UNIVERSITY OF CALIFORNIA,
IRVINE

Development of Nickel-Catalyzed Cross-Electrophile Coupling Reactions

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in Chemistry

by

Taylor A. Thane

Dissertation Committee:
Professor Elizabeth R. Jarvo, Chair
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2022

DEDICATION

For my grandfather, parents, brother, and Joey

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Hewitt, K. A.‡; Xie, P. P.‡; Thane, T. A.; Hirbawi, N.; Zhang, S.-Q.; Matus, A. C.; Lucas, E. L.; Hong, X.; Jarvo, E. R. "A Nickel-Catalyzed Domino Cross-Electrophile Coupling Dicarbofunctionalization Reaction to Afford Vinylcyclopropanes" *ACS Catal.* **2021**, *11*, 14369–14380.

Sanford, A. B.; Thane, T. A.; McGinnis, T. M.; Chen, P.-P.; Hong, X.; Jarvo, E. R. "Nickel-Catalyzed Alkyl-Alkyl Cross-Electrophile Coupling Reaction of 1,3-Dimesylates for the Synthesis of Alkylcyclopropanes." *J. Am. Chem. Soc.* **2020**, *142*, 5017–5023.

Howitz, W. J.; Thane. T. A.; Frey, T. L.; Wang, X. S.; Gonzales, J. C.; Tretbar, C. A.; Seith, D. D.; Saluga, S. J.; Lam, S.; Nguyen, M. M.; Tieu, P.; Link, R. D.; Edwards, K.D. "Online in No Time: Design and Implementation of a Remote Learning First Quarter General Chemistry Laboratory and Second Quarter Organic Chemistry Laboratory." *J. Chem. Educ.* **2020**, *97*, 2624–2634.

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Thane, T. A.; Jarvo, E. R. "Development of Nickel-Catalyzed Cross-Electrophile Coupling Reactions." Presented at the National Meeting of the American Chemical Society, Virtual, April 2021 (Oral Presentation).

Sanford, A. B.; Thane, T. A.; McGinnis, T. M.; Chen, P.-P.; Hong, X.; Jarvo, E. R. "Nickel-Catalyzed Cross-Electrophile Coupling Reactions of Mesylates for Cyclopropane Synthesis." Presented at the National Meeting of the American Chemical Society, San Diego, CA. August 2019 (Oral Presentation).

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Thane, T. A; Clark, T. B. "β-Borylation and β-Silylation of Enals Towards a Method to Access Trisubstituted Vinyl Boronate Esters and Vinyl Silanes." Presented at the Local Symposium of the American Chemical Society, San Diego, CA., March 2016 (Poster Presentation).

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ABSTRACT OF DISSERTATION

Development of Nickel-Catalyzed and Zinc-Mediated Cross-Electrophile Coupling Reactions for Cyclopropane Synthesis and Investigation of Ligand-Based Control of Nickel Catalysts

By

Taylor A. Thane

Doctor of Philosophy in Chemistry

University of California, Irvine, 2022

Professor Elizabeth R. Jarvo, Chair

Cross-coupling (XC) reactions have had a lasting impact on the way synthetic organic chemists approach bond construction. This is evident by the numerous industrial applications of XC methods and the 2010 Nobel prize awarded to Ei-ichi Negishi, Akira Suzuki, and Richard Heck. Palladium-catalyzed XC reactions have dominated the field and are now very well understood transformations. However, development of cross-electrophile coupling (XEC) reactions has moved slower than that of traditional XC reactions. XEC reactions offer attractive counterparts to traditional XC reactions as XEC reactions couple two electrophilic partners together, utilizing a widely accessible pool of halide and pseudohalide starting materials. Additionally, these transformations are commonly achieved using nickel catalysis, which offers practical advantages over the commonly used palladium catalysts. For example, nickel has a smaller carbon footprint associated with the mining of the metal making it a more sustainable alternative to precious metals such as palladium. Thus, the advancement of nickel-catalyzed XEC

reactions will allow for the development of transformations that utilize readily accessible functional group motifs with sustainable base metal catalysis.

Cyclopropane motifs are a common functional group found in pharmaceutical compounds and natural products. There are a variety of methods that synthesize cyclopropane motifs from either alkenes or diazo compounds including the Simmons–Smith reaction. However, there are few cyclopropanation methods that utilize simple C–O and C–N bonds as precursors. We foresaw nickel-catalyzed XEC reactions as a unique way to approach cyclopropane synthesis. Herein, a nickel-catalyzed XEC reaction of 1,3-dimesylates to access aryl- and alkylcyclopropanes is described. Additionally, by developing a mild set of reaction conditions, we foresaw the opportunity to develop a late-stage modification of medicinal agents such as statins. A zinc-mediated XEC reaction of 1,3-dimesylates for cyclopropane synthesis has also been described. Finally, domino reactions have become an attractive way to quickly build molecular complexity by undergoing multiple synthetic manipulations in a single step. Specifically, our lab foresaw the opportunity to build upon our previously developed nickel-catalyzed ring contraction of sulfonamides. Therefore, we have developed a domino XEC dicarbofuntionalization reaction of propargyl *N*-tosyl sulfonamides for cyclopropane synthesis.

The rapid development of palladium-catalyzed XC methods was aided by mechanistic understanding of the various transformations. While mechanistic investigation of nickel-catalyzed XEC reactions has been performed, there are still key features involved in nickel catalysis that have yet to be addressed including the control of reactivity that the ligand imparts on the nickel catalyst. We foresaw the 4-halotetrahydropyrans (THP) as interesting model substrates for the study of ligand-based control of nickel-catalysts. Phosphine ligands were predicted to selectively engage the carbon–oxygen bond via a two-electron oxidative addition pathway to access a

cyclopropane product. Conversely, nitrogen-based ligands were predicted to selectively engage the carbon–halogen bond in a one-electron oxidative addition pathway resulting in the reduced tetrahydropyran. Herein, a series of vinyl, naphthyl, and biphenyl THPs were examined with a series of phosphorous- and nitrogen-based ligands where two factors work in concert to determine chemoselectivity: the degree of C–O bond activation and the type of ligand employed.

Chapter 1

Nickel-Catalyzed Cross-Electrophile Coupling Reaction of 1,3-Dimesylates for Alkyl Cyclopropane Synthesis

1.1 Introduction

Carbon–carbon bond formation has undoubted importance in organic chemistry.[1] The ability to selectively construct new C–C bonds allows for facile and efficient access to complex molecules as well as quickly setting new stereocenters in a molecule. Traditional cross-coupling (XC) reactions, which couple an electrophile with a nucleophile utilizing a transition metal catalyst, have been widely developed for C–C bond formation. Limitations of traditional XC methods can include limited functional group compatibility and the small range of commercially available organometallic nucleophiles compared to their halide counterparts. Cross-electrophile coupling (XEC) reactions are an attractive alternative to traditional XC reactions. By utilizing two different electrophiles as coupling partners, XEC reactions broaden the range of available starting materials and can tolerate a wide range of functional group motifs.[2,3,4] These methods are not only an alternative to traditional methods but complement them quite nicely as XEC reactions offer orthogonal reactivity to traditional XC reactions.

Challenges associated with XEC reactions arise from the similar reactivity between the two coupling partners and can result in homocoupled products over the desired cross-coupled product.[5] Various strategies have been employed to overcome these challenges, such as forging $C(sp^2)$–$C(sp^3)$ bonds where an aryl or vinyl electrophile will react with the catalyst faster than an alkyl

[1] Portions of this work have been published in the Jounal of the American Chemical Society, see: Sanford, A. B.; Thane, T. A.; McGinnis, T. M.; Chen. P.-P.; Hong, X.; Jarvo, E. R. *J. Am. Chem. Soc.* **2020**, *142*, 5017–5023.
[2] Everson, D. A.; Weix, D. J. *J. Org. Chem.* **2014**, *79*, 4793–4798.
[3] Weix, D. J. *Acc. Chem. Rev.* **2015**, *48*, 1767–1775.
[4] Wang, X.; Gong, H. *Top. Curr. Chem.* **2016**, *374*, 43.
[5] Biswas, S.; Weix, D. J. *J. Am. Chem. Soc.* **2013**, *135*, 16192–16197.

electrophile.[6,7] In XEC reactions, it is typical for one electrophile to be activated, such as a vinyl, benzyl or allyl electrophile, and the other electrophile to be unactivated, such as a simple alkyl electrophile.[8] The activated electrophile will undergo oxidative addition faster while the unactivated electrophile will undergo a sequential oxidative addition or a radical recombination with the nickel catalyst. The development of methods that engage two unactivated and readily available electrophiles would broaden the current scope of XEC reactions and provide opportunities to better understand the mechanistic details that govern cross-selectivity in these couplings.

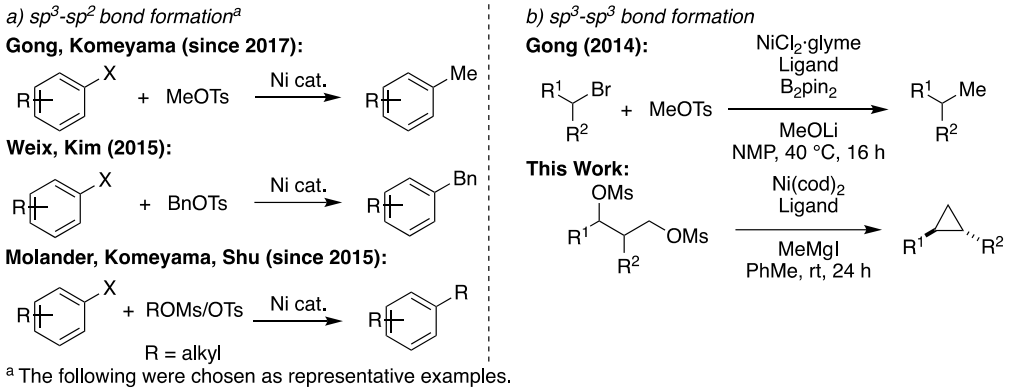
Haloalkanes, haloalkenes and haloarenes have been widely employed as coupling partners in XEC reactions. However, psuedohalides, such as triflates, tosylates, and mesylates, have seen less use in this field.[9,1011] Sulfonates are desirable coupling partners derived from alcohols which are prevalent in steroids, terpenes and polyketides. The accessibility of starting materials and quick conversion of alcohols to sulfonates in one step or in situ make sulfonates attractive alternatives to halides.

Although alkyl sulfonates are attractive electrophiles for XC and XEC reactions, they have seen limited use when compared to their halide counterparts. While the XEC reactions of methyl, alkyl, and benzylic sulfonates with aryl halides have been developed to form new $C(sp^3)$–$C(sp^2)$

[6] Knappke, C. E. I.; Grupe, S.; Gärtner, D.; Corpet, M.; Gosmini, C.; Jacobi Von Wangelin, A. *Chem. – Eur. J.* **2014**, *20*, 6826–6842.
[7] Lucas, E. L.; Jarvo, E. R.; *Nat. Rev. Chem.* **2017**, *1*, 0065.
[8] a) Yu, X.; Yang, T.; Wang, S.; Xu, H.; Gong, G. *Org. Lett.* **2011**, *13*, 2138–2141. b) Xu, H.; Zhao, C.; Qian, Q.; Deng, W.; Gong, H. *Chem. Sci.* **2013**, *4*, 4022–4029. c) Xue, W.; Xu, H.; Liang, Z.; Qian, Q.; Gong, H. *Org. Lett.* **2014**, *16*, 4984–4987.
[9] a) Do, H.; Chandrashekar, E. R. R.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 16288–16291. b) Eno, M. S.; Lu, A. *J. Am. Chem. Soc.* **2016**, *138*, 7824–7827.
[10] Carbonates: a) Dai, Y.; Wu, F.; Zang, Z.; You, H.; Gong, H. *Chem. – Eur. J.* **2012**, *18*, 808–812. b) Yu, Y.; Chen, H.; Qian, Q.; Yao, K.; Gong, H. *Tetrahedron* **2018**, *74*, 5651–5658.
[11] Triflates: a) see reference 4 b) Huang, L.; Ackerman, L. K. G.; Kang, K.; Parsons, A. M.; Weix, D. J. *J. Am. Chem. Soc.* **2019**, *141*, 10978–10983.

bonds (Scheme 1.1a),[12] achieving cross-selectivity between two unactivated alkyl sulfonates remains a challenge. In 2014, the Gong group demonstrated a nickel-catalyzed XEC reaction of methyl tosylate with secondary alkyl halides, but this method was limited to the use of methyl tosylates (Scheme 1.1b).[13] Before our studies, XEC methods that couple two sulfonates had not been reported. Due to the availability and reactivity of sulfonates, we foresaw 1,3-dimesylates as attractive coupling partners. In this Chapter, I report a nickel-catalyzed XEC reaction of alkyl 1,3-dimesylates for cyclopropane synthesis (Scheme 1.1b).

Scheme 1.1 Nickel-Catalyzed XEC Reactions



1.2 Results and Discussion

We began our investigation by examining the reactivity of alkyl 1,3-dimesylates in our standard cross-electrophile coupling conditions.[14] My coworker, Amberly Sanford, optimized the XEC reaction of alkyl 1,3-dimesylates and developed the reaction to include unbranched monosubstituted alkylcyclopropanes.

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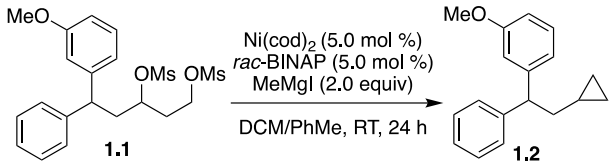
[12] a) Wang, J.; Zhao, J.; Gong, H. *Chem. Commun.* **2017**, *53*, 10180–10183. b) Komeyama, K.; Yamahata, Y.; Osaka, I. *Org. Lett.* **2018**, *20*, 4375–4378. c) Ackerman, L. K. G.; Anka-Lufford, L. L.; Naodovic, M.; Weix, D. J. *Chem. Sci.* **2015**, *6*, 1115–1119. d) Jung, H.-S.; Kim, S.-H. *Synlett.* **2015**, *26*, 666–670. e) Molander, G. A.; Traister, K. M.; O'Neill, B. T. *J. Org. Chem.* **2015**, *80*, 2907–2911. f) Komeyama, K.; Ohata, R.; Kiguchi, S.; Osaka, I. *Chem. Commun.* **2017**, *53*, 6401–6404. g) Duan, J.; Du, Y.-F.; Pang, X.; Shu, X.-Z. *Chem. Sci.* **2019**, *10*, 8706–8712.

[13] a) Liang, Z.; Xue, W.; Lin, K.; Gong, H. *Org. Lett.* **2014**, *16*, 5620–5623. b) Wang, J.; Zhao, J.; Gong, H. *Chem. Commun.* **2017**, *53*, 10180–10183.

[14] Portions of this work have been published: Sanford, A. B.; Thane, T. A.; McGinnis, T. M.; Chen, P.-P.; Hong, X.; Jarvo, E. R. *J. Am. Chem. Soc.* **2020**, *142*, 5017–5023.

To extend the scope of this reaction, the XEC reaction of β-branched alkylcyclopropanes was optimized (Table 1.1). Employing dppm as the ligand provided a higher yield than when *rac*-BINAP was utilized (entry 2). Cooling the reaction to 0 °C improved the yield of the XEC reaction of 1,3-dimesylates when branching was present on the alkyl chain (entry 3), reflected by an increased yield to 75%. A bidentate nitrogen ligand, Bphen, that has also been successful for our previously developed XEC reactions did not improve the yield when run at 0 °C.

Table 1.1 Optimization of Branched Alkylcyclopropanes in the XEC Reaction

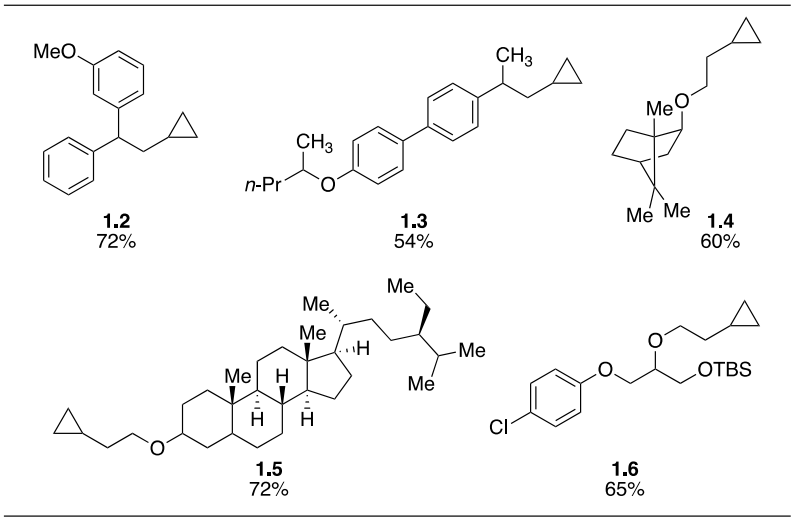


Entry	Deviation From Standard Conditions	Yield (%)[a]
1	none	51
2	dppm	67 (65)[b]
3	dppm, 0 °C	75 (72)[b]
4	Bphen, 0 °C	60

[a]Yield determined by ^{1}H NMR based on comparison to PhTMS as internal standard. [b]Isolated yield.

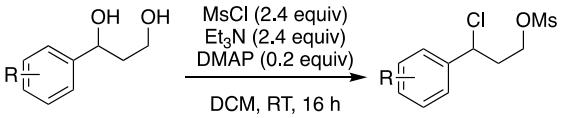
The scope of branched alkylcyclopropanes was extended to show tolerance of both phenyl and methyl substituents in the β-position (cyclopropanes **1.2** and **1.3**, Scheme 1.2). Alkylcyclopropanes derived from borneol **1.4** and β-sitosterol **1.5** were also synthesized. Tolerance of both a silyl ether protecting group and an aryl chloride were also demonstrated in cyclopropane **1.6**.

Scheme 1.2 Alkylcyclopropanes with Branching and Various Funcationality



Previous XEC reactions in our laboratory were limited to benzylic and allylic electrophiles. Due to the success of this XEC reaction with alkyl electrophiles, benzylic electrophiles were also examined for the synthesis of arylcyclopropanes. Conditions for the synthesis of branched alkylcyclopropanes proved equally successful for the synthesis of arylcyclopropanes, although the electrophile precursor was no longer a 1,3-dimesylate, but a benzylic chloride (Scheme 1.3). Under mesylation conditions, the benzylic mesylate undergoes a facile substitution reaction to afford the benzylic chloride (Scheme 1.3).[15]

Scheme 1.3 Synthesis of Benzylic Chloride from 1,3-Diol

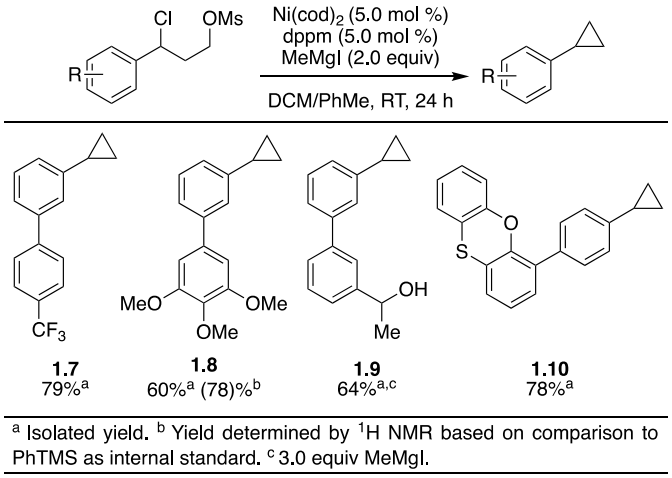


An electron-withdrawing trifluoromethyl substituent in cyclopropane **1.7** was tolerated as well as an electron donating trimethoxy substituted arene on cyclopropane **1.8**. A substrate containing a pendant aldehyde underwent the XEC and concurrent Grignard addition to afford the

[15] Ding, R.; He, Y.; Wang, X.; Xu, J.; Chen, Y.; Feng, M.; Qi, C. *Molecules* **2011**, *141*, 5835–5855.

desired cyclopropane **1.9** bearing a secondary alcohol. The pendant phenoxathiine moiety on cyclopropane **1.10** was also well tolerated (Scheme 1.4).

Scheme 1.4 Expansion of XEC Reaction to the Synthesis of Arylcyclopropanes

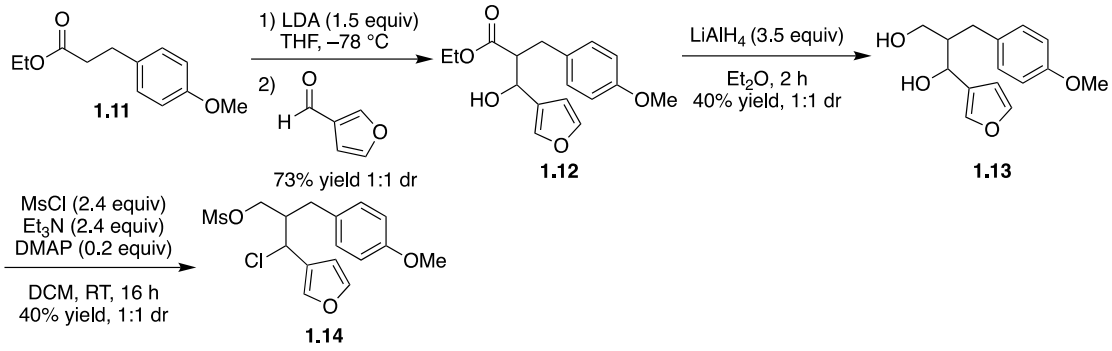


[a] Isolated yield. [b] Yield determined by ^{1}H NMR based on comparison to PhTMS as internal standard. [c] 3.0 equiv MeMgI.

The synthesis of 1,2-disubstituted alkyl- and arylcyclopropanes would be significant based on their prevalence in biologically relevant compounds. The extension of this method for the formation of 1,2-disubstituted cyclopropanes would complement previously developed cyclopropanation reactions which require the use of directing groups to control the stereoselectivity.[16] The desired 1,3-dimesylates for 1,2-disubstituted cyclopropane synthesis are readily accessible via a self-Claisen condensation or a crossed-Claisen reaction. A representative synthesis is outlined in Scheme 1.5. Ester **1.11** underwent a self-Claisen condensation followed by reduction to afford 1,3-diol **1.13**. Subsequent mesylation afforded benzylic chloride **1.14**.

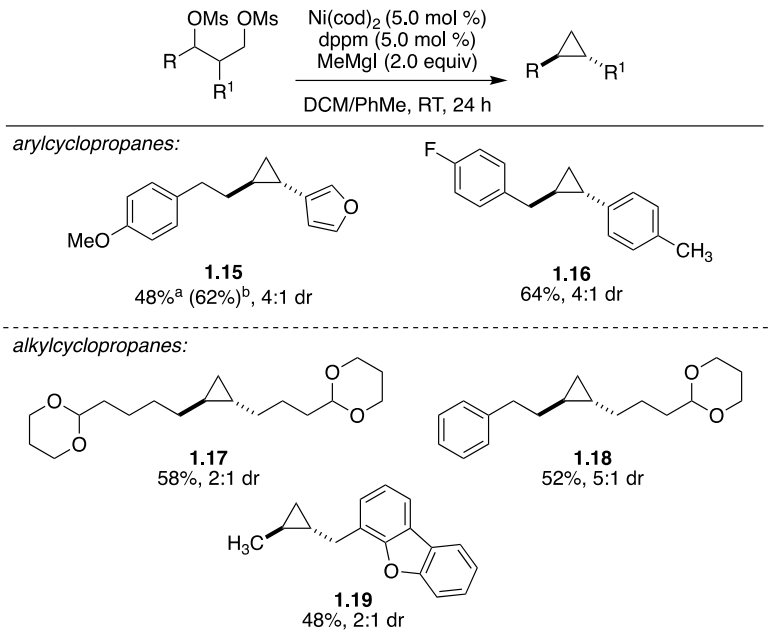
[16] a) Ebner, C.; Carreira, E. *Chem. Rev*. **2017**, *117*, 11651–11679. b) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A.B. *Chem. Rev.* **2003**, *103*, 977–1050. c) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Synthesis* **2014**, *46*, 979–1029.

Scheme 1.5 Synthesis of 1,3-Dimesylate via a Claisen Condensation



Initial examination of a benzylic chloride **1.14** in the XEC reaction for 1,2-disubstituted cyclopropane synthesis demonstrated this transformation as a stereoconvergent method yielding the *trans*-cyclopropane as the major diastereomer. Subjecting a 1:1 mixture of diastereomers of **1.14** to the XEC reaction resulted in a 4:1 mixture favoring the *trans*-cyclopropane **1.15** (Scheme 1.6). A variety of 1,2-disubstituted cyclopropanes were synthesized. Notably, a furanyl cyclopropane, **1.15**, was synthesized (Scheme 1.6). Additionally, acetals as well as a dibenzofuran and an aryl flouride were tolerated yielding cyclopropanes **1.16–1.19** (Scheme 1.6).

Scheme 1.6 XEC Reaction for the Synthesis of 1,2-Alkyl- and 1,2-Arylcyclopropanes



[a] Isolated yield. [b] Yield determined by ^{1}H NMR based on comparison to PhTMS as internal standard.

1.3 Conclusions

This work demonstrates the first cross-electrophile coupling reaction of primary mesylates with secondary mesylates. Monosubstituted branched and unbranched alkylcyclopropanes as well as 1,2-disubsituted alkylcyclopropanes have been synthesized from the corresponding 1,3-dimesylates. This method was also extended to the synthesis of mono- and 1,2-disubstituted arylcyclopropanes from the corresponding benzylic chlorides. Stereoconvergent synthesis of disubstituted cyclopropanes from a 1:1 diastereomeric mixture of 1,3-diols offers a facile route to install stereochemistry in the desired compound and offers a new strategy for cyclopropane synthesis that complements previously developed cyclopropanation methods.

1.4 Experimental Details

1.4.1 General Procedures

All reactions were carried out under a N_2 atmosphere, unless otherwise stated. All glassware was either oven-dried or flame-dried prior to use. Toluene (PhMe), diethyl ether (Et_2O), dichloromethane (DCM), hexanes (hex), triethylamine (Et_3N), and tetrahyrdofuran (THF) were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 °C for 12 hours) to remove H_2O. Other solvents were purchased "anhydrous" commercially, or were purified as described. ^{1}H NMR were recorded on Bruker DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C), CRYO-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C), GN-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C), or AVANCE-600 (150 MHz ^{13}C, 564.6 MHz ^{19}F) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00) unless otherwise noted. Data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (br s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet (t), doublet of triplets (dt), triplet of doublets (td), doublet of doublet of triplets (ddt), quartet (q), quintet (quint), quintet of triplets (quintt), quintet of doublets (quintd), sextet (sext), septet (sept), octet (oct), nonuplet (non), multiplet (m), apparent singlet (ap s), apparent doublet (ad), apparent triplet (at), apparent quartet (aq), apparent quintet (aquint)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). NMR data were collected at 25 °C. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60Å F254 precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with p-anisaldehyde (PAA), cerium ammonium molybdate (CAM), or potassium permanganate ($KMnO_4$) solutions. Flash chromatography was

performed using either SiliaFlash F60 (40–63 μm, 60 Å) from SiliCycle, or Teledyne Isco Combiflash® Rf+ automated flash chromatography system. High resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center. GC/FID analysis for competition experiments was performed on Agilent 7820A system with helium as carrier gas. For reactions performed at rt, average room temperature was 20 ºC.

Bis(1,5-cyclooctadiene)nickel was purchased from Strem, stored in a glove box freezer (–20 °C) under an atmosphere of N_2 and used as received. All ligands were purchased from Strem or Sigma Aldrich and were stored under N_2 atmosphere and used as received. All Grignard reagents were titrated with iodine prior to use. All other chemicals were purchased commercially and used as received, unless otherwise noted.

1.4.2 General Cross-Electrophile Coupling Procedures

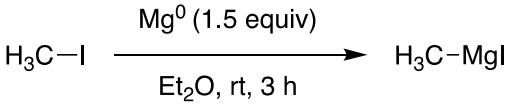
1.4.2.1 Method A: Cross-Electrophile Coupling Reaction of 1,3-Dimesylates

In a glovebox, a flame-dried vial equipped with a stir bar was charged with $Ni(cod)_2$ (5 mol %), *rac*-BINAP (5 mol %), alkyl dimesylate (1 equiv), and PhMe (0.2 M). Methyl magnesium iodide (2 equiv) was added and the reaction mixture was allowed to stir for 24 h at room temperature. The reaction was quenched with MeOH, filtered through silica with Et_2O (neat) and concentrated in vacuo.

1.4.2.2 Method B: Cross-Electrophile Reaction of Benzylic Chlorides

In a glovebox, a flame-dried vial equipped with a stir bar was charged with $Ni(cod)_2$ (5 mol %), *rac*-BINAP (5 mol %), alkyl dimesylate (1 equiv), and toluene (0.2 M). The reaction mixture was cooled to 0 °C then methyl magnesium iodide (2 equiv) was added and the reaction was allowed to stir for 24 h. The reaction was quenched with MeOH, filtered through silica with Et_2O (neat) and concentrated in vacuo.

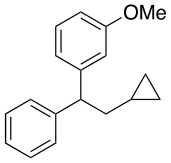
1.4.2.3 Preparation of Methylmagnesium Iodide



Under an N_2 atmosphere, to a 3-necked round bottom flask equipped with a stir bar, reflux condenser, and Schlenk filtration apparatus was added magnesium turnings (2.80 g, 120 mmol, 1.50 equiv). The flask and magnesium turnings were flame-dried under vacuum and the flask was back-filled with N_2. A crystal of iodine (ca. 2 mg) was added to the flask, followed by anhydrous Et_2O (25 mL). The reaction mixture was brought to 0 °C, and freshly distilled iodomethane (5.0 mL, 82 mmol, 1.0 equiv) was slowly added over 30 min to maintain a gentle reflux. The mixture was stirred for 4 h at room temperature then filtered through the fritted Schlenk filter into a pear-shaped flask under N_2 atmosphere. The magnesium turnings were washed with Et_2O (2 x 1.0 mL) then the Schlenk bomb was sealed, removed, and placed under an argon atmosphere. The resulting methyl Grignard reagent was typically between 2.4 and 3.0 M as titrated by Knochel's method[17] and was stored in a glovebox for up to 8 weeks.

1.4.3 Characterization of Cyclopropanes

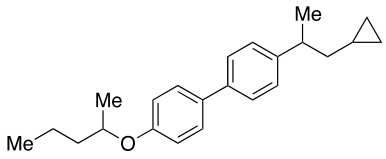
1.4.3.1 Monosubstituted Alkylcyclopropanes



1-(2-Cyclopropyl-1-phenylethyl)-3-methoxybenzene (1.2) was prepared according to Method B. The reaction was performed on a 0.1 mmol scale to obtain a ^1H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used on a 0.1 mmol scale:

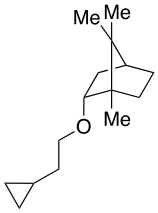
[17] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, *5*, 890–891.

$Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), dppm (3.8 mg, 5.0 µmol, 5.0 mol %), substrate **1.1** (0.13 mL, 0.10 mmol, 1.0 equiv, 0.76 M stock soln in PhMe), PhMe (0.4 mL), MeMgI (0.08 mL, 0.20 mmol, 2.5 M solution in Et_2O, 2 equiv). A ^1H NMR yield of 67% yield was obtained based on comparison to PhTMS as internal standard. The following amounts of reagents were used on a 0.2 mmol scale: $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), rac-BINAP (3.8 mg, 10. µmol, 5.0 mol %), substrate **1.1** (0.26 mL, 0.20 mmol, 1.0 equiv, 0.76 M stock soln in Et_2O), PhMe (1.0 mL, 0.20 M in substrate), MeMgI (0.14 mL, 0.40 mmol, 2.9 M solution in Et_2O, 2.0 equiv). The compound was purified by column chromatography (100% hexanes) to afford the title compound as a clear, colorless oil (34 mg, 0.13 mmol, 67% yield). **TLC R_f =** 0.9 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26–7.13 (m, 6H), 6.85 (d, J = 9.4 Hz, 1H), 6.81 (s, 1H), 6.70 (dd, J = 8.3, 2.7 Hz, 1H), 4.00 (t, J = 7.6 Hz, 1H), 3.75 (s, 3H), 1.96–1.87 (m, 2H), 0.62–0.57 (m, 1H), 0.39–0.35 (m, 2H), 0.07–0.03 (m, 2H); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 159.6, 147.0, 145.2, 129.3, 128.5 (2C), 127.9 (2C), 126.1, 120.5, 114.2, 110.9, 55.2, 51.7, 40.9, 9.8, 4.8 (2C); **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calcd for $C_{18}H_{20}ONa$, 275.1412; found, 275.1409.



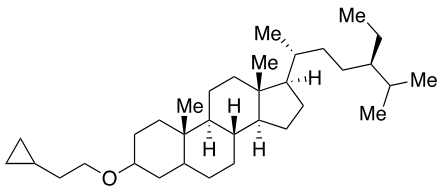
4-(1-Cyclopropylpropan-2-yl)-4'-(pentan-2-yloxy)-1,1'-biphenyl (1.3) was prepared according to Method B. The following amounts of reagents were used: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), dppm (3.8 mg, 5.0 µmol, 5.0 mol %), substrate **1.26** (82.1 mg, 0.100 mmol, 1.00 equiv), PhMe (0.4 mL), MeMgI (0.08 mL, 0.2 mmol, 2.5 M solution in Et_2O, 2 equiv). A ^1H NMR yield of 73% was obtained based on comparison to PhTMS as internal standard. The compound was purified by column chromatography (100% hexanes) to yield the title compound a clear, colorless oil (35 mg, 0.11 mmol, 54% yield, 1:1 dr). **TLC R_f =** 0.8 (10% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$)

δ 7.58 (d, J = 8.9 Hz, 2H), 7.56 (d, J = 8.9 Hz, 2H), 7.33 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 8.6 Hz, 2H), 4.48 (m, 1H), 2.95 (sext, J = 7.1 Hz, 1H), 1.88–1.81 (m, 1H), 1.74–1.44 (m, 5H), 1.41 (d, J = 2.7 Hz, 3H), 1.39 (d, J = 3.6 Hz, 3H), 1.04 (t, J = 7.3 Hz, 3H), 0.75–0.67 (m, 1H), 0.52–43 (m, 2H), 0.14–0.07 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 157.6, 146.4, 138.5, 133.5, 128.0 (2C), 127.4 (2C), 126.7 (2C), 126.6 (2C), 73.7, 43.8, 40.1, 38.8, 21.9, 19.9, 18.9, 14.2, 9.6, 4.8, 4.5; **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calcd for $C_{23}H_{30}ONa$, 322.2297; found, 322.2286.

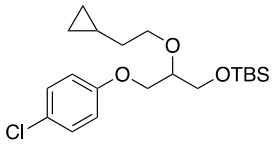


(1*R*,2*R*,4*S*)-2-(2-Cyclopropylethoxy)-1,7,7-trimethylbicyclo[2.2.1]heptane (1.4) was prepared according to Method B. The reaction was performed on a 0.1 mmol scale to obtain a ^{1}H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used on for the 0.1 mmol scale: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), dppm (1.9 mg, 5.0 µmol, 5.0 mol %), substrate **1.32** (7.5 µL, 0.10 mmol, 1.0 equiv, 1.3 M of substrate in PhMe), MeMgI (0.07 mL, 0.2 mmol, 2 equiv, 2.8 M solution in Et_2O), and PhMe (0.40 mL). A ^{1}H NMR yield of 50% was obtained based on comparison to PhTMS as internal standard. The following amounts of reagents were used for the 0.2 mmol scale: $Ni(cod)_2$ (2.7 mg, 10. µmol, 5.0 mol %), dppm (3.8 mg, 10. µmol, 5.0 mol %), substrate **1.32** (0.15 mL, 0.20 mmol, 1.0 equiv), MeMgI (0.14 mL, 0.40 mmol, 2.0 equiv, 2.8 M solution in Et_2O), and PhMe (0.80 mL). The compound was purified by flash column chromatography (100% hexanes) to yield the title compound as a clear oil (22 mg, 0.10 mmol, 60% yield). **TLC R_f =** 0.9 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.57–3.40 (m, 3H), 2.15–2.07 (m, 1H), 2.03–1.96 (m, 1H), 1.73–1.64 (m, 1H), 1.61 (t, J = 5.1 Hz, 1H), 1.44 (q, J = 6.7 Hz, 2H), 1.26–1.14 (m, 2H), 1.01 (dd, J = 12.9, 3.3 Hz, 1H), 0.87 (s, 3H),

0.84 (s, 6H), 0.78–0.68 (m, 1H), 0.43–0.39 (m, 2H), 0.07–0.03 (m, 2H); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 84.8, 70.2, 49.3, 47.9, 45.2, 36.6, 35.4, 28.4, 26.8, 19.9, 19.0, 14.2, 8.2, 4.31, 4.27; **HRMS** (TOF MS Cl+) *m/z:* $[M]^+$ calcd for $C_{15}H_{26}O$, 222.1984; found, 222.1986.

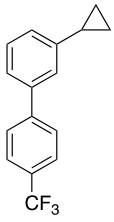


3-(2-Cyclopropylethoxy)-17-(5-ethyl-6-methylheptan-2-yl)-10,13-dimethyhexadecahydro-1H-cyclopenta[a]phenanthrene (1.5) was prepared according to Method A. The reaction was performed on a 0.1 mmol scale to obtain a ^{1}H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used on a 0.1 mmol scale: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), rac-BINAP (3.1 mg, 5.0 µmol, 5.0 mol %), substrate **1.39** (68 mg, 0.10 mmol, 1.0 equiv), PhMe (0.4 mL), MeMgI (0.8 mL, 0.2 mmol, 2.5 M solution in Et_2O, 2.0 equiv). A 1 H NMR yield of 72% yield was obtained based on comparison to PhTMS as internal standard. The following amounts of reagents were used on a 0.2 mmol scale: $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), rac-BINAP (3.8 mg, 10. µmol, 5.0 mol %), substrate **1.39** (135 mg, 0.200 mmol, 1.00 equiv), PhMe (1.0 mL, 0.20 M in substrate), MeMgI (0.14 mL, 0.40 mmol, 2.9 M solution in Et_2O, 2.0 equiv). The compound was characterized without further purification. **TLC R_f =** 0.8 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.55–3.48 (m, 2H), 3.24– 3.19 (m, 1H), 1.97–0.65 (m, 53H), 0.42–0.40 (m, 2H), 0.05–0.04 (m, 2H); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 79.2, 68.6, 57.2, 56.9, 55.1, 46.5, 45.6, 43.2, 40.7, 37.7, 36.8, 36.5, 36.1, 36.0, 35.6, 34.6, 32.8, 29.8, 29.5, 29.0, 28.9, 26.7, 24.9, 23.7, 21.9, 20.4, 19.7, 19.4, 12.9, 12.7, 12.6, 8.5, 4.8 (2C); **HRMS** (TOF MS ES+) *m/z:* $[M]^+$ calcd for $C_{34}H_{60}O$, 484.4644; found, 484.4626.

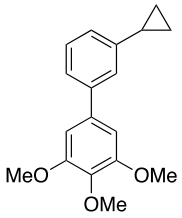


tert-Butyl(3-(4-chlorophenoxy)-2-(2-cyclopropylethoxy)propoxy)dimethylsilane (1.6) was prepared according to Method A. The reaction was performed on a 0.1 mmol scale to obtain a ^{1}H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used for the 0.1 mmol scale: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), rac-BINAP (3.1 mg, 5.0 µmol, 5.0 mol %), substrate **1.46** (68 mg, 0.10 mmol, 1.0 equiv), PhMe (0.40 mL), MeMgI (0.08 mL, 0.2 mmol, 2.5 M solution in Et_2O, 2 equiv). A ^{1}H NMR yield of 66% was obtained. The following amounts of reagents were used for the 0.2 mmol scale: $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), rac-BINAP (3.8 mg, 10. µmol, 5.0 mol %), substrate **1.46** (0.14 g, 0.20 mmol, 1.00 equiv), PhMe (1.0 mL, 0.20 M in substrate), MeMgI (0.14 mL, 0.40 mmol, 2.9 M solution in Et_2O, 2.0 equiv). The desired product was purified by column chromatography (25% EtOAc/hexanes) to yield the title compound a clear, colorless oil (50. mg, 0.13 mmol, 65% yield). **TLC R_f =** 0.8 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, J = 9.2 Hz, 2H), 6.85 (d, J = 9.1 Hz, 2H), 4.11–4.08 (dd, J = 4.2, 10.2 Hz, 1H), 3.99–3.95 (dd, J = 5.6, 10.0 Hz, 1H), 3.75–3.66 (m, 5H), 1.47 (q, J = 7.4 Hz, 2H), 0.88 (s, 9H), 0.77–0.67 (m,1H), 0.42–0.40 (m, 2H), 0.03 (s, 8H); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 157.6, 129.3 (2C), 125.6, 115.9 (2C), 78.7, 70.8, 68.2, 62.4, 35.2, 25.9 (3C), 18.3, 7.8, 4.2 (2C), –5.39, –5.43; **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calcd for $C_{20}H_{33}ClO_3SiNa$, 407.1785; found, 407.1793.

1.4.3.2 Monosubstituted Arylcyclopropanes

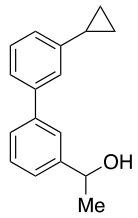


3-Cyclopropyl-4'-(trifluoromethyl)-1,1'-biphenyl (1.7) was prepared according to Method B. The following amounts of reagents were used: $Ni(cod)_2$ (1.9 mg, 7.0 µmol, 5.0 mol %), dppm (2.7 mg, 7.0 µmol, 5.0 mol %), substrate **1.50** (55 mg, 0.14 mmol, 1.0 equiv), MeMgI (0.10 mL, 0.28 mmol, 2.0 equiv), PhMe (1.0 mL). The compound was purified by flash chromatography (0–10% EtOAc/hexanes) to afford the title compound as a clear, colorless oil (30. mg, 0.11 mmol, 79%). **TLC R_f =** 0.8 (5% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (s, 4H), 7.37–7.33 (m, 2H), 7.30 (s, 1H), 7.09 (d, J = 7.0 Hz, 1H), 2.00–1.93 (m, 1H), 1.01 (aq, J = 6.5 Hz, 2H), 0.75 (aq, J = 5.0 Hz, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 145.1, 145.0, 140.0, 129.5 (q, J = 32.8 Hz, 1C), 129.1, 127.6 (2C), 125.8 (q, J = 3.7 Hz, 2C), 125.5, 125.1, 124.6, 124.5 (q, J = 271.9 Hz, 1C), 15.6, 9.5 (2C); **^{19}F NMR** (564.6 MHz, $CDCl_3$) δ –62.4; **HRMS** (TOF MS ES+) *m/z:* $[M]^+$ calculated for $C_{16}H_{13}F_3$, 262.0969; found, 262.0956.



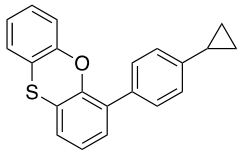
3'-cyclopropyl-3,4,5-trimethoxy-1,1'-biphenyl (1.8) was prepared according to Method B. The following amounts of reagents were used: The reaction was performed on a 0.1 mmol scale to obtain a ^{1}H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used on a 0.1 mmol scale: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), dppm (3.8 mg, 5.0 µmol, 5.0 mol %), substrate **1.52** (0.84 mL, 0.10 mmol, 1.0 equiv, 0.24 M stock soln in DCM/PhMe), DCM (0.10 mL), PhMe (0.40 mL), MeMgI (0.8 mL, 0.2 mmol, 2.6 M solution in Et_2O, 2.0 equiv). A ^{1}H NMR yield of 78% yield was obtained based on comparison to PhTMS as internal standard. The following amounts of reagents were used on a 0.2 mmol scale: $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), dppm (3.8 mg, 10. µmol, 5.0 mol %), substrate **1.52** (83 mg, 0.20 mmol,

1.0 equiv), DCM (0.20 mL), PhMe (0.80 mL, 0.20 M in substrate), MeMgI (0.34 mL, 0.40 mmol, 2.6 M solution in Et_2O, 2.0 equiv). The compound was purified by column chromatography (100% hexanes) to afford a clear oil (34 mg, 0.12 mmol, 60% yield). **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31–7.25 (m, 3H), 7.02 (s, 1H), 6.76 (s, 2H), 3.92 (s, 3H), 3.89 (s, 3H), 3.79 (s, 3H), 1.99–1.93 (m, 1H), 1.01–0.97 (m, 2H), 0.77–0.73 (m, 2H); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 153.5 (2C), 144.5, 141.5, 137.7, 137.6, 128.8, 124.9, 124.41, 124.39, 104.6 (2C), 61.0, 56.3 (2C), 15.5, 9.3 (2C); **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calcd for $C_{18}H_{20}O_3Na$, 307.1310; found, 307.1309.



1-(3'-Cyclopropyl-[1,1'-biphenyl]-3-yl)ethan-1-ol (1.9) was prepared according to Method B. The reaction was performed on a 0.1 mmol scale to obtain a ^{1}H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used on a 0.1 mmol scale: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), dppm (3.8 mg, 5.0 µmol, 5.0 mol %), substrate **1.54** (0.16 mL, 0.10 mmol, 1.0 equiv, 0.62 M stock soln in DCM/PhMe), DCM (0.10 mL), PhMe (0.40 mL), MeMgI (0.16 mL, 0.2 mmol, 2.6 M solution in Et_2O, 2.0 equiv). A ^{1}H NMR yield of 67% yield was obtained based on comparison to PhTMS as internal standard. The following amounts of reagents were used on a 0.2 mmol scale: $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), dppm (3.8 mg, 10. µmol, 5.0 mol %), substrate **1.54** (76 mg, 0.20 mmol, 1.0 equiv), DCM (0.20 mL), PhMe (0.80 mL), MeMgI (0.34 mL, 0.40 mmol, 2.6 M solution in Et_2O, 2.0 equiv). The compound was purified by column chromatography (25% EtOAc/hexanes) to afford a clear oil (33 mg, 0.14 mmol, 64% yield). **TLC R_f =** 0.5 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.49 (d,

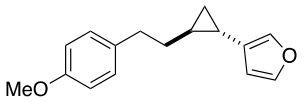
J = 7.7 Hz, 1H), 7.46–7.29 (m, 5H), 7.04 (d, *J* = 7.6 Hz, 1H), 4.94 (q, *J* = 6.6 Hz, 1H), 2.03–1.89 (m, 2H), 1.53 (d, *J* = 6.5 Hz, 3H), 1.00–0.92 (m, 2H), 0.78– 0.73 (m, 2H); **^{13}C NMR** (125.7 MHz, $CDCl_3$**)** δ 146.9, 145.1, 142.3, 141.7, 129.5, 129.3, 126.9, 125.4, 125.2, 125.0, 124.9, 124.8, 71.1, 25.8, 16.1, 9.8 (2C); **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calcd for $C_{17}H_{18}ONa$, 375.0434; found, 375.0421.



3-(4-Cyclopropylphenyl)phenoxathiine (1.10) was prepared according to Method B. The following amounts of reagents were used: The reaction was performed on a 0.1 mmol scale to obtain a ^{1}H NMR yield and on a 0.2 mmol scale to isolate the product. The following amounts of reagents were used on a 0.1 mmol scale: $Ni(cod)_2$ (1.4 mg, 5.0 µmol, 5.0 mol %), dppm (3.8 mg, 5.0 µmol, 5.0 mol %), substrate **1.58** (0.36 mL, 0.10 mmol, 1.0 equiv, 0.28 M stock solution in DCM/PhMe), DCM (0.11 mL), PhMe (0.37 mL), MeMgI (0.80 mL, 0.20 mmol, 2.6 M solution in Et_2O, 2.0 equiv). A ^{1}H NMR yield of 78% yield was obtained based on comparison to PhTMS as internal standard. The following amounts of reagents were used on a 0.2 mmol scale: $Ni(cod)_2$ (3.0 mg, 11 µmol, 5.0 mol %), dppm (4.2 mg, 11 µmol, 5.0 mol %), substrate **1.58** (99 mg, 0.22 mmol, 1.0 equiv), PhMe (1.0 mL, 0.20 M in substrate), MeMgI (0.17 mL, 0.44 mmol, 2.6 M solution in Et_2O, 2.0 equiv). The compound was purified by column chromatography (100% hexanes) to afford a clear oil (54 mg, 0.17 mmol, 78% yield). **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.28–6.98 (m, 8H), 6.90 (d, *J* = 8.1 Hz, 1H), 1.95 (q, *J* = 13.3, 8.6, 5.0 Hz, 1H), 1.03–0.95 (m, 2H), 0.81–0.75 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 152.8, 149.4, 143.5, 134.3, 131.7, 129.5 (2C), 129.3, 127.7, 126.8, 125.9, 125.5 (2C),

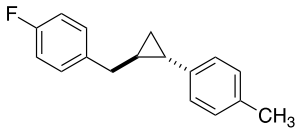
124.7, 124.4, 121.8, 121.4, 117.8, 15.4, 9.5 (2C); **HRMS** (TOF MS Cl+) *m/z:* $[M]^+$ calcd for $C_{21}H_{16}OS$, 316.0922; found, 316.0918.

1.4.3.3 1,2-Disubstituted Arylcyclopropanes



3-(2-(4-Methoxybenzyl)cyclopropyl)furan (1.15) was prepared according to Method B. The following amounts of reagents were used: substrate **1.14** (0.26 mL, 0.20 mmol, 1.0 equiv, 0.77 M soln in PhMe), $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), dppm (3.8 mg, 10. µmol, 5.0 mol %), MeMgI (0.14 mL, 0.20 mmol, 2.0 equiv, 2.9 M soln in Et_2O) and PhMe (0.5 mL). The compound was run through a silica plug with Et_2O (neat) and a 62% ^1H NMR yield was obtained. To remove the β-hydride elimination byproducts, a dihydroxylation was prepared on unpurified cyclopropane. The following amounts of reagents were used: 38 (0.20 mmol, 1.0 equiv), AD mix β (280 mg, 0.36 mmol, 1.8 equiv), *t*BuOH (1 mL), and H_2O (1 mL). After dihydroxylation, the unpurifed residue was purified by column chromatography (100% hexanes) to afford a clear oil (22 mg, 0.096 mmol, 48% yield). The desired compound was characterized as a 4:1 mixture of diastereomers (trans:cis). **TLC R_f =** 0.8 (100% hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (s, 1H, minor diastereomer), 7.29 (m, 1H, major, 1H, minor), 7.21 (s, 1H, major diastereomer), 7.17 (d, *J* = 8.4 Hz, 2H, major diastereomer), 7.06 (d, *J* = 8.4 Hz, 2H, minor diastereomer), 6.84 (d, *J* = 8.6 Hz, 2H, major diastereomer), 6.79 (d, *J* = 8.3 Hz, 2H, minor diastereomer), 6.26 (s, 1H, minor diastereomer), 6.11 (s, 1H, major diastereomer), 3.79 (s, 3H, major diastereomer), 3.77 (s, 3H, minor diastereomer), 2.68 (dd, *J* = 15.3, 7.3 Hz, 1H, major diastereomer), 2.60 (dd, *J* = 15.2, 7.4 Hz, 1H, major diastereomer), 2.49 (dd, *J* = 15.2, 7.3 Hz, 1H, minor diastereomer), 2.34 (dd, *J* = 15.3, 7.3 Hz, 1H, minor diastereomer), 1.90–1.85 (m, 1H, minor diastereomer), 1.58–1.55 (m, 1H, major diastereomer), 1.19–1.12 (m, 1H, major diastereomer), 1.07–1.02 (m, 1H, minor

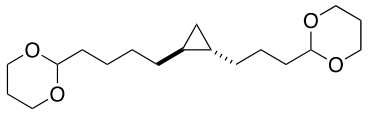
diastereomer), 0.79–0.75 (m, 2H, major diastereomer), 0.54–0.50 (m, 2H, minor diastereomer); The desired compound was characterized by ^{13}C NMR as a single diastereomer. **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 158.1, 142.9, 138.3, 133.6, 129.3 (2C), 127.6, 113.8 (2C), 109.4, 55.4, 38.9, 22.5, 14.4, 13.9; **HRMS** (TOF MS Cl+) *m/z:* $[M+H]^+$ calculated for $C_{15}H_{16}O_2$, 228.1150; observed, 228.1148.



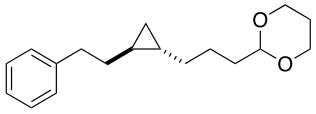
1-Fluoro-4-((2-(p-tolyl)cyclopropyl)methyl)benzene (1.16) was prepared according to Method B. The following amounts of reagents were used: substrate **1.63** (62 mg, 0.17 mmol, 1.0 equiv), $Ni(cod)_2$ (2.2 mg, 8.0 µmol, 5.0 mol %), dppm (3.1 mg, 8.0 µmol, 5.0 mol %), MeMgI (0.13 mL, 0.32 mmol, 2.0 equiv, 2.5 M in Et_2O), and PhMe (0.85 mL). The residue was purified via column chromatography (0–10% EtOAc/hexanes) to afford a clear oil (28 mg, 64% yield, 4% PhTMS by NMR). Due to the volatility of the compound, the desired compound was characterized with a small amount of PhTMS. The desired compound was characterized as a 4:1 mixture of diastereomers (trans:cis). **TLC R_f =** 0.7 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20–7.17 (m, 1H, major, 1H, minor), 7.11–6.89 (m, 8H, major, 8H, minor), 2.69 (qd, J = 14.7, 6.6 Hz, 2H, major diastereomer), 2.43 (qd, J = 15.2, 6.9 Hz, 2H, minor diastereomer), 2.32 (s, 3H, minor diastereomer), 2.29 (s, 3H, minor diastereomer), 2.21–2.17 (m, 1H, minor diastereomer), 1.76–1.72 (m, 1H, major diastereomer), 1.35–1.31 (m, 1H, minor diastereomer), 1.28–1.23 (m, 1H, major diastereomer), 1.07–1.02 (m, 1H, minor diastereomer), 0.96–0.92 (m, 1H, major diastereomer), 0.88–0.84 (m, 1H, major diastereomer), 0.81–0.77 (m, 1H, minor diastereomer); The desired compound was characterized by ^{13}C NMR as a single diastereomer. **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 261.5 (d, J = 243.7 Hz), 140.2, 137.2 (d, J = 3.2 Hz), 135.1, 129.7 (d, J = 7.9 Hz,

2C), 129.1 (2C), 125.8 (2C), 115.1 (d, J = 20.8 Hz, 2C), 39.3, 24.0, 23.1, 21.1, 15.8; **^{19}F NMR** (564.6 MHz, $CDCl_3$) δ –117.55 (major diastereomer), –117.99 (minor diastereomer); **HRMS** (TOF MS CI+) *m/z:* $[M+NH4]^+$ calculated for $C_{17}H_{17}FNH_4$, 258.1658; observed, 258.1650.

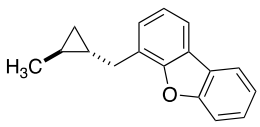
1.4.3.4 1,2-Disubstituted Alkylcyclopropanes



2-(3-(2-(4-(1,3-Dioxan-2-yl)butyl)cyclopropyl)propyl)-1,3-dioxane (1.17) was prepared according to Method B. The following amounts of reagents were used: substrate **1.68** (0.129, 0.256 mmol, 1.00 equiv), $Ni(cod)_2$ (3.5 mg, 13 µmol, 5.0 mol %), dppm (4.9 mg, 13 µmol, 5.0 mol %), MeMgI (0.20 mL, 0.51 mmol, 2.0 equiv, 2.5 M in Et_2O), and PhMe (1.3 mL). To remove the β-hydride elimination byproducts, a dihydroxylation was prepared on unpurified cyclopropane. The following amounts of reagents were used: 36 (0.256 mmol, 1.00 equiv), AD mix β (280 mg, 0.36 mmol, 1.8 equiv), *t*-BuOH (1 mL), and H_2O (1 mL). The residue was purified by column chromatography (0–25% EtOAc/hexanes) to afford a clear oil (48 mg, 0.15 mmol, 58% yield). The desired cyclopropane was characterized as a 2:1 mixture of diastereomers (trans:cis). **TLC R_f** = 0.5 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.51–4.49 (m, 2H, major, 2H, minor), 4.11–4.08 (m, 4H, major, 4H, minor), 3.79–3.73 (m, 4H, major, 4H, minor), 2.11–1.98 (m, 4H, major, 4H, minor), 1.62–1.17 (m, 14H, major, 14H, minor), 0.69–0.62 (m, 2H, minor diastereomer), 0.59–0.54 (m, 1H, minor diastereomer), 0.38– 0.36 (m, 2H, major diastereomer), 0.15–0.12 (m, 2H, major diastereomer), –0.29 to –0.34 (m, 1H, minor diastereomer); The major diastereomer was characterized by ^{13}C NMR. **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 102.55, 102.49, 66.9 (4C), 35.3, 35.1, 34.18, 34.16, 29.5, 25.9 (2C), 24.1, 23.9, 18.7, 18.6, 11.8; **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{18}H_{32}O_4Na$, 335.2198; observed, 225.2200.



2-(3-(2-Phenethylcyclopropyl)propyl)-1,3-dioxane (1.18) was prepared according to Method B. The following amounts of reagents were used: substrate **1.71** (0.4 mL, 0.2 mmol, 1 equiv, 0.5 M soln in PhMe), $Ni(cod)_2$ (2.8 mg, 10. µmol, 5.0 mol %), dppm (3.8 mg, 10. µmol, 5.0 mol %), MeMgI (0.16 mL, 0.40 mmol, 2.0 equiv, 2.5 M in Et_2O), and PhMe (1 mL). To remove the β-hydride elimination byproducts, a dihydroxylation was prepared on unpurified cyclopropane. The following amounts of reagents were used: 34 (0.2 mmol, 1 equiv), AD mix β (280 mg, 0.36 mmol, 1.8 equiv), *t*-BuOH (1 mL), and H_2O (1 mL). The residue was purified by column chromatography (0–25% EtOAc/hexanes) to afford a clear oil (29 mg, 0.10 mmol, 52% yield). The desired compound was characterized as a 4:1 mixture of diastereomers (trans:cis). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27–7.16 (m, 15H, major, 5H, minor), 4.51–4.48 (m, 1H, major, 1H, minor), 4.11–4.08 (m, 2H, major, 2H, minor), 3.77–3.72 (m, 2H, major, 2H, minor), 2.69–2.59 (m, 2H, major, 2H, minor), 2.10–2.03 (m, 2H, major, 2H, minor), 1.71–1.17 (m, 8H, major, 8H, minor), 0.74–0.68 (m, 2H, minor diastereomer), 0.64–0.58 (m, 1H, minor diastereomer), 0.44–0.41 (m, 2H, major diastereomer), 0.20–0.18 (m, 2H, major diastereomer), –0.26 to 0.28 (m, 1H, minor diastereomer); The major diastereomer was characterized by ^{13}C NMR. **^{13}C NMR (125.8 MHz, $CDCl_3$)** δ 142.8, 128.6 (2C), 128.3 (2C), 125.7, 102.6, 67.0 (2C), 36.4, 36.1, 35.2, 34.2, 26.0, 24.2, 18.9, 18.6, 11.9; **HRMS** (TOF MS CI+) *m/z:* $[M+NH_4]^+$ calculated for $C_{18}H_{26}O_2NH_4$, 292.2277; observed, 292.2266.

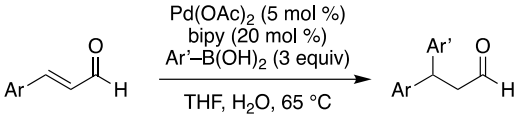


4-((2-Methylcyclopropyl)methyl)dibenzo[b,d]furan (1.19) was prepared according to Method B. The following amounts of reagents were used: **1.75** (0.23 mL, 0.20 mmol, 1.0 equiv), $Ni(cod)_2$ (2.8 mg, 10. μmol, 5.0 mol %), dppm (3.8 mg, 10 μmol, 5.0 mol %), MeMgI (0.14 mL, 0.40 mmol, 2.0 equiv, 2.9 M soln in Et_2O), and PhMe (1.0 mL). To remove the β-hydride elimination byproducts, a dihydroxylation was prepared on unpurified cyclopropane. The following amounts of reagents were used: 31 (0.20 mmol, 1.0 equiv), AD mix β (280 mg, 0.36 mmol, 1.8 equiv), *t*-BuOH (1 mL), and H_2O (1 mL). The residue was purified by column chromatography (100% hexanes) to afford a clear oil (23 mg, 0.97 mmol, 48% yield). The desired compound was characterized as a 2:1 ratio of diastereomers (trans:cis). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.8 Hz, 1H, major, 1H, minor), 7.80 (d, J = 7.6 Hz, 1H, major, 1H, minor), 7.58 (d, J = 8.2 Hz, 1H, major, 1H, minor), 7.45–7.42 (m, 1H, major, 1H, minor), 7.38–7.27 (m, 3H, major, 3H, minor), 3.05–2.95 (m, 2H, minor diastereomer), 2.92–2.90 (m, 2H, major diastereomers), 1.23–1.19 (m, 1H, minor diastereomer), 1.17 (d, J = 6.4 Hz, 3H, major diastereomer), 1.06 (d, J = 6.0 Hz, 3H, major diastereomer), 0.97–0.85 (m, 2H, major diastereomer), 0.78–0.70 (m, 2H, minor diastereomer), 0.48–0.45 (m, 1H, major diastereomer), 0.30–0.27 (m, 1H, major diastereomer), 0.03–0.01 (m, 1H, minor diastereomer); The desired compound was characterized by ^{13}C NMR as a single diastereomer. **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 156.2 (one diastereomer), 154.8 (other diastereomer), 127.03 (2C, both diastereomers), 126.99 (3C, both diastereomers), 126.93 (one diastereomer), 126.52 (other diastereomer), 124.8 (one diastereomer), 123.82 (other diastereomer), 123.78 (one diastereomer), 122.90 (other diastereomer), 122.8 (2C, both diastereomers), 122.6 (3C, both diastereomers), 120.8 (2C, both diastereomers), 118.3 (one diastereomer), 118.2 (other diastereomer), 118.8 (2C, both diastereomers), 33.9 (one diastereomer), 28.3 (other diastereomer), 19.5 (one diastereomer), 19.0

(one diastereomer), 15.5 (other diastereomer), 13.6 (other diastereomer), 13.31 (one diastereomer), 13.29 (one diastereomer), 12.5 (other diastereomer), 10.1 (other diastereomer); **HRMS** (TOF MS CI+) *m/z:* $[M]^+$ calculated for $C_{17}H_{16}O$, 236.1201; observed, 236.1202.

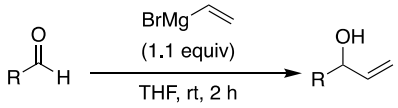
1.4.4 General Procedures for Starting Material Synthesis

1.4.4.1 Method C: Pd-Catalyzed Conjugate Addition



The target compound was prepared using a modified procedure reported by Lin.[18] A Schlenk flask equipped with stir bar was charged with arylboronic acid (3.0 equiv), $Pd(OAc)_2$ (5.0 mol %), and bipy (20 mol %) were added, and flask was placed under vacuum and backfilled with N_2 (x 3). Then, THF (2 M in aldehyde), H_2O (3 M in aldehyde), and acetic acid (1 M in aldehyde) were added. Aldehyde (1.0 equiv) was then added, and reaction was heated at 65 ºC and allowed to stir overnight. The reaction was cooled to rt, quenched with sat. $NaHCO_3$, and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.2 Method D: Vinyl Grignard Addition into Aldehydes

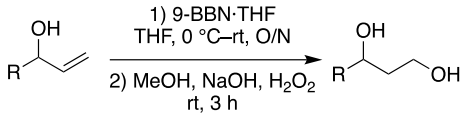


A flame-dried flask with stir bar was charged with vinylmagnesium bromide (1.1 equiv) and cooled to 0 ºC. A solution of aldehyde (1.0 equiv) in anhydrous THF was added in a dropwise. The reaction mixture was stirred at room temperature for at least 2 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and the mixture was extracted with EtOAc (3 x 20 mL).

[18] Lu, X.; Lin, S. *J. Org. Chem.* **2005**, *70*, 9651–9653.

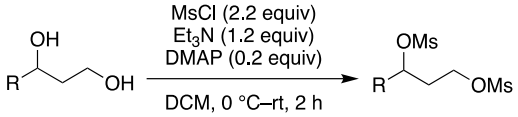
The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.3 Method E: Hydroboration-Oxidation



The target compound was prepared using a modified procedure reported by Hartwig.[19] A round bottom flask equipped with stir bar was charged with alkene (1.0 equiv) and THF (0.4 M). The flask was cooled to 0 ºC, and 9-BBN·THF (2.5 equiv) was added slowly. The reaction mixture was then warmed to rt and stirred overnight. Then, MeOH (3 mL/mmol), H_2O_2 (30%, 1 mL/mmol) and NaOH (3.0 M, 1 mL/mmol) were added, and the reaction stirred for at least 3 h. Once complete, H_2O (10 mL) was added. The reaction mixture was then extracted with EtOAc (3 x 20 mL) and combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo.

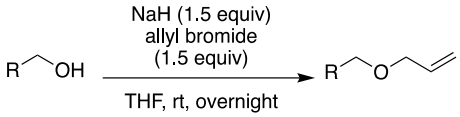
1.4.4.4 Method F: Mesylation of Diols



A round bottom flask equipped with stir bar was charged with alcohol (1.0 equiv) and DCM (0.2 M) under N_2. Then, Et_3N (1.5 equiv), DMAP (0.2 equiv), and MsCl (2.2 equiv) were added. The reaction mixture was then stirred at rt for at least 3 h. Once complete by TLC, sat. $NaHCO_3$ (5 mL) was added and the reaction mixture was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

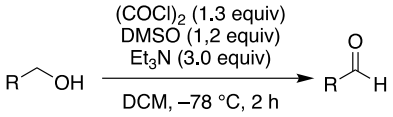
[19] Stanley, L. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 8971–8983.

1.4.4.5 Method G: Allylation of Alcohols



The target compound was prepared using a modified procedure reported by Yang.[20] In a glovebox, a flame-dried flask equipped with stir bar was charged with sodium hydride (1.5 equiv). The flask was sealed with septum, removed from the glovebox, and placed under N_2. Alcohol (1.0 equiv) was slowly added as a solution in anhydrous THF (1.0 M) at rt and allowed to stir. After 2–3 h, allyl bromide (1.5 equiv) was added. The reaction mixture was stirred overnight. To quench, saturated NH_4Cl (10 mL) was added. The reaction mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.6 Method H: Swern Oxidation of Primary Alcohols to Aldehydes



The target compound was prepared using a modified procedure reported by Kobayashi.[21] A flame-dried round bottom flask equipped with stir bar was charged with alcohol (1.0 equiv), and DCM (0.2 M). The reaction flask was cooled to –78 ºC, then oxalyl chloride (1.3 equiv) and DMSO (1.2 equiv) were added under N_2 with vent. The reaction mixture was allowed to stir at –78 ºC for 2 h. Then, trimethylamine (3.0 equiv) was added and the reaction was warmed to rt. To quench, saturated NH_4Cl (10 mL) was added and the reaction was extracted with DCM (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

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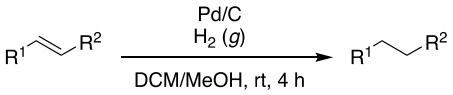
[20] Fu, M.; Chen, L.; Jiang, Y.; Jiang, Z.-X.; Yang, Z. *Org. Lett.* **2016**, *18*, 348–351.

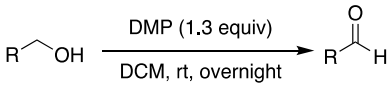
[21] Shinohara, R.; Morita, M.; Ogawa, N.; Kobayashi, Y. *Org. Lett.* **2019**, *21*, 3247–3251.

1.4.4.7 Method I: Palladium on Carbon Reduction of Alkenes



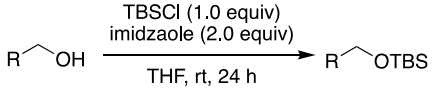
A round-bottom flask with stir bar was charged with palladium on carbon (1.0 mg/ 3.5 mmol of substrate), flushed with N_2, and capped with septum. Slowly DCM was added, until Pd/C was fully submerged. Then, MeOH or EtOH (0.2 M in substrate), and alkene (1.0 equiv) were added. Vacuum was pulled on the flask until the solvent began to bubble, at which point the flask was backfilled with N_2 (x 3). An H_2 balloon was added and the reaction mixture was allowed to stir vigorously for 4 h. The balloon was then removed, and the flask was purged with N_2 for 30 min. The septum was removed, and the reaction mixture was filtered through celite using MeOH (100 mL). The filtrate was then concentrated in vacuo.

1.4.4.8 Method J: DMP Oxidation of Primary Alcohols to Aldehydes



The target compound was prepared using a modified procedure reported by Fernandes.[22] A flame-dried round bottom flask equipped with stir bar was charged with alcohol (1.0 equiv), and DCM (0.2 M). To the reaction flask was added Dess-Martin periodinane (DMP; 1.3 equiv) in one portion. The reaction mixture was stirred overnight. To quench, saturated $NaHCO_3$ (10 mL) was added and the reaction was extracted with DCM (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

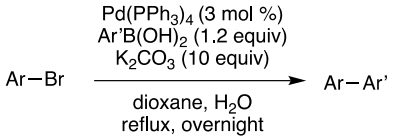
1.4.4.9 Method K: TBS Protection



[22] Halle, M. B.; Fernandes, R. A. *RSC. Adv.* **2014**, *4*, 63342–63348.

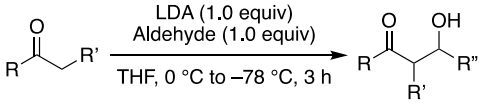
A flame-dried round-bottom flask equipped with a stir bar was charged with alcohol (1.0 equiv), TBSCl (1.0 equiv), imidazole (2.0 equiv), and THF (0.5 M in substrate) were added. The reaction mixture was allowed to stir at rt for 24 h. The reaction mixture was diluted with H_2O and extracted with Et_2O (3 x 150 mL). The combined organic layers were dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.10 Method L: Suzuki–Miyaura Cross-Coupling with $Pd(PPh_3)_4$



The target compound was prepared using a modified procedure reported by Nagano.[23] A two-neck round-bottom flask was equipped with reflux condenser and stir bar. Aryl bromide (1.0 equiv), $Pd(PPh_3)_4$ (0.030 equiv), Ar'–$B(OH)_2$ (1.2 equiv), K_2CO_3 (10. equiv), and dioxane/H_2O (4:1 ratio, 0.1 M) were added under N_2. The reaction mixture was allowed to stir at reflux overnight. Once complete, H_2O (10 mL) was added. The reaction mixture was then extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.11 Method M: Aldol Addition Using LDA

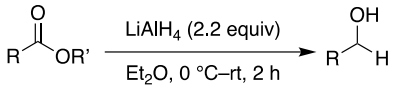


The target compound was prepared using a modified procedure reported by Heathcock.[24] To a flame-dried flask with stir bar, diisopropylamine (1.0 equiv) and THF (0.50 M in amine) were

[23] Terai, T.; Kohno, M.; Boncompain, G.; Sugiyama, S.; Saito, N.; Fujikake, R.; Ueno, T.; Komatsu, T.; Hanaoka, K.; Okabe, T.; Urano, Y.; Perez, F.; Nagano, T. *J. Am. Chem. Soc.* **2015**, *137*, 10464–10467.
[24] Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066–1081.

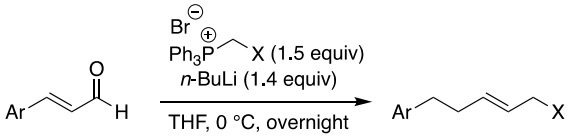
added under N_2. The flask was then cooled to 0 ºC and *n*-BuLi (1.0 equiv) was added slowly. The reaction stirred for 1 h at 0 ºC, then was cooled to –78 ºC and ester or aldehyde (1.0 equiv) was added dropwise. The reaction stirred for 1 h, then electrophile (1.0 equiv) was added and reaction continued to stir for 2 h. The reaction was quenched with sat. NH_4Cl (10 mL) and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried with Na_2SO_4 and concentrated in vacuo.

1.4.4.12 Method N: $LiAlH_4$ Reduction



In a glove box, a flame-dried flask was charged with $LiAlH_4$ (2.2 equiv), capped with stopper and removed from glovebox. An N_2 inlet and anhydrous Et_2O (0.2 M) were added. The reaction flask was cooled to 0 ºC and substrate (1.0 equiv) was added as a solution in Et_2O (1.0 M). The reaction was warmed to rt and stirred for 2 h. To quench, saturated NH_4Cl was added and reaction was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.13 Method O: Wittig Reaction

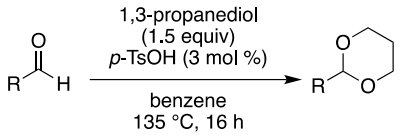


The target compound was prepared using a modified procedure reported by Cossy.[25] A flame-dried flask under N_2 equipped with a stir bar was charged with triphenyl phosphonium salt (1.5 equiv), and THF (0.2 M). At 0 ºC, *n*-BuLi (1.4 equiv, 2.5 M in hexanes) was added dropwise to the solution and the mixture was allowed to stir for 30 min. A solution of aldehyde in THF was slowly over 5

[25] Specklin, S.; Fenneteau, J.; Subramanian, P.; Cossy, J. *Chem. Eur. J.* **2018**, *24*, 332–336.

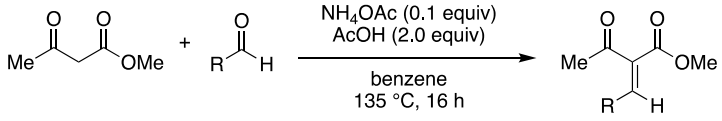
minutes and allowed to stir overnight. To quench, a saturated solution of NH_4Cl was added and the reaction was diluted with H_2O. The reaction was then extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.14 Method P: Acetal Formation



The target compound was prepared using a modified procedure reported by Koshino.[26] To a flame-dried round bottom flask equipped with a stir bar, the desired aldehyde (1.0 equiv), 1,3-propanediol (1.5 equiv), *p*-toluenesulfonic acid (3.0 mol %), and benzene (0.5 M in substrate) were added. The reaction flask was equipped with a Dean–Stark apparatus and a condenser, and was heated to 135 °C overnight. After cooling to rt, the reaction mixture was quenched with H_2O, extracted with EtOAc (3x), dried over Na_2SO_4, and concentrated in vacuo.

1.4.4.15 Method Q: Knoevenagel Condensation



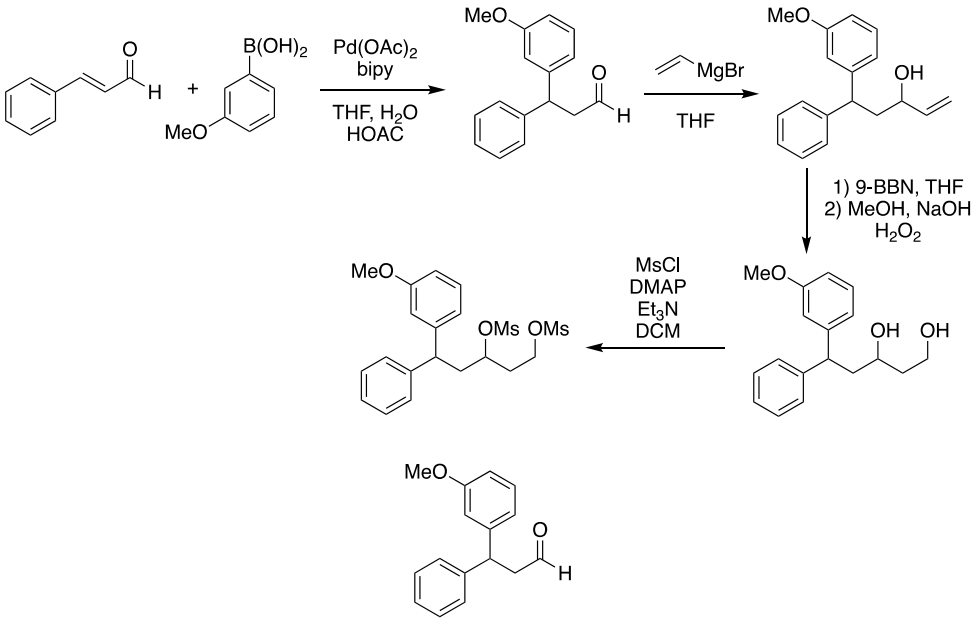
The target compound was prepared using a modified procedure reported by Hong.[27] To a round-bottom flask equipped with a stir bar, the desired aldehyde (1 equiv), the desired ester (1 equiv), NH_4OAc (0.1 equiv), AcOH (2.5 mol %) and benzene (1 M in substrate) were added. The round-bottom flask was then fitted with a Dean–Stark apparatus and reflux condenser. The reaction mixture was heated to 135 °C and allowed to stir overnight. After cooling the reaction flask to rt,

[26] Koshino, J.; Fujikura, Y.; Fujita, M.; Toi, N. Kao Corportation. U.S. Patent 4,978,653, December 18, 1990.
[27] Hong, S.; Lee, M.; Jung, M.; Park, Y.; Kim, M.-H.; Park, H.-G. *Tetrahedron Lett.* **2012**, *53*, 4209–4211.

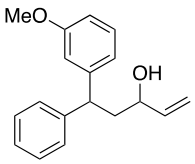
the reaction mixture was quenched with H_2O. The aqueous layer was extracted with EtOAc (3x), dried with Na_2SO_4, and concentrated in vacuo.

1.4.5 Intermediates and 1,3-Dimesylates for Monosubstituted Alkylcyclopropane Synthesis

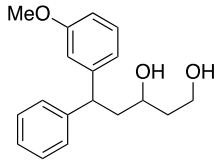
Scheme 1.7 Synthesis of 1,3-dimesylate **1.1** leading to cyclopropane **1.2**.



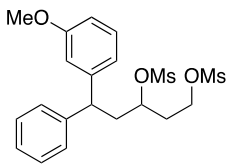
3-(3-Methoxyphenyl)-3-phenylpropanal (1.20) was prepared according to Method C. The following amounts of reagents were used: trans-cinnamaldehyde (0.88 mL, 7.0 mmol, 1.0 equiv), 3-methoxyphenyl boronic acid (3.2 g, 21 mmol, 3.0 equiv), $Pd(OAc)_2$ (78 mg, 0.35 mmol, 5.0 mol %), bipyridine (220 mg, 1.4 mmol, 0.20 equiv), THF (3.5 mL), HOAc (7 mL), and H_2O (2.1 mL). The compound was purified by column chromatography (0–25% EtOAc/hexanes) to afford a clear oil (1.183 g, 4.92 mmol, 70% yield). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.29–7.17 (m, 6H), 6.82–6.72 (m, 3H), 4.57 (t, J = 7.8 Hz, 1H), 3.77 (s, 3H), 3.13 (d, J = 7.6 Hz, 2H).



5-(3-Methoxyphenyl)-5-phenylpent-1-en-3-ol (1.21) was prepared according to Method D. The following amounts of reagents were used: **1.20** (1.2 g, 4.9 mmol, 1.0 equiv), vinylmagnesium bromide (17 mL, 12 mmol, 2.0 equiv), THF (13 mL, 0.20 M in substrate). The compound was purified by column chromatography (25% EtOAc/hexanes) to afford a clear oil (0.88 g, 61% yield, contains 32% EtOAc by NMR). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28–7.17 (m, 6H), 6.88–6.84 (m, 1H), 6.83–6.80 (m, 1H), 6.74–6.69 (m, 1H), 5.89 (ddd, *J* = 17.3, 10.5, 6.4 Hz, 1H), 5.18 (d, *J* = 17.2 Hz, 1H), 5.11 (d, *J* = 10.3 Hz, 1H), 4.15 (td, *J* = 8.1, 2.2 Hz, 1H), 3.98–3.93 (m, 1H), 3.77 (s, 3H), 2.26–2.22 (m, 2H), 1.44 (add, *J* = 4.4, 1.8 Hz, 1H).

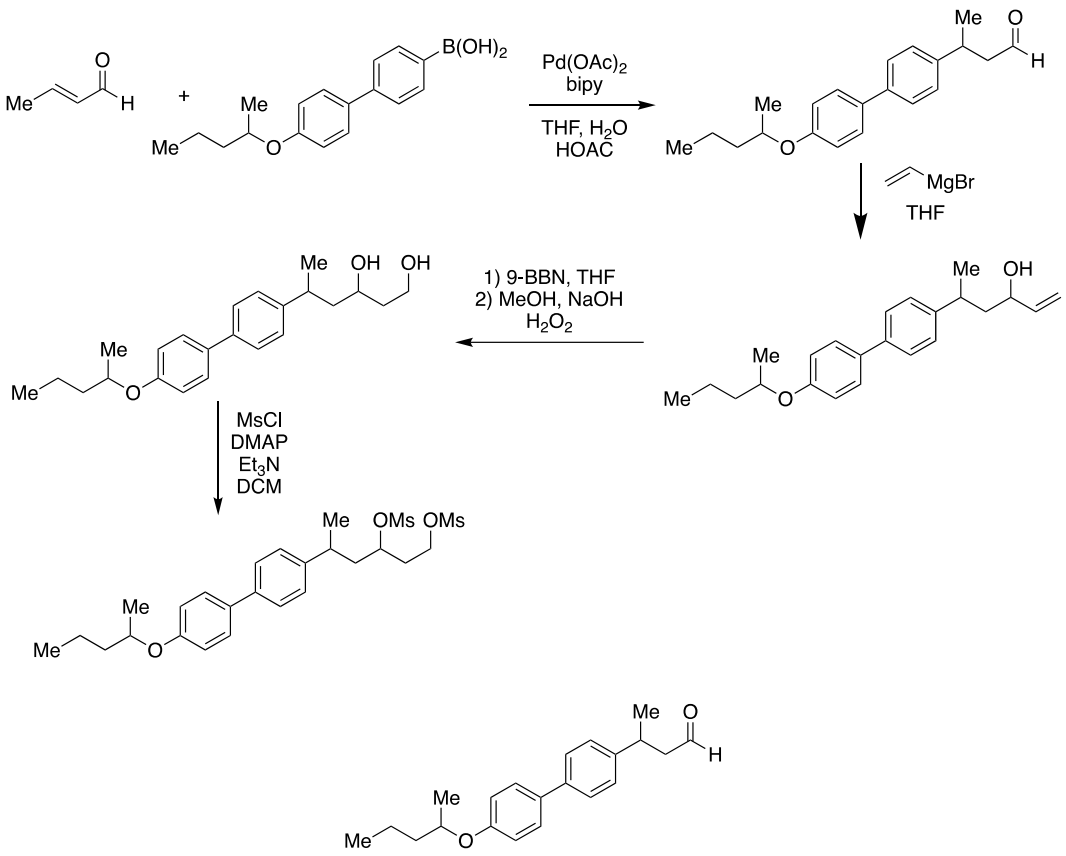


5-(3-Methoxyphenyl)-5-phenylpentane-1,3-diol (1.22) was prepared according to Method E. The following amounts of reagents were used: **1.21** (0.88 g, 3.3 mmol, 1.0 equiv), 9-BBN (17 mL, 8.3 mmol, 2.5 equiv), THF (8 mL, 0.2 M in substrate), MeOH (9.9 mL, 3.0 mL/mmol), NaOH (4.9 mL, 1.5 mL/mmol, 3.0 M aqueous solution), H_2O_2 (4.9 mL, 1.5 mL/mmol, 30% w/w). The compound was purified by flash column chromatography (3% MeOH/DCM) to afford a clear oil (0.79 g, 71% product, contains 33% EtOAc by ^{1}H NMR). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29–7.17 (m, 6H), 6.88–6.86 (m, 1H), 6.81 (s, 1H), 6.74–6.70 (m, 1H), 4.18 (t, *J* = 7.8 Hz, 1H), 3.88–3.83 (m, 1H), 3.79–3.74 (m, 5H), 2.32 (br s, 1H), 2.23–2.07 (m, 3H), 1.75–1.71 (q, *J* = 5.7 Hz, 2H).



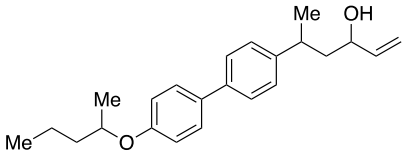
5-(3-Methoxyphenyl)-5-phenylpentane-1,3-diyl dimethanesulfonate (1.1) was prepared according to Method F. The following amounts of reagents were used: **1.22** (0.65 g, 2.4 mmol, 1.0 equiv), methanesulfonyl chloride (0.45 mL, 5.8 mmol, 2.4 equiv), dimethylaminopyridine (59 mg, 0.50 mmol, 0.20 equiv), Et_3N (0.80 mL, 5.8 mmol, 2.4 equiv), and DCM (5 mL, 0.5 M in substrate). The compound was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.54 g, 1.16 mmol, 48% yield). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32–7.18 (m, 6H), 6.85–6.72 (m, 3H), 4.78–4.75 (m, 1H), 4.35– 4.29 (m, 2H), 4.10–4.05 (m, 1H), 3.77 (s, 3H), 2.93 (s, 3H), 2.89 (s, 3H), 2.62–2.56 (m, 1H), 2.45–2.39 (m, 1H), 2.19–2.11 (m, 2H); **^{13}C NMR** (128.5 MHz, $CDCl_3$) δ 159.93 (2C, both diastereomers), 144.8 (2C, both diastereomers), 143.2 (one diastereomer), 143.0 (other diastereomer), 129.89 (one diastereomer), 129.86 (other diastereomer), 128.90 (2C, both diastereomer), 128.86 (2C, both diastereomers), 127.8 (2C, both diastereomers), 127.7 (2C, both diastereomers), 126.90 (one diastereomer), 126.85 (other diastereomer), 120.14 (one diastereomer), 120.08 (other diastereomer), 114.1 (one diastereomer), 113.7 (other diastereomer), 112.0 (one diastereomer), 111.8 (other diastereomer), 77.62 (one diastereomer), 77.57 (other diastereomer), 65.4 (2C, both diastereomers), 55.3 (2C, both diastereomers), 47.32 (one diastereomer), 47.29 (other diastereomer), 40.6 (2C, both diastereomers), 38.5 (2C, both diastereomers), 37.5 (2C, both diastereomers), 34.4 (one diastereomer), 34.3 (other diastereomer); **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calculated for $C_{20}H_{26}O_7S_2Na$, 465.1018; found, 465.1028.

Scheme 1.8 Synthesis of 1,3-dimesylate **1.26** leading to cyclopropane **1.3**.

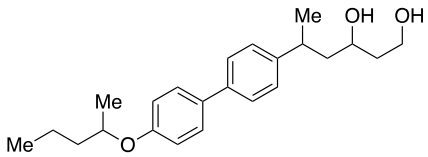


3-(4'-(Pentan-2-yloxy)-[1,1'-biphenyl]-4-yl)butanal (1.23) was prepared according to Method C. The following amounts of reagents were used: crotonaldehyde (0.21 mL, 2.5 mmol, 1.0 equiv), (4-(pentan-2-yloxy)phenyl)boronic acid (2.1 g, 7.5 mmol, 3.0 equiv), $Pd(OAc)_2$ (28 mg, 0.13 mmol, 5.0 mol %), bipyridine (78 mg, 0.50 mmol, 0.20 equiv), THF (1.25 mL), H_2O (0.75 mL), and HOAc (2.5 mL). The compound was purified by column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear, colorless oil (0.55 g, 62% yield, contains 30% DCM and 3% Et_2O by ^1H NMR). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.73 (t, J = 2.1 Hz, 1H), 7.49–7.45 (m, 4H), 7.25 (d, J = 8.2 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 4.40 (sext, J = 6.2 Hz, 1H), 3.39 (sext, J = 7.1 Hz, 1H), 2.74 (ddd, J = 16.6, 6.9, 1.9 Hz, 1H), 2.67 (ddd, J = 16.6,

7.6, 2.3, 7.6 Hz, 1H), 1.80–1.72 (m, 1H), 1.61–1.39 (m, 3H), 1.35 (d, *J* = 6.9 Hz, 3H), 1.32 (d, *J* = 6.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

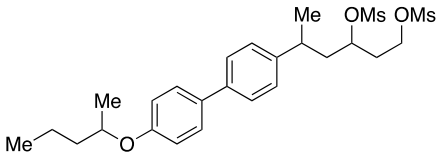


5-(4'-(Pentan-2-yloxy)-[1,1'-biphenyl]-4-yl)hex-1-en-3-ol (1.24) was prepared according to Method D. The following amounts of reagents were used: **1.23** (0.55 g, 1.6 mmol, 1.0 equiv), vinylmagnesium bromide (6.0 mL, 4.0 mmol, 2.5 equiv), and THF (2 mL, 0.2 M in substrate). The compound was purified by column chromatography (0–25% EtOAc/hexanes) to afford a clear oil (0.19 g, 32% yield, contains 29% EtOAc and 2% THF by ^{1}H NMR). The compound was characterized as a 2:1 mixture of diasteromers. **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50–7.46 (m, 12H, both diastereomers), 7.27–7.23 (m, 6H, both diastereomers), 6.95–6.92 (m, 6H, both diastereomers), 5.92–5.83 (m, 3H, both diastereomers), 5.22–5.04 (m, 6H, both diastereomers), 4.40 (sext, *J* = 6.0 Hz, 3H, both diastereomers), 4.20– 4.02 (m, 2H, one diastereomer), 3.96–3.89 (m, 1H, other diastereomer), 3.03 (sext, J = 7.2 Hz, 1H, one diastereomer), 2.89 (sext, *J* = 7.1 Hz, 2H, other diastereomer), 1.97–1.89 (m, 3H, both diastereomers), 1.82–1.72 (m, 6H, both diastereomers), 1.59–1.41 (m, 9H, both diastereomers), 1.32–1.24 (m, 18H, both diastereomers), 0.95 (t, *J* = 7.2 Hz, 9H, both diastereomers), 0.90–0.85 (m, 3H).



5-(4'-(Pentan-2-yloxy)-[1,1'-biphenyl]-4-yl)hexane-1,3-diol (1.25) was prepared according to Method E. The following amounts of reagents were used: **1.24** (190 mg, 0.60 mmol, 1.0 equiv), 9-

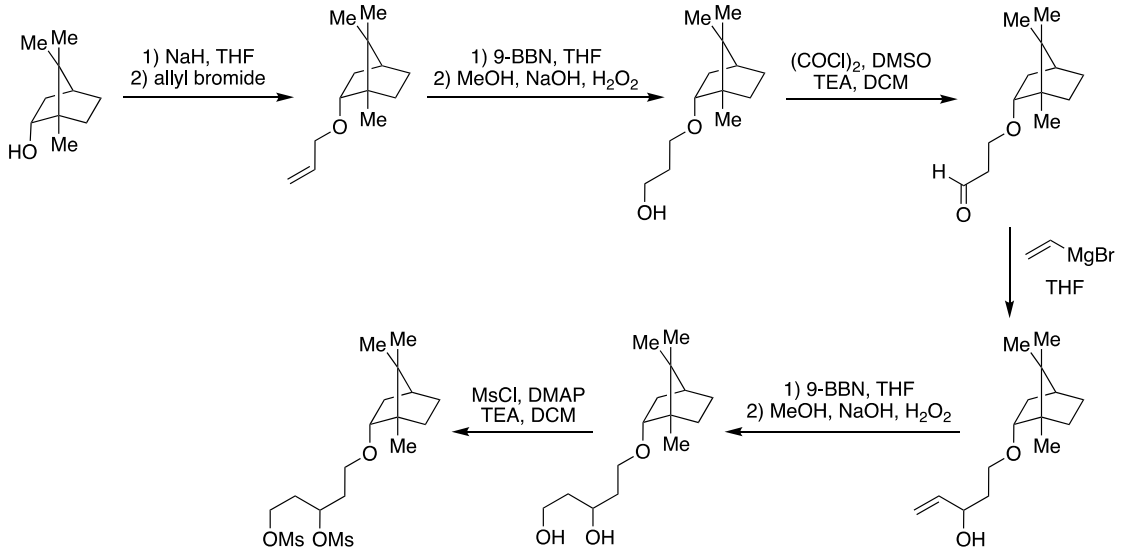
BBN (3.0 mL, 1.5 mmol, 2.5 equiv), THF (1.0 mL, 0.15 M in substrate), MeOH (1.8 mL, 3.0 mL/mmol), NaOH (0.90 mL, 1.5 mL/mmol, 3.0 M aqueous solution), and H_2O_2 (0.90 mL, 1.50 mL/mmol, 30% w/w). The compound was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.16 g, 70% yield, contains 13% DCM and 3% Et_2O). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49–7.46 (m, 8H, both diastereomers), 7.26–7.23 (m, 4H, both diastereomers), 6.93 (d, J = 8.8 Hz, 4H, both diastereomers), 4.39 (sext, J = 6.1 Hz, 2H, both diastereomers), 3.93–3.62 (m, 6H, both diastereomers), 3.06–2.97 (m, 1H, one diastereomer), 2.91 (sext, J = 7.3 Hz, 1H, other diastereomer), 2.43 (br s, 2H, both diastereomers), 2.32 (br s, 2H, both diastereomers), 1.92–1.39 (m, 16H, both diastereomers), 1.32–1.28 (m, 12H, both diastereomers), 0.95 (t, J = 7.1 Hz, 6H, both diastereomers).

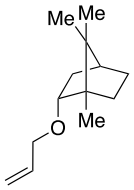


5-(4'-(Pentan-2-yloxy)-[1,1'-biphenyl]-4-yl)hexane-1,3-diyl dimethanesulfonate (1.26) was prepared according to Method F. The following amounts of reagents were used: **1.25** (0.250 g, 1.0 mmol, 1.0 equiv), dimethylaminopyridine (25 mg, 0.20 mmol, 0.20 equiv), Et_3N (0.33 mL, 2.4 mmol, 2.4 equiv), methanesulfonyl chloride (0.19 mL, 2.4 mmol, 2.4 equiv), and DCM (2 mL, 0.5 M in substrate). The compound was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.22 g, 0.44 mmol, 44% yield). **TLC R_f =** 0.5 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52–7.47 (m, 4H, both diastereomers), 7.25 (m, 2H, both diastereomers), 6.94 (d, J = 8.8 Hz, 2H, both diastereomers), 4.77–4.76 (m, 1H, both diastereomers), 4.42–4.38 (m, 1H, both diastereomers), 4.35–4.29 (m, 2H, both diastereomers), 3.12–2.82 (m, 6H, both diastereomers), 2.24–1.94 (m, 4H, both diastereomers), 1.78–1.72 (m, 1H,

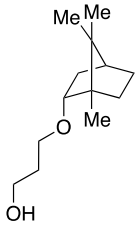
both diastereomers), 1.60–1.40 (m, 4H, both diastereomers), 1.34–1.31 (m, 6H, both diastereomers), 0.95 (t, J = 7.3 Hz, 3H, both diastereomers); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 157.89 (one diastereomer), 157.87 (other diastereomer), 143.8 (one diastereomer), 143.6 (other diastereomer), 139.33 (one diastereomer), 139.31 (other diastereomer), 133.0 (one diastereomer), 132.9 (other diastereomer), 128.0 (4C, both diastereomers), 127.5 (2C, one diastereomer), 127.3 (2C, other diastereomer), 127.0 (4C, both diastereomers), 116.1 (4C, both diastereomers), 77.8 (one diastereomer), 77.6 (other diastereomer), 73.8 (2C, both diastereomers), 65.57 (one diastereomer), 65.54 (other diastereomer), 43.1 (one diastereomer), 42.9 (other diastereomer), 38.7 (2C, both diastereomers), 38.5 (2C, both diastereomers), 37.45 (one diastereomer), 37.41 (other diastereomer), 36.1 (one diastereomer), 35.8 (other diastereomer), 34.6 (one diastereomer), 34.1 (other diastereomer), 23.2 (one diastereomer), 22.8 (other diastereomer), 19.8 (2C, both diastereomers), 18.8 (2C, both diastereomers), 14.1 (2C, both diastereomers); **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calculated for $C_{25}H_{36}O_7S_2Na$ 535.1800, found 535.1807.

Scheme 1.9 Synthesis of 1,3-dimesylate **1.32** leading to cyclopropane **1.4**.



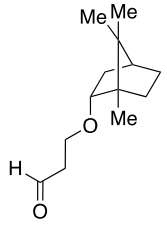


(1R,2R,4S)-2-(Allyloxy)-1,7,7-trimethylbicyclo[2.2.1]heptane (1.27) was prepared according to Method G. The following amounts of reagents were used: borneol (10. g, 65 mmol, 1.0 equiv), NaH (3.1 g, 130 mmol, 2.0 equiv), THF (130 mL, 0.50 M in substrate), and allyl bromide (6.8 mL, 78 mmol, 1.2 equiv). The compound was purified by column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear oil. **TLC R_f =** 0.9 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.92–5.87 (m, 1H), 5.36 (dd, J = 17.2, 1.9 Hz, 1H), 5.12 (dd, J = 10.4, 1.4, 1H), 4.00 (dd, J = 13.1, 5.1 Hz, 1H), 3.92 (dd, J = 13.4, 5.5 Hz, 1H), 3.64–3.60 (m, 1H), 2.12–2.01 (m, 2H), 1.70–1.61 (m, 2H), 1.27–1.20 (m, 2H), 1.02 (dd, J = 12.8, 3.9 Hz, 1H), 0.90 (s, 3H), 0.87 (s, 6H).

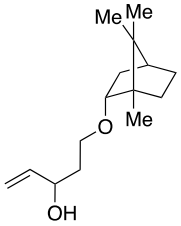


3-(((1R,2R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)oxy)propan-1-ol (1.28) was prepared according to Method E. The following amounts of reagents were used: **1.27** (7.1 g, 37 mmol, 1.0 equiv), 9-BBN (180 mL, 91 mmol, 2.5 equiv), THF (100 mL, 0.4 M in substrate), MeOH (110 mL, 3.0 ml/mmol), NaOH (55 mL, 1.5 mL/mmol, 3.0 M aqueous solution), and H_2O_2 (55 mL, 1.5 mL/mmol, 30% w/w). The compound was purified by flash column chromatography (0–5% MeOH/DCM) to afford the title compound as a clear oil (6.5 g, 31 mmol, 84% yield). **TLC R_f =** 0.5 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.79– 3.77 (m, 2H), 3.70–3.69 (m, 1H),

3.57–3.53 (m, 2H), 2.73 (t, *J* = 5.5 Hz, 1H), 2.17–2.09 (m, 1H), 1.85–1.81 (m, 2H), 1.70–1.63 (m, 3H), 1.27–1.18 (m, 2H), 1.01 (dd, *J* = 12.9, 3.1 Hz, 1H), 0.87 (s, 3H), 0.84 (s, 6H).

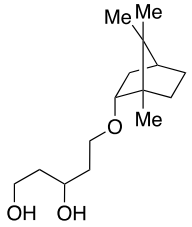


3-(((1R,2R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)oxy)propanal (1.29) was prepared according to Method H. The following amounts of reagents were used: **1.28** (6.5 g, 31 mmol, 1.0 equiv), DMSO (2.6 mL, 37 mmol, 1.2 equiv), oxalyl chloride (3.3 mL, 40. mmol, 1.3 equiv), Et_3N (13 mL, 92 mmol, 3.0 equiv), and DCM (100 mL, 0.3 M in substrate). The unpurified yellow oil was carried into the next step without further purification. **TLC R_f =** 0.9 (25% EtOAc/hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 3.82–3.79 (m, 1H), 3.70–3.67 (m, 1H), 3.59–3.55 (m, 1H), 2.62 (m, 2H), 2.11–0.95 (m, 7H), 0.84 (s, 9H).

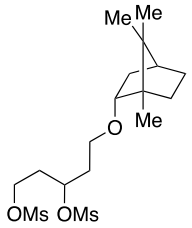


5-(((1R,2R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)oxy)pent-1-en-3-ol (1.30) was prepared according to Method D. The following amounts of reagents were used: **1.29** (4.2 g, 20. mmol, 1.0 equiv), vinylmagnesium bromide (30. mL, 30. mmol, 1.5 equiv), and THF (40 mL, 0.5 M in substrate). The compound was purified by column chromatography (0–10–25% EtOAc/hexanes) to afford the title compound as a clear yellow oil (1.5 g, 6.3 mmol, 21% yield over two steps). **TLC R_f =** 0.5 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.88 (ddd, *J* = 17.1, 10.8, 5.2 Hz, 1H), 5.30 (d, *J* = 16.9 Hz, 1H), 5.11 (d, *J* = 10.6 Hz, 1H), 4.35 (br s, 1H),

3.76–3.64 (m, 1H), 3.62–3.45 (m, 3H), 2.13–2.11 (m, 1H), 1.87–1.63 (m, 4H), 1.27–1.19 (m, 3H), 1.02 (d, *J* = 13.2 Hz, 1H), 0.87 (s, 3H), 0.84 (s, 6H).



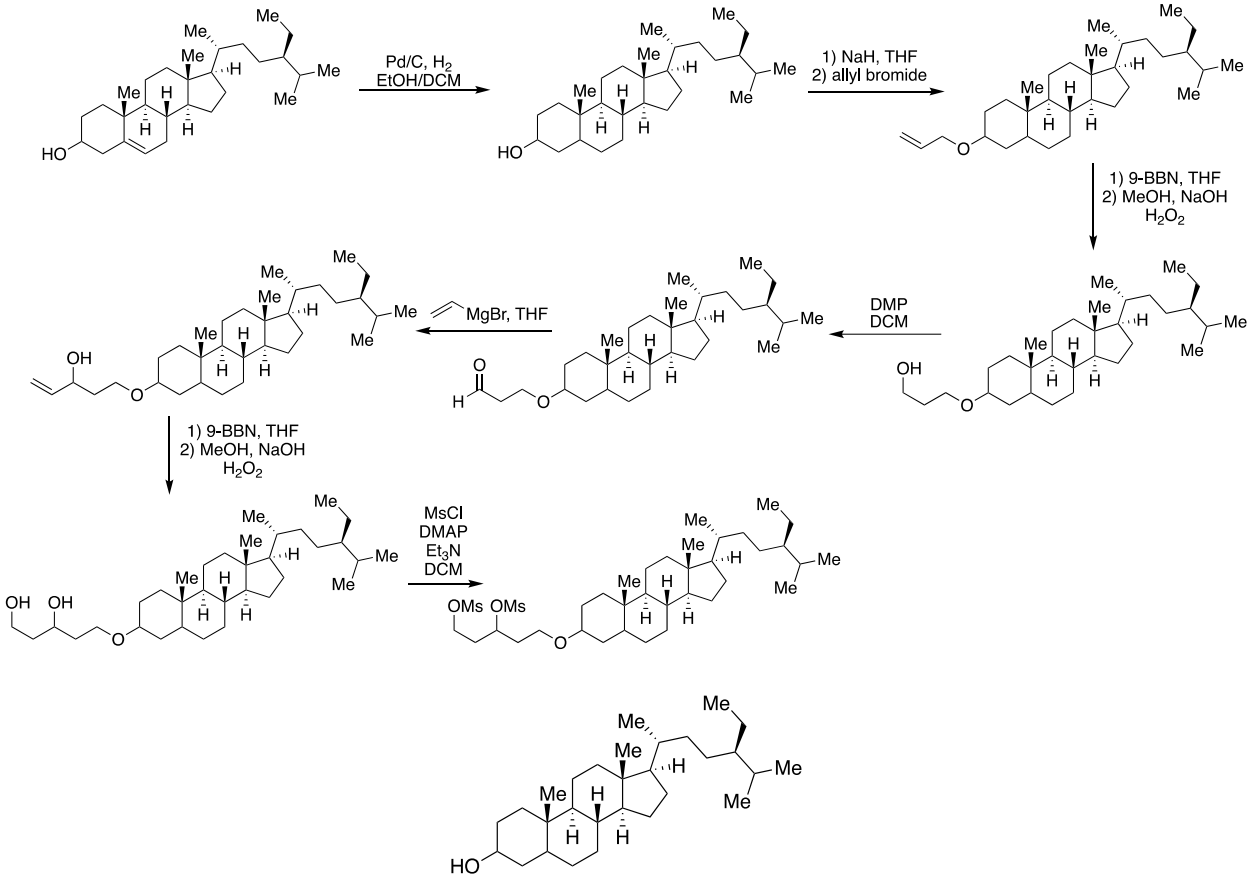
5-(((1R,2R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)oxy)pentane-1,3-diol (1.31) was prepared according to Method E. The following amounts of reagents were used: **1.30** (1.5 g, 6.3 mmol, 1.0 equiv), 9-BBN (31 mL, 16 mmol, 2.5 equiv), THF (15 mL, 0.40 M in substrate), MeOH (19 mL, 3.00 mL/mmol), NaOH (9.4 mL, 1.5 mL/mmol, 3.0 M aqueous solution), and H_2O_2 (9.4 mL, 1.5 mL/mmol, 30% w/w). The compound was purified by column chromatography (0–5% MeOH/DCM) to afford the title compound as a clear, colorless oil (1.4 g, 5.6 mmol, 89% yield). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.12–4.05 (m, 1H), 3.92 (d, *J* = 12.2 Hz, 1H), 3.82–3.85 (aq, *J* = 5.1 Hz, 2H), 3.80–3.49 (m, 3H), 2.84 (q, *J* = 5.3 Hz, 1H), 2.19–2.08 (m, 1H), 1.89–1.64 (m, 7H), 1.29–1.16 (m, 2H), 1.02 (dd, *J* = 13.2, 3.5 Hz, 1H), 0.87 (s, 3H), 0.84 (s, 6H).



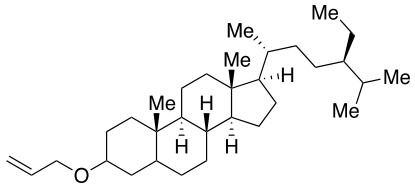
5-(((1R,2R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)oxy)pentane-1,3-diyl dimethanesulfonate (1.32) was prepared according to Method F. The following amounts of reagents were used: **1.31** (1.4 g, 5.6 mmol, 1.0 equiv), DMAP (130 mg, 1.1 mmol, 0.20 equiv), Et_3N (1.9 mL, 13 mmol, 2.4 equiv), MsCl (1.0 mL, 13 mmol, 2.4 equiv), and DCM (20 mL, 0.3 M in substrate). The

compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a clear yellow oil (1.3 g, 3.3 mmol, 59% yield). **TLC R_f =** 0.7 (50% EtOAc/hexanes); The reported NMR data is a 1:1 mixture of diastereomers: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.06–4.99 (m, 2H, both diastereomers), 4.39–4.35 (m, 4H, both diastereomers), 3.62–3.53 (m, 4H, both diastereomers), 3.46–3.41 (m, 2H, both diastereomers), 3.07 (s, 3H, one diastereomer), 3.06 (s, 3H, other diastereomer), 3.05 (s, 6H, both diastereomers), 2.31–1.86 (m, 12H, both diastereomers), 1.75–1.62 (m, 4H, both diastereomers), 1.25–1.15 (m, 4H, both diastereomers), 0.99 (td, J = 1.0, 0.9 Hz, 2H, both diastereomers), 0.86 (s, 6H, both diastereomers), 0.84 (s, 12H, both diastereomers); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 85.3 (one diastereomer), 85.2 (other diastereomer), 77.44 (one diastereomer), 77.42 (other diastereomer), 65.8 (2C, both diastereomers), 64.90 (one diastereomer), 64.86 (other diastereomer), 49.3 (2C, both diastereomers), 47.92 (one diastereomer), 47.87 (other diastereomer), 45.1 (2C, both diastereomers), 38.6 (one diastereomer), 38.5 (other diastereomer), 37.5 (2C, both diastereomers), 36.2 (one diastereomer), 36.0 (other diastereomer), 35.5 (one diastereomer), 35.3 (other diastereomer), 34.6 (2C, both diastereomers), 28.4 (one diastereomer), 28.3 (other diastereomer), 26.88 (one diastereomer), 26.85 (other diastereomer), 19.9 (2C, both diastereomers), 18.9 (2C, both diastereomers), 14.2 (one diastereomer), 14.1 (other diastereomer); **HRMS** (TOF MS ES+) *m/z:* $[M + Na]^+$ calcd for $C_{17}H_{32}O_7S_2Na$, 435.1487; found, 435.1466.

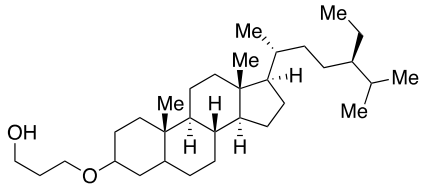
Scheme 1.10 Synthesis of 1,3-dimesylate **1.39** leading to cyclopropane **1.5**.



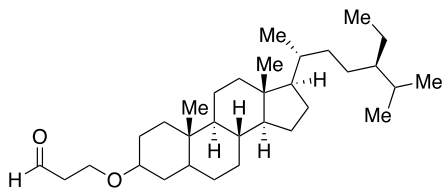
(8R,9S,10S,13R,14S,17R)-17-((2R,5R)-5-Ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (1.33) was prepared according to Method I. Two reactions were performed in parallel on 10 mmol scale. The following amounts of reagents were used for each 10 mmol scale reaction: β-sitosterol (4.2 g, 10. mmol, 1.0 equiv), palladium on carbon (290 mg, 20. mg/0.70 mmol), EtOH (150 mL), DCM (60 mL), and H_2 balloon (x 2). The product obtained was a white waxy solid and carried forward without further purification (3.2 g, 77% yield, contains 27% MeOH by NMR). **TLC R_f =** 0.2 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.63–3.54 (sept, J = 5.3 Hz, 1H), 1.66–0.65 (m, 51H).



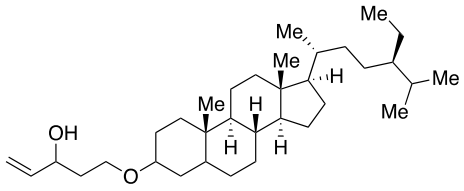
(8R,9S,10S,13R,14S,17R)-3-(Allyloxy)-17-((2R,5R)-5-ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthrene (1.34) was prepared according to Method G. The following amounts of reagents were used: **1.33** (5.0 g, 12 mmol, 1.0 equiv), NaH (0.37 g, 16 mmol, 1.3 equiv), THF (60 mL), allyl bromide (1.4 mL, 16 mmol, 1.30 equiv). The compound was purified by flash column chromatography (10% EtOAc/hexanes) to afford the title compound as a white waxy solid (3.0 g, 6.6 mmol, 55% yield). **TLC R_f =** 0.8 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.93–5.89 (m, 1H), 5.26 (dd, J = 17.2, 2.1 Hz, 1H), 5.13 (dd, J = 10.5, 1.8 Hz, 1H), 4.01 (d, J = 5.7 Hz, 2H), 3.27 (asept, J = 4.9 Hz, 1H), 1.97–0.64 (m, 50H).



3-(((8R,9S,10S,13R,14S,17R)-17-((2R,5R)-5-Ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)propan-1-ol (1.35) was prepared according to Method E. The following amounts of reagents were used: **1.34** (4.9 g, 11 mmol, 1.0 equiv), 9-BBN (55 mL, 28 mmol, 2.5 equiv, 0.50 M in THF), THF (25 mL), MeOH (32 mL, 3.0 mL/mmol), NaOH (16 mL, 1.5 mL/mmol, 3 M solution), and H_2O_2 (16 mL, 1.5 mL/mmol, 30% w/w). The product was purified by column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a white waxy solid (3.9 g, 8.2 mmol, 77% yield). **TLC R_f =** 0.2 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.77 (aq, J = 5.6 Hz, 2H), 3.67 (td, J = 5.8, 1.8 Hz, 2H), 3.22 (asept, J = 4.8 Hz, 1H), 2.65 (t, J = 5.3 Hz, 1H), 1.98–0.65 (m, 52H).

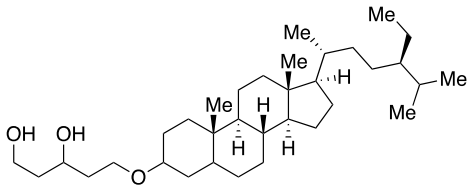


3-(((8R,9S,10S,13R,14S,17R)-17-((2R,5R)-5-Ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)propanal (1.36) was prepared according to Method J. The following amounts of reagents were used: **1.35** (3.4 g, 7.2 mmol, 1.0 equiv), DMP (3.7 g, 8.6 mmol, 1.2 equiv), DCM (36 mL, 0.2 M). The product was purified by column chromatography (0–25% EtOAc/hexanes) to afford a white waxy solid (2.9 g, 69% yield, contains 12% EtOAc by NMR). **TLC R_f =** 0.9 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.79 (t, J = 1.9, 1H), 3.80 (td, J = 6.2, 2.6 Hz, 2H), 3.24 (asept, J = 4.9 Hz, 1H), 2.63 (atd, J = 6.1, 1.9 Hz, 2H), 1.98–0.65 (m, 50H).

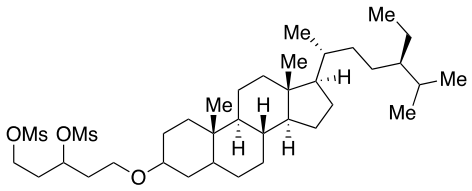


5-(((8R,9S,10S,13R,14S,17R)-17-((2R,5R)-5-Ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)pent-1-en-3-ol (1.37) was prepared according to Method D. The following amounts of reagents were used: **1.36** (2.4 g, 5.0 mmol, 1.0 equiv), vinylmagnesium bromide (21 mL, 15 mmol, 3.0 equiv, 0.70 M in THF), and THF (10 mL, 0.5 M in substrate). The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a white waxy solid (1.1 g, 2.3 mmol, 45% yield). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.3 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.88 (m, 1H), 5.29 (d, J = 17.2 Hz, 1H), 5.11 (d,

J = 10.4 Hz, 1H), 4.33 (m, 1H), 3.73–3.65 (m, 2H), 3.43 (br s, 1H), 3.24 (asept, *J* = 5.2 Hz, 1H), 1.98–0.65 (m, 52H).



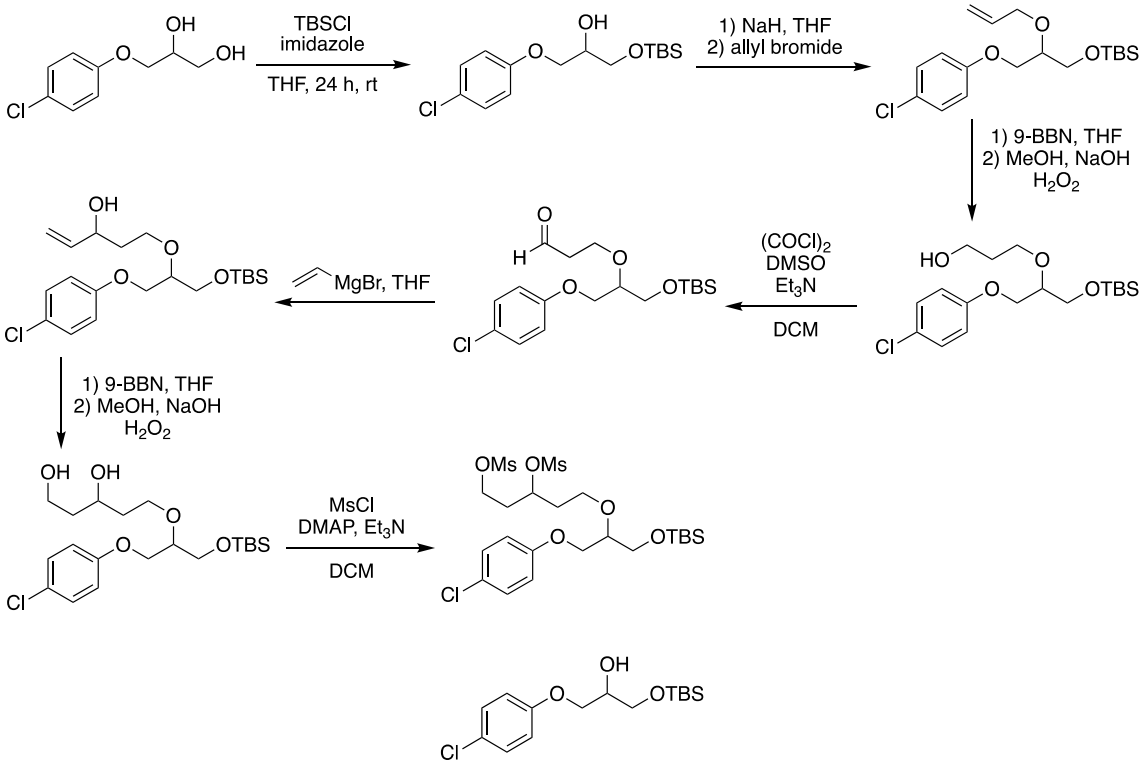
5-(((8R,9S,10S,13R,14S,17R)-17-((2R,5R)-5-Ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)pentane-1,3-diol (1.38) was prepared according to Method E. The following amounts of reagents were used: **1.37** (1.1 g, 2.3 mmol, 1.0 equiv), 9-BBN (11 mL, 5.6 mmol, 2.5 equiv), THF (5 mL), MeOH (6.8 mL, 3 mL/mmol), NaOH (6.8 mmol, 1.5 mL/mmol, 3.0 M aqueous solution), and H_2O_2 (6.8 mmol, 1.50 mL/mmol, 30% w/w). The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a white waxy solid (0.77 g, 1.5 mmol, 67% yield). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.1 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.07 (at, *J* = 10.2 Hz, 1H), 3.91 (br s, 1H), 3.84–3.83 (m, 2H), 3.77–3.64 (m, 2H), 3.24 (asept, *J* = 4.9 Hz, 1H), 2.85 (t, *J* = 5.1 Hz, 1H), 1.97–0.64 (m, 54H).



5-((17-(5-Ethyl-6-methylheptan-2-yl)-10,13-dimethylhexadecahydro-1Hcyclopenta[a]phenanthren-3-yl)oxy)pentane-1,3-diyl dimethanesulfonate (1.39) was prepared according to Method F. The following amounts of reagents were used: **1.38** (0.77 g, 1.5 mmol, 1.0 equiv), methanesulfonyl chloride (0.28 mL, 3.6 mmol, 2.4 equiv), dimethylamino

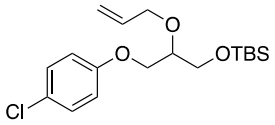
pyridine (37 mg, 0.30 mmol, 0.20 equiv), Et_3N (0.51 mL, 3.6 mmol, 2.4 equiv), DCM (8 mL, 0.2 M in substrate). The compound was purified by flash column chromatography (50% EtOAc/hexanes) to afford the title compound as a white waxy solid (0.44 g, 0.65 mmol, 43% yield). The compound was characterized as a 1:1 mixture of diastereomers. **m.p. =** 145 °C; **TLC R_f =** 0.8 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.09–5.05 (m, 1H), 4.38–4.35 (m, 2H), 3.58–3.55 (m, 2H), 3.31–3.24 (asept, J = 5.0 Hz, 1H), 3.06 (s, 3H), 3.04 (s, 3H), 2.15–0.64 (m, 54H); **^{13}C NMR** (128.5 MHz, $CDCl_3$) δ 78.9, 65.79, 62.9, 56.5, 56.3, 54.4, 45.9, 44.8, 42.7, 40.1, 38.5, 37.5, 37.0, 36.9, 36.2, 35.8, 35.6, 35.4, 34.9, 34.8, 34.6, 34.0, 32.2, 29.2, 28.9, 28.3, 26.1, 24.3, 23.1, 21.3, 19.9, 19.1, 18.8, 12.4, 12.1, 12.0; **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{36}H_{66}O_7S_2Na$, 697.4148; found, 697.4139.

Scheme 1.11 Synthesis of 1,3-Dimesylate **1.46** leading to cyclopropanes **1.6**.

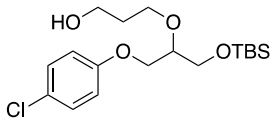


1-((tert-Butyldimethylsilyl)oxy)-3-(4-chlorophenoxy)propan-2-ol (1.40) was prepared according to Method K. The following amounts of reagents were used: 3-(4-chlorophenoxy)-1,2-

propanediol (7.1 g, 35 mmol, 1.0 equiv), TBSCl (5.3 g, 35 mmol, 1.0 equiv), imidazole (4.8 g, 70. mmol, 2.0 equiv), and THF (100 mL, 0.4 M in substrate). The resulting clear oil was a mixture of 90% product and 10% starting material by ^{1}H NMR and was carried forward into the next step without further purification. **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23–7.21 (d, J = 8.8 Hz, 2H), 6.85–6.83 (d, J = 8.8 Hz, 2H), 4.03–3.98 (m, 3H), 3.76–3.75 (m, 2H), 1.85 (br s, 1H), 0.89 (s, 9H), 0.07 (s, 6H).

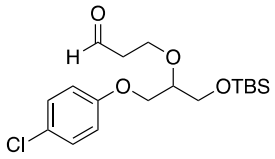


(2-(Allyloxy)-3-(4-chlorophenoxy)propoxy)(tert-butyl)dimethylsilane (1.41) was prepared according to Method G. The following amounts of reagents were used: **1.40** (13 g, 35 mmol, 1.0 equiv), NaH (2.50 g, 104 mmol, 3.00 equiv, 0.200 M in THF), and allyl bromide (4.0 mL, 46 mmol, 1.3 equiv). The compound was purified by flash column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear, colorless oil (9.5 g, 26 mmol, 74% yield over two steps). **TLC R_f =** 0.8 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25–7.21 (d, J = 9.0 Hz, 2H), 6.86–6.84 (d, J = 9.0 Hz, 2H), 5.97–5.86 (m, 1H), 5.28 (dd, J = 17.2, 1.66 Hz, 1H), 5.17 (dd, J = 10.3, 1.6 Hz, 1H), 4.18–4.16 (m, 2H), 4.13–3.95 (m, 2H), 3.78–3.72 (m, 3H), 0.89 (s, 9H), 0.05 (s, 6H).

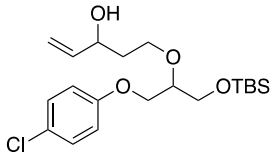


3-((1-((tert-Butyldimethylsilyl)oxy)-3-(4-chlorophenoxy)propan-2-yl)oxy)propan-1-ol (1.42) was prepared according to Method E. The following amounts of reagents were used: **1.41** (4.8 g, 13 mmol, 1.0 equiv), 9-BBN (67 mL, 33 mmol, 2.5 equiv, 0.50 M in THF), THF (60. mL), MeOH (80. mL, 3.0 mL/mmol), NaOH (40. mL, 1.5 mL/mmol), and H_2O_2 (40. mL, 1.5 mL/mmol). The

product was purified by column chromatography (0–5% MeOH/DCM) to the title compound as a clear, colorless oil (2.5 g, 6.7 mmol, 51% yield). **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 4.07 (dd, J = 10.1, 4.7 Hz, 1H), 3.96 (dd, J = 10.1, 5.7 Hz, 1H), 3.83–3.75 (m, 7H), 2.46 (t, J = 5.9 Hz, 1H), 1.83 (quint, J = 5.7 Hz, 2H), 0.89 (s, 9H), 0.07 (s, 6H).

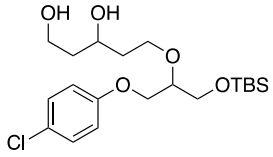


3-((1-((tert-Butyldimethylsilyl)oxy)-3-(4-chlorophenoxy)propan-2-yl)oxy)propanal (1.43) was prepared according to Method H. The following amounts of reagents were used: **1.42** (2.3 g, 6.2 mmol, 1.0 equiv), oxalyl chloride (0.68 mL, 8.1 mmol, 1.3 equiv), DMSO (0.53 mL, 7.5 mmol, 1.2 equiv), Et_3N (2.6 mL, 19 mmol, 3.0 equiv), DCM (30 mL, 0.20 M in substrate). The product was purified by column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear, colorless oil (1.6 g, 4.3 mmol, 69% yield). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.80 (t, J = 1.7 Hz, 1H), 7.24 (d, J = 9.1 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 4.08 (dd, J = 10.1, 3.9 Hz, 1H), 4.02–3.99 (m, 3H), 3.75–3.71 (m, 3H), 2.67 (td, J = 6.1, 1.8 Hz, 2H), 0.90 (s, 9H), 0.06 (s, 6H).

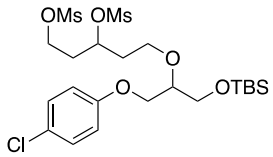


5-((1-((tert-Butyldimethylsilyl)oxy)-3-(4-chlorophenoxy)propan-2-yl)oxy)pent-1-en-3-ol (1.44) was prepared according to Method D. The following amounts of reagents were used: **1.43** (1.6 g, 4.3 mmol, 1.0 equiv), vinylmagnesium bromide (19 mL, 13. mmol, 3.0 equiv, 0.70 M in THF), THF (5 mL). The compound was purified by column chromatography (0–5–25%

EtOAc/hexanes) to afford the title compound as a clear, colorless oil (0.75 g, 1.9 mmol, 43% yield). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 5.87 (ddd, J = 16.0, 10.1, 5.3 Hz, 1H), 5.27 (dd, J = 17.5, 1.5 Hz, 1H), 5.09 (dd, J = 10.6, 1.4 Hz, 1H), 4.34–4.30 (m, 1H), 4.08 (dd, J = 10.4, 3.7 Hz, 1H), 3.98–3.94 (m, 1H), 3.91–3.68 (m, 5H), 3.03–2.91 (br s, 1H), 1.91–1.72 (m, 2H), 0.90 (s, 9H), 0.07 (s, 6H).



5-((1-((tert-Butyldimethylsilyl)oxy)-3-(4-chlorophenoxy)propan-2-yl)oxy)pentane-1,3-diol (1.45) was prepared according to Method E. The following amounts of reagents were used: **1.44** (0.75 g, 1.9 mmol, 1.0 equiv), 9-BBN (9.4 mL, 4.7 mmol, 2.5 equiv), THF (5.0 mL, 0.40 M in substrate), MeOH (5.6 mL, 3.0 mL/mmol), NaOH (2.8 mL, 1.5 mL/mmol), H_2O_2 (2.8 mL, 1.5 mL/mmol). The product was purified by column chromatography (0–5% MeOH/DCM) to afford the title compound as a clear, colorless oil (0.62 g, 72% yield, contains 35% Et_2O by ^{1}H NMR). The compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (d, J = 9.1 Hz, 2H), 6.83 (d, J = 9.1 Hz, 2H), 4.14–4.05 (m, 2H), 3.99–3.90 (m, 2H), 3.85–3.79 (m, 2H), 3.77–3.71 (m, 2H), 3.63 (ad, J = 11.4 Hz, 1H), 2.86–2.79 (br s, 1H), 1.86–1.64 (m, 4H), 1.59, (s, 1H), 1.21 (t, J = 7.1 Hz, 1H), 0.89 (s, 9H), 0.07 (s, 6H).

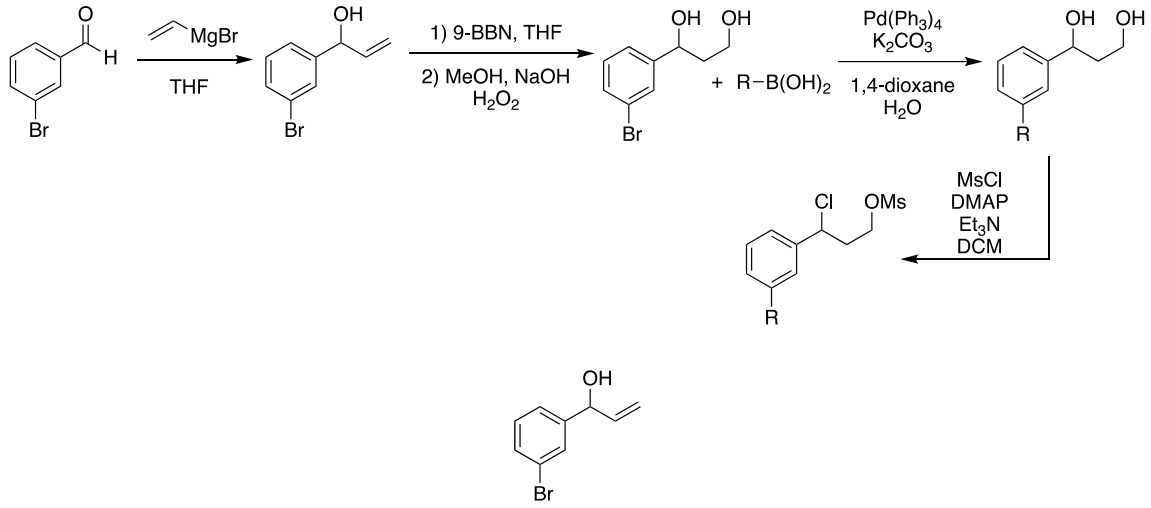


5-((1-((tert-Butyldimethylsilyl)oxy)-3-(4-chlorophenoxy)propan-2-yl)oxy)pentane-1,3-diyl

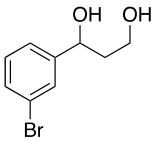
dimethanesulfonate (1.46) was prepared according to Method F. The following amounts of reagents were used: **1.45** (0.56 g, 1.4 mmol, 1.0 equiv), methanesulfonyl chloride (0.25 mL, 3.2 mmol, 2.4 quiv), dimethylaminopyridine (33 mg, 0.27 mmol, 0.20 equiv), Et_3N (0.45 mL, 3.2 mmol, 2.4 equiv), DCM (7 mL, 0.2 M in substrate). The product was purified by column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear, colorless oil (0.40 g 0.72 mmol, 51% yield). **TLC R_f =** 0.4 (50% EtOAc/hexanes); The reported NMR data is a 1:1 mixture of diastereomers: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25–7.22 (add, J = 2.7, 2.5 Hz, 4H, both diastereomers), 6.84 (d, J = 8.6 Hz, 4H, both diastereomers), 5.09–4.98 (m, 2H, both diastereomers), 4.35–4.33 (m, 4H, both diastereomers), 4.12–4.06 (m, 2H, both diastereomers), 4.01–3.95 (m, 2H, both diastereomers), 3.77–3.71 (m, 10H, both diastereomers), 3.04 (s, 6H, both diastereomers), 3.01 (s, 6H, both diastereomers), 2.29–2.08 (m, 4H, both diastereomers), 2.05–1.96 (m, 4H, both diastereomers), 0.88 (s, 18H, both diastereomers), 0.06 (s, 12H, both diastereomers); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 157.4 (2C, both diastereomers), 129.4 (4C, both diastereomers), 125.8 (2C, both diastereomers), 115.8 (4C, both diastereomers), 79.2 (one diastereomer), 79.0 (other diastereomer), 76.71 (one diastereomer), 76.66 (other diastereomer), 68.2 (one diastereomer), 68.0 (other diastereomer), 65.71 (one diastereomer), 65.67 (other diastereomer), 65.66 (one diastereomer), 65.64 (other diastereomer), 62.3 (one diastereomer), 62.2 (other diastereomer), 38.41 (one diastereomer), 38.38 (other diastereomer), 37.4 (2C, both diastereomers), 35.4 (one diastereomer), 35.2 (other diastereomer), 34.6 (one diastereomer), 34.4 (other diastereomer), 25.9 (6C, both diastereomers), 18.3 (2C, both diastereomers), –5.40 (2C, one diastereomer), –5.44 (2C, other diastereomer); **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calculated for $C_{22}H_{39}ClO_9S_2SiNa$, 597.1391; found, 597.1392.

1.4.6 Intermediates and Benzylic Chlorides for Monosubstituted Arylcyclopropanes

Scheme 1.12 Synthesis of benzylic chlorides **1.50**, **1.52**, **1.54** leading to cyclopropanes **1.7–1.9**.

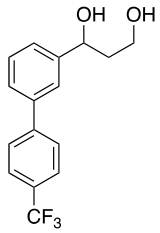


1-(3-Bromophenyl)prop-2-en-1-ol (1.47) was prepared according to Method D. The following amounts of reagents were used: 3-bromobenzaldehyde (2.3 mL, 20 mmol, 1.0 equiv), vinylmagnesium bromide (57 mL, 40. mmol, 2.0 equiv), and THF (20. mL, 0.10 M in substrate). The compound was purified by flash column chromatography (25% EtOAc/hexanes) to afford the title compound as a pale-yellow oil in (2.4 g, 11 mmol, 56%). **TLC R_f =** 0.7 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 6.02–5.96 (m, 1H), 5.35 (d, J = 16.9 Hz, 1H), 5.22 (d, J = 10.3 Hz, 1H), 5.16 (d, J = 5.6 Hz, 1H), 2.05 (s, 1H). Analytical data is consistent with literature values.

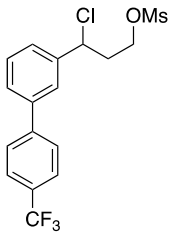


1-(3-Bromophenyl)propane-1,3-diol (1.48) was prepared according to Method E. The following amounts of reagents were used: **1.47** (2.4 mL, 11 mmol, 1.0 equiv), 9-BBN (56 mL, 28 mmol, 2.5 equiv), THF (20. mL), MeOH (34 mL, 3.0 mL/mmol), NaOH (17 mL, 1.5 mL/mmol, 3.0 M aqueous solution), and H_2O_2 (17 mL, 1.5 mL/mmol, 30% w/w). The compound was purified by

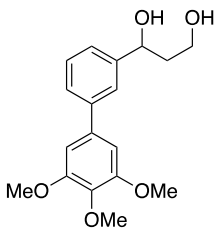
flash chromatography (0–5% MeOH/DCM) to afford the title compound as a pale-yellow oil in (1.4 g, 6.0 mmol, 54%). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR (**500 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.37 (m, 1H), 7.22–7.16 (m, 2H), 4.83 (m, 1H), 4.06 (s, 1H), 3.75 (m, 2H), 3.36 (s, 1H), 1.91–1.81 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 146.7, 130.5, 130.1, 128.8, 124.3, 122.6, 73.1, 60.9, 40.3; **HRMS** (TOF MS ES+) *m/z:* [M+Na]+ calculated for $C_9H_{11}BrO_2Na$, 252.9848; found, 252.9840. Analytical data is consistent with literature values.



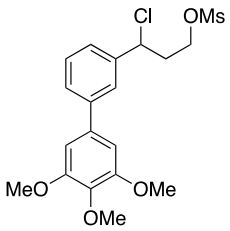
1-(4'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)propane-1,3-diol (1.49) was prepared according to Method L. The following amounts of reagents were used: **1.48** (0.84 g, 3.6 mmol,1.0 equiv), (4-(trifluoromethyl)phenyl)boronic acid (1.1 g, 5.8 mmol, 1.6 equiv), $Pd(PPh_3)_4$ (130 mg, 0.11 mmol, 3.0 mol %), K_2CO_3 (5.0 g, 36 mmol, 10. equiv), dioxane (16 mL), and H_2O (4 mL). The compound was purified by flash column chromatography (0–60% EtOAc/hexanes) to afford the title compound as a pale-yellow oil (560 mg, 1.9 mmol, 53%). **TLC R_f =** 0.6 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (s, 4H), 7.63 (s, 1H), 7.52 (d, J = 7.0, 1H), 7.46 (t, J = 7.5, 1H), 7.40 (d, J = 7.8, 1H), 5.05 (dd, J = 4.8, 3.8 Hz, 1H), 3.95–3.86 (m, 2H), 2.83 (br s, 2H), 2.13–1.94 (m, 2H).



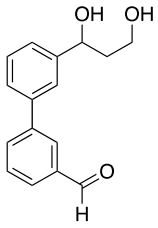
3-Chloro-3-(4'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)propyl methanesulfonate (1.50) was prepared according to Method F. The following amounts of reagents were used: **1.49** (560 mg, 1.9 mmol, 1.0 equiv), MsCl (0.32 mL, 4.2 mmol, 2.2 equiv), DMAP (47 mg, 0.38 mmol, 0.20 equiv), Et_3N (0.80 mL, 5.7 mmol, 2.2 equiv), DCM (10 mL). The compound was purified by flash chromatography (0–40% EtOAc/hexanes) to afford a pale-yellow oil (260 mg, 0.66 mmol, 34%). **TLC R_f =** 0.6 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (at, J = 8.8, 4H), 7.62 (s, 1H), 7.56 (d, J = 7.7, 1H), 7.48 (t, J = 7.7, 1H), 7.44 (d, J = 7.6, 1H), 5.14 (t, J = 7.2 Hz, 1H), 4.51–4.44 (m, 1H), 4.39–4.32 (m, 1H), 3.03 (s, 3H), 2.54–2.48 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 144.1, 141.3, 140.6, 129.8 (q, J = 32.4 Hz, 1C), 129.7, 127.8, 127.6 (2C), 126.7, 126.0, 125.9 (q, J = 3.7 Hz, 2C), 124.3 (q, J = 271.9 Hz, 1C), 66.9, 58.9, 39.3, 37.4; **HRMS** (TOF MS ES+) *m/z:* [M + Na] + calcd for $C_{17}H_{16}ClF_3O_3SNa$, 415.0359; found, 415.0359.



1-(3',4',5'-Trimethoxy-[1,1'-biphenyl]-3-yl)propane-1,3-diol (1.51) was prepared according to Method L. The following amounts of reagents were used: **1.48** (0.35 g, 1.5 mmol, 1.0 equiv), 3,4,5-trimethoxyphenylboronic acid (0.38 g, 1.8 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (52 mg, 45 µmol, 3.0 mol %), K_2CO_3 (2.1 g, 15 mmol, 10. equiv), dioxane (11 mL, 0.14 M in substrate), and H_2O (2.5 mL, 0.60 M in substrate). The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a clear, colorless oil (0.38 g, 62% yield, contains 50% EtOAc by ^{1}H NMR). **TLC R_f =** 0.3 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65–7.34 (m, 6H), 5.04 (dd, J = 8.9, 3.2 Hz, 1H), 3.92–3.89 (m, 11H), 3.11 (br s, 1H), 2.47 (br s, 1H), 2.08–1.97 (m, 2H).

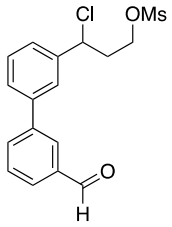


3-Chloro-3-(3',4',5'-trimethoxy-[1,1'-biphenyl]-3-yl)propyl methanesulfonate (1.52) was prepared according to Method F. The following amounts of reagents were used: **1.51** (0.38 g, 1.2 mmol, 1.0 equiv), dimethylaminopyridine (30. mg, 0.24 mmol, 0.20 equiv), Et_3N (0.40 mL, 2.9 mmol, 2.4 equiv), methanesulfonyl chloride (0.22 mL, 2.9 mmol, 2.4 equiv), and DCM (2 mL, 0.8 M in substrate). The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a clear oil (0.18 g, 0.43 mmol, 36% yield). **TLC R_f =** 0.2 (50% EtOAc/hexanes); **^{1}H NMR (**500 MHz, $CDCl_3$) δ 7.55–7.37 (m, 4H), 6.77 (s, 2H), 5.14–5.11 (m, 1H), 4.48–4.43 (m, 1H), 4.36–4.31 (m, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 3.69 (s, 3H), 3.03 (s, 3H), 2.56–2.49 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 153.6 (2C), 142.1, 140.9, 138.0, 136.5, 129.5, 127.6, 125.9, 125.7, 104.6 (2C), 66.9, 61.0, 59.0, 56.4 (2C), 39.2, 37.3; **HRMS** (TOF MS Cl+) *m/z:* [M+Na]+ calculated for $C_{19}H_{23}ClO_6SNa$, 437.0802; found, 437.0801.



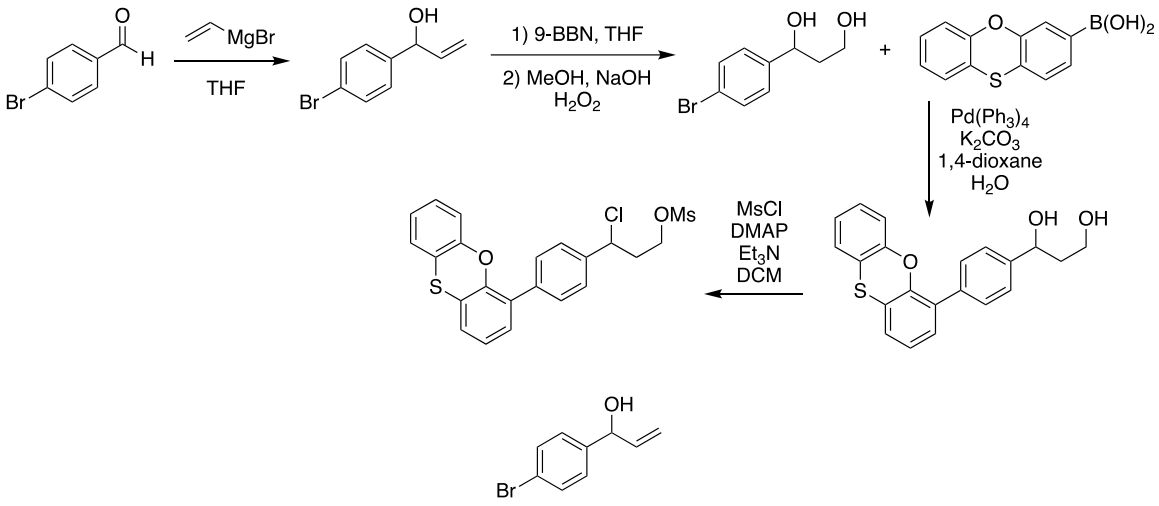
3'-(1,3-Dihydroxypropyl)-[1,1'-biphenyl]-3-carbaldehyde (1.53) was prepared according to Method L. The following amounts of reagents were used: **1.48** (0.35 g, 1.5 mmol, 1.0 equiv), 3-formylphenylboronic acid (270 mg, 1.8 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (52 mg, 45 µmol, 3.0 mol %), K_2CO_3 (2.1 g, 15 mmol, 10. equiv), 1,4-dioxane (11 mL, 0.14 M in substrate), and H_2O (2.5 mL, 0.60 M in substrate). The compound was purified by flash column chromatography (0–50%

EtOAc/hexanes) to afford the title compound as a clear oil (0.31 g, 67% yield, contains 40% EtOAc by ^{1}H NMR). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 8.09 (s, 1H), 7.87–7.84 (m, 2H), 7.65–7.36 (m, 5H), 5.06 (dd, J = 8.8, 3.9 Hz, 1H), 3.92–3.87 (m, 2H), 3.22 (br s, 1H), 2.47 (br s, 1H), 2.08–1.97 (m, 2H).

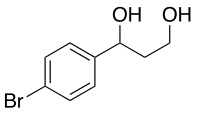


3-Chloro-3-(3'-formyl-[1,1'-biphenyl]-3-yl)propyl methanesulfonate (1.54) was prepared according to Method F. The following amounts of reagents were used: **1.53** (0.31 g, 1.2 mmol, 1.0 equiv), dimethylaminopyridine (29 mg, 0.24 mmol, 0.20 equiv), Et_3N (0.40 mL, 2.9 mmol, 2.4 equiv), methanesulfonyl chloride (0.22 mL, 2.9 mmol, 2.4 equiv), DCM (2 mL, 0.8 M in substrate). The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a clear oil (130 mg, 0.38 mmol, 31% yield). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.11 (s, 1H), 8.10 (s, 1H), 7.89–7.85 (m, 2H), 7.65–7.59 (m, 3H), 7.49 (at, *J* = 7.8 Hz, 1H), 7.45–7.42 (m, 1H), 5.14 (t, *J* = 7.8 Hz, 1H), 4.52–4.46 (m, 1H), 4.39–4.34 (m, 1H), 3.05 (s, 3H), 2.54–2.52 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 192.2, 141.6, 141.3, 140.6, 137.1, 133.1 (2C), 129.7, 129.2, 128.1, 127.7, 126.5, 125.9, 66.8, 58.8, 39.3, 37.4; **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calculated for $C_{17}H_{17}ClO_4SNa$, 375.0434; found, 375.0421.

Scheme 1.13 Synthesis of benzylic chloride **1.58** leading to cyclopropane **1.10**.

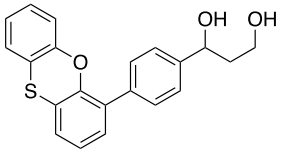


1-(4-Bromophenyl)prop-2-en-1-ol (1.55) was prepared according to Method D. The following amounts of reagents were used: 4-bromobenzaldehyde (1.9 g, 10. mmol, 1.0 equiv), vinylmagnesium bromide (29 mL, 20. mmol, 2.0 equiv), THF (20. mL). The compound was purified by flash chromatography (25% EtOAc/hexanes) to afford the title compound as a yellow oil in (1.4 g, 6.4 mmol, 64% over two steps). **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H), 6.02–5.95 (m, 1H), 5.32 (d, J = 16.9 Hz, 1H), 5.23 (d, J = 10.5 Hz, 1H), 5.15 (d, J = 6.4 Hz, 1H), 2.07 (br s, 1H). Analytical data is consistent with literature values.

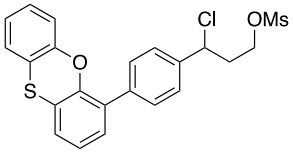


1-(4-Bromophenyl)propane-1,3-diol (1.56) was prepared according to Method E. The following amounts of reagents were used: **1.55** (1.1 g, 5.1 mmol, 1.0 equiv), 9-BBN (26 mL, 22 mmol, 2.5 equiv, 0.50 M in THF), THF (10. mL, 0.50 M in substrate), MeOH (15.4 mL, 3.00 mL/mmol), NaOH (7.7 mL, 1.5 mL/mmol, 3.0 M aqueous solution), and H_2O_2 (7.7 mL, 1.5 mL/mmol, 30% w/w). The compound was purified by flash column chromatography (0–5%MeOH/DCM) to afford

the title compound as a clear oil (1.0 g, 4.4 mmol, 87% yield). **TLC R_f =** 0.3 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.2 Hz, 2H), 4.87–4.83 (m, 1H), 3.8–3.76 (m, 2H), 3.67 (ad, J = 3.13 Hz, 1H), 2.96 (at, J = 4.5 Hz, 1H), 1.95–1.82 (m, 2H); **^{13}C NMR** (500 MHz, $CDCl_3$) δ 143.3, 131.6 (2C), 127.4 (2C), 121.3, 73.4, 61.1, 40.3; **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calculated for $C_9H_{11}BrO_2Na$, 252.9840; found, 252.9834. Analytical data is consistent with literature values.



1-(4-(Phenoxathiin-4-yl)phenyl)propane-1,3-diol (1.57) was prepared according to Method L. The following amounts of reagents were used: **1.56** (0.35 g, 1.5 mmol, 1.0 equiv), phenoxathiin-4-boronic acid (0.40 g, 1.6 mmol, 1.1 equiv), $Pd(OAc)_2$ (2 mg, 0.9 µmol, 6.0 mol %), PPh_3 (7.0 mg, 27 µmol, 18 mol %), Na_2CO_3 (190 mg, 1.8 mmol, 1.2 equiv), propanol (5 mL, 0.3 M in substrate), and H_2O (5 mL). The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a clear oil (0.38 g, 1.1 mmol, 72% yield). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.15–6.88 (m, 6H), 6.87 (dd, J = 8.0, 1.2 Hz, 1H), 5.01 (dd, J = 8.6, 3.7 Hz, 1H), 3.91–3.83 (m, 2H), 3.56 (br s, 1H), 3.03 (br s, 1H), 2.09–1.94 (m, 2H).

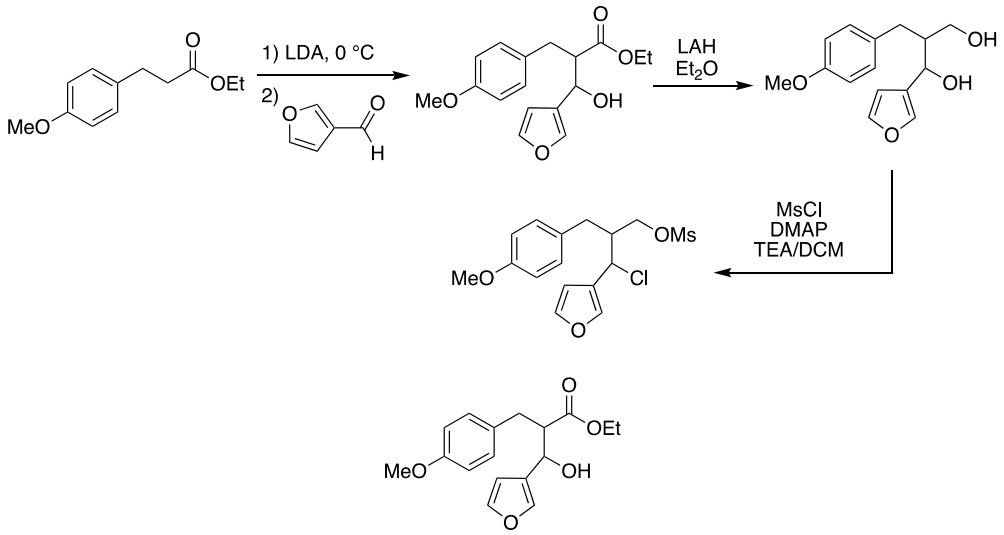


3-Chloro-3-(4-(phenoxathiin-4-yl)phenyl)propyl methanesulfonate (1.58) was prepared according to Method F. The following amounts of reagents were used: **1.57** (1.5 g, 4.3 mmol, 1.0 equiv), dimethylaminopyridine (110 mg, 0.86 mmol, 0.20 equiv), Et_3N (1.4 mL, 10. mmol, 2.4

equiv), methanesulfonyl chloride (0.80 mL, 10. mmol, 2.4 equiv), and DCM (5 mL, 0.8 M in substrate). The compound was purified by column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a clear oil (0.93 g, 2.1 mmol, 49% yield). **TLC R_f =** 0.6 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.25–7.02 (m, 6H), 6.91 (d, J = 8.3 Hz, 1H), 5.14 (t, J = 6.7 Hz, 1H), 4.53–4.37 (m, 2H), 3.05 (s, 3H), 2.56–2.52 (m, 2H); **^{13}C NMR** (500 MHz, $CDCl_3$) δ 152.6, 149.3, 139.5, 137.8, 130.8, 130.1 (2C), 129.3, 127.8, 126.9 (2C), 126.8, 126.5, 124.8, 124.5, 121.9, 121.1, 117.7, 66.9, 58.9, 39.2, 37.4; **HRMS** (TOF MS Cl+) *m/z:* $[M+Na]^+$ calculated for $C_{22}H_{19}ClO_4S_2Na$, 469.0311; found, 469.0303.

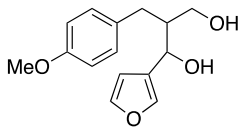
1.4.7 Intermediates and Benzylic Chlorides for Disubstituted Arylcyclopropanes

Scheme 1.14 Synthesis of benzylic chloride **1.14** leading to cyclopropane **1.15**.

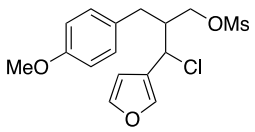


Ethyl 3-(furan-3-yl)-3-hydroxy-2-(4-methoxybenzyl)propanoate (1.12) was prepared according to Method M. The following amounts of reagents were used: *n*-BuLi (6.8 mL, 17 mmol, 1.7 equiv, 2.5 M), diisopropylamine (2.4 mL, 17 mmol, 1.7 equiv), ethyl 3-(4-methoxyphenyl)propanoate **1.11** (2.08 g, 10.0 mmol, 1.00 equiv), 3-furancarboxaldehyde (0.63 mL, 7.5 mmol, 0.75 equiv), and THF (70 mL). The oil was purified by column chromatography

(0–25% EtOAc/hexanes) to afford a clear oil (1.7 g, 5.5 mmol, 73% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.3 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (s, 1H, one diastereomer), 7.39–7.37 (m, 3H, both diastereomers), 7.08 (d, *J* = 7.1 Hz, 2H, one diastereomer), 7.05 (d, *J* = 7.0 Hz, 2H, other diastereomer), 6.82–6.78 (m, 4H, both diastereomers), 6.39–6.38 (m, 2H, both diastereomers), 4.94 (d, *J* = 4.9 Hz, 1H, one diastereomer), 4.73 (m, 1H, other diastereomer), 4.04 (q, *J* = 4.0 Hz, 2H, one diastereomer), 3.96 (q, *J* = 3.9 Hz, 2H, other diastereomer), 3.77 (s, 3H, one diastereomer), 3.76 (s, 3H, other diastereomer), 3.20 (d, *J* = 3.2 Hz, 1H, one diastereomer), 2.96–2.85 (m, 7H, both diastereomers), 1.08 (t, *J* = 1.1 Hz, 3H, one diastereomer), 1.02 (t, *J* = 1.0 Hz, 3H, other diastereomer).



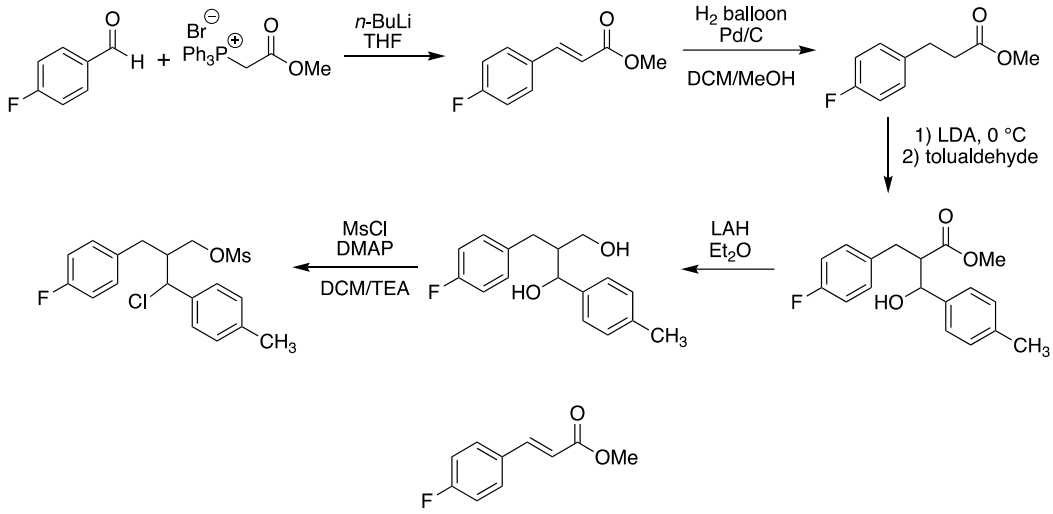
1-(Furan-3-yl)-2-(4-methoxybenzyl)propane-1,3-diol (1.13) was prepared according to Method N. The following amounts of reagents were used: **1.12** (1.67 g, 5.50 mmol, 1.00 equiv), $LiAlH_4$ (0.732 g, 19.3 mmol, 3.50 equiv), and Et_2O (30 mL). The oil was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.58 g, 2.2 mmol, 40% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.5 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43–7.40 (m, 4H both diastereomers), 7.07–7.04 (m, 4H, both diastereomers), 6.81 (d, *J* = 8.7 Hz, 4H, both diastereomers), 6.40 (d, *J* = 11.7 Hz, 2H, both diastereomers), 4.97 (bs, 1H), 4.73 (d, *J* = 6.2 Hz, 1H), 3.84–3.79 (m, 1H, one diastereomer), 3.77 (s, 6H, both diastereomers), 3.64 (d, *J* = 5.6 Hz, 2H, other diastereomer), 3.61–3.56 (m, 1H, one diastereomer), 3.21 (bs, 1H, one diastereomer), 3.18 (bs, 1H, other diastereomer), 2.74–2.66 (m, 2H, both diastereomers), 2.61–2.48 (m, 4H, both diastereomers), 2.19–2.11 (m, 1H, one diastereomer), 2.03–1.95 (m, 1H, other diastereomer).



3-Chloro-3-(furan-3-yl)-2-(4-methoxybenzyl)propyl methanesulfonate (1.14) was prepared according to Method F. The following amounts of reagents were used: **1.13** (0.583 g, 2.20 mmol, 1.00 equiv), dimethylaminopyridine (54 mg, 0.44 mmol, 0.20 equiv), Et_3N (0.74 mL, 5.3 mmol, 2.4 equiv), methanesulfonyl chloride (0.41 mL, 5.3 mmol, 2.4 equiv), and DCM (10 mL). The oil was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.32 g, 0.89 mmol, 40% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.7 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50–7.49 (m, 2H, both diastereomers), 7.46–7.44 (m, 2H, both diastereomers), 7.08 (d, J = 8.8 Hz, 2H, both diastereomers), 7.06 (d, J = 8.6 Hz, 2H, both diastereomers), 6.85–6.83 (m, 4H, both diastereomers), 6.44 (s, 2H, both diastereomers), 5.15 (d, J = 5.1 Hz, 1H, one diastereomer), 4.99 (d, J = 6.9 Hz, 1H, other diastereomer), 4.39 (dd, J = 9.8, 4.6 Hz, 1H, one diastereomer), 4.22–4.18 (m, 2H, both diastereomers), 4.03 (dd, J = 10.0, 4.5 Hz, 1H, other diastereomer), 3.78 (s, 6H, both diastereomers), 3.01–2.98 (m, 1H, one diastereomer), 2.97 (s, 3H, both diastereomers), 2.94 (s, 3H, both diastereomers), 2.76 (dd, J = 13.9, 5.9 Hz, 1H, other diastereomer), 2.64–2.57 (m, 2H, both diastereomers), 2.56–2.45 (m, 2H, both diastereomers). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 158.62 (one diastereomer), 158.59 (other diastereomer), 144.31 (one diastereomer), 144.26 (other diastereomer), 140.82 (one diastereomer), 140.77 (other diastereomer), 130.2 (2C, one diastereomer), 130.14 (one diastereomer), 130.08 (2C, other diastereomer), 130.02 (other diastereomer), 124.8 (one diastereomer), 124.7 (other diastereomer), 114.4 (4C, both diastereomers), 109.2 (one diastereomer), 109.1 (other diastereomer), 68.70 (one diastereomer), 68.65 (other diastereomer), 55.6 (one diastereomer), 55.4 (2C, both diastereomers), 54.9 (other

diastereomer), 47.8 (one diastereomer), 47.5 (other diastereomer), 37.2 (2C, both diastereomers), 33.3 9 (one diastereomer), 31.9 (other diastereomer); **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{16}H_{19}ClO_5SNa$, 381.0540; observed, 381.0529.

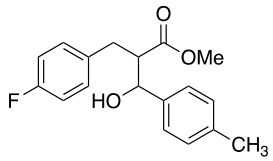
Scheme 1.15 Synthesis of benzylic chloride **1.63** leading to cyclopropane **1.16**.



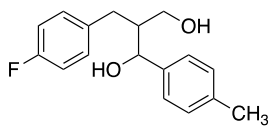
Methyl (E)-3-(4-fluorophenyl)acrylate (1.59) was prepared according to Method O. The following amounts of reagents were used: 4-fluorobenzaldehyde (0.74 mL, 7.0 mmol, 1.0 equiv), (carbomethoxylmethyl)-triphenylphosphonium bromide (3.9 g, 9.1 mmol, 1.3 equiv), *n*-BuLi (3.6 mL, 9.1 mmol, 1.3 equiv), and THF (35 mL). The residue was purified by column chromatography (0–25% EtOAc/hexanes) to afford a white solid (1.1 g, 5.8 mmol, 83% yield). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, J = 15.9 Hz, 1H), 7.53–7.46 (m, 2H), 7.09–7.05 (m, 2H), 6.36 (d, J = 15.9 Hz, 1H), 3.81 (s, 3H).

Methyl 3-(4-fluorophenyl)propanoate (1.60) was prepared according to Method I. The following amounts of reagents were used: **1.59** (1.05 g, 5.8 mmol, 1.0 equiv), palladium on carbon (166 mg, 20.0 mg/0.700 mmol), DCM (10 mL), and MeOH (20 mL). The clear oil was carried forward

without further purification (1.1 g, 94% yield, 15% Et_2O by ^1H NMR). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17–7.13 (m, 2H), 6.99–6.94 (m, 2H), 3.66 (s, 3H), 2.92 (t, J = 7.9 Hz, 2H), 2.61 (t, J = 7.8 Hz, 2H).

