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“Chiral Pool” Based Routes to Terpenoids, Jungermatrobrunin A and Xishacorene B, and Oxidative Coupling Approaches to Scholarinine A and Pleiocarpamine

by

Kerry E. Jones

A dissertation submitted in partial satisfaction of the

requirements for the degree of

Doctor of Philosophy

in

Chemistry

in the

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of the

University of California, Berkeley

Committee in charge:

Professor Richmond Sarpong, Chair
Professor Thomas Maimone
Professor Gregory W. Aponte

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Abstract

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Total synthesis is often pursued for one of two motivations: to showcase a strategy and/or methodology or to investigate the function of a natural product. The work described in this dissertation will span an array of natural products but focus on both of these motivations.

Chapter 1 briefly discusses “chiral pool” syntheses to give context for some of the work outlined in Chapters 2, 3, and 4 of this dissertation.

Chapter 2 discloses work toward rearranged *ent*-kaurene jungermatrobrunin A, utilizing a “chiral pool” starting material. We employed a “chiral pool” building block to synthesize a common decalin intermediate in enantioenriched fashion. Several potential routes to carry the decalin on to the jungermatrobrunin A framework are discussed. Additionally, the formal synthesis of two natural products, erigerol and forskolin, from the decalin intermediate are described.

Chapters 3 and 4 outline the work completed toward the terpene xishacorene B. Chapter 3 focuses on the rearrangements of chrysanthenone derivatives that were discovered while attempting to forge the [3.3.1]bicyclic core of the natural product. These rearrangements were studied experimentally and computationally. The mechanism and underlying principles that were elucidated then aided in the synthesis of the [3.3.1]bicyclic core. Chapter 4 focuses on efforts to take the [3.3.1]bicyclic core to the natural product, highlighting key directed C–H functionalization efforts.

Chapter 5 outlines efforts toward the alkaloid scholarinine A through a key oxidative coupling route. An efficient synthesis of scholarinine A would enable our collaborators, Corteva AgriSciences, to probe insecticidal activity of the natural product. Several attempted routes to the carbocyclic framework of scholarinine A are discussed in addition to a potential route to the alkaloid pleiocarpamine.

Overall, this dissertation spans an array of targets, detailing work toward both terpene and alkaloid derived natural products.

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Acknowledgments

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Experimental General Information

Solvents and Reagents

Unless otherwise stated, commercial reagents were purchased and used without purification. Solvents including tetrahydrofuran (THF), diethyl ether (Et_2O), benzene (PhH), toluene (PhMe), methanol (MeOH), acetonitrile (MeCN), and triethylamine (Et_3N) were dried by passage through activated alumina columns using argon in a Glass Contour solvent purification system. Dichloromethane (DCM) and diisopropylamine (DIPA) were distilled over calcium hydride under nitrogen. Cyclohexane (HPLC grade) and dichloroethane (DCE, dry and packaged under nitrogen) were used without purification. All commercial reagents were used without additional purification unless otherwise specified. Deuterated solvents were purchased from Cambridge Isotope Laboratories and were used without further purification unless otherwise specified.

Experimental Procedures

Unless otherwise stated, all reactions were performed in flame-dried or oven-dried glassware under an atmosphere of positive nitrogen pressure using Teflon-coated stir bars. Air and moisture-sensitive liquids were transferred by syringe through rubber septa. Solids were added under inert gas or were dissolved in the appropriate solvent and added by syringe and needle. Reactions ran above room temperature were heated in a metal block or oil bath with a thermocouple; room temperature is defined as 23 ^{o}C. Low temperature reactions were carried out in a Dewar flask filled with 2-propanol/dry ice (–78 ^{o}C) or water/ice (0 ^{o}C). Reaction progress was monitored by thin layer chromatography (TLC) and gas chromatography mass spec (GCMS). TLC and preparative TLC were performed on glass-backed Silicycle SiliaPlate 250 µm thickness, 60 Å porosity F-254 precoated plates. GCMS analysis was conducted using a Shimadzu GCMS-QP2010 SE. Photoreactions were performed using either a Penn OC M2 photoreactor equipped with a 365 nm light source or a sunlamp (1900 lumens, 90W) with a standing fan. Microwave reactions were carried out using a Biotage Initiator+ microwave synthesizer. Flash column chromatography was performed on Silicycle SiliaFlash P60 silica gel (230−400 mesh, 40−63 µm particle size). Compounds were visualized with UV light (254 nm) and stained with aqueous potassium permanganate (KMnO4), p-anisaldehyde and heat, or cerium ammonium molybdate (CAM) and heat.

Analytical Instrumentation

Nuclear magnetic resonance (NMR) spectra were obtained on Bruker AV-300, AVQ-400, AVB-400, AV-500, NEO-500, AV-600, and AV-700 instruments at UC Berkeley's College of Chemistry NMR Facility. [Note: these instruments are partially funded by the following grants: NSF grant CHE-0130862 and NIH grants 1S10RR016634-01, SRR023679A, and S10OD024998.] Residual solvent was used as an internal reference. For chloroform ($CHCl_3$), ^{1}H (δ = 7.26 ppm) and ^{13}C (δ = 77.16 ppm), for benzene, ^{1}H (δ = 7.16 ppm) and ^{13}C (δ = 128.06 ppm), and for DMSO, ^{1}H (δ = 2.50 ppm) and ^{13}C (δ = 39.52 ppm). Experiments were conducted at 25 ^{o}C unless otherwise stated. The following abbreviations were used to describe the NMR multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, h = heptet, m = multiplet, br = broad. Ethylene carbonate was used as an internal standard for quantitative NMR. Coupling constants (J) are given in Hertz.

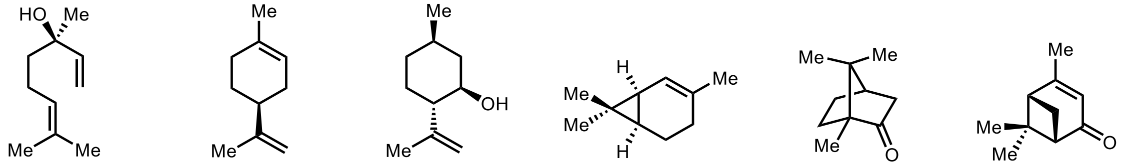
Infrared (IR) spectroscopy data were obtained on a Bruker ALPHA FT-IR spectrophotometer using a diamond attenuated total reflectance (ATR) accessory. Analytes were dissolved in chloroform prior to direct application on the ATR unit. Frequency of absorption is given in cm^{-1}. High-resolution mass spectra (HRMS) were obtained from the Mass Spectral Facility at the University of California, Berkeley, on a Finnigan/Thermo LTQ-FT instrument (ESI) or an AutoSpec Premier mass spectrometer (Waters, Manchester, UK), utilizing electron impact (EI). Optical rotations were measured on a PerkinElmer 241 Polarimeter. Melting points were measured on a Laboratory Devices Mel-Temp II.

Chapter 1

The “Chiral Pool” in Total Synthesis

1.1 Brief Introduction to the Terpenoid “Chiral Pool” in Total Synthesis

Total synthesis is a field of organic synthesis that focuses on making complex compounds (often those found in nature) from simpler starting materials. These syntheses are pursued with the following motivations: to showcase synthetic methodology and strategy on complex substrates, or to investigate the function (i.e. biological activity) of the natural products. Often, “chiral pool” materials are employed as starting points for these synthesis efforts.[1–5] “Chiral pool” molecules are so named because they are a pool of chiral small molecules that are naturally available and enantioenriched. They include amino acids, sugars, and terpenoids. Specifically, we will discuss the terpenoid “chiral pool” in more detail. These compounds, which are derived from isoprene, range in carbocyclic framework and oxidation pattern as demonstrated by representative examples displayed in Figure 1.1 (see **1.1**–**1.6**).



(–)-citronellol (**1.1**) (+)-limonene (**1.2**) (–)-isopulegol (**1.3**) (+)-2-carene (**1.4**) (+)-camphor (**1.5**) (–)–verbenone (**1.6**)

Figure 1.1 Representative “chiral pool” terpenoids.

Maimone and coworkers state that “chiral pool” syntheses are influenced by three major factors: (1) the availability of the starting materials, (2) state-of-the-art methodology that can be implemented, and (3) creativity in the synthesis strategy that is adopted.[5] “Chiral pool” terpenoids are often commercially available and cheap, providing access to enantioenriched material at low cost. Additionally, by starting a synthesis from an enantioenriched material, enantioenriched products can be accessed without the need for an enantioselective step in the synthesis, which can be non-trivial. In terms of the second and third influence, state-of-the-art methodologies coupled with creativity allow researchers to transform the original material into a wide array of compounds, expanding the chemical space accessible by beginning from the “chiral pool”.

The third factor is most evident when the framework of the starting terpene is overlayed with the natural product to showcase the structural similarities (or lack thereof) between the two molecules. On the basis of the structural overlap between the compounds, the syntheses can be categorized into three levels. In Level 1 syntheses, the “chiral pool” material can be directly mapped onto the target.[5] In Level 2 syntheses, the “chiral pool” material can be partially mapped onto the target, and in Level 3 syntheses, the "chiral pool" starting material is not recognizable in the target without an in-depth analysis.[5]

Examples of these types of syntheses are showcased in Figure 1.2. Danishefsky and coworkers developed a Level 1 synthesis of eleutherobin (**1.7**) starting from the "chiral pool" terpene (–)-α-phellandrene (**1.8**) that maps directly onto the eastern-most ring.[6] Smith and coworkers developed a Level 2 synthesis of jatropholone A (**1.9**) starting from (–)-carene (**1.4**) that employed a ring expansion of the "chiral pool" material.[7] In terms of Level 3 syntheses, Kishi and coworkers synthesized ophiobolin C (**1.10**) starting from (+)-camphor (**1.5**). In the Kishi synthesis, cleavage of the [2.2.1]bicycle formed the highly functionalized cyclopentane of the natural product.[8] In this synthesis, the carbons of the starting material can be traced back, step-by-step, to see where they end up in the natural product. However, the retrosynthetic disconnection back to camphor (**1.5**) is not intuitive. Another example of a Level 3 synthesis is Bermejo and coworkers' synthesis of (+)-paeonisuffrone (**1.11**) from (+)-carvone (**1.12**) wherein the remodeling the cyclohexanone core to the pinene derived scaffold of the target molecule is achieved.[9]

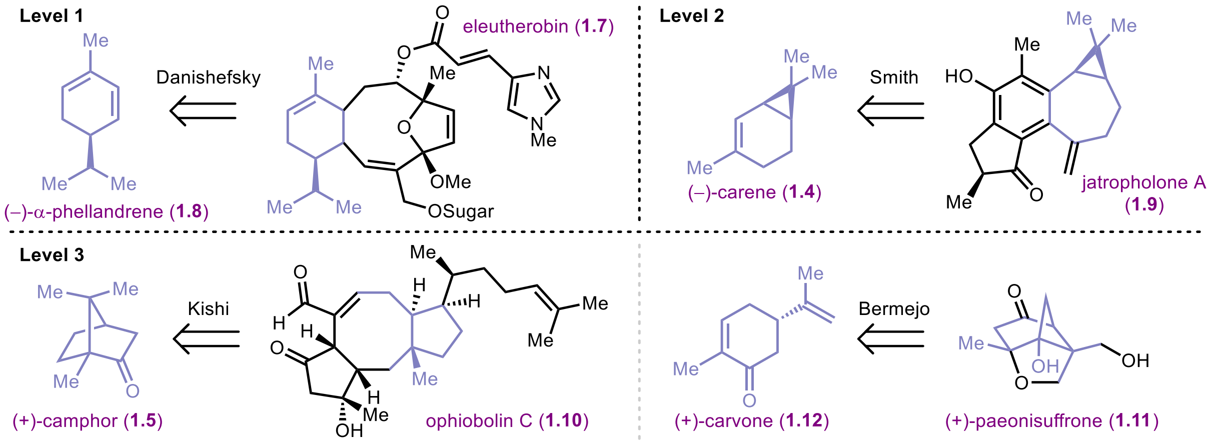


Figure 1.2 Levels 1, 2, and 3 syntheses of natural products originating from "chiral pool" terpenes.

These Level 3 syntheses employ a strategy that has been termed "chiral pool" remodeling, wherein native functional groups are leveraged to remodel the carbon skeleton of the "chiral pool" molecule. This strategy grants access to a broader array of novel structures, allowing entry to a diverse chemical space. This approach allows researchers to overcome the inherent constraints of the terpenoid "chiral pool", specifically, the limited number of available carbocyclic scaffolds.

1.2 Select Examples of "Chiral Pool" Total Syntheses

1.2.1 Reisman's Synthesis of Ryanodol

In 2016, Reisman and coworkers reported a Level 1 synthesis of the highly oxygenated diterpenoid ryanodol (**1.13**) starting from the "chiral pool" terpenoid (–)-pulegone (**1.14**).[10] Starting from (–)-pulgone (**1.14**), highly functionalized cyclohexane **1.15** was formed in four steps

(Figure 1.3). Acetylide addition, followed by a cyclization-elimination cascade, and vinyl conjugate addition subsequently afforded lactone **1.16** in good yield. Lactone **1.16** was well poised for a Pauson–Khand reaction to form the [5.5]-fused system. Oxidation of the cyclopentenone, triflation, and Stille coupling yielded diene **1.17**. Finally, a four-step sequence of functional group manipulations gave rise to ryanodol (**1.13**) in 15 steps from (–)-pulegone (**1.14**).

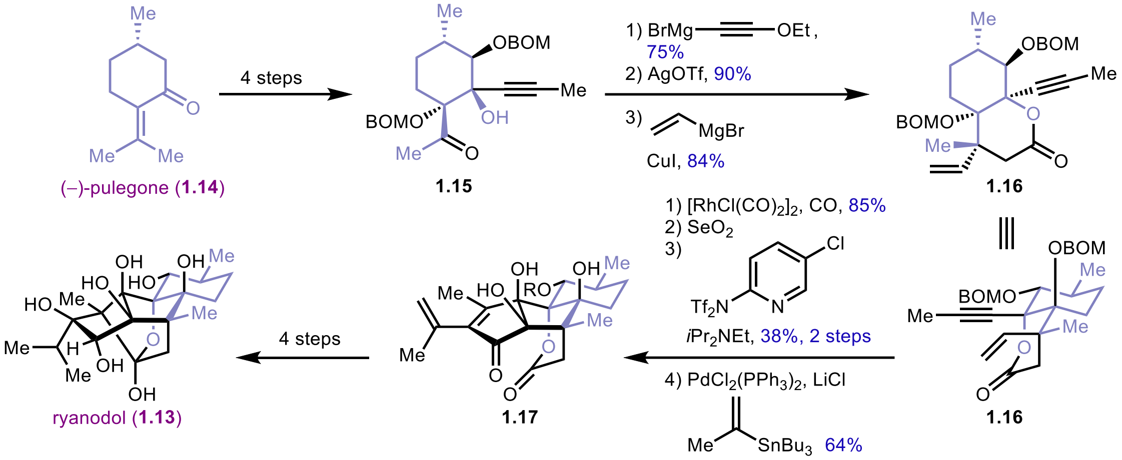


Figure 1.3 Reisman and coworkers' synthesis of ryanodol (**1.13**) from (–)-pulgone (**1.14**).

This Level 1 synthesis showcases the benefits from proper recognition of a suitable "chiral pool" starting material. By starting from (–)-pulegone (**1.14**), Reisman and coworkers were able to install all the requisite functionality of the natural products' cyclohexane ring by leveraging activated positions or the inherent functional groups on the "chiral pool" material. This approach then enabled a rapid synthesis of the highly oxygenated natural product.

1.2.2 Romo's Synthesis of (+)-Omphadiol from (–)-Carvone

In 2011, Romo and coworkers reported a synthesis of the sesquiterpenoid (+)-omphadiol (**1.18**), which is a member of the africanane family of natural products.[11] These natural products all contain a highly functionalized cyclopentane moiety. Therefore, in developing their synthesis, Romo and coworkers initially focused on the cyclopentane fragment, setting the stage for the possibility of a divergent synthesis.

Romo and coworkers started their synthesis from the "chiral pool" terpenoid (–)-carvone (***ent*-1.12**, Figure 1.4), beginning with a Mukaiyama-type hydration followed by oxidative cleavage to afford ketoacid **1.19**. Aldol lactonization of ketoacid **1.19** via enolate **1.20** gave rise to β-lactone **1.21** which was subsequently converted to alkyl bromide **1.22**. An enolate-alkylation then gave δ-lactone **1.23**. Allyl addition and ring-closing metathesis produced enone **1.24** which upon reduction and Simmons–Smith cyclopropanation afforded (+)-omphadiol (**1.18**) in just 10 steps from the commercial "chiral pool" terpene in a total yield of 18% yield.

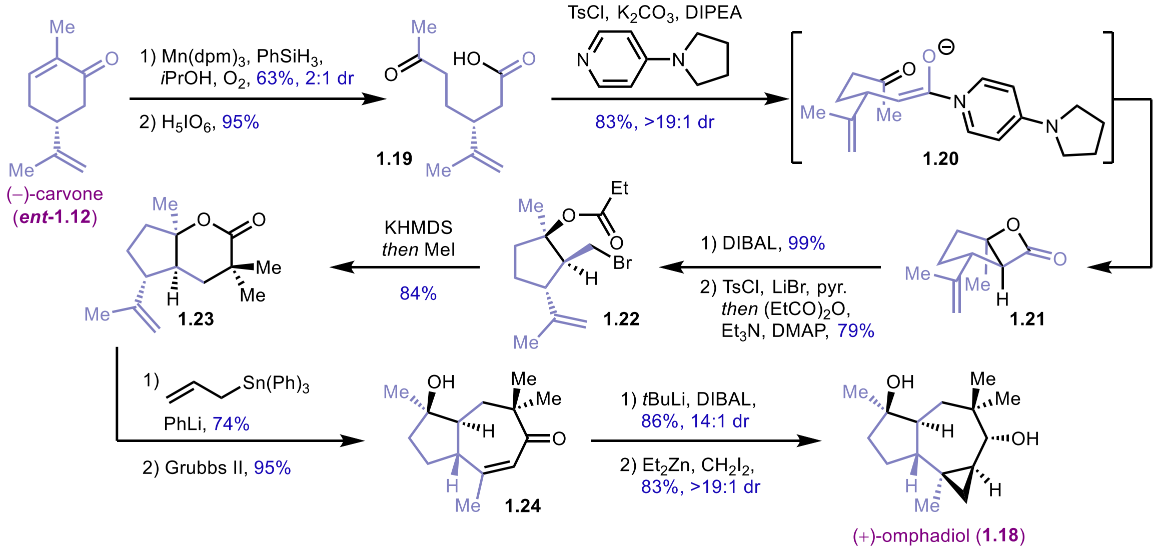


Figure 1.4 Romo and coworkers' synthesis of (+)-omphadiol (**1.18**).

This Level 3 synthesis showcases how chiral pool inputs can be readily transformed to fit the needs of a given synthesis. In this case, the parent cyclohexane ring of carvone was transformed into the requisite cyclopentane in short order through a ring opening-ring closing sequence. Ring contraction (or, analogously, ring expansion) is a common technique utilized in "chiral pool" total synthesis efforts, often transforming the common cyclohexane moieties into other ring sizes, allowing entry to a wider array of targets. This is a modest example of "chiral pool" remodeling, which, nonetheless, expands the utility of available starting inputs and facilitates access to unique chemical space with greater ease and efficiency.

1.2.3 Sarpong's Synthesis of the Longiborneol Sesquiterpenoids from (+)-Carvone

In 2022, Sarpong and coworkers reported a synthesis of longiborneol (**1.25**) as well as oxidized congeners in the family.[12,13] This Level 3 synthesis started from (+)-carvone (**1.12**) and employed a "chiral pool" remodeling strategy to transform the cyclohexane found in **1.12** to pinene derivative **1.26** and, upon semi-pinacol rearrangement, camphor derivative **1.27** was accessed (Figure 1.5). Wittig olefination gave diene **1.28** which was transformed to the corresponding vinyl phenyl sulfonate which upon iron-mediated hydrogen atom transfer (HAT) cyclization formed cycloheptene **1.29**. A series of reductions then afforded longiborneol (**1.25**) in a total of nine steps from (+)-carvone (**1.12**). Oxidized congener culmorin (**1.30**) was synthesized by undirected oxidation with methyl(trifluoromethyl)dioxirane (TFDO) and additional functional group manipulations. Additional oxidized natural products were synthesized from intermediates along the synthetic route, ultimately leading to the total synthesis of nine natural products.

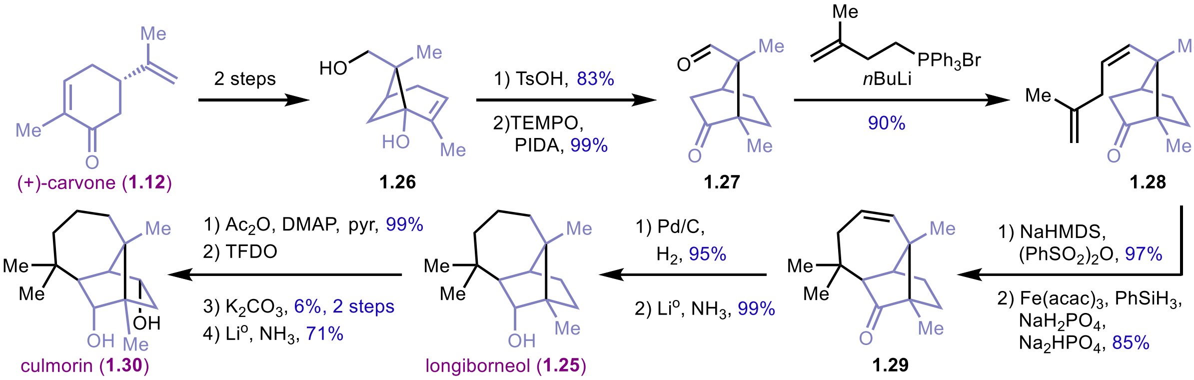


Figure 1.5 Sarpong and coworkers' synthesis of the longiborneol sesquiterpenoids employing "chiral pool" remodeling with C–H functionalization.

Recognition that "chiral pool" remodeling of carvone (**1.12**) could allow access to highly oxidized camphor derivatives was key in this Level 3 synthesis. Additionally, this synthesis leveraged state-of-the-art HAT methodology to forge the seven membered ring of the natural products. Though this synthesis beautifully demonstrates "chiral pool" remodeling, it also showcases how the oxidation and functional group pattern on the starting "chiral pool" material can be constraining, requiring the use of C–H oxidation methodologies to access the more oxygenated congeners.

1.3 Conclusion

As described in this chapter, employing "chiral pool" starting materials in syntheses is a commonly utilized approach in total synthesis. These strategies enable access to enantioenriched material in short order when the optimal "chiral pool" material and strategy are employed. Some of these strategies utilize the "chiral pool" framework as is and build upon it, as demonstrated by the Level 1 syntheses showcased. However, some syntheses employ a "chiral pool" remodeling strategy, transforming the carbocyclic framework and allowing entry to more complex scaffolds and unique chemical space. Examples of these types of syntheses were discussed and hopefully give ample context to work that follows: Chapter 2 will disclose efforts toward a Level 1 synthesis of jungermatrobrunin A and the work outlined in Chapters 3 and 4 showcases a Level 3 route to xishacorene B.

1.4 References for Chapter 1

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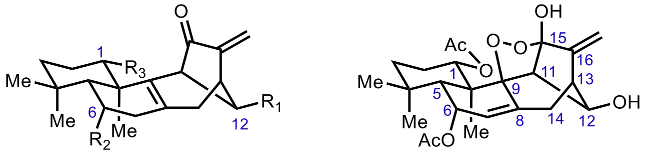
Chapter 2

Progress Toward the Synthesis of Jungermatrobrunin A

2.1 Isolation, Biosynthesis, and Bioactivity

Jungermannenone A (**2.1a**, Figure 2.1) was first isolated in 2003 by Asakawa and coworkers from the *Jungermannia* species of liverworts and represented the first known member of the jungermannenone family.[1] In 2005, Asakawa reported the isolation of several other members of this family.[2] To date, six members of this family have been isolated. They all possess the same carbon skeleton, namely a *trans*-decalin system fused to a bicyclo[3.2.1]octane framework. Jungermannenones A–E (**2.1a–2.1e**) differ in their oxidation patterns at C1, C6, and C12 (Figure 2.1). Jungermatrobrunin A (**2.2**) is the most oxygenated member of the jungermannenone family and was isolated in 2008 by Lou and coworkers from the liverwort *Jungermannia atrobrunnea* in 0.00625% yield from dried plant mass.[3] Notably, jungermatrobrunin A (**2.2**) contains an endoperoxide bridge, which links C9 to C15 and masks the exocyclic enone that is characteristic of the jungermannenone congeners.



jungermannenones:
A (**2.1a**): R_1, R_2= H, R_3= OH
B (**2.1b**): R_1, R_2, R_3 = H
C (**2.1c**): R_1, = OH, R_2, R_3 = H
D (**2.1d**): R_1, R_3 = OH, R_2 = H
E (**2.1e**): R_1, R_3 = H, R_2 = OH

jungermatrobrunin A (**2.2**)

Figure 2.1 Structures of jungermannenones A–E (**2.1a–2.1e**) and jungermatrobrunin A (**2.2**).

Biosynthetically, the jungermannenones are believed to arise from *ent*-kaurene (**2.3**, Figure 2.2), the biosynthesis of which has been extensively studied.[4] From geranylgeranyl pyrophosphate (**2.4**), enzyme-catalyzed cyclization gives *trans*-decalin **2.5**, followed by S_N1-like cyclization to yield tricyclic carbocation **2.6**. This tertiary carbocation (**2.6**) is hypothesized to undergo cation–olefin cyclization, followed by a 1,2-alkyl shift and elimination to furnish the [3.2.1]bicycle of *ent*-kaurene (**2.3**). From *ent*-kaurene (**2.3**), Asakawa and coworkers propose oxidation at C11 to give alcohol **2.7**, followed by either dehydration to give diene **2.8** (Figure 2.2, red pathway) or ionization and subsequent 1,3-alkyl shift to give tetracyclic cation **2.9** (Figure 2.2, blue pathway).[2] Along the red pathway, diene **2.8** could undergo ring opening to afford allylic carbocation **2.10**, followed by ring closing and elimination to give [3.2.1]bicycle **2.11**, which contains the complete carbon skeleton of the jungermannenones. Alternatively, a Cope rearrangement of diene **2.8** could occur to yield the desired [3.2.1]bicycle, bypassing allylic carbocation **2.10**. The blue pathway can terminate through elimination of carbocation **2.9** to give the internal olefin (see **2.11**) and complete the carbocyclic framework of the jungermannenones.

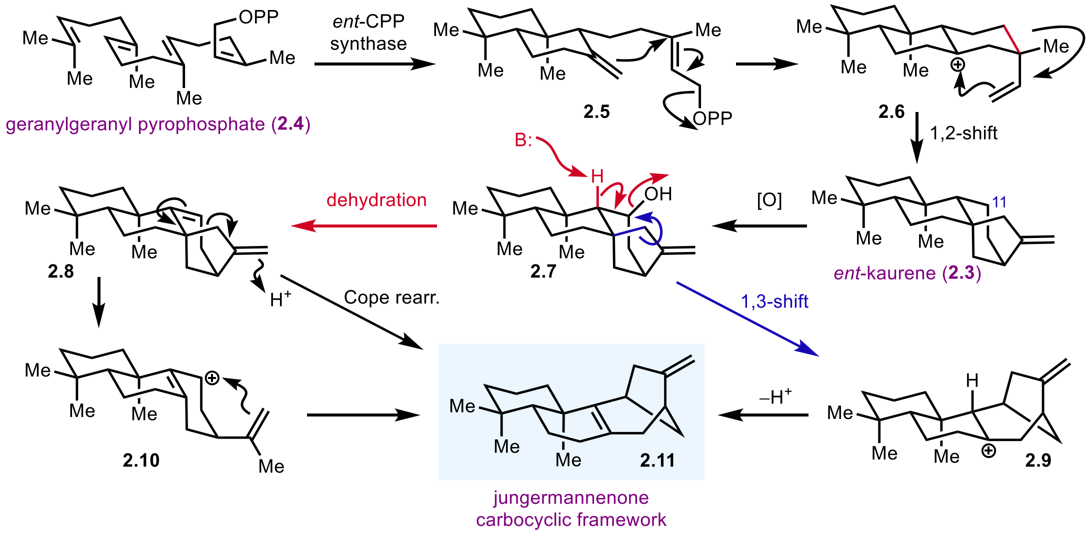


Figure 2.2 Proposed biosynthetic pathways to the jungermannenone skeleton from geranylgeranyl pyrophosphate.

The jungermannenones have shown moderate bioactivity against leukemia cells (HL-60). Specifically, they display IC_{50} values ranging from 0.28–7.8 μM.[1,5] The biological activity of these compounds is attributed to their exocyclic enone functionality, which is hypothesized to undergo a Michael addition in the presence of cysteine containing proteins or glutathione, leading to an increase in reactive oxygen species (ROS) and ultimately apoptosis.[6] Additionally, jungermatrobrunin A (**2.2**) has exhibited weak antifungal ability against *C. albicans*, possessing a minor inhibitory concentration (MIC) of 128 μg/mL.[3]

2.2 Previous Syntheses of the Jungermannenones

2.2.1 Lei's Racemic Synthesis of Jungermannenones B and C

At the onset of this project, relatively few synthetic studies of the jungermannenones had been completed. Lei and coworkers had previously reported the racemic synthesis of jungermannenones B and C (**2.1b** and **2.1c**, Figure 2.1) from the monoterpene geraniol (**2.12**).[7] In a short sequence, geraniol (**2.12**) was elaborated to aryl diene **2.13**. The Lei group then employed two key cyclizations to build the rearranged *ent*-kaurene skeleton in an efficient manner (**2.13**→**2.16**, Figure 2.3). The first was a ruthenium catalyzed intramolecular, electrophilic hydroarylation of aryl diene **2.13** which was followed by benzylic oxidation to afford fused tricycle **2.14**. The second key cyclization forged the [3.2.1]bicycle of **2.16** through a reductive 1,6-dienyne cyclization of **2.15**. Jungermannenones B and C (**2.1b** and **2.1c**) were then accessed through a series of functional group manipulations to install the exocyclic enone, ultimately furnishing the natural products in 10 and 9 steps, respectively.

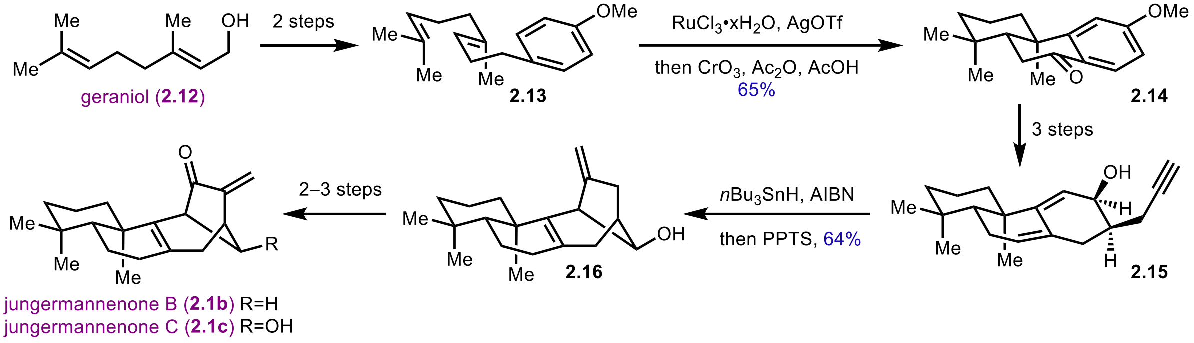


Figure 2.3 Lei's synthesis of jungermannenones B (**2.1b**) and C (**2.1c**) from geraniol (**2.12**).

2.2.2 Lei's Enantioselective Synthesis of Jungermannenone C

In May 2019, Lei and coworkers reported an alternative route to (–)-jungermannenone C (**2.1c**) through a key photoinduced skeletal rearrangement from the *ent*-kaurene skeleton to the jungermannenone skeleton (**2.22→2.1c**, Figure 2.4).[8] Starting from hydroxy alkyne **2.17**, Lei and coworkers quickly built aryl aldehyde **2.18** through sequential carboalumination-iodination and Suzuki–Miyaura[9] cross-coupling reactions. Treatment of aldehyde **2.18** with Cu(OTf)$_2$ and a chiral amine catalyst enabled cyclization of an *in situ* generated radical cation to enantioselectively form tricycle **2.19**. Following a five-step sequence to dienone **2.20**, Lei and coworkers utilized their previously established 1,6-dienyne cyclization to achieve *ent*-kaurene skeleton **2.21**. Ketone **2.21** was further elaborated to enone **2.22** by sequential oxidative cleavage of the exomethylene, alpha methenylation of C16, and Luche reduction of the ketone.[10] Finally, treatment of *ent*-kaurene **2.22** with 254 nm UV light induced a 1,3-acyl migration to yield (–)-jungermannenone C (**2.1c**).

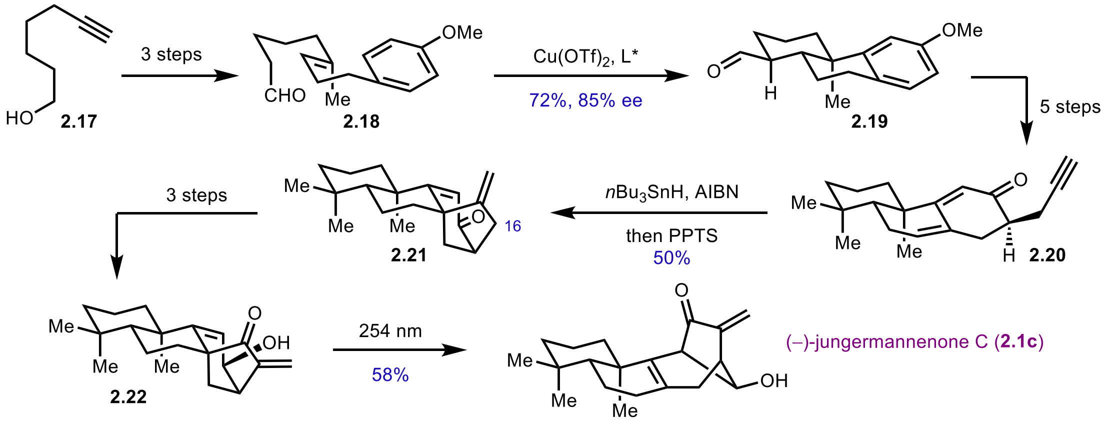


Figure 2.4 Lei's synthesis of (–)-jungermannenone C (**2.1c**) via a key photoinduced rearrangement.

2.2.3 Lei's Enantioselective Synthesis of Jungermatrobrunin A

Shortly after their (–)-jungermannenone C (**2.1c**) report, Lei and coworkers published the first total synthesis of jungermatrobrunin A (**2.2**) in 13 steps from commercial materials (Figure 2.5).[11] Starting from enone **2.23** and vinyl arene **2.24**, they employed an asymmetric hydrozirconation, 1,4-cuprate addition sequence to yield alkyl arene **2.25**. Sequential intramolecular alpha arylation of **2.25**, methylation, and oxidation gave *cis*-decalin **2.26**. Luche reduction[10] of the trione **2.26** set three stereocenters in a single step to give triol **2.27**. The synthesis of the jungermannenone skeleton (**2.28**) was realized in an efficient manner, drawing a series of transformations from their initial jungermannenone synthesis.[12] Finally, the jungermannenone core was converted to jungermatrobrunin A (**2.2**) through a bioinspired Schenck ene[13] reaction.

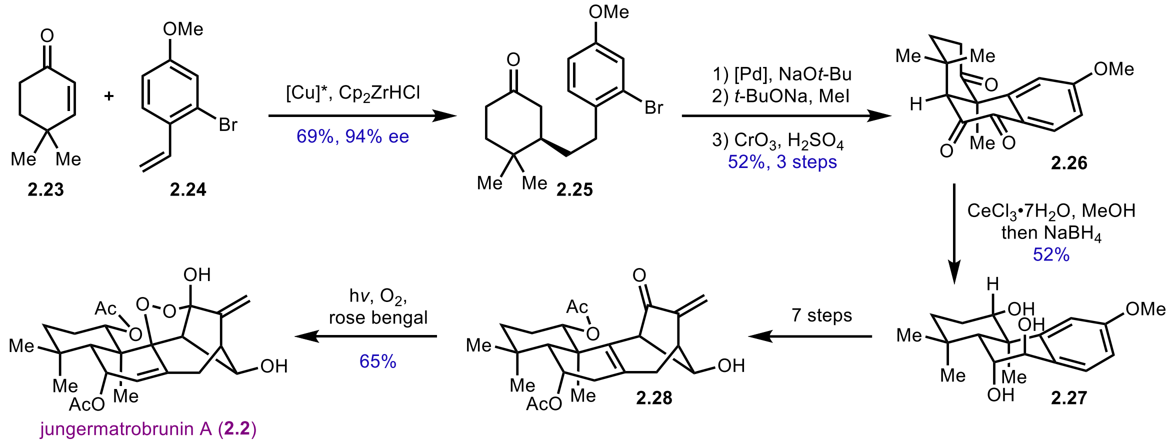


Figure 2.5 Lei's synthesis of jungermatrobrunin A (**2.2**).

2.3 Retrosynthesis

At the outset of this project only one synthesis of the jungermannenones had been reported. Therefore, we envisioned an "chiral pool" approach to jungermatrobrunin A (**2.2**) with the possibility for divergence to the jungermannenones. Retrosynthetically, excision of the endoperoxide bridge would give tetra-substituted olefin **2.28** (Figure 2.6), which, in the forward sense, could be elaborated to the natural product via a Schenck ene reaction[13]. We envisioned tetracycle **2.28** could arise from enone **2.29** by γ-deoxygenation in the forward sense. In turn, enone **2.29** could be simplified to cyclopentadiene **2.30** and silyl dienol ether **2.31** through a retro (4+3) cycloaddition. Silyl dienol ether **2.31** could be constructed by extended enolization of β-hydroxy enedione **2.32**, which could arise from methyl ester **2.33** by Dieckmann condensation,[14] in the forward sense. In turn, ketoester **2.33** could be obtained from (*R*)-carvone (**2.34**) using a reductive olefin coupling reaction. This approach allowed us to start from an inexpensive "chiral pool" material and gain access to the natural product in enantioenriched form.

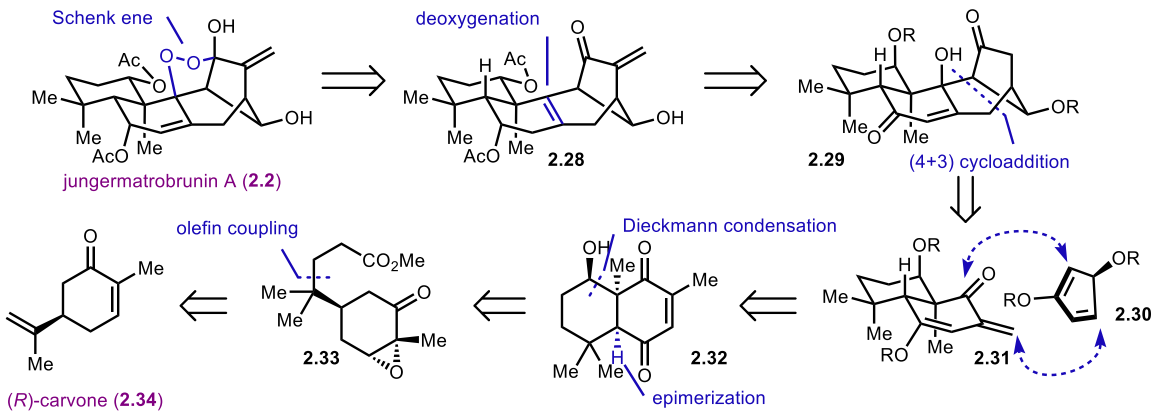


Figure 2.6 Initial retrosynthesis of jungermatrobrunin A (**2.2**).

2.4 Initial Synthesis of the Decalin Core

The synthesis of jungermatrobrunin A (**2.2**) commenced with an Fe(III)-catalyzed reductive olefin coupling, adapted from the work of Baran and coworkers,[15] between (*R*)-carvone (**2.34**) and methyl acrylate. This transformation would install all the carbons of the decalin scaffold in a single step. However, the desired cyclohexanone **2.35** was not obtained, instead, bicyclo[3.3.1]nonane **2.36** was observed, albeit in low yield, likely arising through sequential Giese additions (Figure 2.7).[16]

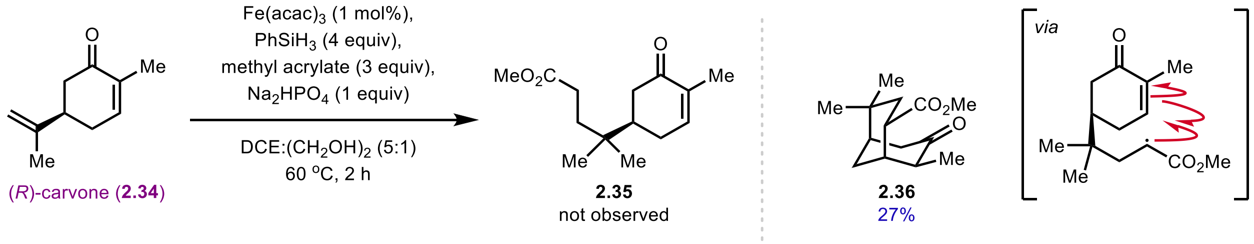


Figure 2.7 Formation of [3.3.1]bicycle **2.36** from (*R*)-carvone (**2.34**).

In order to circumvent this undesired reactivity, a Weitz–Scheffer[17] nucleophilic epoxidation was performed on (*R*)-carvone (**2.34**) to mask the enone moiety, giving epoxide **2.37** (Figure 2.8). Subsequent Fe(III)-mediated reductive olefin coupling was then effected to afford ketoester **2.33**.[15] Solvent choice proved crucial in this Fe(III)-mediated hydrogen atom transfer (HAT) reaction with epoxy carvone (**2.37**) as ethanol gave an inseparable mixture of ketoester **2.33** and an unidentifiable phenylsilane-derived compound. Upon switching the solvent to 1,2-dichloroethane,[15] ketoester **2.33** was obtained cleanly in 62% yield. Dieckmann condensation of ketoester **2.33** delivered ketoenol **2.38**, constructing the decalin core.

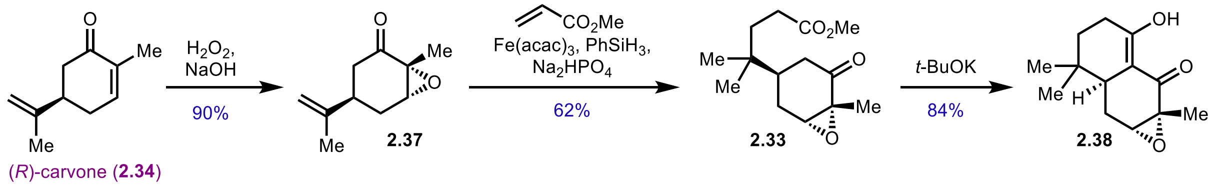


Figure 2.8 Synthesis of ketoenol **2.38** from (*R*)-carvone (**2.34**).

Subsequent methylation of the doubly α-position with methyl iodide (MeI) delivered the *cis*-fused bicyclic system **2.39** (Figure 2.9). Though the target natural product possesses a *trans*-fused decalin, we determined that the ring junction (C5) could be epimerized at a later stage to yield the *trans*-decalin. The reproducibility of this methylation was improved with the addition of tetra-*n*-butyl ammonium bromide (TBAB). Presumably, this is due to the ability of TBAB to improve solubility of potassium carbonate (K_2CO_3), leading to increased conversion, higher yield, and reproducibility. Removal of the epoxide with Cp_2TiCl, generated *in situ* from bis(cyclopentadienyl)titanium(IV) dichloride (Cp_2TiCl_2) and zinc dust, afforded enone **2.40**.[18]

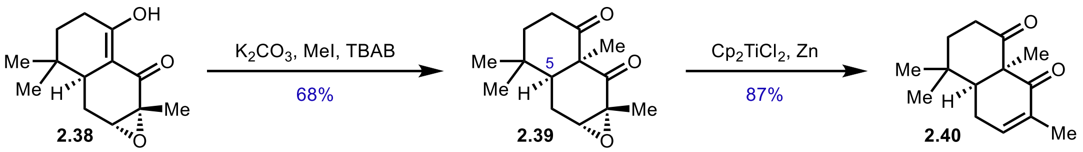


Figure 2.9 Installation of ring fusion methyl group and deoxygenation to give enone **2.40**.

Oxidation of the γ–methylene (C6) of enone **2.40** was effected using chromium trioxide (CrO_3) and 3,5-dimethylpyrazole (3,5-DMP) to afford tricarbonyl **2.41** (Figure 2.10).[19] However, this reaction requires super-stoichiometric quantities of the Cr(VI) reagent. To avoid these forcing conditions, we screened an array of transition metal catalysts and *tert*-butyl hydroperoxide (TBHP) as greener allylic oxidation conditions.[20,21] Unfortunately, we observed a mixture of C8 and C6 oxidation products, favoring the undesired oxidation at C8 (**2.42**, Figure 2.10). Selective reduction of the ketone at C1 was achieved with sodium borohydride yielding an axially disposed hydroxy group, due to addition of hydride from the convex face.[22] Subsequent protection of the resultant hydroxy group yielded known silyl ether **2.43**.[23]

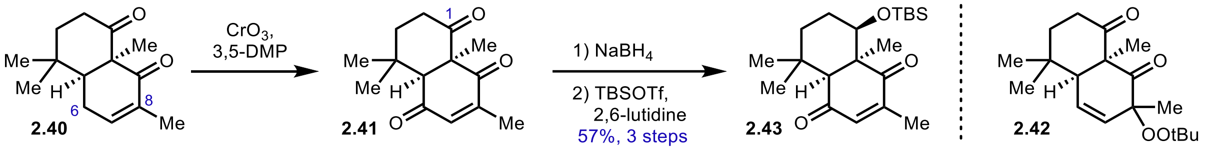


Figure 2.10 Redox manipulations to afford enedione **2.43**.

We then applied conditions developed by Kienzle and coworkers[24] to epimerize *cis*-enedione **2.43** to *trans*-enedione **2.44** by heating at reflux in toluene with aluminum oxide (Al_2O_3) (Figure 2.11). From **2.44**, efforts to form the desired silyl dienol ether **2.45** utilizing a variety of silyl sources and bases were unsuccessful, resulting in unreacted starting material in most cases. We sought to switch the order of operations so that we could form the silyl ether prior to epimerizing. We subjected *cis*-decalin **2.43** to *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) and triethylamine (Et_3N) and were successful in formation of silyl dienol ether **2.46**. From **2.46**, efforts to epimerize the C5 position utilizing numerous bases (e.g., DBU, K_2CO_3, Al_2O_3) were unfruitful, resulting in only recovered starting material. Švenda and coworkers have reported that the success of epimerizations with Al_2O_3 on similar systems is highly substate dependent.[23] Given this observation, we turned our attention to testing the validity of the key proposed cycloaddition using *cis*-fused bicycle **2.46**, believing that we could potentially epimerize the decalin system at a later stage.

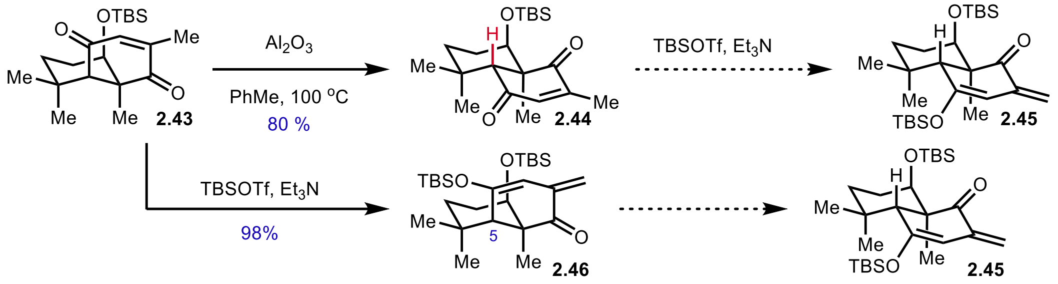


Figure 2.11 Attempted epimerization and silyl ether formation to give *trans*-fused silyl dienol ether **2.45**.

2.5 Formal (4+3) Cycloaddition to Forge the [3.2.1]Bicycle

2.5.1 First Generation Route: Mukaiyama Aldol Mukaiyama–Michael Cascade

We initially sought to forge the [3.2.1]bicycle of jungermatrobrunin A (**2.2**) through tandem Mukaiyama aldol Mukaiyama–Michael reactions (Figure 2.12). Upon treatment of the coupling partners **2.46** and **2.47** with a Lewis acid, we envisioned cyclopentadiene silyl ether **2.47** could add into the ketone of decalin **2.46** in a Mukaiyama aldol fashion. From there the silyl dienol ether could add into the newly formed cyclopentenone of **2.48** in a Mukaiyama–Michael reaction to forge [3.2.1]bicycle **2.49** which is reminiscent of the characteristic jungermannenone core.

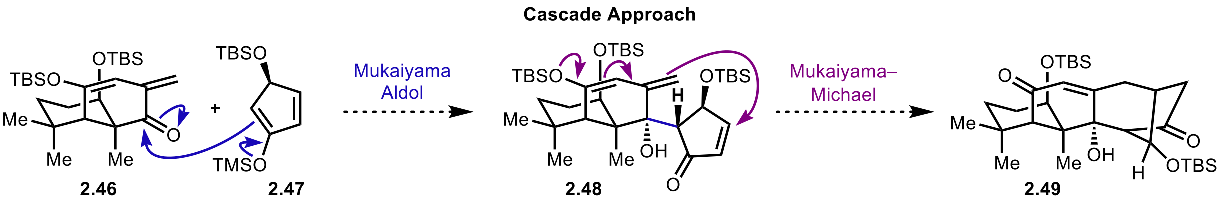


Figure 2.12 Proposed (4+3) cycloaddition of silyl dienol ether **2.46** and cyclopentane **2.47** through a cascade approach.

In terms of the cyclopentadiene coupling partner (**2.47**), we looked to synthesize it in enantioenriched form so that upon coupling with our enantioenriched decalin fragment we would avoid a mixture of diastereomers. Luckily, there was ample literature precedent toward our desired cyclopentane fragment. We utilized a modified procedure by Reiser and coworkers to convert furfural alcohol (**2.50**) to racemic cyclopentenone **2.51** through a Piancatelli-type rearrangement (Figure 2.13).[25] From there, we followed precedent by Curran and coworkers to access enantioenriched cyclopentenone **2.52**.[26] First, silyl protection of the secondary alcohol in **2.51** followed by 1,2-reduction yielded racemic allylic alcohol **2.52**. Enzymatic kinetic resolution of the two enantiomers could be achieved through acylation of the secondary alcohols and selective hydrolysis of one enantiomer by the lipase. Ultimately, hydrolysis of acetate **2.53** afforded allylic alcohol **(+)-2.52**. Following precedent by Rokach and coworkers, Dess–Martin periodinane (DMP) oxidation forged cyclopentenone **2.54**.[27]

It was at this point that we ventured away from known chemistry to access the desired coupling partner. We attempted enolization of enone **2.54** and subsequent trapping with silyl sources to form the desired cyclopentadiene coupling partner (**2.47**), however, **2.47** was not a persistent compound and rapidly decomposed.

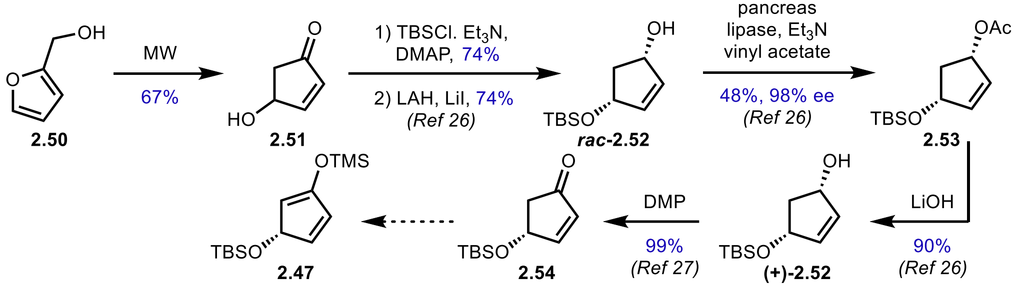


Figure 2.13 Attempted synthesis of the cyclopentadiene coupling partner **2.47**.

Given the challenges associated with forming cyclopentadiene **2.47**, we took a step back and rethought our cyclopentane coupling partner. Having accessed enone **2.54**, we attempted a stepwise approach to forge the [3.2.1]bicycle, focusing on the desired Mukaiyama–Michael reaction first with the goal of forging the C9–C11 bond separately (Figure 2.14). Treating silyl dienol ether **2.46** and cyclopentenone **2.54** with an array of Lewis acids we sought to access the coupled product **2.55**, but unfortunately were faced with only desilylation of the various silyl groups. Due to the lack of success in coupling these fragments, an alternative coupling strategy was devised.

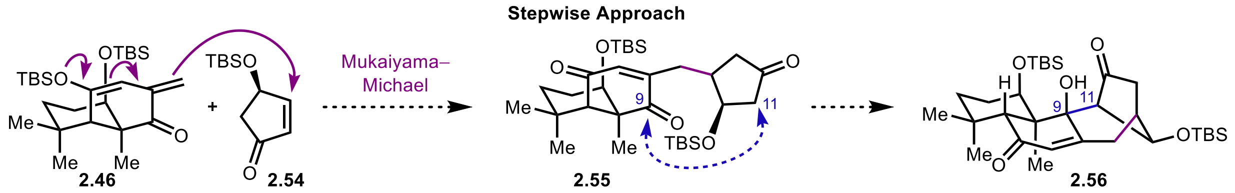


Figure 2.14 Proposed (4+3) cycloaddition of silyl dienol ether **2.46** and cyclopentane **2.54** through a stepwise approach.

2.5.2 Second Generation Route: Cyclopentane Fragment Rethought

We next turned our attention toward alternative cyclopentane derivatives that could change the electronics of the coupling reaction and map differently onto the [3.2.1]bicycle. Realizing that the natural product is functionalized at both C15 and C16, possessing a hemiketal at C15 and an exo-methylene at C16, we believed shifting the oxidation pattern of the cyclopentane fragment would not be detrimental to the end stages of our proposed synthesis. As outlined in Figure 2.15, the first-generation route, highlighted in blue, places a ketone at C15 (**2.56**) after coupling. However, with the second-generation route, highlighted in purple, the other enantiomer of the cyclopentenone (***ent*-2.54**) is utilized and furnishes oxidation at C16 (**2.57**).

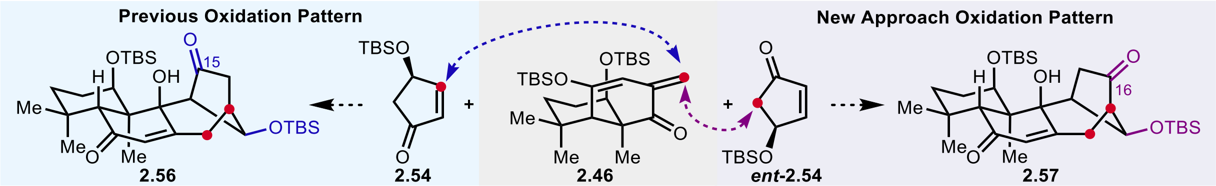


Figure 2.15 Proposed shift in coupling strategy and thus oxidation pattern of the resultant bicycle.

Specifically, we believed a Mn(III)-mediated radical coupling developed by Mohr and coworkers for silyl dienol ethers and 1,3-dicarbonyls would effect our desired transformation.[28] A representative example is displayed in Figure 2.16 where silyl dienol ether **2.58** and ketoester **2.59** forge a C–C bond to afford the coupled product (**2.60**). Mechanistically, the dicarbonyl (**2.61**) is proposed to formally undergo deprotonation/oxidation by manganese triacetate ($Mn(OAc)_3$) to give radical species **2.62**.[29] The electrophilic radical **2.62** can then react with silyldienol ether **2.58** to afford nucleophilic radical **2.63**. Subsequent oxidation affords oxonium **2.64** which can be hydrolyzed to afford the coupled product.

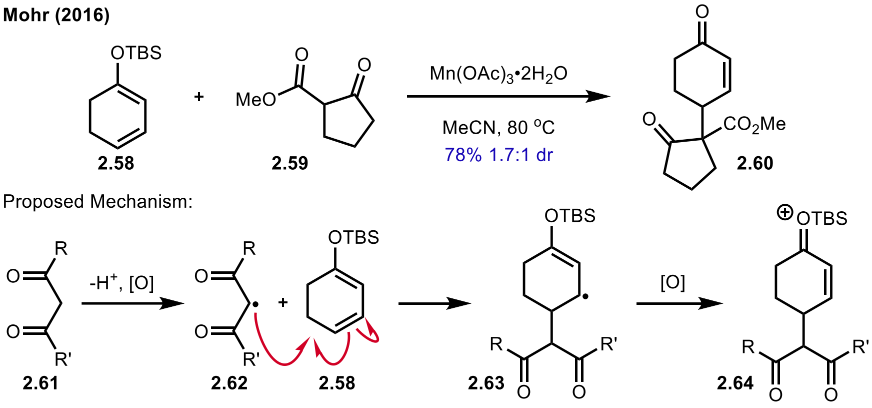


Figure 2.16 Mohr and coworkers' precedent for manganese mediated oxidative coupling.

The cyclopentenone coupling partner that we proposed for this oxidative coupling could be synthesized through a route that was very similar to that used for the previous strategy. Curran and coworkers report allylic alcohol **(–)-2.52** is formed in the aforementioned enzymatic chiral resolution of ***rac*-2.52** (Figure 2.17).[26] Oxidation of alcohol **(–)-2.52** with DMP afforded the desired cyclopentenone ***ent*-2.54**. To utilize the manganese mediated oxidative coupling, a 1,3-dicarbonyl is required in order to effect the initial deprotonation/oxidation. Therefore, ***ent*-2.54** was treated with LDA and Mander's reagent to install a methyl ester, giving rise to **2.65** as an inconsequential mixture of diastereomers. Upon subjecting silyl dienol ether **2.46** and cyclopentenone **2.65** to $Mn(OAc)_3$ we were able to access the desired coupled product (**2.66**) in high yield and moderate diastereoselectivity. Having successfully forged the first of the two requisite C–C bonds (between C13 and C14) we turned our attention toward removal of the methyl ester as it was only beneficial for the coupling reaction. Unfortunately, upon Krapcho decarboxylation of methyl ester **2.66**, the resulting compound (**2.67**) was unstable and this route was deemed untenable.

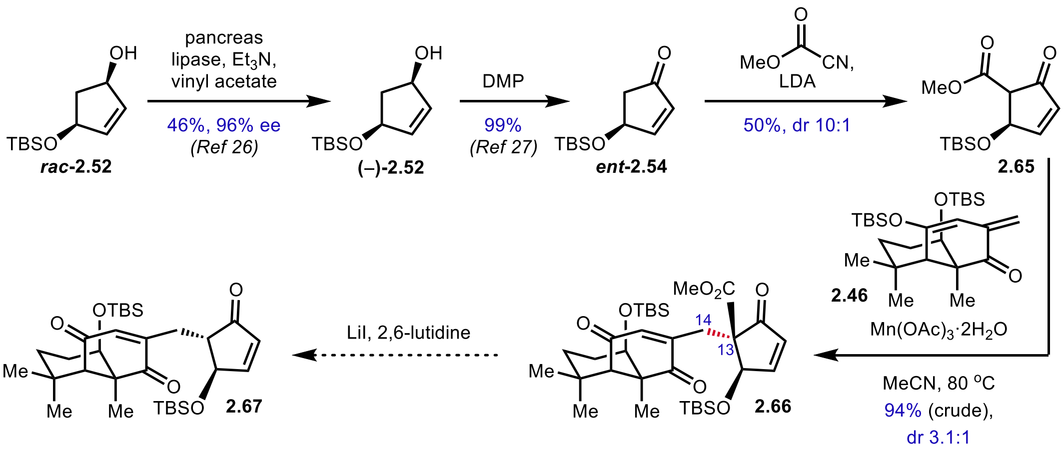


Figure 2.17 Synthesis of ketoester **2.65** and oxidative coupling to give adduct **2.66**.

Given the added steps of installing and removing the methyl ester, the sub-optimal diastereoselectivity in the coupling reaction, as well as the unsuccessful Krapcho decarboxylation, we turned our attention toward simpler, symmetric 1,3-diones. Initial coupling of silyldieneol ether **2.46** with 1,3-cyclopentanedione (**2.68**) did not produce the desired monoalkylated product (**2.69**) but rather produced the dialkylated product (**2.70**) in moderate yields (Figure 2.18). Though Mohr and coworkers do observe formation of dialkylated products, there are cases where they observe monoalkylation on substrates with two alpha protons.[30] To circumvent this additional reactivity, a pre-functionalized cyclopentanedione was utilized as a model coupling partner to eliminate one of the doubly alpha positions and to ascertain the feasibility of the bicyclization step. This coupling proceeded in high yield with 2-methyl-1,3-cyclopentadione (**2.71**) to afford adduct **2.72**.

From **2.72**, we looked to close the [3.2.1]bicycle through an intramolecular aldol reaction between C9 and C11 (Figure 2.18). We realized that differentiating the ketones on the cyclopentanedione would be a challenge, but we were optimistic that we could obtain some of the desired [3.2.1]bicycle (**2.73**). Under strongly basic conditions, only decomposition of the starting material was observed, even at cryogenic temperatures. Attempts at acid-catalyzed aldol cyclizations resulted only in cleavage of the silyl ether of **2.72**. Amine-catalyzed aldol cyclization was also investigated but led to nonspecific decomposition as well as unreacted starting material. At this point we realized that the strain associated with the desired bicyclic system was not insignificant, and that the retro-aldol reaction was likely hindering our chances of obtaining the bicycle.

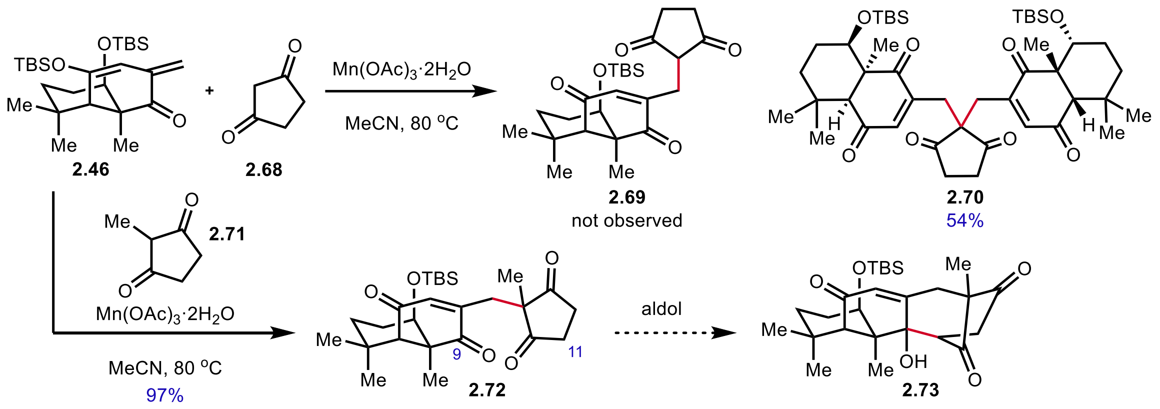


Figure 2.18 Coupling of symmetric cyclopentanediones to silyl dienol ether **2.46**.

To test our hypothesis about the competing retro-aldol reaction, we changed the cyclopentane coupling partner to acyclic pentane **2.74** to alleviate some of the ring strain associated with the [3.2.1]bicycle. Coupling of 2,4-pentanedione **2.74** proceeded smoothly to give **2.75**. Upon treatment with excess potassium hexamethyldisilazane (KHMDS), the desired aldol reaction proceeded, forming the C9–C11 bond, but the resultant alkoxide was well disposed to engage the C16 carbonyl to form hemiketal **2.76** (Figure 2.19). This structure was assigned by 2D NMR, however, the configuration at the newly formed stereocenters has not been confirmed. Despite the initial promise of forming the desired C–C bond by an aldol reaction, we deemed formation of the [3.2.1]bicycle from this compound to be challenging and therefore did not pursue this route any further.

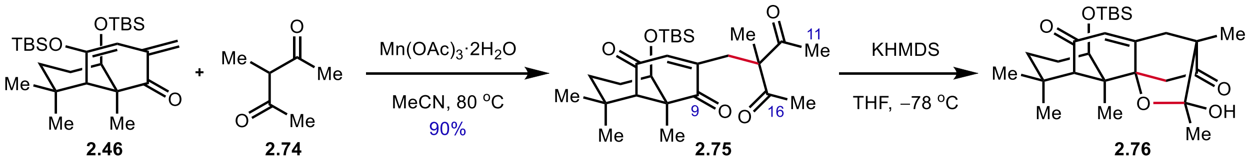


Figure 2.19 Oxidative coupling with acyclic pentane fragment **2.74** and formation of hemiketal **2.76**.

2.5.3 Model Systems: Radical Based Coupling

Considering the undesired reactivity observed in the second-generation route, we envisioned an array of alternative routes to forge the [3.2.1]bicycle of jungermatrobrunin A (**2.2**), focusing on Giese-type radical additions to couple the fragments. Initially, we selectively reduced the carbonyl at C9 of enedione **2.43** (Figure 2.20) through treatment with lithium aluminum hydride (LAH) to give hydroxyenone **2.77,** and then investigated methods to generate α-hydroxy radical **2.78**.[31,32] We believed **2.78** could react with cyclopentenone **2.79** to give hydroxycyclopentone **2.80**, however, no coupled adduct was observed and only decomposition of the decalin starting material occurred.

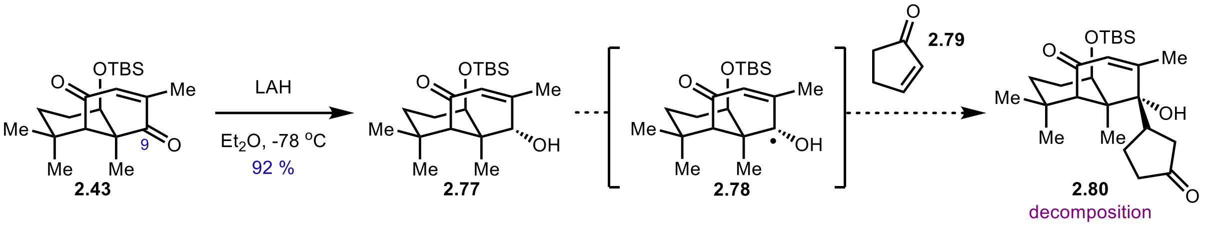


Figure 2.20 Efforts toward α-hydroxy radical fragment couplings.

We next investigated the generation of the radical on the cyclopentane fragment with the embedded enone of silyldienol ether **2.46** acting as the radical acceptor (Figure 2.21). We utilized simple cyclopentane fragments as models to examine proof of concept reactivity. Looking at photochemical decarboxylation methods, we attempted to use photoredox-active esters, such as *N*-hydroxyphthalimide ester **2.81** or cyclopentanecarboxylic acid (**2.82**), however, we were unable to obtain a coupled product (**2.83**) under any of these conditions.

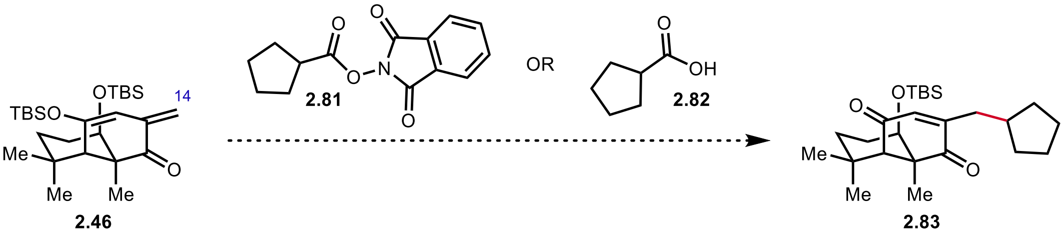


Figure 2.21 Radical decarboxylation couplings with silyl dienol ether **2.46**.

It is worth noting that in these reactions the radical polarities are not well matched. We believe this made the desired coupling very challenging due to the electroneutral nature of the radicals generated. In terms of the cyclopentane fragment, the radical formed is not very polarized in either direction. For the decalin fragment, our system possesses cross conjugation between a silyl dienol ether and an enone, making the exocyclic methylene electronically ambiguous. If a radical were to undergo a 1,4-addition to the enone, the resulting radical would be captodative because it is electrophilic by being adjacent to the carbonyl but also nucleophilic by virtue of the silylenol ether. Furthermore, the lack of an oxidant to oxidize the radical post-coupling could have resulted in an unstable silylenol ether. Given this lack of success even with these highly unfunctionalized model systems and the efficient synthesis of jungermatrobrunin A (**2.2**) by Lei and coworkers, we chose to not explore this project any further.[11]

2.6 Formal Synthesis of Erigerol and Forskolin

During the course of our work toward jungermatrobrunin A (**2.2**), we came to appreciate intermediate **2.48** as a possible point of divergence to access a variety of highly oxygenated decalin containing natural products as decalin **2.48** has been previously utilized in several syntheses.

Erigerol (**2.84**) is a labdane diterpenoid natural product isolated from the leaves of *E. canadensis* in 1983, that consists of a decalin core appended to a spiro-tetrahydrofuran moiety.[33]

Forskolin (**2.85**) is another labdane diterpenoid natural product, isolated in 1977 from the herb *Coleus forskohlii*.[34] This compound possesses a highly oxygenated decalin core with a fused tetrahydropyran ring. Forskolin (**2.85**) has attracted much interest because an analogue of the natural product is a leading heart failure drug in Japan. Both of these natural products have been previously synthesized through a common intermediate, the highly oxygenated decalin **2.43,** making our eight step synthesis of **2.43** (Figure 2.8–2.10) a formal synthesis of erigerol (**2.84**) and forskolin (**2.85**).[24,23,35] In addition to this, we believe decalin **2.43** could play a part in a broad campaign to access a diverse array of decalin containing terpenoids (Figure 2.22).

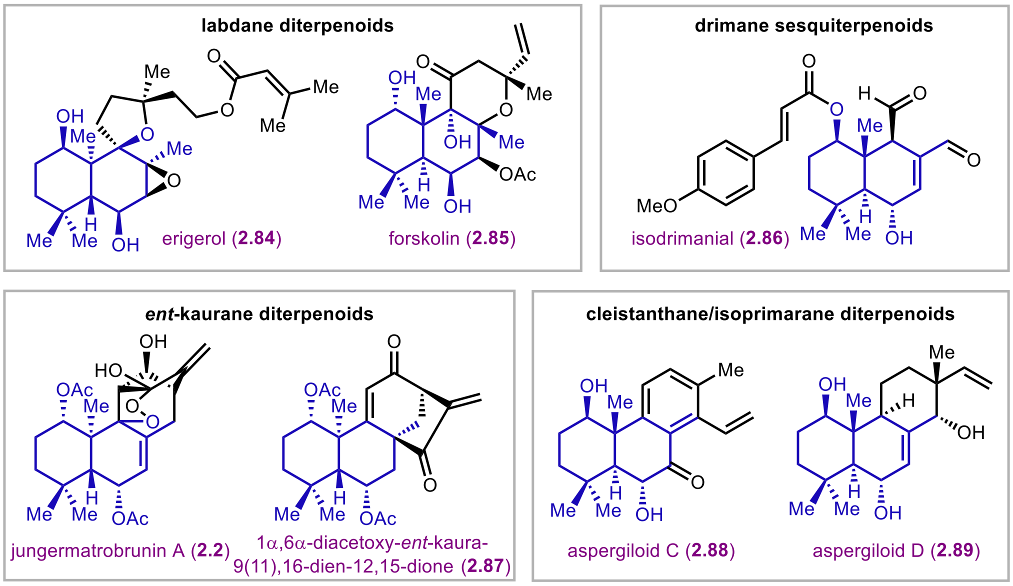


Figure 2.22 Selected terpenoids containing a highly oxygenated decalin core traced back to a plausible common intermediate highlighted in blue.

Compound **2.48** was previously synthesized in racemic fashion based on a protocol reported by Kienzle and coworkers in which diene **2.91** and quinone **2.92** undergo a Diels–Alder cycloaddition to furnish decalin **2.93** (Figure 2.23).[35] Additionally, after we established our route to **2.48**, Pronin and coworkers reported an enantioselective route to **2.48** which hinges on an oxazaborolidine catalyzed enantioselective Diels–Alder to forge [2.2.1]bicycle **2.95**.[36] Quinone derivative **2.95** then undergoes a radical-polar crossover with aldehyde **2.94** to build the decalin core. Finally, silylation of **2.96** and a retro Diels–Alder reaction to extrude cyclopentadiene yields ***ent*-2.48**.

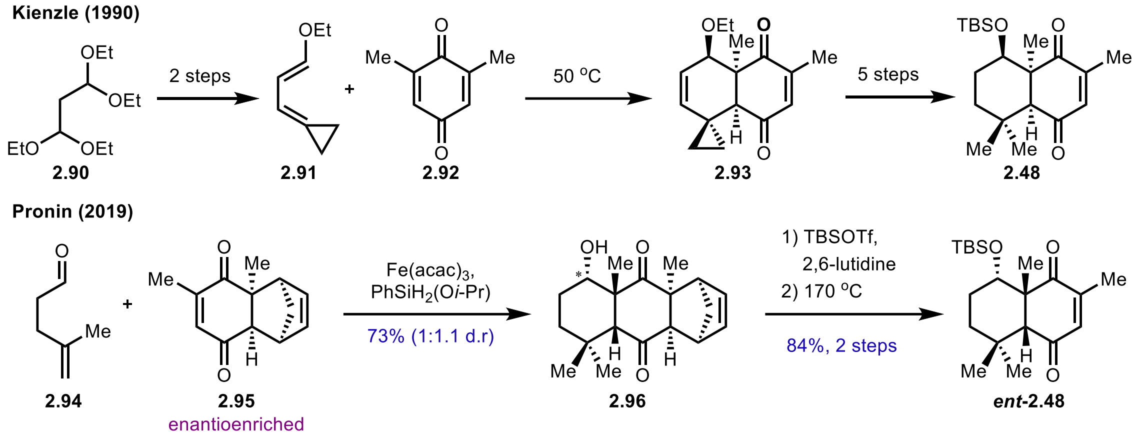


Figure 2.23 Previous routes to common decalin intermediate **2.48**.

The route that we developed to **2.48** is the first enantiospecific entry to this versatile decalin intermediate.[37] This route takes advantage of the inherent asymmetry within carvone (**2.34**), a cheap and commercially available "chiral pool" terpene that can be purchased in both enantiomeric forms. The full route to decalin **2.48** is detailed above in section 2.4.

2.7 Conclusion and Outlook

We envisioned developing a synthetic route to enantioenriched jungermatrobrunin A (**2.2**) by starting from the "chiral pool" terpene carvone (**2.34**), building a decalin and then appending a cyclopentane fragment to achieve the carbocyclic core. We were successful in synthesizing the decalin system using a key reductive olefin coupling and subsequent Dieckmann condensation. The synthesis of this decalin fragment in enantioenriched fashion constituted the formal synthesis of the natural products erigerol (**2.84**) and forskolin (**2.85**), as they had been previously synthesized utilizing the racemic decalin.

Toward jungermatrobrunin A (**2.2**), our initial approach for advancing the decalin to the carbocyclic framework of the jungermannenones was met with challenges associated with synthesis of the desired cyclopentyl fragment. Simplification of the cyclopentyl fragment and a stepwise, formal (4+3) approach was also unsuccessful, yielding no productive reactivity.

We then pivoted in terms of the cyclopentyl fragment, rethinking the oxidation pattern of the coupling partner and subsequent [3.2.1]bicycle. Utilizing manganese mediated oxidative radical coupling conditions by Mohr and coworkers, we were able to forge one of the desired C–C bonds, bringing together our two fragments.[30] Unfortunately, we encountered functional group manipulation issues with the use of our ideal cyclopentyl substrate and development of a model system was met with its own challenges and strayed from the initial target and goal.

The above synthetic efforts were ultimately abandoned when Lei's enantioselective synthesis of jungermatrobrunin A (**2.2**) was published.[11] Though it was possible we could still achieve access to the natural product, it was determined that the concessions that we had taken along our route to the natural product had made our route lengthy, and further investigation of this route would not be fruitful. However, we believe that our strategy and approach will be informational for others.

2.8 Experimental Contributors

Project design was carried out by Prof. Richmond Sarpong. Initial development of the route to the decalin core was done by Dr. Shota Nagasawa (S.N.). Optimization of the decalin route was conducted by Kerry E. Jones (K.E.J.) and S.N. Synthesis of the first-generation cyclopentenone fragment was carried out by K.E.J. and S.N. Experiments toward the first-generation (4+3) cycloaddition were done by S.N. Experiments toward the second-generation fragment coupling were carried out by K.E.J. and S.N., where S.N. investigated the optimal coupling partner and K.E.J. investigated the model coupling partner. Miscellaneous experiments detailed herein were carried out by K.E.J.

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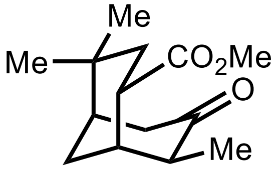
2.9 Experimental Details

2.9.1 Experimental Procedures

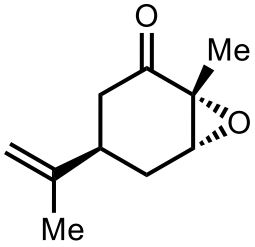
Methyl (1S,2S,5R,8S)-4,4,8-trimethyl-7-oxobicyclo[3.3.1]nonane-2-carboxylate (2.36)



Prepared according to a modification of the procedure by Baran and coworkers:[15] (*R*)-(–)-Carvone (14, 50. mg, 0.33 mmol, 1.0 equiv) was dissolved in a mixture of 1,2-dichloroethane (1.5 mL) and ethylene glycol (0.3 mL) in a flask open to the atmosphere. Iron(III) acetylacetonate (10.6 mg, 30.0 µmol, 0.1 equiv), methyl acrylate (0.11 mL, 0.99 mmol, 3.0 equiv), anhydrous sodium phosphate dibasic (47 mg, 0.33 mmol, 1.0 equiv) were added to the rapidly stirring mixture. Phenylsilane (0.06 mL, 0.66 mmol, 2.0 equiv) was added dropwise. (CAUTION: rapid evolution of gas is observed). The flask was fitted with a water jacketed reflux condenser and the mixture was heated to 60 ˚C for 1 h, and then additional phenylsilane (0.06 mL, 0.66 mmol, 2.0 equiv) was added and stirred 1 h. Upon observed completion by TLC the reaction mixture was cooled to room temperature and diluted with saturated aqueous sodium chloride (5 mL). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 x 8 mL). The combined organic layers were washed with saturated aqueous sodium chloride (5 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The crude oil was then purified via gradient flash chromatography (Yamazen, eluting with 8-29% ethyl acetate in hexanes) to give the title compound **2.36** (21.5 mg, 0.090 mmol, 27%). The ^{1}H NMR and ^{13}C NMR spectra are consistent with that reported in the literature.[16]

^{1}H NMR (400 MHz, CDCl$_3$) δ 3.64 (s, 3H), 2.94 – 2.88 (m, 1H), 2.73 – 2.62 (m, 2H), 2.47 (qdd, *J* = 6.9, 6.4, 0.9 Hz, 1H), 2.32 (ddd, *J* = 15.7, 5.7, 0.9 Hz, 1H), 2.20 (dq, *J* = 13.6, 3.3 Hz, 1H), 1.96 (dt, *J* = 13.6, 3.1 Hz, 1H), 1.88 – 1.83 (m, 1H), 1.48 (dd, *J* = 14.8, 3.8 Hz, 1H), 1.32 (d, *J* = 14.8 Hz, 1H), 1.00 (s, 3H), 0.97 (s, 3H), 0.94 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 212.9, 175.4, 51.6, 48.8, 44.6, 41.9, 41.8, 40.1, 34.0, 33.4, 33.1, 29.2, 27.5, 12.0.

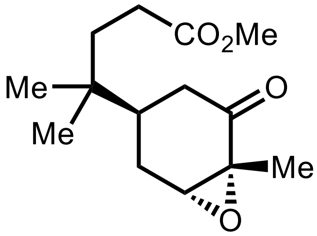
(1R,4R,6R)-1-Methyl-4-(prop-1-en-2-yl)-7-oxabicyclo[4.1.0]heptan-2-one (carvone oxide, 2.37)



Prepared according to a modification of the procedure outlined by Mulzer and coworkers:[38] (*R*)-(–)-Carvone (14, 5.0 g, 33 mmol, 1.0 equiv) was added to HPLC grade methanol (83 mL) in a flask open to the environment and the mixture was cooled to –20 ˚C. A 4.0 M solution of sodium hydroxide (2.5 mL, 9.9 mmol, 0.3 equiv) and a 35% aqueous hydrogen peroxide solution (3.7 mL, 43 mmol, 1.3 equiv) were added sequentially in a dropwise fashion. The solution was warmed to 0 ˚C within 1.5 h, and then additional 35% aqueous hydrogen peroxide solution (1.8 mL, 21 mmol, 0.6 equiv) was added and the reaction mixture was stirred for 1 h. The excess hydrogen peroxide was quenched with 2N hydrochloric acid (4 mL) and sodium thiosulfate (3.0 g, 0.5 equiv) and allowed to stir at room temperature for 30 min before the addition of water (100 mL) was added, and the aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The crude residue was purified via column chromatography (20:1 hexanes:ethyl acetate) to yield carvone oxide **2.37** as a colorless oil (5.0 g, 30. mmol, 90% yield). Full characterization has been reported by Cao and coworkers. The ^{1}H NMR spectrum is consistent with that reported in the literature.[39]

^{1}H NMR (400 MHz, CDCl$_3$) δ 4.79 (s, 1H), 4.72 (s, 1H), 3.45 (dd, *J* = 3.2, 1.2 Hz, 1H), 2.71 (tt, *J* = 11.2, 4.8 Hz, 1H), 2.59 (ddd, *J* = 17.7, 4.7, 1.4 Hz, 1H), 2.37 (dt, *J* = 14.8, 3.3 Hz, 1H), 2.03 (dd, *J* = 17.6, 11.6 Hz, 1H), 1.90 (ddd, *J* = 14.8, 11.1, 1.2 Hz, 1H), 1.71 (s, 3H), 1.41 (s, 3H).

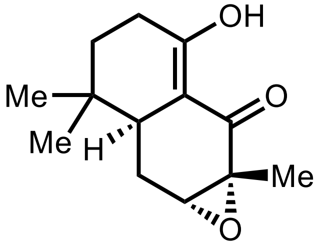
Methyl 4-methyl-4-((1R,3R,6R)-6-methyl-5-oxo-7-oxabicyclo[4.1.0]heptan-3-yl)pentanoate (2.33)



Prepared according to a modification of the procedure by Baran and coworkers:[15] Epoxide **2.37** (1.0 g, 6.0 mmol, 1.0 equiv) was dissolved in a mixture of 1,2-dichloroethane (25 mL) and ethylene glycol (5 mL) in a flask open to the atmosphere. Iron(III) acetylacetonate (0.21 g, 0.59 mmol, 0.1 equiv), methyl acrylate (2.0 mL, 22 mmol, 3.0 equiv), and anhydrous sodium phosphate dibasic (0.85 g, 5.9 mmol, 1.0 equiv) were added to the rapidly stirring mixture. Phenylsilane (1.2 mL, 12 mmol, 2.0 equiv) was added dropwise. (CAUTION: rapid evolution of gas is observed). The mixture was heated to 60 ˚C for 1 h, and then additional phenylsilane (0.6 mL, 6.0 mmol, 1.0 equiv) was added and the reaction mixture was stirred 30 min. Upon observed completion by TLC the reaction mixture was cooled to room temperature and diluted with saturated aqueous sodium chloride (100 mL). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 x 75 mL). The combined organic layers were washed with saturated aqueous sodium chloride, dried over magnesium sulfate, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (10:1 hexanes:ethyl acetate) yielded methyl ester **2.33** as a colorless oil (0.94 g, 3.7 mmol, 62% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.67 (s, 3H), 3.43 (d, *J* = 3.6 Hz, 1H), 2.52 – 2.41 (m, 1H), 2.36 – 2.22 (m, 3H), 2.02 – 1.95 (m, 1H), 1.89 (dd, *J* = 17.4, 11.8 Hz, 1H), 1.69 (dd, *J* = 14.4, 11.6 Hz, 1H), 1.62 – 1.53 (m, 2H), 1.40 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 206.16, 174.22, 61.15, 58.71, 51.57, 38.45, 34.66, 34.44, 33.79, 28.79, 24.30, 23.81, 23.69, 15.15. **IR**: ṽ = 2954, 2874, 1736, 1706, 1437, 1371, 1304, 1197, 1171, 1116 cm^{-1}**.** **$[\alpha]^{20}_D$** = +69.2˚ (c 0.93, $CHCl_3$). **HRMS** (ESI): calcd for ([M+H], $C_{14}H_{23}O_4$)$^+$: *m/z* = 255.1591 found 255.1594. **R_f** = 0.26 (4:1 hexanes:ethyl acetate), red spot (*p*-anisaldehyde).

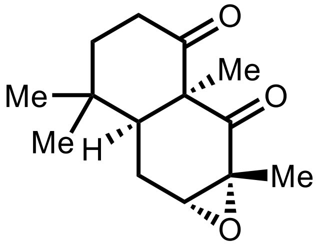
(1aR,6aS,7aR)-3-Hydroxy-1a,6,6-trimethyl-4,5,6,6a,7,7a-hexahydronaphtho[2,3-b]oxiren-2(1aH)-one (2.38)



Methyl ester **2.33** (0.94 g, 3.7 mmol, 1.0 equiv) was dissolved in THF (37 mL) and cooled to 0 ˚C. Potassium *tert*-butoxide (0.50 g, 4.4 mmol, 1.2 equiv) was added and the mixture stirred for 30 min. Upon completion by TLC, saturated aqueous ammonium chloride (50 mL) was added and the reaction mixture was warmed to room temperature. The aqueous layer was extracted with ethyl acetate (3 x 50 mL), the combined organic layers were washed with saturated aqueous sodium chloride (25 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash chromatography (10:1 hexanes:ethyl acetate) to give enol **2.38** as a white solid (0.69 g, 3.1 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.81 (s, 1H), 3.49 (d, *J* = 3.5 Hz, 1H), 2.48 – 2.24 (m, 4H), 1.64 – 1.42 (m, 6H), 1.01 (s, 3H), 0.78 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.08, 182.33, 106.01, 62.42, 57.60, 37.59, 36.33, 30.97, 28.98, 28.10, 23.72, 19.79, 15.79. **mp**: 41-44 °C. **IR**: $\tilde{\nu}$ = 2927, 2868, 1601, 1416, 1379, 1367, 1355, 1290, 1260, 1183, 934, 406 cm^{-1}. **$[\alpha]^{20}_D$** = –45.4° (c 0.97, $CHCl_3$). **HRMS** (ESI): calcd for ([M+H], $C_{13}H_{19}O_3$)$^+$ *m/z* = 223.1329 found 223.1322. **R_f** = 0.55 (4:1 hexanes:ethyl acetate), UV-active, orange spot (*p*-anisaldehyde).

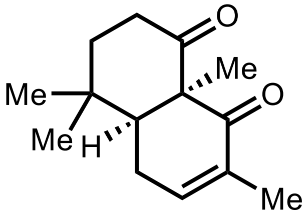
(1aR,2aS,6aS,7aR)-1a,2a,6,6-Tetramethylhexahydronaphtho[2,3-b]oxirene-2,3(1aH,2aH)-dione (2.39)



Enol **2.38** (4.4 g, 20 mmol, 1.0 equiv) was dissolved in anhydrous dimethylformamide (90 mL), followed by subsequent addition of potassium carbonate (12.3 g, 88.9 mmol, 4.5 equiv), tetrabutylammonium bromide (64 mg, 0.2 mmol, 0.01 equiv), and iodomethane (6.15 mL, 98.7 mmol, 5.0 equiv). This mixture was stirred in a closed vessel for 4.5 h at room temperature. Excess solid potassium carbonate removed by filtration through fritted glass and the filtrate was diluted with water (300 mL) and extracted with diethyl ether (4 x 100 mL). The combined organic layers were washed with saturated aqueous sodium chloride (50 mL), dried over magnesium sulfate, and concentrated *in vacuo*. Purification via flash chromatography (9:1 hexanes:ethyl acetate) afforded 1,3-dione **2.39** (3.2 g, 13 mmol, 68% yield) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.47 (d, *J* = 5.2 Hz, 1H), 2.57 (td, *J* = 14.4, 6.0 Hz, 1H), 2.46 (dd, *J* = 16.4, 7.2 Hz, 1H), 2.30 (ddd, *J* = 14.3, 4.6, 3.1 Hz, 1H), 2.15 (ddd, *J* = 16.4, 5.2, 2.2 Hz, 1H), 1.92 (dt, *J* = 7.0, 1.6 Hz, 1H), 1.75 (ddd, *J* = 13.8, 6.2, 3.1 Hz, 1H), 1.59 (td, *J* = 14.0, 4.5 Hz, 1H), 1.48 (s, 3H), 1.40 (s, 3H), 1.00 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.54, 208.54, 64.27, 59.94, 58.82, 56.35, 40.50, 36.56, 34.20, 30.69, 22.88, 22.68, 20.56, 15.86. **mp**: 128-131 °C. **IR**: $\tilde{\nu}$ = 2980, 2962, 2943, 2880, 1716, 1686, 1471, 1380, 1044, 1009, 851 cm^{-1}. **$[\alpha]^{20}_D$** = +122.5° (c 1.13, $CHCl_3$). **HRMS** (ESI): calcd for ([M+Na], $C_{14}H_{20}NaO_3$)$^+$ *m/z* = 259.1305 found 259.1308. **R_f** = 0.37 (4:1 hexanes:ethyl acetate), yellow-orange spot (*p*-anisaldehyde).

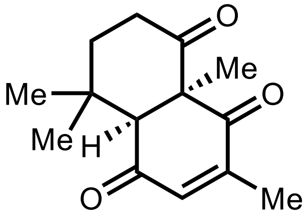
(4aS,8aS)-4,4,7,8a-Tetramethyl-3,4,4a,8a-tetrahydronaphthalene-1,8(2H,5H)-dione (2.40)



Procedure adapted from Nugent and coworkers.[18] THF (25 mL) was added to a flask charged with zinc (4.2 g, 64 mmol, 6.6 equiv) and bis(cyclopentadienyl)titanium(IV) dichloride (5.33 g, 21.4 mmol, 2.2 equiv). After 15 min, 1,3-dione **2.39** (2.3 g, 9.7 mmol, 1.0 equiv) was added dropwise in THF (25 mL). After stirring the solution at room temperature for 1.5 h, saturated aqueous monosodium phosphate (50 mL), saturated aqueous sodium chloride (50 mL), and ethyl acetate (50 mL) were added. After 1 h, the mixture was filtered through Celite® and the filtrate was extracted with ethyl acetate (3 x 75 mL). The combined organic layers were washed with saturated aqueous sodium chloride (25 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The resulting residue was purified via flash chromatography (8:1 hexanes:ethyl acetate). This yielded **2.40** (1.87 g, 8.48 mmol, 87% yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.58 – 6.55 (m, 1H), 2.71 – 2.56 (m, 2H), 2.39 (dd, *J* = 21.0, 4.8 Hz, 1H), 2.28 (dt, *J* = 13.9, 3.3 Hz, 1H), 1.99 (d, *J* = 6.7 Hz, 1H), 1.77 – 1.69 (m, 4H), 1.61 (td, *J* = 13.9, 3.8 Hz, 1H), 1.33 (s, 3H), 0.97 (s, 3H), 0.90 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.45, 200.56, 142.38, 133.79, 59.22, 54.13, 41.76, 37.07, 34.40, 30.40, 24.80, 22.99, 20.71, 16.03. **mp**: 99–104 ˚C. **IR**: ṽ = 2958, 2928, 2874, 1713, 1653, 1455, 1424, 1372, 1361, 1030, 847, 754 cm^{-1}. **$[\alpha]^{20}_D$** = +144.7˚ (c 1.14, $CHCl_3$). **HRMS** (ESI): calcd for ([M+H], $C_{14}H_{21}O_2$)$^+$ *m/z* = 221.1536 found 221.1543. **R_f** = 0.34 (4:1 hexanes:ethyl acetate), UV-active, yellow spot (*p*-anisaldehyde).

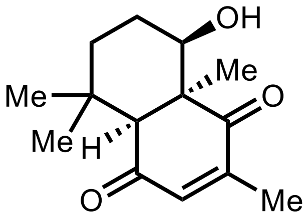
(4aS,8aS)-3,4a,8,8-Tetramethyl-6,7,8,8a-tetrahydronaphthalene-1,4,5(4aH)-trione (2.41)



Diketone **2.40** (1.87 g, 8.49 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (50 mL) in a flask open to the environment. Chromium trioxide (17.0 g, 169 mmol, 20 equiv) and 3,5-dimethylpyrazole (16.2 g, 169 mmol, 20 equiv) were added sequentially at 0 ˚C, and after stirring at 0 ˚C for 10 min the mixture was heated to 50 ˚C. After 20 h, slight starting material remined as evident by TLC, the mixture was cooled to room temperature and filtered through a silica plug. The silica was washed with 1:1 hexanes:ethyl acetate and the filtrate concentrated. The resultant residue was subjected to flash chromatography (1:6 hexanes:ethyl acetate) resulting in triketone **2.41** (1.54 g) as a yellow solid, which contained minimal inseparable starting material. The mixture was carried forward without further purification. *NOTE: reaction goes to completion on small scales, portion of product further purified for full characterization.*

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.58 – 6.52 (m, 1H), 2.68 (s, 1H), 2.67 (td, *J* = 14.4, 6.0 Hz, 1H), 2.40 (dt, *J* = 14.8, 3.4 Hz, 1H), 2.01 (d, *J* = 1.6 Hz, 3H), 1.83 – 1.68 (m, 2H), 1.37 (s, 3H), 1.06 (s, 3H), 0.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.92, 200.06, 197.90, 148.15, 137.23, 68.50, 60.59, 41.14, 36.49, 35.20, 29.70, 24.33, 23.68, 16.44. **mp**: 63–66 °C. **IR**: ṽ = 2962, 2933, 2871, 1721, 1666, 1625, 1428, 1375, 1249, 1191, 1178, 1030, 978, 892 cm^{-1}. **[*α*] $^{20}{}_D$** = +178.9° (c 1.21, $CHCl_3$). **HRMS** (ESI): calcd for ([M+Na], $C_{14}H_{18}NaO_3$)$^+$ *m/z* = 257.1148 found 257.1144. **R_f** = 0.28 (4:1 hexanes:ethyl acetate), UV-active, yellow spot (*p*-anisaldehyde).

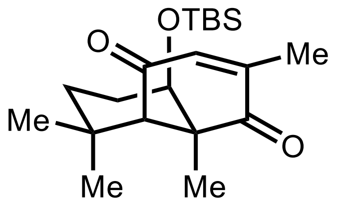
(4aS,8R,8aS)-8-Hydroxy-2,5,5,8a-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalene-1,4-dione (2.32)



Triketone **2.41** (1.54 g, 6.57 mmol, 1.0 equiv), with slight impurities, was dissolved in a mixture of methanol (33 mL) and dichloromethane (33 mL) and the solution was cooled to –78 °C. Sodium borohydride (0.25 g, 6.6 mmol, 1.0 equiv) was added and stirred for 1.5 h, before the addition of a second portion of sodium borohydride (0.25 g, 6.6 mmol, 1.0 equiv). After 1 h, acetone (50 mL) and water (50 mL) were added to quench excess borohydride and the mixture was warmed to room temperature. The mixture was diluted with water (50 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic layers were washed with saturated aqueous sodium chloride (25 mL), dried over magnesium sulfate, and concentrated *in vacuo.* The crude residue was subjected to flash chromatography (1:8 hexanes:ethyl acetate) to yield alcohol **2.32** as a mixture with remaining starting material (1.31 g) as a yellow solid. This was carried forward without further purification. Full characterization has been reported by Švenda and coworkers. The ^{1}H NMR spectrum is consistent with that reported in the literature.[23]

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 – 6.48 (m, 1H), 3.98 (br s, 1H), 3.15 (dd, *J* = 12.0, 4.3 Hz, 1H), 2.35 (d, *J* = 1.3 Hz, 1H), 1.99 (d, *J* = 1.5 Hz, 3H), 1.89 (dq, *J* = 13.4, 3.9 Hz, 1H), 1.77 (qd, *J* = 13.4, 3.5 Hz, 1H), 1.53 (dt, *J* = 13.7, 3.6 Hz, 1H), 1.46 (s, 3H), 1.48 – 1.39 (m, 1H), 0.96 (s, 3H), 0.72 (s, 3H).

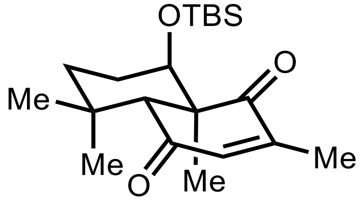
(4aS,8R,8aS)-8-((Tert-butyldimethylsilyl)oxy)-2,5,5,8a-tetramethyl-4a,5,6,7,8,8a-hexahydro-naphthalene-1,4-dione (2.43)



Prepared according to a modification of the procedure outlined by Švenda and coworkers.[23] Alcohol **2.32** (1.31 g, 5.54 mmol, 1.0 equiv), with slight impurities, was dissolved in dichloromethane (28 mL) and the solution was cooled to –78 ˚C. 2,6-lutidine (0.97 mL, 8.3 mmol, 1.5 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.27 mL, 5.54 mmol, 1.0 equiv.) were added sequentially. After 1 h of stirring at –78 ˚C, additional *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.25 mL, 1.1 mmol, 0.2 equiv) was added. After stirring for an additional 20 min, saturated aqueous sodium bicarbonate (30 mL) was added and the reaction mixture was warmed to room temperature. The mixture was extracted with dichloromethane (3 x 30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The crude residue was purified via flash chromatography in (20:1 → 8:1 hexanes:ethyl acetate) to yield **2.43** (1.70 g, 4.85 mmol, 57% over three steps) as a yellow solid. Full characterization has been reported by Švenda and coworkers. The ^{1}H NMR spectrum is consistent with that reported in the literature.[23]

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.39 – 6.38 (m, 1H), 3.23 (dd, *J* = 11.8, 3.8 Hz, 1H), 2.29 (d, *J* = 1.4 Hz, 1H), 2.08 – 1.96 (m, 1H), 1.96 (d, *J* = 1.5 Hz, 3H), 1.63 (dq, *J* = 13.4, 3.7 Hz, 1H), 1.49 (dt, *J* = 13.7, 3.6 Hz, 1H), 1.41 (td, *J* = 13.6, 3.7 Hz, 1H), 1.32 (s, 3H), 0.94 (s, 3H), 0.90 (s, 9H), 0.71 (s, 3H), 0.09 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 200.50, 200.03, 151.65, 135.49, 78.47, 67.72, 51.80, 40.95, 35.27, 30.79, 28.15, 26.95, 25.95, 24.56, 18.21, 16.76, –3.74, –4.76. **$[\alpha]^{20}_{D}$** = +29.5˚ (c 1.02, CHCl$_3$).

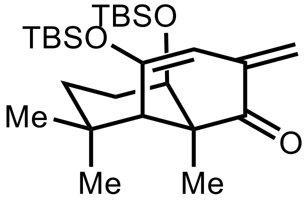
(4aR,8R,8aS)-8-((Tert-butyldimethylsilyl)oxy)-2,5,5,8a-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalene-1,4-dione (2.44)



Prepared according to a modification of the procedure outlined by Švenda and coworkers, originally by Kienzle and coworkers.[24,23] *Cis*-decalin **2.43** (10 mg, 28 μmol, 1.0 equiv) was dissolved in toluene (0.3 mL). Aluminum oxide (40.0 mg, 400 wt%) was added and the heterogeneous mixture was heated to reflux at 100 ˚C and that temperature was held for 24 h. The reaction mixture was cooled and filtered through a silica plug to remove solid aluminum oxide. The silica plug was flushed with ethyl acetate. The filtrate was concentrated *in vacuo*. The resultant crude product was purified via flash chromatography in (20:1 hexanes:ethyl acetate) to yield *trans*-decalin **2.44** (7.8 mg, 22 μmol, 80%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (m, 1H), 4.30 (m, 1H), 3.30 (s, 1H), 1.88 (d, *J* = 1.5 Hz, 3H), 1.86 – 1.66 (m, 2H), 1.59 – 1.49 (m, 1H), 1.24 (s, 3H), 1.14 (s, 6H), 1.10 (dt, *J* = 13.0, 3.1 Hz, 1H), 0.82 (s, 9H), 0.10 (s, 3H), 0.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.45, 201.19, 144.78, 138.70, 70.61, 55.90, 55.58, 35.12, 32.85, 32.41, 25.93, 24.87, 22.30, 21.33, 18.18, 15.94, –4.18, –5.09. **mp**: 43–44 ˚C. **IR**: ṽ = 2936, 2928, 2854, 1683, 1469, 1377, 1251, 1084, 836 cm^{-1}. **[*α*] ^{20}*$_D$*** = –108.4˚ (c 1.02, $CHCl_3$). **HRMS** (EI): calcd for ([M-CH_3], $C_{19}H_{31}O_3Si$)$^+$ *m/z* = 335.2037 found 335.2038. **R$_f$** = 0.61 (8:1 hexanes:ethyl acetate), UV-active, blue spot (*p*-anisaldehyde).

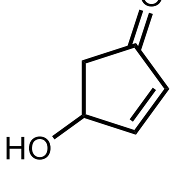
(4a*S*,8*R*,8a*S*)-4,8-bis((tert-butyldimethylsilyl)oxy)-5,5,8a-trimethyl-2-methylene-4a,5,6,7,8,8a-hexahydronaphthalen-1(2H)-one (2.46)



Prepared according to a modification of the procedure outlined by Mohr and coworkers.[30] Enedione **2.43** (50 mg, 143 µmol, 1.0 equiv) was dissolved in acetonitrile (0.72 mL). The mixture was cooled to 0 °C and triethylamine (0.14 mL, 1.0 mmol, 7.0 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.12 mL, 0.5 mmol, 3.5 equiv) were added sequentially. The reaction was allowed to warm to room temperature. After 30 min, saturated aqueous sodium bicarbonate (3 mL) was added and the mixture extracted with ethyl acetate (3 x 3 mL). The combined organic layers were dried over magnesium sulfate and concentrated in *vacuo*. The resultant residue was purified via flash chromatography (50:1 hexanes:ethyl acetate) to yield silyl dienol ether **2.46** (65 mg, 140 µmol, 98% yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.68 (d, *J* = 1.1 Hz, 1H), 5.65 (d, *J* = 1.9 Hz, 1H), 4.90 (d, *J* = 1.8 Hz, 1H), 3.29 (dd, *J* = 11.9, 4.0 Hz, 1H), 2.09 (tdd, *J* = 13.5, 11.9, 3.5 Hz, 1H), 1.81 (d, *J* = 1.2 Hz, 1H), 1.59 (ddd, *J* = 13.2, 9.3, 4.5 Hz, 1H), 1.46 (dt, *J* = 13.6, 3.5 Hz, 1H), 1.39 – 1.31 (m, 1H), 1.31 (s, 3H), 0.98 (s, 3H), 0.94 (s, 9H), 0.90 (s, 9H), 0.73 (s, 3H), 0.25 (s, 3H), 0.23 (s, 3H), 0.09 (s, 3H), 0.04 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 199.76, 155.48, 140.58, 114.66, 107.48, 78.50, 61.27, 51.41, 40.46, 35.83, 32.84, 28.15, 26.05, 25.75, 24.21, 21.90, 18.28, 18.06, -3.67, -3.76, -4.35, -4.64. **mp**: 56-61 °C**. [*α*]^{20}$_D$** = –29.77° (c 0.87, $CHCl_3$). **HRMS** (ESI): calc'd for [$C_{26}H_{49}O_3Si_2$]$^+$ *m/z* = 465.3215 found 465.3201. **R$_f$** = 0.66 (8:1 hexanes:ethyl acetate), UV-active, yellow spot (*p*-anisaldehyde).

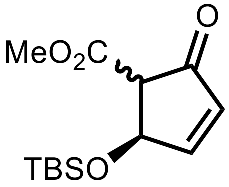
4-hydroxycyclopent-2-en-1-one (2.51)



Prepared according to a modification of the procedure outlined by Reiser and coworkers.[25] Furfuryl alcohol **2.50** (450 mg, 4.6 mmol, 1.0 equiv) in H_2O (18 mL) was heated in the microwave at 180 °C for 10 min. The mixture was extracted with ether (3 x 5 mL) and the combined organic layers were dried over magnesium sulfate and concentrated in *vacuo*. The resultant residue was purified via flash chromatography (1:1 hexanes:ethyl acetate) to yield enone **2.51** (298 mg, 2.0 mmol, 65% yield). Full characterization has been reported by Curran and coworkers. The ^{1}H NMR spectrum is consistent with that reported in the literature.[26]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 5.7, 2.3 Hz, 1H), 6.24 (dd, *J* = 5.7, 1.3 Hz, 1H), 5.07 (dq, *J* = 5.9, 2.0 Hz, 1H), 2.79 (dd, *J* = 18.5, 6.1 Hz, 1H), 2.29 (dd, *J* = 18.6, 2.1 Hz, 1H).

Methyl (2R)-2-((tert-butyldimethylsilyl)oxy)-5-oxocyclopent-3-ene-1-carboxylate (2.65)



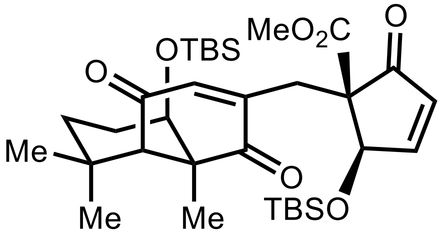
A solution of enone ***ent*-2.54** (60 mg, 0.28 mmol, 1.0 equiv) in THF (1.4 mL) was cooled to –78 °C. A homemade solution of lithium diisopropylamine (1M in THF, 0.37 mL, 0.37 mmol, 1.3 equiv) was added dropwise and the mixture was allowed to stir for 15 min. Methyl cyanoformate (0.07 mL, 0.84 mmol, 3 equiv) was added dropwise and the mixture was allowed to react for 30 min. At that point, ammonium chloride (3 mL) was added, and the mixture was warmed to room temperature and extracted with ethyl acetate (3 x 3 mL). The combined organic layers were dried over magnesium sulfate and concentrated in *vacuo*. The resultant residue was purified via flash chromatography (10:1 hexanes:ethyl acetate) to yield beta-ketoester **2.65** (37 mg, 0.14 mmol, 50% yield, 10:1 dr) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (ddd, *J* = 5.6, 2.3, 1.4 Hz, 1H), 6.16 (dt, *J* = 5.7, 1.6 Hz, 1H), 5.28 (td, *J* = 2.4, 1.3 Hz, 1H), 3.78 (d, *J* = 2.1 Hz, 3H), 3.28 (t, *J* = 2.3 Hz, 1H), 0.88 (q, *J* = 1.2 Hz, 9H), 0.10 (d, *J* = 19.2 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.3, 168.8, 163.6, 132.7, 74.5, 61.9, 52.8, 25.9, 25.8, 25.7, 18.1, -4.8, -4.9.

General Procedure for Manganese Triacetate Mediated Coupling:

Prepared according to a modification of the procedure outlined by Mohr and coworkers.[30] Silyl dienol ether **2.46** (1.0 equiv), 1,3-dicarbonyl (if solid, 1.3 equiv), and manganese triacetate dihydrate (3.0 equiv) were added to a crimp top vial fitted with a stir bar. The vial was sealed with a septa cap, evacuated, and refilled with N_2 three times. Acetonitrile (and 1,3-dicarbonyl, if liquid) was added and the sealed vial was heated to 80 °C for 0.5-2 h. Mixture changes from dark brown/orange to yellow/tan over course of reaction. Upon completion shown by TLC the mixture was cooled to room temperature and filtered through a silica plug with ethyl acetate. The resulting solution was concentrated *in vacuo*. Crude mixture was submitted directly to purification.

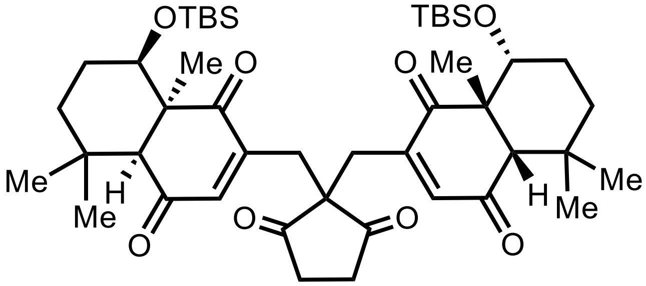
Methyl (1R,2R)-2-((tert-butyldimethylsilyl)oxy)-1-(((4aS,8R,8aS)-8-((tert-butyldimethylsilyl)oxy)-5,5,8a-trimethyl-1,4-dioxo-1,4,4a,5,6,7,8,8a-octahydronaphthalen-2-yl)methyl)-5-oxocyclopent-3-ene-1-carboxylate (2.66)



The title compound was prepared with slight deviation from the general procedure for manganese triacetate medicated coupling using silyl dienol ether **2.46** (10.0 mg, 21 µmol, 1.0 equiv), cyclopentenone **2.65** (6.4 mgs, 24 µmol, 1.1 equiv), manganese triacetate dihydrate (2.5 equiv), and 0.64 mL acetonitrile. Heat at 80 °C for 2 h. Concentrate to yield product **2.66** (94% crude yield) as a 3.1:1 mixture of diastereomers (diastereomers about position of methyl ester, major diastereomer pictured). An analytical sample of the major diastereomer was purified via preparative thin layer chromatography (10:1 hexanes:ethyl acetate, run 5 times).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 5.8, 2.0 Hz, 1H), 6.36 (s, 1H), 6.24 (d, *J* = 5.9 Hz, 1H), 5.05 (s, 1H), 3.65 (s, 3H), 3.28 (d, *J* = 14.4 Hz, 1H), 3.23 (dd, *J* = 11.8, 3.7 Hz, 1H), 2.89 (d, *J* = 14.6 Hz, 1H), 2.26 (s, 1H), 1.99 – 1.92 (m, 1H), 1.66 – 1.57 (m, 2H), 1.45 – 1.40 (m, 1H), 1.28 (s, 3H), 0.91 (s, 3H), 0.90 (s, 18H), 0.51 (s, 3H), 0.22 (s, 3H), 0.21 (s, 3H), 0.09 (s, 3H), 0.02 (s, 3H).

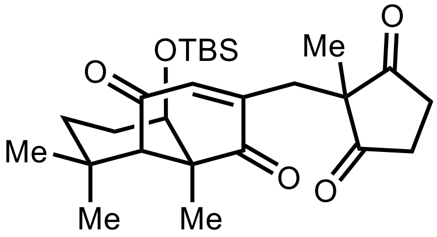
(4a*S*,4a'*S*,5*R*,5'*R*,8a*S*,8a'*S*)-3,3'-((2,5-dioxocyclopentane-1,1-diyl)bis(methylene))bis(5-((tert-butyldimethylsilyl)oxy)-4a,8,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphthalene-1,4-dione) (2.70)



The title compound was prepared according to the general procedure for manganese triacetate medicated coupling using silyl dienol ether **2.46** (10.0 mg, 0.021 mmol, 1.0 equiv), 1,3-cyclopentanedione (**2.68**) (2.4 mgs, 0.025 mmol, 1.2 equiv), 3.0 equiv manganese triacetate dihydrate, and 0.45 mL acetonitrile. Heat at 80 °C for 2 h. Purify via preparative thin layer chromatography (6:1 hexanes:ethyl acetate) to yield the dialkylated product **2.70** (9.0 mg, 0.011 mmol, 54%).

^{1}H NMR (700 MHz, CDCl$_3$) δ 6.34 (d, *J* = 2.0 Hz, 2H), 3.18 (dd, *J* = 11.8, 3.8 Hz, 2H), 2.94 (d, *J* = 14.6 Hz, 2H), 2.86 (d, *J* = 1.4 Hz, 4H), 2.29 (d, *J* = 1.7 Hz, 2H), 2.27 (d, *J* = 14.9 Hz, 2H), 1.90 (qd, *J* = 13.5, 3.3 Hz, 2H), 1.61 – 1.26 (m, 12H), 0.93 – 0.90 (m, 24H), 0.62 (s, 6H), 0.07 (d, *J* = 1.3 Hz, 6H), 0.02 (d, *J* = 1.3 Hz, 6H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 211.24, 200.52, 199.23, 148.73, 138.06, 78.21, 67.91, 57.88, 51.91, 40.77, 35.34, 34.61, 33.21, 30.66, 29.85, 28.01, 27.07, 25.91, 24.51, 18.17, 14.27, -3.65, -4.85. **HRMS** (ESI): calc'd for $[C_{45}H_{71}O_8Si_2]^+$ *m/z* = 795.4682 found 795.3658. **R$_f$** = 0.19 (8:1 hexanes:ethyl acetate), UV-active, dark green spot (*p*-anisaldehyde).

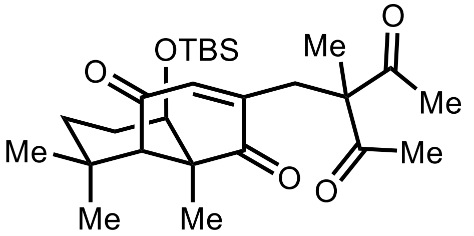
(4a*S*,8*R*,8a*S*)-8-((tert-butyldimethylsilyl)oxy)-5,5,8a-trimethyl-2-((1-methyl-2,5-dioxocyclopentyl)methyl)-4a,5,6,7,8,8a-hexahydronaphthalene-1,4-dione (2.72)



The title compound was prepared according to the general procedure for manganese triacetate medicated coupling using silyl dienol ether **2.46** (30 mgs, 64 µmol, 1.0 equiv), 2-methyl-1,3-cyclopentanedione (**2.71**) (9.4 mg, 0.084 mmol, 1.3 equiv), and 2 mL acetonitrile at 80 °C for 1 h. Purified via gradient flash chromatography (Yamazen, eluting with 12-33% ethyl acetate in hexanes) to yield title compound **2.72** (28.6 mg, 0.062 mmol, 97%) as an off white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.35 (q, *J* = 1.5 Hz, 1H), 3.17 (dd, *J* = 11.8, 4.0 Hz, 1H), 3.06 – 2.65 (m, 5H), 2.44 (dd, *J* = 15.4, 1.4 Hz, 1H), 2.27 (d, *J* = 1.3 Hz, 1H), 1.90 (tdd, *J* = 13.4, 11.7, 3.6 Hz, 1H), 1.57 (dq, *J* = 13.3, 3.7 Hz, 1H), 1.49 – 1.35 (m, 2H), 1.30 (s, 3H), 1.11 (s, 3H), 0.91 (s, 3H), 0.90 (s, 9H), 0.64 (s, 3H), 0.06 (s, 3H), 0.01 (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 214.06, 213.94, 201.22, 199.33, 149.00, 137.67, 78.22, 67.77, 55.03, 51.92, 40.75, 35.31, 34.49, 34.43, 34.40, 30.64, 27.98, 26.98, 25.88, 24.52, 20.99, 18.13, -3.73, -4.85. **HRMS** (ESI): calc'd for $[C_{26}H_{41}O_5Si]^+$ *m/z* = 461.2718 found 461.2730. **R$_f$** = 0.30 (4:1 hexanes:ethyl acetate), UV-active, yellow-green spot (*p*-anisaldehyde).

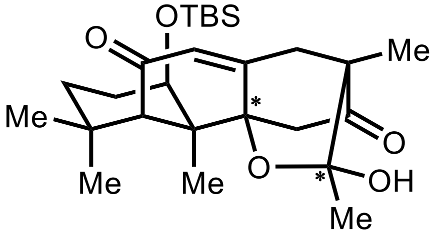
(4a*S*,8*R*,8a*S*)-2-(2-acetyl-2-methyl-3-oxobutyl)-8-((tert-butyldimethylsilyl)oxy)-5,5,8a-trimethyl-4a,5,6,7,8,8a-hexahydronaphthalene-1,4-dione (2.75)



The title compound was prepared according to the general procedure for manganese triacetate medicated coupling using silyl dienol ether **2.46** (30 mgs, 0.064 mmol, 1.0 equiv), 3-methyl-2,4-pentanedione (**2.74**) (10 µL, 0.084 mmol, 1.3 equiv), and 2 mL acetonitrile at 80 °C for 1.5 h. Purified via gradient flash chromatography (Yamazen, eluting with 0-19% ethyl acetate in hexanes) to yield title compound **2.75** (26.6 mg, 0.06 mmol, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (d, *J* = 1.2 Hz, 1H), 3.27 (dd, *J* = 13.8, 1.1 Hz, 1H), 3.19 (dd, *J* = 11.8, 3.9 Hz, 1H), 2.60 (dd, *J* = 13.7, 0.9 Hz, 1H), 2.29 (d, *J* = 1.4 Hz, 1H), 2.14 (d, *J* = 1.8 Hz, 6H), 1.99 (tdd, *J* = 13.4, 11.8, 3.5 Hz, 1H), 1.65 – 1.33 (m, 3H), 1.29 (s, 3H), 1.23 (s, 3H), 0.92 (s, 3H), 0.90 (s, 9H), 0.67 (s, 3H), 0.08 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.15, 205.39, 200.11, 199.45, 150.80, 138.71, 78.24, 67.78, 66.19, 51.86, 40.78, 35.36, 32.98, 30.74, 27.93, 27.17, 26.80, 26.76, 25.88, 24.16, 18.42, 18.14, -3.54, -4.97. **R_f** = 0.53 (4:1 hexanes:ethyl acetate), UV-active, brown spot (*p*-anisaldehyde).

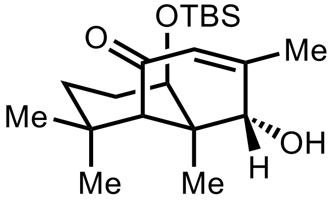
(5*R*,8a*S*)-5-((tert-butyldimethylsilyl)oxy)-12-hydroxy-2,4b,8,8,12-pentamethyl-1,2,4b,5,6,7,8,8a-octahydro-9H-4a,2-(epoxymethano)phenanthrene-3,9(4H)-dione (2.76)



1,3-dione **2.75** (8.2 mg, 18 µmol, 1.0 equiv) was dissolved in THF (0.8 mL). The mixture was cooled to –78 °C and potassium bis(trimethylsilyl)amide solution (1M in THF, 70 µL, 0.071 mmol, 4.0 equiv) was added dropwise. Upon addition of the potassium bis(trimethylsilyl)amide, the solution changed from clear to brown and then over time changed to red. After 1 h, sat. aq. ammonium chloride (3 mL) was added directly into the THF solution. The mixture was warmed to rt and extracted with ethyl acetate (3 x 3 mL). The combined organic layers were dried and concentrated *in vacuo*. The resulting residue was purified via preparative thin layer chromatography (4:1 hexanes:ethyl acetate) to yield hemiketal **2.76.** Absolute stereochemistry at starred carbons not confirmed.

^{1}H NMR (700 MHz, $CDCl_3$) δ 5.93 (s, 1H), 3.71 (d, *J* = 19.0 Hz, 1H), 3.41 (dd, *J* = 11.9, 4.1 Hz, 1H), 3.03 (d, *J* = 18.7 Hz, 1H), 2.59 (qd, *J* = 14.1, 12.5, 3.9 Hz, 1H), 2.46 (s, 1H), 2.37 (dd, *J* = 18.7, 2.6 Hz, 1H), 2.30 (d, *J* = 19.0 Hz, 1H), 1.95 (s, 1H), 1.55 – 1.47 (m, 2H), 1.39 – 1.26 (m, 4H), 1.15 (s, 3H), 1.09 (s, 3H), 1.07 (s, 3H), 0.98 (s, 3H), 0.90 (s, 9H), 0.09 (d, *J* = 6.4 Hz, 6H). **R$_f$** = 0.26 (4:1 hexanes:ethyl acetate), UV-active, yellow spot (*p*-anisaldehyde).

(4*S*,4a*R*,5*R*,8a*S*)-5-((tert-butyldimethylsilyl)oxy)-4-hydroxy-3,4a,8,8-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalen-1(4H)-one (2.77)

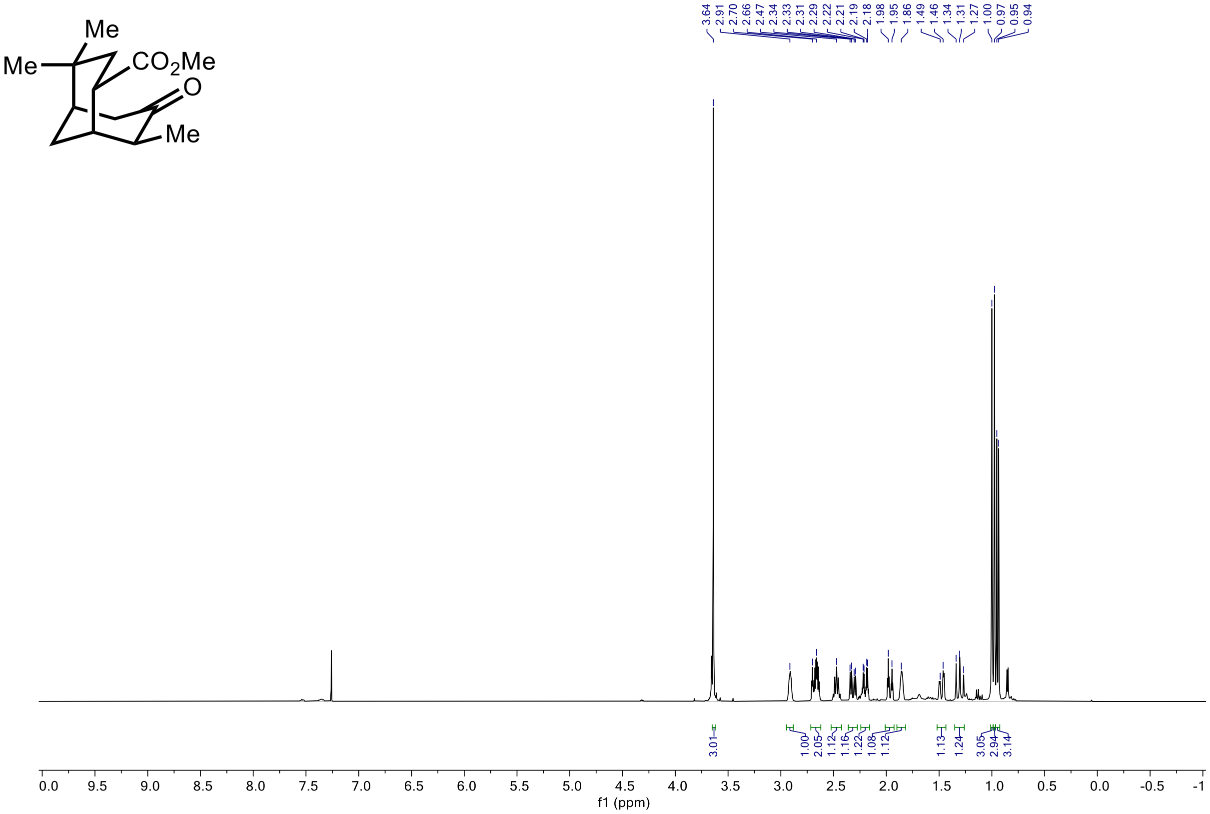


Enedione **2.43** (0.1 g, 0.29 mmol, 1.0 equiv) was dissolved in diethyl ether (1.6 mL) and cooled to –78 °C. Lithium aluminum hydride (13.0 mg, 0.34 mmol, 1,2 equiv) was added in one portion. After 2 h at –78 °C, the resulting grey/green suspension was quenched with sat. aq. Rochelle's salt (10 mL) and methanol (1 mL) and stirred for 1 hr at room temperature. The solution was extracted with ethyl acetate (3 x 10 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The resultant oil was purified via gradient flash chromatography (Yamazen, eluting with 0-13% ethyl acetate in hexanes) to yield hydroxyenone **2.77** as a white solid (92.8 mg, 0.26 mmol, 92%).

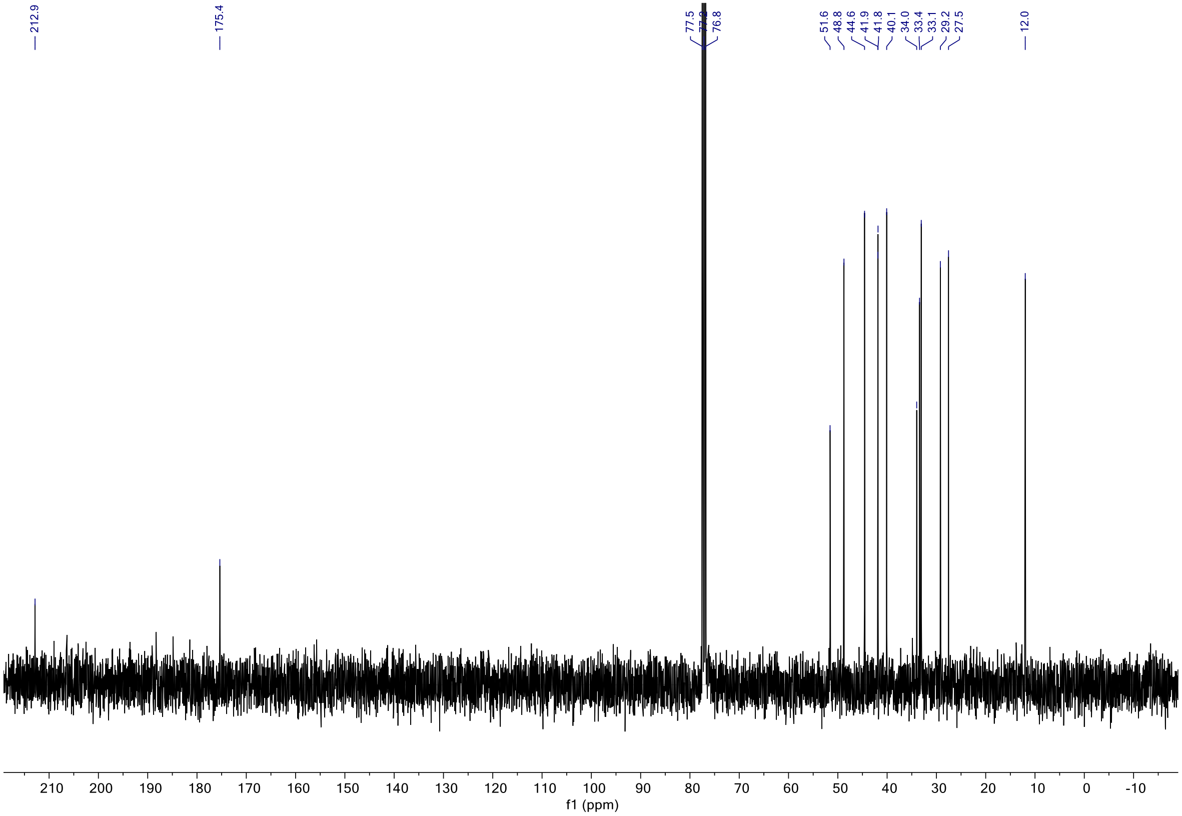
^{1}H NMR (600 MHz, CDCl$_3$): δ 5.87 (s, 1H), 4.04 (d, *J* = 3.9 Hz, 1H), 3.64 (d, *J* = 3.9 Hz, 1H), 3.53 (dd, *J* = 11.9, 5.5 Hz, 1H), 2.24 – 2.12 (m, 1H), 2.03 (s, 2H), 1.87 (s, 1H), 1.63 (dq, *J* = 12.9, 4.4, 3.9 Hz, 1H), 1.48 (dt, *J* = 13.6, 3.6 Hz, 1H), 1.36 – 1.30 (m, 2H), 1.01 (s, 3H), 0.98 (s, 3H), 0.96 (s, 3H), 0.94 (s, 9H), 0.14 (d, *J* = 1.1 Hz, 6H). **mp**: 101-105 °C. **R$_f$** = 0.64 (4:1 hexanes:ethyl acetate), UV-active, purple spot (*p*-anisaldehyde).

2.9.2 NMR Spectral Data for Chapter 2

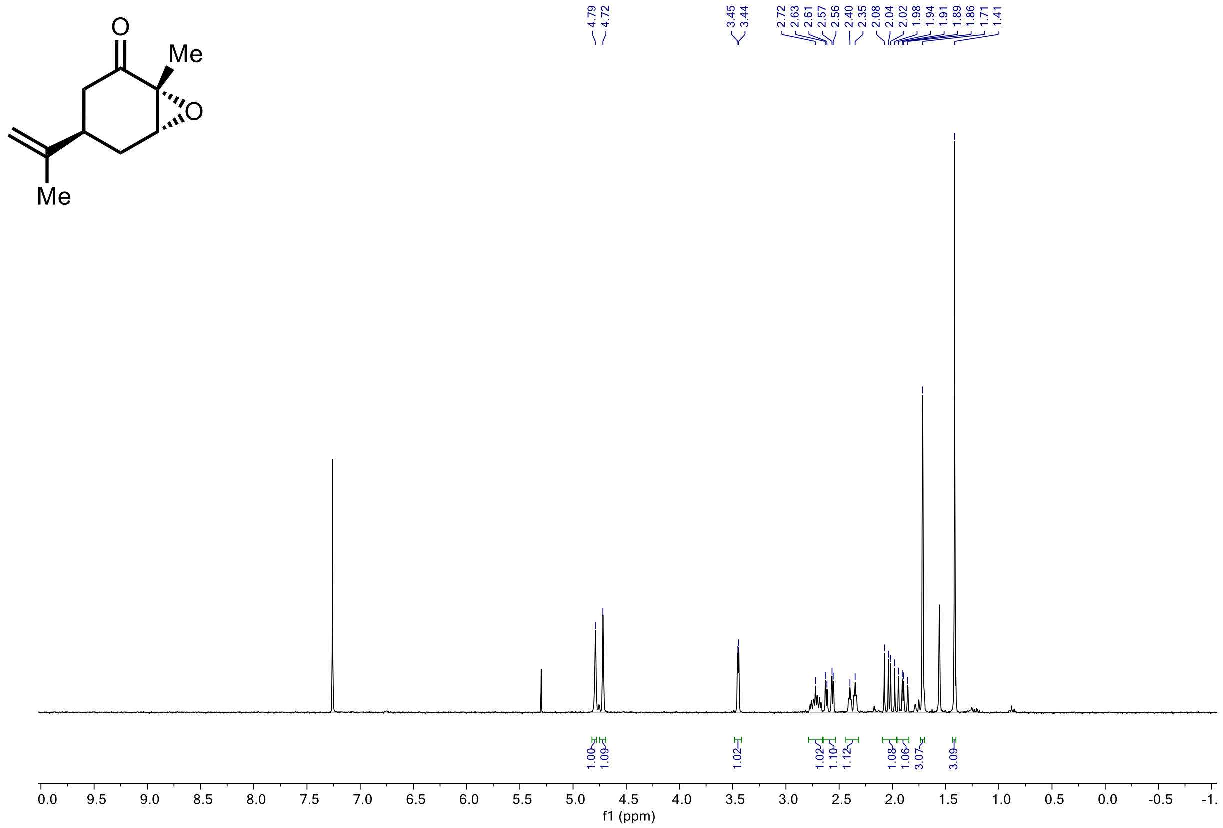
2.36 (^{1}H NMR, 400 MHz, CDCl$_3$)



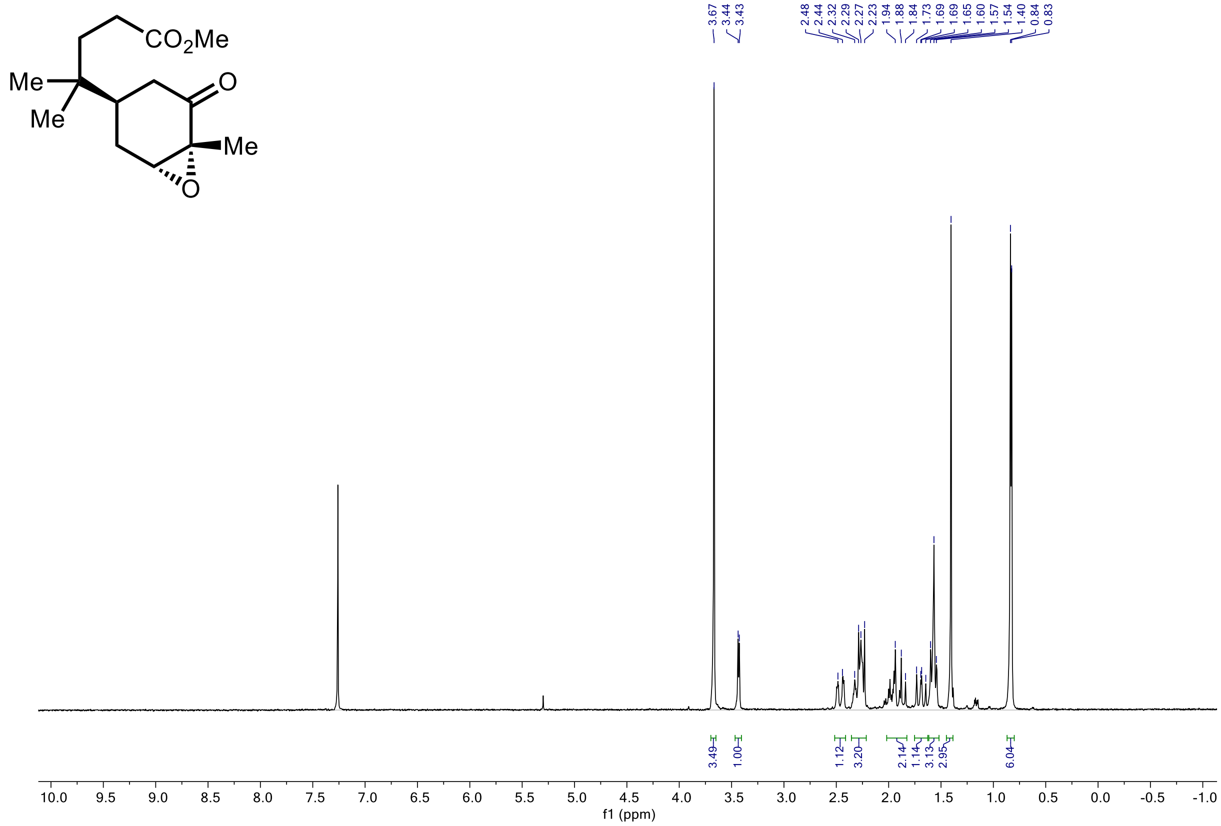
2.36 (^{13}C NMR, 101 MHz, CDCl$_3$)



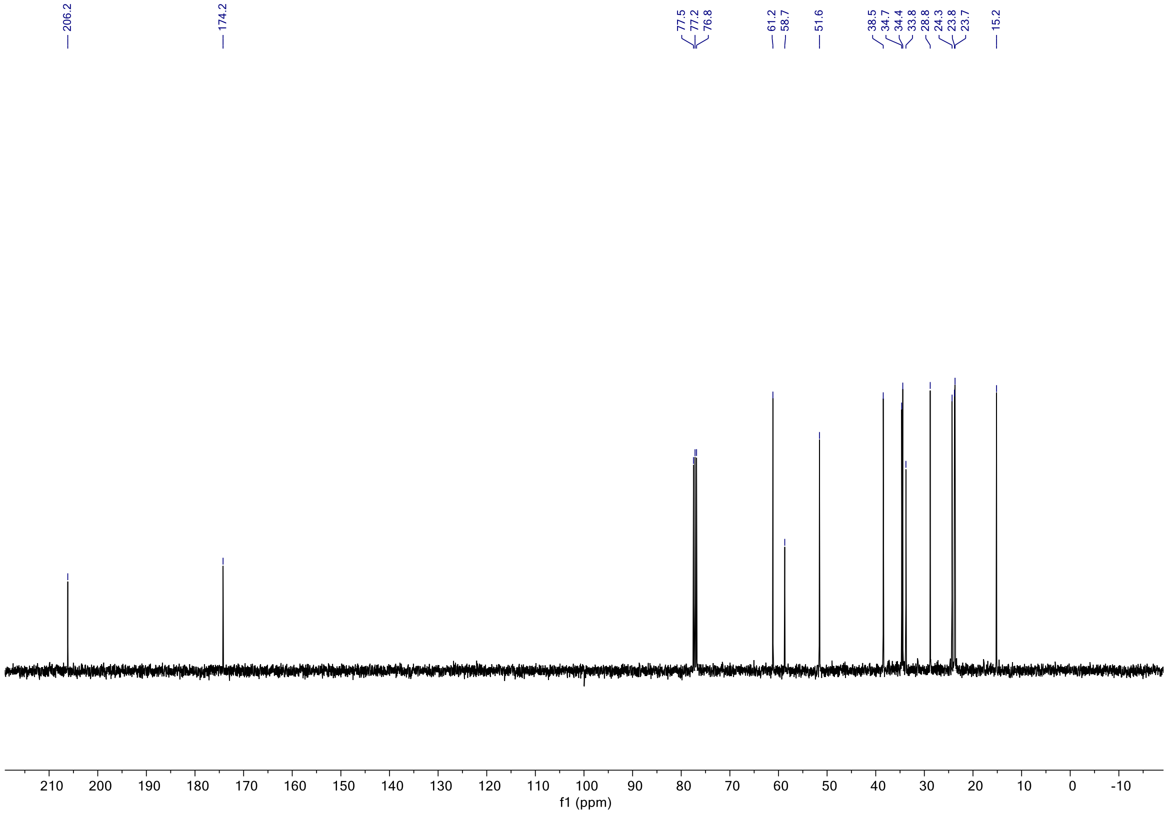
2.37 (^{1}H NMR, 300 MHz, CDCl$_3$)



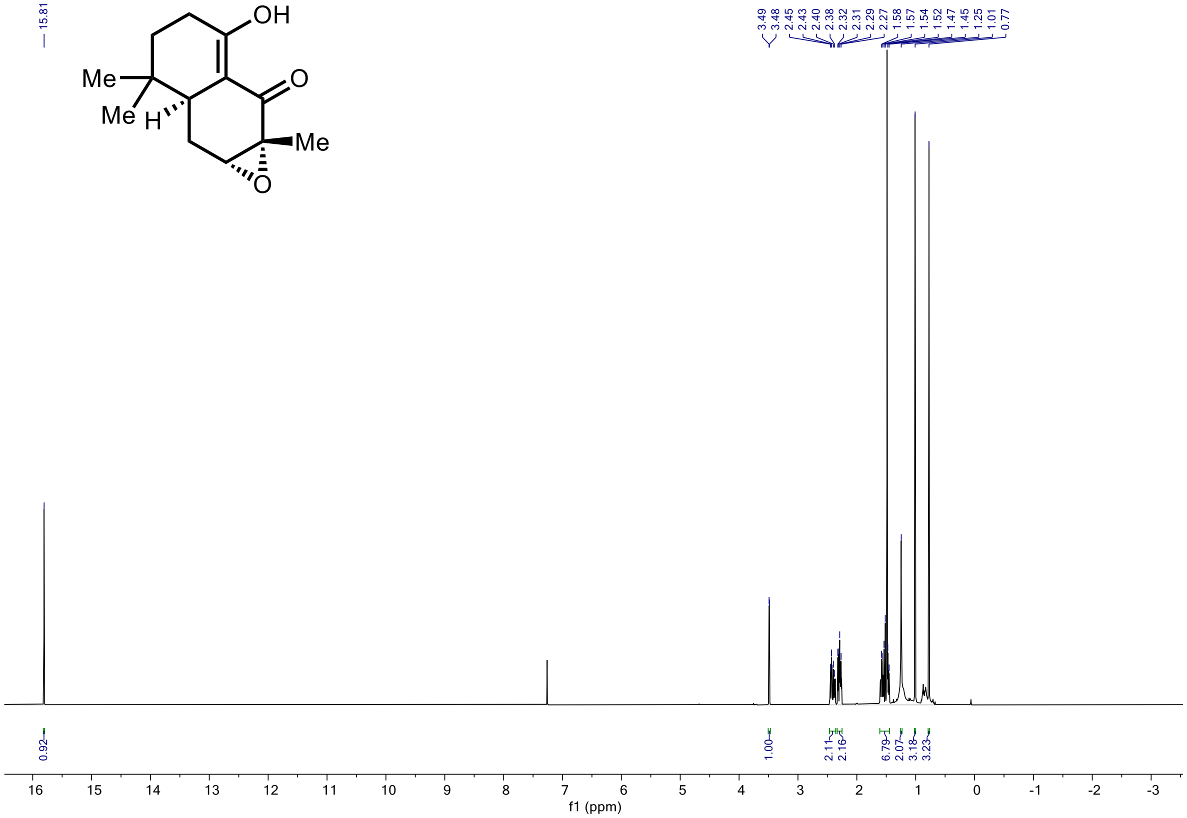
2.33 (^{1}H NMR, 300 MHz, CDCl$_3$)



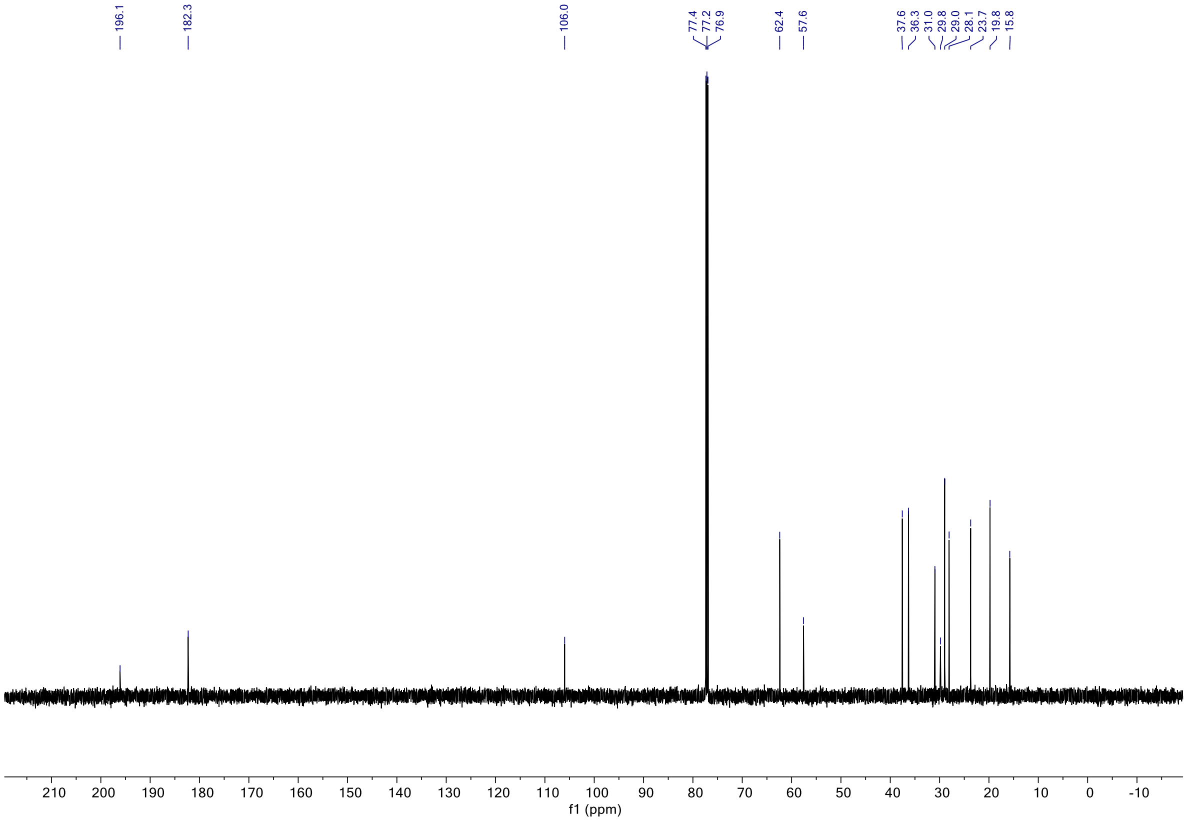
2.33 (^{13}C NMR, 101 MHz, CDCl$_3$)



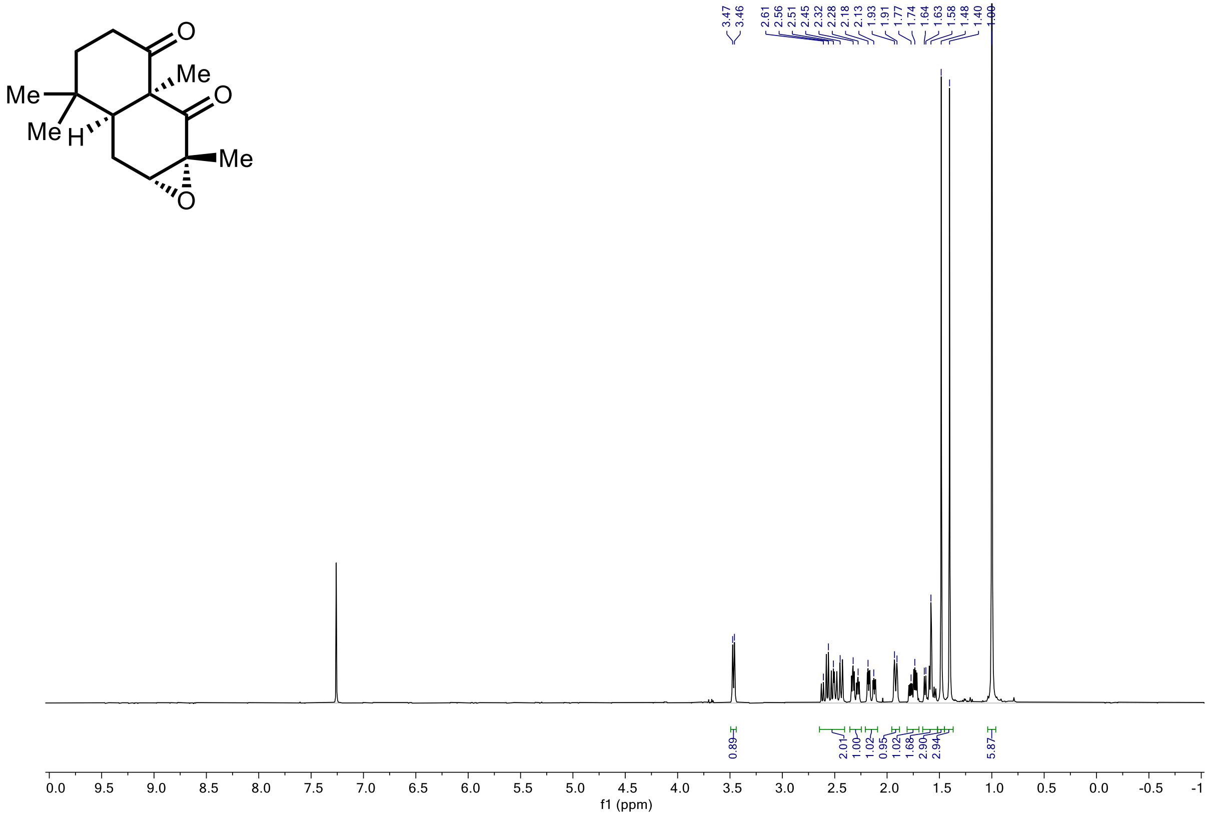
2.38 (^{1}H NMR, 600 MHz, CDCl$_3$)



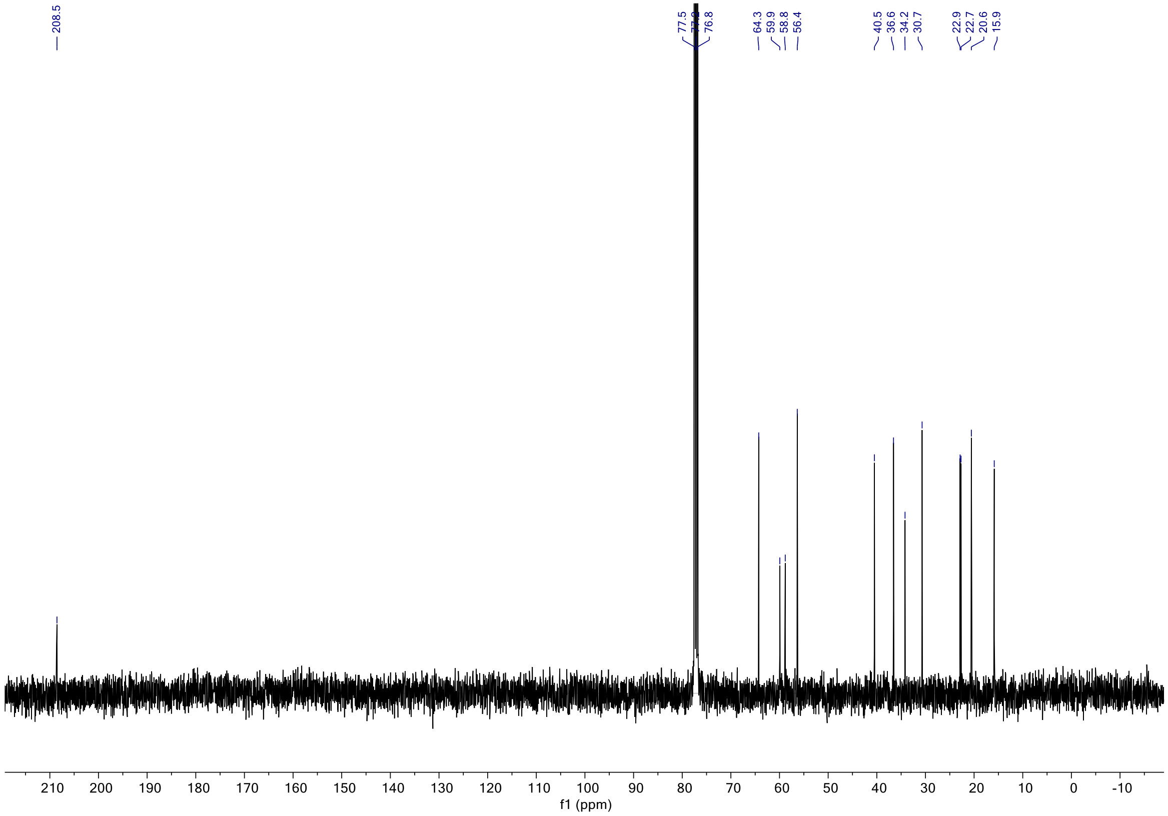
2.38 (^{13}C NMR, 151 MHz, CDCl$_3$)



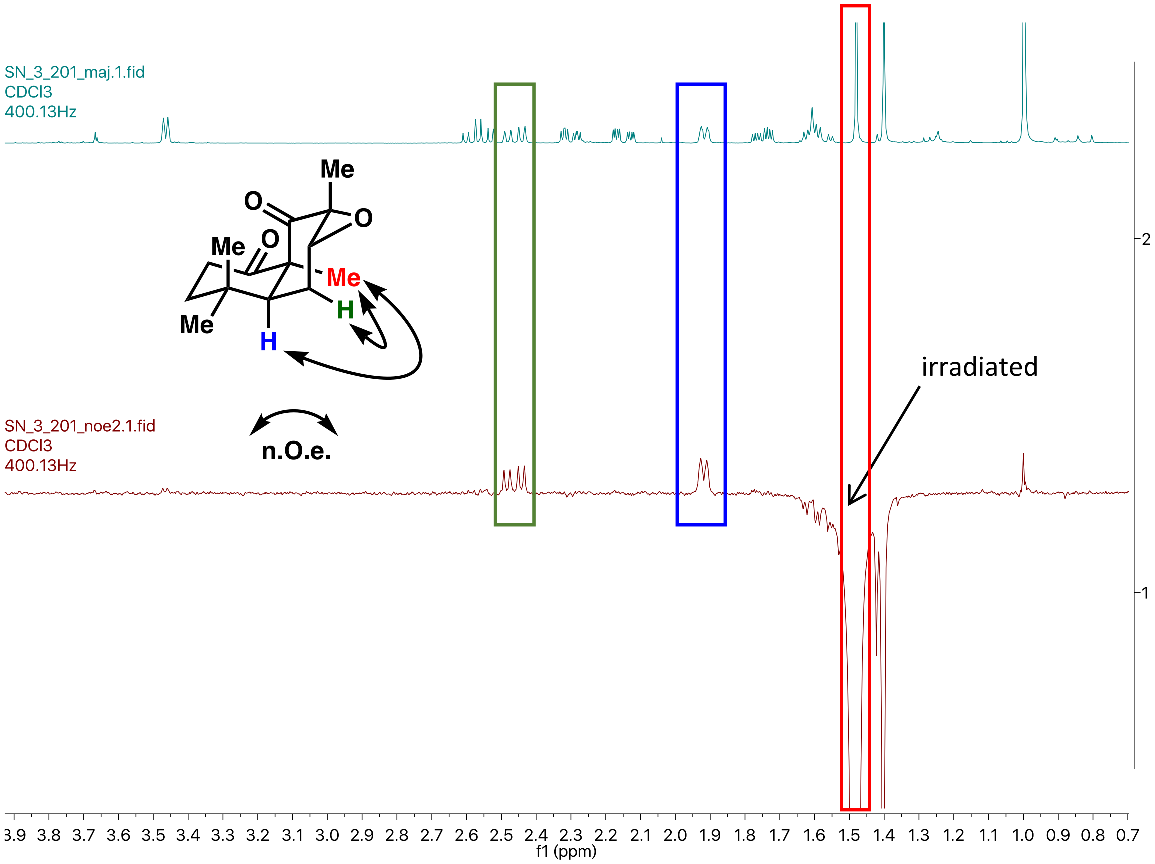
2.39 (^{1}H NMR, 300 MHz, CDCl$_3$)



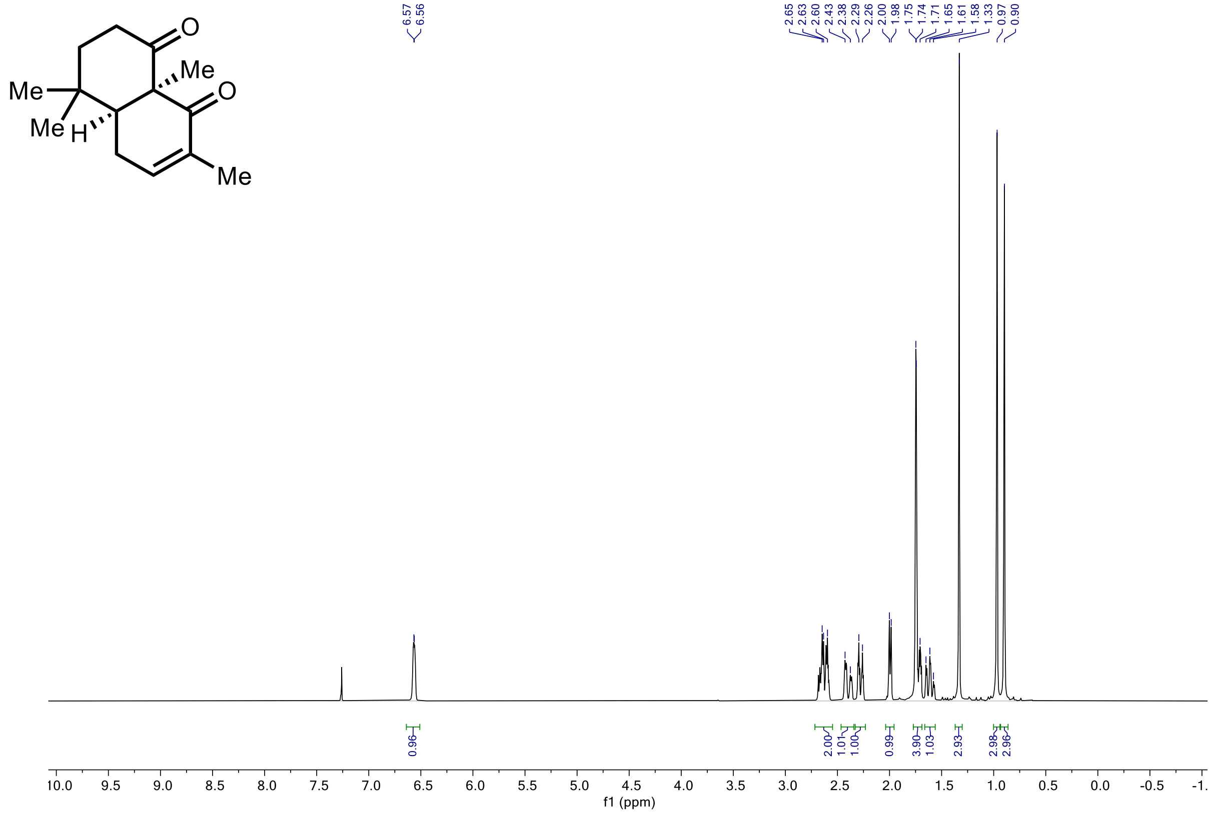
2.39 (^{13}C NMR, 101 MHz, CDCl$_3$)



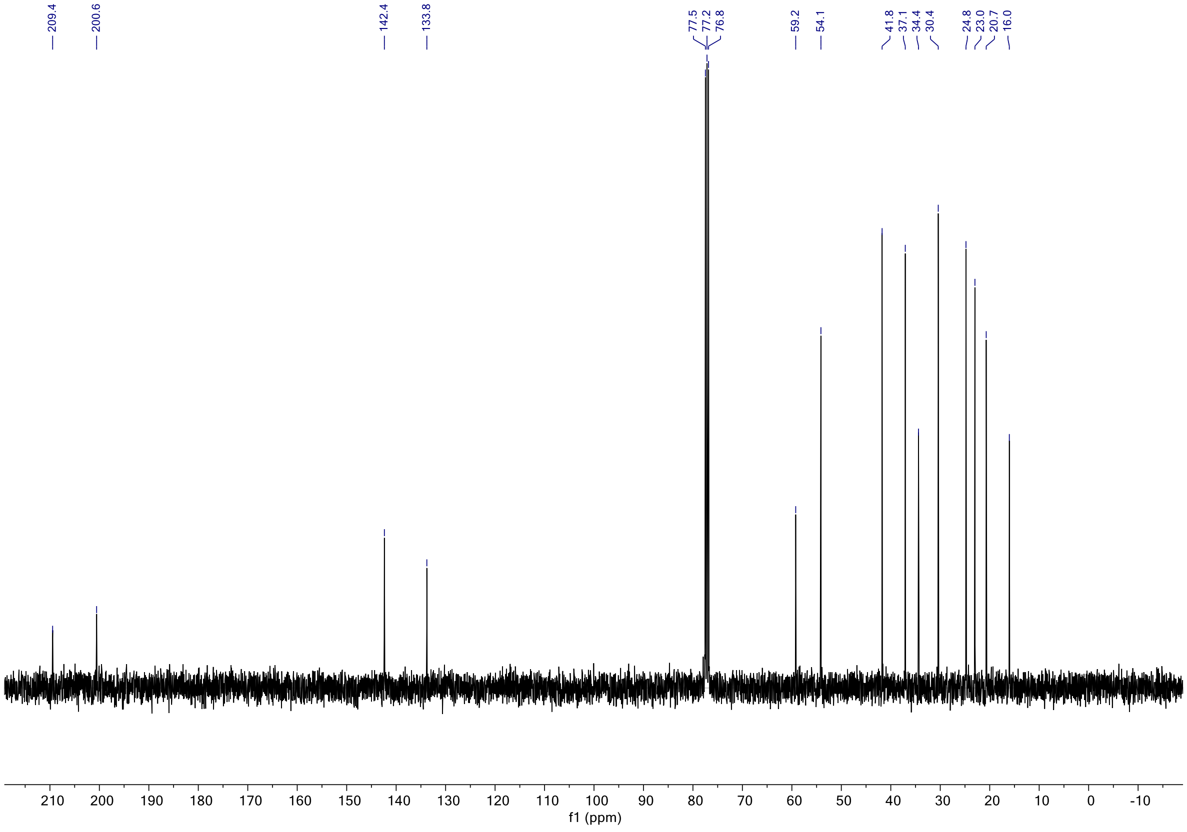
2.39 (NOE, CDCl₃)



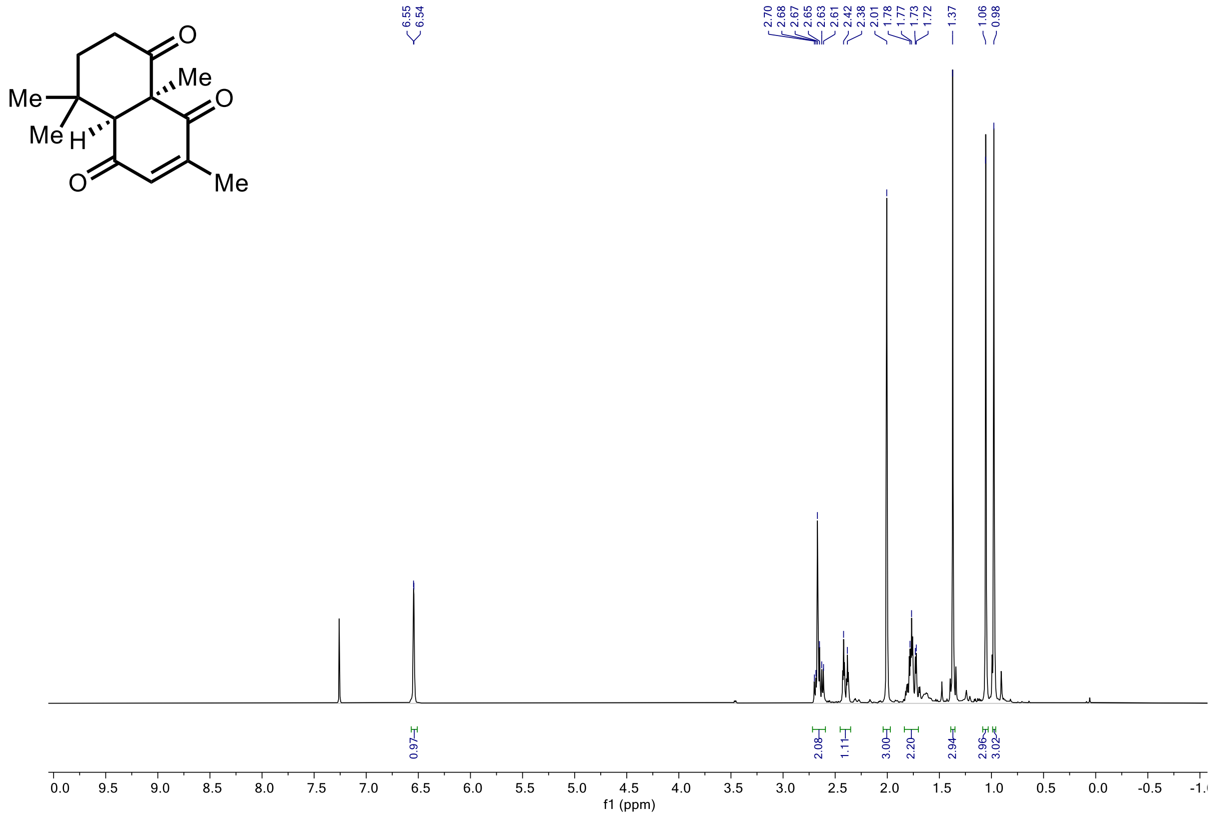
2.40 (^{1}H NMR, 400 MHz, CDCl$_3$)



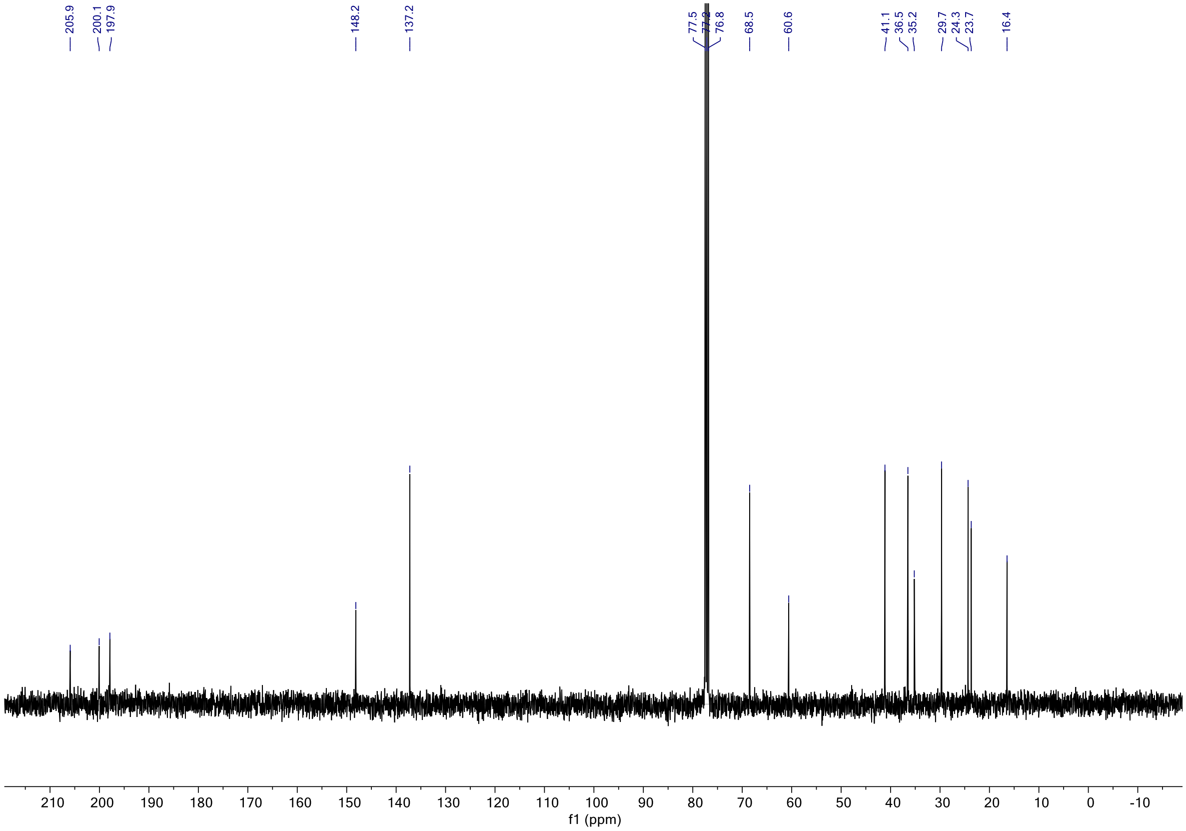
2.40 (^{13}C NMR, 101 MHz, CDCl$_3$)



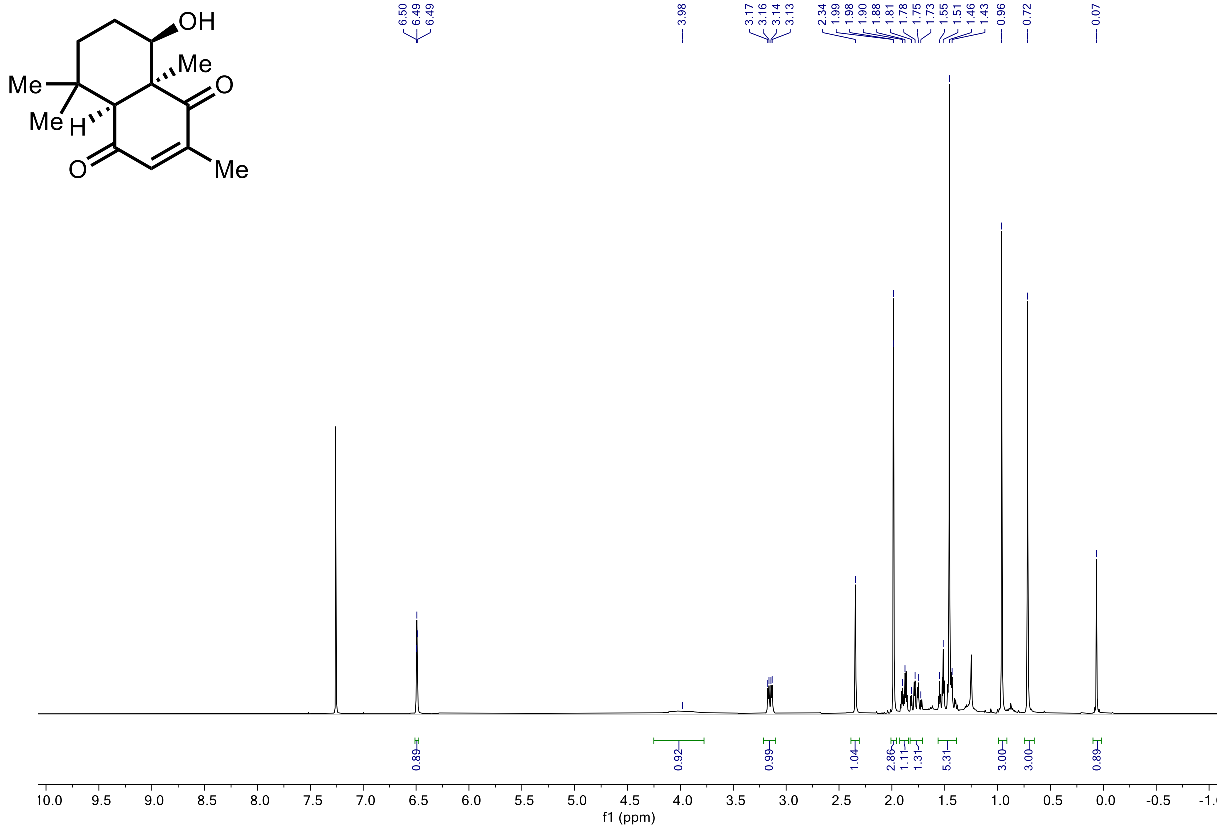
2.41 (^{1}H NMR, 400 MHz, CDCl$_3$)



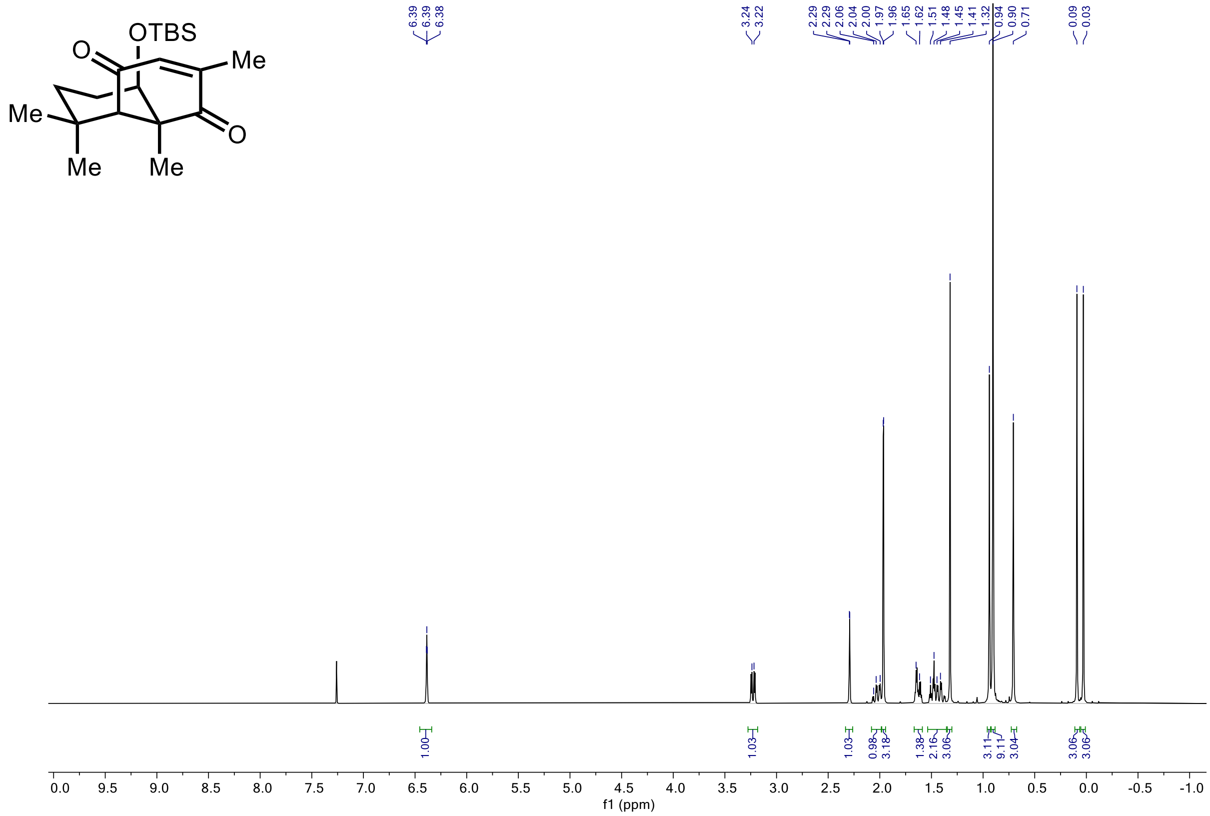
2.41 (^{13}C NMR, 101 MHz, CDCl$_3$)



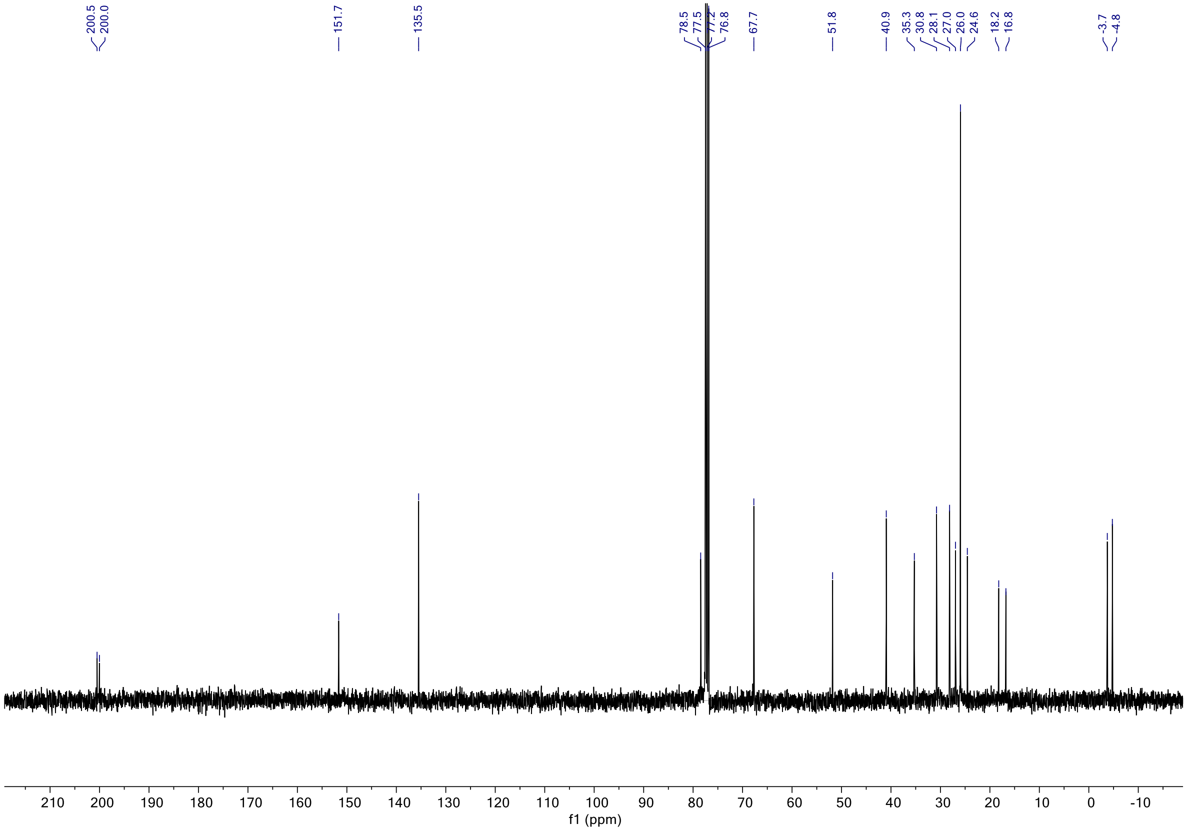
2.32 (^{1}H NMR, 400 MHz, $CDCl_3$)



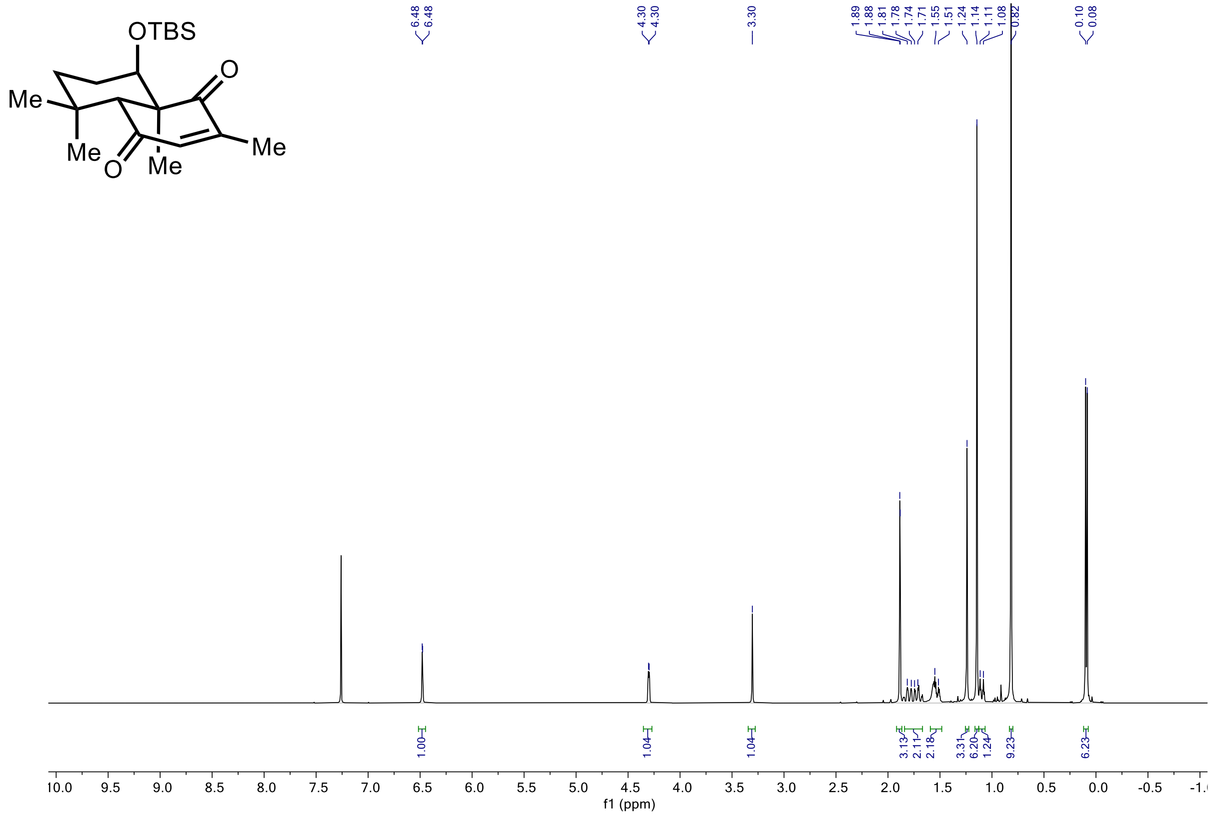
2.43 (^{1}H NMR, 400 MHz, CDCl$_3$)



