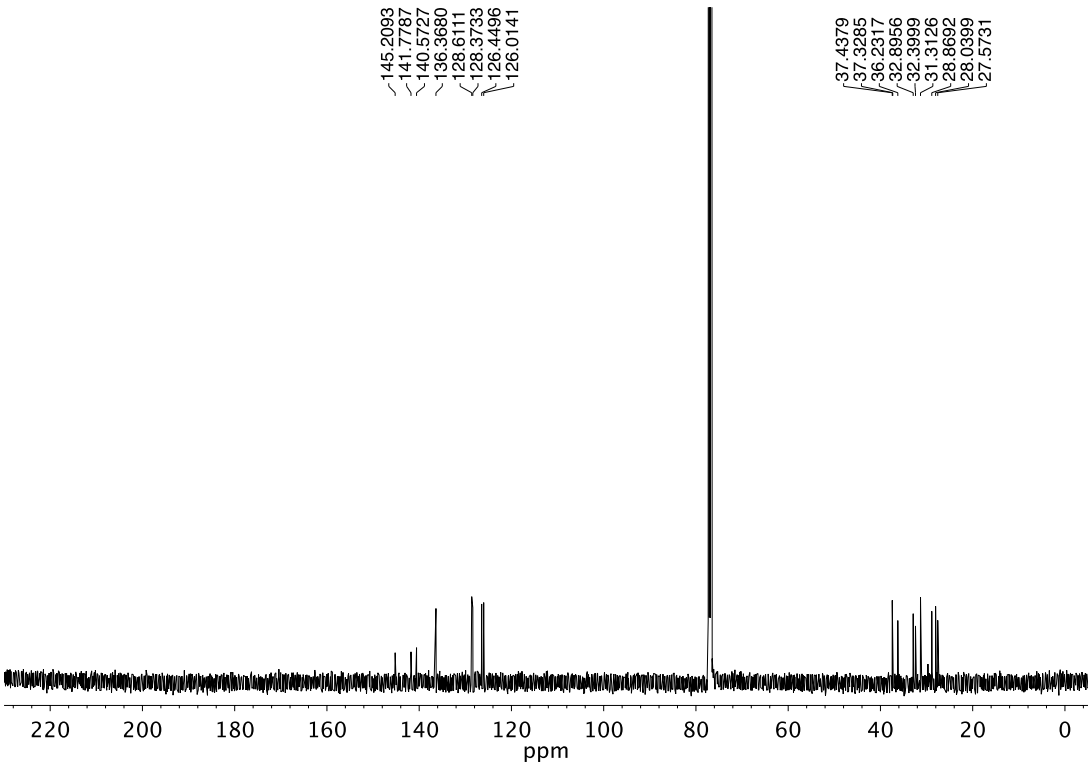


Figure 2.55 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.37.2**

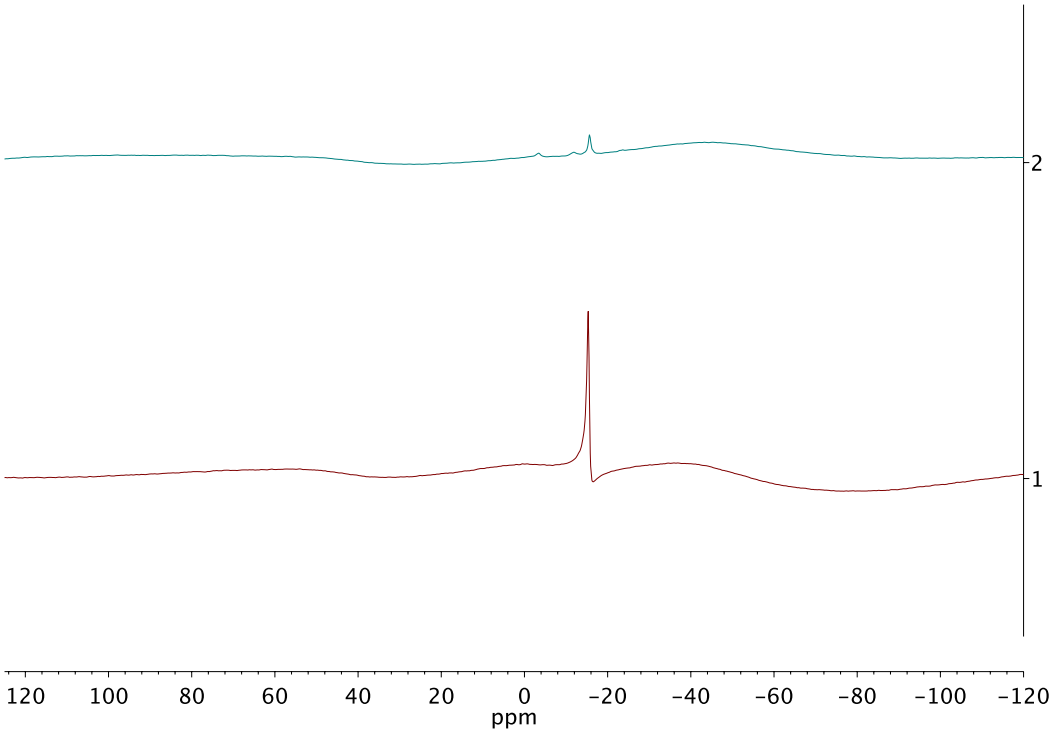


Figure 2.56 ^{11}B NMR (128 MHz, C_6D_6)) comparison of authentic **Li[B(C_6F_5)$_4$] (2.11)** (top) and *in situ* **Li[B(C_6F_5)$_4$]** (bottom).

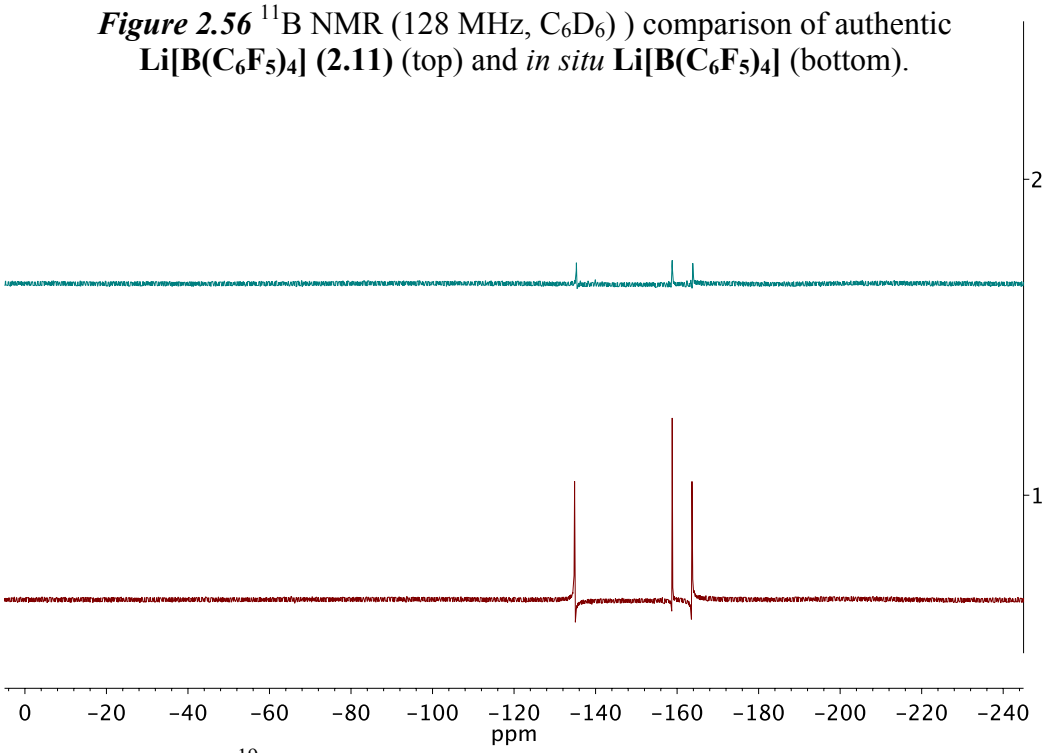


Figure 2.57 ^{19}F NMR (282 MHz, C_6D_6)) comparison of authentic **Li[B(C_6F_5)$_4$] (2.11)** (top) and *in situ* **Li[B(C_6F_5)$_4$]** (bottom).

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CHAPTER THREE

Urea Catalysts Used to Generate Vinyl Carbocations and Further Exploration of Substrate Compatibility

Alex L. Bagdasarian, Stasik Popov, Benjamin Wigman, Wenjing Wei, Woojin Lee, and Hosea M. Nelson *Org. Lett.* **2020**, *22*, 7775–7779.

3.1 Abstract

The previously disclosed basic conditions used demonstrated that the lithium-Lewis acid system could tolerate a variety of functional groups. A commercially available catalyst was utilized, but it was still rather cost prohibitive. Here, in efforts to gain access to even more easily accessible catalysts, we have shown that common hydrogen bonding catalysts, such as ureas and squareamides, in conjunction with a lithium base promote intramolecular C–H insertion reactions of vinyl triflates. Further substrate scope is demonstrated, and mechanistic insight into how vinylogous acyl triflates undergo C–H functionalization is gained. These results demonstrate how C–H functionalization reactions using vinyl triflates is now much more easily accessible to the synthetic organic community.

3.2 Introduction

With the previous work (Chapter **2**) in mind, our lab grew eager to control the selectivity of our C–H insertion reactions. Particularly, enantioselectivity was highly appealing, as an enantioselective insertion reaction of sp^3 C–H bonds to form new C–C bonds would be very powerful. The initial efforts of this work were entirely spearheaded by Alex Bagdasarian, and he was inspired by the usage of urea, thiourea, and squareamide hydrogen bonding catalysts in asymmetric catalysis.[1–5] He tested a variety of organocatalysts using the previously developed benzosuberonyl triflate (**3.1**) to see if any of the C–H insertion product (**3.2**) was observed. What he found was that none of the hydrogen bonding catalysts alone (**3.3–3.4**) promoted this transformation, but in the presence of LiHMDS even at –40ºC the reaction proceeded in high yield (Figure 3.1).

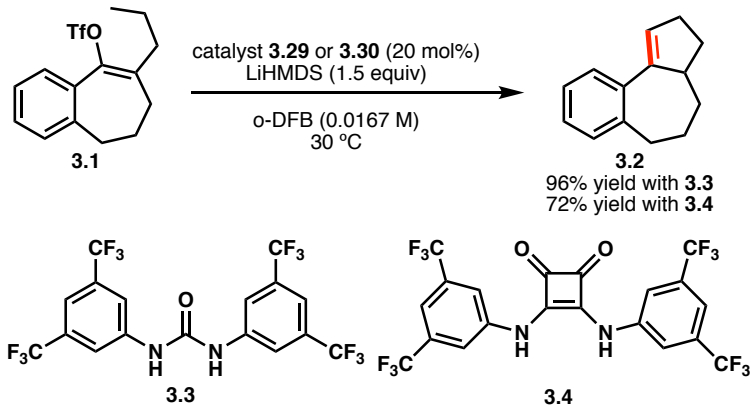


Figure 3.1 C–H insertion promoted by hydrogen bonding catalysts with LiHMDS

This result was promising, as perhaps chiral variants of these catalysts could yield an enantioselective C–H insertion reaction. While further screening not mentioned here was unfruitful, the discovery of this catalytic system was still quite important. Multiple grams of these catalysts can be prepared in a single day, and storage outside of the glovebox is possible. While the previous [Li][$B(C_6F_5)_4$] catalyst could be accessed with commercially available reagents, they were rather expensive and required storage in a glovebox.

3.3 C–H Functionalization of Linear and Vinylogous Acyl Triflates

Around the same time of this discovery I was interested in exploring what other substrate scaffolds could undergo C–H insertion readily. Particularly we had not investigated linear vinyl triflate precursors (**3.5**) or vinylogous acyl triflates (**3.6**). If both of these substrate classes performed C–H insertion reactions, it would drastically increase our substrate scope and appeal to the common organic chemist: moving away from the benzosuberonyl and cyclooctenyl triflate class was necessary.

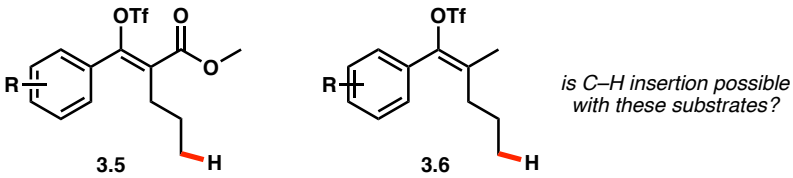


Figure 3.2 Unexplored substrates for C–H insertion

A variety of electron withdrawing arene appended linear vinyl triflates were prepared (Figure 3.3). Linear vinyl carbocation precursors were also demonstrated to undergo intermolecular Friedel-Crafts reactions, but these efforts will not be discussed.

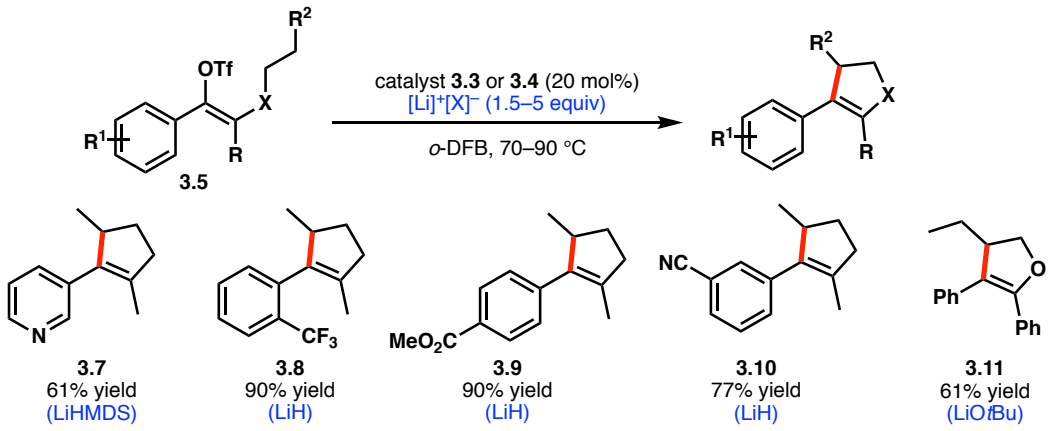


Figure 3.3 Li-urea promoted intramolecular C–H insertion reactions of linear vinyl triflates

The susbstrates shown in Figure 3.3 underwent facile C–H insertion reactions, albeit at elevated temperatures. Particularly interesting was the tolerance of a heterocyclic pyridine moiety in **3.7**. Also an ortho-trifluoromethyl group led to high yielding C–C bond formation

(**3.8**). Surprisingly, utilizing LiH gave essentially a single olefin isomer, whereas using LiHMDS gave at least three products detected by GC-FID and ^{1}H NMR. This unselective reaction was initially discovered when I tested the substrate to yield **3.9**, where the use of LiHMDS at elevated temperatures gave a complex reaction outcome likely due to ester functionalization (observed by GC-MS). By utilizing LiH, no ester functionalization was observed, and again a single olefin isomer was observed (by ^{1}H NMR). Additionally a cyano group (**3.10**) was tolerated as well as a dihydrofuran heterocycle (**3.11**) could accessed.

Around the same time of investigating ester **3.9**, I began to prepare the vinylogous acyl triflates; the productive C–H insertion to form **3.9** was promising and utilizing LiH was key to its success.[6,7] Initially I had prepared **3.12** in hopes that it would undergo C–H functionalization (**3.13**); however, upon heating to 140 ºC, I was only ever able to recover trace amounts of the β-keto ester, the starting material for the vinyl triflate (Figure 3.8).

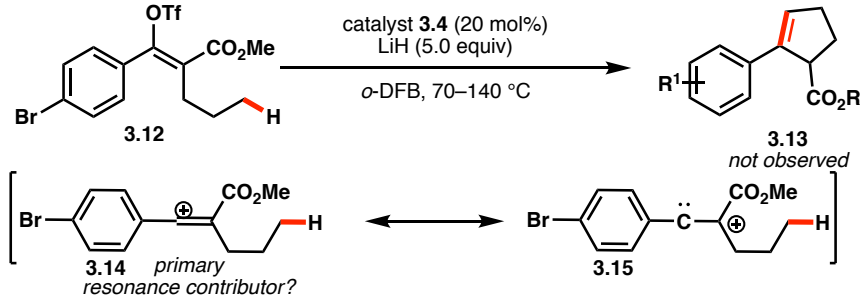


Figure 3.4 Initial attempts at vinyligous acyl triflate C–H functionalization and proposed rationale for lack of reactivity

Upon observing this result, one hypothesis I formed was in regards to how we usually think about the electronic structure of vinyl carbocations that yields their C–H insertion reactivity. In this case after drawing the two resonance structures, **3.14** as the vinyl carbocation and **3.15** as the carbene-like intermediate, it became clear that perhaps **3.15** is no longer a major resonance contributor due to the high-energy α-acyl carbocation.[8] Still with hopes to functionalize a C–H bond, I began to think there was an alternative mechanistic pathway besides concerted C–H insertion.

It had been previously proposed by Stang, Hanack, Olah and others that these dicoordinated carbocations can abstract C–H bonds through a "rebound" pathway.[9–12] In this case doing so would yield a primary carbocation, which is highly unfavored, even more so than that of an α-acyl carbocation.[13] So, to counteract this destabilization, I synthesized the butyl variant that would yield a more favorable 2º carbocation if the rebound pathway were active. This substrate ended up producing the C–H insertion product in moderate yield (**3.16**) (Figure 3.5).

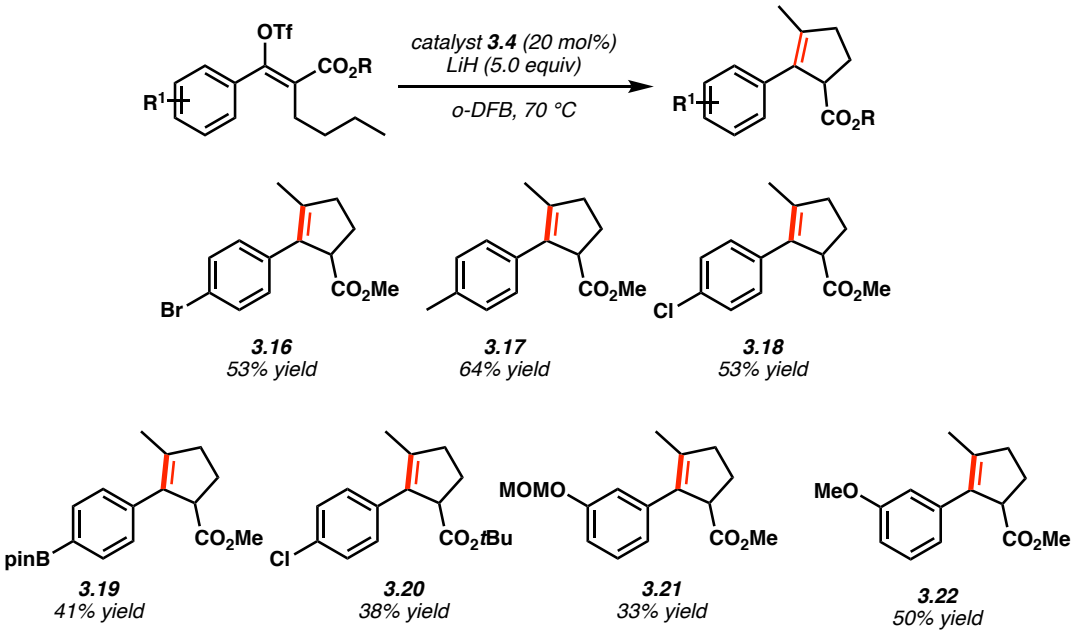


Figure 3.5 Vinyligous acyl triflate C–H functionalization scope

Additionally a variety of other substituents were tolerated (**3.17–3.22**). Particular important to the success of these reactions was the usage of LiH as the base; this was able to protect the acid sensitive methoxymethyl (**3.21**) and *tert*-butyl ester (**3.20**) groups, albeit in low yield. There was also a trend of increasing yield and reaction rate depending on how electron rich the arene conjugated with the vinyl triflate was. For example, **3.17** was formed and fully consumed the starting material in a few hours, whereas **3.18** required 36 hours to go to full conversion.

This trend of reactivity/rate indicated that likely a vinyl carbocation was being formed, however, some of the yields were quite low compared to our other developed C–H insertion reactions. In an attempt to further optimize these yields, I tried to isolate any other side products produced in the reaction to form **3.17**. In doing so, I was able to isolate γ-lactone **3.23**. This provided some evidence for the previously discussed rebound process, as a putative mechanism for its formation is shown in Figure 3.6. It is proposed that **3.24** can be ionized to the vinyl carbocation **3.25**, which can subsequently undergo the rebound/1,5-hydride transfer to yield 2º alkyl carbocation **3.26**. This can then undergo nucleophilic trapping by the styrene to yield the desired C–H functionalization product **3.17**. However, an alternative pathway is isomerization/hydride migration of this carbocation (**3.27**) followed by nucleophilic trapping by the ester to give **3.23**. It is worth noting, while not cleanly isolated, evidence for the six-membered and E/Z olefin isomers of the lactone were also observed by ^{1}H NMR.

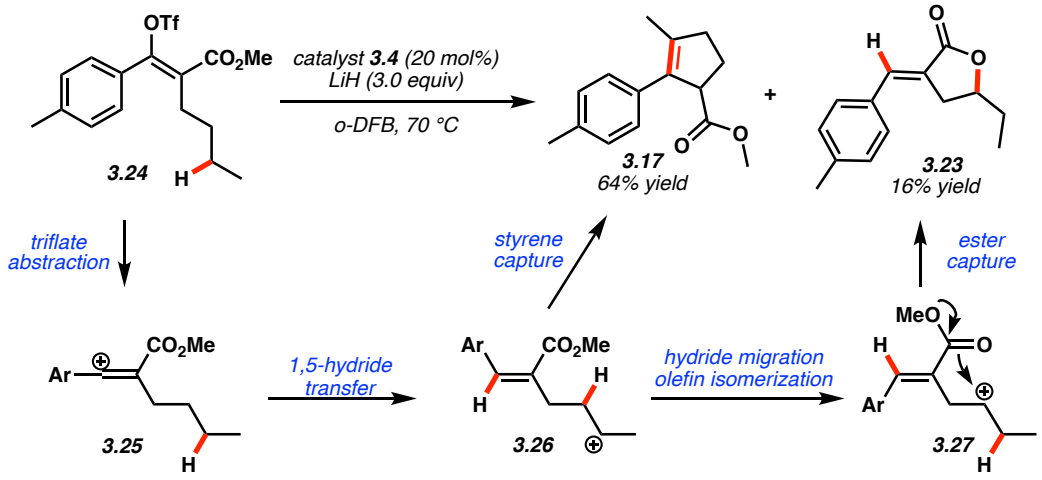


Figure 3.6 Proposed "rebound" pathway to give lactone **3.23**

The observation of this product provides insight on the mechanism and also corroborates with the arene electronics. The more electron rich the arene, likely the more nucleophilic the styrene, and thus lower amounts of the lactone side product would be observed. However, some confounding issues still stand with the proposed mechanism in Figure 3.6. Namely that

carbocation **3.26** does not immediately rearrange to the allylic carbocation. My rationale for this is simply that the observation of other rearranged products is observed, and as these secondary carbocations are often times proposed to be non-classical carbocations[14], *intra*molecular attack of these identical carbocations (or in the case of classical carbocations, in equilibrium) is not unreasonable.

Another potential mechanism is one that does not actually invoke a vinyl carbocation. Particularly the tolyl substrate **3.24** was difficult to handle due to the electron rich arene present attached to the vinyl triflate. Low temperature storage was required (–40ºC). This substrate would produce product **3.17** in 20% yield in the presence of TfOH and also when heated in solution for 48 hours, 25% yield. A colleague mentioned that this may indicate the following mechanism in Figure 3.7. However, I believe that this would yield an opposite trend in reactivity; if this were the case the electron poor styrenyl triflates would serve as the best hydride acceptors and react the most spontaneously.

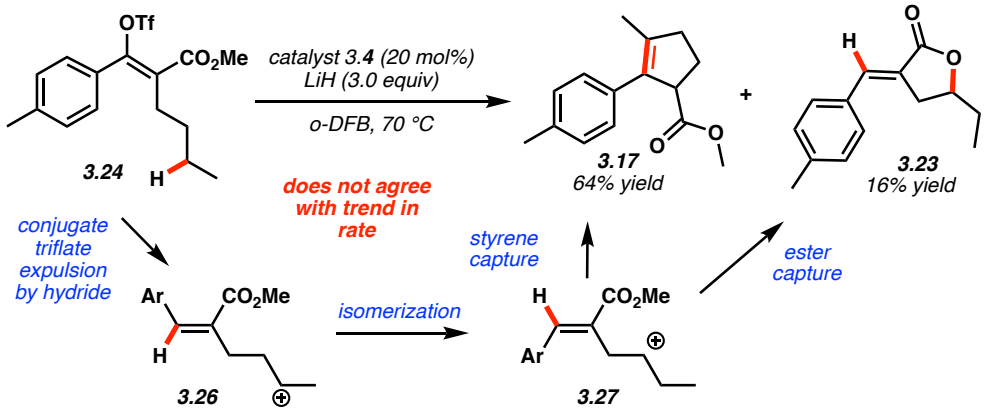


Figure 3.7 *Alternative mechanism without vinyl carbocation by direct hydride donation and triflate expulsion*

Also in the process of developing this substrate class and investigating the mechanism I substituted two other withdrawing groups in place of the ester. In particular, cyano group and aldehyde appended substrates (**3.28** and **3.29**) both yielded alkyne products (**3.30** and **3.31**) (Figure 3.8). This was rather peculiar, however, one proposed mechanism is by the production of

HCN or formaldehyde, see Figure 3.8. Attempts to use LiHMDS as a bulkier base also yielded these alkyne products. Additionally, an appended amide was attempted to be made, however this product (**3.32**) was much more unstable than the esters and difficult to purify. This is likely due to the lesser withdrawing nature of the amide; the reoccurring issue of substrate decomposition will be further addressed in Chapter 5.

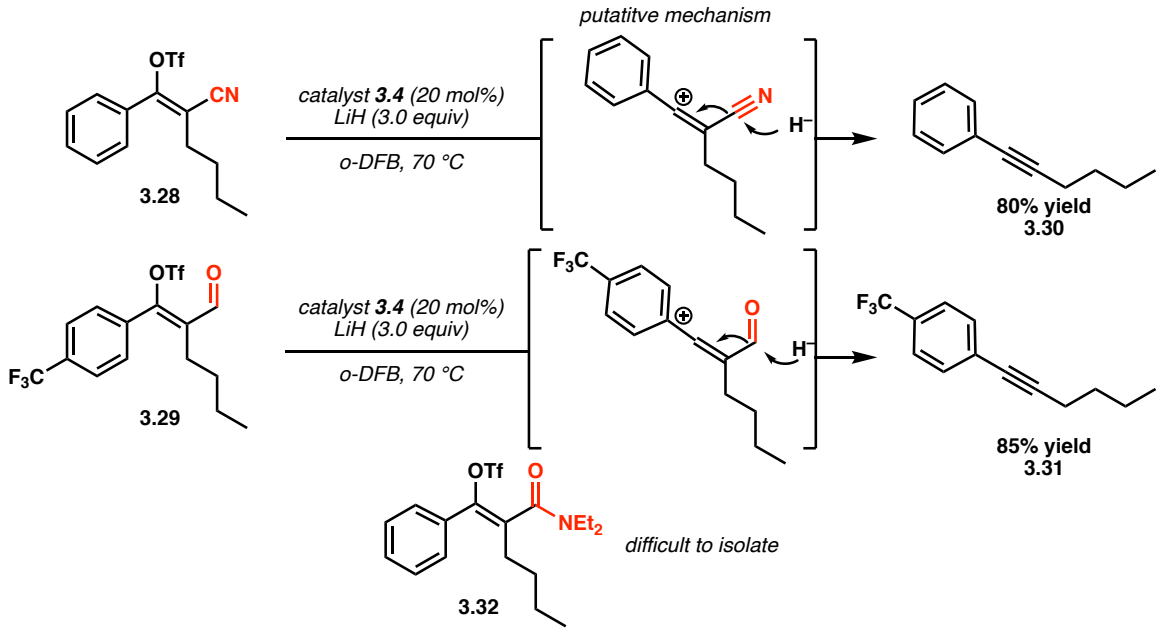


Figure 3.8 *Failed C–H functionalization substrates and side products observed*

3.4 Conclusion

Overall, this portion of work highlights the ability of the new lithium Lewis acid conditions to tolerate a wide variety of functional groups. Besides the production of ester containing cyclopentene products, other linear vinyl cation reactions could tolerate aryl esters, nitriles, alkyl ethers, and even a pyridine moiety. Now, easily accessible urea catalysts can be utilized to generate reactive vinyl carbocations that subsequently undergo high yielding C–H insertion reactions. This increased reaction scope and easily obtainable catalyst make it a true synthetic method.

3.5 Experimental Section

3.5.1 Materials and Methods

Unless otherwise stated, all reactions were performed in an MBraun or Vacuum Atmospheres glovebox under nitrogen atmosphere with ≤ 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and dried *in vacuo* before use. All liquid substrates were either dried over CaH_2 or filtered through dry neutral aluminum oxide. Solid substrates were dried over P_2O_5. All solvents were rigorously dried before use. Benzene, *o*-dichlorobenzene, and toluene were degassed and dried in a JC Meyer solvent system and stored inside a glovebox. Cyclohexane was distilled over potassium. *o*-Difluorobenzene was distilled over CaH_2. Hydrogen-bonding catalysts were prepared according to original or modified literature procedures.[15] Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. $AgNO_3$-Impregnated silica gel was prepared by mixing with a solution of $AgNO_3$ (150% v/w of 10% w/v solution in acetonitrile), removing solvent under reduced pressure, and drying at 120 °C. NMR spectra were recorded on a Bruker AV-300 (^1H, ^{19}F), Bruker AV-400 (^1H, ^{13}C, ^{19}F), Bruker DRX-500 (^1H), and Bruker AV-500 (^1H, ^{13}C). ^1H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^1H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted otherwise. GC spectra were recorded on an Agilent 6850 series GC using an Agilent HP-1 (50 m, 0.32 mm ID, 0.25 mm DF) column. GCMS spectra were

recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 mm DF) column interface at room temperature. IR Spectra were record on a Perkin Elmer 100 spectrometer and are reported in terms of frequency absorption (cm^{-1}). High resolution mass spectra (HR-MS) were recorded on a Waters (Micromass) GCT Premier spectrometer, a Waters (Micromass) LCT Premier, or an Agilent GC EI-MS, and are reported as follows: m/z (% relative intensity). Purification by preparative HPLC was done on an Agilent 1200 series instrument with a reverse phase Alltima C_{18} (5m, 25 cm length, 1 cm internal diameter) column.

3.5.2 Experimental Procedures for Li-Urea Catalysis

*Synthesis of catalysts **3.3** and **3.4** is reported in the adapted article.*

3.5.3 Vinyl Triflate Synthesis

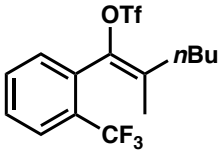
*For synthesis of ketone precursors for vinyl triflates in **Figure 3.3, Figure 3.4, Figure 3.5 and Figure 3.8** see adapted articles. Spectral data for these precursors and vinyl triflates are also reported in the adapted article.*

General Procedure

A: In a flame dried roundbottom flask, the starting ketone (1 equiv) was dissolved in THF to make a 0.413 M solution and this was cooled to –78 °C. To this solution was added a solution of NaHMDS (1.5 equiv, 1M solution in THF). This was warmed up to –40 °C for one hour before being cooled back down to –78 °C. Finally, a solution of $PhNTf_2$ (1 equiv, 1.65M in THF) was added dropwise and the reaction was allowed to warm up to r.t overnight. The reaction was quenched by addition of 1:9 *v/v* solution of methanol:ethyl acetate. The crude mixture was rotovapped and then suspended in 1:1 ether/pentane. The suspension was filtered and the solid

washed with pentane. The supernatant was concentrated giving the crude product. The crude was purified by flash column chromatography to give the pure vinyl triflate.

B: Ketone (1 equiv.) was dissolved in anhydrous DCM to make a 0.65 M solution. 2-chloropyridine (1.21 equiv) was added and the solution was cooled to 0 °C. To this was added triflic anhydride (1.32 equiv) as a 1.7 M solution in DCM. The resulting solution was allowed to warm up to room temperature and stir until all starting material was consumed as determined by GC or NMR (sometimes the product decomposes to the starting material on TLC). After reaction was finished, the reaction was concentrated and the crude sludge was suspended in hexanes. This was sonicated and stirred and then filtered. This process was repeated three more times and the combined hexanes supernatant was concentrated to give product. If necessary, this was heated under reduced pressure to remove residual 2-chloropyridine.



2-Methyl-1-(2-(trifluoromethyl)phenyl)hex-1-en-1-yl trifluoromethanesulfonate (3.8:1 *Z*:*E* isomers) (3.8S).

Synthesized according to general procedure A starting from 2-methyl-1-(2-(trifluoromethyl)phenyl)hexan-1-one. Column chromatography was performed using 95:5:0.1 hexane:diethyl ether:triethylamine. **3.8S** was obtained as colorless oil and as a 3.8:1 mixture of *Z*:*E* isomers (260 mg, 1.8 mmol, 36%). The major isomer was determined by observing an NOE between the allylic methyl peak at 1.57 with aromatic protons.

NMR Data for Major Isomer:

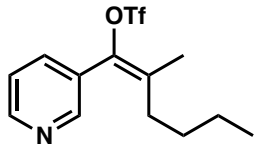
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.59 (td, *J* = 7.4, 1.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.53 – 7.48 (m, 1H), 2.46 (ddd, *J* = 13.4, 9.1, 7.0 Hz, 1H), 2.30 (ddd, *J* = 13.4, 8.9, 6.4 Hz, 1H), 1.57 (s, 3H), 1.55 – 1.49 (m, 2H), 1.48 – 1.36 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.2, 135.1, 133.9, 131.8, 130.1, 130.1 (q, $^{2}J_{C–F}$ = 20.5 Hz), 126.56 (q, $^{3}J_{C–F}$ = 4.9 Hz), 123.5 (q, $^{1}J_{C–F}$ = 273.8 Hz), 118.0 (q, $^{1}J_{C–F}$ = 319.9 Hz), 31.7, 29.0, 22.5, 17.9, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.1, -75.3.

FTIR (Neat film NaCl): 2963, 2936, 2876, 1605, 1411, 1315, 1211, 1136, 1118, 846, 770, 606.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{15}H_{16}F_6O_3S$ 390.0724; Found 390.0730.



(*E*)-2-methyl-1-(pyridin-3-yl)hex-1-en-1-yl trifluoromethanesulfonate (3.7S).

Synthesized according to general procedure A starting from 2-methyl-1-(pyridin-3-yl)hexan-1-one. Purified by column chromatography (first with 20% ether/hexanes and then 8% acetone/hexanes) to afford pure triflate **3.7S** as yellow oil (530 mg, 26%).

Assignment of the *E* configuration of this substrate was based on key cross peaks in ^{1}H NOESY experiments. There were key NOEs present between the two aromatic protons of pyridine (7.68, 8.61 ppm) and the allylic CH_2 protons (2.03-2.09 ppm). This led to the assignment of the (*E*)-isomer.

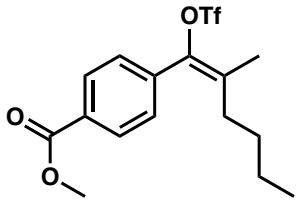
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.61 (d, *J* = 2.0 Hz, 1H), 7.68 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.35 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H), 2.09 – 2.03 (m, 2H), 2.00 (s, 3H), 1.50 – 1.40 (m, 2H), 1.24 (hex, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.4, 150.3, 139.0, 137.0, 134.8, 128.9, 123.2, 118.1 (q, $^{1}J_{C-F}$ = 320.1 Hz), 33.1, 29.9, 22.3, 16.5, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.7.

FTIR (Neat film NaCl): 3033, 2961, 2933, 2865, 1588, 1567, 1411, 1207, 1140, 951, 847, 713, 607.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{13}H_{16}F_3NO_3S$ 323.0803; Found 323.0796.



Methyl (*E*)-4-(2-methyl-1-(((trifluoromethyl)sulfonyl)oxy)hex-1-en-1-yl)benzoate (3.9S)

Synthesized according to general procedure 3.8.3.2.1A starting from corresponding ketone. To a 25 mL round bottom flask was added corresponding ketone (130 mg, 0.52 mmol, 1 equiv) as a solution in dry THF (1mL). This flask was cooled to –78 ºC, and to it was added a solution of NaHMDS (144 mg, 0.79 mmol, 1.5 equiv) as a solution in dry THF (5 mL) drop wise. This solution was allowed to stir for 30 minutes at –78 ºC. To the reaction was added 1,1,1-trifluoro-N-phenyl-N-((trifluoromethyl)sulfonyl)methanesulfonamide (206 mg, 0.58 mmol, 1.1 equiv) as a solution in dry THF (2 mL). The reaction was allowed to warm to room temperature and stir for 8h. The reaction was concentrated and suspended in 1:1 ether:hexanes (15 mL) and filtered. The

solids were washed with cold 1:5 ether:hexanes. The filtrate was concentrated and purified by flash column chromatography (8% ether:hexanes) to give **3.9S** as a clear oil (50 mg, 25% yield).

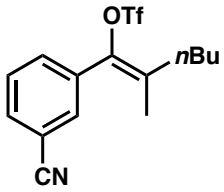
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.9 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 3.94 (s, 3H), 2.07 (t, *J* = 7.8 Hz, 2 H), 1.98 (s, 3H), 1.45 (p, *J* = 8.0, 7.5 Hz, 2H), 1.23 (q, *J* = 7.3 Hz, 2H), 0.83 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 141.3, 137.3, 133.9, 131.1, 129.9, 129.8, 118.3 (q, $^{1}J_{C-F}$ = 320.2 Hz),52.6, 33.4, 30.2, 22.6, 16.8, 14.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -74.66.

FTIR (Neat Film NaCl): 2959, 2938, 2865, 1728, 1414, 1279, 1210, 1141, 1104, 955, 868, 838, 706, 607 cm^{-1}.

HRMS (CI-MS) m/z: [M]+ Calc'd for $C_{16}H_{19}F_3O_5S$ 380.0905; Found 380.0902.



(*Z*)-1-(3-Cyanophenyl)-2-methylhex-1-en-1-yl trifluoromethanesulfonate (3.10S). Synthesized according to general procedure 3.8.3.2.1A starting from corresponding ketone. To a round bottom flask was added corresponding ketone (220 mg, 1.0 mmol, 1 equiv) as a solution in dry THF (2.5 mL). This flask was cooled to –78 ºC, and to it was added a solution of NaHMDS (281 mg, 1.5 mmol, 1.5 equiv) as a solution in dry THF (2 mL) drop wise. This solution was allowed to stir for 30 minutes at –78 ºC. To the reaction was added 1,1,1-trifluoro-N-phenyl-N-((trifluoromethyl)sulfonyl)methanesulfonamide (365 mg, 1.0 mmol, 1.0 equiv) as a solution in dry THF (0.6 mL). The reaction was allowed to warm to room temperature and stir overnight.

The reaction was then cooled to –78 °C and was quenched by addition of MeOH in EtOAc (10% *v/v*). The solution was allowed to warm to room temperature and the combined organics were washed with water and brine. The organic layer was then dried over $MgSO_4$, filtered and concentrated. The crude material was concentrated and purified by flash column chromatography (2.5% ether:hexanes) to give **3.10S** as a clear oil (310 mg, 87% yield).

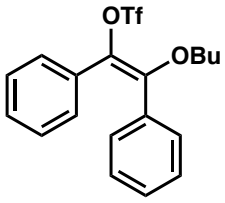
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.65 (s, 1H), 7.62 – 7.57 (m, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 2.07 – 2.00 (m, 3H), 1.99 (d, *J* = 0.8 Hz, 3H), 1.45 (tt, *J* = 7.7, 6.1 Hz, 3H), 1.27 – 1.16 (m, 3H), 0.88 – 0.77 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.6, 134.7, 134.2, 133.2, 133.0, 129.6, 120.7 (q, $^1J_{C–F}$ = 320 Hz), 118.1, 113.0, 33.1, 29.9, 22.4, 16.5, 13.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.64.

HRMS (CI-MS) m/z: [M]+ Calc'd for $C_{15}H_{16}F_3NO_3S$ 347.0803; Found 347.0797.

FTIR (Neat Film NaCl): 2960, 2932, 2864, 2233, 1412, 1244, 1207, 1139, 983, 903, 844, 592 cm^{-1}.



(*Z*)-2-Butoxy-1,2-diphenylvinyl trifluoromethanesulfonate (3.11S). Synthesized according to general procedure 3.8.3.2.1A starting from known butoxy benzoin derivative. To a flame dried flask was added NaHMDS (1.08 g, 5.9 mmol, 1.5 equiv) and anhydrous THF 20 ml, then cool

the solution to –78 °C. 2-butoxy-1,2-diphenylethan-1-one (1.09 g, 3.9 mmol, 1 equiv) in 10 ml THF was added dropwise. Stir the solution at –78 °C for 30min and then warm up to 0 °C and keep at 0 °C for 30 min. 1,1,1-trifluoro-N-phenyl-N-((trifluoromethyl)sulfonyl)methanesulfonamide (1.55 g, 4.3 mmol, 1.1 equiv) in 10 ml THF was added after the solution was cooled to –78 °C then warm up slowly to room temperature. Reaction was quenched with 10 ml 1:5 methanol/ethyl actetate after 1 hour stirring at room temperature. The solvent was evaporated and the crude was purified by flash column chromatography (1% ether:hexanes) to give **3.11S** as white solid (920 mg, 59% yield).

*Note: Vinyl triflate **3.11S** was found to be unstable for long term storage on benchtop and should be stored in a glovebox freezer at – 40 °C after purification in order to maintain purity.

Major *Z* isomer was assigned by a [^{1}H-^{19}F HOESY] experiment where correlations were observed between the trifluoromethyl group with the methylene protons of the butoxy chain.

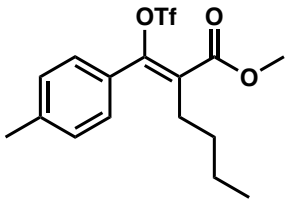
^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.38 – 7.33 (m, 2H), 7.30 – 7.25 (m, 2H), 7.25 – 7.17 (m, 6H), 4.59 (dd, *J* = 9.8, 8.8 Hz, 1H), 4.23 (dd, *J* = 8.8, 7.0 Hz, 1H), 3.49 (dddd, *J* = 10.3, 8.9, 6.9, 3.5 Hz, 1H), 1.61 (dqd, *J* = 13.7, 7.6, 3.5 Hz, 1H), 1.45 – 1.35 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 150.1, 135.6, 132.0, 128.8, 128.4, 128.2, 128.0, 127.6, 126.3, 114.8, 73.3, 49.1, 25.5, 10.6.

^{19}F NMR (282 MHz, CD_2Cl_2) δ –75.29

FTIR (Neat film NaCl): 3085, 3061, 3028, 2961, 2937, 2876, 1651, 1446, 1415, 1258, 1240, 1201, 1139, 1100, 1074, 1001, 986, 897,820, 768, 694, 647, 601, 569, 511.

HRMS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{19}H_{19}F_3O_4SNa$ 423.0854; Found 423.0845.



Methyl (*Z*)-2-(*p*-tolyl(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.17S)

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (170 mg, 60% *w/w*, 4.35 mmol, 1.8 equiv) followed by dry toluene (20 mL). To this was added dropwise corresponding ketone(600 mg, 2.4 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.57 mL, 3.4 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (15 mL), followed by addition of satd. aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with ether (3 x 20 mL). The organic layer was dried with Na_2CO_3, filtered, and concentrated. The crude oil was purified by column chromatography (6% ether:hexanes) to give **3.17S** as a yellow oil (600 mg, 65% yield).

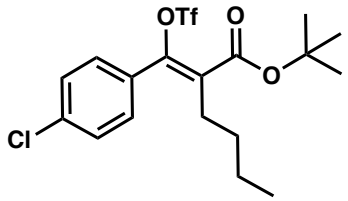
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 3.88 (s, 3H), 2.34 – 2.23 (m, 2H), 1.56 (s, 3H), 1.41 (tdd, J = 9.9, 7.4, 3.9 Hz, 2H), 1.33 – 1.21 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 147.5, 140.9, 129.2, 129.0, 128.2, 128.1, 118.3 (q, $^1J_{C–F}$ = 320.2 Hz), 52.3, 30.6, 29.7, 22.2, 21.5, 13.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -74.55.

FTIR (Neat Film NaCl): 2960, 2934, 2875, 1731, 1421, 1302, 1208, 1139, 969, 842, 608 cm^{-1}.

HRMS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{16}H_{19}F_3O_5SNa$ 403.0803; Found 403.0799.



***tert*-Butyl (*Z*)-2-((4-chlorophenyl)(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.20S).**

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (120 mg, 60% *w/w*, 1.90 mmol, 1.8 equiv) followed by dry toluene (14 mL). To this was added dropwise ester (500 mg, 1.6 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.41 mL, 2.4 mmol, 1.5 equiv) was added dropwise. This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. To the reaction was added triethylamine (3 mL) to quench any remaining trifluoromethanesulfonic acid/anhydride, diluted with ether (10 mL), followed by addition of satd. aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with ether (3 x 20 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated. The crude oil was purified by column chromatography on triethylamine deactivated silica gel (10% ether:hexanes + 0.5% triethylamine) to give **3.20S** as a yellow solid (300 mg, 42% yield).

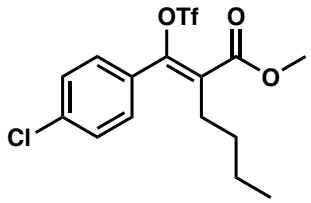
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 2.30 – 2.15 (m, 2H), 1.58 (s, 9H), 1.47 – 1.36 (m, 2H), 1.30 – 1.23 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 143.9, 137.0, 133.1, 131.5, 131.1, 129.3, 118.3 (q, $^1J_{C–F}$ = 320.2 Hz), 84.2, 30.4, 30.2, 28.2, 22.5, 14.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ –74.30.

FTIR (Neat Film NaCl): 2951, 2933, 2874, 1724, 1594, 1489, 1422, 1370, 1310, 1296, 1210, 1145, 1092, 1018, 969, 846, 606 cm^{-1}.

HRMS (ESI-MS): Calculated for [$C_{18}H_{22}ClF_3O_5S$+Na]: 465.0726; Measured: 465.0715.



Methyl (*Z*)-2-((4-chlorophenyl)(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.18S)

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (160 mg, 60% *w/w*, 2.23 mmol, 1.8 equiv) followed by dry toluene (20 mL). To this was added dropwise the ester (600 mg, 4.0 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.57 mL, 3.4 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (15 mL), followed by addition of satd. aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with ether (3 x 20 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated. The crude oil was purified by column chromatography (6% ether:hexanes) to give **3.18S** as a clear oil (593 mg, 66% yield).

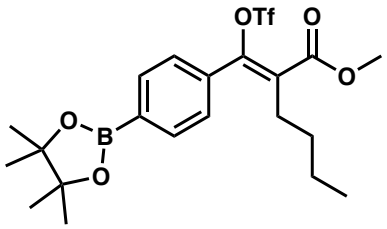
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 8.6 Hz, 2H), 7.35 (d, J = 8.5 Hz, 2H), 3.89 (s, 3H), 2.43 – 2.16 (m, 2H), 1.48 – 1.35 (m, 2H), 1.30 – 1.20 (m, 2H), 0.83 (t, J = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 146.2, 137.2, 130.9, 129.9, 129.7, 129.4, 118.3 (q, $^1J_{C–F}$ = 320.2 Hz), 52.8, 30.8, 30.1, 22.6, 14.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ –74.47.

FTIR (Neat Film NaCl): 2960, 2934, 2875, 1732, 1490, 1422, 1309, 1295, 1209, 1138, 1091, 1019, 970, 846, 605 cm^{-1}.

HRMS (EI-MS): Calculated for $C_{15}H_{16}ClF_3O_5S$: 400.0359; Measured: 400.0412.



Methyl (*Z*)-2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.19S).

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (76 mg, 60% *w/w*, 1.90 mmol, 1.8 equiv) followed by dry toluene (10 mL). To this was added dropwise the ester (381 mg, 1.1 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.27 mL, 1.6 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (10 mL), followed by addition of satd. aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ether (3 x 15 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated. The crude oil was purified by column chromatography (10% ether:hexanes) to give **3.19S** as a clear oil (118 mg, 23% yield).

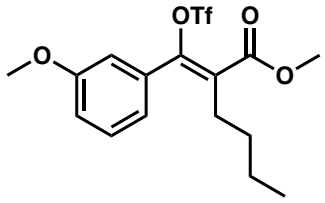
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 7.7 Hz, 2H), 7.40 (d, J = 7.7 Hz, 2H), 3.89 (s, 3H), 2.29 (t, J = 7.7 Hz, 2H), 1.36 (s, 12H), 1.30 – 1.14 (m, 4H), 0.81 (t, J = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 147.1, 134.8, 133.5, 128.8, 128.3, 118.3 (q, $^1J_{C–F}$ = 320.2 Hz), 84.2, 52.4, 30.5, 29.7, 24.9, 22.2, 13.6. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{19}F NMR (376 MHz, $CDCl_3$) δ -74.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.1.

FTIR (Neat Film NaCl): 2978, 2960, 2934, 2874, 1733, 1610, 1422, 1399, 1361, 1209, 1143, 1088, 962, 854, 658, 604 cm^{-1}.

HRMS (EI-MS): Calculated for $C_{21}H_{28}BF_3O_7S$: 492.1600; Measured: 492.1598



Methyl (*Z*)-2-((3-methoxyphenyl)(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.22S).

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (95 mg, 60% *w/w*, 2.4 mmol, 1.8 equiv) followed by dry toluene (12 mL). To this was added dropwise the ester (350 mg, 1.3 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.34 mL, 2.0 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (10 mL), followed by addition of satd. aqueous $NaHCO_3$ (8 mL). The aqueous layer was extracted with ether (3 x 15 mL). The organic layer was dried with Na_2CO_3, filtered, and concentrated. The crude oil was purified by column chromatography (10% ether:hexanes) to give trfilate **3.22S** as a yellow oil (389 mg, 74% yield).

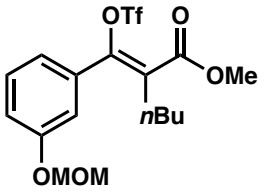
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 2.0 Hz, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 2.45 – 2.22 (m, 2H), 1.43 (tt, *J* = 7.8, 6.4 Hz, 2H), 1.26 (h, *J* = 7.3 Hz, 2H), 0.83 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 159.8, 147.3, 132.5, 130.1, 129.0, 121.8, 118.3 (q, $^1J_{C–F}$ = 320.2 Hz), 116.8, 114.7, 55.7, 52.7, 30.9, 30.1, 22.6, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -74.52.

FTIR (Neat Film NaCl): 2959, 2934, 2875, 2842, 1732, 1599, 1420, 1291, 1244, 1205, 1138, 992, 890, 839, 614 cm^{-1}.

HRMS (CI-MS): Calculated for $C_{16}H_{19}F_3O_6S$: 396.0854; Measured: 396.0853.



Methyl (*Z*)-2-((3-(methoxymethoxy)phenyl)(((trifluoromethyl)sulfonyl)oxy) methylene) hexanoate (3.21S). To a stirring solution of NaH (610 mg, 60% *w/w*, 15.3 mmol, 1.8 equiv) in toluene (8 mL) was added a solution of the ester (2.5 g, 8.5 mmol, 1 equiv) in toluene (9 mL). After H_2 gas evolution ceased, the reaction was heated to 80 °C for 1 hr. The reaction mixture was then cooled to 0 °C and triflic anhydride (3.6 g, 12.7 mmol, 1.5 equiv) was added and this was allowed to stir at 0 °C for 1 hr and then warmed to room temperature overnight. The reaction was diluted with diethyl ether followed by addition of satd. aqueous $NaHCO_3$. The aqueous layer was then extracted with ether (3 x 20 mL). The organics were dried over $MgSO_4$, filtered and concentrated. The crude oil was purified by column chromatography (5% ether:hexanes) to give triflate **3.21S** as an oil (3.1 g, 86% yield).

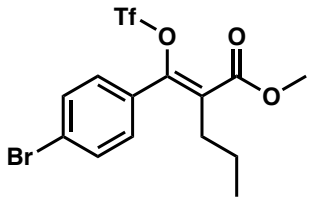
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (ddd, *J* = 8.2, 7.6, 0.6 Hz, 1H), 7.13 (ddd, *J* = 8.2, 2.5, 1.0 Hz, 1H), 7.11 (t, *J* = 2.0 Hz, 1H), 7.05 (ddd, *J* = 7.6, 1.6, 1.1 Hz, 1H), 5.18 (s, 1H), 3.89 (s, 2H), 3.47 (s, 1H), 2.37 – 2.27 (m, 1H), 1.43 (tt, *J* = 7.8, 6.3 Hz, 1H), 1.27 (h, *J* = 7.3 Hz, 1H), 0.83 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 157.3, 147.0, 132.3, 129.8, 128.8, 122.7, 121.3 (q, *J* = 320.3 Hz), 118.8, 117.0, 94.6, 56.0, 52.5, 30.7, 29.9, 22.4, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ –74.58.

HRMS (CI-MS): Calculated for $C_{17}H_{21}F_3O_7S$: 426.0960; Measured: 426.0947.

FTIR (Neat Film NaCl): 2959, 2933, 2865, 1728, 1583, 1419, 1292, 1204, 1135, 1090, 1022, 994, 902, 881, 832, 600 cm^{-1}.



methyl (*Z*)-2-((4-bromophenyl)(((trifluoromethyl)sulfonyl)oxy)methylene)pentanoate (3.12S)

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (194 mg, 60% *w/w*, 4.8 mmol, 1.8 equiv) followed by dry toluene (27 mL). To this was added dropwise the ester (806 mg, 2.7 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.68 mL, 4.0 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (10 mL), followed by addition of satd. aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ether (3 x 20 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated. The crude oil was purified by column chromatography (7% ether:hexanes) to give **3.12S** as a white solid (913 mg, 78% yield).

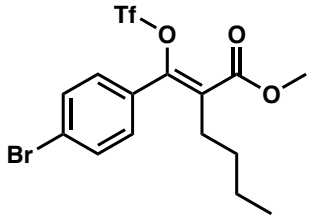
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 3.89 (s, 3H), 2.47 – 2.12 (m, 2H), 1.52 – 1.31 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 146.3, 132.3, 131.0, 130.3, 129.5, 125.5, 118.3 (q, J = 320.6 Hz), 52.8, 32.1, 22.0, 13.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -74.53.

FTIR (Neat film NaCl): 2958, 2933, 2874, 1732, 1487, 1410, 1312, 1296, 1209, 1128, 1090, 968 cm^{-1}

HR-MS (EI-MS): Calculated for $C_{14}H_{14}BrF_3O_5S$: 429.9697; measured: 429.9695.



Methyl (*Z*)-2-((4-bromophenyl)(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.16S)

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (69 mg, 60% *w/w*, 1.7 mmol, 1.8 equiv) followed by dry toluene (10 mL). To this was added dropwise the ester (300 mg, 0.95 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.24 mL, 1.4 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (10 mL), followed by addition of satd. aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ether (3 x 10 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated. The crude oil was purified by column chromatography (6% ether:hexanes) to give **3.16S** as a yellow oil (298 mg, 70% yield).

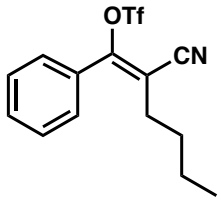
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 3.89 (s, 3H), 2.48 – 2.17 (m, 1H), 1.53 – 1.33 (m, 2H), 1.36 – 1.11 (m, 2H), 0.83 (t, J = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 146.3, 137.3, 130.9, 129.9, 129.7, 129.4, 118.3 (q, J = 320.6 Hz), 52.9, 30.9, 30.1, 22.65, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -74.53.

FTIR (Neat film NaCl): 2960, 2932, 2870, 1731, 1485, 1421, 1310, 1296, 1209, 1135, 1090, 1019, 970 cm^{-1} .

HR-MS (EI-MS): Calculated for $C_{15}H_{16}BrF_3O_5S$: 443.9854; measured: 443.9849.

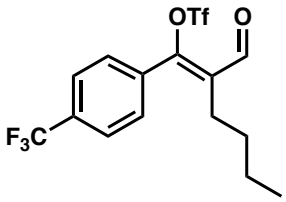


(*Z*)-2-cyano-1-phenylhex-1-en-1-yl trifluoromethanesulfonate (3.28S)

To a flame dried flask equipped with a stir bar was added dry dichloromethane (5 mL). To this was added the ketone (0.20 g, 1 equiv, 0.99 mmol) and triethylamine (0.15 mL, 1.1 equiv, 1.1 mmol). This was cooled to 0ºC with an ice bath and triflic anhydride (0.25 mL, 1.5 equiv, 1.5 mmol) was added dropwise. This solution was warmed to room temperature and allowed to stir for 36 hours. To this solution was added water (5 mL). The solution was extracted with diethyl ether (3x 20 mL), dried over MgSO4, and concentrated. The crude material was purified by flash column chromatography (4% ether in hexanes) to afford **3.28S** as a colorless oil (216 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.59 (m, 2H), 7.59 – 7.51 (m, 1H), 7.51 – 7.39 (m, 2H), 2.83 – 2.26 (m, 2H), 2.00 – 1.58 (m, 2H), 1.45 (h, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 1=3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 132.0, 130.3, 128.8, 128.5, 118.0 (q, *J* = 320.9 Hz), 116.3, 110.42, 29.5, 29.1, 22.1, 13.6.

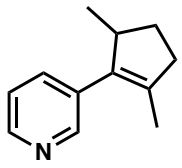


(*Z*)-2-formyl-1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl trifluoromethanesulfonate (3.29S)

To a flame dried flask was added the starting alcohol (150 mg, 1 equiv, 0.37 mmol) and dichloromethane (5 mL). To this was added MnO_2 (321 mg, 10 equiv, 3.7 mmol) and stirred rapidly (1500 rpm) for 18 hours. The reaction was filtered through silica gel with DCM, concentrated, and purified by flash column chromatography (5% ether in hexanes) to yield **3.29S** as a yellow oil (60 mg, 40% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 8.1 Hz, 2H), 2.33 – 2.06 (m, 2H), 1.38 (p, *J* = 7.2 Hz, 2H), 1.23 (dt, *J* = 14.6, 7.2 Hz, 2H), 0.82 (t, *J* = 7.2 Hz, 3H).

3.5.4 C–H Insertion Reactions of Linear Vinyl Triflates



3-(2,5-Dimethylcyclopent-1-en-1-yl)pyridine (3.7).

Synthesized according to a slightly modified general procedure 3.8.3.4.1. To a 20 mL vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.4** (9.6 mg, 0.02 mmol, 0.20 equiv). LiHMDS (56.5 mg, 0.34 mmol, 3.4 equiv) was added followed by cyclohexane (6 mL). After a five minute prestir, vinyl triflate **3.7** (32.3 mg, 0.10 mmol, 1 equiv) was added. The reaction was heated to 70 °C. After 4 hours, the reaction was cooled to room temperature and removed from the glovebox. The reaction was concentrated and then suspended in ether and pushed through a pad of silica. This was concentrated to give crude product as dark solid (80%

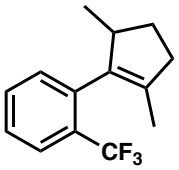
NMR yield). This was purified by silica flash column chromatography (1% MeOH/DCM) and then another flash column chromatography (1:25:175 triethylamine:ethyl acetate:hexanes). This gave cyclopentyl product **3.7** as colorless oil (10.6 mg, 61% yield, 0.061 mmol).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.43 (d, *J* = 2.0 Hz, 1H), 8.41 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.49 (dt, *J* = 7.8, 2.0 Hz, 1H), 7.25 (ddd, *J* = 7.8, 4.8, 0.9 Hz, 1H), 3.22 – 3.12 (m, 1H), 2.60 – 2.46 (m, 1H), 2.44 – 2.32 (m, 1H), 2.22 (dddd, *J* = 12.8, 9.0, 8.1, 4.7 Hz, 1H), 1.74 (dt, *J* = 2.2, 1.2 Hz, 3H), 1.48 (dddd, *J* = 12.8, 9.3, 6.8, 6.1 Hz, 1H), 0.93 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 149.7, 147.2, 137.4, 137.1, 135.5, 133.8, 123.0, 43.2, 37.9, 31.4, 19.9, 15.1.

FTIR (Neat film NaCl): 3083, 3032, 2954, 2928, 2864, 2842, 1654, 1563, 1479, 1453, 1409, 1377, 1324, 1268, 1186, 1100, 1026, 1001, 957, 807, 716, 617.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{12}H_{15}N$ 173.1205; Found 173.1199.



1-(2,5-Dimethylcyclopent-1-en-1-yl)-2-(trifluoromethyl)benzene (3.8).

Synthesized according to general procedure 3.8.3.4.1. To a 20 mL vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.4** (9.6 mg, 0.02 mmol, 0.20 equiv). LiH (2.9 mg, 0.30 mmol, 3.0 equiv) was added followed by 1,2-difluorobenzene (6 mL). After a five minute prestir, vinyl triflate **3.8** (39.0 mg, 0.10 mmol, 1 equiv) was added. The reaction was heated to 70 °C. After 2 hours, the reaction was cooled to room temperature and removed from the glovebox. The reaction was concentrated and then suspended in ether and pushed through a pad of silica. This was concentrated to give crude product as yellow solid. This was purified by

silica flash column chromatography (3% ether/hexanes) to give cyclopentenyl product **3.8** as colorless oil (21.6 mg, 90% yield, 0.90 mmol).

This compound exists as a mixture of rotamers at room temperature due to the *ortho*-CF_3 group interacting with the methyls of the cyclopentene ring: the major rotamer is reported in $CDCl_3$ at room temperature and a spectrum of C_6D_6 at elevated temperature is shown to show the two rotamers converging into one.

Major Rotamer

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.64 (m, 1H), 7.53 – 7.45 (m, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 2.99 (s, 1H), 2.39 (t, J = 6.8 Hz, 2H), 2.22 (dtd, J = 12.3, 7.8, 6.1 Hz, 1H), 1.53 – 1.46 (m, 1H), 1.44 (s, 3H), 0.90 (d, J = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.2, 138.1 (q, $^3J_{C–F}$ = 2.5 Hz), 136.8, 132.3, 131.0, 128.9 (q, $^2J_{C–F}$ = 29.7 Hz), 126.5, 125.9 (q, J = 5.4 Hz), 124.3 (q, $^1J_{C–F}$ = 273.6 Hz), 44.6 (q, $^3J_{C–F}$ = 2.3 Hz), 36.7, 32.3, 19.9, 15.0.

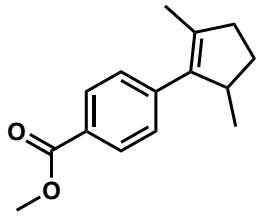
^{19}F NMR (376 MHz, $CDCl_3$) δ –61.7.

VT NMR (70 °C)

^{1}H NMR (500 MHz, C_6D_6, 70 °C) δ 7.52 (d, J = 8.0 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.93 (t, J = 7.6 Hz, 2H), 6.92 (t, J = 7.6 Hz, 2H), 3.10 (s, 1H), 2.30 (br s, 2H), 2.16 (br s, 1H), 1.43 (s, 3H), 1.42 – 1.38 (m, 1H), 0.90 (d, J = 6.9 Hz, 4H).

FTIR (Neat film NaCl): 3072, 2956, 2928, 2857, 2845, 1734, 1448, 1314, 1167, 1127, 1103, 1062, 1035, 768, 756.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{14}H_{15}F_3$ 240.1126; Found 240.1133.



Methyl 4-(2,5-dimethylcyclopent-1-en-1-yl)benzoate (3.9)

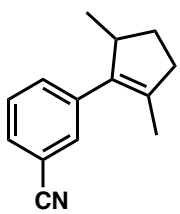
Synthesized according to a modified general procedure 3.8.3.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with the urea catalyst **3.4** (2.4 mg, 0.005 mmol, 0.2 equiv) and LiH (0.6 mg, 0.075 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (1.5 mL). To this was added **3.9** (9.5 mg, 0.025 mmol, 1 equiv) and heated to 70 ºC for 6 hours. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (4% acetone:hexanes) to yield cyclopentene **3.9** as a clear oil (5.2 mg, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 2H), 3.91 (s, 2H), 3.16 – 3.23 (m, 1H), 2.46 – 2.54 (m, 1H), 2.33 – 2.41 (m, 1H), 2.22 (dtt, *J* = 12.9, 8.6, 4.5 Hz, 1H), 1.76 (s, 3H), 1.50 – 1.43 (m, 1H), 0.93 (d, *J* = 6.9 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 143.5, 140.3, 137.2, 129.6, 128.6, 127.9, 52.3, 43.5, 38.4, 31.6, 20.5, 15.8.

FTIR (Neat Film NaCl): 2952, 2927, 2866, 2840, 1722, 1607, 1435, 1275, 1177, 1109, 1000, 857, 775, 709 cm^{-1}.

HRMS (CI-MS) m/z: [M]+ Calc'd for $C_{15}H_{18}O_2$ 230.1307; Found 230.1299.



3-(2,5-Dimethylcyclopent-1-en-1-yl)benzonitrile (3.10).

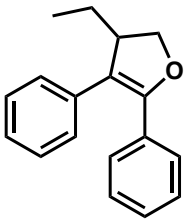
Synthesized according to general procedure 3.8.3.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with the urea catalyst **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (2.0 mg, 0.25 mmol, 5 equiv) followed by dry 1,2-difluorobenzene (3.0 mL). To this was added **3.10** (17.4 mg, 0.050 mmol, 1 equiv) and heated to 70 ºC for 24 hrs. The reaction vial was removed from the glove box, diluted with ether and plugged through silica gel with dichloromethane and concentrated. The crude oil was purified by flash column chromatography (2% ether:hexanes) to yield olefin **3.10** as a clear oil (7.6 mg, 77% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (dt, *J* = 7.1, 1.8 Hz, 1H), 7.47 – 7.45 (m, 1H), 7.45 – 7.39 (m, 1H), 3.15 (dddt, *J* = 8.5, 6.4, 4.3, 2.1 Hz, 1H), 2.59 – 2.45 (m, 1H), 2.44 – 2.31 (m, 2H), 2.22 (dddd, *J* = 12.8, 9.1, 8.2, 4.5 Hz, 1H), 1.79 – 1.64 (m, 1H), 1.52 – 1.40 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.6, 138.8, 137.4, 132.9, 132.0, 129.6, 128.9, 119.3, 112.3, 43.3, 38.0, 31.4, 20.2, 15.4.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{14}H_{15}N$ 197.1205; Found 197.1204.

FTIR (Neat Film NaCl): 3405, 3068, 2956, 2928, 2865, 2230, 1691, 1596, 1574, 1479, 1454, 1413, 1378, 1273, 1211, 1140, 985, 903, 845, 799, 698 cm^{-1}.



3-Ethyl-4,5-diphenyl-2,3-dihydrofuran (3.11).

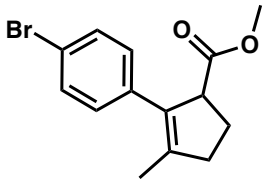
Synthesized according to a slightly modified general procedure 3.8.3.4.1. To an 1-dram vial with a magnetic stir bar in the glove box was added LiOtBu (9.0 mg, 0.11 mmol, 1.5 equiv), 3,4-bis((3,5-bis(trifluoromethyl)phenyl)amino) cyclobut-3-ene-1,2-dione **3.3** (8.0 mg, 0.015 mmol, 0.2 equiv), 1.5 ml DCE, and 0.1 ml hexanes. This was allowed to prestir at room temperature for 1 hour. Then triflate **3.11** (30.0 mg, 0.075 mmol, 1 equiv) was added. The reaction was heated to 70 °C for 12 hours then 90 °C for another 12 hours. The reaction was diluted with ether and pushed through a pad of silica. The crude material was purified by silica flash chromatography (3% acetone/hexanes) to give pure dihydrofuran **3.11** as colorless oil (11.5 mg, 61%, 0.046 mmol).

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.44 – 7.33 (m, 2H), 7.32 – 7.26 (m, 2H), 7.26 – 7.04 (m, 6H), 4.60 (dd, J = 9.8, 8.8 Hz, 1H), 4.24 (dd, J = 8.8, 7.0 Hz, 1H), 3.50 (dddd, J = 10.3, 9.0, 6.9, 3.5 Hz, 1H), 1.62 (dqd, J = 13.7, 7.5, 3.5 Hz, 1H), 1.47 – 1.36 (m, 1H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 150.0, 135.4, 131.8, 128.7, 128.3, 128.1, 127.9, 127.5, 126.1, 114.7, 73.2, 49.0, 25.4, 10.5.

FTIR (Neat film NaCl): 3079, 3055, 3025, 2959, 2929, 2873, 1950, 1886, 1808, 1650, 1601, 1497, 1446, 1365, 1233, 1094, 1067, 1016, 985, 950, 916, 761, 694, 674, 580, 493

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{18}H_{18}O$ 250.1358; Found 250.1354.



Methyl 2-(4-bromophenyl)-3-methylcyclopent-2-ene-1-carboxylate (3.16)

Synthesized according to general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol,

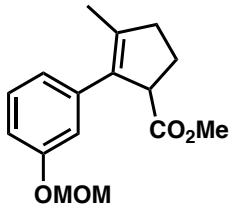
3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.16** (19.1 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 5h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (5% ether:hexanes) to yield **3.16** as a clear oil (43% NMR yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 3.93 (m, 1H), 3.54 (s, 3H), 2.75 – 2.59 (m, 1H), 2.46 (dt, *J* = 16.0, 7.5 Hz, 1H), 2.36 – 2.21 (m, 1H), 2.12 (ddt, *J* = 12.0, 9.1, 5.8 Hz, 1H), 1.79 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 140.7, 136.0, 133.0, 131.5, 129.9, 120.7, 54.8, 52.0, 38.9, 27.4, 15.6.

FTIR (Neat film NaCl):): 2950, 2925, 2860, 2850, 1720, 1607, 1435, 1170, 1115, 1009, 858, 775 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{15}BrO_2$: 294.0255; measured: 295.0248.



Methyl 2-(3-(methoxymethoxy)phenyl)-3-methylcyclopent-2-ene-1-carboxylate (3.21). Synthesized according to a slightly modified general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with the urea catalyst **3.4** (2.4 mg, 0.005 mmol, 0.2 equiv) and LiH (2.0 mg, 0.25 mmol, 10 equiv) followed by dry 1,2-difluorobenzene (1.5 mL). This mixture was sealed and heated to 70 °C for 30 minutes. After cooling to room temperature, to this was added vinyl triflate **3.21** (10.7 mg, 0.025 mmol, 1 equiv) and heated to 90 ºC overnight. The reaction vial was removed from the glove box, diluted with ether, and plugged

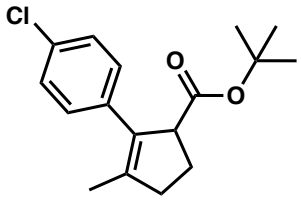
through silica gel with dichloromethane and concentrated. The crude oil was purified by flash column chromatography (90:5:5 hexanes:dichloromethane:ether) to yield cyclopentene **3.21** as a clear oil (2.5 mg, 36% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (td, *J* = 7.7, 0.8 Hz, 1H), 6.91 (d, *J* = 1.1 Hz, 1H), 6.89 – 6.84 (m, 2H), 5.16 (s, 2H), 3.55 (s, 3H), 3.48 (s, 3H), 2.74 – 2.63 (m, 1H), 2.46 (dddd, *J* = 16.4, 9.0, 5.8, 1.4 Hz, 1H), 2.26 (dtd, *J* = 12.9, 9.0, 5.4 Hz, 1H), 2.11 (ddt, *J* = 13.0, 9.2, 5.8 Hz, 1H), 1.83 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 157.1, 140.0, 138.4, 133.5, 129.2, 121.8, 116.1, 114.5, 94.6, 56.1, 54.8, 51.8, 38.8, 27.4, 15.6.

FTIR (Neat Film NaCl): 2953, 2922, 2852, 1735, 1600, 1577, 1486, 1462, 1435, 1377, 1276, 1152, 1080, 1019, 789, 720 cm^{-1}.

MS (EI-MS): Calculated for $C_{16}H_{20}O_4$: 276.1; measured:276.1.



***tert*-Butyl 2-(4-chlorophenyl)-3-methylcyclopent-2-ene-1-carboxylate (3.20).**

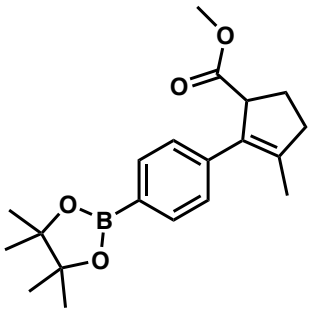
Synthesized according to a slightly modified general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.15 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.20** (22.1 mg, 0.050 mmol, 1 equiv) and heated to 70 ºC for 5h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (40% dichloromethane:hexanes followed by 3% acetone:hexanes) to yield cyclopentene **3.20** as a clear oil (5.6 mg, 38% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.3 Hz, 2H), 3.82 (bs, 1H), 2.61 – 2.68 (m, 1H), 2.40 – 2.48 (m, 1H), 2.26 – 2.02 (m, 1H), 1.79 (s, 3H), 1.21 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 139.9, 135.9, 133.6, 132.3, 130.0, 128.3, 80.5, 56.0, 38.9, 28.1, 26.9, 15.6.

FTIR (Neat Film NaCl): 2975, 2930, 2856, 1726, 1491, 1455, 1367, 1278, 1148, 1092, 1014, 833 cm^{-1}.

HRMS (CI-MS): Calculated for $C_{17}H_{21}ClO_2$: 292.1230; Measured: 292.1219.



Methyl 3-methyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopent-2-ene-1-carboxylate (3.19).

Synthesized according to a slightly modified general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (2.4 mg, 0.005 mmol, 0.2 equiv) and LiH (0.6 mg, 0.15 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (1.5 mL). To this was added vinyl triflate **3.19** (12.3 mg, 0.025 mmol, 1 equiv) and heated to 70 ºC for 4h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (20% ether:hexanes) to yield cyclopentene **3.19** as a clear oil (3.5 mg, 41% yield).

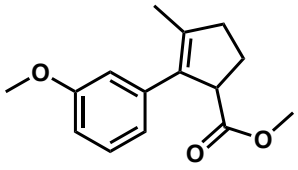
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 4.08 – 3.92 (m, 1H), 3.51 (s, 3H), 2.76 – 2.61 (m, 1H), 2.55 – 2.41 (m, 1H), 2.27 (dtd, *J* = 13.0, 9.0, 5.2 Hz, 1H), 2.12 (ddt, *J* = 13.0, 9.2, 6.0 Hz, 1H), 1.82 (s, 1H), 1.34 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.2, 140.5, 140.1, 134.8, 134.1, 127.6, 84.0, 54.9, 52.0j, 39.1, 27.6, 25.2, 15.7. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (161 MHz, $CDCl_3$) δ 30.78.

FTIR (Neat Film NaCl): 2977, 2955, 2928, 2854, 1735, 1609, 1435, 1398, 1361, 1822, 1276, 1165, 1144, 1091cm^{-1}.

HRMS (EI-MS): Calculated for $C_{20}H_{27}BO_4$: 342.2002; Measured: 342.1997



Methyl 2-(3-methoxyphenyl)-3-methylcyclopent-2-ene-1-carboxylate (3.22).

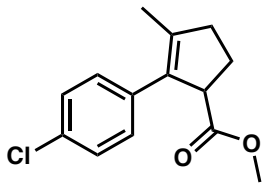
Synthesized according to general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.22** (19.8 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 5 hours. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (2% acetone:hexanes) to yield cyclopentene **3.22** as a yellow oil (6.1 mg, 50% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 1H), 6.81 (dt, *J* = 7.6, 1.3 Hz, 1H), 6.79 – 6.74 (m, 2H), 4.00 – 3.90 (m, 1H), 3.80 (s, 3H), 3.55 (s, 3H), 2.77 – 2.56 (m, 1H), 2.47 (dt, *J* = 16.0, 7.5 Hz, 1H), 2.27 (dtd, *J* = 12.9, 9.0, 5.3 Hz, 1H), 2.11 (ddt, *J* = 13.0, 9.3, 5.8 Hz, 1H), 1.83 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 159.6, 140.1, 138.6, 134.0, 129.3, 120.8, 113.9, 112.4, 55.4, 55.0, 52.0, 39.0, 27.6, 15.8.

FTIR (Neat Film NaCl): 2950, 2842, 1733, 1599, 1577, 1487, 1454, 1432, 1339, 1287, 1231, 1165, 1047, 877, 788, 700 cm^{-1}.

HRMS (CI-MS): Calculated for $C_{15}H_{18}O_3$: 246.1256; Measured: 246.1252.



Methyl 2-(4-chlorophenyl)-3-methylcyclopent-2-ene-1-carboxylate (3.20).

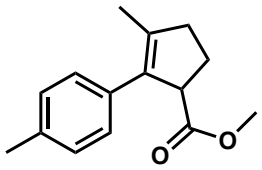
Synthesized according to general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with the urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.20** (20 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 36h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (60% DCM:hexanes) to yield cyclopentene **3.20** as a clear oil (6.6 mg, 53% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 3.94 (td, *J* = 6.4, 5.7, 2.5 Hz, 1H), 3.54 (s, 3H), 2.76 – 2.60 (m, 1H), 2.47 (dt, *J* = 15.9, 7.5 Hz, 1H), 2.37 – 2.18 (m, 1H), 2.21 – 2.02 (m, 1H), 1.80 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 140.6, 135.6, 133.0, 132.5, 129.6, 128.6, 54.9, 52.0, 39.0, 27.5, 15.7.

FTIR (Neat Film NaCl): 2950, 2844, 1734, 1491, 1434, 1337, 1251, 1194, 1165, 1092, 1013, 832 cm^{-1}.

HRMS (EI-MS): Calculated for $C_{14}H_{15}ClO_2$: 250.0760; Measured 250.0758



Methyl 3-methyl-2-(*p*-tolyl)cyclopent-2-ene-1-carboxylate (3.17).

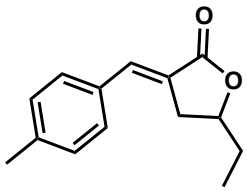
Synthesized according to general procedure 6. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.17** (19.1 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 3h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (2% ether:hexanes) to yield cyclopentene **3.17** as a yellow oil (7.4 mg, 64% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (s, 4H), 3.96 (dddd, *J* = 7.7, 5.8, 4.1, 2.1 Hz, 1H), 3.54 (s, 3H), 2.75 – 2.58 (m, 1H), 2.46 (dt, *J* = 16.2, 7.5 Hz, 1H), 2.26 (dtd, *J* = 13.0, 9.0, 5.4 Hz, 1H), 2.11 (ddt, *J* = 13.0, 9.2, 5.7 Hz, 1H), 1.82 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 143.5, 140.3, 137.2, 129.6, 128.6, 127.9, 52.3, 43.5, 38.4, 31.6, 20.4, 15.8.

FTIR (Neat Film NaCl): 2979, 2930, 2854, 1725, 1491, 1463, 1367, 1278, 1145, 1091, 1013, cm^{-1}.

HRMS (EI-MS): Calculated for $C_{15}H_{18}O_2$: 230.1307; Measured: 230.1309.



(*E*)-5-ethyl-3-(4-methylbenzylidene)dihydrofuran-2(3*H*)-one (3.23)

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.23** (19.1 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 3h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (8→15% ether:hexanes) to yield γ-lactone **3.23** as a yellow oil (16% NMR yield). Product is more polar than the usual isolated product **3.17**.

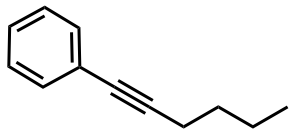
The olefin geometry was assigned based on NOESY NMR. Allylic protons at 3.3 and 2.8 ppm showed NOE with the aromatic protons.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (t, *J* = 2.9 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 4.56 (ddt, *J* = 7.9, 6.9, 5.7 Hz, 1H), 3.43 – 3.18 (m, 1H), 2.82 (ddd, *J* = 17.4, 5.6, 3.0 Hz, 1H), 2.40 (s, 3H), 1.95 – 1.62 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 140.3, 136.5, 132.1, 130.1, 129.7, 123.7, 78.9, 33.3, 29.6, 21.6, 9.2.

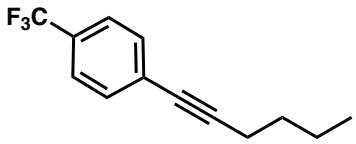
FTIR (Neat film NaCl): 2968, 2923, 2879, 1747, 1654, 1607, 1463, 1415, 1347, 1229, 1177, 1050, 965 cm^{-1}.

HR-MS (EI-MS): Calculated for $C_{14}H_{16}O_2$: 216.1150; measured: 216.1148.



hex-1-yn-1-ylbenzene (3.30)

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.28** (19.1 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 3h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (100% hexanes) to yield alkyne **3.30** as a colorless oil (80% NMR yield). The reported ^{1}H NMR spectrum matched the isolated compound.[16]



1-(hex-1-yn-1-yl)-4-(trifluoromethyl)benzene (3.31)

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with urea **3.4** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (1.2 mg, 0.3 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.29** (19.1 mg, 0.05 mmol, 1 equiv) and heated to 70 ºC for 3h. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (100% hexanes) to yield alkyne **3.31** as a colorless oil (85% NMR yield). The reported ^{1}H NMR spectrum matched the isolated compound.[17]

3.6 Spectra Relevant to Chapter Three:

Urea Catalysts Used to Generate Vinyl Carbocations and Further Exploration of Substrate Compatibility

Alex L. Bagdasarian, Stasik Popov, Benjamin Wigman, Wenjing Wei, Woojin Lee, and Hosea M. Nelson *Org. Lett.* **2020**, *22*, 7775–7779.

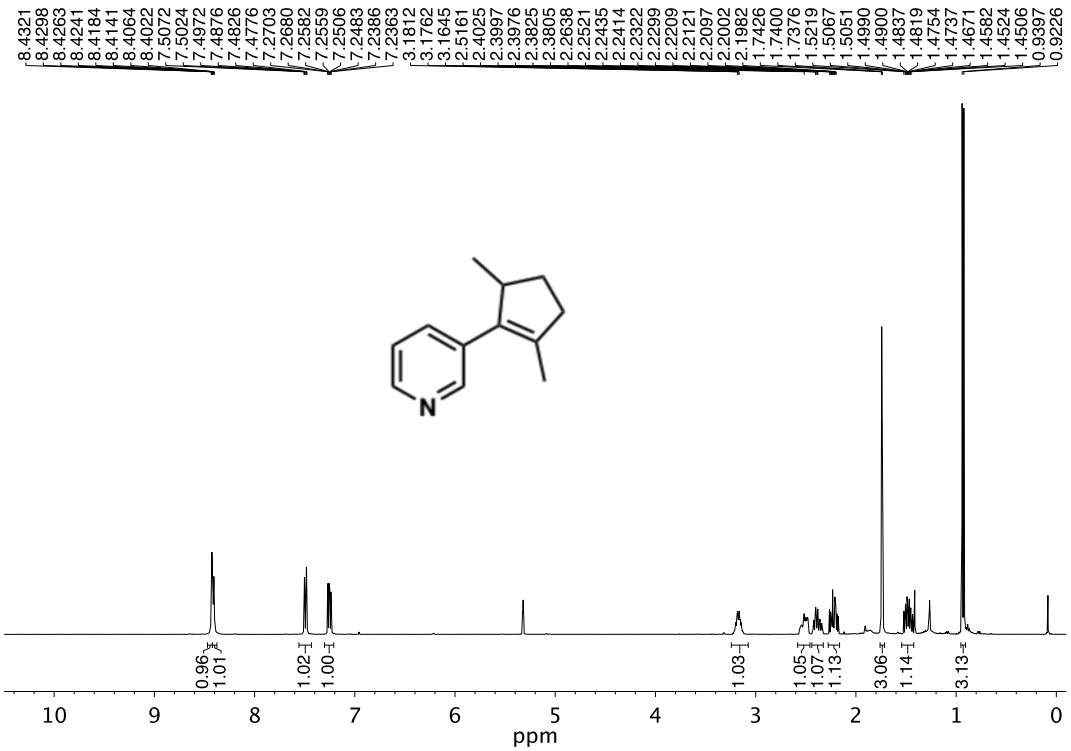


Figure 3.9 ^{1}H NMR (500 MHz, CD_2Cl_2) of compound **3.7**.

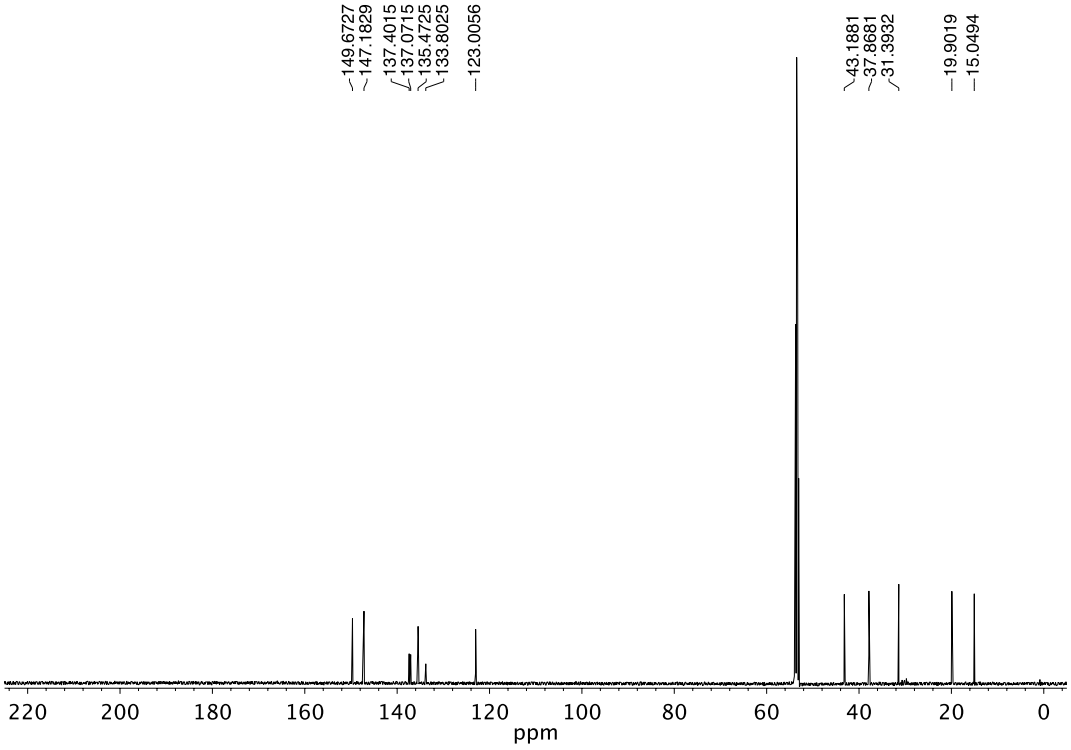


Figure 3.10 ^{13}C NMR (126 MHz, CD_2Cl_2) of compound **3.7**.

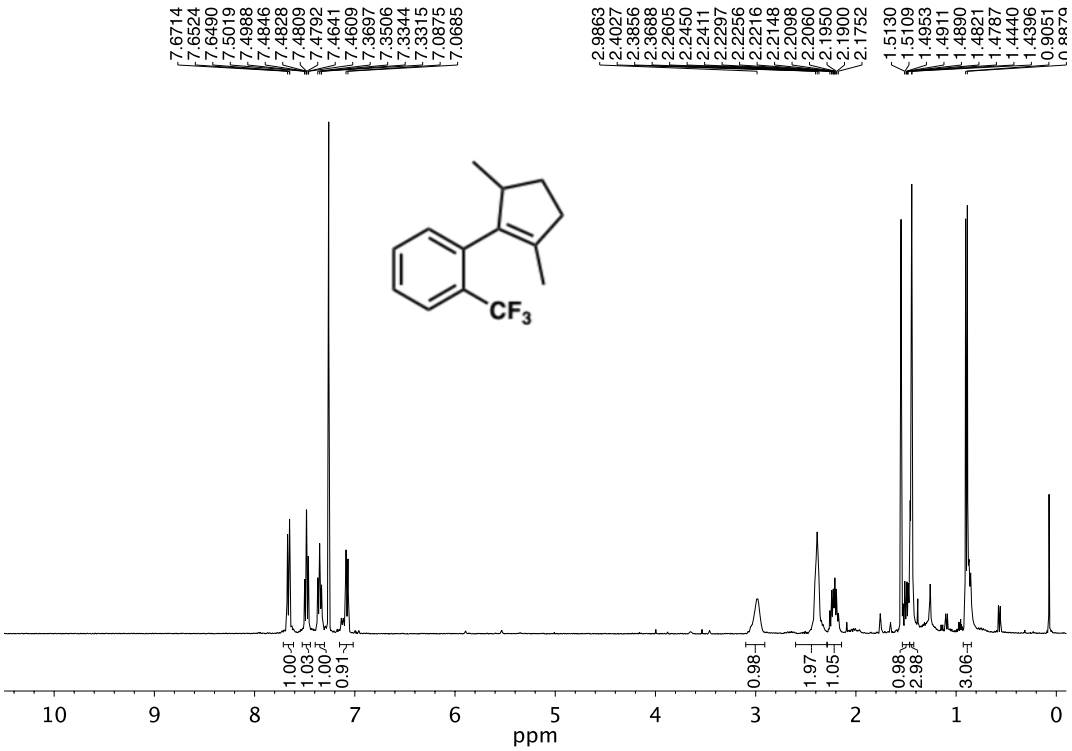


Figure 3.11 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.8**.

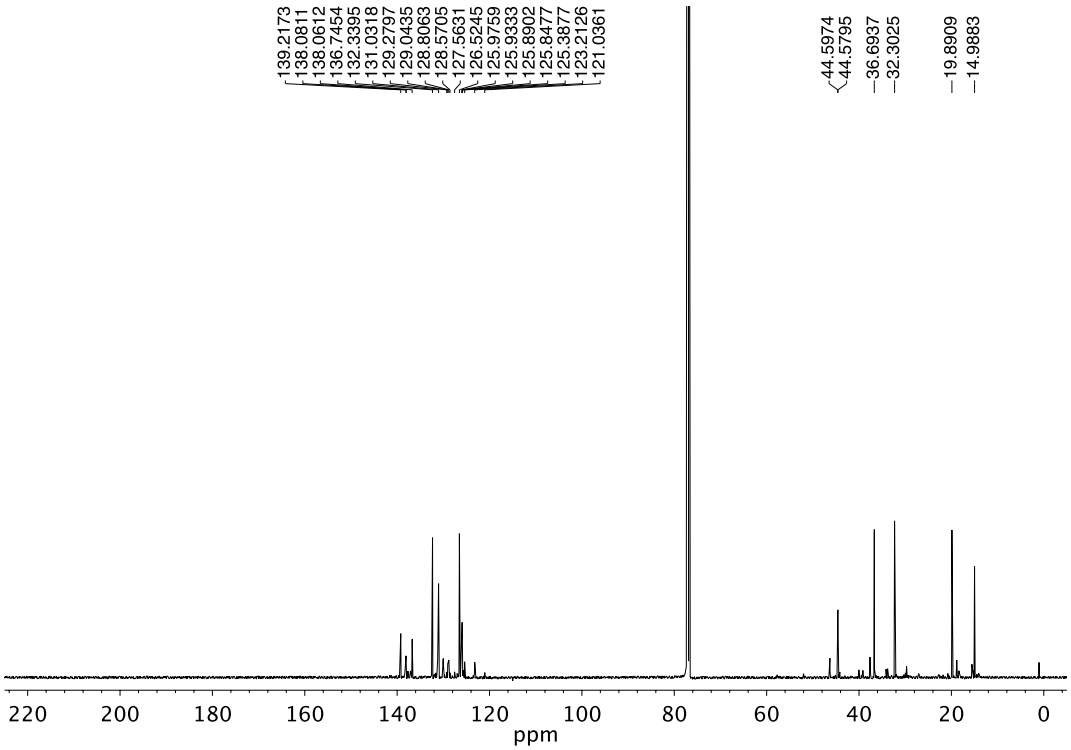


Figure 3.12 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.8**.

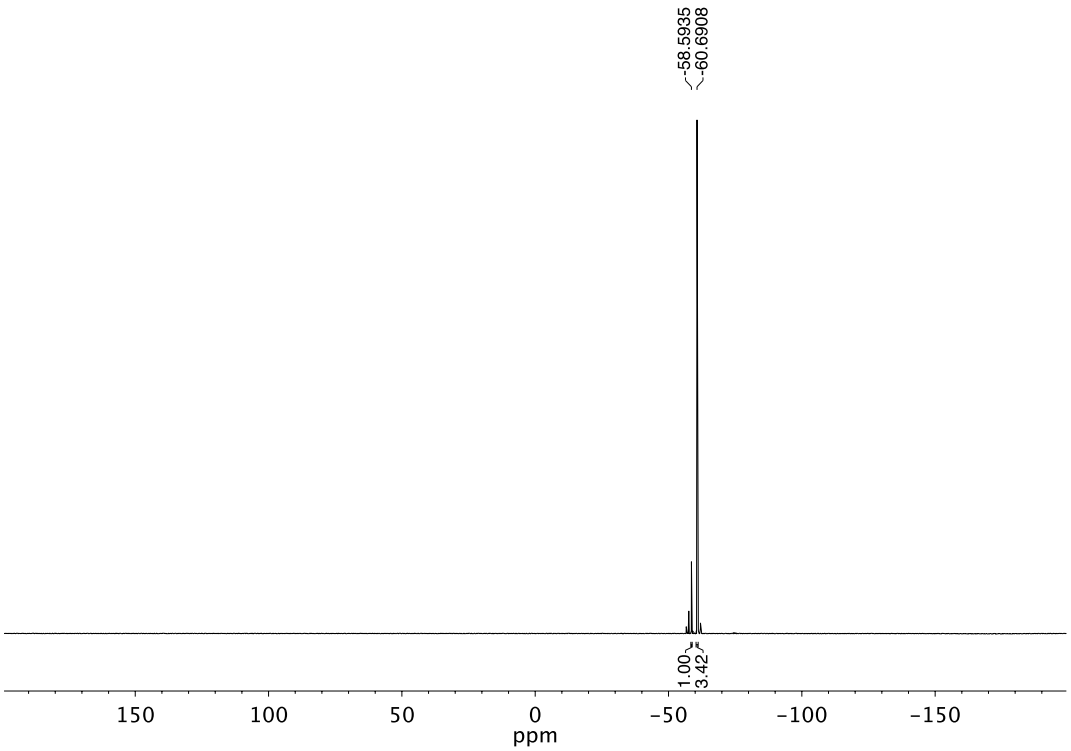


Figure 3.13 ^{19}F NMR (376 MHz, $CDCl_3$) of compound **3.8**.

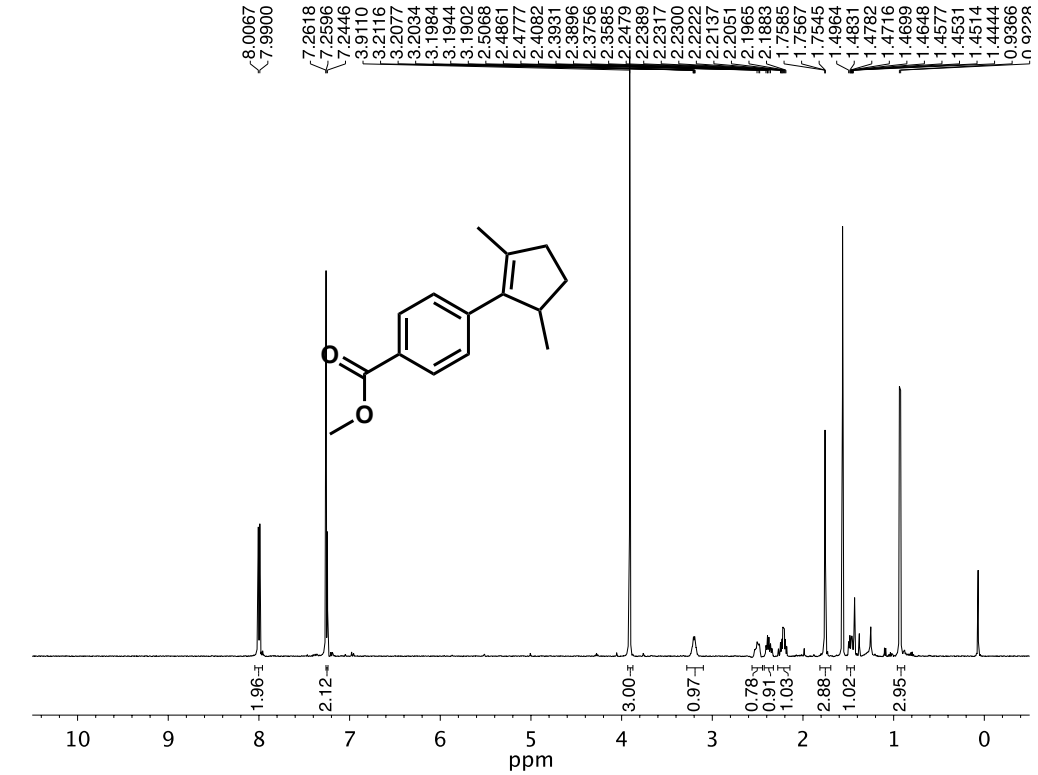
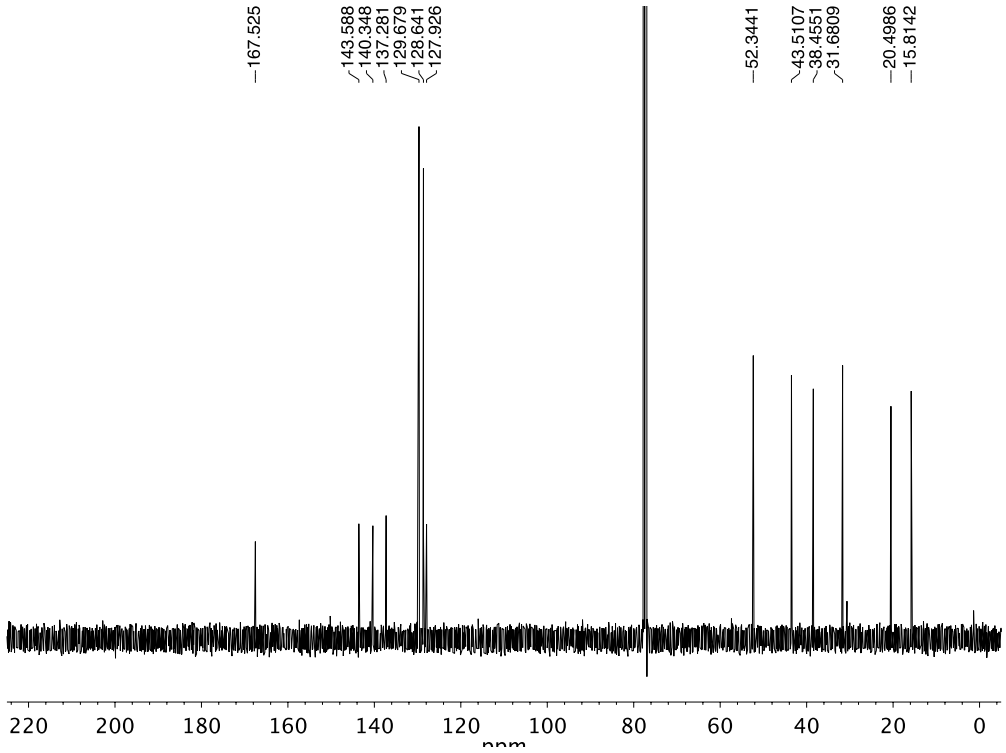


Figure 3.14 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.9**.



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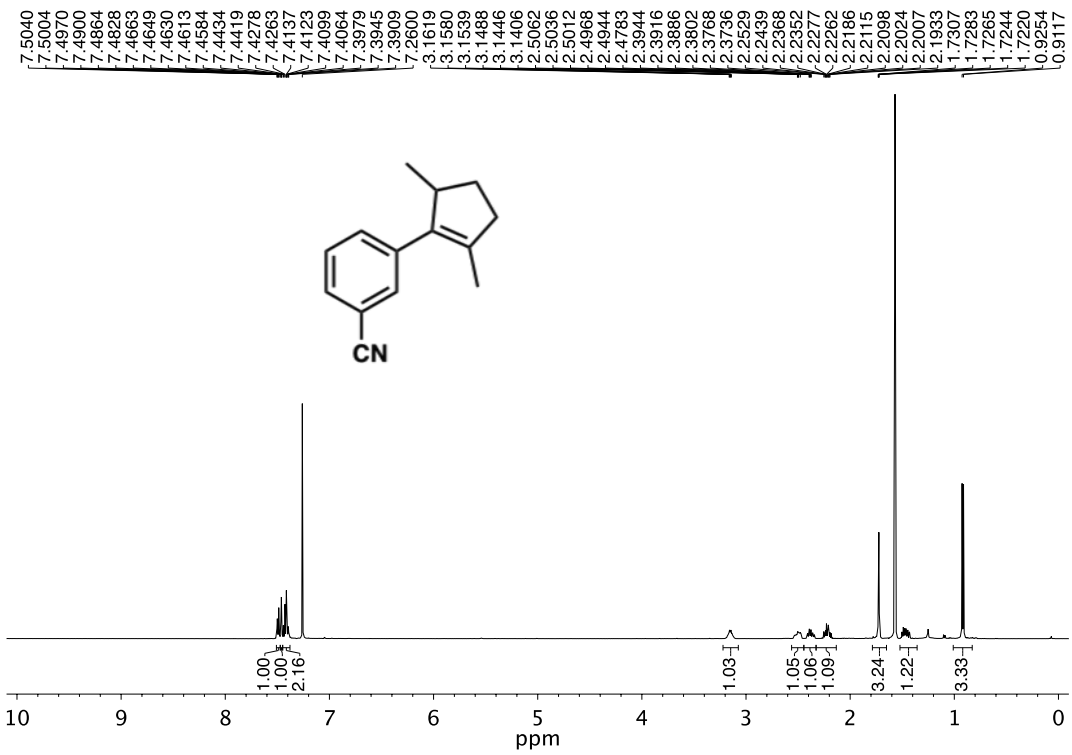

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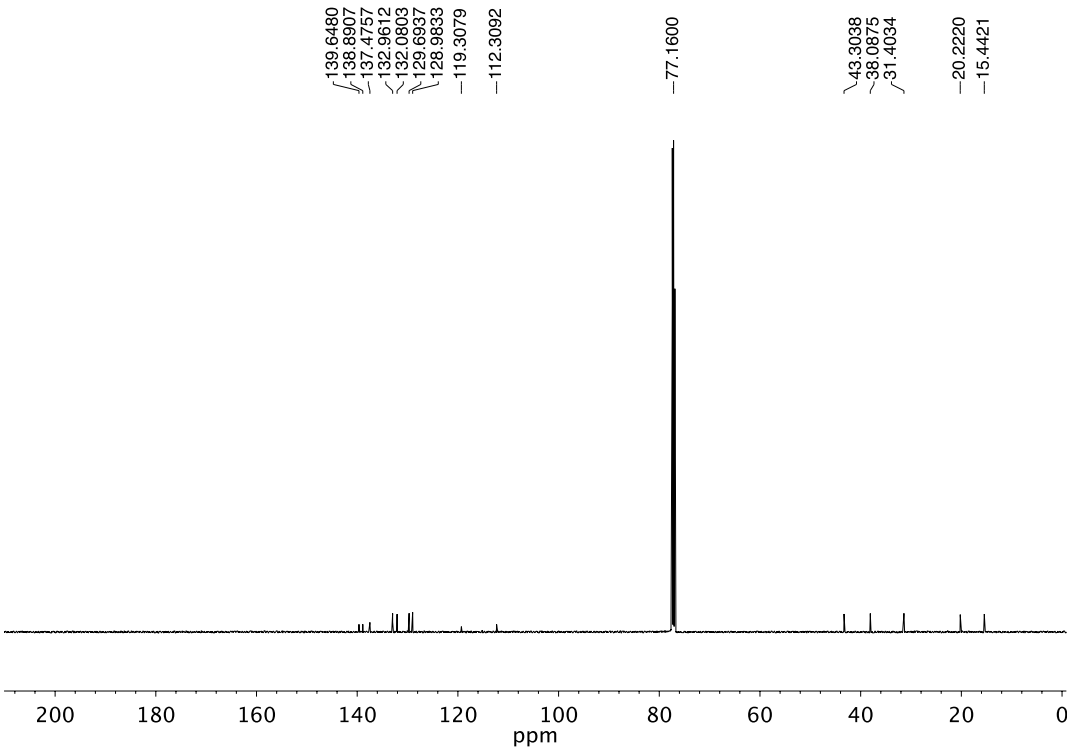

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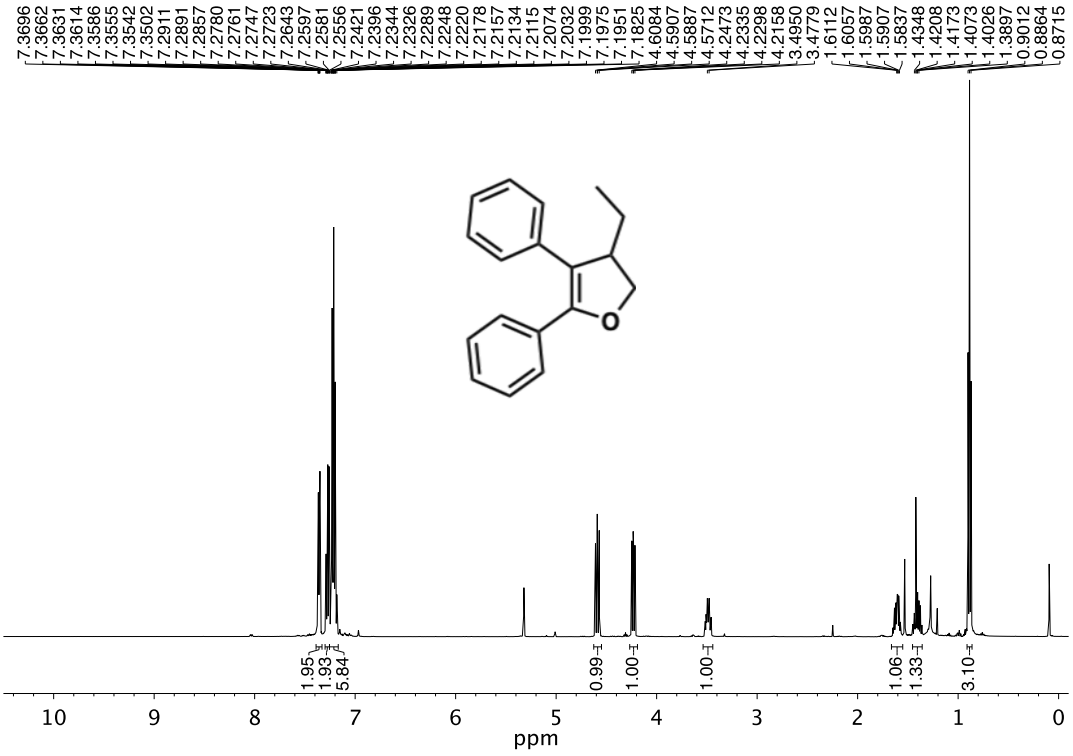

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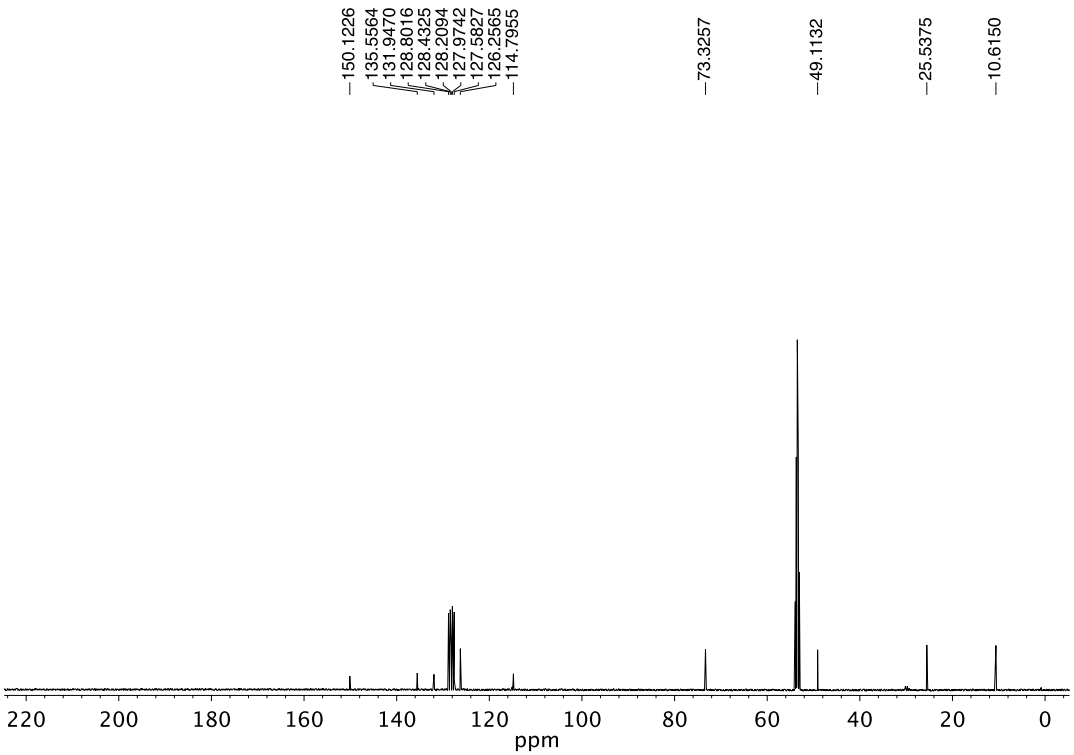
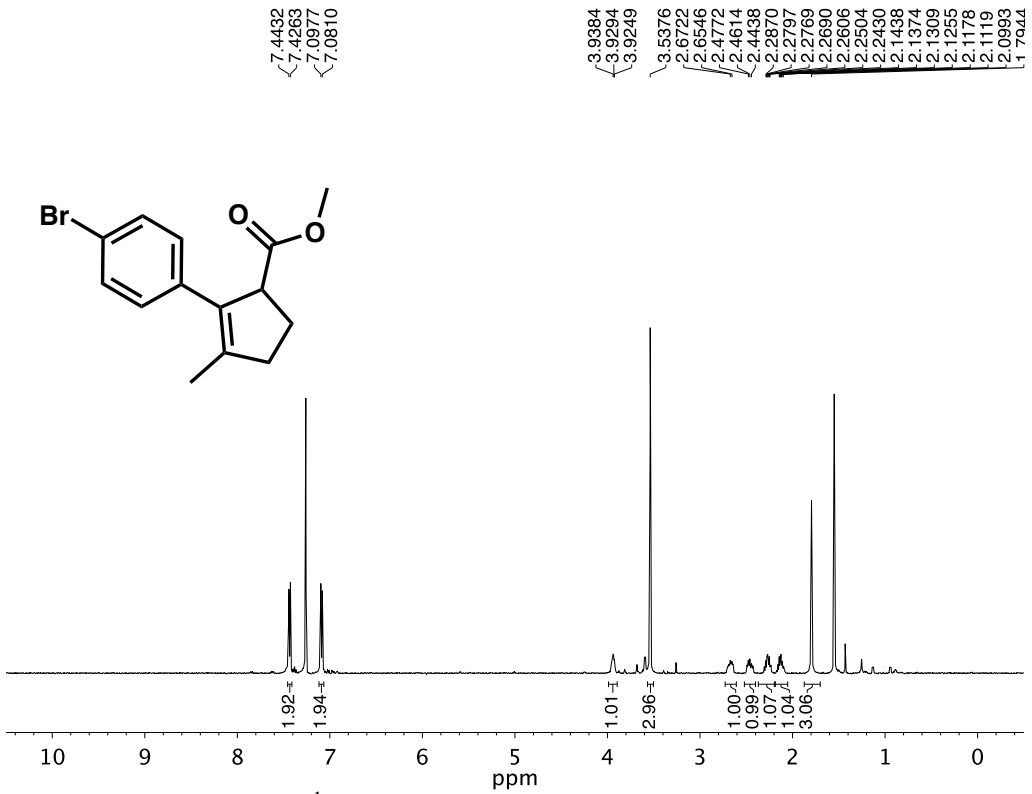


Figure 3.19 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.11**.