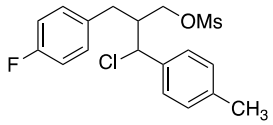


Methyl 2-(4-fluorobenzyl)-3-hydroxy-3-(p-tolyl)propanoate (1.61) was prepared according to Method M. The following amounts of reagents were used: *n*-BuLi (2.6 mL, 6.6 mmol, 1.2 equiv), diisopropylamine (0.94 mL, 6.6 mmol, 1.2 equiv), **1.60** (0.997 g, 5.50 mmol, 1.00 equiv), tolualdehyde (0.65 mL, 5.5 mmol, 1.0 equiv), and THF (20 mL). The residue was purified by column chromatography (0–25–50% EtOAc/hexanes) to afford a clear oil (0.52 g, 1.7 mmol, 18% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.4 (one diastereomer), and 0.5 (other diastereomer) (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27–7.15 (m, 8H, both diastereomers), 7.06–7.02 (m, 4H, both diastereomers), 6.94–6.88 (m, 4H, both diastereomers), 4.98–4.96 (m, 1H, one diastereomer), 4.77 (d, J = 7.3 Hz, other diastereomer), 3.54 (s, 3H, one diastereomer), 3.42 (s, 3H, other diastereomer), 3.04–2.93 (m, 4H, one diastereomer), 2.83 (dd, J = 13.7, 9.8 Hz, 1H, one diastereomer), 2.74 (br s, 1H, one diastereomer), 2.35 (dd, J = 13.7, 5.6 Hz, 1H, other diastereomer), 2.35 (s, 3H, one diastereomer), 2.34 (s, 3H, other diastereomer), 1.60 (br s, 1H, other diastereomer).



2-(4-Fluorobenzyl)-1-(p-tolyl)propane-1,3-diol (1.62) was prepared according to Method N. The following amounts of reagents were used: **1.61** (0.517 g, 1.70 mmol, 1.00 equiv), $LiAlH_4$ (228 mg, 6.00 mmol, 3.50 equiv), and Et_2O (10 mL). The pale yellow oil was carried forward without

further purification (0.32 g, 35% yield, 33% Et_2O by NMR). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 4H, both diastereomers), 7.20–7.17 (m, 4H, both diastereomers), 7.10–7.04 (m, 4H, both diastereomers), 6.96–6.90 (m, 4H, both diastereomers), 5.04 (d, *J* = 4.4, 1H, one diasetereomer), 4.73 (d, *J* = 6.5, 1H, other diastereomer), 3.76 (dd, *J* = 10.8, 2.5 Hz, 1H, one diastereomer), 3.65–3.54 (m, 3H, both diastereomers), 2.69–2.56 (m, 4H, both diastereomers), 2.37 (s, 3H, one diastereomer), 2.35 (s, 3H, other diastereomer), 2.16–2.02 (m, 2H, both diastereomers).

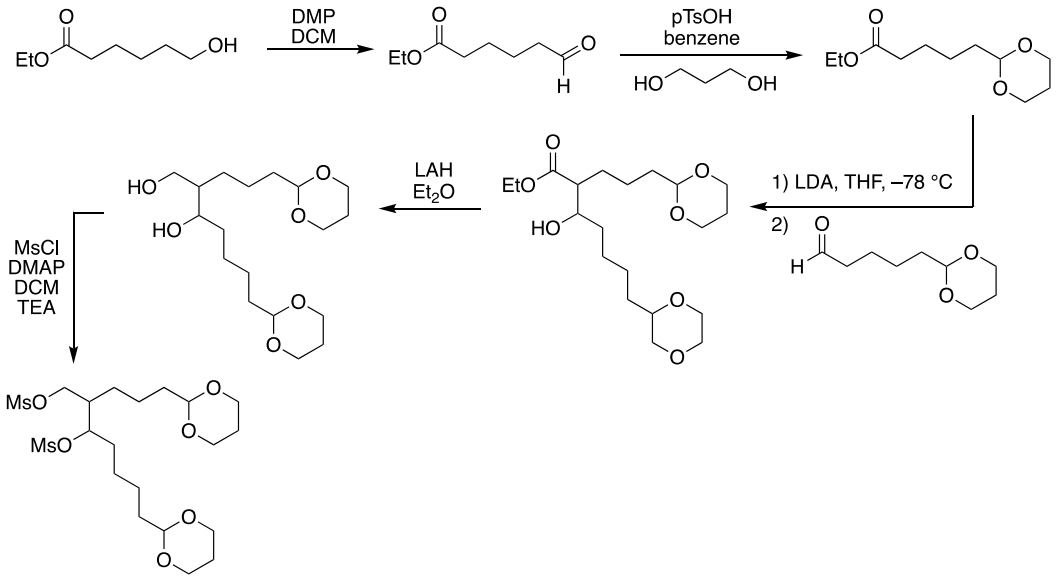


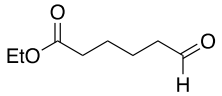
3-Chloro-2-(4-fluorobenzyl)-3-(p-tolyl)propyl methanesulfonate (1.63) was prepared according to Method F. The following amounts of reagents were used: **1.62** (0.163 g, 0.600 mmol, 1.00 equiv), methanesulfonyl chloride (0.11 mL, 1.4 mmol, 2.4 equiv), dimethylaminopyridine (15 mg, 0.12 mmol, 0.20 equiv), Et_3N (0.20 mL, 1.4 mmol, 2.4 equiv), and DCM (4 mL). The residue was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (62 mg, 0.17 mmol, 28% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.8 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 4H, both diastereomers), 7.22–7.17 (m, 4H, both diastereomers), 7.13–7.09 (m, 2H, one diastereomer), 7.07–7.04 (m, 2H, other diastereomer), 6.99–6.94 (m, 4H, both diastereomers), 5.07–5.0-4 (m, 1H, one diastereomer), 4.93–4.91 (m, 1H, other diastereomer), 4.54–4.50 (m, 1H, one diastereomer), 4.17–4.13 (m, 1H, other diastereomer), 4.07–4.03 (m, 1H, one diastereomer), 3.82–3.78 (m, 1H, other diastereomer), 3.18–3.13 (m, 1H, one diastereomer), 3.01 (s, 3H, one diastereomer), 2.85 (s, 3H, other diastereomer), 2.72–2.66 (m, 1H, other diastereomer), 2.56–2.50

(m, 4H, both diastereomers), 2.36 (s, 3H, one diastereomer), 2.35 (s, 3H, other diastereomer); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 161.5 (d, J =245.1 Hz, 2C, both diastereomers), 138.9, 138.7, 136.3, 136.0, 134.05 (d, J = 11.6 Hz, one diastereomer), 134.03 (d, J = 11.6 Hz, other diastereomer), 130.7 (d, J = 8.3 Hz, 2C, one diastereomer), 130.6 (d, J = 8.7 Hz, 2C, other diastereomer), 129.8 (2C, one diastereomer), 129.6 (2C, other diastereomer), 127.4 (2C, one diastereomer), 127.3 (2C, other diastereomer), 115.7 (d, J = 21.3 Hz, 4C, both diastereomers), 68.4 (one diastereomer), 68.2 (other diastereomer), 63.6 (one diastereomer), 62.9 (other diastereomer), 48.6 (2C, both diastereomers), 37.14 (both diastereomers), 37.11 (both diastereomers), 33.3 (one diastereomer), 32.3 (other diastereomer), 21.28 (one diastereomer), 21.26 (other diastereomer); **^{19}F NMR** (564.6 MHz, $CDCl_3$) δ –115.94 (one diastereomer), –116.04 (other diastereomer); **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{18}H_{20}ClFO_3SNa$, 393.0703; observed, 383.0308.

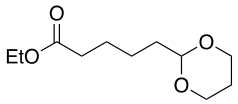
1.4.8 Intermediates and 1,3-Dimesylates for Disusbstituted Alkylcyclopropanes

Scheme 1.16 Synthesis of 1,3-dimesylate **1.68** leading to cyclopropane **1.17**.

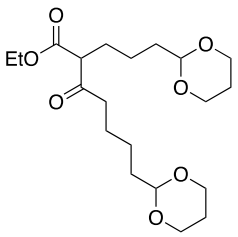




Ethyl 6-oxohexanoate (1.64) was prepared according to Method J. The following amounts of reagents were used: ethyl-6-hydroxyhexanoate (4.9 mL, 30. mmol, 1.0 equiv), Dess-Martin periodinane (15.3 g, 36.0 mmol, 1.20 equiv), and DCM (150 mL). The yellow oil was purified by column chromatography (0–25% EtOAc/hexanes) to afford a pale, yellow oil (5.7 g, 55% yield, 12% Et_2O by ^1H NMR and 30% EtOAC by ^1H NMR). **TLC R_f =** 0.6 (25% EtOAc/hexanes); **^1H NMR** (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 4.15–4.09 (m, 2H), 2.47–2.45 (m, 2H), 2.34–2.31 (m, 2H), 1.69–1.65 (m, 4H), 1.26 (t, J = 7.0 Hz, 3H).

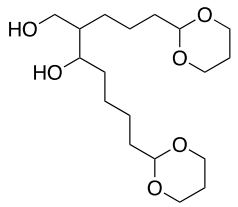


Ethyl 5-(1,3-dioxan-2-yl)pentanoate (1.65) was prepared according to Method P. The following amounts of reagents were used: **1.64** (2.62 g, 16.6 mmol, 1.00 equiv), 1,3- propanediol (1.8 mL, 25 mmol, 1.5 equiv), p-toluenesulfonic acid (86 mg, 0.50 mmol, 3.0 mol %), and benzene (30 mL). The yellow residue was carried forward without further purification (5.1 g, 4% Et_2O by ^1H NMR and 34% EtOAc by ^1H NMR). **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^1H NMR** (400 MHz, $CDCl_3$) δ 4.51 (t, J = 5.2 Hz, 1H), 4.17–4.07 (m, 4H), 3.75 (t, J = 12.4 Hz, 2H), 2.29 (t, J = 7.3 Hz, 2H), 2.09–1.97 (m, 1H), 1.69–1.58 (m, 4H), 1.46–1.31 (m, 3H), 1.25 (t, J = 7.3 Hz, 3H).

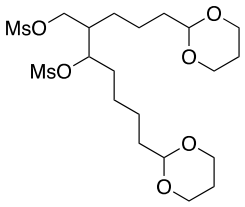


Ethyl 2-(3-(1,3-dioxan-2-yl)propyl)-7-(1,3-dioxan-2-yl)-3-oxoheptanoate (1.66) was prepared according to Method M. The following amounts of reagents were used: *n*-BuLi (5.98 mL, 15.0 mmol, 1.50 equiv), diisopropylamine (2.13 mL, 15.0 mmol, 1.50 equiv), THF (50 mL), **1.65**

portion 1 (1.95 g, 9.00 mmol, 1.00 equiv), and **1.65** portion 2 (1.95 g, 9.00 mmol, 1.00 equiv). The oil was purified by column chromatography (0–25–50% EtOAc/hexanes) to afford a clear oil (0.535 g, 17% yield, 4% DCM by ^{1}H NMR, and 15% EtOAC by ^{1}H NMR). **TLC R_f =** 0.4 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.50 (t, J = 5.1 Hz, 2H), 4.19–4.06 (m, 6H), 3.77–3.70 (m, 4H), 3.40 (t, J = 7.3 Hz, 1H), 2.55–2.46 (m, 2H), 2.36–2.26 (m, 1H), 2.08– 2.04 (m, 2H), 1.87–1.81 (m, 2H), 1.65–1.55 (m, 6H), 1.41–1.30 (m, 5H), 1.25 (t, J = 7.2 Hz, 3H).

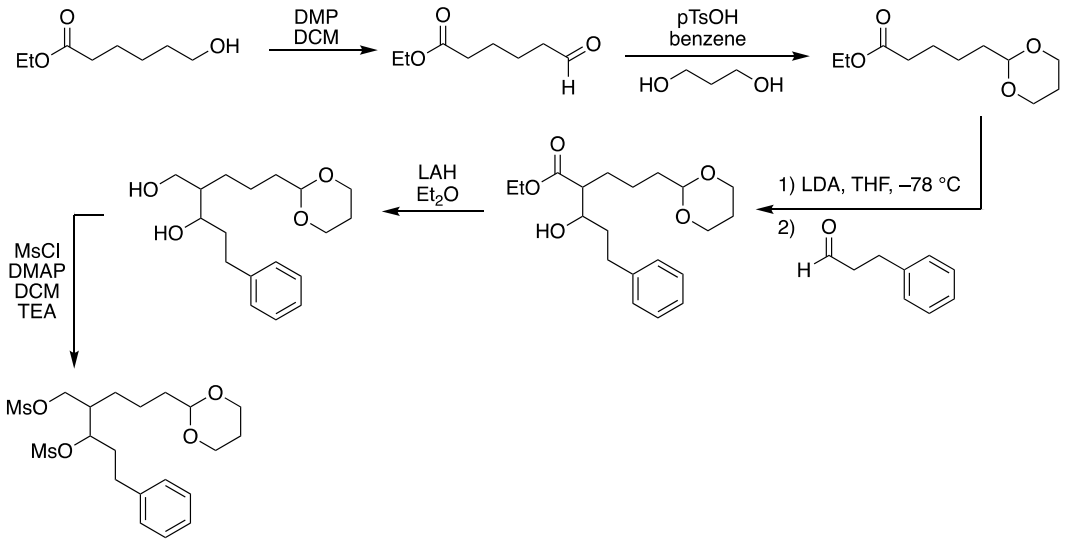


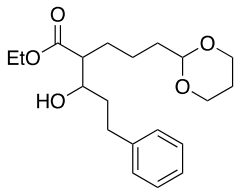
2-(3-(1,3-Dioxan-2-yl)propyl)-7-(1,3-dioxan-2-yl)heptane-1,3-diol (1.67) was prepared according to Method N. The following amounts of reagents were used: **1.66** (0.535 g, 1.54 mmol, 1.00 equiv), $LiAlH_4$ (205 mg, 5.40 mmol, 3.50 equiv), and Et_2O (8 mL). The clear oil was carried forward without further purification (0.373 g, 40% yield, 20% Et_2O by ^{1}H NMR). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.1 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.51 (t, J = 5.1 Hz, 4H, both diastereomers), 4.11–4.07 (m, 8H, both diastereomers), 3.86–3.81 (m, 2H, one diastereomer), 3.79–3.70 (m, 11H, both diastereomers), 3.69–3.63 (m, 1H, other diastereomer), 2.38 (br s, 2H, both diastereomers), 2.36 (br s, 2H, both diastereomers), 2.09–2.02 (m, 4H, both diastereomers), 1.63– 1.28 (m, 34H, both diastereomers).



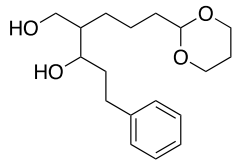
2-(3-(1,3-Dioxan-2-yl)propyl)-7-(1,3-dioxan-2-yl)heptane-1,3-diyl dimethanesulfonate (1.68) was prepared according to Method F. The following amounts of reagents were used: **1.67** (209 mg, 0.600 mmol, 1.00 equiv), methanesulfonyl chloride (0.11 mL, 1.4 mmol, 2.4 equiv), Et_3N (0.20 mL, 1.4 mmol, 2.4 equiv), dimethylaminopyridine (15 mg, 0.12 mmol, 0.20 equiv), and DCM (3 mL). The residue was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.129 g, 0.256 mmol, 43% yield). The desired compound was characterized as a 4:1 ratio of diastereomers. **TLC R_f =** 0.2 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.90–4.86 (m, 1H, major diastereomer), 4.81–4.78 (m, 1H, minor diastereomer), 4.54–4.50 (m, 2H, major, 2H, minor), 4.28–4.18 (m, 2H, major, 2H, minor), 4.10– 4.07 (m, 4H, major, 4H, minor), 3.78–3.73 (m, 4H, major, 4H, minor), 3.05 (s, 3H, major, 3H, minor), 3.03 (s, 3H, major, 3H, minor), 2.11–2.02 (m, 3H, major, 3H, minor), 1.78–1.20 (m, 16H, major, 16H, minor); The major diastereomer was characterized by 13C NMR. **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 102.1, 101.8, 82.1, 68.7, 67.0 (4C), 41.8, 38.9, 37.5, 35.2, 34.9, 31.6, 26.0, 25.9, 25.7, 25.6, 23.7, 21.9; **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{20}H_{38}O_{10}S_2Na$, 525.1804; observed, 525.1809.

Scheme 1.17 Synthesis of 1,3-dimesylate **1.71** leading to cyclopropane **1.18**.



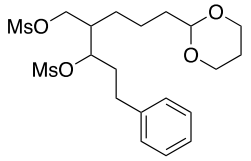


Ethyl 2-(3-(1,3-dioxan-2-yl)propyl)-3-hydroxy-5-phenylpentanoate (1.69) was prepared according to Method M. The following amounts of reagents were used: *n*-BuLi (1.85 mL, 4.62 mmol, 1.20 equiv), diisopropylamine (0.66 mL, 4.6 mmol, 1.2 equiv), **1.65** (0.83 g, 3.9 mmol, 1.00), 3-phenylpropionaldehyde (0.41 mL, 3.1 mmol, 0.80 equiv), and THF (20 mL). The following compound was purified by column chromatography (0–25–50% EtOAc/hexanes) to afford a clear oil (0.18 g, 8% yield, 18% E_2O by ^{1}H NMR and 27% EtOAc by ^{1}H NMR). The desired compound was characterized as a 2:1 mixture of diastereomers. **TLC R_f =** 0.2 (25% EtOAc;hexanes) and 0.6 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30–7.17 (m, 10H, both diastereomers), 4.51–4.48 (m, 2H, both diastereomers), 4.20–4.06 (m, 8H, both diastereomers), 3.85–3.79 (m, 1H, one diastereomer), 3.77–3.71 (m, 4H, both diastereomers), 3.69–3.65 (m, 1H, other diastereomer), 2.90–2.42 (m, 8H, both diastereomers), 1.83–1.30 (m, 20H, both diastereomers), 1.26 (t, J = 7.1 Hz, 6H, both diastereomers).



2-(3-(1,3-Dioxan-2-yl)propyl)-5-phenylpentane-1,3-diol (1.70) was prepared according to Method N. The following amounts of reagents were used: **1.69** (0.578 g, 1.65 mmol, 1.00 equiv), $LiAlH_4$ (220. mg, 5.78 mmol, 3.50 equiv), and Et_2O (8 mL). The residue was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.39 g, 40% yield, 39% EtOAc by ^{1}H NMR). The desired compound was characterized as a 2:1 mixture of diastereomers. **TLC R_f =** 0.2 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30–7.17 (m, 10H, both

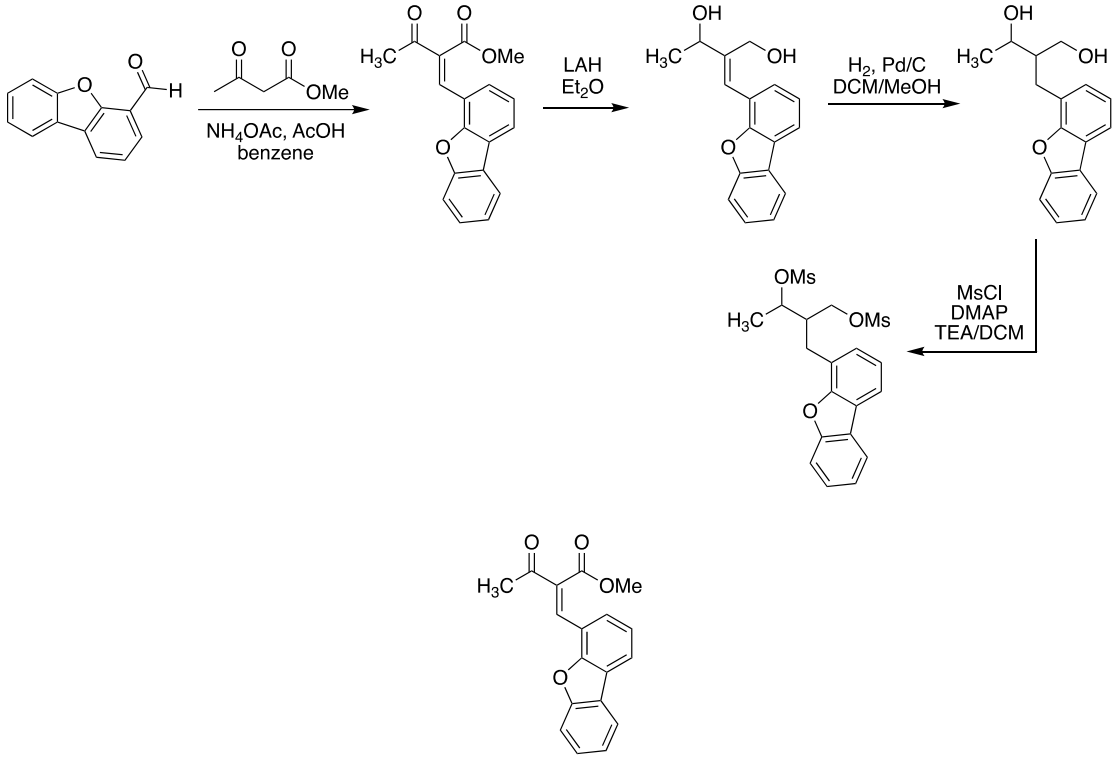
diastereomers), 4.53–4.49 (m, 2H, both diastereomers), 4.15–4.06 (m, 4H, both diastereomers), 3.95–3.91 (m, 1H, one diastereomer), 3.89–3.81 (m, 1H, other diastereomer), 3.79–3.71 (m, 8H, both diastereomers), 2.88–2.81 (m, 2H, both diastereomers), 2.70–2.61 (m, 4H, both diastereomers), 2.49 (br s, 2H, both diastereomers), 2.12–2.04 (m, 2H, both diastereomers), 1.89–1.27 (m, 20H, both diastereomers).



2-(3-(1,3-Dioxan-2-yl)propyl)-5-phenylpentane-1,3-diyl dimethanesulfonate (1.71) was prepared according to Method F. The following amounts of reagents were used: **1.70** (0.20 g, 0.66 mmol, 1.0 equiv), methanesulfonyl chloride (0.12 mL, 1.6 mmol, 2.4 equiv), Et_3N (0.22 mL, 1.6 mmol, 2.4 equiv), dimethylaminopyridine (16 mg, 0.13 mmol, 0.20 equiv), and DCM (3mL). The residue was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.22 g, 0.47 mmol, 72% yield). The desired compound was characterized as a 2:1 mixture of diastereomers. **TLC R_f =** 0.3 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22–7.19 (m, 10H, both diastereomers), 4.94 (ddd, J = 8.1, 5.1, 2.8 Hz, 1H, one diastereomer), 4.88 (q, J = 5.6 Hz, 1H, other diastereomer), 4.53–4.49 (m, 2H, both diastereomers), 4.31–4.20 (m, 4H, both diastereomers), 4.11–4.06 (m, 4H, both diastereomers), 3.78–3.72 (m, 4H, both diastereomers), 3.04 (s, 3H, other diastereomer), 3.03 (s, 3H, one diastereomer), 3.02 (s, 3H, one diastereomer), 3.01 (s, 3H, other diastereomer), 2.78–2.68 (m, 4H, both diastereomers), 2.18–2.04 (m, 6H, both diastereomers), 1.63–1.32 (m, 16H, both diastereomers). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 140.7 (one diastereomer), 140.4 (other diastereomer), 128.8 (4C, both diastereomers), 128.52 (2C, one diastereomer), 128.50 (2C, other diastereomer), 126.5 (one diastereomer), 126.4 (other diastereomer), 101.9 (one diastereomer), 101.8 (other diastereomer), 81.9 (one diastereomer), 81.4

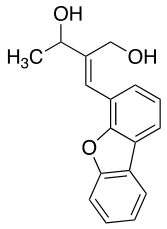
(other diastereomer), 68.6 (one diastereomer), 68.0 (other diastereomer), 67.0 (4C, both diastereomer), 41.9 (one diastereomer), 41.6 (other diastereomer), 38.90 (one diastereomer), 38.86 (other diastereomer), 37.6 (one diastereomer), 37.5 (other diastereomer), 35.1 (one diastereomer), 35.0 (other diastereomer), 33.5 (one diastereomer), 33.4 (other diastereomer), 32.1 (one diastereomer), 31.2 (other diastereomer), 26.6 (one diastereomer), 25.9 (2C, both diastereomers), 25.8 (other diastereomer), 21.8 (one diastereomer), 21.4 (other diastereomer); **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{20}H_{32}O_8S_2Na$, 487.1436; observed, 487.1433.

Scheme 1.18 Synthesis of 1,3-dimesylate **1.75** leading to cyclopropane **1.19**.

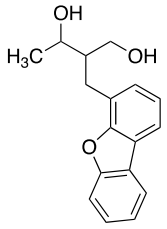


Ethyl-2-(dibenzo[b,d]furan-4-ylmethylene)-3-oxobutanoate (1.72) was prepared according to Method Q. The following amounts of reagents were used: methylacetoacetate (0.54 mL, 5.0 mmol, 1.0 equiv), dibenzofuran-4-carboxaldehyde (0.98 g, 5.0 mmol, 1.0 equiv), ammonium acetate (39 mg, 0.50 mmol, 0.10 equiv), AcOH (7 µL, 0.1 mmol, 3 mol %), and benzene (5 mL). The unpuried residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford a clear oil

(0.75 g, 2.6 mmol, 51% yield). **TLC R_f =** 0.4 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.00 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.97–7.95 (m, 1H), 7.63–7.61 (m, 1H), 7.54–7.48 (m, 2H), 7.41–7.33 (m, 2H), 3.82 (s, 3H), 2.54 (s, 3H).

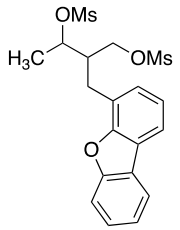


2-(Dibenzo[b,d]furan-4-ylmethylene)butane-1,3-diol (1.73) was prepared according to Method N. The following amounts of reagents were used: **1.72** (0.746 g, 2.55 mmol, 1.00 equiv), $LiAlH_4$ (0.34 g, 8.9 mmol, 3.5 equiv), and Et_2O (13 mL). The residue was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.36 g, 1.4 mmol, 53% yield). The desired compound was characterized as a 2:1 mixture of diastereomers. **TLC R_f =** 0.5 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.7 Hz, 2H, both diastereomers), 7.89–7.87 (m, 2H, both diastereomers), 7.57 (d, *J* = 8.3 Hz, 2H, both diastereomers), 7.49–7.32 (m, 8H, both diastereomers), 6.96 (s, 1H, one diastereomer), 6.87 (s, 1H, other diastereomer), 4.99–4.93 (m, 1H, one diastereomer), 4.80–4.71 (m, 2H, both diastereomers), 4.51–4.38 (m, 3H, both diastereomers), 2.55–2.45 (m, 4H, both diastereomers), 1.59 (d, *J* = 6.5 Hz, 3H, one diastereomer), 1.46 (d, *J* = 6.5 Hz, 3H, other diastereomer).



2-(Dibenzo[b,d]furan-4-ylmethyl)butane-1,3-diol (1.74) was prepared according to Method J. The following amounts of reagents were used: **1.73** (0.361 g, 1.35, 1.00 equiv), Pd/C (40. mg, 20.

mg/0.70 mmol), H_2 balloon, DCM (2 mL), and MeOH (4 mL). The clear unpurified oil was carried forward without further purification (0.31 g, 1.1 mmol, 84% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.5 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.7 Hz, 2H, both diastereomers), 7.83–7.80 (m, 2H, both diastereomers), 7.57 (d, J = 8.2 Hz, 2H, both diastereomers), 7.47–7.43 (m, 2H, both diastereomers), 7.36–7.26 (m, 6H, both diastereomers), 4.22–4.16 (m, 1H, one diastereomer), 4.02–3.95 (m, 2H, both diastereomers), 3.76–3.63 (m, 3H, both diastereomers), 3.21 (dd, J = 14.0, 6.8 Hz, 1H, one diastereomer), 3.11–3.05 (m, 3H, both diastereomers), 2.65 (br s, 2H, both diastereomers), 2.58 (br s, 1H, one diastereomer), 2.41 (br s, 1H, other diasetereomer), 2.23–2.16 (m, 1H, one diastereomer), 2.03–1.95 (m, 1H, other diastereomer), 1.39 (d, J = 6.5 Hz, 3H, one diastereomer), 1.37 (d, J = 7.2 Hz, 3H, other diastereomer).



2-(Dibenzo[b,d]furan-4-ylmethyl)butane-1,3-diyl dimethanesulfonate (1.75) was prepared according to Method F. The following amounts of reagents were used: **1.74** (0.306 g, 1.13 mmol, 1.00 equiv), dimethylaminopyridine (28 mg, 0.23 mmol, 0.20 equiv), Et_3N (0.38 mL, 2.7 mmol, 2.4 equiv), methanesulfonyl chloride (0.21 mL, 2.7 mmol, 2.4 equiv), and DCM (6 mL). The oil was purified by column chromatography (0–50% EtOAc/hexanes) to afford a clear oil (0.37 g, 0.86 mmol, 76% yield). The desired compound was characterized as a 1:1 mixture of diastereomers. **TLC R_f =** 0.6 (50% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.7 Hz, 2H, both diastereomers), 7.86 (d, J = 6.4 Hz, 2H, both diastereomers), 7.57 (d, J = 8.4 Hz, 2H, both diastereomers), 7.49–7.45 (m, 2H, both diastereomers), 7.39–7.28 (m, 5H, both

diastereomers), 7.19–7.16 (m, 1H, one diastereomer), 5.17–5.12 (m, 1H, one diastereomer), 5.05 (quint, J = 6.3 Hz, 1H, other diastereomer), 4.29 (dd, J = 10.4, 4.1 Hz, 1H, one diastereomer), 4.25–4.21 (m, 2H, other diastereomer), 4.17 (dd, J = 10.2, 5.0 Hz, 1H, other diastereomer), 3.35 (dd, J = 14.5, 4.9 Hz, 1H, one diastereomer), 3.25 (dd, J = 13.9, 5.5 Hz, 1H, one diastereomer), 3.09 (s, 3H, one diastereomer), 3.08 (s, 3H, other diastereomer), 3.06–2.98 (m, 1H, other diastereomer), 2.97 (s, 3H, one diastereomer), 2.96 (s, 3H, other diastereomer), 2.95–2.92 (m, 1H, other diastereomer), 2.73–2.65 (m, 2H, one diastereomer), 1.66 (d, J = 6.5 Hz, 6H, both diastereomers); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 156.11 (one diastereomer), 156.09 (other diastereomer), 154.71 (one diastereomer), 154.69 (other diastereomer), 128.4 (one diastereomer), 127.9 (other diastereomer), 127.52 (one diastereomer), 127.50 (other diastereomer), 124.6 (one diastereomer), 124.5 (other diastereomer), 124.40 (one diasetereomer), 124.38 (other diastereomer), 123.31 (one diastereomer), 123.30 (other diastereomer), 123.11 (one diastereomer), 122.1 (other diastereomer), 122.0 (one diastereomer), 121.02 (one diastereomer), 121.00 (other diastereomer), 119.69 (one diastereomer), 119.68 (other diastereomer), 111.86 (3C, both diastereomers), 78.4 (one diastereomer), 77.9 (other diastereomer), 68.1 (one diastereomer), 67.3 (other diastereomer), 44.0 (one diastereomer), 43.8 (other diastereomer), 39.0 (one diastereomer), 38.9 (other diastereomer), 37.40 (one diastereomer), 37.37 (other diastereomer), 27.8 (one diastereomer), 26.6 (other diastereomer), 19.2 (one diastereomer), 18.8 (other diastereomer); **HRMS** (TOF MS ES+) *m/z:* $[M+Na]^+$ calculated for $C_{19}H_{22}O_7S_2Na$, 449.0705; observed, 449.0699.

Chapter 2

Zinc-Mediated Cross-Electrophile Coupling Reaction of 1,3-Dimesylates for Cyclopropane Synthesis

2.1 Introduction

Cyclopropane motifs are prevalent in pharmaceutical and biologically active compounds,[1][2] and many methods have been developed to access these structures with reports dating back to the late 1800s.[3] While a variety of methods have been developed to access these structures,[4] limitations include safety precautions associated with handling diazo compounds, selectivity issues associated with forming substituted cyclopropanes, and the use of alkenes and α,β-unsaturated esters as the primary precursors for these transformations. An early report from Boord and coworkers demonstrated the synthesis of simple cyclopropanes from the corresponding dibromo-alkane in excellent yields using zinc dust in ethanol (Scheme 2.1a).[5] The Simmons-Smith reaction, developed in 1958, utilizes alkene precursors and diiodomethane in the presence of a zinc-copper couple to access the desired cyclopropanes in moderate yields (Scheme 2.1b).[6]

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[1] Portions of this manuscript have been submitted for publication; McGinnis, T. M.; Thane, T. A.; Jarvo, E. R. *Manuscript Submitted.*

[2] Cyclopropane as privileged motif in medicinal chemistry: a) Talele, T. T. *J. Med. Chem.* **2016**, *59*, 8712–8756. b) Salaün, J. Cyclopropane Derivatives and their Diverse Biological Profile. In *Small Ring Compounds in Organic Synthesis* VI. A. Ed. De Meijere, A. Ed. **2000**. 1−67. Berlin Heidelberg: Springer-Verlag.

[3] For early reports of metal-mediated cyclopropanations, see: a) Freund, A. Ueber Trimethylen. *J. Prakt. Chem.* **1882**, *26*, 367–377. b) Gustavson, G. Ueber Eine Neue Darstellungsmethode Des Trimethylens. *J. Prakt. Chem.* **1887**, *36*, 300–303.

[4] For reviews of cyclopropanation methods, see: a) Ebner, C.; Carreira, E. Cyclopropanation Strategies in Recent Total Syntheses. *Chem. Rev.* **2017**, *117*, 11651−11679. b) Lebel, H.; Marcoux, J.−F.; Molinaro, C.; Charette, A. B. *Chem. Rev*. **2003**, *103*, 977−1050. c) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. Asymmetric Cyclopropanation Reactions. *Synthesis* **2014**, *46*, 979−1029. d) Wu, W.; Lin, Z.; Jiang, H. *Org. Biomol. Chem.* **2018**, *16*, 7315−7329.

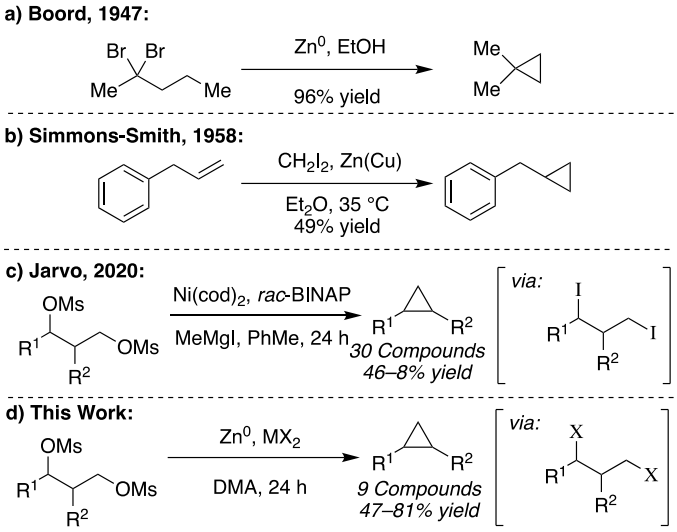
[5] Shortridge, R. W.; Craig, R. A.; Greenlee, K. W.; Derfer, J. M.; Boord, C. E. *J. Am. Chem. Soc.* **1948**, *70*, 946–949.

[6] Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323–5324.

Alcohols and 1,3-diols are prevalent motifs in small molecules,[7] and XEC methods that utilize alcohols and 1,3-diols as precursors have been developed.[8] In 2020, our laboratory identified 1,3-dimesylates as substrates for a nickel-catalyzed cross-electrophile coupling (XEC) reaction to access alkyl- and arylcyclopropanes (Scheme 2.1c).[9] These 1,3-dimesylates could be readily prepared via aldol chemistry followed by a global mesylation. After investigating the mechanism of this transformation, our laboratory discovered that the 1,3-dimesylates are converted in situ with MeMgI to the corresponding 1,3-diiodides, which are the active intermediate for the nickel-catalyzed XEC reaction. With this mechanistic insight in hand, we set out to develop a more tolerant set of reaction conditions for cyclopropane formation that would still employ 1,3-dimesylates prepared by aldol sequences. We envisioned the 1,3-dimesylate could be transformed to the reactive 1,3-dihalide via an in situ S_N2 reaction with a halide salt. The corresponding 1,3-dihalide would then undergo a radical cyclization to provide the desired cyclopropane in the presence of a reducing metal, avoiding the need for the Grignard reagent (Scheme 2.1d).

[7] Prevalence of alcohols in natural products and medicinal agents: a) Henkel, T.; Brunne, R. M.; Müller, H.; Reichel, F. *Angew. Chem. Int. Ed.* **1999**, *38*, 643–647. b) Cramer, J.; Sager, C. P.; Ernst, B. *J. Med. Chem.* **2019**, *62*, 8915–8930.
[8] Jana, S. K.; Maiti, M.; Dey, P.; Maji, B. *Org. Lett.* **2022**, *24*, 1298–1302.
[9] Sanford, A. B.; Thane, T. A.; McGinnis, T. M.; Chen, P.–P.; Hong, X.; Jarvo, E. R. *J. Am. Chem. Soc.* **2020**, *142*, 5017–5023.

Scheme 2.1 Cyclopropanation Methods.



Due to the prevalence of 1,3-diols motifs in natural products and medicinal agents, we foresaw the potential of 1,3-diols to pose as attractive handles for late-stage modification of complex molecules.[10,11] Specifically, polyketides, a common scaffold found in natural products and medicinal agents, consist of 1,3-diols that could undergo further synthetic manipulation (Figure 2.1). Statins are one class of molecules that contain a polyketide backbone.[12] The HMG-CoA reductase inhibitors are among one of the most prescribed classes of medications in the United States and are used to lower cholesterol for those at risk of cardiovascular disease.[13] There are a variety of natural and synthetic statins currently on the market in the United States including

[10] For reviews of synthetic modification of natural products, see: a) Shugrue, C. R.; Miller, S. J. *Chem. Rev.* **2017**, *117*, 11894–11951. b) Robles, O.; Romo, D.; *Nat. Prod. Rep.* **2014**, *31*, 318–334. c) Majhi, S.; Das, D. *Tetrahedron*, **2021**, *78*, 131801–131823.

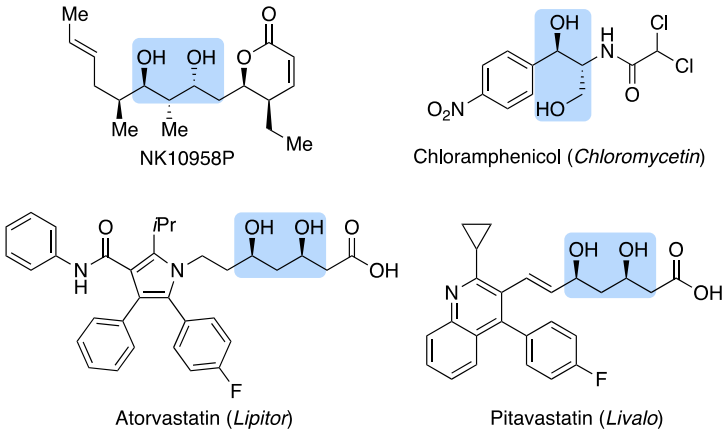
[11] For representative late-stage cross-coupling and cross-electrophile coupling reactions, see: a) Leroux, M.; Vorherr, T.; Lewis, I.; Schaefer, M.; Koch, G.; Karaghiosoff, K.; Knochel, P. *Angew. Chem. Int. Ed.* **2019**, *58*, 8231–8234. b) Mennie, K. M.; Vara, B. A.; Levi, S. M. *Org. Lett.* **2020**, *22*, 556–559. c) Dong, Z.; MacMillan, D. W. C. *Nature*, **2021**, *598*, 451–456

[12] a) Koskinen, A. M. P.; Karisalmi, K. *Chem. Soc. Rev.* **2005**, *34*, 677–690. b) Walsh, C. T.; Tang Y. in *Natural Product Biosynthesis: Chemical Logic and Enzymatic Machinery, Royal Society of Chemistry*, Croyden, 2017; b) Mander, L.; Liu, H.–W. in *Comprehensive Natural Products II Chemistry and Biology, Vol. 1* (Eds.: C. A. Townsend, Y. Ebizuka), Elsevier, Kidlington, **2010**.

[13] a) Endo, A. *Proc. Jpn. Acad., Ser B.* **2010**, *86*, 484–493. b) Brown, M. S.; Goldstein, J. L. *Science* **1986**, *232*, 34–47. c) Schachter, M. *Fundamental & Clinical Pharmacology* **2004**, *19*, 117–125.

Atorvastatin, Pitavastatin, and Rosuvastatin, all of which contain a 1,3-diol motif or can be readily converted to a 1,3-diol in a single step.[14] Our laboratory saw statins as an interesting class of molecules that could undergo a late stage editing to access cyclopropane derivatives.

Figure 2.1 Polyketide Containing Scaffolds.

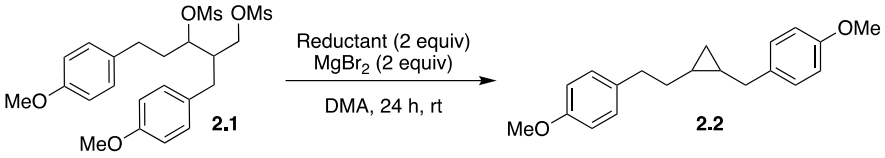


2.2 Results and Discussion

To initiate reaction optimization, a variety of different halide salts were examined. Halide salts, such as $MgBr_2$, are suspected to promote a nucleophilic substitution reaction of the 1,3-dimesylates to give the desired 1,3-dihalide in situ. $MgBr_2$ proved to be the optimal nucleophile source for the desired transformation (Table 2.1, entry 1). Other nucleophile sources including MgI_2, NaBr, and NaI resulted in lower yields of cyclopropane **2.2** (entries 2–4). Higher loadings of different nucleophile sources and mixing $MgBr_2$ and NaI also gave diminished yields of cyclopropane **2.2** (entries 5–8).

[14] Tobert, J. A. *Nature Reviews Drug Discovery* **2003**, *2*, 517–526.

Table 2.1 Optimization of Zinc Mediated XEC Reaction Conditions.

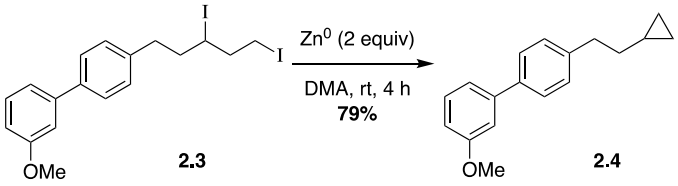


Entry	Deviation From Standard Conditions	4.1(%)	4.2 (%)[a]	dr (trans:cis)[a]
1	None	12	74[b]	3.6:1
2	MgI_2	40	19	3.8:1
3	NaBr	21	52	4.2:1
4	NaI	49	33	4.5:1
5	NaBr (3 equiv)	9	64	3.9:1
6	NaI (8 equiv), THF	35	47	3.7:1
7	$MgBr_2$ (3 equiv)[c]	21	68	3.9:1
8	$MgBr_2$:NaI (2:2 equiv)[c]	11	50	4:1

[a] Yields and dr determined by comparison to PhTMS. [b] Isolated yield. [c] Run at 0.1 M to solubilize salts.

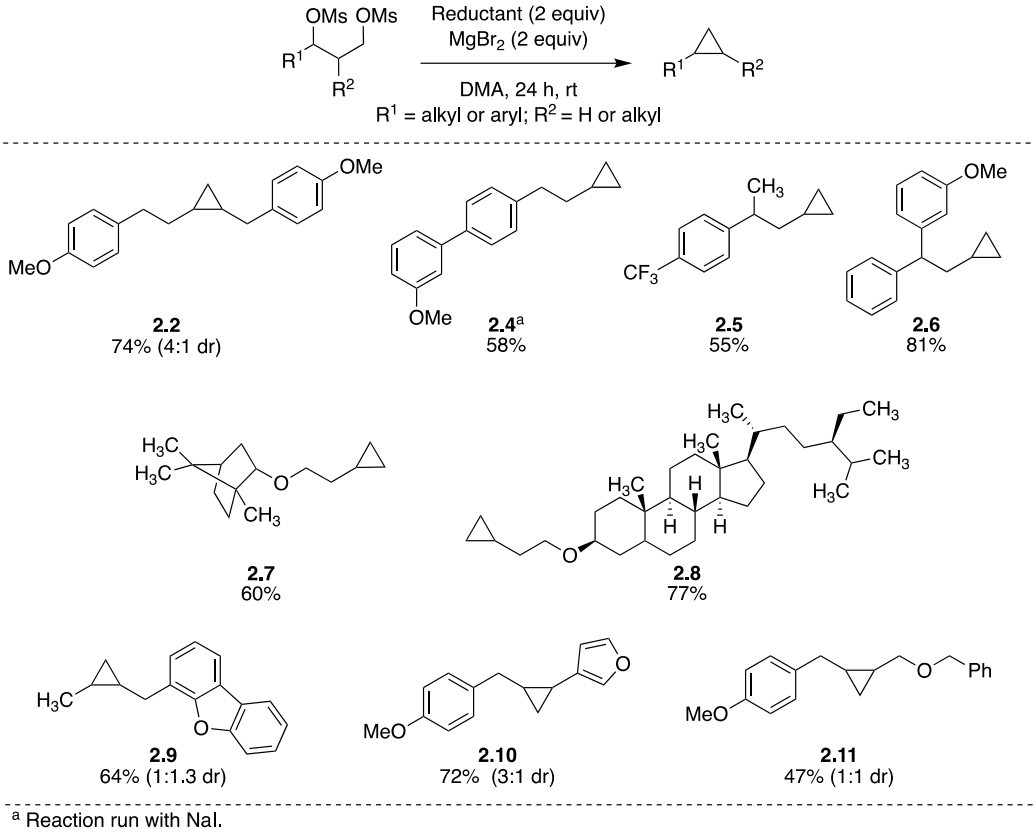
To confirm that the reaction proceeds via a 1,3-dihalide intermediate, 1,3-diioide **2.3** was synthesized and subjected to Zn^0 in DMA at room temperature for four hours (Scheme 2.2). The desired cyclopropane **2.4** was isolated in 79% yield, confirming that 1,3-dihalides are reactive intermediates in the zinc-mediated XEC reaction of 1,3-dimesylates.

Scheme 2.2 Zinc-Mediated XEC of 1,3-Diiodides.



With optimized reaction conditions in hand, a variety of mono- and di-substituted cyclopropanes were synthesized (Scheme 2.3). Electron-donating and electron withdrawing groups were tolerated on the arene (Scheme 2.3, cyclopropanes **2.2**, **2.4** and **2.5**). Cyclopropanes **2.5** and **2.6** showed that substitution on the beta-carbon of the aliphatic carbon chain were well tolerated. (-)-Borneol derivative cyclopropane **2.7** and β-sitosterol derivative cyclopropane **2.8** were synthesized in good yields. Disubstituted cyclopropanes including a dibenzofuran-substituted cyclopropane, a furanyl cyclopropane, and a benzyl ether-substituted cyclopropane were all tolerated under the optimized reaction conditions (Scheme 2.3, cyclopropanes **2.9**–**2.11**).

Scheme 2.3 Reaction Scope of the Zinc-Mediated XEC Reaction.



[a] Reaction run with NaI.

2.3 Conclusions

A zinc-mediated XEC reaction of 1,3-dimesylates for cyclopropane synthesis has been developed. This mild set of reaction conditions allows for increased functional group compatibility, increased yields of di-substituted cyclopropanes, and late-stage modification of complex molecules such as statins.

2.4 Experimental Details

2.4.1 General Procedures

All reactions were carried out under an atmosphere of N_2, or Ar when noted. All glassware was oven- or flame-dried prior to use. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), dimethylformamide (DMF), triethylamine (Et_3N), and toluene (PhMe) were degassed with Ar and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x

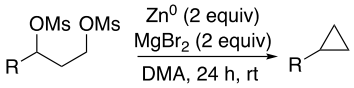
14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 °C for 12 h) to remove H_2O.[15] All other solvents utilized were purchased anhydrous commercially or purified as described. ^{1}H NMR spectra were recorded on Bruker DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C, 376.5 MHz ^{19}F), GN-500 (500 MHz ^{1}H, 125.4 MHz ^{13}C), CRYO-500 (500 MHz ^{1}H, 125.8 MHz ^{13}C) or AVANCE600 (600 MHz ^{1}H, 150 MHz ^{13}C, 564.6 MHz ^{19}F) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), sextet (sext), septet (sept), multiplet (m), broad singlet (bs), broad triplet (bt), doublet of doublet (dd), doublet of triplet (dt), doublet of quartet (dq), doublet of doublet of doublet (ddd), doublet of doublet of triplet (ddt), doublet of triplet of doublet (dtd), triplet of doublet (td), triplet of triplet (tt), triplet of doublet of doublet (tdd), quartet of doublet (qd), quartet of triplet (qt), quartet of doublet of doublet (qdd), apparent singlet (as), apparent triplet (at), apparent quintet (aquin), apparent doublet of quintet (aquin), apparent triplet of doublet (aqd), apparent quartet of doublet (aqd)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). Fluorine chemical shifts are reported in ppm (δ) relative to the absolute frequency of 0.00 ppm in the proton spectrum. Unless otherwise indicated, NMR data were collected at 25 °C. Infrared (IR) spectra were obtained on a Thermo Scientific Nicolet iS5 spectrometer with an iD5 ATR tip (neat) and are reported in terms of frequency of absorption (cm^{-1}). Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with $KMnO_4$ or CAM. Flash chromatography was performed using SiliaFlash F60 (40-63 μm, 60 Å) from SiliCycle. Automated

[15] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518–1520.

chromatography was carried out on a Teledyne Isco CombiFlash Rf Plus. Melting points (m.p.) were obtained using a Mel-Temp melting point apparatus and are uncorrected. All other chemicals were purchased commercially and used as received, unless otherwise noted.

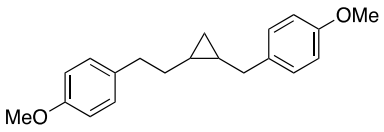
2.4.2 General Cross-Electrophile Coupling Procedures

2.4.2.1 Method A: Zinc-Mediated Cross-Electrophile Coupling Reaction



In a glovebox, a flame-dried 7 mL vial equipped with a stir bar was charged with substrate (1.0 equiv), Zn^0 (2.0 equiv), $MgBr_2$ (2.0 equiv), and DMA (0.10–0.20 M in substrate). The reaction was stirred vigorously for 24 h and then removed from the glovebox. The reaction was filtered through a plug of silica gel (eluting with 100% Et_2O), concentrated in vacuo, and purified by flash column chromatography.

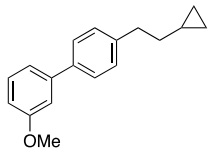
2.4.3 Characterization of Cyclopropane Products



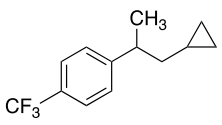
Cyclopropane (2.2) was prepared according to Method A. The following amounts of reagents were used: 1,3-dimesylate **2.1** (0.34 ml, 0.10 mmol, 1.0 equiv, 0.29 M stock solution of substrate in Et_2O), $MgBr_2$ (37 mg, 0.20 mmol, 2.0 equiv), Zn^0 (13 mg, 0.20 mmol, 2.0 equiv) and DMA (0.5 mL, 0.2 M in substrate). The desired compound was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound in a 3.6:1 (trans:cis) mixture of diastereomers as a colorless oil (22 mg, 74 μmol, 74% yield). **TLC R_f =** 0.8 (25% EtOAc/hexanes). Analytical data is consistent with literature values.[8]

Major Diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.7 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.84–6.79 (m, 4H), 3.78 (s, 3H), 3.77 (s, 3H), 2.58 (at, *J* = 9.8 Hz, 2H), 2.47 (t, *J* = 7.3 Hz, 2H), 1.54–1.47 (m, 2H), 0.74–0.66 (m, 1H), 0.63–0.55 (m, 1H), 0.36–0.32 (m, 1H), 0.31–0.26 (m, 1H).

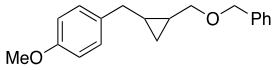
Minor Diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.84–6.79 (m, 4H), 3.78 (s, 3H), 3.77 (s, 3H), 2.67–2.61 (m, 2H), 2.52–2.41 (m, 2H), 1.80–1.71 (m, 2H), 1.04–0.95 (m, 1H), 0.88–0.79 (m, 2H), –0.07 (q, *J* = 5.2 Hz, 1H).



Cyclopropane (2.4) was prepared according to Method A. The following amounts of reagents were used: 1,3-dimesylate **2.12** (25 mg, 0.10 mmol, 1.0 equiv), NaI (30. mg, 0.20 mmol, 2.0 equiv), Zn^0 (13 mg, 0.20 mmol, 2.0 equiv) and DMA (0.5 mL, 0.2 M in substrate). The desired compound was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a colorless oil (16 mg, 65 μmol, 65% yield). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.1 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.11 (s, 1H), 6.87 (dd, *J* = 8.2, 2.6 Hz, 1H), 3.85 (s, 3H), 2.75 (t, *J* = 7.7 Hz, 2H), 1.55 (q, *J* = 7.1 Hz, 2H), 0.78–0.68 (m, 1H), 0.44 (aq, *J* = 5.7 Hz, 2H), 0.06 (q, *J* = 5.1 Hz, 2H). Analytical data is consistent with literature values.[8]



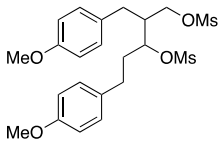
Cyclopropane (2.5) was prepared according to Method A. The following amounts of reagents were used: 1,3-dimesylate **2.13** (42 mg, 0.10 mmol, 1.0 equiv), $MgBr_2$ (37 mg, 0.20 mmol, 2.0 equiv), Zn^0 (13 mg, 0.20 mmol, 2.0 equiv) and DMA (0.5 mL, 0.2 M in substrate). The desired compound was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a colorless oil (12 mg, 54 μmol, 54% yield). **TLC R_f =** 0.8 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 2.89 (sext, *J* = 7.1 Hz, 1H), 1.58 (quint, *J* = 7.1 Hz, 1H), 1.36 (quint, *J* = 7.0 Hz, 1H), 1.29 (d, *J* = 7.0 Hz, 3H), 0.58–0.51 (m, 1H), 0.43–0.37 (m, 1H), 0.36–0.31 (m, 1H), 0.05–0.01 (m, 1H), –0.03 to –0.08 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) *δ* 152.0, 128.1 (q, *J* = 32.1 Hz), 127.4 (2C), 124.5 (q, *J* = 271.4 Hz), 125.2 (q, *J* = 3.7 Hz, 2C), 43.5, 40.5, 21.5, 9.4, 4.7, 4.5; **^{19}F NMR** (564.6 MHz, $CDCl_3$) δ –62.2; **HRMS** (TOF MS CI^+) m/z: $[M]^+$ calculated for $C_{13}H_{15}F_3$, 228.1126; found, 228.1132.



Cyclopropane (2.11) was prepared according to Method A. The following amounts of reagents were used: 1,3-dimesylate **2.14** (43 mg, 0.10 mmol, 1.0 equiv), $MgBr_2$ (37 mg, 0.20 mmol, 2.0 equiv), Zn^0 (13 mg, 0.20 mmol, 2.0 equiv) and DMA (0.5 mL, 0.2 M in substrate). The desired compound was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound in a 1:1 mixture of diastereomers as a colorless oil (12 mg, 47 μmol, 47% yield). **TLC R_f =** 0.9 (25% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34–7.23 (m, 10H, both diastereomers), 7.20–7.16 (m, 4H, both diastereomers), 6.84–6.80 (m, 4H, both diastereomers), 4.53 (aq, *J* = 11.8 Hz, 2H, one diastereomer), 4.48 (s, 2H, other diastereomer), 3.78 (s, 3H, one diastereomer), 3.77 (s, 3H, other diastereomer), 3.63 (dd, *J* = 10.2, 6.5 Hz, 1H, one diastereomer), 3.46 (dd, *J* = 10.2, 8.1 Hz, 1H, other diastereomer), 3.40–3.31 (m, 2H, both diastereomers), 2.78

(dd, J = 15.1, 6.1 Hz, 1H, one diastereomer), 2.60–2.50 (m, 2H, both diastereomers), 2.43 (dd, J = 15.0, 8.2 Hz, 1H, other diastereomer), 1.29–1.21 (m, 1H, one diastereomer), 1.19–1.11 (m, 1H, other diastereomer), 1.05–0.97 (m, 1H, one diastereomer), 0.92–0.86 (m, 1H, other diastereomer), 0.85–0.80 (m, 1H, one diastereomer), 0.50–0.43 (m, 2H, both diastereomers), 0.16 (q, J = 5.5 Hz, 1H, other diastereomer); **^{13}C NMR** ($CDCl_3$, 125.7 MHz) δ 158.01 (one diastereomer), 157.95 (other diastereomer), 138.8 (one diastereomer), 138.7 (other diastereomer), 134.4 (one diastereomer), 133.9 (other diastereomer), 129.5 (2C, one diastereomer), 129.3 (2C, other diastereomer), 128.49 (2C, one diastereomer), 128.45 (2C, other diastereomer), 127.9 (2C, one diastereomer), 127.73 (2C, other diastereomer), 127.69 (one diastereomer), 127.6 (other diastereomer), 113.87 (2C, one diastereomer), 113.85 (2C, other diastereomer), 74.2 (one diastereomer), 72.9 (other diastereomer), 72.4 (one diastereomer), 70.62 (other diastereomer), 55.40 (one diastereomer), 55.39 (other diastereomer), 38.5 (one diastereomer), 33.7 (other diastereomer), 18.6 (one diastereomer), 18.5 (other diastereomer), 17.2 (one diastereomer), 15.9 (other diastereomer), 10.3 (one diastereomer), 10.0 (other diastereomer); **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calculated for $C_{19}H_{22}O_2Na$, 305.1518; found, 305.1525.

2.4.4 Characterization of 1,3-Dimesylates

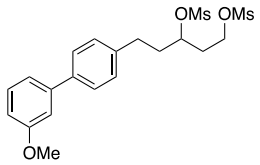


Dimesylate (2.1) was prepared by was charging a flame-dried flask with $LiAlH_4$ (2.2 equiv) in a glovebox. The flask was capped with a stopper and removed from glovebox. An N_2 inlet and anhydrous Et_2O (25 mL, 0.4 M in substrate) were added. The reaction flask was cooled to 0 ºC and the prerequisite beta-keto ester (11 mmol, 1.0 equiv) was added as a solution in Et_2O (11 mL, 1.0 M). The reaction was warmed to rt and stirred for 2 h. To quench, saturated NH_4Cl was added

and reaction was extracted with EtOAc (x3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The diol was carried into the next step without further purification. The unpurified diol (1.1 g, 3.4 mmol, 1.0 equiv) and DMAP (83 mg, 0.68 mmol, 0.20 equiv) in DCM (10. mL, 0.34 M substrate) under Schlenk conditions. Et_3N (1.4 mL, 10. mmol, 3.0 equiv) and MsCl (0.58 mL, 7.5 mL, 2.2 equiv) were added sequentially to the flask and allowed to stir overnight. The resulting solution was quenched with $NaHCO_3$, extracted with DCM (x3), washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The compound was purified by flash column chromatography (0–60% EtOAc/hexanes) to afford the title compound as a clear, light-yellow oil (1.5 g, 3.1 mmol, 92% over two steps). The compound was characterized as a 3:1 mixture of diastereomers. **TLC R_f =** 0.6 (50% EtOAc/hexanes). Analytical data is consistent with literature values.[8]

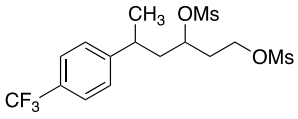
Major Diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.06 (m, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.83 (t, *J* = 8.5 Hz, 4H), 4.95–4.88 (m, 1H), 4.21–4.14 (m, 2H), 3.79–3.88 (m, 6H), 2.97 (s, 3H), 2.85–2.52 (m, 4H), 2.50–2.41 (m, 4H), 2.18–1.97 (m, 2H);

Minor Diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.06 (m, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.83 (t, *J* = 8.5 Hz, 4H), 4.95–4.88 (m, 1H), 4.21–4.14 (m, 2H), 3.79–3.88 (m, 6H), 3.04 (s, 3H), 2.95 (s, 3H), 2.85–2.52 (m, 4H), 2.50–2.41 (m, 1H), 2.18–1.97 (m, 2H).



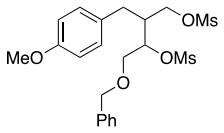
Dimesylate (2.12) was prepared by dissolving the prerequisite diol (0.70 g, 2.4 mmol, 1.0 equiv) and DMAP (60. mg, 0.49 mmol, 0.20 equiv) in DCM (10. mL, 0.24 M in substrate) under Schlenk conditions. Et_3N (1.0 mL, 7.3 mmol, 3.0 equiv) and MsCl (0.42 mL, 5.4 mmol, 2.2 equiv) were

added sequentially to the flask and allowed to stir overnight. The resulting solution was quenched with $NaHCO_3$, extracted with DCM (x3), washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The compound was purified by flash column chromatography (0–50% EtOAc/hexanes) to afford the title compound as a white solid (0.93 g, 2.1 mmol, 86%). **TLC R_f =** 0.7 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.10 (s, 1H), 6.88 (d, *J* = 8.7 Hz, 1H), 4.97–4.93 (m, 1H), 4.40–4.33 (m, 2H), 3.85 (s, 3H), 3.04 (s, 3H), 3.03 (s, 3H), 2.82–2.74 (m, 2H), 2.24–2.05 (m, 4H).Analytical data is consistent with literature values.[9]



Dimesylate (2.13) was prepared by dissolving the prerequisite diol (1.17 g, 4.48 mmol, 1.00 equiv) and DMAP (109 mg, 0.896 mmol, 0.200 equiv) in DCM (9 mL, 0.5 M in substrate) under Schlenk conditions. Et_3N (1.87 mL, 13.4 mmol, 3.00 equiv) and MsCl (0.86 mL, 11 mmol, 2.5 equiv) were added sequentially to the flask and allowed to stir overnight. The resulting solution was quenched with $NaHCO_3$, extracted with DCM (x3), washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The compound was purified by flash column chromatography (50% EtOAc/hexanes) to afford the title compound in a 1:1 mixture of diastereomers as a viscous oil (0.92 mg, 2.2 mmol, 49% yield). **TLC R_f =** 0.6 (50% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) *δ* 7.58 (d, *J* = 7.9 Hz, 4H, both diastereomers), 7.35 (t, *J* = 8.8 Hz, 4H, both diastereomers), 4.77–4.74 (m, 1H, one diastereomer), 4.71–4.67 (m, 1H, other diastereomer), 4.34–4.26 (m, 4H, both diastereomers), 3.03–3.00 (m, 2H, both diastereomers), 2.99–2.95 (m, 12H, both diastereomers), 2.23–1.92 (m, 8H, both diastereomers), 1.33 (d, *J* = 6.9 Hz, 3H, one diastereomer), 1.30 (d, *J* = 7.0 Hz, 3H, other diastereomer); **^{13}C NMR** (500 MHz, $CDCl_3$) *δ* 149.7 (one

diastereomer), 149.6 (other diastereomer), 129.3–128.5 (q, J = 32.3 Hz, 2C, both diastereomers), 127.4–120.6 (q, J = 271.8 Hz, 2C, both diastereomers), 127.6 (2C, one diastereomer), 127.3 (2C, other diastereomer), 125.8–125.6 (quint, J = 3.7 Hz, 4C, both diastereomers), 77.1 (one diastereomer), 76.8 (other diastereomer), 65.4 (one diastereomer), 65.3 (other diastereomer), 42.9 (one diastereomer), 42.6 (other diastereomer), 38.7 (one diastereomer), 38.5 (other diastereomer), 37.43 (one diastereomer), 37.40 (other diastereomer), 36.2 (one diastereomer), 36.0 (other diastereomer), 34.5 (one diastereomer), 34.2 (other diastereomer), 22.9 (one diastereomer), 22.4 (other diastereomer); **^{19}F NMR** (564.6 MHz, $CDCl_3$) δ –62.3; **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calculated for $C_{15}H_{21}F_3O_6S_2Na$, 441.0629; found, 441.0621.



Dimesylate (2.14) was prepared by dissolving the prerequisite diol (240 mg, 0.77 mmol, 1.0 equiv) and DMAP (18 mg, 0.15 mmol, 0.20 equiv) in DCM (4 mL, 0.4 M in substrate) under Schlenk conditions. Et_3N (0.26 mL, 1.9 mmol, 2.4 equiv) and MsCl (0.14 mL, 1.9 mmol, 2.4 equiv) were added sequentially to the flask and allowed to stir overnight. The resulting solution was quenched with $NaHCO_3$, extracted with DCM (x3), washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The compound was purified by flash column chromatography (50% EtOAc/hexanes) to afford the title compound in a 3:1 mixture of diastereomers as a viscous oil (0.30 g, 0.63 mmol, 82% yield). **TLC R_f** = 0.5 (50% EtOAc/hexanes); **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calculated for $C_{21}H_{28}S_2O_8Na$, 495.1123; found, 495.1112.

Major Diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.36 (m, 5H), 7.12 (d, J = 8.6 Hz, 2H), 6.91–6.88 (m, 2H), 5.09–5.06 (m, 1H), 4.65–4.56 (m, 2H), 4.26–4.15 (m, 2H), 3.84 (s, 3H), 3.82–

3.77 (m, 2H), 3.10 (s, 3H), 3.02 (s, 3H), 2.88 (dd, *J* = 14.2, 5.5 Hz, 1H), 2.69–2.61 (m, 1H), 2.55–2.46 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 158.5, 137.2, 129.9 (2C), 129.6, 128.6 (2C), 128.2, 128.1 (2C), 114.3 (2C), 80.7, 73.6, 69.7, 67.9, 55.3, 42.2, 38.7, 37.2, 31.2.

Minor Diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.41 (m, 5H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.91–6.88 (m, 2H), 5.00–4.97 (m, 1H), 4.65–4.56 (m, 2H), 4.26–4.15 (m, 2H), 3.84 (s, 3H), 3.71–3.68 (m, 2H), 3.10 (s, 3H), 3.01 (s, 3H), 2.82 (dd, *J* = 13.8, 5.8 Hz, 1H), 2.69–2.61 (m, 1H), 2.55–2.46 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 158.5, 137.1, 130.2 (2C), 129.6, 128.6 (2C), 128.2, 128.0 (2C), 114.3 (2C), 80.8, 73.5, 69.9, 67.4, 55.3, 42.1, 38.9, 37.2, 32.3.

Chapter 3

Nickel-Catalyzed Domino Dicarbofunctionalization Cross-Electrophile Coupling Reaction for Vinyl Cyclopropane Synthesis

3.1 Introduction

The ability to rapidly build up molecular complexity in a single step has vastly transformed the way organic chemists approach synthesizing molecules.[1] Domino reactions are an efficient way to forge multiple bonds in a single step, as two or more bond forming steps are involved in a single transformation.[2] Developing synthetic methods with sustainable first row transition metals, such as nickel, has allowed for new mechanistic pathways to be invoked.[3,4] Specifically, nickel catalysis has aided in the advancement of new domino transformations because nickel can participate in both one- and two- electron pathways.[5]

Dicarbofunctionalization reactions have become an increasingly popular method to construct two new bonds in a single step.[6] These methods utilize transition metal catalysts, such

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[1] Portions of this chapter have been published in ACS Catalysis, see: Hewitt, K. A.; Xie, P.-P.; Thane, T. A.; Hirbawi, N.; Zhang, S.-Q.; Matus, A. C.; Lucas, E. L.; Hong, X.; Jarvo, E. R. *ACS Catalysis* **2021**, *11*, 14369–14380.

[2] For reviews of transition-metal catalyzed domino reactions see: a) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136. b) Ikeda, S.-I. *Acc. Chem. Res.* **2000**, *33*, 511–519. c) Montgomery, J. *Angew. Chem. Int. Ed.* **2004**, *43*, 3890–3908. d) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186. e) Pellissier, H.. *Chem. Rev.* **2013**, *113*, 442–524. f) Tietze, L. F. *Domino Reactions: Concepts for Efficient Organic Synthesis.* Wiley-VCH: Weinheim, **2014.**

[3] For lead references on sustainable first row transition metal catalysis: a) Hayler, J. D.; Leahy, D. K.; Simmons, E. *Oragnometallics* **2019**, *38*, 36–46. b) Nuss, P.; Eckelman, M. J. *PLOS One: Metals Environmental Impact* **2014**, DOI: 10.1371. c) Ashby, M. F. *Materials and the Environment – Eco-Informed Material Choice, 2nd ed.* **2013**, Butterworth-Heinemann.

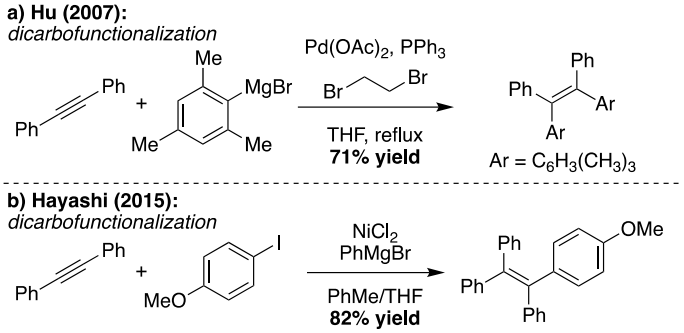
[4] For lead references in first row transition metal catalyzed cross couplings: a) Campeau, L.-C.; Hazari, N. *Organometallics* **2019**, *38*, 3–35. b) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417–1492. c) Singer, R. A.; Monfette, S.; Bernhardson, D.; Tcyrulnikov, S.; Hubbell. A. K.; Hansen, E. C. *Org. Process Res. Dev.* **2021**, *25*, 1802–1815.

[5] a) Tasker, S. Z.; Standely, E. A.; Jamison, T. A. *Nature* **2014**, *509*, 299–309. b) Tamaru, Y. *Modern Organonickel Chemistry.* Wiley-VCH Verlag GmbH & Co., **2005**. c) Lucas, E. L.; Jarvo, E. R. *Acc. Chem. Res.* **2018**, *51*, 567–572. (d) Diccianni, J. B.; Diao, T. *Trends Chem.* **2019**, *1*, 830–844. e) Fu, G. C. *ACS Cent. Sci.* **2017**, *3*, 692–700. f) Greaves, M. E.; Johnson Humphrey, E. L. B.; Nelson, D. J. *Catal. Sci. Technol.*, **2021**, *11*, 2980.

[6] For recent reviews on nickel-catalyzed conjunctive XC reactions see: a) Derosa, J.; Tran, V. T.; van der Puyl, V. A.; Engle, K. M. *Aldrichimica ACTA* **2018**, *51*, 21–32. b) Dhungana, R. K.; KC, S.; Basnet, P.; Giri, R. T. *Chem. Rec.* **2018**, *18*, 1314–1340. c) Luo, Y.-C. Xu, C.; Zhang, X. *Chin. J. Chem.* **2020**, *38*, 1371–1394. For lead examples with alkynes: d) Terao, H.; Bando, F.; Kambe, N. *Chem. Commun.* **2009**, 7336–7338. e) Xue, F.; Zho, J.; Hor, T. S. A.;

as nickel or palladium, and organometallic reagents or alkyl halides to add across alkenes or alkynes affording highly substituted alkane or alkene products. In 2007, the Hu laboratory developed a palladium-catalyzed oxidative dicarbofunctionalization reaction to form *cis*-stilbenes (Scheme 3.1a).[7] This method added hindered Grignard reagents across internal alkynes to access tetrasubstituted alkene products. In a complementary fashion, the Hayashi laboratory developed a nickel-catalyzed dicarbofunctionalization of internal alkynes (Scheme 3.1b).[8] In this report, both a Grignard reagent and an aryl halide were used to functionalize the internal alkyne.

Scheme 3.1. Previous Work in Transition-Metal Catalyzed Dicarbofunctionalization Reactions.



The field of cross-electrophile coupling (XEC) reactions has also had a significant impact on organic synthesis as it has allowed for the coupling of easily accessible halide and pseudohalide building blocks.[9] Specifically, the Jarvo laboratory has been interested in developing new intramolecular XEC reactions utilizing nickel catalysis to activate sluggish C–O and C–N bonds.[10]

Hayashi, T. *J. Am. Chem. Soc.* **2015**, *137*, 3189–3192. (f) Wickham, L. M.; Giri, R. *Acc. Chem. Res.* **2021**, *54*, 3415–3437.

[7] Dong, C.–G.; Yeung, P.; Hu, Q.–S. *Org. Lett.* **2007**, *9*, 363–366.

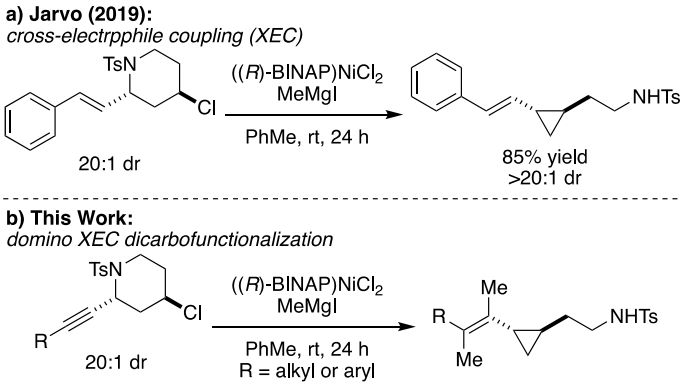
[8] Xue, F.; Zhao, J.; Andy Hor, T. S.; Hayashi, T. *J. Am. Chem. Soc*. **2015**, *137*, 3189−3192.

[9] For reviews of XEC reactions see: a) Knappke, C. E. I.; Grupe, S.; Gärtner, D.; Corpet, M.; Gosmini, C.; Jacobi von Wangelin, A. *Chem. Eur. J.* **2014**, *20*, 6828–6842. b) Goldfogel, M. J.; Huang, L.; Weix, D. J. "Cross-Electrophile Coupling: Principles and New Reactions." In *Nickel Catalysis in Organic Synthesis*; Ogoshi, S., Ed.; Wiley, **2020**; pp 183–222. c) Wang, X.; Dai, Y.; Gong, H. *Top. Curr. Chem. (Z)* **2016**, *374*, 61–89. d) Lucas, E. L.; Jarvo, E. R. *Nat. Rev. Chem*. **2017**, *1*, 0065. e) Poremba, K. E.; Dibrell, S. E.; Reisman, S. E. *ACS Catal.* **2020**, *10*, 8237–8246. f) Campeau, L.-C.; Hazari, N. *Organometallics* **2019**, *38*, 3–35.

[10] a) Tollefson, E. J.; Erickson, L. W.; Jarvo, E. R. *J. Am. Chem. Soc.* **2015**, *137*, 9760–9763. b) Erickson, L. W.; Lucas, E. L.; Tollefson, E. J.; Jarvo, E. R. *J. Am. Chem. Soc.* **2016**, *138*, 14006–14011. c) Chen, P.-P.; Lucas, E. L.; Greene, M. A.; Zhang, S.-Q.; Tollefson, E. J.; Erickson, L. W.; Taylor, B. L. H.; Jarvo, E. R.; Hong, X. *J. Am. Chem. Soc.* **2019**, *141*, 5835– 5855.

In 2019, the Jarvo laboratory reported the nickel-catalyzed XEC of vinyl piperidines to access vinyl disubstituted cyclopropanes in high yield and high diastereoselectivity (Scheme 3.2a).[11] We foresaw alkynyl piperidines as unique substrates to undergo both dicarbofunctionalization and XEC reactions.

Scheme 3.2. Nickel-Catalyzed XEC Reactions.



Herein, we report the first example of a domino XEC dicarbofunctionalization reaction for vinyl cyclopropane synthesis (Scheme 3.2b). Propargyl *N*-tosyl sulfonamides undergo a XEC reaction to install the cyclopropane moiety followed by a dicarbofuncationalization reaction to install a tetrasubstituted olefin, thus forming three new carbon–carbon bonds. An $FeCl_3$-mediated aza-Prins reaction was developed in conjunction with this work to access propargyl *N*-tosyl sulfonamides rapidly in one step from ynal precursors.[12]

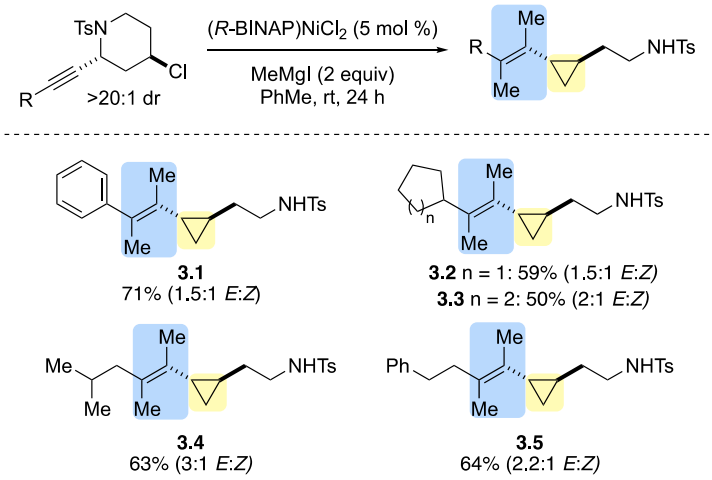
3.2 Results and Discussion

Reaction development was initiated by optimizing reaction conditions. With optimized conditions in hand, a variety of vinyl cyclopropanes were synthesized (Scheme 3.3). While simple aryl substituents were well tolerated, of note was the tolerance of alkyl substituents. Both

[11] Lucas, E. L.; Hewitt, K. A.; Chen, P.-P.; Castro, A. J.; Hong, X.; Jarvo, E. R. *J. Org. Chem.* **2020**, *85*, 1775–1793.
[12] The $FeCl_3$-mediated aza-Prins reaction was developed and optimized by Kirsten A. Hewitt. Further details can be found here: *ACS Catal.* **2021**, *11*, 14369–14380.

cyclopentyl- and cyclohexyl-substituted alkenes, in cyclopropanes **3.2** and **3.3**, were synthesized in 59% and 50% yields respectively. Isobutyl substitution and aliphatic chain substitution were also tolerated as demonstrated by cyclopropanes **3.4** and **3.5**. Notably, vinyl cyclopropanes **3.1**–**3.5** were synthesized in 20:1 dr with respect to the cyclopropane and in a modest *E*:Z ratio.

Scheme 3.3. Scope of the Domino XEC Dicarbofunctionalization.

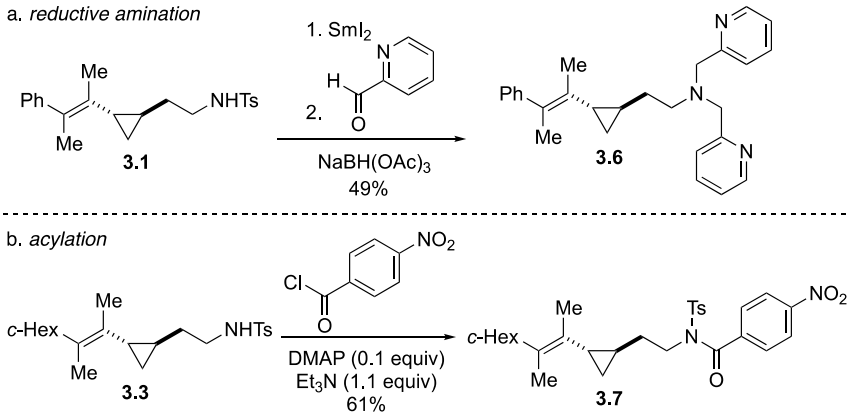


Cyclopropane moieties are prevalent in natural products and pharmaceutical compounds including both vinyl cyclopropanes and cyclopropyl amines.[13][14] Specifically, amine-substituted cyclopropanes have been shown to have potent anti-leukemia activity as lysine specific demethylase inhibitors (LSD1).[15] To demonstrate the synthetic utility of this method, two derivatized vinyl cyclopropanes were synthesized. Cyclopropane **3.6** was accessed in two steps via a SmI_2 deprotection of the sulfonamide followed by a reductive amination with 2-

[13] For reviews on biological activity of substituted vinyl cyclopropanes, see: a) Talele, T. T. *J. Med. Chem.* **2016**, *59*, 8712–8756. b) Salaün, J. "Cyclopropane Derivatives and their Diverse Biological Profile." In *Small Ring Compounds in Organic Synthesis VI*. de Meijere, A. Ed. **2000**. pp. 1–67.
[14] For discussions on the biological activity of substituted alkenes, see: a) Avendano, C.; Menendez, J. C. *Medicinal Chemistry of Anticancer Drugs*, Elsevier, Oxford, **2015**, pp. 87–95. b) Flynn, A. B.; Ogilvie, W. W. *Chem. Rev.* **2007**, *107*, 4698–4745.
[15] Albrecht, B. K.; Audia, J. E.; Cote, A.; Duplessis, M.; Gehling, V. S.; Harmange, J.-C.; Vaswani, R. G. LSD1 Inhibitors and Uses Thereof. WO 2016/172496 A1. **2016**.

pyridylcarboxaldehyde (Scheme 3.4a).[16] Cyclopropane **3.7** was synthesized by acylating the pendant sulfonamide (Scheme 3.4b). Imide **3.7** was shown to have activity against a non-small cell lung cancer cell line (HOP-92) in collaboration with the NIH DPT Program.[17]

Scheme 3.4. Synthesis of Vinyl Cyclopropane Derivatives.

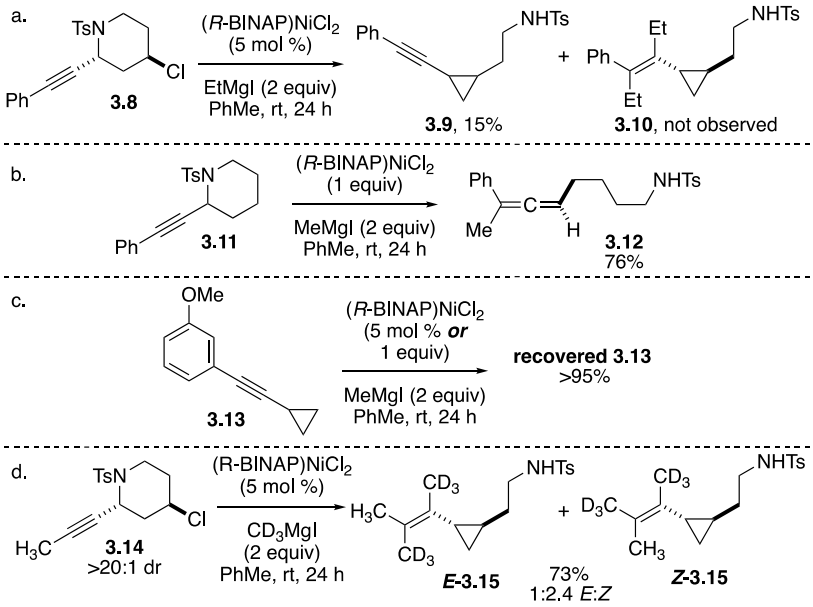


To investigate the operative mechanism of this transformation, a variety of mechanistic experiments were performed to confirm that the reaction initiates by oxidative addition at the propargyl sulfonamide. An initial attempt to employ alternative Grignard reagents, such as EtMgI, resulted in a 15% yield of alkynyl cyclopropane **3.9** (Scheme 3.5a). No difunctionalized alkene **3.10** was observed. Propargyl sulfonamide **3.11**, with no alkyl chloride, was synthesized and subjected to the reaction conditions with stoichiometric nickel (Scheme 3.5b). No difunctionalized alkene was observed, however allene **3.12** was isolated in 76% yield. Additionally, alkynyl cyclopropane **3.13** was subjected to the standard reaction conditions (Scheme 3.5c). Dicarbofunctionalization of the alkyne was not observed, and only alkynyl cyclopropane **3.13** was recovered. These results are consistent with the reaction initiating via oxidative addition at the

[16] a) Szostak, M.; Spain, M.; Procter, D. J. *J. Org. Chem.* **2012**, *77*, 3049– 3059. b) Ankner, T.; Hilmersson, G. *Org. Lett.* **2009**, *11*, 503– 506.
[17] National Institute of Health, "National Cancer Institute Developmental Therapeutics Program," can be found under https://dtp. cancer.gov/, **2021**.

propargyl sulfonamide. Finally, to probe the relative stability of the diastereomers, propargyl sulfonamide **3.14** was synthesized and subjected to reaction conditions utilizing CD_3MgI (Scheme 3.5d). Product diastereomers of cyclopropane **3.15** were isolated in a 1:2.4 *E:Z* ratio confirming that the relative stability of the diastereomers does not determine the selectivity of the reaction.

Scheme 3.5. Mechanistic Experiments.



3.3 Conclusions

This work is the first report of a domino XEC dicarbofunctionalization reaction. In this transformation, the propargyl sulfonamide undergoes an XEC reaction to afford the desired cyclopropane and, in subsequent steps of the catalytic cycle, the alkyne is difunctionalized by methylmagnesium iodide to afford the tetrasubstituted alkene. To demonstrate the synthetic utility of this method, derivatives of these vinyl cyclopropanes were synthesized with one showing activity against a non-small cell lung cancer cell line (HOP-92). Finally, a series of mechanistic studies were carried out to probe the sequence of events that occur in the catalytic cycle. Future efforts include development of new XEC methods to synthesize alkynyl cyclopropanes.

3.4 Experimental Details

3.4.1 General Procedures

All reactions were carried out under an atmosphere of N_2 or Ar when noted. All glassware was oven- or flame-dried prior to use. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), dimethylformamide (DMF), triethylamine (Et_3N), and toluene (PhMe) were degassed with Ar and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 °C for 12 h) to remove H_2O.[18] All other solvents utilized were purchased anhydrous commercially or purified as described. ^{1}H NMR spectra were recorded on Bruker DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C, 376.5 MHz ^{19}F), GN-500 (500 MHz ^{1}H, 125.4 MHz ^{13}C), CRYO-500 (500 MHz ^{1}H, 125.8 MHz ^{13}C) or AVANCE600 (600 MHz ^{1}H, 150 MHz ^{13}C, 564.6 MHz ^{19}F) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), sextet (sext), septet (sept), multiplet (m), broad singlet (bs), broad triplet (bt), doublet of doublet (dd), doublet of triplet (dt), doublet of quartet (dq), doublet of doublet of doublet (ddd), doublet of doublet of triplet (ddt), doublet of triplet of doublet (dtd), triplet of doublet (td), triplet of triplet (tt), triplet of doublet of doublet (tdd), quartet of doublet (qd), quartet of triplet (qt), quartet of doublet of doublet (qdd), apparent singlet (as), apparent triplet (at), apparent quintet (aquin), apparent doublet of quintet (aquin), apparent triplet of doublet (aqd), apparent quartet of doublet (aqd)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). Fluorine chemical shifts are reported in ppm (δ) relative to the absolute frequency of 0.00 ppm in the proton spectrum.

[18] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518–1520.

Unless otherwise indicated, NMR data were collected at 25 °C. Infrared (IR) spectra were obtained on a Thermo Scientific Nicolet iS5 spectrometer with an iD5 ATR tip (neat) and are reported in terms of frequency of absorption (cm^{-1}). Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with $KMnO_4$ or CAM. Flash chromatography was performed using SiliaFlash F60 (40-63 μm, 60 Å) from SiliCycle. Automated chromatography was carried out on a Teledyne Isco CombiFlash Rf Plus. Melting points (m.p.) S-3 were obtained using a Mel-Temp melting point apparatus and are uncorrected.

All ligands were purchased from Strem or Sigma Aldrich and were stored in a glovebox and used as received. The methylmagnesium iodide was titrated with iodine prior to use. All other chemicals were purchased commercially and used as received, unless otherwise noted.

3.4.2 General Procedures for Domino XEC Dicarbofunctionalization Reaction

3.4.2.1 Method A: Domino Cross-Electrophile Coupling Dicarbofunctionalization Reaction

Domino XEC 1,2-Dicarbofunctionalization with (*R*-BINAP)$NiCl_2$ In a glovebox, an oven-dried 7 mL vial equipped with a stir bar was charged with substrate (1 equiv), (*R*-BINAP)$NiCl_2$ (5 mol %), and PhMe (0.2 M in substrate). A solution of MeMgI in Et_2O (2 equiv) was then added dropwise via syringe. After 24 h, the reaction vial was removed from the glovebox, quenched with MeOH, filtered through a plug of silica gel eluting with Et_2O, and concentrated in vacuo. Phenyltrimethylsilane (PhTMS; 8.6 μL, 50. μmol) was added and the yield was determined by ^1H NMR based on comparison to PhTMS as internal standard before purification by column chromatography.

3.4.2.2 Preparation of Methylmagnesium Iodide

Under a N_2 atmosphere, a three-necked flask equipped with a stir bar, reflux condenser, and Schlenk filtration apparatus was charged with magnesium turnings (2.80 g, 115 mmol). The flask and magnesium turnings were then flame-dried under vacuum and the flask was backfilled with N_2. Anhydrous Et_2O (25 mL) and a crystal of iodine (ca. 2 mg) were added to the flask. Freshly distilled iodomethane (5 mL, 80 mmol) was slowly added over 30 min to maintain a gentle reflux. The mixture was stirred for 2 h at room temperature then filtered through the fritted Schlenk filter into a pear-shaped flask under a N_2 atmosphere. The pear-shaped flask was capped with a septum, sealed with parafilm, and stored in the glovebox under a N_2 atmosphere for up to eight weeks. The resulting methyl Grignard reagent was typically between 2.4 and 3.0 M as titrated by Knochel's method.[19]

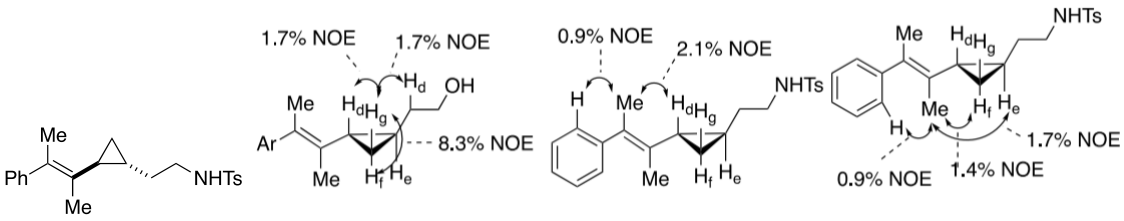
3.4.2.3 Preparation of (*R*-BINAP)$NiCl_2$

(*R*-BINAP)$NiCl_2$ was synthesized according to a procedure reported by Jamison.[20] To a 50 mL round-bottom flask equipped with a stir bar was added $NiCl_2 \cdot 6H_2O$ (152 mg, 0.64 mmol, 1.0 equiv). The flask was placed under vacuum and flame-dried until nearly all of the nickel compound had turned from green to yellow-orange (a small amount of remaining green of the hexahydrate is necessary for the reaction to proceed). After cooling to room temperature, (*R*)-BINAP (0.40 g, 0.64 mmol, 1.0 equiv) was added to the flask and a reflux condenser was attached. The flask was evacuated, backfilled with N_2, and then anhydrous MeCN (20 mL) was added. The reaction mixture was heated to reflux in an oil bath for 24 h, at which point the solution was cooled

[19] Krasoviskiy, A.; Knochel, P. Convenient Titration Method for Organometallic Zinc, Magnesium, and Lanthanide Reagents. *Synthesis* **2006**, *5*, 890–891.
[20] Standley, E. A.; Smith, S. J.; Muller, P.; Jamison, T. F. *Organometallics* **2014**, *33*, 2012–2018.

to room temperature and filtered under vacuum to yield a fine, black powder (0.33 mg, 0.44 mmol, 68% yield).

3.4.3 Characterization of Cyclopropane Products

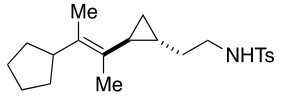


N-(2-trans-2-(3-phenylbut-2-en-2-yl)cyclopropyl)ethyl)4-methylbenzenesulfonamide (3.1): was prepared according to Method A. The following amounts of reagents were used: piperidine **3.8** (37 mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (3.8 mg, 5.0 μmol, 5.0 mol %), MeMgI (90. μL, 0.20 mmol, 2.3 M in Et_2O, 2.0 equiv), PhMe (0.50 mL, 0.20 M in substrate). Before purification a ^{1}H NMR yield of 72% was obtained based on comparison to PhTMS as an internal standard. The residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford the title compound a pale yellow oil (26 mg, 71. μmol, 71% yield, 1.5:1 *E:Z*). The ratio of alkene isomers was determined by integration of the resonances attributed to Hg in the ^{1}H NMR spectrum. The relative configuration of the major (*E*)- and minor (*Z*)-4 were assigned based on NOE analysis. A second column was performed and the diastereomers were separated. The alkene isomers were characterized separately to demonstrate the stereochemical outcome of the reaction. **TLC R_f =** 0.6 (25% EtOAc/hexanes); **IR** (neat) 3284, 2925, 2860, 1599, 1324, 1160, 905, 728, 650 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calculated for $C_{22}H_{27}NO_2SNa$, 392.1660; found, 392.1667;

Major Diastereomer: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.34–7.27 (m, 4H), 7.23–7.14 (m, 1H), 7.11–7.05 (m, 2H), 4.41 (s, 1H), 3.08 (qd, *J* = 6.7, 2.3 Hz, 2H), 2.42 (s, 3H), 2.04 (d, *J* = 1.5 Hz, 3H), 1.71–1.55 (m, 1H), 1.52–1.39 (m, 2H), 1.25 (d, *J* = 1.6 Hz, 3H), 0.87–0.77 (m, 1H), 0.77–0.70 (m, 1H), 0.49 (dt, *J* = 9.3, 4.8 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 125.7 MHz) δ

145.5, 143.5, 137.0, 132.0, 129.8 (2C), 129.5, 128.4 (2C), 128.0 (2C), 127.2 (2C), 125.9, 76.8, 43.4, 34.3, 22.2, 21.6, 20.8, 16.0, 15.6, 11.7.

Minor Diastereomer: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 5H), 7.15 (d, *J* = 7.9 Hz, 2H), 4.30 (t, *J* = 6.2 Hz, 1H), 2.98–2.83 (m, 2H), 2.42 (s, 3H), 1.96 (s, 3H), 1.43 (d, *J* = 1.5 Hz, 3H), 1.30–1.15 (m, 3H), 0.69–0.63 (m, 1H), 0.59 (dt, *J* = 8.8, 5.0 Hz, 1H), 0.16 (dt, *J* = 9.4, 4.9 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 125.7 MHz) δ 143.3, 131.3, 129.7 (2C), 129.5, 128.7 (2C), 128.5, 128.1 (2C), 127.8, 127.1 (2C), 125.9, 43.2, 33.7, 22.9, 21.6, 21.6, 15.6, 13.9, 11.6.

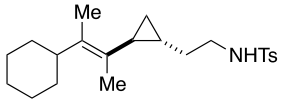


***N*-(2-(Trans-2-(3-cyclopentylbut-2-en-2-yl)cyclopropyl)ethyl)-4-methylbenzenesulfonamide (3.2)** was prepared according to Method A. The following amounts of reagents were used: piperidine **3.20** (36 mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (3.8 mg, 5.0 μmol, 5.0 mol %), MeMgI (80. μL, 0.20 mmol, 2.3 M in Et_2O, 2.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). The residue was purified by flash column chromatography (0–20% EtOAc/hexanes) to afford the title compound as a mixture of alkene diastereomers as a clear oil (22 mg, 0.59 mmol, 59% yield, 1.5:1 *E:Z*). The ratio of alkene isomers was determined by the integration of the resonances attributed to cyclopentyl methine in the ^{1}H NMR spectrum. The relative configuration of the major **(*E*)-3.2** was assigned based on analogy to cyclopropane **3.1**. For clarity, the ^{1}H NMR and ^{13}C NMR data of the major and minor diastereomers have been tabulated individually. **TLC R_f =** 0.5 (25% EtOAc/hexanes); **IR** (neat) 3278, 2949, 2865, 1599 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{21}H_{31}NO_2SNa$, 384.1973; found, 384.1976.

Major Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2

Hz, 2H), 4.56 (bs, 1H), 3.17–3.11 (m, 1H), 3.02 (q, *J* = 6.7 Hz, 2H), 2.42 (s, 3H), 1.65–1.47 (m, 11H), 1.43–1.25 (m, 6H), 0.69–0.63 (m, 1H), 0.61–0.56 (m, 1H), 0.38–0.33 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 137.1, 132.9, 129.8 (2C), 127.3 (2C), 126.6, 43.4, 42.2, 34.5, 30.6, 30.4, 26.2 (2C), 21.64, 21.59, 15.58, 15.55, 14.2, 11.9;

Minor Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.56 (bs, 1H), 3.02 (q, *J* = 6.7 Hz, 2H), 2.90–2.83 (m, 1H), 2.42 (s, 3H), 1.65–1.47 (m, 11H), 1.43–1.25 (m, 6H), 0.69–0.63 (m, 1H), 0.61–0.56 (m, 1H), 0.38–0.33 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 137.1, 132.6, 129.8 (2C), 127.3 (2C), 126.2, 43.5, 43.1, 34.3, 30.4, 30.3, 26.1, 26.0, 22.6, 21.6, 15.7, 14.3, 13.6, 11.8.

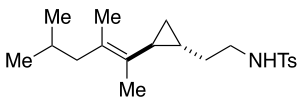


N-(2-(trans-2-(3-cyclohexylbut-2-en-2-yl)cyclopropyl)ethyl)-4-methylbenzenesulfonamide (3.3) was prepared according to Method A. The following amounts of reagents were used: piperidine **3.22** (38 mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (3.8 mg, 5.0 μmol, 5.0 mol %), MeMgI (90. μL, 0.20 mmol, 2.3 M in Et_2O, 2.0 equiv), PhMe (0.50 mL, 0.20 M in substrate). Before purification, a ^{1}H NMR yield of 52% was obtained based on comparison to PhTMS as an internal standard. The residue was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a mixture of alkene diastereomers as a clear yellow oil (19 mg, 51 μmol, 50% yield, 2:1 *E:Z*). The ratio of alkene isomers was determined by integration of the resonances in the ^{13}C NMR spectrum. The relative configuration of the major diastereomer **(*E*)-3.3** was assigned based on analogy to cyclopropane **3.1**. For clarity, the ^{1}H NMR and ^{13}C NMR data of the major and minor diastereomers have been tabulated individually. **TLC** $\mathbf{R_f}$ **=** 0.2 (20% EtOAc/hexanes); **IR** (neat) 3278, 2924, 2851, 1599, 1446, 1325, 1158, 1094, 838,

660 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{22}H_{33}NO_2SNa$, 398.2130; found, 398.2119.

Major Diastereomer: ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.3, 2.8 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.46 (t, *J* = 6.2 Hz, 1H), 3.03 (qt, *J* = 8.1, 4.1 Hz, 2H), 2.71–2.63 (m, 1H), 2.43 (s, 3H), 1.77–1.71 (m, 2H), 1.68–1.64 (m, 1H), 1.61 (d, *J* = 1.7 Hz, 1H), 1.53–1.51 (m, 3H), 1.46–1.34 (m, 3H), 1.34 (s, 3H), 1.32–1.20 (m, 5H), 1.19–1.09 (m, 1H), 0.69–0.60 (m, 1H), 0.58 (dt, *J* = 8.5, 5.1 Hz, 1H), 0.36 (dt, *J* = 9.4, 4.9 Hz, 1H); ^{13}**C NMR** (125.8 MHz, $CDCl_3$) δ 143.4, 137.0, 135.5, 129.7 (2C), 127.1 (2C), 125.2, 43.4, 41.2, 34.4, 31.0, 30.9, 26.9, 26.8, 26.4, 21.6, 21.3, 15.6, 15.5, 14.3, 11.9.

Minor Diastereomer: ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.3, 2.8 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.46 (t, *J* = 6.2 Hz, 1H), 3.03 (qt, *J* = 8.1, 4.1 Hz, 2H), 2.71–2.63 (m, 1H), 2.43 (s, 3H), 1.77–1.71 (m, 2H), 1.68–1.64 (m, 1H), 1.53–1.51 (m, 2H), 1.61 (d, *J* = 1.7 Hz, 3H), 1.47–1.36 (m, 2H), 1.35 (d, *J* = 1.6 Hz, 3H), 1.32–1.20 (m, 5H), 1.19–1.09 (m, 1H), 0.69–0.60 (m, 1H), 0.58 (dt, *J* = 8.5, 5.1 Hz, 1H), 0.36 (dt, *J* = 9.4, 4.9 Hz, 1H); ^{13}**C NMR** (125.8 MHz, $CDCl_3$) δ 143.4, 137.0, 135.3, 129.7 (2C), 127.2 (2C), 125.1, 43.4, 41.9, 34.2, 30.8, 30.7, 26.8, 26.8, 26.4, 22.4, 21.3, 15.7, 15.5, 14.1, 13.7.

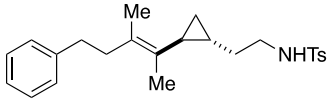


***N*-(2-(Trans-2-(3,5-dimethylhex-2-en-2-yl)cyclopropyl)ethyl)-4-methylbenzenesulfonamide (3.4)** was prepared according to Method A. The following amounts of reagents were used: piperidine **3.25** (35 mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (3.8 mg, 5.0 μmol, 5.0 mol %), MeMgI (90. μL, 0.20 mmol, 2.3 M in Et_2O, 2.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). The residue was purified by flash column chromatography (0–20% EtOAc/hexanes) to afford the title compound as a clear oil (23 mg, 0.66 mmol, 66% yield, 3:1 *E:Z*). The ratio of alkene isomers was determined by integration of the resonances in the ^{13}C NMR spectrum. The relative configuration of the major diastereomer **(*E*)-3.4** was assigned based on analogy to cyclopropane **3.1**. For clarity, the ^{1}H NMR and ^{13}C NMR data of the major and minor diastereomers have been tabulated individually. **TLC R_f =** 0.5 (25% EtOAc/hexanes); **IR** (neat) 3279, 3056, 2951, 2924, 2866 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{20}H_{31}NO_2SNa$, 372.1973; found, 372.1969.

Major Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 7.9 Hz, 2H), 8.30 (d, *J* = 7.9 Hz, 2H), 5.50 (t, *J* = 6.2 Hz, 1H), 4.01 (q, *J* = 6.7 Hz, 2H), 3.01 (d, *J* = 7.6 Hz, 2H), 2.77–2.71 (m, 1H), 2,.61 (s, 3H), 2.58–2.53 (m, 1H), 2.38–2.30 (m, 2H), 2.27 (s, 3H), 1.89–1.79 (m, 6H), 1.69–1.67 (m, 1H), 1.61–1.58 (m, 1H), 1.34–1.31 (m, 1H), 0.73–0.64 (m, 1H), 0.61–0.58 (m, 1H), 0.34–0.31 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.4, 137.2, 129.8 (2C), 129.4, 127.3 (2C), 127.2, 43.43, 43.41, 34.3 (2C), 27.5 (2C), 22.81, 22.76, 21.75, 21.65, 15.3, 11.5.

Minor Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 7.9 Hz, 2H), 8.30 (d, *J* = 7.9 Hz, 2H), 5.50 (t, *J* = 6.2 Hz, 1H), 4.01 (q, *J* = 6.7 Hz, 2H), 2,90 (d, *J* = 7.5 Hz, 2H), 2.77–2.71 (m, 1H), 2.69 (s, 3H), 2.58–2.53 (m, 1H), 2.38–2.30 (m, 2H), 2.33 (s, 3H), 1.89–1.79 (m, 6H), 1.69–1.67 (m, 1H), 1.61–1.58 (m, 1H), 1.37–1.34 (m, 1H), 0.73–0.64 (m, 1H), 0.61–0.58 (m, 1H), 0.39–

0.35 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.4, 137.2, 129.8 (2C), 129.4, 127.3 (2C), 127.2, 44.4, 43.5, 34.4 (2C), 22.7, 22.6, 22.3, 21.8, 19.1, 15.7, 14.9, 11.8.



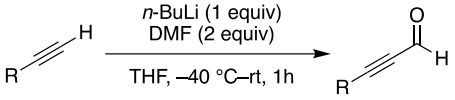
4-Methyl-N-(2-(trans-2-(3-methyl-5-phenylpent-2-en-2-yl)cyclopropyl)ethyl)benzenes-ulfonamide (3.5) was prepared according to Method A. The following amounts of reagents were used: piperidine **3.28** (40. mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (3.8 mg, 5.0 μmol, 5.0 mol %), MeMgI (90. μL, 0.20 mmol, 2.3 M in Et_2O, 2.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). The residue was purified by flash column chromatography (0–20% EtOAc/hexanes) to afford the title compound as a clear oil (26 mg, 0.64 mmol, 64% yield, 2.2:1 *E:Z*). The ratio of alkene isomers was determined by integration of the resonances in the ^{13}C NMR spectrum. The relative configuration of the major diastereomer **(*E*)-3.5** was assigned based on analogy to cyclopropane **3.1**. For clarity, the ^{1}H NMR and ^{13}C NMR data of the major and minor diastereomers have been tabulated individually. **TLC R_f =** 0.5 (25% EtOAc/hexanes); **IR** (neat) 3276, 3062, 3026, 2998, 2924, 2860, 1599 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{24}H_{31}NO_2SNa$, 420.1973; found, 420.1975.

Major Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.72 (m, 2H), 7.31–7.24 (m, 4H), 7.17–7.14 (m, 3H), 4.58–4.52 (m, 1H), 3.04–2.96 (m, 2H), 2.68–2.60 (m, 2H), 2.43–2.41 (m, 2H), 2.39 (s, 3H), 1.68 (s, 3H), 1.55–1.48 (m, 1H), 1.30 (s, 3H), 1.28–1.20 (m, 2H), 0.67–0.62 (m, 1H), 0.58–0.53 (m, 1H), 0.32–0.28 (m, 1H**); ^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.4, 142.6, 137.0, 129.7 (2C), 129.3, 128.4 (2C), 128.3 (2C), 127.3, 127.2 (2C), 125.8, 43.3, 36.6, 34.8, 34.3, 21.6, 21.4, 19.3, 15.2, 14.5, 11.5.

Minor Diastereomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76–7.72 (m, 2H), 7.31–7.24 (m, 4H), 7.17–7.14 (m, 3H), 4.58–4.52 (m, 1H), 3.04–2.96 (m, 2H), 2.68–2.60 (m, 2H), 2.39 (s, 3H), 2.31–2.27 (m, 2H), 1.75 (s, 3H), 1.40–1.36 (m, 1H), 1.28–1.20 (m, 2H), 1.23 (s, 3H), 0.67–0.62 (m, 1H), 0.58–0.53 (m, 1H), 0.38–0.34 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.4, 142.5, 137.0, 129.8 (2C), 129.3, 128.5 (2C), 128.3 (2C), 127.4, 127.2 (2C), 125.7, 43.4, 37.5, 34.5, 34.3, 22.1, 21.6, 18.6, 15.5, 14.1, 11.7.

3.4.4 General Procedures for Starting Material Synthesis

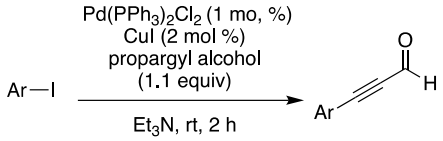
3.4.4.1 Method B: Synthesis of Propargyl Aldehydes with *n*-BuLi and DMF



This method was adapted from a procedure reported by Larsen.[21] To a flame-dried round-bottom flask equipped with a stir bar was added alkyne (1 equiv). The flask was evacuated, backfilled with N_2, and capped with a septum. THF (0.4 M in alkyne) was added, and the solution was cooled to –40 ºC. Then *n*-BuLi (1 equiv) was added dropwise, followed by DMF (2 equiv). The mixture was allowed to warm to room temperature and stir for an additional 30 mins. The solution was poured into a vigorously stirred biphasic solution of 10% aqueous KH_2PO_4 and Et_2O cooled over ice. The layers were separated, and the organic layer was washed with H_2O (x2). The combined aqueous layers were extracted with Et_2O. Then the combined organic layers were dried over Na_2SO_4, concentrated in vacuo, and purified by column chromatography.

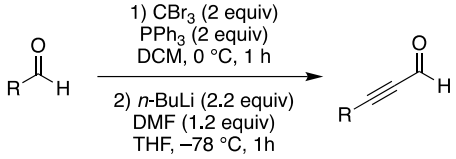
[21] Journet, M.; Cai, D.; DiMichele, L. M.; Larsen, R. D. *Tetrahedron Lett.* **1998**, *39*, 6427–6428.

3.4.4.2 Method C: Sonogashira Cross-Coupling Reaction of Aryl Iodides and Propargyl Alcohol



This method was adapted from a procedure reported by Tambar.[22] To a flame-dried round bottom flask equipped with a stir bar was added $Pd(PPh_3)_2Cl_2$ (1 mol %) and CuI (2 mol %). Et_3N (0.01 M in CuI) was added to the flask, and the suspension was allowed to stir for five minutes. A solution of aryl iodide (1.0 equiv) and propargyl alcohol (1.1 equiv) in Et_3N (1.0 M in aryl iodide) was prepared, and the solution was added dropwise to the reaction mixture. The reaction was allowed to stir at rt until the aryl iodide was consumed. The reaction mixture was filtered through a pad of Celite and washed with excess EtOAc. The combined solution was concentrated in vacuo and purified by column chromatography.

3.4.4.3 Method D: Corey-Fuchs Reaction



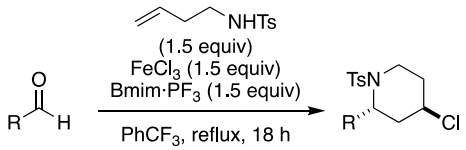
Step 1: This method was adapted from a procedure reported by Ghosh.[23] To a flame-dried round bottom flask equipped with a stir bar was added PPh_3 (4 equiv) and CH_2Cl_2 (0.3 M in substrate). The reaction mixture was cooled to 0 °C and CBr_4 (2 equiv) was added. Then the desired aldehyde (1 equiv) was added dropwise to the reaction flask and was allowed to stir at 0 °C for 1 hour. The reaction mixture was warmed to rt and concentrated in vacuo. The residue was diluted with 1:1

[22] Xu, B.; Gartman, J. A.; Tambar, U. K. *Tetrahedron* **2017**, *73*, 4150–4159.
[23] Ghosh, A. K.; Wang, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11027–11028.

Et_2O:hexanes and filtered through a pad of silica gel. The filter cake was washed with excess 1:1 mixture of Et_2O:hexanes.

Step 2: To a flame-dried round bottom flask, was added the residue (1.0 equiv) and THF (0.4 M in substrate). The reaction mixture was cooled to –78 °C and *n*-BuLi (2.2 equiv) was added dropwise. After stirring at –78 °C for 1 h, the reaction flask was allowed to stir at rt for 1 h. The reaction mixture was cooled to –78 °C and DMF (1.2 equiv) was added in one portion. After stirring at –78 °C for 1 h, the reaction mixture was quenched with an aq. solution of NH_4Cl, extracted with Et_2O (x3), dried over Na_2SO_4, and concentrated in vacuo. The residue was carried forward without purification.

3.4.4.4 Method E: $FeCl_3$/Bmim·PF_6-Promoted aza-Prins Reaction



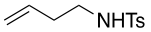
This method was adapted from a procedure reported by Iwamoto.[24] In a glovebox, $FeCl_3$ (1.5 equiv) was added to a flame-dried round-bottom flask equipped with a stir bar. The flask was sealed with a septum and removed from the glovebox. Benzotrifluoride (0.3 M in $FeCl_3$) was added to the flask, followed by dropwise addition of Bmim·PF_6 (1.5 equiv). In a separate flask, a solution of aldehyde (1.5 equiv) and homoallylic sulfonamide **(3.16)** (1.0 equiv) in benzotrifluoride (0.3 M in homoallylic sulfonamide **3.16**) was prepared. Using a syringe, the solution of aldehyde and sulfonamide was added to the flask containing $FeCl_3$. The reaction flask was fitted with a reflux condenser and N_2 inlet. The solution was heated to reflux and allowed to stir for 24 h. The reaction mixture was cooled to rt and was then quenched with H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (x2). The combined organic layers were washed

[24] Hasegawa, E.; Osawa, C.; Tateyama, M.; Miura, K.; Tayama, E.; Iwamoto, H. *Heterocycles* **2012**, *86*, 1211–1226.

sequentially with sat. aq. $Na_2S_2O_3$, sat. aq. $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated in vacuo, and purified by column chromatography. After purification by column chromatography, the bright orange residue was passed through an activated charcoal plug to remove the colored impurities.

Frequently, the desired product was isolated as a mixture with unreacted aldehyde. To remove unreacted aldehyde from the desired product, the mixture was subjected to $NaBH_4$ reduction by a modified procedure reported by Wang and Franzén.[25] The unpurified reaction mixture was concentrated and dissolved in MeOH. $NaBH_4$ (1.6 equiv relative to 1.0 equiv of remaining aldehyde as determined by ^1H NMR integration) was added in one portion and the reaction was stirred 20 min at rt. The reaction mixture was then concentrated in vacuo to remove the MeOH. The resulting solid was dissolved in CH_2Cl_2 and transferred to a separatory funnel. The organic layer was washed with H_2O (x3) and brine (x1), dried over Na_2SO_4, filtered, and concentrated in vacuo.

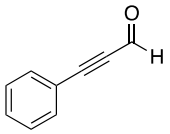
3.4.5 Characterization of Starting Materials



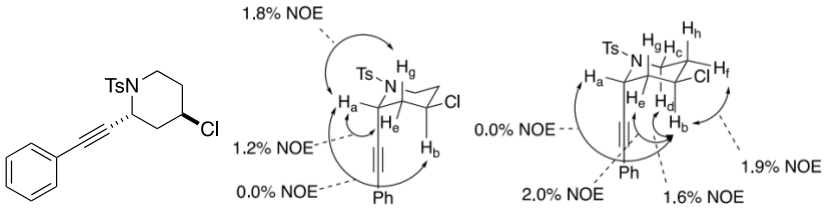
Homoallylic sulfonamide (3.16) was prepared by dissolving 4-bromo-1-butene (1 equiv), p-toluenesulfonamide (1 equiv), and K_2CO_3 (1.2 equiv) were added to a flame-dried round-bottom flask and dissolved in acetonitrile (100 mL, 0.3 M in 4-bromo-1-butene). The reaction flask was heated to 60 °C for 72 h. The reaction flask was cooled back down to rt, quenched with an aq soln of NH_4Cl, and extracted with EtOAc (x3). The combined organic layers were dried over Na_2SO_4, concentrated in vacuo, and purified by flash column chromatography (0–25% EtOAc/hexanes). Analytical data is consistent with literature values.[26] **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* =

[25] Wang, Y.; Franzén, R. *Synlett* **2012**, *23*, 925–929.
[26] Huang, J.; Zheng, J.; Wu, W.; Li, J.; Ma, J.; Ren, Y.; Jiang, H. *J. Org. Chem.* **2017**, *82*, 8191–8198.

8.2, 2H), 7.30 (d, *J* = 8.1, 2H), 5.63 (ddt, *J* = 17.1, 10.4, 6.8, 1H), 5.11 (br s, 1H), 5.02–4.93 (m, 2H), 2.99 (q, *J* = 6.7, 2H), 2.41 (s, 3H), 2.20 (q, *J* = 6.9, 2H).



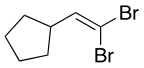
3-phenylpropiolaldehyde (3.17) was prepared according to Method B. The following amounts of reagents were used: phenylacetylene (0.55 mL, 5.0 mmol, 1.0 equiv), *n*-BuLi (4.2 mL, 5.0 mmol, 1.2 equiv, 1.2 M in THF), DMF (0.78 mL, 10. mmol, 2.0 equiv), THF (13 mL, 0.40 M). The residue was purified by column chromatography (0–5% EtOAc/hexanes) to afford the title compound as an orange oil (0.56 g, 4.3 mmol, 86% yield). **TLC R_f =** 0.6 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.63–7.57 (m, 2H), 7.48 (tt, *J* = 7.4, 1.4 Hz, 1H), 7.40 (ddd, *J* = 8.7, 6.7, 1.6 Hz, 2H). Analytical data are consistent with literature values.[27]



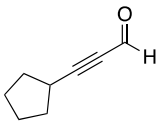
trans-4-Chloro-2-(phenylethynyl)-1-tosylpiperidine (3.8) was prepared according to Method E. The following amounts of reagents were used: 3-phenylpropiolaldehyde **3.17** (0.45 g, 3.5 mmol, 1.5 equiv), homoallylic sulfonamide **3.16** (0.43 mL, 2.3 mmol, 1.0 equiv), $FeCl_3$ (0.56 g, 3.5 mmol, 1.5 equiv), Bmim·PF_6 (0.72 mL, 3.5 mmol, 1.5 equiv), benzotrifluoride (23 mL, 0.10 M in homoallylic sulfonamide). The residue was purified by flash column chromatography (0–20% EtOAc/hexanes) to afford the title compound as a pale yellow solid (0.46 g, 1.2 mmol, 53% yield, >20:1 dr trans:cis). The dr was determined based on the integration of the resonances attributed to

[27] Noro, M.; Masuda, T.; Ichimura, A. S.; Koga, N.; Iwamura, H. *J. Am. Chem. Soc.* **1994**, *116*, 6179–6190.

the propargylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis. **m.p.** 107–109 ºC; **TLC R_f =** 0.5 (20% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.38–7.33 (m, 1H), 7.32–7.25 (m, 4H), 7.04 (d, *J* = 8.5 Hz, 2H), 5.19 (as, 1H), 4.26 (tt, *J* = 12.0, 4.3 Hz, 1H), 3.91 (dt, *J* = 12.4, 2.1 Hz, 1H), 3.04 (td, *J* = 12.4, 2.6 Hz, 1H), 2.44 (ddt, *J* = 12.5, 4.1, 2.3 Hz, 1H), 2.34 (s, 3H), 2.33–2.27 (m, 1H), 2.23 (td, *J* = 12.7, 4.7 Hz, 1H), 2.04 (qd, *J* = 12.6, 4.8 Hz, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.7, 134.7, 131.5 (2C), 129.5 (2C), 128.7, 128.1 (2C), 128.1 (2C), 121.7, 87.7, 82.8, 52.9, 47.3, 42.0, 41.5, 35.9, 21.4; **IR** (neat) 2971, 2934, 2235, 1596, 1488, 1397, 1340, 1160, 1084, 856, 762, 723, 691 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calculated for $C_{20}H_{20}ClNO_2SNa$, 396.0801; found, 396.0807.

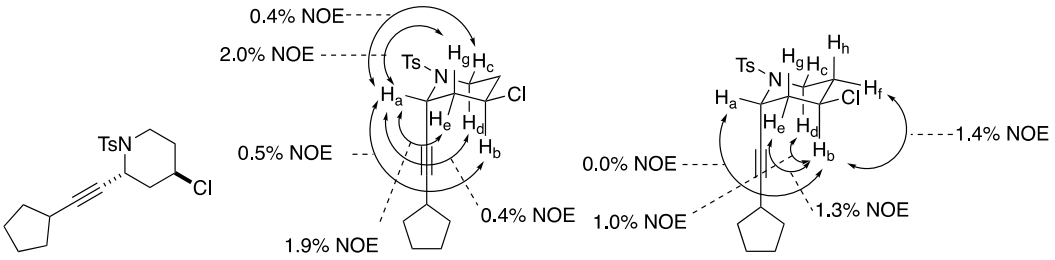


(2,2-dibromovinyl)cyclopentane (3.18) was prepared according to Method D, Step 1. The following amounts of reagents were used: cyclopentanecarboxaldehyde (0.53 mL, 5.0 mmol, 1.0 equiv), CBr_4 (3.3 g, 10. mmol, 2.0 equiv), PPh_3 (5.2 g, 20. mmol, 4.0 equiv), and CH_2Cl_2 (16 mL, 0.30 M in substrate). The residue was carried forward without further purification. **TLC R_f =** 0.9 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 9.0 Hz, 1H), 2.67 (sext, *J* = 8.7 Hz, 1H), 1.91–1.87 (m, 2H), 1.69–1.56 (m, 4H), 1.32–1.26 (m, 2H).

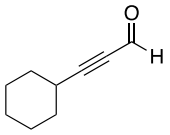


3-cyclopentylpropiolaldehyde (3.19) was prepared according to Method D, Step 2. The following amounts of reagents were used: **3.18** (0.75 g, 2.9 mmol, 1.0 equiv), *n*-BuLi (2.6 mL, 6.5 mmol, 2.2 equiv, 2.5 M in hexanes), DMF (0.28 mL, 3.6 mmol, 1.2 equiv), and THF (8.0 mL, 0.40 M in substrate). The residue was carried forward without further purification. **TLC R_f =** 0.6 (10%

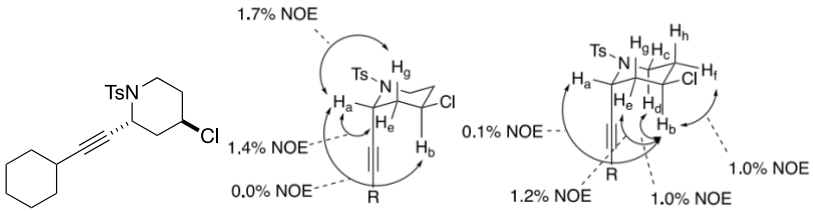
EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 2.86–2.78 (m, 1H), 2.03–1.96 (m, 2H), 1.79–1.67 (m, 4H), 1.66–1.58 (m, 2H).



trans-4-chloro-2-(cyclopentylethynyl)-1-tosylpiperidine (3.20) was prepared according to Method E. The following amounts of reagents were used: aldehyde **3.19** (180 mg, 1.5 mmol, 1.5 equiv), homoallylic sulfonamide **3.16** (230 mg, 1.0 mmol, 1.0 equiv), $FeCl_3$ (240 mg, 1.5 mmol, 1.5 equiv), Bmim·PF_6 (0.31 mL, 1.5 mmol, 1.5 equiv), and benzotrifluoride (15 mL, 0.10 M in aldehyde). The residue was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a pale yellow solid (220 mg, 0.59 mmol, 5.9% yield over 3 steps, >20:1 dr trans:cis). The dr was determined based on the integration of the resonances attributed to the propargylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis. **m.p.** 84–86 °C; **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 4.91–4.88 (m, 1H), 4.13 (tt, *J* = 11.8, 4.4 Hz, 1H), 3.78–3.73 (m, 1H), 2.89 (td, *J* = 12.5, 2.5 Hz, 1H), 2.41 (s, 3H), 2.31–2.15 (m, 3H), 2.05 (td, *J* = 12.3, 4.9 Hz, 1H), 1.90 (qd, *J* = 12.3, 4.9 Hz, 1H), 1.72–1.59 (m, 2H), 1.69–1.62 (m, 2H), 1.51–1.42 (m, 2H), 1.23–1.13 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 135.4, 129.5 (2C), 128.1 (2C), 92.8, 73.3, 53.2, 47.0, 42.0, 41.7, 36.1, 33.6, 33.5, 29.8, 25.04, 25.01, 21.6; **IR** (neat) 2958, 2868, 2232, 1598; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{19}H_{24}ClNO_2SNa$, 388.1114; found, 388.1107.

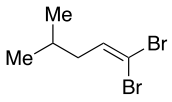


3-cyclohexylpropiolaldehyde (3.21) was prepared according to Method B. The following amounts of reagents were used: ethynylcyclohexane (0.65 mL, 5.0 mmol, 1.0 equiv), *n*-BuLi (4.5 mL, 5.0 mmol, 1.0 equiv, 2.5 M in hexanes), DMF (0.77 mL, 10. mmol, 2.0 equiv), THF (13 mL, 0.38 M in ethynylcyclohexane). The residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a yellow solid (0.39 g, 2.9 mmol, 58% yield). **TLC R_f =** 0.8 (5% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 2.58 (tt, *J* = 8.8, 3.9 Hz, 1H), 1.84 (ddt, *J* = 12.8, 6.7, 3.5 Hz, 2H), 1.75 – 1.65 (m, 2H), 1.51 (ddd, *J* = 13.3, 9.6, 6.9 Hz, 4H), 1.34 (tdd, *J* = 10.1, 5.9, 2.6 Hz, 3H).

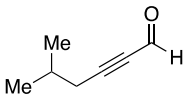


trans-4-Chloro-2-(cyclohexylethynyl)-1-tosylpiperidine (3.22) was prepared according to Method E. The following amounts of reagents were used: aldehyde **3.21** (0.63 g, 4.6 mmol, 1.5 equiv), homoallylic sulfonamide **3.16** (0.56 mL, 3.1 mmol, 1.0 equiv), $FeCl_3$ (0.74 g, 4.6 mmol, 1.5 equiv), Bmim·PF_6 (0.94 mL, 4.6 mmol, 1.5 equiv), benzotrifluoride (31 mL, 0.15 M in aldehyde). The residue was purified by flash column chromatography (0–20% EtOAc/hexanes) to afford the title compound as a white solid (0.67 mg, 1.8 mmol, 57% yield, >20:1 dr trans:cis). The dr was determined based on the integration of the resonances attributed to the propargylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis. **m.p.** 110–113 °C; **TLC R_f =** 0.7 (20% EtOAc/hexanes); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 4.96 (s, 1H), 4.20 (tt, *J* = 12.0, 4.3 Hz, 1H), 3.82

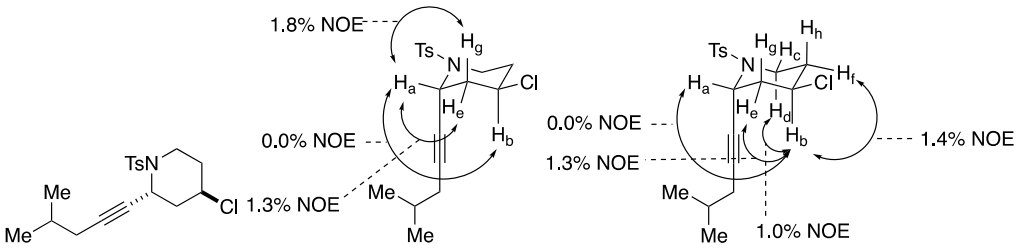
(ddt, *J* = 12.2, 4.6, 2.2 Hz, 1H), 2.96 (td, *J* = 12.5, 2.7 Hz, 1H), 2.47 (s, 3H), 2.35 – 2.20 (m, 2H), 2.16 – 2.04 (m, 2H), 1.97 (qd, *J* = 12.6, 4.9 Hz, 1H), 1.62 – 1.46 (m, 6H), 1.32 – 1.17 (m, 3H), 1.16 – 1.01 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125.8 MHz) δ 143.4, 135.3, 129.4, 128.0, 92.6, 73.6, 53.1, 46.9, 41.9, 41.6, 36.0, 32.3, 32.2, 28.8, 25.7, 24.8, 21.5; **IR** (neat) 2927, 2853, 2230, 1598, 1346, 1185, 933, 726 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calculated for $C_{20}H_{28}ClNO_2SNa$, 402.1270; found, 402.1272.



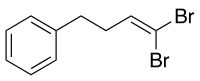
1,1-Dibromo-4-methylpent-1-ene (3.23) was prepared according to Method D, Step 1. The following amounts of reagents were used: isovaleraldehyde (0.54 mL, 5.0 mmol, 1.0 equiv), CBr_4 (3.3 g, 10. mmol, 2.0 equiv), PPh_3 (5.2 g, 20. mmol, 4.0 equiv), and CH_2Cl_2 (15 mL). The residue was passed through a silica plug eluting with 100% hexanes. The resulting oil was carried forward without further purification. **TLC R_f =** 0.9 (100% hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.40 (t, *J* = 7.5 Hz, 1H), 1.99 (t, *J* = 7.1 Hz, 2H), 1.75 (sept, *J* = 6.7 Hz, 1H), 0.93 (d, *J* = 6.6 Hz, 6H).



5-Methylhex-2-ynal (3.24) was prepared according to Method D, Step 2. The following amounts of reagents were used: dibromoalkene **3.23** (0.88 g, 3.7 mmol, 1.0 equiv), *n*-BuLi (3.2 mL, 8.0 mmol, 2.2 equiv, 2.5 M in hexanes), DMF (0.34 mL, 4.4 mmol, 1.2 equiv), and THF (9 mL, 0.4 M in dibromoalkene). The residue was carried forward without further purification. **TLC R_f =** 0.5 (10% hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.19 (s, 1H), 2.31 (d, *J* = 6.6 Hz, 2H), 1.94 (sept, *J* = 6.6 Hz, 1H), 1.02 (d, *J* = 6.8 Hz, 6H).

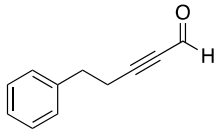


trans-4-Chloro-2-(4-methylpent-1-yn-1-yl)-1-tosylpiperidine (3.25) was prepared according to Method E. The following amounts of reagents were used: aledhyde **3.24** (0.17 g, 1.6 mmol, 1.5 equiv), homoallylic sulfonamide **3.16** (0.23 g, 1.0 mmol, 1.0 equiv), $FeCl_3$ (0.25 g, 1.6 mmol, 1.5 equiv), Bmim·PF_6 (0.32 mL, 1.6 mmol, 1.5 equiv), and benzotrifluoride (15 mL, 0.10 M in aldehyde). The residue was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a pale yellow solid (59 mg, 0.16 mmol, 10% yield, >20:1 dr trans:cis). The dr was determined based on the integration of the resonances attributed to the propargylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis. **m.p.** 63–65 °C; **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 4.94–4.91 (m, 1H), 4.14 (tt, *J* = 12.1, 4.2 Hz, 1H), 3.78–3.74 (m, 1H), 2.90 (td, *J* = 12.4, 2.7 Hz, 1H), 2.41 (s, 3H), 2.27–2.23 (m, 1H), 2.21–2.16 (m, 1H), 2.0 (td, *J* = 12.5, 4.8, 1H), 1.90 (qd, *J* = 12.5, 4.4, 1H), 1.73 (qdd, *J* = 13.8, 6.9, 1.9, 2H), 1.48 (sept, *J* = 6.7, 1H), 0.79 (d, *J* = 6.7, 3H), 0.77 (d, *J* = 6.7, 3H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 135.3, 129.4 (2C), 128.2 (2C), 87.3, 74.8, 53.2, 47.0, 42.0, 41.8, 36.1, 27.82, 27.76, 22.07, 22.05, 21.6; **IR** (neat) 2957, 2927, 2868, 2230 cm^{-1}; **HRMS** (TOF MS ES+) m/z: [M + Na]$^+$ calcd for $C_{18}H_{24}ClNO_2SNa$, 376.1114; found, 376.1108.

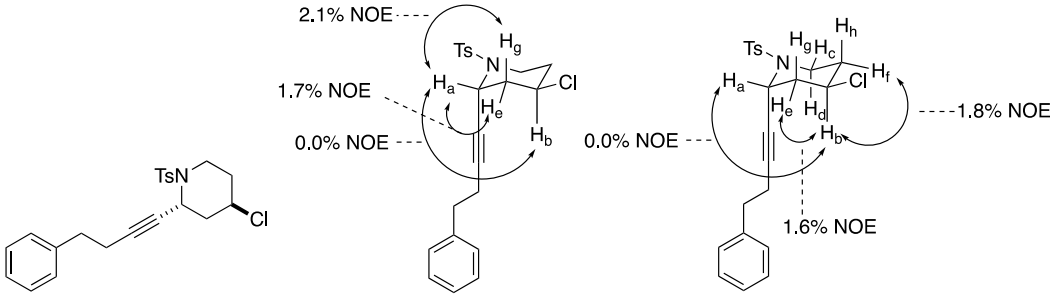


(4,4-Dibromobut-3-en-1-yl)benzene (3.26) was prepared according to Method D, Step 1. The following amounts of reagents were used: phenyl propionaldehyde (0.66 mL, 5.0 mmol, 1.0 equiv),

CBr_4 (3.3 g, 10. mmol, 2.0 equiv), PPh_3 (5.2 g, 20. mmol, 4.0 equiv), and CH_2Cl_2 (16 mL, 0.30 M in substrate). The residue was carried forward without further purification. **TLC R_f =** 0.9 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.24–7.16 (m, 3H), 6.41 (t, *J* = 7.1 Hz, 1H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.41 (q, *J* = 7.5 Hz, 2H).



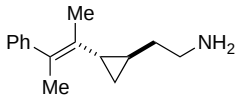
5-Phenylpent-2-ynal (3.27) was prepared according to Method D, Step 2. The following amounts of reagents were used: dibromoalkene **3.26** (0.92 g, 3.1 mmol, 1.0 equiv), *n*-BuLi (3.1 mL, 6.8 mmol, 2.2 equiv, 2.5 M in hexanes), DMF (0.29 mL, 3.7 mmol, 1.2 equiv), and THF (8 mL, 0.4 M in substrate). The residue was carried forward without further purification. **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.34–7.27 (m, 2H), 7.25–7.16 (m, 3H), 2.91 (t, *J* = 7.5 Hz, 2H), 2.71 (t, *J* = 7.4 Hz, 2H).



trans-4-Chloro-2-(4-phenylbut-1-yn-1-yl)-1-tosylpiperidine (3.28) was prepared according to Method E. The following amounts of reagents were used: aldehyde **3.27** (0.28 g, 1.8 mmol, 1.5 equiv), homoallylic sulfonamide **3.16** (0.27 g, 1.2 mmol, 1.0 equiv), $FeCl_3$ (0.29 g, 1.8 mmol, 1.5 equiv), Bmim·PF_6 (0.37 mL, 1.8 mmol, 1.5 equiv), and benzotrifluoride (18 mL, 0.10 M in aldehyde). The residue was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a yellow solid (110 mg, 0.28 mmol, 23% yield, >20:1 dr trans:cis). The dr was determined based on the integration of the resonances attributed to the propargylic

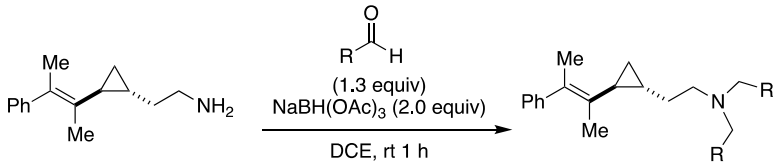
hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis. **m.p.** 111–113°C; **TLC R_f =** 0.7 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.29–7.19 (m, 5H), 7.02 (d, *J* = 7.4 Hz, 2H), 4.84–4.82 (m, 1H), 3.85 (tt, *J* = 11.9, 4.3 Hz, 1H), 3.65–3.60 (m, 1H), 2.60 (td, *J* = 12.4, 2.5 Hz, 1H), 2.56–2.43 (m, 2H), 2.41 (s, 3H), 2.24–2.07 (m, 3H), 2.04–1.94 (m, 2H), 1.81 (qd, *J* = 12.6, 4.9 Hz, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 140.2, 135.1, 129.3 (2C), 128.5 (2C), 128.4 (2C), 128.2 (2C), 126.6, 87.5, 74.9, 52.9, 46.9, 41.7 (2C), 35.9, 34.4, 21.7, 20.3; **IR** (neat) 3062, 3027, 2928, 2860 2232 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{22}H_{24}ClNO_2SNa$, 424.1114; found, 424.1102.

3.4.6 Synthesis and Characterization of Cyclopropane Derivatives



trans-2-(3-Phenylbut-2-en-2-yl)cyclopropyl)ethan-1-amine (3.29) was prepared according to modified procedure reported by Hilmersson.[28] To a flame-dried round bottom flask equipped with a stir bar was added freshly prepared SmI_2 (40. mL, 3.2 mmol, 10. equiv, 80. mM in THF).[29] Then cyclopropane **3.1** (120 mg, 0.32 mmol, 1.0 equiv) was added as a solution in a minimal amount of THF. This was immediately followed by H_2O (0.17 mL, 9.6 mmol, 30. equiv), and pyrrolidine (0.53 mL, 6.4 mmol, 20. equiv). The solution became white upon the addition of the amine. The reaction mixture was diluted with CH_2Cl_2 and treated with a solution of potassium sodium tartrate (50 mL, 10% w/w) and K_2CO_3 (50 mL, 10% w/w). The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The unpurified reaction mixture was carried onto the next step without further purification.

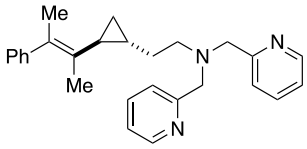
3.4.6.1 Method F: Reductive Amination of Primary Amines



This method was adapted from a procedure reported by Albrecht.[15] To a suspension of amine **3.29** (1.0–1.3 equiv) in dichloroethane (0.10–0.20 M in amine) was added the corresponding ketone or aldehyde (1.0 equiv). Then $NaBH(OAc)_3$ (2.0–3.2 equiv) was added at rt and was allowed to stir for 30 mins. Then additional ketone or aldehyde (0.3 equiv) was added and the reaction mixture

[28] Ankner, T.; Hilmersson, G. *Org. Lett.* **2009**, *11*, 503–506.
[29] For the preparation of SmI_2 see: Szostak, M.; Spain, M.; Procter, D. J. *J. Org. Chem.* **2012**, *77*, 3049– 3059.

was allowed to stir for 30 mins. The mixture was quenched with a saturated aq. solution of $NaHCO_3$ and extracted with methyl t-Butyl ether (x3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography.

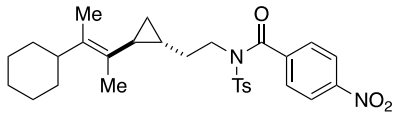


trans-2-(3-Phenylbut-2-en-2-yl)cyclopropyl)-N,N-bis(pyridin-2-ylmethyl)ethan-1-amine (3.6) was prepared according to Method F. The following amounts of reagents were used: amine **3.29** (43 mg, 0.20 mmol, 1.1 equiv), 2-pyridinecarbozaldehyde (17 μL, 0.18 mmol, 1.0 equiv), sodium triacetoxyborohydride (0.11 g, 0.50 mmol, 2.8 equiv), and DCE (2 mL, 0.1 M in amine **3.29**). The residue was purified by flash column chromatography (0–10% MeOH/CH_2Cl_2) to afford the title compound as a clear oil (34 mg, 86 μmol, 49% yield over two steps). For clarity, the ^{1}H NMR and ^{13}C NMR data of the major and minor diastereomers have been tabulated individually.

TLC R_f = 0.3 (10% MeOH/CH_2Cl_2); **HRMS** (TOF MS Cl+) m/z: $[M + H]^+$ calcd for $C_{27}H_{32}N_3$, 398.2596; found, 398.2598.

Major Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53–8.49 (m, 2H), 7.66–7.55 (m, 4H), 7.30–7.23 (m, 2H), 7.22– 7.07 (m, 5H), 3.85 (s, 4H), 2.70 (t, *J* = 7.5 Hz, 2H), 1.98 (s, 3H), 1.70–1.64 (m, 1H), 1.38–1.28 (m, 2H), 1.26 (s, 3H), 0.92–0.84 (m, 1H), 0.71–0.67 (m, 1H), 0.46–0.41 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 160.2 (2C), 149.11 (2C), 145.9, 136.5 (2C), 130.51, 128.5 (2C), 128.1 (2C), 125.8 (2C), 122.9 (2C), 122.0 (2C), 60.7 (2C), 54.4, 32.3, 23.3, 20.8, 16.6, 16.0, 12.0.

Minor Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53–8.49 (m, 2H), 7.66–7.55 (m, 4H), 7.30–7.23 (m, 2H), 7.22– 7.07 (m, 5H), 3.85 (s, 4H), 2.54 (t, *J* = 6.6 Hz, 2H), 1.95 (s, 3H), 1.59–1.52 (m, 1H), 1.44 (s, 3H), 1.37–1.17 (m, 2H), 0.83–0.76 (m, 1H), 0.59–0.54 (m, 1H), 0.17–0.12 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 160.3 (2C), 149.1 (2C), 145.3, 136.4 (2C), 130.48, 128.9 (2C), 128.0 (2C), 125.8 (2C), 122.9 (2C), 121.9 (2C), 60.6 (2C), 54.3, 31.8, 22.6, 21.7, 16.59, 13.9, 11.9.



N-(2-(trans-2-(3-cyclohexylbut-2-en-2-yl)cyclopropyl)ethyl)-4-nitro-*N*-tosylbenzamide (3.7) was prepared according to a procedure reported by Zeng.[30] To a flame-dried round bottom flask equipped with a stir bar was added cyclopropane **3.3** (68 mg, 0.18 mmol, 1.0 equiv), DMAP (2.0 mg, 20. μmol, 0.10 equiv), NEt_3 (29 mL, 0.20 mmol, 1.1 equiv), and CH_2Cl_2 (0.75 mL, 0.24 M in cyclopropane **3.3**). Then 4- nitrobenzoyl chloride (37 mg, 0.20 mmol, 1.1 equiv) was added in one portion and the reaction mixture was allowed to stir overnight at rt. The reaction mixture was diluted with CH_2Cl_2 and washed sequentially with 1.0 M HCl and aq $NaHCO_3$. The combined organic layers were dried over Na_2SO4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a clear oil (59 mg, 0.11 mmol, 61% yield). For clarity, the ^{1}H NMR and ^{13}C NMR data of the major and minor diastereomers have been tabulated individually.

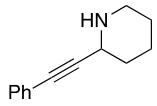
TLC Rf = 0.4 (10% MeOH/CH_2Cl_2); **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calcd for $C_{29}H_{36}N_2O_5SNa$, 547.2242; found, 547.2230.

[30] Wu, H.; Guo, W.; Daniel, S.; Li, Y.; Lio, C.; Zeng, Z. Fluoride-Catalyzed Esterification of Amides. *Chem. Eur. J.* **2018**, *24*, 3444–3447.

Major Diastereomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 3.89–3.84 (m, 2H), 2.75–2.68 (m, 1H), 2.46 (s, 3H), 1.91–1.82 (m, 1H), 1.79–1.64 (m, 4H), 1.58–1.54 (m, 1H), 1.53 (s, 3H), 1.46–1.39 (m, 2H), 1.36 (s, 3H), 1.32–1.20 (m, 5H), 0.73–0.65 (m, 1H), 0.62–0.56 (m, 1H), 0.42–0.36 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 169.4, 149.1, 145.4, 141.6, 135.7, 129.9 (2C), 128.9 (2C), 128.12, 128.07 (2C), 125.2, 123.3 (2C), 47.57, 41.2, 34.31, 31.0, 30.9, 26.9, 26.8, 26.4, 21.7, 21.5, 15.7 (2C), 14.3, 12.0.

Minor Diastereomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 3.89–3.84 (m, 2H), 2.46 (s, 3H), 2.41–2.34 (m, 1H), 1.91–1.82 (m, 1H), 1.79–1.64 (m, 4H), 1.61 (s, 3H), 1.58–1.54 (m, 1H), 1.46–1.39 (m, 2H), 1.36 (s, 3H), 1.32–1.20 (m, 5H), 0.73–0.65 (m, 1H), 0.62–0.56 (m, 1H), 0.42–0.36 (m, 1H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 169.4, 149.1, 145.4, 141.6, 135.5, 129.9 (2C), 128.9 (2C), 128.12, 128.07 (2C), 125.2, 123.3 (2C), 47.62, 41.9, 34.26, 30.8, 30.7, 26.83, 26.81, 26.4, 22.5, 15.5, 14.3, 14.2, 13.8, 12.1.

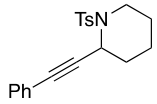
3.4.7 Mechanistic Experiments



2-(phenylethynyl)piperidine (3.30) was prepared according to a procedure reported by Seidel.[31] To a solution of piperidine (0.49 mL, 5.0 mmol, 1.0 equiv) in Et_2O (10 mL, 0.5 M), was added *n*-BuLi (2.0 mL, 5.0 mmol, 1.0 equiv, 2.5 M in hexanes) at –78 °C. The reaction mixture was allowed to stir for 10 mins. Then 2,2,2-trifluoroacetophenone (0.84 mL, 6.0 mmol, 1.2 equiv) was added

[31] Paul, A.; Seidel, D. *J. Am. Chem. Soc.* **2019**, *141*, 8778–8782.

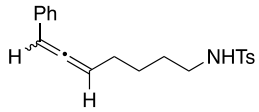
as a solution in Et_2O (6.0 mL, 1.0 M) and allowed to stir for an additional 10 mins. This was followed by the addition of freshly prepared lithium acetylide (7.5 mmol, 1.5 equiv). The reaction mixture was warmed to rt and allowed to stir for 2 h. The lithium acetylide was prepared according to the following method: In a flame dried round bottom flask equipped with a stir bar was added phenylacetylene (0.82 mL, 7.5 mmol, 1.5 equiv), PhMe (7.5 mL, 1.0 M), and THF (2.0 mL, 3.8 M). The flask was cooled to –78 °C and *n*-BuLi (3.0 mL, 7.5 mmol, 1.5 equiv, 2.5 M in hexanes) was added dropwise via syringe. The reaction mixture was allowed to stir for 30 mins at –78 °C. To quench, the flask was warmed to 0 °C and MeOH was added. The mixture was transferred to a separatory funnel, was diluted with Et_2O and washed with 1.0 M NaOH. The aqueous layer was extracted with Et_2O (x3). The combined organic layers were washed sequentially with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (0–5% MeOH/CH_2Cl_2) to afford the title compound as a pale, yellow oil (0.31 g, 1.7 mmol, 33% yield). **TLC R_f =** 0.1 (5% MeOH/CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.34–7.23 (m, 3H), 3.88 (dd, *J* = 7.4, 3.6 Hz, 1H), 3.21–3.10 (m, 1H), 2.91 (bs, 1H), 2.77 (ddd, *J* = 11.7, 6.8, 4.3 Hz, 1H), 1.94 (ddt, *J* = 12.4, 6.9, 3.4 Hz, 1H), 1.88–1.78 (m, 1H), 1.72 (dtd, *J* = 11.6, 7.6, 3.6 Hz, 1H), 1.6–1.47 (m, 3H).



2-(phenylethynyl)-1-tosylpiperidine (3.11) was prepared according to a procedure reported by Smith.[32] To a stirring solution of piperidine **3.30** (0.31 g, 1.7 mmol, 1.0 equiv) in CH_2Cl_2 (3.4 mL, 0.50 M) was added Et_3N (0.48 mL, 3.4 mmol, 2.0 equiv) and TsCl (0.30 g, 1.9 mmol, 1.1 equiv) at rt. The reaction mixture was allowed to stir overnight. To quench, 1.0 M HCl was added slowly.

[32] Spoehrle, S. S. M.; West, T. H.; Taylor J. E.; Slawin, A. M.; Smith, A. D. *J. Am. Chem. Soc.* **2017**, *139*, 11895–11902.

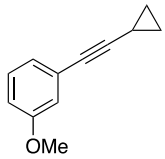
The biphasic mixture was transferred to a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with a saturated aq. solution of $NaHCO_3$ and brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a white solid (350 mg, 1.0 mmol, 67% yield). Analytical data is consistent with literature values.[33] **^{1}H NMR** (500 MHz, $CDCl_3$) 7.71 (d, *J* = 8.3 Hz, 2H), 7.31–7.14 (m, 5H), 6.98 (dt, *J* = 7.0, 1.5 Hz, 2H), 5.05 (s, 1H), 3.76 (dd, *J* = 12.1, 3.6 Hz, 1H), 2.88 (td, *J* = 11.8, 2.8 Hz, 1H), 2.27 (s, 3H), 1.97–1.82 (m, 2H), 1.77–1.61 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.3, 135.1, 131.5 (2C), 129.3 (2C), 128.2, 128.1 (2C), 128.0 (2C), 122.4, 86.9, 84.4, 46.9, 42.4, 31.7, 25.4, 21.4, 19.5.



4-Methyl-N-(7-phenylocta-5,6-dien-1-yl)benzenesulfonamide (3.12) was prepared according to Method A. The following amounts of reagents were used: piperidine **3.11** (28 mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (75 mg, 0.10 mmol, 1.0 equiv), MeMgI (80. μL, 0.20 mmol, 2.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). The residue was purified by flash column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear oil (21 mg, 76 μmol, 76% yield). **TLC R_f =** 0.4 (25% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.8 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.32–7.25 (m, 4H), 7.19 (t, *J* = 7.3 Hz, 1H), 5.37 (bs, 1H), 4.40 (bt, 1H), 2.91 (q, *J* = 6.5 Hz, 2H), 2.41 (s, 3H), 2.06 (s, 3H), 1.54–1.48 (m, 2H), 1.46–1.40 (m, 2H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 204.3, 143.5, 137.6, 137.1, 129.8 (2C), 128.4 (2C), 127.2 (2C),

[33] Daniels, D. S. B.; Jones, A. S.; Thompson, A. L.; Paton, R. S.; Anderson, E. A. *Angew. Chem. Int. Ed.* **2014**, *53*, 1915–1920.

126.6, 125.7 (2C), 100.9, 92.5, 43.2, 29.2, 28.4, 26.0, 21.6, 17.3; **IR** (neat) 3282, 3082, 3060, 3027, 2931, 2858, 1948 cm^{-1}.

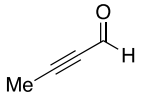


1-(Cyclopropylethynyl)-3-methoxybenzene (3.13) was prepared according to Method C. The following amounts of reagents were used: cyclopropylacetylene (0.13 mL, 1.5 mmol, 1.1 equiv), 3-iodoanisole (0.17 mL, 1.4 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (13 mg, 0.18 mmol, 1.0 mol %), CuI (6.9 mg, 40 μmol, 2.0 mol %), and Et_3N (6 mL, 0.3 M in cyclopropylacetylene). The residue was purified by flash column chromatography (0–10% EtOAc/hexanes) to afford the title compound as a clear oil (94 mg, 0.55 mmol, 39% yield). **TLC R_f =** 0.8 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 7.9, 1H), 6.97–6.95 (m, 1H), 6.91–6.90 (m, 1H), 6.82–6.79 (m, 1H), 3.77 (s, 3H), 1.47–1.40 (m, 1H), 0.88–0.82 (m, 2H), 0.81–0.72 (m, 2H). Analytical data are consistent with literature values.[34]

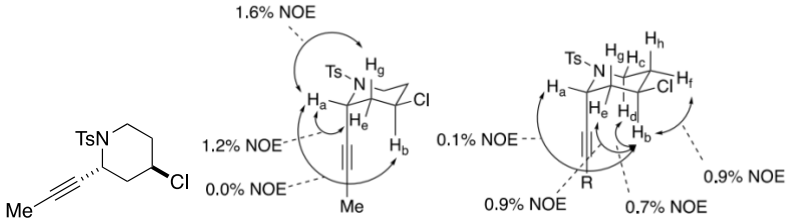
[34] Siebeneicher, H.; Doye, S. *Eur. J. Org. Chem.* **2002**, *7*, 1213–1220

3.4.7.1 Preparation of CD_3MgI

Under a N_2 atmosphere, a three-neck flask equipped with a stir bar, reflux condenser, and Schlenk filtration apparatus was charged with magnesium turnings (2.80 g, 115 mmol). The flask and magnesium turnings were then flame-dried under vacuum and the flask was backfilled with N_2. Anhydrous Et_2O (25 mL) and a crystal of iodine (ca. 2 mg) were added to the flask. Freshly distilled D_3-iodomethane (5.0 mL, 80 mmol) was slowly added over 30 min to maintain a gentle reflux. The mixture was stirred for 2 h at rt then filtered through the fritted Schlenk filter into a pear-shaped flask under a N_2 atmosphere. The pear-shaped flask was capped with a septum, sealed with parafilm, and stored in the glovebox under a N_2 atmosphere for up to eight weeks. The resulting methyl Grignard reagent titrated to 2.9 M as titrated by Knochel's method.[19]

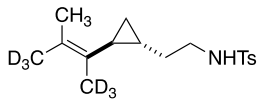


But-2-ynal (3.31) was prepared according to Method B. The following amounts of reagents were used: propyne (0.23 mL, 3.0 mmol, 1.0 equiv, 3% solution in heptane), *n*-BuLi (1.2 mL, 3.0 mmol, 1.0 equiv, 2.5 M in hexanes), DMF (0.46 mL, 6.0 mmol, 2 equiv), THF (7.5 mL, 0.40 M). Due to the volatility of the compound, it was carried onto the next step without further purification.



trans-4-Chloro-2-(prop-1-yn-1-yl)-1-tosylpiperidine (3.14) was prepared according to Method E. The following amounts of reagents were used: aldehyde **3.31** (3.0 mmol, 1.5 equiv), homoallylic sulfonamide **3.16** (0.37 mL, 2.0 mmol, 1.0 equiv), $FeCl_3$ (0.48 g, 3.0 mmol, 1.5 equiv), Bmim·PF_6 (0.62 mL, 3.0 mmol, 1.5 equiv), benzotrifluoride (30 mL, 0.1 M in aldehyde). The residue was

purified by flash column chromatography (0–20% EtOAc/hexanes) to afford the title compound as a white solid (24 mg, 76 μmol, 3.0% yield, >20:1 dr trans:cis). The dr was determined based on the integration of the resonances attributed to the propargylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis. **m.p.** 109–111 °C; **TLC R_f =** 0.3 (20% EtOAc/hexanes); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.88 (dq, *J* = 4.5, 2.3 Hz, 1H), 4.18–4.07 (m, 1H), 3.73 (ddt, *J* = 12.3, 4.6, 2.2 Hz, 1H), 2.87 (td, *J* = 12.5, 2.6 Hz, 1H), 2.42 (s, 3H), 2.27–2.13 (m, 2H), 2.03 (td, *J* = 12.3, 4.7 Hz, 1H), 1.89 (qd, *J* = 12.6, 4.8 Hz, 1H), 1.46 (d, *J* = 2.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125.8 MHz) δ 143.6, 135.0, 129.2 (2C), 128.3 (2C), 83.7, 73.1, 53.1, 47.1, 41.8, 41.7, 36.0, 21.7, 3.3; **IR** (neat) 2918, 2860, 2229, 1596, 1340, 1159, 927, 727 cm^{-1}; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calculated for $C_{15}H_{18}ClNO_2SNa$, 334.0645; found, 334.0642.



4-Methyl-N-(2-(trans-2-(3-methylbut-2-en-2-yl-1,1,1,4,4,4-d6)cyclopropyl)ethyl)benzene-sulfonamide (3.15) was prepared according to Method A. The following amounts of reagents were used: piperidine **3.14** (31 mg, 0.10 mmol, 1.0 equiv), (*R*-BINAP)$NiCl_2$ (3.8 mg, 5.0 μmol, 5.0 mol %), CD_3MgI (80. μL, 0.20 mmol, 2.0 equiv), and PhMe (0.50 mL, 0.20 M in substrate). A ^{1}H NMR yield of 70% was obtained based on comparison to PhTMS as internal standard. The residue was purified by flash column chromatography (0–25% EtOAc/hexanes) to afford the title compound as a clear oil (23 mg, 73 μmol, 73% yield, 1:2.4 *E:Z*). The E:Z ratio was determined based on the integration of the resonances attributed to CD_3 in the ^{2}H NMR spectrum. **TLC R_f =** 0.5 (25% EtOAc/hexanes); **IR** (neat) 3279, 3065, 2996, 2923, 2859, 2236, 2189, 2058, 1598 cm^{-}

[1]; **HRMS** (TOF MS CI+) m/z: $[M + H]^+$ calcd for $C_{17}H_{20}D_6NO_2S$, 314.2061; found, 314.2164. >99% ^2H Incorporation.

Major Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 4.60 (bt, *J* = 6.0 Hz, 1H), 3.05–2.98 (m, 2H), 2.43 (s, 3H), 1.71 (s, 3H), 1.57–1.48 (m, 1H), 1.43 (m, 1H), 1.32–1.25 (m, 1H), 0.68–0.62 (m, 1H), 0.60–0.55 (m, 1H), 0.37–0.33 (m, 1H); **^{2}H NMR** (400 MHz, $CDCl_3$) δ 1.62 (bs, 3H), 1.29 (bs, 3H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 137.1, 129.8 (2C), 127.3 (2C), 126.0, 125.9, 43.6, 43.5, 34.3, 29.8, 21.9, 21.6, 20.41, 15.4, 11.5.

Minor Diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 4.60 (bt, *J* = 6.0 Hz, 1H), 3.05–2.98 (m, 2H), 2.43 (s, 3H), 1.64 (s, 3H), 1.57–1.48 (m, 1H), 1.43 (m, 1H), 1.32–1.25 (m, 1H), 0.68–0.62 (m, 1H), 0.60–0.55 (m, 1H), 0.37–0.33 (m, 1H); **^{2}H NMR** (400 MHz, $CDCl_3$) δ 1.70 (bs, 3H), 1.29 (bs, 3H); **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 143.5, 137.1, 129.8 (2C), 127.3 (2C), 126.0, 125.9, 43.6, 43.5, 34.3, 29.8, 21.9, 21.6, 20.41, 15.4, 11.5.

Chapter 4

Ligand-Based Control of Nickel-Catalysts: Switching Chemoselectivity from One-Electron to Two-Electron Pathways in Competing Reactions of 4-Halotetrahydropyrans

4.1 Introduction

Experimental evidence that provides the basis for a broad-strokes understanding of ligand effects is critical for implementation of new catalytic methods by a broad range of synthetic chemists and can accelerate development of new catalytic transformations.[1] Such experimentally determined design principles have driven powerful advances in palladium-catalyzed coupling reactions.[2,3] Guiding principles for the selection of nickel catalysts are still being identified.[4,5,6] Chemoselectivity for one- or two-electron oxidative addition is a critical feature of many reactions

[1] Portions of this chapter have been published in *Organic Letters*, see: Thane, T. A.; Jarvo, E. R. *Org. Lett.* **2022**, *In Press*.

[2] a) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417–1492. b) Tsuji, J. *Palladium Reagents and Catalysts: New Perspectives for the 21st Century*. John Wiley and Sons, Ltd, 2004. DOI: 10.1992/0470021209.

[3] For example, bulky phosphine ligands are proposed to accelerate reductive elimination from palladium(II) complexes. a) Hartwig, J. F. *Inorg. Chem.* **2007**, *46*, 1936–1947. b) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **1998**, *37*, 3387–3388. c) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685–4696.

[4] a) Tasker, S. Z.; Standely, E. A.; Jamison, T. A. Recent Advances in Homogeneous Nickel Catalysis. *Nature* **2014**, *509*, 299–309. b) Tamaru, Y. *Modern Organonickel Chemistry*. Wiley-VCH Verlag GmbH & Co., **2005**. c) Lucas, E. L.; Jarvo, E. R. *Acc. Chem. Res.* **2018**, *51*, 567–572. d) Diccianni, J. B.; Diao, T. *Trends Chem.* **2019**, *1*, 830–844. e) Fu, G. C. *ACS Cent. Sci.* **2017**, *3*, 692–700. f) Greaves, M. E.; Johnson Humphrey, E. L. B.; Nelson, D. J. *Catal. Sci. Technol.*, **2021**, *11*, 2980.

[5] For seminal examples pinning aspects of nickel-catalyzed XC mechanisms, see: a) Elson, I. H.; Morrell, D. G.; Kochi, J. K. *J. Organomet. Chem.* **1975**, *84*, C7–C10. b) Kochi, J. K. *Pure Appl. Chem.* **1980**, *52*, 571–605. c) Jones, G. D.; Martin, J. L.; McFarland, C.; Allen, O. R.; Hall, R. E.; Haley, A. D.; Brandon, R. J.; Konovalova, T.; Desrochers, P. J.; Pulay, P.; Vicic, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 13175–12183.

