Catalytic Generation and C–C Bond Forming Reactions of Dicoordinated Carbocations

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Catalytic Generation and C–C Bond Forming Reactions of Dicoordinated Carbocations

A dissertation submitted in partial satisfaction of the

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in Chemistry

by

Stanislav Popov

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ABSTRACT OF THE DISSERTATION

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Stanislav Popov

Doctor of Philosophy in Chemistry

University of California, Los Angeles, 2021

Professor Hosea Martin Nelson, Chair

This dissertation describes the development of Lewis acid-based methodology to generate dicoordinated carbocations catalytically. These reactive intermediates were once sparingly accessible synthetically and were mostly the focus of theoretical studies. This dissertation highlights new, mild conditions that can generate these species in a kinetically persistent fashion through the use of weakly coordinating anions in non-polar media. These conditions also enable new carbon–carbon bond forming reactions of these intermediates to take place; either through Friedel-Crafts or C–H insertion. Additionally mechanistic nuances and the key advantages and disadvantages of each developed system

will be highlighted. Overall, this work features the development of this chemistry from a fundamental study to a more broadly applicable reaction.

Chapter One is a brief overview of the current state of research on aryl and vinyl cations. This chapter serves as a prelude to the remaining chapters and will be referenced throughout this dissertation. Strategies to generate these reactive species, specifically ones that inspired our own research in this area are presented. Furthermore, some reactivity of these cations is also highlighted, again focusing on mechanistically similar reactions to our own.

Chapter Two describes our efforts in the development of a silylium-carborane catalyzed reaction to generate aryl and vinyl cations catalytically from aryl fluorides and vinyl triflates respectively. These species were then able to be engaged in intermolecular reactions with inert C–H bonds of both alkanes and arenes resulting in a mild C–H functionalization reaction.

Chapter Three discusses our investigations of lithium-based Lewis acids to generate reaction vinyl cations under highly basic conditions and their ensuing reactivity. Notably, this work also overcomes some of the challenges presented in chapter Two with regards to the functional group compatibility of these systems. This work represents an important advancement of our chemistry towards a more robust, practical reaction.

Chapter Four highlights an ongoing effort in our research group to utilize different vinyl sulfonate precursors in order to access a broader class of vinyl cation intermediates. With these precursors in hand, we utilize similar conditions to Chapter Three to develop some new vinyl cation reactivity. These reactions involve trapping of vinyl cations with allylsilanes, silyl ketene acetals, and methyl ethers.

Chapter Five discusses our ongoing effort to develop a “field guide” for the practicing organic chemist in order to disseminate some of our groups in-house knowledge in developing these cation methodologies over the past few years. Here, mechanistic nuances, substrate design, and choice of catalytic system are discussed.

The dissertation of Stanislav Popov is approved.

Neil Kamal Garg

Ellen May Sletten

Patrick G. Harran

Hosea Martin Nelson, Committee Chair

University of California, Los Angeles

2021

This dissertation is dedicated to my best friend, Nick.

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LIST OF ABBREVIATIONS

Ac = acetyl, acetate

AcOH = acetic acid

α = alpha

app. = apparent

aq. = aqueous

Ar = aryl

β = beta

br = broad

Bu = butyl

t-Bu = *tert*-butyl

°C = degrees Celsius

calcd = calculated

cat. = catalytic

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

d = doublet

dd = doublet of double

dr = diastereomeric ratio

δ = chemical shift

DCB = dichlorobenzene

DFB = difluorobenzene

DMF = dimethylformamide

DMSO = dimethylsulfoxide

equiv = equivalent

ESI = electrospray ionization

Et = ethyl

F_{15} = tris(pentafluorophenyl)borane

F_{20} = tetrakis(pentafluorophenyl)borate

g = gram(s)

h = hour(s)

HMDS = hexamethyldisilazane

HPLC = high performance liquid chromatography

HRMS = high resolution mass spectroscopy

Hz = Hertz

IR = infrared spectroscopy

i-Pr = isopropyl

J = coupling constant

L = liter

Li = lithium

LDA = lithium diisopropylamide

m = multiplet

m = meta

M = molar

m/z = mass to charge ratio

μ = micro

Me = methyl

MHz = megahertz

min = minutes

mol = mole(s)

MOM = methoxymethyl ether

mp = melting point

NMR = nuclear magnetic resonance

o = ortho

OTf = trifluoromethanesulfonate

OTs = *p*-toluenesulfonate

p = para

Ph = phenyl

pin = pinacolato

ppm = parts per million

Pr = propyl

q = quartet

rt = room temperature

s = singlet

t = triplet

temp = temperature

TES = triethylsilyl

Tf = trifluoromethanesulfonyl

TFA = trifluoroacetic acid

THF = tetrahydrofuran

TIPS = triisopropylsilyl

TLC = thin layer chromatography

TMS = trimethylsilyl

Ts = *p*-toluenesulfonyl (tosyl)