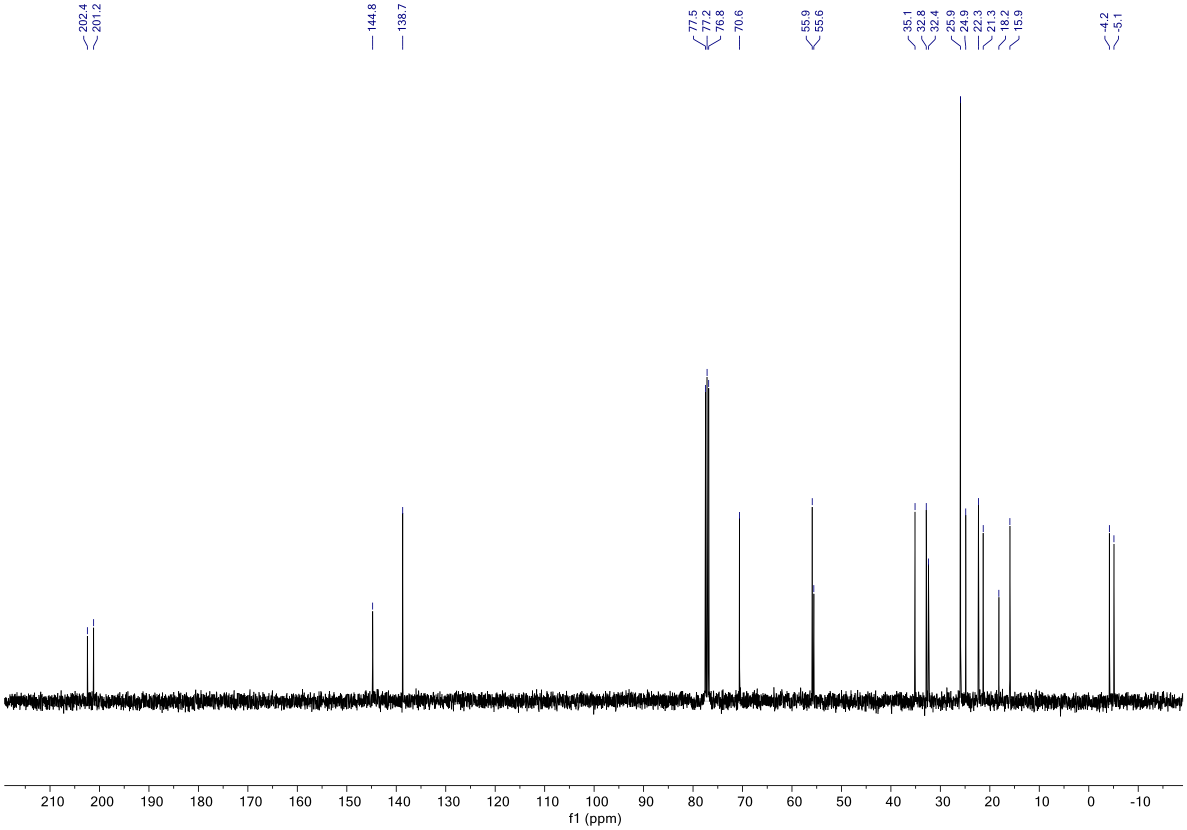
2.43 (^{13}C NMR, 101 MHz, CDCl$_3$)



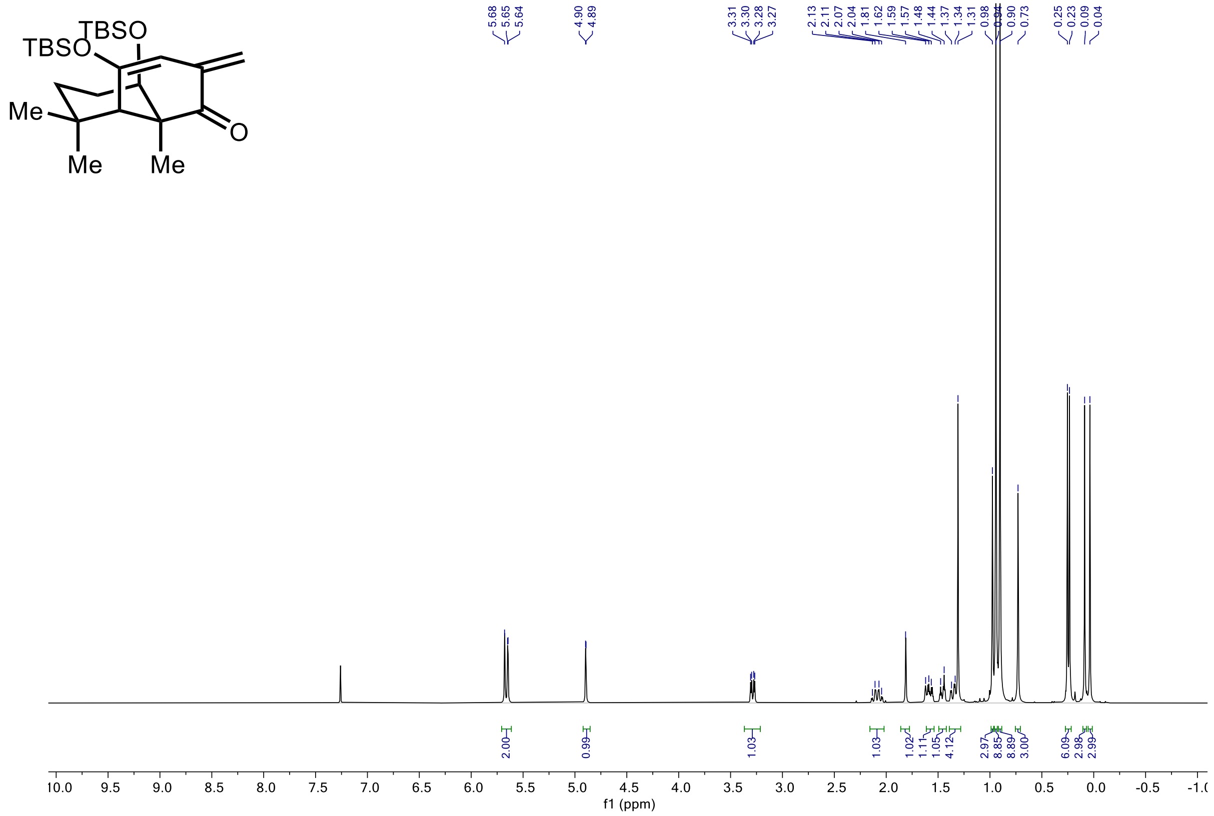
2.44 (^{1}H NMR, 400 MHz, CDCl$_3$)



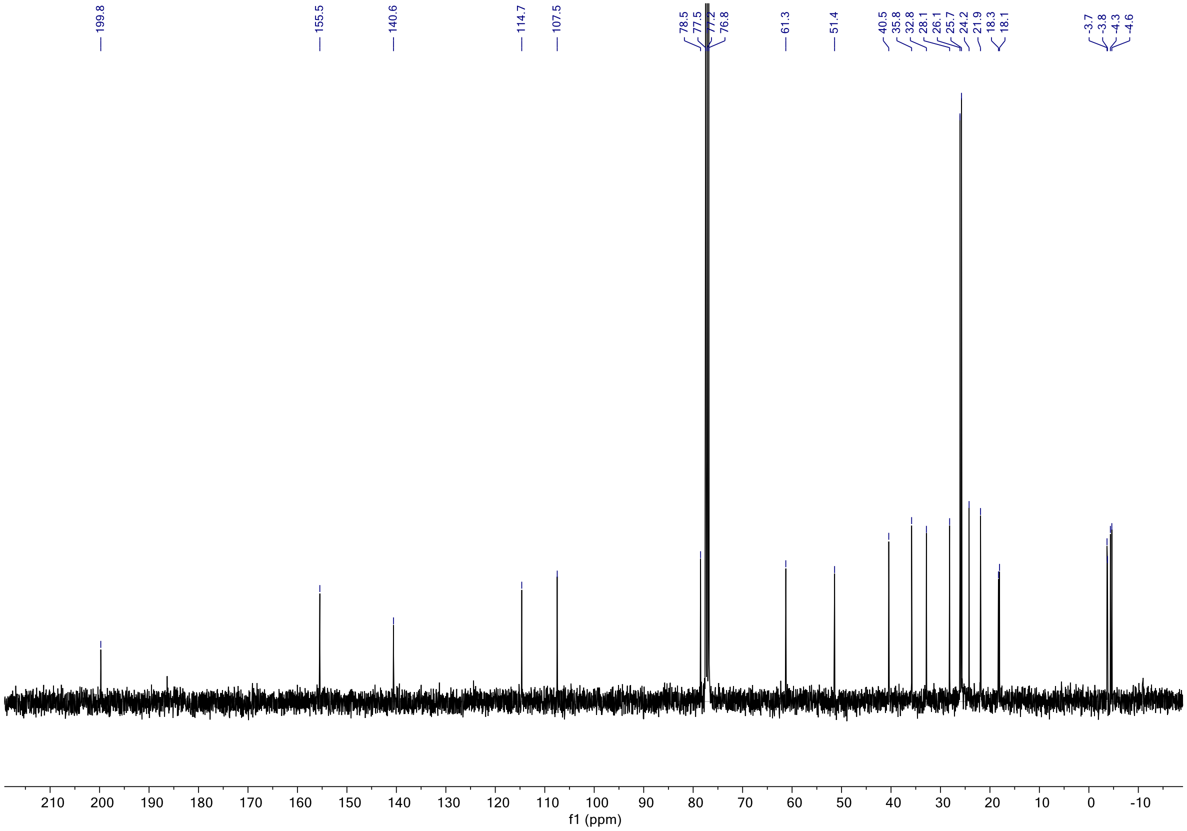
2.44 (^{13}C NMR, 101 MHz, CDCl$_3$)



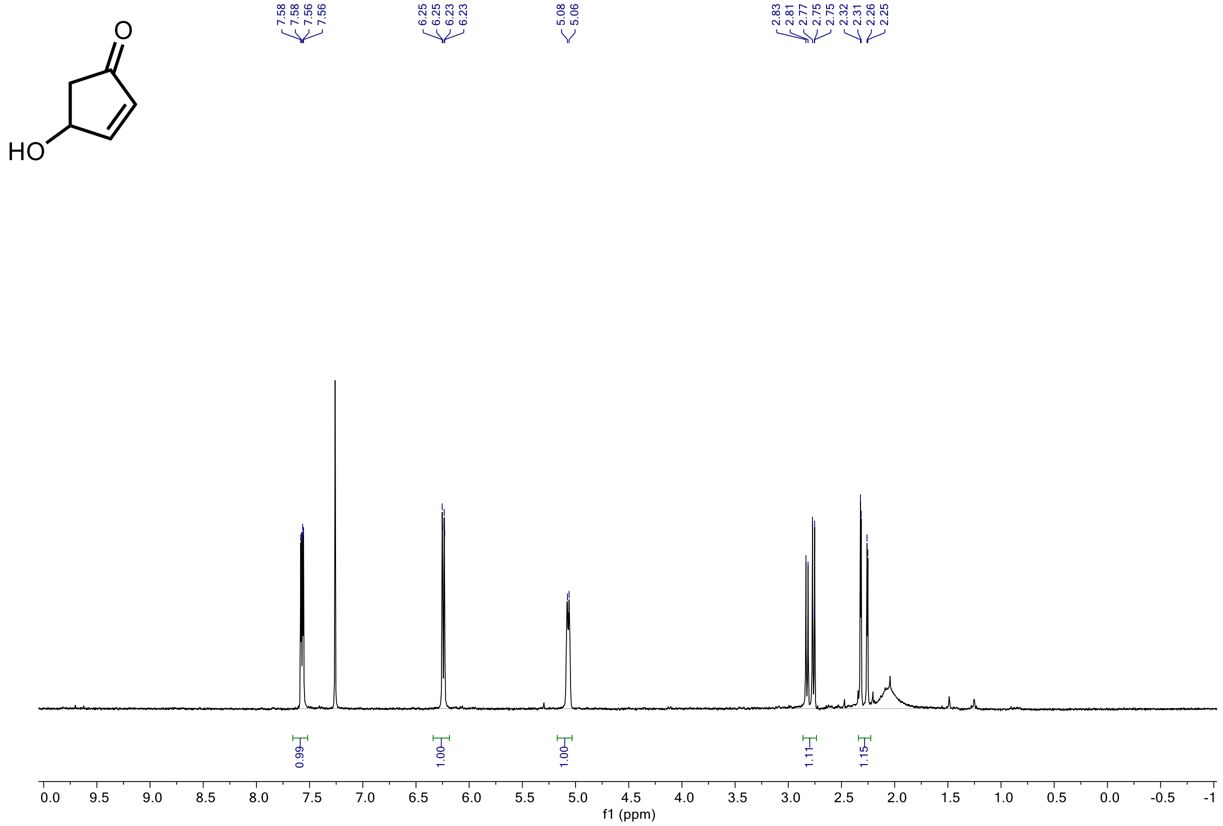
2.46 (^{1}H NMR, 400 MHz, CDCl$_3$)



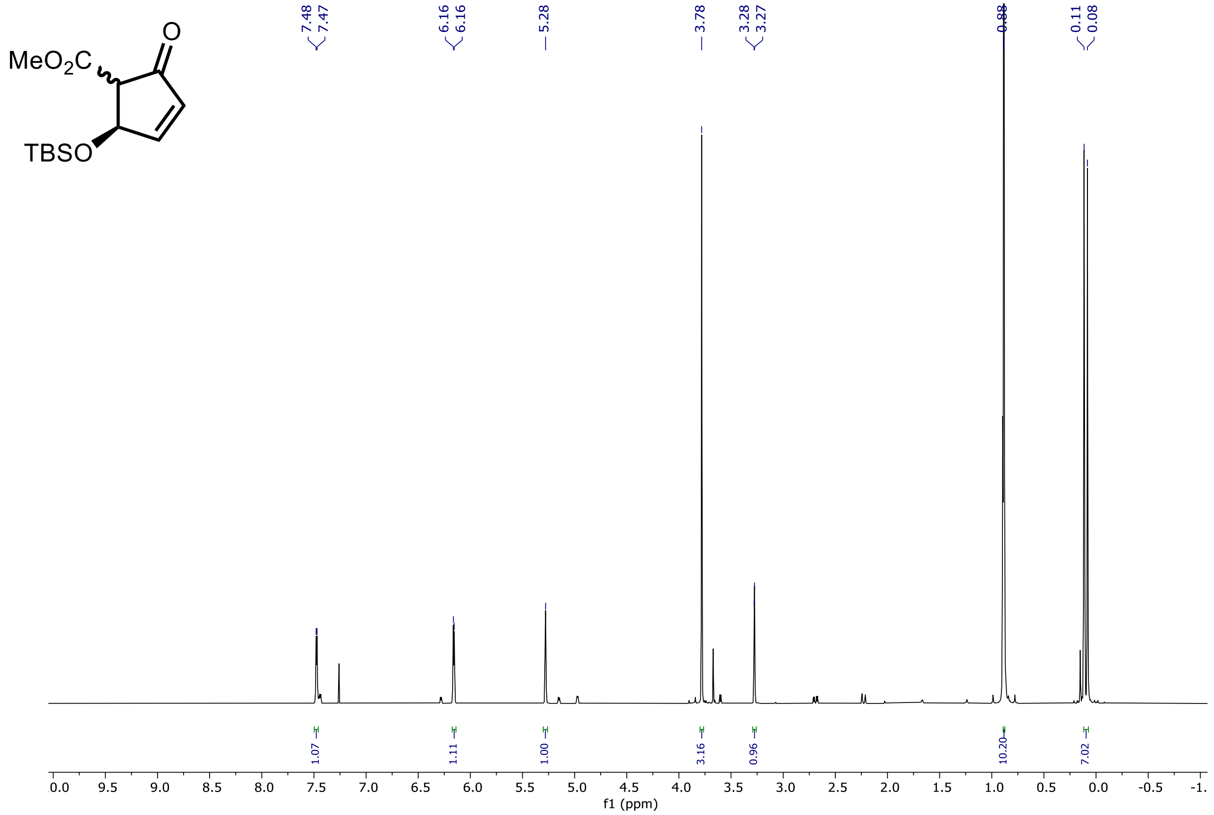
2.46 (^{13}C NMR, 101 MHz, CDCl$_3$)



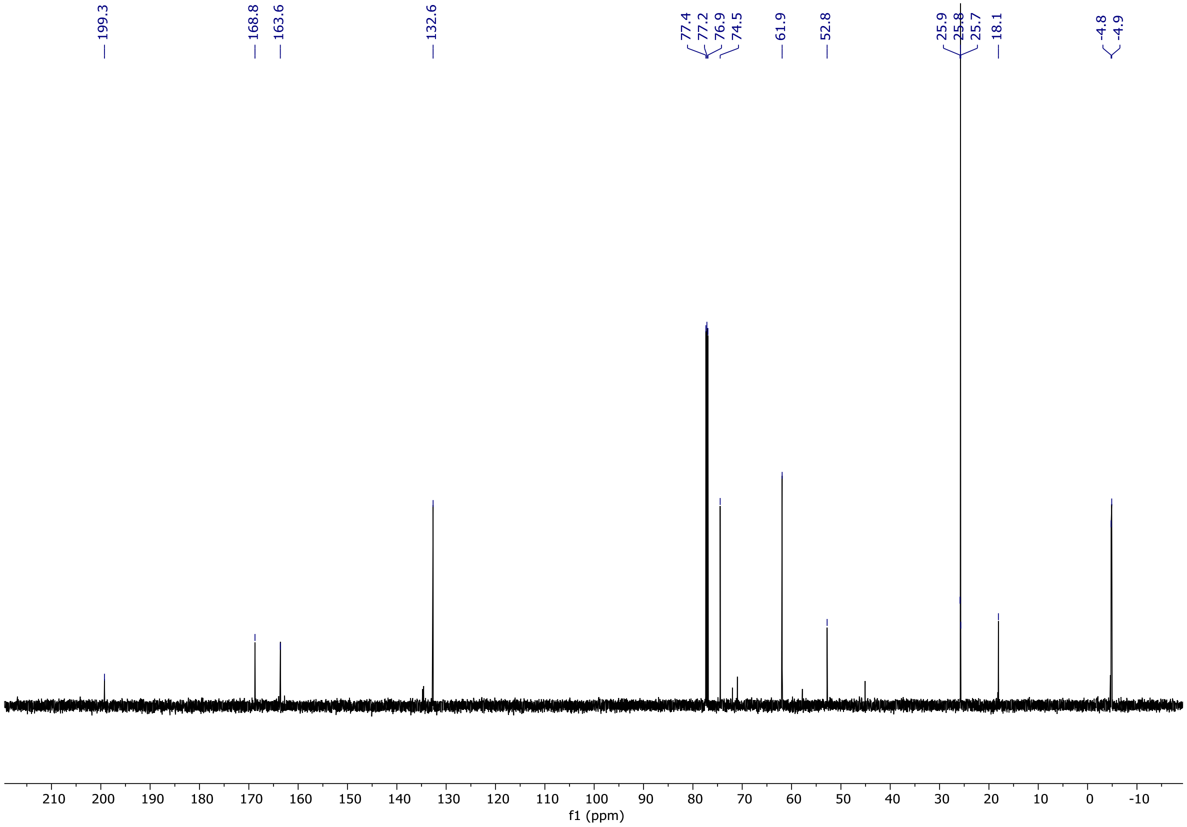
2.51 (^{1}H NMR, 300 MHz, $CDCl_3$)



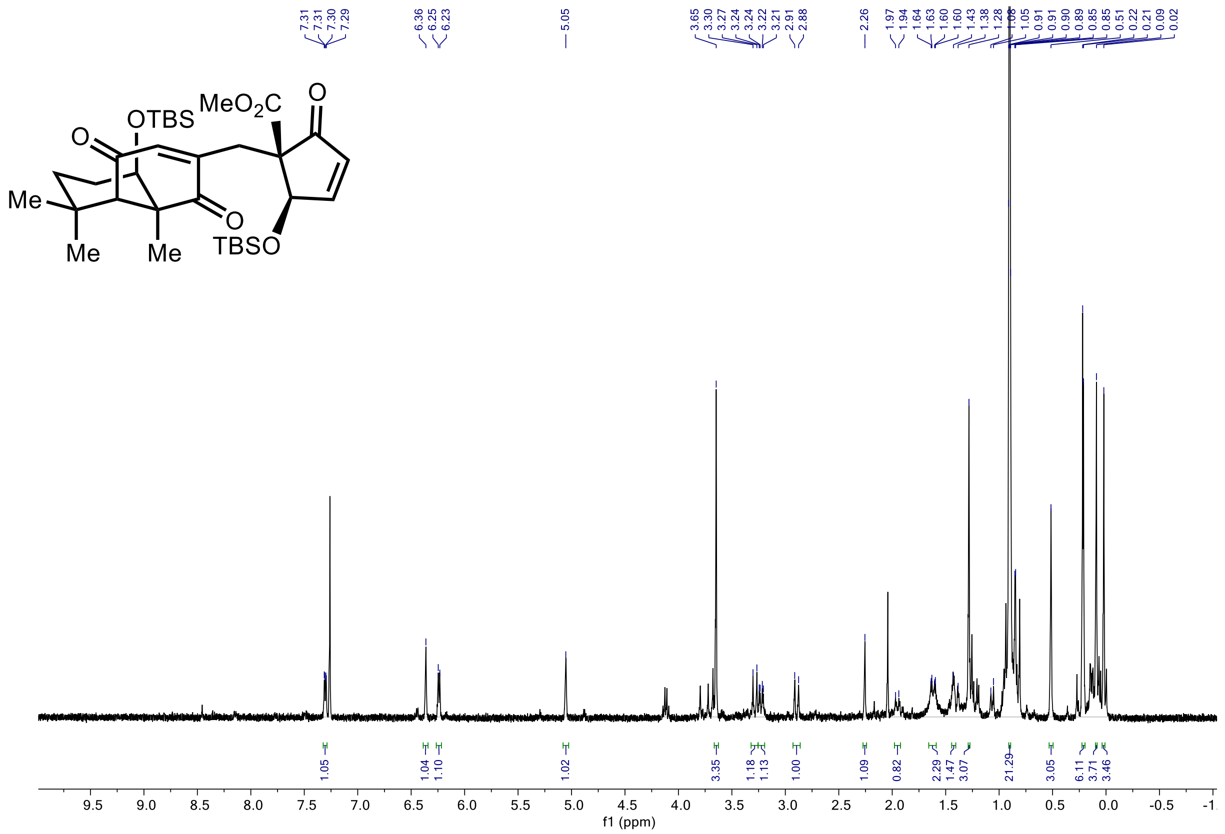
2.65 (^{1}H NMR, 600 MHz, CDCl$_3$)



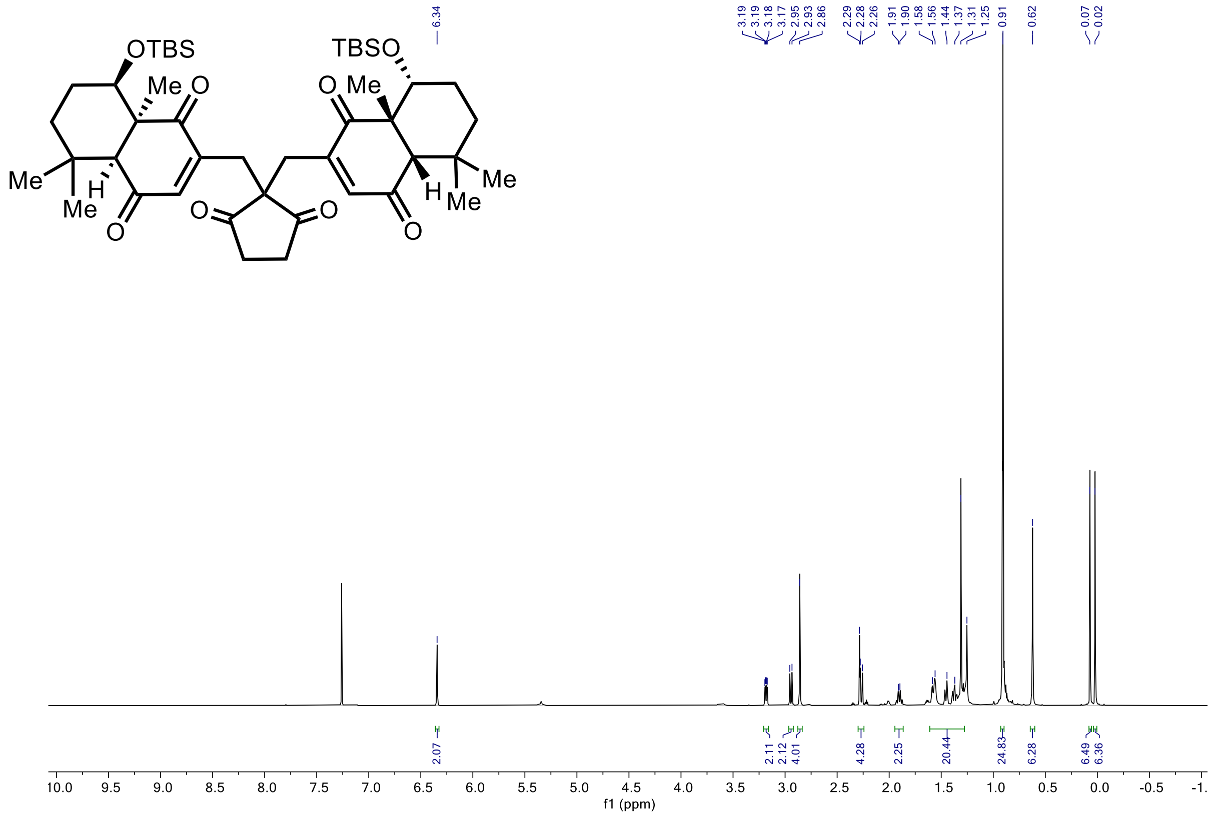
2.65 (^{13}C NMR, 151 MHz, CDCl$_3$)



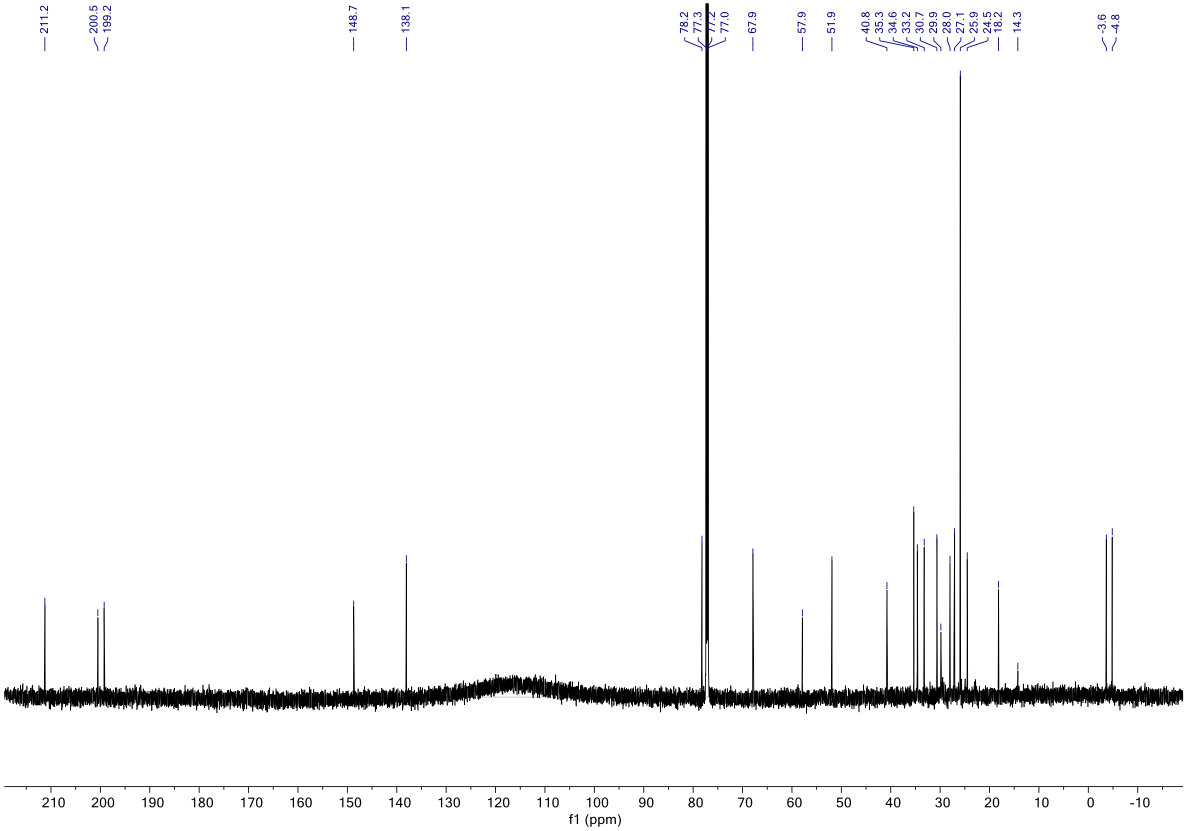
2.66 (^{1}H NMR, 400 MHz, CDCl$_3$)



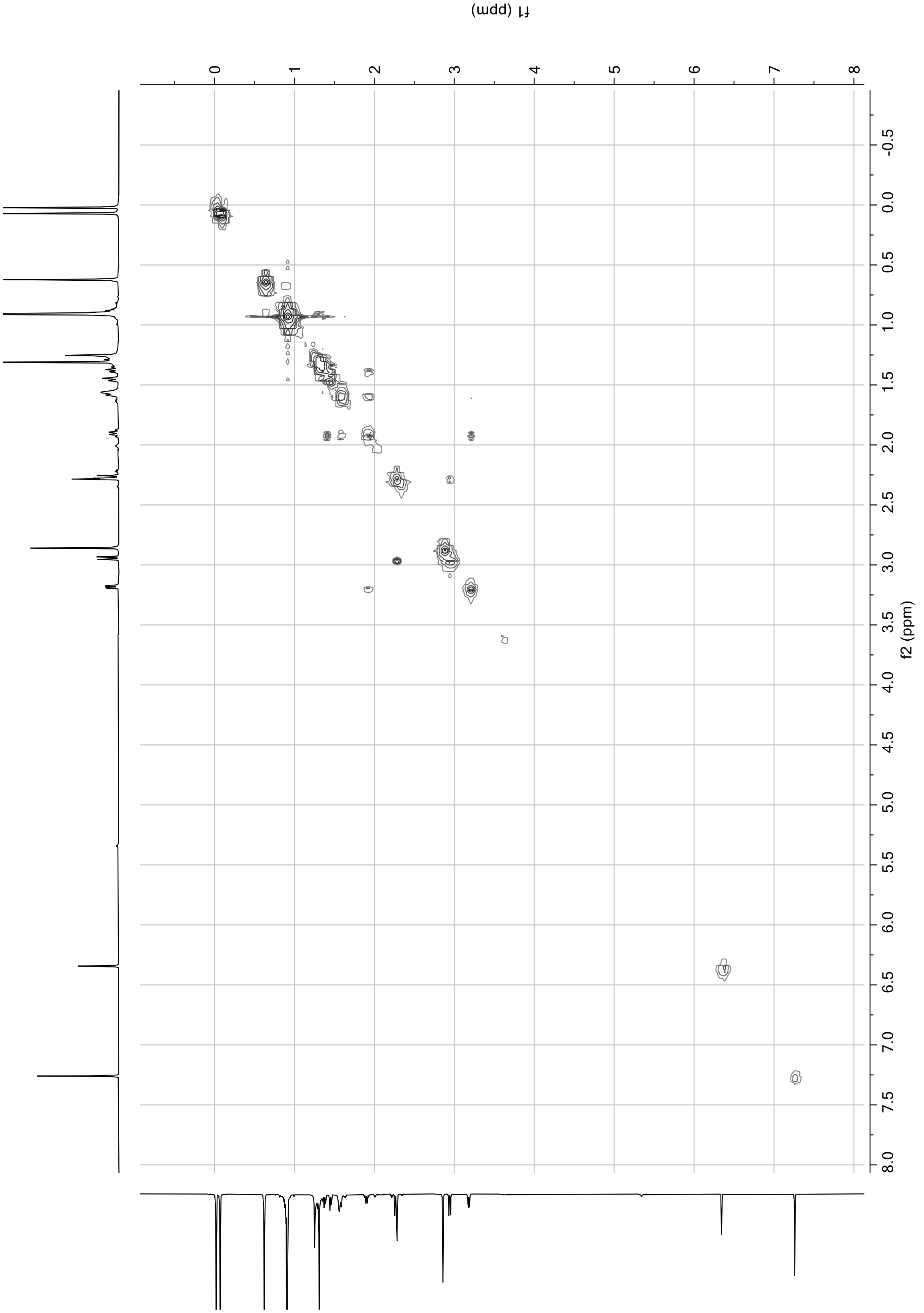
2.70 (^{1}H NMR, 700 MHz, CDCl$_3$)



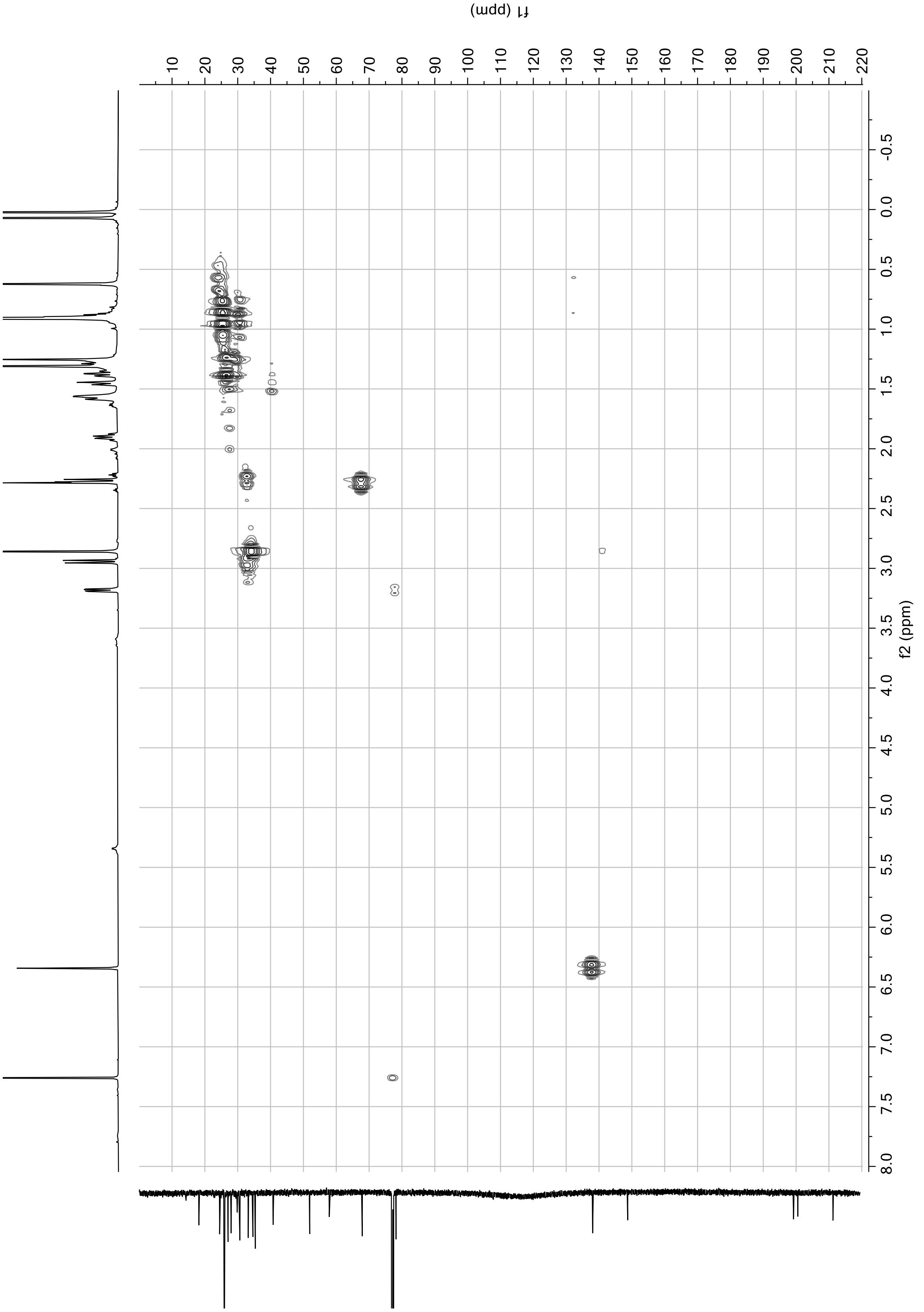
2.70 (^{13}C NMR, 176 MHz, CDCl$_3$)



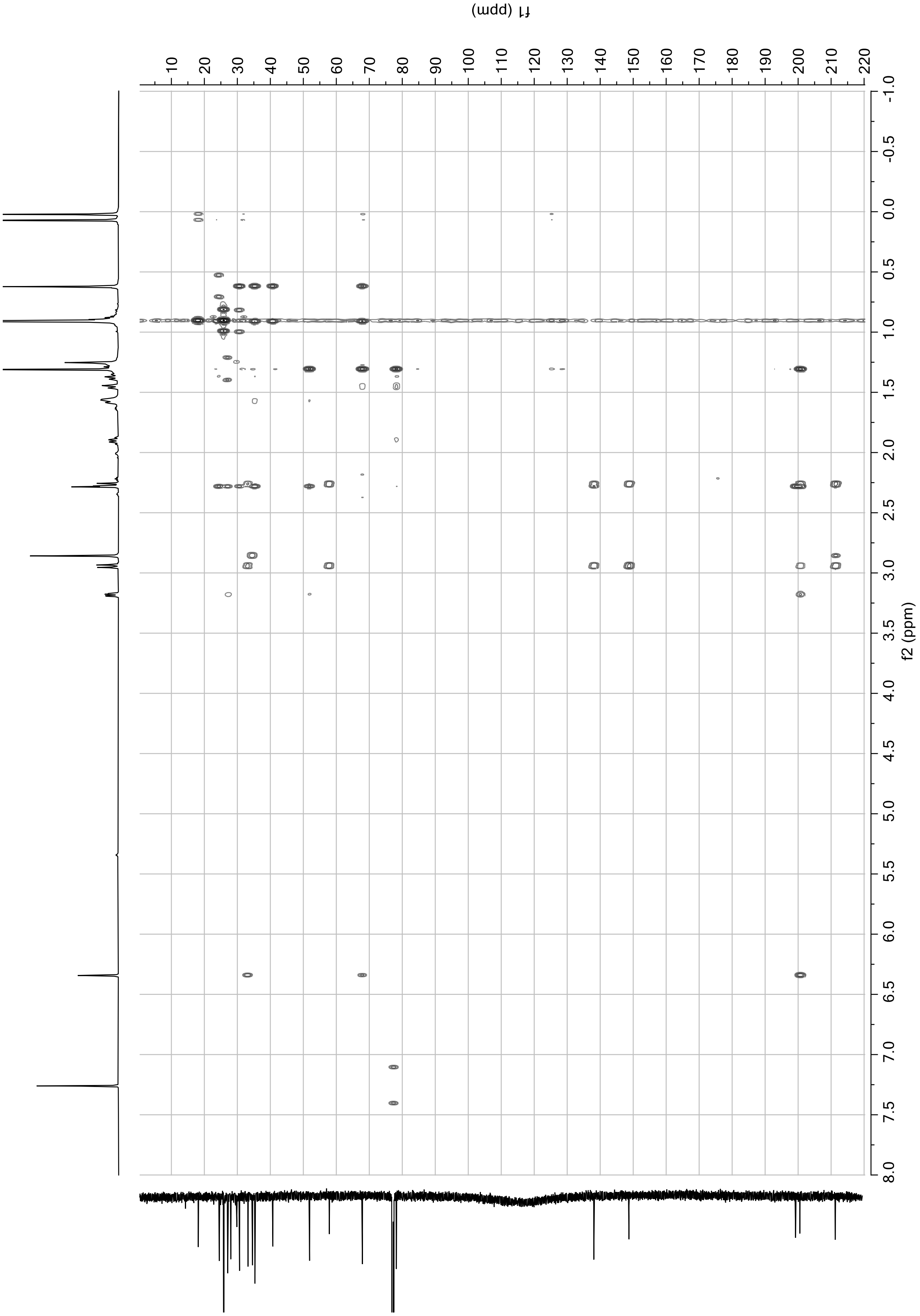
2.70 (COSY, $CDCl_3$)



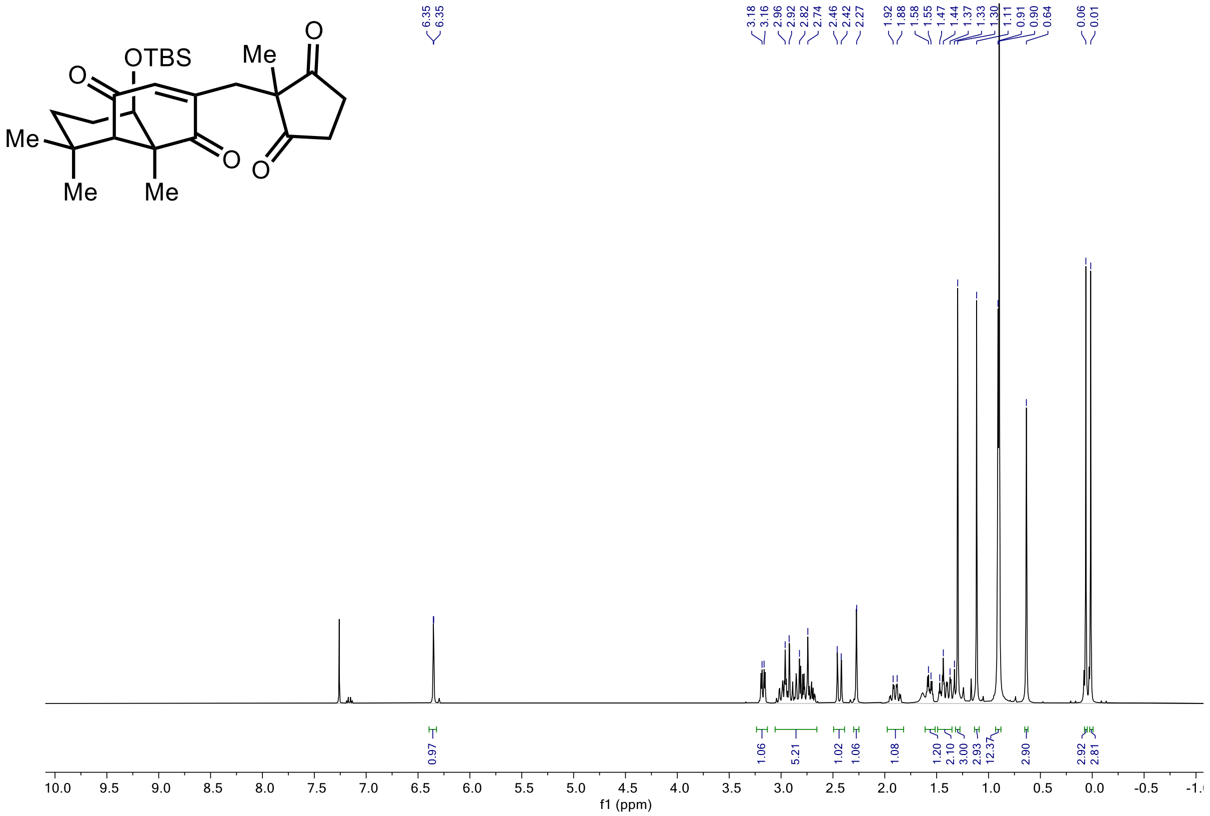
2.70 (HSQC, $CDCl_3$)



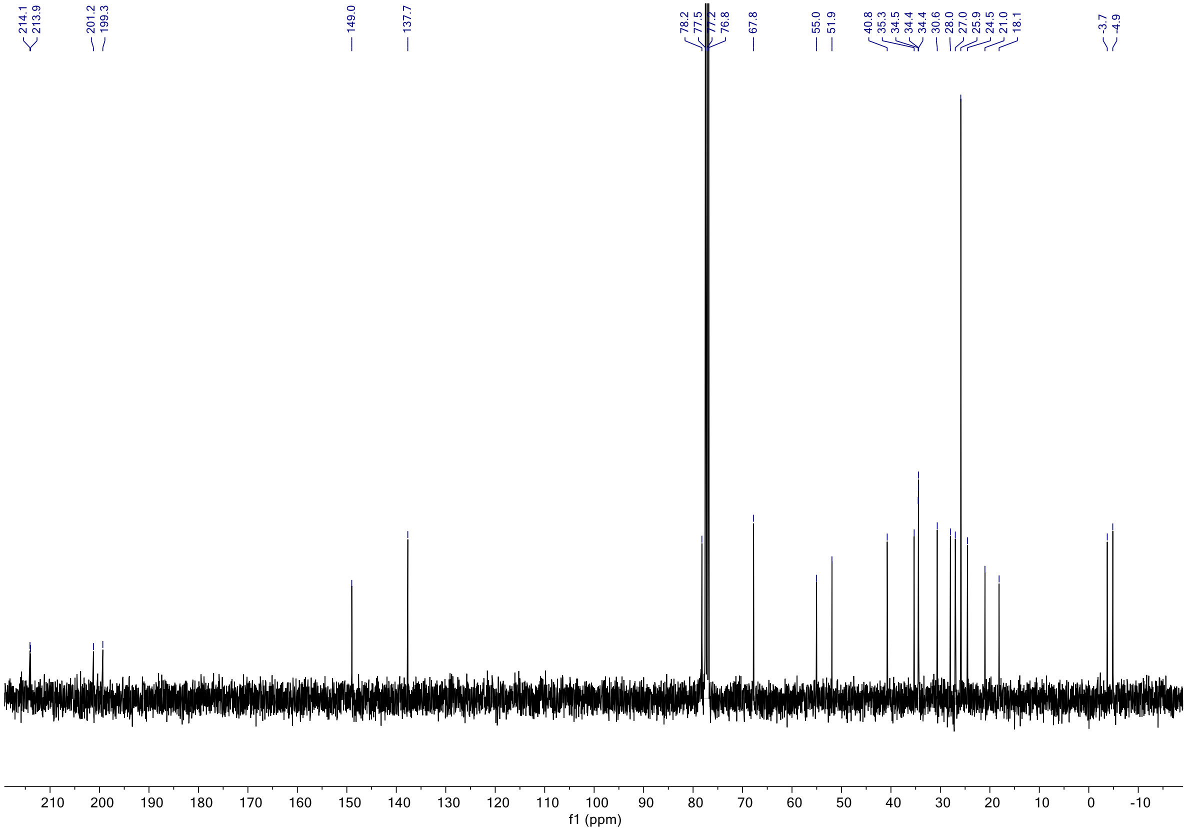
2.70 (HMBC, $CDCl_3$)



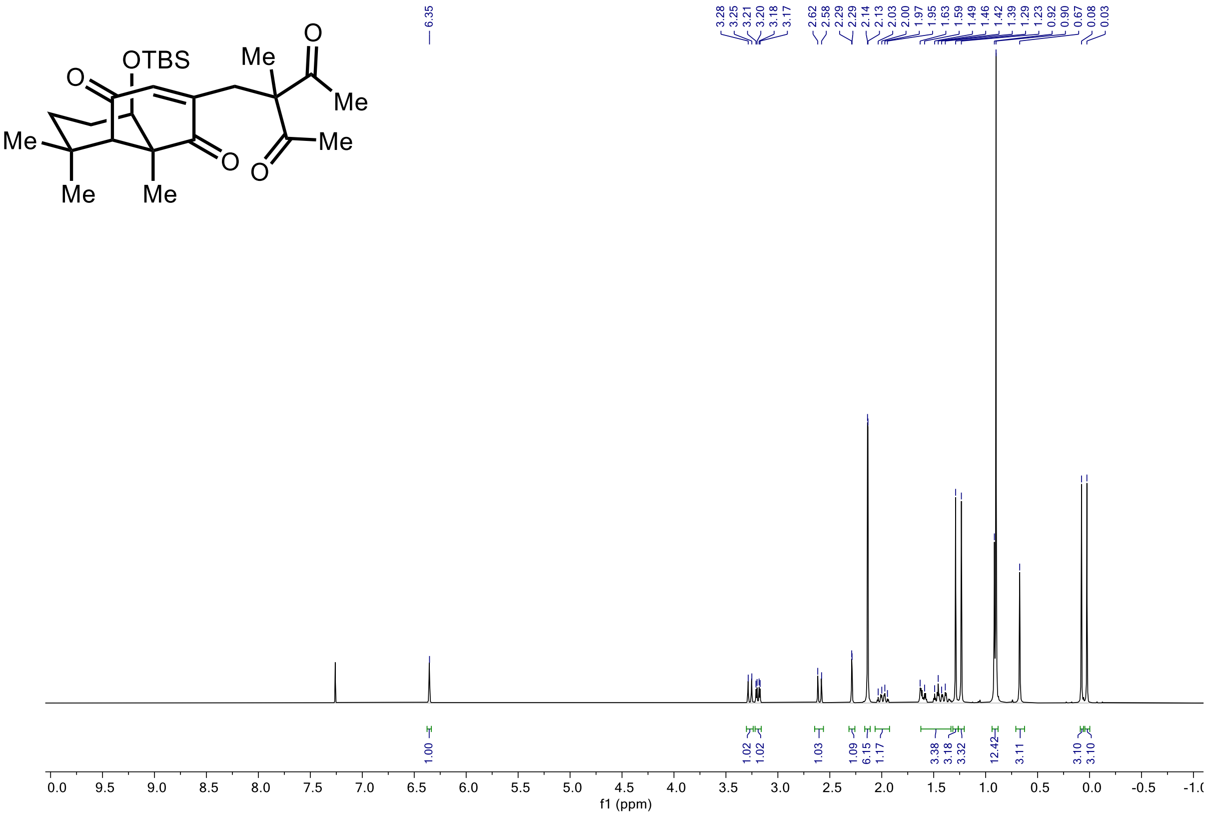
2.72 (^{1}H NMR, 400 MHz, CDCl$_3$)



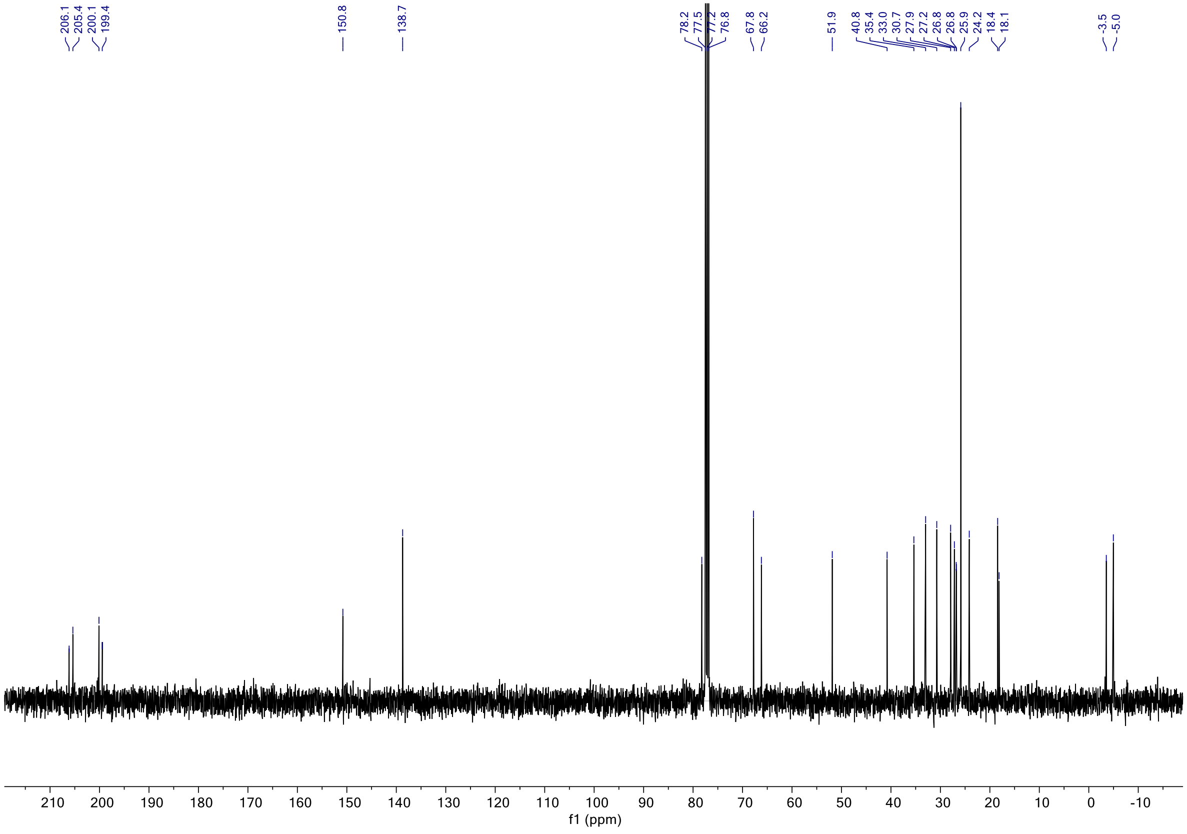
2.72 (^{13}C NMR, 101 MHz, CDCl$_3$)



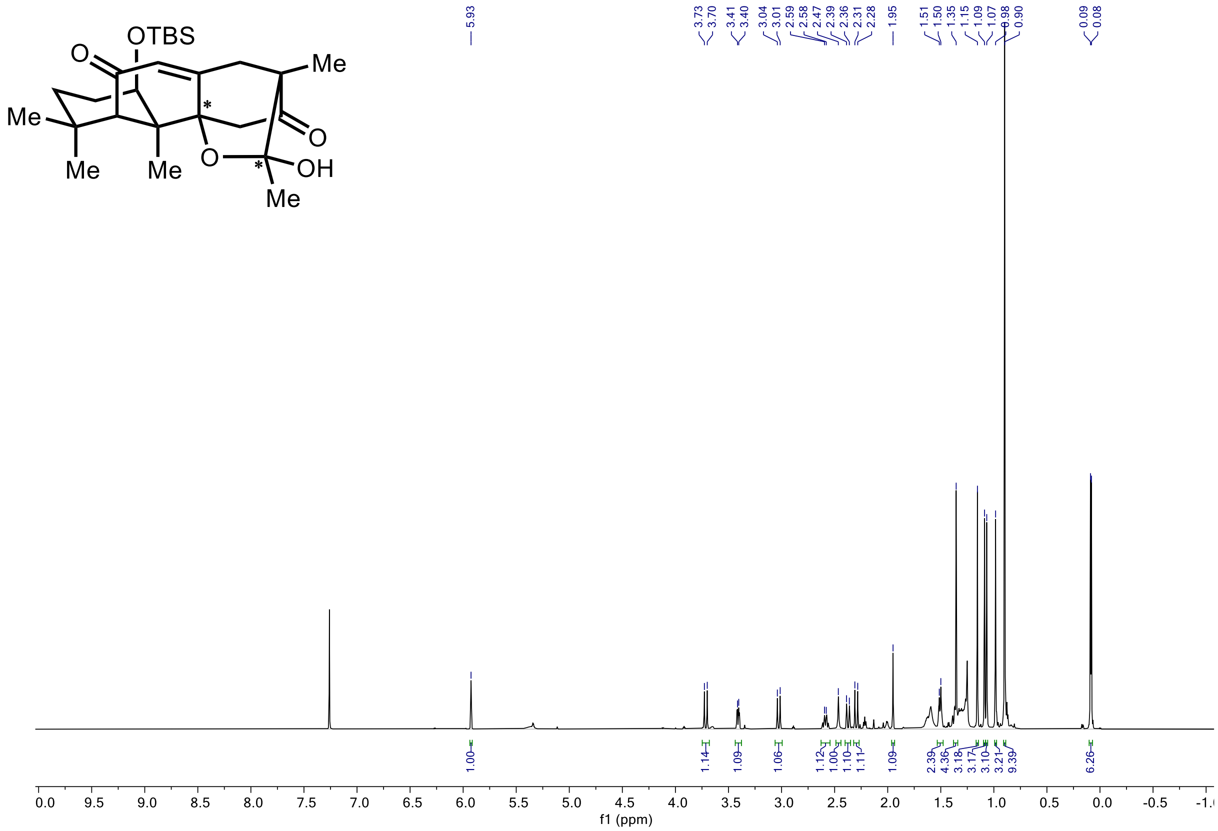
2.75 (^{1}H NMR, 400 MHz, CDCl$_3$)



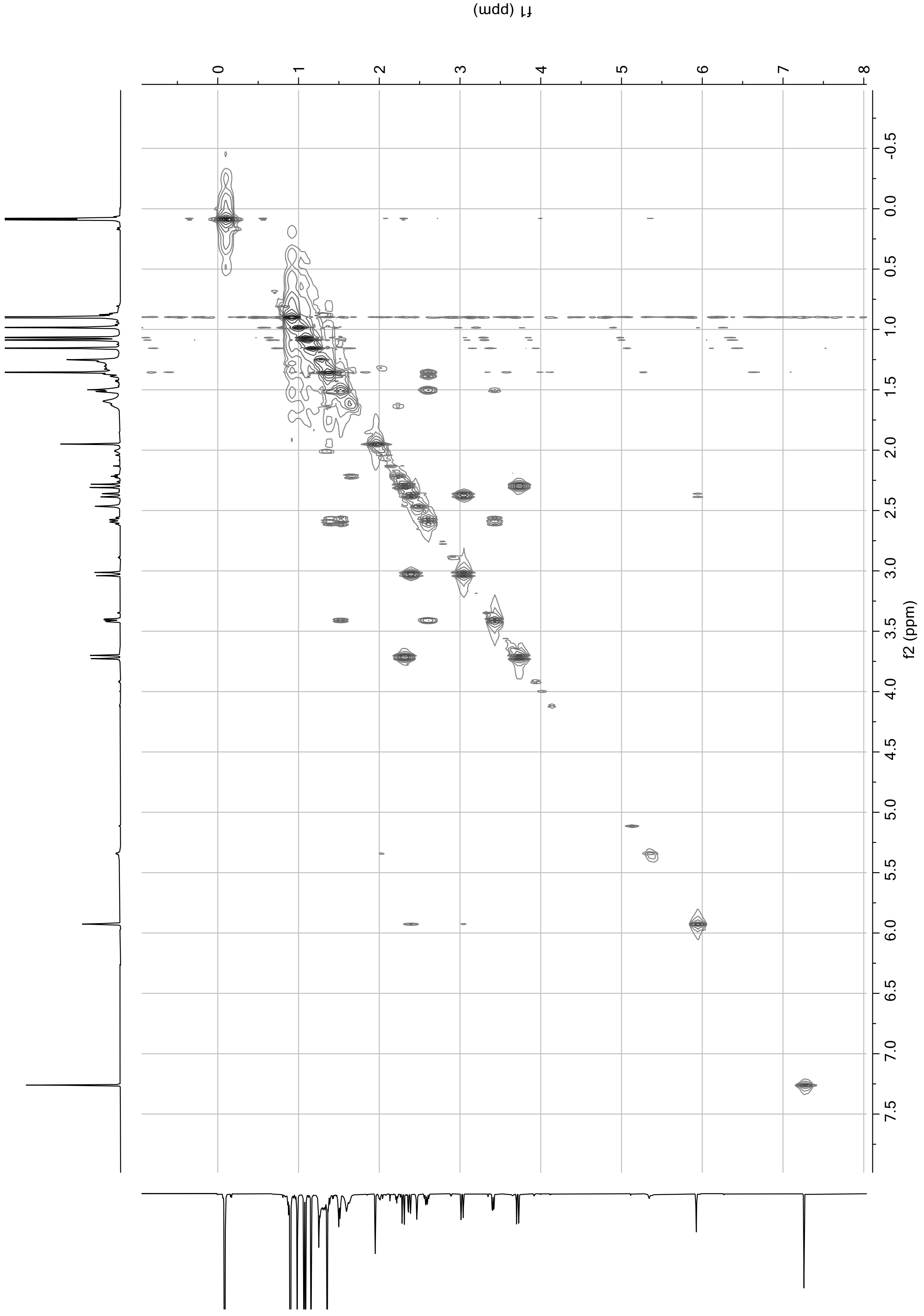
2.75 (^{13}C NMR, 101 MHz, CDCl$_3$)



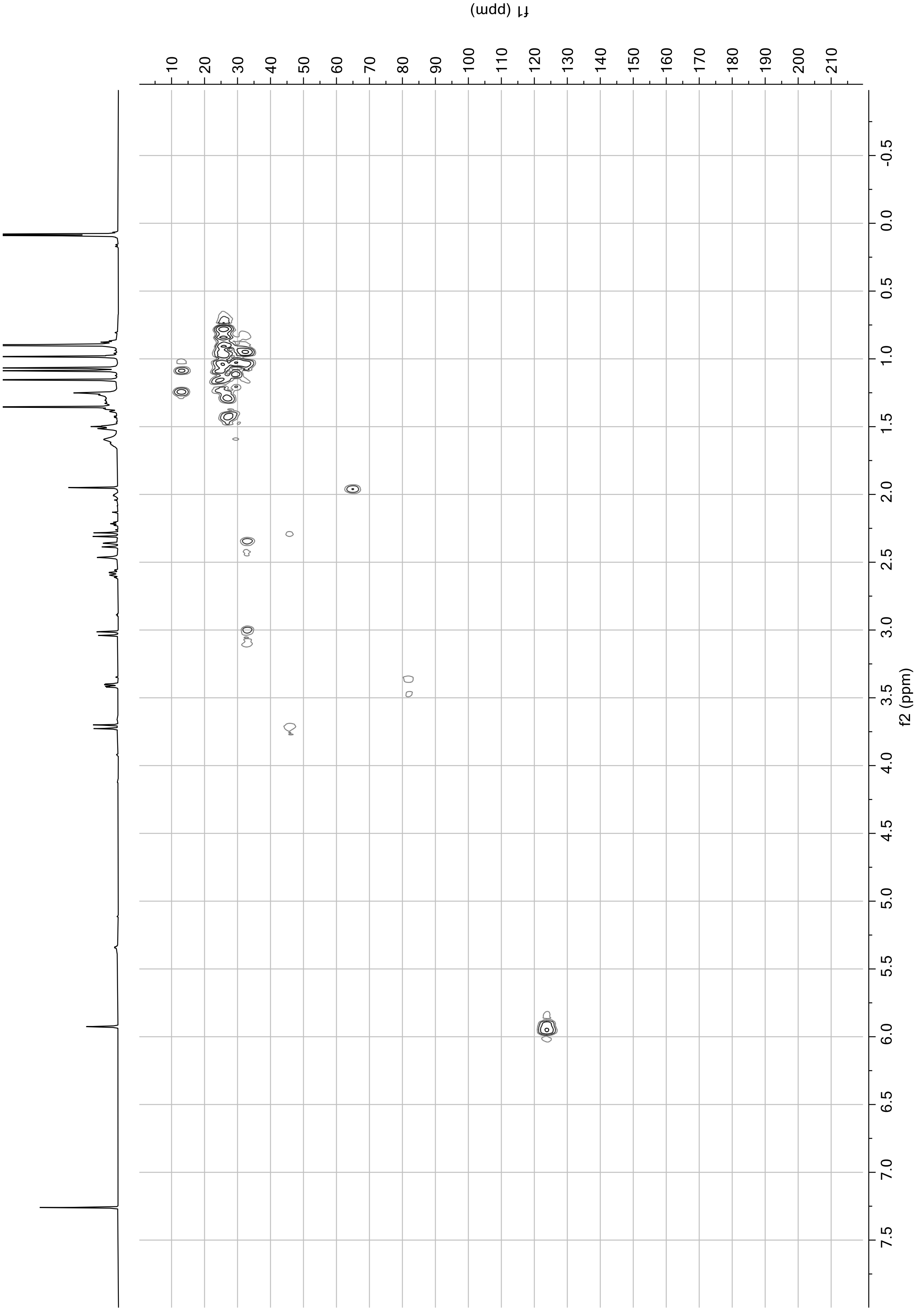
2.76 (^1H NMR, 700 MHz, $CDCl_3$)



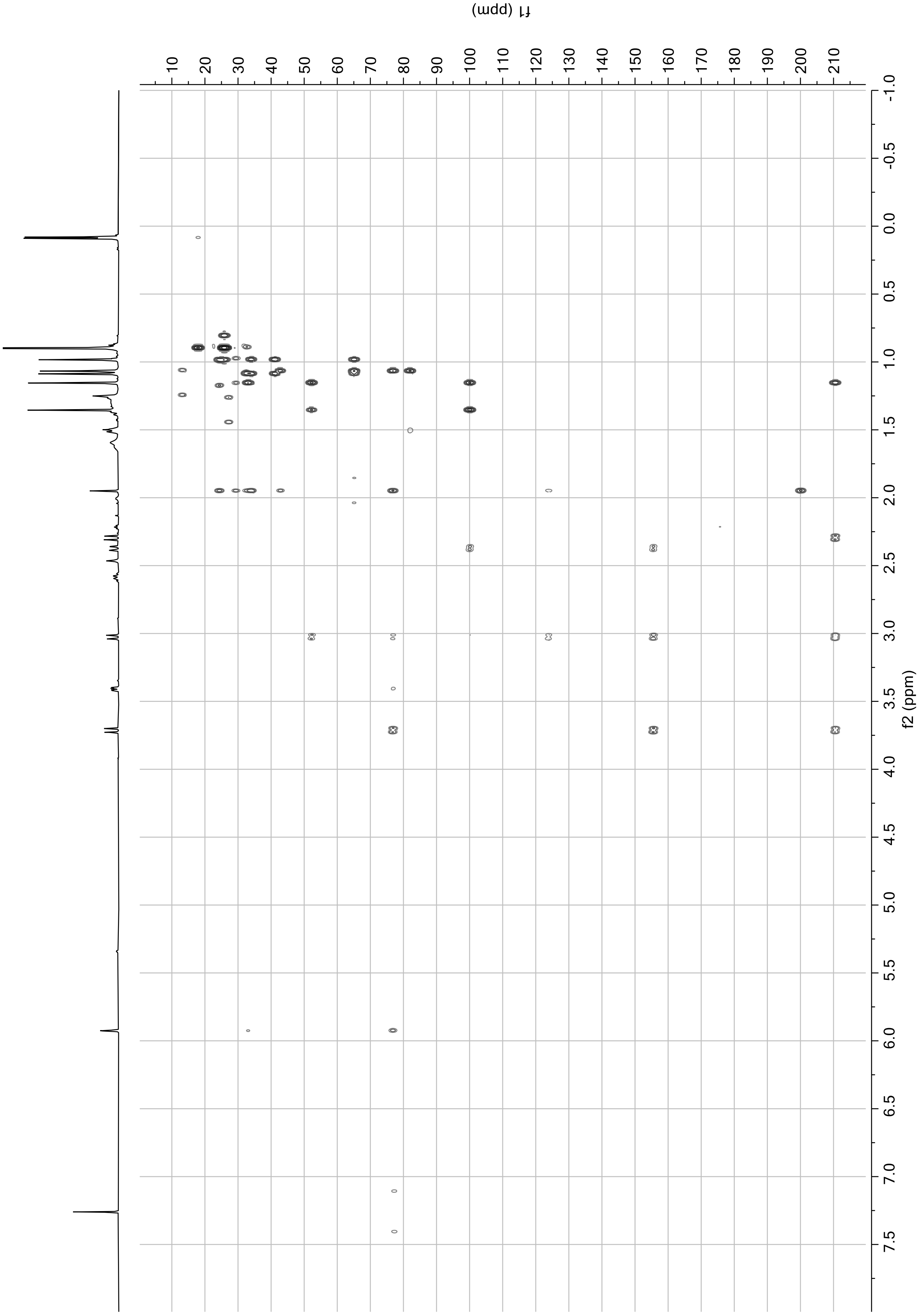
2.76 (COSY, $CDCl_3$)



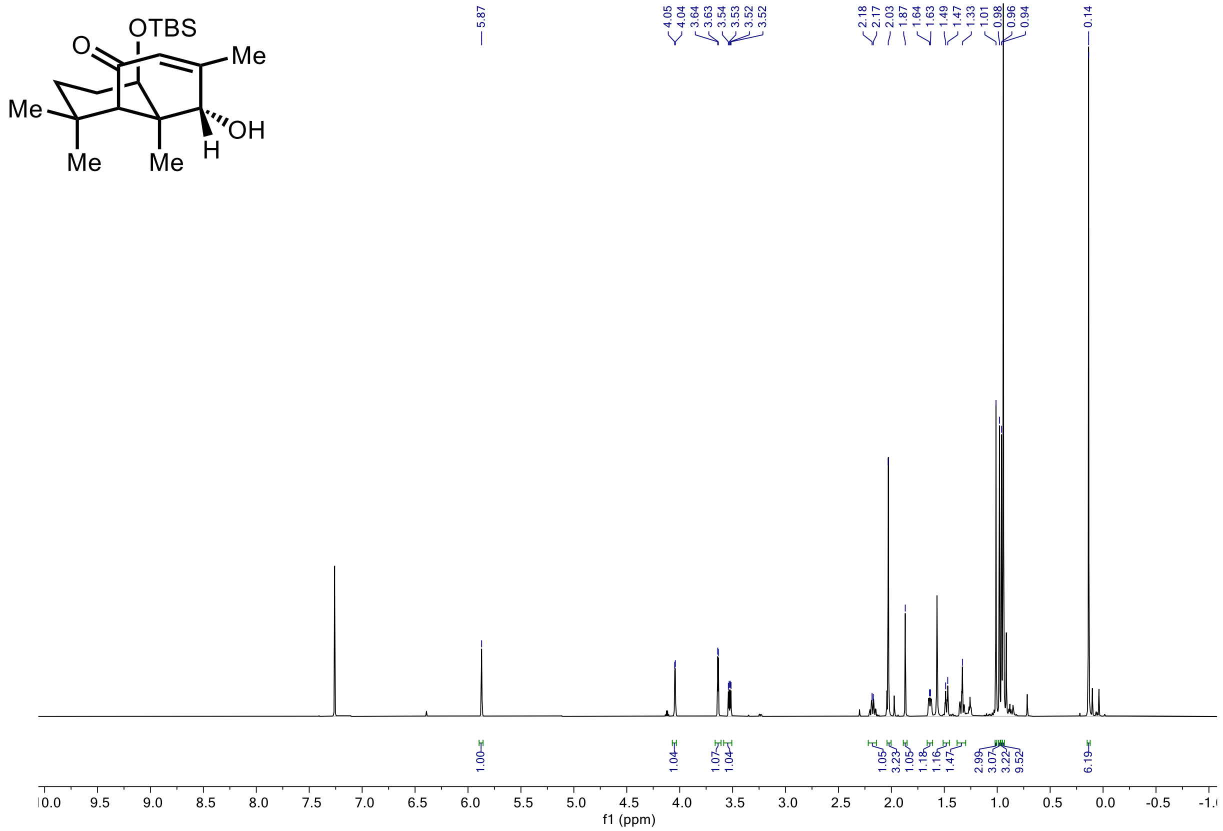
2.76 (HSQC, $CDCl_3$)



2.76 (HMBC, $CDCl_3$)



2.77 (^{1}H NMR, 700 MHz, CDCl$_3$)



2.10 References for Chapter 2

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Chapter 3

Chrysanthenol Rearrangements for the Synthesis of the Xishacorenes

3.1 Isolation, Biosynthesis, and Bioactivity

Xishacorenes A, B, and C (**3.1**, **3.2**, **3.3**, Figure 3.1) were isolated in 2017 from the soft coral *Sinularia poludactyla,* found off the coast of the Xisha Islands in the South China Sea.[1] These diterpene natural products contain a bicyclo[3.3.1]nonane skeleton with an appended diene sidechain, differing in stereochemistry about C13 and the position of unsaturation at C10, C11, or C12 (Figure 3.1). These hydrocarbon compounds were isolated alongside the previously isolated diterpenoid natural product fuscol (**3.4**) which contains a highly decorated cyclohexane ring.

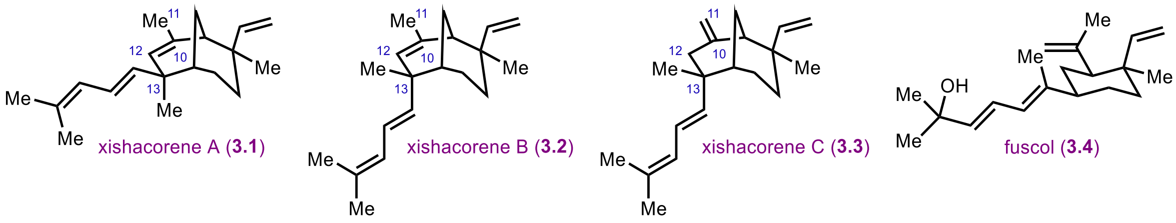


Figure 3.1 Xishacorenes A–C (**3.1**–**3.3**) and co-isolated natural product fuscol (**3.4**).

Though the xishacorene natural products are structurally distinct from fuscol (**3.4**), they do share some common structural motifs such as the cyclohexane core and conjugated diene sidechain. Due to these similarities, it is proposed that fuscol (**3.4**) is the biosynthetic precursor to the xishacorenes.[1] Fuscol (**3.4**) is known to arise from geranylgeranyl pyrophosphate (**3.5**) through initial cyclization to eunicene A (**3.6**, Figure 3.2).[2] Oxidation of the exocyclic olefin group yields eunicol (**3.7**) which upon Cope rearrangement gives rise to fuscol (**3.4**). Fuscol (**3.4**) can then undergo an acid-catalyzed cyclization to forge [3.3.1]bicycle **3.8** containing the core of the xishacorenes. This cyclization is non-specific, giving rise to both epimers at the C13 position. The resulting carbocation can subsequently be eliminated, again in a non-specific fashion, to give either the internal olefin group, characteristic of xishacorene A and B (**3.1** and **3.2**) or the exomethylene, characteristic of xishacorene C (**3.3**).

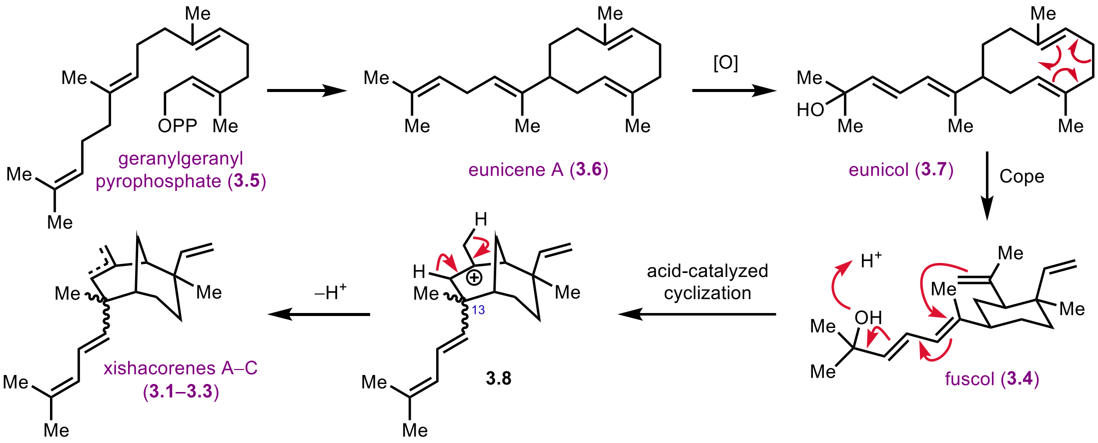


Figure 3.2 Proposed biosynthesis of the xishacorenes from geranylgeranyl pyrophosphate (**3.5**).

The bioactivity of xishacorenes A–C (**3.1**–**3.3**) has been tested in several assays since their isolation, of which, the most notable are included below. Li, Guo, and coworkers found in their immunological activity test that the natural products promoted concanavalin A (ConA)-induced T lymphocyte proliferation in a dose-dependent manner.[1] Additionally, Sarpong, Ndubaku, and coworkers tested the immunogenic activity of the xishacorenes by looking for antagonists of the interferon regulatory factor (IRF) pathway. They found that the parent natural products did not possess notable bioactivity in this test, presumably due to their highly hydrophobic nature, however oxidized derivatives inhibited IRF activity.[2]

3.2 Previous Syntheses of the Xishacorenes

3.2.1 Sarpong's Enantiospecific Synthesis of Xishacorene B

In 2018, the Sarpong group reported the first total synthesis of a member of the xishacorene family, accessing xishacorene B (**3.2**) from the "chiral pool" terpene (*R*)-carvone (**3.9**, Figure 3.3).[3] Starting from (*R*)-carvone (**3.9**), electrophilic epoxidation of the isopropenyl group and subsequent reductive radical cyclization onto the carbonyl afforded cyclobutanol **3.10** as a mixture of diastereomers. The major diastereomer was then subjected to a palladium-mediated C–C bond cleavage-cross-coupling with vinyl iodide **3.11** to access the highly decorated cyclohexane **3.12**. Hydrobromination of the electron rich olefin in **3.12** gave the tertiary bromide, which underwent radical cyclization to afford [3.3.1]bicycle **3.13** as a mixture of diastereomers about C1. Global reduction and subsequent iodination of the primary alcohols yielded diiodide **3.14**. From **3.14**, treatment with potassium *tert*-butoxide (KO*t*-Bu) afforded rearranged primary alcohol **3.15**. This transformation was postulated to proceed first through cyclization of the alkoxide onto the alkyl iodide to form an oxetane; from there, elimination opened the oxetane and led to transposition of the alcohol. Finally, oxidation to the aldehyde and Horner–Wadsworth–Emmons olefination with phosphonate **3.16** afforded xishacorene B (**3.2**) in 10 steps from commercially available (*R*)-carvone (**3.9**).

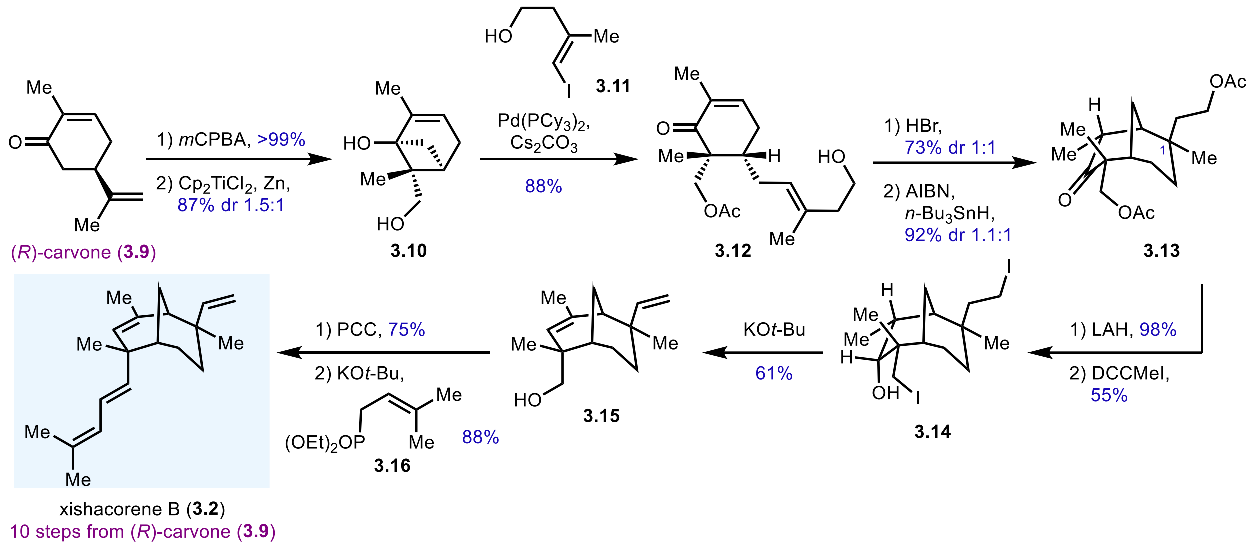


Figure 3.3. Total synthesis of xishacorene B (**3.2**) from (*R*)-carvone (**3.9**).

3.2.2 Sarpong's Bio-inspired Synthesis of the Xishacorenes

In 2019, the Sarpong group reported a bio-inspired synthesis of the xishacorene family of natural products.[2] The initial goal was to explore the bioactivity of glycosylated fuscol derivatives and of the xishacorenes. However, under the attempted glycosylation conditions, fuscol (**3.4**) was found to cyclize to afford the xishacorenes. After some experimentation, it was found that boron trifluoride etherate (BF_3•OEt_2) afforded the xishacorenes in the highest combined yield, with xishacorene C (**3.3**) as the major product (Figure 3.4). The formation of an unnatural product possessing the α-disposed diene sidechain and exomethylene, named xishacorene D (**3.17**), was also isolated. Though not initially anticipated, this transformation provides support for the biosynthetic proposal that the xishacorenes likely originate from fuscol (**3.4**).

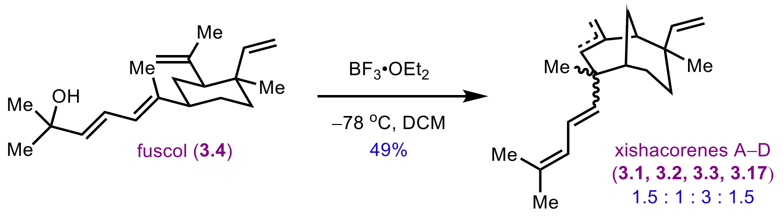


Figure 3.4 Bio-inspired rearrangement of fuscol (**3.4**) to xishacorenes A–D (**3.1, 3.2, 3.3, 3.17**).

3.3 Strategy and Retrosynthesis

The "chiral pool" has been a longstanding starting point for many synthetic efforts, allowing facile entry to enantioenriched materials. As discussed in Chapter 1, skeletal remodeling of these molecules to transform the native skeleton of "chiral pool" materials into novel scaffolds in short order has been well studied. However, "chiral pool" compounds still possess limitations, in terms of their sites and pattern of functional groups. Though some “chiral pool” compounds have many functional groups and activated positions, several are minimally functionalized. We envisioned that this limitation could be overcome by employing C–H functionalization. Therefore, in developing an approach to xishacorene B (**3.2**), we aimed to employ a strategy that coupled the synthetic versatility of the “chiral pool” with the power of C–H functionalization methodologies (Figure 3.5.A).

Retrosynthetically, xishacorene B (**3.2**) could arise from ketone **3.18** through a deoxygenation in the forward sense (Figure 3.5.B). Diene **3.18** could be brought back to [3.3.1]bicycle **3.19** bearing geminal methyl groups through excision of the diene sidechain. We anticipated that the oxidation at C5 could be leveraged to direct C−H functionalization of one of the geminal methyl groups to install the diene sidechain. Simplification of ketone **3.19**’s β-position gives rise to enone **3.20** in the retrosynthetic sense. We envisioned enone **3.20** arising from vinyl chrysanthenol **3.21.V** through an oxy-Cope rearrangement in the forward sense. Finally, [3.1.1]bicycle **3.21.V** could arise from verbenone (**3.22**) through a known photochemical rearrangement and subsequent nucleophile addition.

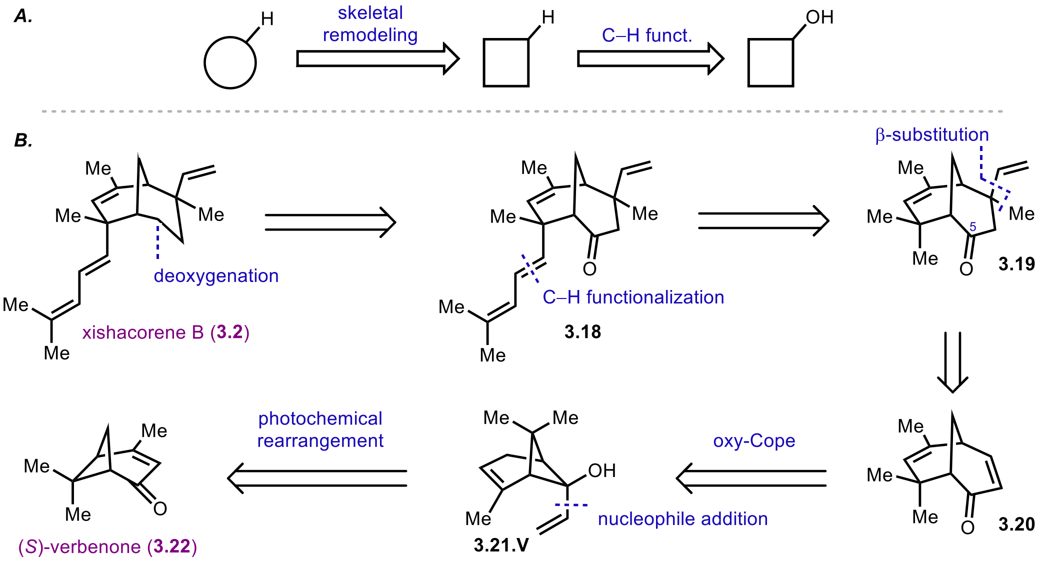


Figure 3.5 (A) General strategy for “chiral pool” skeletal remodeling coupled with C–H functionalization. (B) Retrosynthesis of xishacorene B (**3.2**) starting from commercial verbenone (**3.22**).

This proposed route highlights the strategy outlined above by first remodeling the “chiral pool” [3.1.1]bicycle, (*S*)-verbenone (**3.22**), to access a completely different scaffold, such as [3.3.1]bicycle **3.20**. For [3.3.1]bicycle **3.20** to be brought forward to xishacorene B (**3.2**), installation of functionality at the geminal methyl groups would be required. This requisite oxidation pattern differs from the functional pattern of our starting material. However, by leveraging C–H functionalization we would access our desired oxidation pattern, allowing entry to the natural product.

3.4 Initial Synthesis and Vinyl Chrysanthenol Rearrangements

Starting from (*S*)-verbenone (**3.22**), we carried out a known photochemical rearrangement to access chrysanthenone (**3.23**). This rearrangement was initially reported by Hurst and Whitham, where verbenone was irradiated in cyclohexane with an unfiltered mercury lamp, affording chrysanthenone (**3.23**) in 33% yield.[4] This transformation is postulated to occur through excitation of the enone to biradical **3.24**, δ-scission to open chain biradical **3.25**, and finally, radical recombination at the α-position of the newly formed ketone gives rise to chrysanthenone (**3.23**, Figure 3.6.A). It is worth noting that the enantioenrichment of the material does decline during this rearrangement. The postulated racemization pathway is outlined in Figure 3.6.B, wherein chrysanthenone (**3.23**) undergoes a retro-[2+2] cycloaddition to give achiral ketene **3.26** and subsequent [2+2] cycloaddition affords both enantiomers of chrysanthenone (**3.23**).[5] Erman and coworkers were able to optimize the reaction by employing acetic acid as solvent with a Pyrex filter, obtaining chrysanthenone (**3.23**) in 67% yield.[5] However, in all previously reported cases, this reaction also produces isomeric [3.1.1]bicycle **3.27** regardless of the solvent or filter used, likely through Norrish I-type fragmentation of chrysanthenone (**3.23**), proceeding through biradical **3.28** (Figure 3.6.C). Aiming to minimize racemization and eliminate formation of **3.27**, we screened a variety of longer wavelength light sources, aiming to excite only the starting material's enone and not the product's ketone group. We found that 365 nm LEDs in cyclohexane afforded our desired product in 67% yield as the sole product. Though we do observe some racemization under these conditions, it occurs only to an extent comparable to that of prior reports.

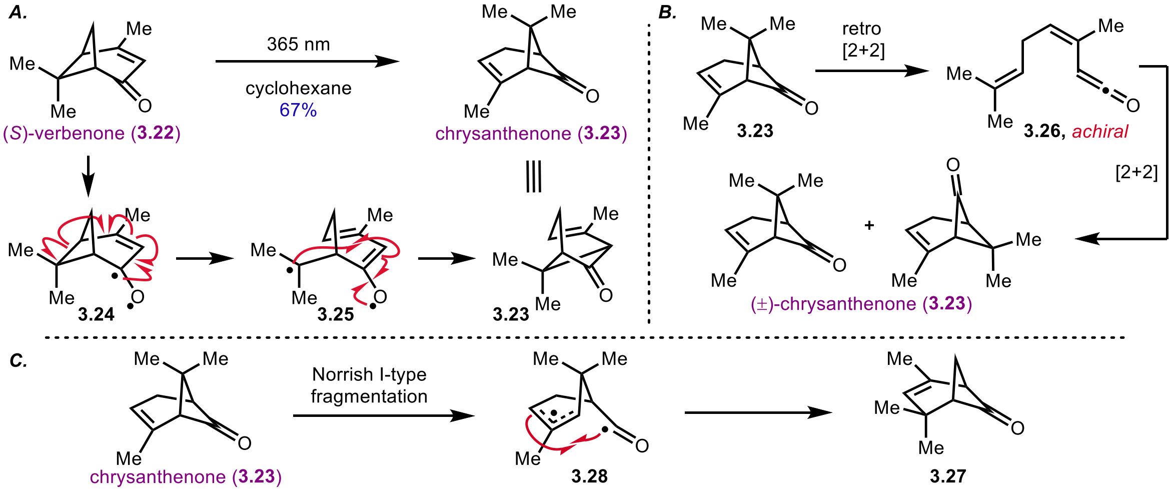


Figure 3.6 (A) Mechanism of (*S*)-verbenone (**3.22**) to chrysanthenone (**3.23**). (B) Pathway for racemization of chrysanthenone (**3.23**). (C) Known rearrangement to **3.27**.

With chrysanthenone (**3.23**) in hand, we turned our investigation toward nucleophile addition into the ketone. Addition of vinyl magnesium bromide to chrysanthenone (**3.23**) would afford the desired alcohol (**3.21.V**) required for the planned [3,3]-sigmatropic (oxy-Cope) rearrangement. When chrysanthenone (**3.23**) was treated with vinyl magnesium bromide, the desired alcohol (**3.21.V**) was obtained in moderate yield along with an unexpected rearranged [3.1.1]bicycle, **3.29.V** (Figure 3.7.A). Bicycle **3.29.V** was unambiguously characterized by X-ray crystallographic analysis. We observed that the yields of **3.21.V** and **3.29.V** differed based on the reaction duration: over prolonged reaction times, **3.29.V** was obtained as the major product. This observation suggested that **3.29.V** likely arose from **3.21.V** through a formal [1,3]-alkyl shift.

To provide support for the proposal that the rearrangement occurred following 1,2-addition of the alkenyl Grignard reagents to chrysanthenone (**3.23**), vinyl 1,2-adduct **3.21.V** was subjected to the reaction conditions. A mixture of starting material (**3.21.V**) as well as rearranged alcohol **3.29.V**, albeit in diminished yields, was obtained (Figure 3.7.B). Under the reaction conditions, rearranged vinyl alcohol **3.29.V** remained unchanged (Figure 3.7.C). This observation indicated that 1,2-addition product **3.21.V** is competent in undergoing the rearrangement but that the rearrangement is not a reversible process. The diminished yields are attributed to the volatility of the compounds.

We found that the rearrangement of **3.23** to **3.29.V** was not exclusive to magnesium alkoxides. Upon treatment of chrysanthenone (**3.23**) with vinyl lithium, we observed only rearranged [3.3.1]bicycle **3.29.V**, albeit in low yield (Figure 3.7.D). However, the lithium alkoxides are likely less stable than their magnesium counter parts as the remainder of the mass had either decomposed or evaporated as there were no other distinguishable compounds in the crude mixture. Furthermore, vinyl chrysanthenol **3.21.V** was found to undergo the rearrangement as the neutral alcohol through microwave irradiation in THF (Figure 3.7.E).

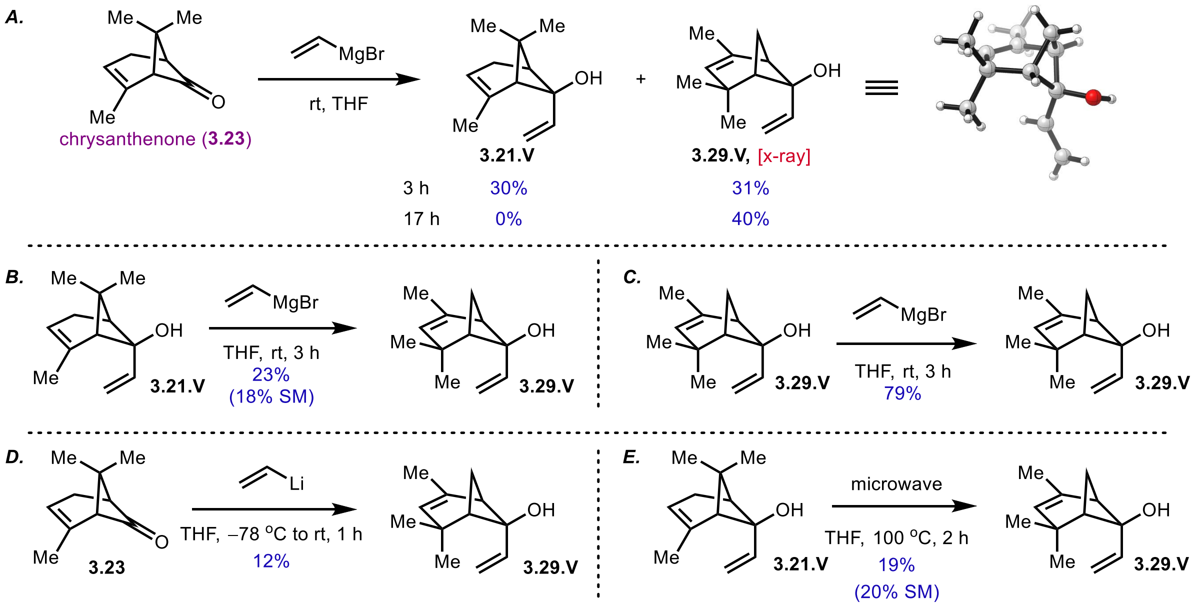
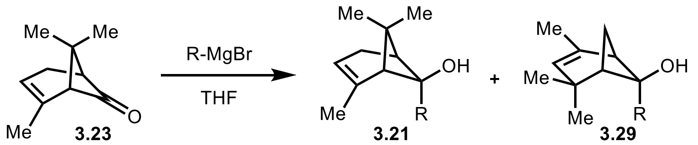


Figure 3.7 (A) Vinyl Grignard reagent addition to chrysanthenone (**3.23**) to yield isomeric [3.1.1]bicycles **3.21.V** and **3.29.V**. (B and C) Resubjecting **3.21.V** and **3.29.V** to the Grignard reagent conditions to test origin of rearrangement. (D) Addition of vinyl lithium to **3.23**. (E) Thermal rearrangement of the neutral alcohol of **3.21.V**.

Looking to explore this unexpected rearrangement further, we sought to determine how broadly applicable this rearrangement was. We took a variety of commercially available Grignard reagents (alkenyl-, alkynyl-, aryl-, and alkyl based) and added them to chrysanthenone (**3.23**) at selected temperatures and quenched excess Grignard reagent at selected time points, as illustrated in Table 3.1.

All the adducts resulting from addition of alkenyl Grignard reagents (Table 3.1, entries 1−3) underwent rearrangement to the isomeric formal 1,3-alkyl migration adduct (**3.29**). In these cases, prolonged reaction times and higher reaction temperatures led to an increase in the amount of **3.29**. However, the extent of rearrangement observed had a strong dependence on the alkenyl Grignard reagent. Interestingly, when an *E/Z* mixture of the 1-propenyl Grignard reagent was used (Table 3.1, entry 2), the rearranged product (**3.29.Pr**) bearing exclusively the *E* olefin group was isolated following prolonged reaction at room temperature, along with the chrysanthenol derivative (**3.21.Pr**) bearing both *E*- and *Z*-disposed olefins. On the other hand, heating the same reaction mixture to higher temperatures (50 °C for 17 h) resulted in formation of the rearranged isomer (**3.29.Pr**) as a mixture of *E* and *Z* olefins. This temperature-dependent outcome suggested that the steric demand posed by the *E*- or *Z*-disposed substituent affected the rate of rearrangement, with the *E* double bond isomer rearranging more readily at room temperature. The combined ratio of *E* and *Z* olefins was maintained in all cases, indicating there was no *E/Z* isomerization occurring throughout the reaction.

While the alkenyl adducts displayed a rearrangement reactivity trend consistent with substitution on the alkene group, alkynyl adducts (Table 3.1, entries 4 and 5), aryl adducts (Table 3.1, entries 6 and 7), as well as alkyl adducts (Table 3.1, entries 8 and 9) did not undergo any observable rearrangement under any of the reaction conditions, delivering solely the 1,2-addition adducts (**3.21**).



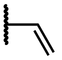
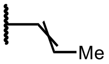
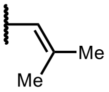
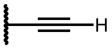
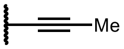
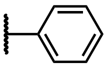
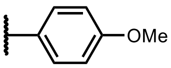
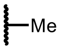
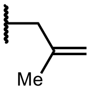
entry, R=	25 °C, 3 h			25 °C, 17 h			50 °C, 17 h		
	yield 3.23	yield 3.21	yield 3.29	yield 3.23	yield 3.21	yield 3.29	yield 3.23	yield 3.21	yield 3.29
1 	0%	30%	31%	0%	0%	40%	0%	0%	53%
2  Me	33%	46%*	9%	31%	41%*	16%	6%	0%	48%*
3  Me Me	23%	69%	0%	22%	71%	3%	9%	39%	25%
4  H	71%	14%	0%	39%	48%	0%	0%	47%	0%
5  Me	15%	70%	0%	0%	77%	0%	0%	70%	0%
6 	0%	95%	0%	0%	96%	0%	0%	96%	0%
7  OMe	0%	96%	0%	0%	79%	0%	0%	80%	0%
8  Me	38%	22%	0%	7%	50%	0%	0%	65%	0%
9  Me	0%	78%	0%	0%	61%	0%	0%	66%	0%

Table 3.1 Reaction of selected Grignard reagents with chrysanthenone (**3.23**). *Combined yield of *E/Z*-olefins.

3.5 Computational Insight into Vinyl Rearrangement

Quantum mechanical calculations using density functional theory (DFT) were conducted, and the most salient results are summarized in Figure 3.8. For each case that was analyzed, our calculations were initiated with the magnesium alkoxide dimer of the 1,2-adduct, which is assumed to be the most stable intermediate under the reaction conditions on the basis of the Schlenk equilibrium.[6] Vinyl adduct **3.21.V** was selected as a representative model. As described above, while the [3,3]-sigmatropic rearrangement to yield [3.3.1]bicycle **3.30.V’** was desired, it was not observed experimentally. Rather, a formal [1,3]- sigmatropic rearrangement of **3.21.V** occurred. As shown in Figure 3.8, the barrier for the anionic oxy-Cope rearrangement (**3.21.V’-**

TSc) was calculated to be 22.2 kcal/mol, which is 4.2 kcal/mol higher than the barrier of the homolytic C–C bond cleavage (**3.21.V'-TS**) associated with a formal [1,3]-sigmatropic rearrangement. These barrier differences are consistent with the experimental observations and suggest that the [1,3]-sigmatropic rearrangement is ~5 orders of magnitude faster than the anionic oxy-Cope rearrangement. Therefore, we focused our attention on the C–C bond homolysis leading to the bicyclo[3.1.1] product, as illustrated (solid black line in Figure 3.8).

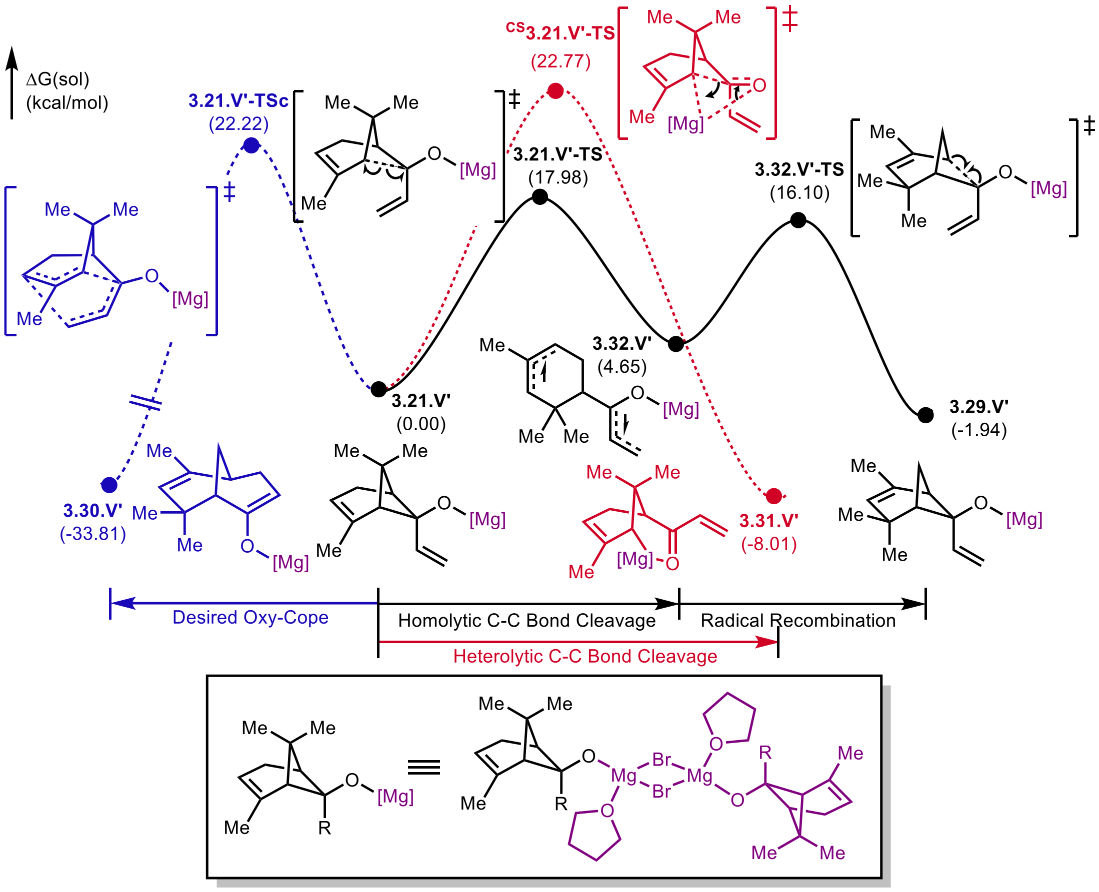


Figure 3.8 Free energy profile of plausible reaction pathways. The black trace represents the homolytic C–C bond cleavage and the blue dotted trace represents the heterolytic C–C bond cleavage. The red dotted line represents the oxy-Cope rearrangement.

We also considered an alternative, heterolytic C–C bond breaking process, with the associated transition state ^{CS}**3.21.V'-TS** (red dotted line in Figure 3.8). This alternative reaction pathway leads to the ring opened intermediate **3.31.V'**, which was calculated to be 6.1 kcal/mol lower in free energy than rearranged product **3.29.V'**. However, the barrier was found to be substantial at 22.8 kcal/mol, which is 4.7 kcal/mol higher than the homolytic cleavage from **3.21.V'**. Therefore, we propose that the [1,3]-sigmatropic rearrangement proceeds through homolytic C–C bond cleavage to afford open-shell singlet intermediate **3.32.V'** at 4.7 kcal/mol with an associated barrier of only 18.0 kcal/mol.

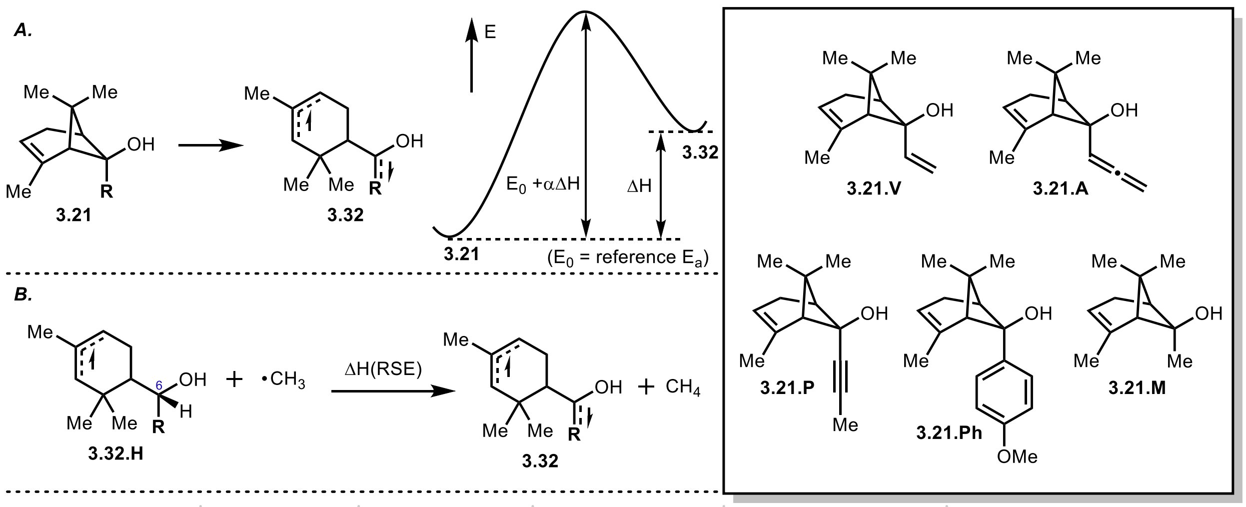
Having established a plausible reaction mechanism for the formal [1,3]-sigmatropic rearrangement, we sought to better understand the factors that affect the rate of the rearrangement. These analyses were conducted using the neutral intermediates **3.21** and **3.32** (Figure 3.9.A) to reduce potential artifacts associated with the computational treatment of the Schlenk equilibrium intermediates, which we have found difficult to model computationally. Although the formal [1,3]-sigmatropic rearrangement of the neutral alcohol only proceeds at higher temperatures experimentally, we believe that the computational modeling of this simpler substrate will capture the key features of the reaction. Experimentally, none of the products arising from an oxy-Cope rearrangement were observed for the neutral alcohol or magnesium alkoxide of the vinyl adduct.

As the formal [1,3]-sigmatropic rearrangement involves homolytic C−C bond breaking, the energies of the open-shell singlet intermediates such as **3.32.V’** or **3.32** are key to the rate constant for C−C bond cleavage. Employing the Bell−Evans−Polanyi principle,[7] we hypothesized that the barrier heights are directly proportional to the enthalpy difference (ΔH) of the open-shell singlet intermediates prepared from the addition of different nucleophiles to chrysanthenone (**3.23**, Figure 3.9.A). Accordingly, we investigated the ΔH between various 1,2-addition products (**3.21**) and their corresponding C−C bond cleaved open-shell singlet intermediates (**3.32**). Specifically, we analyzed vinyl- (**3.21.V**), allenyl- (**3.21.A**), propynyl- (**3.21.P**), *p*-methoxyphenyl- (**3.21.Ph**), and methylchrysanthenol (**3.21.M**) adducts as representative examples (Figure 3.9). In good agreement with our experimental observations, **3.21.V** has the lowest ΔH value of 13.7 kcal/mol (Figure 3.9.C), whereas **3.21.A**, **3.21.P**, **3.21.Ph**, and **3.21.M** show notably higher enthalpies of 17.2, 19.1, 20.5, and 25.6 kcal/mol, respectively.

Because the only difference among the substrates that were examined is the exocyclic radical functionality in the biradical intermediate, the differences in ΔH should be governed by the relative stability of the corresponding radicals formed upon homolytic C−C bond cleavage. To determine the effect of the substituents on the radical intermediates, the radical stabilization energies (RSEs)[8] of the exocyclic radicals were calculated using the following isodesmic reaction

$$\mathbf{3.32.H} + \bullet\mathrm{CH_3} \rightarrow \mathbf{3.32} + \mathrm{CH_4}, \quad \Delta H_{rxn} \qquad (1)$$

where **3.32.H** represents **3.32** bearing a hydrogen at C6 (Figure 3.9.B). Our calculations showed that the biradical bearing a vinyl group (**3.32.V**) is most stable with a RSE of −29.1 kcal/mol, whereas **3.32.M** is the least stable with a RSE of −16.2 kcal/mol, as enumerated in Figure 3.9.C. Notably, the increase in RSE in comparing the vinyl-bearing biradical intermediate to the methyl-bearing biradical reveals a quantitative trend that mirrors the increase in ΔH. This correlation between the ΔH and RSE supports our assertion that the change of ΔH arises from the relative stability of the exocyclic radicals in the biradical intermediates for each adduct.

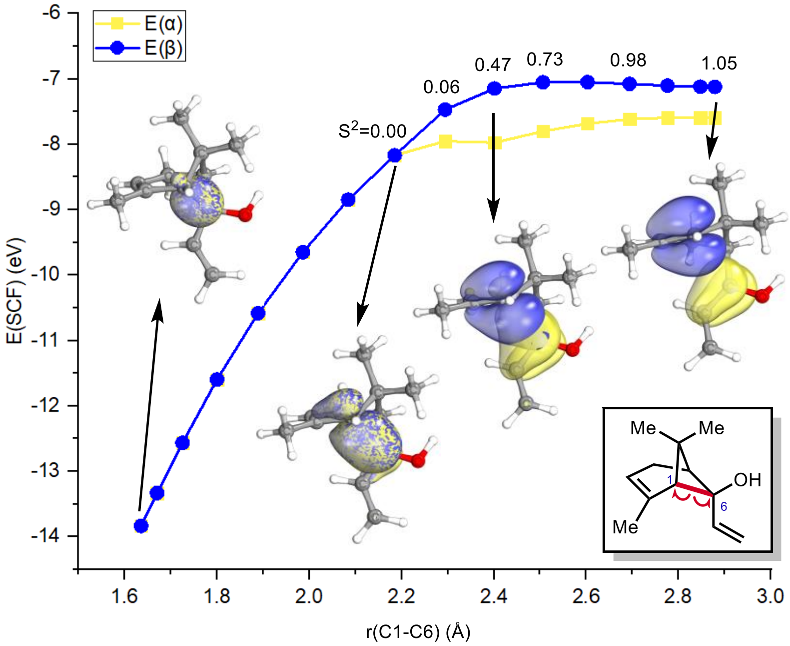


C.

R	Vinyl (**V**)	Allenyl (**A**)	Propynyl (**P**)	(*p*-MeO)Ph (**Ph**)	Methyl (**M**)
ΔH (in kcal/mol)	13.71	17.17	19.06	20.54	25.59
RSE (in kcal/mol)	–29.08	–25.90	–26.38	–23.49	–16.17

Figure 3.9 (A) Homolytic C–C bond cleavage of chrysanthenol derivatives to compare the relative barriers using the Bell–Evans–Polanyi principle. (B) The reaction scheme for the calculation of the radical stabilization energy (RSE). (C) Computed ΔH and RSE values depending on the functional groups, R.

Finally, we conducted intrinsic bond orbital (IBO)[9,10] analysis along the intrinsic reaction coordinate (IRC) of the C–C bond cleavage step to obtain a more quantitative depiction of how the covalent electron pair homolyzes to form the biradical intermediate. Figure 3.10 depicts energy levels of the two orbitals from the breaking of the C1–C6 bond to yield the exocyclic radical (E(α), shown in yellow) and endocyclic radical (E(β), shown in blue), respectively. For each of the chrysanthenol derivatives, the energy levels of the endocyclic allylic radicals E(β) were calculated to be very similar (−7.13 to −6.96 eV when $S^2 \approx 1$ (**3.32**); Figure 3.10). However, the energy levels of the exocyclic radicals (E(α)) varied substantially. Note that for **3.32.V** the exocyclic allylic radical is 0.47 eV lower in energy than the endocyclic allylic radical as a result of the adjacent alkoxide moiety. In the case of **3.32.V** and **3.32.A**, E(α) was calculated to be −7.59 and −7.37 eV, respectively, whereas, for **3.32.P** and **3.32.Ph**, the energies of the propargylic and benzylic radicals were calculated to be −7.30 and −7.15 eV, respectively. Furthermore, **3.32.M** has an E(α) value of −6.59 eV. Therefore, the relative energy of the exocyclic radical on the hydroxy bearing π system plays a key role in determining the overall barrier for the C–C bond homolysis, whereas the endocyclic allylic radical does not play a significant role. Having elucidated the principles governing the unexpected rearrangement, we returned to our initial plan of synthesizing the xishacorenes.



R	E(α) at S^2 = 1, (in eV)	E(β)
Vinyl (**V**)	–7.59	–7.12
Allenyl (**A**)	–7.37	–7.13
Propynyl (**P**)	–7.30	–6.96
(*p*-MeO)Ph (**Ph**)	–7.15	–7.06
Methyl (**M**)	–6.59	–7.05

Figure 3.10 Intrinsic bond orbital (IBO) profile of **3.21.V** along the intrinsic reaction coordinate for the formation of the diradical (**3.21.V** → **3.32.V**). E(α) and E(β) represent the energies of the two radicals associated with the diradical intermediate.

3.6 Rearrangements of Chrysanthenols to [3.3.1]Bicycles

3.6.1 First Generation Oxy-Cope Rearrangement

Despite observing rearrangement to the isomeric [3.1.1]bicycle **3.29**, we attempted to carry forward vinyl chrysanthenol **3.21.V** through the planned oxy-Cope rearrangement to afford [3.3.1]bicycle **3.33** (Figure 3.11.A). We initially investigated anionic oxy-Cope conditions (base and crown ether, Figure 3.11.B), however, we were met with non-specific decomposition of the substrate. We next attempted simply heating our substrate, aiming to effect a standard oxy-Cope rearrangement (Figure 3.11.C). Unfortunately, under a variety of solvents (e.g., 1,4-dioxane, DMF, and DMSO), rearrangement to the isomeric [3.1.1]bicycle **3.29.V** was observed rather than the desired [3.3.1]bicycle. At this stage, we realized that there was not a clear path forward with the vinyl chrysanthenol oxy-Cope given the competing rearrangement to the isomeric [3.1.1]bicycle **3.29.V**.

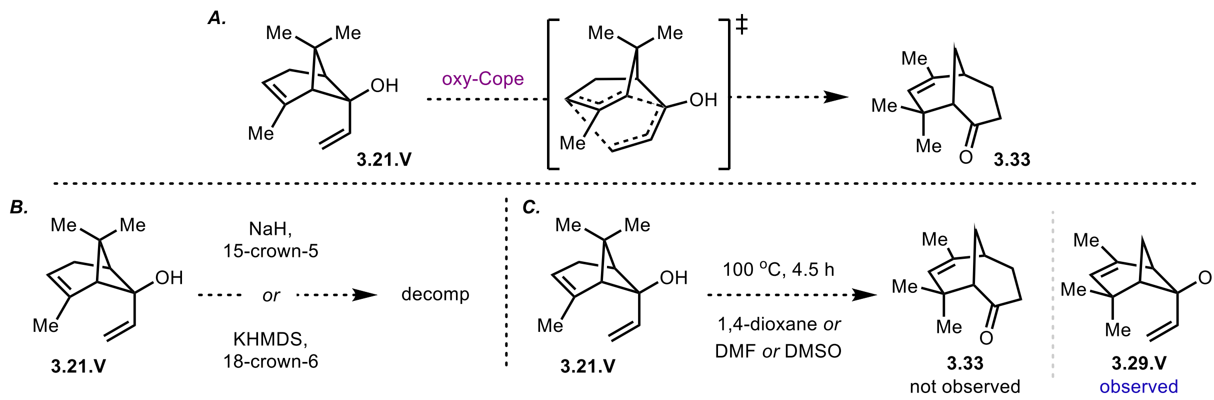


Figure 3.11 Attempted oxy-Cope rearrangements from **3.21.V**.

3.6.2 Strain-Promoted Cyclobutanol Cleavage

Given the challenges associated with the desired oxy-Cope rearrangement, we envisioned a different approach to the key skeletal remodeling step. Drawing on precedent from the initial xishacorene synthesis (Figure 3.3), we envisioned leveraging an embedded cyclobutanol which upon treatment with a metal catalyst could undergo β-carbon elimination of the bond highlighted in red to access a cyclohexyl intermediate (Figure 3.12). In our case, either the 1,2-adduct **3.21.V** or the rearranged [3.1.1]bicycle **3.29.V** could be used to access the cyclohexyl intermediate, metal-allyl **3.34**. Upon migratory insertion of the metal-allyl species into the pendent enone a [3.3.1]bicycle could be formed. The migratory insertion could occur from either end of the allyl system (position A or B) giving rise to either [3.3.1]bicycle **3.20** from A or **3.35** from B.

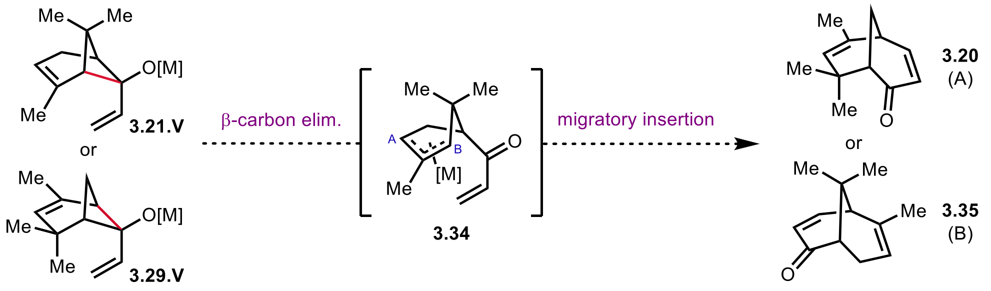


Figure 3.12 Proposed rearrangement of [3.1.1]bicycles **3.21.V** or **3.29.V** to [3.3.1]bicycles **3.20** or **3.35** through metal mediated C–C cleavage.

Attempts toward this transformation utilized a rhodium (I) precatalyst and a ferrocenyl diphosphine ligand (Figure 3.13). However, the desired [3.3.1]bicycle was not observed; rather, diene **3.36** was obtained in moderate yield. The diene likely arises from the desired β-carbon elimination of cyclobutanol **3.29.V**, followed by an unexpected β-hydride elimination and migratory insertion of the rhodium hydride into the enone to give ketone **3.36** following a final ligand exchange.

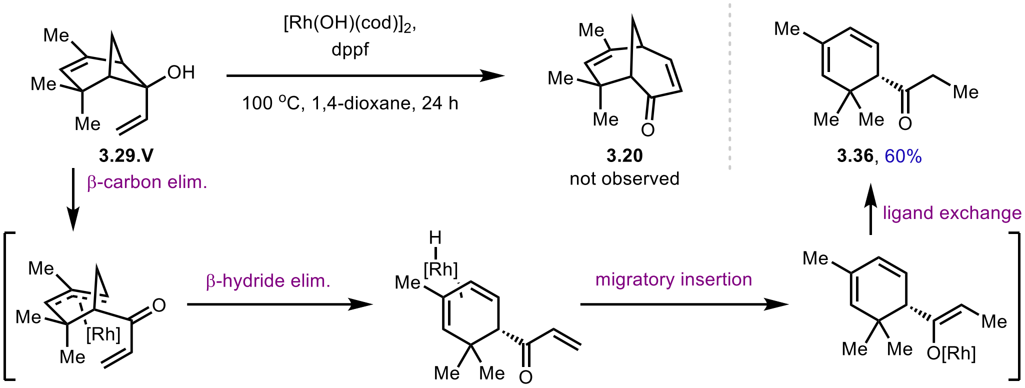


Figure 3.13 Attempted rhodium-mediated conversion of **3.29.V** to **3.20** and proposed mechanistic pathway to observed product **3.36**.

This result is analogous to a report in the literature by Cramer and coworkers, wherein vinyl cyclobutanol **3.37** delivers the product arising from the β-hydride elimination pathway, **3.38** (Figure 3.14).[11] In order to overcome this β-hydride elimination, they switched the alkene to an allene (**3.39**) which suppressed the undesired β-hydride elimination and favored migratory insertion to give the desired cyclohexanone (**3.40**).

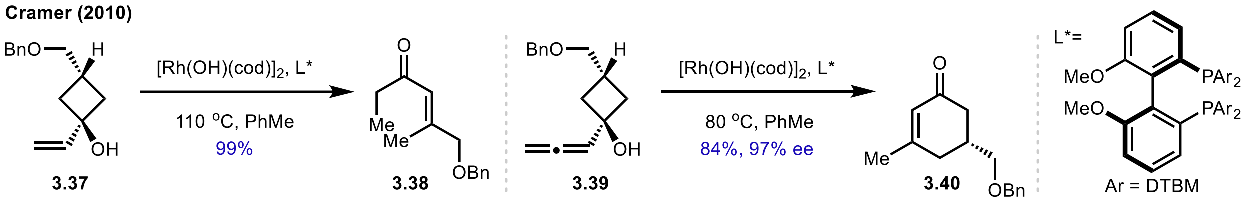


Figure 3.14 Precedent by Cramer and coworkers for overcoming undesired β-hydride elimination by utilizing allenol **3.39** in place of vinyl alcohol **3.37**.

Aiming to observe the same switch in reactivity, we set out to synthesize the allenol chrysanthenol. It is also worth noting that should this transformation work, the addition of one carbon as well as the higher oxidation state of the allenol substrate would simplify the proposed β-substitution en route to xishacorene B (**3.2**). We first attempted a Crabbé homologation[12] from ethynyl chrysanthenol **3.21.E**, however, we never observed formation of the desired allene (Figure 3.15.A). We next investigated metal-mediated addition of a propargyl halide into chrysanthenone (**3.23**) to give either allene **3.21.A** or alkyne **3.41**, depending on which end of the nucleophile adds to the ketone (Figure 3.15.B).[13] Unfortunately, we only observed formation of [5.4]-fused bicycle **3.42**, which is known to arise from chrysanthenone (**3.23**) through treatment with a Lewis acid.[14,15] Additionally, we investigated the addition of lithium acetylides to chrysanthenone (**3.23**) to give compounds such as **3.43**, but observed decomposition in these reactions (Figure 3.15.C).

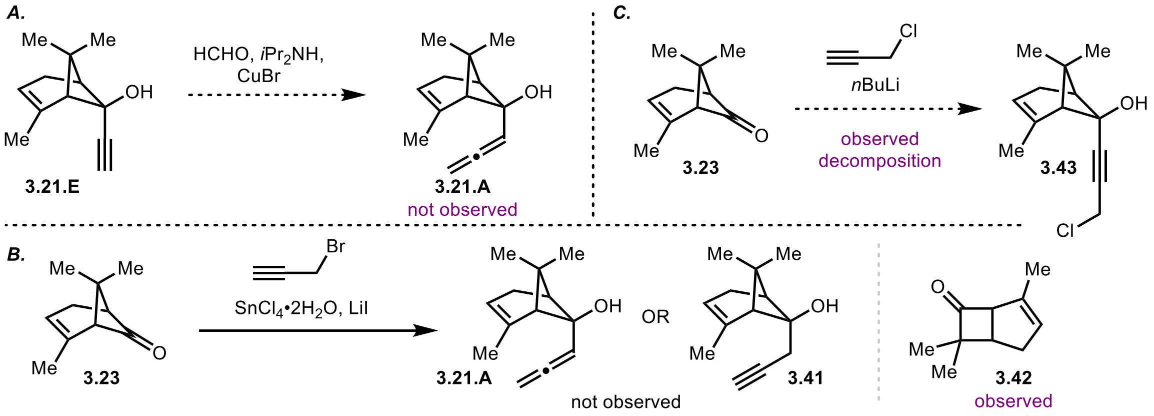


Figure 3.15 Various attempts at synthesizing allenol **3.21.A**.

Knowing that Grignard reagents had worked previously with chrysanthenone (**3.23**), we looked to add a Grignard reagent then convert to the allene. Modifying conditions that Carreira and coworkers employed to build a scope of allenols,[16] we took tetrahydropyran-protected propargyl alcohol **3.44** and converted it into the corresponding Grignard reagent through treatment with ethyl magnesium bromide (EtMgBr) and then subsequently added it to chrysanthenone (**3.23**), affording alkynyl chrysanthenol **3.45** in good yield (Figure 3.16). After some optimization, it was found that irradiation of verbenone (**3.22**) in cyclohexane in a nitrogen filled Schlenk flask followed by addition of the Grignard reagent and heating the sealed Schlenk flask led to formation of alkynyl chrysanthenol **3.45** in 67% in one step on gram scale (see experimental for detailed setup). Reduction of alkynyl chrysanthenol **3.45** with lithium aluminum hydride (LAH) afforded the desired allenol (**3.21.A**) in low yields over short reaction times, with most of the mass being recovered as unreacted starting material. However, when the reaction was run over an extended period, desired allene **3.21.A** and rearranged allenol **3.29.A** were obtained in low yield as an inseparable mixture. Though the throughput for this transformation was low, we proceeded with our modest 25% yield to test the validity of our proposed plan, aiming to optimize this sequence at a later stage.

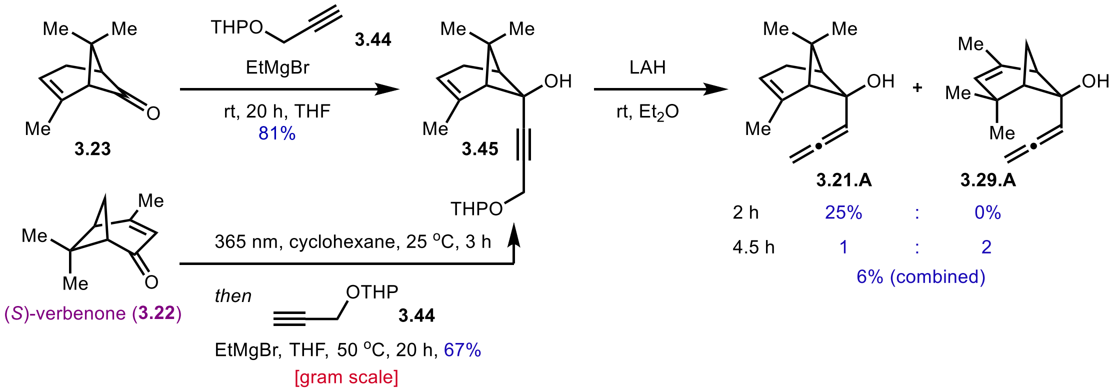


Figure 3.16 Formation of allenol **3.21.A** through a two-step sequence and an optimized one-step procedure to form chrysanthenol **3.45** from (*S*)-verbenone (**3.22**).

With allene **3.21.A** in hand, we subjected the substrate to a rhodium (I) precatalyst and a ferrocenyl ligand, aiming to effect the desired β-carbon elimination and migratory insertion. However, under these conditions, no [3.3.1]bicycle **3.46** was observed, but rather the reaction resulted in non-specific decomposition (Figure 3.17.A). This transformation was also attempted on alkynyl chrysanthenol **3.21.P**, resulting in the formation of several products (Figure 3.17.B). One of the products formed contained only aliphatic resonances, evidenced by ^{1}H and ^{13}C-NMR, but the full structure was never determined. The other product formed in the reaction, which was not identified until much later, was in fact the desired [3.3.1]bicycle (**3.46**). Given that this result was not identified until a later date, we were dissuaded by the formation of the alkyl product and moved away from this cyclobutanol cleavage strategy. We turned to simply investigating how the allene would behave under magnesium alkoxide conditions.

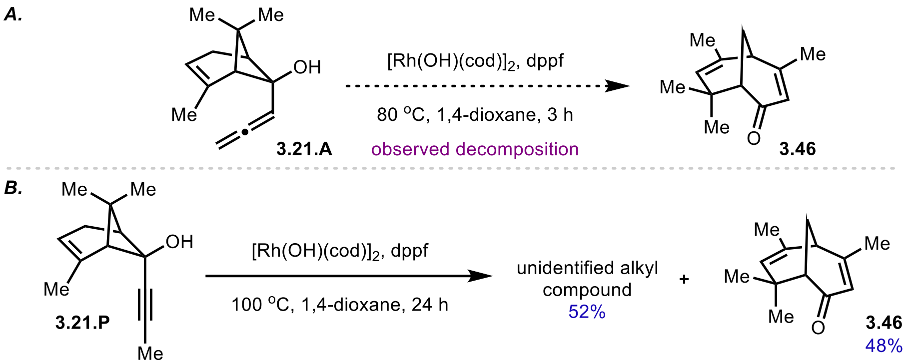
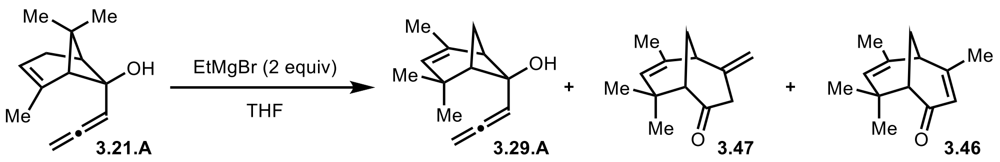


Figure 3.17 (A and B) Attempted rhodium mediated C–C cleavage and re-insertion to form [3.3.1]bicycle **3.46**.

3.6.3 Second Generation Oxy-Cope Rearrangement

Aiming to directly compare how the vinyl, allenyl, and alkynyl chrysanthenol derivatives behave upon formation of the magnesium alkoxide, we sought to subject allenol chrysanthenol **3.21.A** to a Grignard reagent to see if rearrangement to the isomeric [3.1.1]bicycle would occur. Given that the allene has the same hybridization on the central carbon as the alkyne but a similar spatial configuration as the vinyl group, we were not sure which scenario was most likely to occur.

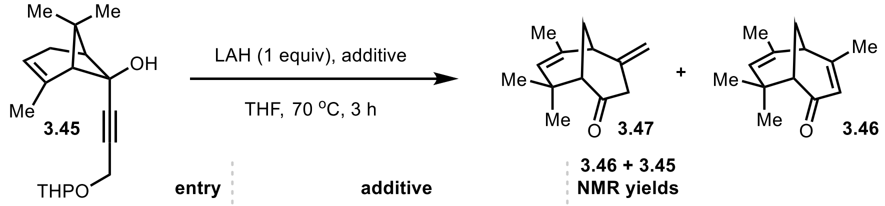
In attempts to mimic the conditions outlined in Table 3.1, we treated allenol chrysanthenol **3.21.A** with EtMgBr to afford the magnesium alkoxide *in situ*, at varying temperatures and reaction durations. At room temperature over 3 h, we observed predominately unreacted allene **3.21.A** as well as some rearranged allene **3.29.A** (Figure 3.18). However, for both entries at 17 h, we observed full conversion of **3.21.A** to [3.3.1]bicycles **3.47** and **3.46** as well as trace rearranged allene **3.29.A**. Fortunately, upon purification by silica gel exo-methylene **3.47** isomerizes to enone **3.46**. This isomerization allowed for the formation of [3.3.1]bicycle **3.46** in 41% from allene **3.21.A**. These results proved to us that though the rearrangement to the [3.1.1]bicycle was possible, the formation of the desired [3.3.1]bicycle through oxy-Cope rearrangement predominates.



	3.29.A	3.47	3.46
rt, 3 h	yes	no	no
rt, 17 h	trace	yes	yes
50 °C, 17 h	trace	yes	yes 41% isolated

Figure 3.18 Formation of the magnesium alkoxide of **3.21.A** and rearrangement to **3.29.A**, **3.47**, and **3.46**.

Upon identifying the [3.3.1]bicycle (**3.46**), we were able to determine that trace amounts of this product were formed upon treating ether **3.45** with LAH in Et_2O. We realized that this transformation circumvents the isolation of the allene, eliminates a bottleneck of the synthesis, and cuts down on step count. Aiming to leverage this discovery, we changed the solvent to THF such that elevated temperature, 70 °C, could be explored. As depicted in Figure 3.19 entry 1, this change in solvent provided the [3.3.1]bicycle as a mixture of olefin isomers **3.47** and **3.46** in a combined 34% yield. Given the success we had previously seen on these systems with magnesium alkoxides, we added EtMgBr to the mixture (entry 2). This marginally improved the combined yield to 39% but led to a cleaner reaction profile, as we observed less decomposition. We then thought about where the mass balance in the reaction could possibly go and hypothesized that the allenol intermediate could undergo homolytic C–C cleavage to form radical intermediates that could potentially initiate radical chain processes. To test this hypothesis, we added 1,4-cyclohexadiene (entry 3) as a radical trap to mitigate any radical initiated reactivity. This improved the combined yield to 53%, which was a significant improvement. Finally, we looked to develop reliable conditions to isomerize the exomethylene of **3.47** to the enone **3.46**. We found that upon workup, the addition of an aqueous sodium hydroxide wash, along with some methanol to help the miscibility, could effect this transformation and afford [3.3.1]bicyclic enone **3.46** in 67% isolated yield on gram scale.



entry	additive	3.46 + 3.45 NMR yields
1	none	34%
2	EtMgBr (1 equiv)	39%
3	EtMgBr (1 equiv), 1,4-cyclohexadiene	53%
4	EtMgBr (1 equiv), 1,4-cyclohexadiene NaOH:MeOH post quench	67%*

*isolated yield of B, gram scale

Figure 3.19 Optimization of a one-step transformation from alkyne **3.45** to enone **3.46**.

3.7 Allenol Anionic Oxy-Cope Rearrangement Computations

To better understand the unique reactivity of allenyl chrysanthenol substrate **3.21.A** relative to the other chrysanthenol-derived substrates, additional computational studies were undertaken. Unlike the vinyl or alkynyl chrysanthenol adducts, allenyl substrate **3.21.A** underwent a formal oxy-Cope rearrangement to give the [3.3.1]bicyclic product (**3.46**). Calculated reaction energy profiles for the anionic oxy-Cope rearrangement and homolytic C–C bond cleavage of **3.21.A'** are illustrated in Figure 3.20.A, showing barriers of 19.2 and 19.8 kcal/mol, respectively. Compared to the vinyl chrysanthenol adduct (**3.21.V'**), the barrier for the C–C bond cleavage is 1.9 kcal/mol higher for **3.21.A'**. This computed value is in good agreement with the rationale discussed above; Figure 3.9.C shows a ΔH value of 17.2 kcal/mol for **3.21.A**, which is 3.5 kcal/mol higher than that for **3.21.V**.

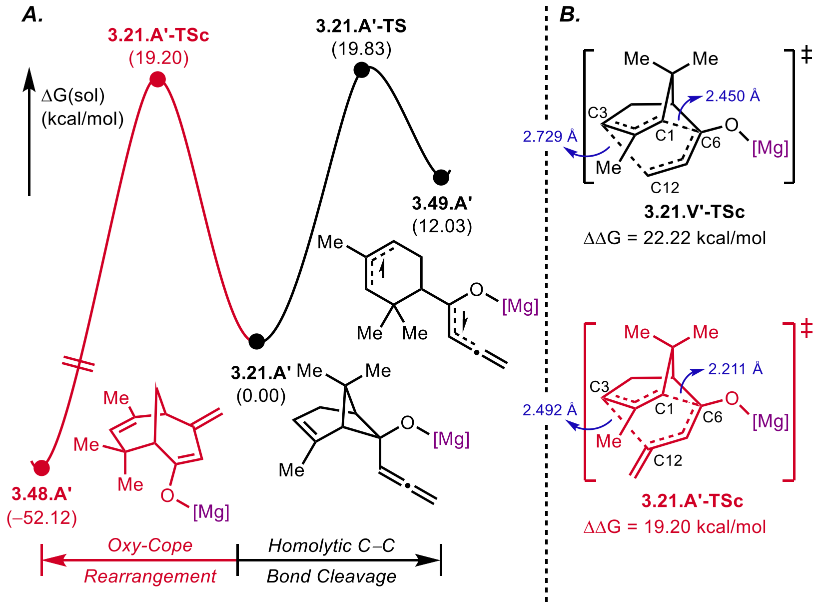


Figure 3.20 (A) Free energy profile of the oxy-Cope rearrangement (red trace) and the homolytic C–C bond cleavage (black trace) of the allenyl substrate **3.21.A'**. (B) Transition state descriptions and FMO energy levels for **3.21.V'**-TSc and **3.21.A'**-TSc.

Despite the relative energies of the associated intermediates and transition states, the anionic oxy-Cope rearrangement of **3.21.A'** has a barrier that is 3.0 kcal/mol lower than that for **3.21.V'**, which can be rationalized by considering the relative energies of the reactant and the product. For the vinyl-substituted case, the free energy difference (ΔG) between the magnesium alkoxide of vinyl adduct **3.21.V'** and the immediate product of anionic oxy-Cope rearrangement, enolate **3.30.V'**, was calculated to be 33.8 kcal/mol (Figure 3.8). On the other hand, the analogous product for the allenyl case, dienolate **3.48.A'**, is 52.1 kcal/mol more stable than **3.21.A'**. On the basis of the Hammond postulate,[17] the related transition state, **3.21.A'**-TSc, should be earlier and have a lower barrier. Figure 3.20.B depicts the two transition states, **3.21.V'**-TSc and **3.21.A'**-TSc, associated with the anionic oxy-Cope rearrangements of **3.21.V'** and **3.21.A'**, respectively. In **3.21.A'**-TSc, the length of the breaking C1–C6 bond was calculated to be 2.21 Å, which is 0.24 Å shorter than what was found in **3.21.V’**-TSc (Figure 3.20.B), consistent with an earlier transition state.

This difference between the reactivity of the vinyl- and allenyl bearing substrates can be rationalized on the basis of the electronic properties of the allenyl moiety. Both **3.21.V’**-TSc and **3.21.A’**-TSc have much higher associated barriers than conventional anionic oxy-Cope rearrangements (Figure 3.20.B)[18] due to the distortion required to achieve the optimal transition state geometry. As illustrated in Figure 3.21.A, C12 must rotate ~90° and break the exocyclic π bond to form the C3−C12 bond. Therefore, **3.21.V’** does not experience a simple suprafacial−suprafacial interaction but rather requires additional energy to break the π bond. As a result, the two allyl synstems in **3.21.V’**-TSc do not possess effective orbital overlap, which leads to a weak interaction and relatively long interatomic distances (2.45, 2.73 Å, Figure 3.20.B). Furthermore, the relatively small HOMO−LUMO gap of 2.76 eV (Figure 3.21.B) and the large HOMO energy change of 1.54 eV from **3.21.V’** toward **3.21.V’**-TSc (Figure 3.21.B) render this transition a higher energy process.

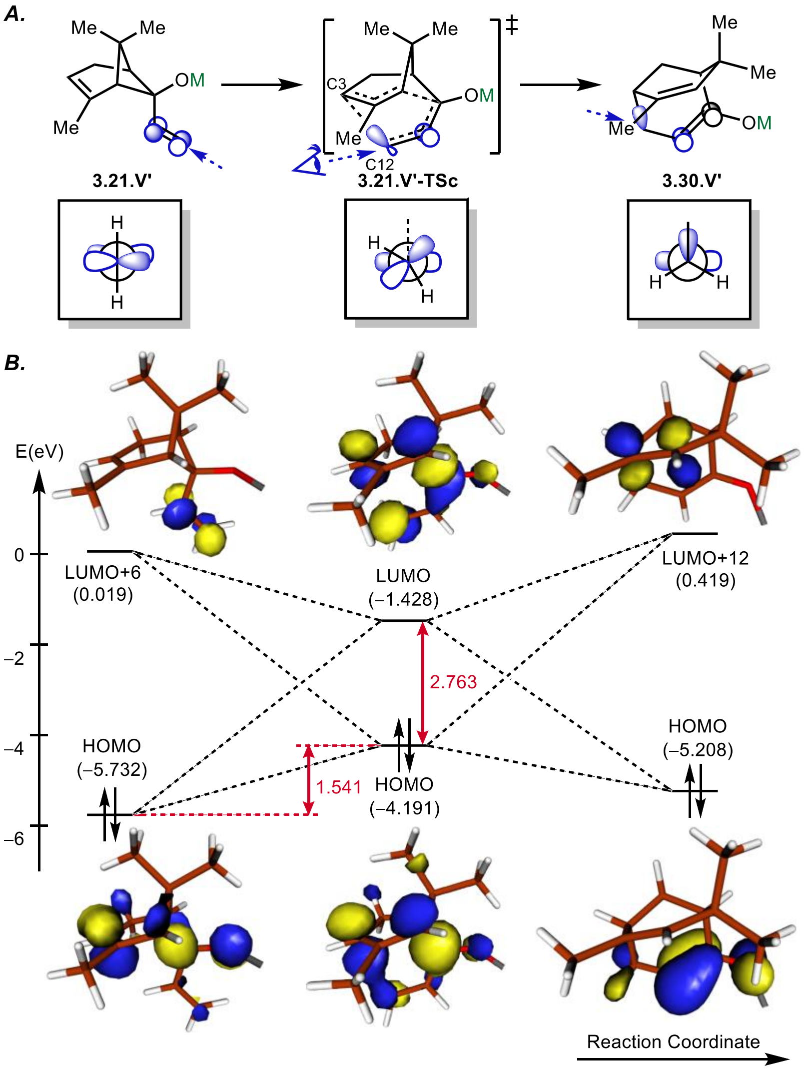


Figure 3.21 (A) Reaction schemes and Newman projections of the oxy-Cope rearrangement of **3.21.V'**. (B) FMO diagrams of part A along the reaction coordinate.

On the other hand, for the allenyl system, significant rotation is not required, since the p-orbital (shown in red, Figure 3.22.A) is productively oriented for C3−C12 bond formation. The p-orbital at the terminal methylene, depicted in red in Figure 3.22.A, rotates by 90° into conjugation with the orthogonal π bond, shown in blue. Consequently, there is less of an energetic penalty associated with the distortion of **3.21.A'**-TSc and, in addition, the two allyl fragments here experience better orbital overlap; compare the larger HOMO−LUMO gap of 3.68 eV in **3.21.A'**-TSc (Figure 3.22.B) and the smaller HOMO energy change of 1.10 eV (from **3.21.A'** toward **3.21.A'**-TSc) to **3.21.V'**-TSc. Overall, these differences lead to an accessible oxy-Cope rearrangement transition state with smaller interatomic distances (2.21 Å, 2.49 Å, Figure 3.20.B) for **3.21.A'**.

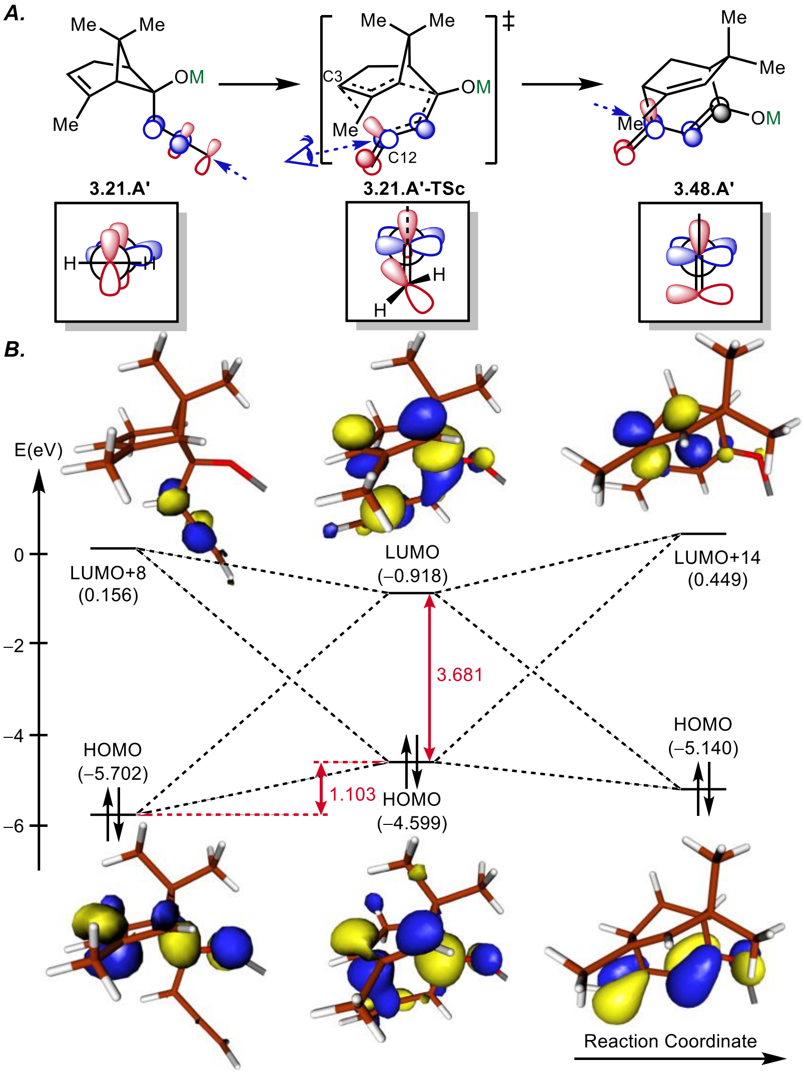


Figure 3.22 (A) Reaction schemes and Newman projections of the oxy-Cope rearrangement of **3.21.A'**. (B) FMO diagrams of part A along the reaction coordinate.

3.8 Conclusion and Outlook

We envisioned coupling a "chiral pool" remodeling strategy with C–H functionalization methodologies to access complex scaffolds, such as the xishacorene natural products from feedstocks such as verbenone (**3.23**). Very early on in our route, we observed unexpected reactivity as vinyl chrysanthenol **3.21.V** rearranged to isomeric [3.1.1]bicycle **3.29.V**. This prompted an investigation into the scope and the underlying principles that govern this rearrangement. By utilizing computational experimentation supported by small mechanistic experiments, we were able to determine that the rearrangement occurs through homolytic cleavage to form a biradical which can then recombine to form isomeric [3.1.1]bicycle **3.29.V**. We were able to correlate the extent of the rearrangement to the radical stabilization energy of the biradical intermediates.

With a greater understanding of this rearrangement, we turned our attention to the desired oxy-Cope rearrangement from vinyl chrysanthenol **3.21.V**, which was ultimately unsuccessful. From here, we changed direction and investigated a cyclobutanol C–C cleavage strategy to effect the desired transformation from a [3.1.1]bicycle to [3.3.1]bicycle. Though this route was effective on propynyl chrysanthenol **3.21.P**, this result was not appreciated until a later date. However, this strategy ultimately led us to synthesizing allenol chrysanthenol **3.21.A** which was then utilized to investigate the rearrangement to isomeric [3.1.1]bicycle **3.29.A**. During this investigation, we were delighted to find allenol **3.21.A** undergoes an anionic oxy-Cope rearrangement to [3.3.1]bicycle **3.46**. We were then able to employ additional computational experiments to determine that the allene leads to a lower degree of distortion in the transition state and in conjunction with better orbital overlap leads to a lower energy barrier.

In the end, through a variety of approaches, as well as unexpected twists and turns, we were able to access the key [3.3.1]bicyclic scaffold of the xishacorenes. The remainder of the route to the natural products, featuring a key C–H functionalization, will be discussed in Chapter 4.

3.9 Experimental Contributors

Project design and development was carried out by Prof. Richmond Sarpong (R.S.) and Kerry E. Jones (K.E.J.). Experiments were conducted by K.E.J. and Nicolle A. Doering (N.A.D.). Specifically, N.A.D. optimized the verbenone (**3.22**) to chrysanthenone (**3.23**) rearrangement and carried out initial investigation of the reaction of non-vinyl Grignard reagents with chrysanthenone (**3.23**). K.E.J. investigated the vinyl Grignard reagent addiitions and their rearrangements, the cyclobutanol cleavage route, and formation of the [3.3.1]bicycle via allenol **3.21.A**. Computations were carried out by Bohyun Park (B.P.) and Prof. Mu-Hyun Baik (M.-H.B.) on the basis of data provided through collaboration with K.E.J. and R.S.

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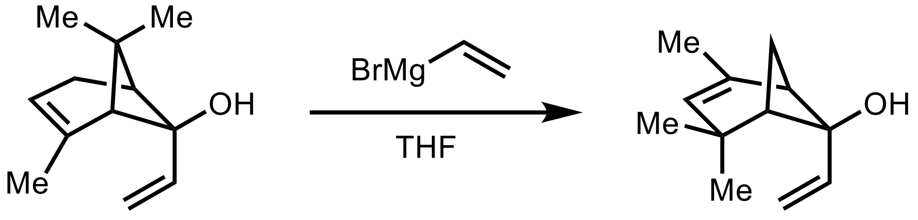
3.10 Experimental Details

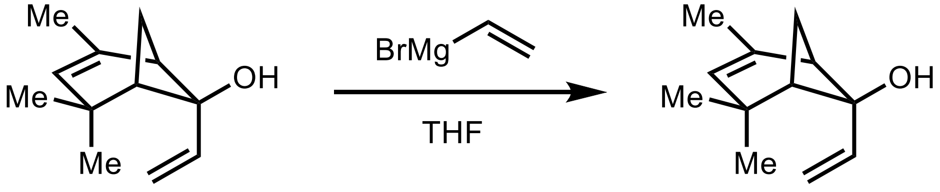
3.10.1 Experimental Procedures

Rearrangement Control Reactions



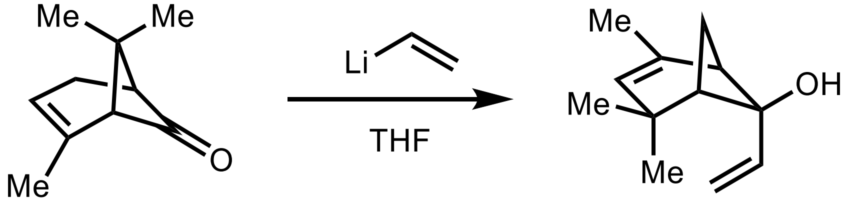
3.21.V **3.29.V**

Vinyl chrysanthenol **3.21.V** (13.4 mg, 75.2 µmol, 1.0 equiv) was dissolved in THF (0.16 mL) under an atmosphere of nitrogen. Vinyl magnesium bromide (0.7 M in THF, 0.21 mL, 15.0 mmol, 2.0 equiv) was added and the reaction mixture was stirred at room temperature for 3 h. The mixture was then quenched by addition of sat. aq. NH_4Cl (1 mL) and extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give **3.29.V** in 23% yield along with 18% of starting material **3.21.V**, as determined by quantitative ^{1}H NMR with ethylene carbonate as an internal standard**.**



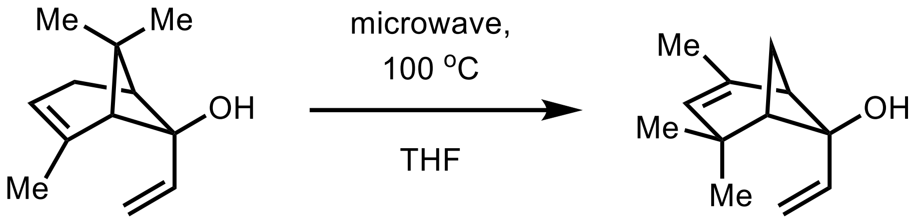
3.29.V **3.29.V**

Rearranged vinyl chrysanthenol **3.29.V** (13.4 mg, 75.2 µmol, 1.0 equiv) was dissolved in THF (0.16 mL) under an atmosphere of nitrogen. Vinyl magnesium bromide (0.7 M in THF, 0.21 mL, 15.0 mmol, 2.0 equiv) was added and the reaction mixture was stirred at room temperature for 3 h. The mixture was then quenched through the addition of sat. aq. NH_4Cl (1 mL) and extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the starting material **3.29.V** in 79% yield as determined by quantitative ^{1}H NMR with ethylene carbonate as an internal standard**.**



3.23 **3.29.V**

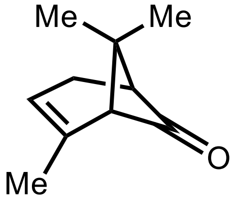
Vinyl iodide (40 µL, 0.52 mmol, 4 equiv) was added in THF (0.15 mL) and cooled to –78 °C. *t*BuLi (1.55 M in pentane, 0.67 mL, 1.04 mmol, 8 equiv) was added dropwise and stirred for 30 min. Chrysanthenone (**3.23**, 20.0 mg, 0.13 mmol, 1 equiv) in THF (0.15 mL) was added and the mixture was warmed to room temperature. After 1 h, NH_4Cl (3 mL) was added and the quenched mixture was extracted with EtOAc (3 x 3 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the title compound **3.29.V** in 12% yield as determined by quantitative ^{1}H NMR with pyrazine as an internal standard. No other products were observed.



3.21.V **3.29.V**

Vinyl chrysanthenol **3.21.V** (13.4 mg, 75.2 µmol, 1.0 equiv) was dissolved in THF (0.16 mL) under an atmosphere of nitrogen. The mixture was heated in a microwave reactor (100 °C, low absorbance) for 2 h. The mixture was concentrated in vacuo to give **3.29.V** in 19% yield along with 20% of starting material as determined by ^{1}H quantitative NMR with ethylene carbonate as an internal standard**.**

(1R,5S)-2,7,7-trimethylbicyclo[3.1.1]hept-2-en-6-one, chrysanthenone (3.23)



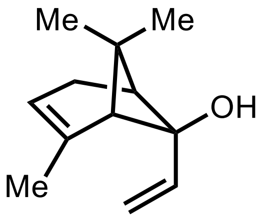
(*S*)-Verbenone (6.50 g, 43.3 mmol) was dissolved in cyclohexane (35 mL) under air. The stirring solution was irradiated with 365 nm light in a fan-cooled Penn OC M2 photoreactor for 3 h, then concentrated *in vacuo* to give a yellow oil. This material was purified by flash column chromatography (eluting with 30:1 hexanes:ethyl acetate) to give chrysanthenone as a pale yellow oil (4.37 g, 29.1 mmol, 67% yield). The ^{1}H NMR spectrum was fully consistent with that reported in the literature.[20]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (s, 1H), 2.70 – 2.59 (m, 3H), 2.56 (dt, *J* = 7.0, 3.1 Hz, 1H), 1.70 (q, *J* = 2.0 Hz, 3H), 1.21 (s, 3H), 1.18 (s, 3H). **$[\alpha]^{20}_D$** = –32.21 (*c* 1.07, $CHCl_3$)

General procedure for Addition of Commercial Grignard Reagents to Chrysanthenone:

To a solution of chrysanthenone (1.0 equiv) in THF (0.2 M, including volume of Grignard reagent solution) was added a solution of Grignard reagent in THF (2.0 equiv). The reaction mixture was allowed to stir at the specified temperature for the specified duration, then quenched through the addition of sat. aq. NH_4Cl (1 mL) and extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product. An analytical sample was obtained by purifying the crude reaction mixture by flash column chromatography (eluting with 30:1 hexanes:ethyl acetate).

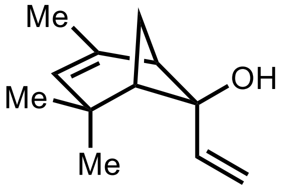
(1R,5S,6R)-2,7,7-trimethyl-6-vinylbicyclo[3.1.1]hept-2-en-6-ol (3.21.V)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.2 mL) was added vinylmagnesium bromide (0.7 M in THF, 0.3 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature to afford the title compound in 30% yield based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared by combining chrysanthenone (40.0 mg, 0.26 mmol, 1.0 equiv) in THF (0.54 mL) and vinylmagnesium bromide (0.7 M in THF, 0.76 mL, 0.4 mmol, 2.0 equiv) for 3 h at room temperature which after purification gave vinyl chrysanthenol **3.21.V** (13.4 mg, 75 µmol, 29%) as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.35 (dd, J = 17.6, 10.8 Hz, 1H), 5.24–5.22 (m, 1H), 5.20 (dd, J = 17.6, 1.6 Hz, 1H), 5.04 (dd, J = 10.9, 1.6 Hz, 1H), 2.25 (dq, J = 21.0, 3.3 Hz, 1H), 2.18 (dq, J = 21.0, 3.3 Hz, 1H), 2.11 (q, J = 1.1 Hz, 2H), 1.67 (s, 3H), 1.66 (d, J = 2.0 Hz, 3H), 0.95 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.7, 141.5, 119.7, 114.3, 78.3, 57.1, 50.6, 36.2, 31.4, 28.3, 23.5, 22.7. **HRMS** (EI): calcd for ([M], $C_{12}H_{18}O$)$^+$: m/z = 178.1353; found 178.1356. **IR**: ṽ = 3393, 2920, 2867, 1440, 1259, 1015, 951, 793 cm^{-1}. **$[\alpha]^{20}_D$** = +6.92 (*c* 0.98, $CHCl_3$).

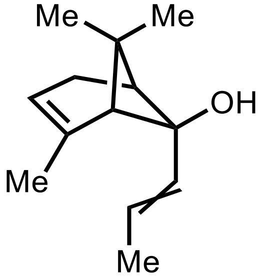
(1R,5S,6R)-2,4,4-trimethyl-6-vinylbicyclo[3.1.1]hept-2-en-6-ol (3.29.V)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.2 mL) was added vinylmagnesium bromide (0.7 M in THF, 0.3 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 31%, 40%, and 53% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with chrysanthenone (0.45 g, 2.9 mmol, 1.0 equiv) in THF (15 mL) and vinyl magnesium bromide (0.7 M in THF, 8.6 mL, 6.1 mmol, 2.0 equiv) for 17 h at room temperature which after purification gave **3.29.V** (0.25 g, 1.4 mmol, 47%) as a white solid. Crystallization through slow diffusion with hexanes/ethyl acetate afford a crystal that was unambiguously characterized by single crystal X-ray crystallography.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (dd, J = 17.5, 10.9 Hz, 1H), 5.23 (dd, J = 17.5, 1.8 Hz, 1H), 5.07 (dd, J = 10.8, 1.8 Hz, 1H), 5.05 (s, 1H), 2.66 (dt, J = 8.3, 5.6 Hz, 1H), 2.23 (ddd, J = 6.5, 5.2, 1.2 Hz, 1H), 2.17 (td, J = 6.3, 1.9 Hz, 1H), 1.75 (bs, 1H), 1.71 (d, J = 1.6 Hz, 3H), 1.50 (d, J = 8.3 Hz, 1H), 1.04 (s, 3H), 0.97 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.4, 140.0, 128.0, 113.6, 81.4, 58.3, 50.6, 39.2, 31.2, 29.0, 26.5, 22.5. **HRMS** (EI): calcd for ([M], $C_{12}H_{18}O)^+$: m/z = 178.1353; found 178.1357. **IR**: ṽ = 3337, 2957, 2925, 2865, 1444, 1081, 920, 830 cm^{-1}. **[α]$^{20}_D$** = +5.75 (*c* 0.33, $CHCl_3$) **MP**: 58–62 °C

(1R,5S,6R)-2,7,7-trimethyl-6-(prop-1-en-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.21.Pr)



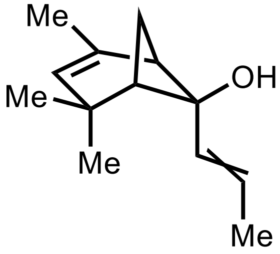
To chrysanthenone (15 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 1-propenylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound as a mixture of *E/Z*-isomers in 46%, 41%, and 0% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared by adding 1-propenylmagnesium bromide (0.5 M in THF, 1.3 mL, 0.67 mmol, 2.0 equiv) to chrysanthenone (50 mg, 0.33 mmol, 1.0 equiv) in THF (0.3 mL) and stirring for 3 h at room temperature, which after purification gave propenyl chrysanthenol **3.21.Pr** in 47% yield (29.8 mg, 0.15 mmol) as a clear oil.

E-isomer: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.92 (dq, *J* = 15.7, 1.7 Hz, 1H), 5.68 – 5.55 (m, 1H), 5.20 (dq, *J* = 2.9, 1.5 Hz, 1H), 2.25 – 2.05 (m, 4H), 1.68 – 1.64 (m, 9H), 0.93 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.5, 134.8, 125.2, 119.5, 78.1, 57.2, 50.6, 36.1, 31.5, 28.3, 23.6, 22.8, 18.1.

Z-isomer: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.68 – 5.55 (m, 1H), 5.41 (dd, *J* = 10.9, 7.1 Hz, 1H), 5.21 (dq, *J* = 3.2, 1.4 Hz, 1H), 2.34 – 2.29 (m, 1H), 2.25 – 2.05 (m, 2H), 1.81 (d, *J* = 1.5 Hz, 1H), 1.71 (dd, *J* = 7.1, 1.7 Hz, 3H), 1.66 – 1.64 (m, 6H), 0.93 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.4, 134.5, 126.1, 120.6, 78.7, 57.4, 50.9, 36.7, 31.5, 28.1, 23.8, 22.6, 14.1.

HRMS (EI): calcd for ([M], $C_{13}H_{20}O)^+$: m/z = 192.1509; found 192.1517. **IR**: ṽ = 3455, 2918, 1441, 1379, 1260, 1175, 1019, 958, 794 cm^{-1}. **[α]$^{20}_D$** = +13.92 (*c* 0.79, $CHCl_3$)

(1R,5S,6R)-2,4,4-trimethyl-6-(prop-1-en-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.29.Pr)



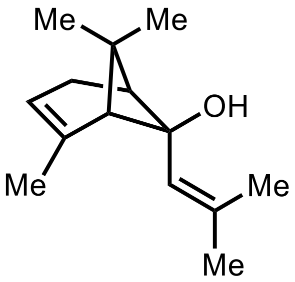
To chrysanthenone (15 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 1-propenylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound as a combined mixture of *E/Z*-isomers in 9%, 16%, and 48% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with chrysanthenone (50 mg, 0.33 mmol, 1.0 equiv) in THF (0.3 mL) and 1-propenylmagnesium bromide (0.5 M in THF, 1.3 mL, 0.67 mmol, 2.0 equiv) for 17 h at 50 °C, which after purification gave propenyl chrysanthenol **3.29.Pr** in 9% yield (5.8 mg, 0.03 mmol) as a clear oil. An analytical sample of the sole *E*-isomer was prepared with chrysanthenone (0.1 g, 0.67 mmol, 1.0 equiv.) in THF (0.7 mL) and 1-propenylmagnesium bromide (0.5 M in THF, 2.7 mL, 1.34 mmol, 2.0 equiv) for 17 h at room temperature which after purification gave the *E*-isomer of propenyl chrysanthenol **3.29.Pr** (19.3 mg, 10.0 µmol, 15%) as a clear oil.

E-isomer: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.86 (dq, *J* = 15.7, 1.7 Hz, 1H), 5.67 – 5.57 (m, 1H), 5.01 (q, *J* = 1.7 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.21 (ddd, *J* = 6.4, 5.2, 1.1 Hz, 1H), 2.13 (td, *J* = 6.3, 1.9 Hz, 1H), 1.71 (d, *J* = 1.6 Hz, 3H), 1.69 (dd, *J* = 6.5, 1.6 Hz, 3H), 1.46 (d, *J* = 8.3 Hz, 1H), 1.03 (s, 3H), 0.96 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.1, 134.7, 127.9, 124.5, 81.2, 58.1, 50.6, 39.3, 31.2, 29.1, 26.4, 22.6, 18.0. *[Note: spectrum of sole E-isomer provided below]*

Z-isomer: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.67 – 5.57 (m, 1H), 5.55 – 5.46 (m, 1H), 5.03 (q, *J* = 1.6 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.39 (td, *J* = 6.3, 1.8 Hz, 1H), 2.25 (ddd, *J* = 6.4, 5.2, 1.1 Hz, 1H), 1.76 (dd, *J* = 7.1, 1.7 Hz, 3H), 1.72 (d, *J* = 1.6 Hz, 3H), 1.52 (d, *J* = 8.4 Hz, 1H), 1.08 (s, 3H), 0.97 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.9, 135.1, 129.6, 128.7, 80.8, 57.7, 50.9, 39.4, 31.4, 29.2, 25.3, 23.1, 15.8.

HRMS (EI): calcd for ([M], $C_{13}H_{20}O$)$^+$: m/z = 192.1509; found 192.1512. **IR**: $\tilde{\nu}$ = 3369, 2957, 2922, 2861, 1445, 1377, 1024, 830 cm^{-1}. **$[\alpha]^{20}_D$** = –11.72 (*c* 0.58, $CHCl_3$)

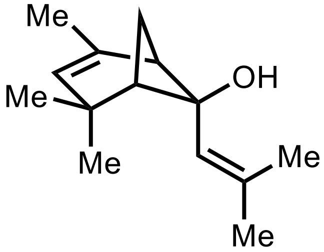
(1R,5S,6R)-2,7,7-trimethyl-6-(2-methylprop-1-en-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.S1)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 2-methyl-1-propenylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 69%, 71%, and 39% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared using the aforementioned quantities, stirring for 3 h at room temperature, to afford the title compound in 43% yield (8.7 mg, 42 µmol) as a white semi-solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.34 (p, *J* = 1.4 Hz, 1H), 5.18 (th, *J* = 3.0, 1.5 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.17 (ddq, *J* = 17.1, 4.9, 2.4 Hz, 1H), 2.13 – 2.03 (m, 2H), 1.69 (d, *J* = 1.2 Hz, 3H), 1.67 – 1.64 (m, 6H), 1.64 (s, 3H), 0.92 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.3, 134.2, 129.3, 120.4, 78.7, 57.4, 50.8, 36.5, 31.5, 28.1, 25.7, 23.8, 22.7, 18.7. **HRMS** (EI): calcd for ([M], $C_{14}H_{22}O)^+$: m/z =206.1666; found 206.1672. **IR**: : ṽ = 3380, 2991, 2917, 1665, 1442, 1378, 1020 cm^{-1}. **$[\alpha]^{20}_D$** = +42.38 (*c* 0.42, $CHCl_3$)

(1R,5S,6R)-2,4,4-trimethyl-6-(2-methylprop-1-en-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.S2)

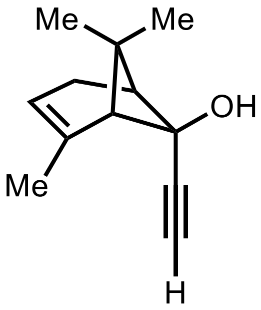


To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 2-methyl-1-propenylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 17 h at room temperature or 17 h at 50 °C to afford the title compound in 3% and 25% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with chrysanthenone (30.0 mg, 0.2 mmol, 1.0 equiv) in THF (0.2 mL) and 2-methyl-1-propenylmagnesium bromide (0.5 M in THF, 0.8 mL, 0.4 mmol, 2.0 equiv) for 17 h at 50 °C, to afford the title compound in 16% yield (6.3 mg, 31 µmol) as a colorless solid after purification.

^{1}H NMR (700 MHz, $CDCl_3$) δ 5.31 (s, 1H), 4.99 (s, 1H), 2.58 (q, *J* = 6.8 Hz, 1H), 2.39 – 2.37 (m, 1H), 2.22 (t, *J* = 6.3 Hz, 1H), 1.73 (s, 5H), 1.71 (s, 3H), 1.65 (s, 2H), 1.49 (d, *J* = 6.0 Hz, 1H), 1.02 (s, 2H), 0.96 (s, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 139.9, 138.0, 129.8, 128.6, 80.6, 57.2, 50.9, 39.5, 31.4, 29.2, 25.9, 25.2, 23.2, 20.5. **HRMS** (EI): calcd for ([M], $C_{14}H_{22}O)^+$: m/z =206.1666; found 206.1673.

IR: : ṽ = 3440, 2962, 2926, 1717, 1658, 1447, 1376, 1031 cm^{-1}. **[α]^{20}$_D$** = –9.09 (*c* 0.33, $CHCl_3$) **MP**: 64–72 °C

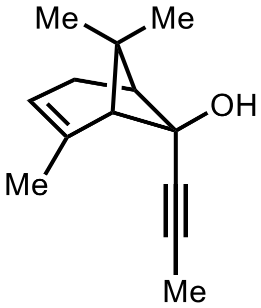
(1R,5S,6R)-6-ethynyl-2,7,7-trimethylbicyclo[3.1.1]hept-2-en-6-ol (3.21.E)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added ethynylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 14%, 48%, and 47% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with the aforementioned quantities, reacting for 17 h at 50 °C, to afford the title compound in 43% yield (7.6 mg, 40 µmol) as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.32 (tq, *J* = 2.9, 1.5 Hz, 1H), 2.53 – 2.45 (m, 1H), 2.39 (s, 1H), 2.31 – 2.23 (m, 3H), 2.19 (dtd, *J* = 6.9, 2.9, 1.2 Hz, 1H), 1.68 (q, *J* = 2.0 Hz, 3H), 1.61 (s, 3H), 0.94 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.9, 120.4, 85.5, 74.3, 71.6, 57.9, 51.0, 36.5, 31.7, 27.9, 23.1, 23.0. **HRMS** (EI): calcd for ([M], $C_{12}H_{16}O)^+$: m/z =176.1196; found 176.1200. **IR**: ṽ = 3304, 2958, 2926, 1706, 1673, 1442, 1369, 1036 cm^{-1}. **[α]^{20}$_D$** = +15.38 (*c* 0.07, $CHCl_3$)

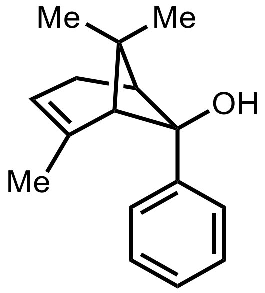
(1R,5S,6R)-2,7,7-trimethyl-6-(prop-1-yn-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.21.P)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 1-propynylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 70%, 77%, and 70% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared using chrysanthenone (50.0 mg, 0.33 mmol, 1.0 equiv) in THF (0.3 mL) and 1-propynylmagnesium bromide (0.5 M in THF, 1.3 mL, 0.66 mmol, 2.0 equiv) for 17 h at room temperature which after purification gave the title compound in 53% yield (33.0 mg, 0.17 mmol) as a colorless solid. Crystallization of the enantiomer of the title compound through slow diffusion with hexanes/ethyl acetate afforded a crystal that led to unambiguous characterization by single crystal X-ray crystallography.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.27 (th, *J* = 3.0, 1.5 Hz, 1H), 2.43 (dq, *J* = 17.1, 2.6 Hz, 1H), 2.26 – 2.15 (m, 3H), 2.12 (dtd, *J* = 6.9, 2.9, 1.2 Hz, 1H), 1.79 (s, 3H), 1.65 (q, *J* = 2.0 Hz, 3H), 1.58 (s, 3H), 0.92 (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 140.9, 120.0, 81.1, 79.4, 74.5, 58.1, 51.2, 36.2, 31.9, 27.9, 23.1, 23.1, 3.8. **HRMS** (EI): calcd for ([M], $C_{13}H_{18}O$)$^+$: m/z = 190.1353; found 190.1359. **IR**: ṽ = 3387, 2920, 2866, 1382, 1180, 1057, 1021, 789 cm^{-1}. **[α]$^{20}_{D}$** = +7.40 (*c* 0.77, CHCl$_3$) **MP**: 42–45 °C

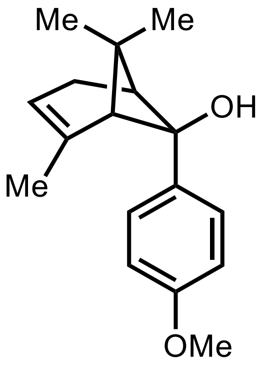
(1R,5S,6R)-2,7,7-trimethyl-6-phenylbicyclo[3.1.1]hept-2-en-6-ol (3.S3)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.3 mL) was added phenylmagnesium bromide (2.0 M in THF, 0.2 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 95%, 96%, and 96% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with the aforementioned quantities, stirring for 3 h at room temperature, to afford the title compound in 83% yield (18.9 mg, 0.08 mmol) as a clear solid without purification.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.30 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.19 (m, 1H), 7.16 – 7.12 (m, 2H), 4.84 (dd, *J* = 3.1, 1.6 Hz, 1H), 2.53 – 2.48 (m, 2H), 2.38 – 2.10 (m, 2H), 1.76 (s, 3H), 1.72 (d, *J* = 2.0 Hz, 3H), 1.03 (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 145.2, 142.2, 128.2, 126.6, 125.7, 119.1, 81.4, 55.4, 48.3, 35.6, 31.7, 28.4, 23.7, 23.1. **HRMS** (ESI): calcd for ([M+Na], $C_{16}H_{20}ONa$)$^+$: m/z = 251.1407; found 251.1410. **IR**: : ṽ = 3434, 2918, 2866, 1445, 1381, 1020, 770, 703 cm^{-1}. **[α]$^{20}_{D}$** = +30.45 (*c* 0.44, CHCl$_3$) **MP**: 52–56 °C

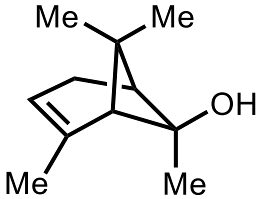
(1R,5S,6R)-6-(4-methoxyphenyl)-2,7,7-trimethylbicyclo[3.1.1]hept-2-en-6-ol (3.21.Ph)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 4-methoxyphenylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 96%, 79%, and 80% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with chrysanthenone (20.0 mg, 0.13 mmol, 1.0 equiv) in THF (0.13 mL) and 4-methoxyphenylmagnesium bromide (0.5 M in THF, 0.53 mL, 0.26 mmol, 2.0 equiv) for 17 h at 50 °C, which after purification gave the title compound in 96% yield (32.3 mg, 0.13 mmol, 96%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.92 – 4.87 (m, 1H), 3.82 (s, 3H), 2.55 – 2.49 (m, 2H), 2.35 – 2.13 (m, 2H), 1.79 (s, 3H), 1.75 (d, *J* = 2.0 Hz, 3H), 1.06 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.1, 142.2, 137.8, 126.9, 119.0, 113.5, 81.0, 55.4, 55.2, 48.3, 35.6, 31.7, 28.3, 23.7, 23.2. **HRMS** (EI): calcd for ([M], $C_{17}H_{22}O_2$)$^+$: m/z =258.1615; found 258.1620. **IR**: ṽ = 3451, 2916, 2838, 1512, 1244, 1173, 832 cm^{-1}. **$[\alpha]^{20}_D$** = +31.36 (*c* 1.07, $CHCl_3$) **MP**: 75–79 °C

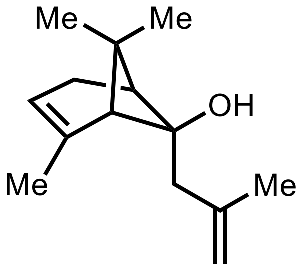
(1R,5S,6R)-2,6,7,7-tetramethylbicyclo[3.1.1]hept-2-en-6-ol (3.21.M)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.3 mL) was added methylmagnesium bromide (1 M in THF, 0.2 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 22%, 50%, and 65% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with the aforementioned quantities, stirring for 17 h at 50 °C to afford the title compound in 57% yield (9.4 mg, 0.10 mmol) as a colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.22 (tq, *J* = 3.0, 1.5 Hz, 1H), 2.23 (dq, *J* = 17.4, 2.6 Hz, 1H), 2.16 (dq, *J* = 17.4, 2.6 Hz, 1H), 2.02 (dd, *J* = 7.0, 1.4 Hz, 1H), 1.93 (dtd, *J* = 7.0, 2.9, 1.1 Hz, 1H), 1.65 (s, 4H), 1.64 (d, *J* = 1.9 Hz, 2H), 1.27 (s, 3H), 0.92 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.3, 119.1, 77.7, 57.6, 49.6, 36.4, 31.2, 28.7, 23.5, 23.0, 22.7. **HRMS** (EI): calcd for ([M], $C_{11}H_{18}O)^+$: m/z =166.1353; found 166.1355. **IR**: ṽ = 3326, 2917, 2865, 1438, 1372, 1292, 1261, 1184, 1087, 923, 791 cm^{-1}. **[α]^{20}$_D$** = +43.04 (*c* 0.79, $CHCl_3$) **MP**: 49–53 °C

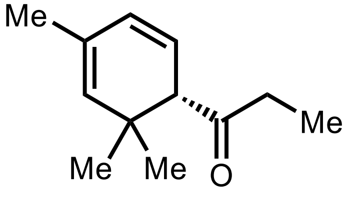
(1R,5S,6R)-2,7,7-trimethyl-6-(2-methylallyl)bicyclo[3.1.1]hept-2-en-6-ol (3.S4)



To chrysanthenone (15.0 mg, 0.1 mmol, 1.0 equiv) in THF (0.1 mL) was added 2-methylallylmagnesium bromide (0.5 M in THF, 0.4 mL, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred for 3 h at room temperature, 17 h at room temperature, or 17 h at 50 °C to afford the title compound in 78%, 61%, and 66% yield respectively based on quantitative ^{1}H NMR. An analytical sample of this compound was prepared with the aforementioned quantities, stirring for 17 h at room temperature, to afford the title compound in 37% yield (7.6 mg, 0.36 µmol) without purification.

^{1}H NMR (700 MHz, $CDCl_3$) δ 5.29 (tq, *J* = 3.1, 1.5 Hz, 1H), 4.91 (p, *J* = 1.6 Hz, 1H), 4.78 (dd, *J* = 2.4, 1.2 Hz, 1H), 2.64 (dd, *J* = 13.9, 1.2 Hz, 1H), 2.35 (s, 1H), 2.27 (dd, *J* = 13.8, 1.0 Hz, 1H), 2.25 – 2.18 (m, 2H), 2.09 (dd, *J* = 6.9, 1.4 Hz, 1H), 2.01 – 1.97 (m, 1H), 1.67 (d, *J* = 3.1 Hz, 9H), 0.94 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.6, 141.6, 119.5, 114.9, 76.1, 57.9, 49.8, 42.0, 37.1, 30.9, 28.3, 23.5, 23.4, 23.1. **HRMS** (ESI): calcd for ([M–H], $C_{14}H_{21}O)^-$: m/z = 205.1597; found 205.1604. **IR**: ṽ = 3541, 2917, 2866, 1643, 1436, 1373, 1053, 888 cm^{-1}. **[α]^{20}$_D$** = +7.09 (*c* 0.62, $CHCl_3$)

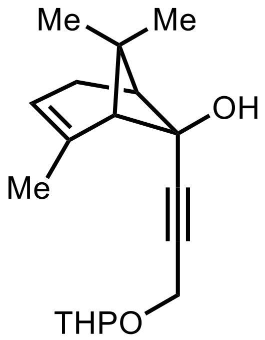
(S)-1-(4,6,6-trimethylcyclohexa-2,4-dien-1-yl)propan-1-one (3.36)



Hydroxy(cyclooctadiene)rhodium(I) dimer (3.8 mg, 8.0 µmol, 5 mol%) and 1,1'-ferrocenediyl-bis(diphenylphosphine) (dppf, 13.9 mg, 0.025 mmol, 15 mol%) were added to a sealable vial in the glovebox. 1,4-dioxane (1 mL) was added and the mixture was stirred for 5 min, resulting in a golden yellow solution. Rearranged [3.1.1]bicycle **3.29.V** (30.0 mg, 0.17 mmol, 1.0 equiv) was added as a solution in 1,4-dioxane (0.5 mL) to the rhodium mixture. The sealed vial was heated to 100 °C for 24 h. Upon allowing the mixture to cool to room temperature, it was filtered through Celite eluting with EtOAc, and then concentrated *in vacuo*. Purification of the crude residue by preparative thin layer chromatography (running in 6:1 hexanes:ethyl acetate) afforded ketone **3.36** (17.6 mg, 0.10 mmol, 59% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90 (dt, *J* = 9.5, 1.6 Hz, 1H), 5.63 (dd, *J* = 9.6, 4.8 Hz, 1H), 5.18 (s, 1H), 3.04 (dd, *J* = 4.8, 1.8 Hz, 1H), 2.66 – 2.44 (m, 2H), 1.75 (d, *J* = 1.7 Hz, 3H), 1.09 (s, 3H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.94 (s, 3H). **HRMS** (ESI): calcd for ([M+H], $C_{12}H_{19}O)^+$: m/z = 179.1431; found 179.1429.

(1R,5S,6R)-2,7,7-trimethyl-6-(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-yn-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.45)

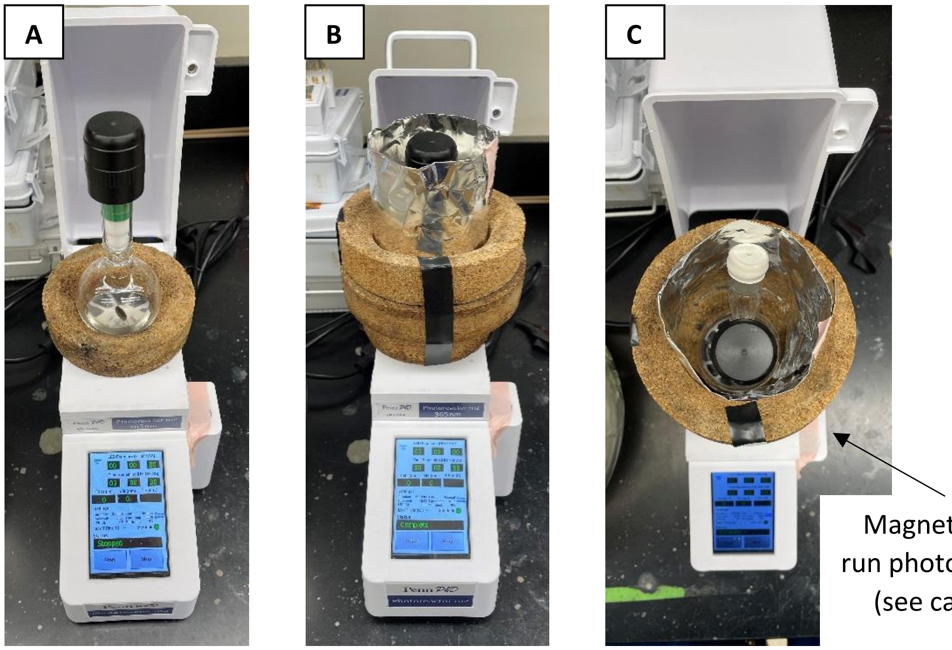


The alkynyl Grignard reagent was prepared according to a procedure reported by Christov and coworkers.[21]

From chrysanthenone: 2-(2-propynyloxy)tetrahydropyran (0.37 mL, 2.6 mmol, 2.0 equiv) was dissolved in THF (3 mL). Ethylmagnesium bromide (1 M in THF, 2.6 mL, 2.6 mmol, 2.0 equiv) was added to the mixture which was then heated at reflux for 2 h. Chrysanthenone (0.20 g, 1.3 mmol, 1.0 equiv) in THF (0.2 mL) was added and the reaction mixture was allowed to stir at room temperature for 20 h after which it was quenched through the addition of sat. aq. NH_4Cl (3 mL) and extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product. Purification of the crude reaction mixture by flash column chromatography (eluting with 10:1 to 6:1 hexanes:ethyl acetate) gave **3.45** in 81% yield (0.31 g, 1.1 mmol) as a white semi-solid.