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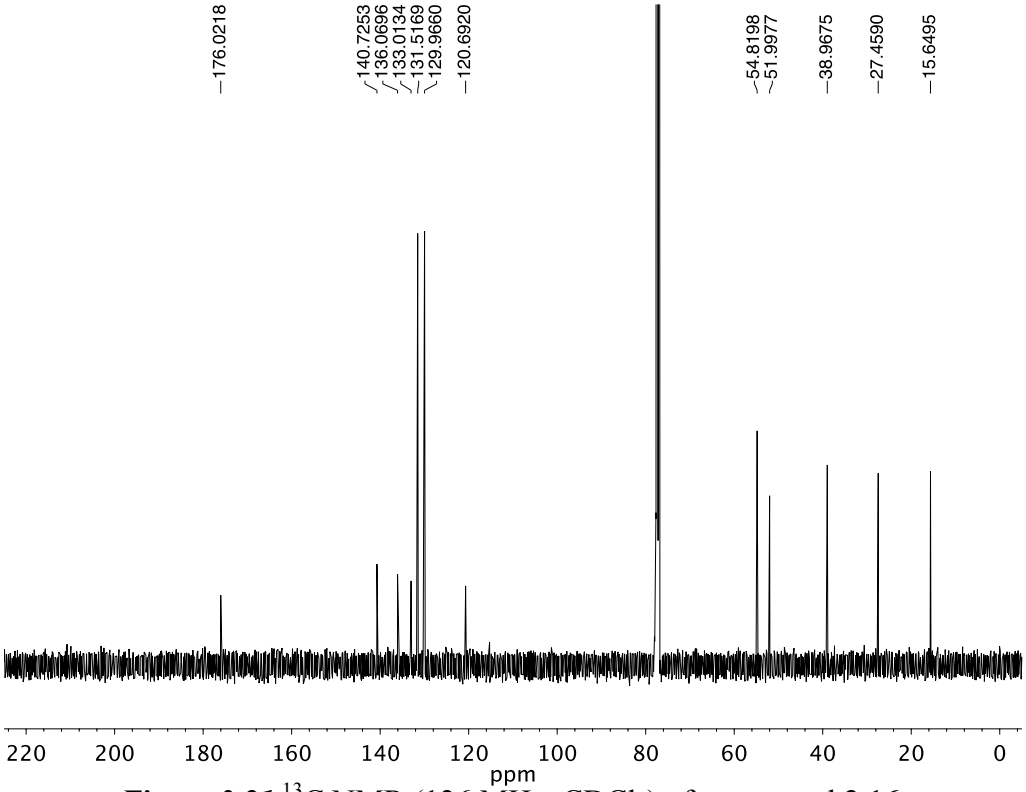


Figure 3.21 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.16**.

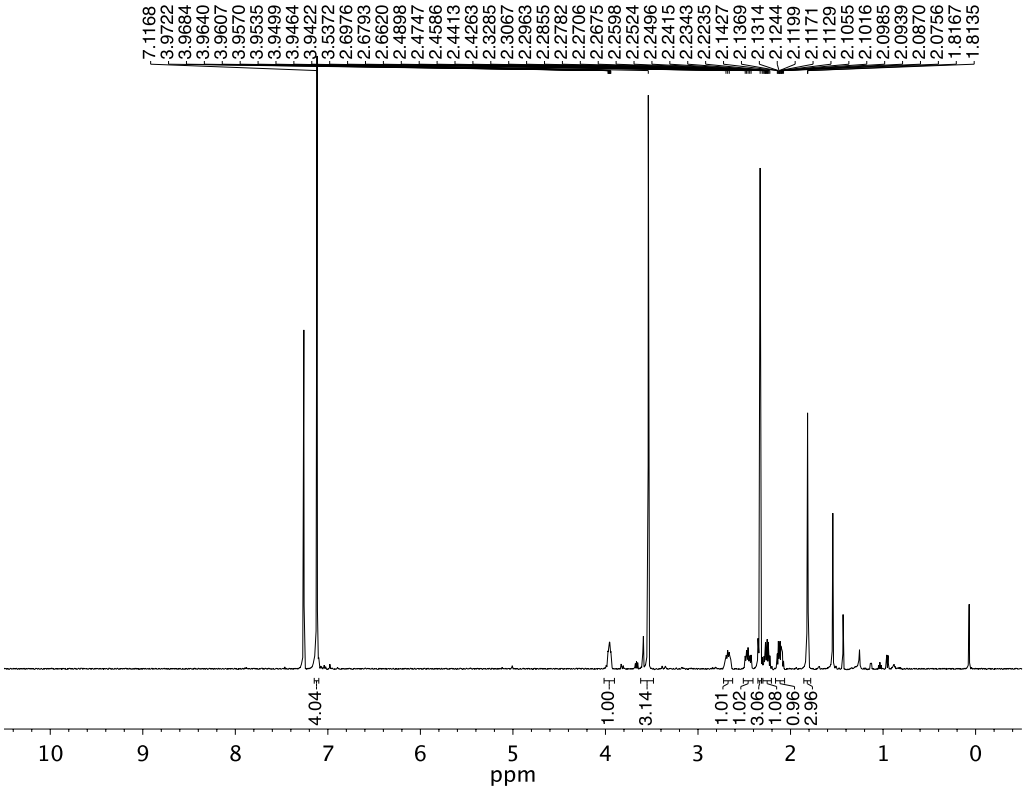


Figure 3.22 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.17**.

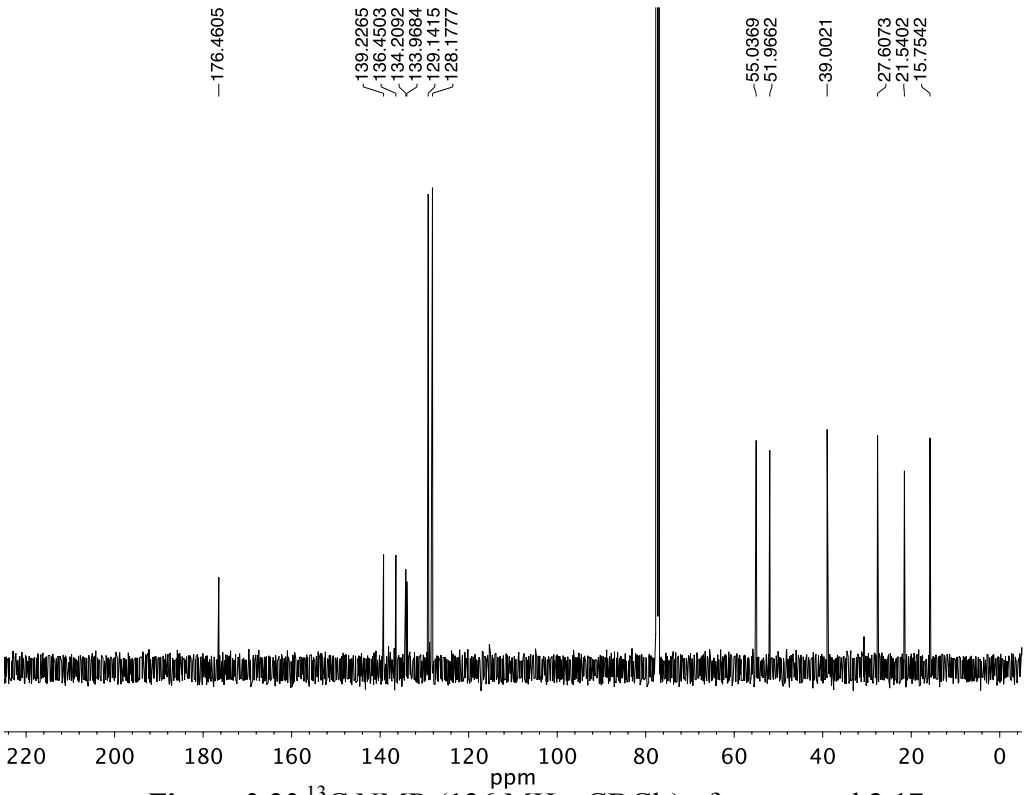


Figure 3.23 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.17**.

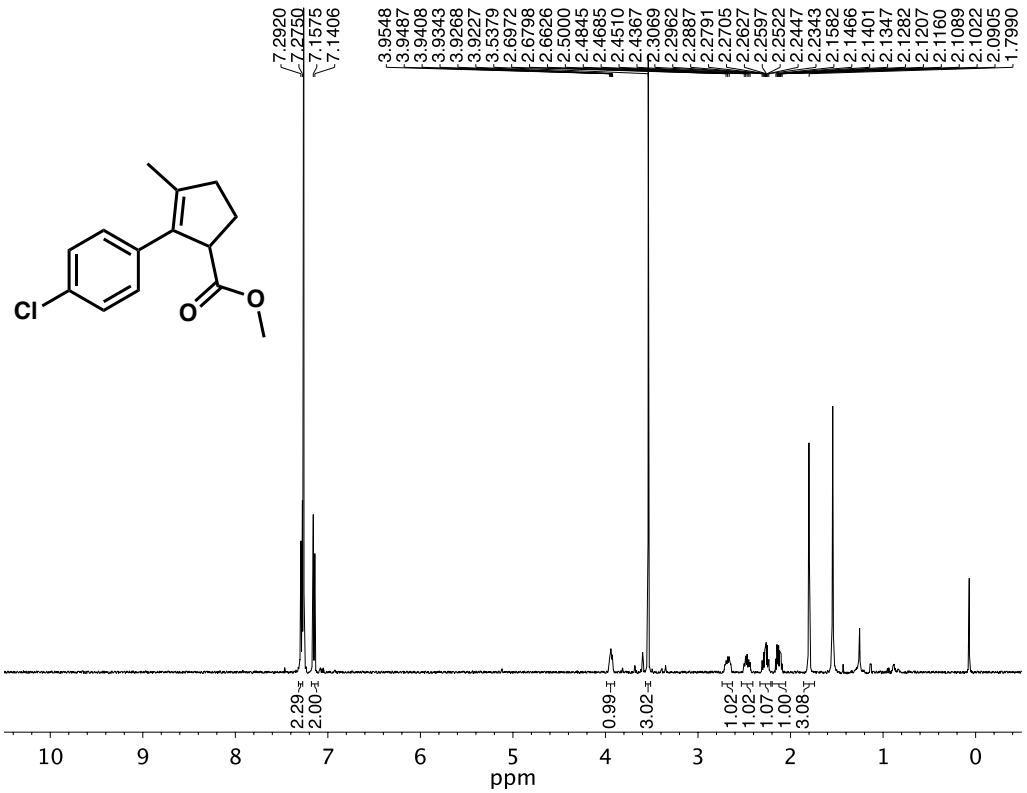
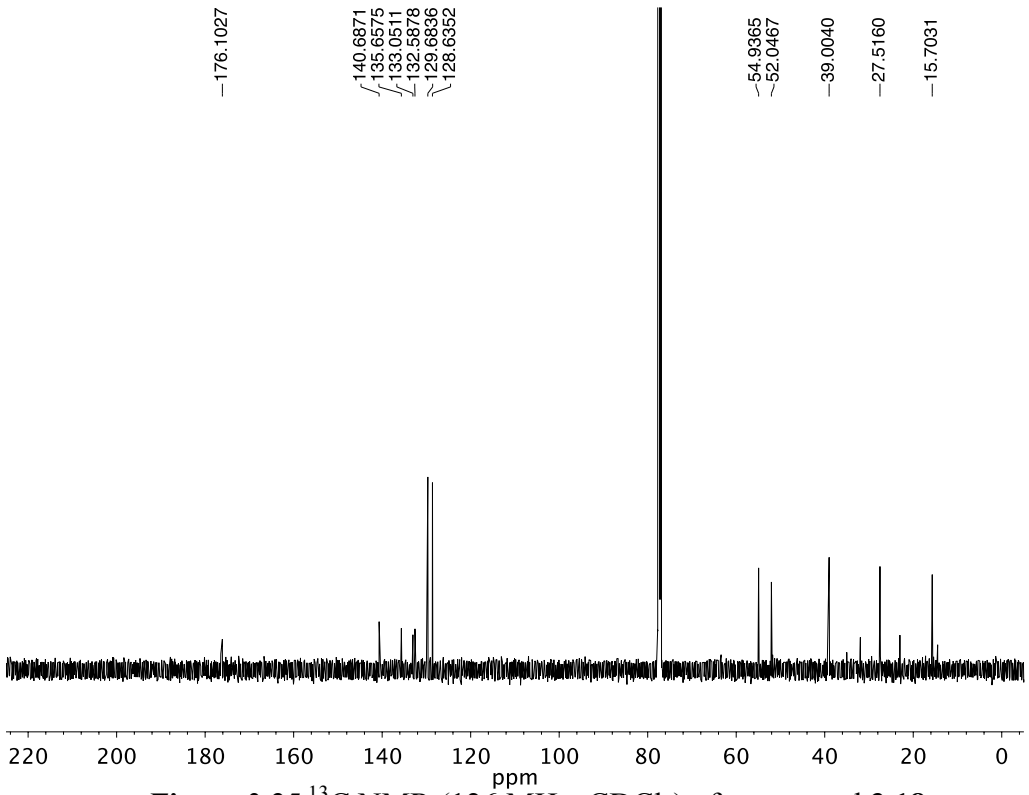


Figure 3.24 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.18**.



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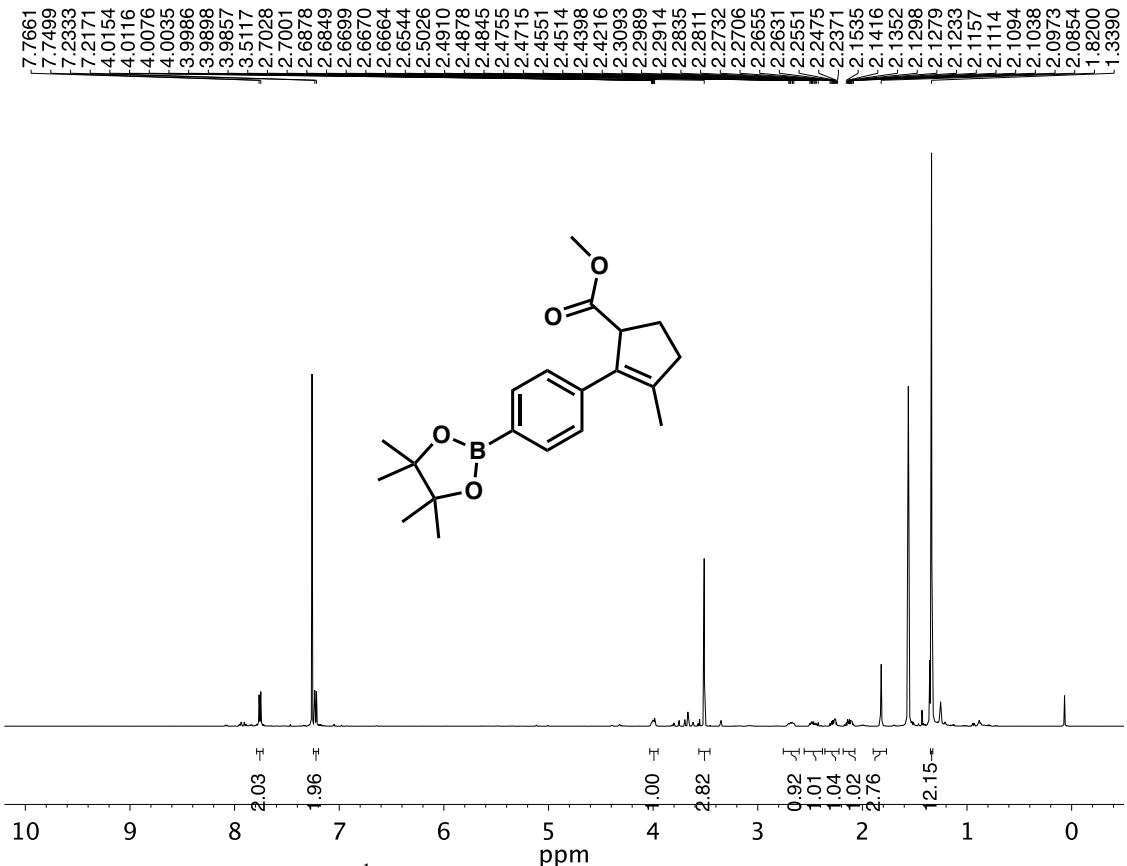

Figure 3.26 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.19**.

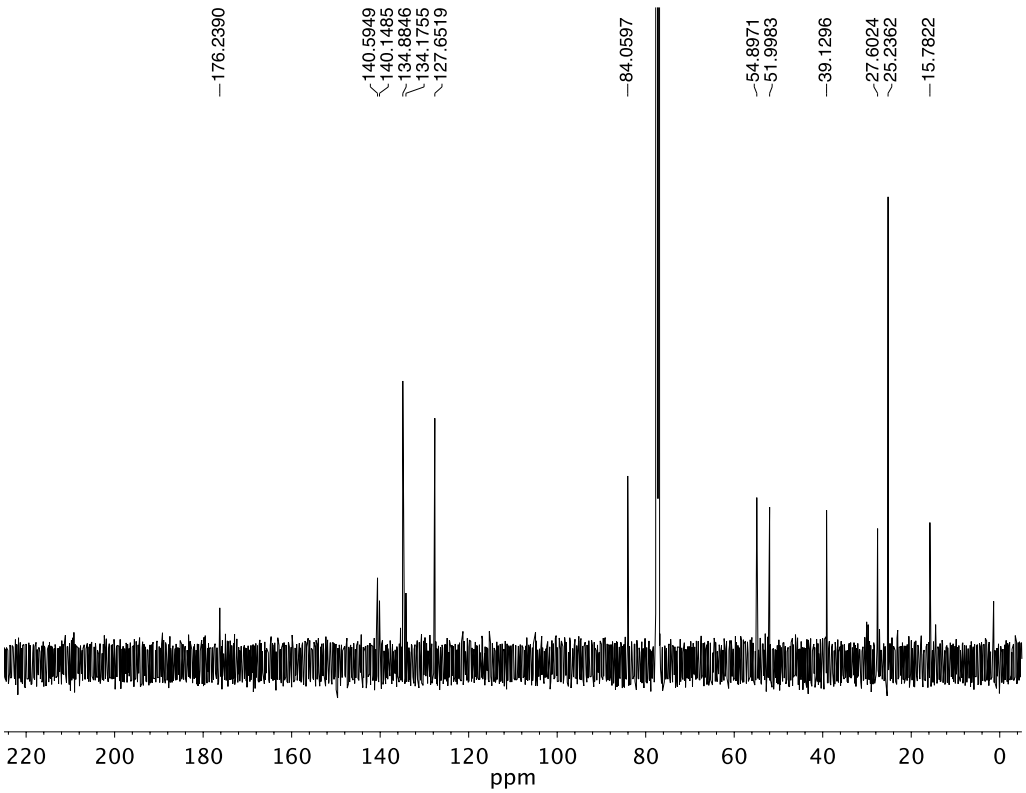

Figure 3.27 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.19**.

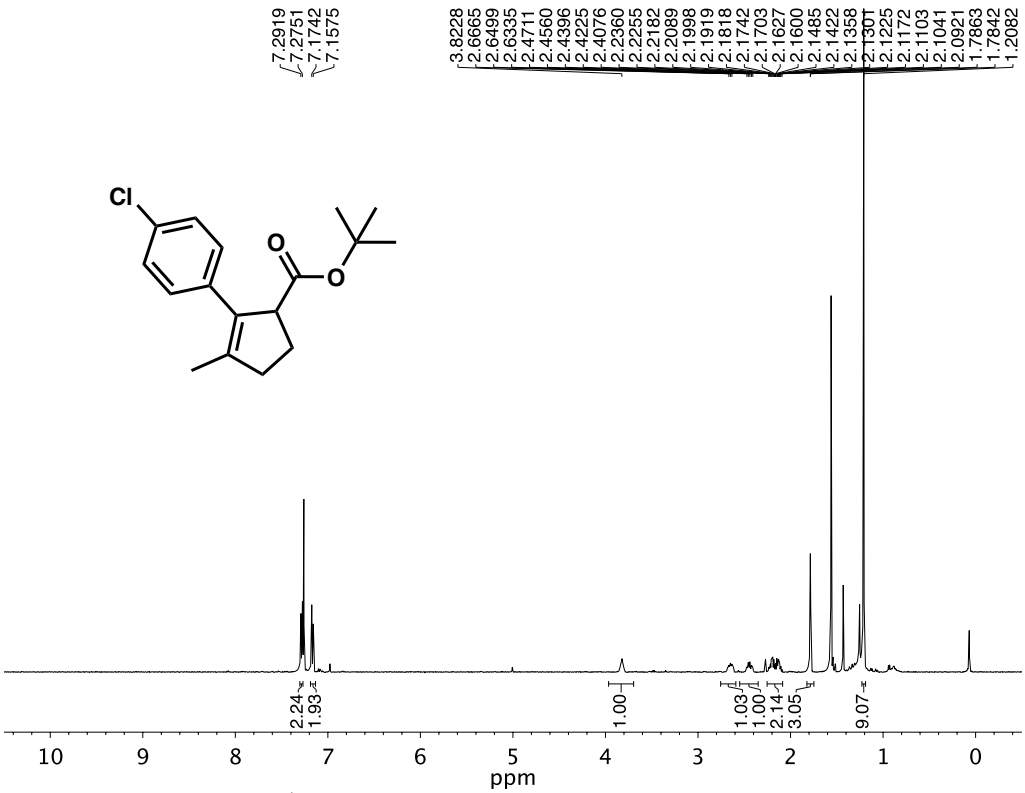

Figure 3.28 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.20**.

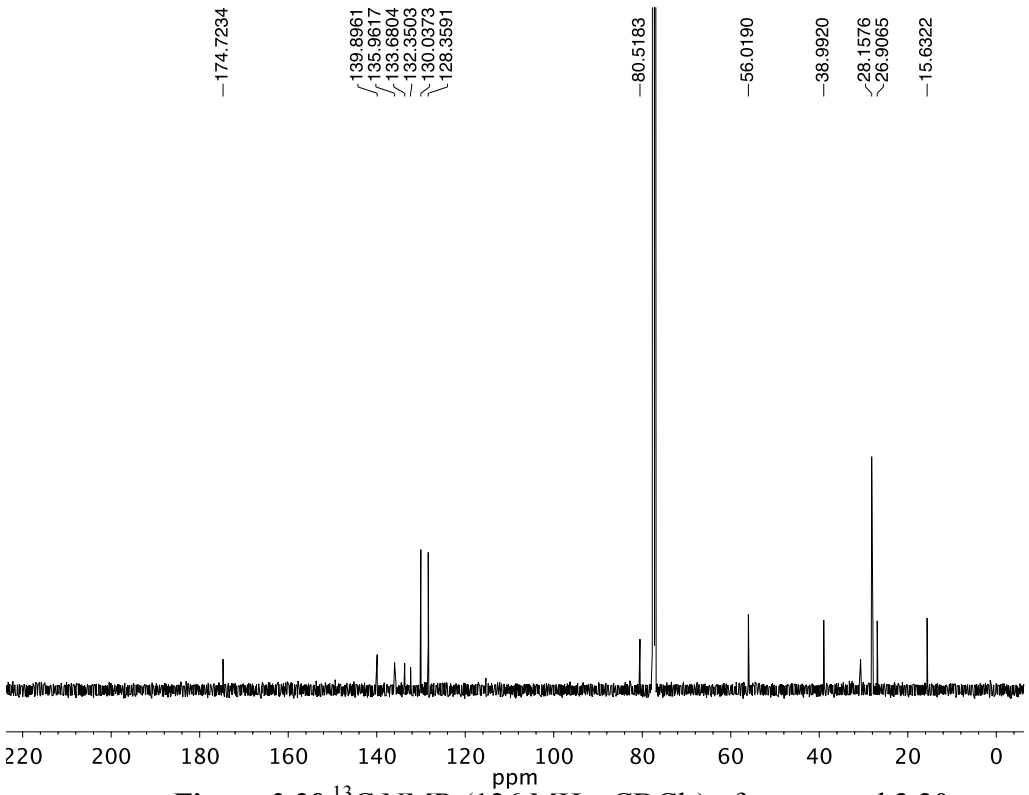

Figure 3.29 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.20**.

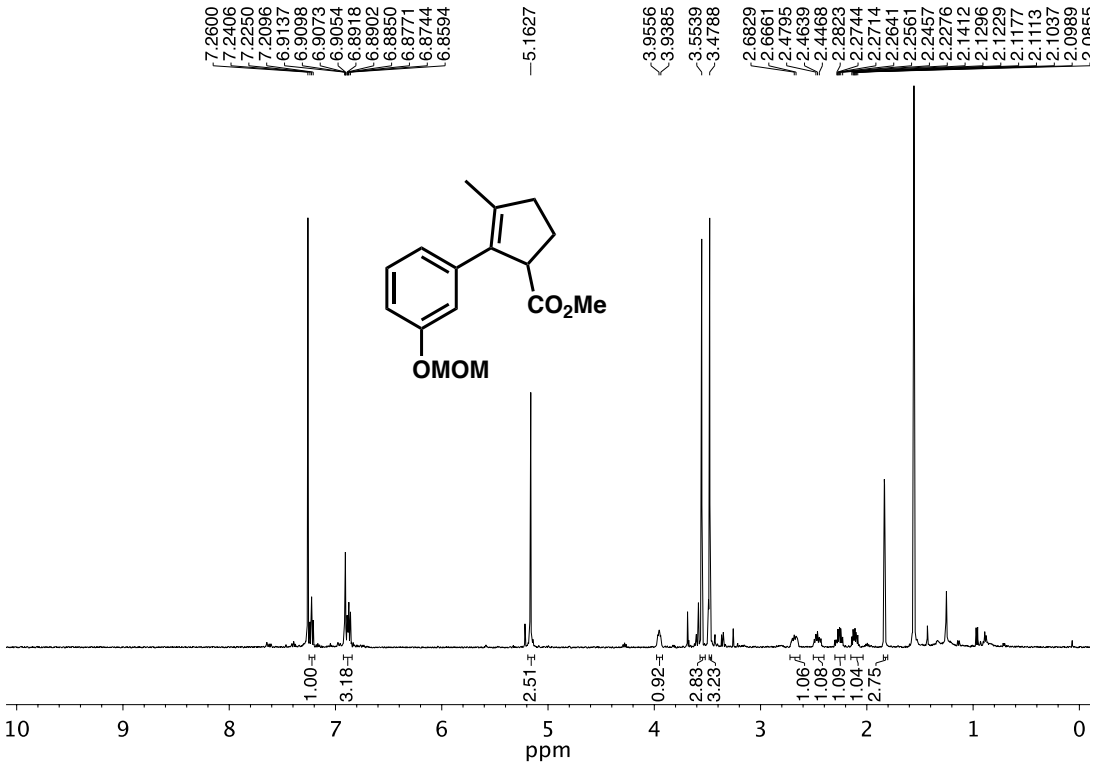

Figure 3.30 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.21**.

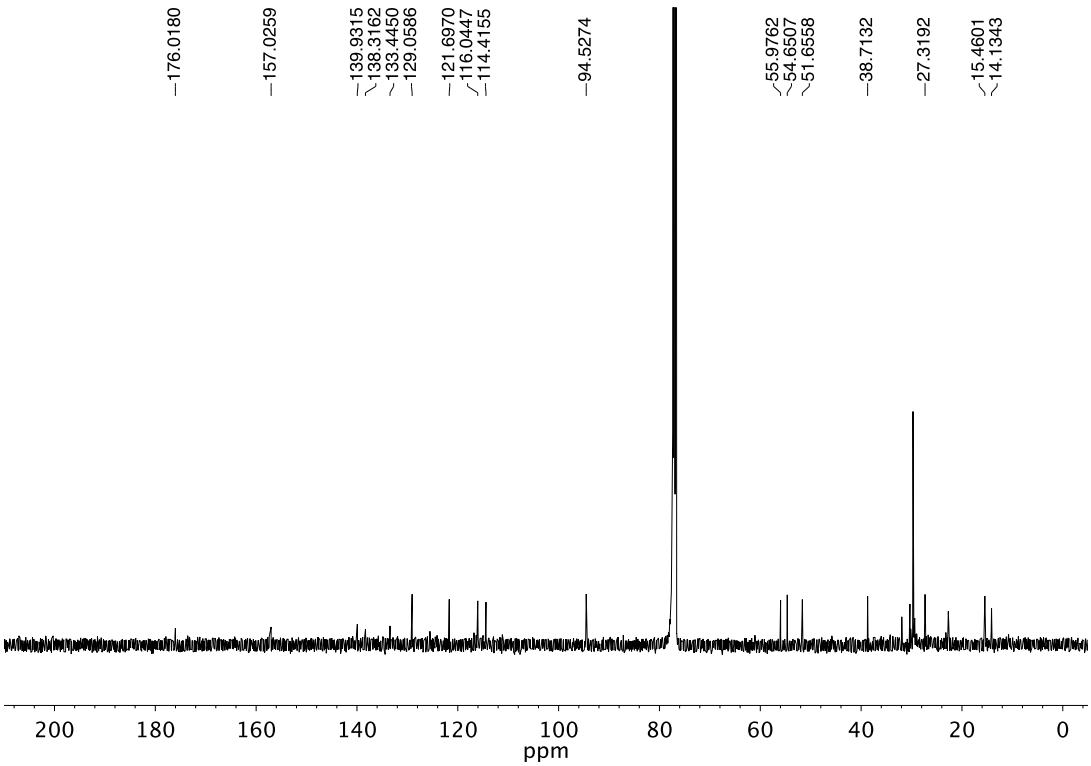

Figure 3.31 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.21**.

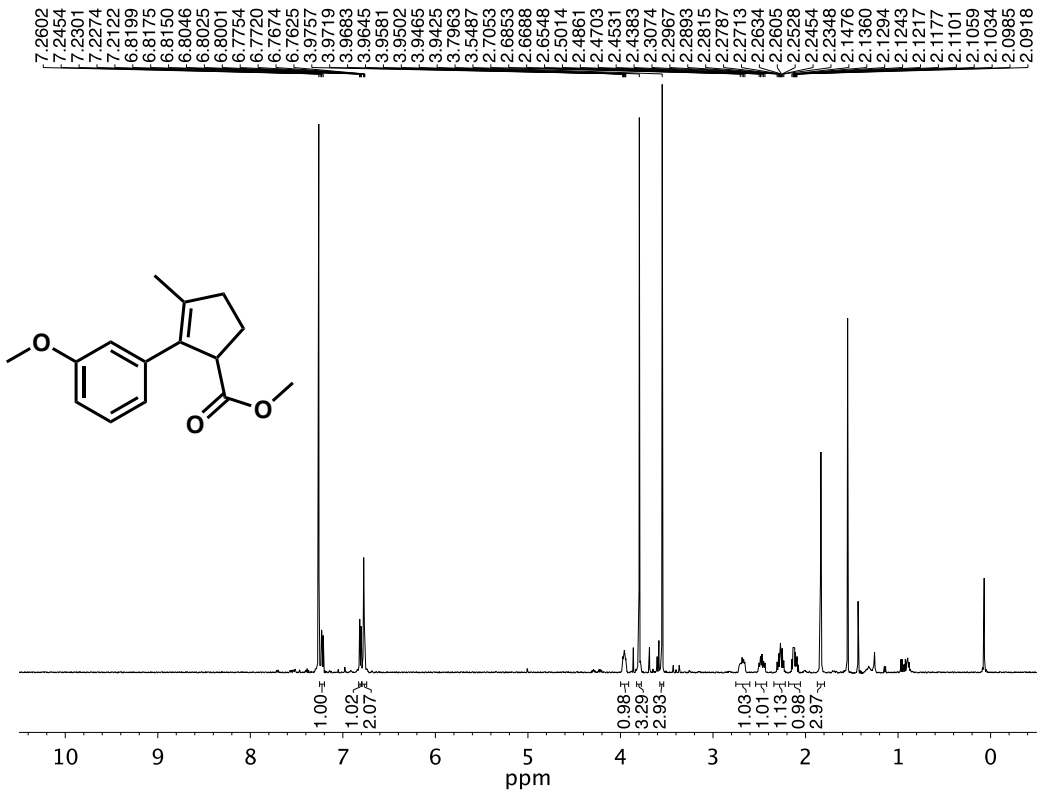

Figure 3.32 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.22**.

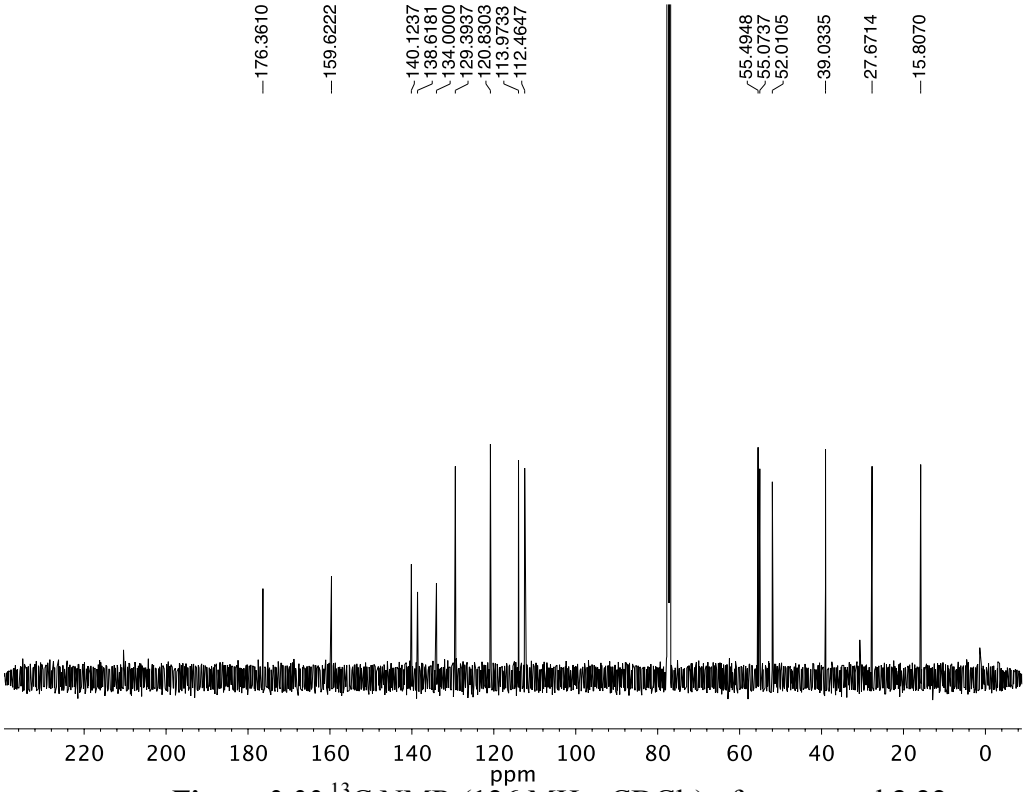

Figure 3.33 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.22**.

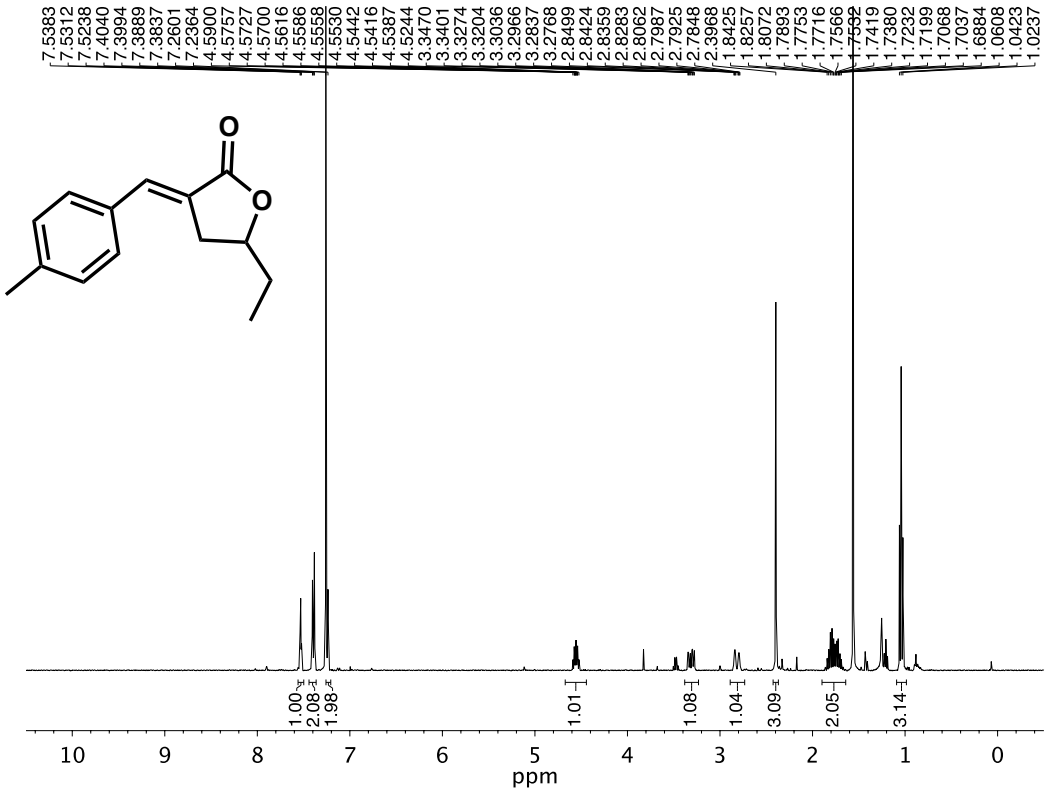

Figure 3.34 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **3.23**.

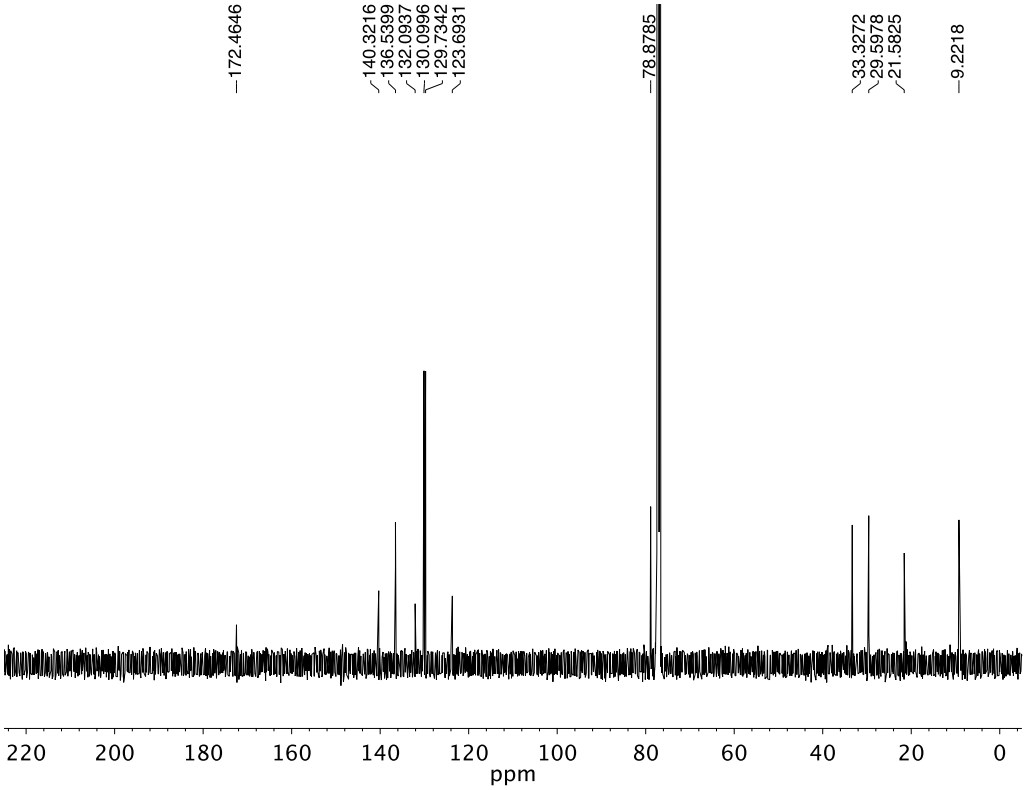

Figure 3.35 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.23**.

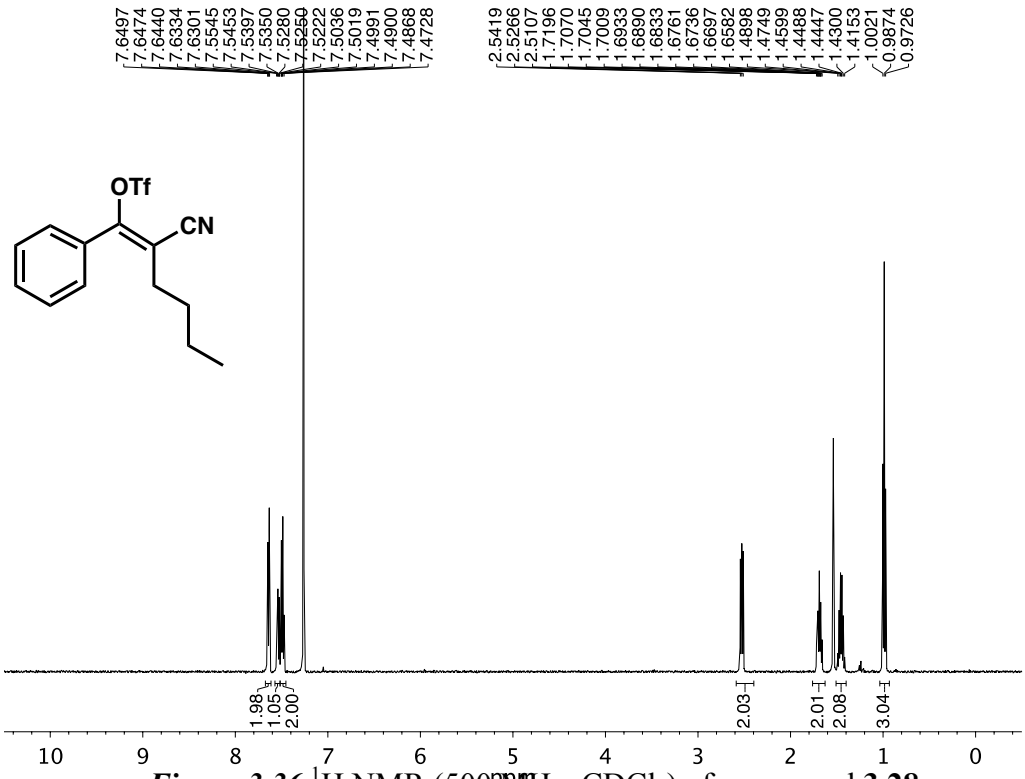

Figure 3.36 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.28**.

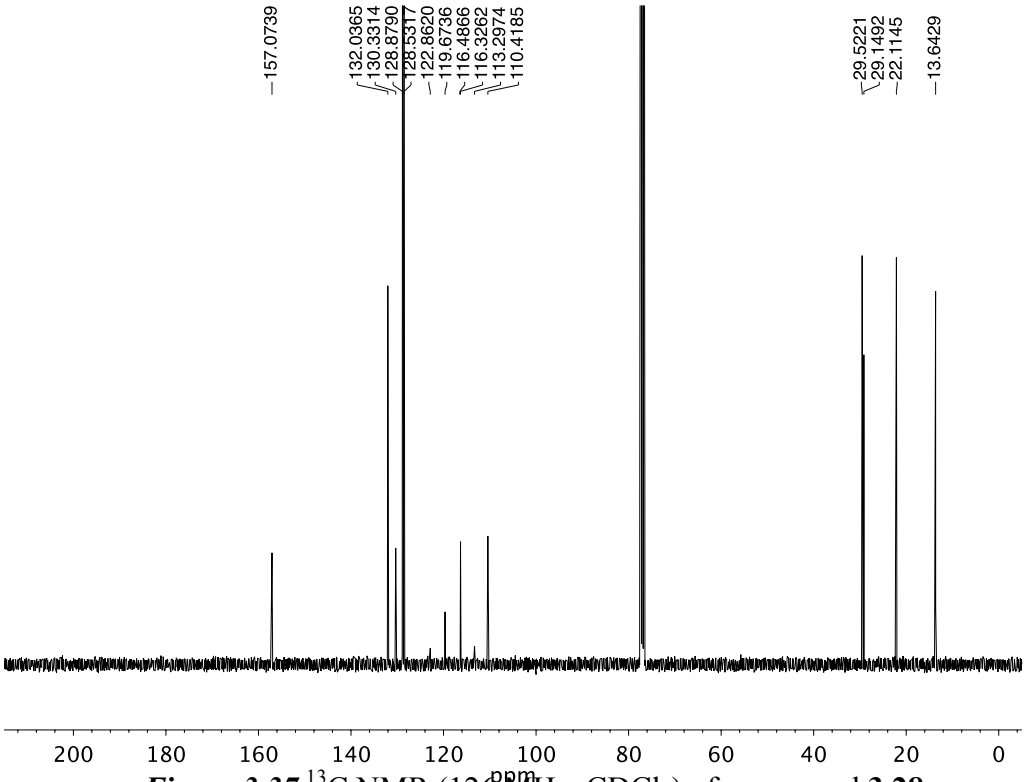

Figure 3.37 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.28**.

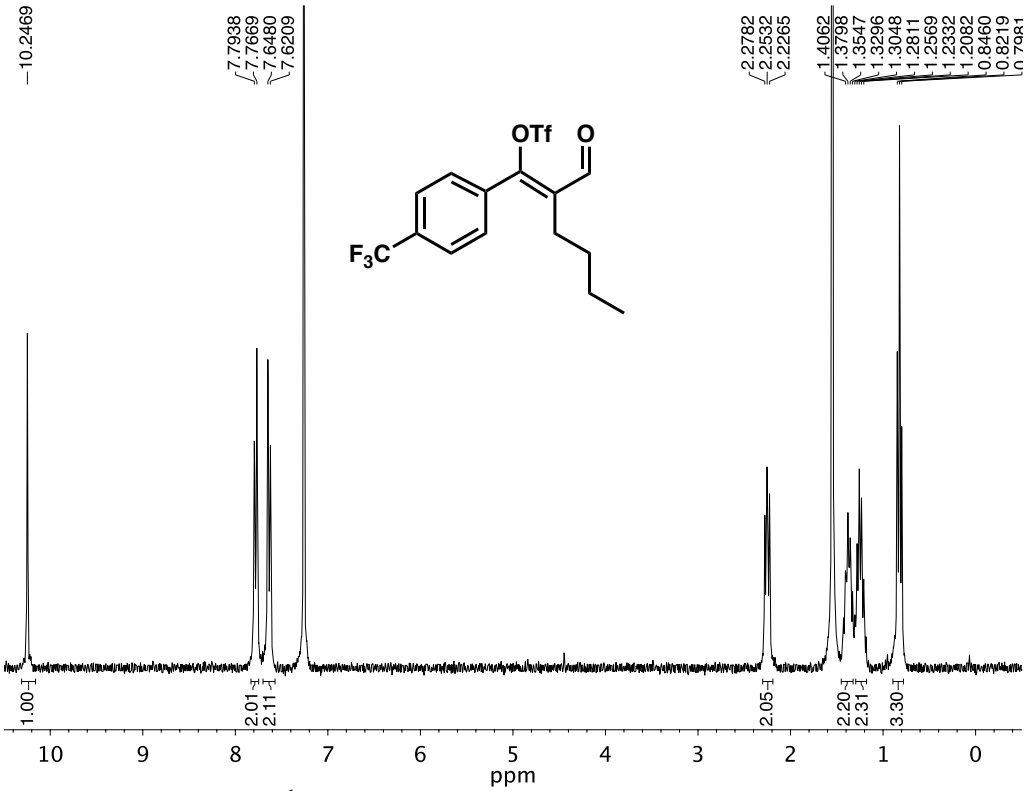

Figure 3.38 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **3.29**.

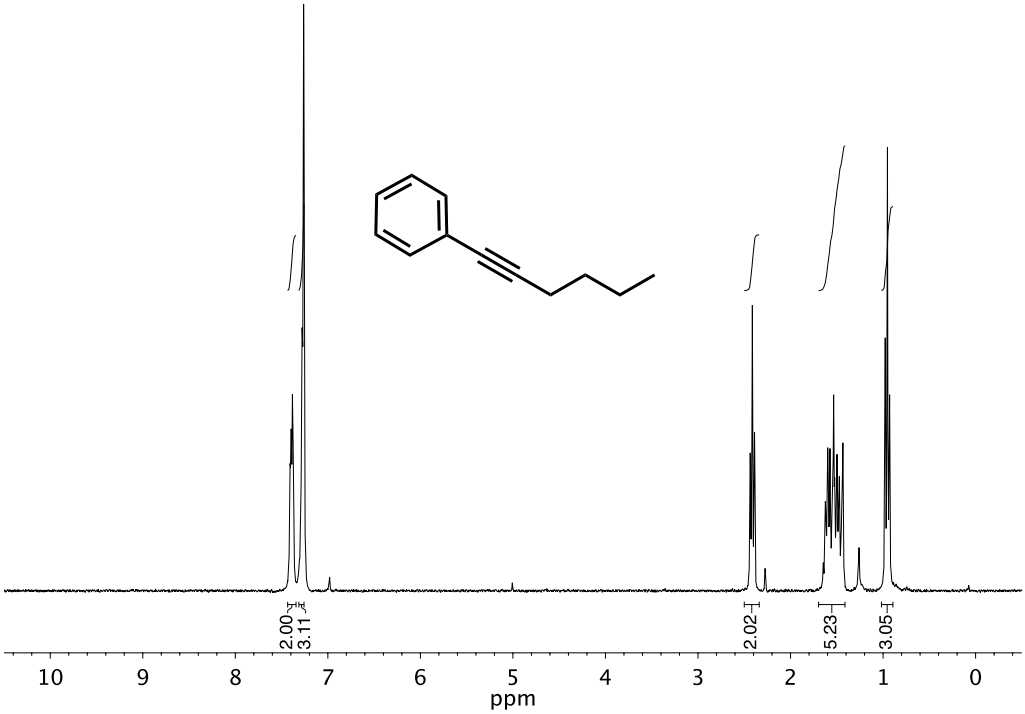

Figure 3.39 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **3.30**.

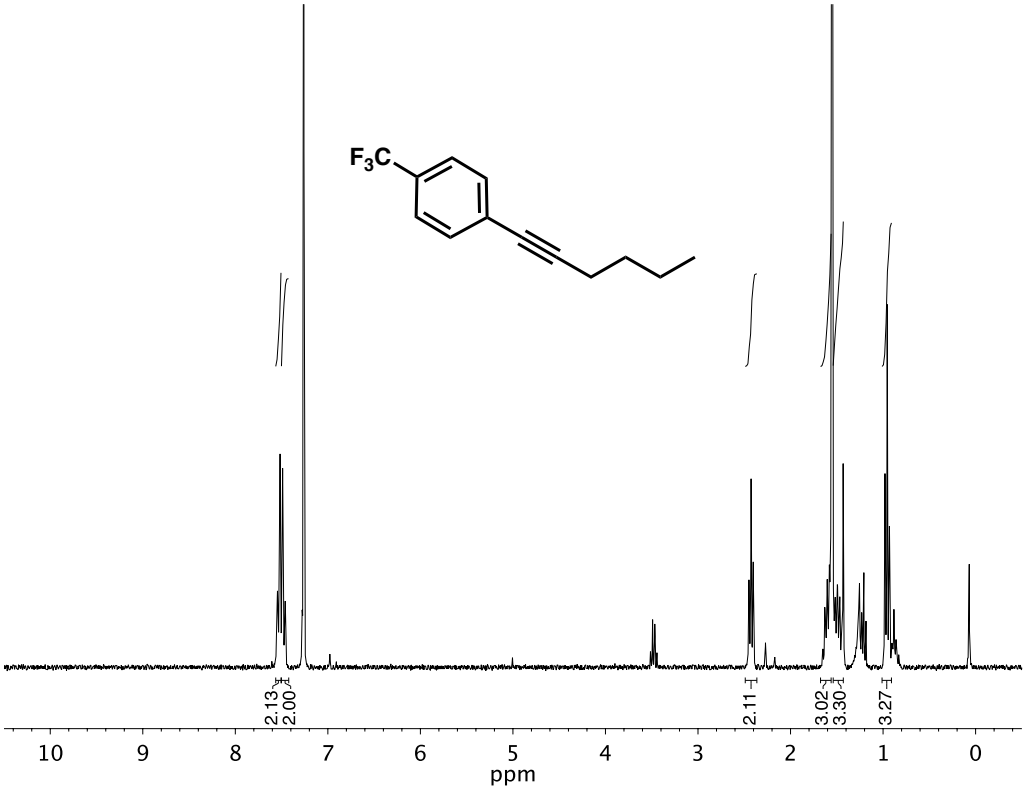

Figure 3.40 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **3.31**.

3.10 Notes and References

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CHAPTER FOUR

Electrochemical Generation of Vinyl Carbocations from Alkenyl Boronates

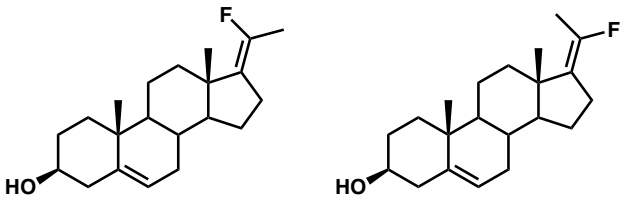
Benjamin Wigman, Woojin Lee, Wenjing Wei, K. N. Houk and Hosea M. Nelson *Angew. Chem. Int. Ed.* **2022**, *61*, e202113972.

4.1 Abstract

Here efforts to generate dicoordinate carbocations without the use of Lewis acids through a single electron oxidation pathway are described. Redox active alkenyl appended substrates were subjected to photochemical, chemical, and electrochemical oxidizing conditions in hopes to generate vinyl carbocations. The electrochemical oxidation of alkenyl boronates was successful, and the ensuing carbocations were trapped with F^-, Cl^-, Br^-, N-Me pyrrole, and one example of a C–H bond. This is the first example of single electron oxidation to gain access to these dicoordinated carbocations. Mechanistic studies are performed to indicate that first a vinyl radical is formed, and a second oxidative event occurs to yield the vinyl carbocation. Notably, these reactions can be performed in Lewis basic acetonitrile solvent and even in the presence of free N–H bonds.

4.2 Introduction

After determining that the lithium Lewis acid conditions could promote C–H insertion to forge new C–C bonds, I became interested in seeing what other nucleophiles could yield value added products. Particularly, I had observed some iodide trapping of vinyl carbocations. With this result I was interested in the possibility of using a nucleophilic fluoride source to generate fluoro olefins; these products have value in medicinal chemistry as they are bioisosteres of the amide bond and act as enol mimics.[1,2] Additionally, since they can be prepared as a single isomer, as opposed to interchanging (E/Z) enols or amides, the drug activity or desired effect can be fine tuned (**1,2** Figure 4.1).



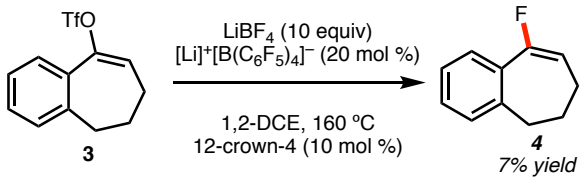
(Z) enol mimic
1
94% inhibition

(E) enol mimic
2
60% inhibition

Figure 4.1 Vinyl fluorides and differing inhibition of cynomolgus monkey testicular $C_{17(20)}$ lyase

4.3 Initial efforts to generate vinyl fluorides

I began to screen fluoride sources with benzosuberonyl triflate **3** to produce the vinyl fluoride **4** (Figure 4.2). I found some success with $LiBF_4$ acting as a fluoride source. However, even at elevated temperatures I was unable to observe even a full catalyst turnover of product, and I found that the lithium-selective 12-crown-4 ether was an essential additive for any reactivity.



3 **4**
7% yield

Figure 4.2 Attempt to gain access to vinyl fluorides, final "optimized" conditions

While the crown ether was likely necessary to solubilize the $LiBF_4$ salt, it was also likely poisoning the catalyst. This issue of finding soluble reagents to use with Lewis acid compatible solvents had been troubling ever since the first attempts to use lithium as an abstraction agent (Chapter 2, Figure 2.8).

4.4 Electrochemical oxidation to generate vinyl carbocations

I figured the only way to get around this issue was to find a new way to generate vinyl carbocations that wouldn't be affected by the usage of polar, Lewis basic solvents. I began to look at redox active groups appended to olefins; particularly I was inspired by the production of alkyl carbocations in methanol dating back to the early 1900's by Hofer and Moest (Figure 4.3).[3,4] This report was also optimized further by Baran and coworkers to yield a broader synthetic method.[5] However, attempts to oxidize both the vinyl carboxylate (**5**) and the redox active ester (in this case a reduction event must precede the oxidation) (**6**) through a variety of means failed to yield any isolable products that indicated the presence of a vinyl carbocation.

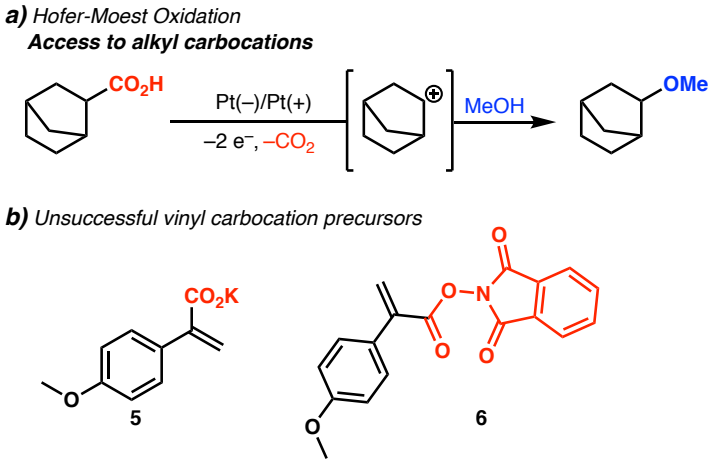
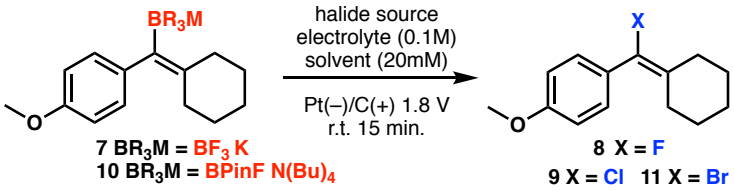


Figure 4.3 (a) Hofer-Moest Oxidation (b) Unsuccessful vinyl carbocation precursors

Inspired by other recent reports to oxidize trifluoroborates I turned my attention to these redox active moieties.[6–10] Electrochemical oxidation (**7** Table 4.1) was rather facile, and one of the first few reactions I tried with this substrate in combination with tetrabutyl ammonium

fluoride (TBAF) ended up yielding the desired vinyl fluoride (**8**) in moderate yield, 42%, however with a substantial amount, ~20%, of the vinyl chloride product (**9**) (Table 4.1, entry 1). This formed likely through the reduction of dichloromethane or reaction of the TBAF with the solvent to produce the chloride anion.[11]



Entry	Starting Material	Solvent	Electrolyte (0.1 M)	Halide Source (equiv)	Yield
1	*7*	*DCM*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*42%*
2	*7*	*THF*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*<5%*
3	*7*	*DMF*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*n.d.*
4	*7*	*MeCN*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*65%*
5	*10*	*MeCN*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*70%*
6	*10*	*MeCN*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (3 equiv)*	*62%*
7	*10*	*MeCN*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (2 equiv)*	*50%*
8	*10*	*MeCN*	*$TBABF_4$*	*$TMAF{\cdot}(H_2O)_4$ (5 equiv)*	*49%*
9	*10*	*MeCN*	*$TBABF_4$*	*$TBAF{\cdot}(tBuOH)_4$ (5 equiv)*	*58%*
10	*10*	*MeCN*	*$TBABF_4$*	*KF+18-Crown-6 (10 equiv)*	*n.d.*
11	*10*	*MeCN*	*$TBABF_4$*	*TBAT (5 equiv)*	*40%*
12	*10*	*MeCN*	*$TBAPF_6$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*54%*
13	*10*	*MeCN*	*$TBABF_4$*	*$TBAF{\cdot}(H_2O)_3$ (5 equiv)*	*19%*
14	*3*	*MeCN*	*$TBABF_4$*	*TBACl (6 equiv)*	*68%*
15	*1*	*MeCN*	*TBABr*	—	*57%*

Table 4.1 Optimization of electrochemical alkenyl boronate fluorination

I found that by utilizing acetonitrile as the solvent and also changing to the pinacol boronic ester (**10**), boronate produced *in situ*, the yield increased to 70% (entry 5). In my experience the electron rich styrenyl trifluoroborates were difficult to handle and must be kept at

cold (–20ºC) temperatures. Even storage at these temperatures gave significant amounts of protodeboronation, which I believe to be the reason for the decrease of yield with **7** compared to the boronate ester (**10**). Additionally the vinyl chloride **9** could be prepared cleanly by utilizing TBACl, and also the vinyl bromide **11** could be produced using TBABr as the electrolyte.

With these results in hand I began to perform preliminary mechanistic studies of this transformation. Very early on I had made substrates **12** and **13** to serve as mechanistic probes. **12** produced the alkyne (**14**), presumably from E1 elimination of the vinyl carbocation (**15**), in 43% yield. Elimination to form alkynes through vinyl carbocation intermediates is well documented in the literature.[12–13] Additionally, when **13** was exposed to the reaction conditions fluoride **16** was produced as a mixture of Z/E isomers in 35% yield and a 6.25:1 ratio (Figure 4.4). This isomerization of the pure starting olefin gives evidence for a linear vinyl carbocation intermediate.

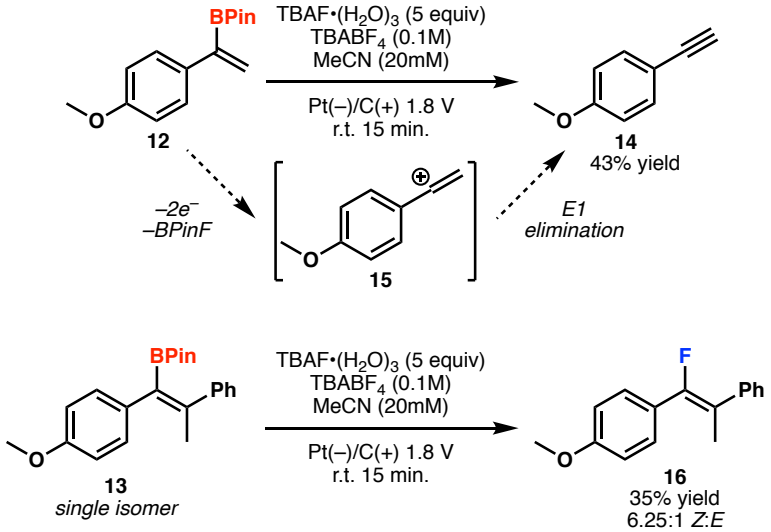


Figure 4.4 Initial mechanistic probe substrates yielding vinyl carbocation-like reactivity

With these two mechanistic substrates yielding vinyl carbocation-like reactivity I decided to explore the scope of this transformation (Figure 4.5). Initially I focused on electron rich arenes as these likely would stabilize a vinyl carbocation intermediate. Strongly electron-donating

substituents produced vinyl fluorides **17–19** in 50–82% yield. Vinyl fluoride **7** was also isolated in good yield utilizing only three equivalents of TBAF on 1 mmol scale. Alkenyl boronic esters bearing *meta* substituents and an *ortho* or *para* donor were also tolerated, yielding vinyl fluorides **20** and **21** in 59% and 47% yield respectively. Additionally, novel fluoro-analogue **23** of chlorotrianisene, a nonsteroidal estrogen[14], was generated in 60% yield. Other appended ring sizes and alkyl chains also led to production of the vinyl fluoride (**24–27**). Constant voltage conditions at a lower +0.8 V *vs* SCE were key to produce electron–rich aniline fluoride product **27.**

Less electron-donating substituents were tolerated, but led to incomplete conversion even at higher applied potentials (**30**). Notably, these N–H containing compounds are not tolerated under routine Lewis acid promoted vinyl carbocation formation, but are commonly seen in natural products and drug molecules.[15] The boronic ester bearing a simple phenyl ring did not lead to formation of vinyl fluoride **31**, even under forcing conditions.

Throughout these studies I observed that only electron-rich arenes were competent in this transformation. Yields increased with decreasing Hammet σ_p parameter, suggesting that there was a carbocation formed at the carbon once bearing the boronic ester. The trend of decreasing yield, **17**>**24**>**28**>**30**, with corresponding σ_p values of $-0.81<-0.27<-0.17<0.00$ for the respective *para* donor substituents, was observed.[16] Additionally, if a *meta*-methoxy group were present on the arene, an electron-*withdrawing* substituent with $\sigma_m=+0.12$, **32** was not formed.[16] This trend suggested the formation of a carbocation intermediate, and so I decided to carry out more rigorous mechanistic studies to investigate the intermediacy of a vinyl carbocation.

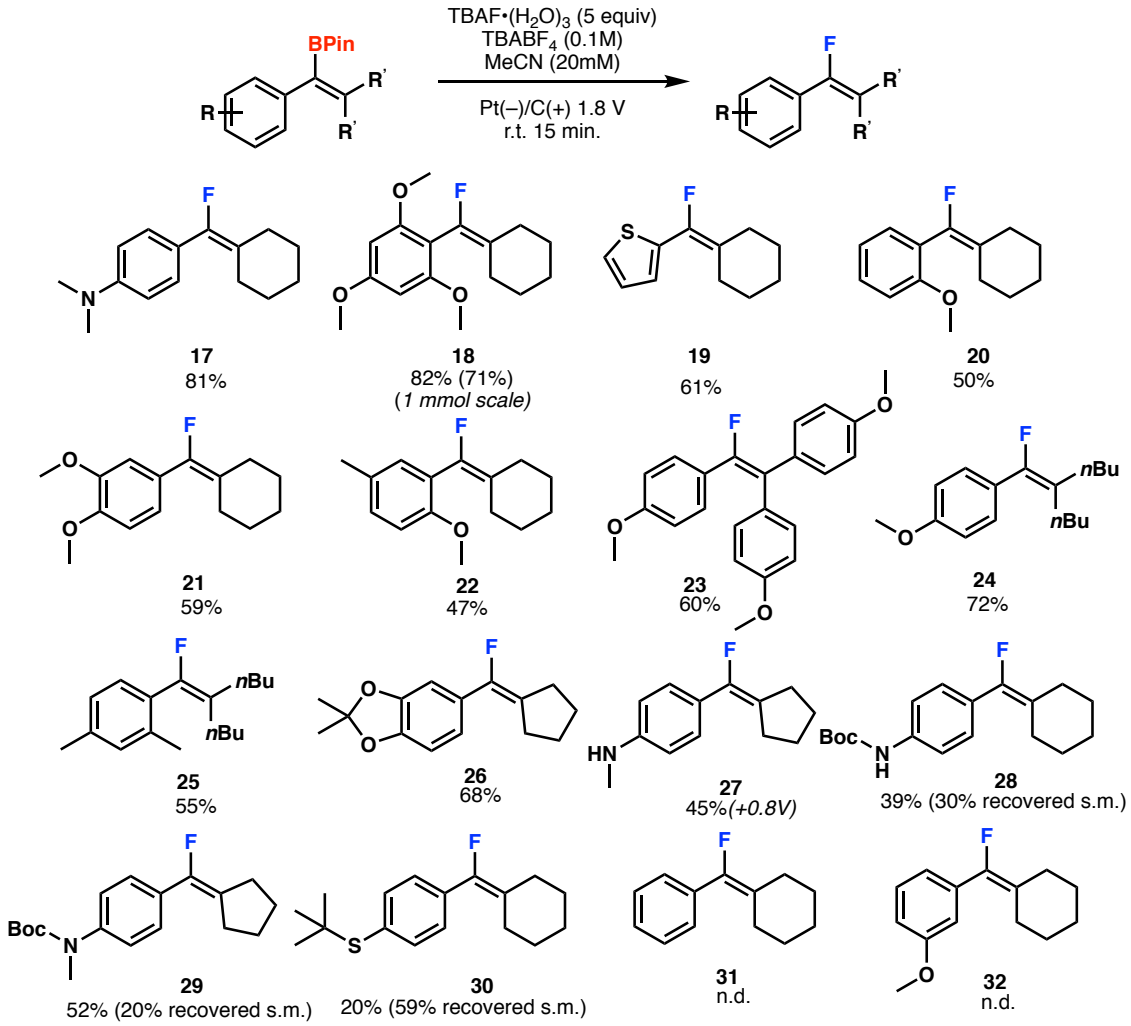


Figure 4.5 Substrate scope for electrochemical fluorination of alkenyl boronates

4.5 Mechanistic Studies

First, other common vinyl carbocation reactivity was tested. Aside from previously described elimination, a variety of methods report arylation[17] with electron rich arenes and also C–H insertion reactions to forge C–C bonds.[18] In this case, to avoid nucleophilic attack by fluoride I prepared the activated trifluoroborate salts to test if this reactivity was observed. First **7** was subjected to the reaction conditions, but with N-Me pyrrole as a nucleophile in place of TBAF. The pyrrole adduct (**33**) was observed in 48% yield in a 2.7:1 ratio (Figure 4.5). Notably,

the selectivity, or rather the lack of it, is highly indicative of a reactive vinyl carbocation being quenched. A similar study with proposed reactive vinyl carbocations being generated from triazines gave a ratio of 2.3:1.[19] Furthermore, if this reaction were proceeding through a vinyl radical likely only the 2-position of the N-Me pyrrole would react, as aryl and vinyl radical additions to pyrroles are highly selective for this position.[20]

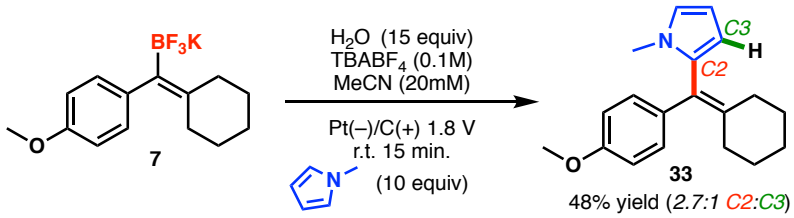


Figure 4.6 Cationic regioselectivity shown in Friedel-Crafts reaction with N-Me pyrrole

Next 2,4-dimethyl substituted vinyl trifluoroborate **34** was prepared to see if an electrochemical promoted C–H insertion could occur. This salt was particularly troublesome to handle, and subsequent reactions needed to be performed within a few hours of preparation of the trifluoroborate salt to avoid significant amounts of protodeboronation. A 5.5:1 ratio (determined by GC-FID) of the cyclopentene products **35** were produced in a meager 12 % yield after divided cell electrolysis of **34** (Figure 4.6). Here a large amount of side product observed was the styrene, however, subjecting this styrene to the previous reaction conditions did not produce any of the desired cyclopentene. It was also demonstrated that the BF_3 likely generated by the electrochemical oxidation was not promoting the reaction by halting electrolysis and determining that product formation had ceased.

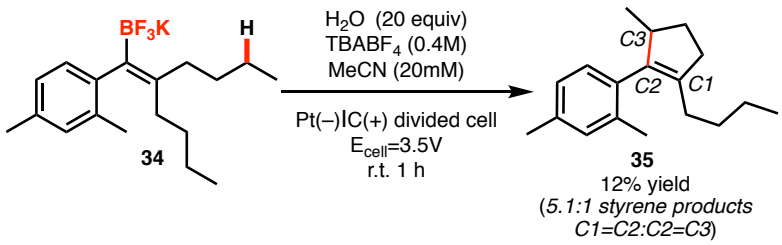


Figure 4.7 Demonstration of C–H functionalization reactivity, giving evidence for vinyl carbocation

With reactivity indicating that a vinyl carbocation was likely being formed under these electrochemical conditions, I decided to perform other electrochemical experiments, namely cyclic voltammetry and bulk electrolysis coulometry, to gain insight into the mechanism of formation of this carbocation. First, bulk electrolysis coulometry of the fluorination of **18** showed a 73% Faradaic efficiency for a 2 electron oxidation. Further evidence for this process was indicated in the cyclic voltammogram of **7** (Figure 4.7).

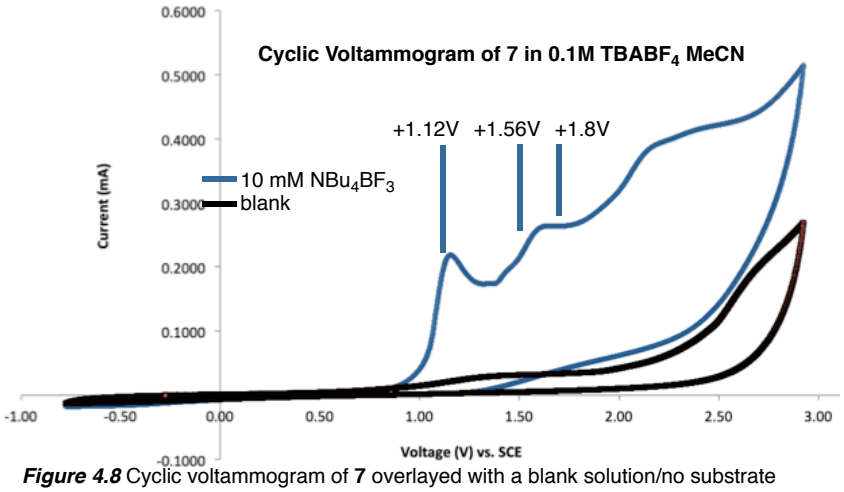


Figure 4.8 Cyclic voltammogram of **7** overlayed with a blank solution/no substrate

Two oxidative currents were observed before reaching the working voltage (+1.8 V *vs* SCE). My hypothesis here was that the initial oxidation (~+1.1 V) produces a vinyl radical and the second oxidation (~+1.5V) produces the vinyl carbocation, and if this was the case controlling the potential applied should be able to control the intermediate that is formed.

To test this hypothesis I tried two radical trapping reagents. First I added a deuterated thiol into the solution, as thiols are known to rapidly undergo HAT reactions.[21] In this case I observed a large amount of the styrene product **36** (Figure 4.8). While the deuterium incorporation was only 25%, the starting thiol had only been 77% deuterium incorporated and importantly deuteration was observed specifically at the styrene position.

Additionally I thought that a lower voltage could change the selectivity for the arylation with N-Me pyrrole. Applying a lower voltage of +1.1 V *vs* SCE to **7** in the presence of N-Me pyrrole now yielded **33,** but exclusively with arylation at the 2 position; albeit in low yield with large amounts of styrene formation (Figure 4.8). This change in regioselectivity of addition suggested that a different radical mechanism was at play at this lower applied potential. Finally, no fluorination products were observed at this potential, indicating that a vinyl carbocation was not formed.

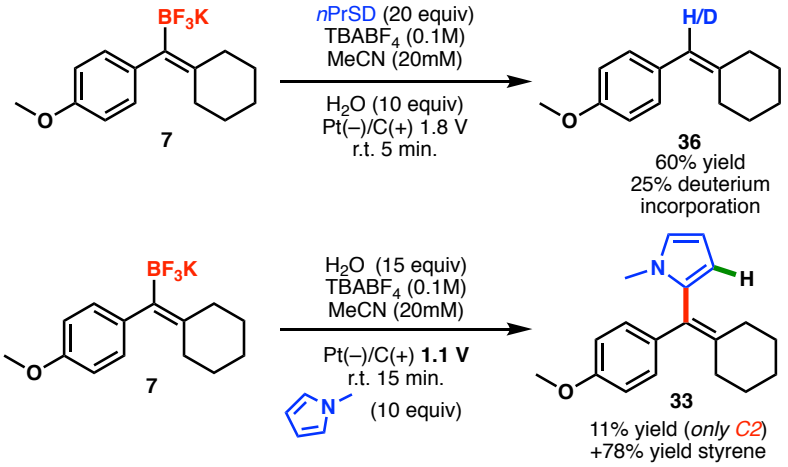


Figure 4.9 Trapping experiments to provide evidence for vinyl radical production

With the production of first a vinyl radical and subsequently a vinyl carbocation evidenced by these experiments, a full proposed mechanism could be formed. However, one question remained unanswered, what part of the trifluoroborate is oxidized first? This question was difficult to address from chemical intuition, as electron rich styrenes are readily oxidizable as are alkyl trifluoroborates. With the help of computations, a HOMO for **7** was calculated and DFT was utilized to predict an initial oxidation (Figure 4.9). The styrene was predicted to be the most easily oxidizable portion of the HOMO yielding the delocalized radical cation **37** in good agreement with the observed oxidation potential (+1.12 V experimental, +1.04 V calculated). This is then proposed to eliminate BF_3, or BPin–F that was detected by ^{19}F and ^{11}B NMR in the

reaction mixture when utilizing the alkenyl boronates, to give a vinyl radical (**38**). This can then finally be oxidized a second time to yield the vinyl carbocation (**39**) that is subsequently trapped by fluoride in solution.

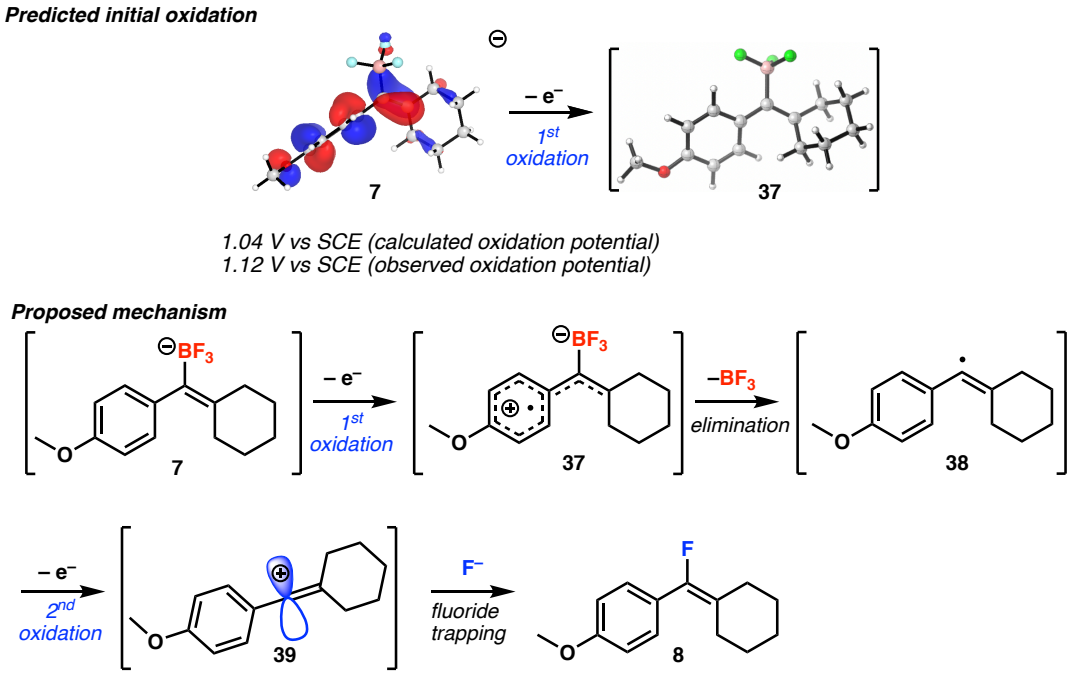


Figure 4.10 Proposed mechanism of boronate oxidation and fluorination, Calculated HOMO and oxidation potential using (uM06-2X/6-311++G(d,p) cpcm=acetonitrile // uM06-2X/6-31+G(d,p) cpcm=acetonitrile)

4.6 Conclusion

Initial efforts to produce vinyl fluorides using lithium Lewis acid conditions were unsuccessful primarily due to solubility of the nucleophilic fluoride reagents. In an attempt to gain access to a wider array of reagents and solvents, I decided to investigate the production of vinyl carbocations in a Lewis acid-free fashion. Electron rich alkenyl boronates were oxidized electrochemically to yield vinyl fluorides in moderate to good yield. Notably, nucleophilic fluoride sources could be used as opposed to the more hazardous electrophilic fluorination reagents. Mechanistic studies were performed to provide evidence for the intermediacy of a vinyl carbocation; in the process new C–C, C–Br, and C–Cl bonds were forged in addition to the initially sought after C–F bond. Overall, this work describes a novel means to generate reactive

vinyl carbocations utilizing an electric potential, and provides hope that other highly reactive dicoordinate carboctaions can be generated in a similar fashion to avoid the pitfalls of current methodologies.

4.7 Experimental Section

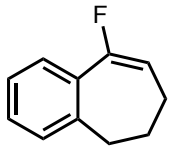
4.7.1 Materials and Methods

All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and allowed to cool *in vacuo* or a desiccator before use. Acetonitrile was freshly distilled over CaH_2 before use. Benzene, dichloromethane, tetrahydrofuran, dimethylformamide, and toluene were degassed and dried in a JC Meyer solvent system. TBAF•$(H_2O)_3$ was purchased from Acros Organics and stored in a Drierite desiccator purged with nitrogen. $TBABF_4$ was purchased from Oakwood chemical and dried over P_2O_5 *in vacuo* before use. Thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. NMR spectra were recorded on a Bruker AV-300 (^1H, ^{19}F), Bruker AV-400 (^1H, ^{13}C, ^{19}F), Bruker DRX-500 (^1H), and Bruker AV-500 (^1H, ^{13}C). ^1H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^1H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted otherwise. GCMS spectra were recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 mm DF) column interface at room temperature. IR Spectra were record on a Perkin Elmer 100 spectrometer and are reported in terms of frequency absorption (cm^{-1}). High resolution mass spectra (HR-MS)

were recorded on a Waters (Micromass) GCT Premier spectrometer, a Waters (Micromass) LCT Premier, or an Agilent GC EI-MS, and are reported as follows: m/z (% relative intensity).

General Procedures

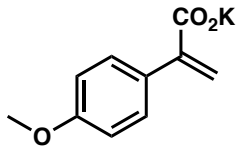
4.7.2 Initial attempts to synthesize benzosuberonyl fluoride 4:



9-fluoro-6,7-dihydro-5*H*-benzo[7]annulene (4.4)

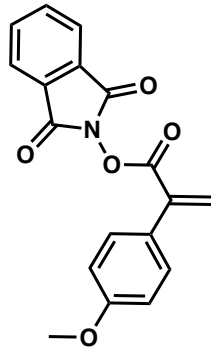
To a dram vial equipped with a stir bar was added Lithium tetrakis(pentafluorophenyl)borate (2.3 mg, 0.2 equiv, 0.01 mmol), $LiBF_4$ (47 mg, 10 equiv, 0.5 mmol), and 1,2-dichloroethane (0.5 mL). To this was added the 12-crown-4 ether (0.88 mg, 0.1 equiv, 0.005 mmol) and the benzosuberonyl triflate (15 mg, 1 equiv, 0.05 mmol). This solution was heated to 160ºC for 18 hours, then plugged through silica gel, concentrated and ^{1}H NMR analysis showed 7% yield of **4**. This material matched the reported spectrum from an authentic sample prepared in our lab as a 85% pure mixture with the styrene.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (dd, J = 7.1, 2.0 Hz, 1H), 7.24 (ddd, J = 6.9, 5.2, 1.8 Hz, 2H), 7.15 (q, J = 2.3, 1.4 Hz, 2H), 5.77 (t, J = 5.0 Hz, 1H), 5.72 (t, J = 5.0 Hz, 1H), 2.84 – 2.78 (m, 2H), 2.32 (tt, J = 6.7, 4.7 Hz, 2H), 1.98 – 1.82 (m, 2H).



potassium 2-(4-methoxyphenyl)acrylate (4.5)

4.5 was prepared according to known procedures, and matched the reported 1H NMR spectral data.[22]

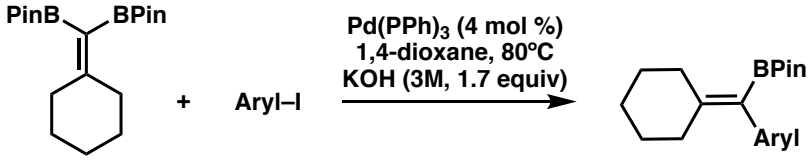


1,3-dioxoisoindolin-2-yl 2-(4-methoxyphenyl)acrylate. (4.6)
(**4.6**) was prepared according to known procedures, and matched the reported ^{1}H NMR spectral data.[23]

4.7.3 Preparation of Alkenyl Boronate Starting Materials

Note: The cross-couplings performed to synthesize the substrates are not optimized.

Cross-Coupling Condition A:

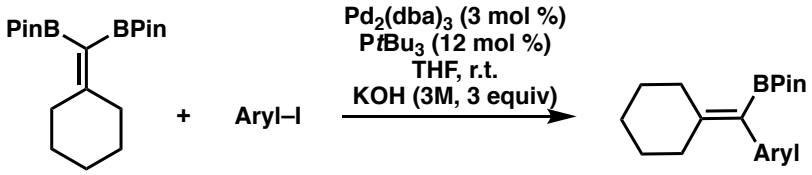


Condition A Scheme

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1 equiv), aryl iodide (1 equiv), 1,4-dioxane (0.15 M), and the aqueous KOH solution (3 molar, 1.7 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tetrakis(triphenylphosphine)palladium(0) (4 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was heated to 80 ºC for 12 hours. The solution was cooled to room temperature and quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organics were dried

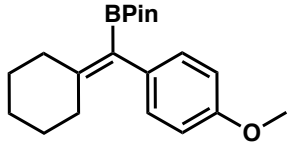
over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

Cross-Coupling Condition B:



Condition B Scheme

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1 equiv), aryl iodide (1 equiv), tetrahydrofuran (0.15 M), and the aqueous KOH solution (3 molar, 1.7 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature. The reaction was monitored carefully by TLC. The solution was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography.



2-(cyclohexylidene(4-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (5.10)
Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (750 mg, 2.15 mmol, 1 equiv), 4-iodoanisole (504 mg, 2.15 mmol, 1 equiv), tetrahydrofuran (12 mL), and the aqueous KOH solution (2.15 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (59 mg, 0.06 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (52 mg, 0.26 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature. The reaction was monitored carefully by TLC (~3 hours). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 12 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (35% dichloromethane in hexanes) to yield 463 mg of **5.10** an off-white solid (66% yield).

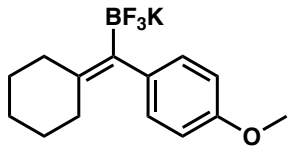
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H), 2.78 – 2.24 (m, 2H), 2.23 – 2.04 (m, 2H), 1.71 – 1.42 (m, 6H), 1.25 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 154.6, 134.7, 130.3, 113.5, 83.4, 55.4, 35.7, 32.1, 29.1, 28.7, 27.0, 24.9. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 31.6.

FT-IR (neat film NaCl): 2976, 2926, 2852, 2835, 1606, 1507, 1464, 1354, 1238, 1104, 1006, 925, 856 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{20}H_{29}BO_3$: 328.2209; Measured: 328.2213.



(cyclohexylidene(4-methoxyphenyl)methyl)trifluoro-λ^4-borane, potassium salt. (5.7)

To 25 mL round bottom flask with a stir bar was added 2-(cyclohexylidene(4-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (286 mg, 0.87 mmol, 1 equiv). This was dissolved in a mixture of methanol/water (7.1mL methanol:1.0 mL water). Diethyl ether was added to the solution until it was homogeneous (~1 mL). To this stirring solution was added KHF_2 (340 mg, 4.35 mmol, 5 equiv). The solution was stirred vigorously and monitored by TLC. Once the starting pinacol boronic ester had been consumed (~25 minutes) the solution was stirred an additional 15 minutes. The solution was concentrated *in vacuo*. The remaining solid was dissolved in hot acetone (~15 mL) and filtered. The filtrate was concentrated *in vacuo*. The resulting off-white solid was washed with cold hexanes (15 mL), cold diethyl ether (5 mL), and finally cold hexanes (10 mL). The white solid remaining white solid was dried *in vacuo* to give the (**5.7**) as a white powder (180 mg, 67% yield). *Note:*This solid should be stored in a freezer for long term storage.

^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 6.91 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.6 Hz, 2H), 3.75 (s, 3H), 2.54 (t, *J* = 5.8 Hz, 2H), 1.91 (t, *J* = 6.0 Hz, 2H), 1.64 – 1.48 (m, 4H), 1.42 (q, *J* = 6.0 Hz, 2H).

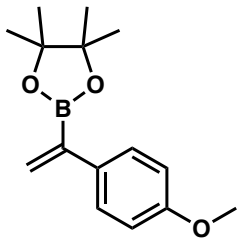
^{13}C NMR (126 MHz, $(CD_3)_2CO$) δ 157.6, 143.3, 141.3, 131.2, 116.6, 113.5, 55.9, 34.8, 34.1, 29.0, 26.0, 25.9. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $(CD_3)_2CO$) δ 3.89 – 2.43 (m).

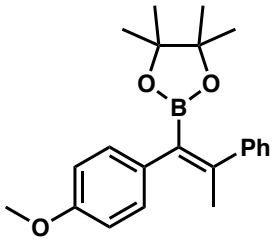
^{19}F NMR (282 MHz, $(CD_3)_2CO$) δ -133.6 – 133.5 (m).

FT-IR (neat film NaCl): 2921, 2849, 1603, 1505, 1276, 1236, 1177, 1135, 1119, 1079, 975, 830, 797 cm^{-1}.

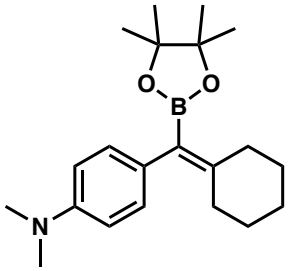
HR-MS (ESI): Calculated for $[M]^-$ $C_{14}H_{17}BF_3O$: 269.1324; Measured: 269.1320.



2-(1-(4-methoxyphenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (5.12)
(**5.12**) was prepared according to known procedures, and matched the reported 1H NMR spectral data.[24]



(*E*)-2-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.13) was prepared according to known procedures, and matched the reported 1H NMR spectral data.



4-(cyclohexylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-*N*,*N*-dimethylaniline. (4.17s)

Synthesized according to condition A.

To a schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (700 mg, 2.0 mmol, 1 equiv), 4-iodo-N,N-dimethylaniline (497 mg, 2.0 mmol, 1 equiv), 1,4-dioxane (14 mL, 0.15 M), and the aqueous KOH solution (1.2 mL, 3 molar, 1.7

equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tetrakis(triphenylphosphine)palladium(0) (93.0 mg, 0.08 mmol, 4 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was heated to 90 ºC for 12 hours. The solution was cooled to room temperature and quenched with saturated aqueous NH_4Cl (14 mL) and extracted with ethyl acetate (3 x 14 mL) The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (70% dichloromethane in hexanes) to yield the 120 mg of **4.17s** (20% yield) of an off-white solid.

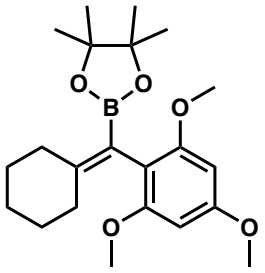
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 – 6.82 (m, 2H), 6.69 (bs, 2H), 2.94 (s, 3H), 2.45 (t, J = 6.0 Hz, 2H), 2.17 (d, J = 6.5 Hz, 2H), 1.65 – 1.46 (m, 6H), 1.25 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 148.6, 130.1, 112.5, 83.3, 41.0, 35.9, 32.0, 29.1, 28.7, 27.1, 25.0. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (161 MHz, $CDCl_3$) δ 29.85.

FT-IR (neat film NaCl): 2978, 2929, 2851, 1610, 1517, 1446, 1348, 1328, 1298, 1223, 1142, 973, 856 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{21}H_{32}BNO_2$: 341.2526; Measured: 341.2530.



2-(cyclohexylidene(2,4,6-trimethoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.18S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (235 mg, 0.675 mmol, 1 equiv), 2-iodo-1,3,5-trimethoxybenzene (199 mg, 0.675 mmol, 1 equiv), tetrahydrofuran (5 mL), and the aqueous KOH solution (0.68 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (19 mg, 0.02 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (17 mg, 0.08 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature. The reaction was monitored carefully by TLC (~3 hours). The solution was quenched with saturated aqueous NH_4Cl (5 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (7→12% ethyl acetate in hexanes) to yield 193 mg of (**4.18S**) as a white solid (73% yield).

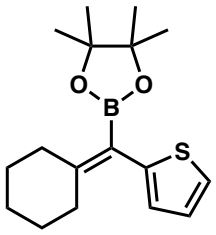
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (s, 2H), 3.80 (s, 3H), 3.73 (s, 6H), 2.83 – 2.34 (m, 2H), 1.92 (t, J = 5.7 Hz, 2H), 1.65 – 1.50 (m, 6H), 1.22 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 158.3, 157.9, 113.2, 91.1, 82.8, 56.0, 55.5, 34.9, 33.9, 29.0, 27.8, 27.2, 25.1. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.03.

FT-IR (neat film NaCl): 2975, 2928, 2851, 1603, 1583, 1464, 1353, 1326, 1223, 1124, 953 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{22}H_{33}BO_5$: 388.2421; Measured: 388.2425.



2-(cyclohexylidene(thiophen-2-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.19S)

Synthesized according to condition A.

To a schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (600 mg, 1.7 mmol, 1 equiv), 2-bromo-thiophene (280 mg, 1.7 mmol, 1 equiv), 1,4-dioxane (11 mL, 0.15 M), and the aqueous KOH solution (1.0 mL, 3 molar, 1.7 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tetrakis(triphenylphosphine)palladium(0) (100 mg, 0.09 mmol, 5 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was heated to 90 ºC for 20 hours. The solution was cooled to room temperature and quenched with saturated aqueous NH_4Cl (11 mL) and extracted with ethyl acetate (3 x 12 mL) The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (5% diethyl ether in hexanes) to yield (**4.19S**) 63 mg (12% yield) of a white solid.

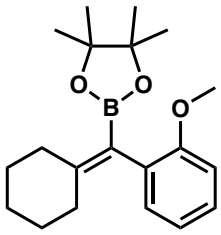
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 1H), 6.95 (dd, J = 5.2, 3.5 Hz, 1H), 6.71 (d, J = 3.5 Hz, 1H), 2.48 (t, J = 6.2 Hz, 2H), 2.32 (t, J = 5.8 Hz, 2H), 1.69 – 1.56 (m, 6H), 1.27 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3, 143.9, 127.0, 125.6, 124.1, 83.8, 35.9, 32.6, 29.1, 28.7, 26.9, 25.0. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $CDCl_3$) δ 31.27.

FT-IR (neat film NaCl): 2977, 2926, 2853, 1608, 1446, 1354, 1300, 1144, 995, 854, 699 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{17}H_{25}BO_2S$: 304.1668; Measured: 304.1663.



2-(cyclohexylidene(2-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.20S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (500 mg, 1.44 mmol, 1 equiv), 1-iodo-2-methoxybenzene (336 mg, 1.44 mmol, 1 equiv), tetrahydrofuran (8 mL), and the aqueous KOH solution (1.44 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (40 mg, 0.04 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (35 mg, 0.17 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature. The reaction was monitored carefully by TLC (~3 hours). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (50% dichloromethane in hexanes) to yield (**4.20S**) 394 mg of an off-white solid (83% yield).

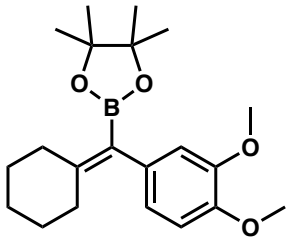
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (ddd, *J* = 8.2, 7.4, 1.8 Hz, 1H), 7.03 (dd, *J* = 7.4, 1.8 Hz, 1H), 6.89 (td, *J* = 7.4, 1.1 Hz, 1H), 6.82 (dd, *J* = 8.1, 1.1 Hz, 1H), 3.76 (s, 3H), 2.60 (t, *J* = 6.0 Hz, 2H), 2.13 (bs, 2H), 1.67 – 1.42 (m, 6H), 1.24 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 156.5, 131.9, 127.2, 120.4, 110.3, 83.2, 55.5, 35.4, 33.0, 29.2, 28.9, 27.1, 25.0. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.29.

FT-IR (neat film NaCl): 2976, 2925, 2852, 1616, 1487, 1354, 1297, 1241, 1146, 972, 857, 750 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{20}H_{39}BO_3$: 328.2209; Measured: 328.2213.



2-(cyclohexylidene(3,4-dimethoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.21S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (400 mg, 1.15 mmol, 1 equiv), 4-iodo-1,2-dimethoxybenzene (316 mg, 1.15 mmol, 1 equiv), tetrahydrofuran (7 mL), and the aqueous KOH solution (1.2 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (33 mg, 0.03 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (29 mg, 0.14 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three

times. The solution was allowed to thaw and stirred at room temperature (24 h). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (15→20% diethyl ether in hexanes) to yield **4.21S** 70 mg of a yellow solid (16% yield).

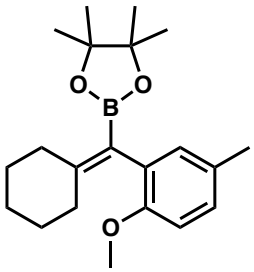
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 – 6.72 (m, 1H), 6.64 (d, *J* = 7.5 Hz, 3H), 3.86 (s, 3H), 3.84 (s, 3H), 2.59 – 2.37 (m, 2H), 2.27 – 2.09 (m, 2H), 1.72 – 1.46 (m, 6H), 1.26 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6, 148.5, 147.0, 135.0, 121.3, 112.7, 111.0, 83.5, 56.1, 56.0, 35.9, 32.3, 29.1, 28.8, 27.0, 25.0. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.10.

FT-IR (neat film NaCl): 2975, 2925, 2852, 1603, 1510, 1463, 1445, 1352, 1296, 1249, 1142, 1030, 858 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{21}H_{31}BO_4$: 358.2315; Measured: 358.2319.



2-(cyclohexylidene(2-methoxy-5-methylphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.22S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (400 mg, 1.15 mmol, 1 equiv), 2-iodo-1-methoxy-4-methylbenzene (285 mg, 1.15 mmol, 1 equiv), tetrahydrofuran (7 mL), and the aqueous KOH solution (1.2 mL, 3 molar,

3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (32 mg, 0.03 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (28 mg, 0.14 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature. The reaction was monitored carefully by TLC (~1 h). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (30→40% diethyl ether in hexanes) to yield (**4.22S**) 378 mg of a brown solid (96% yield).

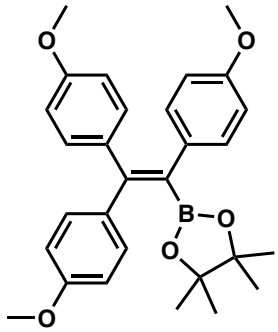
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.85 (bs, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 3.72 (s, 3H), 2.59 (bs, 2H), 2.25 (bs, 3H), 2.15 (s, 3H), 1.67 – 1.52 (m, 6H), 1.24 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 155.2, 132.1, 131.5, 129.3, 127.6, 110.3, 83.2, 55.7, 35.5, 33.0, 29.2, 28.9, 27.1, 25.0, 21.0. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.81.

FT-IR (neat film NaCl): 2976, 2924, 2852, 1617, 1495, 1447, 1350, 1297, 1146, 1036, 856, 801 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{21}H_{31}BO_3$: 342.2366; Measured: 342.2370.



4,4,5,5-tetramethyl-2-(1,2,2-tris(4-methoxyphenyl)vinyl)-1,3,2-dioxaborolane. (4.23S)

(**4.23S**) was prepared by Miyaura-borylation.

To a flame dried schlenk flask with a stir bar was added 4,4',4''-(2-bromoethene-1,1,2-triyl)tris(methoxybenzene) (300 mg, 0.70 mmol, 1 equiv), potassium phenolate (140 mg, 1.05 mmol, 1.5 equiv), 4,4,4',4'5,5,5',5'-octamethyl-2,2'bi(1,3,2-dioxaborolane) (197 mg, 0.775 mmol, 1.1 equiv) and triphenylphosphine (11.1 mg, 0.04 mmol, 6 mol %). To this was added dry toluene (5 mL). The solution was freeze pump-thawed three cycles of 15 minutes. To the frozen solution was added bis(triphenylphosphine)palladium chloride (15 mg, 0.02 mmol, 3 mol %), and the flask was evacuated and back filled with nitrogen three times. The solution was thawed and heated to 70 ºC (1.5 h). The solution was diluted with diethyl ether (10 mL) and quenched with satd. Aqueous NH_4Cl (10 mL). The aqueous solution was extracted with diethyl ether (3 x 15 mL), and the organic layer was dried over Na_2SO_4. The organic solution was filtered and concentrated *in vacuo*. The crude yellow material was purified flash column chromatography (18% diethyl ether in hexanes) to yield 260 mg of a yellow solid (78% yield) (**4.23S**).

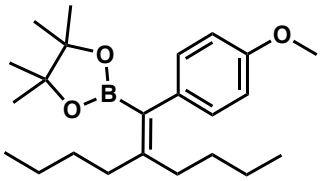
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.7 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.7 Hz, 2H), 6.68 (d, J = 8.8 Hz, 2H), 6.62 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.74 (s, 3H), 3.73 (s, 3H), 1.14 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 158.5, 157.8, 150.3, 138.2, 135.0, 135.1, 132.7, 131.3, 130.9, 113.8, 113.5, 113.2, 83.8, 55.6, 55.4, 55.4, 24.9.*Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 29.93.

FT-IR (neat film NaCl): 2977, 2930, 2885, 1605, 1508, 1346, 1292, 1244, 1173, 1140, 1034, 852, 832 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{29}H_{33}BO_5$: 427.2421; Measured: 427.2426.



2-(2-butyl-1-(4-methoxyphenyl)hex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.24S)

Synthesized according to condition B.

To a schlenk flask was added 2,2'-(2-butylhex-1-ene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (400 mg, 1.02 mmol, 1 equiv), 1-iodo-4-methoxybenzene (239 mg, 1.02 mmol, 1 equiv), tetrahydrofuran (7 mL), and the aqueous KOH solution (1.0 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (46 mg, 0.05 mmol, 5 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (41 mg, 0.20 mmol, 20 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature (18 h). The solution was

quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (10→50% dichloromethane in hexanes) to yield 267 mg of a brown oil (**4.24S**) (70% yield).

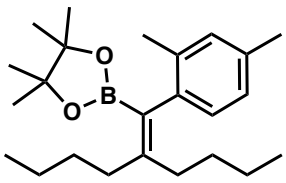
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 2.47 – 2.23 (m, 2H), 2.10 – 1.81 (m, 2H), 1.50 – 1.26 (m, 6H), 1.21 (s, 12H), 1.13 (d, *J* = 7.0 Hz, 2H), 0.94 (t, *J* = 7.1 Hz, 3H), 0.77 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 155.7, 135.3, 130.1, 113.5, 83.3, 55.4, 35.4, 32.5, 32.3, 31.0, 25.0, 23.4, 23.2, 14.4, 14.2. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 29.12.

FT-IR (neat film NaCl): 2957, 2930, 2860, 1602, 1508, 1465, 1352, 1282, 1242, 1173, 1145, 1116, 1036, 973, 857, 829 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{23}H_{37}BO_3$: 372.2835; Measured: 378.2840.



2-(2-butyl-1-(2,4-dimethylphenyl)hex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.25S)

Synthesized according to condition B. To a schlenk flask was added 2,2'-(2-butylhex-1-ene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (400 mg, 1.02 mmol, 1 equiv), 1-iodo-2,4-dimethylbenzene (237 mg, 1.02 mmol, 1 equiv), tetrahydrofuran (7 mL), and the aqueous KOH solution (1.0 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (46 mg, 0.05 mmol, 5 mol %) was added to

the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (41 mg, 0.20 mmol, 20 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature (4 h). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (10→80% dichloromethane in hexanes) to yield **4.24S**, 314 mg of a brown oil (83% yield).

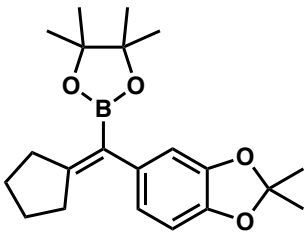
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (s, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 2.49 (d, *J* = 7.9 Hz, 1H), 2.40 (d, *J* = 7.6 Hz, 1H), 2.29 (s, 3H), 2.10 (s, 3H), 1.97 – 1.64 (m, 2H), 1.47 (p, *J* = 7.4 Hz, 2H), 1.39 (p, *J* = 7.1 Hz, 2H), 1.20 (s, 12H), 1.14 – 1.02 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H), 0.72 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 139.9, 135.6, 134.9, 130.4, 129.3, 126.2, 83.0, 34.4, 32.9, 32.7, 30.5, 25.1, 24.9, 23.3, 23.1, 21.4, 20.3, 14.4, 14.2. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $CDCl_3$) δ 30.00.

FT-IR (neat film NaCl): 2976, 2956, 2928, 2871, 2859, 1604, 1496, 1465, 1378, 1348, 1294, 1145, 1007, 973, 857 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{24}H_{39}BO_2$: 370.3043; Measured: 370.3047.



2-(cyclopentylidene(2,2-dimethylbenzo[*d*][1,3]dioxol-5-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.26S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclopentylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (SI-21) (400 mg, 1.2 mmol, 1 equiv), 5-iodo-2,2-dimethylbenzo[d][1,3]dioxole (331 mg, 1.2 mmol, 1 equiv), tetrahydrofuran (8 mL), and the aqueous KOH solution (1.2 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (54.8 mg, 0.06 mmol, 5 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (48.4 mg, 0.24 mmol, 20 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature (1.5 h). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (100% hexanes→2% diethyl ether in hexanes) to yield (**4.26S**) 130 mg of a brown oil (30% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (d, *J* = 7.9 Hz, 1H), 6.56 (d, *J* = 1.5 Hz, 1H), 6.53 (dd, *J* = 7.8, 1.6 Hz, 1H), 2.62 (t, *J* = 7.2 Hz, 2H), 2.29 (t, *J* = 7.1 Hz, 2H), 1.76 – 1.67 (m, 4H), 1.67 (s, 6H), 1.27 (s, 12H).

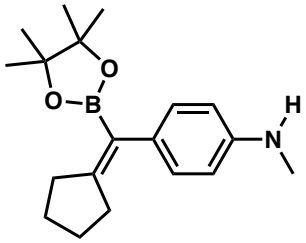
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9, 147.1, 145.2, 136.8, 121.4, 117.5, 109.6, 107.8, 83.3, 34.2, 34.2, 26.7, 26.4, 26.3, 25.1.

Note: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $CDCl_3$) δ 30.63.

FT-IR (neat film NaCl): 2976, 2953, 2866, 1611, 1493, 1438, 1369, 1304, 1245, 1232, 1144, 977, 854, 840, 753 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{21}H_{29}BO_4$: 356.2158; Measured: 356.2163.



4-(cyclopentylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-*N*-methylaniline (4.27S)

To a 20 mL scintillation vial containing *tert*-butyl (4-(cyclopentylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)phenyl)(methyl)carbamate (230 mg, 0.56 mmol, 1 equiv) and a stir bar was added dichloromethane (5.1 mL). This solution was cooled to 0 ºC in an ice bath. To this solution was added dropwise trifluoroacetic acid (214 uL, 2.78 mmol, 5 equiv). This solution was allowed to warm to room temperature and stirred for 4 hours (monitored for consumption of the starting material by LC-MS). To this solution was slowly added triethylamine (0.5 mL) followed by saturated aqueous NH_4Cl (3 mL). This solution was extracted with dichloromethane (3 x 5 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. This essentially pure material was purified by flash column chromatography to yield **4.27S** as a white solid (135 mg, 77%).