TS = transition state

UV = ultraviolet

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First off, I would like to thank my advisor Professor Hosea M. Nelson. I first talked to Hosea in December of 2015 when he called me on the phone telling me that I was accepted to graduate school at UCLA. It was my first graduate acceptance that I was received and I was incredibly excited to come visit. After talking more at the recruiting weekend the following March, I decided to attend UCLA and decided to start in Hosea's lab in the summer before graduate school officially began. Thank you for all the support and mentorship from my first day of summer in 2016 to now, as I'm about to graduate. I have learned a lot about thoughtful and careful designing of hypotheses, as well as theorycrafting about rigorous experiments to test those hypotheses. Thank you for attending all of my practice talks and helping me with my presentation skills and teaching me how to tell a good story both in my talks and my written works. I am excited to start my new position at Merck process and will certainly take the rigorous standards from the lab with me for my future career. Best of luck with your own career with the big move coming up and I'm excited to see all the papers that come out of the group in the coming years. I would also like to thank Professor Ken Houk for being a great collaborator over many years and helping us understand some of the more intricate mechanistic details in our reactions.

I would also like to thank the rest of my doctoral committee members: Professors Ellen Sletten, Neil Garg, and Patrick Harran. They have provided me with a lot of useful feedback and guidance throughout different meetings over my graduate career. I would like to thank Professor Harran for doing a wonderful job teaching Synthesis 244B, as it was a really enjoyable class and really got my mornings off to a good start that quarter being able to see elegant syntheses everyday. I would like to thank Professor Sletten for all the feedback during my first few months in graduate school when we had joint group meeting between our two labs. I enjoyed doing chalk-talk paper presentations and problem sets during that summer; it really helped ease the transition into giving more formal talks down the line.

I am also thankful for all the mentors and peers I have had in my undergraduate studies at Brandeis. Thank you to Professor Isaac Krauss for letting me perform undergraduate research in his group and exposing me to the world of methodology development. Even though I got a late start on undergraduate research, it was valuable crash course in synthetic skills that gave me a kick-start when I first began working at UCLA. Thank you to Leiming Tian, Ashley Klein, and Sebastian Temme for helping me get started in the lab and showing me how to use all of the equipment when I didn't know anything. Thank you to Professor Barry Snider for all the conversations and guidance you've given me over the years. I enjoyed attending journal club on Wednesday nights with Professor Krauss and Professor Snider to learn about new reactions and the world of total synthesis.

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In the class below me, I would like to thank Benjamin Wigman for being a good lab mate and close friend during my time here. He was the first graduate student that I got a chance to mentor even though I had just finished my first year of studies at the time. This was a really valuable and fun experience for me and we have worked together on multiple projects since then. Thanks for sharing your Clif bars and crackers with me during our late nights. Thanks for being the local repair expert for every time anyone had an issue with an instrument, I'll make sure to give you a call if my rotovap every breaks in the future. It's too bad we didn't work in the same room during my last year of graduate school, but you'll still be an eastern block member for life. Sepand Nistanaki has had multiple conversations with me about reaction mechanisms and weird rearrangements even when we weren't working together directly, and we have often designed some cool substrates together. Thanks for starting Dumbledore's Army with me and for all the help in preparing for my job interviews. I know you have a bright future ahead of you dude, and I'm excited to hear about all the exciting developments on your ee project after I leave. Thanks to Jessica Burch for going on hikes and other adventures with me; it was fun exploring all the trails that SoCal has to offer. Good luck with your own graduation in September and I'm sure you'll get be a valuable first employee at your next job. Thanks to Christopher Jones for being a good gym buddy and for developing a new branch of our lab with your initial MicroED studies in 2018. Lee Joon Kim has always been fun to talk to over the years; thanks for teaching me about MicroED and for all of the virtual hangouts we had during COVID. It's been great talking about different videogames over the years and you've done a great job in a new research area in our lab. I still remember helping you with your first vacuum distillation back in your synthesis days in fall of 2017 and I'm glad I was able to show you how to use a glovebox for the first time even though you've left the synthesis world behind. Also, thanks for solving structures of all of my weird unknown compounds that I've made over the past few years even faster than I could finish acquiring all of my 2D NMR data.

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I would also like to thank my two undergraduate researchers: Daniel Lin and Jonathan Wong. You guys have both been a pleasure to mentor and it's been great watching you guys grow as chemists. Congratulations to Daniel on finishing your first year of graduate school at USC and I'm excited to see where graduate school takes you in the future. Jonathan, I'm looking forward to hanging out when you move to the east coast in a few months to start in the Jacobsen lab at Harvard. I'll be sure to show you all of my favorite spots in Boston. You guys have both taught me a lot of valuable things both in terms of being a good mentor as well as a project leader for that I will always be grateful.