From verbenone: (–)-Verbenone (1.50 g, 10.0 mmol, 1.0 equiv) was dissolved in cyclohexane (8.0 mL) in a Schlenk flask under an atmosphere of nitrogen. The stirring solution was irradiated with 365 nm light in a fan-cooled photobox for 3 h. *[Note: see attached images of setup].* In a separate flask, ethylmagnesium bromide (1 M in THF, 26.4 mL, 26.4 mmol) was added to 2-(2-propynyloxy)tetrahydropyran (3.7 mL, 26.4 mmol) in THF (32.0 mL) and the mixture was heated at reflux for 2 h to make a ~0.43 M solution of alkynyl Grignard reagent. The alkynyl Grignard reagent solution (47.0 mL, 20.2 mmol, 2.0 equiv) was then added to the cyclohexane mixture and heated at 50 °C for 20 h after which it was cooled to room temperature and quenched through the addition of sat. aq. NH_4Cl (30 mL), extracted with Et_2O (3 x 75 mL), and washed with brine (50 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product. This material was purified by flash column chromatography (eluting with 10:1 hexanes:ethyl acetate) gave **3.45** in 67% yield (1.94 g, 6.68 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.26 (ddq, *J* = 6.3, 3.0, 1.5 Hz, 1H), 4.80 (q, *J* = 3.0 Hz, 1H), 4.24 (dd, *J* = 5.6, 2.0 Hz, 2H), 3.92 – 3.74 (m, 1H), 3.49 (ddq, *J* = 10.9, 4.3, 2.4 Hz, 1H), 2.67 (br s, 1H), 2.44 (dt, *J* = 17.1, 2.7 Hz, 1H), 2.35 – 2.09 (m, 3H), 1.90 – 1.75 (m, 1H), 1.70 (ddt, *J* = 16.6, 9.9, 3.3 Hz, 2H), 1.64 (dq, *J* = 3.8, 2.0 Hz, 3H), 1.58 (s, 3H), 1.54 – 1.41 (m, 3H), 0.91 (d, *J* = 2.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.8, 140.8, 120.3, 120.3, 96.3, 96.2, 87.7, 87.7, 79.1, 79.1, 74.1, 74.1, 62.2, 62.1, 58.0, 57.9, 54.3, 54.3, 51.0, 51.0, 36.3, 31.8, 31.7, 30.4, 30.4, 27.9, 25.5, 23.1, 23.1, 23.0, 23.0, 19.3, 19.3. *Duplicate carbon peaks from mixture of diastereomers from THP ring. **HRMS** (ESI): calcd for ([M+Na], $C_{18}H_{26}O_3Na)^+$: m/z = 313.1775; found 313.1775. **IR**: $\tilde{\nu}$ = 3415, 2927, 2868, 1441, 1262, 1118, 1023 cm^{-1}. **$[\alpha]^{20}_D$** = –2.16 (*c* 0.19, $CHCl_3$)

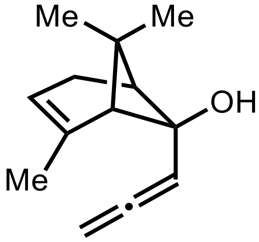


Magnet was placed here to run photoreactor with lid open (see caution note below).

Figure 3.23. (A) Setup of Schlenk flask in photoreactor. (B) Side-view of setup with Schlenk flask wrapped in foil in photoreactor. (C) Top-view of setup with Schlenk flask wrapped in foil in photoreactor.

[Caution Note: This is not the intended setup for this photoreactor and caution was exercised to contain and shield the light by placing an opaque box over the setup.]

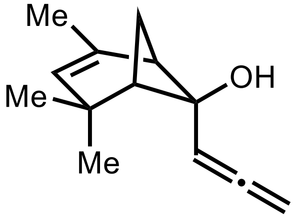
(1R,5S,6R)-2,7,7-trimethyl-6-(propa-1,2-dien-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.21.A)



Allene **3.21.A** was prepared according to the following modification of a procedure reported by Carreira and coworkers.[16] $LiAlH_4$ (2.0 M in THF, 0.17 mL, 0.34 mmol, 1.0 equiv) was added dropwise to alcohol **3.45** (0.1 g, 0.34 mmol, 1.0 equiv) in Et_2O (2.0 mL) at 0 °C. The reaction mixture was warmed to room temperature and allowed to stir for 2 h. The mixture was quenched at 0 °C through sequential additions of H_2O (1 mL), 10% NaOH (1.5 mL), and H_2O (3.0 mL). The biphasic mixture was stirred for 15 min and extracted with Et_2O (3 x 5mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product. Purification of the crude residue by flash column chromatography (eluting with 10:1 hexanes:ethyl acetate) gave allenol **3.21.A** in 31% yield (20.5 mg, 0.11 mmol) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.81 (t, *J* = 6.7 Hz, 1H), 5.29 (dq, *J* = 3.0, 1.5 Hz, 1H), 4.88 (dd, *J* = 6.7, 5.3 Hz, 1H), 4.93 – 4.83 (m, 1H), 2.26 (q, *J* = 2.5 Hz, 2H), 2.16 (dd, *J* = 6.9, 1.3 Hz, 1H), 2.14 – 2.10 (m, 1H), 1.66 (s, 6H), 0.96 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 206.9, 141.7, 119.6, 95.5, 78.7, 75.8, 57.8, 51.0, 36.4, 31.3, 28.1, 23.5, 22.9. **HRMS** (EI): calcd for ([M], $C_{13}H_{18}O)^+$: m/z = 190.1353; found 190.1359. **IR**: ṽ = 3431, 2922, 2842, 1951, 1439, 1258, 1025, 842 cm^{-1}. **$[\alpha]^{20}_D$** = +7.42 (*c* 0.93, $CHCl_3$)

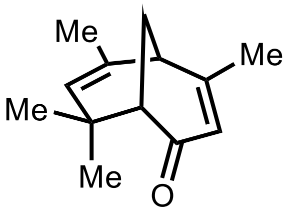
(1R,5S,6R)-2,4,4-trimethyl-6-(propa-1,2-dien-1-yl)bicyclo[3.1.1]hept-2-en-6-ol (3.29.A)



An analytical sample of allenol **3.29.A** was prepared as follows: $LiAlH_4$ (2.0 M in THF, 0.09 mL, 0.17 mmol, 1.0 equiv) was added dropwise to alcohol **3.45** (50. mg, 0.17 mmol, 1.0 equiv) in THF (0.93 mL) at 0 °C. The reaction mixture was warmed to room temperature for 15 min. The mixture was then heated for 3 h in a microwave reactor (50 °C, normal absorbance). The mixture was diluted with Et_2O (3 mL) and quenched at 0 °C with sat. aq. Rochelle's salt (1 mL). The mixture was stirred for 15 min and extracted with Et_2O (3 x 5mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product. Purification of the crude residue by flash column chromatography (eluting with 30:1 hexanes:ethyl acetate) gave allenol **3.29.A** in 9% yield (2.8 mg, 0.015 mmol) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.53 (t, *J* = 6.6 Hz, 1H), 5.31 (q, *J* = 1.7 Hz, 1H), 4.92 (dd, *J* = 6.7, 2.0 Hz, 2H), 3.00 (s, 1H), 2.51 (td, *J* = 5.5, 1.3 Hz, 1H), 2.22 (td, *J* = 5.9, 2.0 Hz, 1H), 1.75 (d, *J* = 1.6 Hz, 3H), **1.30 (d, *J* = 9.3 Hz, 1H)**, 1.19 (s, 3H), 0.99 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.8, 138.7, 129.8, 95.1, 77.6, 73.1, 54.0, 50.5, 38.3, 29.4, 27.4, 25.7, 23.1. **HRMS** (EI): calcd for ([M], $C_{13}H_{18}O$)$^+$: m/z = 190.1353; found 190.1361. **IR**: ṽ = 2956, 2917, 2849, 1733, 1462, 1260, 1167, 802 cm^{-1}. **$[\alpha]^{20}_D$** = +4.85 (*c* 0.33, $CHCl_3$)

(1S,5R)-4,6,8,8-tetramethylbicyclo[3.3.1]nona-3,6-dien-2-one (3.46)



*From alkyne **3.21.P**:* Prepared according to the modified procedure by Cramer and coworkers.[11] Hydroxy(cyclooctadiene)rhodium(I) dimer (1.1 mg, 2.5 µmol, 5 mol%) and 1,1'-ferrocenediyl-bis(diphenylphosphine) (dppf, 4.4 mg, 7.5 µmol, 15 mol%) were added to a sealable vial in the glovebox. 1,4-dioxane (0.25 mL) was added and the mixture was stirred for 5 min, resulting in a golden yellow solution. Alkyne **3.21.P** (10.0 mg, 0.052 mmol, 1.0 equiv) was added as a solution in 1,4-dioxane (0.25 mL) to the rhodium mixture. The sealed vial was heated to 100 °C for 24 h. Upon allowing the mixture to cool to room temperature it was filtered through Celite eluting with EtOAc, and then concentrated *in vacuo*. Purification of the crude residue by preparative thin layer chromatography (running in 30:1 to 15:1 hexanes:ethyl acetate) afforded enone **3.46** (4.8 mg, 0.025 mmol, 48% yield).

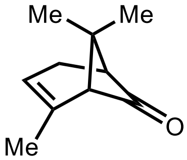
*From allenol **3.21.A**:* Ethyl magnesium bromide (1.0 M in THF, 0.64 mL, 0.64 mmol, 2.0 equiv) was added dropwise to a solution of allenol **3.21.A** (60 mg, 0.32 mmol, 1.0 equiv) dissolved in THF (0.9 mL). After 5 min at room temperature, the reaction mixture was transferred to a 50 °C oil bath for 20 h. At this stage, the reaction mixture was cooled to room temperature and quenched with sat. aq. NH_4Cl. The solution was then extracted with Et_2O (3 x 5 mL), the combined organics phase was dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude oil. Purification of the crude residue by flash column chromatography (eluting with 30:1 hexanes:ethyl acetate) gave enone **3.46** in 41% yield (24.6 mg, 0.13 mmol) as a clear oil.

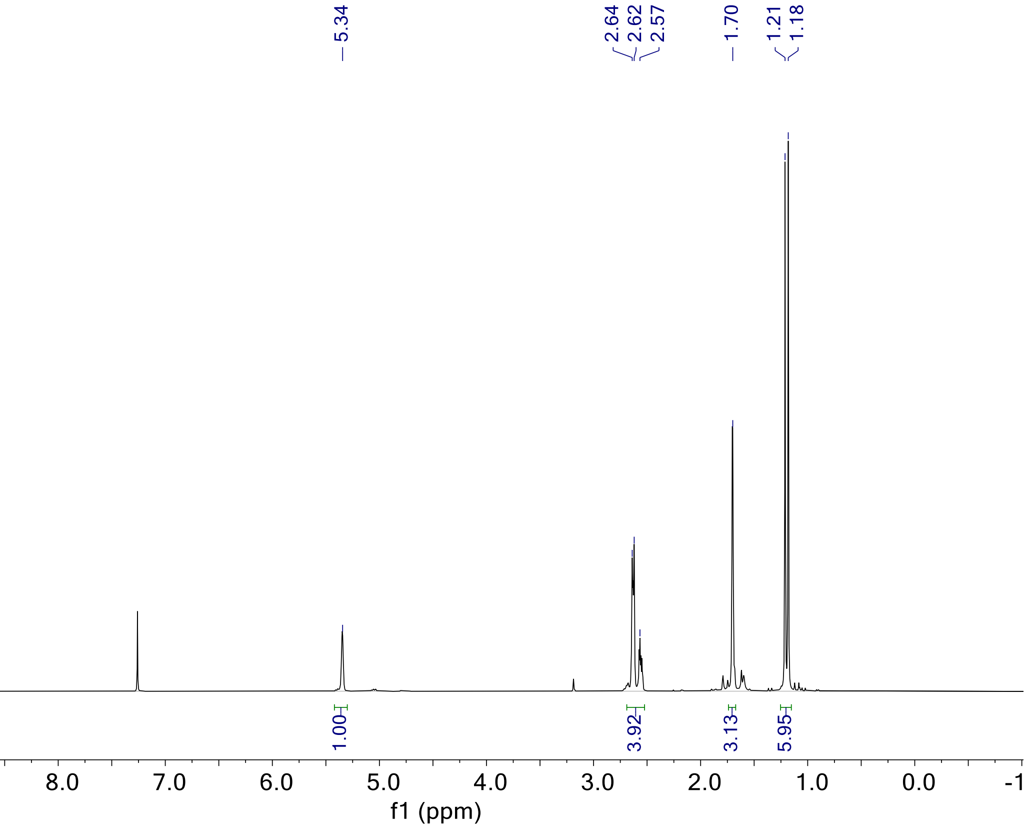
*From THP-propargyl alcohol **3.45**:* Alkyne **3.45** (1.0 g, 3.4 mmol, 1.0 equiv) was dissolved in THF (17 mL) and cooled to 0 °C. Ethylmagnesium bromide (1.0 M in THF, 3.4 mL, 3.4 mmol, 1.0 equiv) was added dropwise followed by addition of 1,4-cyclohexadiene (6.5 mL). After 10 min, $LiAlH_4$ (2 M in THF, 1.7 mL, 3.4 mmol, 1.0 equiv) was added dropwise. The reaction mixture was then warmed to room temperature over 10 min, then transferred to a 70 °C oil bath and heated at this temperature for 3 h. The reaction mixture was then cooled to 0 °C, diluted with Et_2O (15 mL), then quenched with sat. aq. Rochelle's salt (5 mL). 2.0 M NaOH (5 mL) and MeOH (2 mL) were added, and the mixture was vigorously stirred for 15 min, sat. aq. NH_4Cl (4 mL) was added, and the mixture was extracted with Et_2O (3x 25mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude oil. Purification of the crude residue by flash column chromatography (eluting with 10:1 hexanes:ethyl acetate) gave enone **3.46** in 67% yield (442. mg, 2.32 mmol) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.67 (s, 1H), 5.08 (s, 1H), 2.46 (t, *J* = 3.1 Hz, 1H), 2.29 (t, *J* = 3.1 Hz, 1H), 2.20 (dt, *J* = 12.4, 3.2 Hz, 1H), 2.10 – 2.08 (m, 1H), 2.07 (s, 3H), 1.83 (s, 3H), 1.11 (s, 3H), 0.86 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.9, 168.2, 134.4, 132.2, 125.2, 51.1, 41.6, 33.4, 31.5, 31.2, 26.9, 25.0, 24.1. **HRMS** (EI): calcd for $([M],C_{13}H_{18}O)^+$: m/z =190.1353; found 190.1358 **IR**: ṽ = 2959, 2916, 1657, 1628, 1449, 1288, 1026, 878 cm^{-1}. **$[\alpha]^{20}_D$** = –23.14 (*c* 0.35, $CHCl_3$)

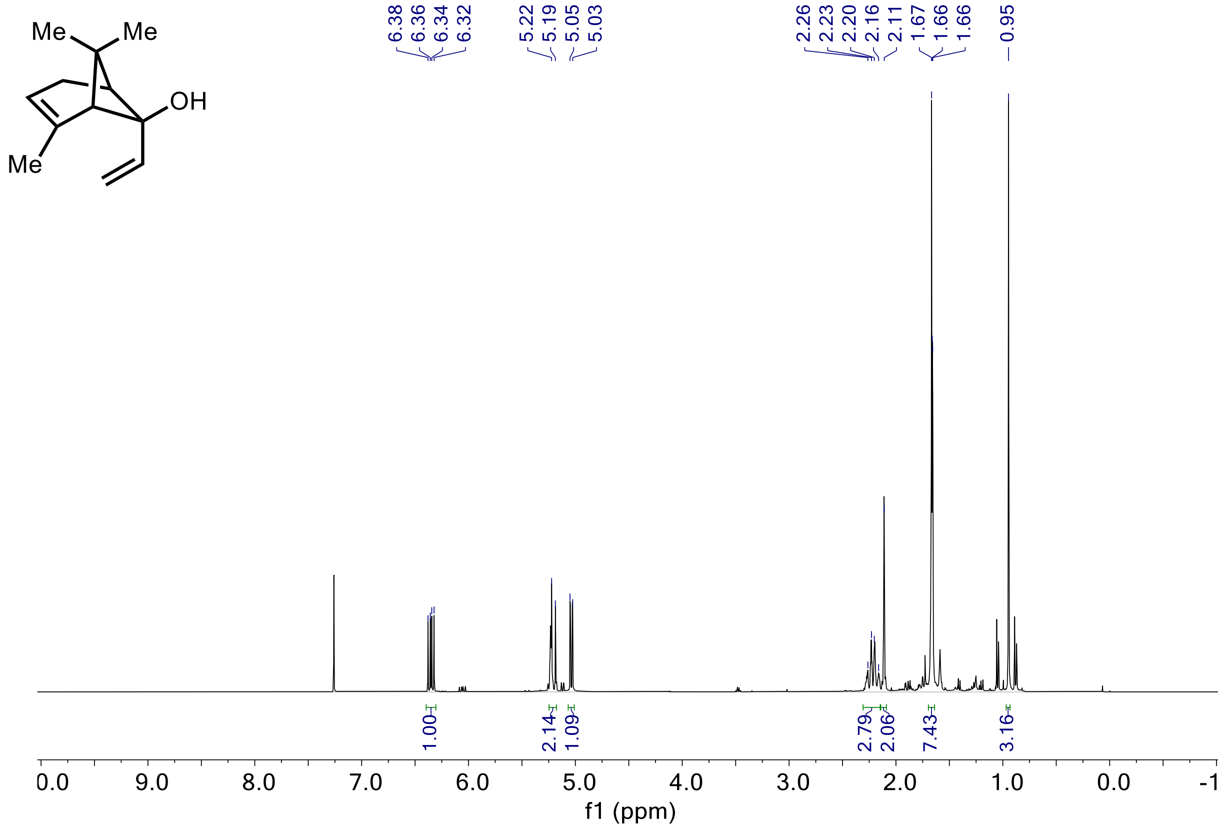
3.10.2 NMR Spectral Data for Chapter 3

3.23 (^{1}H NMR, 400 MHz, CDCl$_3$)

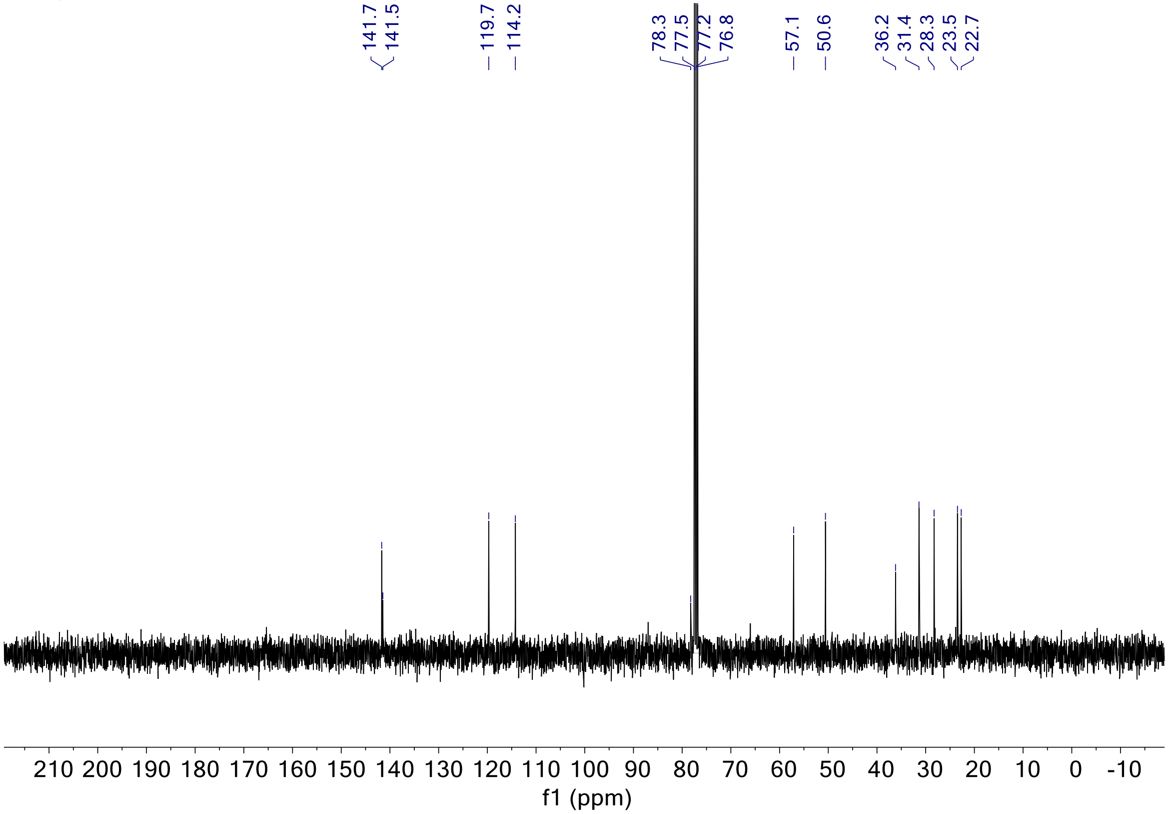




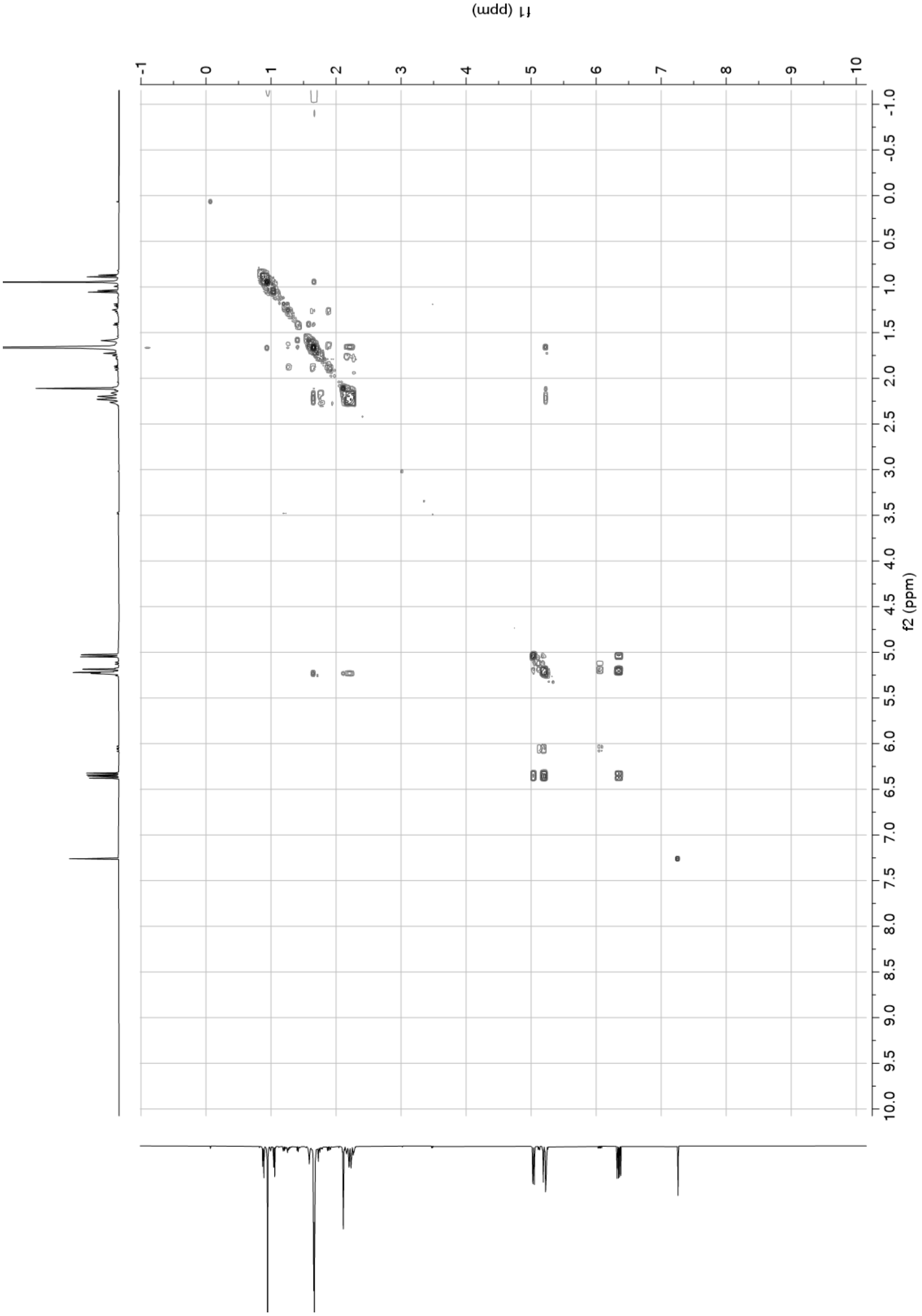
3.21.V (^{1}H NMR, 500 MHz, CDCl$_3$)



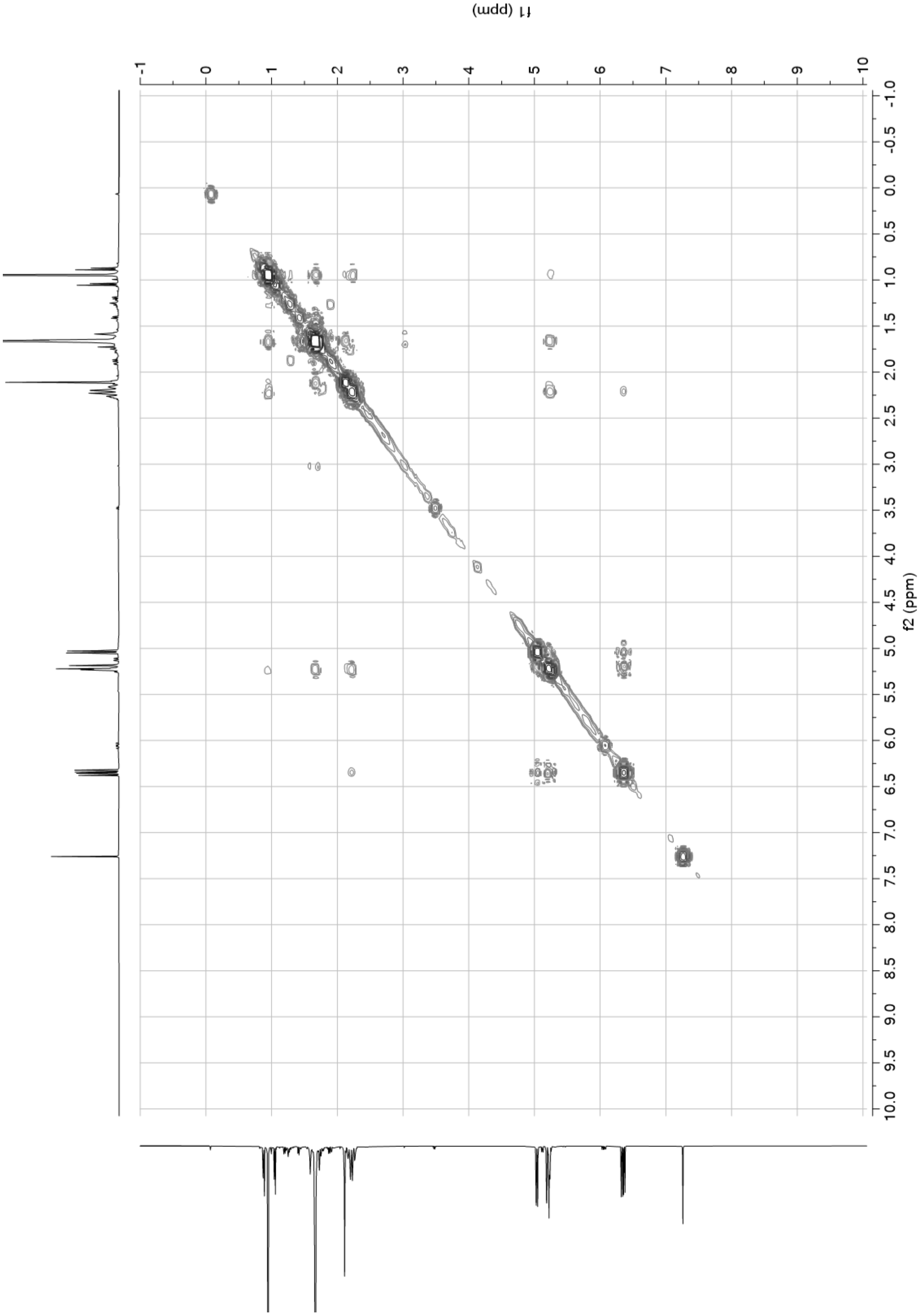
3.21.V (^{13}C NMR, 101 MHz, CDCl$_3$)



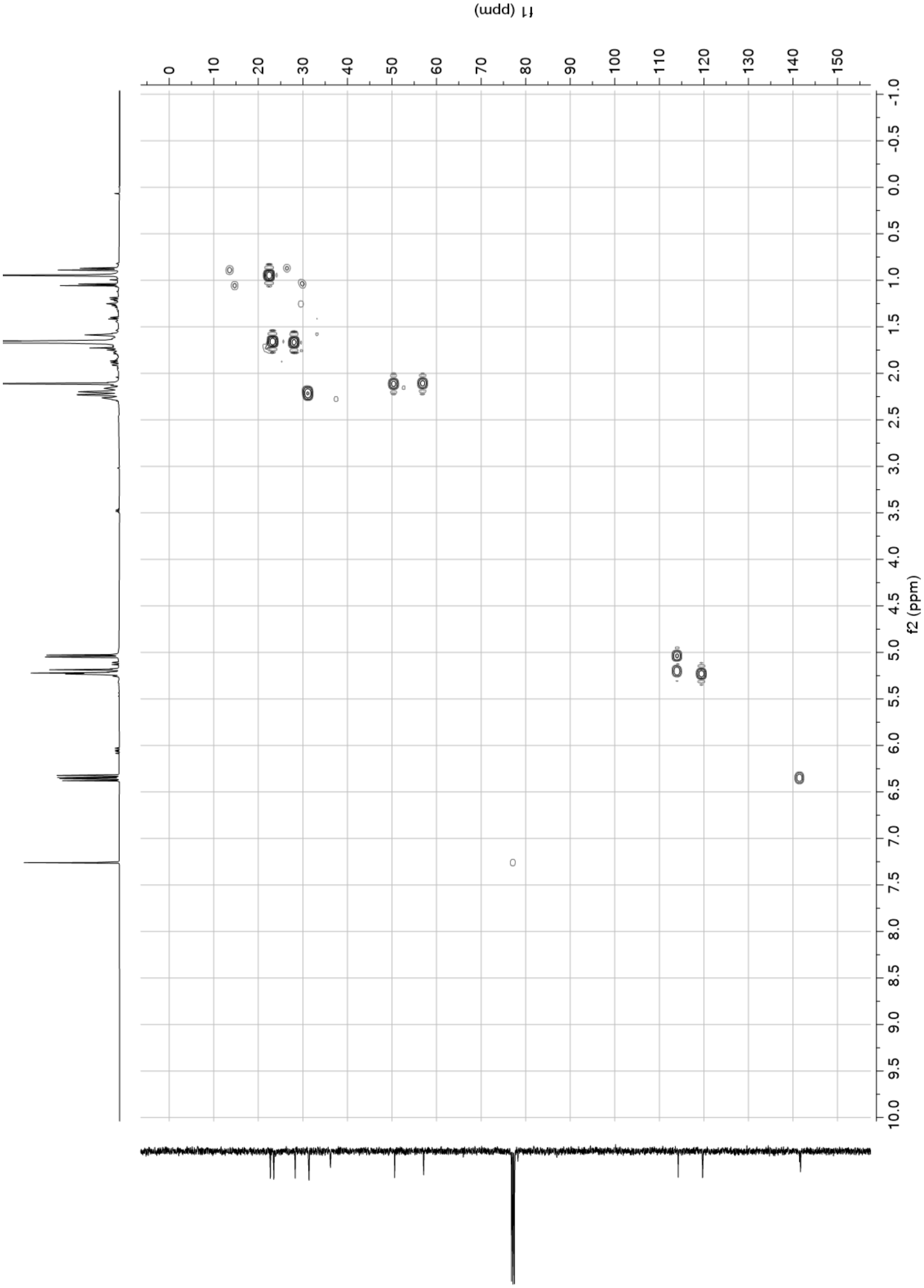
3.21.V (COSY, $CDCl_3$)



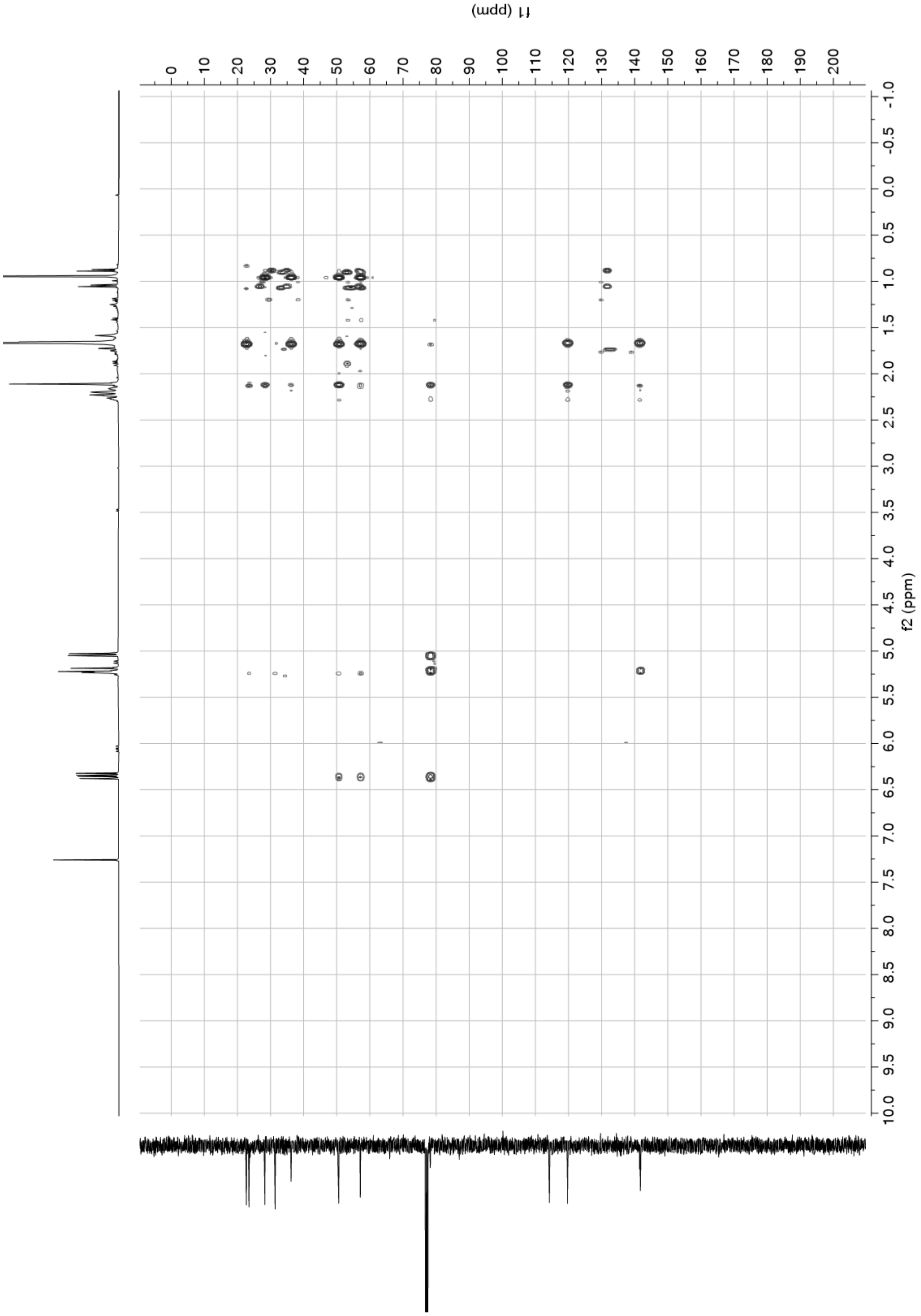
3.21.V (NOESY, $CDCl_3$)



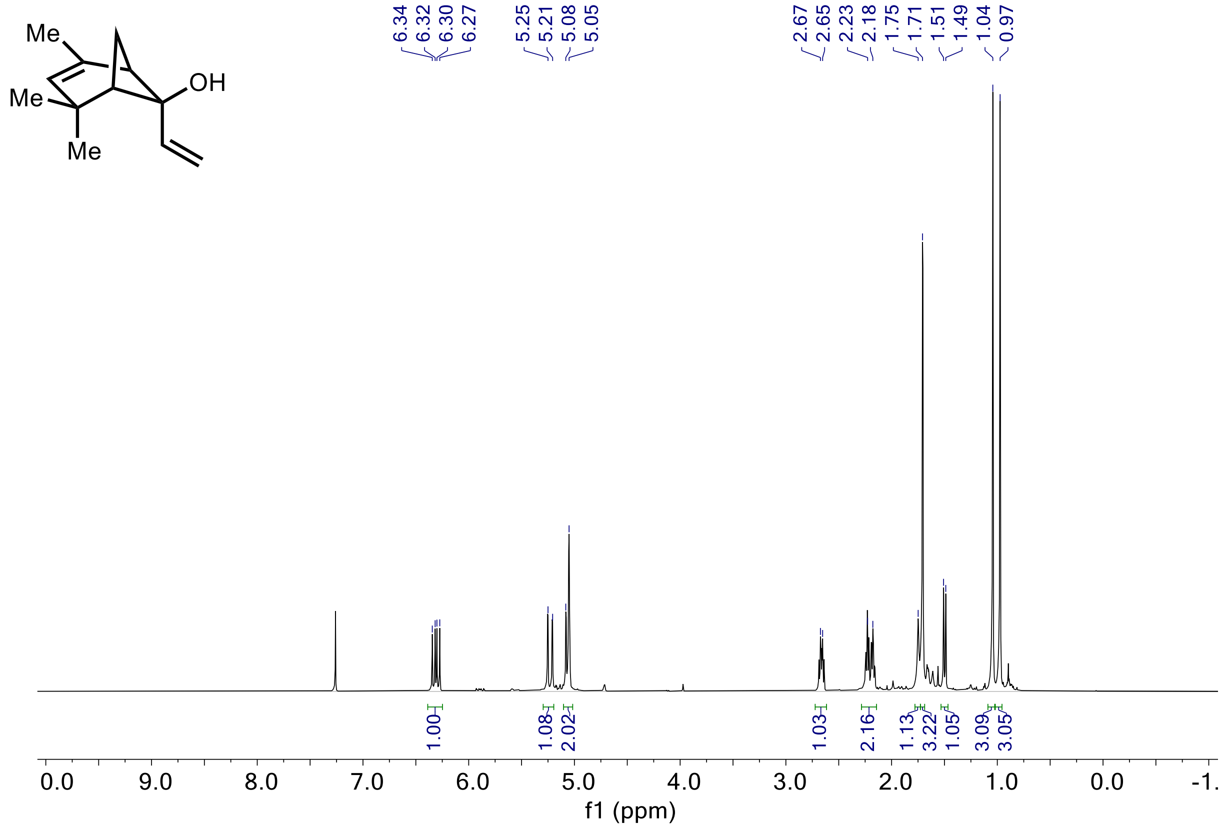
3.21.V (HSQC, $CDCl_3$)



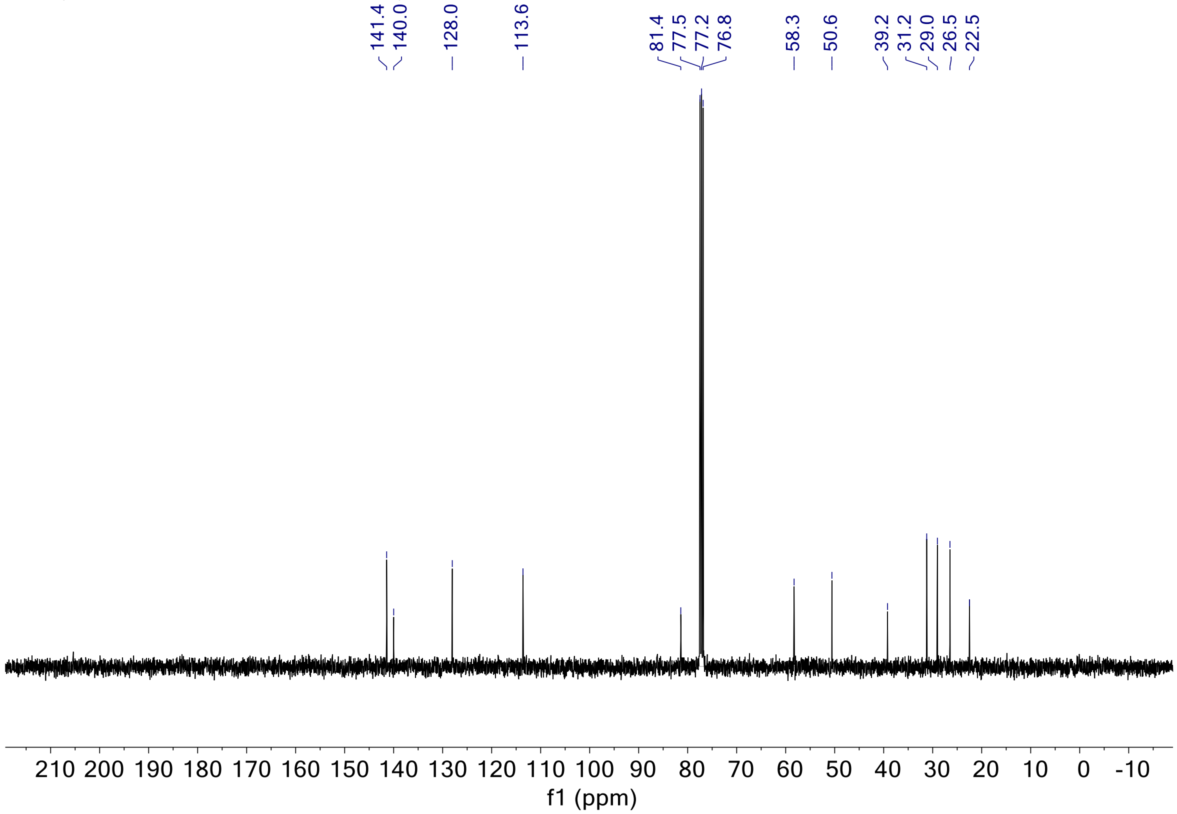
3.21.V (HMBC, $CDCl_3$)



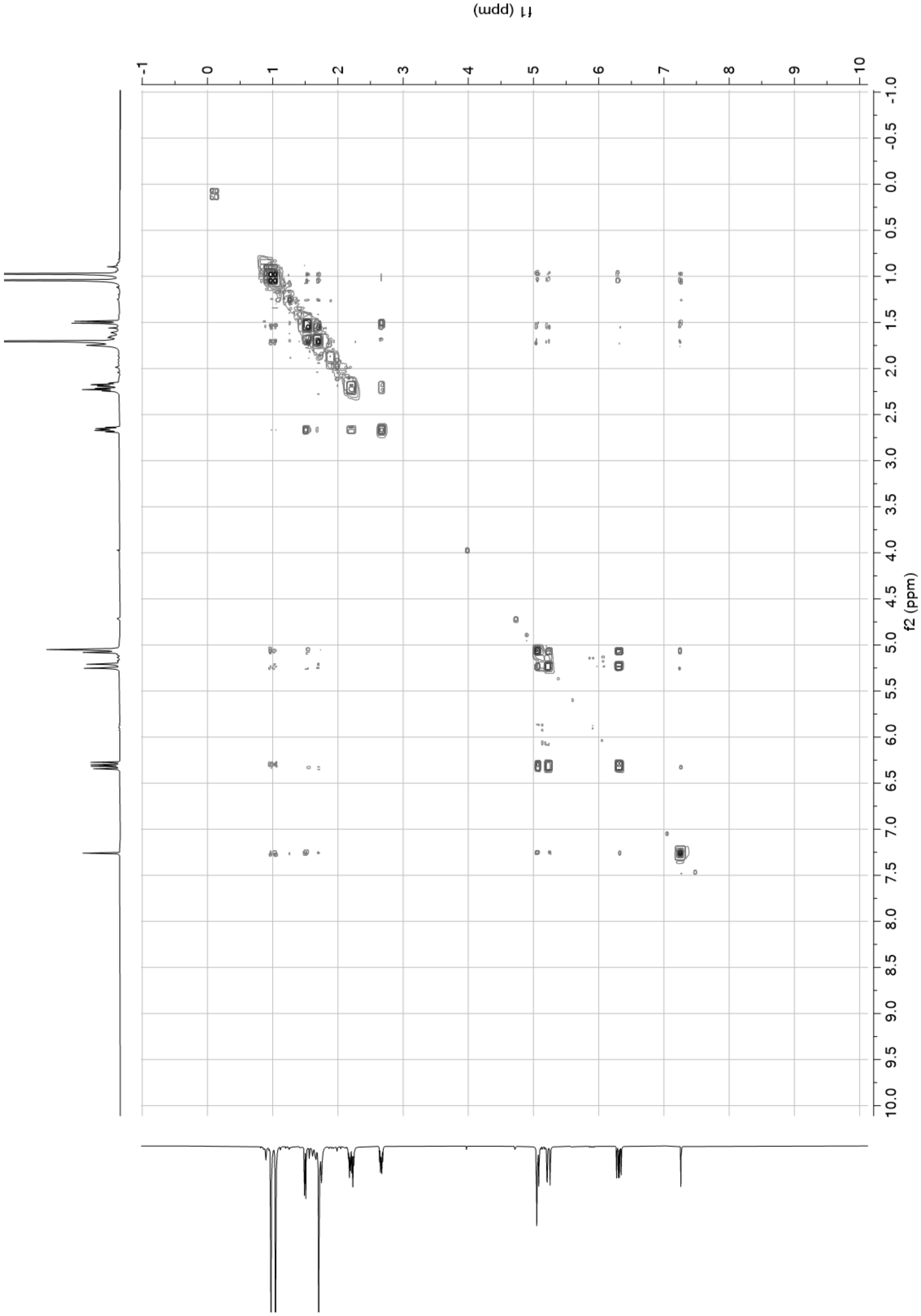
3.29.V (^{1}H NMR, 400 MHz, CDCl$_3$)



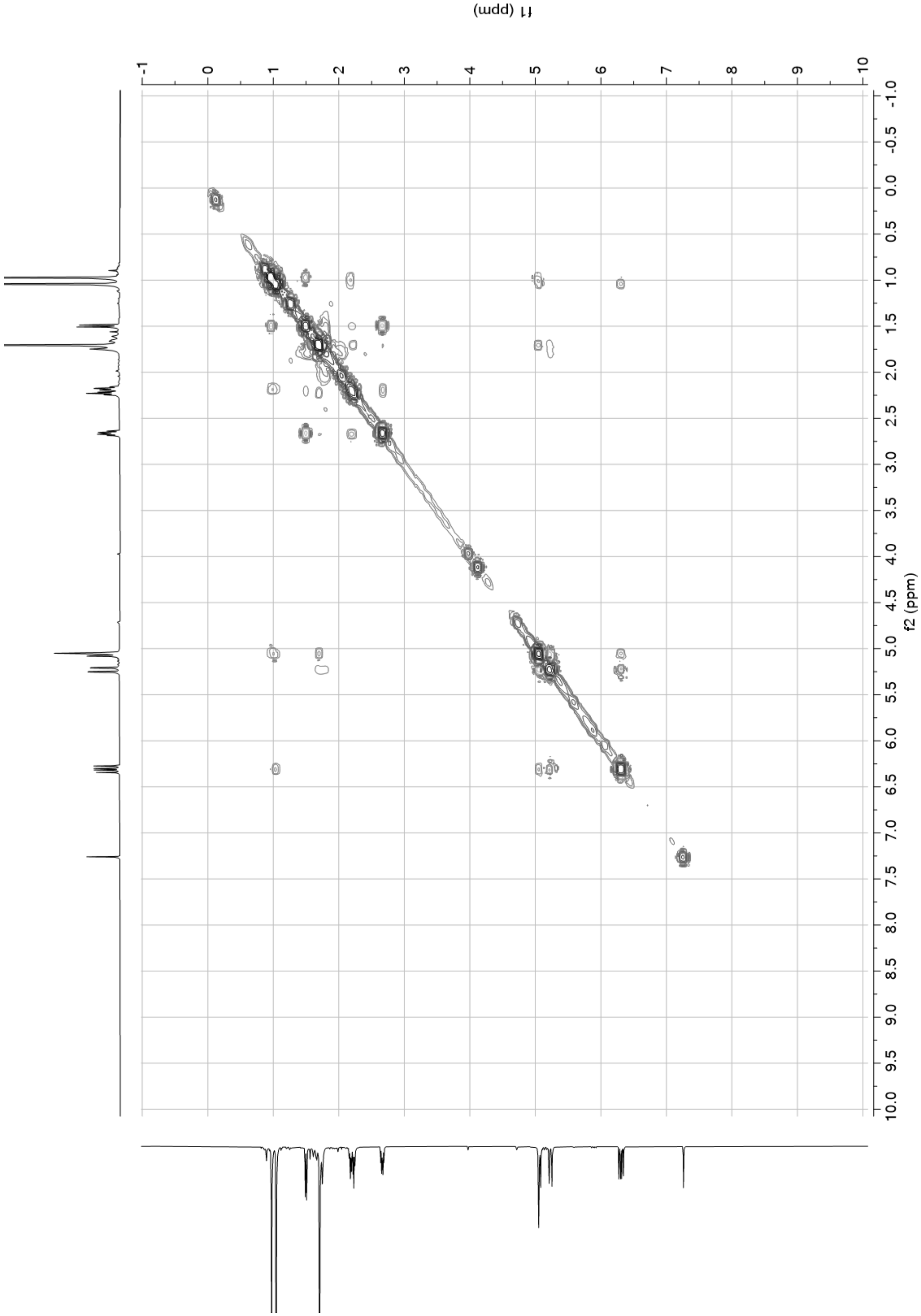
3.29.V (^{13}C NMR, 101 MHz, CDCl$_3$)



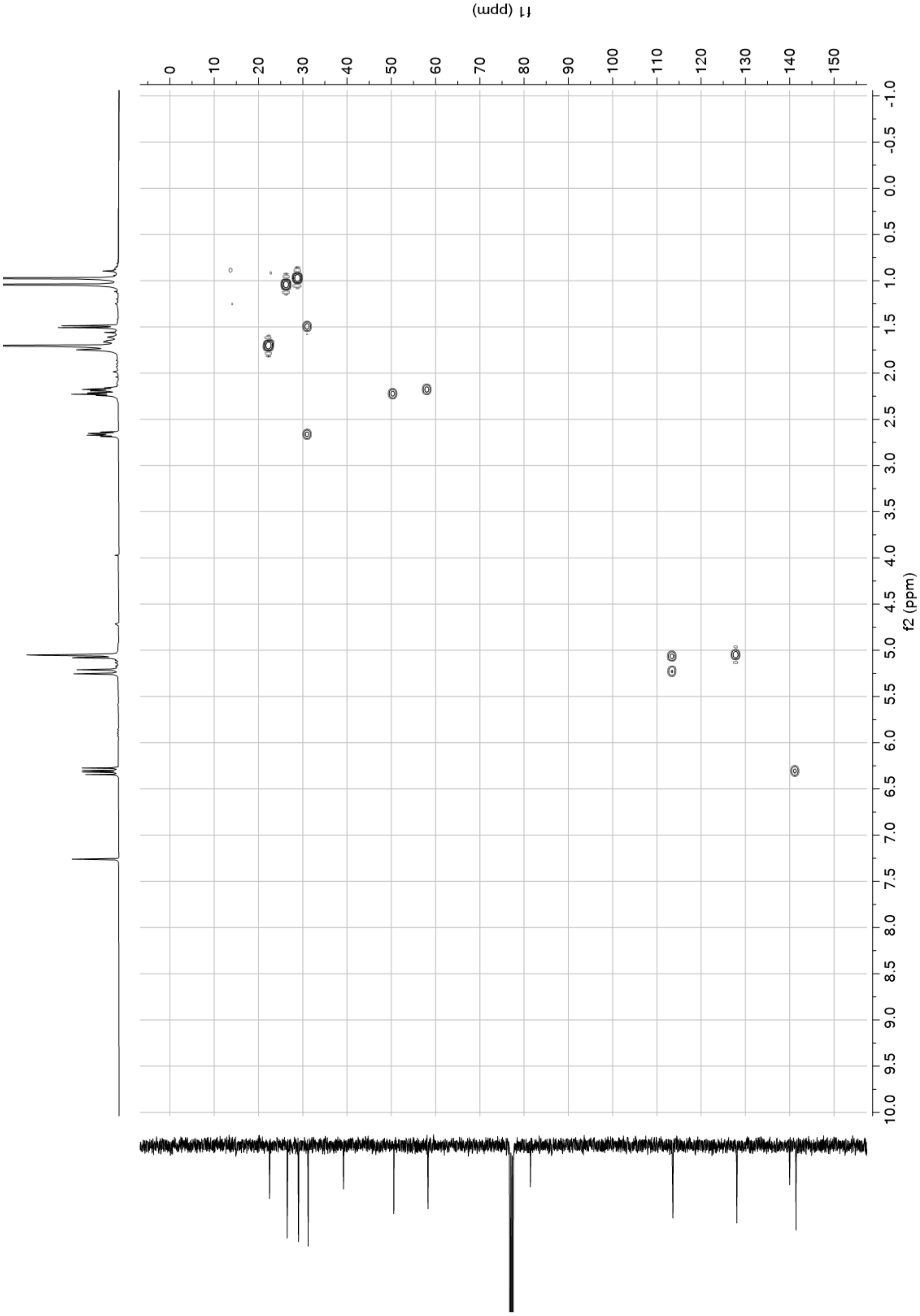
3.29.V (COSY, $CDCl_3$)



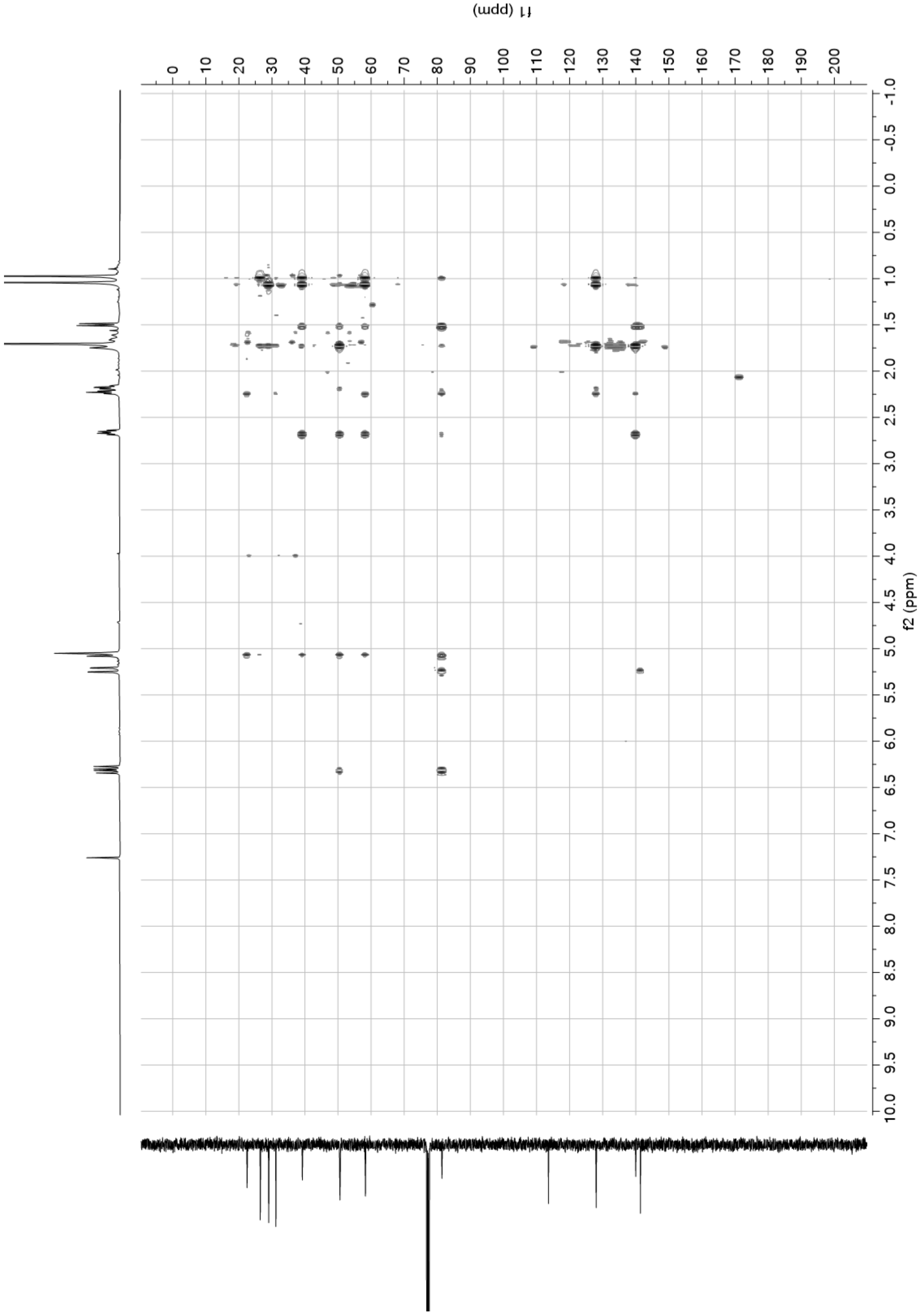
3.29.V (NOESY, $CDCl_3$)



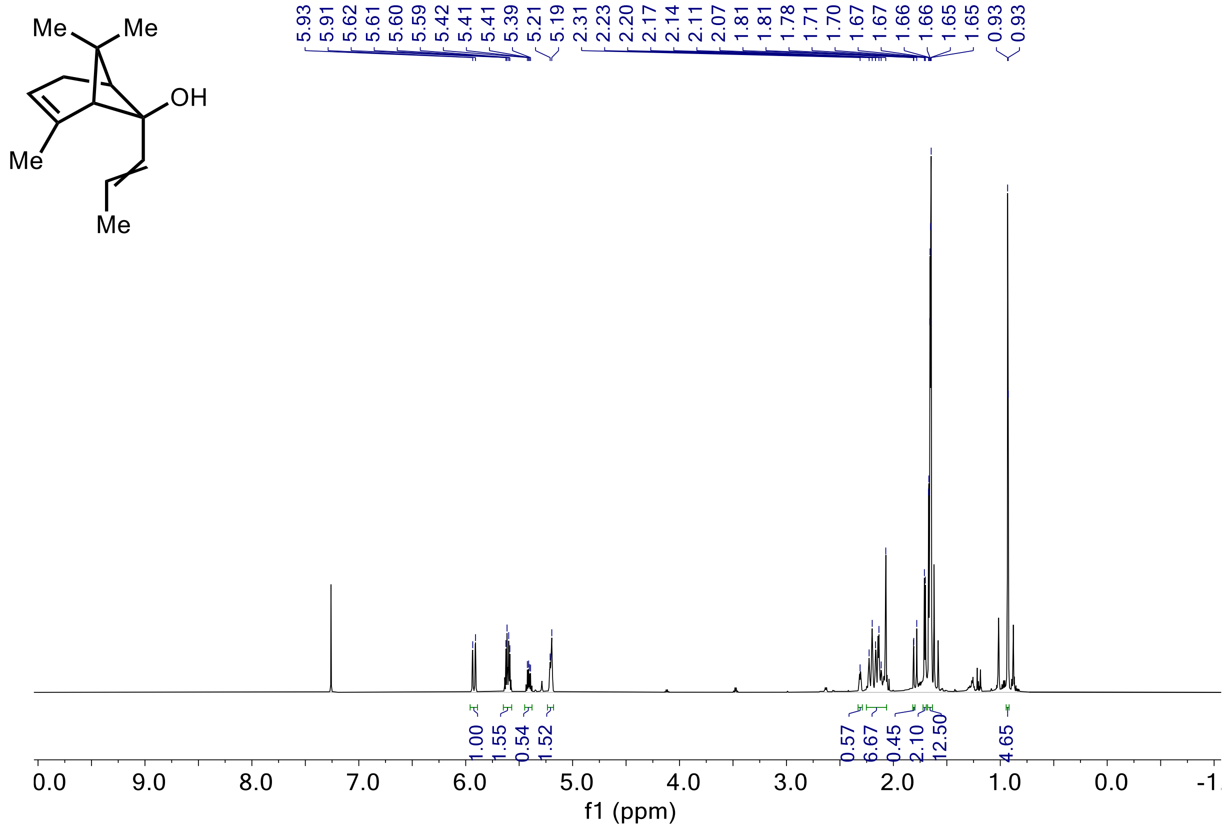
3.29.V (HSQC, $CDCl_3$)



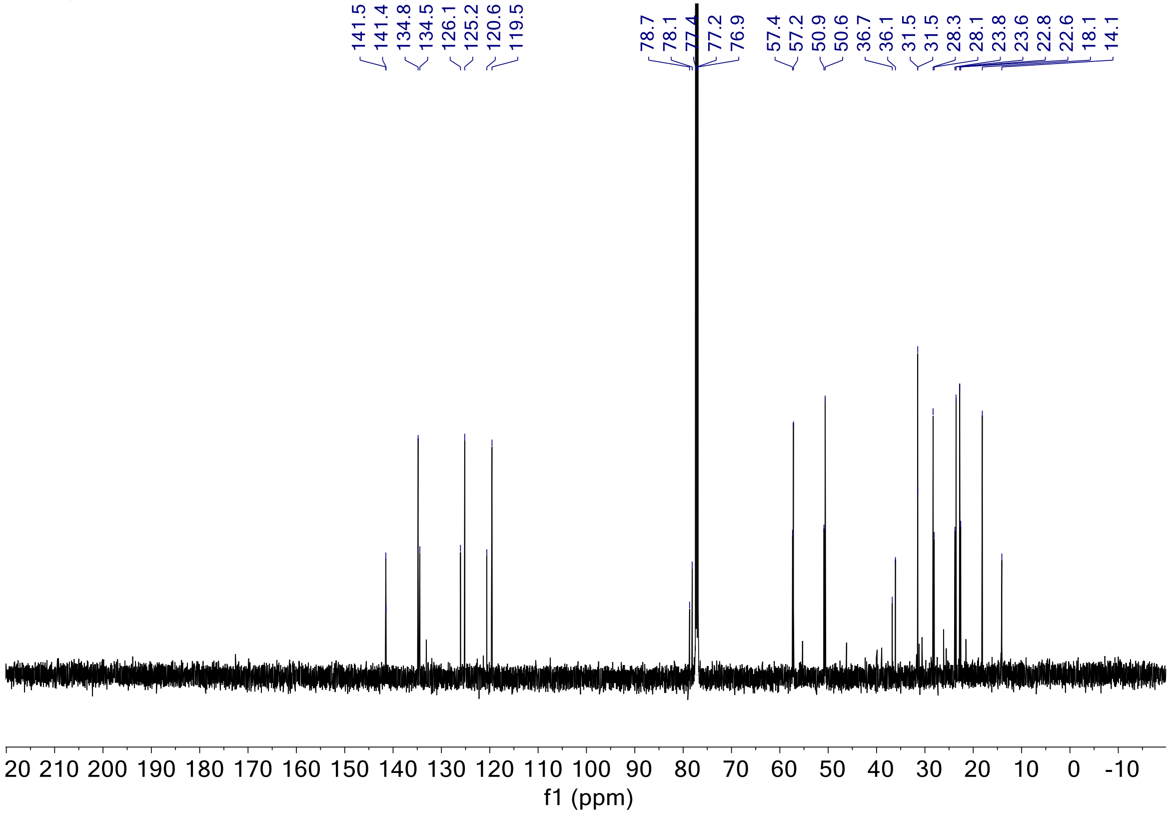
3.29.V (HMBC, CDCl$_3$)



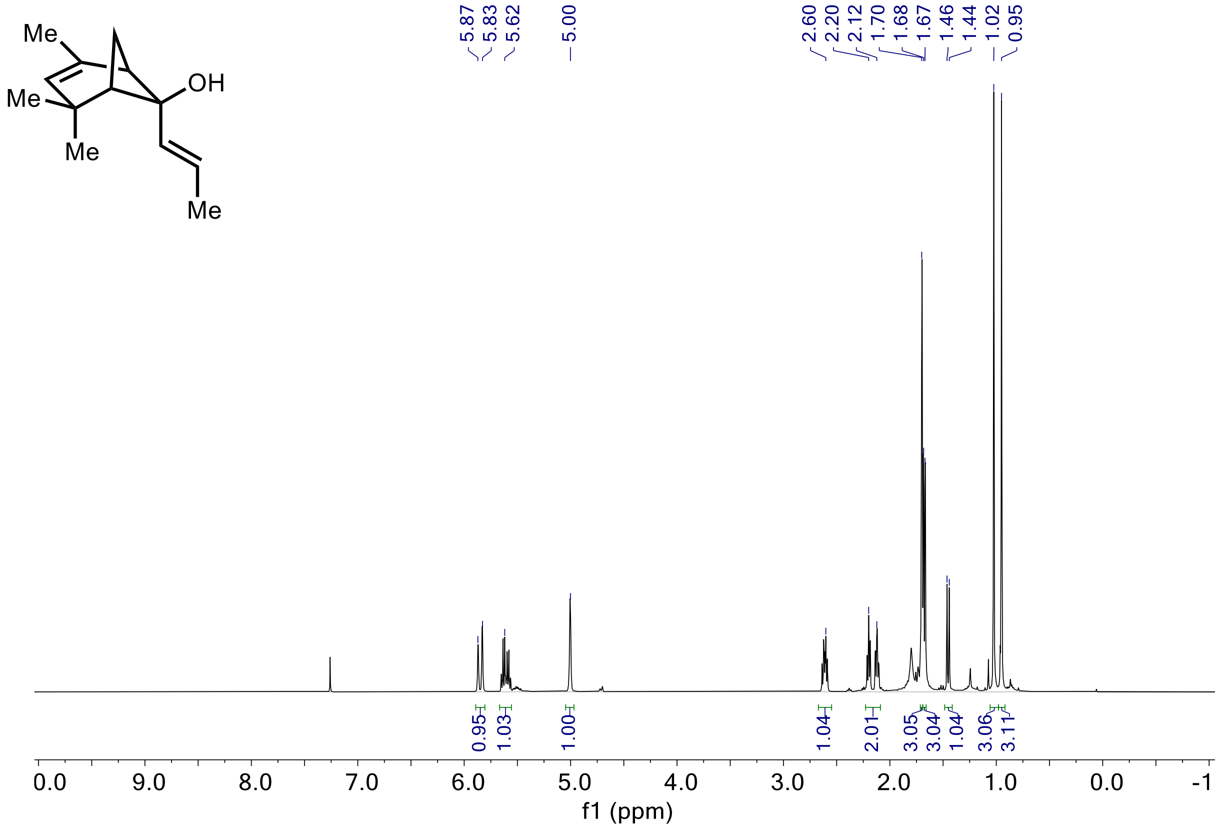
3.21.Pr (^{1}H NMR, 600 MHz, CDCl$_3$)



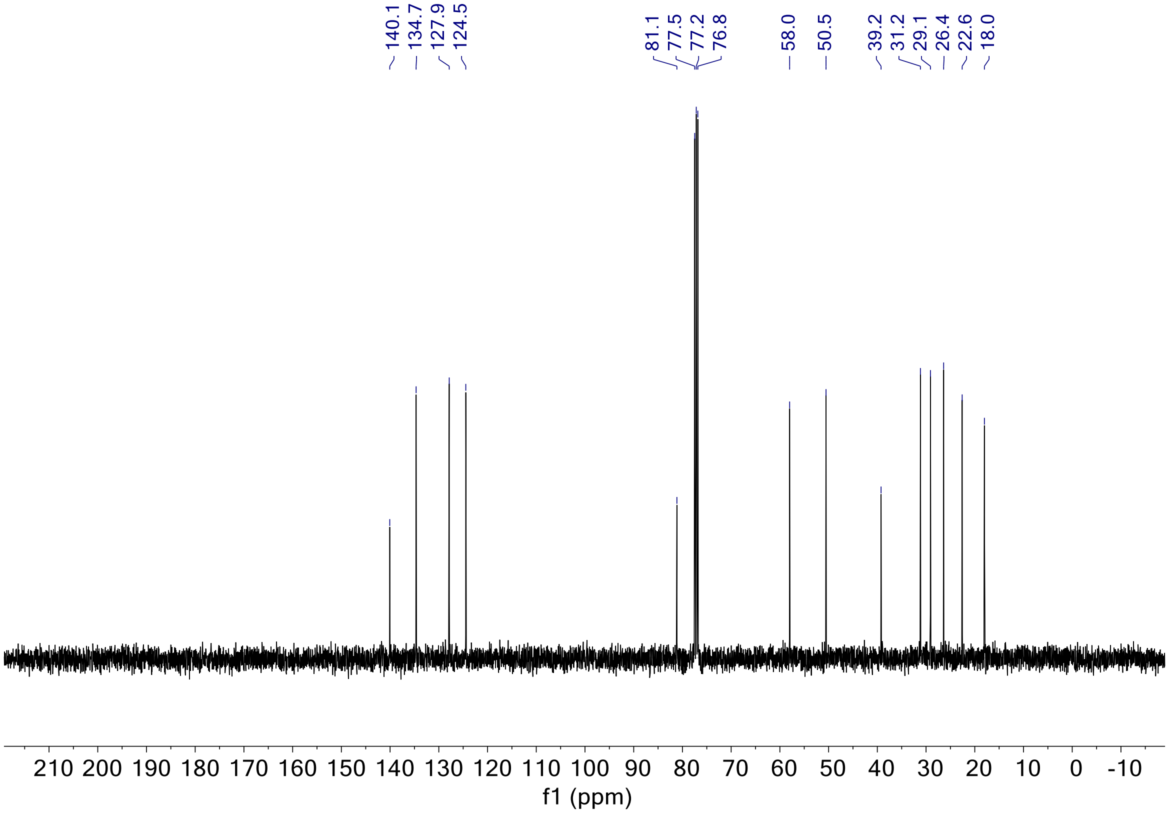
3.21.Pr (^{13}C NMR, 151 MHz, CDCl$_3$)



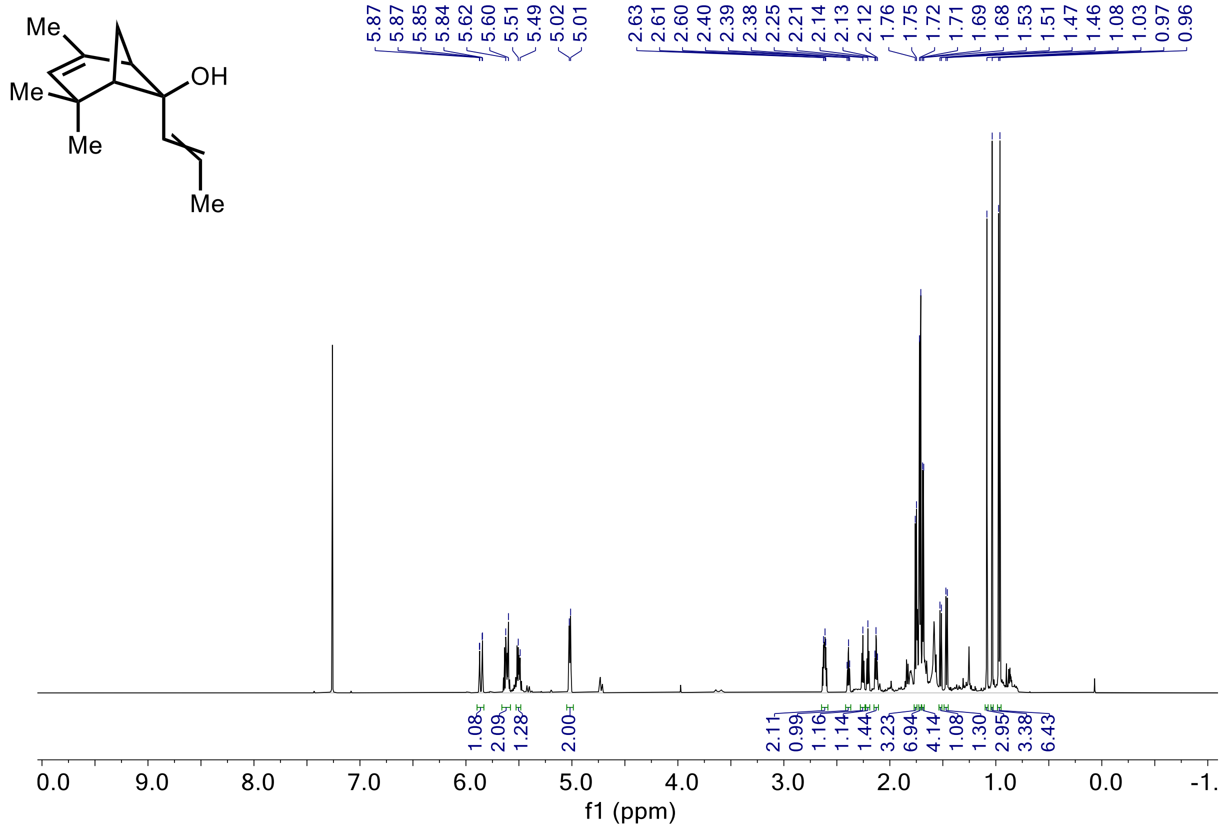
3.29.Pr-*E* isomer (^{1}H NMR, 400 MHz, CDCl$_3$)



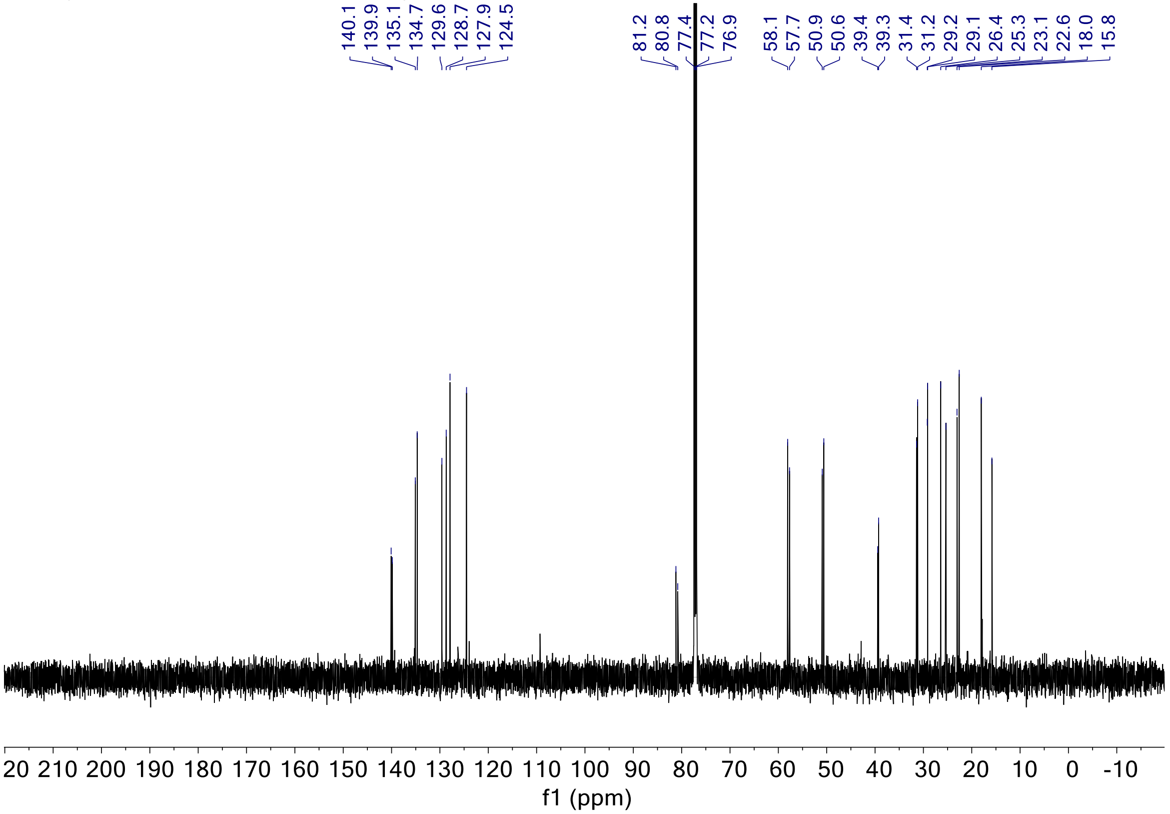
3.29.Pr-*E* isomer (^{13}C NMR, 101 MHz, CDCl$_3$)



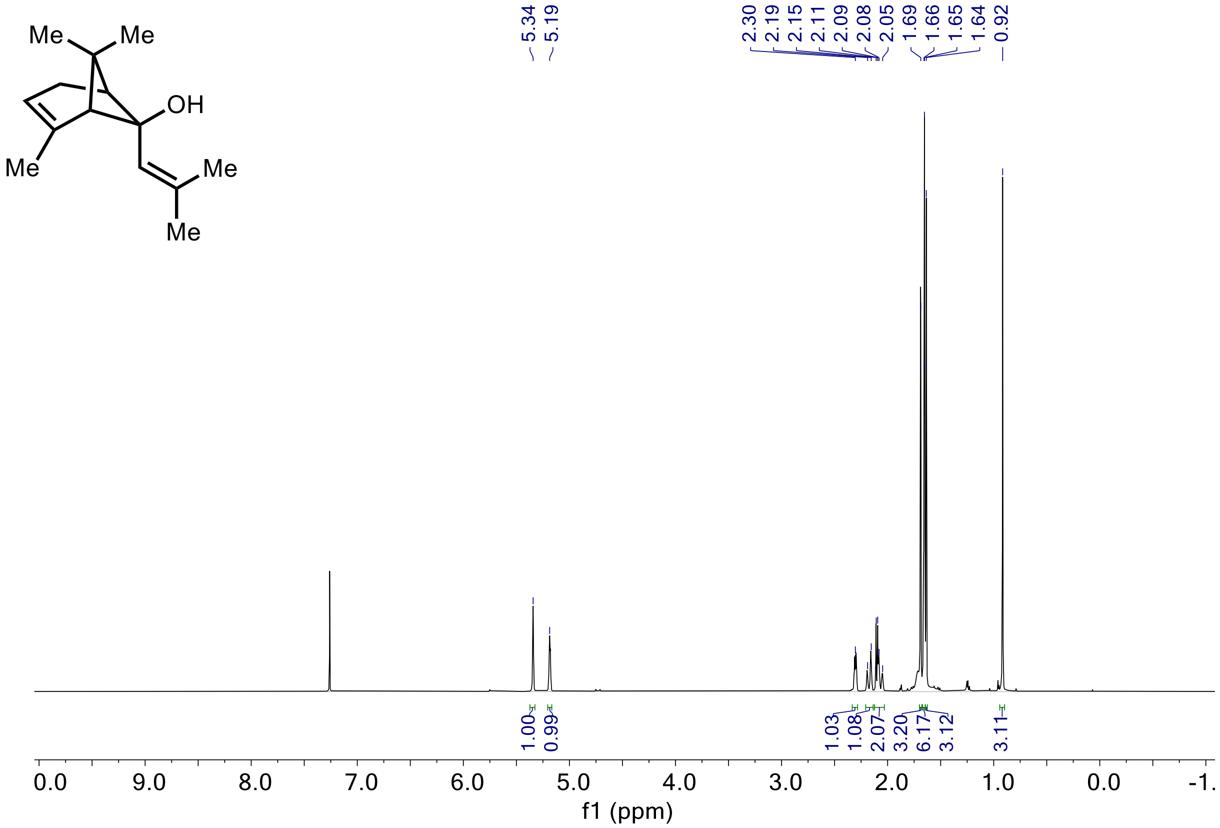
3.29.Pr (^{1}H NMR, 600 MHz, CDCl$_3$)



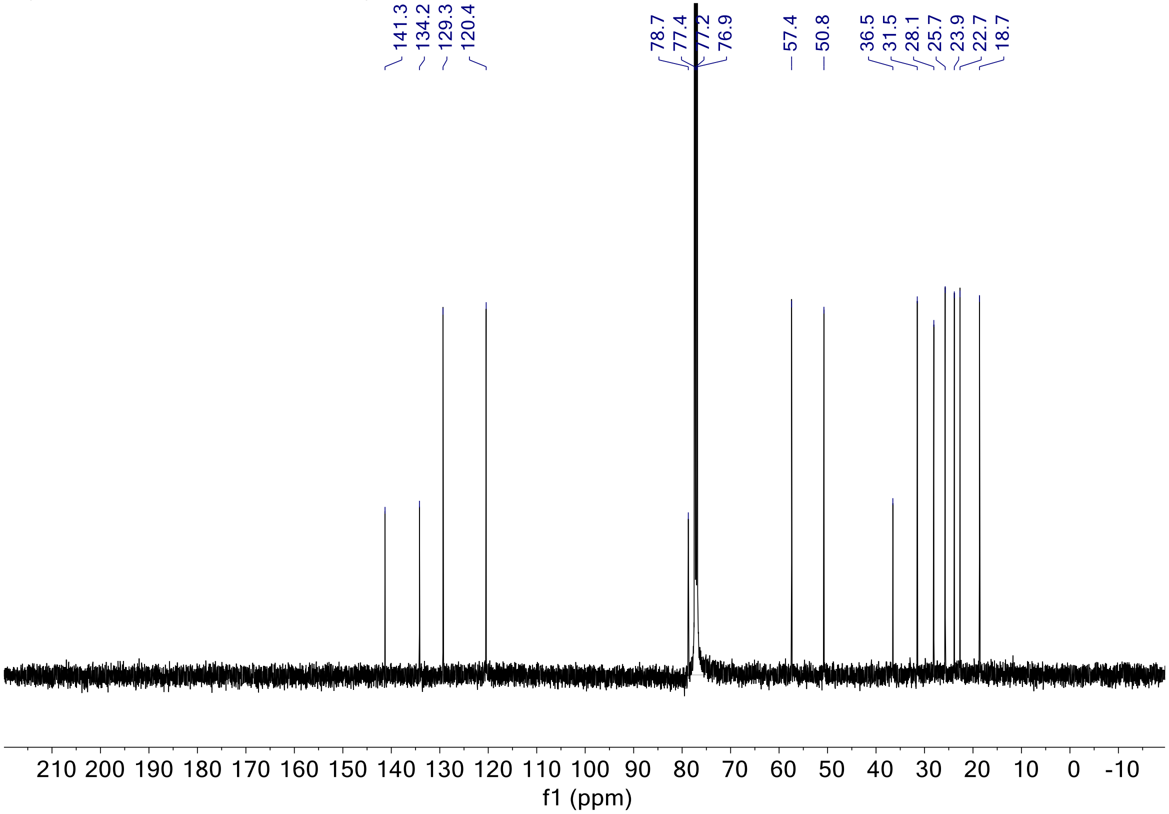
3.29.Pr (^{13}C NMR, 151 MHz, CDCl$_3$)



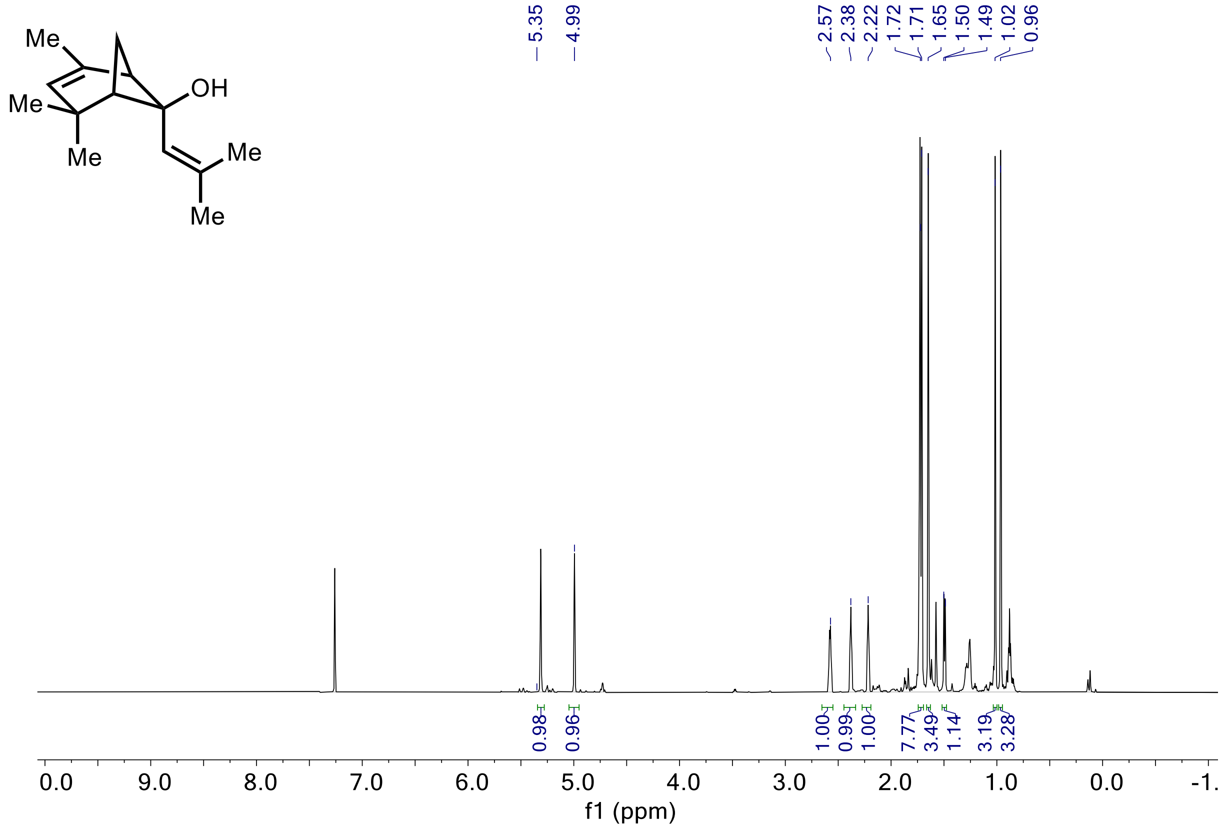
3.S1 (^{1}H NMR, 500 MHz, CDCl$_3$)



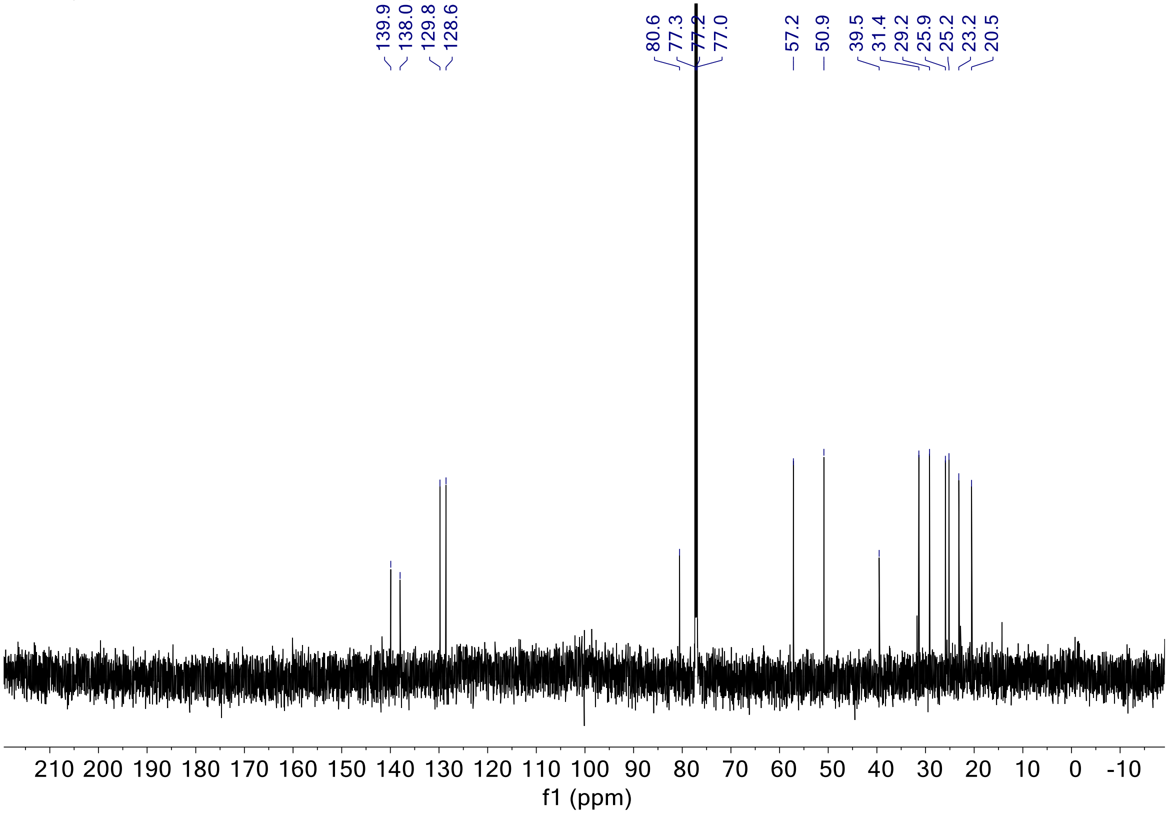
3.S1 (^{13}C NMR, 126 MHz, CDCl$_3$)



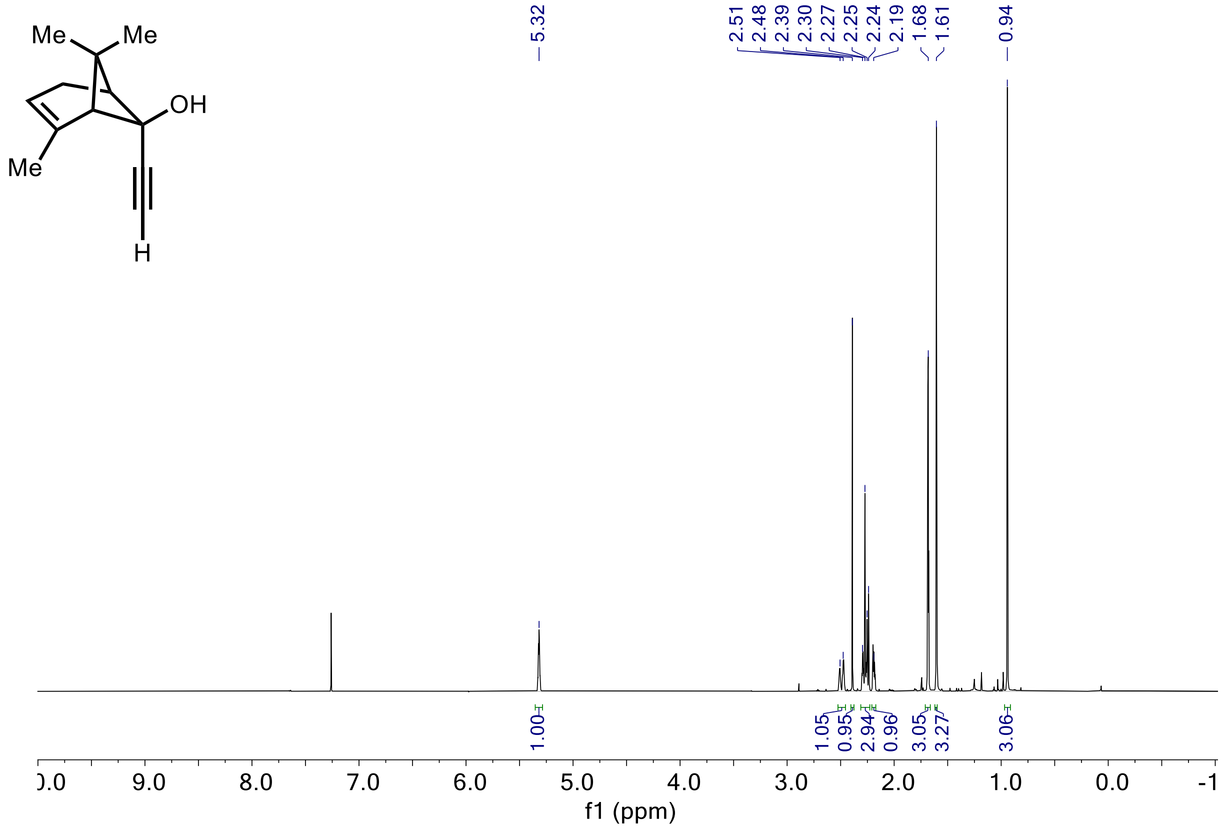
3.S2 (^{1}H NMR, 700 MHz, CDCl$_3$)



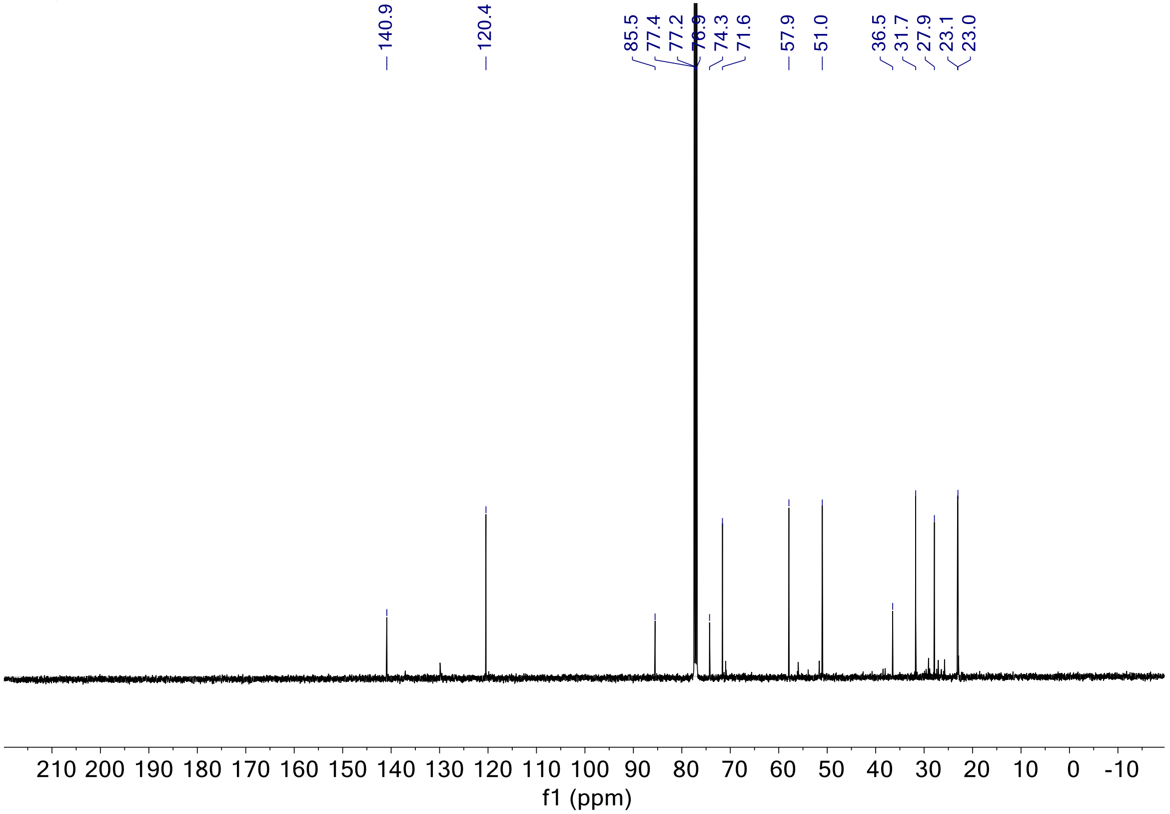
3.S2 (^{13}C NMR, 176 MHz, CDCl$_3$)



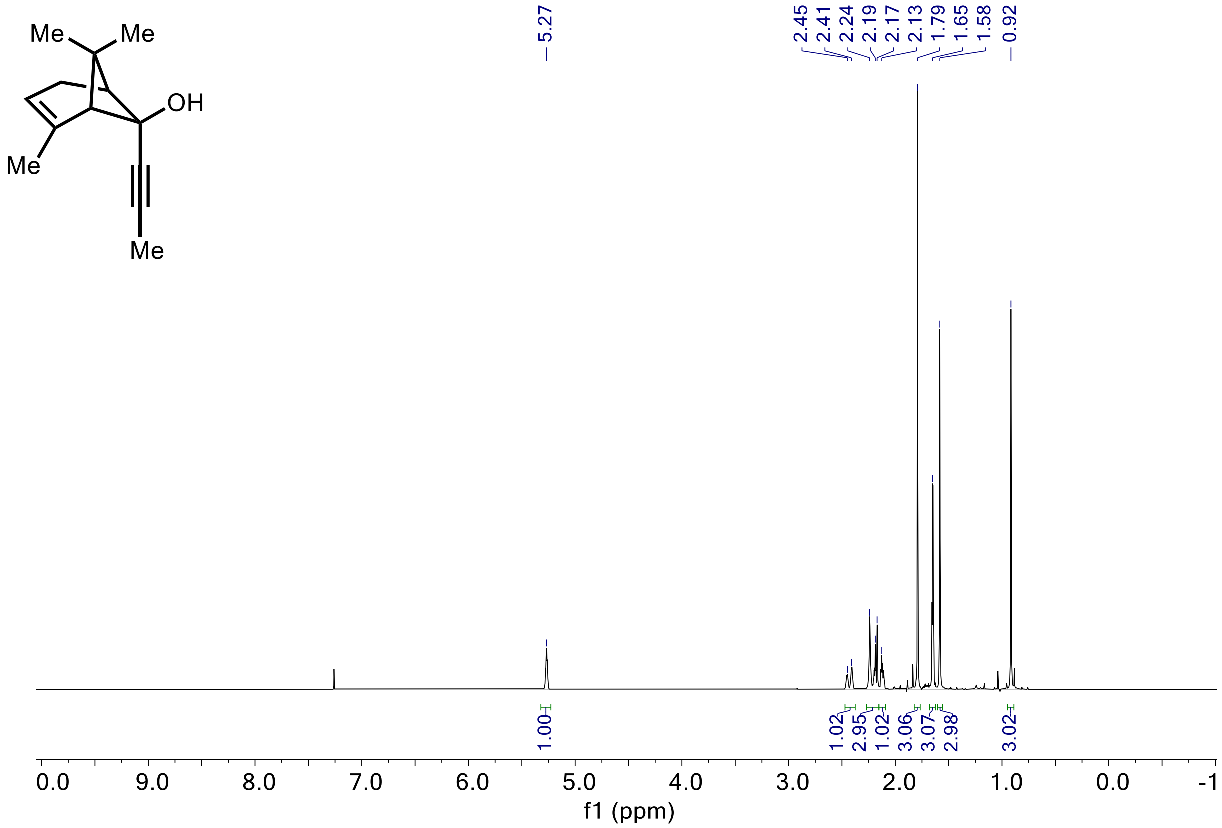
3.21.E (^{1}H NMR, 500 MHz, CDCl$_3$)



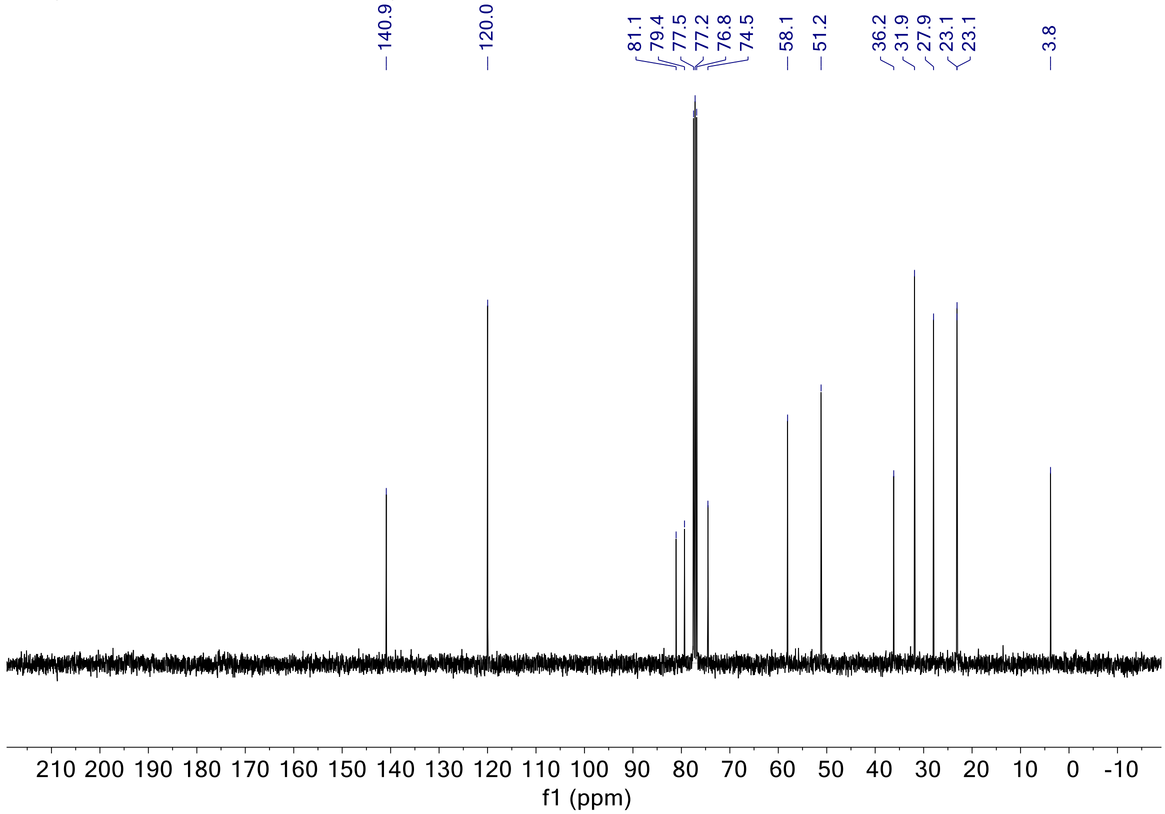
3.21.E (^{13}C NMR, 126 MHz, CDCl$_3$)



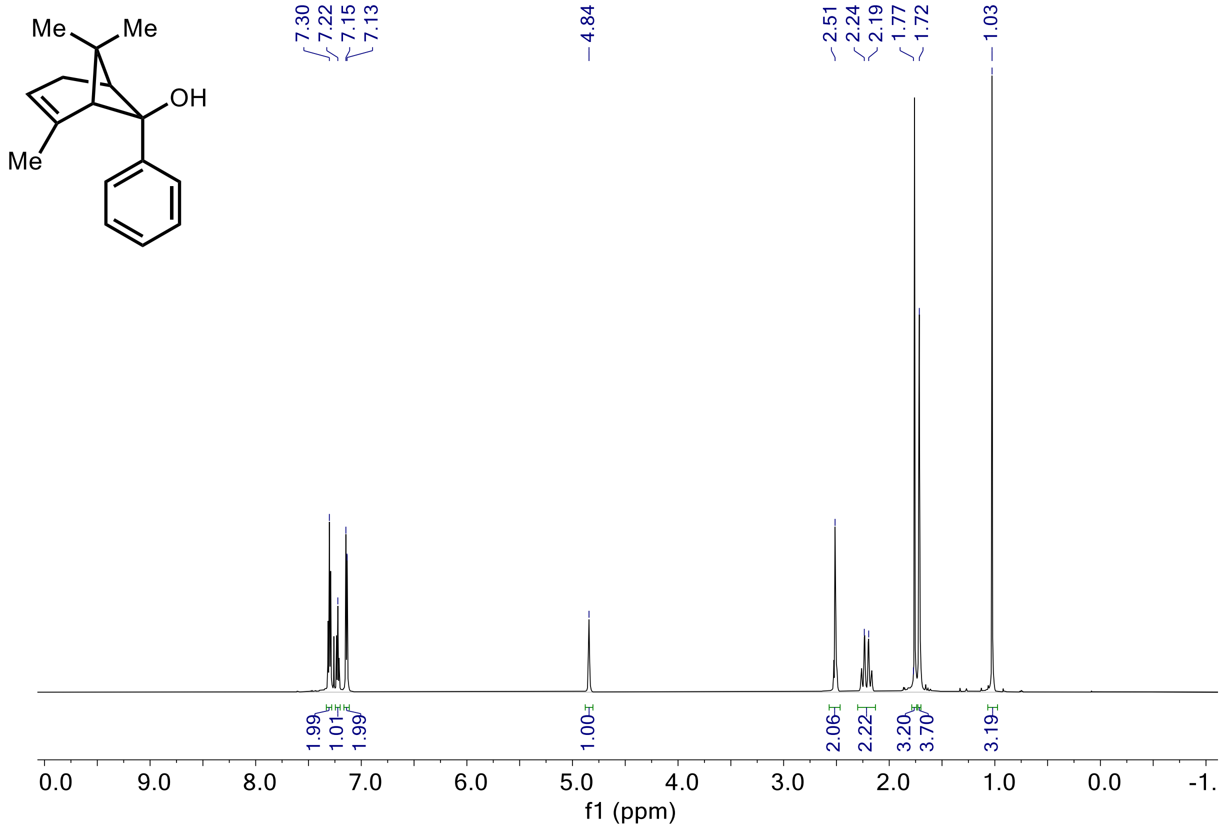
3.21.P (^{1}H NMR, 400 MHz, CDCl$_3$)



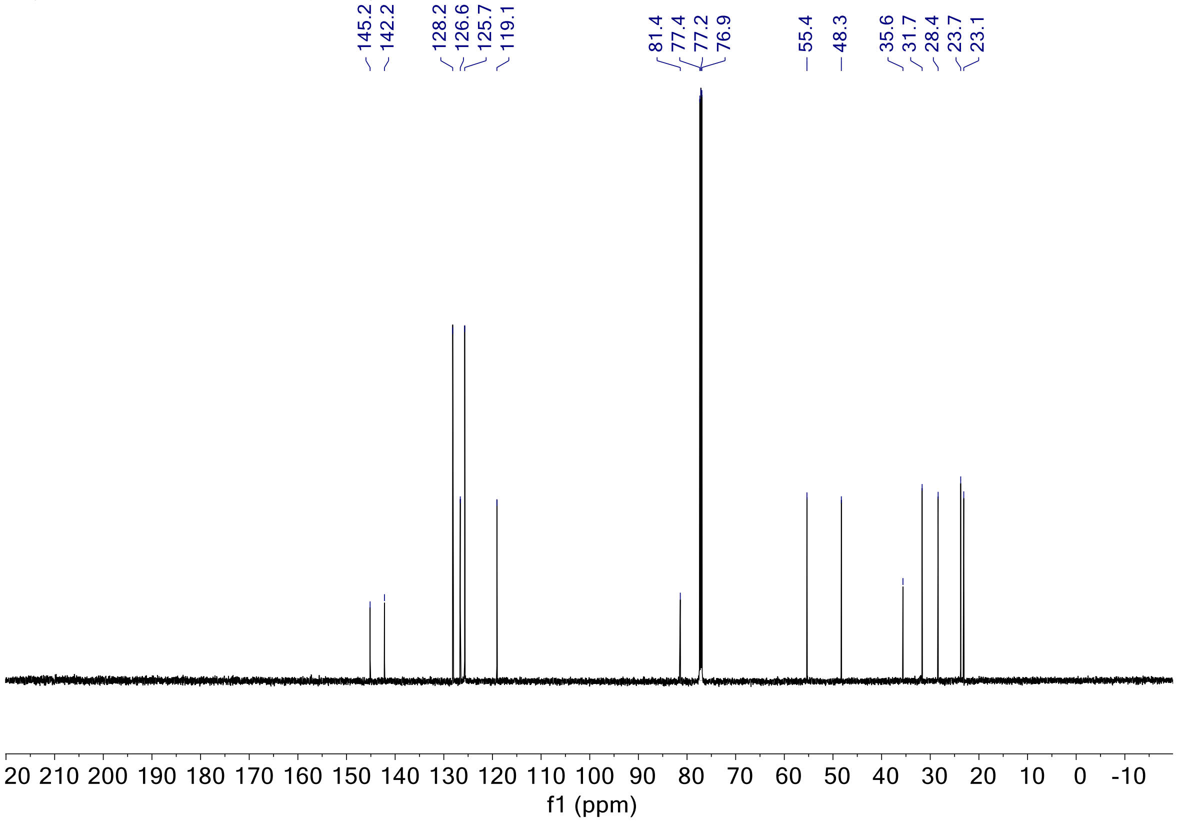
3.21.P (^{13}C NMR, 101 MHz, CDCl$_3$)



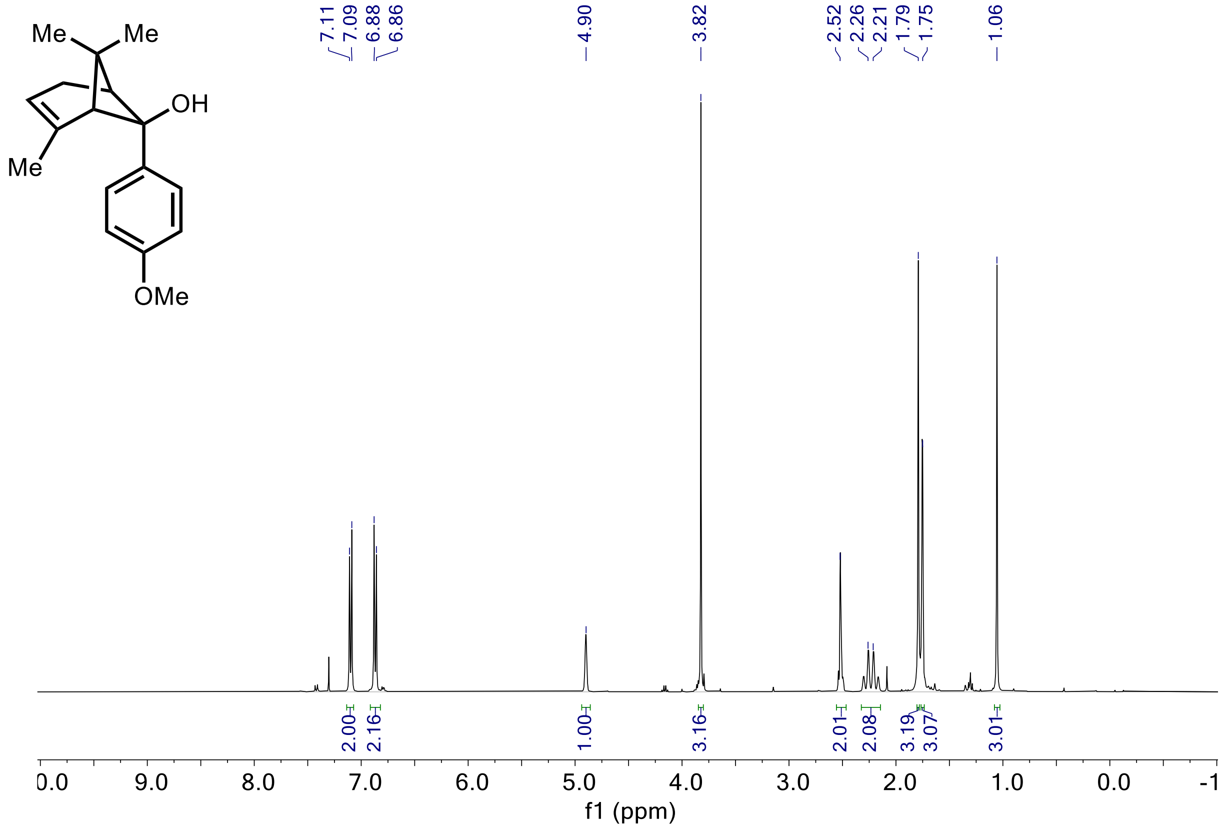
3.S3 (^{1}H NMR, 600 MHz, CDCl$_3$)



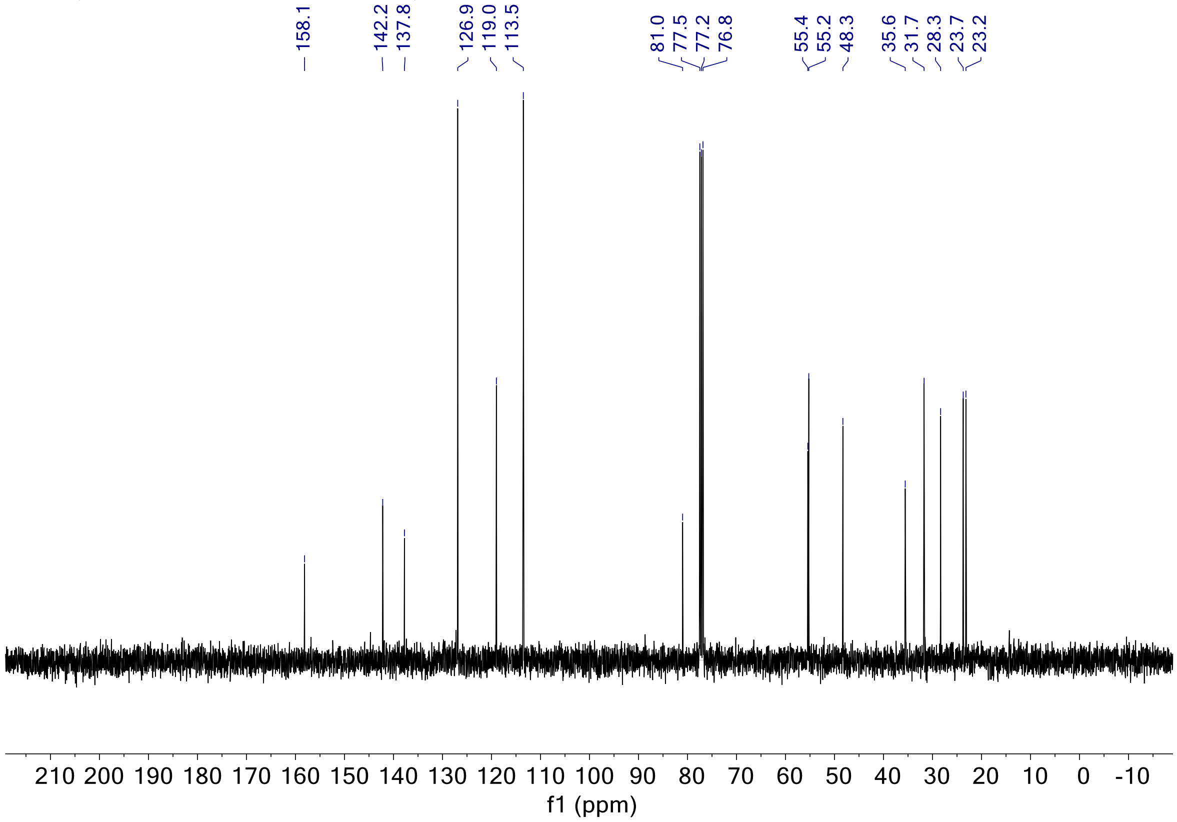
3.S3 (^{13}C NMR, 151 MHz, CDCl$_3$)



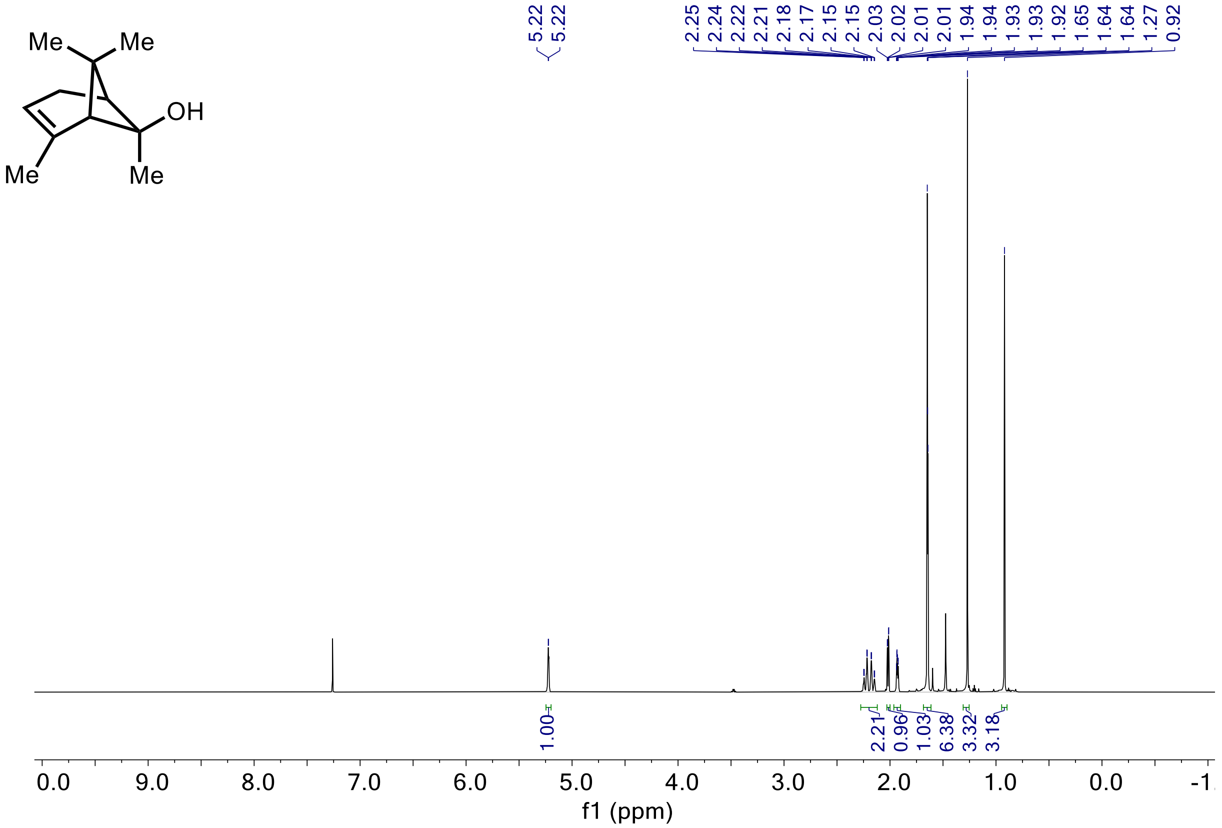
3.21.Ph (^{1}H NMR, 400 MHz, $CDCl_3$)



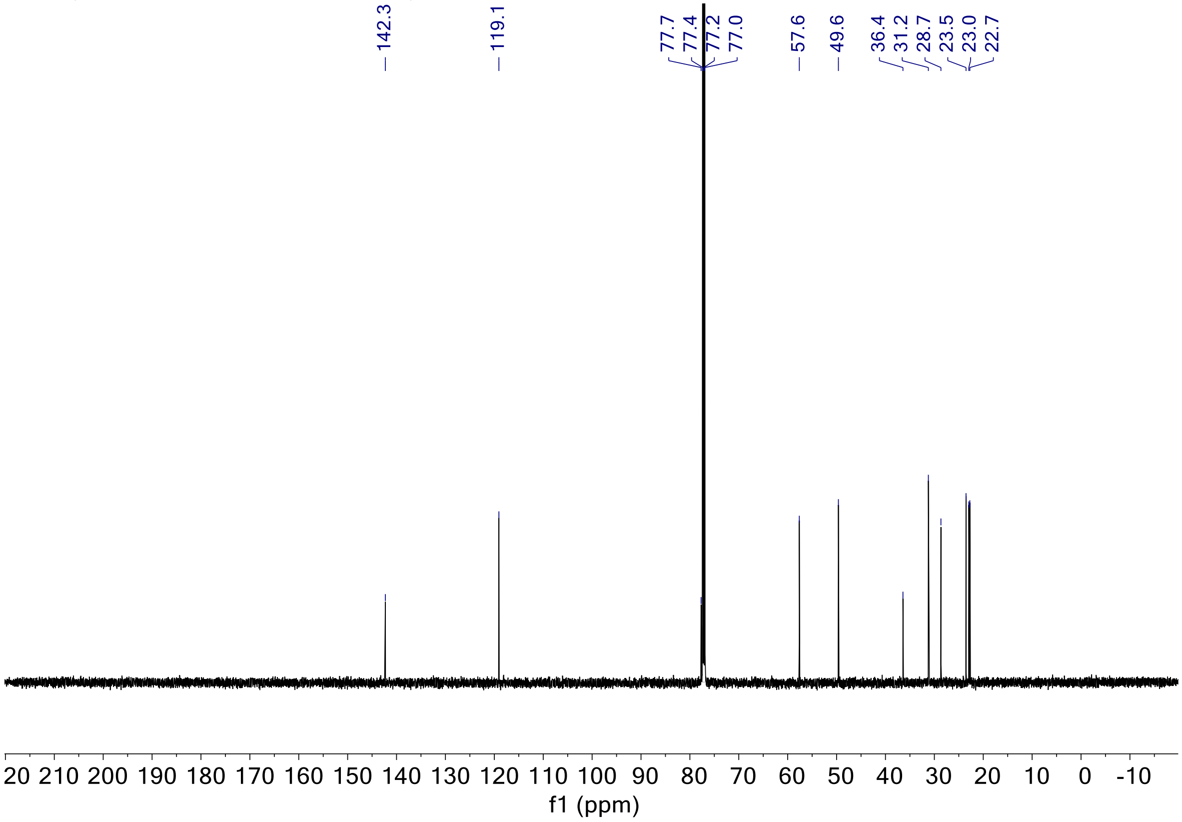
3.21.Ph (^{13}C NMR, 101 MHz, $CDCl_3$)



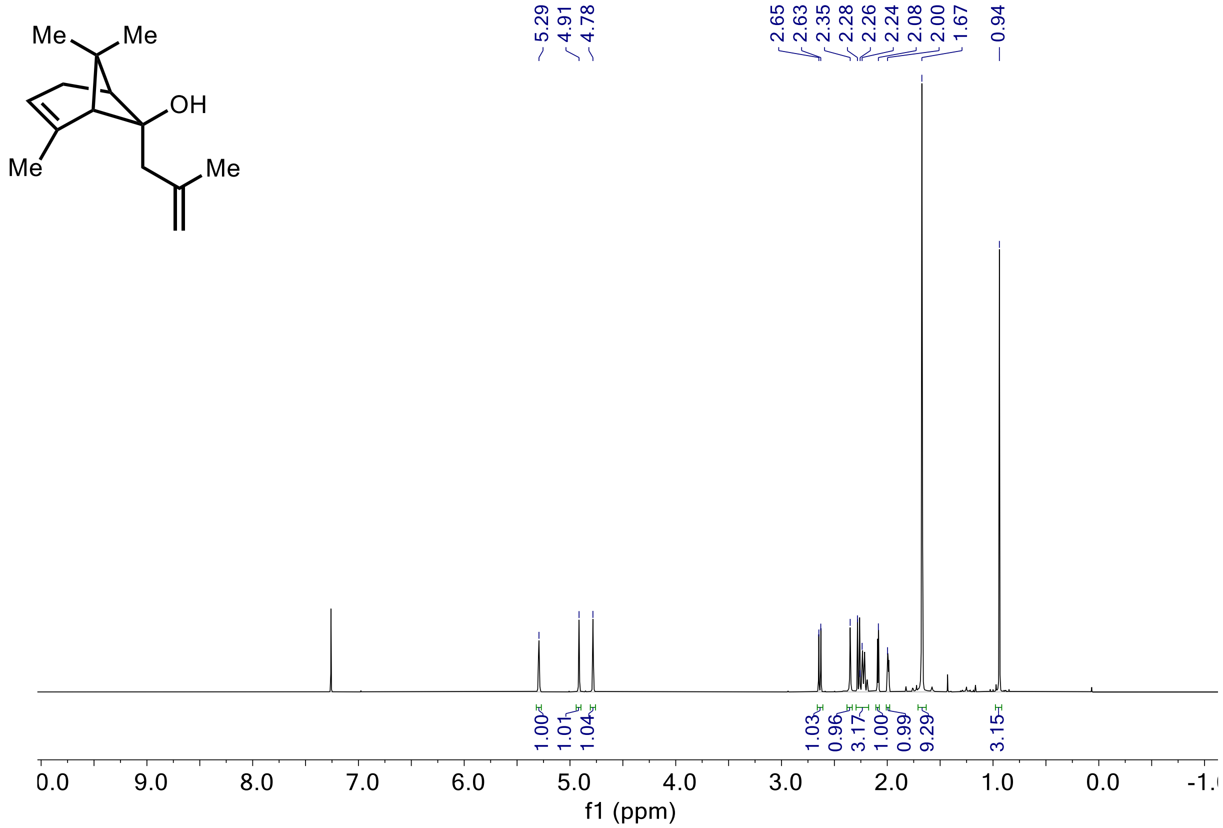
3.21.M (^{1}H NMR, 600 MHz, CDCl$_3$)



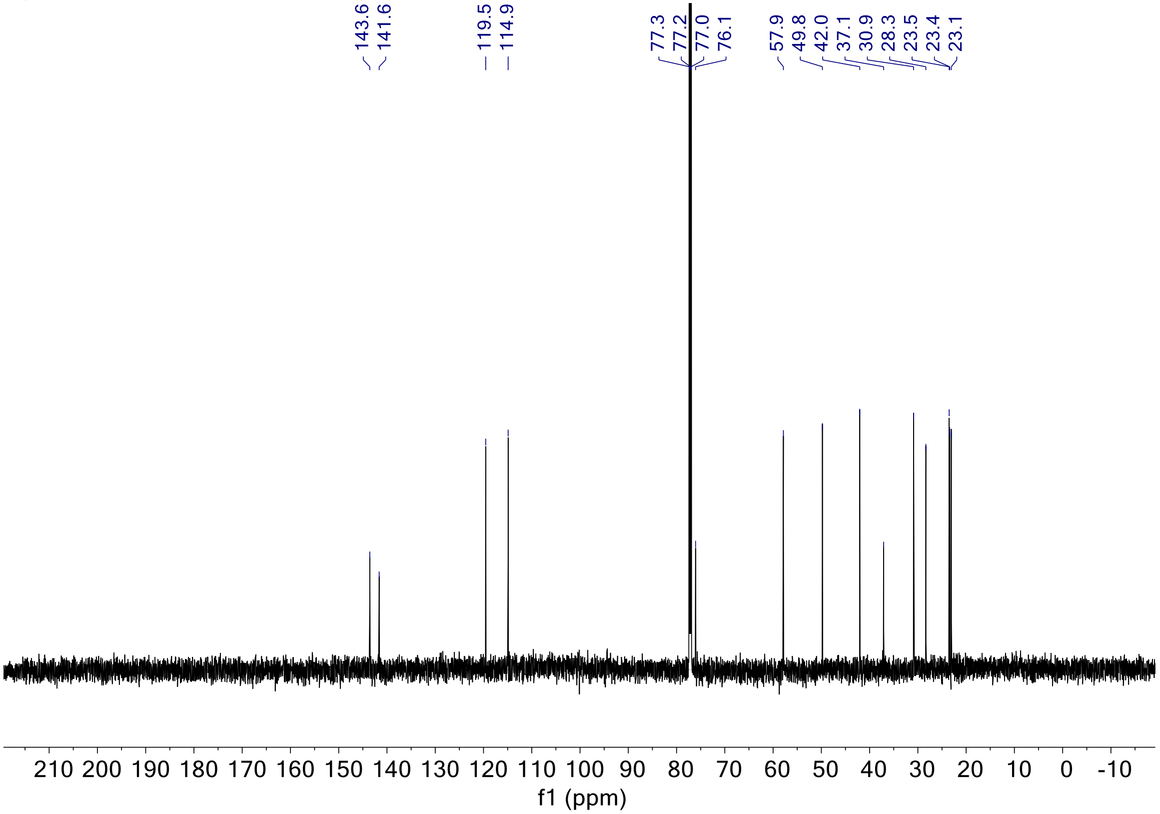
3.21.M (^{13}C NMR, 151 MHz, CDCl$_3$)



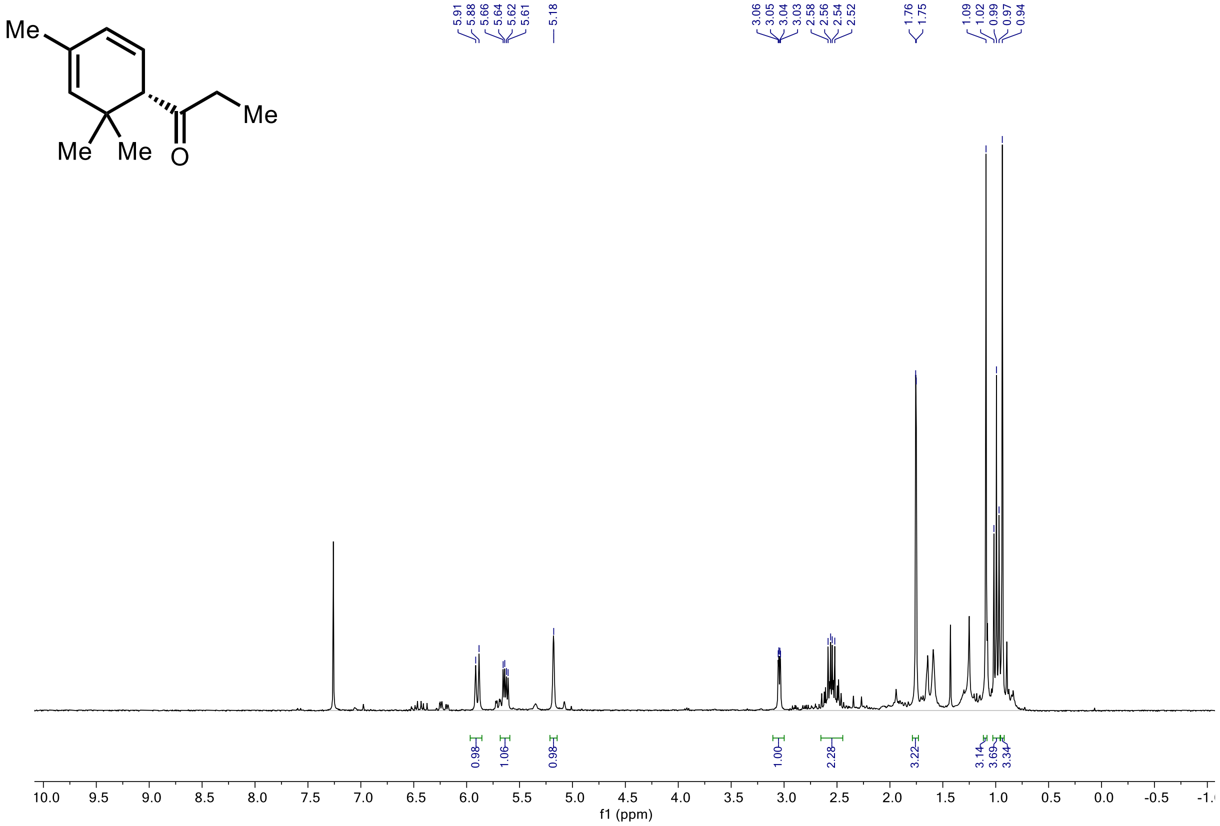
3.S4 (^{1}H NMR, 700 MHz, CDCl$_3$)



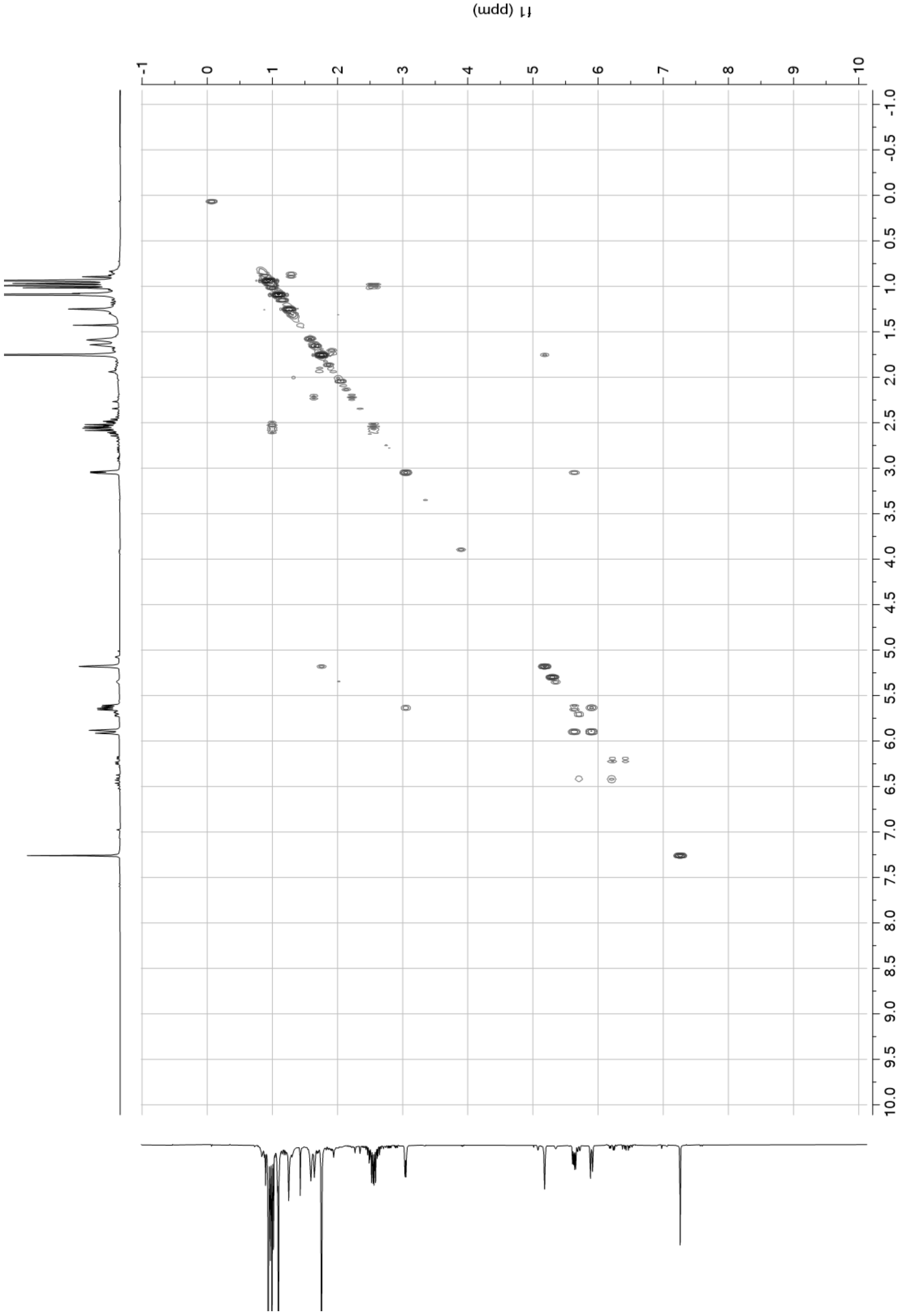
3.S4 (^{13}C NMR, 176 MHz, CDCl$_3$)



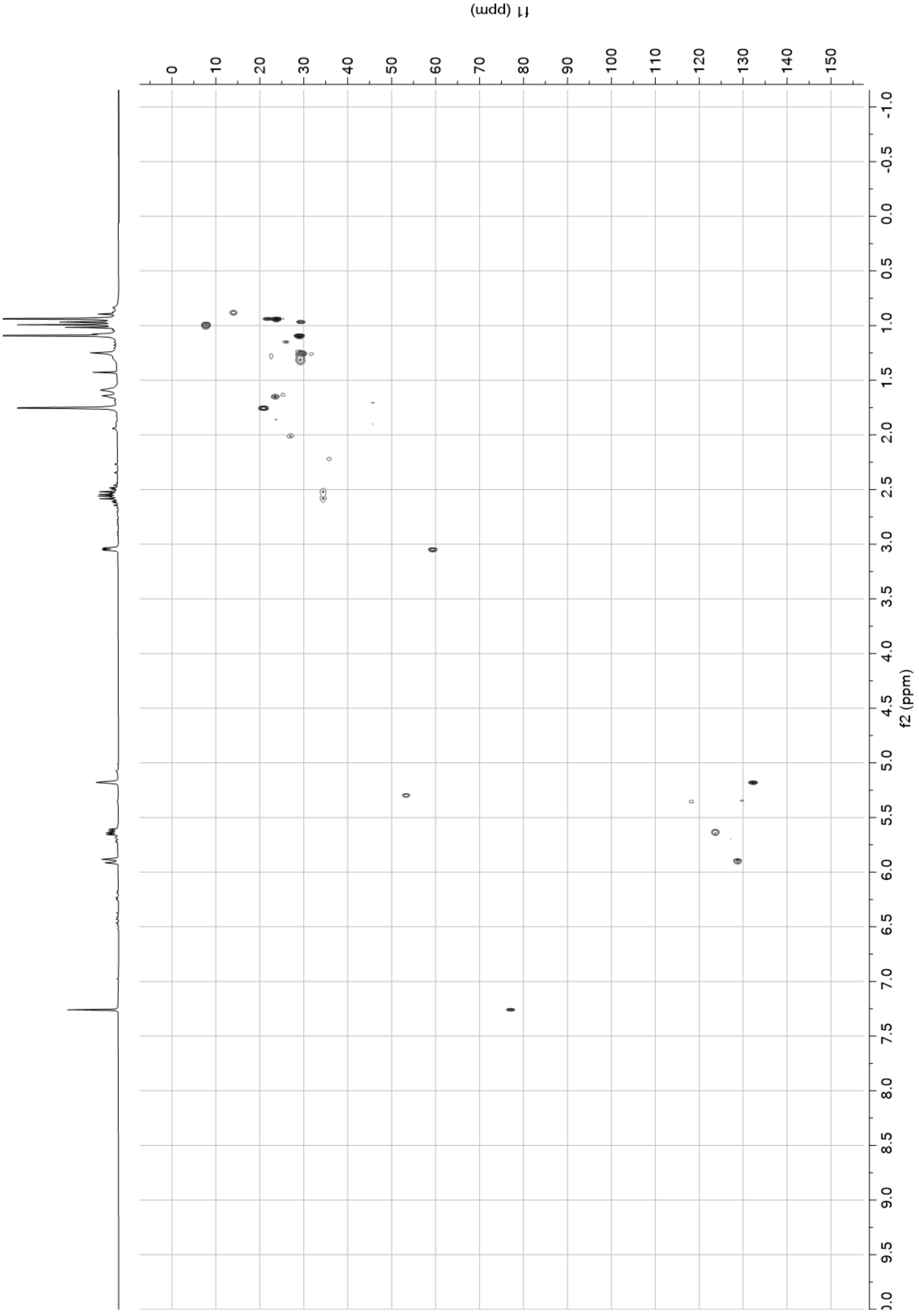
3.36 (^{1}H NMR, 300 MHz, CDCl$_3$)



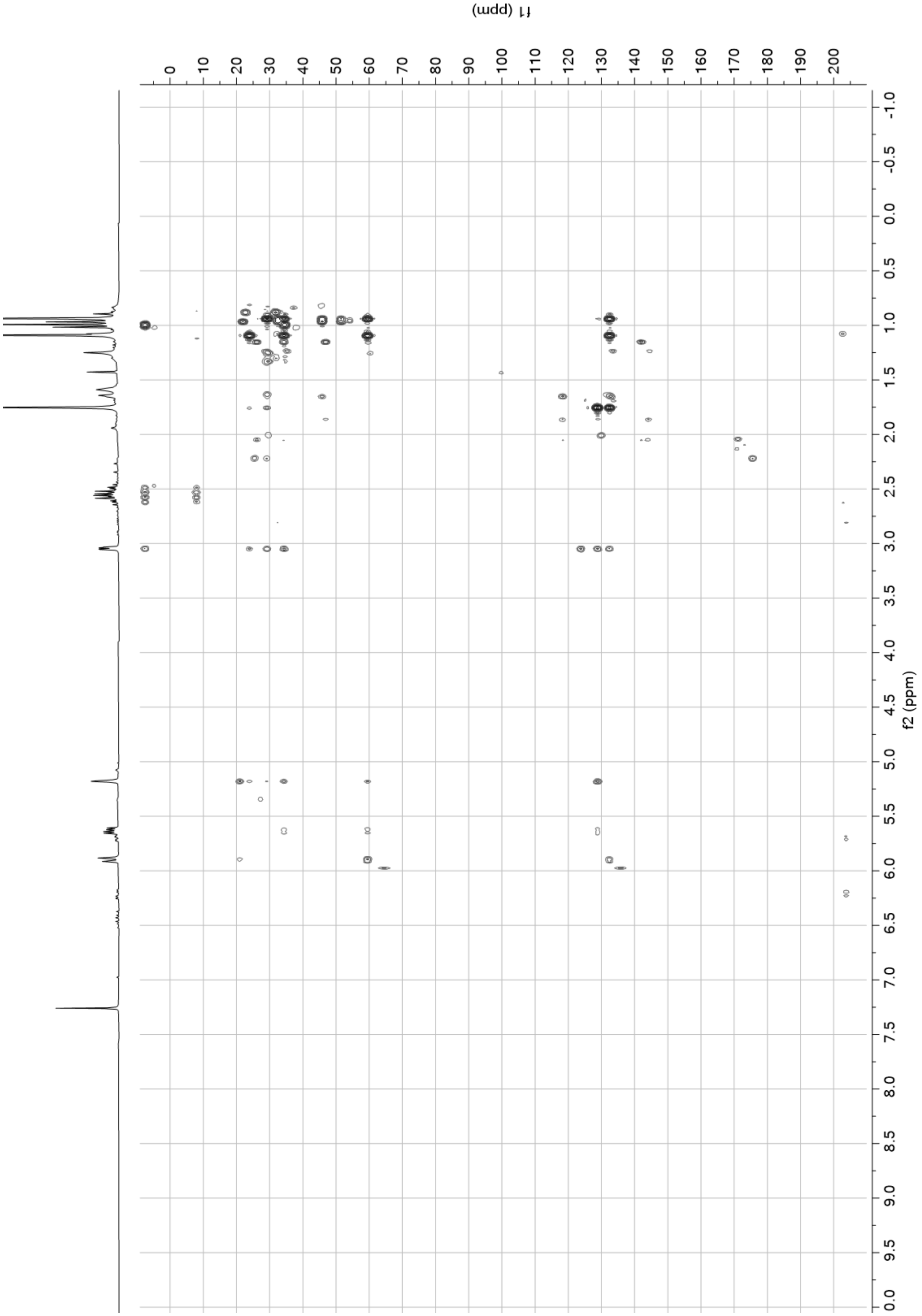
3.36 (COSY, CDCl$_3$)



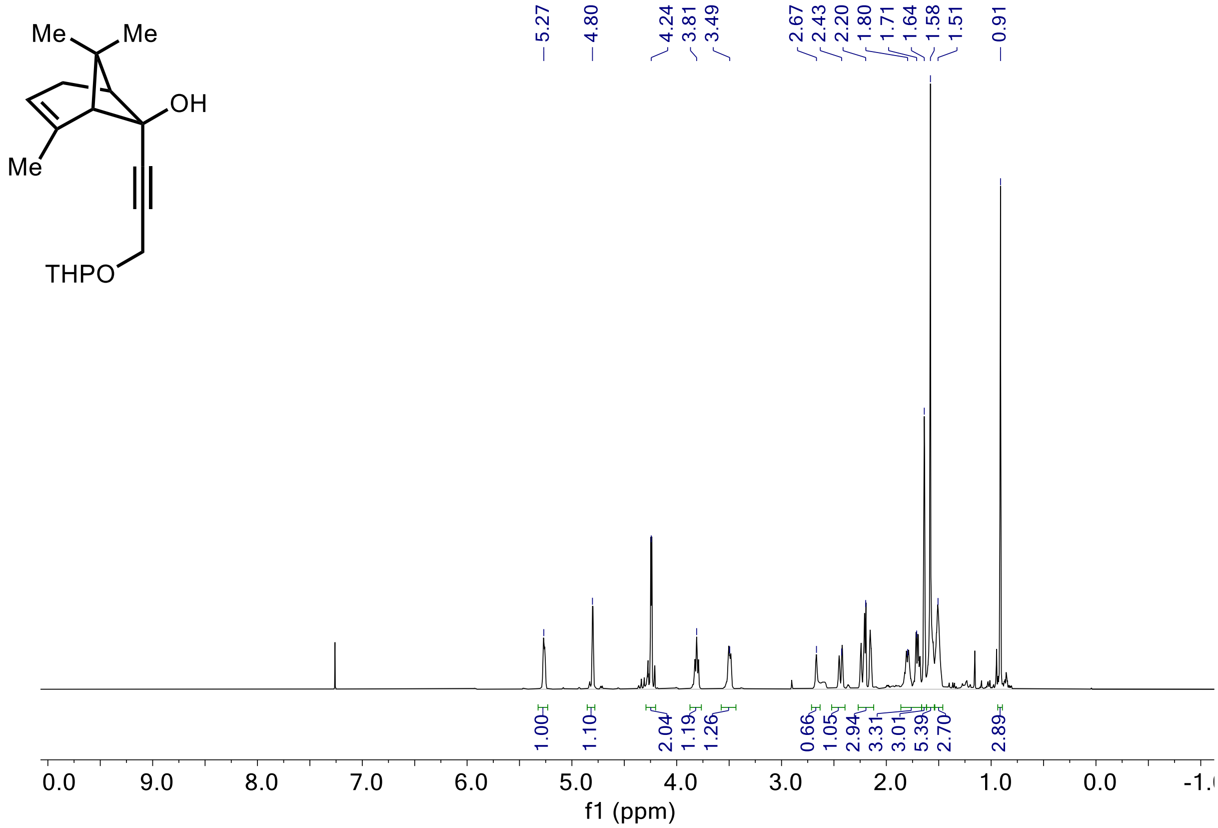
3.36 (HSQC, $CDCl_3$)



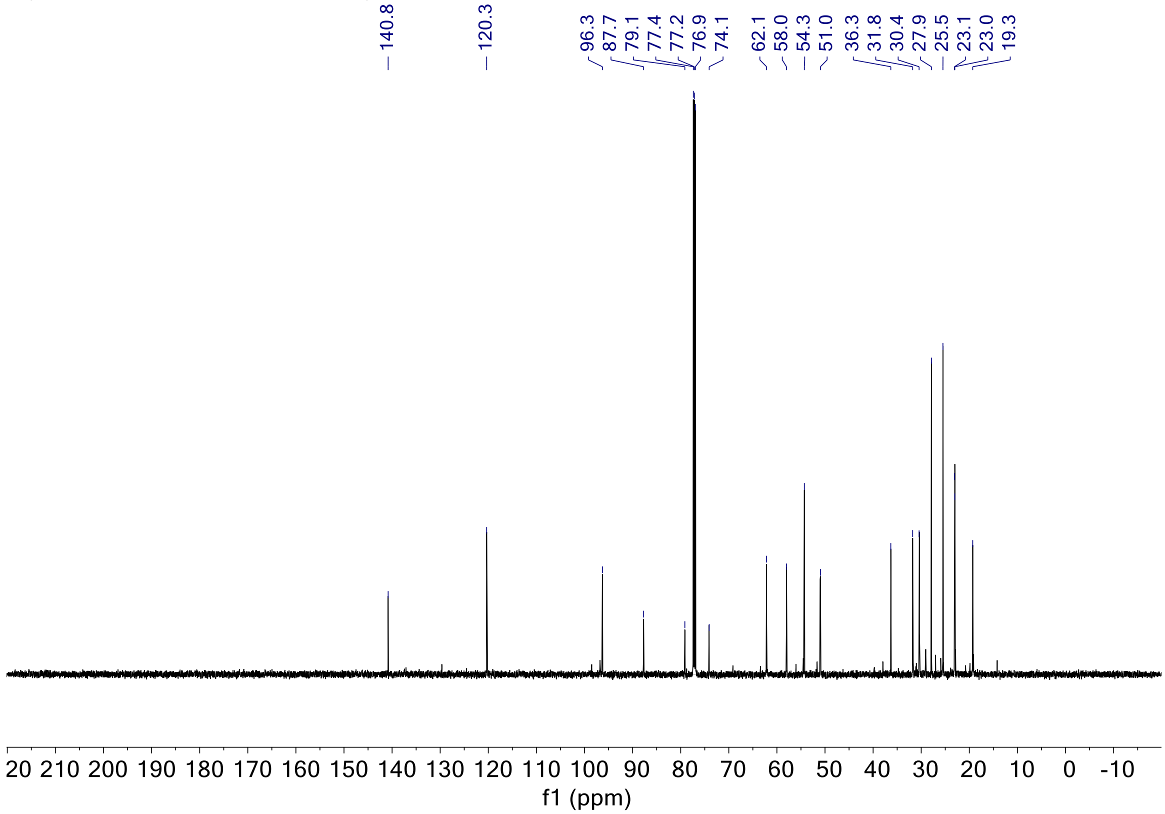
3.36 (HMBC, $CDCl_3$)



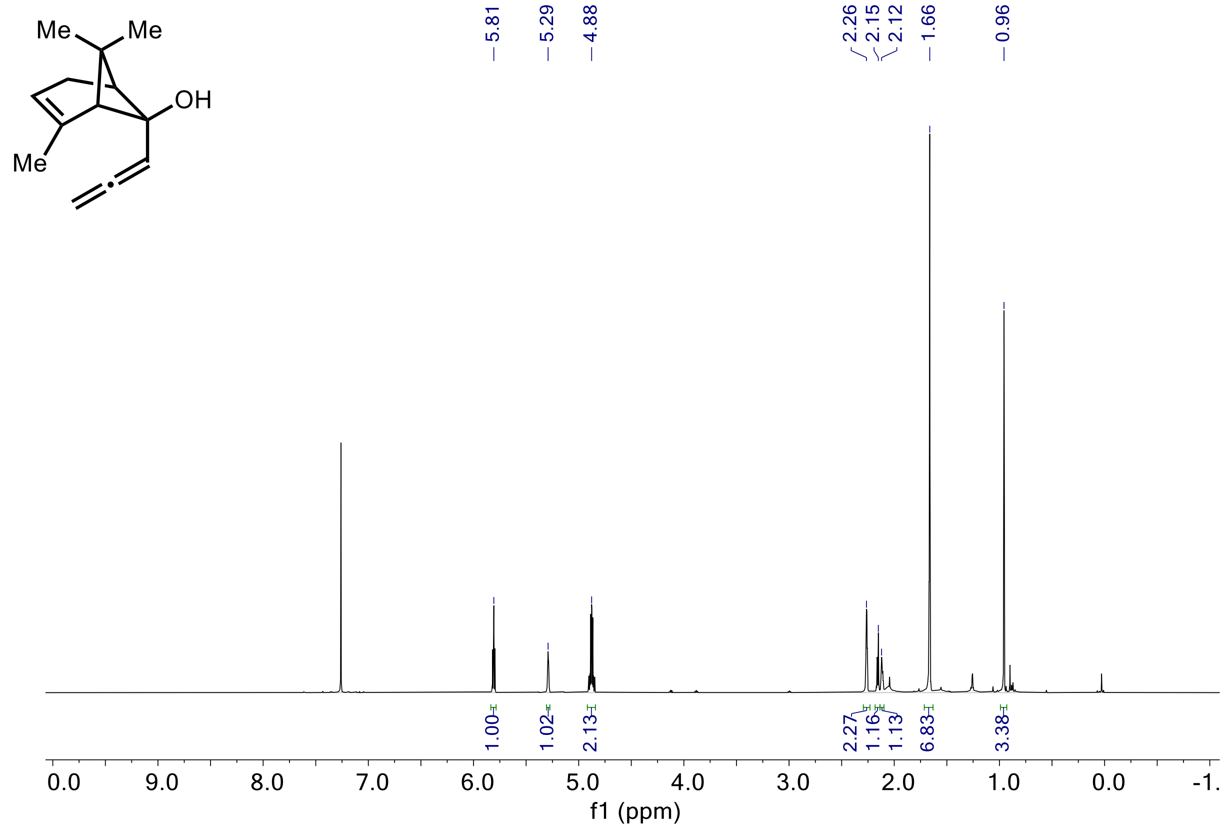
3.45 (^{1}H NMR, 600 MHz, CDCl$_3$)



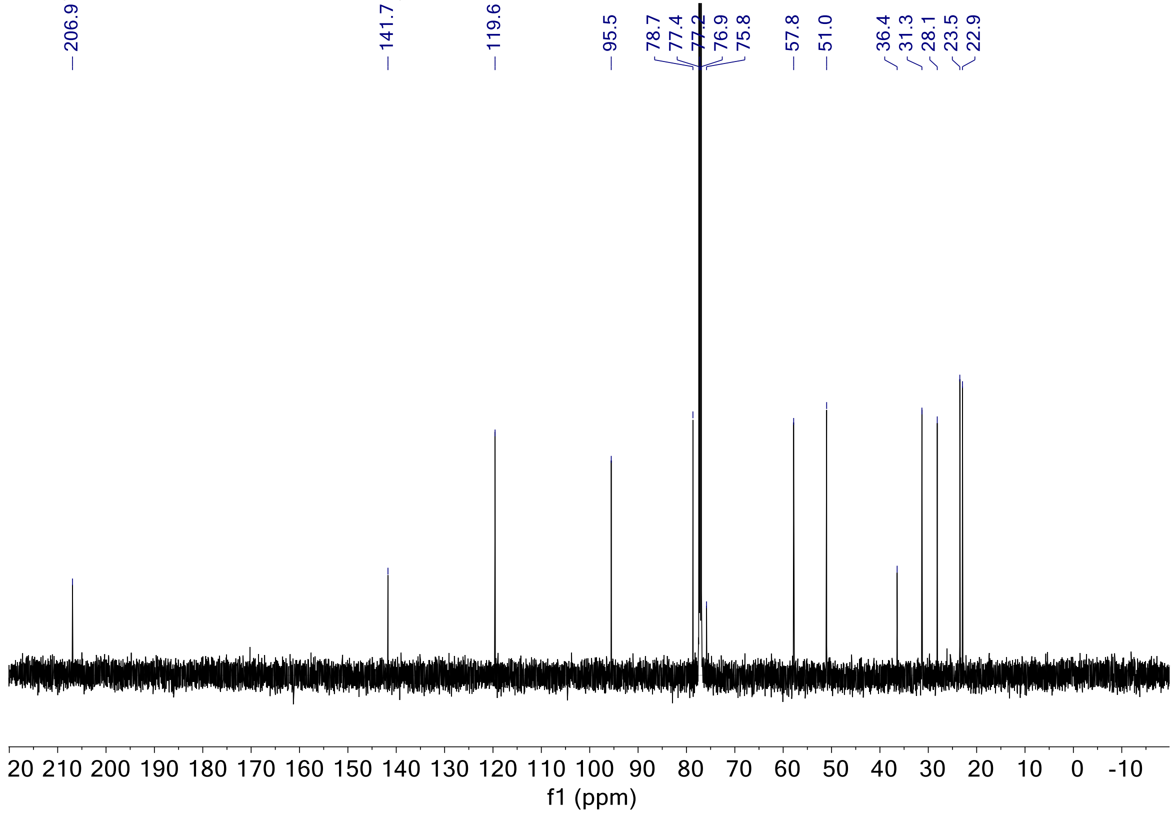
3.45 (^{13}C NMR, 151 MHz, CDCl$_3$)



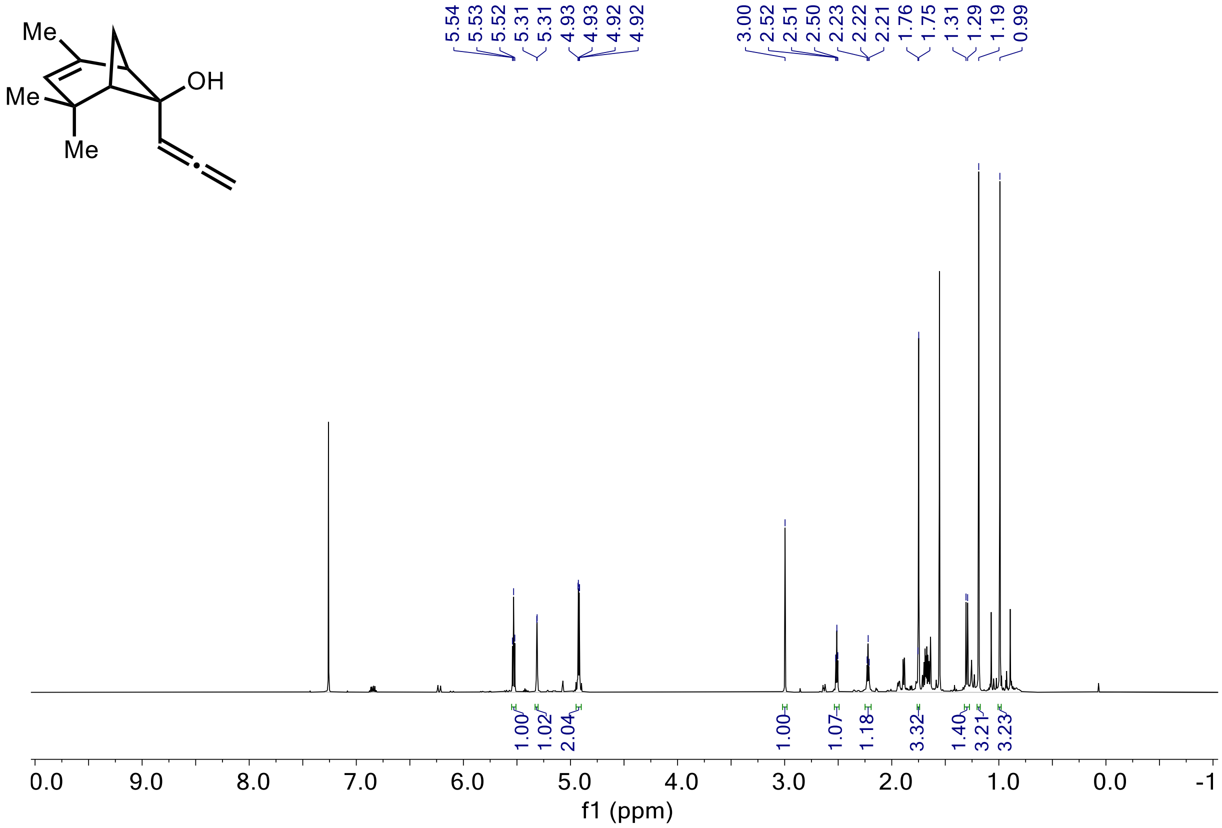
3.21.A (^{1}H NMR, 600 MHz, CDCl$_3$)



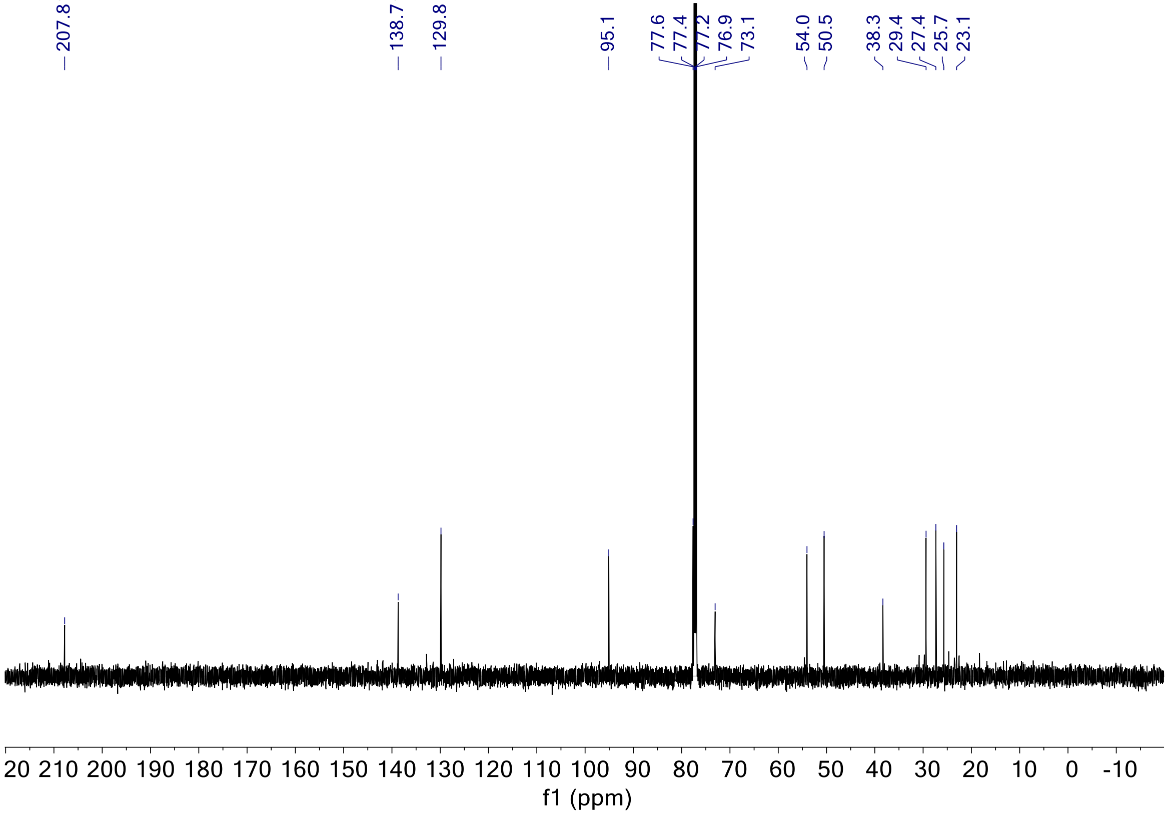
3.21.A (^{13}C NMR, 151 MHz, CDCl$_3$)



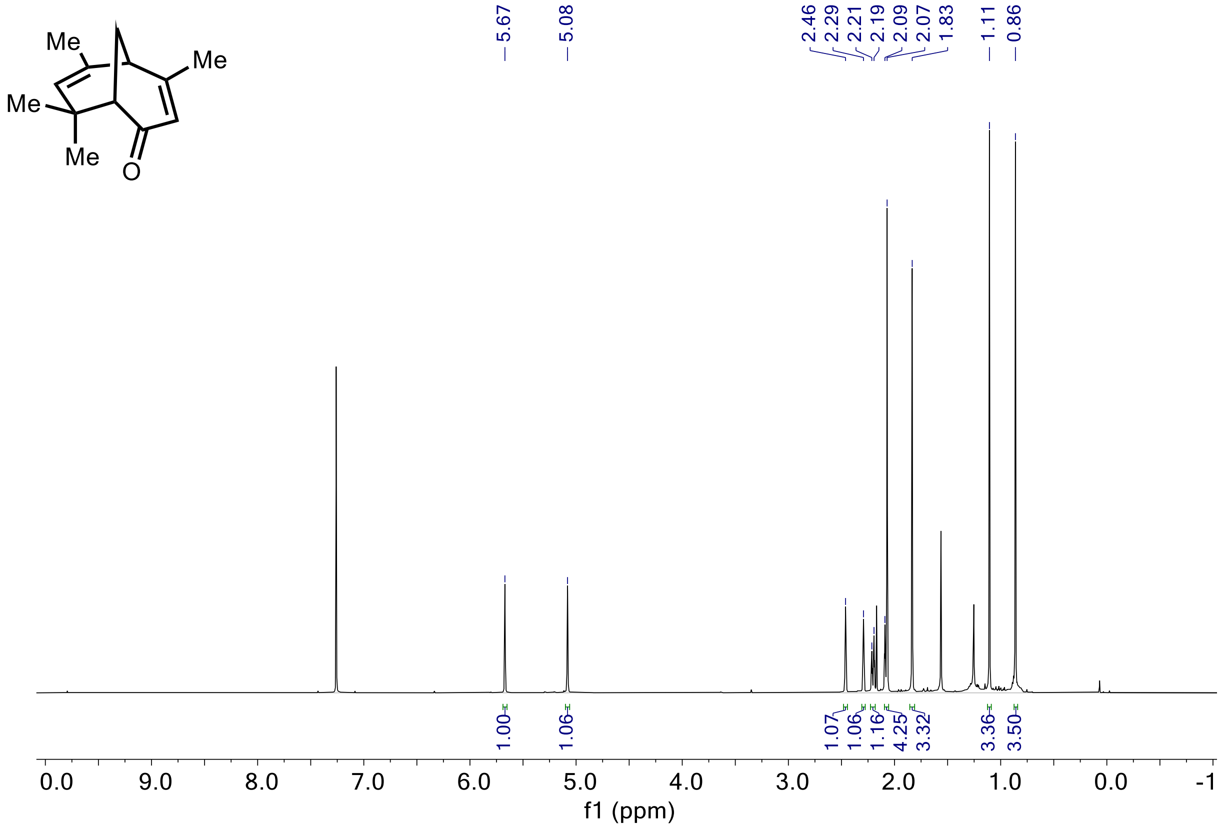
3.29.A (^{1}H NMR, 600 MHz, CDCl$_3$)



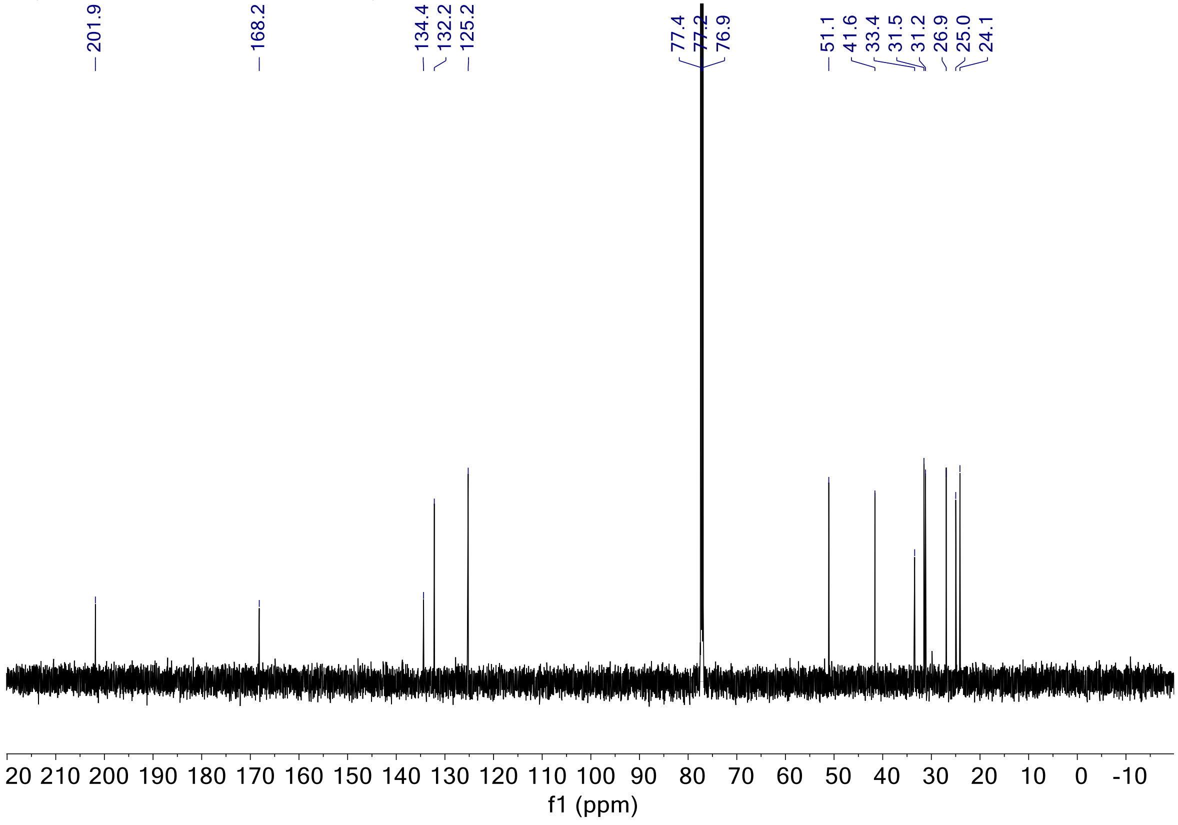
3.29.A (^{13}C NMR, 151 MHz, CDCl$_3$)



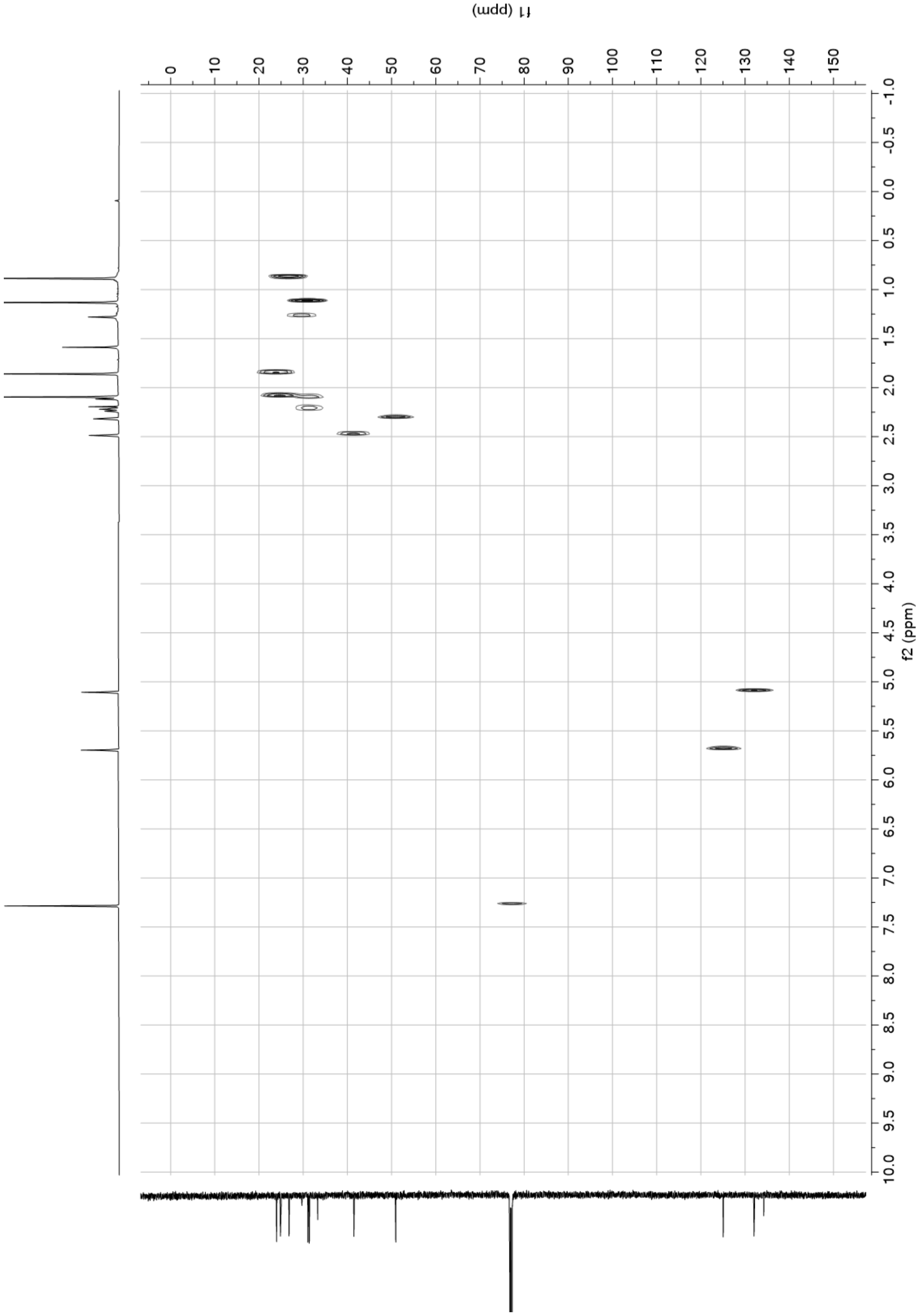
3.46 (^{1}H NMR, 600 MHz, CDCl$_3$)



3.46 (^{13}C NMR, 151 MHz, CDCl$_3$)



3.46 (HSQC, $CDCl_3$)



3.10.3 X-Ray Crystallographic Data for Chapter 3

X-Ray Analysis of 3.29.V

A colorless block 0.23 x 0.10 x 0.07 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 30.23 mm and exposure time was 0.50 seconds per frame at low angles and 2.00 seconds at high angles, using a scan width of 0.5°. Data collection was 100% complete to 74.000° in θ. A total of 22311 reflections were collected covering the indices -6<=h<=10, -14<=k<=14, -28<=l<=22. 4430 reflections were found to be symmetry independent, with an R_{int} of 0.0605. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the CrysAlis^{Pro} 1.171.40.63a software program and scaled using the SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2015) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

[Note: The instruments are supported by an NIH Shared Instrument Grant S10-RR027172.]

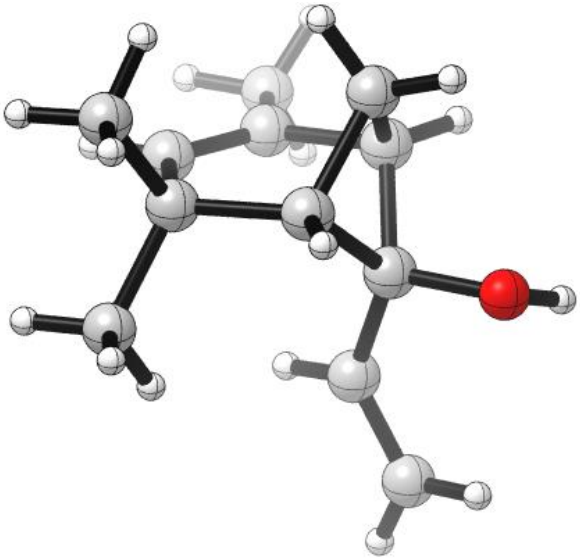


Figure 3.24 CYLview representation of **3.29.V**.

This crystal structure has been deposited at the Cambridge Crystallographic Data Center under CCDC 2108926.

Table 3.2. Crystal data and structure refinement for **3.29.V**.

Identification code	KJones002_Sarpong
Empirical formula	C12 H18 O

Formula weight	178.26	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.33890(10) Å	a= 90°.
	b = 11.5932(2) Å	b= 90°.
	c = 22.6819(3) Å	g = 90°.
Volume	2192.76(5) Å^3	
Z	8	
Density (calculated)	1.080 Mg/m^3	
Absorption coefficient	0.509 mm^{-1}	
F(000)	784	
Crystal size	0.230 x 0.100 x 0.070 mm^3	
Theta range for data collection	3.898 to 74.503°.	
Index ranges	-6<=h<=10, -14<=k<=14, -28<=l<=22	
Reflections collected	22311	
Independent reflections	4430 [R(int) = 0.0605]	
Completeness to theta = 74.000°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.77586	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4430 / 0 / 249	
Goodness-of-fit on F^2	1.102	
Final R indices [I>2sigma(I)]	R1 = 0.0380, wR2 = 0.1050	
R indices (all data)	R1 = 0.0400, wR2 = 0.1076	
Absolute structure parameter	0.07(12)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.182 and -0.171 e.Å^{-3}	

Table 3.3 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **3.29.V**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	7864(3)	4667(2)	4578(1)	32(1)
C(2)	7273(2)	5078(2)	5077(1)	26(1)
C(3)	6048(2)	4491(2)	5451(1)	23(1)
C(4)	6280(2)	4524(2)	6138(1)	25(1)
C(5)	4440(2)	4340(2)	6185(1)	26(1)
C(6)	4324(2)	4997(2)	5586(1)	24(1)

C(7)	4299(3)	6305(2)	5696(1)	29(1)
C(8)	4477(3)	6987(2)	5118(1)	36(1)
C(9)	2671(3)	6646(2)	5965(1)	37(1)
C(10)	5662(3)	6580(2)	6115(1)	31(1)
C(11)	6633(3)	5762(2)	6319(1)	29(1)
C(12)	8070(3)	5985(2)	6701(1)	38(1)
C(13)	10320(3)	3219(2)	6257(1)	38(1)
C(14)	9614(2)	2264(2)	6447(1)	29(1)
C(15)	8468(2)	1549(2)	6095(1)	24(1)
C(16)	8745(2)	210(2)	6102(1)	24(1)
C(17)	6946(2)	86(2)	5942(1)	26(1)
C(18)	6700(2)	1236(2)	6288(1)	24(1)
C(19)	6507(3)	977(2)	6949(1)	28(1)
C(20)	6487(3)	2099(2)	7311(1)	34(1)
C(21)	4877(3)	371(2)	7056(1)	36(1)
C(22)	7870(3)	189(2)	7129(1)	31(1)
C(23)	8948(2)	-179(2)	6738(1)	28(1)
C(24)	10345(3)	-938(2)	6882(1)	37(1)
O(1)	5774(2)	3343(1)	5248(1)	25(1)
O(2)	8314(2)	1980(1)	5510(1)	26(1)

Table 3.4 Bond lengths [Å] and angles [°] for **3.29.V**.