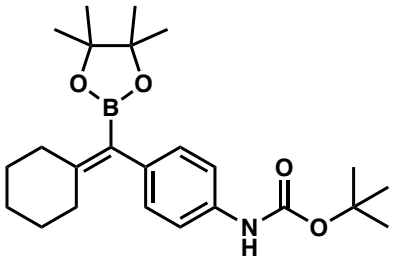
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.5 Hz, 2H), 6.56 (d, *J* = 8.5 Hz, 2H), 2.83 (s, 3H), 2.63 (tt, *J* = 7.3, 1.4 Hz, 2H), 2.32 (tt, *J* = 7.1, 1.4 Hz, 2H), 1.82 – 1.62 (m, 2H), 1.59 – 1.47 (m, 2H), 1.27 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 161.4, 147.1, 132.7, 129.9, 112.3, 83.2, 34.2, 34.0, 31.2, 26.7, 26.4, 25.1. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $CDCl_3$) δ 29.91.

Melting Point: 78–80 ºC

HR-MS (ESI-MS) m/z: [M]+ Calculated for $C_{19}H_{28}BNO_2$: 313.2213; Measured: 313.2217.



***tert*-butyl (4-(cyclohexylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)phenyl)carbamate. (4.28S)**

Synthesized according to condition A.

To a schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (700 mg, 2.1 mmol, 1 equiv), tert-butyl (4-iodophenyl)carbamate (669 mg, 2.1 mmol, 1 equiv), 1,4-dioxane (12 mL, 0.15 M), and the aqueous KOH solution (1.2 mL, 3 molar, 1.7 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tetrakis(triphenylphosphine)palladium(0) (97.0 mg, 0.08 mmol, 4 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was heated to 90 ºC for 20 hours. The solution was cooled to room temperature and quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 10 mL) The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (3→5% ethyl acetate in hexanes) to yield (**4.28S**) 84 mg (10% yield) of a white solid.

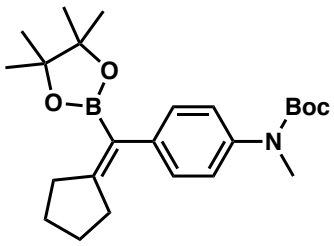
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 2H), 7.01 (d, J = 8.5 Hz, 2H), 6.39 (s, 1H), 2.58 – 2.37 (m, 2H), 2.24 – 2.00 (m, 2H), 1.65 – 1.42 (m, J = 6.1 Hz, 6H), 1.51 (s, 9H), 1.24 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.2, 153.2, 137.4, 135.9, 129.9, 118.6, 83.5, 35.8, 32.3, 29.1, 28.7, 27.0, 25.0. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $CDCl_3$) δ 29.52.

FT-IR (neat film NaCl): 3335, 2976, 2927, 2852, 1726, 1588, 1521, 1448, 1390, 1354, 1270, 1227, 1161, 1052, 972, 855 cm^{-1}.

HR-MS (ESI-MS) m/z: [M–Boc]+ Calculated for $C_{14}H_{28}BNO_2$: 313.2313; Measured: 313.2315.



***tert*-butyl (4-(cyclopentylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)phenyl)(methyl)carbamate (4.29S)**

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclopentylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (SI-21) (850 mg, 2.5 mmol, 1 equiv), tert-butyl (4-iodophenyl)(methyl)carbamate (848 mg, 2.5 mmol, 1 equiv), tetrahydrofuran (15 mL), and the aqueous KOH solution (2.5 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (70 mg, 0.076 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-tertbutyl phosphine (61.7 mg, 0.30 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature (24 h). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (10→20% diethyl ether in hexanes followed by 90% DCM:Hexanes) to yield **4.29S** as 268 mg of a colorless oil

(25% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 2H), 7.11 – 6.97 (m, 2H), 3.25 (s, 3H), 2.68 – 2.54 (m, 2H), 2.27 (tt, *J* = 7.1, 1.2 Hz, 2H), 1.70 (p, *J* = 7.0 Hz, 2H), 1.63 – 1.49 (m, 2H), 1.45 (s, 9H), 1.26 (s, 12H).

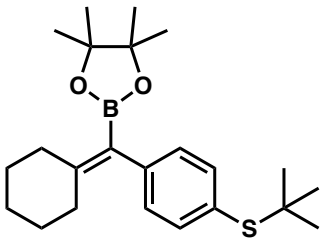
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 155.3, 141.1, 140.7, 129.2, 124.9, 83.3, 80.3, 37.6, 34.3, 34.1, 28.7, 26.7, 26.4, 25.1.

Note: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (96 MHz, $CDCl_3$) δ 31.76.

FT-IR (neat film NaCl): 2975, 2867, 1699, 1606, 1509, 1477, 1452, 1389, 1357, 1305, 1145, 980, 858 cm^{-1}.

HR-MS (CI-MS) m/z: [M]+ Calculated for $C_{24}H_{36}BNO_4$: 413.2737; Measured: 413.2742.



2-((4-(*tert*-butylthio)phenyl)(cyclohexylidene)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.30S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (400 mg, 1.15 mmol, 1 equiv), (4-bromophenyl)(tert-butyl)sulfane (281 mg, 1.15 mmol, 1 equiv), tetrahydrofuran (8 mL), and the aqueous KOH solution (1.15 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (52 mg, 0.06 mmol, 5 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-

tertbutyl phosphine (46.5 mg, 0.23 mmol, 20 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature. The reaction was monitored carefully by TLC (~3 hours). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (20→25% dichloromethane in hexanes) to yield **4.30S** as 187 mg of an yellow solid solid (42% yield).

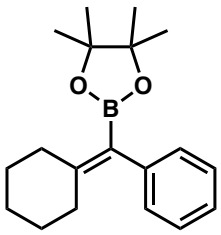
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.2 Hz, 2H), 2.62 – 2.37 (m, 2H), 2.26 – 1.94 (m, 2H), 1.60 – 1.42 (m, 6H), 1.29 (s, 9H), 1.24 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5, 143.1, 137.2, 129.5, 83.6, 46.0, 35.8, 32.3, 31.3, 29.1, 28.8, 27.0, 24.9. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.44.

FT-IR (neat film NaCl): 2974, 2925, 2854, 1614, 1482, 1448, 1352, 1300, 1145, 972, 856, 764 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{23}H_{35}BO_2S$: 386.2451; Measured: 386.2455.

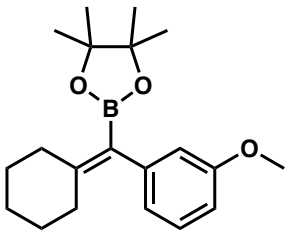


2-(cyclohexylidene(phenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.31S)

Synthesized according to condition A.

To a schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-

dioxaborolane) (500 mg, 1.4 mmol, 1 equiv), iodobenzene (293 mg, 1.4 mmol, 1 equiv), 1,4-dioxane (12 mL, 0.15 M), and the aqueous KOH solution (0.7 mL, 3 molar, 1.7 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tetrakis(triphenylphosphine)palladium(0) (50.0 mg, 0.04 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was heated to 90 ºC for 18 hours. The solution was cooled to room temperature and quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 10 mL) The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (6% diethyl ether in hexanes) to yield **4.31S** as 140 mg (32% yield) of a white solid. This material matched reported literature ^{1}H NMR data.[25]



2-(cyclohexylidene(3-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (4.32S)

Synthesized according to condition B.

To schlenk flask was added 2,2'-(cyclohexylidenemethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **(SI-2)** (370 mg, 1.06 mmol, 1 equiv), 1-iodo-3-methoxybenzene (249 mg, 1.06 mmol, 1 equiv), tetrahydrofuran (7 mL), and the aqueous KOH solution (1.0 mL, 3 molar, 3.0 equiv). The flask was freeze-pump thawed three cycles of 15 minutes. Tris(dibenzylideneacetone)dipalladium(0) (29 mg, 0.03 mmol, 3 mol %) was added to the frozen solution and the flask was evacuated under vacuum and backfilled with nitrogen three times. Tri-

tertbutyl phosphine (26 mg, 0.13 mmol, 12 mol %) was added to the frozen solution under a stream of nitrogen and the flask was evacuated under vacuum and backfilled with nitrogen three times. The solution was allowed to thaw and stirred at room temperature (18 h). The solution was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (20→35% dichloromethane in hexanes) to yield **4.32S** as 203 mg of a brown solid (61% yield).

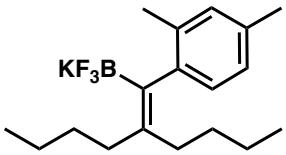
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (dd, J = 8.2, 7.5 Hz, 1H), 6.78 – 6.52 (m, 3H), 3.78 (s, 3H), 2.53 – 2.41 (m, 2H), 2.21 – 2.02 (m, 2H), 1.83 – 1.50 (m, 6H), 1.25 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 155.2, 143.6, 129.3, 121.5, 114.0, 111.4, 83.6, 55.1, 35.3, 32.1, 29.9, 28.3, 27.5, 25.2. *Note*: Carbon attached to boron not seen due to relaxation on B.

^{11}B NMR (128 MHz, $CDCl_3$) δ 31.27.

FT-IR (neat film NaCl): 2977, 2925, 2851, 1618, 1487, 1353, 1297, 1135, 970, 857 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{20}H_{39}BO_3$: 328.2209; Measured: 328.2211.



(2-butyl-1-(2,4-dimethylphenyl)hex-1-en-1-yl)trifluoro-λ^4-borane, potassium salt (4.34S)

To a scintillation vial containing (100 mg, 0.27 mmol, 1 equiv) and a stir bar was added methanol (3.4 mL) and water (1.7 mL). To this was added solid KHF_2 (127 mg, 1.62 mmol, 6 equiv). This solution was stirred vigorously (rpm~1300) for 8 hours. This solution was filtered through a kimwipe pipette to remove solids. The filtrate was concentrated **at or below** room temperature using rotary evaporation followed by high-vac. This was then dissolved in room temperature acetone and decanted away from the solids. The acetone solution was concentrated

to yield a low-melting colorless solid of **4.34S** (89 mg, 94% yield). *Note:* This solid was stable in the freezer (–20ºC) for only a few days at a time without total decomposition to the styrene, presumably through protodeboronation.

^{1}H NMR (300 MHz, $(CD_3)_2O$) δ 6.79 (d, J = 0.8 Hz, 1H), 6.71 (d, J = 0.9 Hz, 2H), 2.69 – 2.47 (m, 1H), 2.29 – 2.22 (m, 1H), 2.19 (s, 3H), 2.15 (d, J = 7.2 Hz, 1H), 2.10 (s, 3H), 2.07 (bs, 1H), 1.66 (q, J = 6.9, 6.3 Hz, 2H), 1.48 (qd, J = 6.8, 6.4, 2.8 Hz, 2H), 1.42 – 1.26 (m, 2H), 1.10 – 0.98 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H), 0.71 (t, J = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $(CD_3)_2O$) δ 147.1, 139.1,135.6 132.0, 129.7, 129.0, 125.1, 33.0, 32.8, 32.7, 31.4, 24.9, 23.7, 23.4, 20.8, 20.33, 14.4, 14.0.

^{19}F NMR (282 MHz, $(CD_3)_2O$) δ -134.99.

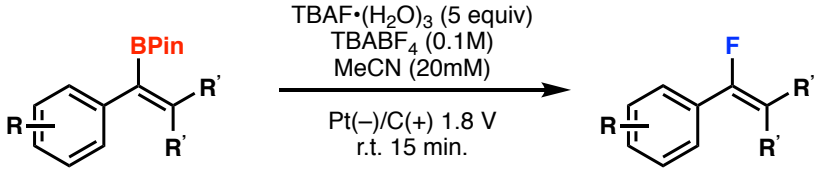
^{11}B NMR (96 MHz, $(CD_3)_2O$) δ 4.83.

FT-IR (neat film NaCl): 2955, 2928, 2858, 1613, 1492, 1465, 1377, 1140, 1072, 932, 857, 818 cm^{-1}.

HR-MS (ESI): $[M]^-$ Calculated for $C_{18}H_{27}BF_3$: 311.2157; Measured: 311.2149.

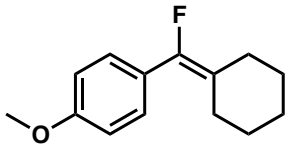
4.7.4 Electrochemical Halogenation of Alkenyl Boronates:

General procedure for fluorination reactions



To an oven dried 2 dram vial equipped with an oven dried stir bar was added the vinyl boronic ester or boronate (0.05–0.025 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by

bubbling nitrogen with stirring (~400 rpm) for 20 minutes. *Degassing showed no effect on yield for this reaction with several substrates, but for consistency was performed before each reaction.* After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-50 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-150 SCE electrode (*usually ~3.5V E_{cell} required, this can allow further ease of use without a reference electrode*) was applied for 15 minutes, or until the starting material was consumed. (*Constant voltage gave optimal yields for this reaction, particularly for substrates that contained redox sensitive moieties such as unprotected anilines and thiols).* Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography to give the resulting vinyl fluoride.



1-(cyclohexylidenefluoromethyl)-4-methoxybenzene. (4.8)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(4-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (16.4 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-50 SCE

electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-150 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (50% dichloromethane in hexanes) to give the resulting vinyl fluoride **4.8** as a colorless oil (7.7 mg, 70% yield).

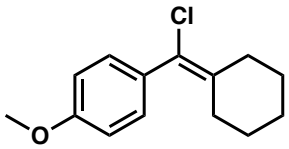
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 9.0, 1.0 Hz, 2H), 6.95 – 6.84 (m, 2H), 3.82 (s, 3H), 2.43 – 2.28 (m, 2H), 2.19 (t, *J* = 5.6 Hz, 2H), 1.69 – 1.47 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7 (d, *J* = 1.6 Hz), 150.0 (d, *J* = 237.2 Hz), 130.2 (d, *J* = 3.5 Hz), 125.9 (d, *J* = 31.7 Hz), 117.7 (d, *J* = 17.9 Hz), 113.7, 55.6, 29.1 (d, *J* = 4.2 Hz), 27.9 (d, *J* = 2.3 Hz), 27.3, 26.8, 26.6 (d, *J* = 7.7 Hz).

^{19}F NMR (282 MHz, $CDCl_3$) δ -107.71.

FT-IR (neat film NaCl): 2927, 2852, 1609, 1510, 1444, 1302, 1247, 1174, 1031, 834 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{14}H_{17}FO$: 220.1263; Measured: 220.1267.



1-(chloro(cyclohexylidene)methyl)-4-methoxybenzene. (4.9)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(4-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (16.4 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBACl (79.0 mg, 0.35 mmol, 7 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile

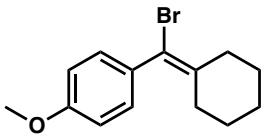
was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 25 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (50% dichloromethane in hexanes) to give the resulting vinyl chloride **(4.9)** as a colorless oil (8.0 mg, 68% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 3H), 2.52 (dd, *J* = 7.0, 5.3 Hz, 2H), 2.15 (dd, *J* = 7.0, 5.2 Hz, 2H), 1.78 – 1.43 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3, 137.7, 132.0, 130.8, 122.9, 113.8, 55.6, 32.3, 32.2, 28.2, 27.5, 26.6.

FT-IR (neat film NaCl): 2927, 2852, 1606, 1508, 1442, 1293, 1243, 1173, 1034, 831, 800cm^{-1}.

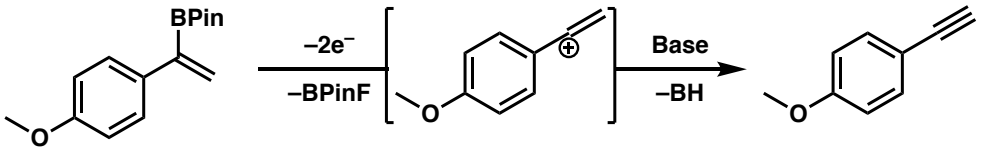
HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{14}H_{17}ClO$: 236.0967; Measured: 236.0968.



1-(bromo(cyclohexylidene)methyl)-4-methoxybenzene. (4.11)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added (cyclohexylidene(4-methoxyphenyl)methyl)trifluoro-λ^4-borane, potassium salt (15.4 mg, 0.05 mmol, 1 equiv). To this was added the TBABr (97.0 mg, 0.300 mmol, 6 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was

degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (50% dichloromethane in hexanes) to give the resulting vinyl bromide **(4.11)** as a colorless oil (8.0 mg, 57% yield). ^{1}H NMR data were in matched those reported in the literature.[26]

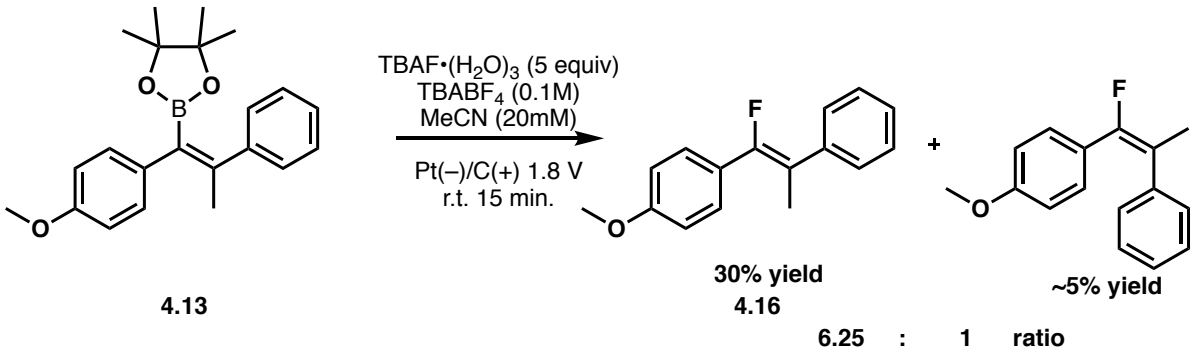


1-ethynyl-4-methoxybenzene. (4.14)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(1-(4-methoxyphenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13.0 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the $TBAF•(H_2O)$ (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution

was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (5% acetone in hexanes) to give the resulting alkyne **(4.14)** as a colorless oil (2.8 mg, 43% yield). The ^{1}H NMR spectrum was in agreement with the reported specta.[27]

Further evidence for the intermediacy of a vinyl carbocation is the mixture of vinyl fluorides produced (6.25:1 Z:E) starting from a single isomer of alkenyl boronic ester **4.13**.



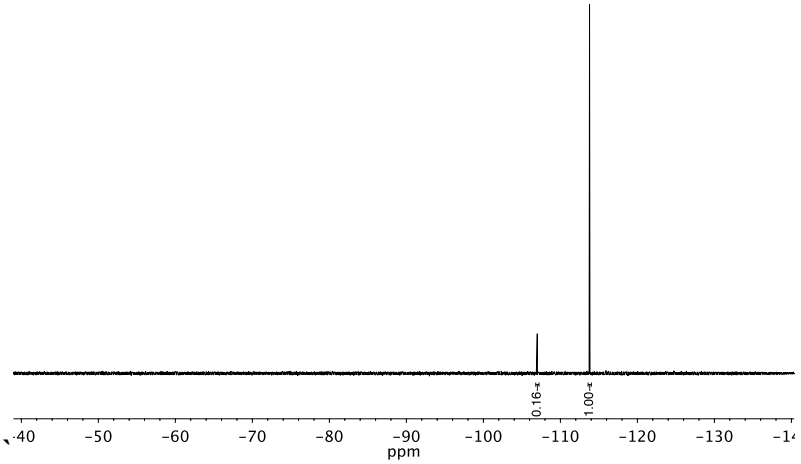
4.13 **30% yield** **4.16** **~5% yield**

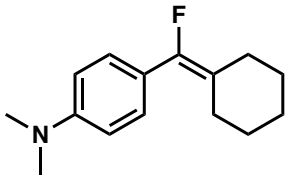
6.25 : 1 ratio

To an oven dried 2 dram vial equipped with an oven dried stir bar was added (*E*)-2-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **(4.13)** (17.5 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The

resulting solution was concentrated *in vacuo* to yield a brown oil. This material was then plugged through silica gel with diethyl ether and concentrated. ^{1}H NMR analysis of this crude material indicated 30% yield of the Z-vinyl fluoride product (*Z*)-1-(1-fluoro-2-phenylprop-1-en-1-yl)-4-methoxybenzene **(4.16).** ^{19}F NMR analysis indicated a 6.25:1 mixture of this material with E isomer.

The crude material was purified by flash column chromatography (40% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.16)**. This matched published literature spectral data.[28] The ^{19}F NMR spectrum of the crude mixture is shown below indicating a 6.25:1 ratio.





4-(cyclohexylidenefluoromethyl)-*N*,*N*-dimethylaniline. (4.17)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 4-(cyclohexylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-*N*,*N*-dimethylaniline (17.1 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly

distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (50% dichloromethane in hexanes) to give the resulting vinyl fluoride **4.17** as a colorless oil (9.5 mg, 81% yield).

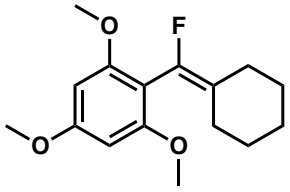
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.21 (m, 2H), 6.70 (d, *J* = 8.5 Hz, 2H), 2.98 (s, 6H), 2.37 (dt, *J* = 6.8, 3.3 Hz, 2H), 2.21 (t, *J* = 5.6 Hz, 2H), 1.56 (dq, *J* = 24.2, 6.5, 5.7 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.3 (d, *J* = 237.5 Hz), 150.2, 130.1, 129.5, 116.2 (d, *J* = 18.6 Hz), 111.5, 40.3, 28.8 (d, *J* = 4.3 Hz), 27.6 (d, *J* = 2.2 Hz), 27.0, 26.5, 26.3 (d, *J* = 7.6 Hz).

^{19}F NMR (282 MHz, $CDCl_3$) δ -107.69.

FT-IR (neat film NaCl): 2923, 2851, 1611, 1523, 1446, 1356, 1288, 1191, 1038, 817 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{15}H_{20}FN$: 233.1579; Measured: 233.1576.



2-(cyclohexylidenefluoromethyl)-1,3,5-trimethoxybenzene. (4.18)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(2,4,6-trimethoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (19.4

mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (50% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.18)** as a colorless oil (11.5 mg, 82% yield).

Note: Reaction was also performed on 1 mmol scale with 3 equiv of TBAF.

To an oven dried 100 mL round bottom flask equipped with an oven dried stir bar was added 2-(cyclohexylidene(2,4,6-trimethoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (388 mg, 1.0 mmol, 1 equiv). To this was added the $TBABF_4$ (1.98 g, 1.50 mmol, 6 equiv) and the TBAF•(H_2O) (947 mg, 0.75 mmol, 3 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (50 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant cell potential (E_{cell}=3.5 V) was applied for 5 hr. Upon completion the applied potential was halted and the electrodes were removed from

solution and rinsed with dichloromethane (5 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (100% hexanes→50% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.18)** as a colorless oil (201 mg, 71% yield).

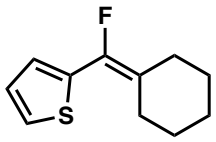
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (s, 2H), 3.83 (s, 3H), 3.80 (s, 6H), 2.41 (td, *J* = 6.2, 2.1 Hz, 2H), 1.85 – 1.73 (m, 2H), 1.65 – 1.59 (m, 2H), 1.51 (ddq, *J* = 14.4, 11.4, 5.9 Hz, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (d, *J* = 2.2 Hz), 160.1, 142.7 (d, *J* = 238.7 Hz), 120.8 (d, *J* = 18.8 Hz), 104.2 (d, *J* = 29.5 Hz), 90.8, 56.2, 55.6, 29.5 (d, *J* = 3.6 Hz), 27.4 (d, *J* = 2.4 Hz), 27.3, 26.9, 26.2 (d, *J* = 5.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.75.

FT-IR (neat film NaCl): 2928, 2841, 1605, 1584, 1466, 1413, 1226, 1205, 1156, 1128, 1030, 812 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{16}H_{21}FO_3$: 280.1474; Measured: 280.1478.



2-(cyclohexylidenefluoromethyl)thiophene. **(4.19)**

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(thiophen-2-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (15.2 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring

(~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (100% hexaness→35% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.19)** as a colorless oil (6.0 mg, 61% yield) as a 9:1 mix with the styrene product.

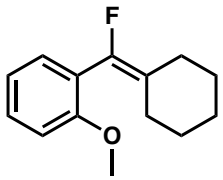
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 5.1 Hz, 1H), 7.19 – 7.10 (m, 1H), 7.02 (q, J = 3.9, 2.8 Hz, 1H), 2.71 – 2.14 (m, 4H), 1.63 – 1.56 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7 (d, J = 232.2 Hz), 134.9 (d, J = 36.3 Hz), 127.3 (d, J = 5.1 Hz), 126.9, 126.1, 120.5 (d, J = 18.1 Hz), 29.2 (d, J = 4.1 Hz), 27.7 (d, J = 2.3 Hz), 27.2, 26.9 (d, J = 7.7 Hz), 26.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -104.80.

FT-IR (neat film NaCl): 2926, 2854, 1719, 1630, 1449, 1413, 1278, 1258, 1038, 799 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{11}H_{13}FS$: 196.0722; Measured: 196.0722.



1-(cyclohexylidenefluoromethyl)-2-methoxybenzene. (4.20)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(2-methoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (16.4 mg,

0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (50% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.20)** as a colorless oil (5.5 mg, 50% yield).

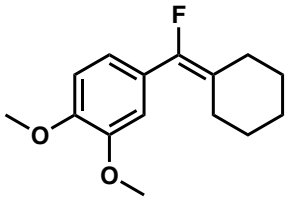
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (ddt, J = 8.2, 7.5, 1.7 Hz, 1H), 7.26 – 7.20 (m, 1H), 7.05 – 6.83 (m, 2H), 3.85 (s, 3H), 2.52 – 2.33 (m, 2H), 2.02 – 1.80 (m, 2H), 1.67 – 1.45 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 147.3 (d, J = 239.3 Hz), 132.0 (d, J = 2.3 Hz), 130.6 (d, J = 2.4 Hz), 122.3 (d, J = 28.9 Hz), 120.4, 119.7 (d, J = 16.9 Hz), 55.9, 29.3 (d, J = 4.0 Hz), 27.8 (d, J = 2.4 Hz), 27.3, 26.8, 26.3 (d, J = 6.7 Hz).

^{19}F NMR (282 MHz, $CDCl_3$) δ -107.51.

FT-IR (neat film NaCl): 2927, 2852, 1701, 1600, 1580, 1491, 1463, 1435, 1299, 1272, 1247, 1209, 1111, 1033, 936, 752 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{14}H_{17}FO$: 220.1263; Measured: 220.1261.



4-(cyclohexylidenefluoromethyl)-1,2-dimethoxybenzene. (SI-38)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(3,4-dimethoxyphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (17.9 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (15% diethyl ether in hexanes) to give the resulting vinyl fluoride **(4.21)** as colorless oil (7.4 mg, 59% yield).

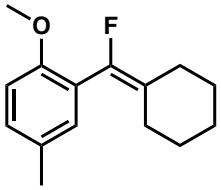
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 – 6.89 (m, 2H), 6.85 (d, J = 8.2 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.38 (t, J = 5.0 Hz, 2H), 2.21 (t, J = 5.8 Hz, 2H), 1.64 – 1.51 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0 (d, J = 237.9 Hz), 148.4 (d, J = 1.6 Hz), 125.7 (d, J = 31.4 Hz), 121.6 (d, J = 4.3 Hz), 117.6 (d, J = 17.8 Hz), 111.5 (d, J = 2.9 Hz), 110.4, 55.8, 28.8 (d, J = 4.2 Hz), 27.6 (d, J = 2.3 Hz), 27.0, 26.4, 26.3 (d, J = 7.7 Hz).

^{19}F NMR (282 MHz, $CDCl_3$) δ -107.48.

FT-IR (neat film NaCl): 2928, 2852, 1604, 1513, 1463, 1447, 1409, 1256, 1233, 1169, 1140, 1027, 812 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{15}H_{19}FO_2$: 250.1369; Measured: 250.1359.



2-(cyclohexylidenefluoromethyl)-1-methoxy-4-methylbenzene. (4.22)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclohexylidene(2-methoxy-5-methylphenyl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (17.1 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (20% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.22)** as colorless oil (5.7 mg, 47% yield).

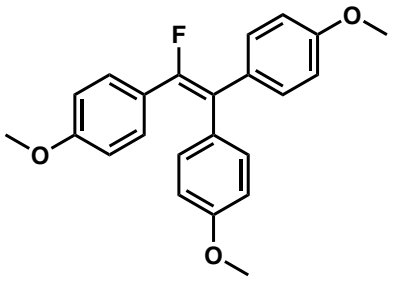
^1H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, J = 8.5 Hz, 1H), 7.05 (s, 1H), 6.82 (d, J = 8.3 Hz, 1H), 3.81 (s, 3H), 2.46 – 2.32 (m, 2H), 2.29 (s, 3H), 1.93 (t, J = 5.6 Hz, 2H), 1.65 – 1.46 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8, 147.3 (d, *J* = 239.3 Hz), 132.4 (d, *J* = 2.0 Hz), 131.0 (d, *J* = 2.4 Hz), 129.7, 122.0 (d, *J* = 29.1 Hz), 119.6 (d, *J* = 17.2 Hz), 111.5, 56.1, 29.3 (d, *J* = 3.9 Hz), 27.8 (d, *J* = 2.4 Hz), 27.3, 26.8, 26.3 (d, *J* = 6.7 Hz), 20.7.

^{19}F NMR (282 MHz, $CDCl_3$) δ -107.18.

FT-IR (neat film NaCl): 2926, 2852, 1501, 1463, 1448, 1273, 1251, 1147, 1112, 1040, 807 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{15}H_{19}FO$: 234.1419; Measured: 234.1420.



4,4',4''-(2-fluoroethene-1,1,2-triyl)tris(methoxybenzene). (4.23)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added **4**,4,5,5-tetramethyl-2-(1,2,2-tris(4-methoxyphenyl)vinyl)-1,3,2-dioxaborolane (23.6 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (5% acetone in hexanes) to give the resulting vinyl fluoride **(4.23)** as a yellow

solid (10.9 mg, 60% yield).

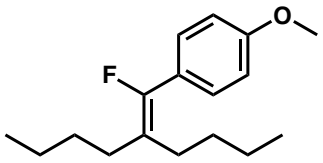
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.17 (d, *J* = 8.9 Hz, 2H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.74 – 6.67 (m, 2H), 3.82 (s, 3H), 3.80 (s, 3H), 3.77 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 159.0, 158.8, 153.4 (d, *J* = 249.5 Hz), 132.5 (d, *J* = 3.2 Hz), 132.0 (d, *J* = 7.4 Hz), 131.6, 131.4 (d, *J* = 4.8 Hz), 130.0 (d, *J* = 6.1 Hz), 126.2 (d, *J* = 29.6 Hz), 120.2 (d, *J* = 18.7 Hz), 114.2, 113.7, 113.6, 55.5, 55.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -104.48.

FT-IR (neat film NaCl): 2002, 2932, 2836, 1738, 1607, 1512, 1462, 1365, 1297, 1247, 1175, 1033, 831 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{23}H_{21}FO_3$: 364.1474; Measured: 364.1475.



1-(2-butyl-1-fluorohex-1-en-1-yl)-4-methoxybenzene (4.24)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(2-butyl-1-(4-methoxyphenyl)hex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (18.6 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected

to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (100% hexanes→30% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.24)** as a colorless oil (9.5 mg, 72% yield).

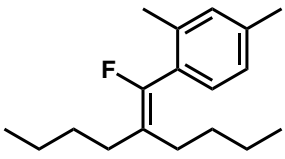
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 2H), 7.04 – 6.82 (m, 2H), 3.83 (s, 3H), 2.35 – 2.13 (m, 2H), 2.11 – 1.92 (m, 2H), 1.52 – 1.32 (m, 6H), 1.27 (q, *J* = 7.2 Hz, 2H), 0.94 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 152.6 (d, *J* = 238.5 Hz), 129.7 (d, *J* = 3.8 Hz), 125.9 (d, *J* = 31.5 Hz), 118.6 (d, *J* = 17.2 Hz), 113.4, 55.2, 30.5 (d, *J* = 3.1 Hz), 30.2, 29.5 (d, *J* = 4.3 Hz), 27.3, 27.2, 22.6, 14.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ -103.34.

FT-IR (neat film NaCl): 2956, 2927, 2858, 1726, 1681, 1610, 1512, 1464, 1378, 1301, 1250, 1175, 1108, 1033, 834 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{17}H_{25}FO$: 264.1889; Measured: 264.1901.



1-(2-butyl-1-fluorohex-1-en-1-yl)-2,4-dimethylbenzene (4.25)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(2-butyl-1-(2,4-dimethylphenyl)hex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (18.5 mg, 0.05 mmol, 1

equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the $TBAF•(H_2O)$ (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (100% hexanes) to give the resulting vinyl fluoride **(4.25)** as a colorless oil (7.2 mg, 55% yield).

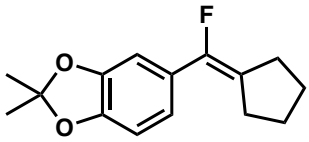
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.0 Hz, 1H), 7.04 (s, 1H), 6.97 (d, *J* = 7.6 Hz, 1H), 2.33 (s, 3H), 2.27 (d, *J* = 2.4 Hz, 3H), 2.24 (d, *J* = 6.8 Hz, 2H), 1.82 (t, *J* = 7.8 Hz, 2H), 1.47 (q, *J* = 7.7 Hz, 2H), 1.39 (dt, *J* = 15.0, 7.5 Hz, 2H), 1.31 (p, *J* = 7.5 Hz, 2H), 1.17 (h, *J* = 7.4 Hz, 2H), 1.01 – 0.89 (m, 3H), 0.85 – 0.73 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6 (d, *J* = 242.2 Hz), 138.7 (d, *J* = 2.9 Hz), 137.7, 130.8, 130.4, 129.9 (d, *J* = 28.0 Hz), 126.0, 119.3 (d, *J* = 15.9 Hz), 114.9, 30.1 (d, *J* = 3.0 Hz), 29.6 (d, *J* = 5.5 Hz), 29.1 (d, *J* = 3.7 Hz), 26.3 (d, *J* = 5.9 Hz), 22.6, 22.4, 21.2, 19.4, 14.0, 13.9.

^{19}F NMR (282 MHz, $CDCl_3$) δ -100.07.

FT-IR (neat film NaCl): 2956, 2926, 2859, 1737, 1693, 1498, 1458, 1378, 1349, 1288, 1261, 1121, 1034 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{18}H_{27}F$: 262.2096; Measured: 262.2097.



5-(cyclopentylidenefluoromethyl)-2,2-dimethylbenzo[*d*][1,3]dioxole (4.26)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclopentylidene(2,2-dimethylbenzo[*d*][1,3]dioxol-5-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (17.8 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (1%DCM:hexanes + 0.1% triethylamine on triethylamine deactivated silica gel) to give the resulting vinyl fluoride **(4.26)** as a yellow oil (8.3 mg, 68% yield). This material was sensitive to mild acids, and decomposition was observed in $CDCl_3$. The NMR spectra are reported in $(CD_3)_2CO$.

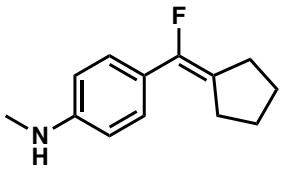
^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 6.95 (dd, J = 8.2, 1.8 Hz, 1H), 6.87 (d, J = 1.8 Hz, 1H), 6.79 (dt, J = 8.2, 0.6 Hz, 1H), 2.49 (dt, J = 6.9, 3.5 Hz, 4H), 1.76 – 1.67 (m, 4H), 1.66 (s, 6H).

^{13}C NMR (126 MHz, $(CD_3)_2CO$) δ 148.8 (d, *J* = 232.5 Hz), 147.0 (d, *J* = 47.4 Hz), 126.8 (d, *J* = 30.9 Hz), 121.5, 120.3 (d, *J* = 21.6 Hz), 119.2 (d, *J* = 7.4 Hz), 118.0, 107.5, 105.5 (d, *J* = 7.2 Hz), 33.5, 33.1, 29.8 (d, *J* = 4.6 Hz), 27.1, 25.3, 24.7.

^{19}F NMR (282 MHz, $(CD_3)_2CO$) δ -105.33.

FT-IR (neat film NaCl): 2980, 2853, 1698, 1495, 1446, 1384, 1359, 1259, 1243, 1151, 1016, 804 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{15}H_{17}FO_2$: 248.1212; Measured: 248.1213.



4-(cyclopentylidenefluoromethyl)-*N*-methylaniline (4.27)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-(cyclopentylidene(2,2-dimethylbenzo[*d*][1,3]dioxol-5-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (17.8 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +0.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes, or until the starting material was consumed. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column

chromatography (100% hexanes→6% ether:hexanes) to give the resulting vinyl fluoride **(4.27)** as a yellow oil (4.7mg, 45% yield).

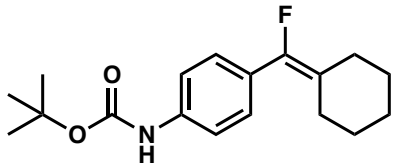
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.60 (d, *J* = 8.4 Hz, 2H), 2.86 (s, 3H), 2.58 – 2.43 (m, 4H), 1.80 – 1.62 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.0 (d, *J* = 232.7 Hz), 148.9, 127.3 (d, *J* = 6.6 Hz), 123.2 (d, *J* = 30.6 Hz), 119.2 (d, *J* = 22.3 Hz), 112.1, 30.9, 30.6 (d, *J* = 4.9 Hz), 29.5 (d, *J* = 4.4 Hz), 28.0, 26.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -109.47.

FT-IR (neat film NaCl): 3417, 2954, 2868, 2890, 2816, 1680, 1613, 1523, 1318, 1261, 1189, 1046, 952, 824 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{13}H_{10}FN$: 205.1266; Measured: 205.1267.



***tert*-butyl (4-(cyclohexylidenefluoromethyl)phenyl)carbamate. (4.28)**

To an oven dried 2 dram vial equipped with an oven dried stir bar was added *tert*-butyl (4-(cyclohexylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)phenyl)carbamate (20.7 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE

electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (70% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.28)** as a white solid (6.0 mg, 39% yield) as well as recovered the unreacted starting material **(4.28S)** (6.2 mg, 30% recovered s.m.).

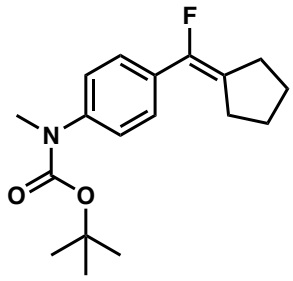
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), 6.50 (s, 1H), 2.37 (bs, 2H), 2.19 (t, *J* = 5.8 Hz, 2H), 1.63 – 1.55 (m, 6H), 1.52 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 149.8 (d, *J* = 237.0 Hz), 138.6 (d, *J* = 1.9 Hz), 129.6 (d, *J* = 3.8 Hz), 128.0 (d, *J* = 31.5 Hz), 118.3 (d, *J* = 17.6 Hz), 118.1, 81.1, 29.1 (d, *J* = 4.2 Hz), 28.6, 27.9 (d, *J* = 2.2 Hz), 27.3, 26.8, 26.6 (d, *J* = 7.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.84.

FT-IR (neat film NaCl): 3330, 2967, 2927, 2852, 1731, 1702, 1590, 1523, 1405, 1367, 1315, 1234, 1159, 1054, 842 cm^{-1}.

HR-MS (ESI): Calculated for $[M]^+$ $C_{18}H_{24}FNO_2$: 305.1791; Measured: 305.1795.



***tert*-butyl (4-(cyclopentylidenefluoromethyl)phenyl)(methyl)carbamate (4.29)**

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2 *tert*-butyl (4-(cyclopentylidene(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)phenyl)(methyl)carbamate (20.6 mg, 0.05 mmol, 1 equiv). To this was added the

$TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (70% dichloromethane:hexanes) to give the resulting vinyl fluoride **(4.29)** as a colorless oil (7.9 mg, 52% yield). 4.0 mg of **4.29S** was also recovered.

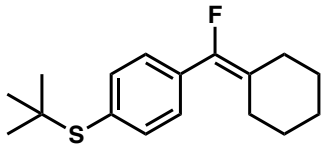
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.7 Hz, 2H), 7.24 (d, J = 8.7 Hz, 2H), 3.27 (s, 3H), 2.66 – 2.43 (m, 4H), 1.85 – 1.61 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 149.2 (d, J = 232.9 Hz), 143.2, 130.8 (d, J = 30.4 Hz), 126.2 (d, J = 6.9 Hz), 125.1, 123.0 (d, J = 21.5 Hz), 80.8, 37.4, 30.8 (d, J = 4.6 Hz), 29.8 (d, J = 4.6 Hz), 28.6, 28.0, 26.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -110.47.

FT-IR (neat film NaCl): 2957, 2928, 2868, 1703, 1608, 1513, 1477, 1366, 1355, 1285, 1152, 1110, 1054, 11013, 840 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{18}H_{24}FNO_2$: 305.1791; Measured: 305.1805.



***tert*-butyl(4-(cyclohexylidenefluoromethyl)phenyl)sulfane. (4.30)**

To an oven dried 2 dram vial equipped with an oven dried stir bar was added 2-((4-(*tert*-butylthio)phenyl)(cyclohexylidene)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (19.3 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and the TBAF•(H_2O) (79.0 mg, 0.25 mmol, 5 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (100% hexanes→20% dichloromethane in hexanes) to give the resulting vinyl fluoride **(4.30)** as a colorless oil (2.8 mg, 20% yield) as well as recovered the unreacted starting material **(4.30S)** (11.3 mg, 59% recovered s.m.).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 – 7.47 (m, 2H), 7.41 – 7.30 (m, 2H), 2.39 (d, J = 6.4 Hz, 2H), 2.24 (d, J = 6.1 Hz, 2H), 1.68 – 1.55 (m, 6H), 1.30 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2 (d, J = 236.9 Hz), 136.9, 133.2 (d, J = 31.0 Hz), 132.8, 128.4 (d, J = 3.8 Hz), 119.4 (d, J = 16.9 Hz), 46.2, 30.9, 28.7 (d, J = 4.3 Hz), 27.5 (d, J = 2.2 Hz), 27.0, 26.4 (d, J = 7.9 Hz), 26.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -109.95.

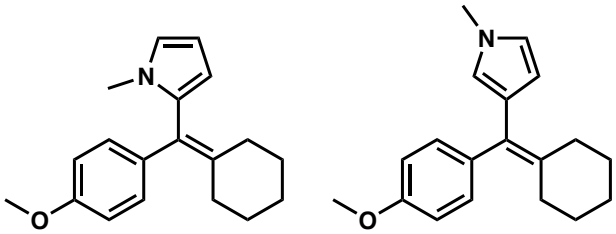
FT-IR (neat film NaCl): 2962, 2927, 2854, 1447, 1393, 1363, 1291, 1214, 1164, 1042, 839 cm^{-1}.

HR-MS (EI-MS) m/z: [M]+ Calculated for $C_{17}H_{23}FS$: 278.1504; Measured: 278.1506.

4.7.5 Mechanistic Studies

Friedel-Crafts Reaction with N-Me Pyrrole

Additional evidence supporting the intermediacy of a vinyl cation is the Friedel-Crafts reactivity with N-Me pyrrole to produce **2-(cyclohexylidene(4-methoxyphenyl)methyl)-1-methyl-1*H*-pyrrole 33.1** and **3-(cyclohexylidene(4-methoxyphenyl)methyl)-1-methyl-1*H*-pyrrole 33.2**.



(33.1) **(33.2)**

To an oven dried 2 dram vial equipped with an oven dried stir bar was added (cyclohexylidene(4-methoxyphenyl)methyl)trifluoro-λ^4-borane, potassium salt **(SI-25)** (15.4 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and water (15 uL, 15 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL) followed by N-Me pyrrole (41 mg, 0.50 mmol, 10 equiv). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied

potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (2% diethyl ether in hexanes) to give the resulting Friedel-Crafts products **(33.1)** and **(33.2)** as colorless oils (6.8 mg, 48% combined yield, 2.7:1 ratio). Analytical samples of each were obtained by further flash column chromatography (100% hexanes → 2% diethyl ether in hexanes).

(33.1) Characterization Data:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.53 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.10 (dd, *J* = 3.5, 2.7 Hz, 1H), 5.99 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.78 (s, 3H), 3.21 (s, 3H), 2.34 (bs, 2H), 2.23 (t, *J* = 5.6 Hz, 2H), 1.60 (bs, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 143.6, 134.5, 134.1, 131.0, 125.4, 121.4, 113.5, 108.9, 106.9, 55.5, 34.5, 33.7, 32.1, 29.0, 29.0, 27.1.

FT-IR (neat film NaCl): 2923, 2850, 1605, 1507, 1447, 1290, 1244, 1174, 1036, 833 cm^{-1}.

HR-MS (ESI): [M]+ Calculated for $C_{19}H_{23}NO$: 281.1779; Measured: 281.1780.

(33.2) Characterization Data:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.48 (t, *J* = 2.5 Hz, 1H), 6.25 (t, *J* = 2.0 Hz, 1H), 5.95 (dd, *J* = 2.7, 1.7 Hz, 1H), 3.80 (s, 3H), 3.57 (s, 3H), 2.53 (s, 2H), 2.27 – 1.95 (m, 2H), 1.81 – 1.48 (m, 6H).

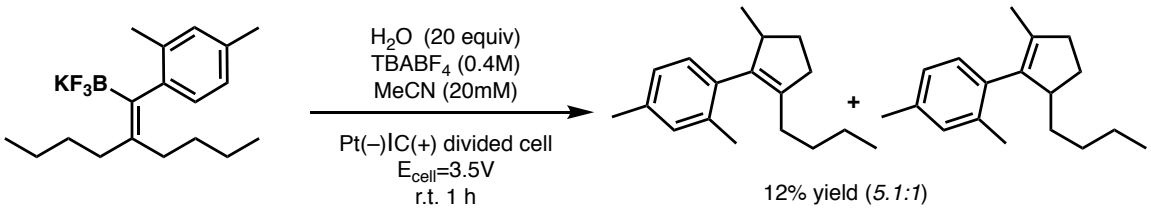
^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 137.4, 136.6, 131.0, 128.1, 126.3, 121.9, 121.1, 113.3, 110.3, 55.5, 36.4, 33.1, 32.5, 29.0, 28.8, 27.3.

FT-IR (neat film NaCl): 2921, 2851, 1606, 1507, 1463, 1289, 1242, 1159, 1102, 1037, 830, 799 cm^{-1}.

HR-MS (ESI): [M]+ Calculated for $C_{19}H_{23}NO$: 281.1779; Measured: 281.1771.

C–H Insertion Reactivity

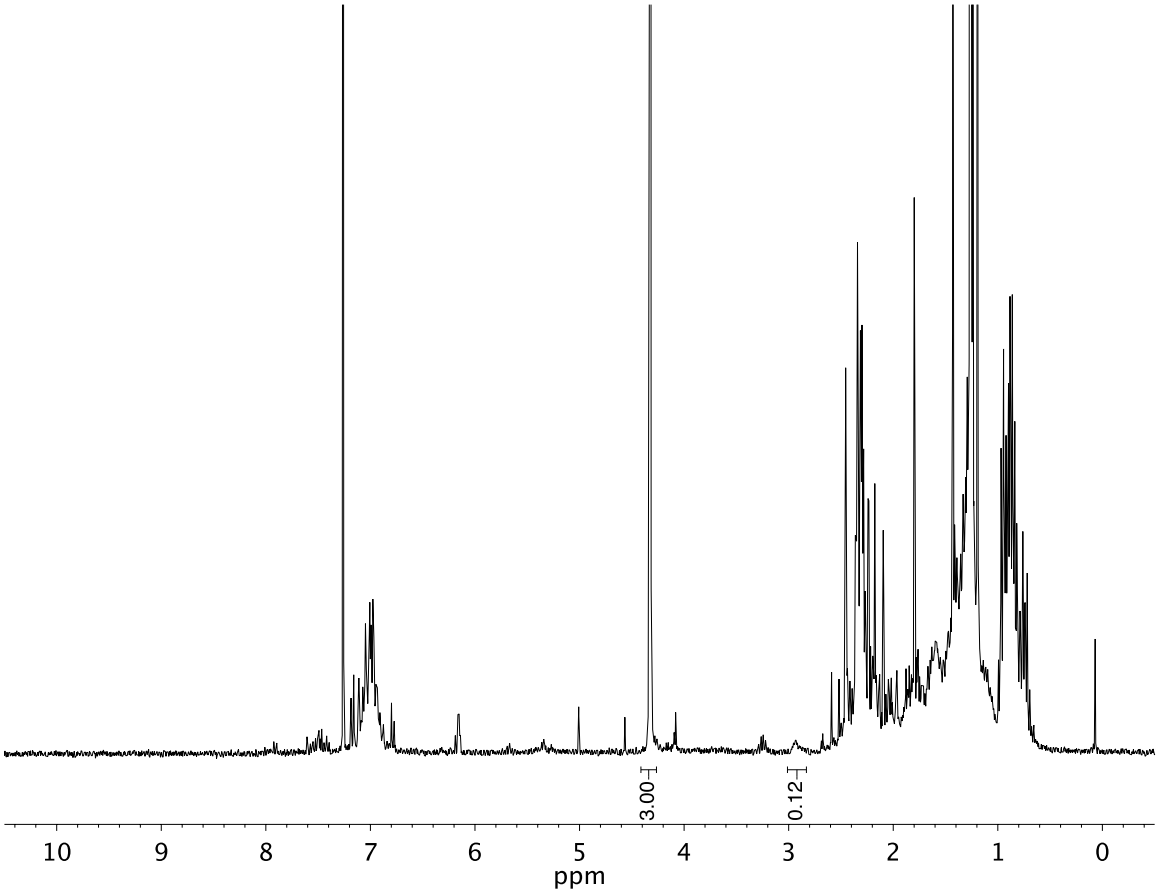
In order to probe for C–H insertion reactivity without halide nucleophilic attack, trifluoroborate salt of **34** was oxidized electrochemically in a divided cell according to the following procedure.



To both cells of an oven dried divided cell (fine glass frit) with an oven dried stir bar in each half-cell was added freshly dried under P_2O_5 $TBABF_4$ (395 mg, 1.20 mmol, 24 equiv) as the electrolyte (increased concentration of electrolyte was used due to the increased resistance of the divided cell). To each half-cell was added freshly distilled acetonitrile (3.0 mL). To the cathodic side was added water (20uL, 1.1 mmol, 22 equiv). To the anodic side was added (2-butyl-1-(2,4-dimethylphenyl)hex-1-en-1-yl)trifluoro-λ^4-borane, potassium salt (**34**) (17.5 mg, 0.050 mmol, 1 equiv). To the cathodic side was quickly placed the platinum electrode. To the anodic side was quickly placed the carbon electrode. Each solution was degassed by bubbling nitrogen with stirring (~300 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a cell potential of 3.5V was applied (enough potential to observe 1-2 mA of current) for 1 hour. After electrolysis was halted, a small aliquot from the anodic chamber (~20 uL) was taken, diluted with hexanes and water (1 mL hexanes:0.25mL water). The hexanes layer was analyzed by GC-FID (indicating a 5.5:1 ratio of desired product). The anode was rinsed with dichloromethane (3 x 4 mL) into the anodic solution, and the solution was concentrated to yield a yellow oil. This yellow oil was plugged through silica gel with diethyl ether. The diethyl ether was concentrated, and analyzed by ^1H

NMR with added 2.5uL of nitromethane as an internal standard (indicating a 12% yield of desired product). The ratio of these olefin isomers was further confirmed by GC-FID. Attempts to purify the mixture by chromatography failed, and so standards of the olefinic products were synthesized.

Additionally subjection of a mixture of **35.1** and **35.2** to the reaction mixtures showed ~65% consumption of the material (10 mg of the mixture/0.04 mmol). 1.25 uL of nitromethane was added as an internal standard indicating ~35% remaining material. (see spectrum below).



Crude 1H NMR indicating 12% NMR yield. (protons at 2.8–2.9 ppm correspond to tertiary allylic protons of **35.1** and **35.2**.

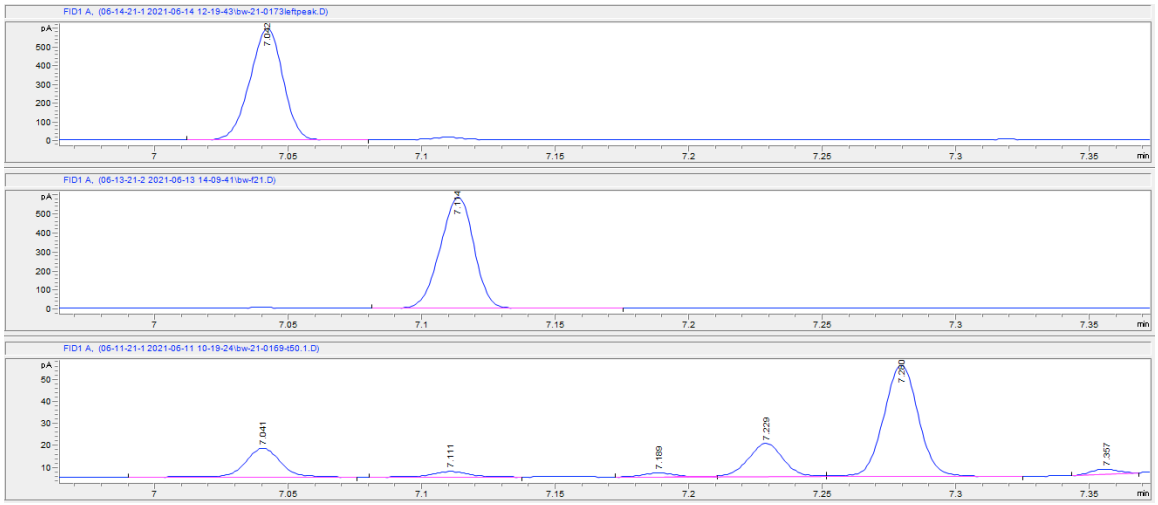


Figure 4.11 GC-FID Trace of pure **35.1** (top) and **35.2** (middle) and crude reaction (bottom).

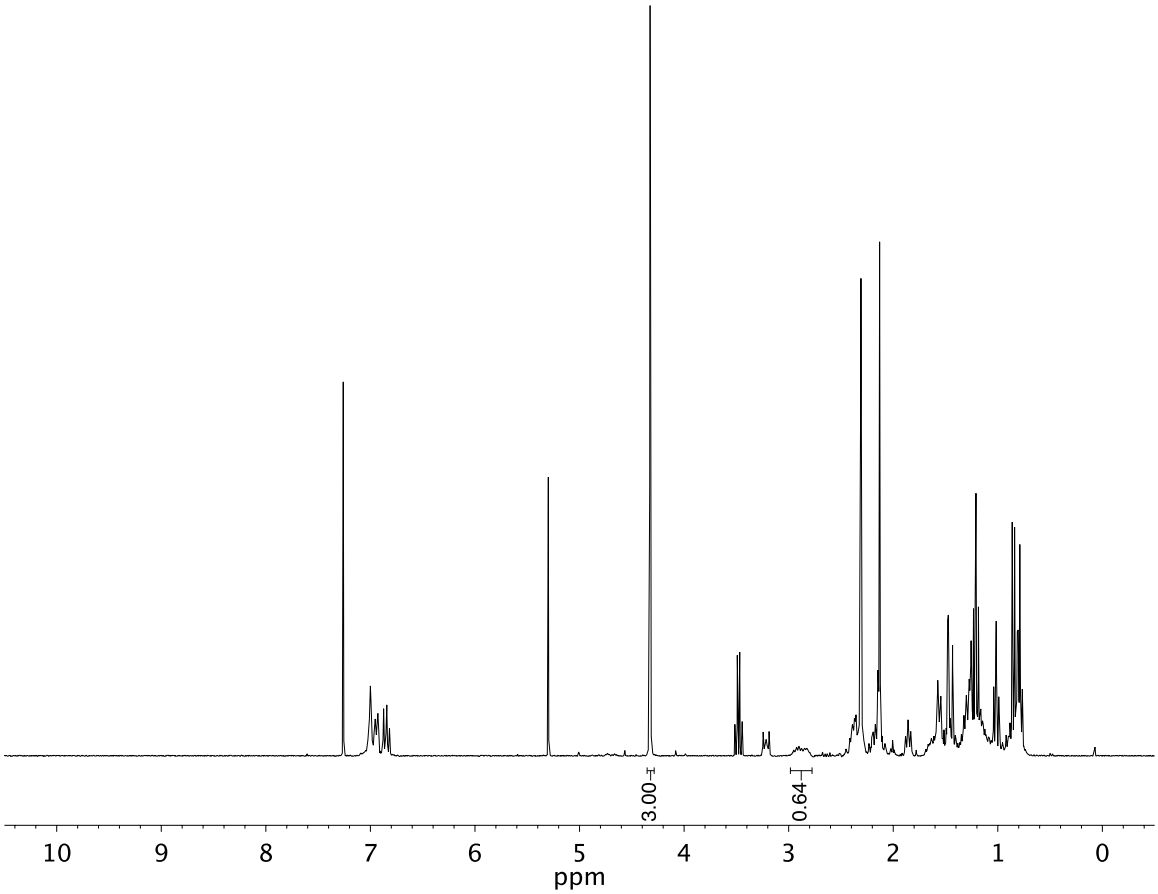


Figure 4.12 Crude 1H NMR with added 1.25uL of nitromethane as an internal standard of resubjected **(35.1)** and **(35.2)** to the reaction conditions after 15 minutes, indicating ~35% remaining starting material.

Additionally two control experiments were performed. The previous procedure for the divided cell electrolysis of **34** were replicated with the addition of 15uL of nonane as an internal standard to the anodic chamber. The solution was prestirred for 30 minutes after degassing and no production of **35.1** and **35.2** was observed (See GC-FID trace below). Then electrolysis was performed for 1 hour (See GC-FID below). To show that this process is promoted only by electrolysis and not BF_3 generated during the reaction an additional 0.05 mmol of **34** was added to the cathodic chamber after electrolysis was halted. This solution was stirred for an additional 2 hours, and the ratio of **35.1** and **35.2** remained unchanged relative to the added nonane internal standard (See GC-FID trace below).

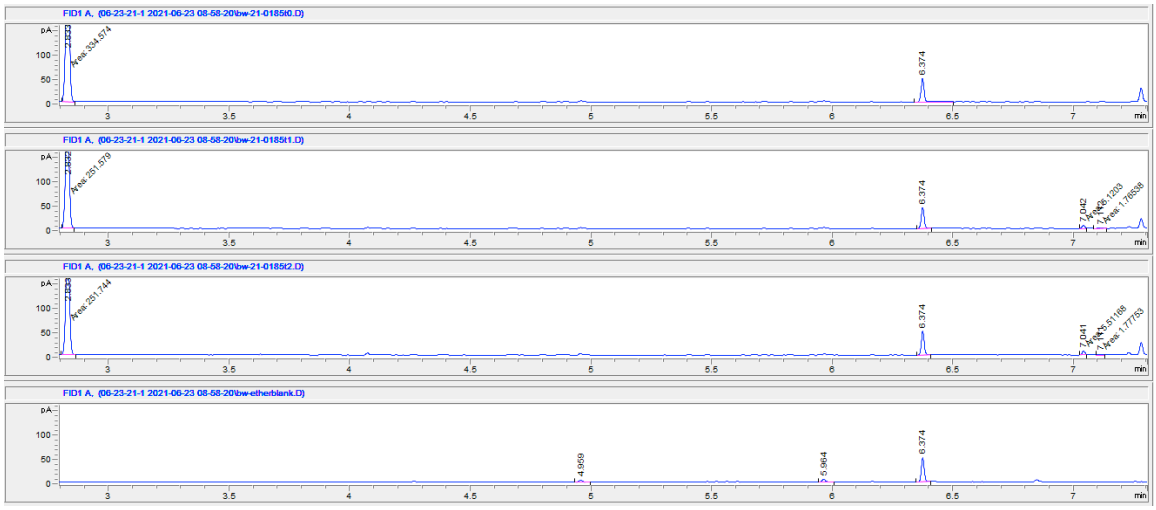


Figure 4.13

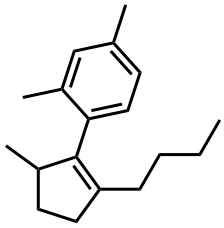
Top GC-FID trace: aliquot after stirring for 30 minutes after degassing

2nd to top GC-FID trace: aliquot after electrolysis for 1 hour

2nd to bottom GC-FID trace: aliquot after addition of more starting material and stirring for 2 hours.

Bottom GC-FID trace: diethyl ether blank (peak at 6.37 is the BHT stabilizer present in commercial samples of diethyl ether)

Characterization Data:



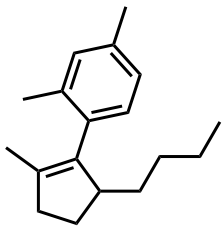
1-(2-butyl-5-methylcyclopent-1-en-1-yl)-2,4-dimethylbenzene (35.1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 – 6.98 (m, 1H), 6.94 (d, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 2.95 – 2.87 (m, *j*1H), 2.46 – 2.33 (m, 2H), 2.31 (s, 3H), 2.23 – 2.15 (m, 1H), 2.13 (s, 3H), 1.86 (t, *J* = 7.7 Hz, 2H), 1.46 (ddd, *J* = 15.5, 12.9, 7.0 Hz, 1H), 1.30 (p, *J* = 7.6 Hz, 2H), 1.23 – 1.10 (m, *J* = 6.7 Hz, 2H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.79 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 136.4, 135.9, 135.6, 130.7, 126.1, 34.1, 32.3, 30.4, 30.0, 29.4, 22.9, 21.4, 20.0, 14.3.

FT-IR (neat film NaCl): 2953, 2926, 2859, 1499, 1455, 1376, 815 cm^{-1}.

HR-MS (CI): Calculated for $C_{18}H_{26}$: [M]+ 242.2034; Measured: 242.2041.



1-(5-butyl-2-methylcyclopent-1-en-1-yl)-2,4-dimethylbenzene (35.2)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 2.83 (s, 1H), 2.45 – 2.33 (m, 2H), 2.31 (s, 3H), 2.18 – 2.14 (m, 1H), 2.13 (s, 3H), 2.11 – 2.0 (m, 1H), 1.54 – 1.49 (m, 1H), 1.48 (s, 3H), 1.36 – 0.96 (m, 6H), 0.80 (t, *J* = 7.0 Hz, 3H).

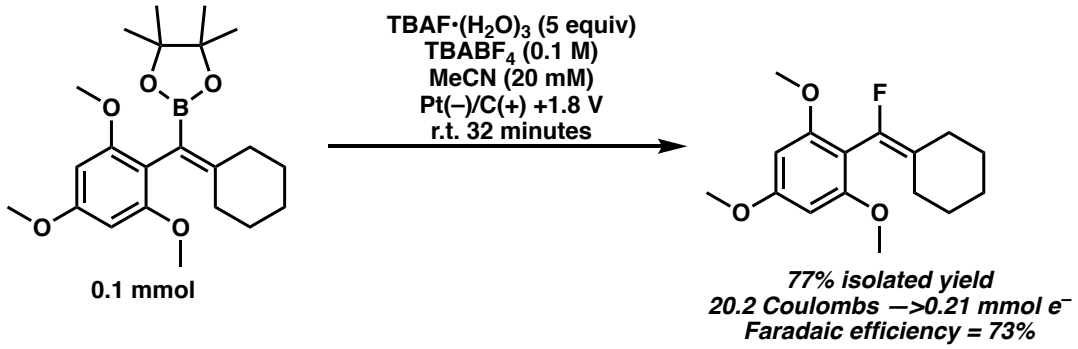
^{13}C NMR (126 MHz, $CDCl_3$) δ 136.4, 135.9, 135.6, 134.9, 130.8, 126.2, 37.3, 34.4, 30.4, 29.7, 23.2, 21.4, 20.0, 15.3, 14.5.

FT-IR (neat film NaCl): 2954, 2923, 2855, 1497, 1456, 1376, 817 cm^{-1}.

HR-MS (CI): Calculated [M]+ $C_{18}H_{26}$: 242.2034; Measured: 242.2043.

Coulometry Experiment

In order to determine the number of electrons required to generate the vinyl fluoride product, **SI-5** was subjected to bulk electrolysis with coulometry using a CHI600E potentiostat.



To an oven dried 20 mL scintillation vial equipped with a septum cap and stir bar was added **18S** (38.8 mg, 0.10 mmol, 1 equiv), $TBABF_4$ (198 mg, 0.6 mmol, 6 equiv), and $TBAF•(H_2O)_3$ (158 mg, 0.5 mmol, 5 equiv). To this was added freshly distilled MeCN (6 mL). The Pt(–), C(+), and SCE reference electrode were placed into the solution through the septum cap under nitrogen. The solution was degassed by bubbling nitrogen for 20 minutes with stirring (400 rpm). The electrodes were connected to the CHI600E potentiostat and a bulk electrolysis with coulometry was carried out at +1.8V *vs* SCE. The reaction was monitored carefully by TLC for full consumption of the starting material. After 32 minutes of electrolysis it was determined that the starting material had been consumed and the data collection and applied potential was halted. The electrodes were rinsed into the solution with dichloromethane and the reaction contents were concentrated *in vacuo*. The material was purified by flash column chromatography (50% dichloromethane:hexanes) to yield the vinyl fluoride **18** (21.6 mg, 77% yield).

20.2 coulombs had been passed, corresponding to 0.21 mmol of electrons at a Faradaic efficiency of 73%. (See graphs of current/charge vs. time below).

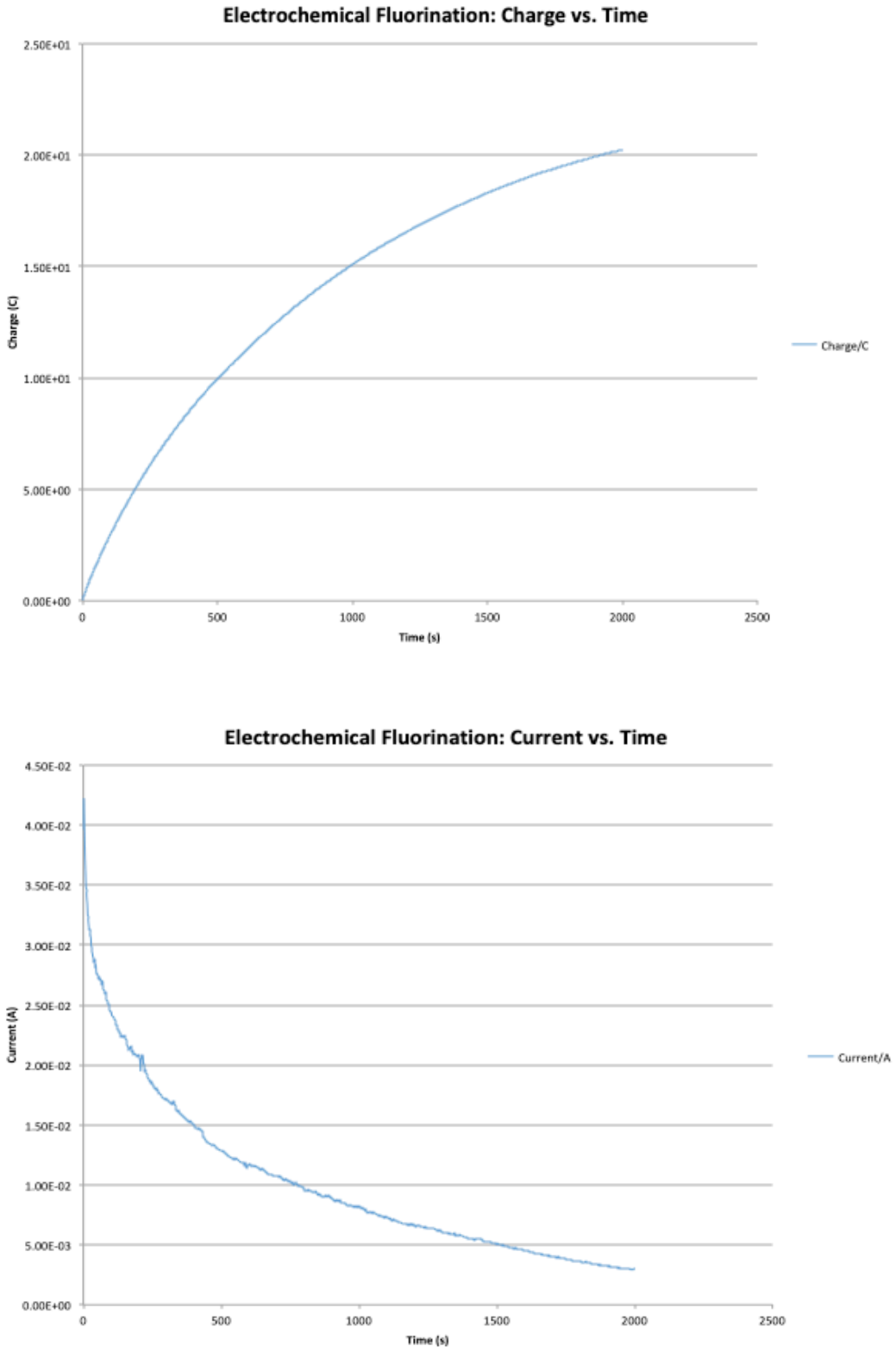
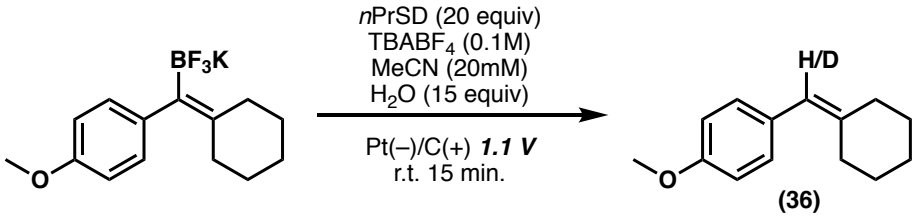


Figure 4.14 Bulk electrolysis coulometry plots

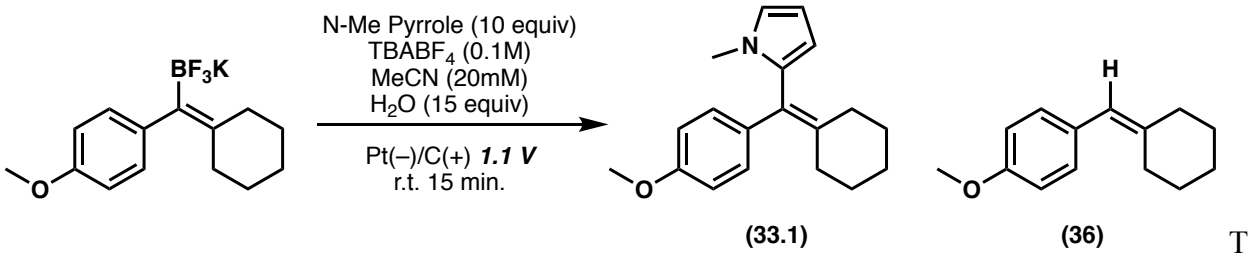
Vinyl Radical Trapping Experiments.



(36)

To an oven dried 2 dram vial equipped with an oven dried stir bar was added (cyclohexylidene(4-methoxyphenyl)methyl)trifluoro-λ^4-borane, potassium salt **(7)** (15.4 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv), water (15 uL, 15 equiv), deuterated propane thiol (77 mg, 20 equiv) as prepared by known methods.[19] The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of +1.8 V (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 5 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was purified by flash column chromatography (2% ether in hexanes) to yield **36** (6.0 mg, 60% yield) with 25% deuterium incorporation as determined by ^1H NMR and ^2D NMR. (See attached NMR spectra at end of SI section 6).

Additionally control experiments were also performed. The same reaction was performed without electrolysis and no styrene product was formed. Additionally, with 20 equivalents of added sodium propanethiolate and no electrolysis, the styrene product was also not formed indicating that electrolysis is necessary and this is likely not a simple protodeboronation process.



(33.1) **(36)**

To an oven dried 2 dram vial equipped with an oven dried stir bar was added (cyclohexylidene(4-methoxyphenyl)methyl)trifluoro-λ^4-borane, potassium salt (15.4 mg, 0.05 mmol, 1 equiv). To this was added the $TBABF_4$ (99.0 mg, 0.300 mmol, 6 equiv) and water (15 uL, 15 equiv). The electrodes [Pt(–)/C(+)] held in place by a septum cap were put in place. The vial was placed under a nitrogen atmosphere. Freshly distilled acetonitrile was added (2.5 mL) followed by N-Me pyrrole (41 mg, 0.50 mmol, 10 equiv). The solution was degassed by bubbling nitrogen with stirring (~400 rpm) for 20 minutes. After degassing the potentiostat (TACKLife MDC01 DC power supply) was connected to the electrodes and a constant working potential *vs.* a CHI-150 SCE electrode of ***+1.1 V*** (measured with a multimeter between the C(+) and reference CHI-50 SCE electrode) was applied for 15 minutes. Upon completion the applied potential was halted and the electrodes were removed from solution and rinsed with dichloromethane (3 x 4 mL). The resulting solution was concentrated *in vacuo* to yield a brown oil. The crude material was plugged through a pipette of silica gel with ether. ^1H NMR analysis of this mixture with added 1.5 uL of nitromethane as an internal standard showed product **(33.1)** and styrene **(36)** in 11% and 78% yield respectively (See spectrum below). **(36)** was isolated by flash column chromatography (2% ether in hexanes) and matched known literature spectra. Styrene product integration at ~6.2 ppm and pyrrole addition product integration ~7.2 ppm.

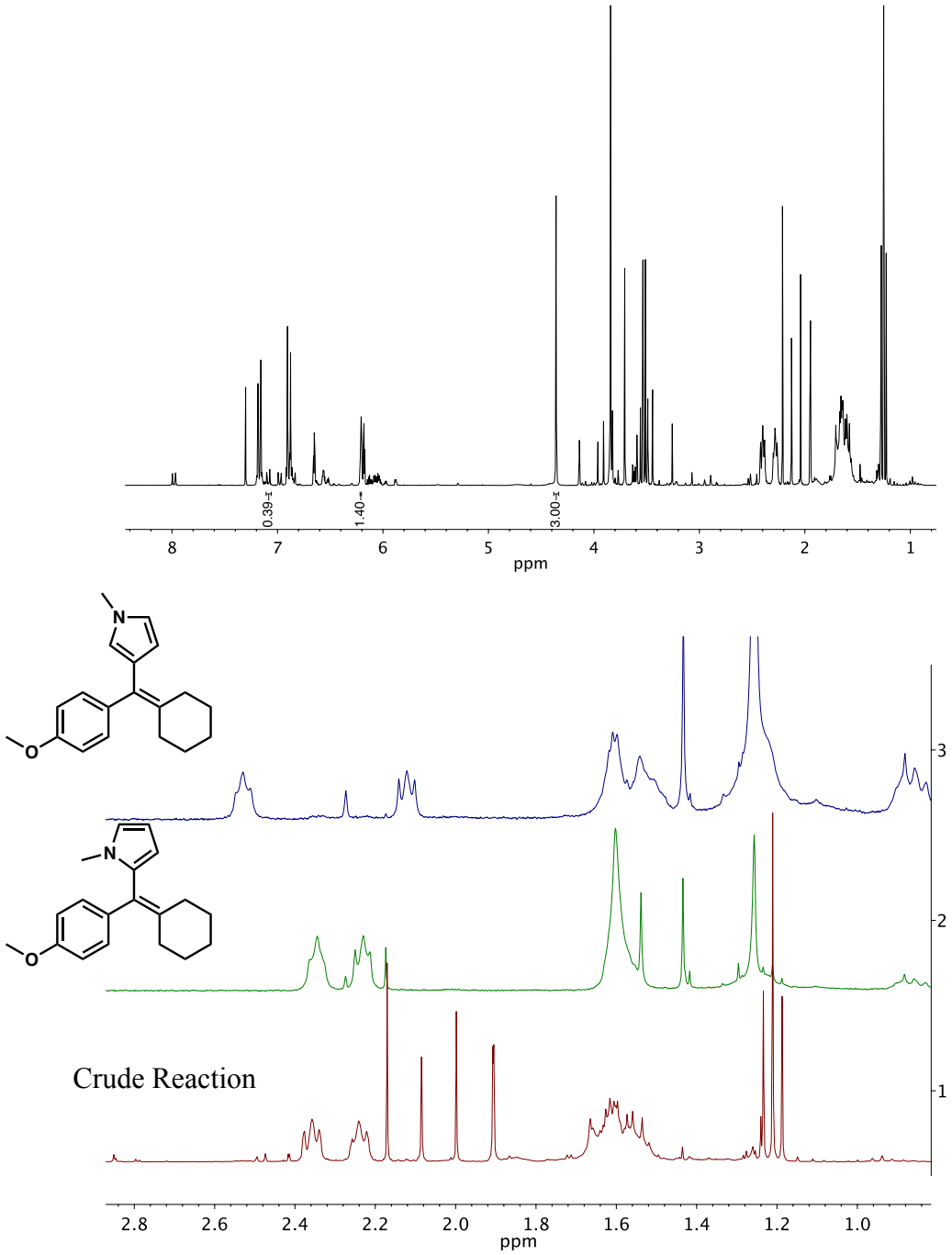


Figure 4.15 Zoomed in view of crude ^{1}H NMR showing no production of the C-3 arylation product. Highlighting allylic protons around 2.0–2.5 ppm. (top 3-addition product, middle 2-addition product, bottom-crude reaction mix).

4.7.6 DFT Calculations

HOMO/Oxidation Potential Calculations

The experimental redox potential of vinyl trifluoroborate **30**, which held the potassium counter ion in the actual experiment, was observed at +1.12 V *vs* SCE. Based on the computational studies, the redox potential from **30** to **31** was 1.04 V *vs* SCE.

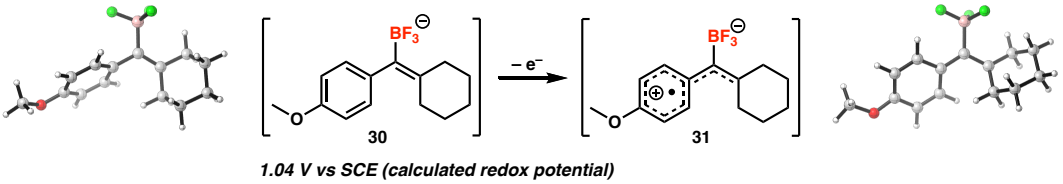


Figure 4.16. Calculated redox potential (uM06-2X/6-311++G(d,p) cpcm=acetonitrile // uM06-2X/6-31+G(d,p) cpcm=acetonitrile)

Intermediate	Electronic Energy (EE)	Zero-Point Energy Correction (ZPE)	EE + Thermal Enthalpy Correction (H)	EE + Thermal Free Energy Correction (G)
30	-943.329406 Hartree	0.291981 Hartree	-943.018678 Hartree	-943.084409 Hartree
31	-943.131918 Hartree	0.292935 Hartree	-942.820389 Hartree	-942.885658 Hartree

Table 4.2. Energies for the intermediates of Figure S1 (uM06-2X/6-31+G(d,p) in CPCM=acetonitrile)

Intermediate	Electronic Energy (EE)	EE + Thermal Free Energy Correction (6-31+G(d,p)) (G)
30	-943.554296 Hartree	-943.309299 Hartree
31	-943.354815 Hartree	-943.108555 Hartree

Table 4.3. Single point energies for the intermediates of Figure S1 (uM06-2X/6-311++G(d,p) in CPCM=acetonitrile)

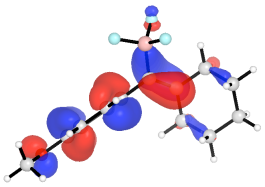


Figure 4.17. HOMO of vinyl trifluoroborate anion (**30**) (uM06-2X/6-31+G(d,p) cpcm=acetonitrile)

Cartesian coordinates for structures of Figure 12, Figure 11, Table 1. (optimized with uM06-2X/6-31+G(d,p) in CPCM=acetonitrile)

Vinyl trifluoroborate anion (7)

Charge: -1

C	3.44265900	-0.45088400	0.21190900
C	2.84105800	0.08002700	-0.93120400
C	1.47870300	0.39252800	-0.90736700
C	0.68260700	0.17618600	0.22129900
C	1.31865300	-0.35061500	1.35810400
C	2.67326400	-0.66175500	1.36103400
H	3.15401000	-1.06893000	2.24549600
H	0.73330400	-0.52037400	2.25868300
C	-0.76761300	0.53371900	0.22222100
C	-1.70599100	-0.41875300	0.41348500
C	-3.18852300	-0.10584700	0.45174600
H	-3.57901400	-0.39222100	1.44167600
C	-3.96022800	-0.90389600	-0.61066300
C	-3.70126300	-2.40463500	-0.47014700
C	-2.20234900	-2.70355200	-0.51766800
C	-1.43390400	-1.90403400	0.54871900
H	-1.76956200	-2.24334100	1.54131900
H	-0.36572900	-2.12161100	0.47855400
H	-2.02055700	-3.77557000	-0.38033100
H	-1.81217600	-2.43582400	-1.50946600
H	-4.10568700	-2.75038400	0.49207100
H	-4.22674300	-2.96046600	-1.25494900
H	-3.63859700	-0.57267800	-1.60778600
H	-5.03265700	-0.69149300	-0.53246700
H	-3.36364400	0.96386500	0.33004800
B	-1.15141900	2.10473400	-0.00066000
F	0.00989700	2.90734600	-0.18214000
F	-1.85737500	2.64550900	1.11831300
F	-1.97759800	2.30302700	-1.14985200
H	1.02431900	0.81645500	-1.79930600
H	3.41191600	0.25825000	-1.83501900
O	4.76388000	-0.78724800	0.30203900
C	5.57053800	-0.58254600	-0.84572400
H	5.20979700	-1.17719100	-1.69216700
H	6.57326700	-0.90858400	-0.57312100
H	5.59382100	0.47581600	-1.12759100

There are no imaginary frequencies

Vinyl trifluoroborate radical (INT31)

Charge: 0

C	3.50461900	-0.55980300	0.16630800
C	3.04586200	0.50767200	-0.62991700

C	1.70721900	0.84295800	-0.61058700
C	0.75732800	0.10226200	0.14828300
C	1.26263200	-0.97334100	0.94595000
C	2.59541000	-1.28964100	0.96742100
H	2.98020400	-2.08994000	1.58979300
H	0.58054400	-1.52620300	1.58360300
C	-0.63172500	0.44941700	0.16745000
C	-1.61113100	-0.53189400	0.39272400
C	-2.97069100	-0.20863200	0.93149900
H	-3.10764500	-0.83404200	1.82626900
C	-4.07375600	-0.58115000	-0.08433400
C	-3.94846800	-2.03794600	-0.52217700
C	-2.55011900	-2.31987600	-1.06687700
C	-1.45797700	-1.96475700	-0.03047000
H	-1.59905400	-2.60992100	0.84896600
H	-0.47108000	-2.16023700	-0.45114300
H	-2.43769800	-3.37333900	-1.33839100
H	-2.37993000	-1.72921800	-1.97562100
H	-4.14589900	-2.69769600	0.33309600
H	-4.69868900	-2.26693700	-1.28605200
H	-3.98414800	0.08264500	-0.95142400
H	-5.04818300	-0.39195100	0.37583500
H	-3.04838100	0.83389200	1.23350000
B	-1.17708000	2.02203700	0.00573200
F	-0.23100600	2.87447600	-0.58483300
F	-1.46463900	2.49573800	1.30567300
F	-2.35099300	2.04759600	-0.77157200
H	1.36242600	1.66764000	-1.21921300
H	3.72914100	1.07170800	-1.25200400
O	4.77623000	-0.94989700	0.23522100
C	5.75799500	-0.25915600	-0.54129500
H	5.53146300	-0.34571400	-1.60696800
H	6.70257400	-0.75074900	-0.32119400
H	5.80646800	0.79208700	-0.24676500

There are no imaginary frequencies

4.7 Spectra Relevant to Chapter Four:

Electrochemical Generation of Vinyl Carbocations from Alkenyl Boronates

Benjamin Wigman, Woojin Lee, Wenjing Wei, K. N. Houk and Hosea M. Nelson *Angew. Chem. Int. Ed.* **2022**, *61*, e202113972.

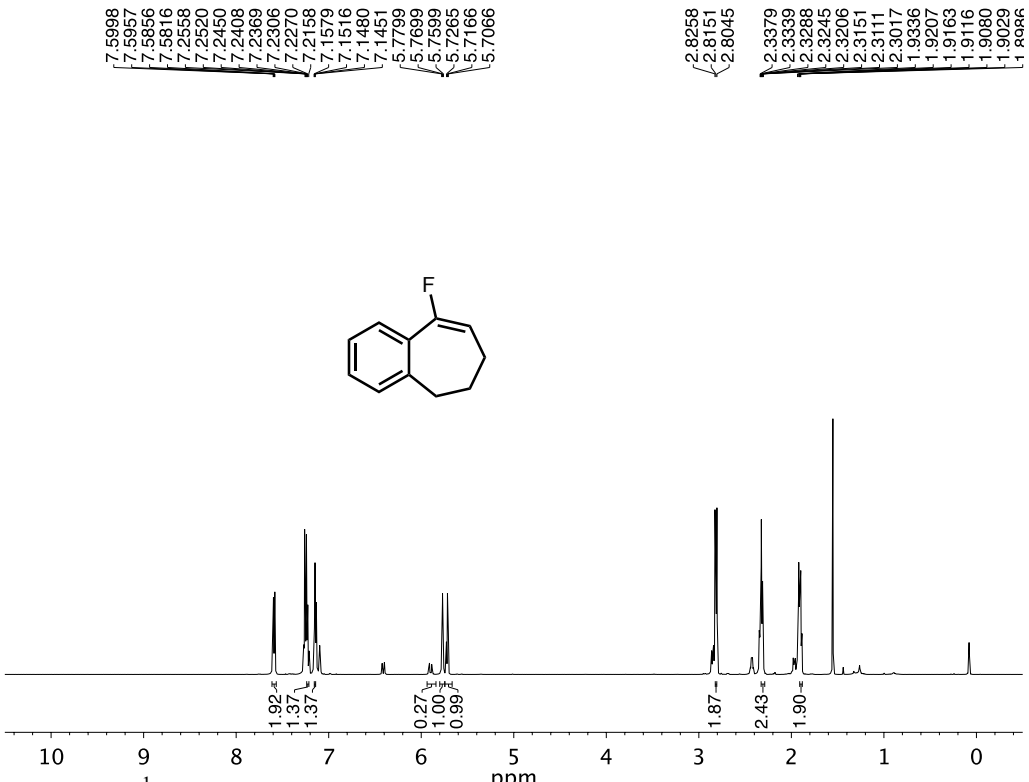


Figure 4.18 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.4** mixed with the styrene.

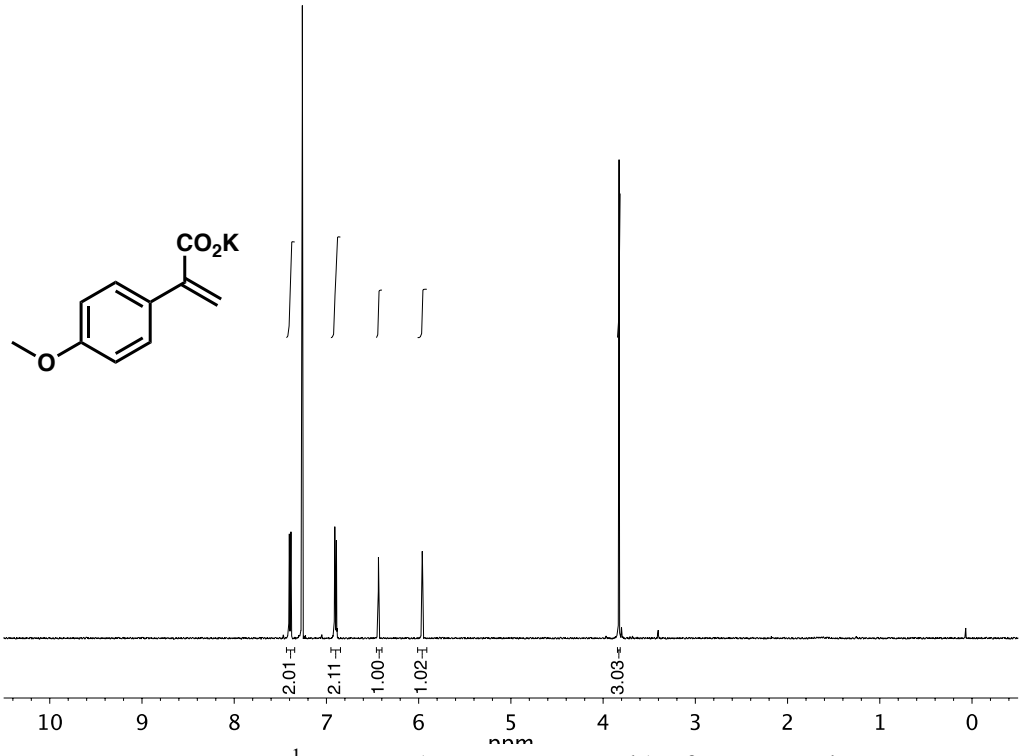


Figure 4.19 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.5.**

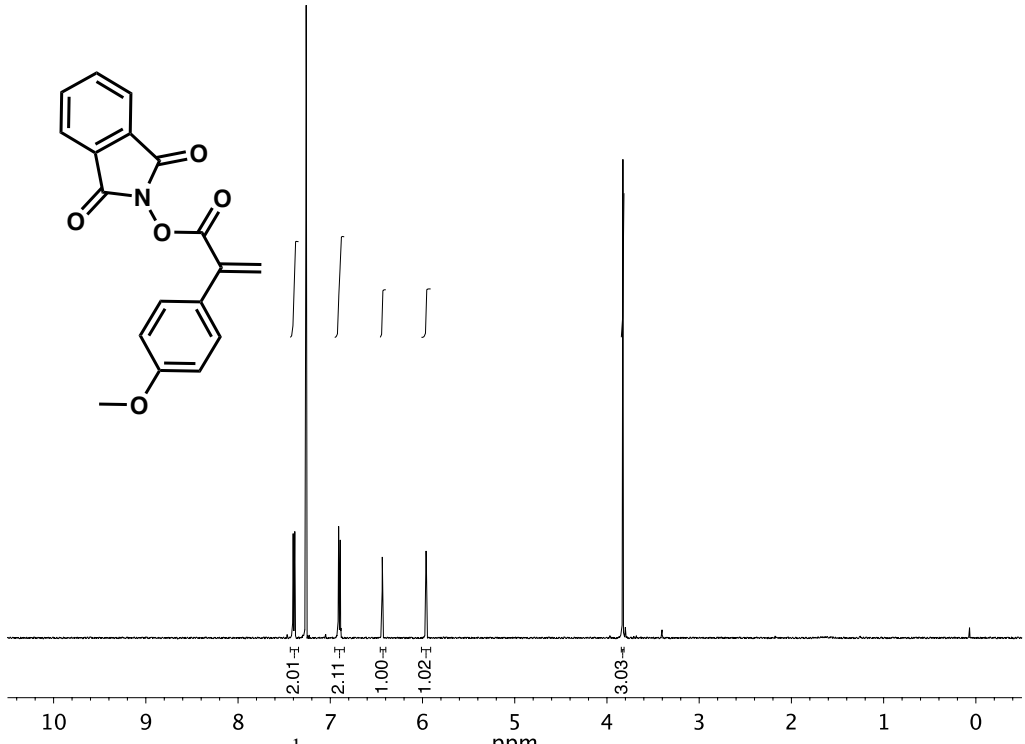


Figure 4.20 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.6**.

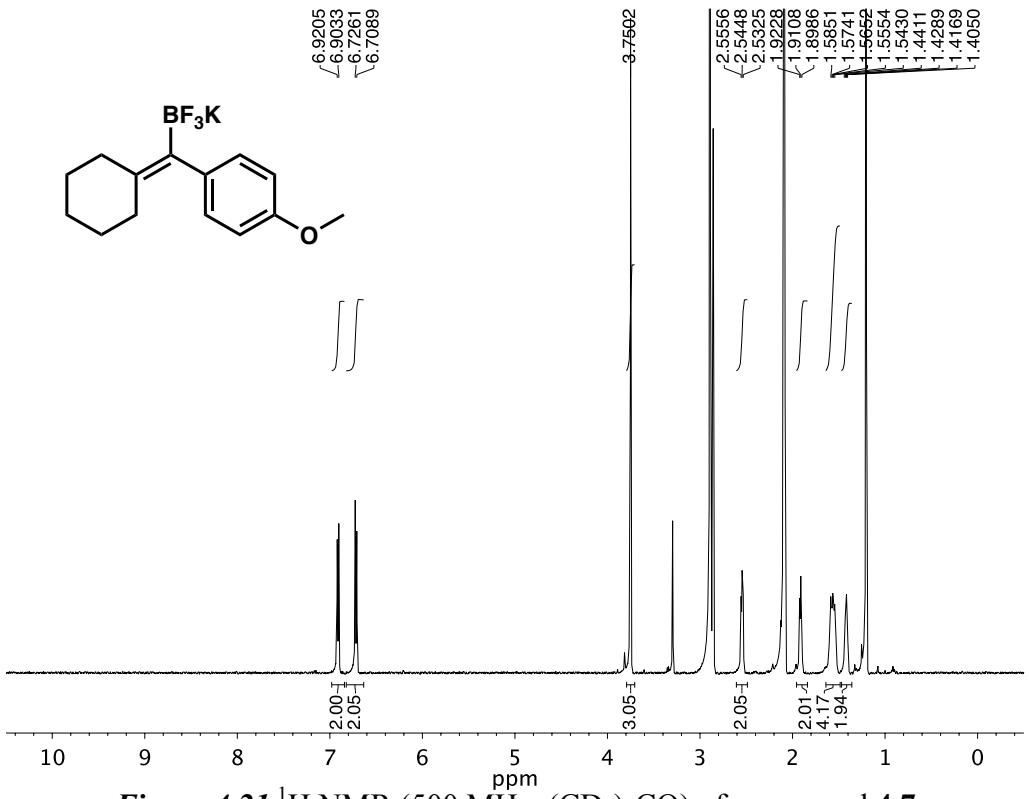


Figure 4.21 ^{1}H NMR (500 MHz, $(CD_3)_2CO$) of compound **4.7**

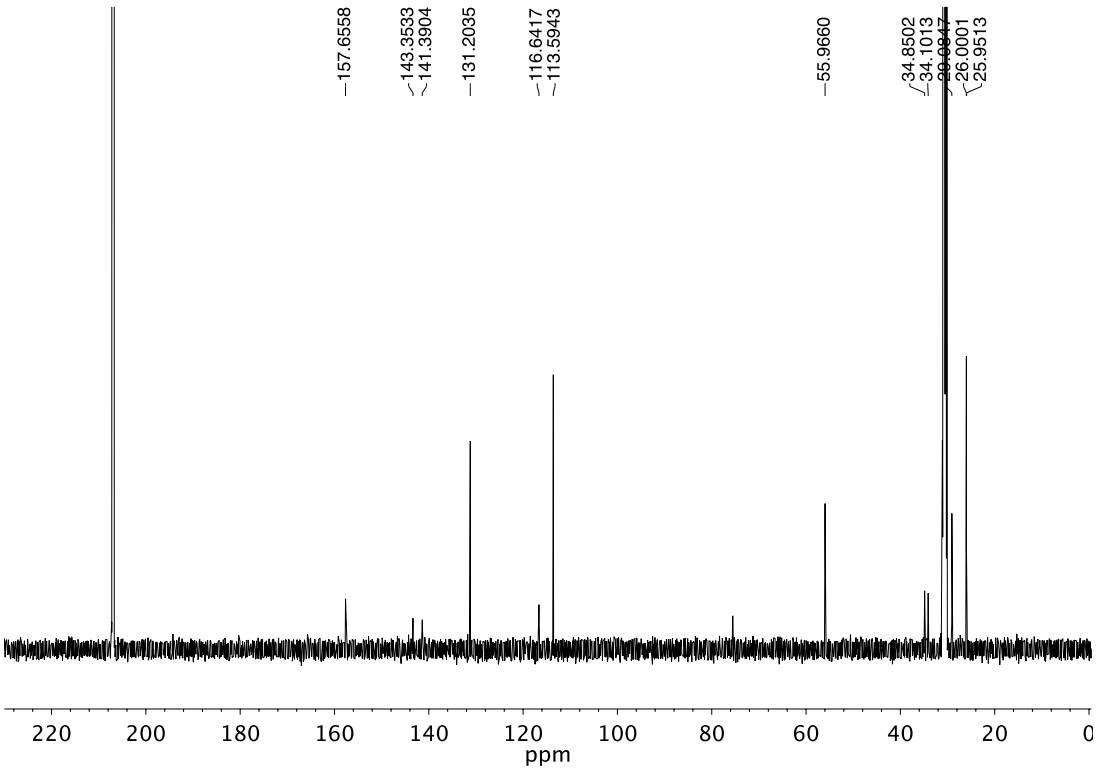


Figure 4.22 ^{13}C NMR (126 MHz, $(CD_3)_2CO$) of compound **4.7.**

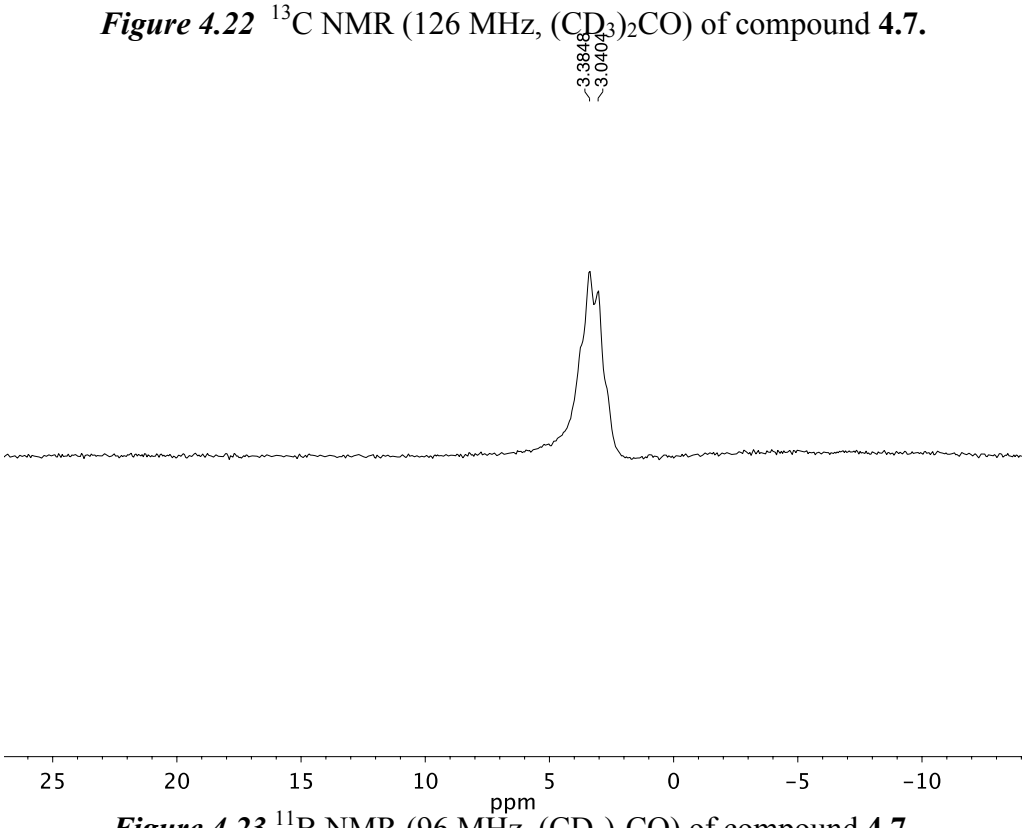


Figure 4.23 ^{11}B NMR (96 MHz, $(CD_3)_2CO$) of compound **4.7.**

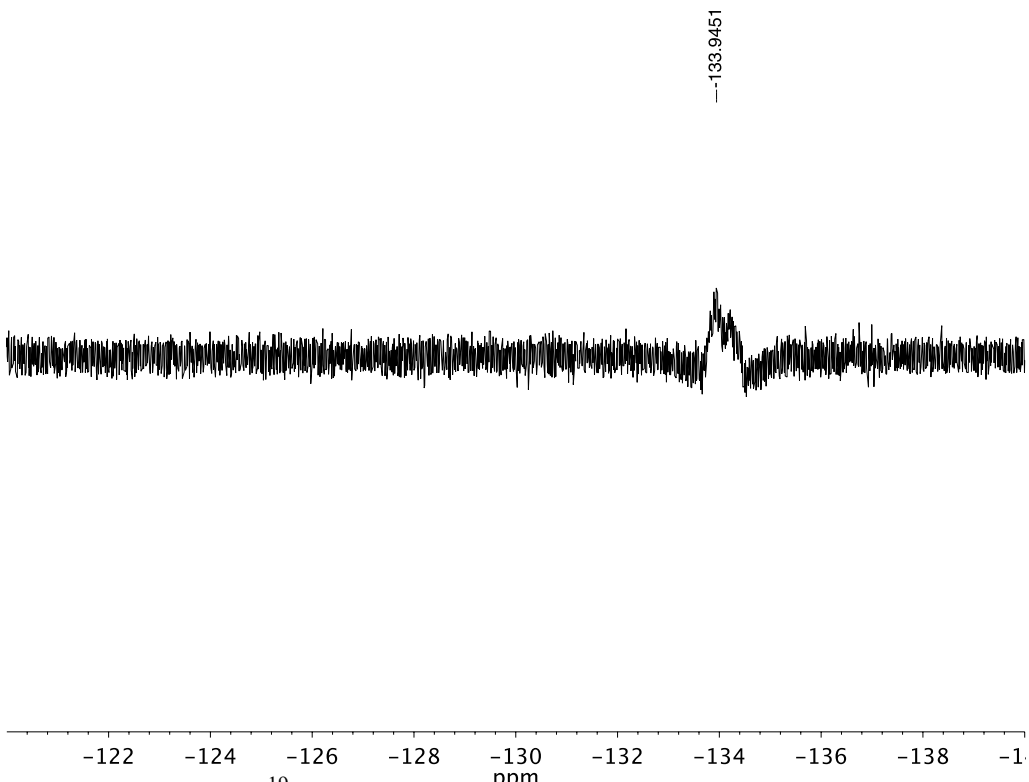


Figure 4.24 ^{19}F NMR (282 MHz, $(CD_3)_2CO$) of compound **4.7.**

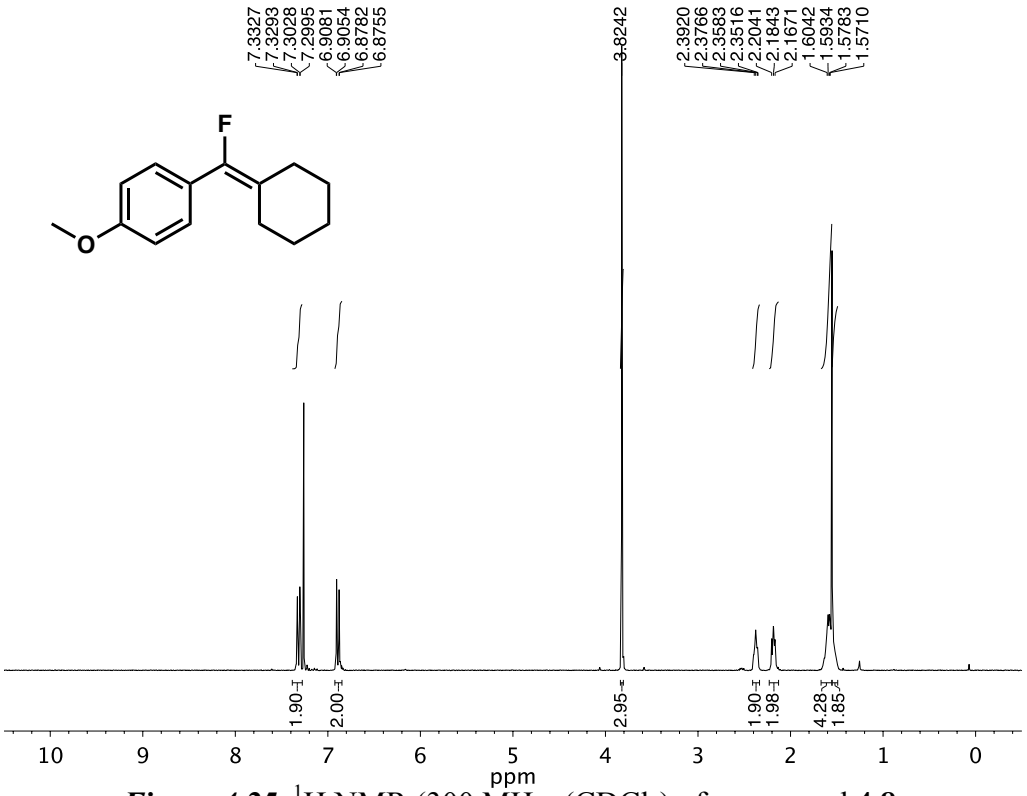


Figure 4.25 ^{1}H NMR (300 MHz, $(CDCl_3)$) of compound **4.8.**

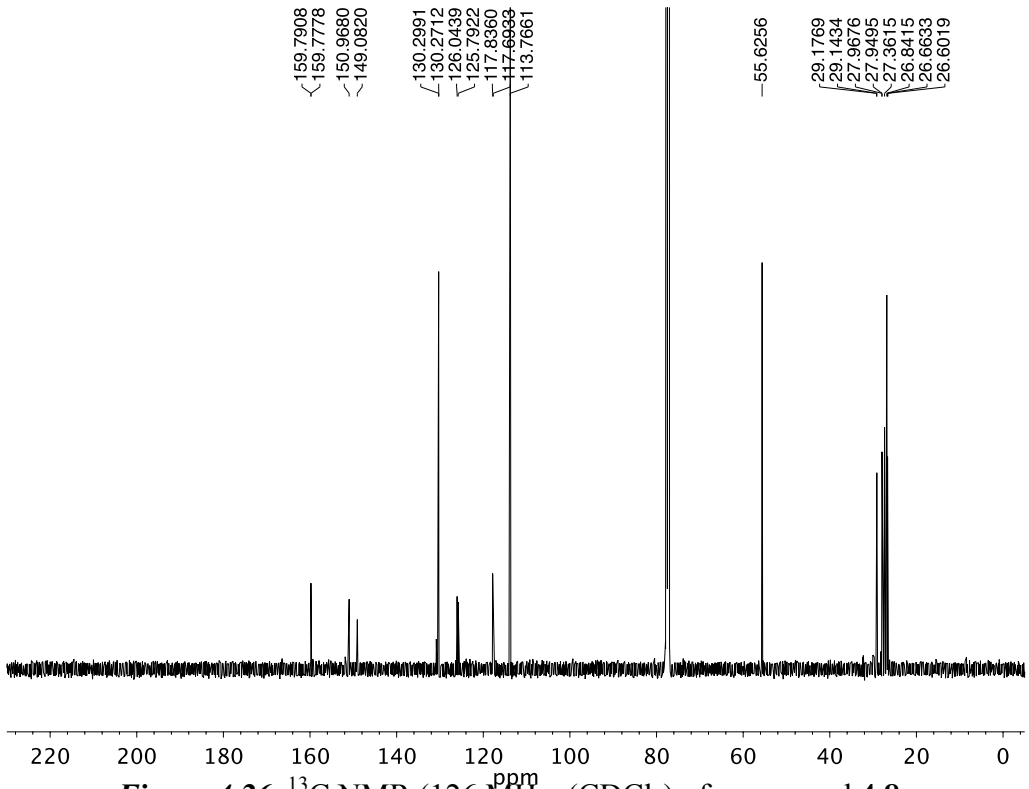


Figure 4.26 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.8**.