[6] For example, electron-poor olefins are proposed to accelerate reductive elimination from nickel(II) complexes. a) Yamamoto, T.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc.* **1971**, *94*, 3350–3359. b) Sustmann, R.; Lau, J.; Zipp, M. *Tetrahedron Lett.* **1986**, *27*, 5207–5210. c) Giovannini, R.; Studemann, T.; Devasagayaraj, A.; Dussin, G.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 3544–3553. d) Piber, M.; Jensen, A. E.; Rottlander, M.; Knochel, P. *Org. Lett.* **1999**, *1*, 1323–1326. e) Estrada, J. G.; Williams, W. L.; Ting, S. I.; Doyle, A. *J. Am. Chem. Soc.* **2020**, *142*, 8928–8937.

of alkyl electrophiles and can be controlled by identity of the substrate.[7,8,9] However, there is little empirical evidence that this selectivity can also be perturbed by the ligand. Many stereoablative reactions employ pyridyl- or imine-based ligands, while stereospecific transformations often employ phosphine ligands. In any given publication, typically either nitrogen- or phosphine-based ligands are evaluated. However, a direct contrast between the two classes is rarely provided. In this manuscript, we report experiments that provide, to our knowledge, the first data set that directly compares stereospecific and stereoablative reaction manifolds under the same reaction conditions.[10,11] As such, we directly interrogate the ligands' control of catalyst propensity for closed-shell and open-shell reactivity. These experiments complement detailed parameterization that has been employed to compare closely related ligands for single reaction pathways.[12,13] This work will impact the development of new base-metal-catalyzed reactions of alkyl electrophiles.

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[7] For a comparison of the two reaction manifolds, see: Lucas, E. L.; Jarvo, E. R. *Nat. Chem. Rev.* **2017**, *1*, 0065.

[8] For representative examples of nickel-catalyzed, stereoablative, one-electron oxidative addition of alkyl electrophiles: a) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 14726–14727. b) Yin, H.; Fu, G. C. *J. Am. Chem. Soc.* **2019**, *141*, 15433–15440. c) Weix, D. J. *Acc. Chem. Res.* **2015**, *48*, 1767–1775. d) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 7442–7445. e) Poremba, K. E.; Dibrell, S. E.; Reisman, S. E. *ACS Catal.* **2020**, *10*, 8237–8246. f) Huang, C.-Y.; Doyle, A. G. *J. Am. Chem. Soc.* **2012**, *134*, 9541–9544.

[9] For nickel-catalyzed, stereospecific, two-electron oxidative addition of benzylic electrophiles: a) Taylor. B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389–391. b) Tollefson, E. J.; Erickson. L. W.; Jarvo. E. R. *J. Am. Chem. Soc.* **2015**, *137*, 9760–9763. c) Tollefson, E. R.; Hanna, L. E.; Jarvo, E. R. *Acc. Chem. Res.* **2015**, *48*, 2344–2353.

[10] For analysis of ligand effects on chemoselectivity of oxidative addition of aryl halides and pseudohalides, see: a) Kalvet, I.; Guo, Q.; Tizzard, G. J.; Schoenebeck, F. *ACS Catal.* **2017**, *7*, 2126–2132. b) Entz, E. D.; Russell, J. E.; Hooker, L. V.; Neufeldt, S. R. *J. Am. Chem. Soc.* **2020**, *142*, 15454–15463. c) Reeves, E. K.; Entz, E. D.; Neufeldt, S. R. *Chem. – A Eur. J.* **2021**, *27*, 6161–6177.

[11] a) For effects of structure of N-based ligands on halogen-atom abstraction and oxidative addition of aryl halides, see: Lin, Q.; Fu, Y.; Liu, P.; Diao, T. *J. Am. Chem. Soc.* **2021**, *143*, 14196–14206. b) For differing preferences of Pd and Ni catalysts for oxidative addition with aryl halides and aryl sulfonates, see: Huang, L.; Ackerman, L. K. G.; Kang, K.; Parsons, A. M.; Weix, D. J. *J. Am. Chem. Soc.* **2019**, *141*, 10978–10983.

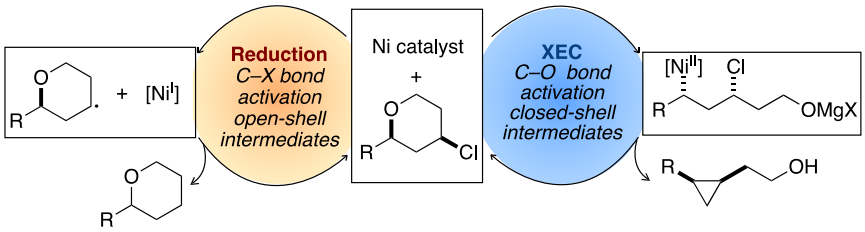
[12] a) Milo, A.; Bess, E. N.; Sigman, M. S. Interrogating Selectivity in Catalysis Using Molecular Vibrations. *Nature* **2014**, *507*, 210. b) Wu, K.; Doyle, A. G. *Nature Chem.* **2017**, *9*, 779–784. c) Zhao, S.; Gensch, T.; Murray, B.; Niemery, Z. L.; Sigman, M. S.; Biscoe, M. R. *Science* **2018**, *80*, 670–674. d) DeLano, T. J; Dibrell, S. E.; Lacker, C. R.; Pancoast, A. R.; Poremba, K. E.; Cleary, L.; Sigman, M. S.; Reisman, S. E. *Chem. Sci.* **2021**, *12*, 7758–7762. e) Woods, B. P.; Orlandi, M.; Huang, C.-Y.; Sigman, M. S.; Doyle, A. G. *J. Am. Chem. Soc.* **2017**, *139*, 5688–5691. f) Newman-Stonebraker, S. H.; Smith, S. R.; Borowski, J. E.; Peters, E.; Gensch, T.; Johnson, H. C.; Sigman, M. S.; Doyle, A. G. *Science* **2021**, *374*, 301–308.

[13] For machine-learning based approaches, see: a) Crawford, J. M.; Kingston, C.; Toste, D. F.; Sigman, M. S. *Acc. Chem. Res.* **2021**, *54*, 3136–3148. b) Żurański, A. M.; Martinez Alvarado, J. I.; Shields, B. J.; Doyle. A. G. *Acc. Chem. Res.* **2021**, *54*, 1856–1865. c) Durand, D. J.; Fey, N. *Acc. Chem. Res.* **2021**, *54*, 837–848.

A major challenge is identifying a suitable control reaction, where a single variable can be changed to systematically compare catalyst systems, and where the reaction mechanisms are well-understood. We hypothesized that reactions of 4-halotetrahydropyrans fit these criteria (Scheme 4.1). These substrates undergo divergent reaction pathways and therefore provide a competition experiment where product outcome is determined by the chemoselectivity of the first elementary step, oxidative addition. One potential reaction product is the cyclopropane, formed by an intramolecular cross-electrophile coupling (XEC).[14] This product forms if the reaction initiates by oxidative addition at the ether. Our laboratory has reported mechanistic details for this XEC reaction and has determined that it proceeds through a robust two-electron pathway, where oxidative addition occurs via an S_N2-type transition state.[15] Radical intermediates are not formed. Alternatively, the tetrahydropyran can be formed as the product if the reaction initiates by halogen atom transfer (XAT) of the alkyl halide.[16] This pathway proceeds through the alkyl radical. Therefore, we hypothesized that correlating the product distribution to ligand identity would allow identification of the key features of the nickel catalyst that pro-mote oxidative addition by one- or two-electron manifolds.

[14] For the ring contraction of 4-halotetrahydropyrans see: a) reference 8b; b) Erickson, L. W.; Lucas, E. L.; Tollefson, E. J.; Jarvo, E. R. *J. Am. Chem. Soc*. **2016**, *138*, 14006–14011.
[15] Chen, P.-P.; Lucas, E. L.; Greene, M. A.; Zhang, S.-Q.; Tollefson, E. J.; Erickson, L. W.; Taylor, B. L. H.; Jarvo, E. R.; Hong, X. *J. Am. Chem. Soc.* **2019**, *141*, 5835–5855.
[16] a) Kehoe, R.; Mahadevan, M.; Manzoor, A.; McMurray, G.; Wienefeld, P.; Baird, M. C.; Budzelaar, P. H. *Organometallics* **2018**, *37*, 2450–2467. b) Diccianni, J. B.; Katigbak, J.; Hu, C.; Diao, T. *J. Am. Chem. Soc.* **2019**, *141*, 1788–1796.

Scheme 4.1 Ligand-Based Control of Nickel Catalysis: Competition Between One- and Two-Electron Pathways.

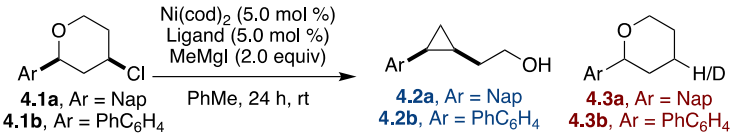


4.2 Results and Discussion

As a first step to validate our approach, we set out to confirm that the reduction products are indeed formed via open-shell intermediates (Table 4.1).[17] We proposed that the nickel catalyst undergoes halogen atom abstraction with the alkyl halide to form a secondary radical.[18,19] Substrates **4.1a** and **4.1b** were chosen for these experiments due to the resolution of the characteristic peaks in ^{1}H NMR. Experiments were performed employing Ni(cod)$_2$ in the presence of IndaBox and Biox ligands since these catalyst-substrate combinations facilitated the reduction pathway (vide infra). Addition of TEMPO to the standard reaction conditions suppressed formation of tetrahydropyrans **4.3a** and **4.3b** (entries 2 and 5). These results are consistent with formation of open-shell intermediates over the course of the reduction pathway. In contrast, the XEC reaction, employing *rac*-BINAP as the ligand, was not significantly inhibited by addition of TEMPO, consistent with closed-shell intermediates for the XEC pathway (entry 8).

[17] Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev*. **2002**, 102, 4009–4091.
[18] See reference 15
[19] Sanford, A. B.; Thane, T. A.; McGinnis, T. M.; Chen, P.-P.; Hong, X.; Jarvo, E. R. *J. Am. Chem. Soc.* **2020**, *142*, 5017–5023.

Table 4.1 TEMPO Trapping and Deuterium Incorporation Studies Provide Evidence of a Radical Mechanism for Reduction.



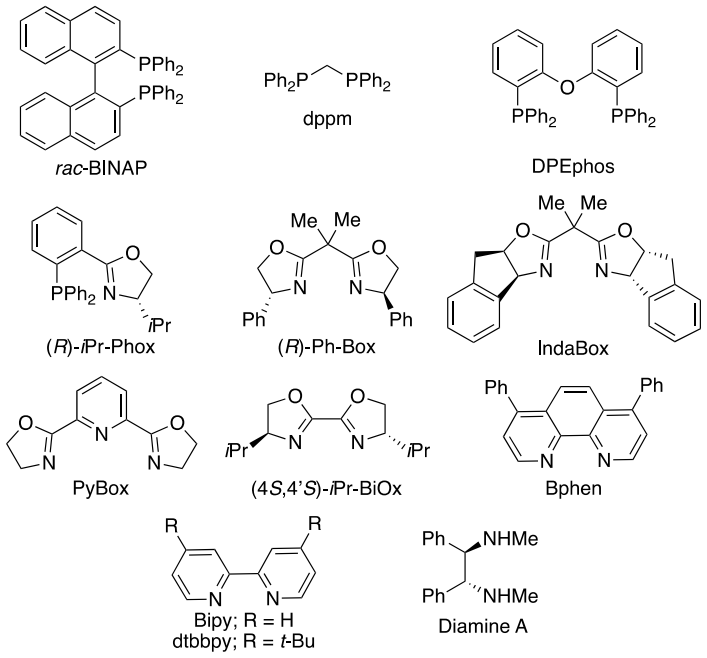
Entry	Ar	Ligand	Deviation from standard conditions	Recovered 4.1 (%)	4.2 (%)	4.3 (%)	D incorporation (%)
1	Nap	IndaBox	none	30	<5	55	-
2	Nap	IndaBox	1 equiv TEMPO added	87	<5	10	-
3	Nap	IndaBox	D_8-PhMe as solvent	32	<5	16	21
4	PhC_6H_4	Biox	none	<5	<5	63	-
5	PhC_6H_4	Biox	1 equiv TEMPO added	54	<5	35	-
6	PhC_6H_4	Biox	D_8-PhMe as solvent	44	<5	33	41
7	Nap	*rac*-BINAP	none	<5	92	<5	-
8	Nap	*rac*-BINAP	1 equiv TEMPO added	9	83	<5	-

To provide additional evidence that the reduction pathway proceeds by initial XAT and an alkyl radical intermediate, we performed deuterium-incorporation experiments to determine the source of the hydrogen atom. Performing the reaction of substrates **4.1a** and **4.1b** in D_8-toluene provided the reduction product with deuterium incorporation, consistent with formation of an alkyl radical by XAT and subsequent HAT from toluene (entries 3 and 6). Importantly, the reaction was stereoablative: product **4.3b** was formed as a 1:1 mixture of diastereomers. Taken together, these experiments are consistent with initiation of reduction by XAT of the alkyl halide with the nickel catalyst.

With robust mechanistic understanding of competing reaction pathways, we designed and evaluated a matrix of cross-electrophile coupling reactions with six racemic 4-halotetrahydropyrans and 11 ligands. Ligands were selected based on their success in previously developed cross-coupling (XC) and XEC reactions, and to span a range of ligand properties including ligand field, bite angle and redox activity (Figure 1). Bidentate phosphines were selected

based on their success in our previously developed ring contractions.[20] A variety of sub-classes of nitrogen-based ligands that have been employed in XC and XEC reactions were examined, including bipyridine-, oxazoline-, and diamine-based ligands. [21,22,23,24,25,26,27]

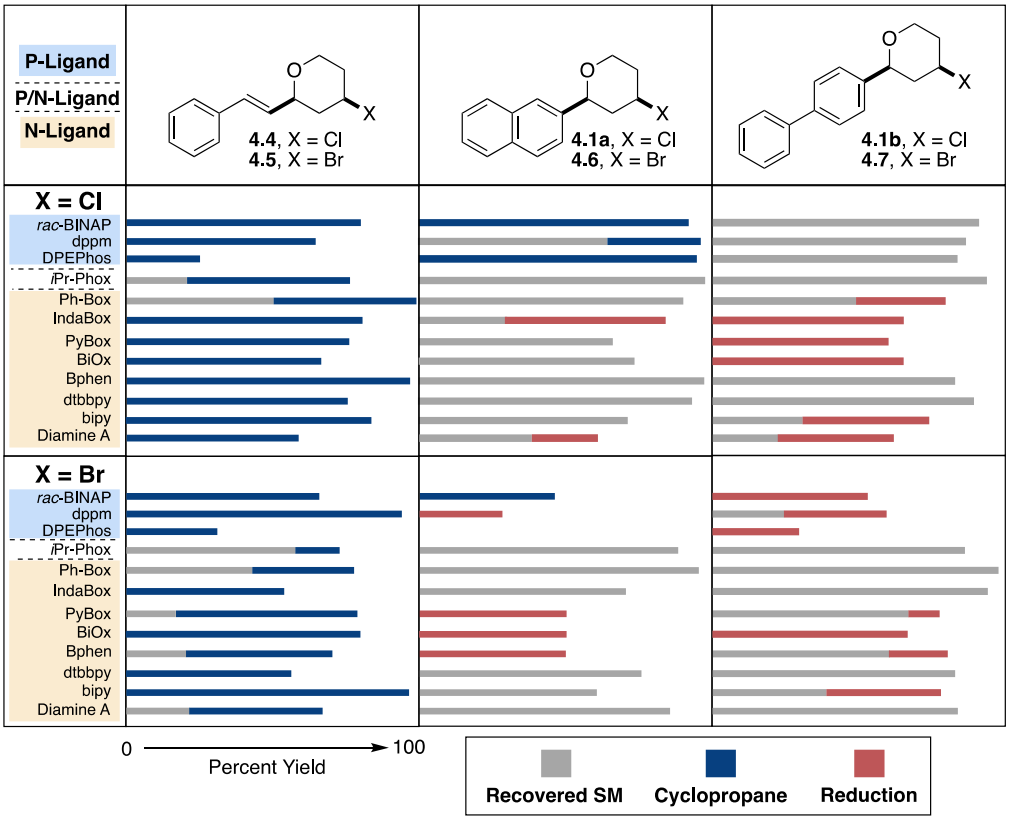
Figure 4.1 Ligands Selected for Initial Evaluation for XEC or Reduction of 4-Halotetrahydropyrans.



[20] See reference 13.
[21] For an overview, see: reference 7e.
[22] For representative examples using bipy and bipy analogs, see: a) Knappke, C. E. I.; Grupe, S.; Gärtner, D.; Corpet, M.; Gosmini, C.; von Wangelin, A. J. *Chem. Eur. J.* **2014**, *20*, 6828–6842. b) Everson, D. A.; Shrestha, R.; Weix, D. J. *J. Am. Chem. Soc.* **2010**, *132*, 920–921. c) Liu, J.; Ren, Q.; Zhang, X.; Gong, H. *Angew. Chem. Int. Ed.* **2016**, *55*, 11544–11548. d) Liao, J.; Basch, C. H.; Hoerrner, M. E.; Talley, M. R.; Boscoe, B. P.; Tucker, J. W.; Garnsey, M. R.; Watson, M. P. *Org. Lett.* **2019**, *21*, 2941–2946.
[23] For representative examples using Box ligands, see: a) references 7b and 7d; b) Ackerman, L. K. G., Anka-Lufford, L. L.; Naodovic, M.; Weix, D. J. *Chem. Sci*. **2015**, *6*, 1115–1119.
[24] For representative example using BiOx ligand: a) Poremba, K.; Kadunce, N. T.; Suzuki, N.; Cherney, A. H.; Reisman, S. E. *J. Am. Chem. Soc.* **2017**, *139*, 5684–5687. b) Woods, B. P.; Orlandi, M.; Huang, C.-Y.; Sigman, M. R.; Doyle, A. G. *J. Am. Chem. Soc.* **2017**, *139*, 5688–5691.
[25] For representative reactions using PyBox ligand, Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 14726–14727.
[26] For a representative example using a Phox ligand, see: Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2015**, *137*, 10480–10483.
[27] For reactions that utilize diamine ligands: a) Cordier, C. J.; Lundgren, R. J.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 10946–10949. b) Schmidt, J.; Liu, A. T.; Slusarczyk, M.; Fu, G. C. *Science* **2016**, *354*, 1265–1269.

Analysis of the data trends supports a working hypothesis that two factors work in concert to predict selectivity: the identity of the electrophile and the identity of the ligand. Allylic ethers (in **4.4** and **4.5**) outcompete alkyl chloride and alkyl bromide moieties, resulting in XEC regardless of ligand structure. Conversely, simple benzylic ethers (in **4.1b** and **4.7**) are sluggish oxidative addition partners, resulting in no XEC. In this series, catalysts with nitrogen-based ligands support XAT of the alkyl chloride moiety, and many catalysts (nitrogen- and phosphine-based) promote XAT of the alkyl bromide.

Figure 4.2 Overview of Results from the THP x Ligand Matrix.[28]



Most illustrative are reactions of naphthyl-substituted tetrahydropyrans **4.1a** and **4.6**, where product selectivity is dictated by the ligand. The C–O bond of these substrates is moderately

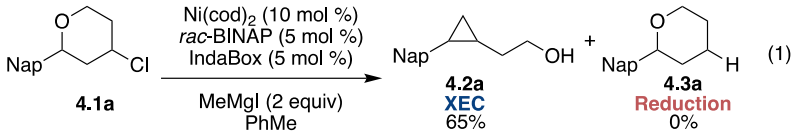
[28] Seeing Supporting Information Tables S-1 through S-6 for data tables with the exact numbers from the bar graph in Figure 2.

activated and, with the correct ligand structure, competes with the alkyl halide for the nickel catalyst. Particularly illustrative are reactions of 4-chlorotetrahydropyran **4.1a**. For this substrate, phosphine-based ligands promote two-electron oxidative addition and nitrogen-based ligands promote one-electron XAT. Therefore, we hypothesize that stronger field phosphine-based ligands favor two-electron oxidative addition, by providing an electron-rich, nucleophilic catalyst.[29] Conversely, weaker field nitrogen-based ligands that can support open-shell nickel complexes favor XAT.[30] In addition to ligand field effects, it is important to note that certain nitrogen-based ligands such as bipyridine are known to be redox active and support Ni(I) intermediates by accommodating ligand-centered radicals.[31] However, this factor does not appear to be a key determinant for this data set, since some of the ligands that favor XAT, such as oxazoline-based ligands, have been shown to provide nickel(I) complexes with metal-centered radicals.[32]

To evaluate which reaction pathway is dominant, we performed a competition experiment, where substrate **4.1a** was exposed to both catalysts (eq 1). Subjecting substrate **4.1a** to the reaction conditions with equivalent loadings of both *rac*-BINAP and IndaBox provided cyclopropane **4.2a** as the exclusive product. This result is consistent with the *rac*-BINAP-ligated nickel catalyst undergoing oxidative addition at the benzylic C–O bond faster than the IndaBox-ligated nickel

[29] Van Hecke, G. R.; Horrocks, W. D. *Inorg. Chem.* **1966**, *5*, 1960–1968.
[30] a) Crabtree, R. H. Crystal Field Theory and Ligand Field Theory. In *The Organometallic Chemistry of the Transition Metals*, 6th ed; John Wiley & Sons, **2014**; pp 11–21. b) Hartwig, J. F. Chapter 2.6 Dative Phosphorous Ligands and Heavier Congeners and Chapter 2.7 Complexes of Ligands Bound Through N, O, and S. In *Organotransition Metal Chemistry*; University of Science Books, **2010**; pp 33–39 and 57–58. c) Chapter 19: Coordination and Organometalic Compound. In *Chemistry of Elements*, 2nd ed.; Greenwood, N. N.; Eearnshaw, A.; Elsevier Ltd., **1997**; pp 922–933.
[31] Redox active ligand in XC/XEC: a) Anderson, T. J.; Jones, G. D.; Vicic, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 8100–8101. b) Jones, G. D.; Martin, J. L.; McFarland, C.; Allen, O. R.; Hall, R. E.; Haley, A. D.; Brandon, R. J.; Konovalova, T.; Desrochers, P. J.; Pulay, P.; Vicic, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 13175–12183. c) Wagner, C. L.; Herrera, G.; Lin, Q.; Chunhua, T. H.; Diao, T. *J. Am. Chem. Soc.* **2021**, *143*, 5295–5300. d) Schley, N. D.; Fu, G. F. *J. Am. Chem. Soc.* **2014**, *136*, 16588–16593. (e) For a discussion, see: Hu, X. *Chem. Sci*. **2011**, *2*, 1867–1886.
[32] For example, nickel(I) complexes ligated by bipyridine ligands, Ph-Box and Biox have been shown to be metal-centered radicals: a) Ting, S. L.; Williams, W. L.; Doyle, A. G. *J. Am. Chem. Soc.* **2020**, doi:10.1021/jacs.2c00462. b) Yin, H.; Fu, G, C. *J. Am. Chem. Soc*. **2019**, *141*, 15433–15440. c) Ju, L.; Lin, Q.; LiBretto, N. J.; Wagner, C. L.; Hu, C. T.; Miller, J. T.; Diao, T. *J. Am. Chem. Soc*. **2021**, *143*, 14458–14463. d) Somerville, R. J.; Odena, C.; Obst, M. F.; Hazari, N.; Hopmann, K. H.; Martin, R. *J. Am. Chem. Soc.* **2020**, *142*, 10936–10941.

catalyst can react with the secondary chloride by XAT. This follows our expectation that phosphine-ligated nickel catalysts have a high nucleophilicity, likely in part due to the strong sigma-donor properties of the ligand, which favors the S_N2-type oxidative addition. The nucleophilicity of the nickel catalyst with *rac*-BINAP coordination drives the chemoselectivity towards the two-electron paradigm.



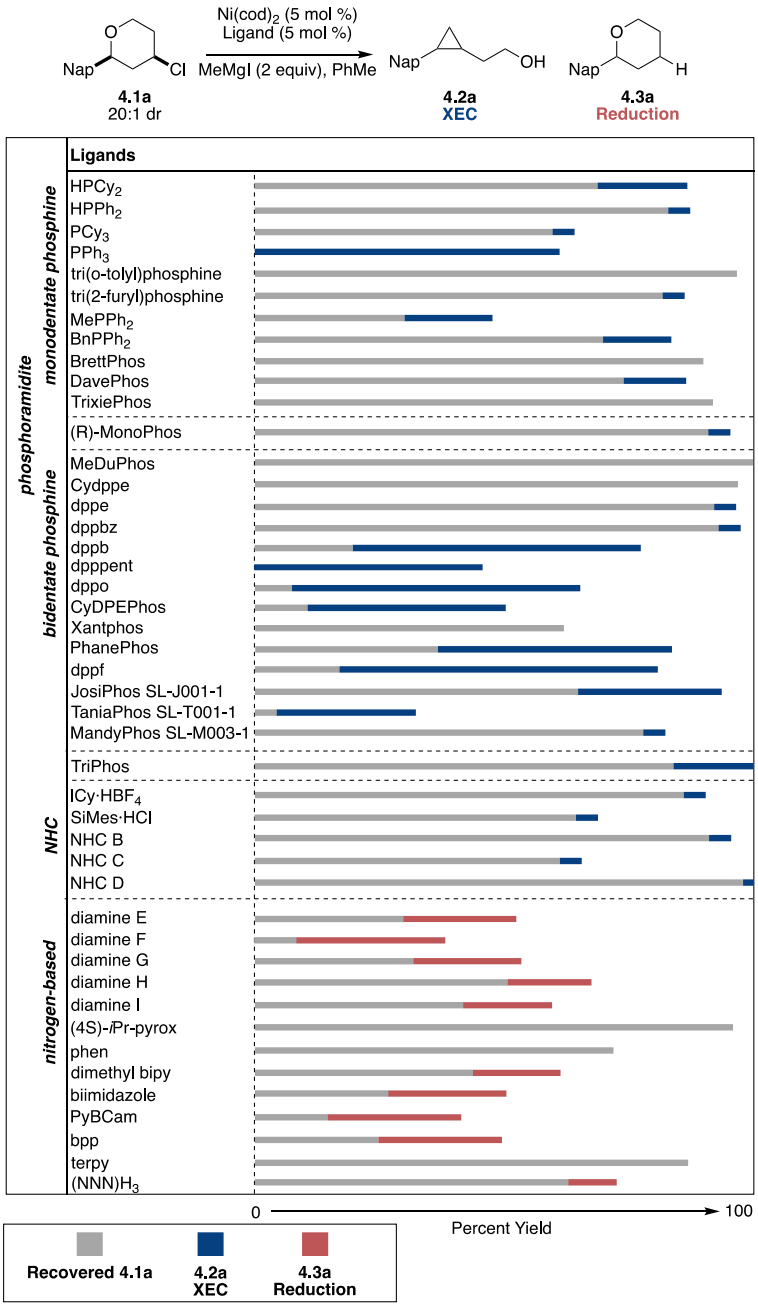
To further evaluate whether this ligand dependency is a predictable trend, we examined a larger sample of a range of ligands in reaction of 4-chlorotetrahydropyran **4.1a** (Figure 3). We evaluated >40 ligands, including monodentate phosphines, phosphoramidites, bidentate phosphines, tridentate phosphines, N-heterocyclic carbenes, diamines and pyridines.[33,34] The overall data trends are clear, with nitrogen-based ligands, including diamines and pyridine-based ligands, providing the reduced THP **4.3a** via XAT. In contrast, only phosphine ligands provided significant yields of cyclopropane **4.2a**, by polar oxidative addition of the benzylic ether. There are clearly additional factors, including steric parameters, that control whether a ligand provides a reactive catalyst, since many ligands provided recovered starting material.[35] However, as a general design principle, the premise that phosphine ligands favor two-electron pathways and nitrogen-based ligands promote one-electron reactions appears to hold. These results are consistent with the

[33] For an overview of phosphine-based ligands in nickel-catalyzed reactions, see: Clevenger, A. L.; Stolley, R. M.; Aderibigbe, J.; Louie, J. *Chem. Rev.* **2020**, *120*, 6124–6196.
[34] a) For methods using NHCs: Zhang, K.; Conda-Sheridan, M.; Cooke, S. R.; Louie, J. *Organometallics* **2011**, *30*, 2546–2552. b) For methods utilizing PyBcam: a) Kim, S.; Goldfogel, M. J.; Gilbert, M. M.; Weix, D. J. *J. Am. Chem. Soc.* **2020**, *142*, 9902–9907. c) For methods using terpy, see: Gong, H.; Gagné, M. R. *J. Am. Chem. Soc.* **2008**, *130*, 12177–12183. d) For a lead example with $(NNN)H_3$: Nguyen, A. I.; Blackmore, K. J.; Carter, S. M.; Zarkesh, R. A.; Heyduk, A. F. *J. Am. Chem. Soc.* **2009**, *131*, 3307–3316.
[35] The majority of reactions (>35 ligands) provided <5% of identifiable byproducts. Only PPh_3 provided >10% byproducts, resulting from reactions initiating by oxidative addition of the benzylic C–O. See Supporting Information for details.

prevalence of phosphine ligands in stereoselective XC and XEC reactions of benzylic and alkyl ethers. These results are also consistent with the prevalence of nitrogen-based ligands in stereoablative XC and XEC reactions of alkyl halides, and, within this series, accommodation of ligand-centered radicals does not appear to be a critical feature.[36]

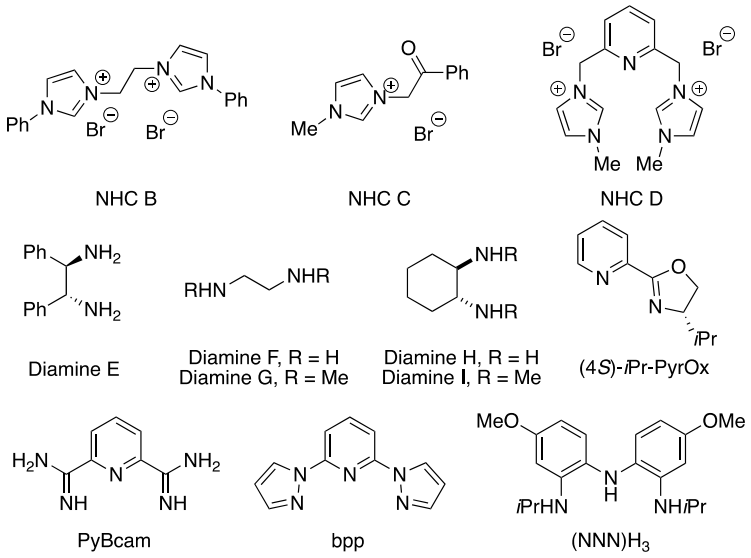
[36] See references 29 and 30.

Figure 4.3 Overview of Results from Expanded Ligand Set with 4-Chlorotetrahydropyran **4.1a**.[37]



[37] See Supporting Information Tables S-7 and S-8 for the exact numbers recorded in bar graph Figure 3 and for byproducts formed.

Figure 4.4 Ligand Key for the Expanded Reaction Matrix.



4.3 Conclusions

In conclusion, we provide experimental evidence for a ligand-based switch in selectivity for one- and two-electron pathways in a nickel catalyzed reaction, by examining competitive XEC and reduction of 4-halotetrahydropyrans. Both phosphorous- and nitrogen-based ligands were examined to determine the preference of the catalysts for activation of C–O or C–X bonds. In general, two factors work in concert to control the preferred pathway: identity of electrophile and the identity of the ligand. These results will inform the development of new cross-electrophile coupling reactions by providing insight into the synergistic effect of the ligand and oxidative addition mechanism evoked. Current investigations include more detailed analysis of these trends and establishing related structure-activity relationships for a broader range stereospecific and stereoablative reactions.

4.4 Experimental Details

4.4.1 General Procedures

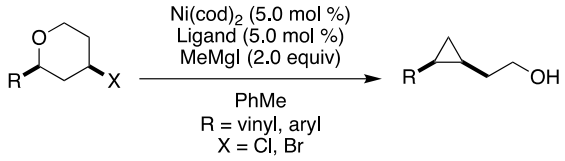
All reactions were carried out under a N_2 atmosphere, unless otherwise stated. All glassware was either oven-dried or flame-dried prior to use. Toluene (PhMe), diethyl ether (Et_2O), dichloromethane (DCM), and tetrahydrofuran (THF) were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 °C for 12 hours) to remove H_2O. Other solvents were purchased "anhydrous" commercially, or were purified as described. ^1H NMR were recorded on Bruker DRX-400 (400 MHz ^1H, 100 MHz ^{13}C), CRYO-500 (500 MHz ^1H, 125.7 MHz ^{13}C), GN-500 (500 MHz ^1H, 125.7 MHz ^{13}C), or AVANCE-600 (150 MHz ^{13}C) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00) unless otherwise noted. Data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (br s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet (t), doublet of triplets (dt), triplet of doublets (td), doublet of doublet of triplets (ddt), quartet (q), quintet (quint), quintet of triplets (quintt), coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). NMR data were collected at 25 °C. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60Å F254 precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with p-anisaldehyde (PAA), cerium ammonium molybdate (CAM), or potassium permanganate ($KMnO_4$) solutions. Flash chromatography was performed using either SiliaFlash F60 (40–63 μm, 60 Å) from SiliCycle, or Teledyne Isco Combiflash® Rf+ automated flash chromatography system. High resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center.

GC/FID analysis for competition experiments was performed on Agilent 7820A system with helium as carrier gas. For reactions performed at rt, average room temperature was 20 ºC.

Bis(1,5-cyclooctadiene)nickel was purchased from Strem, stored in a glove box freezer (–20 °C) under an atmosphere of N_2 and used as received. All ligands were purchased from Strem or Sigma Aldrich and were stored under N_2 atmosphere and used as received. All Grignard reagents were titrated with iodine prior to use.[38] All other chemicals were purchased commercially and used as received, unless otherwise noted.

4.4.2 General Ni-Catalyzed XEC and Reduction Procedures

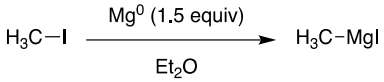
4.4.2.1 Method A: Cross-Electrophile Coupling



In a glovebox, to a 7 mL vial equipped with a stir bar was added $Ni(cod)_2$ (5.0 mol %), ligand (5.0 mol %), tetrahydropyran (1.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). Next, methylmagnesium iodide (2.0 equiv, 2.4 M soln in Et_2O) was added dropwise to the vial and the reaction mixture was allowed to stir at rt. After 24 h, the reaction was quenched with MeOH. The unpurified reaction mixture was plugged in a monstr pipette with silica and washed with Et_2O (neat, x3). Next, the Et_2O washes were concentrated in vacuo and a ^1H NMR yield was obtained by comparison to PhTMS as the internal standard.

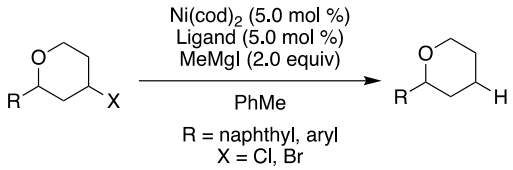
[38] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, *5*, 890–891.

4.4.2.2 Preparation of Methylmagnesium Iodide



Under an N_2 atmosphere, to a three-necked round bottom flask equipped with a stir bar, reflux condenser, and Schlenk filtration apparatus was added magnesium turnings (2.80 g, 120 mmol, 1.50 equiv). The flask and magnesium turnings were flame-dried under vacuum and the flask was back-filled with N_2. A crystal of iodine (ca. 2 mg) was added to the flask, followed by anhydrous Et_2O (25 mL). The reaction mixture was brought to 0 °C, and freshly distilled iodomethane (5.0 mL, 82 mmol, 1.0 equiv) was slowly added over 30 min to maintain a gentle reflux. The mixture was stirred for 4 h at room temperature then filtered through the fritted Schlenk filter into a pear-shaped flask under N_2 atmosphere. The magnesium turnings were washed with Et_2O (2 x 1.0 mL) then the pear-shaped flask was sealed, removed, and placed under an N_2 atmosphere. The resulting methyl Grignard reagent was typically between 2.4 and 3.0 M as titrated by Knochel's method[38] and was stored in a glovebox for up to 8 weeks.

4.4.2.3 Method B: Reduction of THP

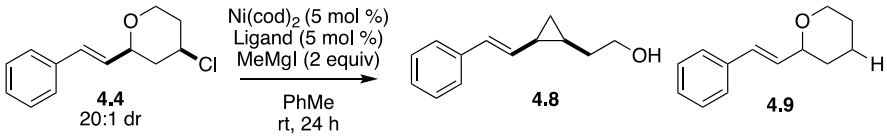


In a glovebox, to a 7 mL vial equipped with a stir bar was added $Ni(cod)_2$ (5.0 mol %), tetrahydropyran (1.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). Next, methylmagnesium iodide (2.0 equiv, 2.4 M soln in Et_2O) was added dropwise to the vial and the reaction mixture was allowed to stir at rt. After 24 h, the reaction was quenched with MeOH. The unpurified reaction mixture was plugged in a monstr pipet with silica gel and washed with Et_2O (neat, x3). Next, the

Et_2O washes were concentrated in vacuo and a ^1H NMR yield was obtained by comparison to PhTMS as the internal standard.

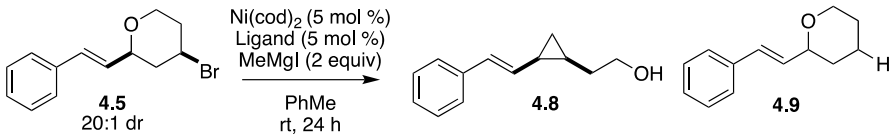
4.4.3 Tables for Ligand Screening with Vinyl, Naphthyl, and Aryl THPs

Table 4.2 Ligand Screen with 4-Chlorotetrahydropyran **4.4**.



Ligand	4.4 (%)	4.8 (%)	4.9 (%)
rac-BINAP	0	79	0
dppm	0	63	0
DPEphos	0	24	0
(*R*)-*i*Pr-Phox	21	56	0
(*R*)-Ph-Box	50	50	0
IndaBox	0	81	0
PyBox	0	75	0
(4*S*, 4'*S*)-*i*Pr-BiOx	0	66	0
Bphen	0	96	0
dtbbp	0	76	0
bipy	0	78	0
Diamine A	0	59	0
No Ligand	0	87	0
No Ligand, No Ni	80	0	0

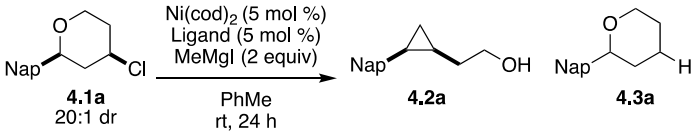
Table 4.3 Ligand Screen with 4-Bromotetrahydropyran **4.5**.



4.5 20:1 dr — **4.8** — **4.9**

Ligand	4.5 (%)	4.8 (%)	4.9 (%)
rac-BINAP	0	65	0
dppm	0	94	0
DPEphos	0	31	0
(*R*)-*i*Pr-Phox	57	17	0
(*R*)-Ph-Box	43	34	0
IndaBox	0	53	0
PyBox	17	62	0
(4*S*, 4'*S*)-*i*Pr-BiOx	0	80	0
Bphen	19	50	0
dtbbp	0	56	0
bipy	0	96	0
Diamine A	22	46	0
No Ligand	81	0	0
No Ligand, No Ni	86	0	0

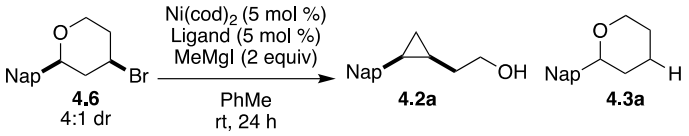
Table 4.4 Ligand Screen with 4-Chlorotetrahydropyran **4.1a**.



4.1a 20:1 dr — **4.2a** — **4.3a**

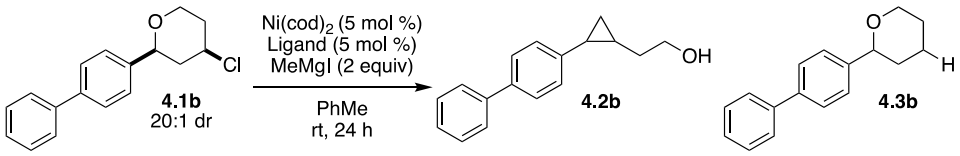
Ligand	4.1a (%)	4.2a (%)	4.3a (%)
rac-BINAP	0	92	0
dppm	64	32	0
DPEPhos	0	95	0
(*R*)-*i*Pr-Phox	97	0	0
(*R*)-Ph-Box	90	0	0
IndaBox	30	0	55
PyBox	66	0	0
(4*S*, 4'*S*)-*i*Pr-BiOx	70	0	0
Bphen	97	0	0
dtbbp	93	0	0
bipy	71	0	0
Diamine A	30	0	23
No Ligand	0	0	62
No Ligand, No Ni	99	0	0
Preformed Catalysts			
((*R*)-BINAP)$NiCl_2$	0	60	0
(Bphen)$NiBr_2$	83	0	0
(Bphen)$NiBr_2$ + cod (10 mol %)	86	0	0
(bipy)$NiCl_2$	33	0	20
(bipy)$NiCl_2$ + cod (10 mol %)	99	0	0

Table 4.5 Ligand Screen with 4-Bromotetrahydropyran **4.6**.



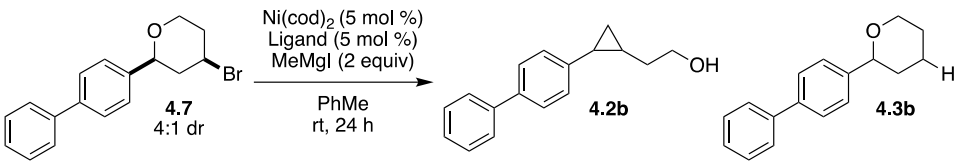
Ligand	4.6 (%)	4.2a (%)	4.3a (%)
rac-BINAP	0	45	0
dppm	0	0	27
DPEPhos	0	0	0
(*R*)-*i*Pr-Phox	88	0	0
(*R*)-Ph-Box	95	0	0
IndaBox	70	0	10
PyBox	0	0	50
(4*S*, 4'*S*)-*i*Pr-BiOx	0	0	50
Bphen	0	0	50
dtbbp	76	0	0
bipy	60	0	10
Diamine A	0	0	86
No Ligand	80	0	10
No Ligand, No Ni	95	0	0

Table 4.6 Ligand Screen with 4-Chlorotetrahydropyran **4.1b**.



Ligand	4.1b (%)	4.2b (%)	4.3b (%)
rac-BINAP	93	0	0
dppm	87	0	0
DPEphos	84	0	0
(*R*)-*i*Pr-Phox	95	0	0
(*R*)-Ph-Box	50	0	32
IndaBox	0	0	66
PyBox	0	0	62
(4*S*, 4'*S*)-*i*Pr-BiOx	0	0	63
Bphen	84	0	0
dtbbp	91	0	0
bipy	32	0	44
Diamine A	23	0	40
No Ligand	0	0	66
No Ligand, No Ni	85	0	0
Preformed Catalysts			
$(Bphen)NiCl_2$	77	0	0
$(bipy)NiCl_2$	0	0	55

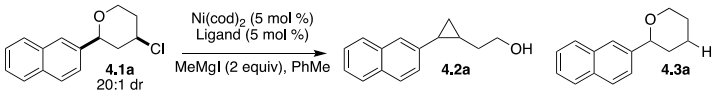
Table 4.7 Ligand Screen with 4-Bromotetrahydropyran **4.7**.



Ligand	4.7 (%)	4.2b (%)	4.3b (%)
rac-BINAP	0	0	55
dppm	24	0	36
DPEphos	0	0	30
(*R*)-*i*Pr-Phox	88	0	0
(*R*)-Ph-Box	>99	0	0
IndaBox	95	0	0
PyBox	67	0	10
(4*S*, 4'*S*)-*i*Pr-BiOx	0	0	70
Bphen	62	0	20
dtbbp	83	0	0
bipy	40	0	40
Diamine A	84	0	0
No Ligand	0	0	66
No Ligand, No Ni	>99	0	0
Preformed Catalysts			
((*R*)-BINAP)$NiCl_2$	0	0	51
(Bphen)$NiBr_2$	0	0	53
(bipy)$NiCl_2$	0	0	60

4.4.4 Tables for Expanded Ligand Screen

Table 4.8. Tabulated ^{1}H NMR Yields for Expanded Ligand Screen with THP **4.1a**.



Ligands	Ligand Type	4.1 (%)[a]	4.2 (%)[a]	4.3 (%)[a]	4.10 (%)[a]	4.11 (%)[a]	4.12 (%)[a]
$HPCy_2$	monodentate phosphine	69	18	0	0	0	0
$HPPh_2$	monodentate phosphine	83	6	0	0	0	0
PCy_3	monodentate phosphine	60	<5	0	0	0	0
PPh_3	monodentate phosphine	0	64	0	21	21	20
tri(o-tolyl)phosphine	monodentate phosphine	97	0	0	0	0	0
tri(2-furyl)phosphine	monodentate phosphine	82	<5	0	0	0	0
$MePPh_2$	monodentate phosphine	30	18	0	6	6	<5
$BnPPh_2$	monodentate phosphine	70	14	0	<5	<5	<5
BrettPhos	monodentate phosphine	90	0	0	0	0	0
DavePhos	monodentate phosphine	74	13	0	0	0	0
TrixiePhos	monodentate phosphine	92	0	0	0	0	0
(R)-MonoPhos	phosphoramidite	91	<5	0	0	0	0
MeDuPhos	bidentate phosphine	>99	0	0	0	0	0
Cydppe	bidentate phosphine	97	0	0	0	0	0
dppe	bidentate phosphine	92	<5	0	0	0	0
dppbz	bidentate phosphine	93	<5	0	0	0	0
dppb	bidentate phosphine	20	58	0	0	0	<5
dpppent	bidentate phosphine	0	46	0	10	10	10
dppo	bidentate phosphine	8	58	0	12	12	9
CyDPEPhos	bidentate phosphine	11	40	0	0	0	0
Xantphos	bidentate phosphine	62	0	0	0	0	0
PhanePhos	bidentate phosphine	37	47	0	0	0	0
dppf	ferrocene - phosphines	17	64	0	0	0	0
SL-J001-1[b]	ferrocene - phosphines	65	29	0	0	0	0
SL-T001-1[b]	ferrocene - phosphines	<5	28	0	10	10	<5
SL-M003-1[b]	ferrocene - phosphines	78	<5	0	0	0	0
TriPhos	tridentate phosphine	88	17	0	0	0	0
ICy·HBF_4	NHC	86	<5	0	0	0	0
SiMes·HCl	NHC	64	<5	0	0	0	0
NHC B	NHC	91	<5	0	0	0	0
NHC C	NHC	61	<5	0	0	0	0
NHC D	NHC	98	<5	0	0	0	0
N-methylethylenediamine	nitrogen	32	0	22	0	0	0
trans-N,N'-dimethylcyclohexanediamine	nitrogen	42	0	18	0	0	0
(1R, 2R)-N,N'-dimethyl-1,2-diphenylethane-1,2-diamine	nitrogen	39	0	23	0	0	0
ethylenediamine	nitrogen	9	0	30	0	0	0
trans-diaminecyclohexane	nitrogen	51	0	17	0	0	0
(1R,2R)-(+)-(1,2)-diphenylethylenediamine	nitrogen	30	0	23	0	0	0
(4S)-*i*Pr-pyrox	nitrogen	96	0	0	0	0	0
phen	nitrogen	72	0	0	0	0	0
dimethyl bipy	nitrogen	44	0	18	0	0	0
biimidazole	nitrogen	27	0	24	0	0	0
PyBCam	nitrogen	15	0	27	0	0	0
bpp	nitrogen	25	0	25	0	0	0
terpy	nitrogen	87	0	0	0	0	0
$(NNN)H_3$	nitrogen	63	0	10	0	0	0

[a] ^{1}H NMR yields are determined by comparison to PhTMS. [b] Ligands from Solvias ligand kit.

Figure 4.5 Legend for Table 4.8 Including Byproducts Assigned by ^{1}H NMR and GCMS.

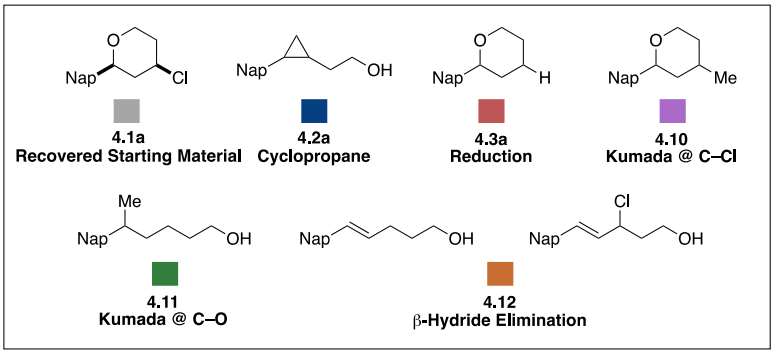


Figure 4.6 Bar Graph of Expanded Ligand Screen Including Byproducts.

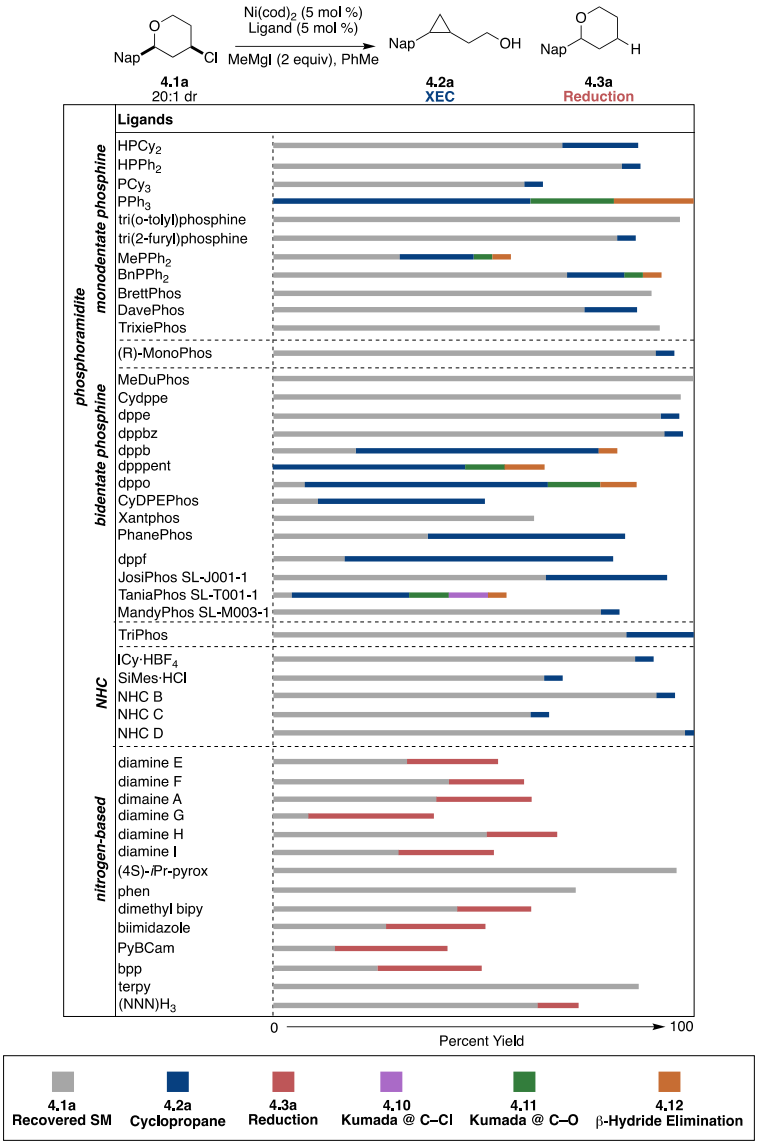
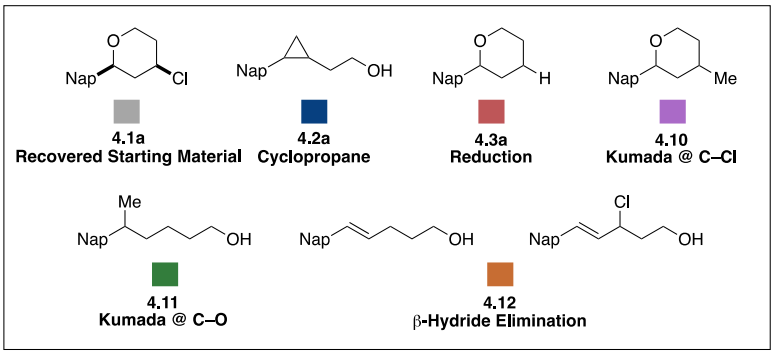
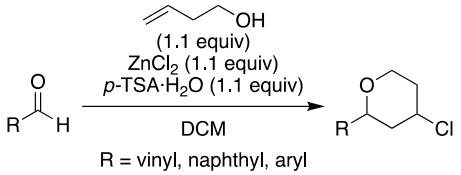


Figure 4.7 Legend for Table Byproduct Structures Assigned Based on ^{1}H NMR and GCMS.



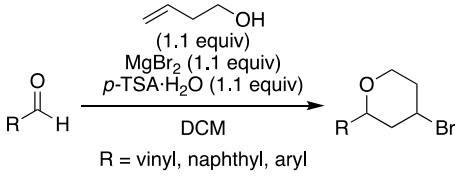
4.4.5 General Procedures for the Synthesis of THP Starting Materials

4.4.5.1 Method C: Prins Cyclization with $ZnCl_2$



The following method was adapted from a procedure reported by Jarvo, et al.[39] To a flame-dried round bottom flask equipped with a stir bar was added $ZnCl_2$ (1.1 equiv), *p*-toluenesulfonic acid monohydrate (1.1 equiv), and DCM (0.5 M in $ZnCl_2$). The solution was allowed to stir for 5 min at rt. In a separate flame dried round bottom flask equipped with a stir bar was added aldehyde (1.0 equiv), 3-buten-1-ol (1.1 equiv) and DCM (0.5 M in substrate) and allowed to stir for 5 min. The aldehyde solution was then transferred to the premixed solution of $ZnCl_2$ via syringe. The reaction mixture was allowed to stir 24–72 h at rt and quenched with an aqueous solution of $NaHCO_3$. The aqueous layer was extracted with DCM (x3), organic layers were combined, dried over Na_2SO_4, concentrated in vacuo, and purified by column chromatography.

4.4.5.2 Method D: Prins Cyclization with $MgBr_2$



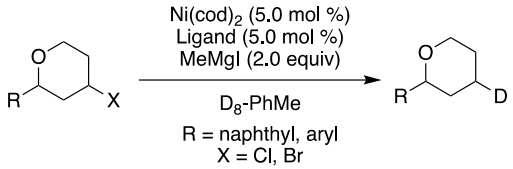
The following method was adapted from a procedure reported by Jarvo, et al.[39] To a flame-dried round bottom flask equipped with a stir bar was added $MgBr_2$ (1.1 equiv), *p*-toluenesulfonic acid monohydrate (1.1 equiv), and DCM (0.5 M in $MgBr_2$). The solution was allowed to stir for 5 min at rt. In a separate flame dried round bottom flask equipped with a stir bar was added aldehyde

[39] Tollefson, E. J.; Erickson, L. W.; Jarvo, E. R. *J. Am. Chem. Soc.* **2015**, *137*, 9760–9763.

(1.0 equiv), 3-buten-1-ol (1.1 equiv) and DCM (0.5 M in substrate) and allowed to stir for 5 min at rt. The aldehyde solution was then transferred to the premixed solution of $MgBr_2$ via syringe. The reaction mixture was allowed to stir 24-72 h at rt and quenched with an aqueous solution $NaHCO_3$. The aqueous layer was extracted with DCM (x3), the organic layers were combined, dried over Na_2SO_4, concentrated in vacuo, and purified by column chromatography.

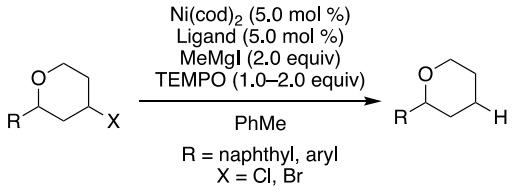
4.4.6 Procedures for Mechanistic Studies

4.4.6.1 Method E: Deuterium Incorporation into Reduction Product



In a glovebox, to a 7 mL vial equipped with a stir bar was added $Ni(cod)_2$ (5.0 mol %), the desired THP (1.0 equiv), and D8-PhMe (0.5 mL, 0.2 M in substrate). Next, methylmagnesium iodide (2.0 equiv, 2.4 M soln in Et_2O) was added dropwise to the vial and the reaction mixture was allowed to stir at rt. After 24 h, the reaction was quenched with MeOH. The unpurified reaction mixture was plugged in a monstr pipet with silica gel and washed with Et_2O (neat, x3). Next, the Et_2O washes were concentrated in vacuo and a ^1H NMR yield was obtained by comparison to PhTMS as the internal standard.

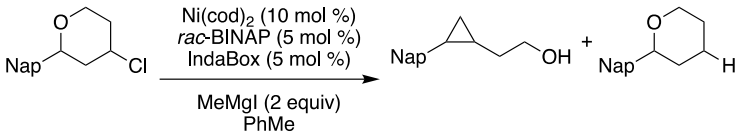
4.4.6.2 Method F: Radical Trapping Experiments with TEMPO



In a glovebox, to a 7 mL vial equipped with a stir bar was added $Ni(cod)_2$ (5.0 mol %), TEMPO (1.1 equiv), tetrahydropyran (1.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). Next, methylmagnesium iodide (2.0 equiv, 2.4 M soln in Et_2O) was added dropwise to the vial and the

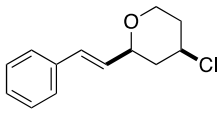
reaction mixture was allowed to stir at rt. After 24 h, the reaction was quenched with MeOH. The unpurified reaction mixture was plugged in a monstr pipet with silica gel and washed with Et_2O (neat, x3). Next, the Et_2O washes were concentrated in vacuo and a ^1H NMR yield was obtained by comparison to PhTMS as the internal standard.

4.4.6.3 Method G: Competition Experiment



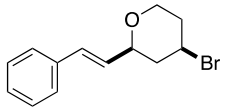
In a glovebox, to a 7 mL vial equipped with a stir bas was added $Ni(cod)_2$ (10. mol %), *rac*-BINAP (5.0 mol %), IndaBox (5.0 mol %), tetrahydropyran **1a** (1.0 equiv), and PhMe (0.5 mL, 0.2 M in substrate). Next, methylmagnesium iodide (2.0 equiv, 2.9 M soln in Et_2O) was added dropwise to the vial and the reaction mixture was allowed to stir at rt. After 24 h, the reaction was quenched with MeOH. The unpurified residue was plugged in a monstr pipet with silica gel and washed with Et_2O (neat, x3). Next, the Et_2O washes were concentrated in vacuo and a ^1H NMR yield was obtained by comparison to PhTMS as the internal standard.

4.4.7 Characterization of THP Starting Materials



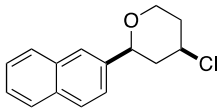
(*trans*)-4-Chloro-2-((*E*)-styryl)tetrahydro-2*H*-pyran (4.4) was prepared according to Method C. The following amounts of reagents were used: *trans*-cinnamaldehyde (0.94 mL, 7.5 mmol, 1.0 equiv), $ZnCl_2$ (1.12 g, 8.25 mmol, 1.10 equiv), *p*-toluenesulfonic acid monohydrate (1.42 g, 8.25 mmol, 1.10 equiv), 3-buten-1-ol (0.71 mL, 8.3 mmol, 1.1 equiv), and DCM (40 mL). The unpurified residue was purified by column chromatography (0–5–10% EtOAc/hexanes) to afford a clear oil (163 mg, 0.700 mmol, 9% yield). The desired compound was characterized as a 20:1

(cis:trans) mixture of diastereomers. The dr was determined based on the integration of the resonances attributed to the benzylic hydrogens in the ^{1}H NMR spectrum: **TLC R_f =** 0.6 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38–7.23 (m, 5H), 6.61 (d, *J* = 16.1 Hz, 1H), 6.17 (dd, *J* = 16.0, 5.9 Hz, 1H), 4.13–4.04 (m, 2H), 3.98 (dd, *J* = 11.2, 6.2 Hz, 1H), 3.52 (td, *J* = 12.2, 2.0 Hz, 1H), 2.32–2.27 (m, 1H), 2.14–2.09 (m, 1H), 1.92 (dq, *J* = 12.2, 4.8 Hz, 1H), 1.78 (q, *J* = 11.7 Hz, 1H). Analytical data is consistent with literature values.[40]

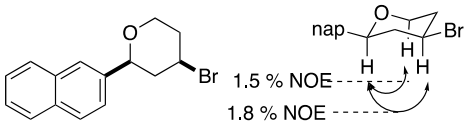


(*trans*)-4-Bromo-2-((*E*)-styryl)tetrahydro-2*H*-pyran (4.5) was prepared according to Method D. The following amounts of reagents were used: *trans*-cinnamaldehyde (1.25 mL, 10.0 mmol, 1.00 equiv), $MgBr_2$ (2.0 g, 11 mmol, 1.1 equiv), *p*-toluenesulfonic acid monohydrate (1.9 g, 11 mmol, 1.1 equiv), 3-buten-1-ol (0.95 mL, 11 mmol, 1.1 equiv), and DCM (50 mL). The unpurified oil was purified by column chromatography (0–5–10% EtOAc/hexanes) to afford a clear oil (99 mg, 0.40 mmol, 4% yield). The desired compound was characterized as a 20:1 (cis:trans) mixture of diastereomers. The dr was determined based on the integration of the resonances attributed to the benzylic hydrogens in the ^{1}H NMR spectrum: **TLC R_f =** 0.6 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 16.1 Hz, 1H), 6.15 (dd, *J* = 15.9, 5.9 Hz, 1H), 4.21 (tt, *J* = 11.9, 4.5 Hz, 1H), 4.08 (ddd, *J* = 11.9, 4.9, 1.6 Hz, 1H), 3.98 (dd, *J* = 11.3, 5.8 Hz, 1H), 3.52 (td, *J* = 11.9, 2.1 Hz, 1H), 2.42–2.37 (m, 1H), 2.23–2.18 (m, 1H), 2.10 (qd, *J* = 12.1, 4.9 Hz, 1H), 1.96 (q, *J* = 12.0 Hz, 1H). Analytical data is consistent with literature values.[40]

[40] Erickson, L. W.; Lucas, E. L.; Tollefson, E. J.; Jarvo, E. R. *J. Am. Chem. Soc.* **2016**, *138*, 14006–14011.

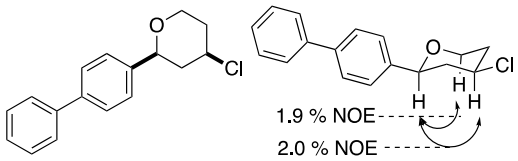


(*trans*)-4-Chloro-2-(naphthalen-2-yl)tetrahydro-2*H*-pyran (4.1a) was prepared according to Method C. The following amounts of reagents were used: naphthaldehyde (1.18 g, 7.50 mmol, 1.00 equiv), $ZnCl_2$ (1.12 g, 8.25 mmol, 1.10 equiv), *p*-toluenesulfonic acid monohydrate (1.42 g, 8.25 mmol, 1.10 equiv), 3-buten-1-ol (0.71 mL, 8.3 mmol, 1.1 equiv), and DCM (40 mL). The unpurified residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford a white solid (1.1 g, 4.4 mmol, 59% yield). The desired compound was characterized as a 20:1 (cis:trans) mixture of diastereomers. The dr was determined based on the integration of the resonances attributed to the benzylic hydrogens in the ^{1}H NMR spectrum: **TLC R_f =** 0.4 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84–7.80 (m, 4H), 7.49–7.44 (m, 3H), 4.50 (dd, *J* = 11.6, 1.3 Hz, 1H), 4.27–4.19 (m, 2H), 3.66 (td, *J* = 12.1, 2.1 Hz, 1H), 2.49–2.45 (m, 1H), 2.22–2.19 (m, 1H), 2.08–1.95 (m, 2H). Analytical data is consistent with literature values.[39]



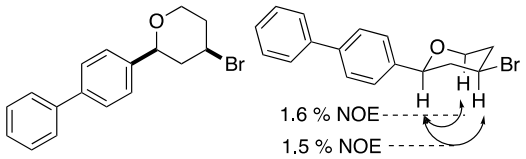
(*trans*)-4-Bromo-2-(naphthalen-2-yl)tetrahydro-2*H*-pyran (4.6) was prepared according to Method D. The following amounts of reagents were used: naphthaldehyde (1.18 g, 7.50 mmol, 1.00 equiv), $MgBr_2$ (1.56 g, 8.25 mmol, 1.10 equiv), *p*-toluenesulfonic acid monohydrate (1.42 g, 8.25 mmol, 1.10 equiv), 3-buten-1-ol (0.71 mL, 8.3 mmol, 1.1 equiv), and DCM (40 mL). The unpurified residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford a white solid (1.1 g, 3.9 mmol, 52% yield). The desired compound was characterized as a 4:1 (cis:trans) mixture of diastereomers. The dr was determined based on the integration of the resonances attributed to the benzylic hydrogens in the ^{1}H NMR spectrum. **TLC R_f =** 0.4 (10%

EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82–7.77 (m, 8H, both diastereomers), 7.47–7.42 (m, 6H, both diastereomers), 5.08–5.04 (m, 1H, minor diastereomer), 4.82–4.77 (m, 1H, minor diastereomer), 4.46 (ad, *J* = 11.5 Hz, 1H, major diastereomer), 4.29 (tt, *J* = 11.7, 4.9 Hz, 1H, major diastereomer), 4.22–4.15 (m, 2H, both diastereomers), 4.09–4.04 (m, 1H, minor diastereomer), 3.62 (td, *J* = 12.2, 1.9 Hz, 1H, major diastereomer), 2.55–2.52 (m, 2H, both diastereomers), 2.29–2.11 (m, 5H, both diasteroemers), 2.00–1.96 (m, 1H, minor diastereomer); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 139.4 (minor diastereomer), 138.7 (major diastereomer), 133.41 (minor diastereomer), 133.36 (major diastereomer), 133.1 (major diastereomer), 133.0 (minor diastereomer), 128.4 (major diastereomer), 128.3 (minor diastereomer), 128.10 (major diastereomer), 128.07 (minor diastereomer), 127.76 (major diastereomer), 127.73 (minor diastereomer), 126.3 (major diastereomer), 126.2 (minor diastereomer), 126.05 (major diastereomer), 125.93 (minor diastereomer), 124.7 (minor diastereomer), 124.6 (major diastereomer), 124.2 (minor diastereomer), 124.0 (major diastereomer), 80.3 (major diastereomer), 74.5 (minor diastereomer), 68.4 (major diastereomer), 63.6 (minor diastereomer), 50.3 (minor diastereomer), 46.5 (major diastereomer), 45.6 (major diastereomer), 41.9 (minor diastereomer), 37.8 (major diastereomer), 34.1 (minor diastereomer); **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calcd for $C_{15}H_{15}BrONa$, 313.0204; found, 313.0201.



(*trans*)-2-([1,1'-Biphenyl]-4-yl)-4-chlorotetrahydro-2*H*-pyran (4.1b) was prepared according to Method C. The following mounts of reagents were used: biphenyl-4-carboxaldehyde (1.3 g, 7.0 mmol, 1.0 equiv), $ZnCl_2$ (1.05 g, 7.70 mmol, 1.10 equiv), *p*-toluenesulfonic acid monohydrate (1.3

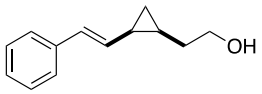
g, 7.7 mmol, 1.1 equiv), 3-buten-1-ol (0.66 mL, 7.7 mmol, 1.1 equiv), and DCM (35 mL). The unpurified residue is purified by column chromatography (0–10% EtOAc/hexanes) to afford a white solid (1.4 g, 5.2 mmol, 74% yield). The desired compound was characterized as a 20:1 (cis:trans) mixture of diastereomers. The dr was determined based on the integration of the resonances attributed to the benzylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis: **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 4H), 7.44–7.39 (m, 4H), 7.33 (at, *J* = 7.6 Hz, 1H), 4.37 (ad, *J* = 11.2 Hz, 1H), 4.21–4.13 (m, 2H), 3.61 (t, *J* = 12.5, 1H), 2.44–2.38 (m, 1H), 2.19–2.14 (m, 1H), 2.05–1.90 (m, 2H); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 140.95, 140.93, 140.4, 128.9 (2C), 127.5, 127.4 (2C), 127.2 (2C), 126.4 (2C), 79.3, 67.5, 55.8, 44.7, 37.0; **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calcd for $C_{17}H_{17}BrONa$, 339.0360; found, 339.0370.



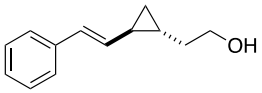
(*trans*)-2-([1,1'-Biphenyl]-4-yl)-4-bromotetrahydro-2*H*-pyran (4.7) was prepared according to Method D. The following amounts of reagents were used: biphenyl-4-carboxaldehyde (1.65 g, 9.00 mmol, 1.00 equiv), $MgBr_2$ (1.82 g, 9.90 mmol, 1.10 equiv), *p*-toluenesulfonic acid monohydrate (1.7 g, 9.9 mmol, 1.1 equiv), 3-buten-1-ol (0.85 mL, 9.9 mmol, 1.1 equiv), and DCM (50 mL). The unpurified residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford a white solid (2.15 g, 6.73 mmol, 75% yield). The desired compound was characterized as a 4:1 mixture (cis:trans) mixture of diastereomers. The dr was determined based on the integration of the resonances attributed to the benzylic hydrogens in the ^{1}H NMR spectrum. The relative configuration was assigned based on NOE analysis: **TLC R_f =** 0.4 (10%

EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 8H, both diastereomers), 7.44–7.39 (m, 8H, both diastereomers), 7.35–7.32 (m, 2H, both diastereomers), 4.97–4.93 (m, 1H, minor diastereomer), 4.84–4.79 (m, 1H, minor diastereomer), 4.38 (ad, *J* = 11.37 Hz, 1H, major diastereomer), 4.34–4.27 (m, 1H, major diastereomer), 4.17 (dd, *J* = 12.4, 5.4 Hz, 2H, both diastereomers), 4.04 (dd, *J* = 11.5, 4.6 Hz, 1H, minor diastereomer), 3.62 (at, *J* = 12.1 Hz, 1H, major diastereomer), 2.55–2.48 (m, 1H, major diastereomer), 2.30–2.09 (m, 6H, both diastereomers), 2.02–1.96 (m, 1H, minor diastereomer); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 141.0 (major diastereomer), 140.9 (minor diastereomer), 140.3 (2C, both diastereomers), 128.9 (4C, both diastereomers), 127.47 (2C, both diastereomer), 127.41 (4C, both diastereomers), 127.35 (major diastereomer), 127.26 (4C, both diastereomers), 126.5 (minor diastereomer), 126.37 (4C, both diastereomer), 80.1 (major diastereomer), 74.2 (minor diastereomer), 68.4 (major diastereomer), 63.6 (minor diastereomer), 50.3 (minor diastereomer), 46.5 (major diastereomer), 45.6 (major diastereomer), 41.8 (minor diastereomer), 37.8 (major diastereomer), 34.1 (minor diastereomer); **HRMS** (TOF MS ES+) m/z: $[M+Na]^+$ calcd for $C_{17}H_{17}ClONa$, 295.0865; found, 295.0873.

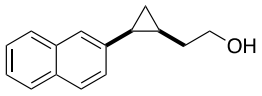
4.4.8 Characterization of Cyclopropane Products



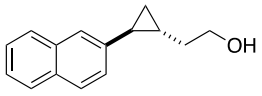
2-((*cis*)-2-((*E*)-styryl)cyclopropyl)ethan-1-ol, cis-(4.8) was prepared according to Method A. **TLC R_f =** 0.8 (20% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33–7.25 (m, 4H), 7.18 (t, *J* = 6.7 Hz, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 5.96 (dd, *J* = 15.8 Hz, 8.9, 1H), 3.72 (t, *J* = 6.7 Hz, 2H), 1.68 (aq, *J* = 6.6 Hz, 3H), 1.49 (br, 1H), 1.12 (q, *J* = 7.6 Hz, 1H), 1.06–1.00 (m, 1H), 0.41 (q, *J* = 5.0 Hz, 1H). Analytical data is consistent with literature values.[39]



2-((*trans*)-2-((*E*)-Styryl)cyclopropyl)ethan-1-ol, trans-(4.8) was prepared according to Method A. **TLC R_f =** 0.2 (20% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36–7.31 (m, 4H), 7.22 (tt, *J* = 6.6, 2.2 Hz, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 5.83 (dd, *J* = 15.8, 8.9 Hz, 1H), 3.80 (t, *J* = 6.6 Hz, 2H), 1.71–1.58 (m, 3H), 1.43 (sept, *J* = 4.7 Hz, 1H), 1.03–0.96 (m, 1H), 0.79 (dt, *J* = 8.4, 4.9 Hz, 1H), 0.76–0.71 (m, 1H). Analytical data is consistent with literature values.[39]

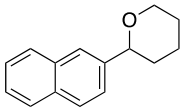


2-((*cis*)-2-(naphthalen-2-yl)cyclopropyl)ethan-1-ol, cis-(4.2a) was prepared according to Method A. **TLC R_f =** 0.3 (20% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80–7.73 (m, 3H), 7.56 (s, 1H), 7.46–7.36 (m, 3H), 3.57–3.52 (m, 2H), 2.30 (aq, *J* = 8.3 Hz, 1H), 1.43–1.38 (m, 1H), 1.27–1.19 (m, 3H), 1.12–1.07 (m, 1H), 0.90–0.86 (m, 1H). Analytical data is consistent with literature values.[39]

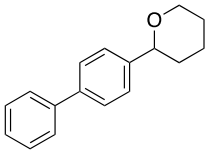


2-((*trans*)-2-(naphthalen-2-yl)cyclopropyl)ethan-1-ol, trans-(4.2a) was prepared according to Method A. **TLC R_f =** 0.3 (20% EtOAc/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.50 (s, 1H), 7.45–7.35 (m, 2H), 7.17 (dd, *J* = 8.6, 1.7 Hz, 1H), 3.78 (t, *J* = 6.5 Hz, 2H), 1.87–1.81 (m, 1H), 1.70 (sept, *J* = 6.6 Hz, 2H), 1.50 (br s, 1H), 1.24–1.16 (m, 1H), 1.05 (dt, *J* = 8.6, 4.9 Hz, 1H), 0.89 (dt, *J* = 8.6, 4.9 Hz, 1H). Analytical data is consistent with literature values.[39]

4.4.9 Characterization of Reduction Products



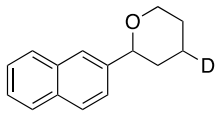
2-(Naphthalen-2-yl)tetrahydro-2*H*-pyran (4.3a) was prepared according to Method B. The following amounts of reagents were used: **1** (25 mg, 0.10 mmol, 1.0 equiv), $Ni(cod)_2$ (1.4 mg, 5.0 μmol, 5.0 mol %), MeMgI (8 mL, 0.2 mmol, 2 equiv, 2.4 M soln in Et_2O), and toluene (0.5 mL, 0.2 M in substrate). The residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford (4 mg, 0.02 mmol, 9% yield). **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89–7.87 (m, 4H), 7.55–7.48 (m, 3H), 4.57–4.55 (m, 1H), 4.28–4.25 (m, 1H), 3.75 (td, *J* = 11.4, 2.3 Hz, 1H), 2.06–1.97 (m, 2H), 1.83–1.67 (m, 4H); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 140.9, 133.4, 132.9, 128.04, 127.98, 127.7, 125.9, 125.6, 124.34, 124.30, 80.2, 69.1, 34.2, 26.0, 24.1; **HRMS** (TOF MS Cl+) m/z: $[M+NH_4]^+$ calcd for $C_{15}H_{16}ONH_4$, 230.1545; found, 230.1550.



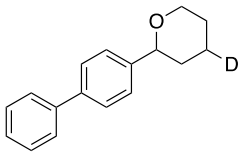
2-([1,1'-Biphenyl]-4-yl)tetrahydro-2*H*-pyran (4.3b) was prepared according to Method B. The following amounts of reagents were used: **7** (27 mg, 0.1 mmol, 1.0 equiv), $Ni(cod)_2$ (1.4 mg, 5.0 μmmol, 5.0 mol %), MeMgI (8 mL, 0.2 mmol, 2 equiv, 2.4 M soln in Et_2O), and toluene (0.5 mL, 0.2 M in substrate). The residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford (14 mg, 0.030 mmol, 30 % yield). **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59–7.54 (m, 4H), 7.43–7.39 (m, 4H), 7.34–7.29 (m, 1H), 4.36 (dd, *J* =10.7, 2.4 Hz, 1H), 4.17–4.13 (m, 1H), 3.63 (td, *J* = 11.4, 2.5 Hz, 1H), 1.97–1.84 (m, 2H), 1.73–1.57 (m, 4H); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 142.5, 141.2, 140.4, 128.9 (2C), 127.3 (2C), 127.24, 127.20

(2C), 126.23 (2C), 80.0, 69.2, 34.1, 26.1, 24.2; **HRMS** (TOF MS Cl+) m/z: $[M]^+$ calcd for $C_{17}H_{18}O$, 238.1358; found, 238.1354.

4.4.10 Characterization of Deuterated Reduction Product



2-(naphthalen-2-yl)tetrahydro-2*H*-pyran-4-*d*, D-labelled-(4.3a) was prepared according to Method E. The following amounts of reagents were used: **1a** (27 mg, 0.10 mmol, 1.0 equiv), $Ni(cod)_2$ (1.4 mg, 5.0 μmol, 5.0 mol %), MeMgI (8 mL, 0.2 mmol, 2 equiv, 2.4 M soln in Et_2O), and toluene (0.5 mL, 0.2 M in substrate). Before purification the compound a ^{1}H NMR yield of 16% was obtained based on comparison to PhTMS as an internal standard. Percent deuterium incorporation was measured by HRMS. **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.84–7.79 (m, 4H), 7.48–4.42 (m, 3H), 4.51–4.48 (m, 1H), 4.21–4.18 (m, 1H), 3.70–3.66 (td, *J* = 11.7, 2.5 Hz, 1H), 1.99–1.90 (m, 1.7H), 1.76–1.60 (m, 4H); **^{2}H NMR** (500 MHz, $CDCl_3$) δ 1.75; **HRMS** (TOF MS Cl+) m/z: $[M]^+$ calcd for $C_{15}H_{15}DO$, 213.1235; found, 213.1240, 21% deuterium incorporation.

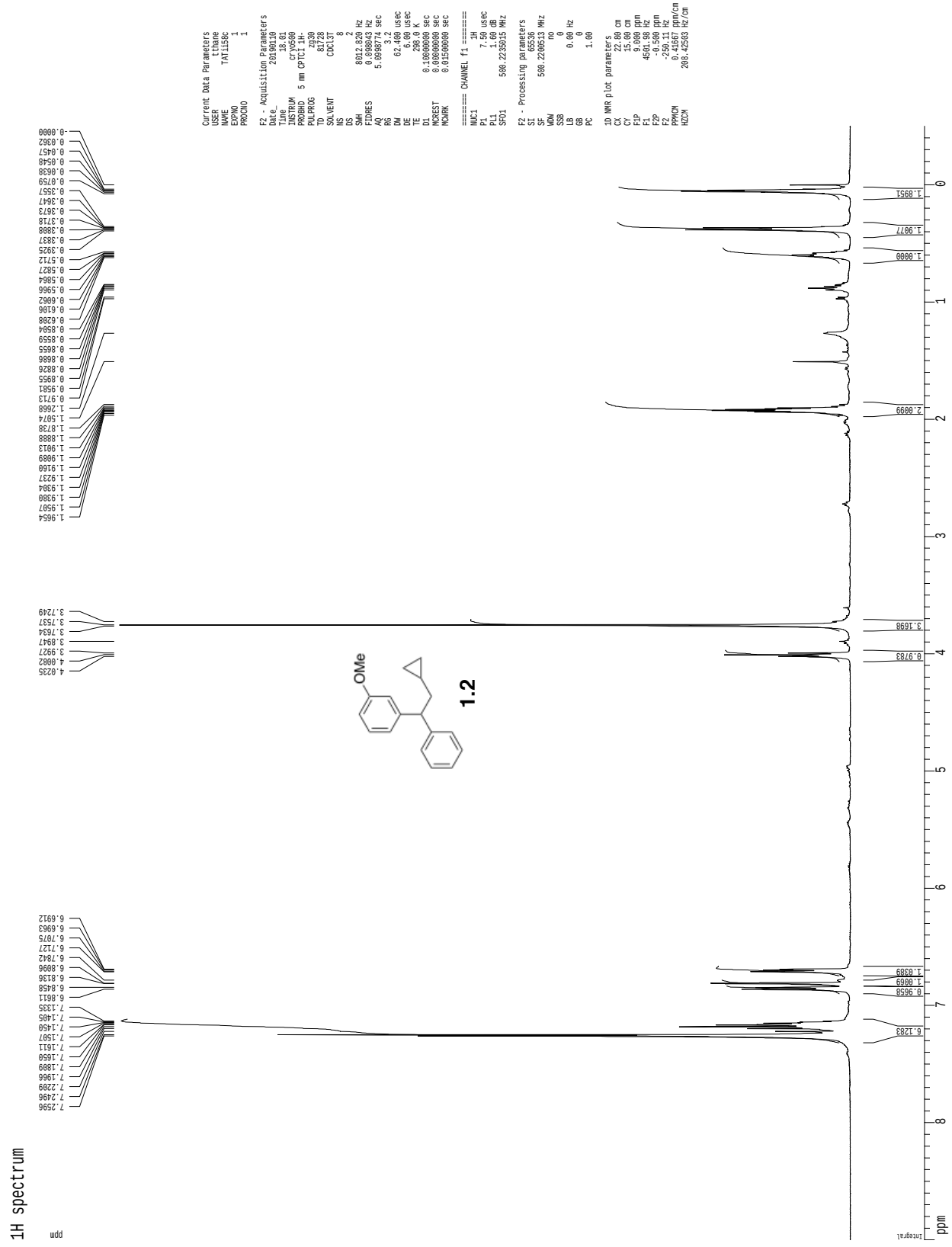


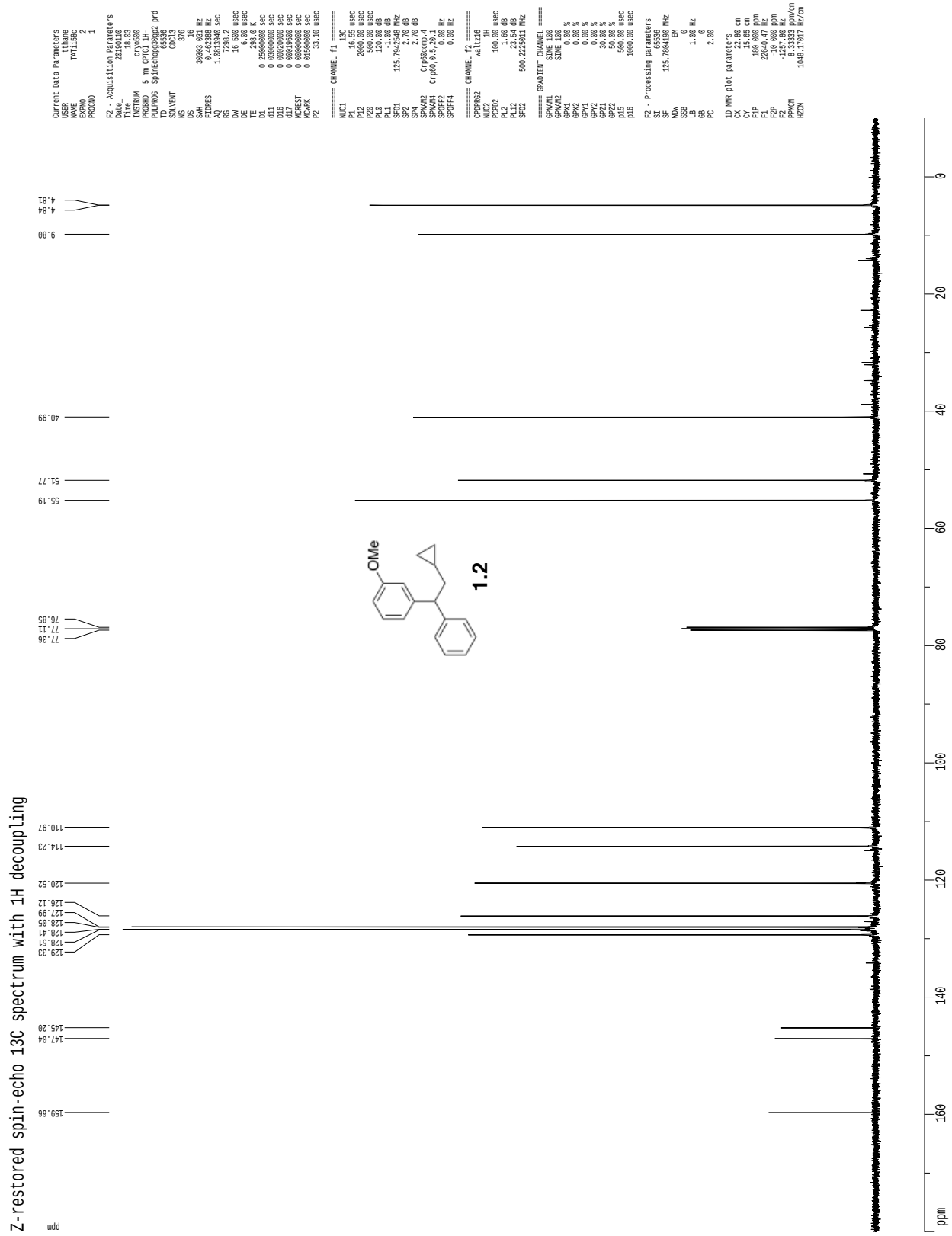
2-([1,1'-Biphenyl]-4-yl)tetrahydro-2*H*-pyran-4-*d*, D-labelled-(4.3b) was prepared according to Method E. The following amounts of reagents were used: **1b** (27 mg, 0.10 mmol, 1.0 equiv), $Ni(cod)_2$ (1.4 mg, 5.0 μmol, 5.0 mol %), MeMgI (8 mL, 0.2 mmol, 2 equiv, 2.4 M soln in Et_2O), and toluene (0.5 mL, 0.2 M in substrate). The residue was purified by column chromatography (0–10% EtOAc/hexanes) to afford (20. mg, 0.084 mmol, 42% yield). Percent deuterium incorporation

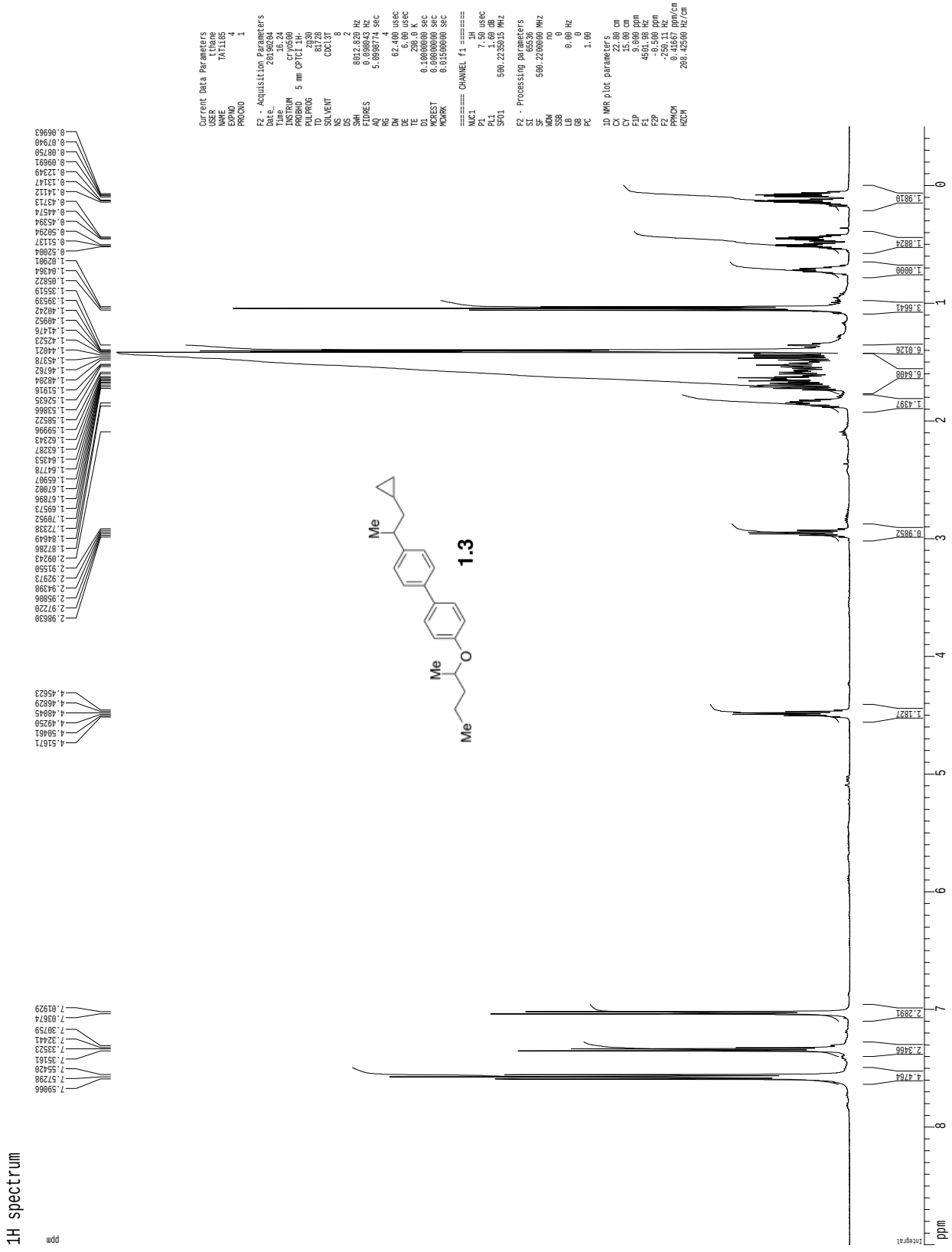
was measured by HRMS. **TLC R_f =** 0.5 (10% EtOAc/hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59–7.54 (m, 4H), 7.43–7.39 (m, 4H), 7.34–7.29 (m, 1H), 4.36 (dd, *J* =10.7, 2.4 Hz, 1H), 4.17–4.13 (m, 1H), 3.63 (td, *J* = 11.4, 2.5 Hz, 1H), 1.97–1.84 (m, 2.5H), 1.73–1.57 (m, 3H); **^{2}H NMR** (500 MHz, $CDCl_3$) δ 2.05, 1.78; **HRMS** (TOF MS Cl+) m/z: $[M]^+$ calcd for $C_{17}H_{17}DO$, 239.1392; found, 239.1468, 35% deuterium incorporation.

APPENDIX: ^{1}H, ^{2}H, ^{13}C, ^{19}F, COSY, NOE NMR Spectra and HRMS Data

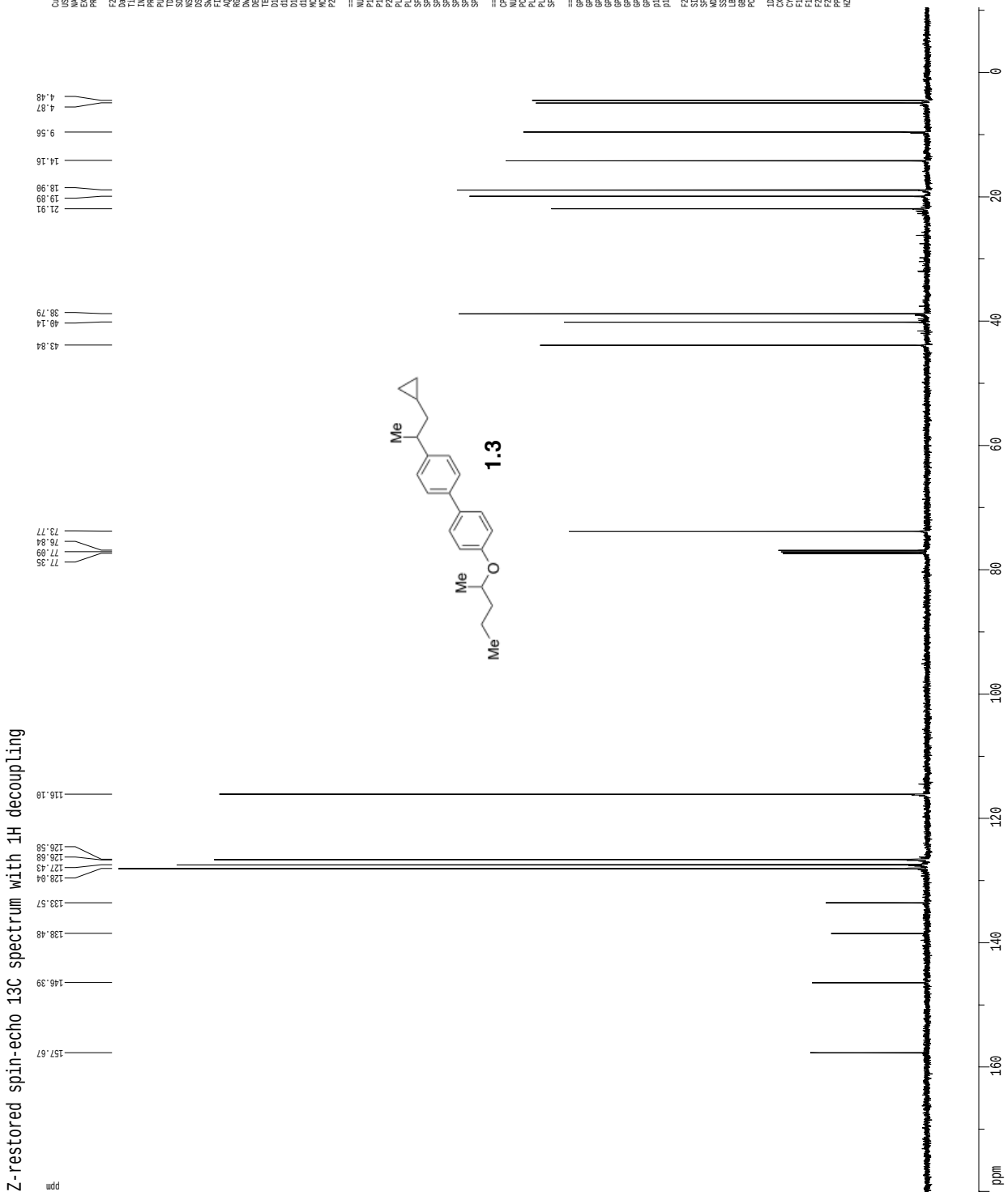
A.1 NMR Data Corresponding to Chapter 1


1H spectrum
Current Data Parameters
USER ttiane
NAME TAT1158c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190110
Time 18.01
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.091843 Hz
AQ 5.0998774 sec
RG 3.2
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200513 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42503 Hz/cm
OMe
1.2
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
OMe
1.2
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
159.66
147.04
145.20
129.33
128.51
128.41
128.05
127.99
126.12
120.52
114.23
110.97
77.36
77.11
76.85
55.19
51.77
40.99
9.80
4.84
4.81
0
20
40
60
80
100
120
140
160
ppm



1H spectrum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PROCNO 1
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Time 13.45
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PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 472
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08139840 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
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NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.79422540 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225911 MHz
===== GRADIENT CHANNEL =====
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GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.000 usec
F2 - Processing parameters
SI 65536
SF 125.78041300 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
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CY 15.00 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.460 ppm
F2 -1315.66 Hz
PPMCM 8.35351 ppm/cm
HZCM 1050.70716 Hz/cm
4.48
4.87
9.56
14.16
18.90
19.89
21.91
38.79
40.14
43.84
73.77
76.84
77.09
77.35
116.10
126.58
126.68
127.43
128.04
133.57
138.48
146.39
157.67
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Me
Me
O
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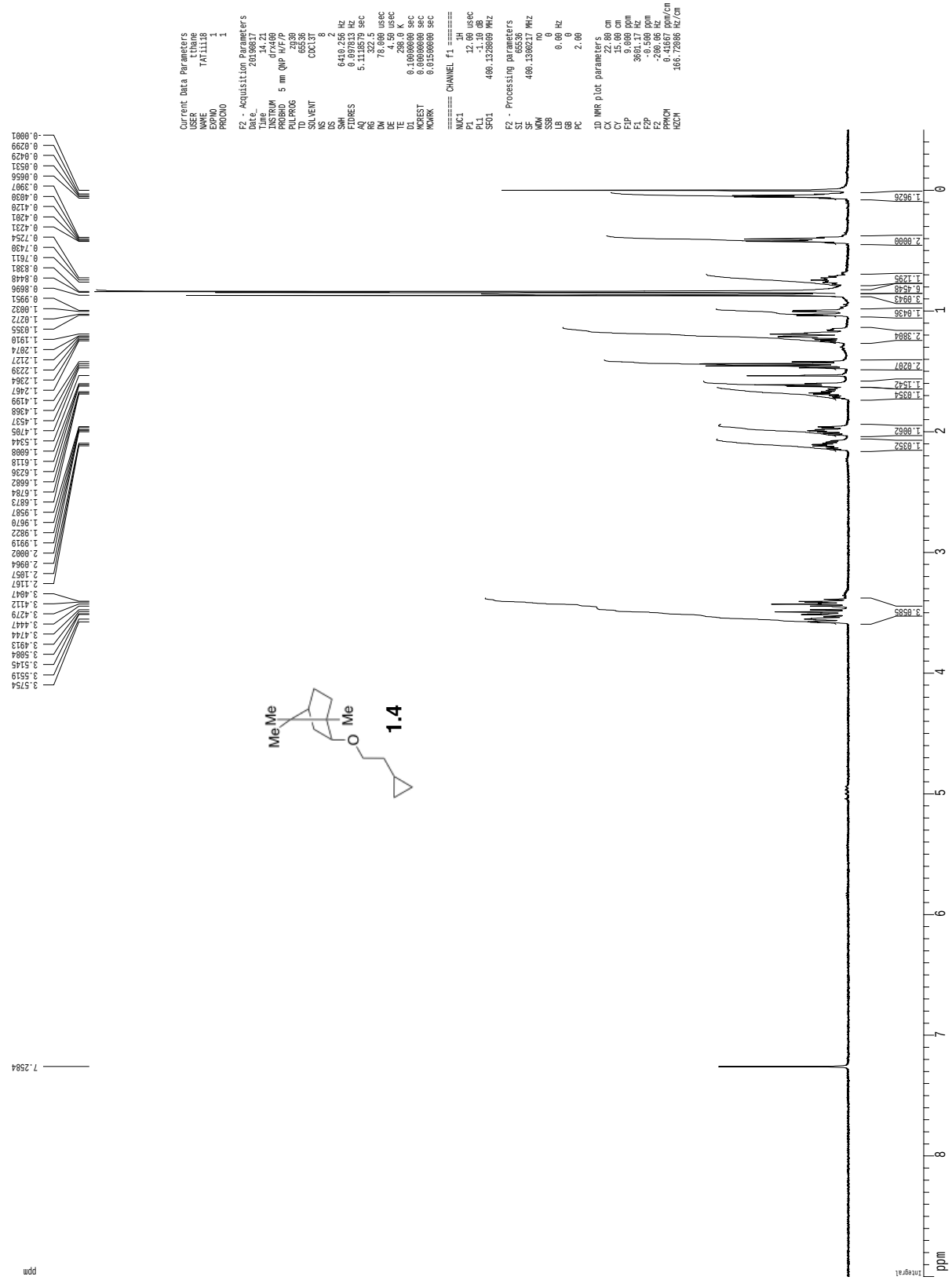
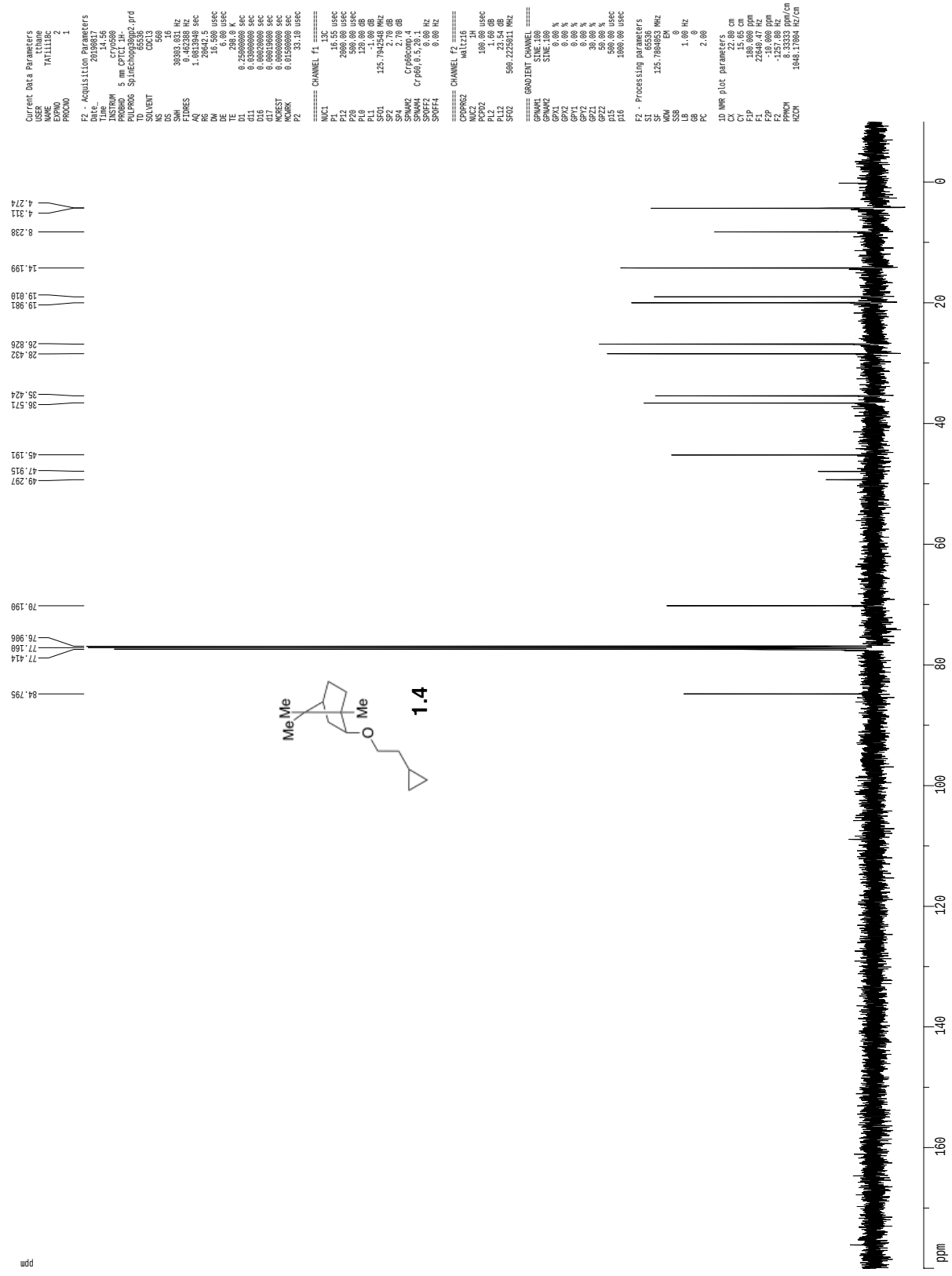
ppm
0
20
40
60
80
100
120
140
160

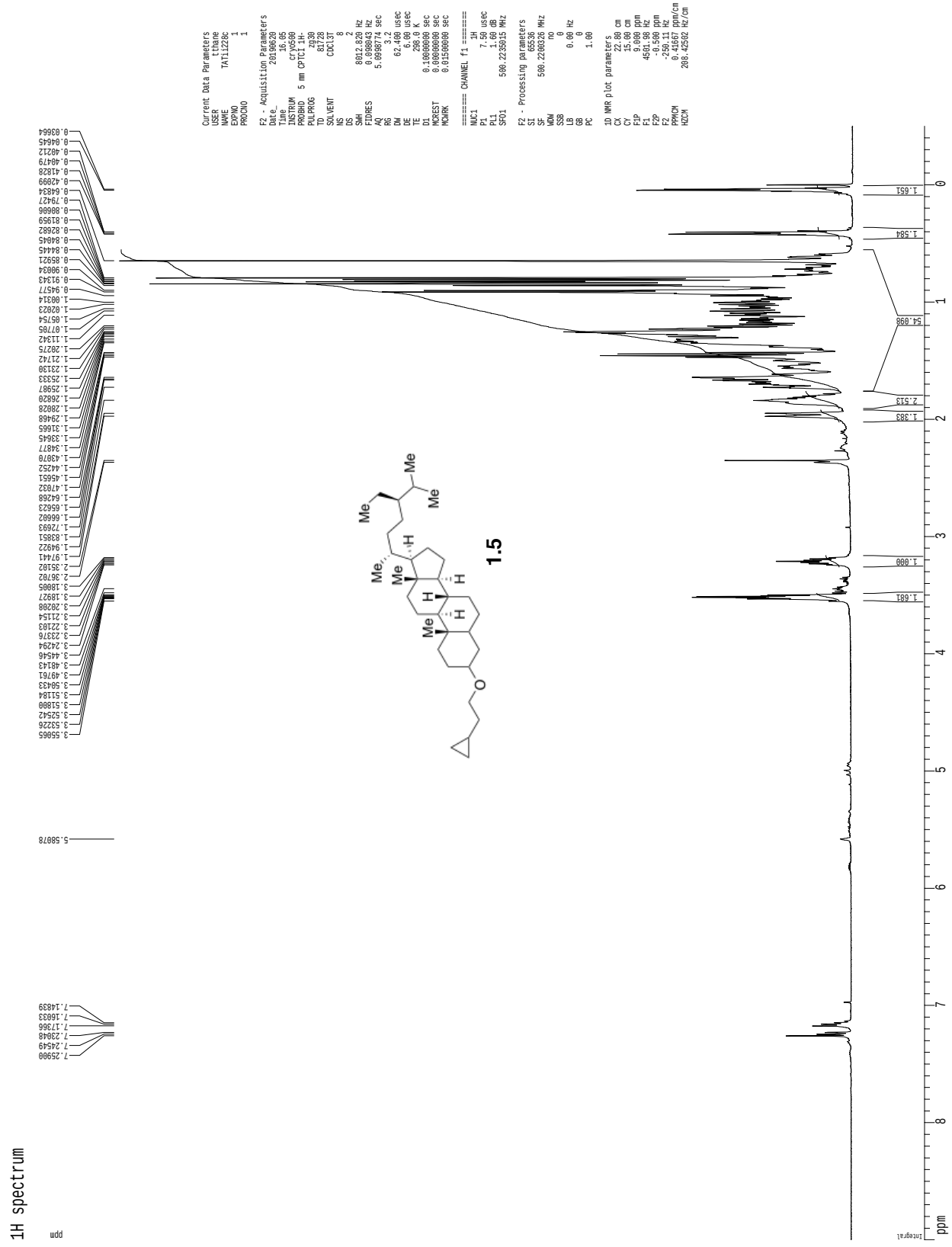
1H spectrum

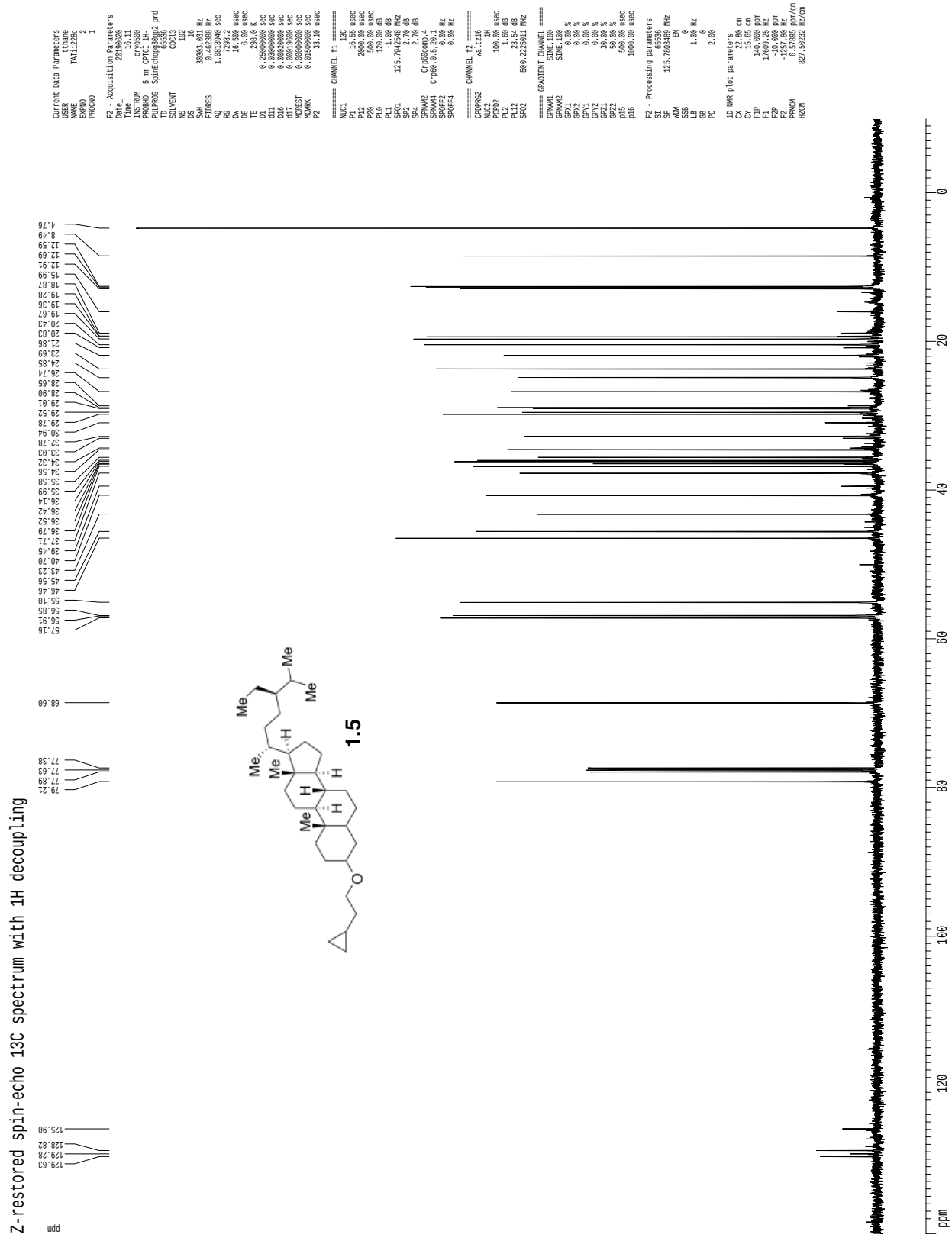


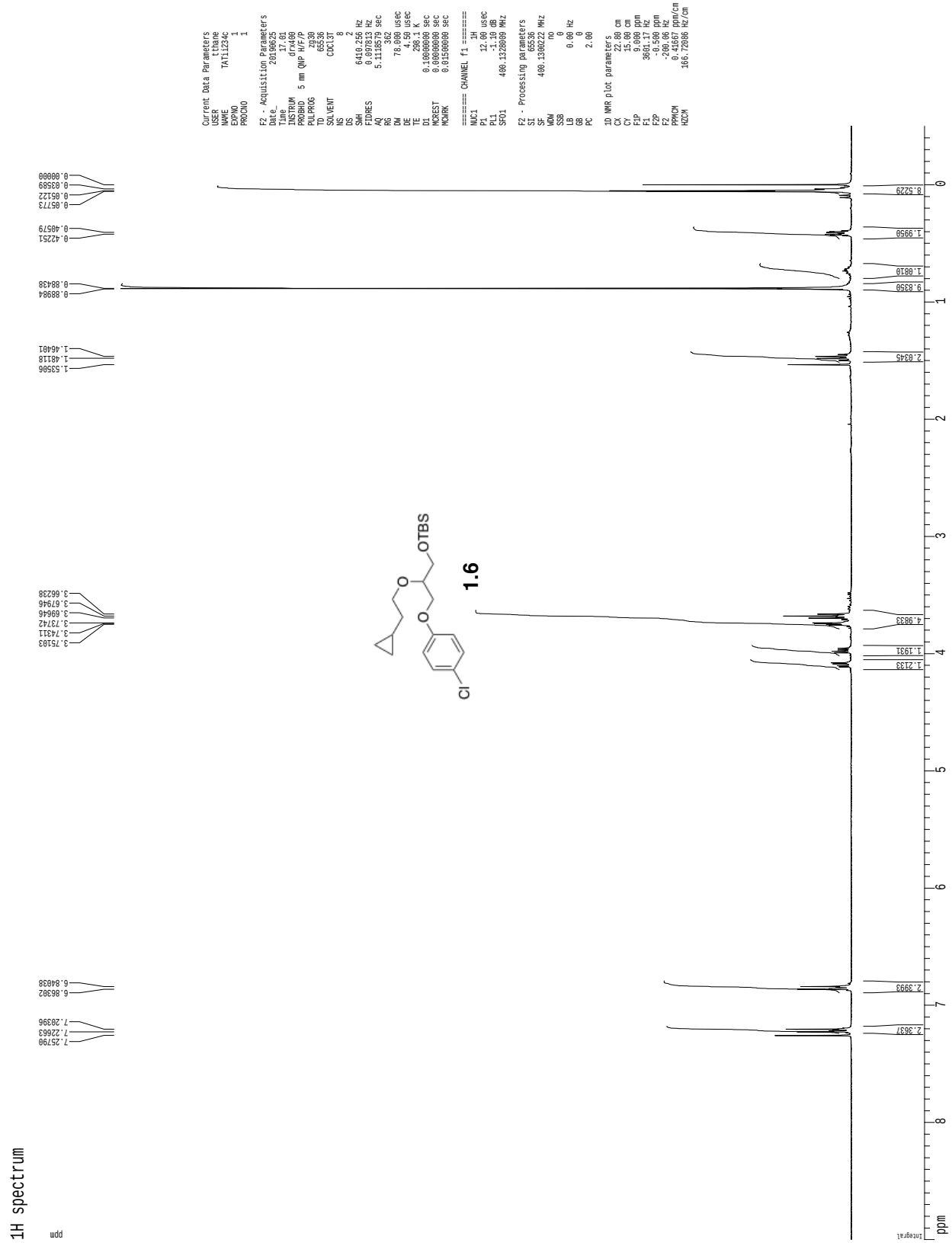
1.4

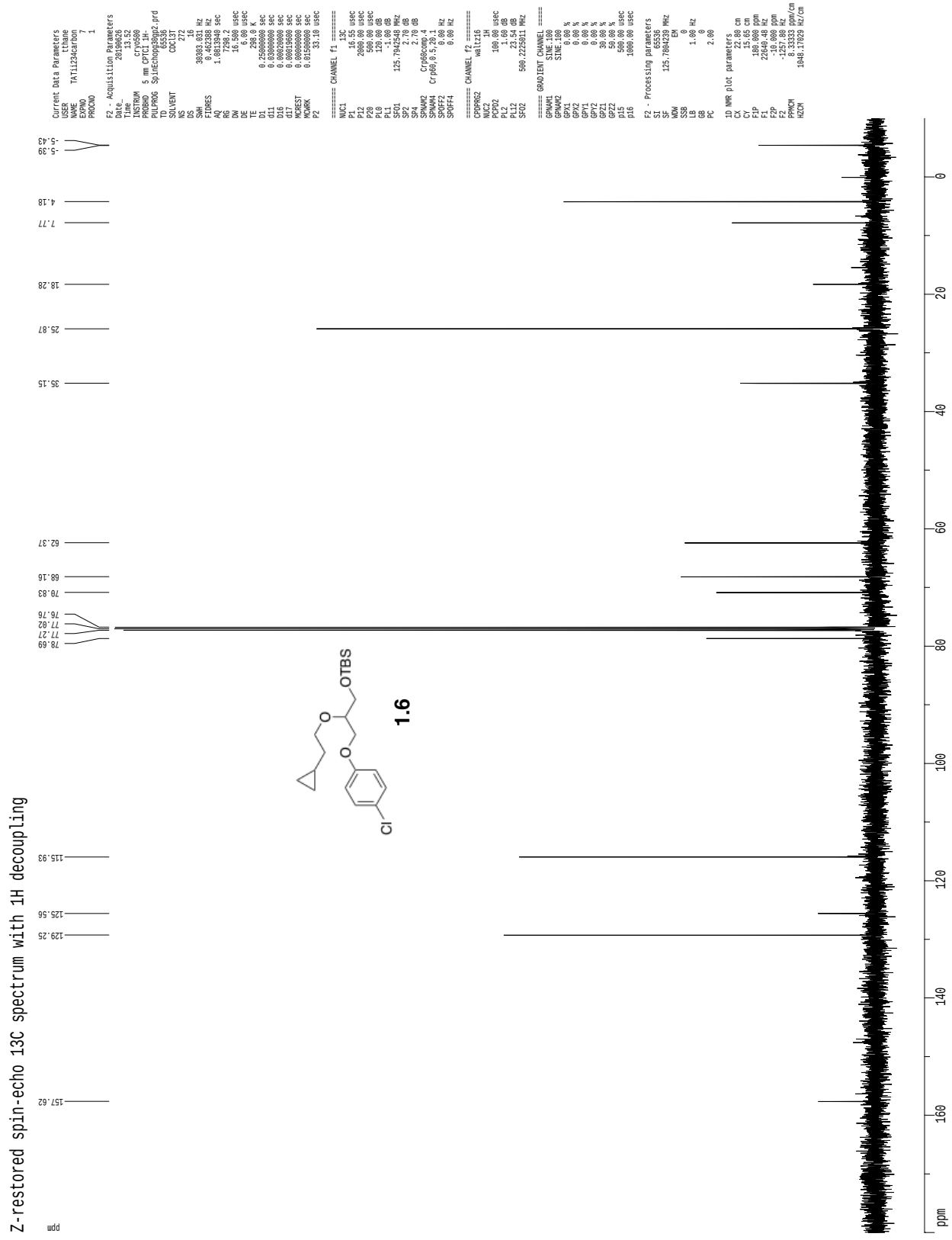
Z-restored spin-echo 13C spectrum with 1H decoupling




1H spectrum
1.5
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
1.5
Current Data Parameters
Acquisition Parameters
F2 - Processing parameters
1D WNR plot parameters
ppm


1H spectrum
1.6
OTBS
Cl
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
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OTBS
O
O
Cl
ppm
0
20
40
60
80
100
120
140
160
180
-5.43
-5.39
4.18
7.77
18.28
25.87
35.15
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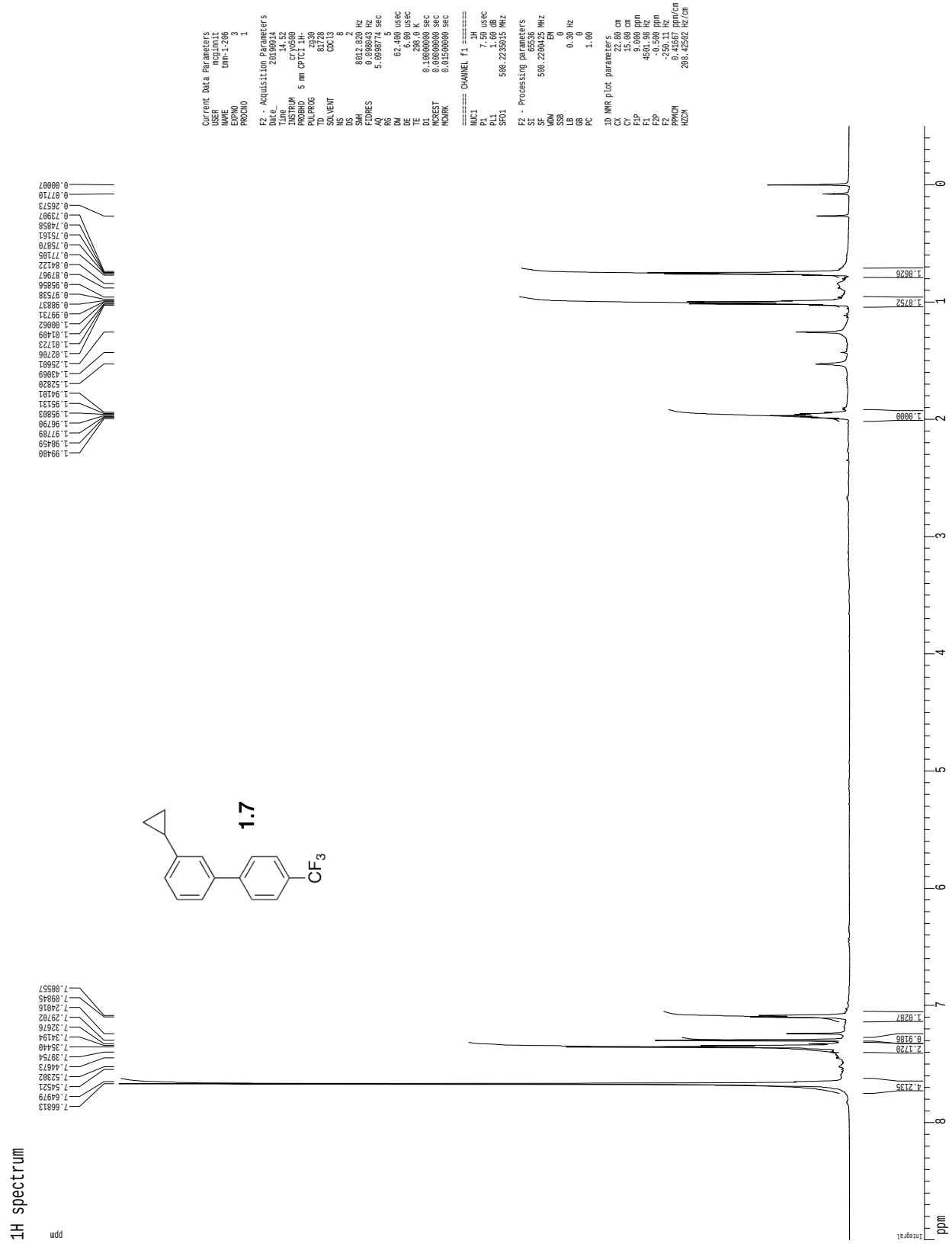
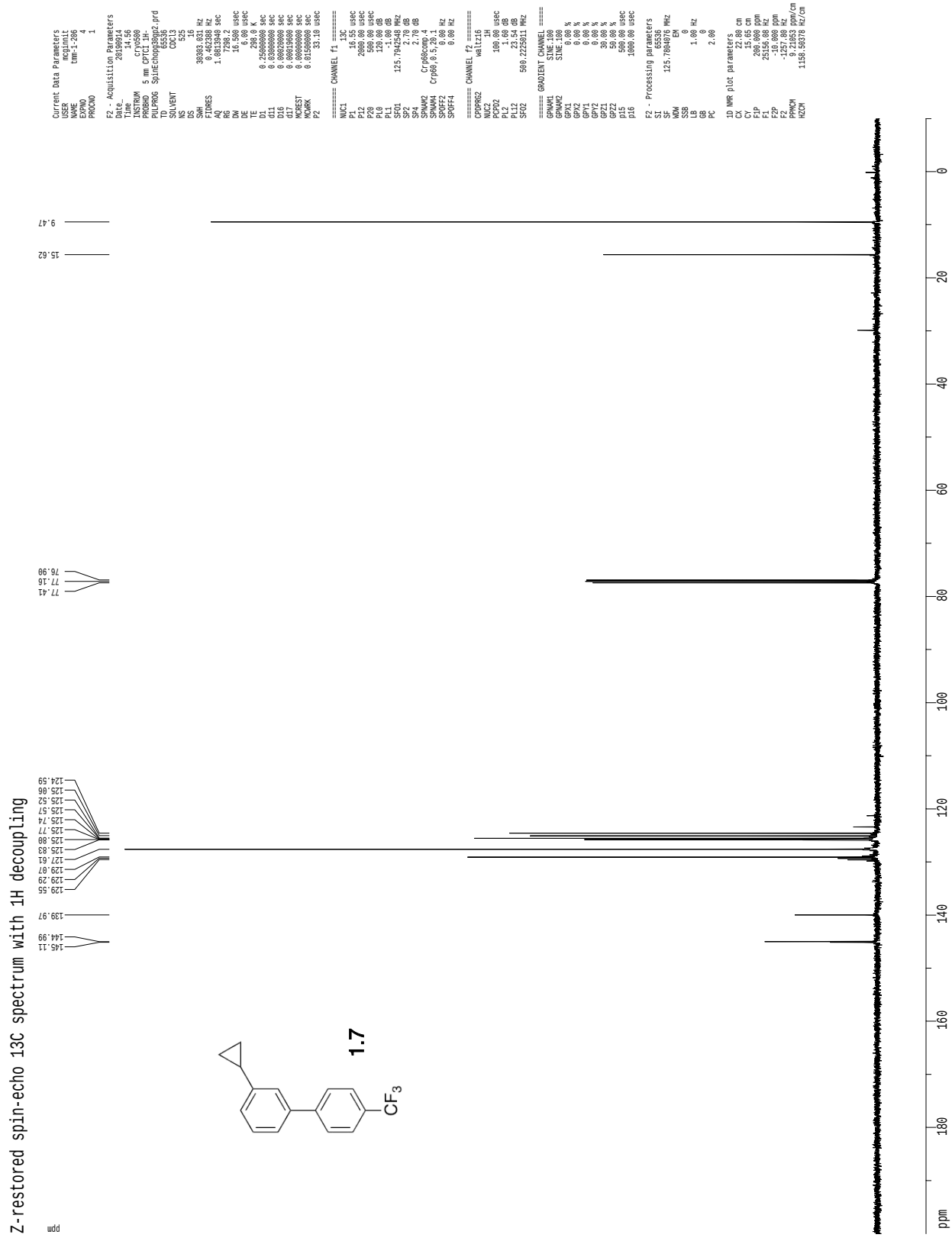
77.27
78.69
115.93
125.56
129.25
157.62


1H spectrum
1.7
CF3
ppm
Integral



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PROCNO 1

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NS 512
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08139840 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
d13 0.00003000 sec
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MCWRK 33.10 usec
P2

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P12 2000.00 usec
P20 500.00 usec
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PL1 -1.00 dB
SFO1 125.79422540 MHz
SP1 2.70 dB
SP4 2.70 dB
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SPNAM4 Crp60,0.5,20.1
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SPOFF4 0.00 Hz

======== CHANNEL f2 ========
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PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225911 MHz

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GPNAM2 SINE.100
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GPZ2 0.00 %
GPY1 0.00 %
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GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
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GB 0
PC 2.00

1D NMR plot parameters
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CY 15.00 cm
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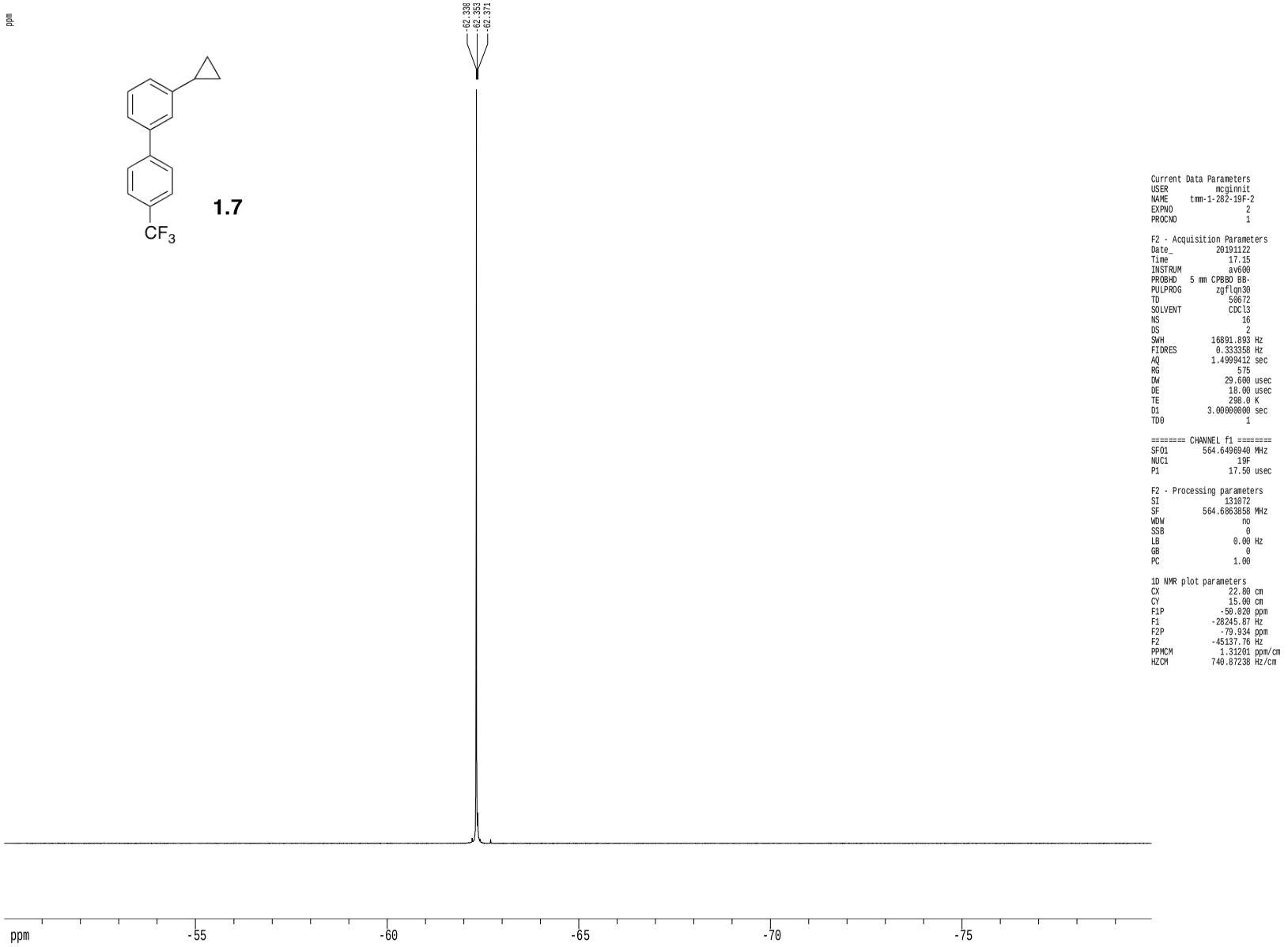
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 9.21053 ppm/cm
HZCM 1158.50378 Hz/cm

19F spectrum

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Current Data Parameters
USER            mcginnit
NAME      tmm-1-282-19F-2
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20191122
Time               17.15
INSTRUM           av600
PROBHD   5 mm CPBBO BB-
PULPROG         zgflqn30
TD                 50672
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           16891.893 Hz
FIDRES         0.333358 Hz
AQ             1.4999412 sec
RG                   575
DW                29.600 usec
DE                18.00 usec
TE                298.0 K
D1            3.00000000 sec
TD0                    1

======= CHANNEL f1 =======
SFO1         564.6496940 MHz
NUC1                19F
P1                17.50 usec

F2 - Processing parameters
SI                131072
SF           564.6863858 MHz
WDW                   no
SSB                    0
LB                 0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                22.80 cm
CY                15.00 cm
F1P              -50.020 ppm
F1            -28245.87 Hz
F2P              -79.934 ppm
F2            -45137.76 Hz
PPMCM           1.31201 ppm/cm
HZCM          740.87238 Hz/cm
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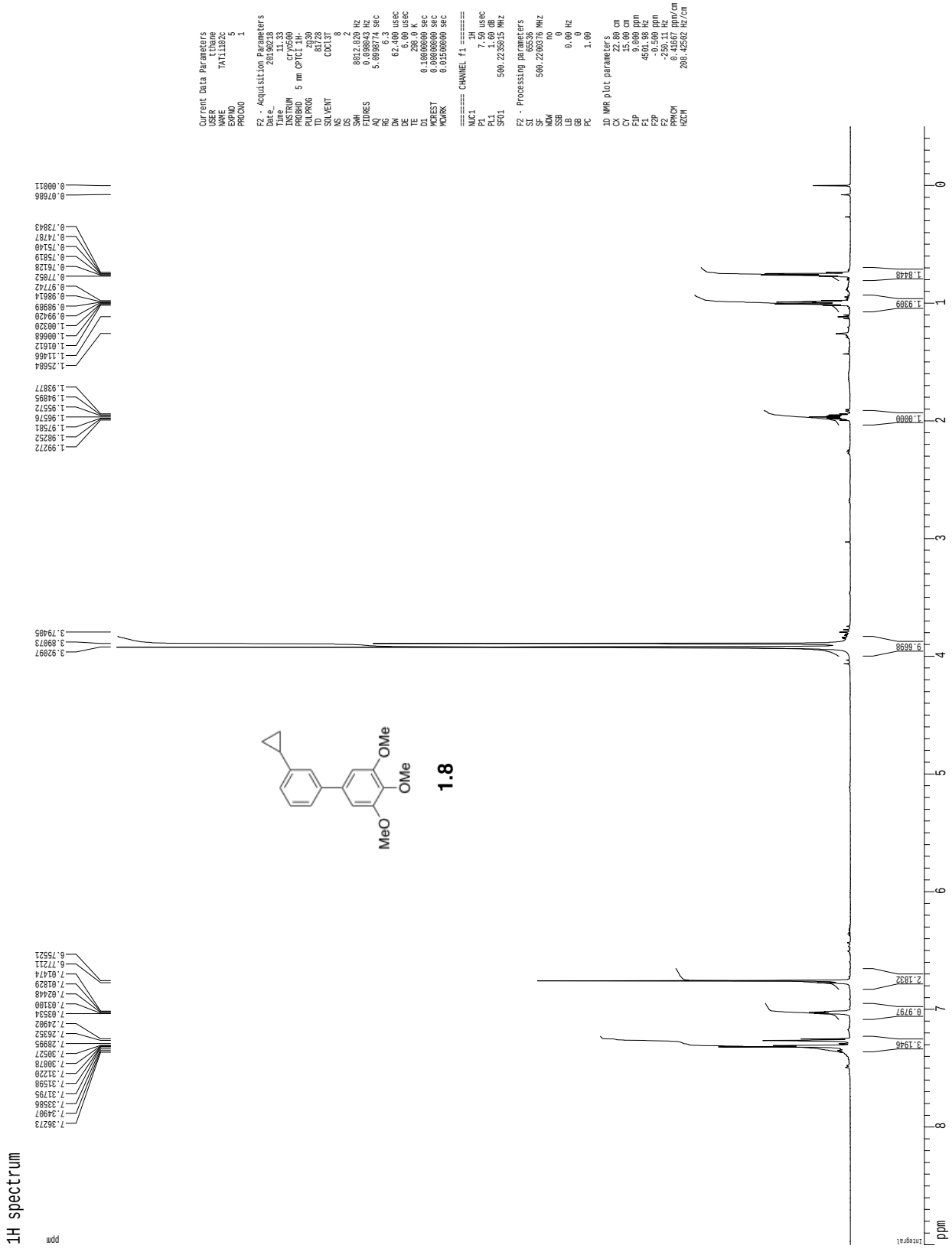
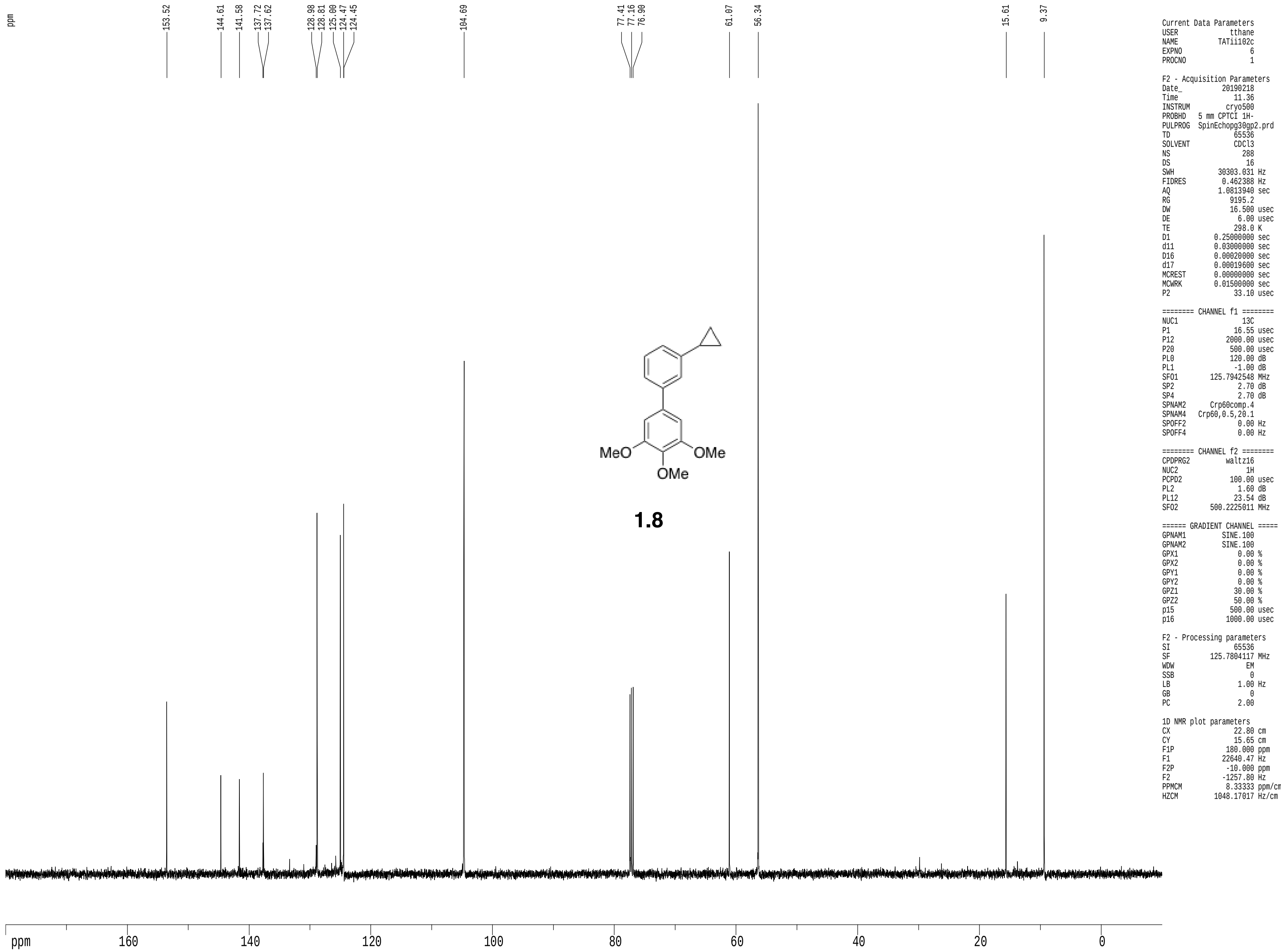
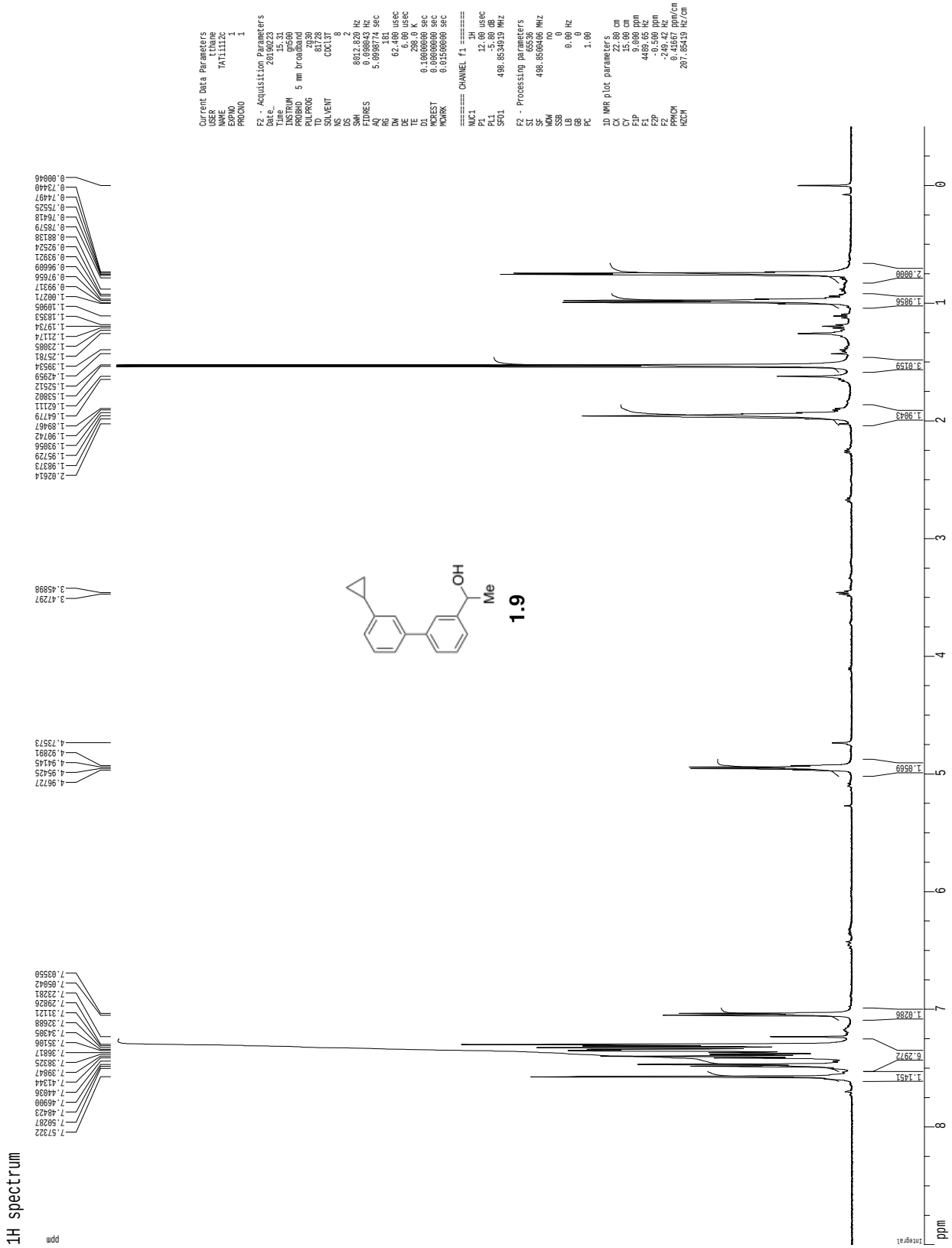
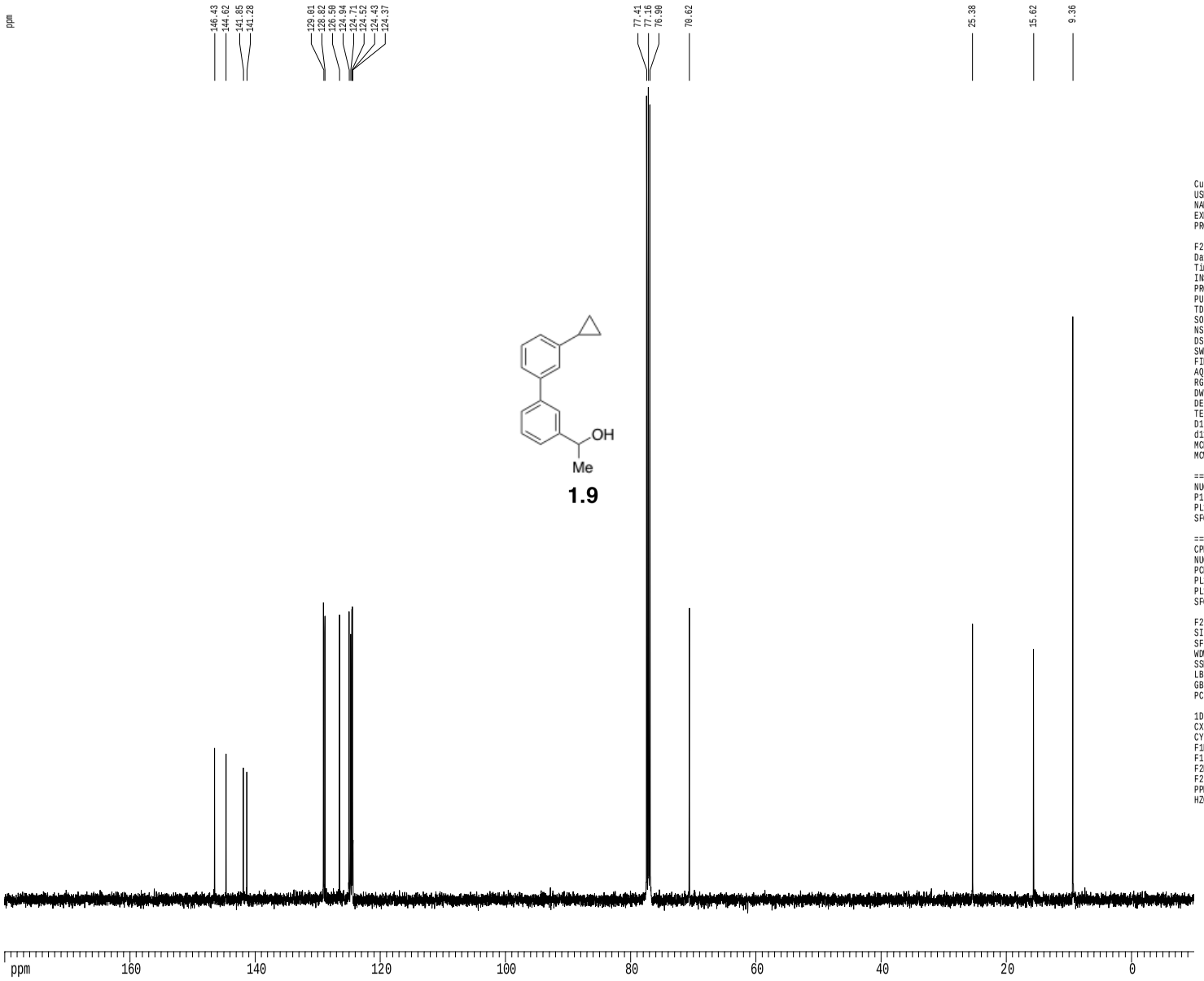

1H spectrum
1.8
OMe
OMe
MeO
Current Data Parameters
Acquisition Parameters
Processing parameters
1D NMR plot parameters
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling




1H spectrum
Current Data Parameters
USER tihane
NAME TA111112c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190223
Time 15.31
INSTRUM qnp500
PROBHD 5 mm broadband
PULPROG zg30
TD 87238
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.091843 Hz
AQ 5.0998774 sec
RG 161
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -5.00 dB
SFO1 498.8534919 MHz
F2 - Processing parameters
SI 65536
SF 498.8500406 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4489.65 Hz
F2P -0.500 ppm
F2 -249.42 Hz
PPMCM 0.41667 ppm/cm
HZCM 207.65419 Hz/cm
OH
Me
1.9
ppm
Integral

13C spectrum with 1H decoupling



Current Data Parameters
USER tthane
NAME TATii112c
EXPNO 2
PROCNO 1

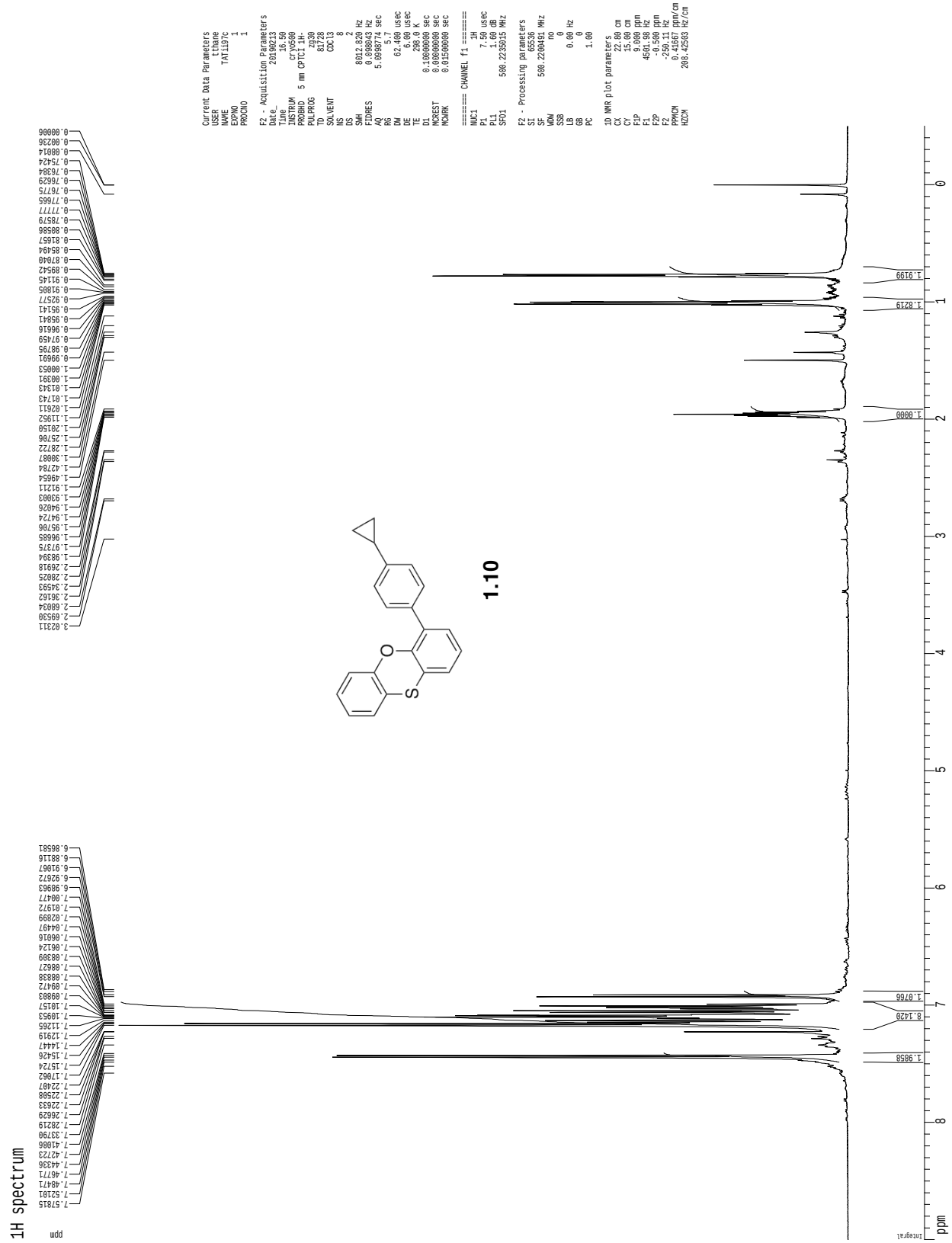
F2 - Acquisition Parameters
Date_ 20190223
Time 15.32
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 408
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 14596.5
DW 16.500 usec
DE 4.50 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

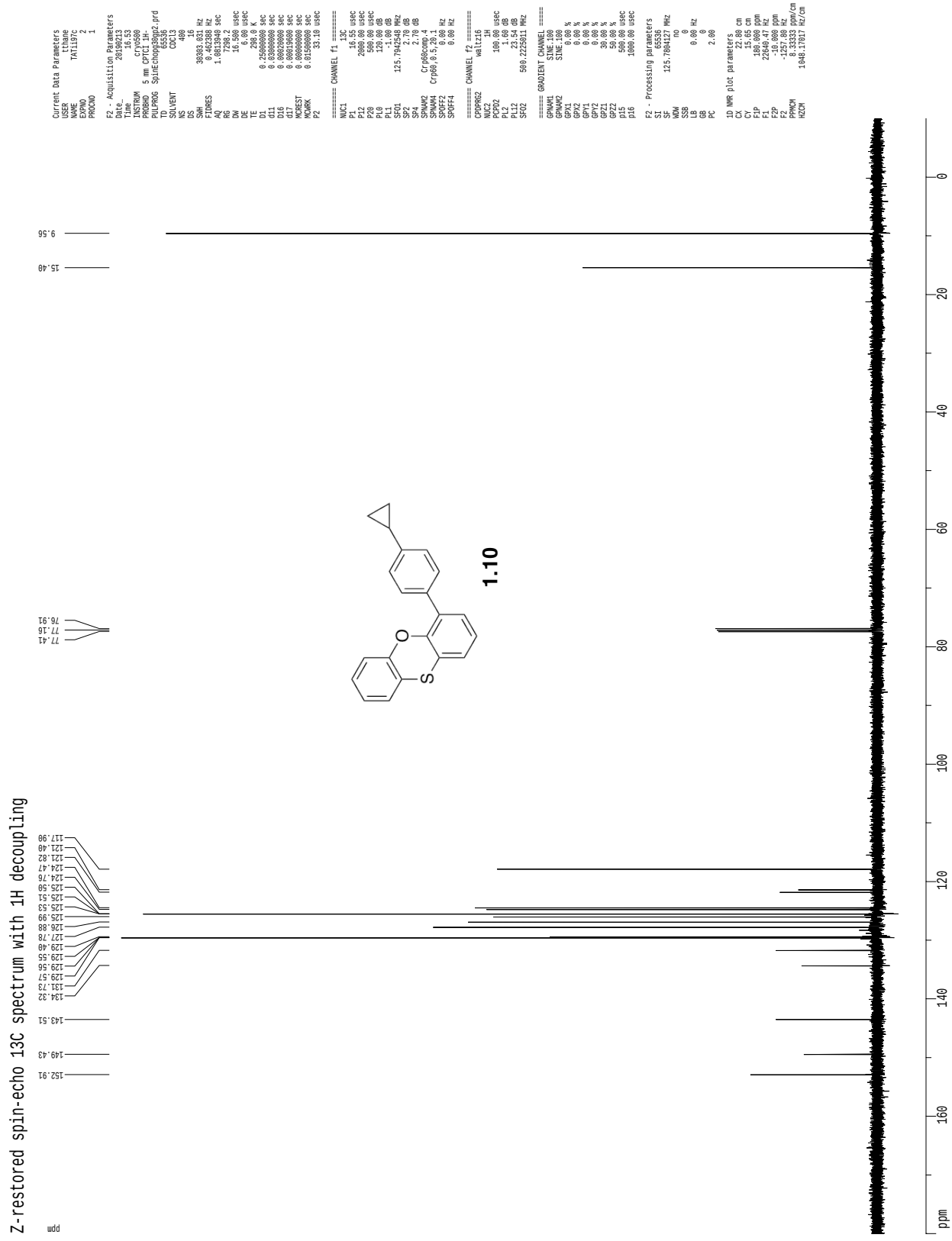
======= CHANNEL f1 =======
NUC1 13C
P1 9.00 usec
PL1 -0.60 dB
SFO1 125.4497300 MHz

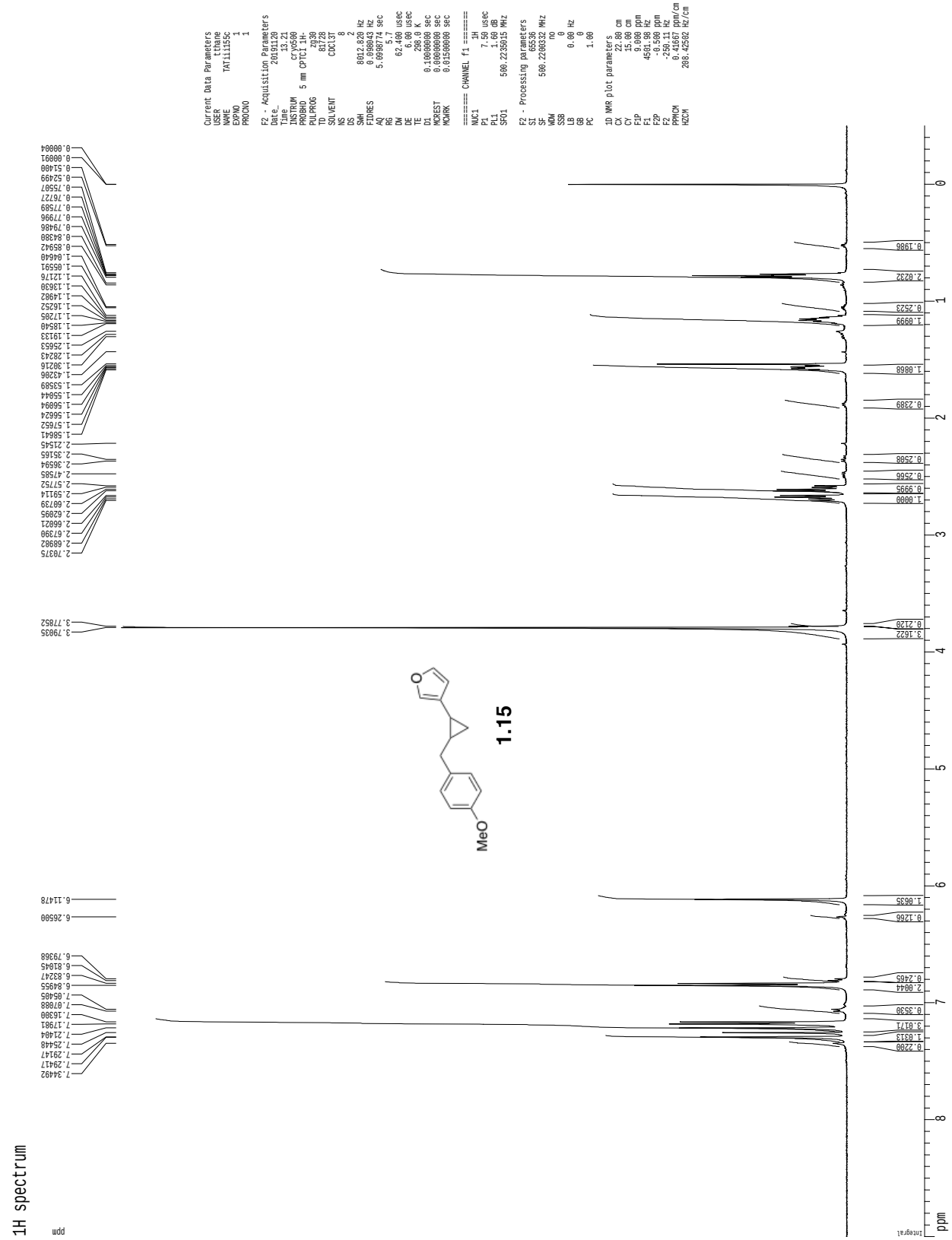
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 12.80 dB
SFO2 498.8524943 MHz