I would also like to thank my own classmates. Luke Boralsky was a great friend and gym buddy over my first few years of graduate school. Thanks for sitting in the front row with me in every class and at all the seminars so that we could make the most out of our free education. It was great working in the hood next to you and I learned a lot from our talks about natural product synthesis. I know you've moved on from the group, but I'm sure you're doing great things and having fun up north.

Sydnee Green started doing research on the same day that I did and now we're going to both graduate at the same time. Thanks for being part of my graduate school journey from beginning to end. We went through everything together from the first group meeting, to the first time we TA'd 30CL together and our first real research talk during winter of 2016. Thanks for bringing your vibrant personality to the group and always making the lab a great place. It was fun TAing graduate synthesis with you and talking about chemistry even though we never got a chance to work on the same project together. Good luck at Terray and I'm sure you're going to have a great career in industry!

Lastly I would like to thank all my friends and family back home for supporting me throughout my journey. I've always looked forward to going home over my winter breaks and seeing everyone and I'm looking forward to moving back and spending more time together now that I won't be so far away. Thanks for the constant phone calls making sure I was doing ok and for helping me make the cross country move in 2016. I would also like to thank my best friend Nick Ouellet for his friendship over the last eight years. Thanks for making time to play videogames with me every Friday night despite the time difference and for all the fun projects we've done together over the winter breaks. I know that we will have many more fun adventures in store for the near future and beyond. I'm looking forward to being able to hang out often again when I move back to the right coast.

BIOGRAPHICAL SKETCH

Education:

University of California, Los Angeles, CA

- Ph.D. in Organic Chemistry, anticipated Spring 2021
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- Current GPA: 4.00/4.00

Brandeis University, Waltham, MA

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Graduate Research Assistant: University of California, Los Angeles, CA

- July 2016 – present; Advisor: Prof. Hosea M. Nelson
- Discovered novel C–H insertion reaction of vinyl cations
- Spearheaded development of milder catalysts for vinyl cation generation
- Experienced in project lead position and demonstrated success on a team
- Propelled projects forward by performing reaction and substrate design

Undergraduate Research Assistant: Brandeis University, Waltham, MA

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- Worked on synthesizing new boron carboxylate compounds
- Tested new compounds for catalysis in homoallylation of aldehydes

Graduate Teaching Assistant: University of California, Los Angeles, CA

- Undergraduate organic chemistry labs and discussion sections (Fall 2016 – Spring 2018): Taught students organic reactions, mechanisms and laboratory techniques.

Honors and Awards:

- Donald J. Cram Dissertation Award (Spring 2021)
- Majeti-Alpati Excellence in Research Award (Spring 2020)
- UCLA Foote Foundation Fellowship (2019–2021)
- NSF Graduate Research Fellowship (2018–2021)

- Hanson Dow Teaching Award (Spring 2018)
- Deans List at Brandeis University (Fall 2013–Spring 2016)
- ACS Organic Division Undergraduate Award 2016
- Provost Undergraduate Summer Research Fellowship (Summer 2015)

Publications:

1. **C–H Functionalization Reactions of Phenyl and Vinyl Carbocations**. Popov, S.; Shao, B.; Bagdasarian, A. L.; Wigman, B.; Nelson, H. M. *Synlett*, **2020**, *31*, 1851– 1856.
2. **Urea Catalyzed Functionalization of Unactivated C–H Bonds.** Bagdasarian, A. L.; Popov, S.; Wigman, B.; Wei, W.; Lee, W.; Nelson, H. M. *Org. Lett.* **2020**, *22*, 7775–7779.
3. **Strong Bases and Weak Anions in Catalytic C–H Insertion Reactions of Vinyl Carbocations.** Wigman, B.; Popov, S.; Bagdasarian, A. L.; Shao, B.; Benton, T. R.; Williams, C. G.; Fisher, S. P.; Lavallo, V.; Houk, K. N.; Nelson, H. M. *J. Am. Chem. Soc.* **2019**, *141*, 9140–9144.
4. **Teaching an Old Carbocation New Tricks: Intermolecular C–H Insertion Reactions of Vinyl Cations.** Popov, S.; Shao, B.; Bagdasarian, A. L.; Benton, T. R.; Zou, L.; Yang, Z.; Houk, K. N.; Nelson, H. M. *Science* **2018**, *361*, 381–387.
5. **Arylation of Hydrocarbons Enabled by Organosilicon Reagents and Weakly Coordinating Anions**. Shao, B.; Bagdasarian, A. L.; Popov, S. *Science,* **2017**, *355*, 1403–1407.