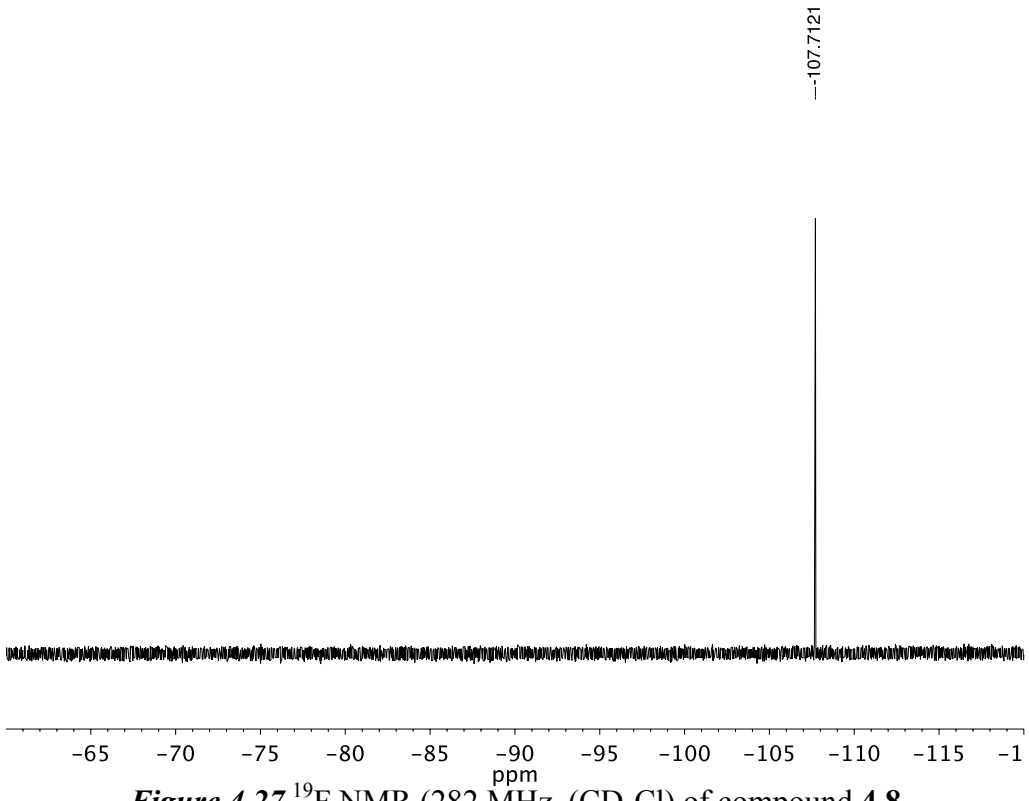


Figure 4.27 ^{19}F NMR (282 MHz, (CD_3Cl) of compound **4.8**

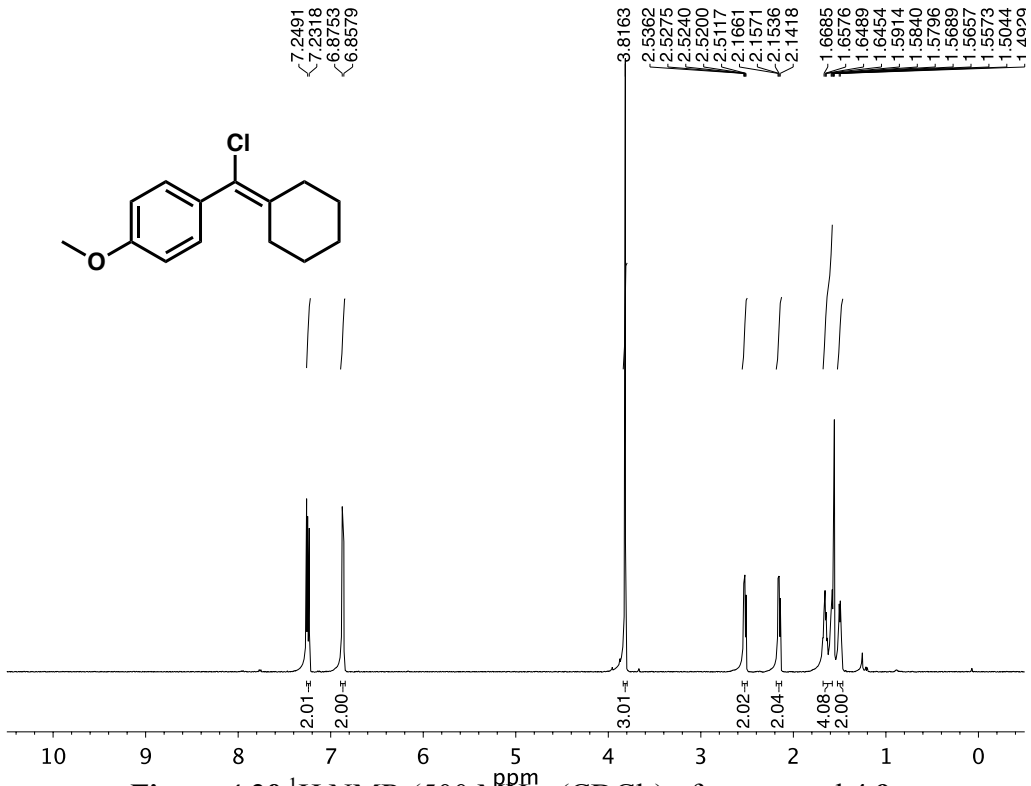


Figure 4.28 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.9.**

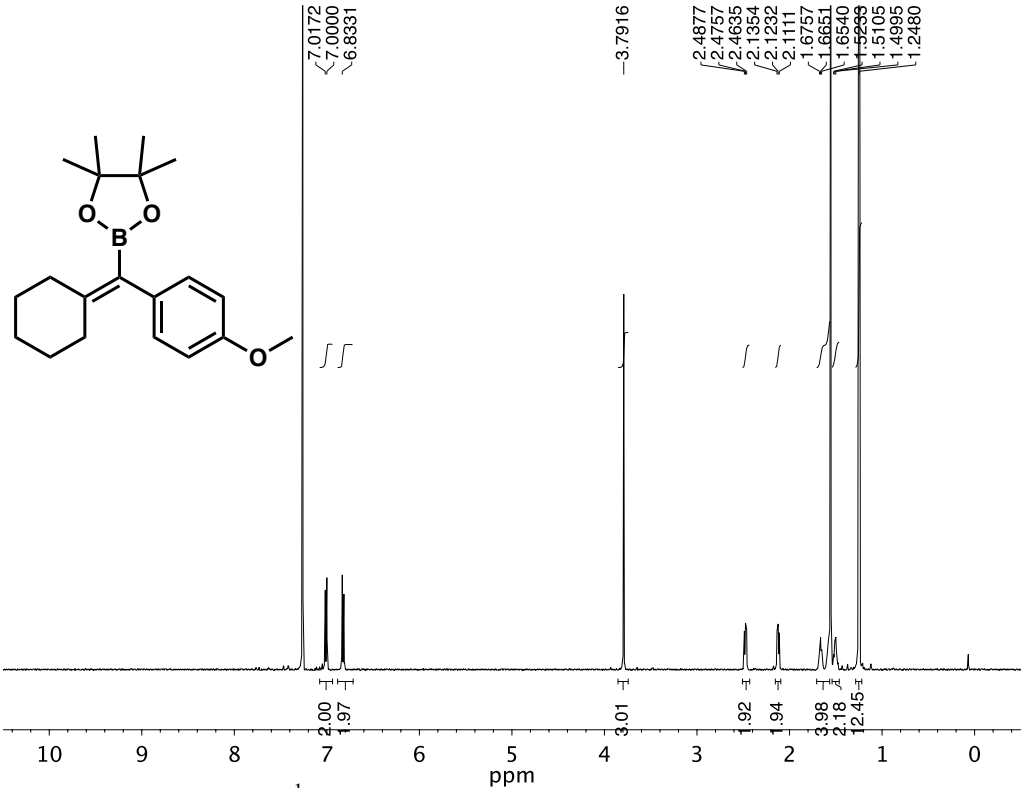


Figure 4.29 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4.10**

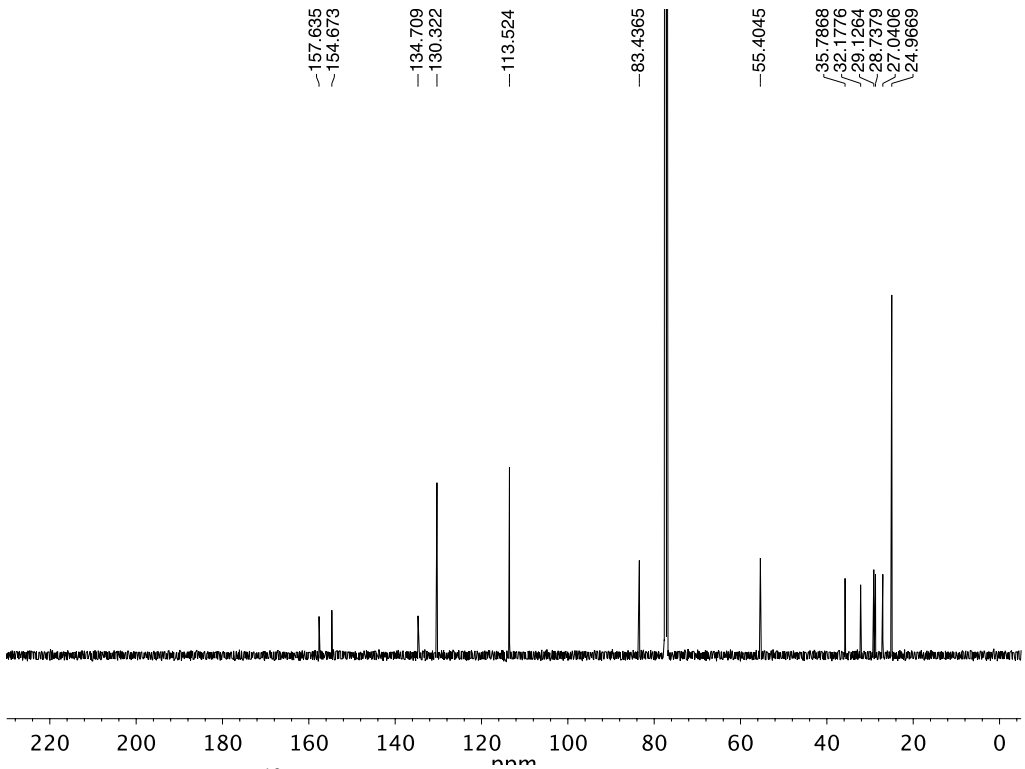


Figure 4.30 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.10**.

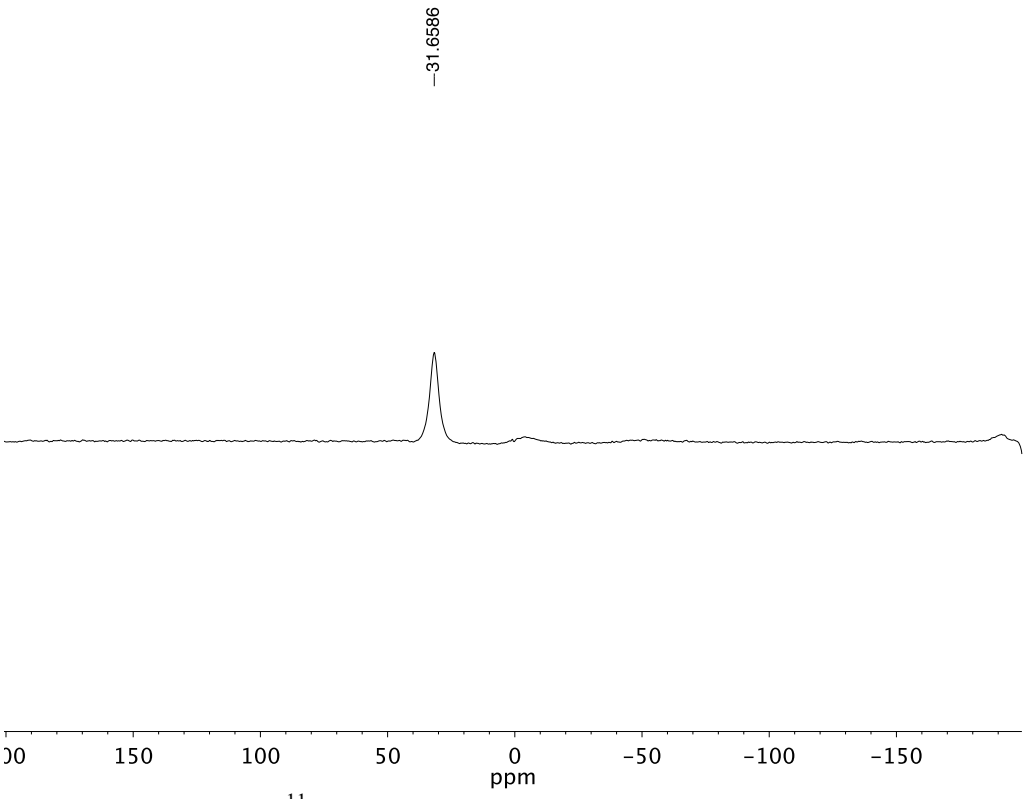


Figure 4.31 ^{11}B NMR (128 MHz, $CDCl_3$) of compound **4.10.**

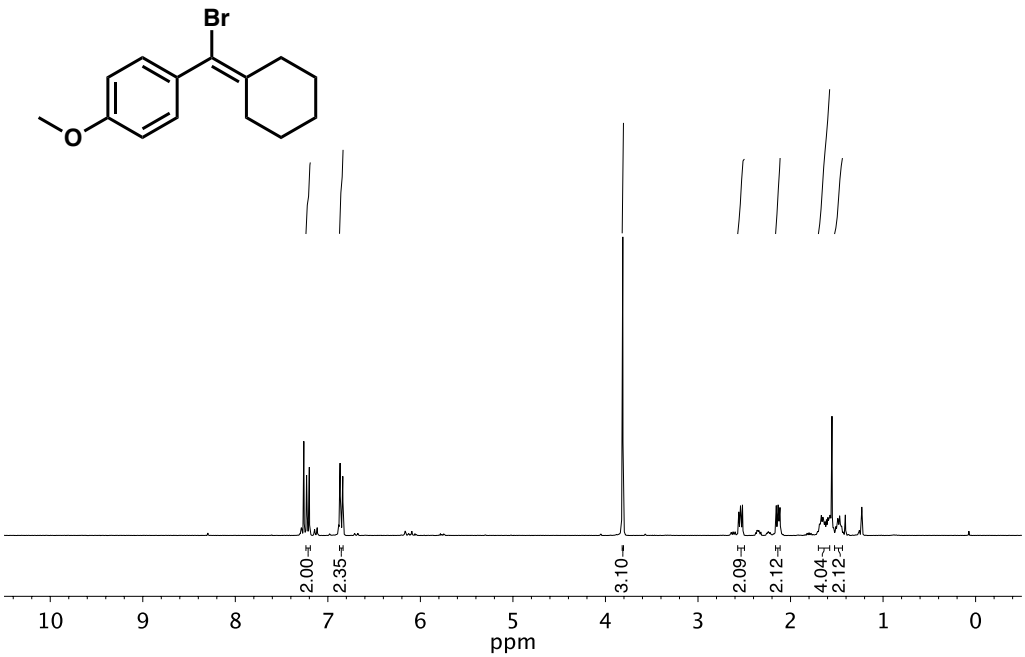


Figure 4.32 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.11.**

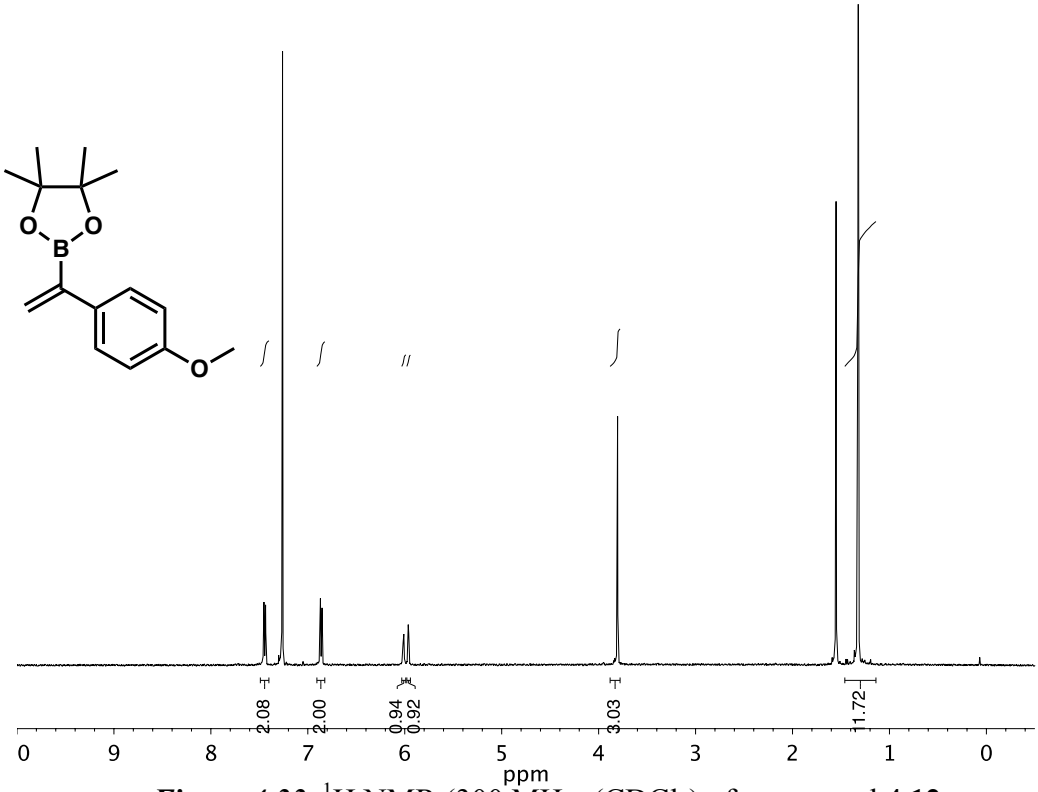


Figure 4.33 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.12.**

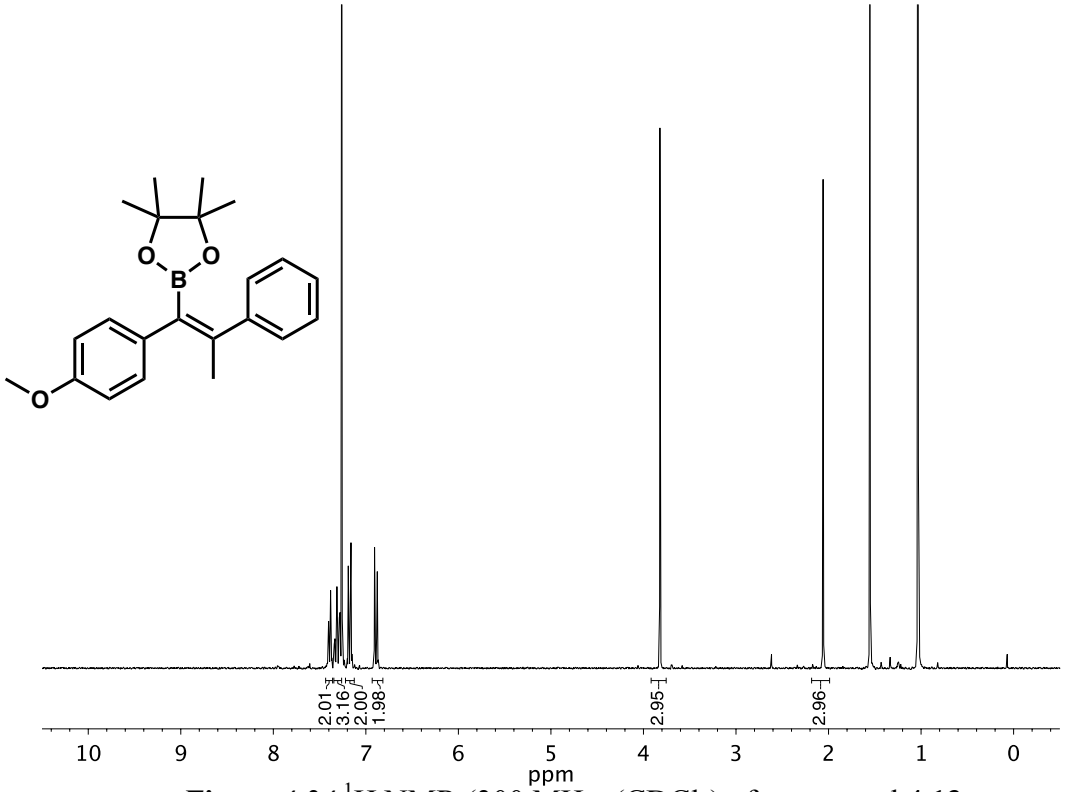


Figure 4.34 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.13.**

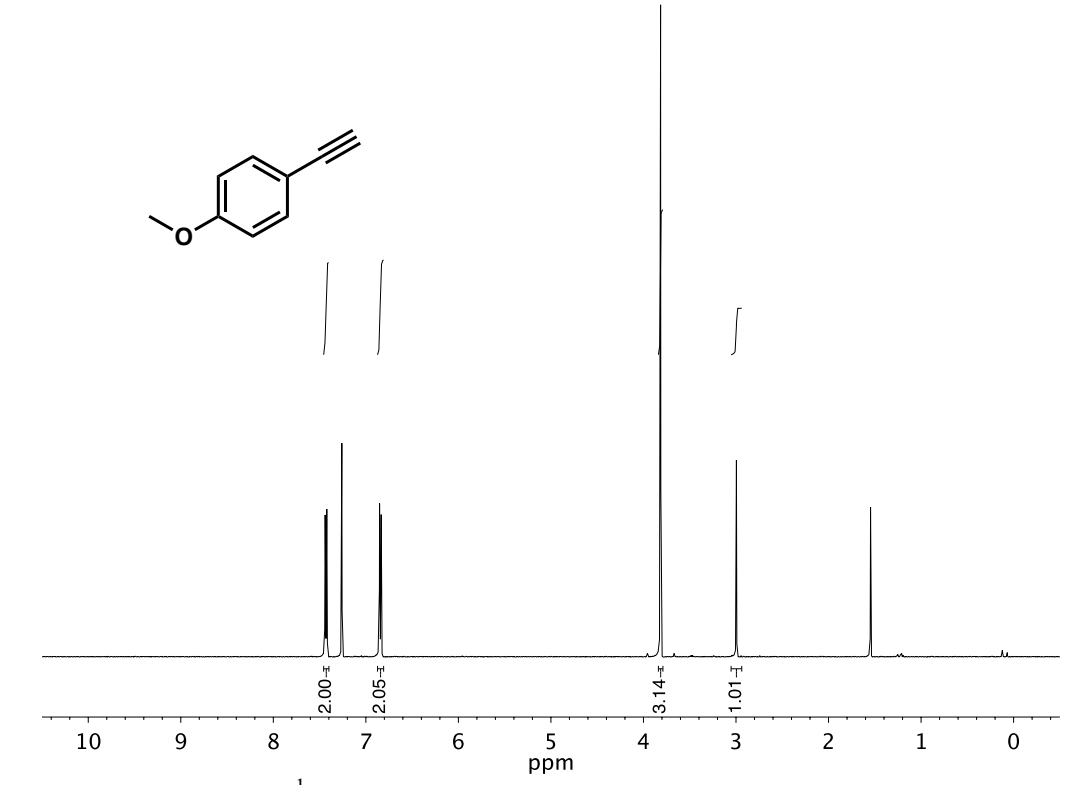


Figure 4.35 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.14.**

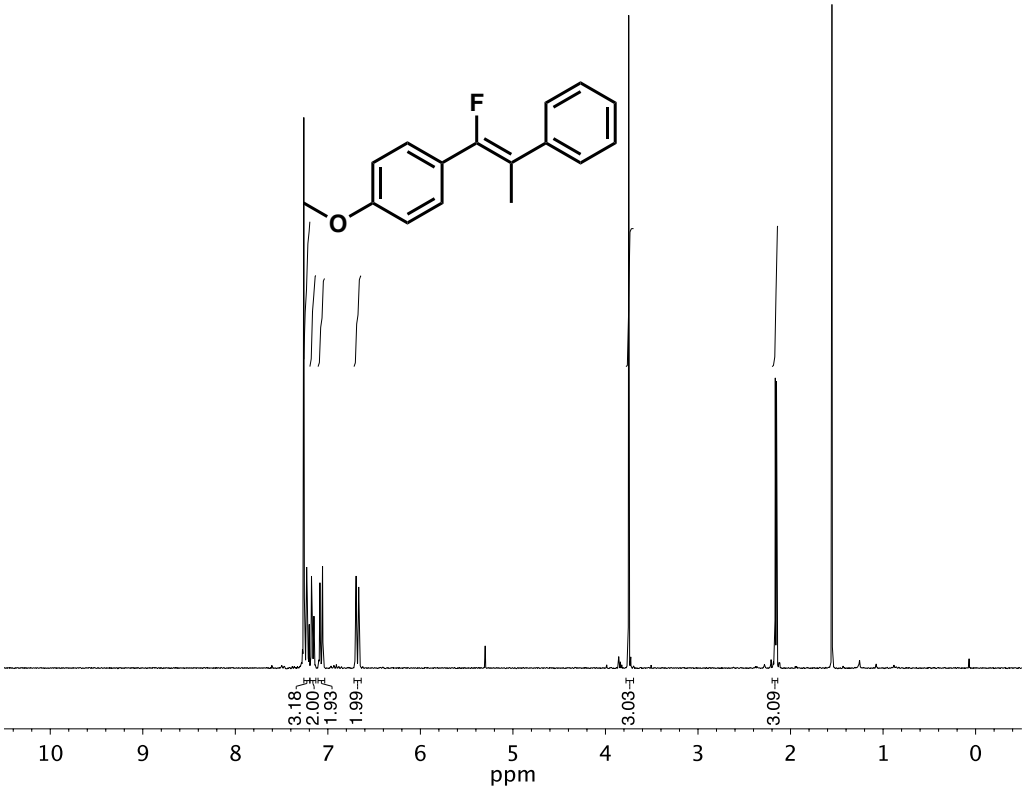


Figure 4.36 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.16.**

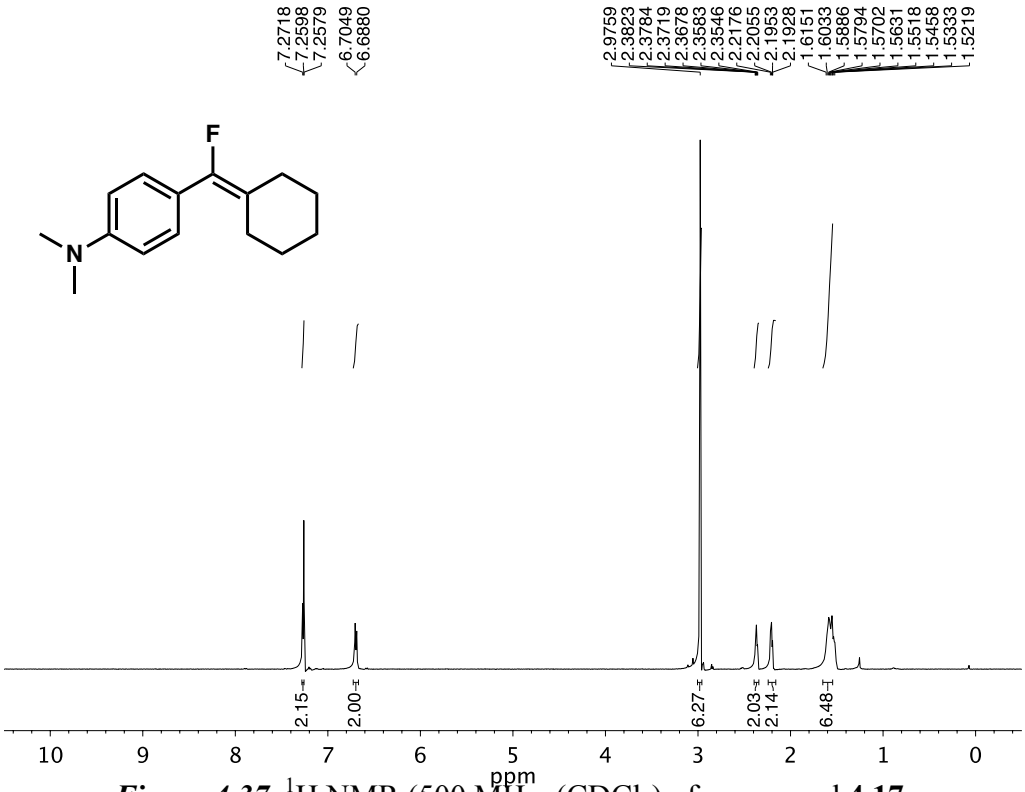


Figure 4.37 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.17.**

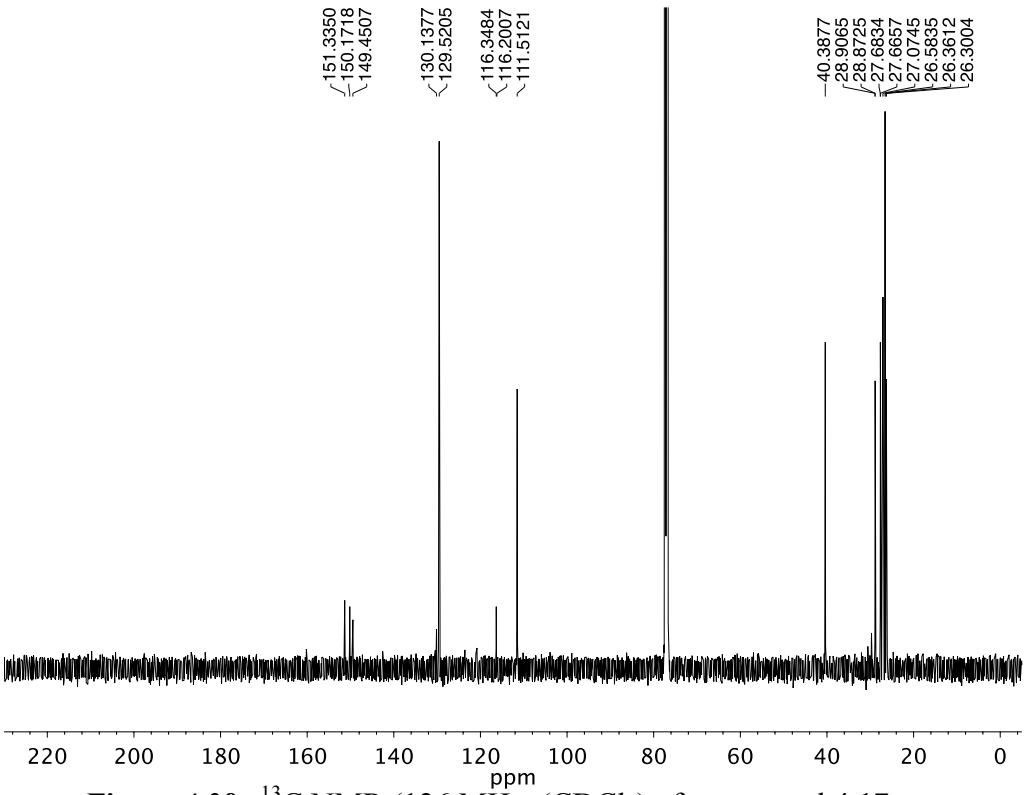


Figure 4.38 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.17.**

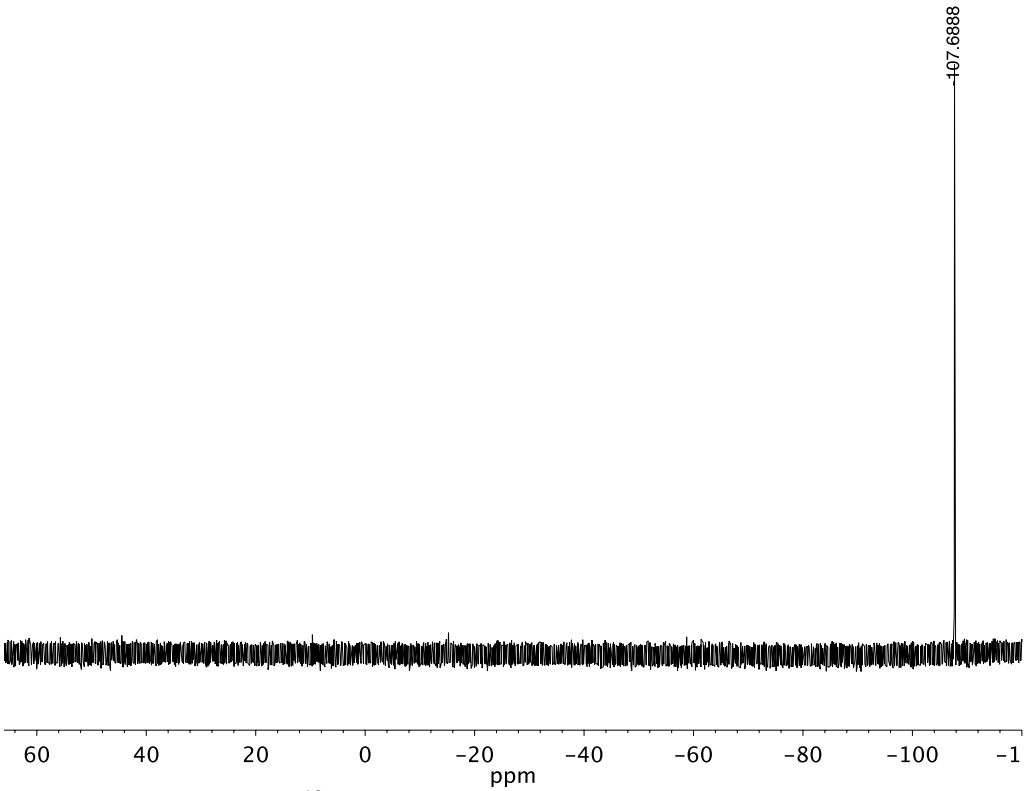


Figure 4.39 ^{19}F NMR (376 MHz, (CD_3Cl) of compound **4.17.**

Figure 4.40 ^{1}H NMR (400 MHz, ($CDCl_3$) of compound **4.18**.

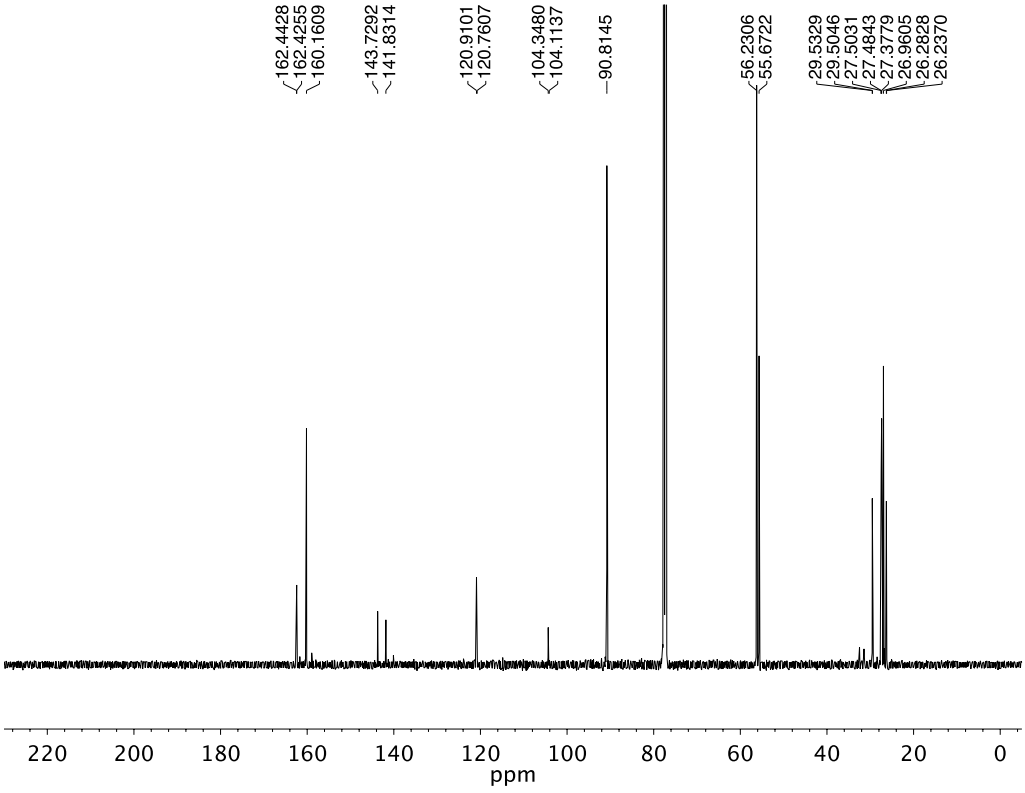


Figure 4.41 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.18.**

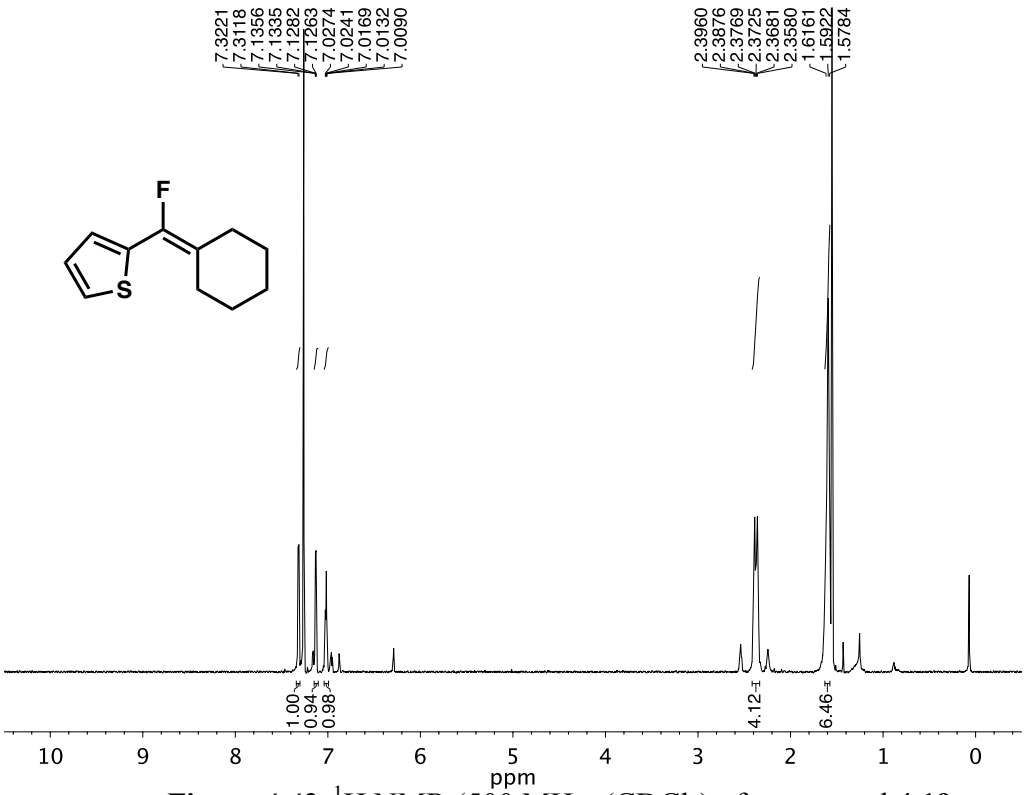


Figure 4.42 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.19.**
(*Note: styrene impurity not integrated)*

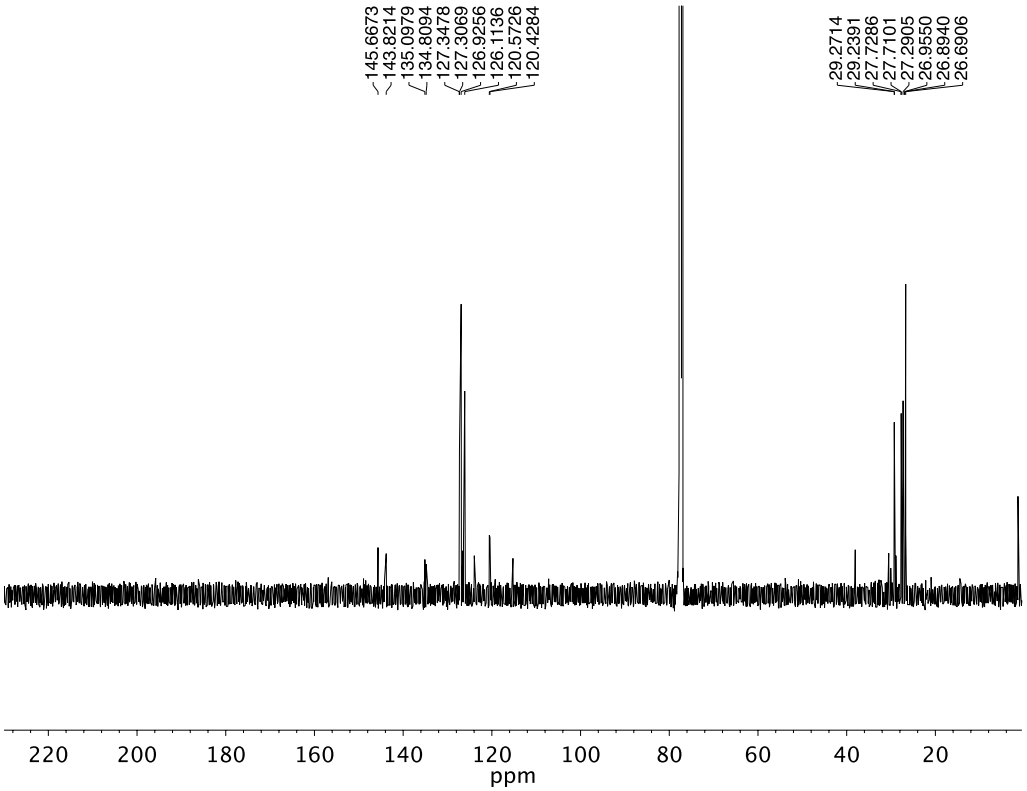


Figure 4.43 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.19**
(Note: styrene impurity peaks not selected for clarity)