C(1)-C(2)	1.323(3)	C(8)-H(8B)	0.9800
C(1)-H(1A)	0.9500	C(8)-H(8C)	0.9800
C(1)-H(1B)	0.9500	C(9)-H(9A)	0.9800
C(2)-C(3)	1.492(3)	C(9)-H(9B)	0.9800
C(2)-H(2)	0.9500	C(9)-H(9C)	0.9800
C(3)-O(1)	1.427(2)	C(10)-C(11)	1.330(3)
C(3)-C(4)	1.570(3)	C(10)-H(10)	0.9500
C(3)-C(6)	1.582(3)	C(11)-C(12)	1.502(3)
C(4)-C(11)	1.522(3)	C(12)-H(12A)	0.9800
C(4)-C(5)	1.553(3)	C(12)-H(12B)	0.9800
C(4)-H(4)	1.0000	C(12)-H(12C)	0.9800
C(5)-C(6)	1.560(3)	C(13)-C(14)	1.326(3)
C(5)-H(5A)	0.9900	C(13)-H(13A)	0.9500
C(5)-H(5B)	0.9900	C(13)-H(13B)	0.9500
C(6)-C(7)	1.538(3)	C(14)-C(15)	1.496(3)
C(6)-H(6)	1.0000	C(14)-H(14)	0.9500
C(7)-C(10)	1.514(3)	C(15)-O(2)	1.425(2)
C(7)-C(8)	1.538(3)	C(15)-C(16)	1.570(3)
C(7)-C(9)	1.540(3)	C(15)-C(18)	1.580(3)
C(8)-H(8A)	0.9800	C(16)-C(23)	1.521(3)

C(16)-C(17)	1.550(3)
C(16)-H(16)	1.0000
C(17)-C(18)	1.560(3)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-C(19)	1.538(3)
C(18)-H(18)	1.0000
C(19)-C(22)	1.514(3)
C(19)-C(20)	1.538(3)
C(19)-C(21)	1.549(3)
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-C(23)	1.334(3)
C(22)-H(22)	0.9500
C(23)-C(24)	1.497(3)
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
O(1)-H(1)	0.89(3)
O(2)-H(2A)	0.93(3)
C(2)-C(1)-H(1A)	120.0
C(2)-C(1)-H(1B)	120.0
H(1A)-C(1)-H(1B)	120.0
C(1)-C(2)-C(3)	125.3(2)
C(1)-C(2)-H(2)	117.4
C(3)-C(2)-H(2)	117.4
O(1)-C(3)-C(2)	110.55(16)
O(1)-C(3)-C(4)	111.27(15)
C(2)-C(3)-C(4)	117.99(17)
O(1)-C(3)-C(6)	105.18(15)
C(2)-C(3)-C(6)	124.28(17)
C(4)-C(3)-C(6)	84.91(14)
C(11)-C(4)-C(5)	107.57(17)
C(11)-C(4)-C(3)	108.32(16)
C(5)-C(4)-C(3)	86.76(14)
C(11)-C(4)-H(4)	116.7
C(5)-C(4)-H(4)	116.7
C(3)-C(4)-H(4)	116.7
C(4)-C(5)-C(6)	86.23(14)
C(4)-C(5)-H(5A)	114.3
C(6)-C(5)-H(5A)	114.3
C(4)-C(5)-H(5B)	114.3
C(6)-C(5)-H(5B)	114.3
H(5A)-C(5)-H(5B)	111.4
C(7)-C(6)-C(5)	109.85(16)
C(7)-C(6)-C(3)	114.15(17)
C(5)-C(6)-C(3)	86.07(14)
C(7)-C(6)-H(6)	114.5
C(5)-C(6)-H(6)	114.5
C(3)-C(6)-H(6)	114.5
C(10)-C(7)-C(6)	107.42(17)
C(10)-C(7)-C(8)	110.72(19)
C(6)-C(7)-C(8)	111.50(17)
C(10)-C(7)-C(9)	111.07(17)
C(6)-C(7)-C(9)	109.27(19)
C(8)-C(7)-C(9)	106.89(18)
C(7)-C(8)-H(8A)	109.5
C(7)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(7)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(7)-C(9)-H(9A)	109.5
C(7)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(7)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(7)	121.7(2)
C(11)-C(10)-H(10)	119.1
C(7)-C(10)-H(10)	119.1
C(10)-C(11)-C(12)	124.4(2)
C(10)-C(11)-C(4)	117.39(19)
C(12)-C(11)-C(4)	118.21(19)
C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(14)-C(13)-H(13A)	120.0
C(14)-C(13)-H(13B)	120.0
H(13A)-C(13)-H(13B)	120.0
C(13)-C(14)-C(15)	124.9(2)

C(13)-C(14)-H(14)	117.5
C(15)-C(14)-H(14)	117.5
O(2)-C(15)-C(14)	111.11(17)
O(2)-C(15)-C(16)	111.68(15)
C(14)-C(15)-C(16)	116.70(17)
O(2)-C(15)-C(18)	104.74(15)
C(14)-C(15)-C(18)	125.16(16)
C(16)-C(15)-C(18)	84.69(14)
C(23)-C(16)-C(17)	107.54(16)
C(23)-C(16)-C(15)	108.57(16)
C(17)-C(16)-C(15)	86.98(15)
C(23)-C(16)-H(16)	116.6
C(17)-C(16)-H(16)	116.6
C(15)-C(16)-H(16)	116.6
C(16)-C(17)-C(18)	86.02(15)
C(16)-C(17)-H(17A)	114.3
C(18)-C(17)-H(17A)	114.3
C(16)-C(17)-H(17B)	114.3
C(18)-C(17)-H(17B)	114.3
H(17A)-C(17)-H(17B)	111.5
C(19)-C(18)-C(17)	109.72(17)
C(19)-C(18)-C(15)	114.34(16)
C(17)-C(18)-C(15)	86.25(14)
C(19)-C(18)-H(18)	114.5
C(17)-C(18)-H(18)	114.5
C(15)-C(18)-H(18)	114.5
C(22)-C(19)-C(20)	112.00(18)
C(22)-C(19)-C(18)	107.59(17)
C(20)-C(19)-C(18)	110.85(18)
C(22)-C(19)-C(21)	110.08(18)
C(20)-C(19)-C(21)	106.91(19)
C(18)-C(19)-C(21)	109.41(17)
C(19)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(19)-C(21)-H(21A)	109.5
C(19)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(19)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(23)-C(22)-C(19)	121.30(19)
C(23)-C(22)-H(22)	119.3
C(19)-C(22)-H(22)	119.3
C(22)-C(23)-C(24)	124.6(2)
C(22)-C(23)-C(16)	117.49(19)
C(24)-C(23)-C(16)	117.89(19)
C(23)-C(24)-H(24A)	109.5
C(23)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(23)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(3)-O(1)-H(1)	109.6(19)
C(15)-O(2)-H(2A)	109.7(18)

Symmetry transformations used to generate equivalent atoms:

Table 3.5 Anisotropic displacement parameters (Å^{2}x 10^3) for **3.29.V**. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	28(1)	38(1)	30(1)	0(1)	6(1)	0(1)
C(2)	25(1)	26(1)	29(1)	1(1)	1(1)	-1(1)
C(3)	23(1)	22(1)	24(1)	1(1)	2(1)	0(1)
C(4)	22(1)	26(1)	25(1)	2(1)	-1(1)	0(1)
C(5)	22(1)	30(1)	24(1)	2(1)	2(1)	-1(1)

C(6)	22(1)	28(1)	23(1)	0(1)	1(1)	2(1)
C(7)	34(1)	28(1)	26(1)	0(1)	2(1)	5(1)
C(8)	47(1)	28(1)	35(1)	2(1)	2(1)	8(1)
C(9)	38(1)	41(1)	32(1)	-4(1)	1(1)	12(1)
C(10)	36(1)	27(1)	29(1)	-5(1)	6(1)	-2(1)
C(11)	28(1)	33(1)	25(1)	-2(1)	5(1)	-5(1)
C(12)	32(1)	45(1)	39(1)	-8(1)	-1(1)	-10(1)
C(13)	28(1)	35(1)	50(1)	-10(1)	3(1)	-6(1)
C(14)	22(1)	32(1)	33(1)	-6(1)	-1(1)	1(1)
C(15)	23(1)	25(1)	23(1)	1(1)	1(1)	0(1)
C(16)	22(1)	26(1)	25(1)	0(1)	1(1)	0(1)
C(17)	24(1)	28(1)	26(1)	0(1)	-1(1)	-3(1)
C(18)	20(1)	28(1)	23(1)	2(1)	0(1)	0(1)
C(19)	30(1)	33(1)	22(1)	3(1)	3(1)	3(1)
C(20)	37(1)	41(1)	25(1)	-2(1)	1(1)	5(1)
C(21)	31(1)	45(1)	32(1)	9(1)	7(1)	1(1)
C(22)	31(1)	37(1)	26(1)	6(1)	-1(1)	1(1)
C(23)	27(1)	28(1)	29(1)	2(1)	-3(1)	1(1)
C(24)	32(1)	37(1)	41(1)	7(1)	-2(1)	6(1)
O(1)	24(1)	22(1)	28(1)	-1(1)	-2(1)	1(1)
O(2)	24(1)	30(1)	24(1)	4(1)	4(1)	2(1)

Table 3.6 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **3.29.V**.

	x	y	z	U(eq)
H(1A)	7509	3942	4433	38
H(1B)	8644	5096	4366	38
H(2)	7660	5805	5208	32
H(4)	6976	3912	6313	29
H(5A)	3931	4746	6520	31
H(5B)	4100	3523	6166	31
H(6)	3460	4712	5317	29
H(8A)	5485	6773	4925	54
H(8B)	4483	7816	5205	54
H(8C)	3576	6808	4857	54
H(9A)	1808	6438	5692	55
H(9B)	2651	7480	6036	55
H(9C)	2519	6238	6340	55
H(10)	5827	7356	6234	37

H(12A)	8016	5495	7053	58
H(12B)	8083	6798	6820	58
H(12C)	9049	5808	6480	58
H(13A)	10111	3494	5870	45
H(13B)	11036	3627	6507	45
H(14)	9854	2016	6837	35
H(16)	9533	-102	5810	29
H(17A)	6414	-592	6122	31
H(17B)	6714	140	5515	31
H(18)	5856	1753	6120	28
H(20A)	7501	2512	7253	52
H(20B)	6353	1915	7729	52
H(20C)	5595	2586	7179	52
H(21A)	4004	879	6928	54
H(21B)	4756	201	7477	54
H(21C)	4839	-349	6830	54
H(22)	7958	-47	7529	37
H(24A)	10283	-1647	6648	55
H(24B)	10323	-1134	7303	55
H(24C)	11345	-532	6791	55
H(1)	6660(40)	2920(30)	5295(12)	43(8)
H(2A)	9270(40)	1890(30)	5310(13)	48(8)

Table 3.7 Torsion angles [°] for **3.29.V**.

C(1)-C(2)-C(3)-O(1)	8.9(3)
C(1)-C(2)-C(3)-C(4)	138.6(2)
C(1)-C(2)-C(3)-C(6)	-117.5(2)
O(1)-C(3)-C(4)-C(11)	177.73(16)
C(2)-C(3)-C(4)-C(11)	48.4(2)
C(6)-C(3)-C(4)-C(11)	-77.94(17)
O(1)-C(3)-C(4)-C(5)	-74.82(17)
C(2)-C(3)-C(4)-C(5)	155.88(18)
C(6)-C(3)-C(4)-C(5)	29.51(14)
C(11)-C(4)-C(5)-C(6)	78.30(17)
C(3)-C(4)-C(5)-C(6)	-29.90(14)
C(4)-C(5)-C(6)-C(7)	-84.61(18)
C(4)-C(5)-C(6)-C(3)	29.67(14)
O(1)-C(3)-C(6)-C(7)	-168.68(15)
C(2)-C(3)-C(6)-C(7)	-40.0(3)
C(4)-C(3)-C(6)-C(7)	80.64(17)
O(1)-C(3)-C(6)-C(5)	81.31(16)
C(2)-C(3)-C(6)-C(5)	-150.0(2)
C(4)-C(3)-C(6)-C(5)	-29.37(14)
C(5)-C(6)-C(7)-C(10)	48.8(2)
C(3)-C(6)-C(7)-C(10)	-45.9(2)
C(5)-C(6)-C(7)-C(8)	170.27(17)
C(3)-C(6)-C(7)-C(8)	75.6(2)
C(5)-C(6)-C(7)-C(9)	-71.8(2)
C(3)-C(6)-C(7)-C(9)	-166.49(16)
C(6)-C(7)-C(10)-C(11)	0.2(3)
C(8)-C(7)-C(10)-C(11)	-121.8(2)
C(9)-C(7)-C(10)-C(11)	119.7(2)
C(7)-C(10)-C(11)-C(12)	175.7(2)
C(7)-C(10)-C(11)-C(4)	-2.6(3)
C(5)-C(4)-C(11)-C(10)	-43.0(2)
C(3)-C(4)-C(11)-C(10)	49.4(2)
C(5)-C(4)-C(11)-C(12)	138.58(19)
C(3)-C(4)-C(11)-C(12)	-128.99(19)
C(13)-C(14)-C(15)-O(2)	4.1(3)
C(13)-C(14)-C(15)-C(16)	133.7(2)

C(13)-C(14)-C(15)-C(18)	-123.2(2)
O(2)-C(15)-C(16)-C(23)	178.31(16)
C(14)-C(15)-C(16)-C(23)	49.0(2)
C(18)-C(15)-C(16)-C(23)	-77.92(16)
O(2)-C(15)-C(16)-C(17)	-74.20(17)
C(14)-C(15)-C(16)-C(17)	156.48(18)
C(18)-C(15)-C(16)-C(17)	29.57(13)
C(23)-C(16)-C(17)-C(18)	78.60(17)
C(15)-C(16)-C(17)-C(18)	-29.92(13)
C(16)-C(17)-C(18)-C(19)	-84.81(17)
C(16)-C(17)-C(18)-C(15)	29.73(14)
O(2)-C(15)-C(18)-C(19)	-168.37(16)
C(14)-C(15)-C(18)-C(19)	-38.5(3)
C(16)-C(15)-C(18)-C(19)	80.58(18)
O(2)-C(15)-C(18)-C(17)	81.67(16)
C(14)-C(15)-C(18)-C(17)	-148.5(2)
C(16)-C(15)-C(18)-C(17)	-29.38(13)
C(17)-C(18)-C(19)-C(22)	49.7(2)
C(15)-C(18)-C(19)-C(22)	-45.2(2)
C(17)-C(18)-C(19)-C(20)	172.46(17)
C(15)-C(18)-C(19)-C(20)	77.5(2)
C(17)-C(18)-C(19)-C(21)	-69.9(2)
C(15)-C(18)-C(19)-C(21)	-164.80(17)
C(20)-C(19)-C(22)-C(23)	-123.6(2)
C(18)-C(19)-C(22)-C(23)	-1.5(3)
C(21)-C(19)-C(22)-C(23)	117.6(2)
C(19)-C(22)-C(23)-C(24)	178.7(2)
C(19)-C(22)-C(23)-C(16)	-0.7(3)
C(17)-C(16)-C(23)-C(22)	-44.2(3)
C(15)-C(16)-C(23)-C(22)	48.5(3)
C(17)-C(16)-C(23)-C(24)	136.3(2)
C(15)-C(16)-C(23)-C(24)	-131.0(2)

Symmetry transformations used to generate equivalent atoms:

X-Ray Analysis of *ent*-3.21.P

A colorless block 0.38 x 0.24 x 0.21 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 30.23 mm and exposure time was 0.50 seconds per frame at low and high angles, using a scan width of 0.5°. Data collection was 100% complete to 74.000° in θ. A total of 76677 reflections were collected covering the indices -13<=h<=13, -27<=k<=26, -12<=l<=12. 4715 reflections were found to be symmetry independent, with an R_{int} of 0.0589. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21/c (No. 14). The data were integrated using the $\text{CrysAlis}^{\text{Pro}}$ 1.171.40.68a software program and scaled using the SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2015) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

[Note: The instruments are supported by an NIH Shared Instrument Grant S10-RR027172.]

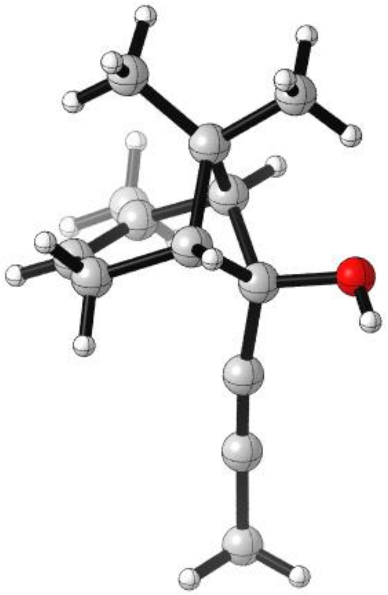


Figure 3.25 CYLview representation of ***ent*-3.21.P**.

This crystal structure has been deposited at the Cambridge Crysrallographic Data Center under CCDC 2108936.

Table 3.8 Crystal data and structure refinement for ***ent*-3.21.P**.

Identification code	NDoering001_Sarpong	
Empirical formula	C13 H18 O	
Formula weight	190.27	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 10.94100(10) Å	a= 90°.
	b = 21.9317(2) Å	b= 112.2260(10)°.
	c = 10.39670(10) Å	g = 90°.
Volume	2309.38(4) Å^{3}	
Z	8	
Density (calculated)	1.095 Mg/m^{3}	
Absorption coefficient	0.514 mm^{-1}	
F(000)	832	
Crystal size	0.380 x 0.240 x 0.210 mm^{3}	
Theta range for data collection	4.031 to 74.484°.	
Index ranges	-13<=h<=13, -27<=k<=26, -12<=l<=12	
Reflections collected	76677	
Independent reflections	4715 [R(int) = 0.0589]	
Completeness to theta = 74.000°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.81955	
Refinement method	Full-matrix least-squares on F^{2}	
Data / restraints / parameters	4715 / 0 / 269	
Goodness-of-fit on F^{2}	1.051	
Final R indices [I>2sigma(I)]	R1 = 0.0568, wR2 = 0.1506	
R indices (all data)	R1 = 0.0573, wR2 = 0.1510	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.816 and -0.332 e.Å^{-3}	

Table 3.9 Atomic coordinates (x 10^{4}) and equivalent isotropic displacement parameters (Å^{2}x 10^{3}) for ***ent*-3.21.P**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1A)	6279(2)	5767(1)	525(2)	39(1)
C(1B)	3342(2)	6007(1)	7166(2)	45(1)
C(2A)	5161(2)	5764(1)	972(2)	30(1)

C(2B)	4423(2)	6095(1)	6683(2)	32(1)
C(3A)	4249(2)	5760(1)	1339(2)	27(1)
C(3B)	5305(2)	6154(1)	6286(2)	28(1)
C(4A)	3244(2)	5714(1)	1955(2)	25(1)
C(4B)	6367(1)	6129(1)	5742(2)	25(1)
C(5A)	1841(2)	5469(1)	1074(2)	30(1)
C(5B)	7804(2)	6297(1)	6717(2)	29(1)
C(6A)	1264(2)	5903(1)	1906(2)	31(1)
C(6B)	8044(2)	6537(1)	5409(2)	30(1)
C(7A)	-122(2)	6160(1)	1124(2)	43(1)
C(7B)	8981(2)	7078(1)	5629(2)	40(1)
C(8A)	1270(2)	5647(1)	3284(2)	36(1)
C(8B)	8492(2)	6050(1)	4626(2)	36(1)
C(9A)	2498(2)	6310(1)	2080(2)	31(1)
C(9B)	6504(1)	6658(1)	4800(2)	26(1)
C(10A)	2211(2)	6670(1)	736(2)	38(1)
C(10B)	6199(2)	7241(1)	5406(2)	29(1)
C(11A)	2488(2)	7336(1)	820(2)	47(1)
C(11B)	5181(2)	7666(1)	4472(2)	33(1)
C(12A)	1716(2)	6361(1)	-434(2)	39(1)
C(12B)	6816(2)	7314(1)	6774(2)	34(1)
C(13A)	1447(2)	5688(1)	-427(2)	39(1)
C(13B)	7753(2)	6834(1)	7639(2)	36(1)
O(1A)	3794(1)	5369(1)	3203(1)	28(1)
O(1B)	6282(1)	5553(1)	5070(1)	26(1)

Table 3.10 Bond lengths [Å] and angles [°] for ***ent*-3.21.P**.

C(1A)-C(2A)	1.463(2)
C(1A)-H(1AA)	0.9800
C(1A)-H(1AB)	0.9800
C(1A)-H(1AC)	0.9800
C(1B)-C(2B)	1.462(2)
C(1B)-H(1BA)	0.9800
C(1B)-H(1BB)	0.9800
C(1B)-H(1BC)	0.9800
C(2A)-C(3A)	1.196(2)
C(2B)-C(3B)	1.192(2)
C(3A)-C(4A)	1.471(2)
C(3B)-C(4B)	1.473(2)
C(4A)-O(1A)	1.4244(17)
C(4A)-C(5A)	1.556(2)
C(4A)-C(9A)	1.573(2)
C(4B)-O(1B)	1.4300(17)
C(4B)-C(5B)	1.559(2)
C(4B)-C(9B)	1.5622(19)
C(5A)-C(13A)	1.531(2)
C(5A)-C(6A)	1.571(2)
C(5A)-H(5A)	1.0000
C(5B)-C(13B)	1.533(2)
C(5B)-C(6B)	1.569(2)
C(5B)-H(5B)	1.0000
C(6A)-C(7A)	1.531(2)
C(6A)-C(8A)	1.536(2)
C(6A)-C(9A)	1.571(2)
C(6B)-C(7B)	1.528(2)
C(6B)-C(8B)	1.531(2)
C(6B)-C(9B)	1.581(2)

C(7A)-H(7AA)	0.9800
C(7A)-H(7AB)	0.9800
C(7A)-H(7AC)	0.9800
C(7B)-H(7BA)	0.9800
C(7B)-H(7BB)	0.9800
C(7B)-H(7BC)	0.9800
C(8A)-H(8AA)	0.9800
C(8A)-H(8AB)	0.9800
C(8A)-H(8AC)	0.9800
C(8B)-H(8BA)	0.9800
C(8B)-H(8BB)	0.9800
C(8B)-H(8BC)	0.9800
C(9A)-C(10A)	1.531(2)
C(9A)-H(9A)	1.0000
C(9B)-C(10B)	1.517(2)
C(9B)-H(9B)	1.0000
C(10A)-C(12A)	1.317(3)
C(10A)-C(11A)	1.487(3)
C(10B)-C(12B)	1.333(2)
C(10B)-C(11B)	1.496(2)
C(11A)-H(11A)	0.9800
C(11A)-H(11B)	0.9800
C(11A)-H(11C)	0.9800
C(11B)-H(11D)	0.9800
C(11B)-H(11E)	0.9800
C(11B)-H(11F)	0.9800
C(12A)-C(13A)	1.507(3)
C(12A)-H(12A)	0.9500
C(12B)-C(13B)	1.507(2)
C(12B)-H(12B)	0.9500
C(13A)-H(13A)	0.9900
C(13A)-H(13B)	0.9900
C(13B)-H(13C)	0.9900
C(13B)-H(13D)	0.9900
O(1A)-H(1A)	0.85(3)
O(1B)-H(1B)	0.84(3)
C(2A)-C(1A)-H(1AA)	109.5
C(2A)-C(1A)-H(1AB)	109.5
H(1AA)-C(1A)-H(1AB)	109.5
C(2A)-C(1A)-H(1AC)	109.5
H(1AA)-C(1A)-H(1AC)	109.5
H(1AB)-C(1A)-H(1AC)	109.5
C(2B)-C(1B)-H(1BA)	109.5
C(2B)-C(1B)-H(1BB)	109.5
H(1BA)-C(1B)-H(1BB)	109.5
C(2B)-C(1B)-H(1BC)	109.5
H(1BA)-C(1B)-H(1BC)	109.5
H(1BB)-C(1B)-H(1BC)	109.5
C(3A)-C(2A)-C(1A)	179.73(18)
C(3B)-C(2B)-C(1B)	178.54(18)
C(2A)-C(3A)-C(4A)	172.51(16)
C(2B)-C(3B)-C(4B)	171.45(16)
O(1A)-C(4A)-C(3A)	107.80(12)
O(1A)-C(4A)-C(5A)	109.58(12)
C(3A)-C(4A)-C(5A)	120.07(13)
O(1A)-C(4A)-C(9A)	114.86(12)
C(3A)-C(4A)-C(9A)	118.42(12)
C(5A)-C(4A)-C(9A)	84.75(11)
O(1B)-C(4B)-C(3B)	107.78(12)
O(1B)-C(4B)-C(5B)	112.98(12)
C(3B)-C(4B)-C(5B)	119.35(12)
O(1B)-C(4B)-C(9B)	110.70(11)
C(3B)-C(4B)-C(9B)	119.35(12)
C(5B)-C(4B)-C(9B)	85.36(11)
C(13A)-C(5A)-C(4A)	109.07(13)
C(13A)-C(5A)-C(6A)	110.76(13)
C(4A)-C(5A)-C(6A)	88.79(11)
C(13A)-C(5A)-H(5A)	115.1
C(4A)-C(5A)-H(5A)	115.1
C(6A)-C(5A)-H(5A)	115.1
C(13B)-C(5B)-C(4B)	108.75(13)
C(13B)-C(5B)-C(6B)	109.99(13)
C(4B)-C(5B)-C(6B)	88.53(11)
C(13B)-C(5B)-H(5B)	115.5
C(4B)-C(5B)-H(5B)	115.5
C(6B)-C(5B)-H(5B)	115.5
C(7A)-C(6A)-C(8A)	106.51(13)
C(7A)-C(6A)-C(9A)	119.21(14)
C(8A)-C(6A)-C(9A)	113.59(14)
C(7A)-C(6A)-C(5A)	116.99(14)
C(8A)-C(6A)-C(5A)	115.46(13)
C(9A)-C(6A)-C(5A)	84.32(11)
C(7B)-C(6B)-C(8B)	106.79(13)
C(7B)-C(6B)-C(5B)	116.98(14)
C(8B)-C(6B)-C(5B)	114.73(13)
C(7B)-C(6B)-C(9B)	118.88(13)
C(8B)-C(6B)-C(9B)	114.22(13)
C(5B)-C(6B)-C(9B)	84.37(10)

C(6A)-C(7A)-H(7AA)	109.5
C(6A)-C(7A)-H(7AB)	109.5
H(7AA)-C(7A)-H(7AB)	109.5
C(6A)-C(7A)-H(7AC)	109.5
H(7AA)-C(7A)-H(7AC)	109.5
H(7AB)-C(7A)-H(7AC)	109.5
C(6B)-C(7B)-H(7BA)	109.5
C(6B)-C(7B)-H(7BB)	109.5
H(7BA)-C(7B)-H(7BB)	109.5
C(6B)-C(7B)-H(7BC)	109.5
H(7BA)-C(7B)-H(7BC)	109.5
H(7BB)-C(7B)-H(7BC)	109.5
C(6A)-C(8A)-H(8AA)	109.5
C(6A)-C(8A)-H(8AB)	109.5
H(8AA)-C(8A)-H(8AB)	109.5
C(6A)-C(8A)-H(8AC)	109.5
H(8AA)-C(8A)-H(8AC)	109.5
H(8AB)-C(8A)-H(8AC)	109.5
C(6B)-C(8B)-H(8BA)	109.5
C(6B)-C(8B)-H(8BB)	109.5
H(8BA)-C(8B)-H(8BB)	109.5
C(6B)-C(8B)-H(8BC)	109.5
H(8BA)-C(8B)-H(8BC)	109.5
H(8BB)-C(8B)-H(8BC)	109.5
C(10A)-C(9A)-C(6A)	108.51(14)
C(10A)-C(9A)-C(4A)	106.69(12)
C(6A)-C(9A)-C(4A)	88.19(11)
C(10A)-C(9A)-H(9A)	116.6
C(6A)-C(9A)-H(9A)	116.6
C(4A)-C(9A)-H(9A)	116.6
C(10B)-C(9B)-C(4B)	106.05(11)
C(10B)-C(9B)-C(6B)	110.05(12)
C(4B)-C(9B)-C(6B)	87.97(11)
C(10B)-C(9B)-H(9B)	116.4
C(4B)-C(9B)-H(9B)	116.4
C(6B)-C(9B)-H(9B)	116.4
C(12A)-C(10A)-C(11A)	124.29(17)
C(12A)-C(10A)-C(9A)	116.63(16)
C(11A)-C(10A)-C(9A)	119.08(17)
C(12B)-C(10B)-C(11B)	124.73(15)
C(12B)-C(10B)-C(9B)	116.28(14)
C(11B)-C(10B)-C(9B)	118.85(13)
C(10A)-C(11A)-H(11A)	109.5
C(10A)-C(11A)-H(11B)	109.5
H(11A)-C(11A)-H(11B)	109.5
C(10A)-C(11A)-H(11C)	109.5
H(11A)-C(11A)-H(11C)	109.5
H(11B)-C(11A)-H(11C)	109.5
C(10B)-C(11B)-H(11D)	109.5
C(10B)-C(11B)-H(11E)	109.5
H(11D)-C(11B)-H(11E)	109.5
C(10B)-C(11B)-H(11F)	109.5
H(11D)-C(11B)-H(11F)	109.5
H(11E)-C(11B)-H(11F)	109.5
C(10A)-C(12A)-C(13A)	120.88(15)
C(10A)-C(12A)-H(12A)	119.6
C(13A)-C(12A)-H(12A)	119.6
C(10B)-C(12B)-C(13B)	120.53(15)
C(10B)-C(12B)-H(12B)	119.7
C(13B)-C(12B)-H(12B)	119.7
C(12A)-C(13A)-C(5A)	109.38(15)
C(12A)-C(13A)-H(13A)	109.8
C(5A)-C(13A)-H(13A)	109.8
C(12A)-C(13A)-H(13B)	109.8
C(5A)-C(13A)-H(13B)	109.8
H(13A)-C(13A)-H(13B)	108.2
C(12B)-C(13B)-C(5B)	109.95(13)
C(12B)-C(13B)-H(13C)	109.7
C(5B)-C(13B)-H(13C)	109.7
C(12B)-C(13B)-H(13D)	109.7
C(5B)-C(13B)-H(13D)	109.7
H(13C)-C(13B)-H(13D)	108.2
C(4A)-O(1A)-H(1A)	111.9(16)
C(4B)-O(1B)-H(1B)	109.7(17)

Symmetry transformations used to generate equivalent atoms:

Table 3.11 Anisotropic displacement parameters ($Å^2$x 10^3) for ***ent*-3.21.P**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1A)	35(1)	41(1)	52(1)	6(1)	29(1)	6(1)
C(1B)	41(1)	62(1)	43(1)	-4(1)	29(1)	-8(1)
C(2A)	30(1)	29(1)	35(1)	5(1)	18(1)	4(1)
C(2B)	35(1)	36(1)	31(1)	0(1)	18(1)	-2(1)
C(3A)	28(1)	25(1)	30(1)	4(1)	14(1)	4(1)
C(3B)	32(1)	28(1)	28(1)	3(1)	16(1)	1(1)
C(4A)	28(1)	24(1)	28(1)	5(1)	16(1)	3(1)
C(4B)	28(1)	25(1)	27(1)	2(1)	15(1)	0(1)
C(5A)	26(1)	36(1)	32(1)	2(1)	14(1)	2(1)
C(5B)	28(1)	33(1)	29(1)	4(1)	13(1)	0(1)
C(6A)	28(1)	34(1)	38(1)	5(1)	20(1)	4(1)
C(6B)	27(1)	33(1)	33(1)	5(1)	15(1)	-1(1)
C(7A)	33(1)	52(1)	52(1)	12(1)	25(1)	11(1)
C(7B)	32(1)	43(1)	46(1)	8(1)	17(1)	-7(1)
C(8A)	37(1)	41(1)	42(1)	7(1)	26(1)	4(1)
C(8B)	33(1)	42(1)	41(1)	7(1)	24(1)	5(1)
C(9A)	33(1)	28(1)	40(1)	3(1)	23(1)	3(1)
C(9B)	28(1)	25(1)	27(1)	3(1)	14(1)	-1(1)
C(10A)	33(1)	35(1)	55(1)	17(1)	27(1)	12(1)
C(10B)	32(1)	25(1)	35(1)	1(1)	19(1)	-3(1)
C(11A)	50(1)	37(1)	62(1)	11(1)	31(1)	8(1)
C(11B)	39(1)	26(1)	40(1)	2(1)	21(1)	1(1)
C(12A)	33(1)	53(1)	36(1)	15(1)	20(1)	14(1)
C(12B)	40(1)	30(1)	36(1)	-5(1)	18(1)	-5(1)
C(13A)	29(1)	59(1)	31(1)	3(1)	13(1)	6(1)
C(13B)	38(1)	40(1)	30(1)	-2(1)	13(1)	-6(1)
O(1A)	26(1)	30(1)	30(1)	8(1)	12(1)	0(1)
O(1B)	31(1)	23(1)	29(1)	4(1)	16(1)	1(1)

Table 3.12 Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for ***ent*-3.21.P**.

	x	y	z	U(eq)
H(1AA)	5969	5666	-466	59
H(1AB)	6932	5464	1061	59
H(1AC)	6687	6172	680	59
H(1BA)	2577	6248	6590	67

H(1BB)	3624	6138	8136	67
H(1BC)	3100	5574	7096	67
H(5A)	1708	5024	1183	36
H(5B)	8372	5947	7213	35
H(7AA)	-175	6328	231	64
H(7AB)	-304	6482	1679	64
H(7AC)	-774	5833	961	64
H(7BA)	8996	7207	4732	60
H(7BB)	9872	6957	6249	60
H(7BC)	8677	7417	6046	60
H(8AA)	667	5298	3094	54
H(8AB)	982	5964	3771	54
H(8AC)	2166	5515	3864	54
H(8BA)	7887	5702	4422	54
H(8BB)	9386	5915	5201	54
H(8BC)	8488	6222	3755	54
H(9A)	2890	6544	2968	37
H(9B)	6037	6601	3775	31
H(11A)	2032	7535	1355	70
H(11B)	2175	7509	-120	70
H(11C)	3441	7404	1278	70
H(11D)	5466	7815	3742	49
H(11E)	5069	8012	5014	49
H(11F)	4339	7450	4047	49
H(12A)	1526	6566	-1294	46
H(12B)	6665	7672	7206	41
H(13A)	1959	5463	-882	47
H(13B)	497	5607	-953	47
H(13C)	7454	6689	8373	43
H(13D)	8646	7011	8094	43
H(1A)	4600(30)	5460(11)	3660(30)	54(7)
H(1B)	6300(20)	5270(12)	5620(30)	54(7)

Table 3.13 Torsion angles [°] for ***ent*-3.21.P**.

O(1A)-C(4A)-C(5A)-C(13A)	-161.64(13)	C(9B)-C(4B)-C(5B)-C(13B)	82.87(13)
C(3A)-C(4A)-C(5A)-C(13A)	-36.13(19)	O(1B)-C(4B)-C(5B)-C(6B)	82.77(13)
C(9A)-C(4A)-C(5A)-C(13A)	83.81(14)	C(3B)-C(4B)-C(5B)-C(6B)	-149.00(14)
O(1A)-C(4A)-C(5A)-C(6A)	86.78(13)	C(9B)-C(4B)-C(5B)-C(6B)	-27.77(11)
C(3A)-C(4A)-C(5A)-C(6A)	-147.71(13)	C(13A)-C(5A)-C(6A)-C(7A)	37.8(2)
C(9A)-C(4A)-C(5A)-C(6A)	-27.76(11)	C(4A)-C(5A)-C(6A)-C(7A)	147.80(14)
O(1B)-C(4B)-C(5B)-C(13B)	-166.60(12)	C(13A)-C(5A)-C(6A)-C(8A)	164.40(14)
C(3B)-C(4B)-C(5B)-C(13B)	-38.37(18)	C(4A)-C(5A)-C(6A)-C(8A)	-85.64(15)

C(13A)-C(5A)-C(6A)-C(9A)	-82.14(14)	C(5B)-C(4B)-C(9B)-C(6B)	27.54(11)
C(4A)-C(5A)-C(6A)-C(9A)	27.82(11)	C(7B)-C(6B)-C(9B)-C(10B)	-38.82(18)
C(13B)-C(5B)-C(6B)-C(7B)	37.64(19)	C(8B)-C(6B)-C(9B)-C(10B)	-166.41(12)
C(4B)-C(5B)-C(6B)-C(7B)	147.08(14)	C(5B)-C(6B)-C(9B)-C(10B)	78.97(13)
C(13B)-C(5B)-C(6B)-C(8B)	163.90(14)	C(7B)-C(6B)-C(9B)-C(4B)	-145.18(14)
C(4B)-C(5B)-C(6B)-C(8B)	-86.66(14)	C(8B)-C(6B)-C(9B)-C(4B)	87.24(13)
C(13B)-C(5B)-C(6B)-C(9B)	-82.00(13)	C(5B)-C(6B)-C(9B)-C(4B)	-27.39(11)
C(4B)-C(5B)-C(6B)-C(9B)	27.44(11)	C(6A)-C(9A)-C(10A)-C(12A)	-47.15(19)
C(7A)-C(6A)-C(9A)-C(10A)	-38.3(2)	C(4A)-C(9A)-C(10A)-C(12A)	46.62(19)
C(8A)-C(6A)-C(9A)-C(10A)	-165.16(13)	C(6A)-C(9A)-C(10A)-C(11A)	132.31(16)
C(5A)-C(6A)-C(9A)-C(10A)	79.50(13)	C(4A)-C(9A)-C(10A)-C(11A)	-133.93(15)
C(7A)-C(6A)-C(9A)-C(4A)	-145.34(15)	C(4B)-C(9B)-C(10B)-C(12B)	48.45(17)
C(8A)-C(6A)-C(9A)-C(4A)	87.83(14)	C(6B)-C(9B)-C(10B)-C(12B)	-45.33(18)
C(5A)-C(6A)-C(9A)-C(4A)	-27.51(11)	C(4B)-C(9B)-C(10B)-C(11B)	-127.52(14)
O(1A)-C(4A)-C(9A)-C(10A)	169.81(13)	C(6B)-C(9B)-C(10B)-C(11B)	138.70(14)
C(3A)-C(4A)-C(9A)-C(10A)	40.47(19)	C(11A)-C(10A)-C(12A)-C(13A)	-179.14(16)
C(5A)-C(4A)-C(9A)-C(10A)	-81.02(14)	C(9A)-C(10A)-C(12A)-C(13A)	0.3(2)
O(1A)-C(4A)-C(9A)-C(6A)	-81.39(14)	C(11B)-C(10B)-C(12B)-C(13B)	175.34(15)
C(3A)-C(4A)-C(9A)-C(6A)	149.27(14)	C(9B)-C(10B)-C(12B)-C(13B)	-0.4(2)
C(5A)-C(4A)-C(9A)-C(6A)	27.77(11)	C(10A)-C(12A)-C(13A)-C(5A)	-0.3(2)
O(1B)-C(4B)-C(9B)-C(10B)	164.42(12)	C(4A)-C(5A)-C(13A)-C(12A)	-48.10(17)
C(3B)-C(4B)-C(9B)-C(10B)	38.48(17)	C(6A)-C(5A)-C(13A)-C(12A)	48.05(17)
C(5B)-C(4B)-C(9B)-C(10B)	-82.75(13)	C(10B)-C(12B)-C(13B)-C(5B)	-1.4(2)
O(1B)-C(4B)-C(9B)-C(6B)	-85.29(13)	C(4B)-C(5B)-C(13B)-C(12B)	-45.59(17)
C(3B)-C(4B)-C(9B)-C(6B)	148.77(14)	C(6B)-C(5B)-C(13B)-C(12B)	49.85(17)

Symmetry transformations used to generate equivalent atoms:

3.10.4 Computational Data for Chapter 3

Computational Details

All calculations were conducted using DFT[22] implemented in the Gaussian 09 suite[23] of ab initio quantum chemistry programs with Becke's three-parameter exchange functional B3LYP including Grimme's D3 dispersion correction.[24–29] Geometry optimizations were conducted using Pople's 6-31G(d,p) basis set[30–35] for the main group elements. Copper was calculated using the Los Alamos ECP plus DZ basis (LANL2DZ)[36] that includes relativistic effective core potentials. The energies of the optimized structures were reevaluated by additional single point calculations on each optimized geometry using the same functional and Pople's 6-311++G(d,p) basis set.[37–40] Bromine was calculated using Stuttgart group effective core potential SDD.[41] Solvation effects were adopted at the same level of single-point calculations and at the self-consistent reaction field polarizable continuum model (IEF-PCM) with the dielectric constant of 7.4257 for tetrahydrofuran.[42] The Gibbs free energies were computed with the following equations.

$$G(sol) = e(sol) + G(corr) \quad (1)$$

$$G(corr) = H(corr) – TS(tot) \quad (2)$$

$$H(corr) = E(tot) + k_B T \quad (3)$$

$$E(tot) = E(t)+E(r)+E(v)+E(e) \quad (4)$$

$$S(tot) = S(t)+S(r)+S(v)+S(e) \quad (5)$$

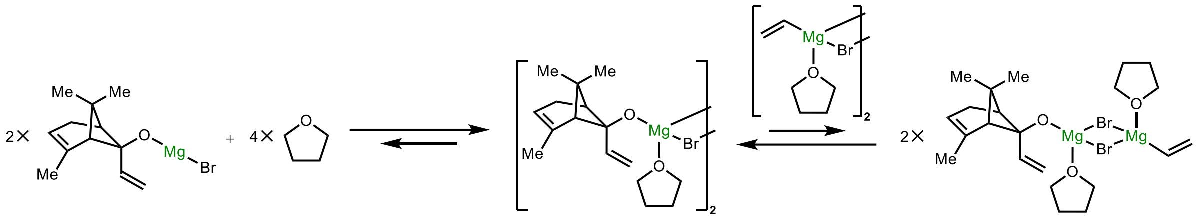
$$\Delta E(SCF) = \Sigma E(SCF) \text{ for products} – \Sigma E(SCF) \text{ for reactants} \quad (6)$$

$$\Delta G(sol) = \Sigma G(sol) \text{ for products} – \Sigma G(sol) \text{ for reactants} \quad (7)$$

E(sol) is the electronic energy in solution phase computed from the SCF (self-consistent field) procedure with the IEF-PCM calculations; G(sol) is the free energy in solution phase; G(corr) is the thermal correction to the free energy; T is the temperature (293.15 K); S(tot) is the entropy; E(tot) is the total internal thermal energy; E(t), E(r), E(v), and E(e) are the internal thermal energies from translation, rotation, vibration, and electronic motions, respectively; S(t), S(r), S(v), and S(e) are the entropies from translation, rotation, vibration, and electronic motions, respectively; The entropy we refer to is specifically of the solute(s), and the entropy of the solvent is implicitly comprised in the continuum solvation model.

Free Energy Calculations of Schlenk Equilibrium Intermediates

On the basis of the detailed study of the Schlenk equilibrium of the Grignard reagent reported by Cascella and colleagues,[6] we conducted free energy calculations to look into the relative free energy of magnesium vinylchrysanthenolate bromide monomer (**3.49**), dimer 3.21.V', and **3.50**, which were hypothesized as the active intermediates in the rearrangement. In good agreement with the previous work and as shown in Figure S5, dimer **3.21.V’** was calculated to be 23.3 kcal/mol more stable than monomer **3.50**. Additionally, the asymmetric magnesium dimer **3.51** is 1.9 kcal/mol higher in energy than **3.21.V’**. We concluded that **3.21.V’** is likely the most abundant intermediate en route to the 1,3 rearrangement, and therefore employed **3.21.V’** as a representative model for our calculations.



3.50+4THF
(ΔG = 23.25 kcal/mol)

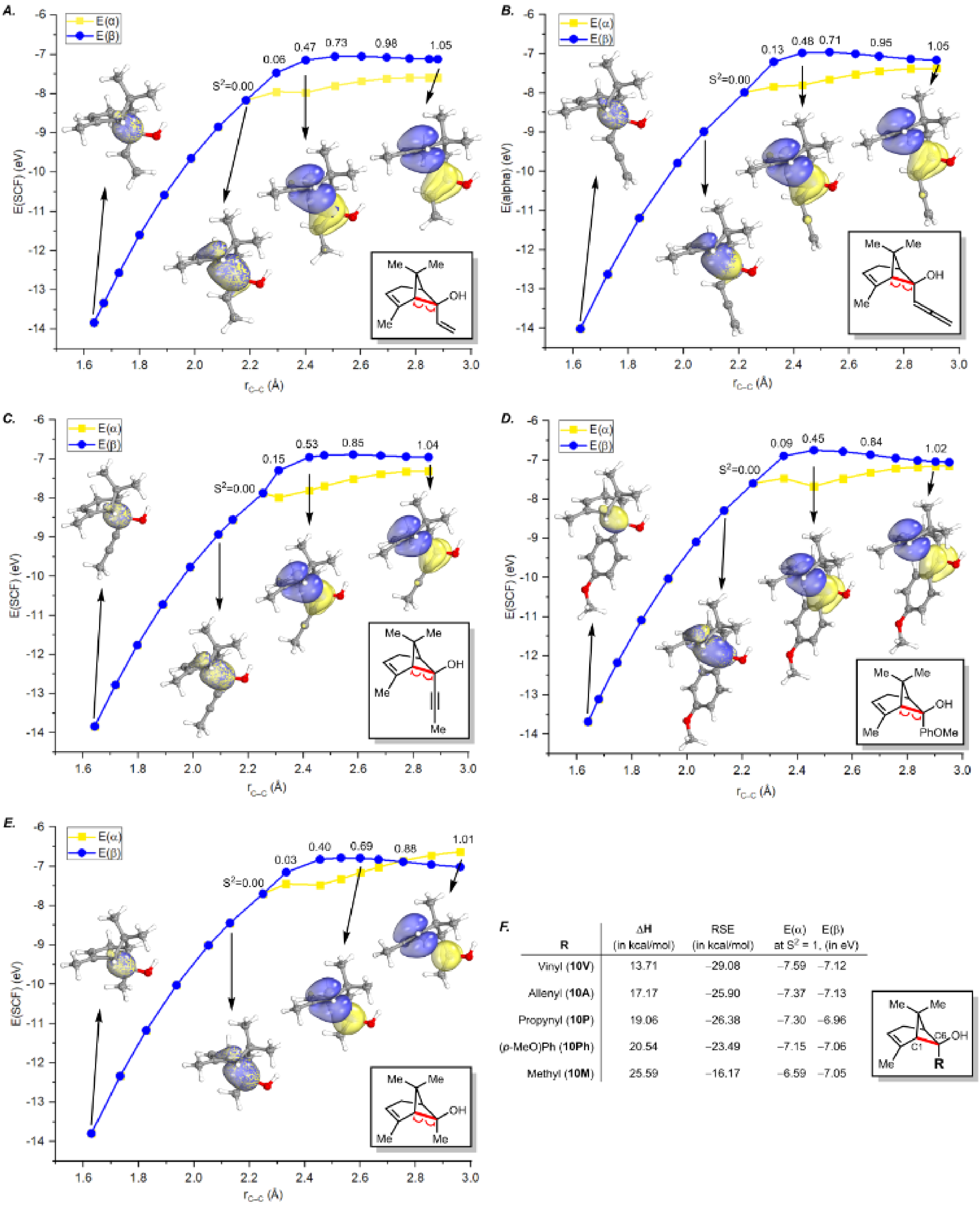
3.21.V'
(ΔG = 0.00 kcal/mol)

2 **3.51**
(ΔG = 1.89 kcal/mol)

Figure 3.26 Relative free energy of **3.50**, **3.21.V’**, and **3.51**. B3LYP-D3/6-311++G**/SDD level of theory. Single point: B3LYP-D3/6-31G**/LANL2DZ. ε=7.4257 for THF.

Intrinsic Bond Orbital Calculations

Intrinsic bond orbital (IBO) calculations of all other intermediates have been conducted. The results are shown in Figure 3.27.



R	ΔH (in kcal/mol)	RSE (in kcal/mol)	E(α) at S^2 = 1, (in eV)	E(β)
Vinyl (**10V**)	13.71	–29.08	–7.59	–7.12
Allenyl (**10A**)	17.17	–25.90	–7.37	–7.13
Propynyl (**10P**)	19.06	–26.38	–7.30	–6.96
(*p*-MeO)Ph (**10Ph**)	20.54	–23.49	–7.15	–7.06
Methyl (**10M**)	25.59	–16.17	–6.59	–7.05

Figure 3.27 Intrinsic bond orbital (IBO) profile of (a) **3.21.V**, (b) **3.21.A**, (c) **3.21.P**, (d) **3.21.Ph**, and (e) **3.21.M** along the intrinsic reaction coordinate for the formation of the diradical (**3.21**→**3.32**). (f) Computed ΔH, RSE, E(α), and E(β) values depending on the functional groups, R. E(α) and E(β) represent the energy of the two radicals associated with the diradical intermediate. Orbital energies were reevaluated by IBO exponent 2 orbital localization method based on the DFT calculation results using B3LYP-D3/def2TZVP level of theory.

Table 3.14 Computed energy components for structures along intrinsic reaction coordinates of C–C homolysis. Numbers in names represent C1–C6 bond length.

	E(α)/(eV)	E(β)/(eV)	S^2
	B3LYP-D3/def2TZVP//IBO exponent 2 orbital localization	B3LYP-D3/def2TZVP//IBO exponent 2 orbital localization	
3.21.V_1.635	-13.83	-13.83	0.00
3.21.V_1.670	-13.33	-13.33	0.00
3.21.V_1.725	-12.56	-12.56	0.00
3.21.V_1.800	-11.59	-11.59	0.00
3.21.V_1.889	-10.58	-10.58	0.00
3.21.V_1.986	-9.65	-9.65	0.00
3.21.V_2.084	-8.85	-8.85	0.00
3.21.V_2.185	-8.17	-8.17	0.00
3.21.V_2.294	-7.95	-7.47	0.06
3.21.V_2.401	-7.97	-7.15	0.47
3.21.V_2.506	-7.80	-7.05	0.73
3.21.V_2.603	-7.68	-7.05	0.89
3.21.V_2.694	-7.61	-7.07	0.98
3.21.V_2.776	-7.59	-7.10	1.02
3.21.V_2.847	-7.59	-7.12	1.05
3.21.V_2.879	-7.59	-7.12	1.05
3.21.A_1.626	-14.01	-14.01	0.00
3.21.A_1.725	-12.62	-12.62	0.00
3.21.A_1.840	-11.19	-11.19	0.00

3.21.A_1.978	-9.79	-9.79	0.00
3.21.A_2.074	-8.99	-8.99	0.00
3.21.A_2.221	-7.98	-7.98	0.00
3.21.A_2.327	-7.84	-7.21	0.13
3.21.A_2.430	-7.80	-6.98	0.48
3.21.A_2.529	-7.65	-6.96	0.71
3.21.A_2.623	-7.52	-7.00	0.86
3.21.A_2.709	-7.44	-7.06	0.95
3.21.A_2.824	-7.38	-7.13	1.03
3.21.A_2.917	-7.37	-7.16	1.05
3.21.P_1.642	-13.84	-13.84	0.00
3.21.P_1.718	-12.78	-12.78	0.00
3.21.P_1.797	-11.76	-11.76	0.00
3.21.P_1.889	-10.72	-10.72	0.00
3.21.P_1.989	-9.76	-9.76	0.00
3.21.P_2.091	-8.93	-8.93	0.00
3.21.P_2.144	-8.55	-8.55	0.00
3.21.P_2.253	-7.87	-7.87	0.00
3.21.P_2.310	-7.98	-7.30	0.15
3.21.P_2.421	-7.81	-6.96	0.53
3.21.P_2.476	-7.70	-6.90	0.66
3.21.P_2.581	-7.51	-6.89	0.85
3.21.P_2.681	-7.38	-6.91	0.96

3.21.P_2.773	-7.32	-6.94	1.01
3.21.P_2.854	-7.30	-6.96	1.03
3.21.Ph_1.640	-13.68	-13.68	0.00
3.21.Ph_1.680	-13.11	-13.11	0.00
3.21.Ph_1.750	-12.17	-12.17	0.00
3.21.Ph_1.830	-11.09	-11.09	0.00
3.21.Ph_1.930	-10.04	-10.04	0.00
3.21.Ph_2.030	-9.09	-9.09	0.00
3.21.Ph_2.130	-8.29	-8.29	0.00
3.21.Ph_2.240	-7.6	-7.6	0.00
3.21.Ph_2.350	-7.47	-6.9	0.09
3.21.Ph_2.450	-7.67	-6.75	0.45
3.21.Ph_2.570	-7.47	-6.78	0.69
3.21.Ph_2.670	-7.32	-6.87	0.84
3.21.Ph_2.760	-7.21	-6.95	0.94
3.21.Ph_2.840	-7.18	-7.01	1.00
3.21.Ph_2.900	-7.16	-7.04	1.02
3.21.Ph_2.950	-7.15	-7.06	1.04
3.21.M_1.629	-13.79	-13.79	0.00
3.21.M_1.733	-12.33	-12.33	0.00
3.21.M_1.827	-11.17	-11.17	0.00
3.21.M_1.936	-10.02	-10.02	0.00
3.21.M_2.052	-9.01	-9.01	0.00

3.21.M_2.129	-8.44	-8.44	0.00
3.21.M_2.249	-7.70	-7.70	0.00
3.21.M_2.333	-7.45	-7.15	0.03
3.21.M_2.455	-7.47	-6.82	0.40
3.21.M_2.531	-7.32	-6.78	0.57
3.21.M_2.600	-7.16	-6.79	0.69
3.21.M_2.667	-7.02	-6.82	0.78
3.21.M_2.755	-6.86	-6.88	0.88
3.21.M_2.857	-6.72	-6.96	0.96
3.21.M_2.962	-6.63	-7.02	1.01

Detailed MO Diagram for the Oxy-Cope Rearrangement

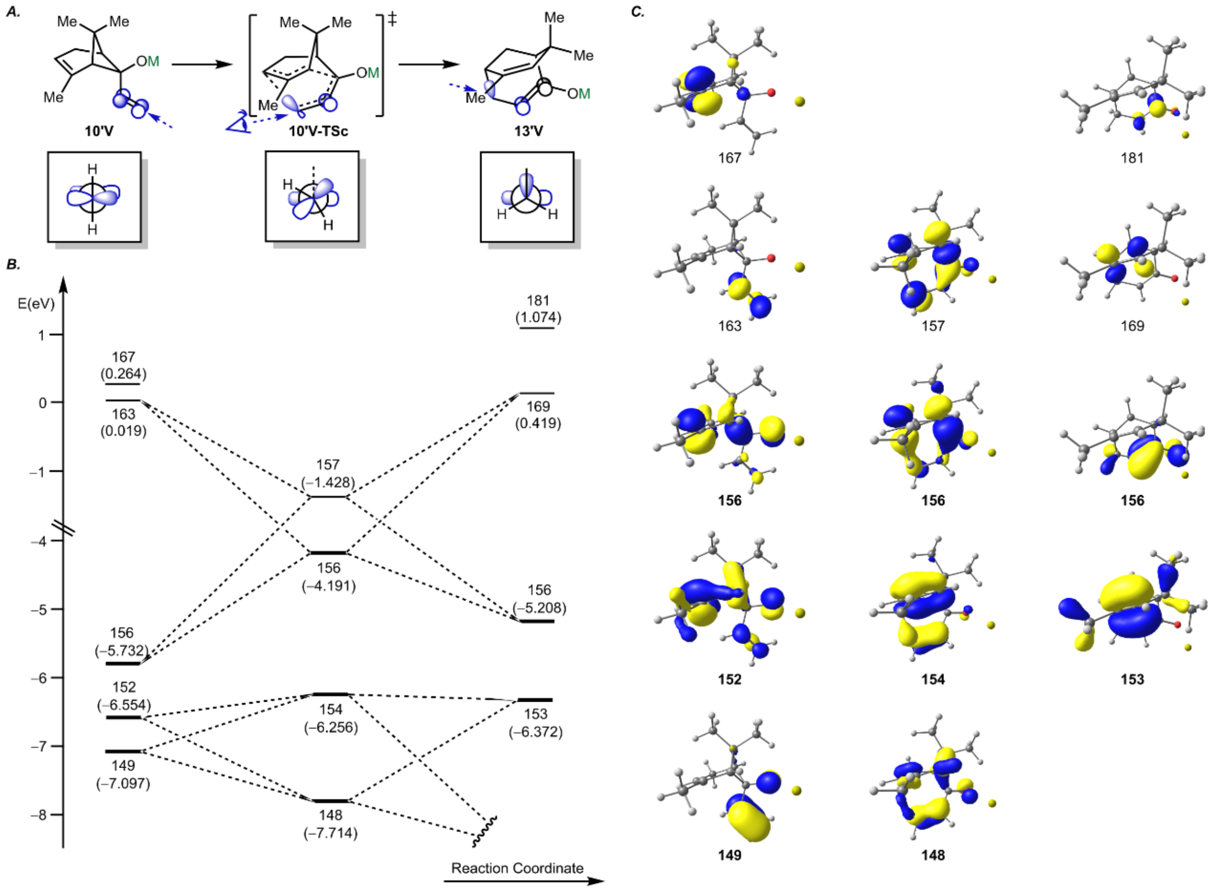


Figure 3.28 (a) Reaction scheme and Newman projection of the oxy-Cope rearrangement of **3.21.V'**. (b) MO diagram of (a) along the reaction coordinate. (c) Isodensity surface plots of the molecular orbitals shown in (b). Unnecessary fragments which have no contribution to FMOs are omitted for clarity. Bold and normal represent filled and unfilled orbitals, respectively. Isodensity value = 0.05 a.u.

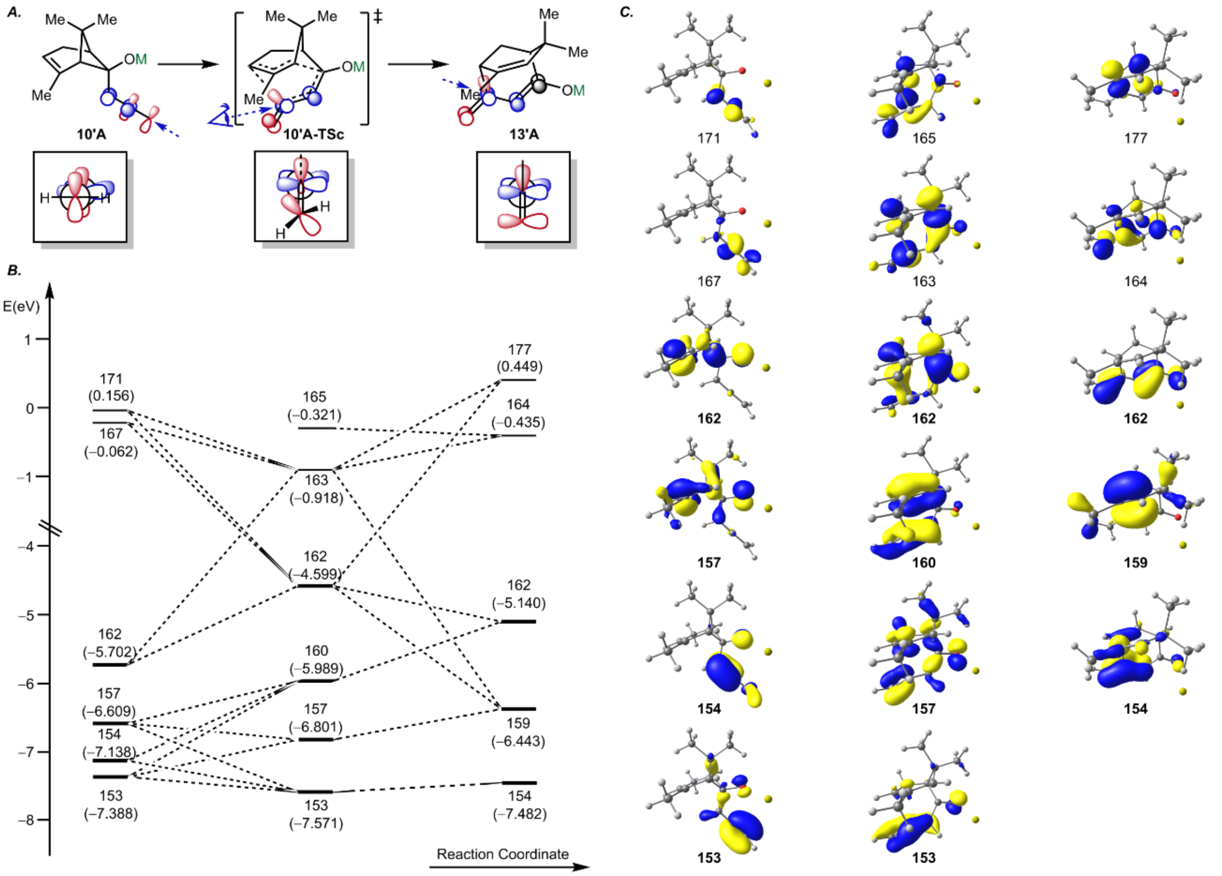


Figure 3.29 (a) Reaction scheme and Newman projection of the oxy-Cope rearrangement of **3.21.A'**. (b) MO diagram of (a) along the reaction coordinate. (c) Isodensity surface plots of the molecular orbitals shown in (b). Unnecessary fragments which have no contribution to FMOs are omitted for clarity. Bold and normal represent filled and unfilled orbitals, respectively. Isodensity value = 0.05 a.u.

DFT-optimized structure's energy components

Table 3.15 Computed energy components for optimized structures

	E(sol)(SCF)/(Hartree)	E(gas)(SCF)/(Hartree)	Thermal Correction to G/(Hartree)	Thermal Correction to H/(Hartree)
	B3LYP-D3/6-311++G(d,p)/SDD	B3LYP-D3/6-311++G(d,p)/SDD	B3LYP-D3/6-31G(d,p)/LANL2DZ	B3LYP-D3/6-31G(d,p)/LANL2DZ
3.21.V'	-1978.127150		0.682738	
3.21.V'-TSc	-1978.093407		0.684404	
3.29.V'	-1978.187895		0.689585	
^{cs}3.21.V'-TS	-1978.096154		0.688032	
^{cs}3.31.V'	-1978.141084		0.683914	
3.21.V'-TS	-1978.097329		0.681571	
3.31.V'	-1978.114768		0.677769	
3.31.V'-TS	-1978.100118		0.681356	
3.29.V'	-1978.131438		0.683934	
3.21.A'	-2054.289731		0.687284	
3.21.A'-TSc	-2054.260264		0.688409	
3.48.A'	-2054.382597		0.697085	
3.21.A'-TS	-2054.260643		0.689792	
3.49.A'	-2054.271970		0.688692	
CH_4		-40.5341158		0.048804
CH_3 radical		-39.8552997		0.033782
3.21.V		-543.445307		0.287489

3.32.V		-543.420800		0.284836
3.21.A		-581.524283		0.292402
3.32.A		-581.494333		0.289821
3.21.P		-581.525211		0.293236
3.32.P		-581.492292		0.290692
3.21.Ph		-811.704865		0.372835
3.32.Ph		-811.670026		0.370733
3.21.M		-505.355727		0.281539
3.32.M		-505.312089		0.278677
$((C_2H_3)(THF)MgBr)_2$	-1048.350016		0.261954	
3.50	-756.481761		0.219104	
THF	-232.529459		0.088439	
3.51	-1513.23689		0.472156	

Table 3.16 Cartesian coordinates of the optimized geometries

The cartesian coordinates of optimized geometries are given below in the standard XYZ format, and units are in Å.

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3.21.V’

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C	3.739716	-0.947911	-0.388285
C	3.347860	-1.785403	0.901830
C	5.705933	-2.547778	-0.228701
C	4.869975	-3.568546	0.016127
C	3.514342	-3.296405	0.640547
C	5.228114	-1.159689	0.161391
C	4.627854	-1.218720	1.621610
O	3.312243	0.364912	-0.322333
C	3.423248	-1.528129	-1.751546
C	2.777788	-0.868781	-2.718029
C	7.059281	-2.692883	-0.859797

C	4.448889	0.161662	2.283622
C	5.307068	-2.104826	2.676705
H	2.372086	-1.544969	1.342255
H	5.140013	-4.594433	-0.226977
H	2.712221	-3.652064	-0.023541
H	3.398909	-3.863980	1.575193
H	5.946143	-0.367244	-0.074457
H	3.765084	-2.538124	-1.950865
H	2.588419	-1.331784	-3.683115
H	2.432300	0.149273	-2.577180
H	7.294115	-3.736054	-1.092621
H	7.117501	-2.110581	-1.788976
H	7.843493	-2.302597	-0.197802
H	3.634600	0.126492	3.018333
H	5.362652	0.439749	2.822347
H	4.229963	0.942919	1.561695
H	6.282684	-1.683277	2.946372
H	4.698440	-2.123687	3.588929
H	5.474112	-3.132937	2.358501
Mg	1.792847	1.294942	0.159661
Br	0.095377	0.651310	1.994000
C	-4.556295	0.406955	-0.155215
C	-5.771475	0.759144	0.799141
C	-5.871887	-1.770676	-0.226053
C	-7.012847	-1.080554	-0.375851
C	-7.104772	0.342007	0.142904
C	-4.732111	-1.056993	0.476181
C	-5.285995	-0.364502	1.787460
O	-3.386457	1.039350	0.226289
C	-4.766151	0.559000	-1.649201
C	-4.038865	1.370121	-2.424214
C	-5.669079	-3.178450	-0.705943
C	-4.201336	0.085406	2.781831
C	-6.338323	-1.113468	2.619282
H	-5.789668	1.791650	1.164299
H	-7.881679	-1.520270	-0.862459
H	-7.347714	1.030990	-0.678462
H	-7.930536	0.429588	0.864126
H	-3.819820	-1.662247	0.556599
H	-5.557730	-0.027272	-2.104801
H	-4.227837	1.449933	-3.491412
H	-3.252193	1.990986	-2.006955
H	-6.575837	-3.590722	-1.159345
H	-4.866233	-3.229168	-1.454603
H	-5.367320	-3.836052	0.119891
H	-4.666449	0.608379	3.626524
H	-3.679954	-0.790579	3.189329
H	-3.472755	0.750725	2.329264
H	-5.858244	-1.914352	3.194916
H	-6.796364	-0.426979	3.341267
H	-7.135548	-1.564193	2.029095
Mg	-1.624998	0.537395	0.035395
Br	-0.027415	1.776655	-1.643701
C	-0.812520	-2.366342	-2.706734
C	0.068860	-3.031394	-1.638201
C	0.026075	-2.008143	-0.509142

O	-1.278779	-1.348583	-0.631863
C	-1.939341	-1.782523	-1.866769
H	-0.257307	-1.563128	-3.202557
H	1.094445	-3.194226	-1.973894
H	0.801494	-1.251390	-0.650304
H	-2.447802	-0.916962	-2.297062
H	0.096685	-2.421529	0.497648
H	-0.361046	-3.986837	-1.319180
H	-1.179343	-3.063326	-3.464272
H	-2.686646	-2.533906	-1.592112
C	3.378304	4.548512	-1.098712
C	2.325501	5.372224	-0.331335
C	1.635832	4.335207	0.575425
O	2.495261	3.149227	0.548549
C	3.772601	3.496376	-0.073575
H	2.929784	4.062206	-1.971103
H	1.611964	5.865383	-0.995101
H	0.658596	4.024814	0.200269
H	4.186772	2.568380	-0.472351
H	1.542514	4.660466	1.614408
H	2.813639	6.142955	0.273021
H	4.227647	5.149205	-1.433484
H	4.433308	3.897698	0.703941

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3.21.V’-TSc

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C	-6.454960	-1.607145	-0.519060
C	-4.211951	-0.052779	-1.910812
C	-5.107826	-0.701298	-2.712271
C	3.453011	-1.043504	0.546223
C	4.456409	-0.934140	-0.678951
C	4.807858	-3.166493	0.839747
C	5.942176	-2.489889	0.604835
C	5.902716	-1.220679	-0.225895
C	3.534914	-2.606743	0.227539
C	3.811453	-2.237004	-1.284491
O	2.213109	-0.493453	0.274997
C	3.928936	-0.592890	1.913851
C	3.235140	0.212698	2.724833
C	4.719142	-4.418548	1.661340
C	2.540638	-2.007864	-2.121957
C	4.709217	-3.158240	-2.123835
H	4.381865	-0.008244	-1.267368
H	6.897527	-2.827689	1.001421
H	6.287147	-0.371345	0.358271
H	6.568556	-1.309856	-1.096359
H	2.644162	-3.196116	0.468169
H	4.886436	-0.968534	2.257677
H	5.695852	-4.728517	2.044935
H	4.043991	-4.273883	2.515346
H	4.302464	-5.245318	1.071119
H	2.786069	-1.449222	-3.034017
H	2.123575	-2.972708	-2.436348
H	1.773848	-1.462350	-1.581556
H	4.181360	-4.093263	-2.345391

H	4.935324	-2.678945	-3.083894
H	5.651466	-3.421359	-1.645107
Mg	1.657435	1.149458	-0.366093
Br	0.044731	2.467906	1.259105
Mg	-1.609179	1.238628	-0.309298
Br	0.017921	1.332791	-2.362724
C	-0.594412	-2.922791	0.063311
C	-0.812056	-2.586018	1.547183
C	-0.650072	-1.068515	1.578436
O	-1.066218	-0.616848	0.240689
C	-1.286302	-1.766086	-0.643149
H	0.472015	-2.918540	-0.173313
H	-0.085387	-3.074209	2.201735
H	0.394124	-0.774924	1.693211
H	-0.854674	-1.511840	-1.613444
H	-1.287729	-0.561537	2.304715
H	-1.816883	-2.880981	1.865084
H	-1.022175	-3.886482	-0.224120
H	-2.367223	-1.900123	-0.729927
C	3.717861	3.819515	1.170576
C	2.869607	4.763658	0.277460
C	2.594029	3.945162	-1.000636
O	3.042986	2.586070	-0.702302
C	4.168673	2.719434	0.214880
H	4.563345	4.324623	1.643401
H	3.408361	5.682571	0.032804
H	3.171531	4.297912	-1.860764
H	5.050511	2.999640	-0.373221
H	1.540601	3.879559	-1.276454
H	1.937220	5.035213	0.775487
H	3.096753	3.379617	1.955834
H	4.325341	1.748880	0.686444
C	-4.386383	0.629816	-0.663602
C	-5.647691	0.664133	0.228895
C	-5.316497	-2.109089	0.069726
C	-6.835647	-0.150508	-0.336933
C	-4.508462	-1.271764	0.876537
C	-5.153653	-0.047855	1.526624
O	-3.465807	1.520600	-0.339837
C	-4.821524	-3.490728	-0.293866
C	-4.141061	0.752650	2.365597
C	-6.298125	-0.426026	2.500829
H	-5.946905	1.709726	0.385031
H	-7.121004	-2.253968	-1.082774
H	-7.169701	0.293845	-1.282933
H	-7.698297	-0.039038	0.335285
H	-3.643570	-1.710226	1.372514
H	-3.168449	-0.067662	-2.236320
H	-4.305307	-3.975389	0.542915
H	-5.642066	-4.142393	-0.610136
H	-4.115887	-3.433401	-1.134525
H	-4.578509	1.694701	2.714145
H	-3.858813	0.166070	3.248844
H	-3.231884	1.000702	1.825041
H	-5.879095	-0.924848	3.381747
H	-6.835733	0.466709	2.845498

H	-7.015130	-1.115935	2.054347
H	-4.736288	-1.265663	-3.564018
H	-6.172914	-0.561242	-2.675094
H	2.256540	0.595264	2.451368
H	3.622233	0.495516	3.699883

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3.29.V’

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Mg	1.195997	1.113976	0.688130
Br	-0.378413	1.984194	2.567917
C	-4.432672	-0.465595	0.336895
C	-4.110599	-0.734114	-1.195445
C	-6.629993	-1.441056	-0.452913
C	-5.977740	-2.399643	-1.128691
C	-4.559196	-2.149760	-1.607525
C	-5.889899	-0.133441	-0.224325
C	-5.214393	0.318919	-1.578995
O	-3.774440	0.645563	0.847111
C	-4.329599	-1.619938	1.318395
C	-3.864669	-1.490213	2.564930
C	-8.022260	-1.583281	0.087161
C	-4.734923	1.781523	-1.582135
C	-5.971991	0.112993	-2.898760
H	-3.082125	-0.516247	-1.519551
H	-6.440617	-3.361809	-1.339188
H	-3.874916	-2.899971	-1.181437
H	-4.492094	-2.273233	-2.698181
H	-6.463263	0.604327	0.344970
H	-4.693418	-2.590952	1.001158
H	-3.832222	-2.334442	3.248390
H	-3.542798	-0.523014	2.940368
H	-8.453470	-2.562603	-0.142067
H	-8.028571	-1.449217	1.176947
H	-8.682886	-0.809511	-0.325491
H	-3.973644	1.924098	-2.359486
H	-5.574742	2.446438	-1.817597
H	-4.316225	2.080199	-0.625502
H	-6.807235	0.820331	-2.963181
H	-5.304555	0.322895	-3.743370
H	-6.381904	-0.887958	-3.029552
Mg	-1.934792	0.846132	0.786968
Br	-0.507803	1.733419	-1.233934
C	0.008387	-3.017148	0.310907
C	-0.589953	-2.986799	1.724554
C	-0.415930	-1.527556	2.107571
O	-0.671262	-0.793303	0.853375
C	-0.484710	-1.707712	-0.293912
H	1.100317	-3.013857	0.354582
H	-0.078883	-3.654611	2.422831
H	0.609508	-1.297137	2.403463
H	0.231290	-1.245989	-0.972216
H	-1.129010	-1.161514	2.845415
H	-1.655336	-3.236921	1.704320
H	-0.318176	-3.878765	-0.276886
H	-1.459098	-1.808948	-0.777217

C	3.059122	3.230291	-1.787052
C	2.179880	4.387177	-1.246276
C	1.934631	4.028082	0.234198
O	2.465904	2.679377	0.408719
C	3.577189	2.546200	-0.526451
H	2.446906	2.522871	-2.352998
H	1.237926	4.450247	-1.794092
H	0.881967	3.995221	0.517360
H	3.789445	1.481895	-0.642457
H	2.474794	4.685877	0.922380
H	2.688055	5.351725	-1.325868
H	3.871152	3.575384	-2.431530
H	4.445792	3.056282	-0.093186
C	2.994025	-1.050787	-0.156307
C	3.956716	-2.092073	0.404936
C	6.072303	-1.453600	-1.409458
C	4.909741	-2.314498	-1.880787
C	4.311593	-3.098493	-0.703244
C	6.204787	-1.094272	-0.125689
C	5.265258	-1.475505	1.001954
O	2.226106	-0.450164	0.755502
C	2.928984	-0.793249	-1.485883
C	3.788639	-1.464794	-2.526398
C	7.059805	-1.028844	-2.466005
C	5.966503	-2.514161	1.912487
C	4.978160	-0.231361	1.869455
H	3.423817	-2.591596	1.224539
H	5.288637	-3.013581	-2.638788
H	3.410191	-3.632612	-1.027276
H	5.020974	-3.849661	-0.343557
H	7.064245	-0.488995	0.167554
H	2.191054	-0.070023	-1.836501
H	3.174940	-2.117982	-3.167309
H	4.224814	-0.717823	-3.204493
H	6.563046	-0.493080	-3.285364
H	7.838204	-0.376050	-2.059831
H	7.548818	-1.901571	-2.919191
H	6.909673	-2.110922	2.297377
H	5.333197	-2.763222	2.772243
H	6.200752	-3.438395	1.377910
H	4.280100	-0.472985	2.676448
H	5.909613	0.136458	2.315679
H	4.535424	0.577683	1.288032

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^{cs}3.21.V'-TS

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Br	-0.449724	0.063141	2.006836
C	4.110066	0.534253	0.179155
C	3.840131	-0.968188	-0.263991
C	6.476079	-0.327800	-0.048673
C	6.161389	-0.935962	-1.202648
C	4.726310	-1.354838	-1.464401
C	5.348169	-0.114009	0.947637
C	4.510287	-1.447769	1.076183
O	3.141414	1.034576	1.036238

C	4.431223	1.559229	-0.894480
C	4.033458	2.834478	-0.844339
C	7.850746	0.156508	0.306850
C	3.572471	-1.477274	2.295028
C	5.247113	-2.795341	1.069338
H	2.787321	-1.222463	-0.435454
H	6.912873	-1.127665	-1.966517
H	4.345168	-0.876079	-2.378019
H	4.670015	-2.437917	-1.651506
H	5.660755	0.395801	1.864400
H	5.038276	1.242851	-1.735091
H	4.295229	3.540423	-1.627941
H	3.467025	3.209892	0.003040
H	8.577591	-0.052463	-0.484357
H	7.842116	1.239175	0.490079
H	8.204629	-0.313337	1.234070
H	2.852917	-2.300686	2.196045
H	4.155044	-1.665747	3.205514
H	3.027265	-0.546481	2.417487
H	5.761624	-2.945997	2.025854
H	4.522553	-3.612396	0.960639
H	5.990108	-2.894331	0.278472
Mg	1.361139	1.267283	0.566211
Br	0.433905	0.332425	-1.680958
C	-0.818499	3.952278	-1.246338
C	-1.548683	4.210906	0.091121
C	-0.578666	3.674392	1.165462
O	0.577726	3.147880	0.440971
C	0.641864	3.853732	-0.833595
H	-1.141567	2.995245	-1.661841
H	-2.500646	3.679340	0.114076
H	-0.980267	2.851112	1.754566
H	1.273582	3.267184	-1.501850
H	-0.218019	4.459859	1.837164
H	-1.733774	5.277477	0.247225
H	-0.989408	4.740091	-1.984426
H	1.105508	4.832357	-0.658236
C	0.562242	-3.368627	-1.389736
C	0.579836	-3.363924	0.162719
C	-0.888686	-3.193903	0.538666
O	-1.412619	-2.348652	-0.524013
C	-0.859747	-2.899833	-1.753715
H	1.310071	-2.679611	-1.786471
H	1.146649	-2.508326	0.535610
H	-1.065458	-2.685189	1.485164
H	-0.897177	-2.111992	-2.504287
H	-1.442668	-4.140381	0.520332
H	1.012697	-4.271878	0.589399
H	0.757272	-4.362918	-1.799836
H	-1.508215	-3.729590	-2.058202
C	-3.827150	0.546329	-0.946347
C	-5.148475	0.832680	-0.200499
C	-4.898465	-1.907612	0.206074
C	-6.004611	-1.519878	-0.468711
C	-6.306209	-0.052966	-0.708674
C	-3.998140	-0.891536	0.799367

C	-4.753305	0.389602	1.239499
O	-2.807445	1.332739	-0.775925
C	-3.770635	-0.314818	-2.165211
C	-2.918469	-0.041307	-3.166977
C	-4.522103	-3.361871	0.332461
C	-3.857838	1.411809	1.960760
C	-5.942561	0.130870	2.188507
H	-5.393327	1.898547	-0.300631
H	-6.683532	-2.256678	-0.892322
H	-6.477312	0.131202	-1.778420
H	-7.238122	0.245596	-0.208301
H	-3.330904	-1.313926	1.565593
H	-4.427151	-1.175053	-2.210788
H	-2.856367	-0.681498	-4.041707
H	-2.273612	0.830218	-3.131163
H	-5.301013	-4.021295	-0.061621
H	-3.596492	-3.558784	-0.221114
H	-4.334227	-3.636159	1.378023
H	-4.439630	2.310931	2.197872
H	-3.490425	0.988983	2.901731
H	-2.999391	1.719387	1.371855
H	-5.563618	-0.162129	3.174020
H	-6.536155	1.043648	2.322022
H	-6.604414	-0.664109	1.843870
Mg	-1.763402	-0.318872	-0.234619

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^{cs}3.31.V’

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Br	-0.177688	0.152523	2.449989
C	3.733812	0.639683	-0.162247
C	3.205013	-0.859508	-0.233510
C	5.827102	-0.568136	-0.878729
C	5.128996	-1.287335	-1.771191
C	3.649403	-1.537663	-1.542763
C	5.075840	-0.058361	0.341395
C	4.199548	-1.227220	0.931990
O	3.103482	1.399135	0.813867
C	3.849104	1.448898	-1.445161
C	3.778924	2.782562	-1.469073
C	7.278730	-0.219437	-1.023320
C	3.658161	-0.952249	2.344751
C	4.802369	-2.640698	0.969935
H	2.131520	-0.992383	-0.045763
H	5.596355	-1.683655	-2.670730
H	3.058154	-1.147752	-2.384507
H	3.443161	-2.619389	-1.509009
H	5.695737	0.528131	1.026729
H	4.034516	0.923802	-2.375461
H	3.894068	3.342147	-2.393424
H	3.632287	3.340119	-0.549140
H	7.716288	-0.643433	-1.932619
H	7.407075	0.870709	-1.054390
H	7.856580	-0.577348	-0.161094
H	2.802701	-1.606776	2.554735
H	4.432993	-1.173018	3.089342

H	3.337332	0.077757	2.467404
H	5.632370	-2.664400	1.686317
H	4.057218	-3.362522	1.325780
H	5.188965	-2.992059	0.013706
Mg	1.245263	1.548446	0.860540
Br	-0.128060	1.008574	-1.303450
C	-0.648951	4.797497	-0.527445
C	-1.536595	4.727449	0.725508
C	-1.015770	3.475416	1.424120
O	0.406220	3.398393	1.065953
C	0.710217	4.375733	0.017268
H	-0.986274	4.073272	-1.274857
H	-2.600896	4.642981	0.491873
H	-1.502943	2.570229	1.052399
H	1.353481	3.890075	-0.720068
H	-1.078444	3.493647	2.512871
H	-1.389815	5.613161	1.352904
H	-0.620470	5.790411	-0.983218
H	1.252594	5.203820	0.485434
C	0.614182	-4.088530	-1.023718
C	1.009644	-3.987138	0.458044
C	-0.177367	-3.243468	1.056638
O	-0.586343	-2.317476	0.009591
C	-0.048962	-2.737220	-1.286809
H	1.469419	-4.253800	-1.683617
H	1.918423	-3.389726	0.570059
H	0.060505	-2.650197	1.939898
H	0.666163	-1.973280	-1.601295

H	-1.022530	-3.907234	1.271544
H	1.172202	-4.959105	0.930457
H	-0.100092	-4.905246	-1.174225
H	-0.880648	-2.765754	-1.991361
C	-3.746084	-0.678294	-2.027325
C	-4.925212	-0.542016	-1.109577
C	-3.924501	-1.649748	1.398321
C	-4.629906	-2.463346	0.566921
C	-5.357214	-1.969361	-0.647554
C	-3.647249	-0.244892	1.079144
C	-4.652669	0.401337	0.118325
O	-2.638034	-1.062289	-1.601158
C	-3.898860	-0.360246	-3.459356
C	-2.834495	-0.262889	-4.269408
C	-3.342102	-2.203456	2.681985
C	-4.134225	1.763974	-0.381338
C	-6.007465	0.629407	0.831078
H	-5.747466	-0.106741	-1.689391
H	-4.720709	-3.523769	0.792711
H	-5.245464	-2.675015	-1.485486
H	-6.439613	-1.923442	-0.459007
H	-3.497203	0.374581	1.970392
H	-4.903702	-0.163894	-3.823309
H	-2.937109	0.002295	-5.316769
H	-1.834040	-0.428598	-3.880168
H	-3.445414	-3.291259	2.744109
H	-2.282492	-1.947930	2.795037
H	-3.851976	-1.762946	3.547650

H	-4.856109	2.256651	-1.044439
H	-3.961775	2.426775	0.474578
H	-3.184051	1.670430	-0.919838
H	-5.879333	1.358833	1.637975
H	-6.776171	1.014434	0.147525
H	-6.374546	-0.296790	1.280876
Mg	-1.681327	-0.600259	0.173177

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3.21.V’-TS

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Mg	1.461930	0.983085	0.319062
Br	-0.039191	1.022717	2.411528
C	-4.490359	-0.130915	0.525593
C	-4.477946	-0.853609	-0.889137
C	-6.915732	-0.830285	0.317612
C	-6.545033	-2.041888	-0.124139
C	-5.206744	-2.210854	-0.819269
C	-5.952274	0.318113	0.069412
C	-5.452880	0.255157	-1.430360
O	-3.603051	0.931886	0.605895
C	-4.382219	-0.999893	1.764437
C	-3.638617	-0.698075	2.833716
C	-8.200959	-0.547825	1.037715
C	-4.757809	1.538398	-1.918236
C	-6.448098	-0.137676	-2.532226
H	-3.492180	-0.942113	-1.363929
H	-7.180679	-2.915005	0.010266
H	-4.586788	-2.943029	-0.279387
H	-5.345686	-2.625487	-1.828547
H	-6.299910	1.277877	0.463215
H	-4.963536	-1.914995	1.788552
H	-3.600852	-1.356630	3.697145
H	-3.074700	0.227041	2.892626
H	-8.811793	-1.448047	1.156794
H	-8.000987	-0.131857	2.033917
H	-8.793792	0.203497	0.499614
H	-4.145343	1.317197	-2.802648
H	-5.509173	2.277798	-2.220803
H	-4.125254	1.981024	-1.154593
H	-7.157346	0.680827	-2.702862
H	-5.911222	-0.300874	-3.474851
H	-7.029567	-1.032603	-2.313133
Mg	-1.767388	0.885652	0.425570
Br	-0.232640	2.355641	-1.127039
C	-0.325871	-2.695490	-1.629702
C	-1.024053	-3.170831	-0.345044
C	-0.791758	-1.999746	0.596472
O	-0.902485	-0.824480	-0.275266
C	-0.642784	-1.200991	-1.669889
H	0.754774	-2.835954	-1.546017
H	-0.607816	-4.101724	0.048443
H	0.215117	-1.994854	1.020933
H	0.189587	-0.596478	-2.025944
H	-1.544616	-1.887108	1.379261
H	-2.097436	-3.311881	-0.512586

H	-0.679137	-3.210127	-2.526574
H	-1.546911	-0.968540	-2.238673
C	4.159794	3.493434	-0.795141
C	3.062727	4.439961	-0.223389
C	2.532826	3.706482	1.017565
O	2.890474	2.311144	0.797597
C	4.221939	2.333804	0.202368
H	3.866571	3.110809	-1.775606
H	2.258762	4.580739	-0.949250
H	1.450505	3.750145	1.146869
H	4.399515	1.350158	-0.231702
H	3.023316	4.029802	1.942093
H	3.455837	5.424019	0.043130
H	5.130605	3.984782	-0.896577
H	4.937520	2.513754	1.013258
C	3.229981	-1.101931	-0.819014
C	3.644649	-2.525763	-0.393033
C	6.189774	-1.377600	-0.346649
C	6.018632	-2.383299	-1.252482
C	4.711533	-3.147250	-1.323993
C	5.167269	-1.122451	0.637093
C	4.257460	-2.290856	1.016186
O	2.093364	-0.683104	-0.299344
C	3.726321	-0.417434	-1.995485
C	3.031946	0.522280	-2.685512
C	7.400797	-0.474677	-0.380973
C	3.236615	-1.883445	2.093660
C	5.021381	-3.512701	1.577671
H	2.747917	-3.163755	-0.377455
H	6.791756	-2.614248	-1.981112
H	4.336648	-3.153161	-2.356108
H	4.855954	-4.205239	-1.060506
H	5.355458	-0.347693	1.380808
H	4.728652	-0.674713	-2.321159
H	3.479105	1.040871	-3.527350
H	1.998039	0.767270	-2.461652
H	8.095073	-0.753092	-1.179162
H	7.098013	0.567533	-0.550540
H	7.944325	-0.495551	0.571053
H	2.461564	-2.650272	2.209155
H	3.745570	-1.776733	3.058444
H	2.737949	-0.941191	1.879262
H	5.453431	-3.264666	2.553289
H	4.341963	-4.362488	1.720752
H	5.841325	-3.828872	0.931161

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3.31.V’

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Mg	1.400113	1.143699	0.395254
Br	-0.146685	1.170433	2.438149
C	-4.505864	-0.267827	0.515712
C	-4.421127	-1.024137	-0.879683
C	-6.887810	-1.093456	0.264812
C	-6.445979	-2.295492	-0.135695
C	-5.082989	-2.414154	-0.792054

C	-5.976314	0.095431	0.011345
C	-5.435235	0.020703	-1.472951
O	-3.673718	0.839425	0.591162
C	-4.388282	-1.099133	1.779307
C	-3.679273	-0.737915	2.853730
C	-8.204141	-0.857885	0.944527
C	-4.792049	1.325139	-1.975566
C	-6.380597	-0.447693	-2.589316
H	-3.419976	-1.074732	-1.326568
H	-7.041079	-3.195780	0.005273
H	-4.440911	-3.099829	-0.218009
H	-5.174660	-2.860671	-1.793218
H	-6.381942	1.045998	0.370783
H	-4.931490	-2.036901	1.816257
H	-3.631951	-1.370678	3.735863
H	-3.155144	0.211332	2.896246
H	-8.772049	-1.784492	1.073860
H	-8.051574	-0.405570	1.933280
H	-8.819756	-0.152448	0.370981
H	-4.145217	1.113453	-2.837448
H	-5.570909	2.018019	-2.316532
H	-4.203742	1.817520	-1.207034
H	-7.127376	0.328227	-2.795209
H	-5.812209	-0.602260	-3.514765
H	-6.919377	-1.367502	-2.364310
Mg	-1.834092	0.836883	0.415899
Br	-0.351595	2.324193	-1.159426
C	-0.075262	-2.749781	-1.397063

C	-0.786069	-3.226138	-0.119436
C	-0.731591	-1.983527	0.754986
O	-0.940011	-0.886031	-0.191448
C	-0.545829	-1.301968	-1.543766
H	1.009034	-2.769191	-1.261196
H	-0.294538	-4.081664	0.350988
H	0.250652	-1.837947	1.212265
H	0.240563	-0.631879	-1.886637
H	-1.524825	-1.911838	1.501989
H	-1.828146	-3.493386	-0.327507
H	-0.327834	-3.348029	-2.276033
H	-1.431977	-1.202927	-2.176673
C	3.372148	3.818817	-1.283975
C	2.480303	4.743953	-0.410874
C	2.289790	3.968004	0.906775
O	2.760846	2.613390	0.631448
C	3.865165	2.749347	-0.312610
H	2.776195	3.341084	-2.065965
H	1.519203	4.923220	-0.896258
H	1.253528	3.885836	1.239379
H	4.033503	1.771299	-0.766846
H	2.900975	4.366277	1.723031
H	2.954576	5.710003	-0.220812
H	4.199754	4.349649	-1.760220
H	4.750705	3.060787	0.253677
C	3.115895	-1.080732	-0.698450
C	3.766614	-2.194458	0.099629
C	6.588191	-1.964916	-0.575647

C	5.816736	-2.927363	-1.227824
C	4.427803	-3.279069	-0.784885
C	6.101991	-1.333786	0.561340
C	4.780422	-1.690143	1.197604
O	2.072326	-0.514436	-0.104428
C	3.540479	-0.659917	-1.970998
C	2.945659	0.337849	-2.724801
C	7.946550	-1.591380	-1.135275
C	4.230039	-0.473434	1.966450
C	5.016791	-2.831817	2.221891
H	2.934362	-2.657495	0.647428
H	6.227440	-3.449935	-2.088823
H	3.791255	-3.468219	-1.659030
H	4.448116	-4.230673	-0.231255
H	6.716719	-0.590471	1.066188
H	4.412355	-1.160868	-2.381731
H	3.326698	0.601195	-3.705092
H	2.053344	0.858992	-2.391869
H	8.489992	-2.475573	-1.484438
H	7.845327	-0.913684	-1.991558
H	8.566457	-1.089600	-0.386418
H	3.247528	-0.687800	2.397800
H	4.911562	-0.202250	2.780817
H	4.128195	0.396759	1.314254
H	5.716276	-2.508747	2.999974
H	4.075169	-3.114106	2.708987
H	5.442177	-3.718948	1.745687

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3.31.V’-TS

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Mg	-0.947388	1.385392	0.195825
Br	0.167568	-0.154043	-1.530391
C	3.985702	-1.390526	-0.272119
C	5.456327	-1.093531	0.230146
C	4.855925	0.048560	-2.179734
C	6.004531	-0.644990	-2.181962
C	6.465634	-1.338063	-0.912707
C	4.095196	0.093453	-0.870550
C	5.092306	0.436433	0.305676
O	3.082784	-1.502215	0.776534
C	3.778748	-2.524318	-1.257549
C	3.051114	-3.615353	-0.995930
C	4.273892	0.750807	-3.371084
C	4.409823	0.864618	1.615636
C	6.204721	1.463659	0.046980
H	5.742194	-1.600787	1.158004
H	6.614564	-0.731163	-3.079303
H	6.568616	-2.418218	-1.088682
H	7.465962	-0.982795	-0.624752
H	3.154475	0.650579	-0.942764
H	4.250921	-2.434858	-2.230354
H	2.922883	-4.400007	-1.736004
H	2.589703	-3.765688	-0.023697
H	4.899903	0.639595	-4.261707
H	3.273107	0.360662	-3.599008

H	4.150487	1.824162	-3.170577
H	5.152172	0.914680	2.421923
H	3.987779	1.873601	1.505796
H	3.618932	0.183925	1.914845
H	5.780574	2.475782	0.018392
H	6.928884	1.441069	0.869939
H	6.745907	1.309834	-0.885894
Mg	1.260590	-1.257831	0.561851
Br	0.334500	0.539088	2.270952
C	-1.467641	-2.997222	2.972336
C	-2.305530	-3.279558	1.716065
C	-1.500317	-2.584564	0.624625
O	-0.099776	-2.653846	1.079160
C	-0.044641	-3.153892	2.455208
H	-1.629814	-1.966235	3.300572
H	-3.311599	-2.861611	1.779981
H	-1.787394	-1.534555	0.532442
H	0.693627	-2.558110	2.998794
H	-1.546403	-3.057181	-0.356881
H	-2.377649	-4.355821	1.526580
H	-1.683915	-3.675766	3.801101
H	0.283295	-4.197562	2.416588
C	1.090229	4.501930	1.580324
C	2.081581	4.289504	0.424192
C	1.506176	3.065325	-0.282706
O	0.056810	3.120018	-0.030908
C	-0.244537	4.201506	0.910522
H	1.277435	3.778380	2.379661
H	3.103933	4.108937	0.764643
H	1.880777	2.136562	0.153110
H	-1.025874	3.847842	1.588497
H	1.651378	3.044606	-1.363630
H	2.087740	5.157571	-0.243292
H	1.124868	5.510047	2.000224
H	-0.627224	5.048952	0.332817
C	-3.827384	0.842983	0.164762
C	-4.713728	1.227840	-1.044206
C	-4.842068	-1.522823	-1.407891
C	-3.646482	-0.758479	-1.642572
C	-3.818842	0.654686	-2.153940
C	-6.034197	-0.895590	-1.186274
C	-6.142585	0.617543	-1.120040
O	-2.785523	1.645622	0.294486
C	-4.161917	-0.029031	1.263554
C	-3.553649	0.010593	2.476662
C	-4.734937	-3.030910	-1.358144
C	-6.997657	1.070731	0.084994
C	-6.861360	1.134819	-2.393067
H	-4.798206	2.323571	-1.062060
H	-2.727844	-1.295405	-1.867639
H	-2.864199	1.189775	-2.164418
H	-4.232274	0.715968	-3.171496
H	-6.947041	-1.471473	-1.044581
H	-4.939454	-0.760706	1.071029
H	-3.810982	-0.699491	3.255960
H	-2.811895	0.765168	2.714220

H	-4.064052	-3.348741	-0.550091
H	-5.706886	-3.501825	-1.184142
H	-4.320813	-3.434019	-2.290119
H	-7.132118	2.158682	0.068126
H	-7.992656	0.612721	0.042251
H	-6.546707	0.805075	1.042462
H	-7.882987	0.740862	-2.434375
H	-6.922059	2.230947	-2.388772
H	-6.351822	0.821679	-3.306882

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3.29.V’

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Mg	1.008465	1.296967	-0.096529
Br	-0.307468	-0.159760	1.599881
C	-4.120947	-1.306956	0.196289
C	-5.559840	-0.949846	-0.358221
C	-5.019763	0.119662	2.098608
C	-6.190210	-0.533806	2.039681
C	-6.622620	-1.183330	0.737615
C	-4.205996	0.167521	0.821907
C	-5.142592	0.567761	-0.385310
O	-3.179255	-1.428012	-0.815819
C	-3.995458	-2.468711	1.162766
C	-3.290457	-3.575937	0.908229
C	-4.460691	0.771726	3.328765
C	-4.391852	0.999781	-1.656361
C	-6.229136	1.627278	-0.147996
H	-5.824377	-1.427934	-1.307669
H	-6.837754	-0.619697	2.910400
H	-6.769185	-2.262784	0.885073
H	-7.597988	-0.788064	0.417816
H	-3.252156	0.693401	0.943403
H	-4.511356	-2.387259	2.113864
H	-3.222938	-4.382301	1.632932
H	-2.785925	-3.715496	-0.043866
H	-5.122626	0.658043	4.192742
H	-3.482034	0.342643	3.581501
H	-4.294947	1.844980	3.161885
H	-5.100244	1.114643	-2.486213
H	-3.922046	1.980733	-1.497250
H	-3.625988	0.288560	-1.949941
H	-5.772688	2.623611	-0.085654
H	-6.923877	1.643176	-0.996136
H	-6.807854	1.475074	0.762372
Mg	-1.361075	-1.216857	-0.537499
Br	-0.291173	0.504502	-2.215390
C	1.441237	-3.266571	-2.728997
C	2.168430	-3.471162	-1.390705
C	1.361743	-2.579541	-0.459428
O	-0.018090	-2.672988	-0.954280
C	-0.025604	-3.233478	-2.309761
H	1.729319	-2.303279	-3.160281
H	3.212811	-3.154804	-1.426892
H	1.691087	-1.540244	-0.544314
H	-0.646075	-2.588615	-2.937930

H	1.349197	-2.877669	0.589045
H	2.121768	-4.517638	-1.071255
H	1.642038	-4.055120	-3.458207
H	-0.474850	-4.228925	-2.246143
C	-0.953360	4.430515	-1.601603
C	-1.932999	4.298996	-0.423723
C	-1.400481	3.072000	0.308825
O	0.048415	3.071483	0.054451
C	0.379646	4.090167	-0.946022
H	-1.187476	3.692415	-2.374838
H	-2.968300	4.155563	-0.742191
H	-1.810173	2.147639	-0.105131
H	1.122011	3.663973	-1.626036
H	-1.542913	3.079733	1.390175
H	-1.888096	5.185448	0.217838
H	-0.949496	5.425970	-2.052104
H	0.821066	4.941500	-0.418343
C	3.900700	0.487943	0.011076
C	3.777956	-0.294042	1.391364
C	6.423205	0.549426	0.847505
C	6.148375	-0.889732	1.260654
C	4.899814	-1.308103	1.519844
C	5.058730	1.281628	0.765768
C	4.236235	1.025275	2.065350
O	2.836413	1.348276	-0.199449
C	4.179084	-0.352203	-1.210236
C	3.585534	-0.180519	-2.395086
C	4.544794	-2.716734	1.901975
C	7.175962	0.612985	-0.500812
C	7.332276	1.227590	1.901341
H	2.791426	-0.703362	1.633877
H	6.998912	-1.566035	1.344017
H	5.178074	2.315978	0.426179
H	3.421550	1.741484	2.169268
H	4.772986	0.927579	3.011579
H	4.895896	-1.158769	-1.084475
H	3.815217	-0.822633	-3.241472
H	2.863375	0.613838	-2.547822
H	5.429030	-3.355881	1.985301
H	4.007417	-2.743701	2.858872
H	3.871897	-3.164776	1.157208
H	7.418131	1.653353	-0.747148
H	8.118867	0.056538	-0.442566
H	6.591626	0.205866	-1.326718
H	8.298848	0.714015	1.960168
H	7.524336	2.271975	1.627997
H	6.888064	1.212401	2.899187

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3.21.A’

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C	-3.858587	-0.857389	0.120831
C	-3.273225	-1.988512	-0.821500
C	-5.763096	-2.523978	0.156133
C	-4.891539	-3.531770	0.315257
C	-3.465869	-3.378467	-0.180632

C	-5.249198	-1.275633	-0.539273
C	-4.444977	-1.697372	-1.832453
O	-3.448356	0.412877	-0.220418
C	-3.739918	-1.037832	1.632322
C	-3.417806	-0.059985	2.442134
C	-7.187650	-2.552264	0.625470
C	-4.181727	-0.537947	-2.810958
C	-4.961615	-2.865352	-2.685946
H	-2.247661	-1.829838	-1.178537
H	-5.181900	-4.462130	0.799765
H	-2.762646	-3.505245	0.655134
H	-3.218322	-4.173002	-0.899451
H	-5.998459	-0.481910	-0.626173
H	-3.973621	-2.005037	2.067565
H	-7.443453	-3.501254	1.106686
H	-7.374435	-1.741041	1.341672
H	-7.878739	-2.393021	-0.212687
H	-3.329272	-0.779073	-3.457627
H	-5.055311	-0.391725	-3.457918
H	-3.972907	0.396024	-2.297499
H	-5.879119	-2.568911	-3.207994
H	-4.219095	-3.116891	-3.452656
H	-5.186135	-3.769406	-2.120942
Mg	-1.852250	1.309705	-0.494847
Br	0.039803	0.339718	-1.921947
C	4.600299	0.246757	0.085169
C	5.758662	0.906225	-0.764185
C	6.312425	-1.621828	0.110483
C	7.285797	-0.734211	0.368191
C	7.121513	0.711085	-0.066831
C	5.090218	-1.102033	-0.621827
C	5.549434	-0.216223	-1.848853
O	3.351243	0.651840	-0.304191
C	4.716484	0.287225	1.611064
C	3.698039	0.597142	2.371051
C	6.352778	-3.067593	0.510803
C	4.433050	0.078021	-2.865052
C	6.769200	-0.668079	-2.666101
H	5.583176	1.945748	-1.061319
H	8.196292	-1.026401	0.888427
H	7.197572	1.381335	0.801745
H	7.941230	1.002404	-0.739553
H	4.320456	-1.863379	-0.792279
H	5.656613	0.023619	2.085068
H	7.278083	-3.324233	1.035699
H	5.507388	-3.313159	1.169020
H	6.261632	-3.720502	-0.367238
H	4.774667	0.839511	-3.577429
H	4.206036	-0.828786	-3.439947
H	3.522256	0.429541	-2.390746
H	6.495435	-1.512788	-3.309555
H	7.093598	0.146812	-3.324182
H	7.623443	-0.976952	-2.063797
Mg	1.595544	0.576773	0.232316
Br	-0.173877	2.165179	1.345742
C	1.265923	-3.157514	2.325869

C	-0.211077	-3.001220	1.927541
C	-0.300924	-1.528036	1.531268
O	1.045638	-1.176006	1.086934
C	1.965955	-2.286875	1.289412
H	1.440261	-2.760011	3.331770
H	-0.909763	-3.248116	2.729825
H	-0.557497	-0.873690	2.367707
H	2.919822	-1.862295	1.605605
H	-0.992798	-1.336200	0.710632
H	-0.439003	-3.639696	1.068097
H	1.612791	-4.193458	2.300372
H	2.096637	-2.805194	0.332784
C	-3.639480	4.249216	0.579869
C	-2.352391	5.042404	0.225210
C	-1.794872	4.328280	-1.024596
O	-2.569582	3.101670	-1.151441
C	-3.912885	3.421541	-0.673283
H	-3.452163	3.572703	1.419216
H	-1.632807	5.007678	1.045484
H	-0.747061	4.038628	-0.940021
H	-4.416932	2.469518	-0.503031
H	-1.943183	4.908922	-1.940970
H	-2.568668	6.090616	0.002978
H	-4.480514	4.896294	0.840860
H	-4.419363	3.996532	-1.458071
C	2.643348	0.895550	3.092483
H	2.420483	1.916395	3.393119
H	1.952623	0.127040	3.434676
C	-3.105448	0.910744	3.262432
H	-3.870131	1.549562	3.701074
H	-2.073077	1.127826	3.526135

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3.21.A’-TSc

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Mg	1.360372	1.488704	0.857105
Br	-0.209589	1.401649	2.897605
C	-4.526939	-0.318009	0.234221
C	-4.277270	-0.383124	-1.329065
C	-6.891029	-0.670208	-0.606531
C	-6.455917	-1.616852	-1.453435
C	-5.018927	-1.588395	-1.941640
C	-5.889667	0.392820	-0.192585
C	-5.141557	0.922413	-1.482326
O	-3.649358	0.514780	0.896569
C	-4.653831	-1.640737	0.987164
C	-3.889972	-1.973686	1.996093
C	-8.282654	-0.606600	-0.049148
C	-4.370654	2.234657	-1.259618
C	-5.937556	1.106136	-2.782843
H	-3.226020	-0.335443	-1.643302
H	-7.112902	-2.411088	-1.803068
H	-4.505856	-2.521565	-1.663718
H	-4.987270	-1.544524	-3.040106
H	-6.290166	1.126502	0.513504
H	-5.433602	-2.336266	0.689316

H	-8.910970	-1.423346	-0.417824
H	-8.263442	-0.653390	1.047755
H	-8.764415	0.344584	-0.310940
H	-3.633297	2.375470	-2.059325
H	-5.066309	3.082085	-1.297638
H	-3.851874	2.251198	-0.306231
H	-6.603800	1.972402	-2.693587
H	-5.247814	1.312580	-3.610189
H	-6.551286	0.249099	-3.058429
Mg	-1.820758	0.395599	1.098790
Br	-0.499608	1.626596	-0.903444
C	0.054044	-3.180129	-0.383324
C	0.289853	-3.396150	1.120380
C	0.169517	-1.983377	1.681399
O	-0.794867	-1.318523	0.798434
C	-1.046269	-2.124852	-0.395706
H	0.955249	-2.782614	-0.858382
H	1.267301	-3.833937	1.338139
H	1.106794	-1.426364	1.622486
H	-1.008156	-1.451827	-1.255237
H	-0.227553	-1.927686	2.695731
H	-0.483156	-4.048781	1.541234
H	-0.246728	-4.091347	-0.906139
H	-2.051606	-2.547464	-0.296908
C	3.978790	2.988631	-1.221517
C	2.724578	3.793735	-1.673616
C	2.039423	4.195502	-0.361591
O	2.463000	3.173906	0.588935
C	3.883806	2.963350	0.309447
H	3.950602	1.966578	-1.605684
H	2.053220	3.161971	-2.260674
H	0.949800	4.180056	-0.395094
H	4.164693	2.011878	0.756285
H	2.386417	5.163177	0.017779
H	2.977078	4.670599	-2.274356
H	4.914225	3.446742	-1.551204
H	4.433278	3.783980	0.783583
C	3.184656	-0.714867	-0.117523
C	3.927344	-1.938799	0.484719
C	5.577196	-1.049939	-1.558043
C	5.039384	-2.302411	-1.730313
C	4.294109	-2.980912	-0.595463
C	5.358679	-0.368605	-0.322499
C	5.233255	-1.227992	0.946740
O	2.609981	0.090864	0.772989
C	2.628308	-0.660454	-1.450847
C	2.795226	-1.512903	-2.472101
C	6.145451	-0.287324	-2.728872
C	6.444337	-2.155243	1.188180
C	5.071806	-0.386426	2.225021
H	3.339443	-2.403633	1.289703
H	5.220393	-2.866510	-2.639778
H	3.391384	-3.467694	-0.980853
H	4.890847	-3.784485	-0.141633
H	5.762174	0.640355	-0.226797
H	2.102902	0.269872	-1.673344

H	5.412912	0.451765	-3.083233
H	7.055683	0.259604	-2.458560
H	6.375940	-0.947270	-3.570440
H	7.304570	-1.559280	1.513006
H	6.226119	-2.881754	1.980955
H	6.748133	-2.697189	0.291655
H	4.942267	-1.043406	3.093366
H	5.978543	0.207679	2.394045
H	4.212810	0.277901	2.183636
C	-3.149247	-2.313828	3.022814
H	-2.243096	-2.903308	2.903478
H	-3.432557	-2.054198	4.040835
C	2.472386	-2.270139	-3.498241
H	3.184339	-2.540010	-4.273797
H	1.467318	-2.681837	-3.597833

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3.48.A’

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Mg	-1.423513	1.434817	0.316205
Br	0.230025	2.173346	2.197736
C	3.462117	-1.291998	0.317961
C	4.359844	-1.622942	-0.942522
C	4.051575	-3.711282	0.784691
C	5.328434	-3.472714	0.446655
C	5.654349	-2.343238	-0.512905
C	2.999362	-2.809775	0.167667
C	3.273138	-2.671080	-1.386632
O	2.465119	-0.389030	0.047149
C	4.197097	-0.899560	1.599638
C	3.982576	0.253232	2.176468
C	3.608188	-4.789953	1.729004
C	2.113098	-2.061389	-2.194373
C	3.738045	-3.912030	-2.161661
H	4.555655	-0.776408	-1.611888
H	6.142633	-4.075855	0.843837
H	6.340485	-1.626594	-0.038560
H	6.188215	-2.730992	-1.392561
H	1.983608	-3.042815	0.501034
H	4.924948	-1.578982	2.032547
H	4.451446	-5.368871	2.117451
H	3.063605	-4.361512	2.581355
H	2.915070	-5.482270	1.232991
H	2.490435	-1.705400	-3.161439
H	1.360583	-2.830109	-2.410880
H	1.641302	-1.225962	-1.683990
H	2.906038	-4.618340	-2.267866
H	4.046922	-3.622279	-3.173028
H	4.564254	-4.447473	-1.694975
Mg	2.017776	1.358653	0.481277
Br	0.283118	1.866255	-1.571570
C	3.551308	3.706096	-2.358811
C	3.403817	4.895169	-1.395289
C	2.752927	4.253500	-0.170516
O	3.221176	2.863834	-0.171679
C	3.939649	2.573376	-1.417239

H	2.593588	3.479344	-2.835114
H	2.789389	5.701284	-1.802862
H	1.662254	4.233417	-0.246529
H	3.631342	1.580114	-1.752918
H	3.048768	4.698490	0.781872
H	4.385593	5.307659	-1.138974
H	4.302760	3.872306	-3.134690
H	5.009862	2.564120	-1.185497
C	-1.015257	-2.867916	-0.189469
C	-0.948391	-2.728122	1.340353
C	-0.444176	-1.302908	1.511405
O	-1.116575	-0.567915	0.443443
C	-1.472310	-1.483477	-0.652810
H	-0.026527	-3.099442	-0.592014
H	-0.280918	-3.457488	1.807651
H	0.634321	-1.212019	1.347867
H	-0.963915	-1.128271	-1.551545
H	-0.724827	-0.830561	2.454170
H	-1.945388	-2.830555	1.781694
H	-1.711675	-3.644767	-0.514604
H	-2.551621	-1.409172	-0.780042
C	-4.050058	1.187151	-0.266201
C	-5.358023	0.804488	0.418772
C	-5.365103	-1.889985	-0.562888
C	-5.780832	-0.742263	-1.480111
C	-6.383622	0.406848	-0.657378
C	-5.132627	-1.688420	0.741455
C	-5.223365	-0.357050	1.463174

O	-3.235050	1.977383	0.426923
C	-3.757941	0.740893	-1.526505
C	-4.566205	-0.225486	-2.248327
C	-5.192732	-3.235300	-1.216378
C	-6.460449	-0.359842	2.394812
C	-3.977720	-0.197816	2.360546
H	-5.684409	1.700482	0.960359
H	-6.516762	-1.121491	-2.200233
H	-6.596381	1.260963	-1.308324
H	-7.329906	0.091576	-0.207916
H	-4.846346	-2.538930	1.363728
H	-2.865029	1.123258	-2.023123
H	-4.478043	-3.162605	-2.045432
H	-4.833585	-3.990636	-0.510285
H	-6.138028	-3.590756	-1.647563
H	-6.415581	-1.207157	3.088133
H	-6.494386	0.559996	2.990185
H	-7.395905	-0.442509	1.835796
H	-3.945726	0.795083	2.817140
H	-3.991843	-0.950372	3.158288
H	-3.061833	-0.337804	1.786622
C	3.712981	1.425419	2.709647
H	4.277603	2.314844	2.436341
H	2.954338	1.540950	3.480182
C	-4.260271	-0.684519	-3.478713
H	-3.378171	-0.336751	-4.009789
H	-4.893284	-1.403256	-3.990031

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3.21.A’-TS

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Mg	1.207588	0.856442	-0.416859
Br	0.276532	1.839463	1.916978
C	-4.572937	-0.337251	0.437352
C	-4.843954	-1.756648	-0.210118
C	-7.108440	-0.353012	0.381348
C	-7.117525	-1.613955	0.841896
C	-5.924313	-2.516690	0.587597
C	-5.874029	0.088972	-0.381862
C	-5.492239	-1.023654	-1.442576
O	-3.419365	0.247368	-0.012996
C	-4.651869	-0.245298	1.960392
C	-3.657133	0.232630	2.658193
C	-8.223565	0.630975	0.581148
C	-4.487903	-0.550810	-2.508248
C	-6.619028	-1.744378	-2.196141
H	-3.954948	-2.376249	-0.384728
H	-7.966632	-2.010437	1.395341
H	-5.503268	-2.870732	1.540027
H	-6.236800	-3.421202	0.045658
H	-5.908365	1.130987	-0.714425
H	-5.548330	-0.577341	2.474073
H	-9.054103	0.201070	1.149435
H	-7.865175	1.521536	1.114280
H	-8.611331	0.982383	-0.383983
H	-4.047734	-1.421040	-3.014005
H	-5.008385	0.038118	-3.273092
H	-3.689961	0.054505	-2.087940
H	-7.073381	-1.064629	-2.926515
H	-6.205933	-2.592005	-2.756333
H	-7.417456	-2.118454	-1.555821
Mg	-1.813552	0.985097	0.533843
Br	-0.814542	2.151198	-1.620632
C	-0.110840	-2.659701	-1.107545
C	-0.187050	-2.982734	0.396093
C	-0.277057	-1.608303	1.078341
O	-0.513107	-0.628729	-0.014017
C	-0.932754	-1.389154	-1.208653
H	0.920031	-2.457501	-1.411158
H	0.684052	-3.541936	0.744629
H	0.647496	-1.295609	1.556567
H	-0.722288	-0.755499	-2.068655
H	-1.121545	-1.532937	1.768638
H	-1.082244	-3.573316	0.612683
H	-0.513595	-3.459898	-1.733618
H	-2.010468	-1.542753	-1.128973
C	4.562896	3.479904	-0.033084
C	3.387095	4.458774	0.119171
C	2.267907	3.771363	-0.664770
O	2.591531	2.343561	-0.622852
C	3.860013	2.135452	0.074341
H	5.034221	3.587324	-1.016348
H	3.600747	5.459465	-0.264567
H	2.246022	4.062958	-1.718843

H	4.363235	1.292855	-0.400303
H	1.275627	3.907403	-0.232969
H	3.105865	4.547734	1.173650
H	5.331356	3.605889	0.733834
H	3.639070	1.875439	1.114748
C	3.330166	-1.262163	-0.338241
C	3.840709	-2.464468	0.476829
C	6.313316	-1.672710	-0.548706
C	5.876307	-2.904698	-0.949645
C	4.602888	-3.498540	-0.382477
C	5.626640	-0.971403	0.501233
C	4.814445	-1.802346	1.492134
O	2.368317	-0.573429	0.206294
C	3.538137	-1.101606	-1.772603
C	2.689184	-0.393562	-2.504276
C	7.481038	-0.992693	-1.226183
C	4.105760	-0.916964	2.531932
C	5.675780	-2.819221	2.277265
H	2.977031	-2.946874	0.959367
H	6.409541	-3.461302	-1.716174
H	3.952730	-3.848604	-1.196187
H	4.814698	-4.391482	0.224315
H	6.041378	-0.021031	0.836885
H	4.404982	-1.572142	-2.230464
H	7.893856	-1.600653	-2.036556
H	7.168829	-0.030603	-1.652591
H	8.286260	-0.777881	-0.513520
H	3.472505	-1.526763	3.187708
H	4.855578	-0.423115	3.161731
H	3.474301	-0.156026	2.079490
H	6.333433	-2.288532	2.974623
H	5.041503	-3.494644	2.865329
H	6.310019	-3.418774	1.622187
C	1.826959	0.381107	-3.124176
H	1.951030	1.464357	-3.159826
H	0.984519	-0.012231	-3.693451
C	-2.622970	0.742831	3.290424
H	-2.558028	1.803672	3.523778
H	-1.810854	0.124491	3.666403

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3.49.A’

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Mg	1.168031	0.626445	-0.505303
Br	0.234191	1.512699	1.930785
C	-4.685289	-0.379529	0.471280
C	-5.200890	-1.552352	-0.460585
C	-7.192405	-0.086715	0.694086
C	-7.341245	-1.412625	0.841333
C	-6.310983	-2.356180	0.248719
C	-5.972955	0.384532	-0.075851
C	-5.835451	-0.465828	-1.405332
O	-3.502987	0.163855	0.044793
C	-4.625809	-0.656412	1.972200
C	-3.538912	-0.433655	2.662500
C	-8.138969	0.939855	1.243323

C	-4.858557	0.126867	-2.435456
C	-7.110361	-0.835847	-2.176862
H	-4.424961	-2.205611	-0.878725
H	-8.190586	-1.832575	1.377027
H	-5.870714	-2.985105	1.036447
H	-6.790504	-3.051956	-0.455356
H	-5.886853	1.473546	-0.145042
H	-5.504716	-1.035861	2.483627
H	-8.975541	0.482429	1.780583
H	-7.618192	1.619916	1.930468
H	-8.546614	1.564655	0.437846
H	-4.629356	-0.627307	-3.200054
H	-5.327602	0.976085	-2.947301
H	-3.929924	0.462551	-1.983520
H	-7.508520	0.050859	-2.684068
H	-6.872266	-1.572699	-2.953495
H	-7.907196	-1.243684	-1.555177
Mg	-1.824520	0.741034	0.536860
Br	-0.862648	2.006506	-1.586004
C	-0.311576	-2.813680	-1.470756
C	0.142600	-3.130724	-0.018675
C	-0.334141	-1.935349	0.813741
O	-0.597123	-0.866826	-0.164681
C	-1.159758	-1.552227	-1.341508
H	0.560461	-2.614822	-2.098122
H	1.228895	-3.214242	0.029543
H	0.407781	-1.537958	1.502419
H	-1.087364	-0.846503	-2.167033
H	-1.282648	-2.133332	1.324545
H	-0.295210	-4.058515	0.358470
H	-0.886882	-3.626672	-1.920948
H	-2.213655	-1.737182	-1.121029
C	4.557127	3.028269	0.091602
C	3.325361	3.710855	0.728908
C	2.252500	3.522191	-0.333816
O	2.507823	2.173977	-0.809854
C	3.953240	2.017691	-0.909019
H	5.183099	3.756862	-0.431625
H	3.497822	4.761762	0.974245
H	2.364804	4.216478	-1.176374
H	4.244547	2.230212	-1.943313
H	1.226645	3.551439	0.029850
H	3.015714	3.184847	1.636950
H	5.177662	2.527729	0.837634
H	4.185646	0.978513	-0.683845
C	3.308591	-1.381754	-0.345008
C	4.267176	-2.109055	0.580666
C	6.761537	-1.124703	-0.478598
C	6.318228	-2.392637	-0.867623
C	5.186257	-3.093909	-0.173240
C	6.199381	-0.495911	0.624348
C	5.145798	-1.153641	1.482371
O	2.315830	-0.748308	0.235337
C	3.403620	-1.383678	-1.754131
C	2.433804	-0.809572	-2.526706
C	7.842904	-0.434672	-1.285662

C	4.307594	-0.091556	2.221477
C	5.858380	-2.007605	2.567833
H	3.624992	-2.672904	1.273230
H	6.806484	-2.897162	-1.698446
H	4.595869	-3.674077	-0.893481
H	5.580689	-3.838829	0.533706
H	6.574328	0.477220	0.936339
H	4.226904	-1.887319	-2.249922
H	8.669765	-1.117001	-1.509732
H	7.448484	-0.078676	-2.244992
H	8.253367	0.428248	-0.753326
H	3.539085	-0.561813	2.841372
H	4.960281	0.499691	2.875020
H	3.789226	0.581554	1.541357
H	6.434642	-1.360521	3.237020
H	5.123461	-2.550766	3.174814
H	6.553563	-2.728506	2.132009
C	1.719804	0.116419	-3.135969
H	2.056969	1.154198	-3.239554
H	0.767041	-0.098236	-3.622450
C	-2.427372	-0.164902	3.309572
H	-2.253401	0.803090	3.773635
H	-1.645385	-0.907369	3.453027

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CH_4

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C	-1.064529	0.000000	-1.523738
H	-0.533984	-0.951533	-1.447532
H	-0.347831	0.822032	-1.466219
H	-1.781227	0.083862	-0.703974
H	-1.595075	0.045639	-2.477227

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CH_3 radical

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C	-1.016408	0.015644	-1.542331
H	-0.607800	-0.982101	-1.449821
H	-0.365612	0.876476	-1.461985
H	-2.075846	0.152556	-1.715173

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3.21.V

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C	0.915103	-0.504809	0.203320
C	-0.289905	-0.674534	1.191226
C	-0.408737	1.545877	-0.397533
C	-0.576369	1.803122	0.908240
C	-0.530428	0.668264	1.913183
C	-0.181682	0.091261	-0.778335
C	-1.257542	-0.809134	-0.044521
O	1.382637	-1.798289	-0.168671
C	2.094549	0.350335	0.599534
C	3.288782	-0.141677	0.936623
C	-0.424073	2.581788	-1.482099
C	-1.386829	-2.235226	-0.608516

C	-2.690310	-0.274794	0.095109
H	-0.213668	-1.516331	1.887053
H	-0.747886	2.815004	1.269359
H	0.268075	0.843015	2.647387
H	-1.467029	0.626506	2.486322
H	-0.023717	-0.056856	-1.852292
H	2.021533	-1.667861	-0.883483
H	1.939154	1.423773	0.607317
H	4.109247	0.514585	1.210504
H	3.477307	-1.210542	0.962403
H	-0.603214	3.585782	-1.086301
H	0.529296	2.593005	-2.027278
H	-1.202925	2.359761	-2.223172
H	-1.974635	-2.851120	0.082950
H	-1.929209	-2.207301	-1.561503
H	-0.429200	-2.721596	-0.766655
H	-3.195668	-0.305358	-0.877367
H	-3.259749	-0.918484	0.775432
H	-2.753428	0.747911	0.464329

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3.32.V

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C	-8.561223	0.619465	1.828016
C	-7.808180	1.213323	0.665470
C	-6.884812	-1.133487	-0.785451
C	-5.999862	-0.483162	0.071865
C	-6.302242	0.851067	0.684634
C	-8.075165	-0.521421	-1.157123
C	-8.435063	0.885711	-0.748217
O	-9.652850	1.319867	2.283599
C	-8.298927	-0.600078	2.452457
C	-9.040930	-1.147217	3.478285
C	-6.564371	-2.530549	-1.277261
C	-9.965553	1.054101	-0.735123
C	-7.847520	1.868983	-1.794437
H	-7.879890	2.307458	0.783671
H	-5.051457	-0.952586	0.321494
H	-5.939207	0.883009	1.719167
H	-5.742215	1.637549	0.156547
H	-8.762809	-1.042455	-1.819679
H	-9.709288	2.159340	1.811364
H	-7.438958	-1.146609	2.077955
H	-8.761407	-2.096497	3.920653
H	-9.919002	-0.645897	3.868407
H	-5.489060	-2.661659	-1.433881
H	-6.883150	-3.283721	-0.547076
H	-7.072322	-2.750469	-2.220780
H	-10.248717	2.086990	-0.496099
H	-10.375702	0.830638	-1.725862
H	-10.440849	0.390937	-0.009408
H	-8.284471	1.680787	-2.780371
H	-8.069058	2.908349	-1.520624
H	-6.764630	1.757344	-1.888570

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3.21.A

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C	0.949428	-0.576585	-0.106424
C	-0.123974	-0.772528	1.016374
C	-0.376856	1.535304	-0.426067
C	-0.377321	1.722311	0.902565
C	-0.241632	0.531743	1.832893
C	-0.240491	0.100955	-0.911059
C	-1.239598	-0.819847	-0.095791
O	1.337492	-1.848934	-0.598934
C	-0.498877	2.631387	-1.442545
C	-1.470009	-2.209178	-0.715748
C	-2.630017	-0.269733	0.251866
H	0.013978	-1.653793	1.651161
H	-0.476023	2.715874	1.334890
H	0.642237	0.648751	2.475379
H	-1.103833	0.475883	2.511513
H	-0.218989	0.009261	-2.002134
H	2.005633	-1.700470	-1.282538
H	-0.588997	3.615814	-0.974093
H	0.374137	2.645743	-2.108302
H	-1.376189	2.473212	-2.083288
H	-1.995573	-2.849433	0.003139
H	-2.112572	-2.115677	-1.599732
H	-0.549609	-2.706108	-1.006336
H	-3.260509	-0.256352	-0.644770
H	-3.116347	-0.930031	0.979252
H	-2.622102	0.739082	0.662260
C	2.191250	0.248767	0.169596
H	2.059066	1.295348	0.424737
C	3.406688	-0.233983	0.094126
C	4.620627	-0.711518	0.009154
H	5.182497	-0.682059	-0.922196
H	5.118270	-1.154009	0.869365

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3.32.A

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C	3.108619	-1.306678	-0.308343
C	3.933428	-2.354920	0.386026
C	6.654912	-1.703718	-0.415382
C	5.978034	-2.715625	-1.092964
C	4.678272	-3.282318	-0.607000
C	6.157841	-1.210577	0.784937
C	4.938588	-1.781120	1.464838
O	1.961976	-0.880420	0.314847
C	3.459269	-0.640839	-1.492547
C	2.773159	0.366993	-2.065191
C	7.910147	-1.105192	-1.017782
C	4.263784	-0.700447	2.329518
C	5.387178	-2.938929	2.393919
H	3.218483	-2.982726	0.943424
H	6.394879	-3.117798	-2.012967
H	4.019077	-3.501582	-1.455929
H	4.855690	-4.251646	-0.117087
H	6.687361	-0.409363	1.295930

H	4.373479	-0.972743	-1.979661
H	8.471842	-1.848594	-1.591810
H	7.661754	-0.283484	-1.699906
H	8.572846	-0.702852	-0.245951
H	3.396426	-1.106541	2.864521
H	4.965914	-0.331729	3.085037
H	3.927965	0.148225	1.729677
H	6.066359	-2.564164	3.166166
H	4.523718	-3.393641	2.896036
H	5.917520	-3.717789	1.840542
C	2.135697	1.349189	-2.637064
H	2.362080	2.395081	-2.418489
H	1.332137	1.180038	-3.357089
H	1.800115	-1.436989	1.086677

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3.21.P

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C	0.958384	-0.447306	0.136318
C	-0.209888	-0.679107	1.152160
C	-0.383768	1.590470	-0.360418
C	-0.510507	1.800724	0.957227
C	-0.447607	0.633770	1.923405
C	-0.171099	0.150281	-0.799125
C	-1.204722	-0.793995	-0.065186
O	1.490216	-1.705650	-0.280850
C	-0.396452	2.667351	-1.403311
C	-1.304360	-2.203698	-0.671230
C	-2.640851	-0.294239	0.131125
H	-0.096642	-1.544864	1.812143
H	-0.649055	2.802172	1.358500
H	0.365739	0.789411	2.644420
H	-1.373858	0.564756	2.510283
H	-0.034004	0.036252	-1.879583
H	2.167458	-1.513917	-0.943988
H	-0.568385	3.655311	-0.966128
H	0.559634	2.693814	-1.942918
H	-1.175978	2.481932	-2.153727
H	-1.859064	-2.860355	0.009927
H	-1.864230	-2.161694	-1.613505
H	-0.334040	-2.652998	-0.863421
H	-3.178226	-0.315305	-0.824228
H	-3.174540	-0.960932	0.818407
H	-2.704703	0.720573	0.521923
C	2.079421	0.421600	0.503238
C	3.060302	1.079669	0.766634
C	4.226308	1.892112	1.098684
H	4.341789	1.991424	2.183994
H	5.148083	1.446462	0.707650
H	4.139727	2.901212	0.679919

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3.32.P

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C	-2.715153	-1.333983	-0.390477
C	-3.611943	-2.443252	-0.874622

C	-5.980746	-1.980924	0.729126
C	-5.071191	-2.952390	1.140277
C	-3.953775	-3.432591	0.265977
C	-5.917019	-1.457694	-0.555769
C	-4.930826	-1.945960	-1.588165
O	-1.831912	-0.762243	-1.284205
C	-2.785486	-0.755469	0.860691
C	-2.870758	-0.283606	1.988523
C	-7.003566	-1.451084	1.712952
C	-4.620374	-0.824732	-2.596872
C	-5.561606	-3.133822	-2.359793
H	-3.037030	-2.994255	-1.637669
H	-5.146379	-3.368046	2.141785
H	-3.055078	-3.609458	0.868526
H	-4.210021	-4.407754	-0.175111
H	-6.625159	-0.690238	-0.860789
H	-7.338973	-2.232373	2.402374
H	-6.573665	-0.642460	2.316313
H	-7.884269	-1.049478	1.203037
H	-3.932314	-1.175960	-3.376333
H	-5.539486	-0.503290	-3.098555
H	-4.172649	0.045478	-2.111882
H	-6.460380	-2.805293	-2.891523
H	-4.859563	-3.536510	-3.101263
H	-5.855878	-3.941039	-1.684761
C	-3.005245	0.278599	3.324138
H	-3.907657	-0.105411	3.814898
H	-2.149703	0.029304	3.965703
H	-3.085443	1.372507	3.294276
H	-1.864838	-1.268573	-2.106424

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3.21.Ph

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C	0.831900	-0.994228	0.254541
C	-0.338278	-0.592217	1.224218
C	0.131258	1.118391	-0.856608
C	0.079654	1.717858	0.340548
C	-0.198068	0.902941	1.586694
C	-0.072837	-0.390735	-0.869936
C	-1.336615	-0.757462	0.014340
O	0.960427	-2.409491	0.050649
C	0.369154	1.829183	-2.155236
C	-1.859905	-2.190455	-0.181820
C	-2.562636	0.163579	-0.046198
H	-0.499493	-1.223538	2.105932
H	0.220722	2.791676	0.441242
H	0.608221	1.048778	2.316054
H	-1.115851	1.257944	2.076805
H	0.010966	-0.838043	-1.864989
H	1.510130	-2.744176	0.772120
H	0.492427	2.906651	-2.012017
H	1.268219	1.447321	-2.656598
H	-0.466855	1.667299	-2.848195
H	-2.586298	-2.425258	0.606125
H	-2.384125	-2.266189	-1.142201

H	-1.071726	-2.936965	-0.159019
H	-3.092843	0.012626	-0.993694
H	-3.260060	-0.093662	0.759587
H	-2.327593	1.224451	0.032460
C	2.229454	-0.461916	0.495928
C	2.767718	-0.442486	1.790926
C	3.071315	-0.125569	-0.566019
C	4.088655	-0.072835	2.020130
C	4.398093	0.252176	-0.358546
C	4.912188	0.283346	0.944752
H	2.141550	-0.717622	2.636118
H	2.685850	-0.160647	-1.580250
H	4.505442	-0.049815	3.021548
H	5.015805	0.513713	-1.209274
O	6.190796	0.639125	1.269601
C	7.071668	1.003733	0.218554
H	7.226113	0.177221	-0.487950
H	6.706255	1.880233	-0.333051
H	8.022453	1.250725	0.693454

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3.32.Ph

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C	3.300944	0.793533	-0.199553
C	3.492637	2.204292	-0.677779
C	6.273967	3.223739	-0.850520
C	5.502252	3.557559	0.250636
C	4.055336	3.203424	0.380278
C	5.705676	2.537674	-1.925506
C	4.224712	2.354804	-2.083062
O	2.078239	0.227122	-0.496503
C	7.757377	3.531381	-0.870283
C	3.929705	1.137007	-2.975769
C	3.652899	3.629858	-2.759656
H	2.467578	2.550491	-0.877359
H	5.962855	4.065479	1.094167
H	3.857832	2.803247	1.384128
H	3.455375	4.123823	0.317119
H	6.343573	2.177858	-2.729757
H	8.001401	4.252091	-1.658922
H	8.097776	3.947197	0.082137
H	8.340406	2.625244	-1.069386
H	2.852553	0.967709	-3.076863
H	4.343106	1.294942	-3.977793
H	4.372485	0.228574	-2.559325
H	4.139352	3.803281	-3.724445
H	2.574632	3.528111	-2.938672
H	3.821635	4.514309	-2.138613
C	4.225525	-0.104594	0.401284
C	5.585987	0.231512	0.655777
C	3.813515	-1.418093	0.766985
C	6.453816	-0.674633	1.238534
C	4.688056	-2.326357	1.345994
C	6.022842	-1.962998	1.588344
H	5.955383	1.209727	0.393838
H	2.786721	-1.713643	0.589974

H	7.488669	-0.408417	1.428812
H	4.323982	-3.313623	1.605849
O	6.967669	-2.777821	2.148539
C	6.586362	-4.095893	2.506448
H	5.792235	-4.098835	3.265343
H	6.246819	-4.672382	1.635313
H	7.478735	-4.567459	2.921549
H	1.480421	0.919376	-0.803654

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3.21.M

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C	0.947678	-0.599690	0.031941
C	-0.185801	-0.772778	1.088182
C	-0.326923	1.509591	-0.413820
C	-0.405353	1.723907	0.907791
C	-0.341219	0.550847	1.868668
C	-0.175505	0.062884	-0.857219
C	-1.236933	-0.828795	-0.085844
O	1.357417	-1.892547	-0.424042
C	-0.387331	2.584108	-1.458629
C	-1.452415	-2.226443	-0.691990
C	-2.637337	-0.252861	0.168184
H	-0.105278	-1.641483	1.750163
H	-0.521509	2.726912	1.313249
H	0.498363	0.675436	2.567023
H	-1.245923	0.518137	2.491199
H	-0.094817	-0.050589	-1.944728
H	1.867959	-1.759831	-1.234622
H	-0.492078	3.579184	-1.016338
H	0.517235	2.578305	-2.081111
H	-1.233551	2.419708	-2.138749
H	-2.037210	-2.842546	0.001937
H	-2.032171	-2.140852	-1.619344
H	-0.523312	-2.745478	-0.906681
H	-3.213757	-0.249150	-0.764294
H	-3.175247	-0.891519	0.878493
H	-2.640085	0.764223	0.558508
C	2.225062	0.168118	0.369943
H	2.798099	-0.407193	1.103148
H	2.842965	0.264952	-0.532510
H	2.051053	1.170302	0.756524

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3.32.M

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C	-2.636365	-1.497951	-0.333067
C	-3.595789	-2.513229	-0.849881
C	-5.980095	-2.023916	0.757869
C	-5.117093	-3.049278	1.128864
C	-3.996713	-3.525045	0.259349
C	-5.858004	-1.412194	-0.487266
C	-4.900883	-1.908083	-1.533175
O	-1.706061	-0.960568	-1.197437
C	-7.006955	-1.511583	1.748151
C	-4.520607	-0.773388	-2.501393

C	-5.585922	-3.039173	-2.344316
H	-3.076745	-3.074592	-1.643839
H	-5.230521	-3.514692	2.105011
H	-3.109588	-3.744701	0.870177
H	-4.261605	-4.479914	-0.218793
H	-6.494235	-0.566536	-0.739324
H	-7.325538	-2.298926	2.438121
H	-6.594087	-0.693854	2.351357
H	-7.896847	-1.127490	1.240339
H	-3.845893	-1.135871	-3.286135
H	-5.415864	-0.378133	-2.993812
H	-4.020326	0.050843	-1.987713
H	-6.459578	-2.648808	-2.875938
H	-4.897610	-3.459162	-3.089093
H	-5.930825	-3.846156	-1.693489
H	-1.622286	-1.543351	-1.964142
C	-2.955031	-0.607243	0.807482
H	-3.245735	-1.186777	1.691520
H	-2.102059	0.032766	1.047359
H	-3.827926	0.035102	0.579221

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3.21.V_1.635

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C	1.001863	-0.354724	-0.078738
C	-0.021398	-0.799042	1.017171
C	-0.782550	1.468075	-0.312043
C	-0.828668	1.576020	1.023458
C	-0.418235	0.407137	1.889885
C	-0.351440	0.112476	-0.868925
C	-1.094513	-1.053527	-0.108698
O	1.721388	-1.491263	-0.560049
C	2.025901	0.727410	0.130128
C	3.333087	0.600429	-0.106481
C	-1.097671	2.613556	-1.236747
C	-0.968280	-2.359651	-0.924593
C	-2.555222	-0.956773	0.348840
H	0.293589	-1.647731	1.641813
H	-1.124075	2.504059	1.508032
H	0.442332	0.688192	2.513128
H	-1.220609	0.134722	2.589057
H	-0.338257	0.078308	-1.961969
H	1.362891	-2.280654	-0.141650
H	1.640857	1.692950	0.436616
H	3.999670	1.449281	0.016436
H	3.768628	-0.338227	-0.428540
H	-1.295374	3.532410	-0.676693
H	-0.261060	2.803244	-1.921128
H	-1.973658	2.399384	-1.862679
H	-0.989603	-3.245088	-0.275754
H	-1.826086	-2.439277	-1.600946
H	-0.074503	-2.398798	-1.544897
H	-3.242214	-1.037156	-0.500480
H	-2.770053	-1.795570	1.022724
H	-2.788516	-0.030640	0.874230

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3.21.V_1.670

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C	1.008561	-0.369062	-0.078760
C	-0.025664	-0.799630	1.008813
C	-0.796245	1.476778	-0.316877
C	-0.826836	1.582152	1.019631
C	-0.415540	0.409408	1.880257
C	-0.375058	0.117312	-0.876720
C	-1.101155	-1.050531	-0.110528
O	1.744695	-1.511222	-0.523588
C	2.029377	0.715992	0.124552
C	3.338894	0.605533	-0.113783
C	-1.101929	2.636147	-1.231783
C	-0.962106	-2.347161	-0.938249
C	-2.558834	-0.974028	0.361924
H	0.280783	-1.648889	1.636960
H	-1.107407	2.511959	1.510159
H	0.448628	0.687126	2.499859
H	-1.215145	0.139587	2.583697
H	-0.377691	0.081345	-1.970066
H	1.335230	-2.303323	-0.157871
H	1.636115	1.680369	0.424648
H	3.991532	1.466316	0.002645
H	3.790591	-0.327828	-0.429508
H	-1.273074	3.554336	-0.661494
H	-0.269081	2.814221	-1.923778
H	-1.989932	2.446834	-1.849034
H	-0.973108	-3.240422	-0.299689
H	-1.818724	-2.429130	-1.615795
H	-0.068868	-2.370139	-1.561118
H	-3.254740	-1.062737	-0.479331
H	-2.754716	-1.815777	1.038057
H	-2.797275	-0.050783	0.890603

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3.21.V_1.725

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C	1.022296	-0.386583	-0.074773
C	-0.028394	-0.801014	0.999266
C	-0.814628	1.485598	-0.320961
C	-0.824725	1.588151	1.016405
C	-0.413065	0.410225	1.870699
C	-0.410314	0.125787	-0.886674
C	-1.107062	-1.046459	-0.112380
O	1.767884	-1.530541	-0.493134
C	2.036063	0.703987	0.123681
C	3.347060	0.611387	-0.119368
C	-1.105856	2.656228	-1.228891
C	-0.956464	-2.336201	-0.947620
C	-2.561422	-0.987433	0.372427
H	0.264648	-1.652288	1.631541
H	-1.083986	2.520826	1.513111
H	0.452417	0.684568	2.489686
H	-1.211573	0.140155	2.575438
H	-0.436806	0.087734	-1.979658

H	1.327707	-2.323679	-0.170813
H	1.631314	1.665675	0.417012
H	3.985362	1.484228	-0.014471
H	3.814243	-0.316615	-0.428234
H	-1.254193	3.574679	-0.653101
H	-0.272967	2.820771	-1.924132
H	-2.000594	2.489302	-1.842215
H	-0.958642	-3.233525	-0.314727
H	-1.811201	-2.422637	-1.626951
H	-0.062915	-2.345829	-1.571062
H	-3.263133	-1.081761	-0.463312
H	-2.743705	-1.831534	1.049253
H	-2.804105	-0.066697	0.903816

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3.21.V_1.800

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C	1.043756	-0.406023	-0.063684
C	-0.029526	-0.802061	0.989786
C	-0.833327	1.493344	-0.324718
C	-0.822578	1.593169	1.013647
C	-0.411157	0.410321	1.862500
C	-0.455082	0.137404	-0.899325
C	-1.111265	-1.041729	-0.114994
O	1.788693	-1.547808	-0.469235
C	2.043754	0.693114	0.125471
C	3.355522	0.617240	-0.124148
C	-1.108743	2.672737	-1.227153
C	-0.951636	-2.327163	-0.954412
C	-2.562640	-0.997732	0.380622
H	0.247273	-1.656149	1.626494
H	-1.060010	2.529091	1.515279
H	0.453966	0.681671	2.482962
H	-1.209607	0.138103	2.566569
H	-0.503882	0.096875	-1.991178
H	1.328436	-2.342361	-0.177994
H	1.625460	1.651031	0.411870
H	3.981307	1.500719	-0.033699
H	3.835444	-0.307181	-0.424766
H	-1.239118	3.592203	-0.648462
H	-0.274202	2.824370	-1.923489
H	-2.007452	2.523343	-1.839109
H	-0.947227	-3.226047	-0.323804
H	-1.804818	-2.418479	-1.635037
H	-0.057605	-2.327182	-1.577920
H	-3.267915	-1.095369	-0.451741
H	-2.735852	-1.843565	1.057632
H	-2.808448	-0.078592	0.913553

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3.21.V_1.889

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C	1.070960	-0.426130	-0.046793
C	-0.029678	-0.802471	0.980846
C	-0.850345	1.499625	-0.328406
C	-0.820505	1.597221	1.011211

C	-0.409785	0.410172	1.855789
C	-0.505500	0.151226	-0.913618
C	-1.113803	-1.036801	-0.118367
O	1.806595	-1.562969	-0.450369
C	2.051146	0.683569	0.128382
C	3.363319	0.622669	-0.128475
C	-1.110611	2.686131	-1.226061
C	-0.947582	-2.319851	-0.959684
C	-2.562761	-1.005889	0.387092
H	0.230553	-1.659622	1.621702
H	-1.037646	2.536240	1.516067
H	0.454003	0.678834	2.478945
H	-1.208810	0.134731	2.558105
H	-0.570477	0.107549	-2.004075
H	1.332487	-2.357653	-0.182148
H	1.618809	1.636914	0.408718
H	3.978100	1.515071	-0.053347
H	3.853610	-0.299226	-0.420375
H	-1.226552	3.606375	-0.645685
H	-0.274271	2.826443	-1.922670
H	-2.011677	2.550545	-1.837504
H	-0.938502	-3.218961	-0.329425
H	-1.799555	-2.415773	-1.641131
H	-0.053179	-2.312858	-1.583146
H	-3.270236	-1.105433	-0.443197
H	-2.729695	-1.852902	1.064082
H	-2.810811	-0.087679	0.920773

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3.21.V_1.986

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C	1.101069	-0.446016	-0.025926
C	-0.029269	-0.802402	0.972537
C	-0.866003	1.504830	-0.332186
C	-0.818456	1.600708	1.008935
C	-0.408812	0.409942	1.850093
C	-0.558116	0.165898	-0.928808
C	-1.115244	-1.031872	-0.122404
O	1.822335	-1.576655	-0.434822
C	2.058118	0.674803	0.132018
C	3.370513	0.627794	-0.132752
C	-1.111810	2.697645	-1.225409
C	-0.943983	-2.313697	-0.964196
C	-2.562148	-1.012805	0.392543
H	0.214492	-1.662812	1.616880
H	-1.016447	2.542649	1.515866
H	0.453076	0.676026	2.476633
H	-1.208783	0.130652	2.549952
H	-0.638206	0.119249	-2.017485
H	1.337838	-2.371020	-0.183840
H	1.611930	1.622993	0.407740
H	3.974967	1.528113	-0.073378
H	3.870030	-0.291967	-0.415953
H	-1.215350	3.618434	-0.643700
H	-0.273598	2.827901	-1.921760
H	-2.014426	2.574005	-1.836814

H	-0.931532	-3.212291	-0.333205
H	-1.794999	-2.413804	-1.646165
H	-0.049352	-2.301611	-1.587752
H	-3.271171	-1.113561	-0.436288
H	-2.724167	-1.860738	1.069502
H	-2.811812	-0.095141	0.926566

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3.21.V_2.084

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C	1.131913	-0.465233	-0.002087
C	-0.028394	-0.801890	0.964527
C	-0.881141	1.509216	-0.336240
C	-0.816378	1.603852	1.006692
C	-0.408052	0.409606	1.844883
C	-0.611712	0.180590	-0.943885
C	-1.115804	-1.026752	-0.127114
O	1.836663	-1.589493	-0.421637
C	2.064846	0.666159	0.136674
C	3.377404	0.632810	-0.137366
C	-1.112484	2.708066	-1.225192
C	-0.940564	-2.308161	-0.968353
C	-2.560805	-1.018927	0.397370
H	0.198649	-1.665897	1.611429
H	-0.995554	2.548630	1.514905
H	0.451401	0.673126	2.475453
H	-1.209306	0.125805	2.541582
H	-0.708115	0.131596	-2.030544
H	1.344533	-2.383309	-0.182799
H	1.605314	1.608852	0.409340
H	3.971422	1.540707	-0.094740
H	3.885856	-0.284822	-0.411727
H	-1.204722	3.629061	-0.642057
H	-0.272205	2.829085	-1.920701
H	-2.016085	2.595814	-1.837020
H	-0.925671	-3.205586	-0.335692
H	-1.790829	-2.412184	-1.650588
H	-0.045763	-2.292708	-1.592109
H	-3.271055	-1.120582	-0.430290
H	-2.718496	-1.867651	1.074347
H	-2.811705	-0.101581	0.931462

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3.21.V_2.185

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C	1.163272	-0.483724	0.025426
C	-0.026873	-0.800573	0.956331
C	-0.895691	1.512678	-0.340686
C	-0.814500	1.606302	1.004348
C	-0.407273	0.409072	1.840189
C	-0.666490	0.194744	-0.958046
C	-1.115533	-1.021165	-0.132777
O	1.849470	-1.601288	-0.411435
C	2.071584	0.657833	0.142635
C	3.384091	0.637697	-0.142501
C	-1.112549	2.717172	-1.225440

C	-0.937451	-2.303121	-0.972134
C	-2.558681	-1.024065	0.401500
H	0.182680	-1.668537	1.605379
H	-0.975975	2.553723	1.513127
H	0.449165	0.670283	2.475409
H	-1.209868	0.119803	2.533309
H	-0.777864	0.144209	-2.041899
H	1.352732	-2.394421	-0.178119
H	1.598701	1.594533	0.414023
H	3.967983	1.552511	-0.117287
H	3.900630	-0.278228	-0.407594
H	-1.195249	3.637842	-0.640569
H	-0.270166	2.830261	-1.919649
H	-2.016631	2.615087	-1.838048
H	-0.921278	-3.198556	-0.336506
H	-1.787251	-2.411050	-1.654275
H	-0.042489	-2.286390	-1.596082
H	-3.269774	-1.126136	-0.425423
H	-2.713149	-1.873246	1.078635
H	-2.810390	-0.106564	0.935066

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3.21.V_2.294

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C	1.198575	-0.499304	0.059327
C	-0.023885	-0.797445	0.948405
C	-0.905475	1.513113	-0.346479
C	-0.813576	1.606646	1.003409
C	-0.406146	0.408614	1.837042
C	-0.724159	0.210133	-0.971540
C	-1.113741	-1.015929	-0.139139
O	1.858537	-1.610543	-0.406855
C	2.075080	0.650737	0.148144
C	3.389821	0.641346	-0.147410
C	-1.111769	2.722892	-1.226195
C	-0.935597	-2.300019	-0.974810
C	-2.556526	-1.026751	0.403867
H	0.168978	-1.670833	1.596272
H	-0.961880	2.556523	1.510906
H	0.447886	0.668940	2.475521
H	-1.209349	0.113565	2.527112
H	-0.823565	0.154996	-2.055254
H	1.362663	-2.403076	-0.168426
H	1.593405	1.582055	0.423352
H	3.966528	1.560456	-0.134014
H	3.911219	-0.273349	-0.406970
H	-1.188904	3.642392	-0.638892
H	-0.268613	2.833461	-1.919671
H	-2.016531	2.627634	-1.838416
H	-0.919158	-3.192671	-0.335241
H	-1.785257	-2.411309	-1.656494
H	-0.039922	-2.284614	-1.598013
H	-3.267867	-1.129587	-0.422655
H	-2.707791	-1.876460	1.081136
H	-2.809065	-0.109209	0.936907

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3.21.V_2.401

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C	1.265341	-0.514518	0.099176
C	0.013184	-0.795520	0.943524
C	-0.881918	1.510916	-0.350483
C	-0.779780	1.603966	1.006109
C	-0.371646	0.406265	1.836833
C	-0.749457	0.222271	-0.979685
C	-1.079285	-1.012342	-0.143150
O	1.899849	-1.621969	-0.400294
C	2.110325	0.640575	0.158105
C	3.429650	0.643175	-0.150449
C	-1.077722	2.726662	-1.224151
C	-0.900895	-2.298727	-0.974837
C	-2.521282	-1.031383	0.409515
H	0.186001	-1.675739	1.587476
H	-0.915385	2.556656	1.511496
H	0.480397	0.667124	2.477468
H	-1.175596	0.107277	2.524244
H	-0.821689	0.162173	-2.063801
H	1.409885	-2.414607	-0.150572
H	1.625709	1.567977	0.441032
H	3.998912	1.566495	-0.145077
H	3.954654	-0.269343	-0.409502
H	-1.150158	3.644196	-0.633345
H	-0.233653	2.836406	-1.916269
H	-1.983151	2.639106	-1.835889
H	-0.883471	-3.188073	-0.330876
H	-1.750402	-2.414260	-1.655947
H	-0.003462	-2.284545	-1.595481
H	-3.233990	-1.136618	-0.415325
H	-2.666656	-1.881912	1.087009
H	-2.775828	-0.114608	0.942675

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3.21.V_2.506

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C	1.264283	-0.525770	0.132555
C	-0.015890	-0.789721	0.932192
C	-0.925725	1.513342	-0.361258
C	-0.811827	1.605381	1.001507
C	-0.403166	0.408059	1.829543
C	-0.839973	0.237394	-0.993560
C	-1.111572	-1.004449	-0.154061
O	1.875341	-1.629936	-0.399479
C	2.080775	0.633595	0.163140
C	3.403806	0.649313	-0.161041
C	-1.109526	2.735386	-1.228872
C	-0.931969	-2.292646	-0.982146
C	-2.552011	-1.032783	0.409258
H	0.134610	-1.676928	1.572216
H	-0.933355	2.561044	1.504792
H	0.446678	0.669766	2.472442
H	-1.208152	0.105943	2.514268
H	-0.888782	0.173378	-2.077933

H	1.393926	-2.423309	-0.135475
H	1.594066	1.556948	0.455496
H	3.964946	1.577223	-0.163054
H	3.932764	-0.260229	-0.421778
H	-1.176625	3.650727	-0.634170
H	-0.263631	2.843579	-1.918685
H	-2.015030	2.657090	-1.841186
H	-0.913391	-3.178589	-0.333697
H	-1.780987	-2.412860	-1.663046
H	-0.032210	-2.279126	-1.599319
H	-3.266803	-1.141395	-0.413186
H	-2.690139	-1.883999	1.087362
H	-2.809134	-0.116843	0.942425

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3.21.V_2.603

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C	1.292319	-0.539499	0.168300
C	-0.012178	-0.786348	0.924364
C	-0.939158	1.515126	-0.369150
C	-0.810303	1.605049	0.998410
C	-0.401464	0.408193	1.824327
C	-0.894843	0.248538	-1.002854
C	-1.112296	-0.997929	-0.162537
O	1.884364	-1.640766	-0.393470
C	2.087143	0.623327	0.174553
C	3.411117	0.654099	-0.170593
C	-1.108523	2.743983	-1.230510
C	-0.929395	-2.286813	-0.988075
C	-2.549398	-1.038243	0.413840
H	0.112348	-1.680485	1.560220
H	-0.915169	2.563737	1.499793
H	0.446177	0.671173	2.469364
H	-1.207556	0.104413	2.506853
H	-0.933961	0.183168	-2.087151
H	1.416328	-2.436253	-0.111741
H	1.599797	1.542350	0.479114
H	3.962740	1.587406	-0.178658
H	3.944340	-0.250425	-0.439496
H	-1.169595	3.656517	-0.630937
H	-0.259377	2.849579	-1.916414
H	-2.013130	2.677526	-1.845083
H	-0.908520	-3.169519	-0.335466
H	-1.777414	-2.412687	-1.669230
H	-0.026632	-2.272138	-1.600682
H	-3.268071	-1.152840	-0.404279
H	-2.676602	-1.889949	1.093463
H	-2.810380	-0.123555	0.947173

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3.21.V_2.694

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C	1.316990	-0.553693	0.201735
C	-0.009054	-0.783528	0.917120
C	-0.954405	1.517958	-0.377284
C	-0.808006	1.605376	0.993668

C	-0.399671	0.409004	1.818155
C	-0.946602	0.258632	-1.011245
C	-1.114029	-0.991143	-0.171308
O	1.893878	-1.652173	-0.384808
C	2.096041	0.612250	0.188661
C	3.417631	0.658838	-0.181752
C	-1.108149	2.753876	-1.232223
C	-0.926142	-2.279264	-0.996013
C	-2.546369	-1.046031	0.420089
H	0.088889	-1.683712	1.548958
H	-0.894745	2.566976	1.493127
H	0.445964	0.673064	2.465260
H	-1.206841	0.104774	2.499072
H	-0.990160	0.193051	-2.095309
H	1.440374	-2.450146	-0.086349
H	1.609146	1.526799	0.507076
H	3.959723	1.597517	-0.192856
H	3.954184	-0.239069	-0.465638
H	-1.163435	3.663233	-0.627324
H	-0.254469	2.856337	-1.912712
H	-2.010591	2.700317	-1.850868
H	-0.902121	-3.159728	-0.340623
H	-1.772720	-2.410766	-1.677946
H	-0.020231	-2.261477	-1.603770
H	-3.270310	-1.169327	-0.392020
H	-2.659303	-1.897700	1.102327
H	-2.812389	-0.132745	0.953318

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3.21.V_2.776

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C	1.338009	-0.567906	0.231510
C	-0.006737	-0.781184	0.910521
C	-0.970619	1.521905	-0.385491
C	-0.804376	1.606859	0.987332
C	-0.397819	0.410808	1.811142
C	-0.994992	0.268182	-1.018601
C	-1.116537	-0.984342	-0.179977
O	1.904061	-1.664297	-0.372595
C	2.106872	0.600447	0.205016
C	3.422710	0.662737	-0.194113
C	-1.108896	2.764779	-1.233994
C	-0.922064	-2.269683	-1.006531
C	-2.542636	-1.056732	0.428217
H	0.066193	-1.686057	1.538883
H	-0.872135	2.571139	1.484688
H	0.446036	0.675169	2.460432
H	-1.206187	0.107276	2.490880
H	-1.055140	0.202627	-2.101992
H	1.461783	-2.464096	-0.062803
H	1.621655	1.510491	0.538572
H	3.956311	1.606169	-0.204523
H	3.960427	-0.227236	-0.499883
H	-1.159897	3.670632	-0.623519
H	-0.249604	2.864479	-1.907603
H	-2.007788	2.723716	-1.858433

H	-0.894144	-3.149750	-0.350822
H	-1.766855	-2.405894	-1.689808
H	-0.013275	-2.246402	-1.609752
H	-3.273045	-1.191944	-0.376112
H	-2.637607	-1.907483	1.114412
H	-2.815006	-0.144883	0.960787

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3.21.V_2.847

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C	1.354638	-0.581394	0.256119
C	-0.005476	-0.779041	0.904393
C	-0.986767	1.527191	-0.393242
C	-0.798597	1.610053	0.979677
C	-0.395920	0.413818	1.803478
C	-1.039259	0.277351	-1.024408
C	-1.119696	-0.977775	-0.188107
O	1.914857	-1.677303	-0.356350
C	2.118610	0.588136	0.222456
C	3.425830	0.665030	-0.207261
C	-1.111253	2.776378	-1.235729
C	-0.916865	-2.257675	-1.020193
C	-2.537845	-1.071046	0.438379
H	0.045101	-1.687236	1.530081
H	-0.845929	2.576910	1.474510
H	0.446236	0.677101	2.455403
H	-1.206114	0.112210	2.481860
H	-1.125839	0.211917	-2.106086
H	1.477838	-2.477674	-0.041106
H	1.636775	1.493594	0.573017
H	3.952869	1.612143	-0.213504
H	3.961581	-0.215848	-0.541508
H	-1.160766	3.678574	-0.619730
H	-0.245402	2.874792	-1.900952
H	-2.005150	2.746124	-1.867666
H	-0.884348	-3.139878	-0.367581
H	-1.759418	-2.396864	-1.705692
H	-0.005490	-2.225852	-1.619168
H	-3.275835	-1.222588	-0.356035
H	-2.610111	-1.919547	1.130299
H	-2.818440	-0.160720	0.969470

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3.21.V_2.879

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C	1.361127	-0.587713	0.266310
C	-0.005254	-0.777946	0.901498
C	-0.994591	1.530375	-0.396740
C	-0.794763	1.612415	0.975428
C	-0.394983	0.415828	1.799473
C	-1.059728	0.281778	-1.026411
C	-1.121524	-0.974617	-0.191873
O	1.920422	-1.684243	-0.346568
C	2.124511	0.581982	0.230890
C	3.426639	0.665202	-0.213752
C	-1.113254	2.782269	-1.236652

C	-0.913767	-2.250628	-1.028327
C	-2.534911	-1.079685	0.444053
H	0.035373	-1.687271	1.526226
H	-0.831442	2.580437	1.468765
H	0.446237	0.677948	2.453038
H	-1.206509	0.115554	2.476826
H	-1.161455	0.216489	-2.106622
H	1.482700	-2.484365	-0.030513
H	1.644958	1.485217	0.589944
H	3.951542	1.613564	-0.217339
H	3.959965	-0.210991	-0.563095
H	-1.163669	3.682740	-0.618136
H	-0.243741	2.880952	-1.896977
H	-2.004040	2.756220	-1.873074
H	-0.878738	-3.134955	-0.378705
H	-1.754987	-2.390481	-1.715377
H	-0.001199	-2.213335	-1.625187
H	-3.276668	-1.240883	-0.344705
H	-2.594221	-1.926447	1.139160
H	-2.820460	-0.170363	0.974293

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3.21.A_1.626

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C	0.692582	-0.404528	-0.049406
C	-0.333260	-0.839248	1.046377
C	-1.066953	1.425102	-0.304337
C	-1.117646	1.544319	1.030441
C	-0.725868	0.376899	1.908553
C	-0.644256	0.063777	-0.848006
C	-1.403033	-1.091702	-0.084414
O	1.416184	-1.530670	-0.537499
C	-1.373101	2.559844	-1.243665
C	-1.287846	-2.407935	-0.885608
C	-2.865251	-0.973319	0.363401
H	-0.025985	-1.686206	1.676795
H	-1.408022	2.478624	1.505984
H	0.131690	0.653458	2.537916
H	-1.537309	0.116997	2.601889
H	-0.617414	0.021110	-1.940979
H	1.060816	-2.325802	-0.124610
H	-1.561166	3.488709	-0.697483
H	-0.537250	2.731071	-1.933668
H	-2.252802	2.343083	-1.863236
H	-1.322932	-3.285159	-0.226500
H	-2.142616	-2.485544	-1.565996
H	-0.391150	-2.464690	-1.500453
H	-3.547779	-1.058542	-0.488992
H	-3.093026	-1.799942	1.047795
H	-3.091754	-0.037315	0.873932
C	1.719969	0.677807	0.172646
H	1.351334	1.650206	0.484284
C	3.005570	0.572716	-0.060989
C	4.291303	0.579301	-0.293321
H	4.686022	0.815439	-1.279279
H	5.014571	0.328636	0.479417

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3.21.A_1.725

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C	0.711038	-0.439885	-0.047733
C	-0.343713	-0.840448	1.024339
C	-1.104021	1.445909	-0.316891
C	-1.111360	1.559309	1.020043
C	-0.719407	0.381898	1.884744
C	-0.713574	0.078002	-0.870287
C	-1.420691	-1.084060	-0.089233
O	1.465722	-1.578751	-0.454305
C	-1.382472	2.612142	-1.234574
C	-1.275572	-2.379712	-0.916265
C	-2.875005	-1.014145	0.395463
H	-0.059642	-1.689475	1.663201
H	-1.357784	2.499589	1.509229
H	0.146050	0.649448	2.506691
H	-1.525279	0.127353	2.586699
H	-0.735925	0.031222	-1.963141
H	1.008154	-2.375248	-0.163464
H	-1.504287	3.540104	-0.667629
H	-0.556000	2.751286	-1.942781
H	-2.289044	2.456649	-1.833649
H	-1.285074	-3.273421	-0.278538
H	-2.128010	-2.464811	-1.598642
H	-0.380346	-2.398291	-1.537704
H	-3.578256	-1.119163	-0.437657
H	-3.058394	-1.847412	1.085343
H	-3.113962	-0.084746	0.913477
C	1.732528	0.648639	0.164552
H	1.343531	1.622302	0.447428
C	3.023811	0.568762	-0.061599
C	4.309048	0.598944	-0.301863
H	4.690723	0.812949	-1.298290
H	5.044905	0.391787	0.472254

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3.21.A_1.84

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C	0.743150	-0.467906	-0.031016
C	-0.345465	-0.841466	1.010012
C	-1.130871	1.456456	-0.322916
C	-1.107264	1.566323	1.015510
C	-0.716542	0.382065	1.872982
C	-0.783387	0.095678	-0.890601
C	-1.427183	-1.077244	-0.093389
O	1.493542	-1.603369	-0.420862
C	-1.386017	2.634926	-1.232622
C	-1.269198	-2.367225	-0.925873
C	-2.877092	-1.029280	0.407716
H	-0.084247	-1.694225	1.655137
H	-1.320933	2.511356	1.510731
H	0.148350	0.644888	2.497294
H	-1.522561	0.124368	2.573820
H	-0.838472	0.045362	-1.981635

H	1.011027	-2.399399	-0.171590
H	-1.481180	3.563584	-0.661936
H	-0.558390	2.755153	-1.943036
H	-2.297984	2.504777	-1.829093
H	-1.269368	-3.263003	-0.291024
H	-2.119406	-2.459511	-1.610048
H	-0.373112	-2.371826	-1.547163
H	-3.585391	-1.139187	-0.420483
H	-3.047463	-1.864773	1.098066
H	-3.120572	-0.101927	0.927640
C	1.742275	0.634141	0.168784
H	1.332083	1.603369	0.436452
C	3.035004	0.572480	-0.060607
C	4.318930	0.605058	-0.306865
H	4.695780	0.796785	-1.309795
H	5.059353	0.424143	0.469579

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3.21.A_1.978

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C	0.784571	-0.496518	-0.003826
C	-0.345438	-0.841306	0.996931
C	-1.154368	1.464291	-0.328866
C	-1.103205	1.571756	1.011649
C	-0.714714	0.381865	1.863932
C	-0.861159	0.116584	-0.913406
C	-1.430543	-1.070124	-0.099091
O	1.516936	-1.624326	-0.395933
C	-1.387829	2.652480	-1.231653
C	-1.263914	-2.357610	-0.933132
C	-2.877085	-1.040767	0.416933
H	-0.107535	-1.698314	1.647423
H	-1.287319	2.521142	1.509994
H	0.147894	0.640317	2.492802
H	-1.522018	0.119098	2.561629
H	-0.941722	0.062387	-2.001751
H	1.017722	-2.418717	-0.174492
H	-1.462610	3.581506	-0.658745
H	-0.558586	2.757093	-1.942727
H	-2.302736	2.541535	-1.827093
H	-1.258266	-3.253302	-0.298107
H	-2.112458	-2.456247	-1.618395
H	-0.367253	-2.353041	-1.554322
H	-3.588249	-1.153248	-0.408480
H	-3.039002	-1.877701	1.107457
H	-3.123500	-0.114411	0.937533
C	1.750924	0.621937	0.174420
H	1.318382	1.584563	0.430535
C	3.044624	0.577086	-0.060337
C	4.326933	0.609396	-0.311348
H	4.700840	0.778244	-1.319664
H	5.070465	0.453279	0.467755

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3.21.A_2.074

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C	0.813752	-0.515007	0.017869
C	-0.344872	-0.840724	0.988653
C	-1.169194	1.468522	-0.333059
C	-1.100361	1.575001	1.009207
C	-0.713847	0.381611	1.858618
C	-0.914372	0.130878	-0.928712
C	-1.431766	-1.065225	-0.103652
O	1.531041	-1.637247	-0.382060
C	-1.388438	2.662761	-1.231462
C	-1.260605	-2.351974	-0.937507
C	-2.876261	-1.047423	0.422258
H	-0.122440	-1.700890	1.641718
H	-1.265581	2.527083	1.508655
H	0.146613	0.637082	2.491351
H	-1.522472	0.114772	2.553378
H	-1.012500	0.074583	-2.014750
H	1.023413	-2.430246	-0.173836
H	-1.451257	3.591655	-0.657044
H	-0.557860	2.758065	-1.942287
H	-2.304575	2.563503	-1.826787
H	-1.252314	-3.246933	-0.301389
H	-2.108216	-2.454452	-1.623286
H	-0.363637	-2.343261	-1.558698
H	-3.588880	-1.161107	-0.401732
H	-3.033428	-1.885152	1.112893
H	-3.124134	-0.121452	0.942990
C	1.756180	0.614128	0.178945
H	1.308920	1.571650	0.429448
C	3.050587	0.580367	-0.060638
C	4.331783	0.611871	-0.314304
H	4.704427	0.764777	-1.325821
H	5.077022	0.472537	0.466626

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3.21.A_2.221

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C	0.858563	-0.541275	0.056566
C	-0.342887	-0.838535	0.976111
C	-1.190028	1.473052	-0.340090
C	-1.096389	1.578649	1.005579
C	-0.712692	0.380892	1.851674
C	-0.995932	0.151883	-0.949745
C	-1.432066	-1.057207	-0.112075
O	1.550010	-1.654968	-0.366357
C	-1.388368	2.675760	-1.232033
C	-1.256104	-2.344414	-0.943320
C	-2.873747	-1.055505	0.428873
H	-0.145168	-1.704341	1.631368
H	-1.234970	2.534411	1.505145
H	0.143553	0.632303	2.491258
H	-1.523499	0.106069	2.540998
H	-1.120953	0.093937	-2.031693
H	1.035010	-2.445976	-0.166301
H	-1.436354	3.603641	-0.654830
H	-0.555588	2.759826	-1.941559
H	-2.305381	2.592200	-1.827884

H	-1.245921	-3.236811	-0.303407
H	-2.102555	-2.452590	-1.629564
H	-0.358442	-2.333039	-1.564106
H	-3.587803	-1.170317	-0.393705
H	-3.025367	-1.894013	1.119842
H	-3.123044	-0.129505	0.948993
C	1.763489	0.602909	0.187330
H	1.294024	1.551367	0.434013
C	3.059037	0.585678	-0.062135
C	4.338617	0.614922	-0.318715
H	4.710877	0.742912	-1.334125
H	5.085640	0.500953	0.465077

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3.21.A_2.327

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C	0.891667	-0.556488	0.088527
C	-0.340042	-0.835511	0.968151
C	-1.199747	1.473439	-0.345970
C	-1.094869	1.579011	1.004518
C	-0.711645	0.380338	1.848477
C	-1.053632	0.167215	-0.962786
C	-1.430845	-1.052059	-0.118365
O	1.559669	-1.664687	-0.361427
C	-1.387479	2.681439	-1.232970
C	-1.254166	-2.341038	-0.946197
C	-2.871866	-1.058466	0.431560
H	-0.158838	-1.706687	1.622122
H	-1.220009	2.537015	1.502738
H	0.142040	0.630585	2.491685
H	-1.523404	0.099814	2.534503
H	-1.168259	0.104796	-2.044379
H	1.045146	-2.454770	-0.155120
H	-1.429360	3.607927	-0.653175
H	-0.554222	2.762937	-1.942063
H	-2.305264	2.605247	-1.828174
H	-1.243923	-3.230897	-0.302691
H	-2.100032	-2.452483	-1.632557
H	-0.355319	-2.330460	-1.565519
H	-3.586410	-1.174256	-0.390366
H	-3.019892	-1.897519	1.122756
H	-3.122073	-0.132506	0.951256
C	1.766147	0.596669	0.192319
H	1.286713	1.539926	0.441362
C	3.063785	0.588563	-0.063664
C	4.342233	0.616328	-0.321257
H	4.716190	0.732716	-1.337861
H	5.089988	0.513727	0.464020

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3.21.A_2.430

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C	1.270386	-0.524249	0.118258
C	0.011369	-0.786102	0.955052
C	-0.862128	1.519726	-0.357577
C	-0.745300	1.624564	0.998966

C	-0.362455	0.425559	1.840146
C	-0.763787	0.227103	-0.977965
C	-1.082676	-1.000861	-0.129715
O	1.917157	-1.629159	-0.361685
C	-1.038579	2.733484	-1.238985
C	-0.904217	-2.291030	-0.954347
C	-2.522068	-1.015952	0.430043
H	0.171828	-1.663628	1.605883
H	-0.856761	2.585057	1.495281
H	0.488486	0.675960	2.486469
H	-1.176041	0.140860	2.522097
H	-0.856683	0.159892	-2.060042
H	1.410222	-2.420093	-0.141225
H	-1.074612	3.657889	-0.655666
H	-0.204345	2.812949	-1.946841
H	-1.956771	2.666084	-1.834020
H	-0.893032	-3.178256	-0.307285
H	-1.749004	-2.406547	-1.641318
H	-0.002710	-2.279729	-1.569602
H	-3.238914	-1.134234	-0.389320
H	-2.663083	-1.855766	1.121732
H	-2.773485	-0.090733	0.950267
C	2.116222	0.635197	0.193727
H	1.632248	1.574904	0.446649
C	3.417260	0.637334	-0.070344
C	4.694578	0.664066	-0.328978
H	5.071252	0.771974	-1.346111
H	5.443409	0.570387	0.457310

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3.21.A_2.529

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C	0.950818	-0.583487	0.156932
C	-0.333186	-0.828301	0.952028
C	-1.222220	1.475230	-0.360640
C	-1.092484	1.578352	1.001192
C	-0.708927	0.380125	1.840158
C	-1.168102	0.194310	-0.983182
C	-1.430612	-1.040599	-0.133285
O	1.578194	-1.686610	-0.351185
C	-1.386001	2.695384	-1.235826
C	-1.249951	-2.332204	-0.955157
C	-2.867903	-1.066708	0.437877
H	-0.195769	-1.712551	1.598837
H	-1.189256	2.541569	1.495196
H	0.140054	0.631741	2.488332
H	-1.523087	0.093699	2.520663
H	-1.245451	0.124342	-2.065632
H	1.075426	-2.476960	-0.119459
H	-1.417309	3.616968	-0.647909
H	-0.549145	2.774047	-1.940345
H	-2.303462	2.637942	-1.832464
H	-1.236449	-3.215890	-0.303519
H	-2.094776	-2.453440	-1.641090
H	-0.346664	-2.321433	-1.567812
H	-3.586912	-1.189192	-0.378874

H	-3.000460	-1.907737	1.129736
H	-3.123811	-0.143055	0.958546
C	1.772644	0.580501	0.207252
H	1.285682	1.516495	0.467474
C	3.076044	0.593955	-0.068692
C	4.352267	0.620664	-0.329377
H	4.730986	0.722273	-1.347042
H	5.102970	0.533605	0.456847

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3.21.A_2.623

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C	0.976530	-0.597298	0.190481
C	-0.330657	-0.825105	0.944074
C	-1.236168	1.477697	-0.368336
C	-1.090880	1.578556	0.997707
C	-0.707721	0.380550	1.834634
C	-1.222236	0.206120	-0.991733
C	-1.432178	-1.034380	-0.141354
O	1.587516	-1.698684	-0.343735
C	-1.385806	2.704355	-1.237508
C	-1.247071	-2.325685	-0.961951
C	-2.865921	-1.073344	0.442654
H	-0.218275	-1.715655	1.587327
H	-1.170783	2.544433	1.489750
H	0.138903	0.633136	2.485149
H	-1.523400	0.092990	2.512677
H	-1.293649	0.134615	-2.074129
H	1.095923	-2.490629	-0.093260
H	-1.411705	3.622863	-0.644578
H	-0.545307	2.780940	-1.937647
H	-2.301684	2.658572	-1.837177
H	-1.230698	-3.206841	-0.307095
H	-2.090696	-2.452556	-1.648384
H	-0.340689	-2.312403	-1.569840
H	-3.589080	-1.202029	-0.369377
H	-2.986476	-1.915291	1.135646
H	-3.126247	-0.151454	0.964183
C	1.778381	0.570644	0.217689
H	1.289369	1.503358	0.484973
C	3.083229	0.595874	-0.072186
C	4.358540	0.623998	-0.335173
H	4.738822	0.722427	-1.353137
H	5.111338	0.542082	0.450532

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3.21.A_2.709

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C	0.998629	-0.611391	0.222393
C	-0.328944	-0.822346	0.936527
C	-1.251764	1.481380	-0.376106
C	-1.088456	1.579438	0.992611
C	-0.706606	0.381657	1.828106
C	-1.272854	0.216733	-0.998877
C	-1.435048	-1.027836	-0.149812
O	1.596709	-1.711422	-0.333591

C	-1.386411	2.714467	-1.239343
C	-1.243566	-2.317207	-0.971100
C	-2.863735	-1.082472	0.449014
H	-0.242287	-1.718338	1.576238
H	-1.149961	2.547825	1.482602
H	0.137945	0.634933	2.480796
H	-1.523892	0.094466	2.504218
H	-1.351048	0.145147	-2.080799
H	1.119832	-2.505689	-0.061843
H	-1.407545	3.629626	-0.641102
H	-0.541077	2.788566	-1.933684
H	-2.299478	2.680840	-1.843745
H	-1.223741	-3.196951	-0.314571
H	-2.085293	-2.449426	-1.658911
H	-0.333587	-2.299432	-1.573344
H	-3.592449	-1.220352	-0.356459
H	-2.968579	-1.924774	1.144187
H	-3.129927	-0.162639	0.971246
C	1.786368	0.559686	0.230198
H	1.296604	1.489683	0.504748
C	3.090723	0.596553	-0.076501
C	4.365301	0.628491	-0.342145
H	4.745951	0.730229	-1.360048
H	5.120401	0.546994	0.442143

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3.21.A_2.824

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C	1.025825	-0.632293	0.265229
C	-0.328015	-0.818568	0.926218
C	-1.275859	1.488679	-0.387404
C	-1.082670	1.582843	0.982831
C	-0.705165	0.385134	1.817218
C	-1.342352	0.231911	-1.007473
C	-1.440597	-1.017948	-0.162502
O	1.609869	-1.731813	-0.312064
C	-1.389871	2.730586	-1.242252
C	-1.237191	-2.300928	-0.989598
C	-2.859377	-1.100990	0.461007
H	-0.276429	-1.720450	1.561416
H	-1.115973	2.554416	1.469329
H	0.136906	0.637728	2.473246
H	-1.525003	0.100299	2.491138
H	-1.444174	0.160394	-2.087508
H	1.151959	-2.527998	-0.015212
H	-1.407972	3.640630	-0.636236
H	-0.535773	2.802478	-1.925768
H	-2.296556	2.712180	-1.856320
H	-1.211664	-3.181932	-0.335022
H	-2.075402	-2.438753	-1.680685
H	-0.322185	-2.272981	-1.583616
H	-3.597763	-1.258035	-0.331956
H	-2.934748	-1.942079	1.161492
H	-3.136750	-0.184361	0.983269
C	1.801400	0.541320	0.251770
H	1.313031	1.468273	0.538256

C	3.101850	0.593919	-0.083798
C	4.375100	0.637162	-0.354775
H	4.753159	0.758186	-1.371854
H	5.134333	0.545751	0.425210

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3.21.A_2.917

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C	1.044279	-0.651662	0.298311
C	-0.329102	-0.814602	0.917232
C	-1.298889	1.498321	-0.396923
C	-1.073314	1.589738	0.971276
C	-0.704006	0.391209	1.805738
C	-1.401531	0.246098	-1.012666
C	-1.446962	-1.008339	-0.174272
O	1.622329	-1.754439	-0.281353
C	-1.397961	2.746893	-1.245358
C	-1.228991	-2.279867	-1.014286
C	-2.852791	-1.125726	0.475121
H	-0.306894	-1.719816	1.549367
H	-1.076827	2.564055	1.453419
H	0.135646	0.640317	2.466113
H	-1.527619	0.110356	2.476665
H	-1.539409	0.175647	-2.088721
H	1.167693	-2.549254	0.024663
H	-1.421327	3.652485	-0.632756
H	-0.533130	2.821186	-1.914870
H	-2.295414	2.737269	-1.872776
H	-1.197300	-3.167175	-0.368554
H	-2.062760	-2.418887	-1.710601
H	-0.309697	-2.236656	-1.600764
H	-3.601336	-1.308900	-0.302300
H	-2.891331	-1.963280	1.182854
H	-3.144924	-0.213151	0.996718
C	1.818397	0.521063	0.274267
H	1.334386	1.445582	0.575416
C	3.112316	0.586179	-0.090224
C	4.383156	0.647255	-0.370216
H	4.753045	0.801121	-1.385837
H	5.149506	0.537632	0.400739

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3.21.P_1.642

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C	0.151211	-0.999914	-0.214846
C	-0.804697	-0.718829	0.983502
C	0.034270	1.546120	-0.330047
C	0.214415	1.578739	0.996905
C	-0.197547	0.400696	1.852190
C	-0.623235	0.285282	-0.882633
C	-1.869800	-0.141414	-0.015025
O	-0.028505	-2.321702	-0.737013
C	1.591868	-0.836515	-0.070293
C	0.519824	2.631754	-1.253868
C	-2.702065	-1.171163	-0.809580
C	-2.852296	0.859210	0.604323

H	-1.075216	-1.593228	1.591494
H	0.698462	2.423163	1.482513
H	0.684908	-0.000510	2.367935
H	-0.900813	0.708340	2.637968
H	-0.742988	0.295451	-1.969428
H	-0.841427	-2.685131	-0.366492
H	1.047903	3.413681	-0.699993
H	1.209201	2.219698	-2.001839
H	-0.304489	3.100866	-1.806599
H	-3.237579	-1.860771	-0.144339
H	-3.458286	-0.641580	-1.398859
H	-2.111016	-1.751734	-1.517533
H	-3.519750	1.284574	-0.152717
H	-3.478711	0.330982	1.334099
H	-2.360373	1.688395	1.114027
C	2.778344	-0.620510	0.003056
C	4.190016	-0.261753	0.060797
H	4.335934	0.636551	0.672243
H	4.802394	-1.062138	0.490841
H	4.579845	-0.046807	-0.940904

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3.21.P_1.718

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C	0.152003	-1.027479	-0.216296
C	-0.806684	-0.717390	0.967439
C	0.021516	1.575565	-0.335969
C	0.225425	1.582723	0.988385
C	-0.190680	0.398991	1.834328
C	-0.655337	0.329441	-0.892518
C	-1.872314	-0.131215	-0.015815
O	-0.016952	-2.367792	-0.697778
C	1.592498	-0.863682	-0.064301
C	0.537223	2.658302	-1.251550
C	-2.685270	-1.162524	-0.826470
C	-2.868202	0.841950	0.626453
H	-1.089343	-1.583102	1.582790
H	0.737950	2.407597	1.478996
H	0.691190	-0.007244	2.346626
H	-0.890367	0.705164	2.624069
H	-0.806062	0.361572	-1.975390
H	-0.873444	-2.693584	-0.395927
H	1.092475	3.416292	-0.690749
H	1.212807	2.229726	-2.002927
H	-0.270054	3.160933	-1.799926
H	-3.212369	-1.870051	-0.173313
H	-3.446703	-0.638849	-1.414340
H	-2.080356	-1.722862	-1.539970
H	-3.547508	1.268806	-0.119158
H	-3.480935	0.293162	1.352702
H	-2.384838	1.670907	1.145113
C	2.776592	-0.627686	0.007247
C	4.185915	-0.252480	0.056926
H	4.325705	0.646899	0.668149
H	4.809889	-1.046301	0.482531
H	4.566908	-0.032591	-0.947135

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3.21.P_1.797

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C	0.159132	-1.056339	-0.209698
C	-0.806856	-0.717401	0.956948
C	0.011257	1.594279	-0.338785
C	0.231014	1.584421	0.983812
C	-0.188176	0.397793	1.824877
C	-0.685245	0.371275	-0.901016
C	-1.872198	-0.125044	-0.017510
O	-0.010917	-2.395336	-0.679569
C	1.596085	-0.881470	-0.057701
C	0.546089	2.671148	-1.251111
C	-2.676543	-1.158332	-0.833586
C	-2.874903	0.833646	0.636403
H	-1.102110	-1.575032	1.578716
H	0.763847	2.395686	1.475421
H	0.692177	-0.009738	2.338414
H	-0.889030	0.702124	2.614453
H	-0.854923	0.415738	-1.980543
H	-0.882546	-2.706008	-0.406631
H	1.114575	3.418195	-0.689025
H	1.214982	2.230836	-2.001750
H	-0.251102	3.188473	-1.800220
H	-3.198503	-1.872250	-0.183315
H	-3.441298	-0.639164	-1.421126
H	-2.065250	-1.710368	-1.548594
H	-3.557811	1.261294	-0.105470
H	-3.482956	0.277130	1.360553
H	-2.395121	1.662621	1.158508
C	2.778030	-0.629894	0.009196
C	4.185986	-0.247782	0.054911
H	4.323862	0.651790	0.666206
H	4.813769	-1.039556	0.478824
H	4.563850	-0.026298	-0.950010

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3.21.P_1.889

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C	0.170107	-1.089823	-0.197587
C	-0.806222	-0.717474	0.947351
C	0.001516	1.610408	-0.341487
C	0.235457	1.585522	0.979865
C	-0.186509	0.396850	1.817355
C	-0.717897	0.417584	-0.910741
C	-1.870956	-0.119685	-0.020208
O	-0.006155	-2.419350	-0.665797
C	1.600380	-0.897477	-0.050955
C	0.553499	2.680995	-1.251022
C	-2.669371	-1.155080	-0.839136
C	-2.879619	0.826682	0.644025
H	-1.115161	-1.566562	1.575511
H	0.787193	2.384266	1.470920
H	0.691995	-0.011169	2.333388
H	-0.889750	0.699028	2.605786

H	-0.904340	0.472958	-1.986587
H	-0.888347	-2.717986	-0.413786
H	1.132331	3.419543	-0.688385
H	1.217088	2.230436	-2.000334
H	-0.235301	3.209296	-1.801493
H	-3.187007	-1.872878	-0.189679
H	-3.437152	-0.640008	-1.426312
H	-2.053584	-1.701233	-1.555232
H	-3.564443	1.255090	-0.095666
H	-3.484720	0.264922	1.366466
H	-2.402311	1.655788	1.168339
C	2.780078	-0.630934	0.010535
C	4.186634	-0.243902	0.053160
H	4.323367	0.655639	0.664659
H	4.816543	-1.034675	0.475967
H	4.562708	-0.021485	-0.952272

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3.21.P_1.989

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C	0.183695	-1.125500	-0.181368
C	-0.805052	-0.717543	0.938598
C	-0.007668	1.624345	-0.344328
C	0.239177	1.586254	0.976383
C	-0.185327	0.396101	1.811184
C	-0.751864	0.465929	-0.921099
C	-1.868979	-0.114989	-0.023724
O	-0.002400	-2.440642	-0.655143
C	1.604796	-0.912019	-0.044340
C	0.560015	2.688864	-1.251181
C	-2.663189	-1.152467	-0.843872
C	-2.883048	0.820437	0.650239
H	-1.127921	-1.558170	1.572574
H	0.808361	2.373465	1.465833
H	0.691119	-0.012020	2.330415
H	-0.891613	0.695965	2.597915
H	-0.953799	0.531596	-1.992898
H	-0.892325	-2.729095	-0.418268
H	1.147164	3.420342	-0.688051
H	1.219376	2.229418	-1.998835
H	-0.221489	3.225951	-1.803248
H	-3.177206	-1.872593	-0.194064
H	-3.433656	-0.641051	-1.430692
H	-2.044136	-1.694311	-1.560812
H	-3.568886	1.249578	-0.088113
H	-3.486083	0.254774	1.371267
H	-2.407508	1.649727	1.176028
C	2.782313	-0.631250	0.011394
C	4.187481	-0.240546	0.051537
H	4.323465	0.658845	0.663314
H	4.818528	-1.030941	0.473612
H	4.562640	-0.017597	-0.954185