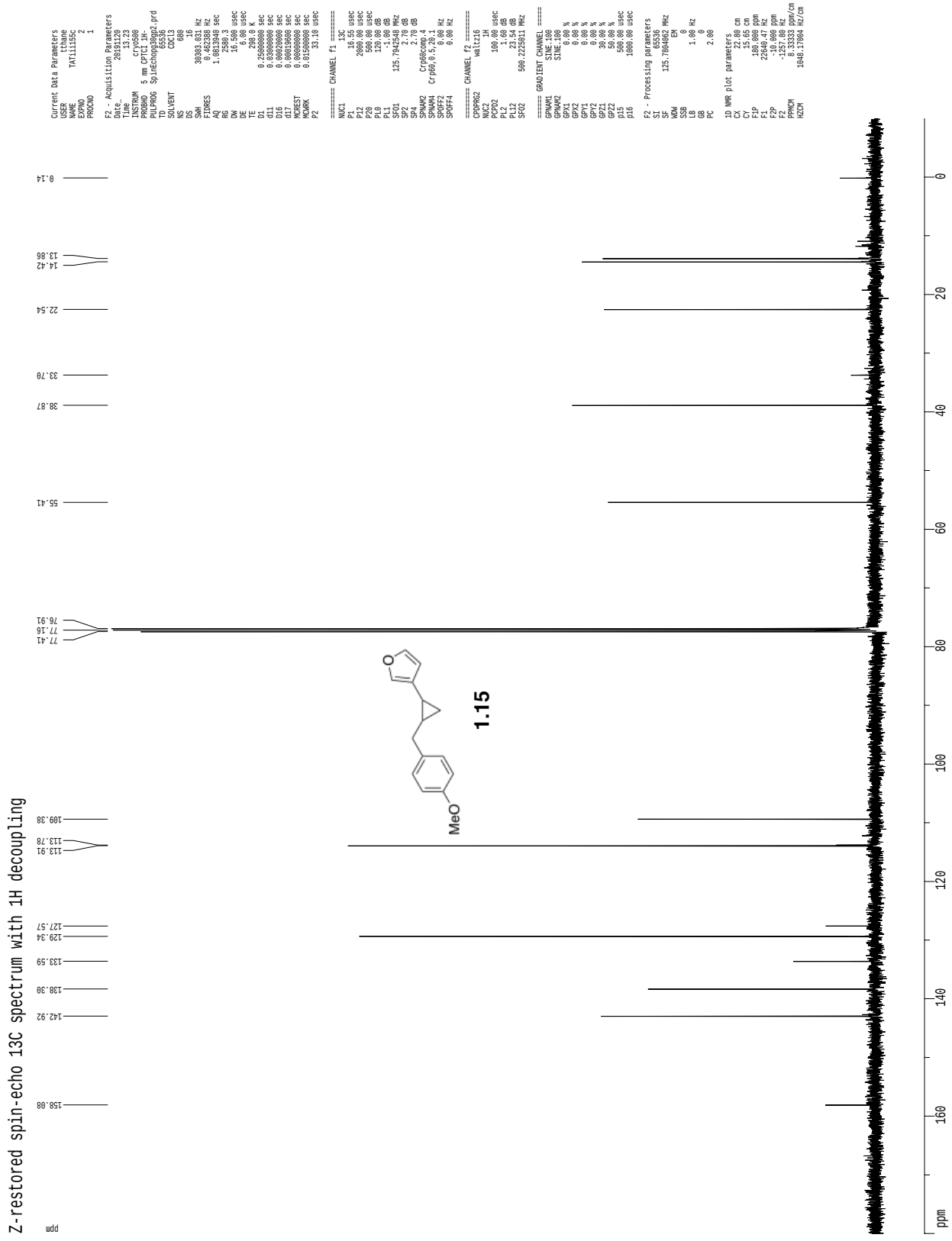
F2 - Processing parameters
SI 65536
SF 125.4359245 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

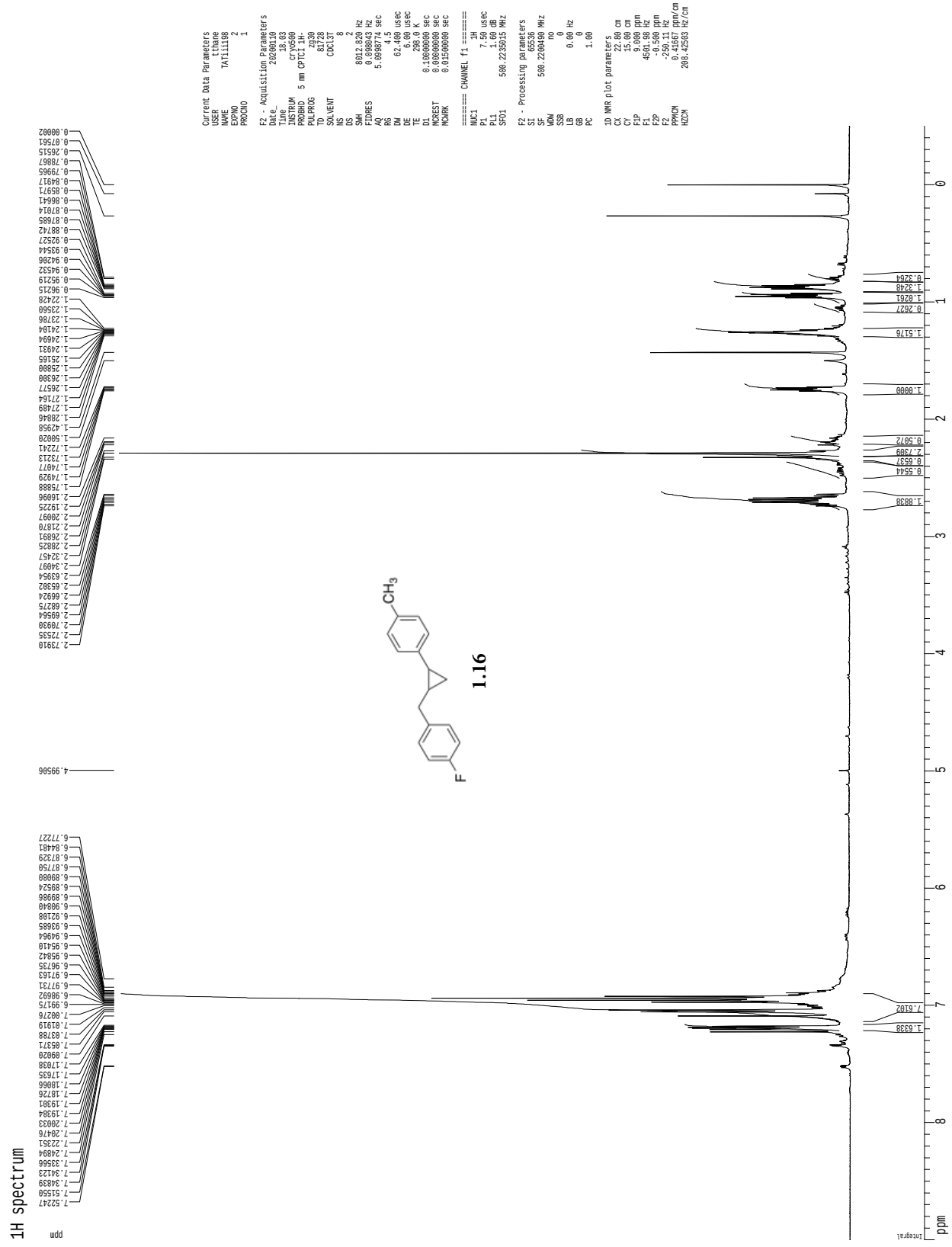
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 180.000 ppm
F1 22578.46 Hz
F2P -10.000 ppm
F2 -1254.36 Hz
PPMCM 8.33333 ppm/cm
HZCM 1045.29932 Hz/cm

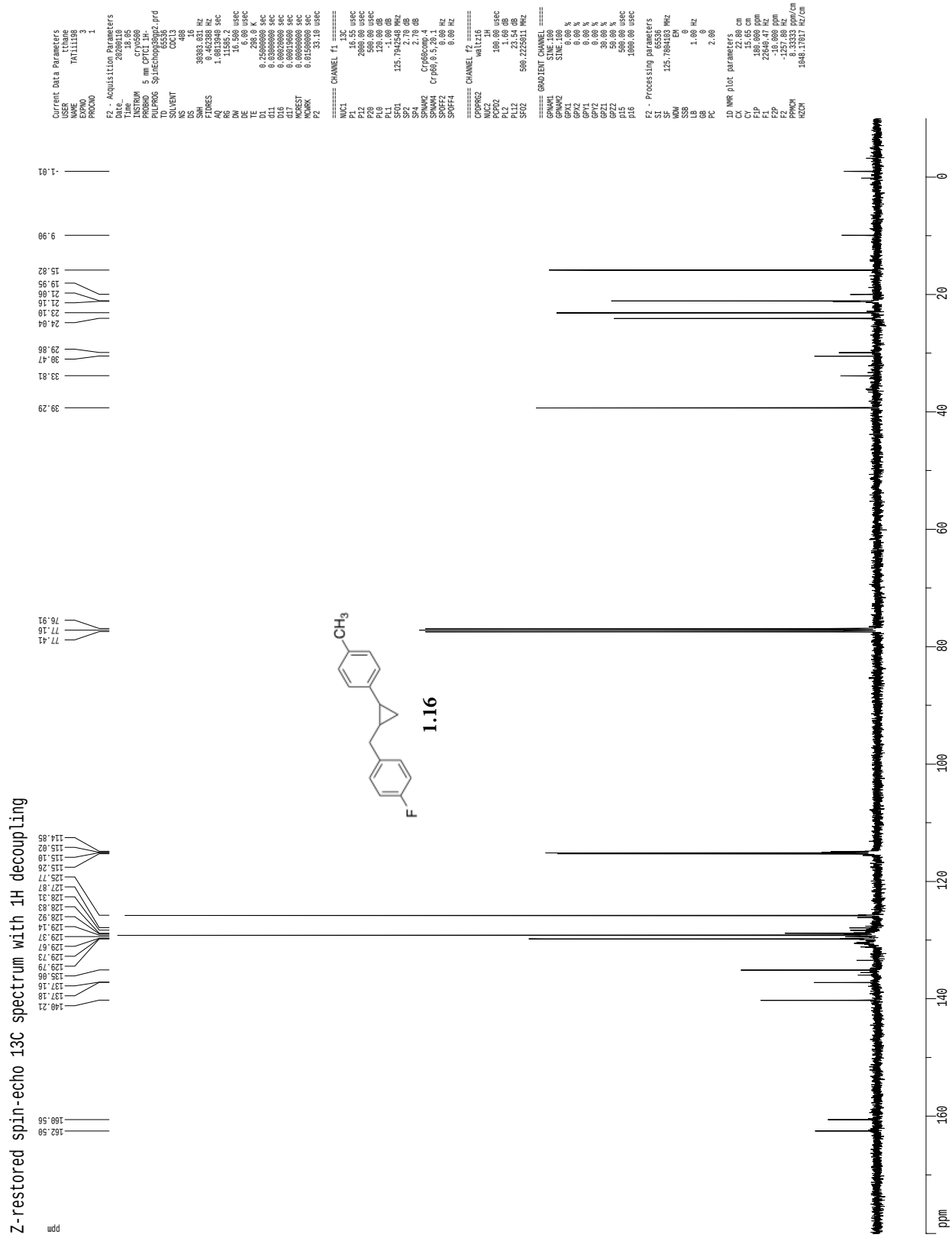

1H spectrum
Current data Parameters
USER ttiane
NAME TAT1197c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190213
Time 16.50
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 82128
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200491 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42503 Hz/cm
1.9199
1.8219
1.0000
1.0766
8.1420
1.9858
Integral
ppm
1.10


Z-restored spin-echo 13C spectrum with 1H decoupling
1.10
Current Data Parameters
Acquisition Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm

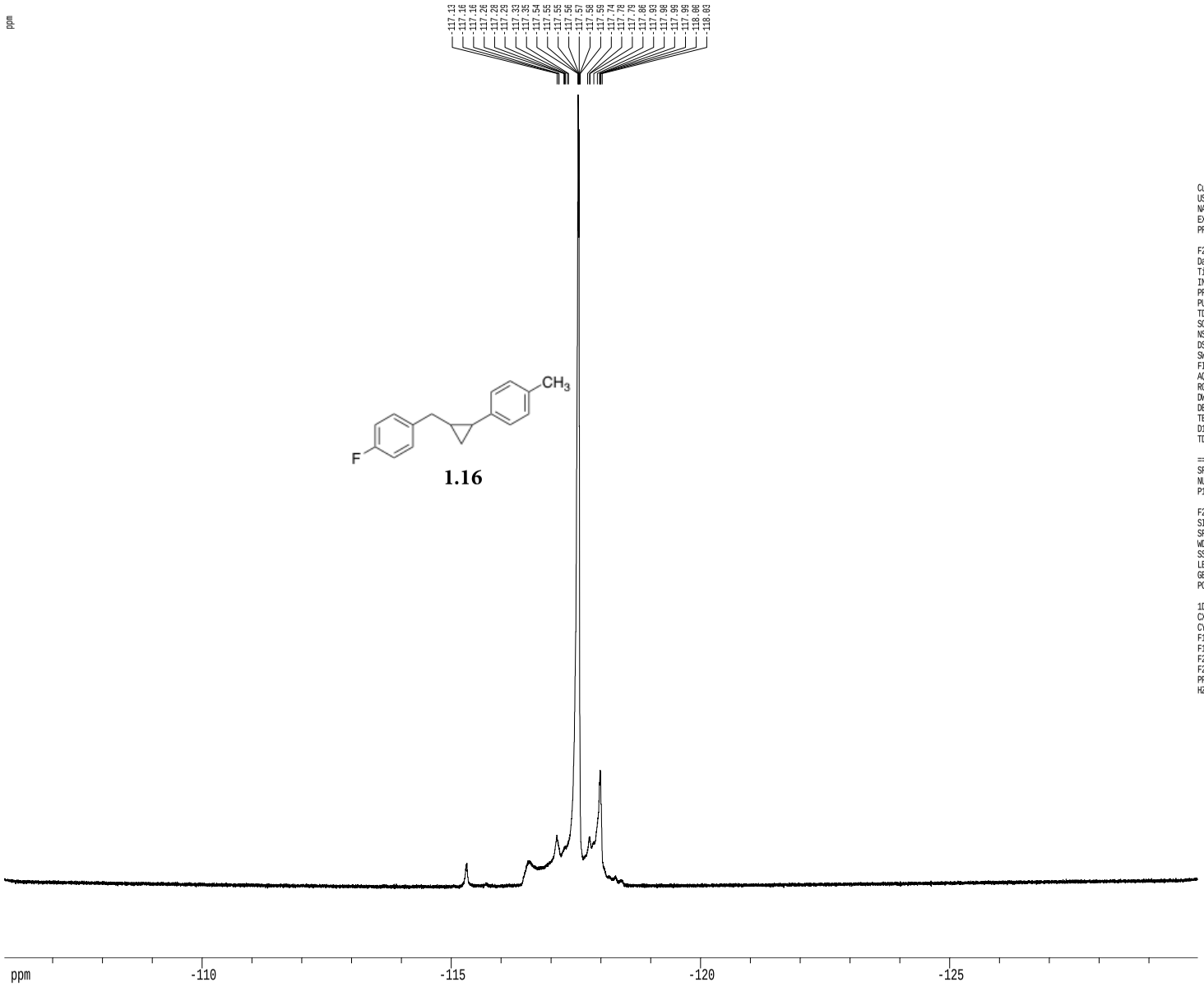

1H spectrum
1.15
MeO
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
1.15
MeO
Current Data Parameters
Acquisition Parameters
Processing parameters
1D NMR plot parameters
ppm


1H spectrum
Current Data Parameters
USER tihane
NAME TA1111196
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200110
Time 18.03
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200490 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42503 Hz/cm
1.16
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
1.16
F
CH3
Current Data Parameters
NAME TAT111108
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200110
Time 13.05
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 400
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08139840 sec
RG 11585.2
DW 16.500 usec
DE 6.50 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
====== CHANNEL f1 ======
NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.79422540 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225911 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPV1 0.00 %
GPV2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.78041103 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 8.33333 ppm/cm
HZCM 1040.17917 Hz/cm
-1.01
9.90
15.82
19.95
21.06
21.16
23.10
24.04
29.86
30.47
33.81
39.29
76.91
77.16
77.41
114.85
115.02
115.10
115.26
125.77
127.87
128.31
128.83
128.92
129.14
129.37
129.67
129.73
129.79
135.06
137.16
137.18
140.21
160.56
162.50
0
20
40
60
80
100
120
140
160

19F spectrum



1.16

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Current Data Parameters
USER              tthane
NAME          TATiii198F
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200115
Time               9.54
INSTRUM           av600
PROBHD   5 mm CPBBO BB-
PULPROG        zgflqn30
TD                40538
SOLVENT           CDCl3T
NS                   16
DS                    2
SWH           13513.514 Hz
FIDRES         0.333354 Hz
AQ             1.4999560 sec
RG                 575
DW                37.000 usec
DE                18.00 usec
TE                298.0 K
D1            3.00000000 sec
TD0                    1

======= CHANNEL f1 =======
SFO1         564.6197485 MHz
NUC1                19F
P1                17.50 usec

F2 - Processing parameters
SI                131072
SF           564.6863858 MHz
WDW                   no
SSB                    0
LB                 0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                22.80 cm
CY                15.00 cm
F1P             -106.042 ppm
F1            -59880.53 Hz
F2P             -129.973 ppm
F2            -73394.04 Hz
PPMCM           1.04961 ppm/cm
HZCM          592.69781 Hz/cm
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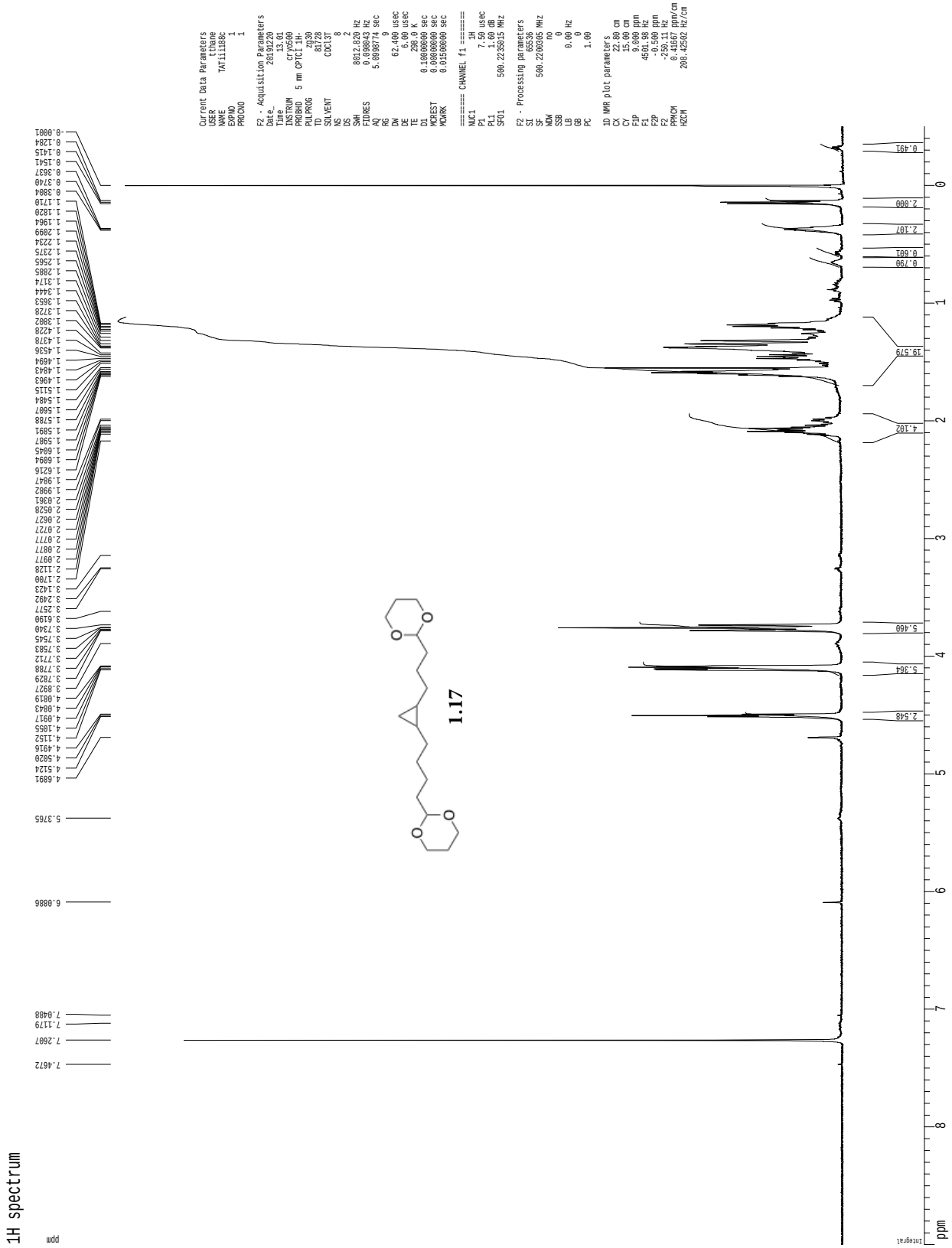
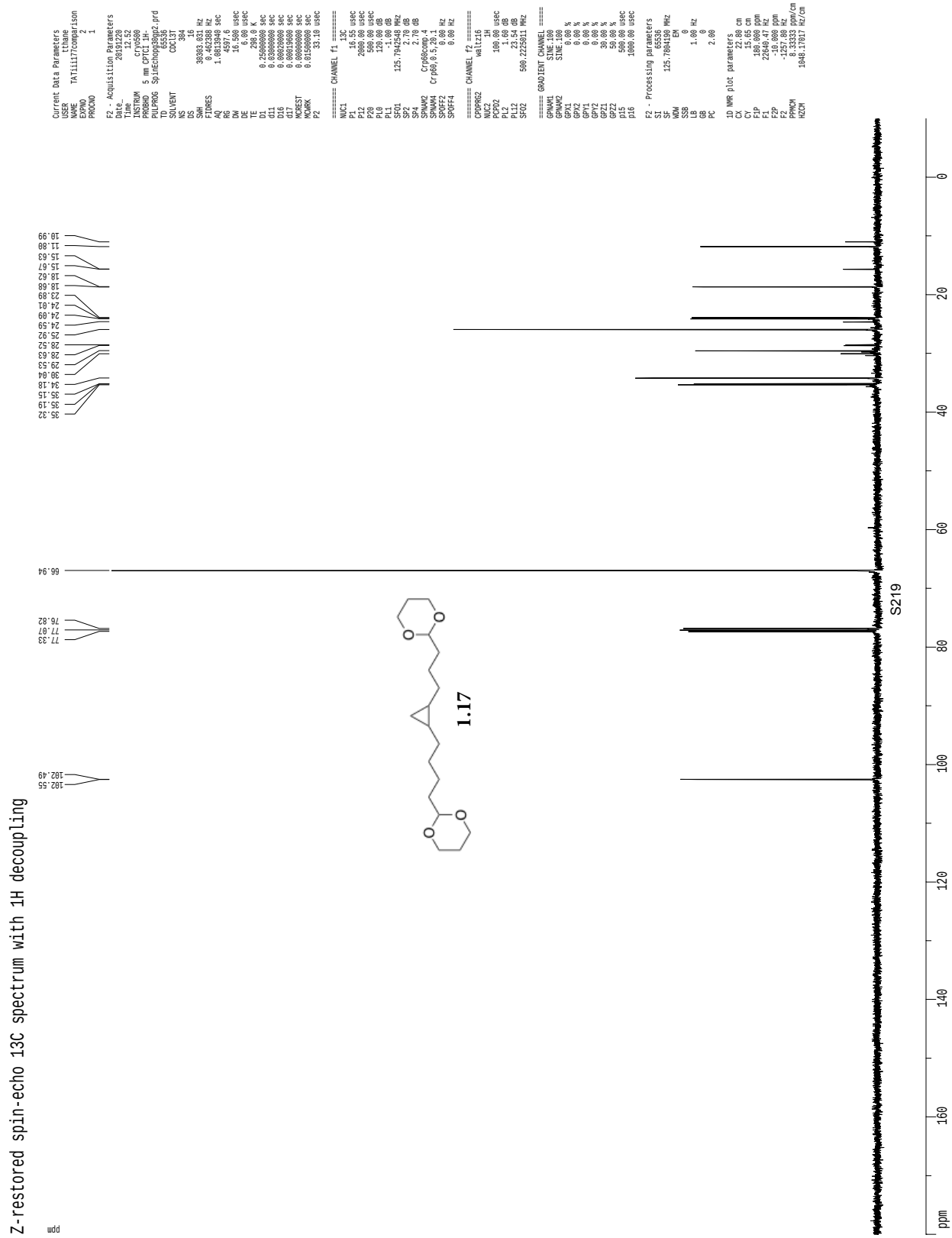
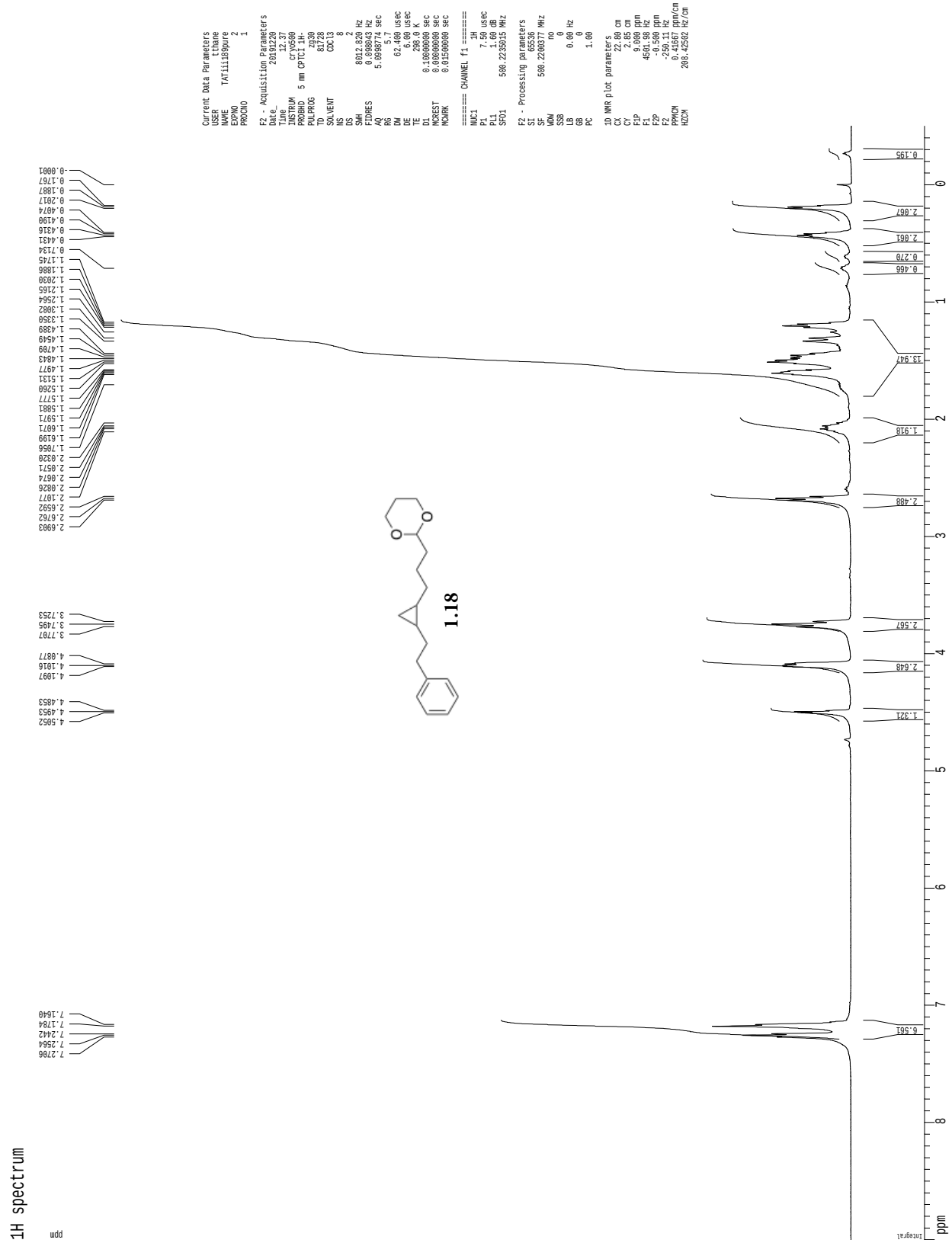
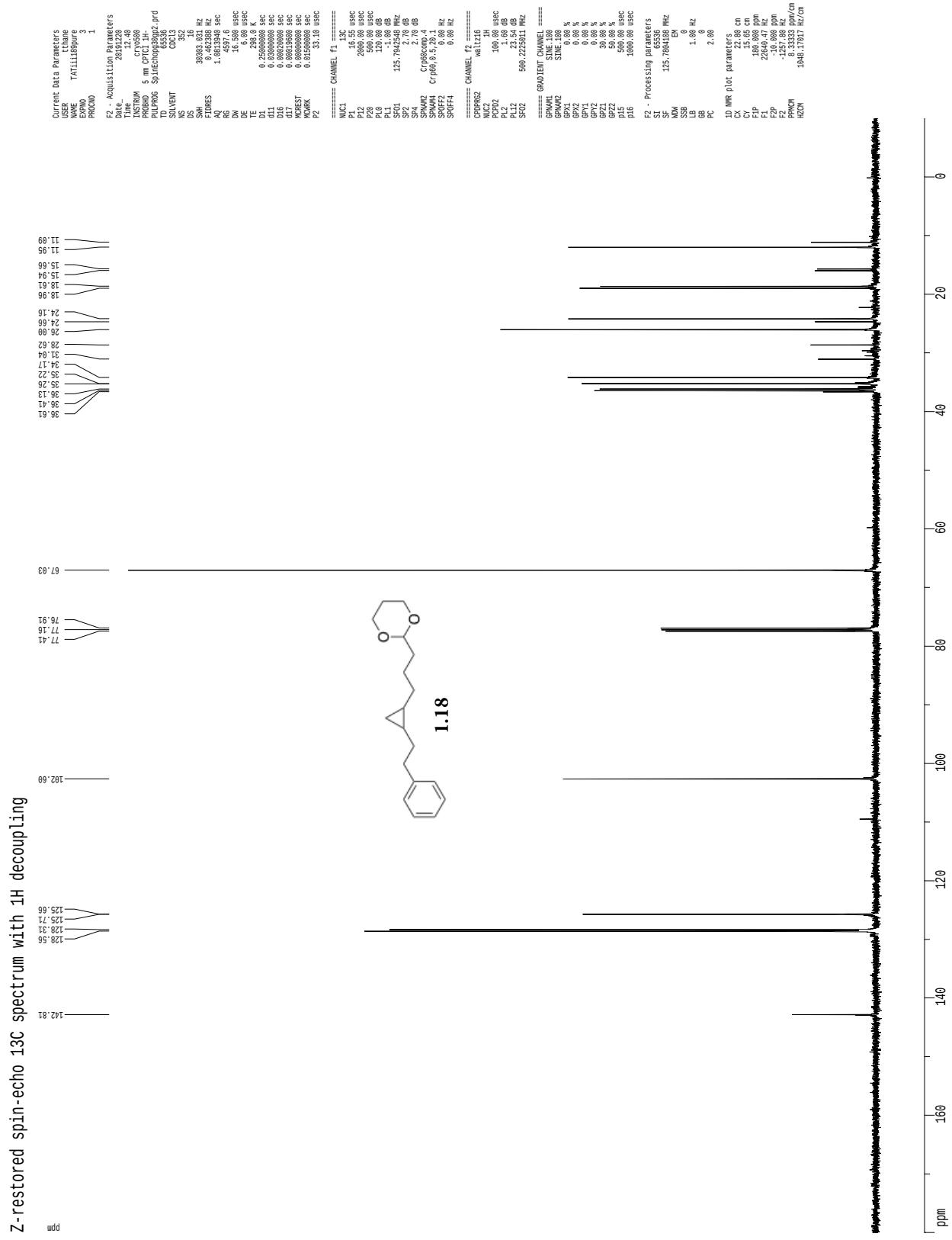
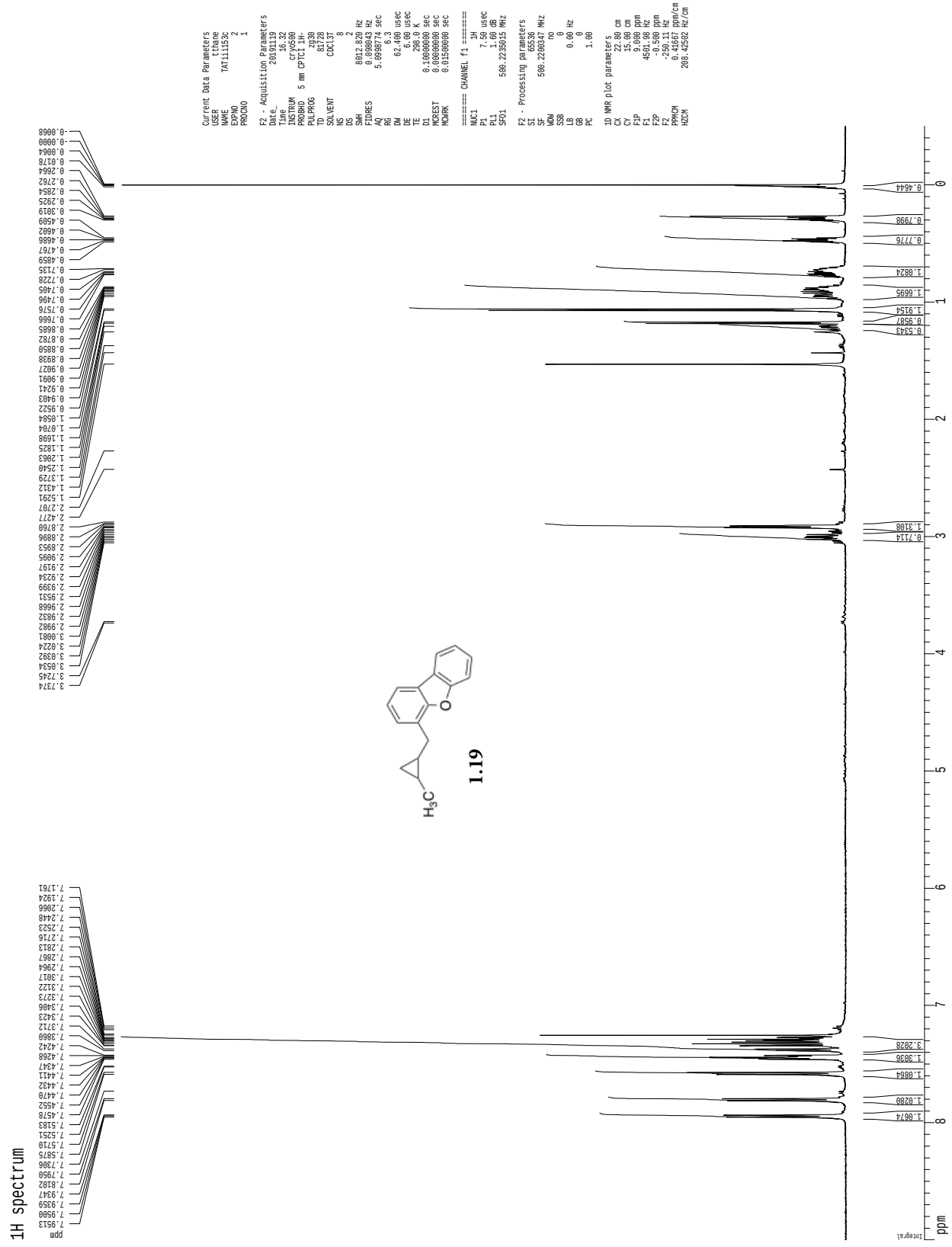
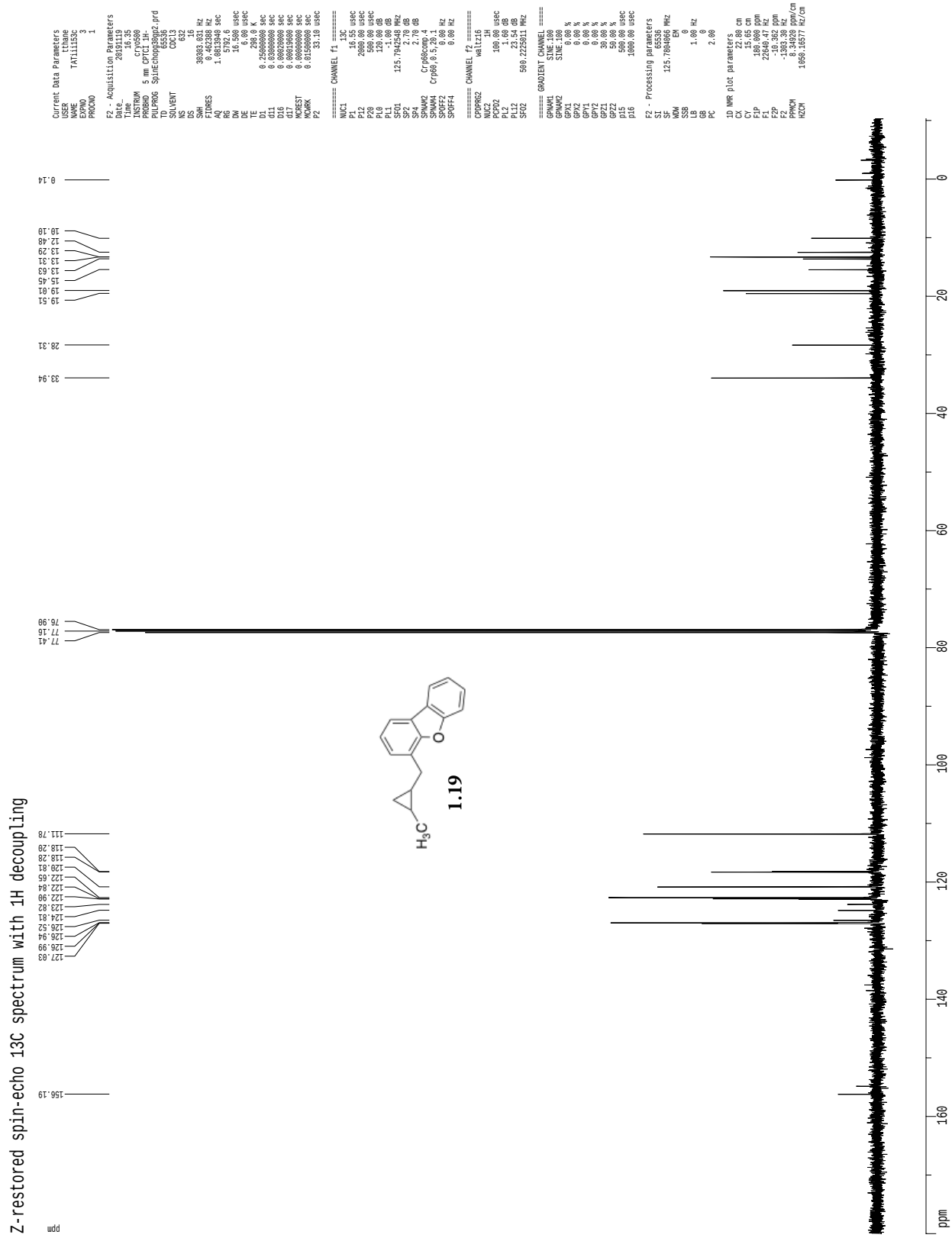

1H spectrum
Current Data Parameters
USER ttihane
NAME TAT1111108c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191220
Time 13.01
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 9
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200305 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
0.0001
0.1284
0.1415
0.1541
0.3637
0.3740
0.3804
1.1710
1.1820
1.1964
1.2099
1.2234
1.2375
1.2565
1.2885
1.3174
1.3444
1.3653
1.3728
1.3802
1.4228
1.4378
1.4536
1.4694
1.4843
1.4963
1.5115
1.5484
1.5607
1.5788
1.5981
1.5987
1.6045
1.6094
1.6216
1.9847
1.9982
2.0361
2.0528
2.0627
2.0727
2.0877
2.0877
2.0977
2.1128
2.1700
3.1423
3.2492
3.2577
3.6190
3.7340
3.7545
3.7583
3.7712
3.7788
3.7829
3.8927
4.0819
4.0843
4.0917
4.1065
4.1152
4.4916
4.5020
4.5124
4.6891
5.3765
6.0886
7.0488
7.1179
7.2607
7.4672
1.17
0.491
2.000
2.187
0.601
0.790
19.579
4.102
5.460
5.364
2.548
Integral
ppm
0
1
2
3
4
5
6
7
8

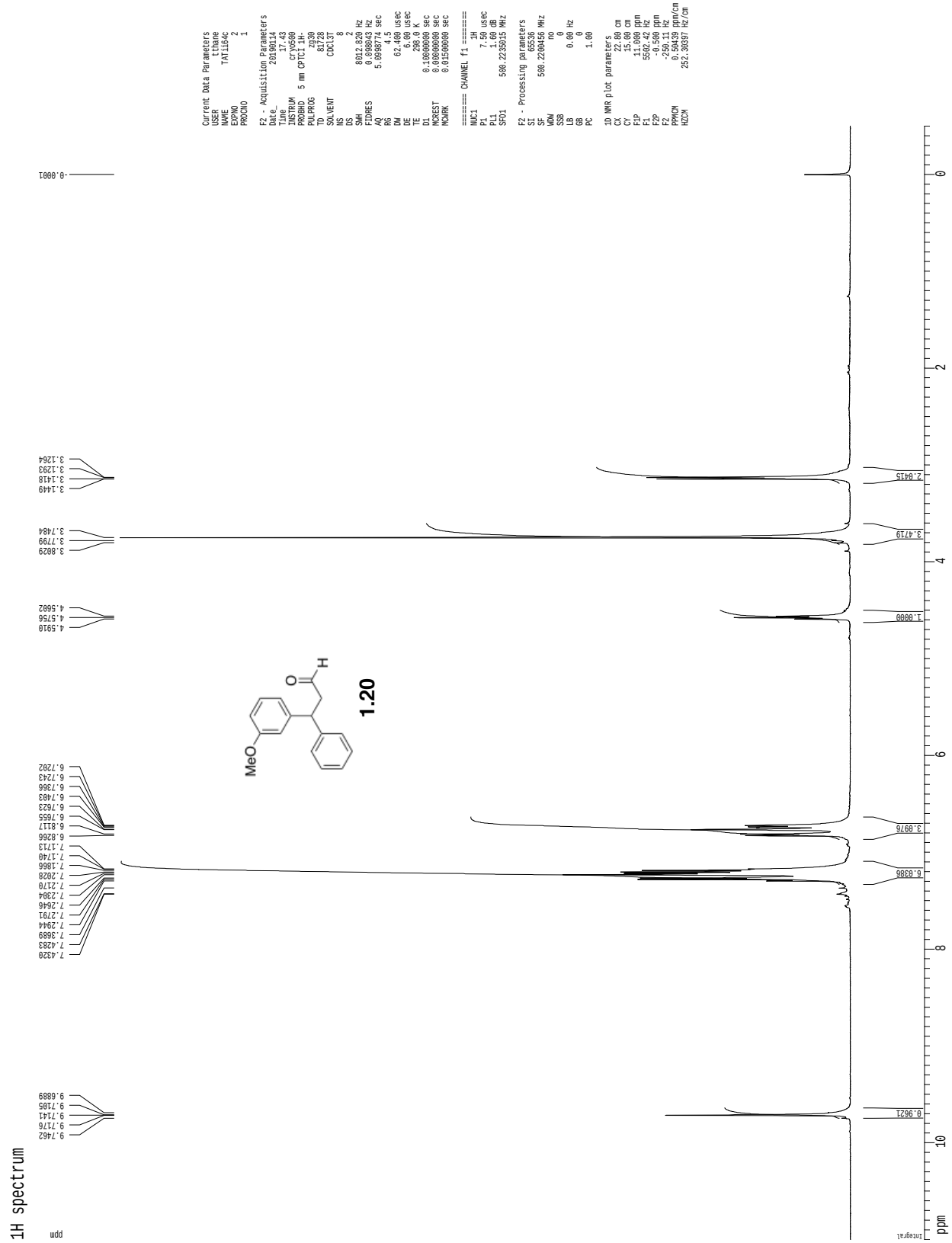

Z-restored spin-echo 13C spectrum with 1H decoupling
1.17
S219
ppm

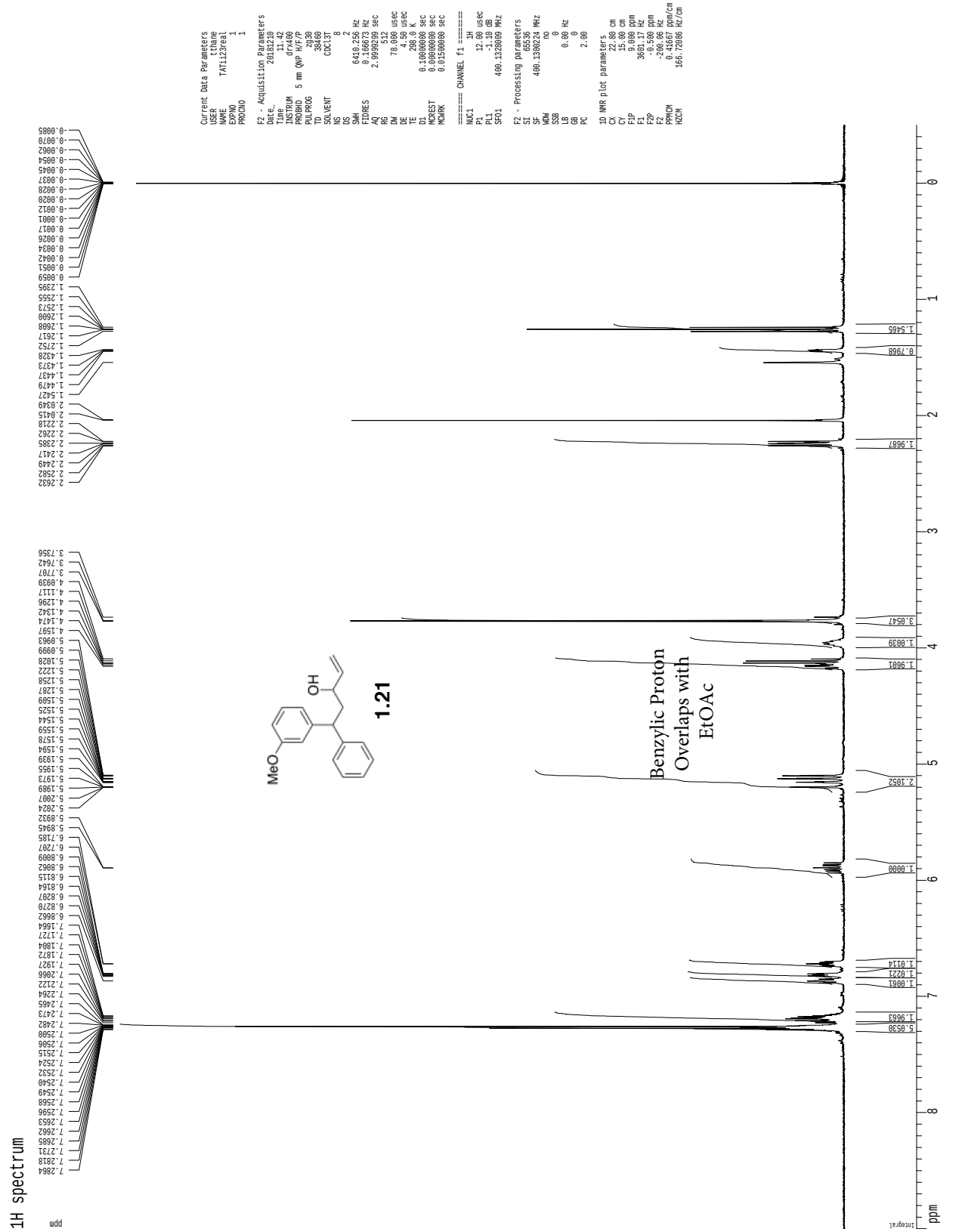

1H spectrum
Current Data Parameters
USER tthane
NAME TAT1iii109pure
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191220
Time 12.37
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 82128
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200377 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 2.85 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
1.18
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
1.18
Current Data Parameters
Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm


1H spectrum
Current Data Parameters
USER ttlahe
NAME TAT1111552
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191119
Time 16.32
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200347 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
1.17
1.19
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
1.19
H3C
O
0.14
10.10
12.48
13.29
13.31
13.63
15.45
19.01
19.51
28.31
33.94
76.90
77.16
77.41
111.78
118.20
118.28
120.81
122.65
122.84
122.90
123.82
124.81
126.52
126.94
126.99
127.03
156.19


1H spectrum
1.20
MeO
O
H
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral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NAME TATi123reai
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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Time 11.42
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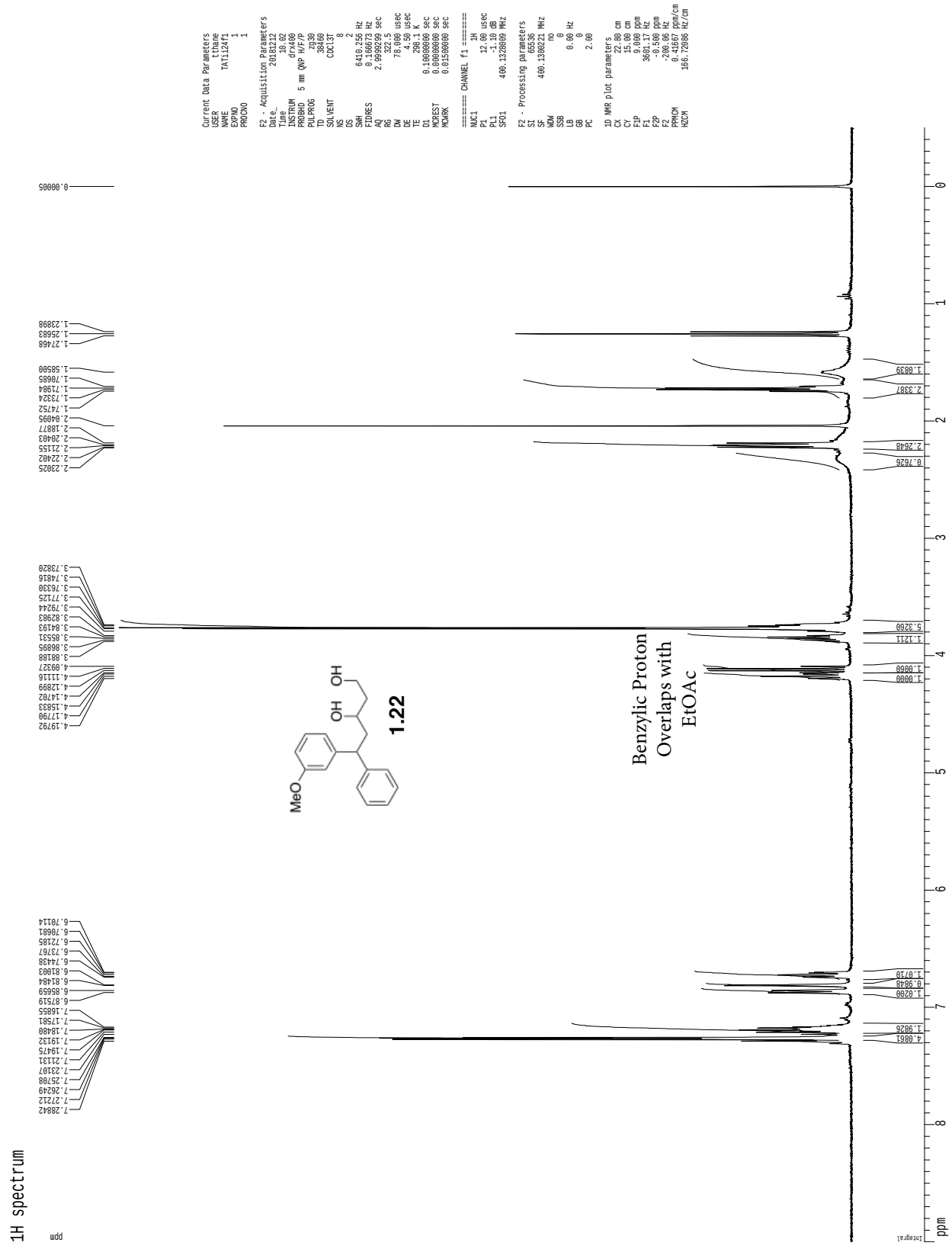
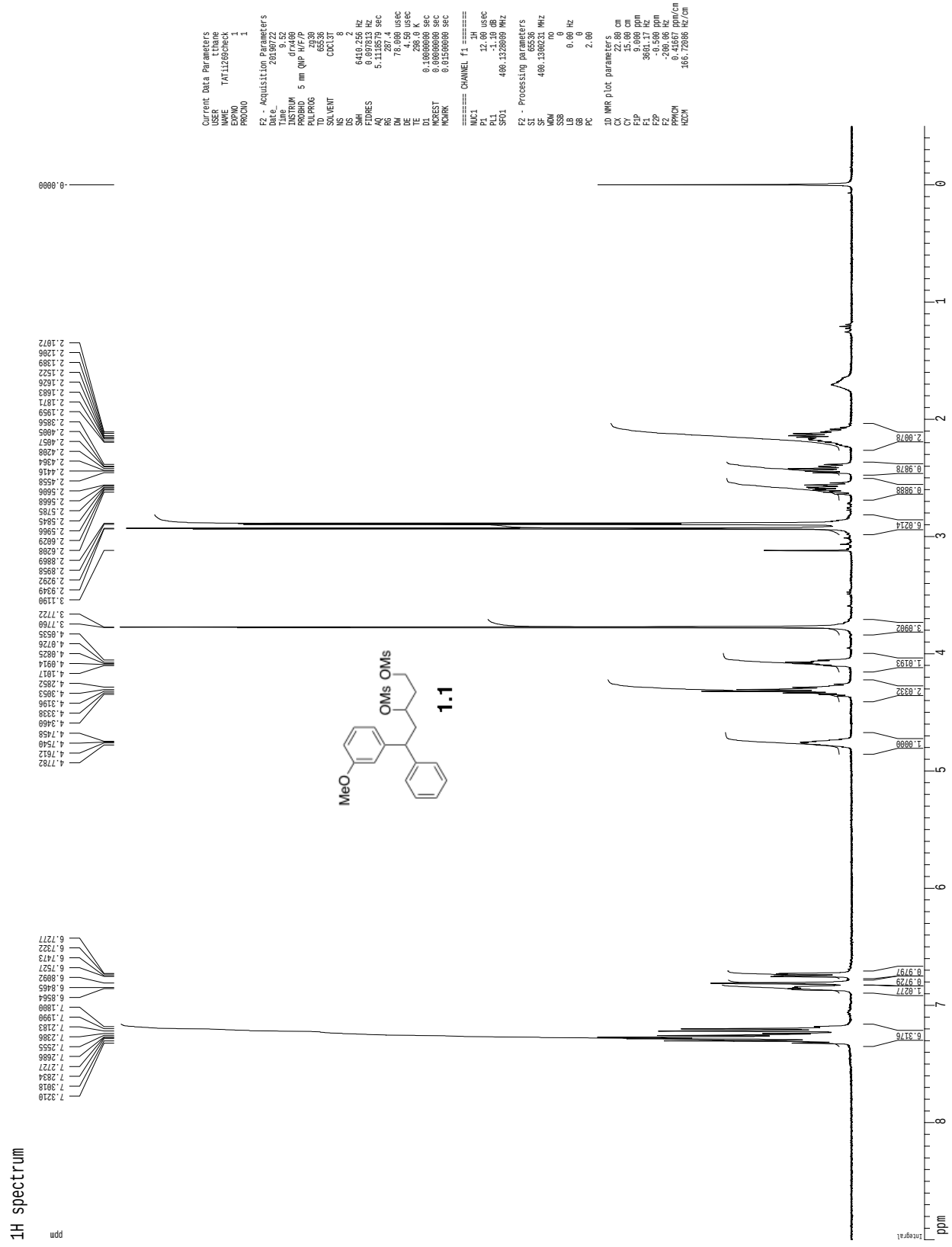
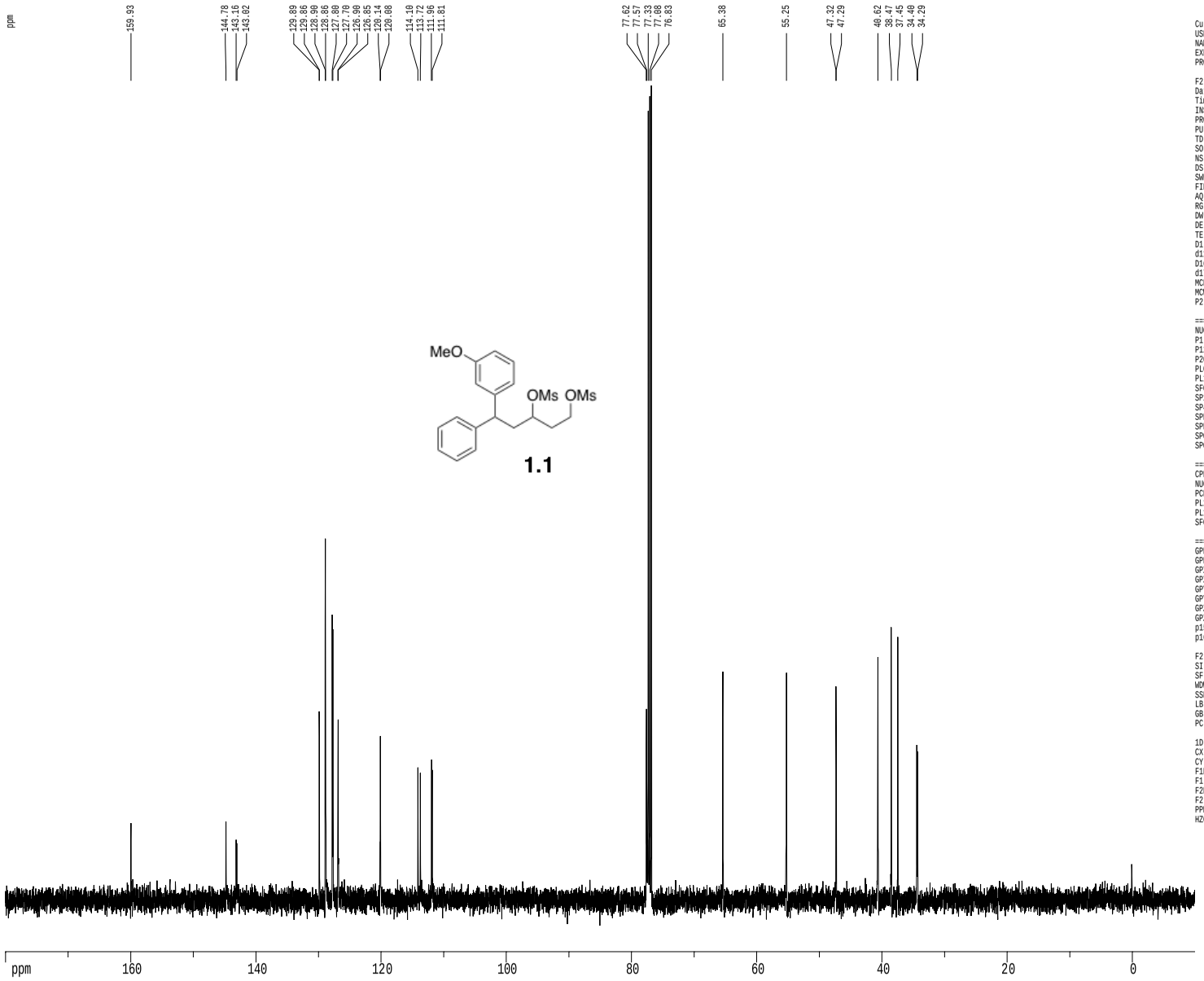
PULPROG zg30
TD 32768
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.166673 Hz
AQ 2.9999209 sec
RG 512
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300224 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
MeO
OH
1.21
Benzylic Proton
Overlaps with
EtOAc
1.5465
0.7968
1.9887
3.8547
1.0039
1.9601
2.1052
1.0000
1.0061
1.0221
1.0114
1.9653
5.0530
integral
ppm


1H spectrum
Benzylic Proton Overlaps with EtOAc
1.22
MeO
OH
OH
ppm


1H spectrum
Current Data Parameters
USER tthane
NAME TAT1i2690check
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190722
Time 9.52
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 287.4
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300231 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OMs OMs
MeO
1.1
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER tthane
NAME TATi1269c
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190722
Time 10.13
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3T
NS 360
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 6502
DW 16.500 usec
DE 6.00 usec
TE 298.2 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

======== CHANNEL f1 ========
NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804190 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
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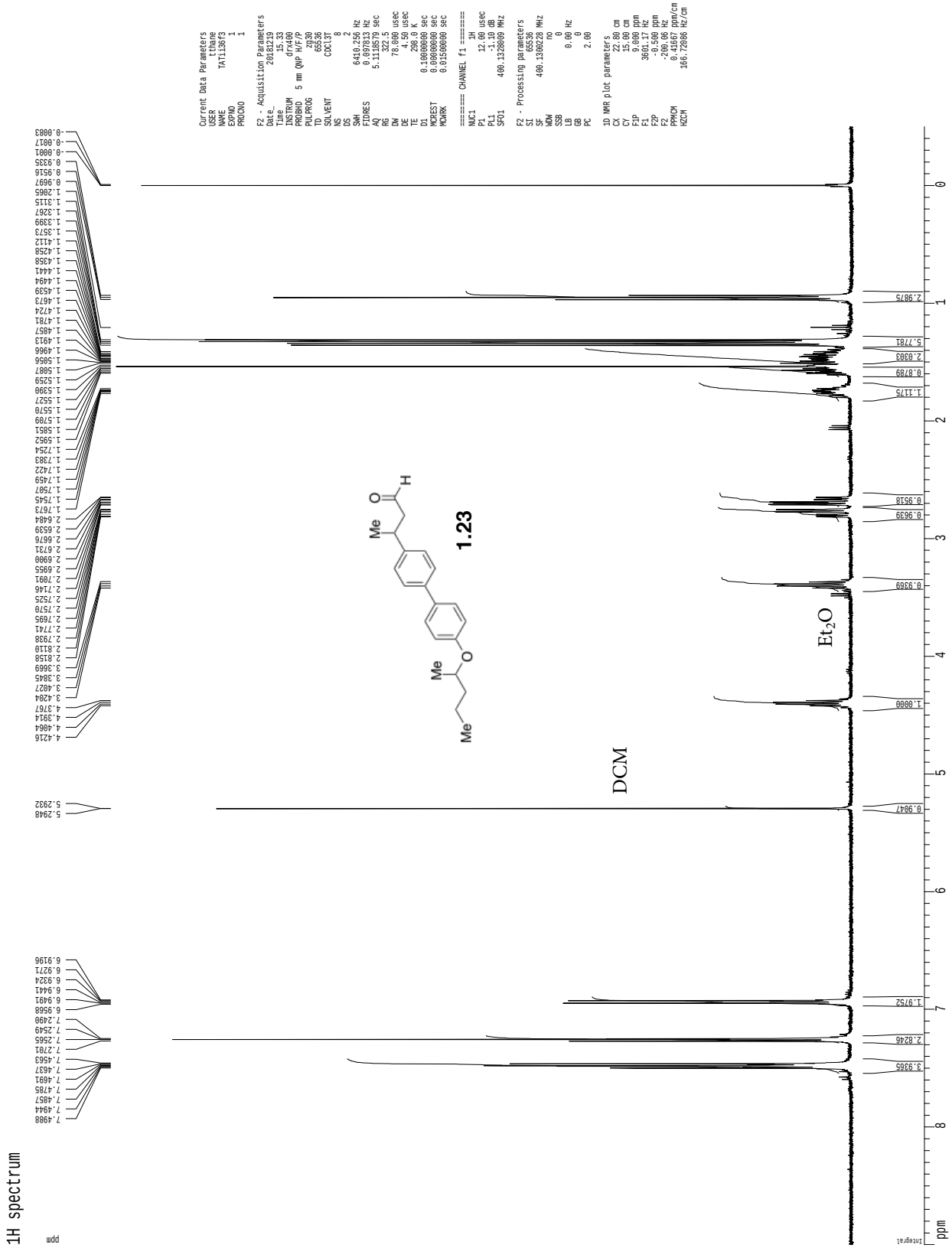
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 8.33333 ppm/cm
HZCM 1048.17017 Hz/cm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Current Data Parameters
USER tihane
NAME TA1113675
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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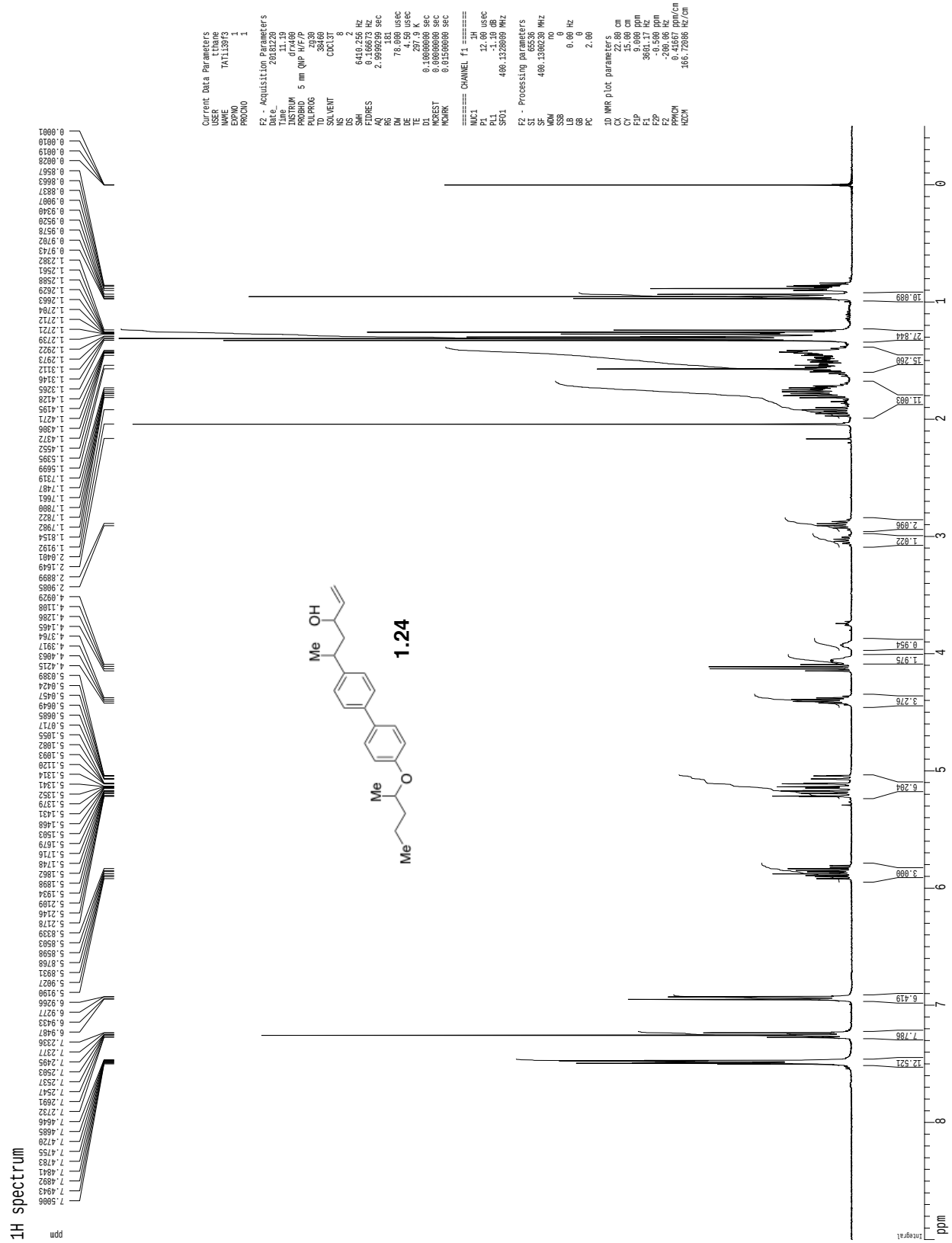
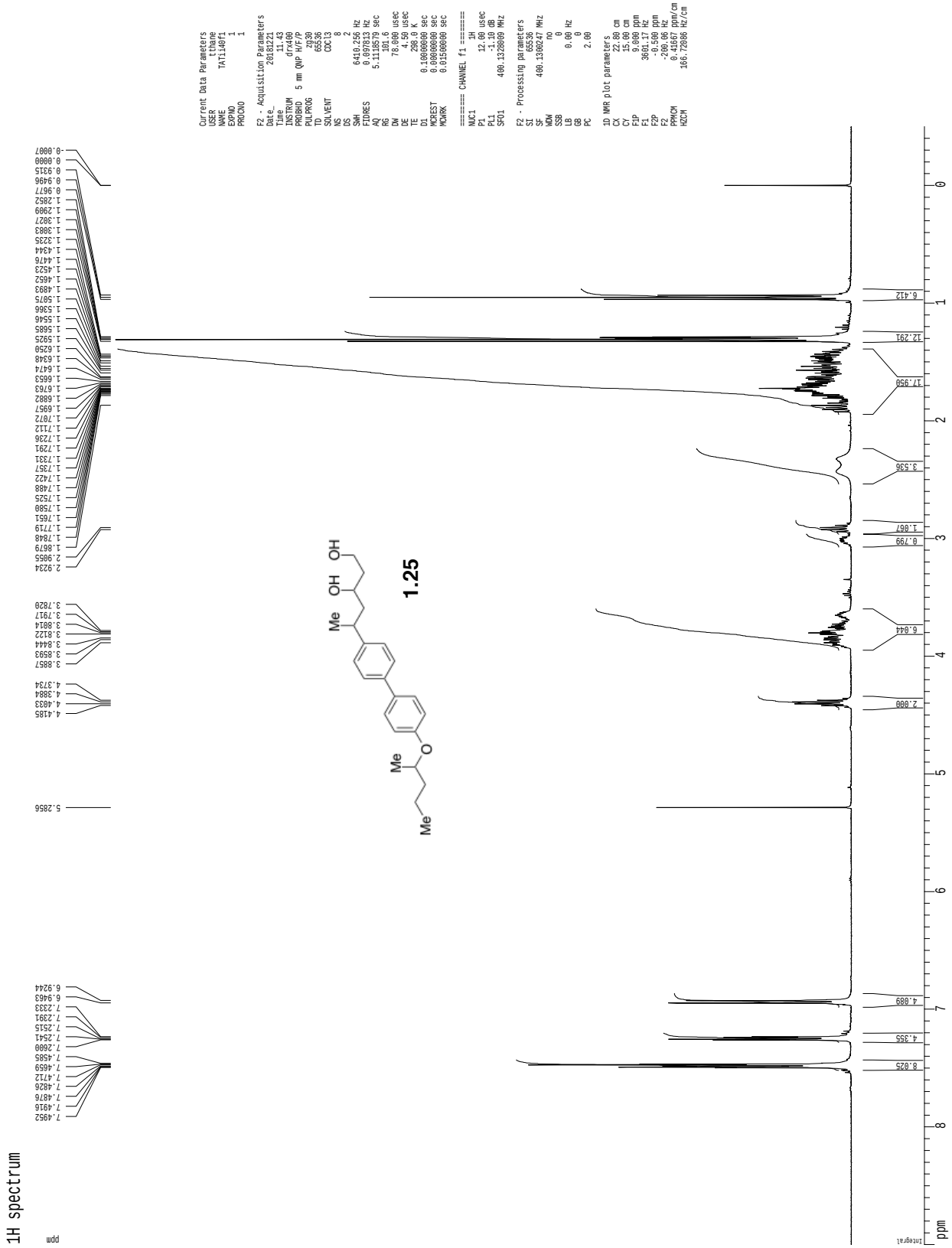
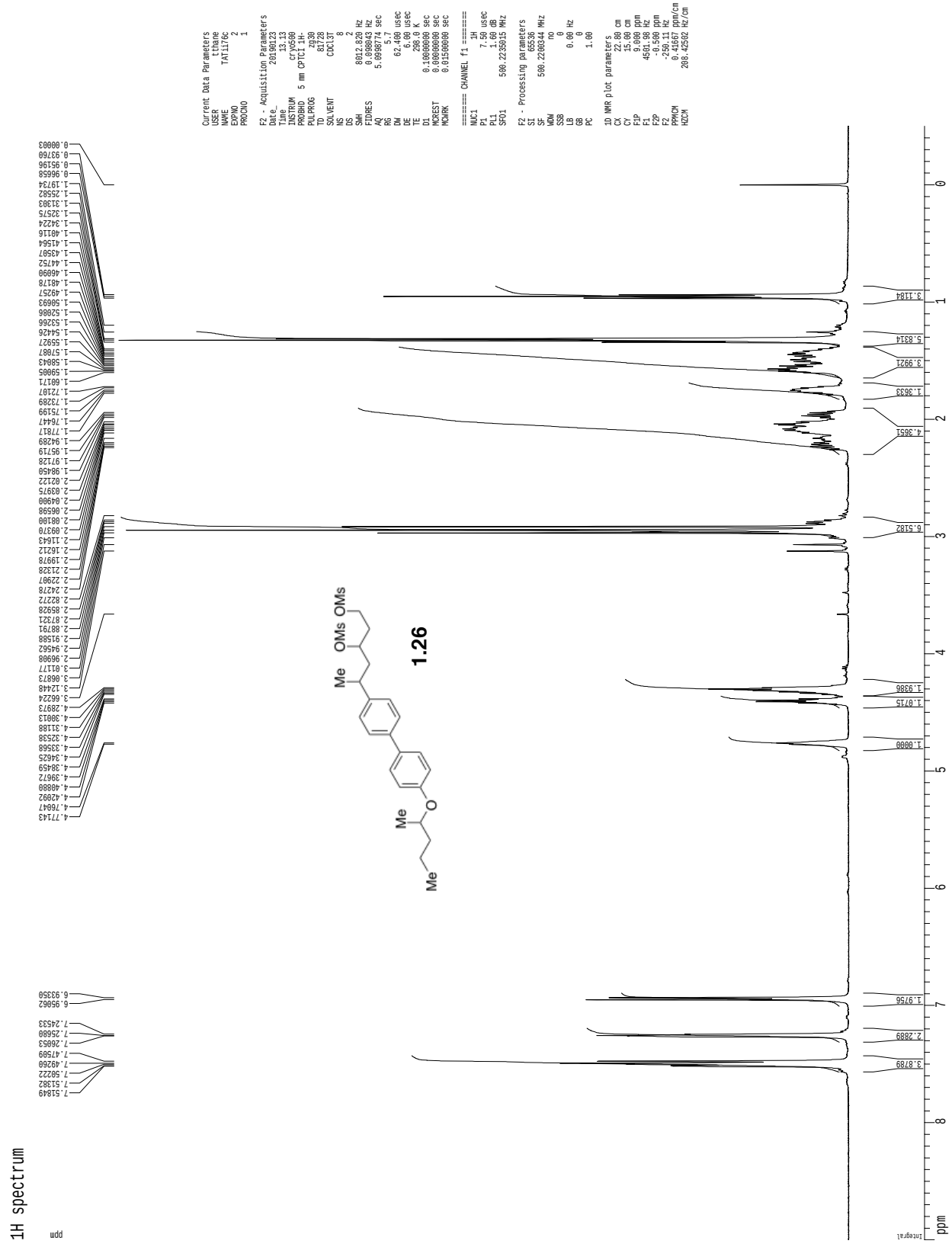
Time 15.33
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 322.5
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300228 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
1.23
DCM
Et2O
ppm
Integral


1H spectrum
Current Data Parameters
USER tihane
NAME TA1113973
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181220
Time 11.19
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 36848
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.166673 Hz
AQ 2.9999209 sec
RG 181
DW 78.000 usec
DE 4.50 usec
TE 297.3 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300230 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
Me
OH
Me
O
Me
1.24
10.089
27.844
15.260
11.003
2.096
1.022
0.954
1.975
3.276
6.204
3.000
6.419
7.786
12.521
ppm
Integral


1H spectrum
Current data Parameters
USER tihane
NAME TA1114071
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181221
Time 11.43
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 101.6
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300247 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
1.25
Me
OH
OH
Me
Me
O
7.4952
7.4916
7.4876
7.4826
7.4712
7.4659
7.4585
7.2600
7.2541
7.2515
7.2391
7.2333
6.9463
6.9244
5.2856
4.4185
4.4033
4.3884
4.3734
3.8857
3.8593
3.8444
3.8122
3.8014
3.7917
3.7620
2.9234
2.9055
1.8679
1.7848
1.7719
1.7661
1.7580
1.7525
1.7488
1.7422
1.7357
1.7331
1.7291
1.7236
1.7112
1.7072
1.6957
1.6882
1.6763
1.6653
1.6474
1.6348
1.6250
1.5925
1.5685
1.5546
1.5366
1.5075
1.4893
1.4652
1.4523
1.4476
1.4344
1.4236
1.3827
1.3083
1.2909
1.2852
0.9677
0.9496
0.9315
0.0000
-0.0007
6.412
12.291
17.950
3.536
1.067
0.799
6.044
2.000
4.089
4.355
8.025
Integral
ppm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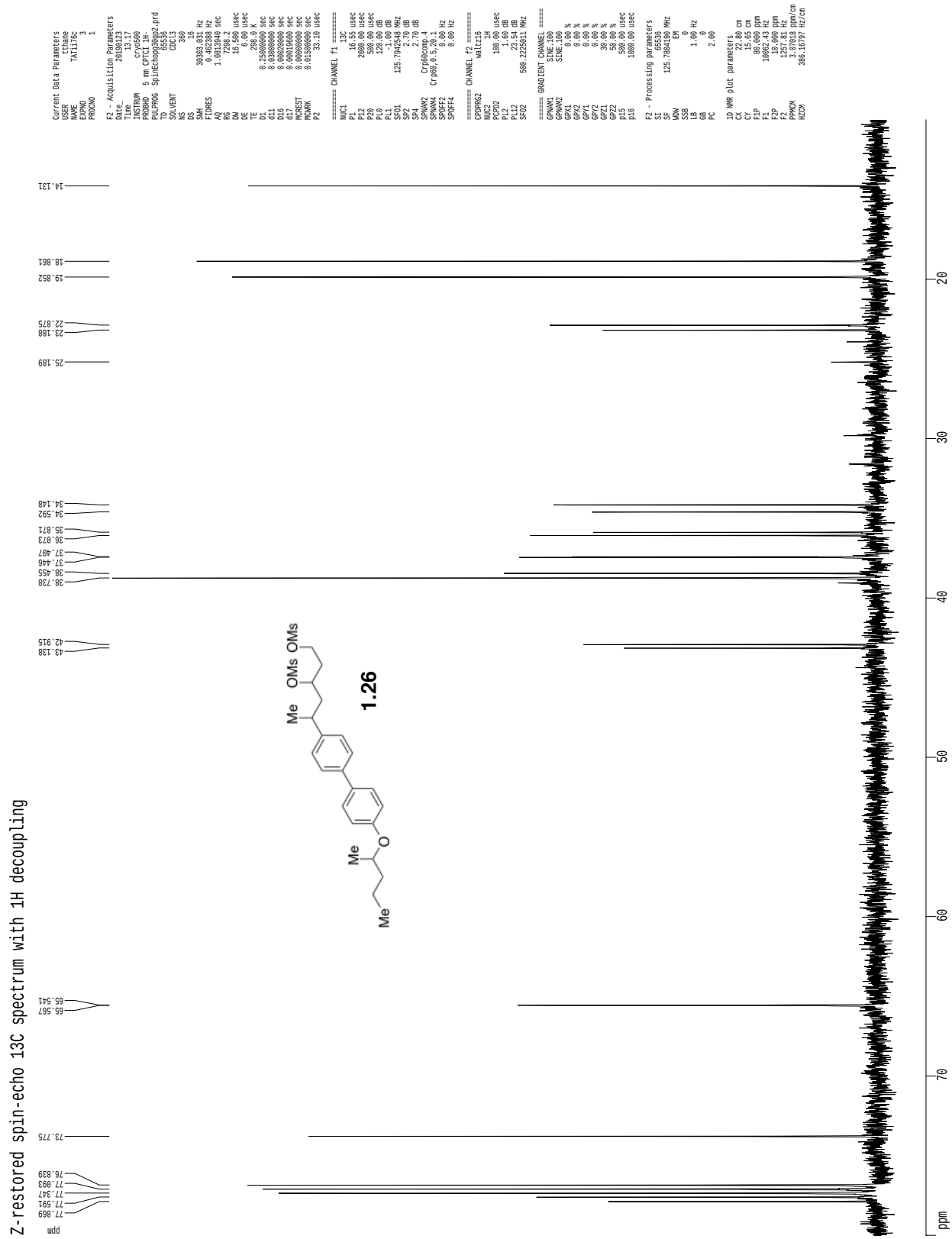
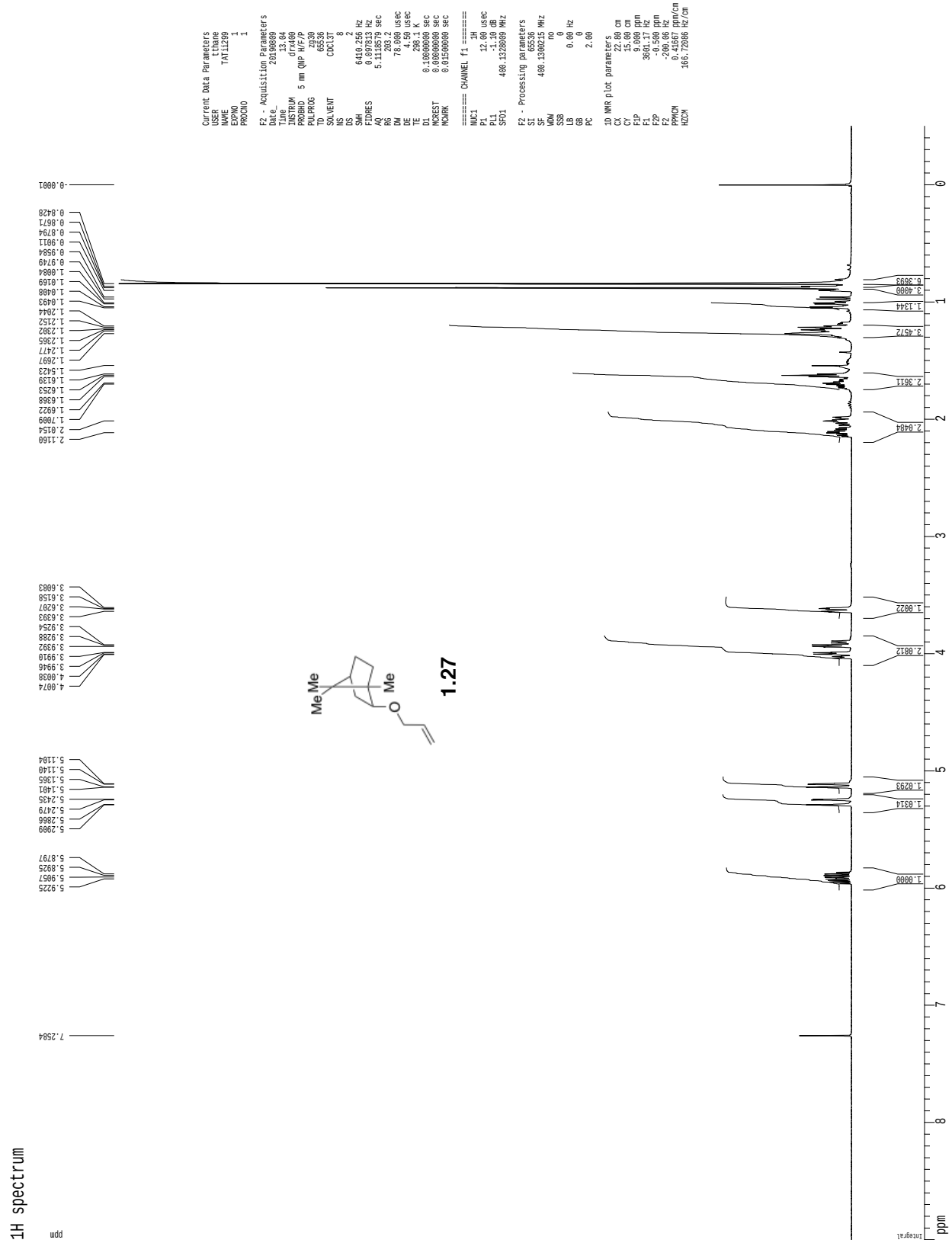
USER tihane
NAME TAT1176c
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190123
Time 13.13
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.090843 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200344 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
Me
OMs
OMs
Me
O
Me
1.26
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
Me OMs OMs
1.26
Me
O
Me
ppm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Current data Parameters
USER ttihane
NAME TAT11299
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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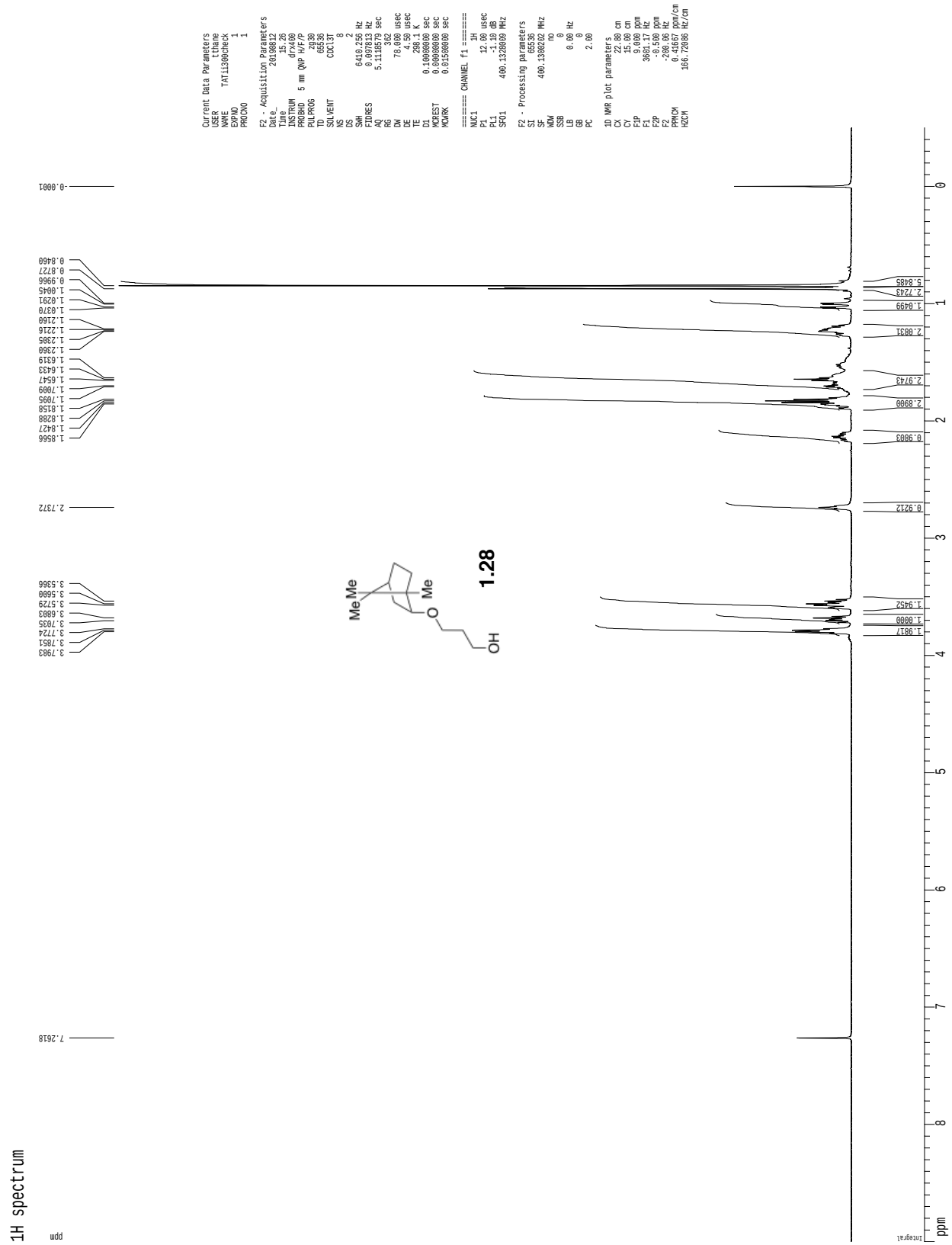
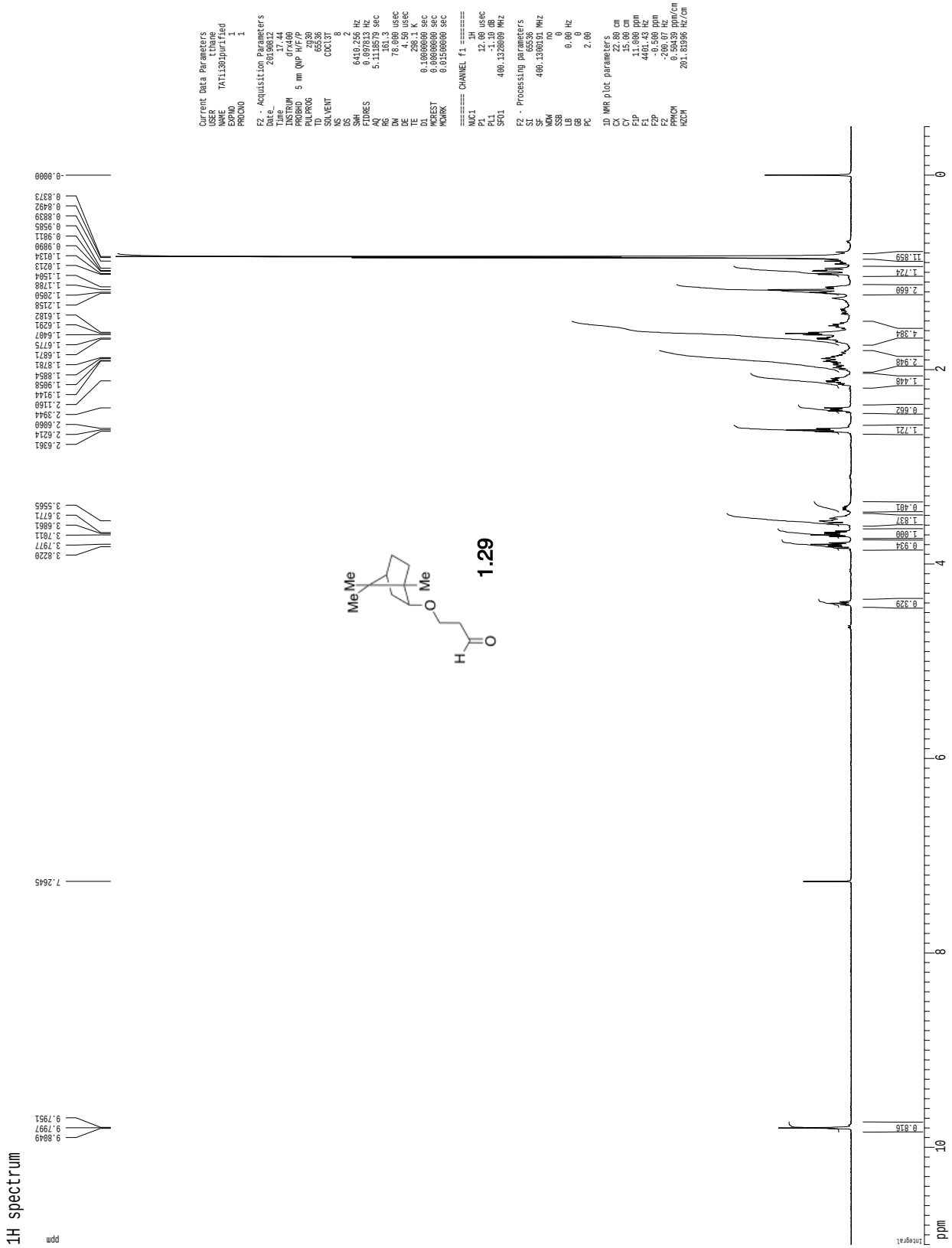
Time 13.04
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 203.2
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.09000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300215 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
Me
Me
Me
O
1.27
ppm
Integral


1H spectrum
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
1.28
ppm
Integral


1H spectrum
Current data Parameters
NAME tthane
EXPNO TATi130purified 1
PROCNO 1
F2 - Acquisition Parameters
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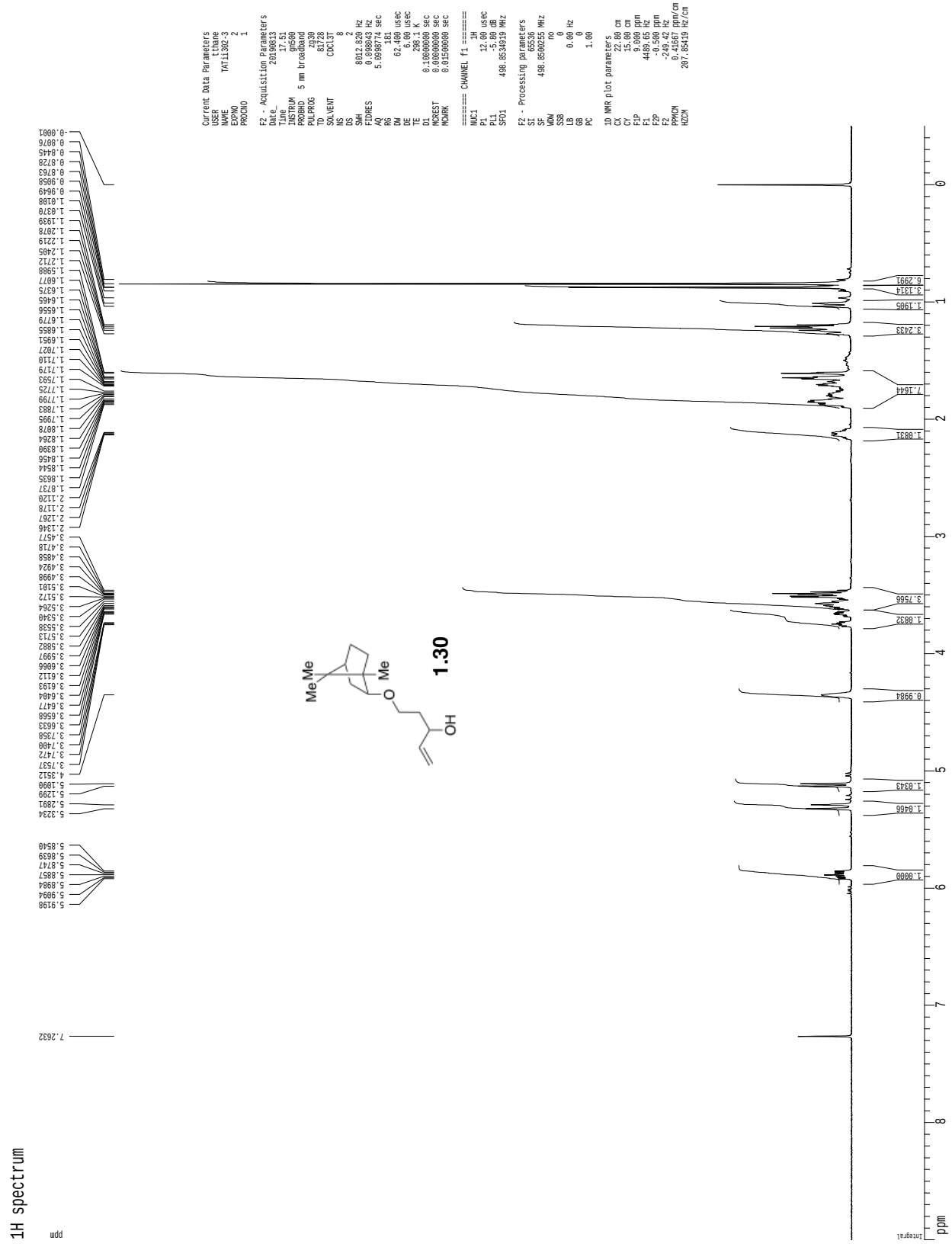
Time 17.44
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 161.3
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300191 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 11.000 ppm
F1 4401.43 Hz
F2P -0.500 ppm
F2 -200.07 Hz
PPMCM 0.50439 ppm/cm
HZCM 201.61996 Hz/cm
Me
Me
Me
O
O
H
1.29
ppm
Integral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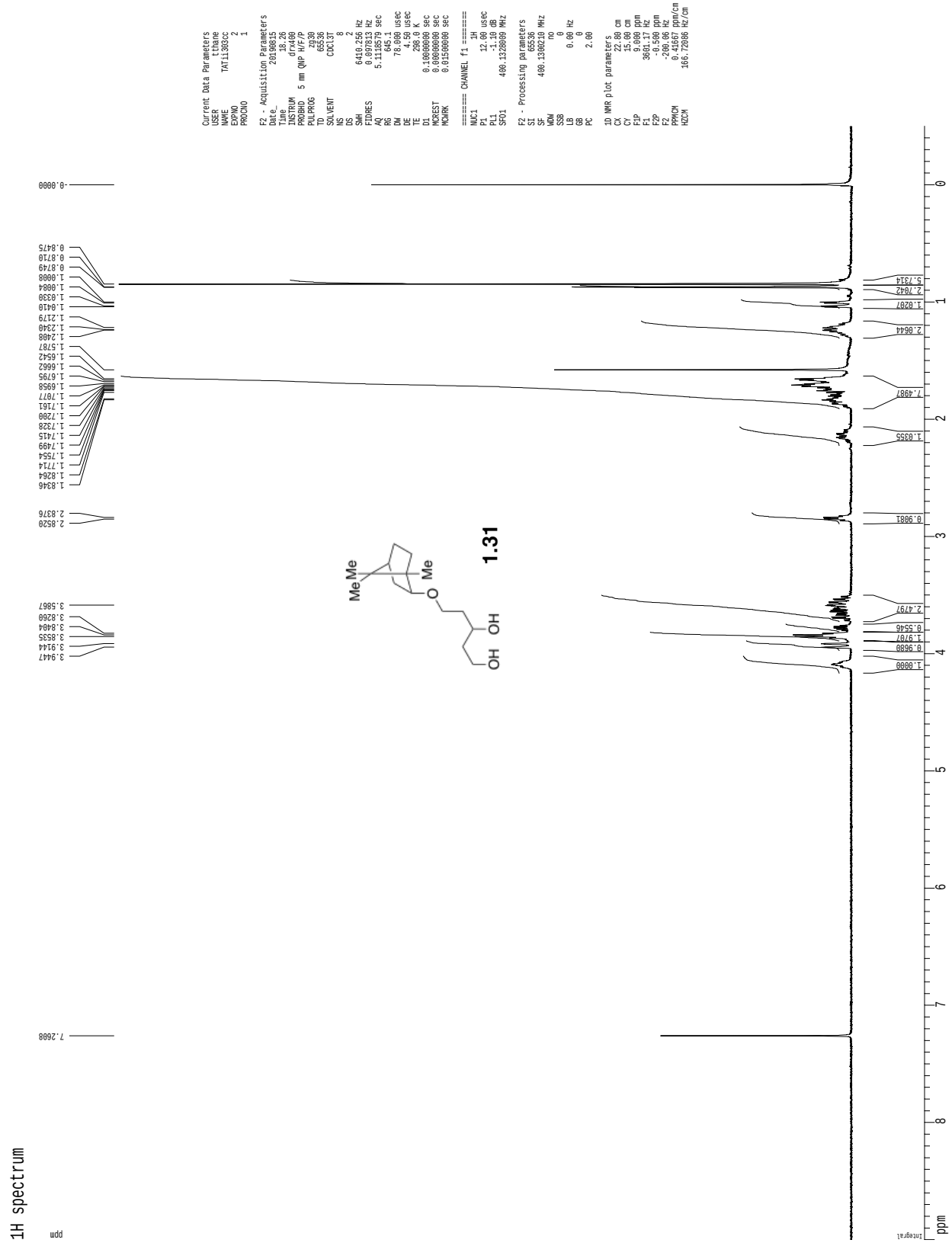
1.30
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral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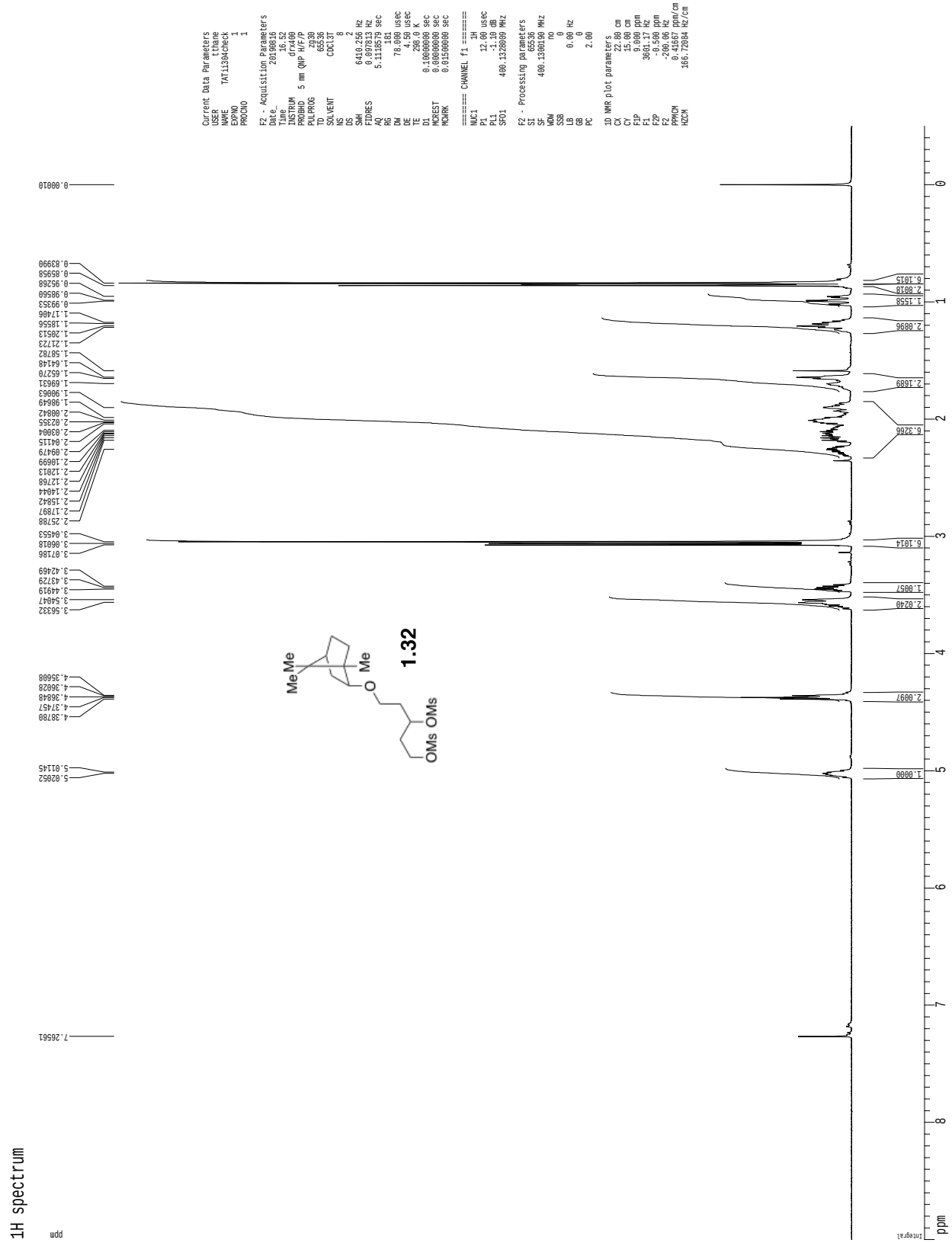
Current data Parameters
USER tthane
NAME TAT113030cc
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190815
Time 18.26
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 645.1
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300210 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
Me
Me
Me
O
OH
OH
1.31
ppm
Integral


1H spectrum
Current Data Parameters
USER tihane
NAME TAT113904check
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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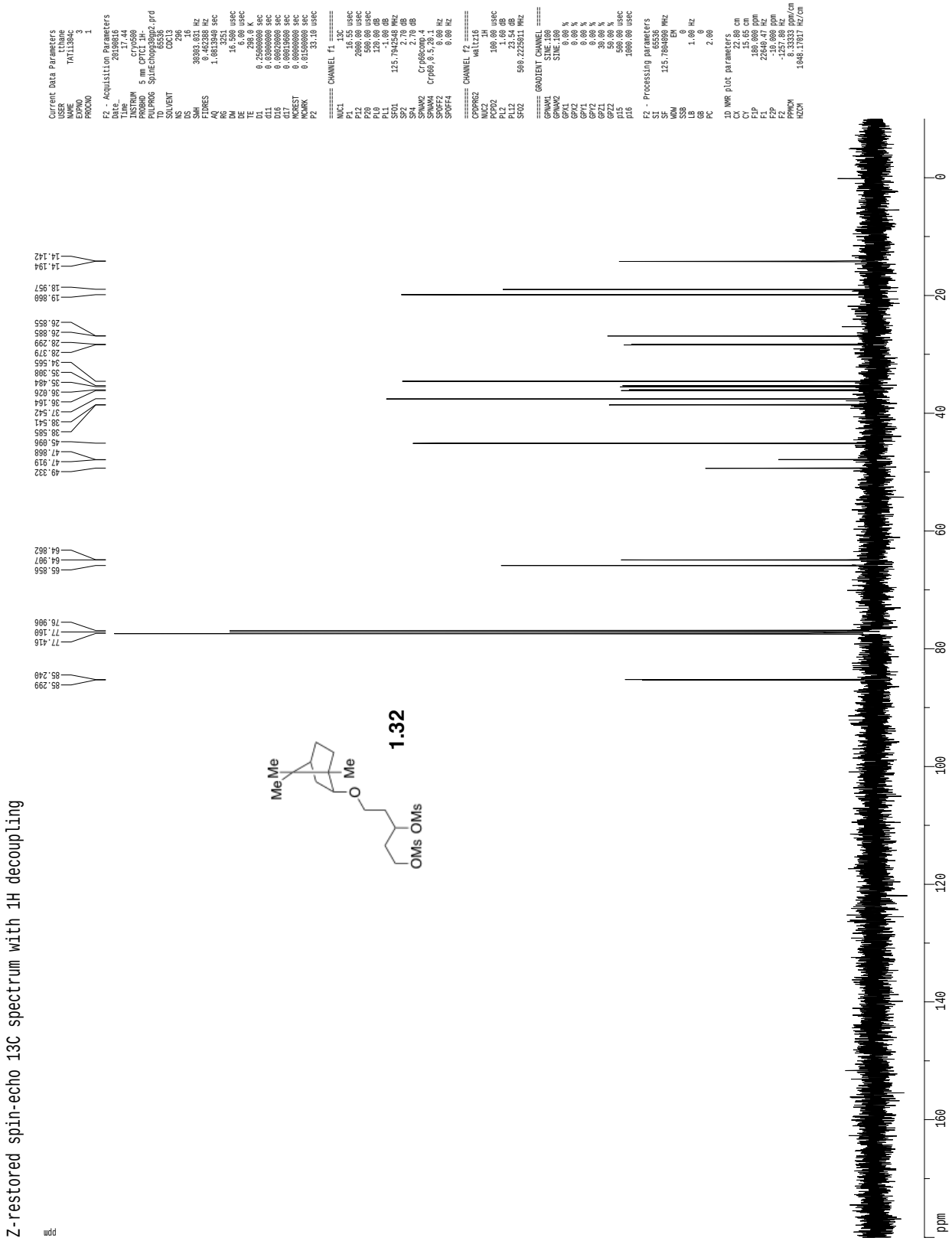
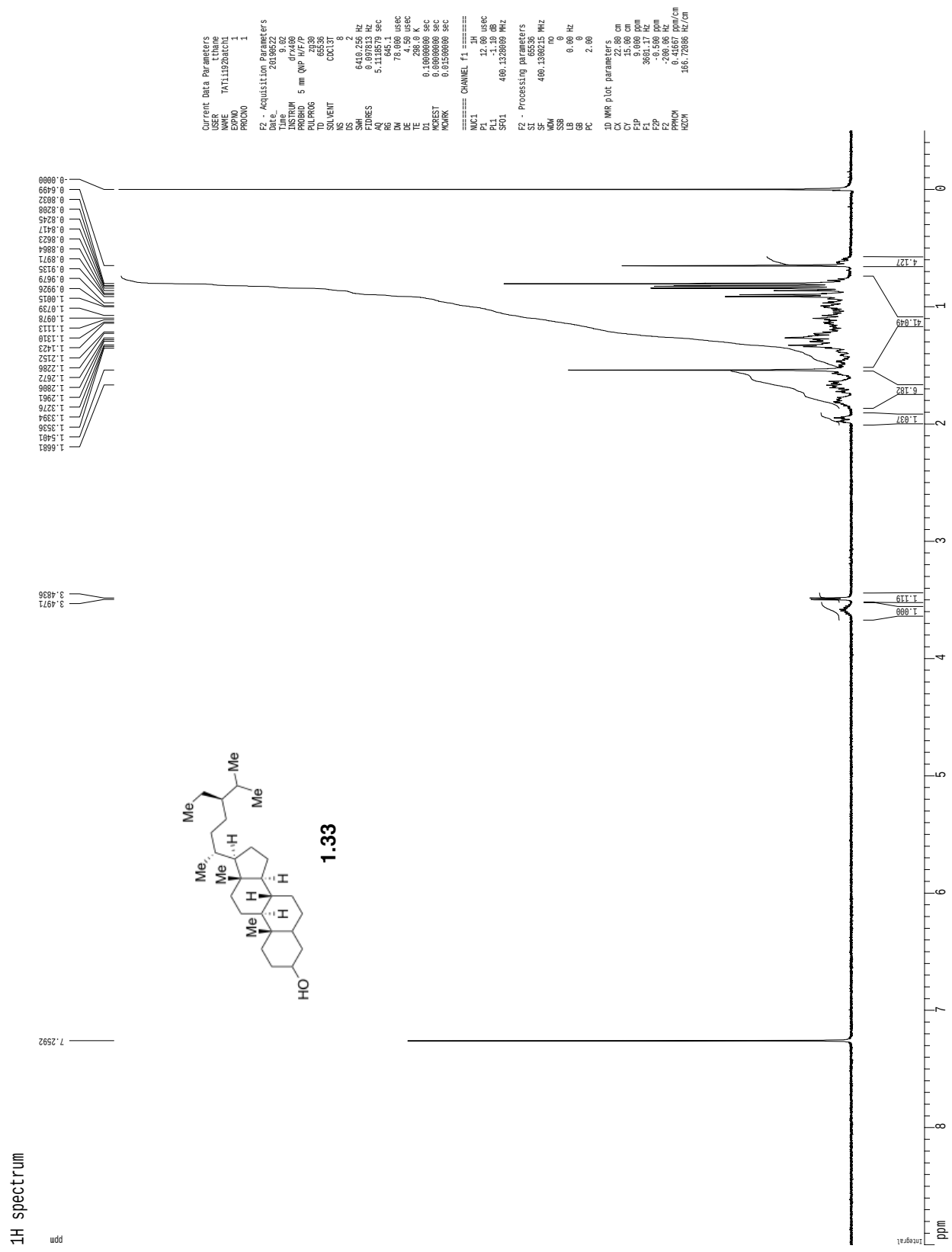
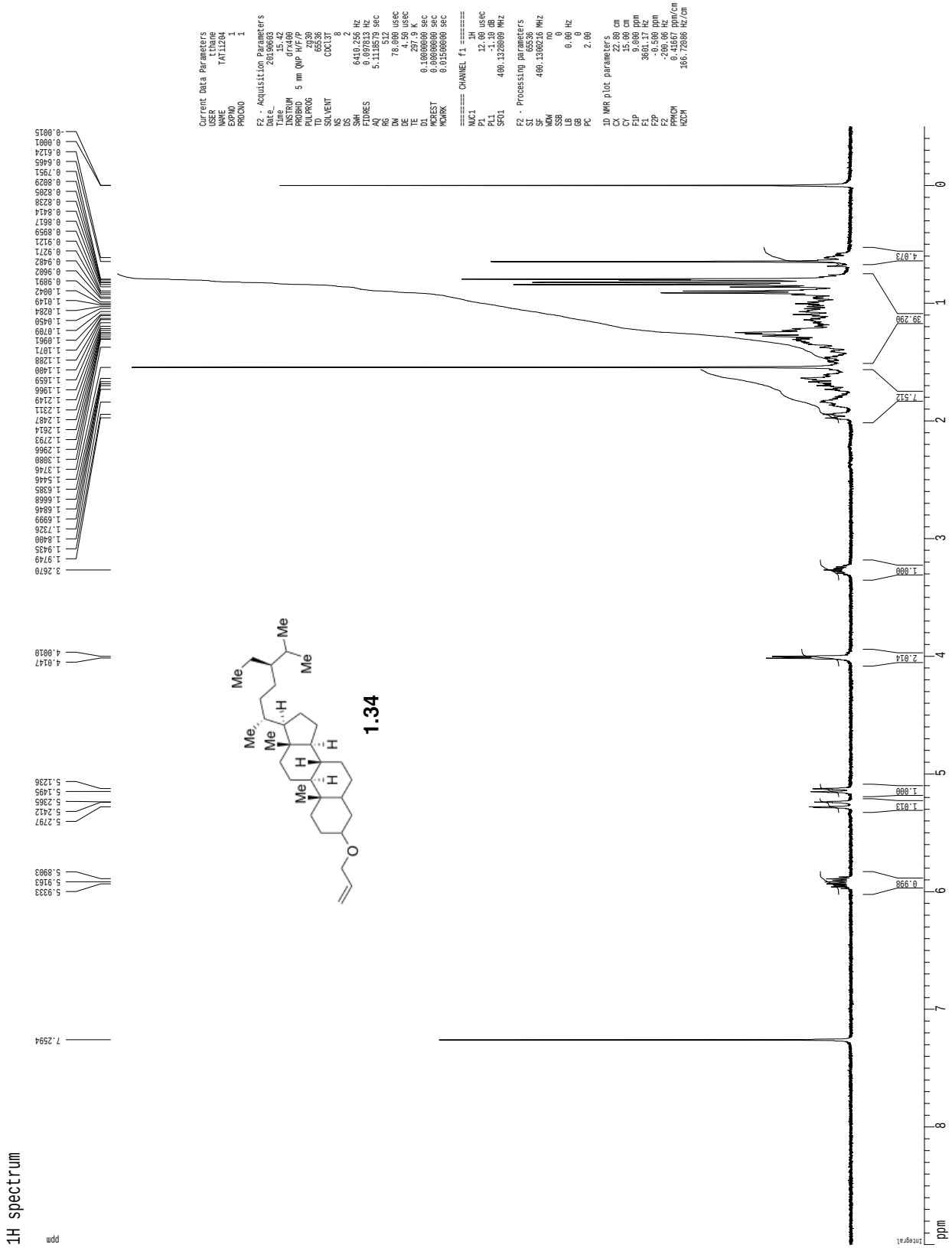
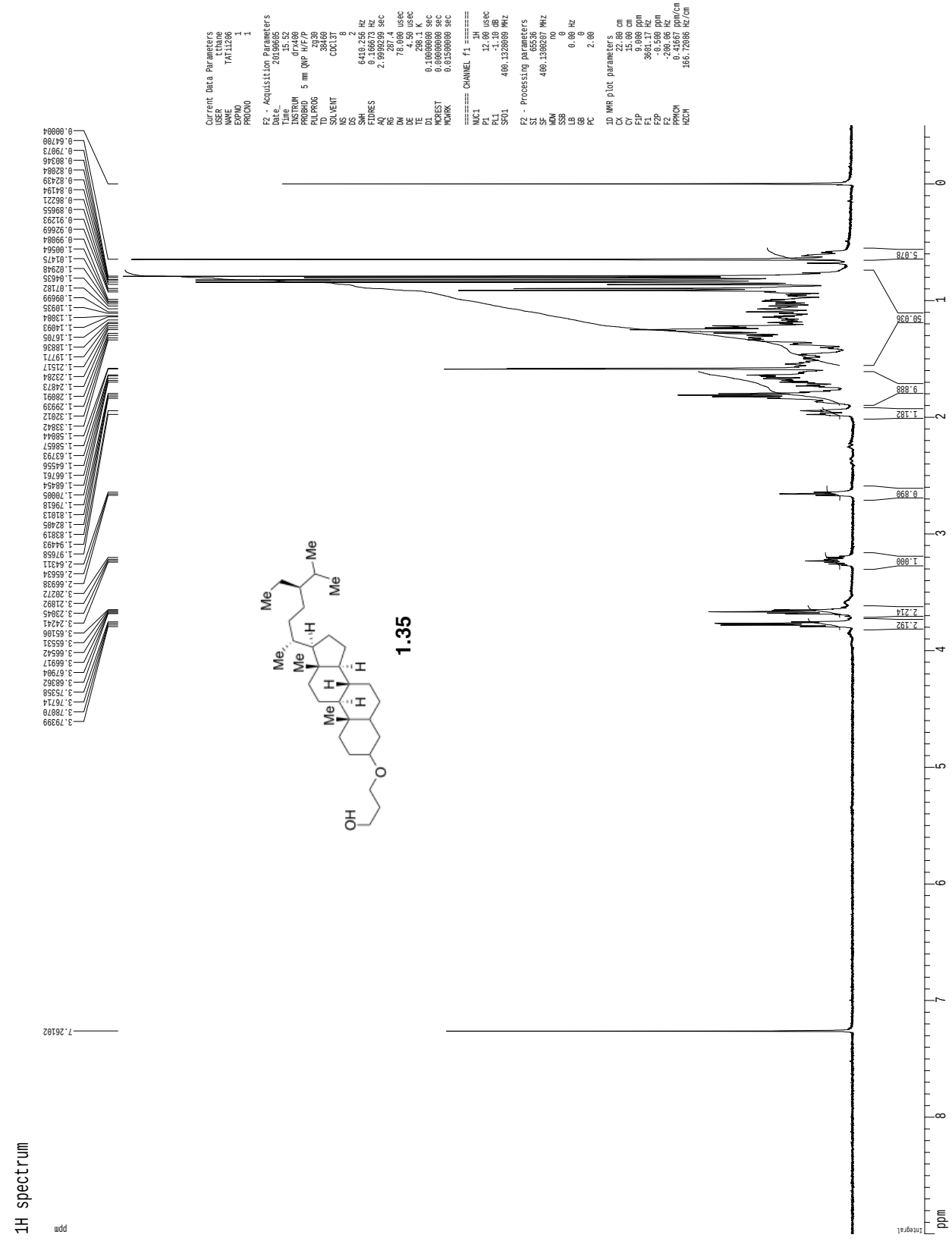
Time 16.52
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 161
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300190 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72604 Hz/cm
Me
Me
Me
O
OMs
OMs
1.32
ppm
Integral

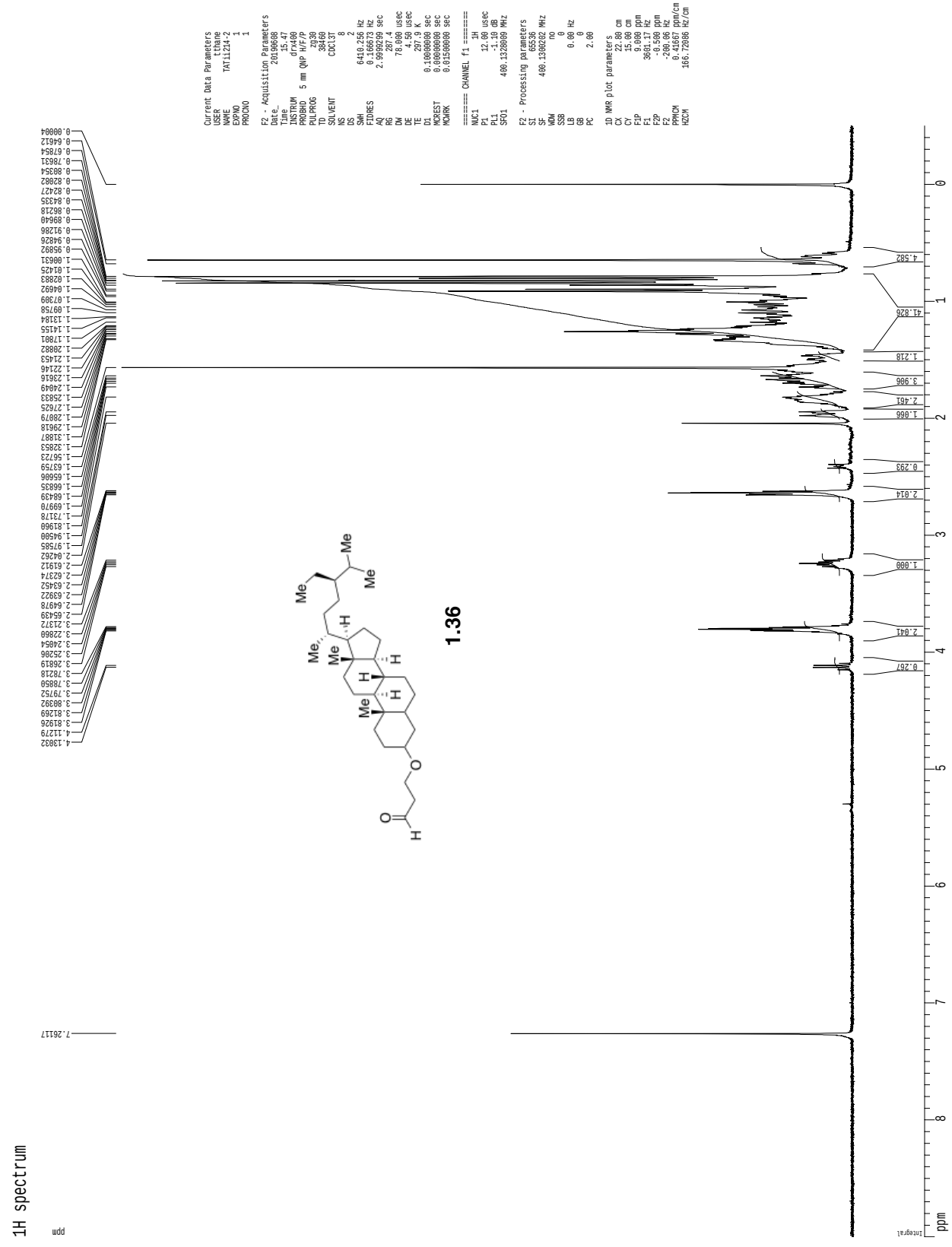
Z-restored spin-echo 13C spectrum with 1H decoupling

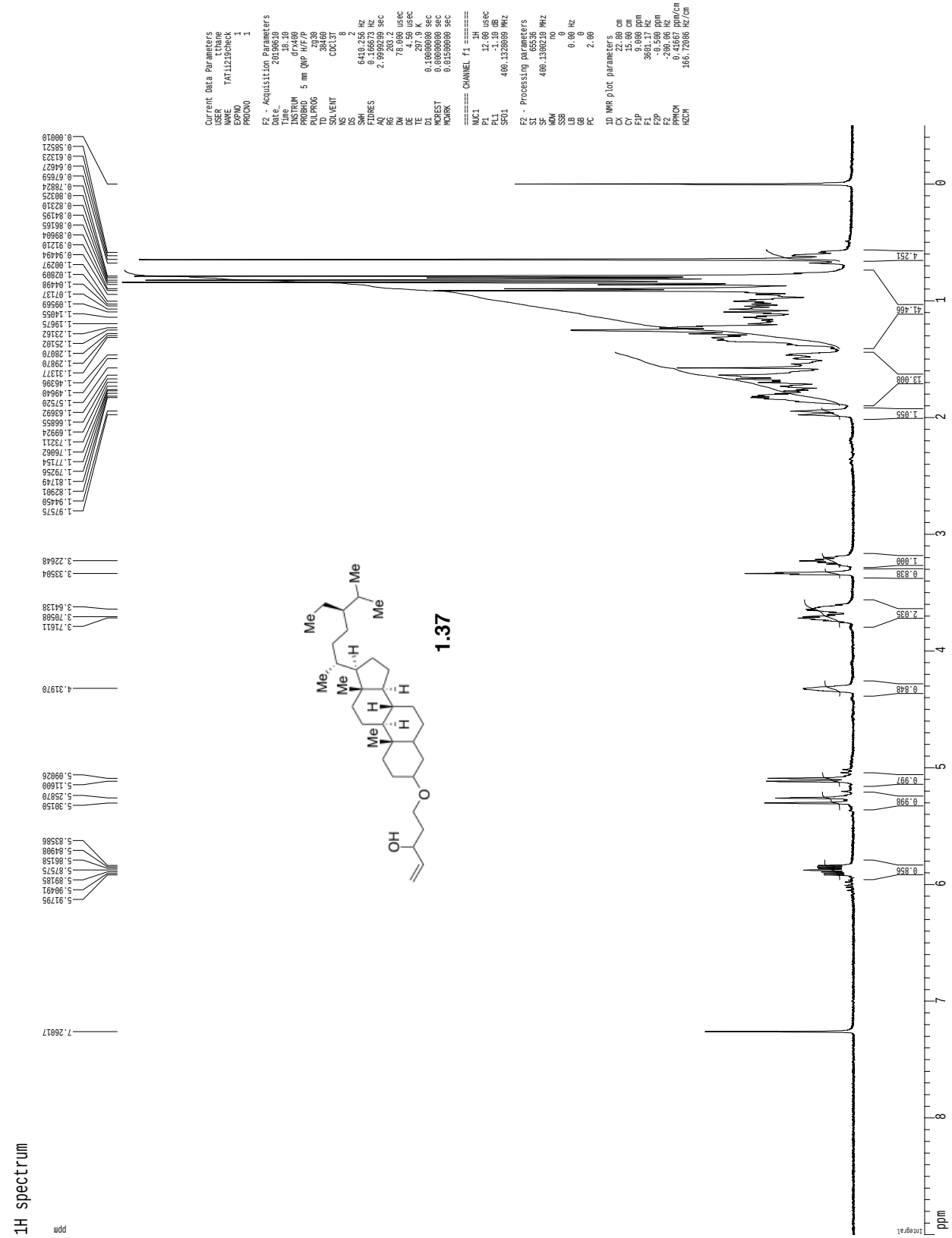


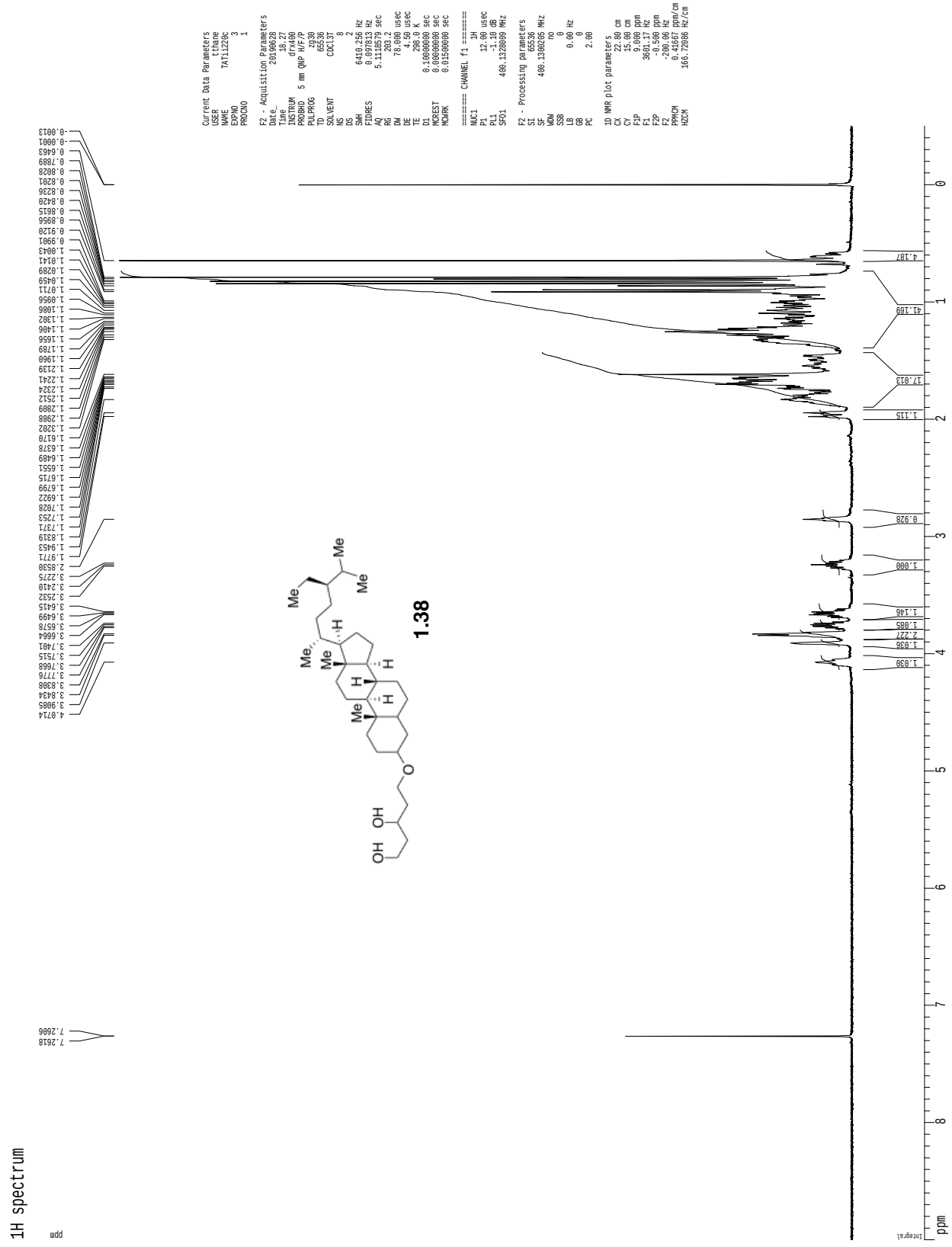

1H spectrum
1.33
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral

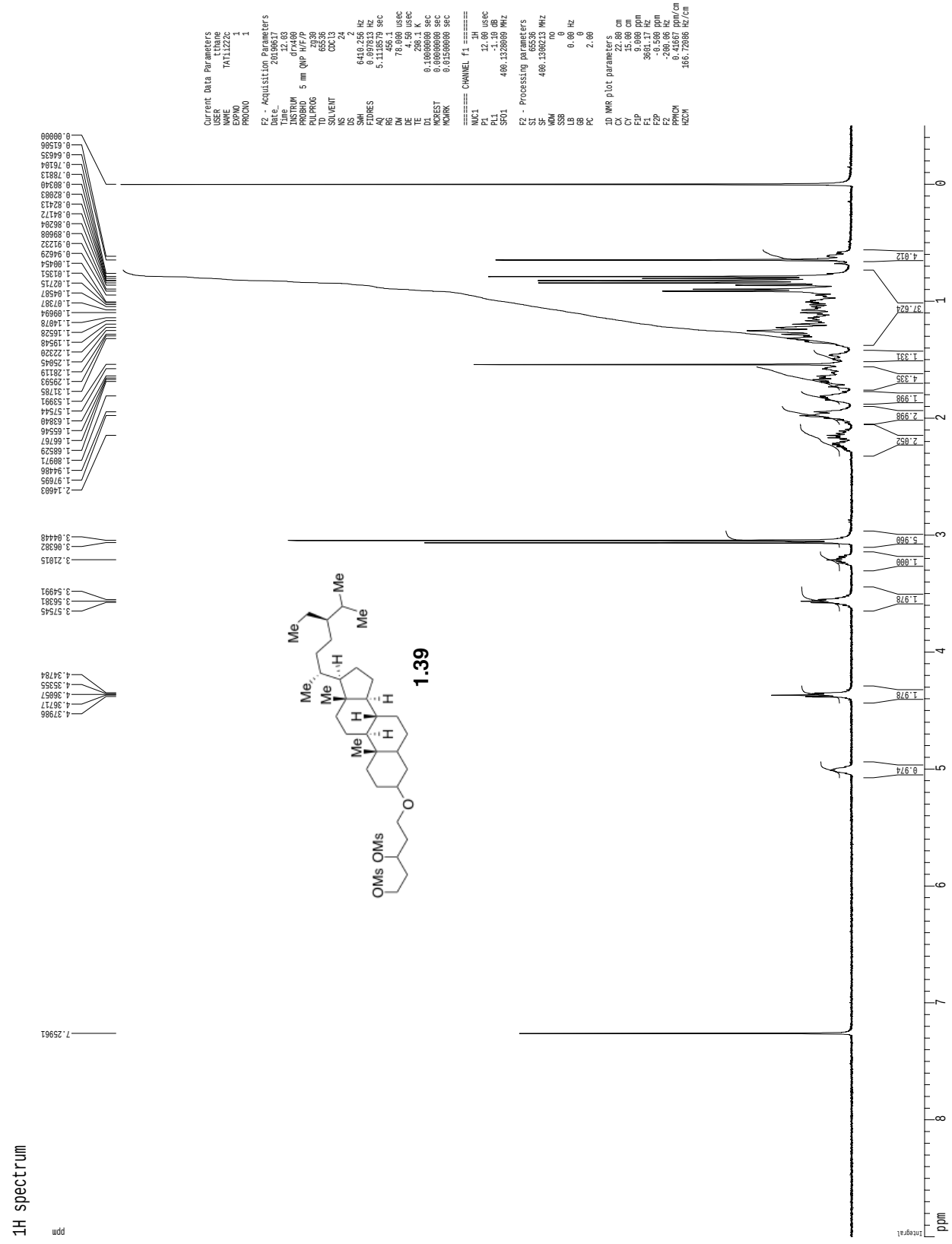

1H spectrum
1.34
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral


1H spectrum
ppm
Integral
1.35
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters

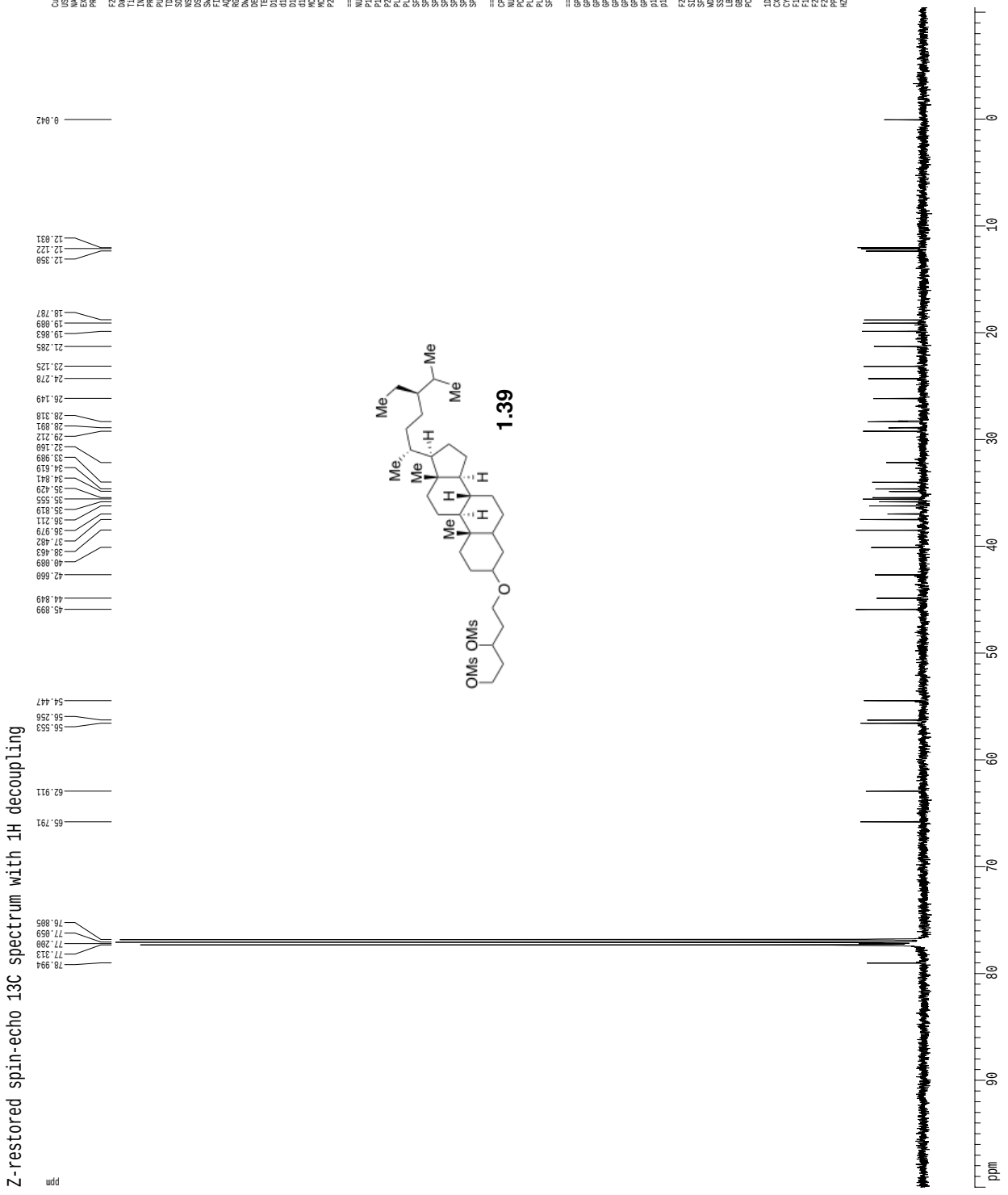

1H spectrum
1.36
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral

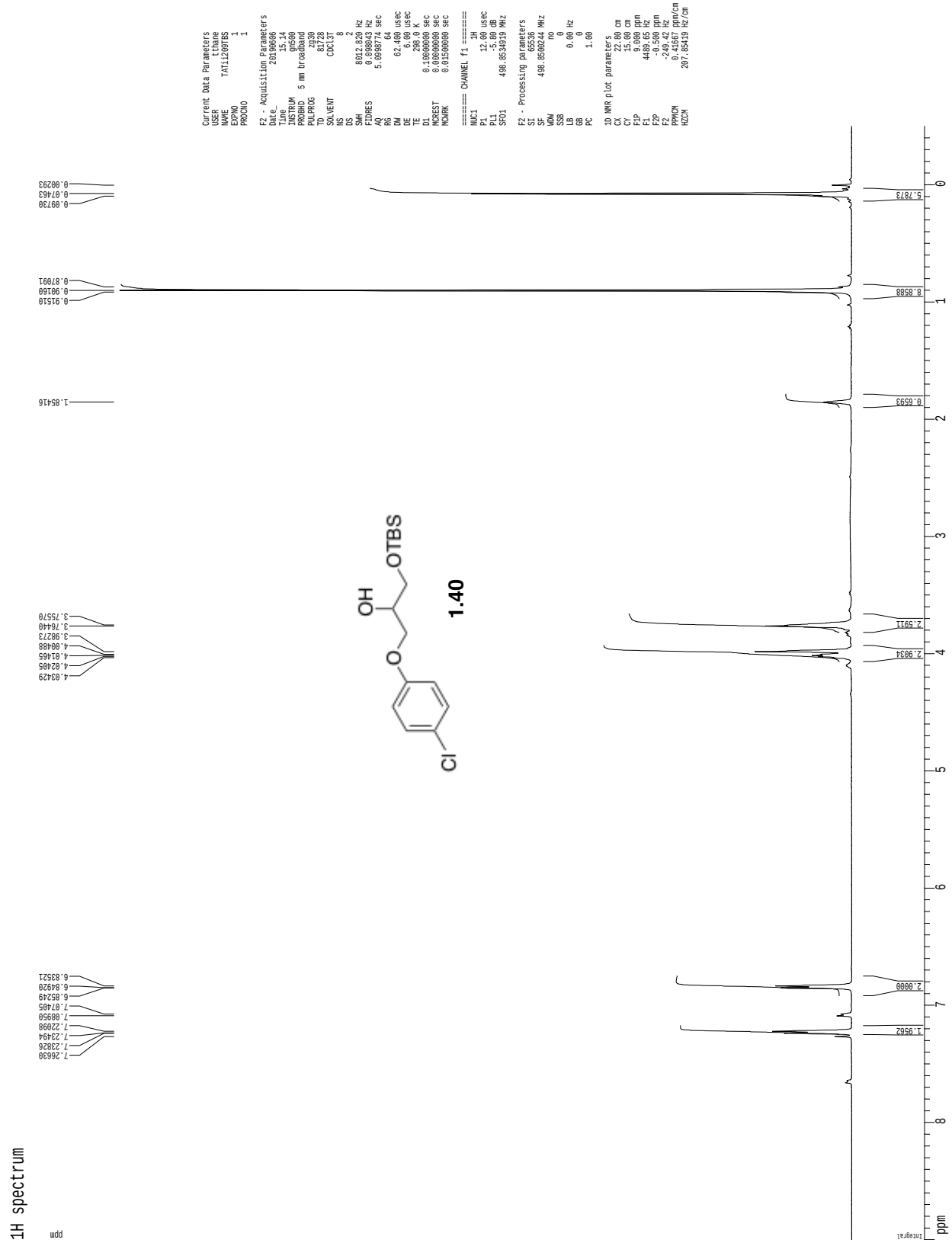

1H spectrum
1.37
Me
H
OH
O
ppm
Integral

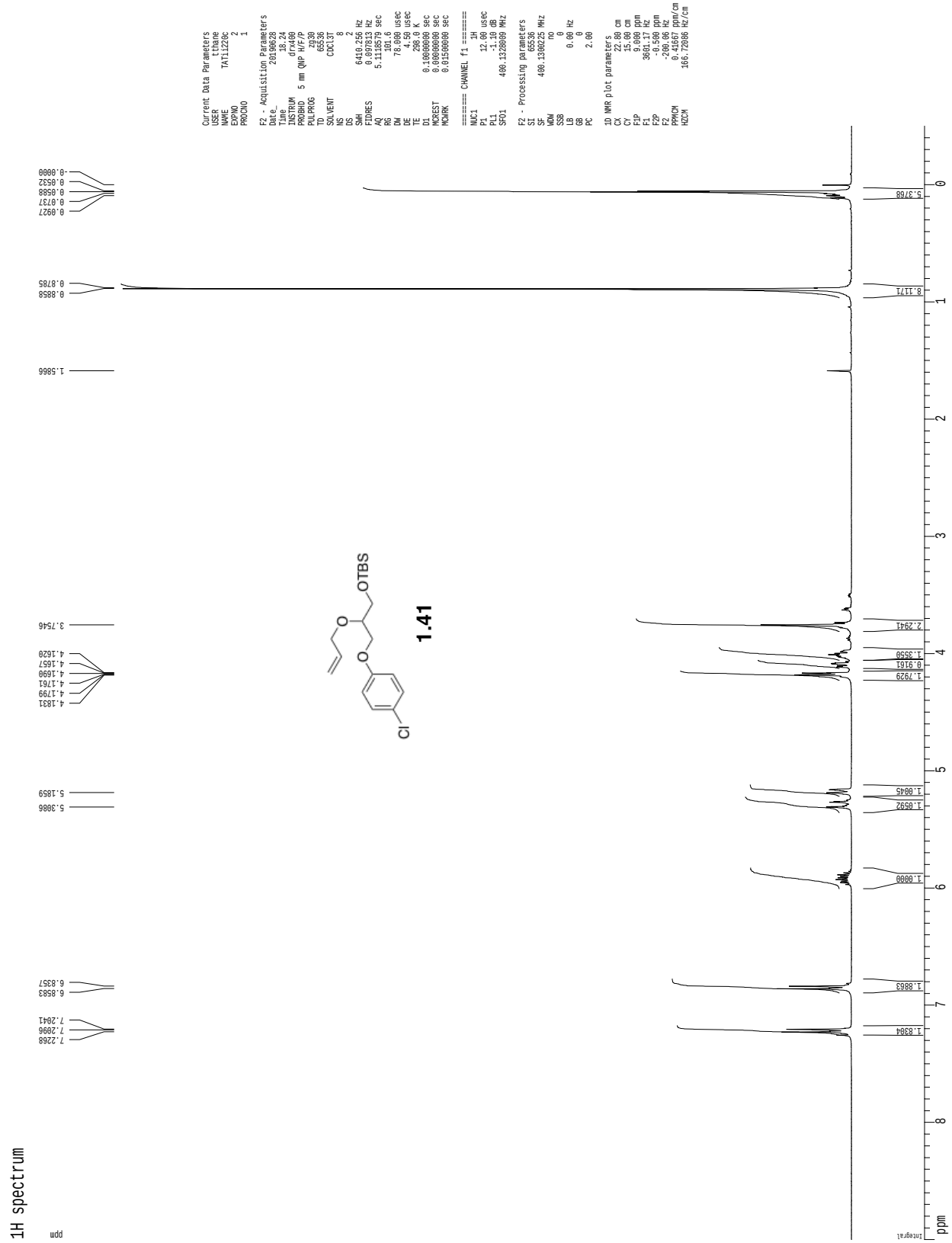

1H spectrum
ppm
Integral
1.38
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters

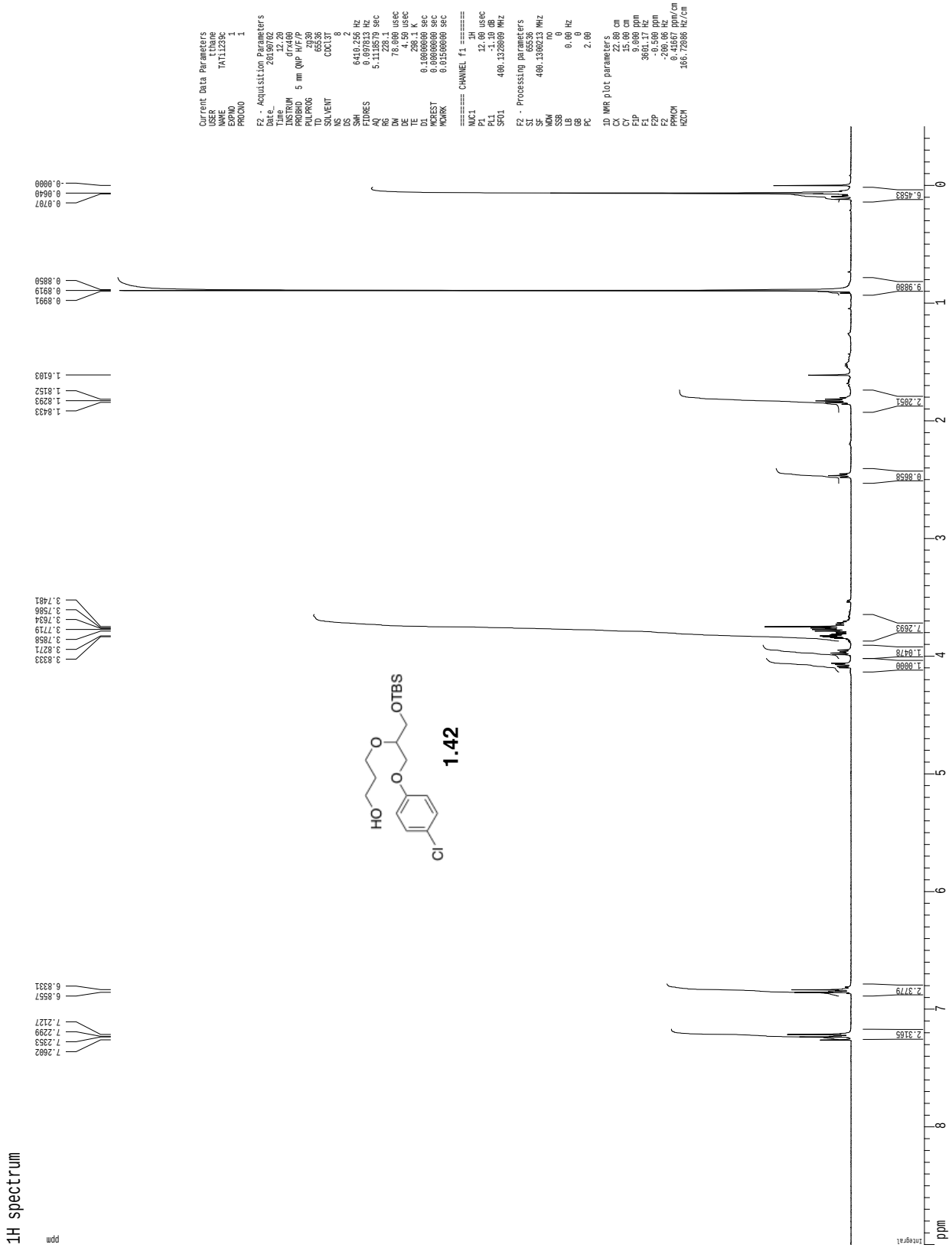

1H spectrum
1.39
OMs OMs
Me
H
O
ppm
Integral
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters

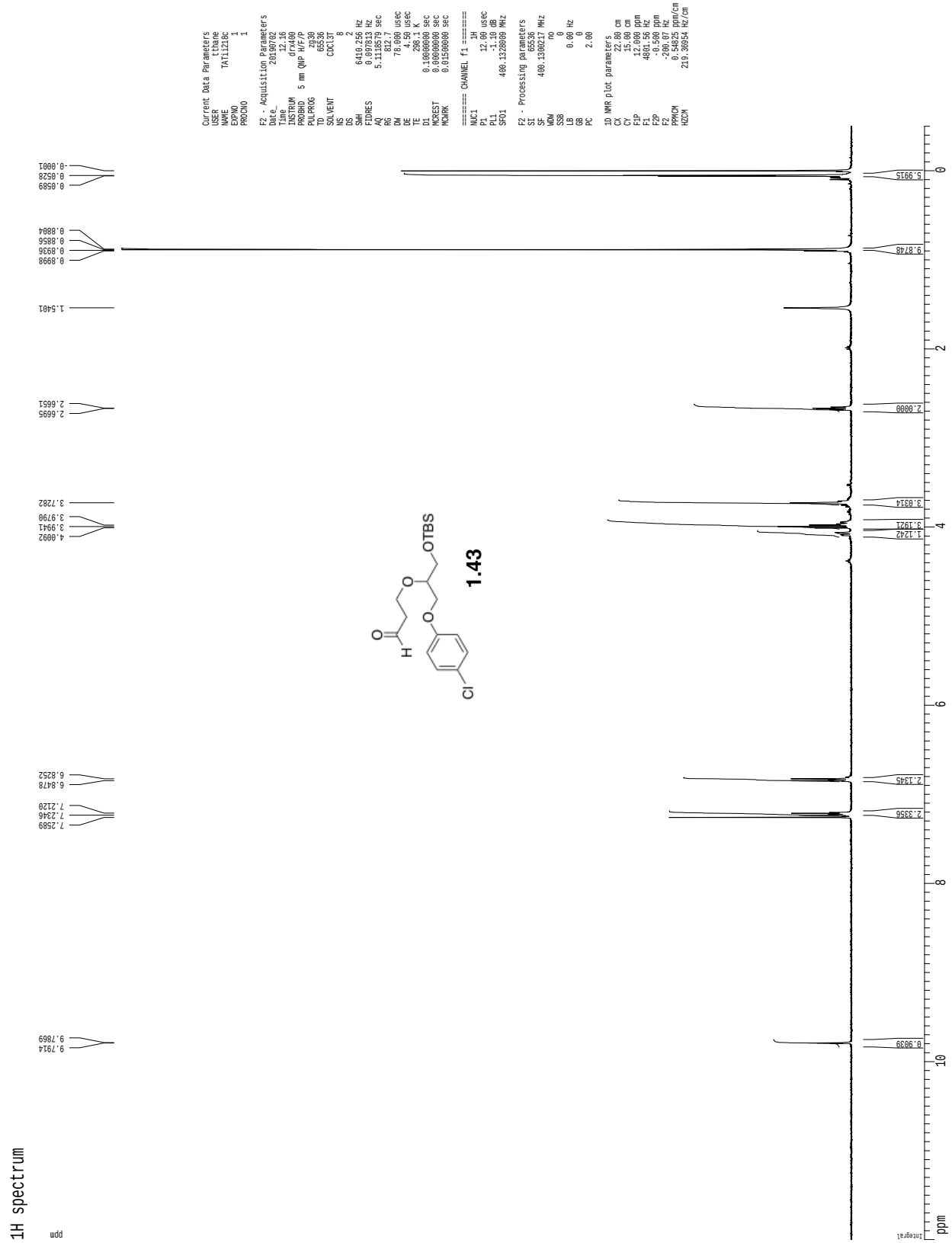
Z-restored spin-echo 13C spectrum with 1H decoupling

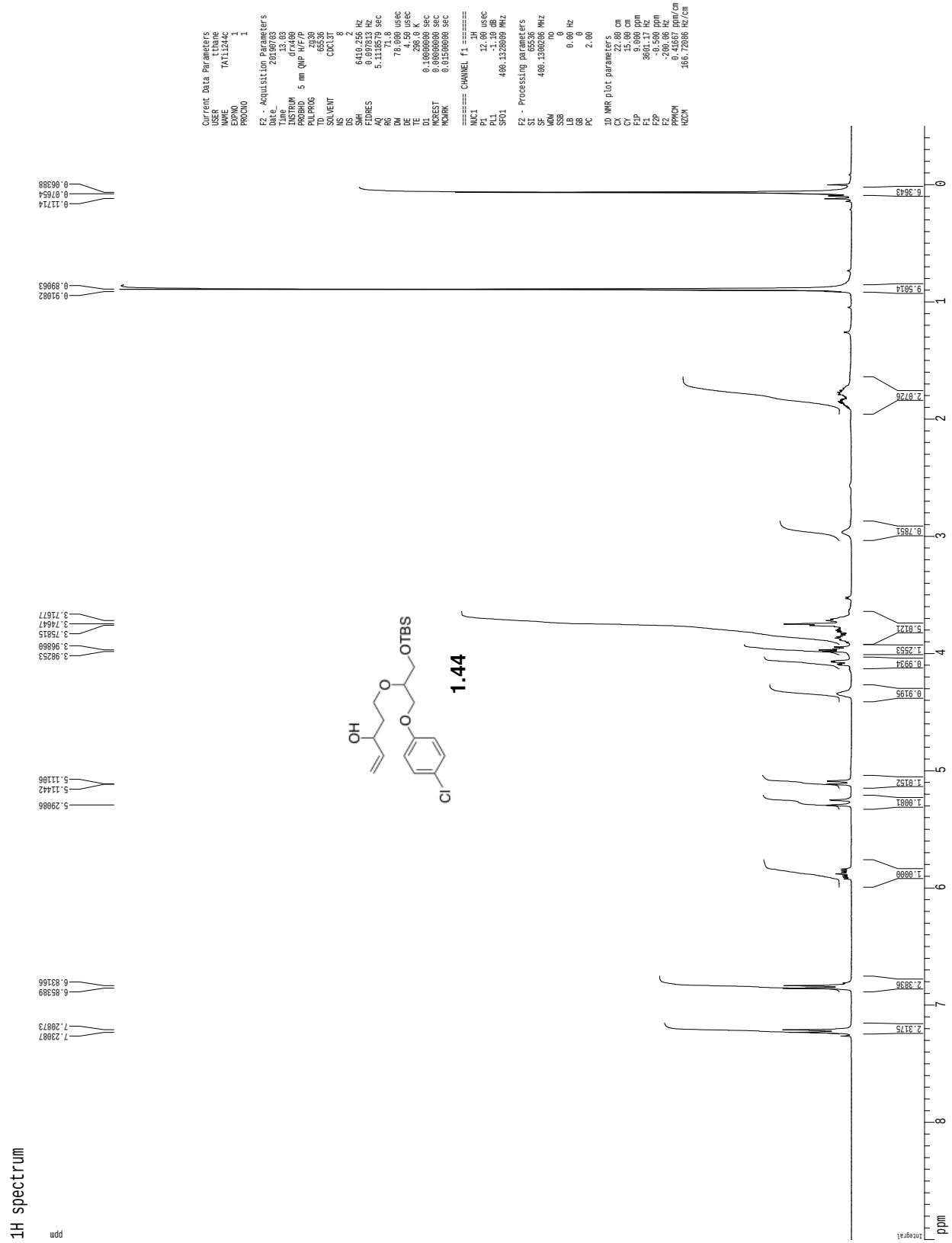


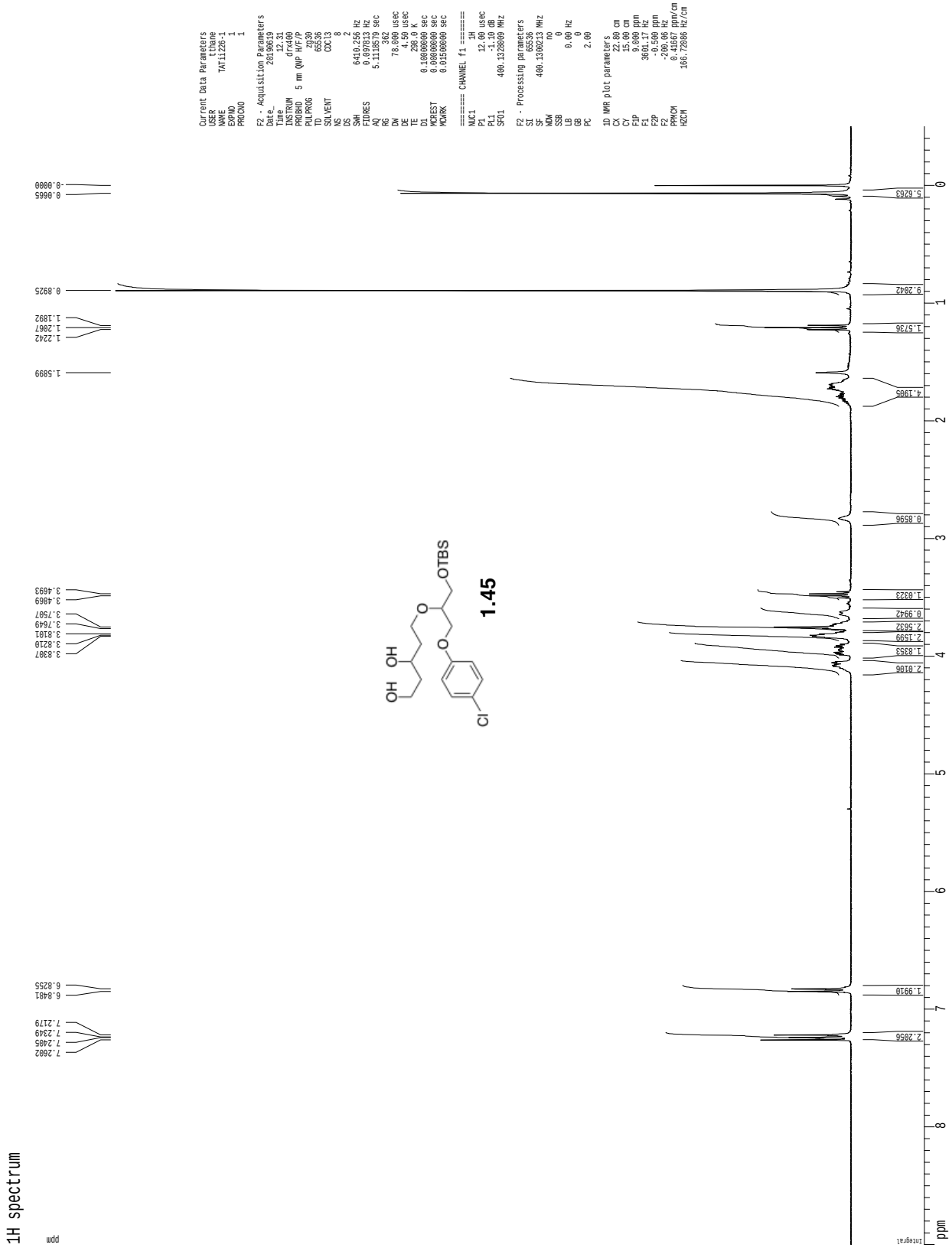

1H spectrum
ppm
Integral
OH
OTBS
Cl
1.40

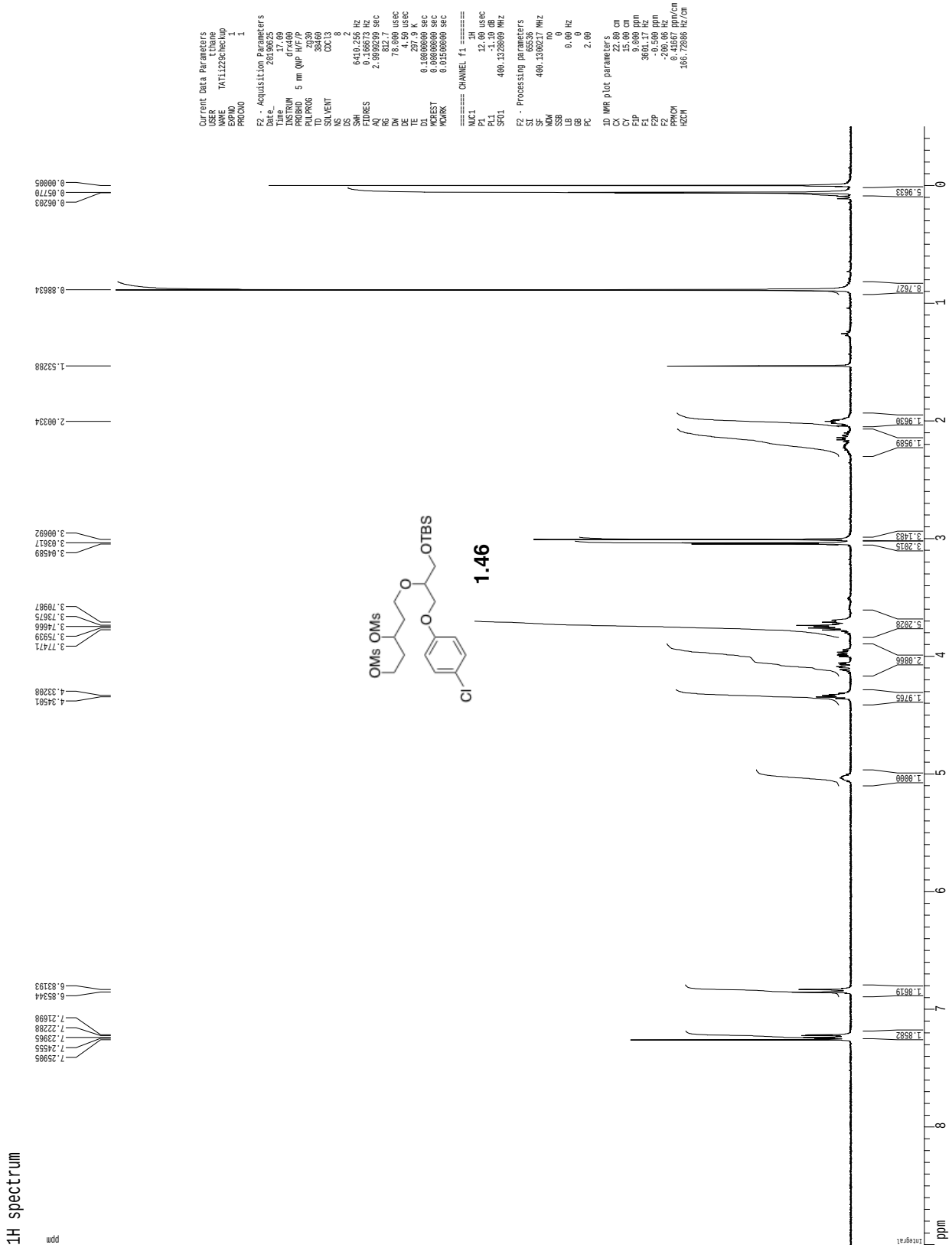

1H spectrum
Current data Parameters
NAME tihane
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190628
Time 18.24
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 101.6
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300225 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OTBS
Cl
1.41
0.0000
0.0532
0.0588
0.0737
0.0927
0.8785
0.8858
1.5866
3.7546
4.1620
4.1657
4.1690
4.1761
4.1799
4.1831
5.3086
5.1859
6.8537
6.8583
7.2041
7.2268
7.2396
5.3768
8.1171
2.2941
1.3550
0.9161
1.7929
1.0045
1.0592
1.0000
1.8863
1.8304
Integral
ppm