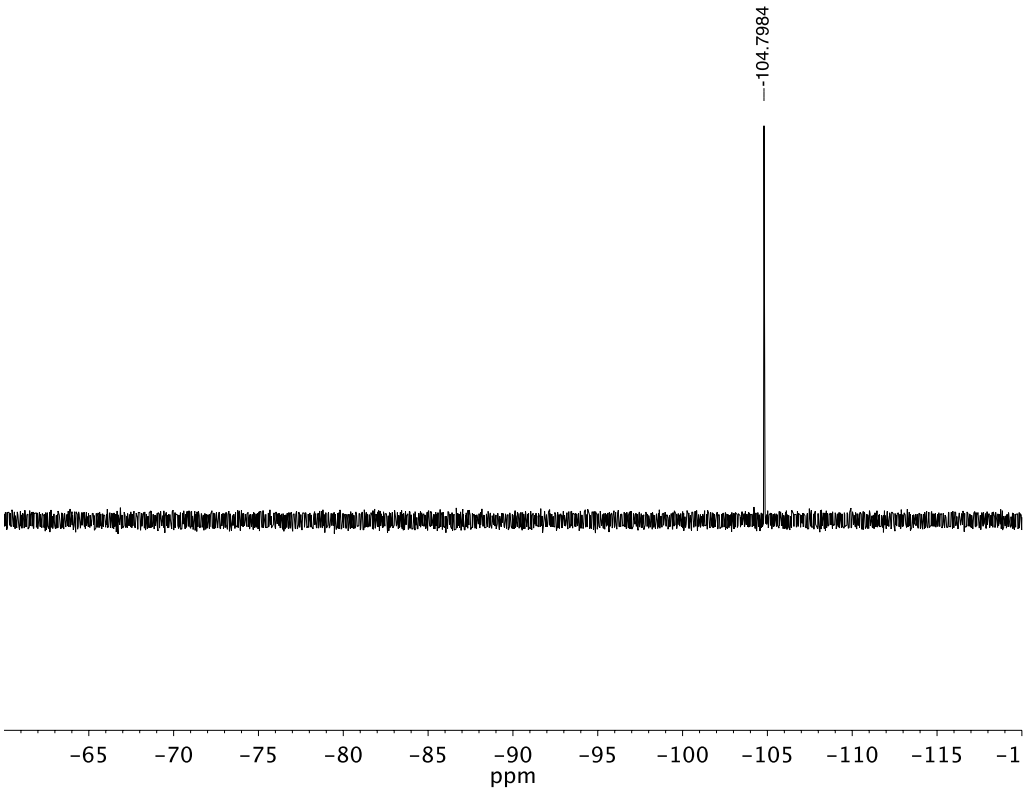


Figure 4.44 ^{19}F NMR (282 MHz, (CD_3Cl) of compound **4.19.**

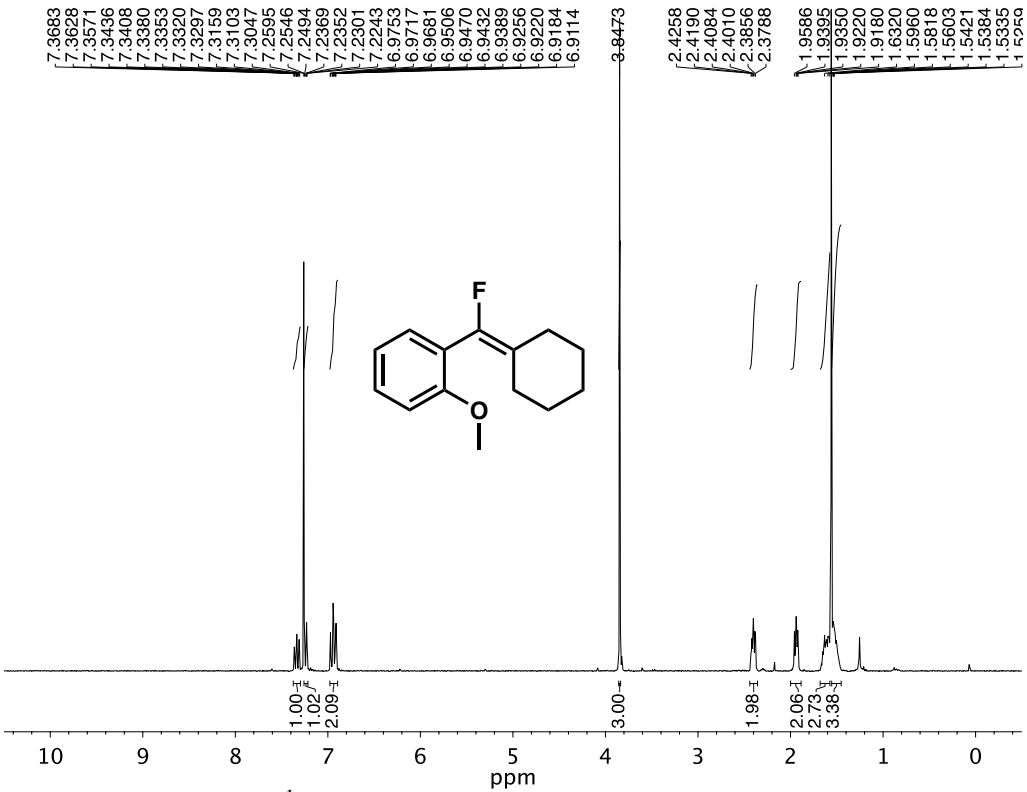


Figure 4.45 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.20.**

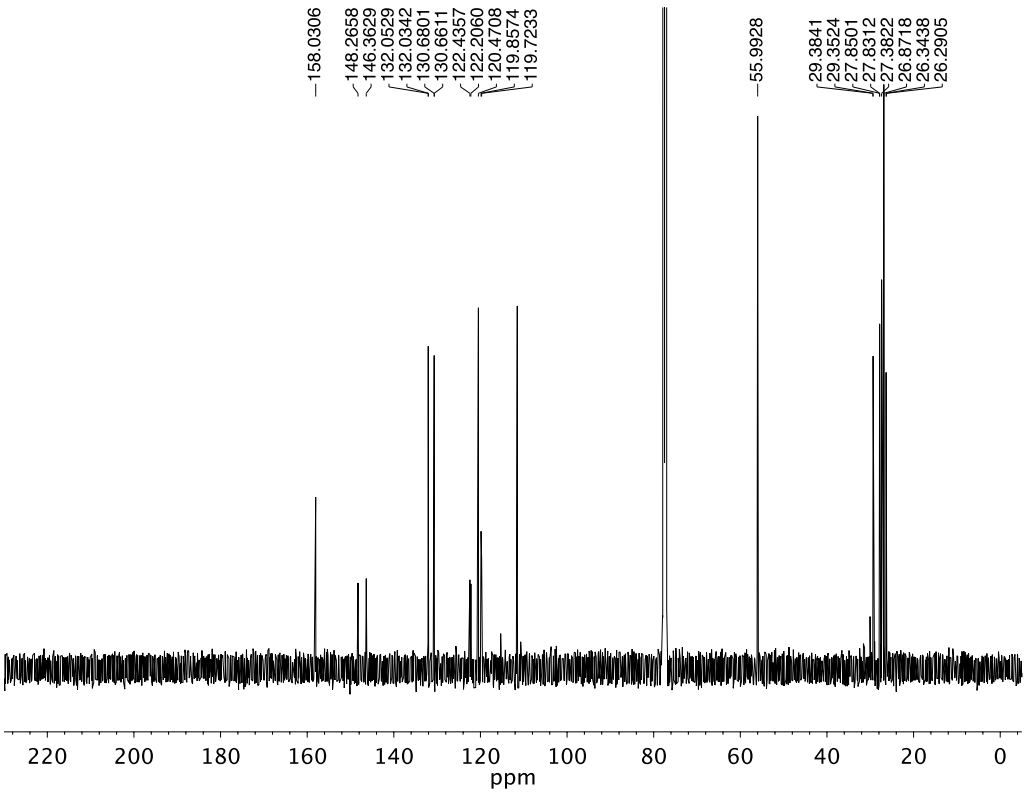


Figure 4.46 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.20.**

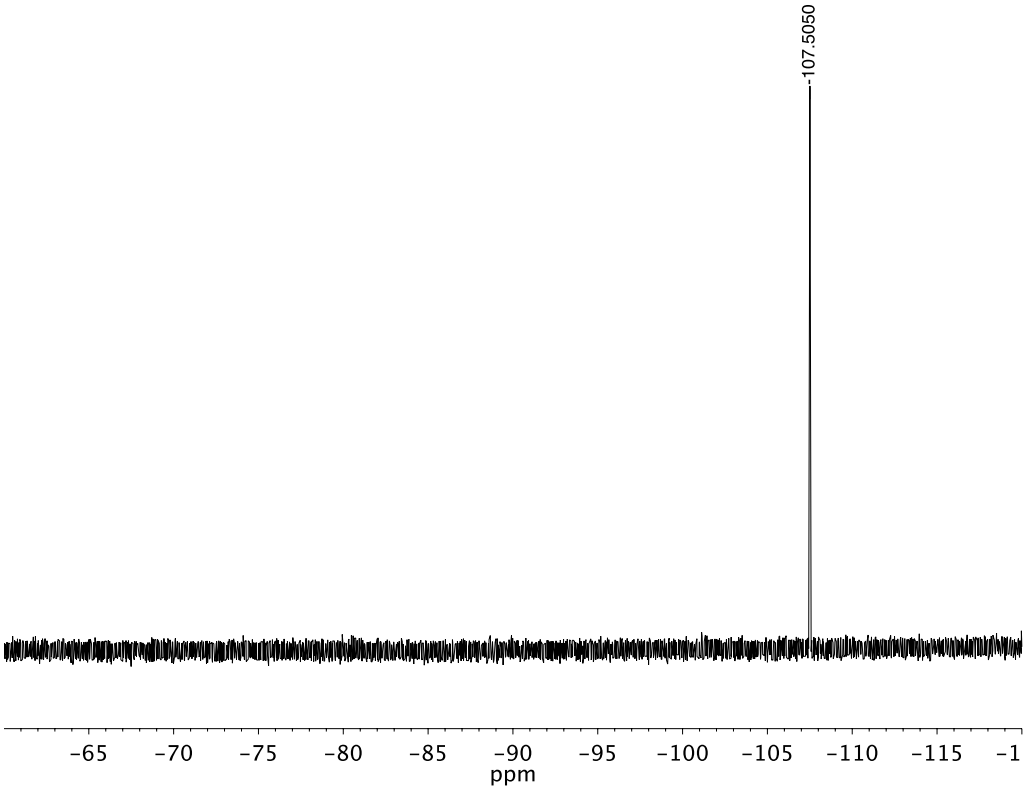


Figure 4.47 ^{19}F NMR (282 MHz, (CD_3Cl) of compound **4.20.**

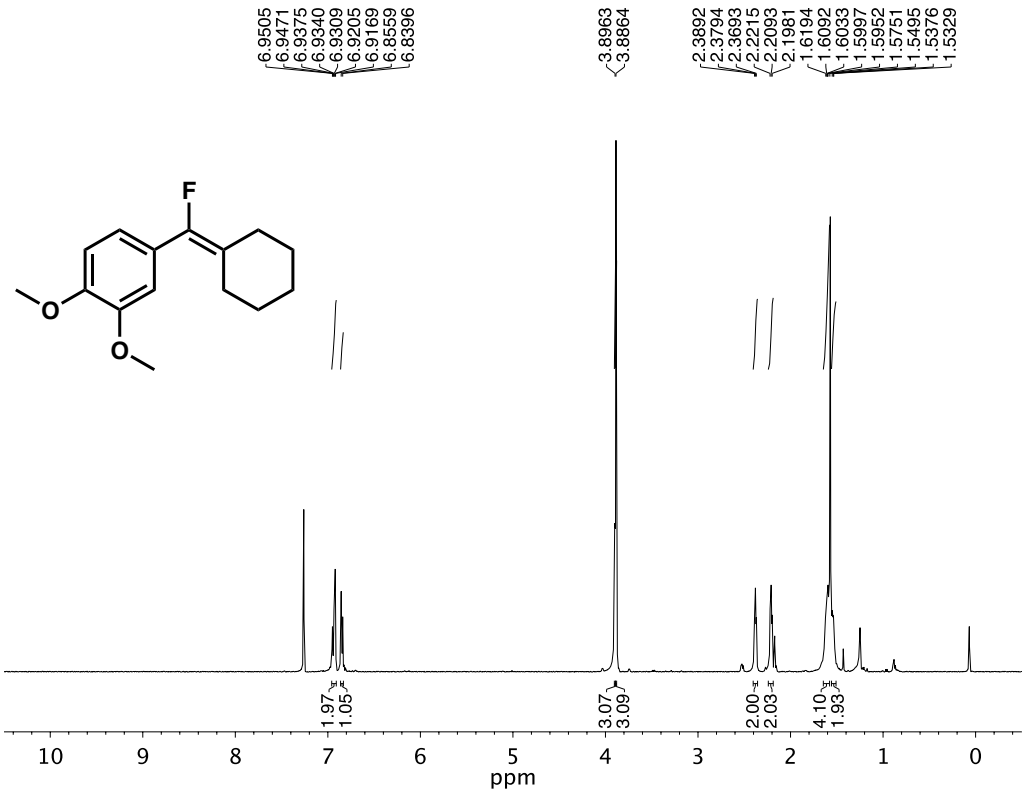


Figure 4.48 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.21.**

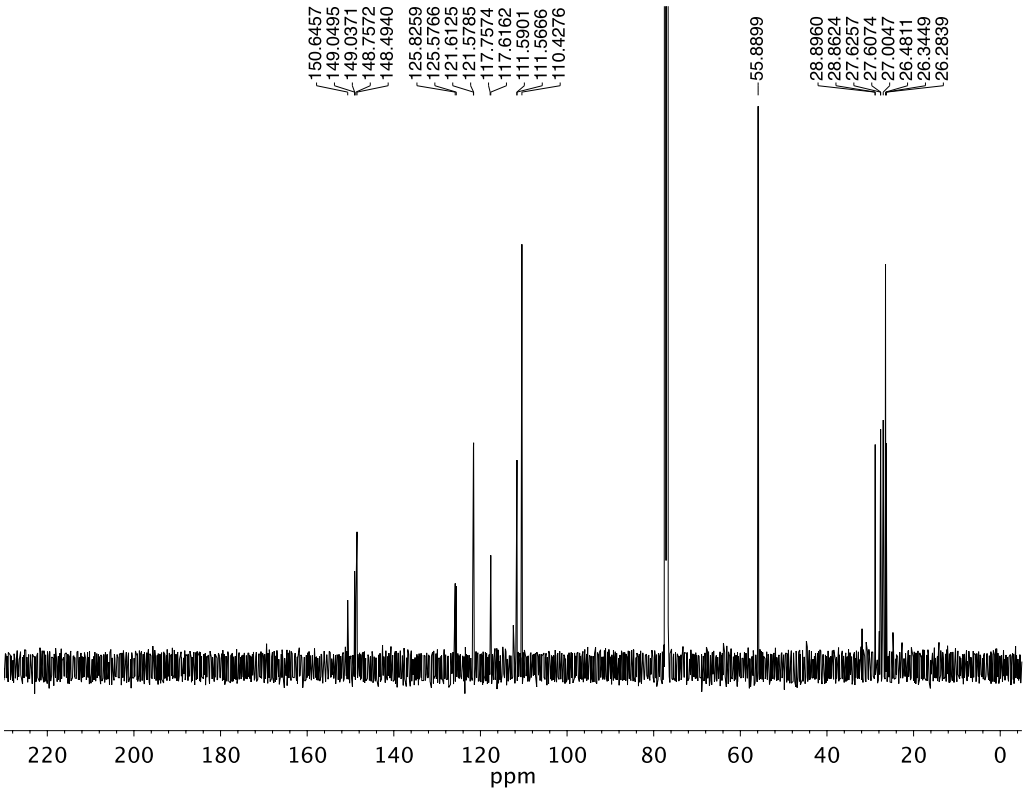


Figure 4.49 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.21.**

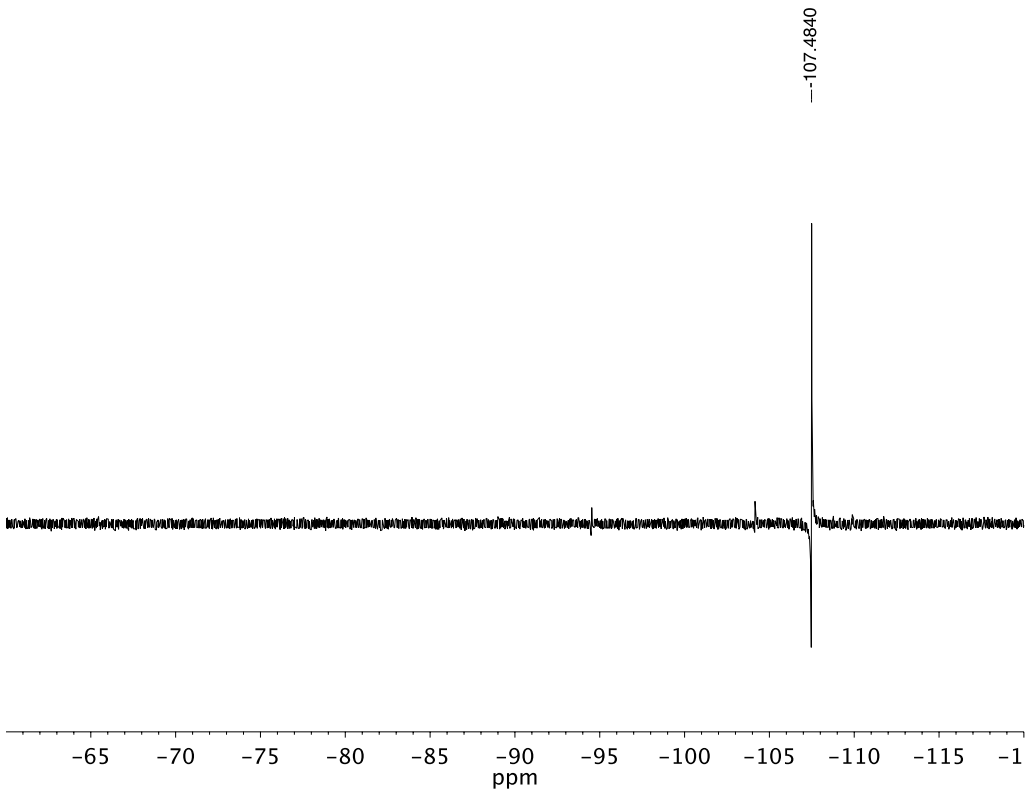


Figure 4.50 ^{19}F NMR (282 MHz, ($CDCl_3$) of compound **4.21.**

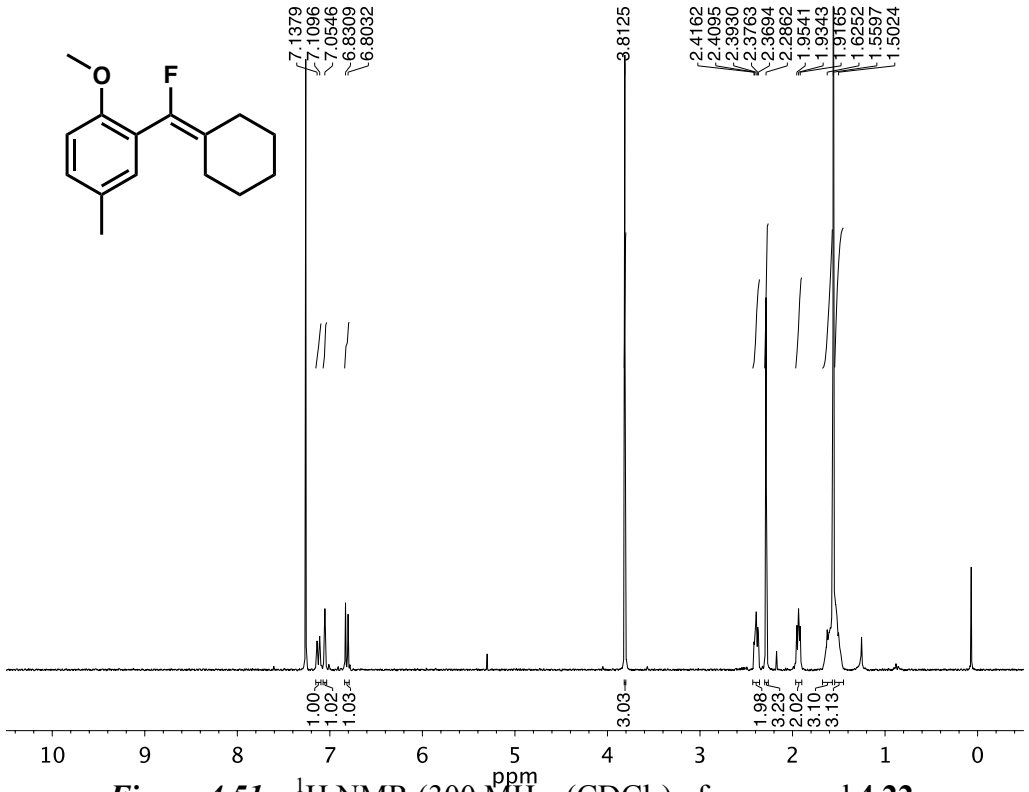


Figure 4.51 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.22.**

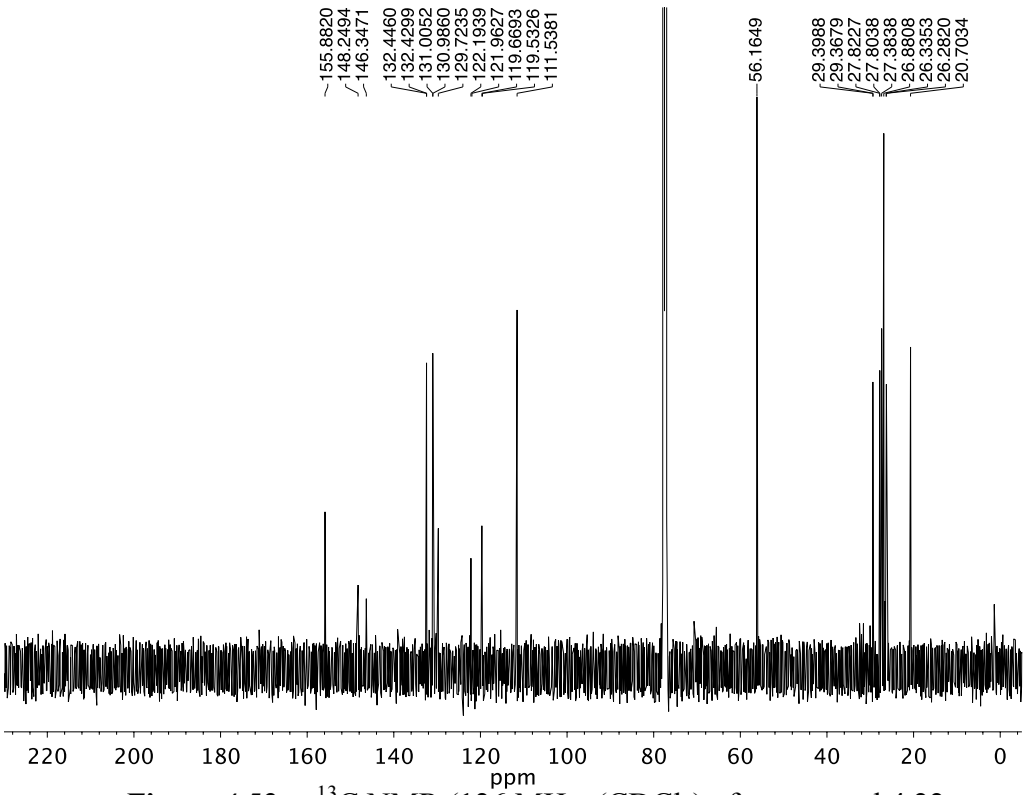


Figure 4.52 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.22.**

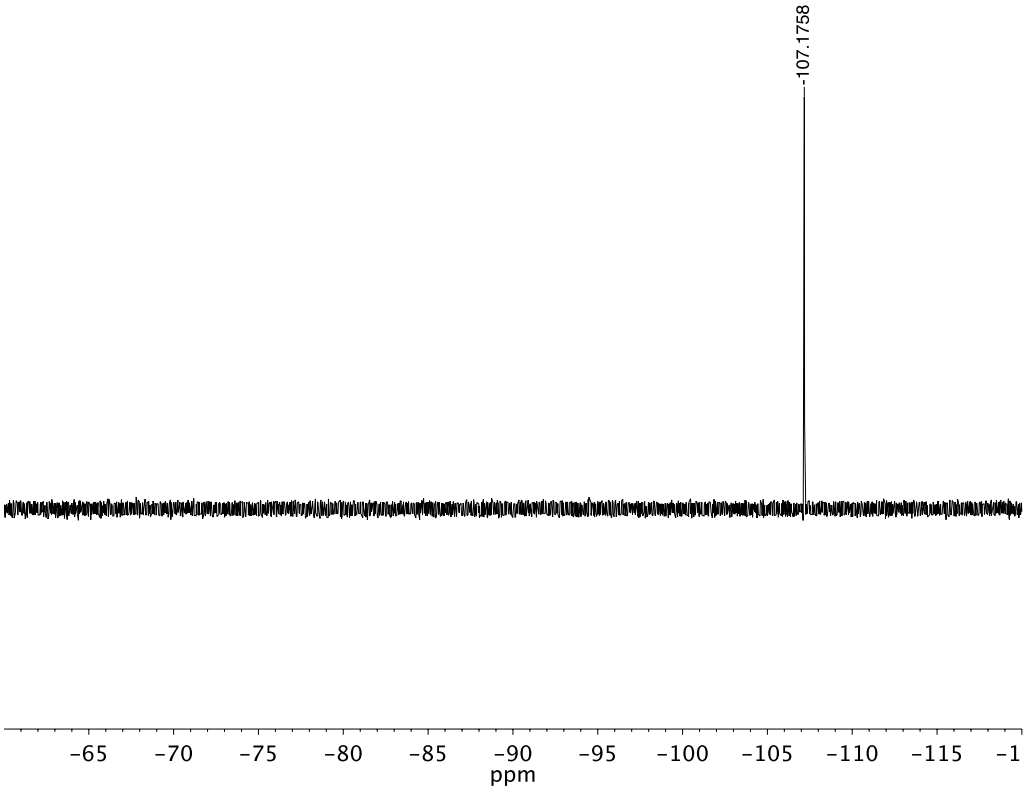


Figure 4.53 ^{19}F NMR (282 MHz, ($CDCl_3$) of compound **4.22.**

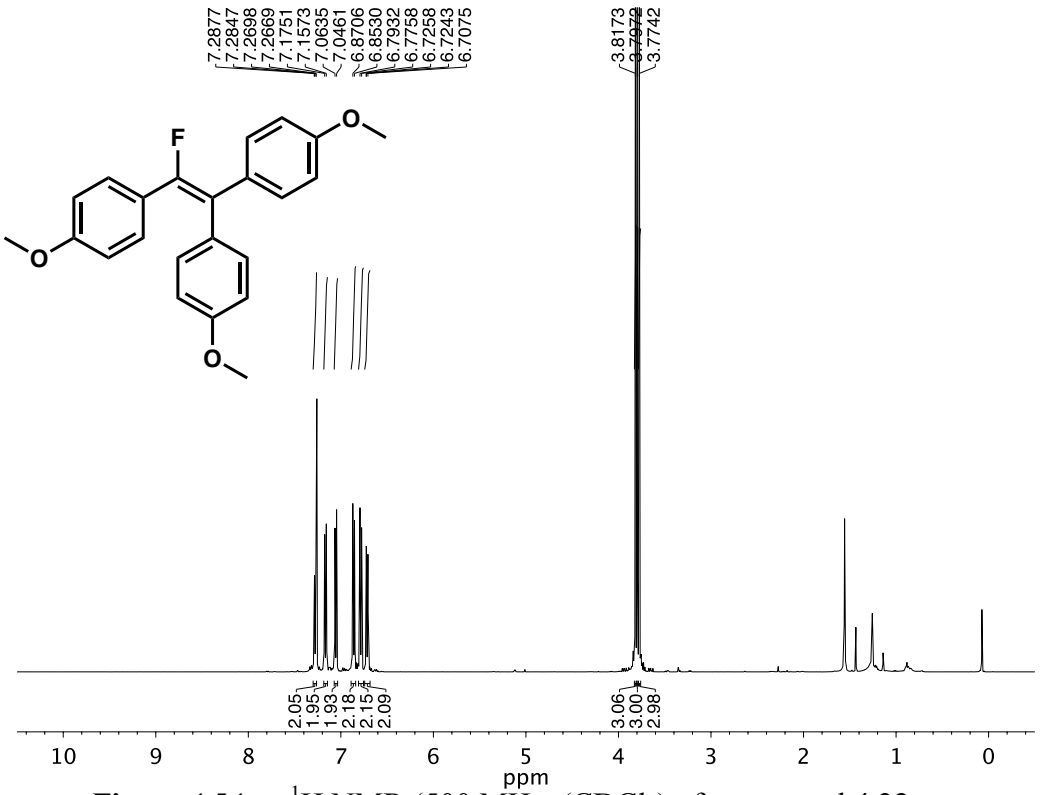


Figure 4.54 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.23.**

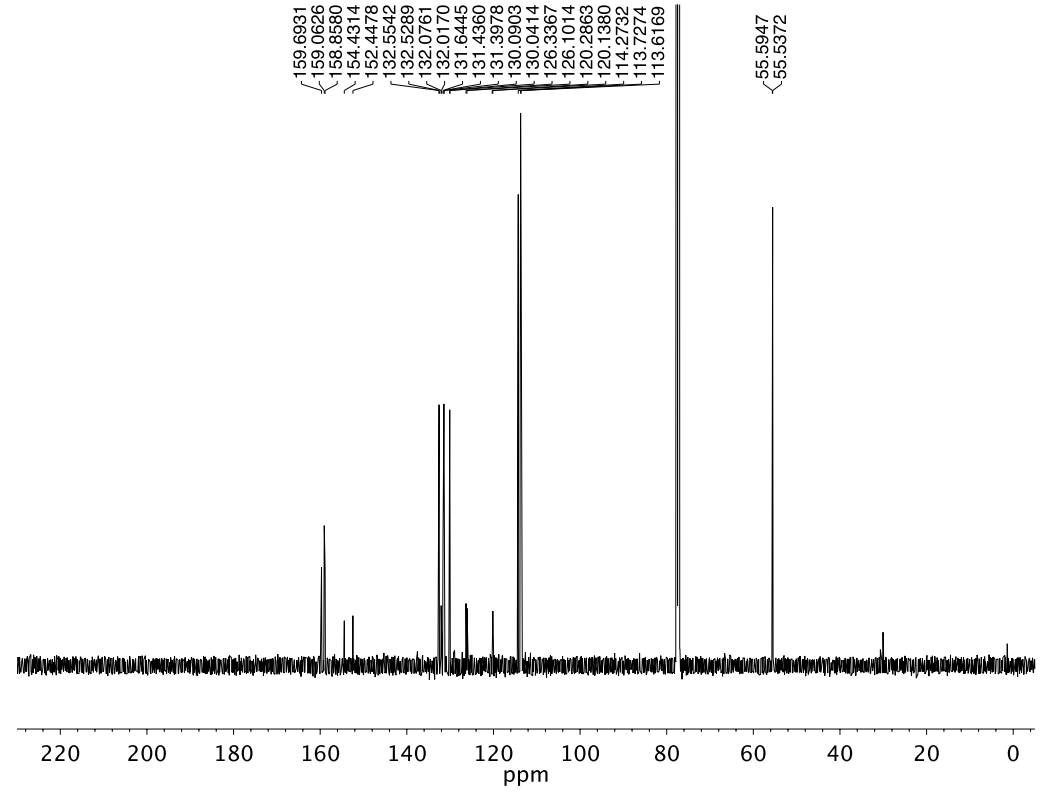


Figure 4.55 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.23.**

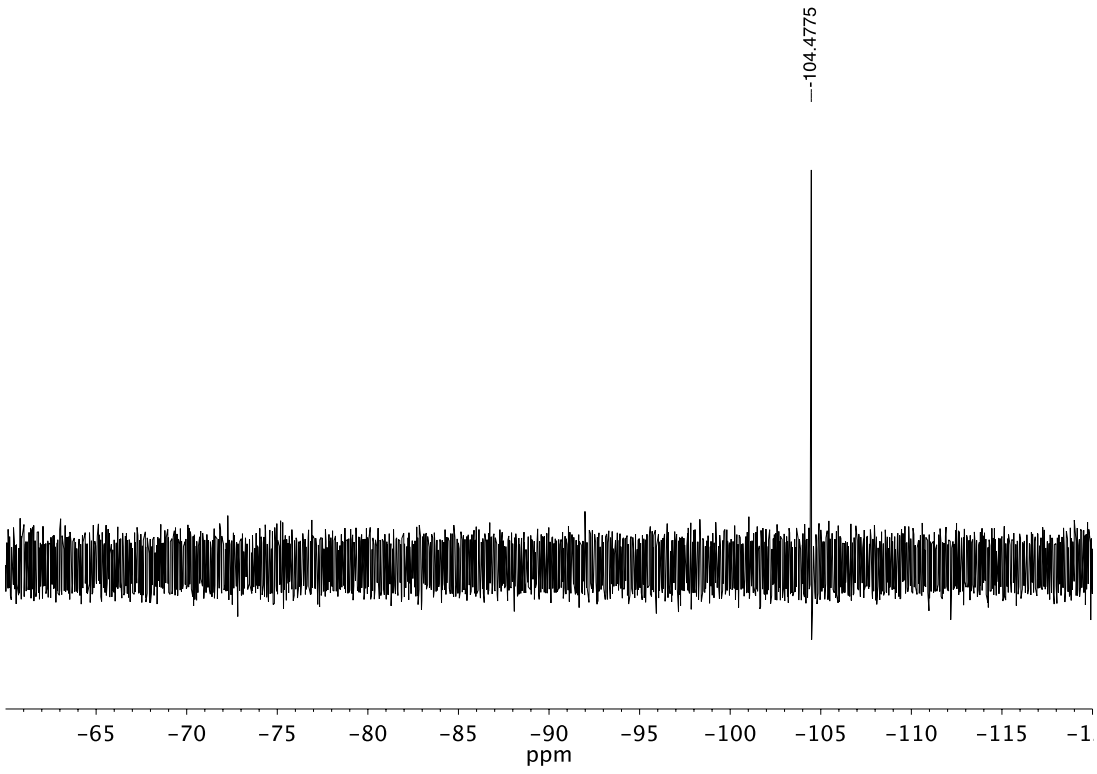


Figure 4.56 ^{19}F NMR (282 MHz, ($CDCl_3$) of compound **4.23.**

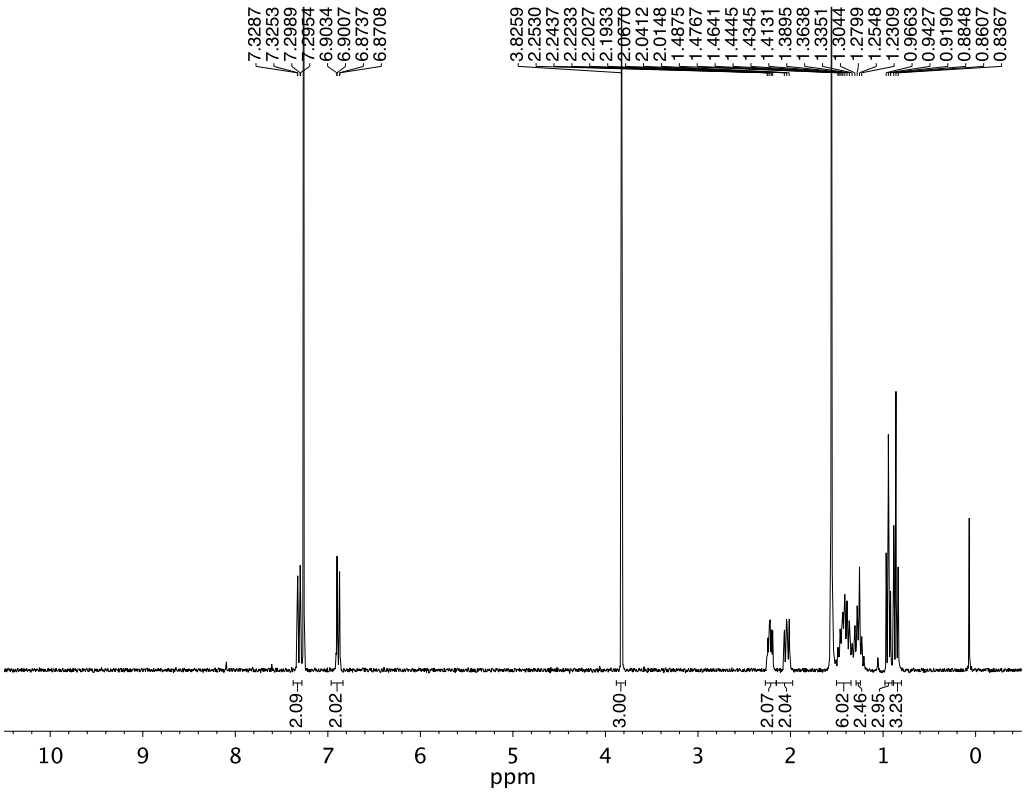


Figure 4.57 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.24.**

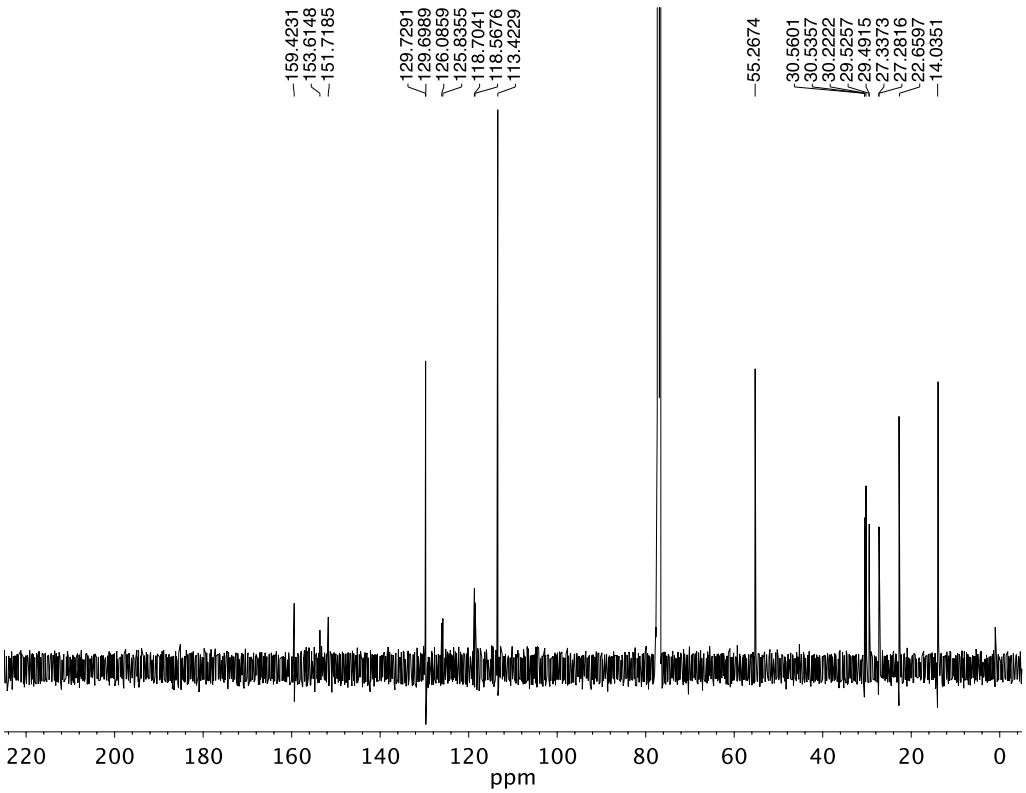


Figure 4.58 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.24.**

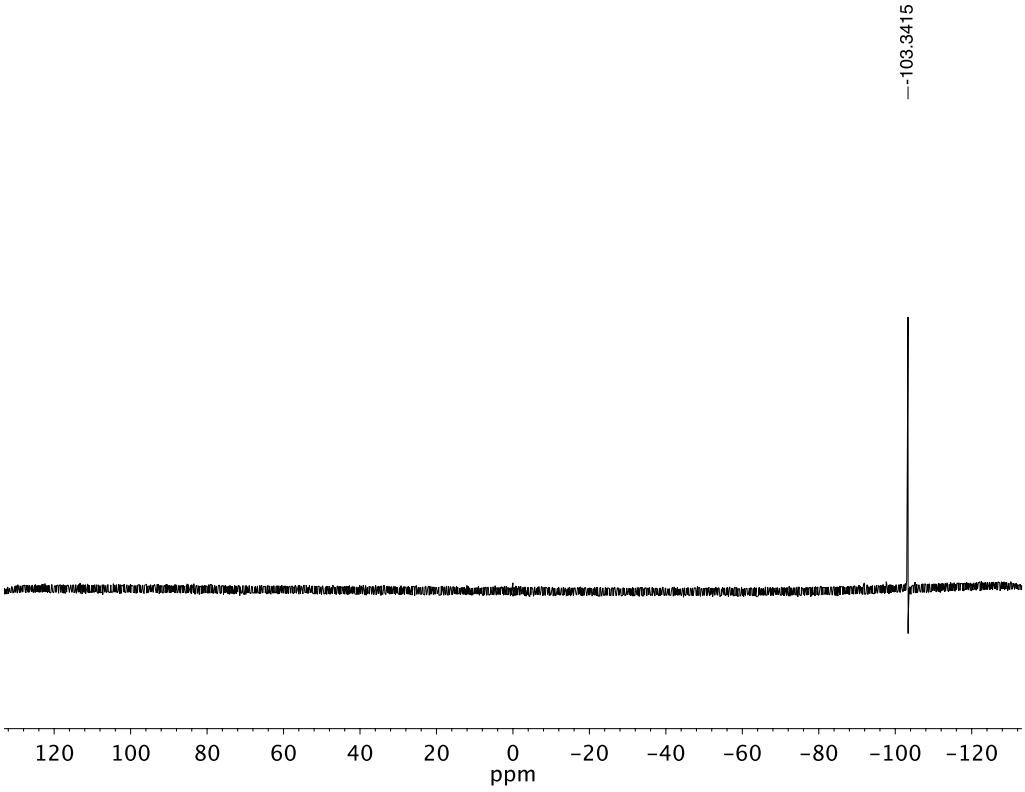


Figure 4.59 ^{19}F NMR (282 MHz, ($CDCl_3$) of compound **4.24.**

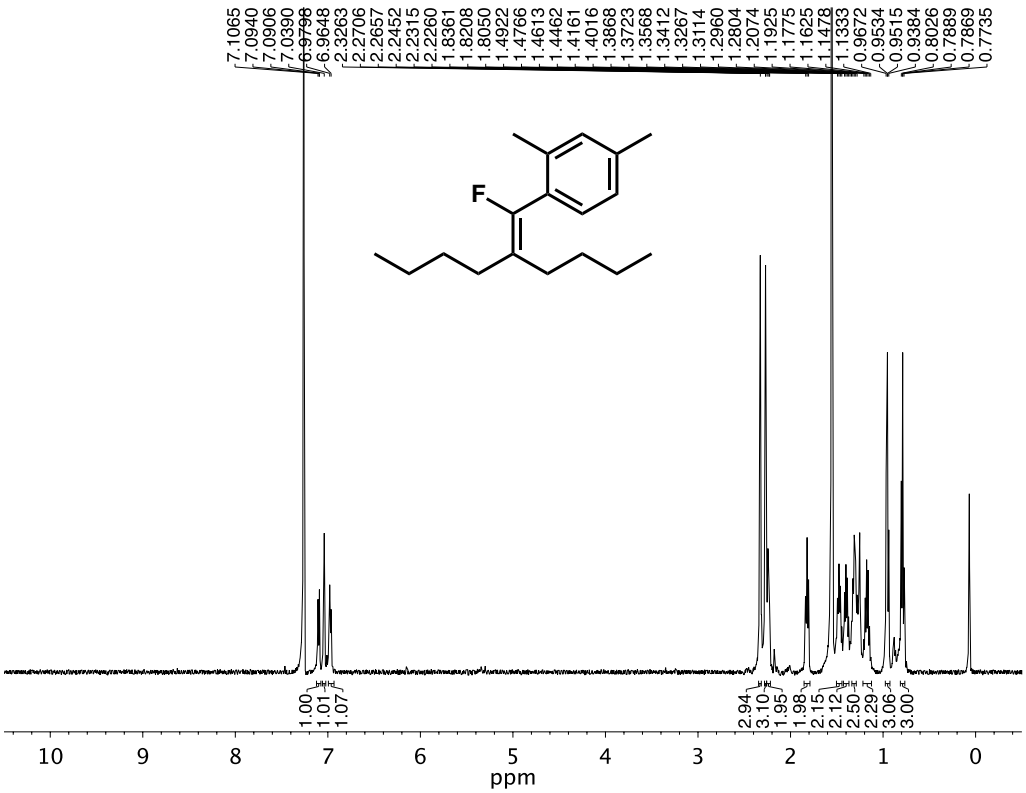


Figure 4.60 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.25.**

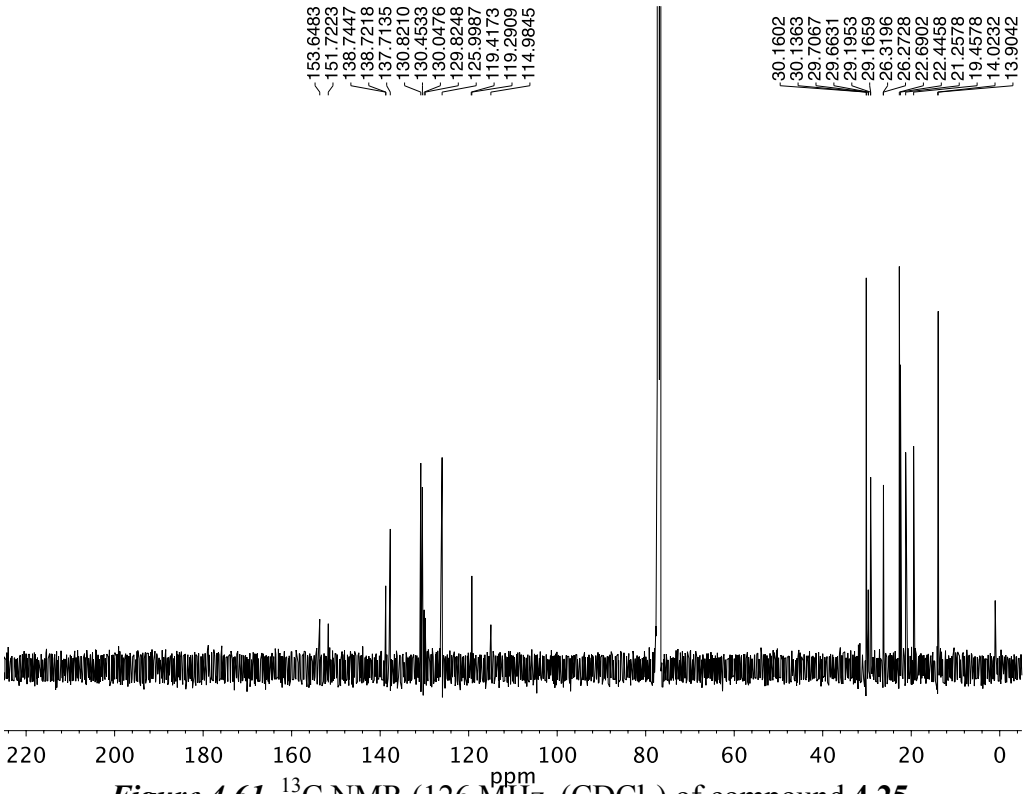


Figure 4.61 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.25.**

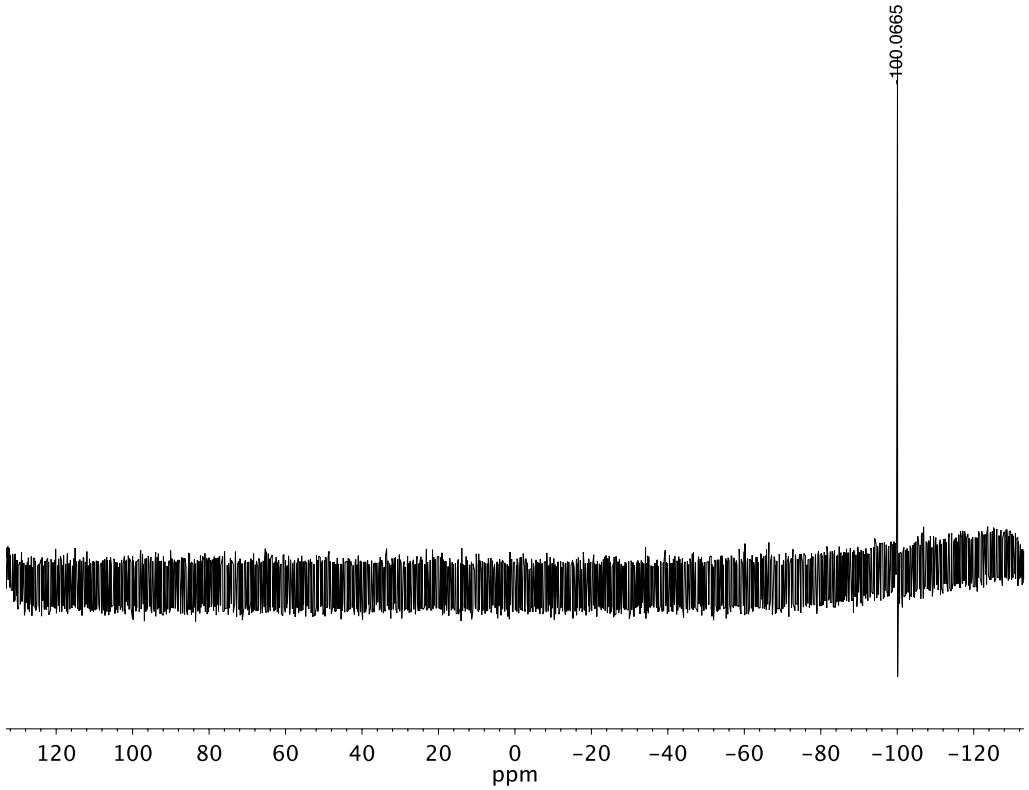


Figure 4.62 ^{19}F NMR (282 MHz, ($CDCl_3$) of compound **4.25.**

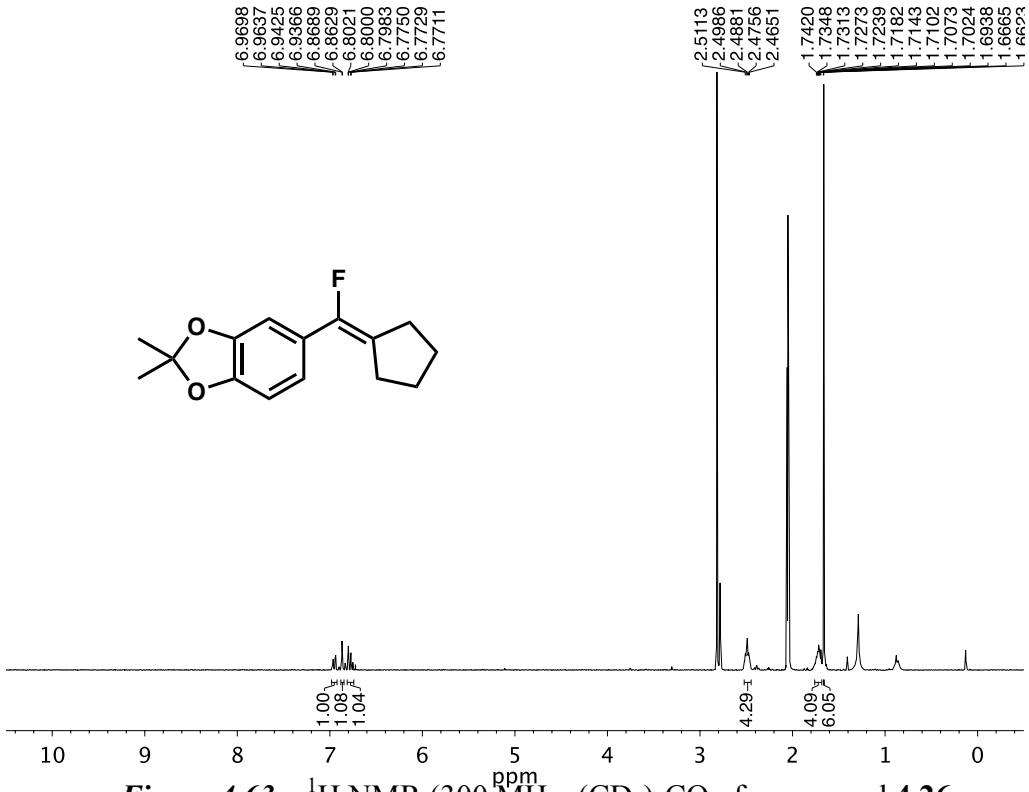


Figure 4.63 ^{1}H NMR (300 MHz, $(CD_3)_2CO$ of compound **4.26.**

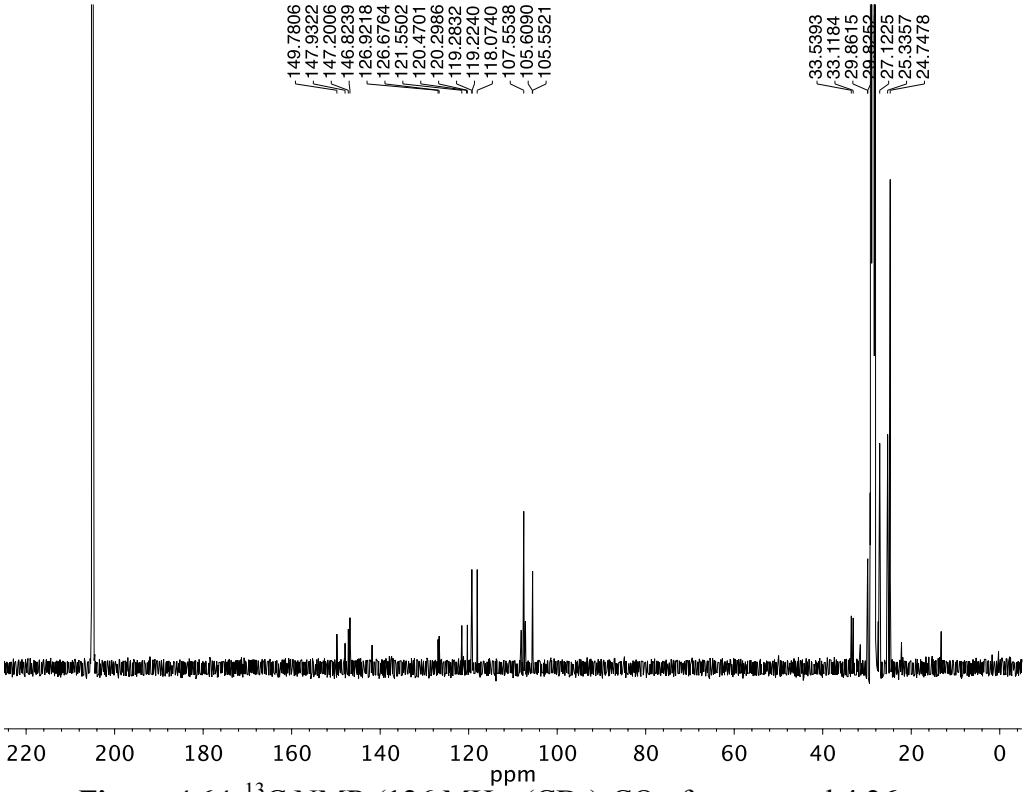


Figure 4.64 ^{13}C NMR (126 MHz, $(CD_3)_2CO$ of compound **4.26.**

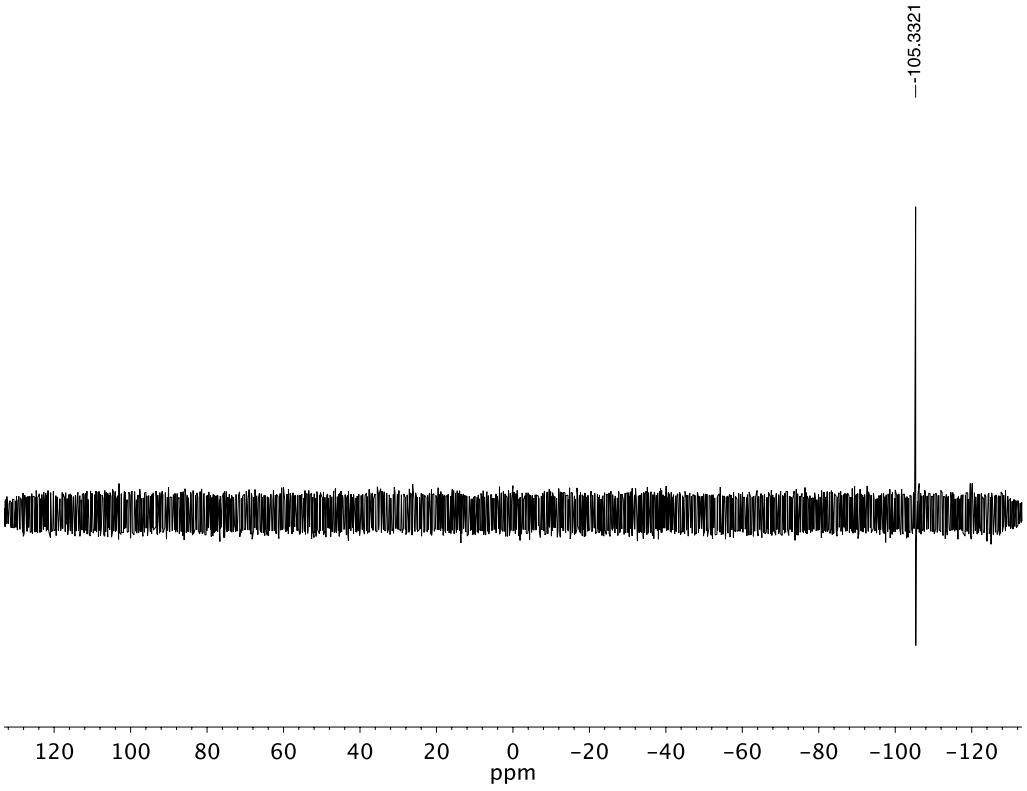


Figure 4.65 ^{19}F NMR (282 MHz, $(CD_3)_2CO$ of compound **4.26.**

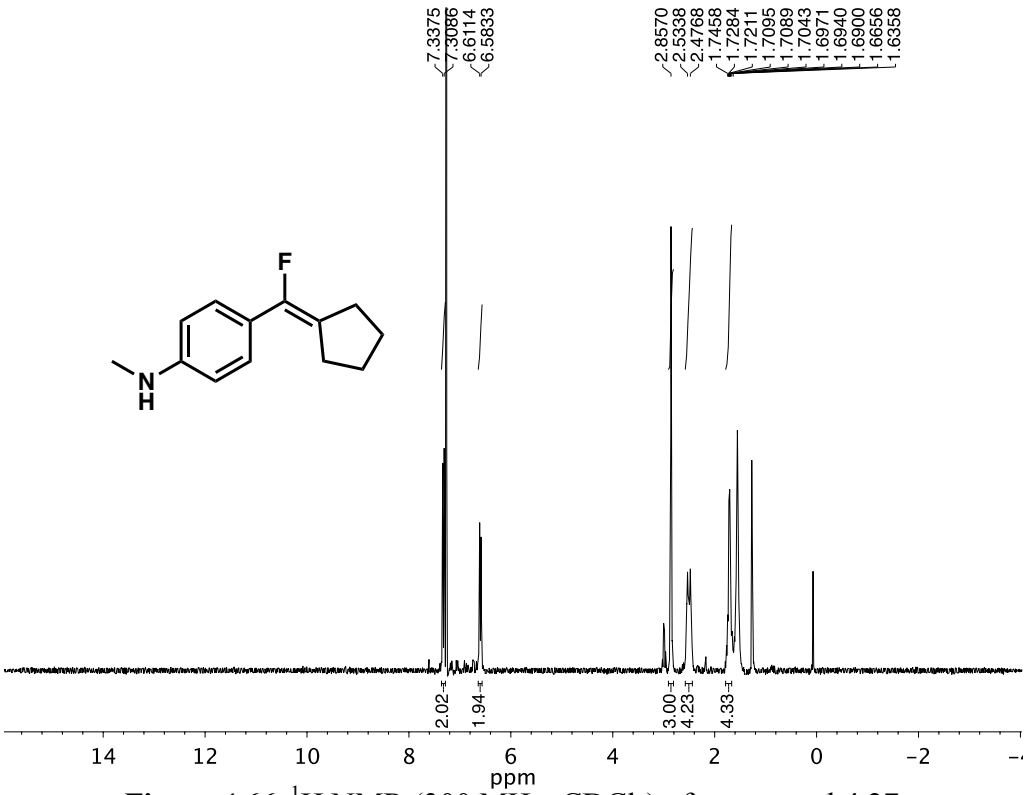


Figure 4.66 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4.27.**

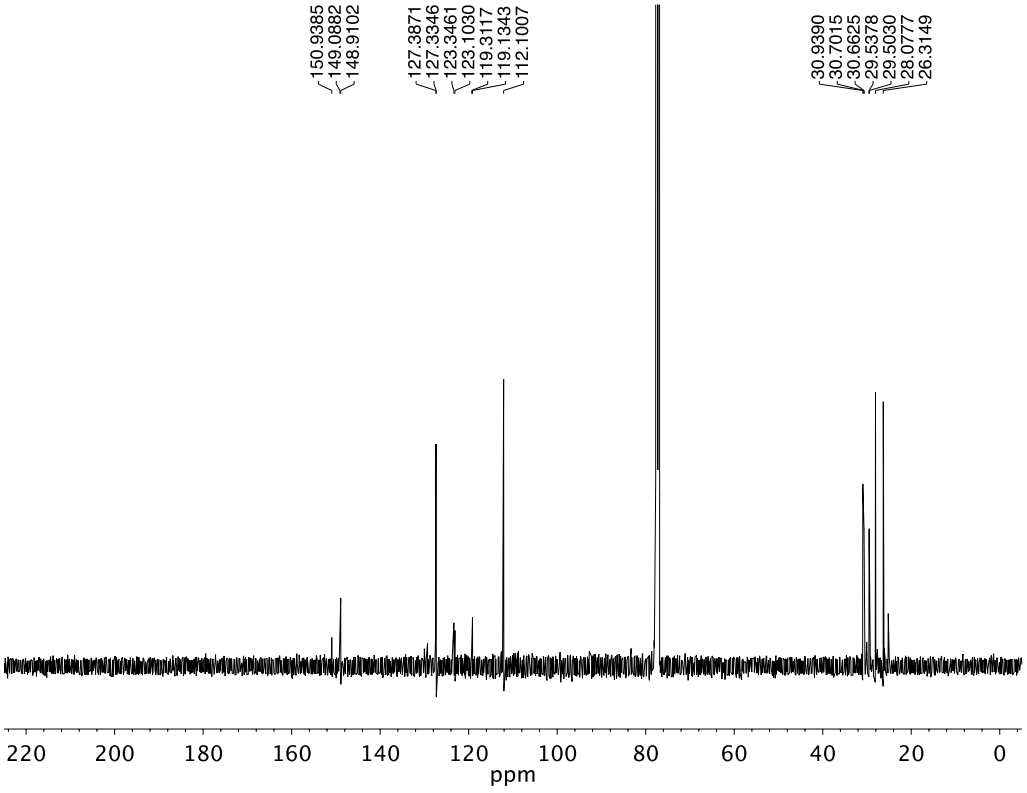


Figure 4.67 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.27.**

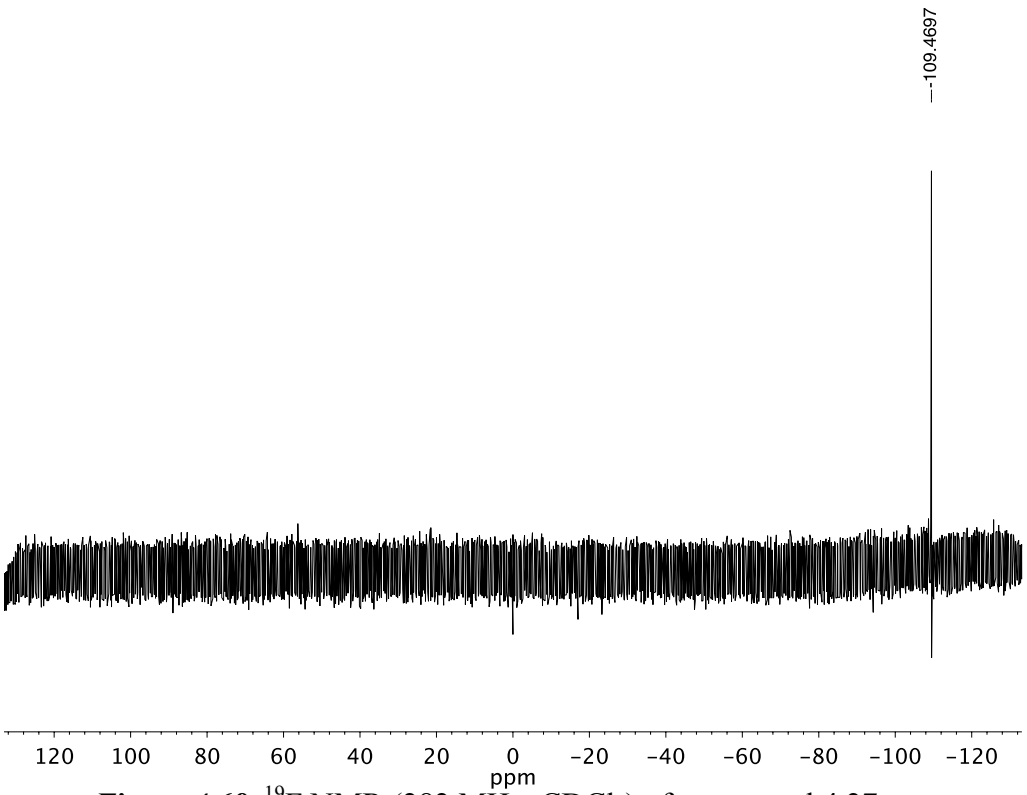


Figure 4.68 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **4.27.**

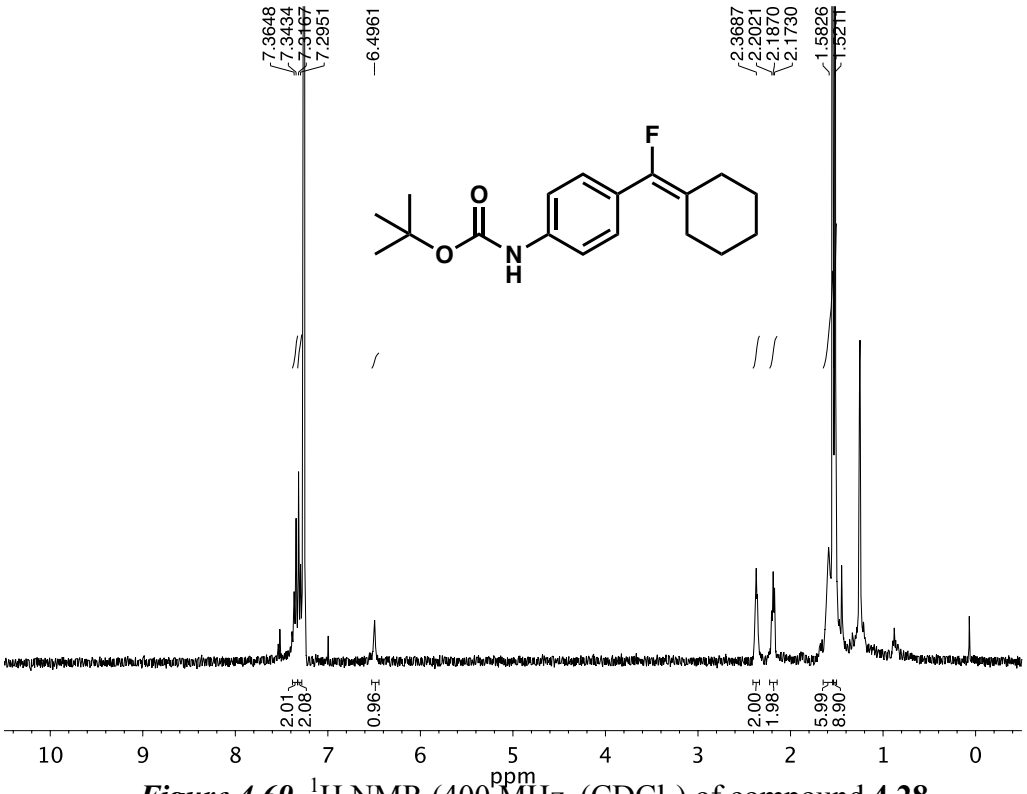


Figure 4.69 ^{1}H NMR (400 MHz, ($CDCl_3$) of compound **4.28.**

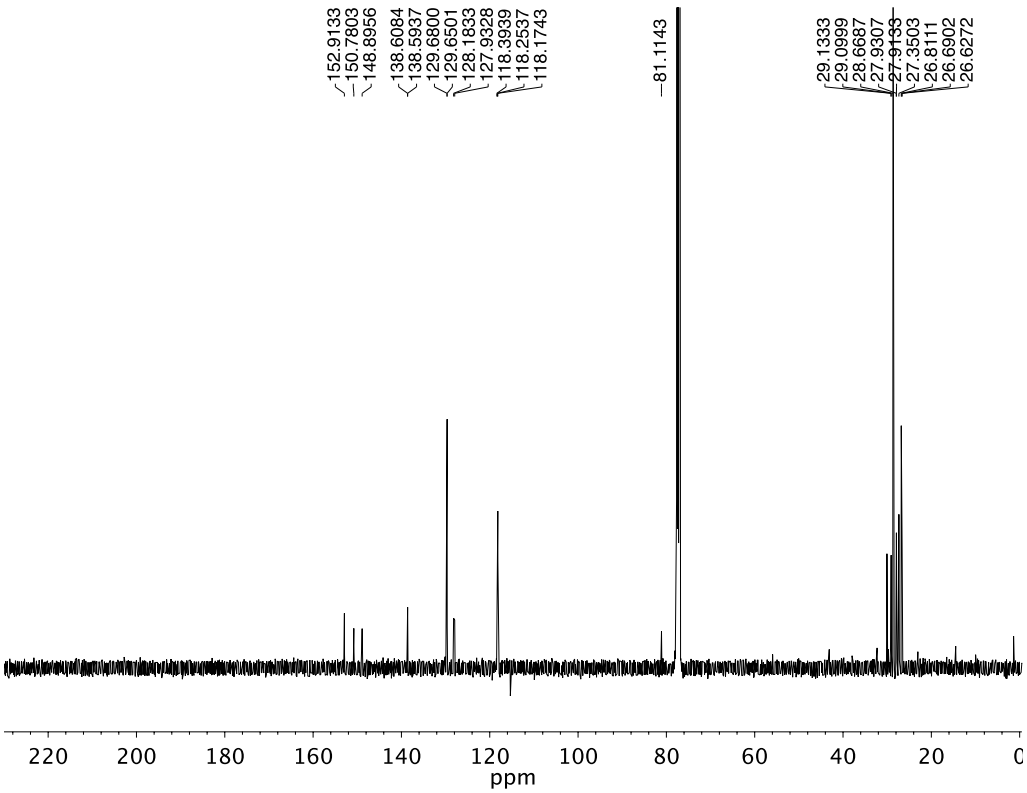


Figure 4.70 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.28.**

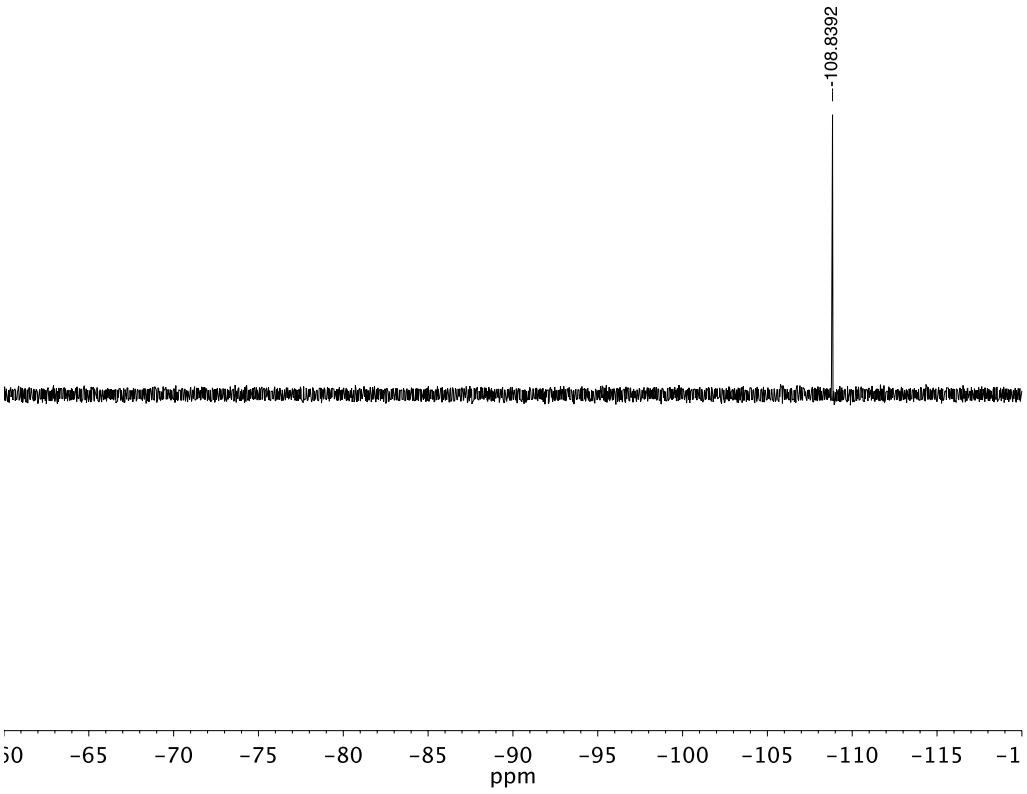


Figure 4.71 ^{19}F NMR (376 MHz, (CD_3Cl) of compound **4.28.**

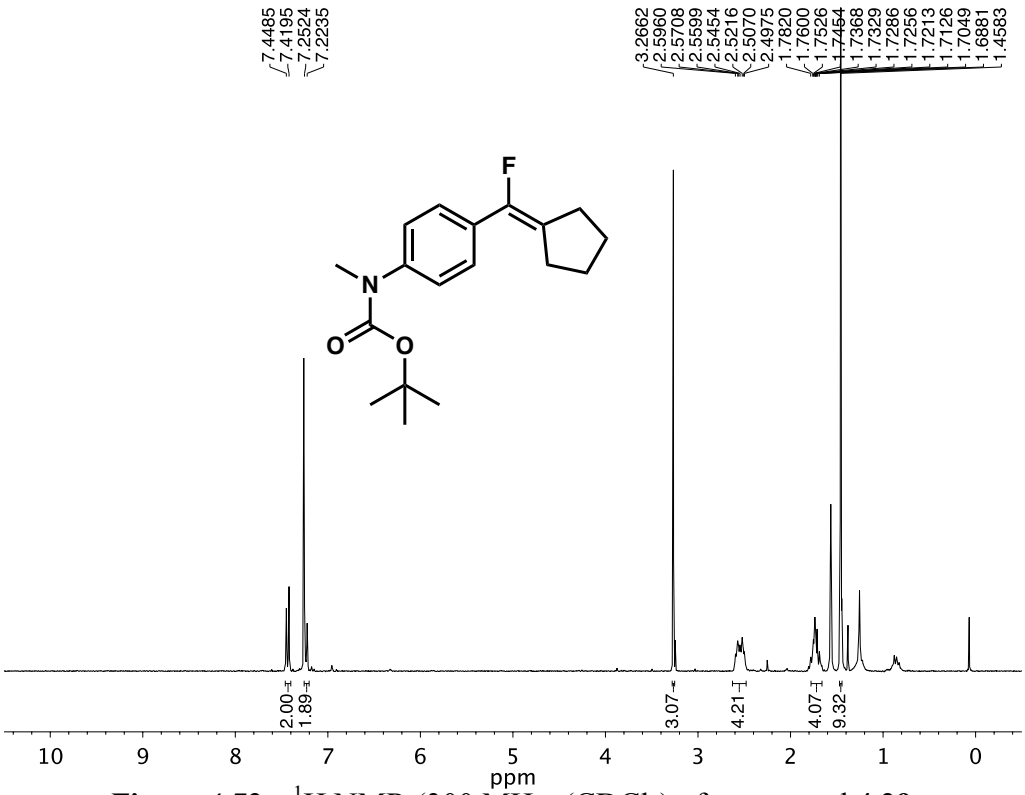


Figure 4.72 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.29.**

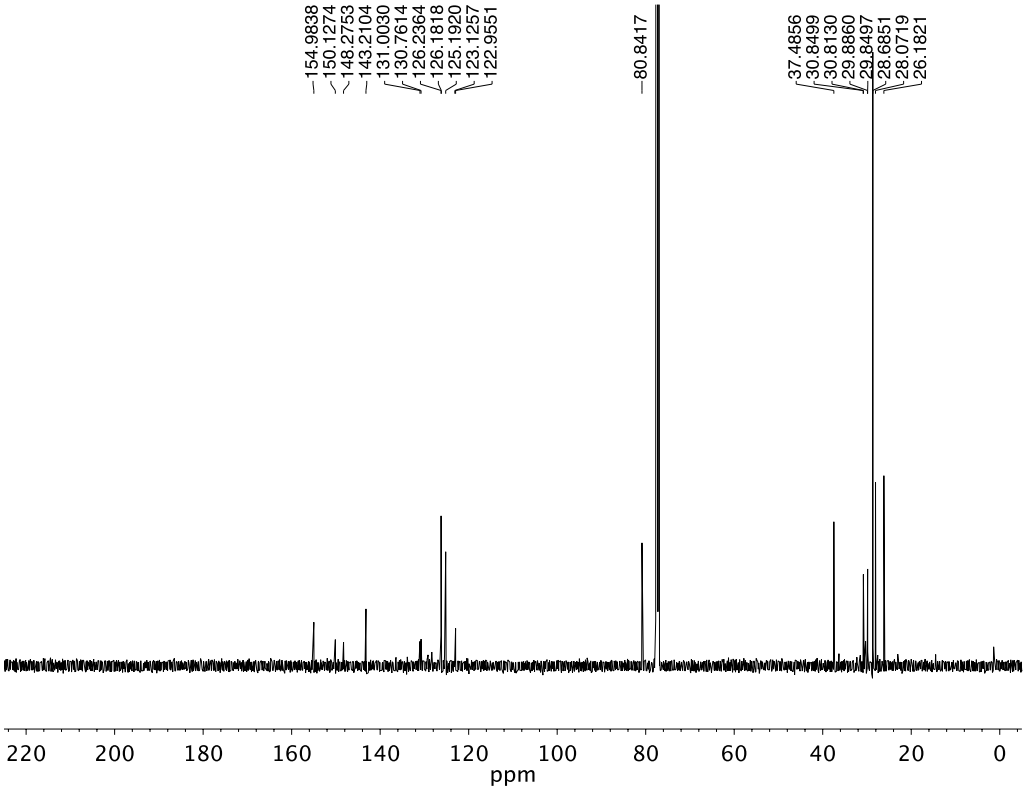


Figure 4.73 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.29.**

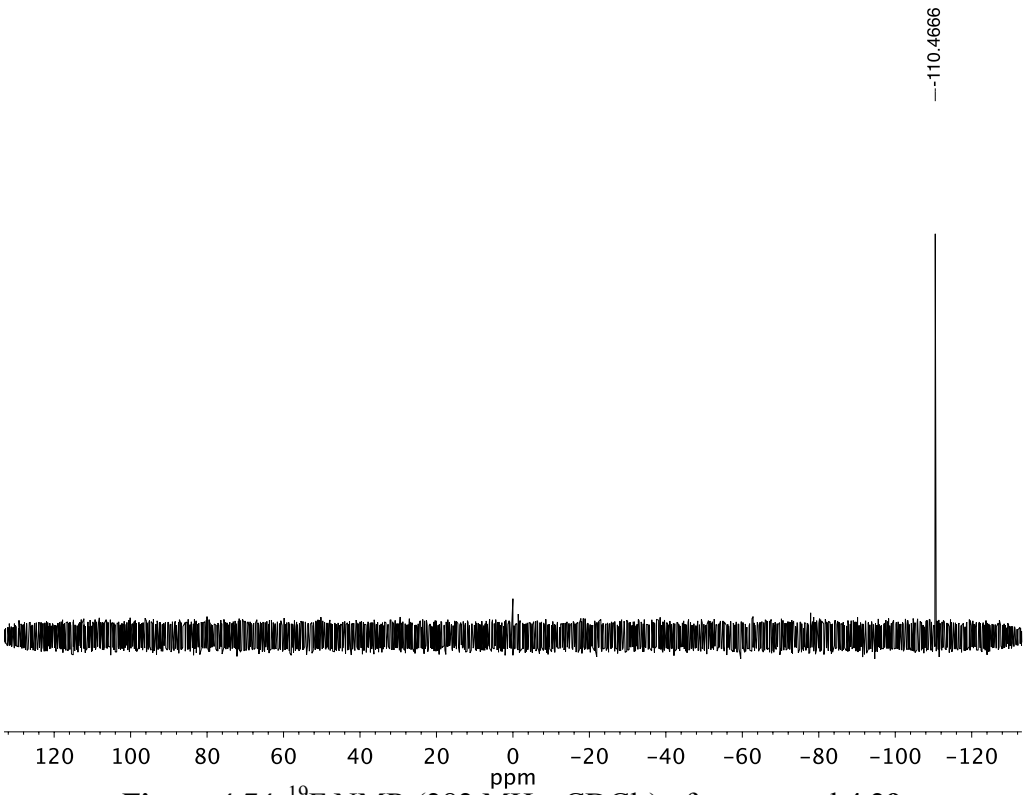


Figure 4.74 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **4.29.**

Figure 4.75 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.30.**

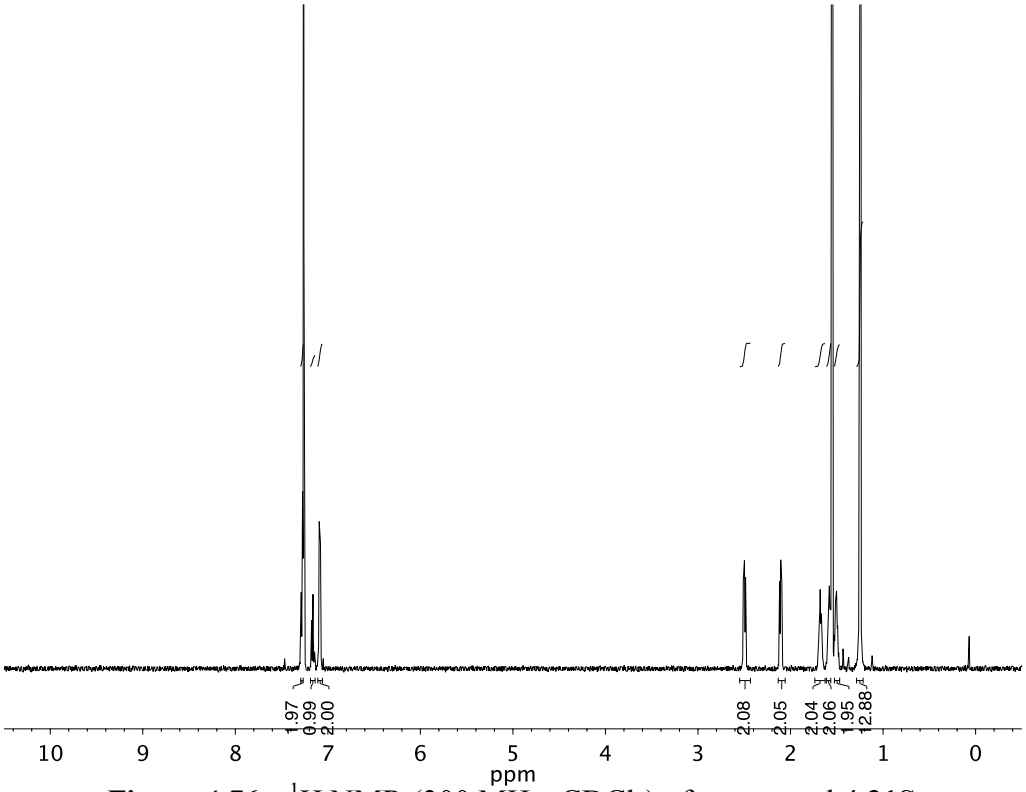


Figure 4.76 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4.31S.**

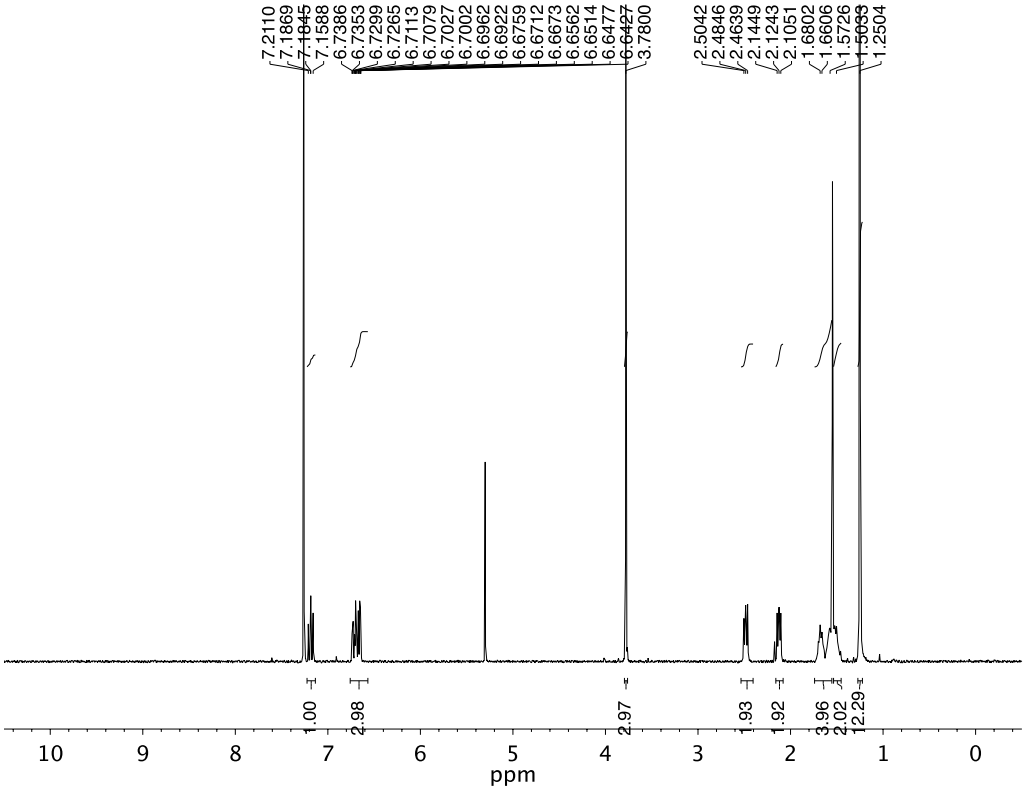


Figure 4.77 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.32S.**

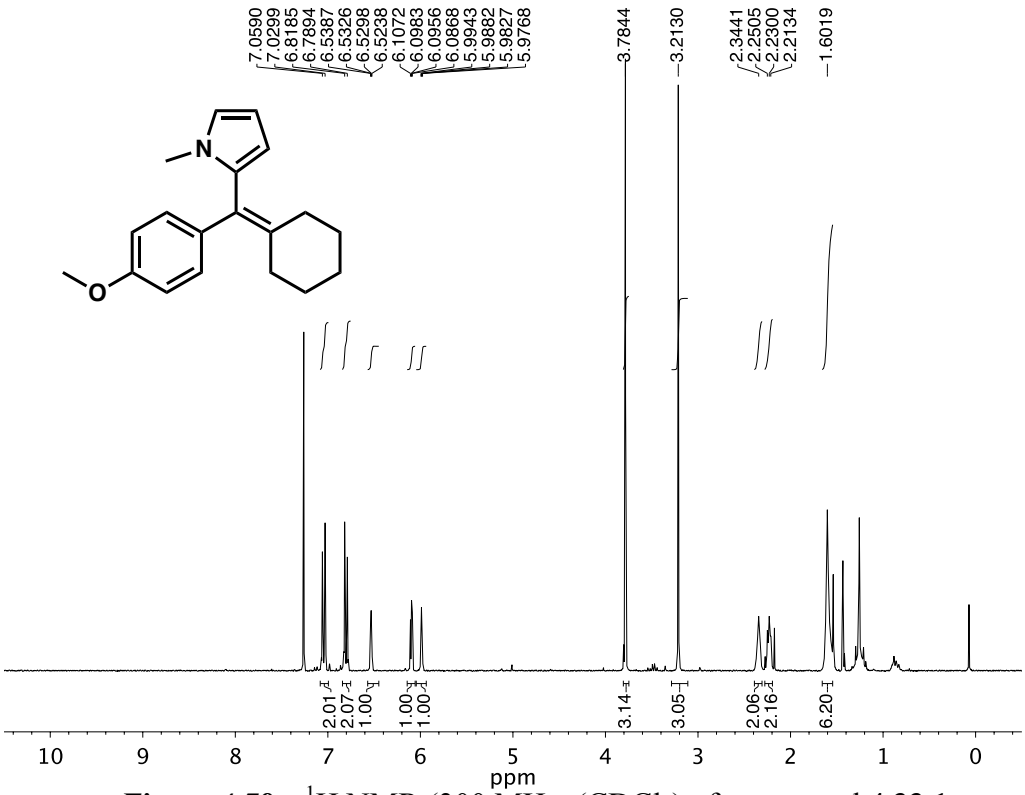


Figure 4.78 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.33.1.**

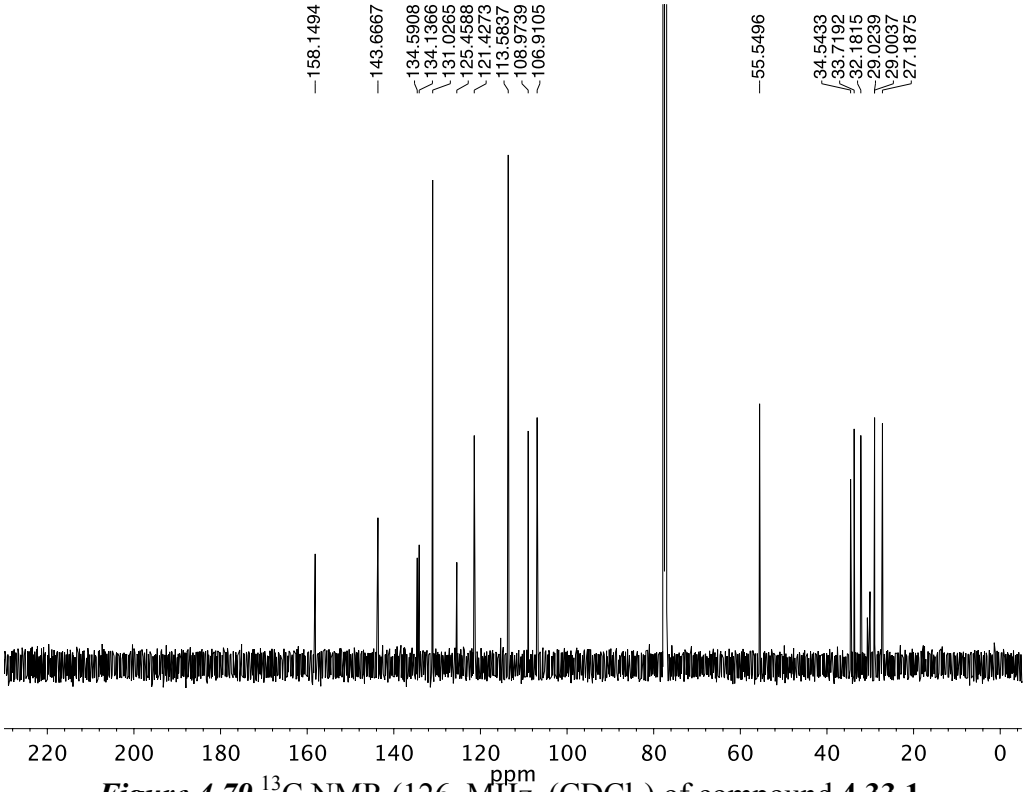


Figure 4.79 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.33.1.**

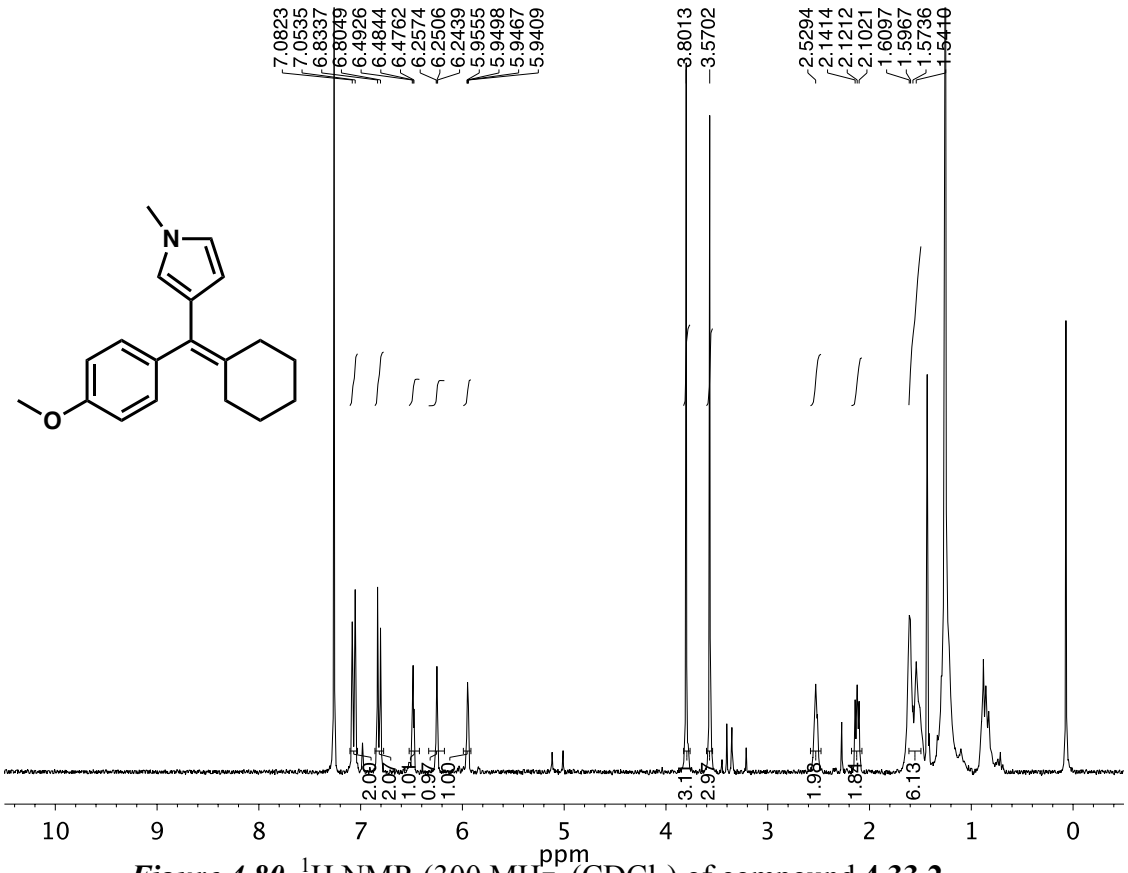


Figure 4.80 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.33.2.**

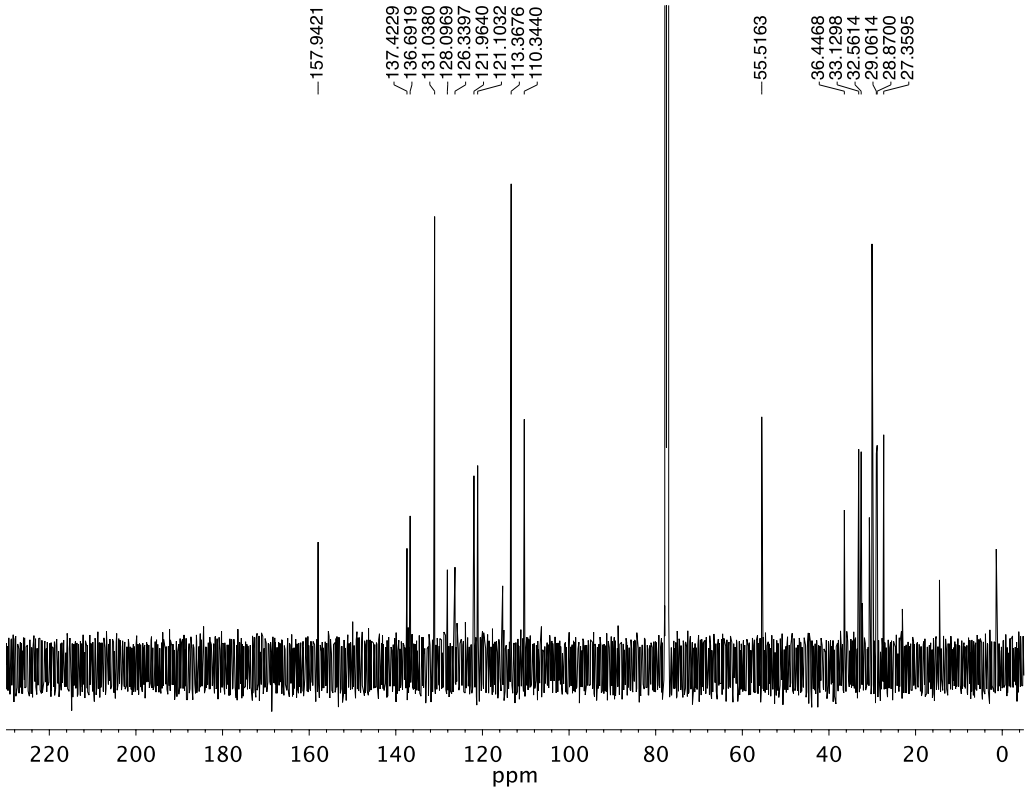


Figure 4.81 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.33.2.**

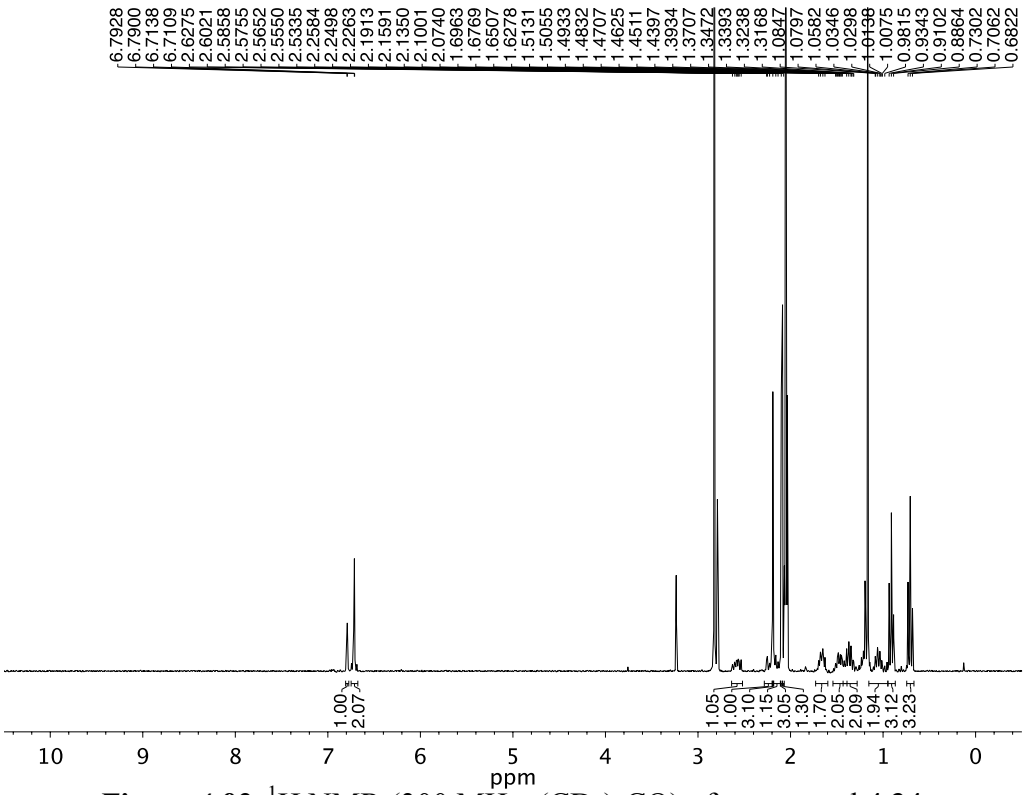


Figure 4.82 ^{1}H NMR (300 MHz, $(CD_3)_2CO$) of compound **4.34.**

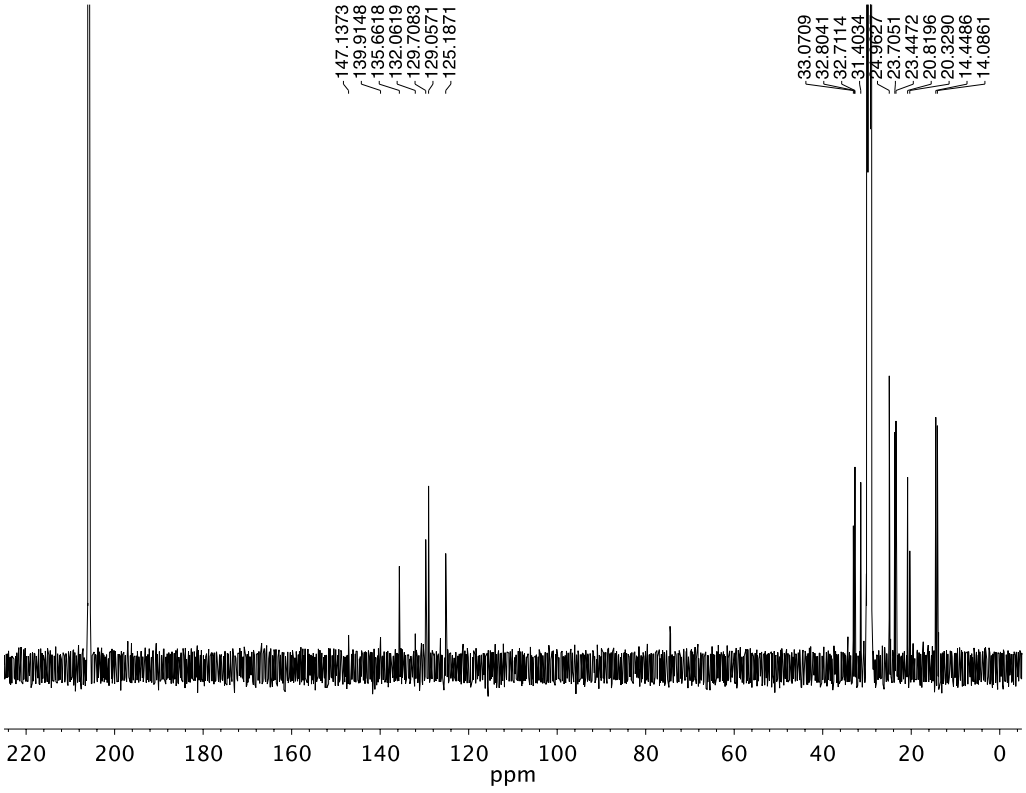


Figure 4.83 ^{13}C NMR (126 MHz, $(CD_3)_2CO$) of compound **4.34.**

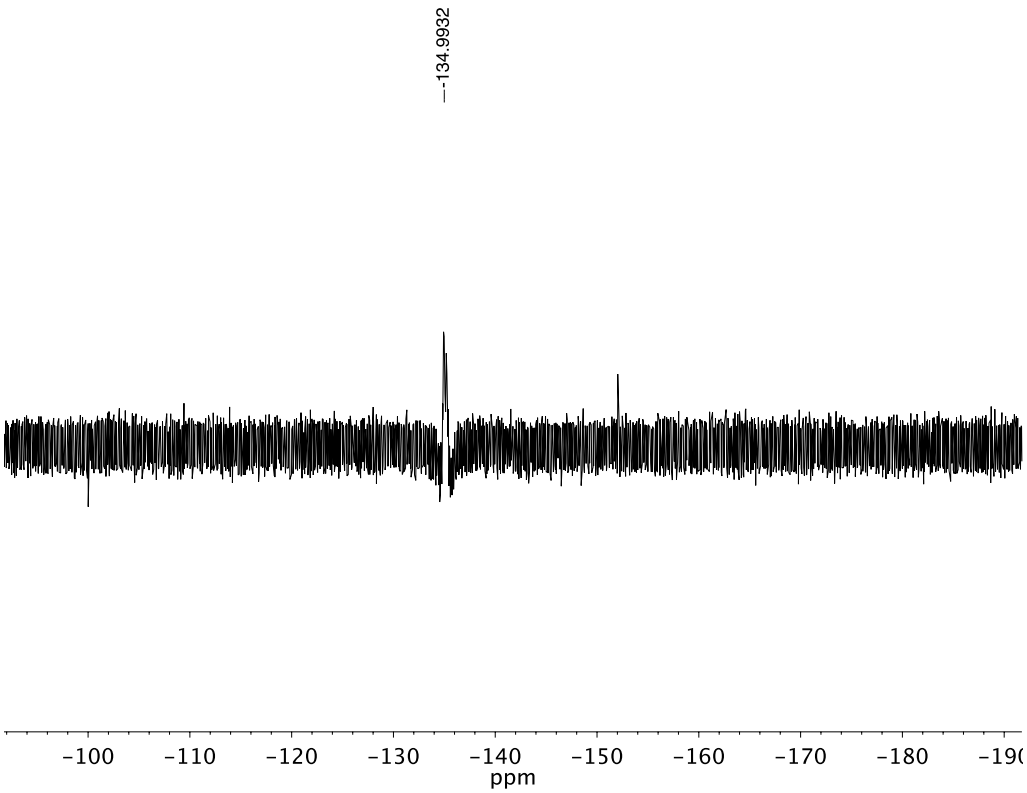


Figure 4.84 ^{19}F NMR (282 MHz, ($(CD_3)_2CO$) of compound **4.34.**

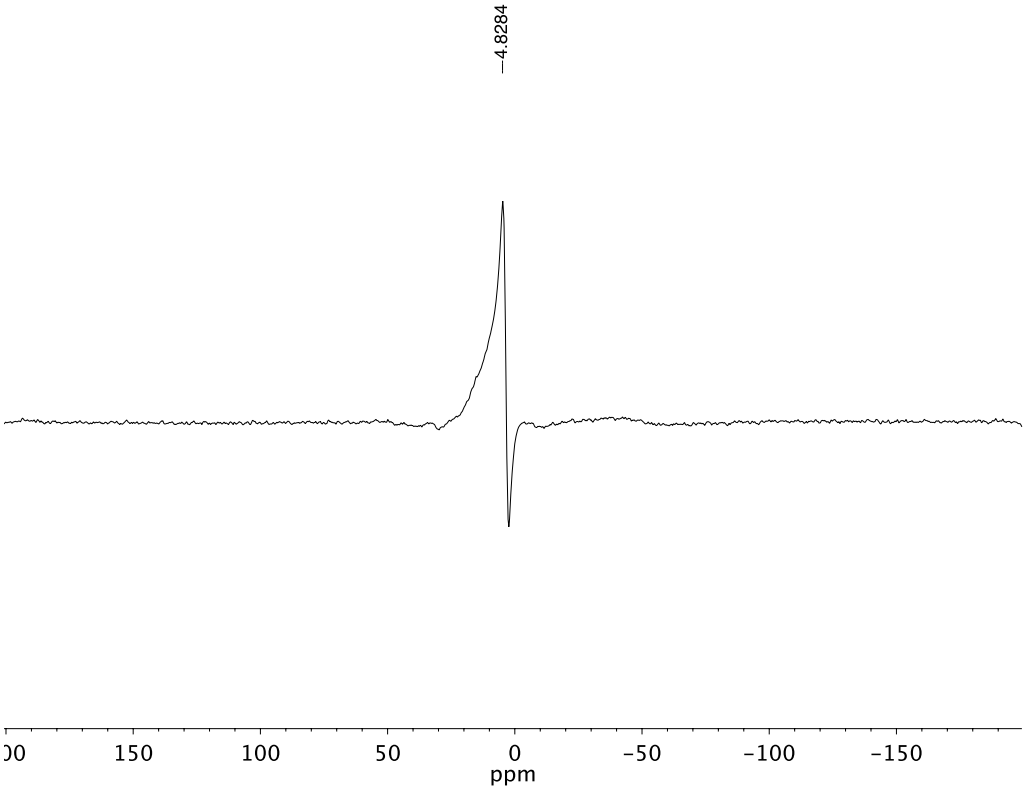


Figure 4.85 ^{11}B NMR (96 MHz, $(CD_3)_2CO$) of compound **4.34.**

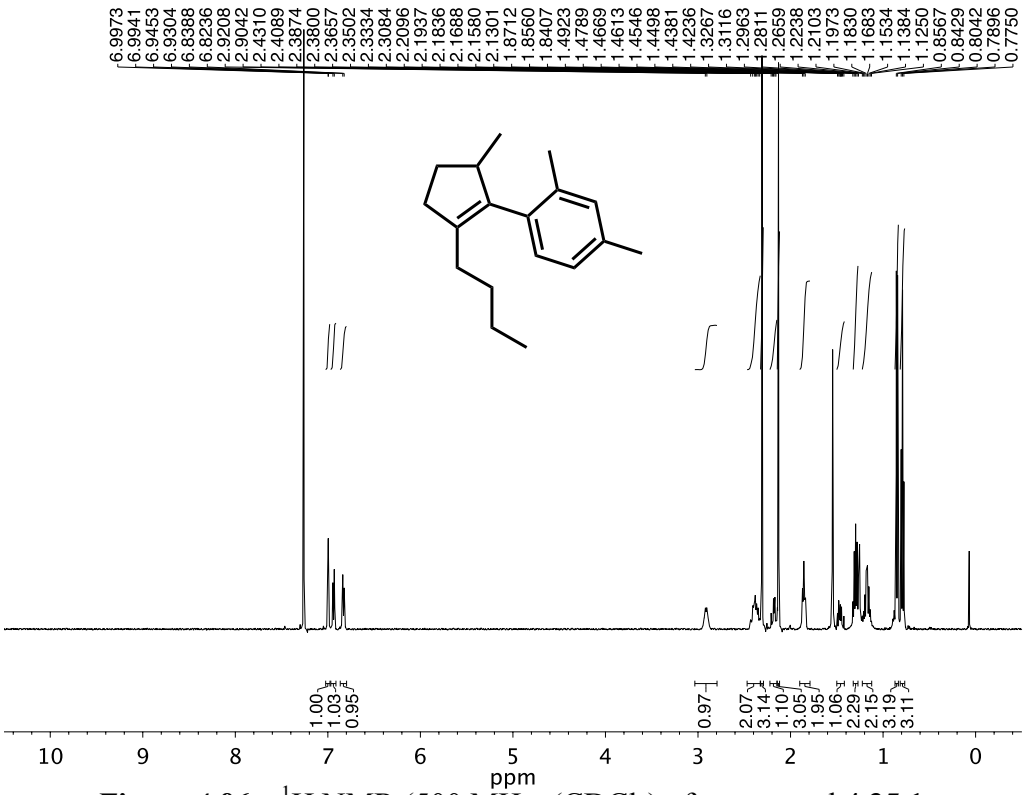


Figure 4.86 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.35.1.**

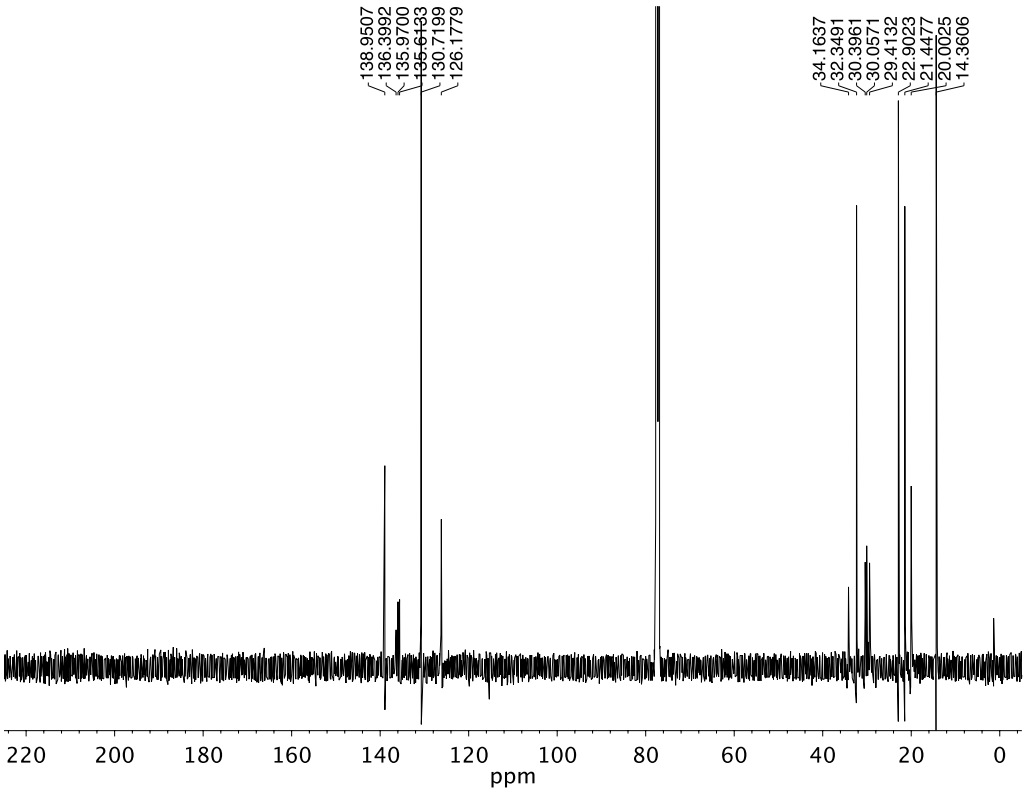


Figure 4.87 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.35.1.**

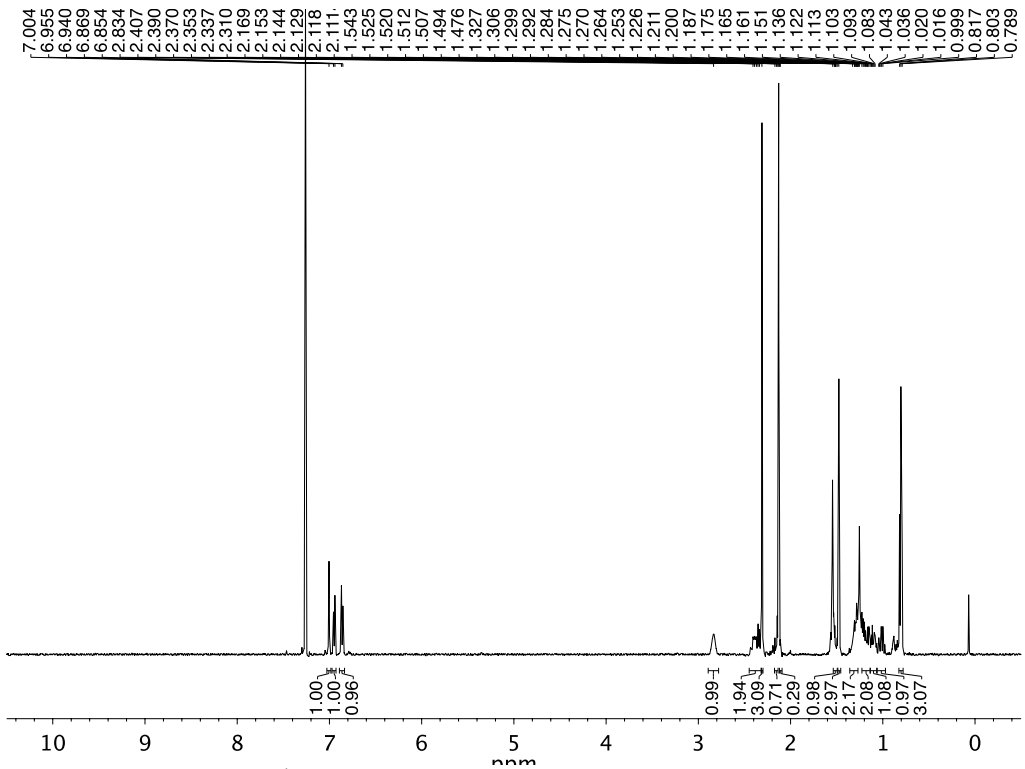


Figure 4.88 ^{1}H NMR (500 MHz, ($CDCl_3$) of compound **4.35.2.**

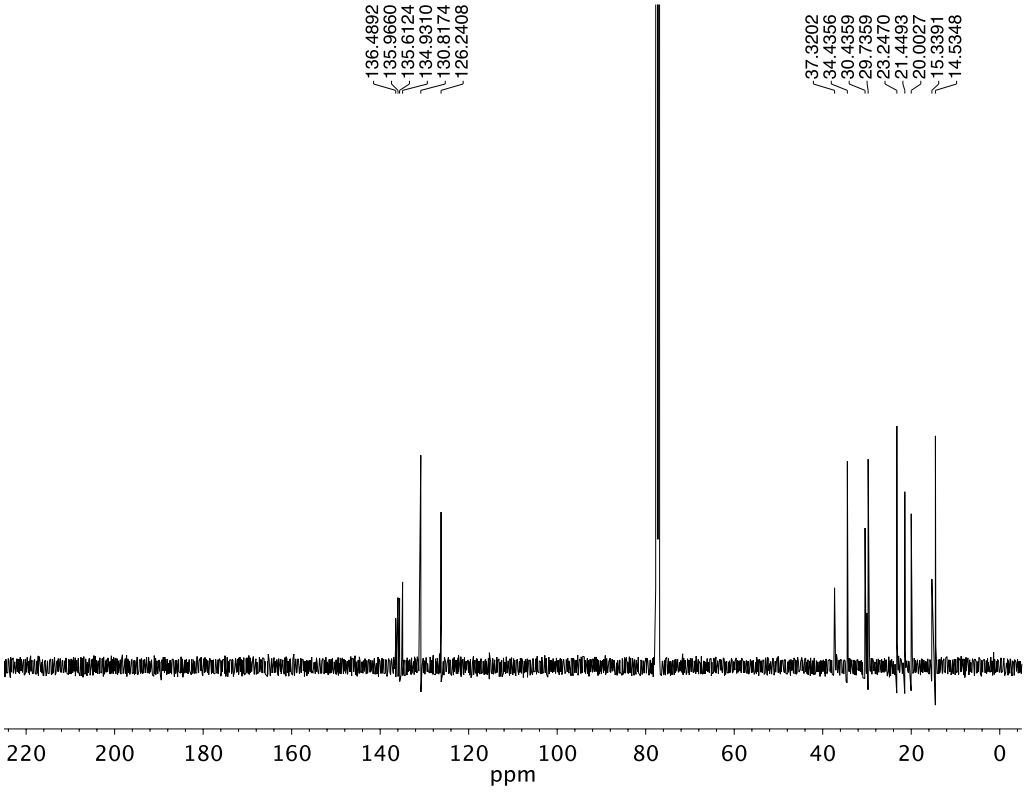


Figure 4.89 ^{13}C NMR (126 MHz, ($CDCl_3$) of compound **4.35.2.**

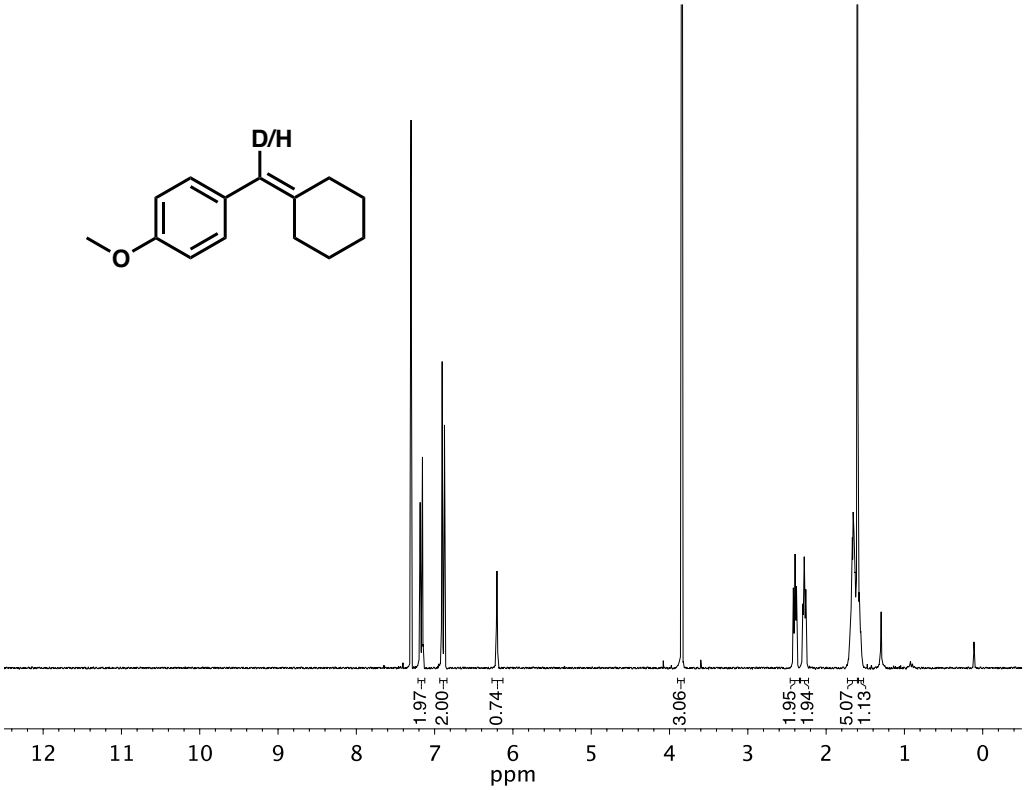


Figure 4.90 ^{1}H NMR (300 MHz, ($CDCl_3$) of compound **4.36.**
Indicating ~25% deuterium incorporation

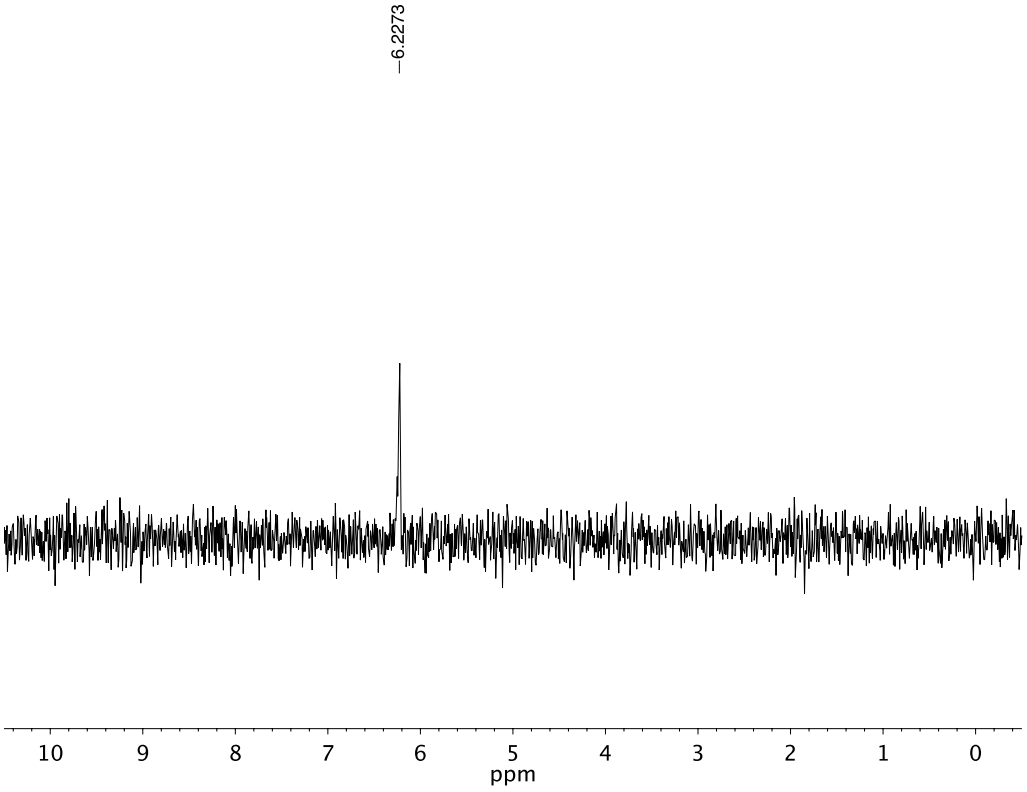


Figure 4.91 ^{2}H NMR (77 MHz, ($CHCl_3$)) of compound **4.36.**

4.8 Notes and References

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CHAPTER FIVE

Vinyl Tosylates as Precursors to Vinyl Carbocations and Efforts to Control the Enantioselectivity of C–H Insertion Reactions

(Unpublished Work)

Hosea M. Nelson, Sepand Nistanaki, Stasik Popov, Benjamin Wigman, Chloe Williams

(authors alphabetically listed by last name)

5.1 Abstract

Vinyl triflates act as good leaving groups and serve as excellent precursors to vinyl carbocations, but they often are too unstable to isolate which prevents their usage in synthetic transformations altogether. Here, vinyl tosylates are utilized as precursors for vinyl carbocations that can undergo C–H insertion reactions; these greatly broaden the substrates accessible and still act as good enough leaving groups to observe high yielding reactivity. While some efforts are discussed to achieve stereoselective vinyl carbocation reactions, no enantioselectivity was ever observed with the usage of vinyl triflates. The broadened substrate scope accessed by vinyl tosylates was ultimately necessary in order to achieve highly enantioselective C–H insertion reactions using chiral acids. These efforts are discussed and a brief scope is shown demonstrating the selectivity achieved.

5.2 Introduction

Throughout my efforts to prepare vinyl triflates I have experienced easily isolable products, semi-isolable products (some care must be taken to isolate these), and some products that are difficult to observe even in the crude reaction mixture. The reasoning behind this relates back to Figure 1.3 in Chapter 1; the more linear and electron rich a vinyl carbocation, the easier it is to generate.[1,2] Thus, the easier it is to generate a vinyl carbocation, usually the more difficult it is to purify or handle the vinyl carbocation precursor. This can to some degree be alleviated by the usage of a less labile leaving group, which will be discussed shortly.

One of the first vinyl triflates I was tasked with preparing ended up being an example of an unstable vinyl triflate. In this case (Figure 5.1, **1**), column chromatography on a variety of stationary phases, silica, basic silica, acidic silica, neutral alumina, basic alumina, and acidic alumina, yielded decomposition products of the vinyl triflate. This was surprising, as there is no electron rich arene appended, but likely rearrangement with the adjacent cyclohexyl ring is the major cause for instability. At this point HPLC to access small amounts of material or distillation likely would have allowed isolation of this product. However, even with distillation some products are difficult to isolate. Particularly styrenyl triflate **2** was difficult to distill; in general these styrenyl triflates with no electron withdrawing group appended to the arene were difficult to handle. However, in Chapter 3, several substrates (i.e. **3**) with withdrawing groups were easily isolable even by column chromatography on silica gel. Substrate **2** could be prepared and isolated, but even in a glovebox freezer at –40ºC decomposition was observed to yield a black tar within six months.

Some other substrates could be isolated by column chromatography, but I noticed that in preparing them that they could not be in contact with dry silica gel without decomposing. These

substrates (**4,5**) sit in the middle of unstable and stable in my mind. They both contain electron rich arenes, however the benzosuberonyl triflate (**4**) is part of a 7-membered ring making it slightly more difficult to ionize due to ring strain and the vinylogous acyltriflate (**5**) has an appended ester withdrawing group on the alkene making up for the increased reactivity of a linear vinyl triflate. Both of these substrates required storage at <–20ºC.

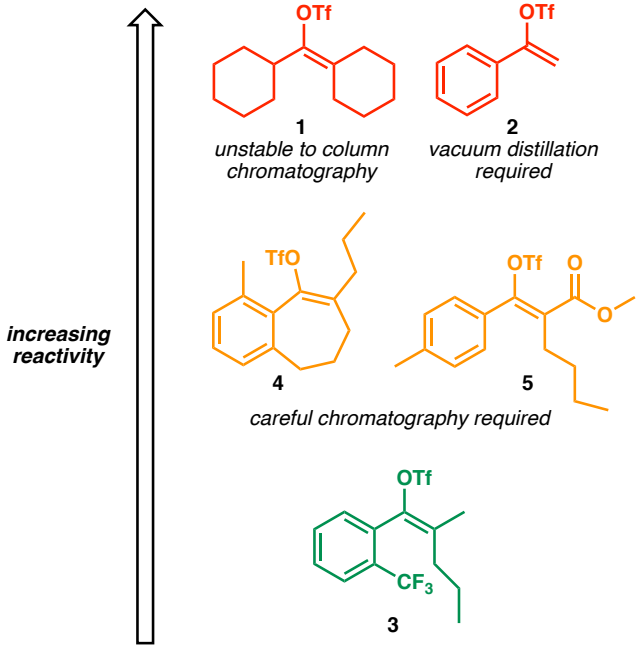


Figure 5.1 Substrates and attempted substrates prepared ranked in terms of reactivity

5.3 Efforts Towards Enantioselective Vinyl Carbocation Reactions

With this in mind most of my and my colleagues screening efforts focused on the benzosuberonyl triflates, which drastically limited opportunities for research in enantioselective catalysis by a lack of substrate diversity. My colleagues tested a variety of chiral urea catalysts with the propylated benzosuberonyltriflate and vinylogous triflate **5**, all to no avail. Below is a short summary of failed efforts on my part to perform reductive C–H insertion reactions (Figure 5.2). The goal was to deliver a hydride, hopefully with the lithium chelated to a chiral ligand, enantioselectively. Some efforts were also made to perform reductive Friedel-Crafts reactions,

where only one stereocenter is set, but elimination to the styrene always outcompeted the desired reduction.

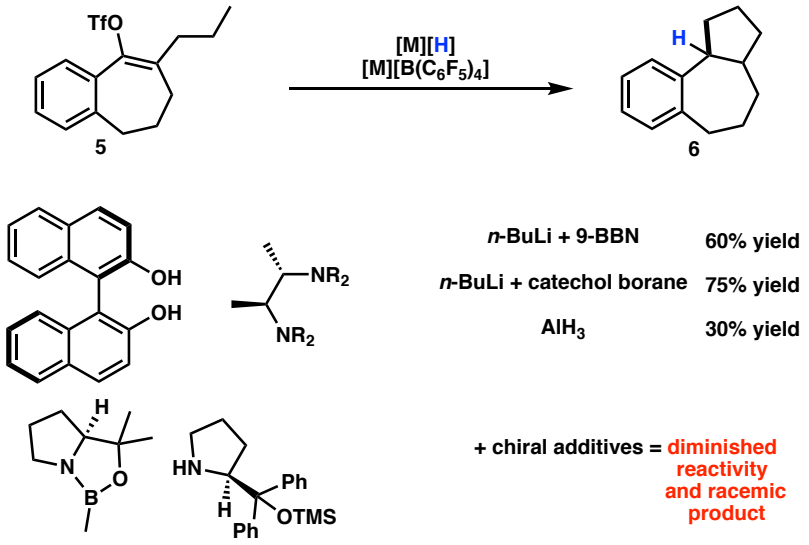


Figure 5.2 Failed attempts at enantioselective reductive C–H insertions

While the reductive C–H insertion without the use of silylium itself may be interesting, the reactions still required rather harsh reagents and led to no enantiocontrol. This short effort was eventually stopped, and it was not until Sepand Nistanaki started to utilize more complex chiral catalysts that any stereoselectivity was achieved in C–H insertion reactions.

According to the small amounts of effort in figure 5.2, it may not be immediately obvious, but the lack of substrate diversity stood as a large challenge to gain any enantioselectivity. Particularly, because the vinyl carbocations we typically generate are not very stabilized, it would likely be difficult to gain catalyst control over such a fast ensuing reaction. This is evident in a variety of systems that demonstrate enantioselectivity over reactions with carbocations. One particular case is shown in Figure 5.3.[3]

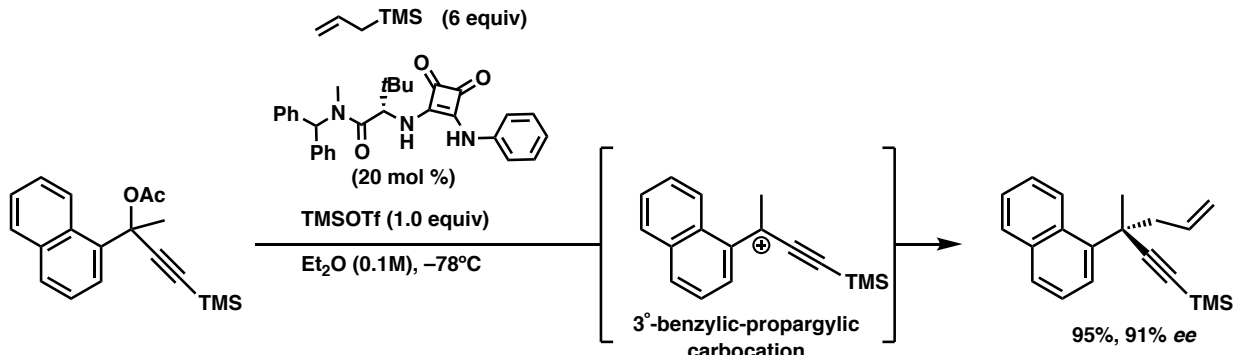


Figure 5.3 Enantioselective allylation of stabilized alkyl carbocation.

Enantioselective reactions of carbocations are generally performed with stabilized carbocation intermediates, such as the enantiocontrol involving alkyl carbocations or even iminium and oxocarbenium ions.[4–11] Increasing enantiocontrol over these intermediates has been gained in the past decade, with a variety of studies utilizing chiral phosphates in ion pairing catalysis.[12] While these were initially tested in our system, we found that most popular chiral anions are too basic to be used in our system. These typically led to no production of the vinyl carbocation.

This left us in a bit of a conundrum: how do we gain access to salts in which the chiral anion doesn't diminish Lewis acidity of the counter-cation, yet provides enough coordination to give control over a highly-reactive carbocation intermediate. Sepand spearheaded this effort, and he found that electron-deficient IDPi (imidodiphosphorimidates) acids paired with allylsilanes are able to abstract vinyl tosylates to vinyl carbocations that subsequently undergo C–H insertion reactions. Initial experiments showed 30% enantiomeric excess (*ee*) on known C–H insertion products, and from there myself and two others joined Sepand to optimize the enantioselectivity.

Most of the efforts will be heavily summarized here, but to give a small insight into the vast array of substrates tested I will give one example. In addition to this substrate, the appeneded cyclohexyl, cyclopentyl, and cycloheptyl analogues were also tested (not shown here) (Figure 5.4).

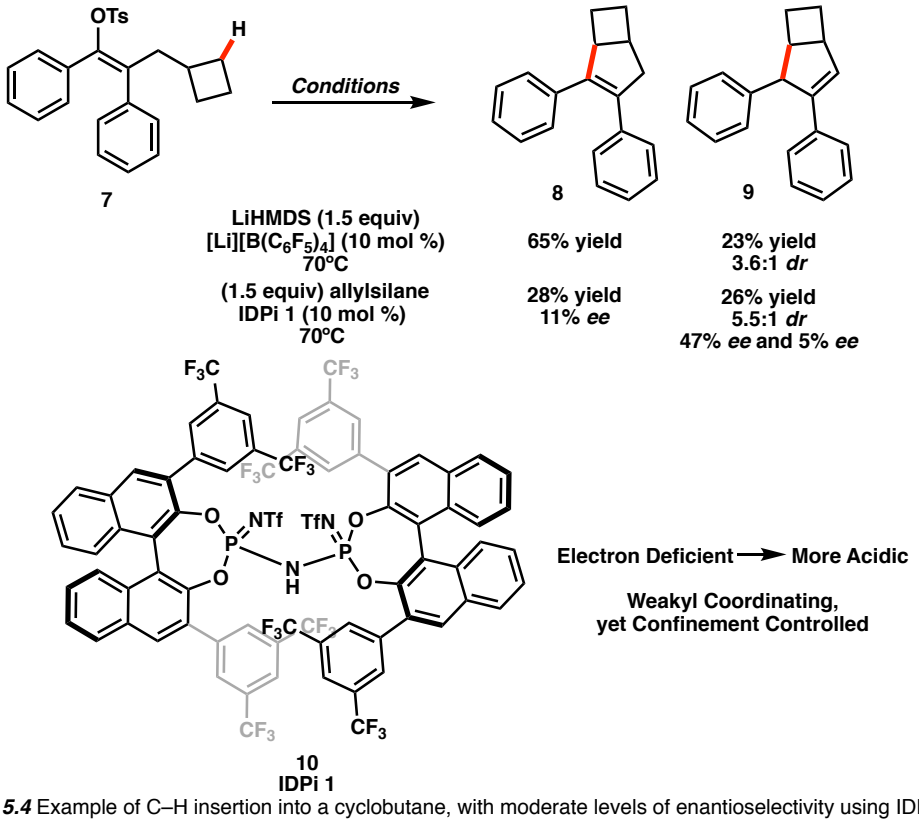


Figure 5.4 Example of C–H insertion into a cyclobutane, with moderate levels of enantioselectivity using IDPi's

Here, cyclobutyl substrate **7** underwent facile C–H insertion to yield olefin products **8** and **9** (a mixture of diastereomers). This substrate demonstrates how important the usage of vinyl tosylates was, as this diaryl vinyl triflate would have been highly unstable, but the vinyl tosylate was an easily handled crystalline solid. Particularly interesting are the differences in reaction outcome with IDPi 1 (**10**); a different ratio of both olefin isomers and diastereomers was observed. This gave us an early clue, besides the modest levels of enantioselectivity, that different catalysts are able to give different outcomes to these reactions. Previously, optimization of olefin isomer ratios was almost entirely substrate dependent, and usage of various bases made little to no difference in reaction outcome.

With this result in hand and hopes that high enantioselectivty can be achieved by confinement,[13] we began to fully optimize this system. After the exploration of many different substrate classes and >50 catalysts we finally arrived at the optimized system shown in Figure

5.5. These NTf-appended piperidines yielded high regioselectivity, diastereoselectivity, and enantioselectivity; this selectivity was very exciting.

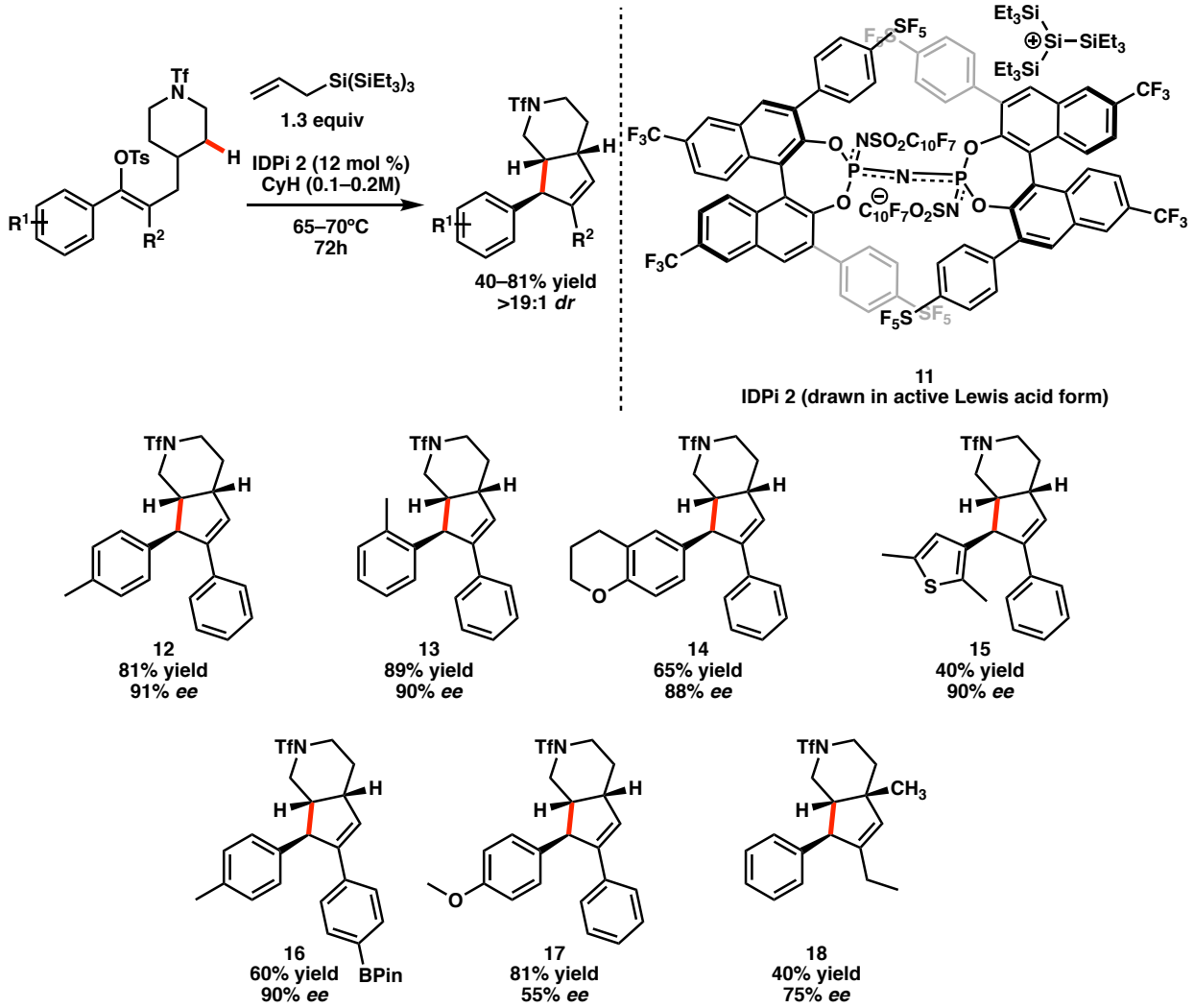


Figure 5.5 Short scope of enantioselective C–H insertion into piperidine C–H bonds

This was a combined result of the usage of the optimized catalyst **11**, drawn as the active "silylium" Lewis acid that can abstract the vinyl tosylate, in addition to the substrate design. This is again an example of an instance where the electron rich vinyl triflate would have been entirely unstable, but we found that electron rich arenes, utilizing stable vinyl tosylates, were crucial to give us high levels of enantioselectivity. This is likely due to stabilization of the intermediate vinyl carbocation by the electron rich arene, that yields a later transition state/slower C–H

insertion reaction and gives higher levels of enantioselectivity.[14] Mechanistic investigations are still ongoing at this time.

In addition to these high levels of enantiocontrol, the substrate scope is also noteworthy. Even utilizing "silylium" **11** as the active Lewis acid, aryl ethers, thiophenes and boronic esters are all tolerated in moderate to good yield (**12–17**). Other highlights include the ability to perform an insertion reaction adjacent to a quaternary center (**17**) and also the ability to retain moderate levels of enantioselectivity when one of the aryl groups is swapped to a much smaller ethyl moiety (**18**).

5.4 Conclusion

Here, the usage of vinyl tosylate precursors is shown to give access to increased substrate diversity, all while still acting as competent precursors to vinyl carbocations. Additionally, efforts to gain access to enantioselective C–H insertion reactions are described. Ultimately the usage of imidiodiphosphorimidate acid catalysts in combination with N-triflyl piperidine appended linear vinyl tosylate substrates demonstrates for the first time highly enantio-, diasterio-, and regio- selective C–H insertion reactions of vinyl carbocations. Good functional group tolerance is also retained in this system. While only my portion of the substrates are shown, this effort is the culmination of the work of four PhD students over the course of almost two years; with these efforts and key findings there is now more hope to gain selectivity over canonically-uncontrollable reactive intermediates in organic chemistry.

5.5 Experimental Section

5.5.1 Materials and Methods

Unless otherwise stated, all reactions were performed in an MBraun or Vacuum Atmospheres glovebox under nitrogen atmosphere with ≤ 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and dried *in vacuo* before use. All liquid substrates were either dried over CaH_2 or filtered through dry neutral aluminum oxide. Solid substrates were dried over P_2O_5. All solvents were rigorously dried before use. Benzene, *o*-dichlorobenzene, and toluene were degassed and dried in a JC Meyer solvent system and stored inside a glovebox. Cyclohexane was distilled over potassium. *o*-Difluorobenzene was distilled over CaH_2. Hydrogen-bonding catalysts were prepared according to original or modified literature procedures.[15] Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. $AgNO_3$-Impregnated silica gel was prepared by mixing with a solution of $AgNO_3$ (150% v/w of 10% w/v solution in acetonitrile), removing solvent under reduced pressure, and drying at 120 °C. Measurements of enantiomeric excess (*ee*) were performed using an Agilent 1260 inifity chiral HPLC using hexanes and isopropanol as the mobile phase. NMR spectra were recorded on a Bruker AV-300 (^1H, ^{19}F), Bruker AV-400 (^1H, ^{13}C, ^{19}F), Bruker DRX-500 (^1H), and Bruker AV-500 (^1H, ^{13}C). ^1H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^1H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted

otherwise. GC spectra were recorded on an Agilent 6850 series GC using an Agilent HP-1 (50 m, 0.32 mm ID, 0.25 mm DF) column. GCMS spectra were recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 mm DF) column interface at room temperature. IR Spectra were record on a Perkin Elmer 100 spectrometer and are reported in terms of frequency absorption (cm^{-1}). High resolution mass spectra (HR-MS) were recorded on a Waters (Micromass) GCT Premier spectrometer, a Waters (Micromass) LCT Premier, or an Agilent GC EI-MS, and are reported as follows: m/z (% relative intensity). Purification by preparative HPLC was done on an Agilent 1200 series instrument with a reverse phase Alltima C_{18} (5m, 25 cm length, 1 cm internal diameter) column.

General Procedures

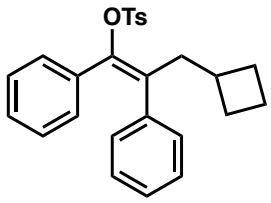
Spectral data and procedures for the preparation of **2,3,5** *are previously reported in the literature and this thesis in Chapters 2,3.*

5.5.2 Initial attempts at enantioselective C–H insertion of Benzosuberonyltriflate 5

The following were performed in a glovebox with a well maintained atmosphere, <0.5 ppm O_2 and H_2O. To a dram vial was added cyclohexane (0.5 mL) and a stir bar. To this was added the hydride source (*n*-BuLi 1.5 equiv + 9-BBN 1.7 equiv) or (*n*-BuLi 1.5 equiv + catechol borane) or (AlH_3 1.5 equiv). This solution was stirred for 15 minutes at room temperature. To this solution was added [Li][$B(C_6F_5)_4$] (0.1 equiv, 0.005 mmol) followed by benzosuberonyltriflate **5** (0.05 mmol, 1 equiv, 16.7 mg). The solution was stirred at room temperature for 18 hours, and subsequently quenched (carefully!) by adding satd. aq. NH_4Cl and plugged through silica gel with diethyl ether to remove the water and yield the crude product. An NMR yield was obtained with 1,4-dioxane as an internal standard to show 60% (9-BBN), 75% (catechol borane), and 30%

(AlH_3) yield respectively. The material could be purified by flash column chromatography (100% hexanes) to yield **6** as a colorless oil. The spectra was in agreement with the literature.[15] This spectrum is shown in the supporting information of Chapter 2. Various chiral additives were also utilized in each case (see Figure 5.2), and in each case the yield was either diminished or yielded no product even at elevated temperatures. Additionally, all products produced were racemic.

5.5.3 Preparation of Substrates and Catalysts

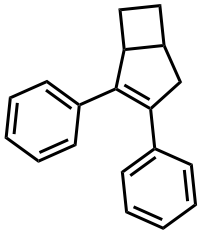


(*E*)-3-cyclobutyl-1,2-diphenylprop-1-en-1-yl 4-methylbenzenesulfonate (7)

To a flame dried flask was added KOtBu (369 mg, 1.5 equiv, 3.3 mmol) and THF (8 mL). This solution was cooled to 0ºC and **2-phenyl-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.12B)** (0.79 g, 1 equiv, 1.8 mmol) was added dropwise as a solution in THF (6 mL). This solution was stirred at 0ºC for 1h. To this was quickly added solid toluenesulfonic anhydride (1.05 g, 1.5 equiv, 3.3 mmol). This solution was allowed to warm to room temperature and stirred for 1 h. The reaction was diluted with ethyl acetate (15 mL) and 1M aqueous NaOH (5 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (1% ether in hexanes → 20% ether in hexanes) to give **(*E*)-3-cyclobutyl-1,2-diphenylprop-1-en-1-yl 4-methylbenzenesulfonate (7)** (600 mg, 70% yield) as a single isomer.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.17 – 7.10 (m, 3H), 7.07 (dt, *J* = 8.0, 0.7 Hz, 2H), 7.01 – 6.93 (m, 3H), 6.91 – 6.82 (m, 4H), 2.77 (d, *J* = 7.7 Hz, 2H), 2.35 (s, 3H), 2.22 – 2.09 (m, 1H), 1.84 (dddd, *J* = 9.6, 8.3, 5.4, 2.5 Hz, 2H), 1.77 – 1.70 (m, 2H), 1.70 – 1.65 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 143.2, 138.6, 134.4, 134.3, 133.8, 129.8, 129.2, 128.0, 127.4, 126.9, 39.6, 34.0, 28.1, 21.5, 18.3.

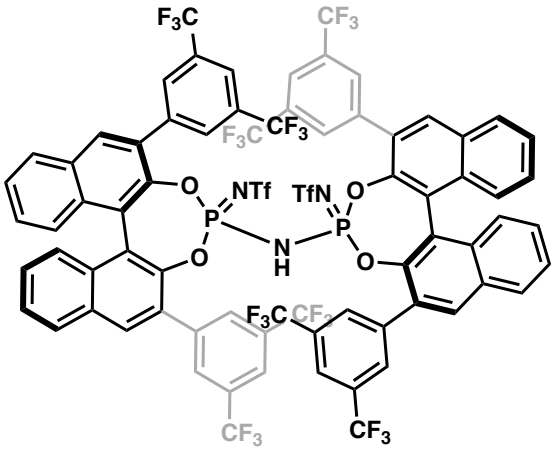


2,3-diphenylbicyclo[3.2.0]hept-2-ene (8)

In a well-kept glove box (O_2, H_2O) to a dram vial was added [Li][$B(C_6F_5)_4$] (2.1 mg, 0.005 mmol, 0.1 equiv) and LiHMDS (12.5 mg, 1.5 equiv, 0.075 mmol). To this was added cylcohexane (0.5 mL) followed by **(*E*)-3-cyclobutyl-1,2-diphenylprop-1-en-1-yl 4-methylbenzenesulfonate** (12.3 mg, 1 equiv, 0.050 mmol). This solution was heated to 70ºC overnight and then removed from the glovebox and plugged through silica gel with diethyl ether. This was concentrated and analyzed by ^{1}H NMR with nitromethane as an internal standard to show that **8** was produced in 65% yield. This crude material was further purified by preparative TLC (5% benzene in hexanes) to yield **8** as a colorless oil.

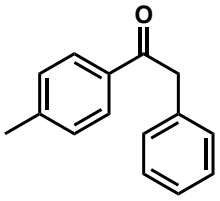
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 – 7.07 (m, 10H), 3.92 – 3.59 (m, 1H), 3.36 – 2.91 (m, 2H), 2.87 – 2.61 (m, 1H), 2.49 – 2.17 (m, 2H), 2.10 – 1.80 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 138.7, 137.6, 137.4, 128.4, 128.2, 128.0, 128.0, 126.6, 126.4, 51.5, 46.7, 33.9, 27.3, 27.1.

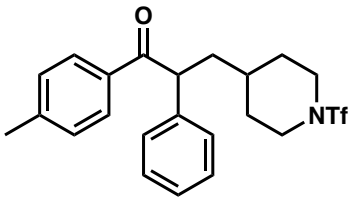


10
IDPi 1

IDPi 1 (10) was prepared according to the literature procedure, and ^{1}H NMR matched the reported spectrum.[16]



2-phenyl-1-(*p*-tolyl)ethan-1-one (12A) was prepared according to literature procedures and matched the ^{1}H NMR data in the literature.[17]



2-phenyl-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.12B)

To a flamed dried flask was added KOtBu (293 mg, 1.1 equiv, 2.6 mmol). This flask was evacuated under vacuum and backfilled with nitrogen three times. To this was added THF (8 mL), and the flask was cooled to 0ºC. To this flask was added **2-phenyl-1-(*p*-tolyl)ethan-1-one**

(0.50 g, 1 equiv, 2.4 mmol) in THF (4 mL), and the solution was stirred at 0ºC for 20 minutes. To this was added a solution of the **4-(iodomethyl)-1-((trifluoromethyl)sulfonyl)piperidine** (892 mg, 1.05 equiv, 2.50 mmol) in THF (4 mL). The reaction flask was allowed to warm up to room temperature overnight, and quenched by addition of saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ethyl acetate (3x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (5% ethyl acetate in hexanes) to yield **2-phenyl-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one** as a white solid (788 mg, 75% yield).

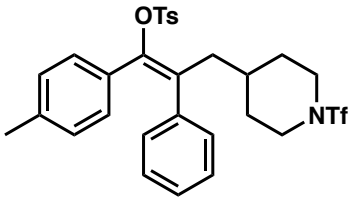
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.23 (m, 5H), 7.17 (d, *J* = 8.1 Hz, 2H), 4.63 (t, *J* = 7.5 Hz, 1H), 4.09 – 3.66 (m, 2H), 2.90 (q, *J* = 13.0 Hz, 2H), 2.29 – 2.04 (m, 3H), 1.98 – 1.63 (m, 1H), 1.50 – 1.13 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 144.1, 139.3, 133.9, 129.3, 129.0, 128.7, 127.9, 127.2, 120.0 (q, *J* = 323.7 Hz), 50.0, 46.7, 40.08, 32.82, 31.91, 21.57.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1.

FT-IR (neat film NaCl): 2919, 1675, 1604, 1460, 1387, 1182, 1149, 1118, 1047, 949, 937, 706 cm^{-1}.

HR-MS (EI-MS) m/z: [M+H]+ Calculated for $C_{22}H_{25}F_3NO_3S$: 440.1507; Measured: 440.1509.



(5.12C)

To a flame dried flask was added KOtBu (302 mg, 1.5 equiv, 2.7 mmol) and THF (7 mL). This solution was cooled to 0ºC and **2-phenyl-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.12B)** (0.79 g, 1 equiv, 1.8 mmol) was added dropwise as a solution in

THF (5 mL). This solution was stirred at 0ºC for 1h. To this was quickly added solid toluenesulfonic anhydride (0.88 g, 1.5 equiv, 2.7 mmol). This solution was allowed to warm to room temperature and stirred for 1 h. The reaction was diluted with ethyl acetate (15 mL) and 1M aqueous NaOH (5 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (1% ether in hexanes → 20% ether in hexanes) to give **(*E*)-2-phenyl-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate** (780 mg, 73% yield). The olefin isomer is assigned to be *E* on the basis of NOESY NMR (observe NOE correlations between tosylate and piperidine fragments). Consistent with this assignment, the chemical shift of the allylic methylene protons (2.73 ppm) is congruent to similarly reported *E* diaryl vinyl tosylates (typically ~2.7 ppm for allylic methylene), which are distinct from the reported *Z* isomer chemical shift (typically ~2.3 ppm for allylic methylene of corresponding *Z* vinyl tosylate). Additionally, this product was crystallized in hexanes to yield X-ray quality crystals to definitively assign the olefin geometry.

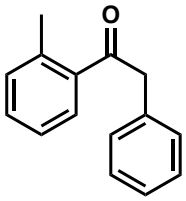
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.21 – 7.14 (m, 3H), 7.09 (d, *J* = 8.1 Hz, 1H), 7.02 (dd, *J* = 6.6, 2.9 Hz, 2H), 6.80 – 6.62 (m, 2H), 3.84 (d, *J* = 13.0 Hz, 2H), 2.89 (s, 1H), 2.69 (d, *J* = 6.3 Hz, 2H), 2.37 (s, 3H), 2.18 (s, 3H), 1.71 (d, *J* = 11.8 Hz, 2H), 1.44 – 1.17 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 144.4, 138.2, 137.9, 134.3, 131.6, 130.2, 129.8, 129.2, 129.2, 128.4, 128.1, 127.9, 127.3, 120.1 (q, *J* = 323.3 Hz), 46.6, 38.7, 33.0, 31.4, 21.5, 21.2.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.0.

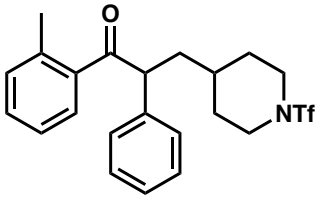
FT-IR (neat film NaCl): 2927, 1598, 1386, 1226, 1188, 1150, 1049, 971, 941, 849 cm^{-1}.

HR-MS (EI-MS) m/z: [M+K]+ Calculated for $C_{29}H_{30}F_3NO_5S_2K$: 632.1155; Measured: 632.1166.



2-phenyl-1-(*o*-tolyl)ethan-1-one (5.13A)

5.13A was prepared according to known procedures, and matched the reported ^{1}H NMR spectrum.[18]



2-phenyl-1-(*o*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.13B)

To a flamed dried flask was added KOtBu (576 mg, 1.1 equiv, 5.1 mmol). This flask was evacuated under vacuum and backfilled with nitrogen three times. To this was added THF (15 mL), and the flask was cooled to 0ºC. To this flask was added **2-phenyl-1-(*o*-tolyl)ethan-1-one (13A)** (0.98 g, 1 equiv, 4.7 mmol) in THF (10 mL), and the solution was stirred at 0ºC for 20 minutes. To this was added a solution of the **4-(iodomethyl)-1 ((trifluoromethyl)sulfonyl)piperidine** (1.75 g, 1.05 equiv, 4.9 mmol) in THF (10 mL). The reaction flask was allowed to warm up to room temperature overnight, and quenched by addition of saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ethyl acetate (3x 20 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→5%→7% ethyl acetate in hexanes) to yield **2-phenyl-1-(*o*-**

tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one as a white solid (805 mg, 40% yield).

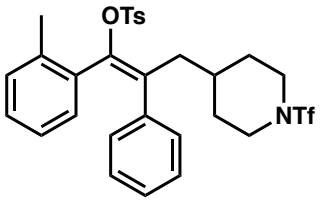
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.47 (m, 1H), 7.38 – 7.27 (m, 2H), 7.24 – 7.01 (m, 5H), 4.49 (t, *J* = 7.5 Hz, 1H), 4.05 – 3.74 (m, 2H), 2.99 – 2.86 (m, 2H), 2.30 (s, 3H), 2.17 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.99 – 1.80 (m, 2H), 1.75 (d, *J* = 11.8 Hz, 1H), 1.46 – 1.20 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.1, 138.2, 138.2, 138.1, 131.8, 131.1, 129.0, 128.2, 127.7, 127.3, 125.5, 120.0 (q, *J* = 323.6 Hz), 53.3, 46.7, 39.2, 32.8, 32.1, 31.7, 20.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1.

FT-IR (neat film NaCl): 2938, 2874, 1684, 1599, 1571, 1491, 1452, 1386, 1356, 1251, 1226, 1146, 1052, 997, 948, 761, 738, 708 cm^{-1}.

HR-MS (ESI) m/z: [M+] Calculated for $C_{22}H_{24}F_3NO_3S$: 439.1419; Measured: 439.1412.



(*E*)-2-phenyl-1-(*o*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate 5.13C

To a flame dried flask was added KOtBu (308 mg, 1.5 equiv, 2.75 mmol) and THF (7 mL). This solution was cooled to 0ºC and **2-phenyl-1-(*o*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.13B)** (0.81 g, 1 equiv, 1.83 mmol) was added dropwise as a solution in THF (5 mL). This solution was stirred at 0ºC for 1h. To this was quickly added solid toluenesulfonic anhydride (0.90 g, 1.5 equiv, 2.75 mmol). This solution was allowed to warm to room temperature and stirred for 1 h. The reaction was diluted with ethyl acetate (15 mL) and 1M aqueous NaOH (5 mL). The organic layer was separated, and the aqueous layer was

extracted with ethyl acetate (3 x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (1% ether in hexanes → 20% ether in hexanes) to give **(*E*)-2-phenyl-1-(*o*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate** (720 mg, 67% yield) as a singler isomer. The olefin isomer is assigned to be *E.* Consistent with this assignment, the chemical shift of the allylic methylene protons (2.9 ppm) is congruent to similarly reported *E* diaryl vinyl tosylates (typically ~2.7 ppm for allylic methylene), which are distinct from the reported *Z* isomer chemical shift (typically ~2.3 ppm for allylic methylene of corresponding *Z* vinyl tosylate).

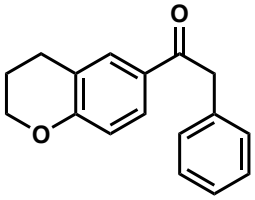
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.4 Hz, 2H), 7.17 – 7.05 (m, 3H), 7.06 – 6.99 (m, 2H), 6.95 (dq, *J* = 6.9, 3.1, 2.3 Hz, 2H), 6.90 – 6.85 (m, 1H), 6.79 (t, *J* = 8.1 Hz, 2H), 3.88 (d, *J* = 12.9 Hz, 2H), 2.92 (dd, *J* = 13.7, 7.2 Hz, 3H), 2.74 (dd, *J* = 13.9, 4.8 Hz, 1H), 2.33 (s, 3H), 1.99 (s, 3H), 1.85 – 1.70 (m, 2H), 1.52 – 1.03 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 144.2, 137.7, 137.4, 134.1, 133.0, 132.6, 132.1, 129.6, 129.0, 128.7, 128.6, 128.1, 127.5, 127.3, 125.0, 120.0 (q, *J* = 323.5 Hz), 46.6, 37.9, 33.3, 31.7, 31.1, 21.5, 19.8.

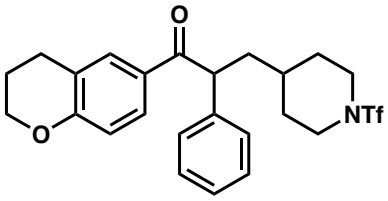
^{19}F NMR (282 MHz, $CDCl_3$) δ -75.0.

FT-IR (neat film NaCl): 2927, 2875, 1598, 1494, 1387, 1226, 1138, 1150, 1117, 1050, 1006, 940, 837, 807, 789, 709 cm^{-1}.

HR-MS (ESI) m/z: [M+Na]+ Calculated for $C_{29}H_{30}F_3NO_5S_2Na$: 616.1415; Measured: 616.1416.



1-(chroman-6-yl)-2-phenylethan-1-one (**5.14A**) was prepared according to known procedures, and matched the reported ^{1}H NMR spectrum.[19]



1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.14B)

To a flamed dried flask was added KOtBu (452 mg, 1.1 equiv, 3.9 mmol). This flask was evacuated under vacuum and backfilled with nitrogen three times. To this was added THF (10 mL), and the flask was cooled to 0ºC. To this flask was added **1-(chroman-6-yl)-2-phenylethan-1-one** (0.92 g, 1 equiv, 3.7 mmol) in THF (8 mL), and the solution was stirred at 0ºC for 20 minutes. To this was added a solution of the **4-(iodomethyl)-1 ((trifluoromethyl)sulfonyl)piperidine** (1.37 g, 1.05 equiv, 3.9 mmol) in THF (7 mL). The reaction flask was allowed to warm up to room temperature overnight, and quenched by addition of saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ethyl acetate (3x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→10%→15% ethyl acetate in hexanes) to yield **1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one** as a white solid (1.23 g, 70% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.57 (m, 2H), 7.32 – 7.27 (m, 2H), 7.25 – 7.15 (m, 2H), 6.73 (d, J = 9.2 Hz, 2H), 4.59 (dd, J = 8.2, 6.6 Hz, 1H), 4.28 – 4.08 (m, 2H), 3.87 (t, J = 11.8 Hz,

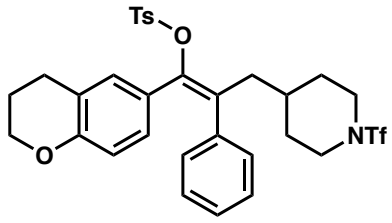
2H), 2.91 (q, *J* = 12.8 Hz, 2H), 2.76 (t, *J* = 6.4 Hz, 2H), 2.19 (ddd, *J* = 14.4, 8.2, 6.3 Hz, 1H), 2.04 – 1.90 (m, 2H), 1.91 – 1.82 (m, 1H), 1.80 – 1.61 (m, 2H), 1.44 – 1.13 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 159.3, 139.6, 131.2, 129.0, 128.5, 127.9, 127.1, 122.2, 120.0 (q, *J* = 323.9 Hz), 116.7, 107.9, 67.6, 66.9, 49.6, 46.7, 40.2, 32.9, 31.9, 29.1, 24.8, 21.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1.

FT-IR (neat film NaCl): 2943, 2875, 1723, 1668, 1601, 1574, 1497, 1445, 1336, 1358, 1316, 1251, 1147, 1117, 1058, 1003, 939, 826, 708 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{24}H_{26}F_3NO_4S$: 482.1612; Measured: 481.1611.



(*E*)-1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.14C)

To a flame dried flask was added KOtBu (419 mg, 1.5 equiv, 3.7 mmol) and THF (12 mL). This solution was cooled to 0ºC and **1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.14B)** (1.2 g, 1 equiv, 2.5 mmol) was added dropwise as a solution in THF (8 mL). This solution was stirred at 0ºC for 1h. To this was quickly added solid toluenesulfonic anhydride (1.2 g, 1.5 equiv, 3.7 mmol). This solution was allowed to warm to room temperature and stirred for 1 h. The reaction was diluted with ethyl acetate (15 mL) and 1M aqueous NaOH (5 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (5%→20%→25% ether in

hexanes) to give **(*E*)- 1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate** (460 mg, 29% yield) as a singler isomer. The olefin isomer is assigned to be *E* by NOESY NMR (observe NOE between the chromane arene and the adjacent phenyl ring). Consistent with this assignment, the chemical shift of the allylic methylene protons (2.72 ppm) is congruent to similarly reported *E* diaryl vinyl tosylates (typically ~2.7 ppm for allylic methylene), which are distinct from the reported *Z* isomer chemical shift (typically ~2.3 ppm for allylic methylene of corresponding *Z* vinyl tosylate).

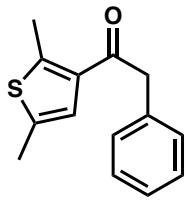
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.24 – 7.15 (m, 3H), 7.13 – 7.09 (m, 2H), 7.07 – 7.00 (m, 2H), 6.52 – 6.42 (m, 2H), 6.28 (d, *J* = 8.3 Hz, 1H), 4.05 (dd, *J* = 5.8, 4.4 Hz, 2H), 3.86 (dd, *J* = 13.2, 4.0 Hz, 2H), 2.99 – 2.82 (m, 2H), 2.72 (d, *J* = 6.3 Hz, 2H), 2.37 (s, 3H), 2.30 (t, *J* = 6.5 Hz, 2H), 1.96 – 1.77 (m, 2H), 1.73 (dd, *J* = 12.6, 2.7 Hz, 2H), 1.51 – 1.27 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 145.0, 144.1, 138.4, 134.6, 131.2, 130.6, 129.4, 129.2, 129.0, 128.3, 127.9, 127.1, 124.8, 121.1, 120.0 (q, *J* = 323.7 Hz), 115.6, 66.4, 46.6, 38.7, 33.1, 31.4, 24.4, 22.0, 21.56.

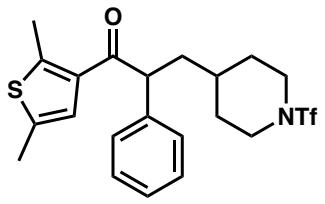
^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9.

FT-IR (neat film NaCl): 2925, 2360, 2241, 1652, 1497, 1385, 1227, 1188, 1176, 1150, 1061, 942, 822, 763, 708 cm^{-1}.

HR-MS (ESI) m/z: [M+Na]+ Calculated for $C_{31}H_{32}F_3NO_6S_2Na$: 658.1520; Measured: 658.1515.



1-(2,5-dimethylthiophen-3-yl)-2-phenylethan-1-one (5.15A) was prepared according to known procedures, and matched literature reported ^{1}H NMR spectra.[20]



1-(2,5-dimethylthiophen-3-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.15B)

To a flamed dried flask was added KOtBu (890 mg, 1.1 equiv, 7.9 mmol). This flask was evacuated under vacuum and backfilled with nitrogen three times. To this was added THF (15 mL), and the flask was cooled to 0ºC. To this flask was added **1-(2,5-dimethylthiophen-3-yl)-2-phenylethan-1-one** (1.66 g, 1 equiv, 7.2 mmol) in THF (10 mL), and the solution was stirred at 0ºC for 20 minutes. To this was added a solution of the **4-(iodomethyl)-1 ((trifluoromethyl)sulfonyl)piperidine** (2.7 g, 1.05 equiv, 7.6 mmol) in THF (10 mL). The reaction flask was allowed to warm up to room temperature overnight, and quenched by addition of saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ethyl acetate (3x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→5% ethyl acetate in hexanes) to yield **1-(2,5-dimethylthiophen-3-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one** as an off-white solid (1.81 g, 55% yield).

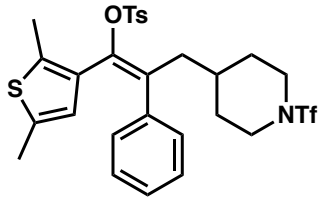
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H), 7.27 – 7.18 (m, 3H), 6.95 (d, J = 1.3 Hz, 1H), 4.32 (dd, J = 7.9, 7.0 Hz, 1H), 3.90 (tdd, J = 11.4, 4.2, 2.2 Hz, 2H), 2.94 (q, J = 12.5 Hz, 2H), 2.64 (s, 3H), 2.35 (d, J = 1.0 Hz, 3H), 2.15 (ddd, J = 14.4, 8.0, 6.6 Hz, 1H), 1.87 (dt, J = 12.5, 2.5 Hz, 1H), 1.77 – 1.60 (m, 2H), 1.53 – 1.15 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 149.1, 139.3, 135.1, 134.9, 129.0, 128.0, 127.1, 125.5, 120.0 (q, J = 323.7 Hz), 52.9, 46.7, 39.9, 32.8, 31.9, 31.8, 16.2, 15.0.

^{19}F NMR (282 MHz, $CDCl_e$) δ -75.1.

FT-IR (neat film NaCl): 2921, 1668, 1476, 1450, 1387, 1361, 1186, 1149, 1114, 1052, 949, 937, 738, 709 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{21}H_{25}F_3NO_3S_2$: 460.1221; Measured: 460.1221.



(*E*)-1-(2,5-dimethylthiophen-3-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.15C)

To a flame dried flask was added KOtBu (366 mg, 1.5 equiv, 3.2 mmol) and THF (9 mL). This solution was cooled to 0ºC and **1-(2,5-dimethylthiophen-3-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.15B)** (1.0 g, 1 equiv, 2.1 mmol) was added dropwise as a solution in THF (9 mL). This solution was stirred at 0ºC for 1h. To this was quickly added solid toluenesulfonic anhydride (1.1 g, 1.5 equiv, 3.2 mmol). This solution was allowed to warm to room temperature and stirred for 3 h. The reaction was diluted with ethyl acetate (15 mL) and 1M aqueous NaOH (5 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (2%→20% ether in hexanes) to give **(*E*)- 1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate** (460 mg, 29% yield) as a singler isomer. The olefin isomer is assigned to be *E* by NOESY-NMR (correlation between thiophene CH_3 group

and adjacent phenyl arene). Consistent with this assignment, the chemical shift of the allylic methylene protons (2.81 ppm) is congruent to similarly reported *E* diaryl vinyl tosylates (typically ~2.7 ppm for allylic methylene), which are distinct from the reported *Z* isomer chemical shift (typically ~2.3 ppm for allylic methylene of corresponding *Z* vinyl tosylate).

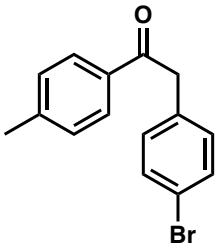
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.14 (m, 4H), 7.11 (d, *J* = 7.9 Hz, 2H), 7.04 – 6.95 (m, 2H), 5.98 (s, 1H), 3.86 (d, *J* = 12.9 Hz, 2H), 2.90 (s, 1H), 2.81 (s, 2H), 2.48 – 2.34 (m, 4H), 2.04 (s, 2H), 1.74 (d, *J* = 12.9 Hz, 2H), 1.69 (s, 3H), 1.50 – 1.14 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 140.5, 137.9, 137.7, 135.4, 134.4, 132.8, 129.5, 129.0, 128.6, 128.2, 127.5, 127.2, 126.3, 120.0 (q, *J* = 323.6 Hz), 46.6, 37.8, 33.5, 31.3, 21.5, 14.6, 13.8.

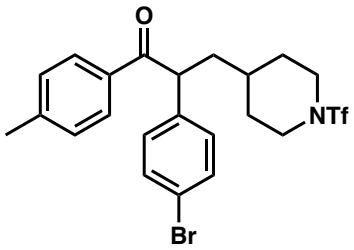
^{19}F NMR (282 MHz, $CDCl_3$) δ -75.0.

FT-IR (neat film NaCl): 2899, 1387, 1274, 1223, 1172, 1150, 1110, 1048, 958, 784, 753, 734 cm^{-1}.

HR-MS (ESI) m/z: [M+Na]+ Calculated for $C_{28}H_{30}F_3NO_5S_3Na$: 636.1136; Measured: 636.1147.



2-(4-bromophenyl)-1-(*p*-tolyl)ethan-1-one (5.16A) was prepared according to known procedures, and the ^{1}H NMR spectrum matched reported literature spectra.[18]



2-(4-bromophenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.16B)

To a flamed dried flask was added KOtBu (615 mg, 1.1 equiv, 5.5 mmol). This flask was evacuated under vacuum and backfilled with nitrogen three times. To this was added THF (15 mL), and the flask was cooled to 0ºC. To this flask was added **2-(4-bromophenyl)-1-(*p*-tolyl)ethan-1-one** (1.44 g, 1 equiv, 4.9 mmol) in THF (10 mL), and the solution was stirred at 0ºC for 20 minutes. To this was added a solution of the **4-(iodomethyl)-1 ((trifluoromethyl)sulfonyl)piperidine** (1.87 g, 1.05 equiv, 5.2 mmol) in THF (10 mL). The reaction flask was allowed to warm up to room temperature overnight, and quenched by addition of saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with ethyl acetate (3x 15 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (2%→10% ethyl acetate in hexanes) to yield **2-(4-bromophenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one** as a white solid (1.35 g, 52% yield).

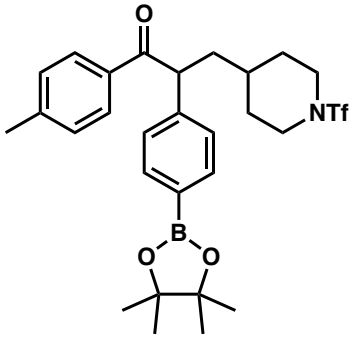
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.3, 2.6 Hz, 2H), 7.42 (dd, J = 8.5, 2.6 Hz, 2H), 7.29 – 7.03 (m, 4H), 4.62 (t, J = 7.8 Hz, 1H), 3.90 (t, J = 13.1 Hz, 2H), 2.93 (d, J = 14.7 Hz, 2H), 2.37 (s, 4H), 2.19 (dt, J = 14.9, 7.5 Hz, 1H), 1.87 (d, J = 13.2 Hz, 1H), 1.75 (dt, J = 13.3, 7.5 Hz, 2H), 1.35 (d, J = 16.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.2, 144.3, 138.3, 133.6, 132.2, 129.7, 129.4, 128.7, 120.0 (q, J = 323.6 Hz), 49.3, 46.7, 39.9, 32.8, 31.9, 31.8, 21.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.0.

FT-IR (neat film NaCl): 2942, 2870, 1677, 1606, 1486, 1386, 1362, 1227, 1149, 1048, 948, 708 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{22}H_{24}BrF_3NO_3S$: 518.0612; Measured: 518.0587.



2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one (5.16C)

To a 100 mL Schlenk flask was added **2-(4-bromophenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one** (800 mg, 1 equiv, 1.5 mmol), potassium acetate (530 mg, 3.5 equiv, 5.4 mmol), bis(pinacolato)diboron (470 mg, 1.2 equiv, 1.8 mmol), and 1,4-dioxane (10 mL). This solution was degassed by freeze-pump-thaw (3 x cycles of 10 minutes under vacuum when frozen). To this degassed solution was added $Pd(dppf)Cl_2$ under a stream of nitrogen. The reaction was then sealed and heated to 80ºC for 15 h. Saturated aqueous NH_4Cl (10 mL) was added and the solution was diluted with ethyl acetate (15 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The organics were washed with brine, dried over Na_2SO_4, concentrated, filtered, and purified by flash column chromatography (100% hexanes→3%→10%→20% ethyl acetate in hexanes) to give an orange oil (799 mg, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 7.19 – 7.14 (m, 2H), 4.64 (t, J = 7.4 Hz, 1H), 4.01 – 3.75 (m, 2H), 2.91 (q, J = 13.3 Hz,

2H), 2.35 (s, 3H), 2.18 (dt, *J* = 14.3, 7.2 Hz, 1H), 1.95 – 1.85 (m, 1H), 1.80 (dt, *J* = 13.7, 6.6 Hz, 1H), 1.71 (dd, *J* = 12.8, 2.8 Hz, 1H), 1.31 (s, 12H).

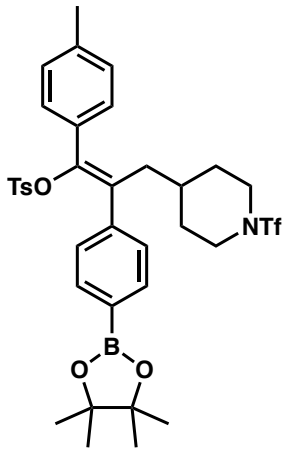
^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 144.0, 142.4, 135.5, 133.8, 129.3, 128.7, 127.4, 120.0 (q, *J* = 323.1 Hz), 83.8, 50.4, 46.7, 39.8, 32.7, 32.0, 31.8, 24.8 (d, *J* = 1.9 Hz), 21.5.

^{11}B NMR (128 MHz, $CDCl_3$) δ 30.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.8.

FT-IR (neat film NaCl): 2978, 2925, 1774, 1677, 1607, 1513, 1445, 1388, 1362, 1272, 1252, 1226, 1182, 1145, 1090, 1050, 948, 828, 709 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{28}H_{35}BF_3NO_5S$: 566.2359; Measured: 566.2355.



(*Z*)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.16D)

To a 50 mL Schlenk flask was added **2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)propan-1-one** (435 mg, 1 equiv, 0.77 mmol) and THF (8 mL). To this solution was added KH (309 mg, 3.0 equiv, 2.3 mmol, 30% w/w). The flask was heated to 75ºC for 3h and cooled to room temperature. Toluenesulfonic anhydride (502 mg, 2.0 equiv, 1.5 mmol) was added under a stream of nitrogen and the reaction was allowed to stir at room temperature for 30 minutes. To this was added satd.

aq. NH_4Cl (5 mL carefully!) and then diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes →10%→20%→30%ether in hexanes) to yield (*Z*)**-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate** (143 mg, 26% yield) as an off-white solid. The olefin isomer is assigned to be *Z* by NOESY-NMR (correlation of tolyl arene not on tosylate and the allyl CH_2). Consistent with this assignment, the chemical shift of the allylic methylene protons (2.33 ppm) is congruent to similarly reported *Z* diaryl vinyl tosylates (typically ~2.3 ppm for allylic methylene), which are distinct from the reported *E* isomer chemical shift (typically ~2.7 ppm for allylic methylene of corresponding *Z* vinyl tosylate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.16 (dd, *J* = 9.5, 8.1 Hz, 4H), 7.05 (dd, *J* = 8.1, 4.0 Hz, 4H), 6.85 (d, *J* = 8.0 Hz, 2H), 3.63 (d, *J* = 12.9 Hz, 2H), 2.66 (t, *J* = 12.7 Hz, 2H), 2.33 (d, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 2.26 (s, 3H), 1.53 (dd, *J* = 13.8, 3.2 Hz, 2H), 1.31 (s, 12H), 1.17 – 1.06 (m, 2H), 1.04 – 0.81 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 143.5, 139.8, 139.0, 134.5, 133.9, 130.6, 130.3, 129.7, 128.9, 128.9, 127.8, 127.5, 119.9 (q, *J* = 323.0 Hz), 83.8, 46.4, 38.6, 33.1, 31.2, 30.3, 24.9, 21.5, 21.3.