CHAPTER ONE

Strategies for Catalytic Carbon–Carbon Bond-Forming Reactions of Dicoordinate Carbocations

1.1 Abstract

Carbocations have long been heralded as reactive intermediates of great synthetic importance. From their significance in biological processes to their implementation and exploitation in synthetic organic chemistry, the unique reactivity of these fleeting species has allowed for the development of previously inaccessible synthetic methods. Not nearly as prominent as their trivalent counterparts, the dicoordinated subclass of carbocations has seen little utility due to their inherent reactivity and lack of applications. The focus of this chapter is not to provide a complete overview of the reactivity and generation of dicoordinated carbocations, but rather to provide historical context for the work presented in this thesis. This chapter will focus on dicoordinated carbocation generation that has inspired some of our research and on reactions that proceed in a mechanistically similar fashion to our own.

1.2 Introduction

Carbocations have a rich history embedded in physical organic chemistry, mechanistic inquiry, and structure and bonding.[1–3] This can be seen specifically in the great classical vs. nonclassical carbocation debate of the 20th century.[4–7] They are also often used in the context of complex molecule total synthesis and retrosynthetic disconnections. The large impact of carbocations on the field of chemistry and science in general has resulted in a 1994 Nobel Prize awarded to George Olah "for his contribution to carbocation chemistry." During his research, Olah focused mostly on the study of "carbenium" ions.[8] Carbenium ions are typically tricoordinated electron-deficient carbon centers (**1.1**, Figure 1.1). In conjunction with this nomenclature, another class of so-called "dicoordinated carbocations" is appropriately named as it consists of an electron deficient carbon center that is disubstituted (**1.2**, **1.3**).[9] Although tri- and dicoordinated carbocations are under the same branch as "carbenium" ions, they possess markedly different reactivity profiles.

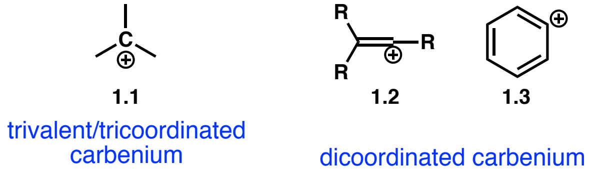


Figure 1.1 Different types of carbenium ions

Tricoordinate carbocations, compared to their dicoordinate counterparts, are more frequently employed in organic chemistry.[10] This is largely due to the relative ease of generation of stabilized trivalent cations, like the tripheynylmethyl (trityl) cation, that can be obtained from commercial sources. Dicoordinated carbocations are much higher in energy since the charge is more localized on a single electrophilic carbon without an extended π-system over which it can be delocalized through resonance, unlike most stabilized trivalent cations. This chapter highlights some common strategies used to generate these high-energy intermediates and their ensuing reactivity.

1.3 Phenyl Carbocations

When compared to vinyl cations, phenyl cations have remained understudied in the area of dicoordinated carbocations. This is likely due to their highly difficult generation that often requires harsh conditions, which limits their potential synthetic utility/applicability.[11] One reason for this is the inability of phenyl cations to adopt a *sp*-hybridized linear geometry that would be ideal for a dicoordinated cation. Some exceptions and breakthroughs are highlighted below.