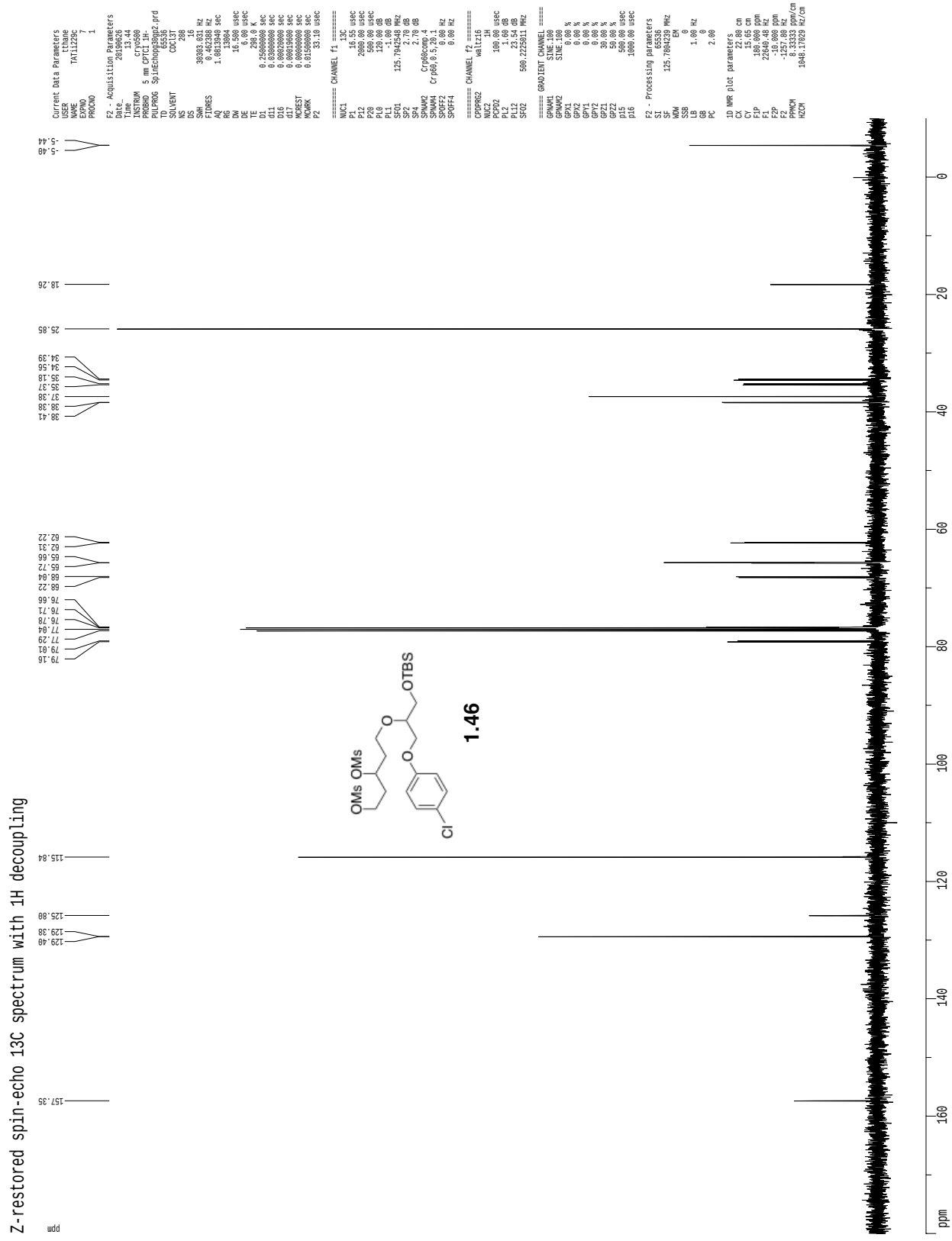

1H spectrum
ppm
Integral
1.42
OTBS
HO
Cl

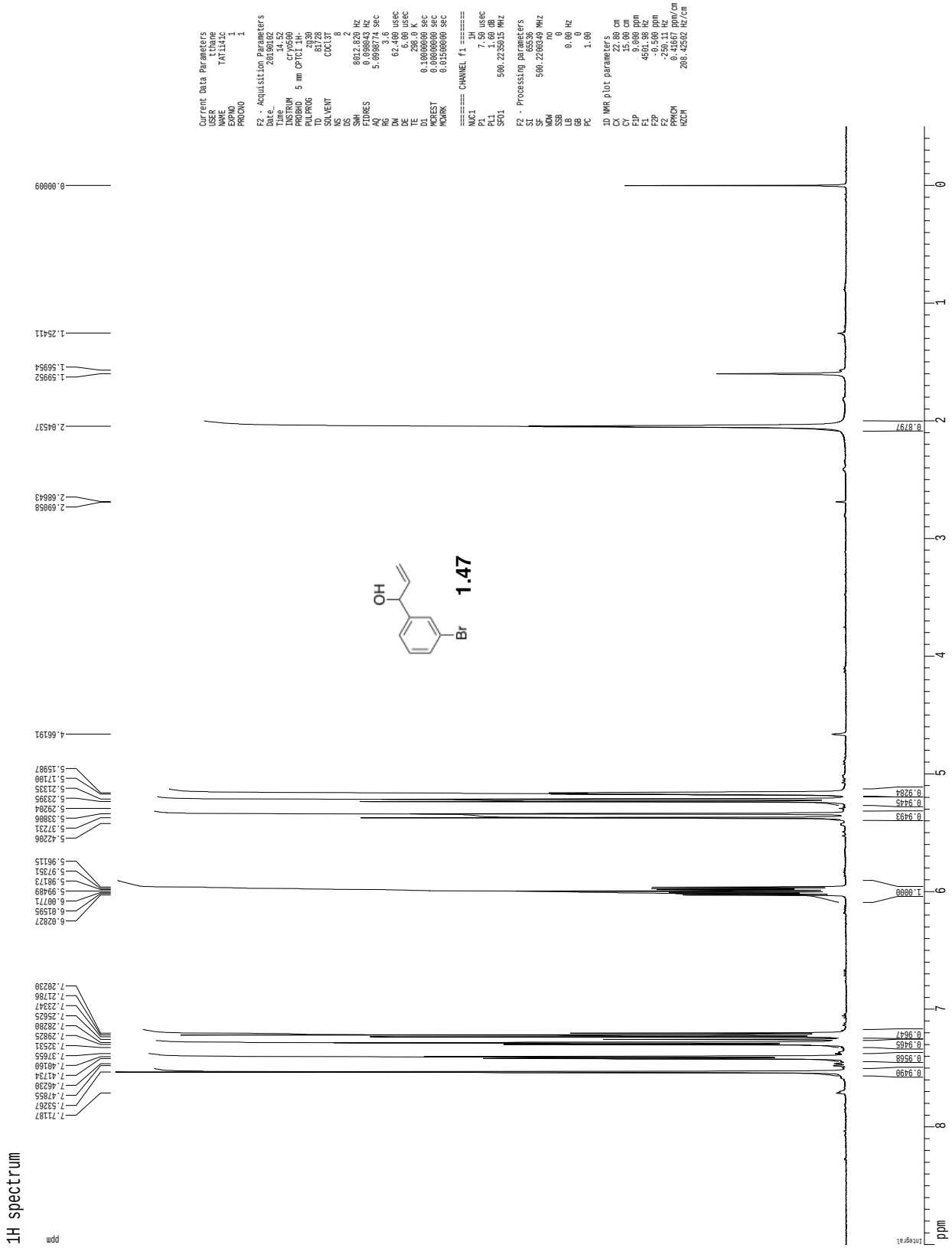

1H spectrum
1.43
OTBS
Cl
O
H
ppm

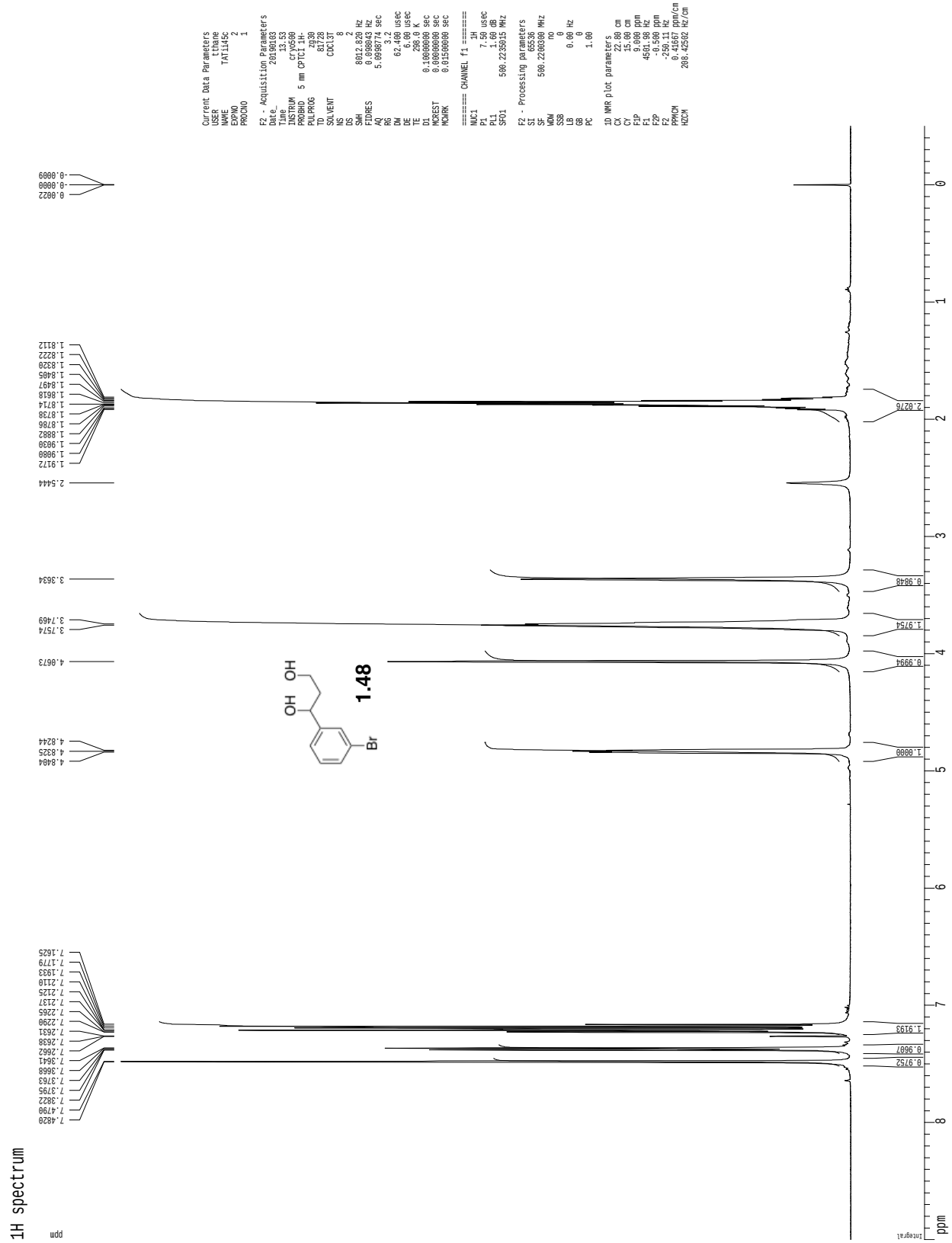

1H spectrum
Current Data Parameters
USER tihane
NAME TA1112244c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190703
Time 13.03
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 71.8
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300206 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OH
O
O
OTBS
Cl
1.44
0.06388
0.07654
0.11714
0.89063
0.91082
3.71677
3.74647
3.75815
3.98680
3.98253
5.11442
5.11106
5.29086
6.83166
6.85389
7.20873
7.23087
6.36431
9.50147
2.07276
0.78517
5.01721
1.25537
0.99347
0.91957
1.01527
1.00817
1.00000
2.38367
2.31757
ppm
Integral


1H spectrum
ppm
Integral
Current Data Parameters
USER ithane
NAME TAT11226-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190619
Time 12.31
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 362
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300213 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 9.41667 ppm/cm
HZCM 166.72086 Hz/cm
0.0000
0.0665
0.8925
1.1892
1.2067
1.2242
1.5899
3.4693
3.4869
3.7507
3.7649
3.8101
3.8210
3.8307
6.8255
6.8481
7.2179
7.2349
7.2485
7.2602
5.6263
9.2042
1.5736
4.1985
0.8596
1.0323
0.9942
2.5632
2.1599
1.8353
2.0106
1.9910
2.2856
OTBS
OH
OH
Cl
1.45


1H spectrum
Current Data Parameters
USER tihane
NAME TATi1229checklup
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190625
Time 17.00
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 36416
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.166673 Hz
AQ 2.9999299 sec
RG 812.7
DW 78.000 usec
DE 4.50 usec
TE 297.3 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300217 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OMs
OMs
O
O
OTBS
Cl
1.46
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
1.46
OMs OMs
OTBS
Cl
ppm


1H spectrum
1.47
OH
Br
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral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Current Data Parameters
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NAME TAT11455c
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
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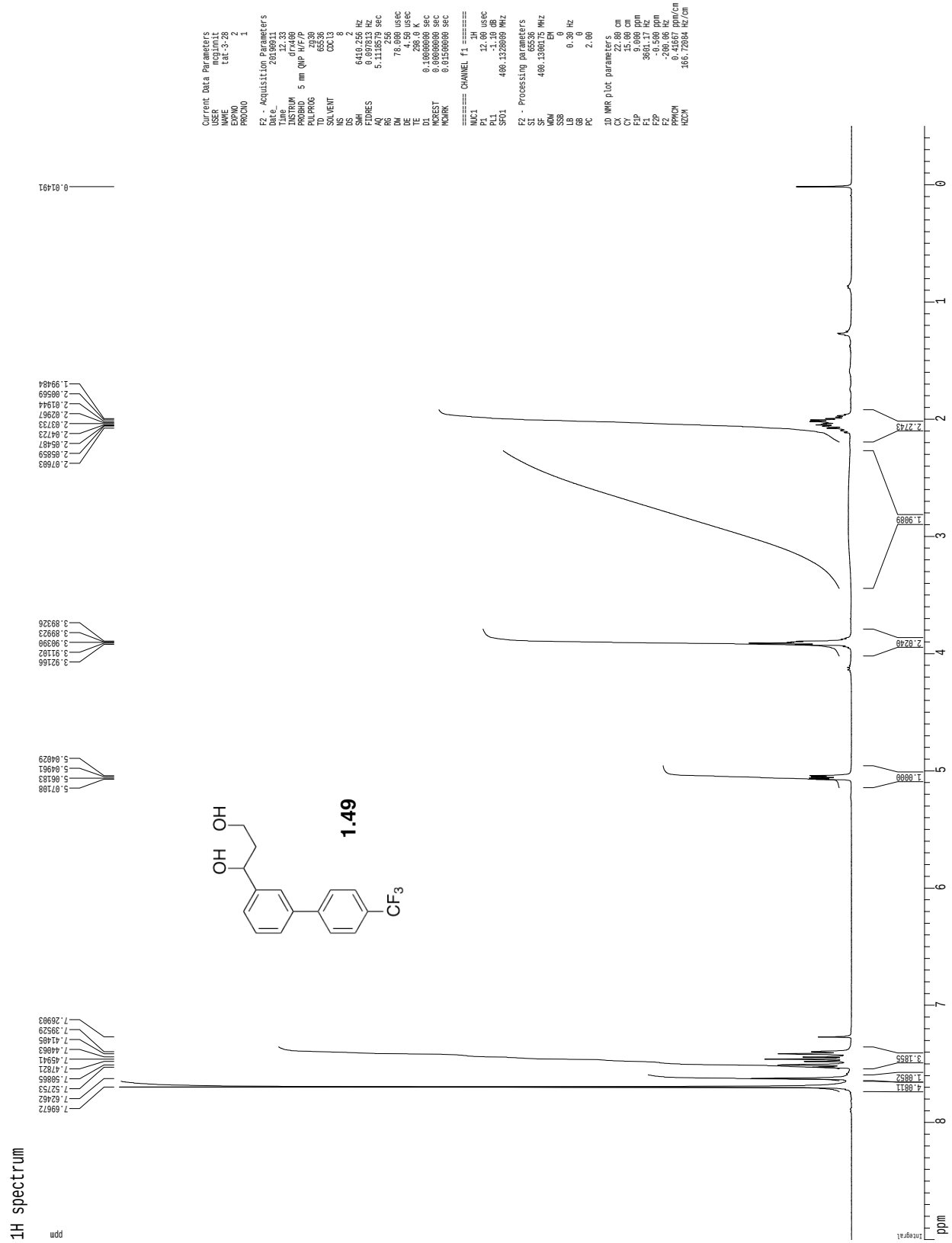
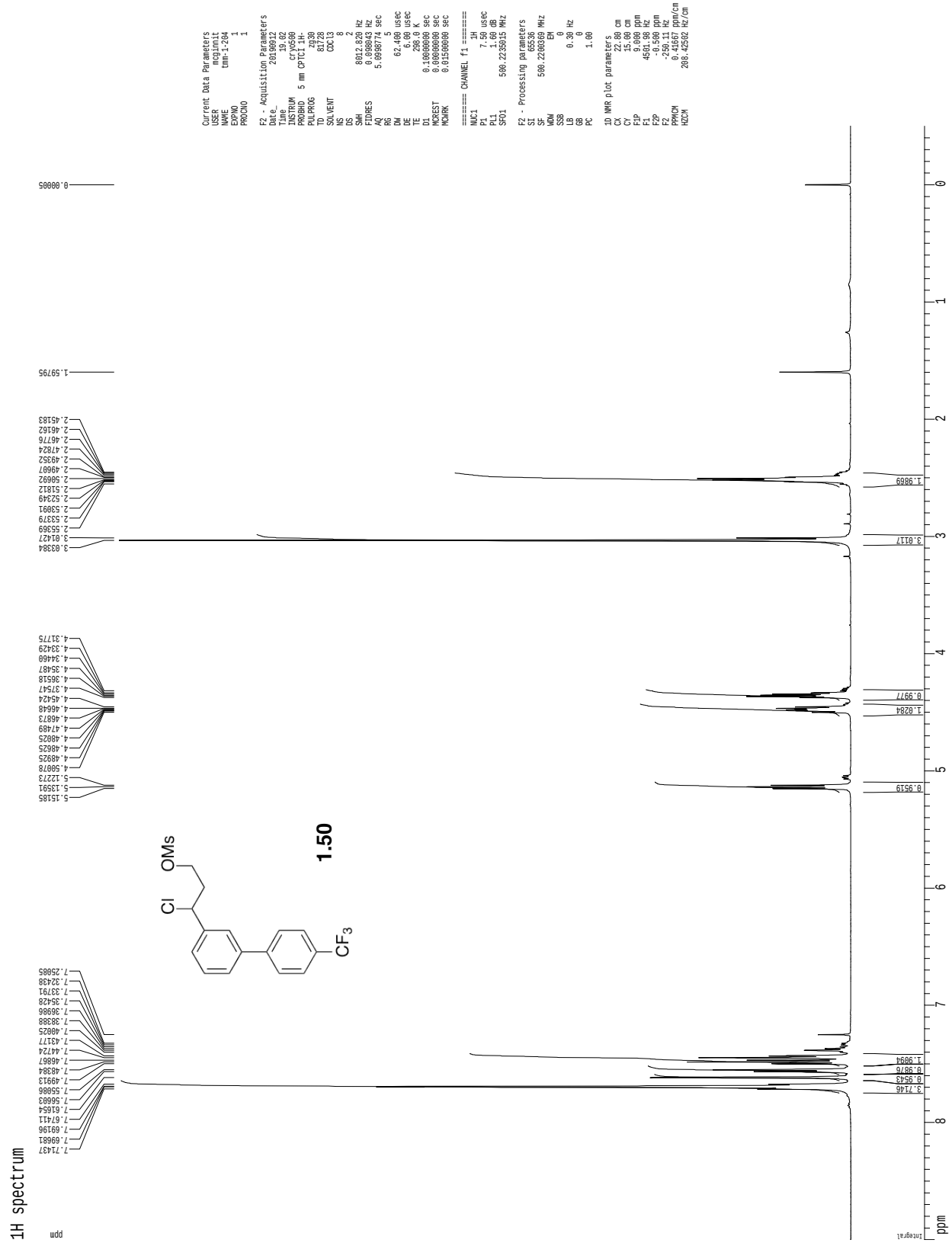
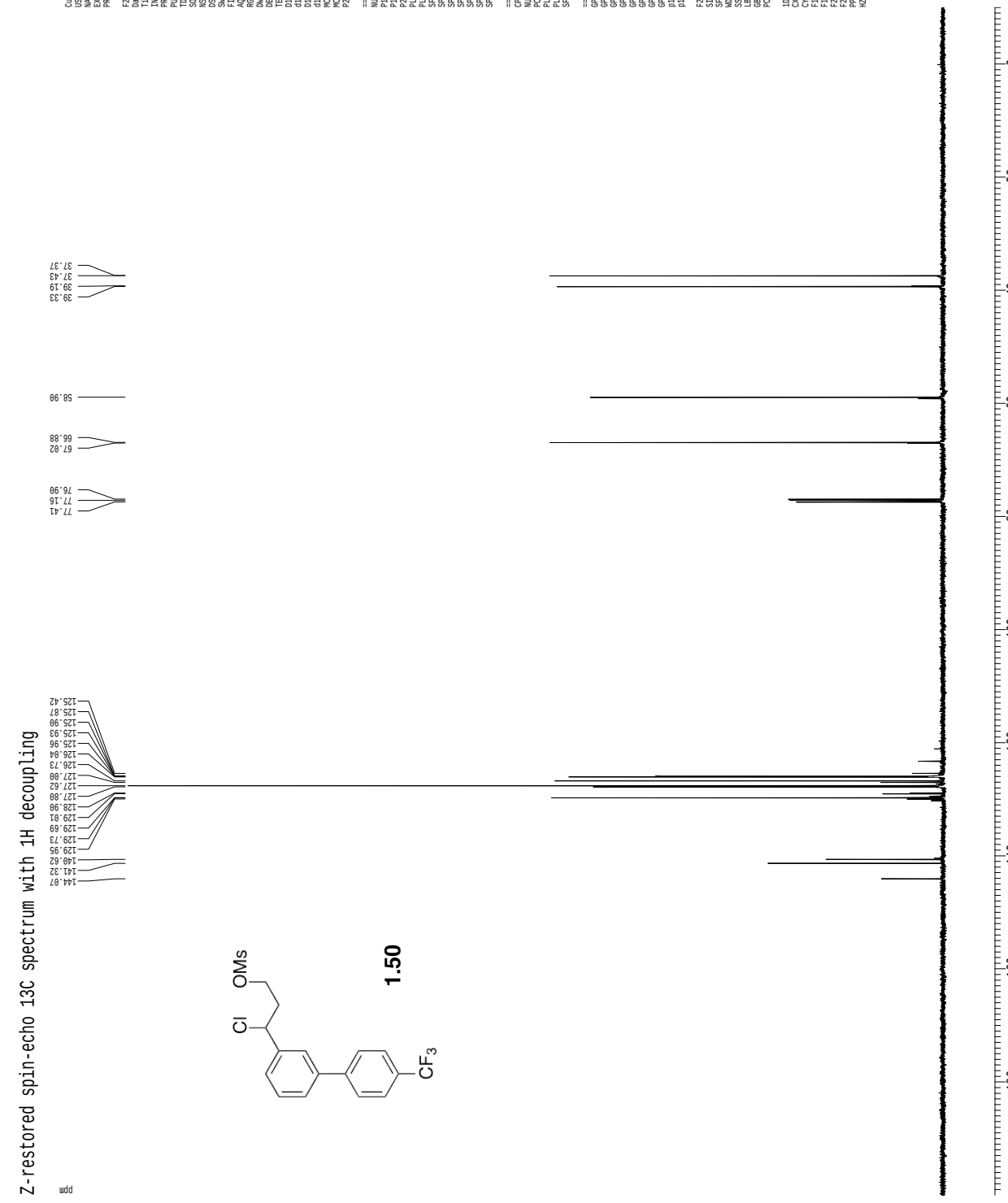
Time 13.53
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.090843 Hz
AQ 5.0998774 sec
RG 3.2
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.09000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200300 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
1.48
Br
OH
OH
ppm
Integral


1H spectrum
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
1.49
OH
OH
CF3
ppm
Integral

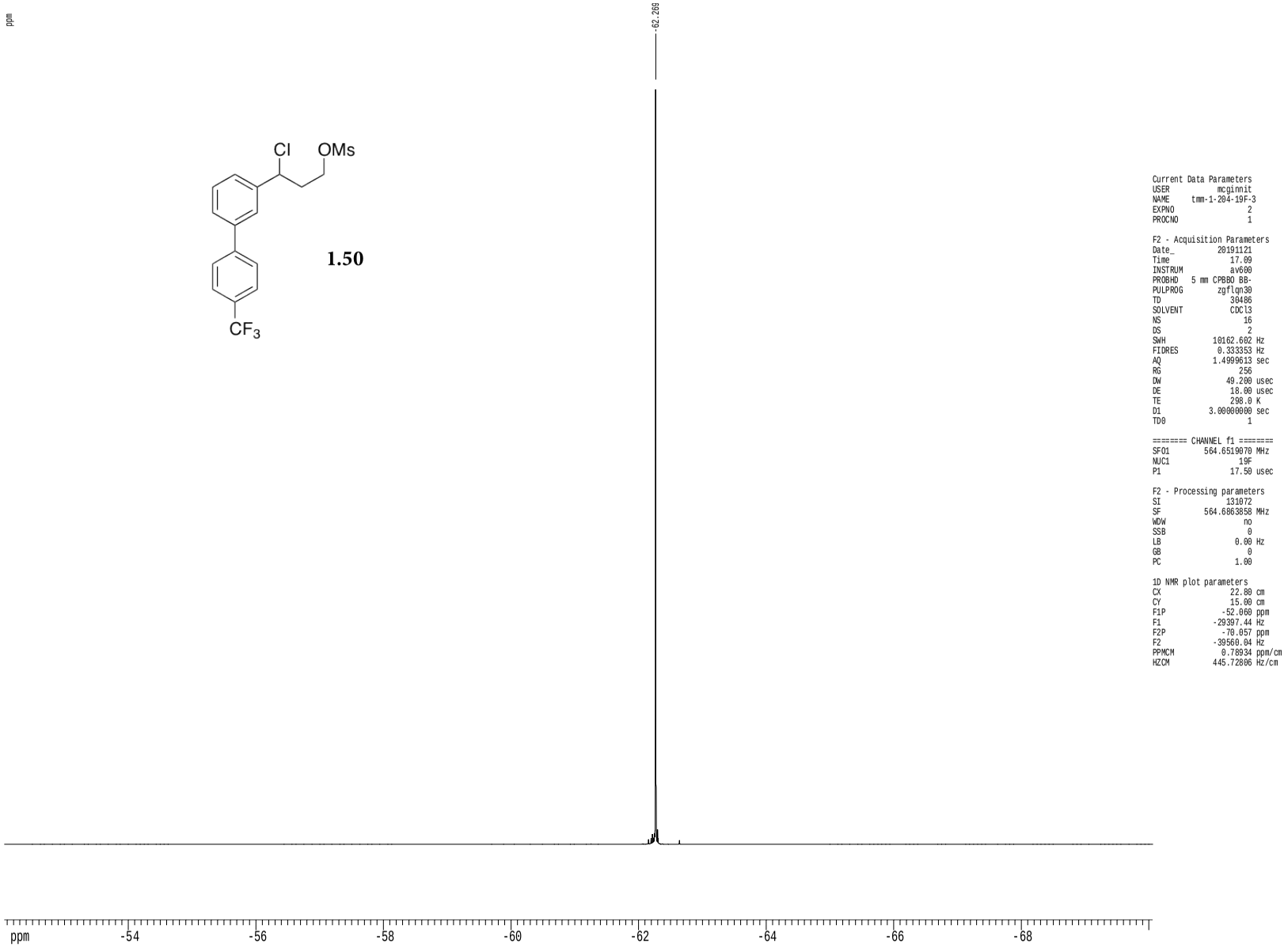

1H spectrum
Current data Parameters
USER mcginnit
NAME comm-1-204
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190912
Time 19.02
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 82728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.096843 Hz
AQ 5.0998774 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200369 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
Cl
OMs
CF3
1.50
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling



1.50

19F spectrum

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Current Data Parameters
USER            mcginnit
NAME      tmm-1-204-19F-3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191121
Time              17.09
INSTRUM           av600
PROBHD   5 mm CPBBO BB-
PULPROG         zgflqn30
TD                30486
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           10162.602 Hz
FIDRES         0.333353 Hz
AQ             1.4999613 sec
RG                  256
DW               49.200 usec
DE               18.00 usec
TE                298.0 K
D1            3.00000000 sec
TD0                   1

======= CHANNEL f1 =======
SFO1         564.6519070 MHz
NUC1                19F
P1                17.50 usec

F2 - Processing parameters
SI                131072
SF           564.6863858 MHz
WDW                 no
SSB                  0
LB                0.00 Hz
GB                   0
PC                1.00

1D NMR plot parameters
CX                22.80 cm
CY                15.00 cm
F1P              -52.060 ppm
F1            -29397.44 Hz
F2P              -70.057 ppm
F2            -39560.04 Hz
PPMCM           0.78934 ppm/cm
HZCM          445.72806 Hz/cm
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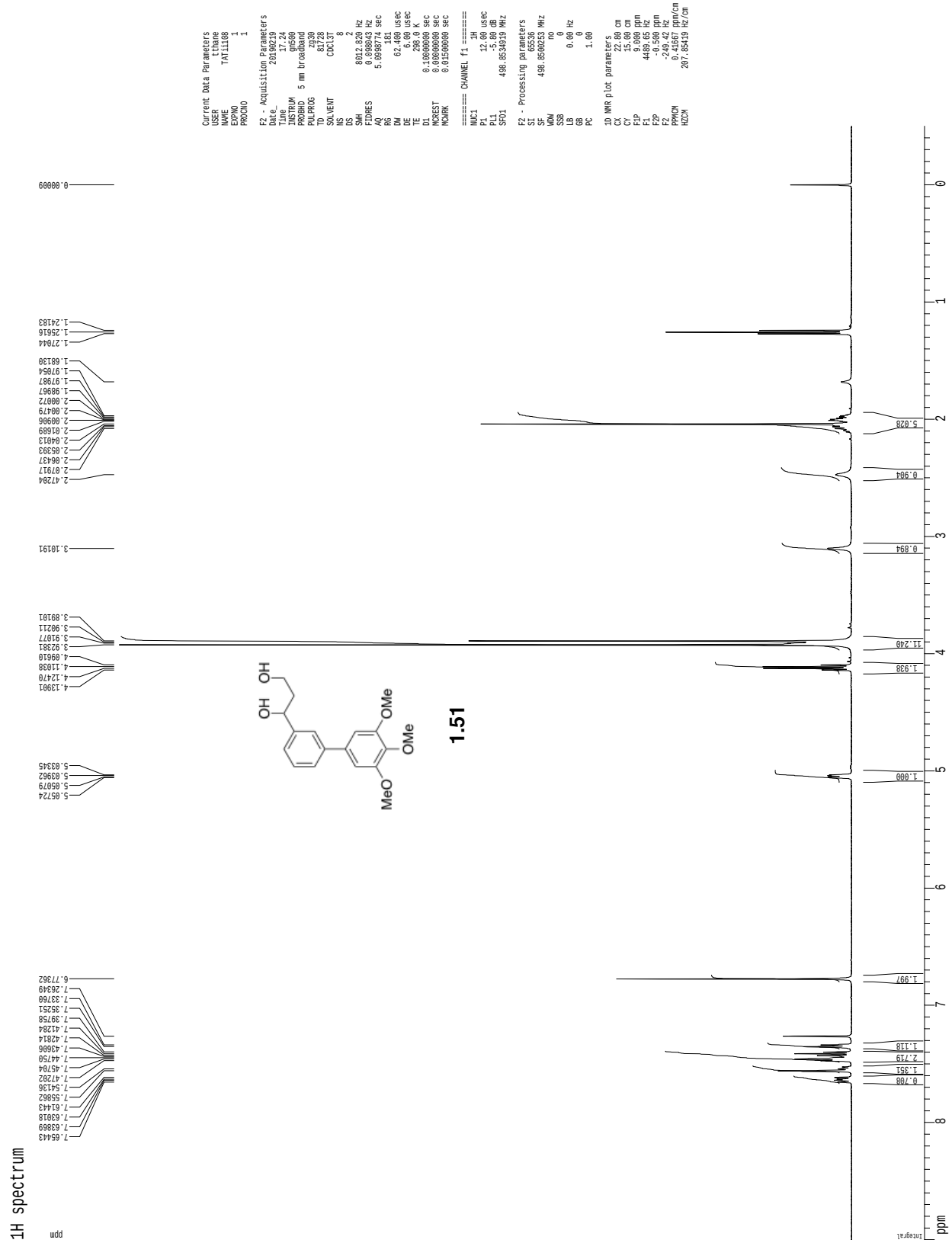
1H spectrum
Current data Parameters
USER ttiane
NAME TAT11108
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190219
Time 17.24
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.091843 Hz
AQ 5.0998774 sec
RG 161
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -5.00 dB
SFO1 498.8534919 MHz
F2 - Processing parameters
SI 65536
SF 498.8500253 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4489.65 Hz
F2P -0.500 ppm
F2 -249.42 Hz
PPMCM 0.41667 ppm/cm
HZCM 207.65419 Hz/cm
OH
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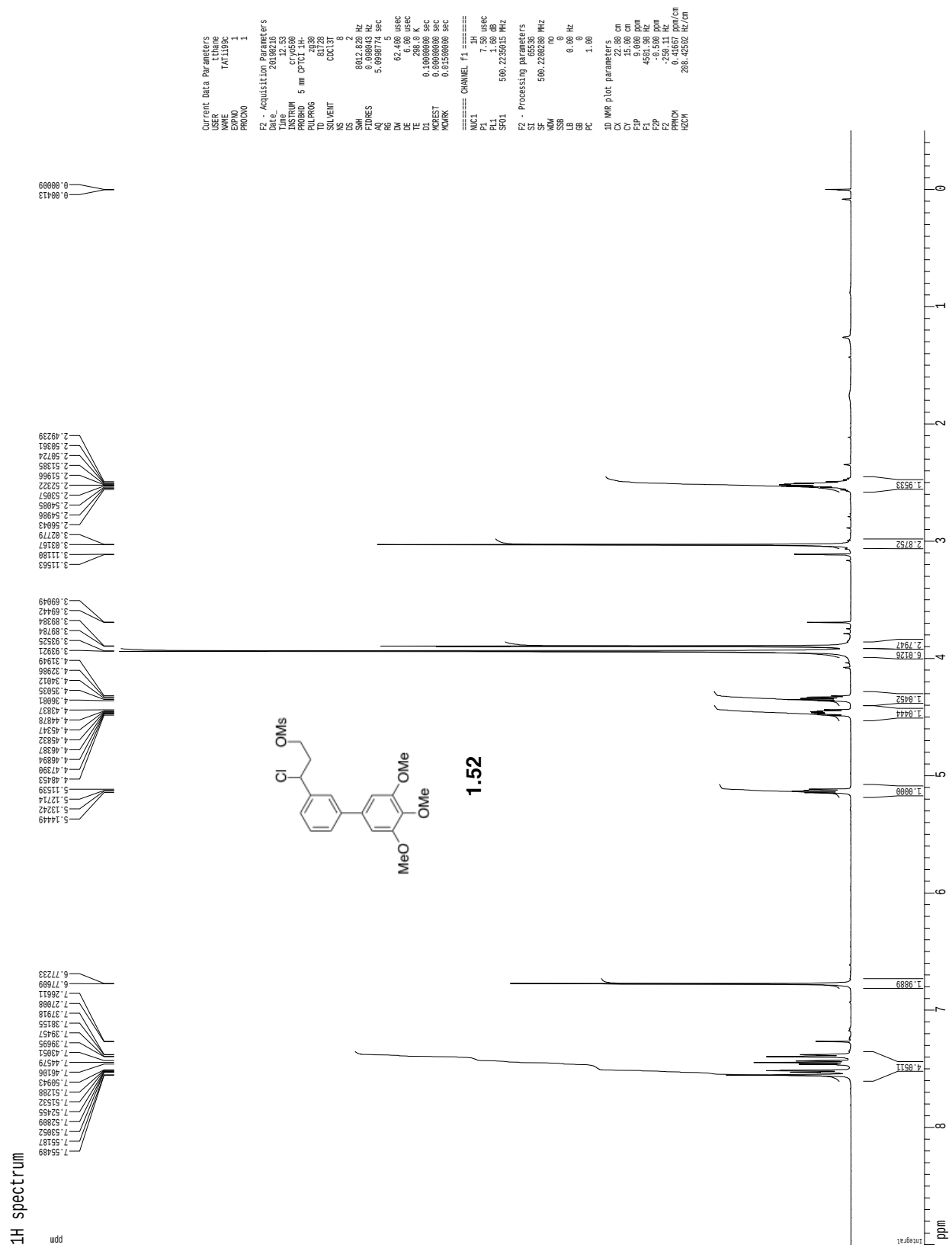
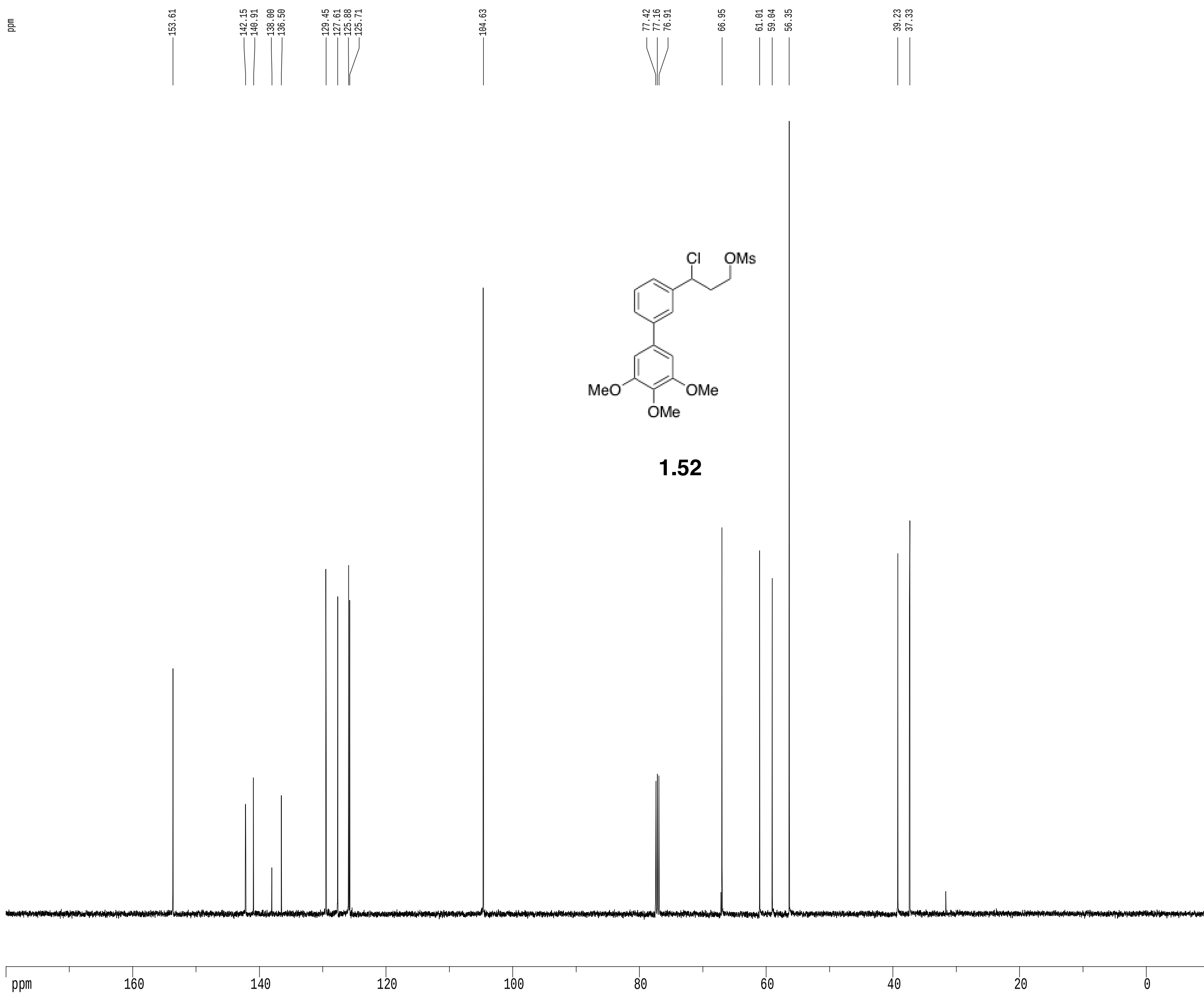
OMe
OMe
MeO
1.51
ppm
Integral


1H spectrum
1.52
Cl
OMs
OMe
OMe
MeO
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



1.52

```
Current Data Parameters
USER              tthane
NAME            TATii99c
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190216
Time               12.55
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                 65536
SOLVENT            CDCl3
NS                   224
DS                    16
SWH          30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG                5160.6
DW              16.500 usec
DE                6.00 usec
TE               298.0 K
D1          0.25000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

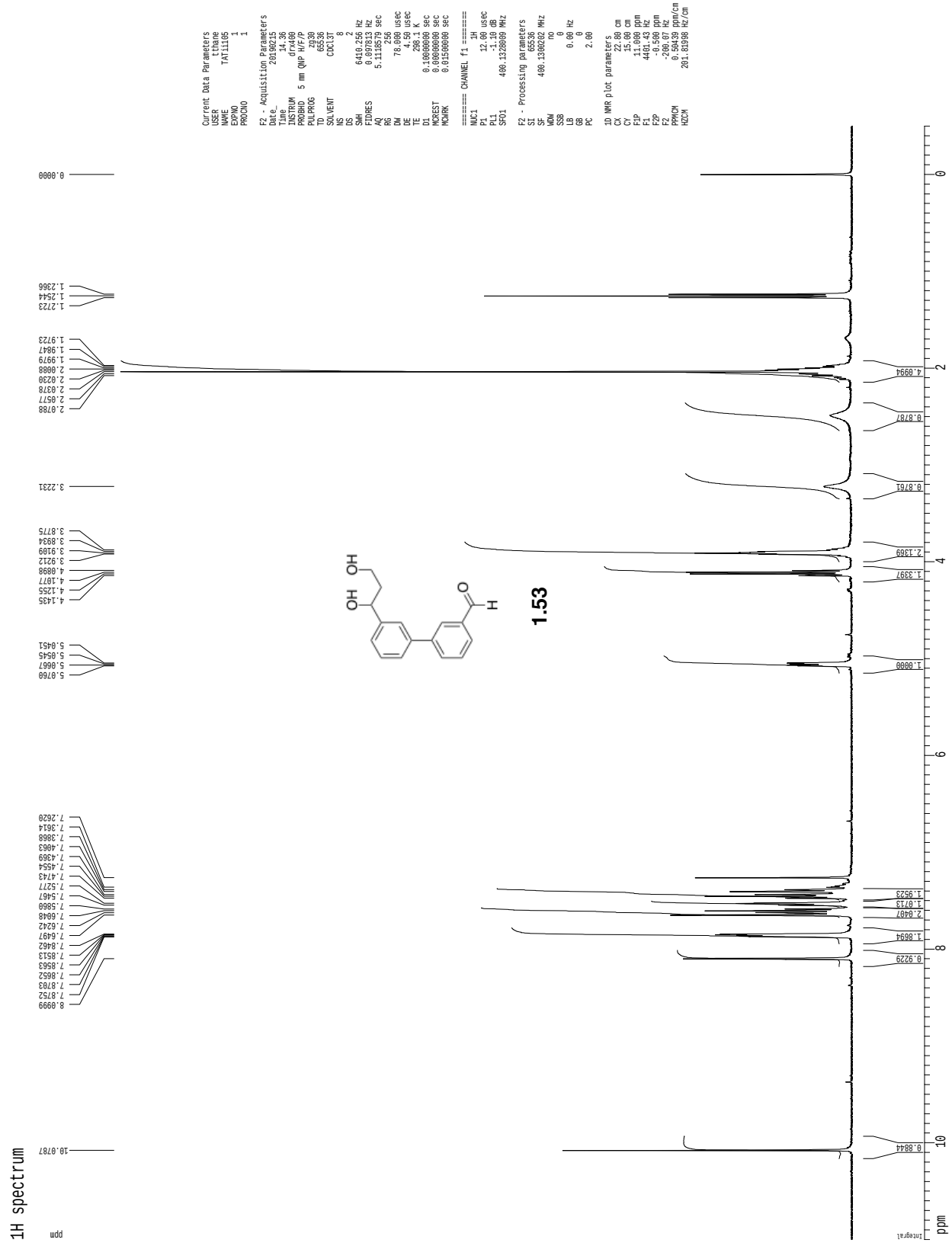
======== CHANNEL f1 ========
NUC1                 13C
P1               16.55 usec
P12            2000.00 usec
P20             500.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP2               2.70 dB
SP4               2.70 dB
SPNAM2      Crp60comp.4
SPNAM4   Crp60,0.5,20.1
SPOFF2            0.00 Hz
SPOFF4            0.00 Hz

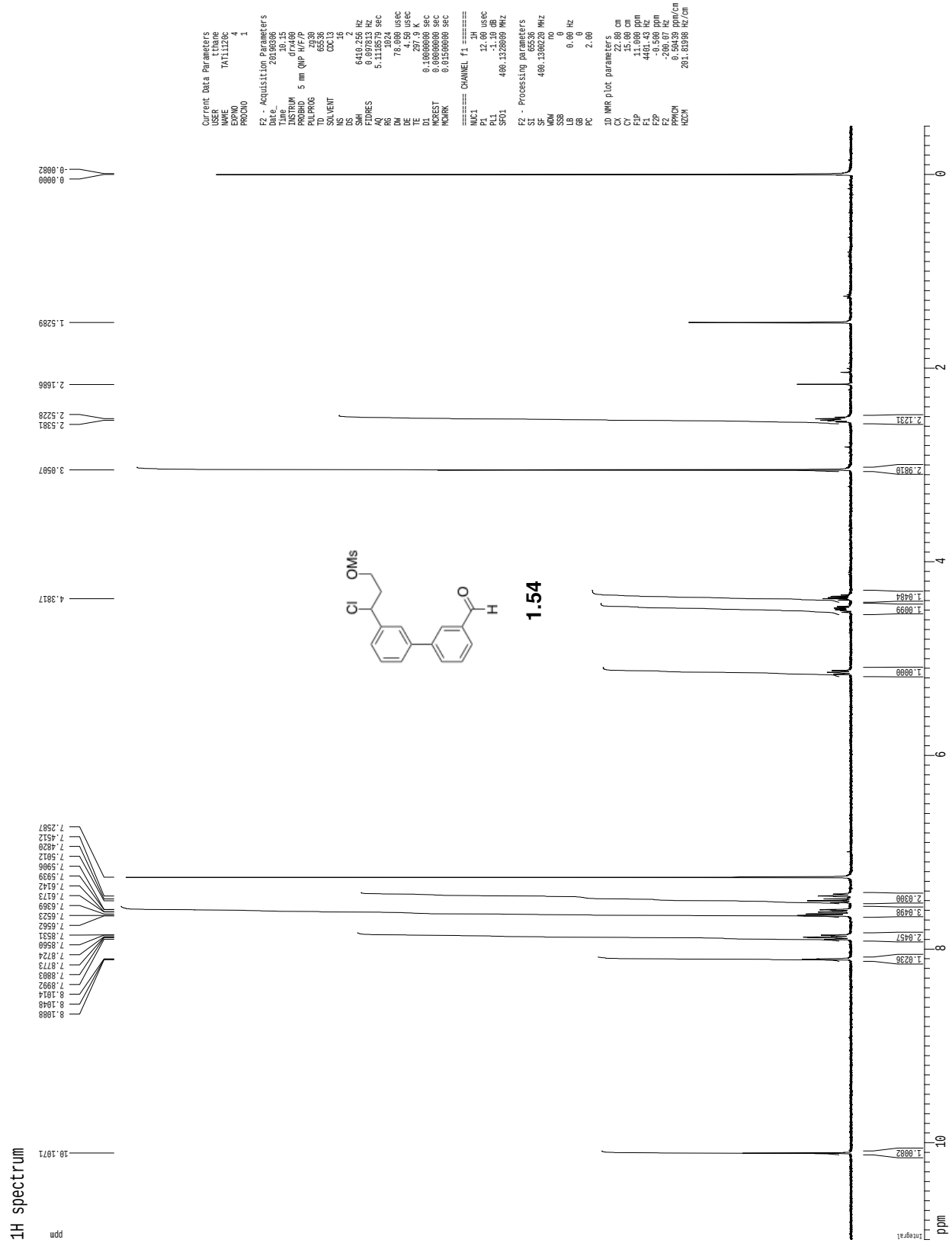
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             23.54 dB
SFO2       500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

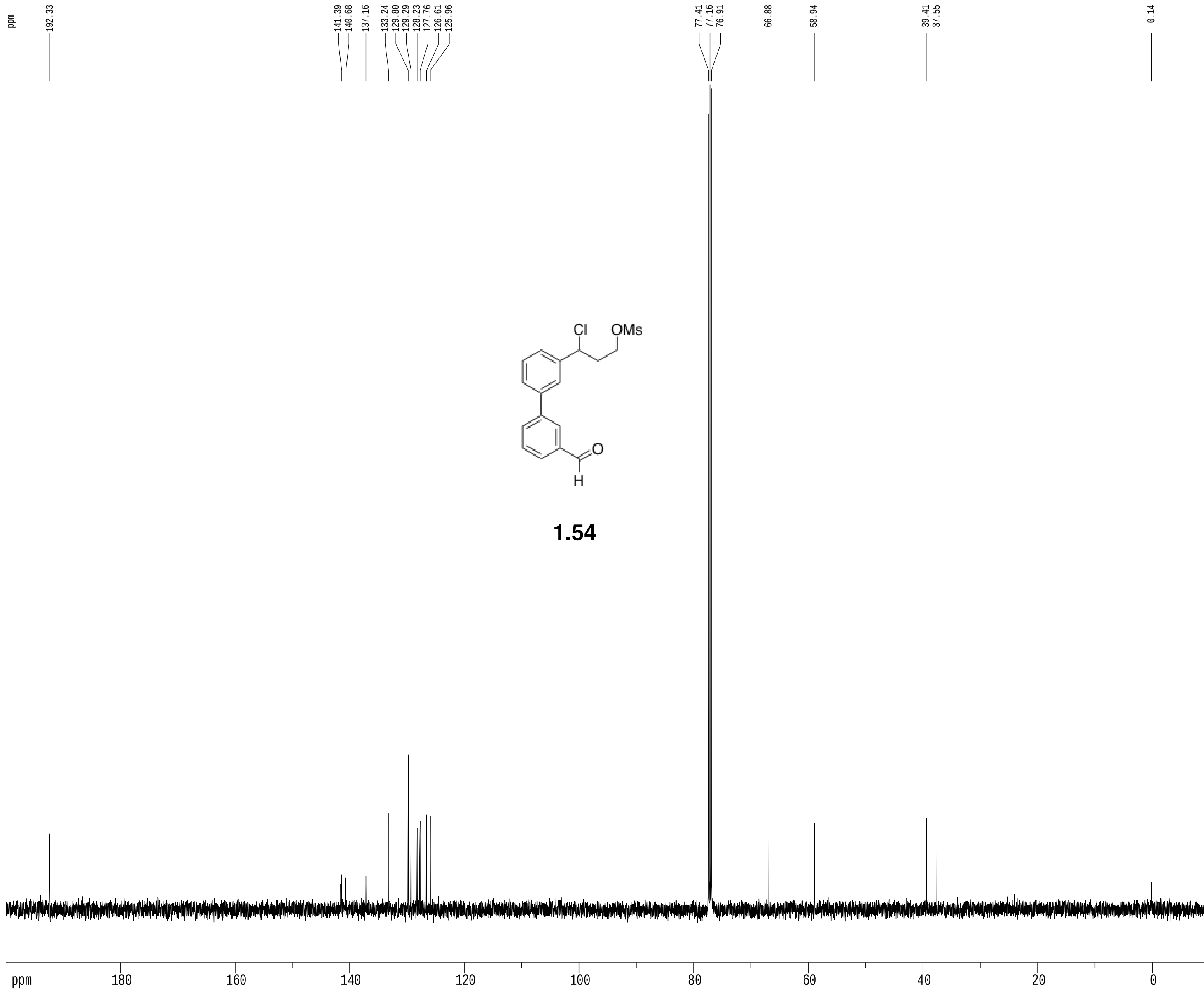
F2 - Processing parameters
SI                 65536
SF           125.7804190 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX               22.80 cm
CY               15.65 cm
F1P            180.000 ppm
F1            22640.47 Hz
F2P            -10.000 ppm
F2            -1257.80 Hz
PPMCM          8.33333 ppm/cm
HZCM        1048.17017 Hz/cm
```


1H spectrum
Current Data Parameters
USER ttiane
NAME TAT11105
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190215
Time 14.36
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 256
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300202 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 11.000 ppm
F1 4401.43 Hz
F2P -0.500 ppm
F2 -200.07 Hz
PPMCM 0.50439 ppm/cm
HZCM 201.61998 Hz/cm
1.53
ppm
Integral


1H spectrum
1.54
Cl
OMs
O
H
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



1.54

```
Current Data Parameters
USER              tthane
NAME           TATii120c
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190305
Time               17.19
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                 65536
SOLVENT            CDCl3
NS                   680
DS                    16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ            1.0813940 sec
RG               10321.3
DW                16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2                 33.10 usec

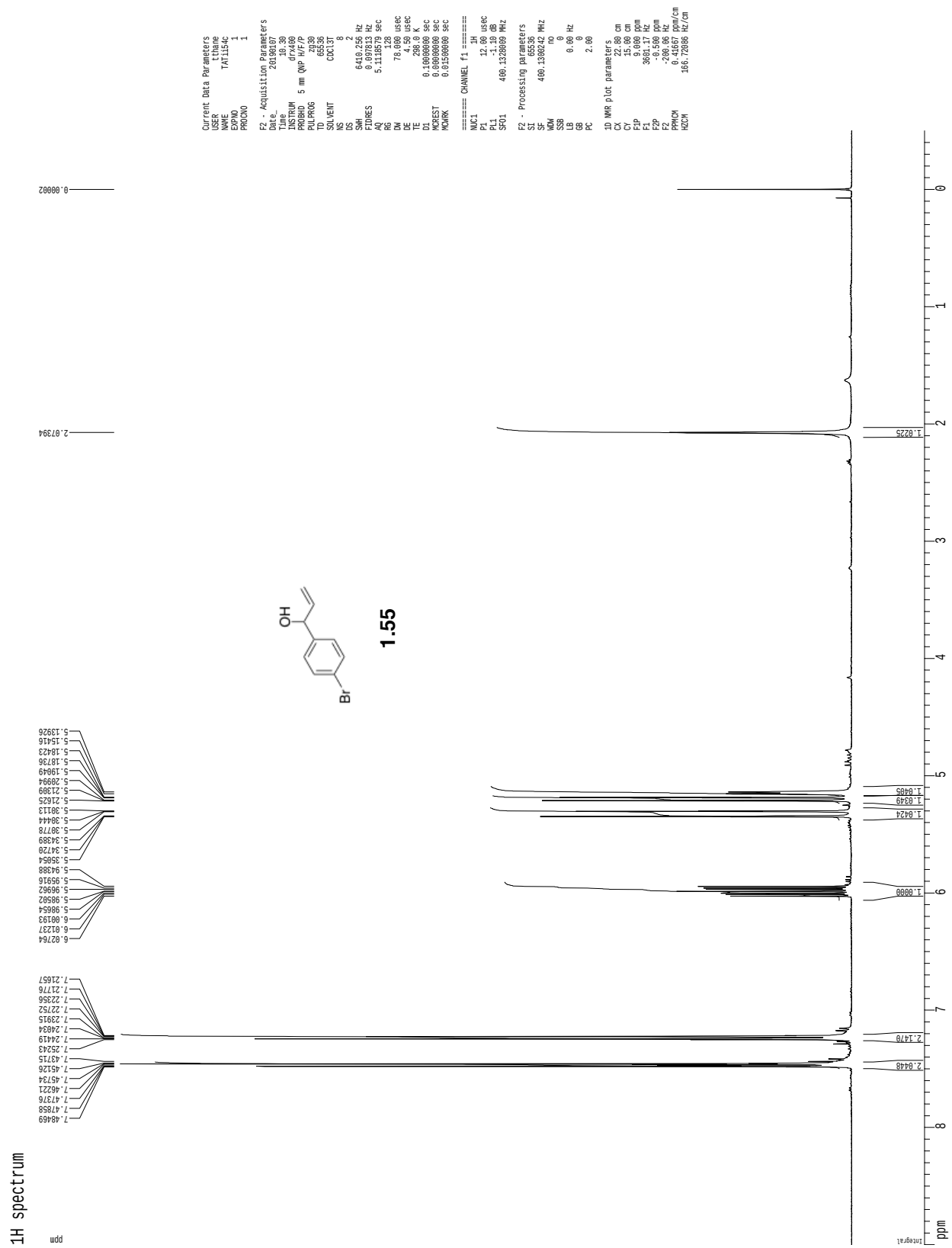
======== CHANNEL f1 ========
NUC1                 13C
P1                 16.55 usec
P12              2000.00 usec
P20               500.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP2                 2.70 dB
SP4                 2.70 dB
SPNAM2       Crp60comp.4
SPNAM4   Crp60,0.5,20.1
SPOFF2              0.00 Hz
SPOFF4              0.00 Hz

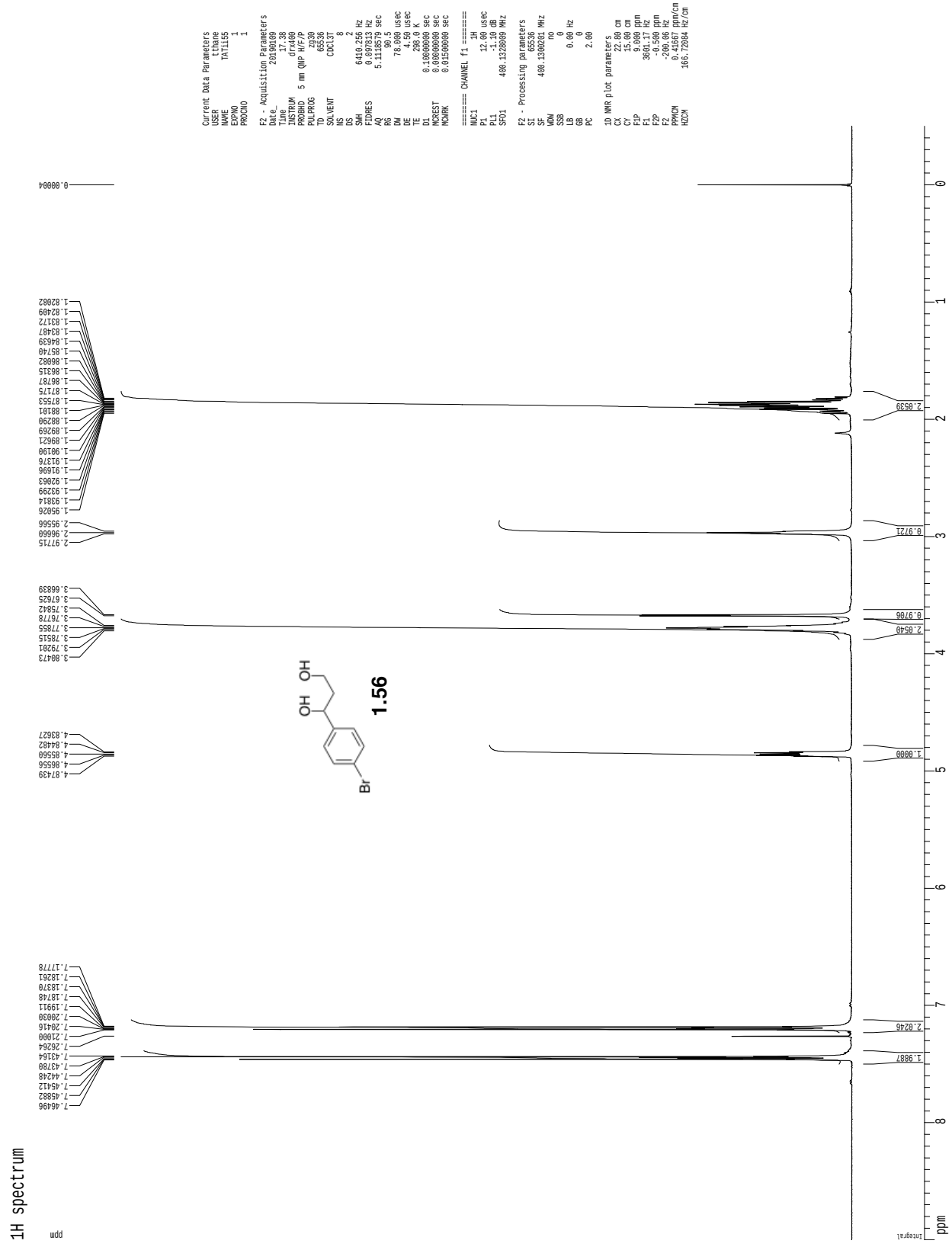
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               23.54 dB
SFO2         500.2225011 MHz

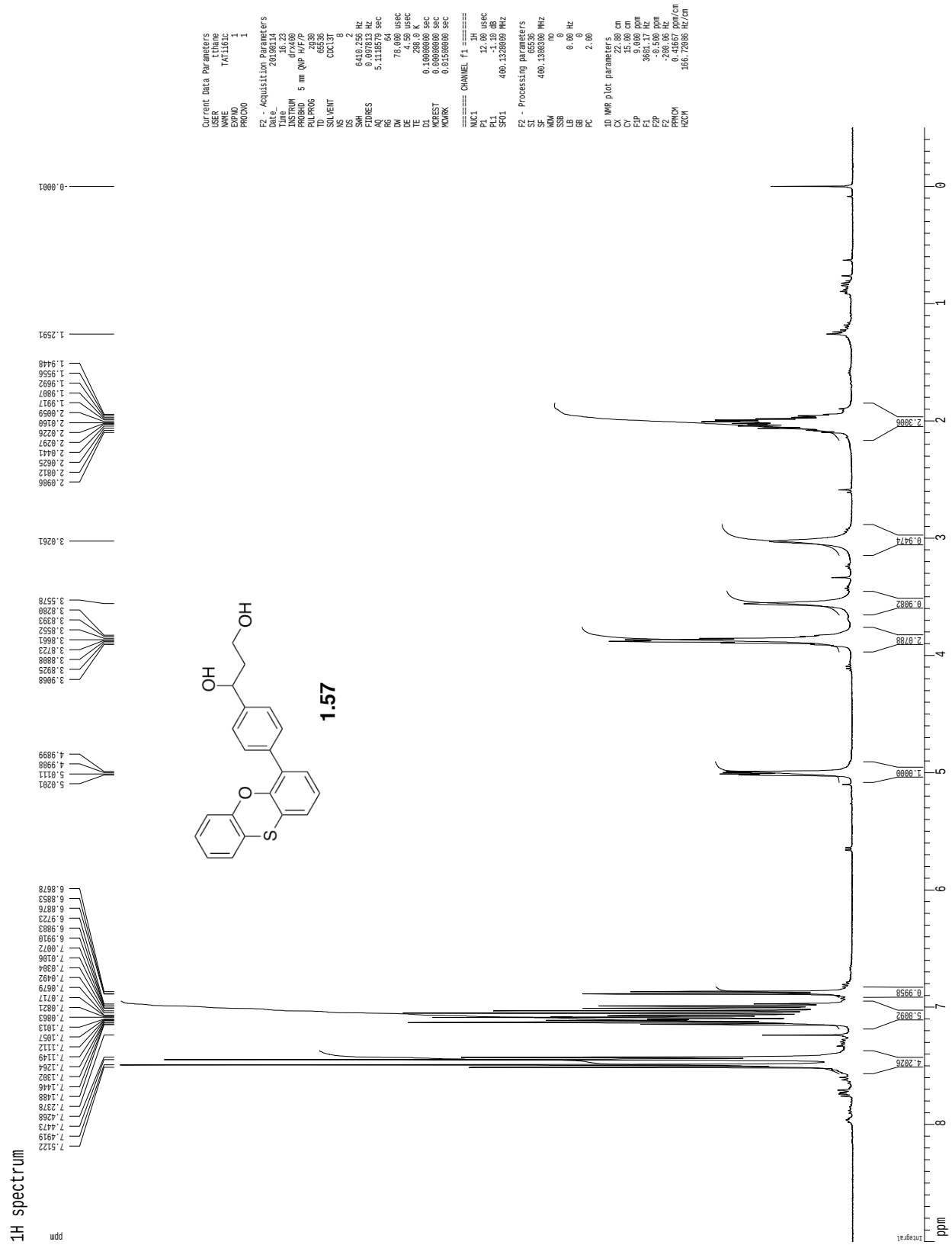
====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

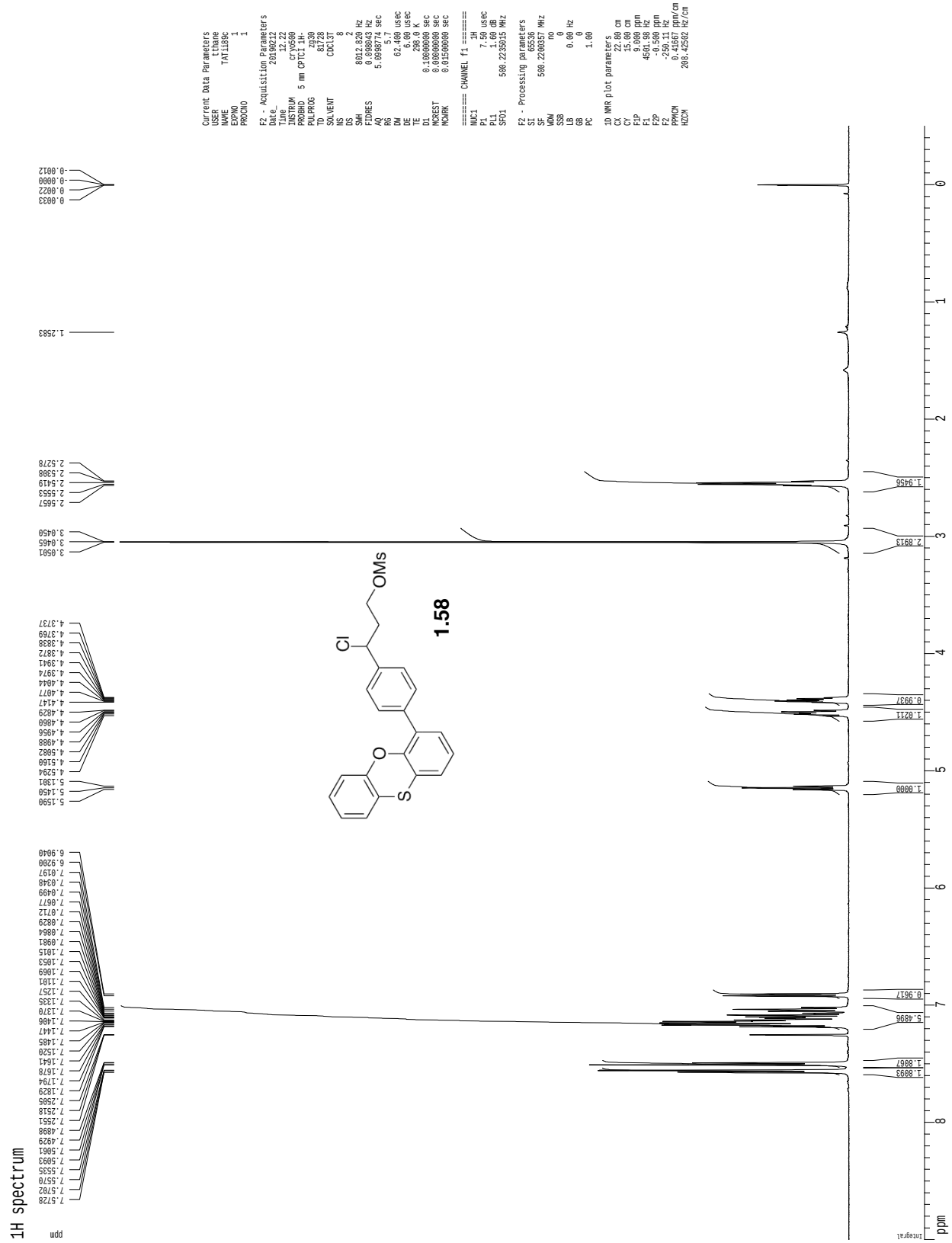
F2 - Processing parameters
SI                 65536
SF           125.7804062 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

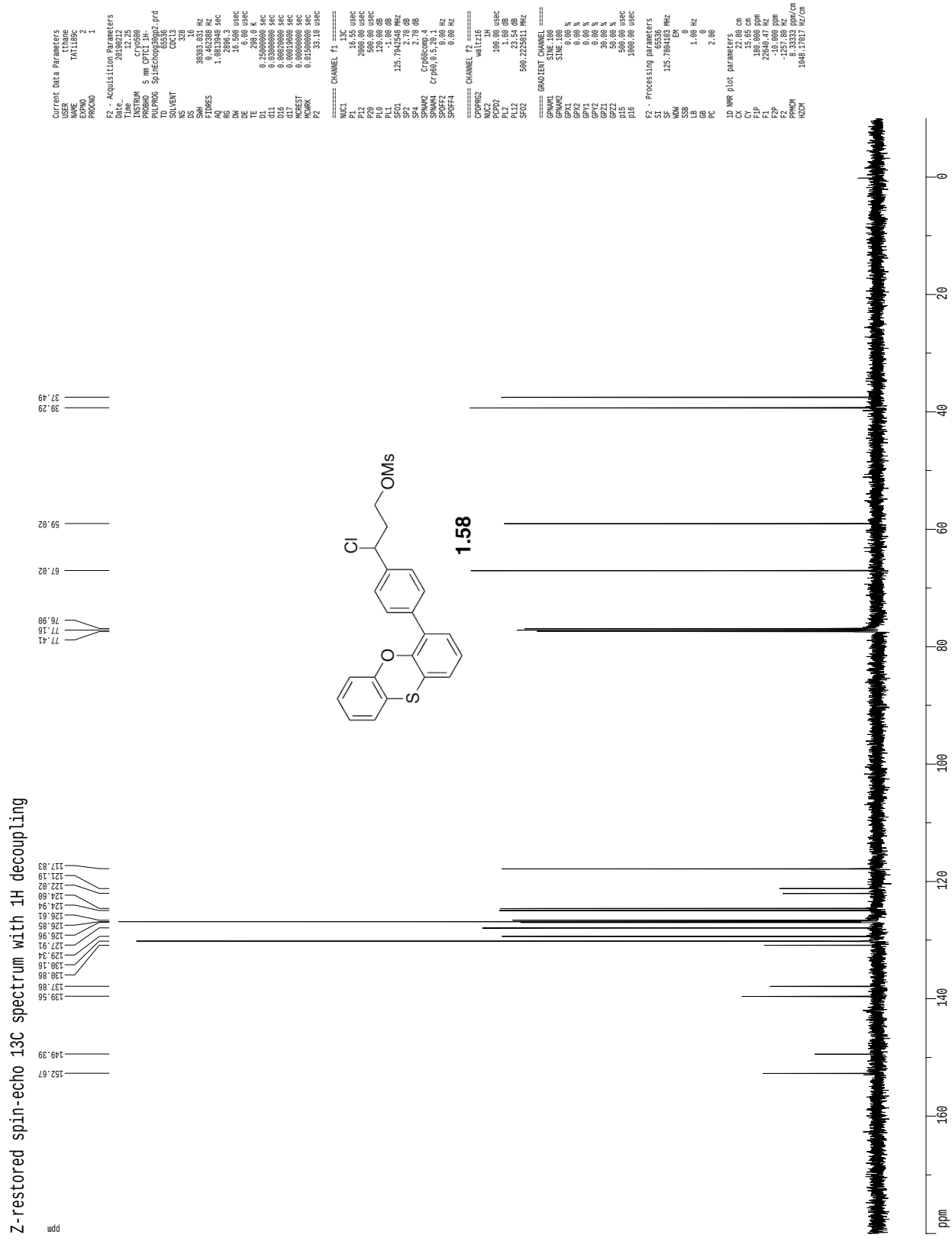
1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              200.000 ppm
F1              25156.08 Hz
F2P              -10.000 ppm
F2              -1257.80 Hz
PPMCM            9.21053 ppm/cm
HZCM          1158.50366 Hz/cm
```

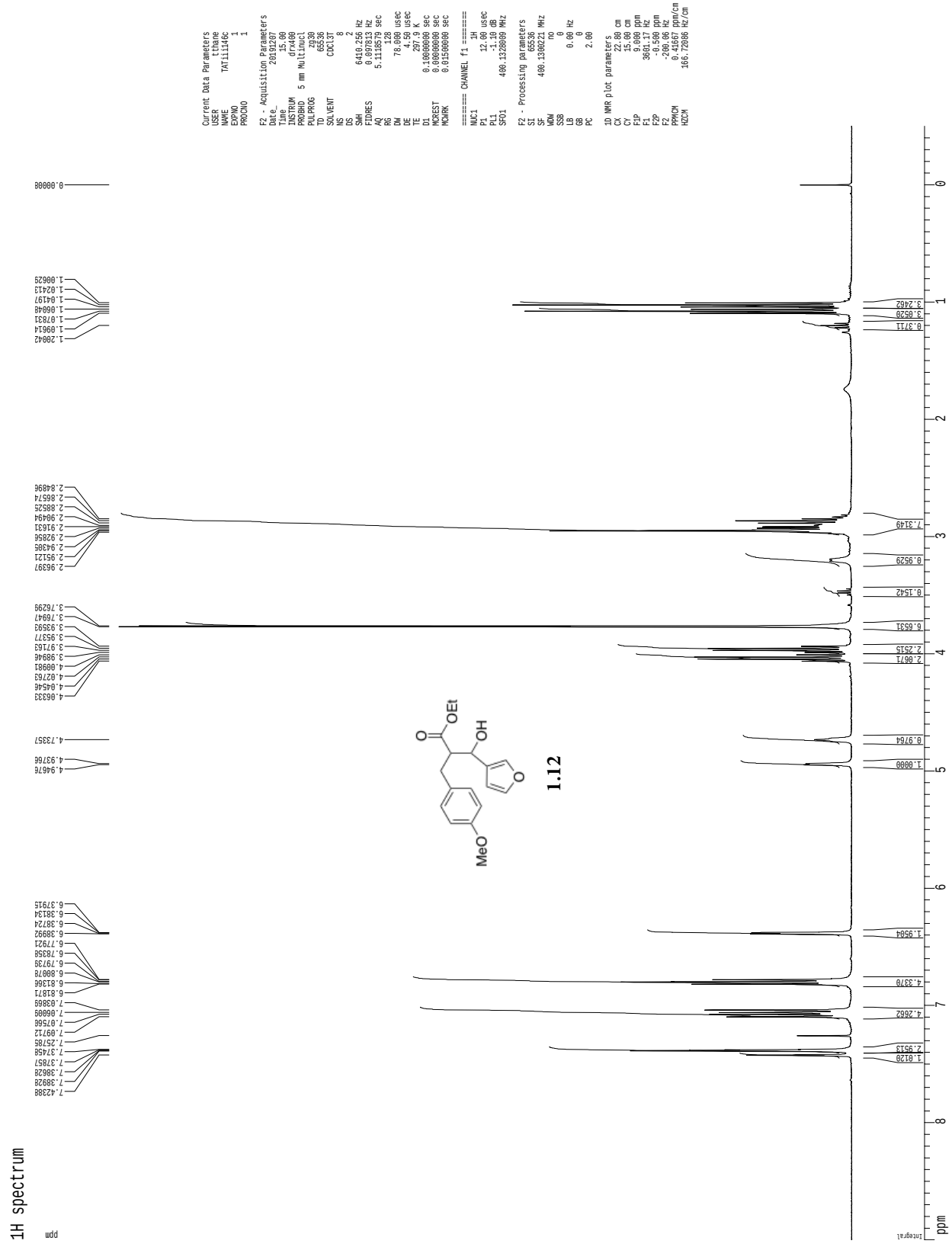

1H spectrum
1.55
OH
Br
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm

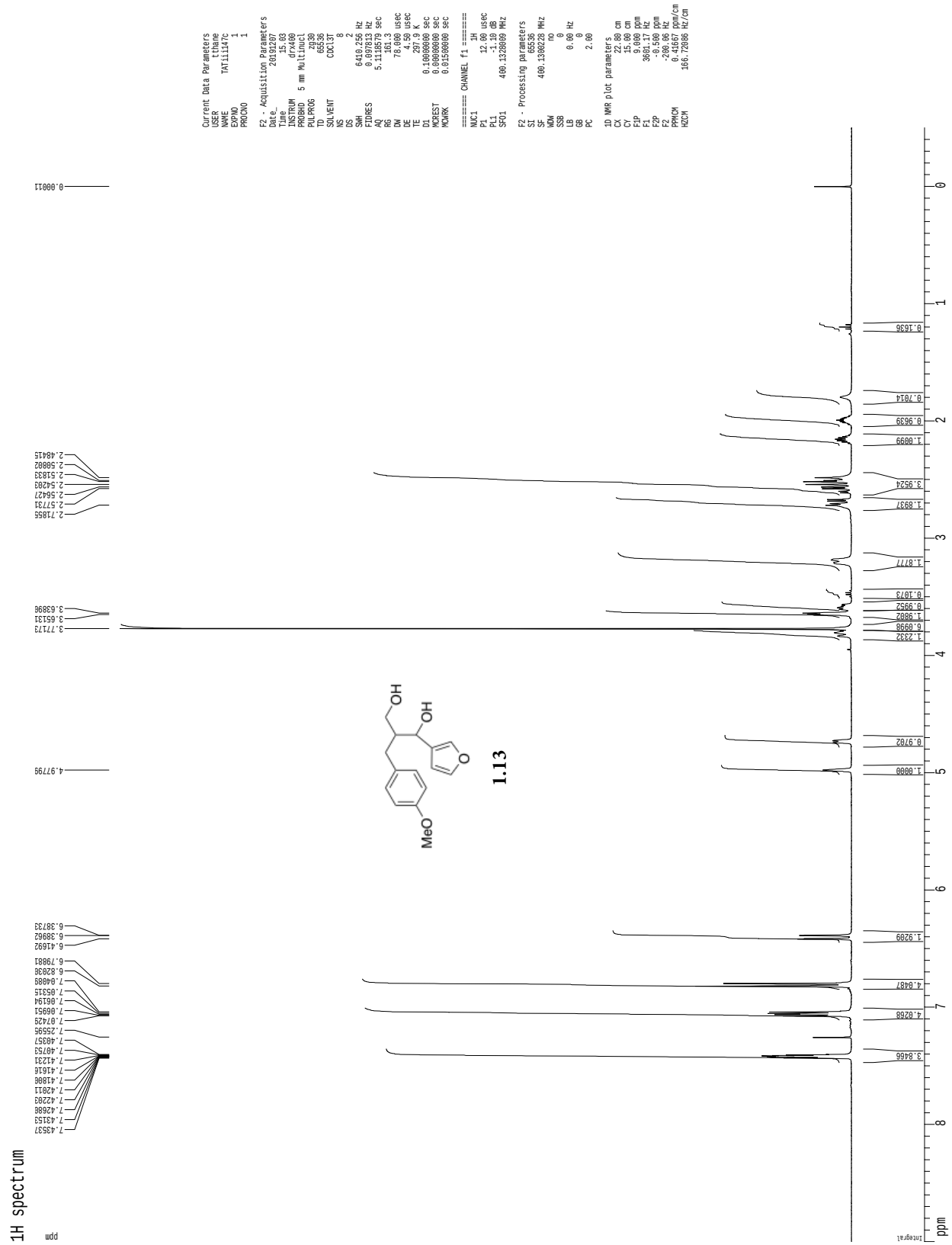

1H spectrum
Current Data Parameters
USER tthane
NAME TA11155
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190109
Time 17.38
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 90.5
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300201 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72084 Hz/cm
OH
OH
Br
1.56
0.00004
1.82082
1.82409
1.83172
1.83487
1.84639
1.85740
1.86082
1.86315
1.86787
1.87175
1.87553
1.88101
1.88290
1.88269
1.89621
1.90190
1.91376
1.91696
1.92063
1.92299
1.93814
1.95026
2.95566
2.96660
2.97715
3.66839
3.67625
3.75842
3.76778
3.77855
3.78515
3.79201
3.80473
4.83627
4.84482
4.85560
4.86556
4.87439
7.17778
7.18261
7.18370
7.18748
7.19931
7.20030
7.20416
7.21000
7.26264
7.43164
7.43780
7.44248
7.45412
7.45882
7.46496
2.06539
0.97721
0.97706
2.05540
1.00000
2.02646
1.98867
Integral
ppm
0
1
2
3
4
5
6
7
8

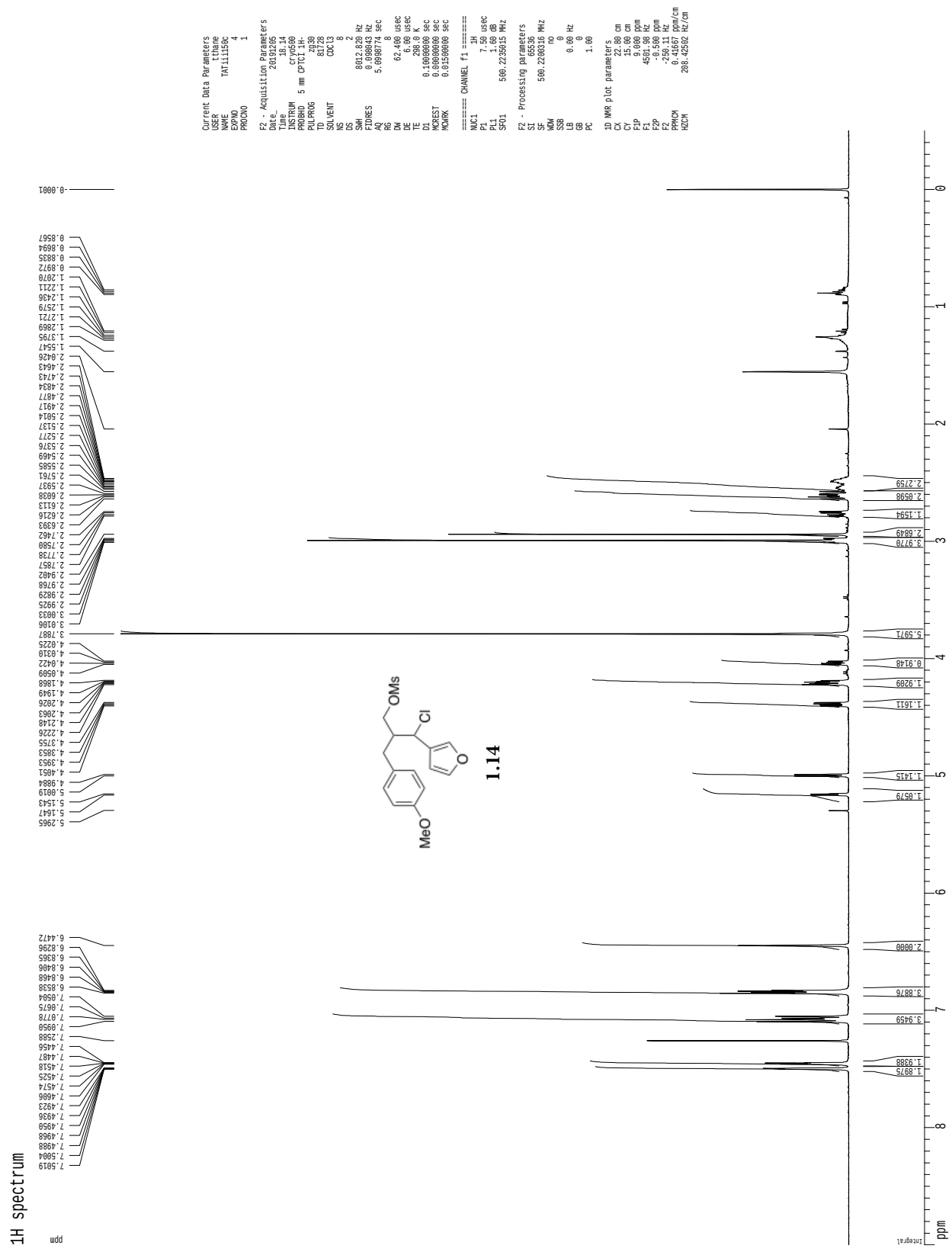

1H spectrum
Current Data Parameters
USER ttiane
NAME TAT1161c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190114
Time 16.23
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 64
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300300 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OH
OH
O
S
1.57
ppm
Integral

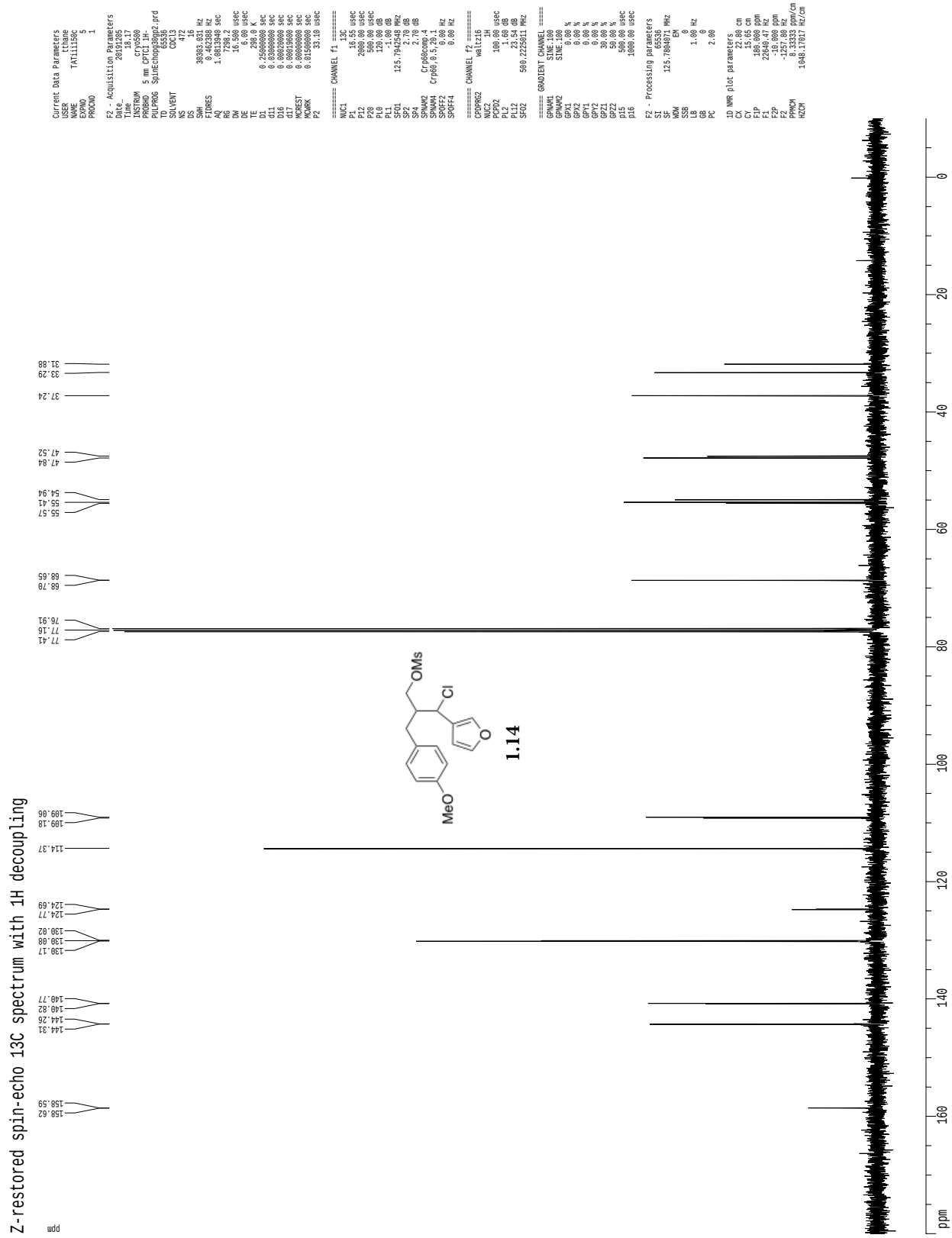

1H spectrum
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral
OMs
Cl
O
S
1.58

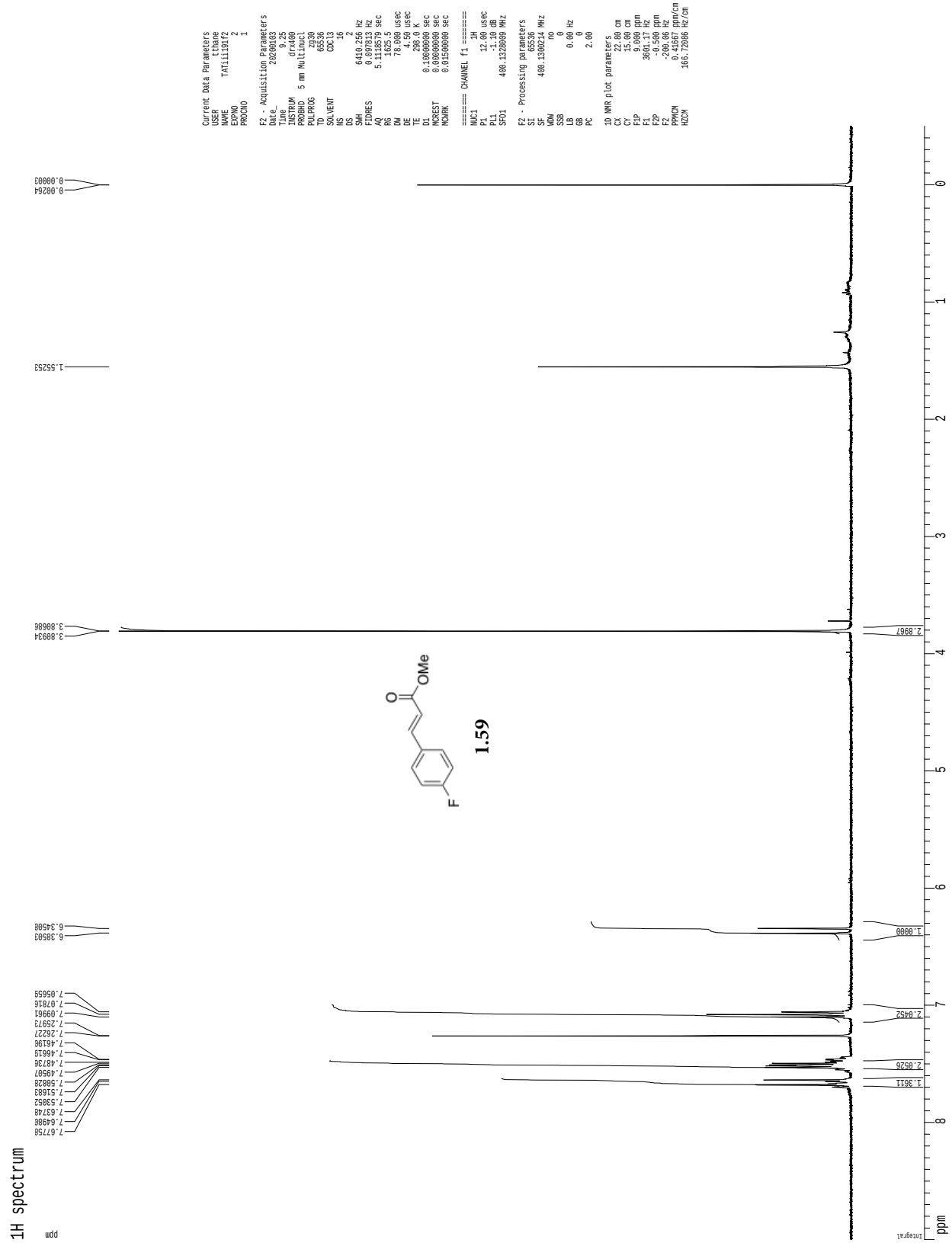

Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
Current Data Parameters
USER tw
NAME TAT1180c
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190212
Time 7.25
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 256
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08139840 sec
RG 2896.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
======== CHANNEL f1 ========
NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.79422540 MHz
SP1 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225911 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPV1 0.00 %
GPV2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.78041833 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 6.33333 ppm/cm
HZCM 1040.17917 Hz/cm
1.58
Cl
OMs
O
S
37.49
39.29
59.02
67.02
76.90
77.16
77.41
117.83
121.19
122.02
124.60
124.94
126.61
126.85
126.96
127.91
129.34
130.16
130.86
137.86
139.56
149.39
152.67
0
20
40
60
80
100
120
140
160

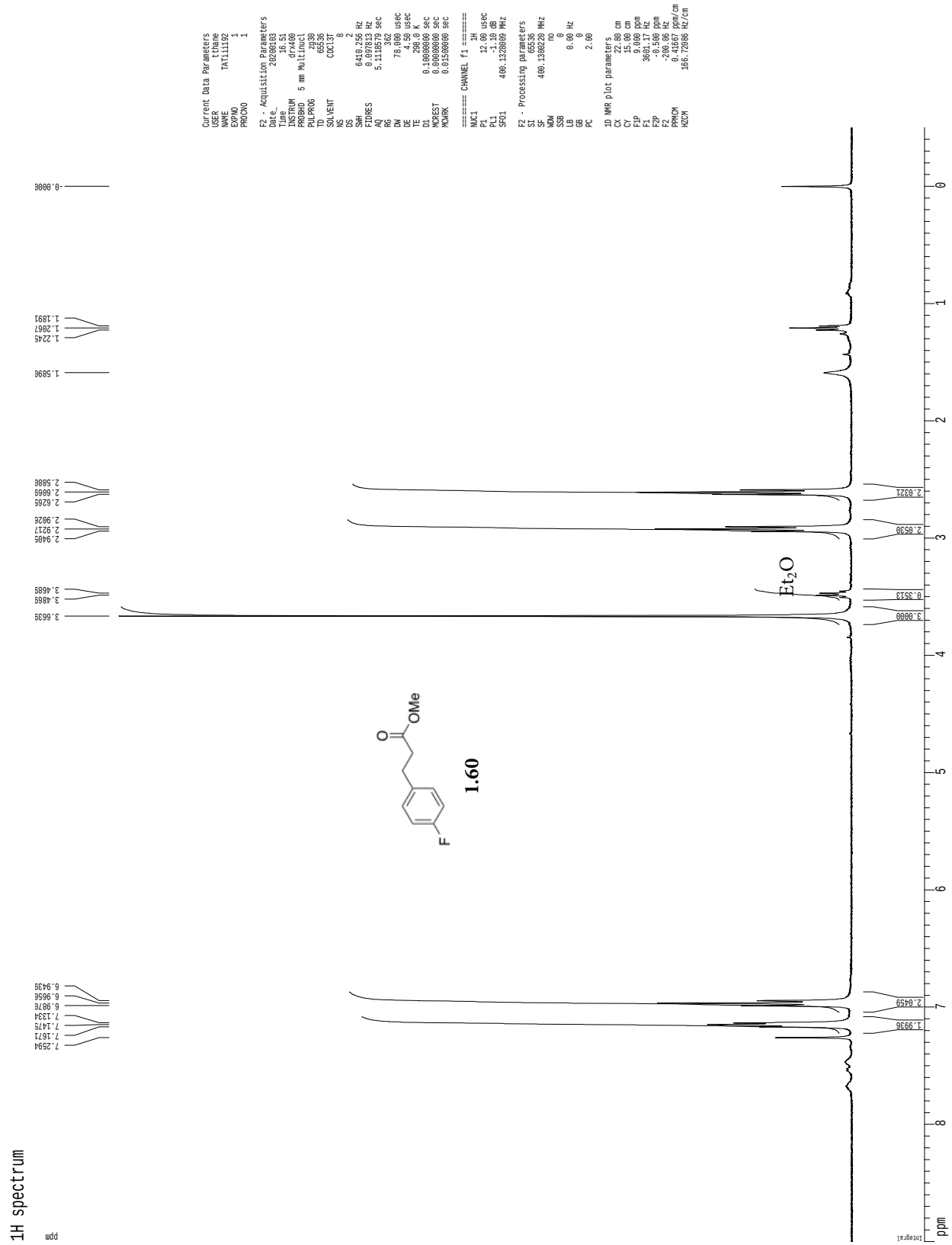

1H spectrum
ppm
Integral
1.12
OEt
OH
O
MeO

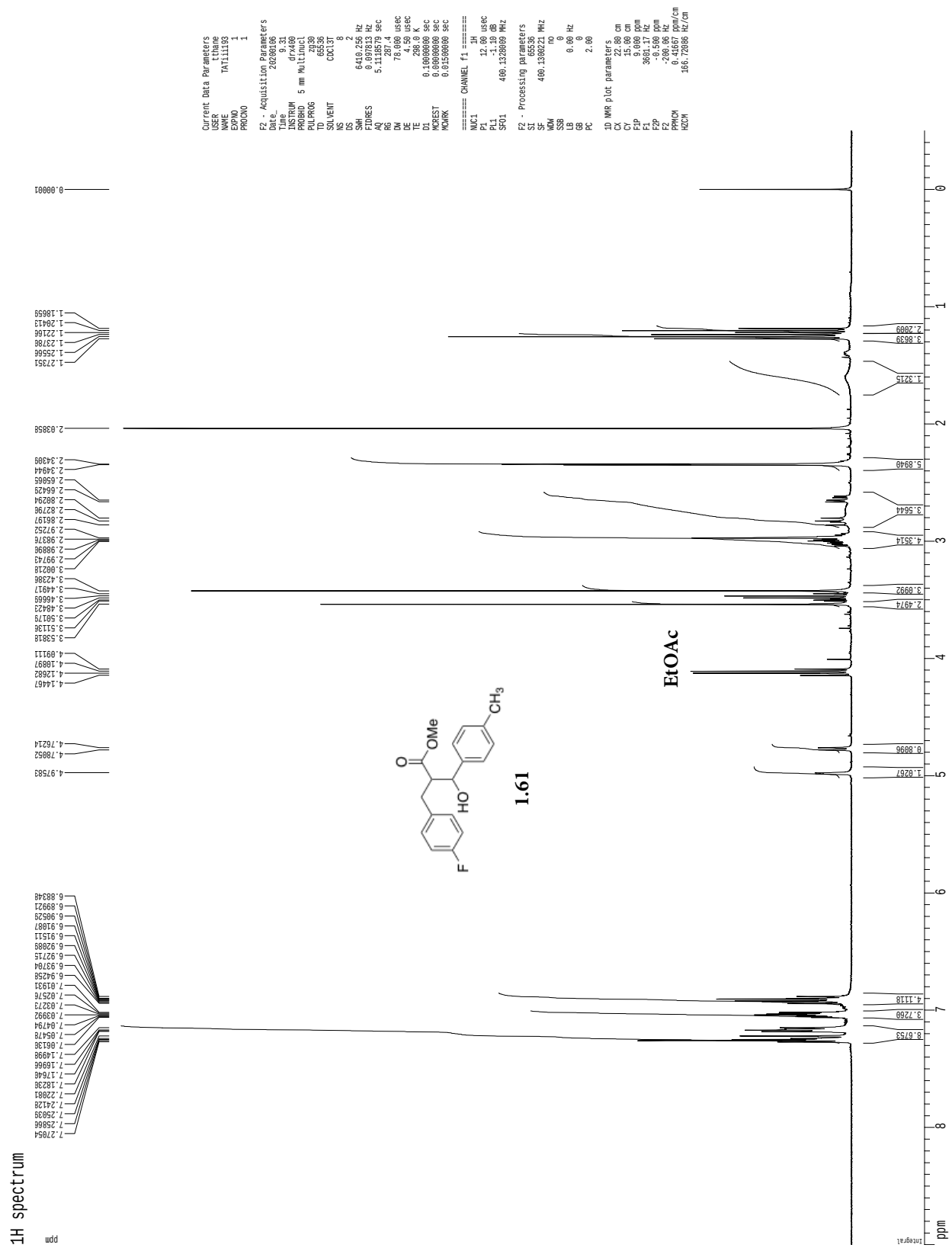

1H spectrum
Current Data Parameters
USER ttihane
NAME TAT111147c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191207
Time 15.03
INSTRUM drx400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 161.3
DW 78.000 usec
DE 4.50 usec
TE 297.3 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300228 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OH
OH
O
MeO
1.13
ppm
Integral

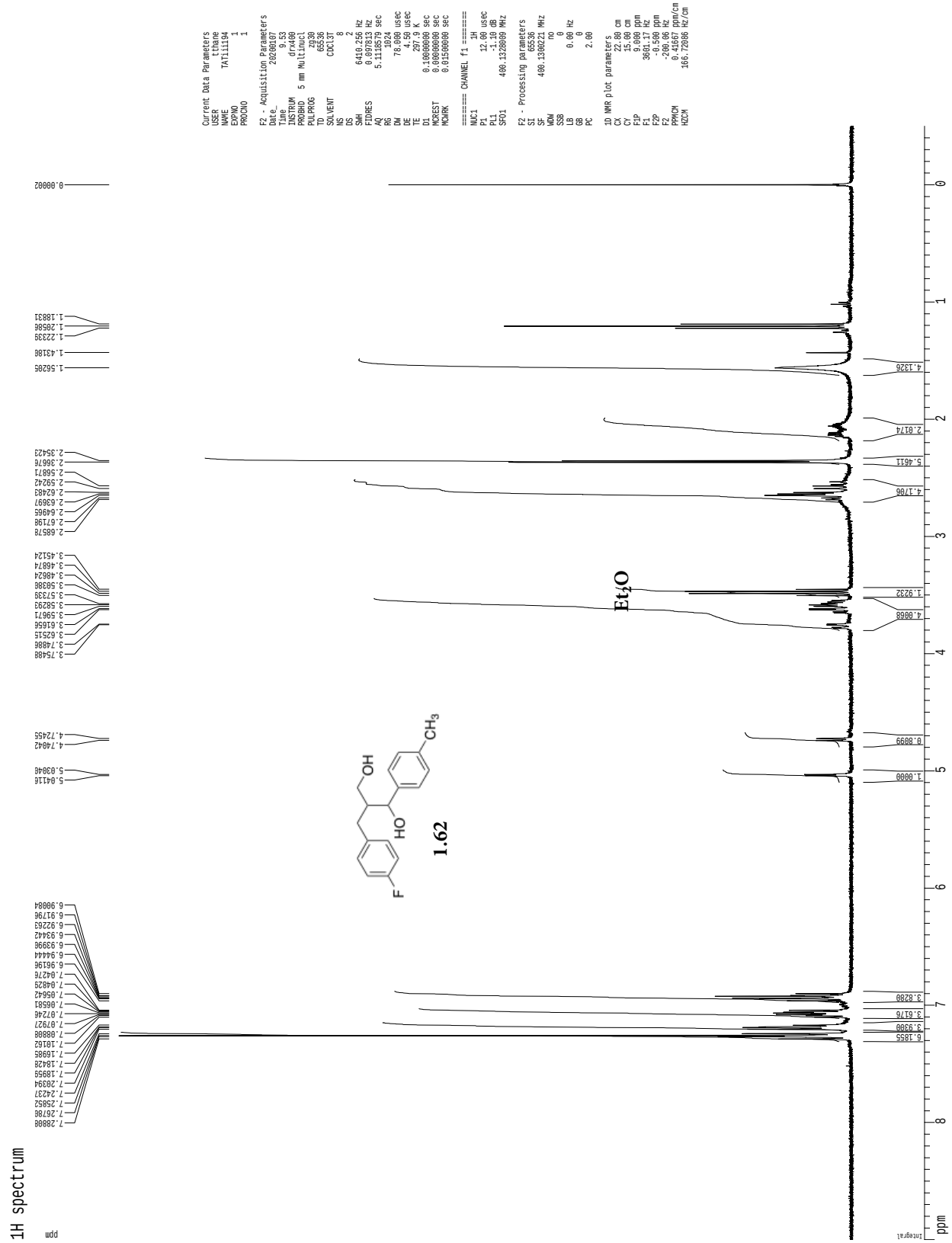

1H spectrum
Current Data Parameters
USER ttlahe
NAME TAT1111150c
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191205
Time 18.14
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 82728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098843 Hz
AQ 5.0998774 sec
RG 8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200316 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
OMs
Cl
O
MeO
1.14
ppm
Integral

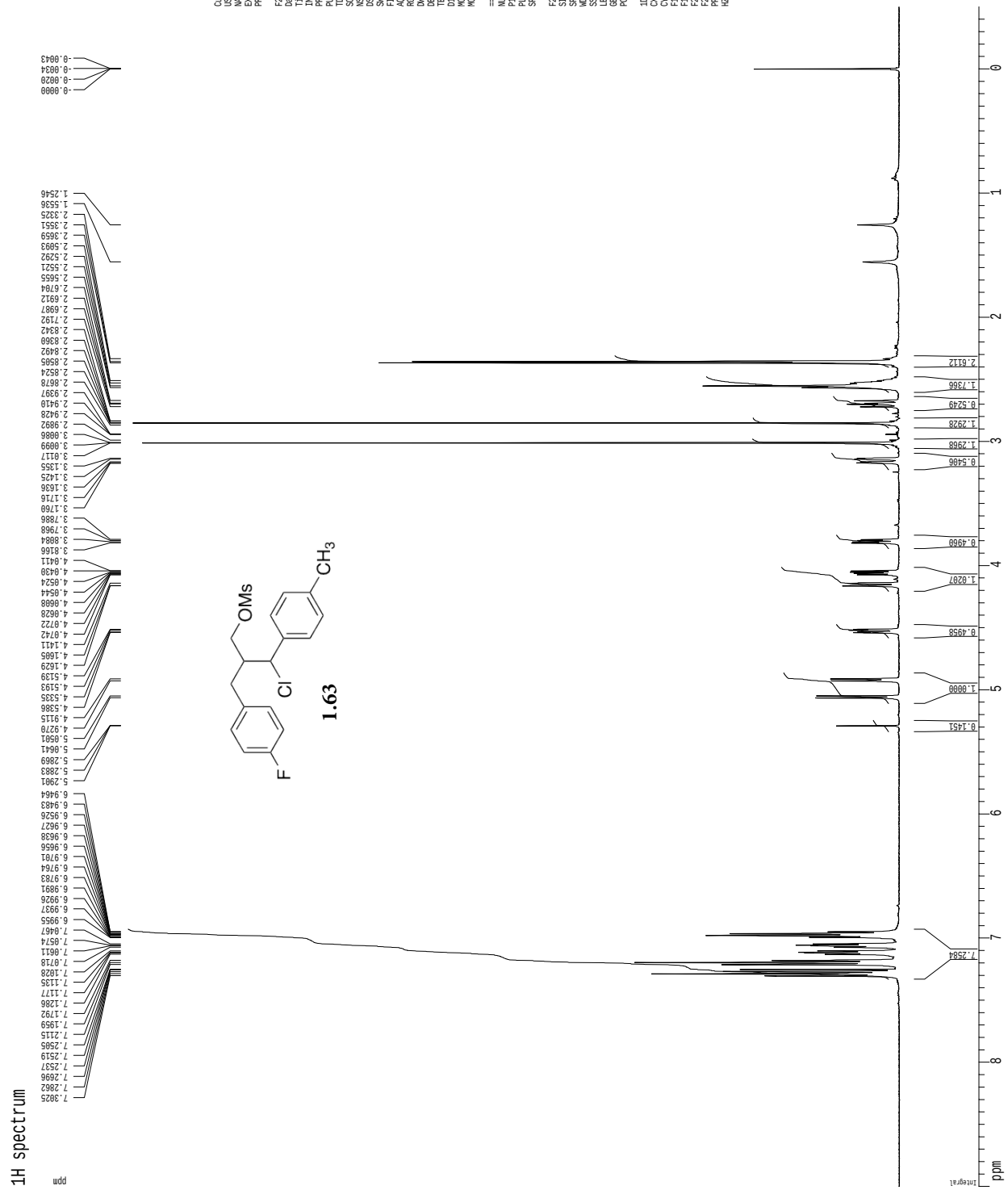

Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
158.62
158.59
144.31
144.26
140.82
140.77
130.17
130.08
130.02
124.77
124.69
114.37
109.18
109.06
77.41
77.16
76.91
68.70
68.65
55.57
55.41
54.94
47.84
47.52
37.24
33.29
31.88
OMs
Cl
O
MeO
1.14
Current Data Parameters
USER tATiliibec
NAME tATiliibec
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131205
Time 11.17
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 472
DS 16
SWH 30303.031 Hz
FIDRES 0.462398 Hz
AQ 1.08139840 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
d13 0.00003000 sec
MCWREST 0.01500000 sec
MCWRK 33.10 usec
P2
====== CHANNEL f1 ======
NUC1 13C
P1 10.50 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.79422540 MHz
SP1 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225911 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPV1 0.00 %
GPV2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.000 usec
F2 - Processing parameters
SI 65536
SF 125.78044071 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 8.33333 ppm/cm
HZCM 1048.17917 Hz/cm
ppm
0
20
40
60
80
100
120
140
160

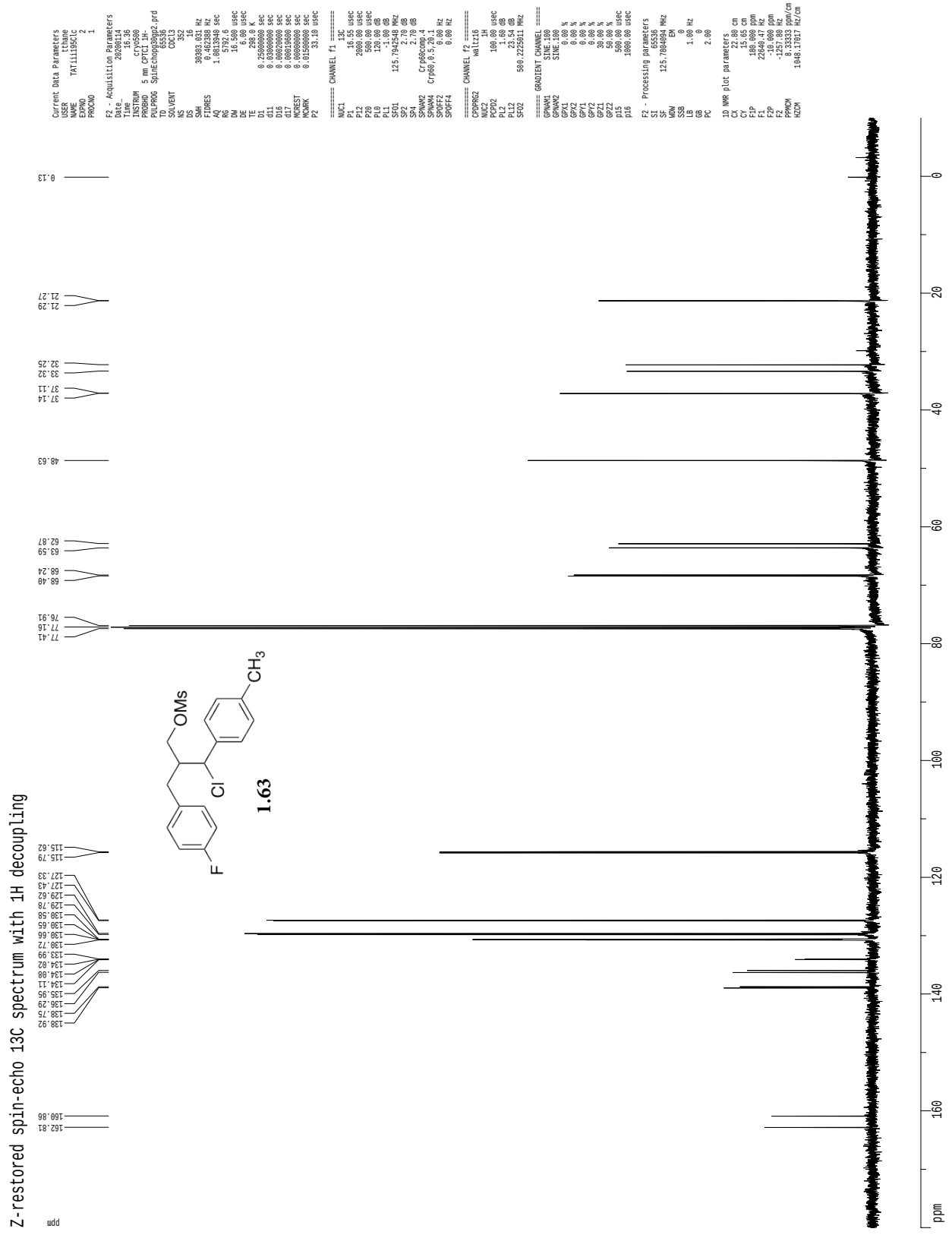

1H spectrum
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
OMe
F
1.59
ppm


1H spectrum
Current data Parameters
USER tihane
NAME TA1111192
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200103
Time 16.51
INSTRUM drx400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 362
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.09000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300220 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
0.0000
1.1891
1.2067
1.2245
1.5898
2.5886
2.6066
2.6265
2.9026
2.9217
2.9486
3.4689
3.4865
3.6639
6.9439
6.9656
6.9876
7.1334
7.1475
7.1671
7.2594
2.8321
2.8530
0.3513
3.0000
2.0459
1.9936
Et2O
OMe
O
F
1.60
ppm
Integral


1H spectrum
EtOAc
1.61
OMe
HO
F
CH3


1H spectrum
Et2O
1.62


1H spectrum
Current data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
OMs
Cl
F
CH3
1.63
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
OMs
Cl
F
CH3
1.63

19F spectrum


```
Current Data Parameters
USER              tthane
NAME         TATiii195clF
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200115
Time               9.41
INSTRUM          av600
PROBHD   5 mm CPBBO BB-
PULPROG          zgflqn30
TD                18938
SOLVENT           CDCl3T
NS                   16
DS                    2
SWH            6313.131 Hz
FIDRES         0.333358 Hz
AQ             1.4999396 sec
RG                  575
DW                79.200 usec
DE                18.00 usec
TE                298.0 K
D1             3.00000000 sec
TD0                    1

======= CHANNEL f1 =======
SFO1         564.6210276 MHz
NUC1                19F
P1                17.50 usec

F2 - Processing parameters
SI                131072
SF           564.6863858 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                22.80 cm
CY                15.00 cm
F1P             -112.000 ppm
F1            -63244.88 Hz
F2P             -120.000 ppm
F2            -67762.37 Hz
PPMCM           0.35088 ppm/cm
HZCM          198.13559 Hz/cm
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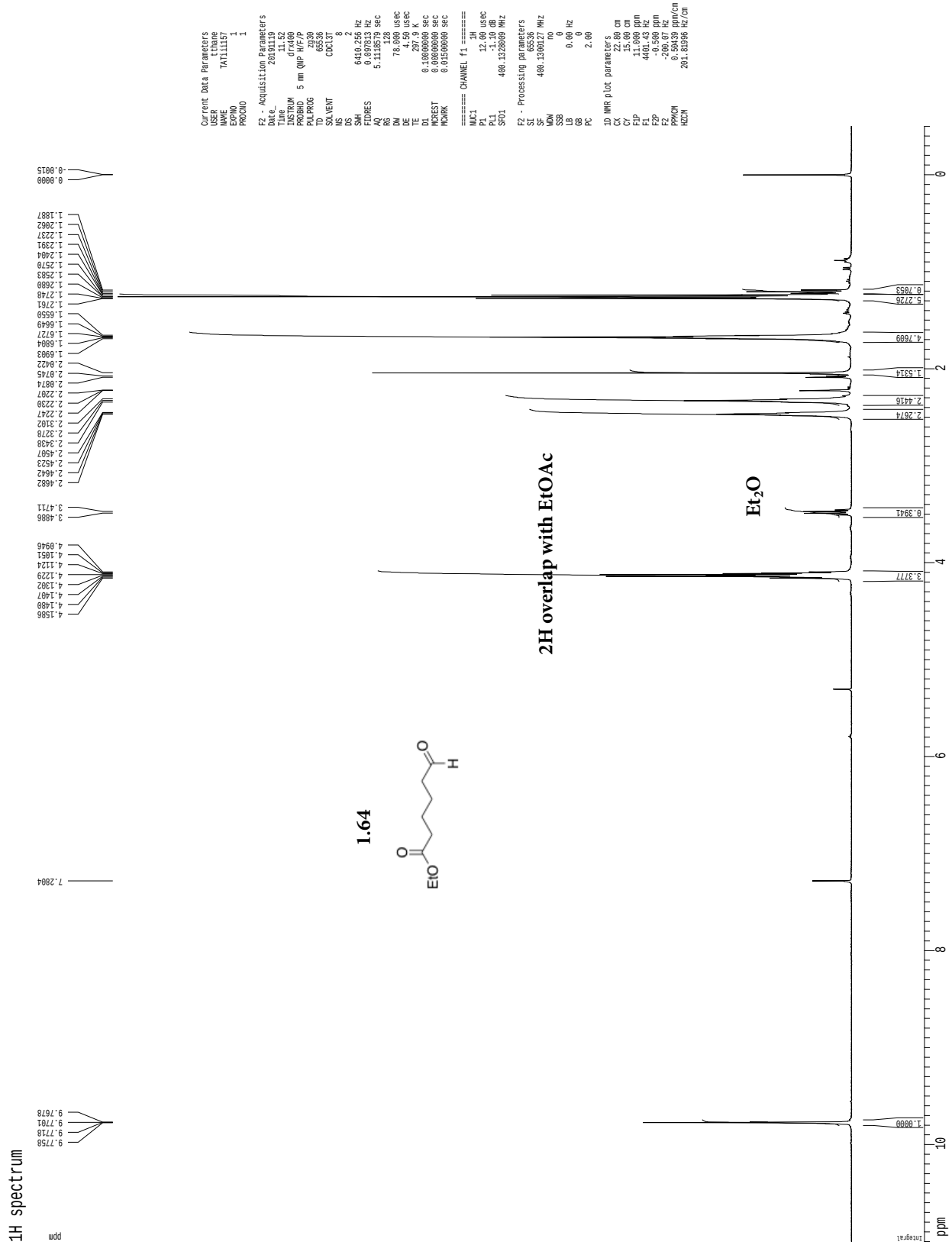
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Current Data Parameters
USER tihane
NAME TA1111157
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191119
Time 11.52
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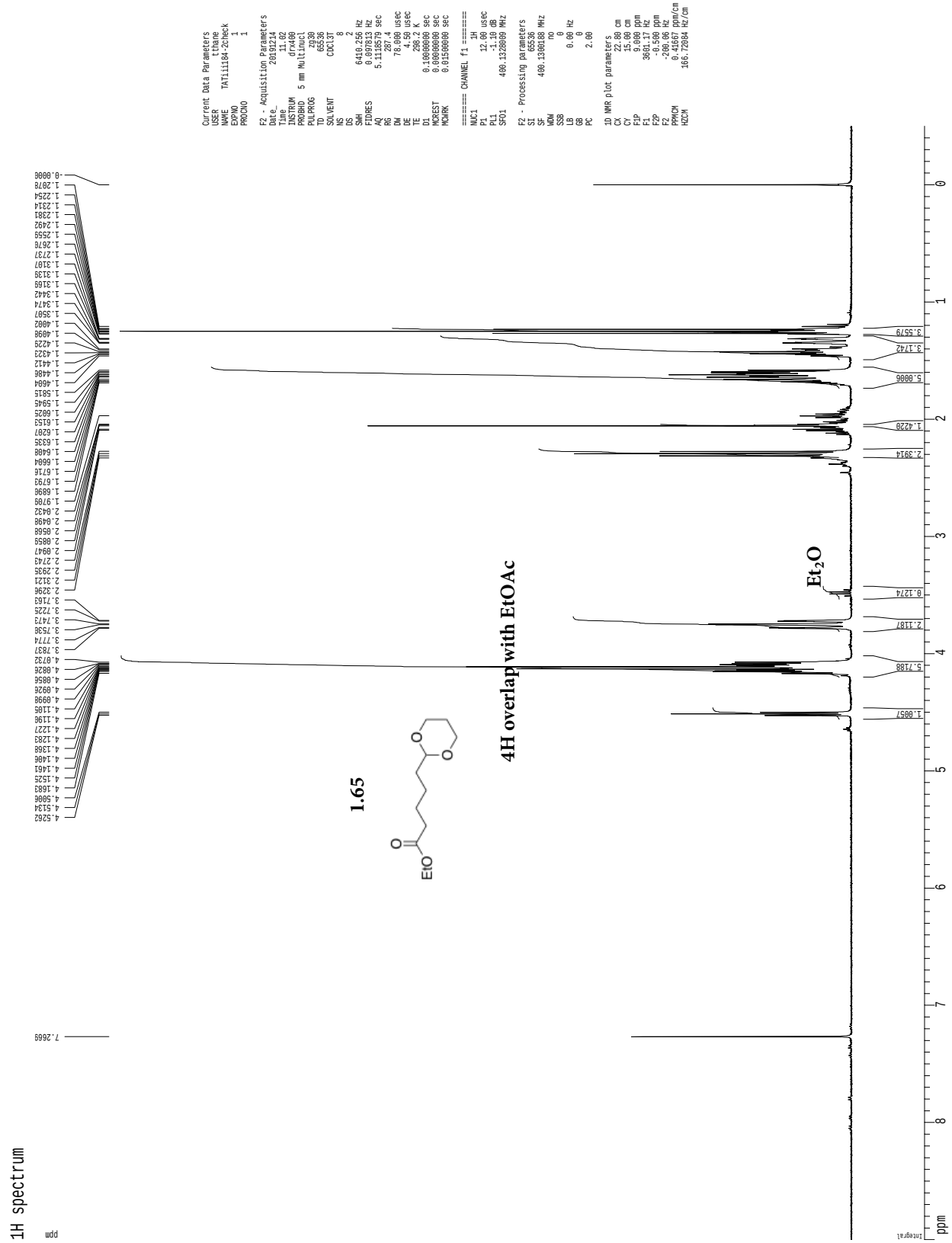
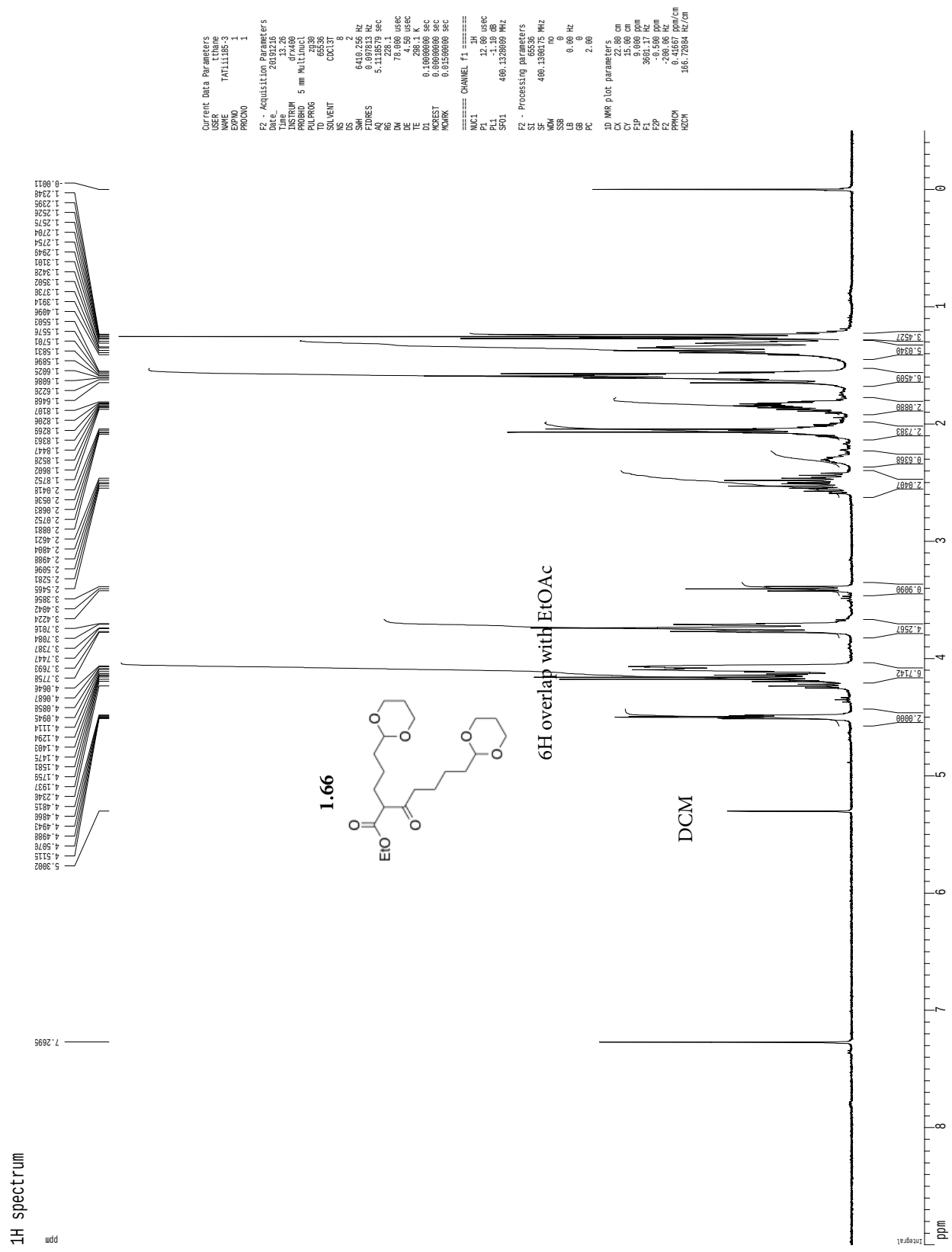
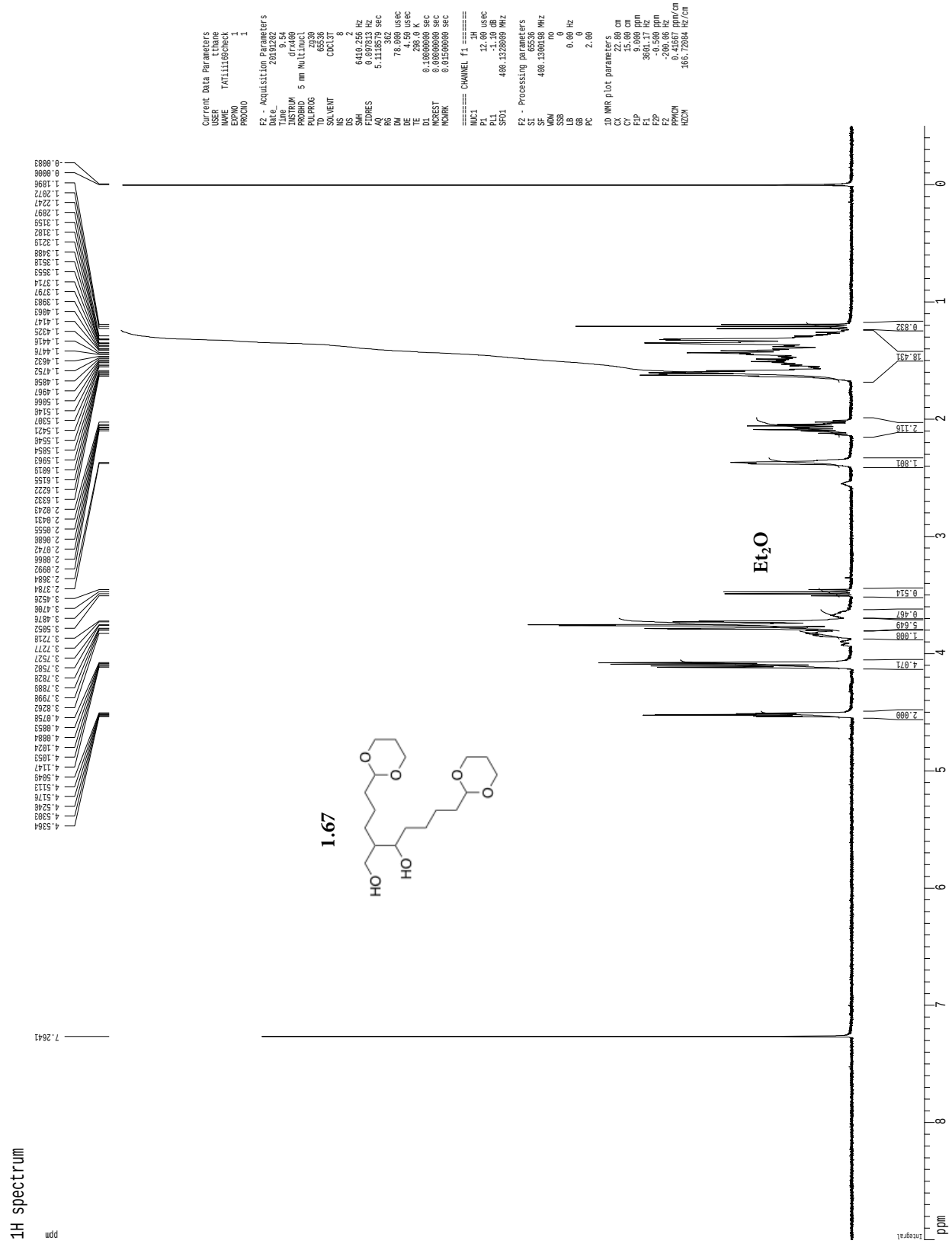
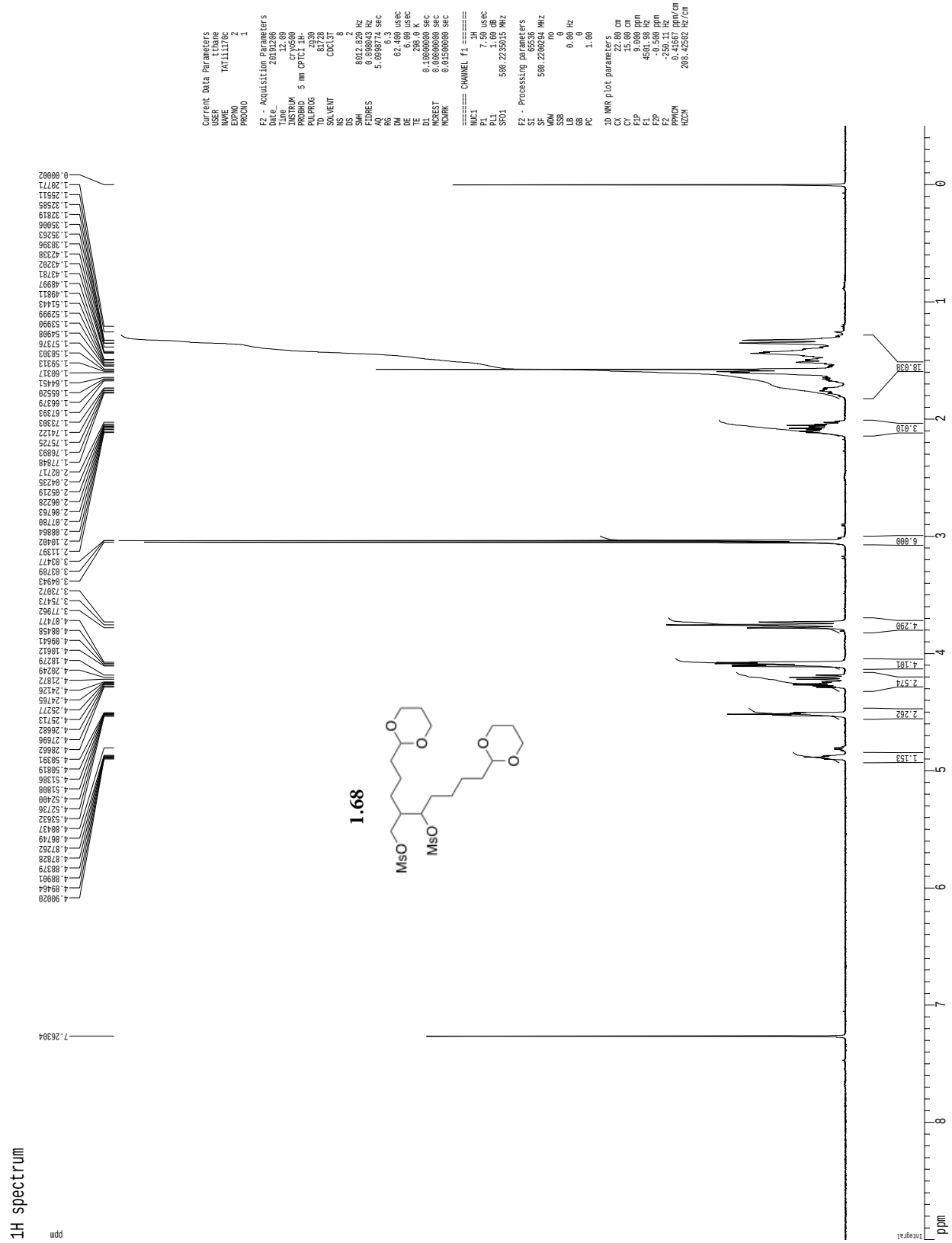
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.0978813 Hz
AQ 5.1118579 sec
RG 128
DW 78.000 usec
DE 4.50 usec
TE 297.3 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300127 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 11.000 ppm
F1 4401.43 Hz
F2P -0.500 ppm
F2 -200.07 Hz
PPMCM 0.50439 ppm/cm
HZCM 201.61996 Hz/cm
0.0015
0.0000
1.1887
1.2062
1.2237
1.2391
1.2404
1.2570
1.2583
1.2680
1.2748
1.2761
1.6550
1.6649
1.6727
1.6804
1.6903
2.0422
2.0745
2.0874
2.2207
2.2230
2.2247
2.3182
2.3278
2.3438
2.4507
2.4523
2.4642
2.4682
3.4711
3.4886
4.0946
4.1051
4.1124
4.1229
4.1392
4.1487
4.1480
4.1586
7.2804
9.7678
9.7701
9.7718
9.7758
1.64
EtO
O
O
H
2H overlap with EtOAc
Et2O
1.0000
3.3777
0.3941
7.2674
2.4416
1.5314
4.7609
5.2726
0.7053
Integral
ppm
0
2
4
6
8
10

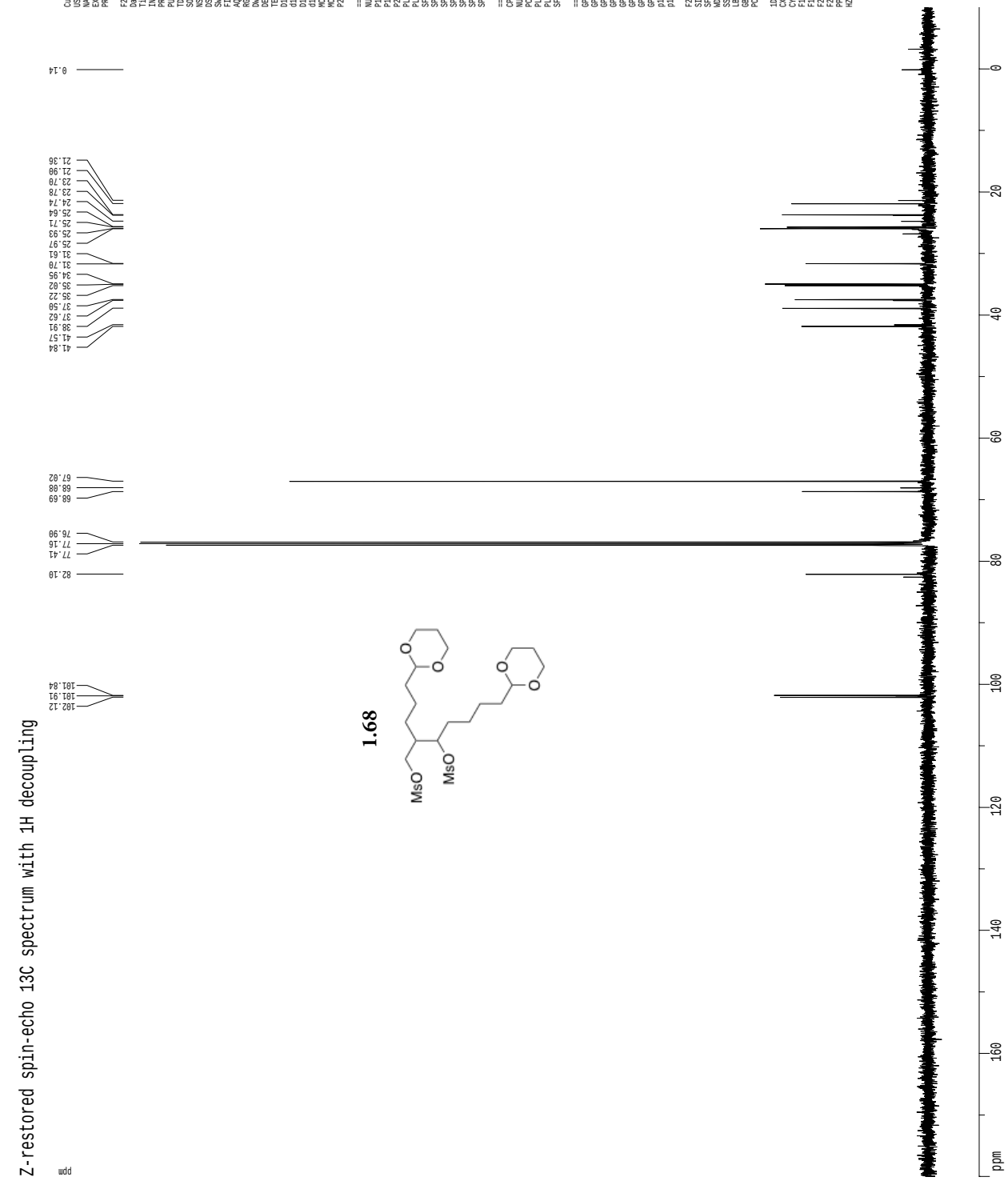

1H spectrum
Current Data Parameters
USER tthane
NAME TATiii104-2dcheck
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191214
Time 11.02
INSTRUM drx400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 287.4
DW 78.000 usec
DE 4.50 usec
TE 298.2 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300188 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72604 Hz/cm
7.2669
4.5262
4.5134
4.5006
4.1683
4.1525
4.1461
4.1406
4.1368
4.1283
4.1227
4.1196
4.1105
4.0998
4.0926
4.0856
4.0826
4.0732
3.7837
3.7774
3.7536
3.7473
3.7225
3.7163
2.3296
2.2743
2.2321
2.2295
2.0947
2.0859
2.0568
2.0498
2.0432
1.9708
1.6993
1.6896
1.6774
1.6684
1.6488
1.6328
1.6297
1.6153
1.6025
1.5945
1.5815
1.4604
1.4486
1.4412
1.4323
1.4225
1.4098
1.4002
1.3674
1.3597
1.3442
1.3165
1.3139
1.3107
1.2737
1.2676
1.2559
1.2492
1.2381
1.2314
1.2254
1.2078
1.0000
1.65
4H overlap with EtOAc
Et2O
EtO
3.5579
3.1742
5.0006
1.4220
2.3914
0.1274
2.1187
5.7188
1.0057
Integral
ppm


1H spectrum
1.66
6H overlap with EtOAc
DCM
EtO

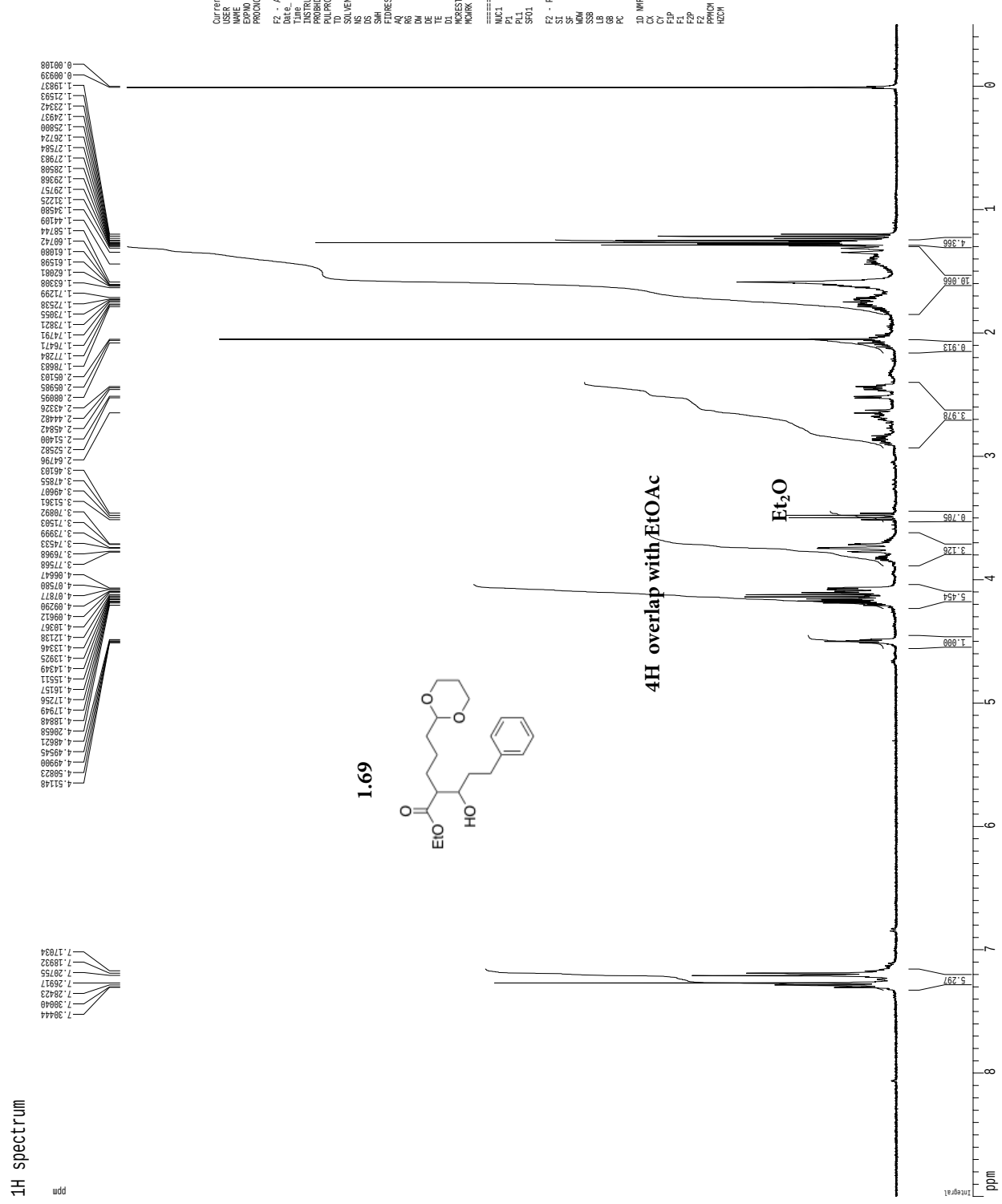

1H spectrum
Current data Parameters
Date_ 20191202
Time 9.54
INSTRUM drx400
PROBHD 5 mm Multinuci
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1138579 sec
RG 362
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
F2 - Processing parameters
SI 65536
SF 400.1300198 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72084 Hz/cm
Et2O
1.67
HO
HO
ppm
Integral

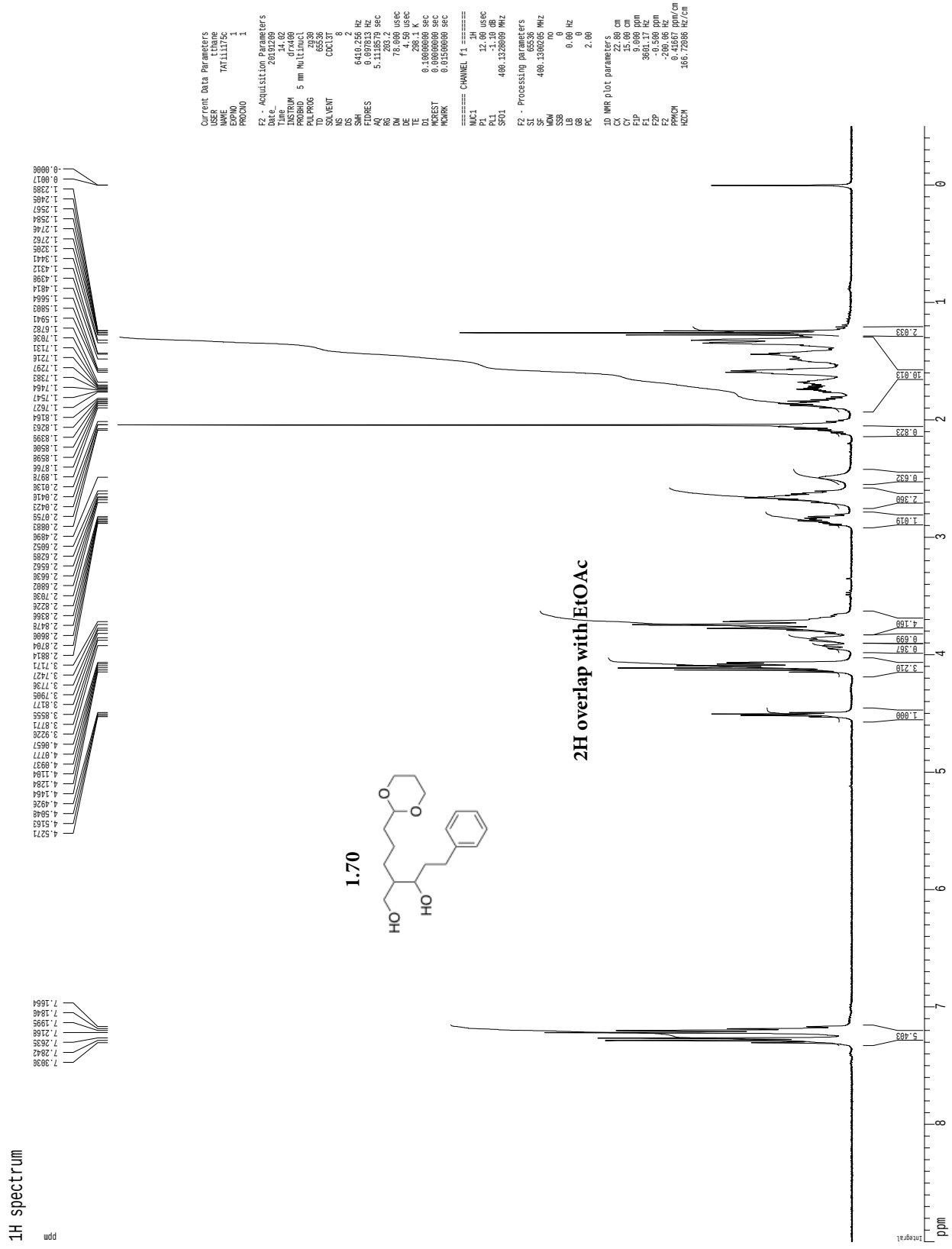

1H spectrum
1.68
MsO
MsO
ppm
Integral
7.26304
6.000
4.290
4.101
3.010
2.574
2.262
1.153
18.038

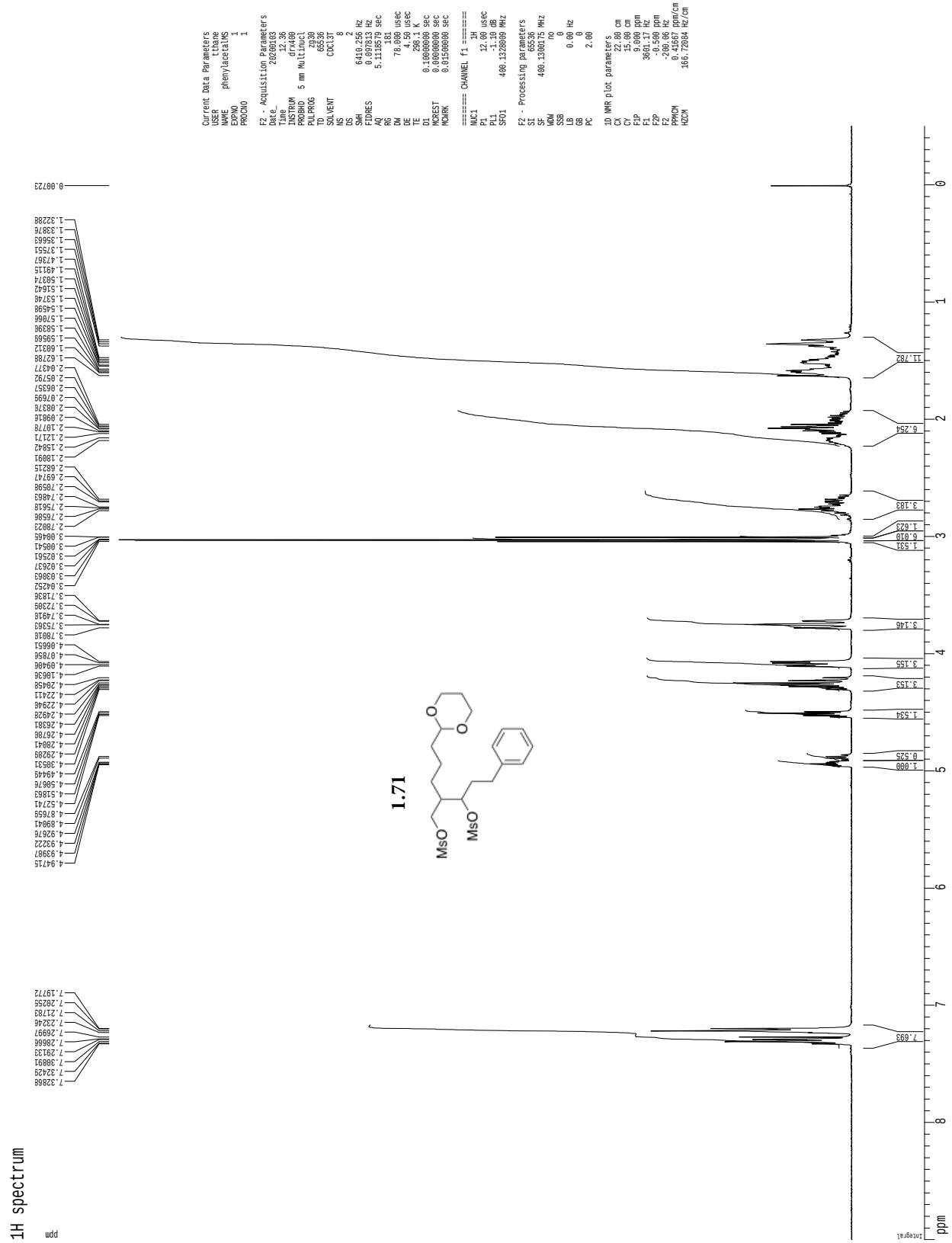
Z-restored spin-echo 13C spectrum with 1H decoupling



1.68


1H spectrum
4H overlap with ÆtOAc
Et2O
1.69
EtO
HO
Current Data Parameters
Acquisition Parameters
Processing parameters
1D NMR plot parameters
ppm
Integral


1H spectrum
Current data Parameters
Date_ Time INSTRUM PROBHD PULPROG TD SOLVENT NS DS SWH FIDRES AQ RG DW DE TE D1 MCREST MCWRK
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
2H overlap with EtOAc
1.70
HO
HO
ppm
Integral


1H spectrum
Current Data Parameters
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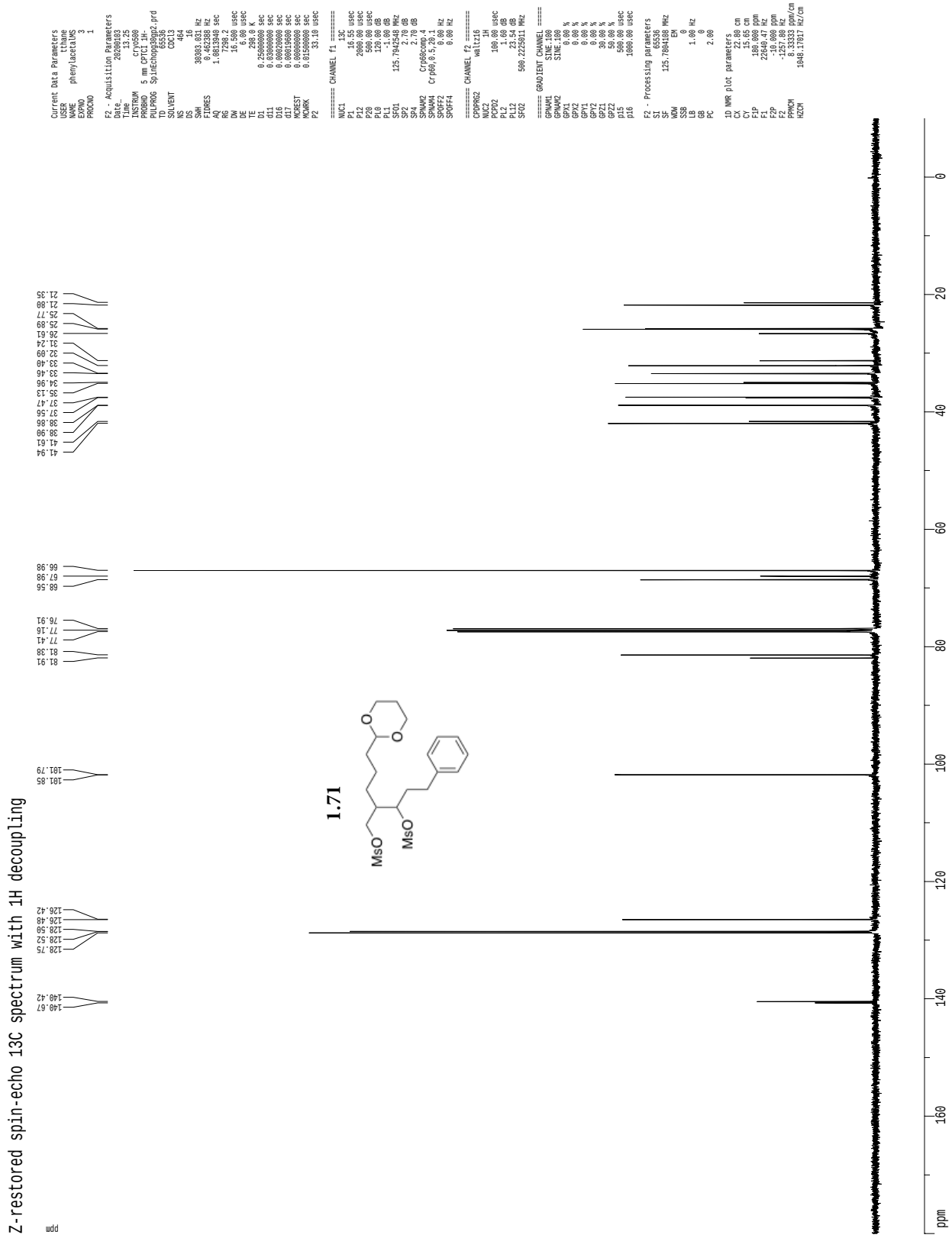
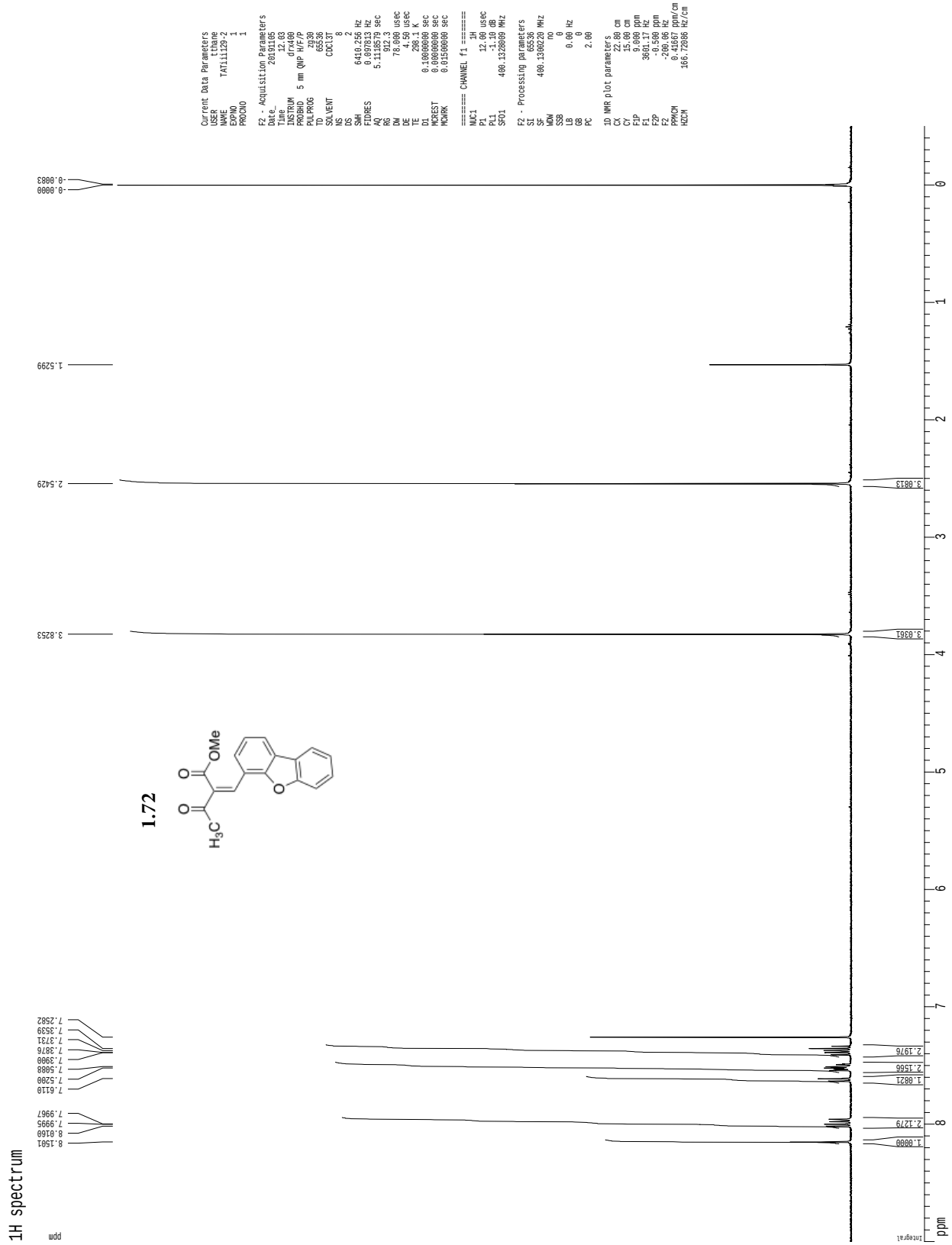
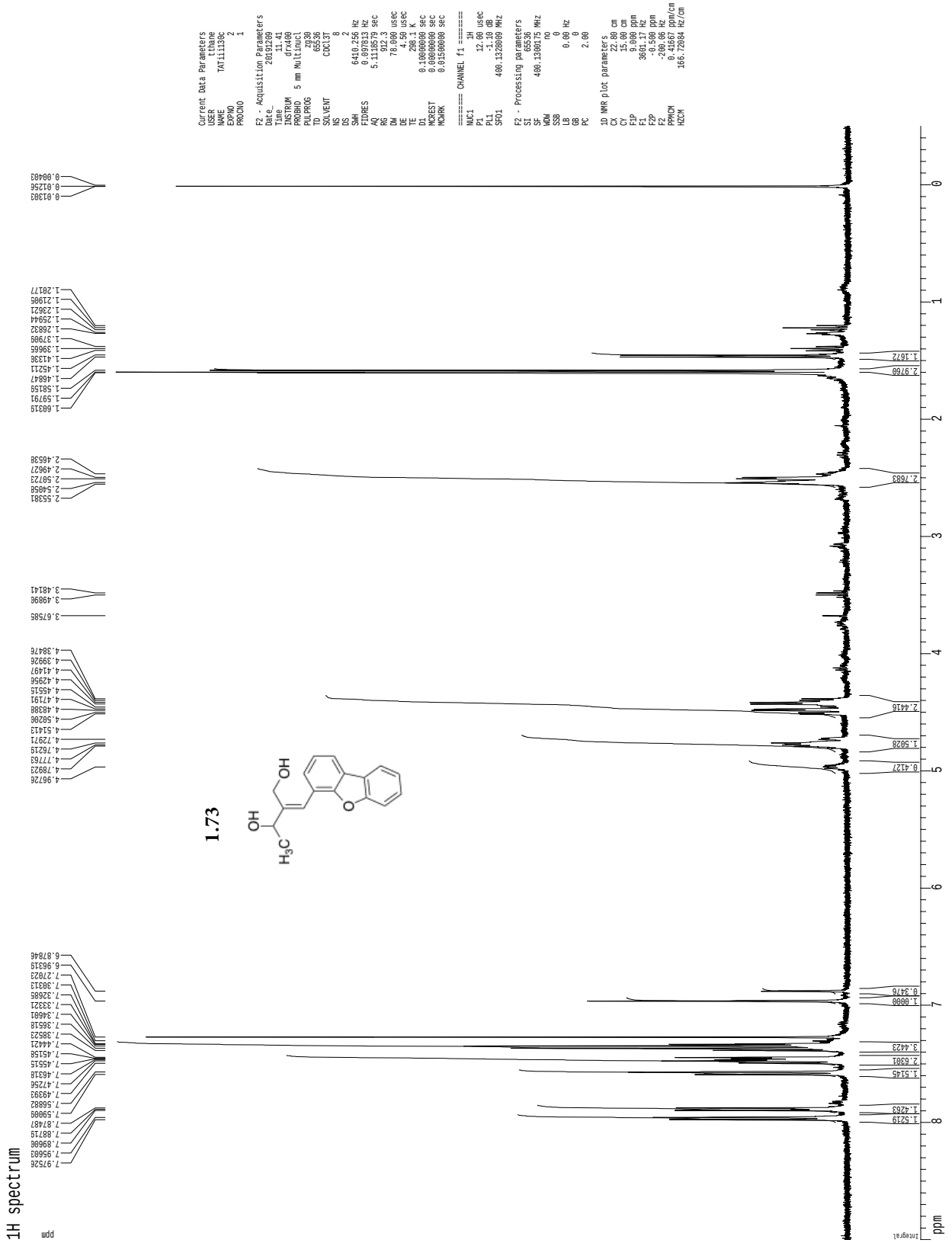
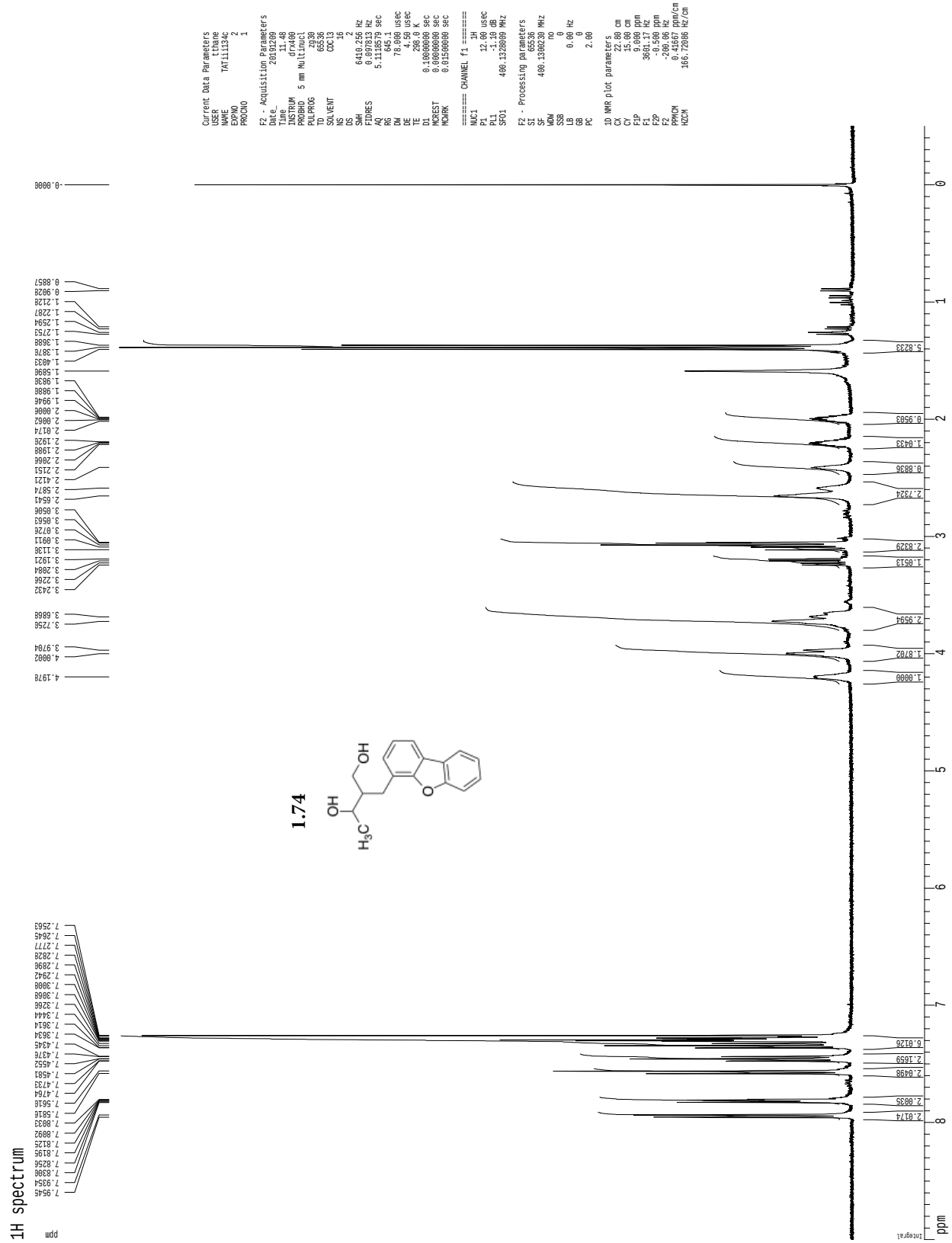
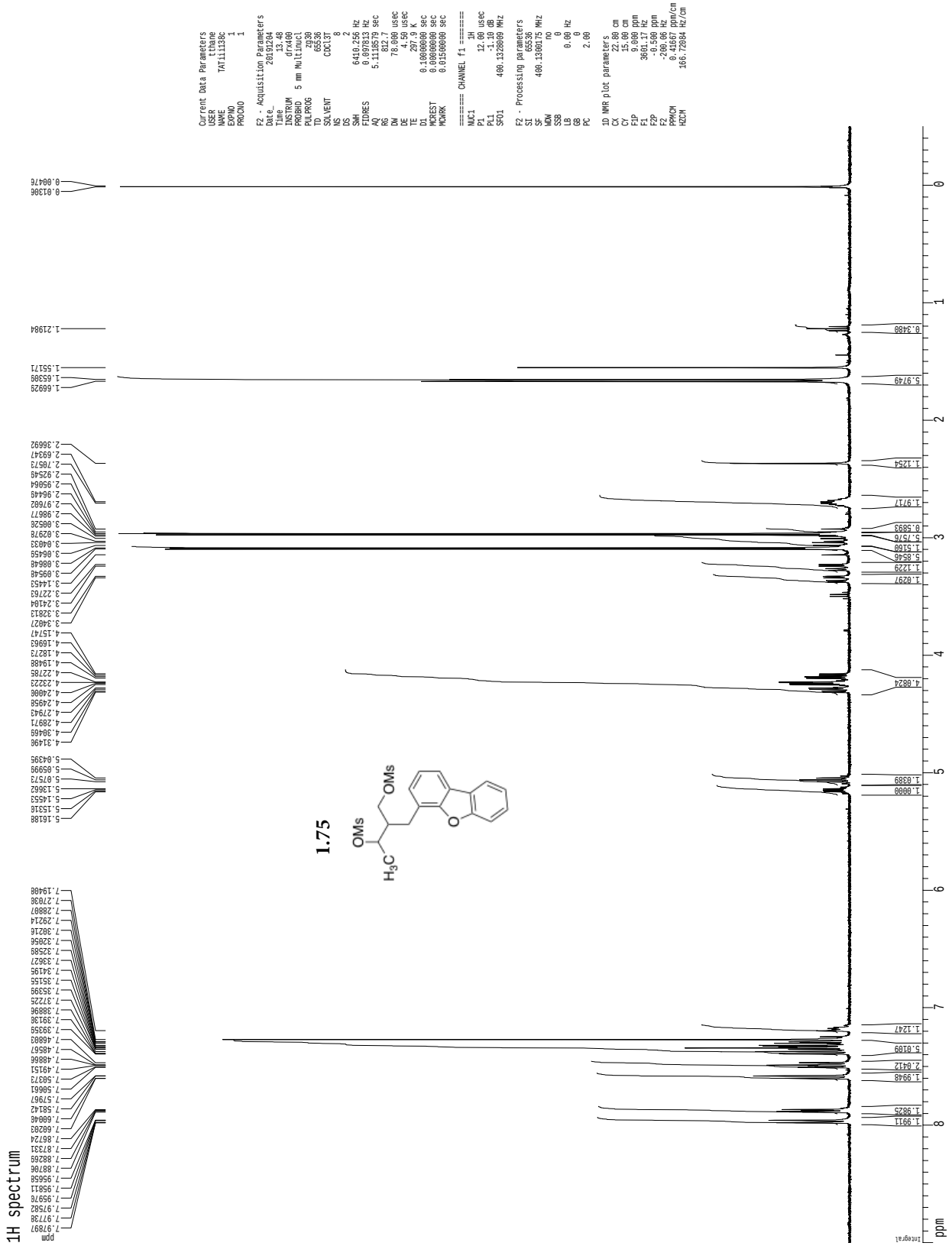
NAME phenylacetaline
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200103
Time 12.36
INSTRUM drx400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 161
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300175 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72604 Hz/cm
1.71
MsO
MsO
11.782
6.254
3.183
1.673
6.010
1.531
3.146
3.155
3.152
1.534
0.525
1.000
7.693
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
1.71
MsO
MsO
ppm
0
20
40
60
80
100
120
140
160
180
140.67
140.42
128.75
128.52
128.50
128.48
126.42
101.85
101.79
81.91
81.38
77.41
77.16
76.91
68.56
67.98
66.98
41.94
41.61
38.90
38.86
37.56
37.47
35.13
34.96
33.46
33.40
32.09
31.24
26.61
25.89
25.77
21.80
21.35
Current Data Parameters
USERNAME
NAME phenylacetalMS
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200103
Time 13.25
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 464
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08139840 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
====== CHANNEL f1 ======
NUC1 13C
P1 10.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.78942540 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPV1 0.00 %
GPV2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.000 usec
F2 - Processing parameters
SI 65536
SF 125.78041388 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.000 ppm
F2 -1257.800 Hz
PPMCM 0.33333 ppm/cm
HZCM 1040.17917 Hz/cm

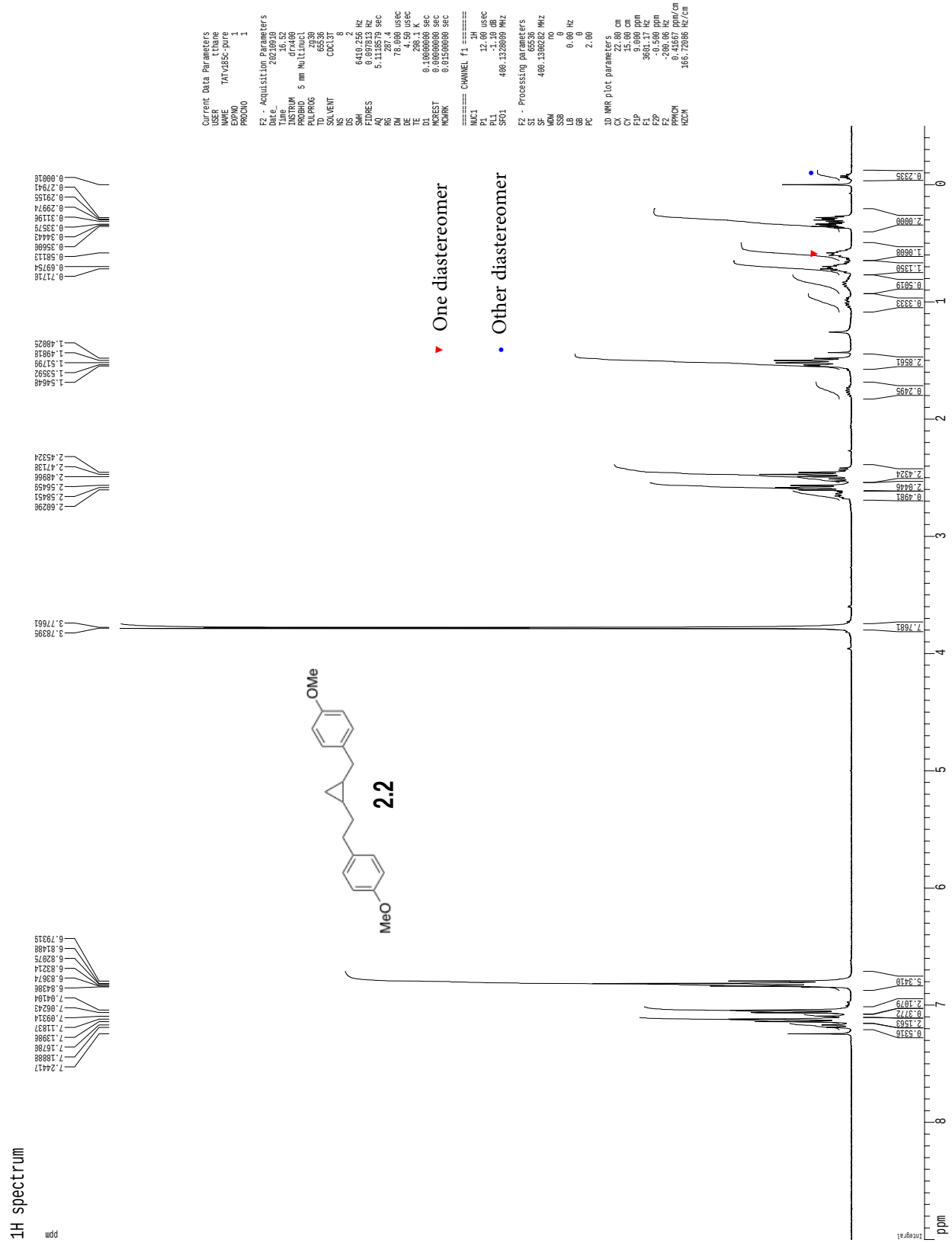

1H spectrum
1.72
OMe
O
O
H3C
Current Data Parameters
USER tithane
NAME TATi111129-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191105
Time 12.03
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 912.3
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300220 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
0.0083
0.0000
1.5299
2.5429
3.8253
8.1501
8.0160
7.9995
7.9967
7.6110
7.5200
7.5088
7.3900
7.3876
7.3731
7.3539
7.2582
3.0813
3.0361
2.1976
2.1566
1.0821
1.0000
2.1279
Integral
ppm

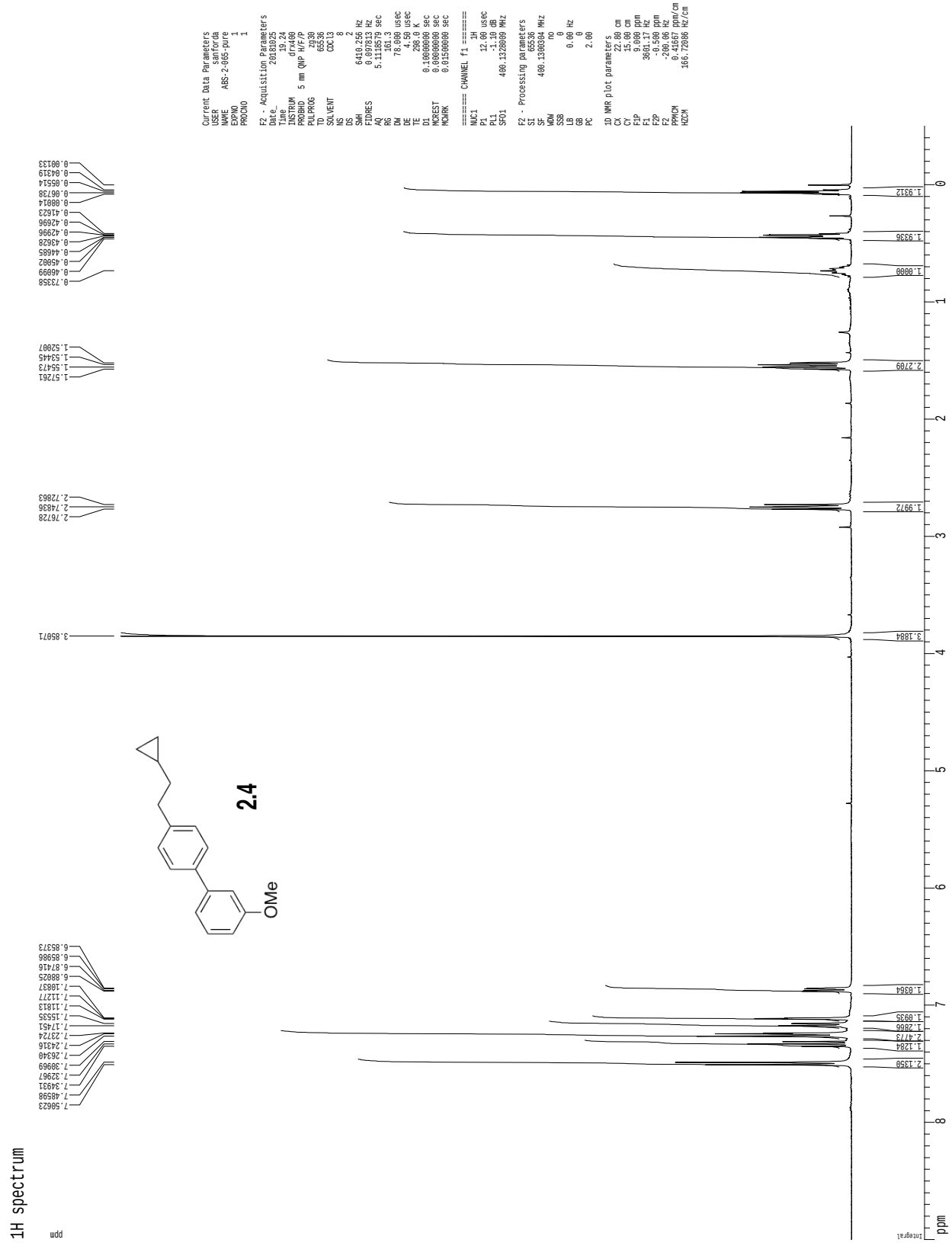

1H spectrum
1.73
OH
OH
H3C
Current Data Parameters
Acquisition Parameters
Processing parameters
1D NMR plot parameters
ppm
Integral

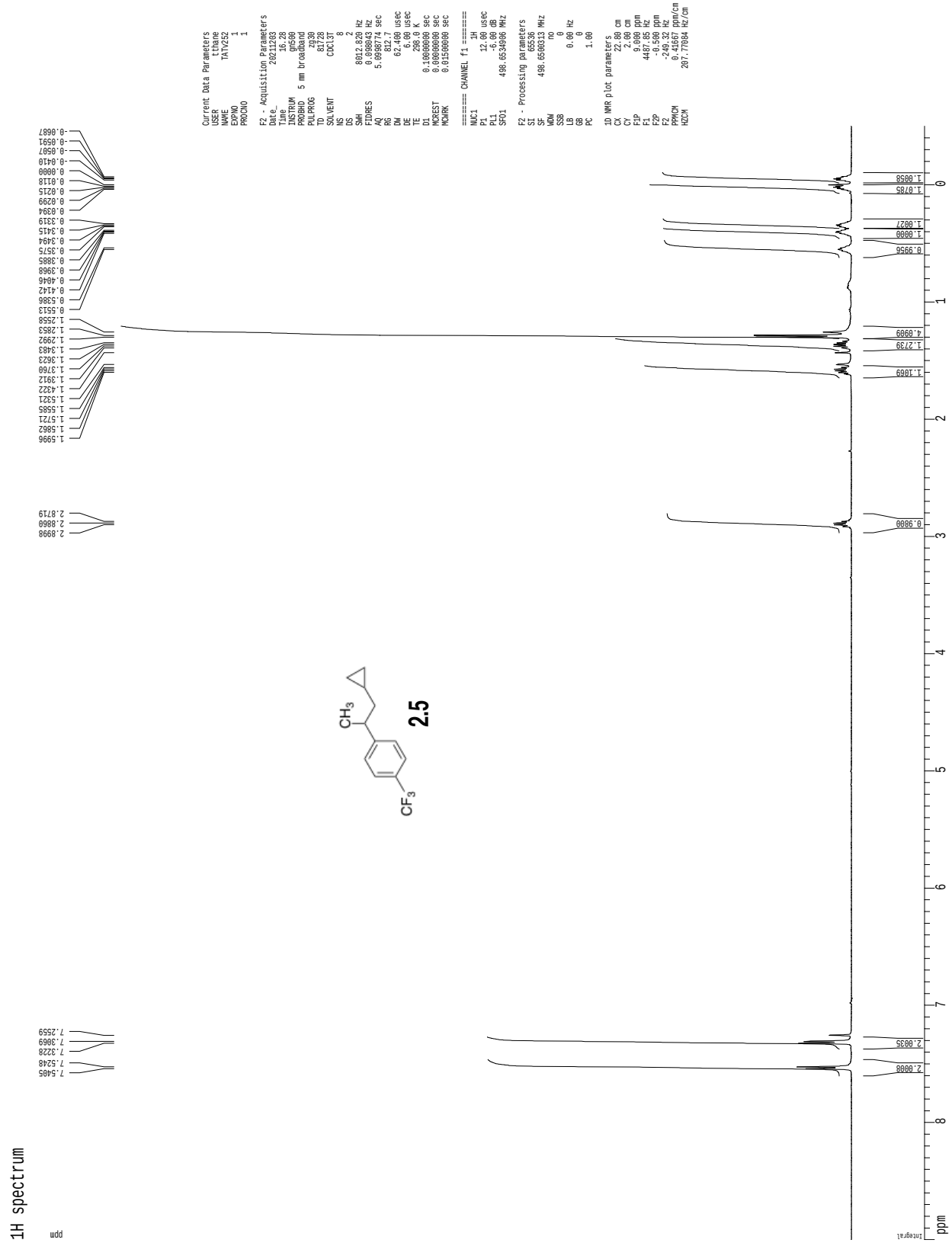

1H spectrum
1.74
OH
OH
H_3C
Current Data Parameters
Acquisition Parameters
Processing parameters
1D NMR plot parameters
ppm
Integral


1H spectrum
1.75
OMs
OMs
H3C
O
ppm
Integral

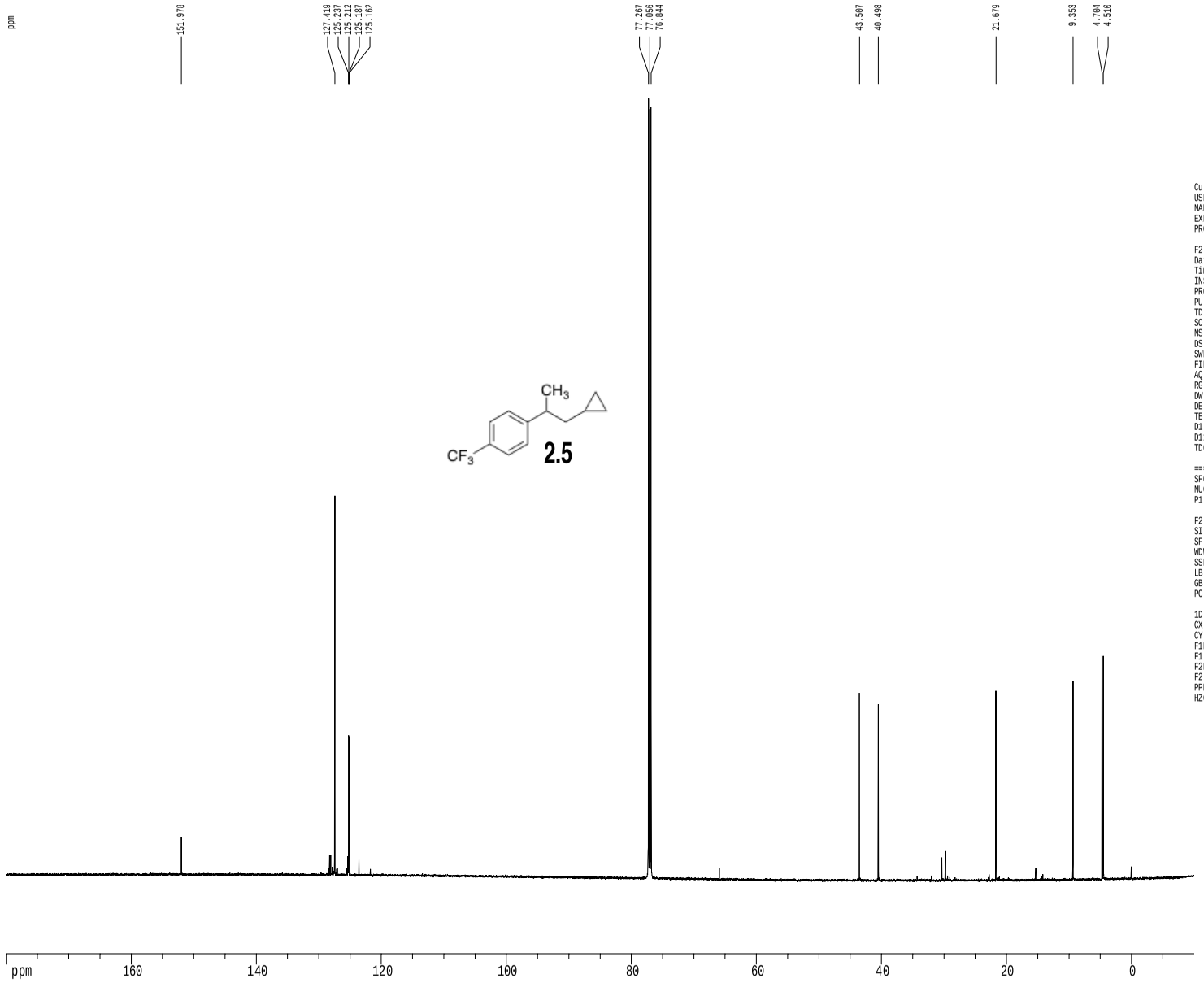
A.2 NMR Data Corresponding to Chapter 2


1H spectrum
One diastereomer
Other diastereomer
2.2
OMe
MeO


1H spectrum
2.4
OMe
ppm


1H spectrum
Current Data Parameters
USER ttihane
NAME TATV252
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211203
Time 16.28
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.6998774 sec
RG 812.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -6.00 dB
SFO1 498.6534906 MHz
F2 - Processing parameters
SI 65536
SF 498.6500313 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 2.00 cm
F1P 9.000 ppm
F1 4487.85 Hz
F2P -0.500 ppm
F2 -249.32 Hz
PPMCM 0.41667 ppm/cm
HZCM 207.77084 Hz/cm
2.5
ppm
Integral

13C spectrum with 1H decoupling



Current Data Parameters
USER tthane
NAME TATv252carbon
EXPNO 2
PROCNO 1

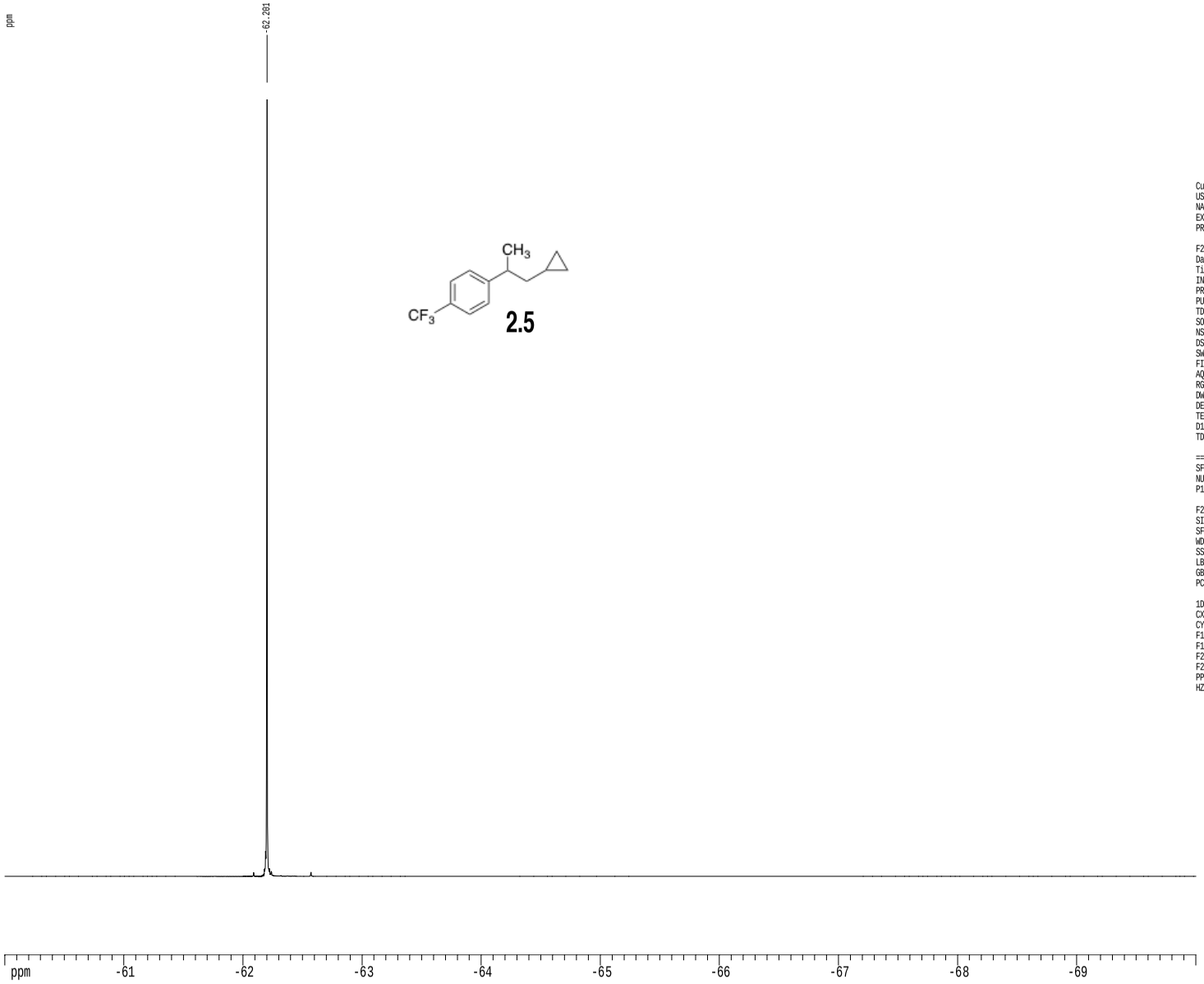
F2 - Acquisition Parameters
Date_ 20211220
Time 15.46
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3T
NS 1024
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9044468 sec
RG 2050
DW 13.800 usec
DE 19.63 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1

======= CHANNEL f1 =======
SFO1 150.9194080 MHz
NUC1 13C
P1 10.10 usec

F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 180.000 ppm
F1 27162.50 Hz
F2P -10.000 ppm
F2 -1509.03 Hz
PPMCM 8.33333 ppm/cm
HZCM 1257.52344 Hz/cm

19F spectrum



2.5

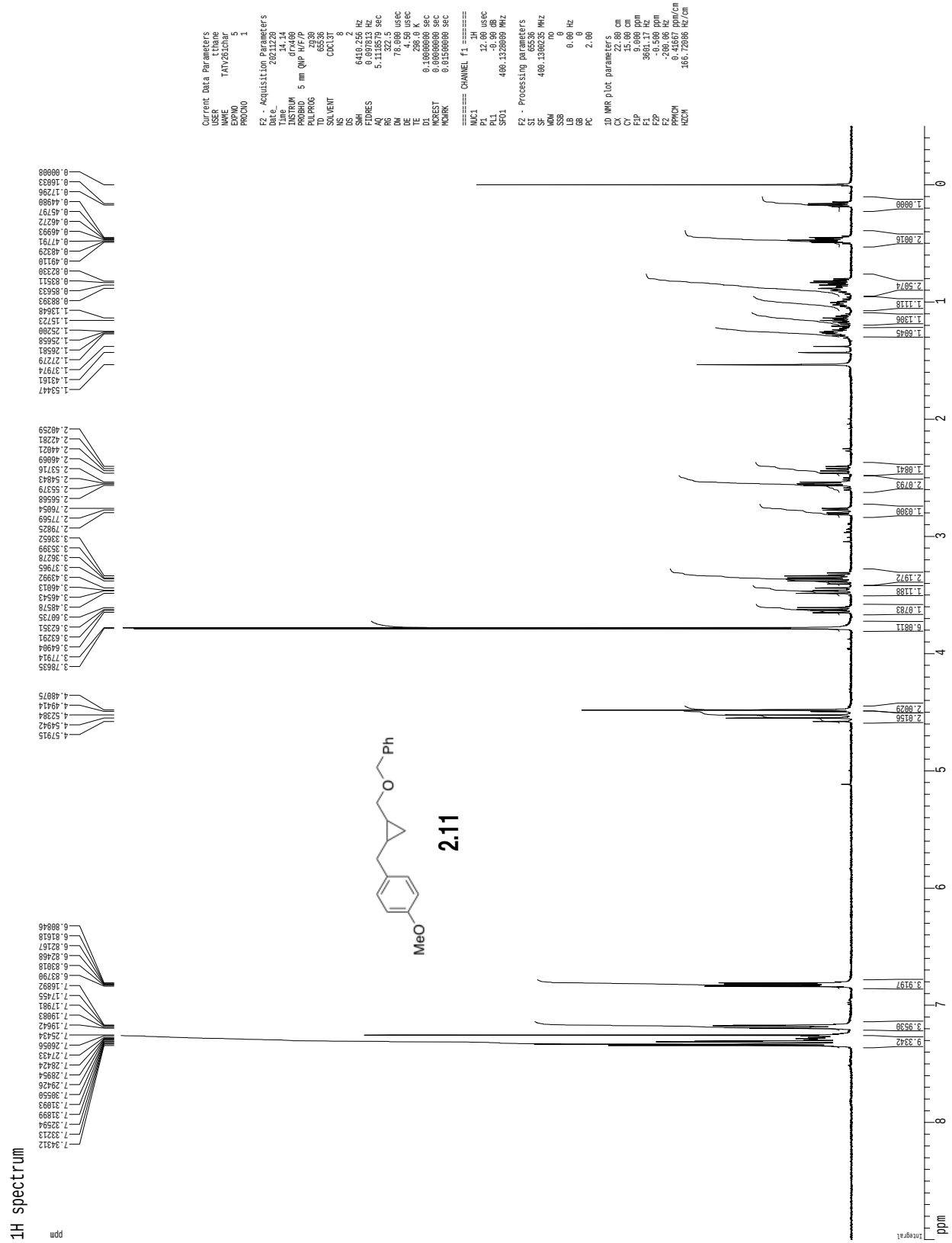
```
Current Data Parameters
USER              tthane
NAME      TATv252fluorine
EXPNO                   1
PROCNO                  1