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3.21.P_2.091

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C	0.198630	-1.161659	-0.161638
C	-0.803418	-0.717630	0.930335
C	-0.016640	1.636614	-0.347478
C	0.242370	1.586665	0.973180
C	-0.184455	0.395365	1.805770
C	-0.786700	0.515056	-0.931064
C	-1.866197	-0.110721	-0.028096
O	0.000497	-2.460031	-0.646987
C	1.609177	-0.925693	-0.037656
C	0.566016	2.695370	-1.251625
C	-2.657514	-1.150220	-0.848208
C	-2.885421	0.814544	0.655489
H	-1.140893	-1.549705	1.569340
H	0.828107	2.362902	1.460191
H	0.689721	-0.012545	2.328802
H	-0.894391	0.692703	2.590295
H	-1.004454	0.592083	-1.998215
H	-0.894904	-2.740000	-0.420020
H	1.159916	3.420607	-0.687652
H	1.222120	2.228099	-1.997232
H	-0.208713	3.239993	-1.805520
H	-3.168345	-1.871446	-0.197024
H	-3.430431	-0.642121	-1.434632
H	-2.036107	-1.689075	-1.565722
H	-3.571793	1.244338	-0.082008
H	-3.486806	0.245701	1.375334
H	-2.411228	1.644097	1.182230
C	2.784668	-0.630985	0.011762
C	4.188531	-0.237508	0.049935
H	4.323974	0.661648	0.662064
H	4.819999	-1.027968	0.471617
H	4.563566	-0.014311	-0.955869

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3.21.P_2.144

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C	0.206576	-1.179926	-0.150112
C	-0.802353	-0.717598	0.926235
C	-0.021051	1.642028	-0.349296
C	0.243633	1.586689	0.971694
C	-0.184104	0.394935	1.803337
C	-0.804474	0.539817	-0.935530
C	-1.864463	-0.108668	-0.030711
O	0.001588	-2.468973	-0.644020
C	1.611361	-0.932084	-0.034358
C	0.568797	2.698076	-1.251973
C	-2.654892	-1.149175	-0.850225
C	-2.886160	0.811777	0.657710
H	-1.147543	-1.545288	1.567610
H	0.837035	2.357868	1.457238
H	0.688899	-0.012696	2.328476
H	-0.896086	0.690863	2.586625
H	-1.029025	0.621735	-2.000204
H	-0.895675	-2.745353	-0.419656
H	1.165320	3.420577	-0.687357
H	1.223708	2.227497	-1.996473

H	-0.202868	3.245931	-1.806784
H	-3.164297	-1.870430	-0.197861
H	-3.429023	-0.642657	-1.436391
H	-2.032714	-1.687141	-1.567885
H	-3.572644	1.241873	-0.079533
H	-3.486877	0.241698	1.377101
H	-2.412466	1.641541	1.184648
C	2.785938	-0.630630	0.011726
C	4.189140	-0.236129	0.049143
H	4.324333	0.662868	0.661500
H	4.820530	-1.026788	0.470798
H	4.564458	-0.012909	-0.956602

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3.21.P_2.253

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C	0.224691	-1.217856	-0.122466
C	-0.799378	-0.717352	0.918446
C	-0.028846	1.650029	-0.353348
C	0.244997	1.586268	0.969064
C	-0.183472	0.393886	1.799625
C	-0.840163	0.590043	-0.944170
C	-1.860450	-0.105102	-0.036846
O	0.002816	-2.483872	-0.640878
C	1.615301	-0.942351	-0.028782
C	0.573442	2.701842	-1.252935
C	-2.650783	-1.147566	-0.853532
C	-2.886633	0.807174	0.660961
H	-1.161161	-1.536248	1.563583
H	0.851785	2.348572	1.451263
H	0.687282	-0.012839	2.329165
H	-0.900112	0.686003	2.580219
H	-1.072946	0.676695	-2.006066
H	-0.896111	-2.755542	-0.416086
H	1.173265	3.419837	-0.686183
H	1.227455	2.227534	-1.995760
H	-0.193363	3.254966	-1.808923
H	-3.157596	-1.867683	-0.197720
H	-3.427136	-0.643933	-1.439163
H	-2.028057	-1.685211	-1.571311
H	-3.573034	1.237418	-0.076293
H	-3.486233	0.235187	1.379871
H	-2.413508	1.637449	1.187784
C	2.788350	-0.629698	0.011279
C	4.190258	-0.233962	0.047736
H	4.324748	0.664744	0.660551
H	4.821107	-1.025137	0.469742
H	4.567041	-0.010769	-0.957625

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3.21.P_2.310

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C	0.235251	-1.236780	-0.106159
C	-0.797066	-0.717153	0.914599
C	-0.032500	1.651812	-0.356765
C	0.245145	1.585618	0.969185

C	-0.183069	0.393254	1.798225
C	-0.858158	0.616238	-0.947759
C	-1.858176	-0.103743	-0.040235
O	0.002790	-2.489749	-0.640765
C	1.616149	-0.945974	-0.026911
C	0.575288	2.702973	-1.253592
C	-2.649479	-1.146980	-0.854849
C	-2.886427	0.805638	0.661946
H	-1.167847	-1.532464	1.559296
H	0.857085	2.344980	1.449223
H	0.686923	-0.012823	2.329335
H	-0.901925	0.683782	2.577365
H	-1.084086	0.692345	-2.010928
H	-0.895642	-2.760582	-0.413290
H	1.175666	3.419257	-0.685309
H	1.229881	2.228696	-1.995719
H	-0.189755	3.258316	-1.809383
H	-3.155032	-1.866452	-0.197361
H	-3.426867	-0.644575	-1.440104
H	-2.026620	-1.685274	-1.572080
H	-3.573225	1.235579	-0.075010
H	-3.484922	0.231995	1.380503
H	-2.414122	1.636167	1.189005
C	2.789491	-0.629259	0.010887
C	4.190770	-0.233223	0.047104
H	4.325043	0.665429	0.660109
H	4.821798	-1.024200	0.469635
H	4.568722	-0.009757	-0.957890

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3.21.P_2.421

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C	0.276989	-1.305918	-0.073824
C	-0.769986	-0.749872	0.904638
C	-0.018528	1.624558	-0.365889
C	0.267828	1.551063	0.966203
C	-0.159919	0.358996	1.792606
C	-0.872259	0.634035	-0.955341
C	-1.831757	-0.132649	-0.049976
O	0.024544	-2.534906	-0.642974
C	1.640547	-0.987382	-0.024204
C	0.601851	2.673269	-1.257334
C	-2.623894	-1.177946	-0.860701
C	-2.864120	0.768776	0.662652
H	-1.162574	-1.555486	1.548481
H	0.891290	2.303597	1.441691
H	0.708753	-0.045171	2.326885
H	-0.882770	0.647313	2.568793
H	-1.086141	0.693158	-2.020748
H	-0.870873	-2.807226	-0.406197
H	1.203144	3.385665	-0.685275
H	1.258140	2.197952	-1.996871
H	-0.158162	3.233853	-1.814002
H	-3.125981	-1.896170	-0.199213
H	-3.404106	-0.678913	-1.444982
H	-2.000155	-1.717694	-1.576041

H	-3.553232	1.197987	-0.072371
H	-3.458840	0.190424	1.380616
H	-2.394099	1.599969	1.190551
C	2.814092	-0.661133	0.007715
C	4.214256	-0.264181	0.043422
H	4.347932	0.634576	0.656560
H	4.846246	-1.054295	0.466985
H	4.594482	-0.039986	-0.960872

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3.21.P_2.476

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C	0.264363	-1.291187	-0.054280
C	-0.789717	-0.717147	0.902792
C	-0.044937	1.660395	-0.367339
C	0.246003	1.582836	0.967643
C	-0.181567	0.390971	1.792797
C	-0.912508	0.691756	-0.955769
C	-1.851854	-0.097802	-0.051817
O	0.002109	-2.508408	-0.640965
C	1.619584	-0.959213	-0.019492
C	0.582046	2.707690	-1.256108
C	-2.644180	-1.144162	-0.860744
C	-2.886289	0.799287	0.666286
H	-1.193733	-1.517558	1.546209
H	0.875413	2.331781	1.440860
H	0.686429	-0.012183	2.328709
H	-0.906370	0.678377	2.567471
H	-1.120850	0.743184	-2.022199
H	-0.891404	-2.782111	-0.398806
H	1.183752	3.418067	-0.682022
H	1.239356	2.231607	-1.994041
H	-0.175121	3.271003	-1.813543
H	-3.144486	-1.861803	-0.197278
H	-3.425824	-0.646907	-1.444601
H	-2.019828	-1.684609	-1.574993
H	-3.576788	1.228111	-0.067579
H	-3.478887	0.218331	1.383927
H	-2.417536	1.630847	1.194661
C	2.793159	-0.627962	0.009192
C	4.192799	-0.230503	0.044707
H	4.326103	0.668309	0.657933
H	4.825285	-1.020133	0.468882
H	4.574241	-0.005942	-0.959194

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3.21.P_2.581

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C	0.281415	-1.326038	-0.018325
C	-0.785360	-0.717432	0.895004
C	-0.054301	1.668875	-0.374493
C	0.247357	1.580360	0.964784
C	-0.180429	0.389328	1.788015
C	-0.947880	0.739173	-0.959608
C	-1.848308	-0.092410	-0.060390
O	0.001254	-2.521020	-0.640941

C	1.622548	-0.969973	-0.012681
C	0.587806	2.712104	-1.258013
C	-2.639094	-1.141168	-0.867016
C	-2.887110	0.793126	0.670604
H	-1.215279	-1.505205	1.537516
H	0.890469	2.320565	1.433313
H	0.686179	-0.011569	2.327343
H	-0.908619	0.676241	2.559579
H	-1.151442	0.783729	-2.026745
H	-0.885109	-2.803029	-0.382118
H	1.189821	3.418223	-0.679053
H	1.248467	2.232782	-1.990498
H	-0.161386	3.281350	-1.819558
H	-3.135405	-1.858182	-0.199900
H	-3.423764	-0.648224	-1.450478
H	-2.011992	-1.682539	-1.577986
H	-3.582804	1.220600	-0.059013
H	-3.472934	0.204727	1.387825
H	-2.421915	1.625751	1.200337
C	2.795598	-0.627372	0.007609
C	4.194380	-0.228270	0.043038
H	4.326349	0.670942	0.656169
H	4.828320	-1.016343	0.468818
H	4.578298	-0.002985	-0.960023

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3.21.P_2.681

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C	0.295960	-1.359722	0.018077
C	-0.781606	-0.717795	0.887673
C	-0.064305	1.679714	-0.381542
C	0.249945	1.577367	0.959920
C	-0.178807	0.387874	1.782233
C	-0.981639	0.783462	-0.962528
C	-1.845449	-0.085831	-0.069496
O	0.000304	-2.533192	-0.639799
C	1.626077	-0.982293	-0.004284
C	0.593998	2.717823	-1.260041
C	-2.632516	-1.137093	-0.875560
C	-2.888822	0.784628	0.676856
H	-1.238703	-1.491095	1.529129
H	0.908149	2.307438	1.423488
H	0.686412	-0.011060	2.324803
H	-0.909382	0.675641	2.551115
H	-1.189922	0.832034	-2.028487
H	-0.875674	-2.829188	-0.360990
H	1.195143	3.420383	-0.675878
H	1.259389	2.233587	-1.984720
H	-0.145576	3.292174	-1.828607
H	-3.124687	-1.854460	-0.205768
H	-3.420167	-0.648948	-1.459073
H	-2.001092	-1.678405	-1.582501
H	-3.593012	1.209524	-0.046013
H	-3.464241	0.186416	1.394503
H	-2.428141	1.618951	1.207800
C	2.797702	-0.627521	0.005556

C	4.195736	-0.225623	0.040716
H	4.325700	0.674480	0.653133
H	4.831853	-1.011432	0.468119
H	4.581148	0.000146	-0.961848

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3.21.P_2.773

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C	0.307414	-1.391298	0.053061
C	-0.778834	-0.717837	0.881041
C	-0.074383	1.692684	-0.388355
C	0.254583	1.574030	0.952836
C	-0.176537	0.387091	1.775465
C	-1.013119	0.824741	-0.964733
C	-1.843235	-0.078446	-0.078781
O	-0.000413	-2.545063	-0.635909
C	1.629775	-0.996189	0.005888
C	0.600237	2.725180	-1.262093
C	-2.623965	-1.131668	-0.887345
C	-2.891710	0.772826	0.685423
H	-1.262065	-1.476017	1.521473
H	0.929493	2.292357	1.410943
H	0.686959	-0.010836	2.321205
H	-0.908497	0.677171	2.542084
H	-1.235458	0.886897	-2.027309
H	-0.864612	-2.857975	-0.338258
H	1.198167	3.425983	-0.672484
H	1.272661	2.234992	-1.976083
H	-0.128486	3.302499	-1.841233
H	-3.112745	-1.851079	-0.217268
H	-3.413762	-0.647980	-1.471730
H	-1.986366	-1.671031	-1.590005
H	-3.608298	1.193106	-0.027876
H	-3.452074	0.162102	1.404647
H	-2.436732	1.609796	1.217116
C	2.799073	-0.629279	0.003396
C	4.196190	-0.222699	0.037638
H	4.323089	0.679027	0.648411
H	4.835360	-1.005250	0.466870
H	4.581749	0.002961	-0.964956

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3.21.P_2.854

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C	0.315142	-1.418339	0.083080
C	-0.777101	-0.717005	0.875064
C	-0.083576	1.707523	-0.394531
C	0.262398	1.570676	0.943508
C	-0.173252	0.387615	1.767750
C	-1.041770	0.863463	-0.965478
C	-1.841717	-0.070774	-0.087467
O	-0.000642	-2.558115	-0.626937
C	1.633070	-1.011657	0.017705
C	0.605582	2.734762	-1.264132
C	-2.612738	-1.124514	-0.903565
C	-2.896197	0.756435	0.696520

H	-1.281717	-1.461319	1.515200
H	0.954927	2.275816	1.395448
H	0.687853	-0.010757	2.316715
H	-0.905539	0.681868	2.532469
H	-1.283234	0.943192	-2.022439
H	-0.856089	-2.883462	-0.318367
H	1.195895	3.437664	-0.669330
H	1.288328	2.238904	-1.964081
H	-0.112611	3.310304	-1.857599
H	-3.099678	-1.848833	-0.237339
H	-3.403376	-0.643909	-1.489424
H	-1.967172	-1.658861	-1.602569
H	-3.628720	1.169425	-0.004531
H	-3.436405	0.130873	1.418155
H	-2.448517	1.597289	1.228357
C	2.799456	-0.633889	0.002124
C	4.194878	-0.219668	0.033324
H	4.317357	0.684768	0.640993
H	4.838721	-0.997264	0.464702
H	4.578494	0.004849	-0.970235

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3.21.Ph_1.640

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C	0.915390	-0.884509	-0.186626
C	2.148161	-0.484984	-1.064575
C	1.331387	1.504416	0.612481
C	1.534909	1.903202	-0.651487
C	2.010858	0.912817	-1.690160
C	1.664950	0.050443	0.933327
C	3.018401	-0.379047	0.254598
O	0.938117	-2.313122	-0.030516
C	0.716838	2.394186	1.658813
C	3.517784	-1.689031	0.909002
C	4.242297	0.542009	0.144229
H	2.436249	-1.227340	-1.821780
H	1.308285	2.919365	-0.966773
H	1.307181	0.865262	-2.530936
H	2.965220	1.227499	-2.133835
H	1.522701	-0.200625	1.989141
H	1.799467	-2.644979	-0.297273
H	0.503560	3.389446	1.258283
H	-0.228219	1.961114	2.011213
H	1.365285	2.505744	2.536996
H	4.089426	-2.307685	0.204161
H	4.197465	-1.437000	1.729632
H	2.721692	-2.291778	1.344126
H	4.753796	0.635559	1.107732
H	4.954667	0.097177	-0.561966
H	4.006766	1.549574	-0.197460
C	-0.565946	-0.581848	-0.366933
C	-1.106972	0.491063	-1.091283
C	-1.469646	-1.360211	0.376150
C	-2.450045	0.830661	-0.997855
C	-2.825188	-1.042151	0.470337
C	-3.315366	0.089756	-0.189055

H	-0.485575	1.099921	-1.726710
H	-1.101148	-2.223109	0.916532
H	-2.848951	1.680273	-1.542081
H	-3.473278	-1.666032	1.074565
O	-4.600487	0.550217	-0.118046
C	-5.529631	-0.185492	0.659397
H	-5.654248	-1.210019	0.283543
H	-5.233201	-0.229394	1.716198
H	-6.480569	0.343564	0.576571

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3.21.Ph_1.680

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C	0.915398	-0.897501	-0.187399
C	2.147889	-0.485043	-1.053958
C	1.338280	1.520700	0.622426
C	1.524013	1.906532	-0.648396
C	2.002056	0.910849	-1.681260
C	1.683488	0.070913	0.950074
C	3.020705	-0.372347	0.257588
O	0.932129	-2.330594	-0.065045
C	0.708360	2.415635	1.658354
C	3.500838	-1.683898	0.921037
C	4.256169	0.530641	0.127532
H	2.443879	-1.223589	-1.811808
H	1.278796	2.914886	-0.974610
H	1.298137	0.856325	-2.521103
H	2.953959	1.227744	-2.128587
H	1.565716	-0.166489	2.011663
H	1.811947	-2.656453	-0.278103
H	0.481176	3.402150	1.243831
H	-0.232293	1.972725	2.010423
H	1.349408	2.549142	2.538734
H	4.067428	-2.315285	0.223441
H	4.178901	-1.436163	1.744335
H	2.694392	-2.272505	1.357492
H	4.781491	0.623804	1.083573
H	4.953305	0.072052	-0.585169
H	4.028643	1.538907	-0.218111
C	-0.565101	-0.594104	-0.371546
C	-1.103465	0.483441	-1.091659
C	-1.472862	-1.371514	0.368929
C	-2.444159	0.831803	-0.991626
C	-2.825996	-1.045195	0.468924
C	-3.312308	0.091508	-0.185567
H	-0.482087	1.090252	-1.728581
H	-1.107876	-2.237984	0.906200
H	-2.839136	1.685709	-1.531974
H	-3.475966	-1.667881	1.072361
O	-4.597055	0.553311	-0.115248
C	-5.528353	-0.184052	0.658314
H	-5.651070	-1.208156	0.280745
H	-5.235401	-0.229008	1.716032
H	-6.479323	0.344535	0.572983

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3.21.Ph_1.750

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C	0.910205	-0.917695	-0.198206
C	2.146279	-0.486604	-1.043354
C	1.348561	1.537305	0.632802
C	1.514577	1.909027	-0.645885
C	1.994789	0.908037	-1.673128
C	1.711675	0.101104	0.972962
C	3.021223	-0.365905	0.260949
O	0.926106	-2.349423	-0.094083
C	0.701120	2.432879	1.658970
C	3.487060	-1.679376	0.929117
C	4.265917	0.521819	0.114800
H	2.454952	-1.219620	-1.802187
H	1.249351	2.909068	-0.982577
H	1.292355	0.848826	-2.513618
H	2.946145	1.224632	-2.121997
H	1.613346	-0.128404	2.038417
H	1.816437	-2.670450	-0.269388
H	0.462480	3.412969	1.235690
H	-0.235941	1.978889	2.006735
H	1.333599	2.581529	2.543050
H	4.048790	-2.318322	0.234392
H	4.165443	-1.436768	1.753689
H	2.673183	-2.258067	1.365972
H	4.798826	0.615168	1.066696
H	4.953556	0.054103	-0.601115
H	4.043849	1.530651	-0.233249
C	-0.565976	-0.606329	-0.379163
C	-1.101143	0.477928	-1.093198
C	-1.476675	-1.380516	0.362826
C	-2.439791	0.833737	-0.986342
C	-2.826854	-1.046469	0.469103
C	-3.310128	0.093432	-0.182816
H	-0.480196	1.081603	-1.733151
H	-1.114152	-2.249334	0.898156
H	-2.832130	1.690896	-1.523499
H	-3.478100	-1.667062	1.073277
O	-4.594967	0.554999	-0.113820
C	-5.527544	-0.183287	0.657623
H	-5.649013	-1.207280	0.279382
H	-5.236810	-0.228408	1.715931
H	-6.478541	0.344944	0.570526

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3.21.Ph_1.830

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C	0.900332	-0.942759	-0.218297
C	2.143814	-0.488424	-1.033863
C	1.358807	1.551609	0.642266
C	1.506737	1.910557	-0.643760
C	1.989194	0.905434	-1.666590
C	1.744338	0.136760	1.000172
C	3.019849	-0.360471	0.264723
O	0.920952	-2.366480	-0.116921
C	0.695075	2.445937	1.659626

C	3.476229	-1.675772	0.934936
C	4.272386	0.514660	0.105078
H	2.467748	-1.215052	-1.793552
H	1.221529	2.902110	-0.988854
H	1.288978	0.843013	-2.508503
H	2.941176	1.220049	-2.115650
H	1.665311	-0.085003	2.068524
H	1.817801	-2.682993	-0.265801
H	0.447517	3.421269	1.230629
H	-0.239178	1.982327	2.002336
H	1.319548	2.605279	2.547308
H	4.033700	-2.319017	0.240745
H	4.155751	-1.437709	1.759865
H	2.657127	-2.247041	1.372612
H	4.809744	0.608076	1.054499
H	4.953788	0.040858	-0.612668
H	4.054082	1.523961	-0.244316
C	-0.567720	-0.616991	-0.387204
C	-1.099361	0.474458	-1.094724
C	-1.480280	-1.387491	0.358148
C	-2.436502	0.835776	-0.982029
C	-2.827397	-1.047037	0.469897
C	-3.308456	0.095134	-0.180791
H	-0.479165	1.073864	-1.739048
H	-1.119658	-2.258220	0.891765
H	-2.827018	1.695336	-1.516657
H	-3.479564	-1.665449	1.075255
O	-4.593500	0.555844	-0.113057
C	-5.527017	-0.182909	0.657172
H	-5.647743	-1.206866	0.278662
H	-5.237784	-0.227851	1.715866
H	-6.477934	0.345206	0.568726

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3.21.Ph_1.930

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C	0.887563	-0.969722	-0.244585
C	2.140726	-0.490117	-1.025291
C	1.368252	1.563612	0.651019
C	1.499904	1.911522	-0.642007
C	1.984597	0.903185	-1.661248
C	1.778723	0.174818	1.029267
C	3.017221	-0.355911	0.268964
O	0.916596	-2.381914	-0.135534
C	0.689744	2.456356	1.660238
C	3.467236	-1.672871	0.939710
C	4.276992	0.508395	0.097035
H	2.480313	-1.210404	-1.785437
H	1.196530	2.895177	-0.993628
H	1.286996	0.838270	-2.505048
H	2.937813	1.214962	-2.109801
H	1.716522	-0.040524	2.099307
H	1.818646	-2.693278	-0.263824
H	0.435605	3.428047	1.226965
H	-0.242519	1.984972	1.997727
H	1.307035	2.623536	2.551281

H	4.021316	-2.318555	0.245010
H	4.148197	-1.438661	1.764510
H	2.644543	-2.238625	1.378613
H	4.817214	0.601841	1.044862
H	4.953827	0.030198	-0.622038
H	4.061293	1.518156	-0.252946
C	-0.569371	-0.626290	-0.394703
C	-1.097705	0.472318	-1.096008
C	-1.483608	-1.393374	0.354392
C	-2.433751	0.837727	-0.978332
C	-2.827606	-1.047396	0.470887
C	-3.307040	0.096670	-0.179203
H	-0.478467	1.067041	-1.745190
H	-1.124559	-2.265679	0.886552
H	-2.822939	1.699073	-1.511027
H	-3.480478	-1.663708	1.077563
O	-4.592296	0.556268	-0.112573
C	-5.526657	-0.182714	0.656862
H	-5.646925	-1.206651	0.278239
H	-5.238562	-0.227343	1.715835
H	-6.477416	0.345444	0.567278

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3.21.Ph_2.030

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C	0.873218	-0.997051	-0.274570
C	2.137190	-0.491706	-1.017442
C	1.377171	1.574060	0.659444
C	1.493532	1.912217	-0.640592
C	1.980530	0.901177	-1.656611
C	1.813808	0.213906	1.058988
C	3.013850	-0.351927	0.273610
O	0.912836	-2.396366	-0.151439
C	0.684754	2.465250	1.660891
C	3.459173	-1.670419	0.944039
C	4.280472	0.502522	0.089854
H	2.492154	-1.206081	-1.777368
H	1.173640	2.888480	-0.997455
H	1.285853	0.834068	-2.502636
H	2.935364	1.209615	-2.104158
H	1.766945	0.004246	2.130010
H	1.819365	-2.702072	-0.262727
H	0.425888	3.434009	1.223992
H	-0.246281	1.987480	1.992626
H	1.295036	2.638557	2.555368
H	4.010498	-2.317510	0.248359
H	4.141590	-1.439576	1.768530
H	2.633941	-2.231973	1.384365
H	4.822865	0.595902	1.036472
H	4.953451	0.020744	-0.630432
H	4.066687	1.512735	-0.260241
C	-0.570556	-0.634720	-0.401715
C	-1.096046	0.471054	-1.097130
C	-1.486751	-1.398752	0.351108
C	-2.431260	0.839610	-0.974975
C	-2.827487	-1.047694	0.471988

C	-3.305762	0.098130	-0.177855
H	-0.477913	1.060953	-1.751326
H	-1.129115	-2.272437	0.881991
H	-2.819384	1.702409	-1.506062
H	-3.480888	-1.661893	1.080178
O	-4.591235	0.556436	-0.112223
C	-5.526437	-0.182631	0.656651
H	-5.646401	-1.206546	0.277992
H	-5.239290	-0.226855	1.715840
H	-6.476977	0.345683	0.566022

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3.21.Ph_2.130

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C	0.858769	-1.023557	-0.306591
C	2.132994	-0.493202	-1.009527
C	1.386289	1.583720	0.668034
C	1.487327	1.912647	-0.639286
C	1.976673	0.899119	-1.652104
C	1.849642	0.253327	1.087551
C	3.009565	-0.348213	0.278720
O	0.909401	-2.410684	-0.165704
C	0.679801	2.473263	1.661731
C	3.451252	-1.668053	0.948277
C	4.283002	0.496668	0.083061
H	2.503749	-1.201913	-1.768287
H	1.151808	2.881682	-1.000659
H	1.285385	0.830065	-2.500772
H	2.933563	1.203624	-2.098086
H	1.819681	0.051425	2.159814
H	1.819853	-2.710246	-0.263140
H	0.417783	3.439545	1.221379
H	-0.250756	1.990052	1.986578
H	1.282433	2.651751	2.560136
H	4.000274	-2.315665	0.251134
H	4.135141	-1.440378	1.772369
H	2.624082	-2.226394	1.389826
H	4.827291	0.589837	1.028628
H	4.952368	0.011671	-0.638457
H	4.070825	1.507377	-0.266744
C	-0.571132	-0.642885	-0.408849
C	-1.094318	0.470473	-1.098179
C	-1.489702	-1.403975	0.347987
C	-2.428930	0.841524	-0.971754
C	-2.827052	-1.047950	0.473284
C	-3.304623	0.099567	-0.176645
H	-0.477587	1.055399	-1.757726
H	-1.133465	-2.278931	0.877743
H	-2.816192	1.705608	-1.501358
H	-3.480777	-1.659848	1.083405
O	-4.590340	0.556409	-0.111958
C	-5.526403	-0.182641	0.656540
H	-5.646172	-1.206525	0.277888
H	-5.240054	-0.226385	1.715894
H	-6.476667	0.345930	0.564940

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3.21.Ph_2.240

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C	0.843570	-1.049612	-0.342668
C	2.128068	-0.494585	-1.001984
C	1.395293	1.591912	0.676842
C	1.482324	1.912619	-0.638051
C	1.973458	0.897058	-1.648140
C	1.886525	0.293091	1.114849
C	3.004431	-0.344781	0.284622
O	0.906402	-2.424530	-0.176885
C	0.675101	2.479796	1.662845
C	3.444257	-1.665850	0.952101
C	4.284286	0.491363	0.077259
H	2.515920	-1.197636	-1.758380
H	1.133430	2.875244	-1.002784
H	1.285768	0.826906	-2.499745
H	2.932896	1.196643	-2.092180
H	1.870964	0.097993	2.187627
H	1.820073	-2.717489	-0.266849
H	0.411846	3.444257	1.219356
H	-0.255827	1.992773	1.980343
H	1.270083	2.662330	2.565280
H	3.991686	-2.312420	0.252537
H	4.129709	-1.441264	1.775690
H	2.616075	-2.222767	1.394232
H	4.829849	0.584213	1.022139
H	4.950758	0.003990	-0.645425
H	4.073096	1.502604	-0.271655
C	-0.571232	-0.650366	-0.415896
C	-1.092830	0.470906	-1.099055
C	-1.492471	-1.408613	0.345616
C	-2.427279	0.843263	-0.968982
C	-2.826427	-1.048241	0.474759
C	-3.303978	0.100845	-0.175797
H	-0.477836	1.050814	-1.764216
H	-1.137539	-2.284716	0.874362
H	-2.814030	1.708306	-1.497380
H	-3.480228	-1.657810	1.087102
O	-4.589850	0.556286	-0.111785
C	-5.526635	-0.182734	0.656558
H	-5.646299	-1.206551	0.277876
H	-5.240745	-0.226012	1.715973
H	-6.476633	0.346112	0.564271

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3.21.Ph_2.350

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C	0.826762	-1.075309	-0.384819
C	2.122174	-0.495842	-0.995620
C	1.402496	1.596616	0.685601
C	1.480545	1.912248	-0.637668
C	1.971133	0.895107	-1.645479
C	1.924718	0.334660	1.141993
C	2.998658	-0.342192	0.290933
O	0.904313	-2.436967	-0.183336

C	0.671002	2.484016	1.664170
C	3.439517	-1.664274	0.955154
C	4.284286	0.487642	0.073412
H	2.528947	-1.194094	-1.747510
H	1.120694	2.869805	-1.004143
H	1.286433	0.825611	-2.499646
H	2.933479	1.189004	-2.087137
H	1.903185	0.129881	2.211582
H	1.819710	-2.724462	-0.275090
H	0.408894	3.447333	1.217582
H	-0.261479	1.996742	1.975969
H	1.260412	2.669665	2.569334
H	3.985772	-2.308212	0.252143
H	4.126672	-1.442425	1.778005
H	2.611420	-2.222167	1.396653
H	4.830878	0.579655	1.017728
H	4.947909	-0.002096	-0.650439
H	4.074158	1.499385	-0.274541
C	-0.570725	-0.655934	-0.421220
C	-1.092776	0.471798	-1.099516
C	-1.494452	-1.411736	0.344661
C	-2.426585	0.844290	-0.967211
C	-2.826004	-1.048459	0.475916
C	-3.304109	0.101417	-0.175234
H	-0.478975	1.049275	-1.767606
H	-1.140715	-2.289243	0.871845
H	-2.813103	1.709800	-1.495020
H	-3.479774	-1.656481	1.089835
O	-4.590040	0.556379	-0.111633
C	-5.526919	-0.182762	0.656600
H	-5.646352	-1.206564	0.277887
H	-5.241098	-0.225839	1.716003
H	-6.476953	0.345949	0.564191

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3.21.Ph_2.460

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C	0.768113	-1.109085	-0.447964
C	2.071632	-0.508169	-1.007757
C	1.366199	1.590800	0.677384
C	1.436580	1.900569	-0.655597
C	1.925023	0.881961	-1.660871
C	1.920688	0.364961	1.148513
C	2.949585	-0.349775	0.280202
O	0.859237	-2.460801	-0.206369
C	0.623097	2.477738	1.647676
C	3.390912	-1.673058	0.941134
C	4.240899	0.472835	0.051033
H	2.502473	-1.200815	-1.751164
H	1.064711	2.852901	-1.023111
H	1.242821	0.815384	-2.516864
H	2.889871	1.172375	-2.098976
H	1.881444	0.143176	2.212889
H	1.773994	-2.745732	-0.308819
H	0.364018	3.440452	1.198136
H	-0.312012	1.991186	1.951570

H	1.205440	2.665870	2.556486
H	3.934965	-2.313959	0.233771
H	4.080481	-1.454977	1.762942
H	2.562346	-2.232487	1.379636
H	4.791234	0.563307	0.993193
H	4.898776	-0.021392	-0.674959
H	4.034053	1.485261	-0.296538
C	-0.613530	-0.672298	-0.445098
C	-1.137559	0.461340	-1.118124
C	-1.539051	-1.425463	0.325298
C	-2.469276	0.834400	-0.983851
C	-2.869429	-1.059058	0.458613
C	-3.347929	0.090452	-0.192347
H	-0.524881	1.039282	-1.787128
H	-1.186681	-2.304985	0.849932
H	-2.855826	1.700610	-1.510677
H	-3.522993	-1.666081	1.073882
O	-4.634311	0.546020	-0.129563
C	-5.570625	-0.193419	0.638334
H	-5.689602	-1.217415	0.259729
H	-5.284921	-0.236772	1.697863
H	-6.521094	0.334662	0.546203

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3.21.Ph_2.570

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C	0.798070	-1.120424	-0.474256
C	2.108259	-0.499263	-0.983207
C	1.417688	1.608393	0.706098
C	1.479067	1.910057	-0.636303
C	1.965426	0.889912	-1.639156
C	2.003112	0.415462	1.189997
C	2.987910	-0.335002	0.306848
O	0.901162	-2.463533	-0.193286
C	0.661659	2.494356	1.667558
C	3.427735	-1.659529	0.965430
C	4.285234	0.478218	0.063778
H	2.565068	-1.185496	-1.717023
H	1.094024	2.856345	-1.005645
H	1.285492	0.826444	-2.496724
H	2.932367	1.177817	-2.073846
H	1.951335	0.182214	2.250684
H	1.813966	-2.748052	-0.311431
H	0.406962	3.456865	1.215091
H	-0.276893	2.008272	1.960462
H	1.234433	2.684146	2.581721
H	3.969157	-2.298100	0.254073
H	4.119598	-1.445730	1.786458
H	2.597603	-2.219442	1.400055
H	4.841467	0.566883	1.002544
H	4.935136	-0.022085	-0.665196
H	4.082939	1.491432	-0.283925
C	-0.569615	-0.667896	-0.433711
C	-1.095691	0.471813	-1.100607
C	-1.496458	-1.418038	0.341771
C	-2.425112	0.845973	-0.963732

C	-2.825823	-1.048096	0.477907
C	-3.304859	0.100934	-0.172621
H	-0.484507	1.050409	-1.770753
H	-1.145488	-2.299575	0.863886
H	-2.811549	1.713123	-1.489282
H	-3.478940	-1.653916	1.095002
O	-4.591760	0.557287	-0.110816
C	-5.527545	-0.182461	0.656606
H	-5.645715	-1.206779	0.278335
H	-5.242245	-0.225791	1.716359
H	-6.478560	0.344744	0.564386

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3.21.Ph_2.670

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C	0.786782	-1.141385	-0.517460
C	2.102148	-0.501096	-0.976655
C	1.426639	1.617395	0.717088
C	1.477210	1.908645	-0.634136
C	1.961851	0.887077	-1.634756
C	2.040548	0.453236	1.211463
C	2.983444	-0.330097	0.316119
O	0.899859	-2.477044	-0.199612
C	0.656547	2.501799	1.669374
C	3.418807	-1.655880	0.973859
C	4.287408	0.470757	0.056275
H	2.586151	-1.180047	-1.700104
H	1.077401	2.847889	-1.005994
H	1.283822	0.826665	-2.493558
H	2.930293	1.173830	-2.066333
H	1.985761	0.216949	2.270991
H	1.808533	-2.764411	-0.341812
H	0.408992	3.465380	1.215089
H	-0.287044	2.016464	1.946532
H	1.216195	2.690530	2.591625
H	3.957402	-2.293348	0.259494
H	4.112150	-1.447009	1.794971
H	2.585179	-2.214579	1.402916
H	4.853124	0.556224	0.989620
H	4.925581	-0.037481	-0.677677
H	4.091362	1.485161	-0.291453
C	-0.569533	-0.675005	-0.442098
C	-1.097661	0.470692	-1.101909
C	-1.496899	-1.421829	0.338822
C	-2.424587	0.846687	-0.961409
C	-2.825479	-1.048074	0.478898
C	-3.305271	0.100502	-0.170619
H	-0.488306	1.050522	-1.773035
H	-1.147315	-2.305608	0.858042
H	-2.810676	1.715424	-1.484765
H	-3.477784	-1.652773	1.098135
O	-4.592647	0.557873	-0.109769
C	-5.528080	-0.182356	0.656817
H	-5.645158	-1.206957	0.278695
H	-5.243468	-0.225797	1.716863
H	-6.479689	0.343851	0.564324

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3.21.Ph_2.760

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C	0.778559	-1.160579	-0.557904
C	2.096968	-0.502653	-0.969750
C	1.436489	1.629079	0.728264
C	1.473924	1.907205	-0.630580
C	1.957693	0.884609	-1.629209
C	2.075174	0.488496	1.230300
C	2.979846	-0.324276	0.326504
O	0.898886	-2.490027	-0.208699
C	0.652243	2.511532	1.671289
C	3.406633	-1.651056	0.986067
C	4.291118	0.460144	0.046359
H	2.606514	-1.173676	-1.682845
H	1.059186	2.838767	-1.005310
H	1.281098	0.826232	-2.488900
H	2.926765	1.171746	-2.058782
H	2.027892	0.257308	2.291377
H	1.800545	-2.783529	-0.378482
H	0.416149	3.478327	1.217707
H	-0.297946	2.028148	1.927458
H	1.195580	2.693954	2.604120
H	3.943356	-2.289636	0.271303
H	4.099520	-1.447108	1.808883
H	2.567223	-2.206376	1.407538
H	4.869791	0.540468	0.972081
H	4.913288	-0.057233	-0.694674
H	4.102943	1.476322	-0.300637
C	-0.570370	-0.682948	-0.452286
C	-1.100100	0.467959	-1.104357
C	-1.496639	-1.426021	0.334314
C	-2.424333	0.846930	-0.958834
C	-2.824858	-1.048497	0.479721
C	-3.305568	0.099722	-0.167972
H	-0.492496	1.049470	-1.775990
H	-1.147980	-2.311748	0.850805
H	-2.809901	1.717725	-1.479255
H	-3.475895	-1.652361	1.101251
O	-4.593114	0.558438	-0.107695
C	-5.528771	-0.182439	0.657434
H	-5.644509	-1.207163	0.279056
H	-5.245319	-0.226183	1.717854
H	-6.480822	0.342916	0.564207

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3.21.Ph_2.840

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C	0.772983	-1.176929	-0.592647
C	2.092994	-0.503274	-0.962386
C	1.446232	1.642498	0.738739
C	1.469021	1.906529	-0.626463
C	1.953304	0.883145	-1.622840
C	2.106148	0.521406	1.246663
C	2.976829	-0.318178	0.337231

O	0.898243	-2.502124	-0.222034
C	0.649731	2.523748	1.673234
C	3.390602	-1.645325	1.002482
C	4.296344	0.445747	0.034511
H	2.625476	-1.166731	-1.665991
H	1.038781	2.829831	-1.004365
H	1.278132	0.825257	-2.483391
H	2.922554	1.171536	-2.050869
H	2.073371	0.301040	2.310574
H	1.792280	-2.802582	-0.419070
H	0.432503	3.497076	1.223966
H	-0.310557	2.046840	1.902099
H	1.173273	2.692526	2.619624
H	3.927116	-2.287899	0.291223
H	4.079795	-1.445249	1.829463
H	2.542862	-2.194626	1.414577
H	4.891649	0.517864	0.950240
H	4.897708	-0.082096	-0.716258
H	4.118105	1.464411	-0.310702
C	-0.571640	-0.691249	-0.463409
C	-1.102789	0.463747	-1.108321
C	-1.495936	-1.430996	0.328305
C	-2.424333	0.846290	-0.956531
C	-2.823757	-1.049926	0.480161
C	-3.305469	0.098428	-0.164898
H	-0.497041	1.046713	-1.780678
H	-1.147753	-2.318642	0.841862
H	-2.809477	1.719366	-1.473492
H	-3.473166	-1.653103	1.104186
O	-4.592745	0.558854	-0.104068
C	-5.529330	-0.182969	0.658700
H	-5.643635	-1.207529	0.279358
H	-5.247699	-0.227547	1.719613
H	-6.481600	0.341834	0.564323

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3.21.Ph_2.900

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C	0.769872	-1.189285	-0.619270
C	2.089965	-0.502588	-0.954891
C	1.455283	1.657423	0.747485
C	1.462676	1.907322	-0.622549
C	1.949109	0.883233	-1.616128
C	2.132386	0.551636	1.259584
C	2.974058	-0.312257	0.347698
O	0.897706	-2.513452	-0.241208
C	0.650507	2.538945	1.675189
C	3.370159	-1.638886	1.023136
C	4.302706	0.427308	0.022335
H	2.640601	-1.159499	-1.650838
H	1.017860	2.822443	-1.003663
H	1.275908	0.824355	-2.477954
H	2.918494	1.173363	-2.042496
H	2.116287	0.344273	2.326500
H	1.786915	-2.817647	-0.454861
H	0.460595	3.522285	1.235043

H	-0.323172	2.074874	1.871657
H	1.152168	2.685509	2.636851
H	3.908074	-2.288985	0.319897
H	4.052546	-1.441018	1.856398
H	2.512009	-2.179192	1.425192
H	4.915903	0.488593	0.926921
H	4.880307	-0.111688	-0.739174
H	4.136693	1.448968	-0.320521
C	-0.573164	-0.699505	-0.474422
C	-1.105473	0.458145	-1.113762
C	-1.495030	-1.437166	0.321032
C	-2.424563	0.844272	-0.955114
C	-2.822228	-1.052939	0.479914
C	-3.304758	0.096318	-0.161668
H	-0.501581	1.041721	-1.787496
H	-1.146739	-2.326575	0.831551
H	-2.809712	1.719294	-1.468788
H	-3.469926	-1.655638	1.106265
O	-4.591218	0.559065	-0.098370
C	-5.529288	-0.184268	0.660985
H	-5.642437	-1.208137	0.279430
H	-5.249846	-0.230901	1.722406
H	-6.481474	0.340538	0.565656

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3.21.Ph_2.950

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C	0.768555	-1.197514	-0.637721
C	2.087550	-0.500568	-0.947848
C	1.463265	1.673307	0.753630
C	1.455863	1.910015	-0.619821
C	1.945682	0.884951	-1.609857
C	2.153020	0.578723	1.268591
C	2.970924	-0.306975	0.357300
O	0.897203	-2.524048	-0.266034
C	0.655618	2.557397	1.676852
C	3.345431	-1.632415	1.046316
C	4.309567	0.405735	0.012587
H	2.651219	-1.152383	-1.638265
H	0.998490	2.817631	-1.004176
H	1.275383	0.824264	-2.473664
H	2.915656	1.176687	-2.033729
H	2.152972	0.384860	2.338331
H	1.787488	-2.825575	-0.478287
H	0.499044	3.552453	1.249485
H	-0.333199	2.112332	1.839827
H	1.135586	2.676080	2.653303
H	3.885455	-2.293037	0.354628
H	4.018991	-1.435549	1.887068
H	2.475606	-2.161053	1.438685
H	4.938418	0.455495	0.907062
H	4.863922	-0.145184	-0.757754
H	4.158127	1.430178	-0.329218
C	-0.574577	-0.707191	-0.484054
C	-1.107901	0.451829	-1.119720
C	-1.494159	-1.444600	0.313144

C	-2.425014	0.840791	-0.954736
C	-2.820557	-1.057860	0.478653
C	-3.303540	0.093151	-0.158640
H	-0.505720	1.035209	-1.795345
H	-1.145323	-2.335738	0.820398
H	-2.810701	1.717167	-1.465693
H	-3.466755	-1.660460	1.106704
O	-4.588671	0.558962	-0.090598
C	-5.528230	-0.186643	0.664625
H	-5.641060	-1.209076	0.279159
H	-5.250471	-0.237258	1.726311
H	-6.480051	0.338915	0.569711

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3.21.M_1.629

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C	0.781642	0.995827	-0.197350
C	0.801381	0.001870	0.989209
C	-1.608441	0.095262	-0.330049
C	-1.703210	0.253928	0.997767
C	-0.456377	0.236267	1.854798
C	-0.200645	-0.109085	-0.880404
C	0.576881	-1.186209	-0.016923
O	2.102824	1.180499	-0.726043
C	-2.805116	0.124523	-1.245215
C	1.805705	-1.679931	-0.814788
C	-0.079770	-2.427269	0.599377
H	1.711017	0.000825	1.606806
H	-2.664085	0.408997	1.484021
H	-0.348388	1.196184	2.379281
H	-0.538597	-0.524772	2.642867
H	-0.174142	-0.225912	-1.968450
H	2.674633	0.479833	-0.398105
H	-3.707107	0.431222	-0.707282
H	-2.650168	0.820550	-2.078961
H	-2.994370	-0.861293	-1.690160
H	2.629618	-1.978042	-0.153123
H	1.522413	-2.567637	-1.390500
H	2.176838	-0.953253	-1.536869
H	-0.290743	-3.190235	-0.157650
H	0.619091	-2.867710	1.321756
H	-1.013435	-2.212515	1.120325
C	0.291980	2.428098	-0.029752
H	0.811748	2.892360	0.814682
H	0.559584	2.991219	-0.928315
H	-0.782024	2.504580	0.131157

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3.21.M_1.733

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C	0.818335	1.002529	-0.204874
C	0.798135	-0.003242	0.963615
C	-1.644098	0.065629	-0.341547
C	-1.714191	0.271667	0.981836
C	-0.458296	0.251702	1.825076
C	-0.245375	-0.176472	-0.898969

C	0.565233	-1.196703	-0.019260
O	2.164779	1.217535	-0.656802
C	-2.860081	0.132258	-1.237913
C	1.786849	-1.655834	-0.845523
C	-0.038521	-2.444208	0.637696
H	1.700763	-0.021373	1.591852
H	-2.662003	0.475750	1.476196
H	-0.340220	1.215220	2.339982
H	-0.542487	-0.498441	2.623540
H	-0.237710	-0.348488	-1.979710
H	2.706118	0.457052	-0.417388
H	-3.730925	0.506322	-0.690764
H	-2.682524	0.797980	-2.091606
H	-3.117939	-0.850906	-1.653152
H	2.634138	-1.938074	-0.206691
H	1.512711	-2.544521	-1.424222
H	2.121140	-0.913563	-1.571189
H	-0.240547	-3.232218	-0.095707
H	0.686263	-2.844431	1.358063
H	-0.968960	-2.242069	1.170444
C	0.317561	2.431146	-0.025147
H	0.776989	2.868263	0.868578
H	0.640631	3.026033	-0.883764
H	-0.765454	2.496935	0.068977

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3.21.M_1.827

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C	0.849177	1.019533	-0.198425
C	0.798051	-0.003681	0.950752
C	-1.661363	0.047684	-0.345080
C	-1.717886	0.278936	0.975825
C	-0.457651	0.256641	1.813121
C	-0.281635	-0.226740	-0.910614
C	0.558551	-1.199015	-0.021939
O	2.193408	1.234753	-0.631899
C	-2.880203	0.135751	-1.236531
C	1.779483	-1.646451	-0.854793
C	-0.024777	-2.448699	0.650081
H	1.696001	-0.037978	1.586296
H	-2.658334	0.510925	1.471894
H	-0.336563	1.219384	2.328488
H	-0.539610	-0.492885	2.612556
H	-0.283812	-0.427978	-1.986182
H	2.724542	0.458018	-0.422527
H	-3.740971	0.532303	-0.689443
H	-2.689346	0.793527	-2.093570
H	-3.160652	-0.843079	-1.646843
H	2.632158	-1.921351	-0.219973
H	1.511644	-2.536567	-1.434233
H	2.101877	-0.898991	-1.581169
H	-0.225204	-3.242189	-0.077848
H	0.707256	-2.838824	1.368465
H	-0.954230	-2.250515	1.186323
C	0.329087	2.439630	-0.019924
H	0.761026	2.878466	0.887497

H	0.659766	3.045378	-0.867736
H	-0.756722	2.484667	0.053417

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3.21.M_1.936

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C	0.883657	1.042146	-0.185919
C	0.797810	-0.003198	0.938792
C	-1.676269	0.031022	-0.348375
C	-1.720567	0.285407	0.970532
C	-0.456989	0.260499	1.803375
C	-0.322019	-0.281410	-0.923371
C	0.552131	-1.199877	-0.025840
O	2.218895	1.249733	-0.611710
C	-2.896280	0.139122	-1.235747
C	1.773316	-1.638609	-0.862352
C	-0.013300	-2.451592	0.659922
H	1.691149	-0.054789	1.581283
H	-2.654208	0.543287	1.466473
H	-0.333366	1.221841	2.320645
H	-0.535801	-0.489800	2.602551
H	-0.333747	-0.510403	-1.992794
H	2.740889	0.460545	-0.425333
H	-3.748836	0.553831	-0.689410
H	-2.693465	0.790608	-2.094905
H	-3.194564	-0.835563	-1.642905
H	2.629239	-1.907494	-0.229285
H	1.511405	-2.530159	-1.442258
H	2.086420	-0.887230	-1.589354
H	-0.212819	-3.248661	-0.064368
H	0.724003	-2.834511	1.376637
H	-0.942192	-2.256366	1.198463
C	0.339256	2.449242	-0.014627
H	0.744383	2.894643	0.903146
H	0.672466	3.063631	-0.854980
H	-0.748491	2.469137	0.041913

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3.21.M_2.052

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C	0.919011	1.067389	-0.169707
C	0.797251	-0.002032	0.927364
C	-1.689371	0.015296	-0.351699
C	-1.722717	0.291643	0.965644
C	-0.456404	0.263784	1.794859
C	-0.364089	-0.338113	-0.936036
C	0.545911	-1.199954	-0.030677
O	2.242560	1.263281	-0.594265
C	-2.909982	0.142445	-1.235404
C	1.767776	-1.631581	-0.869211
C	-0.002895	-2.453492	0.668428
H	1.686347	-0.071050	1.575739
H	-2.649865	0.573935	1.460127
H	-0.330267	1.223319	2.314908
H	-0.531460	-0.488153	2.592983
H	-0.386099	-0.595215	-1.998237

H	2.755900	0.463691	-0.426542
H	-3.754990	0.572962	-0.689711
H	-2.696347	0.788631	-2.095976
H	-3.223882	-0.828103	-1.640245
H	2.625766	-1.895482	-0.236739
H	1.511411	-2.524360	-1.449644
H	2.072997	-0.876781	-1.596597
H	-0.201741	-3.253268	-0.053075
H	0.738739	-2.830459	1.383733
H	-0.931464	-2.260663	1.208593
C	0.348728	2.459074	-0.009507
H	0.727360	2.913047	0.916743
H	0.682309	3.080851	-0.844079
H	-0.740184	2.452462	0.032603

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3.21.M_2.129

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C	0.942249	1.084620	-0.157370
C	0.796542	-0.000881	0.919563
C	-1.697377	0.004933	-0.354005
C	-1.723892	0.295712	0.962410
C	-0.455993	0.265737	1.789479
C	-0.392290	-0.376601	-0.943450
C	0.541720	-1.199597	-0.034459
O	2.257905	1.271867	-0.583703
C	-2.918239	0.144652	-1.235465
C	1.764186	-1.627123	-0.873630
C	0.003672	-2.454264	0.673571
H	1.682977	-0.081927	1.571227
H	-2.646722	0.593972	1.455276
H	-0.328180	1.223835	2.311833
H	-0.528113	-0.487768	2.586473
H	-0.422887	-0.654553	-1.999817
H	2.765556	0.466129	-0.426387
H	-3.758297	0.584804	-0.689917
H	-2.697896	0.787836	-2.096589
H	-3.241977	-0.822981	-1.639202
H	2.622923	-1.888212	-0.240910
H	1.511399	-2.520609	-1.454500
H	2.065001	-0.870268	-1.601086
H	-0.194748	-3.255560	-0.046359
H	0.747851	-2.827641	1.388080
H	-0.924808	-2.262829	1.214496
C	0.354977	2.465955	-0.006046
H	0.715645	2.926872	0.924904
H	0.687846	3.091842	-0.837716
H	-0.734364	2.440925	0.027324

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3.21.M_2.249

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C	0.976866	1.111906	-0.135625
C	0.794997	0.001616	0.907809
C	-1.708035	-0.010011	-0.357912
C	-1.725024	0.300984	0.957750

C	-0.455284	0.268201	1.782369
C	-0.434978	-0.435694	-0.952982
C	0.535218	-1.198627	-0.041182
O	2.279900	1.283766	-0.570331
C	-2.928994	0.147876	-1.236103
C	1.759112	-1.621126	-0.879794
C	0.012539	-2.454597	0.680158
H	1.677588	-0.098664	1.563627
H	-2.641639	0.621859	1.447311
H	-0.325336	1.223971	2.308730
H	-0.521963	-0.488282	2.577146
H	-0.479164	-0.743969	-1.999727
H	2.779353	0.470195	-0.423609
H	-3.762098	0.600312	-0.690093
H	-2.700233	0.787593	-2.097573
H	-3.265953	-0.815475	-1.638750
H	2.617663	-1.879031	-0.245274
H	1.511560	-2.515501	-1.461497
H	2.055349	-0.861735	-1.607040
H	-0.185286	-3.257635	-0.037982
H	0.759633	-2.823506	1.393939
H	-0.916136	-2.264722	1.221430
C	0.364153	2.477306	-0.000829
H	0.697347	2.951857	0.934999
H	0.694276	3.107156	-0.830462
H	-0.725328	2.422710	0.021457

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3.21.M_2.333

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C	0.999495	1.131749	-0.118284
C	0.793684	0.004393	0.900591
C	-1.712876	-0.018578	-0.361522
C	-1.724916	0.303283	0.955585
C	-0.454714	0.269552	1.778753
C	-0.466118	-0.477300	-0.958185
C	0.531284	-1.197253	-0.046306
O	2.293685	1.290508	-0.564016
C	-2.934379	0.149815	-1.236948
C	1.756382	-1.618158	-0.883331
C	0.016973	-2.454212	0.683244
H	1.674477	-0.109543	1.557586
H	-2.638302	0.636592	1.442337
H	-0.324565	1.223904	2.307743
H	-0.517639	-0.489199	2.571791
H	-0.508960	-0.788979	-2.002754
H	2.788139	0.473301	-0.419289
H	-3.763421	0.607990	-0.689734
H	-2.702882	0.788010	-2.098698
H	-3.278004	-0.811466	-1.638412
H	2.613905	-1.874553	-0.246626
H	1.511899	-2.513162	-1.465276
H	2.051987	-0.857422	-1.609658
H	-0.180279	-3.258197	-0.033987
H	0.765960	-2.820141	1.396612
H	-0.911895	-2.265353	1.224584

C	0.369518	2.485104	0.002604
H	0.686180	2.972246	0.938737
H	0.697022	3.114709	-0.828299
H	-0.719799	2.413913	0.018356

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3.21.M_2.455

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C	1.029990	1.158975	-0.092750
C	0.791530	0.009561	0.889540
C	-1.720324	-0.032139	-0.368576
C	-1.724285	0.306992	0.952574
C	-0.453866	0.272188	1.772540
C	-0.513075	-0.540964	-0.962731
C	0.524881	-1.195667	-0.054394
O	2.316509	1.300786	-0.553932
C	-2.943260	0.152575	-1.238766
C	1.751392	-1.613441	-0.890007
C	0.024519	-2.453861	0.688555
H	1.668819	-0.129329	1.546623
H	-2.632914	0.660292	1.433662
H	-0.324916	1.224550	2.304833
H	-0.513601	-0.489906	2.562630
H	-0.547486	-0.845532	-2.008002
H	2.804763	0.480525	-0.407629
H	-3.765615	0.618858	-0.688508
H	-2.709110	0.789638	-2.100345
H	-3.298403	-0.804753	-1.638697
H	2.607494	-1.866929	-0.250306
H	1.511902	-2.509262	-1.472761
H	2.046522	-0.849173	-1.612899
H	-0.170289	-3.261648	-0.024925
H	0.778499	-2.811389	1.400966
H	-0.904094	-2.268137	1.231301
C	0.378667	2.497661	0.008555
H	0.671089	3.006474	0.942148
H	0.703280	3.124931	-0.825599
H	-0.709919	2.408337	0.010589

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3.21.M_2.531

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C	1.048530	1.174775	-0.077458
C	0.789840	0.012990	0.881730
C	-1.726910	-0.042155	-0.373350
C	-1.724108	0.310515	0.949144
C	-0.453678	0.274840	1.767228
C	-0.542687	-0.582406	-0.964017
C	0.519828	-1.195618	-0.059675
O	2.333487	1.307926	-0.545060
C	-2.950544	0.154019	-1.240333
C	1.746806	-1.609679	-0.895778
C	0.031128	-2.454049	0.693592
H	1.664056	-0.143439	1.539153
H	-2.628993	0.678371	1.426202
H	-0.325519	1.226013	2.301351

H	-0.512526	-0.489073	2.555628
H	-0.574497	-0.886310	-2.008922
H	2.818187	0.486310	-0.395874
H	-3.768171	0.625147	-0.687282
H	-2.714477	0.791499	-2.100896
H	-3.313889	-0.799868	-1.640535
H	2.602464	-1.861224	-0.254775
H	1.510908	-2.505607	-1.479860
H	2.040961	-0.841926	-1.615388
H	-0.160871	-3.266063	-0.015798
H	0.789593	-2.803357	1.405353
H	-0.897231	-2.271329	1.237736
C	0.386462	2.506708	0.012575
H	0.662658	3.028734	0.944452
H	0.710949	3.132139	-0.823285
H	-0.701604	2.407842	0.003982

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3.21.M_2.600

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C	1.081593	1.202642	-0.060821
C	0.803659	0.030155	0.876646
C	-1.718931	-0.038259	-0.374954
C	-1.708808	0.329223	0.947484
C	-0.438177	0.293660	1.763408
C	-0.554312	-0.606873	-0.960962
C	0.529932	-1.181743	-0.061730
O	2.367272	1.330358	-0.531272
C	-2.943013	0.168967	-1.239256
C	1.756125	-1.591438	-0.900146
C	0.055102	-2.440463	0.702239
H	1.673996	-0.143387	1.535199
H	-2.609722	0.711899	1.420141
H	-0.310592	1.245146	2.296676
H	-0.497206	-0.469248	2.552888
H	-0.586578	-0.915118	-2.004195
H	2.852757	0.511064	-0.373333
H	-3.756893	0.642638	-0.682974
H	-2.705003	0.809015	-2.097247
H	-3.312945	-0.780974	-1.642239
H	2.612703	-1.841210	-0.259680
H	1.522498	-2.487673	-1.484633
H	2.048210	-0.820265	-1.616640
H	-0.131165	-3.257914	-0.002392
H	0.818014	-2.779242	1.414298
H	-0.873870	-2.262322	1.246452
C	0.412352	2.530899	0.018786
H	0.672703	3.063008	0.949905
H	0.741968	3.154203	-0.816906
H	-0.675344	2.428119	-0.004567

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3.21.M_2.667

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C	1.080779	1.201219	-0.051114
C	0.786149	0.018700	0.865232

C	-1.743339	-0.063691	-0.381552
C	-1.724292	0.319227	0.940179
C	-0.453823	0.280370	1.754618
C	-0.597426	-0.659599	-0.963099
C	0.509031	-1.197515	-0.070751
O	2.367976	1.323084	-0.522691
C	-2.967933	0.155372	-1.242621
C	1.734817	-1.599421	-0.913095
C	0.050633	-2.456055	0.705551
H	1.653590	-0.171000	1.523410
H	-2.620335	0.717913	1.409048
H	-0.326410	1.229145	2.292174
H	-0.513136	-0.486708	2.539906
H	-0.631294	-0.972688	-2.004586
H	2.847896	0.500834	-0.363987
H	-3.775323	0.637392	-0.684068
H	-2.726555	0.793313	-2.101073
H	-3.348988	-0.790798	-1.643789
H	2.592127	-1.847132	-0.272815
H	1.505940	-2.494614	-1.501220
H	2.023554	-0.822037	-1.624421
H	-0.133006	-3.279815	0.007686
H	0.820981	-2.782618	1.415353
H	-0.876757	-2.282357	1.254352
C	0.404618	2.525229	0.021987
H	0.654879	3.068083	0.950239
H	0.731044	3.146907	-0.816438
H	-0.682352	2.414230	-0.006295

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3.21.M_2.755

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C	1.101618	1.216978	-0.034518
C	0.782805	0.022064	0.852562
C	-1.758105	-0.080404	-0.386427
C	-1.725355	0.327492	0.931776
C	-0.454956	0.285120	1.743693
C	-0.634968	-0.711616	-0.959961
C	0.500471	-1.199873	-0.079717
O	2.394160	1.334175	-0.500510
C	-2.983606	0.152779	-1.243272
C	1.722881	-1.588448	-0.932183
C	0.071591	-2.458541	0.715413
H	1.644905	-0.190217	1.511328
H	-2.613864	0.749839	1.394326
H	-0.326961	1.232122	2.283495
H	-0.516278	-0.483847	2.526951
H	-0.676168	-1.040451	-1.996269
H	2.871813	0.512764	-0.331510
H	-3.784293	0.640860	-0.680492
H	-2.739193	0.791998	-2.099771
H	-3.375736	-0.787890	-1.646081
H	2.584143	-1.834752	-0.296627
H	1.497794	-2.481203	-1.525563
H	2.004240	-0.801091	-1.635308
H	-0.102437	-3.293760	0.028845

H	0.853386	-2.762069	1.422947
H	-0.854662	-2.294938	1.269396
C	0.420744	2.539112	0.029497
H	0.657526	3.092516	0.955542
H	0.750998	3.158048	-0.809836
H	-0.665583	2.424982	-0.011973

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3.21.M_2.857

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C	1.127438	1.232900	-0.015957
C	0.777173	0.026353	0.836995
C	-1.779281	-0.101353	-0.391930
C	-1.728693	0.341893	0.918177
C	-0.459017	0.294187	1.727909
C	-0.679883	-0.771680	-0.953390
C	0.488614	-1.202786	-0.090953
O	2.430201	1.344818	-0.463584
C	-3.006710	0.142336	-1.244018
C	1.703776	-1.571364	-0.961516
C	0.103154	-2.461221	0.728576
H	1.631631	-0.211844	1.497394
H	-2.607241	0.793846	1.371879
H	-0.328661	1.239118	2.269949
H	-0.524819	-0.476399	2.509271
H	-0.733960	-1.127628	-1.980237
H	2.902806	0.523295	-0.281421
H	-3.804031	0.628395	-0.674778
H	-2.762953	0.788860	-2.095097
H	-3.403729	-0.793150	-1.653438
H	2.572909	-1.818187	-0.336893
H	1.480669	-2.458626	-1.563952
H	1.972922	-0.769367	-1.652657
H	-0.056605	-3.311846	0.057714
H	0.901478	-2.731744	1.431093
H	-0.820419	-2.313228	1.291652
C	0.446288	2.556169	0.036428
H	0.672337	3.119748	0.959415
H	0.783167	3.170329	-0.804204
H	-0.639439	2.443170	-0.018984

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3.21.M_2.962

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C	1.157691	1.246370	0.002444
C	0.768912	0.032157	0.820737
C	-1.806724	-0.125148	-0.396160
C	-1.735539	0.363749	0.899473
C	-0.467439	0.309382	1.707970
C	-0.728459	-0.832563	-0.942126
C	0.474533	-1.204278	-0.103684
O	2.475501	1.351347	-0.408360
C	-3.038786	0.117178	-1.242887
C	1.677099	-1.545449	-1.001844
C	0.145785	-2.463203	0.740536
H	1.613154	-0.231624	1.484801

H	-2.602408	0.848749	1.341478
H	-0.332308	1.252227	2.251718
H	-0.540526	-0.462069	2.488008
H	-0.799725	-1.225309	-1.954763
H	2.934564	0.522762	-0.223312
H	-3.840364	0.585506	-0.664780
H	-2.804594	0.779987	-2.084035
H	-3.426370	-0.816179	-1.665412
H	2.560020	-1.791997	-0.396707
H	1.453857	-2.425638	-1.614620
H	1.925660	-0.726024	-1.680096
H	-0.001865	-3.328327	0.085755
H	0.967095	-2.698223	1.429262
H	-0.769462	-2.335164	1.322157
C	0.482852	2.574436	0.039001
H	0.707124	3.149079	0.955772
H	0.825885	3.178960	-0.806551
H	-0.602729	2.467354	-0.024479

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$((C_2H_3)(THF)MgBr)_2$

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C	-0.567798	3.250654	-0.705075
Mg	-1.074539	1.345487	-0.027027
Br	-0.100158	0.510375	2.247577
Mg	1.218667	-1.246137	0.808804
Br	-0.130646	-0.705970	-1.415435
C	3.720870	0.261068	-1.844129
C	3.703509	1.612850	-1.110998
C	2.800737	1.336216	0.094551
O	2.858337	-0.115749	0.309409
C	3.745064	-0.720657	-0.681615
H	2.800166	0.124397	-2.419253
H	3.306688	2.428058	-1.720455
H	1.764144	1.606514	-0.112548
H	3.357737	-1.717563	-0.906094
H	3.117633	1.824064	1.018321
H	4.713723	1.885557	-0.787731
H	4.579238	0.141486	-2.509988
H	4.741683	-0.816349	-0.235239
C	-4.115486	-0.786332	-1.500540
C	-4.354339	-1.338960	-0.086041
C	-3.248161	-0.666351	0.725647
O	-2.980198	0.603290	0.035211
C	-3.741768	0.661657	-1.211373
H	-3.272601	-1.298216	-1.974620
H	-4.285311	-2.428040	-0.035002
H	-2.321451	-1.245302	0.715507
H	-3.105989	1.120898	-1.973494
H	-3.516642	-0.429432	1.756272
H	-5.341655	-1.039619	0.281667
H	-4.990936	-0.866505	-2.149615
H	-4.617484	1.297218	-1.041913
C	0.193580	4.067224	0.047680
H	0.528488	5.059422	-0.270585
H	0.525739	3.782141	1.048696

H	-0.826370	3.662462	-1.688573
C	1.271853	-4.161607	0.172244
C	1.573835	-3.270967	1.136009
H	2.010565	-3.714005	2.038781
H	1.441238	-5.239603	0.259545
H	0.823519	-3.853078	-0.775080

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C	-0.729687	-0.213623	0.385090
C	-1.965863	-0.806852	1.138321
C	-2.482869	1.291866	-0.523721
C	-2.969231	1.445015	0.718516
C	-2.795963	0.341925	1.743906
C	-1.729936	0.002862	-0.814450
C	-2.546927	-1.231716	-0.262989
O	0.307383	-1.137003	0.181734
C	-0.026488	1.008588	0.961255
C	0.673426	1.893935	0.219064
C	-2.609659	2.314683	-1.613195
C	-2.014270	-2.584499	-0.761389
C	-4.068396	-1.241235	-0.445996
H	-1.746394	-1.600628	1.859835
H	-3.509257	2.345264	1.004360
H	-2.305820	0.732061	2.648006
H	-3.775421	-0.027348	2.080064
H	-1.327234	-0.054420	-1.831623
H	0.060028	1.045907	2.048848
H	1.282579	2.672200	0.667127
H	0.553944	1.927254	-0.864586
H	-3.168580	3.195985	-1.285284
H	-1.620580	2.647116	-1.957834
H	-3.116286	1.890580	-2.489708
H	-2.471316	-3.397198	-0.183711
H	-2.293587	-2.729551	-1.812128
H	-0.933081	-2.662520	-0.670801
H	-4.317566	-1.448656	-1.493186
H	-4.510330	-2.042311	0.158029
H	-4.551351	-0.302731	-0.172103
Mg	1.957051	-0.280750	0.102247
Br	4.325765	-0.087191	-0.138646

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THF

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C	0.731699	0.995570	-0.232080
C	-0.731730	0.995546	0.232089
C	-1.164716	-0.429246	-0.134331
O	0.000014	-1.252561	0.000016
C	1.164733	-0.429216	0.134310
H	0.785448	1.144089	-1.316614
H	-1.345197	1.763238	-0.247581
H	-1.529110	-0.473469	-1.172549
H	1.953547	-0.821550	-0.517869
H	-1.953550	-0.821605	0.517808

H	-0.785485	1.144037	1.316627
H	1.345144	1.763270	0.247606
H	1.529173	-0.473445	1.172511

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3.51

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C	-4.200967	2.302768	0.806456
Mg	-3.293338	0.443000	0.554254
Br	-1.348127	-0.268949	2.139980
C	2.887993	-0.973973	-0.608109
C	3.864235	-2.070848	-0.011462
C	4.988999	0.408495	-0.231567
C	5.735774	-0.572976	-0.760415
C	5.237317	-2.005316	-0.713535
C	3.672254	-0.003011	0.399269
C	3.913581	-1.256871	1.333584
O	1.569358	-1.192711	-0.255200
C	2.985841	-0.672435	-2.091065
C	1.964012	-0.792842	-2.944742
C	5.370876	1.860001	-0.239914
C	2.761170	-1.562551	2.307024
C	5.199440	-1.304866	2.173221
H	3.456803	-3.087271	0.017414
H	6.696077	-0.365493	-1.229278
H	5.155474	-2.411151	-1.731865
H	5.965254	-2.644157	-0.192263
H	3.098450	0.840425	0.804399
H	3.946493	-0.340572	-2.471423
H	2.082311	-0.566423	-4.001058
H	0.990472	-1.139400	-2.612603
H	6.352963	2.023535	-0.694375
H	4.636604	2.455247	-0.800556
H	5.390646	2.268390	0.779140
H	2.989795	-2.470907	2.878020
H	2.653285	-0.743425	3.029941
H	1.813208	-1.709535	1.798951
H	5.104787	-0.637146	3.038253
H	5.348579	-2.318853	2.563078
H	6.098936	-1.015906	1.630306
Mg	0.172325	-0.030509	0.043936
Br	-1.828796	0.125072	-1.642138
C	0.453550	3.562021	-1.593027
C	-0.161364	4.165450	-0.318396
C	-0.334815	2.945087	0.589509
O	0.628894	1.948254	0.102227
C	1.385837	2.506898	-1.017903
H	-0.317387	3.078801	-2.201674
H	-1.117396	4.663929	-0.494108
H	-1.334919	2.517692	0.499323
H	1.639038	1.685908	-1.692920
H	-0.120830	3.129950	1.643846
H	0.526451	4.890002	0.130165
H	0.981966	4.295996	-2.206562
H	2.309186	2.940024	-0.617174
C	-5.002679	-2.380834	-1.644016

C	-4.371450	-3.436078	-0.721381
C	-3.617862	-2.583424	0.300655
O	-4.334585	-1.299173	0.340340
C	-5.410372	-1.303412	-0.648856
H	-4.255159	-1.981304	-2.336101
H	-3.700363	-4.118103	-1.248391
H	-2.593662	-2.372230	-0.015570
H	-5.480623	-0.297647	-1.072086
H	-3.610337	-2.989002	1.313573
H	-5.149442	-4.030983	-0.231384
H	-5.851939	-2.760149	-2.217496
H	-6.346492	-1.540676	-0.131751
C	-3.866006	3.095717	1.841981
H	-4.277643	4.096342	2.006372
H	-3.148704	2.776239	2.601698
H	-4.928954	2.750724	0.118634

Table 3.17 Vibrational frequencies (in cm-1) of the optimized structures

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3.21.V'
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   9.19   16.56   18.57   23.62   26.59
  31.25   33.05   39.72   43.47   45.96
  53.91   60.13   60.77   65.32   79.42
  84.42   93.88   94.82  103.22  104.69
 111.04  120.81  124.15  137.15  138.86
 149.84  155.20  159.91  164.28  165.65
 185.82  190.16  195.46  196.32  198.58
 199.76  209.55  212.09  219.40  226.63
 229.98  243.05  251.92  284.23  288.50
 289.60  292.20  301.17  302.69  313.25
 332.58  352.01  356.85  367.58  371.31
 374.05  380.85  386.10  397.37  402.03
 412.64  414.29  437.04  450.86  470.79
 473.82  485.37  486.88  503.04  506.75
 567.54  569.71  580.79  584.55  590.74
 605.57  647.51  650.57  684.93  686.83
 692.79  698.45  711.23  713.30  762.85
 764.82  812.79  814.13  834.59  837.23
 838.98  865.33  879.47  880.42  882.02
 886.54  889.36  896.08  914.06  916.76
 924.69  935.05  937.09  937.45  943.74
 946.53  951.35  951.52  954.97  955.19
 955.58  959.13  972.21  977.89  979.41
 980.78  996.82  998.84 1026.72 1027.13
1035.79 1036.78 1038.68 1039.41 1051.09
1052.49 1055.38 1057.22 1061.54 1062.69
1063.48 1068.60 1071.24 1071.89 1074.13
1074.92 1140.84 1142.99 1146.98 1149.69
1153.33 1154.19 1170.71 1173.94 1194.85
1199.54 1200.09 1200.65 1219.73 1224.38
1224.86 1235.55 1237.77 1240.39 1242.18
1244.75 1254.10 1256.51 1264.90 1275.04
1286.55 1291.16 1292.27 1295.87 1331.27
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1333.36 1336.16 1336.91 1338.05 1344.59
1352.88 1354.93 1357.76 1360.93 1366.74
1367.87 1392.77 1397.24 1403.79 1405.82
1420.02 1420.72 1422.69 1424.88 1427.49
1432.08 1441.66 1445.80 1488.92 1489.09
1489.84 1492.61 1493.76 1493.88 1497.04
1499.23 1501.22 1501.42 1507.41 1509.34
1510.12 1515.60 1522.92 1523.90 1527.15
1536.23 1547.35 1548.99 1549.57 1550.31
1696.60 1700.77 1725.21 1725.60 3003.65
3008.62 3014.23 3019.20 3024.99 3027.30
3029.41 3034.77 3035.88 3038.04 3041.89
3049.89 3053.99 3062.49 3067.36 3069.47
3069.99 3073.81 3074.29 3074.44 3074.62
3076.29 3078.91 3083.40 3087.44 3091.31
3091.79 3092.98 3112.17 3114.47 3126.31
3129.96 3134.71 3141.82 3146.59 3146.98
3150.37 3151.99 3154.07 3155.49 3158.02
3160.30 3160.77 3162.53 3194.64 3197.19
3201.26 3202.43 3244.49 3253.61

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3.21.V’-TSc
==============================
 -225.68   15.84   21.65   23.33   29.72
   35.21   36.21   43.67   46.76   56.85
   62.42   66.80   68.34   76.73   81.30
   81.84   90.32   92.23   97.88  101.38
  105.19  113.46  118.64  122.15  130.00
  144.42  146.54  150.02  155.82  165.85
  166.20  176.18  181.27  191.39  196.70
  201.92  206.79  212.95  215.40  231.78
  241.74  250.95  255.09  256.62  271.12
  279.47  289.72  294.51  297.94  306.09
  315.73  320.68  334.87  359.28  375.65
  378.64  384.05  401.08  403.82  405.99
  415.26  416.24  437.59  441.55  449.35
  472.86  488.56  493.89  507.85  513.77
  567.74  573.27  575.32  578.53  581.55
  592.52  617.19  629.48  648.06  682.21
  683.60  687.26  699.99  710.73  717.28
  721.55  729.56  756.47  763.09  807.82
  813.02  832.71  836.37  869.70  870.72
  872.87  876.11  881.73  891.11  898.12
  902.96  916.74  917.46  926.82  930.42
  934.24  938.36  948.41  950.20  950.50
  952.94  954.36  962.45  962.98  973.41
  976.11  977.45  990.72 1002.76 1015.05
1025.88 1033.11 1034.71 1037.04 1037.24
1038.64 1054.43 1055.27 1055.33 1060.02
1061.84 1063.56 1069.42 1072.20 1073.41
1076.22 1140.97 1148.42 1152.89 1158.65
1158.87 1178.03 1181.33 1189.80 1198.08
1201.45 1216.99 1225.54 1226.20 1231.41
1236.08 1240.25 1240.55 1247.98 1254.17
1262.25 1266.58 1281.49 1286.93 1288.29
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1293.82 1304.41 1316.21 1327.54 1335.09
1336.36 1336.53 1339.14 1340.97 1353.04
1353.59 1364.16 1367.29 1369.70 1383.33
1383.70 1403.68 1403.84 1405.49 1408.42
1414.00 1426.07 1428.04 1429.13 1430.87
1447.17 1459.62 1479.78 1487.63 1489.77
1491.66 1495.51 1497.16 1498.53 1500.35
1500.49 1501.97 1502.85 1506.62 1508.58
1511.61 1516.86 1517.42 1522.44 1525.74
1526.95 1540.96 1542.13 1542.51 1550.88
1586.96 1627.93 1697.35 1727.97 3002.21
3007.86 3015.78 3019.33 3020.70 3027.12
3027.84 3029.62 3030.20 3037.29 3038.88
3039.68 3056.36 3069.61 3072.82 3073.07
3074.82 3075.71 3079.63 3081.32 3087.05
3089.66 3091.76 3091.84 3093.91 3094.16
3097.25 3099.28 3110.61 3116.55 3123.99
3130.37 3142.15 3142.24 3142.91 3149.41
3154.89 3155.31 3157.73 3160.66 3161.66
3165.30 3168.10 3169.62 3182.85 3191.62
3204.52 3207.60 3245.30 3331.02

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3.29.V'
==============================
   4.55   16.55   18.55   27.03   31.20
  33.66   35.78   45.80   51.75   54.51
  67.20   71.75   78.38   88.96   89.26
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  98.53   99.63  102.05  112.21  115.93
 121.14  123.05  126.53  141.01  149.94
 155.52  161.08  177.42  179.97  186.56
 190.88  191.60  198.21  202.09  204.71
 218.50  220.96  231.24  242.10  250.01
 252.85  273.91  277.93  284.36  286.90
 289.51  293.74  296.30  304.14  314.48
 322.01  337.11  365.34  377.00  379.48
 387.70  391.12  395.66  400.89  412.44
 429.34  439.35  456.61  473.22  483.28
 494.41  508.61  517.04  539.93  564.68
 573.82  575.83  606.03  614.79  618.42
 645.69  646.71  658.18  687.30  688.05
 689.88  717.29  744.97  747.00  805.60
 809.90  811.89  820.26  834.74  840.02
 850.46  864.86  873.14  875.12  877.32
 890.06  900.71  902.41  918.17  919.30
 921.37  929.96  933.72  939.59  945.69
 949.39  952.80  953.95  955.68  958.07
 964.52  973.08  979.22  982.87  983.66
 992.29 1001.02 1024.54 1030.23 1033.56
1039.28 1040.35 1046.21 1049.02 1056.30
1059.14 1060.43 1063.92 1066.64 1068.61
1070.93 1075.94 1089.50 1108.67 1140.22
1147.47 1155.35 1158.01 1160.36 1171.90
1173.09 1188.84 1201.62 1202.90 1214.41
1224.78 1227.56 1228.73 1230.79 1233.19
1239.86 1240.78 1250.54 1251.32 1266.94
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1278.41 1287.72 1294.34 1295.88 1296.32

1304.74 1318.91 1327.45 1337.03 1337.63

1342.07 1346.22 1346.85 1353.57 1354.26

1367.95 1369.09 1369.14 1376.30 1384.66

1393.87 1403.68 1406.33 1407.83 1409.84

1412.94 1423.05 1426.80 1427.98 1430.41

1435.86 1437.35 1487.40 1489.40 1490.17

1492.31 1496.67 1497.72 1499.08 1501.67

1501.75 1502.79 1503.07 1505.02 1509.67

1509.78 1515.18 1517.69 1518.38 1522.08

1527.00 1529.13 1534.85 1543.24 1547.74

1684.24 1694.67 1725.15 1739.89 2983.47

2993.45 3014.71 3018.46 3019.94 3023.52

3023.55 3027.17 3028.24 3030.78 3034.38

3038.71 3044.57 3050.91 3051.35 3069.00

3071.13 3071.17 3075.64 3082.47 3083.25

3088.12 3088.17 3089.35 3093.57 3097.02

3097.22 3101.29 3101.62 3114.59 3114.63

3115.26 3122.92 3124.80 3126.60 3129.35

3130.51 3140.82 3145.08 3146.29 3146.77

3157.07 3157.19 3163.65 3164.35 3176.17

3178.98 3195.75 3208.10 3238.34

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^{cs}3.21.V’-TS

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-171.89 10.75 19.50 29.44 35.89

43.41 48.14 51.93 58.58 67.28

74.81 75.60 77.24 81.93 90.04

93.75 98.81 105.60 109.67 113.53

114.70 118.53 120.35 129.11 132.81

144.32 152.50 164.03 167.68 167.97

180.25 191.23 191.84 196.02 203.74

208.05 214.14 216.81 220.03 241.06

244.55 247.10 248.34 268.46 280.09

285.72 288.53 295.33 296.73 303.92

320.01 347.63 354.07 360.52 373.29

374.26 382.83 385.60 388.64 398.29

411.20 414.98 428.10 437.72 444.03

460.32 466.50 494.36 505.43 506.63

523.39 533.62 570.67 589.91 606.87

617.83 622.40 643.47 653.11 673.69

689.07 689.80 699.84 716.27 728.32

743.06 759.71 785.03 810.46 812.40

819.43 838.02 845.21 873.22 877.67

879.48 889.42 898.20 901.93 908.68

916.84 919.62 923.55 934.54 937.94

948.20 948.91 949.77 952.02 953.03

958.40 961.07 970.93 975.66 978.16

978.39 981.52 1000.93 1007.12 1027.35

1028.63 1037.72 1037.94 1040.21 1040.93

1042.85 1057.26 1058.71 1062.30 1063.54

1064.47 1069.56 1071.42 1072.68 1074.54

1082.75 1138.52 1144.54 1145.01 1151.60

1157.51 1158.31 1160.36 1178.39 1200.98

1208.82 1219.77 1226.51 1227.72 1228.67

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1234.11 1239.26 1239.48 1243.40 1250.30
1251.23 1256.86 1264.30 1269.29 1291.85
1297.12 1300.52 1302.79 1319.99 1329.80
1331.93 1336.02 1339.54 1343.03 1343.89
1347.27 1353.79 1364.78 1368.80 1382.27
1383.00 1384.57 1402.90 1403.50 1409.20
1412.29 1417.26 1422.89 1425.98 1428.17
1439.19 1441.25 1447.36 1488.07 1488.88
1491.43 1492.46 1499.53 1499.69 1501.90
1505.01 1505.06 1508.81 1510.91 1512.14
1518.73 1519.55 1521.42 1524.54 1526.38
1526.84 1541.53 1543.54 1547.31 1548.07
1662.59 1682.69 1695.12 1726.16 3000.43
3012.43 3013.53 3018.36 3022.18 3025.91
3031.41 3032.58 3033.89 3036.42 3038.89
3043.62 3050.17 3051.78 3055.78 3059.18
3068.72 3069.25 3074.56 3082.26 3082.37
3085.86 3087.31 3089.35 3089.76 3094.57
3095.48 3103.82 3112.73 3119.02 3135.68
3142.21 3147.14 3148.43 3150.28 3150.91
3152.13 3155.09 3159.05 3165.52 3165.84
3169.40 3169.58 3171.13 3204.04 3205.26
3208.62 3213.84 3238.05 3263.78

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cs3.31.V’
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  16.30   20.93   24.61   28.41   35.45
  37.68   44.16   46.64   53.09   58.94
  59.51   64.24   66.11   74.35   81.86
  83.46   91.79   93.92   98.31  106.26
 109.22  112.95  119.38  122.37  129.19
 142.94  148.66  150.11  153.67  160.83
 169.48  179.91  182.66  192.43  197.98
 205.22  211.89  214.28  215.84  218.59
 243.22  251.96  266.73  268.57  276.39
 277.49  281.81  286.70  291.23  303.32
 305.44  318.14  330.62  340.23  350.95
 359.13  363.79  372.03  384.95  387.20
 397.57  415.30  416.11  431.22  436.00
 470.61  495.14  500.32  509.93  511.21
 529.24  539.51  572.84  580.29  585.56
 607.98  628.16  640.23  657.20  687.67
 689.98  697.58  699.92  713.79  739.22
 741.67  791.78  809.91  825.41  833.21
 839.85  855.98  859.79  862.50  877.24
 879.15  882.96  892.13  892.67  895.11
 924.84  927.56  929.31  929.81  934.39
 934.98  937.44  948.57  953.27  954.61
 958.41  958.96  973.08  981.13  986.10
 994.55  998.77 1000.01 1014.21 1017.46
1027.71 1028.90 1034.32 1038.51 1041.34
1041.99 1051.34 1054.05 1055.79 1061.59
1063.26 1066.79 1070.63 1081.53 1095.70
1100.43 1138.28 1142.08 1146.70 1164.06
1166.25 1173.36 1174.21 1183.37 1197.94
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1199.57 1203.87 1203.98 1208.80 1215.46
1217.45 1229.30 1234.76 1236.05 1240.10
1250.64 1269.87 1274.94 1278.75 1279.38
1282.79 1299.78 1332.42 1333.21 1335.74
1338.58 1341.76 1349.33 1355.93 1363.84
1365.42 1365.81 1371.97 1387.82 1396.02
1399.73 1404.93 1412.59 1413.80 1414.74
1422.81 1424.47 1429.03 1429.35 1435.54
1435.81 1451.84 1486.03 1488.01 1488.84
1493.10 1497.56 1499.25 1499.45 1501.46
1502.45 1503.97 1506.76 1507.30 1511.11
1513.54 1519.30 1520.09 1529.31 1532.91
1533.62 1542.56 1545.35 1546.41 1620.55
1659.20 1697.75 1705.92 1725.17 2986.63
2994.94 3015.35 3017.33 3018.77 3020.90
3025.32 3026.00 3032.54 3037.12 3043.51
3050.28 3058.06 3063.95 3065.53 3066.93
3068.77 3070.43 3079.75 3079.84 3083.49
3088.23 3088.58 3089.43 3090.46 3092.72
3095.95 3096.42 3101.69 3112.06 3115.12
3125.49 3125.50 3129.40 3130.58 3141.47
3142.62 3149.42 3154.16 3154.98 3156.31
3158.46 3160.40 3160.66 3164.67 3192.36
3202.85 3209.21 3243.53 3263.24
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3.21.V’-TS
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-395.81   14.67   16.98   22.68   26.96
  30.42   36.77   41.07   46.51   48.03
  53.19   59.67   62.50   71.64   75.40
  77.49   84.59   93.59   96.62  103.05
 106.39  108.26  114.83  118.01  127.12
 139.19  148.40  153.58  157.19  161.08
 162.98  174.77  182.98  188.75  198.05
 201.39  202.90  205.51  211.82  223.73
 227.46  233.88  250.39  253.28  274.63
 282.37  282.53  288.87  291.77  298.44
 304.29  316.38  331.96  361.85  362.97
 371.01  379.22  387.74  389.00  400.51
 402.78  412.42  412.90  438.01  442.53
 468.41  479.96  489.83  503.38  507.53
 527.78  567.29  571.81  579.26  595.77
 612.80  632.74  640.09  645.30  654.25
 656.13  688.80  698.55  710.79  715.03
 717.38  742.60  752.49  795.45  810.60
 813.38  838.83  852.23  860.57  865.66
 868.59  874.74  884.42  892.29  902.76
 907.88  915.55  918.30  927.35  929.91
 936.60  938.78  945.99  949.07  952.03
 954.71  959.07  959.48  974.47  975.05
 975.18  988.95 1000.94 1009.41 1022.12
1027.31 1027.35 1035.46 1037.83 1038.61
1038.73 1042.16 1058.71 1061.78 1062.21
1062.97 1065.36 1070.36 1071.06 1073.02
1086.22 1137.84 1144.07 1153.19 1154.39
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1156.60 1169.80 1170.96 1188.76 1196.96
1198.44 1206.24 1224.98 1226.69 1230.01
1232.32 1237.18 1238.38 1247.09 1247.87
1251.76 1262.35 1265.82 1266.52 1289.62
1292.08 1299.81 1304.77 1315.87 1333.18
1335.03 1335.11 1337.12 1344.08 1349.80
1354.10 1366.09 1367.59 1368.11 1383.52
1391.13 1403.42 1404.24 1409.04 1409.62
1417.17 1422.20 1424.35 1425.46 1428.81
1432.76 1446.16 1446.36 1489.12 1490.21
1491.10 1492.62 1495.80 1498.68 1499.53
1501.31 1501.97 1504.77 1505.59 1509.28
1509.92 1510.86 1517.79 1520.08 1521.75
1524.81 1533.68 1538.17 1541.92 1547.35
1601.48 1620.33 1698.11 1725.98 2997.20
2997.36 3011.34 3020.29 3021.20 3022.17
3022.71 3032.41 3036.00 3039.00 3041.81
3048.28 3054.95 3066.44 3068.44 3071.69
3077.13 3077.94 3082.91 3085.47 3087.07
3087.97 3088.58 3091.24 3091.29 3092.52
3100.70 3114.39 3118.43 3125.71 3126.74
3129.49 3141.61 3143.03 3146.79 3155.67
3155.77 3156.61 3156.85 3160.87 3162.46
3166.86 3173.71 3173.90 3186.08 3193.55
3198.66 3205.02 3246.56 3248.67

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3.31.V’
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 12.90   14.39   17.57   23.55   27.90
 28.72   36.17   40.12   44.65   50.44
 51.89   54.71   63.70   68.68   75.99
 77.66   87.21   90.95   93.79   96.03
 100.55  105.88  108.72  110.39  115.71
 120.96  138.44  149.68  154.08  159.31
 166.90  184.79  189.59  193.13  197.28
 201.96  204.58  205.99  211.98  226.11
 249.01  252.16  254.16  272.55  274.29
 284.92  286.90  288.52  293.01  299.88
 309.40  319.51  324.55  344.68  352.42
 363.58  369.99  374.17  387.68  400.51
 406.01  412.36  418.79  436.09  437.38
 468.36  488.65  491.04  507.17  514.20
 520.02  527.98  571.98  581.02  593.51
 600.57  612.28  624.05  645.54  657.14
 676.20  688.43  690.18  691.31  701.23
 713.20  714.62  727.71  749.66  810.31
 812.00  817.85  839.95  851.14  853.89
 871.70  881.36  884.44  890.49  896.31
 899.17  916.20  918.59  925.90  934.43
 937.20  938.47  943.96  948.57  949.71
 951.23  952.12  956.99  957.89  968.08
 973.28  976.97  990.66 1000.68 1022.74
1026.71 1036.27 1036.67 1037.30 1038.74
1041.11 1047.17 1058.70 1059.08 1060.47
1063.18 1063.82 1069.87 1072.38 1084.65
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1102.33 1137.96 1144.14 1154.25 1157.46
1162.02 1170.75 1171.52 1188.00 1197.50
1199.91 1221.86 1224.61 1227.21 1227.33
1232.73 1235.64 1237.90 1244.85 1248.78
1251.48 1266.51 1269.70 1272.91 1290.62
1292.31 1300.45 1302.46 1328.95 1329.83
1335.52 1336.51 1338.13 1341.80 1350.15
1353.83 1362.48 1366.99 1368.01 1382.31
1392.55 1403.27 1405.75 1409.06 1418.20
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1440.57 1445.18 1488.09 1488.57 1489.67
1495.29 1496.19 1499.00 1499.69 1501.78
1502.48 1504.98 1505.67 1507.87 1509.11
1509.85 1514.51 1518.51 1518.52 1522.12
1526.38 1531.73 1534.78 1542.98 1545.77
1547.95 1563.66 1697.47 1725.89 2991.34
2996.86 3019.03 3019.63 3020.65 3022.71
3033.32 3036.07 3037.59 3044.25 3044.93
3050.89 3055.39 3064.34 3069.75 3071.11
3077.71 3080.98 3082.81 3084.16 3086.67
3086.75 3090.86 3091.42 3098.20 3102.59
3112.98 3113.28 3121.13 3123.70 3130.03
3130.19 3139.60 3140.42 3142.11 3149.68
3152.52 3153.90 3155.13 3155.57 3155.85
3161.28 3163.79 3170.63 3177.31 3184.46
3198.12 3206.31 3247.19 3252.84

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3.31.V’-TS

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   33.59   38.24   41.54   42.31   48.02
   53.98   55.67   61.51   64.30   70.13
   72.89   79.72   84.56   90.44   95.68
  101.65  101.77  111.38  119.57  131.27
  138.25  144.87  151.19  153.39  155.91
  162.35  170.00  187.93  189.85  193.24
  200.19  201.17  205.79  214.75  230.14
  231.79  234.96  238.11  263.13  270.72
  278.58  284.93  287.58  295.69  302.76
  310.12  336.11  343.39  356.66  358.19
  362.39  370.97  373.58  376.70  386.31
  397.74  409.66  416.98  446.79  449.49
  473.34  473.87  489.27  502.63  508.23
  549.66  562.60  571.08  579.28  583.01
  590.13  618.07  626.19  650.72  656.16
  686.58  690.88  694.57  695.89  707.99
  744.54  754.23  768.25  813.71  819.74
  836.78  841.92  855.00  857.33  860.75
  871.99  875.76  880.31  880.70  890.27
  897.45  913.68  931.15  933.44  934.03
  935.49  936.32  936.61  950.20  951.65
  953.15  953.76  956.96  974.56  977.01
  979.08  987.21  997.43 1020.04 1025.94
 1032.40 1034.07 1034.66 1036.24 1036.99
 1051.08 1052.16 1056.70 1058.69 1060.58
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1064.33 1064.87 1070.28 1071.60 1076.89
1085.08 1144.23 1146.95 1150.87 1157.31
1157.62 1166.27 1171.60 1175.66 1196.47
1197.53 1201.07 1209.81 1212.33 1216.48
1225.32 1228.69 1233.60 1240.05 1243.52
1252.70 1274.81 1275.92 1278.67 1282.75
1291.02 1293.15 1309.17 1312.83 1331.58
1332.93 1333.12 1335.99 1336.77 1354.86
1364.46 1365.82 1367.72 1368.28 1390.02
1393.98 1400.15 1405.61 1412.45 1413.85
1418.56 1421.58 1424.36 1426.75 1429.46
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1493.18 1496.11 1496.37 1496.90 1501.25
1502.07 1503.25 1504.65 1506.87 1507.31
1510.24 1514.56 1518.16 1522.45 1524.41
1525.47 1534.05 1536.49 1540.73 1547.01
1593.76 1610.02 1693.90 1727.12 3003.35
3009.08 3014.31 3014.83 3021.91 3026.83
3030.79 3031.83 3035.87 3038.94 3064.34
3065.79 3067.72 3068.92 3069.51 3071.27
3071.32 3074.47 3079.33 3080.11 3082.19
3084.62 3086.57 3093.36 3096.50 3097.57
3100.15 3114.70 3117.88 3122.97 3124.84
3130.79 3136.67 3141.11 3142.66 3146.42
3147.91 3149.38 3155.94 3158.46 3159.55
3161.66 3162.04 3164.23 3164.33 3194.98
3196.72 3206.12 3236.77 3256.16
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3.29.V’
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  77.52   87.23   92.66   94.43  102.55
 105.54  118.06  124.55  133.80  140.73
 149.22  152.02  155.29  157.13  163.47
 188.18  195.71  200.11  203.01  204.30
 208.48  213.02  219.64  228.11  228.99
 232.00  248.64  252.06  274.83  278.84
 281.03  286.67  292.81  297.18  301.20
 322.78  337.45  353.65  356.90  366.39
 370.75  375.77  382.50  397.48  409.05
 413.95  442.42  449.18  453.93  470.11
 473.09  488.48  491.56  501.11  515.65
 563.30  570.20  579.49  581.04  582.10
 624.30  644.79  650.46  686.09  690.04
 693.56  705.75  708.07  739.95  754.27
 778.54  814.34  824.69  838.43  855.77
 861.32  863.67  872.37  874.18  879.21
 881.37  889.94  907.35  913.99  921.97
 929.39  931.72  934.21  935.35  935.83
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 982.24  997.59 1005.51 1026.40 1028.19
1035.08 1035.42 1037.34 1038.25 1050.04
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1108.68 1131.57 1144.24 1147.92 1148.29
1156.60 1158.87 1171.54 1172.27 1180.57
1195.43 1200.70 1201.39 1202.23 1211.95
1213.26 1224.72 1234.81 1240.62 1241.86
1252.75 1253.34 1272.74 1275.92 1277.80
1278.36 1283.00 1284.77 1291.45 1293.32
1331.26 1331.43 1332.13 1332.71 1337.11
1354.46 1355.13 1364.64 1365.12 1367.82
1374.51 1393.51 1394.37 1400.70 1412.11
1416.90 1420.98 1423.78 1424.28 1427.90
1436.99 1439.03 1442.17 1486.53 1488.16
1490.10 1494.99 1495.13 1495.97 1500.96
1501.40 1502.13 1502.56 1505.56 1505.64
1507.38 1510.56 1519.27 1521.10 1521.71
1525.13 1532.25 1533.98 1538.89 1547.35
1694.30 1699.42 1722.87 1726.89 3008.59
3014.71 3015.13 3016.40 3030.97 3033.27
3035.03 3039.26 3064.81 3065.03 3065.51
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3086.60 3087.20 3094.89 3095.37 3096.63
3101.62 3114.11 3114.78 3124.40 3124.68
3130.06 3133.18 3139.39 3141.83 3145.33
3146.02 3149.53 3152.40 3154.35 3155.23
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3195.77 3205.66 3237.02 3253.22
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3.21.A’
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  75.27   80.61   84.88   96.47   99.67
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 133.94  136.48  144.15  150.92  154.68
 158.51  162.97  169.13  178.24  184.65
 195.30  197.76  200.52  201.66  206.93
 211.82  224.29  235.73  254.93  259.47
 263.67  276.71  280.17  281.22  291.84
 295.55  312.75  329.80  344.85  348.26
 349.30  362.47  369.29  377.46  381.26
 390.77  402.22  404.87  408.66  423.26
 427.58  431.59  447.64  461.90  464.28
 483.84  486.60  500.32  508.86  563.32
 565.49  586.56  613.67  617.23  621.75
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 692.97  697.60  705.12  809.50  810.46
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3048.99 3050.20 3058.31 3061.85 3063.53
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3.21.A’-TSc

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 132.96  140.08  145.23  149.22  158.06
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 193.80  196.95  199.72  204.25  210.41
 214.18  226.78  231.75  238.84  261.77
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 294.60  311.31  324.28  327.22  337.47
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3.48.A’

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110.68 119.88 124.99 127.43 137.66
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200.51 213.26 225.33 229.98 232.71
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306.25 310.37 334.15 337.07 345.81
354.82 367.63 373.19 385.22 391.89
398.43 410.18 430.00 431.10 448.59
455.47 467.15 486.40 502.87 506.64
518.31 535.61 566.30 569.82 580.22
584.83 585.86 602.92 629.84 648.87
652.12 675.37 677.57 689.83 700.26
701.04 707.49 724.96 814.19 817.36
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1493.02 1494.76 1496.54 1499.13 1501.44
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1510.36 1511.44 1521.07 1521.60 1530.96
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3119.13 3120.86 3127.03 3127.52 3128.92
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3.21.A’-TS

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82.50 92.12 93.67 95.88 104.59
109.49 115.74 119.59 124.86 130.84
134.26 144.60 155.74 163.41 165.82
169.29 172.55 174.56 193.67 199.29
201.40 206.07 209.14 213.10 217.70
223.19 226.22 239.18 247.28 249.30
259.19 260.59 263.95 272.38 281.09
283.95 294.93 301.53 305.79 328.01
337.59 342.50 345.63 354.73 365.24
374.46 386.77 390.77 408.24 413.29
419.80 422.90 448.92 466.80 469.62
486.00 492.09 499.24 504.93 527.14
561.83 568.93 583.48 584.48 594.51
628.54 631.80 648.77 652.88 677.04
694.25 697.38 698.11 700.87 708.88

```
 734.94  811.01  824.19  826.17  833.42
 842.82  857.68  862.56  868.34  871.82
 881.50  887.96  889.32  894.21  905.11
 913.51  916.10  919.68  925.18  927.01
 929.22  930.48  938.51  939.90  943.89
 945.56  953.94  958.52  958.80  974.70
 977.81  978.21  985.32  996.67 1010.58
1012.18 1015.07 1025.13 1028.88 1029.05
1037.00 1040.31 1045.33 1054.03 1061.22
1062.52 1064.89 1065.76 1074.72 1076.01
1089.51 1116.68 1138.32 1144.31 1151.77
1154.72 1158.54 1163.28 1171.60 1187.77
1198.79 1199.45 1202.08 1210.22 1215.85
1227.54 1235.62 1236.59 1240.00 1242.92
1243.71 1252.13 1262.52 1271.14 1273.12
1291.48 1292.11 1303.89 1308.13 1324.88
1330.45 1334.76 1335.61 1338.75 1353.53
1356.11 1361.25 1362.44 1369.39 1370.57
1389.48 1395.14 1406.95 1407.27 1411.76
1424.07 1424.18 1425.08 1425.87 1430.03
1430.18 1443.54 1481.24 1487.83 1488.86
1491.08 1492.23 1495.55 1498.58 1499.99
1500.41 1501.23 1502.15 1504.07 1505.88
1509.82 1510.29 1512.69 1518.08 1520.55
1524.90 1532.04 1541.23 1542.43 1543.72
1554.87 1609.85 1723.85 1958.09 2042.67
2993.18 3006.06 3007.62 3019.15 3020.15
3026.42 3029.14 3030.00 3030.71 3036.81
3037.04 3043.41 3063.88 3070.89 3071.03
3073.82 3074.75 3076.33 3077.73 3080.80
3084.22 3085.50 3088.08 3089.19 3093.74
3097.06 3098.48 3114.91 3117.91 3118.95
3124.41 3128.38 3131.44 3133.34 3133.99
3142.44 3146.19 3153.08 3154.55 3156.57
3160.74 3161.39 3163.12 3173.53 3190.10
3191.70 3196.48 3197.04 3200.37 3205.06


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3.49.A’
================================
  13.46   17.64   24.17   29.25   30.92
  43.00   49.03   50.66   55.33   62.05
  65.83   72.19   80.29   81.17   83.94
  88.00   91.63   96.47   99.13  108.22
 115.55  119.25  121.47  125.59  127.17
 132.53  134.04  140.28  154.23  156.87
 160.09  164.05  174.01  177.46  184.84
 188.54  195.94  198.02  201.99  209.55
 221.63  223.05  233.94  241.73  243.76
 259.33  261.29  268.86  280.27  281.45
 292.99  296.30  310.89  316.53  325.67
 340.19  345.90  348.13  361.24  368.73
 374.39  385.63  386.39  397.58  408.82
 413.81  424.90  450.15  451.38  464.42
 486.11  503.42  503.71  512.40  525.11
 528.73  568.46  578.25  600.98  611.11
```

```
626.84  639.60  649.84  653.24  676.47
679.38  691.33  697.47  698.63  701.22
731.53  789.96  811.33  812.22  817.20
828.91  834.08  849.95  852.05  869.65
883.05  887.37  888.04  893.38  901.30
905.45  915.72  917.47  924.01  926.50
930.24  935.97  942.65  944.71  947.50
952.48  953.77  957.26  958.76  976.71
977.89  984.92  986.94  996.60 1013.63
1019.57 1024.95 1025.87 1027.91 1035.26
1036.48 1043.85 1046.85 1047.88 1054.85
1059.67 1063.29 1064.91 1074.99 1075.49
1095.17 1121.19 1138.78 1146.03 1151.84
1154.81 1160.03 1160.47 1162.06 1187.26
1198.03 1214.76 1215.50 1225.13 1235.36
1236.02 1236.41 1241.48 1245.88 1246.16
1248.89 1254.95 1257.27 1265.73 1292.85
1293.33 1297.68 1297.78 1322.60 1323.87
1331.81 1332.49 1337.53 1341.09 1343.52
1350.86 1355.63 1362.80 1368.89 1383.84
1389.73 1406.55 1407.52 1409.76 1410.61
1415.05 1418.08 1424.39 1424.74 1429.55
1439.27 1477.44 1483.94 1488.33 1488.58
1490.53 1492.32 1495.53 1497.74 1499.97
1500.10 1500.17 1501.40 1505.89 1509.73
1510.38 1512.11 1515.79 1519.63 1522.03
1524.10 1530.30 1532.35 1542.80 1544.35
1550.75 1560.38 1724.73 1848.26 2044.28
 2999.06 3004.99 3010.58 3019.67 3023.49
 3028.75 3034.75 3037.51 3037.57 3043.25
 3044.05 3046.55 3048.38 3050.37 3060.61
 3064.64 3070.51 3078.50 3079.37 3079.84
 3082.04 3082.26 3090.32 3093.35 3097.76
 3104.82 3107.31 3113.64 3116.74 3121.42
 3122.98 3127.87 3130.49 3137.14 3138.96
 3140.58 3152.21 3154.58 3156.33 3161.07
 3169.13 3174.02 3178.65 3184.27 3186.62
 3193.57 3196.49 3196.96 3204.75 3208.51

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CH4
===============================
 1355.89 1355.89 1355.89 1577.98 1577.98
 3043.35 3160.93 3160.93 3160.93

===============================
CH3_radical
===============================
  464.61 1419.61 1419.77 3127.97 3311.02
 3311.41

===============================
3.21.V
===============================
   81.57  113.38  138.93  171.38  177.38
  202.26  204.64  225.42  285.59  289.48
```

```
 351.84  358.39  367.14  399.54  403.93
 415.73  441.29  479.16  492.94  504.49
 577.03  653.76  676.29  699.51  724.36
 818.96  837.25  892.25  910.01  947.70
 950.03  961.04  961.75  971.66  995.91
1022.60 1036.20 1042.06 1057.51 1065.85
1068.73 1079.45 1142.71 1146.60 1156.37
1200.54 1222.39 1229.16 1241.72 1244.73
1296.53 1326.44 1336.69 1348.49 1362.52
1370.29 1411.76 1426.23 1433.42 1453.02
1489.80 1491.82 1493.39 1502.34 1511.47
1518.92 1545.27 1708.14 1727.10 3017.25
3018.19 3029.30 3039.40 3045.81 3066.53
3067.39 3079.89 3084.00 3095.36 3115.99
3155.65 3157.06 3165.42 3201.94 3204.75
3246.56 3790.94

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3.31.V
==============================
  51.16   62.22   74.49  113.00  144.46
 189.07  223.20  237.27  257.34  290.86
 296.15  313.17  329.19  338.22  355.99
 370.31  414.78  430.99  481.02  516.68
 519.90  546.82  588.18  640.59  669.10
 691.95  722.03  757.79  792.14  844.98
 894.95  936.17  941.55  956.08  960.82
 967.55 1021.65 1037.33 1046.86 1055.98
1060.31 1100.04 1146.14 1170.10 1191.80
1203.98 1229.06 1239.56 1262.12 1294.30
1302.38 1338.70 1351.63 1371.63 1411.95
1418.16 1426.99 1427.82 1438.22 1488.46
1497.83 1506.59 1508.23 1510.65 1519.27
1526.71 1531.18 1543.07 1564.84 2964.48
2998.72 3025.95 3031.86 3038.86 3055.23
3092.91 3100.90 3101.90 3121.66 3134.14
3141.94 3163.62 3171.41 3172.92 3191.28
3268.83 3835.94

==============================
3.21.A
==============================
  34.66  102.40  125.72  138.69  174.03
 181.93  200.14  214.04  243.66  271.57
 289.22  298.19  346.39  361.61  379.00
 386.38  399.61  424.91  456.26  475.30
 491.03  507.11  568.37  630.56  674.22
 693.18  786.81  817.08  835.37  867.97
 891.99  910.25  926.28  945.72  957.55
 961.49  972.49 1000.16 1018.50 1023.93
1033.52 1047.03 1065.05 1073.08 1118.71
1143.09 1147.39 1152.08 1198.74 1220.33
1228.24 1240.40 1243.15 1296.01 1321.66
1336.34 1353.78 1367.06 1389.83 1412.23
1426.32 1432.94 1489.47 1489.75 1493.26
1498.15 1502.39 1512.34 1519.85 1545.86
```

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 1725.62 2062.12 3017.83 3018.72 3029.36
 3039.79 3044.77 3069.14 3072.47 3080.57
 3084.12 3095.84 3116.75 3130.69 3156.80
 3164.94 3190.18 3204.75 3205.32 3791.27


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3.32.A
==============================
   45.25   47.61   58.93  104.87  106.29
  130.62  187.07  204.72  246.72  250.88
  273.54  289.86  298.71  312.48  340.79
  350.39  364.70  396.69  411.17  431.89
  467.66  511.27  516.60  550.46  561.95
  625.95  677.13  690.95  726.37  837.77
  845.41  876.83  878.08  890.91  935.38
  938.57  957.49  965.52  997.26 1020.57
 1038.60 1045.32 1058.79 1063.39 1099.48
 1142.32 1168.10 1189.36 1199.34 1227.13
 1238.62 1279.72 1295.50 1326.83 1339.63
 1365.58 1408.45 1412.79 1422.27 1425.98
 1437.07 1461.77 1487.51 1497.93 1506.24
 1507.20 1510.42 1513.60 1518.03 1530.53
 1563.41 1941.58 2966.46 2999.27 3028.40
 3034.27 3038.51 3054.86 3075.84 3094.97
 3100.93 3103.43 3121.85 3130.85 3132.91
 3138.47 3162.06 3162.36 3173.98 3830.25


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3.21.P
==============================
    1.71   62.16   72.49  120.07  164.95
  184.01  201.53  216.69  219.68  245.79
  262.48  280.77  290.31  329.23  344.28
  353.20  379.30  407.67  420.93  459.57
  482.45  507.47  538.68  593.48  609.93
  675.87  693.29  816.07  832.80  892.30
  909.73  913.29  952.76  961.93  970.73
  987.12  997.20 1027.32 1044.48 1053.43
 1054.95 1064.13 1068.46 1082.79 1143.05
 1150.47 1179.67 1200.27 1212.22 1232.43
 1242.05 1249.28 1298.31 1334.59 1349.21
 1362.25 1376.66 1411.51 1424.65 1426.24
 1433.30 1489.13 1490.10 1490.18 1490.33
 1494.30 1503.04 1511.64 1521.69 1548.05
 1732.22 2358.48 3017.49 3020.85 3030.14
 3030.47 3039.73 3051.85 3067.98 3072.74
 3084.05 3086.10 3094.72 3095.47 3095.76
 3115.91 3157.89 3167.76 3196.33 3801.09


==============================
3.32.P
==============================
   28.63   44.77   50.42   53.27   91.12
  103.11  137.18  171.61  202.05  257.52
  267.36  277.91  291.18  304.39  311.70
  320.80  353.65  364.82  368.36  424.05
```

```
 440.42  492.91  512.20  529.87  536.89
 610.76  636.07  687.14  691.23  724.06
 841.56  890.18  904.13  935.93  944.74
 958.79 1010.40 1029.37 1038.47 1040.81
1045.66 1048.82 1057.07 1100.01 1168.14
1180.50 1189.57 1200.88 1228.60 1238.90
1263.17 1296.58 1337.79 1357.19 1378.02
1409.37 1418.75 1420.79 1422.27 1435.87
1478.10 1480.23 1488.73 1490.94 1499.39
1505.16 1506.30 1511.92 1517.08 1532.58
1563.66 2201.40 2965.18 2999.81 3011.56
3025.19 3030.58 3034.85 3061.38 3065.86
3083.75 3092.33 3096.96 3101.30 3119.00
3132.96 3138.64 3160.56 3174.45 3818.70

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3.21.Ph
===============================
  41.05   48.92   88.86  101.68  132.13
 161.95  179.17  181.26  194.09  199.16
 218.49  223.83  259.94  261.46  282.96
 294.59  308.39  315.16  364.61  394.85
 411.25  431.82  437.72  458.51  482.90
 491.91  510.48  522.15  578.76  592.32
 612.17  652.16  677.69  689.56  751.16
 807.16  820.77  830.52  835.94  852.83
 888.38  911.91  938.16  954.08  955.72
 961.90  965.98  977.04  995.59 1019.09
```

```
1030.40 1033.18 1042.17 1065.10 1068.99
1076.89 1089.04 1138.06 1147.38 1155.54
1180.18 1199.29 1204.07 1210.98 1213.85
1222.15 1228.62 1241.14 1269.25 1296.67
1297.94 1333.37 1338.33 1346.11 1352.48
1365.51 1379.17 1412.97 1428.20 1434.02
1458.56 1489.62 1490.71 1493.66 1495.14
1500.93 1506.80 1512.74 1520.23 1521.08
1548.35 1561.57 1627.34 1672.15 1733.38
3008.20 3017.44 3018.37 3028.70 3039.08
3054.07 3059.04 3067.62 3069.30 3083.00
3084.77 3095.13 3116.34 3144.88 3156.38
3168.02 3172.41 3194.49 3202.83 3209.79
3222.27 3801.55

===============================
3.32.Ph
===============================
  23.79   33.65   49.13   72.69   77.66
 107.93  113.69  121.67  163.87  202.58
 218.01  254.25  264.17  280.15  283.45
 302.07  313.63  319.80  327.24  337.16
 355.78  396.51  419.71  426.75  430.10
 483.38  504.43  514.91  519.90  541.00
 566.91  590.30  636.81  648.01  678.61
 698.93  716.24  720.62  806.60  809.35
 825.08  842.88  890.96  910.49  936.84
 940.16  941.00  945.08  961.43 1015.45
```

```
1018.96 1032.27 1048.62 1056.30 1063.58
1079.66 1106.17 1152.14 1168.36 1179.57
1184.62 1191.46 1196.47 1213.23 1225.44
1231.61 1237.65 1265.64 1292.42 1303.40
1338.30 1345.38 1349.89 1357.07 1400.58
1412.10 1423.19 1432.15 1439.90 1466.84
1474.64 1487.15 1493.03 1498.67 1499.22
1506.75 1508.86 1511.65 1515.14 1521.42
1528.75 1547.04 1570.06 1584.00 1643.63
2976.57 2998.88 3005.75 3025.05 3037.46
3037.54 3040.92 3065.85 3096.74 3099.89
3108.69 3121.62 3125.92 3131.75 3141.35
3163.01 3173.90 3200.74 3208.77 3230.36
3282.92 3830.44

==============================
3.21.M
==============================
  114.09  148.50  175.00  188.83  203.34
  214.80  216.60  259.42  286.43  296.78
  317.28  365.31  388.16  404.73  421.94
  442.16  482.80  493.91  503.97  580.60
  597.54  686.12  702.82  814.15  830.25
  888.74  895.65  921.47  944.76  958.00
  968.39  983.08  987.30 1027.66 1039.76
1056.35 1068.39 1102.41 1124.49 1141.69
1154.05 1161.35 1205.90 1213.44 1234.09
1242.08 1255.05 1294.22 1334.81 1343.36
1365.60 1384.33 1411.23 1419.10 1426.85
1433.60 1490.00 1493.20 1493.87 1499.23
1502.84 1510.83 1520.60 1528.58 1548.36
1728.03 3015.91 3017.14 3028.25 3032.96
3038.69 3042.24 3056.99 3066.68 3075.91
3082.58 3094.95 3105.33 3115.61 3153.46
3163.76 3177.00 3203.75 3794.65

==============================
3.32.M
==============================
   63.11   84.32  104.44  119.92  164.21
  214.02  245.66  254.80  272.88  292.24
  297.48  311.14  342.15  361.25  378.32
  392.84  415.28  464.47  488.56  522.17
  543.91  561.79  634.51  692.77  702.91
  768.84  831.11  883.24  928.72  939.03
  952.28  958.76 1010.09 1018.79 1026.55
1040.56 1043.21 1058.31 1099.68 1136.97
1165.49 1185.61 1194.86 1216.40 1237.52
1269.82 1294.05 1337.02 1358.49 1394.49
1401.04 1409.79 1423.60 1429.14 1435.86
1446.73 1473.89 1485.41 1489.54 1500.11
1506.33 1508.76 1509.79 1516.65 1528.53
1563.60 2913.35 2975.80 3001.65 3025.88
3028.38 3034.89 3035.69 3053.55 3094.84
3097.75 3100.89 3120.12 3128.04 3133.89
3136.54 3160.74 3169.57 3810.45
```

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===============================
((C2H3)(THF)MgBr)2
===============================
  16.65   24.18   30.29   37.64   42.29
  46.04   56.33   59.46   61.67   65.25
  77.04   86.50   92.57   99.96  110.55
 115.94  140.38  148.11  165.57  171.70
 186.25  193.88  209.90  229.50  247.48
 278.12  289.36  301.13  330.23  346.60
 397.91  399.72  559.62  566.31  580.00
 585.66  689.37  692.13  846.14  852.01
 877.49  877.93  880.66  884.82  928.12
 932.12  932.66  932.73  970.56  971.15
 974.44  976.93 1005.16 1005.81 1039.91
1040.22 1049.64 1050.31 1085.54 1086.57
1168.71 1172.65 1193.87 1195.23 1216.72
1222.43 1267.81 1272.28 1279.16 1280.16
1282.66 1283.90 1328.57 1331.96 1365.39
1367.79 1387.63 1392.36 1411.44 1416.76
1443.43 1443.78 1501.25 1502.43 1511.44
1513.57 1526.96 1528.65 1542.04 1544.80
1630.26 1631.01 3046.90 3052.70 3054.80
3061.70 3067.98 3069.34 3072.51 3074.82
3080.64 3081.74 3090.55 3098.04 3118.69
3125.63 3128.30 3129.68 3135.08 3135.37
3141.06 3141.65 3154.15 3158.38
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===============================
3.50
===============================
  24.42   48.72   98.30  117.75  138.52
 148.49  160.75  176.59  190.41  200.04
 210.53  229.52  266.29  274.16  287.70
 324.42  356.59  386.25  399.72  412.92
 433.68  474.22  496.27  526.33  560.70
 602.62  680.38  699.79  730.57  755.89
 820.30  835.89  890.34  920.14  944.86
 953.72  955.99  965.66  975.47  990.46
1029.09 1036.91 1059.40 1060.80 1067.08
1093.82 1099.25 1137.82 1157.01 1168.85
1202.97 1208.52 1233.71 1242.18 1267.21
1295.43 1311.70 1336.90 1353.72 1369.68
1412.60 1426.72 1433.51 1448.23 1489.06
1494.33 1498.92 1499.91 1511.75 1520.34
1543.57 1642.98 1723.34 3008.87 3017.47
3030.53 3032.43 3040.71 3067.61 3069.77
3080.79 3087.37 3097.82 3119.39 3130.17
3138.28 3149.53 3168.14 3183.89 3236.08

===============================
THF
===============================
  46.03  264.87  584.28  674.03  852.82
 891.38  912.94  920.26  931.62  977.60
1035.65 1108.02 1177.40 1188.98 1196.06
```

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1262.81 1264.37 1320.99 1354.35 1375.14
1412.20 1501.74 1512.69 1537.86 1552.12
2991.03 2997.03 3052.70 3054.93 3070.03
3071.18 3112.27 3121.43

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3.51
===============================
  10.85   15.62   27.51   34.51   40.31
  44.50   46.42   50.80   53.63   57.54
  62.11   66.01   71.49   81.14   86.25
  93.04  104.18  106.59  112.46  123.00
 140.50  147.98  151.69  164.70  172.45
 181.67  189.94  195.07  202.85  208.48
 224.61  227.13  233.01  243.28  276.31
 289.23  295.57  300.20  307.55  340.78
 346.20  354.72  369.36  376.64  396.04
 398.69  409.88  449.21  475.03  488.14
 500.11  560.87  567.54  580.96  586.99
 603.67  649.98  687.56  688.61  694.80
 712.15  763.75  813.14  836.57  850.52
 851.35  878.53  879.39  882.14  885.84
 887.28  913.77  928.85  932.65  933.80
 935.47  945.08  948.59  953.90  955.90
 971.51  975.10  976.79  981.07  997.09
1006.71 1024.66 1035.82 1036.71 1039.10
1051.10 1052.48 1058.11 1062.84 1064.44
1071.30 1072.87 1085.81 1142.88 1146.51
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3141.99 3152.24 3153.95 3155.62 3157.64
3159.30 3196.70 3205.03 3245.28
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3.11 References for Chapter 3

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Chapter 4

Formal Synthesis of Xishacorene B

4.1 C–H Functionalization Strategic Approach to Xishacorene B

"Chiral pool" skeletal remodeling has been a useful strategy in accessing complex molecules in enantioenriched fashion and short order. Examples of this strategy are discussed in Chapter 1. However, the specific functionalization patterns of some "chiral pool" building blocks leave certain positions unactivated, limiting the synthetic targets for which the "chiral pool" skeletal remodeling strategy can be applied. We envisioned coupling skeletal remodeling strategies with C–H functionalization to broaden the scope of targets accessible from the "chiral pool" through this combination. Specifically, we sought to demonstrate the power of this strategy through skeletal remodeling of (*S*)-verbenone (**4.1**), readily available from the "chiral pool", followed by C–H functionalization to access xishacorene B (**4.2,** Figure 4.1).

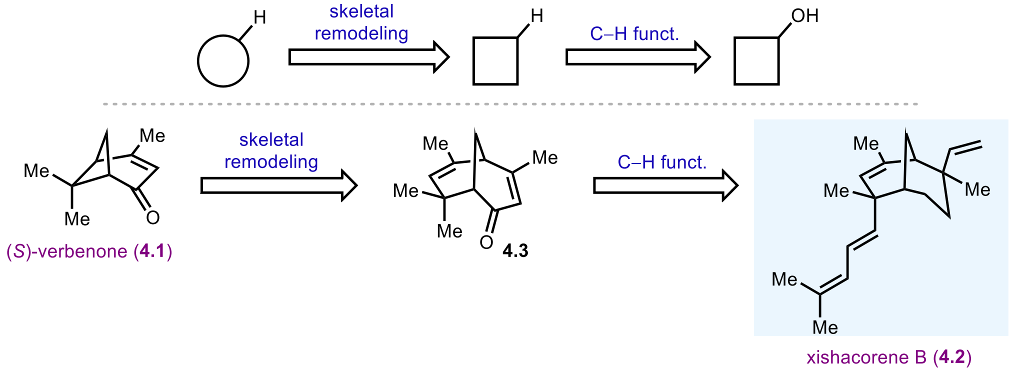


Figure 4.1 Our two-part skeletal remodeling-C–H functionalization strategy conceptually and applied to our synthesis of xishacorene B (**4.2**).

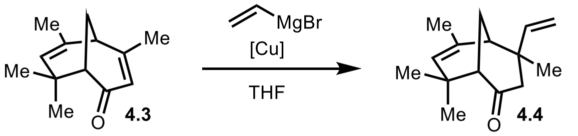
To this end, we investigated the skeletal remodeling of the "chiral pool" terpene (*S*)-verbenone (**4.1**) to [3.3.1]bicycle **4.3**. This work is discussed in Chapter 3. Subsequently, we sought to effect the C–H functionalization of the pseudo-axially disposed methyl group of the gem-dimethyl motif to install a functional handle for appending the diene sidechain. Efforts to carry [3.3.1]bicycle **4.3** to xishacorene B (**4.2**) are discussed below.

4.2 Initial Functionalization of the [3.3.1]Bicycle

Having successfully remodeled the carbocyclic framework of (*S*)-verbenone (**4.1**) to the [3.3.1]bicycle characteristic of the xishacorene family, we next turned our attention to functionalizing the framework to access xishacorene B (**4.2**). From [3.3.1]bicycle **4.3**, we needed to install a vinyl group, functionalize the geminal methyl groups to add the diene sidechain, and deoxygenate to access xishacorene B (**4.2**). Enone **4.3** was well poised for a conjugate addition of a vinyl nucleophile, which we believed would proceed diastereoselectively from the top, or convex, face of the bicycle, minimizing steric clashes with the approaching nucleophile. However, initial attempts to achieve this conjugate addition, using a slight excess of reagents were unsuccessful, observing no reaction and only recovered starting material (Table 4.1, entry 1). We screened other copper sources (entry 2) as well as the addition of trimethylsilyl chloride (TMSCl) to activate the enone (entry 3) but were met with a lack of reactivity in both cases.[1]

It wasn't until treatment of enone **4.3** with superstoichiometric quantities of vinyl magnesium bromide and copper iodide (CuI) that the desired product (**4.4**) was observed (Table 4.1, entry 4). We postulate that this large excess of reagents is required due to the low reactivity of the substrate and low stability of the vinyl cuprate species formed *in situ*. Interestingly, this reaction was highly sensitive to the reagents used, only proceeding using vinyl magnesium bromide sourced from Acros was used — substate decomposition was observed using vinyl magnesium bromide sourced from Sigma-Aldrich. This reaction was also not scalable, displaying a significant drop in yield, down to ~40% yield, on scales of over 500 milligrams (Table 4.1, entry 5).

Given the challenges encountered with the conditions reported above, we continued to screen conditions aiming to improve the reaction efficiency. We found precedent by Tanino and coworkers wherein sequential additions of copper bromide dimethyl sulfide ($CuBr•Me_2S$) and gradually increasing temperatures afforded vinyl conjugate addition adducts.[2] When these conditions were employed on our substrate, we observed conversion to ketone **4.4** in 70% yield (Table 4.1, entry 6). We hypothesized these conditions were successful due to the sequential additions of copper, leading to a consistent, significant, concentration of the cuprate nucleophile. With ketone **4.4** in hand, we next turned our attention to the key C–H functionalization.



entry	Grignard equiv	[Cu] source	temp, duration	additive/notes	result
1	2.0	$CuBr•Me_2S$, 0.5 equiv	–78 °C for 1 h → 50 °C for 20 h		no reaction
2	2.0	CuI, 0.5 equiv	–78 °C for 1 h → 50 °C for 20 h		no reaction
3	3.2	CuI, 1.6 equiv	25 °C, 20 h	TMSCl (2.3 equiv)	no reaction
4	16	CuI, 3 equiv	–78 °C, 45 min	40 mg scale	64%
5	16	CuI, 3 equiv	–78 °C, 45 min	700 mg scale	39%
6	3.0	$CuBr•Me_2S$, 3 x 0.06 equiv	–20 °C, 40 min → 0 °C, 20 min → 25 °C, 30 min		70%

Table 4.1 Optimization of the vinyl conjugate addition transformation.

4.3 Ketone Directed C–H Functionalization Approach

Aiming to install oxidation on the geminal methyl groups by means of a C–H functionalization, we initially investigated conditions reported by Sanford and coworkers for acetoxylation of the unactivated β-position of oximes (Figure 4.2.A).[3,4] The seminal report from Sanford and coworkers utilizes *O*-methyl oximes as the directing group. A subsequent report employed *O*-acetyl oximes as a directing group, which proved more labile and were more easily removed following the C–H functionalization. Mechanistically, treatment of oxime **4.5** with palladium acetate ($Pd(OAc)_2$) and phenyliodine(III) diacetate (PIDA) in acetic acid and acetic anhydride forms the *O*-acetyl oxime (**4.6**) *in situ* and subsequently acetate **4.7**. It is proposed that the acetoxylation occurs by means of a Pd(II/IV) cycle wherein the oxime first coordinates a Pd(II) species, that then undergoes a concerted metalation-deprotonation (CMD) at the position of C–H functionalization. Oxidation of the resulting Pd(II) intermediate to Pd(IV) by PIDA is followed by reductive elimination to afford the product. The CMD step is the site-determining step in this reaction, occurring exclusively at the β-position due to the formation of a five-membered palladacycle.

We postulated that these conditions could potentially be applied to our system to effect C–H functionalization of the geminal methyl groups. In our case, we desired functionalization of the ɣ-position, requiring us to override the inherent β-selectivity. We believed this may be possible due to the rigidity of the bicyclic system locking the conformation of the oxime, positioning the nitrogen atom proximal to the geminal dimethyl substituents. Though we were envisioning C–H functionalization at C14 position, which could lead to xishacorene B (**4.2**), achieving C–H functionalization at C15 position could lead to another xishacorene congener.

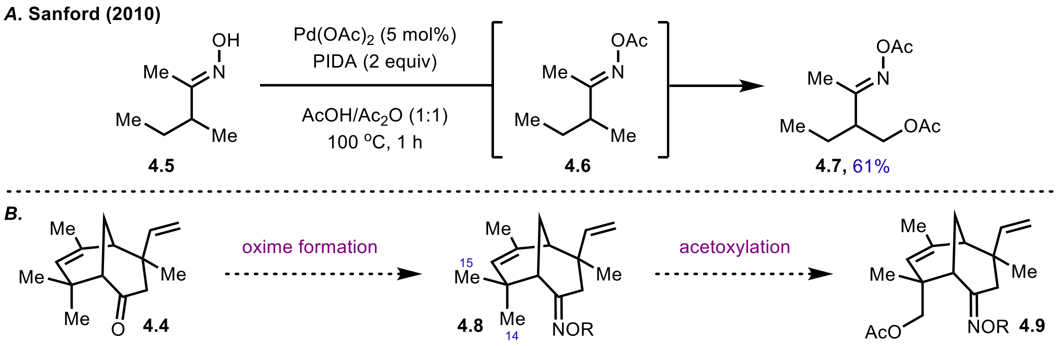
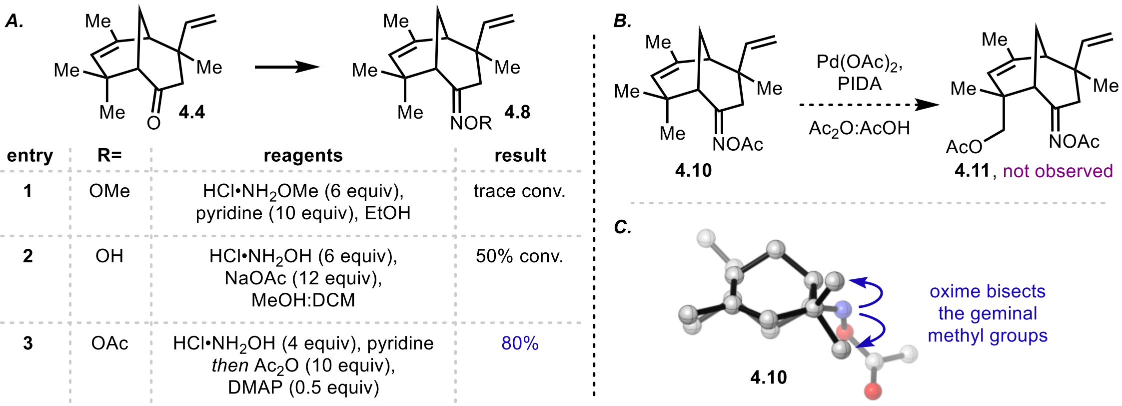


Figure 4.2 (A) Sanford acetoxylation of unactivated C–H bonds with *O*-acetyl oximes. (B) Our proposed C–H functionalization.

In terms of synthesizing the oxime, we screened a variety of conditions to access either the *O*-methyl or *O*-acetyl oxime (**4.8**, Figure 4.3.A). We found that hydroxylamine was the only competent nucleophile for the condensation reaction with ketone **4.4**, which then underwent subsequent acetylation to give oxime **4.10** (Figure 4.3.A, entry 2) in a one-pot procedure. We subjected oxime **4.10** to Sanford's conditions but observed solely recovered starting material (Figure 4.3.B). At this point, we looked more closely at a model of oxime **4.10** and saw that the oxime bisects the geminal methyl groups (Figure 4.3.C). Given the size of the palladacycle we were targeting and the position of our oxime relative to C–H bond in question, we realized that this system was not well poised to undergo the C–H functionalization. It is worth noting that there are reports in the literature that show that the nature of the directing group or added ligands can influence the site-selectivity of C–H functionalization, however these studies focus on ɣ-arylation.[5,6] Given the challenges we faced with formation of oximes on our system, and the lack of direct precedent, these alternative directing groups were not investigated.



entry	R=	reagents	result
1	OMe	HCl•NH$_2$OMe (6 equiv), pyridine (10 equiv), EtOH	trace conv.
2	OH	HCl•NH$_2$OH (6 equiv), NaOAc (12 equiv), MeOH:DCM	50% conv.
3	OAc	HCl•NH$_2$OH (4 equiv), pyridine *then* Ac$_2$O (10 equiv), DMAP (0.5 equiv)	80%

Figure 4.3 (A) Various condensation conditions screened to form oxime **4.8**. (B) Attempted Sanford acetoxylation of *O*-acetyl oxime **4.10**. (C) 3D conformational model of oxime **4.10** showing how oxime is positioned relative to the geminal methyl groups.

4.4 Alcohol Directed C–H Functionalization Approach

Having encountered issues with the oxime directing group, we posited that, by reducing the ketone to the α-disposed hydroxy group, we could establish a more favorable conformation to functionalize the desired methyl group. We found that both dissolving metal reduction (with Li^0 and NH_3) and hydride reduction (with LAH) proceeded with the same diastereoselectivity, giving rise to alcohol **4.12** (Figure 4.4).

From here, we believed that our system was well poised for a Suárez reaction[7] given the 1,5-relationship between the alcohol and the C–H bond in question. Employing classical Suárez conditions, we were able to successfully functionalize the pseudo-axially disposed methyl group to afford ether **4.13**, which was unambiguously characterized by X-ray crystallography (Figure 4.4). Given the low reactivity of ethers in ring opening processes, we also investigated variants of the Suárez reaction, aiming to access a product that could more readily be brought forward to the natural product. Following precedent from Shenvi and coworkers,[8] we treated alcohol **4.12** with lead tetraacetate ($Pb(OAc)_4$), iodine (I_2), and calcium carbonate ($CaCO_3$) anticipating the formation of lactone **4.14**. Unfortunately, these conditions only led to the formation of ether **4.13**. On the basis of precedent from Baran and coworkers,[9] we attempted the Suárez reaction with bromine rather than iodine, attempting to intercept bromide **4.15** prior to the ring closure. However, under these conditions only non-specific decomposition was observed. Though the Suárez reaction variants were unsuccessful, we had a reliable, high yielding way to access the C–H functionalized compound, ether **4.13**.

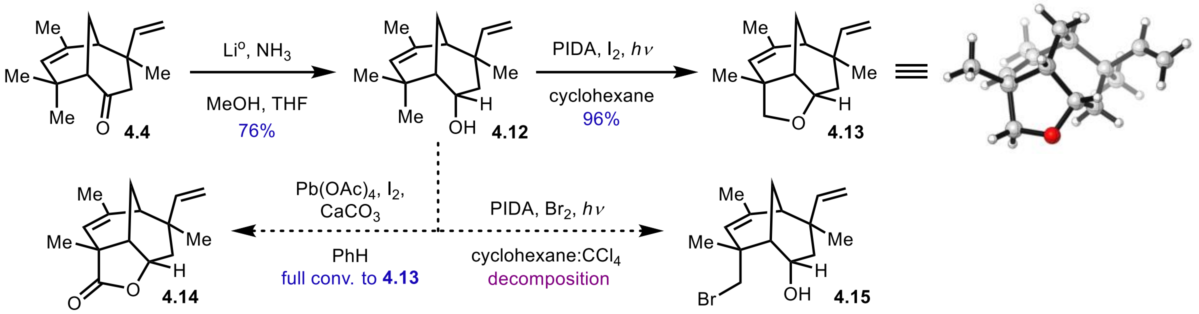


Figure 4.4 Reduction of ketone **4.4** and attempted modified Suárez reactions.

Having functionalized one of the geminal methyl groups, we next sought to carry ether **4.13** forward to xishacorene B (**4.2**). The most direct route was anticipated to be an ionic reduction of ether **4.13** to intercept alcohol **4.16**, which is a known intermediate from the prior Sarpong group synthesis of xishacorene B (**4.2**, Figure 4.5).[10] We postulated that ether **4.13** would open to give the more substituted carbocation (**4.17**), followed by reduction to afford the desired product (**4.16**, Figure 4.5). However, upon treatment of ether **4.13** with triethylsilane (Et_3SiH) and tris(pentafluorophenyl)borane ($B(Ar_F)_3$), alcohol **4.12,** arising from reduction at the undesired position of the tetrahydrofuran moiety, was observed.

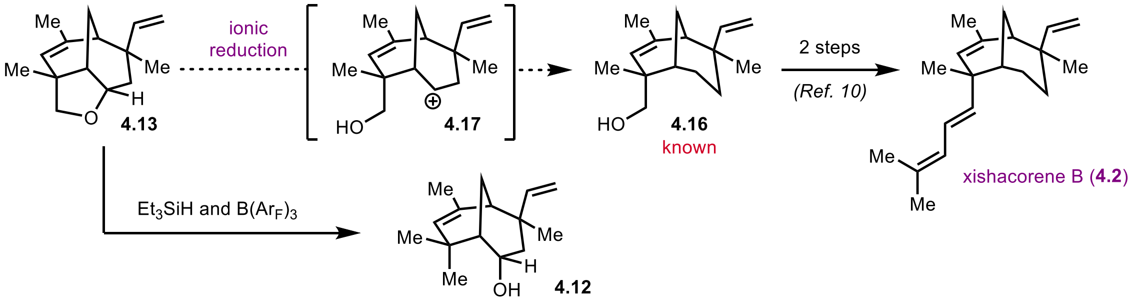


Figure 4.5 Attempted ionic reduction of ether **4.13**.

Our next approach toward opening cyclic ether **4.13** was based on precedent from Mouriño and coworkers where opening of a cyclic tetrahydrofuran (THF) ring to the corresponding diol was achieved.[11] Treatment of ether **4.13** with boron trifluoride diethyl etherate ($BF_3{\bullet}OEt_2$) in acetic anhydride afforded diacetate **4.18**, notably with inversion of stereochemistry at the more substituted carbon (Figure 4.6). Subsequent acetate cleavage gave rise to diol **4.19** and treatment with Dess–Martin periodinane (DMP) afforded ketoaldehyde **4.20**. At this stage we sought to install the diene sidechain of the xishacorenes onto the aldehyde of **4.20**. We first attempted a Horner–Wadsworth–Emmons (HWE) reaction[12] analogous to that reported in the Sarpong group's initial xishacorene B synthesis (Figure 3.3),[10] employing phosphonate **4.21** and potassium *tert*-butoxide (KO*t*-Bu). Diene **4.22** was not observed but rather we saw decomposition of our [3.3.1]bicyclic compound (**4.20**). We also attempted Julia–Kocienski olefination with sulfone **4.23** but were met with a lack of reactivity, observing only recovered starting material.

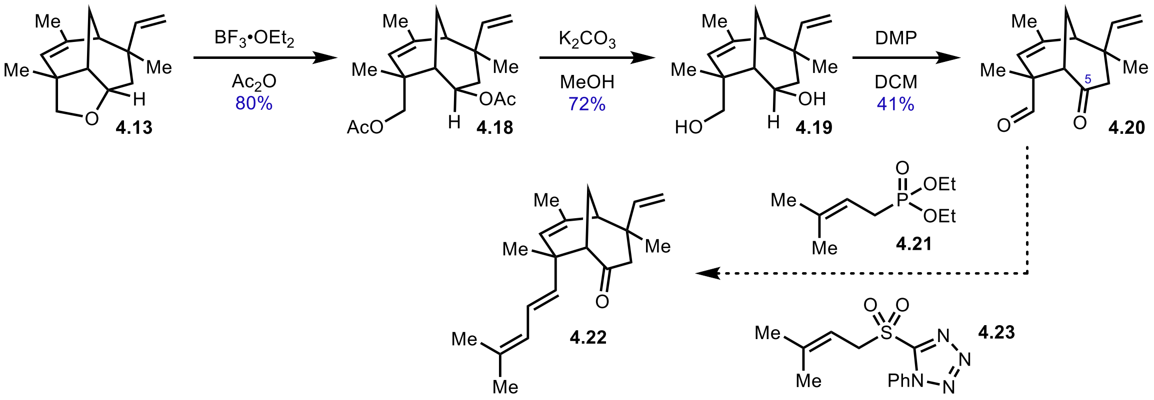


Figure 4.6 Cleavage of ether **4.13** to diol **4.19** and attempted olefinations.

Given that the only difference between our system and the known system was the oxidation at C5, we aimed to change the oxidation state at C5 to see if that may mitigate the decomposition we previously observed using phosphonate **4.21**. From diol **4.19** we aimed to selectively oxidize the primary alcohol to yield aldehyde **4.24** (Figure 4.7). Employing 2,2,6,6-tetramethylphperidine 1-oxyl (TEMPO) and PIDA we were able to obtain aldehyde **4.24** in modest yields. This reaction was unfortunately not reproducible, giving significantly variable and diminished yields. Utilizing tetrapropylammonium perruthenate (TPAP) and *N*-methylmorpholine *N*-oxide (NMO), we observed oxidation to aldehyde **4.24**, albeit unselectively, in a 1:1 ratio with ketoaldehyde **4.20**. Nevertheless, we were able to attempt the HWE and Julia–Kocienski olefinations on aldehyde **4.24**. However, as in the case above with ketoaldehyde **4.24**, we observed no productive reactivity, observing instead a complex mixture of products.

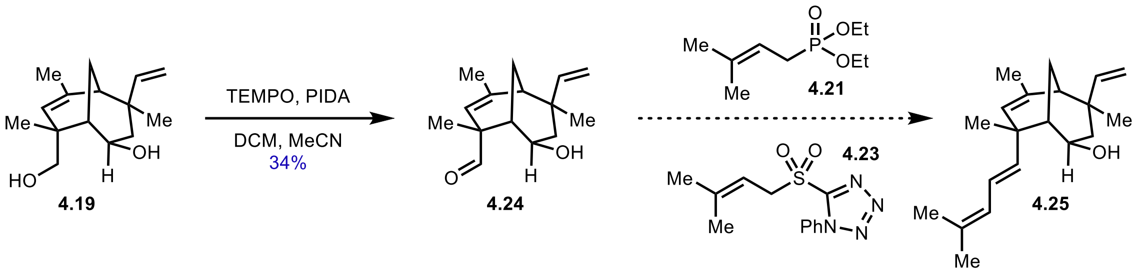


Figure 4.7 Oxidation of diol **4.19** to aldehyde **4.24** and attempted olefinations.

At this point, given the lack of success in installing the diene sidechain using the diol derivatives, coupled with the difficulty we faced differentiating the two alcohols, we chose to reassess the opening of ether **4.13**. If we could differentiate C5 and C14 with two orthogonal functional groups, we could more easily install the diene sidechain. We attempted standard ether cleavage conditions such as boron tribromide (BBr_3) or trimethylsilyl bromide (TMSBr), aiming to access primary bromide **4.26** (Figure 4.8), however BBr_3 led to a complex mixture of products and TMSBr led to no reaction. Fortunately, conditions reported by Shin and coworkers (acetyl chloride and iron) worked on our system and we were able to access chloroester **4.27**.[13]

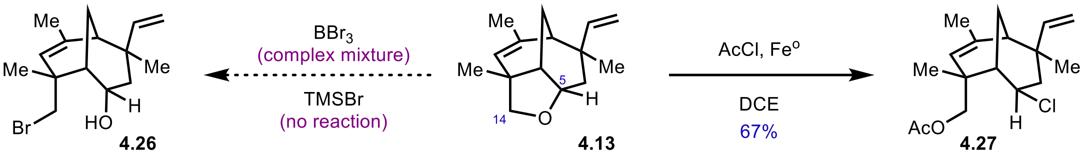


Figure 4.8 Opening of ether **4.13** to give orthogonal functional groups at C14 and C5.

Shin and coworkers propose a mechanism for the aforementioned transformation as illustrated in Figure 4.9.[13] Acid chloride **4.28** presumably undergoes a series of single electron reductions from iron to generate iron trichloride ($FeCl_3$) *in situ*. Another equivalent of acid chloride **4.28** can then engage the Lewis acid to form acylium ion **4.29**. From here, incorporation of the ether (**4.30**) forms intermediate **4.31** which can undergo ring opening yielding the more substituted carbocation (**4.32**). Trapping of carbocation **4.32** with a chloride (presumably generated from the formation of acylium ion **4.29**) gives rise to chloroester **4.33**.

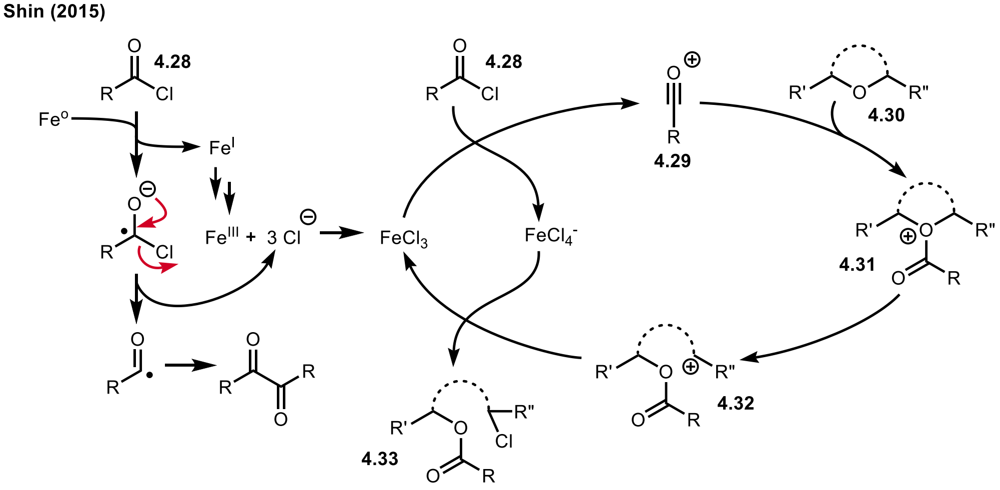


Figure 4.9 Shin and coworkers' proposed mechanism for the transformation of a cyclic ether (**4.30**) to a chloroester (**4.33**).

Having successfully cleaved the cyclic ether to afford two distinct functional handles in chloroester **4.27**, we once again turned our attention to the end game of the synthesis, aiming to install the diene sidechain and remove the chloride functionality at C5. We noted the similarity of this compound with known alcohol **4.16** from the initial Sarpong synthesis of xishacorene B (**4.2**) and realized that we were only a short series of functional group manipulations away from a formal synthesis the natural product.[10] From chloroester **4.27**, we were able to reduce the secondary chloride at C5, using tributyltin hydride (Bu_3SnH) and azobisisobutyronitrile (AIBN), to give the methylene containing compound **4.34** (Figure 4.10). Removal of the acetate protecting group afforded primary alcohol **4.16**, constituting a formal synthesis of xishacorene B (**4.2**).

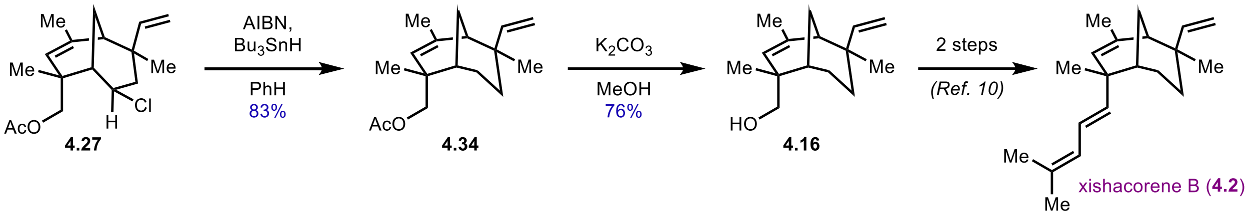


Figure 4.10 Conversion of chloroester **4.27** to known alcohol **4.16**.

4.5 Complete Formal Synthesis of Xishacorene B

As discussed in detail throughout both Chapters 3 and 4, studies to skeletally remodel the "chiral pool" terpene (*S*)-verbenone (**4.1**) to access the natural product xishacorene B (**4.2**) were undertaken. The final 10-step formal synthesis of xishacorene B (**4.2**) is summarized below.

Starting from (*S*)-verbenone (**4.1**), irradiation in cyclohexane followed by addition of an alkynyl Grignard derived from **4.35** gave rise to chrysanthenol **4.36** (Figure 4.11). Treatment of chrysanthenol **4.36** with LAH produced an allene *in situ* which underwent an anionic oxy-Cope rearrangement to afford enone **4.3**. Conjugate addition of a vinyl moiety yielded ketone **4.4** which was reduced with dissolving metal conditions to β-disposed alcohol **4.12**. A Suárez reaction effected a formal C–H functionalization of the pseudo-axially disposed methyl group to form cyclic ether **4.13,** which was opened to chloroester **4.27**. Reduction of the secondary chloride and protecting group cleavage yielded known alcohol **4.16**, which can be converted to xishacorene B (**4.2**) in two known steps (oxidation and olefination) following the previously reported Sarpong group total synthesis.[10]

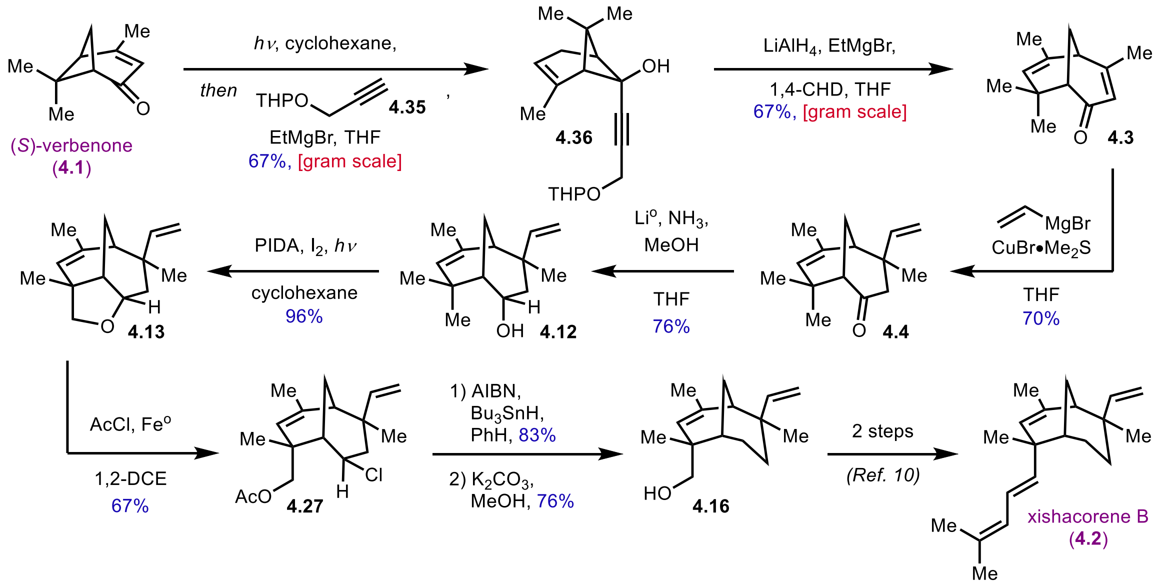


Figure 4.11 Complete formal synthesis of xishacorene B (**4.2**) starting from the "chiral pool" terpene (*S*)-verbenone (**4.1**).

4.6 Conclusion and Outlook

In conclusion, we were able to synthesize xishacorene B (**4.2**) in 10 steps from the "chiral pool" terpene (*S*)-verbenone (**4.1**). This work highlighted a skeletal remodeling strategy of the starting terpene that was discussed in Chapter 3 in addition to a key C–H functionalization to install a functional handle at an unactivated position that was discussed within this chapter.

We were able to take enone **4.3** and effect a conjugate addition of a vinyl group to yield ketone **4.4** by employing sequential additions of the copper reagent. This conjugate addition set the stage for the key C–H functionalization. We synthesized *O*-acetyl oxime **4.10** and investigated Sanford's acetoxylation conditions[3,4] aiming to access the acetoxylated [3.3.1]bicycle (**4.11**), however, this was unsuccessful. Postulating that this was due to the conformation of the bicycle, we changed the directing/mediating group and its conformation relative to the geminal methyl groups by reducing the ketone to alcohol **4.12**. A Suárez reaction[7] afforded cyclic ether **4.13,** effecting the net C–H functionalization of one of the geminal methyl groups we required.

From here, opening of the cyclic ether to install the diene sidechain characteristic of the xishacorenes was investigated. Ultimately, we were able to convert ether **4.13** into chloroester **4.27** which we converted to the known alcohol **4.16** through a series of functional group manipulations.[10] This completed our formal synthesis of xishacorene B (**4.2**) in a total of 10 steps from the commercially available (*S*)-verbenone (**4.1**).

4.7 Experimental Contributors

Project design was carried out by Kerry E. Jones (K.E.J.) and Prof. Richmond Sarpong (R.S.). All experiments for this chapter were conducted by K.E.J.

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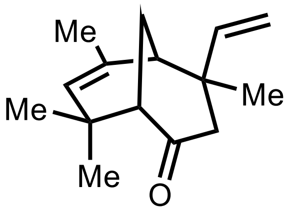
4.8 Experimental Details

4.8.1 Experimental Procedures

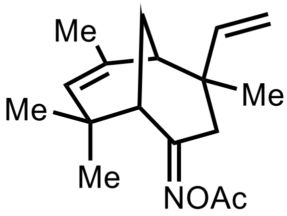
(1S,4R,5R)-4,6,8,8-tetramethyl-4-vinylbicyclo[3.3.1]non-6-en-2-one (4.4)



Ketone **4.4** was prepared according to the following modification of a procedure reported by Tanino and coworkers.[2] Vinyl magnesium bromide (0.7 M in THF, 9.95 mL, 3.0 equiv) was cooled to –40 °C. Copper (I) bromide dimethyl sulfide complex (28.6 mg, 0.139 mmol, 0.06 equiv) was added under an atmosphere of nitrogen. The resulting tan mixture was stirred for 30 min at –30 °C. Enone **4.3** (442. mg, 2.32 mmol, 1.0 equiv) was added dropwise as a solution in THF (7.7 mL) to the reaction mixture. A second portion of copper (I) bromide dimethyl sulfide complex (28.6 mg, 0.139 mmol, 0.06 equiv) was added under an atmosphere of nitrogen and the reaction mixture was warmed to –20 °C. After 40 min, a third portion of copper (I) bromide dimethyl sulfide complex (28.6 mg, 0.139 mmol, 0.06 equiv) was added under an atmosphere of nitrogen. The reaction mixture was stirred at 0 °C for 20 min. The black reaction mixture was then quenched with sat. aq. NH_4Cl (5 mL), extracted with Et_2O (3 x 50 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 30:1 hexanes:ethyl acetate) gave ketone **4.4** in 70% yield (355. mg, 1.63 mmol) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.33 – 5.27 (m, 1H), 5.04 (d, *J* = 17.6 Hz, 1H), 5.03 (d, *J* = 10.9 Hz, 1H), 2.39 (dt, *J* = 14.8, 1.6 Hz, 1H), 2.30 (d, *J* = 14.7 Hz, 1H), 2.19 – 2.15 (m, 1H), 2.00 (dt, *J* = 13.1, 3.1 Hz, 1H), 1.89 (s, 1H), 1.87 (d, *J* = 1.1 Hz, 3H), 1.82 (dt, *J* = 13.0, 3.0 Hz, 1H), 1.07 (s, 3H), 1.01 (s, 3H), 0.89 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 213.5, 146.3, 133.8, 133.4, 113.4, 55.1, 47.6, 46.4, 43.3, 35.2, 30.7, 28.9, 27.1, 26.1, 25.9. **HRMS** (EI): calcd for ([M], $C_{15}H_{22}O)^+$: m/z =218.1666; found 218.1674. **IR:** ṽ = 2958, 2873, 1706, 1455, 1429, 1294, 1245, 919 cm^{-1}. **[α]$^{20}_D$** = –31.00 (*c* 1.00, $CHCl_3$)

(1S,4R,5R,E)-4,6,8,8-tetramethyl-4-vinylbicyclo[3.3.1]non-6-en-2-one O-acetyl oxime (4.10)

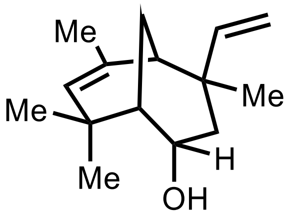


Ketone **4.4** (52 mg, 0.27 mmol, 1.0 equiv) was dissolved in pyridine (9 mL). HCl•NH_2OH (75 mg, 1.08 mmol, 4 equiv) was added and the mixture was heated to 80 °C for 18 h. The mixture was cooled to room temperature and DMAP (17 mg, 0.14 mmol, 0.5 equiv) and Ac_2O (0.26 mL, 2.70 mmol, 10 equiv) were added sequentially. After 1.5 h, the mixture was diluted with toluene (5 mL) and concentrated *in vacuo* followed by dilution with EtOAc and brine wash. The aqueous layer was back extracted with EtOAc (3 x 5 mL). The organic layers were combined and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 6:1 hexanes:ethyl acetate) gave O-acetyl oxime **4.10**, as a mixture of oxime diastereomers, in 63% yield (48 mg, 0.17 mmol) as a clear oil.

Mixture of *E/Z*-isomer, approximately 1:1 ratio: ^{1}H NMR (400 MHz, C_6D_6) δ 5.64 – 5.48 (m, 2H), 5.34 (dd, *J* = 17.7, 1.0 Hz, 1H), 5.19 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.11 – 4.92 (m, 4H), 3.31 – 3.23 (m, 2H), 2.57 (d, *J* = 14.8 Hz, 1H), 2.47 (s, 1H), 2.12 (d, *J* = 14.7 Hz, 1H), 1.85 (dt, *J* = 12.9, 3.1 Hz, 1H), 1.81 (d, *J* = 3.0 Hz, 6H), 1.79 – 1.73 (m, 2H), 1.66 – 1.61 (m, 1H), 1.60 (d, *J* = 1.4 Hz, 6H), 1.57 – 1.47 (m, 3H), 0.92 (s, 3H), 0.90 (d, *J* = 1.6 Hz, 6H), 0.84 (s, 3H), 0.83 (s, 3H), 0.79 (s, 3H). *[Note:*

contains Et_2O and two proton signals are covered by Et_2O] **HRMS (ESI):** calcd for ([M+Na], $C_{17}H_{25}NO_2Na)^+$: m/z =298.1778; found 298.1777.

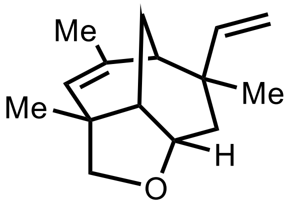
(1S,2S,4R,5R)-4,6,8,8-tetramethyl-4-vinylbicyclo[3.3.1]non-6-en-2-ol (4.12)



Ketone **4.4** (320. mg, 1.47 mmol, 1.0 equiv) was dissolved in THF (9.8 mL) and MeOH (0.3 mL, 7.34 mmol, 5.0 equiv) under a balloon of argon. Li^0 was added (102 mg, 14.7 mmol, 10.0 equiv) and the mixture was cooled to –78 °C. NH_3 (~9.80 mL) was condensed into the reaction flask until the mixture turned a deep blue and maintained the blue color. The mixture was stirred at –78 °C for 1 h then quenched with sat. aq. NH_4Cl (10 mL) then warmed to room temperature and stirred for 15 min. The biphasic mixture was extracted with Et_2O (3 x 15 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 12:1 hexanes:ethyl acetate) gave alcohol **4.12** in 76% yield (247 mg, 1.12 mmol) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.84 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.21 (s, 1H), 5.08 (d, *J* = 17.8 Hz, 1H), 5.04 (d, *J* = 10.9 Hz, 1H), 3.99 – 3.90 (m, 1H), 1.79 – 1.76 (m, 1H), 1.75 (d, *J* = 1.4 Hz, 3H), 1.74 – 1.71 (m, 2H), 1.67 (d, *J* = 2.8 Hz, 1H), 1.67 – 1.62 (m, 2H), 1.21 (s, 3H), 0.97 (s, 3H), 0.94 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.6, 136.3, 133.0, 111.9, 73.1, 43.7, 43.0, 42.6, 39.0, 36.3, 33.0, 29.9, 28.2, 27.3, 26.1. **HRMS** (EI): calcd for ([M], $C_{15}H_{24}O)^+$: m/z =220.1822; found 220.1827 **IR**: $\tilde{\nu}$ = 3319, 2957, 2935, 2874, 1455, 1057, 1023, 910 cm^{-1}. **$[\alpha]^{20}_D$** = +7.64 (*c* 0.17, $CHCl_3$) **MP**: 84–87 °C

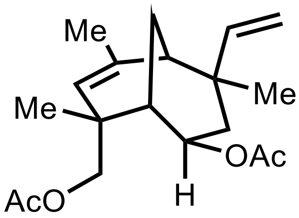
3,6,8-trimethyl-6-vinyl-2,3,3a,4,5,6,7,7a-octahydro-3,5-ethenobenzofuran (4.13)



Ether **4.13** was prepared according to the following modification of a procedure outlined by Maimone and coworkers.[15] Alcohol **4.12** (125 mg, 0.567 mmol, 1.0 equiv) and PIDA (548 mg, 1.70 mmol, 3.0 equiv) were dissolved in cyclohexane (19.0 mL). I_2 (144 mg, 0.567 mmol, 1.0 equiv) was added and the mixture was irradiated using a sunlamp that was simultaneously cooled with a fan for 1.5 h. Upon completion of the reaction, as determined by TLC, the mixture was cooled to 0 °C and quenched with 3:1 sat. aq. $NaHCO_3$: sat. aq. $Na_2S_2O_3$ (10 mL) until the purple color disappeared. The mixture was extracted with Et_2O (3 x 10 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 15:1 hexanes:ethyl acetate) gave ether **4.13** in 96% yield (119 mg, 0.546 mmol) as a colorless oil that spontaneously crystallized at room temperature. This was unambiguously characterized by single crystal X-ray crystallography.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.77 (ddd, *J* = 17.6, 10.8, 1.3 Hz, 1H), 5.44 – 5.33 (m, 1H), 5.07 (dd, *J* = 17.6, 1.1 Hz, 1H), 5.03 (dd, *J* = 10.8, 1.1 Hz, 1H), 4.31 (dt, *J* = 9.2, 7.2 Hz, 1H), 3.88 (d, *J* = 8.5 Hz, 1H), 3.70 (d, *J* = 8.5 Hz, 1H), 1.98 (dt, *J* = 6.8, 3.2 Hz, 1H), 1.94 – 1.89 (m, 1H), 1.87 (ddd, *J* = 13.0, 3.6, 2.5 Hz, 1H), 1.81 (d, *J* = 1.4 Hz, 3H), 1.79 – 1.76 (m, 1H), 1.56 – 1.50 (m, 1H), 1.39 (ddd, *J* = 14.0, 9.2, 1.2 Hz, 1H), 1.13 (s, 3H), 0.97 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.3, 134.8, 132.8, 111.6, 78.7, 76.6, 43.6, 43.2, 43.2, 40.8, 34.3, 30.1, 26.8, 26.3, 23.9. **HRMS** (EI): calcd for ([M], $C_{15}H_{22}O)^+$: m/z =218.1666; found 218.1672 **IR**: ṽ = 2953, 2923, 2865, 1450, 1267, 1034, 909, 821 cm^{-1}. **$[\alpha]^{20}_D$** = +6.89 (*c* 1.17, $CHCl_3$) **MP**: 43–49 °C

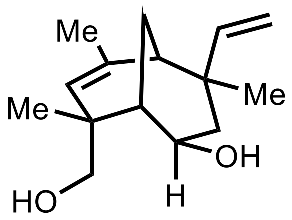
((1S,2R,5R,6R,8S)-8-acetoxy-2,4,6-trimethyl-6-vinylbicyclo[3.3.1]non-3-en-2-yl)methyl acetate (4.18)



Prepared according to the following modification of a procedure outlined by Mouriño and coworkers.[11] Ether **4.13** (50 mg, 0.23 mmol, 1.0 equiv) was dissolved in Ac_2O (2.0 mL) then cooled to –30 °C. BF_3•OEt_2 (0.41 mL, 3.2 mmol, 14 equiv) was added dropwise to the solution. The mixture was maintained at to –30 °C for 3.5 h. The mixture was quenched with sat. aq. $NaHCO_3$ (10 mL) was added dropwise to quench the reaction mixture. The mixture was extracted with Et_2O (3 x 10 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 15:1 hexanes:ethyl acetate) gave diacetate **4.18** in 80% yield (59 mg, 0.18 mmol) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.17 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.16 (p, *J* = 1.3 Hz, 1H), 5.04 – 4.96 (m, 3H), 3.98 (d, *J* = 11.2 Hz, 1H), 3.89 (d, *J* = 11.2 Hz, 1H), 2.20 (ddd, *J* = 13.1, 3.5, 2.4 Hz, 1H), 2.10 (s, 3H), 2.00 (s, 3H), 1.79 (d, *J* = 1.4 Hz, 3H), 1.75 – 1.70 (m, 2H), 1.68 (dt, *J* = 2.8, 1.5 Hz, 1H), 1.61 – 1.51 (m, 2H), 1.06 (s, 3H), 0.92 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.5, 170.4, 148.2, 136.9, 128.5, 110.8, 71.2, 69.2, 43.0, 39.2, 39.0, 38.2, 35.9, 29.9, 26.4, 26.3, 22.3, 21.6, 21.1. **HRMS (ESI):** calcd for ([M+Na], $C_{19}H_{28}O_4Na)^+$: m/z =343.1880; found 343.1879

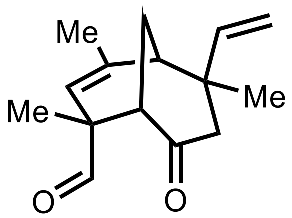
(1S,2S,4R,5R,8R)-8-(hydroxymethyl)-4,6,8-trimethyl-4-vinylbicyclo[3.3.1]non-6-en-2-ol (4.19)



Diacetate **4.18** (59 mg, 0.18 mmol, 1.0 equiv) was dissolved in MeOH (7.2 mL) in a scintillation vial under an atmosphere of air. K_2CO_3 (0.25 g, 1.8 mmol, 10 equiv) was added and the mixture sealed with a Teflon cap and heated to 50 °C for 3.5 h. The mixture was quenched with $NaHCO_3$ (5 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 6:1 to 3:1 hexanes:ethyl acetate) gave diol **4.19** in 72% yield (30. mg, 0.13 mmol) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.22 (dd, *J* = 17.8, 11.0 Hz, 1H), 5.19 (d, *J* = 17.8 Hz, 1H), 5.17 – 5.12 (m, 1H), 5.09 (d, *J* = 11.0 Hz, 1H), 4.09 – 4.04 (m, 1H), 3.54 (d, *J* = 11.0 Hz, 1H), 3.38 (d, *J* = 10.9 Hz, 1H), 2.14 (dt, *J* = 13.4, 3.0 Hz, 1H), 2.00 (d, *J* = 3.0 Hz, 1H), 1.77 (d, *J* = 1.4 Hz, 3H), 1.73 (d, *J* = 15.1 Hz, 1H), 1.69 – 1.61 (m, 2H), 1.54 (dt, *J* = 13.5, 3.4 Hz, 1H), 1.05 (s, 3H), 0.90 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 149.6, 136.0, 129.6, 112.2, 68.9, 68.4, 43.4, 40.9, 40.7, 39.2, 38.0, 30.6, 26.3, 26.0, 21.9. **HRMS (ESI):** calcd for ([M+Na], $C_{15}H_{24}O_2Na)^+$: m/z =259.1669; found 259.1671

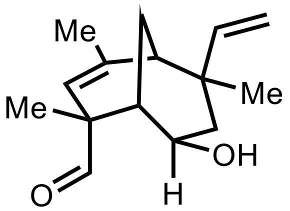
(1S,2R,5R,6R)-2,4,6-trimethyl-8-oxo-6-vinylbicyclo[3.3.1]non-3-ene-2-carbaldehyde (4.20)



Diol **4.19** (30. mg, 0.13 mmol, 1.0 equiv) was dissolved in DCM (4.9 mL) and cooled to 0 °C under an atmosphere of air. DMP (0.16 g, 0.38 mmol, 3.0 equiv) was added and the mixture was warmed to room temperature and stirred for 1.5 h. The mixture was quenched with 1:1 $NaHCO_3$:$Na_2S_2O_3$ (5 mL) then extracted with DCM (3 x 5 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 6:1 hexanes:ethyl acetate) gave ketoaldehyde **4.20** in 41% yield (12 mg, 0.05 mmol) as a clear semi-solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.43 (s, 1H), 5.71 (ddd, *J* = 17.6, 10.9, 0.9 Hz, 1H), 5.51 (p, *J* = 1.4 Hz, 1H), 5.06 (d, *J* = 3.7 Hz, 1H), 5.03 (d, *J* = 2.9 Hz, 1H), 2.54 (s, 1H), 2.38 (d, *J* = 14.8 Hz, 1H), 2.26 (d, *J* = 14.8 Hz, 1H), 2.11 (ddd, *J* = 13.3, 3.6, 2.5 Hz, 1H), 1.97 (s, 1H), 1.95 (d, *J* = 1.4 Hz, 3H), 1.84 (dt, *J* = 13.2, 3.0 Hz, 1H), 1.23 (s, 3H), 1.08 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 211.2, 202.4, 145.7, 138.5, 124.7, 114.0, 52.0, 51.3, 47.2, 46.4, 43.2, 28.7, 26.7, 26.4, 23.0. **HRMS (EI):** calcd for ([M], $C_{15}H_{20}O)^+$: m/z =232.1458; found 232.1459

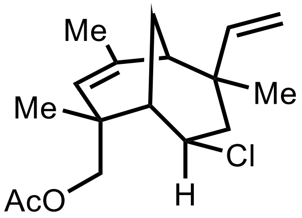
(1S,2R,5R,6R,8R)-8-hydroxy-2,4,6-trimethyl-6-vinylbicyclo[3.3.1]non-3-ene-2-carbaldehyde (4.24)



Diol **19** (3.0 mg, 13 µmol, 1 equiv) was dissolved in DCM (0.2 mL) and MeCN (0.2 mL). TEMPO (0.2 mg, 1.5 µmol, 0.12 equiv) and PIDA (4.1 mg, 13 µmol, 1 equiv) were added to the mixture. The mixture was stirred for 2 h in the dark before sat. aq. $Na_2S_2O_3$ was added. The aqueous layer was separated and extracted with DCM (3 x 3 mL). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The crude reside was purified by preparative thin layer chromatography to yield aldehyde **4.24** (1.0 mg, 4.3 µmol, 34%).

^{1}H NMR (700 MHz, $CDCl_3$) δ 9.60 (s, 1H), 6.19 (dd, *J* = 17.8, 11.0 Hz, 1H), 5.41 (s, 1H), 5.22 (d, *J* = 17.8 Hz, 1H), 5.14 (d, *J* = 11.0 Hz, 1H), 3.82 (s, 1H), 2.23 (dt, *J* = 13.5, 3.0 Hz, 1H), 2.05 (d, *J* = 10.6 Hz, 2H), 1.85 (d, *J* = 1.5 Hz, 3H), 1.68 – 1.58 (m, 3H), 1.22 (s, 3H), 0.93 (s, 3H).