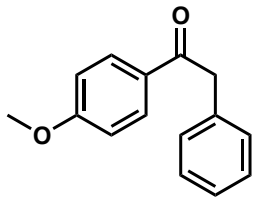
^{11}B NMR (128 MHz, $CDCl_3$) δ 29.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1.

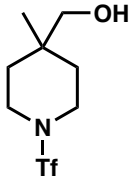
FT-IR (neat film NaCl): 2943, 1398, 1225, 1177, 1144, 1092, 858, 829, 709 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{35}H_{41}BF_3NO_7S_2K$: 758.2006; Measured:

758.2027.



1-(4-methoxyphenyl)-2-phenylethan-1-one (5.17 A) was prepared according to known procedures, and matched the reported ^{1}H NMR spectrum.[18]



(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methanol (5.17 B)

To a flame dried flask with anhydrous dichloromethane (50 mL) was added **(4-methylpiperidin-4-yl)methanol** (5.46 g, 1.0 equiv, 42.3 mmol) in dichloromethane (18 mL) and triethylamine (5.13 g, 7.0 mL, 1.2 equiv, 50.7 mmol). This solution was cooled to 0ºC and freshly distilled trifluoromethanesulfonic anhydride (11.9 g, 7.1 mL, 1.0 equiv, 42.3 mmol) and the solution was allowed to warm up to room temperature overnight. Saturated aqueous $NaHCO_3$ (30 mL) was added and the aqueous layer was extracted further with dichloromethane (3 x 20 mL). The crude material was concentrated and purified by flash column chromatography (100% dichloromethane → 20% ether in dichloromethane) to give a colorless solid (4.0 g, 37% yield).

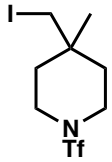
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (d, J = 13.3 Hz, 2H), 3.43 (s, 2H), 3.36 (d, J = 11.4 Hz, 2H), 1.65 (ddd, J = 14.3, 10.2, 4.4 Hz, 2H), 1.55 (bs, 1H), 1.53 – 1.35 (m, 2H), 1.02 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 120.3 (q, J = 323.3 Hz), 42.8, 33.3, 33.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.6.

FT-IR (neat film NaCl): 3360, 2922, 1463, 1385, 1340, 1165, 1140, 1057, 938, 708 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_8H_{15}F_3NO_3S$: 262.0724; Measured: 262.0735.



4-(iodomethyl)-4-methyl-1-((trifluoromethyl)sulfonyl)piperidine ()

To a flame round bottom flask was added dichloromethane (60 mL) and PPh_3 (4.9 g, 1.2 equiv, 18.7 mmol). This solution was cooled to 0ºC and iodine (4.94 g, 1.25 equiv, 19.5 mmol) was added portionwise followed by imidazole (1.59 g, 1.5 equiv, 23.4 mmol). Then **(4-methylpiperidin-4-yl)methanol** (4.07 g, 1.0 equiv, 15.6 mmol) was added in one portion and the reaction was allowed to warm to room temperature over the course of 3h. Once the starting material had been consumed, monitored by TLC, satd. aq. $Na_2S_2O_3$ was added until the orange/yellow color had gone to colorless (~100 mL). This organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 50 mL), the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to yield a yellow solid. This solid was determined to be the phosphonium iodide salt, and so a portion of this material (3 g) was heated in anhydrous benzene (50 mL) to 80ºC for 2 hours. This material was concentrated and purified by flash column chromatography (30% ethyl acetate in hexanes) to give **4-(iodomethyl)-4-methyl-1-((trifluoromethyl)sulfonyl)piperidine** as a yellow solid (1.52 g, 27% yield).

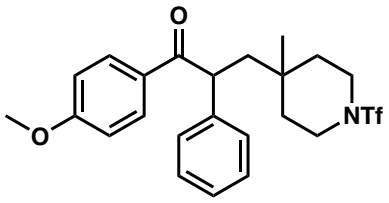
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (bs, 2H), 3.34 (bs, 2H), 3.19 (s, 2H), 1.72 – 1.56 (m, 4H), 1.10 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 120.0 (q, J = 323.3 Hz), 43.1, 35.9, 31.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.6.

FT-IR (neat film NaCl): 2945, 2887, 1470, 1388, 1339, 1262, 1184, 1141, 1056, 939, 707 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_8H_{14}F_3INO_2S$: 371.9742; Measured: 371.9738.



1-(4-methoxyphenyl)-3-(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)-2-phenylpropan-1-one (5.17D)

To a flame dried 100 mL 3-neck flask equipped with a stir bar and reflux condenser was added KOtBu (546 mg, 1.1 equiv, 4.9 mmol). This was evacuated under vacuum and back filled with nitrogen (3 times). To this was added THF (25 mL) and cooled to 0ºC. To this solution was added **1-(4-methoxyphenyl)-2-phenylethan-1-one** (1.0 g, 1.0 equiv, 4.4 mmol) in THF (10 mL) dropwise. This was stirred at 0ºC for 45 minutes, and to this was added **4-(iodomethyl)-4-methyl-1-((trifluoromethyl)sulfonyl)piperidine** (1.72 g, 1.05 equiv, 4.6 mmol) under a stream of nitrogen. This was stirred at 0ºC for 1 h, and then refluxed for 48 h. Then saturated aqueous NH_4Cl (10 mL) was added and the reaction was diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted further with ethyl acetate (3 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash column chromatography (5%→15%→20%→25% ether in hexanes) to give **1-(4-methoxyphenyl)-3-(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)-2-phenylpropan-1-one** (744 mg, 36% yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 7.32 – 7.26 (m, 4H), 7.19 (ddt, *J* = 6.1, 5.0, 2.9 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 2H), 4.68 (dd, *J* = 8.7, 3.4 Hz, 1H), 3.83 (s, 3H), 3.52 (d, *J*

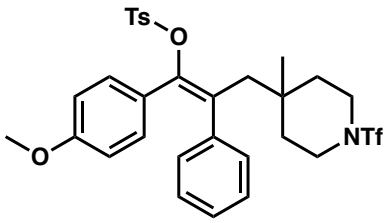
= 20.5 Hz, 2H), 3.33 (bs, 2H), 2.74 (dd, *J* = 14.3, 8.7 Hz, 1H), 1.63 (dd, *J* = 14.2, 3.4 Hz, 3H), 1.50 – 1.29 (m, 2H), 1.00 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 163.5, 140.7, 130.9, 129.27, 129.10, 127.89, 127.05, 120.06 (q, *J* = 323.5 Hz), 113.8, 55.4, 48.0, 42.8, 42.7, 37.0, 36.5, 31.7.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.8.

FT-IR (neat film NaCl): 2921, 1673, 1598, 1385, 1258, 1225, 1140, 1059, 1029, 938, 835, 709, 699 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{23}H_{27}F_3NO_4S$: 470.1612; Measured: 470.1610.



(*E*)-1-(4-methoxyphenyl)-3-(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)-2-phenylprop-1-en-1-yl 4-methylbenzenesulfonate (5.17E)

To a flame dried 50 mL Schlenk flask equipped with a stir bar was added **methoxyphenyl)-3-(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)-2-phenylpropan-1-one** (500 mg, 1.0 equiv, 1.10 mmol). To this was added THF (9 mL) and KH (440 mg, 3.0 equiv, 3.3 mmol, 30% w/w). This solution was heated to 75ºC for 6 h after which it was cooled to room temperature and toluenesulfonic anhydride (645 mg, 1.8 equiv, 2.0 mmol) under a stream of nitrogen and the reaction mixture was stirred further for 1 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (10 mL, Careful!). The solution was further diluted with ethyl acetate (10 mL) and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo*,

and purified by flash column chromatography (1% → 5% → 15% → 20% ether in hexanes) to give **(*E*)-1-(4-methoxyphenyl)-3-(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)-2-phenylprop-1-en-1-yl 4-methylbenzenesulfonate** (340 mg, 51% yield) as an off-white solid. The olefin isomer is assigned to be *E* by NOESY-NMR (correlation of anisole C–H with adjacent phenyl arene, COSY confirm these are not interractions with the tosylate arene). Consistent with this assignment, the chemical shift of the allylic methylene protons (2.79 ppm) is congruent to similarly reported *E* diaryl vinyl tosylates (typically ~2.7 ppm for allylic methylene), which are distinct from the reported *Z* isomer chemical shift (typically ~2.3 ppm for allylic methylene of corresponding *Z* vinyl tosylate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.21 – 6.96 (m, 7H), 6.75 (d, *J* = 8.3 Hz, 2H), 6.41 (d, *J* = 8.4 Hz, 2H), 3.68 (s, 3H), 3.48 (bs, 2H), 3.27 (bs, 2H), 2.79 (s, 2H), 2.37 (s, 3H), 1.50 – 1.46 (m, 2H), 1.34 – 1.21 (m, 3H), 0.88 (s, 3H).

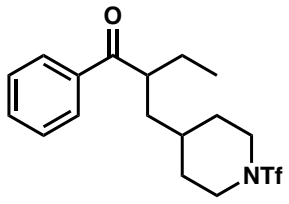
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.11, 145.7, 144.3, 139.8, 134.5, 131.5, 130.0, 129.5, 129.2, 128.3, 127.8, 127.1,

125.7, 120.09 (q, *J* = 323.8 Hz), 113.8, 112.8, 55.0, 42.8, 36.9, 33.6, 21.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.6.

FT-IR (neat film NaCl): 2948, 1389, 1232, 1174, 1143, 1080, 1027, 856, 710 cm^{-1}.

HR-MS (ESI) m/z: [M+K]+ Calculated for $C_{30}H_{32}F_3NO_6S_2K$: 662.1260; Measured: 662.1257.



1-phenyl-2-((1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methyl)butan-1-one (5.18A)

To a 100 mL 3-neck flask equipped with stir bar and reflux condenser was added 1-phenyl-

butanone (0.45 g, 1.0 equiv, 3.00 mmol) in THF (10 mL) and the solution was cooled to 0ºC. To this was added NaH (0.13 g, 1.1 equiv, 3.3 mmol, 60% w/w). To this was added **4-(iodomethyl)-4-methyl-1-((trifluoromethyl)sulfonyl)piperidine** (1.30 g, 1.2 equiv, 3.6 mmol) in THF (12 mL). The reaction was then refluxed overnight, and then diluted with diethyl ether (15 mL), saturated aqueous NH_4Cl (10 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 x 15 mL), the combined organics were dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (100% hexanes → 5% ethyl aceate in hexanes) to give **1-phenyl-2-((1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methyl)butan-1-one** as a colorless oil (281 mg, 24% yield).

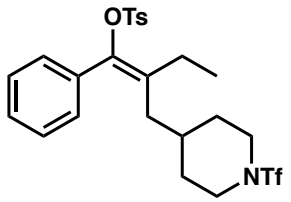
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 7.86 (m, 2H), 7.64 – 7.55 (m, 1H), 7.55 – 7.42 (m, 2H), 4.11 – 3.67 (m, 2H), 3.65 – 3.23 (m, 1H), 2.91 (dt, *J* = 22.7, 12.6 Hz, 2H), 2.02 – 1.88 (m, 1H),1.85 – 1.71 (m, 3H), 1.55 (ddd, *J* = 13.7, 7.6, 6.1 Hz, 1H), 1.48 – 1.12 (m, 4H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.5, 137.1, 133.2, 128.8, 128.0, 120.0 (1, *J* = 323.4 Hz), 46.8, 46.7, 44.2, 37.4, 33.1, 32.3, 31.8, 26.3, 11.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.7.

FT-IR (neat film NaCl): 2928, 2874, 1678, 1447, 1387, 1185, 1148, 1054, 947, 708 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{17}H_{23}F_3NO_3S$: 378.1350; Measured: 378.1346.



(*E/Z*)-1-phenyl-2-((1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methyl)but-1-en-1-yl 4-methylbenzenesulfonate (5.18B)

To a flame dried 25 mL schlenk flask was added **1-phenyl-2-((1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methyl)butan-1-one** (281 mg, 1.0 equiv, 0.74 mmol) and THF (6.0 mL). To this as added KH (299 mg, 3.0 equiv, 2.2 mmol, 30% w/w). This solution was sealed and heated to 75ºC for 12 h. The solution was cooled and toluenesulfonic anhydride (437 mg, 1.8 equiv, 1.3 mmol) was added under a stream of nitrogen. The solution was further stirred at room temperature for 1.5 h. The reaction was diluted with ethyl acetate (5 mL) and saturated aqueous NH_4Cl (5 mL, careful!) was added. The aqueous layer was separated and further extracted with ethyl acetate (3 x 8 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified flash column chromatography (100% hexanes→8% ethyl acetate in hexanes) to give **(*E/Z*)-1-phenyl-2-((1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methyl)but-1-en-1-yl 4-methylbenzenesulfonate** as a colorless semi-solid as mixture of isomers (255 mg, 65% yield). The following NMR data show spectral characterization for a single isomer, but in order to isolate usable amounts of this material the combined isomers were used (^{1}H NMR indicates a 1:1.5 mixture, see attached spectra of mixture).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.3 Hz, 2H), 7.22 – 7.18 (m, 1H), 7.14 (t, *J* = 7.4 Hz, 2H), 7.12 – 7.06 (m, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 3.80 (d, *J* = 12.9 Hz, 2H), 2.94 (t, *J* = 12.7 Hz, 2H), 2.38 (q, *J* = 7.5 Hz, 2H), 2.34 (s, 3H), 2.09 (d, *J* = 7.2 Hz, 2H), 1.75 – 1.60 (m, 3H), 1.14 (t, *J* = 7.5 Hz, 3H), 1.09 – 0.98 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 142.9, 134.5, 133.2, 132.1, 130.0, 129.1, 128.4, 128.0, 127.6, 46.8, 46.9, 35.4, 33.2, 31.5, 29.7, 22.2, 21.5, 12.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.0.

FT-IR (neat film NaCl): 2944, 1381, 1362, 1225, 1198, 1116, 1007, 942, 813 cm^{-1}.

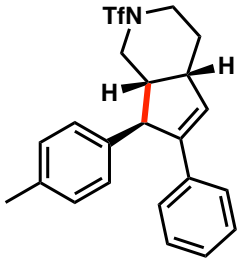
HR-MS (ESI) m/z: [M+K]+ Calculated for $C_{24}H_{28}F_3NO_5S_2K$: 570.0998; Measured: 570.0994.

Mixture of 5.18B isomers ^{13}C NMR, see below for ^{1}H NMR indication 1:1.5 ratio of isomers:

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 144.1, 143.2, 142.9, 134.5 133.4, 133.2, 132.2, 130.0, 129.8, 129.4, 129.1, 128.4, 128.3, 127.9, 127.8, 127.6, 127.6, 46.8, 46.7, 35.4, 34.5, 33.5, 33.2, 31.8, 31.5, 24.0, 22.2, 21.5, 21.5, 13.1, 12.3.

5.5.4 Enantioselective C–H Insertion Reactions of Vinyl Tosylates

Note: all NMR spectra obtained in $(CD_3)_2SO$ are at 90ºC. This was necessary to prevent peak broadening and get accurate integration values.



(4a*R*,7*R*)-6-phenyl-7-(*p*-tolyl)-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.12)

In a well maintained glove box (O_2,H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (28.7 mg, 0.12 equiv, 0.012 mmol), cylcohexane (0.5 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (53.9 mg, 1.3 equiv, 0.13 mmol).

To this solution was added **(*E*)-2-phenyl-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.12C)** (59.4 mg, 1.0 equiv, 0.1 mmol). The reaction was sealed with a teflon cap and heated to 65ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 5% ethyl acetate in hexanes) to give **(4a*R*,7*R*)-**

6-phenyl-7-(*p*-tolyl)-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine as a white solid (34.1 mg, 81% yield). This solid was determined by chiral HPLC to be in 91% enantiomeric excess.

Additionally this material was recrystallized in hexanes to give material that was >99% enantiomeric excess.

Absolute stereochemistry was determined by X-ray crystallography by slow evaporation of the isolated material after column chromatography in cyclohexane, this material also determined to be >99% *ee*.

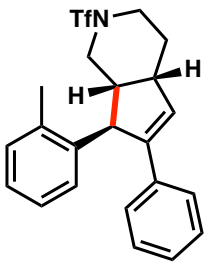
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.39 – 7.31 (m, 2H), 7.28 – 7.21 (m, 2H), 7.21 – 7.15 (m, 1H), 7.14 – 7.07 (m, 4H), 6.40 (dd, *J* = 2.4, 1.5 Hz, 1H), 4.08 (d, *J* = 5.2 Hz, 1H), 3.73 (dd, *J* = 13.3, 5.4 Hz, 1H), 3.57 (ddd, *J* = 12.0, 7.6, 4.1 Hz, 1H), 3.47 (td, *J* = 13.1, 5.6 Hz, 2H), 3.29 – 3.11 (m, 1H), 2.39 (tt, *J* = 7.1, 5.3 Hz, 1H), 2.27 (s, 3H), 2.07 (dddd, *J* = 13.9, 7.6, 6.1, 4.1 Hz, 1H), 1.76 (dtd, *J* = 14.5, 7.5, 4.1 Hz, 1H).

^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 143.8, 138.6, 135.0, 134.9, 130.4, 128.6, 127.6, 126.9, 126.5, 125.73, 119.5 (q, *J* = 324.8 Hz), 52.9, 46.8, 45.6, 43.9, 26.4, 19.9.

^{19}F NMR (376 MHz, $(CD_3)_2SO$) δ -75.3.

FT-IR (neat film NaCl): 2916, 1383, 1225, 1214, 1189, 1055, 1008, 764 cm^{-1}.

HR-MS (ESI) m/z: [M]+ Calculated for $C_{22}H_{22}F_3NO_2S$: 421.1323; Measured: 421.1317



(4a*R*,7*R*)-6-phenyl-7-(*o*-tolyl)-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.13)

In a well maintained glove box (O_2, H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (28.7 mg, 0.12 equiv, 0.012 mmol), cylcohexane (0.5 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (53.9 mg, 1.3 equiv, 0.13 mmol).

To this solution was added **(*E*)-2-phenyl-1-(*o*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.13C)** (59.4 mg, 1.0 equiv, 0.1 mmol). The reaction was sealed with a teflon cap and heated to 65ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 5% ethyl acetate in hexanes) to give **(4a*R*,7*R*)-6-phenyl-7-(*o*-tolyl)-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine** as a colorless low-melting point solid (37.4 mg, 89% yield). This solid was determined by chiral HPLC to be in 90% enantiomeric excess.

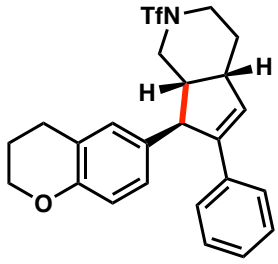
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.33 (dt, *J* = 8.1, 1.8 Hz, 2H), 7.30 – 7.16 (m, 4H), 7.15 – 6.95 (m, 3H), 6.46 (dd, *J* = 2.4, 1.3 Hz, 1H), 4.26 (d, *J* = 1.7 Hz, 1H), 3.81 (dd, *J* = 13.2, 5.6 Hz, 1H), 3.65 – 3.32 (m, 3H), 3.28 – 3.14 (m, 1H), 2.46 (s, 3H), 2.42 (ddd, *J* = 6.6, 3.1, 1.5 Hz, 1H), 2.04 (dddd, *J* = 13.9, 10.8, 5.3, 3.3 Hz, 1H), 1.92 (dtd, *J* = 14.2, 5.9, 3.9 Hz, 1H).

^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 143.9, 138.9, 135.1, 134.8, 130.2, 130.1, 127.7, 126.7, 126.1, 125.8, 125.5, 125.6, 119.51 (q, *J* = 324.9 Hz), 50.5, 46.2, 45.2, 43.6, 25.6, 18.6.

^{19}F NMR (376 MHz, $(CD_3)_2SO$) δ -75.2.

FT-IR (neat film NaCl): 2955, 1383, 1357, 1269, 1222, 1194, 1153, 1040, 827, 758 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{22}H_{23}F_3NO_2S$: 422.1401; Measured: 422.140



(4a*R*,7*R*)-7-(chroman-6-yl)-6-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.14)

In a well maintained glove box (O_2, H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (28.7 mg, 0.12 equiv, 0.012 mmol), cylcohexane (1.0 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (53.9 mg, 1.3 equiv, 0.13 mmol).

To this solution was **(*E*)-1-(chroman-6-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.14C)** (63.6 mg, 1.0 equiv, 0.1 mmol). The reaction was sealed with a teflon cap and heated to 60ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 6% ethyl acetate in hexanes) to give **(4a*R*,7*R*)-7-(chroman-6-yl)-6-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine** as a white solid (30.0 mg, 65% yield). This solid was determined by chiral HPLC to be in 88% enantiomeric excess.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.36 (d, J = 7.4 Hz, 2H), 7.26 (t, J = 7.4 Hz, 2H), 7.22 – 7.16 (m, 1H), 6.97 – 6.82 (m, 2H), 6.64 (d, J = 8.1 Hz, 1H), 6.38 (t, J = 1.9 Hz, 1H), 4.11 (dd, J = 5.9, 4.4 Hz, 2H), 3.99 (d, J = 4.2 Hz, 1H), 3.74 (dd, J = 13.2, 5.5 Hz, 1H), 3.51 (q, J = 5.0 Hz, 2H),

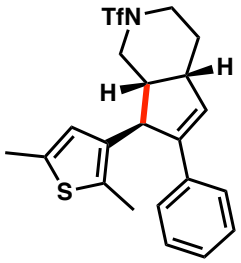
3.41 (dd, *J* = 13.3, 7.4 Hz, 1H), 3.20 (q, *J* = 7.0 Hz, 1H), 2.85 – 2.59 (m, 2H), 2.37 (ddd, *J* = 12.4, 7.1, 5.1 Hz, 1H), 2.13 – 1.99 (m, 1H), 1.97 – 1.87 (m, 2H), 1.78 (ddd, *J* = 14.0, 11.5, 6.5 Hz, 1H).

^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 152.9, 143.9, 135.1, 132.8, 130.1, 128.1, 127.6, 126.5, 125.7, 125.6, 121.8, 119.5 (q, *J* = 325.0 Hz), 115.8, 65.3, 52.7, 46.7, 45.7, 43.8, 26.3, 23.8, 21.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.3.

FT-IR (neat film NaCl): 2966, 1381, 1362, 1224, 1186, 1153, 1051, 1008, 824, 762 cm^{-1}.

HR-MS (ESI) m/z: [M]+ Calculated for $C_{24}H_{24}F_3NO_3S$: 463.1429; Measured: 463.1418.



(4a*R*,7*S*)-7-(2,5-dimethylthiophen-3-yl)-6-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.15)

In a well maintained glove box (O_2, H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (14.3 mg, 0.12 equiv, 0.006 mmol), cylcohexane (0.5 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (27.0 mg, 1.3 equiv, 0.065 mmol).

To this solution was **(*E*)-1-(2,5-dimethylthiophen-3-yl)-2-phenyl-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.15C)** (31.0 mg, 1.0 equiv, 0.05 mmol). The reaction was sealed with a teflon cap and heated to 70ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 2% ether in hexanes) to give **(4a*R*,7*S*)-7-(2,5-**

dimethylthiophen-3-yl)-6-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine as a colorless semi-solid (9.0 mg, 40% yield). This solid was determined by chiral HPLC to be in 90% enantiomeric excess.

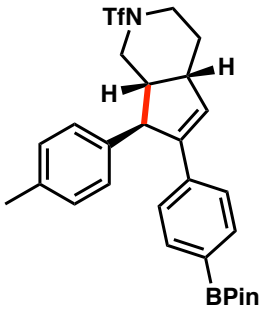
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.35 – 7.31 (m, 2H), 7.32 – 7.24 (m, 2H), 7.24 – 7.17 (m, 1H), 6.36 (d, *J* = 1.3 Hz, 1H), 6.32 (dd, *J* = 2.4, 1.6 Hz, 1H), 4.10 (dt, *J* = 5.2, 1.8 Hz, 1H), 3.70 (dd, *J* = 13.2, 5.4 Hz, 1H), 3.56 (ddd, *J* = 12.1, 7.7, 4.1 Hz, 1H), 3.53 – 3.34 (m, 2H), 3.22 (dtd, *J* = 9.6, 7.6, 2.2 Hz, 1H), 2.46 (tt, *J* = 7.0, 5.3 Hz, 1H), 2.41 (s, 3H), 2.27 (s, 3H), 2.08 (dddd, *J* = 13.9, 7.7, 6.0, 4.1 Hz, 1H), 1.76 (dtd, *J* = 14.5, 7.4, 4.1 Hz, 1H).

^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 144.2, 137.1, 135.1, 134.2, 130.0, 129.7, 127.6, 126.6, 125.4, 125.0, 119.5 (q, *J* = 325.0 Hz), 46.7, 45.6, 45.1, 43.8, 26.2, 14.1, 11.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.2.

FT-IR (neat film NaCl): 2890, 1371, 1265, 1052, 942, 763 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{21}H_{23}F_3NO_2S_2$: 441.1044; Measured: 441.1039.



(4a*R*,7*R*)-6-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-7-(*p*-tolyl)-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.16)

In a well maintained glove box (O_2, H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (14.3 mg, 0.12 equiv, 0.006 mmol), cylcohexane (0.5 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (27.0 mg, 1.3 equiv, 0.065 mmol).

To this solution was added **(*Z*)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)-3-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (5.16D)** (36.0 mg, 1.0 equiv, 0.05 mmol). The reaction was sealed with a teflon cap and heated to 70ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 5% → 10% ethyl acetate in hexanes) to give **(4a*R*,7*R*)-6-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-7-(*p*-tolyl)-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine** as a white solid (16.1 mg, 60% yield). This solid was determined by chiral HPLC to be in 90% enantiomeric excess.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 1.0 Hz, 4H), 6.47 (dd, *J* = 2.5, 1.5 Hz, 1H), 4.10 (dt, *J* = 5.4, 1.7 Hz, 1H), 3.82 – 3.66 (m, 1H), 3.57 (ddd, *J* = 12.0, 6.0, 3.1 Hz, 1H), 3.47 (dt, *J* = 12.9, 5.7 Hz, 2H), 3.32 – 3.11 (m, 1H), 2.40 (tt, *J* = 6.8, 5.3 Hz, 1H), 2.27 (s, 3H), 2.07 (dddd, *J* = 13.7, 7.3, 6.0, 4.0 Hz, 1H), 1.75 (dtd, *J* = 14.1, 7.7, 4.0 Hz, 1H), 1.31 (s, 12H).

^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 143.84, 138.57, 137.82, 134.99, 133.73, 131.83, 128.66, 126.98, 125.16, 119.51 (q, *J* = 325.0 Hz), 83.10, 52.74, 46.83, 45.55, 43.97, 26.45, 24.15 (d, *J* = 3.5 Hz), 19.95.

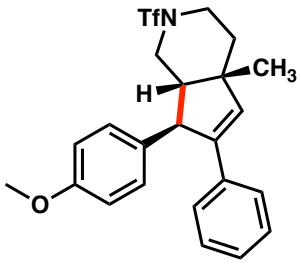
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.2.

^{11}B NMR (128 MHz, $CDCl_3$) δ 32.2.

FT-IR (neat film NaCl): 2875, 1458, 1383, 1363, 1223, 1190, 1169, 1142, 1045, 824, 763 cm^{-1}.

HR-MS (ESI) m/z: [M+K]+ Calculated for $C_{28}H_{33}BF_3NO_4SK$: 586.1812; Measured:

586.1815.



(4a*R*,7*R*)-7-(4-methoxyphenyl)-4a-methyl-6-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.18)

In a well maintained glove box (O_2, H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (14.3 mg, 0.12 equiv, 0.006 mmol), cylcohexane (0.5 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (29.6mg, 1.3 equiv, 0.065 mmol).

To this solution was added **(*E*)-1-(4-methoxyphenyl)-3-(4-methyl-1-((trifluoromethyl)sulfonyl)piperidin-4-yl)-2-phenylprop-1-en-1-yl-4-methylbenzenesulfonate** (31.0 mg, 1.0 equiv, 0.05 mmol). The reaction was sealed with a teflon cap and heated to 65ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 2% → 7% ether in hexanes) to give **(4a*R*,7*R*)-7-(4-methoxyphenyl)-4a-methyl-6-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine** as a white solid (18.1 mg, 81% yield). This solid was determined by chiral HPLC to be in 55% enantiomeric excess.

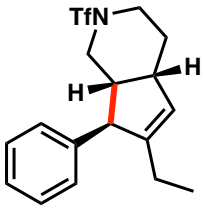
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 – 6.92 (m, 7H), 6.78 (d, *J* = 8.6 Hz, 2H), 6.13 (d, *J* = 2.1 Hz, 1H), 4.27 – 4.12 (m, 1H), 3.80 (t, *J* = 8.1 Hz, 2H), 3.74 (s, 3H), 3.30 – 3.04 (m, 2H), 1.88 (d, *J* = 9.3 Hz, 1H), 1.75 (t, *J* = 5.9 Hz, 2H), 1.30 (s, 3H), 1.29 – 1.15 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 142.8, 137.3, 135.5, 134.5, 129.2, 128.1, 127.0, 126.5, 120.2 (d, *J* = 323.9 Hz), 114.0, 55.4, 55.1, 52.4, 43.6, 43.0, 42.8, 35.2, 31.9, 29.7, 24.4, 22.7, 14.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1.

FT-IR (neat film NaCl): 2865, 1384, 1362, 1220, 1189, 1165, 1043, 824, 763 cm^{-1}.

HR-MS (ESI) m/z: [M+H]+ Calculated for $C_{23}H_{25}F_3NO_3S$: 452.1507; Measured: 452.1511.



(4a*R*,7*S*)-6-ethyl-4a-methyl-7-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine (5.18)

In a well maintained glove box (O_2, H_2O <0.5 ppm) to a dram vial equipped with a stir bar was added **IDPi 2 (11)** (28.7 mg, 0.12 equiv, 0.012 mmol), cylcohexane (0.5 mL), and 2-allyl-1,1,1,3,3,3-hexaethyl-2-(triethylsilyl)trisilane (59.3 mg, 1.3 equiv, 0.13 mmol). To this solution was added **(*E/Z*)-1-phenyl-2-((1-((trifluoromethyl)sulfonyl)piperidin-4-yl)methyl)but-1-en-1-yl 4-methylbenzenesulfonate** (50.9 mg, 1.0 equiv, 0.1 mmol). The reaction was sealed with a teflon cap and heated to 70ºC for 72h, the reaction was removed from the glovebox and a few drops of triethylamine were added to quench the reaction. This mixture was then plugged through silica gel with diethyl ether, concentrated *in vacuo*, and purified by flash column chromatography (100% hexanes→ 2% → 5% ethyl acetate in hexanes: Note product is not

highly UV active, $KMnO_4$ should be used to visualize the TLC plate) to give **((4a*R*,7*S*)-6-ethyl-4a-methyl-7-phenyl-2-((trifluoromethyl)sulfonyl)-2,3,4,4a,7,7a-hexahydro-1*H*-cyclopenta[*c*]pyridine** as a white solid (14.9 mg, 40% yield). This solid was determined by chiral HPLC to be in 75% enantiomeric excess.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.41 – 7.33 (m, 2H), 7.32 – 7.22 (m, 1H), 7.23 – 7.11 (m, 2H), 5.64 (p, *J* = 1.9 Hz, 1H), 3.62 (dt, *J* = 11.3, 5.2 Hz, 1H), 3.55 (ddd, *J* = 10.2, 4.8, 1.4 Hz, 2H), 3.44 (dd, *J* = 13.3, 5.1 Hz, 1H), 3.40 – 3.30 (m, 1H), 2.97 (tdt, *J* = 8.0, 5.9, 2.0 Hz, 1H), 2.36 (tt, *J* = 7.4, 5.1 Hz, 1H), 2.03 (dtd, *J* = 14.1, 6.1, 3.6 Hz, 1H), 1.93 (dtdd, *J* = 8.7, 7.4, 6.0, 1.3 Hz, 1H), 1.87 – 1.72 (m, 1H), 1.55 (dddd, *J* = 14.0, 9.5, 8.4, 4.2 Hz, 1H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz $(CD_3)_2SO$) δ 147.5, 141.6, 128.0, 127.3, 127.0, 126.0, 119.5 (q, *J* = 324.8 Hz), 54.4, 46.3, 45.2, 44.0, 38.8, 27.1, 21.5, 11.2.

^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1.

FT-IR (neat film NaCl): 2955, 1379, 1340, 1220, 1112, 1008, 939, 764 cm^{-1}.

HR-MS (ESI) m/z: [M+Na]+ Calculated for $C_{17}H_{20}F_3NO_2SNa$: 382.1064; Measured: 382.1059.

5.6 Spectra Relevant to Chapter Five:

Vinyl Tosylates as Precursors to Vinyl Carbocations and Efforts to Control the Enantioselectivity of C–H Insertion Reactions

(Unpublished Work)

Hosea M. Nelson, Sepand Nistanaki, Stasik Popov, Benjamin Wigman, Chloe Williams

(authors alphabetically listed by last name)

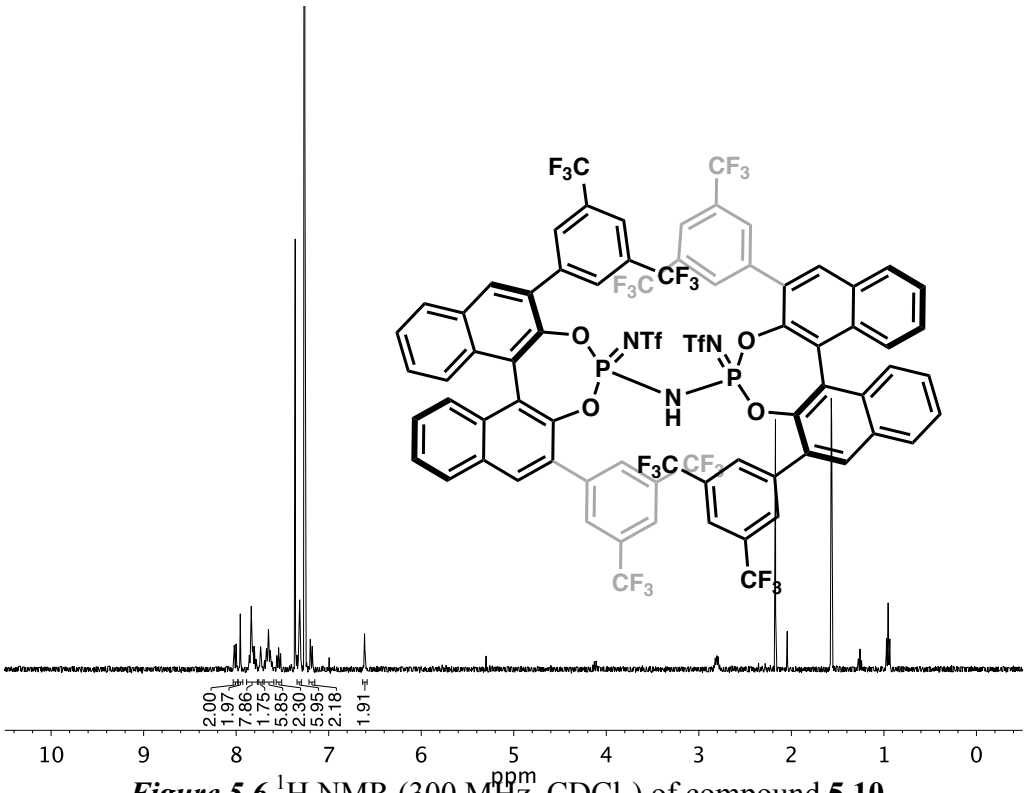


Figure 5.6 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.10**.

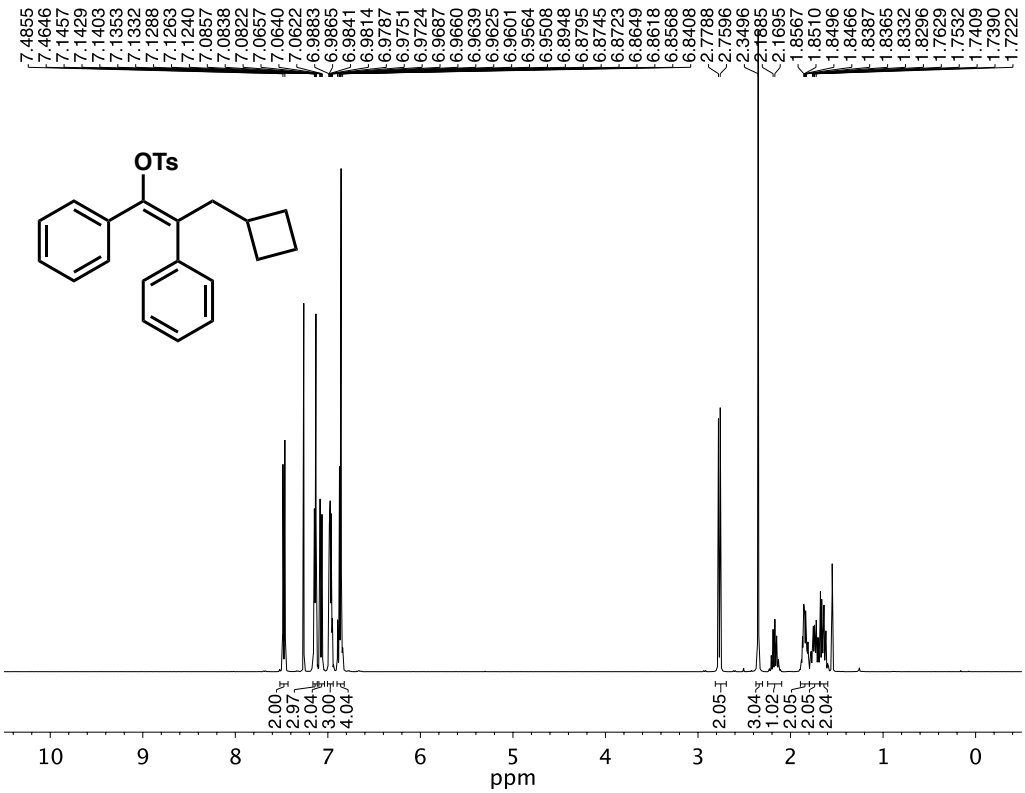


Figure 5.7 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.7**.

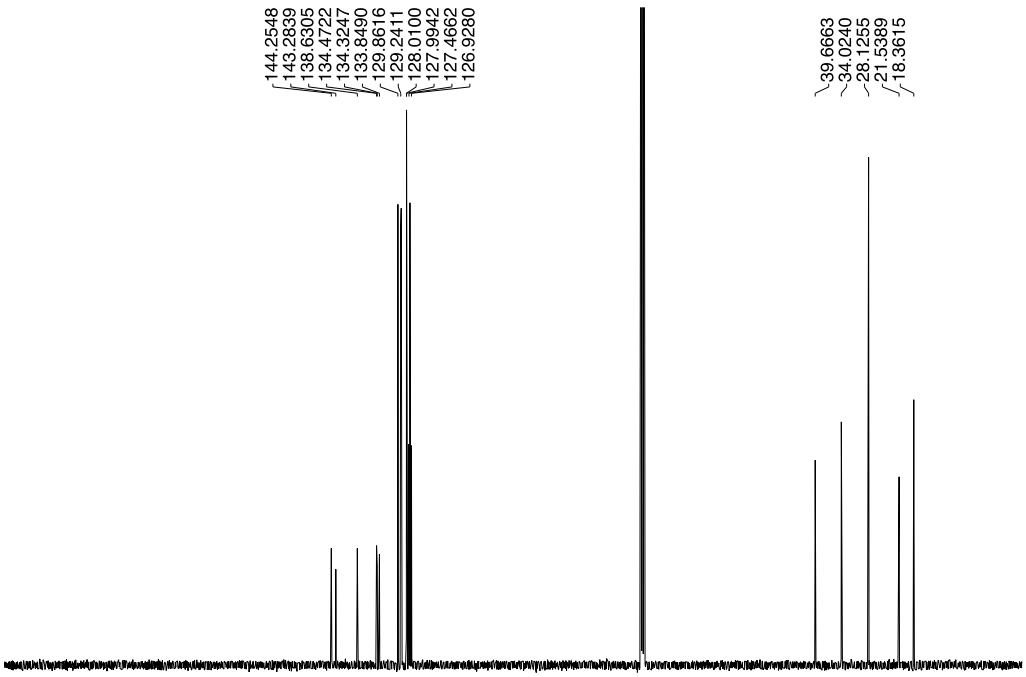


Figure 5.8 ^{13}C NMR (128 MHz, $CDCl_3$) of compound **5.7**.

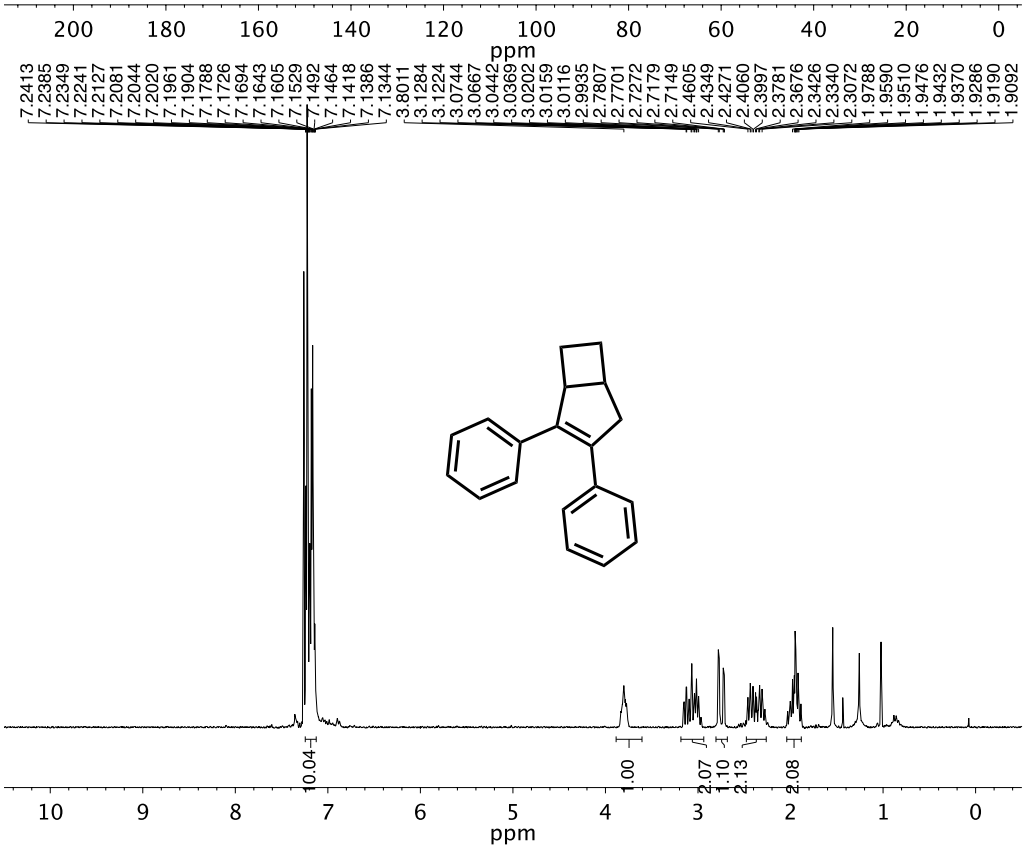


Figure 5.9 ^{1}H NMR (128 MHz, $CDCl_3$) of compound **5.8**.

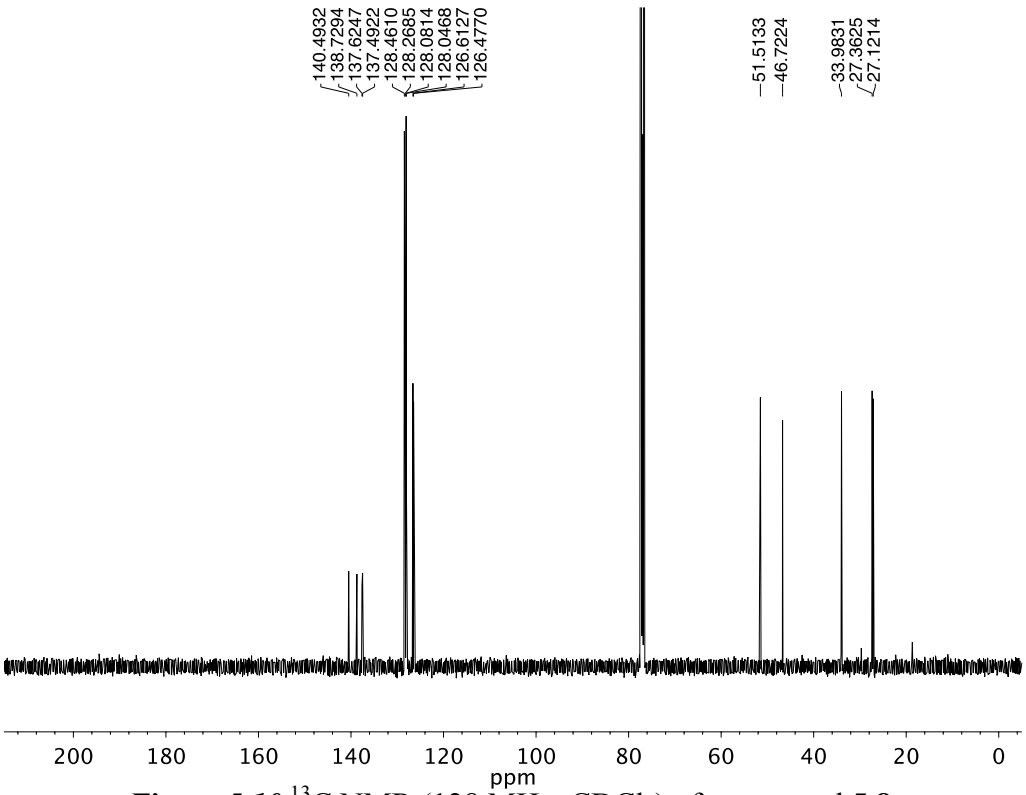


Figure 5.10 ^{13}C NMR (128 MHz, $CDCl_3$) of compound **5.8.**

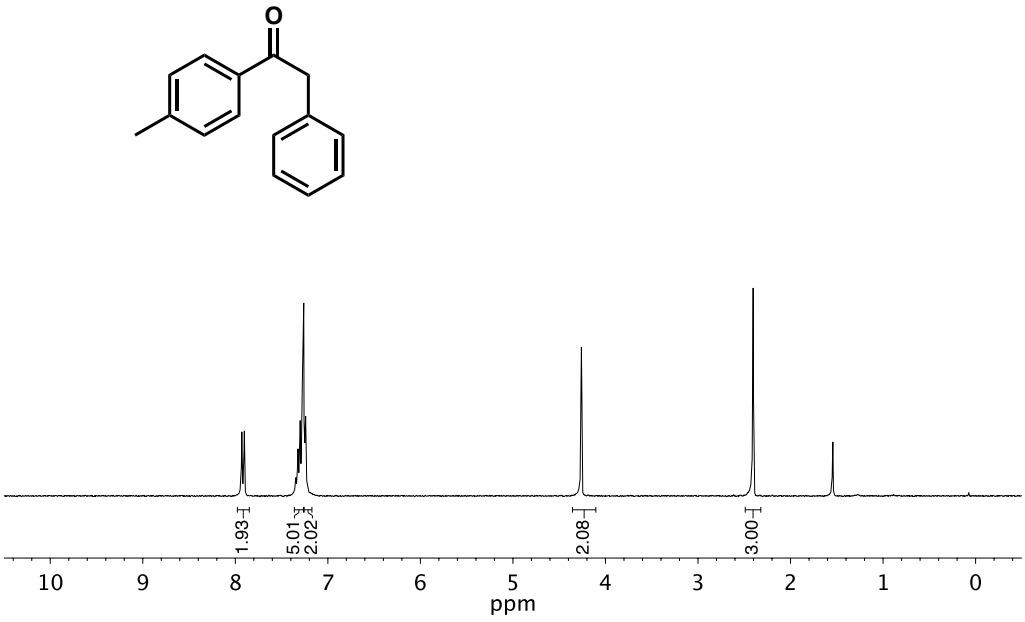


Figure 5.11 ^{1}H NMR (300MHz, $CDCl_3$) of compound **5.12A**.