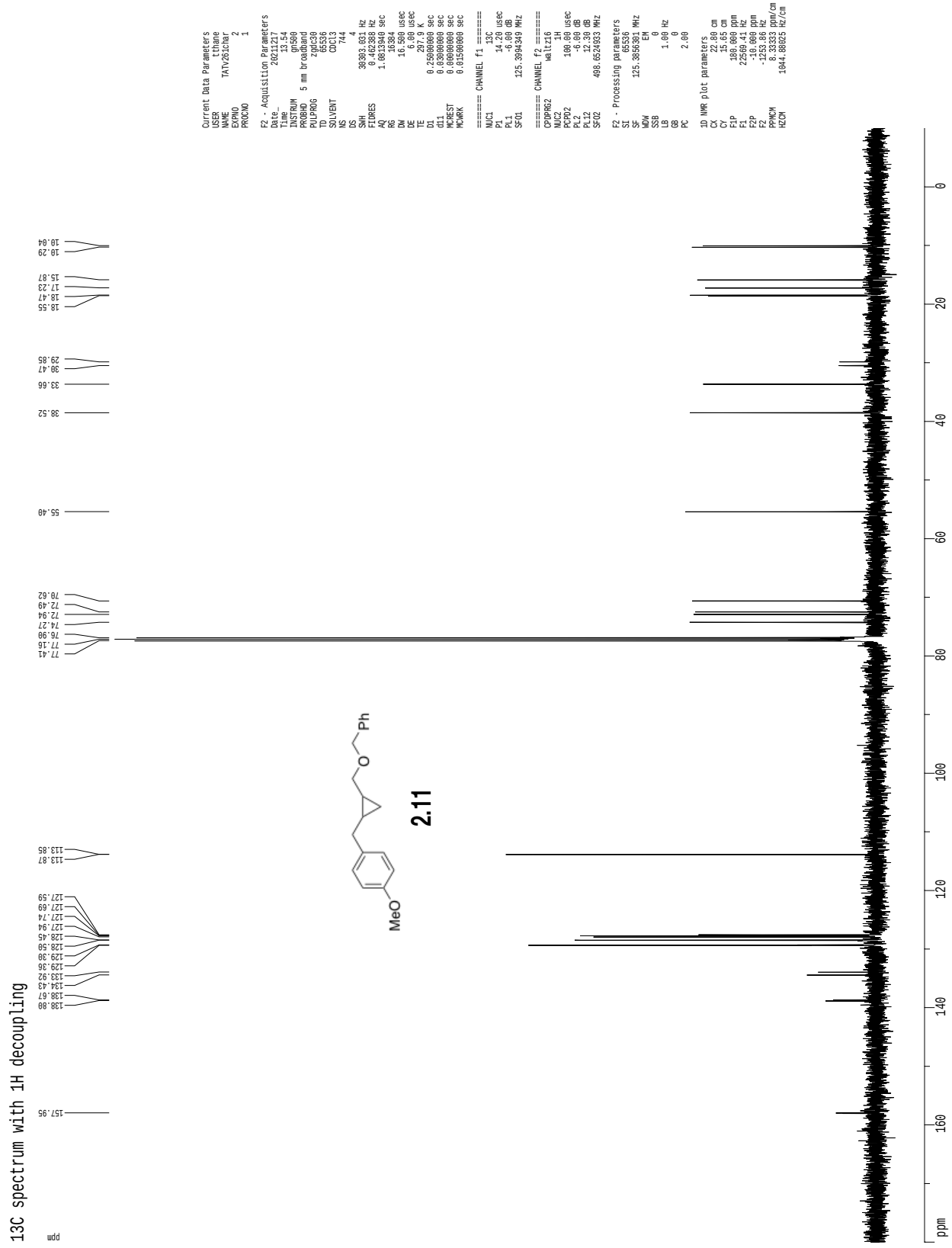
F2 - Acquisition Parameters
Date_           20211217
Time               15.12
INSTRUM          av600
PROBHD   5 mm CPBBO BB-
PULPROG          zgflqn30
TD                131072
SOLVENT           CDCl3T
NS                    16
DS                     2
SWH           178571.422 Hz
FIDRES          1.362392 Hz
AQ              0.3670516 sec
RG                   575
DW                2.800 usec
DE                18.00 usec
TE                298.0 K
D1            3.00000000 sec
TD0                    1

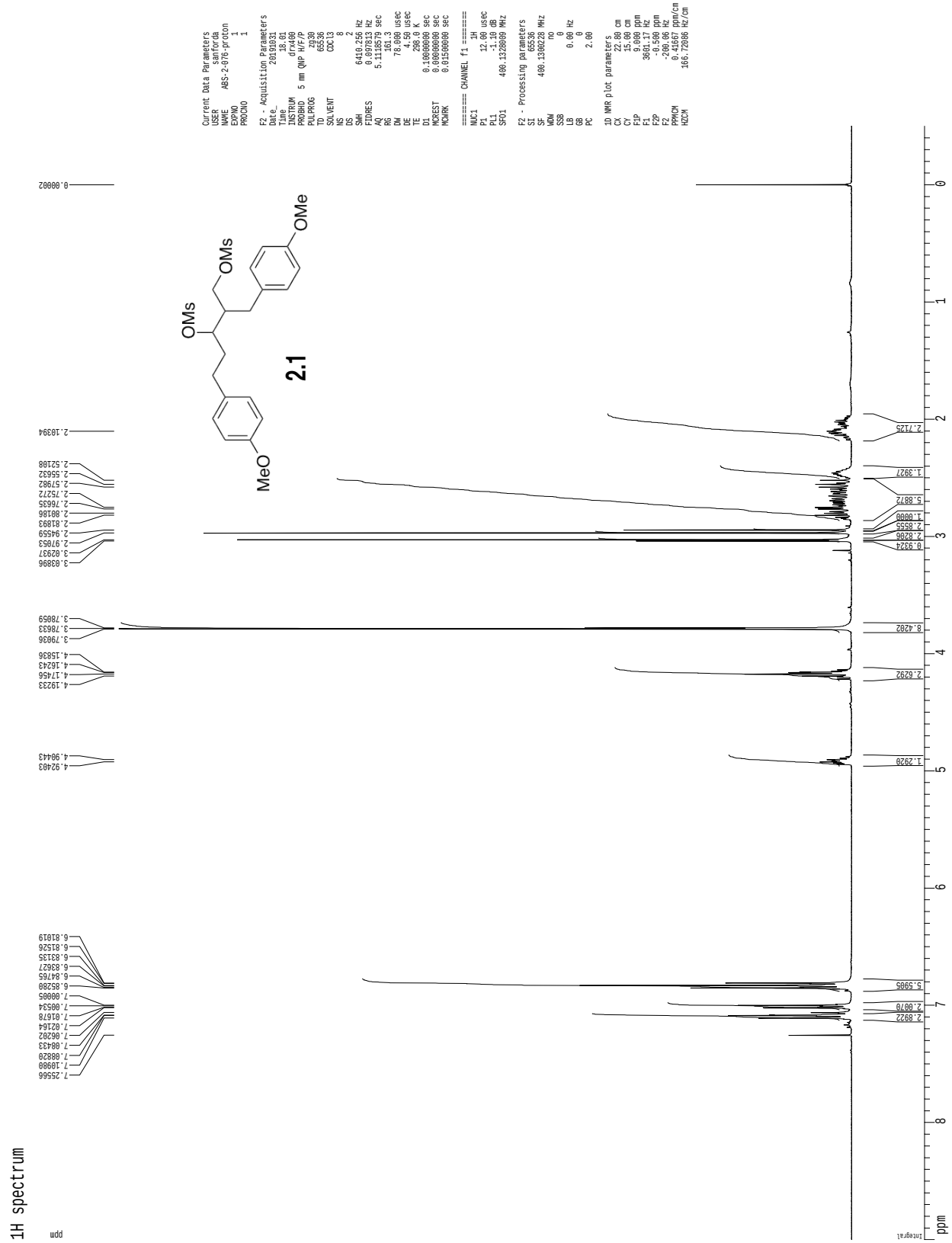
======= CHANNEL f1 =======
SFO1         564.6299196 MHz
NUC1                19F
P1                18.25 usec

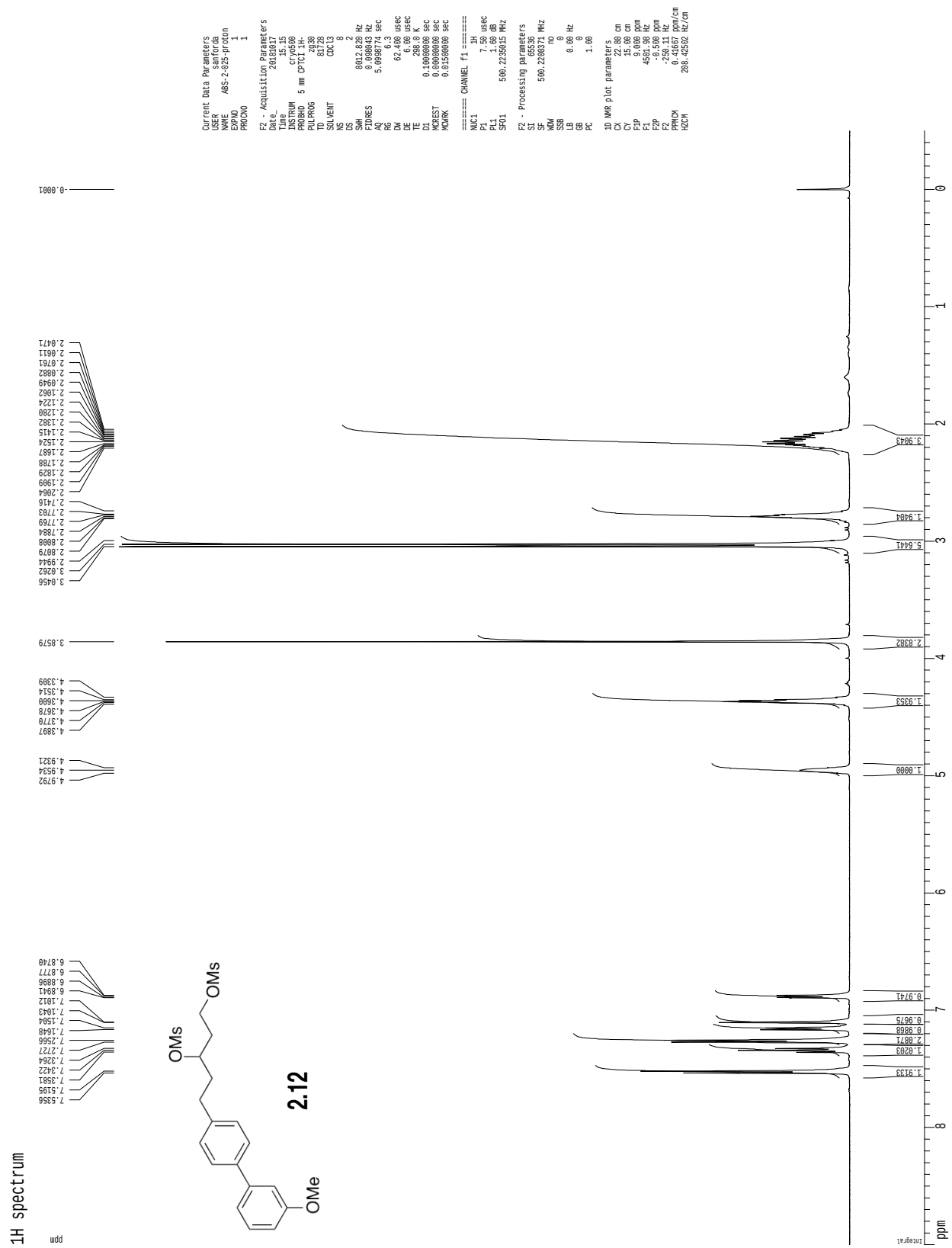
F2 - Processing parameters
SI                131072
SF           564.6863858 MHz
WDW                   no
SSB                    0
LB                 0.00 Hz
GB                     0
PC                  1.00

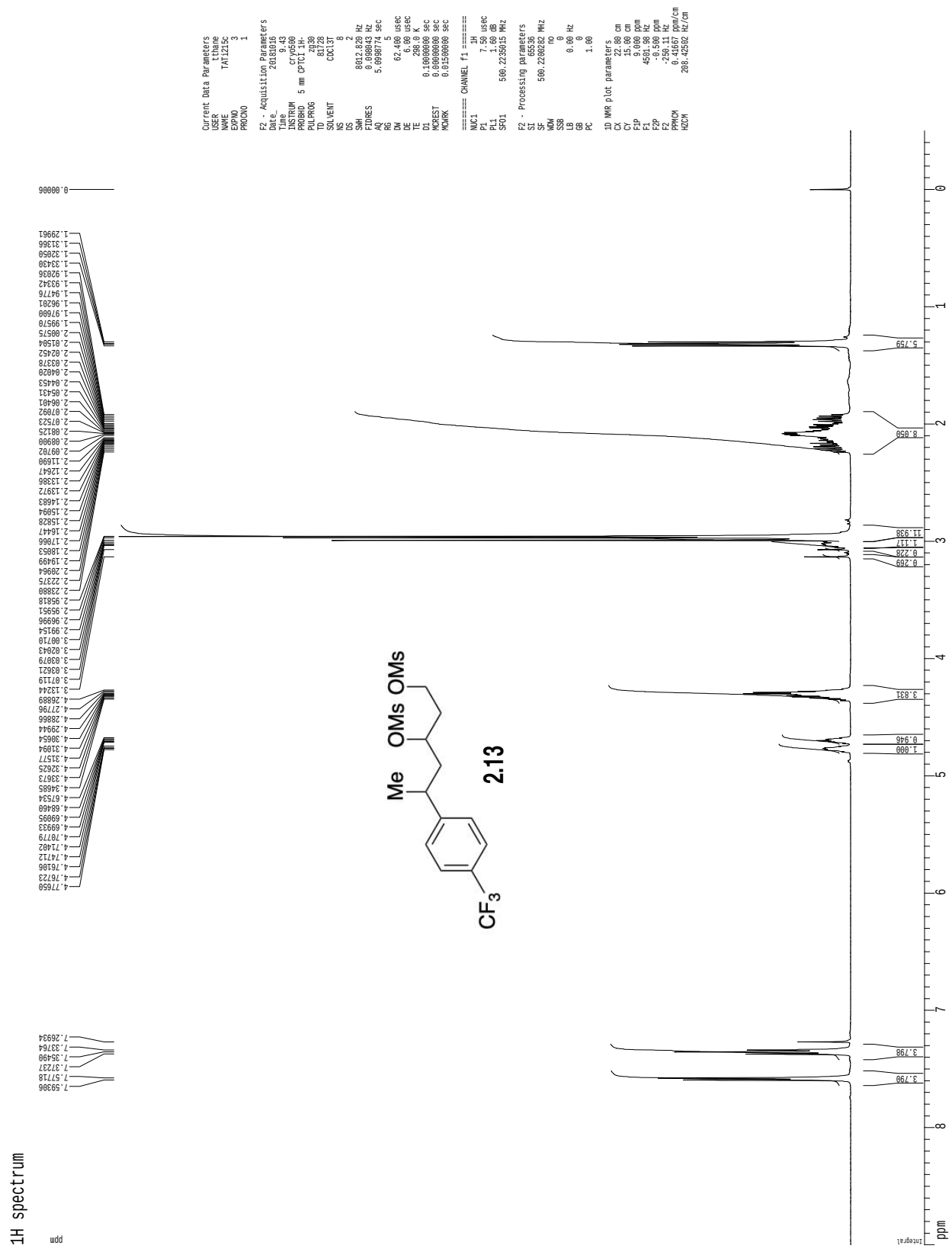
1D NMR plot parameters
CX                22.80 cm
CY                15.00 cm
F1P              -60.000 ppm
F1            -33881.19 Hz
F2P              -70.000 ppm
F2            -39528.05 Hz
PPMCM           0.43860 ppm/cm
HZCM          247.66939 Hz/cm
```


1H spectrum
2.11
MeO
Ph

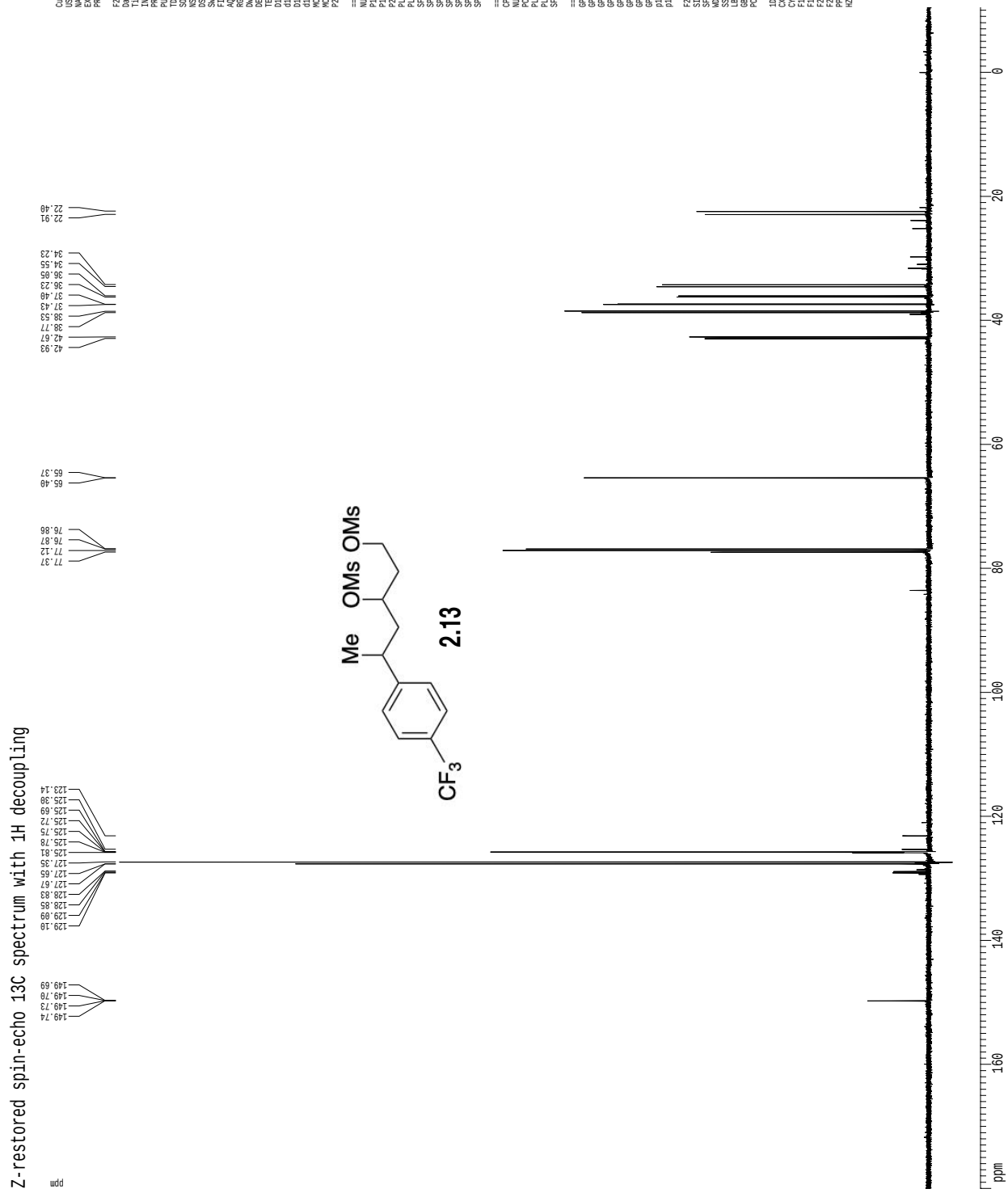

13C spectrum with 1H decoupling
Current Data Parameters
USER ttihane
NAME TATv2612thar 2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211217
Time 13.54
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 744
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 16384
DW 16.500 usec
DE 6.00 usec
TE 297.9 K
D1 0.25000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
====== CHANNEL f1 ======
NUC1 13C
P1 14.20 usec
PL1 -6.00 dB
SFO1 125.3994349 MHz
====== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 2.00 dB
PL12 12.00 dB
SFO2 498.6524933 MHz
F2 - Processing parameters
SI 65536
SF 125.3856301 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 188.000 ppm
F1 22569.41 Hz
F2P -10.000 ppm
F2 -1253.86 Hz
PPMCM 8.33333 ppm/cm
HZCM 1044.88825 Hz/cm
MeO
Ph
O
2.11
ppm
0
20
40
60
80
100
120
140
160
ppm
157.95
138.80
138.67
134.43
133.92
129.36
129.30
128.50
128.45
127.94
127.74
127.69
127.59
113.87
113.85
77.41
77.16
76.90
74.27
72.94
72.49
70.62
55.40
38.52
33.66
30.47
29.85
18.55
18.47
17.23
15.87
10.29
10.04


1H spectrum
Current Data Parameters
USER sanforda
NAME ABS-2-076-prodcon
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191031
Time 18.01
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 161.3
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300228 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
OMs
OMs
OMe
MeO
2.1
ppm
Integral

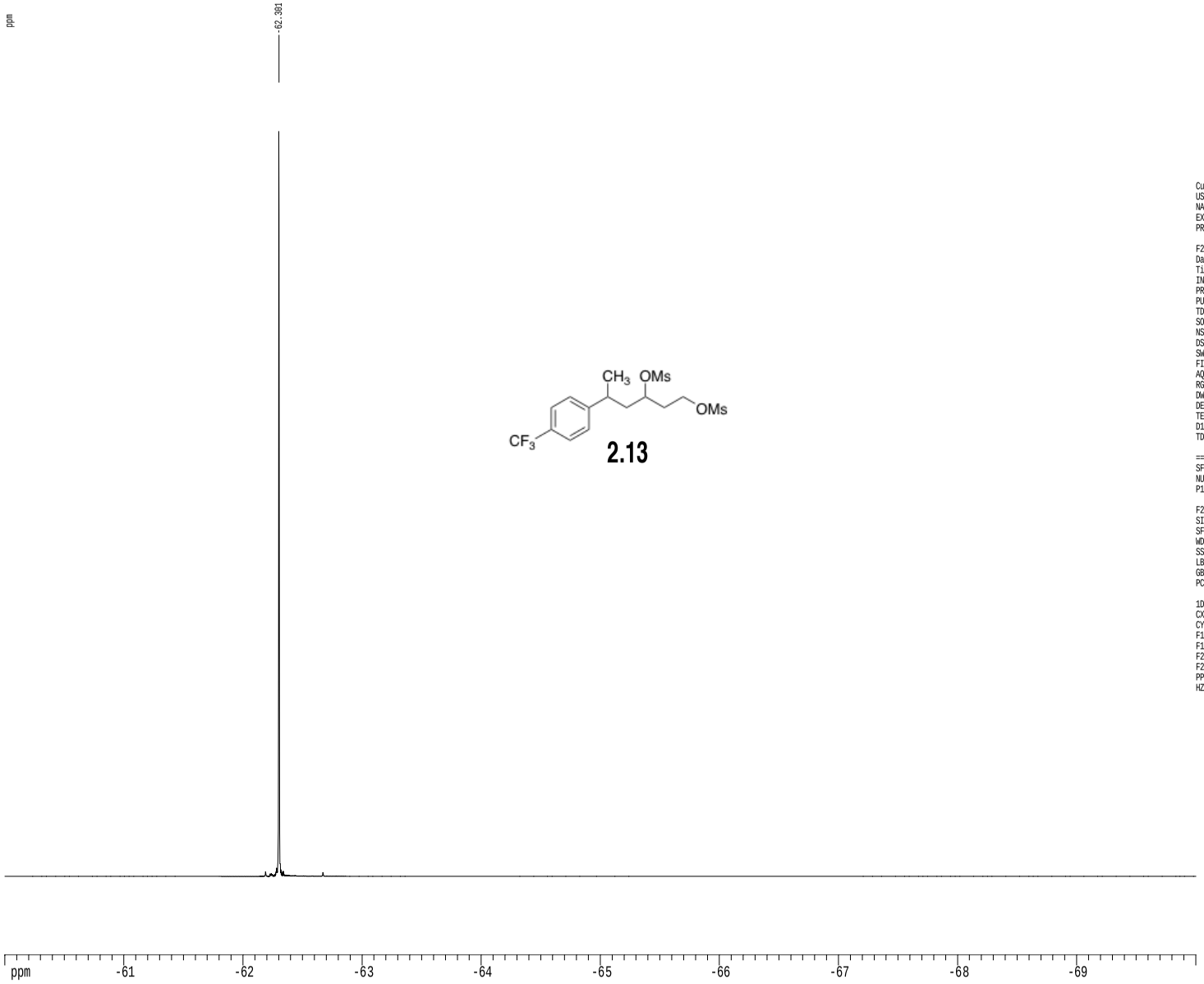

1H spectrum
Current Data Parameters
USER samforda
NAME ABS-2-025-prodcon
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181017
Time 15.15
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 82128
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0898774 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200371 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
OMs
OMs
OMe
2.12
ppm
Integral


Current Data Parameters
USER ttlane
NAME TAT1215c
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181016
Time 9.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.091774 Hz
AQ 5.0998774 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200282 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
Me
OMs
OMs
CF3
2.13
5.759
8.050
11.938
1.117
0.228
0.269
3.831
0.946
1.000
3.798
3.796
ppm
Integral

1H spectrum


Z-restored spin-echo 13C spectrum with 1H decoupling
Me OMs OMs
CF3
2.13
ppm

19F spectrum



2.13

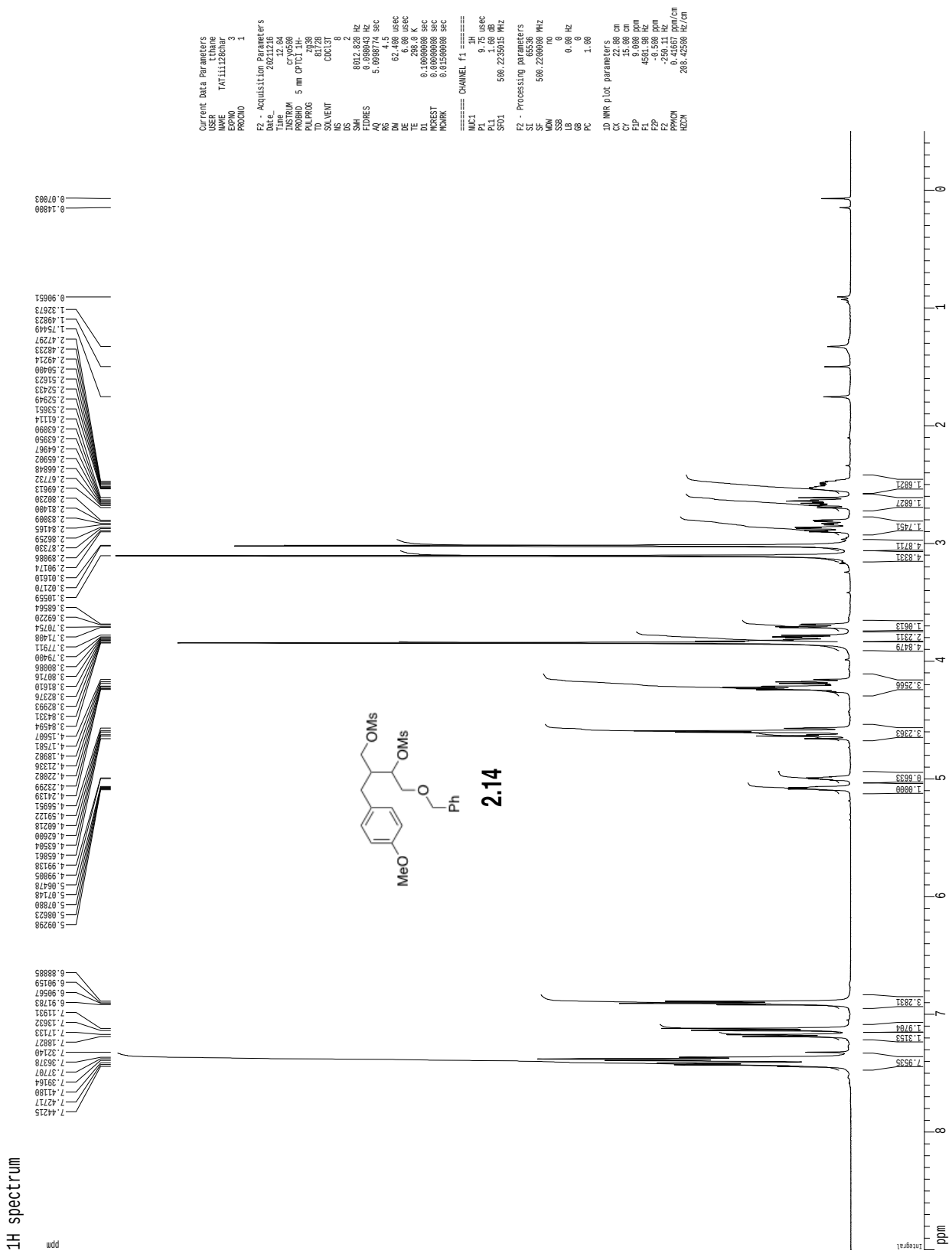
```
Current Data Parameters
USER              tthane
NAME      TAT1215fluorine
EXPNO                  1
PROCNO                 1

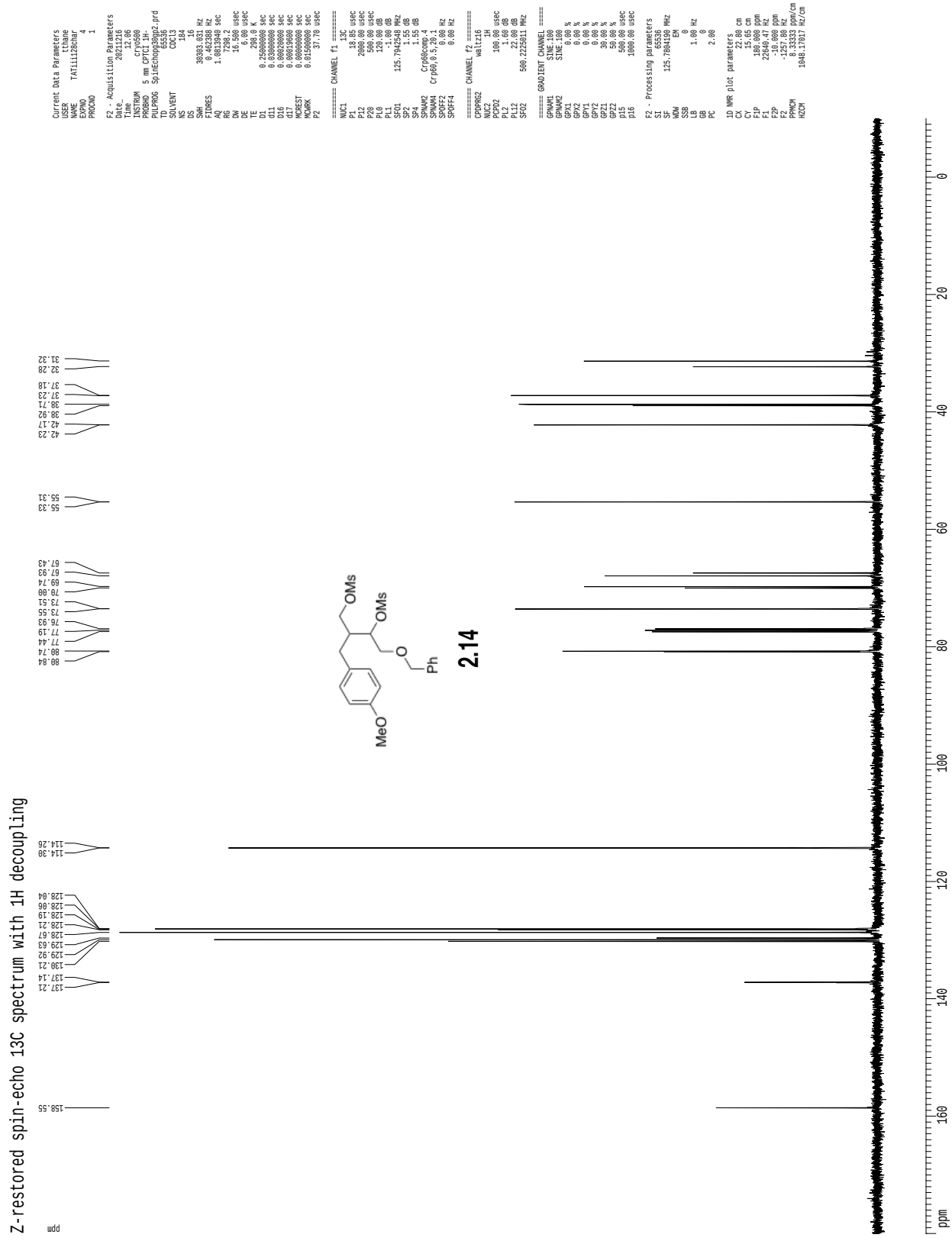
F2 - Acquisition Parameters
Date_           20211217
Time              15.06
INSTRUM           av600
PROBHD   5 mm CPBBO BB-
PULPROG         zgflqn30
TD                131072
SOLVENT           CDCl3T
NS                   16
DS                    2
SWH          178571.422 Hz
FIDRES         1.362392 Hz
AQ             0.3670516 sec
RG                 575
DW                2.800 usec
DE                18.00 usec
TE                298.0 K
D1            3.00000000 sec
TD0                   1

======= CHANNEL f1 =======
SFO1         564.6299196 MHz
NUC1                19F
P1                 18.25 usec

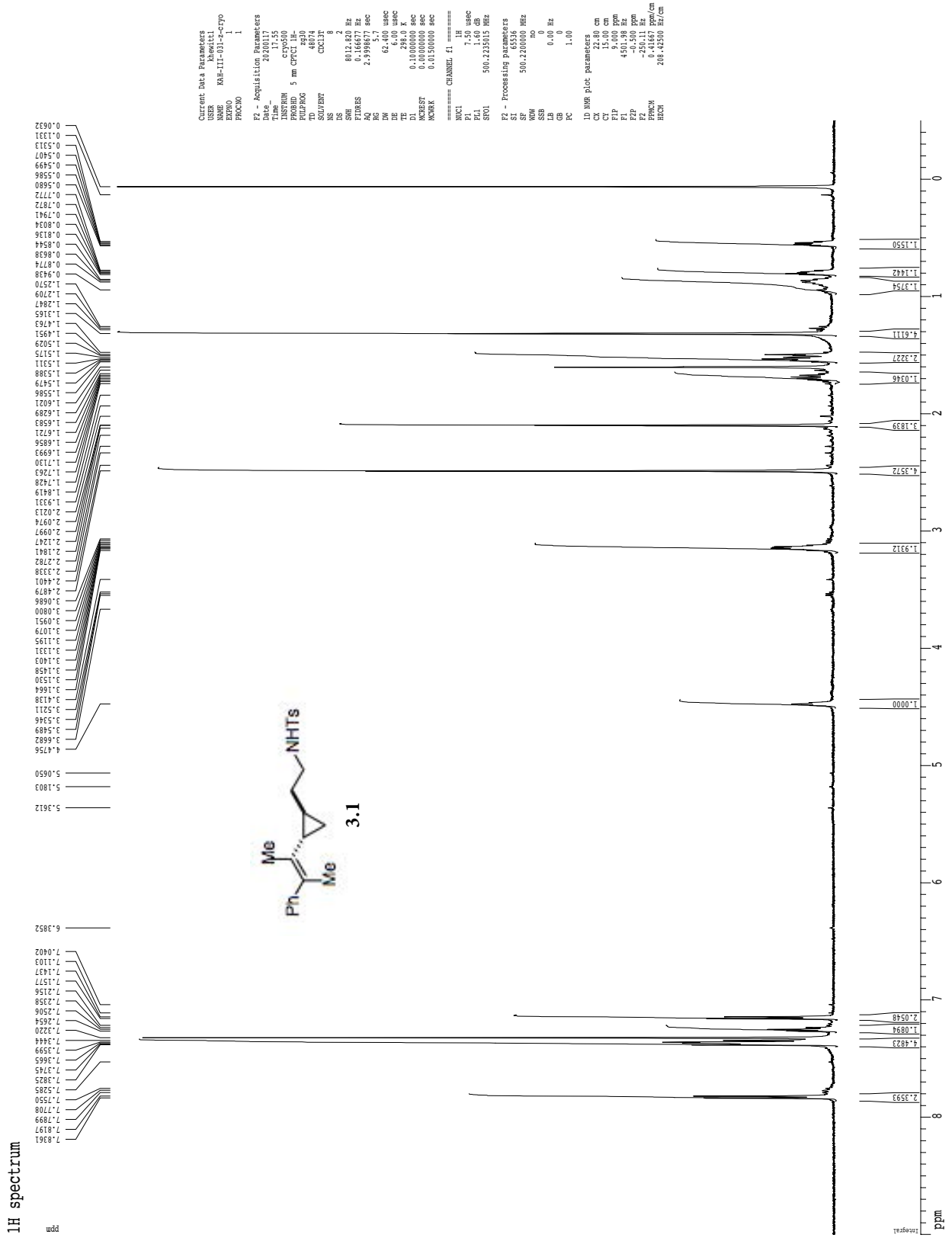
F2 - Processing parameters
SI                131072
SF           564.6863858 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                22.80 cm
CY                15.00 cm
F1P              -60.000 ppm
F1            -33881.19 Hz
F2P              -70.000 ppm
F2            -39528.05 Hz
PPMCM           0.43860 ppm/cm
HZCM          247.66939 Hz/cm
```

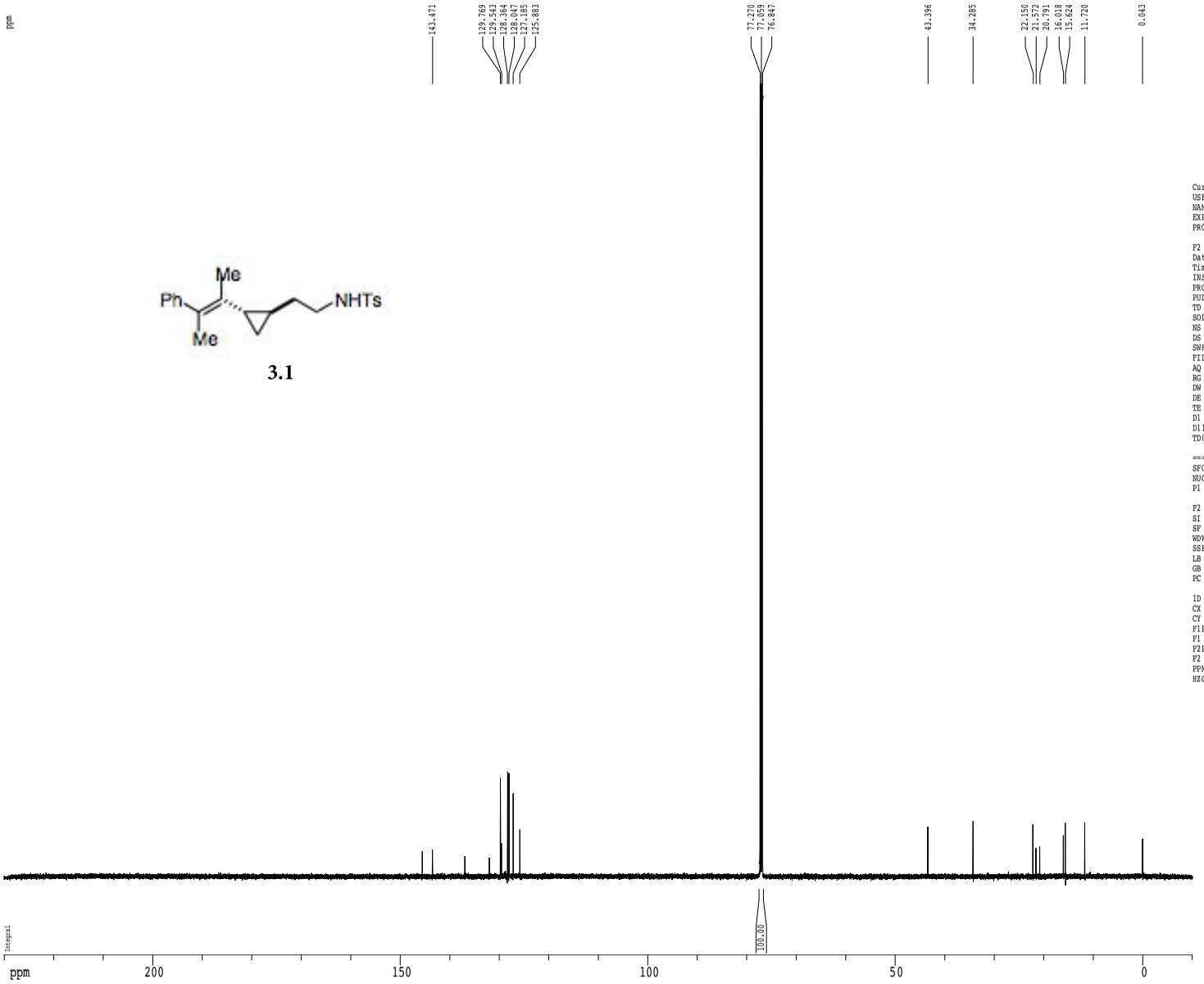

1H spectrum
Current Data Parameters
USER tihane
NAME TAT1iii126char
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211216
Time 12.04
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 9.75 usec
PL1 1.00 dB
SFO1 500.2235915 MHz
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -249.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42500 Hz/cm
OMs
OMs
O
Ph
MeO
2.14
ppm
Integral


Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
158.55
137.21
137.14
130.21
129.92
129.63
128.67
128.21
128.19
128.06
128.04
114.30
114.26
80.84
80.74
77.44
77.19
76.93
73.55
73.51
70.00
69.74
67.93
67.43
55.33
55.31
42.23
42.17
38.92
38.71
37.23
37.18
32.28
31.32
OMs
OMs
O
Ph
MeO
2.14
Current Data Parameters
USER TATiii128chur
NAME TATiii128chur
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20221216
Time 12.06
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30pg2.prd
TD 65536
SOLVENT CDCl3
NS 314
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08139840 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
CNST2 0.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 37.70 usec
======== CHANNEL f1 ========
NUC1 13C
P1 10.85 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942540 MHz
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.00 dB
PL12 21.00 dB
SFO2 500.2225911 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPV1 0.00 %
GPV2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7884100 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 0.33333 ppm/cm
HZCM 1040.17917 Hz/cm
ppm
0
20
40
60
80
100
120
140
160

A.3 NMR Data Corresponding to Chapter 3


1H spectrum
Current Data Parameters
NAME Maxwell
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200117
Time 17:55
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 48074
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.166677 Hz
AQ 2.9998677 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 5.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42500 Hz/cm
NHTs
Me
Me
Ph
3.1
ppm
Integral

1H spectrum



3.1

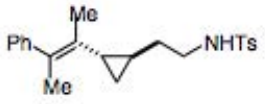
Current Data Parameters
USER khewitt1
NAME KAH-III-031-C-600
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200120
Time 11.25
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3T
NS 736
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9044468 sec
RG 2050
DW 13.800 usec
DE 19.63 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1

======= CHANNEL f1 =======
SFO1 150.9194080 MHz
NUC1 13C
P1 10.10 usec

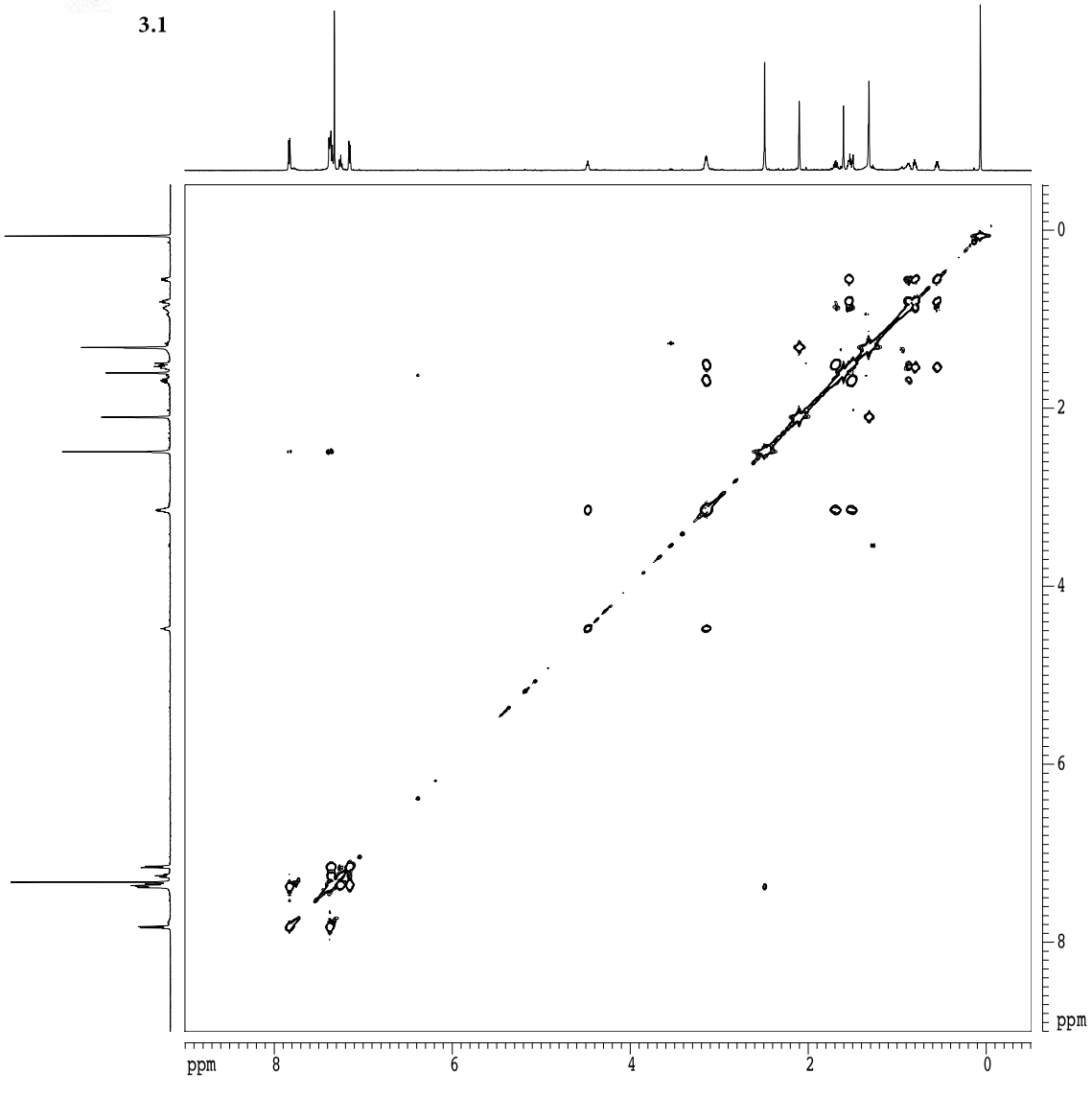
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 24.30 cm
F1P 230.052 ppm
F1 34715.42 Hz
F2P -10.049 ppm
F2 -1516.47 Hz
PPMCM 10.53074 ppm/cm
HZCM 1589.11780 Hz/cm



3.1

gcosy60




```
        Current Data Parameters
  USER              khewitt1
NAME      KAH-III-031-z-cryo
  EXPNO                    2
  PROCNO                   1

      F2 - Acquisition Parameters
  Date_              20200117
  Time                 17.57
  INSTRUM            cryo500
  PROBHD   5 mm CPTCI 1H-
  PULPROG     cosygp60.prd
  TD                    2048
  SOLVENT            CDCl3
  NS                       1
  DS                      16
  SWH              8012.820 Hz
  FIDRES           3.912510 Hz
  AQ               0.1278452 sec
  RG                   812.7
  DW                62.400 usec
  DE                 6.00 usec
  TE                298.0 K
  d0             0.00000300 sec
  D1             1.00000000 sec
  d13            0.00000300 sec
  D16            0.00020000 sec
  IN0            0.00012480 sec

      ======== CHANNEL f1 ========
  NUC1                     1H
  P1                    7.50 usec
  PL1                   1.60 dB
  SFO1          500.2235015 MHz

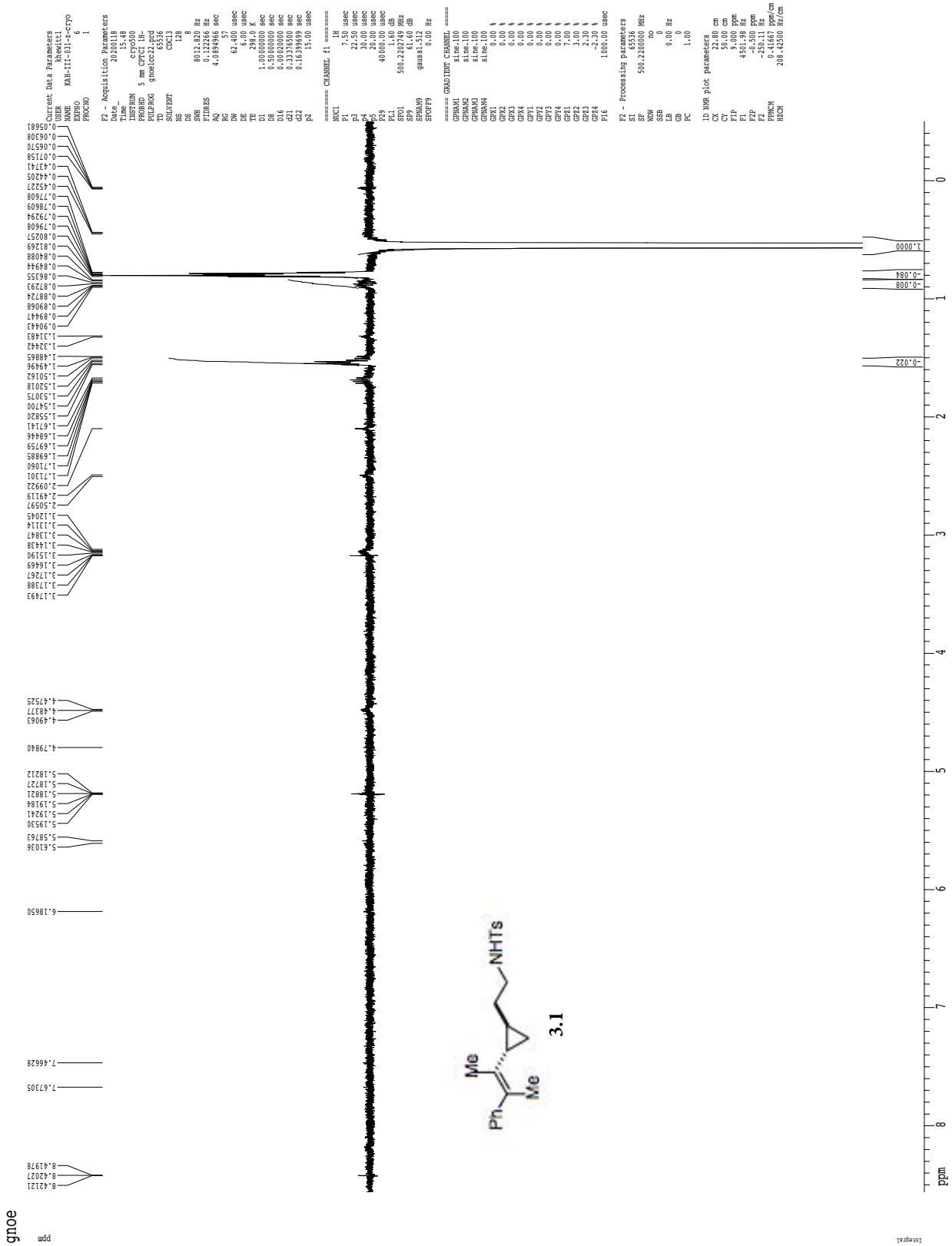
      ====== GRADIENT CHANNEL =====
  GPNAM1           sine.100
  GPNAM2           sine.100
  GPX1                 0.00 %
  GPX2                 0.00 %
  GPY1                 0.00 %
  GPY2                 0.00 %
  GPZ1                17.00 %
  GPZ2                17.00 %
  P16               1000.00 usec

      F1 - Acquisition parameters
  ND0                      1
  TD                     512
  SFO1            500.2235 MHz
  FIDRES          15.650040 Hz
  SW                16.018 ppm
  FnMODE                  QF

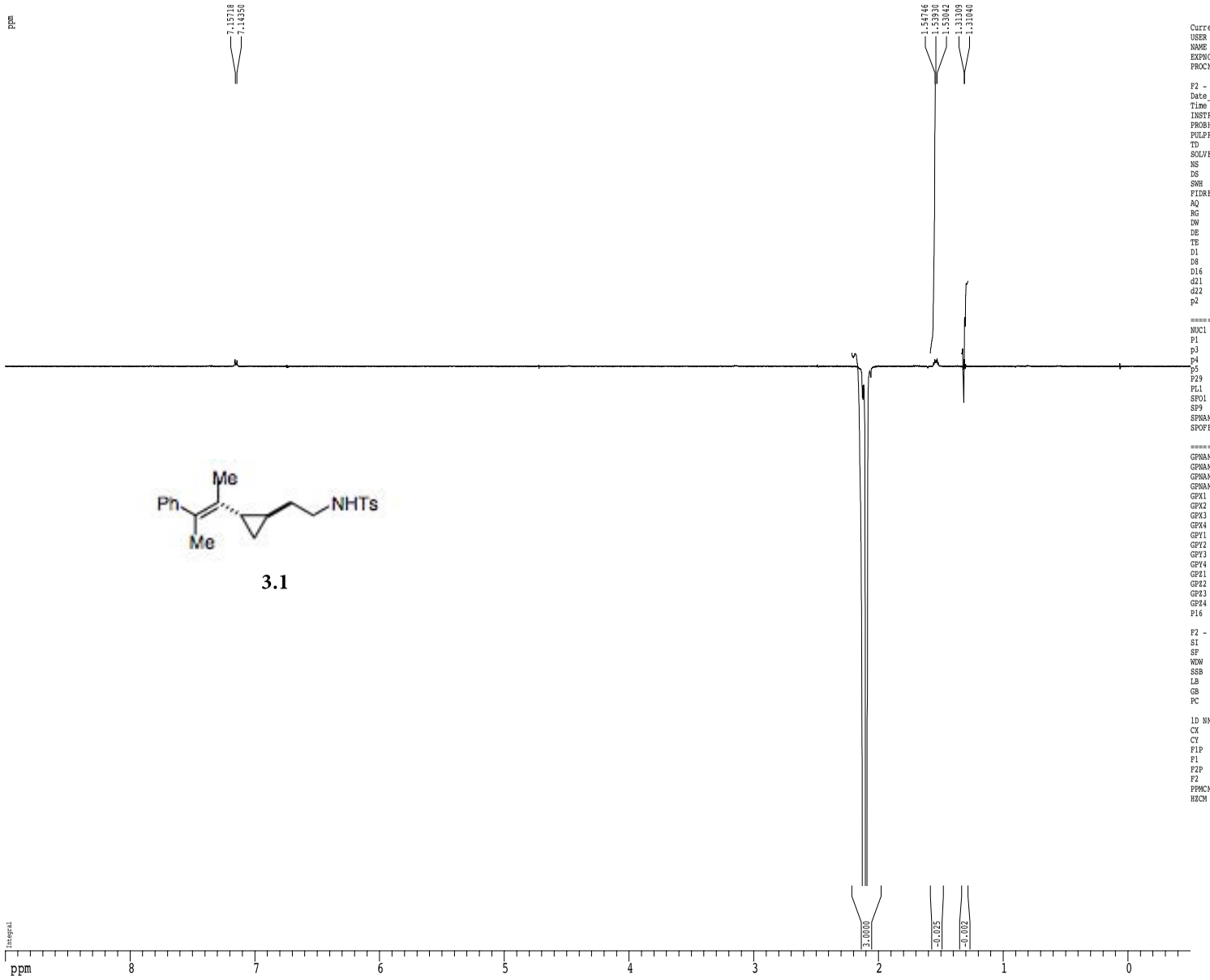
      F2 - Processing parameters
  SI                    1024
  SF           500.2200000 MHz
  WDW                   SINE
  SSB                      0
  LB                    0.00 Hz
  GB                       0
  PC                    1.00

      F1 - Processing parameters
  SI                    1024
  MC2                     QF
  SF           500.2200000 MHz
  WDW                   SINE
  SSB                      0
  LB                    0.00 Hz
  GB                       0

      2D NMR plot parameters
  CX2                  15.00 cm
  CX1                  15.00 cm
  F2PLO                9.002 ppm
  F2LO               4503.14 Hz
  F2PHI               -0.509 ppm
  F2HI               -254.47 Hz
  F1PLO                9.002 ppm
  F1LO               4503.14 Hz
  F1PHI               -0.509 ppm
  F1HI               -254.47 Hz
  F2PPMCM           0.63407 ppm/cm
  F2HZCM          317.17416 Hz/cm
  F1PPMCM           0.63407 ppm/cm
  F1HZCM          317.17416 Hz/cm
```


gnoe
ppm
Integral
Me
Me
Ph
NHTs
3.1

gnoe



3.1

```
Current Data Parameters
USER            khewittl
NAME      KAH-III-031-z-cryo
EXPNO                    7
PROCNO                   1

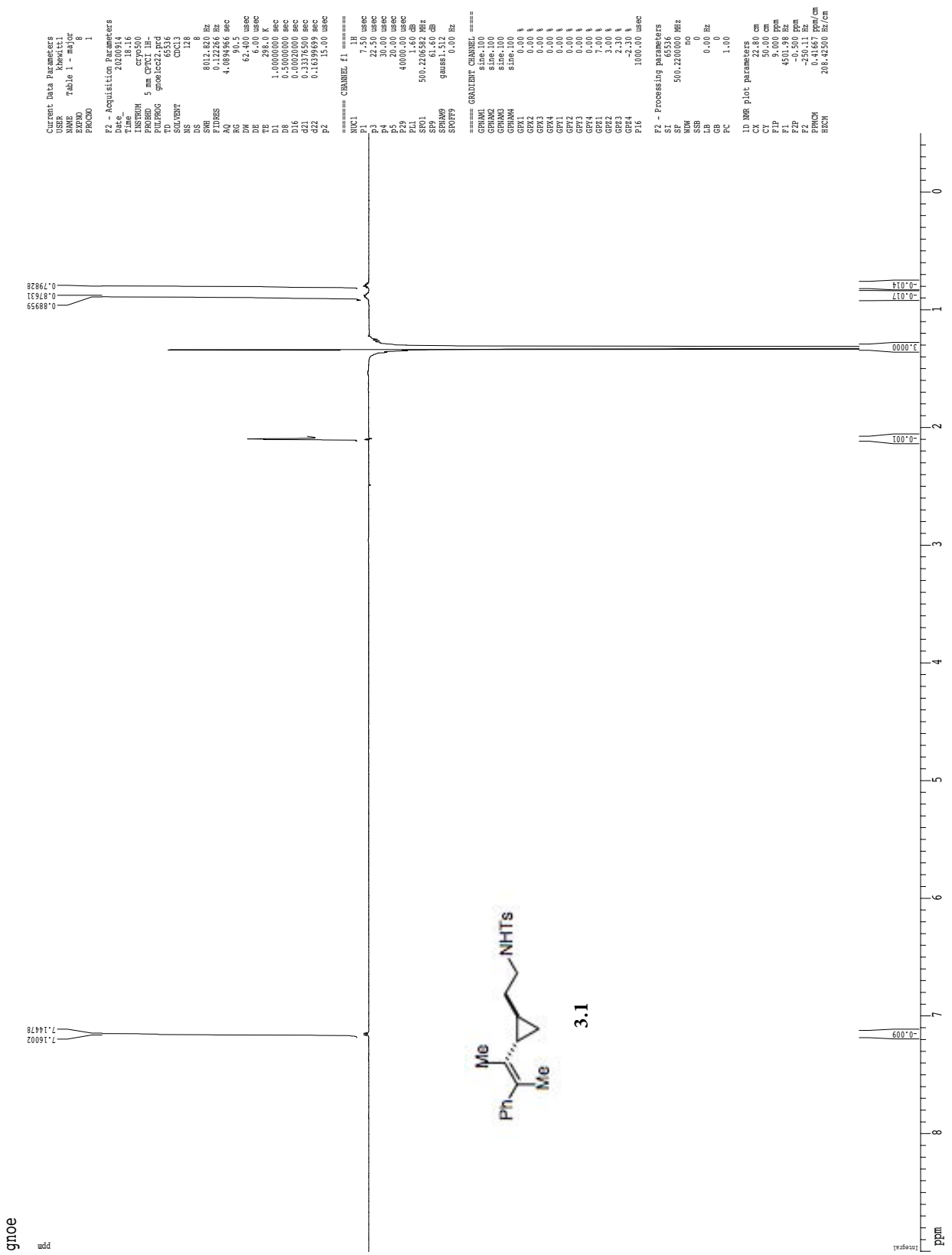
F2 - Acquisition Parameters
Date_          20200118
Time              16.02
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG   gnoelcc22.prd
TD                65536
SOLVENT           CDCl3
NS                  128
DS                    8
SWH            8012.820 Hz
FIDRES         0.122266 Hz
AQ             4.0894966 sec
RG                 80.6
DW                62.400 usec
DE                 6.00 usec
TE                298.0 K
D1             1.00000000 sec
D8             0.50000000 sec
D16            0.00020000 sec
d21            0.33376500 sec
d22            0.16399699 sec
p2                15.00 usec

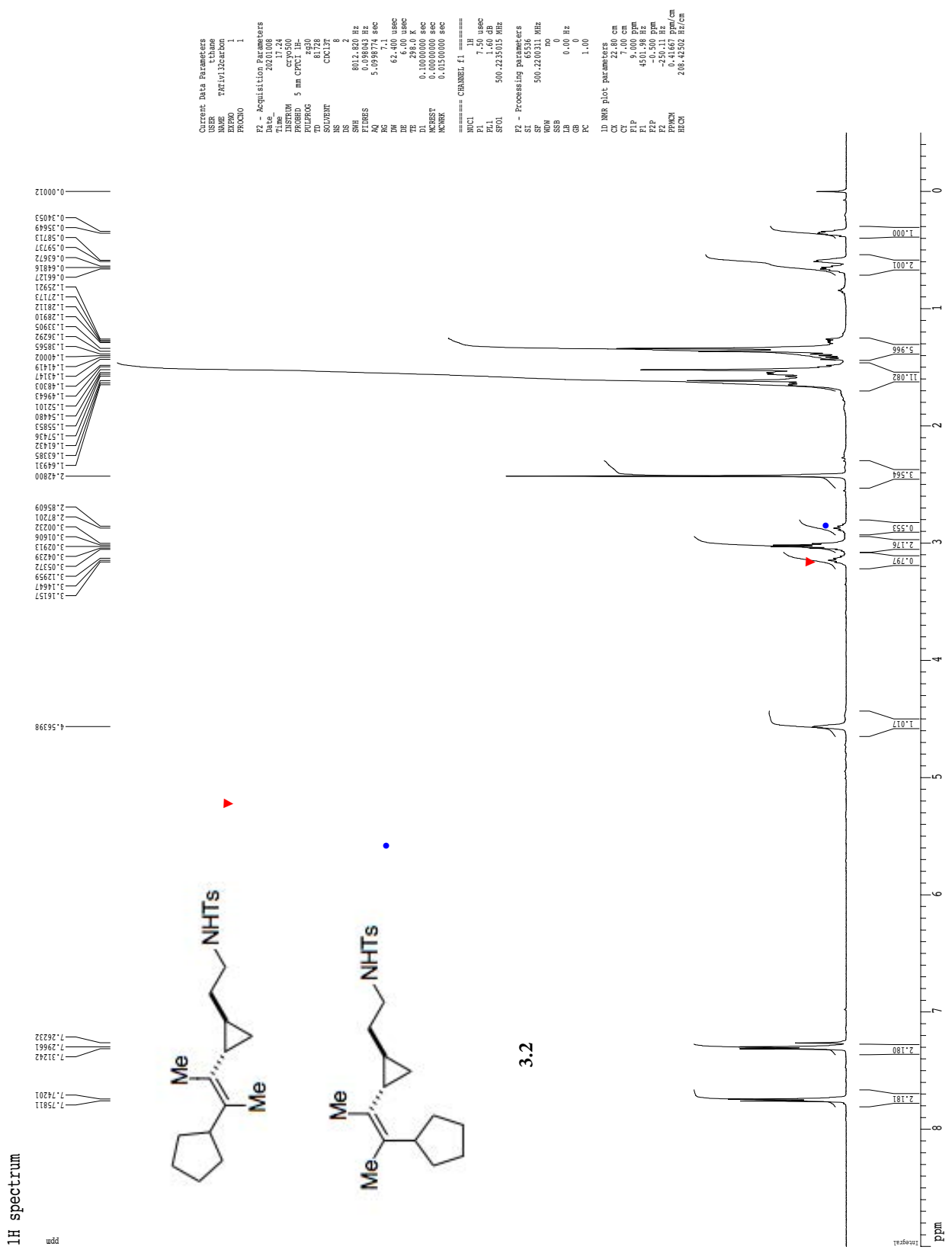
======== CHANNEL f1 =======
NUC1                1H
P1                 7.50 usec
p3                22.50 usec
p4                30.00 usec
p5                20.00 usec
P29            40000.00 usec
PL1                1.60 dB
SFO1         500.2210495 MHz
SP9               61.60 dB
SPNAM9        gauss1.512
SPOFF9             0.00 Hz

===== GRADIENT CHANNEL =====
GPNAM1          sine.100
GPNAM2          sine.100
GPNAM3          sine.100
GPNAM4          sine.100
GPX1               0.00 %
GPX2               0.00 %
GPX3               0.00 %
GPX4               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPY3               0.00 %
GPY4               0.00 %
GPZ1               7.00 %
GPZ2               3.00 %
GPZ3               2.30 %
GPZ4              -2.30 %
P16             1000.00 usec

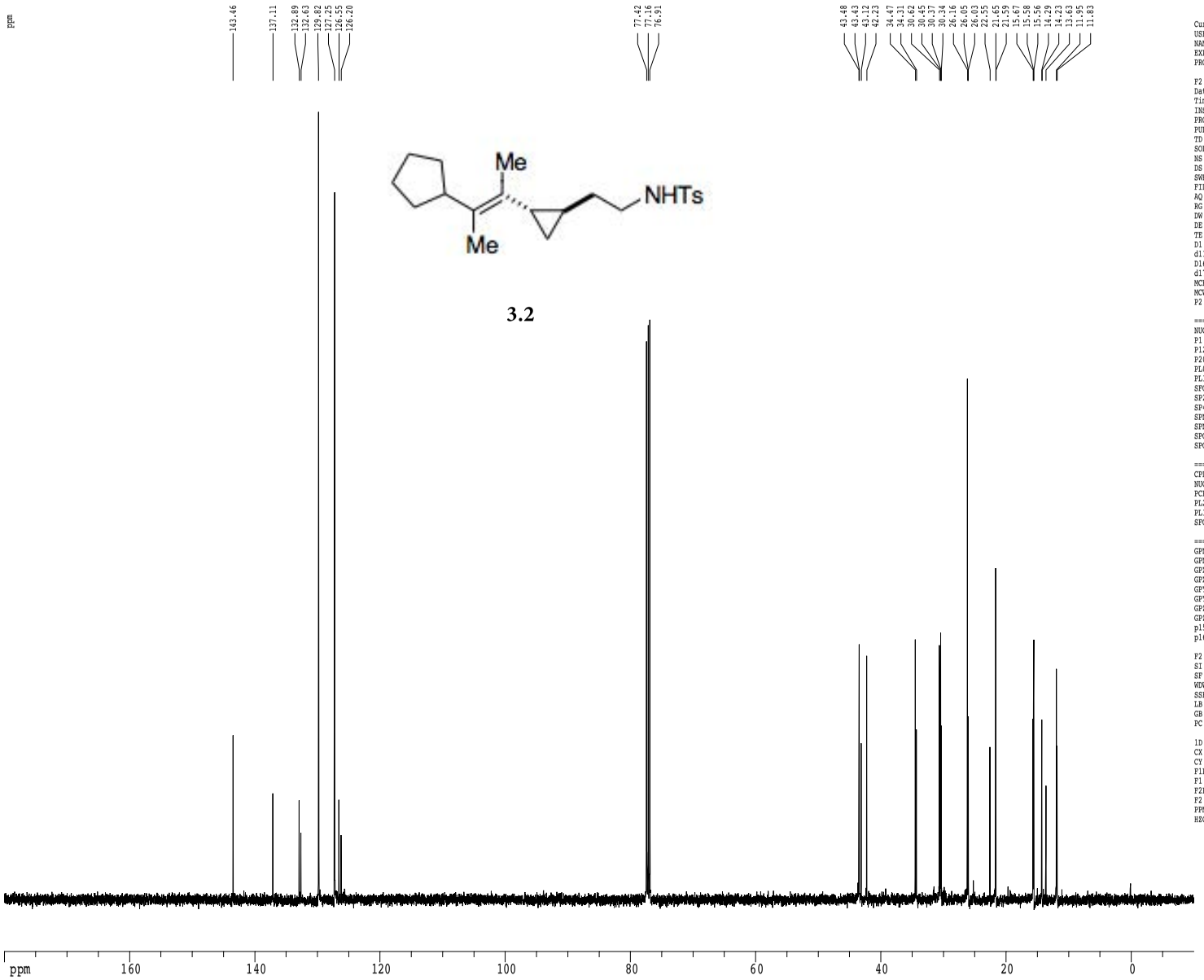
F2 - Processing parameters
SI                65536
SF          500.2200000 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                22.80 cm
CY                50.00 cm
F1P               9.000 ppm
F1             4501.98 Hz
F2P              -0.500 ppm
F2             -250.11 Hz
PPMCM          0.41667 ppm/cm
HZCM         208.42500 Hz/cm
```


gnoe
ppm
Integral
ppm
Current Data Parameters
USER khewitt1
NAME Table 1 - major
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200914
Time_ 18.16
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG gnoe1cc22.pcd
TD 65536
SOLVENT CDCl3
NS 128
DS 8
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 90.5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.13376500 sec
d22 0.16339699 sec
p2 15.00 usec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
p5 20.00 usec
P29 40000.00 usec
PL1 1.60 dB
SFO1 500.2206582 MHz
SP01 61.60 dB
SPNAM9 gauss1.512
SPOFF9 0.00 Hz
====== GRADIENT CHANNEL ====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPNAM4 sine.100
GPX1 0.00 %
GPX2 0.00 %
GPX3 0.00 %
GPX4 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPY3 0.00 %
GPY4 0.00 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 50.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42500 Hz/cm
0.88959
0.87631
0.79828
7.16002
7.14478
3.0000
~0.014
~0.017
~0.001
~0.009
NHTs
Me
Me
Ph
3.1


1H spectrum
NHTs
Me
Me
NHTs
Me
Me
3.2
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                tthane
NAME        TATiv132carbon
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20201008
Time                 17.26
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp2.prd
TD                   65536
SOLVENT              CDCl3
NS                     448
DS                      16
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                    6502
DW                 16.500 usec
DE                  6.00 usec
TE                298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                 33.10 usec

======== CHANNEL f1 ========
NUC1                  13C
P1                  16.55 usec
P12               2000.00 usec
P20                500.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1         125.7942548 MHz
SP2                  2.70 dB
SP4                  2.70 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2               0.00 Hz
SPOFF4               0.00 Hz

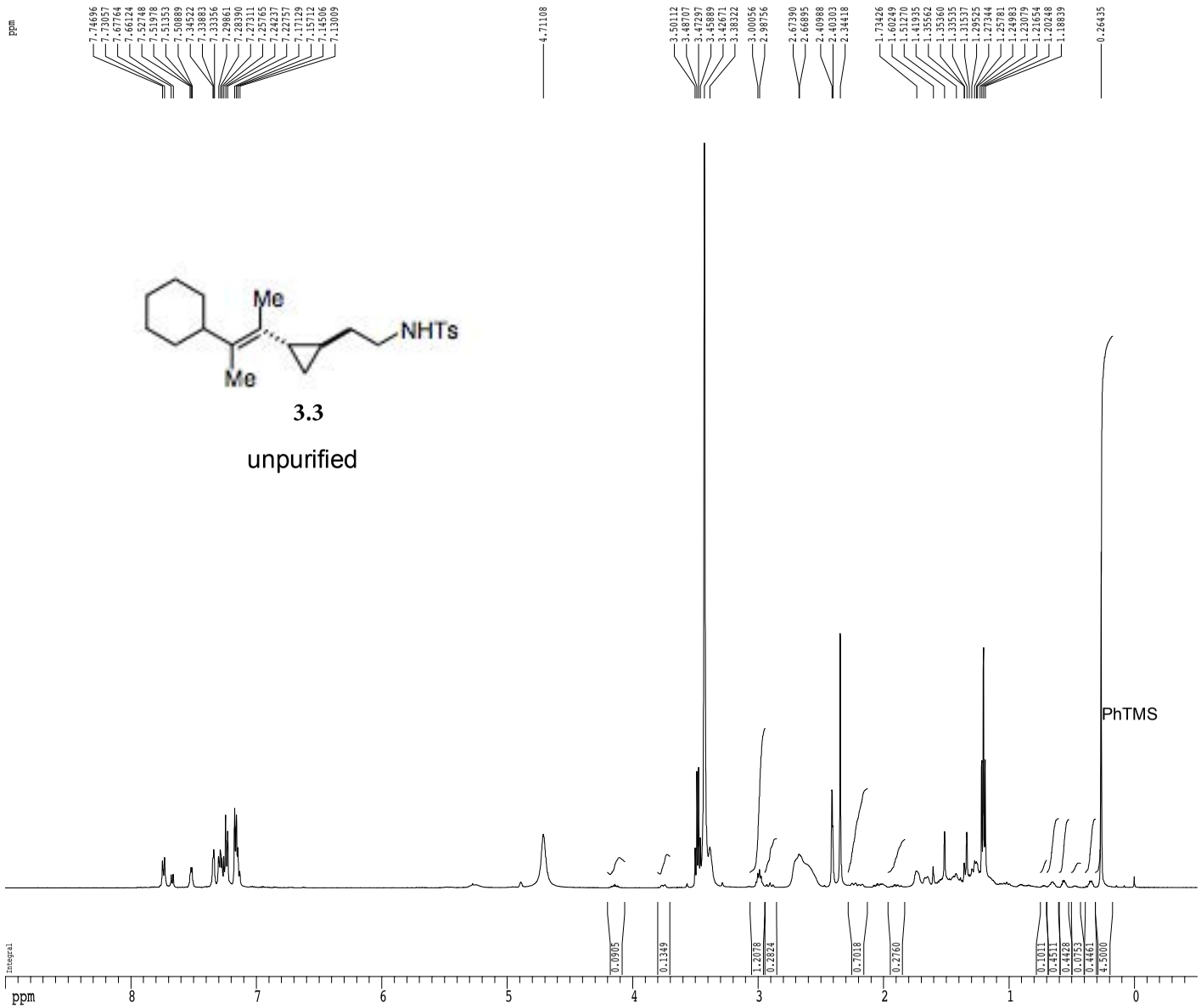
======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                23.54 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF           125.7804085 MHz
WDW                     EM
SSB                      0
LB                   1.00 Hz
GB                       0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               180.000 ppm
F1                22640.47 Hz
F2P               -10.000 ppm
F2                -1257.80 Hz
PPMCM             8.33333 ppm/cm
HZCM           1048.17017 Hz/cm
```

1H spectrum



3.3

unpurified

Current Data Parameters

USER	khewitt1
NAME	KAH-III-145-crude
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20200617
Time	18.55
INSTRUM	gn500
PROBHD	5 mm broadband
PULPROG	zg30
TD	81728
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.098043 Hz
AQ	5.0998774 sec
RG	40.3
DW	62.400 usec
DE	6.00 usec
TE	298.0 K
D1	0.10000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

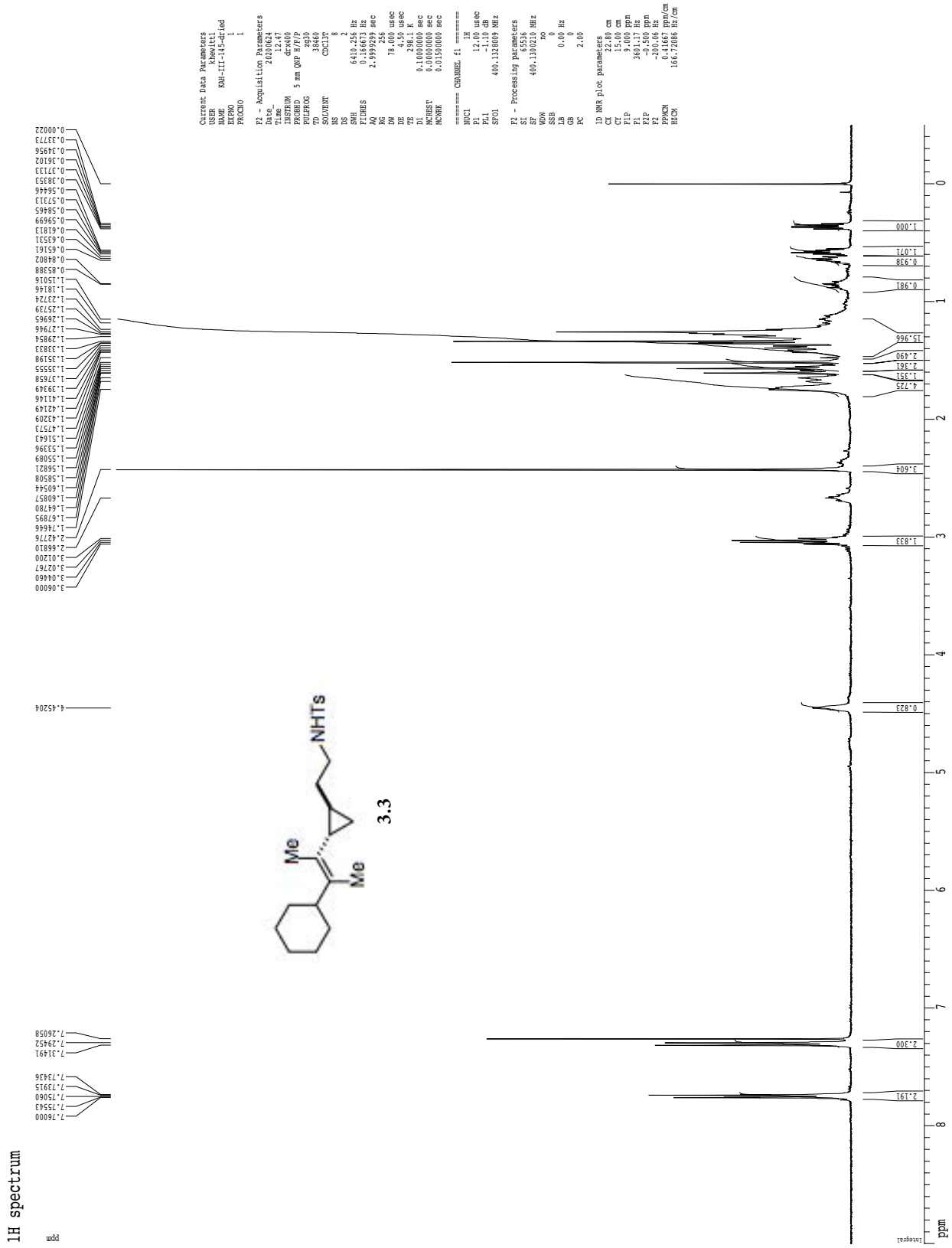
NUC1	1H
P1	12.00 usec
PL1	-6.00 dB
SFO1	498.7534913 MHz

F2 - Processing parameters

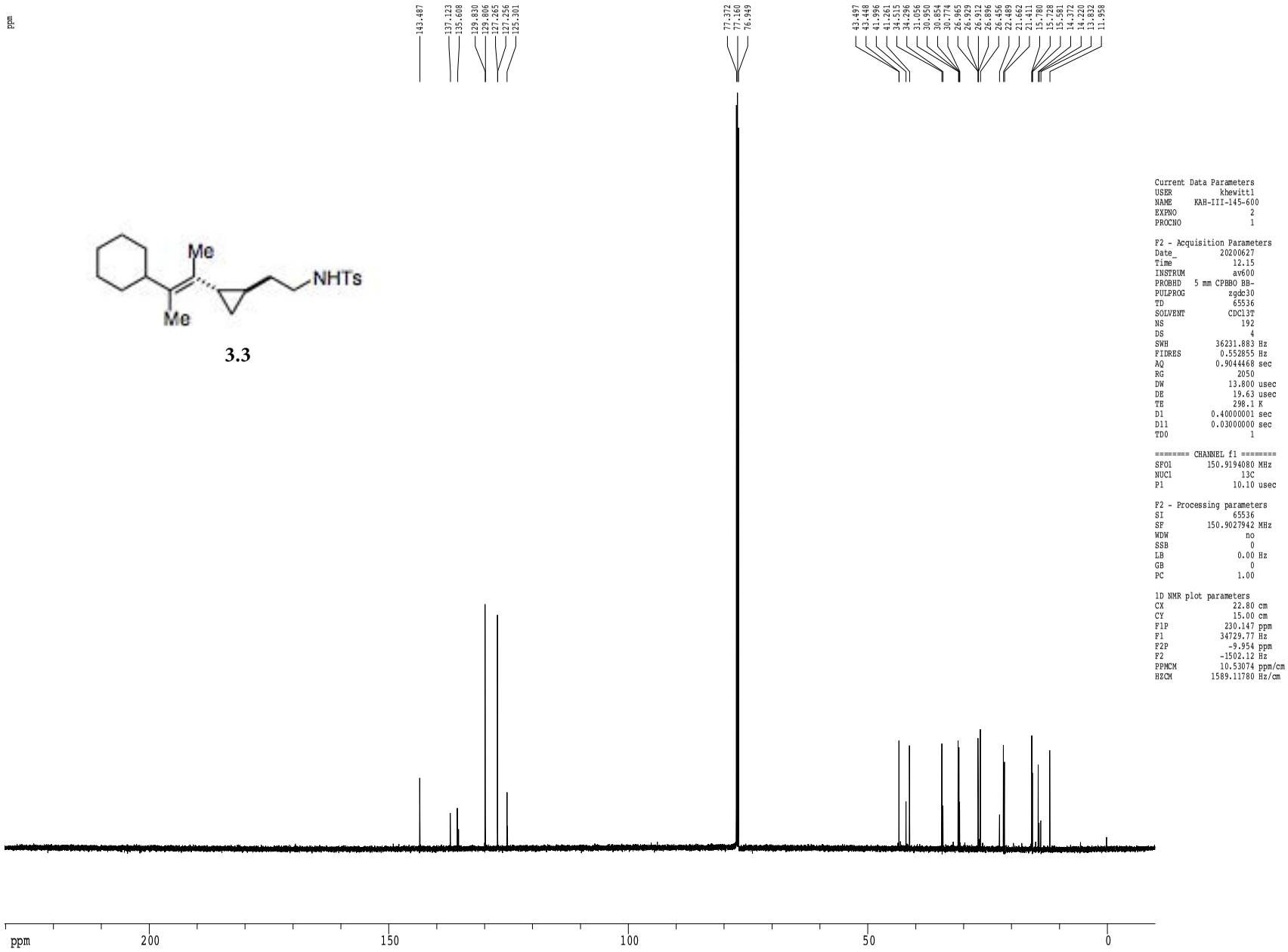
SI	65536
SF	498.7500244 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

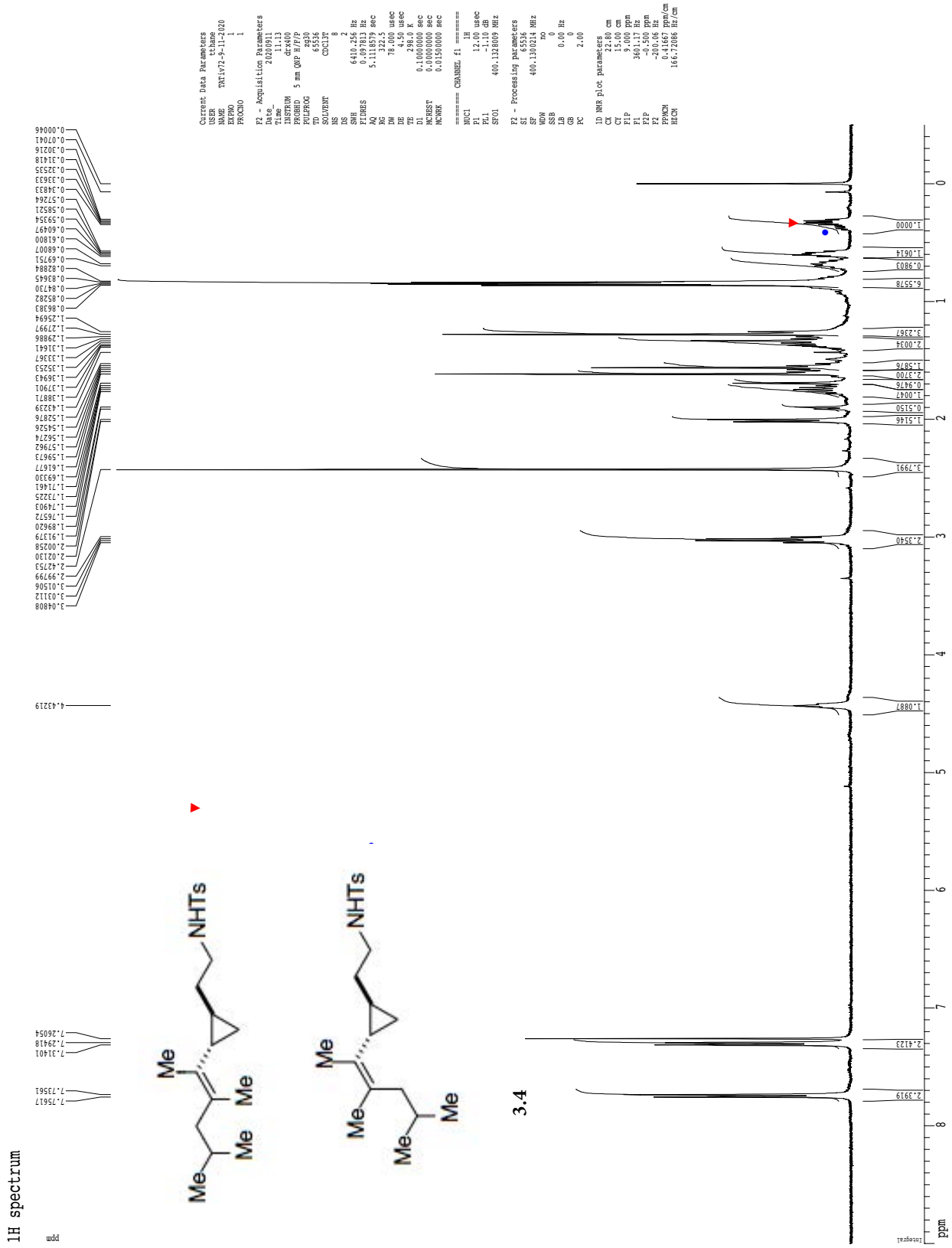
1D NMR plot parameters

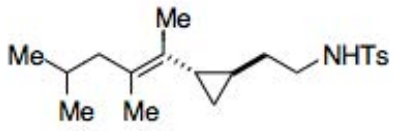
CX	20.00 cm
CY	12.50 cm
F1P	9.000 ppm
F1	4488.75 Hz
F2P	-0.500 ppm
F2	-249.38 Hz
PPMCM	0.47500 ppm/cm
HZCM	236.90627 Hz/cm



1H spectrum

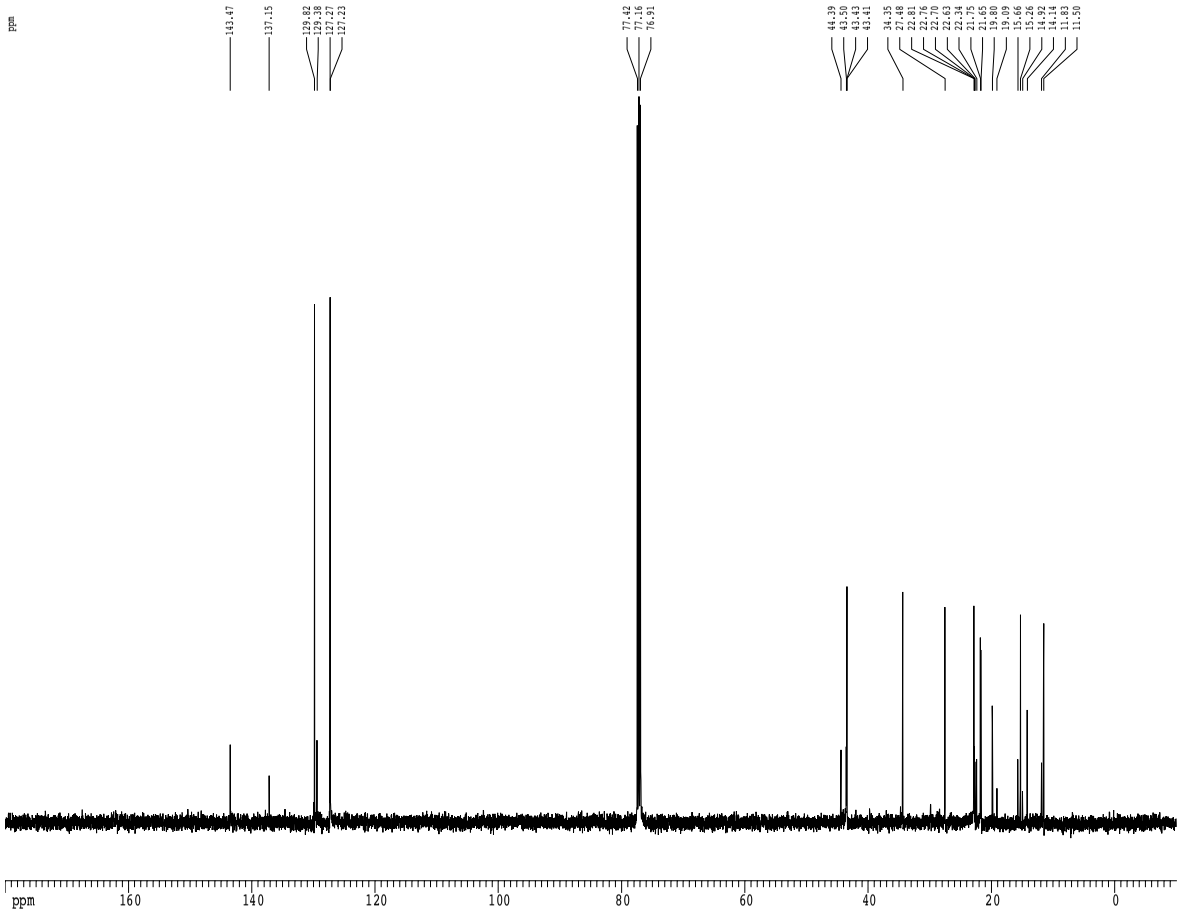

ppm
143.487
137.123
135.608
129.830
129.806
127.265
127.256
125.301
77.372
77.160
76.949
43.497
43.448
41.996
41.261
34.515
34.296
31.056
30.950
30.854
30.774
26.965
26.929
26.912
26.896
26.456
22.489
21.662
21.411
15.780
15.728
15.581
14.372
14.220
13.832
11.958
Me
Me
NHTs
3.3
Current Data Parameters
USER khewitt1
NAME KAB-III-145-600
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200627
Time 12.15
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3T
NS 192
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9044468 sec
RG 2050
DW 13.800 usec
DE 19.63 usec
TE 298.1 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9194080 MHz
NUC1 13C
P1 10.10 usec
F2 - Processing parameters
SI 65536
SF 150.9027942 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 230.147 ppm
F1 34729.77 Hz
F2P -9.954 ppm
F2 -1502.12 Hz
PPMCM 10.53074 ppm/cm
HZCM 1589.11780 Hz/cm
ppm
200
150
100
50
0


1H spectrum
NHTs
Me
Me
Me
Me
NHTs
Me
Me
Me
3.4
ppm



3.4

13C spectrum with 1H decoupling




```
Current Data Parameters
USER              tthane
NAME       TATiv72carbon
EXPNO                2
PROCNO               1

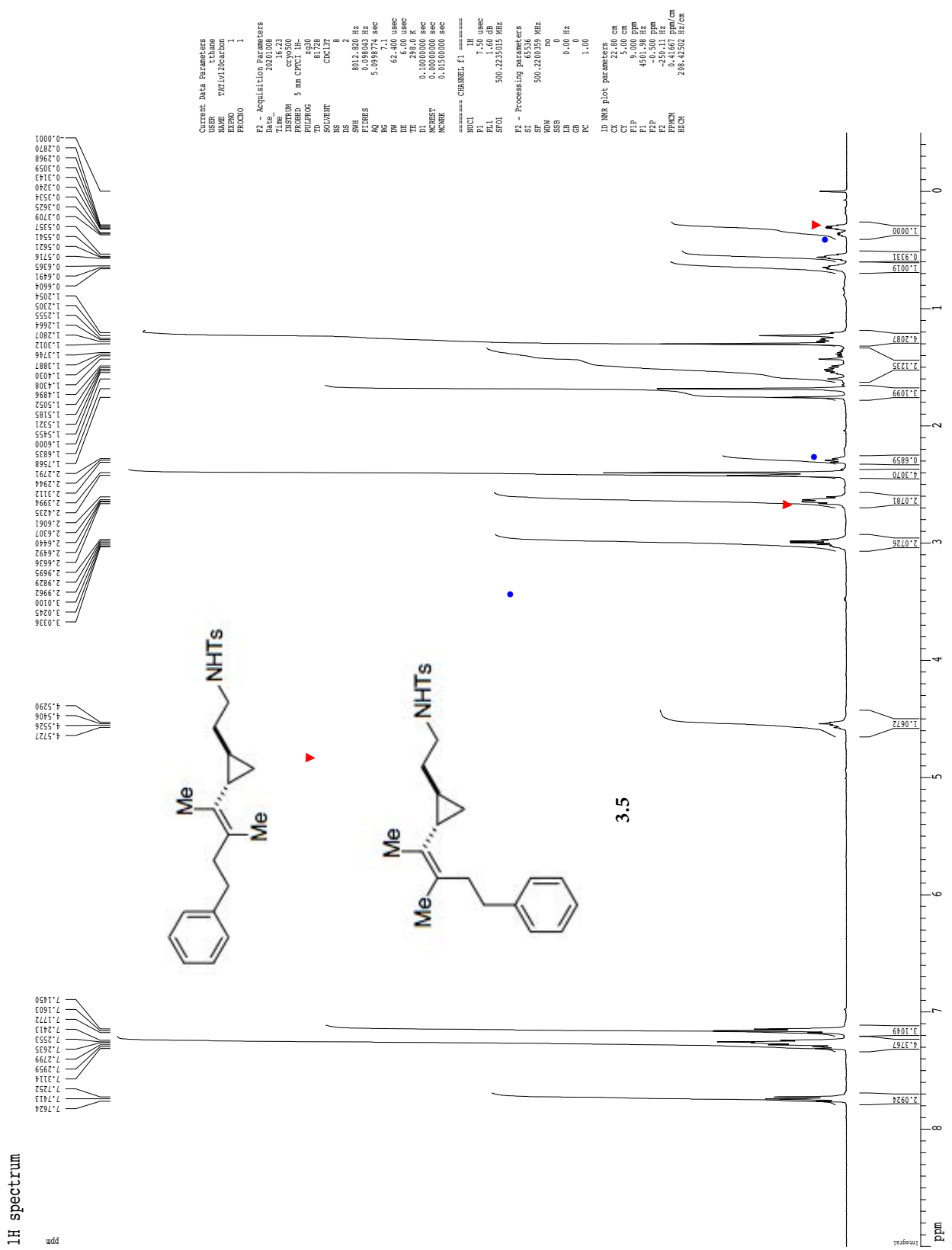
F2 - Acquisition Parameters
Date_          20200718
Time              11.45
INSTRUM           gn500
PROBHD   5 mm broadband
PULPROG         zgdc30
TD               65536
SOLVENT           CDCl3
NS                 704
DS                   4
SWH          30303.031 Hz
FIDRES         0.462388 Hz
AQ           1.0813940 sec
RG              5792.6
DW               16.500 usec
DE                6.00 usec
TE               297.9 K
D1           0.25000000 sec
d11          0.03000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1               13C
P1               14.20 usec
PL1              -6.00 dB
SFO1        125.4245824 MHz

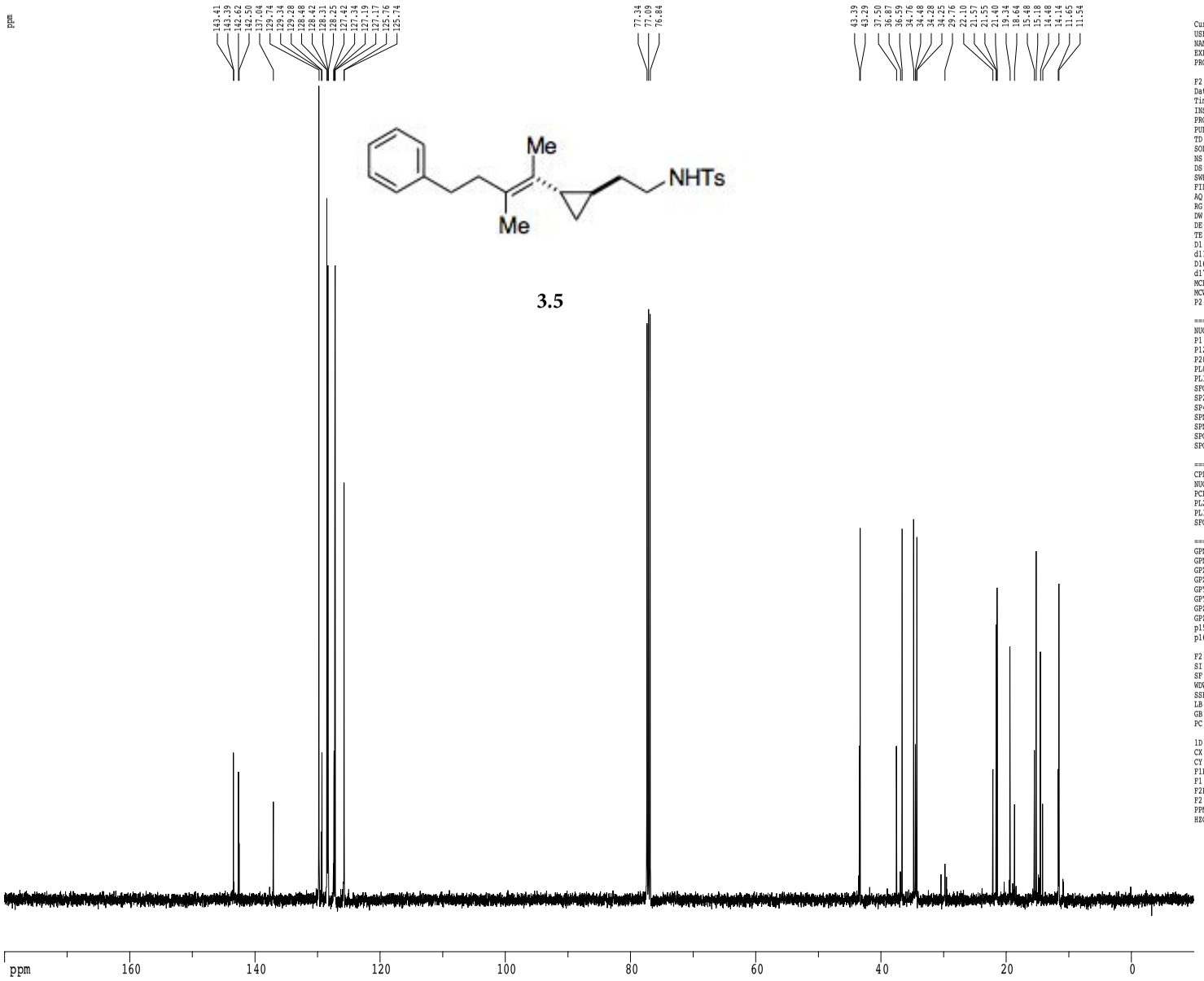
======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2               1H
PCPD2            80.00 usec
PL2              -6.00 dB
PL12             12.30 dB
SFO2        498.7524937 MHz

F2 - Processing parameters
SI               65536
SF          125.4107752 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC               2.00

1D NMR plot parameters
CX               20.00 cm
CY               12.50 cm
F1P             180.000 ppm
F1            22573.94 Hz
F2P            -10.000 ppm
F2            -1254.11 Hz
PPMCM          9.50000 ppm/cm
HZCM        1191.40234 Hz/cm
```


1H spectrum
Current Data Parameters
USER ttahae
NAME TAT1v12bcatdoon
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201008
Time 16.23
INSTRUM czyo500
PROBHD 5 mm CPPICI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 294.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200359 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 5.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
NHTs
Me
Me
NHTs
Me
Me
3.5
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                tthane
NAME          TATiv120carbon
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20201008
Time                16.25
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                  65536
SOLVENT             CDCl3
NS                    520
DS                     16
SWH             30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                   6502
DW                 16.500 usec
DE                  6.00 usec
TE                298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                 33.10 usec

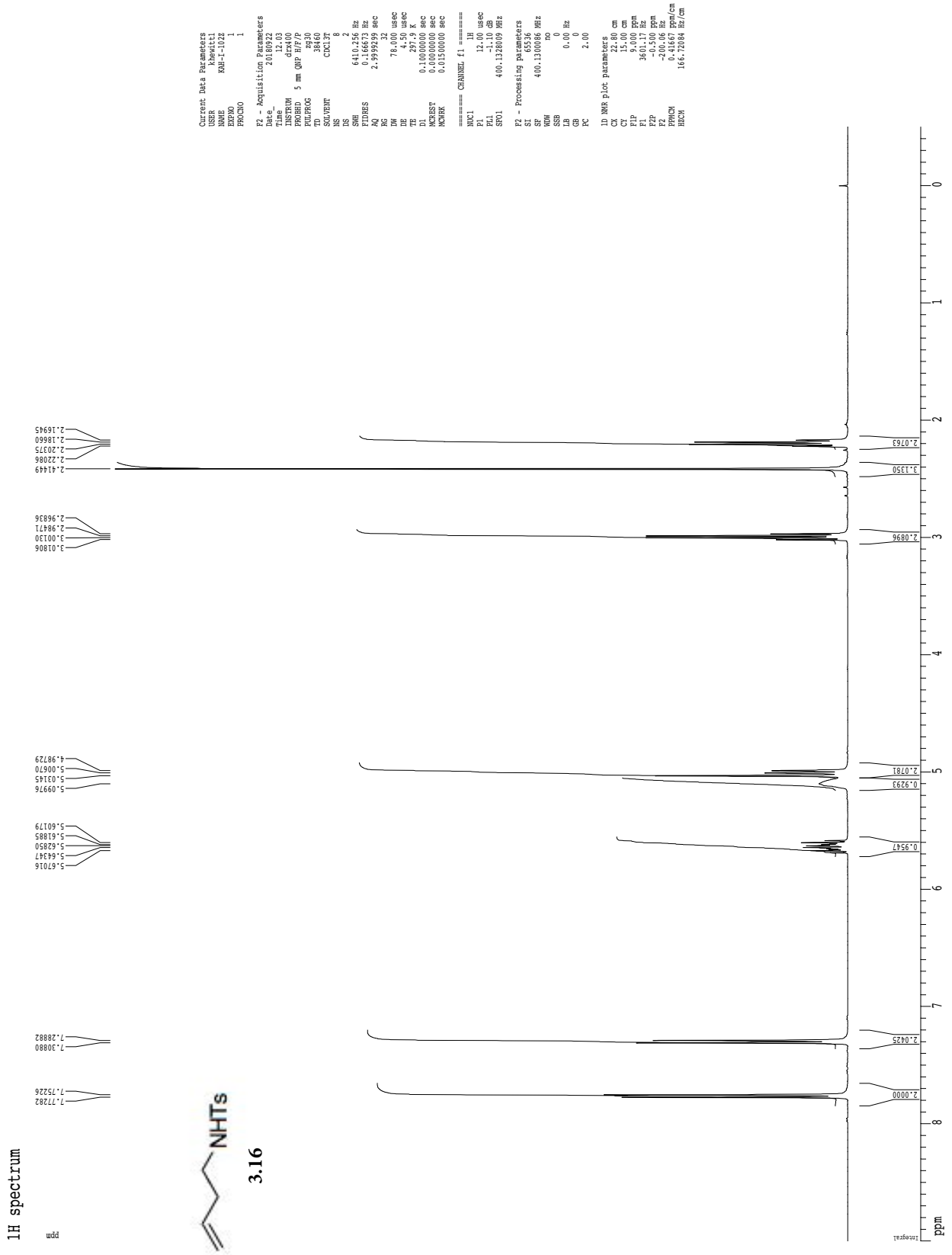
======== CHANNEL f1 ========
NUC1                 13C
P1                 16.55 usec
P12              2000.00 usec
P20               500.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP2                 2.70 dB
SP4                 2.70 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2              0.00 Hz
SPOFF4              0.00 Hz

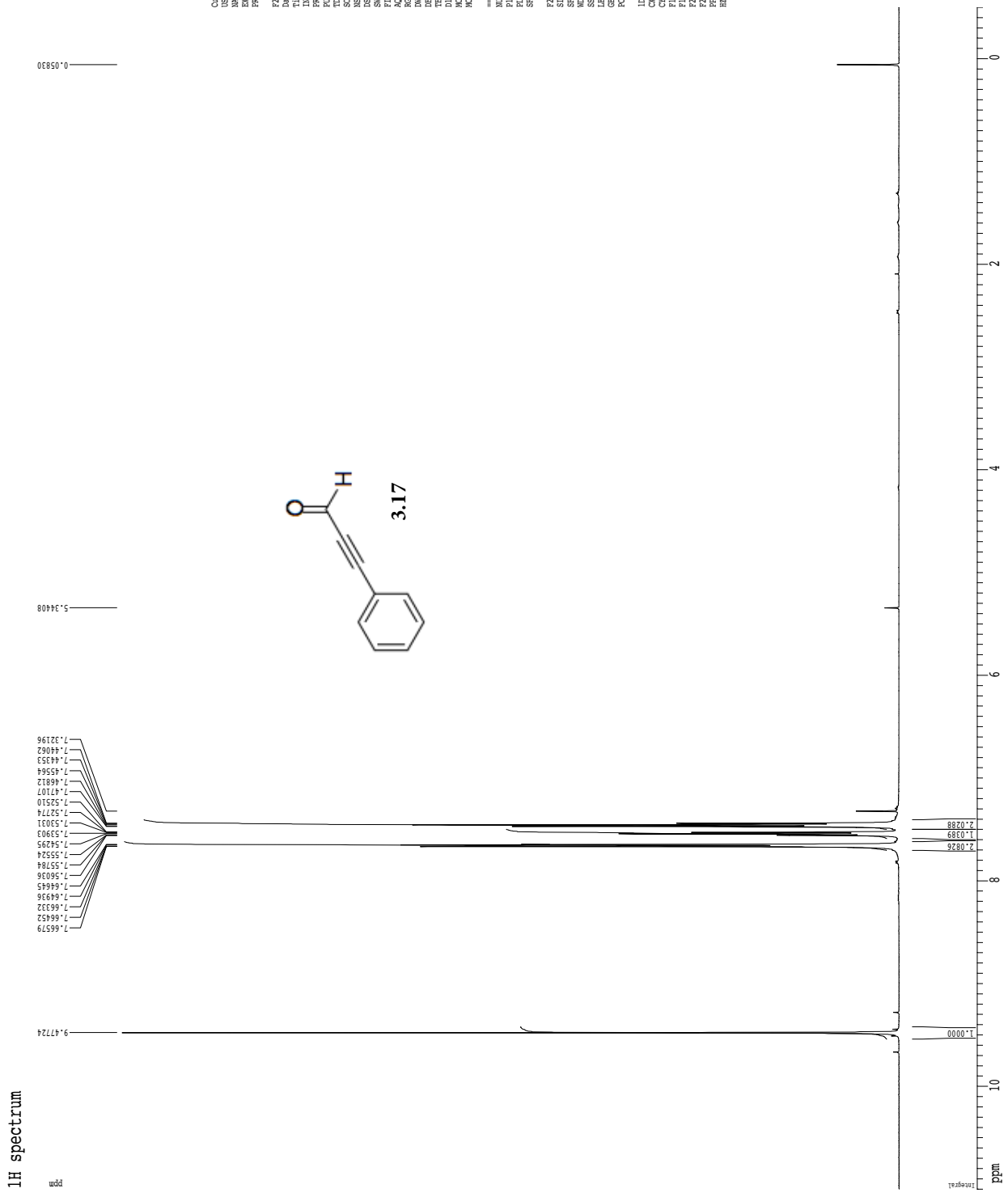
======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               23.54 dB
SFO2         500.2225011 MHz

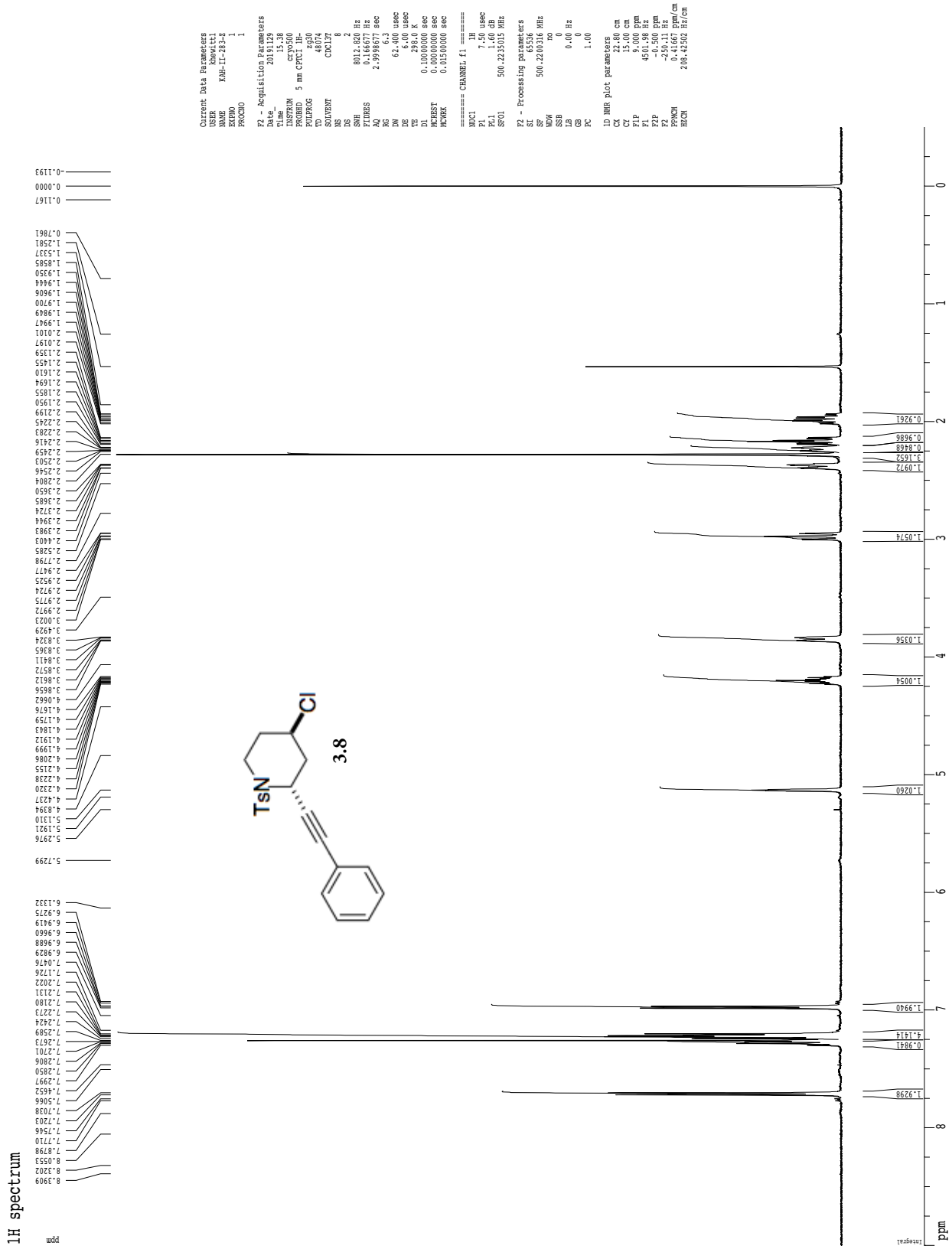
====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                  65536
SF           125.7804190 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