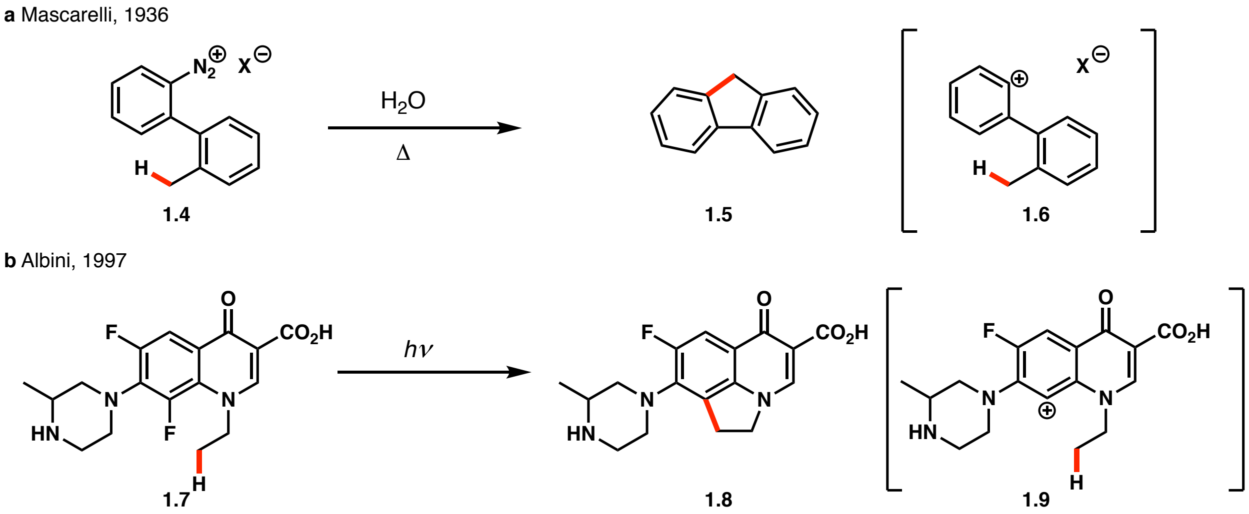


Figure 1.2 Early generation and C–H insertion reactions of phenyl cations

In a seminal example from Mascarelli in 1936, biaryldiazonium salt **1.4**, under thermolytic conditions, could be converted to fluorene (**1.5**).[12] While the underlying mechanism of this reaction was not fully understood at the time, several decades of investigations concluded that functionalization of the methyl group was attributed to a C–H insertion event into a transient phenyl cation **1.6**. Building off of these results, Albini studied the reactivity of phenyl cations **1.9** formed *via* photochemical irradiation of aryl fluorides **1.7**.[11,13] An advantage of this strategy is the use of fluorides as leaving groups, which are easier to carry through a synthesis than

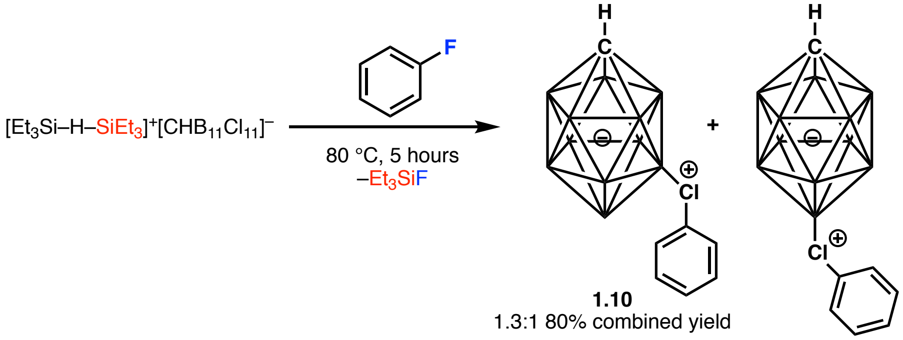
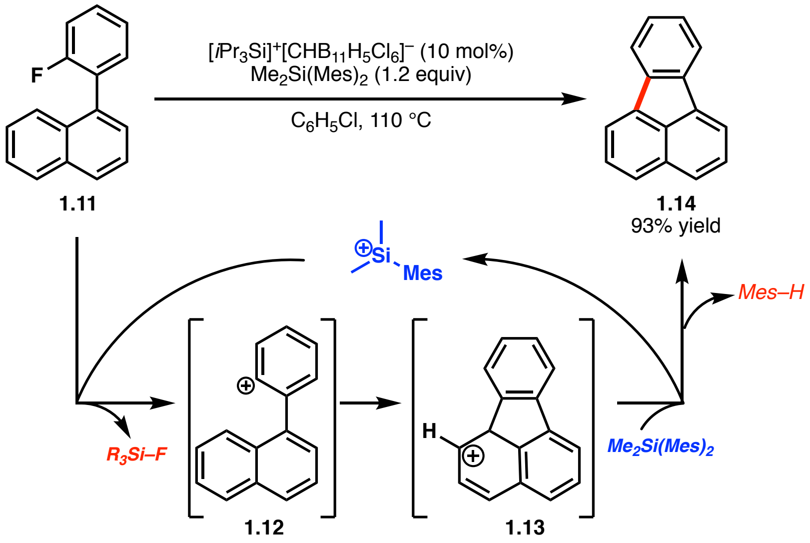


Figure 1.3 Stoichiometric generation of phenyl cations with silylium-carborane salts
(Other chlorines omitted for clarity)

diazonium salts. Furthermore, using this strategy, Albini has accessed both singlet and triplet phenyl cations, which have reactivity analogous to singlet and triplet carbenes respectively.

Some of the more modern work that informed our initial efforts in the field was a 2010 report from Reed and Siegel.[14] They show that a stoichiometric amount of triethylsilylium-carborane salts can successfully perfrom a C–F bond cleavage on fluorobenzene to yield chloronium adducts **1.10**, which result from the attack of the incipient phenyl cation by the chlorines of the carborane. Following up on this reactivity, Siegel has developed a catalytic system to generate phenyl cations based on silylium-carborane reagents. In their first report, they showed that biaryl fluorides **1.11** could react with silylium-carborane salts to yield an intermediate phenyl carbocation **1.12** (Figure 1.4a).[15]