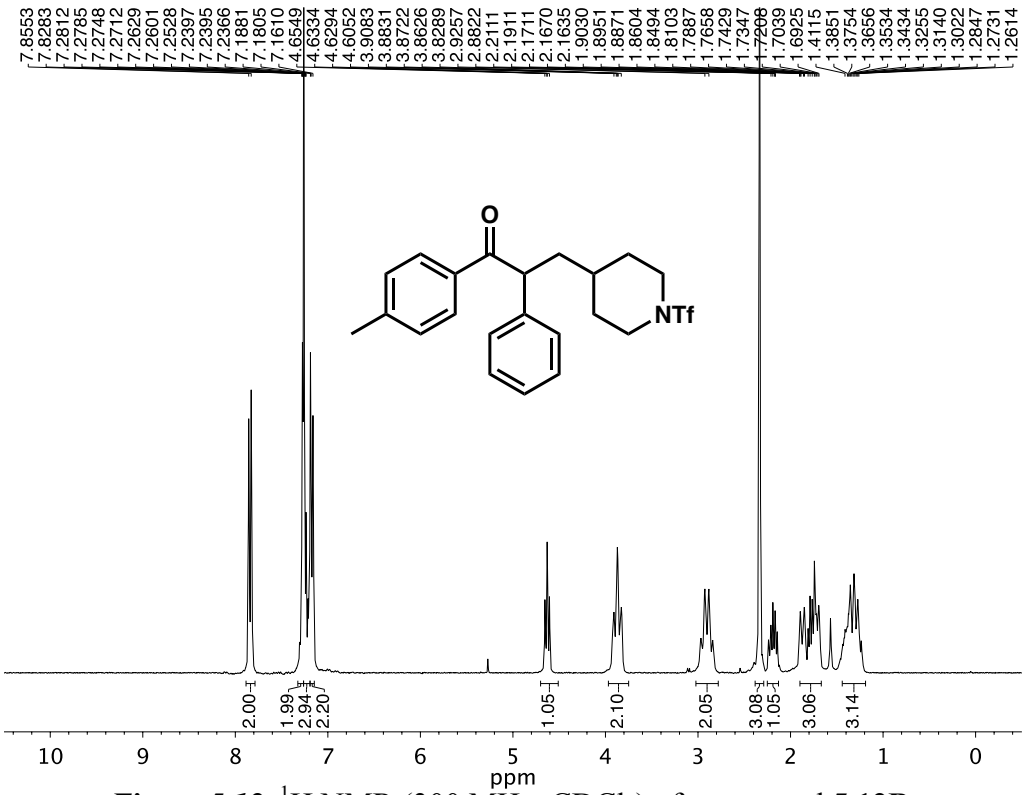


Figure 5.12 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.12B.**

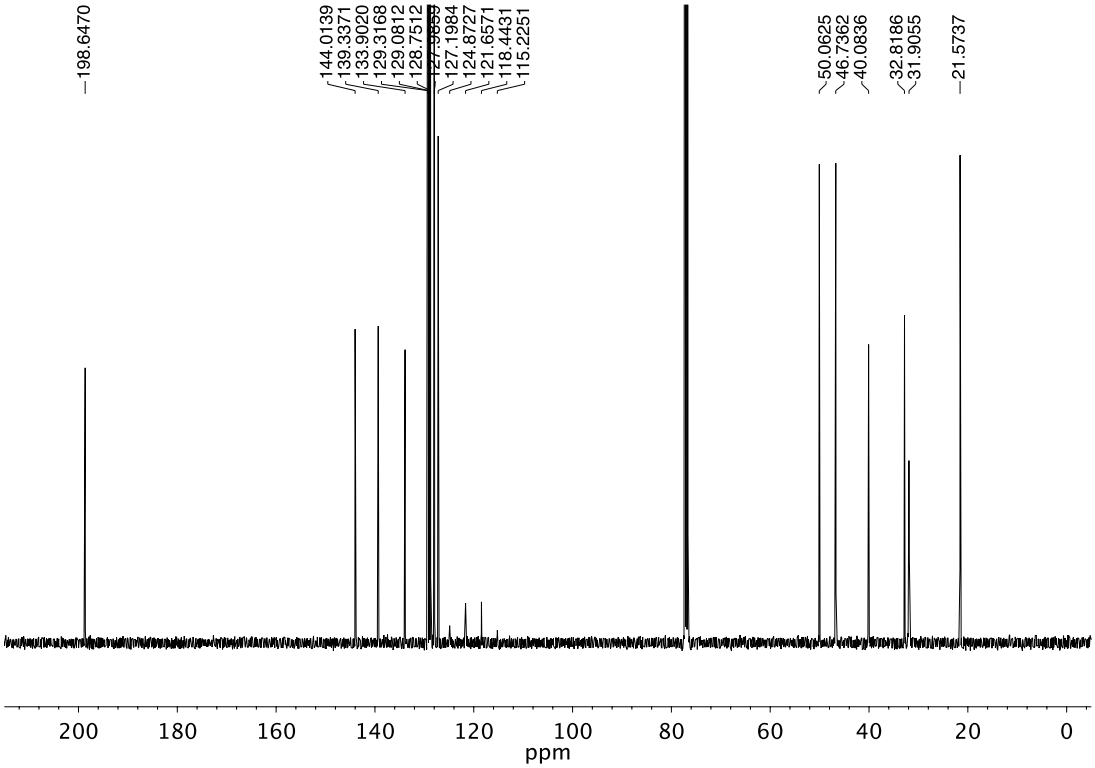


Figure 5.13 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.12B.**

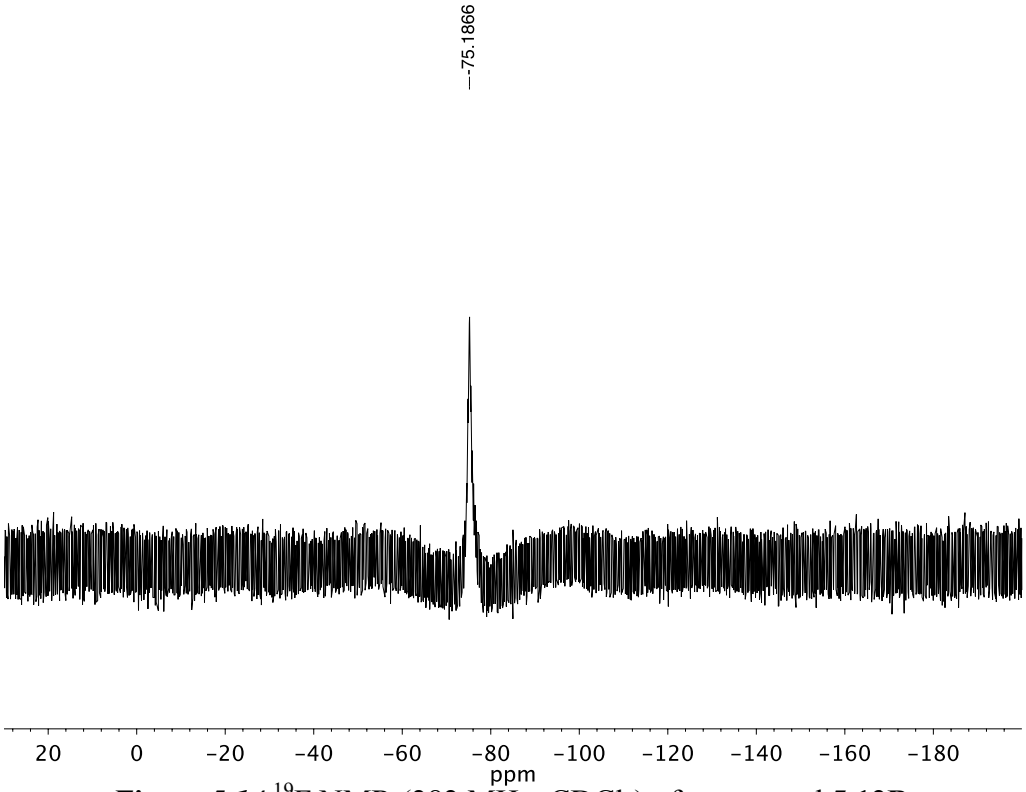


Figure 5.14 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.12B.**

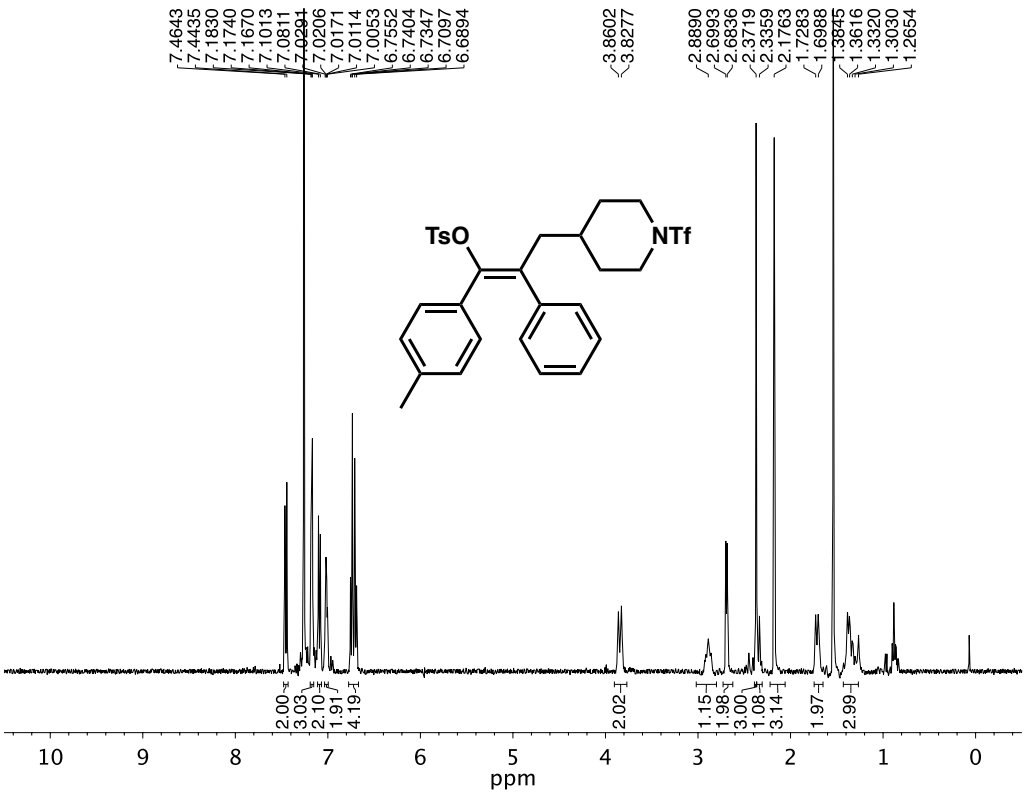


Figure 5.15 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.12C.**

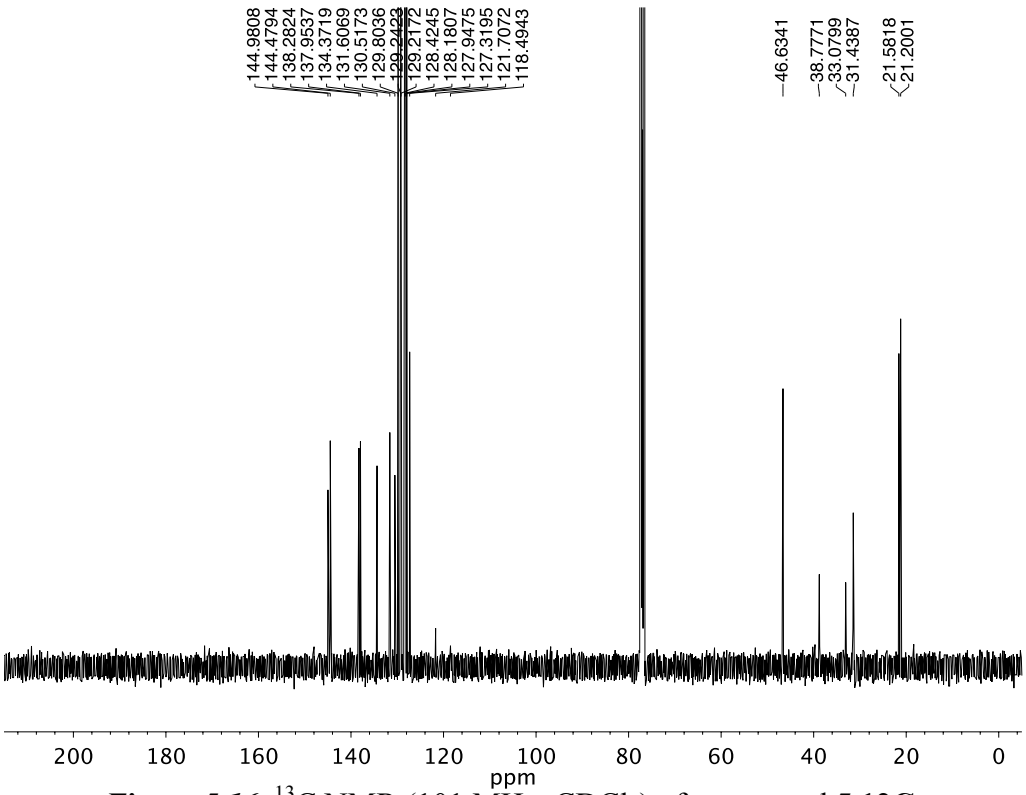


Figure 5.16 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.12C.**

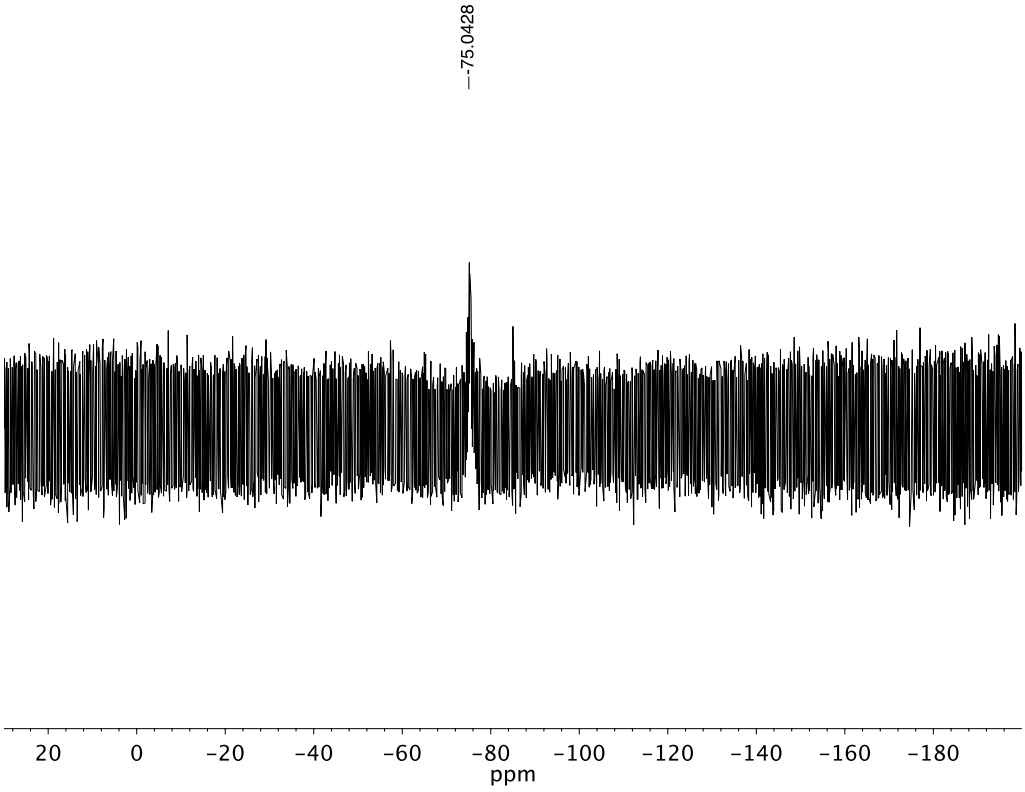


Figure 5.17 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.12C.**

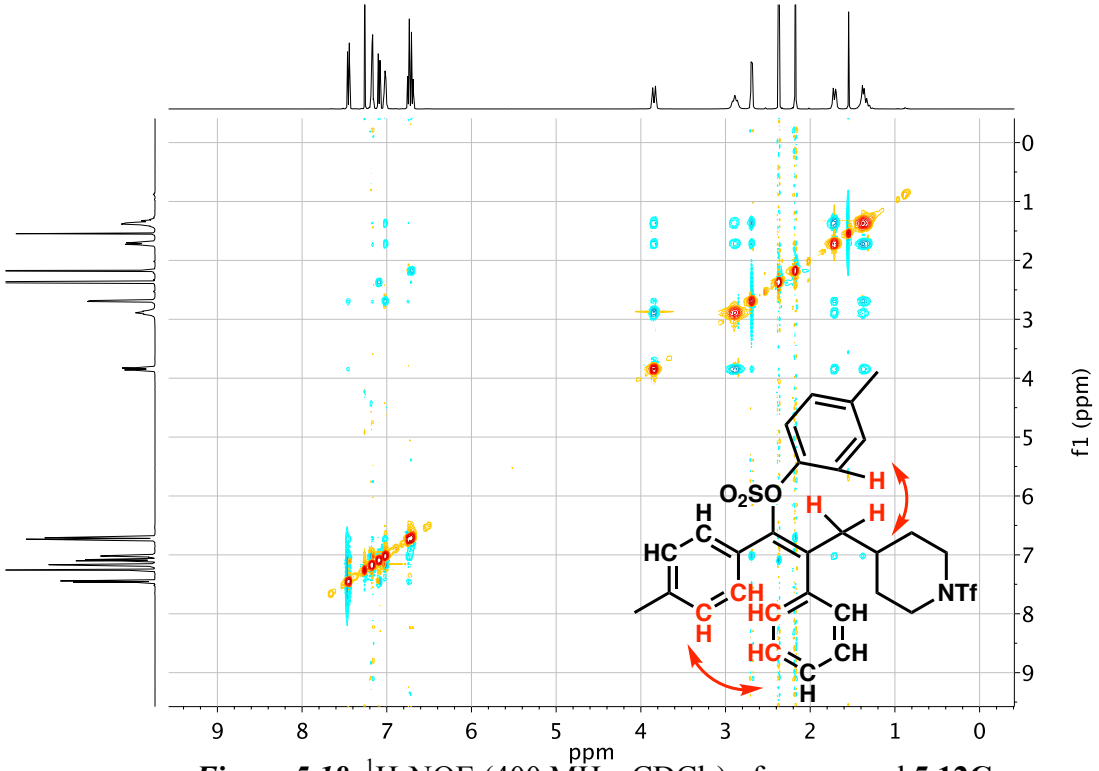


Figure 5.18 ^{1}H-NOE (400 MHz, $CDCl_3$) of compound **5.12C.**

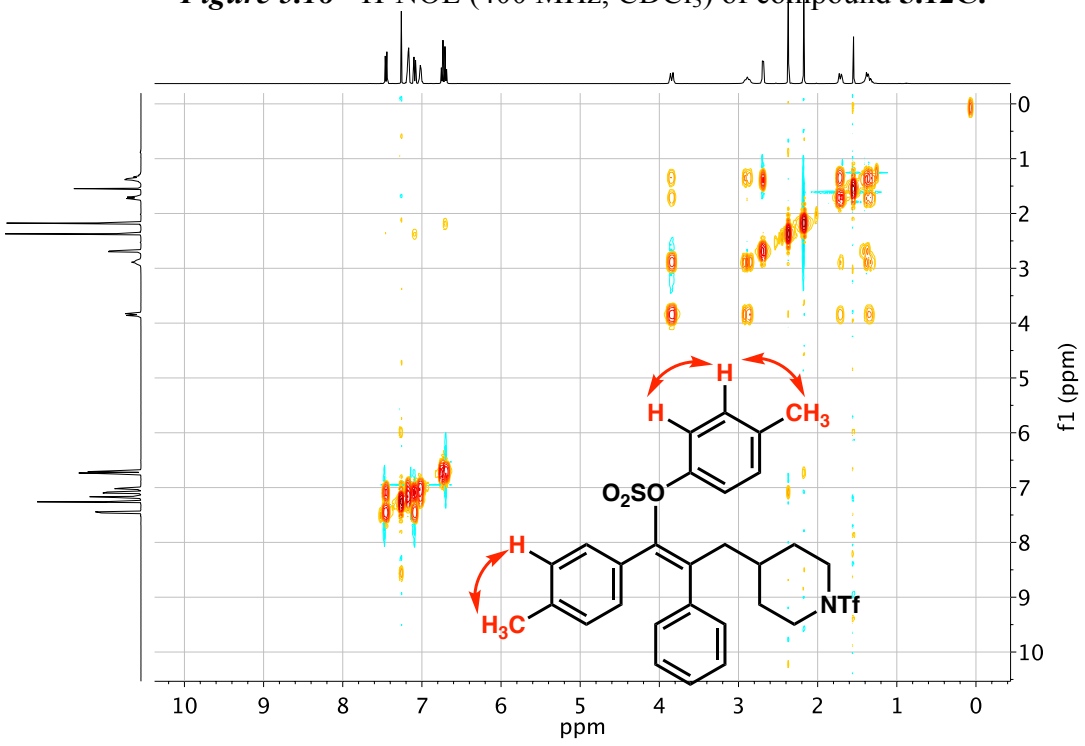


Figure 5.19 ^{1}H-COSY (400 MHz, $CDCl_3$) of compound **5.12C.**

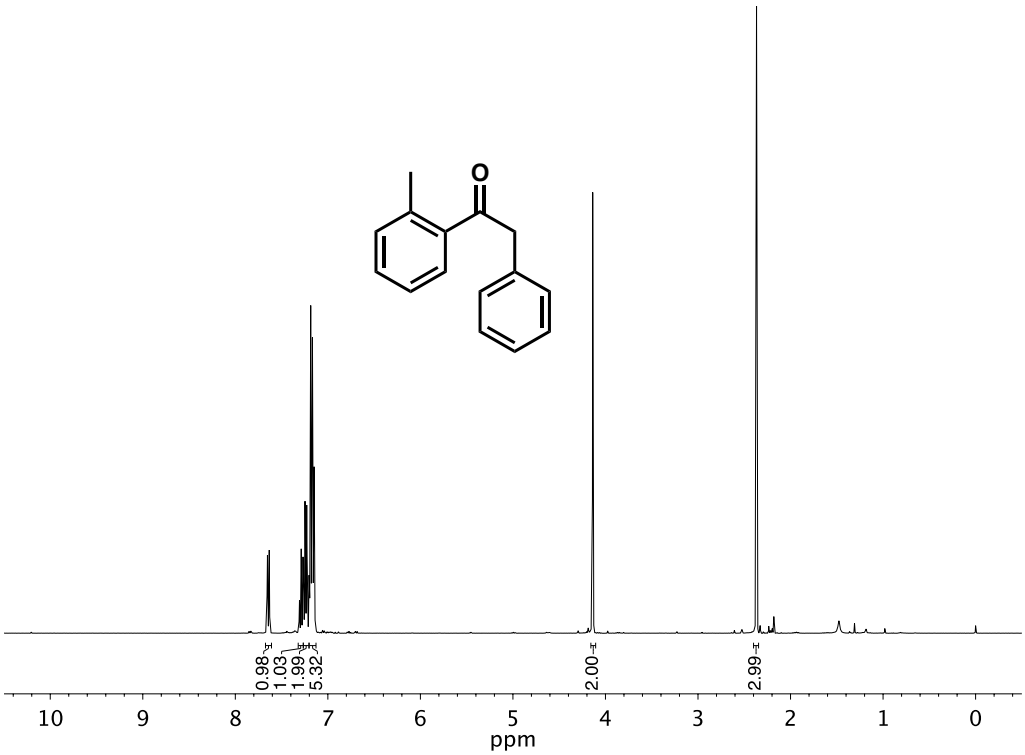


Figure 5.20 ^{1}HNMR (400 MHz, $CDCl_3$) of compound **5.13A.**

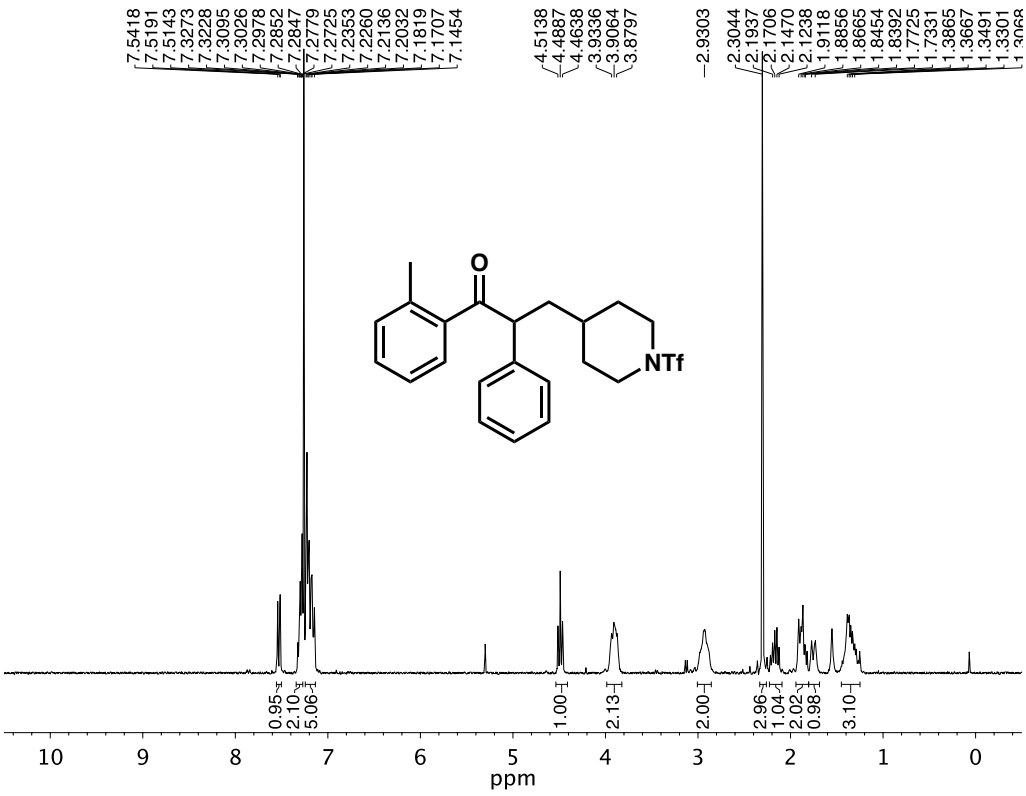


Figure 5.21 ^{1}HNMR (300 MHz, $CDCl_3$) of compound **5.13B.**

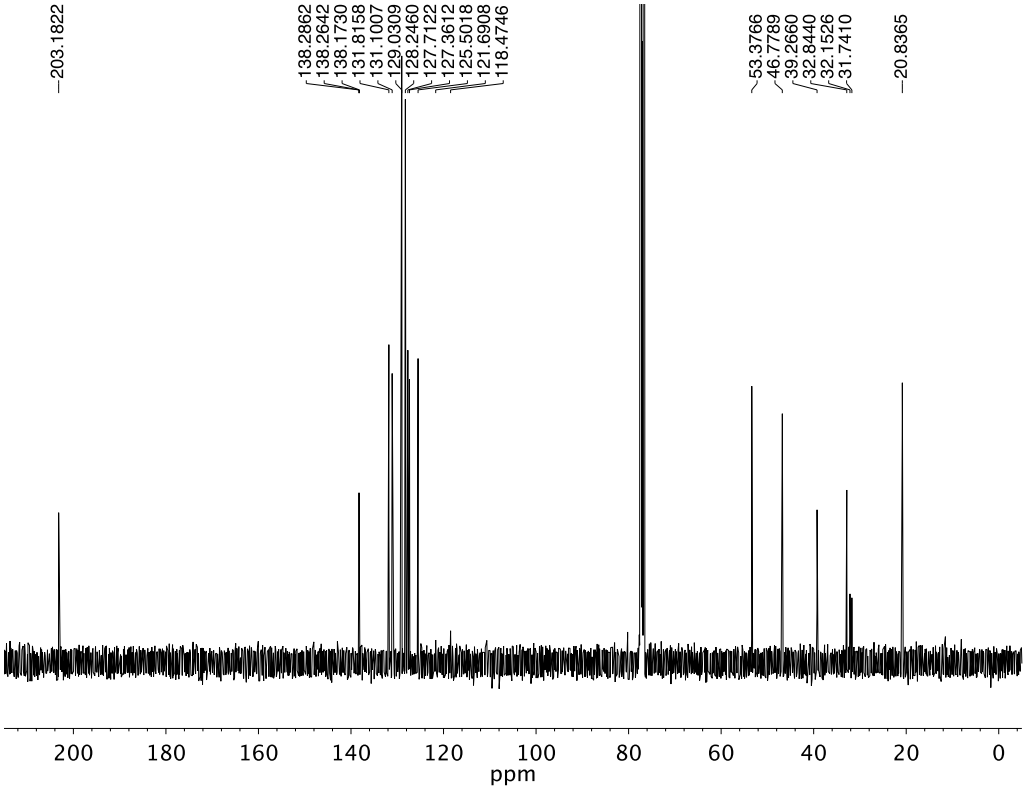


Figure 5.22 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.13B.**

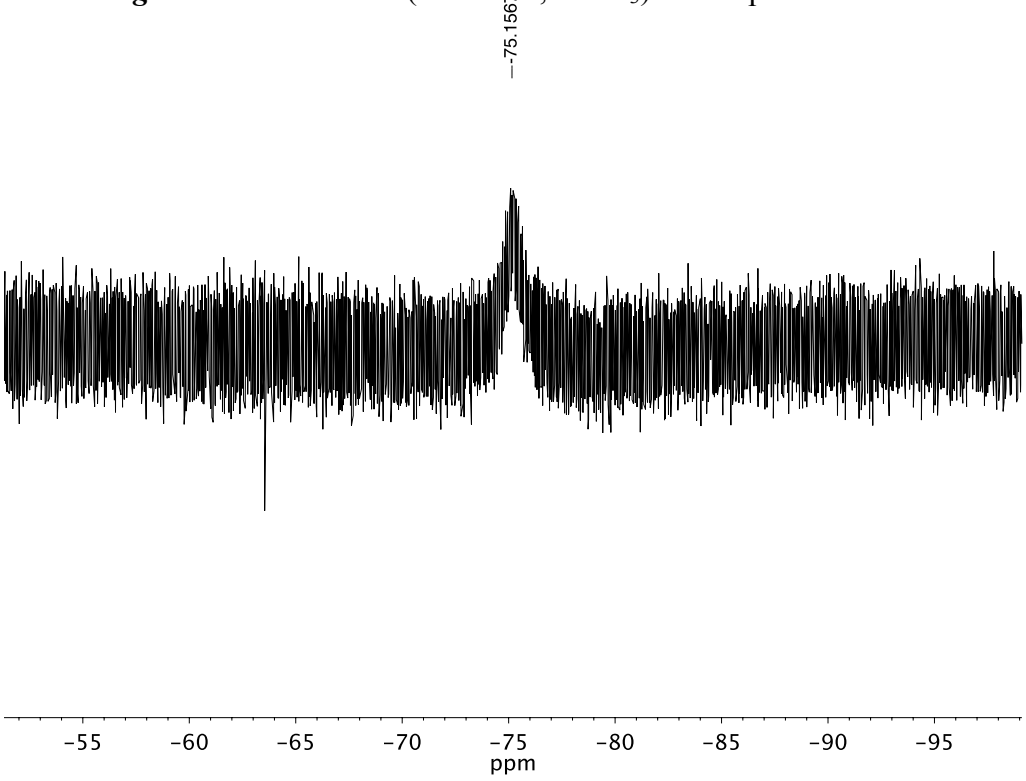


Figure 5.23 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.13B.**

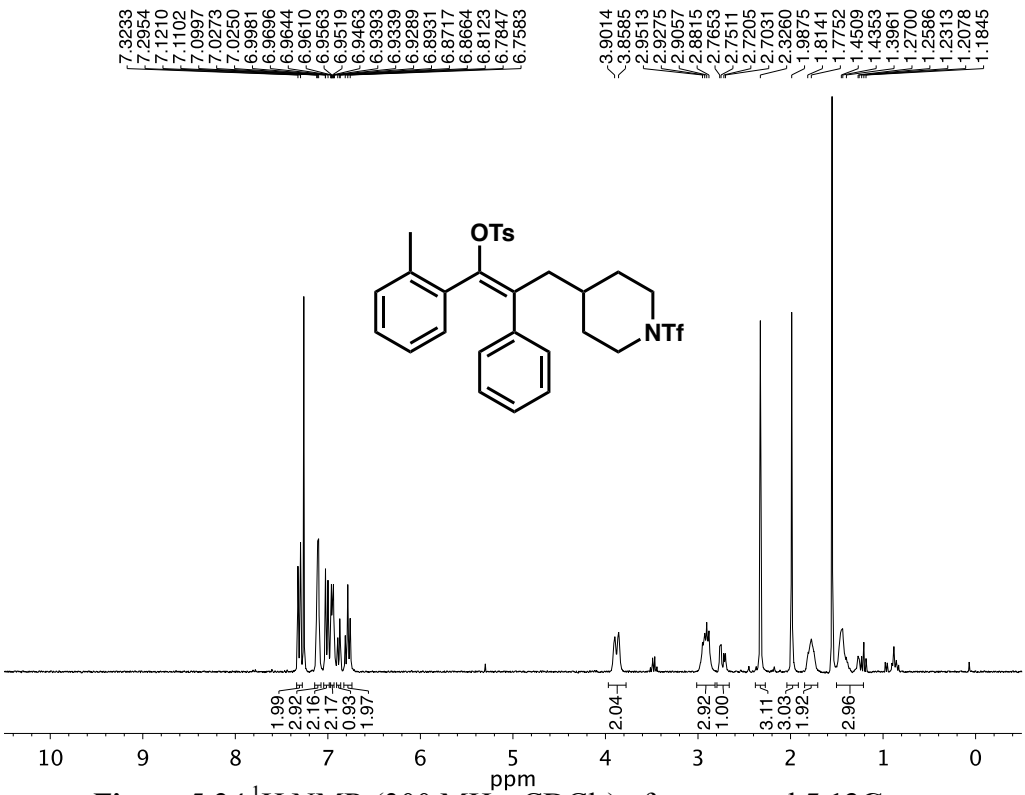


Figure 5.24 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.13C.**

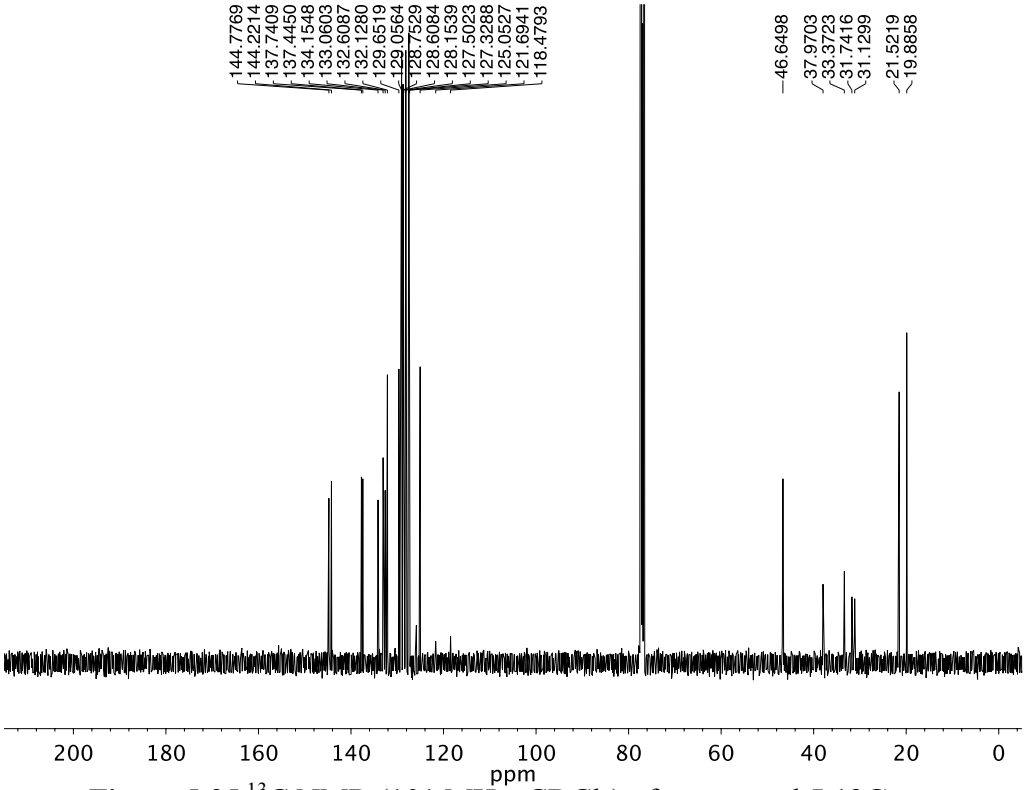


Figure 5.25 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.13C.**

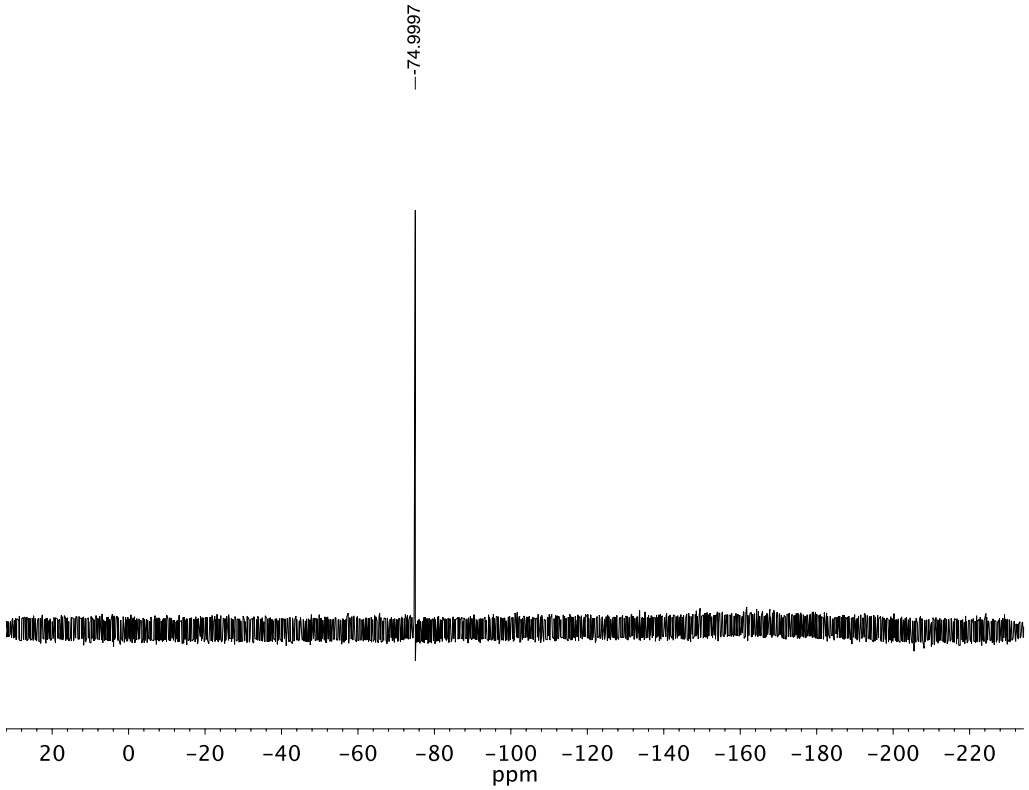


Figure 5.26 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.13C.**

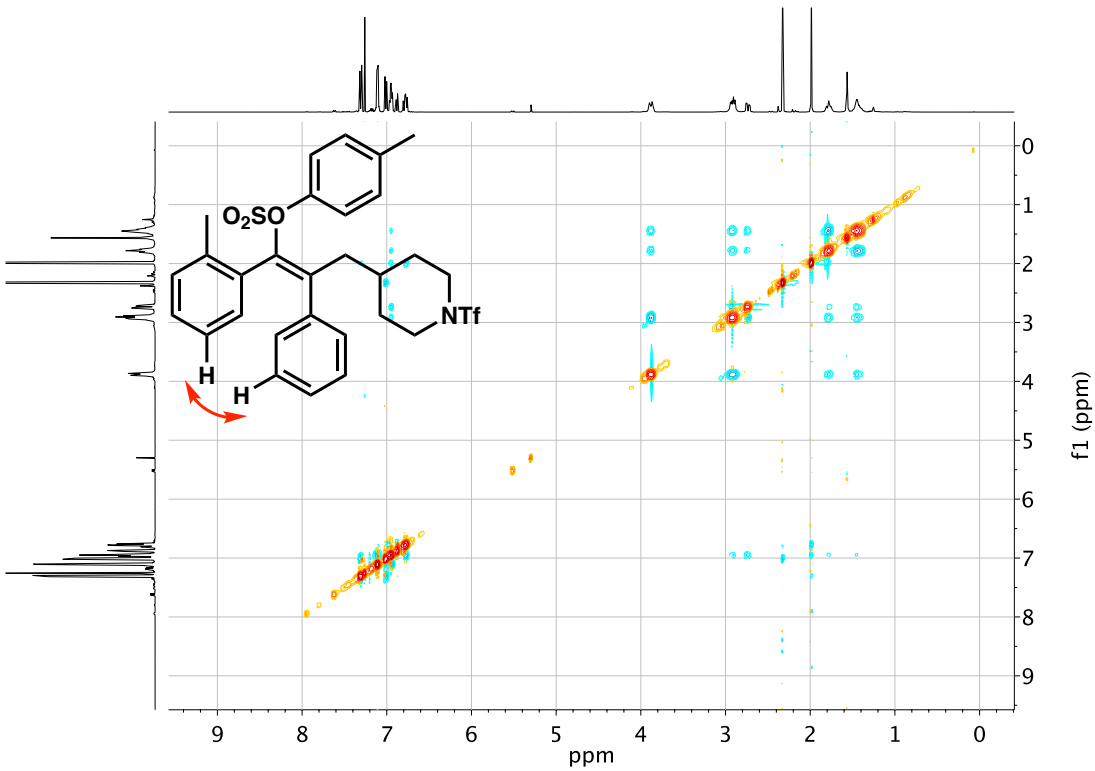


Figure 5.27 ^{1}H-NOE (400 MHz, $CDCl_3$) of compound **5.13C.**

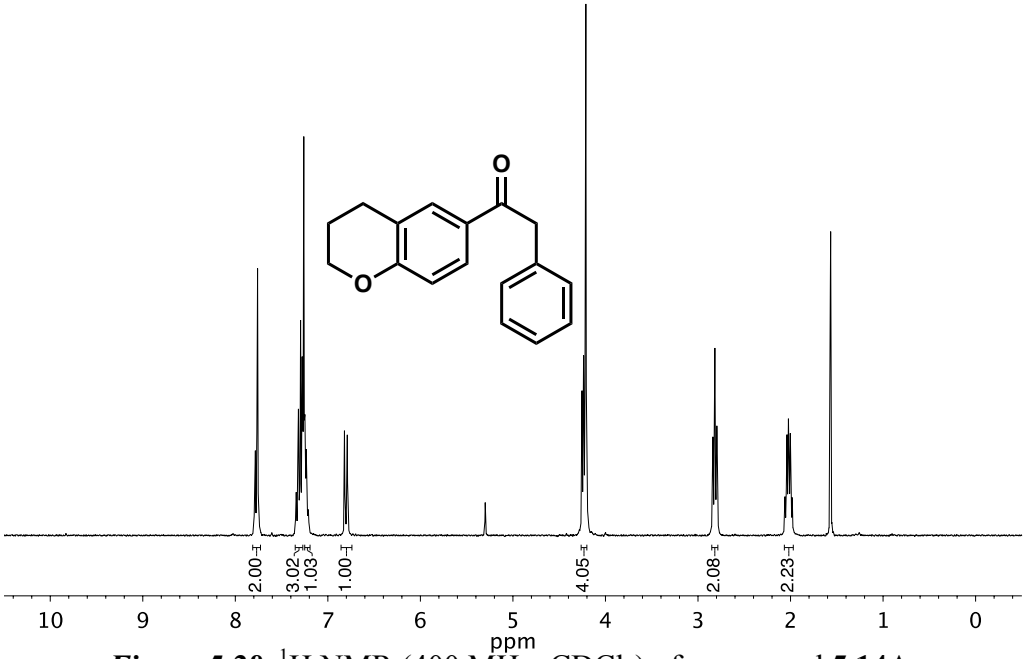


Figure 5.28 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.14A.**

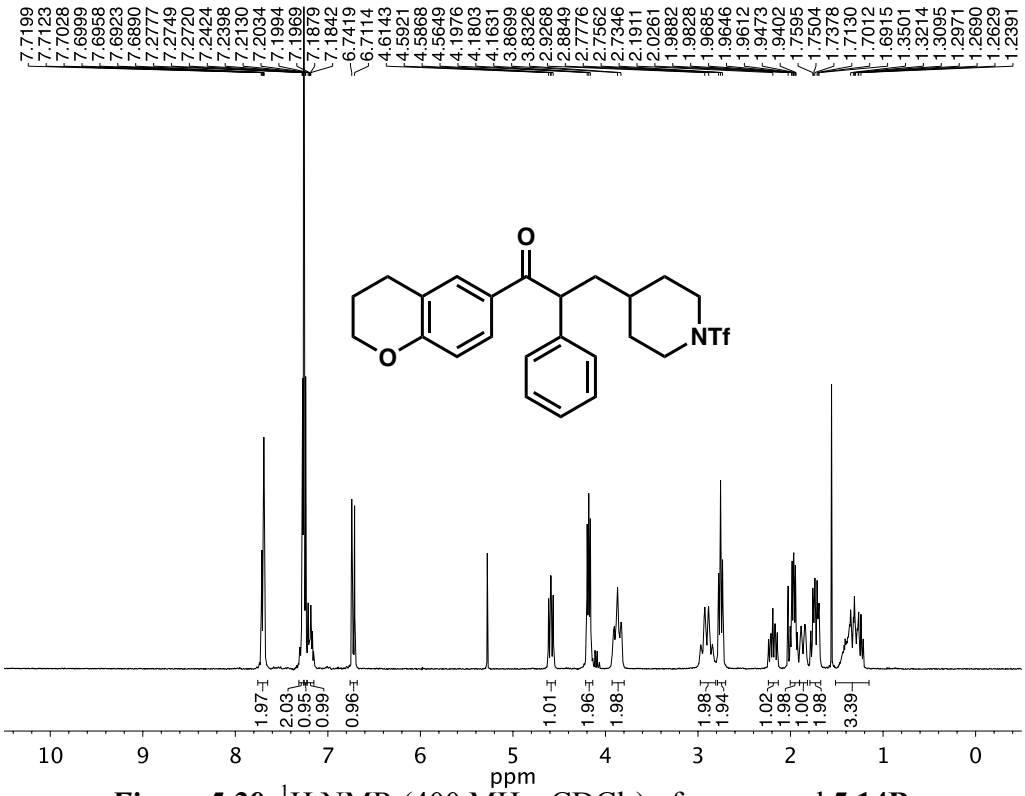


Figure 5.29 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.14B.**

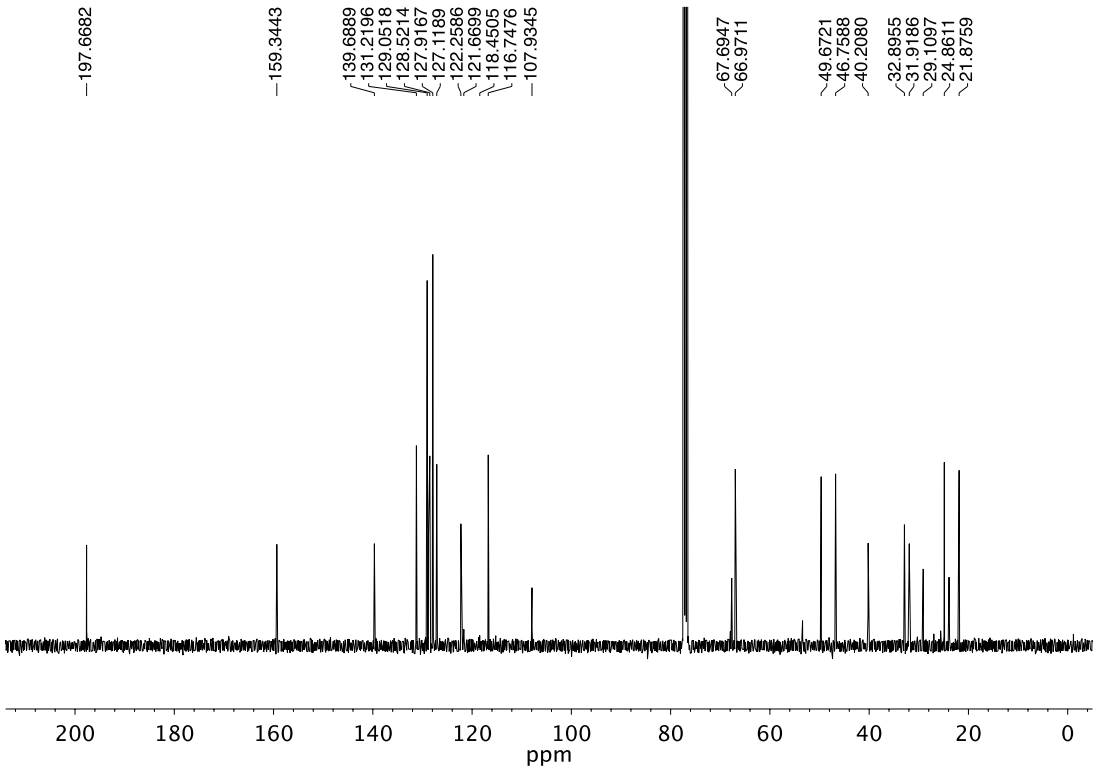


Figure 5.30 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.14B.**

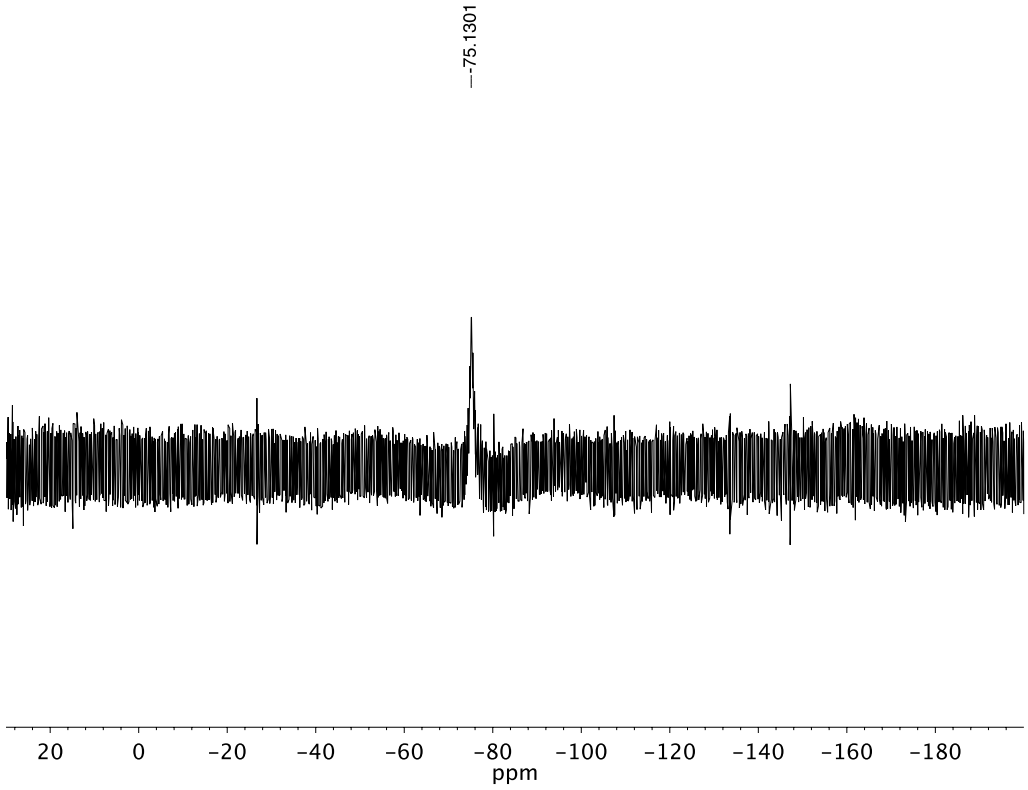


Figure 5.31 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.14B.**

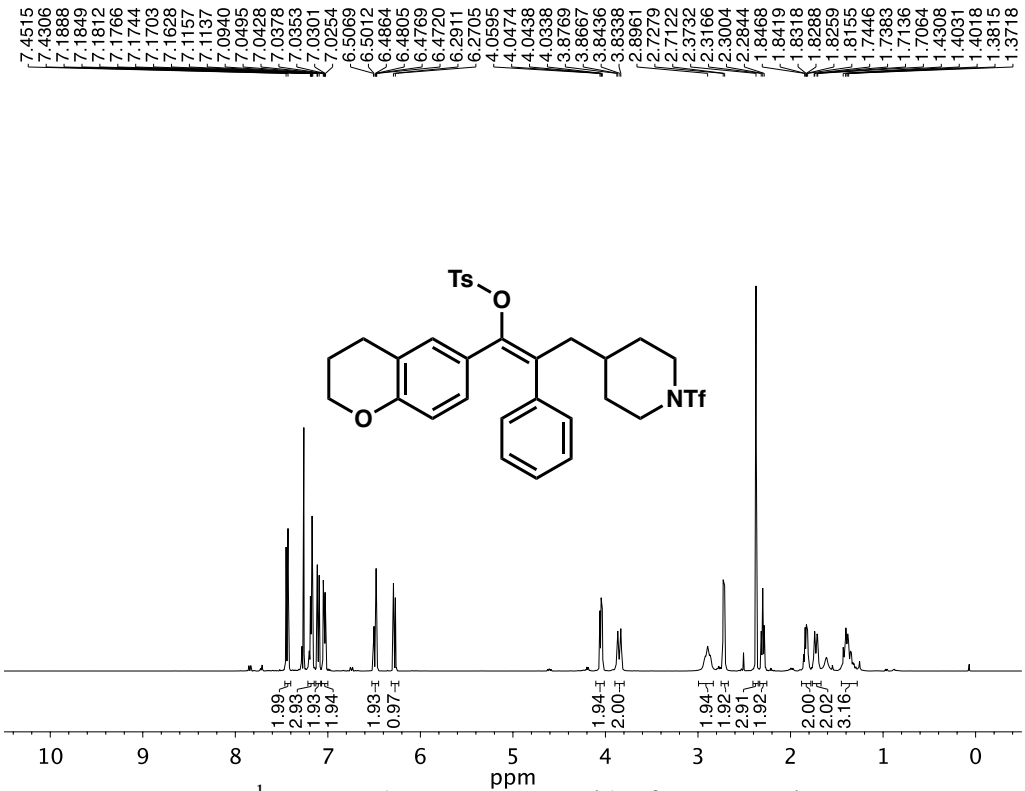


Figure 5.32 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.14C.**

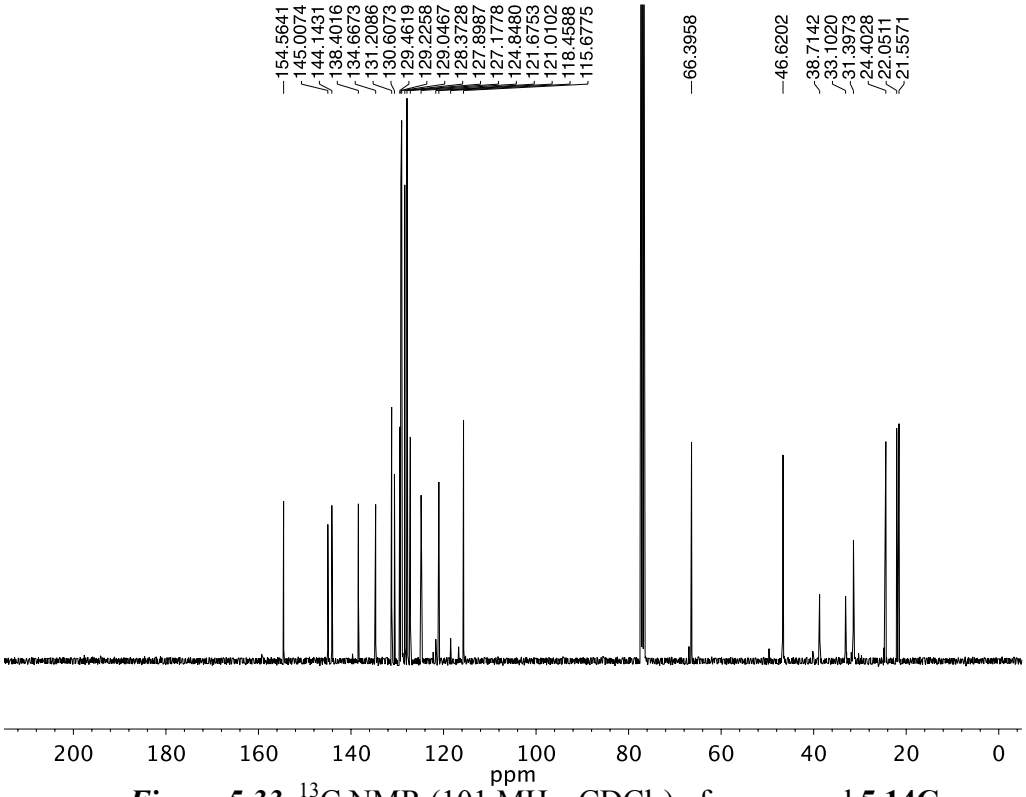


Figure 5.33 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.14C.**

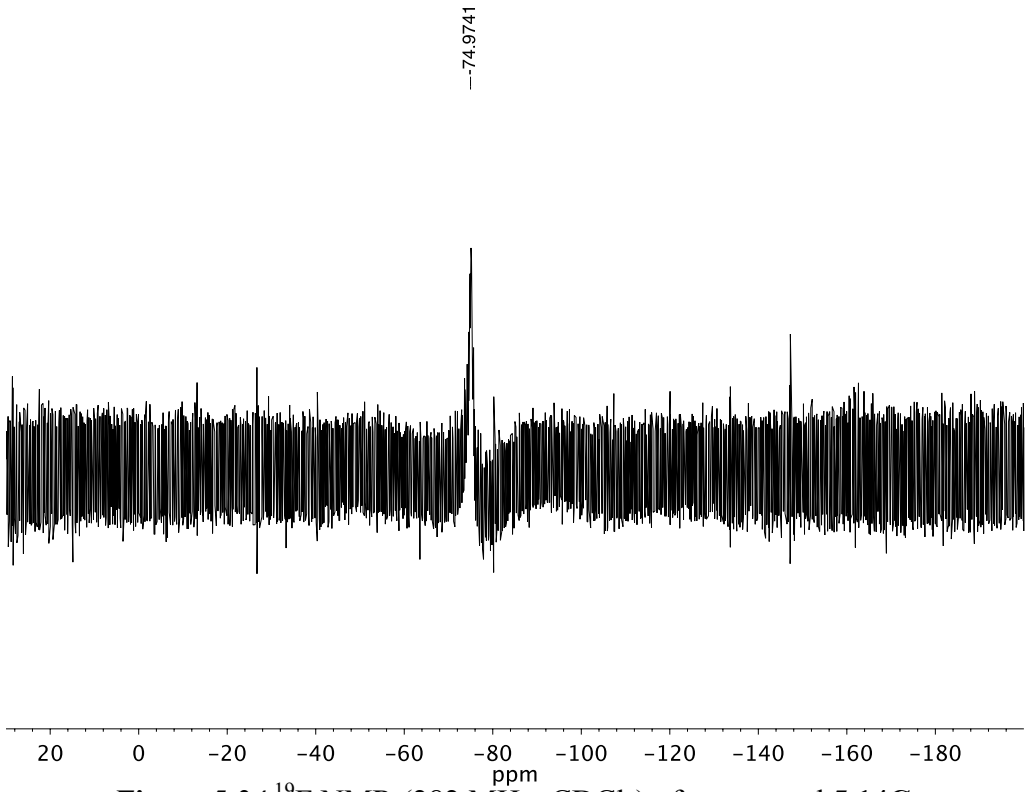


Figure 5.34 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.14C.**

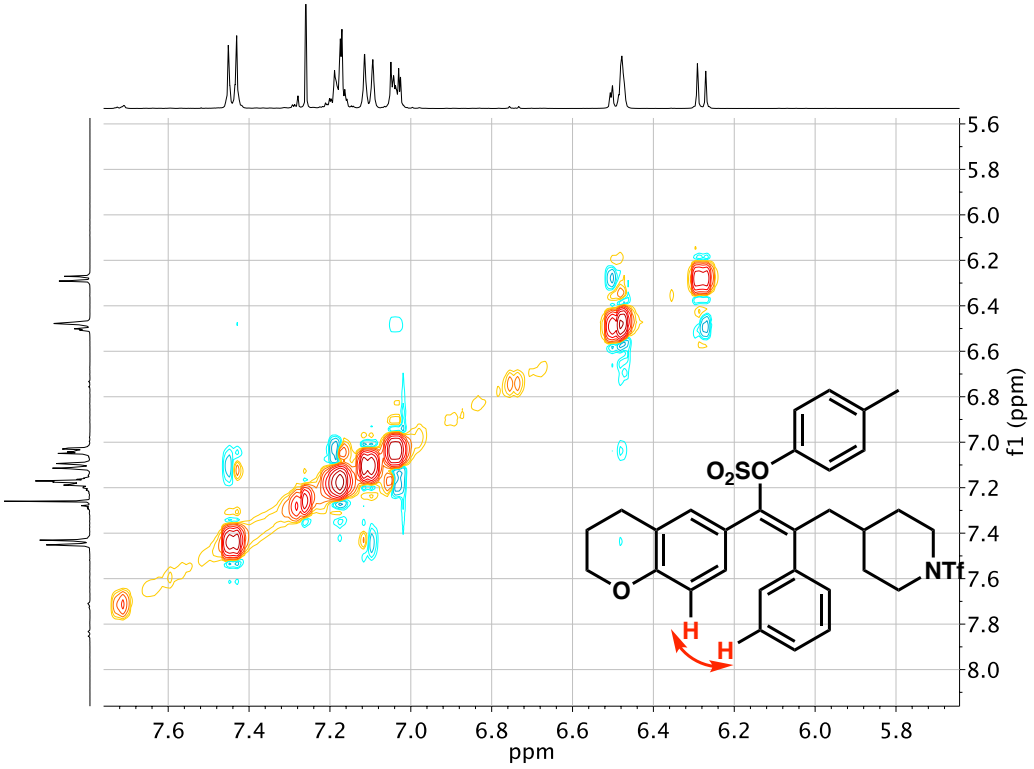


Figure 5.35 ^{1}H-NOE (400 MHz, $CDCl_3$) of compound **5.14C.**

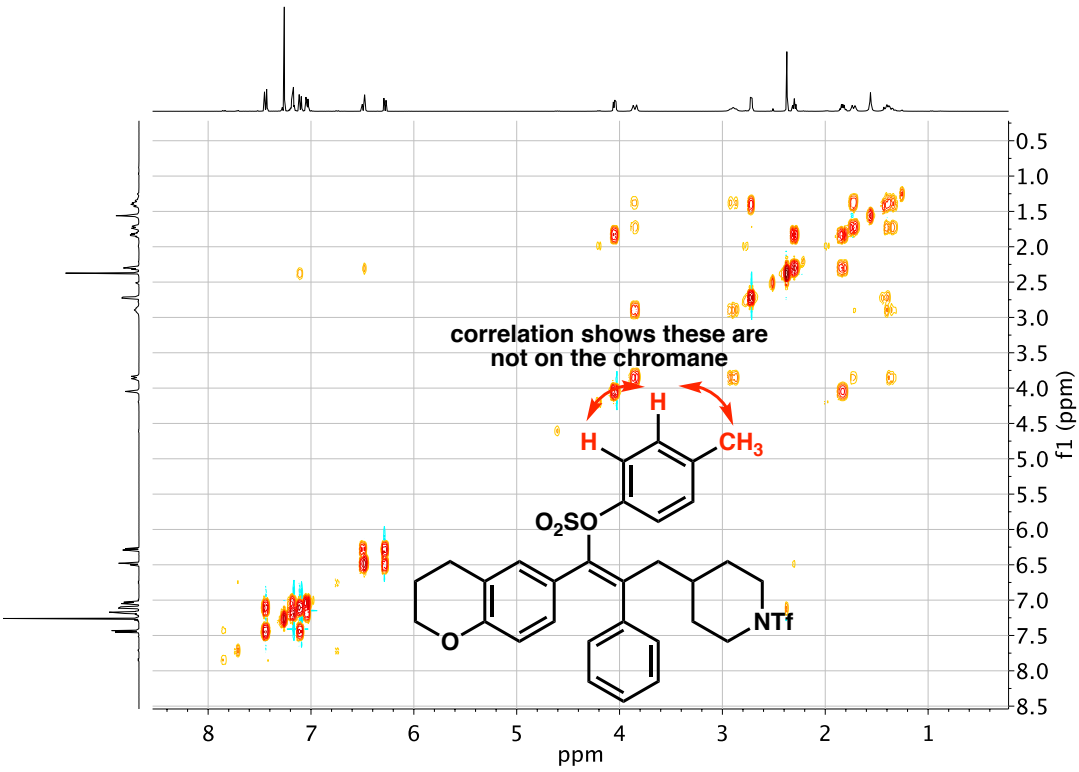


Figure 5.36 ^{1}H COSY (400 MHz, $CDCl_3$) of compound **5.14C.**

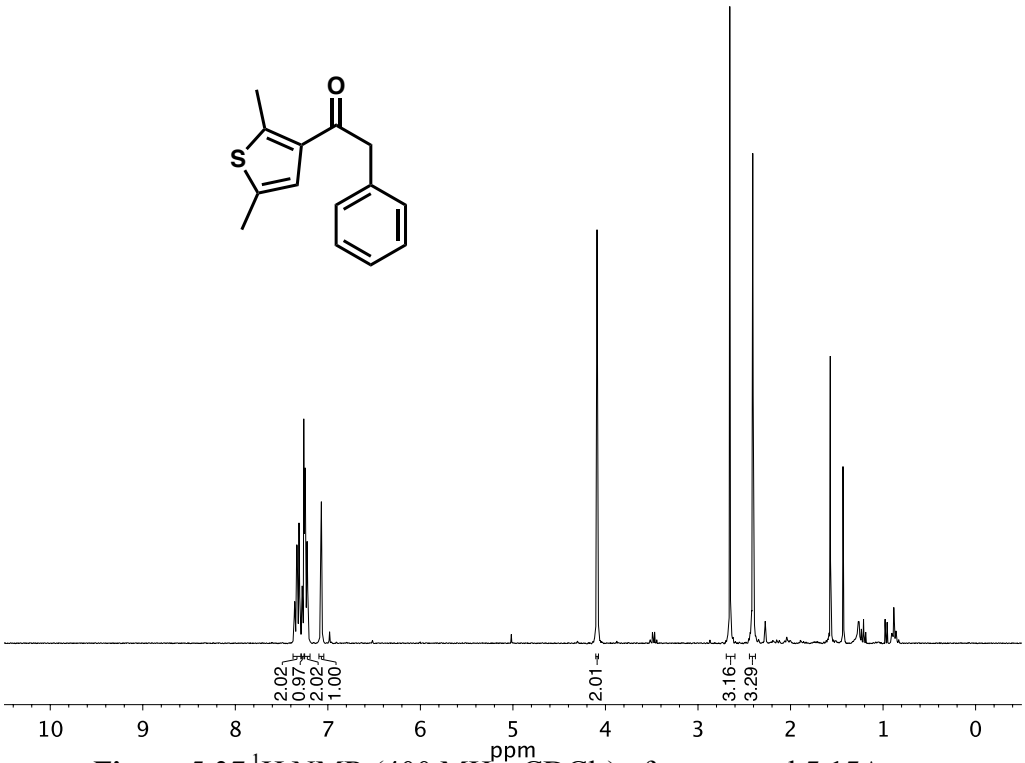


Figure 5.37 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.15A.**

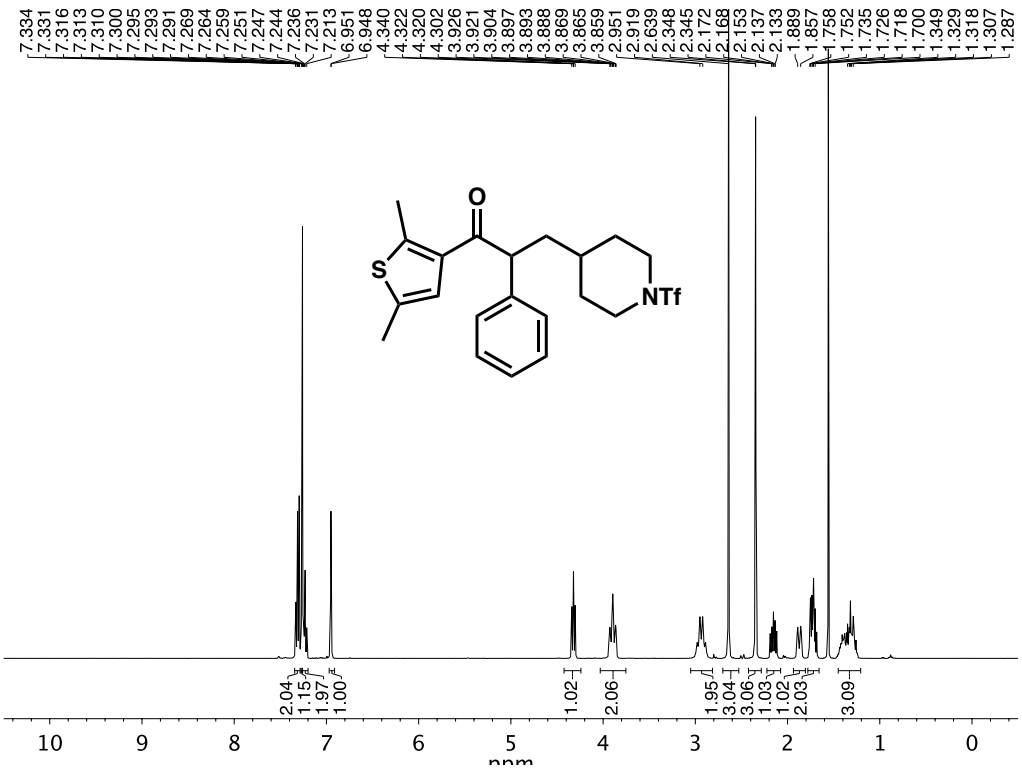


Figure 5.38 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.15B.**

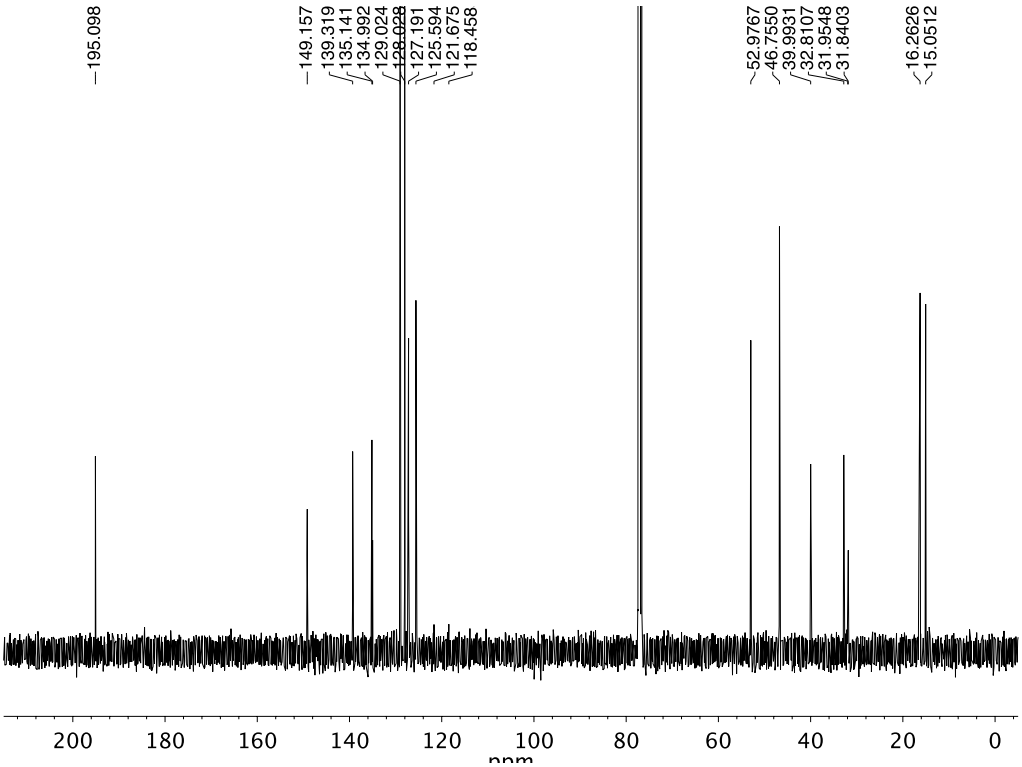


Figure 5.39 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.15B.**

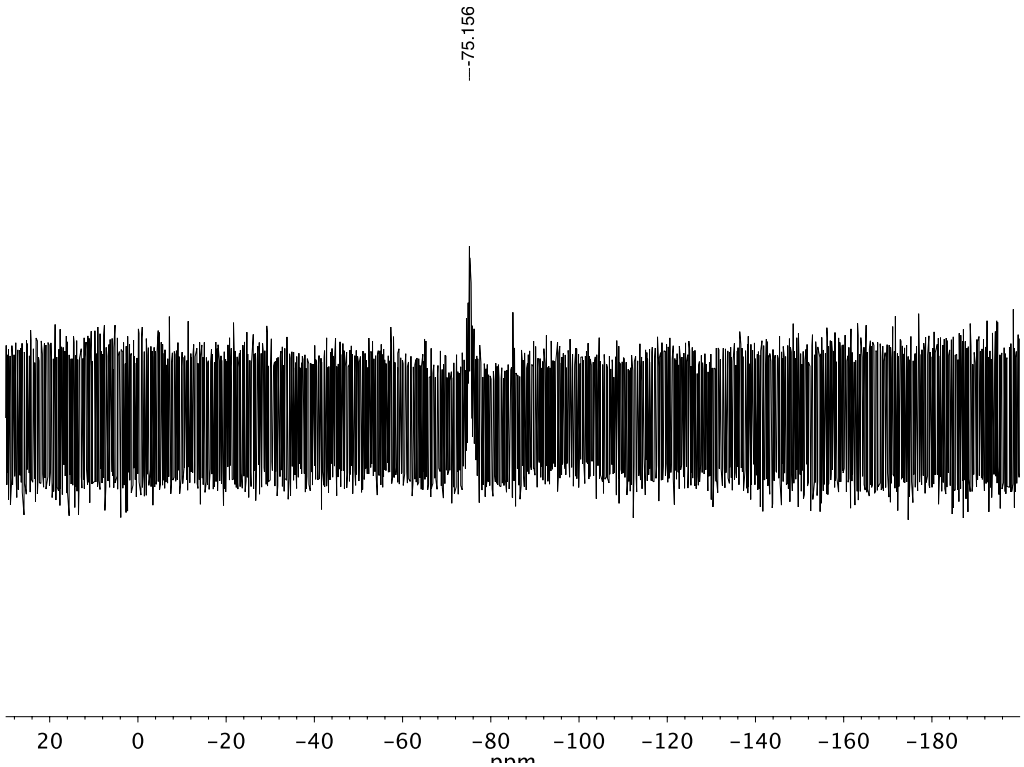


Figure 5.40 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.15B.**

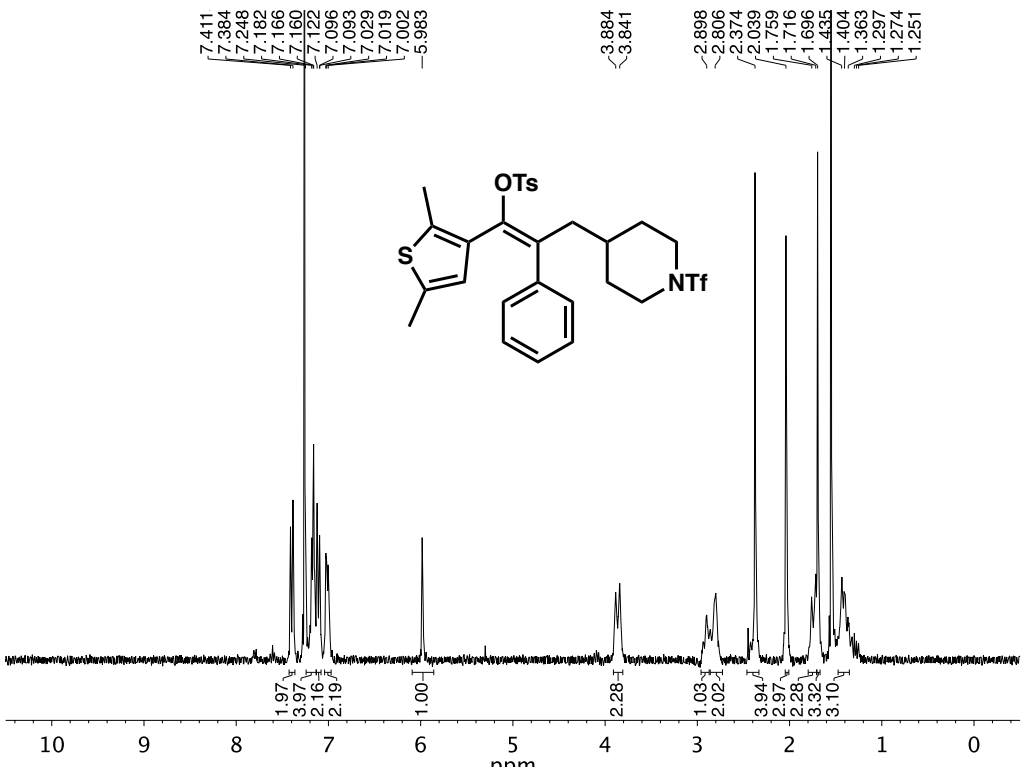


Figure 5.41 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.15C.**

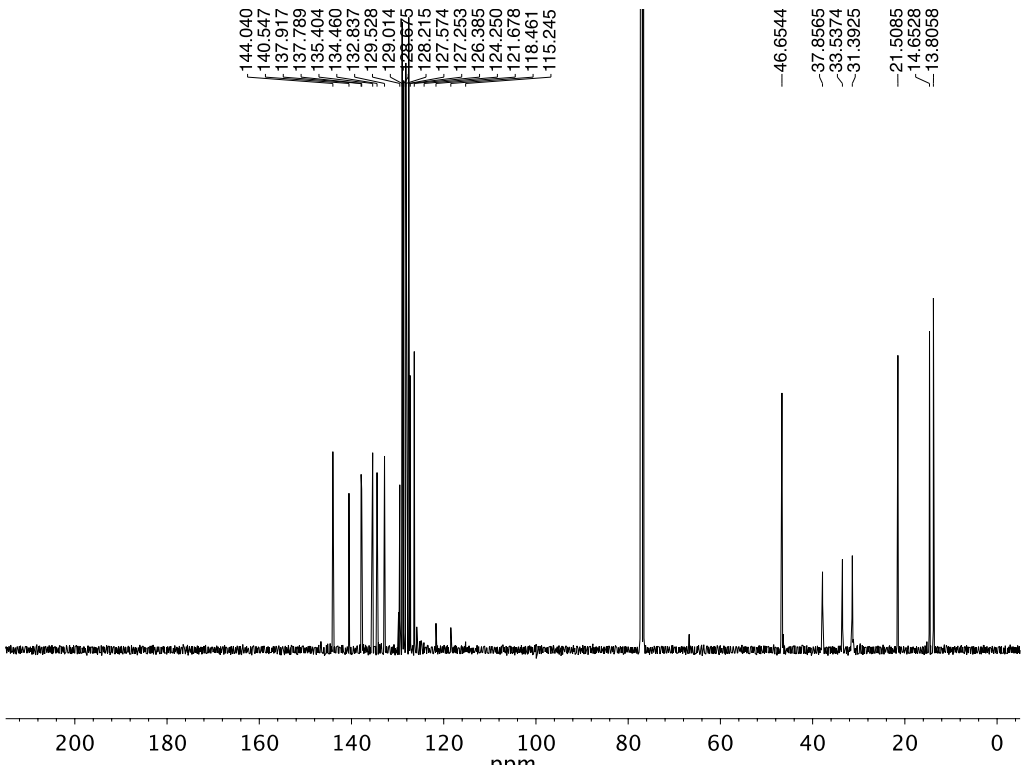


Figure 5.42 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.15C.**

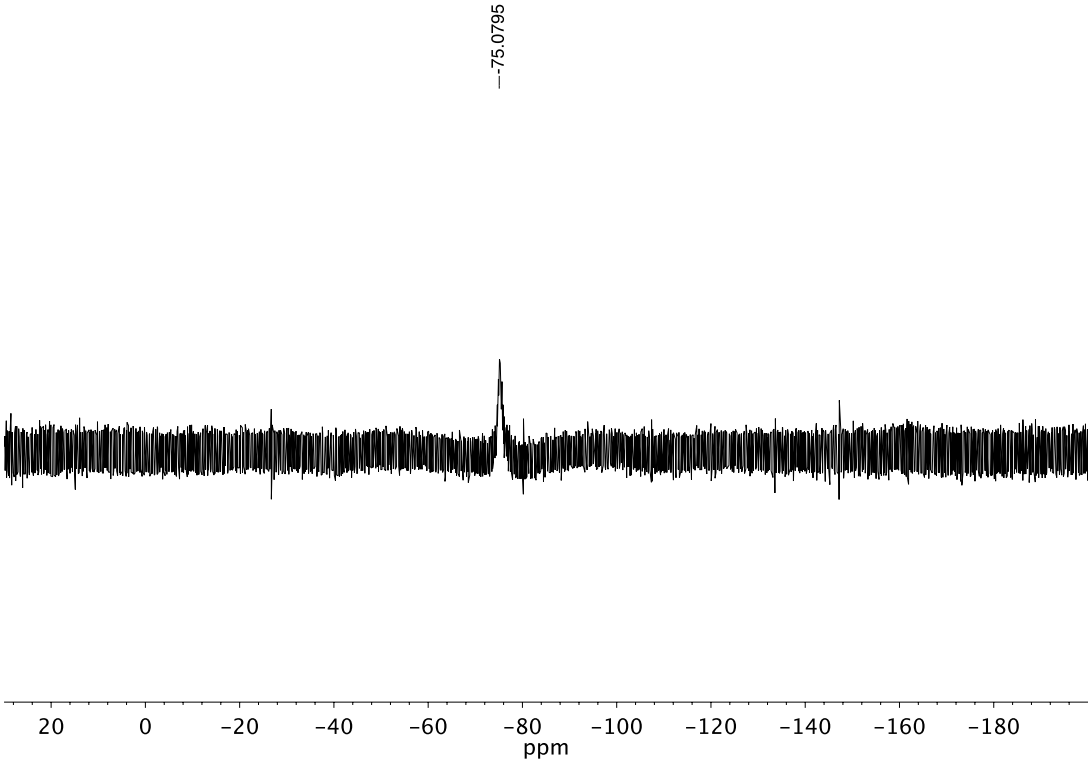


Figure 5.43 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.15C.**

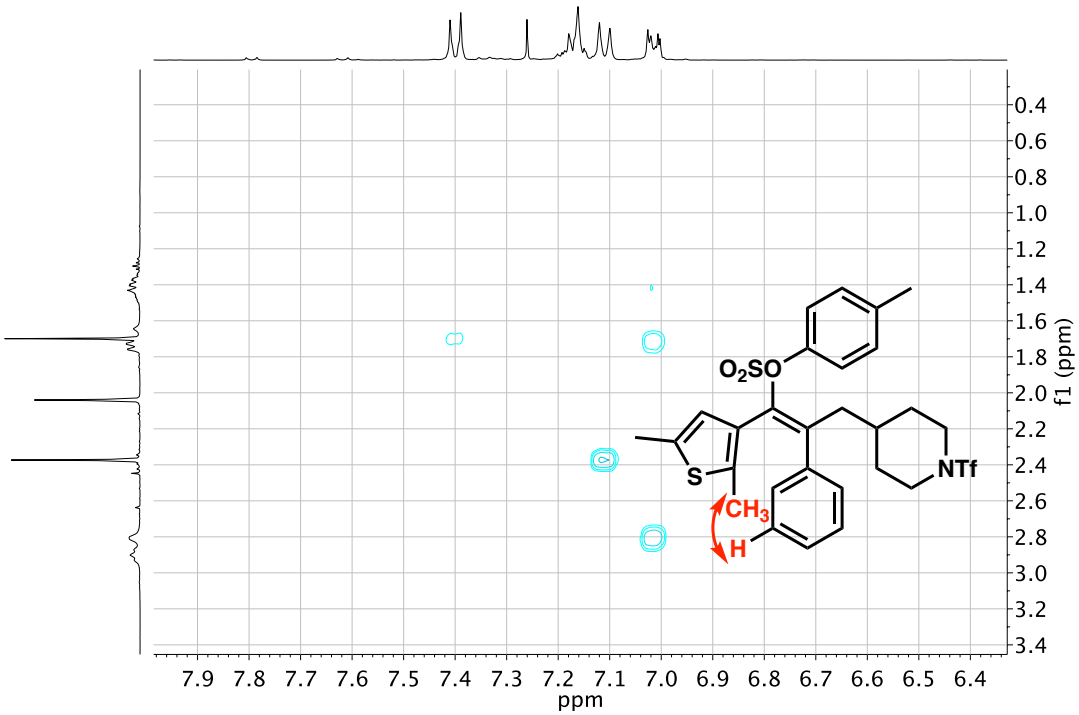


Figure 5.44 ^{1}H-NOE (400 MHz, $CDCl_3$) of compound **5.15C.**

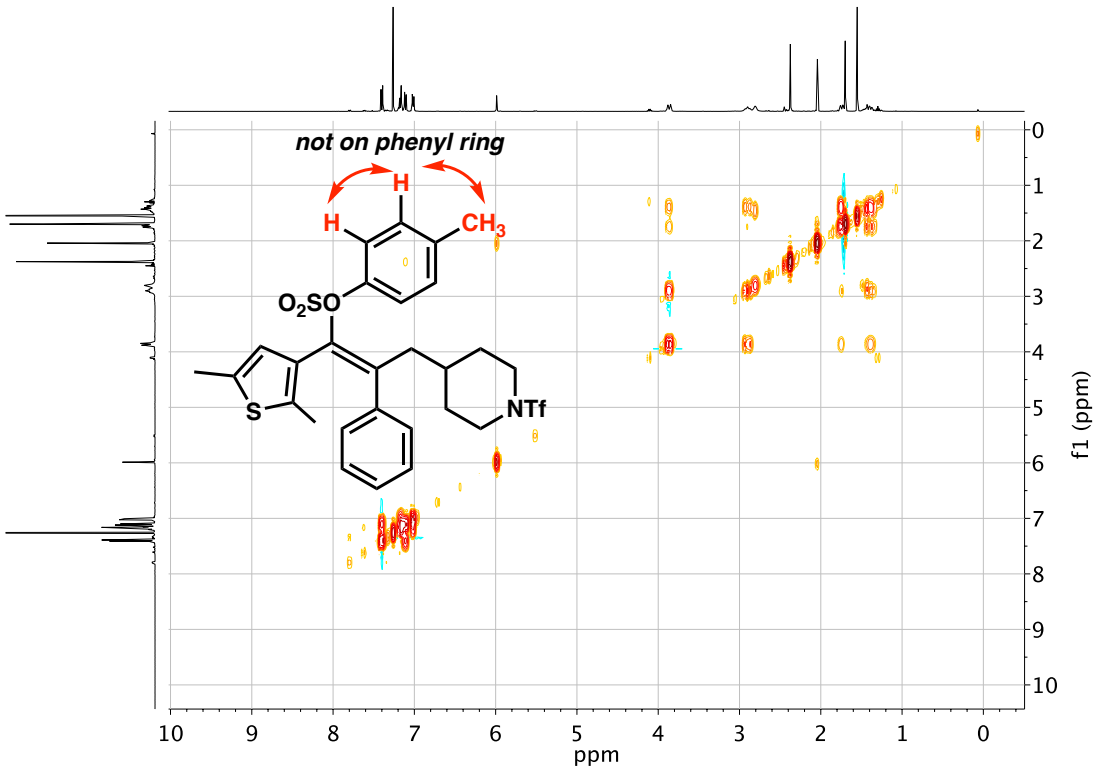


Figure 5.45 ^{1}H-COSY (400 MHz, $CDCl_3$) of compound **5.15C.**

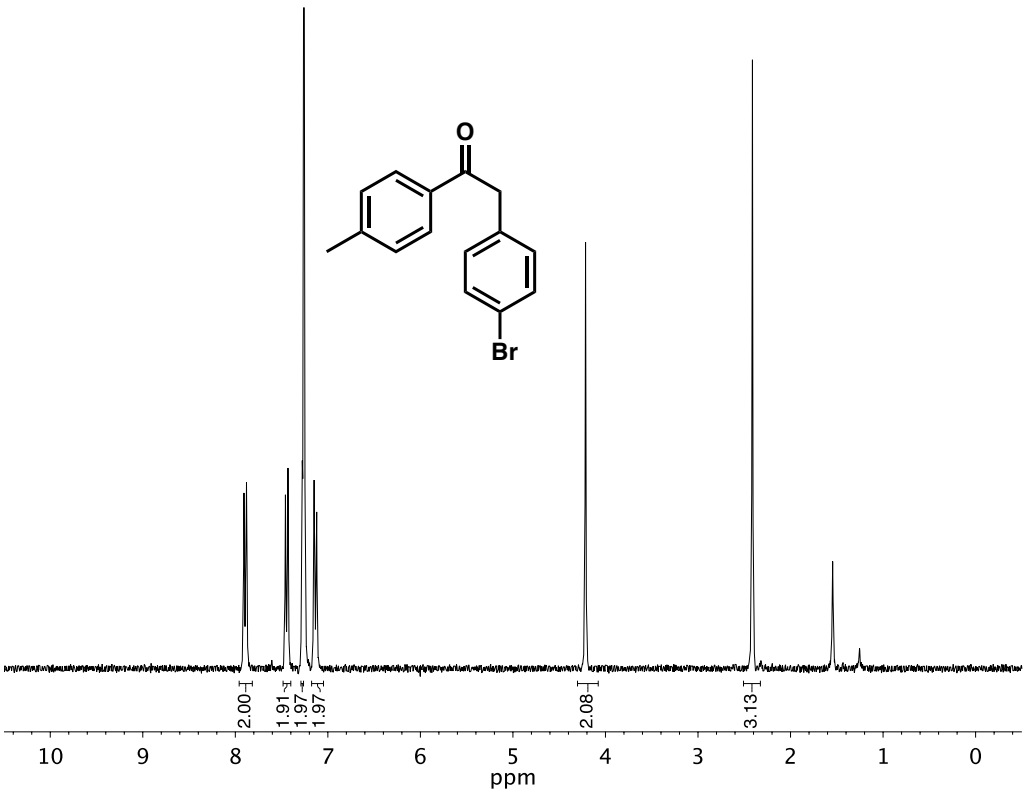


Figure 5.46 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.16A.**

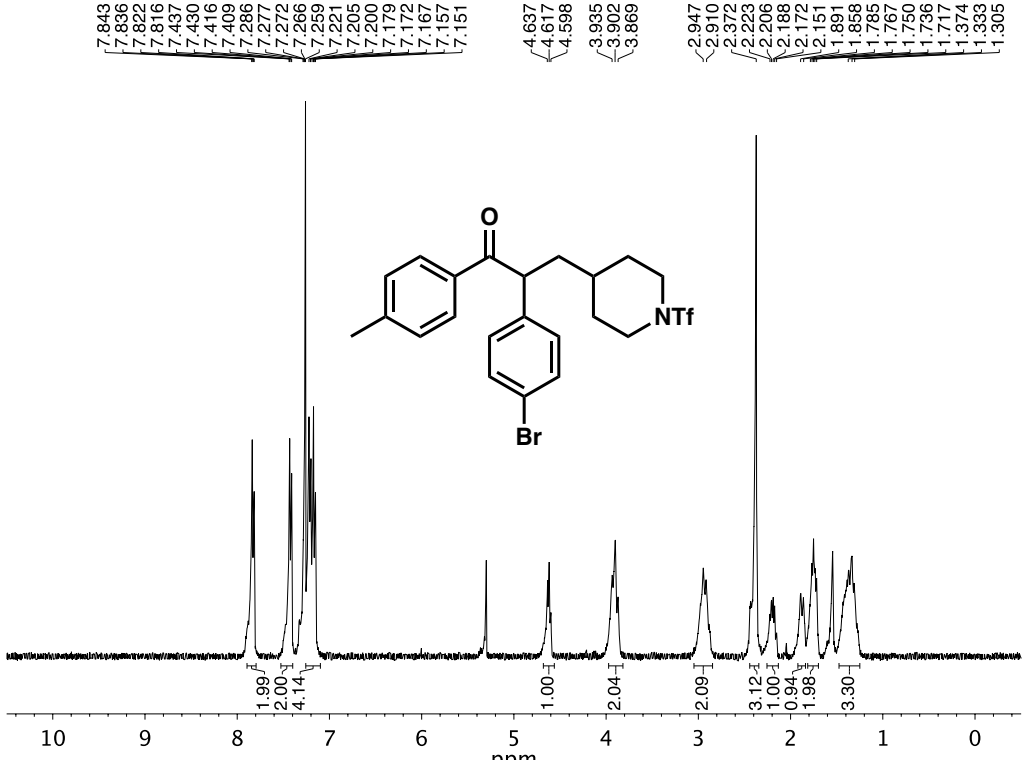


Figure 5.47 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.16B.**

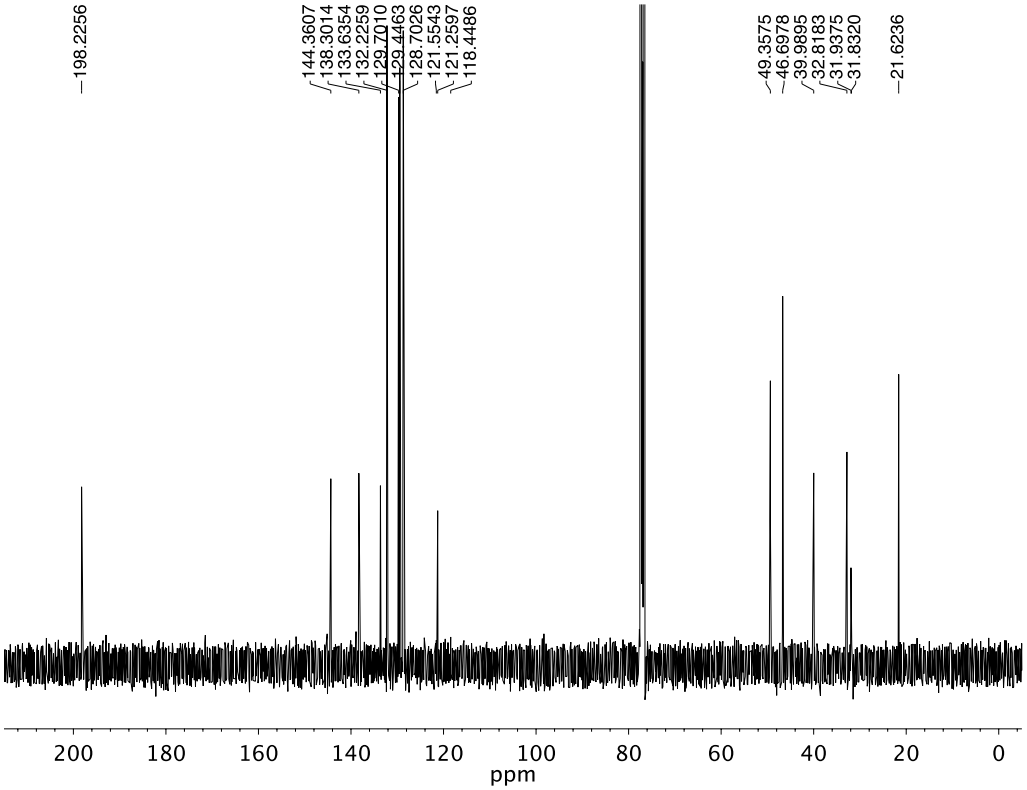


Figure 5.48 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.16B.**

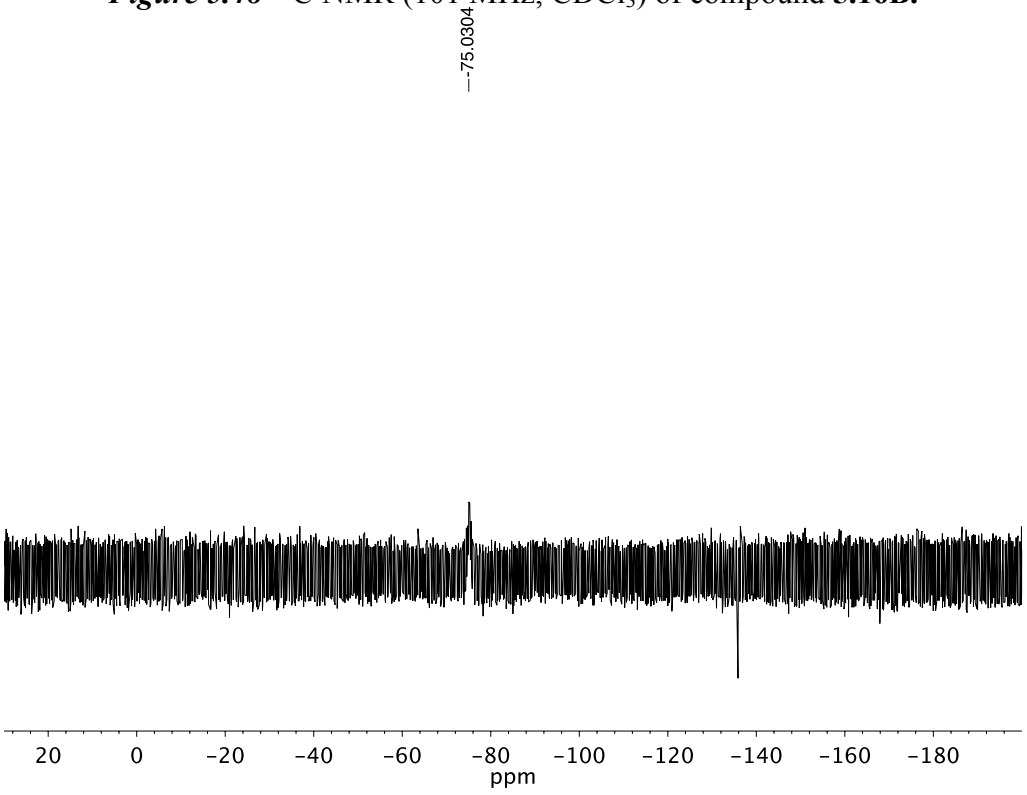


Figure 5.49 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.16B.**

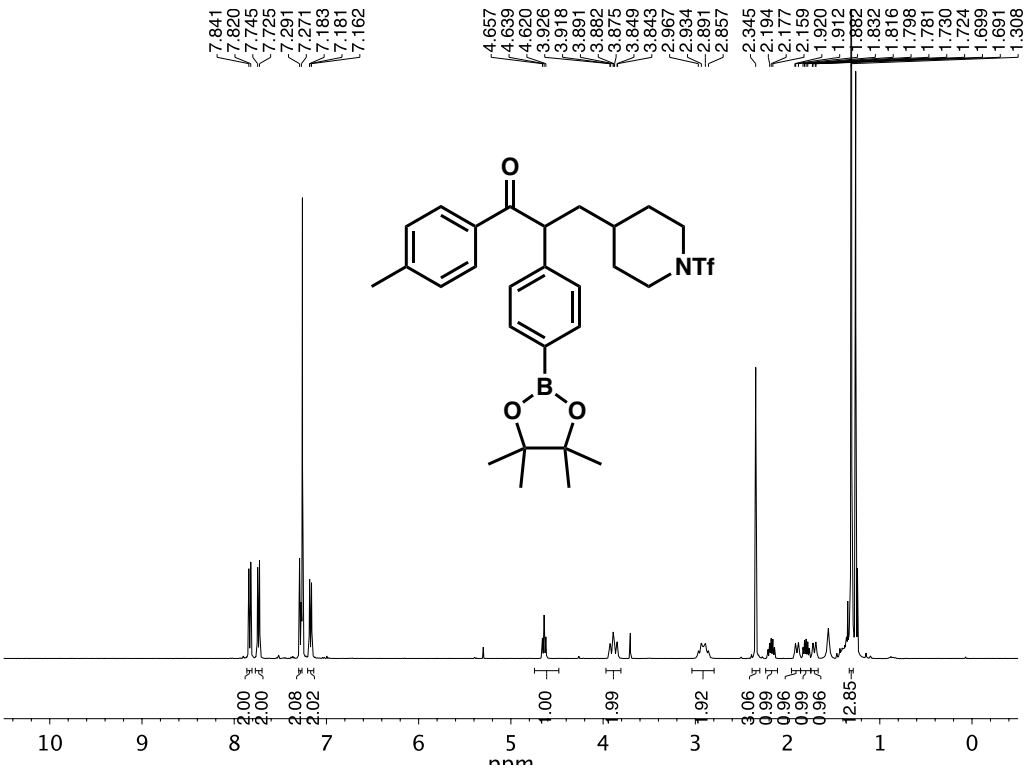


Figure 5.50 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.16C.**

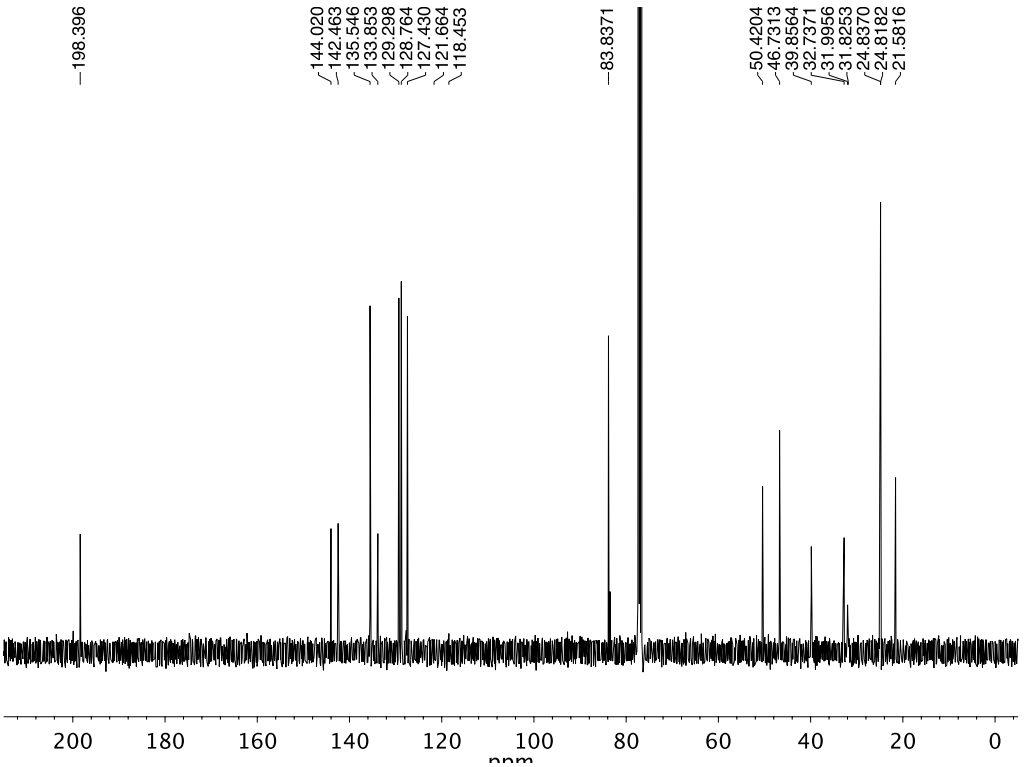


Figure 5.51 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.16C.**

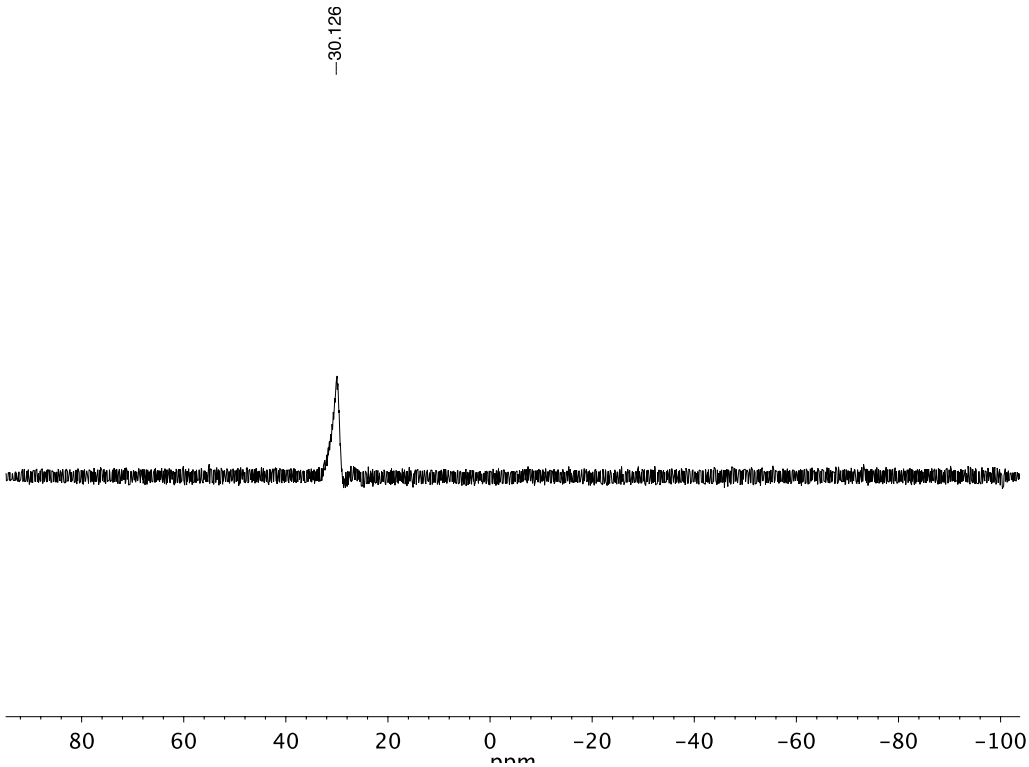


Figure 5.52 ^{11}B NMR (128 MHz, $CDCl_3$) of compound **5.16C.**

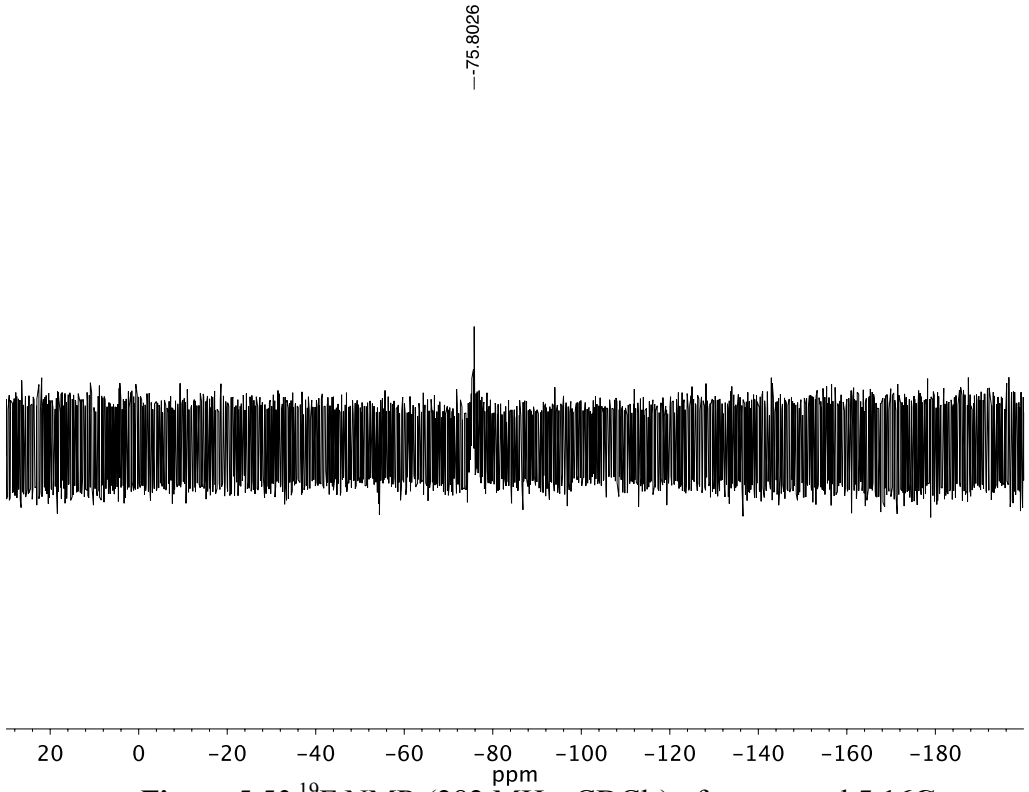


Figure 5.53 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.16C.**

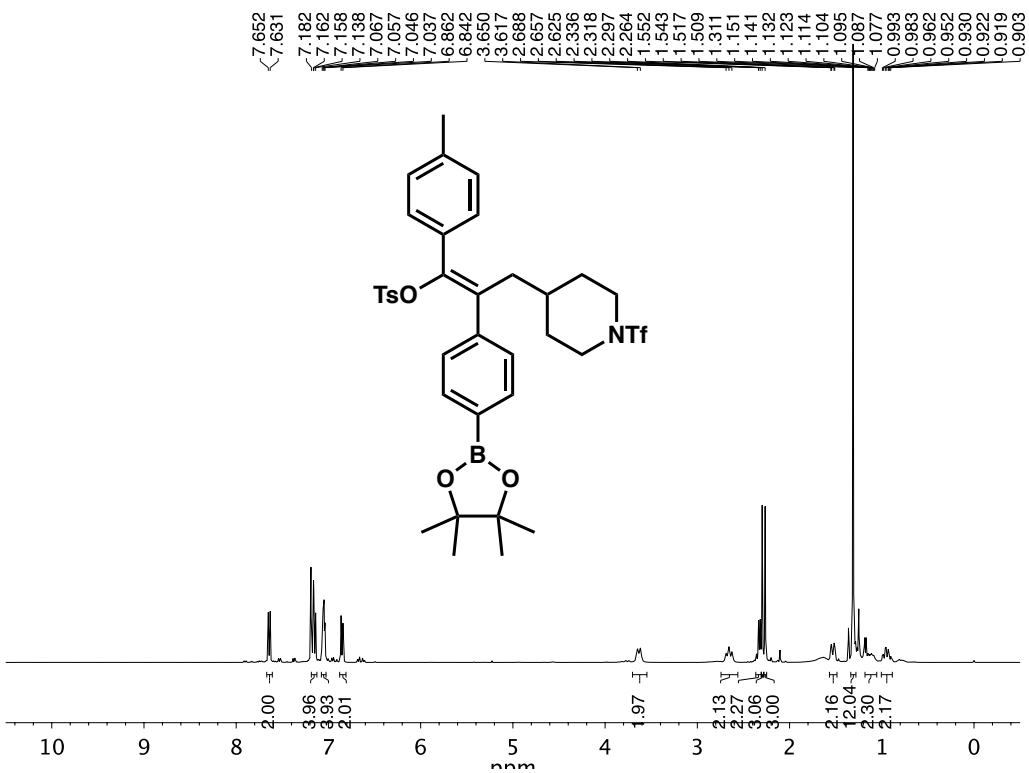


Figure 5.54 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.16D.**

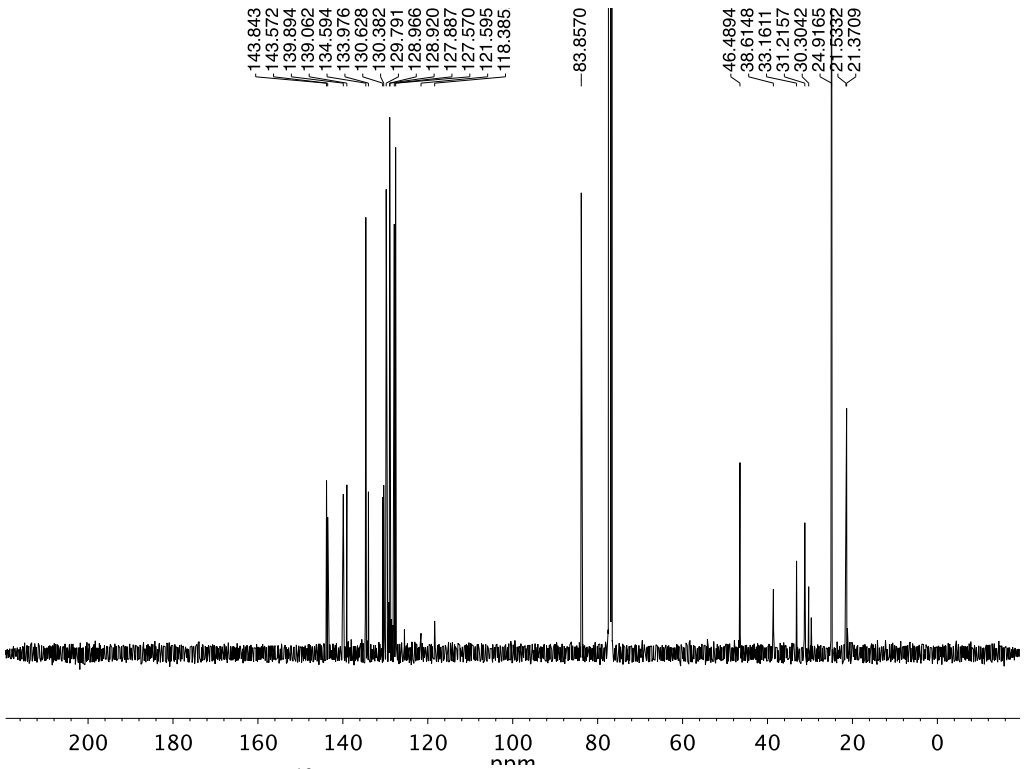


Figure 5.55 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.16D.**

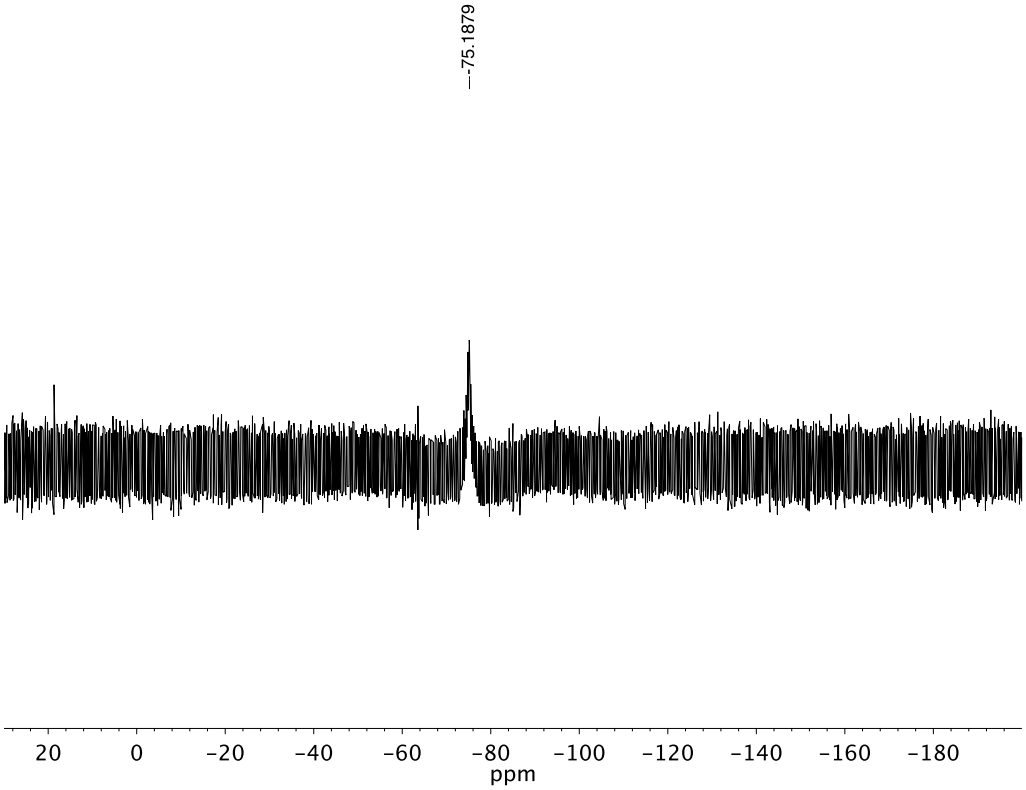


Figure 5.56 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.16D.**

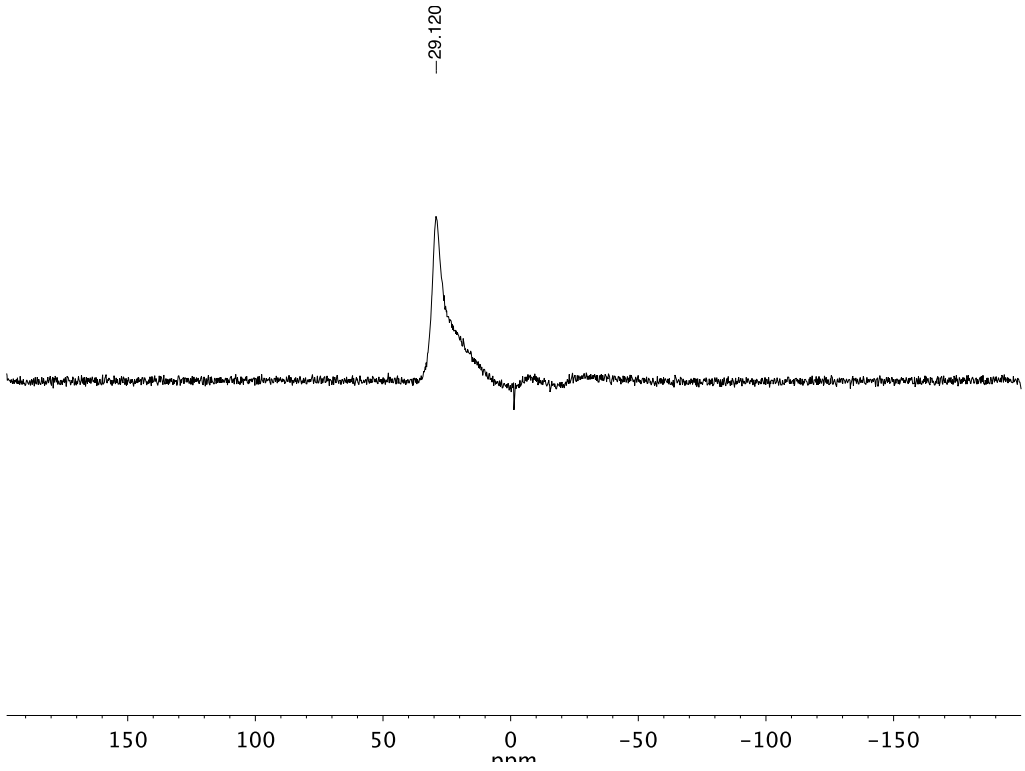


Figure 5.57 ^{11}B NMR (128 MHz, $CDCl_3$) of compound **5.16D.**

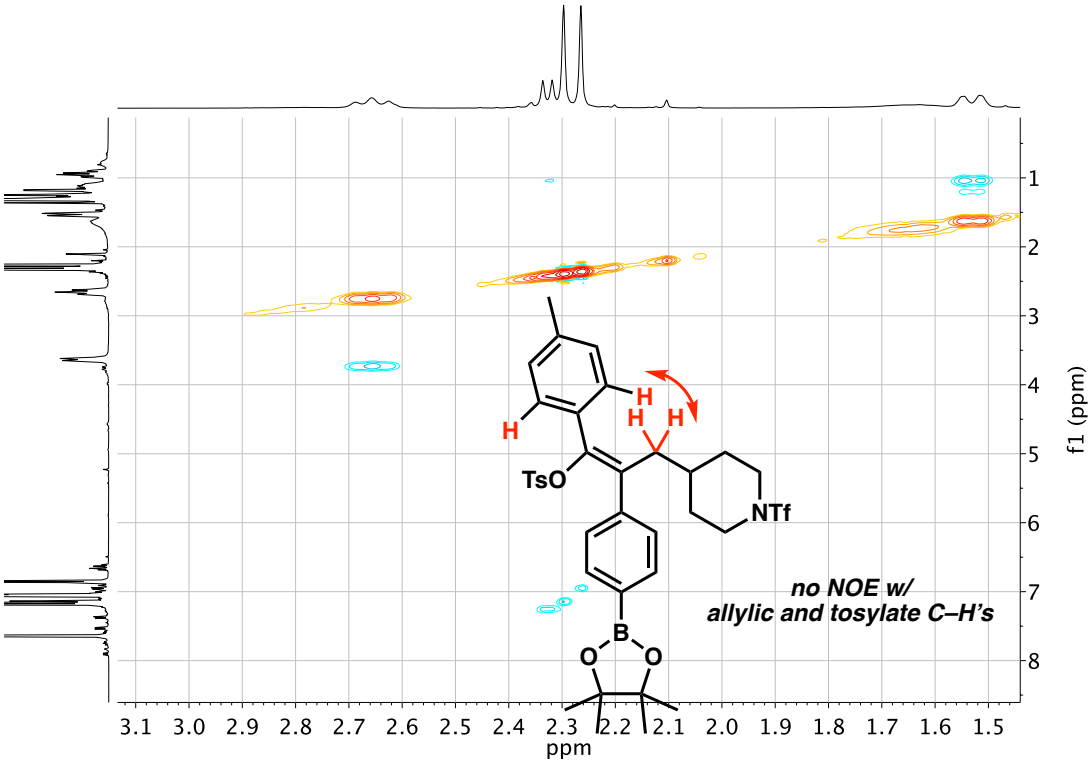


Figure 5.58 ^{1}H NOE NMR (400 MHz, $CDCl_3$) of compound **5.16D.**

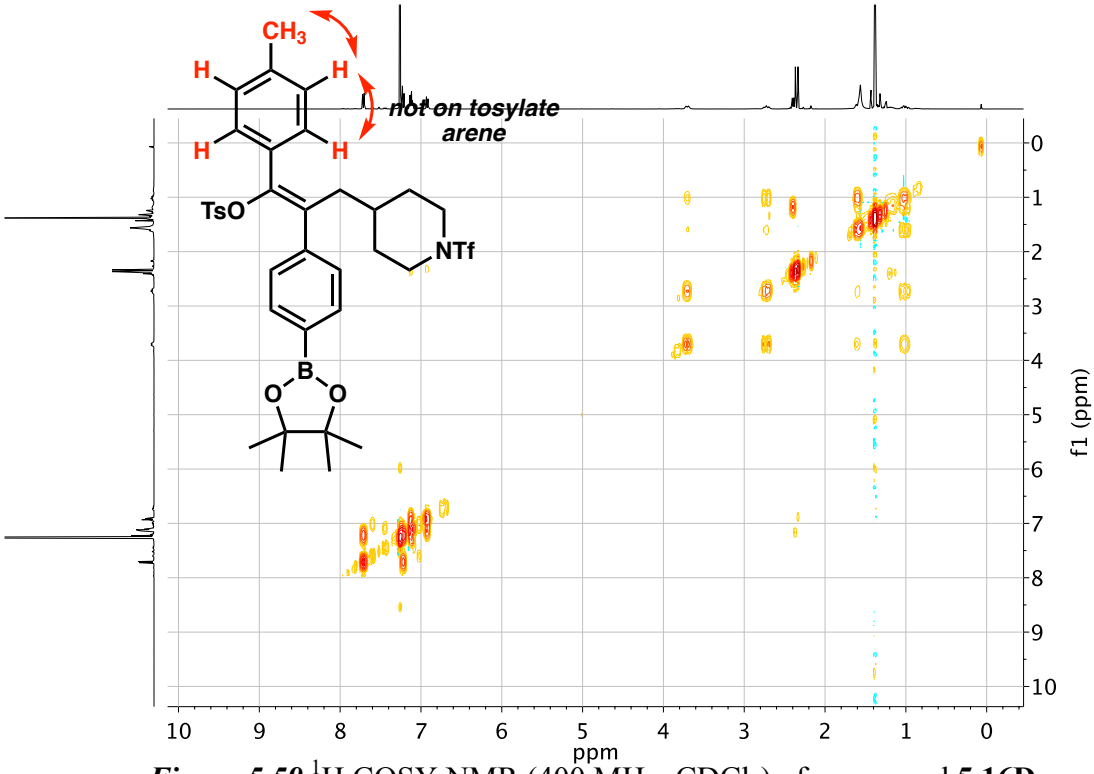


Figure 5.59 ^{1}H COSY NMR (400 MHz, $CDCl_3$) of compound **5.16D.**

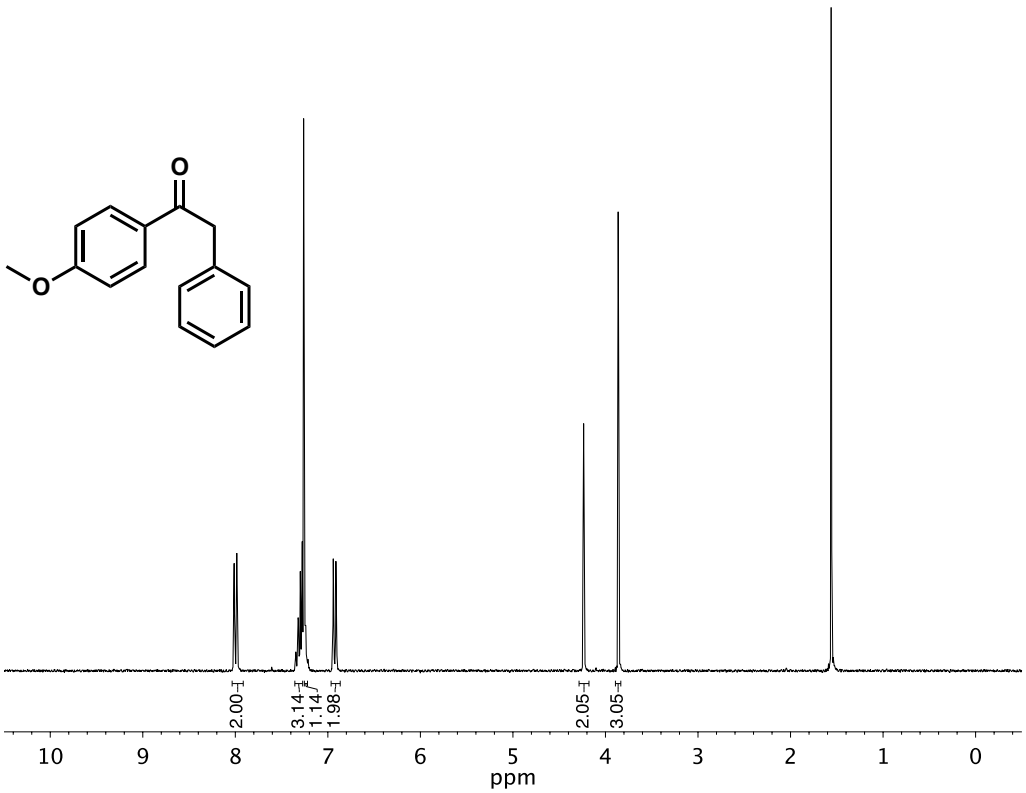


Figure 5.60 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.17A.**

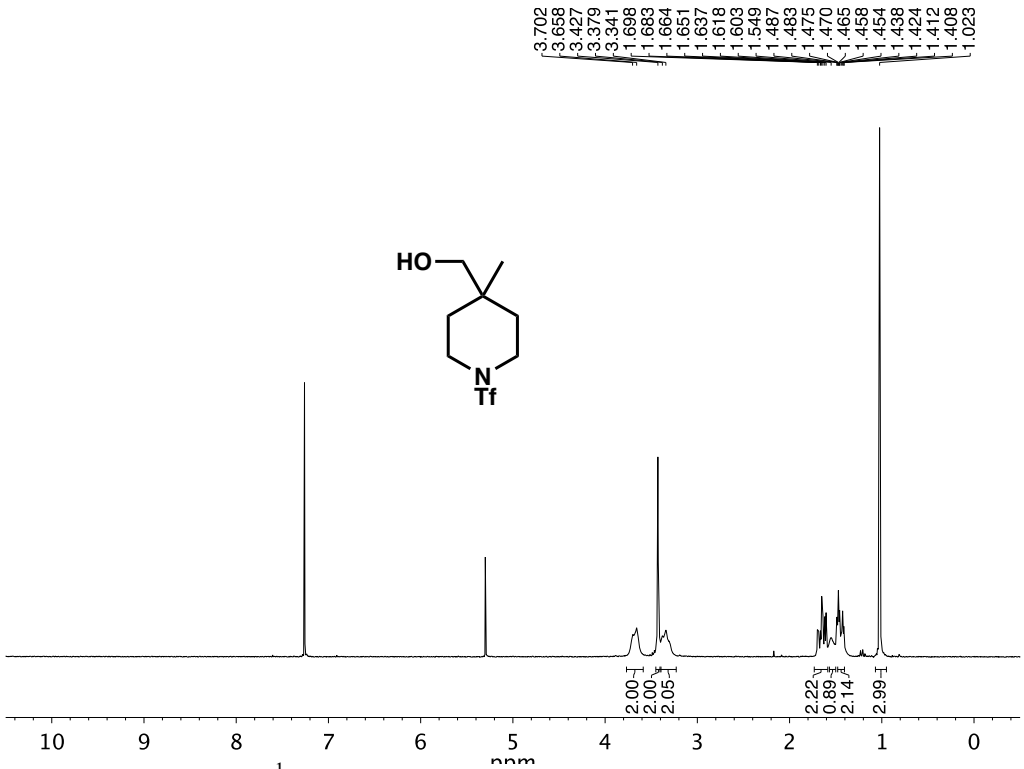


Figure 5.61 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.17B.**

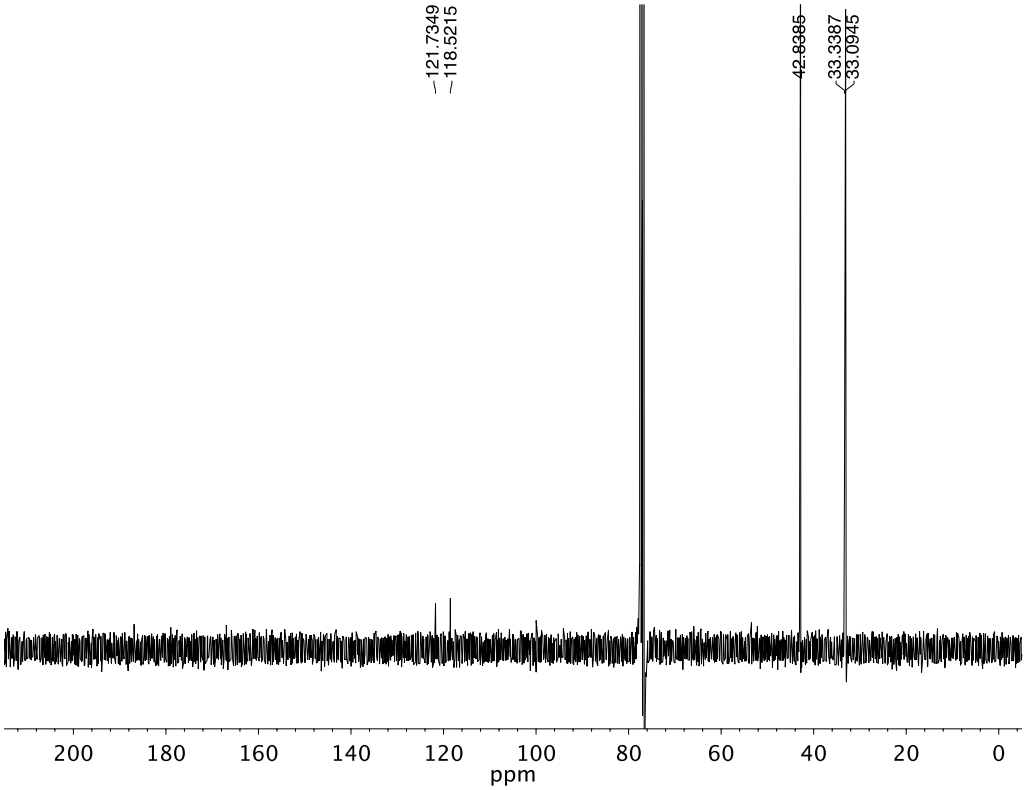


Figure 5.62 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.17B.**

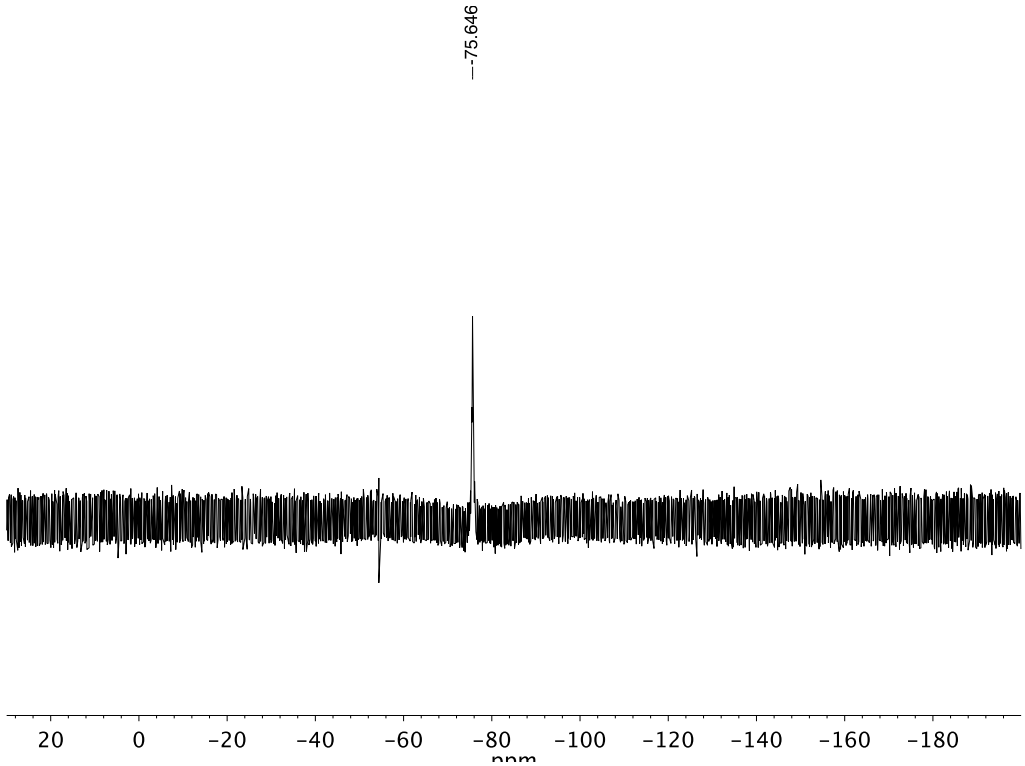


Figure 5.63 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.17B.**

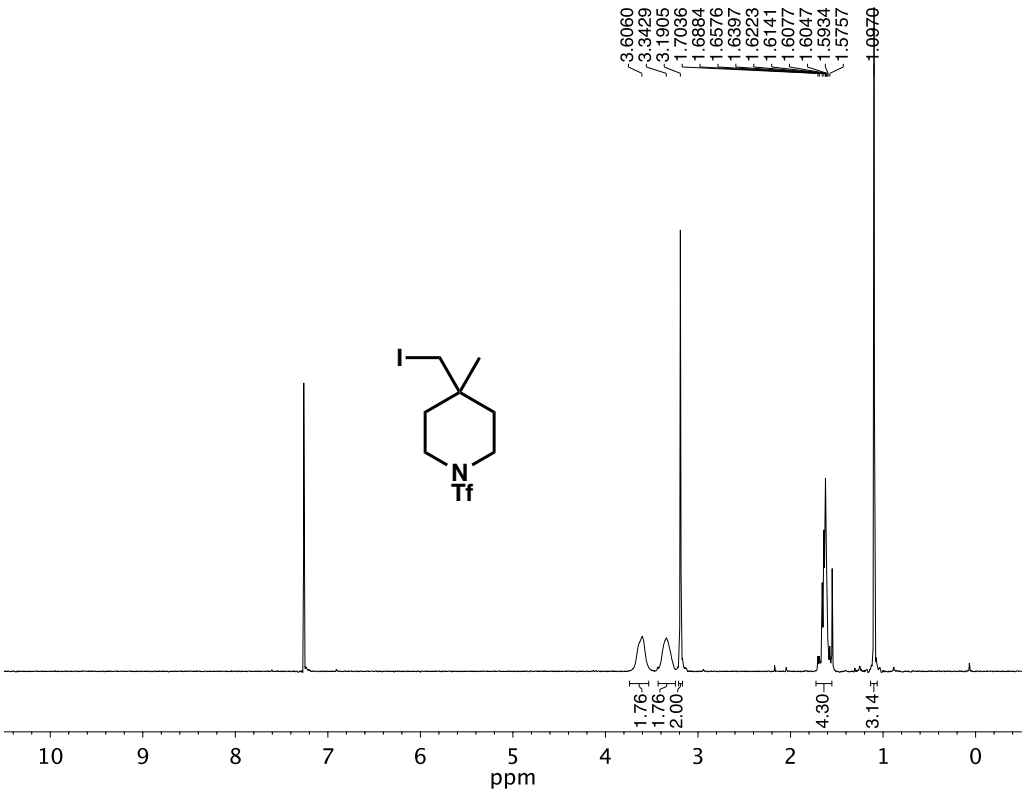


Figure 5.64 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.17C.**

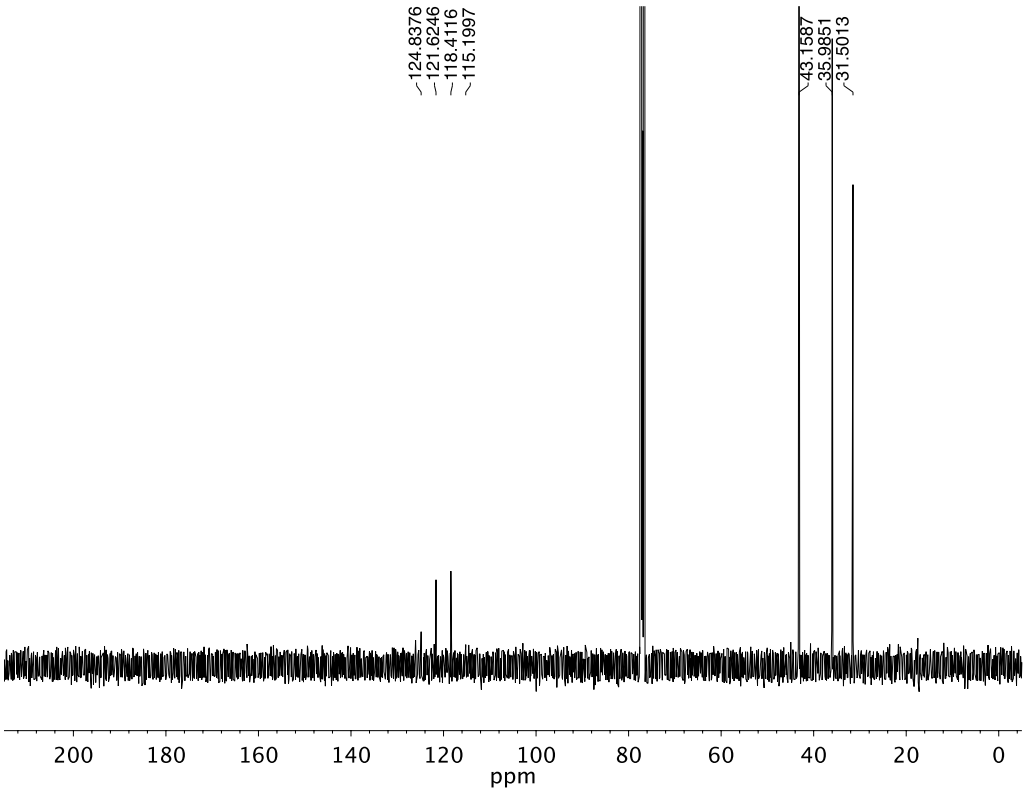


Figure 5.65 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.17C.**

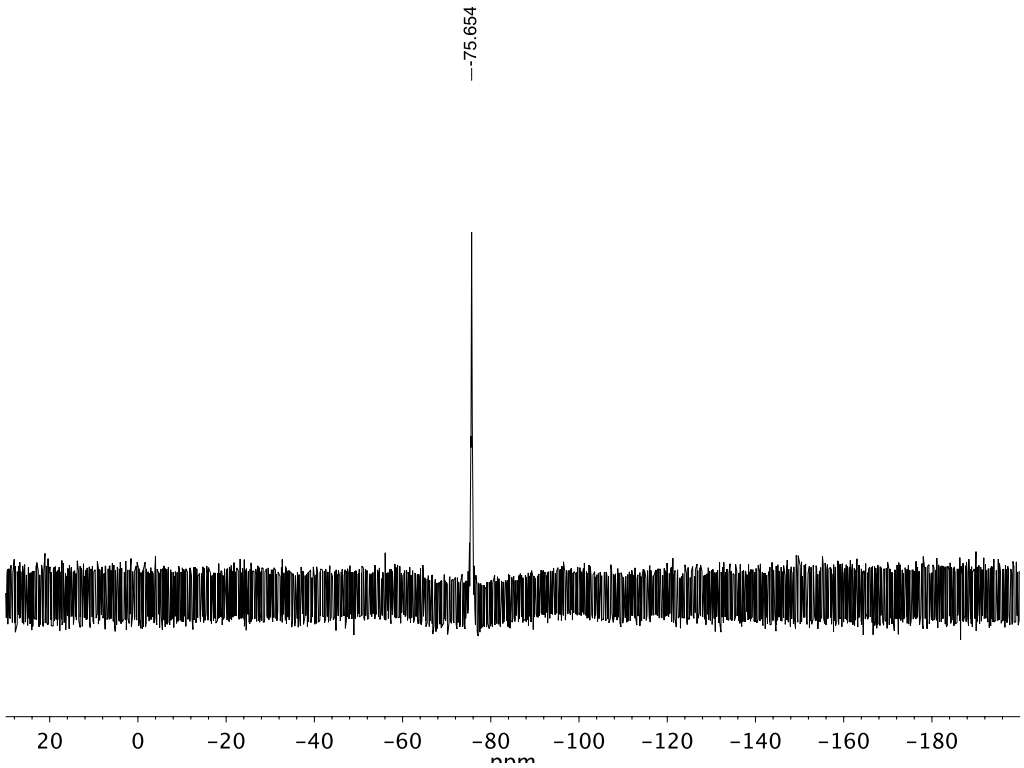


Figure 5.66 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.17C.**

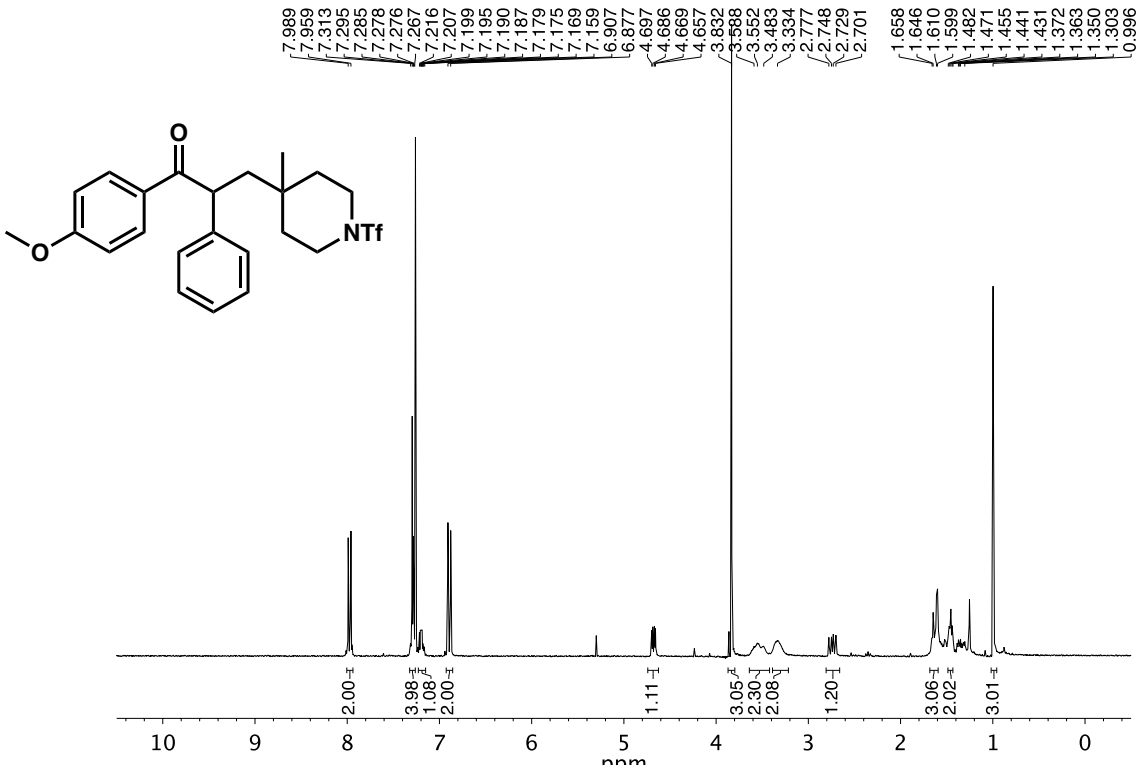


Figure 5.67 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.17D.**

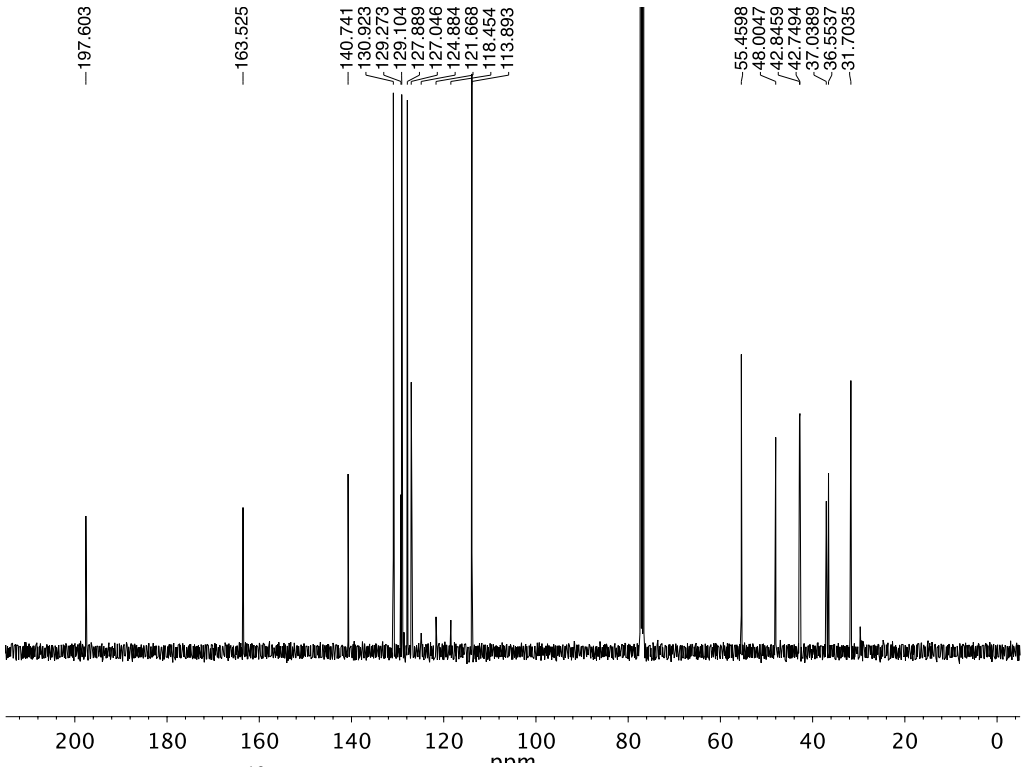


Figure 5.68 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.17D.**

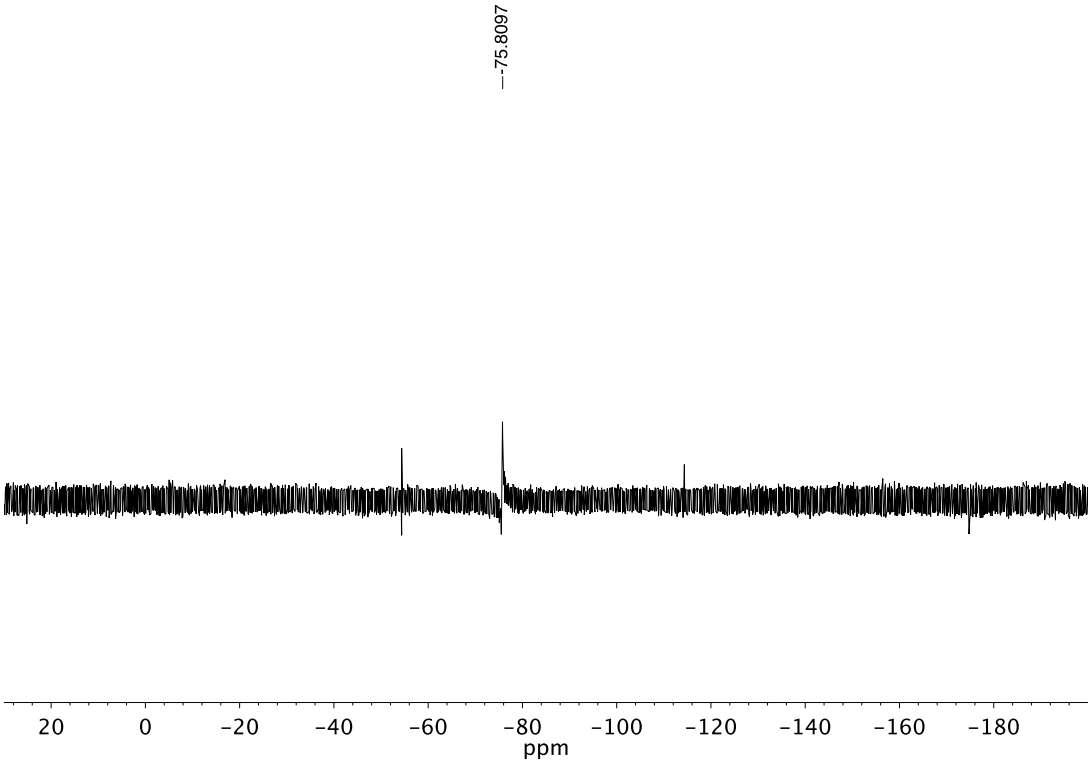


Figure 5.69 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.17D.**

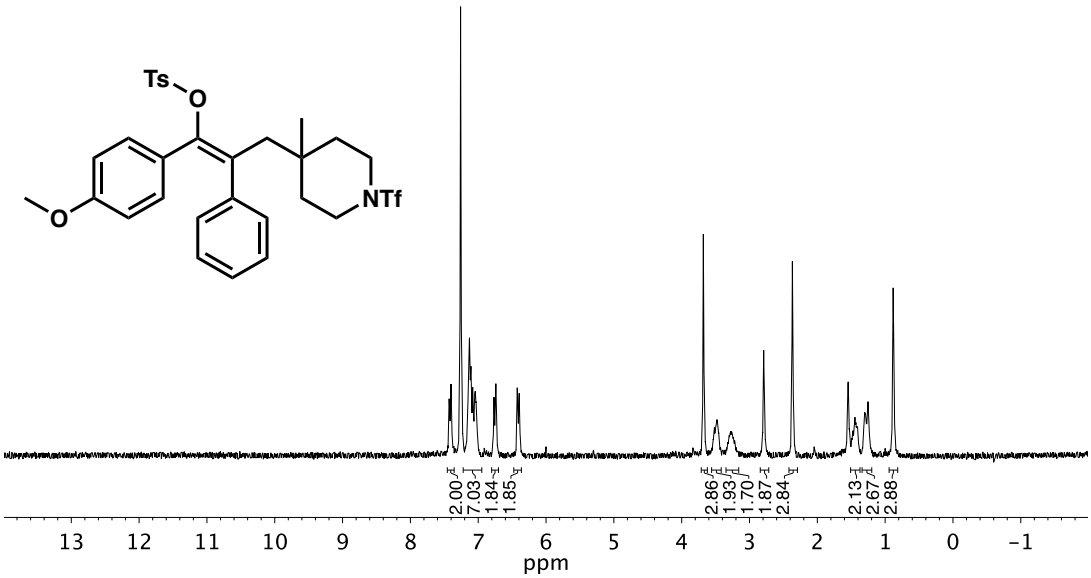


Figure 5.70 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.17E.**

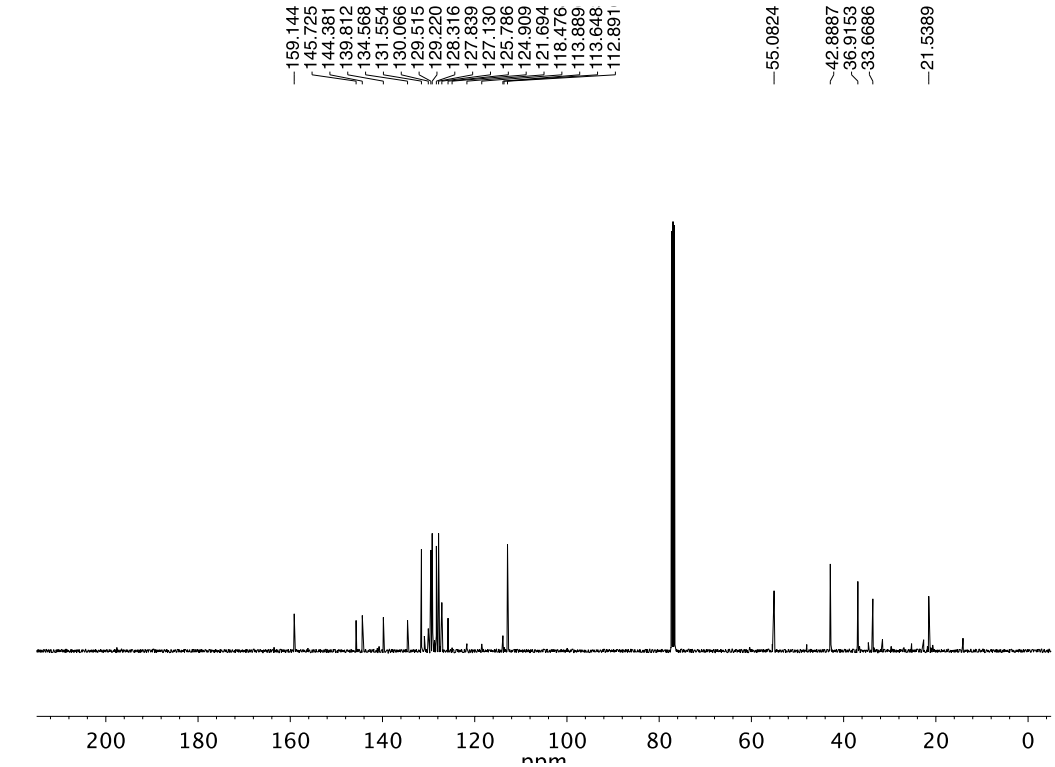


Figure 5.71 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.17E.**

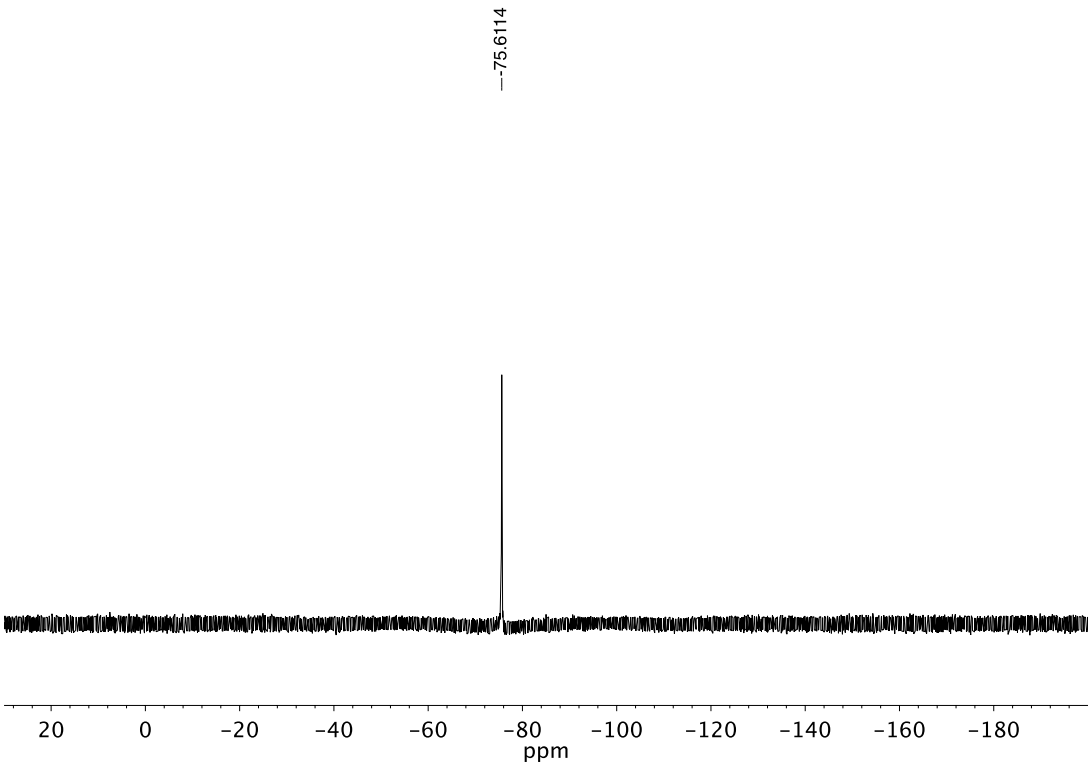


Figure 5.72 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.17E.**

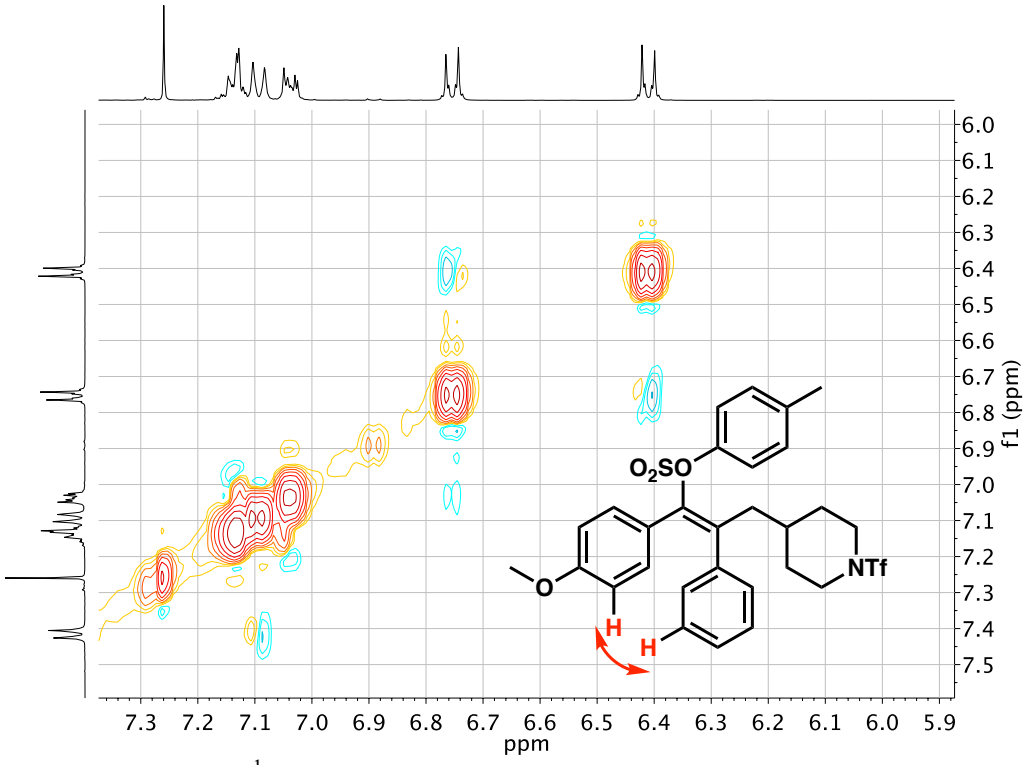


Figure 5.73 ^{1}H NOE NMR (400 MHz, $CDCl_3$) of compound **5.17E.**

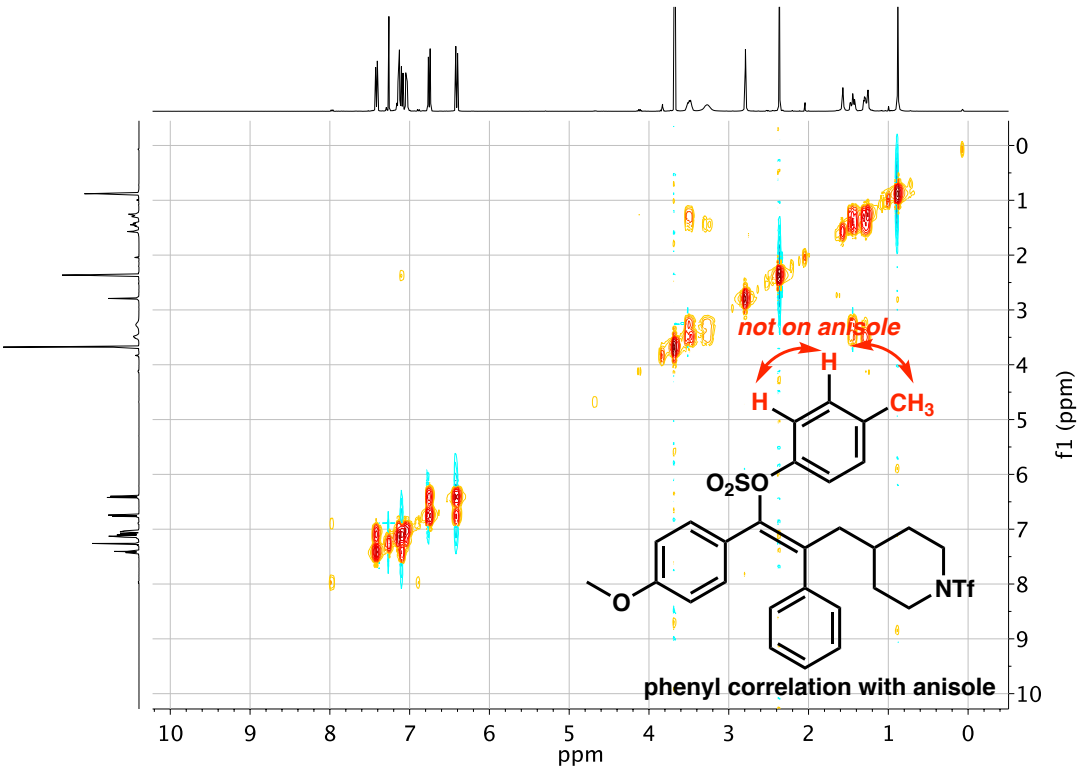


Figure 5.74 ^{1}H COSY NMR (400 MHz, $CDCl_3$) of compound **5.17E.**

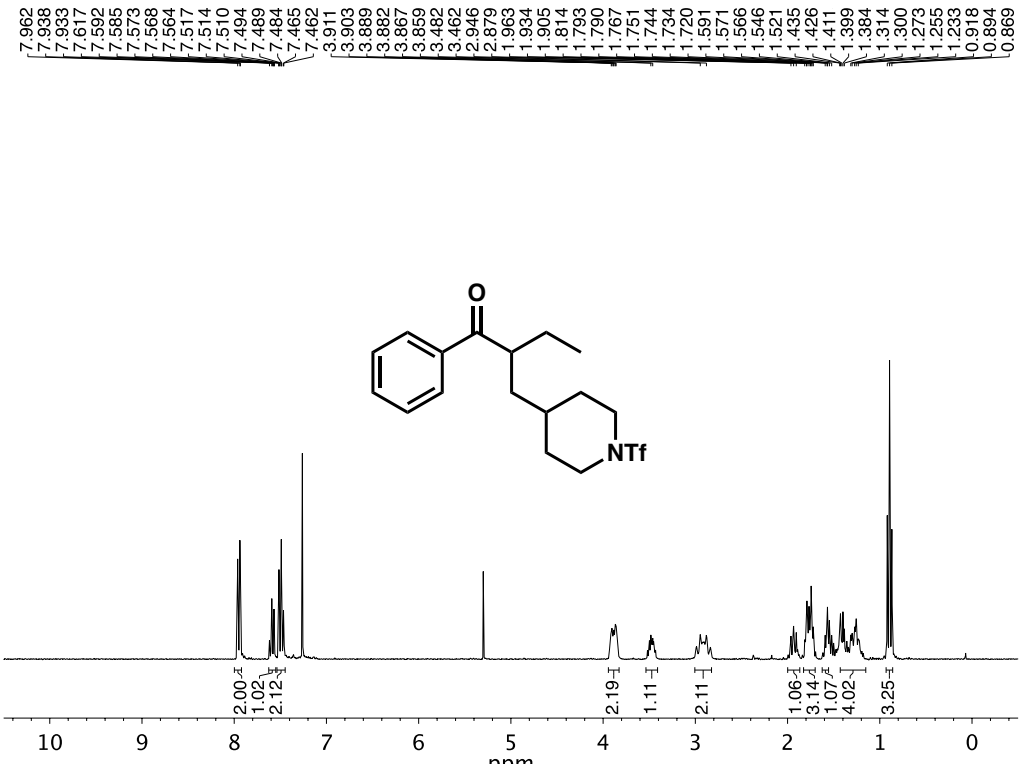


Figure 5.75 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.18A.**

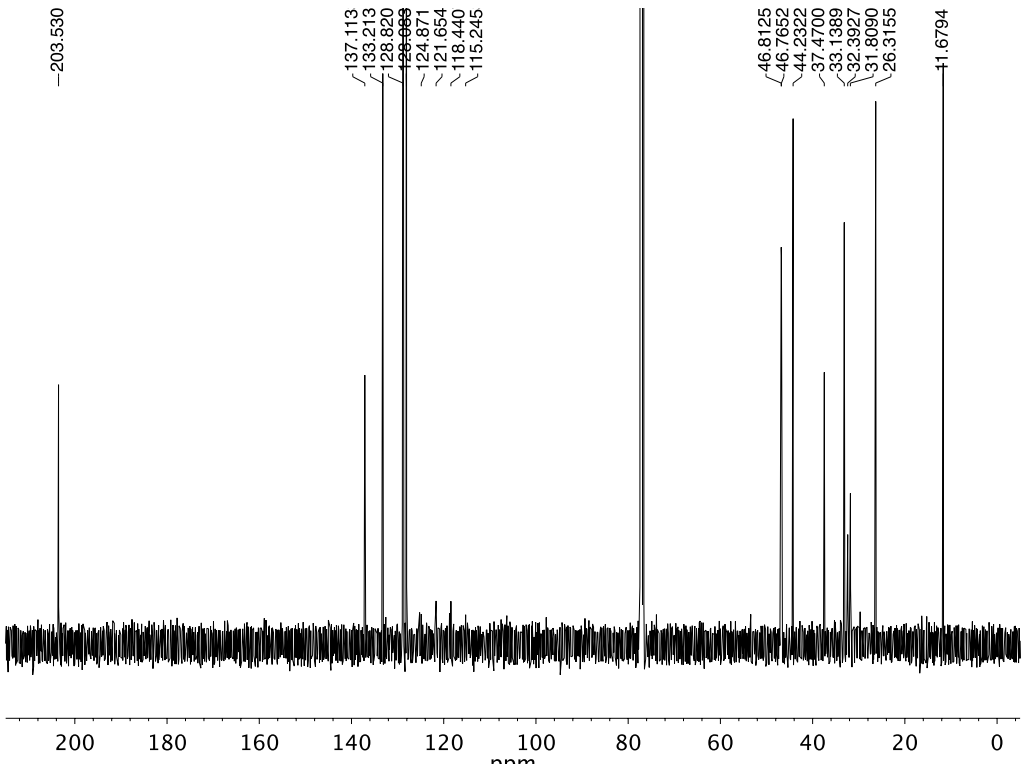


Figure 5.76 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.18A.**

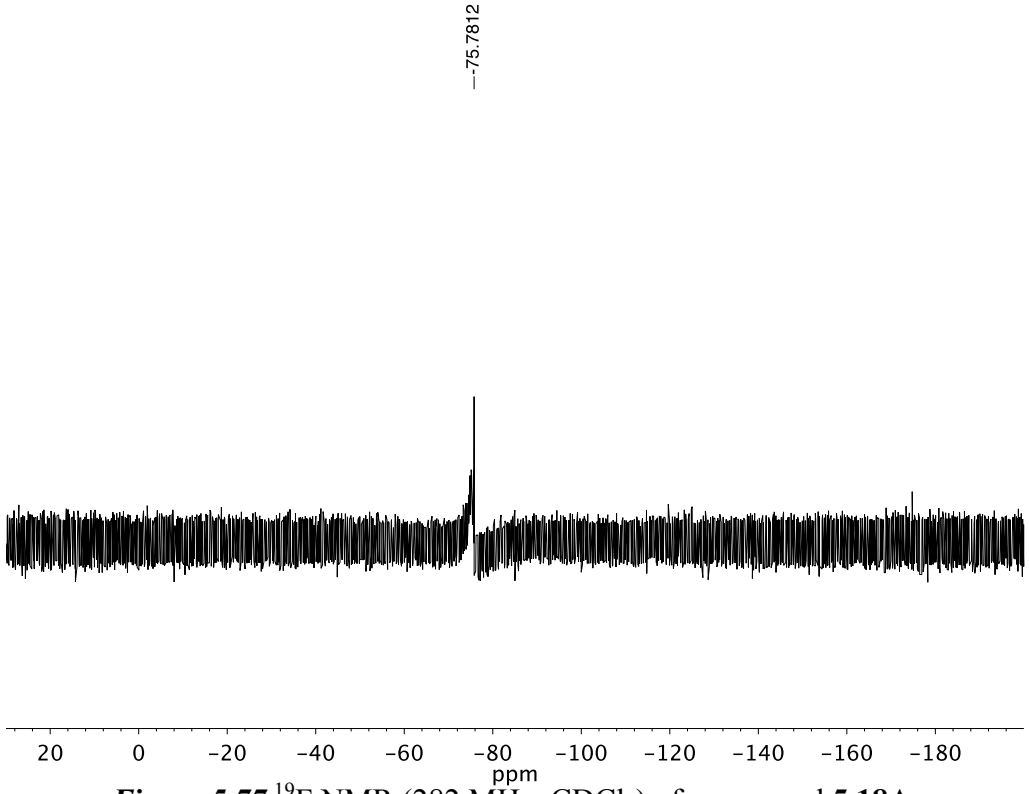


Figure 5.77 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.18A.**

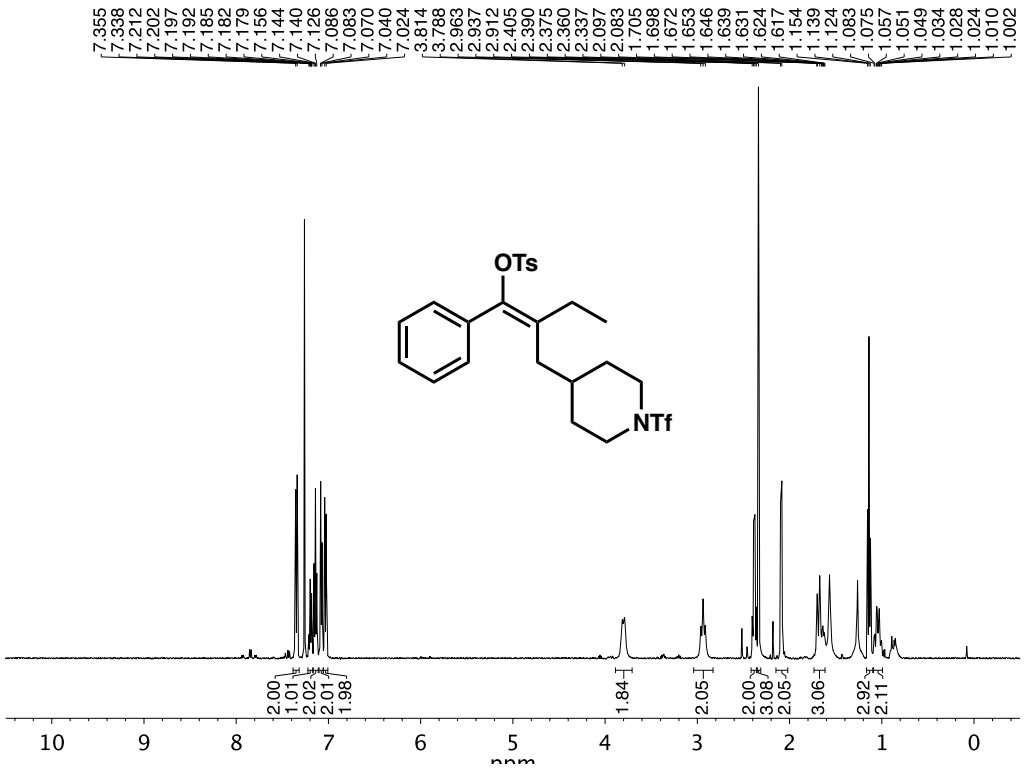


Figure 5.78 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.18B** as a single isomer.