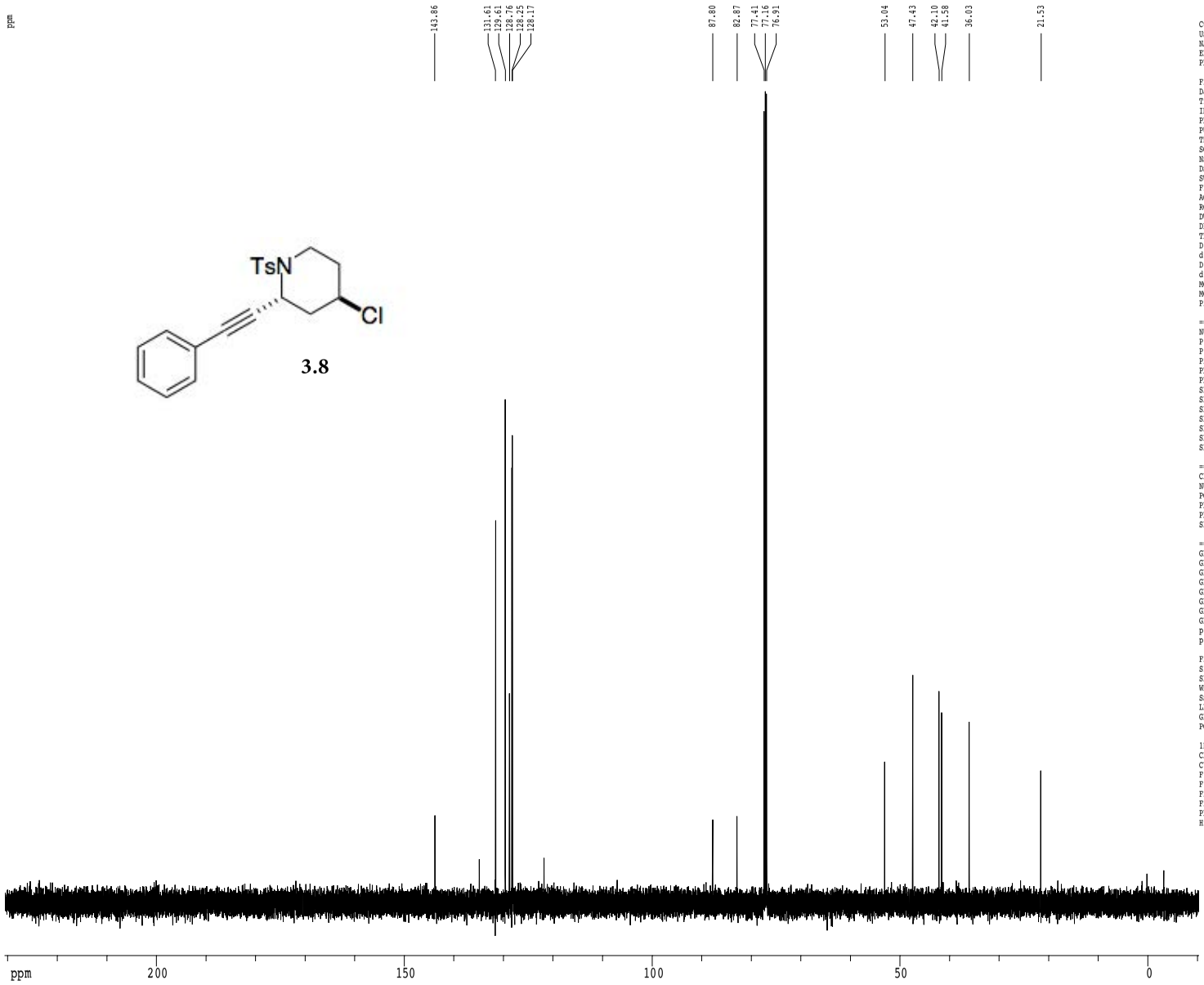
1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               180.000 ppm
F1              22640.47 Hz
F2P               -10.000 ppm
F2              -1257.80 Hz
PPMCM             8.33333 ppm/cm
HZCM           1048.17017 Hz/cm
```


1H spectrum
ppm
NHTs
3.16
Current Data Parameters
USER Rawaitl
NAME KAH-1-102B
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20180922
Time 12.03
INSTRUM drx400
PROBHD 5 mm QNP H/P/P
PULPROG zg30
TD 78560
SOLVENT CDCl3_PT
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.166673 Hz
AQ 2.9999299 sec
RG 32
DW 78.000 usec
DE 4.50 usec
TE 293.3 K
D1 0.10000000 sec
MCREST 0.10000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300086 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72084 Hz/cm
7.77282
7.75226
7.30880
7.28882
5.67016
5.64347
5.62850
5.61885
5.60179
4.98729
5.00670
5.03145
5.09976
3.01806
3.00130
2.98471
2.96836
2.41449
2.22086
2.20375
2.18660
2.16945
2.0000
2.0425
0.9547
2.0781
0.9293
2.0896
3.1350
2.0763
Integral
ppm


1H spectrum
Current Data Parameters
USER khewitt1
NAME KAH-11-282-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200116
Time 16.55
INSTRUM cryo500
PROBHD 5 mm CPPrCI 1H-
PULPROG 6g30
TD 40814
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.166677 Hz
AQ 2.9998677 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 294.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 11.000 ppm
F1 5502.42 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.50439 ppm/cm
HZCM 252.30396 Hz/cm
3.17
0.05830
5.34408
9.47724
1.0000
2.0288
1.0389
2.0826
7.32196
7.44062
7.44353
7.45564
7.46812
7.47107
7.52510
7.52774
7.53031
7.53903
7.54295
7.55524
7.55784
7.56036
7.64645
7.64936
7.66332
7.66452
7.66579
ppm
Integral


1H spectrum
Current Data Parameters
USER khewitt1
NAME KAH-11-203-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191129
Time 15.38
INSTRUM czry500
PROBHD 5 mm CPDCI 1H-
PULPROG zg30
TD 40014
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.166677 Hz
AQ 2.9998677 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200316 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
TsN
Cl
3.8
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              khewitt1
NAME         KAH-II-283-2
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191129
Time               15.57
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                 65536
SOLVENT            CDCl3
NS                   488
DS                    16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                7298.2
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                33.10 usec

======== CHANNEL f1 ========
NUC1                13C
P1                16.55 usec
P12             2000.00 usec
P20              500.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1         125.7942548 MHz
SP2                2.70 dB
SP4                2.70 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2             0.00 Hz
SPOFF4             0.00 Hz

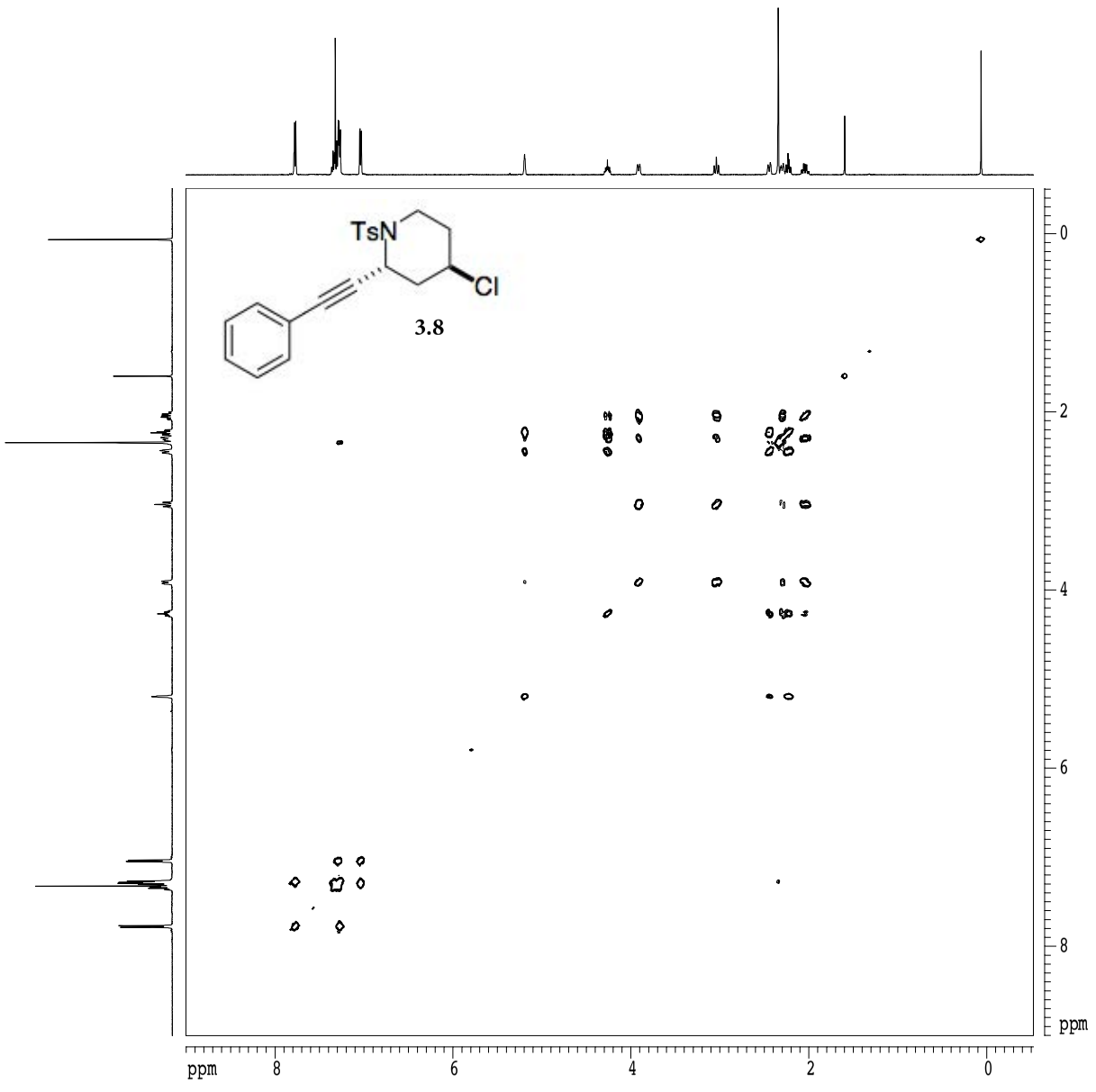
======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              23.54 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1               0.00 %
GPX2               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804057 MHz
WDW                   no
SSB                    0
LB                0.00 Hz
GB                     0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                15.65 cm
F1P              230.637 ppm
F1             29009.68 Hz
F2P              -10.287 ppm
F2             -1293.96 Hz
PPMCM          10.56688 ppm/cm
HZCM         1329.10693 Hz/cm
```

gcosy60




```
        Current Data Parameters
USER            khewitt1
NAME        KAH-II-283-Z
EXPNO                   2
PROCNO                  1

      F2 - Acquisition Parameters
Date_            20191129
Time                15.40
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG     cosygp60.prd
TD                   2048
SOLVENT             CDCl3
NS                      1
DS                     16
SWH             8012.820 Hz
FIDRES          3.912510 Hz
AQ              0.1278452 sec
RG                  912.3
DW                 62.400 usec
DE                  6.00 usec
TE                 298.0 K
d0              0.00000300 sec
D1              1.00000000 sec
d13             0.00000300 sec
D16             0.00020000 sec
IN0             0.00012480 sec

     ======== CHANNEL f1 ========
NUC1                    1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1         500.2235015 MHz

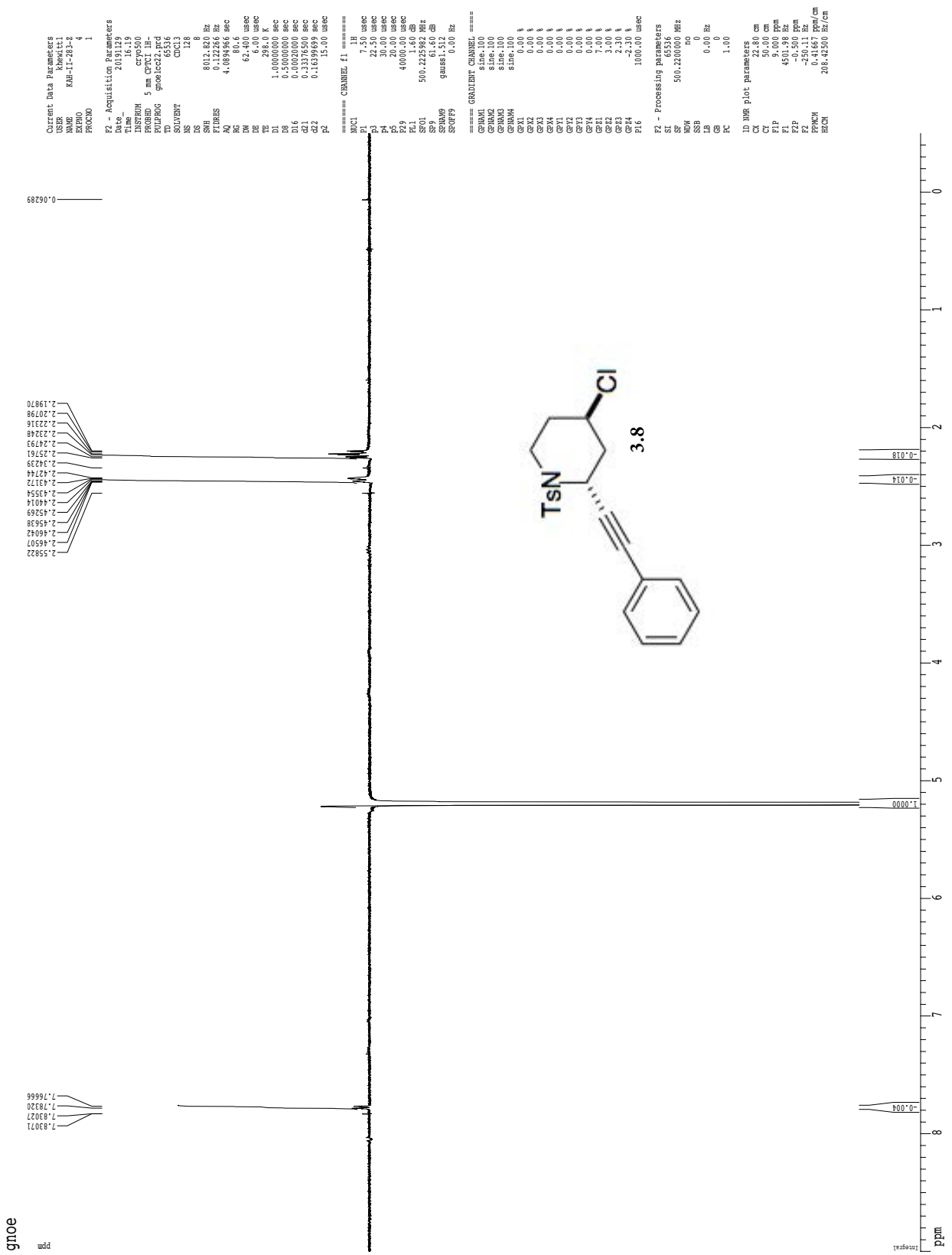
     ====== GRADIENT CHANNEL =====
GPNAM1           sine.100
GPNAM2           sine.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               17.00 %
GPZ2               17.00 %
P16              1000.00 usec

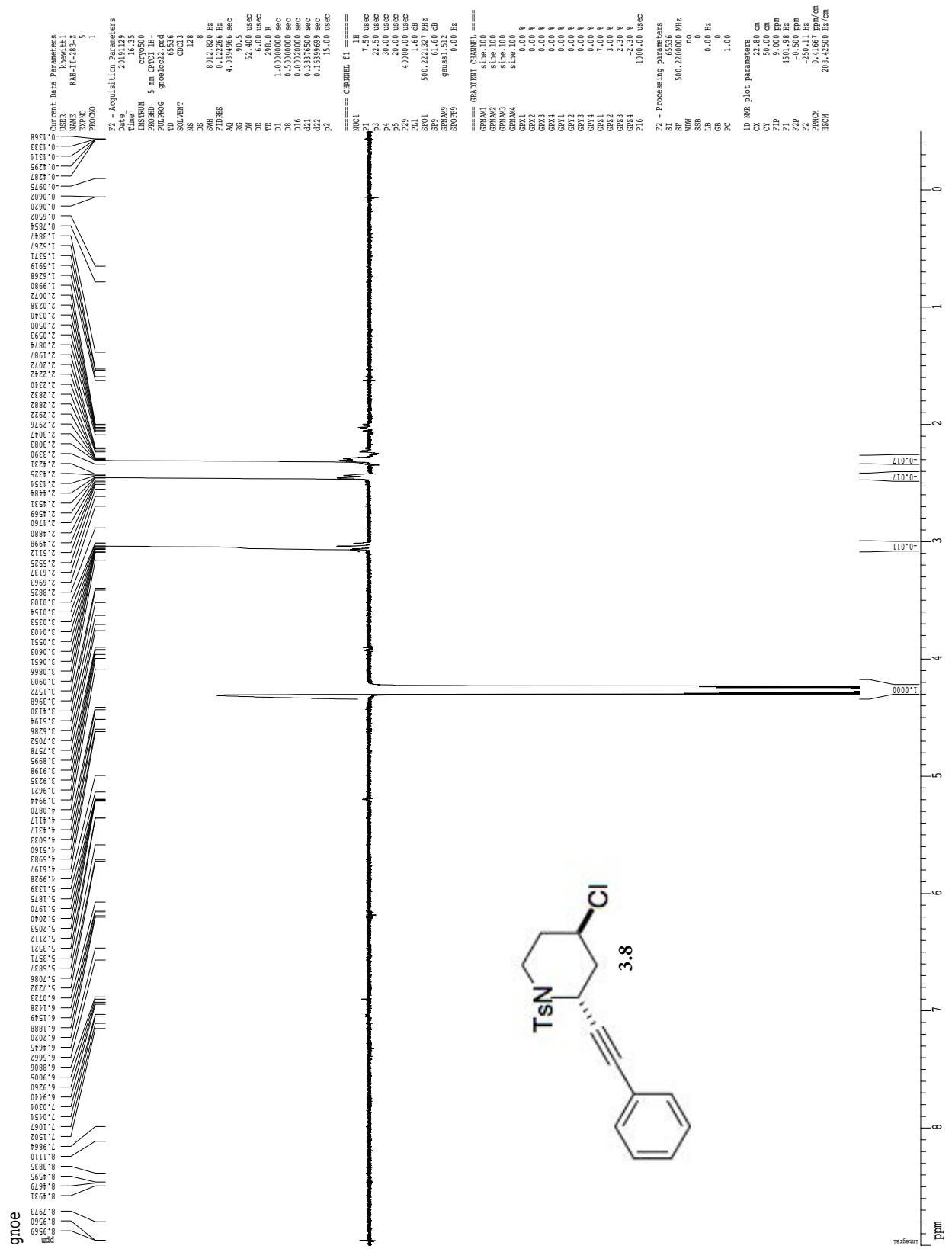
      F1 - Acquisition parameters
ND0                     1
TD                    512
SFO1            500.2235 MHz
FIDRES         15.650040 Hz
SW                16.018 ppm
FnMODE                 QF

      F2 - Processing parameters
SI                    1024
SF           500.2200000 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00

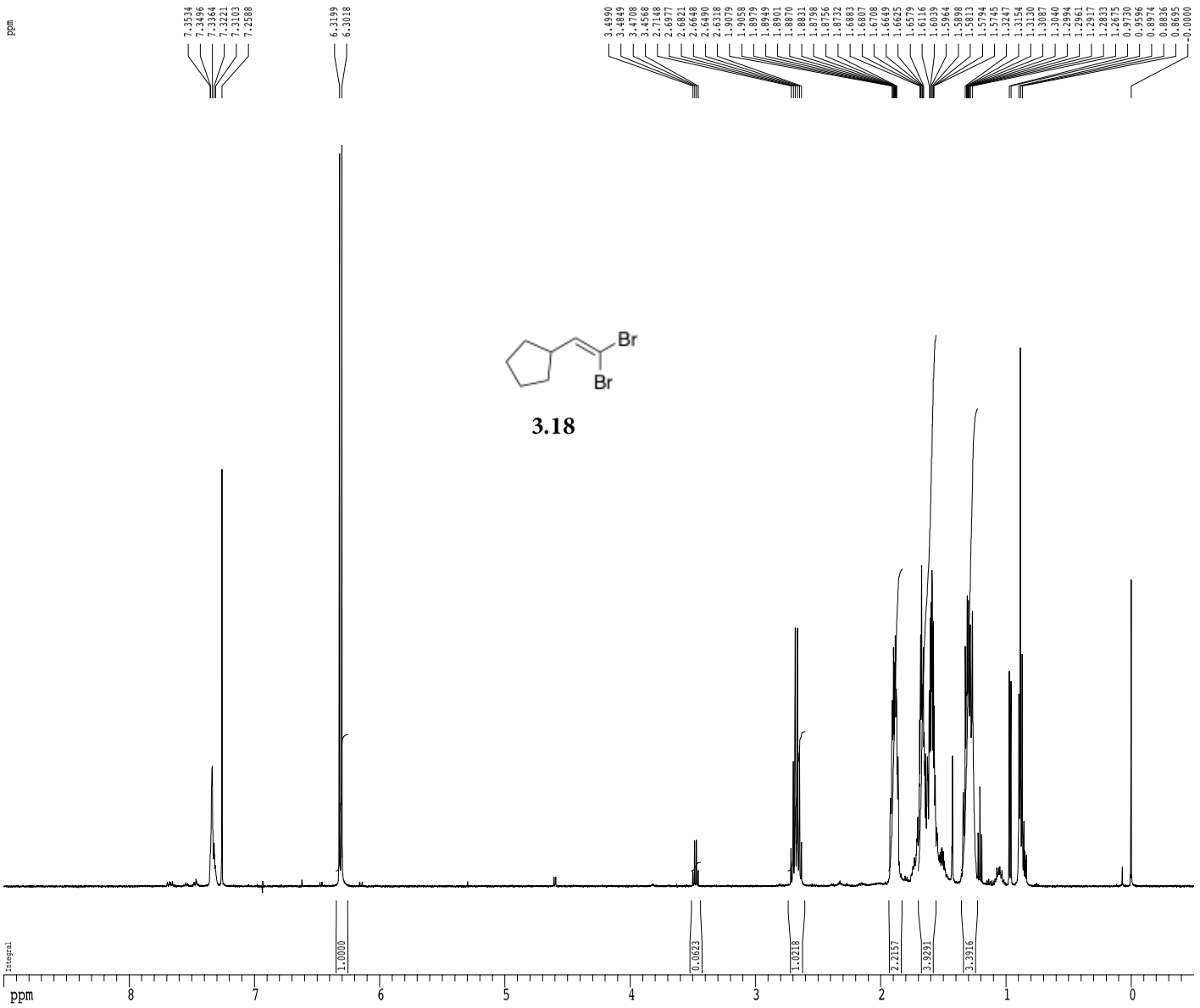
      F1 - Processing parameters
SI                    1024
MC2                    QF
SF           500.2200000 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0

       2D NMR plot parameters
CX2                15.00 cm
CX1                15.00 cm
F2PLO               9.002 ppm
F2LO             4503.14 Hz
F2PHI              -0.524 ppm
F2HI             -262.29 Hz
F1PLO               9.002 ppm
F1LO             4503.14 Hz
F1PHI              -0.509 ppm
F1HI             -254.47 Hz
F2PPMCM          0.63511 ppm/cm
F2HZCM         317.69583 Hz/cm
F1PPMCM          0.63407 ppm/cm
F1HZCM         317.17416 Hz/cm
```


gnoe
ppm
Integral
Current Data Parameters
USER khewitt1
NAME KAH-II-283-2
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191129
Time_ 16.19
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG gnoe1cc22.pcd
TD 65536
SOLVENT CDCl3
NS 128
DS 8
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 80.6
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.13376500 sec
d22 0.16394699 sec
p2 15.00 usec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
p5 20.00 usec
P29 40000.00 usec
PL1 1.60 dB
SFO1 500.2225982 MHz
SPNAM0 Crp60,0.5
SPNAM9 gauss1.512
SPOFF9 0.00 Hz
===== GRADIENT CHANNEL =====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPNAM4 sine.100
GPX1 0.00 %
GPX2 0.00 %
GPX3 0.00 %
GPX4 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPY3 0.00 %
GPY4 0.00 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 50.00 cm
F1P 7.000 ppm
F1 4501.20 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42500 Hz/cm
0.06289
2.55822
2.46507
2.46042
2.45638
2.45269
2.44014
2.43554
2.43172
2.42744
2.34239
2.25761
2.24793
2.23248
2.22316
2.20798
2.19870
7.83071
7.83027
7.78320
7.76666
1.0000
0.014
0.018
0.004
TsN
Cl
3.8


gnoe
ppm
Integral
3.8
TsN
Cl

1H spectrum



3.18

Current Data Parameters

USER	tthane
NAME	TATiv118-1
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20200826
Time	15.29
INSTRUM	gn500
PROBHD	5 mm broadband
PULPROG	zg30
TD	81728
SOLVENT	CDCl3T
NS	8
DS	2
SWH	8012.820 Hz
FIDRES	0.098043 Hz
AQ	5.0998774 sec
RG	181
DW	62.400 usec
DE	6.00 usec
TE	298.0 K
D1	0.10000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

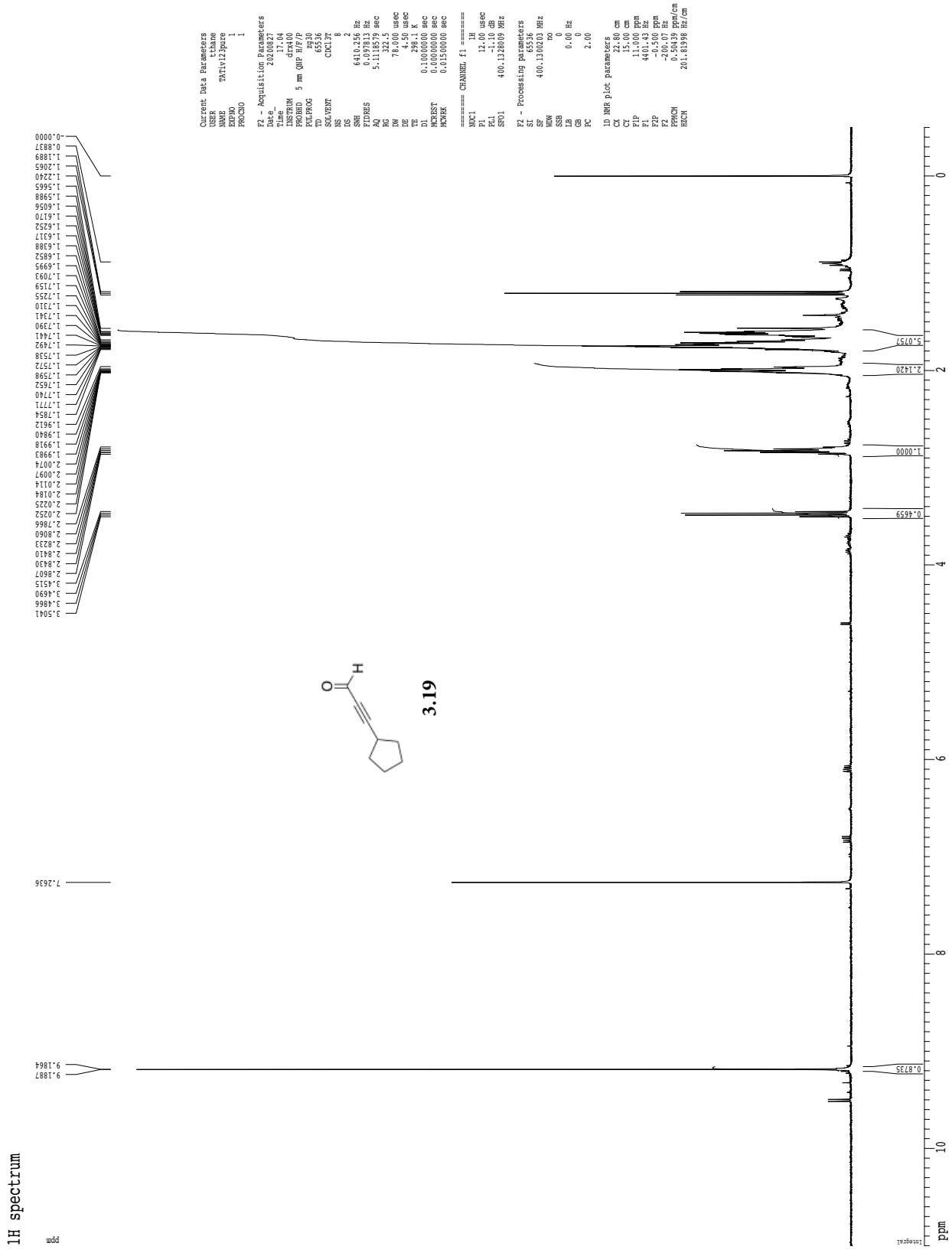
NUC1	1H
P1	12.00 usec
PL1	-6.00 dB
SFO1	498.7534913 MHz

F2 - Processing parameters

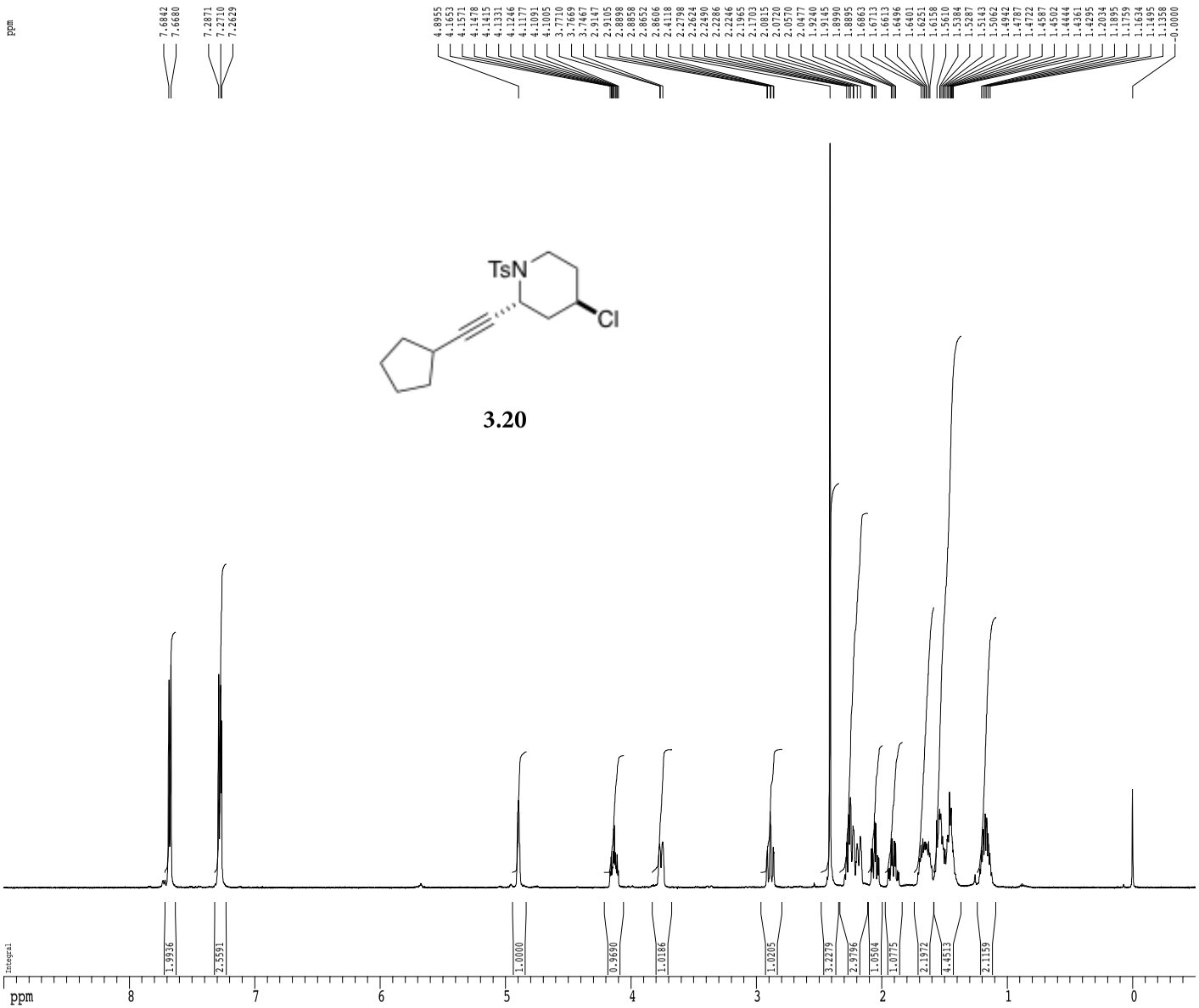
SI	65536
SF	498.7500319 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	9.000 ppm
F1	4488.75 Hz
F2P	-0.500 ppm
F2	-249.38 Hz
PPMCM	0.47500 ppm/cm
HZCM	236.90627 Hz/cm


1H spectrum
3.19
ppm

1H spectrum



3.20

```
Current Data Parameters
USER              tthane
NAME      TATiv129carbon
EXPNO                  1
PROCNO                 1

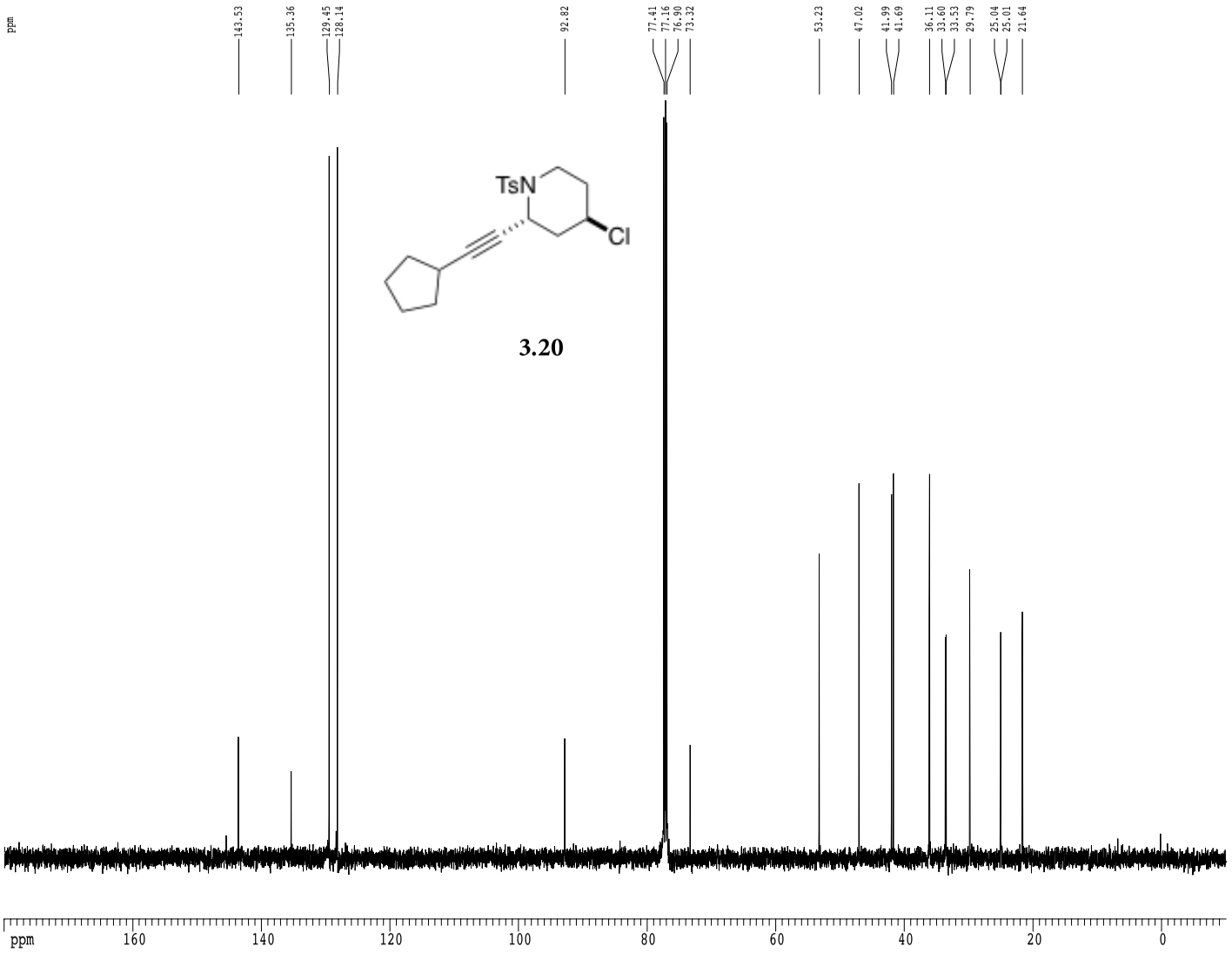
F2 - Acquisition Parameters
Date_           20201009
Time               15.43
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3T
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES             0.098043 Hz
AQ              5.0998774 sec
RG                 724.1
DW                 62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.00 usec
PL1                -6.00 dB
SFO1         498.7534913 MHz

F2 - Processing parameters
SI                 65536
SF           498.7500301 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 20.00 cm
CY                 12.50 cm
F1P                9.000 ppm
F1               4488.75 Hz
F2P                -0.500 ppm
F2               -249.38 Hz
PPMCM           0.47500 ppm/cm
HZCM          236.90627 Hz/cm
```

13C spectrum with 1H decoupling




```
Current Data Parameters
USER              tthane
NAME      TATiv129carbon
EXPNO                 2
PROCNO                1

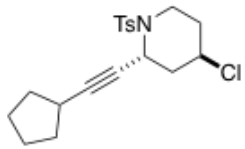
F2 - Acquisition Parameters
Date_          20201009
Time              15.45
INSTRUM           gn500
PROBHD   5 mm broadband
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                  512
DS                    4
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                46341
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                14.20 usec
PL1               -6.00 dB
SFO1        125.4245824 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2             80.00 usec
PL2               -6.00 dB
PL12              12.30 dB
SFO2        498.7524937 MHz

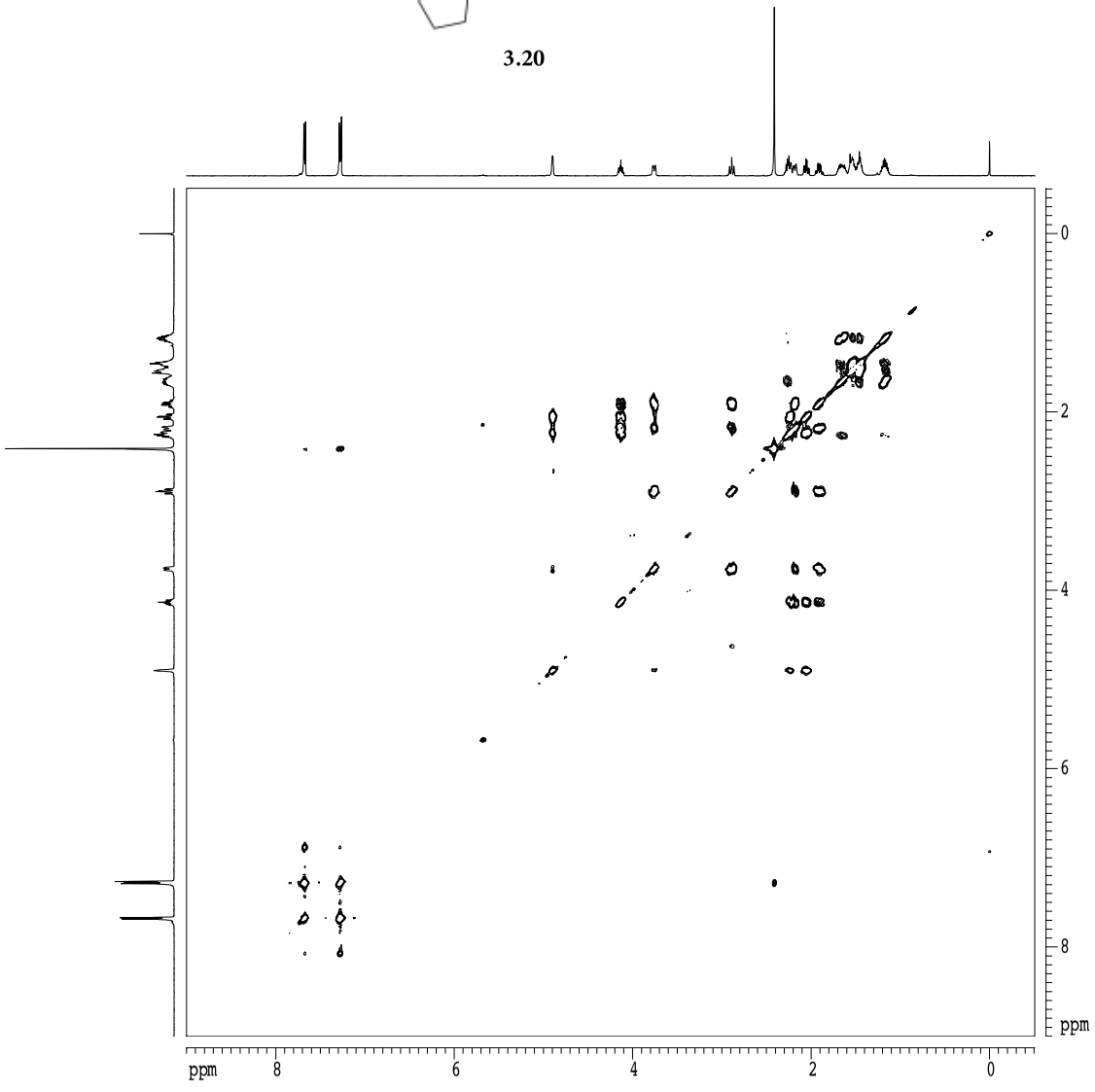
F2 - Processing parameters
SI                65536
SF          125.4107762 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                20.00 cm
CY                12.50 cm
F1P              180.000 ppm
F1             22573.94 Hz
F2P              -10.000 ppm
F2             -1254.11 Hz
PPMCM           9.50000 ppm/cm
HZCM         1191.40234 Hz/cm
```



3.20

gcosy60




```
        Current Data Parameters
USER              tthane
NAME        TATiv129COSY
EXPNO                  2
PROCNO                 1

      F2 - Acquisition Parameters
Date_           20201010
Time              14.56
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG    cosygp60.prd
TD                2048
SOLVENT           CDCl3
NS                   2
DS                  16
SWH           8012.820 Hz
FIDRES        3.912510 Hz
AQ            0.1278452 sec
RG                456.1
DW               62.400 usec
DE                6.00 usec
TE               298.0 K
d0           0.00000300 sec
D1           1.00000000 sec
d13          0.00000300 sec
D16          0.00020000 sec
IN0          0.00012480 sec

     ======= CHANNEL f1 =======
NUC1                 1H
P1                7.50 usec
PL1               1.60 dB
SFO1        500.2235015 MHz

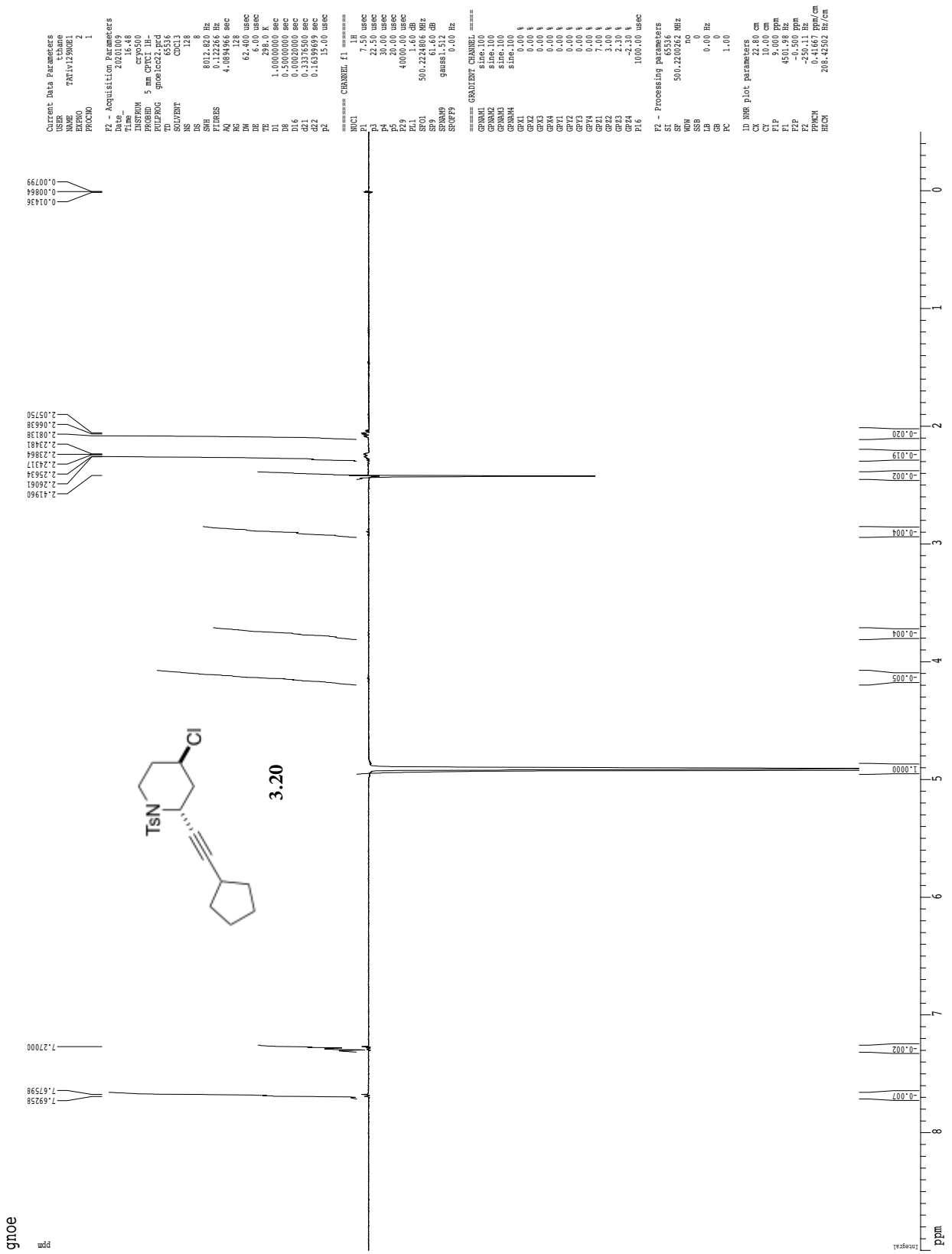
     ===== GRADIENT CHANNEL ====
GPNAM1          sine.100
GPNAM2          sine.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             17.00 %
GPZ2             17.00 %
P16            1000.00 usec

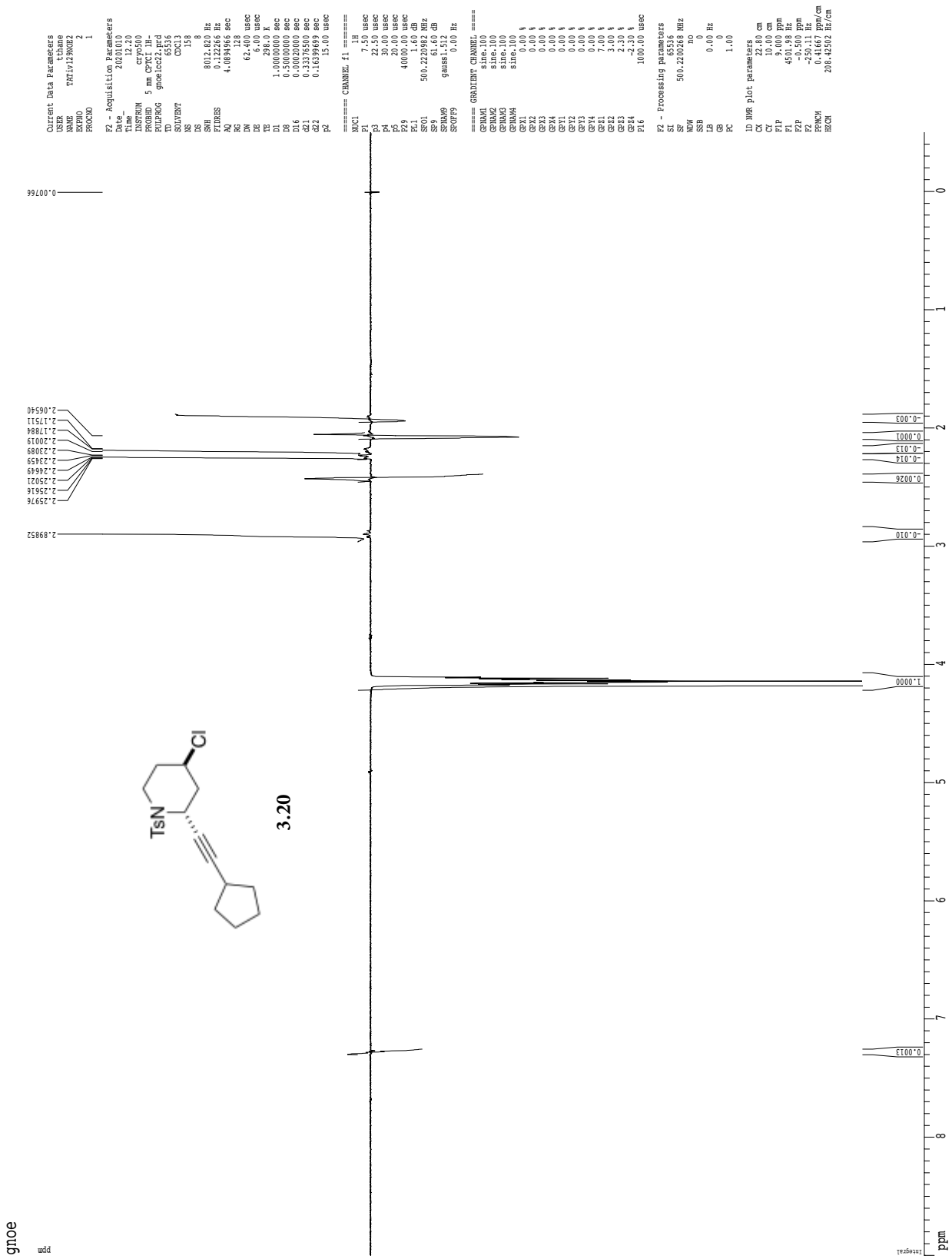
      F1 - Acquisition parameters
ND0                  1
TD                 512
SFO1        500.2235 MHz
FIDRES       15.650040 Hz
SW              16.018 ppm
FnMODE              QF

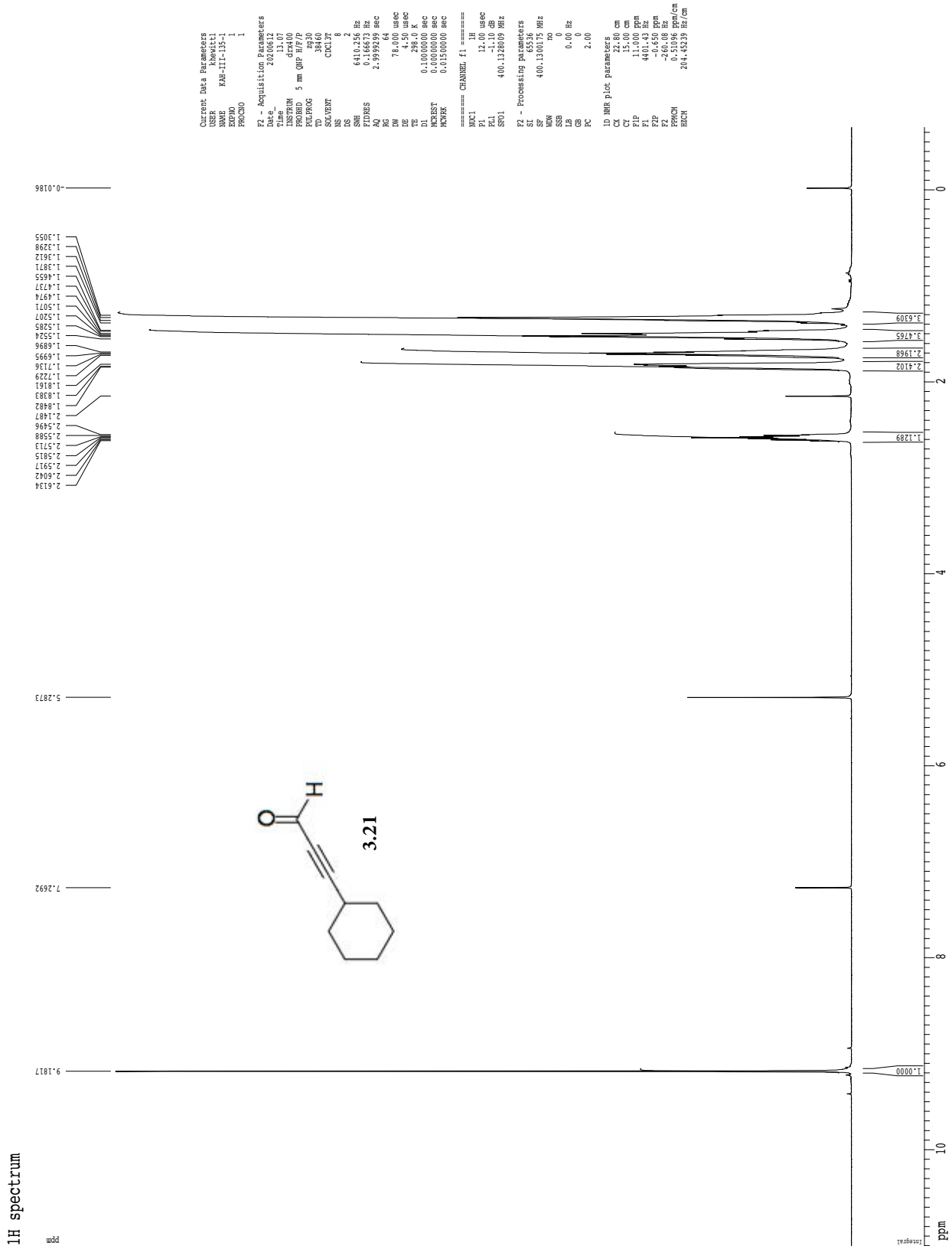
      F2 - Processing parameters
SI                1024
SF          500.2200309 MHz
WDW               SINE
SSB                  0
LB                0.00 Hz
GB                   0
PC                1.00

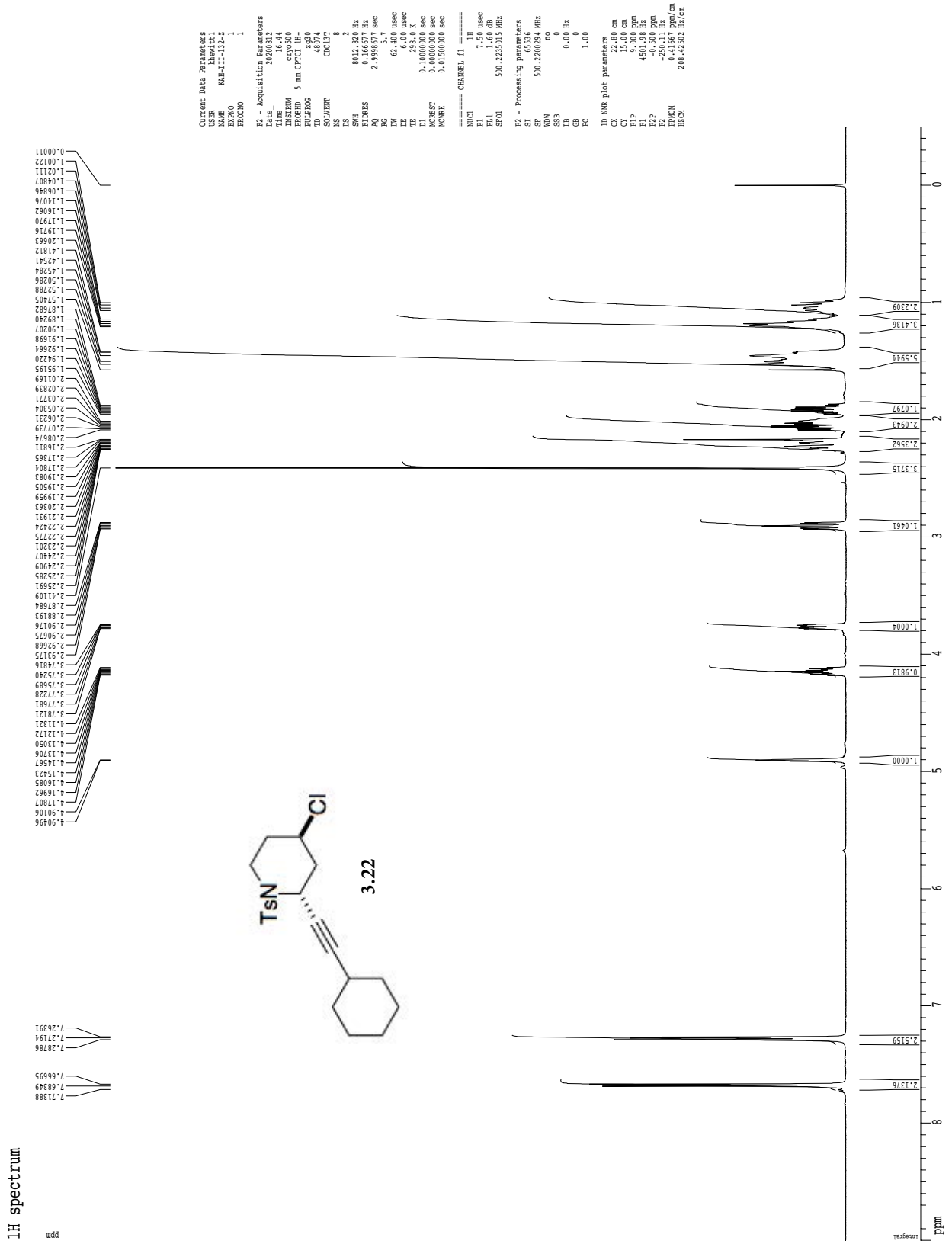
      F1 - Processing parameters
SI                1024
MC2                 QF
SF          500.2200309 MHz
WDW               SINE
SSB                  0
LB                0.00 Hz
GB                   0

      2D NMR plot parameters
CX2              15.00 cm
CX1              15.00 cm
F2PLO             9.000 ppm
F2LO           4501.98 Hz
F2PHI            -0.508 ppm
F2HI           -254.07 Hz
F1PLO             9.003 ppm
F1LO           4503.54 Hz
F1PHI            -0.508 ppm
F1HI           -254.07 Hz
F2PPMCM       0.63386 ppm/cm
F2HZCM      317.07007 Hz/cm
F1PPMCM       0.63407 ppm/cm
F1HZCM      317.17413 Hz/cm
```

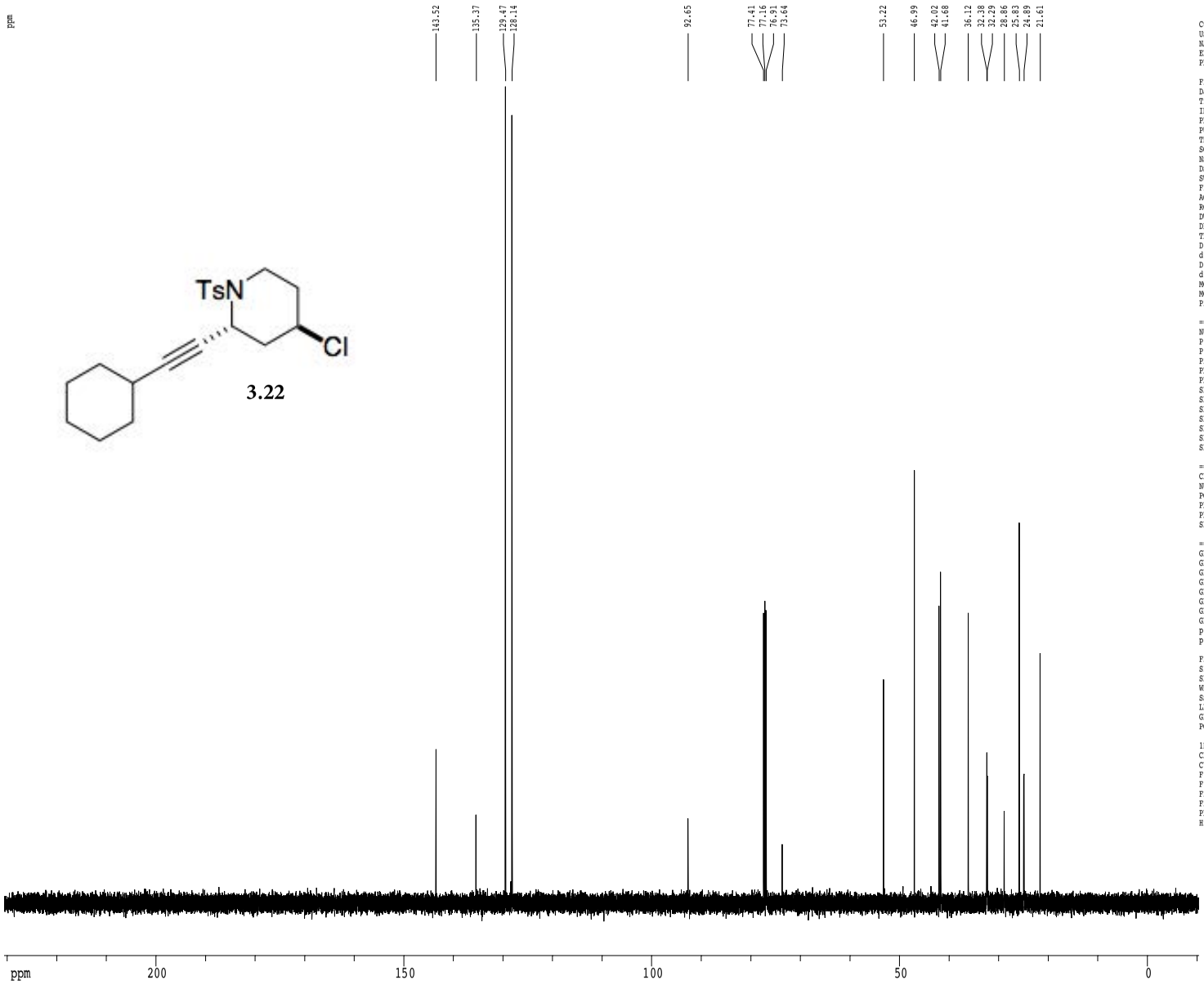

Current Data Parameters
USER ttihane
NAME TAT1v1129NOB1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201009
Time_ 16.48
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG gnoe1cc22.pcd
TD 65536
SOLVENT CDCl3
NS 128
DS 8
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.13376500 sec
d22 0.16394699 sec
p2 15.00 usec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
p5 20.00 usec
PZ9 40000.00 usec
PL1 1.60 dB
SFO1 500.2224806 MHz
SP1 61.60 dB
SPNAM9 gauss1.512
SPOFF9 0.00 Hz
===== GRADIENT CHANNEL =====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPNAM4 sine.100
GPX1 0.00 %
GPX2 0.00 %
GPX3 0.00 %
GPX4 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPY3 0.00 %
GPY4 0.00 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200262 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 10.00 cm
F1P 9.000 ppm
F1 4501.80 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
0.01436
0.00864
0.00799
2.07750
2.06638
2.08138
2.23481
2.23864
2.24317
2.25634
2.26061
2.41960
7.27000
7.69258
7.67598
1.0000
-0.020
-0.019
-0.002
-0.004
-0.004
-0.005
-0.002
-0.007
TsN
Cl
3.20
gnoe
ppm
Integral


gnoe
ppm
3.20
TsN
Cl


1H spectrum
Current Data Parameters
USER kiewiti
NAME KAH-III-135-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200612
Time 13.07
INSTRUM drx400
PROBHD 5 mm QNP H/P/P
PULPROG zg30
TD 34496
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.166673 Hz
AQ 2.9999299 sec
RG 64
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300175 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 11.000 ppm
F1 4401.43 Hz
F2P -0.650 ppm
F2 -260.08 Hz
PPMCM 0.51096 ppm/cm
HZCM 204.45239 Hz/cm
0.0186
1.3055
1.3298
1.3612
1.3871
1.4655
1.4737
1.4974
1.5071
1.5207
1.5285
1.5524
1.6896
1.6995
1.7136
1.7229
1.8161
1.8383
1.8482
2.1487
2.5496
2.5588
2.5713
2.5815
2.5917
2.6042
2.6134
5.2873
7.2692
9.1817
3.6309
3.4765
2.1968
2.4102
1.1289
1.0000
3.21
ppm
Integral


1H spectrum
3.22
TsN
Cl
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                khewitt1
NAME          KAH-III-132-2
EXPNO                     3
PROCNO                    1

F2 - Acquisition Parameters
Date_            20200812
Time                16.58
INSTRUM           cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp2.prd
TD                  65536
SOLVENT             CDCl3
NS                    192
DS                     16
SWH              30303.031 Hz
FIDRES            0.462388 Hz
AQ                1.0813940 sec
RG                   13004
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1               0.25000000 sec
d11              0.03000000 sec
D16              0.00020000 sec
d17              0.00019600 sec
MCREST           0.00000000 sec
MCWRK            0.01500000 sec
P2                  33.10 usec

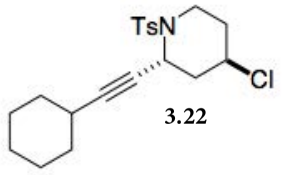
======== CHANNEL f1 ========
NUC1                  13C
P1                  16.55 usec
P12               2000.00 usec
P20                500.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP2                  2.70 dB
SP4                  2.70 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2               0.00 Hz
SPOFF4               0.00 Hz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                23.54 dB
SFO2          500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

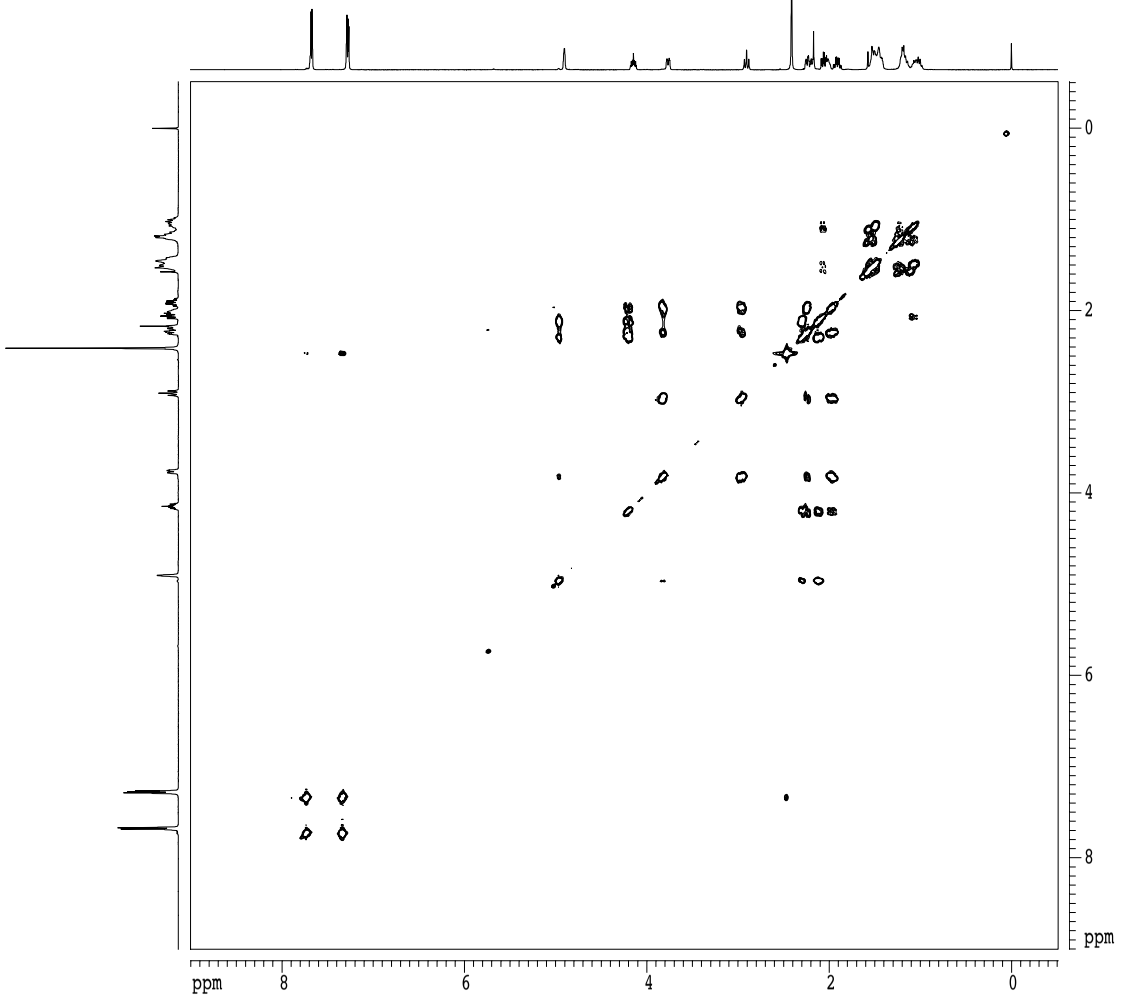
F2 - Processing parameters
SI                  65536
SF            125.7804080 MHz
WDW                    no
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               230.547 ppm
F1              28998.34 Hz
F2P               -10.373 ppm
F2              -1304.69 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```



3.22

gcosy60




```
      Current Data Parameters
USER           khewitt1
NAME      KAH-III-132-Z
EXPNO                 2
PROCNO                1

      F2 - Acquisition Parameters
Date_          20200812
Time              16.45
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG    cosygp60.prcd
TD                 2048
SOLVENT           CDCl3
NS                    1
DS                   16
SWH            8012.820 Hz
FIDRES         3.912510 Hz
AQ             0.1278452 sec
RG                  114
DW                62.400 usec
DE                 6.00 usec
TE                298.0 K
d0             0.00000300 sec
D1             1.00000000 sec
d13            0.00000300 sec
D16            0.00020000 sec
IN0            0.00012480 sec

     ======= CHANNEL f1 =======
NUC1                  1H
P1                  7.50 usec
PL1                 1.60 dB
SFO1         500.2235015 MHz

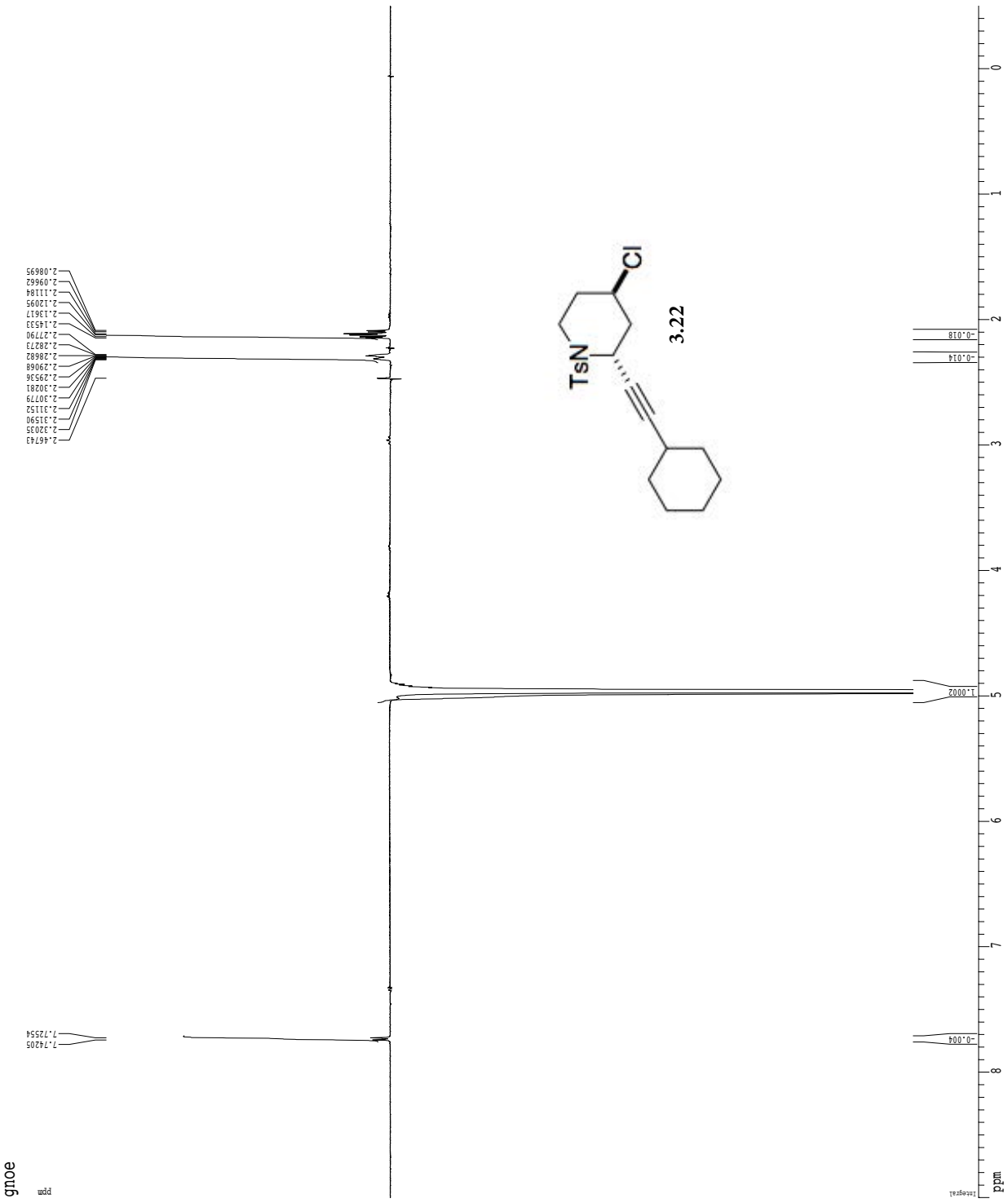
     ====== GRADIENT CHANNEL ====
GPNAM1          sine.100
GPNAM2          sine.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               17.00 %
GPZ2               17.00 %
P16              1000.00 usec

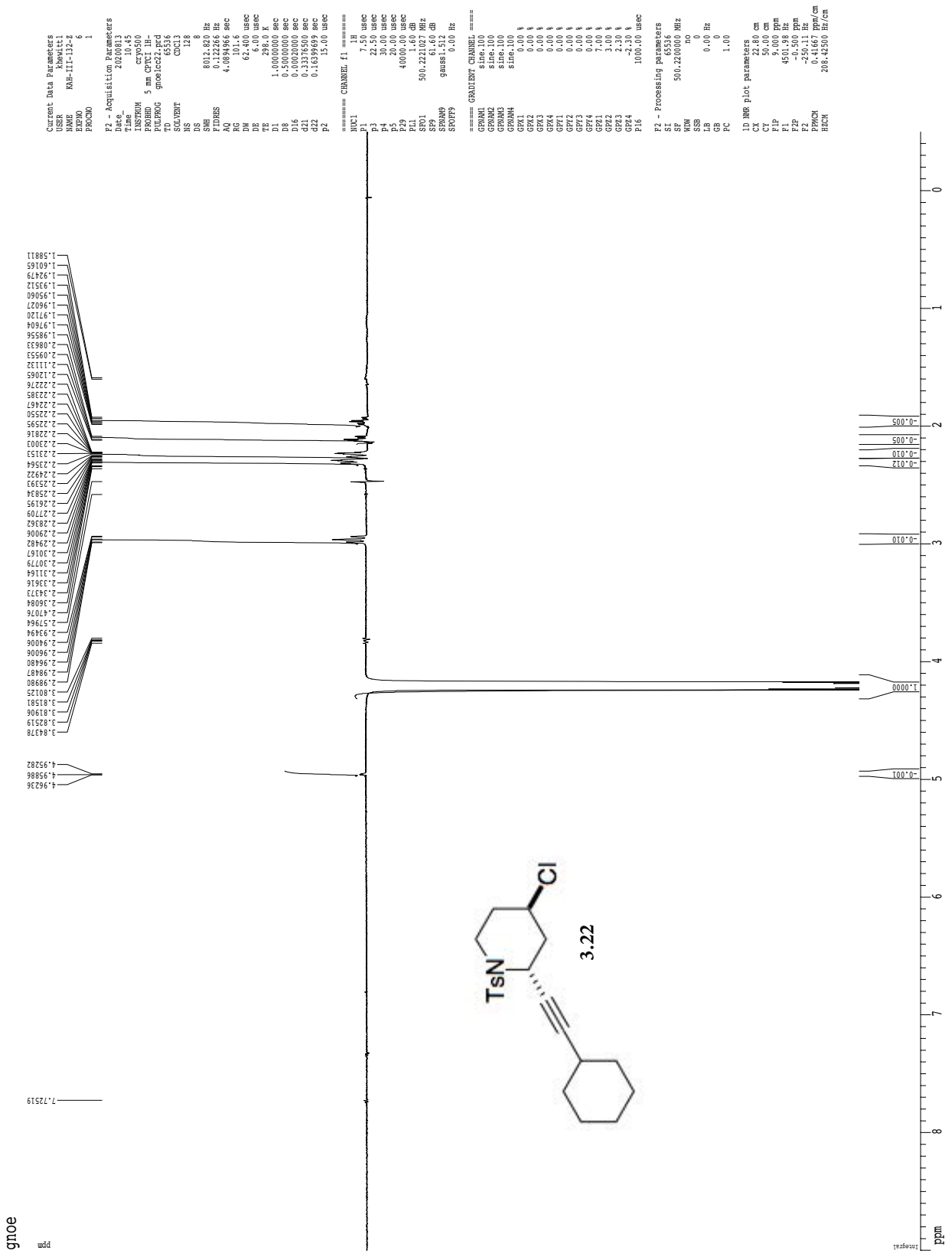
      F1 - Acquisition parameters
ND0                   1
TD                  512
SFO1           500.2235 MHz
FIDRES        15.650040 Hz
SW               16.018 ppm
FnMODE                QF

      F2 - Processing parameters
SI                 1024
SF          500.2200000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00

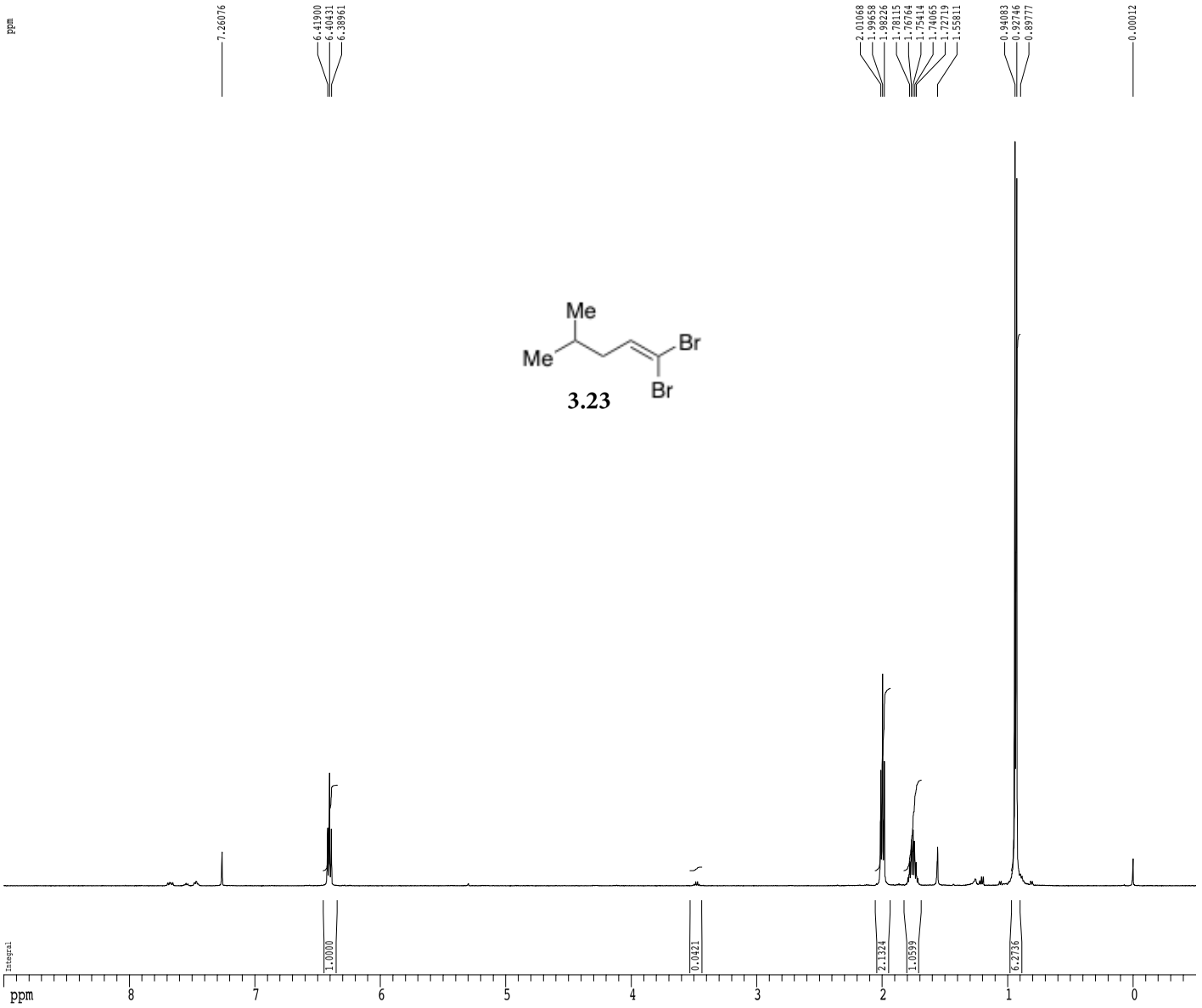
      F1 - Processing parameters
SI                 1024
MC2                   QF
SF          500.2200000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0

      2D NMR plot parameters
CX2               15.00 cm
CX1               15.00 cm
F2PLO              9.002 ppm
F2LO            4503.14 Hz
F2PHI             -0.509 ppm
F2HI            -254.47 Hz
F1PLO              9.002 ppm
F1LO            4503.14 Hz
F1PHI             -0.509 ppm
F1HI            -254.47 Hz
F2PPMCM         0.63407 ppm/cm
F2HZCM        317.17416 Hz/cm
F1PPMCM         0.63407 ppm/cm
F1HZCM        317.17416 Hz/cm
```


gnoe
ppm
Integral
ppm
7.74205
7.72554
2.46743
2.32035
2.31590
2.31152
2.30779
2.30281
2.29536
2.29068
2.28682
2.28273
2.27790
2.13617
2.11284
2.08695
1.0002
0.018
0.014
0.004
TsN
Cl
3.22


gnoe
ppm
TsN
Cl
3.22

1H spectrum



3.23

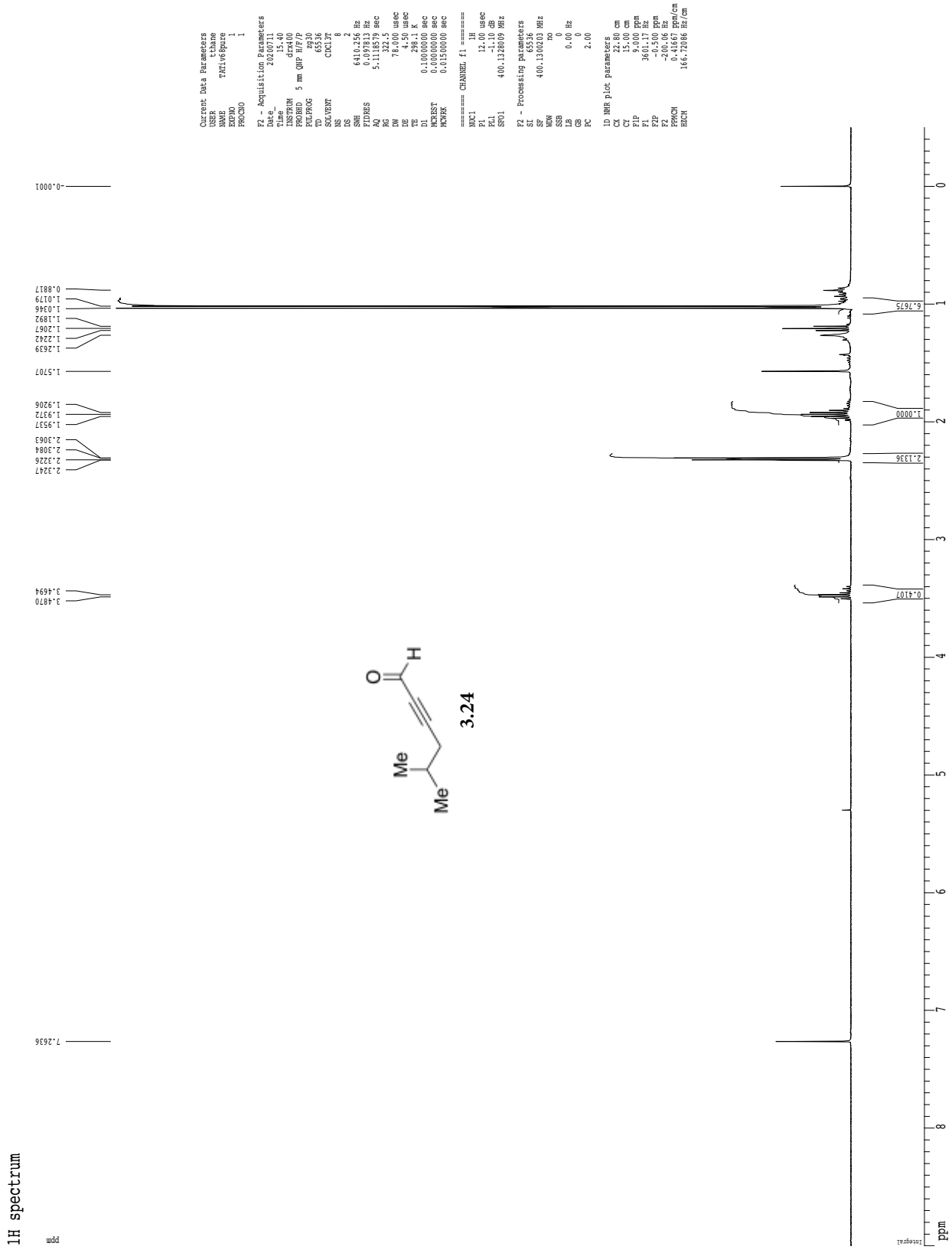
```
Current Data Parameters
USER                tthane
NAME              TATiv66c
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20200715
Time                 11.43
INSTRUM              gn500
PROBHD    5 mm broadband
PULPROG               zg30
TD                   81728
SOLVENT             CDCl3T
NS                       8
DS                       2
SWH               8012.820 Hz
FIDRES            0.098043 Hz
AQ                5.0998774 sec
RG                     512
DW                  62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

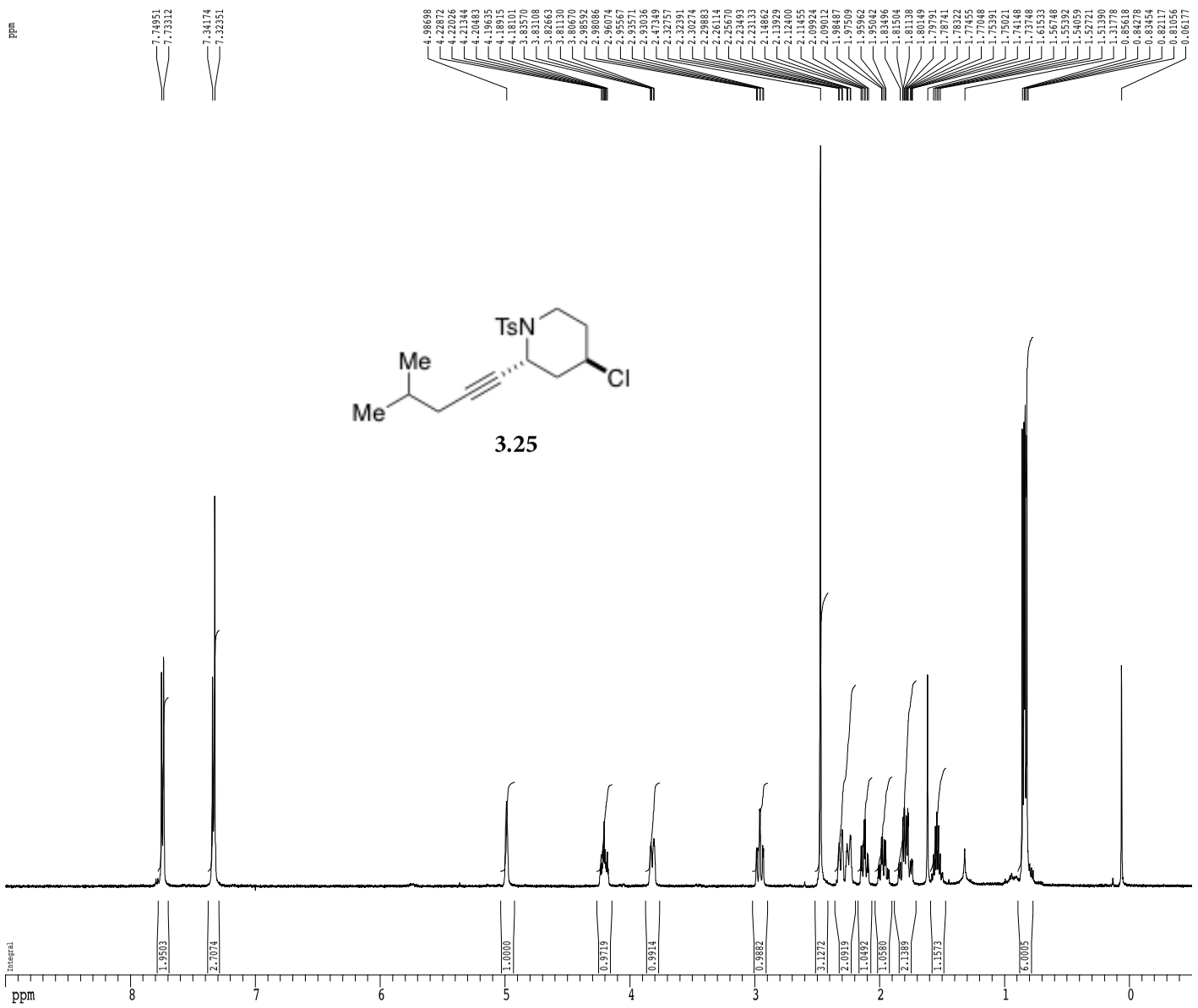
======== CHANNEL f1 ========
NUC1                    1H
P1                  12.00 usec
PL1                 -6.00 dB
SFO1          498.7534913 MHz

F2 - Processing parameters
SI                   65536
SF            498.7500309 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00

1D NMR plot parameters
CX                   20.00 cm
CY                   12.50 cm
F1P                  9.000 ppm
F1                4488.75 Hz
F2P                 -0.500 ppm
F2                -249.38 Hz
PPMCM             0.47500 ppm/cm
HZCM            236.90627 Hz/cm
```


1H spectrum
Current Data Parameters
USER ttshane
NAME YAMi406pure
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200711
Time 15.40
INSTRUM drx400
PROBHD 5 mm QNP H/P/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 322.5
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300203 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
0.0001
0.8817
1.0179
1.0346
1.1892
1.2067
1.2242
1.2639
1.5707
1.9206
1.9372
1.9537
2.3063
2.3084
2.3226
2.3247
3.4670
3.4694
7.2636
6.7675
1.0000
2.1336
0.4107
Integral
ppm
O
H
Me
Me
3.24

1H spectrum




```
Current Data Parameters
USER                tthane
NAME             TATiv69c
EXPNO                   1
PROCNO                  1

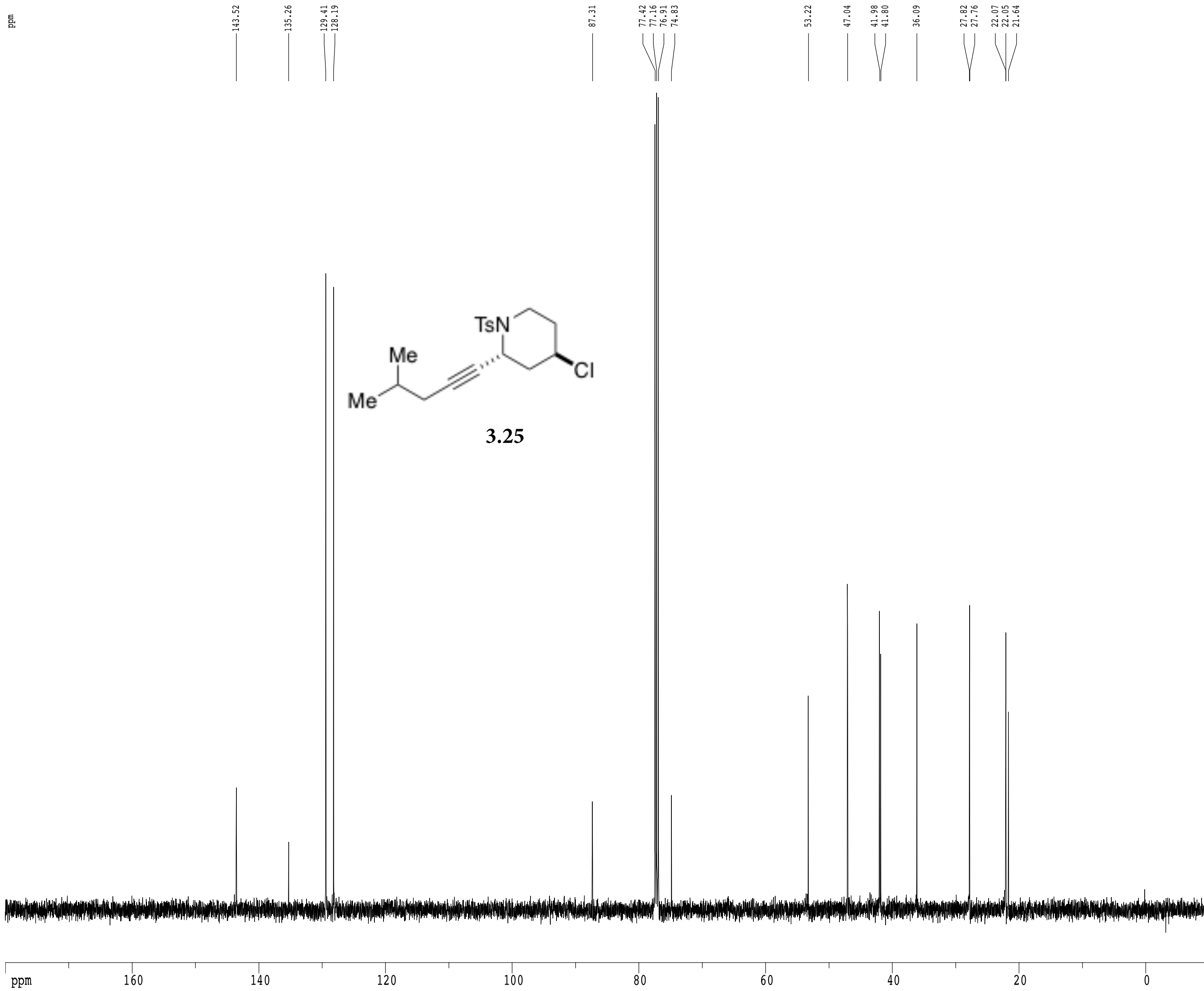
F2 - Acquisition Parameters
Date_            20200715
Time                11.46
INSTRUM             gn500
PROBHD   5 mm broadband
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3T
NS                      8
DS                      2
SWH              8012.820 Hz
FIDRES           0.098043 Hz
AQ               5.0998774 sec
RG                  912.3
DW                  62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.00 usec
PL1                 -6.00 dB
SFO1          498.7534913 MHz

F2 - Processing parameters
SI                  65536
SF            498.7500000 MHz
WDW                    no
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                  20.00 cm
CY                  12.50 cm
F1P                 9.000 ppm
F1                4488.75 Hz
F2P                -0.500 ppm
F2                -249.38 Hz
PPMCM             0.47500 ppm/cm
HZCM            236.90625 Hz/cm
```

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER tthane
NAME TATiv69carbon
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200715
Time 15.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3T
NS 408
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

======== CHANNEL f1 ========
NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz

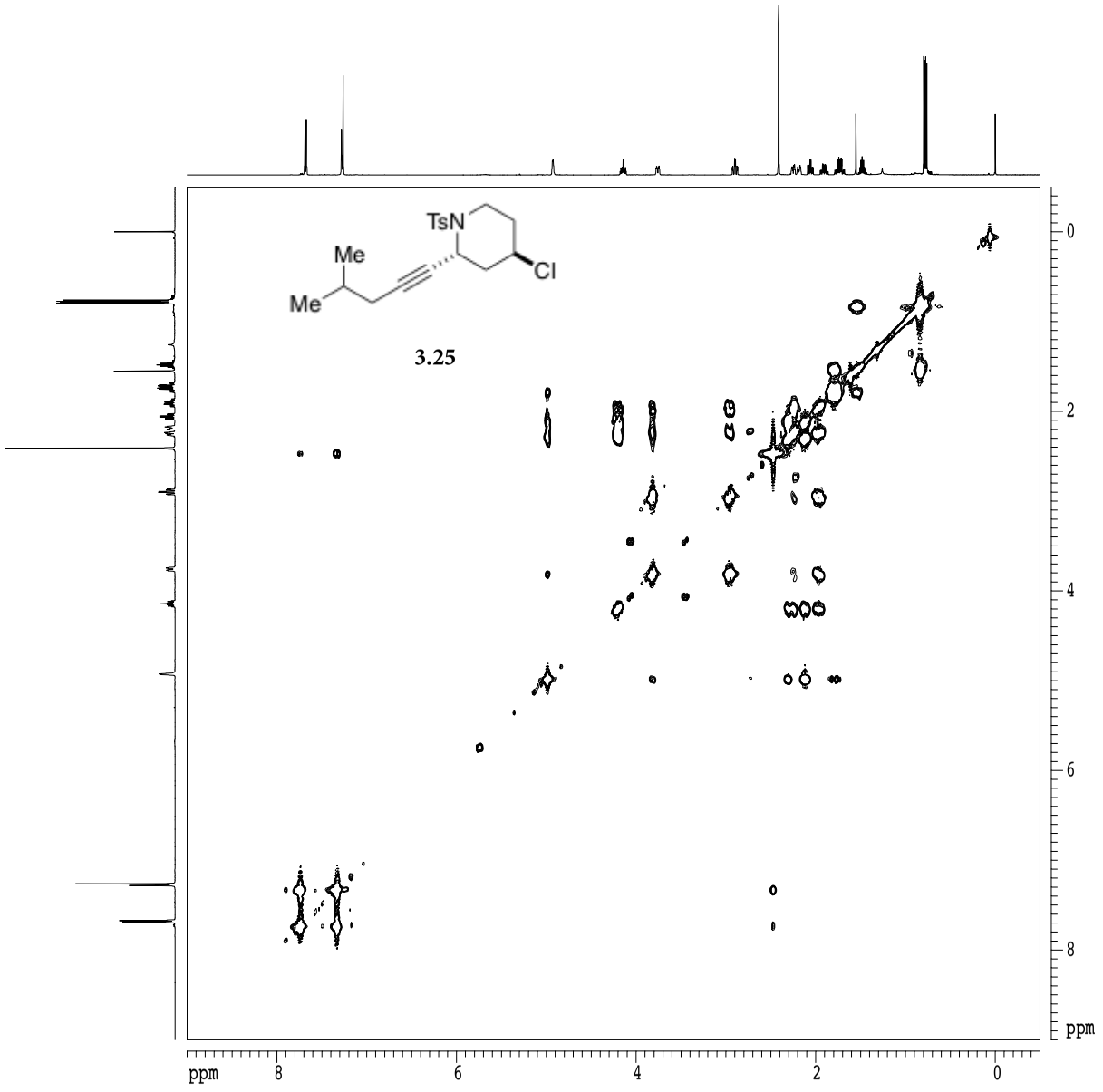
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804062 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 180.000 ppm
F1 22640.47 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 8.33333 ppm/cm
HZCM 1048.17004 Hz/cm

gcosy60




```
      Current Data Parameters
USER              tthane
NAME         TATiv69cosy
EXPNO                 2
PROCNO                1

      F2 - Acquisition Parameters
Date_          20200715
Time              15.57
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG    cosygp60.prd
TD                 2048
SOLVENT            CDCl3
NS                    2
DS                   16
SWH            8012.820 Hz
FIDRES         3.912510 Hz
AQ             0.1278452 sec
RG                456.1
DW               62.400 usec
DE                6.00 usec
TE                298.0 K
d0             0.00000300 sec
D1             1.00000000 sec
d13            0.00000300 sec
D16            0.00020000 sec
IN0            0.00012480 sec

     ======== CHANNEL f1 ========
NUC1                  1H
P1                 7.50 usec
PL1                1.60 dB
SFO1         500.2235015 MHz

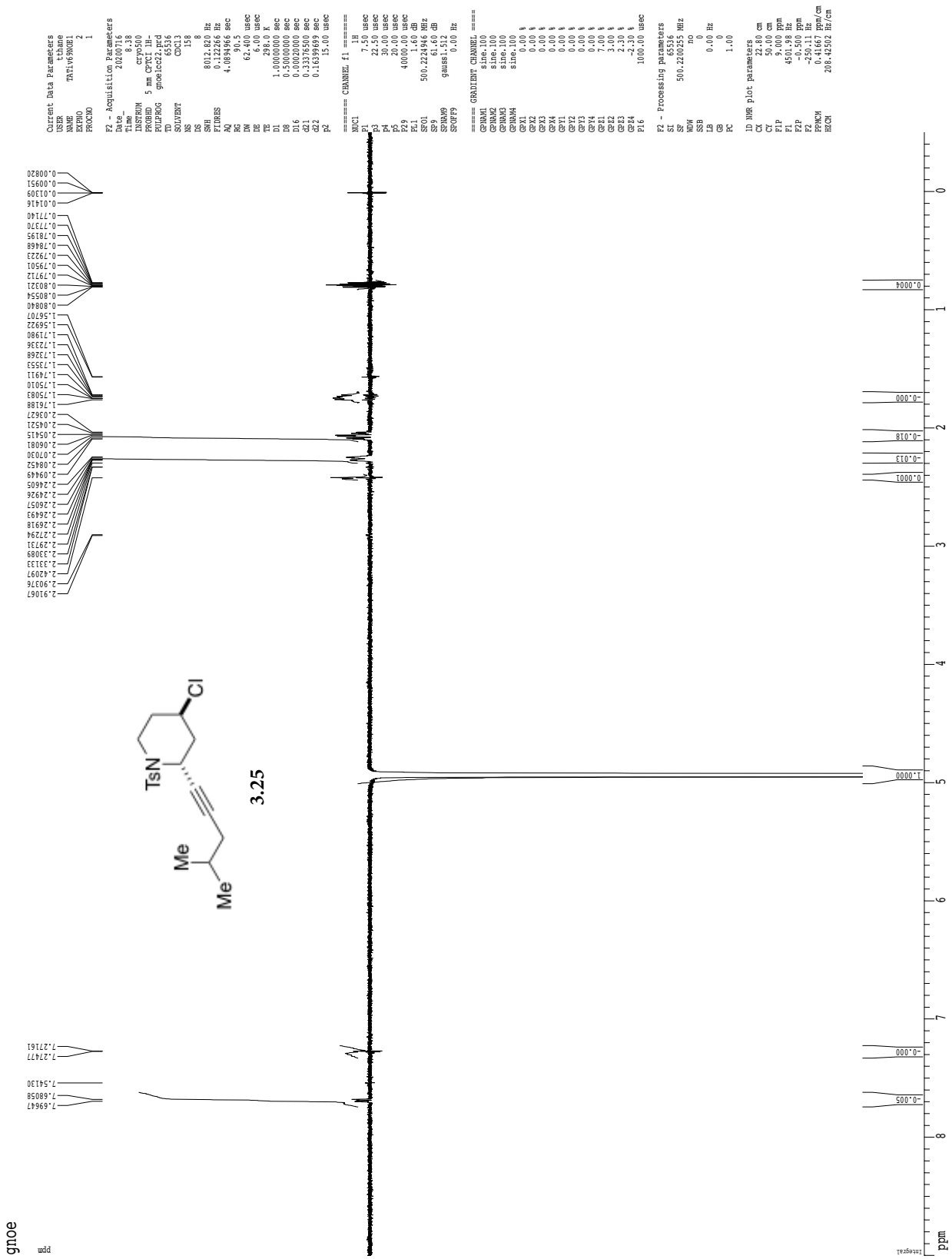
     ====== GRADIENT CHANNEL =====
GPNAM1           sine.100
GPNAM2           sine.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               17.00 %
GPZ2               17.00 %
P16              1000.00 usec

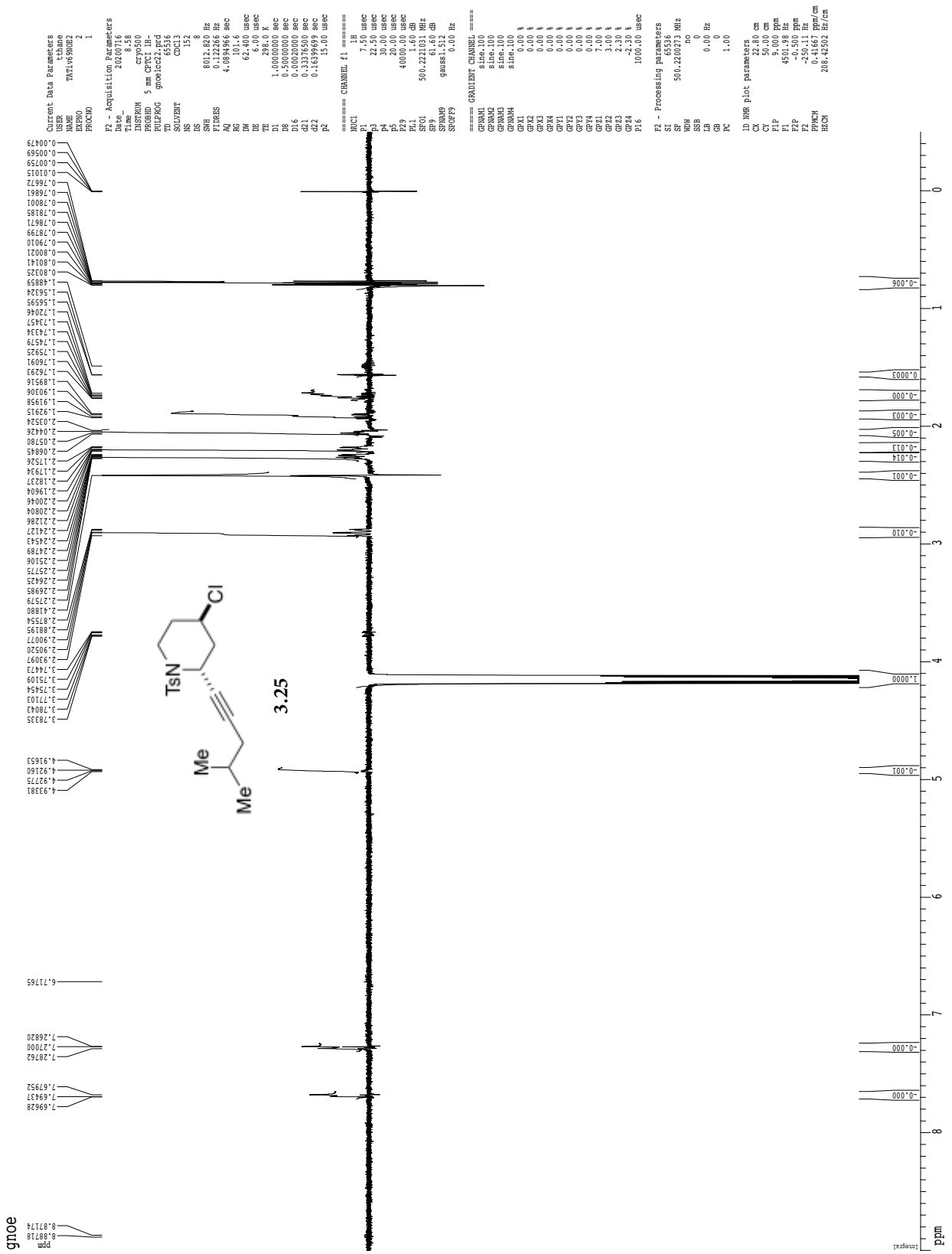
      F1 - Acquisition parameters
ND0                   1
TD                  274
SFO1           500.2235 MHz
FIDRES        29.243870 Hz
SW               16.018 ppm
FnMODE                QF

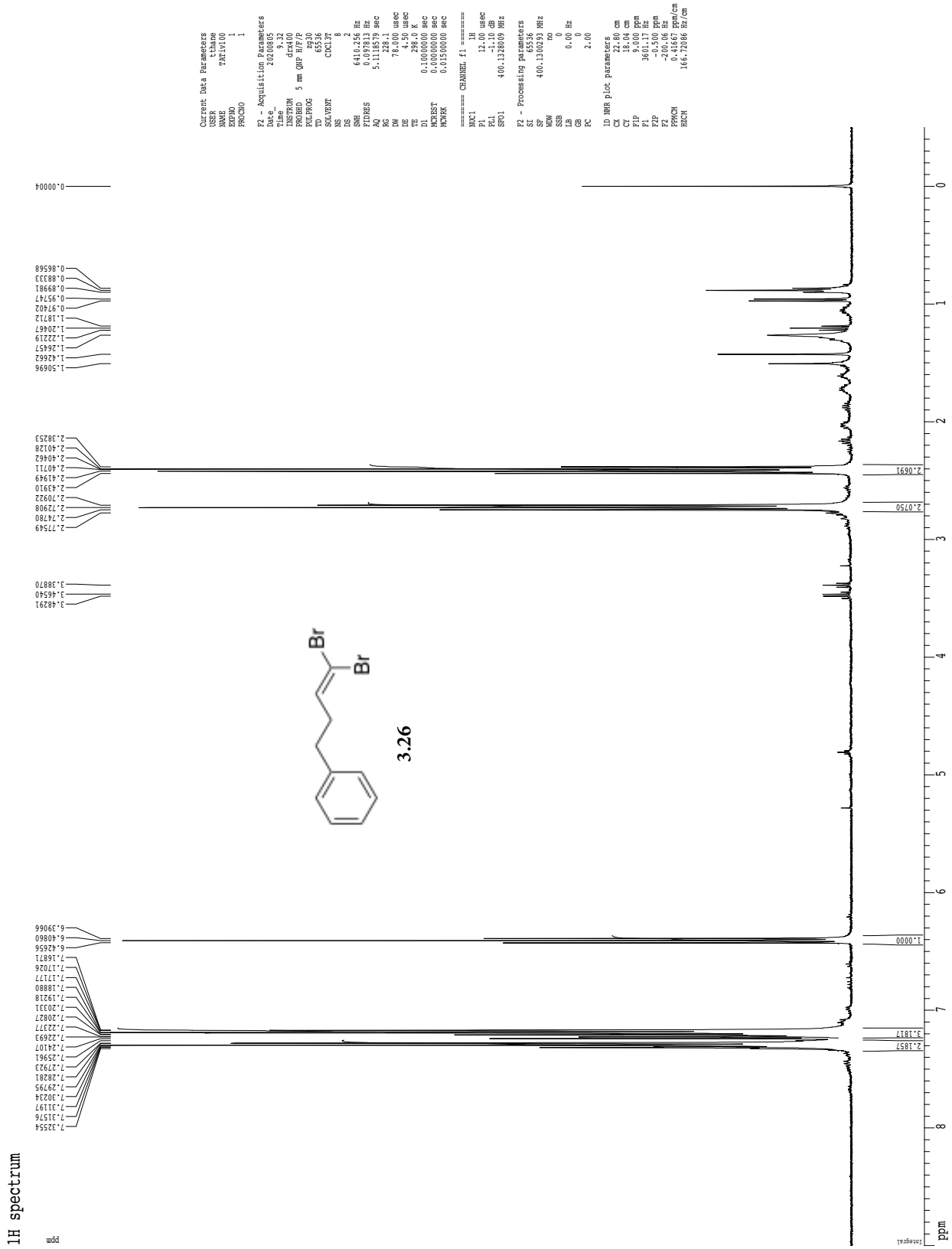
      F2 - Processing parameters
SI                 1024
SF          500.2200000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00

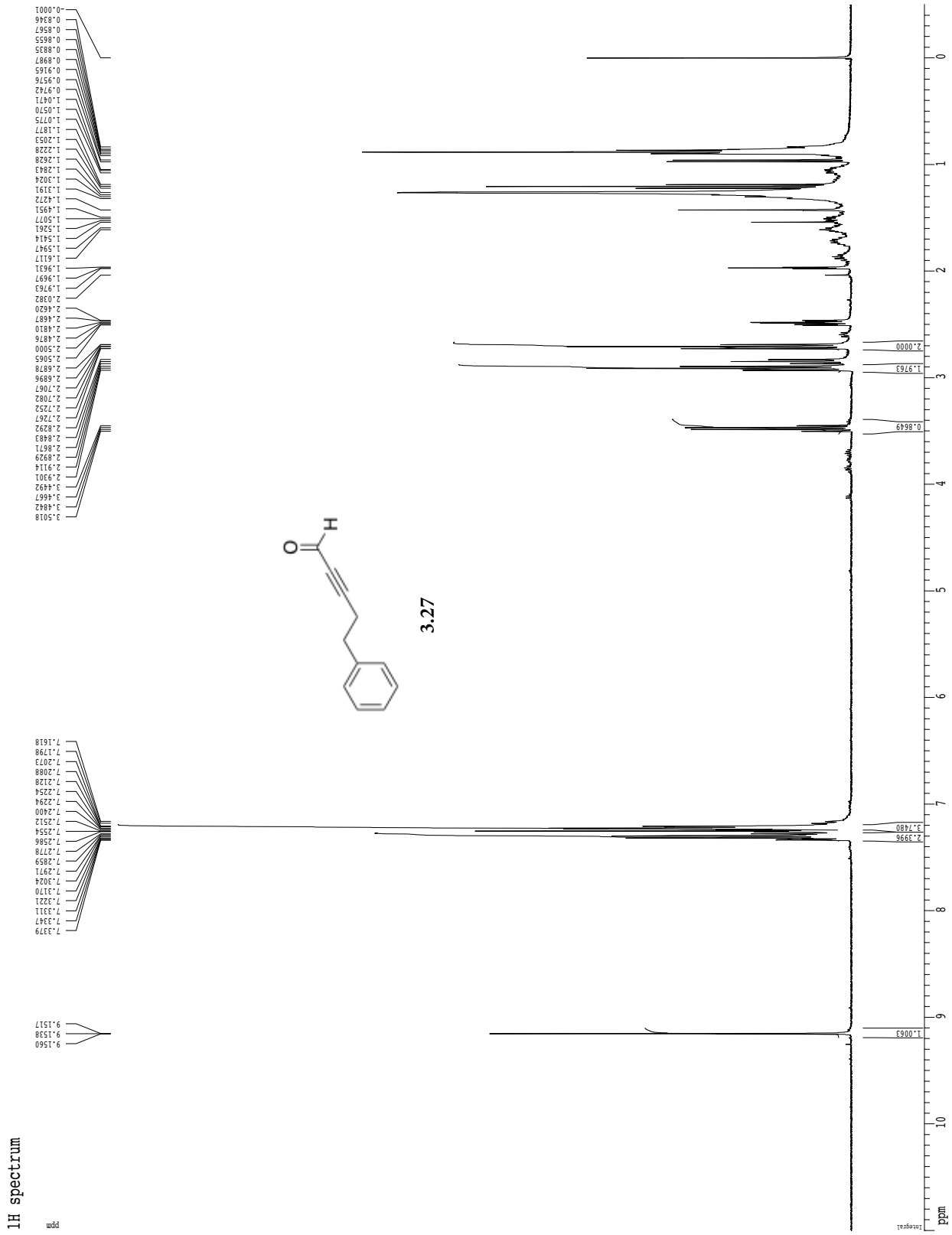
      F1 - Processing parameters
SI                 1024
MC2                  QF
SF          500.2200000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0

      2D NMR plot parameters
CX2               15.00 cm
CX1               15.00 cm
F2PLO              9.000 ppm
F2LO            4501.98 Hz
F2PHI             -0.500 ppm
F2HI            -250.11 Hz
F1PLO              9.000 ppm
F1LO            4501.98 Hz
F1PHI             -0.500 ppm
F1HI            -250.11 Hz
F2PPMCM         0.63333 ppm/cm
F2HZCM        316.80600 Hz/cm
F1PPMCM         0.63333 ppm/cm
F1HZCM        316.80600 Hz/cm
```

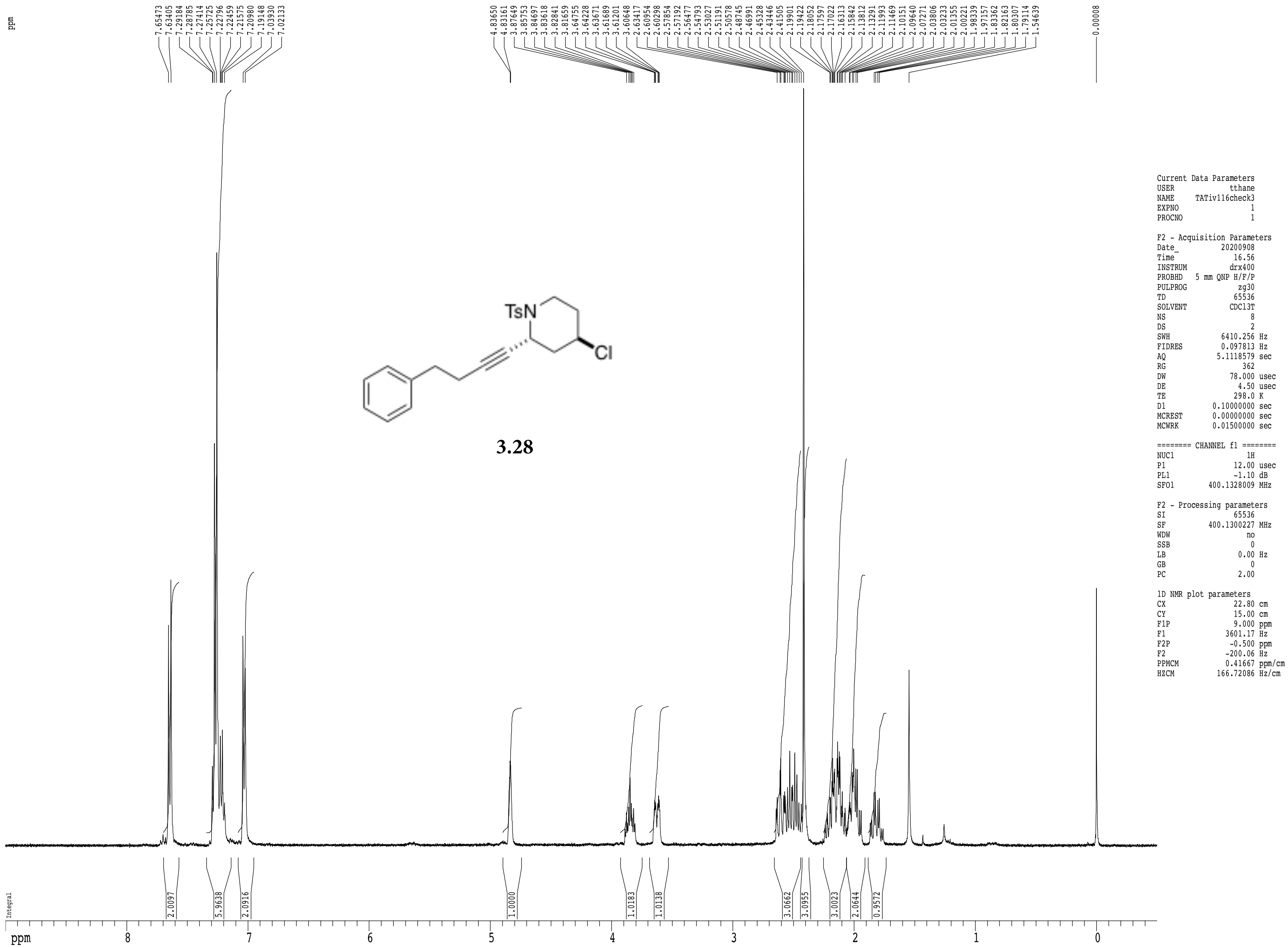

gnoe
3.25
TsN
Cl
Me
Me
ppm


gnoe
ppm
TsN
Cl
Me
Me
3.25


Br
Br
3.26
1H spectrum
ppm

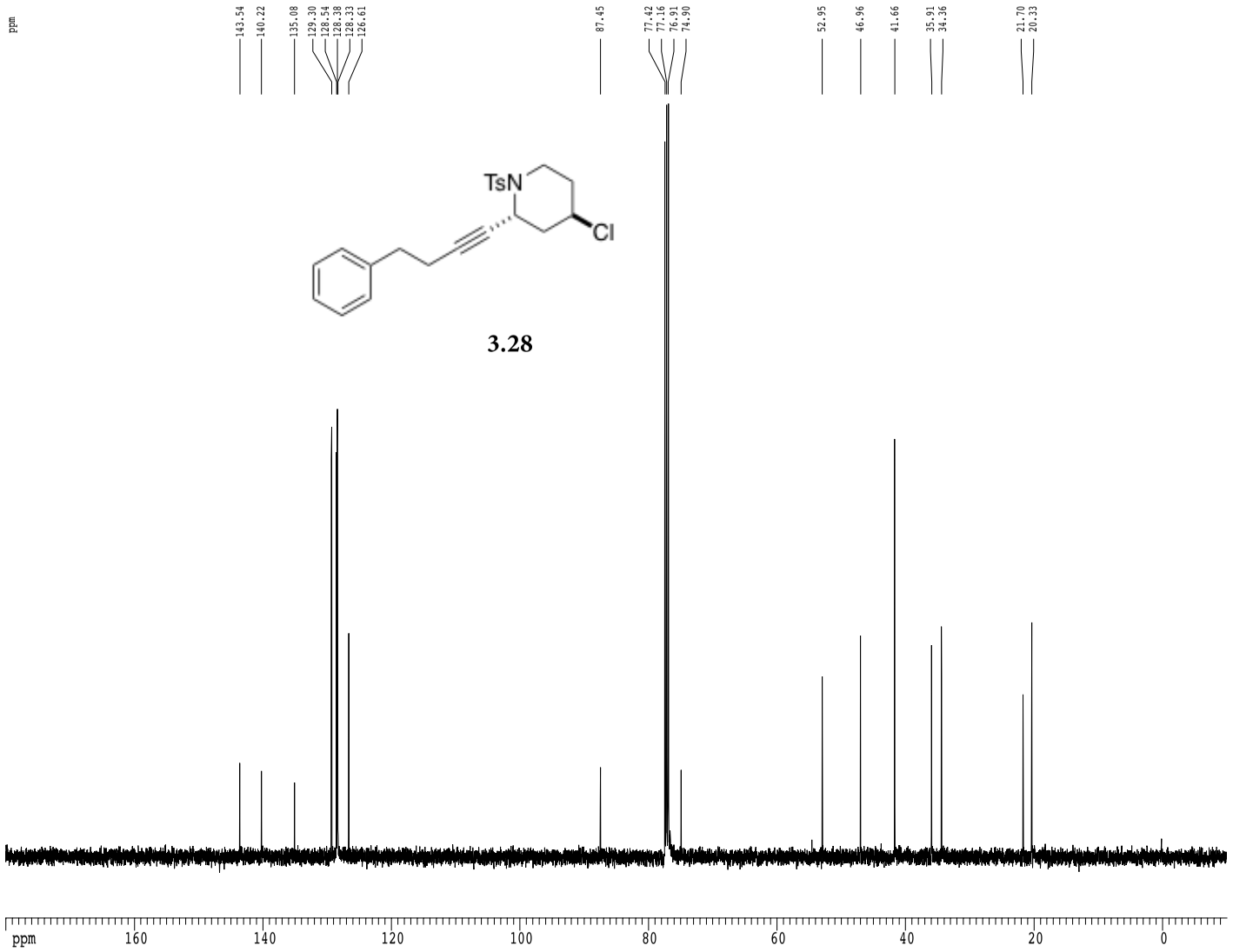

1H spectrum
ppm
Integral
3.27

1H spectrum



3.28

13C spectrum with 1H decoupling




```
Current Data Parameters
USER              tthane
NAME      TATiv116carbon
EXPNO                  1
PROCNO                 1

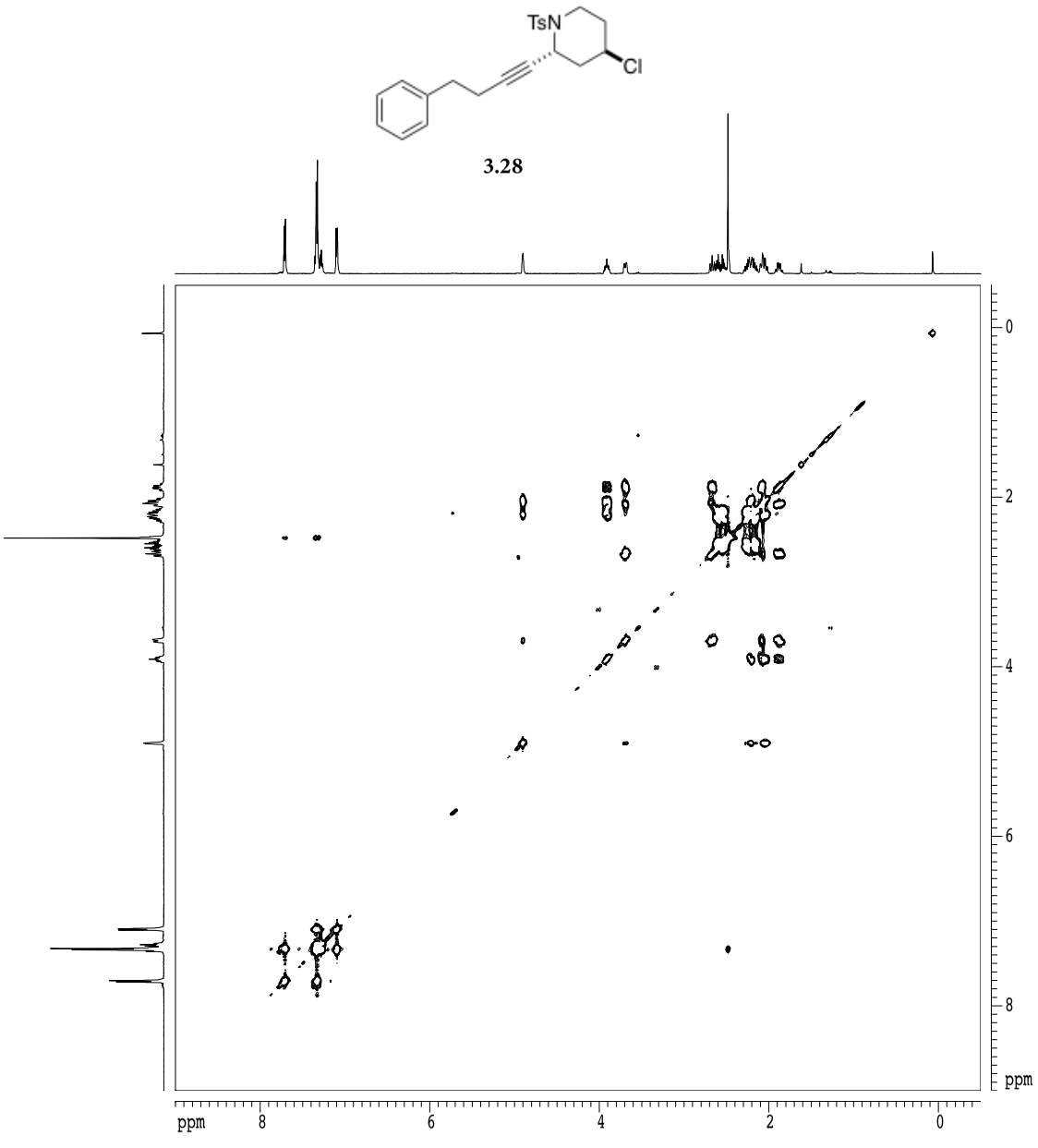
F2 - Acquisition Parameters
Date_           20200825
Time               10.06
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3T
NS                   568
DS                     4
SWH            30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                  8192
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                14.20 usec
PL1               -6.00 dB
SFO1        125.4245824 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                1H
PCPD2             80.00 usec
PL2               -6.00 dB
PL12              12.30 dB
SFO2        498.7524937 MHz

F2 - Processing parameters
SI                 65536
SF          125.4107757 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 20.00 cm
CY                 12.50 cm
F1P               180.000 ppm
F1              22573.94 Hz
F2P               -10.000 ppm
F2              -1254.11 Hz
PPMCM            9.50000 ppm/cm
HZCM          1191.40234 Hz/cm
```



Current Data Parameters

USER	tthane
NAME	TATiv116COSY
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20201012
Time	17.47
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	cosygp60.prd
TD	2048
SOLVENT	CDCl3
NS	2
DS	16
SWH	8012.820 Hz
FIDRES	3.912510 Hz
AQ	0.1278452 sec
RG	574.7
DW	62.400 usec
DE	6.00 usec
TE	298.0 K
d0	0.00000300 sec
D1	1.00000000 sec
d13	0.00000300 sec
D16	0.00020000 sec
IN0	0.00012480 sec

======= CHANNEL f1 =======

NUC1	1H
P1	7.50 usec
PL1	1.60 dB
SFO1	500.2235015 MHz

====== GRADIENT CHANNEL =====

GPNAM1	sine.100
GPNAM2	sine.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	17.00 %
GPZ2	17.00 %
P16	1000.00 usec

F1 - Acquisition parameters

ND0	1
TD	512
SFO1	500.2235 MHz
FIDRES	15.650040 Hz
SW	16.018 ppm
FnMODE	QF

F2 - Processing parameters

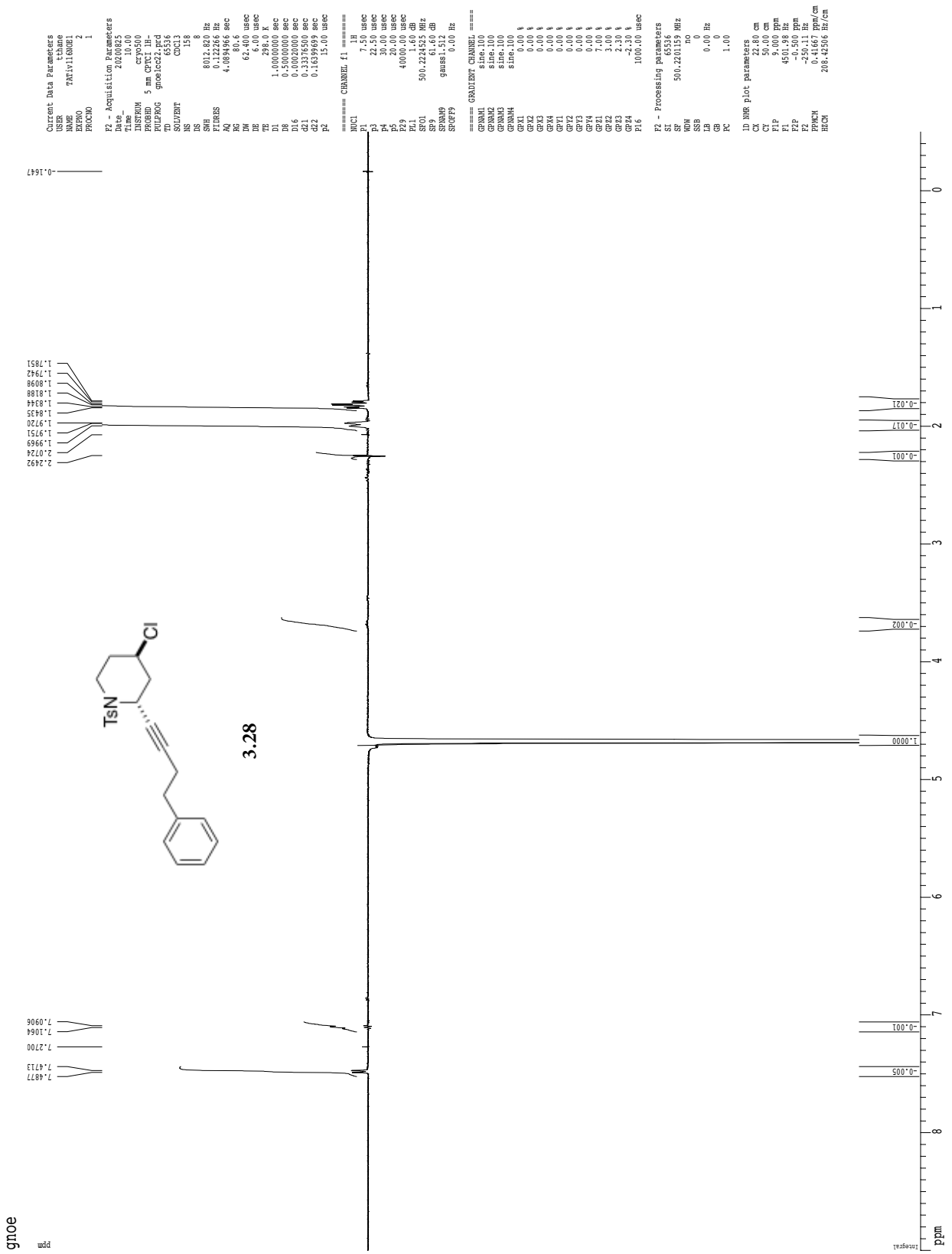
SI	1024
SF	500.2200000 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

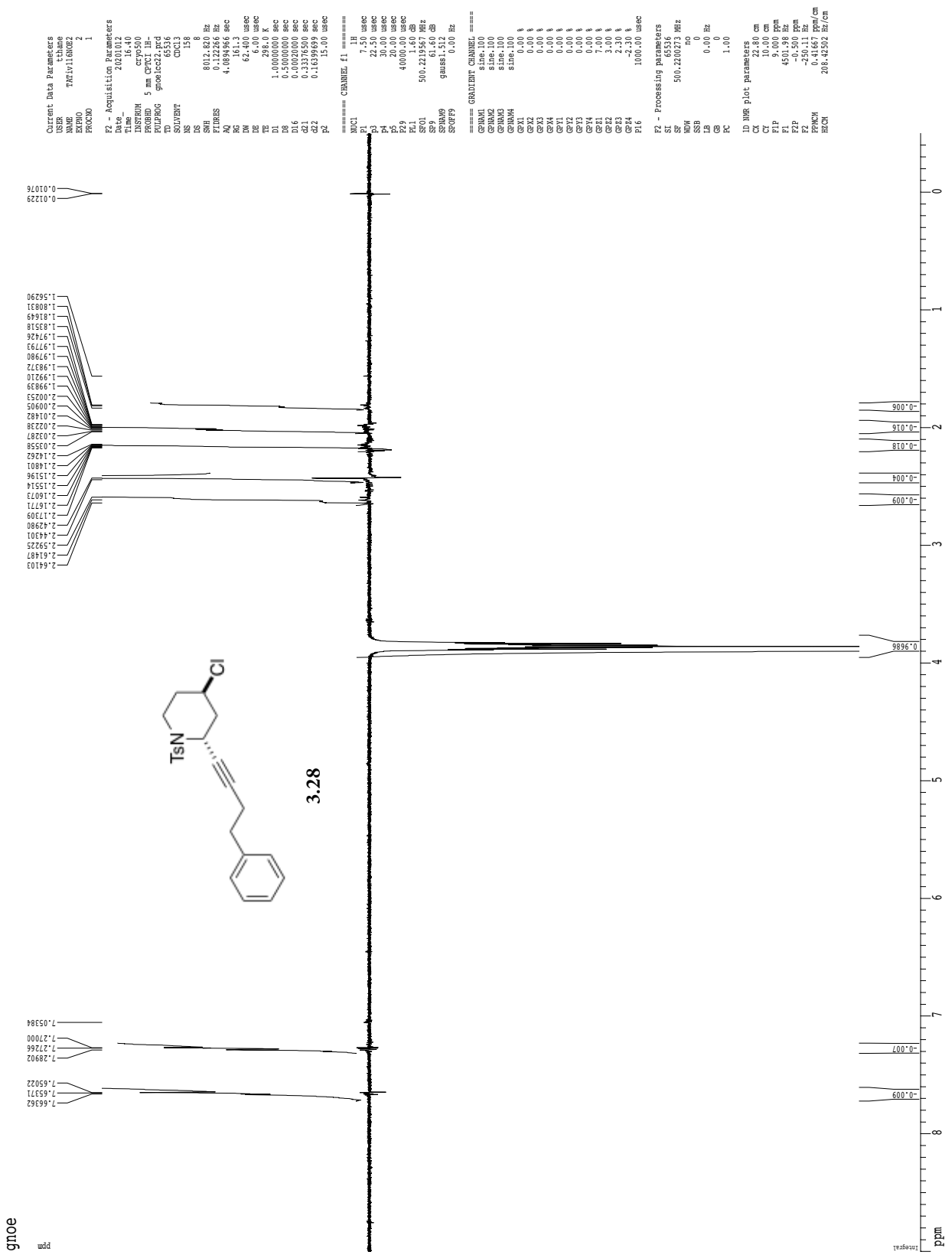
F1 - Processing parameters

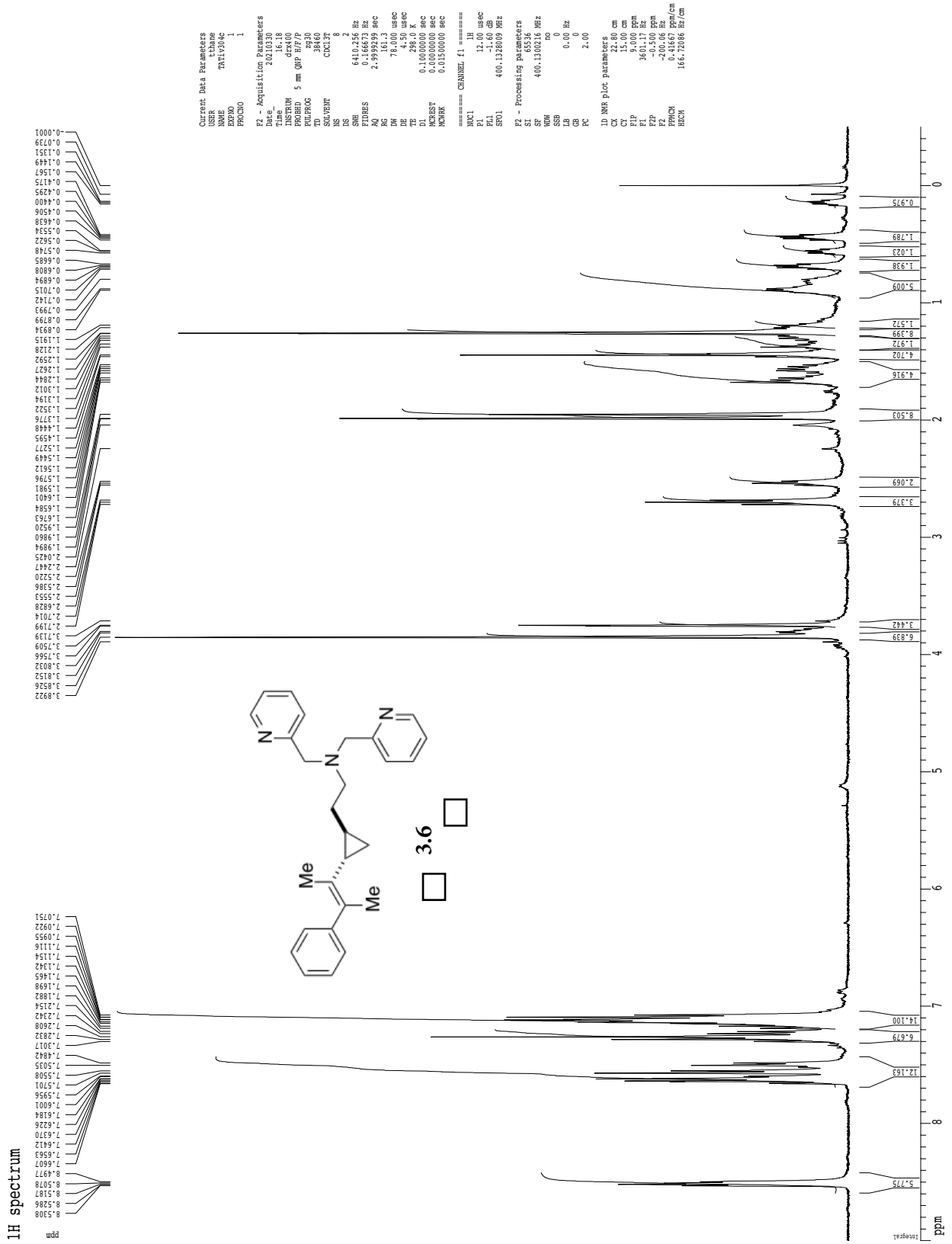
SI	1024
MC2	QF
SF	500.2200000 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

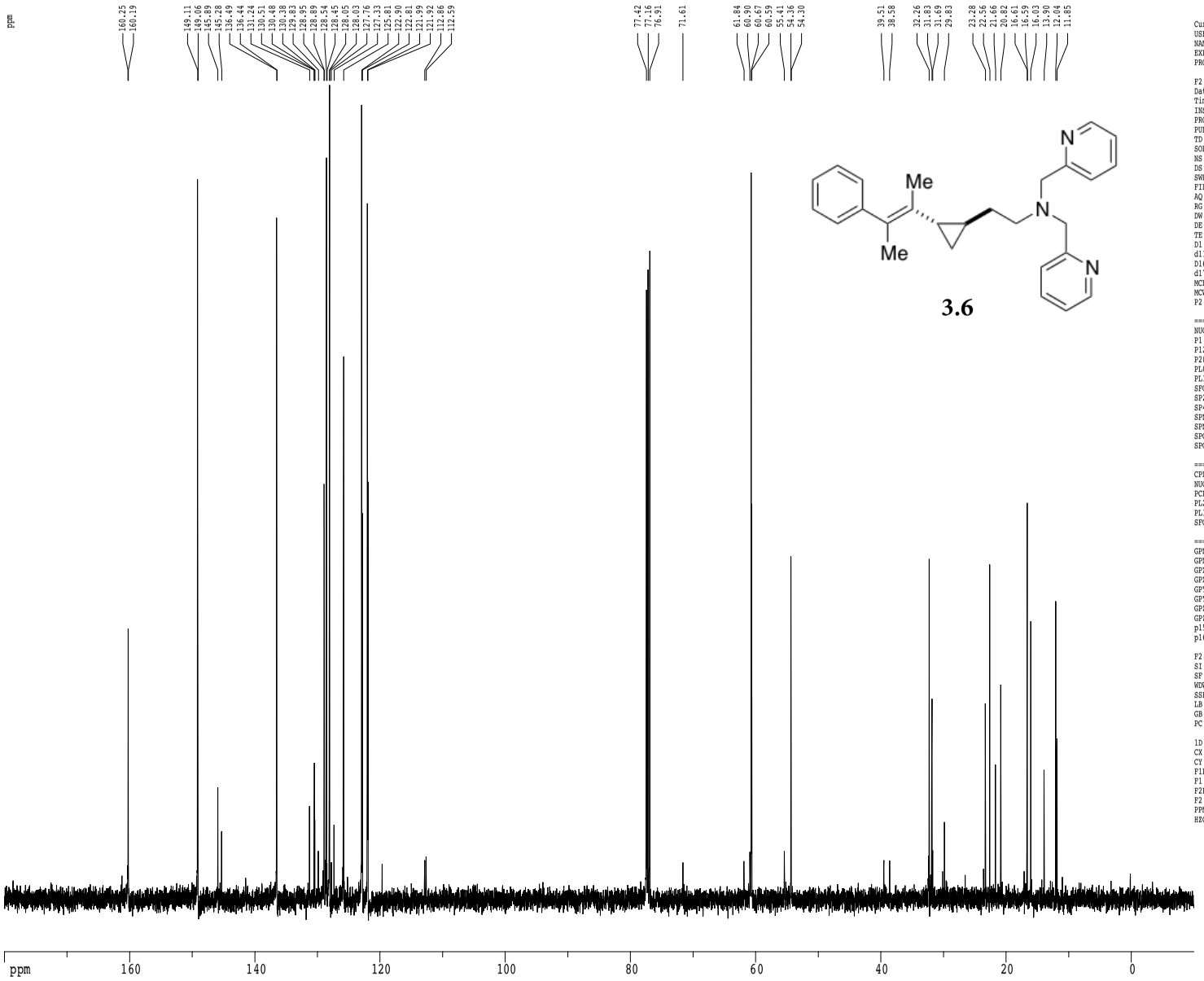
CX2	15.00 cm
CX1	15.00 cm
F2PLO	9.000 ppm
F2LO	4501.98 Hz
F2PHI	-0.500 ppm
F2HI	-250.11 Hz
F1PLO	9.000 ppm
F1LO	4501.98 Hz
F1PHI	-0.500 ppm
F1HI	-250.11 Hz
F2PPMCM	0.63333 ppm/cm
F2HZCM	316.80600 Hz/cm
F1PPMCM	0.63333 ppm/cm
F1HZCM	316.80600 Hz/cm


gnoe
ppm
Integral
3.28
TsN
Cl


gnoe
ppm
3.28
TsN
Cl


1H spectrum
Current Data Parameters
USER ttshane
NAME TA11v304c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210330
Time 16.18
INSTRUM drx400
PROBHD 5 mm QNP H/P/P
PULPROG zg30
TD 34496
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.166673 Hz
AQ 2.9999299 sec
RG 161.3
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.60 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300216 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
Me
Me
3.6
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER            khewitt1
NAME        TATiv304carbon
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20210330
Time                17.24
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                  65536
SOLVENT             CDCl3
NS                    272
DS                     16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                7298.2
DW                 16.500 usec
DE                  6.00 usec
TE                298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                 37.70 usec

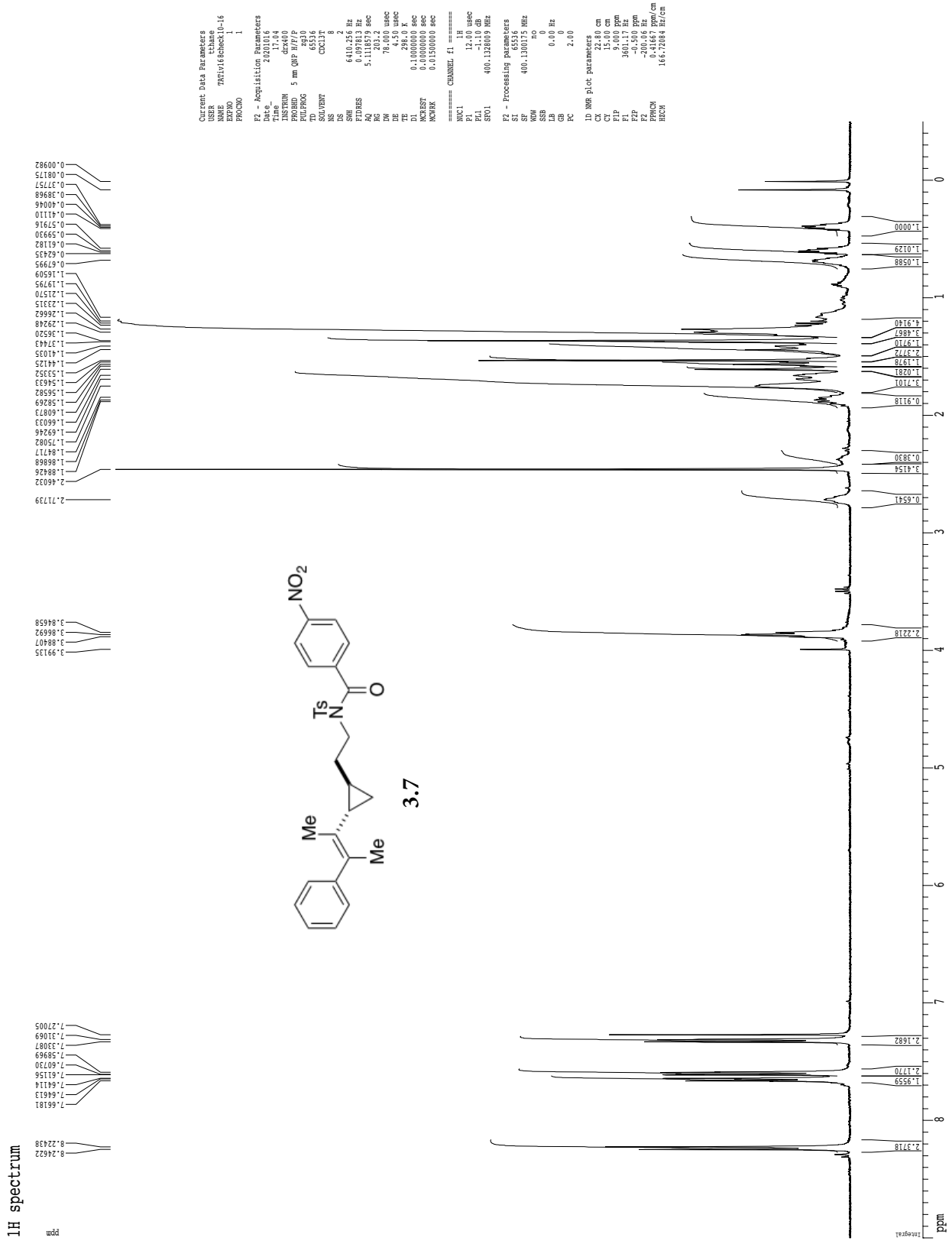
======== CHANNEL f1 ========
NUC1                13C
P1                 18.85 usec
P12              2000.00 usec
P20               500.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP2                 1.55 dB
SP4                 1.55 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2              0.00 Hz
SPOFF4              0.00 Hz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                 1H
PCPD2              100.00 usec
PL2                 1.60 dB
PL12               22.00 dB
SFO2         500.2225011 MHz

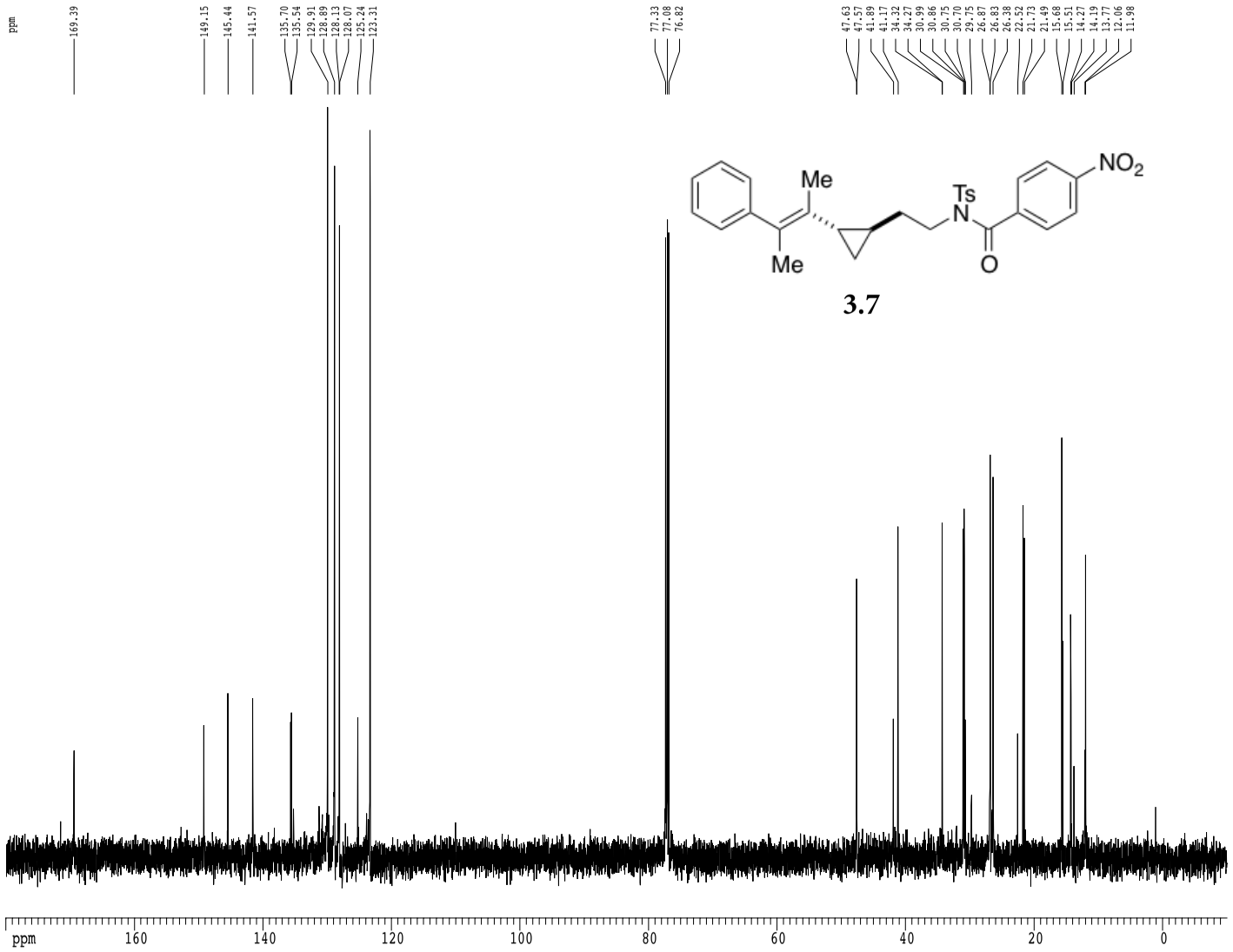
====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                  65536
SF           125.7804094 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               180.000 ppm
F1              22640.47 Hz
F2P               -10.000 ppm
F2              -1257.80 Hz
PPMCM             8.33333 ppm/cm
HZCM           1048.17017 Hz/cm
```


1H spectrum
Current Data Parameters
NAME tkhan
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201016
Time 21.04
INSTRUM spect
PROBHD 5 mm QNP H/P/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 203.2
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
WCBEST 0.00000000 sec
WCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.00 dB
SFO1 400.1320809 MHz
F2 - Processing parameters
SI 65536
SF 400.1300175 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.60 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72084 Hz/cm
NO2
Ts
N
O
Me
Me
3.7
ppm
Integral

13C spectrum with 1H decoupling



3.7

Current Data Parameters
USER tthane
NAME TATiv168carbon1
EXPNO 1
PROCNO 1

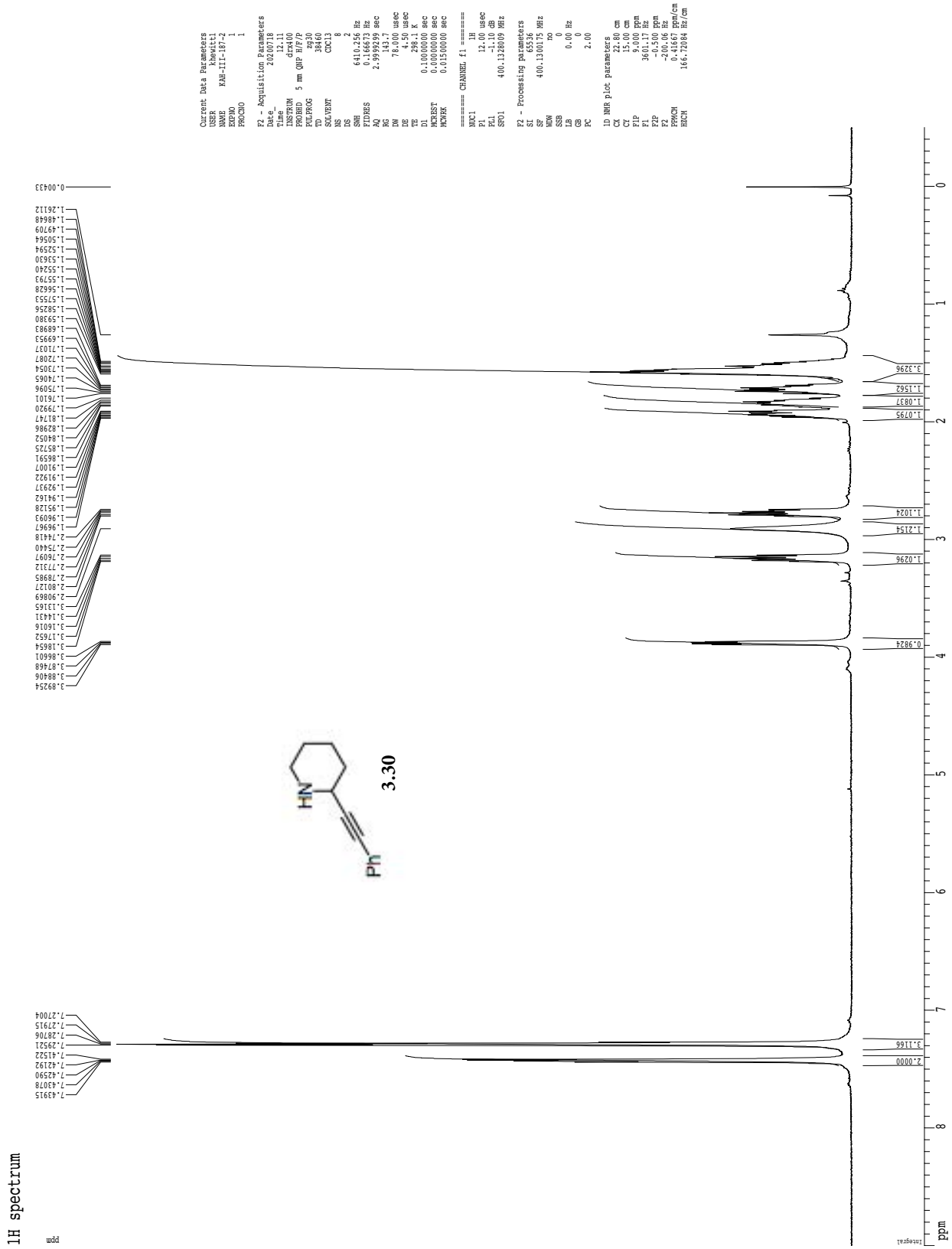
F2 - Acquisition Parameters
Date_ 20210416
Time 17.55
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3T
NS 344
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 5792.6
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

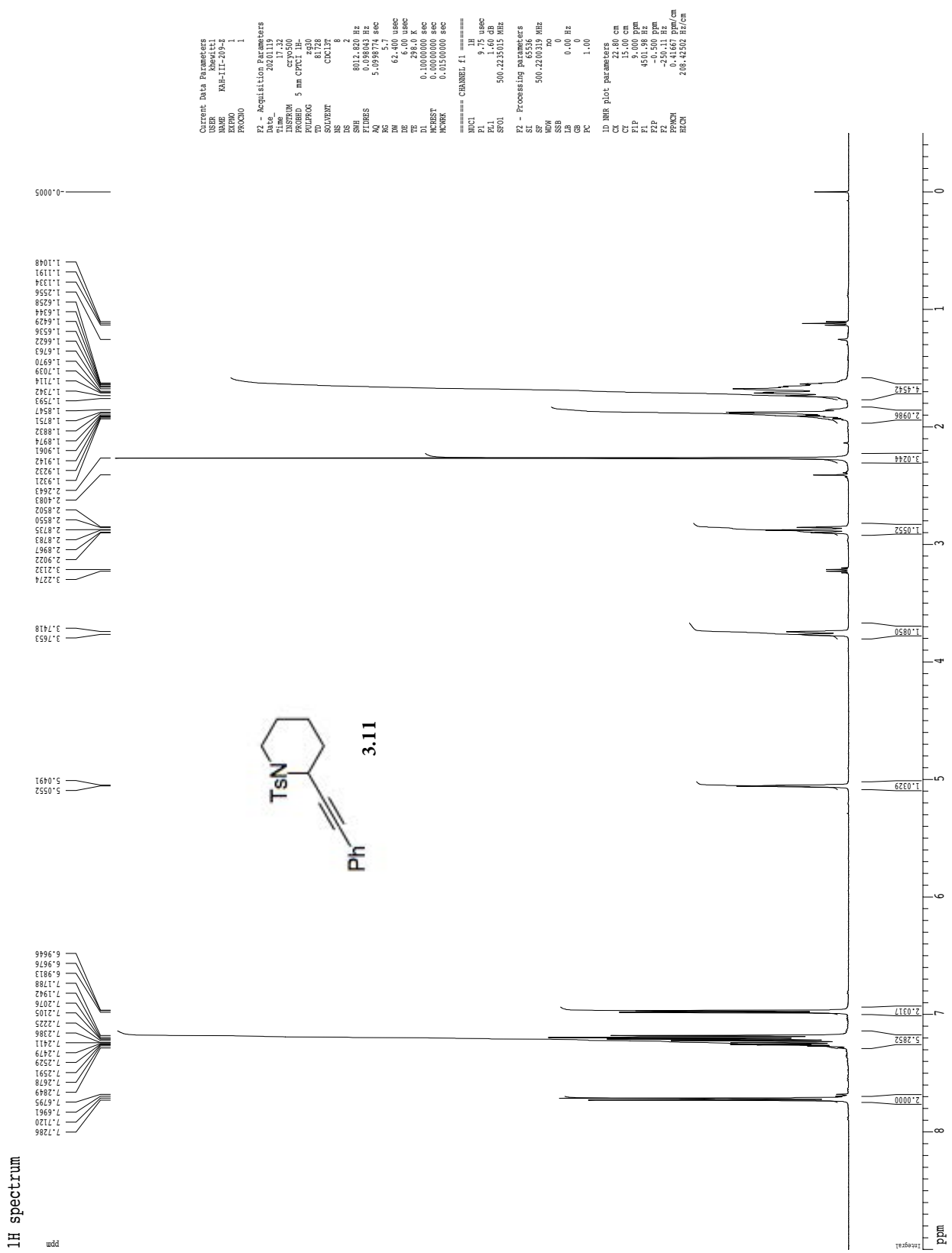
======== CHANNEL f1 ========
NUC1 13C
P1 14.20 usec
PL1 -6.00 dB
SFO1 125.4245824 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 12.30 dB
SFO2 498.7524937 MHz

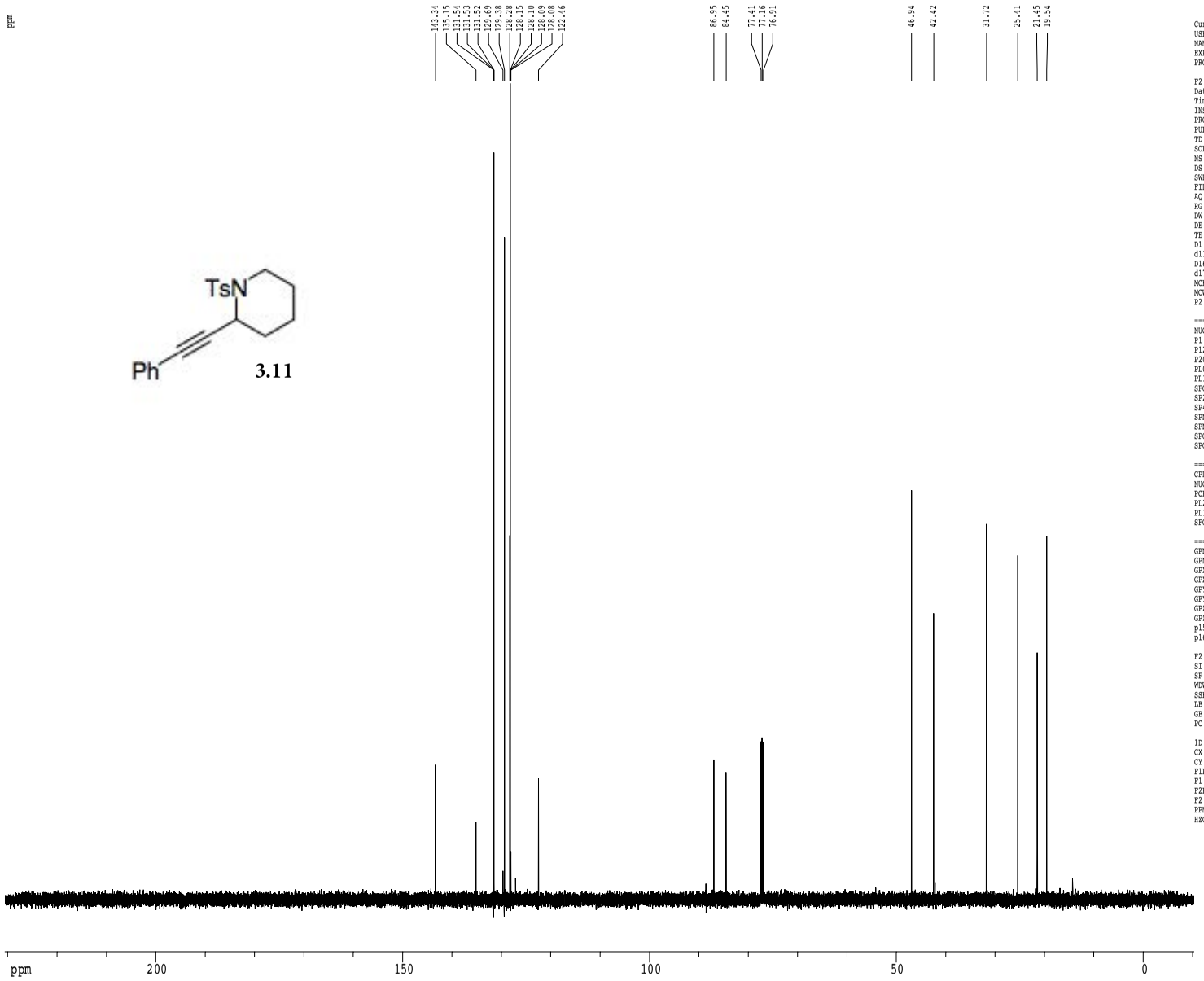
F2 - Processing parameters
SI 65536
SF 125.4107870 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 20.00 cm
CY 12.50 cm
F1P 180.000 ppm
F1 22573.94 Hz
F2P -10.000 ppm
F2 -1254.11 Hz
PPMCM 9.50000 ppm/cm
HZCM 1191.40247 Hz/cm


1H spectrum
3.30
HN
Ph
ppm
Integral


1H spectrum
Current Data Parameters
USER khewitt1
NAME KAH-III-209-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201119
Time 17.32
INSTRUM czyo500
PROBHD 5 mm CPDCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 294.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 9.75 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200319 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
TsN
Ph
3.11
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              khewitt1
NAME        KAH-III-209-Z
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20201119
Time              17.33
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                65536
SOLVENT             CDCl3
NS                   48
DS                   16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG               18390.4
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                37.70 usec

======== CHANNEL f1 ========
NUC1                13C
P1                18.85 usec
P12             2000.00 usec
P20              500.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1         125.7942548 MHz
SP2                1.55 dB
SP4                1.55 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2             0.00 Hz
SPOFF4             0.00 Hz

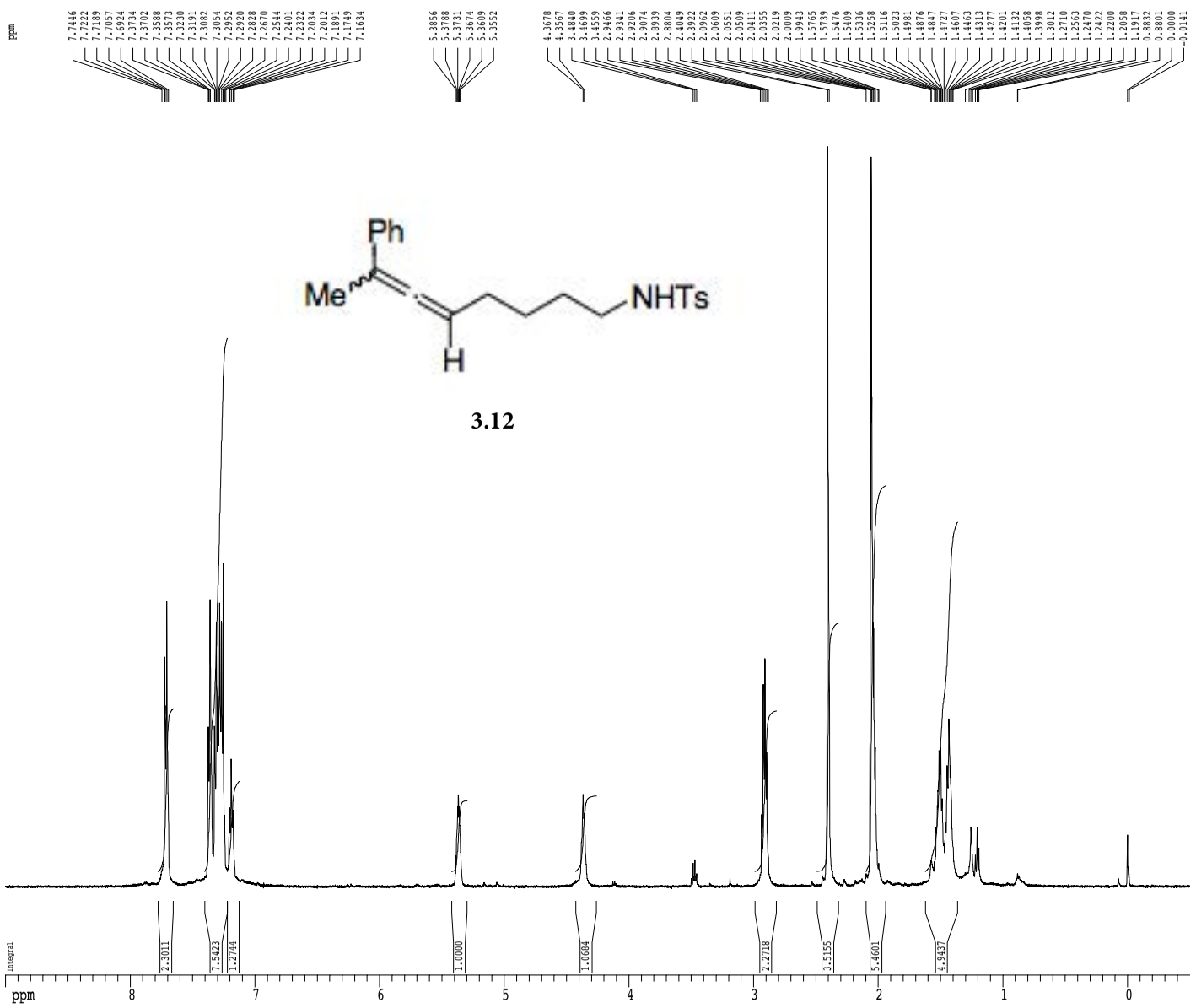
======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              22.00 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1               0.00 %
GPX2               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804122 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                15.65 cm
F1P              230.637 ppm
F1             29009.68 Hz
F2P              -10.287 ppm
F2             -1293.96 Hz
PPMCM          10.56688 ppm/cm
HZCM         1329.10693 Hz/cm
```