a Intramolecular Friedel-Crafts through intermediacy of a phenyl cation



b Intramolecular C–H insertion through intermediacy of a phenyl cation

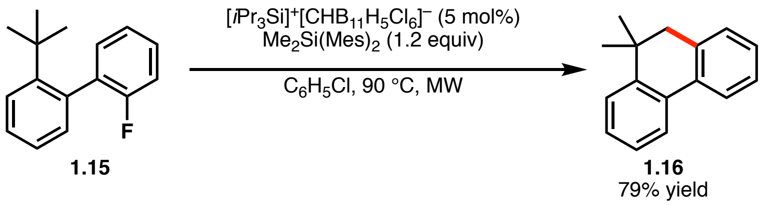


Figure 1.4 Siegel's Intramolecular C–C bond forming phenyl cation reactions

This phenyl cation could then be attacked by a tethered arene to generate Wheland intermediate **1.13**. Using dimethyldimesityl silane as a proton sponge, this Wheland intermediate could be deprotonated, resulting in release of mesitylene and concomitant regeneration of active silylium-carborane catalyst. All in all, this process provides high yields of polycyclic aromatic hydrocarbons **1.14**. In a follow-up report, Siegel has also shown that under similar conditions, intramolecular C–H insertion reactions were also possible yielding tricyclic product **1.16** from *tert*-butyl biphenyl **1.15** (Figure 1.4b).[16] Here, a concerted 1,1-C–H insertion of intermediate phenyl cation **1.17** would directly produce Wheland intermediate **1.18**, which can undergo elimination to form cyclized product **1.19** (Figure 1.5, green pathway). In contrast, a stepwise mechanism would result in a hydride shift whereupon a highly unstable primary cation **1.20** would be formed and trapped by the nearby benzene ring to give the same Wheland intermediate

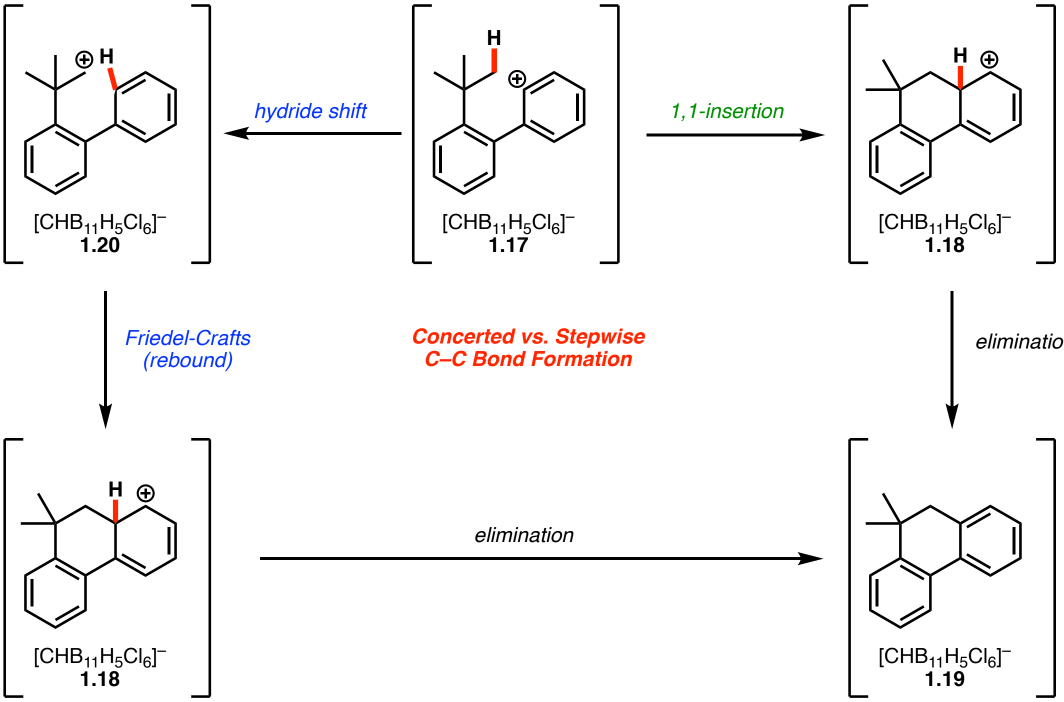


Figure 1.5 Possible mechanisms of C–C bond formation from phenyl cations

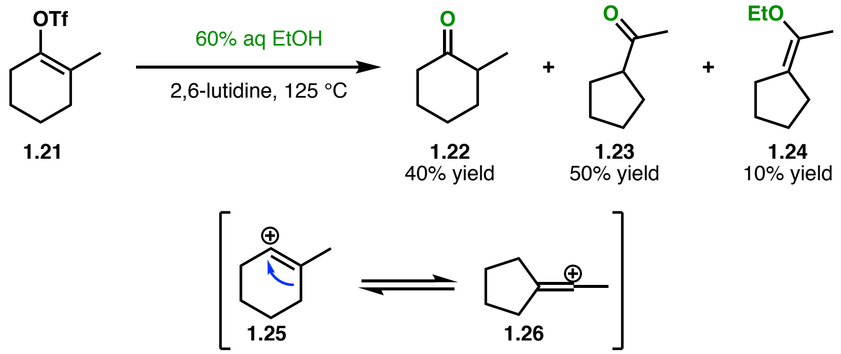
1.18 as above (Figure 1.5 blue pathway). In this case, the C–C bond forming reaction is with a primary, non-benzylic methyl group and is likely to be a concerted process and not a “rebound” type stepwise mechanism due to instability of primary cation **1.20**. Furthermore, they show in the same report that a C–H insertion into benzylic C–H bonds is also possible.[16] This mechanistic continuum of C–H insertion vs. stepwise rebound is something that we observed in much of the work outlined in this document; the preference for one over the other is often found to be substrate/cation dependent.