((1S,2R,5R,6R,8R)-8-chloro-2,4,6-trimethyl-6-vinylbicyclo[3.3.1]non-3-en-2-yl)methyl acetate (4.27)

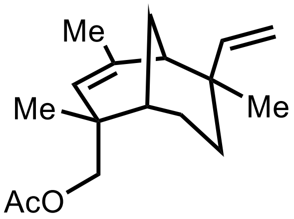


Chloride **4.27** was prepared according to the following modification of a procedure outlined by Shin and coworkers.[13] Ether **4.13** (36.8 mg, 0.17 mmol, 1.0 equiv) and Fe powder (9.4 mg, 0.17 mmol, 1.0 equiv) were dissolved in DCE (2.6 mL). Acetyl chloride (0.02 mL, 0.34 mmol, 2.0 equiv) were added and the mixture was heated at 45 °C for 20 h. The mixture was cooled to room temperature, filtered through silica and Celite (eluting with EtOAc), and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 1.5:1 hexanes:DCM) gave chloride **4.27** in 67% yield (33.6 mg, 0.11 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.34 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.17 (t, *J* = 1.4 Hz, 1H), 5.06 (dd, *J* = 17.7, 1.0 Hz, 1H), 5.02 (dd, *J* = 11.0, 1.0 Hz, 1H), 4.46 (dq, *J* = 4.3, 2.2 Hz, 1H), 3.93 (d, *J* = 11.3 Hz, 1H), 3.90 (d, *J* = 11.2 Hz, 1H), 2.46 (dt, *J* = 13.3, 2.9 Hz, 1H), 2.15 (t, *J* = 1.8 Hz, 1H), 2.10 (s, 3H), 2.12 – 2.07 (m, 1H), 1.99 – 1.96 (m, 1H), 1.85 (d, *J* = 4.4 Hz, 1H), 1.82 (t, *J* = 1.8 Hz, 1H), 1.80 (d, *J* = 1.4 Hz, 3H), 1.06 (s, 3H), 0.91 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.3, 148.1, 137.2, 128.4, 110.4, 69.2, 60.1, 42.3, 41.7, 40.4, 40.2, 39.2, 30.2, 26.6, 26.3, 21.7, 21.1. **HRMS** (ESI): calcd for

([M+Na], $C_{17}H_{25}O_2ClNa)^+$: m/z =319.1436; found 319.1437 **IR**: ṽ = 2963, 1742, 1460, 1372, 1232, 1035, 990, 908 cm^{-1}. **[α]^{20}$_D$** = +9.37 (*c* 1.11, $CHCl_3$)

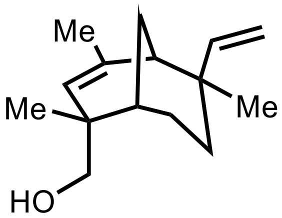
((1S,2S,5R,6R)-2,4,6-trimethyl-6-vinylbicyclo[3.3.1]non-3-en-2-yl)methyl acetate (4.34)



Chloride **4.27** (31.2 mg, 0.11 mmol, 1.0 equiv) and AIBN (3.5 mg, 0.02 mmol, 0.2 equiv) were dissolved in benzene (9.4 mL). Tributyltin hydride (0.06 mL, 0.21 mmol, 2.0 equiv) was added and the mixture was heated to 80 °C for 3 h. The mixture was cooled to room temperature, diluted with Et_2O (5 mL), and washed with 1.0 M aq. KF (5 mL). The aqueous layer was back extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 99:1 to 6:1 hexanes:ethyl acetate) gave acetate **4.34** in 83% yield (23.0 mg, 87.7 µmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.89 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.27 (t, *J* = 1.4 Hz, 1H), 5.05 (dd, *J* = 11.0, 1.3 Hz, 1H), 5.03 (dd, *J* = 17.7, 1.3 Hz, 1H), 4.00 (d, *J* = 10.8 Hz, 1H), 3.95 (d, *J* = 10.7 Hz, 1H), 2.08 (s, 3H), 1.85 (t, *J* = 2.9 Hz, 1H), 1.78 (d, *J* = 1.4 Hz, 3H), 1.78 – 1.71 (m, 1H), 1.67 – 1.56 (m, 3H), 1.54 – 1.51 (m, 1H), 1.46 – 1.39 (m, 2H), 0.98 (s, 3H), 0.89 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.6, 147.6, 136.9, 130.1, 111.8, 70.2, 44.7, 40.3, 39.1, 34.0, 30.4, 30.0, 27.6, 26.4, 26.2, 24.5, 21.2. **HRMS** (EI): calcd for ([M], $C_{17}H_{26}O_2)^+$: m/z =262.1928; found 262.1931 **IR**: ṽ = 2960, 2931, 2872, 1743, 1459, 1375, 1238, 1033 cm^{-1}. **[α]^{20}$_D$** = +13.98 (*c* 1.03, $CHCl_3$)

((1S,2S,5R,6R)-2,4,6-trimethyl-6-vinylbicyclo[3.3.1]non-3-en-2-yl)methanol (4.16)

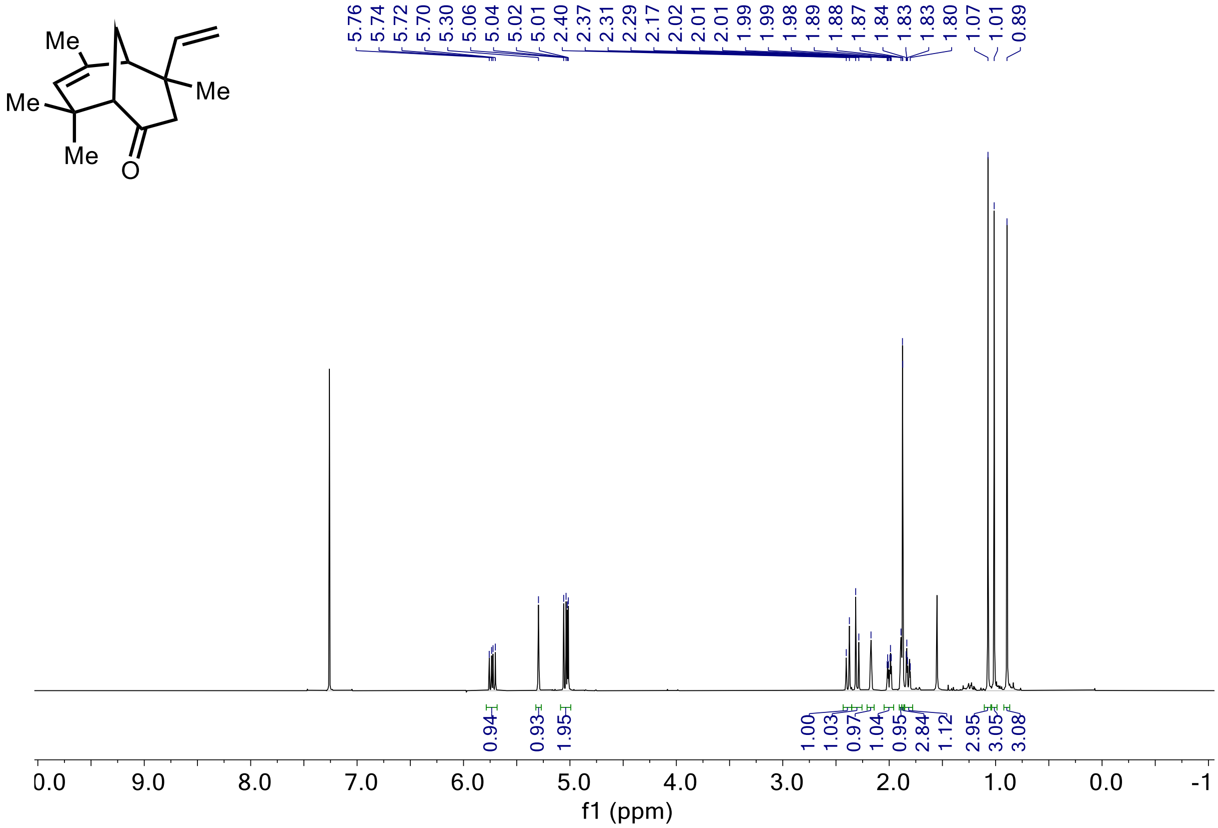


Acetate **4.34** (20.6 mg, 78.5 µmol, 1.0 equiv) was dissolved in MeOH (3.2 mL) in an open flask. K_2CO_3 (108 mg, 0.78 mmol, 10.0 equiv) was added and the mixture sealed with a Teflon cap and heated to 50 °C and held at this temperature for 2 h. The mixture was quenched with sat. aq. $NaHCO_3$ (5 mL) and extracted with Et_2O (5 x 5 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification of the crude residue by flash column chromatography (eluting with 12:1 to 6:1 hexanes:ethyl acetate) gave primary alcohol **4.16** (13.2 mg, 59.9 µmol) in 76% yield. The ^{1}H NMR spectrum was fully consistent with that reported in the literature.[10]

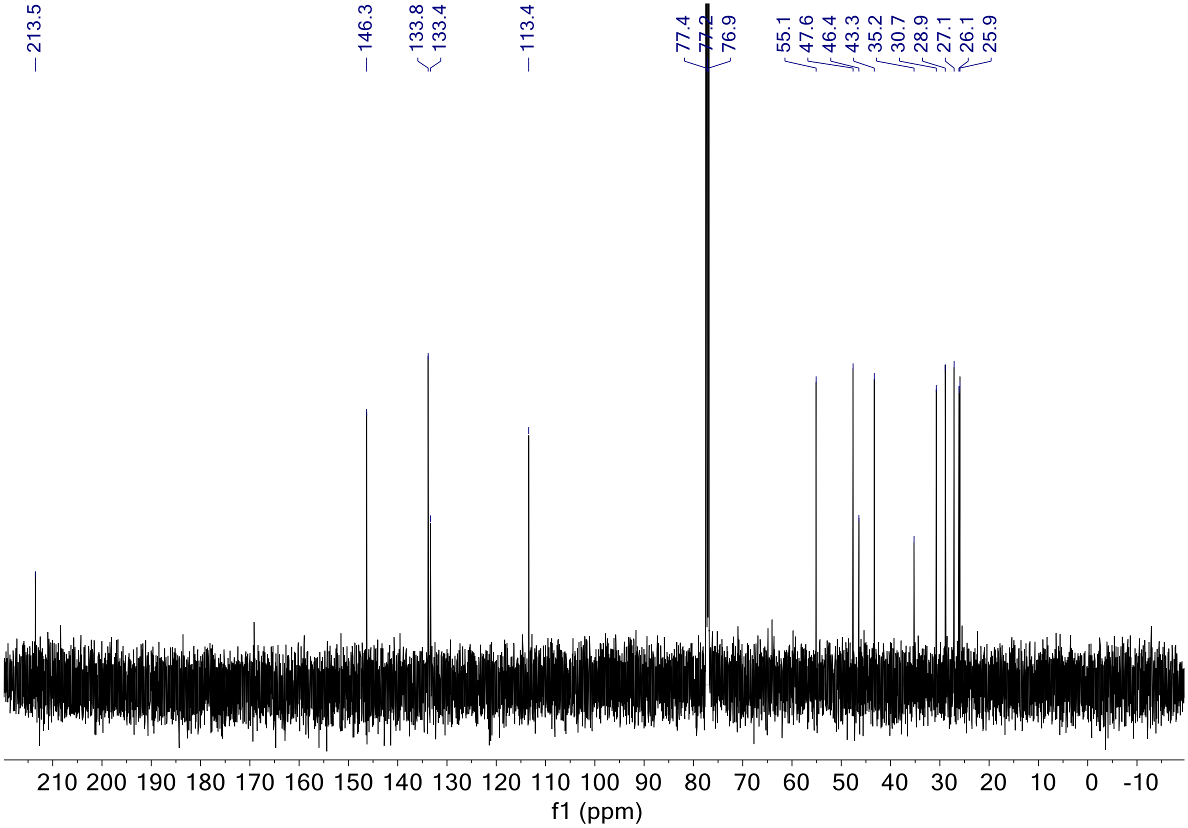
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.90 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.25 (p, *J* = 1.4 Hz, 1H), 5.07 – 5.01 (m, 2H), 3.65 (d, *J* = 10.6 Hz, 1H), 3.45 (d, *J* = 10.6 Hz, 1H), 1.85 (t, *J* = 3.0 Hz, 1H), 1.78 (d, *J* = 1.4 Hz, 3H), 1.75 (dt, *J* = 12.5, 2.9 Hz, 1H), 1.67 – 1.58 (m, 3H), 1.56 (q, *J* = 3.4 Hz, 1H), 1.50 – 1.39 (m, 2H), 1.00 (s, 3H), 0.89 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.7, 136.5, 130.8, 111.7, 68.9, 44.9, 40.8, 40.2, 33.7, 30.5, 30.2, 27.8, 26.5, 25.6, 24.6. **$[\alpha]^{20}_{D}$** = +21.06 (*c* 0.66, $CHCl_3$)

4.8.2 NMR Spectral Data for Chapter 4

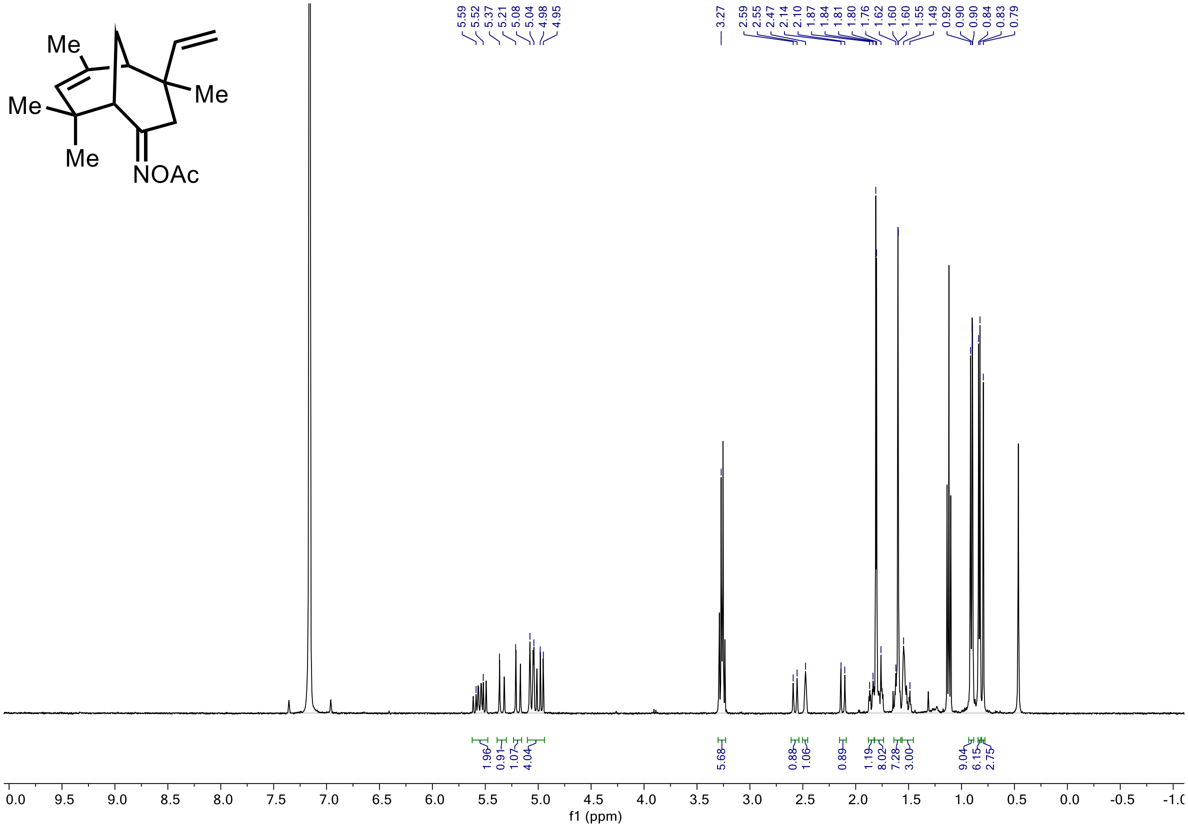
4.4 (^{1}H NMR, 500 MHz, CDCl$_3$)



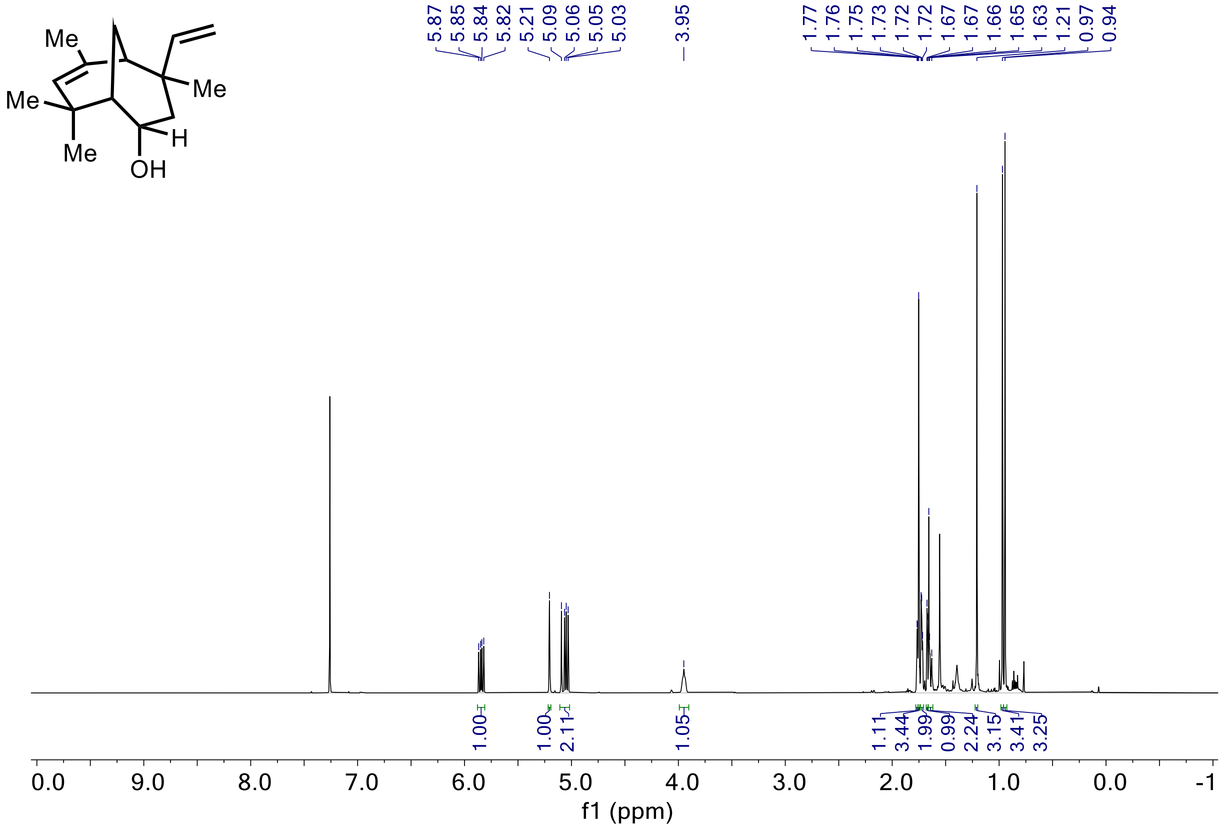
4.4 (^{13}C NMR, 126 MHz, CDCl$_3$)



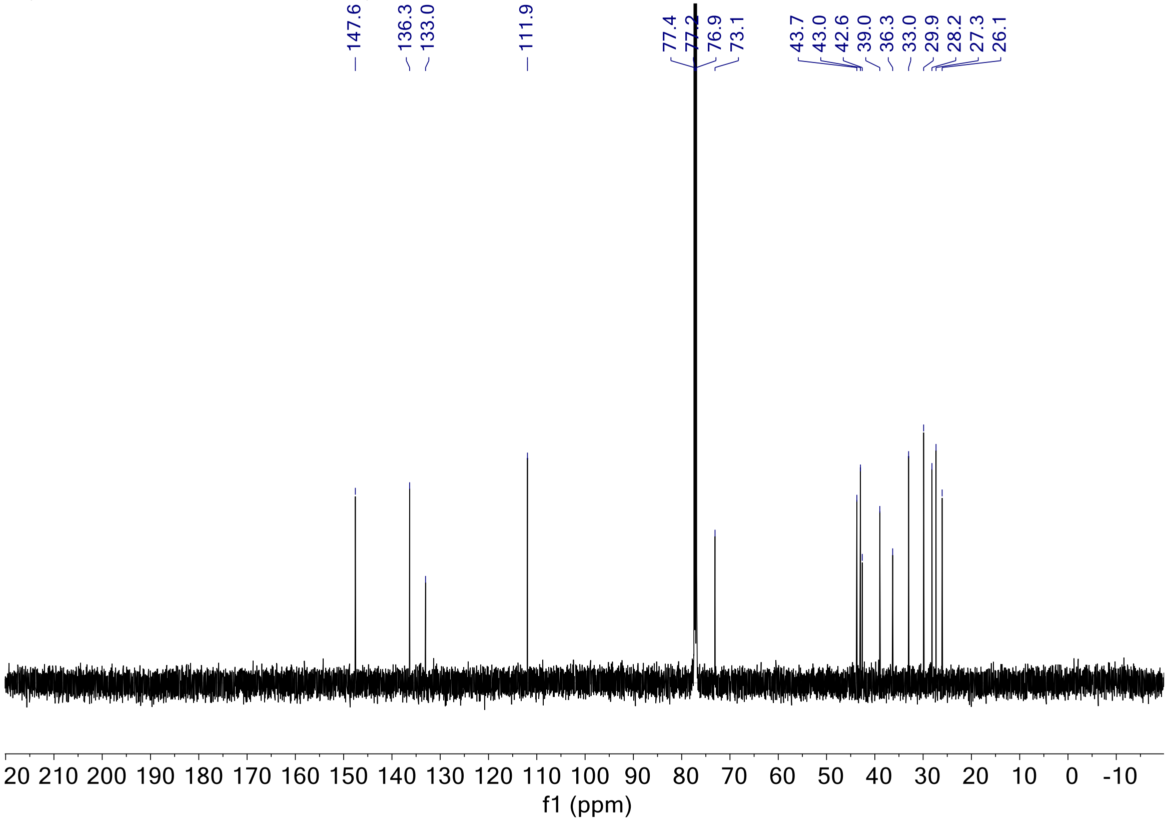
4.10 (^{1}H NMR, 400 MHz, C_6D_6)



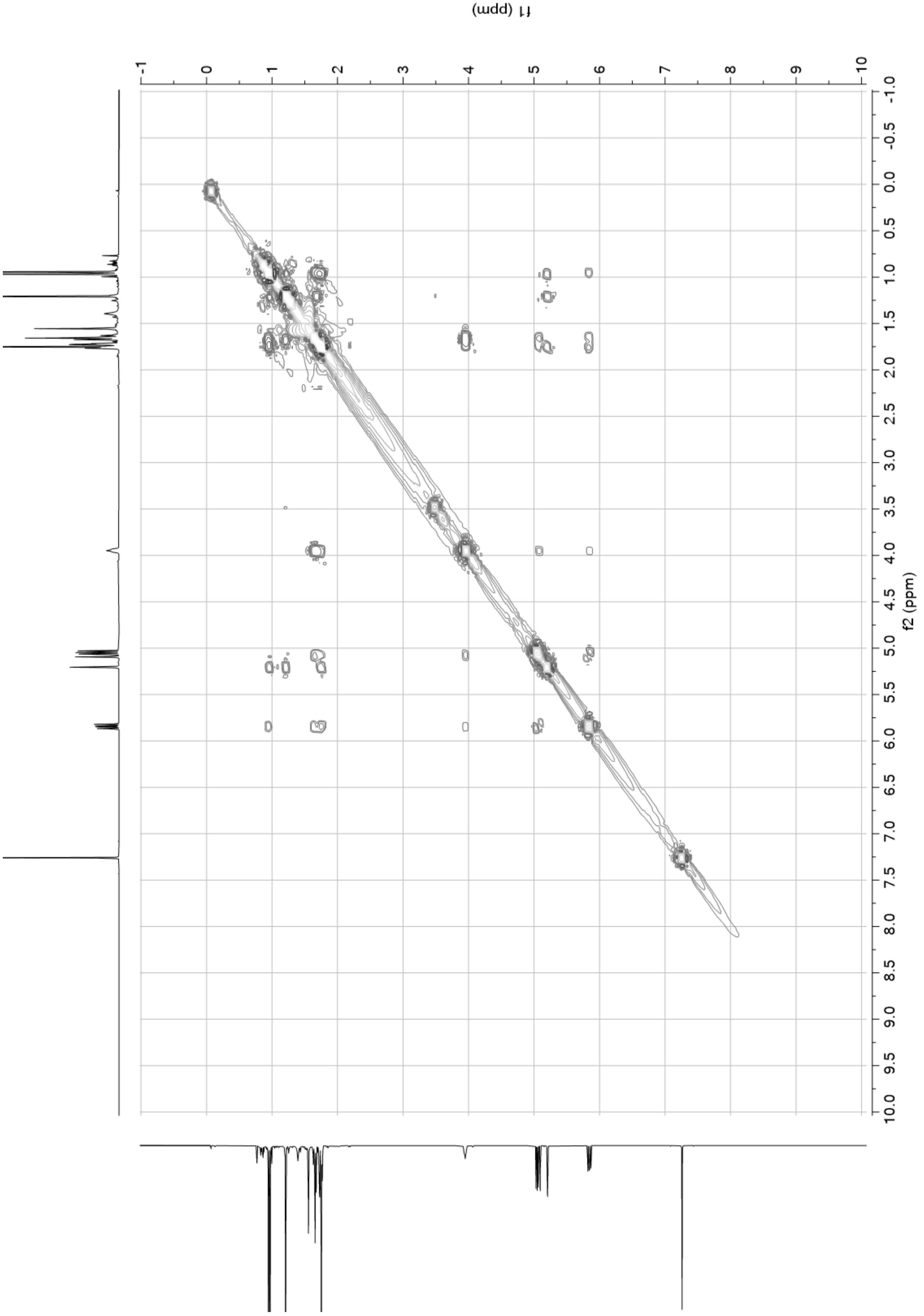
4.12 (^{1}H NMR, 600 MHz, CDCl$_3$)



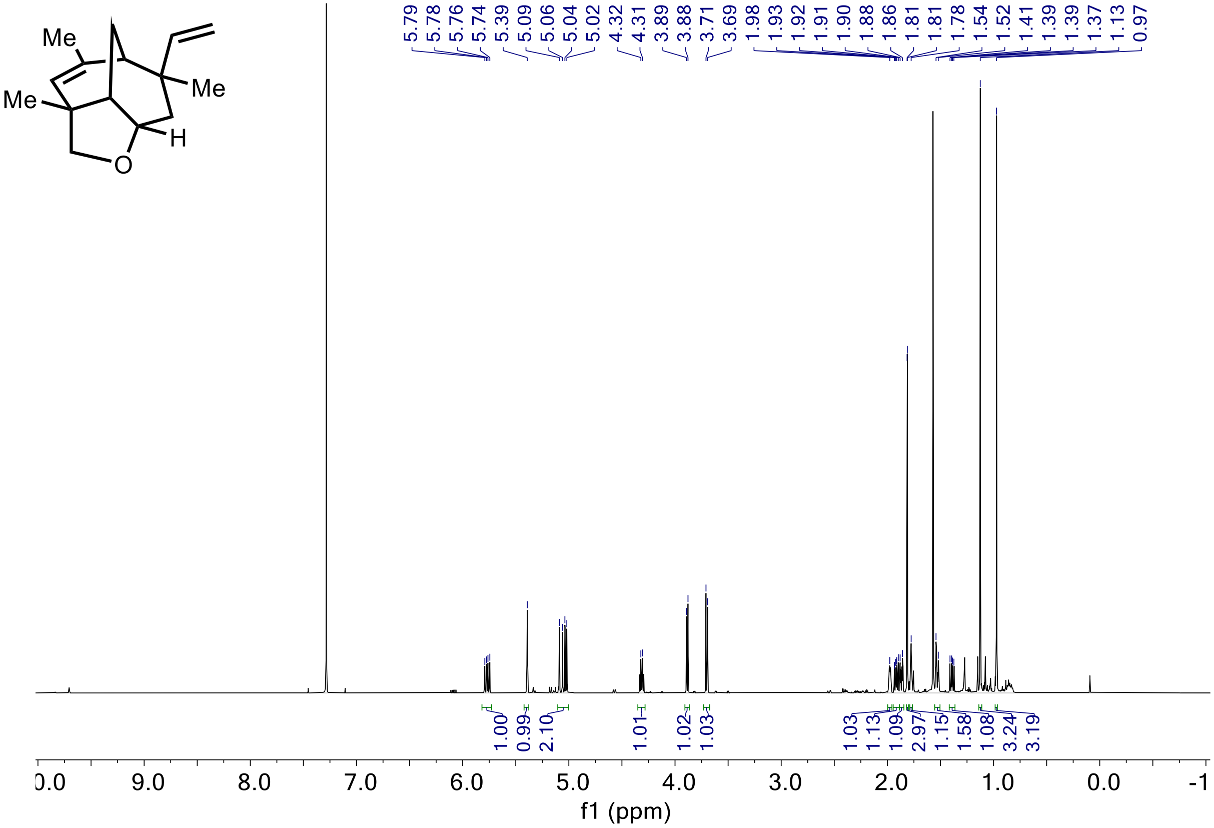
4.12 (^{13}C NMR, 151 MHz, CDCl$_3$)



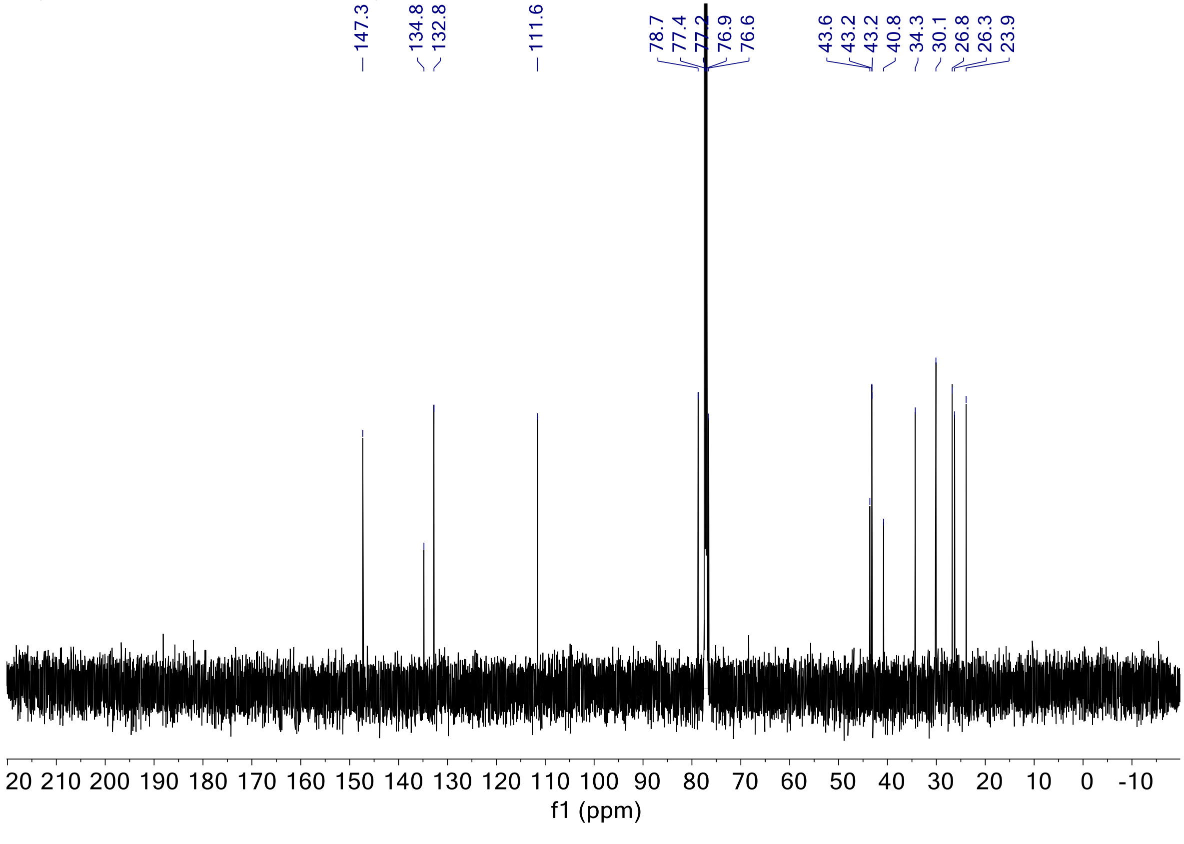
4.12 (NOESY, $CDCl_3$)



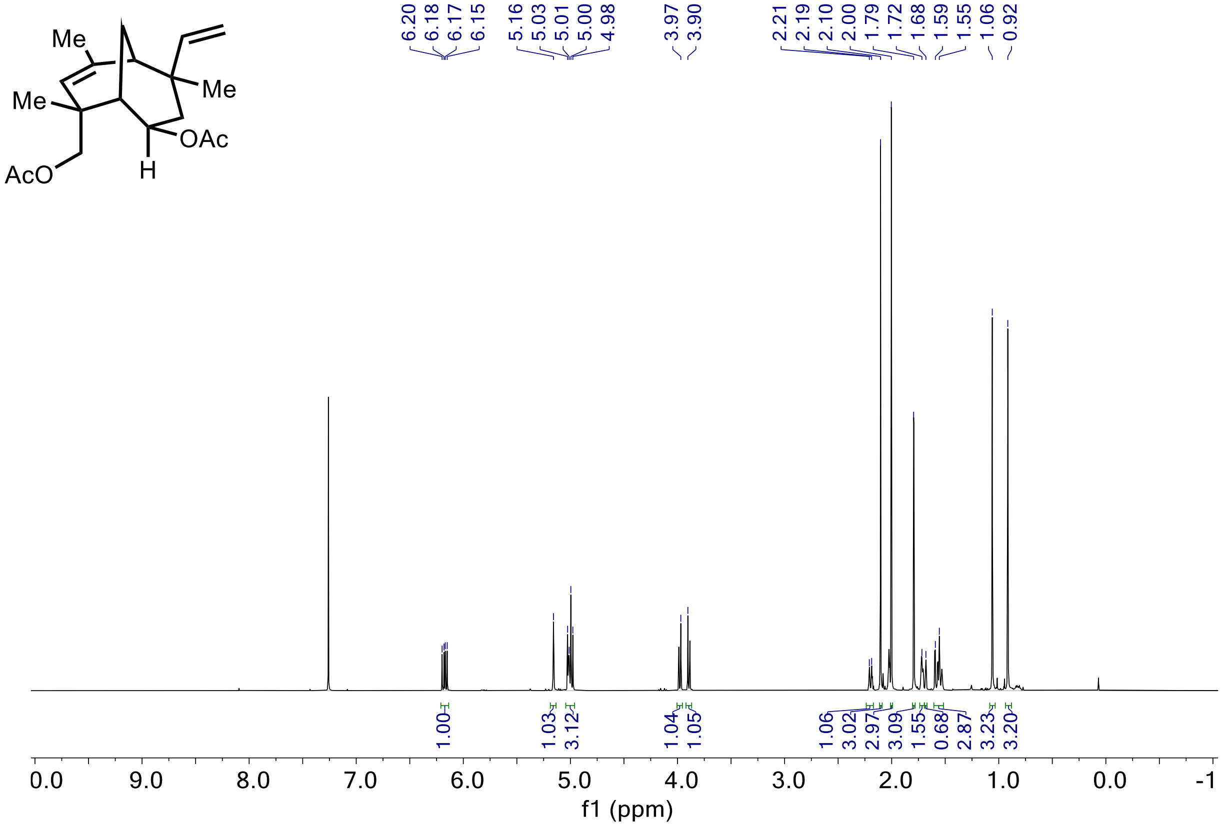
4.13 (^{1}H NMR, 600 MHz, CDCl$_3$)



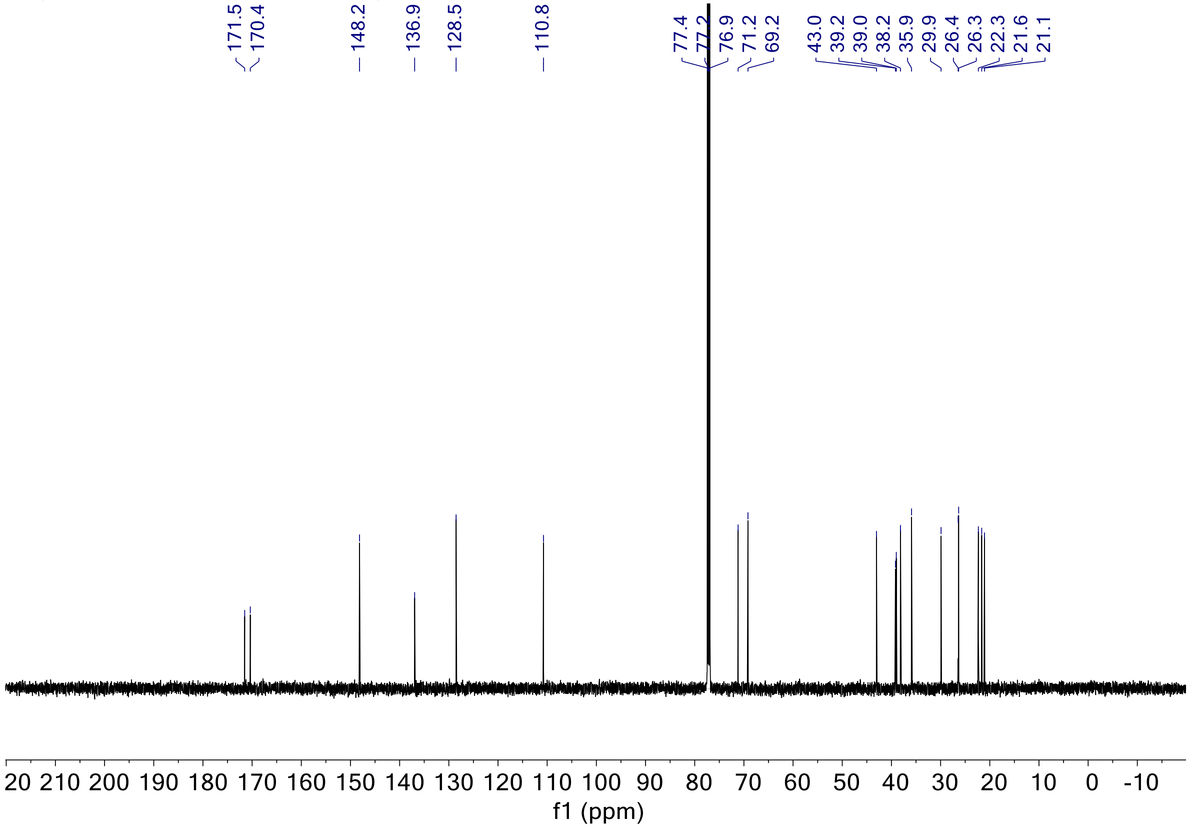
4.13 (^{13}C NMR, 151 MHz, CDCl$_3$)



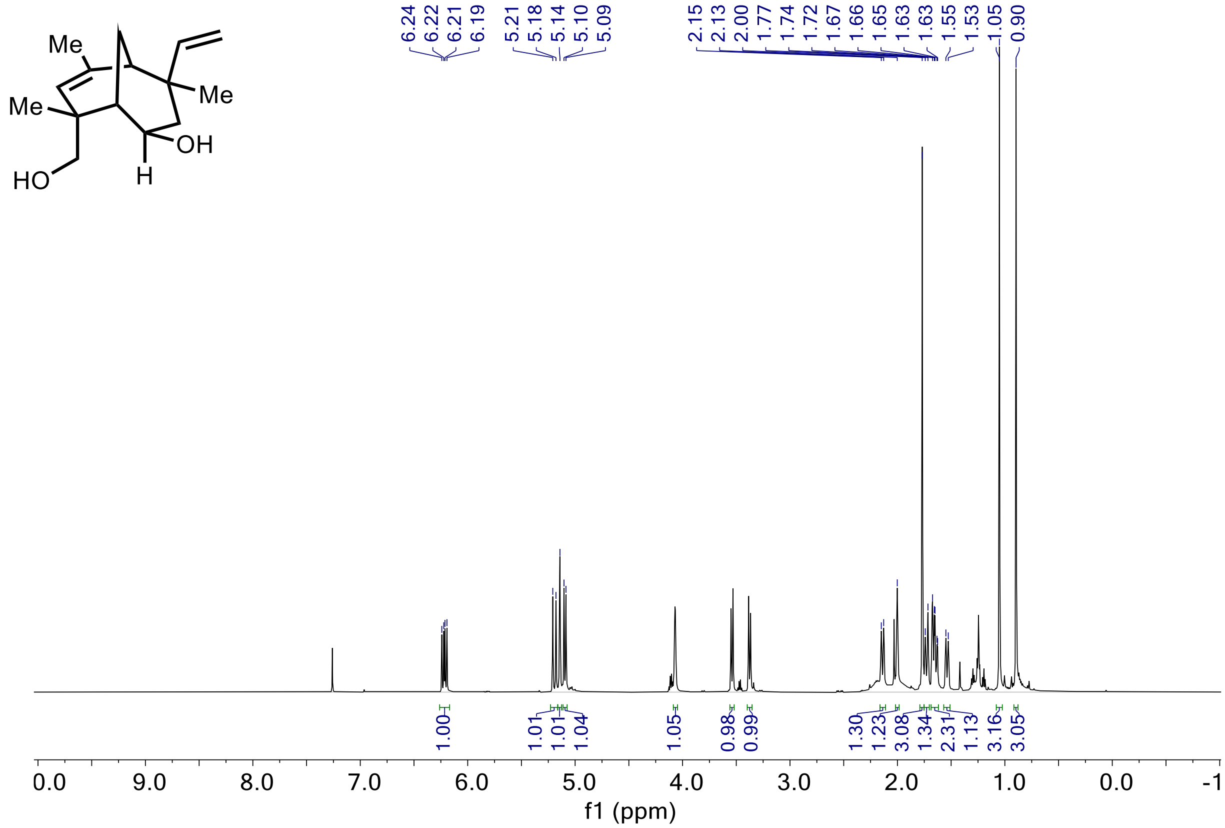
4.18 (^{1}H NMR, 600 MHz, CDCl$_3$)



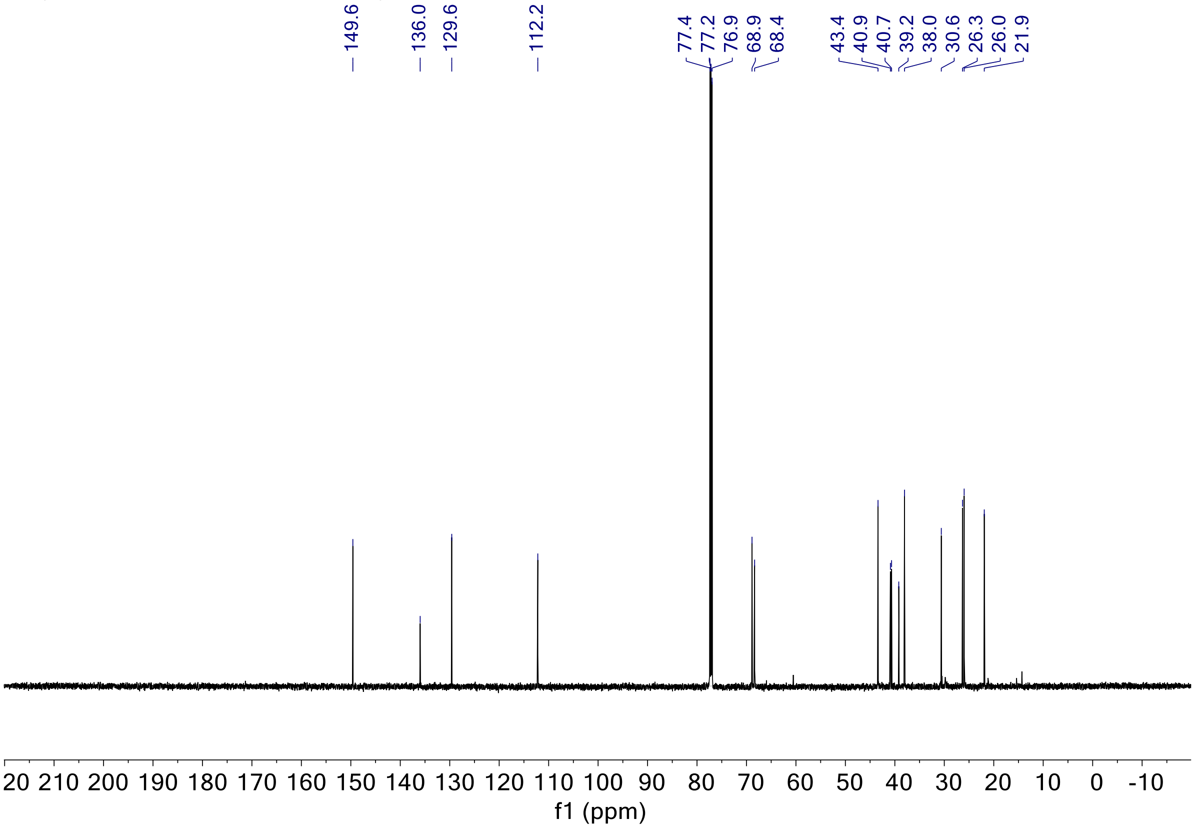
4.18 (^{13}C NMR, 151 MHz, CDCl$_3$)



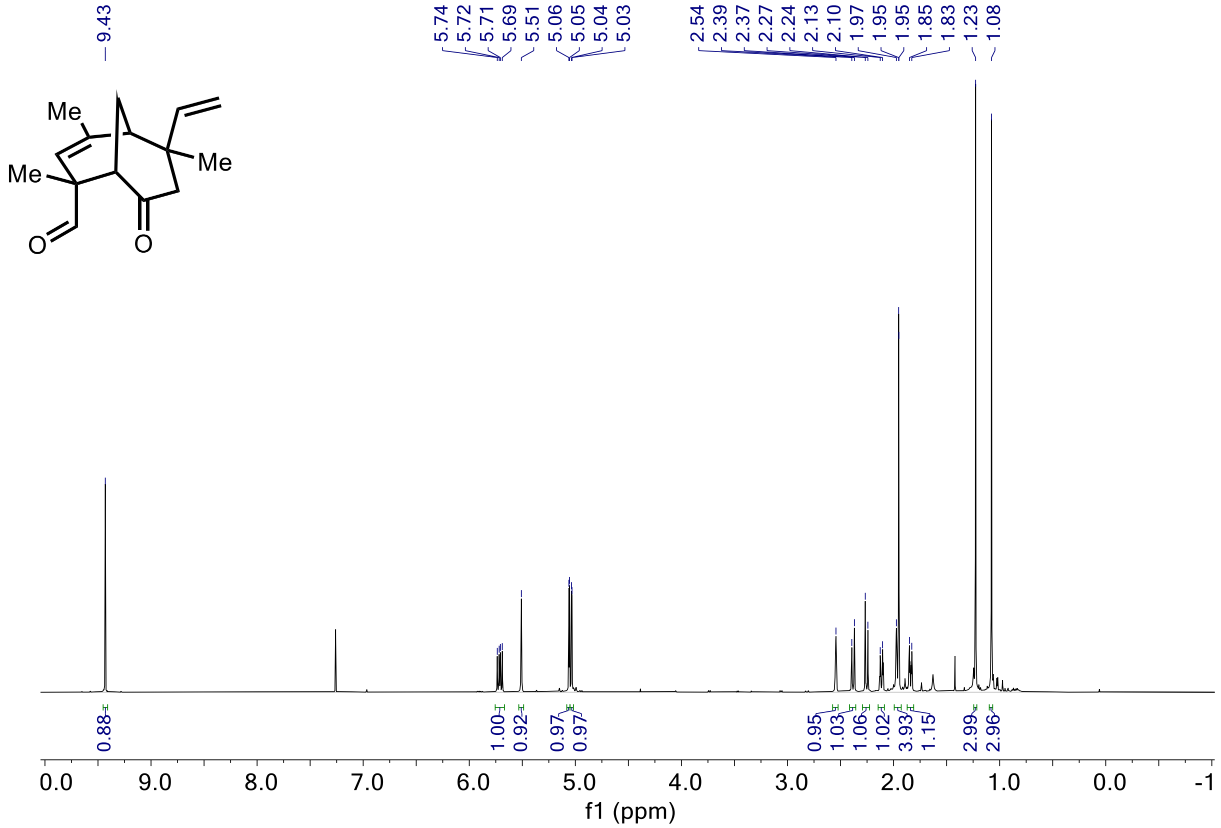
4.19 (^{1}H NMR, 600 MHz, CDCl$_3$)



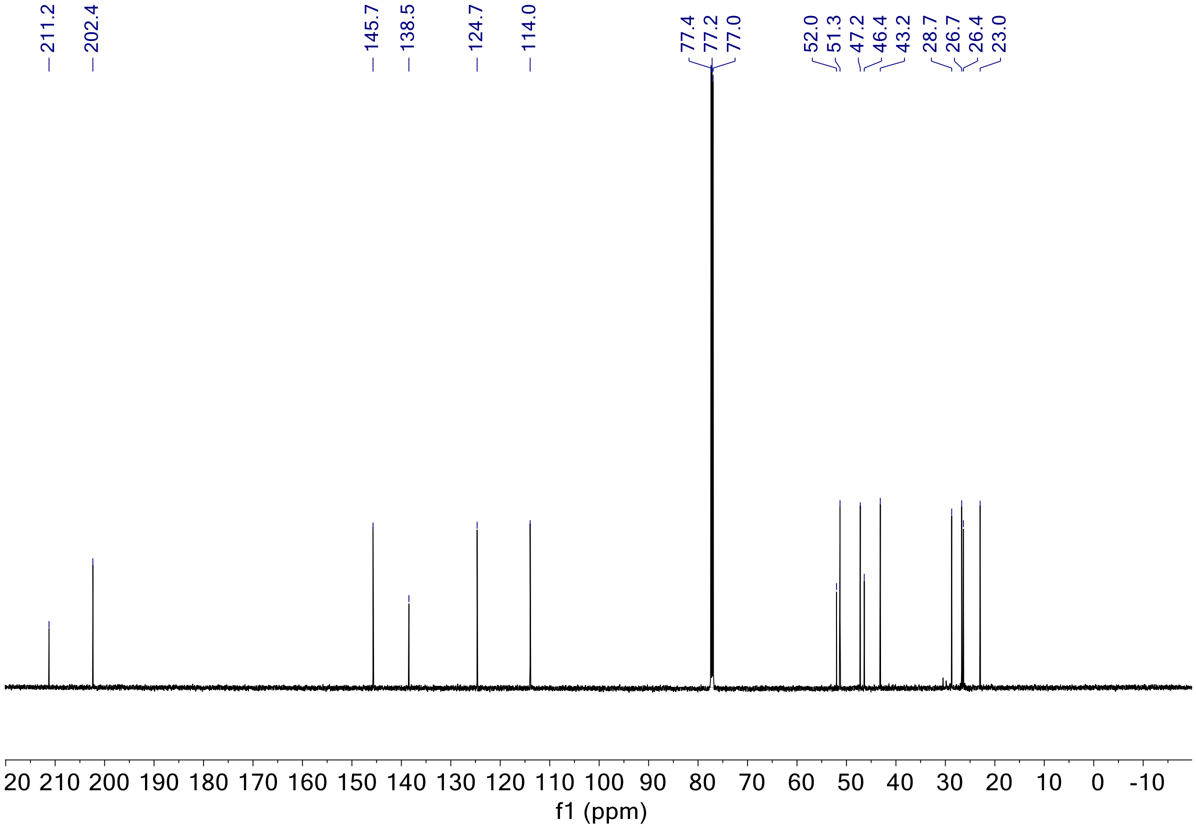
4.19 (^{13}C NMR, 151 MHz, CDCl$_3$)



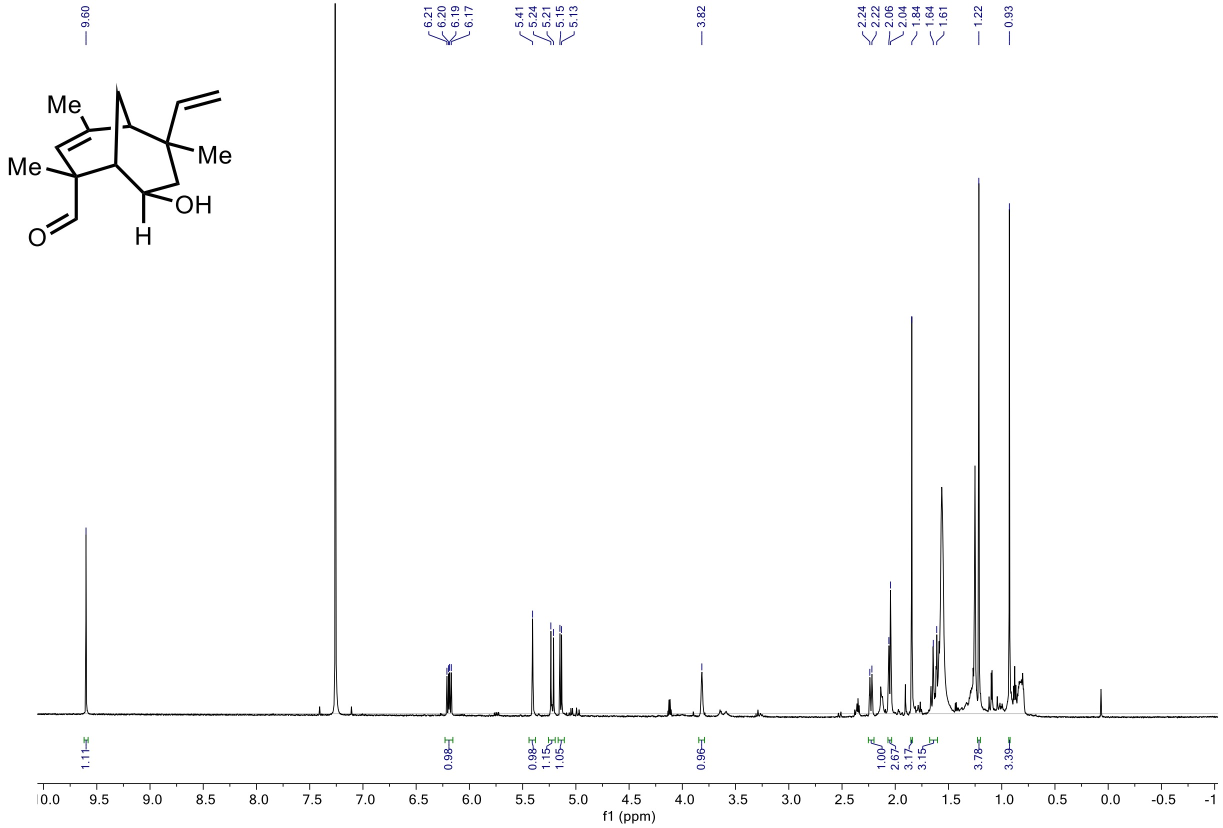
4.20 (^{1}H NMR, 600 MHz, CDCl$_3$)



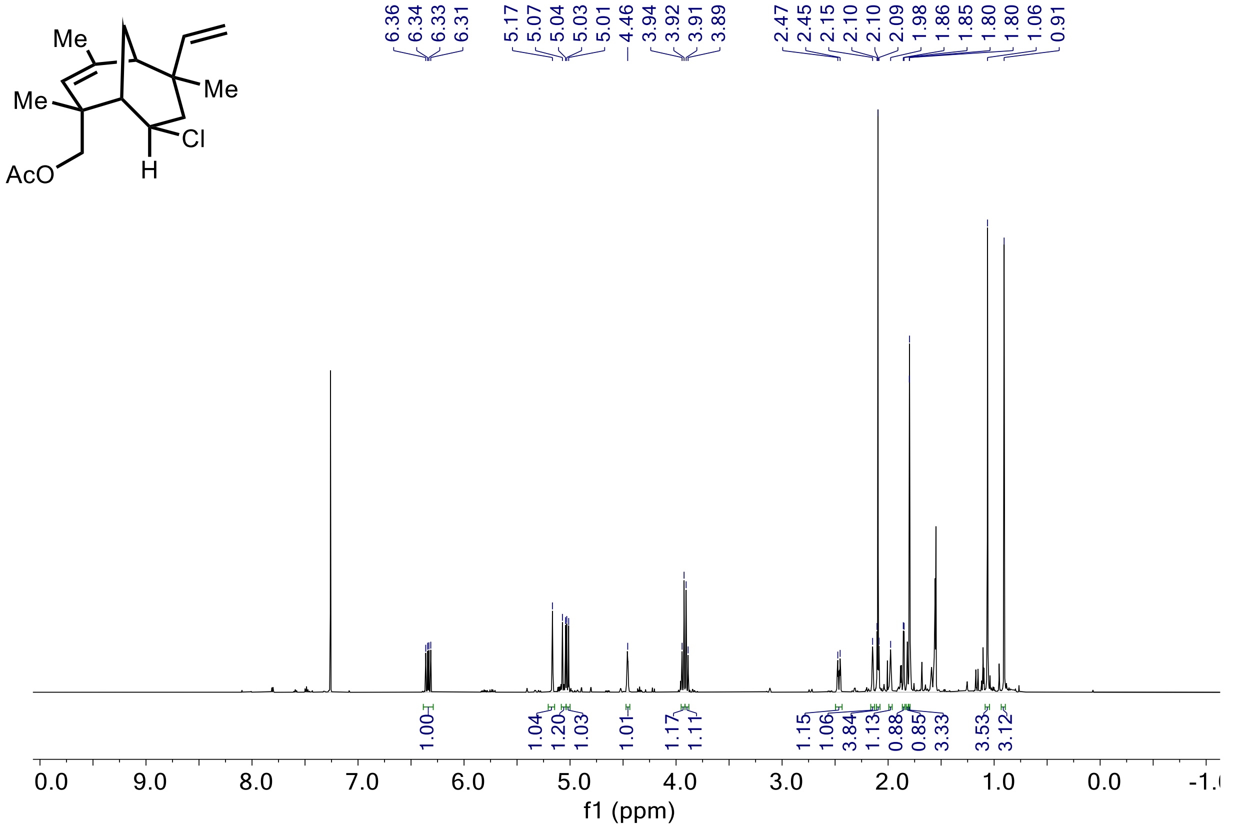
4.20 (^{13}C NMR, 151 MHz, CDCl$_3$)



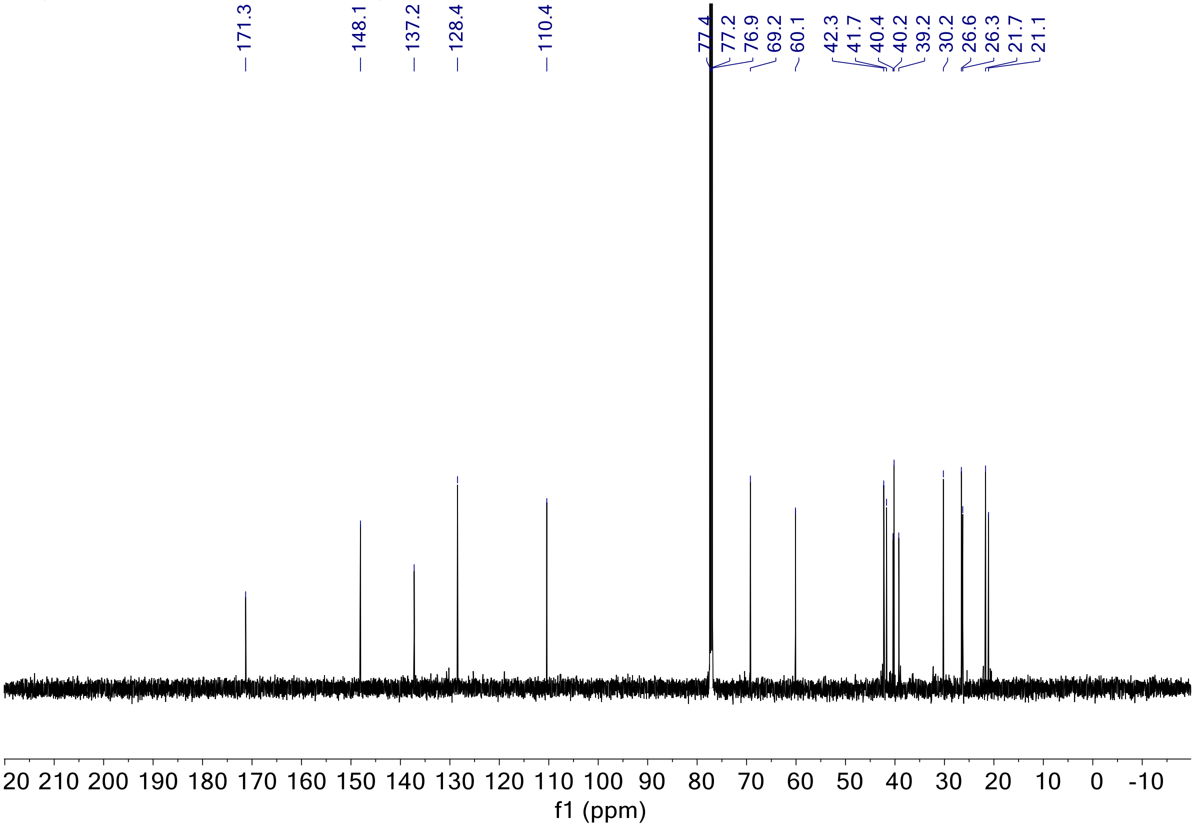
4.24 (^{1}H NMR, 700 MHz, CDCl$_3$)



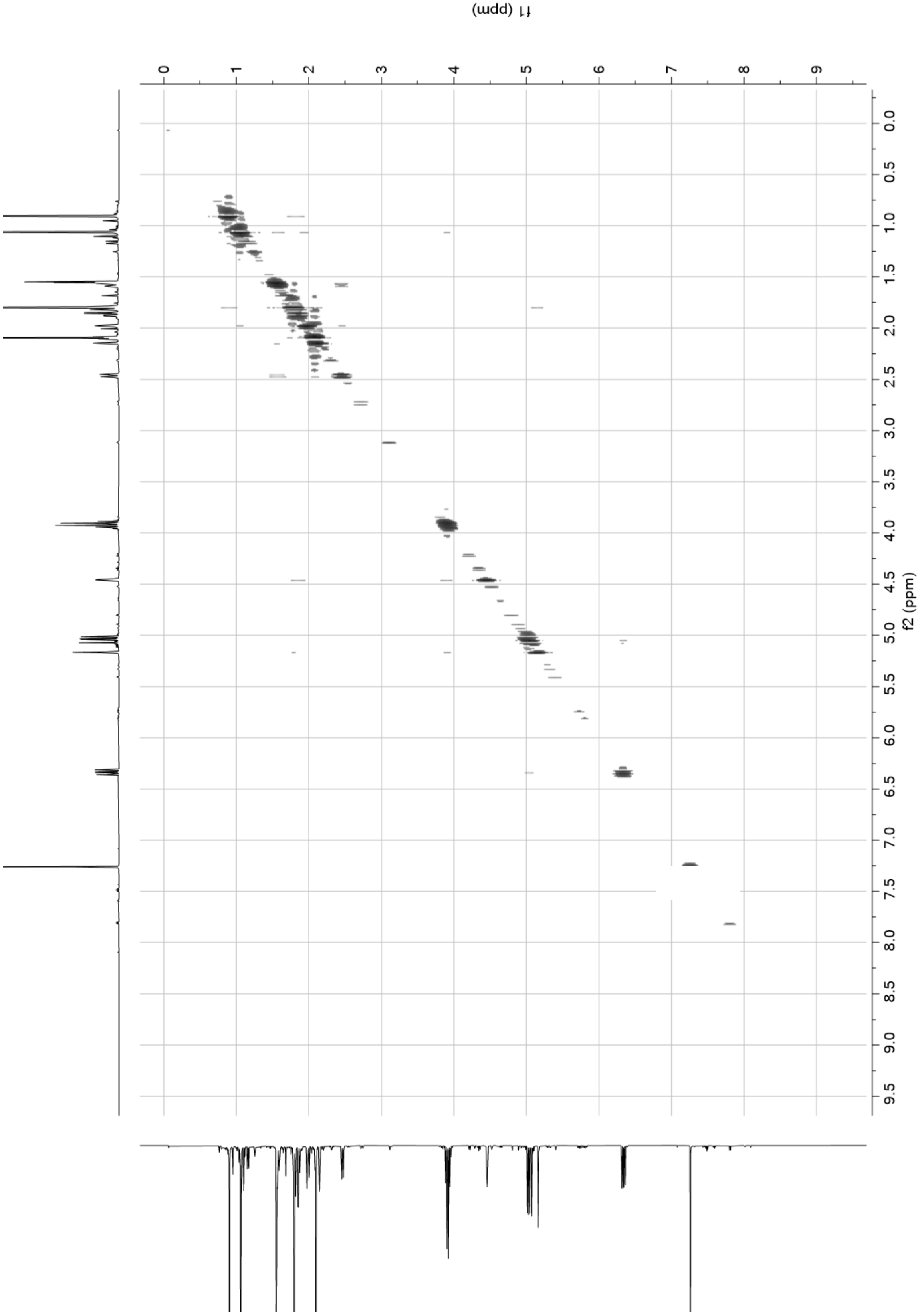
4.27 (^{1}H NMR, 600 MHz, CDCl$_3$)



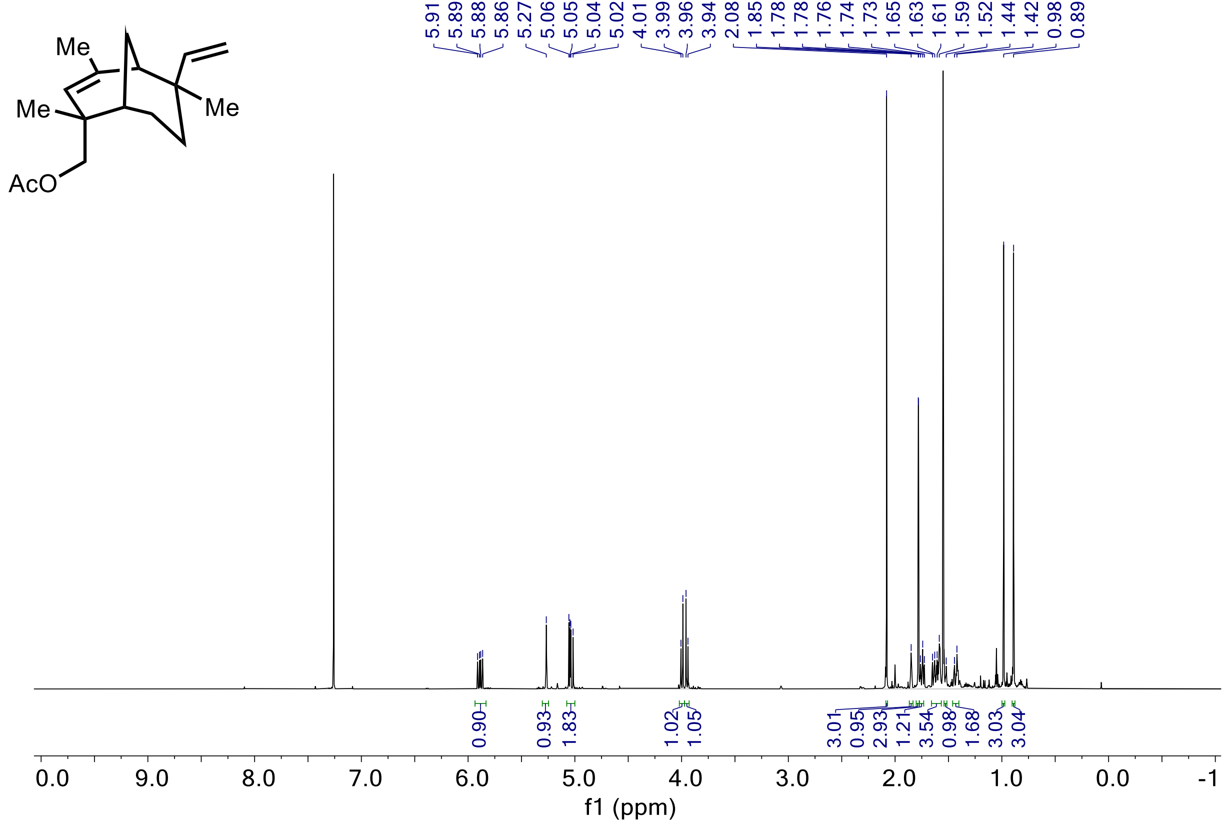
4.27 (^{13}C NMR, 151 MHz, CDCl$_3$)



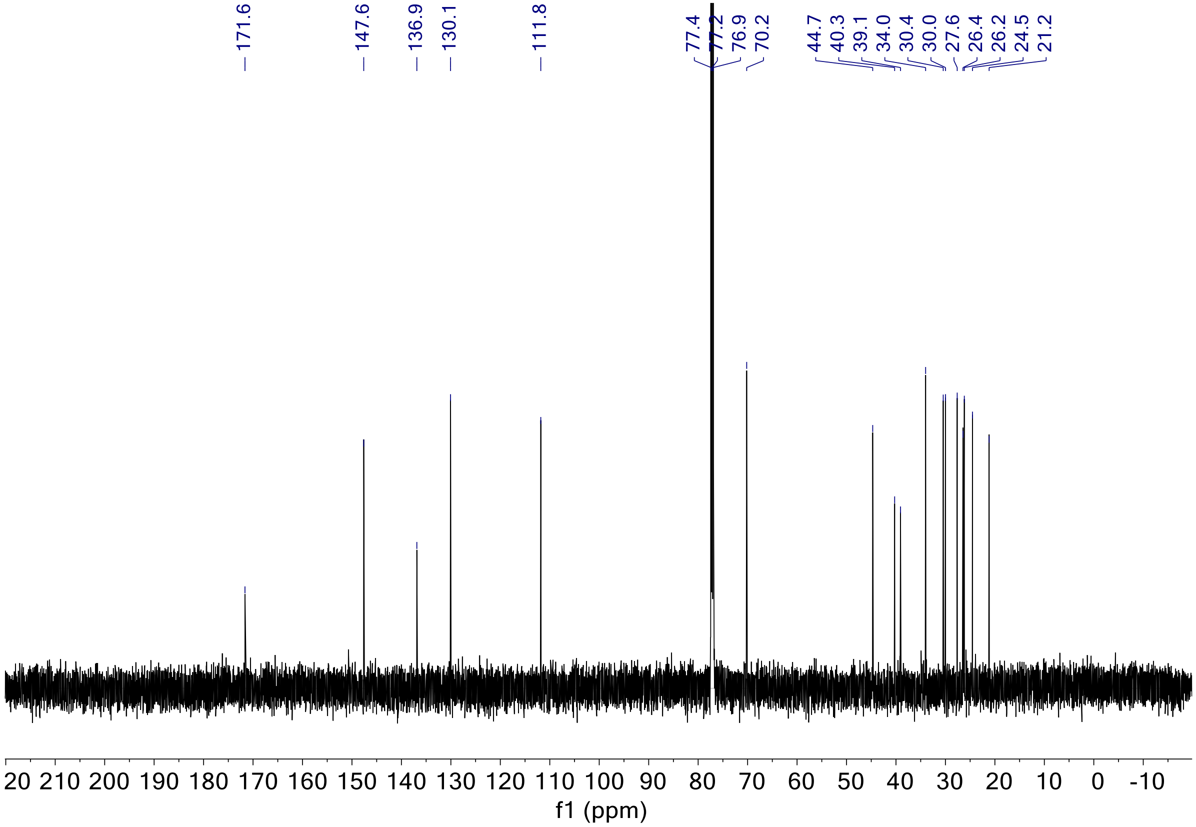
4.27 (NOESY, 600 MHz, $CDCl_3$)



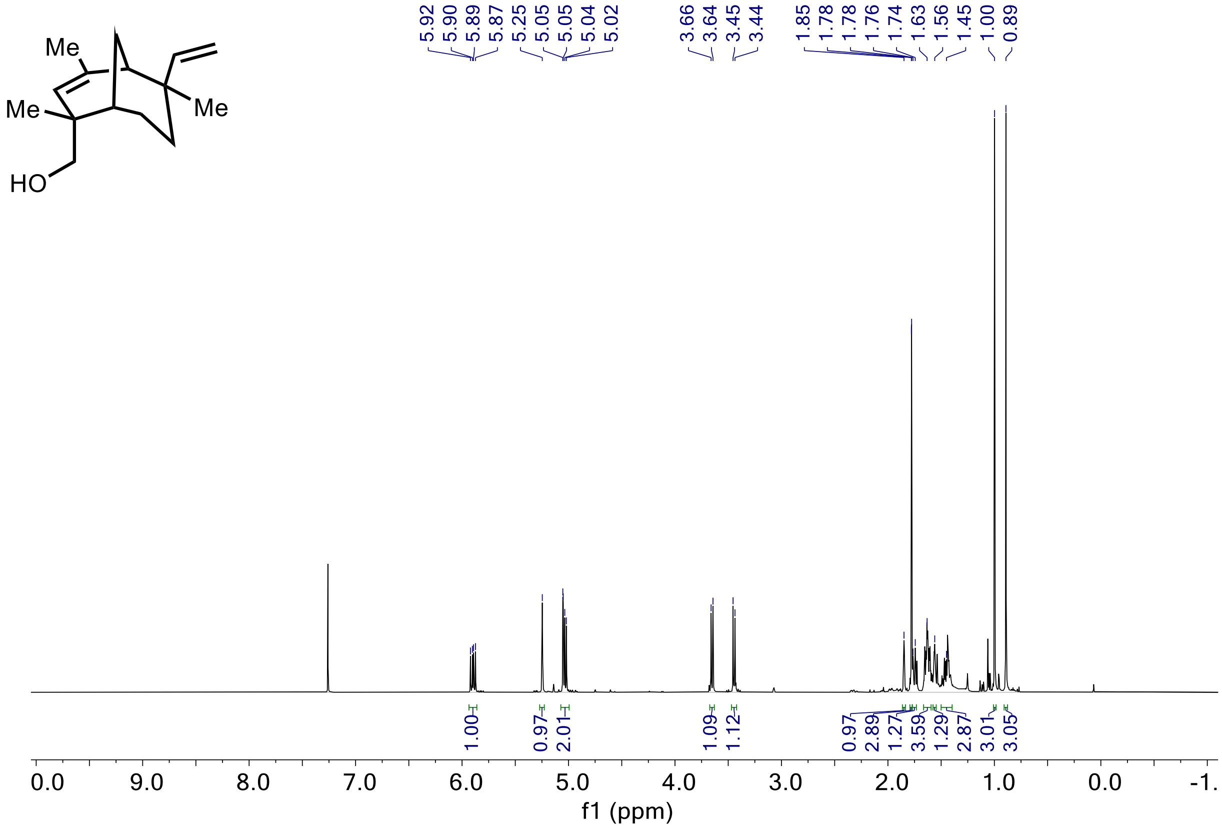
4.34 (^{1}H NMR, 600 MHz, CDCl$_3$)



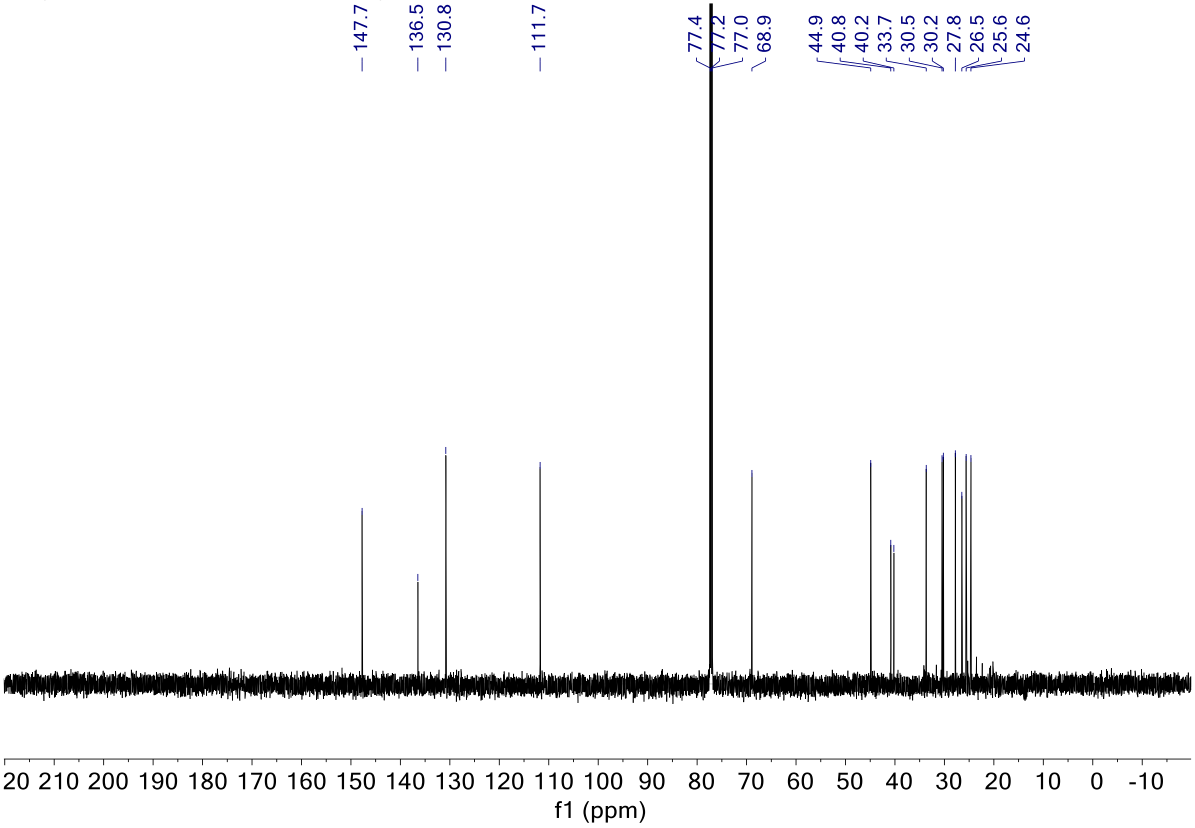
4.34 (^{13}C NMR, 151 MHz, CDCl$_3$)



4.16 (^{1}H NMR, 600 MHz, CDCl$_3$)



4.16 (^{13}C NMR, 151 MHz, CDCl$_3$)



4.8.3 Spectral Comparison of Previously Reported Compounds

Table 4.2 ^{1}H Comparison for 4.16

Sarpong, *J. Am. Chem. Soc.* **2018** (700 MHz, $CDCl_3$)	Our synthetic data (600 MHz, $CDCl_3$)	Δδ (ppm)
5.89 (dd, *J* = 17.7, 11.0 Hz, 1H)	5.90 (dd, *J* = 17.5, 11.0 Hz, 1H)	0.01
5.24 (p, J = 1.4 Hz, 1H)	5.25 (p, *J* = 1.4 Hz, 1H)	0.01
5.06 – 5.01 (m, 2H)	5.07 – 5.01 (m, 2H)	-
3.65 (d, J = 10.7 Hz, 1H)	3.65 (d, *J* = 10.6 Hz, 1H)	0
3.44 (d, J = 10.7 Hz, 1H)	3.45 (d, *J* = 10.6 Hz, 1H)	0.01
1.85 (t, J = 3.0 Hz, 1H)	1.85 (t, *J* = 3.0 Hz, 1H)	0
1.78 (d, J = 1.5 Hz, 3H)	1.78 (d, *J* = 1.4 Hz, 3H)	0
1.75 (dt, J = 12.5, 3.1 Hz, 1H)	1.75 (dt, *J* = 12.5, 2.9 Hz, 1H)	0
1.65 – 1.58 (m, 3H)	1.67 – 1.58 (m, 3H),	-
1.56 (q, J = 3.6 Hz, 1H)	1.56 (q, *J* = 3.4 Hz, 1H)	0
1.49 – 1.41 (m, 2H)	1.50 – 1.39 (m, 2H)	-
1.00 (s, 3H)	1.00 (s, 3H)	0
0.89 (s, 3H)	0.89 s, 3H)	0

Table 4.3 ^{13}C Comparison for 4.16

Sarpong, *J. Am. Chem. Soc.* **2018** (176 MHz, $CDCl_3$)	Our synthetic data (151 MHz, $CDCl_3$)	Δδ (ppm)
147.7	147.7	0
136.5	136.5	0
130.8	130.8	0
111.7	111.7	0
68.9	68.9	0
44.9	44.9	0
40.8	40.8	0
40.2	40.2	0
33.6	33.7	0.1
30.5	30.5	0
30.2	30.2	0
27.8	27.8	0
26.5	26.5	0
25.6	25.6	0
24.6	24.6	0

4.8.4 X-Ray Crystallographic Data for Chapter 4

X-Ray Analysis of 4.13

A colorless block 0.23 x 0.19 x 0.18 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 33.00 mm and exposure time was 0.50 seconds per frame using a scan width of 0.5°. Data collection was 100% complete to 74.000° in θ. A total of 20636 reflections were collected covering the indices -9<=h<=9, -14<=k<=14, -18<=l<=18. 2516 reflections were founded to be symmetry independent, with an R_{int} of 0.0294. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the CrysAlis^{Pro} 1.171.41.109a software program and scaled using the SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2015) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

[Note: The instruments are supported by an NIH Shared Instrument Grant S10-RR027172.]

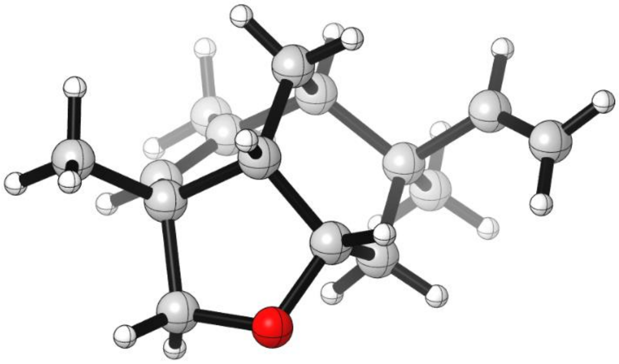


Figure 4.12 CYLview representation of **4.13**.

This crystal structure has been deposited at the Cambridge Crystallographic Data Center under CCDC 2108934.

Table 4.4 Crystal data and structure refinement for **4.13**.

Identification code	KJones03_Sarpong	
Empirical formula	C15 H22 O	
Formula weight	218.32	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.25200(10) Å	a= 90°.
	b = 11.7846(2) Å	b= 90°.
	c = 14.5051(2) Å	g = 90°.
Volume	1239.63(3) Å^3	
Z	4	
Density (calculated)	1.170 Mg/m^3	
Absorption coefficient	0.538 mm^{-1}	
F(000)	480	
Crystal size	0.290 x 0.230 x 0.180 mm^3	
Theta range for data collection	4.835 to 74.376°.	
Index ranges	-9<=h<=9, -14<=k<=14, -18<=l<=18	
Reflections collected	20636	
Independent reflections	2516 [R(int) = 0.0294]	
Completeness to theta = 74.000°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.65867	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2516 / 0 / 148	
Goodness-of-fit on F^2	1.056	
Final R indices [I>2sigma(I)]	R1 = 0.0290, wR2 = 0.0758	
R indices (all data)	R1 = 0.0291, wR2 = 0.0758	
Absolute structure parameter	0.04(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.248 and -0.170 e.Å^{-3}	

Table 4.5 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **4.13**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	7217(2)	6480(1)	5700(1)	23(1)
C(1)	5359(2)	6909(1)	5659(1)	21(1)
C(2)	4092(2)	6063(1)	6184(1)	17(1)

C(3)	2532(2)	5617(1)	5569(1)	23(1)
C(4)	3269(2)	6612(1)	7031(1)	17(1)
C(5)	3643(2)	6342(1)	7904(1)	16(1)
C(6)	2659(2)	6919(1)	8690(1)	22(1)
C(7)	4986(2)	5392(1)	8128(1)	16(1)
C(8)	4925(2)	4520(1)	7346(1)	16(1)
C(9)	5449(2)	5106(1)	6447(1)	16(1)
C(10)	7313(2)	5709(1)	6470(1)	18(1)
C(11)	7681(2)	6374(1)	7364(1)	17(1)
C(12)	7031(2)	5797(1)	8257(1)	17(1)
C(13)	7194(2)	6655(1)	9055(1)	23(1)
C(14)	8180(2)	4774(1)	8525(1)	20(1)
C(15)	9750(2)	4432(1)	8148(1)	23(1)

Table 4.6 Bond lengths [Å] and angles [°] for **4.13**.

O(1)-C(1)	1.4407(19)	C(3)-C(2)-C(1)	111.77(11)
O(1)-C(10)	1.4410(16)	C(9)-C(2)-C(1)	102.29(11)
C(1)-C(2)	1.5545(19)	C(5)-C(4)-C(2)	126.14(13)
C(2)-C(4)	1.5119(18)	C(4)-C(5)-C(6)	121.01(13)
C(2)-C(3)	1.534(2)	C(4)-C(5)-C(7)	120.60(12)
C(2)-C(9)	1.5448(19)	C(6)-C(5)-C(7)	118.28(12)
C(4)-C(5)	1.333(2)	C(5)-C(7)-C(8)	108.54(11)
C(5)-C(6)	1.5078(19)	C(5)-C(7)-C(12)	114.04(11)
C(5)-C(7)	1.5192(19)	C(8)-C(7)-C(12)	108.65(11)
C(7)-C(8)	1.5309(18)	C(9)-C(8)-C(7)	108.82(10)
C(7)-C(12)	1.5688(18)	C(8)-C(9)-C(10)	114.36(11)
C(8)-C(9)	1.5244(18)	C(8)-C(9)-C(2)	112.53(12)
C(9)-C(10)	1.5278(19)	C(10)-C(9)-C(2)	103.25(11)
C(10)-C(11)	1.5380(18)	O(1)-C(10)-C(9)	103.51(11)
C(11)-C(12)	1.5370(18)	O(1)-C(10)-C(11)	109.91(11)
C(12)-C(14)	1.517(2)	C(9)-C(10)-C(11)	114.17(11)
C(12)-C(13)	1.5416(18)	C(12)-C(11)-C(10)	115.59(11)
C(14)-C(15)	1.326(2)	C(14)-C(12)-C(11)	113.53(12)
C(1)-O(1)-C(10)	107.36(10)	C(14)-C(12)-C(13)	106.65(11)
O(1)-C(1)-C(2)	107.91(11)	C(11)-C(12)-C(13)	108.64(11)
C(4)-C(2)-C(3)	109.15(12)	C(14)-C(12)-C(7)	107.94(11)
C(4)-C(2)-C(9)	111.30(11)	C(11)-C(12)-C(7)	108.91(11)
C(3)-C(2)-C(9)	111.35(11)	C(13)-C(12)-C(7)	111.19(11)
C(4)-C(2)-C(1)	110.87(11)	C(15)-C(14)-C(12)	127.42(14)

Symmetry transformations used to generate equivalent atoms:

Table 4.7 Anisotropic displacement parameters (Å^{2}x 10^3)for **4.13**. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	24(1)	28(1)	18(1)	5(1)	4(1)	-1(1)
C(1)	26(1)	20(1)	18(1)	3(1)	1(1)	0(1)
C(2)	20(1)	15(1)	16(1)	1(1)	-1(1)	0(1)
C(3)	24(1)	23(1)	22(1)	-1(1)	-6(1)	1(1)
C(4)	16(1)	13(1)	22(1)	-1(1)	1(1)	1(1)
C(5)	16(1)	13(1)	20(1)	-2(1)	2(1)	-2(1)
C(6)	21(1)	21(1)	23(1)	-5(1)	5(1)	1(1)
C(7)	18(1)	15(1)	14(1)	0(1)	2(1)	-2(1)
C(8)	17(1)	12(1)	18(1)	0(1)	0(1)	0(1)
C(9)	19(1)	14(1)	15(1)	-2(1)	0(1)	1(1)
C(10)	19(1)	19(1)	16(1)	1(1)	2(1)	1(1)
C(11)	17(1)	16(1)	19(1)	0(1)	1(1)	-2(1)
C(12)	18(1)	17(1)	16(1)	-2(1)	-1(1)	-1(1)
C(13)	22(1)	26(1)	20(1)	-7(1)	-1(1)	-2(1)
C(14)	21(1)	21(1)	18(1)	2(1)	-3(1)	-2(1)
C(15)	21(1)	21(1)	26(1)	0(1)	-3(1)	1(1)

Table 4.8 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **4.13**.

	x	y	z	U(eq)
H(1A)	4956	6977	5009	26
H(1B)	5294	7668	5949	26
H(3A)	3042	5369	4976	34
H(3B)	1630	6223	5464	34
H(3C)	1926	4975	5873	34
H(4)	2404	7205	6932	20
H(6A)	1889	6365	9015	33
H(6B)	1880	7530	8449	33
H(6C)	3568	7237	9118	33
H(7)	4574	5015	8710	19
H(8A)	5798	3894	7476	19
H(8B)	3670	4195	7296	19
H(9)	5465	4528	5941	20
H(10)	8325	5147	6366	22

H(11A)	9024	6514	7412	21
H(11B)	7067	7122	7315	21
H(13A)	6676	6322	9617	34
H(13B)	6513	7347	8898	34
H(13C)	8495	6841	9156	34
H(14)	7723	4327	9020	24
H(15A)	10273	4845	7650	27
H(15B)	10352	3772	8375	27

Table 4.9 Torsion angles [°] for **4.13**.

C(10)-O(1)-C(1)-C(2)	-21.22(14)
O(1)-C(1)-C(2)-C(4)	115.04(12)
O(1)-C(1)-C(2)-C(3)	-122.93(12)
O(1)-C(1)-C(2)-C(9)	-3.71(14)
C(3)-C(2)-C(4)-C(5)	124.07(16)
C(9)-C(2)-C(4)-C(5)	0.8(2)
C(1)-C(2)-C(4)-C(5)	-112.38(16)
C(2)-C(4)-C(5)-C(6)	-177.07(13)
C(2)-C(4)-C(5)-C(7)	-1.0(2)
C(4)-C(5)-C(7)-C(8)	-29.40(18)
C(6)-C(5)-C(7)-C(8)	146.80(12)
C(4)-C(5)-C(7)-C(12)	91.86(16)
C(6)-C(5)-C(7)-C(12)	-91.93(15)
C(5)-C(7)-C(8)-C(9)	59.20(14)
C(12)-C(7)-C(8)-C(9)	-65.32(14)
C(7)-C(8)-C(9)-C(10)	55.55(15)
C(7)-C(8)-C(9)-C(2)	-61.84(14)
C(4)-C(2)-C(9)-C(8)	30.73(16)
C(3)-C(2)-C(9)-C(8)	-91.30(14)
C(1)-C(2)-C(9)-C(8)	149.18(11)
C(4)-C(2)-C(9)-C(10)	-93.07(13)
C(3)-C(2)-C(9)-C(10)	144.90(11)
C(1)-C(2)-C(9)-C(10)	25.38(13)
C(1)-O(1)-C(10)-C(9)	37.64(13)
C(1)-O(1)-C(10)-C(11)	-84.69(13)
C(8)-C(9)-C(10)-O(1)	-161.56(11)
C(2)-C(9)-C(10)-O(1)	-38.96(13)
C(8)-C(9)-C(10)-C(11)	-42.11(16)
C(2)-C(9)-C(10)-C(11)	80.49(13)
O(1)-C(10)-C(11)-C(12)	155.20(12)
C(9)-C(10)-C(11)-C(12)	39.42(17)
C(10)-C(11)-C(12)-C(14)	71.26(15)
C(10)-C(11)-C(12)-C(13)	-170.28(12)
C(10)-C(11)-C(12)-C(7)	-49.03(15)
C(5)-C(7)-C(12)-C(14)	177.04(11)
C(8)-C(7)-C(12)-C(14)	-61.75(13)
C(5)-C(7)-C(12)-C(11)	-59.28(14)
C(8)-C(7)-C(12)-C(11)	61.92(13)
C(5)-C(7)-C(12)-C(13)	60.40(15)
C(8)-C(7)-C(12)-C(13)	-178.40(11)
C(11)-C(12)-C(14)-C(15)	8.9(2)
C(13)-C(12)-C(14)-C(15)	-110.74(16)
C(7)-C(12)-C(14)-C(15)	129.69(15)

Symmetry transformations used to generate equivalent atoms:

4.9 References for Chapter 4

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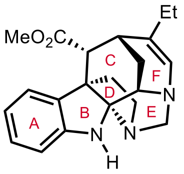
Chapter 5

Oxidative Coupling Approach to Scholarinine A and Pleiocarpamine

5.1 Scholarinine A Isolation, Bioactivity, and Biosynthesis

Scholarinine A (**5.1**), the initial target of this project, was isolated in 2020 by Zhan and coworkers from the branches and leaves of the evergreen tropical tree, *Alstonia scholaris*.[1] This akuammiline alkaloid features a unique 6/5/6/5/5/6 carbocyclic framework with an unprecedented imidazolidine ring (see ring E in **5.1**, Figure 5.1). Furthermore, scholarinine A (**5.1**) contains three nitrogens, which is a rare feature in monoterpene indole alkaloids. This natural product was reported to inhibit T-type $Ca_v3.1$ calcium channels with an IC_{50} of 4.28 µM through allosteric binding to the channel.



scholarinine A (**5.1**)

Figure 5.1 Structure of scholarinine A (**5.1**).

Calcium ion channels are underexploited targets for insecticide development, as such, we pursued the synthesis of scholarinine A (**5.1**) in collaboration with Corteva AgriScience. Currently, most insecticides target voltage-gated sodium channels, GABA receptors, or acetylcholinesterase.[2] Contrary to these established modes of action (MoA), calcium channels have been identified as an underexplored target that could potentially provide a novel MoA.[3] Numerous polypeptides from arachnid venoms selectively inhibit insect calcium channels and have led to insect mortality, demonstrating the potential of this MoA.[2,4] Beyond agrochemical development, the synthesis of scholarinine A (**5.1**) and its derivatives could provide a platform for studying the therapeutic potential of these compounds for various human diseases associated with the inhibition of T-type $Ca_v3.1$ calcium channels, such as absence seizures.[5]

Biosynthetically, monoterpene indole alkaloids are a large, diverse family of natural products that arise from strictosidine (**5.2**).[6] From strictosidine (**5.2**), deglucosylation unveils an aldehyde which can undergo intramolecular condensation to afford geissoschizine (**5.3**), which features a *corynanthe* skeleton (Figure 5.2). Geissoschizine (**5.3**) can undergo various oxidative cyclizations to yield different natural product families. For example, **5.3** can be cyclized to form the *excelsinidine* scaffold (**5.4**) by creating an N4–C16 bond, the *mavacuran* alkaloids (such as pleiocarpamine, **5.5**) by creating an N1–C16 bond, or the *akuammilan* scaffold (such as strictamine, **5.6**) by creating a C7–C16 bond. After the core scaffolds are built, many rearrangements and redox manipulations give rise to the immense structural diversity that exists in the monoterpene indole alkaloids.

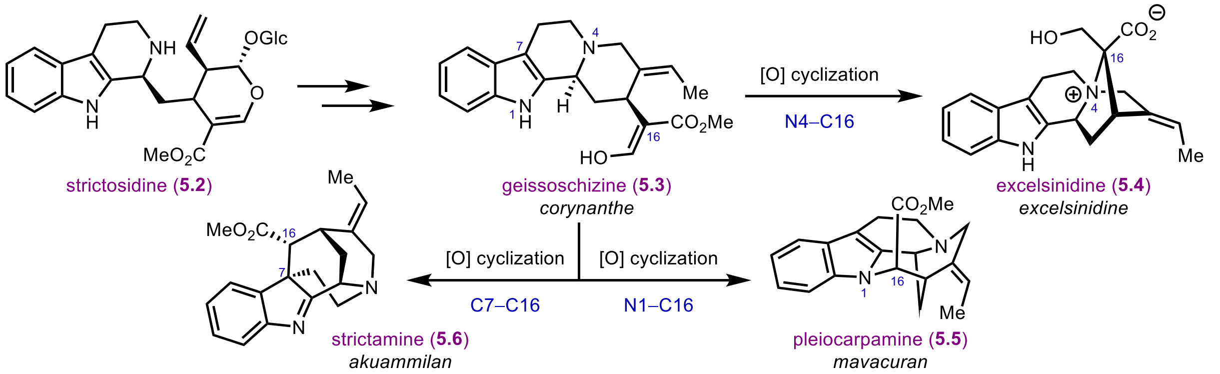


Figure 5.2 Biosynthesis of various monoterpene indole alkaloid families through oxidative cyclization.

Zhan and coworkers propose that scholarinine A (**5.1**) biosynthetically arises from picrinine (**5.7**), an abundant natural product that is produced by the same organism.[1] From picrinine (**5.7**), an oxidative ring opening would furnish α,β-unsaturated imine **5.8** (Figure 5.3). Reduction of the α,β-unsaturated imine would give enamine **5.9**. The aldehyde in enamine **5.9** would subsequently undergo reductive amination to form a primary amine, which could cyclize to afford pentacyclic intermediate **5.10**. Finally, aminal formation between triamine **5.10** and formaldehyde is proposed to forge the imidazolidine ring to deliver scholarinine A (**5.1**).

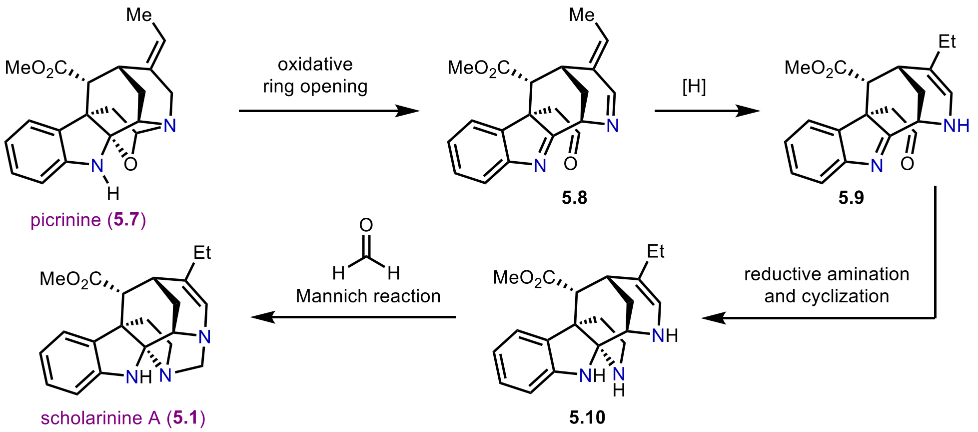


Figure 5.3 Zhan and coworkers' proposed biosynthesis of scholarinine A (**5.1**).

Alternatively, Lim and coworkers propose a biosynthesis of alstobrogaline (**5.11**), which is structurally related to and may inform the biosynthesis of scholarinine A (**5.1**).[7] They suggest oxidation of an akuammiline-type precursor, such as strictamine (**5.6**) would form iminium ion **5.12** and that upon hydrolysis could afford aldehyde **5.13** (Figure 5.4). Transamination to amine **5.14** and cyclization would give rise to pyrroloindoline **5.15**. Oxidation of **5.15** would afford alstrobrogaline (**5.11**). Aminal formation from the same intermediate (**5.15,** analogous to what is shown in Figure 5.3) and isomerization of the exocyclic olefin could afford scholarinine A (**5.1**).

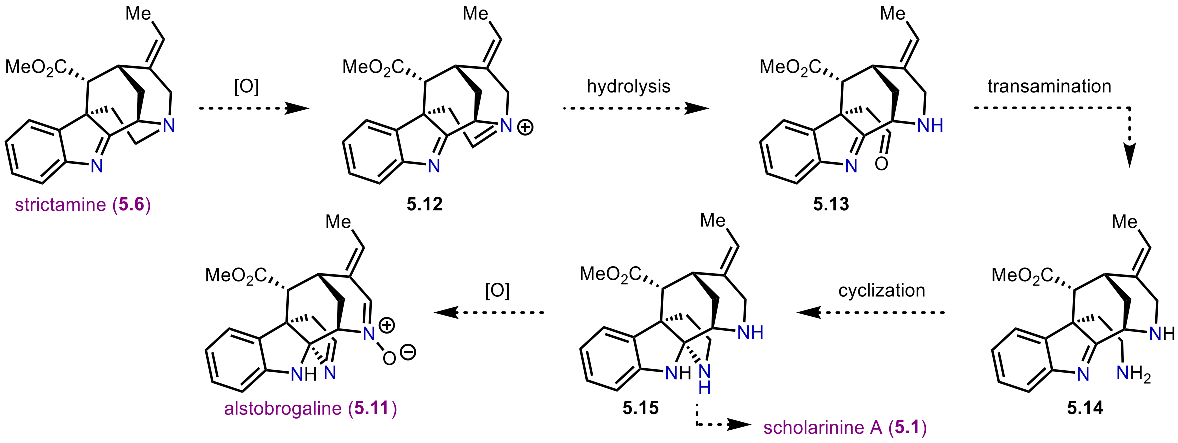


Figure 5.4 Lim and coworkers' proposed biosynthesis of alstobrogaline (**5.11**).

5.2 Previous Syntheses of Related Natural Products

Scholarinine A (**5.1**) has not been synthesized to date. Therefore, the syntheses of structurally related natural products are discussed. Due to the large number of compounds in the akuammiline alkaloid family, it is not feasible to provide a comprehensive review of the syntheses of all structurally related natural products in this context. Additionally, most of the natural products that closely resemble scholarinine A (**5.1**), shown in Figure 5.5, have not yet been synthesized. As such, the syntheses highlighted here cover a range of approaches to structurally-related aspidophylline A (**5.17**).

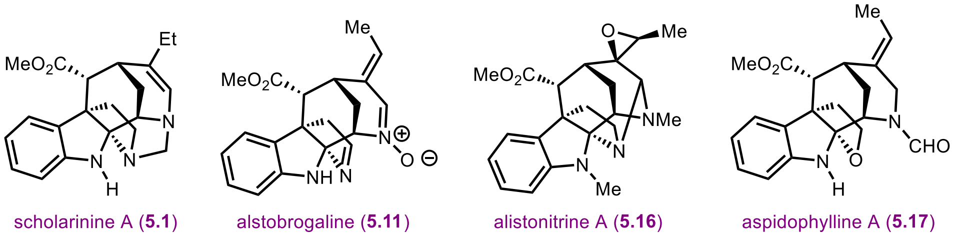


Figure 5.5 Scholarinine A (**5.1**) and structurally-related natural products alistonitrine A (**5.16**), alstogrogaline (**5.11**), and aspidophylline A (**5.17**).

5.2.1 Garg's Synthesis of Aspidophylline A

In 2011, Garg and coworkers reported the first total synthesis of the akuammiline alkaloid aspidophylline A (**5.17**) which featured a key interrupted Fischer indolization (Figure 5.6).[8] Pyridinone **5.18** was elaborated to vinyl iodide **5.19** in seven steps. Heck cyclization of vinyl iodide **5.19** onto the endocyclic α,β-unsaturated ester afforded [3.3.1]bicycle **5.20** in excellent yield. Another series of functional group manipulations built the δ-lactone of **5.21**, which was poised to undergo the key indole formation. Upon treatment of ketone **5.21** with phenylhydrazine, condensation, and partial Fischer indole synthesis, imine **5.22** was formed. Methanolysis of the lactone of **5.22** forged furanoindoline **5.23**. Subsequent reductive cleavage of the tosyl group and formylation of the resulting secondary amine gave aspidophylline A (**5.17**). In 2016, Garg and coworkers reported a similar enantiospecific route to this natural product.[9]

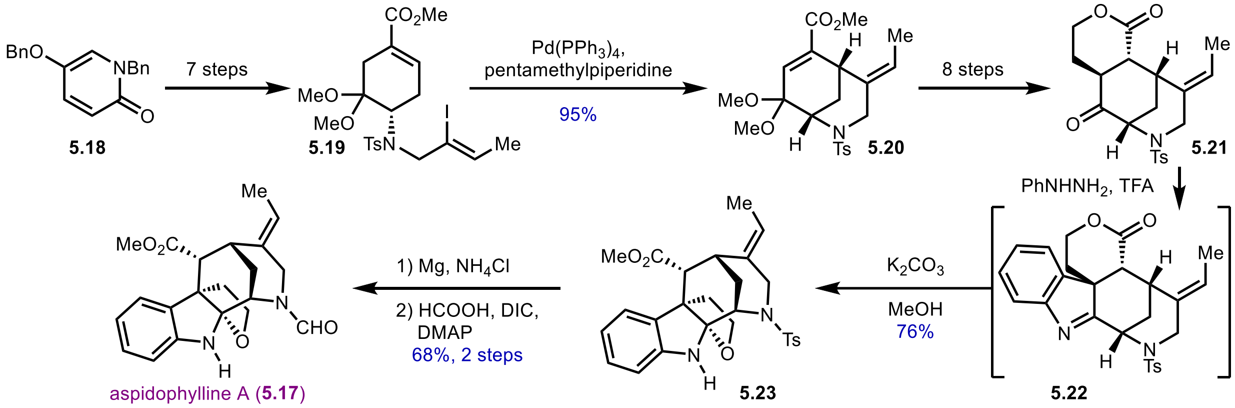


Figure 5.6 Garg and coworkers' 2011 synthesis of aspidophylline A (**5.17**).

5.2.2 Zhu's Synthesis of Aspidophylline A

In 2014, Zhu and coworkers reported their synthesis of aspidophylline A (**5.17**) which constructed the essential furanoindoline core first then created the [3.3.1]bicycle in a subsequent step (Figure 5.7).[10] At the outset of the Zhu synthesis, readily accessible nitroarene **5.24** was elaborated to indoline **5.25**. Oxidative cleavage of the pendant allyl group and reduction set the stage for spontaneous cyclization to afford furanoindoline **5.26**. Alkoxycarbonylation of the resulting vinyl triflate gave α,β-unsaturated ester **5.27**. Reduction of the azide and alkylation with allyl bromide **5.28** gave vinyl iodide **5.29**. Formation of a vinyl lithium nucleophile led to Michael addition to forge the [3.3.1]bicycle featured in aspidophylline A (**5.17**). Final protecting group manipulations gave rise to the natural product.

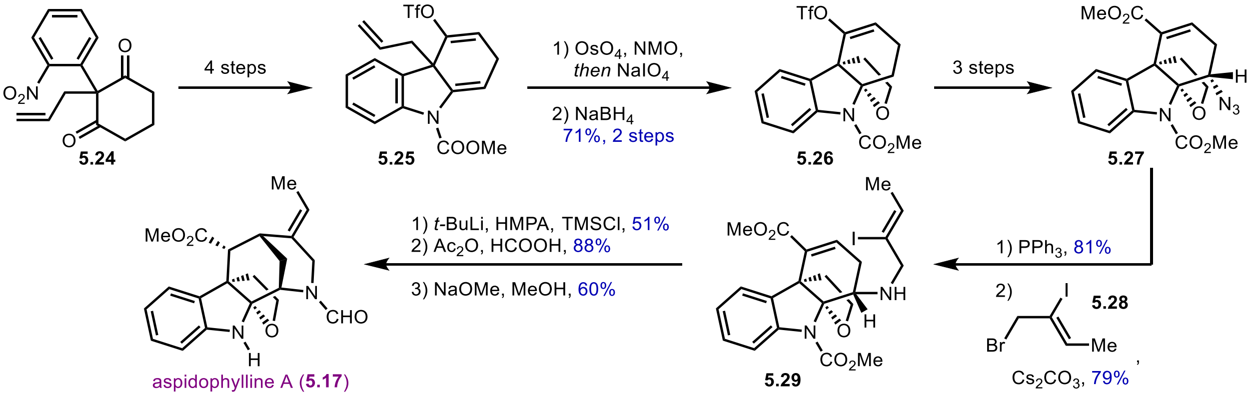


Figure 5.7 Zhu and coworkers' synthesis of aspidophylline A (**5.17**).

5.3 Oxidative Coupling Investigations of Related Natural Products

Oxidative couplings are powerful reactions that allow for two-fragment coupling without requiring pre-functionalization. In 2004, Baran and coworkers reported an intermolecular oxidative coupling between indole (**5.30**) and carvone (**5.31**) mediated by lithium bis(trimethylsilyl)amide (LHMDS) and copper(II)2-ethylhexanoate to afford adduct **5.32** (Figure 5.8).[11] Mechanistically, this transformation is proposed to proceed through deprotonation of both the α-position of carvone (**5.31**) and the indole nitrogen to yield anions **5.33** and **5.34**, respectively.[12] Oxidation of enolate **5.33** is believed to deliver copper-coordinated radical intermediate **5.35**, which could undergo cyclization onto the pendant indole to give α-amino radical **5.36**. Subsequent oxidation and aromatization afforded the C3-alkylated indole **5.32**.

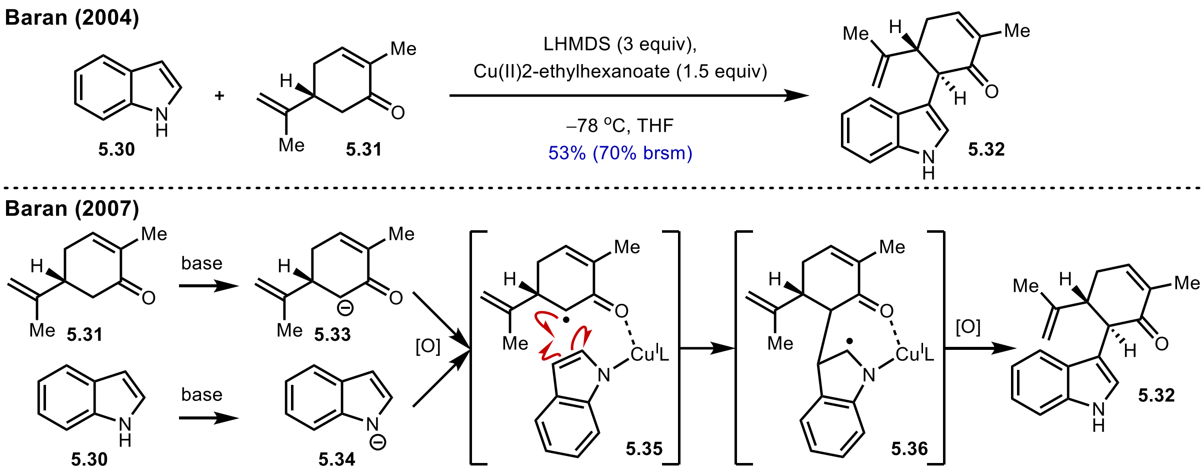


Figure 5.8 Oxidative coupling of indole (**5.31**) and carvone (**5.30**) as reported by Baran and coworkers.

There are numerous examples in the literature of oxidative coupling approaches to complex alkaloid natural products. As such, this is by no means an exhaustive survey of these approaches but, instead, a discussion of several illustrative examples that help frame our approach.

5.3.1 Ma's Synthesis of (–)-Vincorine

In 2012, Ma and coworkers reported an enantioselective synthesis of the akuammiline alkaloid vincorine (**5.37**), which featured an intramolecular oxidative coupling (Figure 5.9).[13] Starting from 5-methoxytryptamine (**5.38**), the vinylidene malonate sidechain of **5.39** was installed in six steps. In six subsequent steps, the vinylidene malonate sidechain of **5.39** was elongated to form malonate **5.40**. At this stage, an intramolecular oxidative coupling was carried out to forge the C–C bond between the positions highlighted in blue and cyclize the tryptamine sidechain to forge pyrroloindoline **5.41**. Krapcho mono-decarboxylation of the geminal methyl diester motifs followed by chlorination of the allylic silyl ether afforded allylic chloride **5.42**.

Deprotection of the secondary amine, followed by alkylative cyclization, and reductive amination of the benzylic amine afforded vincorine (**5.37**) in 18 steps from 5-methoxytryptamine (**5.38**).

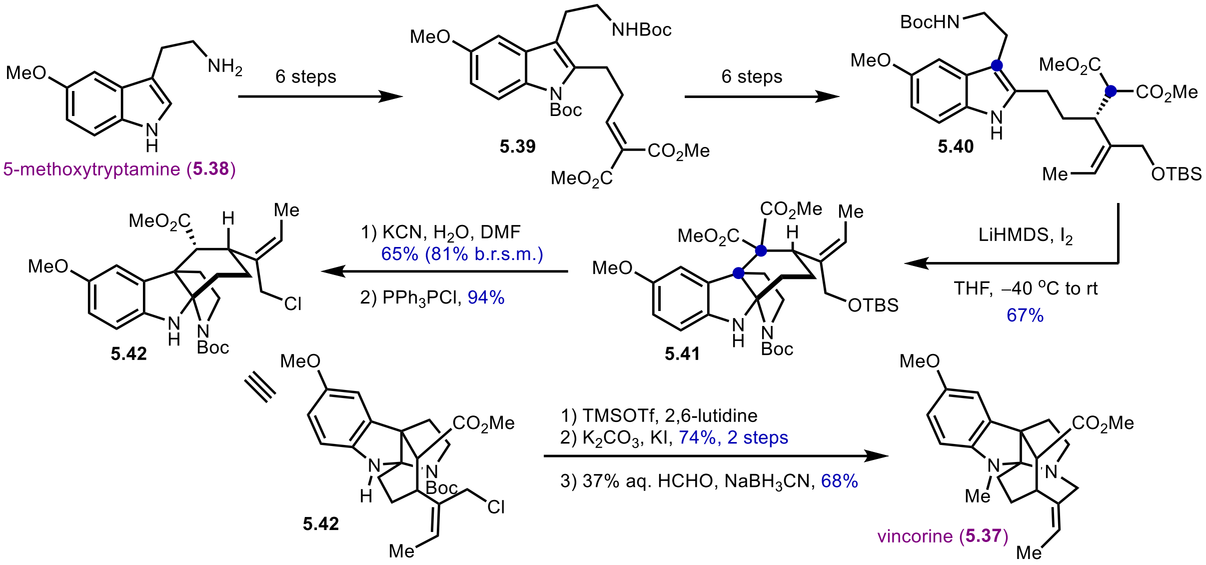


Figure 5.9 Ma and coworkers' synthesis of (–)-vincorine (**5.37**).

5.3.2 Ma's Synthesis of Aspidophylline A

Ma and coworkers continued their interest in intramolecular oxidative coupling strategies in their 2014 synthesis of aspidophylline A (**5.17**), another akuammiline alkaloid.[14] This synthesis draws from their synthesis of vincorine (**5.37**, Figure 5.9) in terms of constructing the furanoindoline, but differs in late stage steps. Their synthesis begins from bis-protected tryptophol **5.43**. Alkylation of the indole C2 position, reductive cleavage of the tosyl group, and azidation afforded azide **5.45** in high yield. Azide **5.45** was subsequently subjected to oxidative coupling conditions, but undesired tricycle **5.46** formed rather than the desired furanoindoline **5.47**. Tricycle **5.46** is formed by competitive oxidative coupling between the malonate and the indole nitrogen rather than the indole C3 position. Ma and coworkers found that cleavage of the silyl ether gave primary alcohol **5.48** that underwent oxidative coupling between the desired positions to afford furanoindoline **5.47** as a mixture of diastereomers. This change in reactivity is proposed to be a result of the additional site of coordination the *in situ* generated alkoxide of alcohol **5.48** provides to enforce the conformation that leads to C–C bond formation. From furanoindoline **5.47**, a series of steps enabled the installation of the remaining carbons and led to vinyl iodide **5.49**. From vinyl iodide **5.49**, the piperidine ring of the natural product was forged by a nickel-mediated cyclization. Finally, deprotection of the benzylic amine afforded aspidophylline A (**5.17**) in 15 steps from commercially available materials.

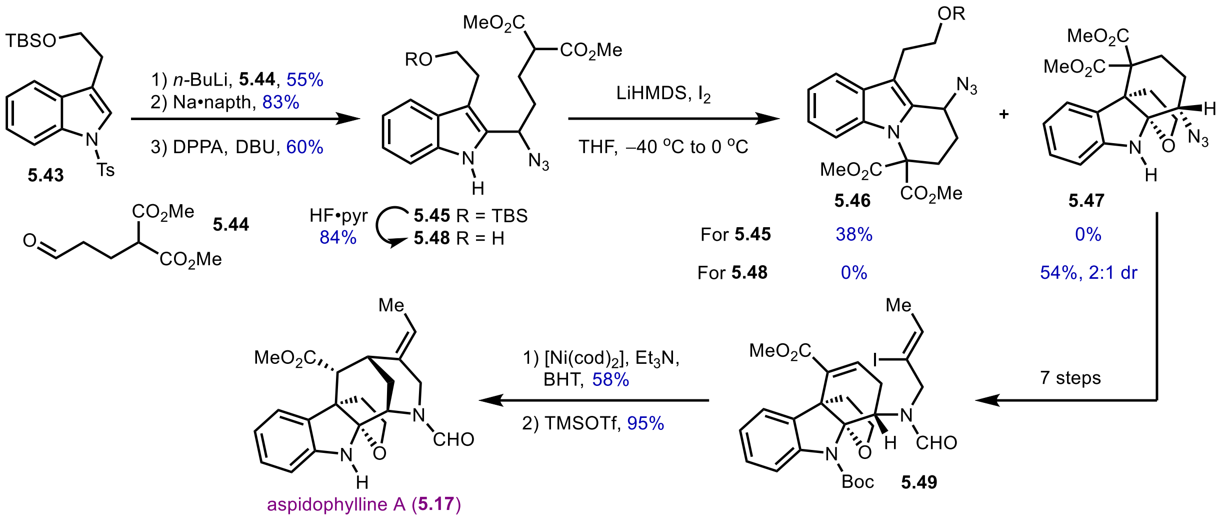


Figure 5.10 Ma and coworkers' synthesis of aspidophylline A (**5.17**).

5.4 Retrosynthesis

In developing our route to scholarinine A (**5.1**), we aspired to incorporate opportunities for divergence that would allow our collaborators at Corteva AgriSciences to probe the bioactivity of the natural product as well as structurally similar compounds through a small SAR campaign. We also saw an opportunity to highlight methodology previously developed within our group. With both these goals in mind, we developed a retrosynthesis that highlighted a key oxidative coupling cascade to forge the carbocyclic framework of the natural product.

From scholarinine A (**5.1**), we envisioned initial excision of the E ring to give enamine **5.10**. This intermediate (**5.10**) could be accessed from pentacycle **5.50** through late stage piperidine functionalization in the forward sense. The core pentacyclic pyrroloindoline scaffold could be constructed by intramolecular oxidative coupling of C2-piperidinyl indole **5.51**, which could arise from known compounds, α-hydroxy-β-lactam **5.52** and bromotryptamine **5.53**.

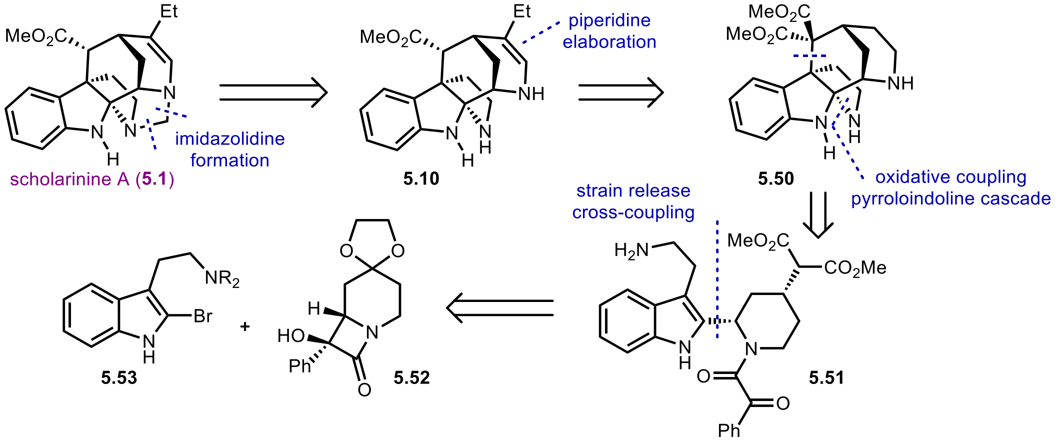


Figure 5.11 Our initial retrosynthesis of scholarinine A (**5.1**).

5.5 Initial α-Hydroxy β-Lactam Cross Coupling Approach

At the outset of our synthesis of scholarinine A (**5.1**), we sought to form piperidinyl indole **5.51** through a strain-release cross-coupling reported by Sarpong and coworkers.[15] In the initial report of this transformation, α-hydroxy-β-lactam **5.54** and an aryl bromide couple to form α-aryl piperidine **5.55** in high yield (Figure 5.12.A). The transformation is proposed to begin with oxidative addition of a ligated Pd(0) to the aryl bromide (Figure 5.12.B). The resulting Pd(II) intermediate undergoes a ligand exchange with α-hydroxy-β-lactam **5.54** to give alkoxy palladium species **5.56**. At this point, β-carbon elimination can occur to cleave either the proximal bond (highlighted in purple) or the distal bond (highlighted in red) to give either α-palladated intermediate **5.57** or α-aroylated intermediate **5.58**, respectively. From these intermediates, reductive elimination presumably turns over the catalyst and gives either α-arylated piperidine **5.55** or α-aroylated piperidine **5.59**. The selectivity of the β-carbon elimination, and thus selectivity of the products, can be biased by the ligand employed in the reaction, with RuPhos giving the proximal cleavage product (**5.55**) with the best selectivity and yield.

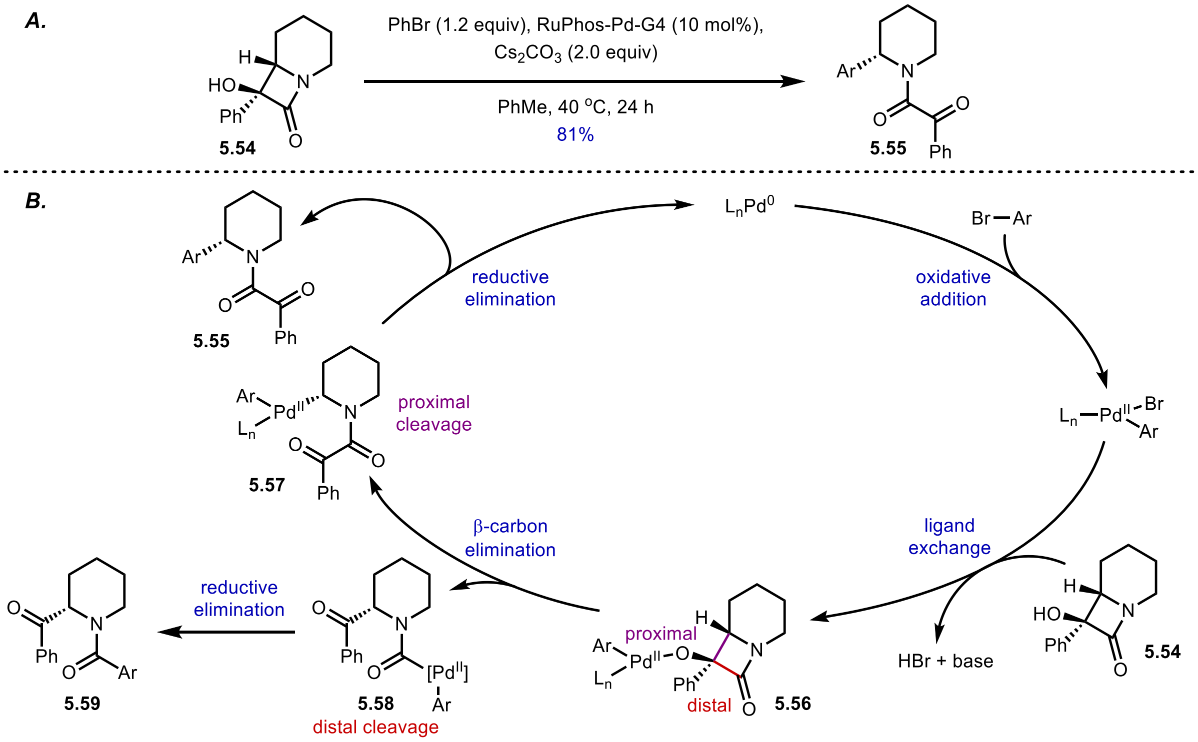


Figure 5.12 (A) Sarpong's α-arylation of piperidine leveraging strain promoted C–C cleavage. (B) The proposed mechanism for the α-arylation.

To implement this strategy in our synthesis, we prepared known compounds α-hydroxy-β-lactam **5.52** and indole **5.60** according to precedented protocols from the groups of Sarpong and Hsung, respectively.[16,17] We then subjected these two coupling partners to the strain-release cross-coupling reaction conditions, anticipating the formation of α-arylated piperidine **5.61** (Figure 5.13.A). Unfortunately, we observed either base promoted distal cleavage of the lactam or protodebromination of the indole coupling partner. Postulating that our coupling partners were not competent in the reaction, we aimed to test our coupling partners with known substrates that had been successful in previous studies of this type of cross-coupling. To this end, ketal lactam **5.52** was subjected to coupling conditions with known competent partner phenylbromide (**5.62**), which gave the desired α-aryl piperidine (**5.63**, Figure 5.13.B). We then attempted the coupling reaction with tryptamine **5.60** and simpler α-hydroxy-β-lactam **5.54**. Rather than producing the desired α-arylated piperidine (**5.64**), α-aroylated piperidine **5.65** was observed (Figure 5.13.B), arising from β-carbon elimination of the distal bond rather than the desired proximal bond.

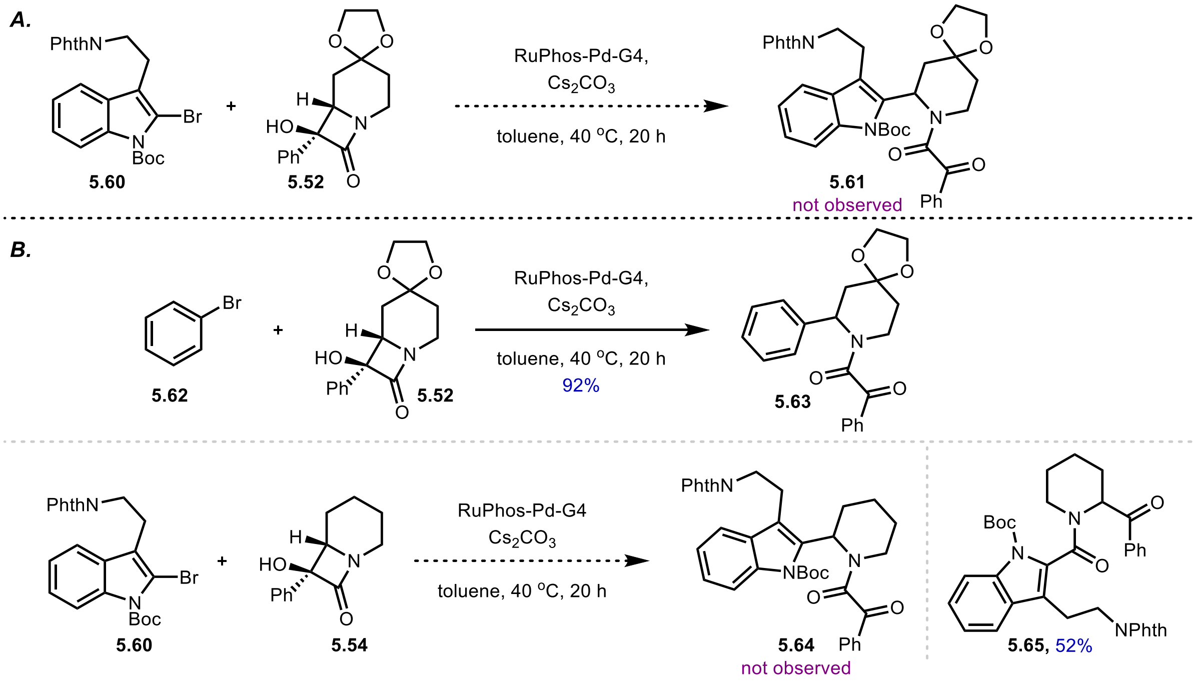


Figure 5.13 (A) Attempted coupling of ideal coupling partners tryptamine **5.60** and piperidine **5.52**. (B) Control reaction to test viability of the coupling partners.

Musaev, Sarpong, and coworkers reported a computational investigation into factors that govern proximal vs distal β-carbon elimination.[18] Their investigations boiled down to a complex interplay between the steric environment of the ligand and substrate, as well as, the electronics at the palladium center due to the substrate and the ligand. These factors lead to either a stabilizing interaction energy or a destabilizing distortion energy which when combined can inform us as to the energy of the barrier for each process. Given the selectivity issues in the β-carbon elimination step that we observed with our indole coupling partner, and the complexity of the system, we decided to opt for a different route toward piperidinyl indole **5.51**.

5.6 Aza-Diels–Alder Approach to Indole-Piperidine Adduct

Having encountered difficulty with the strain-release cross-coupling approach, we decided to employ a longer, but known route to the desired indole-piperidine adduct. Additionally, beginning with tryptophol (**5.67**, Figure 5.14) enabled the possibility for the synthesis to diverge to furanoindoline-containing natural products, such as aspidophylline A (**5.17**). Following precedent by Kuethe and coworkers, we synthesized vinylogous amide **5.66** through an aza-Diels–Alder cycloaddition.[19] Protection of the primary alcohol in tryptophol (**5.67**) followed by protection of the indole nitrogen yielded phenylsulfonyl indole **5.68**.[20,21] Formylation of the indole C2 position with lithium diisopropylamine (LDA) and dimethylformamide (DMF) gave aldehyde **5.69**. Condensation of chiral amine **5.70** onto aldehyde **5.69** afforded the imine, which underwent aza-Diels–Alder cycloaddition with Danishefsky's diene (**5.71**) to give vinylogous amide **5.66** with moderate diastereoselectivity. We found that the literature reported conditions for the aza-Diels–Alder cycloaddition afforded the desired adduct (**5.66**) in only moderate yield, but by modifying the procedure to incorporate sequential additions of diene **5.71**, we were able to access the adduct (**5.66**) in appreciable quantities.

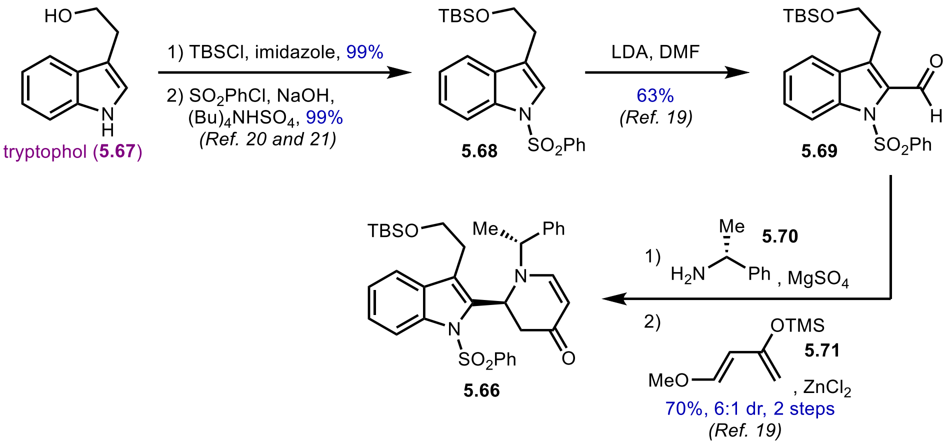


Figure 5.14 Synthesis of known vinylogous amide **5.66**.

With vinylogous amide **5.66** in hand, we turned our attention to incorporation of the malonate moiety required for the key oxidative cyclization step. Attempted 1,4-reduction of vinylogous amide **5.66** afforded alcohol **5.72** rather than the anticipated ketone, even with an equimolar quantity of reductant. The diastereoselecivity of this reduction is likely governed by the steric bulk of the large incoming hydride, which favors equatorial attack to give the axial alcohol. From α-disposed alcohol **5.72**, we envisioned conversion of the secondary hydroxy group to a leaving group followed by stereoinvertive displacement to give desired malonate **5.73**. Conversion of alcohol **5.72** to the mesylate or tosylate was unfortunately unsuccessful, with elimination to the corresponding olefin preferentially taking place.

At this stage we decided to go back to vinylogous amide **5.66**, aiming to reduce the ketone group to a β-disposed alcohol and then effect a double inversion to access the desired malonate. This reduction was accomplished using excess sodium borohydride ($NaBH_4$), presumably occurring by reduction of a zwitterionic resonance form of vinylogous amide **5.66** comprised of an enolate and an iminium ion. Reduction of the iminium ion, protonation of the enolate from the protic solvent, and subsequent 1,2-reduction furnishes alcohol **5.74.** Iodination with inversion followed by displacement with dimethyl malonate afforded malonate **5.73**. In the iodination reaction, we found that pre-stirring of the reagents prior to the addition of the substrate was crucial for reproducibility.

With the malonyl moiety installed, we sought to globally deprotect intermediate **5.73** to set the stage for the key oxidative coupling cyclization. Employing sodium napthalenide, reductive cleavage of the phenylsulfonyl group of **5.73** was accomplished to afford the free indole N–H. Cleavage of the silyl ether with tetrabutylammonium fluoride (TBAF) afforded primary alcohol **5.75**. A one-step cleavage of both the phenylsulfonyl group and silyl ether using TBAF was attempted but only trace phenylsulfonyl cleavage was observed. The stereochemistry about the piperidine of **5.75** was confirmed by derivatization of the primary alcohol with ferrocenyl acid chloride **5.76** to give highly crystalline ferrocenyl ester **5.77**, which was analyzed by single crystal X-ray diffraction.

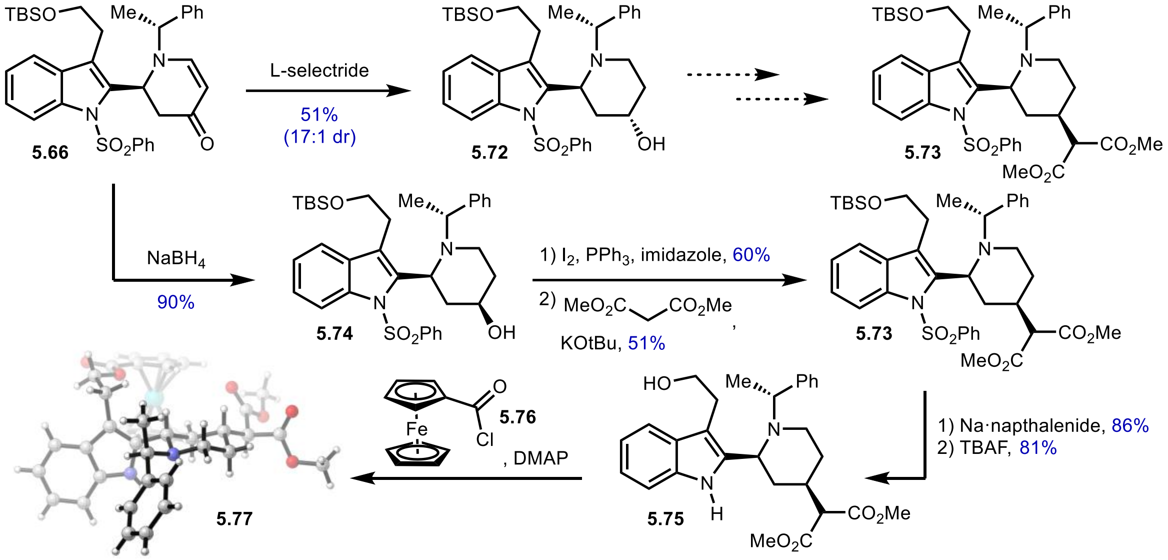


Figure 5.15 Synthesis of malonate containing indole-piperidine adduct **5.75**.

5.7 Oxidative Coupling of the Tryptophol Derivative

5.7.1 Phenethyl Protected Piperidine

With tryptophol derived malonate **5.78** in hand, we attempted the key oxidative cyclization to access the furanoindoline core (**5.79**, Figure 5.16). We expected the oxidative cyclization conditions would translate to a tryptamine derivative to access the pyrroloindoline core characteristic of scholarinine A (**5.1**). We envisioned this cyclization would proceed through deprotonation of the indole nitrogen and malonate methine group to access di-anionic intermediate **5.80** (Figure 5.16). Oxidation would then afford radical species **5.81** (it is possible the indole anion is alternatively oxidized to the corresponding radical), which could cyclize onto the indole to afford radical anion **5.82**. Additional oxidation to imine **5.83** and oxa-Mannich cyclization with the pendant alkoxide would afford furanoindoline **5.79**.

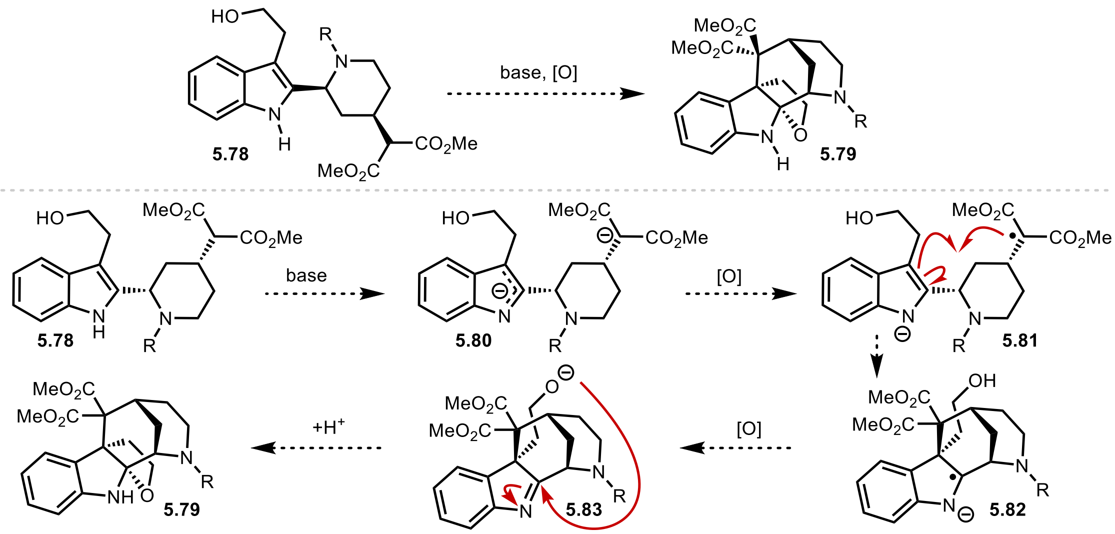
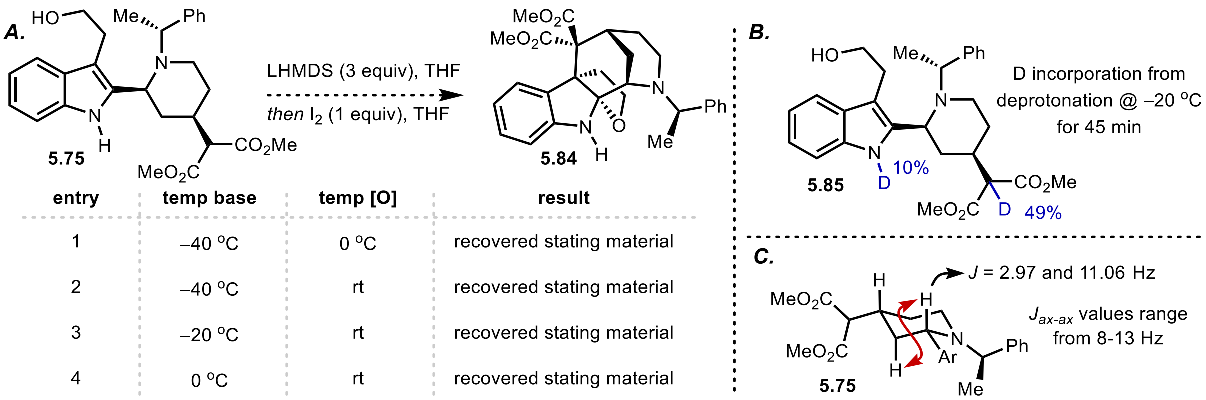


Figure 5.16 Proposed oxidative cascade to form furanoindoline **5.79**.

From phenethyl-protected piperidine **5.75**, we attempted the oxidative coupling to access pentacycle **5.84**. Despite Ma and coworkers' close precedent, no reaction was observed when piperidine **5.75** was subjected to LHMDS and iodine (Figure 5.17.A).[14] Varying the reaction duration and temperature did not change the reaction outcome – only unreacted starting material was observed.

At this stage, we sought to troubleshoot this reaction in stages. To investigate the deprotonation step, we treated piperidine **5.75** with LHMDS and then quenched the reaction mixture with deuterated methanol to confirm deprotonation through deuterium incorporation. We saw 49% deuteration at the malonate methine carbon and 10% deuteration at the indole N–H (see **5.85**, Figure 5.17.B). It is possible that the primary alcohol was deprotonated as well, but the hydroxy group proton was never visible by ^{1}H NMR. Though deprotonation under these conditions was evidently incomplete (and should have been pushed to full deuterium incorporation), this was not expected to completely prevent the desired reaction. Therefore, we then investigated the oxidation and cyclization steps. These steps were not as straightforward to test experimentally as the deprotonation. We believed the oxidation step would proceed smoothly due to its similarity to that reported in the literature, but the cyclization could differ given the substate differences.[14]

When analyzing the cyclization step, we specifically looked at the conformation of the piperidine substrate (**5.75**). We believe piperidine **5.75** is likely to rest as a chair, as drawn in Figure 5.17.C, wherein the indole and malonate fragments are equatorial. By looking at the coupling constants of the piperidine α-methine proton, we observed an axial-axial coupling, confirming the equatorial configuration of the substituents on the piperidine. This hypothesis was additionally supported by the single crystal structure of **5.77**. We postulated that the lack of reactivity was because the reactive substituents were not in close enough proximity to each other to couple.



entry	temp base	temp [O]	result
1	–40 °C	0 °C	recovered stating material
2	–40 °C	rt	recovered stating material
3	–20 °C	rt	recovered stating material
4	0 °C	rt	recovered stating material

Figure 5.17 (A) Attempted oxidative coupling of phenethyl piperidine **5.75**. (B) Deuteration of phenethyl piperidine **5.75**. (C) NMR based conformational analysis of phenethyl piperidine **5.75**.

5.7.2 Carbonyl Containing Piperidine Protecting Groups

Since the piperidine protecting group would not be incorporated into the natural product, we saw this as an ideal handle to conformationally bias the substrate. We looked to install a carbonyl-containing protecting group such that the piperidine nitrogen lone pair could engage in resonance and planarize the nitrogen. Utilizing a sterically encumbering protecting group would introduce pseudo-1,3-allylic strain between the protecting group and the α-aryl group (see **5.86**, Figure 5.18.A) further biasing the molecule toward di-axial conformer **5.87**.

From alcohol **5.75**, hydrogenolysis of the phenethyl group and *tert*-butoxycarbonyl (Boc) protection of the free amine afforded carbamate **5.88**. When carbamate **5.88** was subjected to the oxidative coupling conditions (base and oxidant), urea **5.89** was formed as the sole product. Urea **5.89** formed at temperatures as low as –40 °C, with unreacted starting material accounting for the remainder of the material. This product arises through a base-mediated process wherein cyclization of the deprotonated indole nitrogen into the carbamate and subsequent elimination of *tert*-butoxide affords tetracyclic urea **5.89**. Since no productive reactivity occurred even at low temperature, we surmised that accessing the desired [3.3.1]bicycle from this substrate was unlikely.

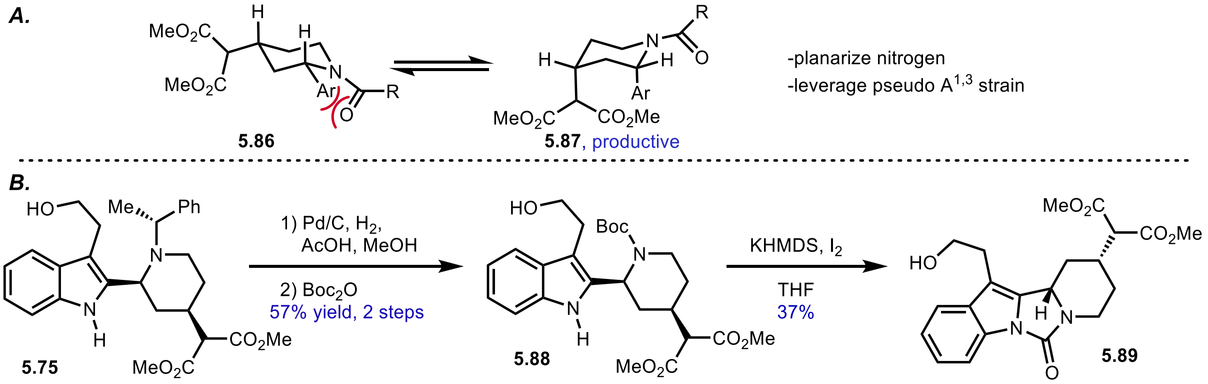


Figure 5.18 (A) Strategy to bias piperidine toward conformation **5.87**. (B) Synthesis and investigation of Boc-protected piperidine substrate.

We turned our attention to synthesis of a pivalyl (Piv) protected piperidine, anticipating that this protecting group would mitigate unwanted cyclization due to the lack of a good leaving group (*tert*-butoxide in the case of **5.88**). Hydrogenolysis of the phenethyl group from silyl ether **5.90** and subsequent protection of the free amine afforded amide **5.91** (Figure 5.19.A). Silyl ether **5.90** was utilized for this transformation instead of alcohol **5.75** to avoid bis-pivalylation. We subjected amide **5.91** to the oxidative coupling conditions and observed oxidized product **5.92**, arising from cyclization at the indole nitrogen rather than the C3 position. Similar competitive C–N bond formation has been previously reported by Ma and coworkers' in their synthesis of aspidophylline A (**5.17**, Figure 5.10).[14] Though this cyclization was initially undesired, [3.3.1]bicycle **5.92** could be advanced to realize the synthesis of pleiocarpamine (**5.5**).[22] It is worth noting that Poupon, Vincent, and Evanno reported a similar oxidative coupling in their synthesis of 16-*epi*-pleiocarpamine (**5.95**, Figure 5.19.B).[6,23]

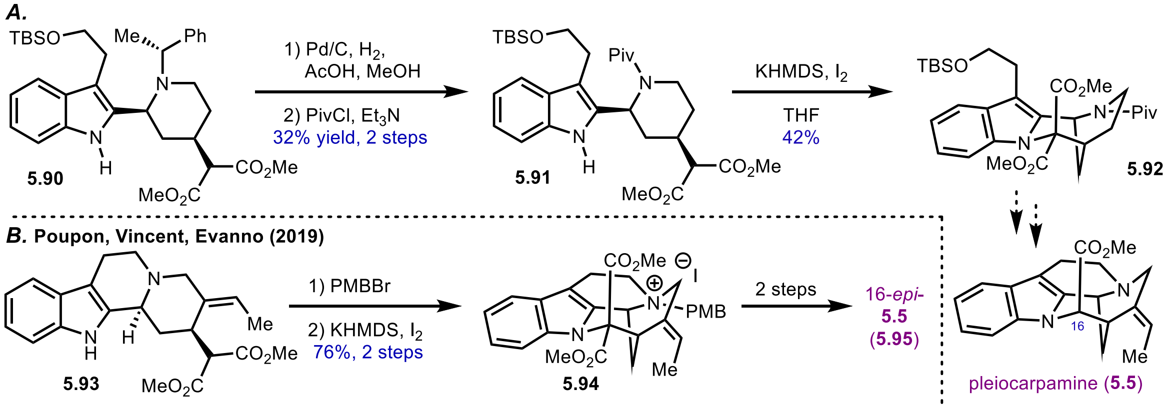


Figure 5.19 Synthesis and oxidative coupling of Piv-protected piperidine toward the natural product pleiocarpamine (**5.5**) and a similar report toward 16-*epi*-pleiocarpamine (**5.95**).

At this stage, we tried to rationalize why the C–N coupled product was forming exclusively over the desired C–C coupled product. We hypothesized that the steric bulk from the silyl ether sidechain was favoring a conformation wherein the indole nitrogen was in close proximity to the malonate. We postulated that alcohol **5.96** (arising from silyl ether cleavage of **5.91**) would add an additional site of coordination and minimize any steric encumbrance caused by the indole sidechain. This small change was found to be successful in overriding competitive C–N bond formation for Ma and coworkers (Figure 5.10).[14] However, cleavage of the silyl ether in amide **5.91** was challenging. We initially employed TBAF as our fluoride source but observed piperidine ring opening to yield olefin **5.97** (Figure 5.20). We propose olefin **5.97** is formed through ejection of the amide group by the indole and subsequent aromatization. We attempted to buffer the reaction, changed the fluoride source, and employed other silyl cleavage conditions but observed the same ring opened piperidine (**5.97** or **5.98**) in all cases. Notably, this piperidine cleavage was also sporadically observed during the pivalyl protecting group installation but could often be overcome by using freshly distilled pivalyl chloride (PivCl). Seeing unproductive reactivity in both the oxidative coupling and the silyl cleavage reactions, we deemed this route untenable to access scholarinine A (**5.1**).

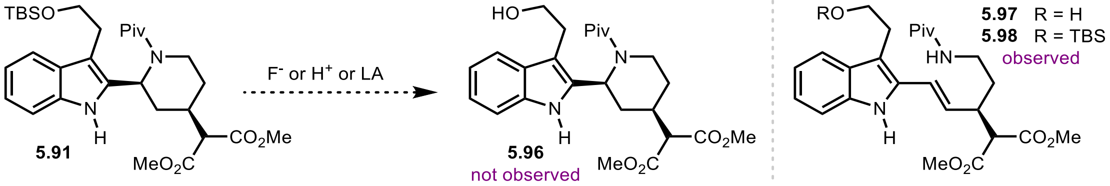


Figure 5.20 Attempted silyl ether cleavage of **5.91** to alcohol **5.96**.

5.8 Synthesis and Oxidative Coupling of a Simplified Indole Derivative

Having encountered several challenges in our proposed oxidative coupling cascade, we sought to simplify the approach. We reasoned that transitioning to a substrate without an indole sidechain, we would eliminate the formation of vicinal quaternary centers in the cascade and would maintain the aromaticity of the indole, potentially leading to a favorable C–C bond formation.

For the synthesis of the proposed simplified indole precursor, we again utilized precedent from Kuethe and coworkers to access known vinylogous amide **5.99** through a Diels–Alder cycloaddition.[19] We aimed to follow the same sequence as outlined in Figure 5.15 to elaborate vinylogous amide **5.99** to the malonate-containing cyclization precursor. Reduction of vinylogous amide **5.99** with $NaBH_4$ produced the desired alcohol (**5.100**), albeit in low yield (Figure 5.22). From alcohol **5.100**, we attempted to iodinate with inversion of stereochemistry; however, these conditions led solely to indole C3 iodination instead of the desired product (**5.101**).

At this stage, we realized that our previously established route would not be directly transferrable to this new substrate. We sought to transform vinylogous amide **5.99** into ketone **5.102** to avoid the challenges associated with alcohol substrates we had previously encountered (elimination in the case of **5.72** or iodination in the case of **5.100**). Treatment of **5.99** with lithium aluminum hydride (LAH) effected the desired reduction, affording ketone **5.102**. Knoevenagel condensation with dimethyl malonate (**5.103**) gave rise to vinylidene malonate **5.104**. Reduction of vinylidene malonate **5.104** was carried out with a variety of reductive conditions (e.g., Pd/C with H_2, Stryker's reagent, SmI_2, Shenvi hydrogen atom transfer (HAT) reduction[24]) to give a mixture of diastereomers, favoring the undesired diastereomer. This is likely because the β-face of **5.104** is more sterically accessible, rendering hydride delivery to this face kinetically favorable. However, formation of the cis-substituted piperidine is likely more thermodynamically favorable. Aiming to access the thermodynamic product, we attempted a dissolving metal reduction of **5.104**. Exposure to lithium metal and liquid ammonia gave rise to cis-substituted piperidine **5.105** with moderate diastereoselectivity. The phenylsulfonyl group was concomitantly cleaved under these conditions.

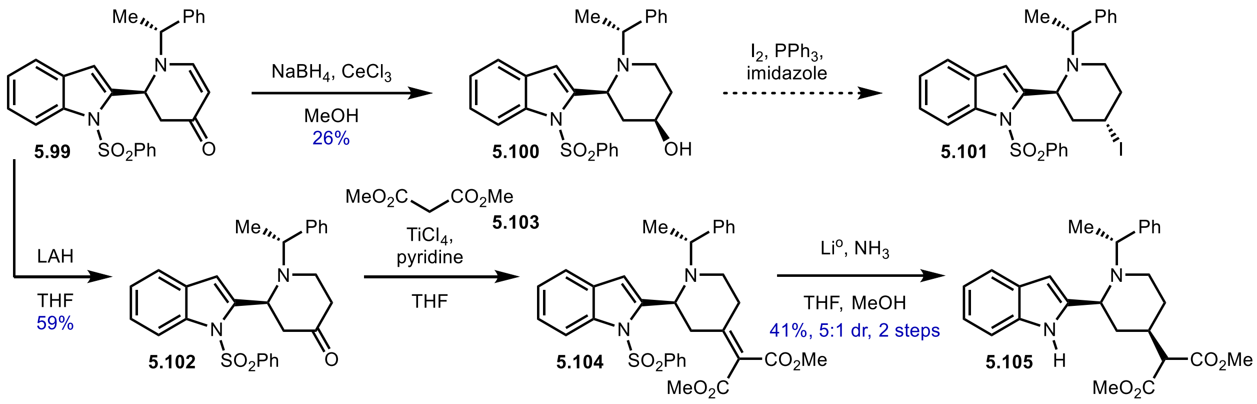


Figure 5.21 Synthesis of malonate **5.105** from vinylogous amide **5.99**.

With malonate **5.105** in hand, we attempted the oxidative coupling of this substrate to access [3.3.1]bicyclic indole **5.106**. We once again screened bases (e.g., KHMDS or LHMDS) and oxidants (e.g., iodine or Cu(II) 2-ethylhexanoate) and observed iodination when iodine was employed and no reaction when the copper oxidant was used. With oxidative coupling remaining elusive, we drew from previous lessons with the C3 substituted indole and aimed to change the protecting group on the piperidine to bias the substrate into a productive conformation (see Figure 5.18 and 5.19).

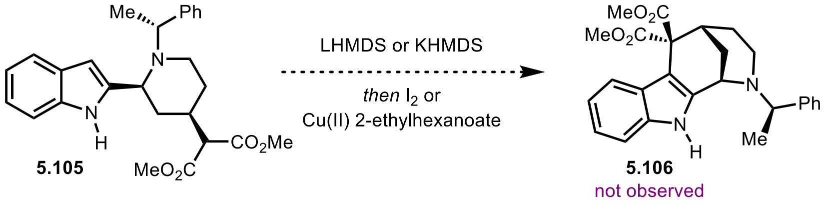


Figure 5.22 Oxidative coupling attempts with phenethyl piperidine **5.105**.

From phenethyl piperidine **5.105**, hydrogenolysis afforded the secondary amine (Figure 5.23). It was found that trace thiophenol, produced in the preceding reaction from reductive cleavage of the phenylsulfonyl group, poisoned the catalyst, thereby shutting down reactivity. Luckily, any residual thiophenol could be easily removed during workup in the previous step by incorporating an aqueous base wash. From the secondary amine, treatment with PivCl afforded amide **5.107**, which was poised to undergo oxidative coupling to furnish the carbocyclic framework characteristic of the target natural products.

From amide **5.107**, several oxidative coupling conditions were screened, aiming to forge the [3.3.1]bicycle of the natural product (see **5.106**, Figure 5.22). Employing bases such as KHMDS or LHMDS with an oxidant (e.g., Cu(II) 2-ethylhexanoate, PIDA, PIFA), we observed either no reaction of the starting material or decomposition. When we employed KHMDS and iodine, the conditions that previously facilitated the formation of the C–N bond in **5.92**, we once again observed C–N bond formation to give **5.108** (Figure 5.23). We believe this reaction proceeds by iodination of the indole C3 position and subsequent oxidative coupling at the indole nitrogen to give iodide **5.108**.

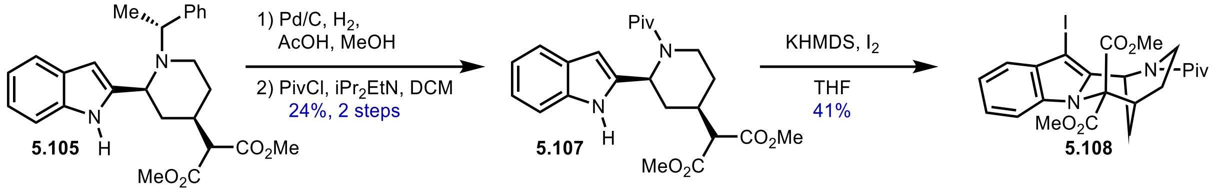


Figure 5.23 Synthesis of Piv-piperidine **5.107** and subsequent formation of iodo-indole **5.108**.

Though this reactivity with iodine is not ideal, it is in accordance with the prior oxidative coupling result (see **5.91** → **5.92**, Figure 5.19). It is possible that the strategic pairing of protecting group and reagent should enable the successful oxidative coupling, however, given the significant reliance of reaction efficiency on conformation, a more flexible cyclization precursor is likely required.

5.9 Conclusion and Outlook

Working in collaboration with Corteva AgriSciences, we pursued the synthesis of scholarinine A (**5.1**) to explore its utility as an insecticide. We envisioned that employing a strain-release cross-coupling followed by a key oxidative cyclization would allow access to the core framework, which could be functionalized at a later stage to afford the natural product. Initial attempts at accessing the indole-piperidine adduct (**5.61**) through the strain release cross-coupling were not successful. We discovered that successful transformations fall within certain steric or electronic constraints that were not met by our attempted transformation.

We next turned to precedent by Kuethe and coworkers to synthesize tryptophol derived vinylougous amide **5.66** which we were able to elaborate to malonate **5.75**.[19] Unfortunately, the oxidative coupling cascade did not give rise to the desired furanoindoline. We investigated multiple facets of this reaction (i.e., deprotonation and substate conformation) and hypothesized that the lack of reactivity we observed was due to the distance between the coupling fragments. To address this issue, we opted to switch the piperidine protecting group, aiming to bias the piperidine ring such that the coupling substituents were axially disposed. We found that Piv-protected piperidine **5.91** underwent oxidative coupling, but unfortunately formed a C–N bond to give [3.3.1]bicycle **5.92**, which we believe could be carried forward to pleiocarpamine (**5.5**).

Aiming to mitigate the undesired C–N bond formation, we opted for a simplified cyclization precursor lacking the indole C3 sidechain. Once again, oxidative cyclization of phenethyl protected malonate **5.105** did not undergo oxidative coupling. However, Piv-protected piperidine **5.107** underwent C–N bond formation when exposed to the oxidative cyclization conditions, giving rise to iodide **5.108**. It is likely that the rigidity of the system leads to the unfavorable reactivity we observed. To access the desired carbocyclic framework, it is likely that a more conformationally labile system will need to be investigated.

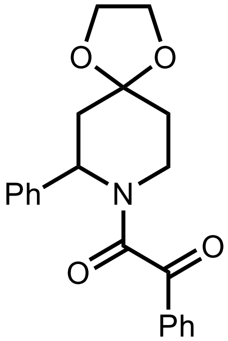
5.10 Experimental Contributors

Project design was carried out by Kerry E. Jones (K.E.J.) and Prof. Richmond Sarpong (R.S.) in collaboration with Dr. Jessica Herrick and Dr. Blane Zavesky from Corteva AgriScience. Experiments were conducted by K.E.J. and Fernando Martínez Lara (F.M.L.).

5.11 Experimental Details

5.11.1 Experimental Procedures

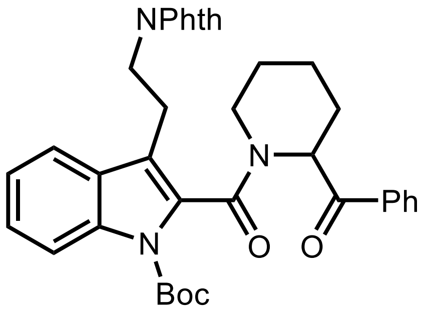
1-phenyl-2-(7-phenyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)ethane-1,2-dione (5.63)



Lactam **5.52** (3.3 mg, 0.012 mmol, 1 equiv) and phenyl bromide (2.3 mg, 0.015 mmol, 1.2 equiv) were added to a 1-dram vial. RuPhos-Pd-G4 (1.0 mg, 1.2 µmol, 0.1 equiv), Cs_2CO_3 (8.0 mg, 0.025 mmol, 2 equiv), and toluene (0.2 mL) were added in a glovebox. The sealed vial was heated to 40 ^oC for 20 h. The mixture was then filtered through Celite, eluting with EtOAc. The organic layers were concentrated *in vacuo* and the crude residue was purified by preparative thin layer chromotography (eluting with 3:1 hexanes:ethyl acetate) to afford piperidine **5.63** (4.0 mg, 0.011 mmol, 92%) as a mixture of rotamers in a 1:0.6 ratio.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.00 (m, 2H), 7.92 – 7.88 (m, 2x0.6H), 7.72 – 7.43 (m, 5H + 0.6H), 7.39 (d, *J* = 4.3 Hz, 2H + 3x0.6H), 7.28 (d, *J* = 6.2 Hz, 1H + 4x0.6H), 6.10 (d, *J* = 6.9 Hz, 1H), 5.01 (d, *J* = 3.7 Hz, 0.6H), 4.68 (dt, *J* = 12.4, 3.0 Hz, 0.6H), 4.05 – 3.81 (m, 4H + 4x0.6H), 3.56 (dd, *J* = 14.4, 4.9 Hz, 1H), 3.46 (td, *J* = 13.4, 3.2 Hz, 1H), 3.25 (td, *J* = 12.9, 3.5 Hz, 0.6H), 2.58 (dt, *J* = 14.6, 2.6 Hz, 1H), 2.48 (dt, *J* = 14.0, 2.4 Hz, 0.6H), 2.31 – 1.79 (m, 3H + 3x0.6H).

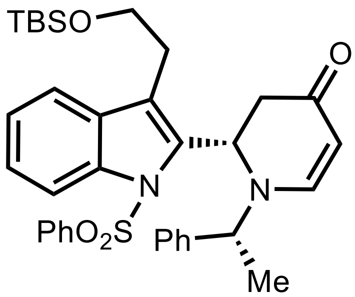
Tert-butyl 2-(2-benzoylpiperidine-1-carbonyl)-3-(2-(1,3-dioxoisoindolin-2-yl)ethyl)-1H-indole-1-carboxylate (5.65)



Lactam **5.54** (5.4 mg, 0.025 mmol, 1 equiv) and indole **5.60** (14.0 mg, 0.030 mmol, 1.2 equiv) were added to a 1-dram vial. RuPhos-Pd-G4 (2.1 mg, 2.5 µmol, 0.1 equiv), Cs_2CO_3 (16 mg, 0.05 mmol, 2 equiv), and toluene (0.4 mL) were added in a glovebox. The sealed vial was heated to 40 °C for 20 h. The mixture was then filtered through Celite, eluting with EtOAc. The organic layers were concentrated *in vacuo* and the crude residue was purified by flash column chromatography (eluting with 3:1 hexanes:ethyl acetate) to afford piperidine **5.65** (8.0 mg, 0.013 mmol, 52%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 8.02 – 7.95 (m, 2H), 7.74 (td, *J* = 5.0, 3.1 Hz, 2H), 7.67 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.34 (dd, *J* = 6.3, 2.0 Hz, 1H), 3.86 (dt, *J* = 13.6, 8.0 Hz, 1H), 3.77 (ddd, *J* = 13.6, 8.5, 4.7 Hz, 1H), 3.68 (d, *J* = 13.5 Hz, 1H), 3.57 (td, *J* = 12.7, 3.4 Hz, 1H), 3.01 (dt, *J* = 14.3, 8.2 Hz, 1H), 2.74 (ddd, *J* = 13.4, 8.1, 4.7 Hz, 1H), 2.26 (d, *J* = 13.7 Hz, 1H), 1.69 (s, 7H), 1.66 – 1.58 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 200.0, 168.2, 163.9, 149.4, 136.0, 135.4, 134.1, 133.9, 133.1, 132.4, 132.4, 130.1, 129.5, 128.8, 128.8, 128.7, 128.6, 125.3, 123.4, 123.2, 123.1, 119.5, 117.7, 115.8, 84.8, 54.6, 45.8, 37.5, 28.4, 25.9, 25.1, 23.2, 20.5.

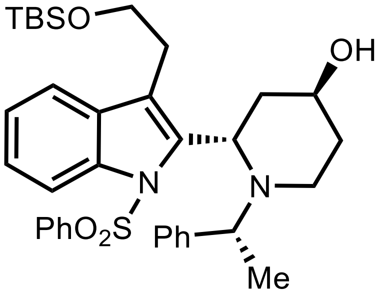
(S)-2-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-(phenylsulfonyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)-2,3-dihydropyridin-4(1H)-one (5.66)



Prepared according to a modified procedure by Kuethe and coworkers.[19] Aldehyde **5.69** (4.0 g, 9.1 mmol, 1 equiv) and $MgSO_4$ (2.8 g, 23.7 mmol, 2.6 equiv) were dissolved in toluene (36 mL). (*R*)-1-phenylethan-1-amine (1.3 mL, 10.0 mmol, 1.1 equiv) was added and the mixture was heated to reflux for 16 h. The mixture was then allowed to cool to room temperature, filtered through Celite (eluting with toluene), and concentrated *in vacuo* to afford the intermediary imine as a crude oil. The crude imine was then dissolved in DCM (70 mL) and cooled to –20 °C. $ZnCl_2$ (1 M in Et_2O, 13.6 mL, 13.6 mmol, 1.5 equiv) was added dropwise. After 10 min, *trans*-1-methoxy-3-trimethylsiloxy-1,3-butadiene (**5.71**, 2.1 mL, 10.9 mmol, 1.2 equiv) was added and the mixture was stirred at –20 °C for 2 h before a second portion of *trans*-1-methoxy-3-trimethylsiloxy-1,3-butadiene (**5.71,** 2.1 mL, 10.9 mmol, 1.2 equiv) was added and the mixture stirred an additional 2 h. The mixture was then quenched with 1 M HCl (35 mL) and warmed to room temperature. The organic and aqueous layers separated and the aqueous layer was extracted with DCM (3 x 25 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (3:1 hexanes/ethyl acetate gradient) yielded vinylogous amide **5.66** (3.9 g, 6.3 mmol, 70% yield).

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.57 (t, *J* = 7.1 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.34 – 7.22 (m, 4H), 7.13 (d, *J* = 7.5 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.05 (dd, *J* = 14.7, 6.2 Hz, 1H), 5.11 (d, *J* = 8.0 Hz, 1H), 4.15 (q, *J* = 6.7 Hz, 1H), 3.80 – 3.71 (m, 2H), 3.29 – 3.23 (m, 1H), 3.02 (t, *J* = 15.8 Hz, 1H), 2.84 (dt, *J* = 13.8, 6.7 Hz, 1H), 2.20 (dt, *J* = 13.9, 5.1 Hz, 1H), 1.53 (d, *J* = 6.7 Hz, 3H), 0.75 (s, 9H), -0.17 (d, *J* = 18.1 Hz, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 190.5, 151.9, 139.9, 138.7, 137.3, 134.5, 133.9, 130.8, 129.7, 128.8, 128.1, 127.7, 126.3, 126.0, 124.1, 123.9, 120.4, 115.9, 100.9, 62.5, 58.2, 54.1, 42.7, 29.1, 26.0, 18.4, 18.1, -5.3, -5.4.

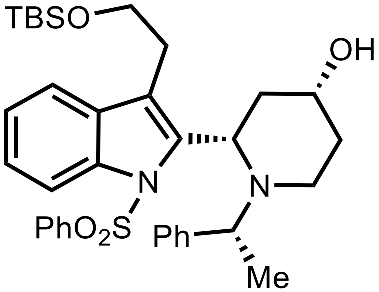
(2S,4S)-2-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-(phenylsulfonyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-ol (5.72)



L-selectride (1M in THF, 0.24 mL, 0.24 mmol, 2.5 equiv) was added dropwise to a solution of vinylogous amide **5.66** (60 mg, 98 µmol, 1 equiv) in THF (1 mL) at –78 °C. After 30 minutes, 0.2 mL 1M NaOH and 0.1 mL H_2O_2 (~35% aqueous) were sequentially added to quench the reaction mixture. The mixture was warmed to room temperature, brine (1 mL) was added, and the organic and aqueous layers separated. The aqueous layer was extracted with EtOAc (3 x 1 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (3:1 to 1:1 hexanes/ethyl acetate gradient) yielded alcohol **5.72** as a white foam. (31 mgs, 50 µmol, 51% yield, 17:1 dr).

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.4 Hz, 1H), 7.83 – 7.77 (m, 2H), 7.58 (dd, *J* = 9.3, 7.4 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.34 – 7.29 (m, 1H), 7.29 – 7.24 (m, 4H), 7.03 – 7.00 (m, 2H), 4.97 (dd, *J* = 12.2, 4.5 Hz, 1H), 3.87 – 3.76 (m, 3H), 3.63 (d, *J* = 2.9 Hz, 1H), 3.48 (q, *J* = 6.5 Hz, 1H), 3.02 (t, *J* = 4.3 Hz, 1H), 2.99 (t, *J* = 3.7 Hz, 1H), 2.98 – 2.90 (m, 1H), 2.32 (dd, *J* = 14.4, 12.2 Hz, 1H), 1.69 (dt, *J* = 14.4, 4.3 Hz, 1H), 1.31 – 1.23 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.91 – 0.83 (m, 1H), 0.78 (s, 9H), -0.13 (d, *J* = 4.7 Hz, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 141.9, 140.3, 138.7, 137.1, 133.9, 131.0, 129.6, 128.6, 127.8, 127.1, 126.7, 124.9, 123.3, 120.9, 119.9, 115.2, 85.6, 63.3, 57.1, 50.3, 48.8, 47.4, 29.6, 28.1, 26.1, 26.1, 18.5, 12.6, -5.2, -5.3.

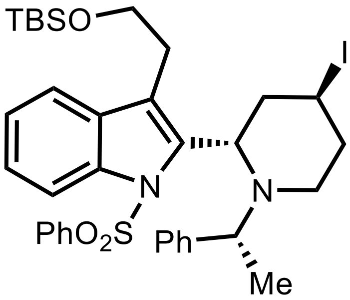
(2S,4R)-2-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-(phenylsulfonyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-ol (5.74)



Vinylogous amide **5.66** (3.84 g, 6.25 mmol, 1.0 equiv) was dissolved in anhydrous ethanol (156 mL) and cooled to 0 °C. Sodium borohydride (2.37 g, 62.5 mmol, 10 equiv) was added and the mixture was warmed to room temperature and stirred vigorously. After 36 h, the mixture was cooled to 0 °C and quenched through the addition of H_2O (25 mL) and brine (25 mL). The aqueous layer was extracted with EtOAc (3 x 50 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (3:1 hexanes/ethyl acetate) yielded alcohol **5.74** as a white foam (3.49 g, 5.63 mmol, 91% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.4 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.59 – 7.50 (m, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.28 (m, 4H), 7.28 – 7.22 (m, 2H), 7.18 – 7.11 (m, 1H), 4.73 (dd, *J* = 11.4, 2.7 Hz, 1H), 3.88 – 3.72 (m, 4H), 3.61 (tt, *J* = 10.6, 4.5 Hz, 1H), 2.99 (ddd, *J* = 12.8, 7.4, 5.6 Hz, 1H), 2.68 (dt, *J* = 12.0, 3.6 Hz, 1H), 2.27 (td, *J* = 12.2, 2.3 Hz, 1H), 1.94 – 1.81 (m, 2H), 1.71 (dp, *J* = 12.4, 2.6 Hz, 1H), 1.51 (qd, *J* = 11.9, 3.9 Hz, 1H), 1.36 (s, 1H), 1.21 (d, *J* = 6.9 Hz, 3H), 0.84 (s, 9H), -0.06 (d, *J* = 13.8 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.1, 139.6, 137.3, 134.0, 131.2, 129.4, 128.0, 127.4, 126.4, 126.2, 124.9, 123.7, 122.2, 120.0, 115.8, 69.8, 63.1, 55.3, 55.2, 43.5, 42.6, 35.3, 28.9, 26.1, 18.5, 10.2, -5.1, -5.1. *Note: two aryl carbons are overlapping* **HRMS** (ESI) calc'd for ([M+H], $C_{35}H_{47}N_2O_4SSi)^+$: m/z = 619.3021, found 619.3022. **IR**: ṽ = 2927, 2855, 1369, 1175, 1087, 835, 749, 582 cm^{-1}. **$[\alpha]^{20}_D$** = –71.90 (c 0.21, $CHCl_3$).

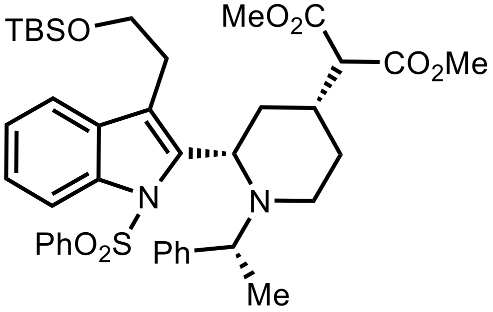
3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-((2S,4S)-4-iodo-1-((R)-1-phenylethyl)piperidin-2-yl)-1-(phenylsulfonyl)-1H-indole (5.109)



Prepared according to a modified procedure by Hanessian and coworkers.[25] Imidazole (0.39 g, 5.86 mmol, 2.5 equiv), triphenylphosphine (1.35 g, 5.15 mmol, 2.2 equiv), and iodine (1.19 g, 4.69 mmol, 2.0 equiv) were added to a flask under nitrogen. The flask was submerged in an ice bath, DCM (68 mL) was added via syringe, and the yellow mixture was vigorously stirred for 30 min at 0 °C. Alcohol **5.74** (1.45 g, 2.34 mmol, 1.0 equiv) was added in DCM (10 mL). The mixture turned from dark yellow to light yellow. After 1.5 h at 0 °C, the mixture was quenched with the addition of H_2O (50 mL) and brought to room temperature. The aqueous layer was extracted with DCM (3 x 50 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (50:1 hexanes/ethyl acetate) yielded iodide **5.109** as a white foam (1.03 g, 1.41 mmol, 60% yield).

^{1}H NMR (500 MHz, C_6D_6) δ 8.74 (d, *J* = 8.5 Hz, 1H), 7.93 (dd, *J* = 8.1, 1.7 Hz, 2H), 7.44 – 7.37 (m, 1H), 7.29 – 7.17 (m, 5H), 7.13 – 7.02 (m, 2H), 6.84 – 6.74 (m, 3H), 5.46 (dd, *J* = 10.8, 2.7 Hz, 1H), 4.46 – 4.38 (m, 1H), 4.01 (dt, *J* = 13.8, 7.8 Hz, 1H), 3.91 – 3.76 (m, 2H), 3.70 (dt, *J* = 10.0, 7.5 Hz, 1H), 3.05 (ddd, *J* = 13.4, 7.7, 5.3 Hz, 1H), 2.82 (td, *J* = 11.9, 2.2 Hz, 1H), 2.42 (dt, *J* = 12.3, 3.5 Hz, 1H), 2.24 (ddd, *J* = 14.6, 10.8, 3.6 Hz, 1H), 1.93 (dq, *J* = 14.8, 2.7 Hz, 1H), 1.58 (dq, *J* = 14.6, 2.6 Hz, 1H), 1.33 (ddt, *J* = 14.9, 11.7, 3.6 Hz, 1H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H), -0.10 (s, 3H), -0.14 (s, 3H). **^{13}C NMR** (126 MHz, C_6D_6) δ 144.2, 140.3, 138.2, 137.9, 133.5, 131.3, 129.3, 128.4, 128.2, 126.9, 126.5, 125.4, 123.9, 122.0, 119.8, 116.5, 63.1, 56.5, 53.1, 42.2, 42.0, 35.4, 33.3, 29.5, 26.1, 18.5, 10.7, -5.2, -5.2. **HRMS** (ESI) calc'd for ([M+H], $C_{35}H_{46}IN_2O_3SSi)^+$: m/z = 729.2038, found 729.2037. **IR**: ṽ = 2951, 2927, 2855, 1447, 1372, 1092, 749, 581 cm^{-1}. **$[\alpha]^{20}_D$** = –78.96 (c 0.58, $CHCl_3$).

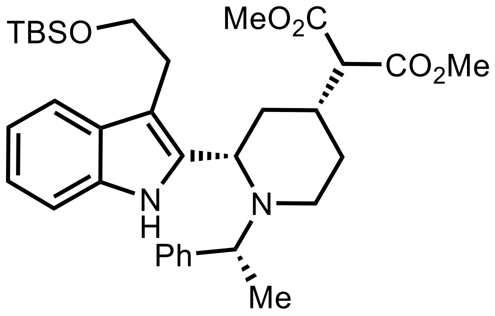
Dimethyl 2-((2S,4R)-2-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-(phenylsulfonyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-yl)malonate (5.73)



Dimethyl malonate (0.076 mL, 0.66 mmol, 1.2 equiv) was added to a solution of potassium tert-butoxide (74 mg, 0.66 mmol, 1.2 equiv) in DMSO (15 mL). After 5 min, iodide **5.109** (0.40 g, 0.55 mmol, 1.0 equiv) was added in DMSO (3 mL). The resulting mixture was heated to 80 °C for 20 h, then cooled to room temperature and H_2O (15 mL) was added. The aqueous layer was extracted with EtOAc (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (5:1 hexanes/ethyl acetate) yielded diester **5.73** as a white foam (0.20 g, 0.28 mmol, 51% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.5 Hz, 1H), 8.04 – 7.73 (m, 2H), 7.57 – 7.44 (m, 4H), 7.35 – 7.29 (m, 3H), 7.26 – 7.21 (m, 3H), 7.19 – 7.10 (m, 1H), 5.02 – 4.75 (m, 1H), 3.84 – 3.74 (m, 3H), 3.73 (s, 3H), 3.66 (s, 3H), 3.16 (d, *J* = 9.3 Hz, 1H), 3.08 – 2.92 (m, 1H), 2.72 (dt, *J* = 11.7, 3.5 Hz, 1H), 2.33 (td, *J* = 12.1, 2.4 Hz, 1H), 2.31 – 2.24 (m, 1H), 1.69 (t, *J* = 9.0 Hz, 2H), 1.65 – 1.61 (m, 1H), 1.57 (s, 1H), 1.37 (qd, *J* = 12.2, 3.7 Hz, 1H), 1.22 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 9H), -0.12 (d, *J* = 9.7 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.8, 168.7, 144.2, 139.5, 137.6, 137.2, 133.8, 131.4, 129.6, 128.0, 127.5, 126.7, 126.2, 124.9, 123.6, 121.7, 120.0, 115.9, 63.1, 57.3, 56.4, 55.7, 52.6, 52.4, 45.5, 38.1, 37.4, 30.3, 28.9, 26.1, 18.5, 10.4, -5.2, -5.2. **HRMS** (ESI) calc'd for ([M+H], $C_{40}H_{53}N_2O_7SSi)^+$: m/z = 733.3338, found 733.3340. **IR**: ṽ = 2952, 2928, 2855, 1734, 1371, 1087, 835, 748, 581 cm^{-1}. **$[\alpha]^{20}_D$** = –95.74 (c 1.22, $CHCl_3$).

Dimethyl 2-((2S,4R)-2-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-yl)malonate (5.90)

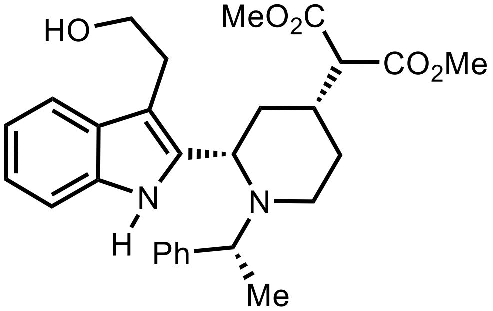


A mixture of malonate **5.73** (0.98 mg, 1.34 mmol, 1.0 equiv) in DME (27 mL) was cooled to –78 °C. A freshly prepared solution of sodium naphthalide (~1.0 M in DME, 8.0 mL, 6.0 equiv), formed though addition of sodium metal to napthelene dissolved in DME at room temperature, was added dropwise via syringe. The resulting deep blue solution was allowed to stir for 5 minutes before sat. aq. $NaHCO_3$ (10 mL) was added, and the mixture was warmed to room temperature. The mixture was extracted with EtOAc (3 x 15 mL), washed with H2O (10 mL), and then the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude residue via column chromatography (5:1 hexanes/ethyl acetate) yielded the title compound (**5.90**) as a white foam (0.69 g, 1.16 mmol, 86% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.61 – 7.50 (m, 1H), 7.35 (dt, *J* = 8.2, 1.1 Hz, 2H), 7.33 – 7.27 (m, 3H), 7.20 (tq, *J* = 7.0, 1.1 Hz, 1H), 7.14 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.08 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 4.01 (dd, *J* = 11.1, 3.0 Hz, 1H), 3.87 – 3.77 (m, 3H), 3.72 (s, 3H), 3.68 (s, 3H), 3.21

(d, *J* = 8.8 Hz, 1H), 3.14 – 2.99 (m, 2H), 2.71 (dt, *J* = 11.7, 3.5 Hz, 1H), 2.38 (td, *J* = 12.0, 2.4 Hz, 1H), 2.33 – 2.24 (m, 1H), 1.87 (dq, *J* = 12.9, 3.1 Hz, 1H), 1.74 – 1.61 (m, 2H), 1.36 (qd, *J* = 12.3, 3.8 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 3H), 0.94 (s, 9H), 0.11 (d, *J* = 3.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.7, 168.7, 143.7, 136.6, 135.6, 128.6, 128.2, 127.3, 126.6, 121.9, 119.4, 118.8, 110.9, 109.3, 64.3, 57.3, 55.8, 52.6, 44.3, 39.3, 36.9, 30.1, 28.5, 26.2, 18.7, 9.5, -5.0, -5.0. *Note: two aliphatic carbons are overlapping* **HRMS** (ESI) calc'd for ([M+H], $C_{34}H_{49}N_2O_5Si)^+$: m/z = 593.3406, found 593.3401. **IR**: ṽ = 3409, 2951, 2929, 1731, 1246, 1085, 834, 743, 699 cm^{-1}. **[α]^{20}$_D$** = +51.94 (c 1.03, $CHCl_3$).

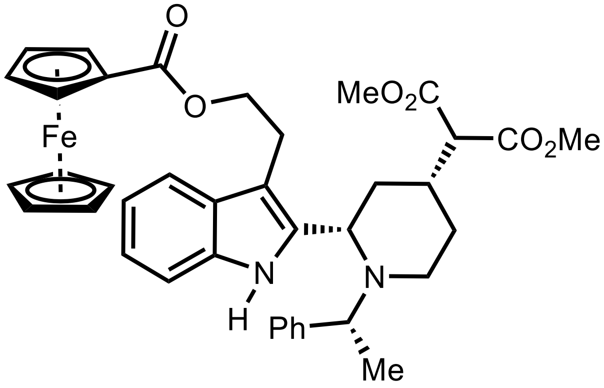
Dimethyl 2-((2S,4R)-2-(3-(2-hydroxyethyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-yl)malonate (5.75)



Tetrabutylammonium fluoride (1.0 M in THF, 2.3 mL, 2.31 mmol, 2.0 equiv) was added to a solution of silyl ether **5.90** (0.69 mg, 1.16 mmol, 1.0 equiv) in THF (9.3 mL). The mixture was stirred at room temperature for 3.5 h then H_2O (5 mL) and NH_4Cl (5 mL) were added. The aqueous layer was extracted with EtOAc (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (1:1 hexanes/ethyl acetate) yielded alcohol **5.75** as a white powder (0.45 g, 0.94 mmol, 81% yield).

^{1}H NMR (500 MHz, C_6D_6) δ 7.98 (s, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.30 – 7.18 (m, 5H), 7.14 – 7.04 (m, 2H), 3.81 (d, *J* = 10.8 Hz, 1H), 3.68 (dt, *J* = 16.8, 6.7 Hz, 3H), 3.33 (s, 3H), 3.32 (s, 3H), 3.29 (d, *J* = 8.7 Hz, 1H), 3.02 – 2.91 (m, 1H), 2.87 (dt, *J* = 14.0, 7.0 Hz, 1H), 2.57 (dt, *J* = 11.8, 3.5 Hz, 1H), 2.38 (dtt, *J* = 12.2, 8.7, 3.6 Hz, 1H), 2.05 (dt, *J* = 12.5, 6.0 Hz, 2H), 1.59 (ddd, *J* = 12.4, 7.9, 4.7 Hz, 2H), 1.29 (qd, *J* = 12.3, 3.8 Hz, 1H), 0.97 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, C_6D_6) δ 168.7, 168.6, 144.1, 137.1, 136.2, 129.1, 128.4, 128.2, 128.0, 127.8, 126.8, 122.3, 119.7, 119.1, 111.2, 109.6, 63.0, 57.6, 56.0, 52.0, 51.9, 44.4, 39.3, 37.0, 30.3, 28.3, 9.2. **HRMS** (ESI) calc'd for ([M-H], $C_{28}H_{33}N_2O_5)^-$: m/z = 477.2394, found 477.2399. **IR**: ṽ = 3405, 2950, 1727, 1459, 1243, 1021, 745, 700 cm^{-1}. **[α]^{20}$_D$** = +53.44 (c 0.30, $CHCl_3$).

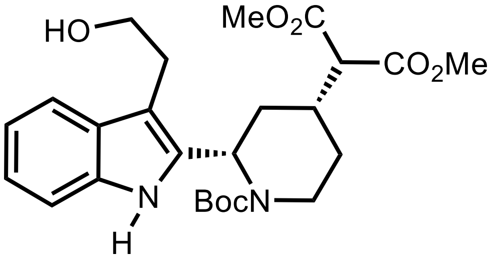
Acyl Ferrocene Derivative of dimethyl 2-((2S,4R)-2-(3-(2-hydroxyethyl)-1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-yl)malonate (5.77)



Prepared according to a modified procedure by Holstein and coworkers.[26] Alcohol **5.75** (5.0 mg, 0.010 mmol, 1 equiv) and DMAP (1.5 mg, 0.012 mmol, 1.2 equiv) were dissolved in DCM (0.3 mL). Ferrocenoyl chloride (3.7 mg, 0.015 mmol , 1.5 equiv) was added to the mixture and after 10 minutes, stirring at room temperature, the mixture was filtered over silica and concentrated *in vacuo* to afford the title compound as a red-orange solid. The compound was recrystallized by vapor diffusion of ethyl acetate and hexanes to afford crystalline solid that was utilized for single crystal x-ray diffraction.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.42 (s, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 3H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.23 – 7.11 (m, 3H), 4.81 (ddt, *J* = 7.0, 2.6, 1.3 Hz, 2H), 4.47 – 4.41 (m, 1H), 4.42 – 4.36 (m, 3H), 4.11 (s, 5H), 4.08 (dd, *J* = 11.1, 2.9 Hz, 1H), 3.84 (q, *J* = 6.9 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.39 – 3.12 (m, 3H), 2.74 (dt, *J* = 11.1, 2.9 Hz, 1H), 2.42 (td, *J* = 11.9, 2.0 Hz, 1H), 2.39 – 2.28 (m, 1H), 1.93 (dd, *J* = 13.0, 3.0 Hz, 1H), 1.71 (q, *J* = 12.1 Hz, 2H), 1.43 – 1.35 (m, 1H), 1.30 (d, *J* = 6.8 Hz, 3H).

Dimethyl 2-((2S,4R)-1-(tert-butoxycarbonyl)-2-(3-(2-hydroxyethyl)-1H-indol-2-yl)piperidin-4-yl)malonate (5.88)

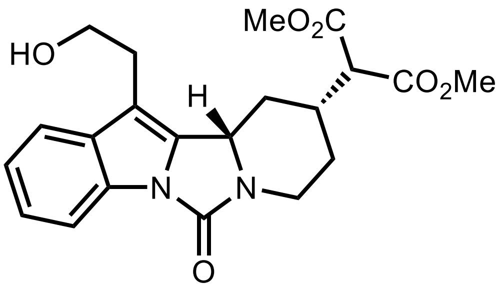


Phenethyl piperidine **5.75** (125 mg, 0.26 mmol, 1.0 equiv) and palladium on carbon (10 wt%, 69.5 mg, 65 µmol, 0.25 equiv) were added to a vial. MeOH (10.6 mL) and AcOH (0.75 mL) were added, and the resultant mixture was sparged with a balloon of hydrogen gas for 10 min. The mixture was stirred at room temperature for 18 h under a hydrogen atmosphere. The heterogeneous catalyst was removed from the mixture by filtering through Celite and flushing with EtOAc. The filtrate was neutralized with sat. aq. NaHCO$_3$ (5 mL), extracted with EtOAc (3 x 5 mL), and the combined organic layers were dried over MgSO$_4$, and concentrated *in vacuo*. The crude residue then dissolved in DCM (1.68 mL) and MeOH (2.11 mL) and the mixture was cooled to 0 °C. Et$_3$N

(0.073 mL, 0.52 mmol, 2.0 equiv) was added dropwise followed by Boc_2O (0.072 mL, 0.31 mmol, 1.2 equiv). The mixture was stirred at room temperature for 20 h then H_2O (3 mL) was added. The aqueous layer was extracted with DCM (3 x 5 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (1:1 hexanes/ethyl acetate) yielded carbamate **5.88** (71.1 mg, 0.15 mmol, 57% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.51 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.30 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.15 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.09 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 4.98 (dd, *J* = 11.8, 5.0 Hz, 1H), 3.86 (dd, *J* = 7.6, 4.5 Hz, 2H), 3.73 (s, 3H), 3.71 (s, 3H), 3.71 – 3.66 (m, 2H), 3.31 (d, *J* = 8.1 Hz, 1H), 3.03 – 2.97 (m, 1H), 2.75 (s, 1H), 2.53 – 2.39 (m, 1H), 2.08 – 1.94 (m, 2H), 1.79 (dt, *J* = 13.6, 12.1 Hz, 1H), 1.59 – 1.41 (m, 2H), 1.30 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.7, 168.6, 156.2, 137.8, 135.5, 128.5, 121.9, 119.5, 118.5, 110.9, 107.6, 80.9, 63.0, 56.5, 52.7, 52.7, 51.7, 42.0, 34.2, 32.9, 28.3, 27.9, 27.6. **HRMS** (ESI) calc'd for ([M-H], $C_{25}H_{33}N_2O_7)^-$: m/z = 473.2293, found 473.2296. **IR**: ṽ = 3396 2953, 2929, 1730, 1669, 1246, 1146, 747 cm^{-1}. **$[\alpha]^{20}_D$** = +6.62 (c 1.54, $CHCl_3$).