1H spectrum



3.12

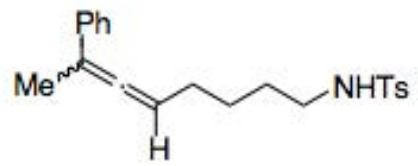
```
Current Data Parameters
USER            khewitt1
NAME          TATiv187f2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          20201116
Time               10.32
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG             zg30
TD                 81728
SOLVENT           CDCl3T
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES             0.098043 Hz
AQ              5.0998774 sec
RG                 812.7
DW                 62.400 usec
DE                  6.00 usec
TE                298.0 K
D1             0.10000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.00 usec
PL1                -6.00 dB
SFO1         498.7534913 MHz

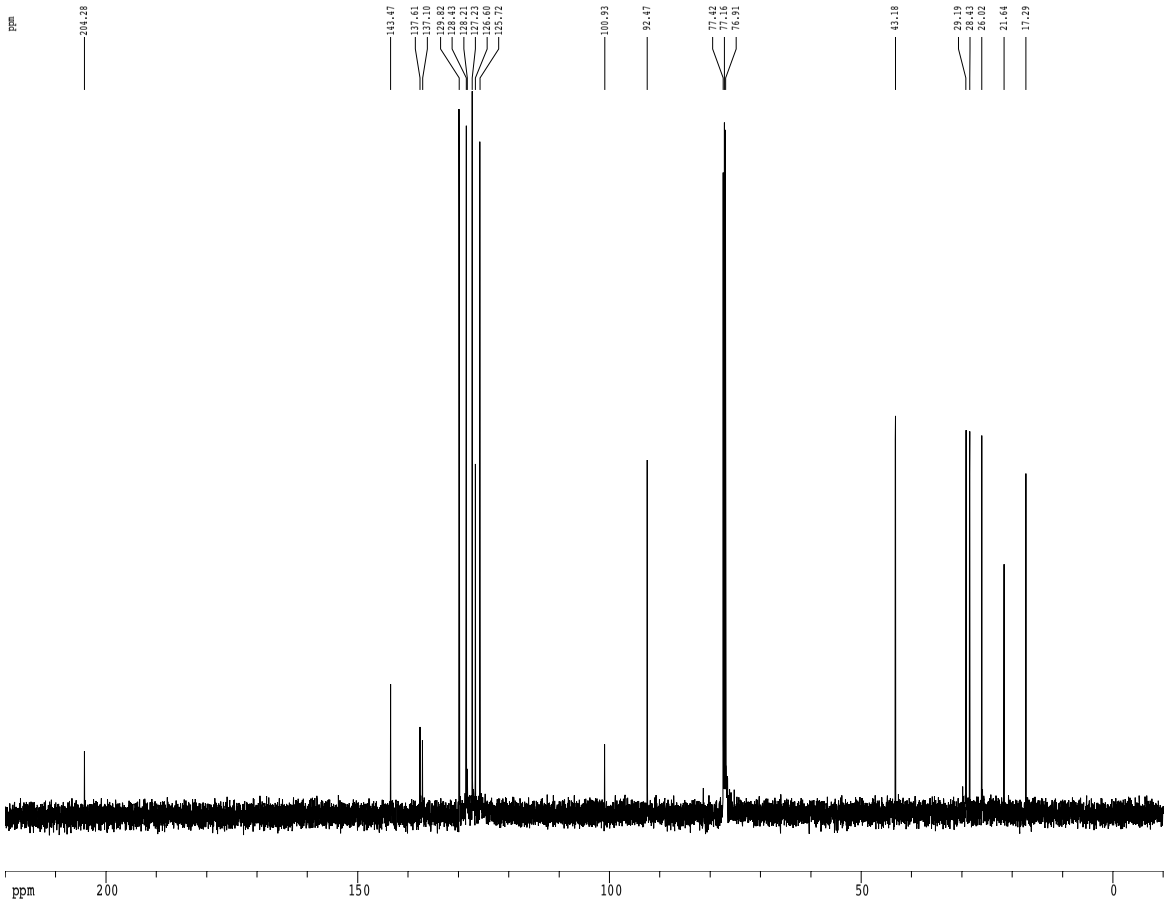
F2 - Processing parameters
SI                 65536
SF           498.7500352 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 20.00 cm
CY                 12.50 cm
F1P                9.000 ppm
F1               4488.75 Hz
F2P                -0.500 ppm
F2               -249.38 Hz
PPMCM            0.47500 ppm/cm
HZCM           236.90627 Hz/cm
```



13C spectrum with 1H decoupling

3.12




```
Current Data Parameters
USER            khewitt1
NAME          TATiv187f2
EXPNO                  3
PROCNO                 1

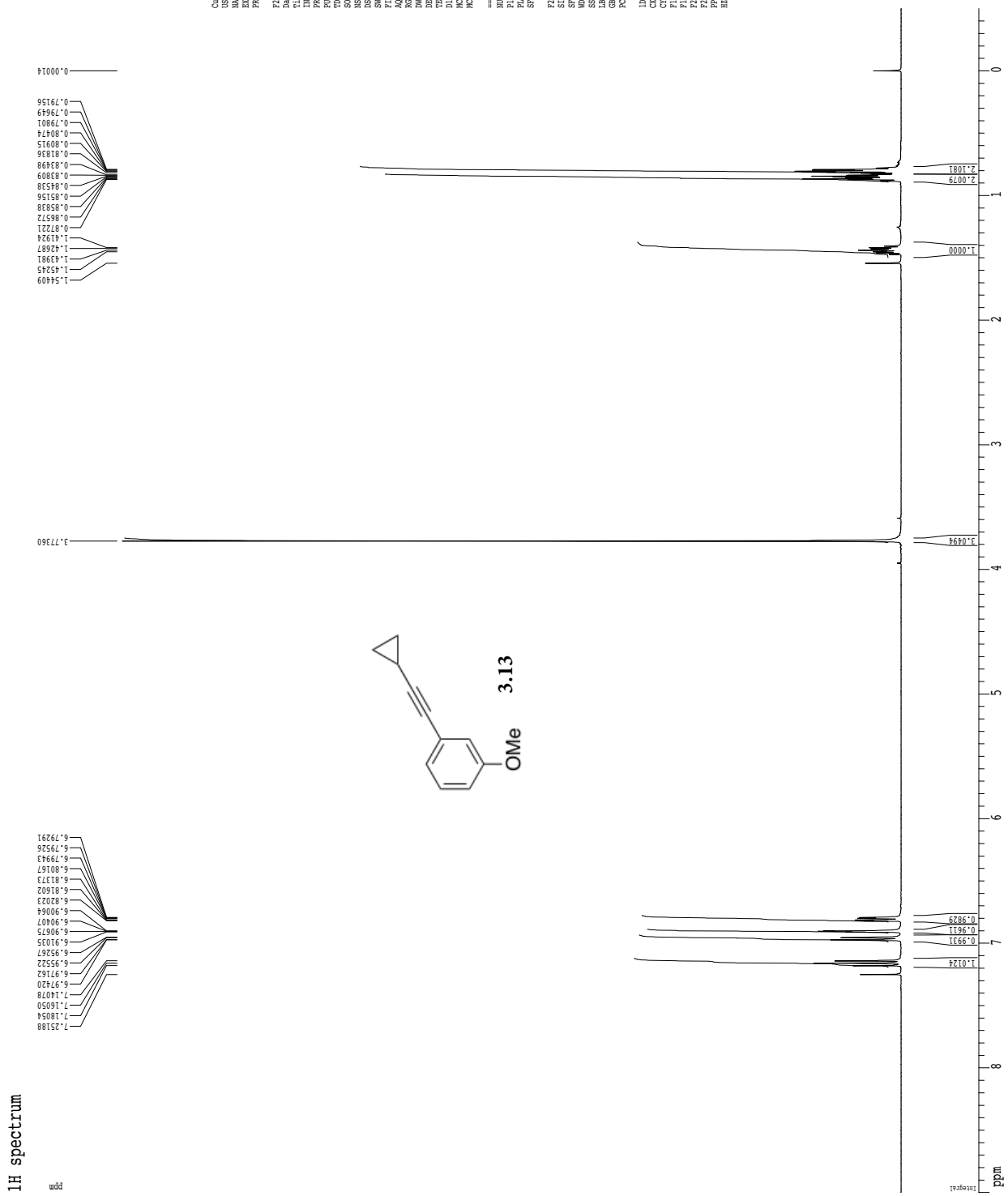
F2 - Acquisition Parameters
Date_           20201116
Time               10.34
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG           zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   616
DS                     4
SWH            30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                  4096
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

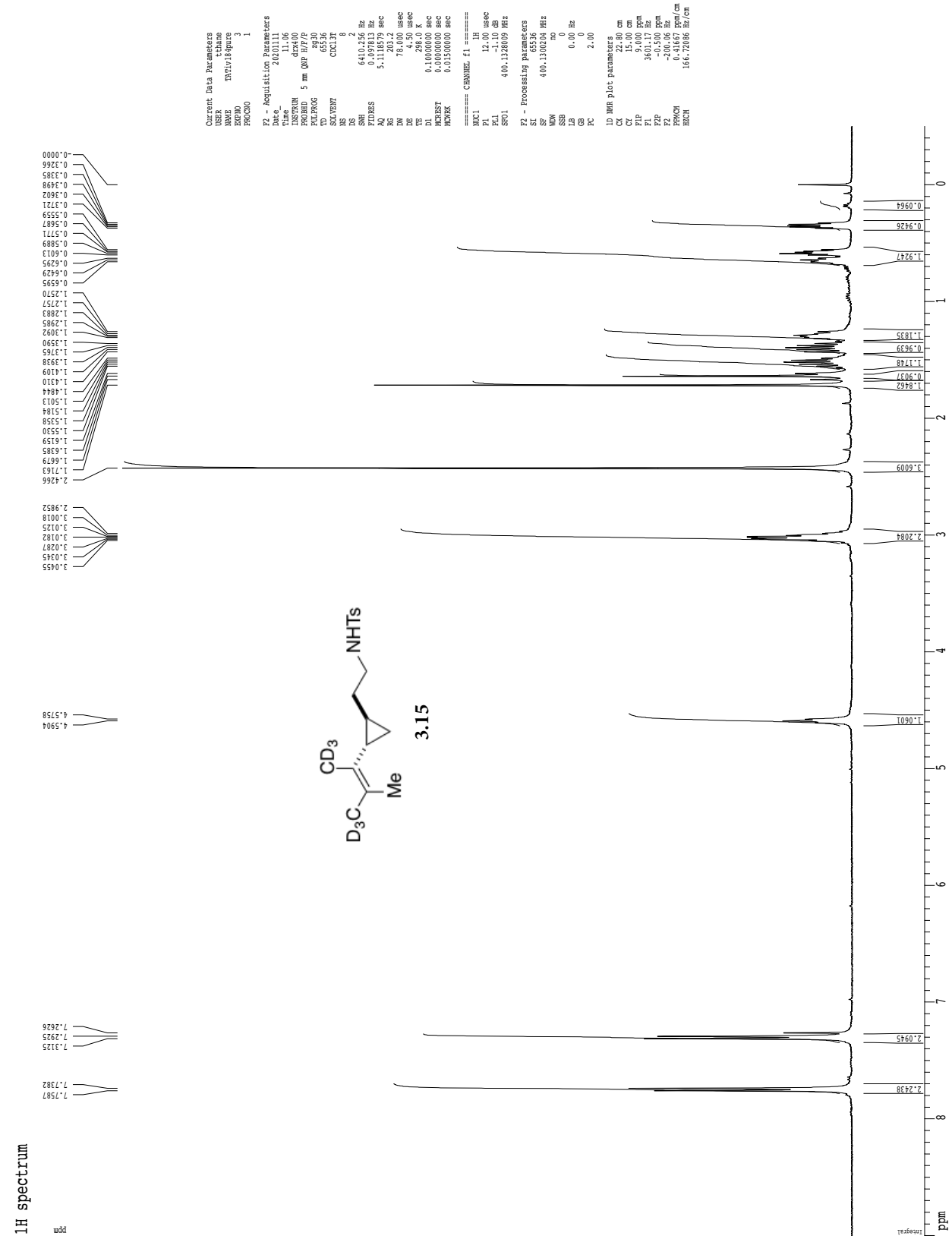
======== CHANNEL f1 ========
NUC1                13C
P1                14.20 usec
PL1               -6.00 dB
SFO1         125.4245824 MHz

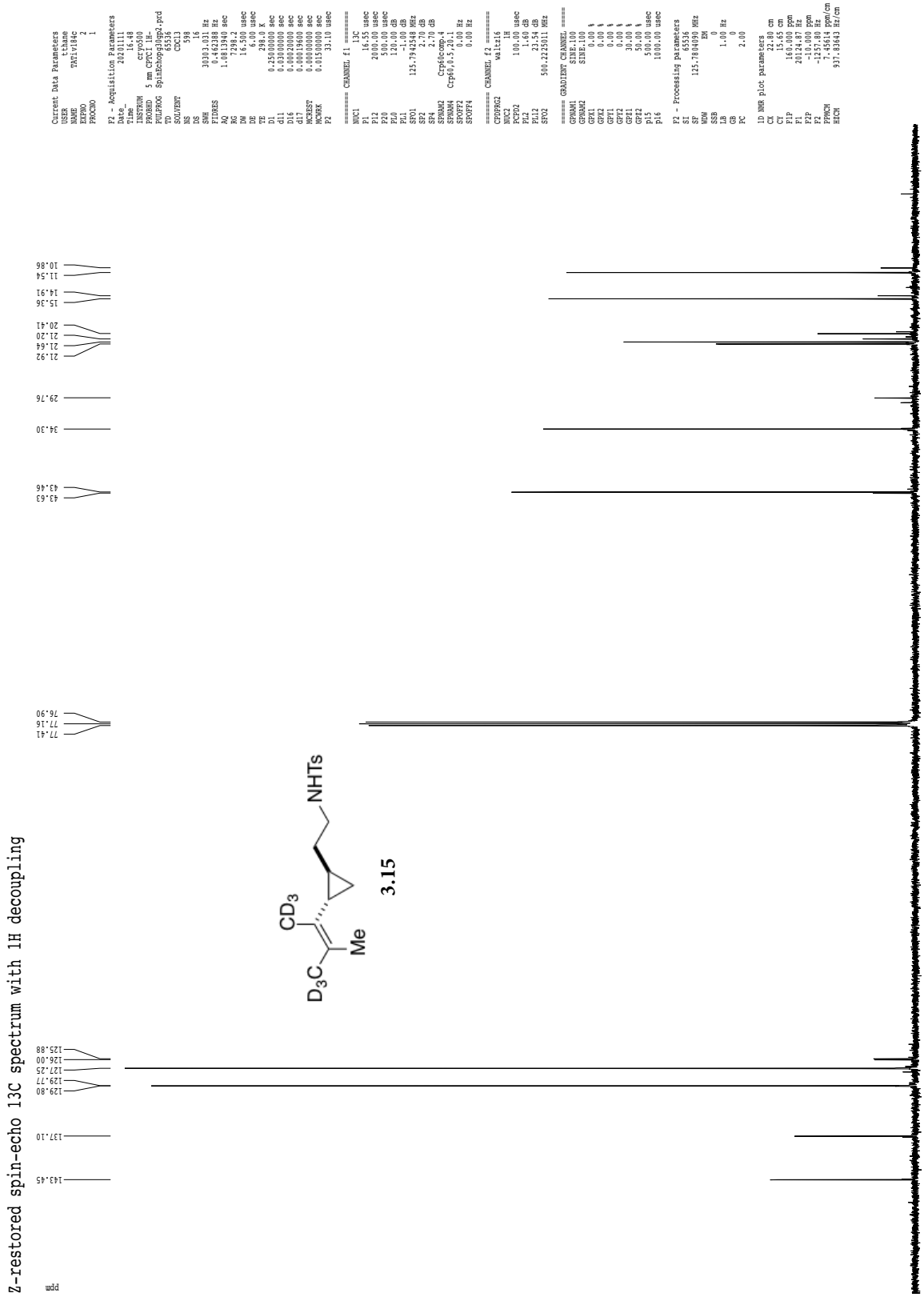
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                1H
PCPD2             80.00 usec
PL2               -6.00 dB
PL12              12.30 dB
SFO2         498.7524937 MHz

F2 - Processing parameters
SI                 65536
SF           125.4107762 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 2.00

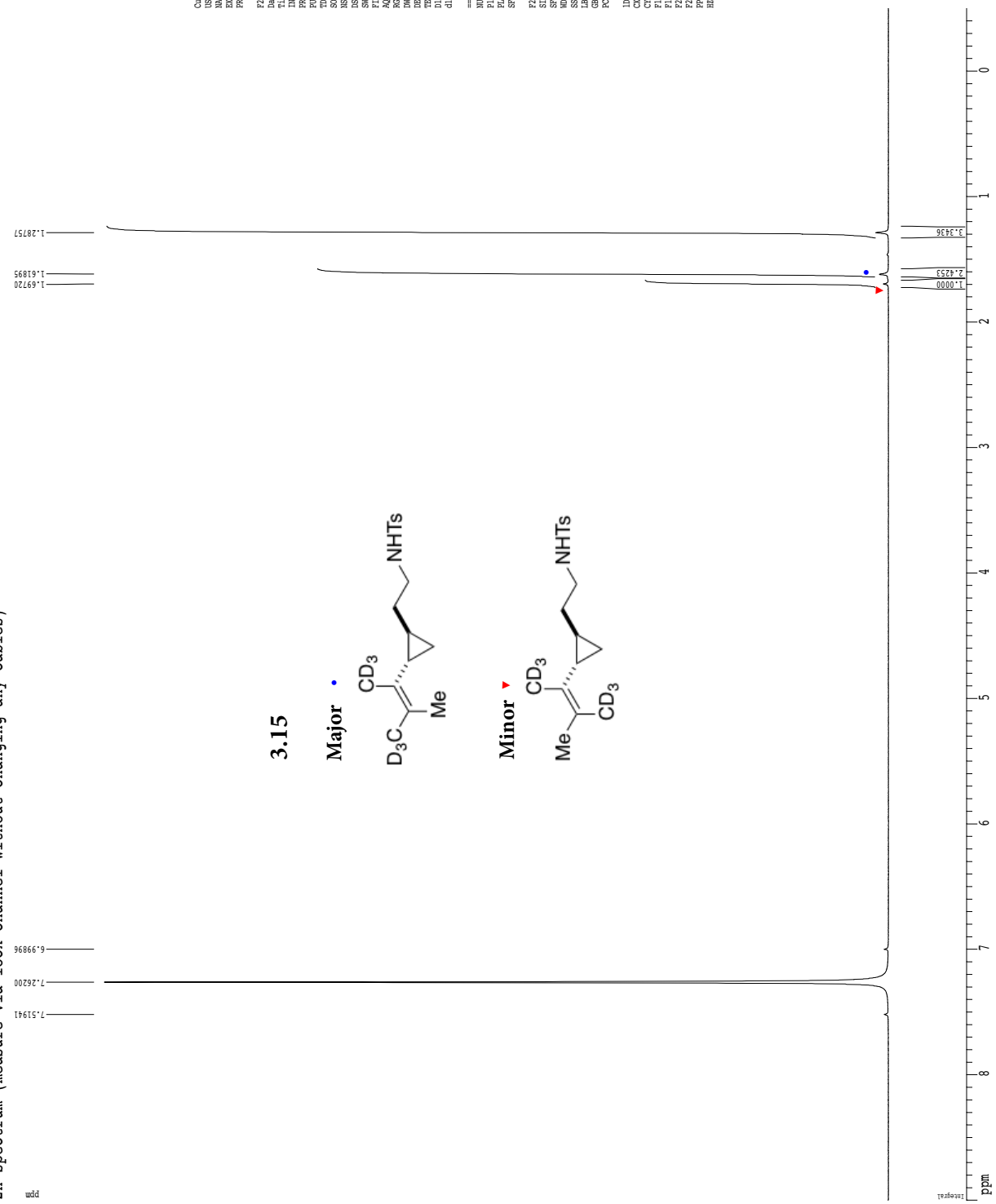
1D NMR plot parameters
CX                20.00 cm
CY                12.50 cm
F1P              220.000 ppm
F1             27590.37 Hz
F2P              -10.000 ppm
F2             -1254.11 Hz
PPMCM          11.50000 ppm/cm
HZCM         1442.22388 Hz/cm
```

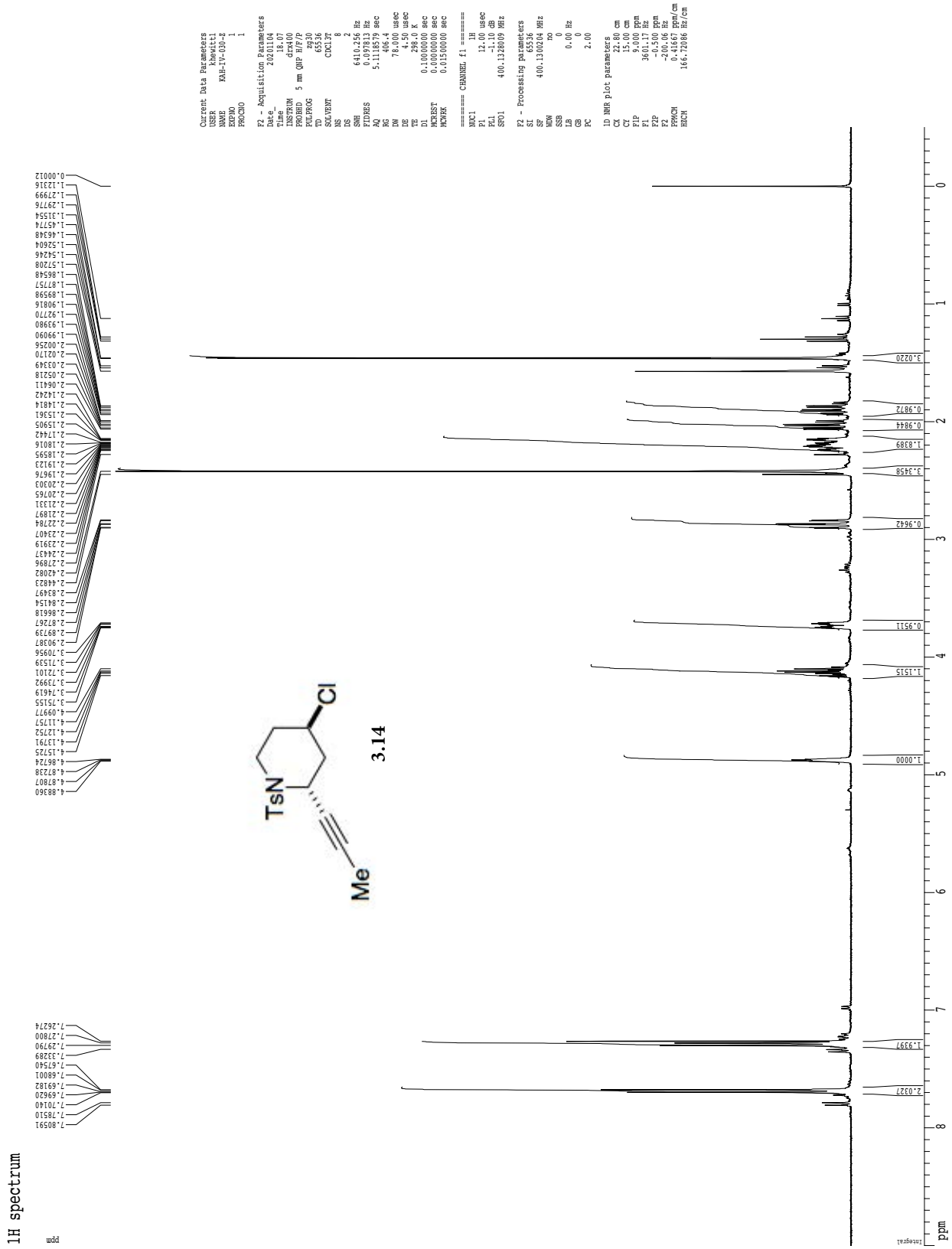

1H spectrum
3.13
OMe
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
Integral


1H spectrum
3.15
NHTs
CD3
Me
D3C

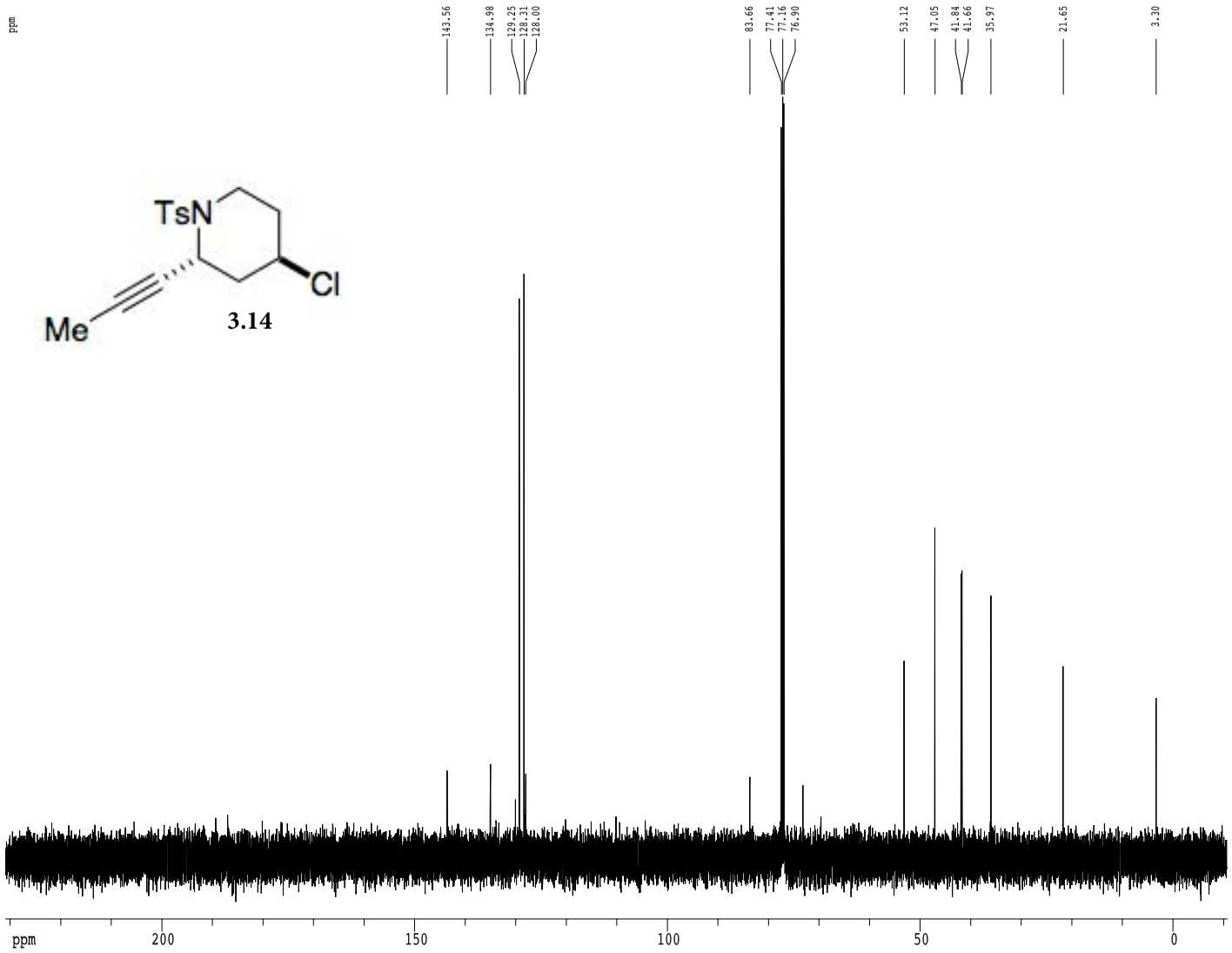

Z-restored spin-echo 13C spectrum with 1H decoupling
3.15
NHTs
Me
CD3
D3C
ppm

2H spectrum (measure via lock channel without changing any cables)




1H spectrum
Current Data Parameters
USER kinewiti
NAME KAH-IV-030-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201104
Time 18.07
INSTRUM drx400
PROBHD 5 mm QNP H/P/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 406.4
DW 78.000 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300204 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm
TsN
Cl
Me
3.14
3.0220
0.9872
0.9844
1.8389
3.3458
0.9642
0.9511
1.1515
1.0000
1.9397
2.0327
ppm
Integral

13C spectrum with 1H decoupling




```
Current Data Parameters
USER            khewitt1
NAME        KAH-IV-030-Z
EXPNO                 8
PROCNO                1

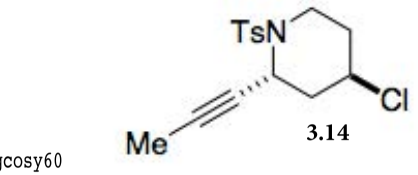
F2 - Acquisition Parameters
Date_          20201104
Time              19.16
INSTRUM           gn500
PROBHD   5 mm broadband
PULPROG         zgdc30
TD                65536
SOLVENT           CDCl3
NS                  224
DS                    4
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                3649.1
DW               16.500 usec
DE                6.00 usec
TE                298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                14.20 usec
PL1               -6.00 dB
SFO1         125.4245824 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2             80.00 usec
PL2               -6.00 dB
PL12              12.30 dB
SFO2         498.7524937 MHz

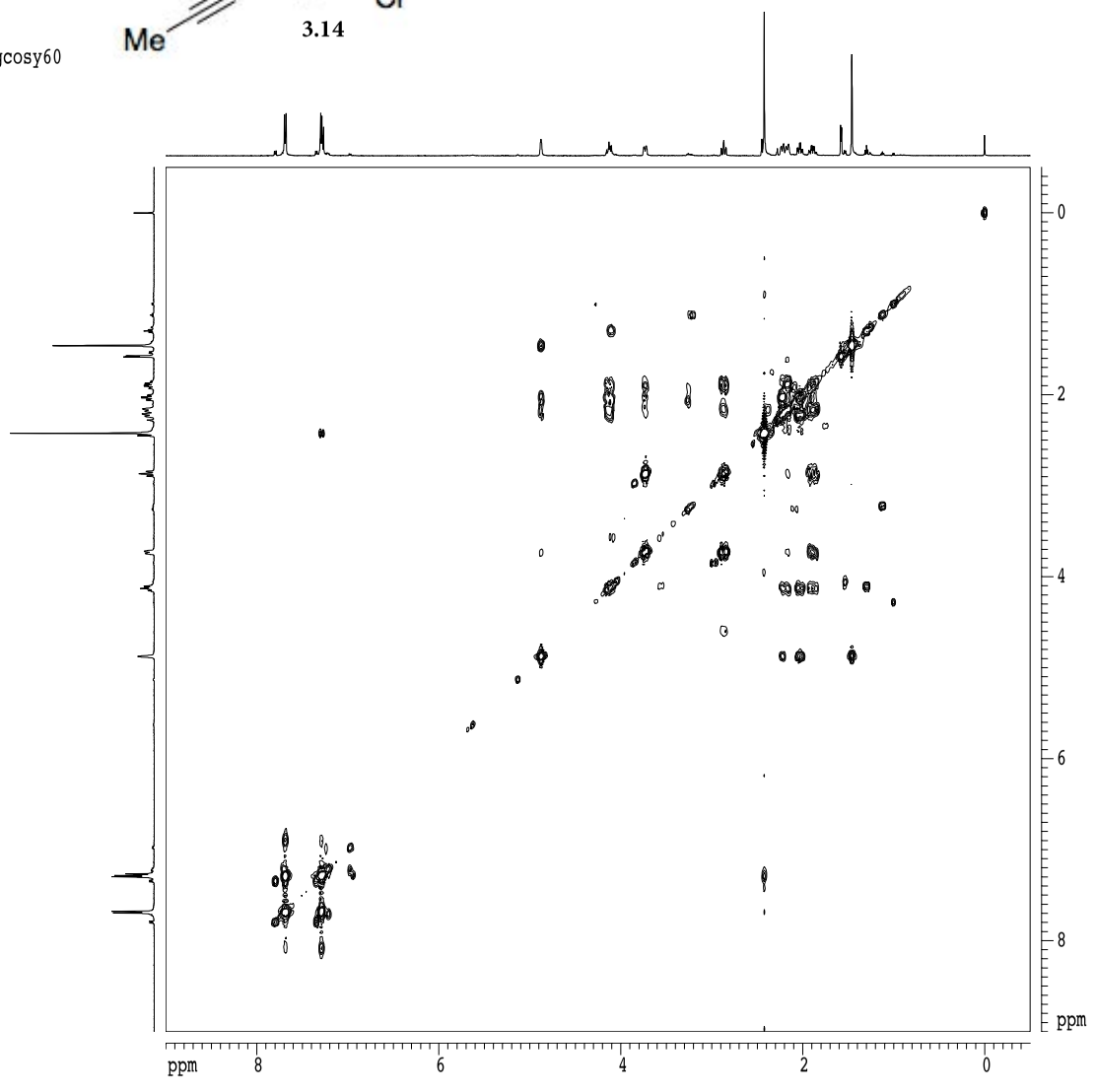
F2 - Processing parameters
SI                65536
SF           125.4107757 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                20.00 cm
CY                12.50 cm
F1P              230.907 ppm
F1             28958.25 Hz
F2P              -10.723 ppm
F2             -1344.78 Hz
PPMCM          12.08151 ppm/cm
HZCM         1515.15149 Hz/cm
```



3.14

gcosy60




```
        Current Data Parameters
USER            khewitt1
NAME        KAH-IV-030-E
EXPNO                  7
PROCNO                 1

      F2 - Acquisition Parameters
Date_           20201104
Time              19.05
INSTRUM           gn500
PROBHD   5 mm broadband
PULPROG    cosygp60.prd
TD                2048
SOLVENT           CDCl3
NS                   1
DS                  16
SWH            8012.820 Hz
FIDRES         3.912510 Hz
AQ             0.1278452 sec
RG                5792.6
DW                62.400 usec
DE                 6.00 usec
TE                298.0 K
d0             0.00000300 sec
D1             1.00000000 sec
d13            0.00000300 sec
D16            0.00020000 sec
IN0            0.00012480 sec

    ======== CHANNEL f1 ========
NUC1                 1H
P1                12.00 usec
PL1                -6.00 dB
SFO1         498.7534913 MHz

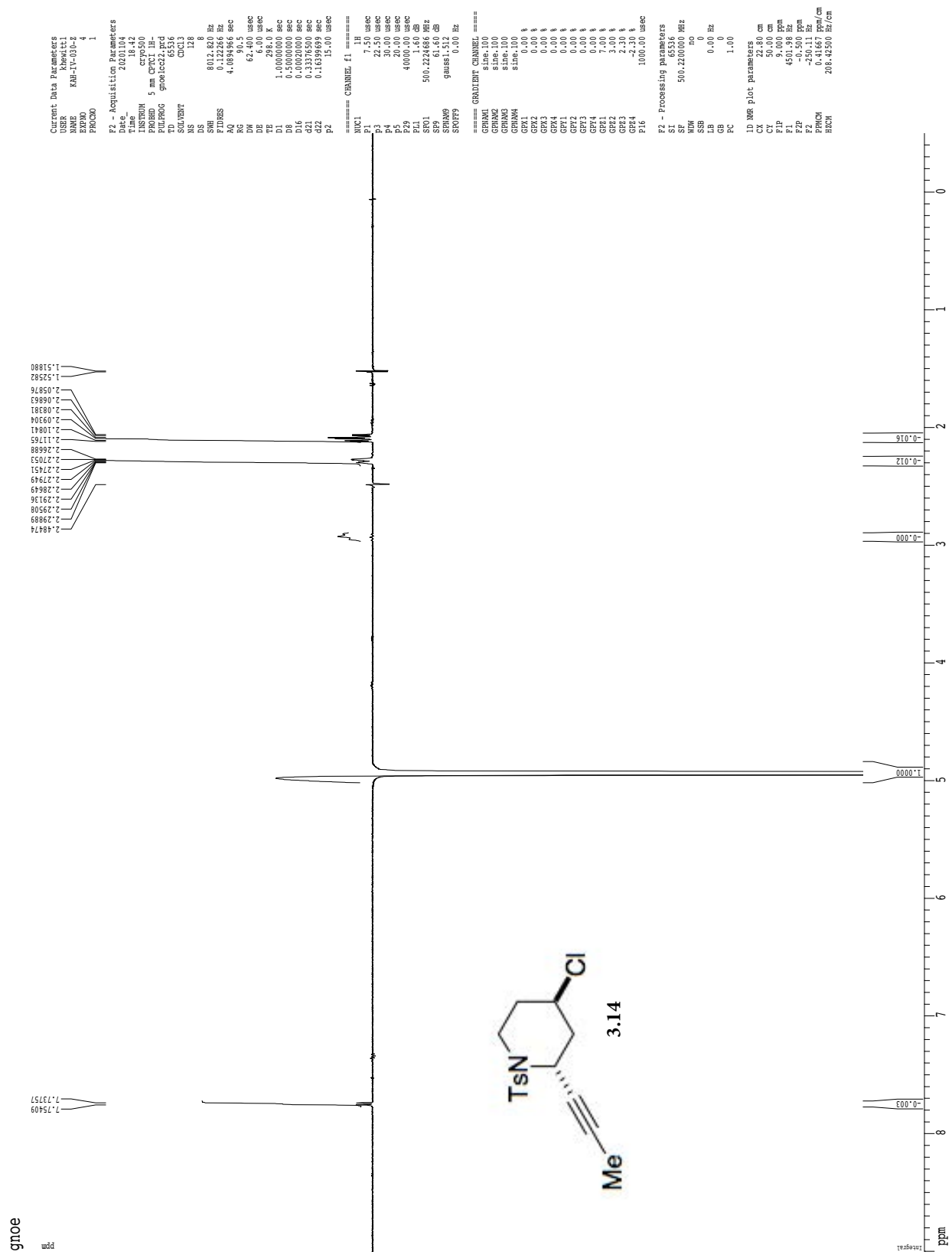
    ====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               17.00 %
GPZ2               17.00 %
P16              1000.00 usec

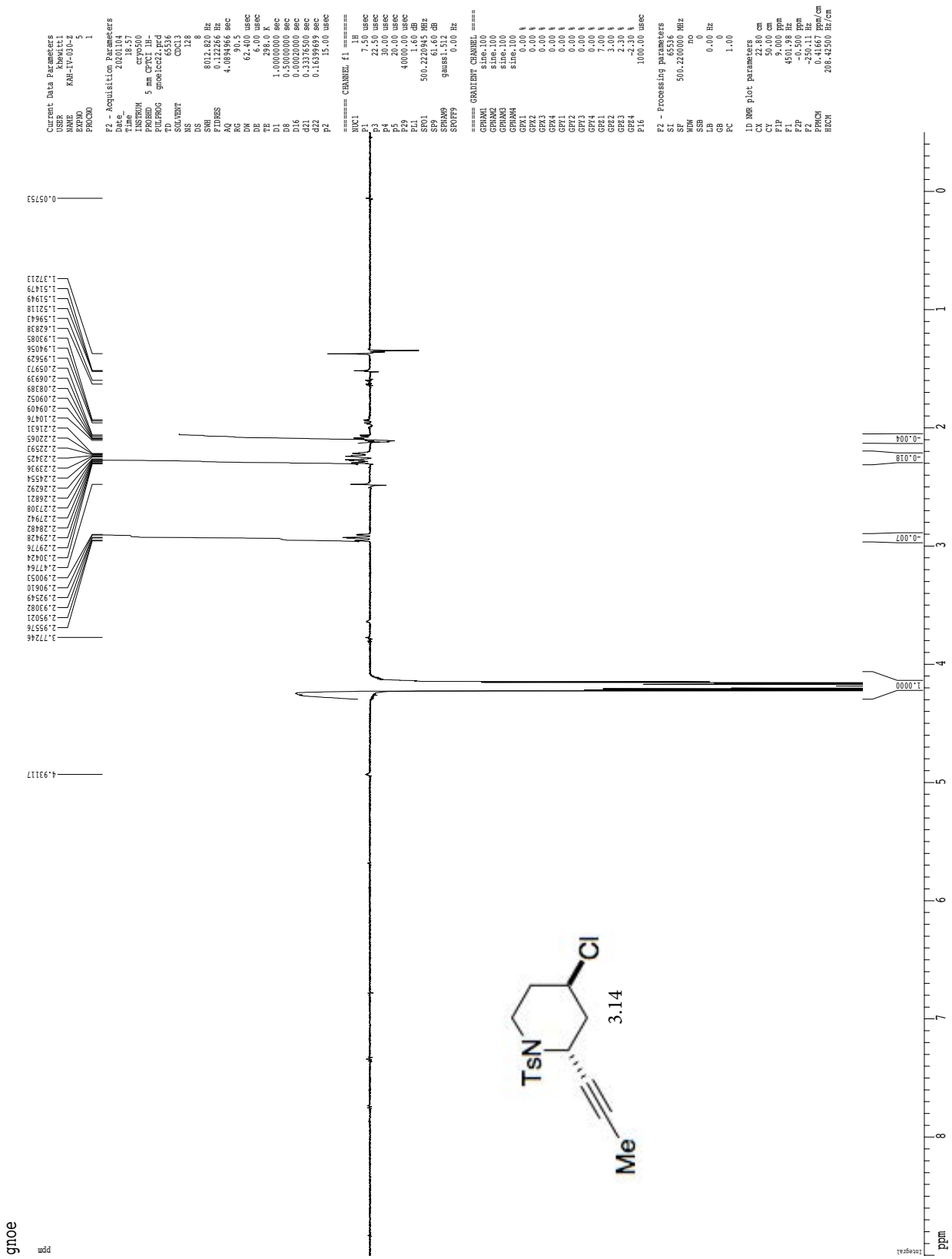
      F1 - Acquisition parameters
ND0                  1
TD                 256
SFO1           498.7535 MHz
FIDRES        31.300079 Hz
SW               16.066 ppm
FnMODE              QF

      F2 - Processing parameters
SI                 1024
SF           498.7500295 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00

      F1 - Processing parameters
SI                 1024
MC2                QF
SF           498.7500295 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0

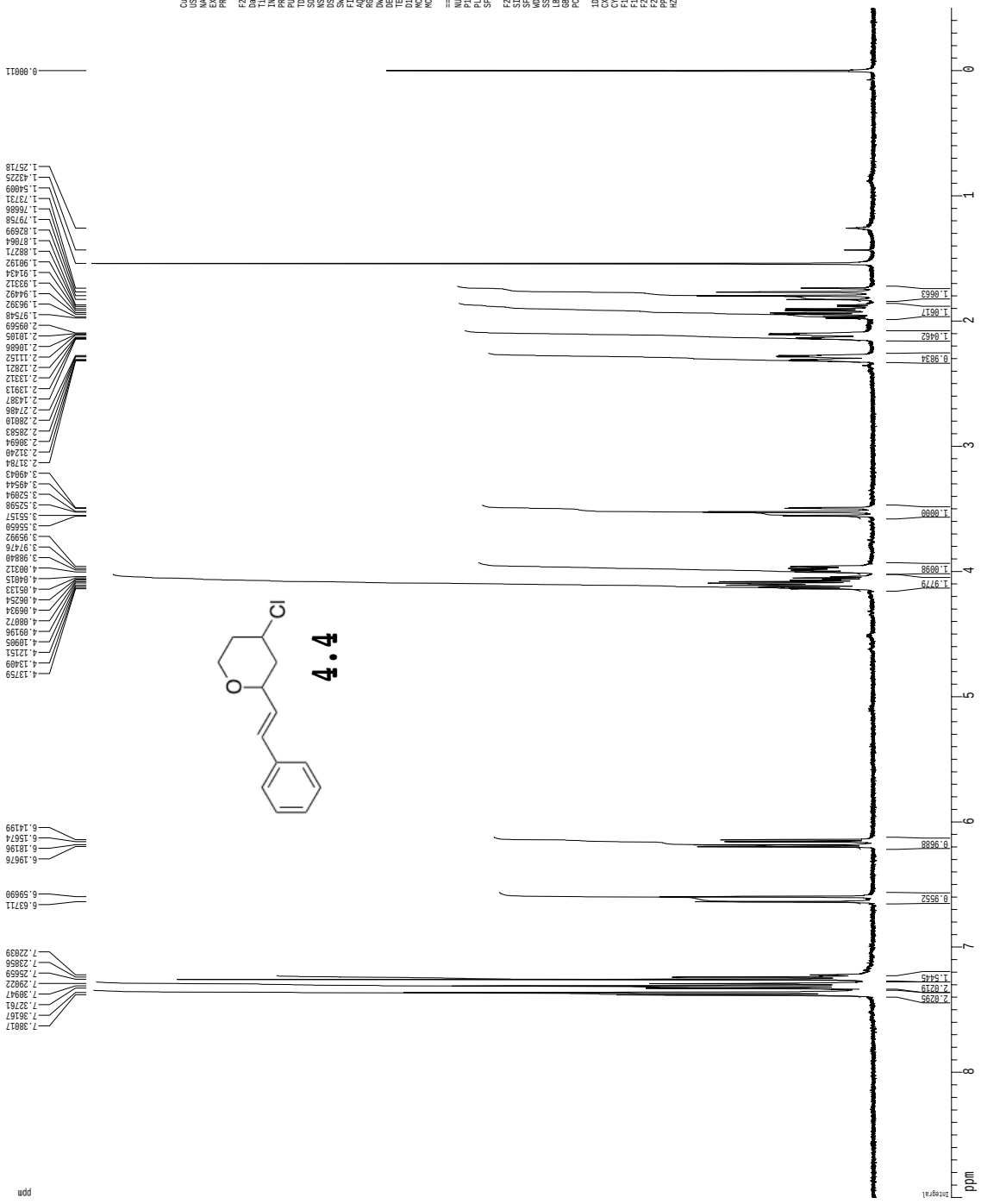
       2D NMR plot parameters
CX2               15.00 cm
CX1               15.00 cm
F2PLO             9.000 ppm
F2LO            4488.75 Hz
F2PHI             -0.500 ppm
F2HI            -249.38 Hz
F1PLO             9.000 ppm
F1LO            4488.75 Hz
F1PHI             -0.500 ppm
F1HI            -249.38 Hz
F2PPMCM         0.63333 ppm/cm
F2HZCM        315.87503 Hz/cm
F1PPMCM         0.63333 ppm/cm
F1HZCM        315.87503 Hz/cm
```

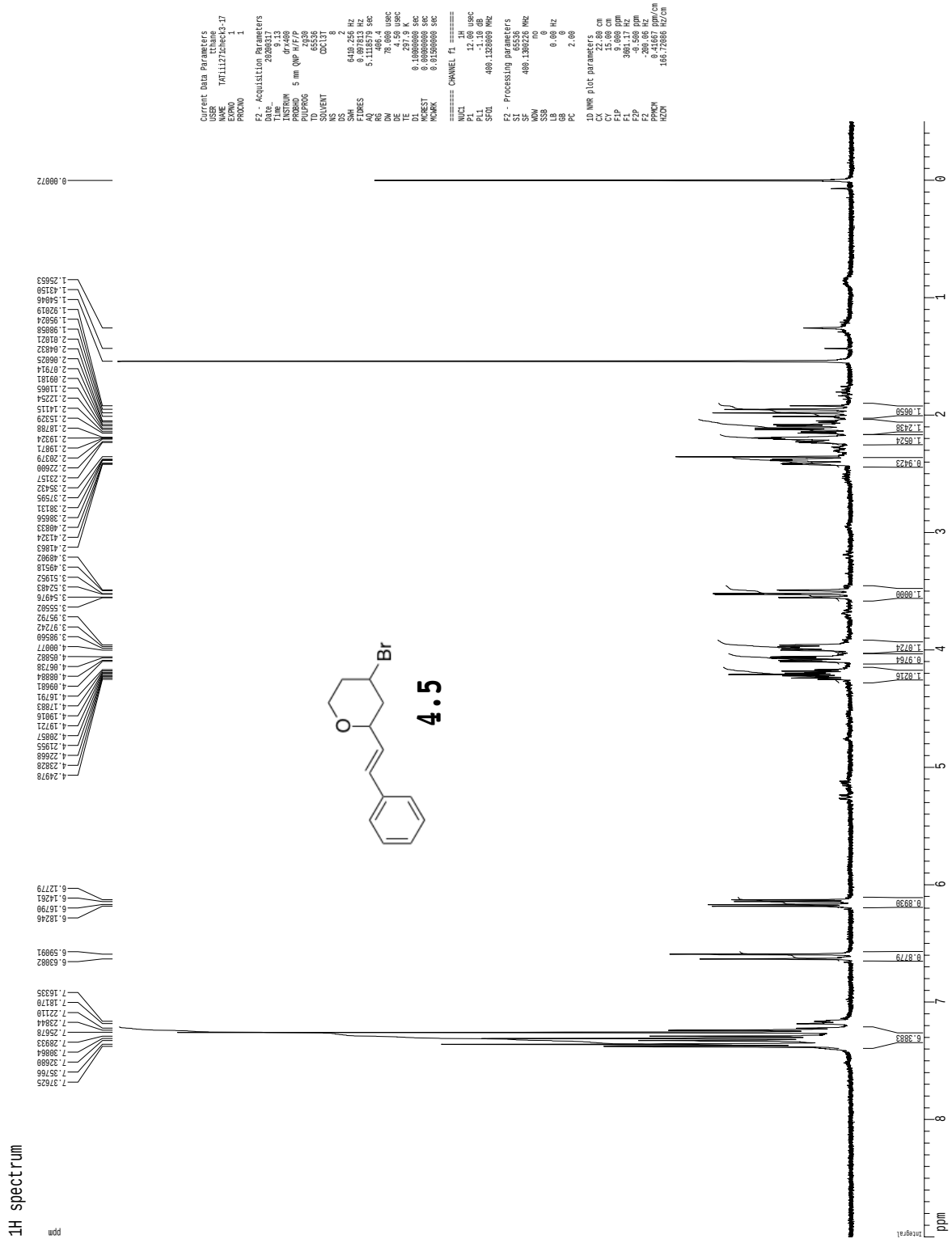

gnoe
ppm
Integral
Cl
TsN
Me
3.14


gnoe
ppm
Integral
TsN
Cl
Me
3.14

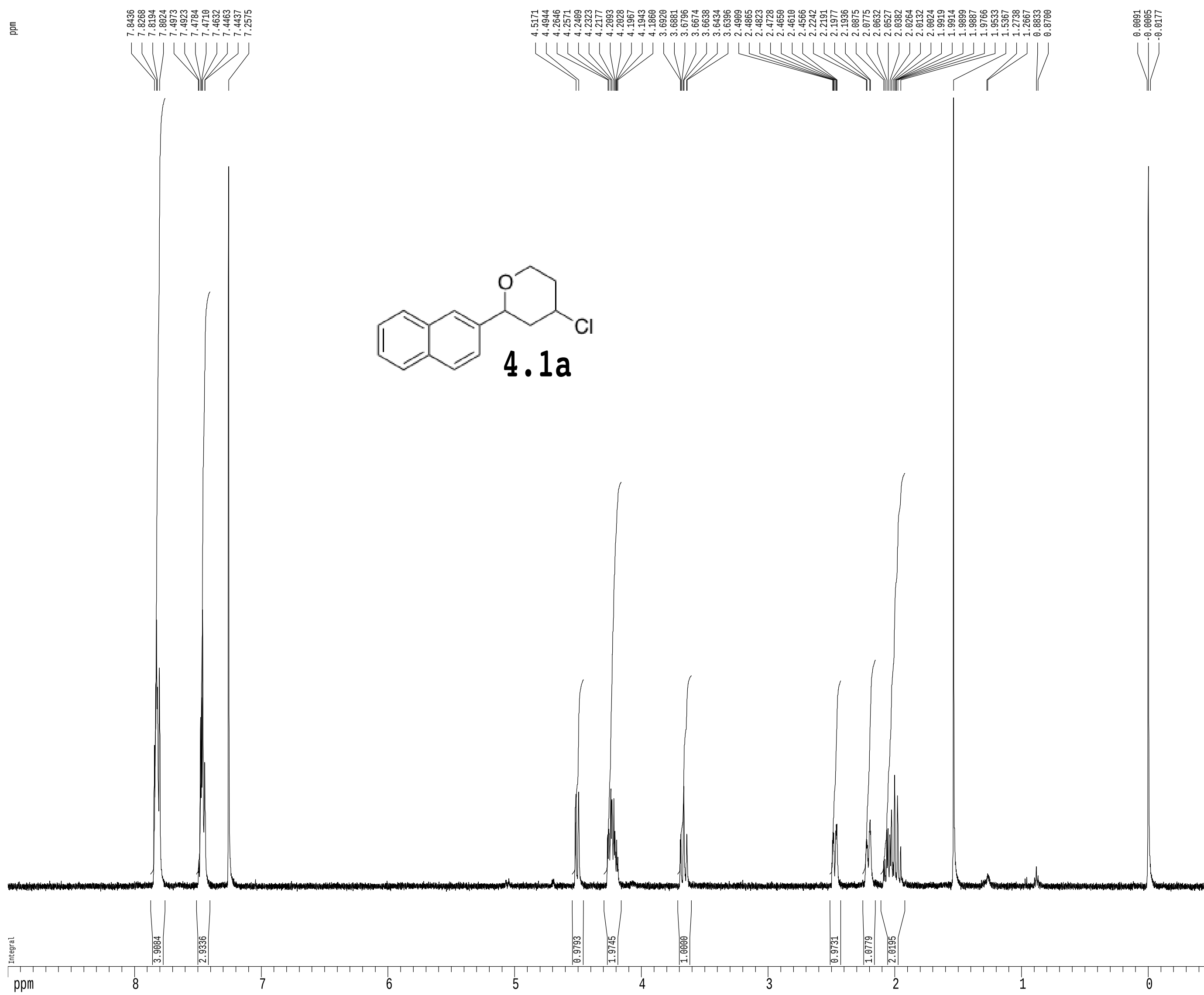
A.4 NMR Data Corresponding to Chapter 4

1H spectrum




Current Data Parameters
USER TITUS
NAME TATli27tcheck3-17
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200317
Time 9.13
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3T
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097781 Hz
AQ 5.11118579 sec
RG 406.4
DW 78.000 usec
DE 4.50 usec
TE 297.1 K
D1 0.10000000 sec
D11 0.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.10 dB
SFO1 400.1320009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300226 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3801.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72886 Hz/cm
0.00072
1.25653
1.43150
1.54046
1.92019
1.95624
1.98058
2.01021
2.04832
2.06025
2.07914
2.09181
2.11065
2.12254
2.14115
2.15329
2.16788
2.19324
2.19871
2.20379
2.22600
2.23157
2.25432
2.27595
2.28131
2.30656
2.40833
2.41324
2.41863
3.48902
3.49518
3.51952
3.54976
3.55502
3.95792
3.97242
3.98560
4.00077
4.05602
4.06738
4.08884
4.09681
4.16791
4.17883
4.19016
4.19721
4.20057
4.21955
4.22668
4.23828
4.24978
6.12779
6.14261
6.15790
6.18246
6.59091
6.63002
7.16335
7.18170
7.22110
7.23844
7.25678
7.28933
7.30064
7.32680
7.35766
7.37625
4.5
Br
O
1.8000
1.0724
0.9764
1.0216
0.8930
0.8779
6.3883
1.0650
1.2438
1.0524
0.9423
ppm
Integral
1H spectrum
ppm

1H spectrum



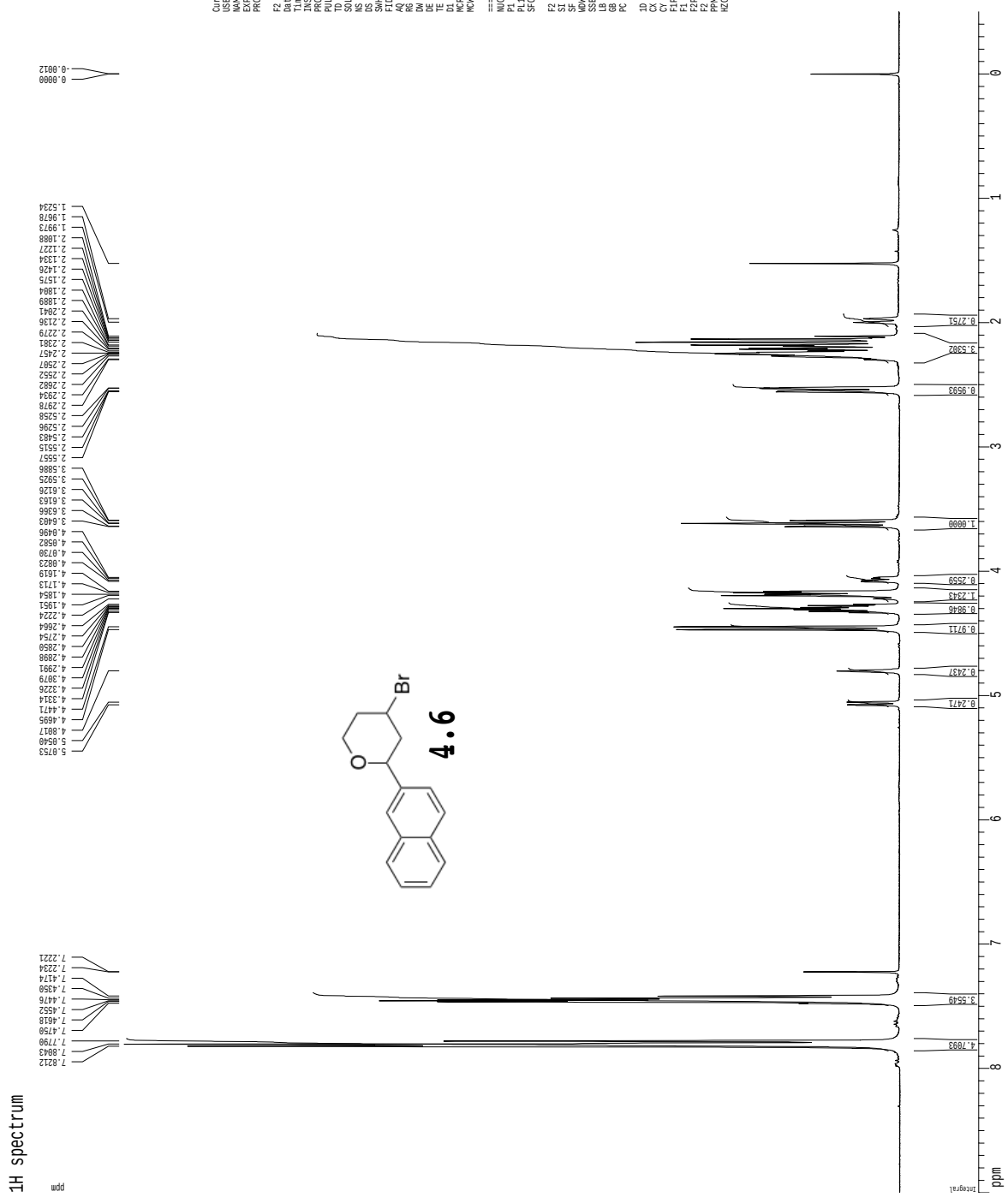

```
Current Data Parameters
USER              tthane
NAME        TATiii288pure
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200227
Time               13.21
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3T
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                  2048
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

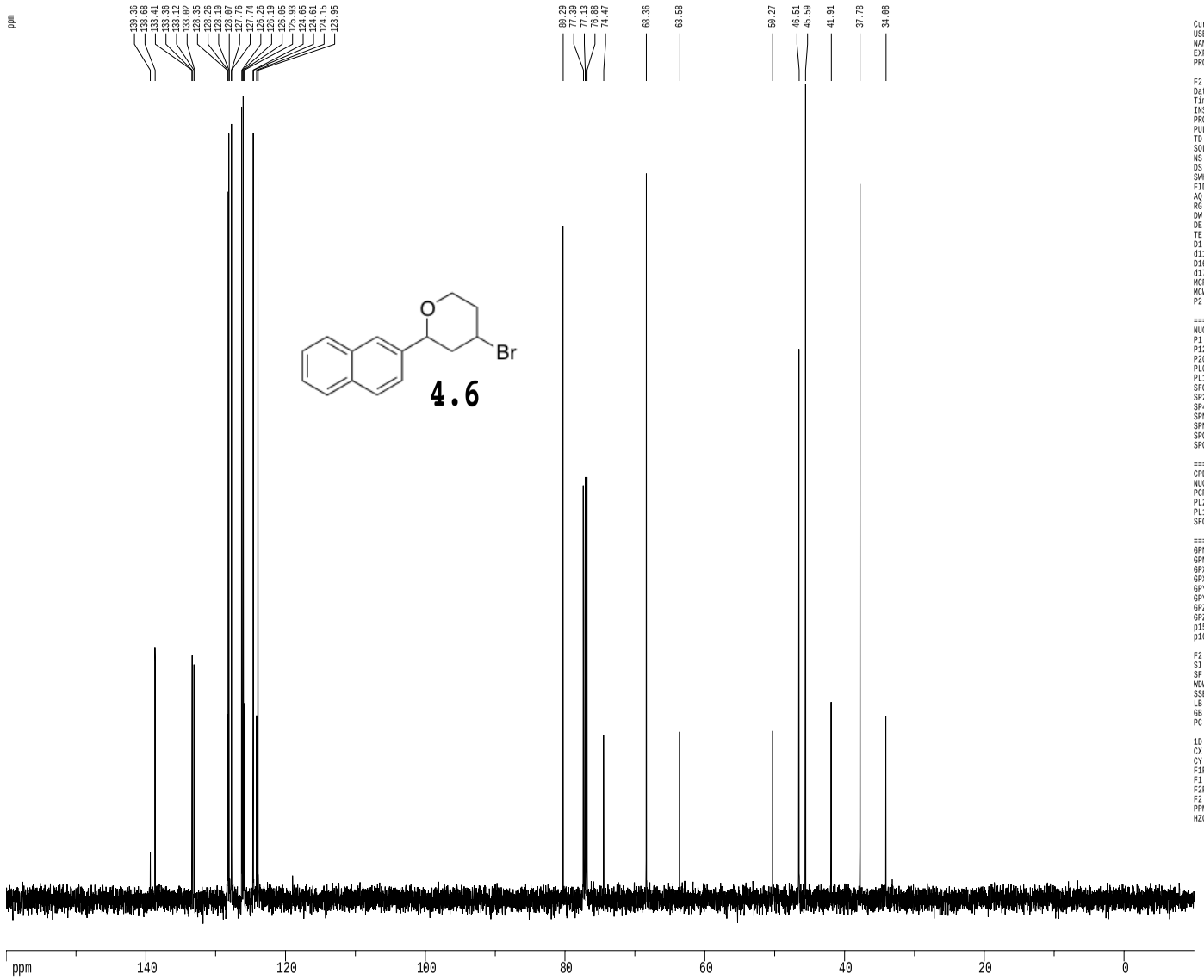
======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -5.00 dB
SFO1         498.8534919 MHz

F2 - Processing parameters
SI                 65536
SF           498.8500284 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.00 cm
F1P                9.000 ppm
F1               4489.65 Hz
F2P               -0.500 ppm
F2               -249.42 Hz
PPMCM            0.41667 ppm/cm
HZCM           207.85419 Hz/cm
```


1H spectrum
4.6
Br
O
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
integral

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER tthane
NAME TATiii289char
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200318
Time 9.25
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 104
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 3649.1
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

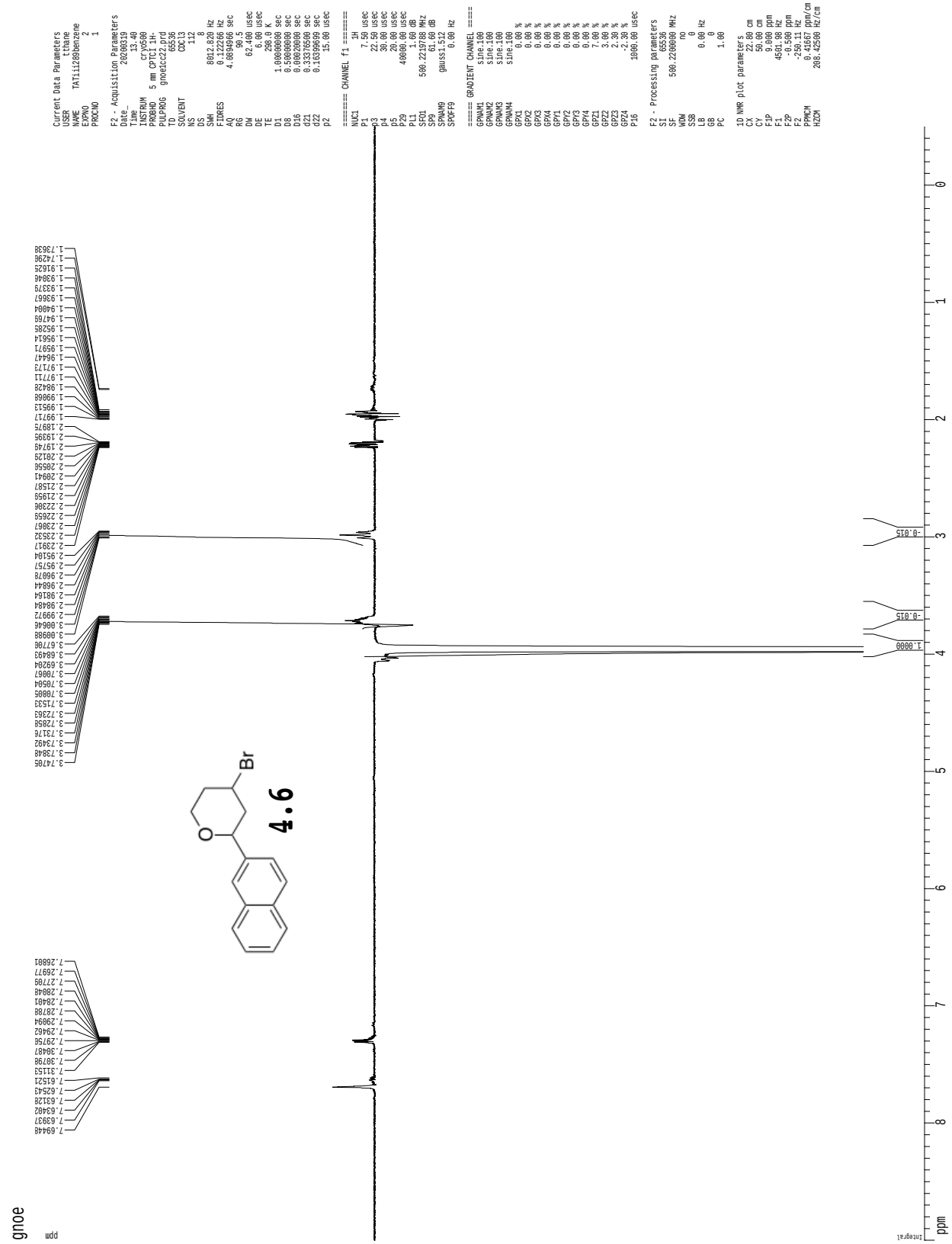
======== CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz

======== CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225011 MHz

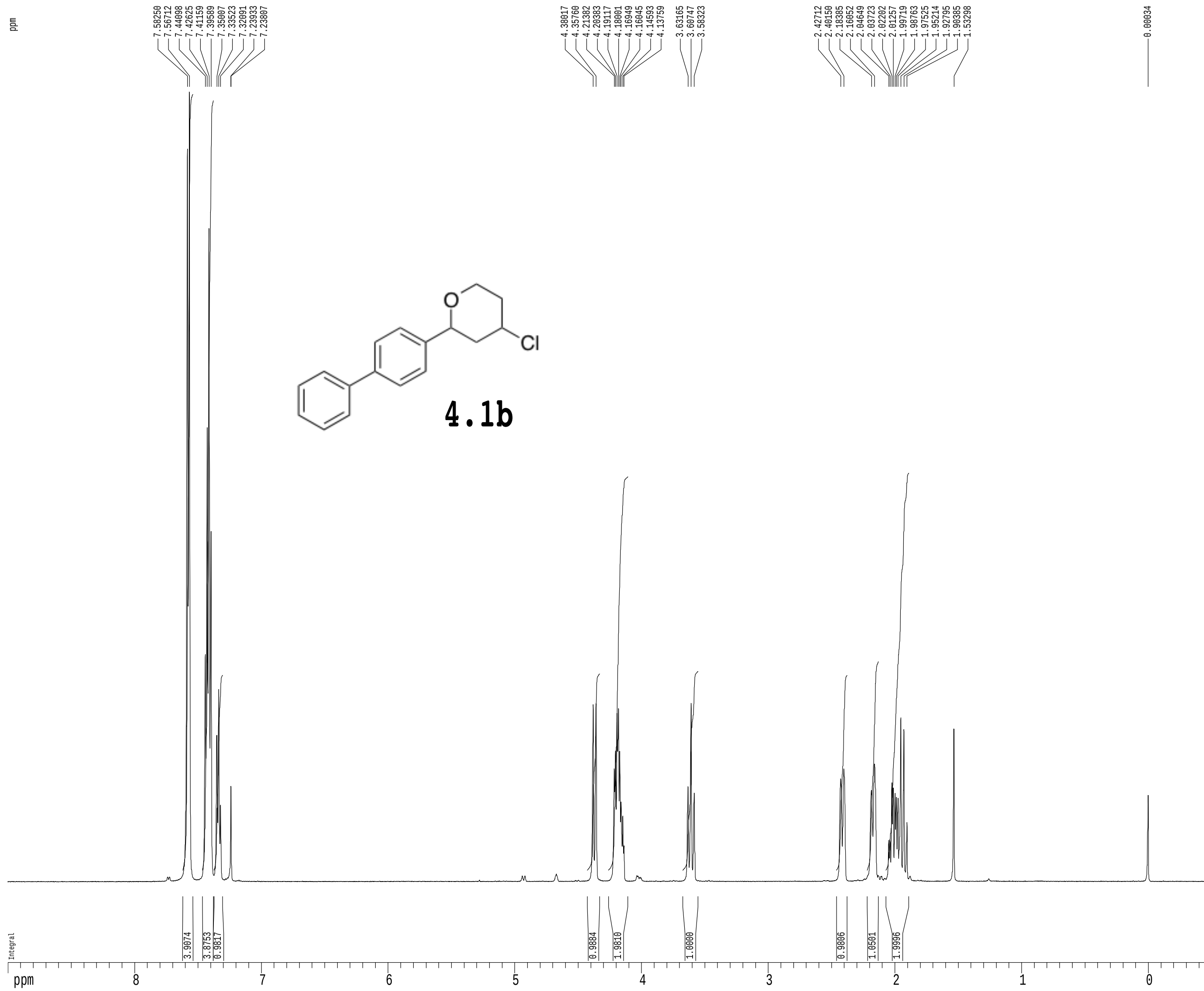
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804198 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 160.000 ppm
F1 20124.87 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 7.45614 ppm/cm
HZCM 937.83649 Hz/cm


gnoe
ppm
4.6
Br
O
Integral

1H spectrum



4.1b

```
Current Data Parameters
USER              tthane
NAME       TATiii215char
EXPNO                  1
PROCNO                 1

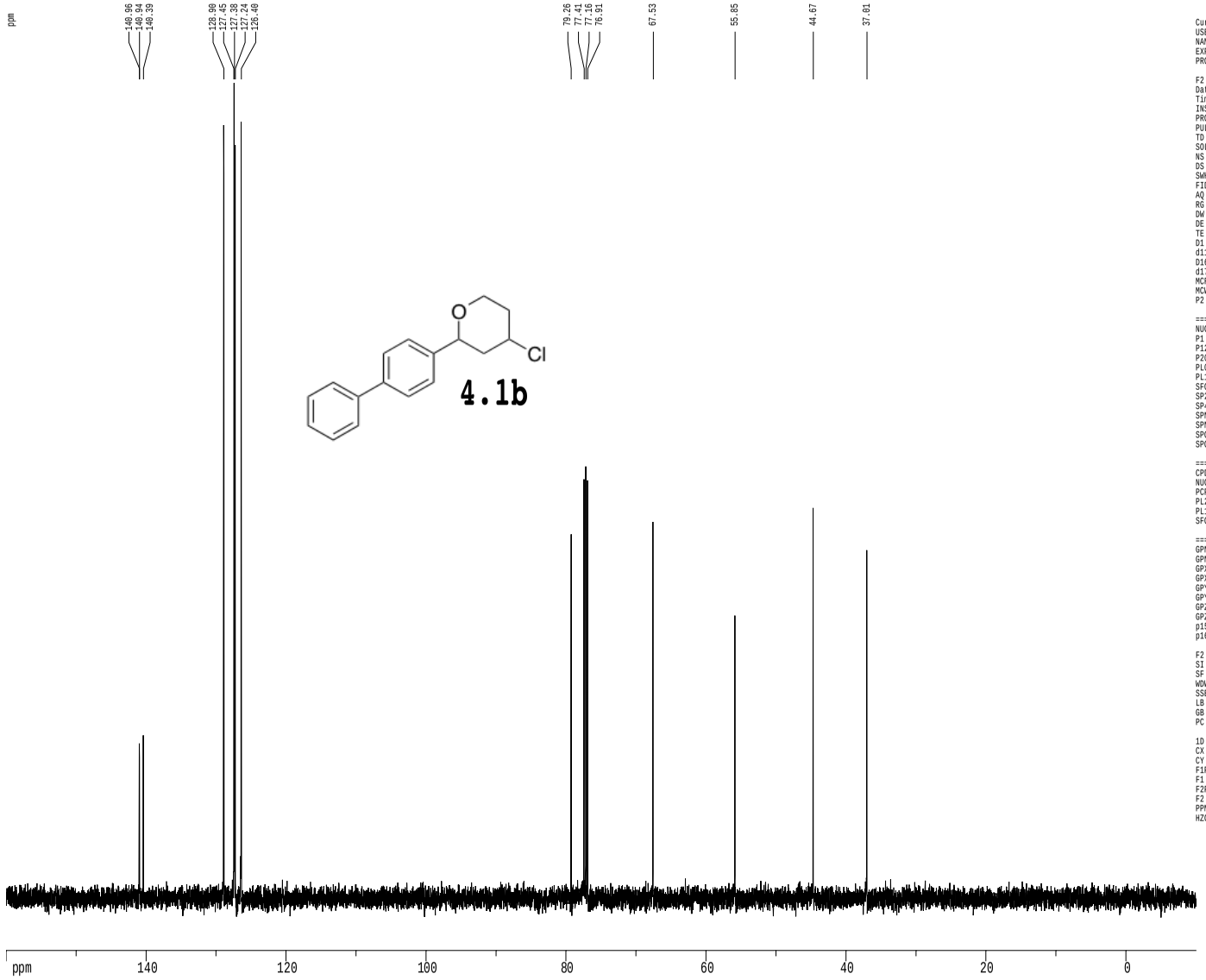
F2 - Acquisition Parameters
Date_           20200318
Time                9.10
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 48074
SOLVENT            CDCl3T
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.166677 Hz
AQ             2.9998677 sec
RG                   5.7
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  7.50 usec
PL1                 1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2200429 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.00 cm
F1P                9.000 ppm
F1               4501.98 Hz
F2P               -0.500 ppm
F2               -250.11 Hz
PPMCM            0.41667 ppm/cm
HZCM           208.42502 Hz/cm
```

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                tthane
NAME       TATiii215char
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_            20200318
Time                 9.12
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                   65536
SOLVENT              CDCl3
NS                      80
DS                      16
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  13004
DW                 16.500 usec
DE                  6.00 usec
TE                298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                 33.10 usec

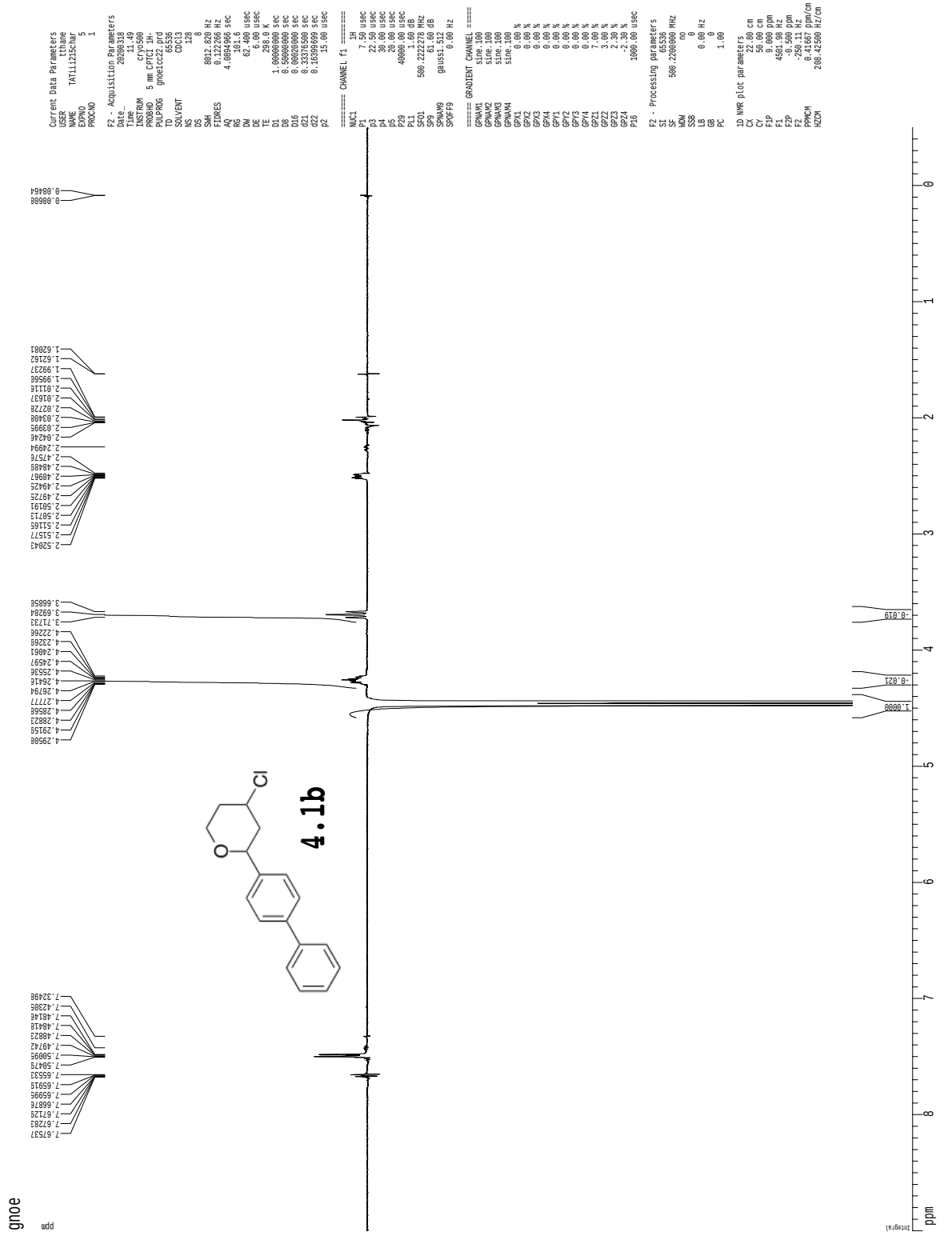
======== CHANNEL f1 =======
NUC1                  13C
P1                  16.55 usec
P12               2000.00 usec
P20                500.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP2                 2.70 dB
SP4                 2.70 dB
SPNAM2       Crp60comp.4
SPNAM4    Crp60,0.5,20.1
SPOFF2                0.00 Hz
SPOFF4                0.00 Hz

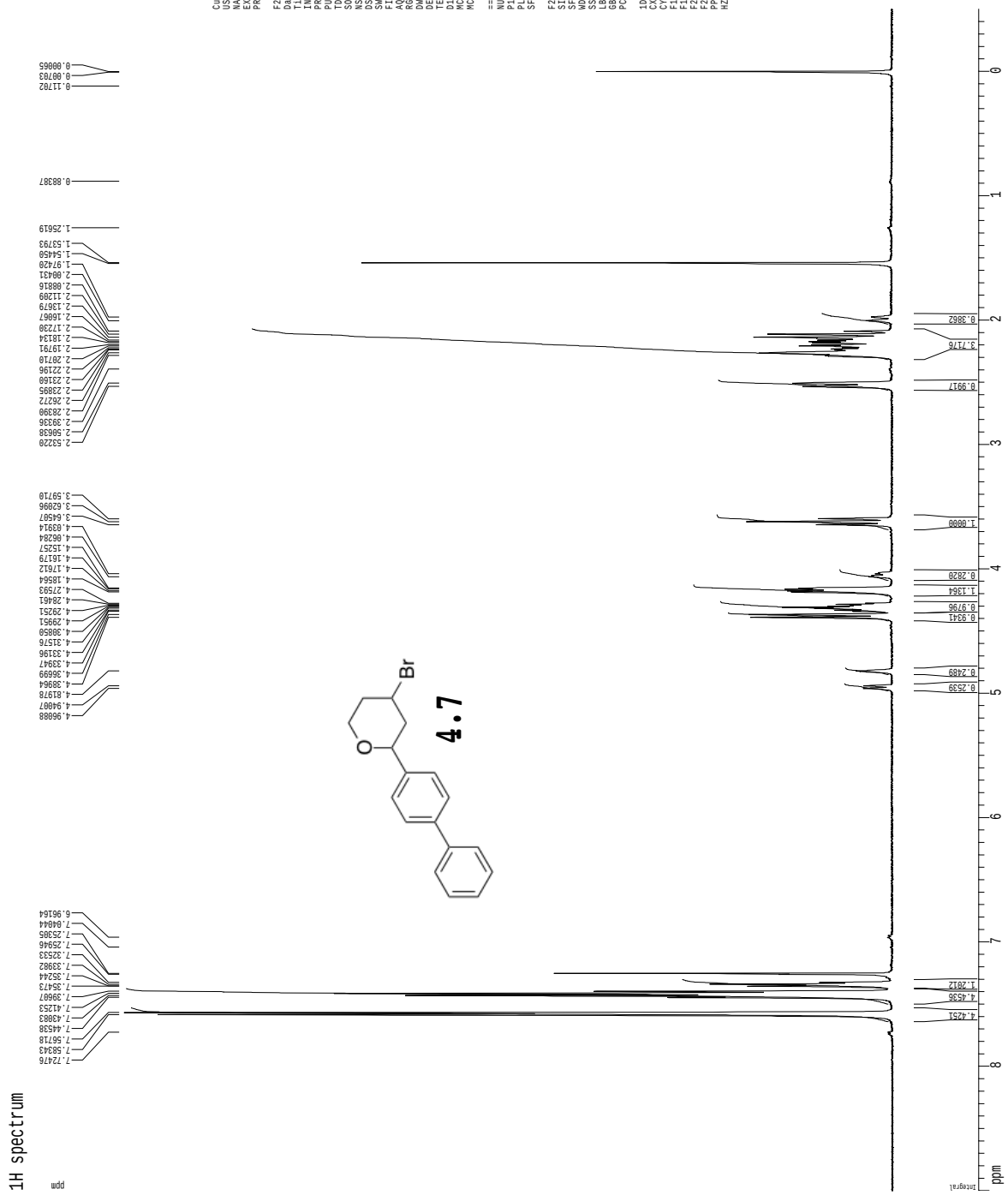
======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                  1H
PCPD2               100.00 usec
PL2                   1.60 dB
PL12                 23.54 dB
SFO2          500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                  0.00 %
GPX2                  0.00 %
GPY1                  0.00 %
GPY2                  0.00 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p15                 500.00 usec
p16                1000.00 usec

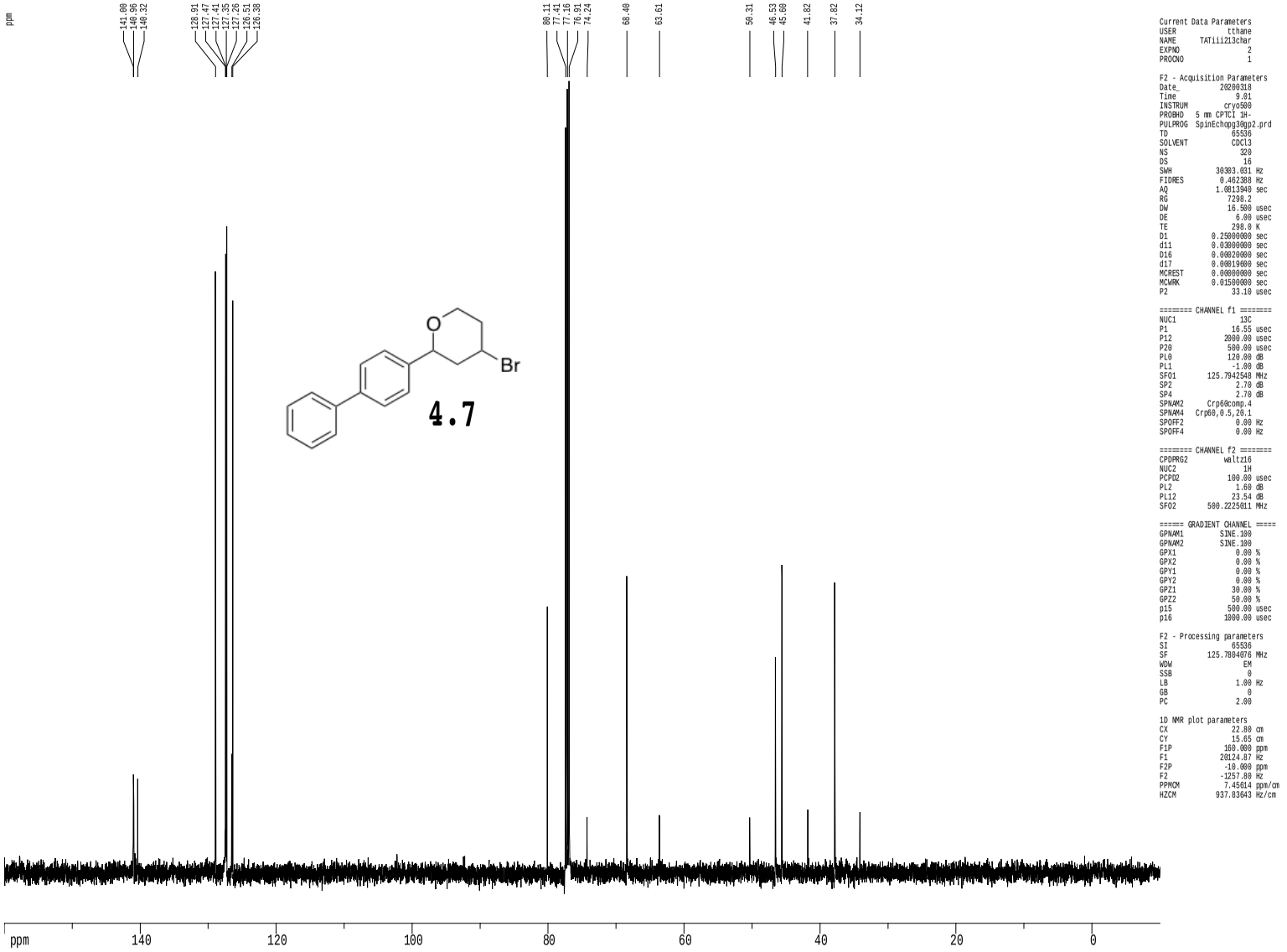
F2 - Processing parameters
SI                   65536
SF            125.7804113 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00

1D NMR plot parameters
CX                   22.80 cm
CY                   15.65 cm
F1P                160.000 ppm
F1              20124.87 Hz
F2P                -10.000 ppm
F2              -1257.80 Hz
PPMCM             7.45614 ppm/cm
HZCM            937.83643 Hz/cm
```


gnoe
4.1b
Cl
O
ppm
Integral


1H spectrum
4.7
Br
O

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER tthane
NAME TATiii213char
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200318
Time 9.01
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp2.prd
TD 65536
SOLVENT CDCl3
NS 320
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7208.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

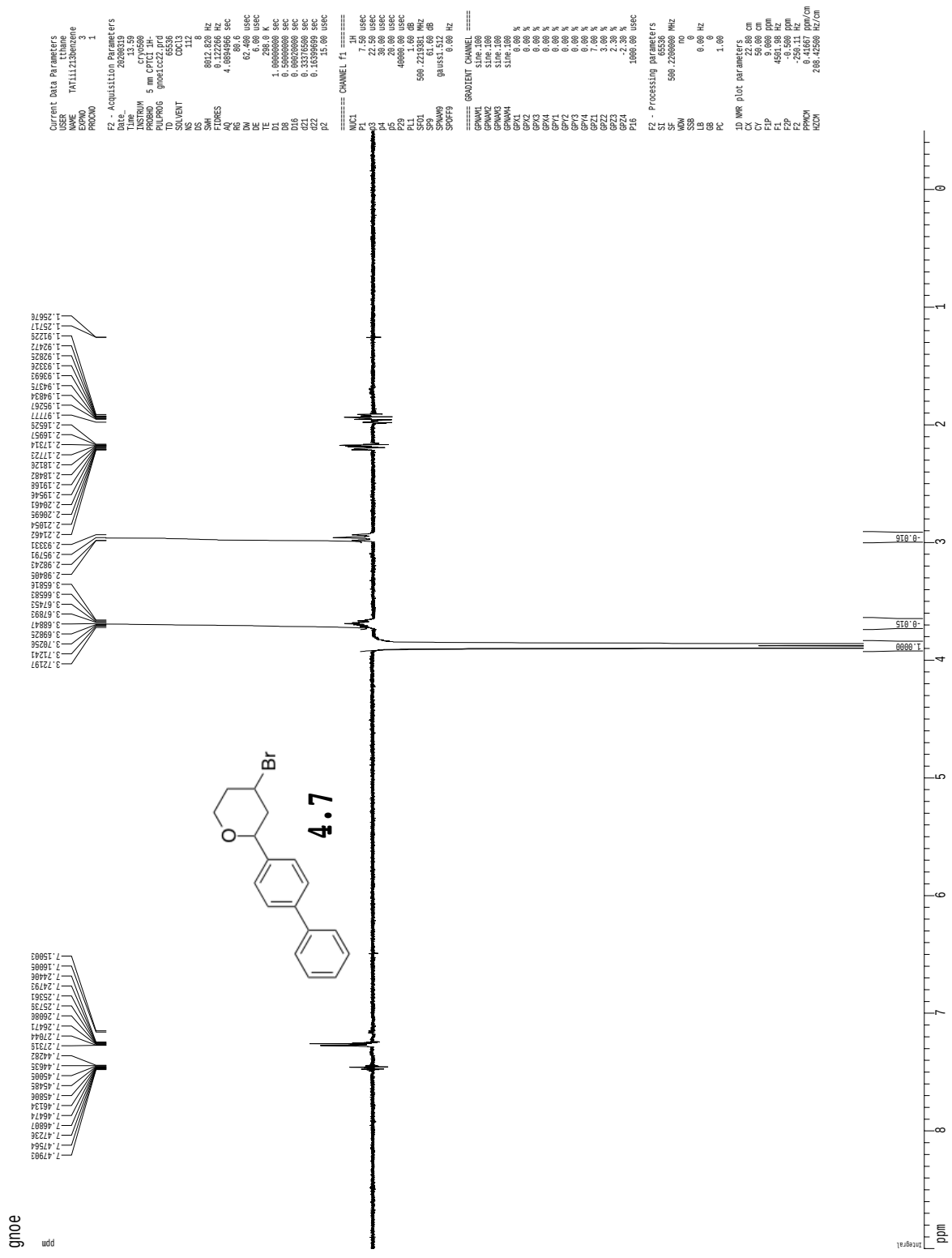
======== CHANNEL f1 ========
NUC1 13C
P1 16.55 usec
P12 2000.00 usec
P20 500.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP2 2.70 dB
SP4 2.70 dB
SPNAM2 Crp60comp.4
SPNAM4 Crp60,0.5,20.1
SPOFF2 0.00 Hz
SPOFF4 0.00 Hz

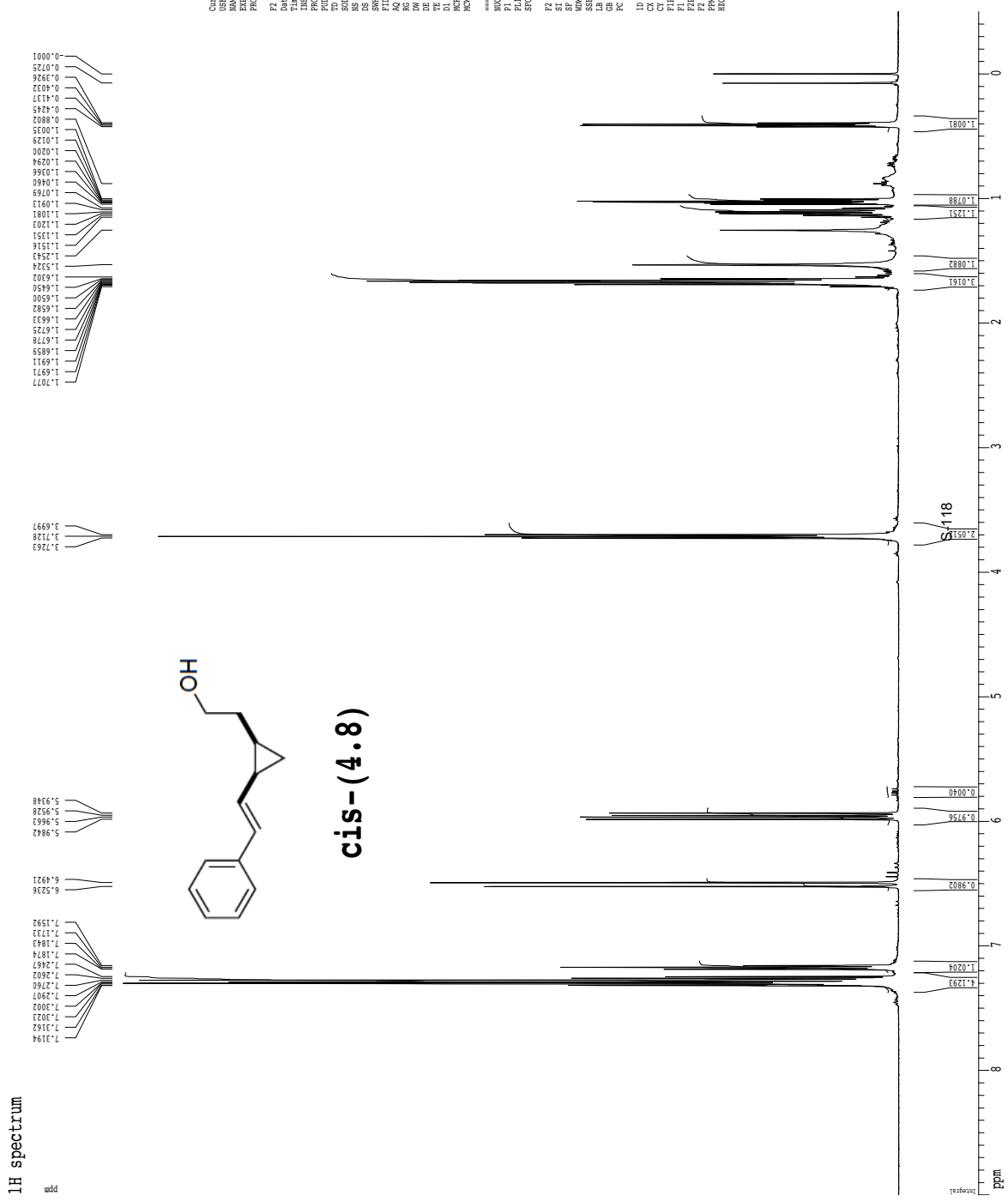
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 23.54 dB
SFO2 500.2225011 MHz

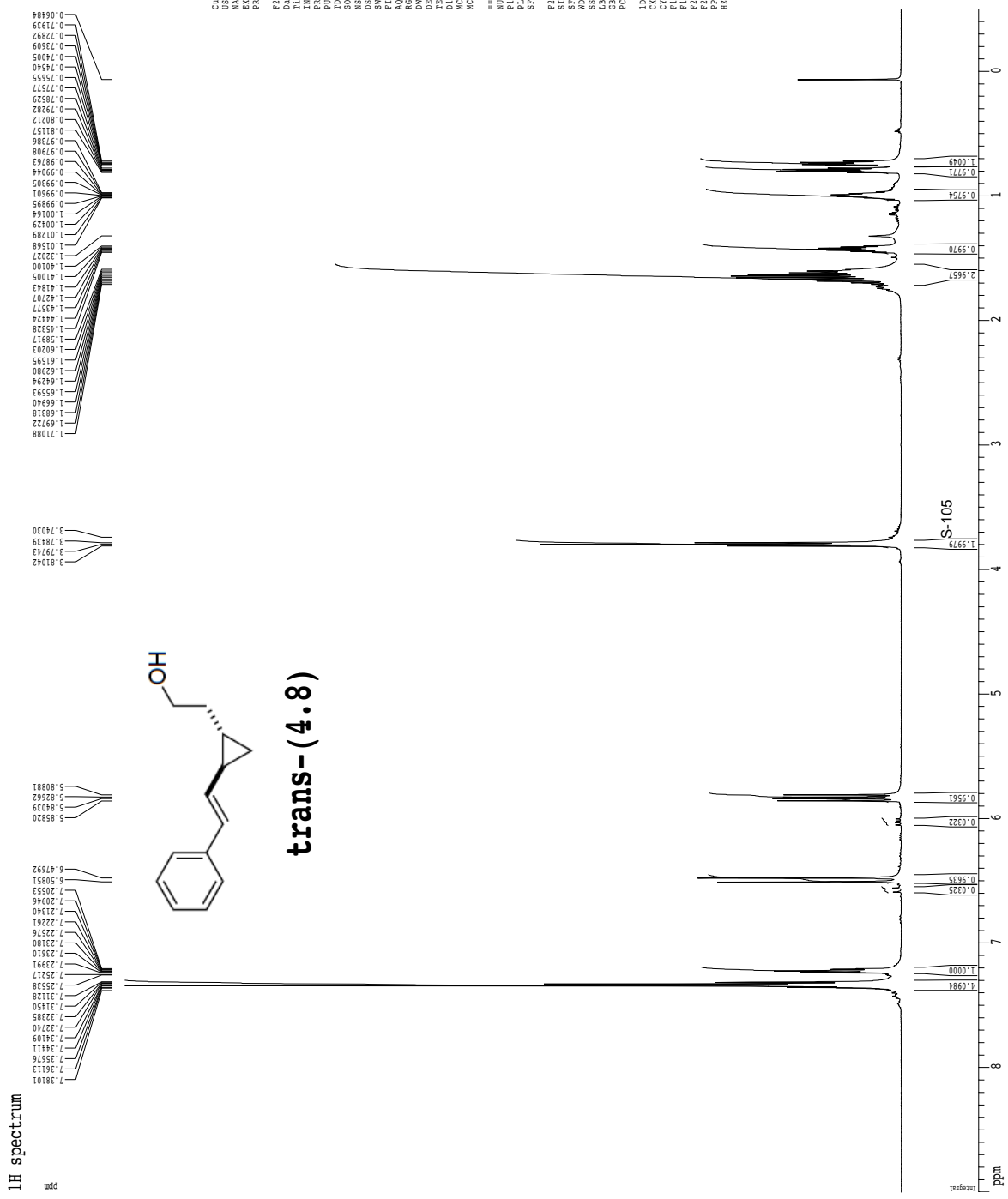
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804076 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

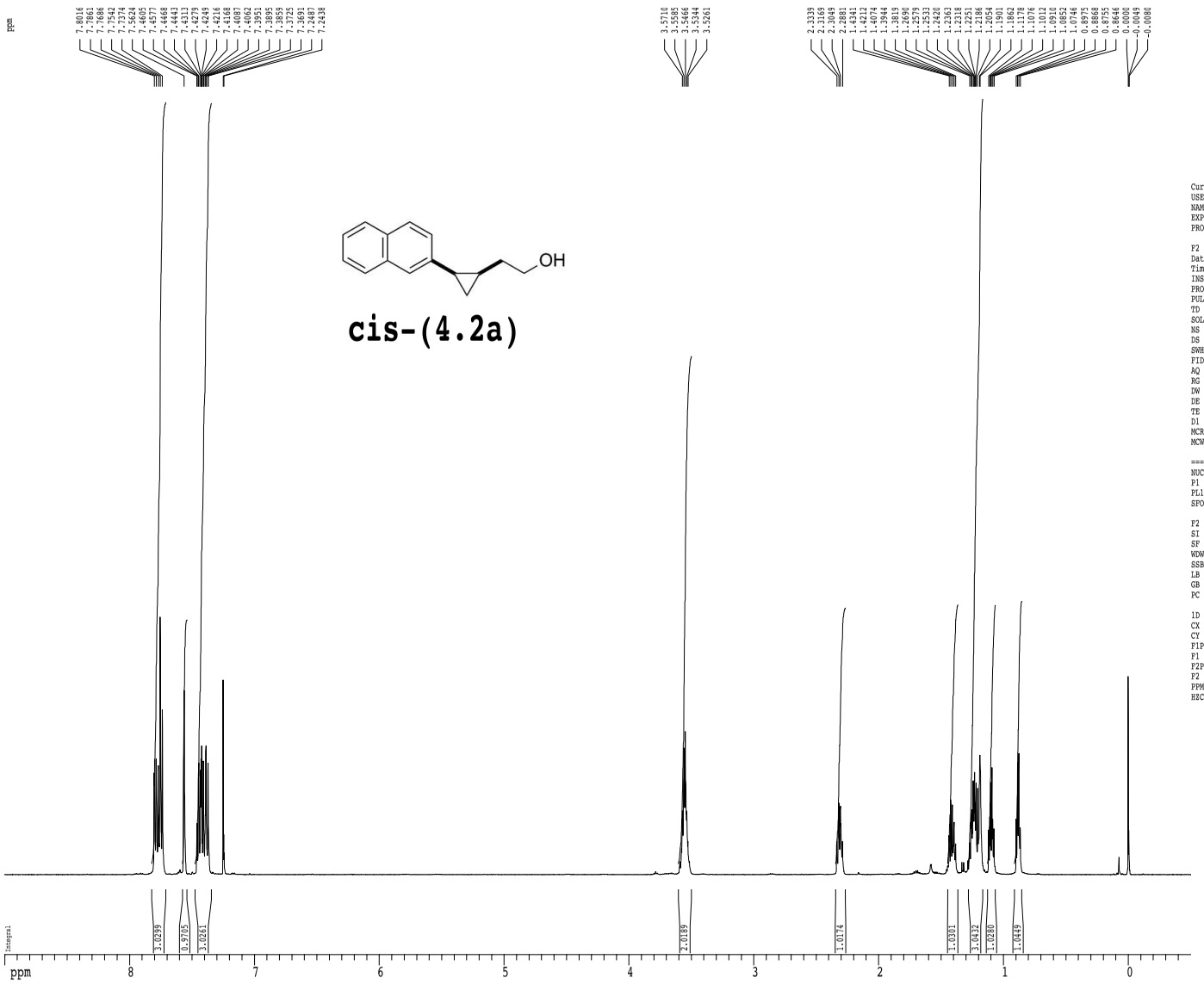
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 160.000 ppm
F1 20124.87 Hz
F2P -10.000 ppm
F2 -1257.80 Hz
PPMCM 7.45614 ppm/cm
HZCM 937.83643 Hz/cm


4.7
Br
O
gnoe
ppm
Integral


1H spectrum
cis-(4.8)
OH
Current Data Parameters
USER erika1
NAME ELL-1-209#3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151120
Time_ 8.04
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 48014
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.166677 Hz
AQ 2.9998677 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200386 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.91 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
7.3194
7.3162
7.3023
7.3002
7.2907
7.2760
7.2602
7.2467
7.1874
7.1843
7.1733
7.1592
6.4921
6.4736
5.9842
5.9663
5.9528
5.9348
3.7263
3.7128
3.6997
1.7077
1.6971
1.6911
1.6859
1.6778
1.6725
1.6633
1.6582
1.6450
1.6308
1.6302
1.5324
1.2549
1.1516
1.1351
1.1203
1.1081
1.0912
1.0769
1.0460
1.0366
1.0294
1.0200
1.0129
1.0035
0.8802
0.4245
0.4137
0.4032
0.3924
0.0725
-0.0001
4.1293
1.0204
0.9802
0.0040
0.9756
2.0518
3.0161
1.0882
1.1251
1.0788
1.0081
S118
ppm


1H spectrum
trans-(4.8)
OH
S-105
ppm

1H spectrum



Current Data Parameters
USER emilyt
NAME EJT-I-173-A
EXPNO 19
PROCNO 1

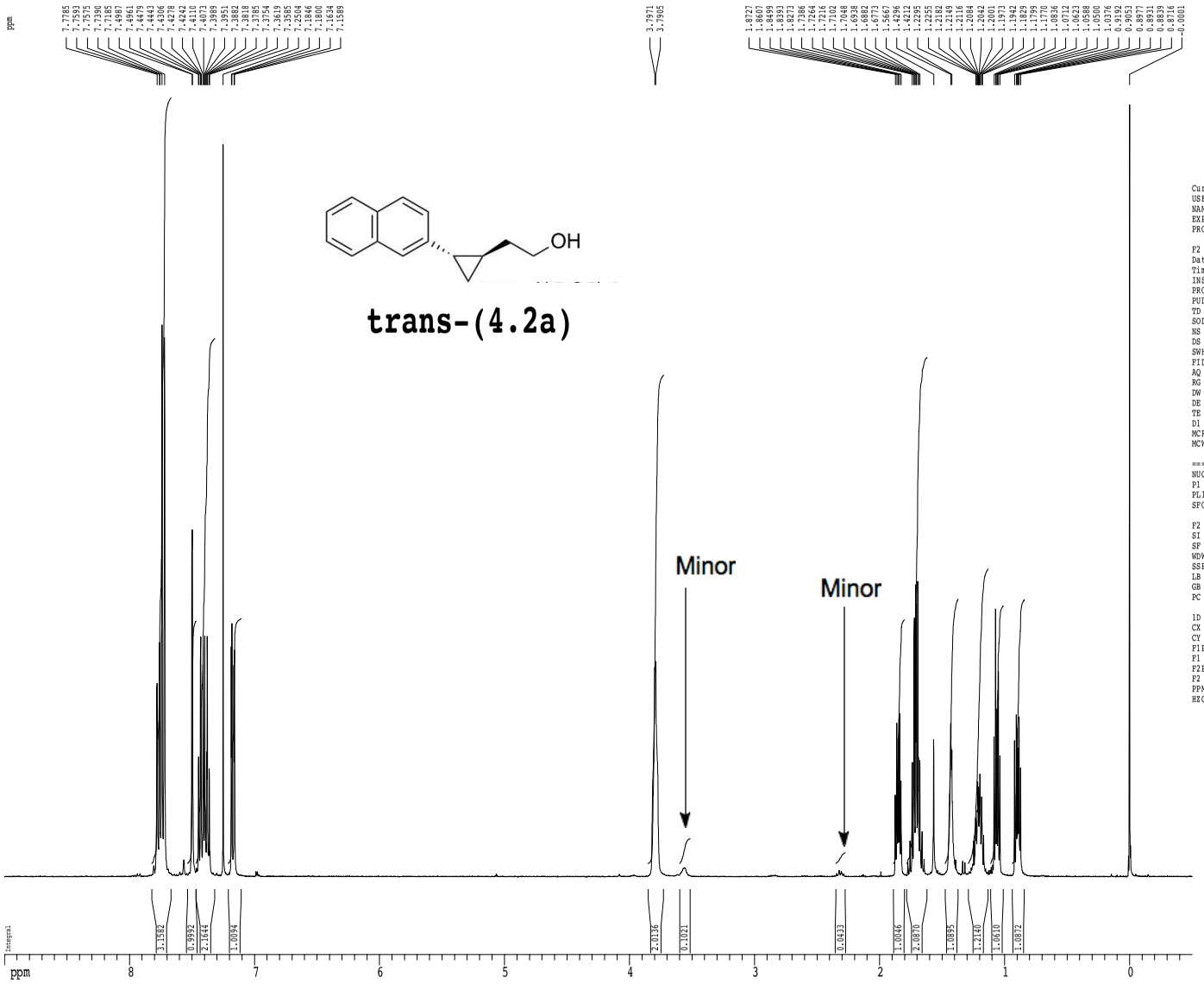
F2 - Acquisition Parameters
Date_ 20121113
Time 19.14
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200365 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 5.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm

PI Jarvo
h1 CDCl3 v emilyt 109



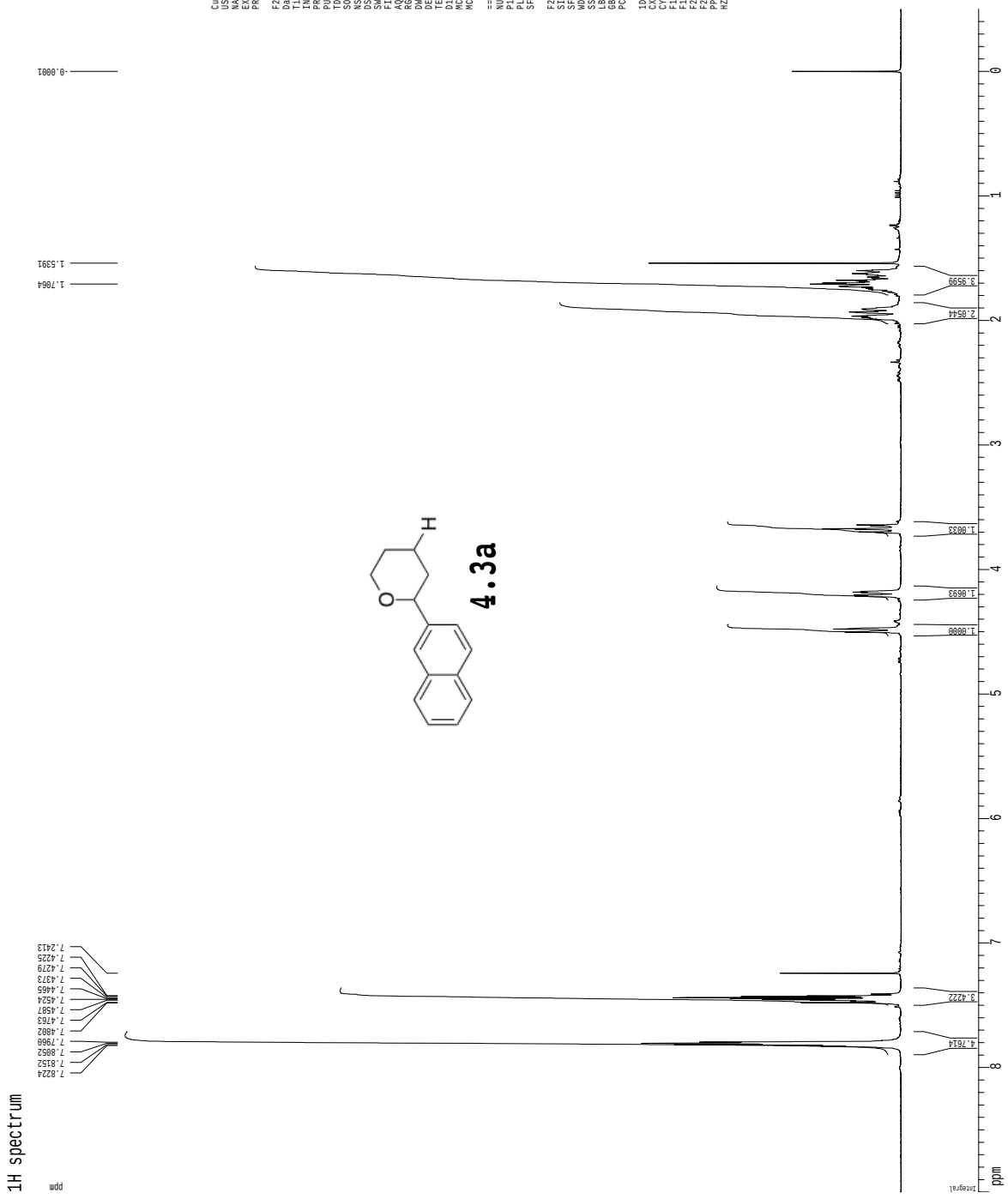
Current Data Parameters
USER emilyt
NAME EJT-IV-172 auto
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150410
Time 5.08
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 73274
SOLVENT CDCl3
NS 8
DS 2
SWH 7183.908 Hz
FIDRES 0.098042 Hz
AQ 5.0999203 sec
RG 287.4
DW 69.600 usec
DE 4.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

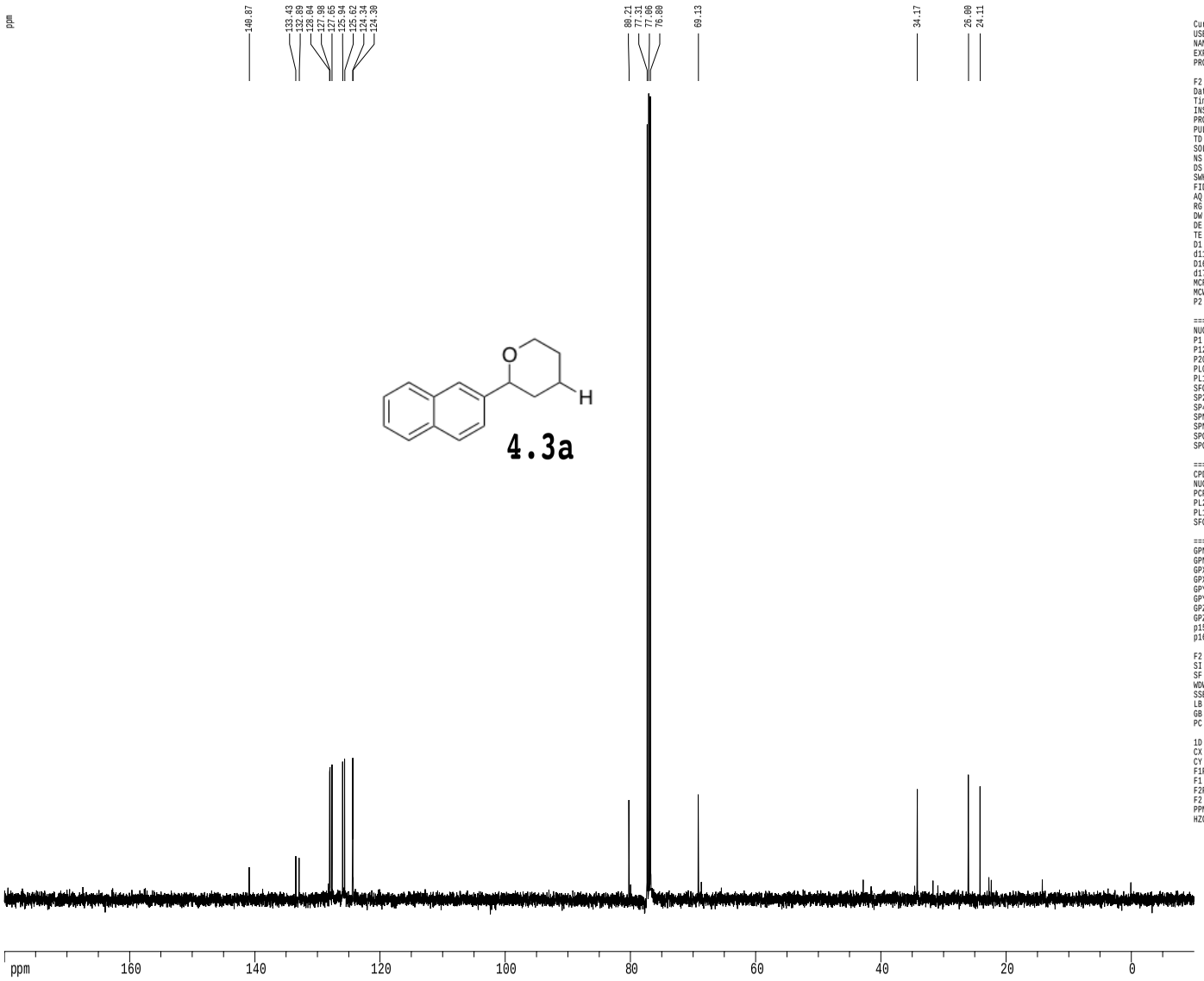
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 0.00 dB
SFO1 400.1328009 MHz

F2 - Processing parameters
SI 65536
SF 400.1300246 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3601.17 Hz
F2P -0.500 ppm
F2 -200.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 166.72086 Hz/cm


1H spectrum
4.3a
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm
integral
7.8224
7.8152
7.8052
7.7960
7.4802
7.4763
7.4587
7.4524
7.4465
7.4373
7.4279
7.4225
7.2413
1.5391
1.7064
3.9599
2.8644
1.0833
1.0693
1.0000
3.4222
4.7614

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                tthane
NAME      TATiii200f1invex
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_            20200111
Time                14.26
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp2.prd
TD                  65536
SOLVENT             CDCl3
NS                    352
DS                     16
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                 7208.2
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                33.10 usec

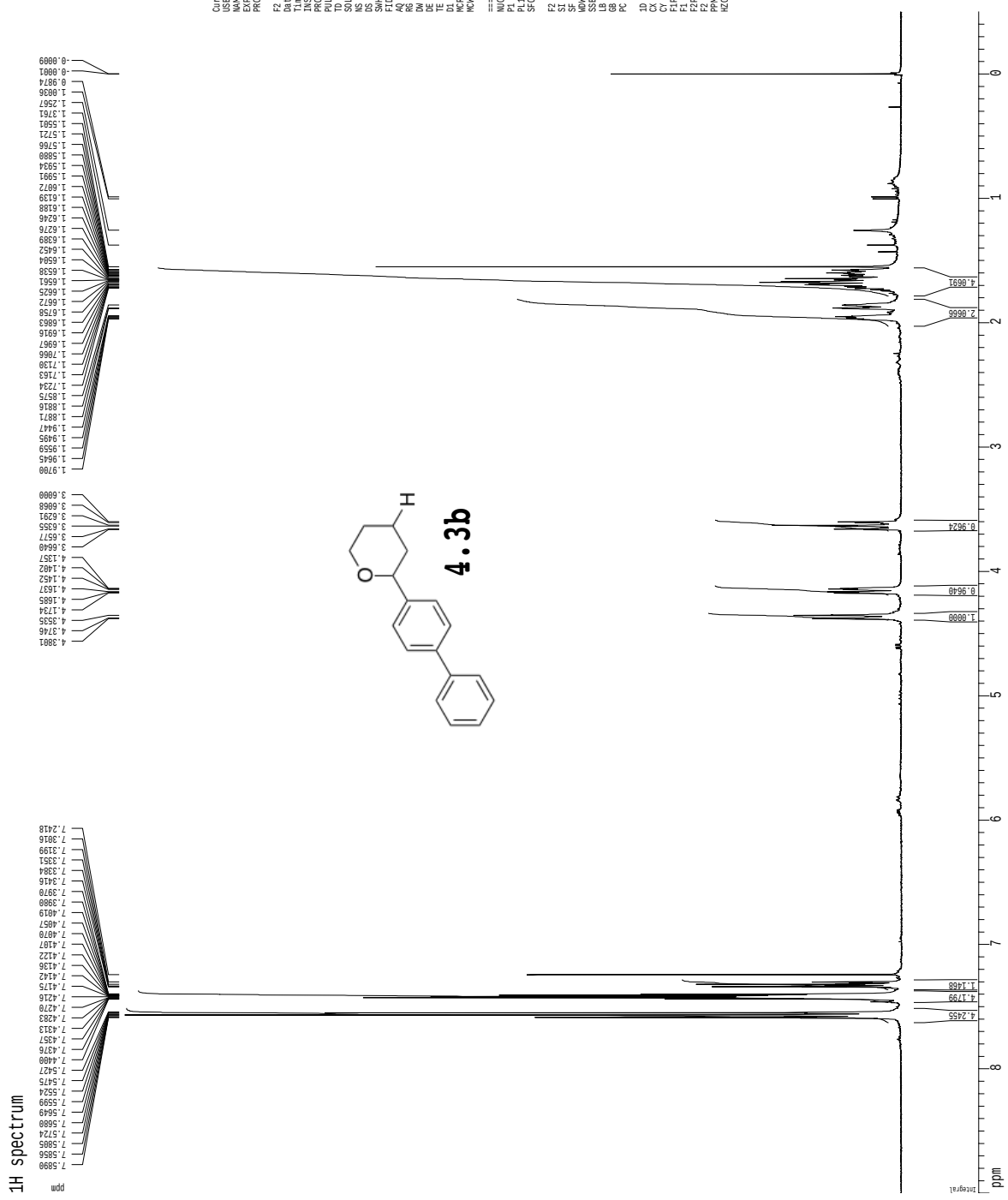
======== CHANNEL f1 =======
NUC1                 13C
P1                 16.55 usec
P12              2000.00 usec
P20               500.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP2                2.70 dB
SP4                2.70 dB
SPNAM2      Crp60comp.4
SPNAM4   Crp60,0.5,20.1
SPOFF2               0.00 Hz
SPOFF4               0.00 Hz

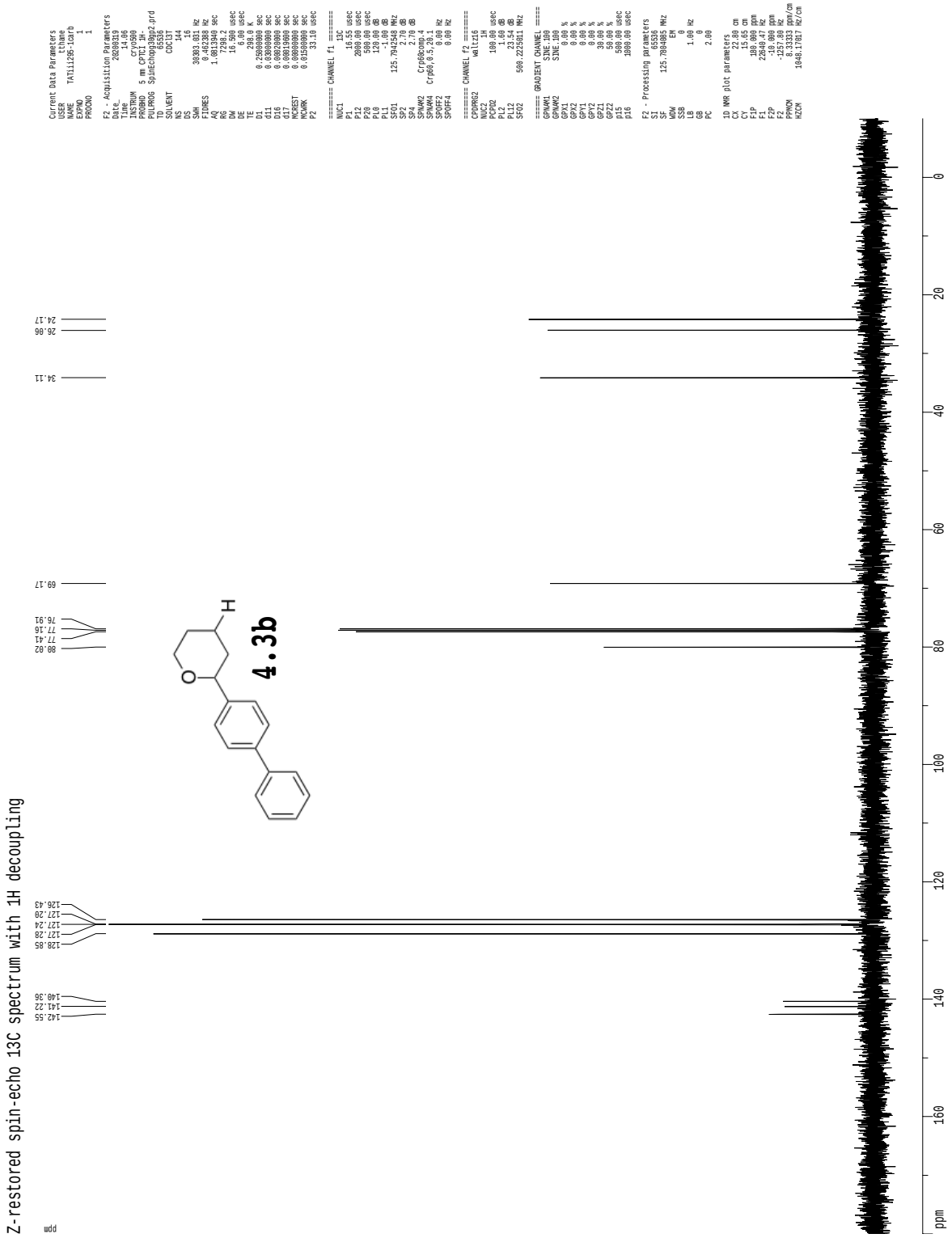
======== CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              23.54 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

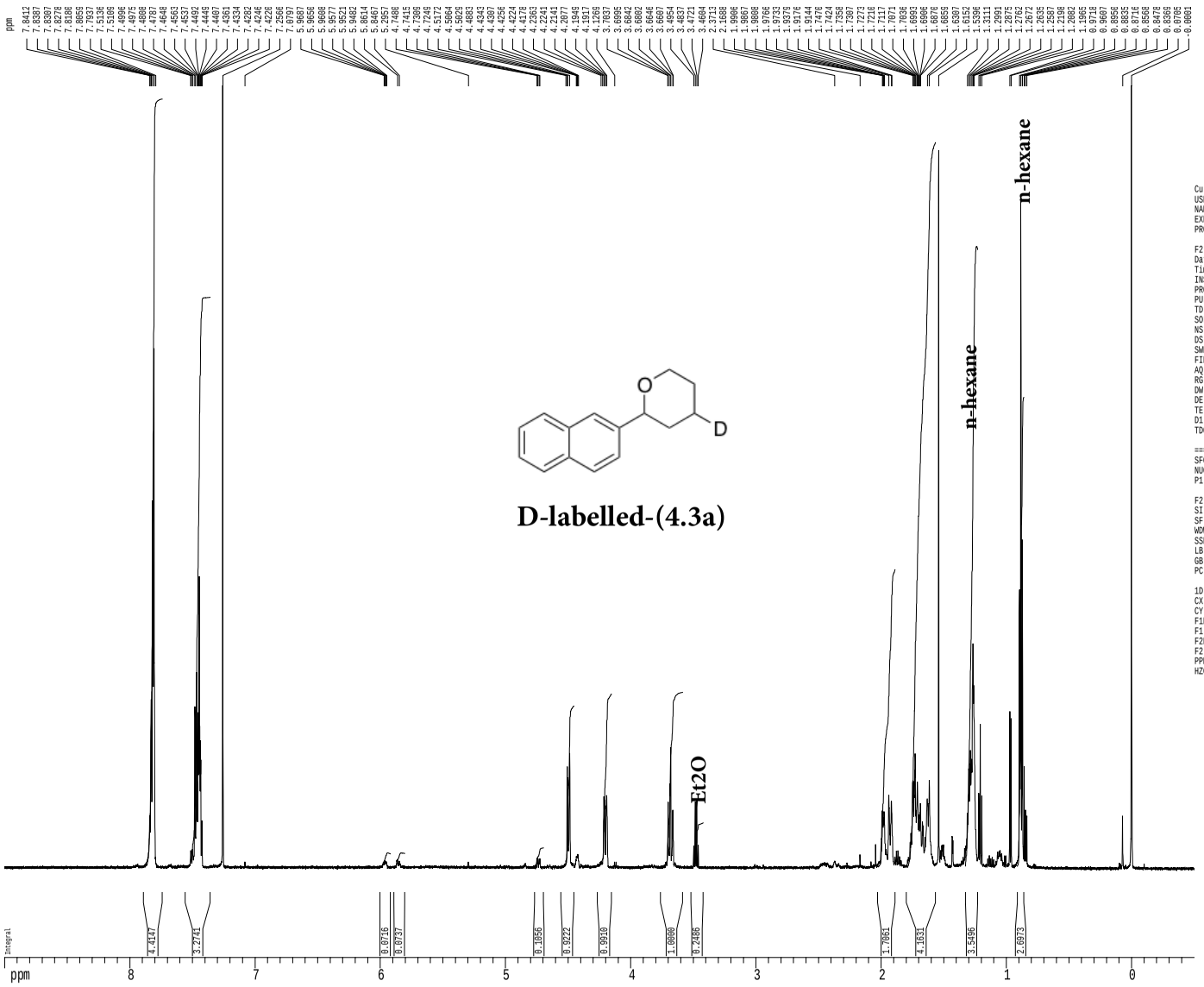
F2 - Processing parameters
SI                  65536
SF           125.7804198 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               180.000 ppm
F1              22640.47 Hz
F2P               -10.000 ppm
F2              -1257.80 Hz
PPMCM             8.33333 ppm/cm
HZCM           1048.17017 Hz/cm
```


1H spectrum
4.3b
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
4.3b
ppm

1H spectrum



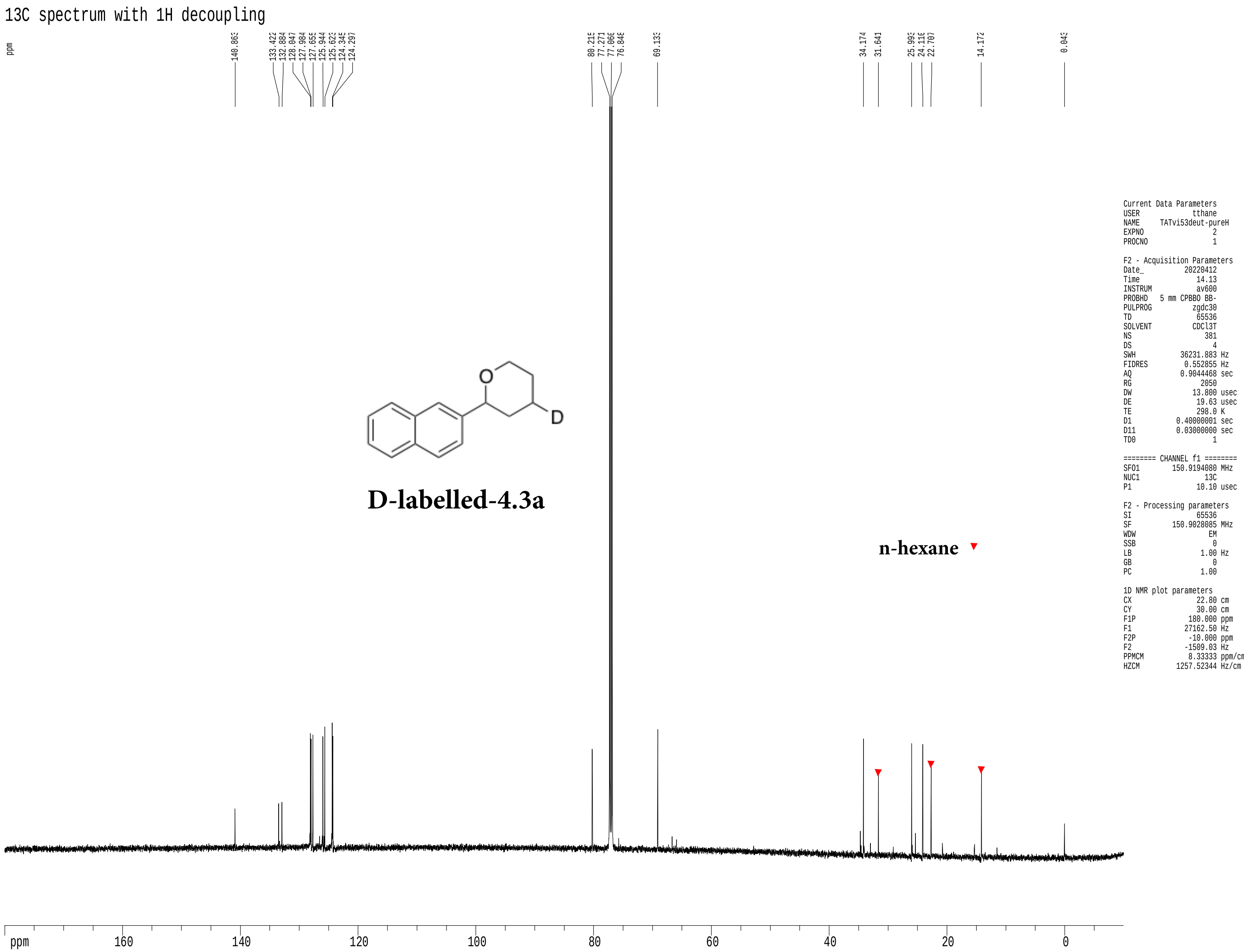
Current Data Parameters
USER tthane
NAME TATvi53deut-pureH
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220412
Time 14.08
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zg30
TD 98074
SOLVENT CDCl3T
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998979 sec
RG 10
DW 52.000 usec
DE 14.23 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1

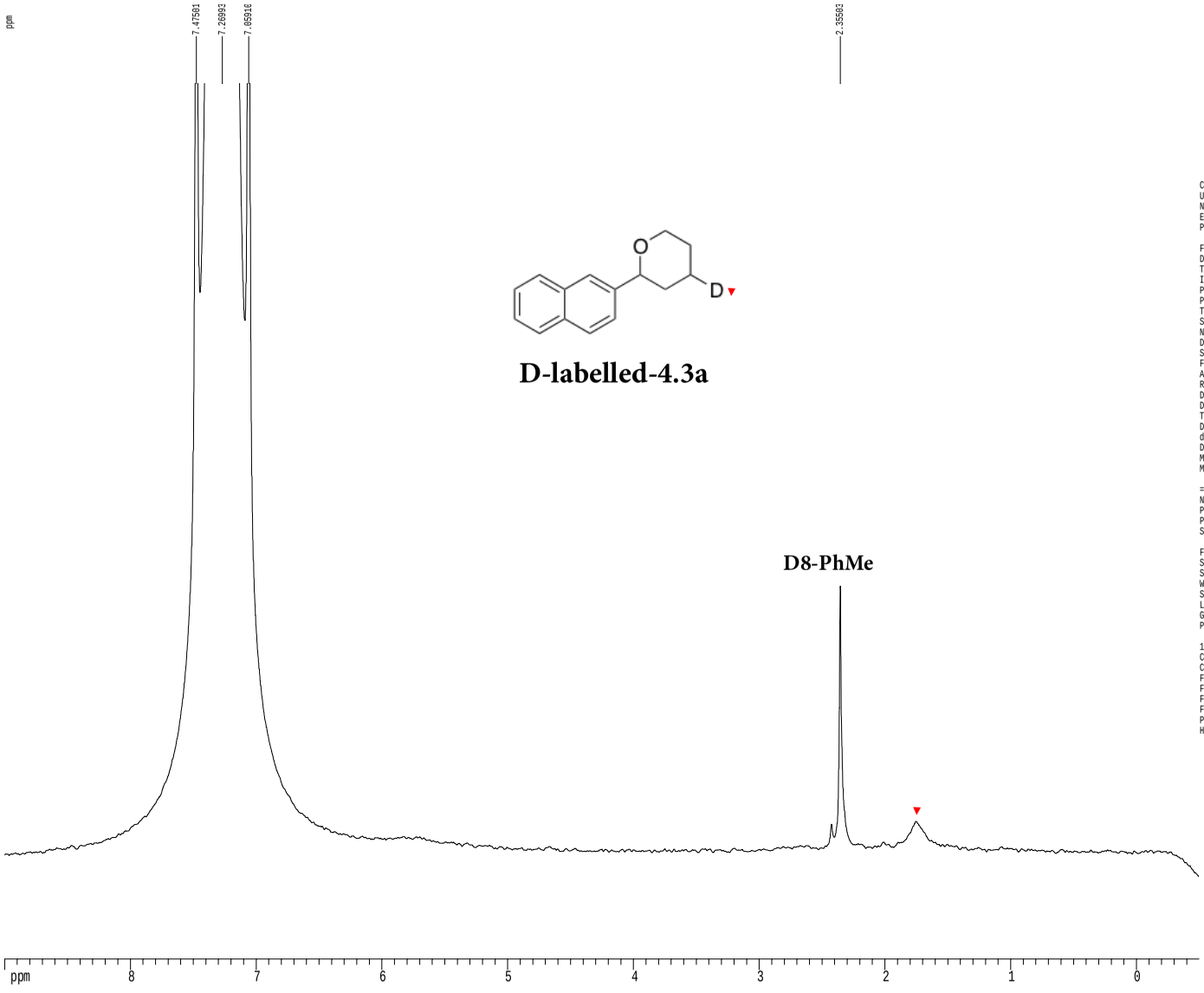
======== CHANNEL f1 =======
SFO1 600.1342009 MHz
NUC1 1H
P1 9.50 usec

F2 - Processing parameters
SI 65536
SF 600.1300372 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 20.00 cm
F1P 9.000 ppm
F1 5401.17 Hz
F2P -0.500 ppm
F2 -300.06 Hz
PPMCM 0.41667 ppm/cm
HZCM 250.05420 Hz/cm


13C spectrum with 1H decoupling
140.863
133.422
132.884
128.047
127.984
127.655
125.944
125.623
124.345
124.297
80.215
77.271
77.060
76.848
69.133
34.174
31.641
25.993
24.116
22.707
14.172
0.043
D
O
D-labelled-4.3a
n-hexane
Current Data Parameters
USER tthane
NAME TATvi53deut-pureH
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220412
Time 14.13
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3T
NS 381
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9044468 sec
RG 2050
DW 13.800 usec
DE 19.63 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9194080 MHz
NUC1 13C
P1 10.10 usec
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 30.00 cm
F1P 180.000 ppm
F1 27162.50 Hz
F2P -10.000 ppm
F2 -1509.03 Hz
PPMCM 8.33333 ppm/cm
HZCM 1257.52344 Hz/cm
ppm
160
140
120
100
80
60
40
20
0

2H spectrum (measure via the lock channel without changing any cables)



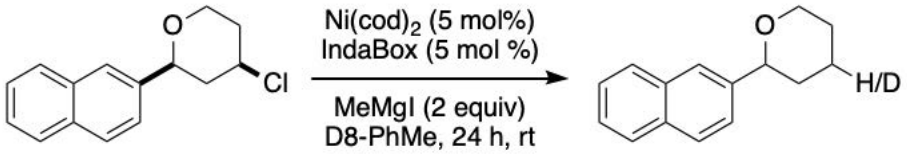

```
Current Data Parameters
USER                tthane
NAME            TATvi53-2H
EXPNO                   4
PROCNO                  1

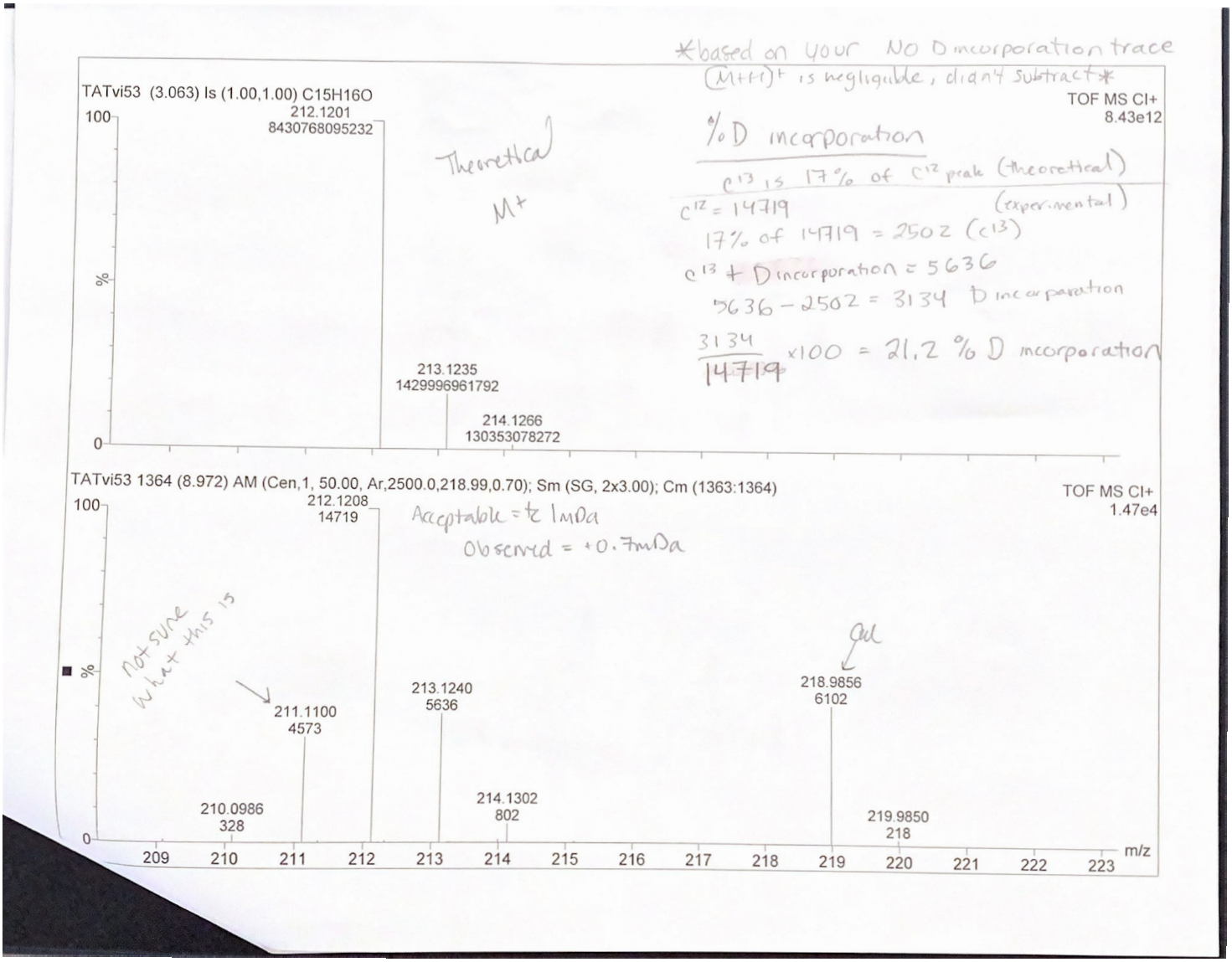
F2 - Acquisition Parameters
Date_            20220401
Time                15.17
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg302h
TD                  16384
SOLVENT             CDCl3
NS                     64
DS                      2
SWH              1230.315 Hz
FIDRES           0.075092 Hz
AQ               6.6585078 sec
RG                  456.1
DW                406.400 usec
DE                 20.39 usec
TE                 298.0 K
D1              5.00000000 sec
d11             0.03000000 sec
D20             0.02000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

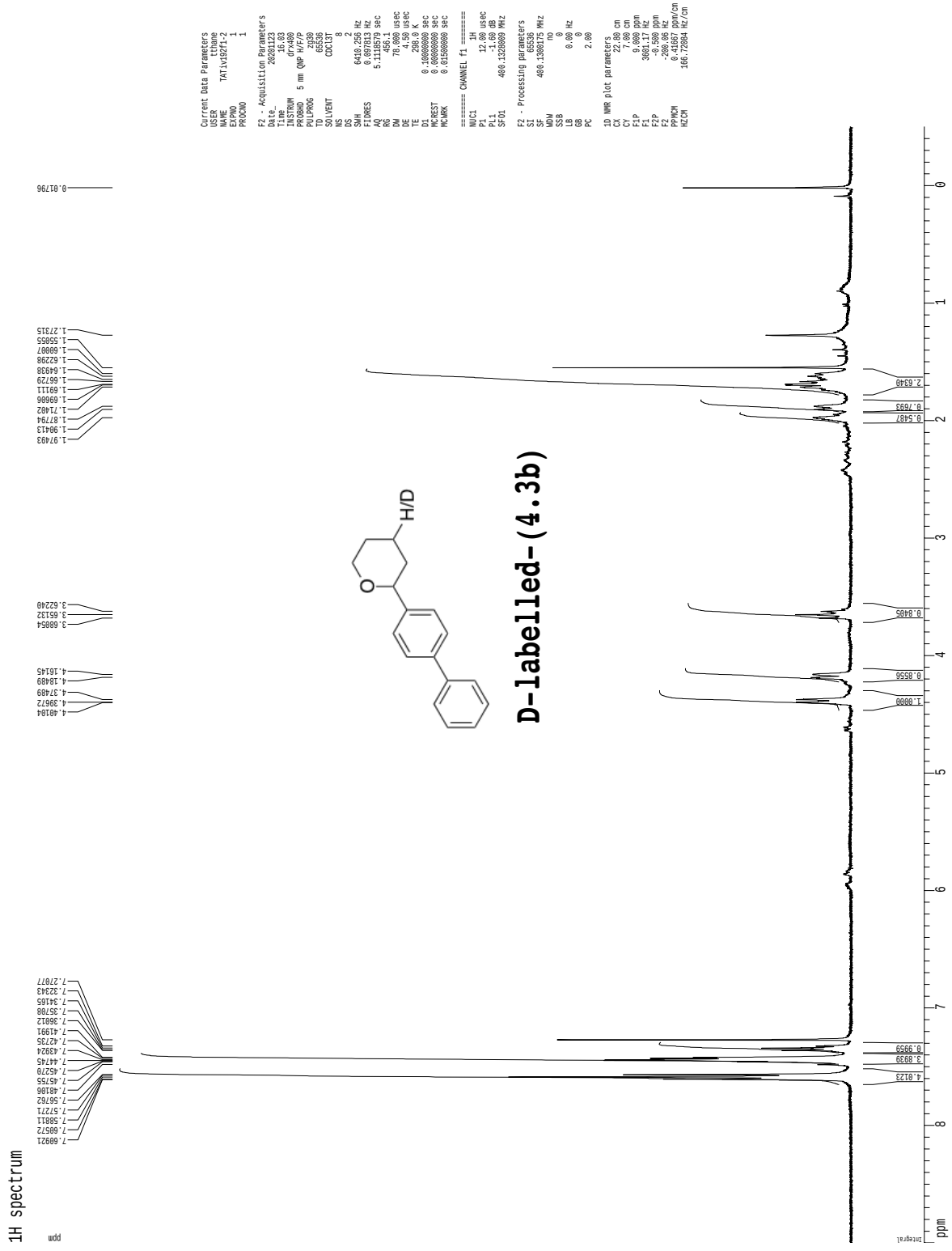
======== CHANNEL f1 ========
NUC1                    2H
P1                 130.00 usec
PL1                  0.50 dB
SFO1            76.7873535 MHz

F2 - Processing parameters
SI                   65536
SF              76.7867765 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.00

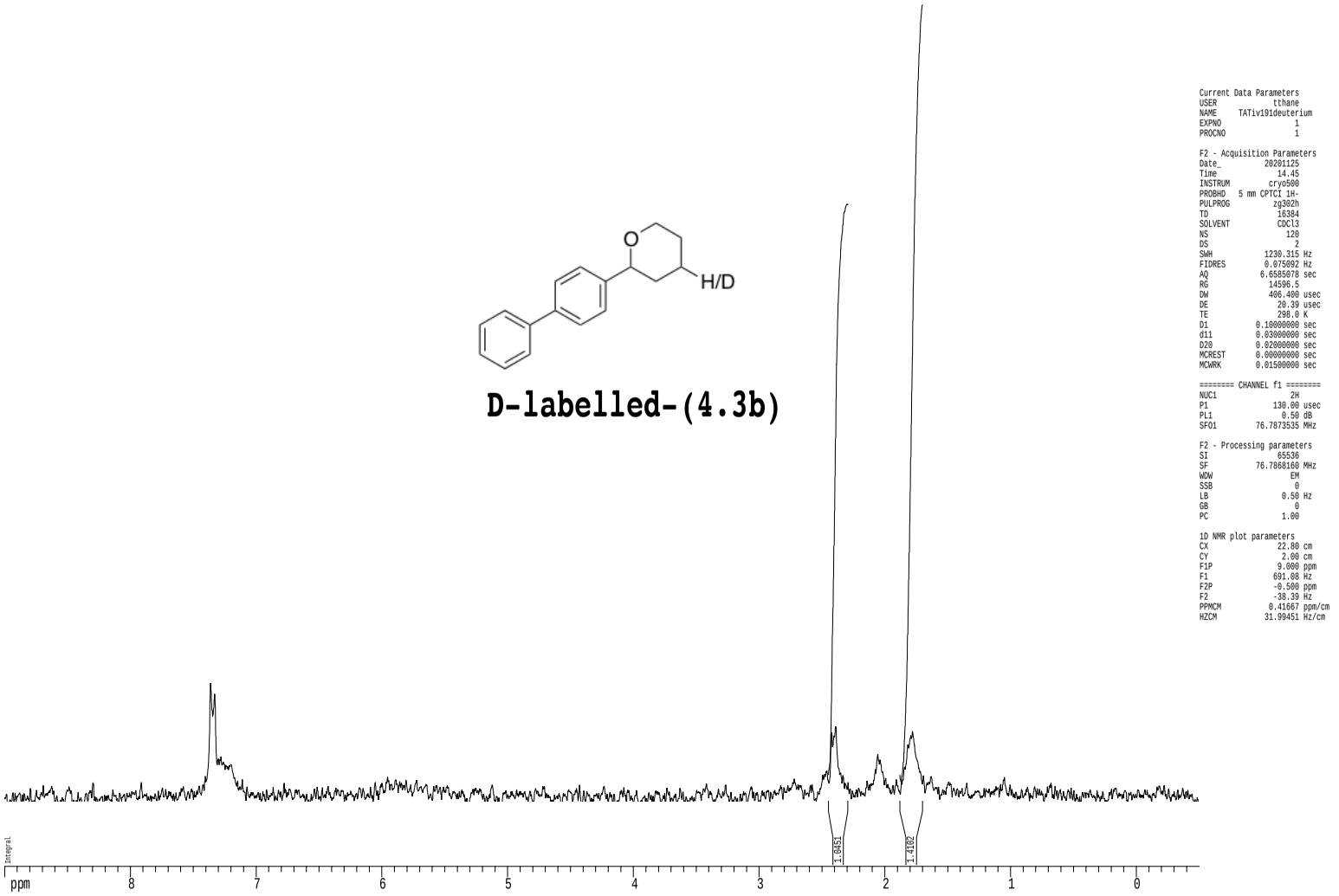
1D NMR plot parameters
CX                   22.80 cm
CY                 4000.00 cm
F1P                   9.000 ppm
F1                  691.08 Hz
F2P                  -0.500 ppm
F2                   -38.39 Hz
PPMCM             0.41667 ppm/cm
HZCM             31.99449 Hz/cm
```


Ni(cod)2 (5 mol%)
IndaBox (5 mol %)
MeMgI (2 equiv)
D8-PhMe, 24 h, rt
Cl
H/D


based on your NO D incorporation trace (M+H)+ is negligible, didn't subtract
TATvi53 (3.063) Is (1.00,1.00) C15H16O
TOF MS CI+
8.43e12
212.1201
8430768095232
213.1235
1429996961792
214.1266
130353078272
Theoretical M+
% D incorporation
C13 is 17% of C12 peak (theoretical)
C12 = 14719 (experimental)
17% of 14719 = 2502 (C13)
C13 + D incorporation = 5636
5636 − 2502 = 3134 D incorporation
3134 / 14719 x100 = 21.2 % D incorporation
TATvi53 1364 (8.972) AM (Cen,1, 50.00, Ar,2500.0,218.99,0.70); Sm (SG, 2x3.00); Cm (1363:1364)
TOF MS CI+
1.47e4
212.1208
14719
Acceptable = ± 1mDa
Observed = +0.7mDa
not sure what this is
211.1100
4573
213.1240
5636
214.1302
802
210.0986
328
218.9856
6102
219.9850
218
m/z


1H spectrum
D-labelled-(4.3b)
H/D
O
ppm
Integral
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters

2H spectrum (measure via the lock channel without changing any cables)



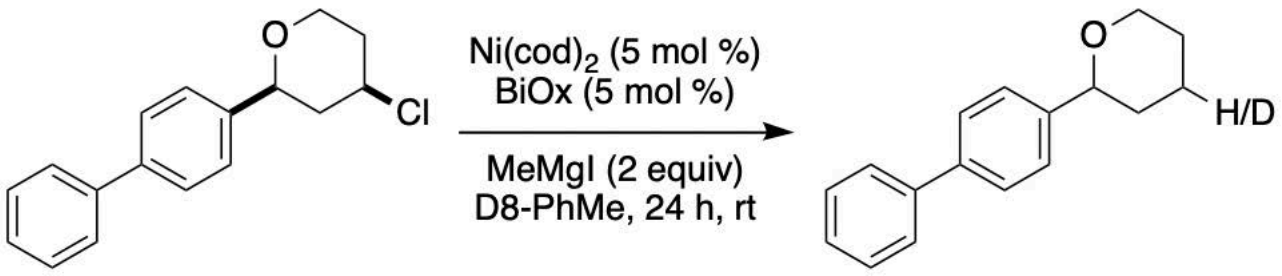

```
Current Data Parameters
USER              tthane
NAME      TATiv191deuterium
EXPNO                 1
PROCNO                1

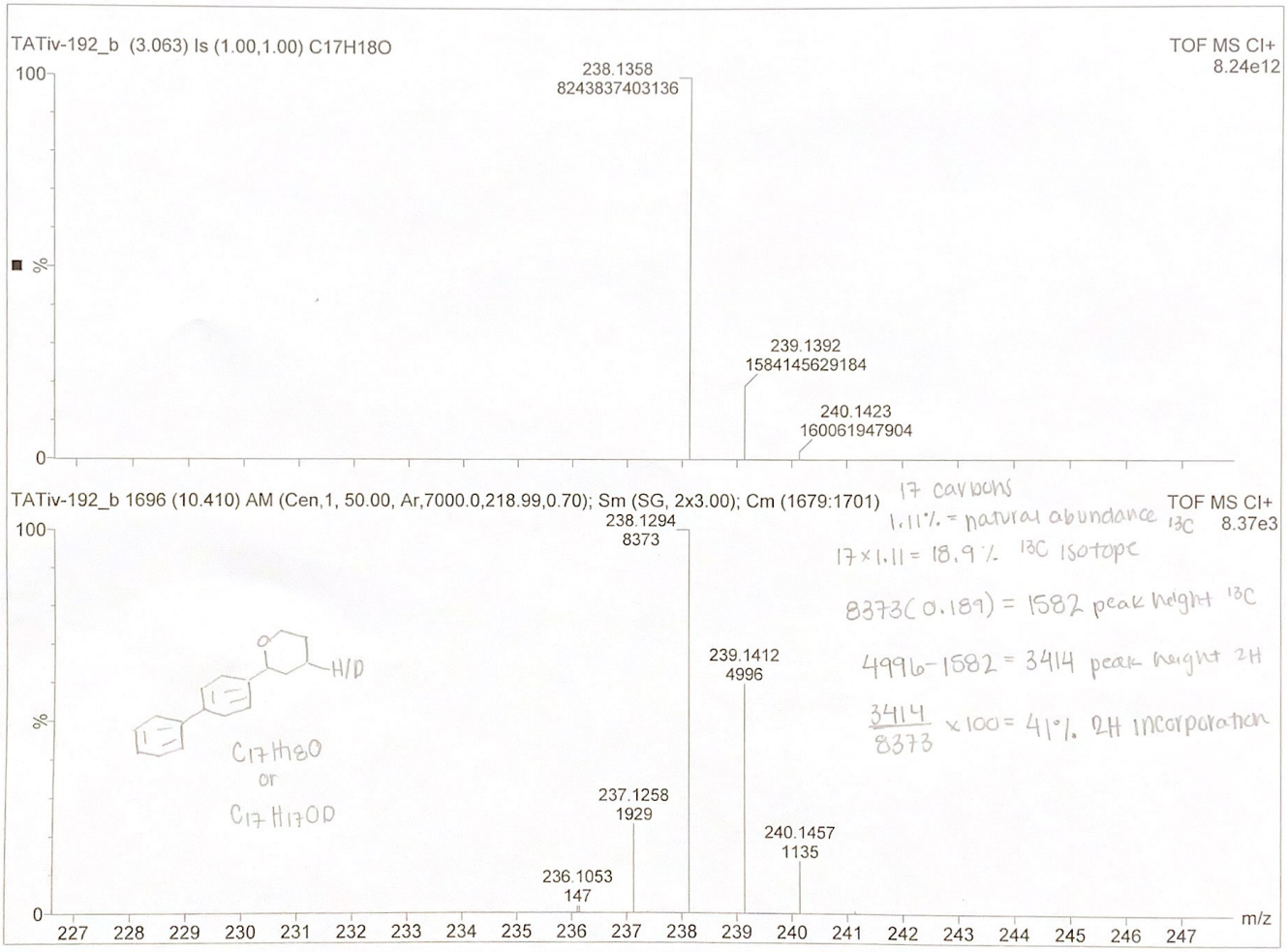
F2 - Acquisition Parameters
Date_          20201125
Time              14.45
INSTRUM         cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG          zg302h
TD                16384
SOLVENT           CDCl3
NS                  120
DS                    2
SWH            1230.315 Hz
FIDRES        0.075092 Hz
AQ             6.6585078 sec
RG               14596.5
DW               406.400 usec
DE                20.39 usec
TE                298.0 K
D1            0.10000000 sec
d11           0.03000000 sec
D20           0.02000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======= CHANNEL f1 =======
NUC1                  2H
P1               130.00 usec
PL1                0.50 dB
SFO1          76.7873535 MHz

F2 - Processing parameters
SI                 65536
SF            76.7868160 MHz
WDW                   EM
SSB                    0
LB                  0.50 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 22.80 cm
CY                  2.00 cm
F1P                9.000 ppm
F1                 691.08 Hz
F2P               -0.500 ppm
F2                 -38.39 Hz
PPMCM           0.41667 ppm/cm
HZCM           31.99451 Hz/cm
```


O
Cl
Ni(cod)2 (5 mol %)
BiOx (5 mol %)
MeMgI (2 equiv)
D8-PhMe, 24 h, rt
O
H/D


TATiv-192_b (3.063) Is (1.00,1.00) C17H18O
TOF MS CI+
8.24e12
238.1358
8243837403136
239.1392
1584145629184
240.1423
160061947904
TATiv-192_b 1696 (10.410) AM (Cen,1, 50.00, Ar,7000.0,218.99,0.70); Sm (SG, 2x3.00); Cm (1679:1701)
TOF MS CI+
8.37e3
238.1294
8373
239.1412
4996
237.1258
1929
240.1457
1135
236.1053
147
H/D
C17H18O
or
C17H17OD
17 carbons
1.11% = natural abundance 13C
17 × 1.11 = 18.9 % 13C isotope
8373(0.189) = 1582 peak height 13C
4996 − 1582 = 3414 peak height 2H
3414/8373 × 100 = 41% 2H incorporation
m/z