1.4 Vinyl Carbocations

Vinyl carbocations are the locally isoelectronic analogs of phenyl carbocations. However, these species have been studied in much greater detail since the early 20th century with some early pioneering work from Jacobs and Grob.[17,18] The ensuing discussion will not nearly cover the breadth of vinyl cation research that has been done in the field to date.[19] Instead, it will focus on some recent advancements in C–C bond-forming reactions of vinyl cations that are inspirational or mechanistically important to our own work later in this document. Furthermore, early solvolytic studies that studied both relative ionization rates and rearrangements will be discussed, as the former is pervasive throughout Chapters 2–5 while the latter will be covered extensively in Chapter 5.9.

Historically, there are multiple strategies available to generate vinyl carbocations. The most common approaches are electrophilic additions to alkynes, electrophilic additions to allenes, and heterolytic cleavage of vinyl halides/pseudohalide precursors.[19] While we have done some preliminary exploration of alkyne chemistry, most of our work and, accordingly, most of this discussion will focus on heterolytic cleavage. Particularly, direct solvolytic generation was often the method of choice for simple generation of vinyl cations in early studies. While there are multiple leaving groups that have been used such as diazonium salts[20], iodoniums salts[21], and simple halides[22], the most popular ones have been the so-called "super leaving groups", triflates[23] and nonaflates[24].

a Solvolysis of 2-substituted cyclohexenyl triflates



b Solvolysis of 6-substituted cyclohexenyl triflates

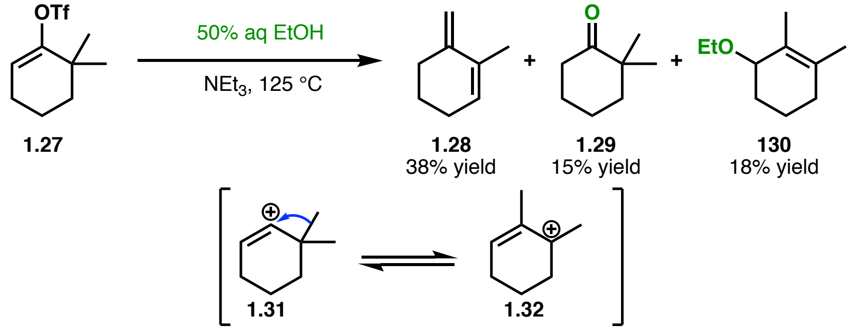


Figure 1.6. Solvolysis of substituted cyclic vinyl triflates

While ring size effects on stability and ionization will be further discussed in Chapter 5.3, generally vinyl cations in larger rings are more stable and their vinyl sulfonate precursors undergo solvolysis at much higher rates. During early studies of cyclic vinyl triflates, it was found that adding substitution on the alkene adjacent to the triflate not only increases the rate of solvolysis, but also introduces the possibility for rearrangement reactions.[25] For example, upon solvolysis of 2-methylcyclohexenyl triflate (**1.21**), Stang and coworkers observed formation of 2-methylcyclohexanone (**1.22**) and cyclopentylmethylketone (**1.23**) in an almost 1:1 ratio along with a small amount of vinyl ether **1.24**. Notably, this occurs through ring contraction of vinyl cation **1.25** to yield more stable acyclic vinyl cation **1.26**. Subjection of 6,6-dimethylcyclohexenyl triflate **1.27** to similar conditions gave the direct quenched product **1.29** in a meager 15% yield and most of the obtained SN1/E1 products **1.28** and **1.30** had a methyl shift occur. This methyl shift occurs from vinyl cation **1.31** to give the more stable allyl cation **1.32**. In solvolytic kinetic studies, it was also found that both vinyl triflates **1.21** and **1.27** undergo solvolytic cleavage 10 and 920 times faster, respectively, than the parent cyclohexenyl triflate. This is a combination of steric buttressing effects and electron-donation from the electron-rich methyl group. These substitution effects are also present in other rings sizes as well as acyclic systems and examples of similar rearrangements will be further discussed in Chapter 5.7.