Dimethyl 2-((10R,11aS)-12-(2-hydroxyethyl)-6-oxo-9,10,11,11a-tetrahydro-6H,8H-pyrido [1',2':3,4]imidazo [1,5-a]indol-10-yl)malonate (5.89)

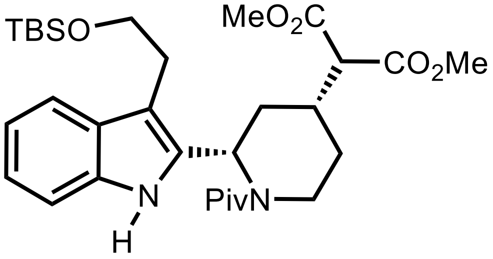


A solution of alcohol **5.88** (7.0 mg, 15 µmol, 1.0 equiv) in THF (0.9 mL) was cooled to 0 °C. Potassium hexamethyldisilazide (1.0 M in THF, 0.04 mL, 44 µmol, 3.0 equiv) was added and the mixture was allowed to warm to room temperature over 2.5 h. MeOH (0.3 mL) and H_2O (2 mL) were added to quench the mixture and the aqueous layer was extracted with EtOAc (3 x 3 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via preparative thin layer chromatography (2:1 hexanes/ethyl acetate) yielded urea **5.89** (2.2 mg, 5.5 µmol, 37% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.30 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 7.23 (td, *J* = 7.6, 1.1 Hz, 1H), 4.60 (dd, *J* = 11.7, 3.8 Hz, 1H), 4.28 (dd, *J* = 13.9, 4.9 Hz, 1H), 3.89 (ddt, *J* = 17.0, 10.6, 5.6 Hz, 2H), 3.76 (d, *J* = 2.0 Hz, 6H), 3.29 (d, *J* = 7.9 Hz, 1H), 3.12 – 3.04 (m, 1H), 2.96 (t, *J* = 6.3 Hz, 2H), 2.57 – 2.46 (m, 1H), 2.44 (d, *J* = 13.0 Hz, 1H), 1.82 (d, *J* = 13.1 Hz, 1H), 1.37 (qd, *J* = 12.7, 5.1 Hz, 1H), 1.32 – 1.23 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.5, 150.3, 136.0, 132.9, 130.7, 123.5, 122.3, 119.2, 112.7, 107.5, 62.4, 56.6, 53.8, 52.8, 39.8, 35.2, 35.1, 29.4, 27.9. *Note*: two malonate carbonyls overlap. **HRMS** (ESI) calc'd for ([M+H],

$C_{21}H_{25}N_2O_6)^+$: m/z = 401.1708, found 401.1707. **IR**: $\tilde{\nu}$ = 2953, 2926, 2855, 1733, 1430, 1252, 1158, 745 cm^{-1}. **$[\alpha]^{20}_{D}$** = –14.38 (c 0.15, $CHCl_3$).

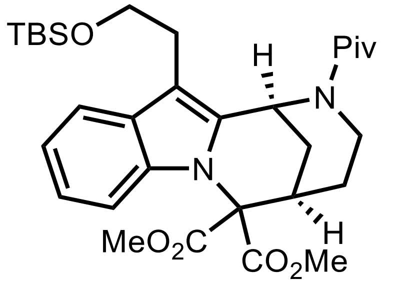
Dimethyl 2-((2S,4R)-2-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-indol-2-yl)-1-pivaloyl-piperidin-4-yl) malonate (5.91)



Phenethyl piperidine **5.90** (150 mg, 0.25 mmol, 1.0 equiv) and palladium on carbon (10 wt%, 135 mg, 0.13 mmol, 0.5 equiv) were added to a vial. MeOH (13 mL) and AcOH (0.9 mL) were added, and the resultant mixture was sparged with a balloon of hydrogen gas for 10 min. The mixture was stirred at room temperature for 18 h under a hydrogen atmosphere. The heterogeneous catalyst was removed from the mixture by filtering through Celite and flushing with EtOAc. The filtrate was neutralized with sat. aq. $NaHCO_3$ (5 mL), extracted with EtOAc (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The crude residue then dissolved in DCM (8.2 mL) and cooled to 0 °C. Et_3N (0.092 mL, 0.66 mmol, 2.6 equiv) followed by PivCl (0.034 mL, 0.28 mmol, 1.1 equiv) were added dropwise. The mixture was warmed to room temperature and stirred for 16 h. The mixture was diluted with DCM (3 mL) and quenched with sat. aq. $NaHCO_3$ (5 mL) and the aqueous layer was extracted with DCM (3 x 5 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (1:1 hexanes/ethyl acetate) yielded amide **5.91** (46.6 mg, 0.08 mmol, 32% yield). *Note: piperidine ring cleavage (**5.98**) has occurred with these reagents; using SureSeal iPr_2EtN and freshly distilled PivCl can circumvent this issue.*

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.15 – 7.10 (m, 1H), 7.09 – 7.03 (m, 1H), 5.31 (dd, *J* = 11.2, 6.3 Hz, 1H), 4.07 – 3.96 (m, 1H), 3.88 – 3.75 (m, 3H), 3.74 (s, 3H), 3.73 (s, 3H), 3.36 (d, *J* = 8.1 Hz, 1H), 3.04 (ddd, *J* = 9.8, 6.7, 3.1 Hz, 2H), 2.45 (ddt, *J* = 15.6, 11.9, 8.2 Hz, 1H), 2.18 – 2.03 (m, 3H), 1.59 (tdd, *J* = 13.3, 7.6, 4.7 Hz, 1H), 1.25 (s, 9H), 0.91 (s, 9H), 0.05 (d, *J* = 2.4 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.8, 168.6, 168.6, 135.4, 135.3, 129.0, 121.8, 119.2, 118.7, 111.0, 108.6, 64.0, 56.2, 52.9, 52.7, 52.7, 39.3, 32.2, 31.3, 28.9, 28.7, 28.5, 27.3, 26.2, 18.6, -5.1. **HRMS** (ESI) calc'd for ([M+H], $C_{31}H_{49}N_2O_6Si)^+$: m/z = 573.3355, found 573.3354. **IR**: $\tilde{\nu}$ = 2953, 2929, 1734, 1608, 1250, 1089, 835, 752 cm^{-1}. **$[\alpha]^{20}_{D}$** = –7.69 (c 0.55, $CHCl_3$).

Dimethyl (1S,5R)-12-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-pivaloyl-2,3,4,5-tetrahydro-1,5-methano[1,4] diazocino[1,2-a]indole-6,6(1H)-dicarboxylate (5.92)



Indole **5.91** (3.0 mg, 5.2 µmol, 1.0 equiv) was dissolved in THF (0.3 mL) and the resulting solution was cooled to 0 °C. *Note: azeotrope starting material with toluene prior to reaction to remove any trace water.* KHMDS (0.1 M in THF, 0.1 mL, 10 µmol, 2.0 equiv) was added dropwise. The mixture was stirred at 0 °C for 1.5 h. An iodine solution (0.1 M in THF, 0.05 mL, 5.2 µmol, 1.0 equiv) was added dropwise along the edge of the reaction vessel. After 15 min, the mixture was quenched with sat. aq. $Na_2S_2O_3$ (1 mL). The aqueous layer was extracted with EtOAc (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified via preparative thin layer chromatography (2:1 hexanes/ethyl acetate) yielded [3.3.1]bicycle **5.92** (1.8 mg, 3.2 µmol, 61% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 – 7.59 (m, 1H), 7.18 – 7.07 (m, 2H), 7.04 (d, *J* = 8.1 Hz, 1H), 6.25 (s, 1H), 3.88 (s, 4H), 3.81 – 3.70 (m, 4H), 3.67 (s, 3H), 3.27 (s, 1H), 3.11 (td, *J* = 13.8, 2.9 Hz, 1H), 2.95 – 2.88 (m, 1H), 2.21 (dd, *J* = 13.6, 3.0 Hz, 1H), 2.09 (dt, *J* = 13.7, 3.4 Hz, 1H), 1.85 (tt, *J* = 14.0, 5.0 Hz, 1H), 1.67 (d, *J* = 14.6 Hz, 1H), 1.23 (s, 9H), 0.83 (s, 9H), -0.08 (d, *J* = 13.3 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.00, 168.34, 168.20, 136.54, 132.02, 129.00, 121.73, 119.92, 119.66, 113.02, 111.83, 77.37, 77.16, 76.95, 71.91, 63.79, 53.35, 53.34, 41.82, 40.80, 38.85, 33.93, 29.85, 29.34, 28.85, 28.38, 27.69, 26.14, 18.48, 1.16, -5.19, -5.25. **HRMS** (ESI) calc'd for ([M+Na], $C_{31}H_{46}N_2O_6SiNa)^+$: m/z = 593.3018, found 593.3017. **IR**: ṽ = 2953, 2927, 2853, 1741, 1626, 1257, 1099, 835 cm^{-1}. **[α]$^{20}_{D}$** = –59.37 (c 0.16, $CHCl_3$).

Silyl Ether Cleavage of 5.91:

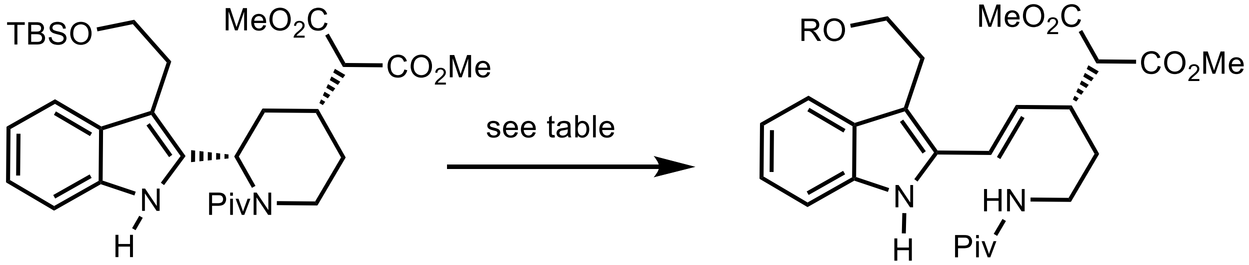
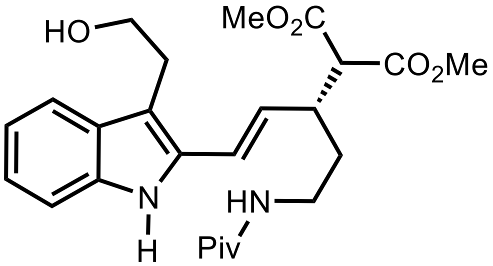


Table 5.1 Conditions employed to cleave silyl ether. Characterization of these products shown below.

Entry	Conditions	Result	Notes
1	TBAF, THF, rt	R = H (**5.97**)	
2	TBAF, THF, –78 °C	R = TBS (**5.98**)	

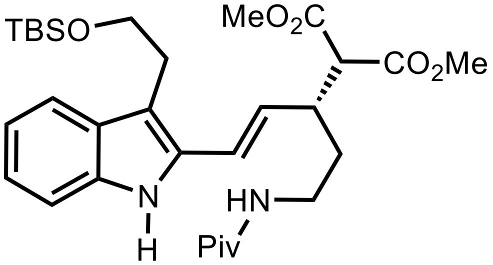
3	TBAF, K_2HPO_4:KH_2PO_4 (pH =7), THF, rt	R = TBS (**5.98**)	*(Ref 27)*[27]
4	TASF, THF, rt	R = H (**5.97**)	
5	HF•pyr, THF, 0 °C to rt	R = H (**5.97**)	
6	HCl, MeOH, rt	R = H (**5.97**)	
7	Al_2O_3, hexanes, rt	R = TBS (**5.98**)	*(Ref 28)*[28]
8	$CeCl_3$, NaI, MeCN, rt	R = TBS (**5.98**)	*(Ref 29)*[29]

Dimethyl (R,E)-2-(1-(3-(2-hydroxyethyl)-1H-indol-2-yl)-5-pivalamidopent-1-en-3-yl)malonate (5.97)



^{1}H NMR (700 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 16.0 Hz, 1H), 5.85 (dd, *J* = 15.8, 8.8 Hz, 2H), 3.87 (dt, *J* = 12.2, 6.3 Hz, 1H), 3.80 (dt, *J* = 19.2, 7.3 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.52 (d, *J* = 8.2 Hz, 1H), 3.34 – 3.28 (m, 2H), 3.05 (qt, *J* = 13.9, 6.4 Hz, 2H), 2.98 (q, *J* = 8.7 Hz, 1H), 1.82 – 1.75 (m, 1H), 1.70 – 1.62 (m, 1H), 1.21 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.9, 168.7, 168.6, 136.5, 132.7, 128.8, 126.2, 123.2, 122.7, 119.8, 119.0, 112.4, 110.8, 63.2, 56.6, 52.8, 52.7, 41.0, 38.9, 37.4, 32.6, 28.0, 27.7.

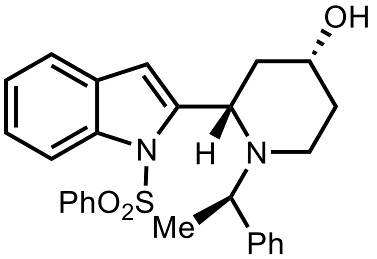
Dimethyl (R,E)-2-(1-(3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-indol-2-yl)-5-pivalamidopent-1-en-3-yl)-malonate (5.98)



^{1}H NMR (700 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.23 (m, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 5.90 – 5.84 (m, 2H), 3.77 (t, *J* = 7.6 Hz, 2H), 3.75 (s, 3H), 3.67 (s, 3H), 3.53 (d, *J* = 8.1 Hz, 1H), 3.36 (dq, *J* = 13.1, 6.3 Hz, 1H), 3.21 (dq, *J* = 13.7, 7.0 Hz, 1H), 2.99 (t, *J* = 7.5 Hz, 3H), 1.82 – 1.76 (m, 1H), 1.73 – 1.66 (m, 1H), 1.19 (s, 9H), 0.88 (s, 9H), 0.01 (s, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 178.7, 168.7, 168.6, 136.4, 132.0, 129.0, 126.6, 123.0, 122.2, 119.6, 119.1, 112.5, 110.7, 64.0, 56.7, 52.8, 52.6, 41.6, 38.8, 37.8, 32.8, 28.2, 27.7, 26.1, 18.5, -5.2. **HRMS** (ESI) calc'd for ([M+H], $C_{31}H_{49}N_2O_6Si)^+$: m/z = 573.3355, found

573.3348. **IR**: ṽ = 2954, 2927, 2855, 1735, 1643, 1256, 1090, 1020, 835, 741 cm^{-1}. **[α]^{20}$_D$** = +3.07 (c 0.13, $CHCl_3$).

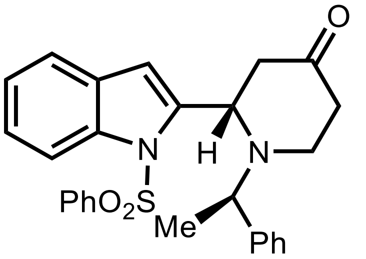
(2S,4R)-1-((R)-1-phenylethyl)-2-(1-(phenylsulfonyl)-1H-indol-2-yl)piperidin-4-ol (5.100)



Known vinylogous amide **5.99** (30. mg, 0.066 mmol, 1 equiv) was dissolved in MeOH (1.3 mL) and cooled to 0 °C. Anhydrous $CeCl_3$ (33 mg, 0.13 mmol, 2 equiv) and $NaBH_4$ (5.0 mg, 0.13 mmol, 2 equiv) were added and the mixture was allowed to warm to room temperature. After stirring for 20 h, H_2O (3 mL) and brine (3 mL) were added, the aqueous layers were extracted with EtOAc (3 x 5 mL), and the combined organic layers were concentrated *in vacuo* to afford a crude reside. Purification by flash column chromatography (eluting with 2:1 to 1:1 hexanes:ethyl acetate) afforded alcohol **5.100** (7.8 mg, 0.017, 26%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (q, *J* = 8.7 Hz, 5H), 7.30 (t, *J* = 7.8 Hz, 3H), 7.22 (dt, *J* = 17.4, 7.5 Hz, 2H), 6.88 (s, 1H), 4.83 (dd, *J* = 10.0, 3.3 Hz, 1H), 4.06 – 3.97 (m, 2H), 2.80 (td, *J* = 11.9, 3.1 Hz, 1H), 2.43 (dt, *J* = 12.1, 4.1 Hz, 1H), 2.02 – 1.94 (m, 1H), 1.87 (ddd, *J* = 13.5, 10.0, 2.7 Hz, 1H), 1.79 – 1.70 (m, 1H), 1.68 – 1.61 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H).

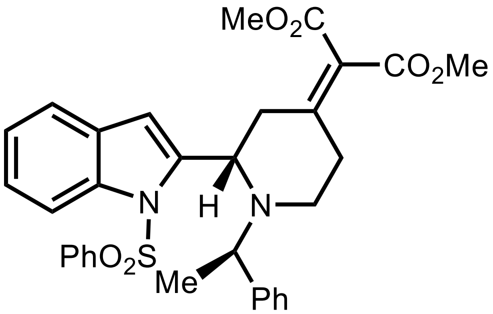
(S)-1-((R)-1-phenylethyl)-2-(1-(phenylsulfonyl)-1H-indol-2-yl)piperidin-4-one (5.102)



Known vinylogous amide **5.99** (2.50 g, 5.48 mmol, 1.0 equiv) was dissolved in THF (71 mL) and cooled to –78 °C. LAH (2.0 M in THF, 3.29 mL, 6.57 mmol, 1.2 equiv) was added dropwise. The mixture was stirred for 1 h and then quenched with sat. aq. Rochelle's salt (15 mL) and brine (30 mL). The mixture was allowed to warm to room temperature and then was extracted with EtOAc (3 x 40 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (1:1 hexanes:EtOAc) yielded ketone **5.102** (1.88 g, 4.10 mmol, 75% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.24 (d, *J* = 8.4 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.45 – 7.37 (m, 4H), 7.32 (t, *J* = 7.6 Hz, 3H), 7.24 (d, *J* = 7.7 Hz, 2H), 6.95 (s, 1H), 5.07 (t, *J* = 6.3 Hz, 1H), 3.88 (q, *J* = 6.8 Hz, 1H), 2.89 (dtd, *J* = 23.0, 10.8, 4.8 Hz, 2H), 2.70 (dd, *J* = 14.8, 5.8 Hz, 1H), 2.63 (dd, *J* = 14.8, 6.9 Hz, 1H), 2.48 (ddd, *J* = 16.6, 10.6, 6.3 Hz, 1H), 2.36 (dt, *J* = 16.1, 3.6 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 208.4, 143.8, 143.7, 139.2, 137.9, 134.1, 129.6, 129.5, 128.4, 127.3, 126.9, 126.3, 125.0, 124.2, 121.1, 115.5, 111.3, 56.9, 55.5, 48.3, 42.7, 41.3, 12.3. **HRMS** (ESI) calc'd for ([M+H], $C_{27}H_{27}N_2O_3S$)$^+$: m/z = 459.1737, found 459.1735. **IR**: ṽ = 2970, 2918, 1718, 1365, 1171, 747, 587 cm^{-1}. **[α]^{20}$_D$** = +6.36 (c 0.66, CHCl$_3$).

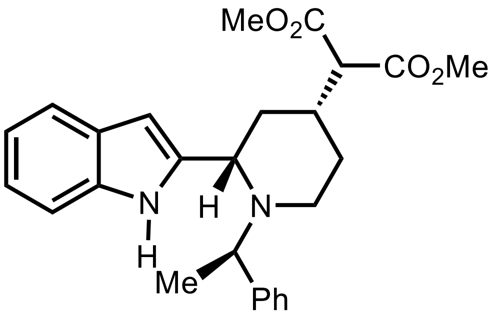
Dimethyl 2-((S)-1-((R)-1-phenylethyl)-2-(1-(phenylsulfonyl)-1H-indol-2-yl)piperidin-4-ylidene) malonate (5.104)



Ketone **5.102** (1.0 g, 2.2 mmol, 1.0 equiv) was dissolved in THF (53 mL) and cooled to 0 °C. TiCl$_4$ (1 M in DCM, 6.5 mL, 6.5 mmol, 3.0 equiv) was added dropwise followed by addition of dimethyl malonate (0.5 mL, 4.4 mmol, 2.0 equiv) and pyridine (1.4 mL, 17.0 mmol, 8.0 equiv). The mixture was stirred at 0 °C for 30 min and then warmed to 25 °C for approximately 18 h. A white precipitate forms over the course of the reaction. The mixture was quenched upon addition of H$_2$O (10 mL) and was subsequently extracted with EtOAc (3 x 10 mL). The organic layers were combined, dried over MgSO$_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (1:1 hexanes:EtOAc) yielded vinylidene malonate **5.104** with trace dimethylmalonate (0.68 g). The impure product was subjected directly to the next step; however, an analytical sample was obtained through additional column chromatography (100% hexanes → 1:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.22 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.54 – 7.49 (m, 1H), 7.49 – 7.44 (m, 1H), 7.44 – 7.35 (m, 4H), 7.34 – 7.27 (m, 3H), 7.24 – 7.17 (m, 2H), 6.96 (s, 1H), 4.85 (dd, *J* = 6.9, 5.0 Hz, 1H), 3.79 – 3.74 (m, 1H), 3.73 (s, 3H), 3.60 (s, 3H), 3.33 (dd, *J* = 14.1, 4.9 Hz, 1H), 2.90 – 2.83 (m, 1H), 2.80 – 2.74 (m, 1H), 2.74 – 2.57 (m, 3H), 1.17 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 166.2, 165.3, 157.2, 144.1, 143.9, 139.1, 137.8, 133.9, 129.8, 129.5, 128.3, 127.3, 126.7, 126.5, 124.6, 124.0, 123.4, 121.1, 115.3, 111.4, 56.9, 56.3, 52.3, 52.1, 43.0, 39.3, 32.1, 12.1. **HRMS** (ESI) calc'd for ([M+H], $C_{32}H_{33}N_2O_6S$)$^+$: m/z = 573.2054, found 573.2055. **IR**: ṽ = 2951, 2924, 1721, 1215, 747, 588, 571 cm^{-1}. **[α]^{20}$_D$** = +67.83 (c 0.23, CHCl$_3$).

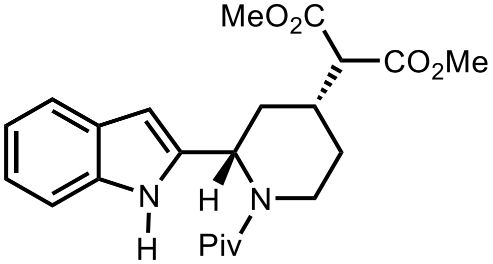
Dimethyl 2-((2S,4R)-2-(1H-indol-2-yl)-1-((R)-1-phenylethyl)piperidin-4-yl)malonate (5.105)



Vinylidene malonate **5.104** (0.68 mg, 1.2 mmol, 1.0 equiv), with slight impurities, was dissolved in THF (7.8 mL) and MeOH (0.24 mL, 6.9 mmol, 5.0 equiv). Lithium metal (82 mg, 12 mmol, 10.0 equiv) was added and then the mixture was cooled to –78 °C. Ammonia (5 mL) was condensed into the reaction vessel producing a deep blue colored solution. The blue solution was allowed to stir for 5 minutes before sat. aq. NH_4Cl (5 mL) and sat. aq. $NaHCO_3$ (5 mL) were added to quench the mixture. The solution was allowed to warm to room temperature to boil off the ammonia and then extracted with EtOAc (3 x 50 mL). The organic layers were combined, washed with brine (2 x 20 mL) 1 M NaOH (2 x 20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. *Note: thiophenol is produced in this reaction, NaOH wash should remove it from solution, but caution should be taken in case some remains in the organic mixture.* Purification of the crude residue via column chromatography (5% MeOH in DCM) yielded malonate **5.105** (0.39 mg, 0.90 mmol, 5:1 dr, 41% yield over two steps).

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 8.6 Hz, 3H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.17 – 7.13 (m, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 3.92 (dd, *J* = 11.2, 2.9 Hz, 1H), 3.85 (q, *J* = 6.8 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.21 (d, *J* = 9.1 Hz, 1H), 2.69 (dt, *J* = 11.8, 3.6 Hz, 1H), 2.36 (td, *J* = 12.0, 2.4 Hz, 1H), 2.33 – 2.26 (m, 1H), 1.97 (dq, *J* = 13.0, 3.1 Hz, 1H), 1.67 (dd, *J* = 16.0, 8.0 Hz, 2H), 1.34 (qd, *J* = 12.2, 3.8 Hz, 1H), 1.26 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 168.8, 168.8, 143.7, 140.4, 136.1, 128.1, 127.5, 126.6, 121.8, 120.3, 119.9, 111.0, 101.1, 58.0, 57.3, 55.9, 52.6, 52.6, 44.2, 39.3, 36.9, 30.2, 8.8. *Note: Two aryl peaks are overlapping.* **HRMS** (ESI) calc'd for ([M+H], $C_{26}H_{31}N_2O_4$)$^+$: m/z = 435.2278, found 435.2283. **IR**: ṽ = 2953, 2919, 1731, 1632, 1454, 1289, 1090, 1021 cm^{-1}. **$[\alpha]^{20}_D$** = +26.03 (c 0.78, $CHCl_3$).

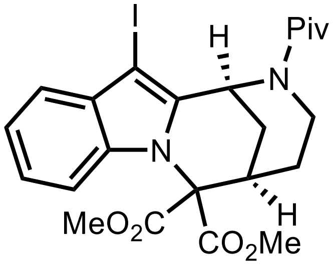
Dimethyl 2-((2S,4R)-2-(1H-indol-2-yl)-1-pivaloylpiperidin-4-yl)malonate (5.107)



Phenethyl piperidine **5.105** (100 mg, 0.23 mmol, 1.0 equiv) and palladium on carbon (10 wt%, 123 mg, 0.12 mmol, 0.5 equiv) were added to a vial. MeOH (15 mL) and AcOH (0.42 mL) were added, and the resultant mixture was sparged with a balloon of hydrogen gas for 10 min. The mixture was stirred at room temperature for 18 h under a hydrogen atmosphere. The heterogeneous catalyst was removed from the mixture by filtering through Celite and flushing with EtOAc. The filtrate was concentrated *in vacuo,* diluted with EtOAc (10 mL), neutralized with sat. aq. $NaHCO_3$ (5 mL), extracted with EtOAc (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The crude residue then dissolved in DCM (7 mL) and cooled to 0 °C. *i*Pr_2EtN (0.1 M in THF, 4.2 mL, 0.42 mmol, 1.8 equiv) followed by PivCl (0.1 M in THF, 4.2 mL, 0.42 mmol, 1.8 equiv) were added dropwise. The mixture was warmed to room temperature and stirred for 16 h. The mixture was diluted with DCM (3 mL) and quenched with H_2O (3 mL) and sat. aq. $NaHCO_3$ (3 mL) and the aqueous layer was extracted with DCM (3 x 5 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude residue via column chromatography (2:1 to 1:1 hexanes/ethyl acetate) yielded amide **5.107** (23 mg, 0.05 mmol, 24% yield).

Major rotamer: ^{1}H NMR (600 MHz, DMSO) δ 10.46 (s, 1H), 7.43 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.34 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.06 – 7.00 (m, 1H), 6.99 – 6.92 (m, 1H), 6.15 (dt, *J* = 2.1, 1.0 Hz, 1H), 5.53 – 5.48 (m, 1H), 4.07 (ddt, *J* = 14.6, 8.1, 1.9 Hz, 1H), 3.66 (s, 3H), 3.66 (s, 3H), 3.43 (d, *J* = 9.1 Hz, 1H), 3.42 – 3.36 (m, 1H), 2.30 (dtdd, *J* = 10.3, 8.6, 7.0, 3.8 Hz, 1H), 2.20 (dddd, *J* = 13.8, 7.3, 3.8, 1.1 Hz, 1H), 2.03 – 1.92 (m, 2H), 1.49 (dddd, *J* = 13.7, 8.3, 5.6, 2.6 Hz, 1H), 1.26 (s, 9H). *[Note: NMR spectra of the rotamers were taken using VT NMR at 100 °C]*
Minor rotamer: ^{1}H NMR (600 MHz, DMSO) δ 10.27 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.39 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.06 – 7.00 (m, 1H), 6.99 – 6.92 (m, 1H), 6.31 (dt, *J* = 2.2, 1.1 Hz, 1H), 5.92 – 5.89 (m, 1H), 4.24 (d, *J* = 14.1 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.43 (d, *J* = 8.0 Hz, 1H), 3.01 – 2.93 (m, 1H), 2.55 – 2.46 (m, 1H), 2.41 (dq, *J* = 13.6, 2.7 Hz, 1H), 2.03 – 1.92 (m, 1H), 1.70 – 1.61 (m, 2H), 1.31 (s, 9H). *[Note: NMR spectra of the rotamers were taken using VT NMR at 100 °C]*
Mixture of rotamers: ^{13}C NMR (151 MHz, DMSO) δ 176.0, 175.5, 167.8, 167.7, 167.7, 140.1, 137.4, 136.1, 135.9, 127.6, 127.4, 120.2, 120.0, 119.0, 118.9, 118.3, 118.2, 110.7, 110.5, 99.3, 96.8, 55.8, 54.4, 51.5, 51.5, 51.5, 51.5, 49.6, 48.5, 41.1, 38.5, 38.1, 37.9, 31.5, 31.3, 30.3, 30.2, 28.7, 27.8, 27.7, 26.6. *[Note: NMR spectra of the rotamers were taken using VT NMR at 100 °C]*
HRMS (ESI) calc'd for ([M+Na], $C_{23}H_{30}N_2NaO_5)^+$: m/z = 437.2047, found 437.2052. **IR**: ṽ = 3384, 2954, 1734, 1606, 1432, 1297, 1200, 736 cm^{-1}. **[α]$^{20}_D$** = –79.45 (c 0.15, $CHCl_3$).

Dimethyl (1S,5R)-12-iodo-2-pivaloyl-2,3,4,5-tetrahydro-1,5-methano[1,4]diazocino[1,2-a]indole-6,6(1H)-dicarboxylate (5.108)

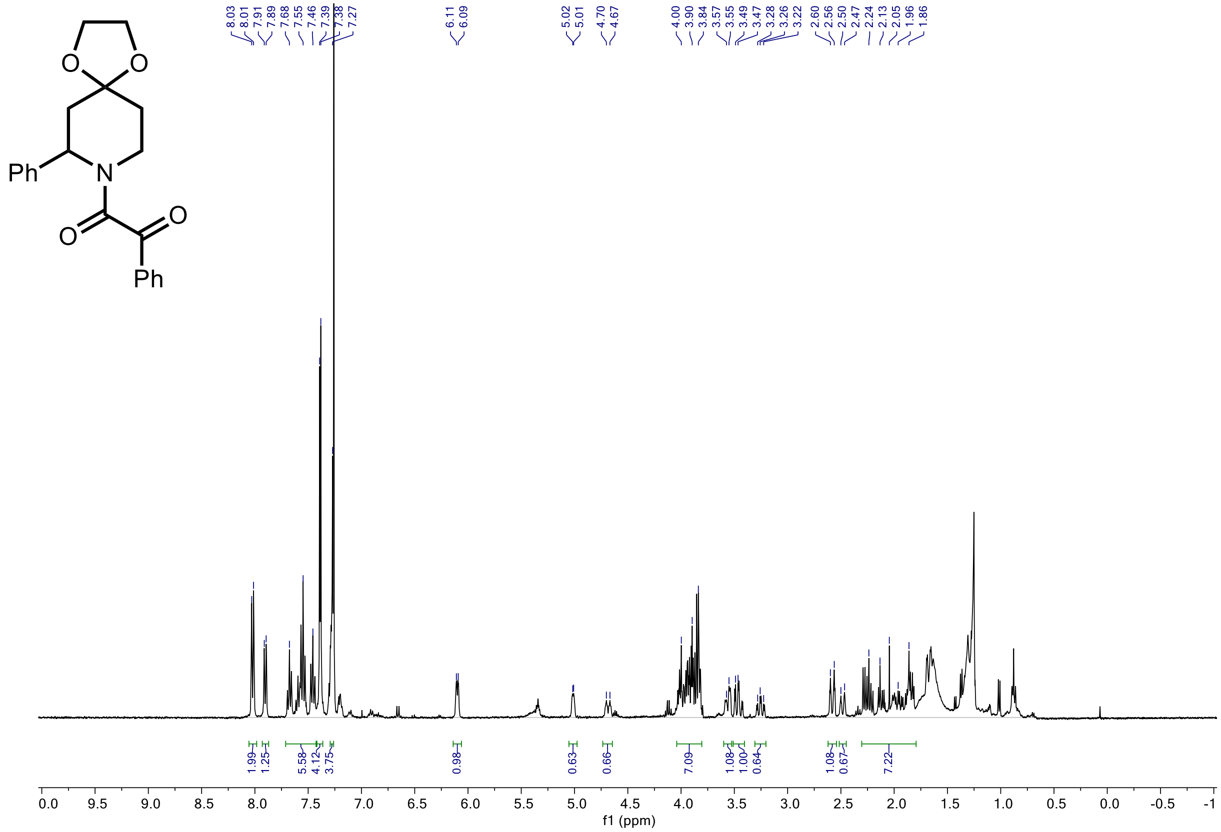


Amide **5.107** (3.0 mg, 7.2 µmol, 1.0 equiv) was dissolved in THF (0.3 mL) and the resulting solution was cooled to 0 °C. *Note: azeotrope starting material with toluene prior to reaction to remove any trace water.* KHMDS (0.5 M in THF, 35 µL, 17 µmol*,* 2.4 equiv) was added dropwise. The mixture was stirred at 0 °C for 1.5 h. An iodine solution (0.1 M in THF, 87 µL, 8.7 µmol, 1.2 equiv) was added dropwise along the edge of the reaction vessel. The mixture was warmed to room temperature and after 30 min it was quenched with sat. aq. $Na_2S_2O_3$ (1 mL). The aqueous layer was extracted with EtOAc (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified via preparative thin layer chromatography (1:1 hexanes/ethyl acetate) yielded iodinated [3.3.1]bicycle **5.108** (1.6 mg, 3.0 µmol, 41% yield).

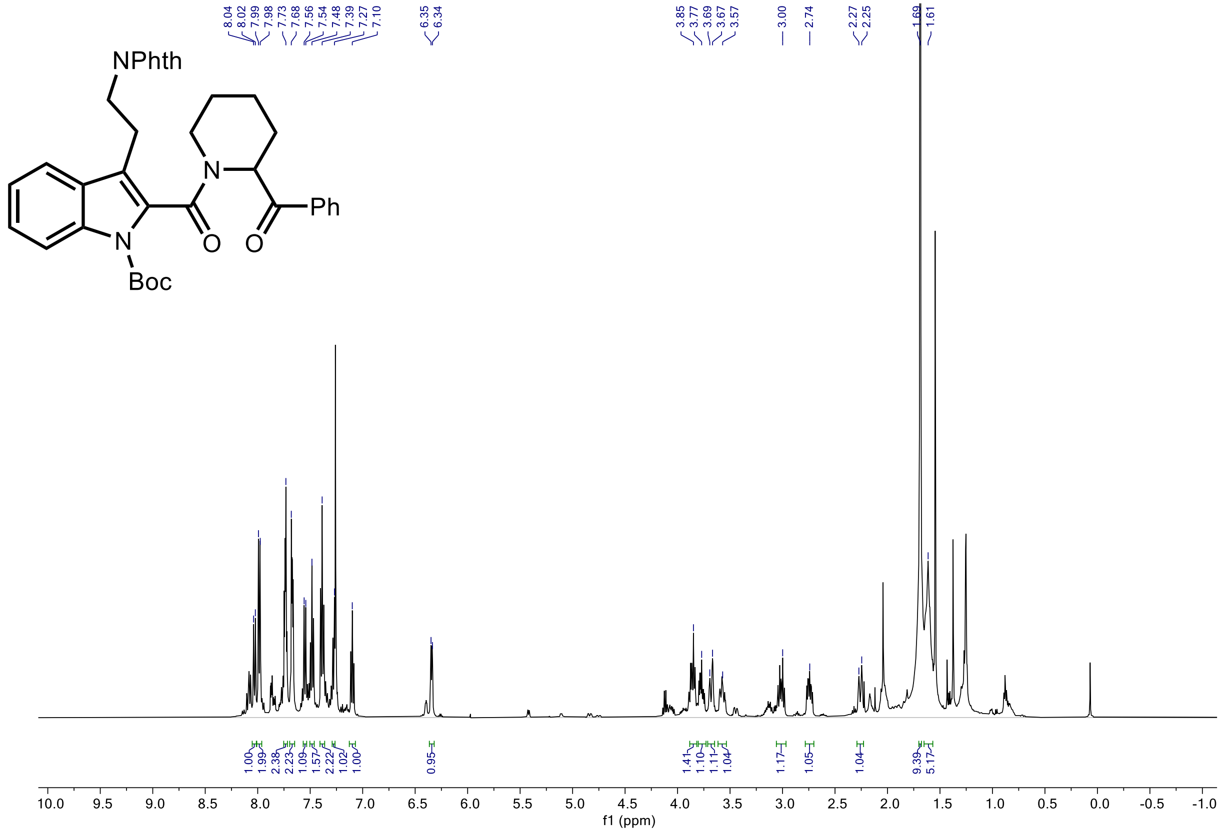
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 6.4, 2.7 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.07 – 7.04 (m, 1H), 6.15 (s, 1H), 3.87 (s, 3H), 3.87 – 3.82 (m, 1H), 3.72 (s, 3H), 3.34 (s, 1H), 3.01 (td, *J* = 13.8, 2.9 Hz, 1H), 2.24 – 2.13 (m, 2H), 1.84 (tt, *J* = 13.9, 5.0 Hz, 1H), 1.66 (d, *J* = 14.7 Hz, 1H), 1.26 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.3, 167.7, 167.7, 136.9, 136.4, 130.6, 123.0, 121.5, 121.4, 113.4, 72.3, 61.7, 53.6, 53.5, 44.5, 41.0, 39.0, 34.4, 29.3, 28.5, 28.4. **HRMS** (ESI) calc'd for ([M+H], $C_{23}H_{28}IN_2O_5$)$^+$: m/z = 539.1038, found 539.1043. **IR**: ṽ = 2954, 2926, 1740, 1627, 1411, 1262, 1175, 745 cm^{-1}. **$[\alpha]^{20}_D$** = –115.22 (c 0.05, $CHCl_3$).

5.11.2 NMR Spectral Data for Chapter 5

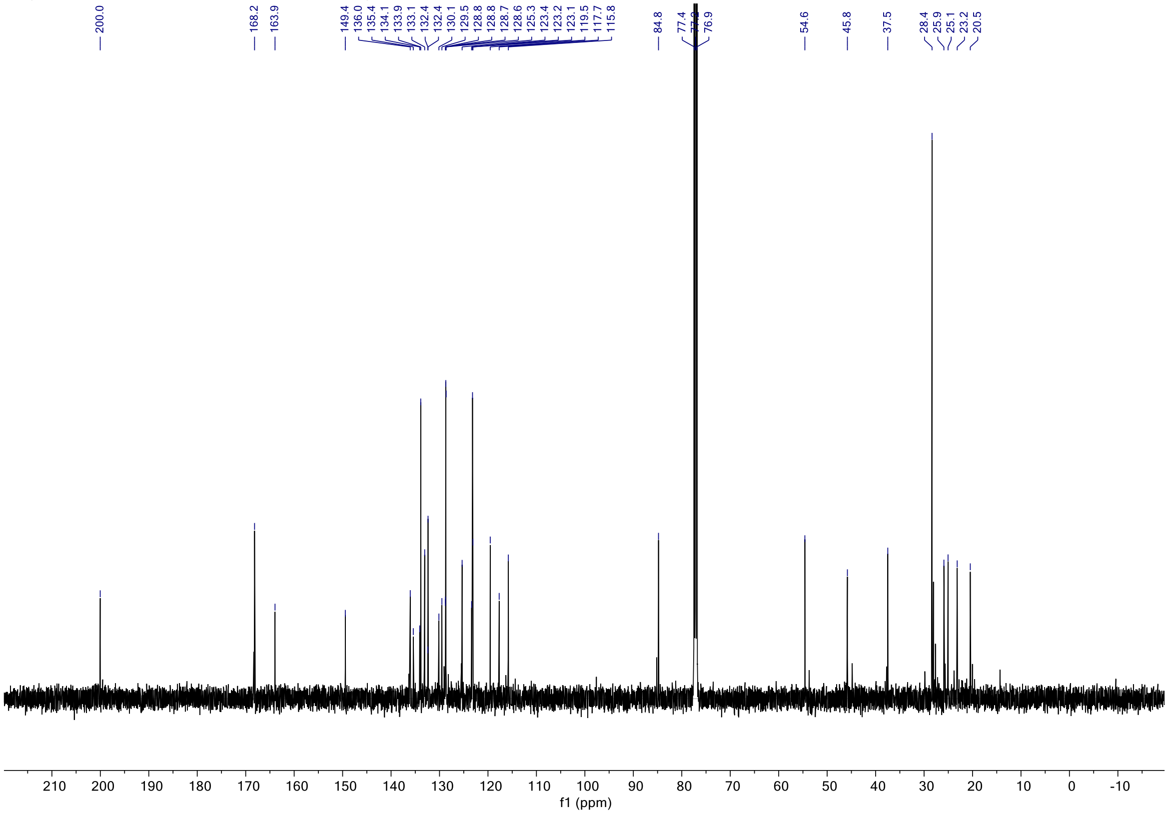
5.63 (^{1}H NMR, 400 MHz, $CDCl_3$)



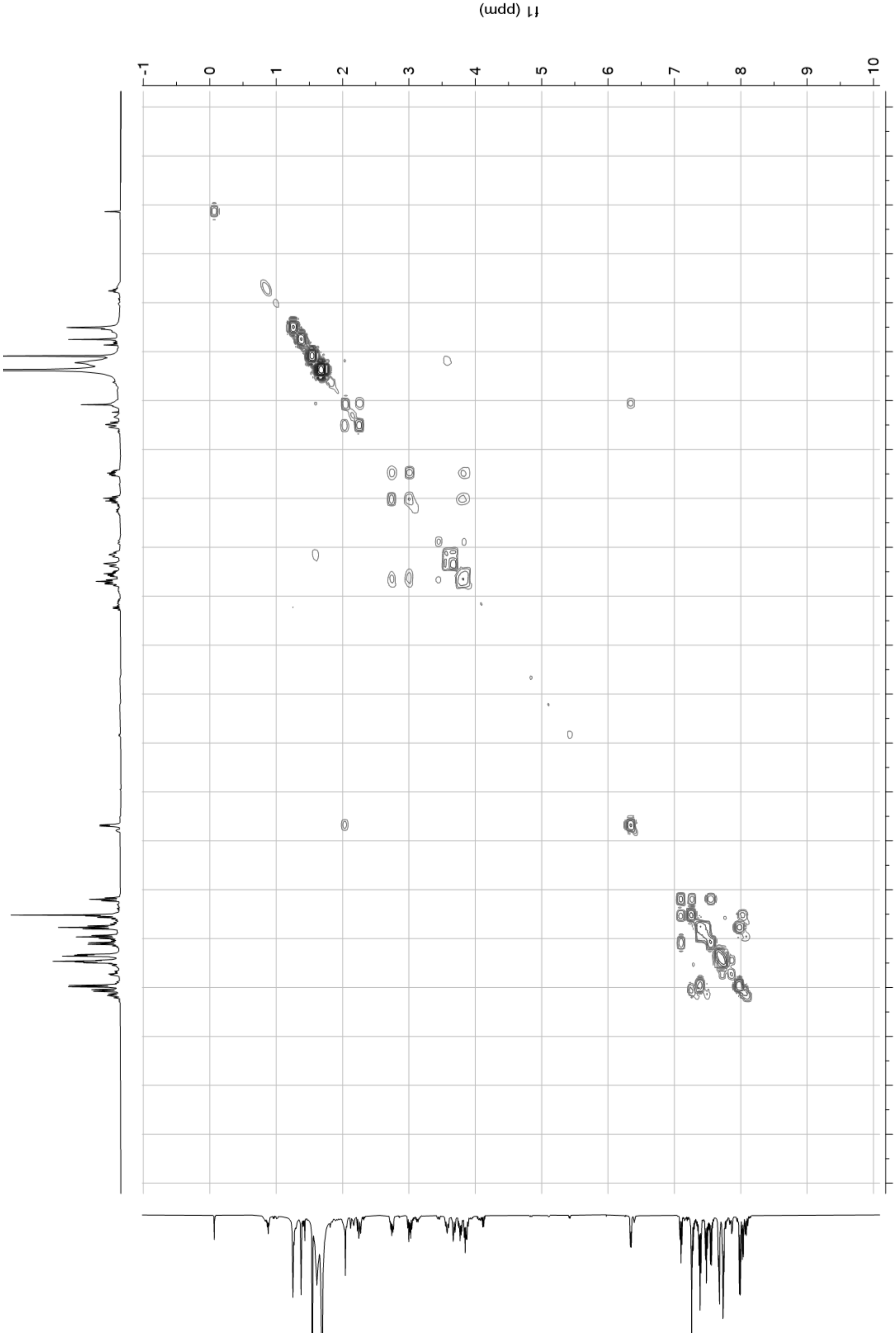
5.65 (^{1}H NMR, 500 MHz, CDCl$_3$)



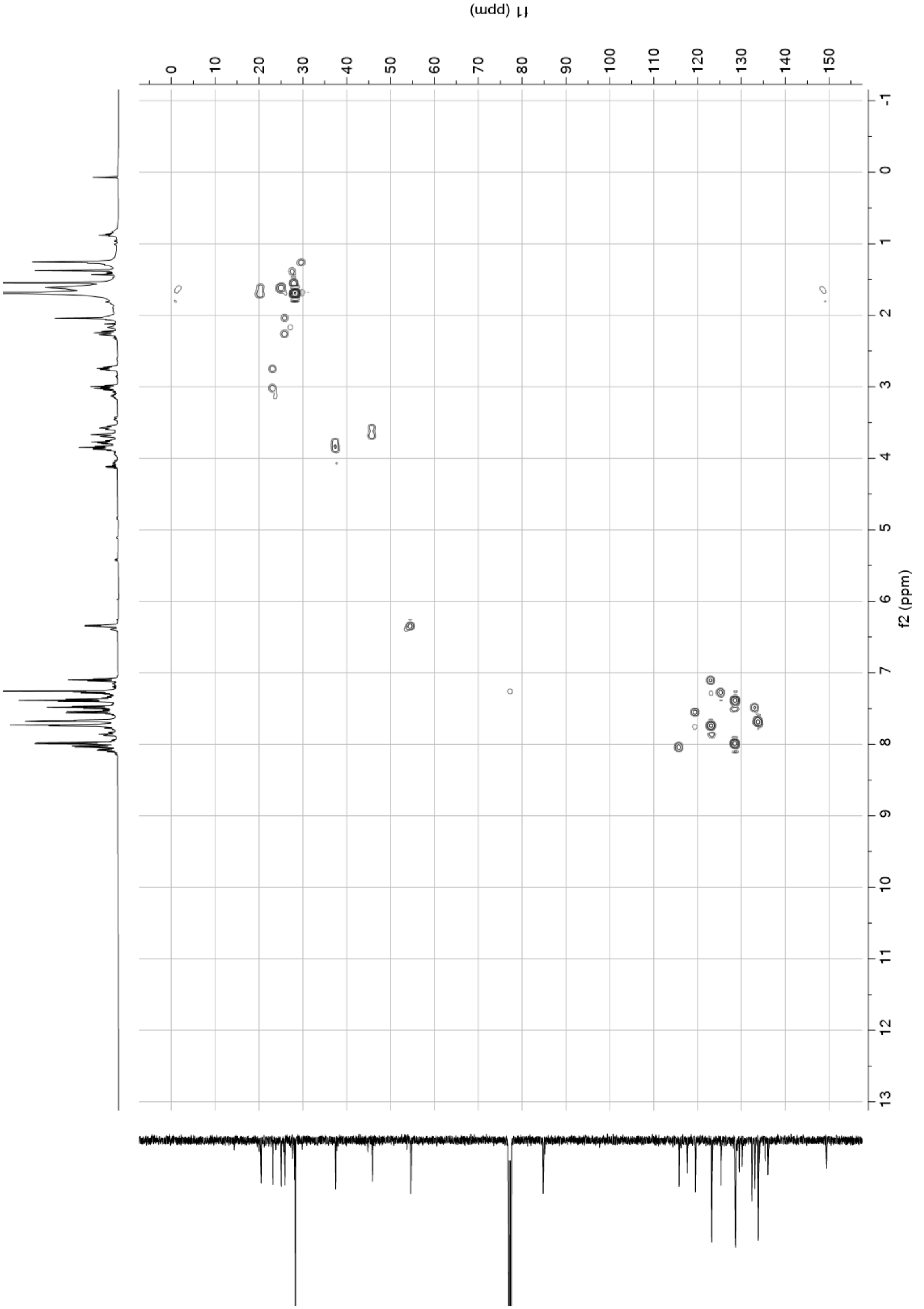
5.65 (^{13}C NMR, 126 MHz, CDCl$_3$)



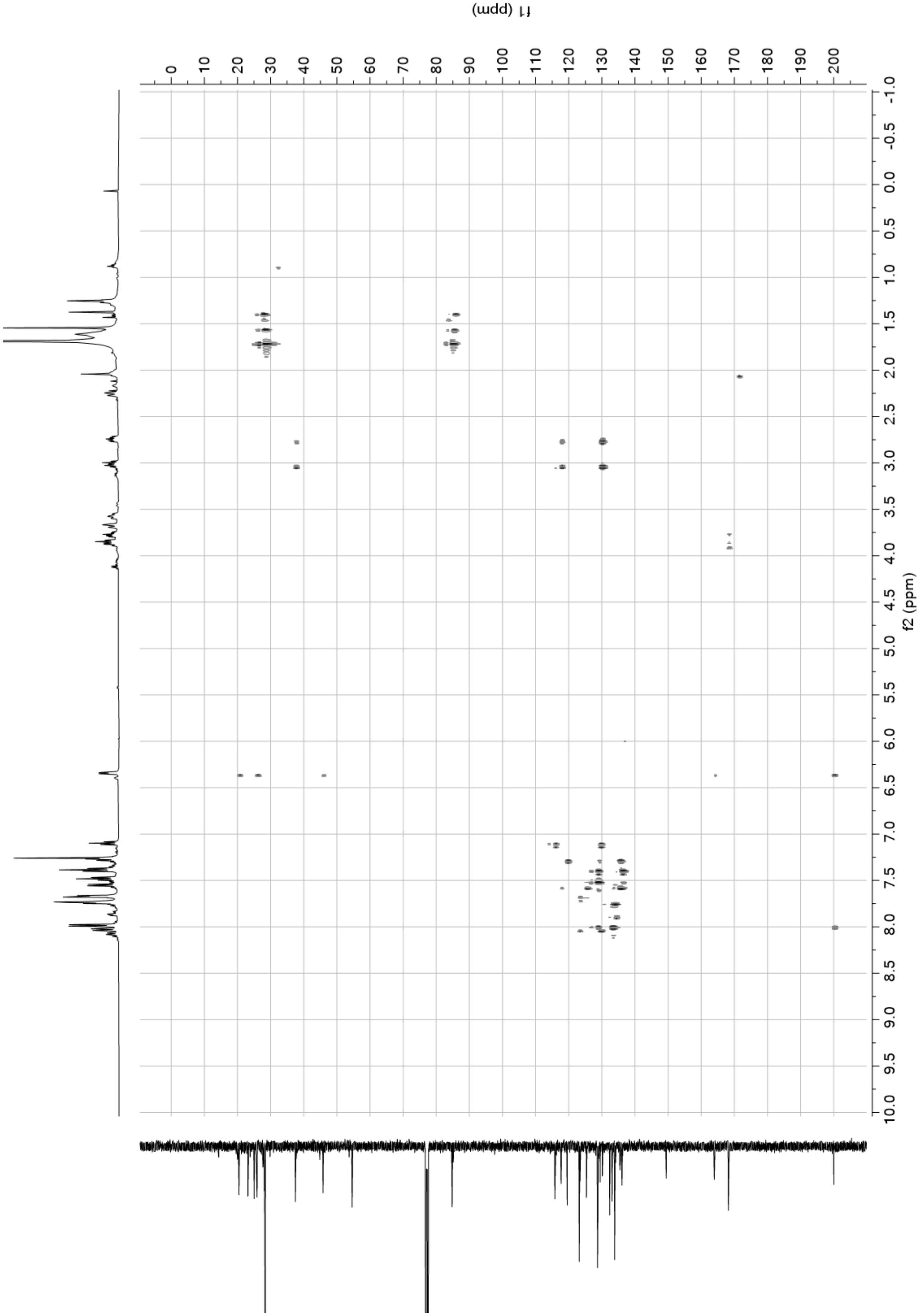
5.65 (COSY, $CDCl_3$)



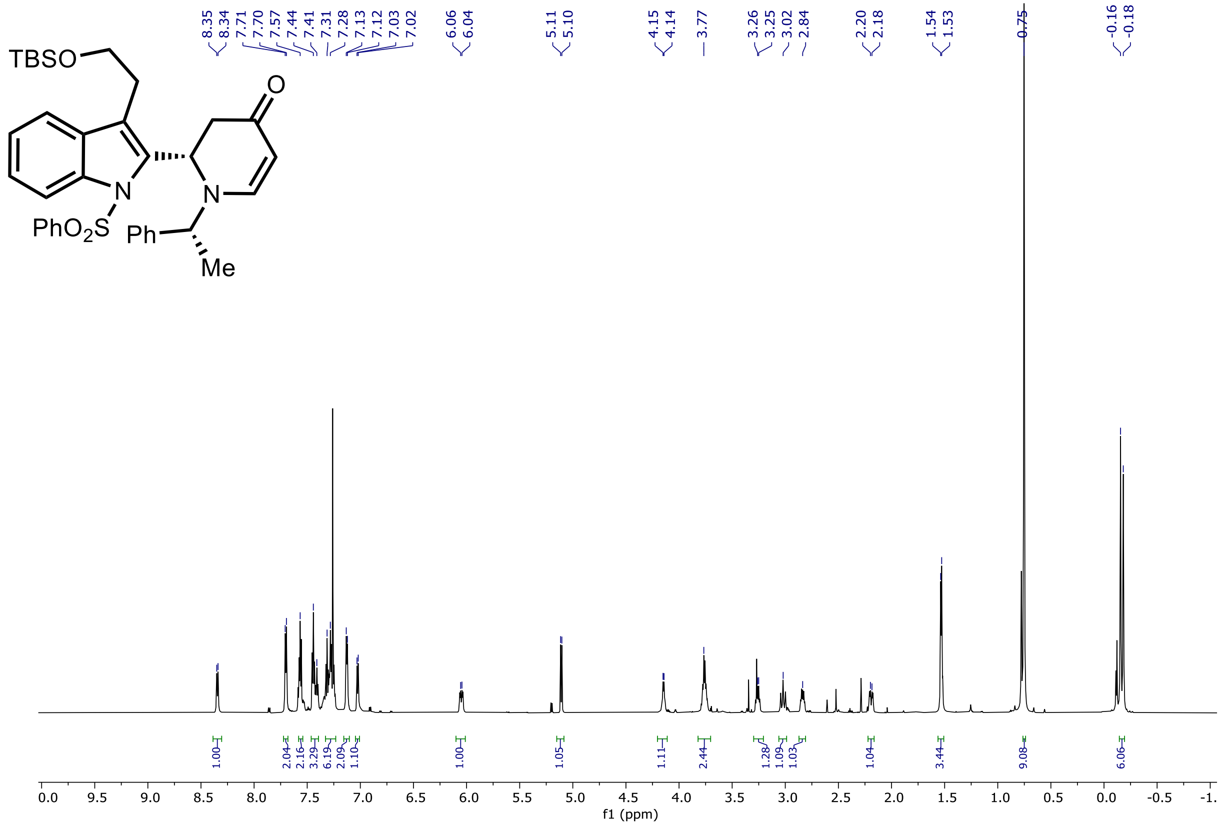
5.65 (HSQC, $CDCl_3$)



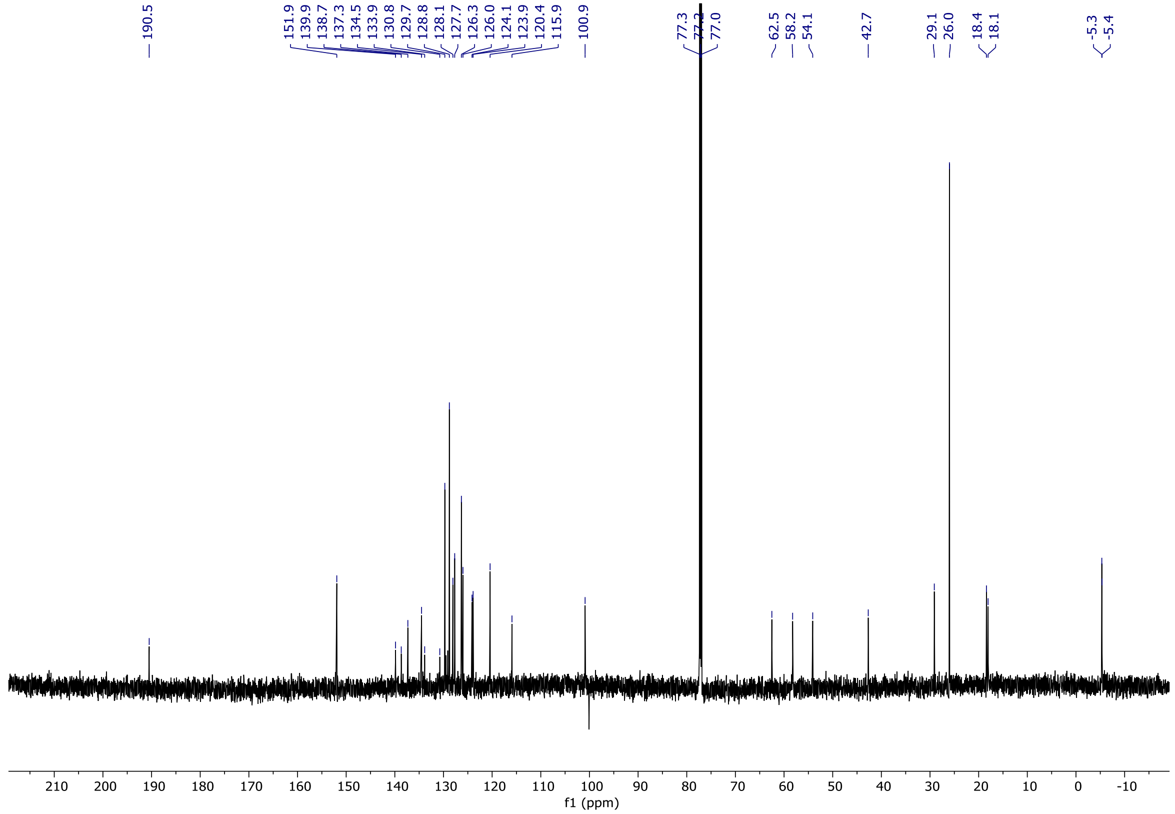
5.65 (HMBC, $CDCl_3$)



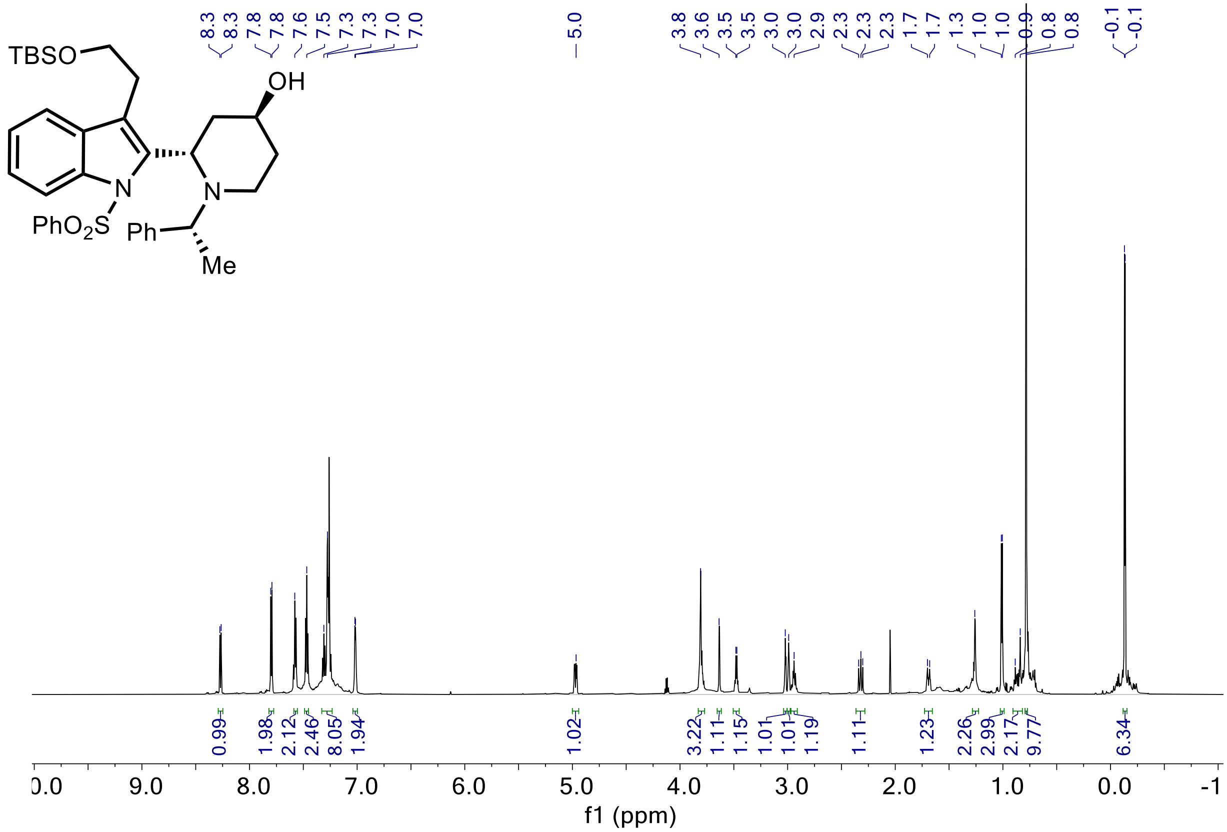
5.66 (^{1}H NMR, 700 MHz, CDCl$_3$)



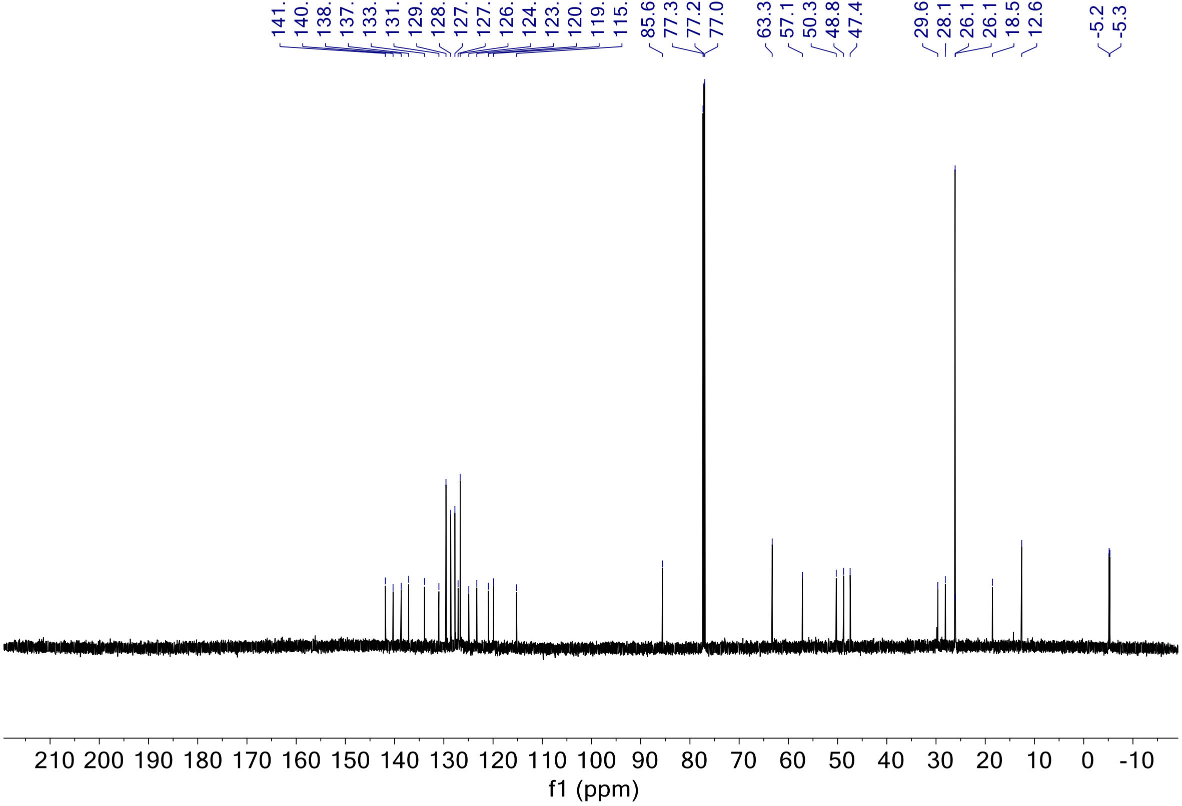
5.66 (^{13}C NMR, 176 MHz, CDCl$_3$)



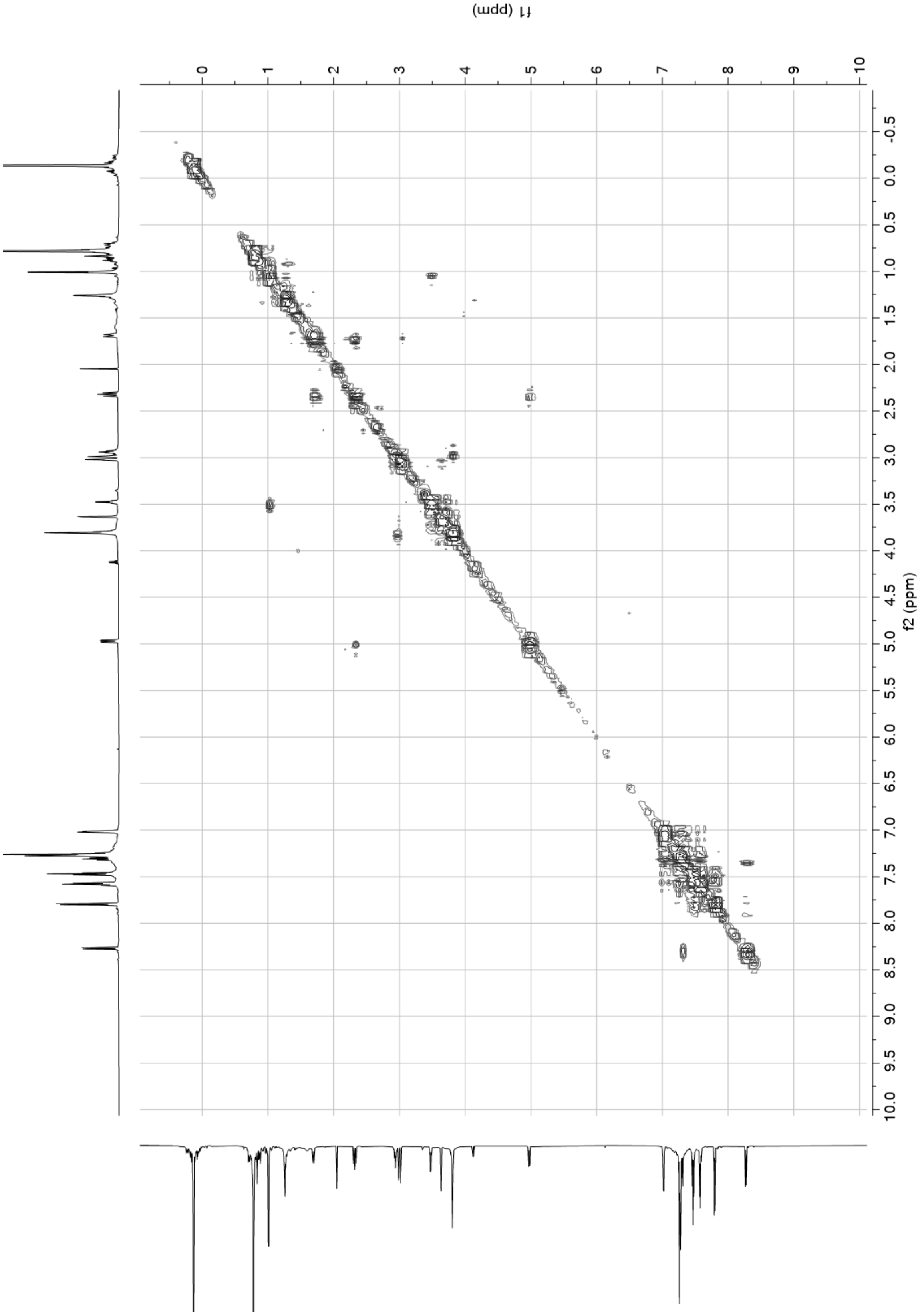
5.72 (^{1}H NMR, 700 MHz, CDCl$_3$)



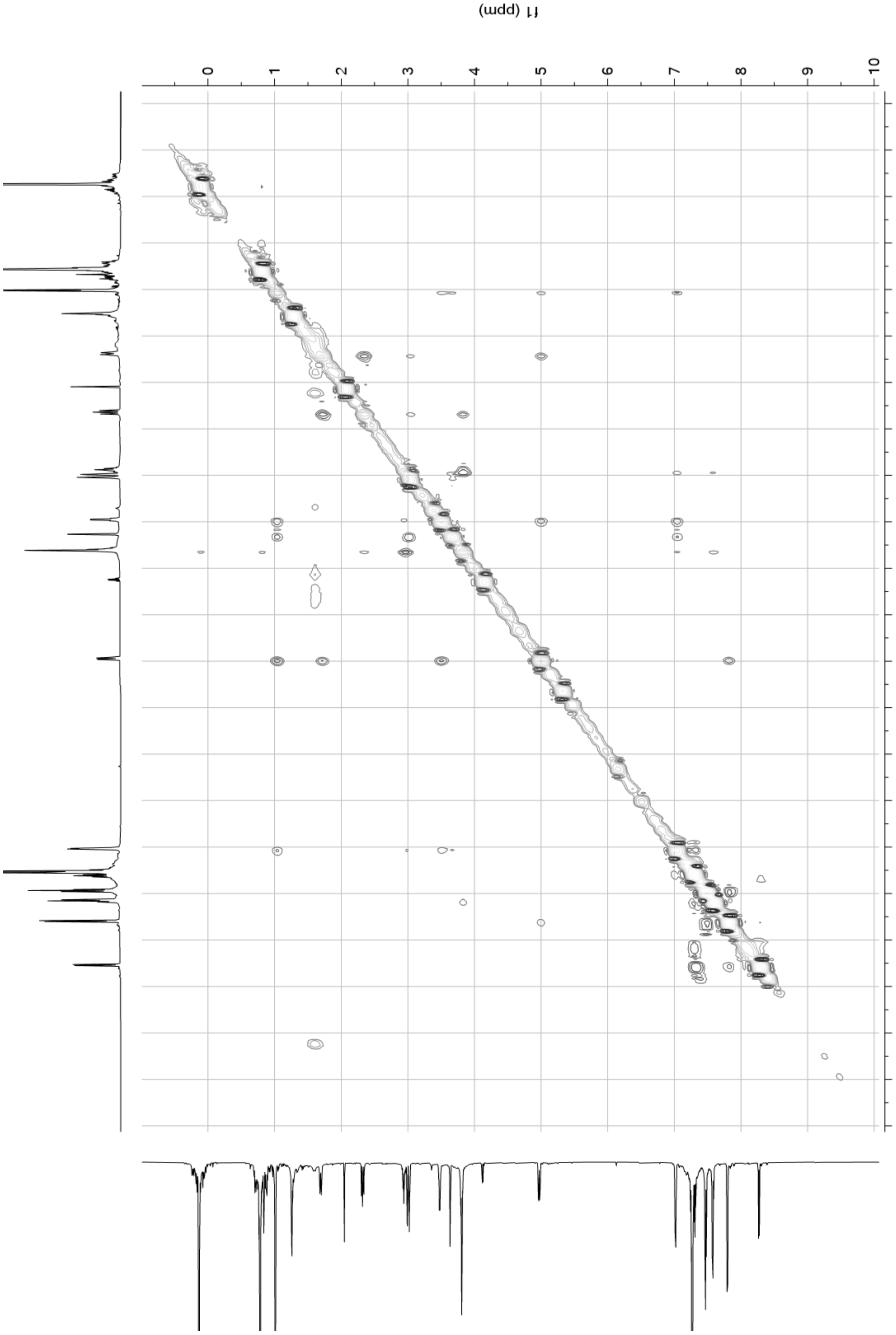
5.72 (^{13}C NMR, 176 MHz, CDCl$_3$)



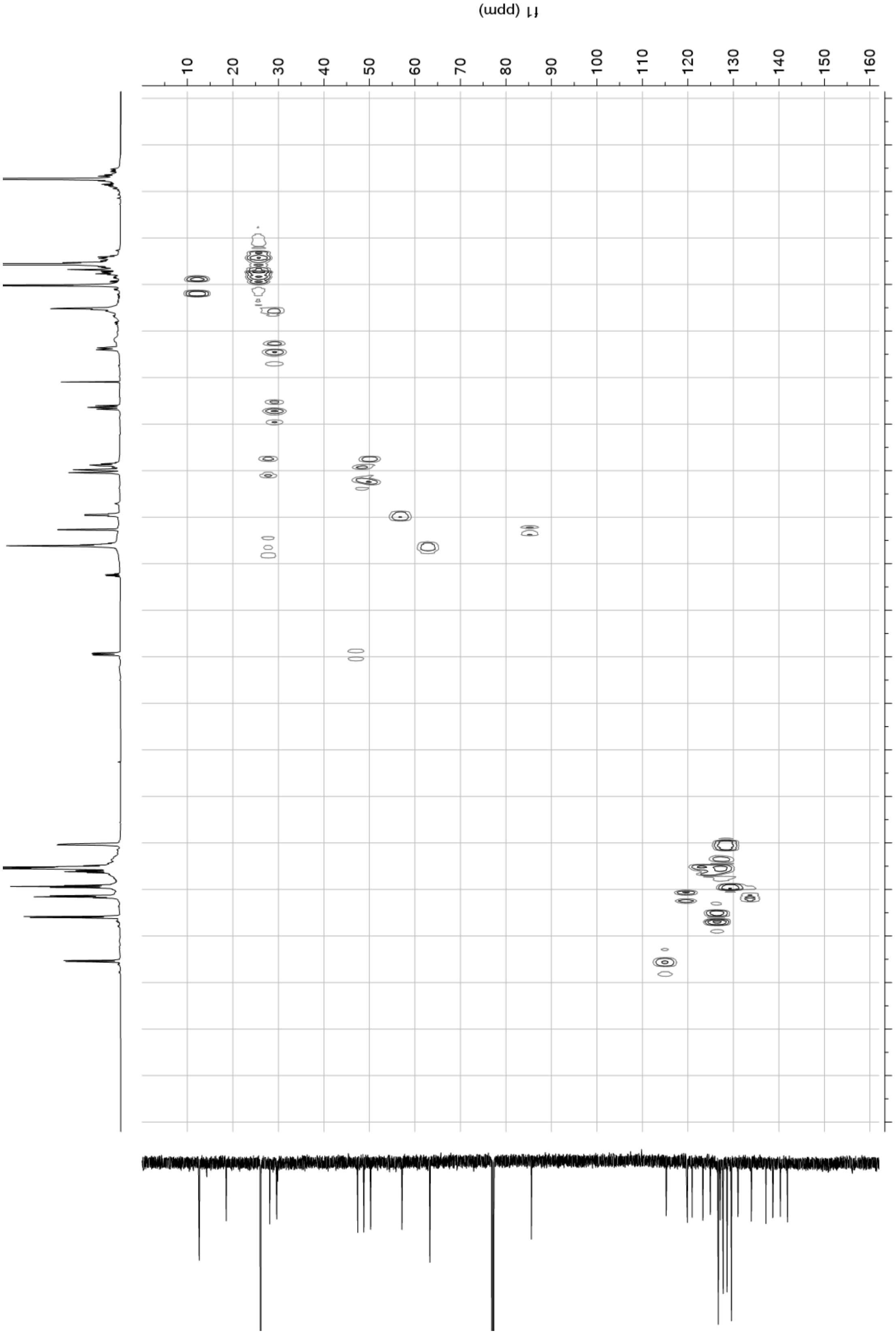
5.72 (COSY, $CDCl_3$)



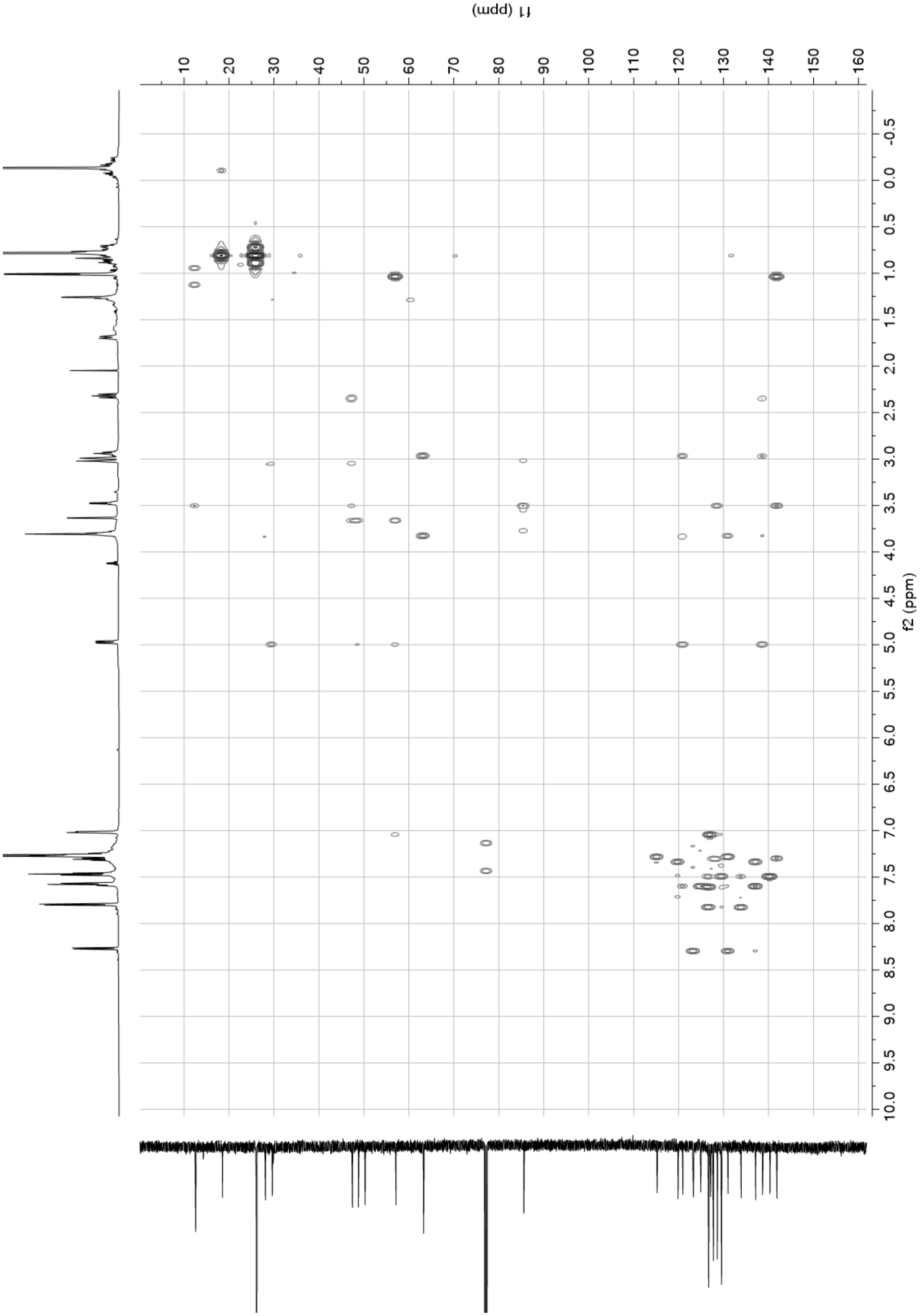
5.72 (NOESY, $CDCl_3$)



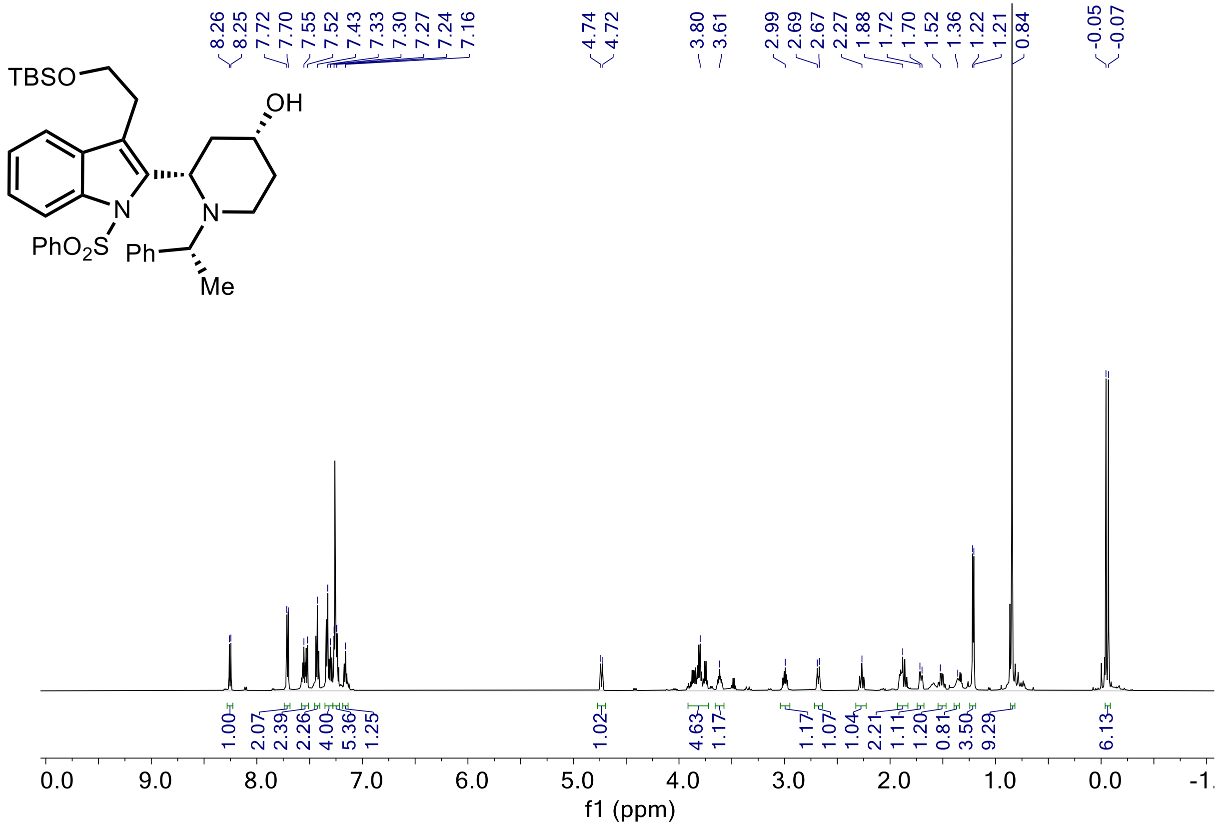
5.72 (HSQC, $CDCl_3$)



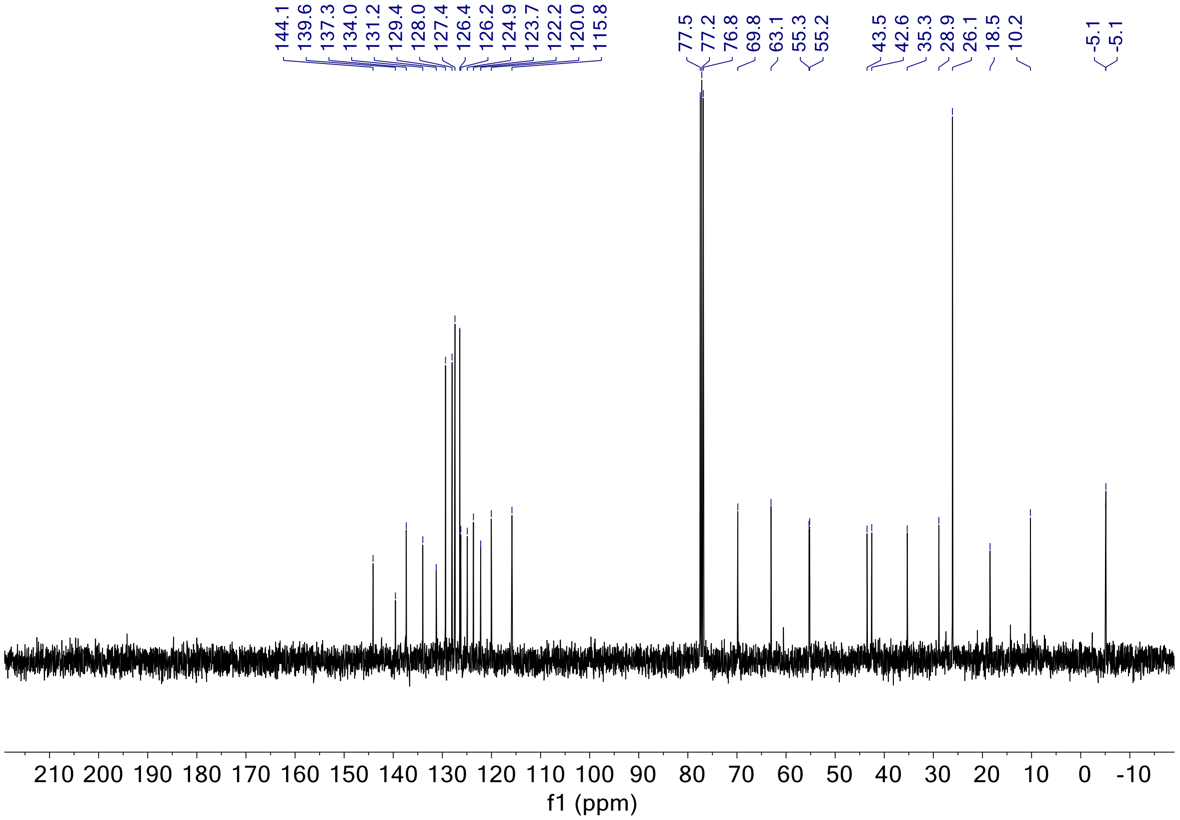
5.72 (HMBC, CDCl$_3$)



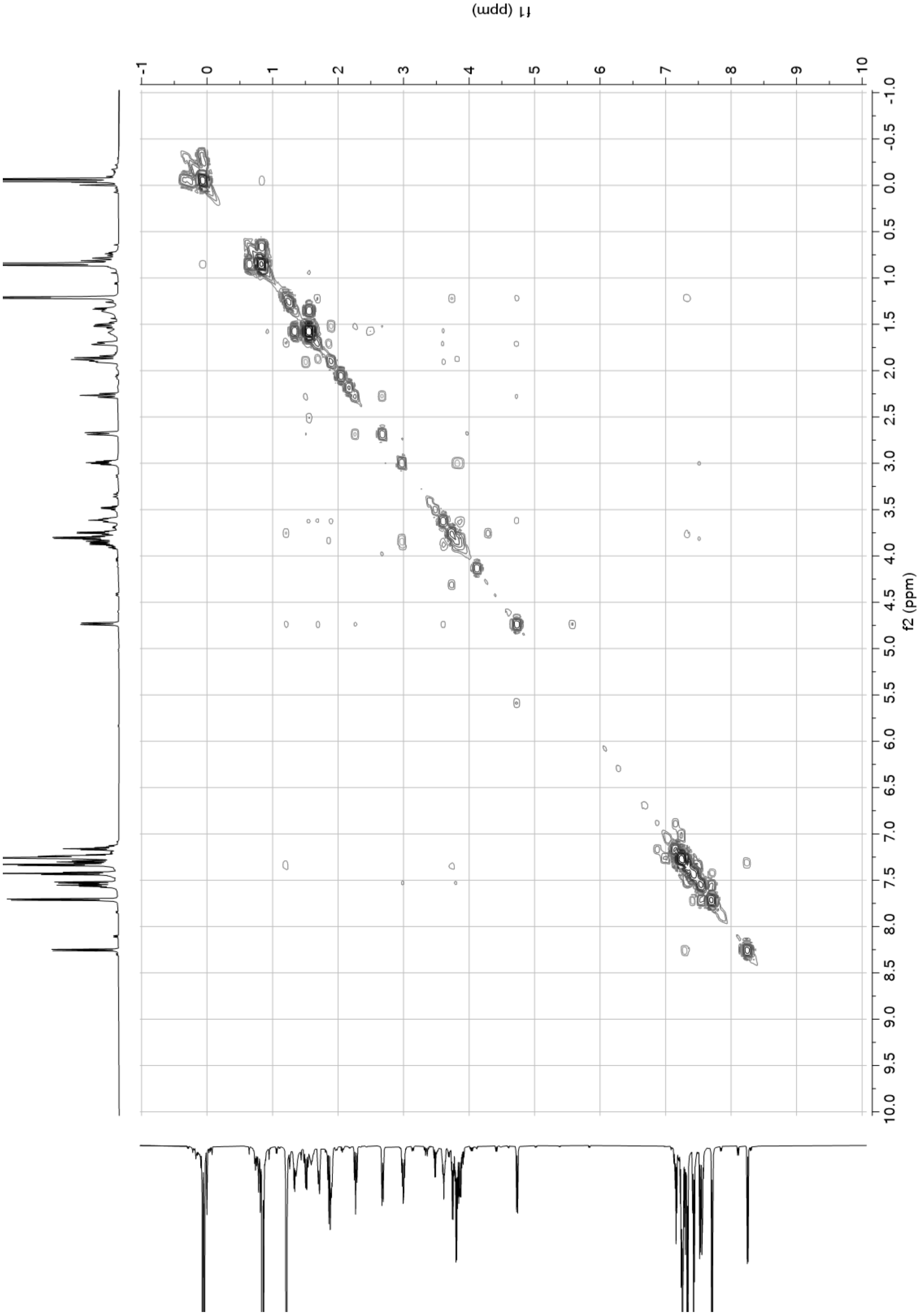
5.74 (^{1}H NMR, 600 MHz, CDCl$_3$)



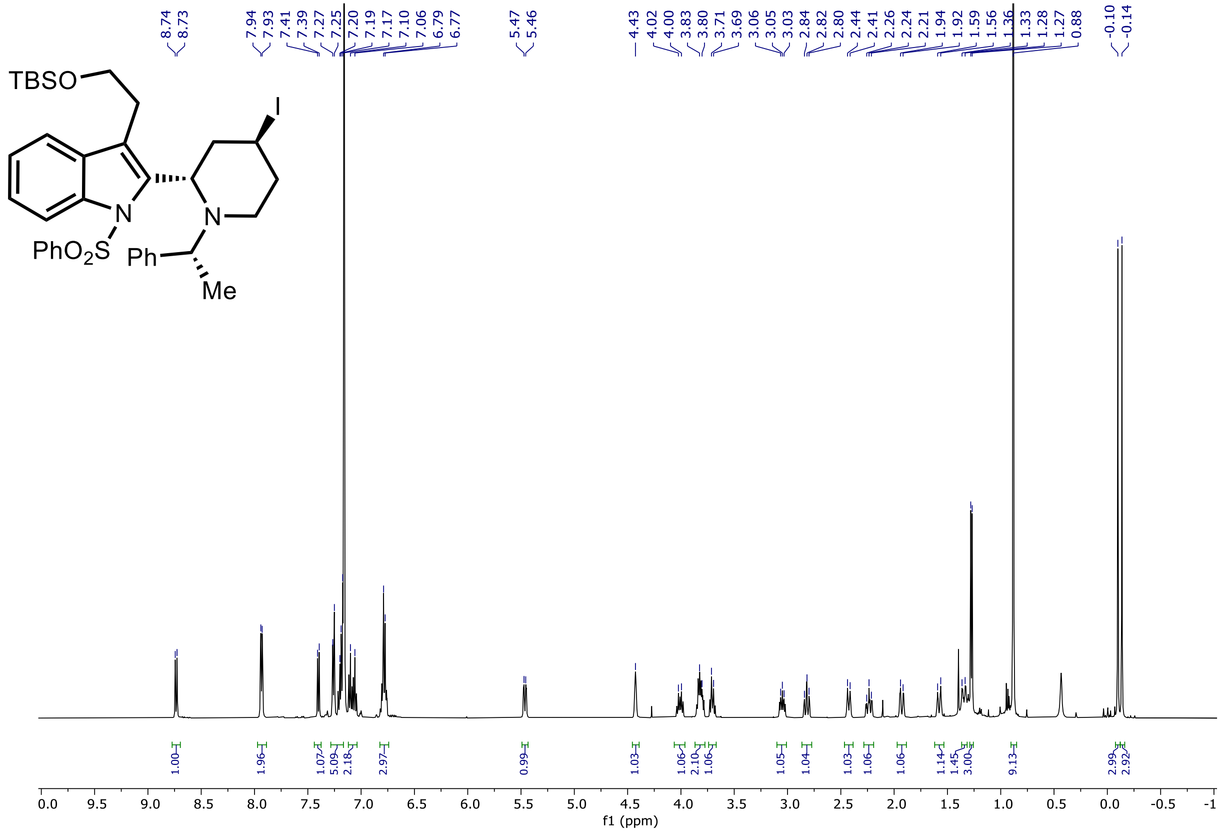
5.74 (^{13}C NMR, 101 MHz, CDCl$_3$)



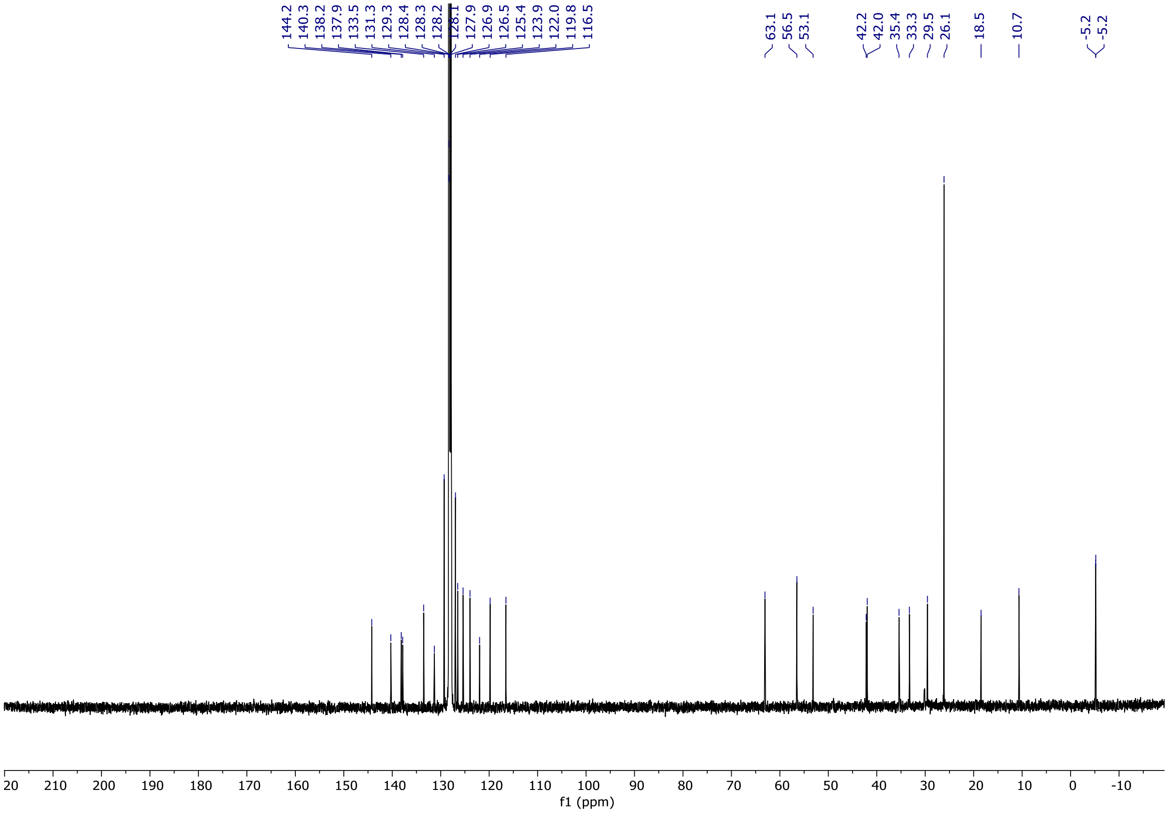
5.74 (NOESY, $CDCl_3$)



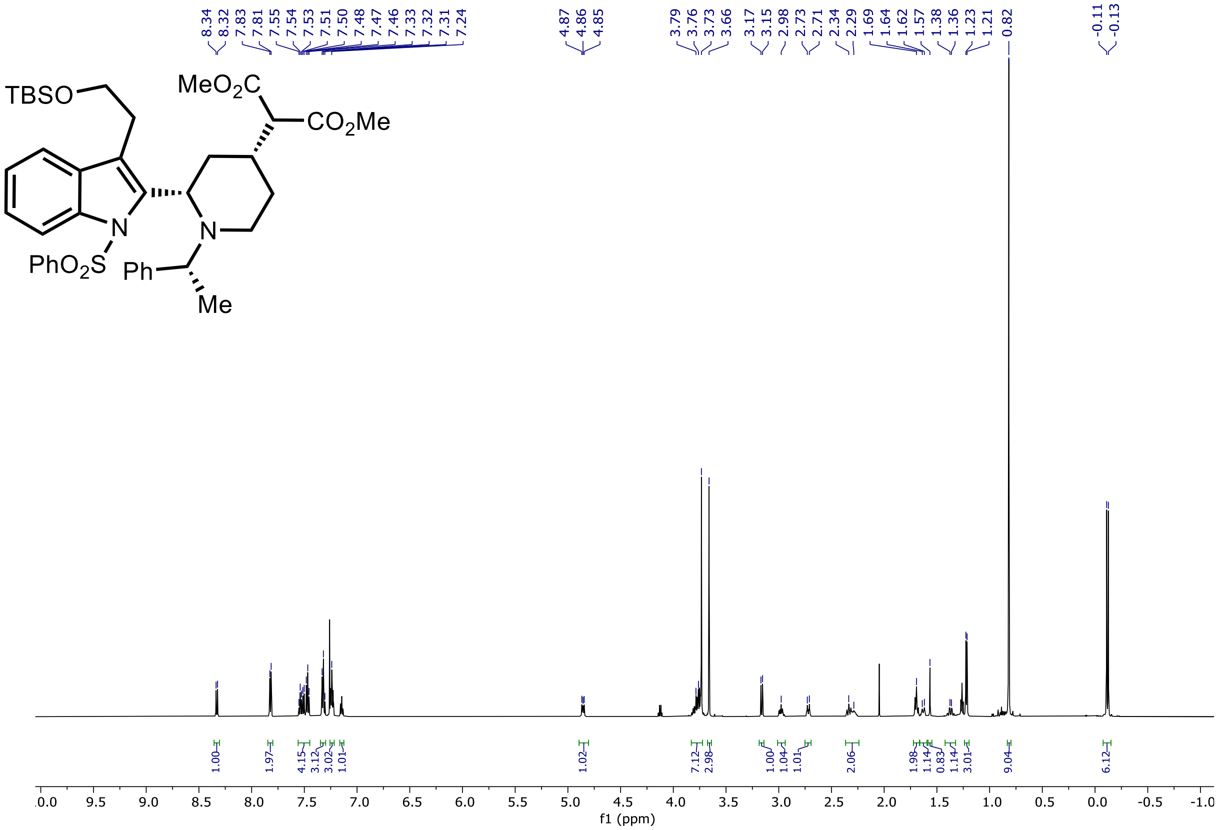
5.109 (^{1}H NMR, 500 MHz, C_6D_6)



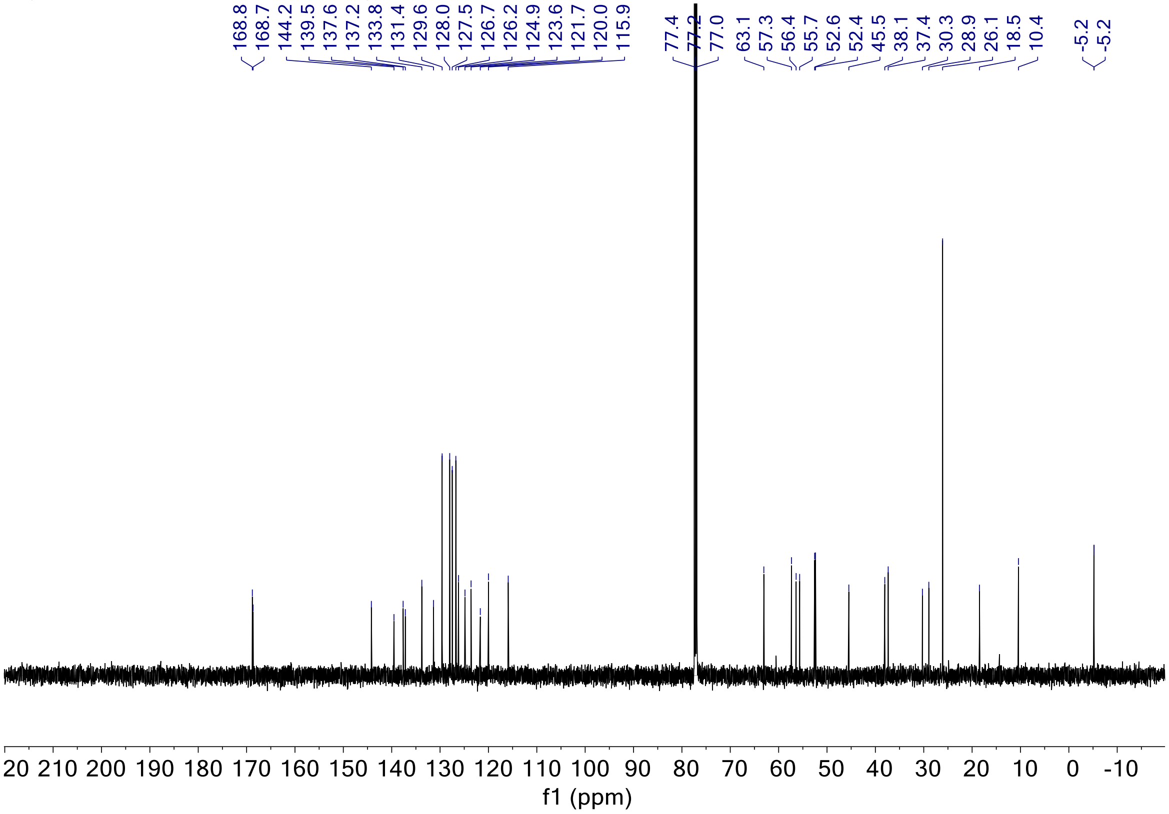
5.109 (^{13}C NMR, 126 MHz, C_6D_6)



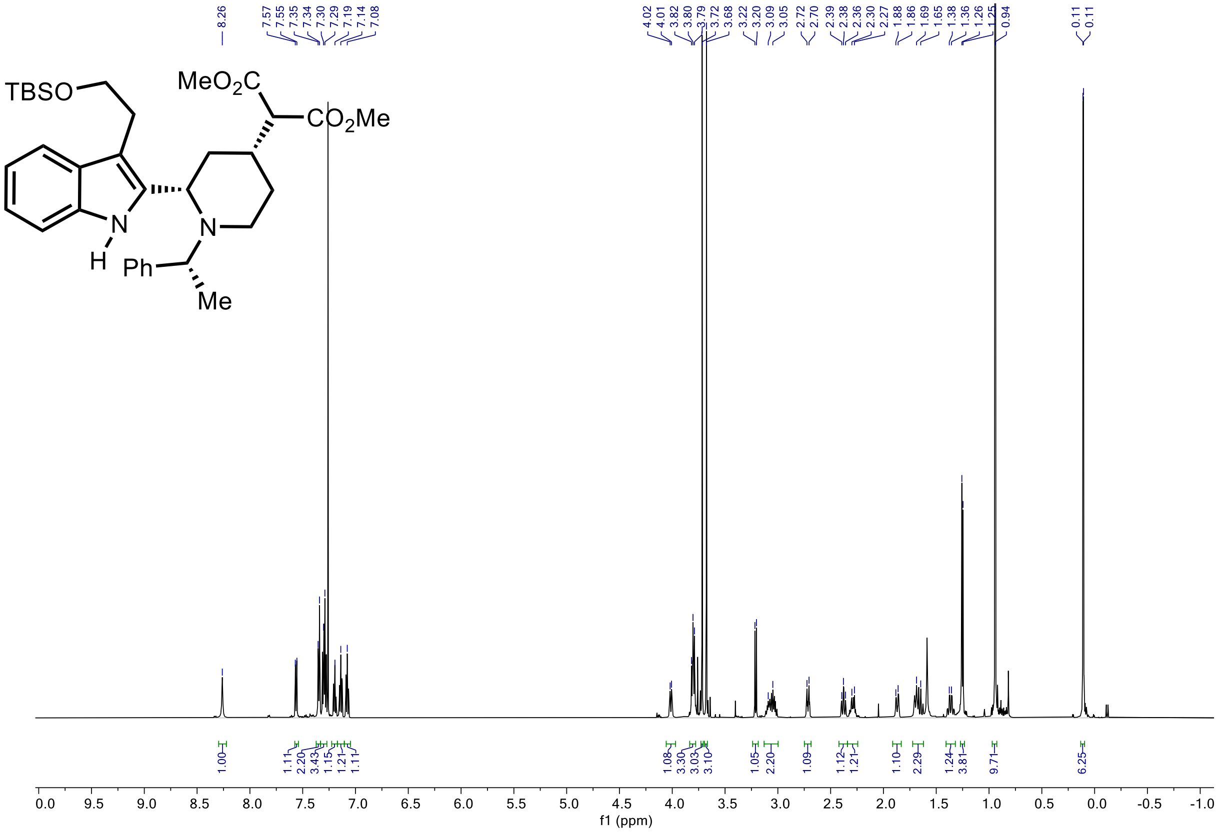
5.73 (^{1}H NMR, 600 MHz, CDCl$_3$)



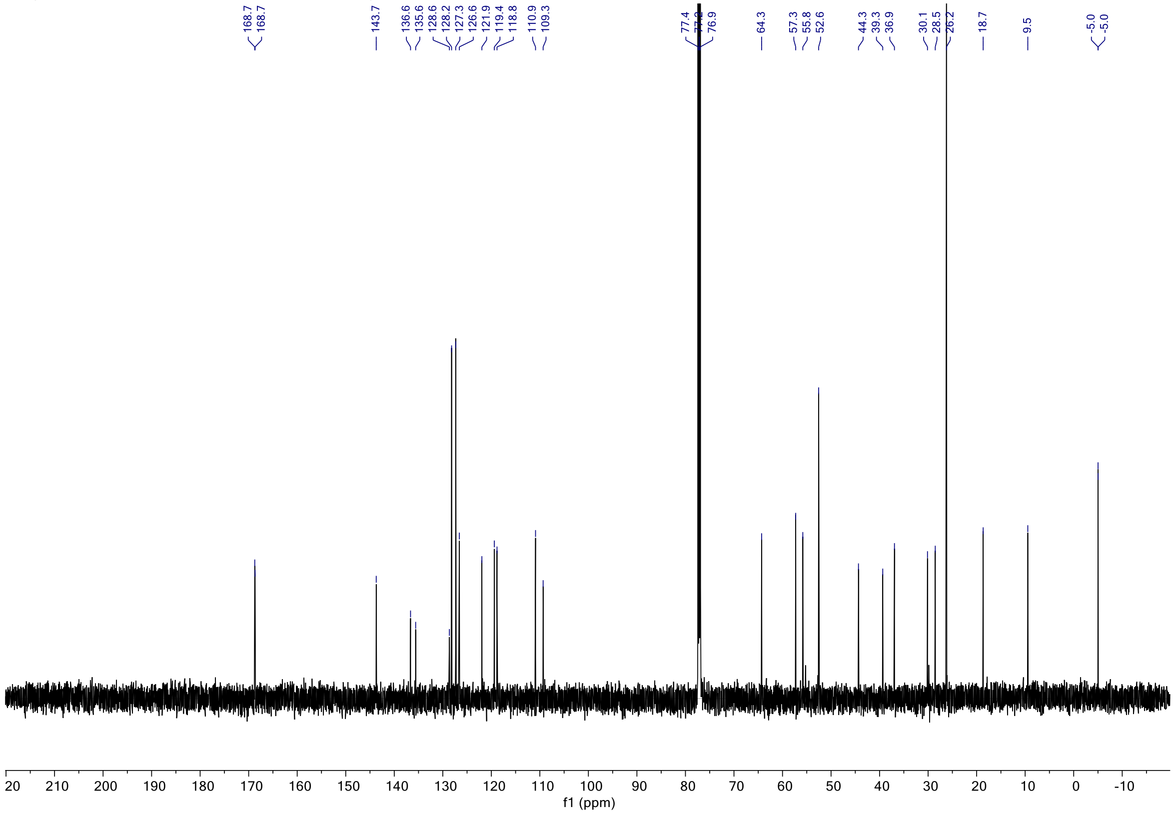
5.73 (^{13}C NMR, 151 MHz, CDCl$_3$)



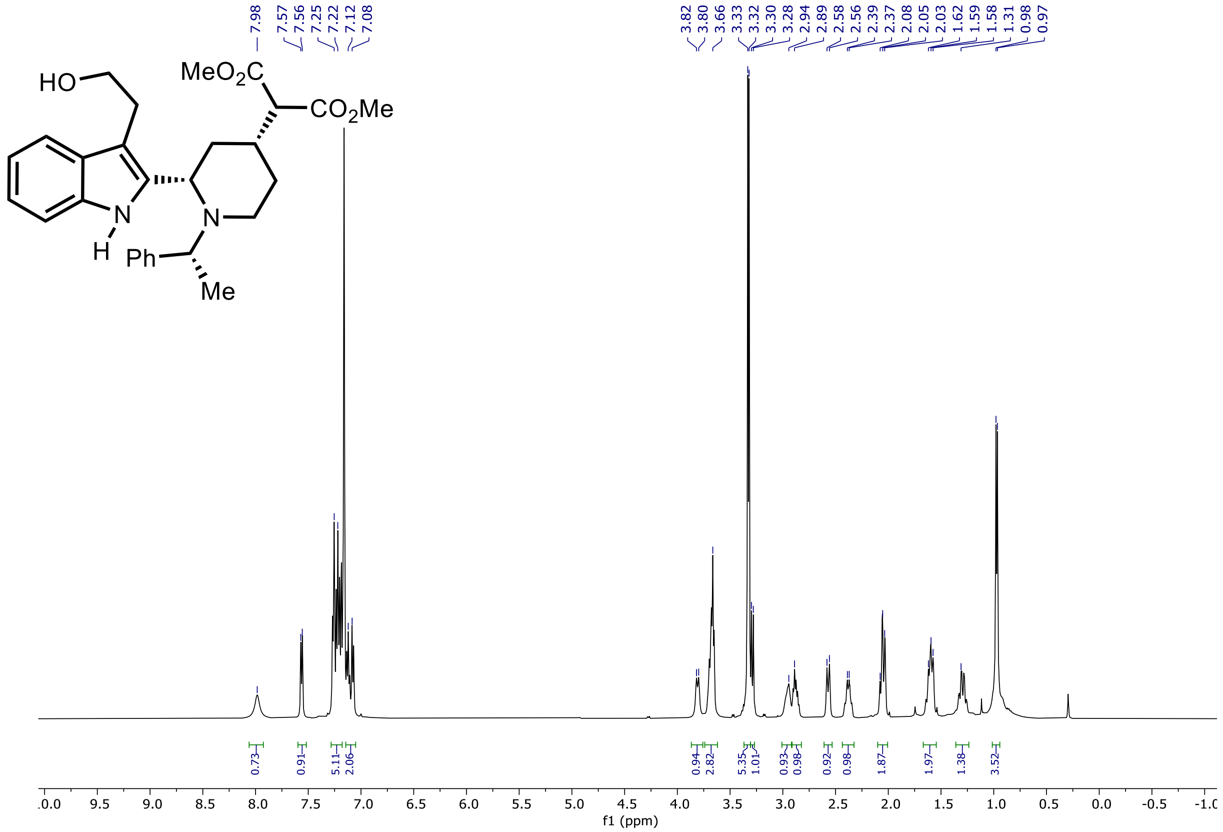
5.90 (^{1}H NMR, 600 MHz, $CDCl_3$)



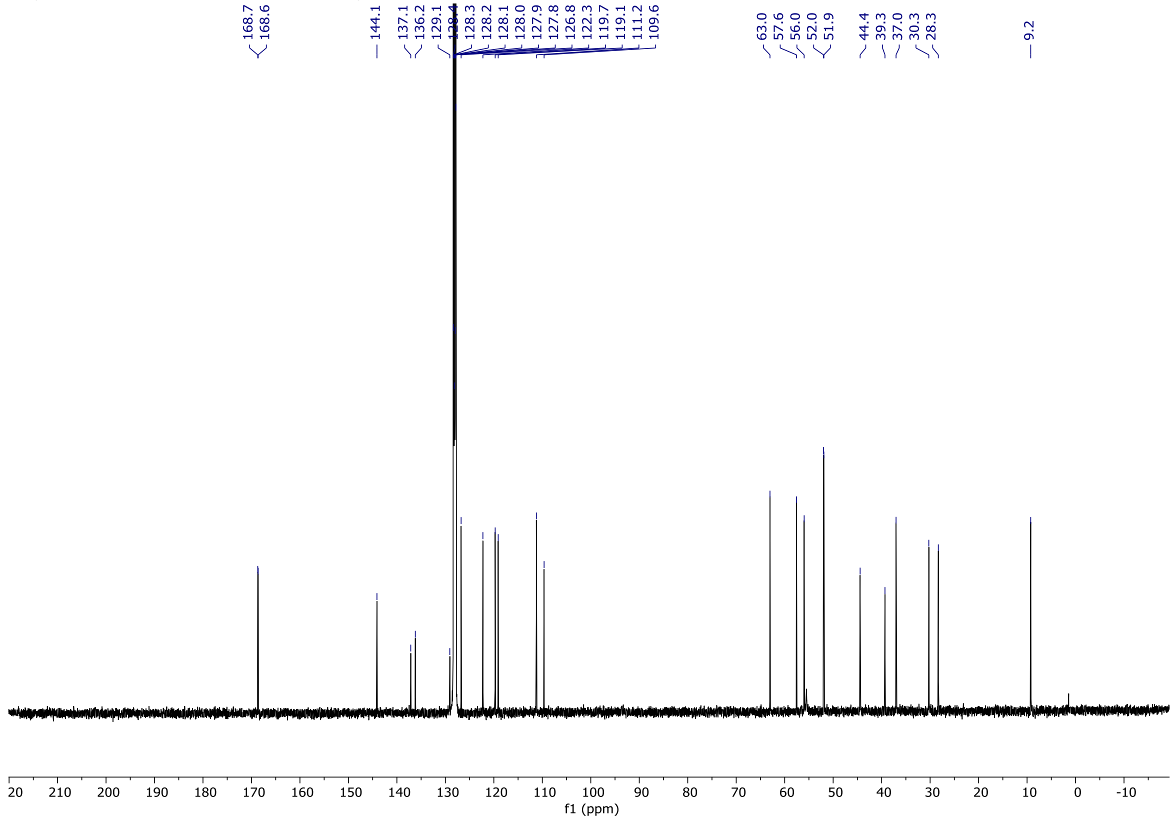
5.90 (^{13}C NMR, 151 MHz, $CDCl_3$)



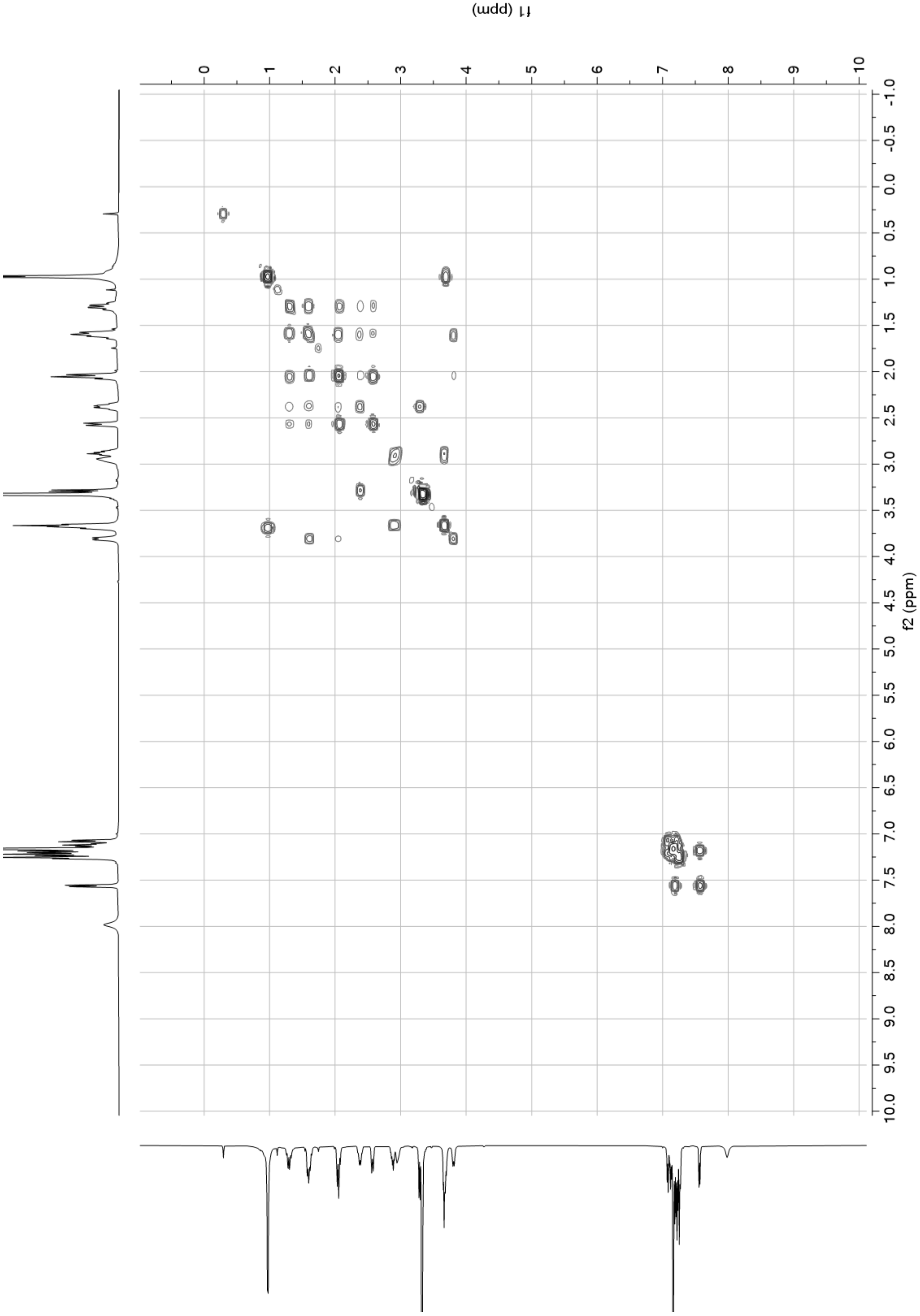
5.75 (^{1}H NMR, 500 MHz, C_6D_6)



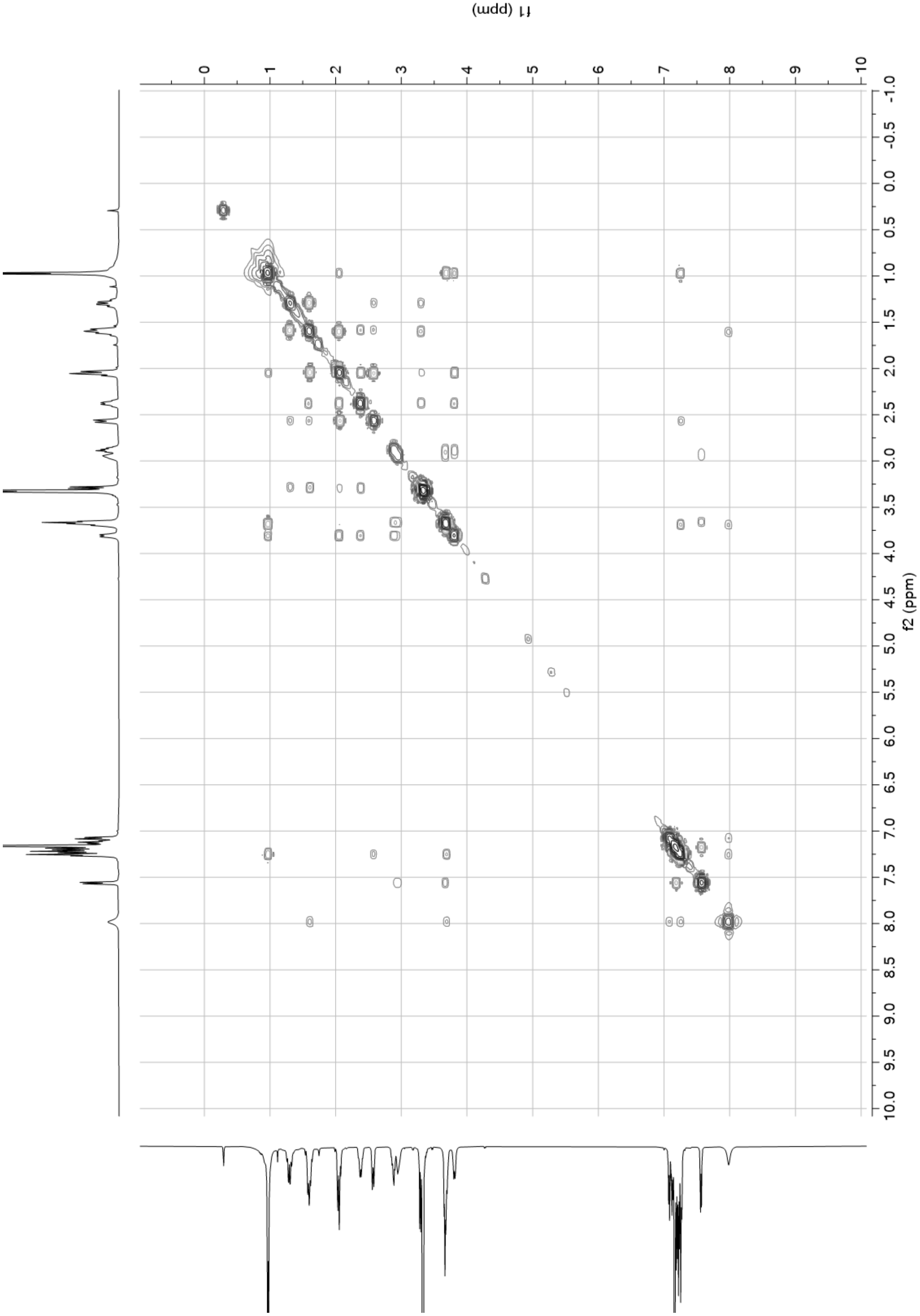
5.75 (^{13}C NMR, 126 MHz, C_6D_6)



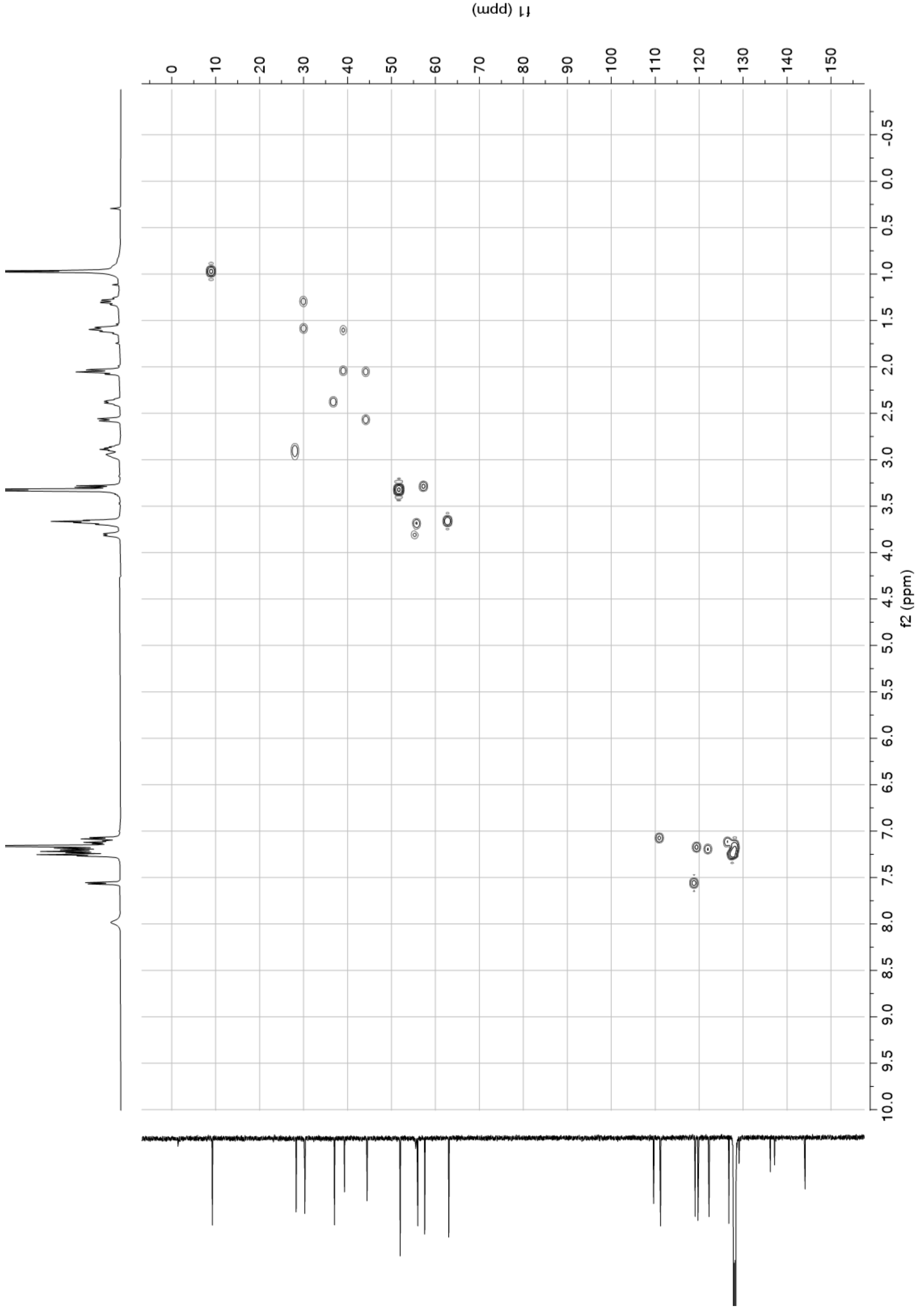
5.75 (COSY, C_6D_6)



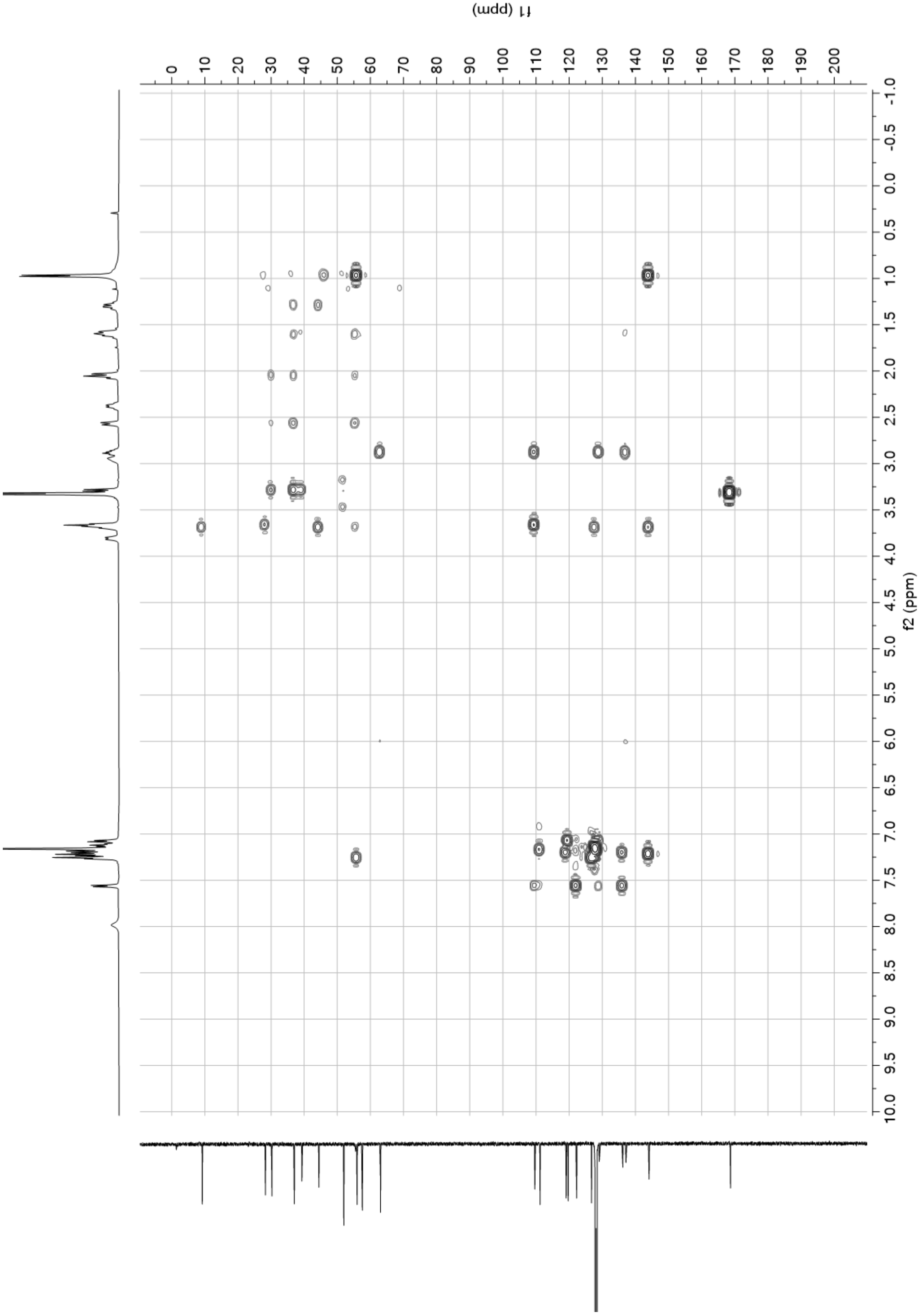
5.75 (NOESY, C_6D_6)



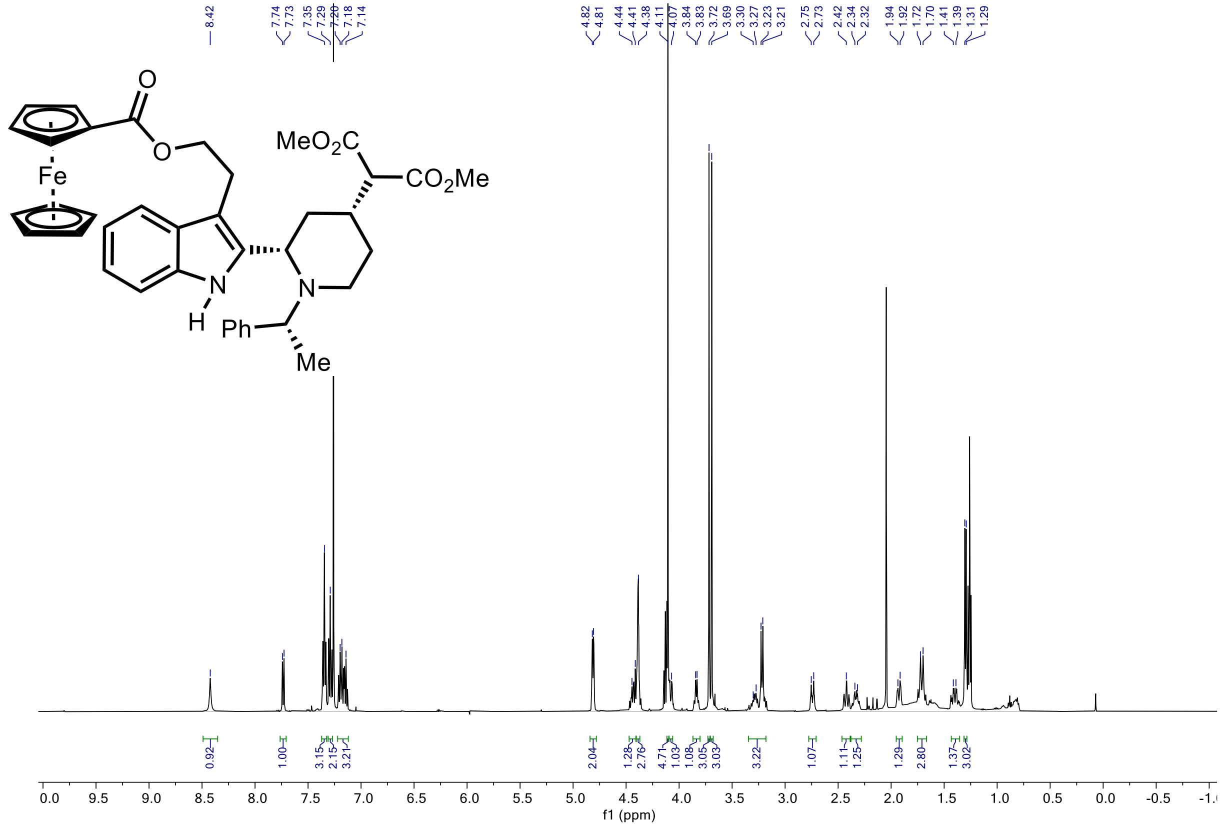
5.75 (HSQC, C_6D_6)



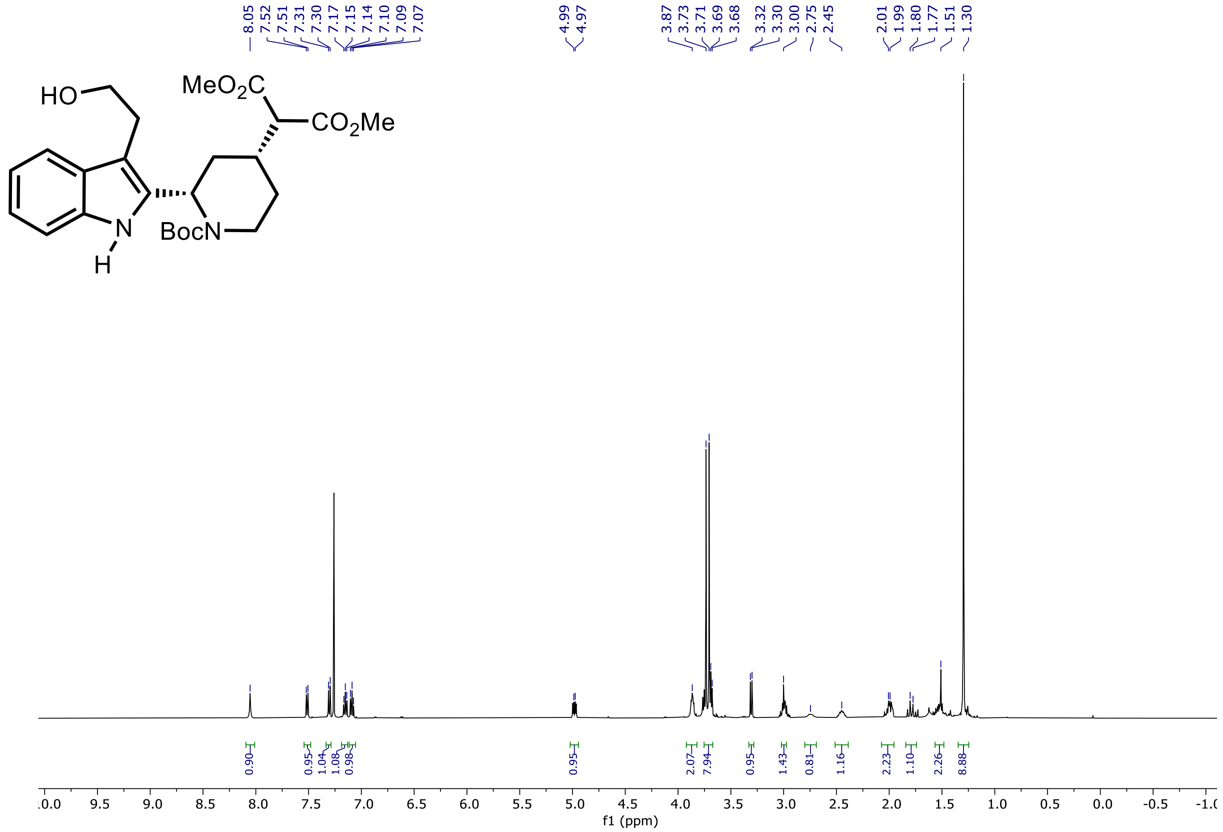
5.75 (HMBC, C_6D_6)



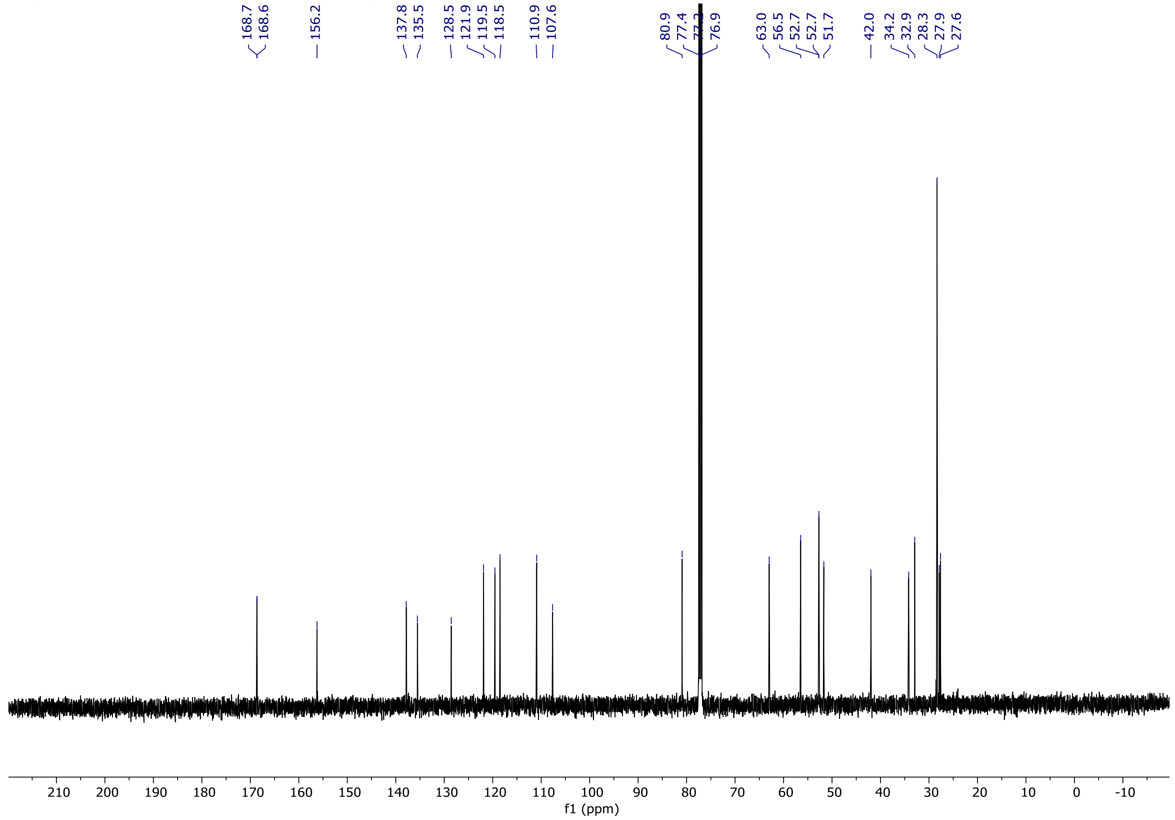
5.77 (^{1}H NMR, 500 MHz, CDCl$_3$)



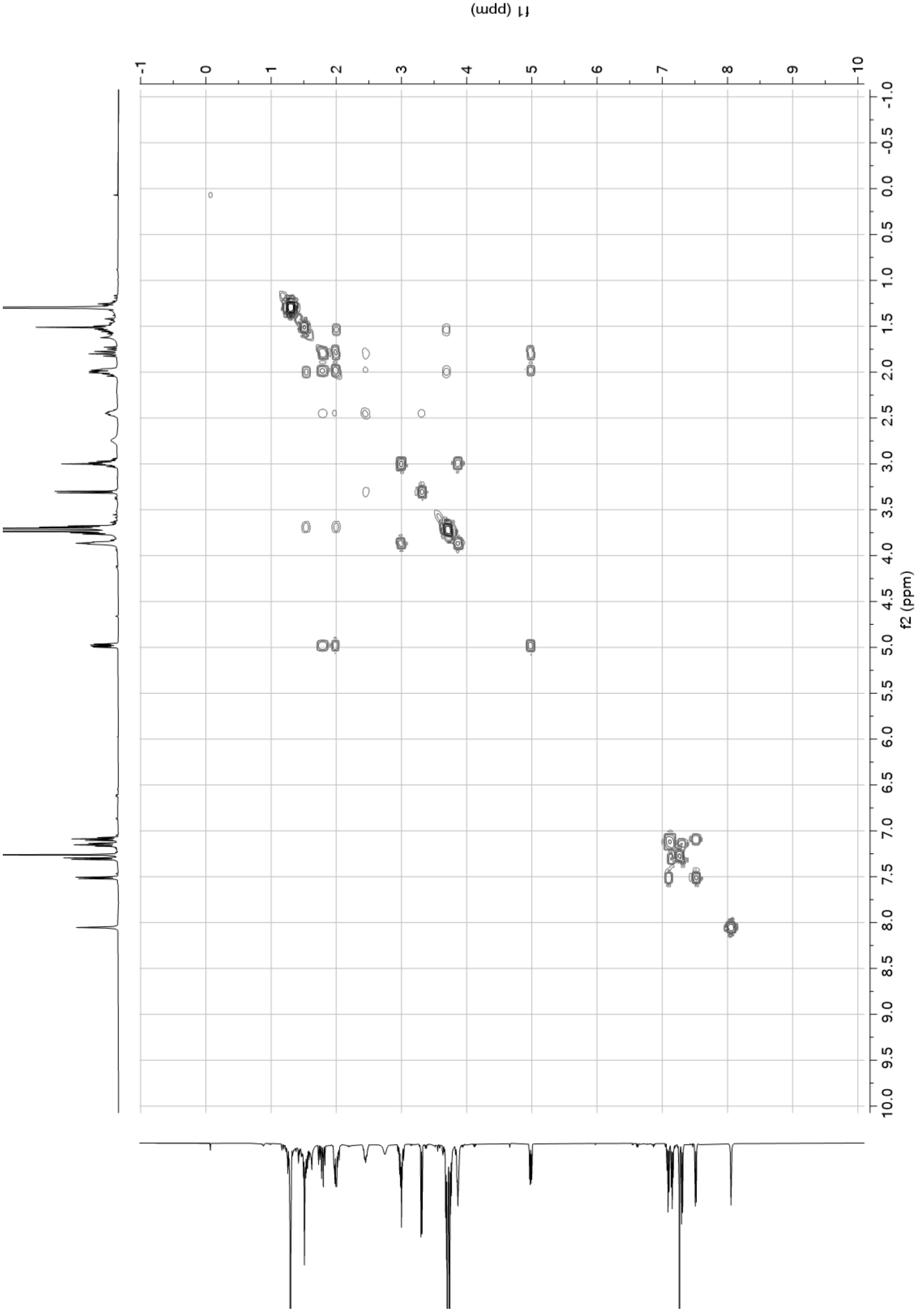
5.88 (^{1}H NMR, 500 MHz, CDCl$_3$)



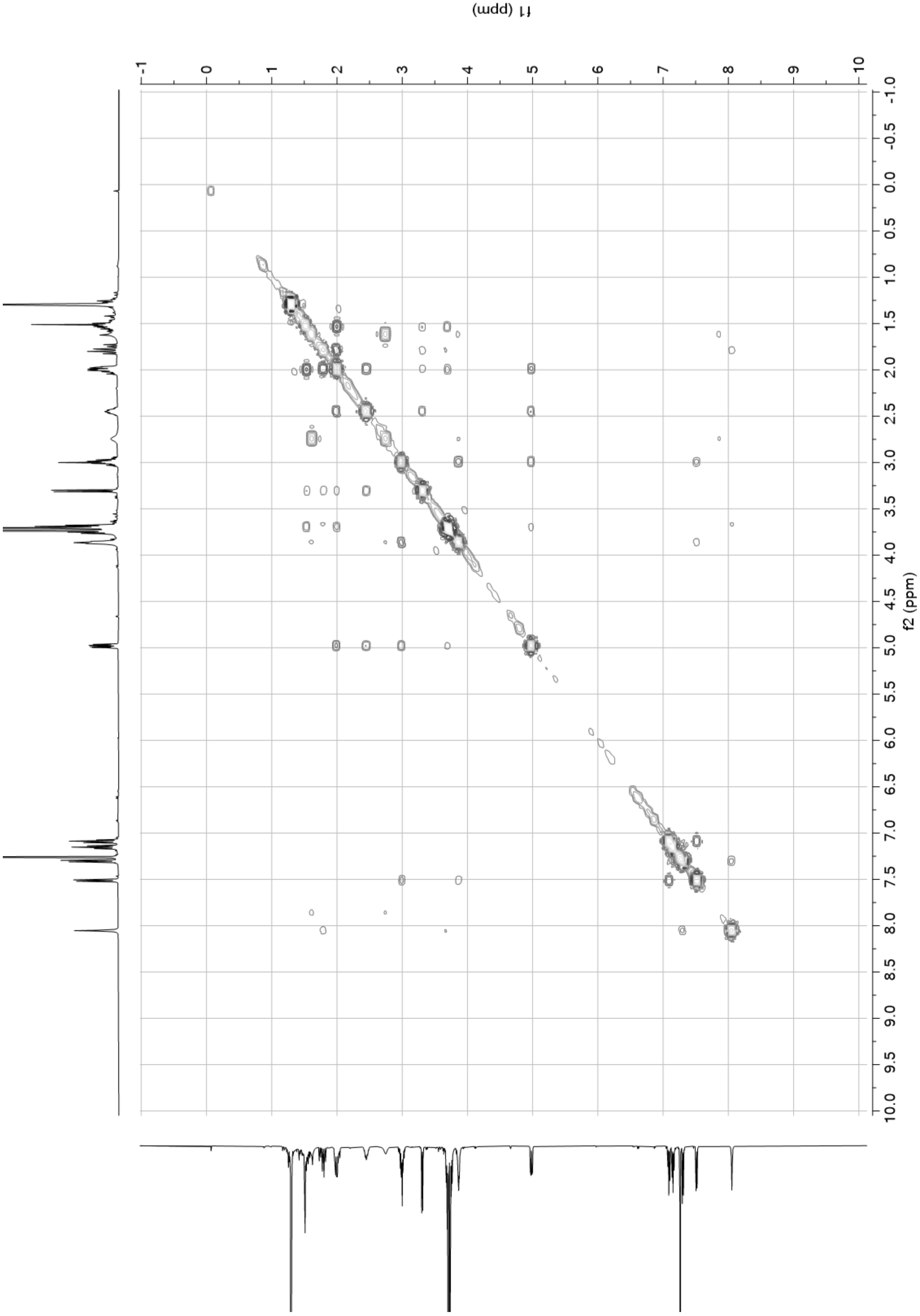
5.88 (^{13}C NMR, 126 MHz, CDCl$_3$)



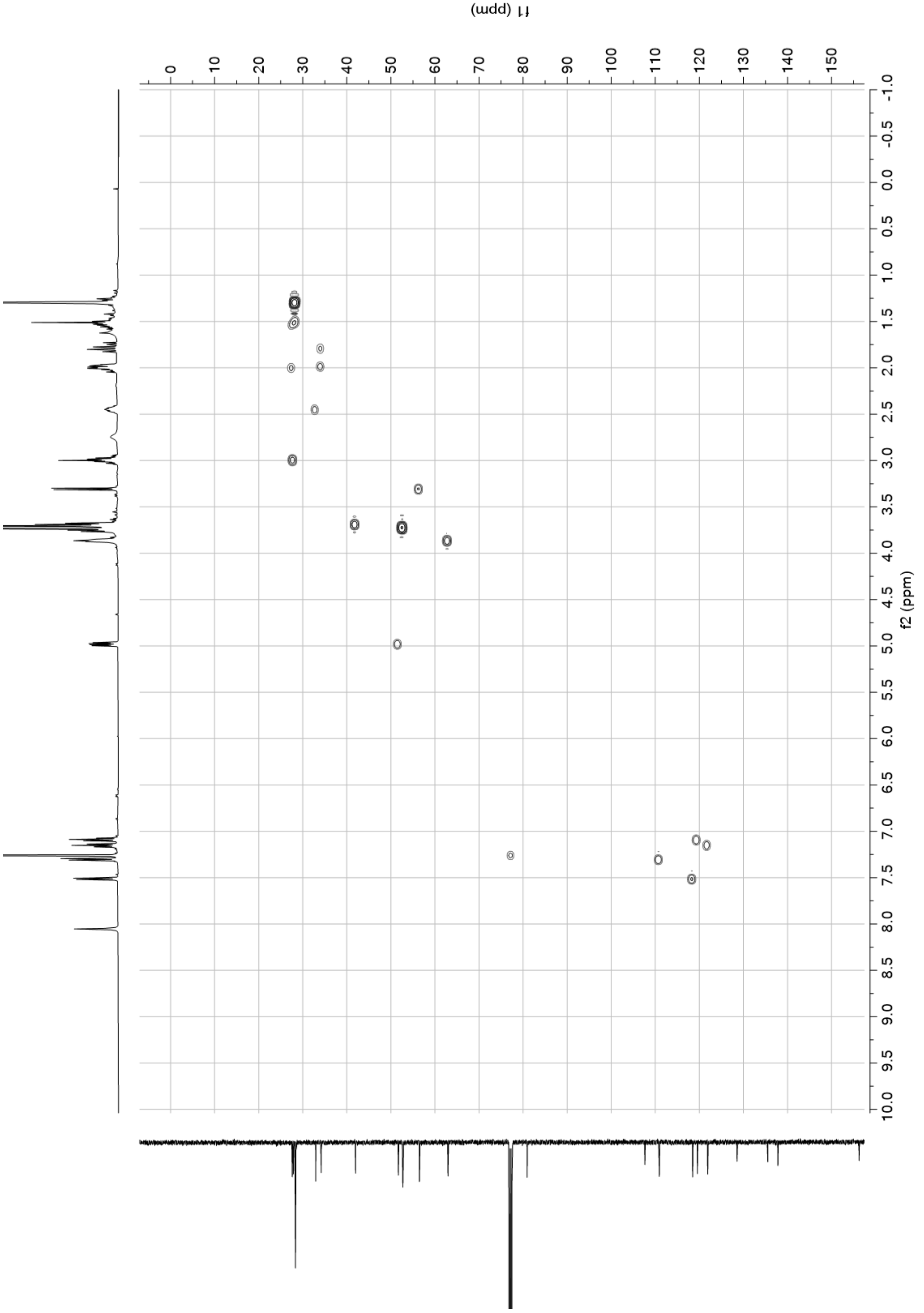
5.88 (COSY, $CDCl_3$)



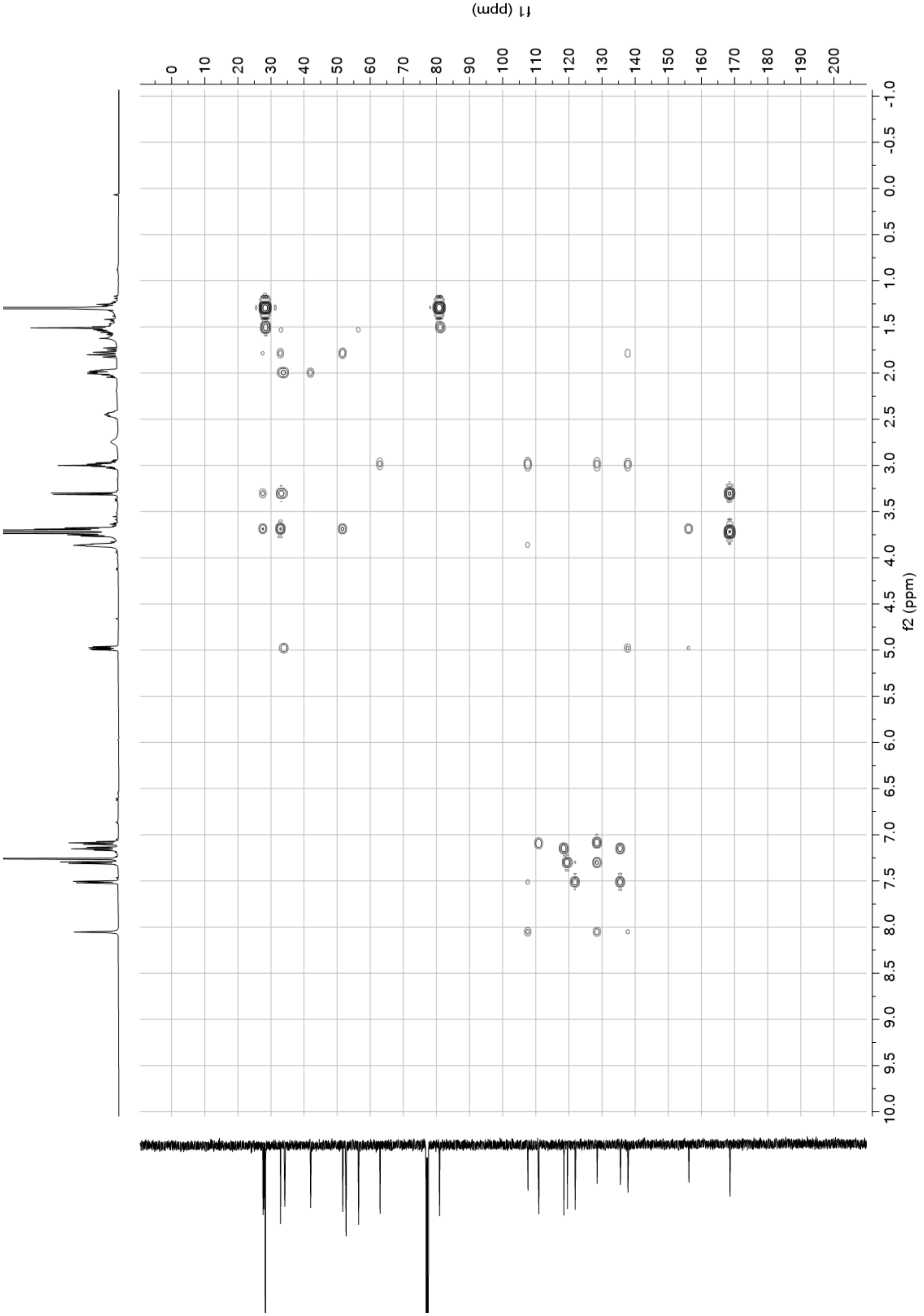
5.88 (NOESY, $CDCl_3$)



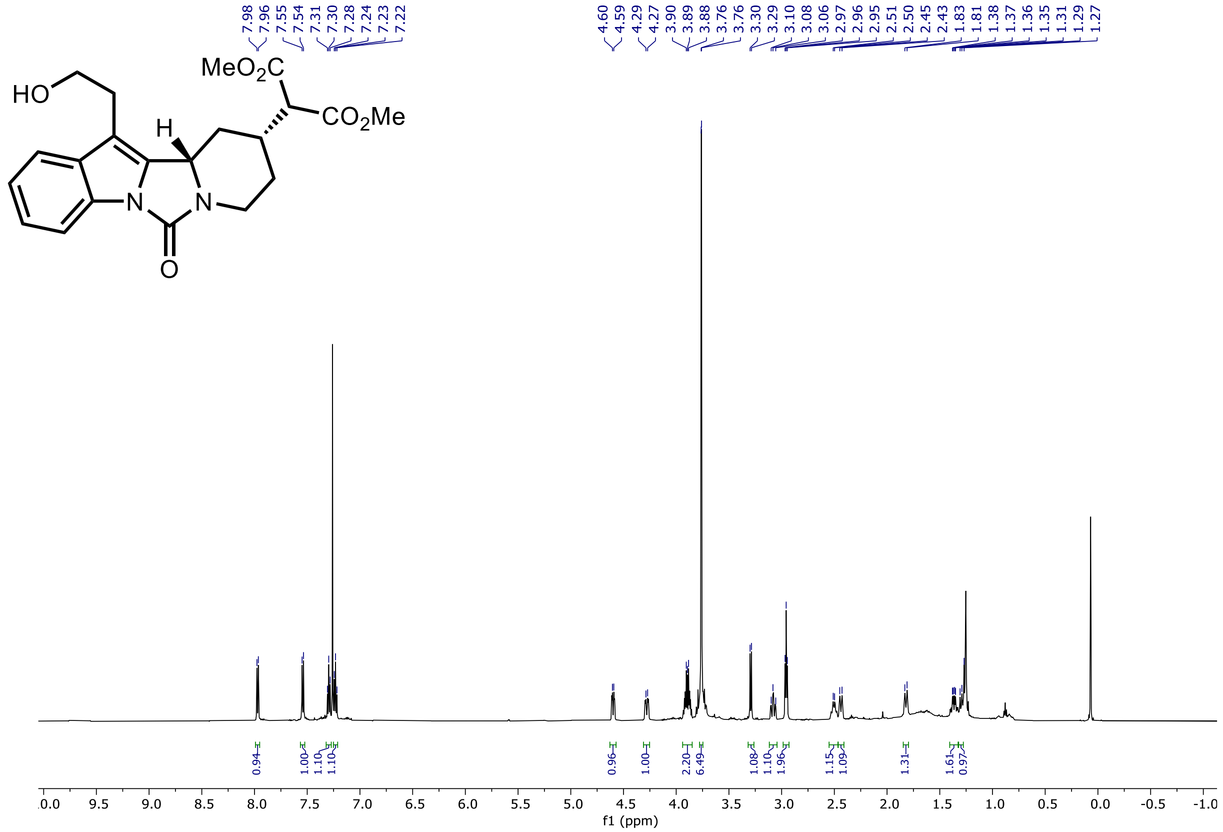
5.88 (HSQC, $CDCl_3$)



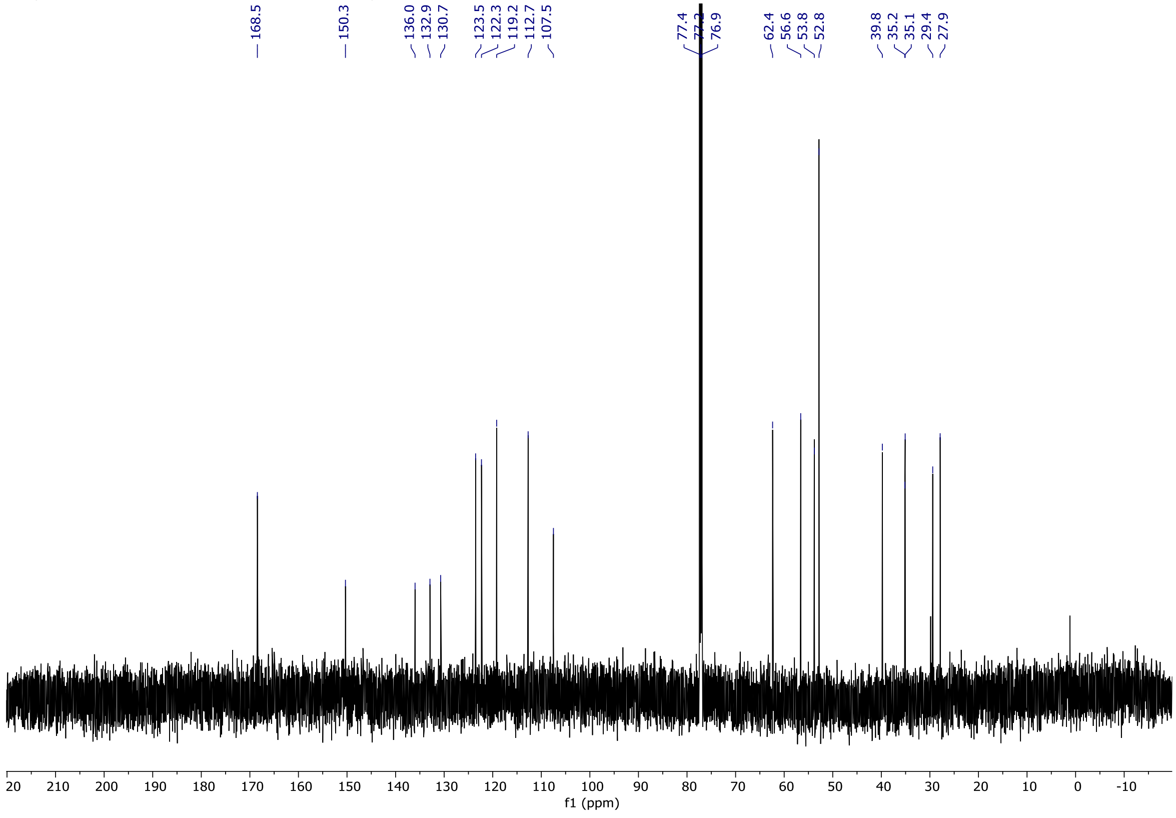
5.88 (HMBC, CDCl$_3$)



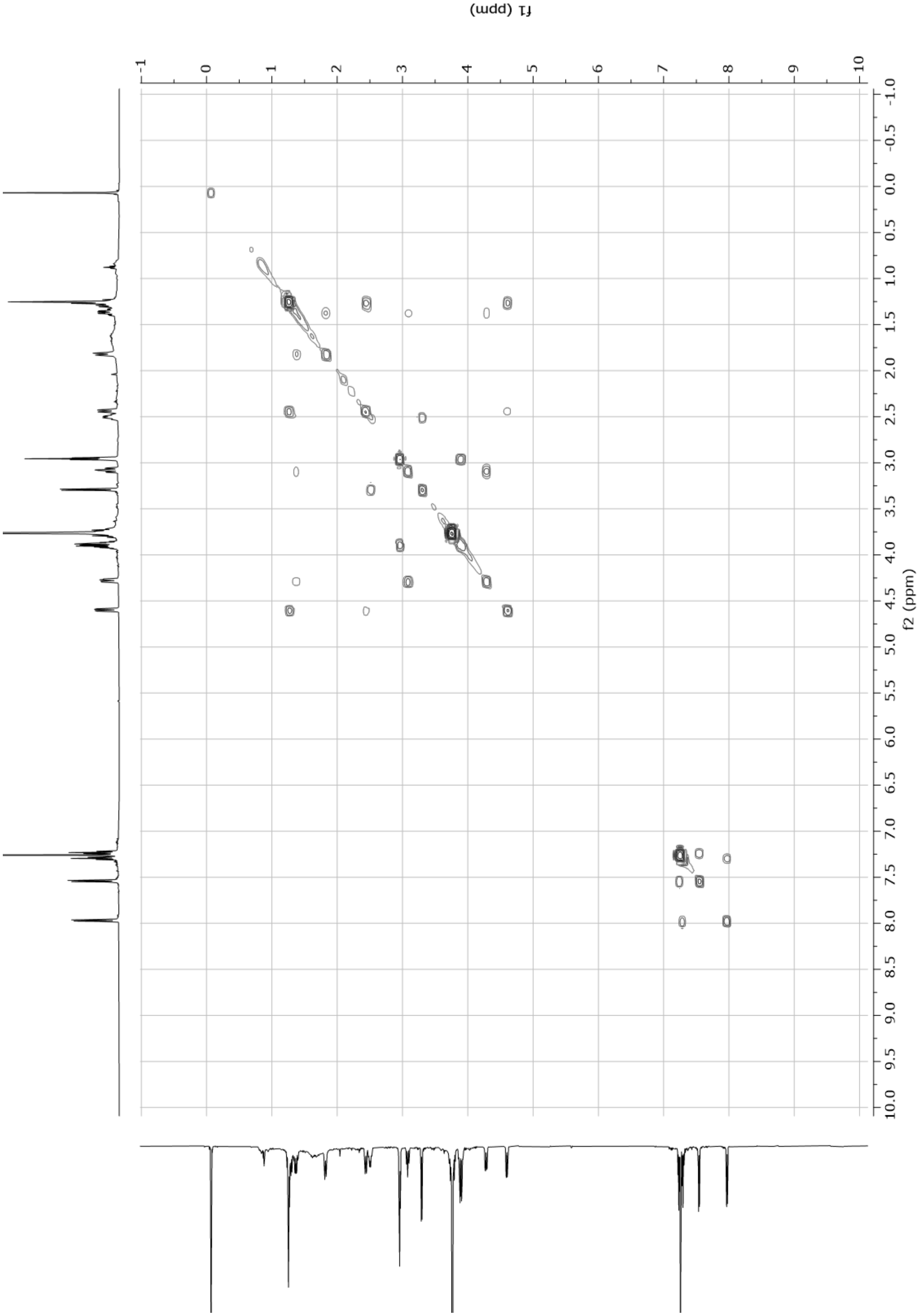
5.89 (^{1}H NMR, 600 MHz, CDCl$_3$)



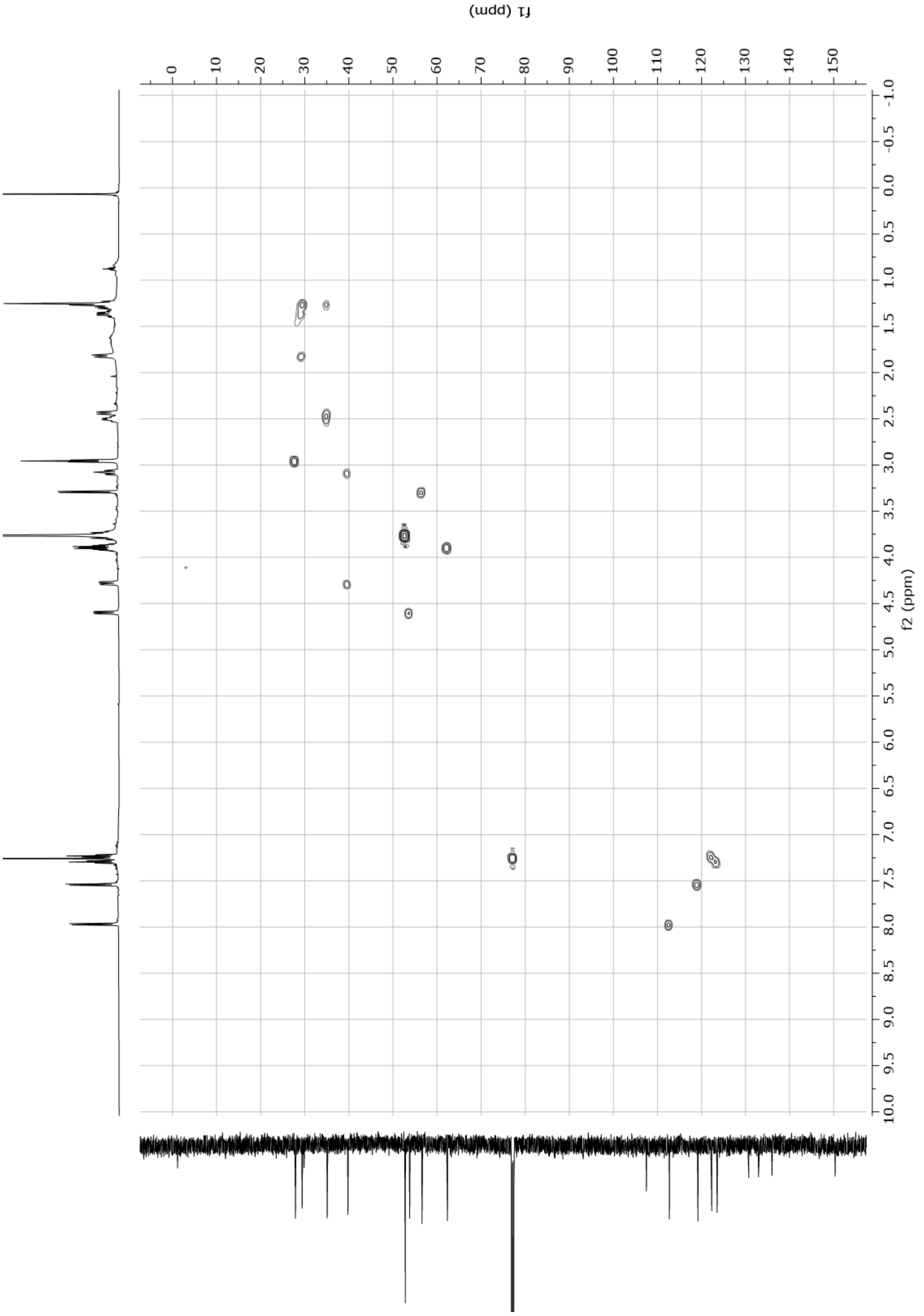
5.89 (^{13}C NMR, 151 MHz, CDCl$_3$)



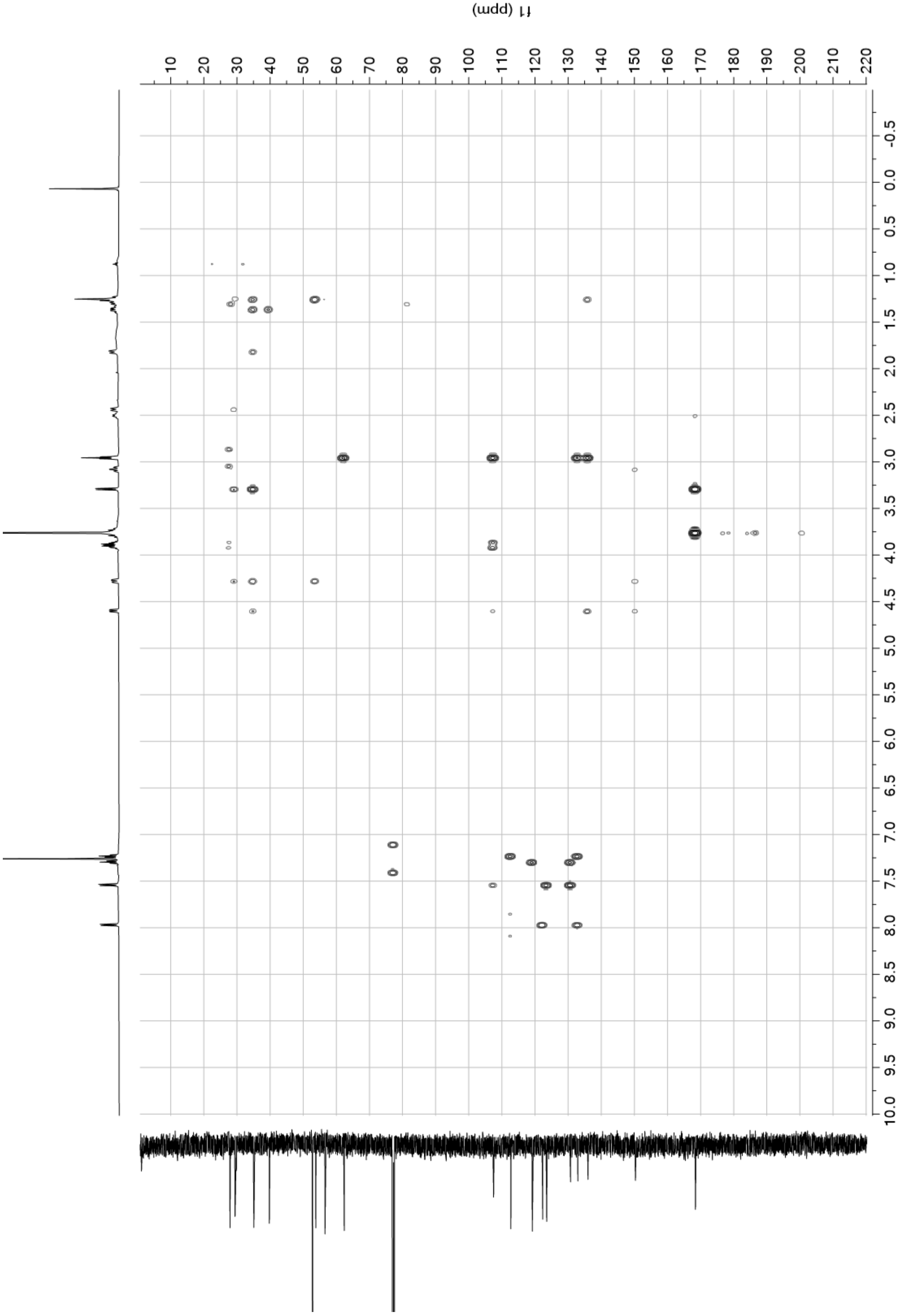
5.89 (COSY, $CDCl_3$)



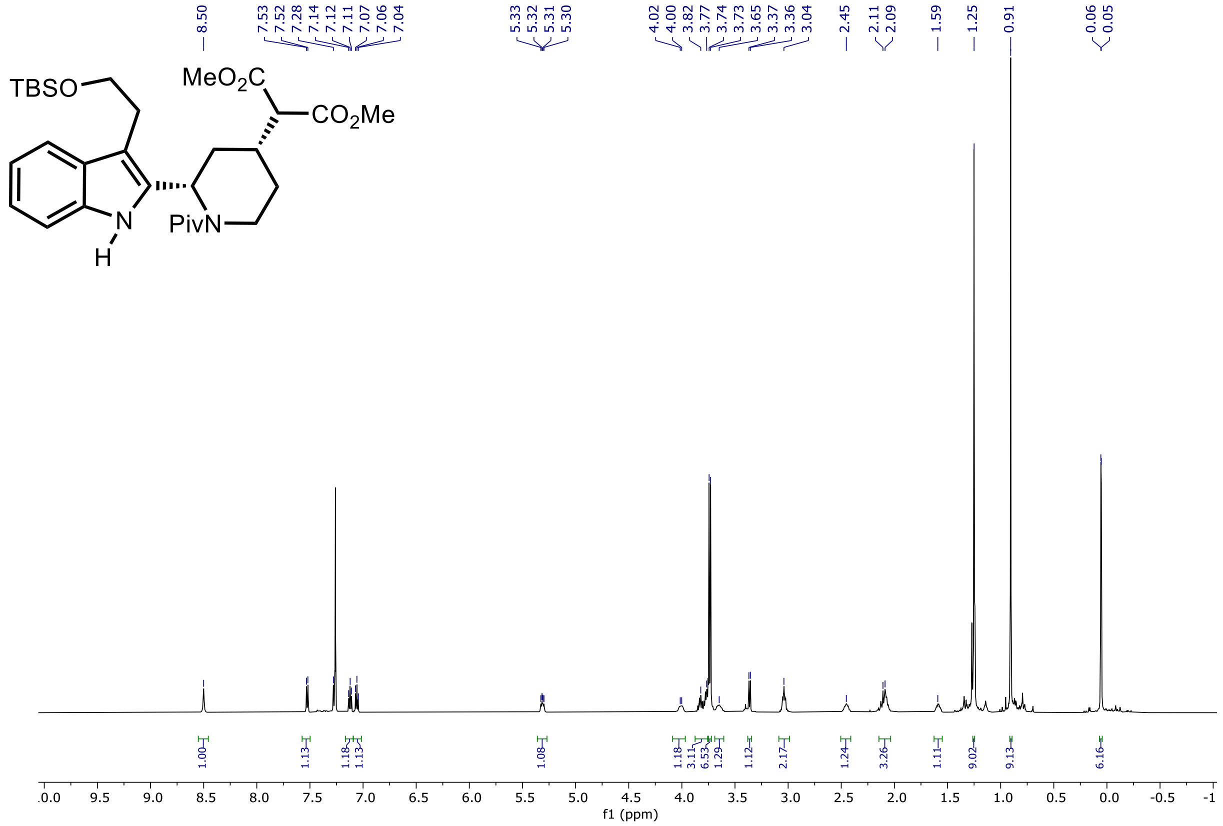
5.89 (HSQC, $CDCl_3$)



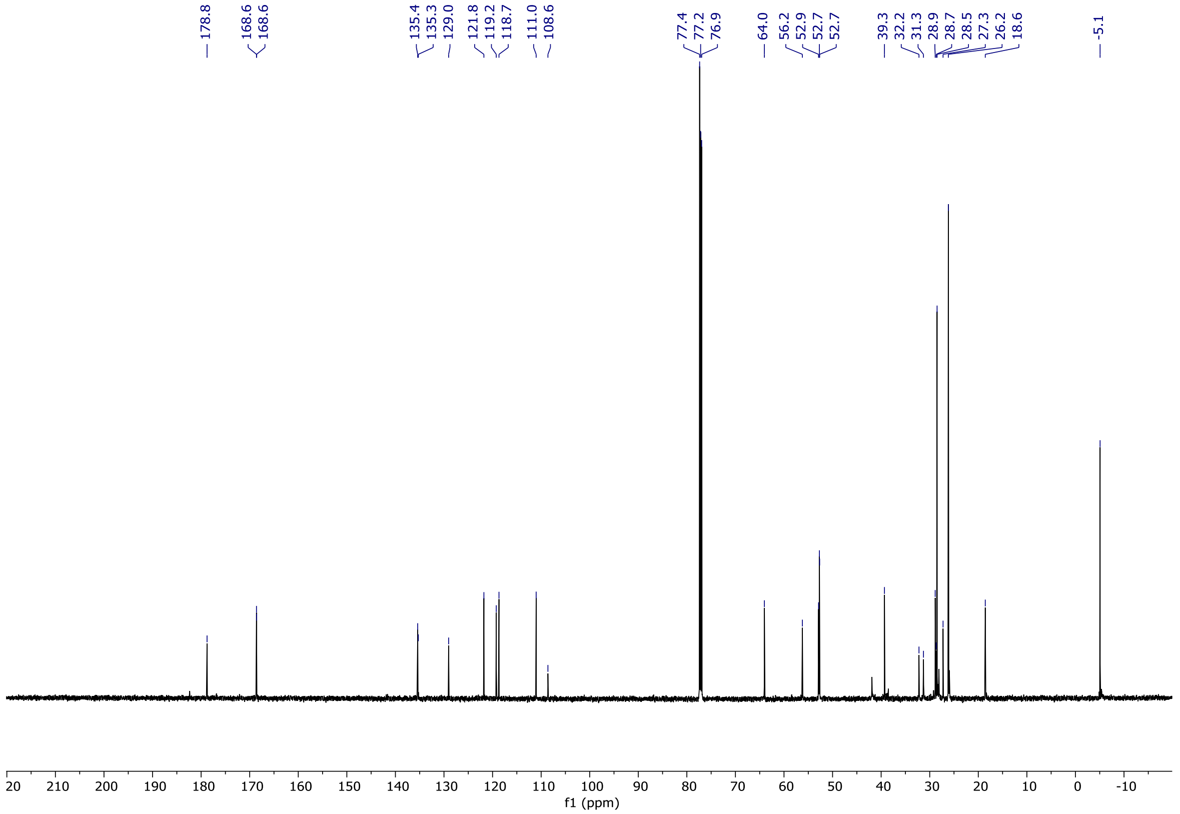
5.89 (HMBC, $CDCl_3$)