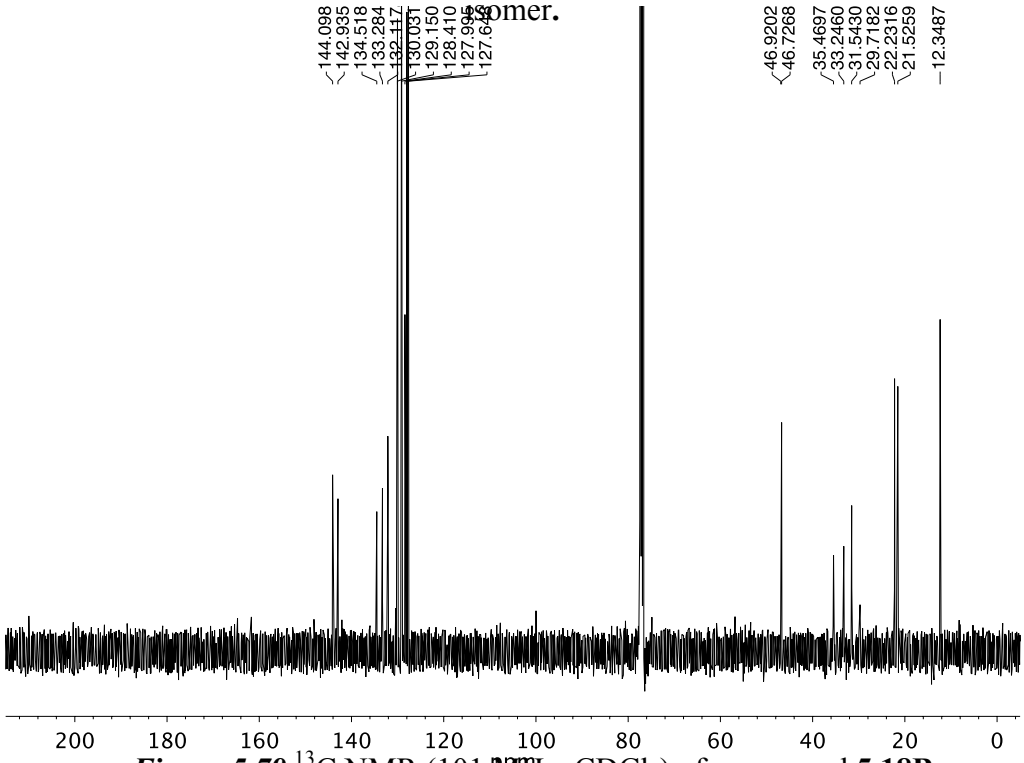


Figure 5.79 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.18B.**

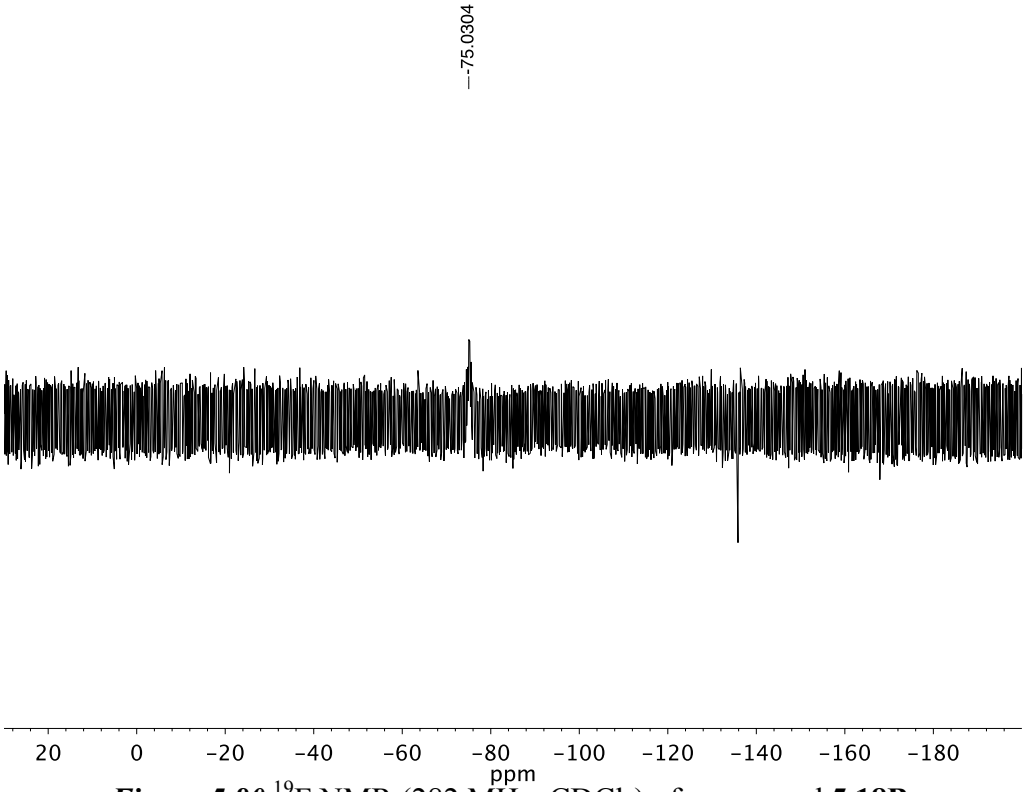


Figure 5.80 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.18B.**

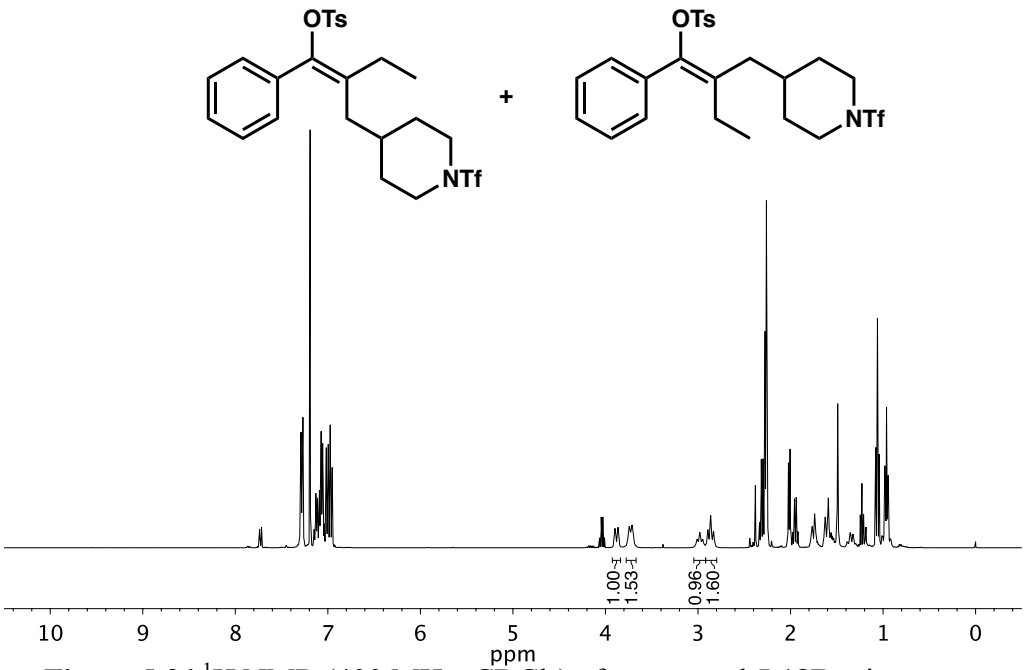


Figure 5.81 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **5.18B** mixture indicating ~1:1.5 ratio.

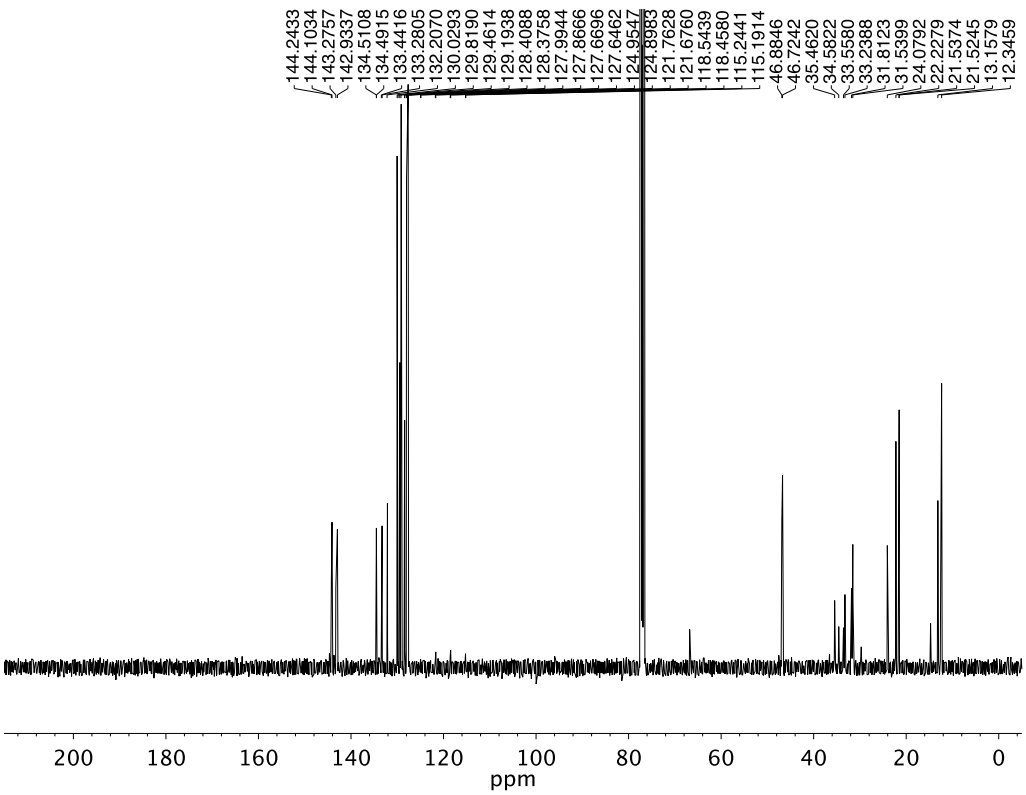


Figure 5.82 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.18B** mixture.

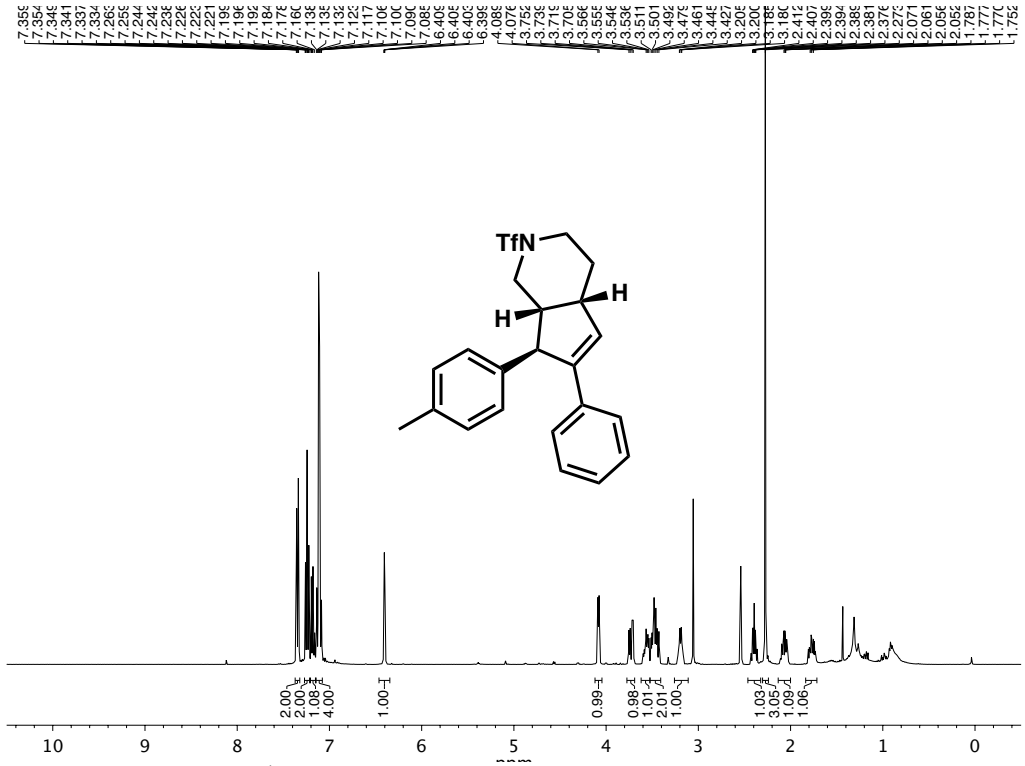


Figure 5.83 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.12.**

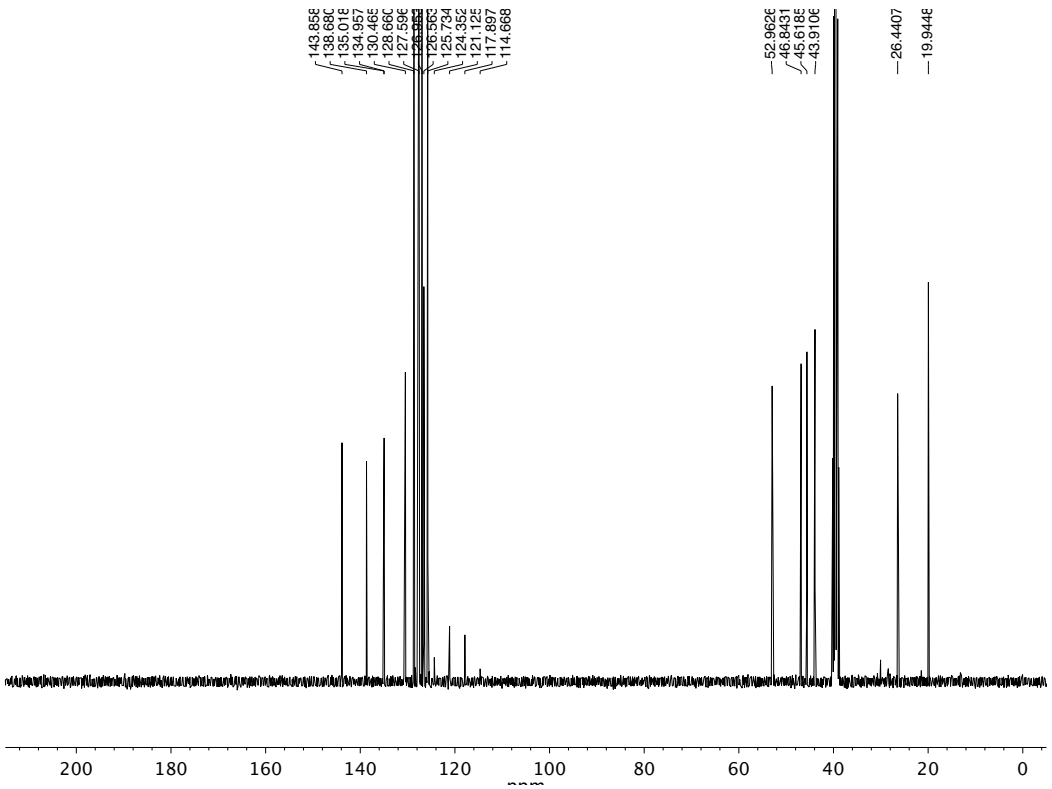


Figure 5.84 ^{13}C NMR (101 MHz, $(CD_3)_2SO$) of compound **5.12.**

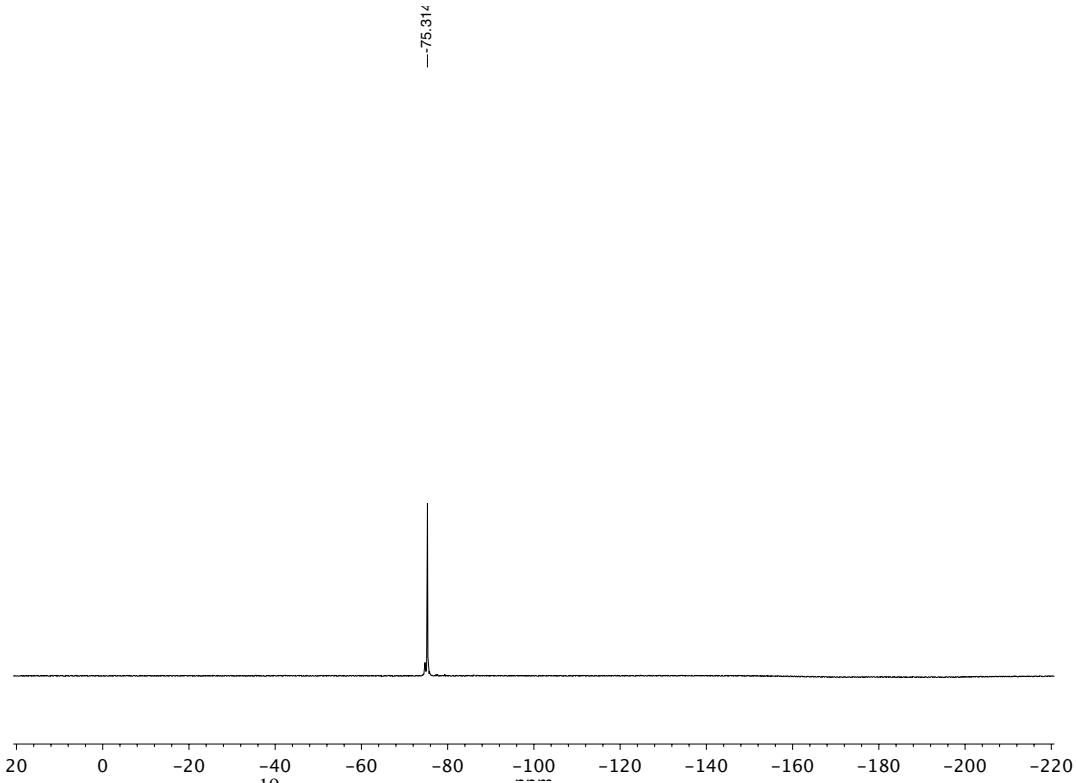


Figure 5.85 ^{19}F NMR (376 MHz, $(CD_3)_2SO$) of compound **5.12.**

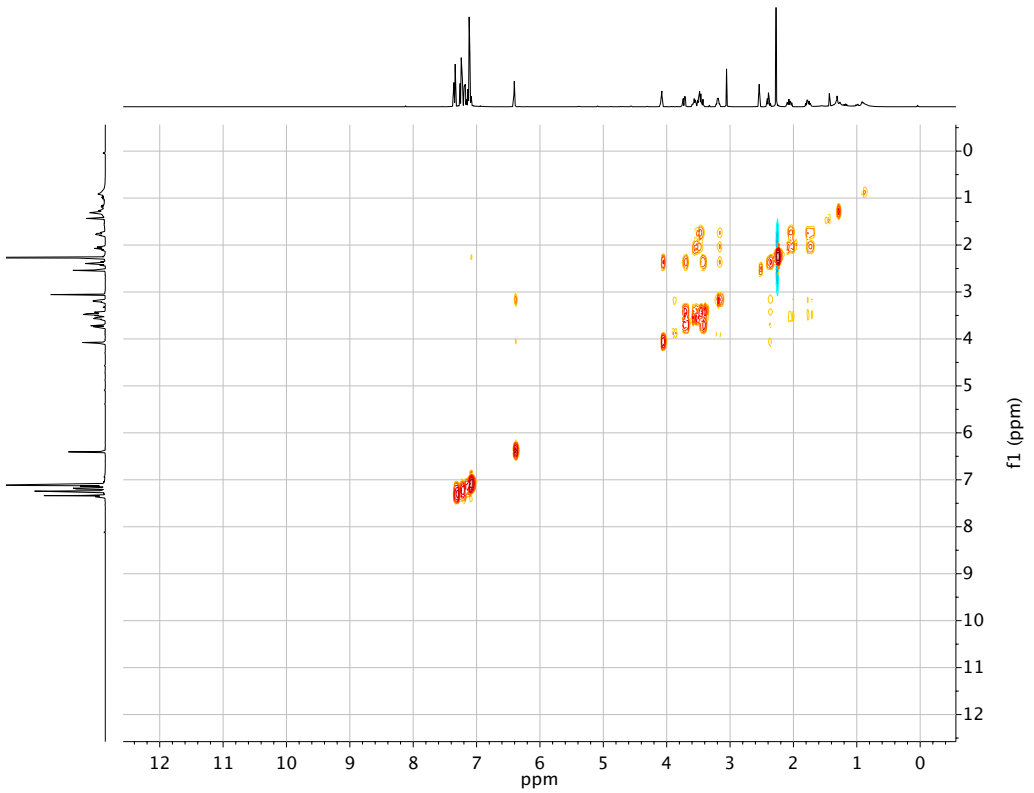


Figure 5.86 COSY NMR (400 MHz, $(CD_3)_2SO$) of compound **5.12.**

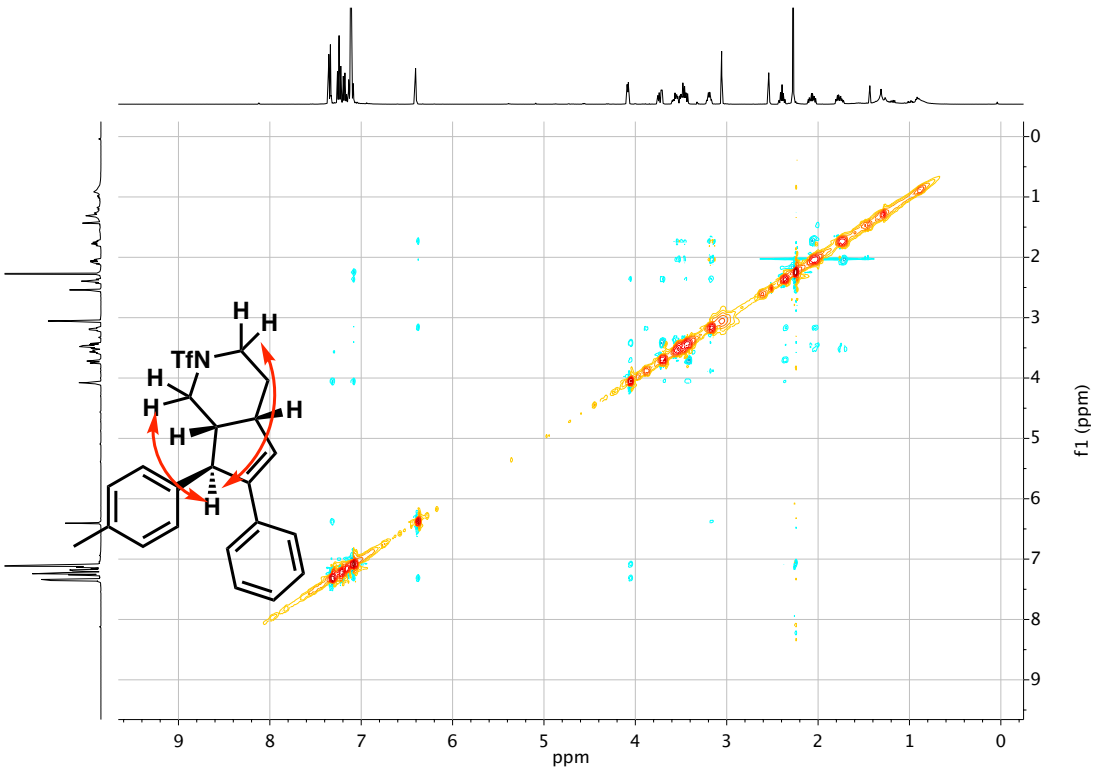


Figure 5.87 NOE ^1H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.12.**

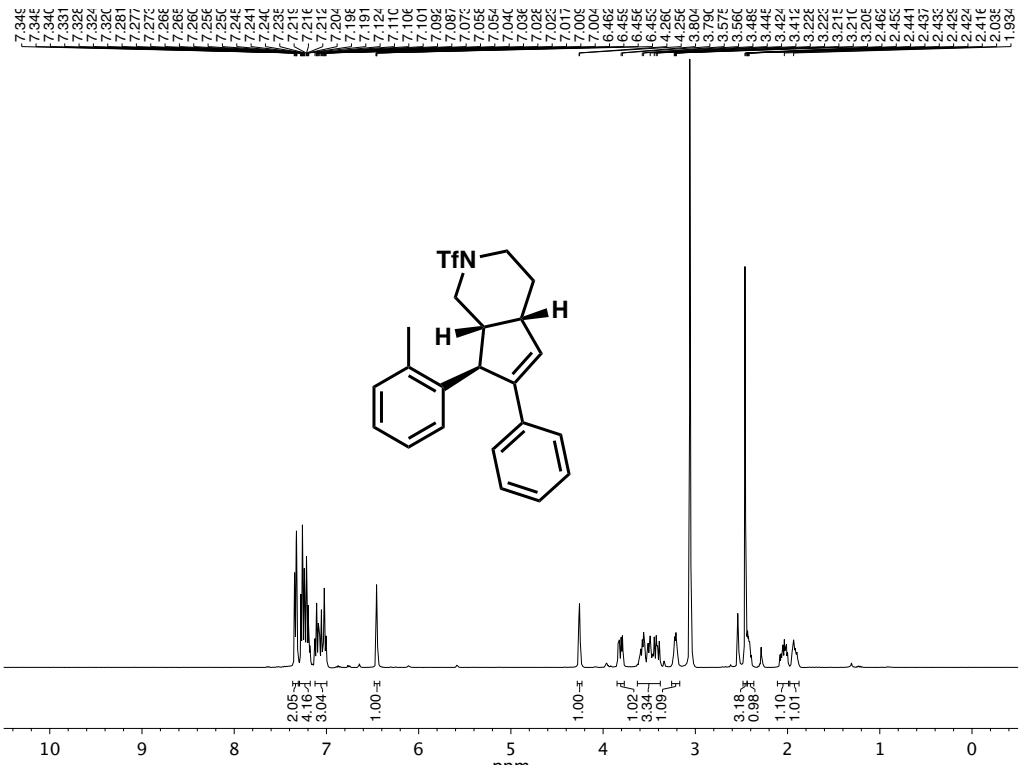


Figure 5.88 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.13.**

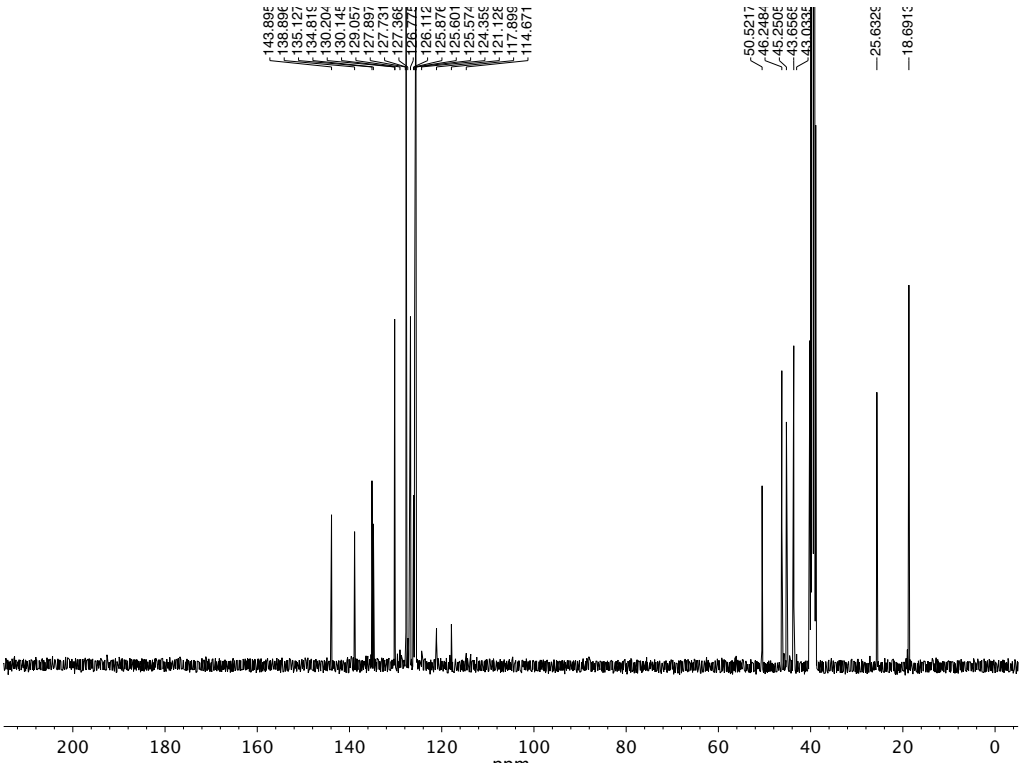


Figure 5.89 ^{13}C NMR (101 MHz, $(CD_3)_2SO$) of compound **5.13.**

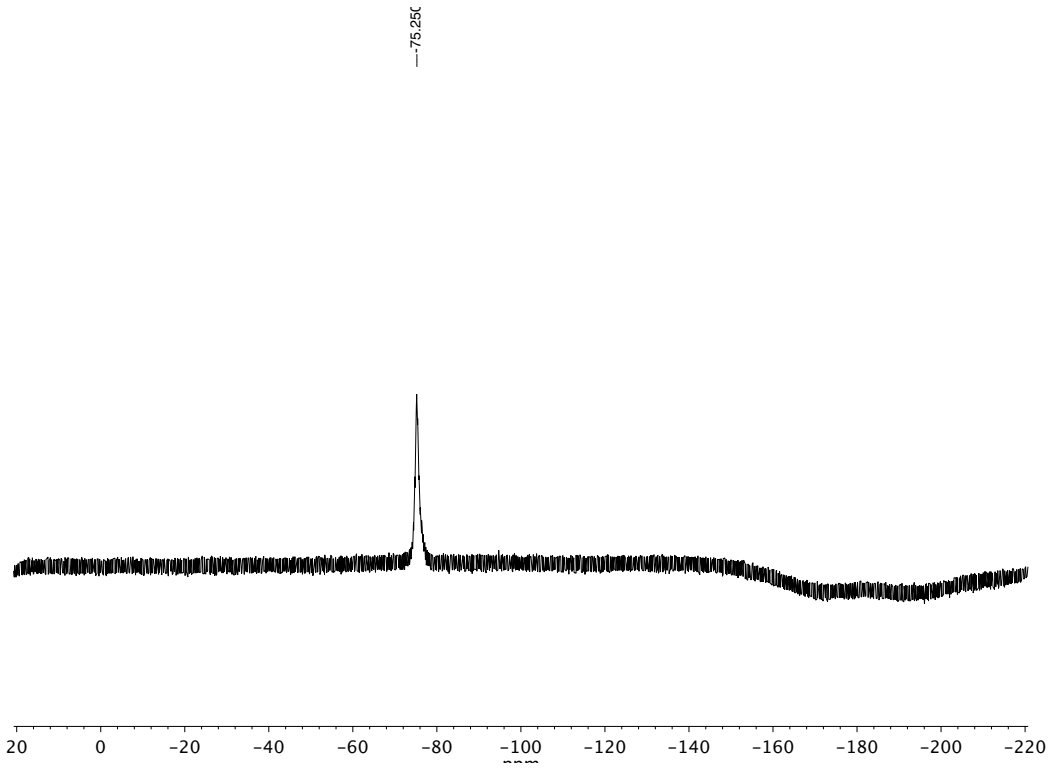


Figure 5.90 ^{19}F NMR (376 MHz, $(CD_3)_2SO$) of compound **5.13.**

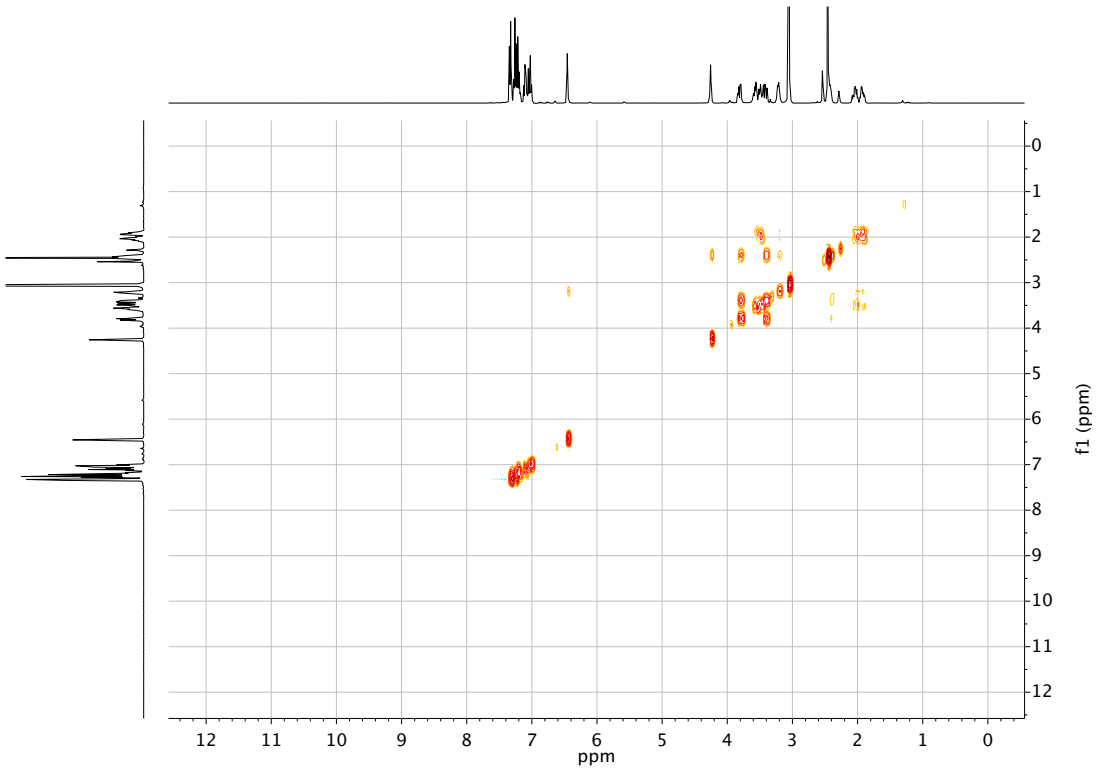


Figure 5.91 COSY (400 MHz, $(CD_3)_2SO$) of compound **5.13.**

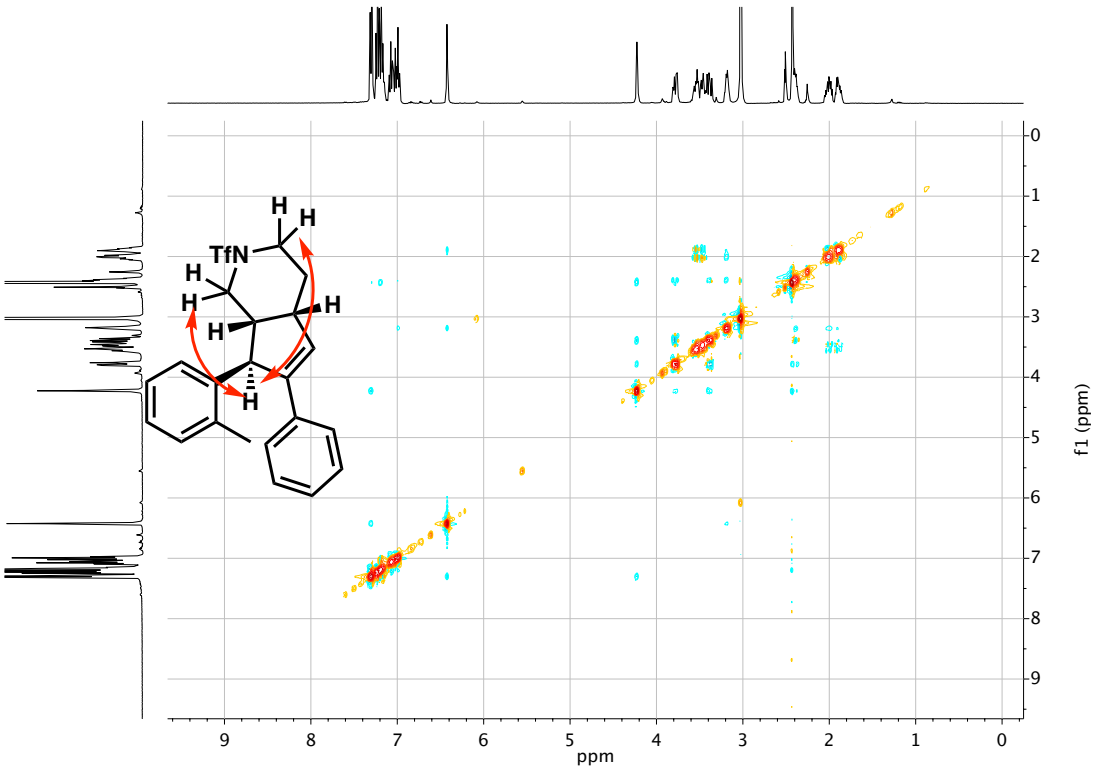


Figure 5.92 ^{1}H NOE NMR (400 MHz, $(CD_3)_2SO$) of compound **5.13.**

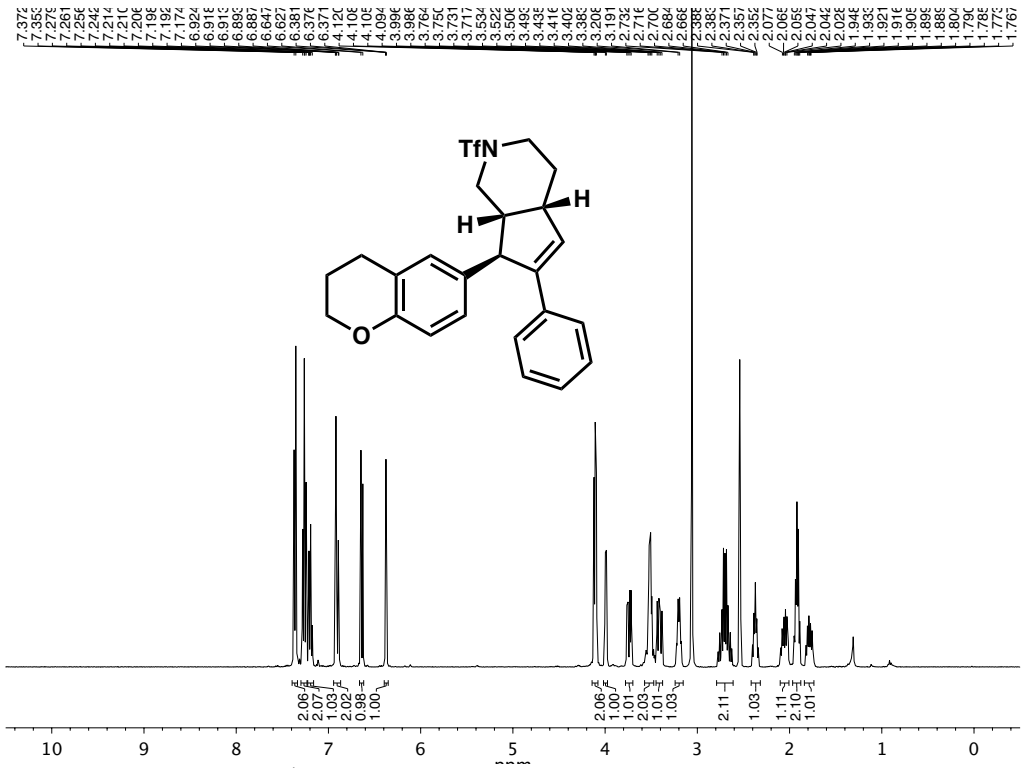


Figure 5.93 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.14.**

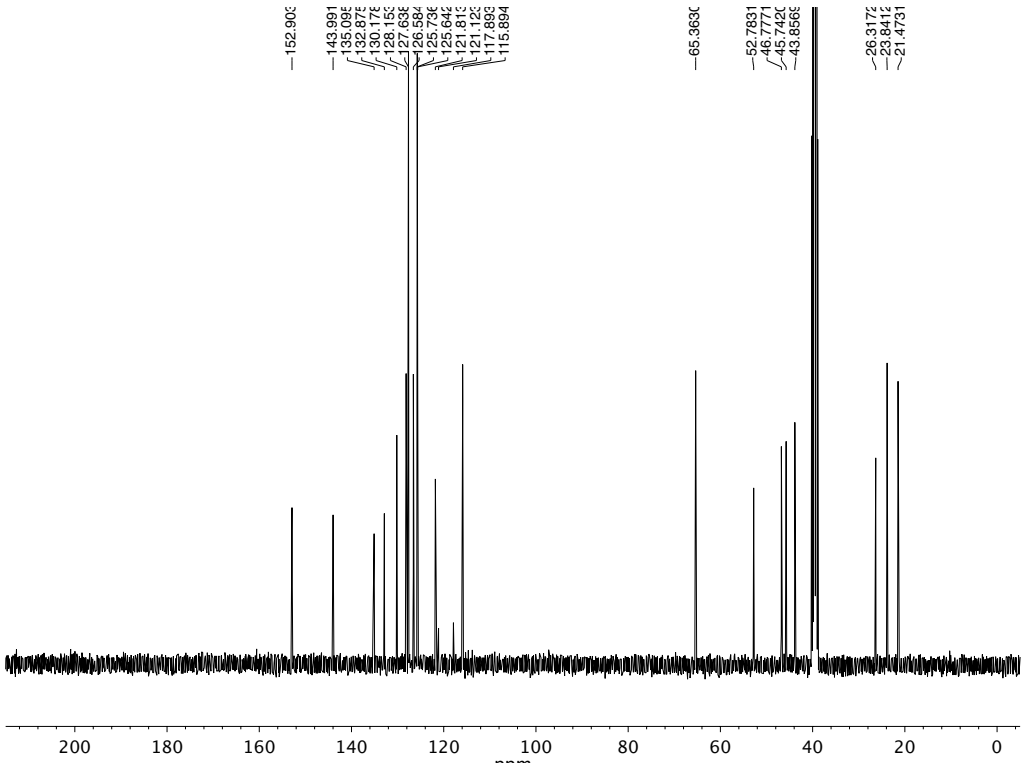


Figure 5.94 ^{13}C NMR (101 MHz, $(CD_3)_2SO$) of compound **5.14.**

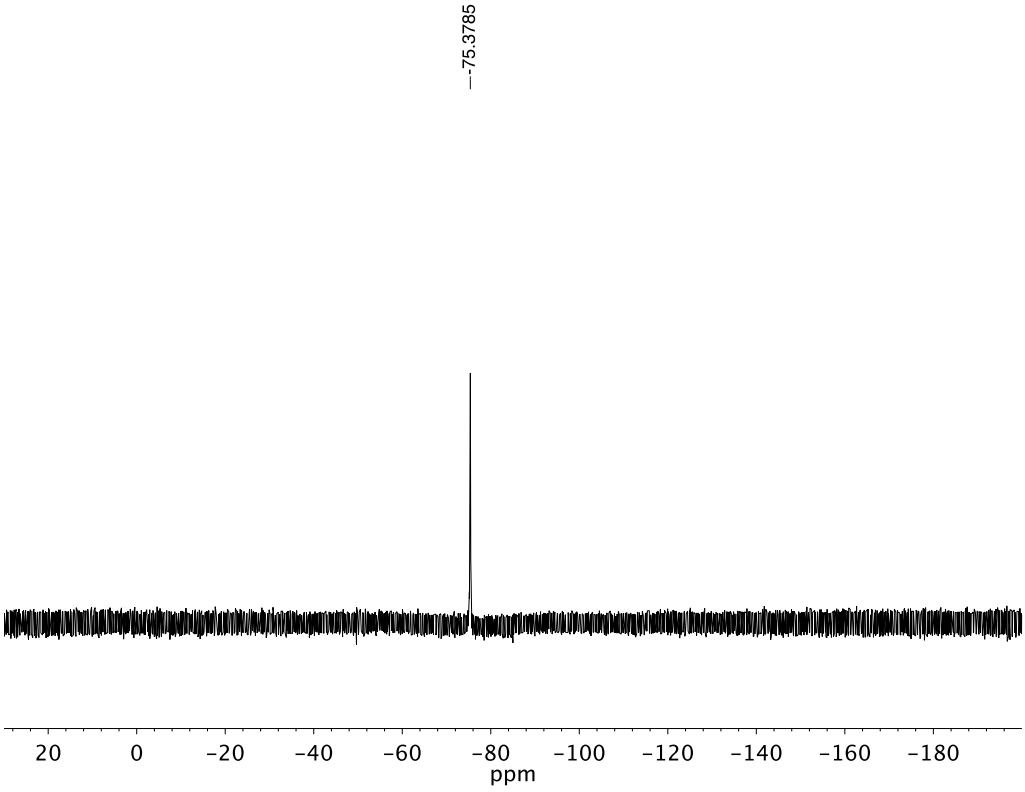


Figure 5.95 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.14.**

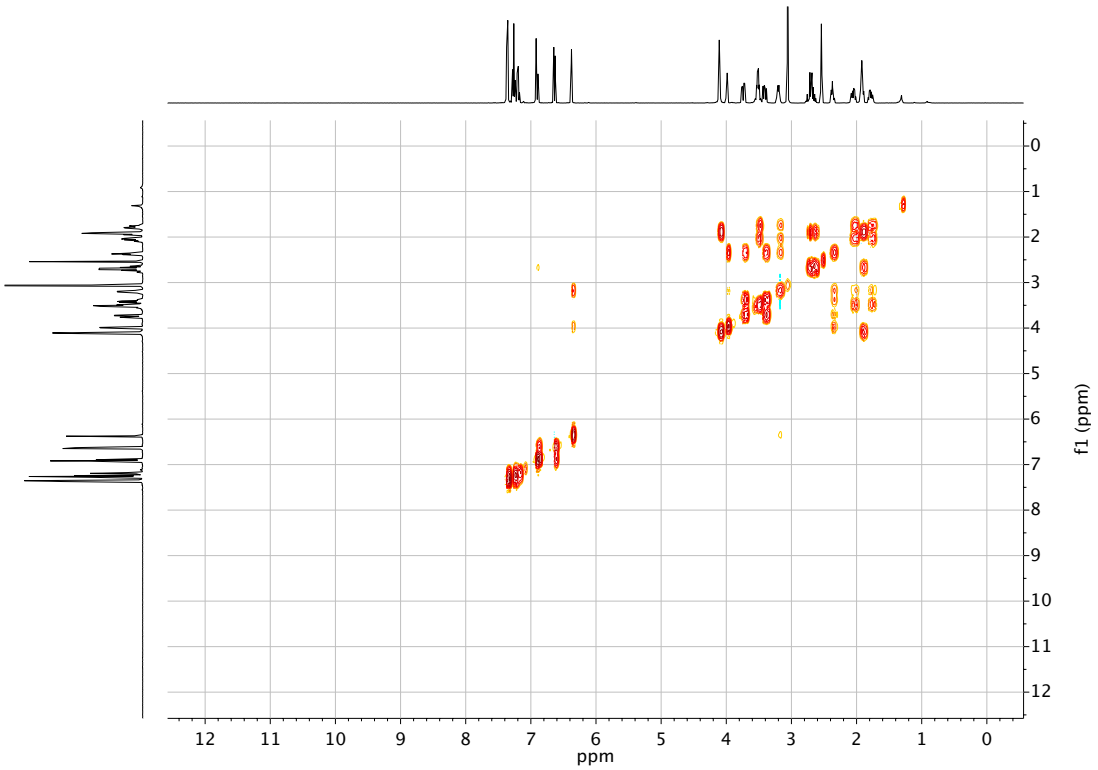


Figure 5.96 COSY NMR (400 MHz, $(CD_3)_2SO$) of compound **5.14.**

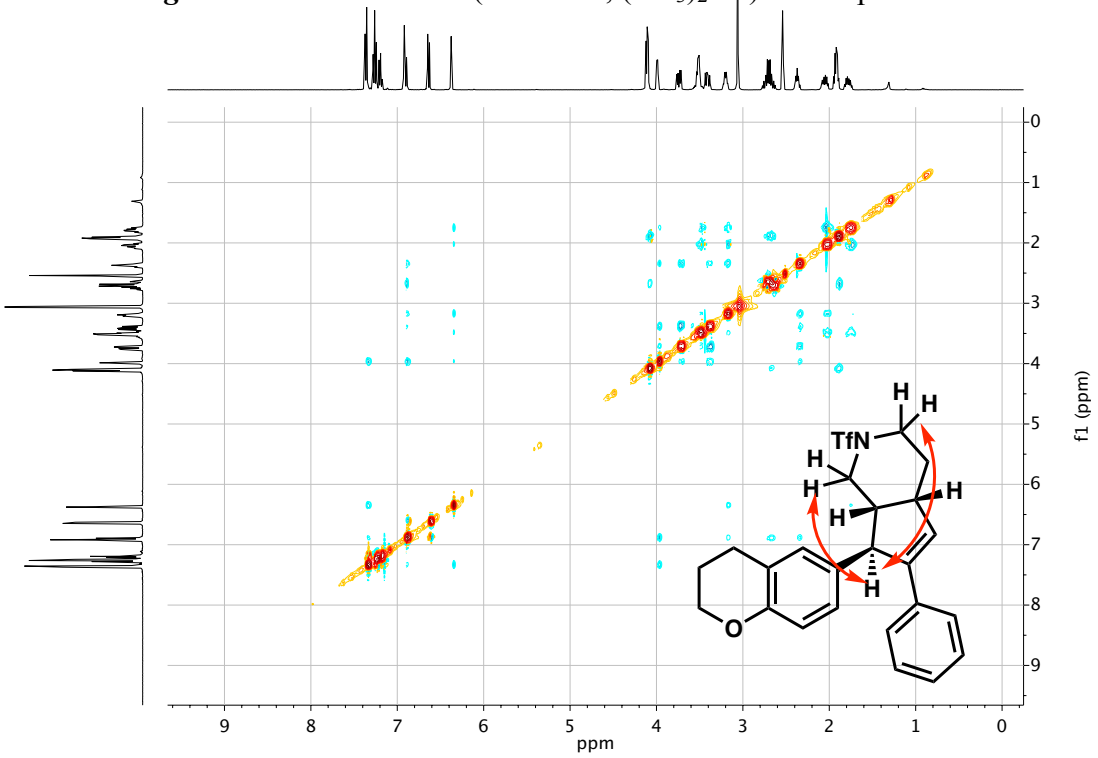


Figure 5.97 ^{1}H NOE NMR (400 MHz, $(CD_3)_2SO$) of compound **5.14.**

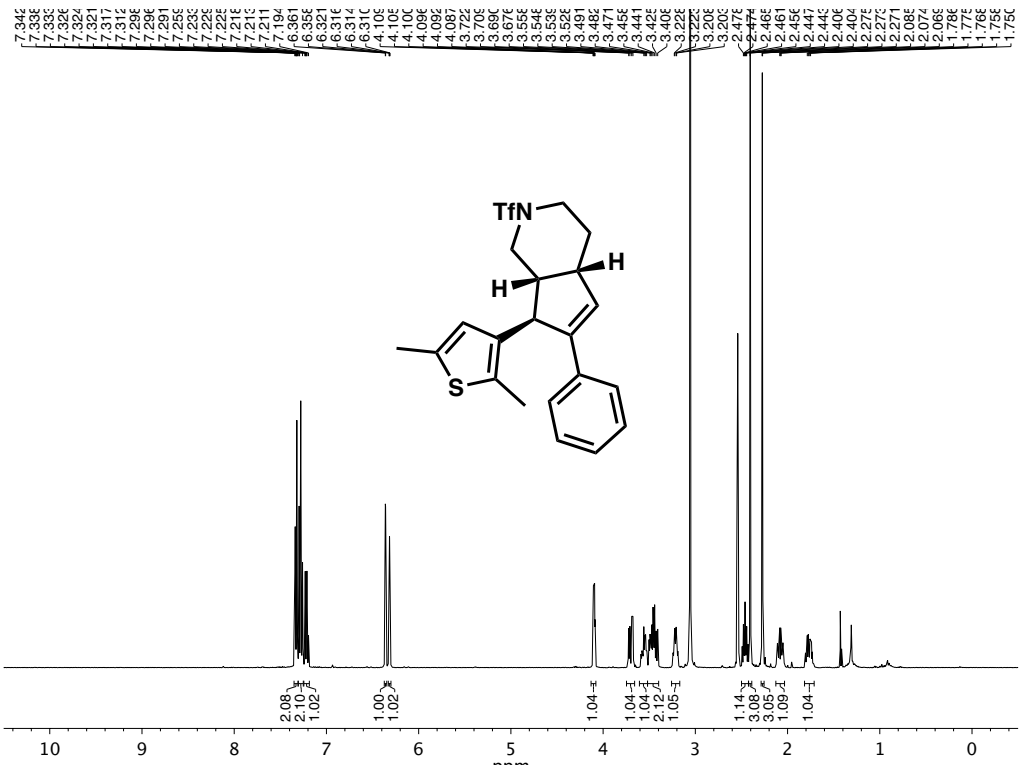


Figure 5.98 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.15.**

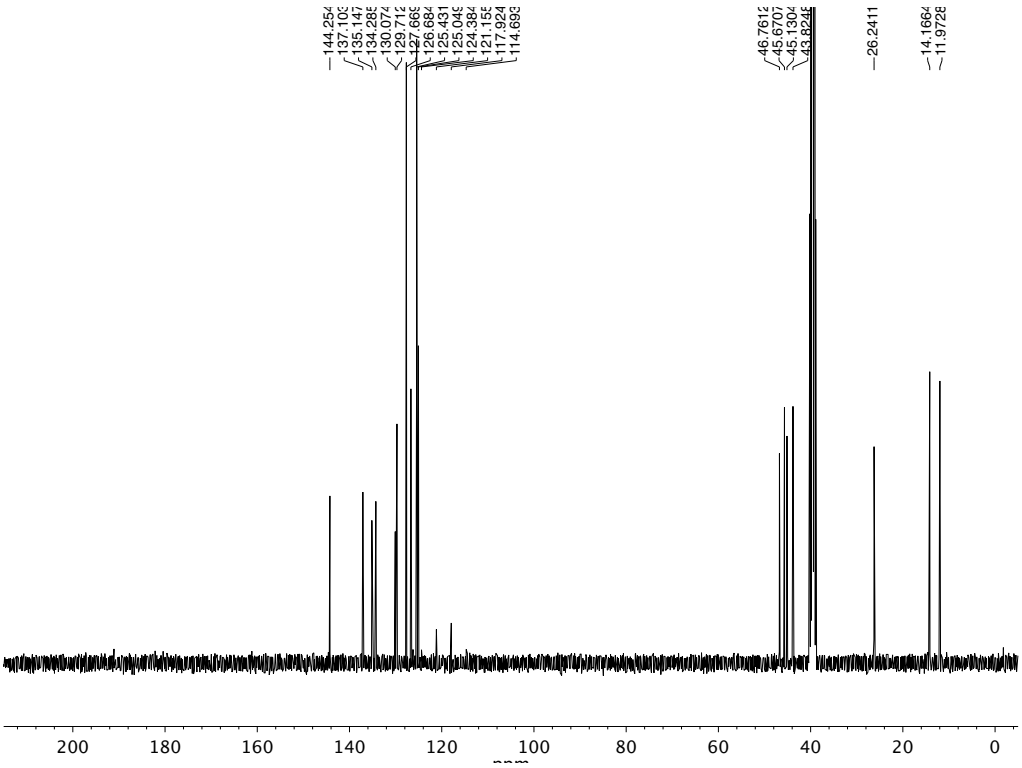


Figure 5.99 ^{13}C NMR (101 MHz, $(CD_3)_2SO$) of compound **5.15.**

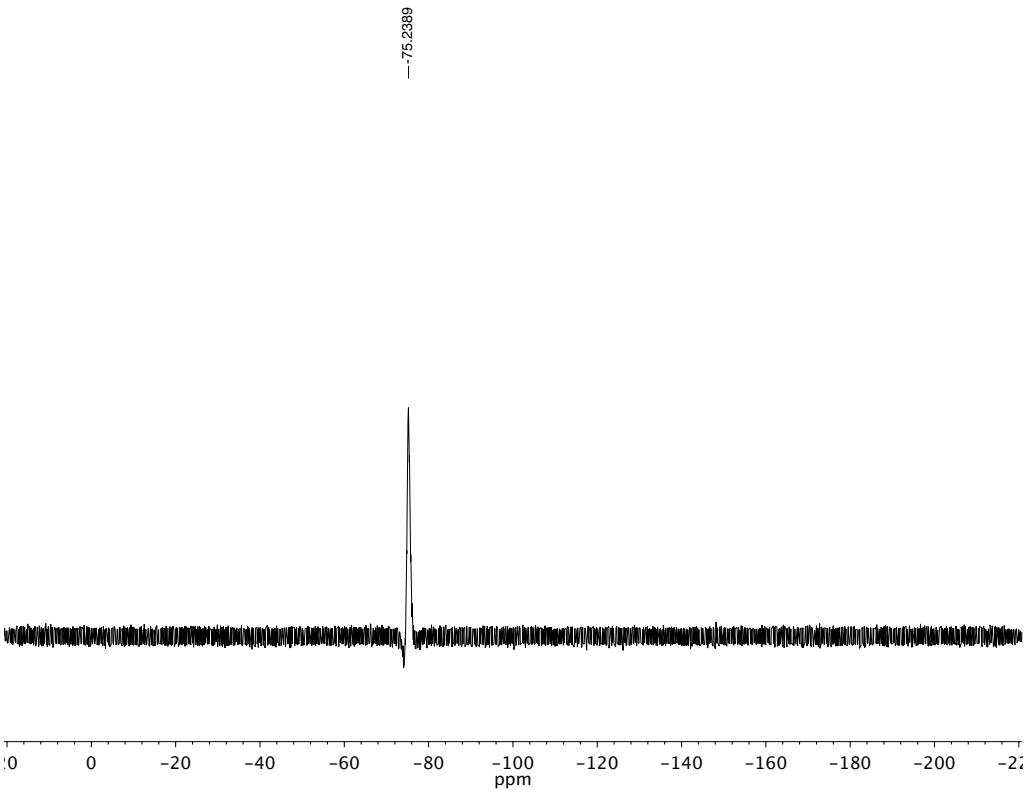


Figure 5.100 ^{19}F NMR (376 MHz, ($CDCl_3$) of compound **5.15.**

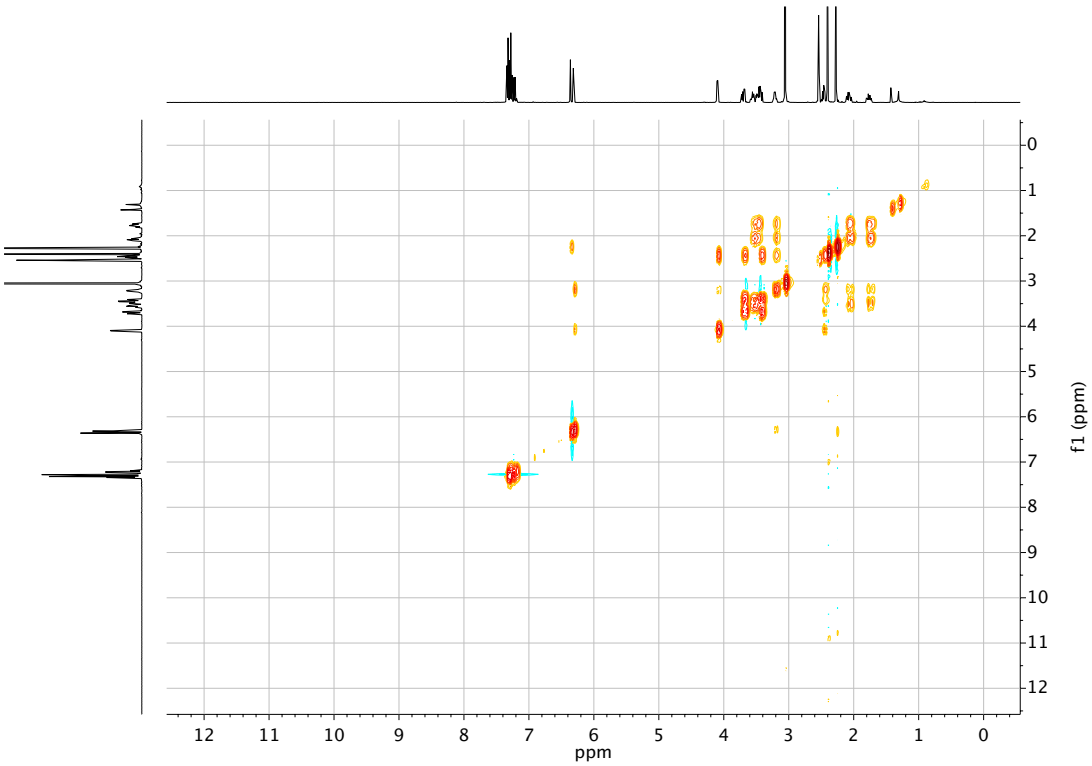


Figure 5.101 COSY NMR (400 MHz, $(CD_3)_2SO$) of compound **5.15.**

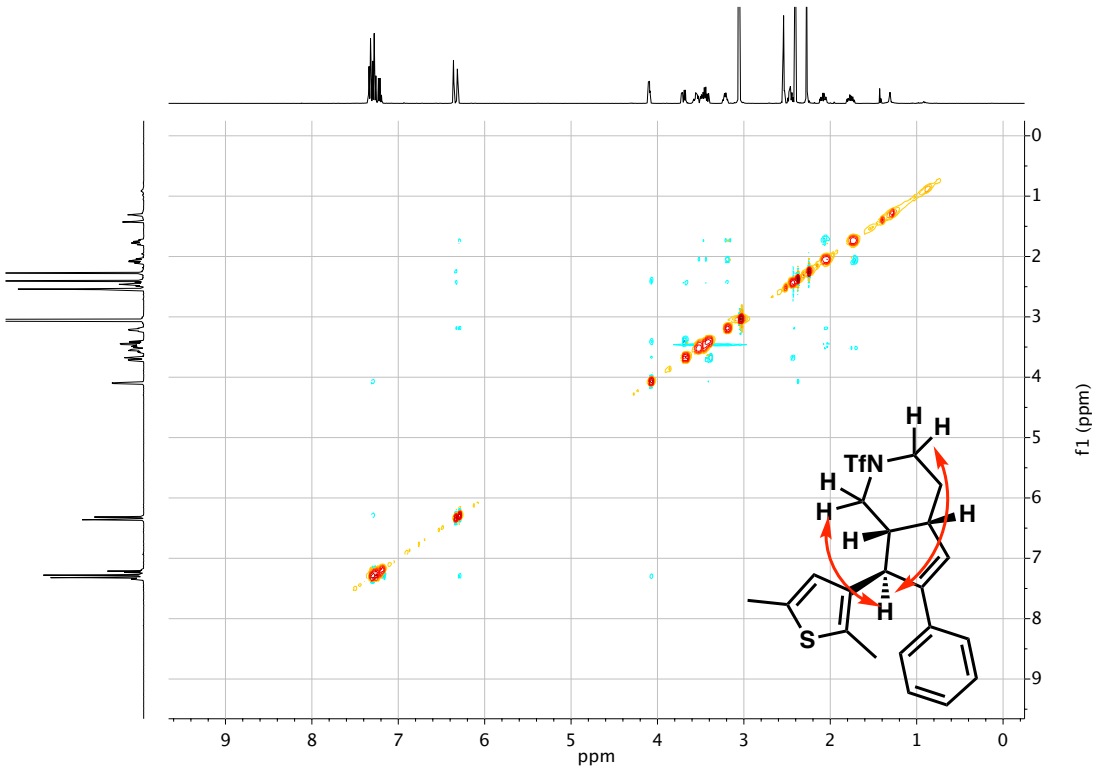


Figure 5.102 ^{1}H NOE NMR (400 MHz, $(CD_3)_2SO$) of compound **5.15.**

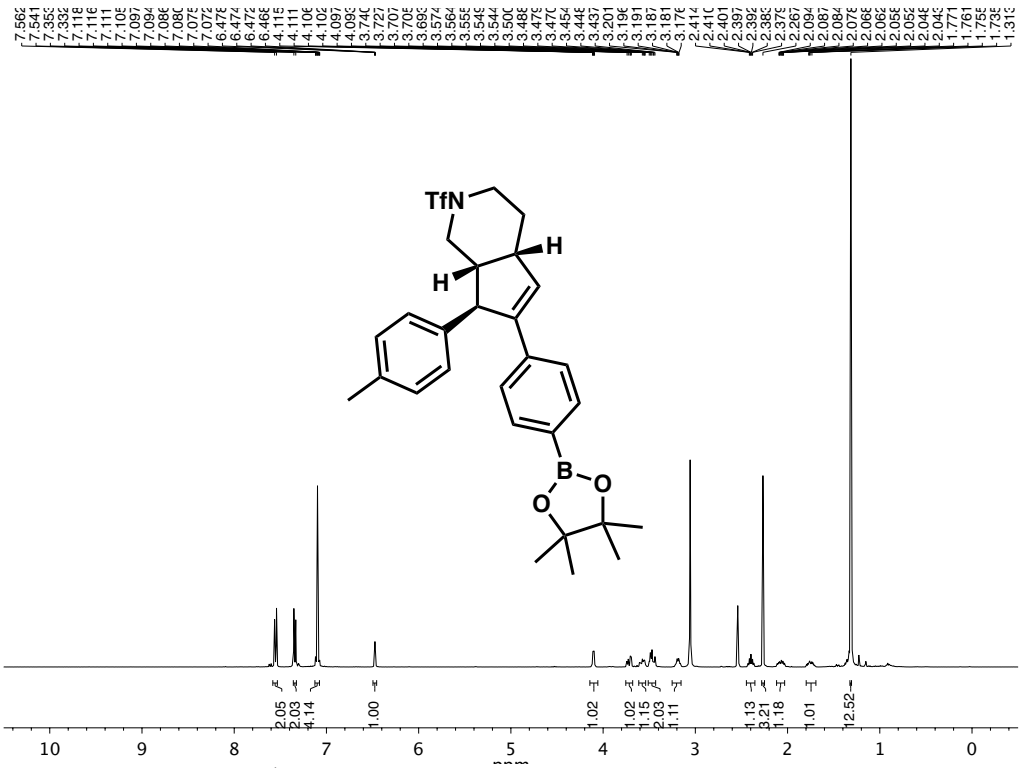


Figure 5.103 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.16.**

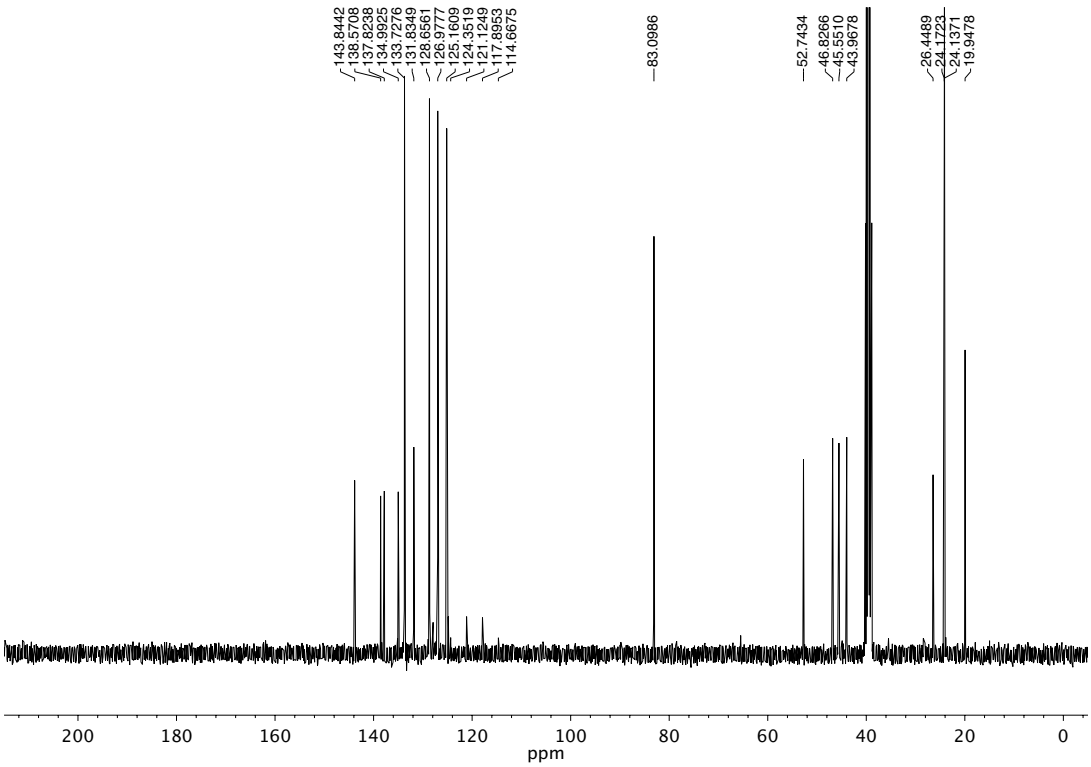


Figure 5.104 ^{13}C NMR (101 MHz, $(CD_3)_2SO$) of compound **5.16.**

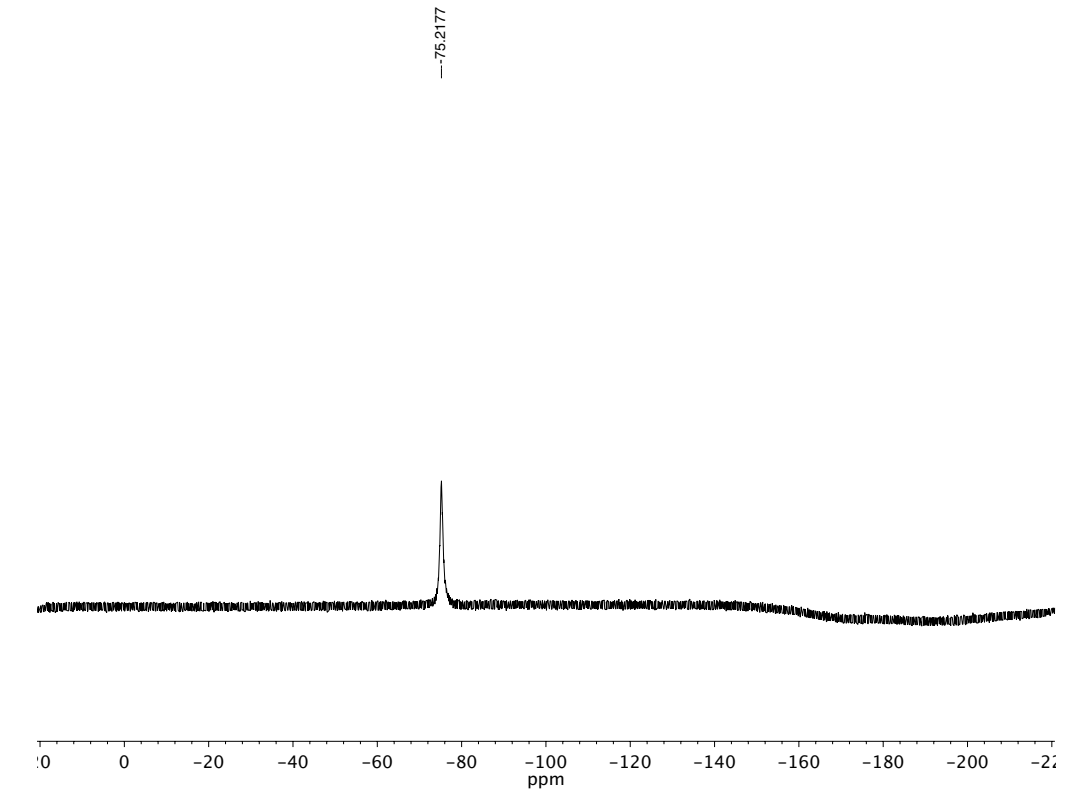


Figure 5.105 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.16.**

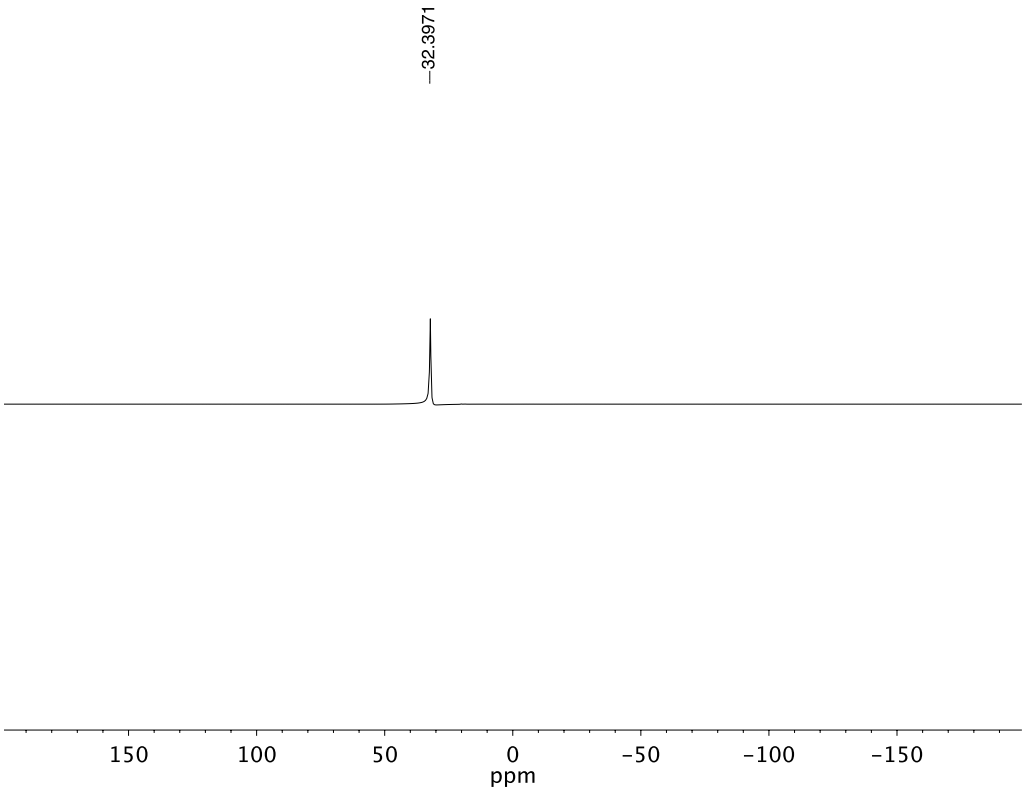


Figure 5.106 ^{11}B NMR (128 MHz, ($CDCl_3$) of compound **5.16.**

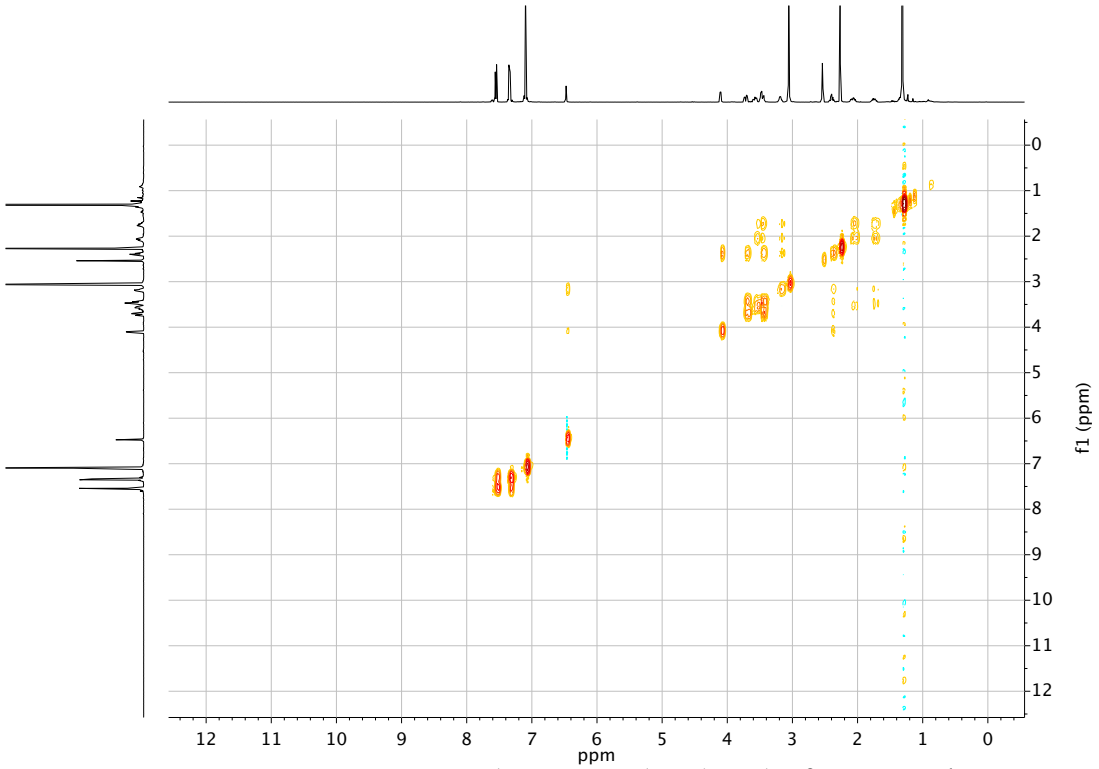


Figure 5.107 COSY NMR (400 MHz, $(CD_3)_2SO$) of compound **5.16.**

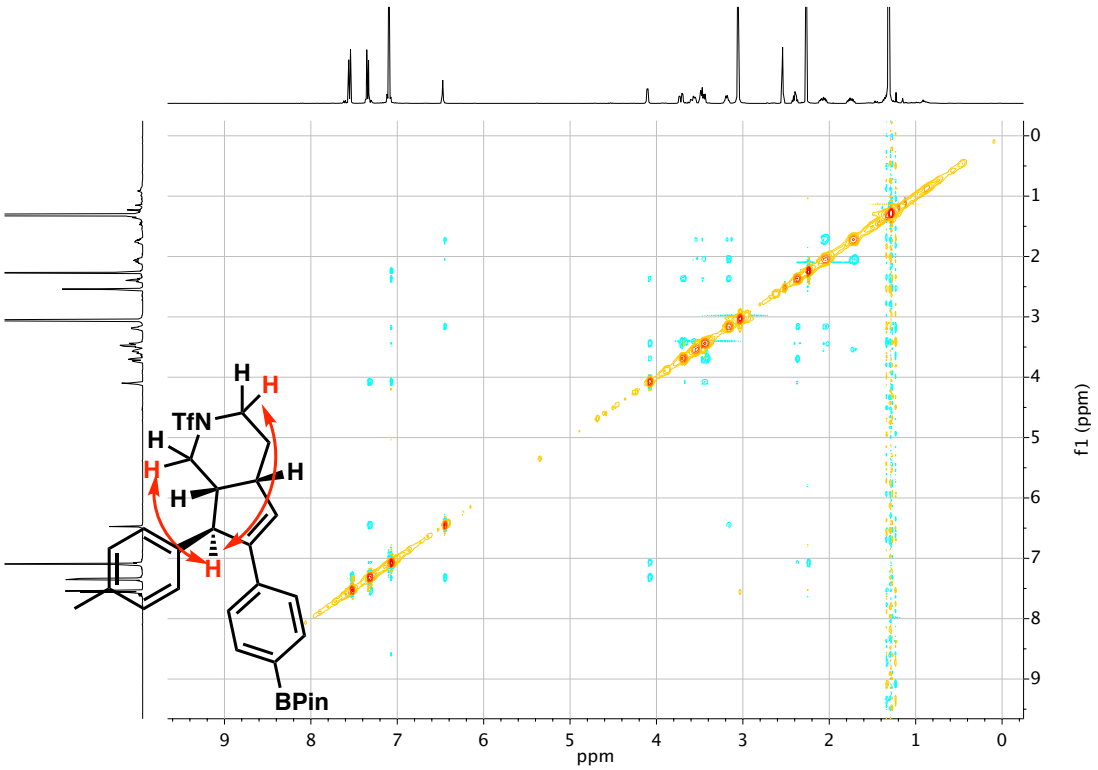


Figure 5.108 ^{1}H NOE NMR (400 MHz, $(CD_3)_2SO$) of compound **5.16.**

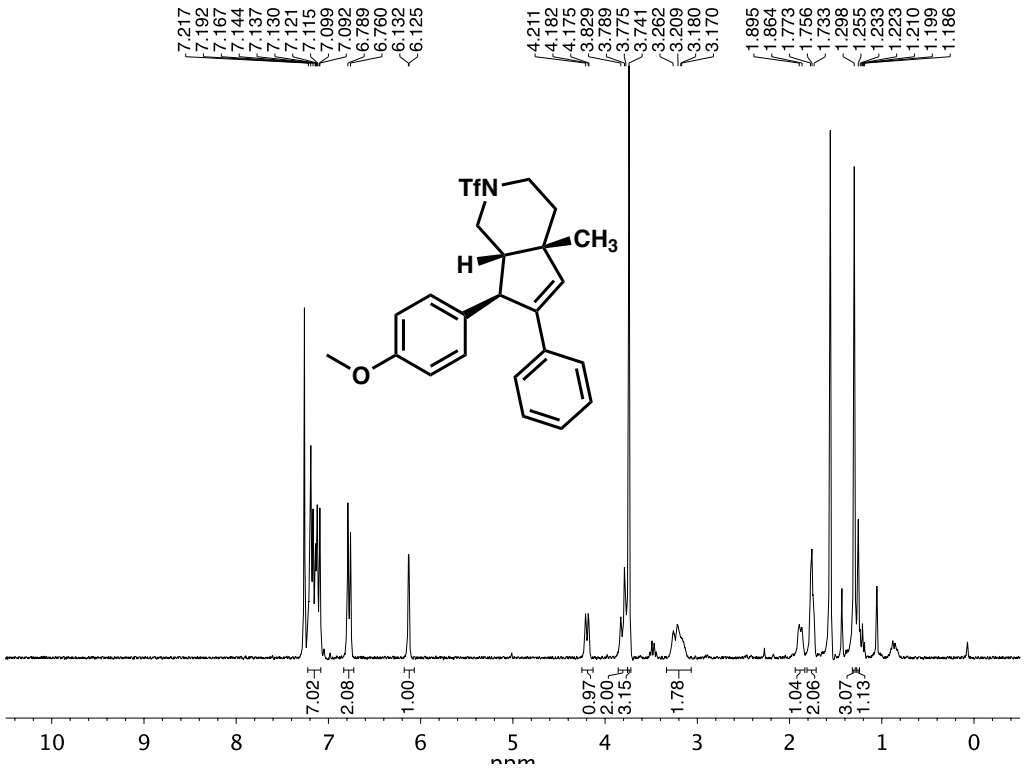


Figure 5.109 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5.17.**

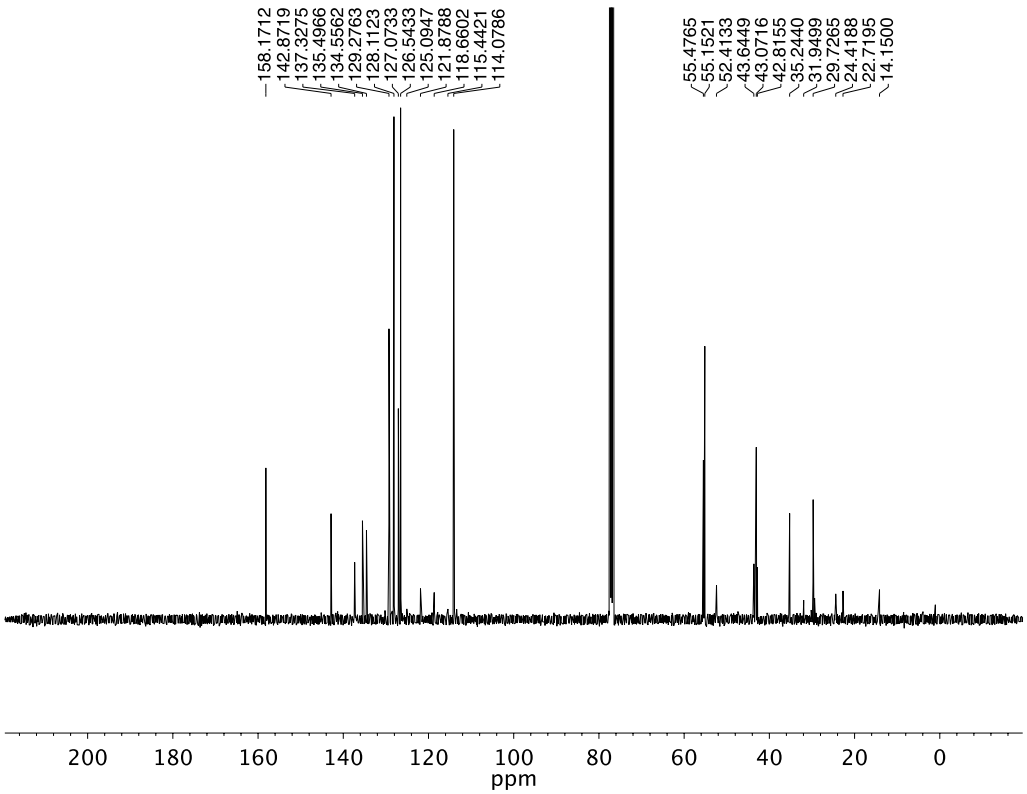


Figure 5.110 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **5.17.**

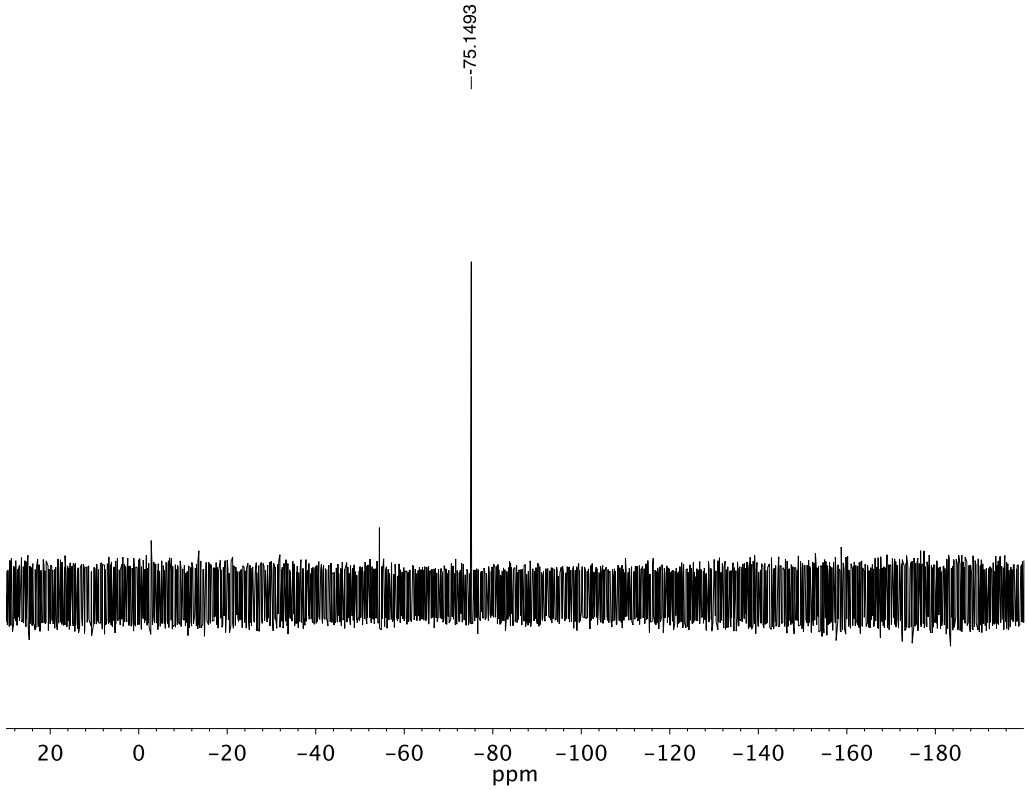


Figure 5.111 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.17.**

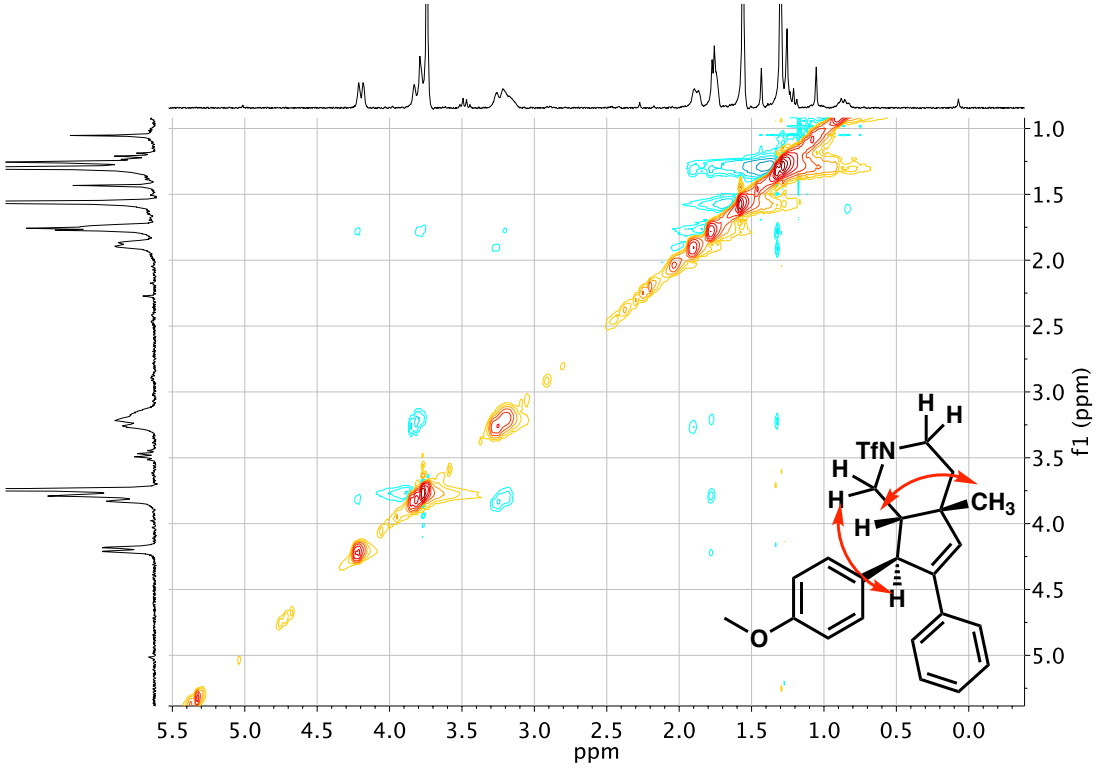


Figure 5.112 ^{1}H NOE NMR (400 MHz, $CDCl_3$) of compound **5.17.** (zoomed in)

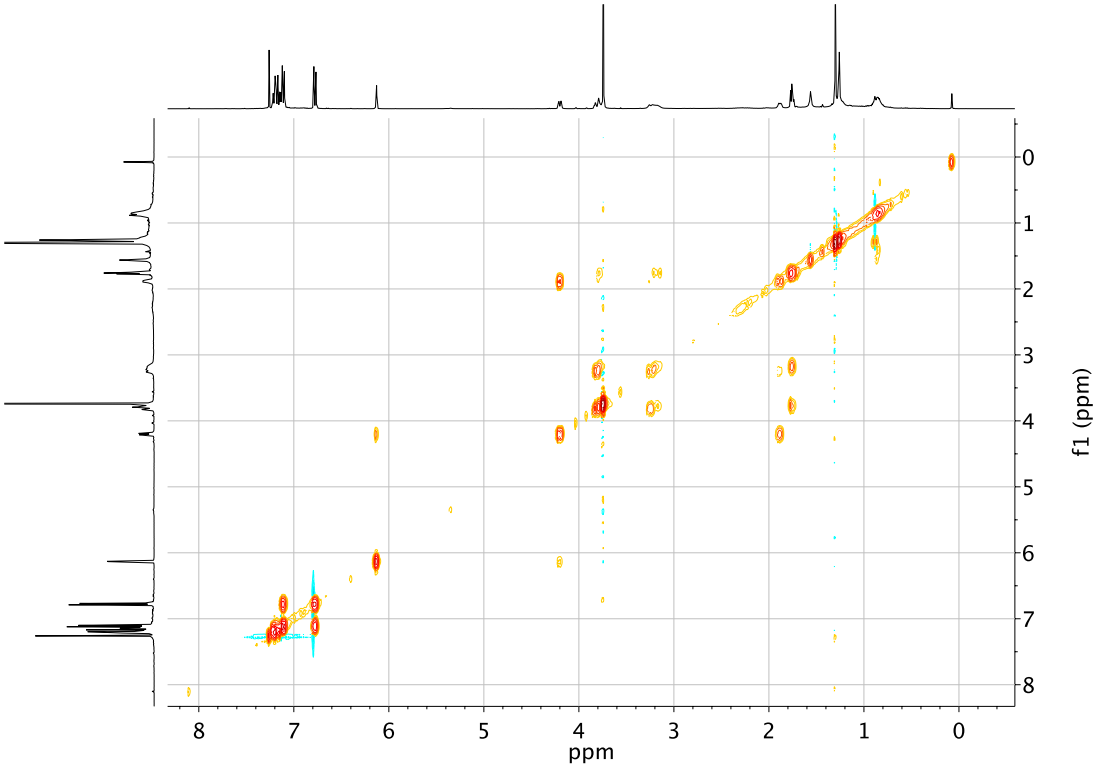


Figure 5.112 COSY NMR (400 MHz, $CDCl_3$) of compound **5.17.** (zoomed in)

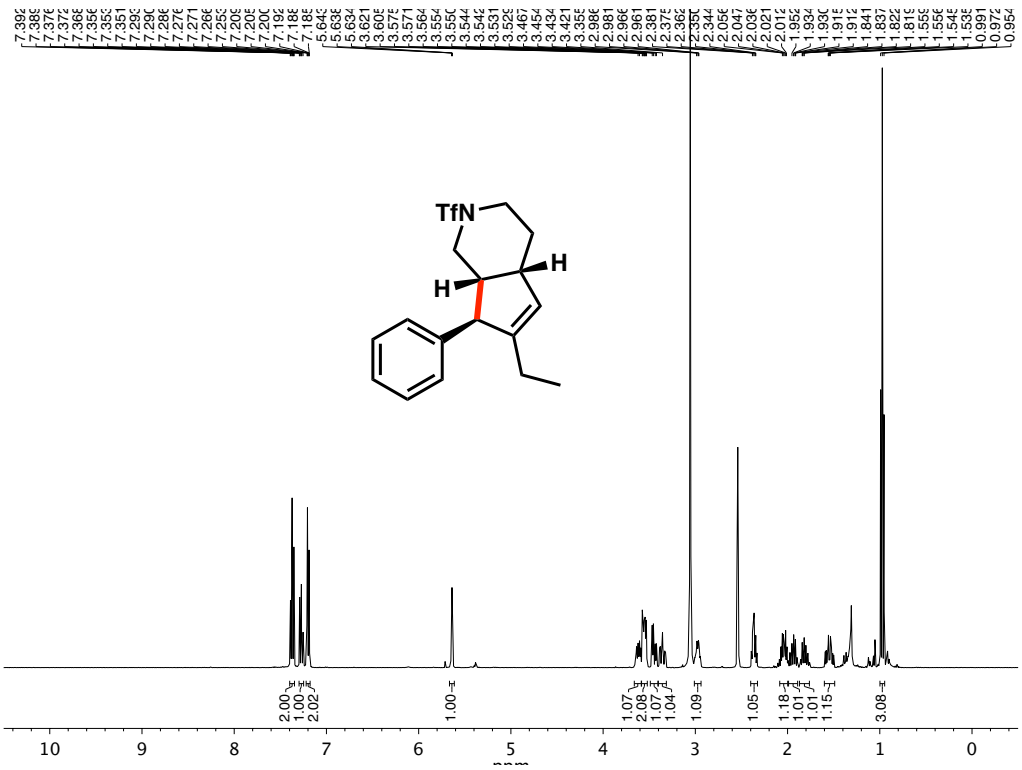


Figure 5.113 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **5.18.**

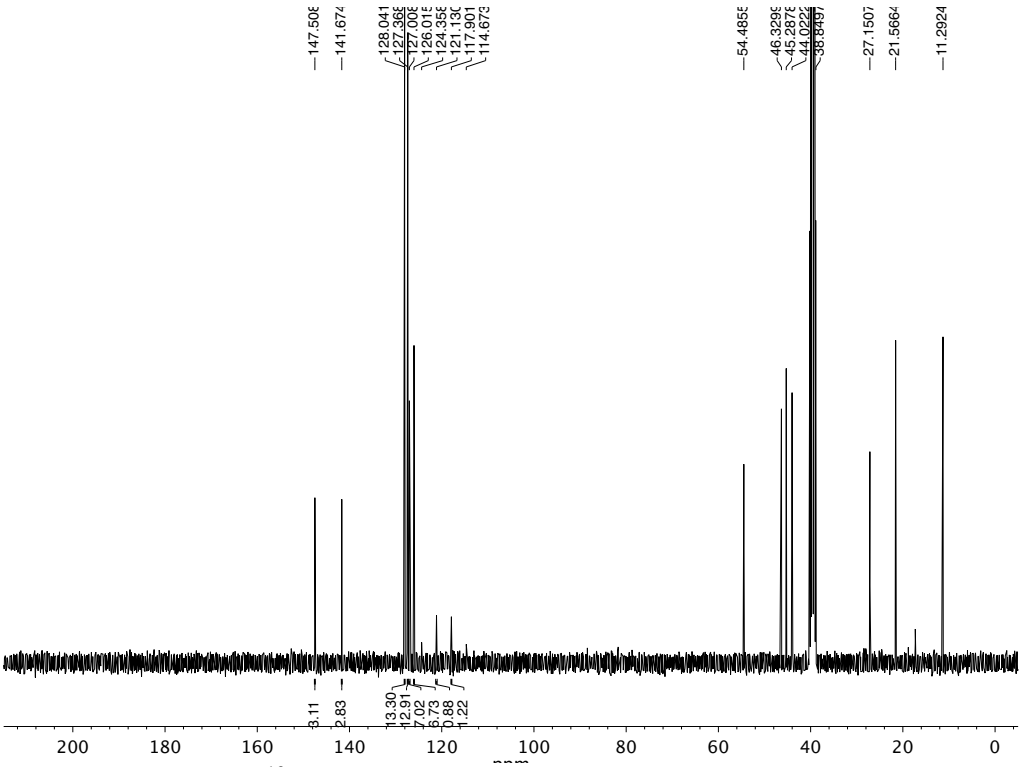


Figure 5.114 ^{13}C NMR (101 MHz, $(CD_3)_2SO$) of compound **5.18.**

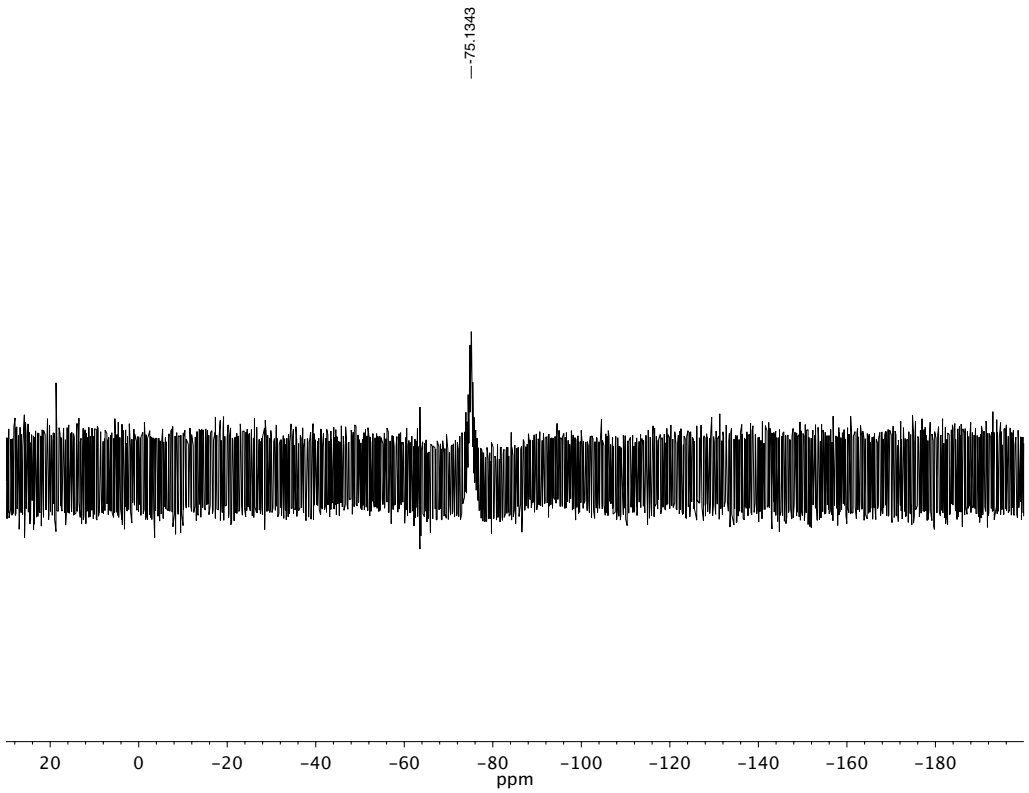


Figure 5.115 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.18.**

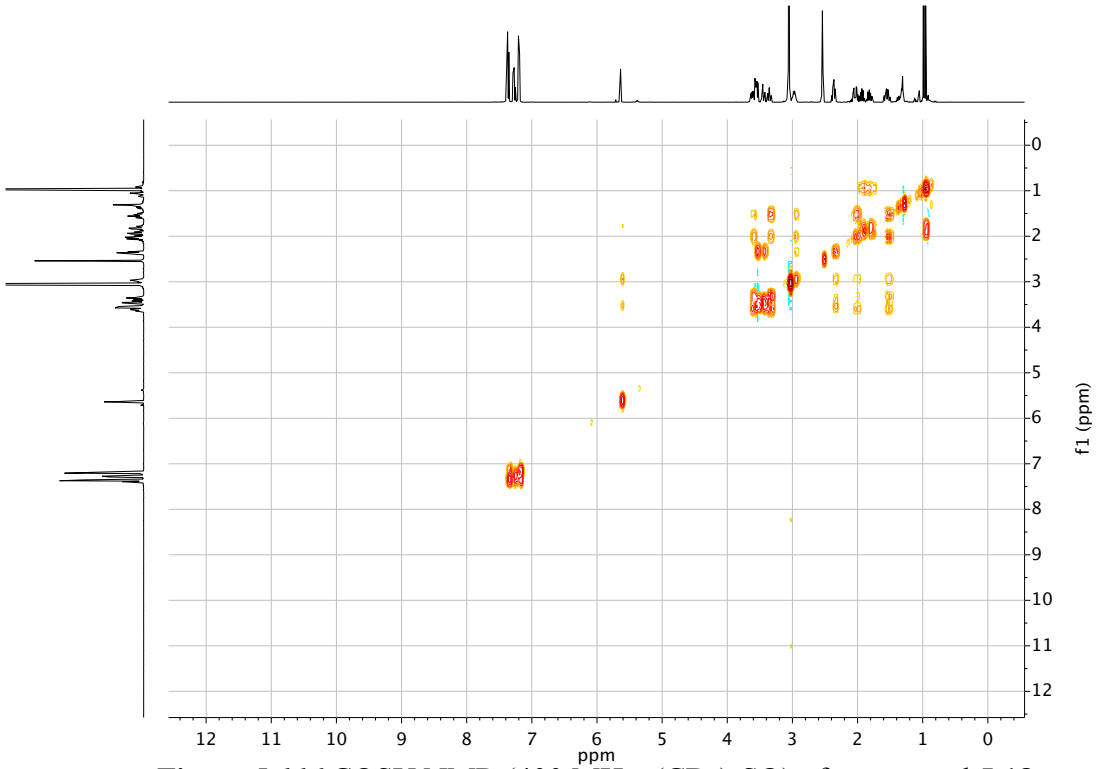


Figure 5.116 COSY NMR (400 MHz, $(CD_3)_2SO$) of compound **5.18.**

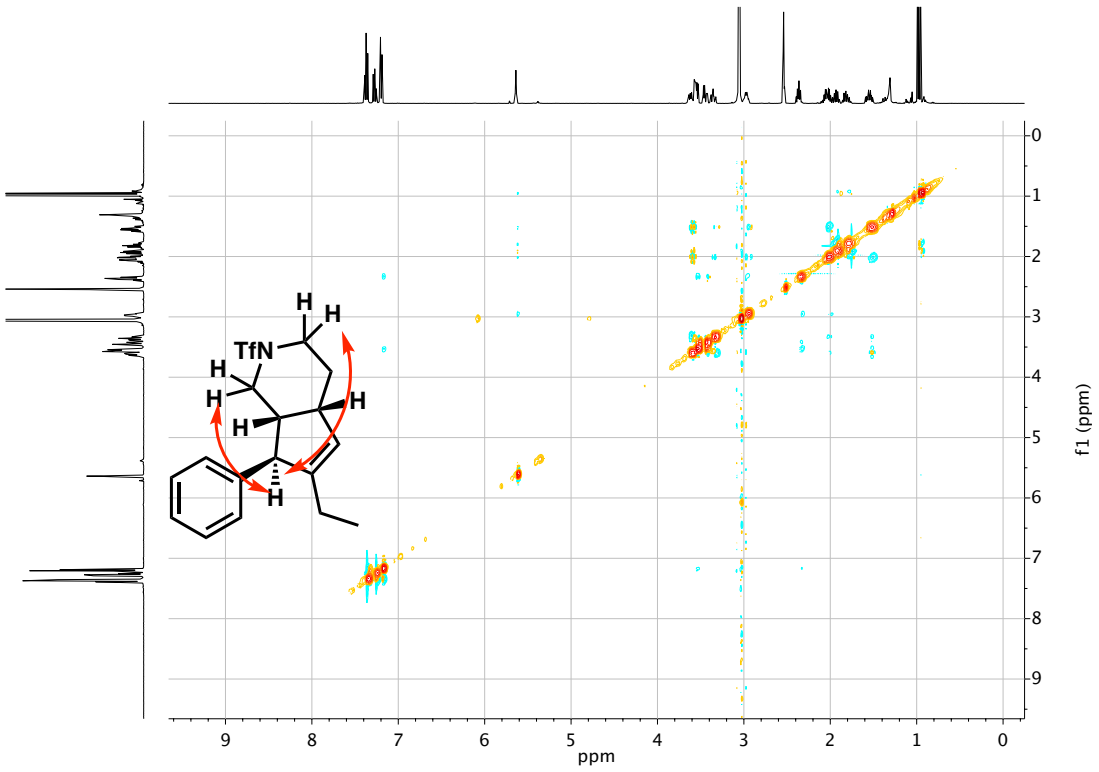


Figure 5.117 ^{1}H NOE NMR (400 MHz, $(CD_3)_2SO$) of compound **5.18.**

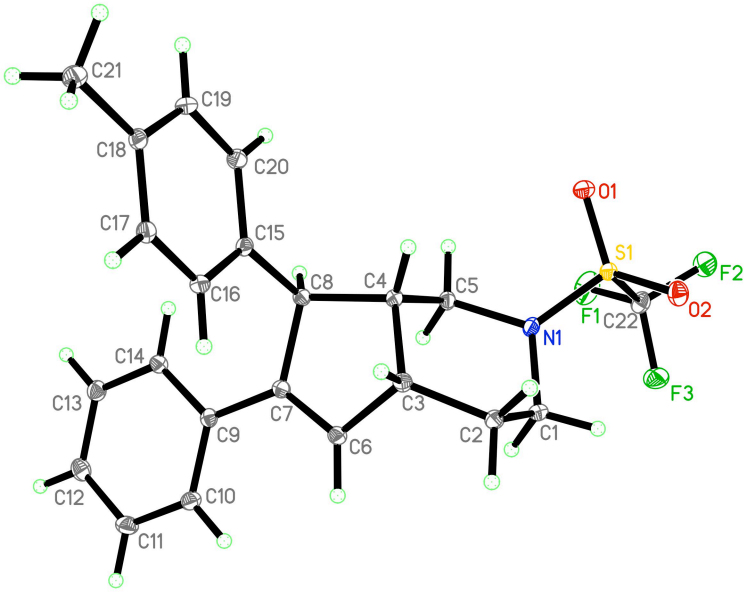


Figure 5.118 Crystal Structure of compound **5.12.**

5.7 Notes and References

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