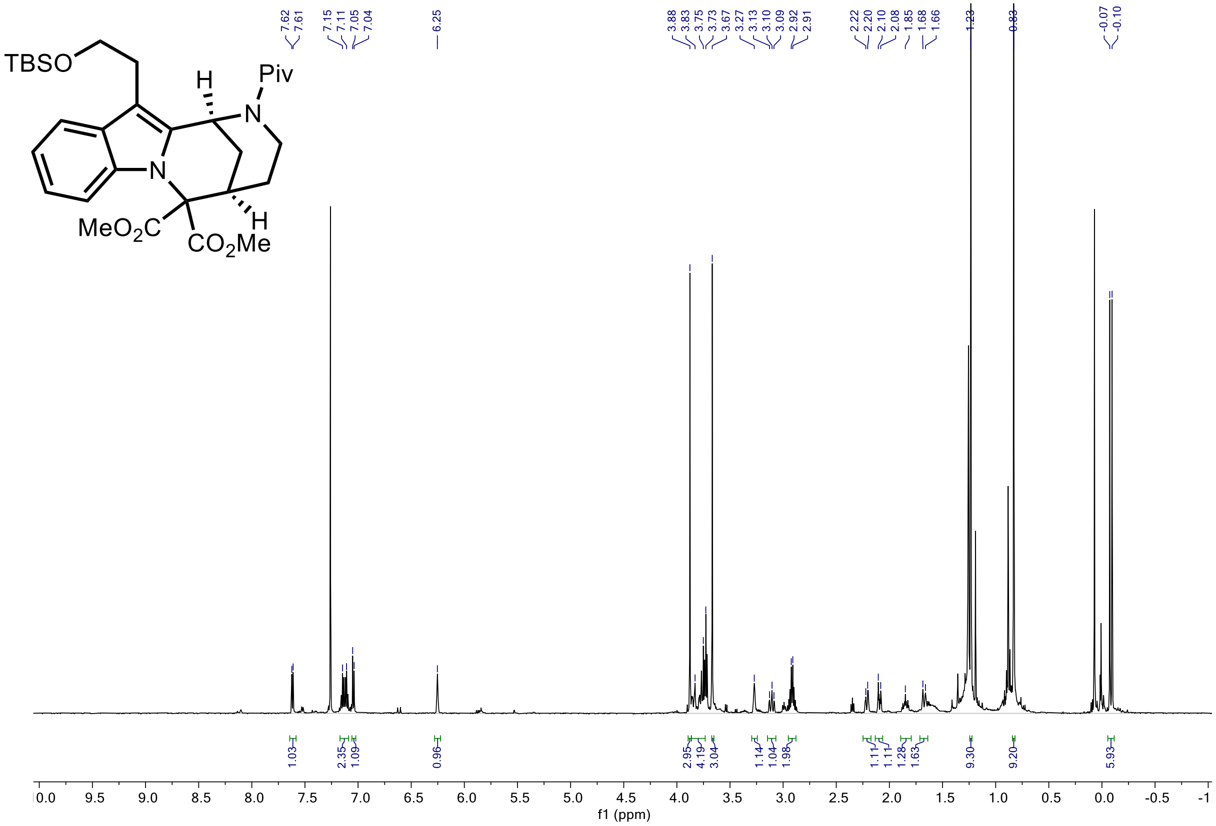
5.91 (^{1}H NMR, 600 MHz, CDCl$_3$)



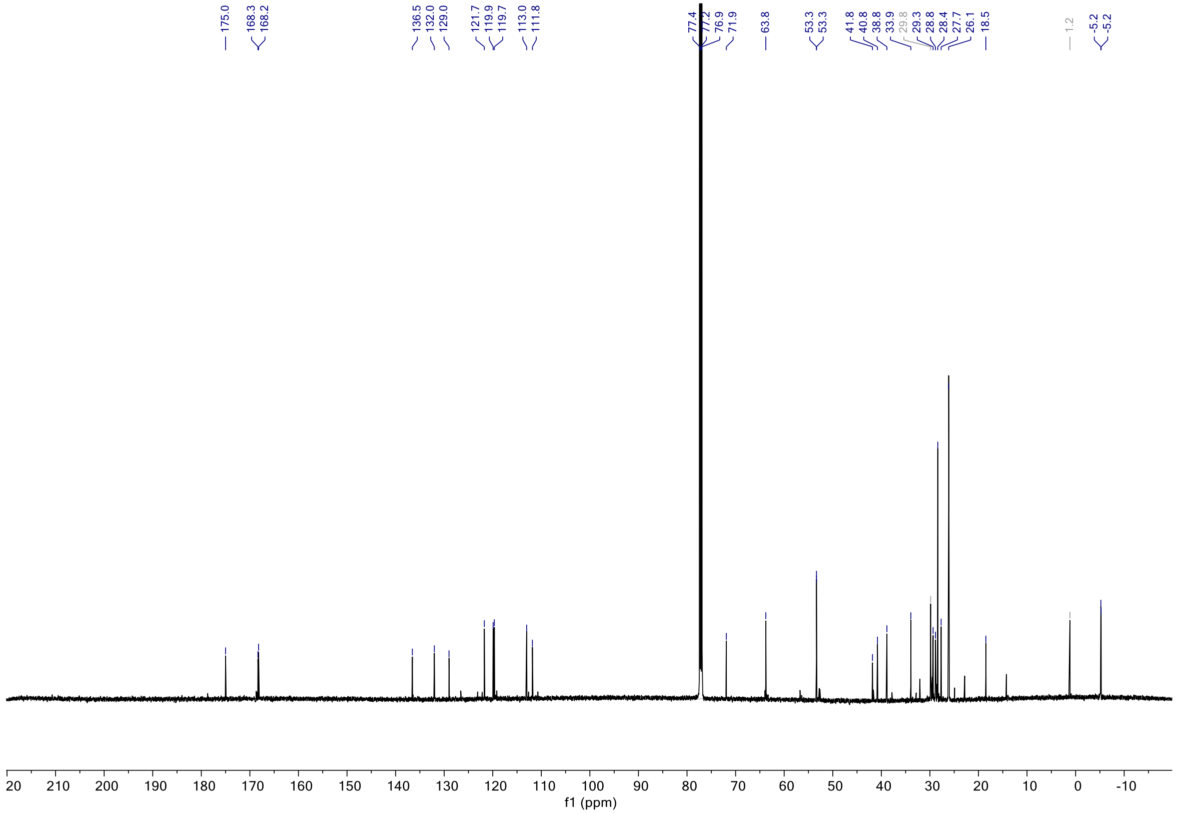
5.91 (^{13}C NMR, 151 MHz, CDCl$_3$)



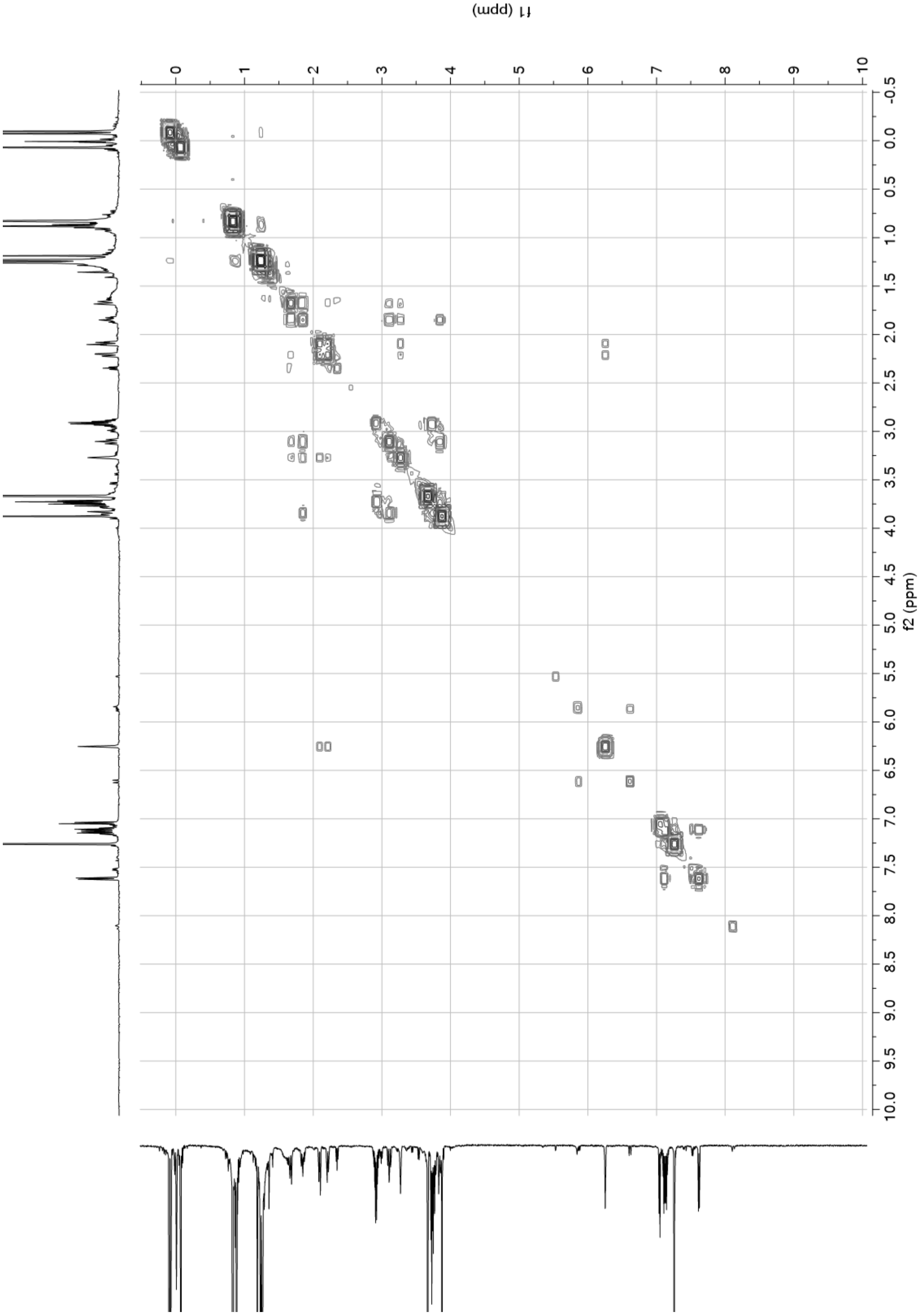
5.92 (^{1}H NMR, 600 MHz, CDCl$_3$)



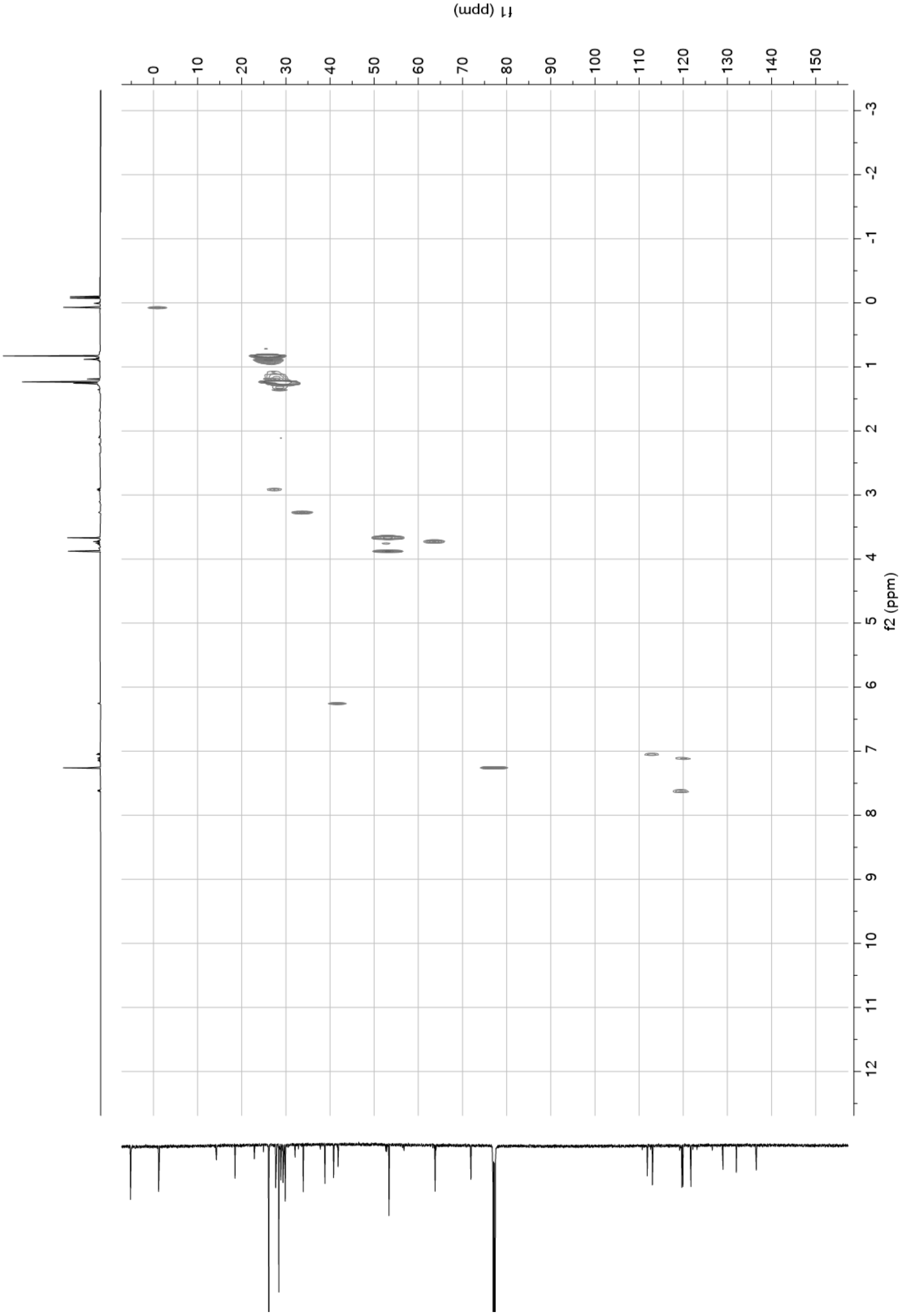
5.92 (^{13}C NMR, 151 MHz, CDCl$_3$)



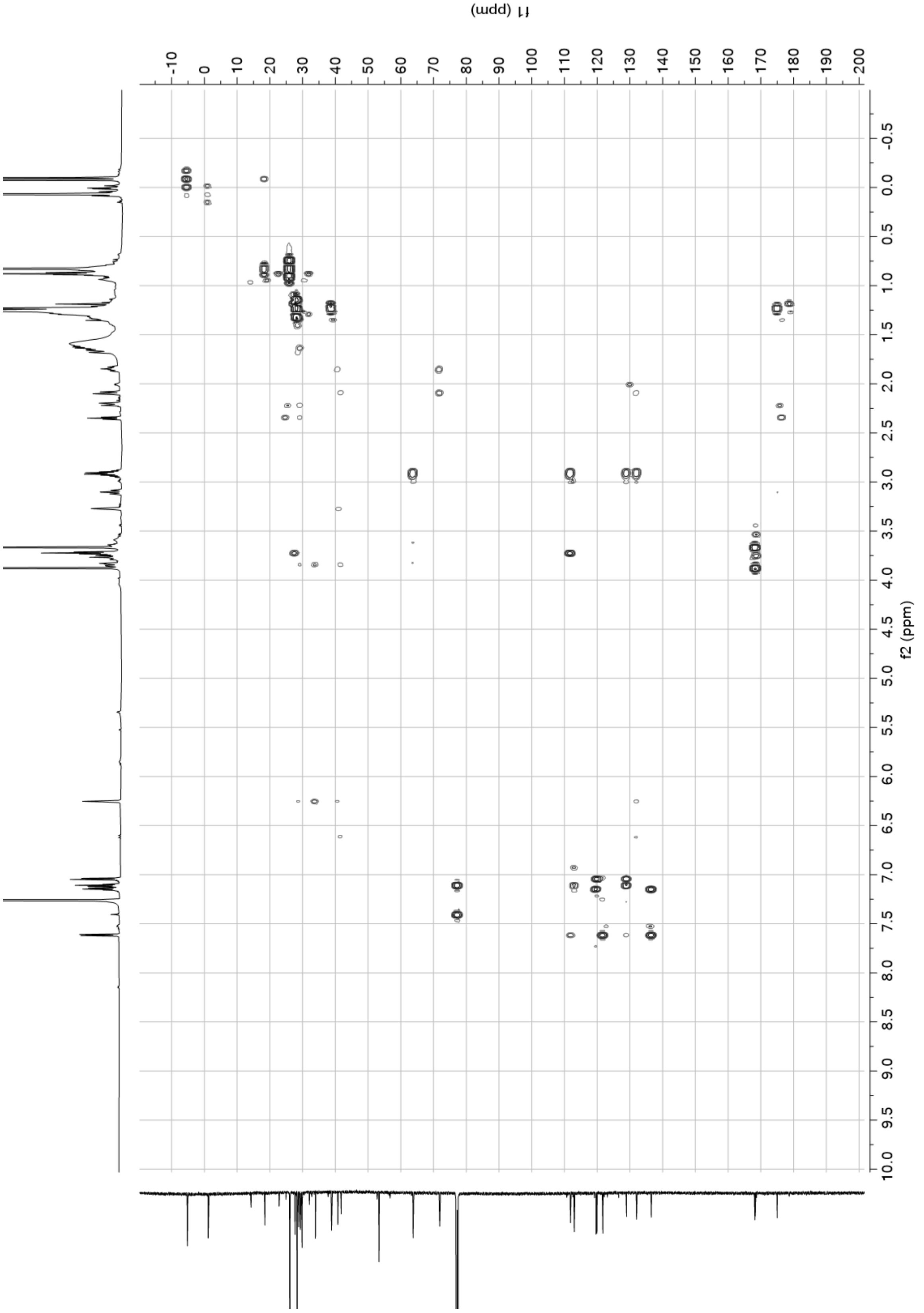
5.92 (COSY, $CDCl_3$)



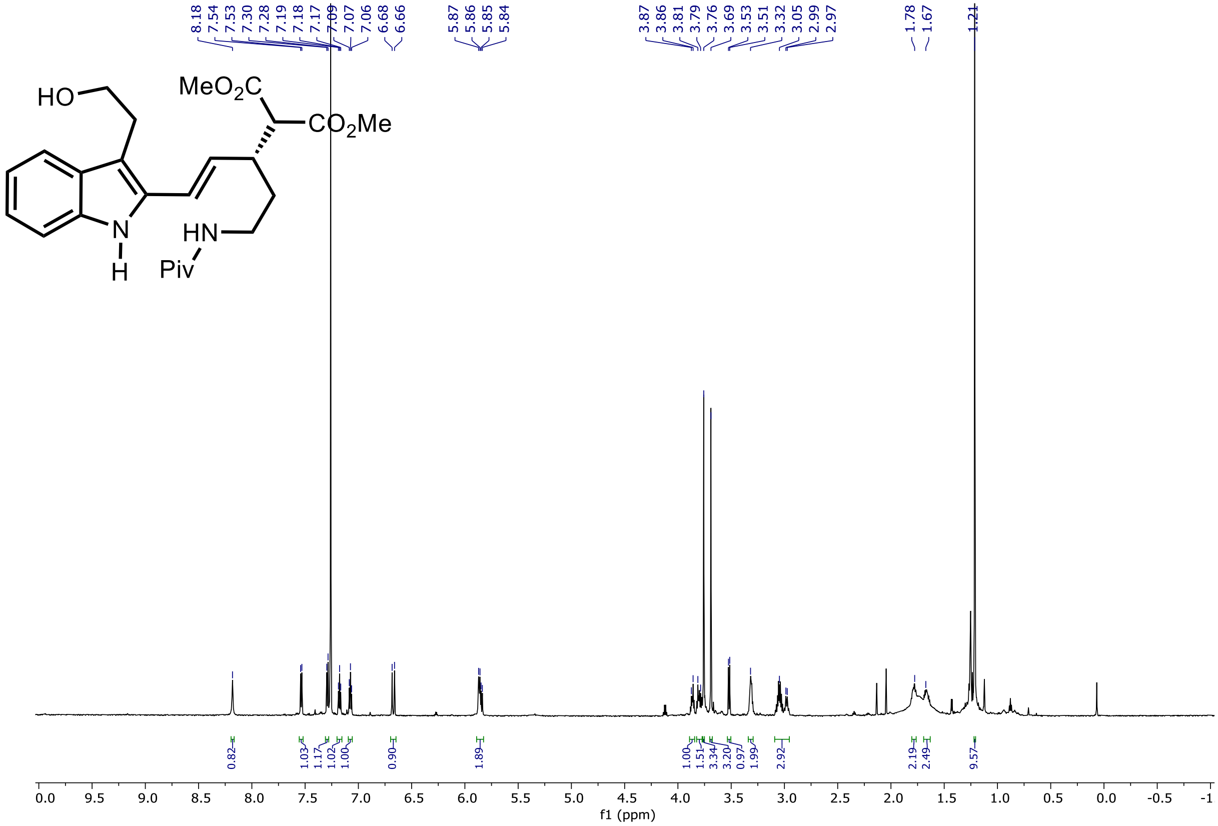
5.92 (HSQC, $CDCl_3$)



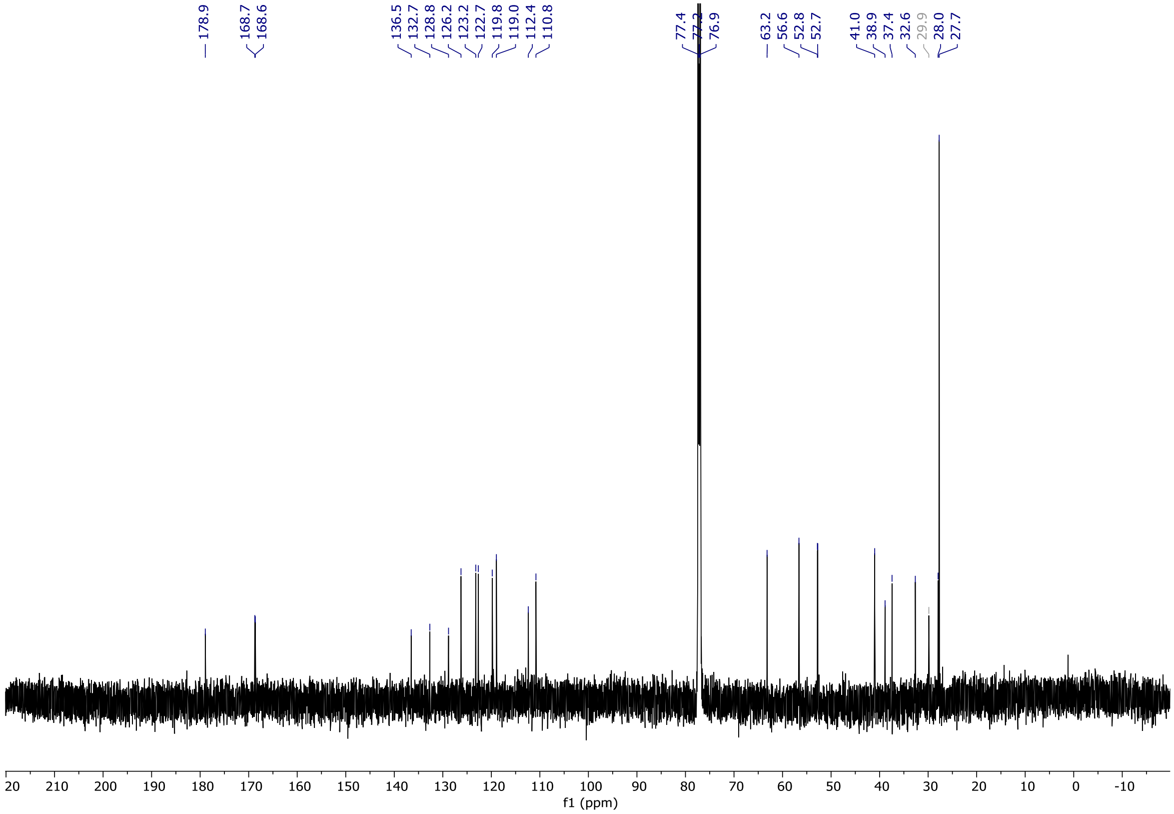
5.92 (HMBC, $CDCl_3$)



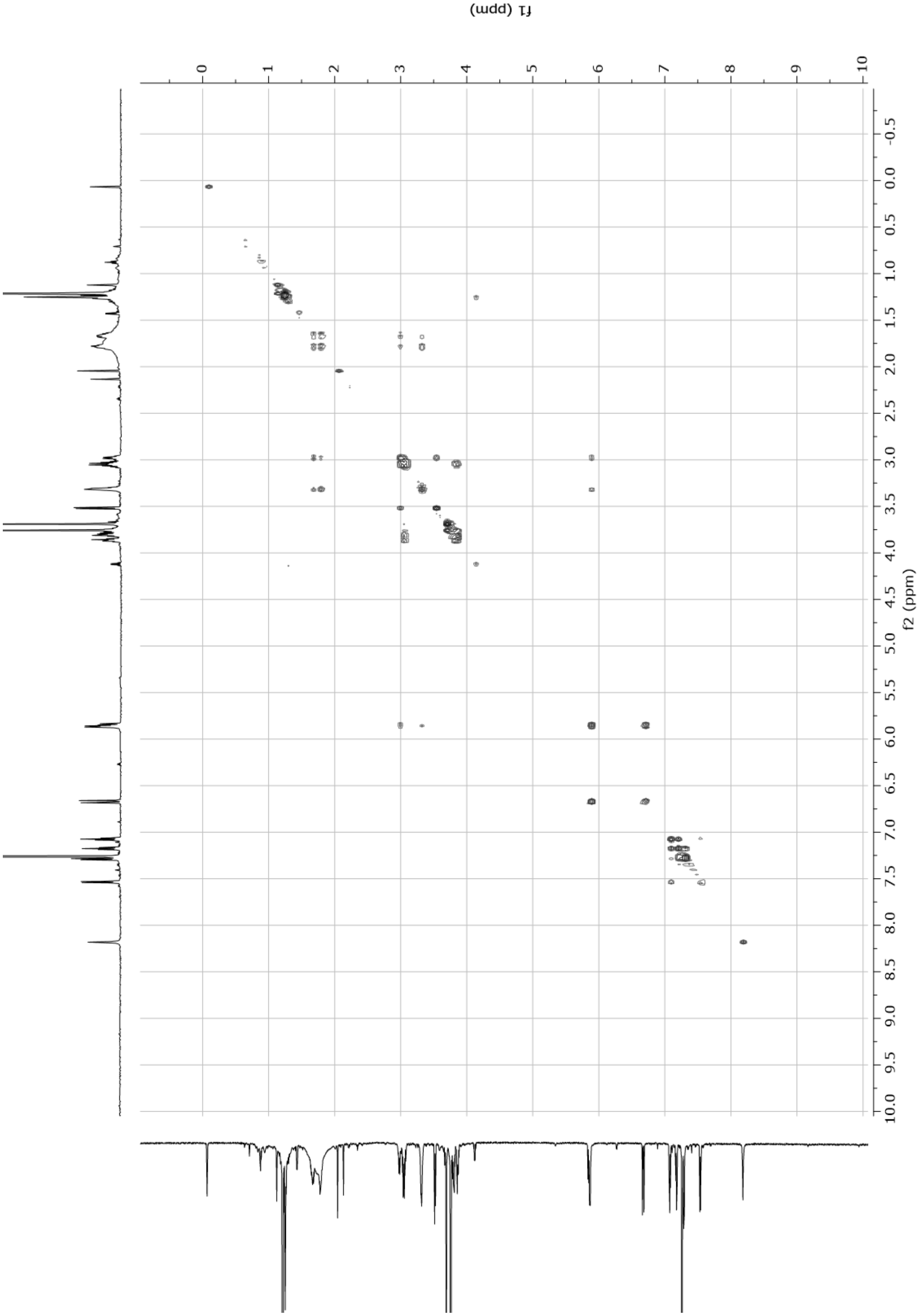
5.97 (^{1}H NMR, 700 MHz, CDCl$_3$)



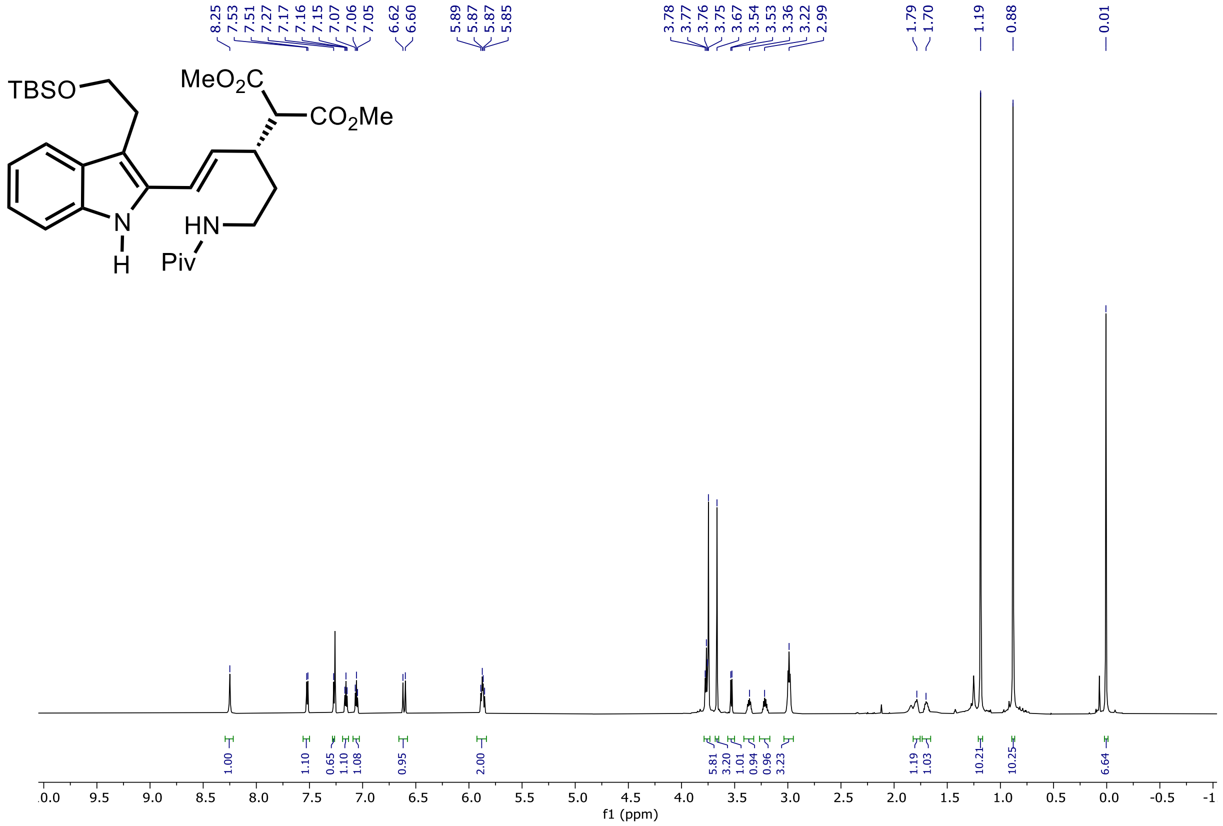
5.97 (^{13}C NMR, 151 MHz, CDCl$_3$)



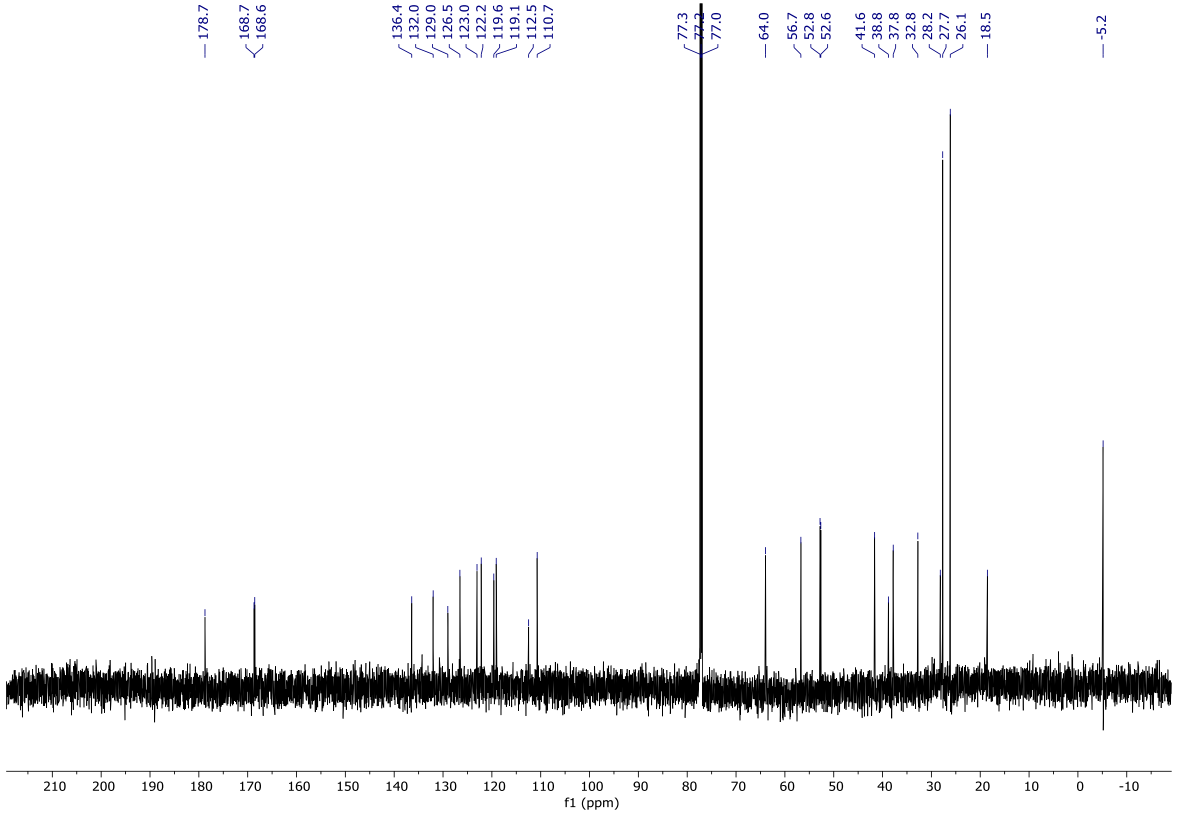
5.97 (COSY, $CDCl_3$)



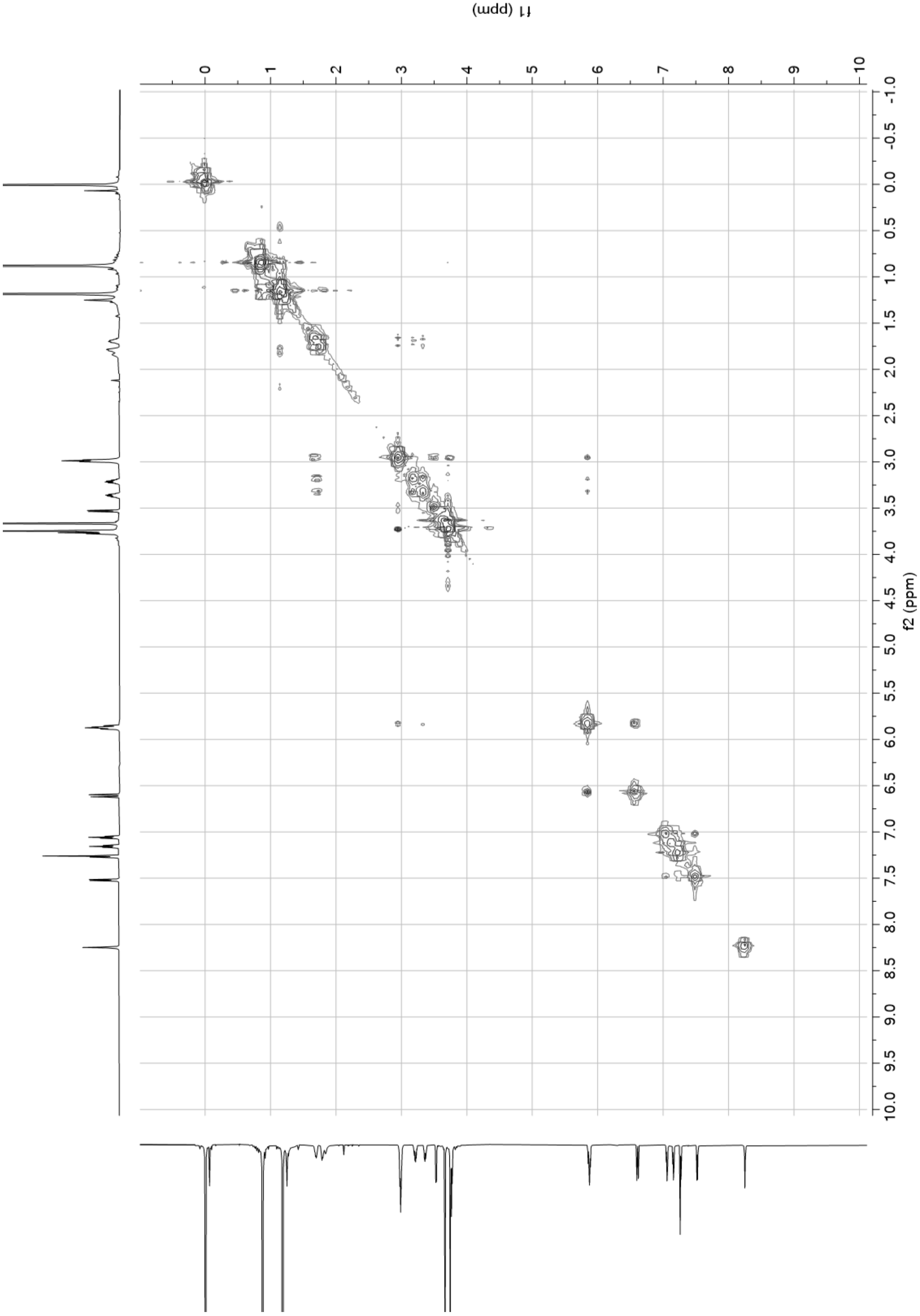
5.98 (^{1}H NMR, 700 MHz, CDCl$_3$)



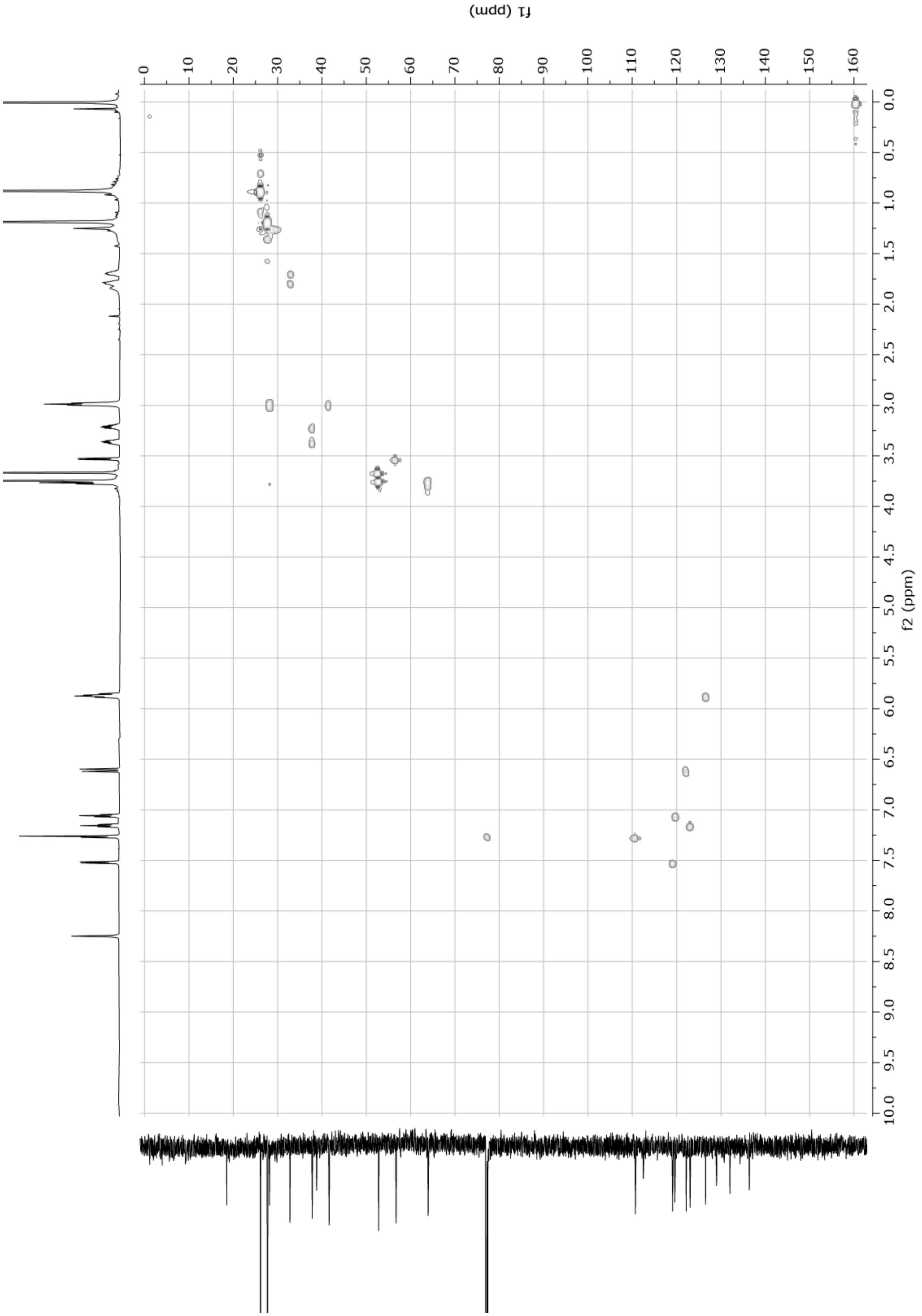
5.98 (^{13}C NMR, 176 MHz, CDCl$_3$)



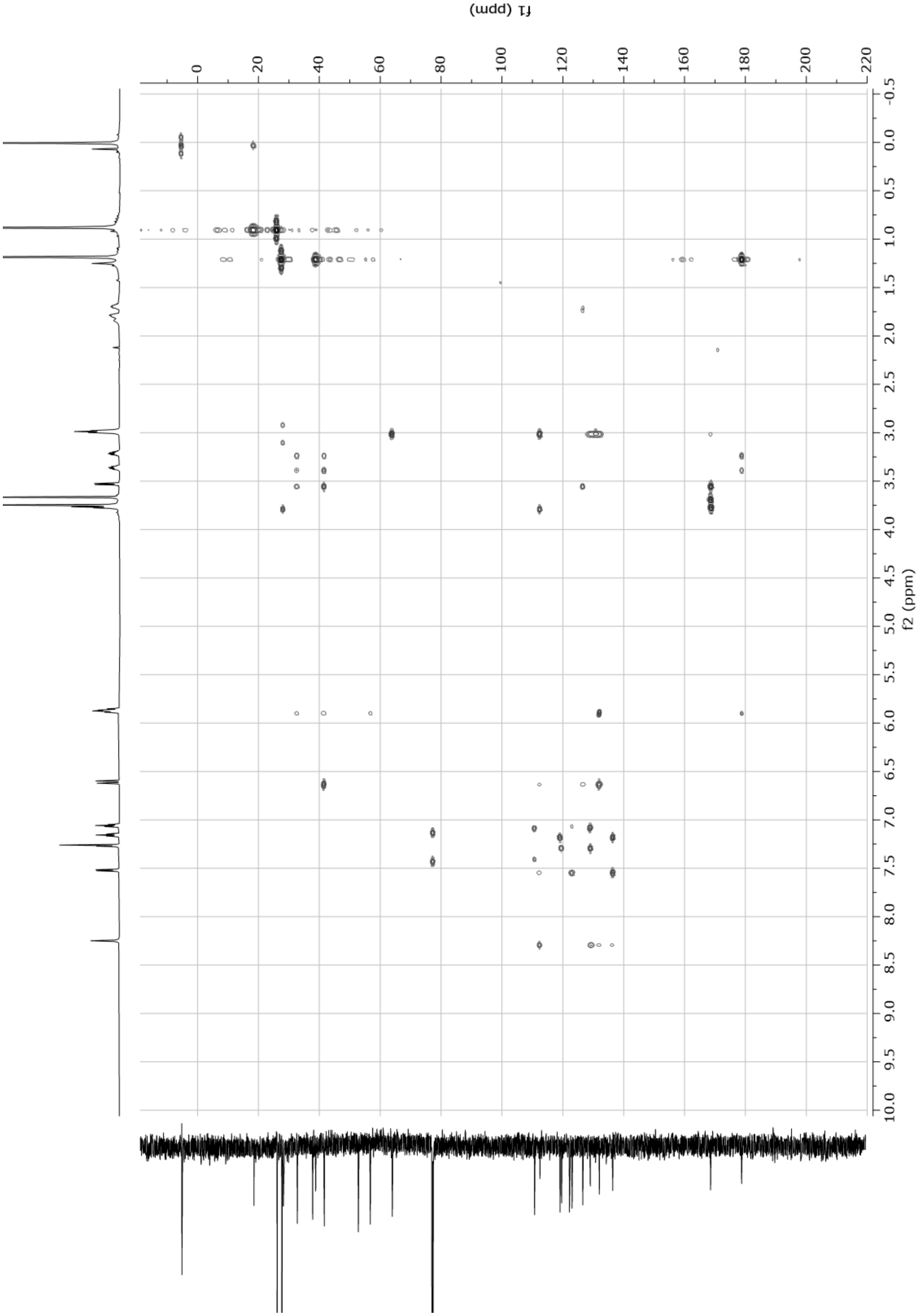
5.98 (COSY, $CDCl_3$)



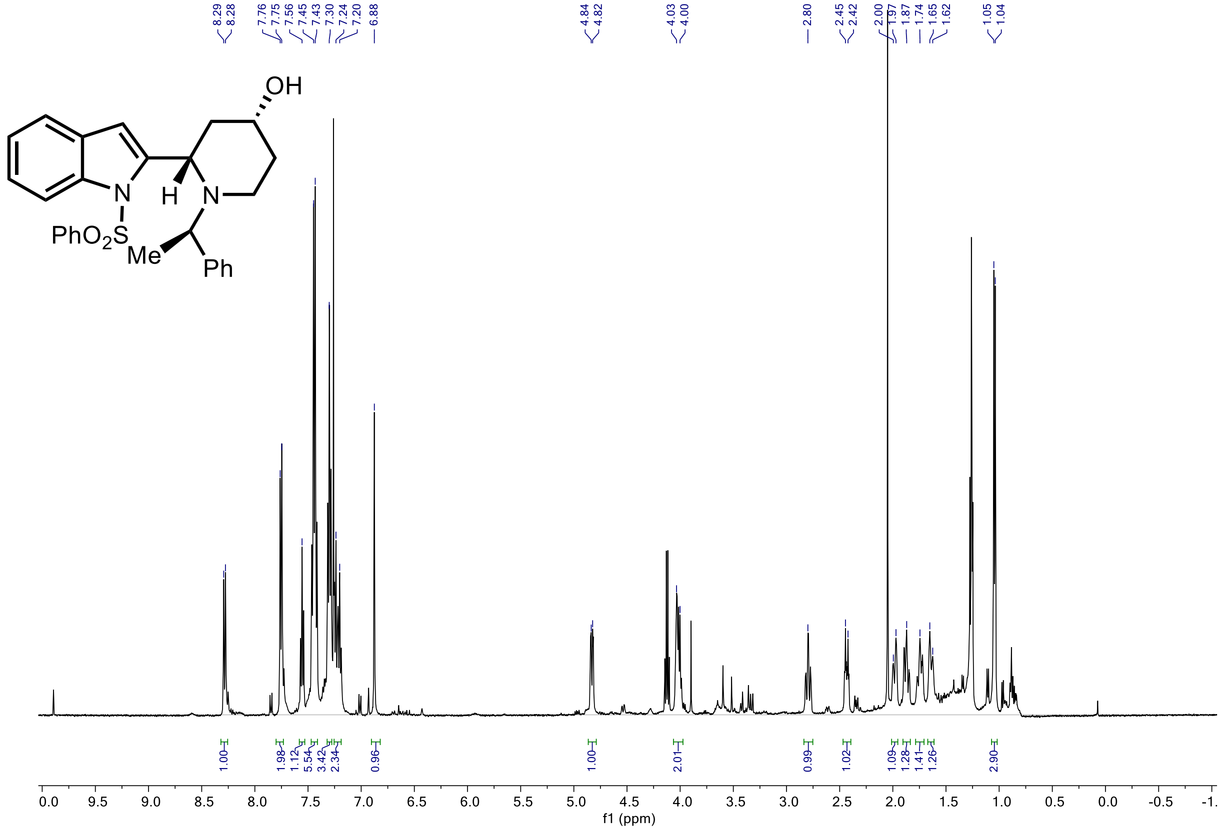
5.98 (HSQC, $CDCl_3$)



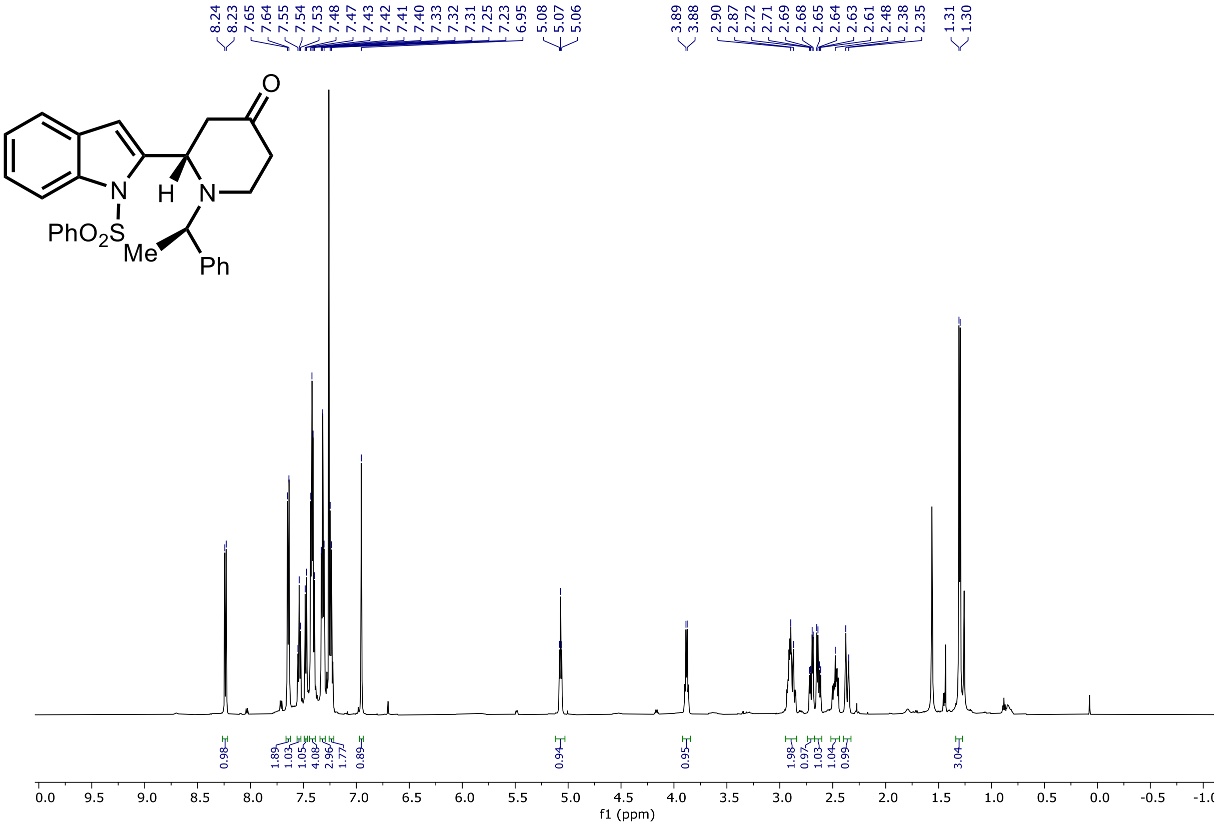
5.98 (HMBC, $CDCl_3$)



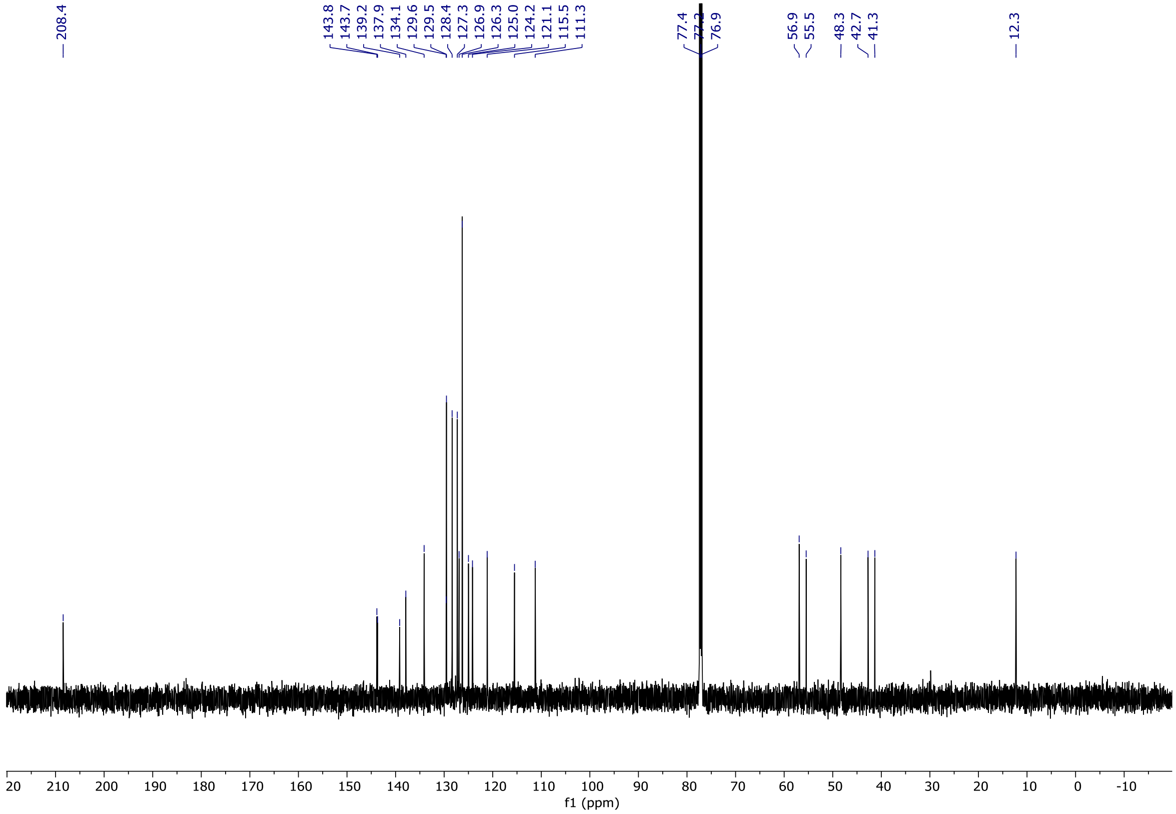
5.100 (^{1}H NMR, 500 MHz, CDCl$_3$)



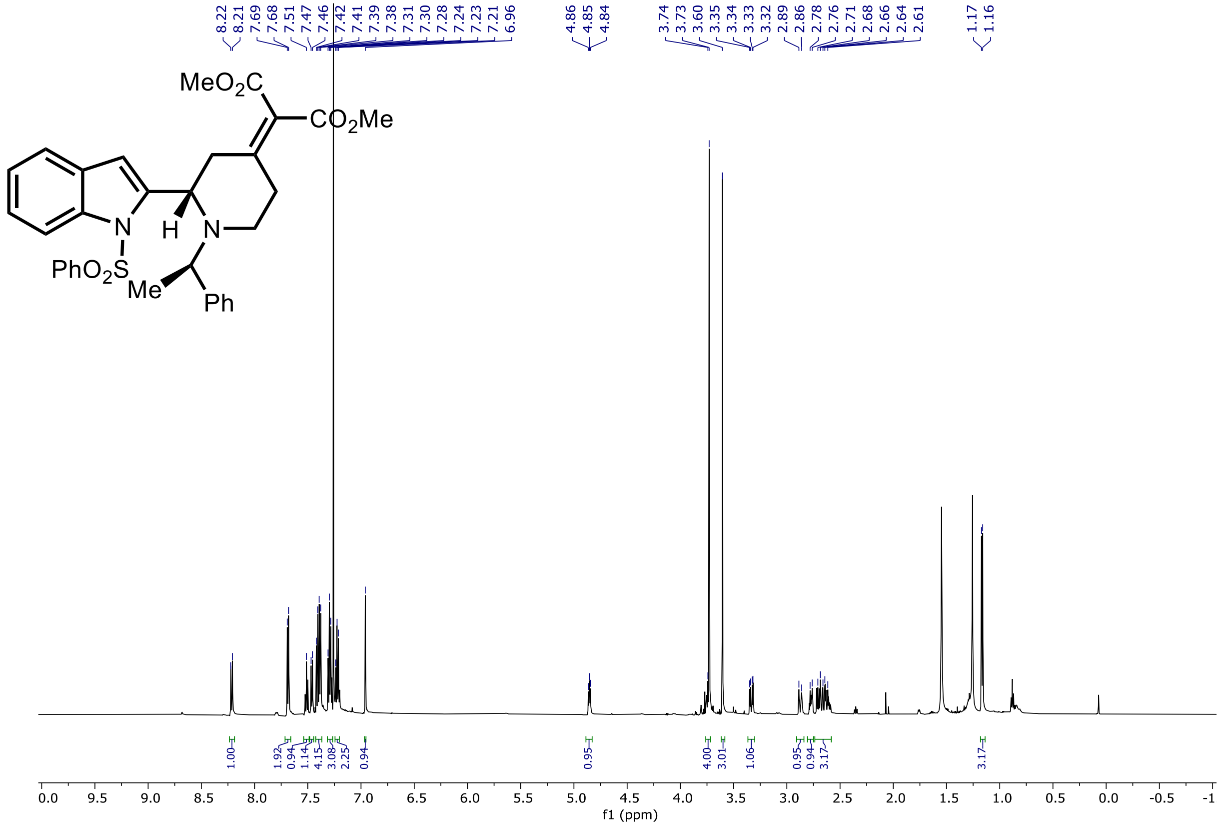
5.102 (^{1}H NMR, 600 MHz, CDCl$_3$)



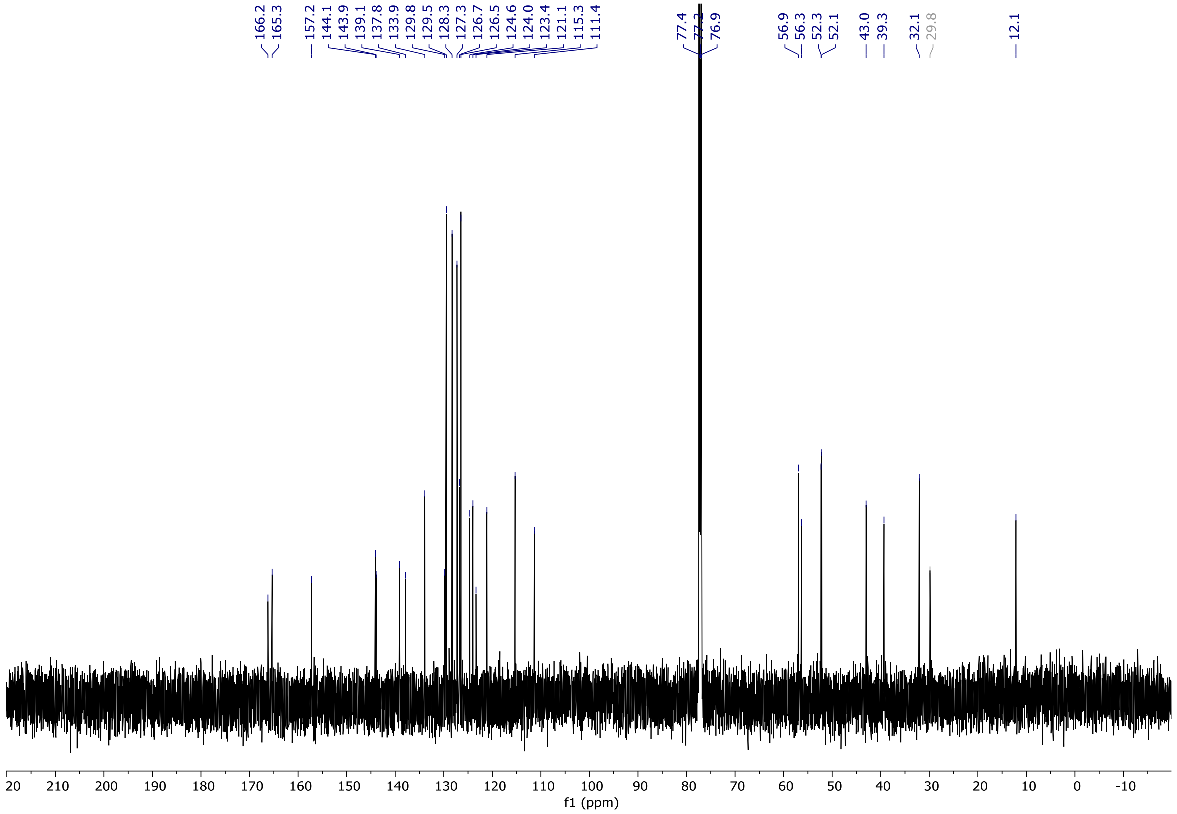
5.102 (^{13}C NMR, 151 MHz, CDCl$_3$)



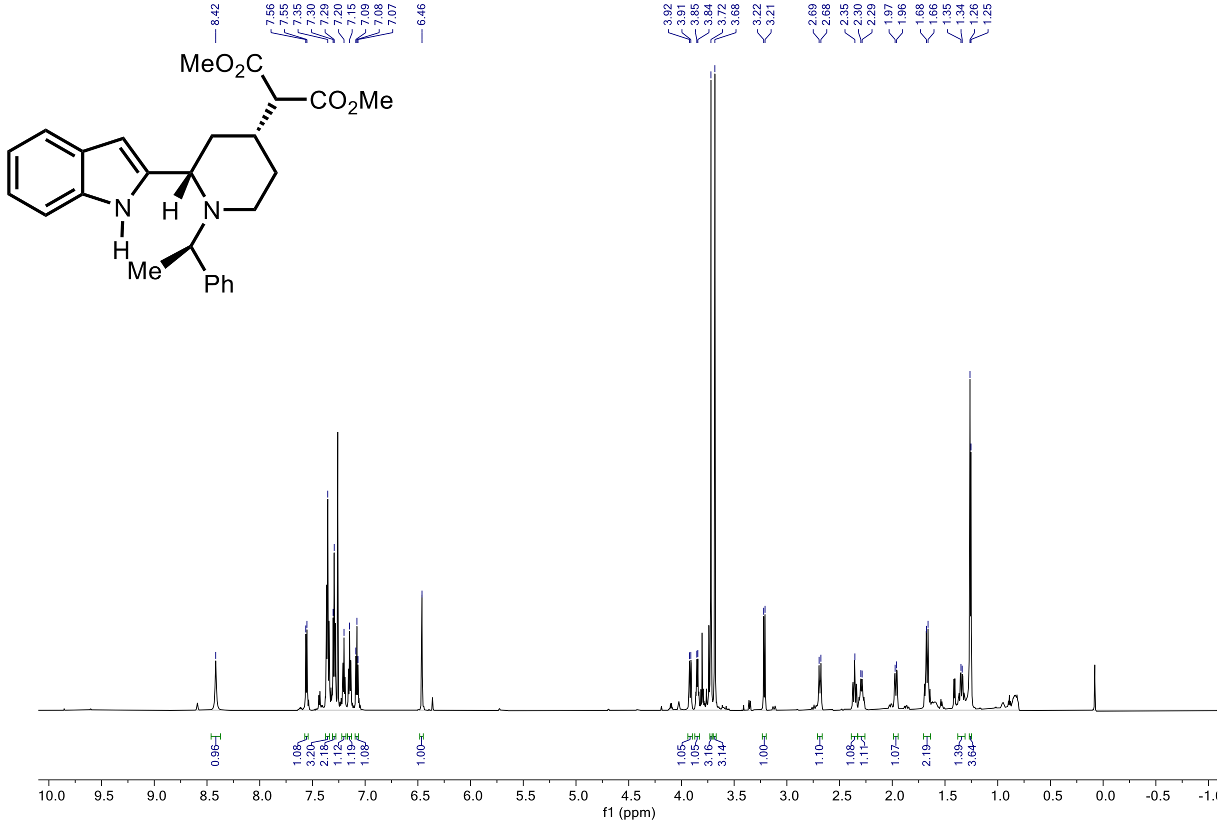
5.104 (^{1}H NMR, 600 MHz, CDCl$_3$)



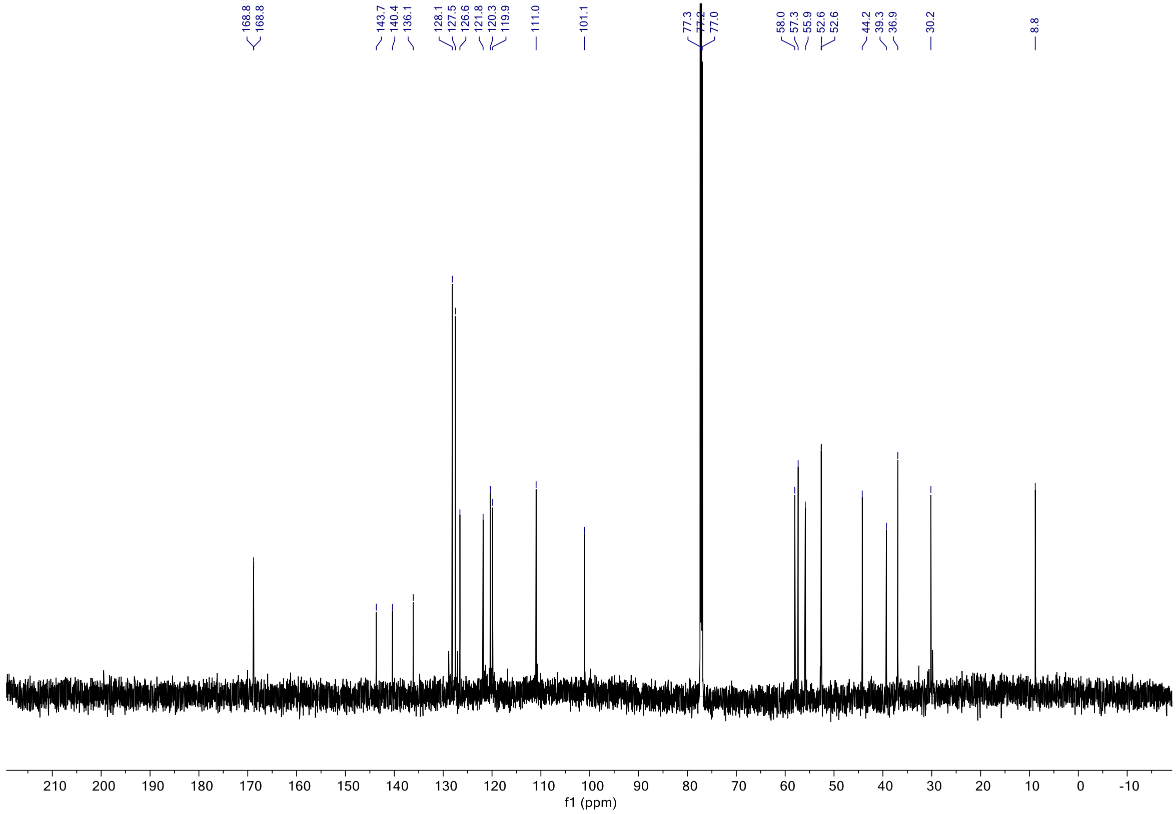
5.104 (^{13}C NMR, 151 MHz, CDCl$_3$)



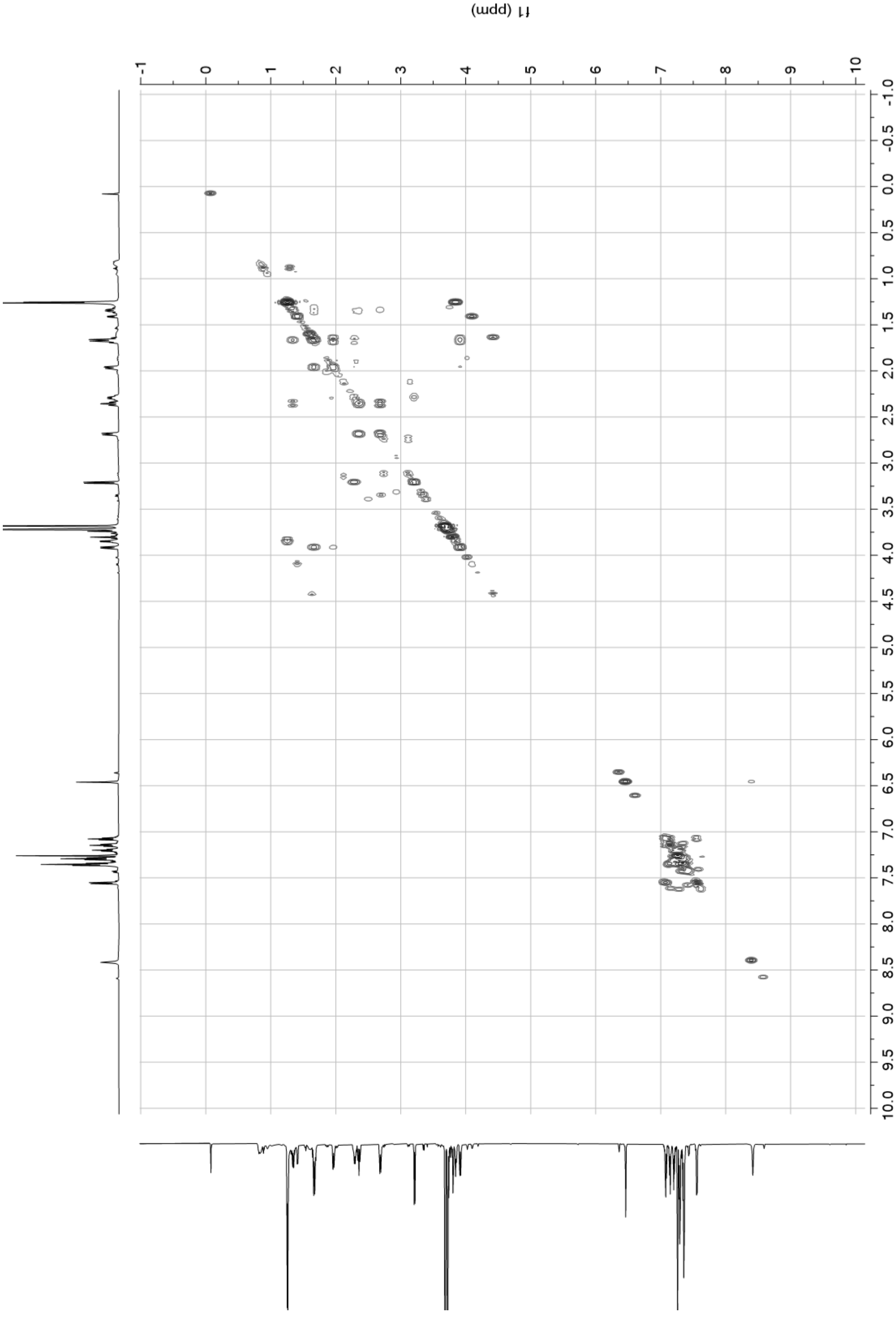
5.105 (^{1}H NMR, 700 MHz, $CDCl_3$)



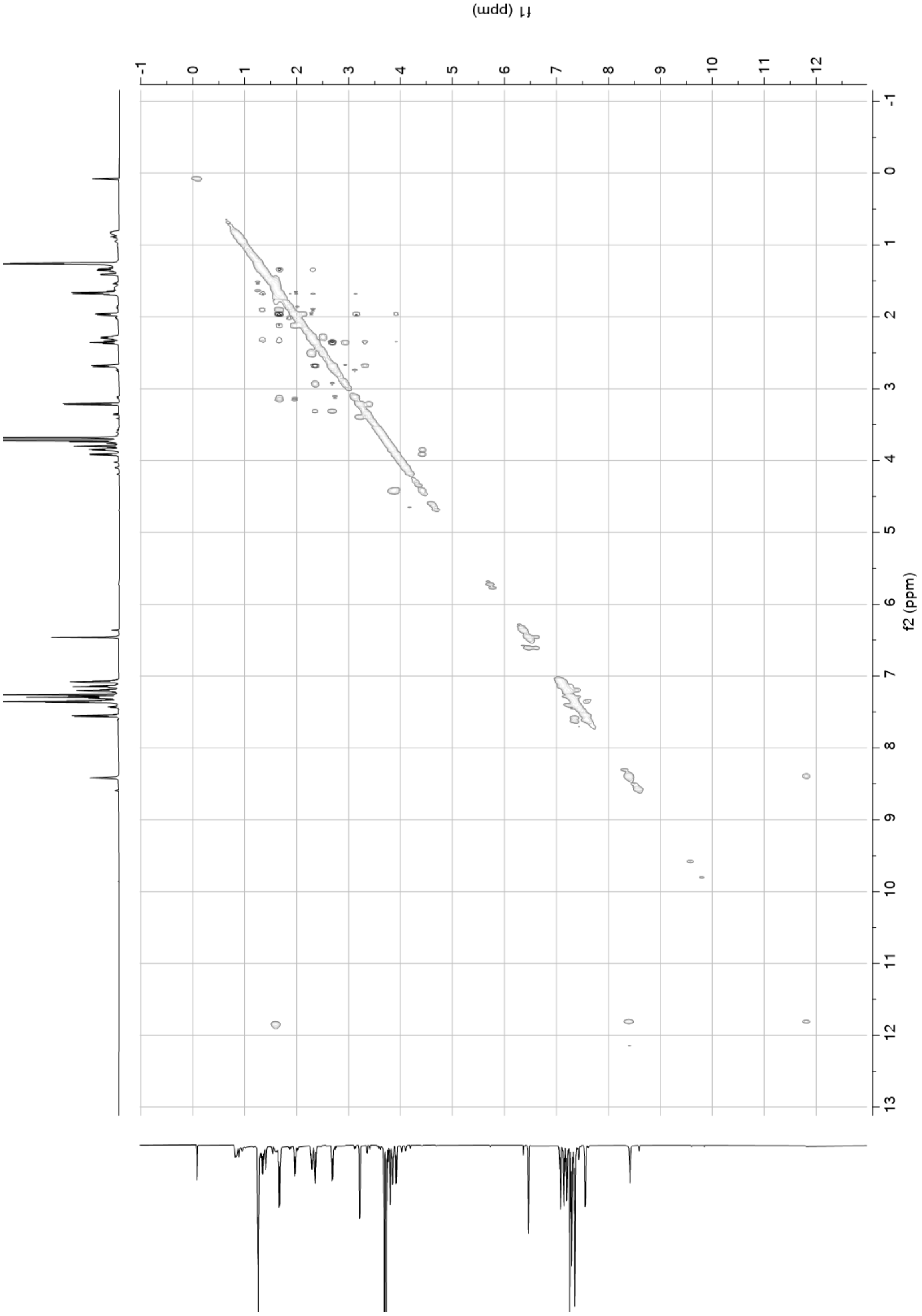
5.105 (^{13}C NMR, 176 MHz, $CDCl_3$)



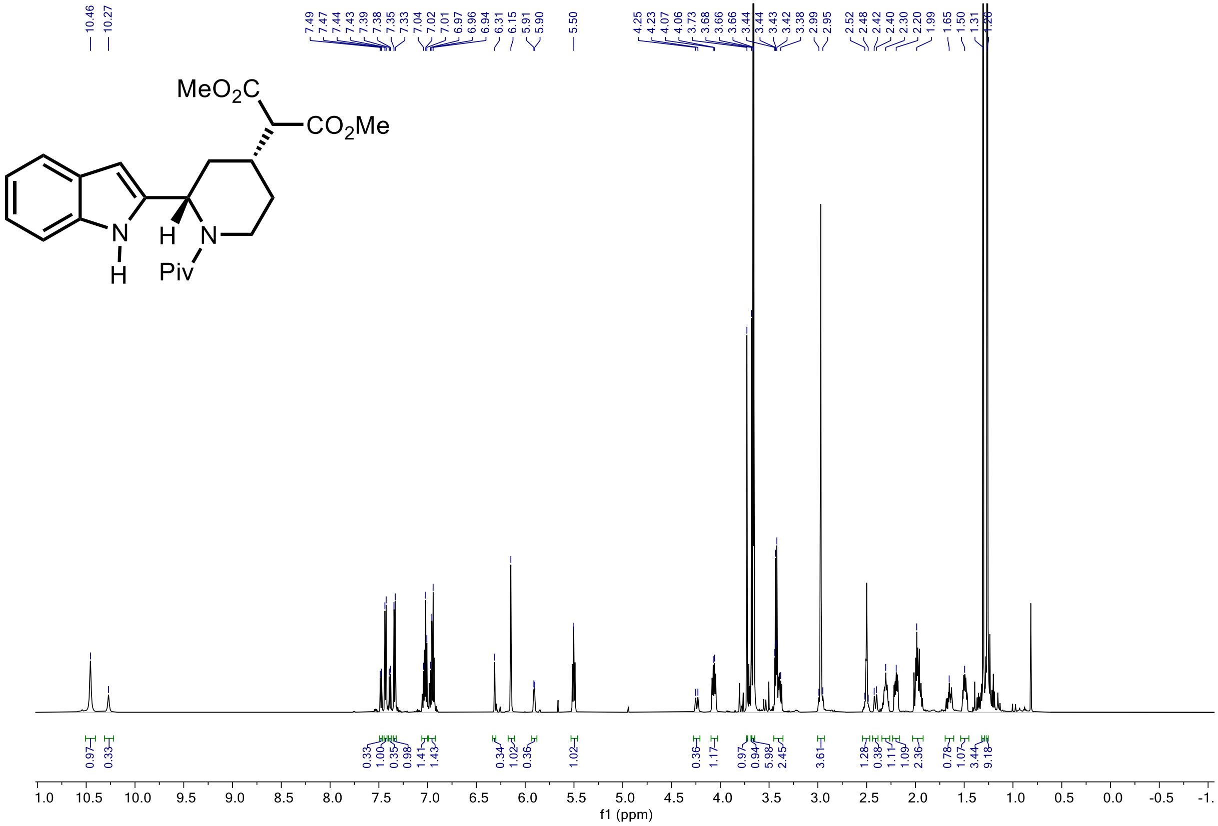
5.105 (COSY, CDCl$_3$)



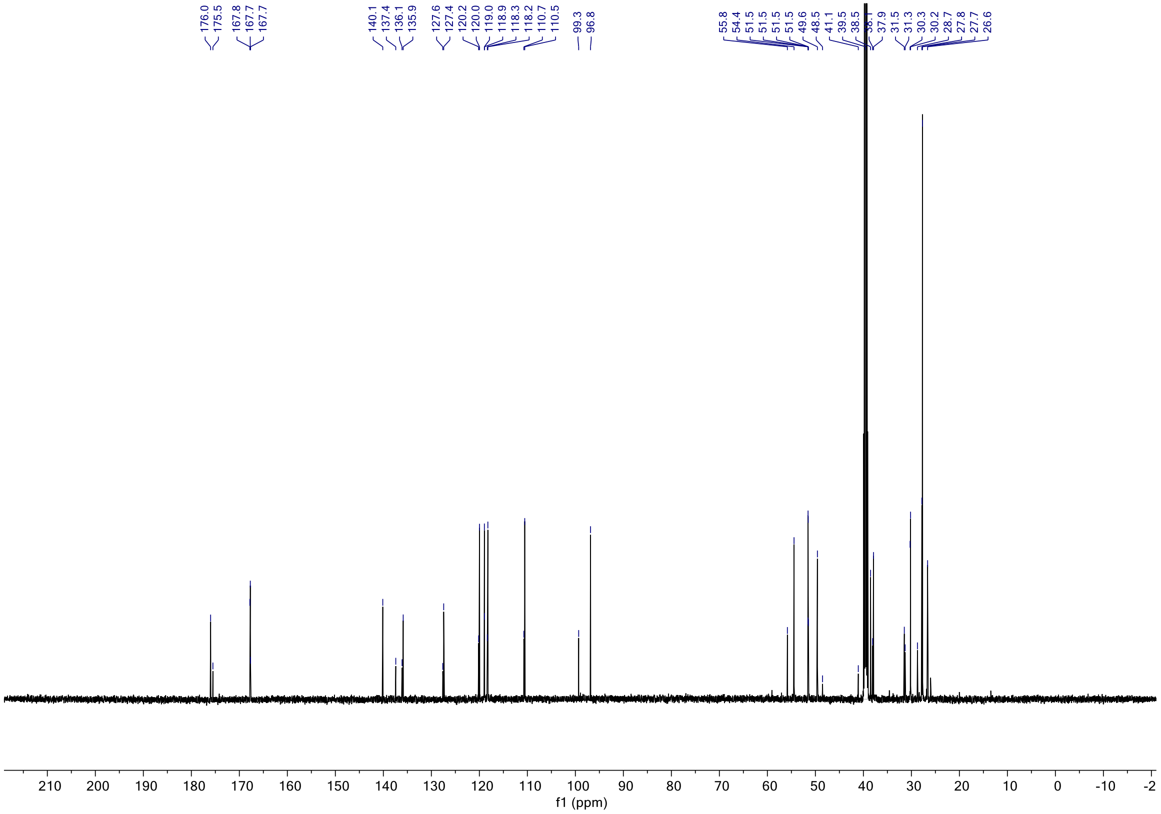
5.105 (NOESY, $CDCl_3$)



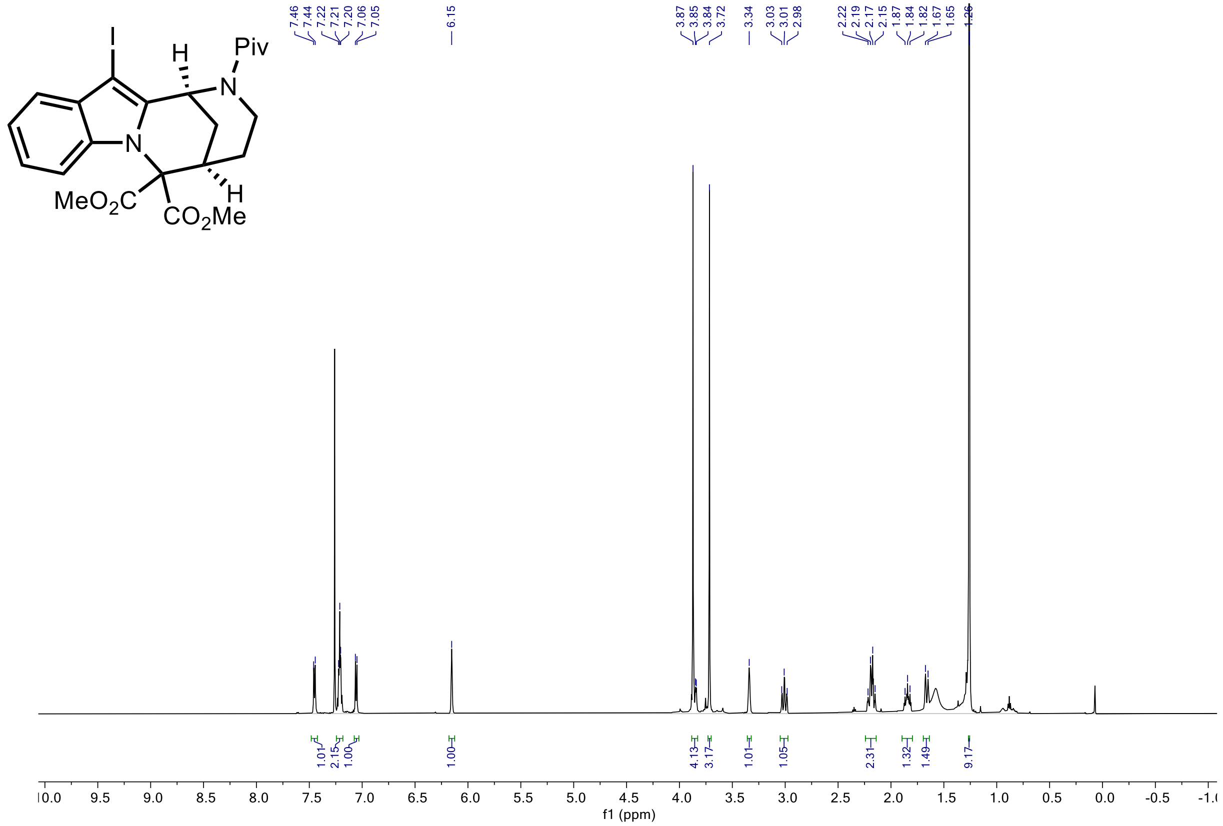
5.107 (^{1}H NMR, 600 MHz, DMSO, 100 ^{o}C)



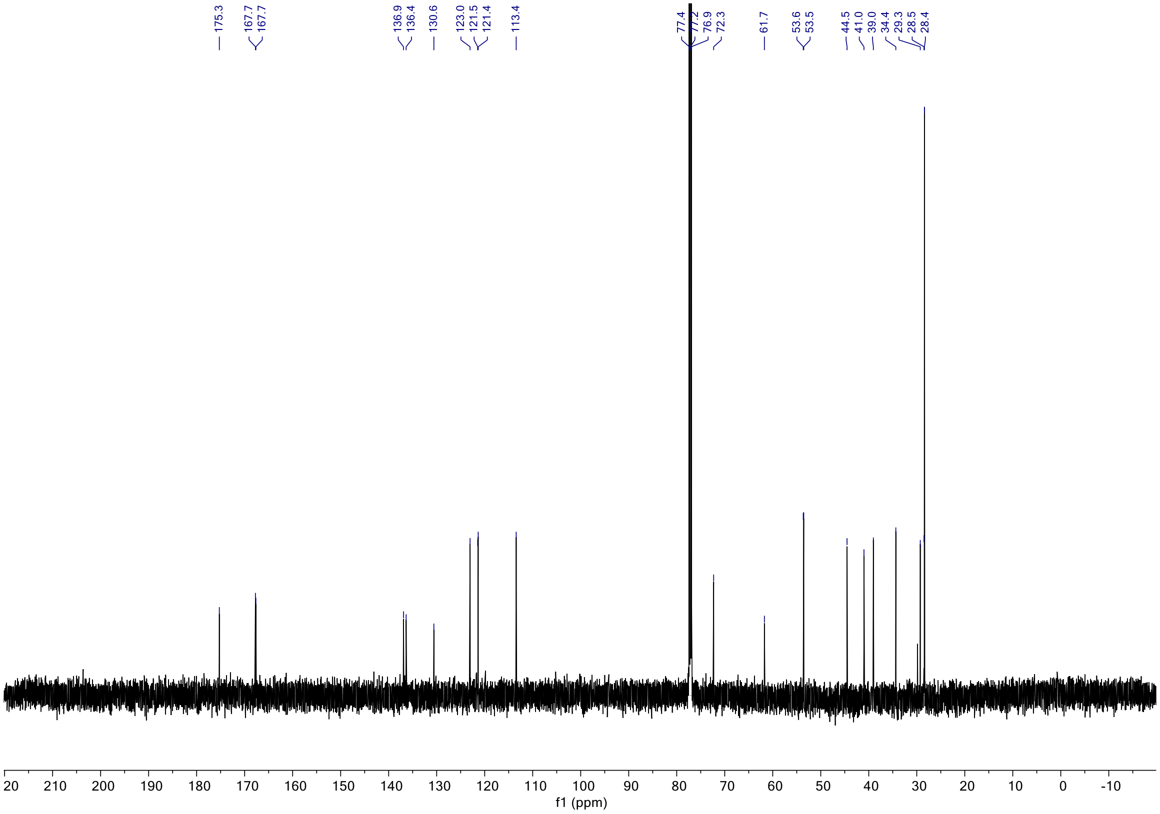
5.107 (^{13}C NMR, 151 MHz, DMSO, 100 ^{o}C)



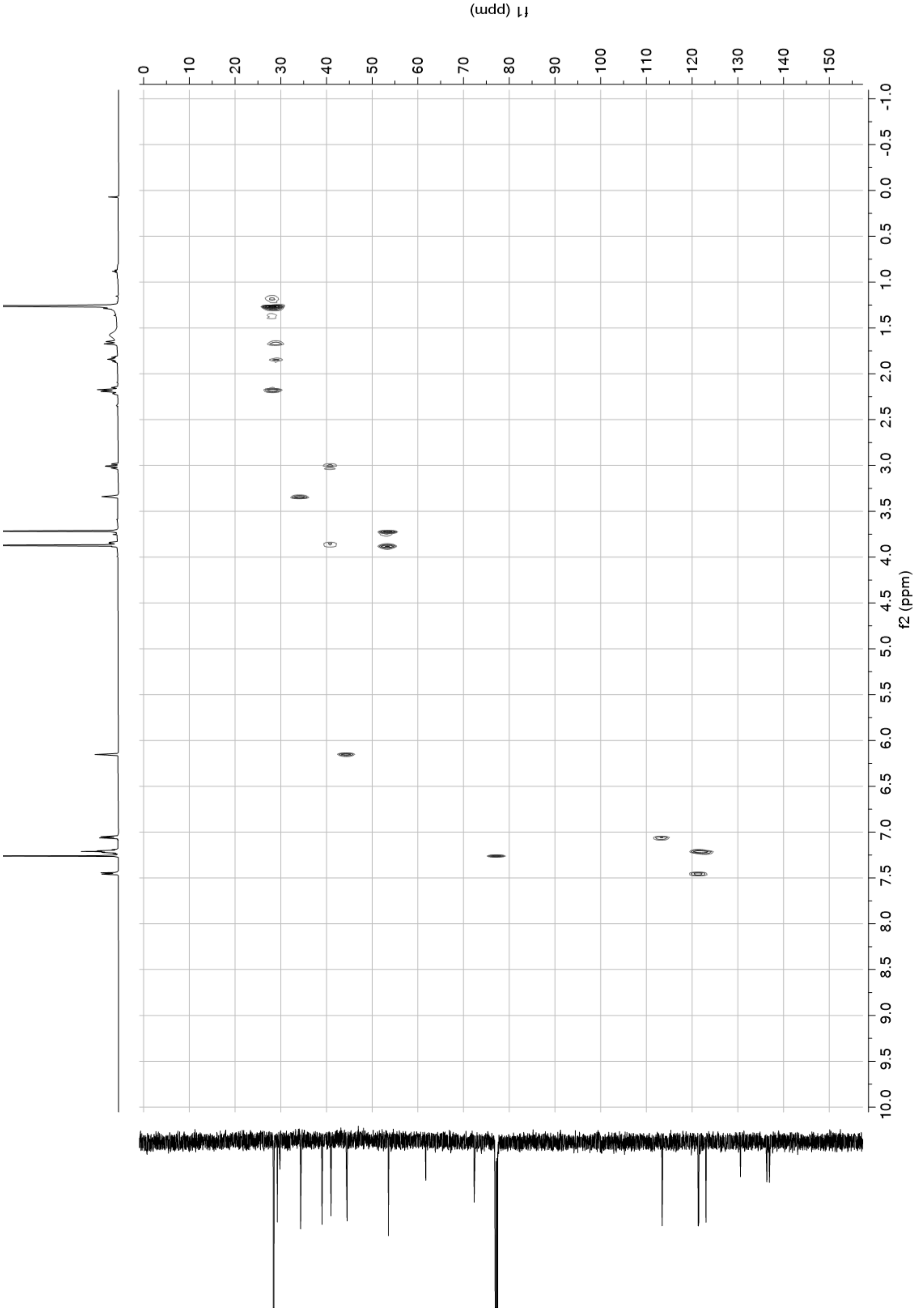
5.108 (^{1}H NMR, 600 MHz, CDCl$_3$)



5.108 (^{13}C NMR, 151 MHz, CDCl$_3$)



5.108 (HSQC, $CDCl_3$)



5.11.3 X-Ray Crystallographic Data for Chapter 5

X-Ray Analysis of 5.77

An orange block 0.21 x 0.19 x 0.13 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 33.00 mm and exposure time was 0.50 seconds per frame at low and high angles, using a scan width of 0.5°. Data collection was 100% complete to 74.000° in θ. A total of 35546 reflections were collected covering the indices -10<=h<=10, -10<=k<=10, -29<=l<=29. 6888 reflections were founded to be symmetry independent, with an R_{int} of 0.0318. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the CrysAlis^{Pro} 1.171.41.116a software program and scaled using the SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2015) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

[Note: The instruments are supported by an NIH Shared Instrument Grant S10-RR027172.]

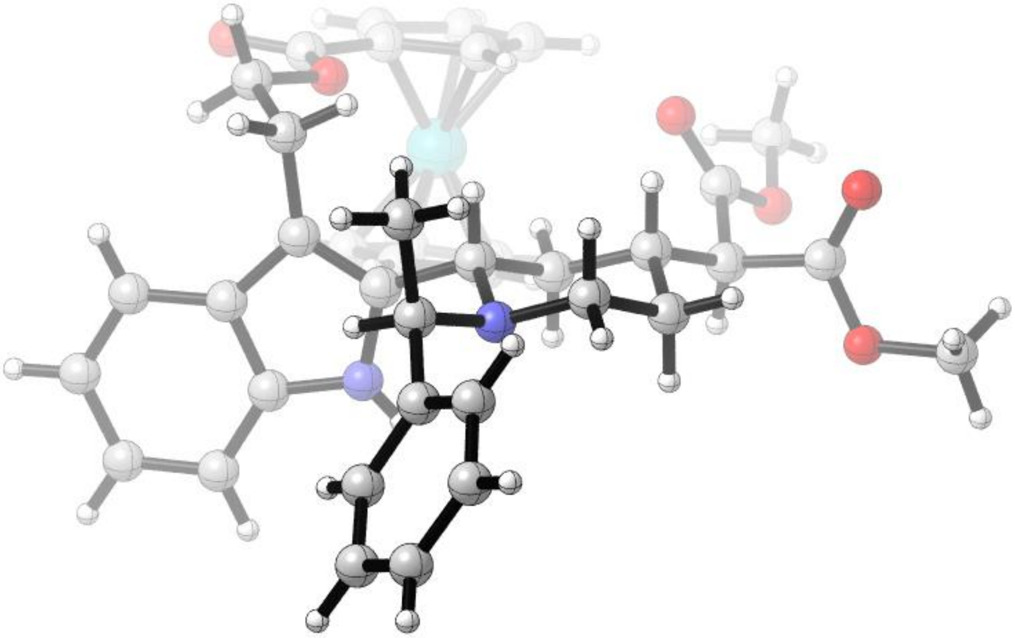


Figure 24. CYLview representation of **5.77**.

Table 5.2 Crystal data and structure refinement for **5.77**.

Identification code	KJones04_Sarpong	
Empirical formula	C39 H42 Fe N2 O6	
Formula weight	690.59	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 8.44320(10) Å	a= 90°.
	b = 8.65900(10) Å	b= 90.8560(10)°.
	c = 23.3610(2) Å	g = 90°.
Volume	1707.72(3) Å^3	
Z	2	
Density (calculated)	1.343 Mg/m^3	
Absorption coefficient	3.947 mm^{-1}	
F(000)	728	
Crystal size	0.210 x 0.190 x 0.130 mm^3	
Theta range for data collection	3.785 to 74.463°.	
Index ranges	-10<=h<=10, -10<=k<=10, -29<=l<=29	
Reflections collected	35546	
Independent reflections	6888 [R(int) = 0.0318]	
Completeness to theta = 74.000°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.71348	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6888 / 1 / 440	
Goodness-of-fit on F^2	1.064	
Final R indices [I>2sigma(I)]	R1 = 0.0263, wR2 = 0.0694	
R indices (all data)	R1 = 0.0275, wR2 = 0.0699	
Absolute structure parameter	-0.0102(15)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.211 and -0.266 e.Å^{-3}	

Table 5.3 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **5.77**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Fe(1)	2049(1)	1621(1)	6725(1)	24(1)
O(1)	-641(2)	3367(2)	7849(1)	27(1)
O(2)	1354(2)	4998(2)	7643(1)	23(1)
O(3)	4753(2)	5926(2)	5919(1)	29(1)

O(4)	6434(2)	4492(3)	5418(1)	44(1)
O(5)	8015(2)	8096(2)	5495(1)	35(1)
O(6)	10033(2)	6548(3)	5750(1)	32(1)
N(1)	6520(2)	4614(2)	8413(1)	19(1)
N(2)	7473(2)	7558(2)	7927(1)	19(1)
C(1)	489(2)	3299(3)	6930(1)	22(1)
C(2)	1521(3)	3831(3)	6489(1)	26(1)
C(3)	1301(3)	2846(3)	6012(1)	32(1)
C(4)	154(3)	1701(4)	6148(1)	31(1)
C(5)	-355(3)	1978(3)	6714(1)	26(1)
C(6)	2682(4)	295(5)	7403(2)	63(1)
C(7)	3729(5)	1533(5)	7355(2)	65(1)
C(8)	4437(3)	1445(5)	6835(2)	63(1)
C(9)	3878(4)	163(5)	6547(2)	57(1)
C(10)	2784(4)	-574(4)	6895(2)	58(1)
C(11)	337(2)	3867(3)	7516(1)	22(1)
C(12)	1167(3)	5696(3)	8205(1)	26(1)
C(13)	2647(2)	6634(3)	8334(1)	23(1)
C(14)	4077(2)	5649(3)	8451(1)	19(1)
C(15)	4271(2)	4576(3)	8917(1)	20(1)
C(16)	3318(3)	4126(3)	9378(1)	24(1)
C(17)	3933(3)	3103(3)	9778(1)	28(1)
C(18)	5469(3)	2508(3)	9732(1)	28(1)
C(19)	6433(3)	2929(3)	9285(1)	24(1)
C(20)	5815(2)	3963(3)	8882(1)	19(1)
C(21)	5477(2)	5648(3)	8160(1)	19(1)
C(22)	6060(2)	6714(3)	7703(1)	19(1)
C(23)	7138(3)	8348(3)	8482(1)	22(1)
C(24)	5975(3)	9698(3)	8439(1)	31(1)
C(25)	8661(2)	8785(3)	8800(1)	22(1)
C(26)	9249(3)	7780(3)	9220(1)	24(1)
C(27)	10570(3)	8161(3)	9554(1)	30(1)
C(28)	11350(3)	9553(3)	9467(1)	32(1)
C(29)	10804(3)	10548(3)	9044(1)	31(1)
C(30)	9457(3)	10178(3)	8716(1)	27(1)
C(31)	8077(3)	8617(3)	7494(1)	22(1)
C(32)	8574(2)	7751(3)	6960(1)	21(1)
C(33)	7149(2)	6905(2)	6700(1)	19(1)
C(34)	6465(2)	5830(3)	7154(1)	20(1)
C(35)	7562(2)	5999(3)	6155(1)	21(1)
C(36)	6080(3)	5494(3)	5831(1)	24(1)
C(37)	5082(4)	3956(5)	5081(2)	58(1)
C(38)	8529(3)	7003(3)	5755(1)	24(1)
C(39)	11100(3)	7467(4)	5410(1)	38(1)

Table 5.4 Bond lengths [Å] and angles [°] for **5.77**.

Fe(1)-C(6)	2.023(3)
Fe(1)-C(1)	2.024(2)
Fe(1)-C(7)	2.031(3)
Fe(1)-C(8)	2.034(3)
Fe(1)-C(10)	2.037(3)
Fe(1)-C(2)	2.039(2)
Fe(1)-C(9)	2.042(3)
Fe(1)-C(5)	2.053(2)
Fe(1)-C(3)	2.065(2)
Fe(1)-C(4)	2.077(2)
O(1)-C(11)	1.221(3)
O(2)-C(11)	1.333(3)
O(2)-C(12)	1.455(3)
O(3)-C(36)	1.202(3)
O(4)-C(36)	1.334(3)
O(4)-C(37)	1.454(3)
O(5)-C(38)	1.203(3)
O(6)-C(38)	1.330(3)
O(6)-C(39)	1.448(3)
N(1)-C(20)	1.374(3)
N(1)-C(21)	1.382(3)
N(1)-H(1)	0.80(3)
N(2)-C(31)	1.463(3)
N(2)-C(22)	1.487(3)
N(2)-C(23)	1.496(3)
C(1)-C(5)	1.435(3)
C(1)-C(2)	1.436(3)
C(1)-C(11)	1.463(3)
C(2)-C(3)	1.412(4)
C(2)-H(2)	0.9500
C(3)-C(4)	1.426(4)
C(3)-H(3)	0.9500
C(4)-C(5)	1.416(3)
C(4)-H(4)	0.9500
C(5)-H(5)	0.9500
C(6)-C(7)	1.395(6)
C(6)-C(10)	1.409(6)
C(6)-H(6)	0.9500
C(7)-C(8)	1.364(6)
C(7)-H(7)	0.9500
C(8)-C(9)	1.378(6)
C(8)-H(8)	0.9500
C(9)-C(10)	1.395(6)
C(9)-H(9)	0.9500
C(10)-H(10)	0.9500
C(12)-C(13)	1.517(3)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.499(3)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-C(21)	1.373(3)
C(14)-C(15)	1.440(3)
C(15)-C(16)	1.409(3)
C(15)-C(20)	1.411(3)
C(16)-C(17)	1.382(4)
C(16)-H(16)	0.9500
C(17)-C(18)	1.402(4)
C(17)-H(17)	0.9500
C(18)-C(19)	1.382(3)
C(18)-H(18)	0.9500
C(19)-C(20)	1.396(3)
C(19)-H(19)	0.9500
C(21)-C(22)	1.500(3)
C(22)-C(34)	1.537(3)
C(22)-H(22)	1.0000
C(23)-C(25)	1.524(3)
C(23)-C(24)	1.529(3)
C(23)-H(23)	1.0000
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-C(26)	1.396(3)
C(25)-C(30)	1.396(3)
C(26)-C(27)	1.392(3)
C(26)-H(26)	0.9500
C(27)-C(28)	1.390(4)
C(27)-H(27)	0.9500
C(28)-C(29)	1.385(4)
C(28)-H(28)	0.9500
C(29)-C(30)	1.398(3)
C(29)-H(29)	0.9500
C(30)-H(30)	0.9500
C(31)-C(32)	1.520(3)

C(31)-H(31A)	0.9900
C(31)-H(31B)	0.9900
C(32)-C(33)	1.527(3)
C(32)-H(32A)	0.9900
C(32)-H(32B)	0.9900
C(33)-C(34)	1.530(3)
C(33)-C(35)	1.539(3)
C(33)-H(33)	1.0000
C(34)-H(34A)	0.9900
C(34)-H(34B)	0.9900
C(35)-C(36)	1.518(3)
C(35)-C(38)	1.522(3)
C(35)-H(35)	1.0000
C(37)-H(37A)	0.9800
C(37)-H(37B)	0.9800
C(37)-H(37C)	0.9800
C(39)-H(39A)	0.9800
C(39)-H(39B)	0.9800
C(39)-H(39C)	0.9800
C(6)-Fe(1)-C(1)	112.76(12)
C(6)-Fe(1)-C(7)	40.26(19)
C(1)-Fe(1)-C(7)	107.77(12)
C(6)-Fe(1)-C(8)	66.93(15)
C(1)-Fe(1)-C(8)	132.17(15)
C(7)-Fe(1)-C(8)	39.20(17)
C(6)-Fe(1)-C(10)	40.62(17)
C(1)-Fe(1)-C(10)	145.17(14)
C(7)-Fe(1)-C(10)	67.40(15)
C(8)-Fe(1)-C(10)	66.84(15)
C(6)-Fe(1)-C(2)	143.01(16)
C(1)-Fe(1)-C(2)	41.39(9)
C(7)-Fe(1)-C(2)	112.27(14)
C(8)-Fe(1)-C(2)	108.50(13)
C(10)-Fe(1)-C(2)	173.43(14)
C(6)-Fe(1)-C(9)	67.48(14)
C(1)-Fe(1)-C(9)	171.52(15)
C(7)-Fe(1)-C(9)	66.58(15)
C(8)-Fe(1)-C(9)	39.52(18)
C(10)-Fe(1)-C(9)	39.99(16)
C(2)-Fe(1)-C(9)	133.50(14)
C(6)-Fe(1)-C(5)	110.13(12)
C(1)-Fe(1)-C(5)	41.21(9)
C(7)-Fe(1)-C(5)	133.94(15)
C(8)-Fe(1)-C(5)	172.11(16)
C(10)-Fe(1)-C(5)	116.15(12)
C(2)-Fe(1)-C(5)	69.10(9)
C(9)-Fe(1)-C(5)	147.24(15)
C(6)-Fe(1)-C(3)	175.89(17)
C(1)-Fe(1)-C(3)	68.28(10)
C(7)-Fe(1)-C(3)	143.71(17)
C(8)-Fe(1)-C(3)	115.59(14)
C(10)-Fe(1)-C(3)	136.53(15)
C(2)-Fe(1)-C(3)	40.26(10)
C(9)-Fe(1)-C(3)	112.13(12)
C(5)-Fe(1)-C(3)	67.82(10)
C(6)-Fe(1)-C(4)	135.94(16)
C(1)-Fe(1)-C(4)	68.39(10)
C(7)-Fe(1)-C(4)	173.88(15)
C(8)-Fe(1)-C(4)	146.87(15)
C(10)-Fe(1)-C(4)	112.77(13)
C(2)-Fe(1)-C(4)	68.31(11)
C(9)-Fe(1)-C(4)	117.79(13)
C(5)-Fe(1)-C(4)	40.10(10)
C(3)-Fe(1)-C(4)	40.27(11)
C(11)-O(2)-C(12)	115.30(17)
C(36)-O(4)-C(37)	114.7(2)
C(38)-O(6)-C(39)	116.4(2)
C(20)-N(1)-C(21)	109.01(18)
C(20)-N(1)-H(1)	126(2)
C(21)-N(1)-H(1)	125(2)
C(31)-N(2)-C(22)	110.52(16)
C(31)-N(2)-C(23)	112.64(18)
C(22)-N(2)-C(23)	111.63(16)
C(5)-C(1)-C(2)	107.9(2)
C(5)-C(1)-C(11)	123.2(2)
C(2)-C(1)-C(11)	128.8(2)
C(5)-C(1)-Fe(1)	70.49(13)
C(2)-C(1)-Fe(1)	69.87(13)
C(11)-C(1)-Fe(1)	122.00(15)
C(3)-C(2)-C(1)	107.3(2)
C(3)-C(2)-Fe(1)	70.85(15)
C(1)-C(2)-Fe(1)	68.74(13)
C(3)-C(2)-H(2)	126.3
C(1)-C(2)-H(2)	126.3
Fe(1)-C(2)-H(2)	125.7
C(2)-C(3)-C(4)	109.0(2)
C(2)-C(3)-Fe(1)	68.89(14)
C(4)-C(3)-Fe(1)	70.33(14)

C(2)-C(3)-H(3)	125.5
C(4)-C(3)-H(3)	125.5
Fe(1)-C(3)-H(3)	126.9
C(5)-C(4)-C(3)	107.9(2)
C(5)-C(4)-Fe(1)	69.04(12)
C(3)-C(4)-Fe(1)	69.40(14)
C(5)-C(4)-H(4)	126.1
C(3)-C(4)-H(4)	126.1
Fe(1)-C(4)-H(4)	127.1
C(4)-C(5)-C(1)	107.9(2)
C(4)-C(5)-Fe(1)	70.87(13)
C(1)-C(5)-Fe(1)	68.30(12)
C(4)-C(5)-H(5)	126.0
C(1)-C(5)-H(5)	126.0
Fe(1)-C(5)-H(5)	126.3
C(7)-C(6)-C(10)	107.2(3)
C(7)-C(6)-Fe(1)	70.20(18)
C(10)-C(6)-Fe(1)	70.23(18)
C(7)-C(6)-H(6)	126.4
C(10)-C(6)-H(6)	126.4
Fe(1)-C(6)-H(6)	124.8
C(8)-C(7)-C(6)	108.4(3)
C(8)-C(7)-Fe(1)	70.50(18)
C(6)-C(7)-Fe(1)	69.54(18)
C(8)-C(7)-H(7)	125.8
C(6)-C(7)-H(7)	125.8
Fe(1)-C(7)-H(7)	125.7
C(7)-C(8)-C(9)	109.3(4)
C(7)-C(8)-Fe(1)	70.30(18)
C(9)-C(8)-Fe(1)	70.56(18)
C(7)-C(8)-H(8)	125.4
C(9)-C(8)-H(8)	125.4
Fe(1)-C(8)-H(8)	125.4
C(8)-C(9)-C(10)	107.9(3)
C(8)-C(9)-Fe(1)	69.91(18)
C(10)-C(9)-Fe(1)	69.79(18)
C(8)-C(9)-H(9)	126.1
C(10)-C(9)-H(9)	126.1
Fe(1)-C(9)-H(9)	125.8
C(9)-C(10)-C(6)	107.3(3)
C(9)-C(10)-Fe(1)	70.22(19)
C(6)-C(10)-Fe(1)	69.16(18)
C(9)-C(10)-H(10)	126.4
C(6)-C(10)-H(10)	126.4
Fe(1)-C(10)-H(10)	125.8
O(1)-C(11)-O(2)	124.0(2)
O(1)-C(11)-C(1)	123.1(2)
O(2)-C(11)-C(1)	112.95(18)
O(2)-C(12)-C(13)	107.63(17)
O(2)-C(12)-H(12A)	110.2
C(13)-C(12)-H(12A)	110.2
O(2)-C(12)-H(12B)	110.2
C(13)-C(12)-H(12B)	110.2
H(12A)-C(12)-H(12B)	108.5
C(14)-C(13)-C(12)	113.0(2)
C(14)-C(13)-H(13A)	109.0
C(12)-C(13)-H(13A)	109.0
C(14)-C(13)-H(13B)	109.0
C(12)-C(13)-H(13B)	109.0
H(13A)-C(13)-H(13B)	107.8
C(21)-C(14)-C(15)	106.56(18)
C(21)-C(14)-C(13)	127.4(2)
C(15)-C(14)-C(13)	125.94(18)
C(16)-C(15)-C(20)	118.7(2)
C(16)-C(15)-C(14)	134.2(2)
C(20)-C(15)-C(14)	107.01(18)
C(17)-C(16)-C(15)	118.7(2)
C(17)-C(16)-H(16)	120.6
C(15)-C(16)-H(16)	120.6
C(16)-C(17)-C(18)	121.5(2)
C(16)-C(17)-H(17)	119.3
C(18)-C(17)-H(17)	119.3
C(19)-C(18)-C(17)	121.1(2)
C(19)-C(18)-H(18)	119.4
C(17)-C(18)-H(18)	119.4
C(18)-C(19)-C(20)	117.4(2)
C(18)-C(19)-H(19)	121.3
C(20)-C(19)-H(19)	121.3
N(1)-C(20)-C(19)	129.7(2)
N(1)-C(20)-C(15)	107.74(19)
C(19)-C(20)-C(15)	122.5(2)
C(14)-C(21)-N(1)	109.65(19)
C(14)-C(21)-C(22)	130.3(2)
N(1)-C(21)-C(22)	119.32(18)
N(2)-C(22)-C(21)	108.75(16)
N(2)-C(22)-C(34)	110.57(16)
C(21)-C(22)-C(34)	111.58(19)
N(2)-C(22)-H(22)	108.6

C(21)-C(22)-H(22)	108.6
C(34)-C(22)-H(22)	108.6
N(2)-C(23)-C(25)	111.54(17)
N(2)-C(23)-C(24)	115.01(18)
C(25)-C(23)-C(24)	112.2(2)
N(2)-C(23)-H(23)	105.7
C(25)-C(23)-H(23)	105.7
C(24)-C(23)-H(23)	105.7
C(23)-C(24)-H(24A)	109.5
C(23)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(23)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(26)-C(25)-C(30)	118.1(2)
C(26)-C(25)-C(23)	118.4(2)
C(30)-C(25)-C(23)	123.4(2)
C(27)-C(26)-C(25)	121.3(2)
C(27)-C(26)-H(26)	119.3
C(25)-C(26)-H(26)	119.3
C(28)-C(27)-C(26)	120.0(2)
C(28)-C(27)-H(27)	120.0
C(26)-C(27)-H(27)	120.0
C(29)-C(28)-C(27)	119.4(2)
C(29)-C(28)-H(28)	120.3
C(27)-C(28)-H(28)	120.3
C(28)-C(29)-C(30)	120.4(2)
C(28)-C(29)-H(29)	119.8
C(30)-C(29)-H(29)	119.8
C(25)-C(30)-C(29)	120.7(2)
C(25)-C(30)-H(30)	119.6
C(29)-C(30)-H(30)	119.6
N(2)-C(31)-C(32)	111.25(18)
N(2)-C(31)-H(31A)	109.4
C(32)-C(31)-H(31A)	109.4
N(2)-C(31)-H(31B)	109.4
C(32)-C(31)-H(31B)	109.4
H(31A)-C(31)-H(31B)	108.0
C(31)-C(32)-C(33)	109.74(17)
C(31)-C(32)-H(32A)	109.7
C(33)-C(32)-H(32A)	109.7
C(31)-C(32)-H(32B)	109.7
C(33)-C(32)-H(32B)	109.7
H(32A)-C(32)-H(32B)	108.2
C(32)-C(33)-C(34)	108.64(16)
C(32)-C(33)-C(35)	112.73(17)
C(34)-C(33)-C(35)	110.83(18)
C(32)-C(33)-H(33)	108.2
C(34)-C(33)-H(33)	108.2
C(35)-C(33)-H(33)	108.2
C(33)-C(34)-C(22)	111.53(18)
C(33)-C(34)-H(34A)	109.3
C(22)-C(34)-H(34A)	109.3
C(33)-C(34)-H(34B)	109.3
C(22)-C(34)-H(34B)	109.3
H(34A)-C(34)-H(34B)	108.0
C(36)-C(35)-C(38)	107.71(18)
C(36)-C(35)-C(33)	111.33(17)
C(38)-C(35)-C(33)	110.29(18)
C(36)-C(35)-H(35)	109.2
C(38)-C(35)-H(35)	109.2
C(33)-C(35)-H(35)	109.2
O(3)-C(36)-O(4)	123.1(2)
O(3)-C(36)-C(35)	126.1(2)
O(4)-C(36)-C(35)	110.85(19)
O(4)-C(37)-H(37A)	109.5
O(4)-C(37)-H(37B)	109.5
H(37A)-C(37)-H(37B)	109.5
O(4)-C(37)-H(37C)	109.5
H(37A)-C(37)-H(37C)	109.5
H(37B)-C(37)-H(37C)	109.5
O(5)-C(38)-O(6)	124.4(2)
O(5)-C(38)-C(35)	124.6(2)
O(6)-C(38)-C(35)	110.96(19)
O(6)-C(39)-H(39A)	109.5
O(6)-C(39)-H(39B)	109.5
H(39A)-C(39)-H(39B)	109.5
O(6)-C(39)-H(39C)	109.5
H(39A)-C(39)-H(39C)	109.5
H(39B)-C(39)-H(39C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 5.5 Anisotropic displacement parameters (Å^{2}x 10^3)for **5.77**. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Fe(1)	23(1)	25(1)	25(1)	2(1)	-1(1)	4(1)
O(1)	20(1)	29(1)	32(1)	4(1)	6(1)	1(1)
O(2)	18(1)	29(1)	23(1)	0(1)	1(1)	-1(1)
O(3)	20(1)	42(1)	26(1)	-4(1)	-3(1)	2(1)
O(4)	22(1)	63(1)	46(1)	-34(1)	-1(1)	-1(1)
O(5)	23(1)	51(1)	31(1)	18(1)	0(1)	4(1)
O(6)	16(1)	42(1)	36(1)	6(1)	4(1)	4(1)
N(1)	15(1)	22(1)	21(1)	2(1)	2(1)	2(1)
N(2)	18(1)	22(1)	18(1)	0(1)	0(1)	-2(1)
C(1)	18(1)	23(1)	27(1)	6(1)	-2(1)	3(1)
C(2)	25(1)	27(1)	26(1)	8(1)	-1(1)	0(1)
C(3)	39(1)	34(1)	23(1)	7(1)	-2(1)	3(1)
C(4)	34(1)	31(1)	28(1)	1(1)	-11(1)	0(1)
C(5)	20(1)	27(1)	32(1)	5(1)	-4(1)	-1(1)
C(6)	50(2)	90(3)	48(2)	42(2)	12(2)	42(2)
C(7)	73(2)	49(2)	70(2)	-17(2)	-50(2)	32(2)
C(8)	24(1)	58(2)	107(3)	31(2)	-9(2)	3(2)
C(9)	52(2)	72(3)	48(2)	-4(2)	5(2)	43(2)
C(10)	44(2)	23(2)	104(3)	10(2)	-30(2)	7(1)
C(11)	14(1)	23(1)	29(1)	5(1)	-1(1)	5(1)
C(12)	18(1)	34(1)	26(1)	-2(1)	2(1)	3(1)
C(13)	20(1)	24(1)	26(1)	-3(1)	2(1)	3(1)
C(14)	17(1)	19(1)	20(1)	-2(1)	1(1)	-1(1)
C(15)	20(1)	21(1)	20(1)	-3(1)	1(1)	-4(1)
C(16)	22(1)	26(1)	24(1)	-5(1)	4(1)	-4(1)
C(17)	32(1)	31(1)	22(1)	-1(1)	6(1)	-10(1)
C(18)	36(1)	26(1)	22(1)	5(1)	-3(1)	-1(1)
C(19)	24(1)	24(1)	23(1)	1(1)	-3(1)	0(1)
C(20)	20(1)	21(1)	18(1)	-2(1)	0(1)	-2(1)
C(21)	17(1)	20(1)	19(1)	-1(1)	-2(1)	-1(1)
C(22)	15(1)	21(1)	21(1)	0(1)	0(1)	0(1)
C(23)	20(1)	26(1)	21(1)	-2(1)	-1(1)	-2(1)
C(24)	26(1)	32(1)	34(1)	-12(1)	-6(1)	5(1)
C(25)	20(1)	27(1)	19(1)	-4(1)	0(1)	-1(1)
C(26)	23(1)	29(1)	21(1)	-2(1)	1(1)	1(1)
C(27)	27(1)	40(2)	22(1)	-2(1)	-4(1)	5(1)
C(28)	26(1)	41(2)	30(1)	-11(1)	-7(1)	-1(1)
C(29)	27(1)	32(1)	35(1)	-9(1)	-1(1)	-9(1)

C(30)	27(1)	30(1)	25(1)	-2(1)	-1(1)	-4(1)
C(31)	24(1)	22(1)	22(1)	2(1)	-1(1)	-6(1)
C(32)	19(1)	24(1)	21(1)	4(1)	-1(1)	-4(1)
C(33)	18(1)	21(1)	19(1)	1(1)	-2(1)	1(1)
C(34)	17(1)	21(1)	20(1)	0(1)	-2(1)	-1(1)
C(35)	17(1)	26(1)	20(1)	1(1)	-2(1)	2(1)
C(36)	21(1)	32(1)	18(1)	0(1)	0(1)	-2(1)
C(37)	30(1)	86(3)	56(2)	-45(2)	-4(1)	-7(2)
C(38)	18(1)	36(1)	18(1)	-1(1)	-2(1)	1(1)
C(39)	19(1)	57(2)	40(1)	5(1)	7(1)	-6(1)

Table 5.6 Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **5.77**.

	x	y	z	U(eq)
H(2)	2222	4687	6513	31
H(3)	1833	2933	5658	38
H(4)	-205	895	5903	37
H(5)	-1119	1393	6915	32
H(6)	2023	79	7719	75
H(7)	3918	2306	7637	77
H(8)	5195	2155	6694	76
H(9)	4185	-162	6176	69
H(10)	2213	-1491	6806	69
H(12A)	1032	4884	8498	31
H(12B)	222	6372	8205	31
H(13A)	2862	7319	8005	28
H(13B)	2456	7296	8672	28
H(16)	2273	4519	9414	29
H(17)	3299	2797	10091	34
H(18)	5854	1802	10012	34
H(19)	7476	2530	9254	29
H(22)	5209	7481	7611	23
H(23)	6612	7556	8726	27
H(24A)	6472	10558	8237	46
H(24B)	5689	10033	8825	46
H(24C)	5020	9370	8229	46
H(26)	8737	6817	9278	29
H(27)	10939	7469	9842	36
H(28)	12249	9820	9695	39
H(29)	11349	11488	8975	37

H(30)	9080	10881	8434	33
H(31A)	8998	9188	7654	27
H(31B)	7246	9378	7391	27
H(32A)	9417	6999	7059	25
H(32B)	9002	8488	6677	25
H(33)	6324	7689	6596	23
H(34A)	7244	5009	7246	23
H(34B)	5496	5330	6998	23
H(35)	8196	5066	6264	25
H(37A)	5455	3334	4759	86
H(37B)	4486	4847	4934	86
H(37C)	4395	3326	5321	86
H(39A)	10695	7526	5015	57
H(39B)	12151	6988	5414	57
H(39C)	11175	8510	5571	57
H(1)	7390(40)	4430(40)	8303(12)	24(7)

Table 5.7 Torsion angles [°] for **5.77**.

C(5)-C(1)-C(2)-C(3)	0.1(3)	C(6)-C(7)-C(8)-Fe(1)	59.5(2)
C(11)-C(1)-C(2)-C(3)	176.1(2)	C(7)-C(8)-C(9)-C(10)	0.2(4)
Fe(1)-C(1)-C(2)-C(3)	60.65(17)	Fe(1)-C(8)-C(9)-C(10)	-59.7(2)
C(5)-C(1)-C(2)-Fe(1)	-60.53(15)	C(7)-C(8)-C(9)-Fe(1)	59.9(2)
C(11)-C(1)-C(2)-Fe(1)	115.4(2)	C(8)-C(9)-C(10)-C(6)	0.3(3)
C(1)-C(2)-C(3)-C(4)	-0.3(3)	Fe(1)-C(9)-C(10)-C(6)	-59.5(2)
Fe(1)-C(2)-C(3)-C(4)	59.02(18)	C(8)-C(9)-C(10)-Fe(1)	59.8(2)
C(1)-C(2)-C(3)-Fe(1)	-59.30(16)	C(7)-C(6)-C(10)-C(9)	-0.6(3)
C(2)-C(3)-C(4)-C(5)	0.3(3)	Fe(1)-C(6)-C(10)-C(9)	60.2(2)
Fe(1)-C(3)-C(4)-C(5)	58.48(17)	C(7)-C(6)-C(10)-Fe(1)	-60.8(2)
C(2)-C(3)-C(4)-Fe(1)	-58.14(18)	C(12)-O(2)-C(11)-O(1)	-3.8(3)
C(3)-C(4)-C(5)-C(1)	-0.3(3)	C(12)-O(2)-C(11)-C(1)	175.08(18)
Fe(1)-C(4)-C(5)-C(1)	58.45(16)	C(5)-C(1)-C(11)-O(1)	-8.1(3)
C(3)-C(4)-C(5)-Fe(1)	-58.70(17)	C(2)-C(1)-C(11)-O(1)	176.5(2)
C(2)-C(1)-C(5)-C(4)	0.1(3)	Fe(1)-C(1)-C(11)-O(1)	-94.5(2)
C(11)-C(1)-C(5)-C(4)	-176.2(2)	C(5)-C(1)-C(11)-O(2)	173.06(19)
Fe(1)-C(1)-C(5)-C(4)	-60.05(16)	C(2)-C(1)-C(11)-O(2)	-2.4(3)
C(2)-C(1)-C(5)-Fe(1)	60.14(15)	Fe(1)-C(1)-C(11)-O(2)	86.6(2)
C(11)-C(1)-C(5)-Fe(1)	-116.1(2)	C(11)-O(2)-C(12)-C(13)	165.54(19)
C(10)-C(6)-C(7)-C(8)	0.7(3)	O(2)-C(12)-C(13)-C(14)	-70.8(2)
Fe(1)-C(6)-C(7)-C(8)	-60.1(2)	C(12)-C(13)-C(14)-C(21)	121.0(2)
C(10)-C(6)-C(7)-Fe(1)	60.8(2)	C(12)-C(13)-C(14)-C(15)	-63.0(3)
C(6)-C(7)-C(8)-C(9)	-0.6(4)	C(21)-C(14)-C(15)-C(16)	176.1(2)
Fe(1)-C(7)-C(8)-C(9)	-60.0(2)	C(13)-C(14)-C(15)-C(16)	-0.6(4)

C(21)-C(14)-C(15)-C(20)	-0.3(2)
C(13)-C(14)-C(15)-C(20)	-177.0(2)
C(20)-C(15)-C(16)-C(17)	0.1(3)
C(14)-C(15)-C(16)-C(17)	-176.0(2)
C(15)-C(16)-C(17)-C(18)	-0.2(4)
C(16)-C(17)-C(18)-C(19)	0.4(4)
C(17)-C(18)-C(19)-C(20)	-0.3(4)
C(21)-N(1)-C(20)-C(19)	-176.1(2)
C(21)-N(1)-C(20)-C(15)	1.4(2)
C(18)-C(19)-C(20)-N(1)	177.3(2)
C(18)-C(19)-C(20)-C(15)	0.1(3)
C(16)-C(15)-C(20)-N(1)	-177.71(19)
C(14)-C(15)-C(20)-N(1)	-0.7(2)
C(16)-C(15)-C(20)-C(19)	0.0(3)
C(14)-C(15)-C(20)-C(19)	177.0(2)
C(15)-C(14)-C(21)-N(1)	1.1(2)
C(13)-C(14)-C(21)-N(1)	177.7(2)
C(15)-C(14)-C(21)-C(22)	-168.6(2)
C(13)-C(14)-C(21)-C(22)	8.1(4)
C(20)-N(1)-C(21)-C(14)	-1.6(2)
C(20)-N(1)-C(21)-C(22)	169.41(19)
C(31)-N(2)-C(22)-C(21)	-179.82(18)
C(23)-N(2)-C(22)-C(21)	-53.6(2)
C(31)-N(2)-C(22)-C(34)	57.3(2)
C(23)-N(2)-C(22)-C(34)	-176.45(18)
C(14)-C(21)-C(22)-N(2)	115.4(2)
N(1)-C(21)-C(22)-N(2)	-53.4(3)
C(14)-C(21)-C(22)-C(34)	-122.4(2)
N(1)-C(21)-C(22)-C(34)	68.8(2)
C(31)-N(2)-C(23)-C(25)	-72.4(2)
C(22)-N(2)-C(23)-C(25)	162.61(19)
C(31)-N(2)-C(23)-C(24)	56.9(2)
C(22)-N(2)-C(23)-C(24)	-68.1(2)
N(2)-C(23)-C(25)-C(26)	-95.5(2)
C(24)-C(23)-C(25)-C(26)	133.8(2)
N(2)-C(23)-C(25)-C(30)	88.0(3)
C(24)-C(23)-C(25)-C(30)	-42.7(3)
C(30)-C(25)-C(26)-C(27)	1.3(3)
C(23)-C(25)-C(26)-C(27)	-175.4(2)
C(25)-C(26)-C(27)-C(28)	-1.2(4)
C(26)-C(27)-C(28)-C(29)	-0.3(4)
C(27)-C(28)-C(29)-C(30)	1.7(4)
C(26)-C(25)-C(30)-C(29)	0.0(3)
C(23)-C(25)-C(30)-C(29)	176.6(2)
C(28)-C(29)-C(30)-C(25)	-1.6(4)
C(22)-N(2)-C(31)-C(32)	-60.6(2)
C(23)-N(2)-C(31)-C(32)	173.78(17)
N(2)-C(31)-C(32)-C(33)	60.7(2)
C(31)-C(32)-C(33)-C(34)	-56.8(2)
C(31)-C(32)-C(33)-C(35)	179.99(18)
C(32)-C(33)-C(34)-C(22)	55.1(2)
C(35)-C(33)-C(34)-C(22)	179.45(16)
N(2)-C(22)-C(34)-C(33)	-55.5(2)
C(21)-C(22)-C(34)-C(33)	-176.72(16)
C(32)-C(33)-C(35)-C(36)	-166.47(18)
C(34)-C(33)-C(35)-C(36)	71.5(2)
C(32)-C(33)-C(35)-C(38)	-47.0(2)
C(34)-C(33)-C(35)-C(38)	-168.98(17)
C(37)-O(4)-C(36)-O(3)	-0.1(4)
C(37)-O(4)-C(36)-C(35)	-179.4(3)
C(38)-C(35)-C(36)-O(3)	-109.5(3)
C(33)-C(35)-C(36)-O(3)	11.5(3)
C(38)-C(35)-C(36)-O(4)	69.7(3)
C(33)-C(35)-C(36)-O(4)	-169.3(2)
C(39)-O(6)-C(38)-O(5)	0.9(4)
C(39)-O(6)-C(38)-C(35)	-176.6(2)
C(36)-C(35)-C(38)-O(5)	51.7(3)
C(33)-C(35)-C(38)-O(5)	-70.0(3)
C(36)-C(35)-C(38)-O(6)	-130.8(2)
C(33)-C(35)-C(38)-O(6)	107.5(2)

Symmetry transformations used to generate equivalent atoms:

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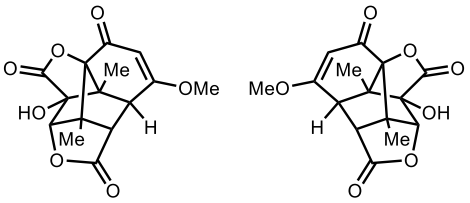
Appendix A

Progress Toward the Synthesis of Preuisolactone A

A.1 Isolation, Bioactivity, and Biosynthesis Proposals

Preuisolactone A (**A.1**, Figure A.1) was isolated from the endophytic fungus *Preussia isomera* XL-1326 in 2019 by Yang, Abe, and coworkers.[1] The natural product was isolated as a scalemic mixture in a ratio of approximately 1.05:1 (–):(+) preuisolactone A (**A.1**). This natural product has an unprecedented 6/5/5/5/5 pentacyclic scaffold featuring a caged tricyclo[$4.4.0^{1,6}.0^{2,8}$]decane carbon skeleton as well as two ɣ-lactone rings. Preuisolactone A (**A.1**) also contains four contiguous quaternary stereocenters and seven adjacent stereocenters. The structure of preuisolactone A (**A.1**) was unambiguously confirmed by single crystal X-ray diffraction.



(–)-preuisolactone A
(–)-**A.1**

(+)-preuisolactone A
(+)-**A.1**

Figure A.1 Structure of both enantiomers of preuisolactone A (**A.1**).

Yang, Abe, and coworkers also tested the racemate of **A.1** for antifungal and antibacterial properties.[1] Preuisolactone A (**A.1**) was found to possess antibacterial activity against *M. luteus* and *B. megaterium* with MIC values of 10.2 and 163.4 µM, respectively. Additionally, the natural product exhibited antifungal activity against *A. alternata* with a MIC value of 163.4 µM. The natural product was also evaluated for cytotoxicity but did not exhibit any significant activity against the selected cell lines.

It was initially proposed by Yang, Abe, and coworkers that preuisolactone A (**A.1**) was a norsesquiterpenoid, arising from farnesyl pyrophosphate (**A.2**, Figure A.2).[1] From farnesyl pyrophosphate (**A.2**), cationic cyclization could give rise to cyclobutane **A.3**. A 1,2-alkyl shift would result in ring expansion of the cyclobutane to cyclopentane **A.4,** which could undergo further cyclization and a 1,3-hydride shift to furnish tricycle **A.5**. A 1,2-hydride and 1,2-alkyl shift would give rise to cation **A.6** which could be quenched with water. A series of oxidations would then afford tetraol **A.7**. Oxidative cleavage of the tricyclic core would give carboxylic acid **A.8** which would undergo an aldol condensation to afford [2.2.1]bicycle **A.9**. Additional oxidation to diacid **A.10** would result in spontaneous lactonization to afford di-ɣ-lactone **A.11**. Oxidation of the α-methyl group to methyl ester **A.12** and subsequent decarboxylation would give **A.13**. Finally, isomerization of the trisubstituted olefin, addition of methoxide, and reoxidation would afford preuisolactone A **(A.1)**.

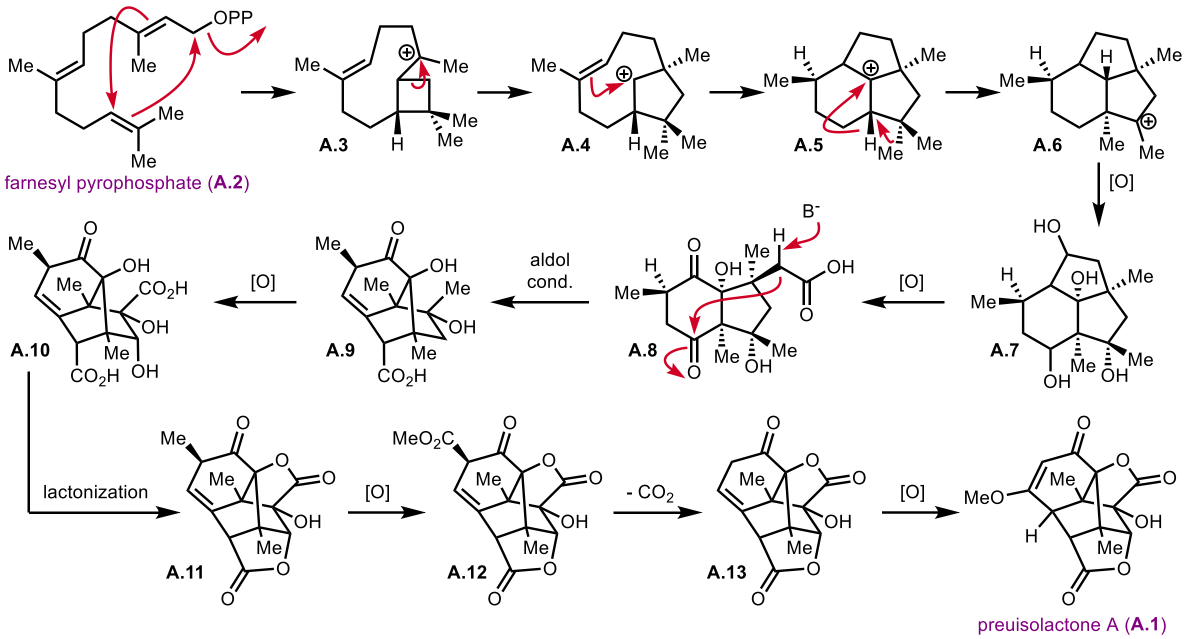


Figure A.2 Yang, Abe, and coworkers' proposed biosynthesis of preuisolactone A (**A.1**) from farnesyl pyrophosphate (**A.2**).

In 2019, Trauner and coworkers proposed a different biosynthesis, claiming that preuisolactone A (**A.1**) was a phenolic polyketide natural product.[2] They stated that their biosynthesis is likely more plausible given that the natural product is isolated as a scalemic mixture since it is unlikely that the terpene cyclase and oxidation sequences occur with equal efficiency on both enantiomers.

Trauner's proposal begins from catechol **A.14** and pyrogallol **A.15** which upon oxidation would give the corresponding *ortho*-quinones **A.16** and **A.17** (Figure A.3). A (5+2) cycloaddition between the quinones would furnish tricycle **A.18** which could undergo a retro-Dieckmann condensation affording bicycle **A.19**. Vinylogous aldol reaction from the dienol would give [3.2.1]bicycle **A.20**. Subsequent oxa-Michael addition of the carboxylic acid into the enone of **A.20** would afford **A.21** which could be oxidized to vicinal diketones **A.22**. From here, a benzilic acid-type rearrangement could give rise to oxetane **A.23** which upon collapse of the cyclobutanol and 1,2-alkyl shift would yield preuisolactone A (**A.1**), converting the [3.2.1]bicycle to the [2.2.1]bicycle characteristic of the natural product.

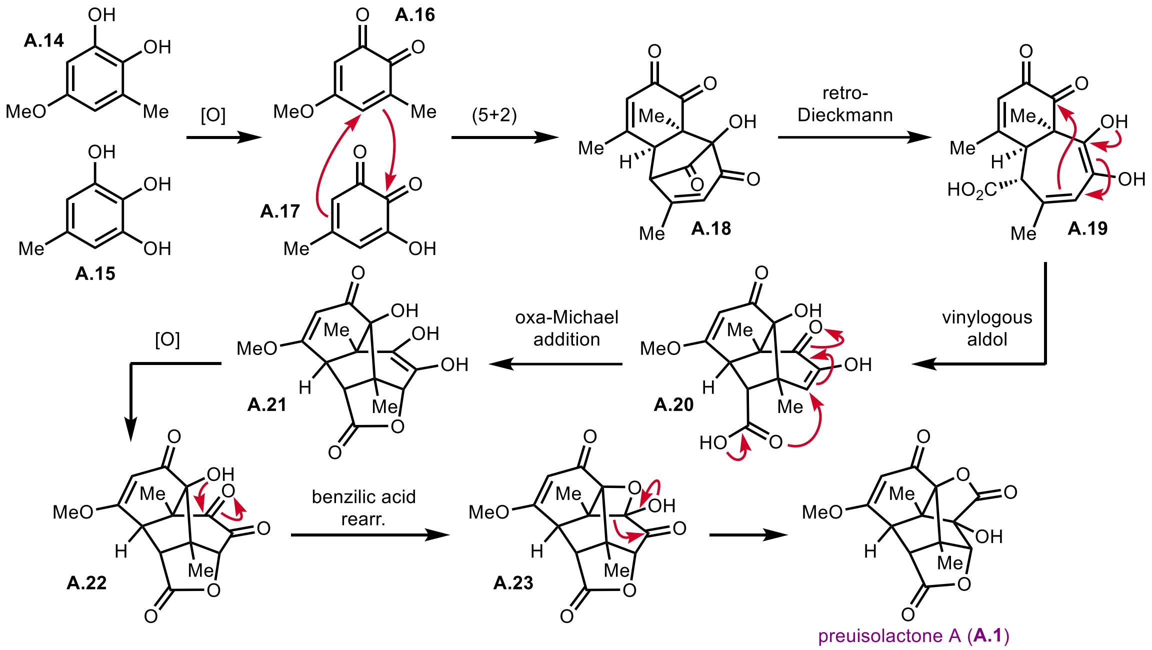


Figure A.3 Trauner and coworkers' proposed biosynthesis of preuisolactone A (**A.1**) from arene building blocks catechol **A.14** and pyrogallol **A.15**.

A.2 Previous Synthesis

At the outset of this project there were no previous syntheses of preuisolactone A (**A.1**). However, shortly after we started on the project, Trauner and coworkers published a biomimetic route that mimics the biosynthesis outlined in Figure A.3 and supported their proposal.[2] Starting from known resorcinol **A.24**, Dakin oxidation afforded catechol **A.14** which upon treatment with pyrogallol **A.15** and potassium ferricyanide ($K_3Fe(CN)_6$) underwent cyclization to afford tricycle **A.20** as well as isomer **A.25**, which resulted from lactonization of the acid into the ketone tautomer. When subjected to base, followed by acid, the mixture of isomers favored formation of **A.20**, which upon treatment with Koser's reagent, led to the formation of the southern lactone. This intermediate was not isolated and upon workup with phosphate buffer underwent the proposed benzilic acid-type rearrangement to afford preuisolactone A (**A.1**) in a short four step sequence from the known resorcinol **A.24**.

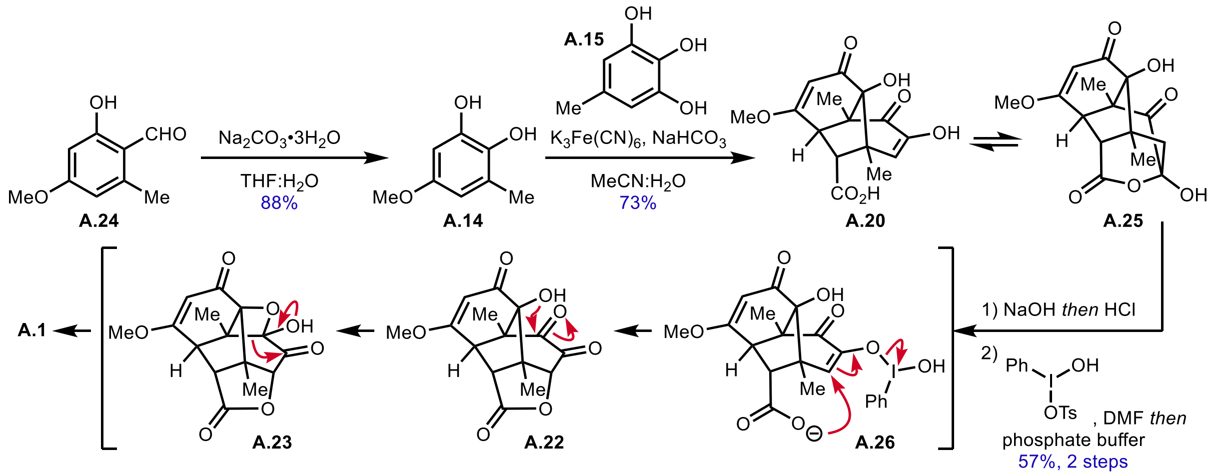


Figure A.4 Trauner and coworkers' synthesis of preuisolactone A (**A.1**).

A.3 Retrosynthesis

We had envisioned accessing preuisolactone A (**A.1**) through a strategy that utilized a symmetric, densely functionalized bicyclo[2.2.1]heptane that has the requisite peripheral functionality built-in. From the natural product, retrosynthetic excision of the A ring would give cyanohydrin **A.27** (Figure A.5). Further simplification of the D ring would lead to [2.2.1]bicycle **A.28,** this could arise from desymmetrization of meso bicycle **A.29** in the forward sense. We envisioned highly functionalized bicycle **A.29** could be traced back to tetrabromide **A.30**, employing sequential sp^2 and sp^3 cross-couplings in the forward sense to effect the transformation. Finally, bicycle **A.30** could be built through a Diels–Alder cycloaddition between known tetrabromo cyclopentadiene **A.31** and vinylene carbonate (**A.32**).

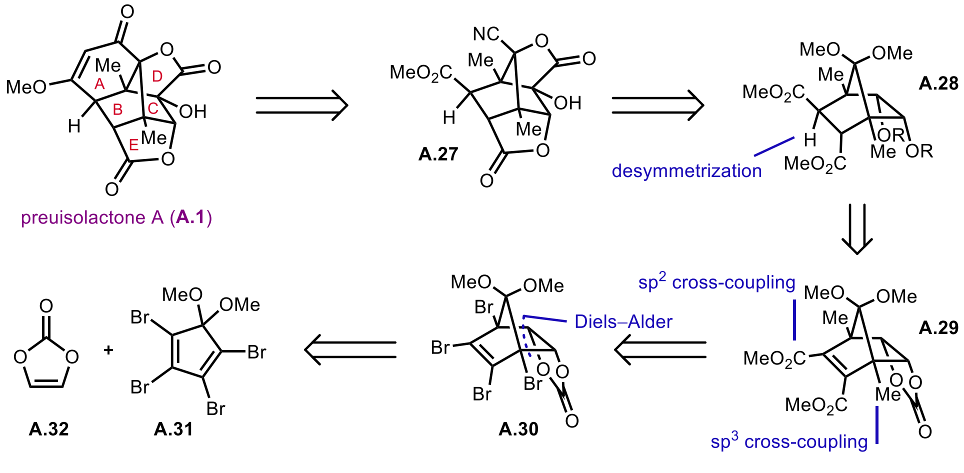


Figure A.5 Our retrosynthesis of preuisolactone A (**A.1**) using a symmetry-based strategy.

This proposal features the use of symmetry to construct the highly functionalized bicycle in short order. A symmetry-based approach such as is described here would lead to a higher degree of complexity with fewer synthetic operations. Additionally, this strategy implements novel and modern cross-coupling methodologies in a complex system through the sequential cross-couplings of **A.30**, which would require differentiating between C(sp^2) and C(sp^3) bromides.

A.4 Cross-Coupling Approach

We commenced our synthesis with the formation of known tetrabromo [2.2.1]bicycle **A.30** (Figure A.6). Drawing from precedent by Breslow and coworkers,[3] retro Diels–Alder cycloaddition of commercially available dicyclopentadiene (**A.33**) gave cyclopentadiene, which then underwent hexabromination upon treatment with molecular bromine and potassium hydroxide to afford **A.34**. Substitution of hexabromide **A.34** with sodium methoxide (NaOMe) delivered di-methoxy tetrabromide **A.31**. As reported by Khan and coworkers, Diels–Alder cycloaddition of diene **A.31** and vinylene carbonate (**A.32**) afforded known [2.2.1]bicycle **A.30**[4] – exclusively the endo product as confirmed by X-ray crystallography. This procedure occurred in slightly diminished yields in our hands but was still synthetically viable.

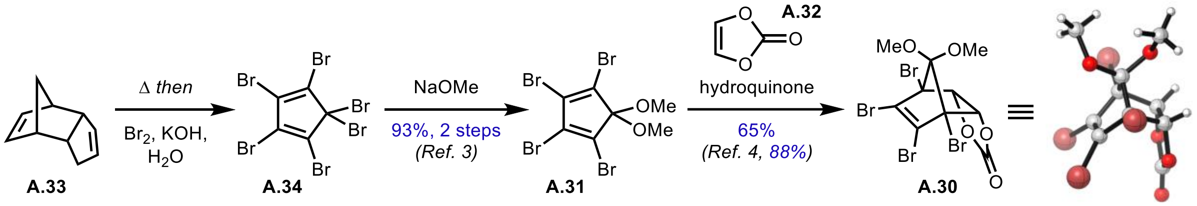


Figure A.6 Synthesis of known tetrabromo [2.2.1]bicycle **A.30**.

With the [2.2.1]bicycle in hand, we turned our attention to the installation of esters on the vicinal vinyl bromides of **A.30**. We believed this conversion could be accomplished through a palladium-catalyzed alkoxycarbonylation of the sp^2 hybridized bromides (Figure A.7.A). A variety of ligated Pd(0) sources (Pd^0 and Buchwald type palladium pre-catalysts) in the presence of carbon monoxide (CO), triethylamine (Et$_3$N), and methanol were screened. However, no desired product was ever detected, with only recovered starting material observed.

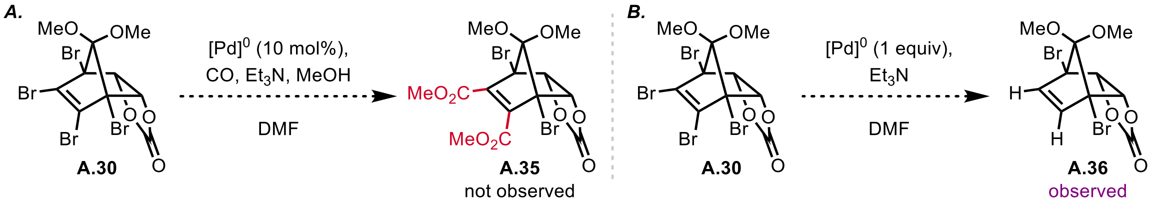


Figure A.7 (A) Attempted alkoxycarbonylation of vicinal vinyl bromides. (B) Oxidative addition control reaction.

To assist in elucidating whether the substate was amenable to palladium catalyzed reactivity of any sort, we subjected the starting material to stoichiometric Pd(0) in the absence of carbon monoxide and methanol (Figure A.7.B). Under these conditions we observed the reduced product, **A.36**, indicating that our substate was indeed undergoing oxidative addition.

Although this was promising and showed that oxidative addition was feasible on this substrate, we opted to explore an alternative route in tandem with further investigation of this reaction.

A.5 Oxidation Approach

Given the challenges we had encountered with the cross-coupling of the vicinal bromides, we investigated an alternative approach to access a highly functionalized bicycle. We recognized that instead of using an alkoxycarbonylation to install the ester moieties, they could be pre-installed in the Diels–Alder cycloaddition partners. Therefore, by turning to a dienophile such as dimethyl acetylenedicarboxylate (**A.37**) we could access symmetric [2.2.1]bicycle **A.38**. This approach allowed for a different transformation of the vinyl bromides by circumventing the challenging alkoxycarbonylation (Figure A.8).

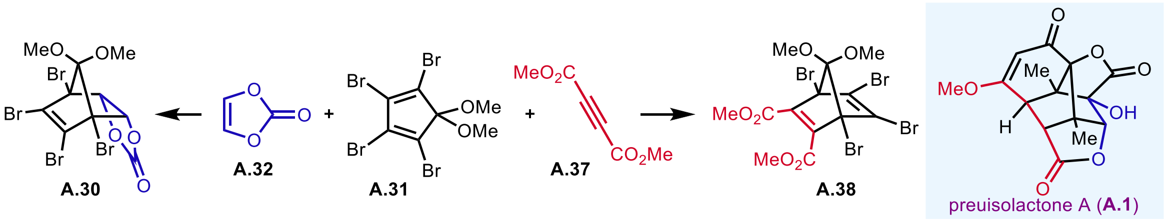


Figure A.8 Second-generation approach to a functionalized bicycle contrasted with the first-generation route.

Taking the same diene (tetrabromide **A.31**) from our previous strategy we sought to conduct the desired Diels–Alder cycloaddition with dimethyl acetylenedicarboxylate (**A.37**). However, after a short literature search, it was found that Hand and coworkers had conducted the desired reaction and obtained aromatic tribromide **A.39** rather than the desired [2.2.1]bicycle (Figure A.9).[5] This reaction presumably occurs by formation of the desired [2.2.1]bicycle and then spontaneous cleavage and aromatization of the carbocyclic framework with ejection of a bromide to give arene **A.39.**

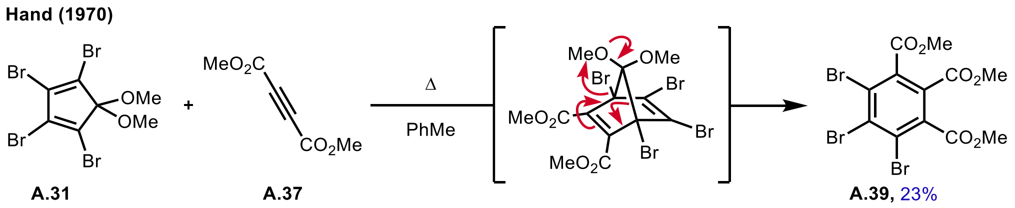


Figure A.9 Formation of aryl **A.39** by Diels–Alder cycloaddition and spontaneous fragmentation of bicyclic system.

At this point, we discovered that a similar Diels–Alder cycloaddition was known with commercially available tetrachlorocyclopentadiene **A.40** and dimethyl fumarate (**A.41**, Figure A.10).[6] This route would similarly allow for pre-installation of the desired ester moieties but would desymmetrize the molecule at an earlier stage than described in the initial synthetic proposal. Known bicycle **A.42** was accessed by following the precedent of Clive and coworkers.[6] On the basis of a report by Khan and coworkers, the vicinal vinyl chlorides of **A.42** were oxidized to the 1,2-diketone (**A.43**) by treatment with ruthenium trichloride and sodium periodate, which generates ruthenium tetraoxide *in situ.*[7]

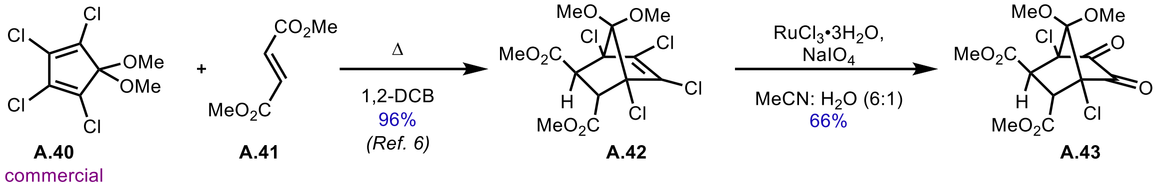


Figure A.10 Construction of the perchlorinated [2.2.1]bicycle **A.42** and oxidation to dione **A.43**.

At this point, most of the requisite functionalization was in place, however, the peripheral rings had yet to be built. From here, we envisioned that installation of the bridgehead methyl groups followed by site-selective reduction and spontaneous lactonization would give **A.44** (Figure A.11). At that stage, a series of functional group manipulations would give rise to cyanohydrin **A.27** which closely resembles the natural product.

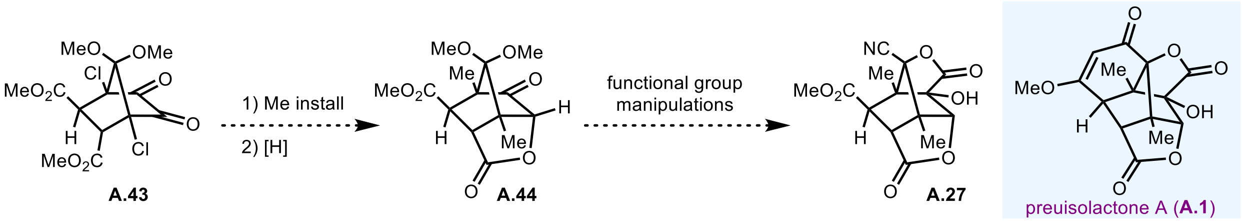


Figure A.11 Proposed next steps for accessing preuisolactone A (**A.1**).

A.6 Conclusion and Outlook

In conclusion, we envisioned accessing preuisolactone A (**A.1**) through a symmetry-based approach to construct the highly functionalized core of the natural product in short order. Initial work leveraged known routes to access perbrominated [2.2.1]bicycle **A.30** which we believed could undergo sequential cross-couplings to install the desired functional groups. Unfortunately, the desired alkoxycarbonylation proved to be more challenging than initially anticipated, and an alternate route to the natural product was investigated.

This second-generation route maintained construction of a highly halogenated [2.2.1]bicyclic framework but leveraged oxidation of the vicinal vinyl dihalides to the corresponding 1,2-diketone (**A.43**). Though this was successful in installing the oxidation and the route showed promise, minimal time and effort had been spent on this project and the synthetic efforts outlined above were ultimately abandoned after the extremely efficient synthesis by Trauner and coworkers was published.[2]

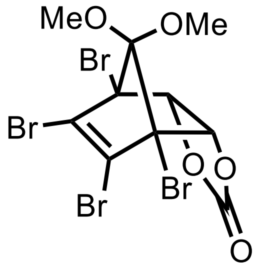
A.7 Experimental Contributions

Initial project generation was carried out by Prof. Richmond Sarpong. Experiments and further project developments were carried out by Kerry E. Jones (K.E.J.) and Prof. Hirofumi Ueda.

A.8 Experimental Details

A.8.1 Experimental Procedures

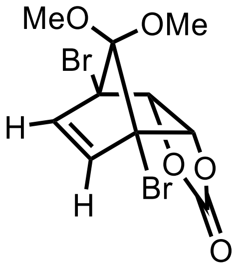
(3aR,7S,7aS)-4,5,6,7-tetrabromo-8,8-dimethoxy-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d][1,3]dioxol-2-one (A.30)



Prepared according to a modification of the procedure outlined by Khan and coworkers.[4] Tetrabromocyclopentadiene **A.31** (100 mg, 0.23 mmol, 1 equiv), vinylene carbonate (14 µL, 0.23 mmol, 1 equiv), and hydroquinone (1.2 mg, 0.01 mmol, 0.05 equiv) were added to a sealed vial under nitrogen. Toluene (0.5 mL) was added and the mixture was heated to 110 °C for 32 h. The mixture was then cooled to room temperature, filtered through a Celite plug, eluting with DCM, and concentrated *in vacuo*. The crude residue was purified by silica gel column chromatography (eluting with a gradient of 8:1 to 6:1 to 4:1 hexanes:ethyl acetate) to afford [2.2.1]bicycle **A.30** (79 mg, 0.15 mmol) as a pale yellow solid in 65% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.21 (s, 2H), 3.64 (d, *J* = 9.0 Hz, 6H).

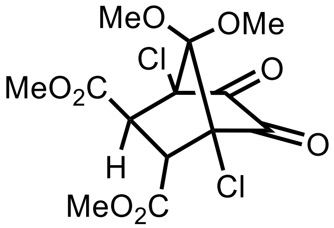
(3aR,7S,7aS)-4,7-dibromo-8,8-dimethoxy-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d][1,3]dioxol-2-one (A.36)



[2.2.1]bicycle **A.30** (3.0 mg, 5.7 µmol, 1 equiv) and P(*t*-Bu)$_3$-Pd-G4 (3.3 mg, 5.7 µmol, 1 equiv) were added to a vial under nitrogen. Degassed DMF (0.2 mL) and Et_3N (1 µL, 5.7 µmol, 1 equiv) were added and the sealed vial was heated to 80 °C for 20 h. The mixture was then cooled to room temperature, quenched by the addition of sat. aq. NH_4Cl (1 mL) and extracted with EtOAc (3 x 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was comprised of starting material and reduced product in an approximate 1:2 ratio. The crude residue was purified by preparatory thin layer chromatography (utilizing 4:1 hexanes:ethyl acetate as the mobile phase) to give the title compound **A.36**.

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.16 (s, 2H), 5.16 (s, 2H), 3.62 (d, *J* = 5.6 Hz, 6H).

Dimethyl (1S,2S,3S)-1,4-dichloro-7,7-dimethoxy-5,6-dioxobicyclo[2.2.1]heptane-2,3-dicarboxylate (A.43)

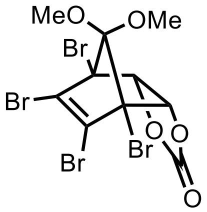


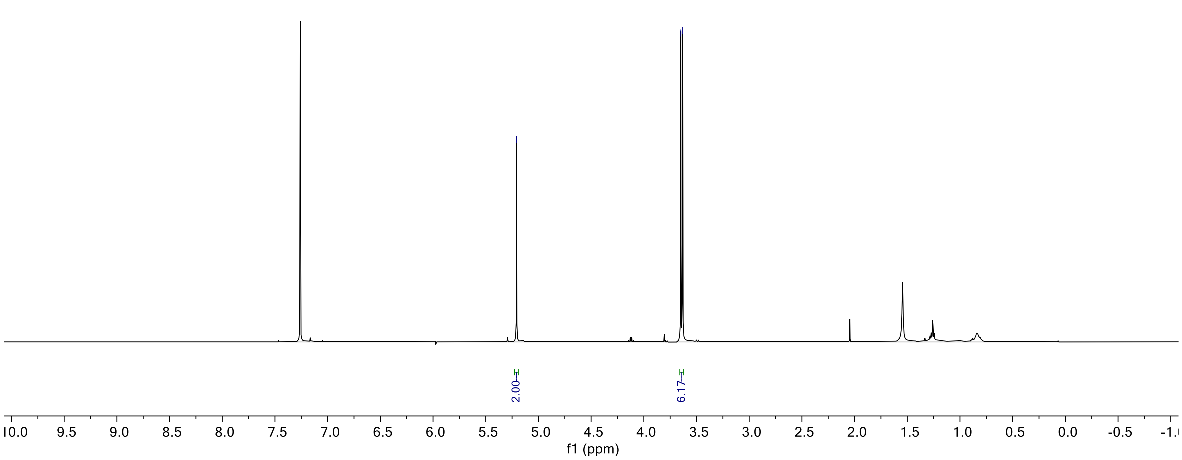
Prepared according to a modification of the procedure outlined by Khan and coworkers.[7] Under an atmosphere of air, tetrachloride **A.42** (50 mgs, 0.12 mmol, 1 equiv) was dissolved in MeCN (1.5 mL) and cooled to 0 °C. A solution of $RuCl_3$ (1.6 mg, 8.5 µmol, 0.07 equiv) and sodium periodate (39 mg, 0.18 mmol, 1.5 equiv) in H_2O was added to the starting material in a dropwise manner. The solution was allowed to warm to room temperature and stirred for 20 h. The mixture was then filtered through a silica plug, eluting with ethyl acetate and then concentrated *in vacuo.* The crude residue was then purified by column chromatography (eluting with 4:1 to 2:1 hexanes:ethyl acetate) to afford dione **A.43** in 66% (30 mg, 0.08 mmol) as a bright yellow oil.

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 4.20 (d, *J* = 6.5 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H), 3.67 (s, 3H), 3.54 (s, 3H), 3.25 (d, *J* = 6.5 Hz, 1H).

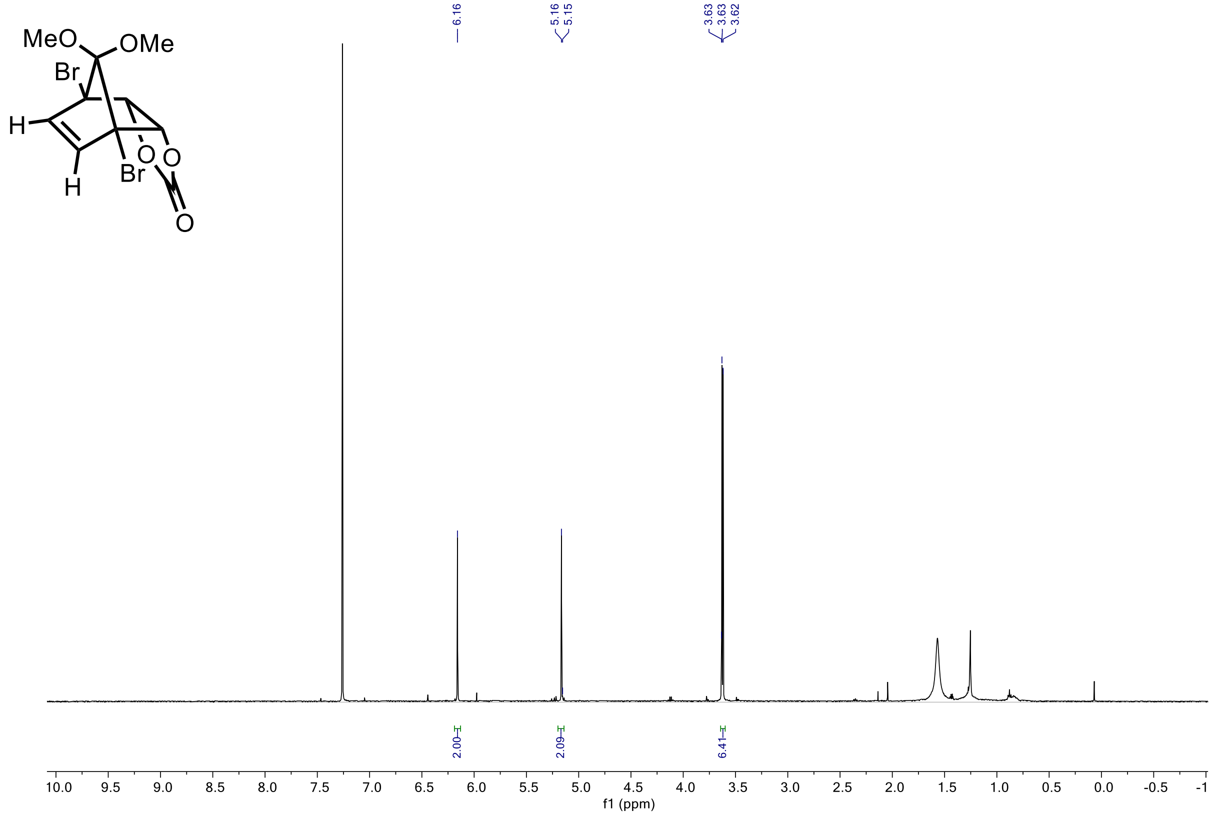
A.8.2 NMR Spectral Data for Appendix A

A.30 (^{1}H NMR, 500 MHz, CDCl$_3$)

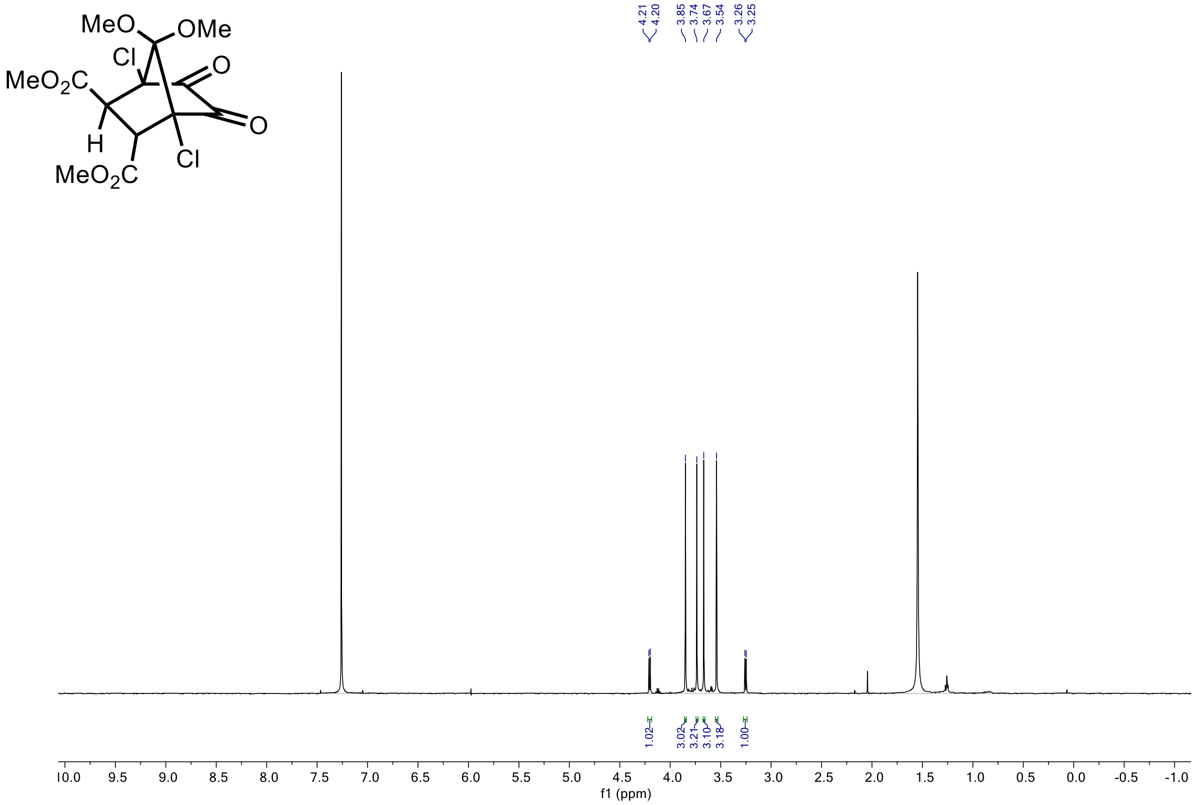




A.36 (^{1}H NMR, 500 MHz, CDCl$_3$)



A.43 (^{1}H NMR, 500 MHz, CDCl$_3$)



A.8.3 X-Ray Crystallographic Data for Appendix A

X-Ray Analysis of A.30

A colorless block 0.44 x 0.27 x 0.15 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 33.00 mm and exposure time was 0.50 seconds per frame using a scan width of 0.5°. Data collection was 99% complete to 26.368° in θ. A total of 15690 reflections were collected covering the indices -11<=h<=11, -12<=k<=13, -18<=l<=16. 2923 reflections were found to be symmetry independent, with an R_{int} of 0.0634. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the CrysAlis^{Pro} 1.171.40.54a software program and scaled using the SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2015) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

[Note: The instruments are supported by an NIH Shared Instrument Grant S10-RR027172.]

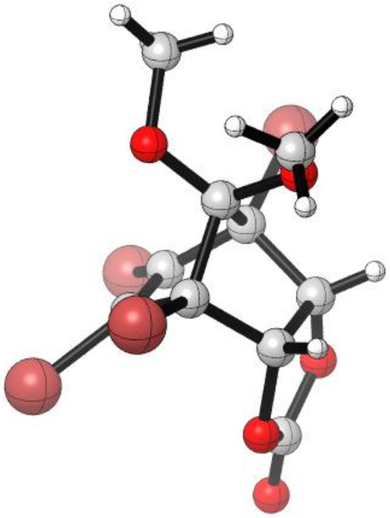


Figure A.12 CYLview representation of **A.30**

Table A.1 Crystal data and structure refinement for **A.30**.

Identification code	KEJ_2_037	
Empirical formula	C10 H8 Br4 O5	
Formula weight	527.80	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 9.0463(3) Å	a= 90°.
	b = 10.6177(4) Å	b= 90°.
	c = 14.9126(5) Å	g = 90°.
Volume	1432.37(9) Å^3	
Z	4	
Density (calculated)	2.448 Mg/m^3	
Absorption coefficient	11.249 mm^{-1}	
F(000)	992	
Crystal size	0.440 x 0.270 x 0.150 mm^3	
Theta range for data collection	2.958 to 26.368°.	
Index ranges	-11<=h<=11, -12<=k<=13, -18<=l<=16	
Reflections collected	15690	
Independent reflections	2923 [R(int) = 0.0634]	
Completeness to theta = 26.368°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.15658	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2923 / 0 / 174	
Goodness-of-fit on F^2	1.034	
Final R indices [I>2sigma(I)]	R1 = 0.0237, wR2 = 0.0545	
R indices (all data)	R1 = 0.0253, wR2 = 0.0548	
Absolute structure parameter	-0.004(9)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.674 and -0.868 e.Å^{-3}	

Table A.2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **A.30**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5165(5)	3488(5)	5563(3)	14(1)
C(2)	5164(6)	2869(5)	4089(3)	17(1)
C(3)	3774(5)	3998(5)	5083(3)	14(1)
C(4)	3981(5)	5427(5)	5119(3)	10(1)
C(5)	5305(5)	5759(5)	4539(3)	13(1)
C(6)	6498(5)	5313(5)	4943(3)	11(1)
C(7)	6027(5)	4707(5)	5807(3)	13(1)
C(8)	4685(5)	5567(5)	6079(3)	12(1)
C(9)	2616(6)	5513(6)	7108(3)	23(1)
C(10)	5692(7)	7167(6)	7057(3)	23(1)
Br(1)	2208(1)	6362(1)	4877(1)	16(1)
Br(2)	5143(1)	6507(1)	3415(1)	15(1)
Br(3)	8424(1)	5252(1)	4493(1)	21(1)
Br(4)	7509(1)	4419(1)	6702(1)	21(1)
O(1)	5903(4)	2763(4)	4879(2)	17(1)
O(2)	5614(4)	2432(4)	3409(2)	25(1)
O(3)	3885(4)	3507(4)	4188(2)	17(1)
O(4)	3958(4)	4949(4)	6770(2)	16(1)
O(5)	4948(4)	6835(3)	6233(2)	13(1)

Table A.3 Bond lengths [Å] and angles [°] for **A.30**.

C(1)-O(1)	1.442(6)	C(6)-C(7)	1.502(7)
C(1)-C(3)	1.546(7)	C(6)-Br(3)	1.868(5)
C(1)-C(7)	1.554(7)	C(7)-C(8)	1.573(7)
C(1)-H(1)	1.0000	C(7)-Br(4)	1.915(4)
C(2)-O(2)	1.187(6)	C(8)-O(5)	1.385(6)
C(2)-O(3)	1.348(6)	C(8)-O(4)	1.388(6)
C(2)-O(1)	1.359(6)	C(9)-O(4)	1.444(6)
C(3)-O(3)	1.436(6)	C(9)-H(9A)	0.9800
C(3)-C(4)	1.530(7)	C(9)-H(9B)	0.9800
C(3)-H(3)	1.0000	C(9)-H(9C)	0.9800
C(4)-C(5)	1.519(6)	C(10)-O(5)	1.446(6)
C(4)-C(8)	1.574(6)	C(10)-H(10A)	0.9800
C(4)-Br(1)	1.920(5)	C(10)-H(10B)	0.9800
C(5)-C(6)	1.324(7)	C(10)-H(10C)	0.9800
C(5)-Br(2)	1.860(5)	O(1)-C(1)-C(3)	103.6(4)

O(1)-C(1)-C(7)	112.2(4)	C(6)-C(7)-C(8)	101.0(4)
C(3)-C(1)-C(7)	103.0(4)	C(1)-C(7)-C(8)	99.0(4)
O(1)-C(1)-H(1)	112.4	C(6)-C(7)-Br(4)	117.9(3)
C(3)-C(1)-H(1)	112.4	C(1)-C(7)-Br(4)	112.4(4)
C(7)-C(1)-H(1)	112.4	C(8)-C(7)-Br(4)	117.0(3)
O(2)-C(2)-O(3)	125.7(5)	O(5)-C(8)-O(4)	114.7(4)
O(2)-C(2)-O(1)	122.6(5)	O(5)-C(8)-C(7)	118.3(4)
O(3)-C(2)-O(1)	111.6(4)	O(4)-C(8)-C(7)	106.4(4)
O(3)-C(3)-C(4)	112.6(4)	O(5)-C(8)-C(4)	108.2(4)
O(3)-C(3)-C(1)	104.3(4)	O(4)-C(8)-C(4)	116.0(4)
C(4)-C(3)-C(1)	103.4(4)	C(7)-C(8)-C(4)	91.3(3)
O(3)-C(3)-H(3)	112.0	O(4)-C(9)-H(9A)	109.5
C(4)-C(3)-H(3)	112.0	O(4)-C(9)-H(9B)	109.5
C(1)-C(3)-H(3)	112.0	H(9A)-C(9)-H(9B)	109.5
C(5)-C(4)-C(3)	107.9(4)	O(4)-C(9)-H(9C)	109.5
C(5)-C(4)-C(8)	100.2(3)	H(9A)-C(9)-H(9C)	109.5
C(3)-C(4)-C(8)	100.1(4)	H(9B)-C(9)-H(9C)	109.5
C(5)-C(4)-Br(1)	115.6(3)	O(5)-C(10)-H(10A)	109.5
C(3)-C(4)-Br(1)	113.9(3)	O(5)-C(10)-H(10B)	109.5
C(8)-C(4)-Br(1)	117.4(3)	H(10A)-C(10)-H(10B)	109.5
C(6)-C(5)-C(4)	107.5(4)	O(5)-C(10)-H(10C)	109.5
C(6)-C(5)-Br(2)	128.8(4)	H(10A)-C(10)-H(10C)	109.5
C(4)-C(5)-Br(2)	123.4(3)	H(10B)-C(10)-H(10C)	109.5
C(5)-C(6)-C(7)	108.2(4)	C(2)-O(1)-C(1)	109.9(4)
C(5)-C(6)-Br(3)	127.5(4)	C(2)-O(3)-C(3)	110.1(4)
C(7)-C(6)-Br(3)	123.9(4)	C(8)-O(4)-C(9)	117.5(4)
C(6)-C(7)-C(1)	107.4(4)	C(8)-O(5)-C(10)	117.2(4)

Symmetry transformations used to generate equivalent atoms:

Table A.4 Anisotropic displacement parameters (Å^{2}x 10^3) for **A.30**. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	18(3)	12(3)	12(2)	-3(2)	1(2)	4(2)
C(2)	13(3)	17(3)	21(3)	-6(2)	0(2)	-4(2)
C(3)	10(2)	17(3)	15(2)	-1(2)	1(2)	0(2)
C(4)	5(2)	15(3)	11(2)	1(2)	1(2)	4(2)
C(5)	15(3)	14(3)	9(2)	-2(2)	-1(2)	-4(2)
C(6)	10(2)	12(3)	12(2)	-4(2)	0(2)	-1(2)
C(7)	8(2)	20(3)	9(2)	-1(2)	-3(2)	3(2)

C(8)	10(2)	15(3)	12(2)	0(2)	2(2)	2(2)
C(9)	23(3)	26(3)	22(3)	0(2)	14(2)	0(3)
C(10)	27(3)	24(3)	17(3)	-6(2)	-2(2)	-4(2)
Br(1)	8(1)	20(1)	20(1)	-1(1)	-1(1)	4(1)
Br(2)	14(1)	21(1)	10(1)	2(1)	1(1)	-1(1)
Br(3)	8(1)	28(1)	26(1)	-2(1)	4(1)	1(1)
Br(4)	20(1)	25(1)	18(1)	-2(1)	-10(1)	7(1)
O(1)	20(2)	15(2)	17(2)	-5(2)	-1(1)	4(2)
O(2)	24(2)	28(2)	22(2)	-13(2)	1(2)	-2(2)
O(3)	16(2)	20(2)	15(2)	-6(2)	-3(1)	-1(2)
O(4)	19(2)	18(2)	11(2)	2(1)	6(1)	1(2)
O(5)	15(2)	13(2)	13(2)	1(1)	1(1)	-1(2)

Table A.5 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **A.30**.

	x	y	z	U(eq)
H(1)	4916	2971	6103	17
H(3)	2842	3724	5386	17
H(9A)	1772	5211	6757	35
H(9B)	2683	6432	7057	35
H(9C)	2482	5280	7738	35
H(10A)	6764	7123	6968	34
H(10B)	5401	6578	7532	34
H(10C)	5415	8025	7231	34

Table A.6 Torsion angles [°] for **A.30**.

O(1)-C(1)-C(3)-O(3)	-0.1(5)	C(8)-C(4)-C(5)-C(6)	35.6(5)
C(7)-C(1)-C(3)-O(3)	117.0(4)	Br(1)-C(4)-C(5)-C(6)	162.7(4)
O(1)-C(1)-C(3)-C(4)	-117.9(4)	C(3)-C(4)-C(5)-Br(2)	105.6(4)
C(7)-C(1)-C(3)-C(4)	-0.9(5)	C(8)-C(4)-C(5)-Br(2)	-150.2(4)
O(3)-C(3)-C(4)-C(5)	-45.3(5)	Br(1)-C(4)-C(5)-Br(2)	-23.1(5)
C(1)-C(3)-C(4)-C(5)	66.6(4)	C(4)-C(5)-C(6)-C(7)	-1.5(6)
O(3)-C(3)-C(4)-C(8)	-149.5(4)	Br(2)-C(5)-C(6)-C(7)	-175.3(4)
C(1)-C(3)-C(4)-C(8)	-37.7(4)	C(4)-C(5)-C(6)-Br(3)	171.9(4)
O(3)-C(3)-C(4)-Br(1)	84.4(4)	Br(2)-C(5)-C(6)-Br(3)	-1.9(8)
C(1)-C(3)-C(4)-Br(1)	-163.8(3)	C(5)-C(6)-C(7)-C(1)	69.9(5)
C(3)-C(4)-C(5)-C(6)	-68.6(5)	Br(3)-C(6)-C(7)-C(1)	-103.7(4)

C(5)-C(6)-C(7)-C(8)	-33.3(5)
Br(3)-C(6)-C(7)-C(8)	153.1(3)
C(5)-C(6)-C(7)-Br(4)	-162.0(4)
Br(3)-C(6)-C(7)-Br(4)	24.4(6)
O(1)-C(1)-C(7)-C(6)	45.2(5)
C(3)-C(1)-C(7)-C(6)	-65.6(5)
O(1)-C(1)-C(7)-C(8)	149.8(4)
C(3)-C(1)-C(7)-C(8)	39.0(4)
O(1)-C(1)-C(7)-Br(4)	-86.0(4)
C(3)-C(1)-C(7)-Br(4)	163.2(3)
C(6)-C(7)-C(8)-O(5)	-61.4(5)
C(1)-C(7)-C(8)-O(5)	-171.2(4)
Br(4)-C(7)-C(8)-O(5)	67.9(5)
C(6)-C(7)-C(8)-O(4)	167.8(4)
C(1)-C(7)-C(8)-O(4)	58.0(4)
Br(4)-C(7)-C(8)-O(4)	-62.9(5)
C(6)-C(7)-C(8)-C(4)	50.1(4)
C(1)-C(7)-C(8)-C(4)	-59.7(4)
Br(4)-C(7)-C(8)-C(4)	179.4(4)
C(5)-C(4)-C(8)-O(5)	69.9(5)
C(3)-C(4)-C(8)-O(5)	-179.7(4)
Br(1)-C(4)-C(8)-O(5)	-56.0(5)
C(5)-C(4)-C(8)-O(4)	-159.6(4)
C(3)-C(4)-C(8)-O(4)	-49.2(5)
Br(1)-C(4)-C(8)-O(4)	74.5(5)
C(5)-C(4)-C(8)-C(7)	-50.6(4)
C(3)-C(4)-C(8)-C(7)	59.8(4)
Br(1)-C(4)-C(8)-C(7)	-176.5(3)
O(2)-C(2)-O(1)-C(1)	174.4(5)
O(3)-C(2)-O(1)-C(1)	-6.3(6)
C(3)-C(1)-O(1)-C(2)	3.6(5)
C(7)-C(1)-O(1)-C(2)	-106.8(5)
O(2)-C(2)-O(3)-C(3)	-174.5(5)
O(1)-C(2)-O(3)-C(3)	6.2(6)
C(4)-C(3)-O(3)-C(2)	107.8(5)
C(1)-C(3)-O(3)-C(2)	-3.6(5)
O(5)-C(8)-O(4)-C(9)	50.9(6)
C(7)-C(8)-O(4)-C(9)	-176.3(4)
C(4)-C(8)-O(4)-C(9)	-76.5(6)
O(4)-C(8)-O(5)-C(10)	52.9(6)
C(7)-C(8)-O(5)-C(10)	-74.0(5)
C(4)-C(8)-O(5)-C(10)	-175.8(4)

Symmetry transformations used to generate equivalent atoms:

A.9 References for Appendix A

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