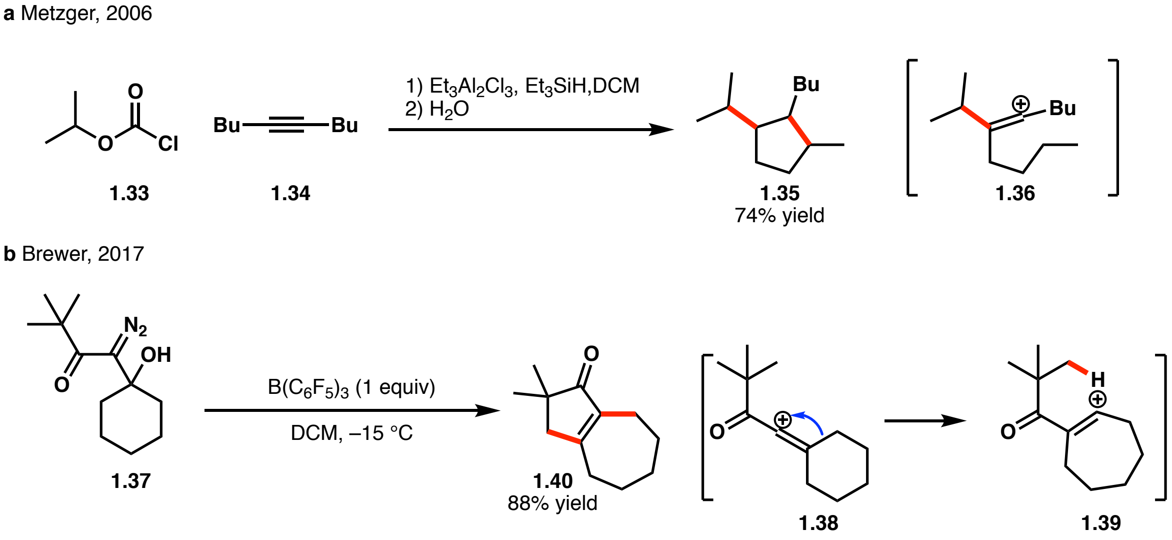


Figure 1.7 Intramolecular C–H insertion reactions of vinyl cations with stoichiometric Lewis acids

Although there were a lot of early studies on vinyl cations, this work was largely limited to solvolytic studies. Before our first report in the area, there were few scattered examples of vinyl cation C–H insertion reactions. These scattered reports piqued our interest and prompted us to start doing research in this largely unexplored area. First, Metzger reported that mixing an alkyne **1.34** with an alkyl chloroformate **1.33** under strongly Lewis acidic conditions (ethylaluminum sesquichloride) can yield cyclopentane product **1.35** in 74% yield (Figure 1.7a).[26] This reaction proceeds by initial ionization of chloroformate **1.33** to yield a 2-propyl cation which can be attacked by alkyne **1.34** to yield intermediate vinyl cation **1.36**. This vinyl cation is perfectly positioned to undergo a C–H insertion with the methylene of the butyl chain that is adjacent to the terminal methyl. Upon terminal reduction by triethylsilane, the alkane product **1.35** is formed. While this work relies on stoichiometric use of both Lewis acid and reactant, it was the first report in the literature that proposed a concerted C–H insertion mechanism with a vinyl cation.

Over ten years later, Brewer and coworkers reported their seminal vinyl cation C–H insertion studies (Figure 1.7b).[27] Here, β-hydroxy-α-diazoketones **1.37** are treated with stoichiometric amounts of strong Lewis acids such as trispentafluorophenyl borane (F_{15}), which yields ring-expanded, bicyclic cyclopentenone products. Mechanistically, the initial vinyl cation **1.38** is generated through Lewis acid-mediated hydroxide abstraction followed by loss of nitrogen. This vinyl cation **1.38** can undergo a 1,2-carbon shift, similar to some observed in Figure 1.6, to generate cycloheptenyl cation **1.39**. This cation can then undergo a C–H insertion with a methyl group on the *tert*-butylketone, and upon terminal deprotonation yield final enone product **1.40**. Because this C–H insertion proceeds with a primary C–H bond, it is also proposed to be a concerted mechanism (instead of a stepwise "rebound" process). While most modern papers discussed here propose a concerted mechanism, there have been some early reports by Stang and Caple that propose a stepwise 1,5-hydride shift, "rebound-type" mechanism.[28–30]

Another type of C–C bond forming reaction of vinyl cations that will be discussed heavily in Chapter 2–5 is the trapping of vinyl cations with arenes (Friedel-Crafts) to give styrenes or arylalkanes depending on the conditions. These types of reactions have also been reported with vinyl cations both in early reports, as well as some more recent 21st century studies. In early reports, Stang studied the Friedel-Crafts vinylation of arenes with vinyl cations. He found that acyclic and medium-sized ring-derived vinyl triflates could undergo solvolytic

Friedel-Crafts reactions with arene solvent.[31] However, these reactions were often sluggish and low-yielding. For example, after heating an anisole solution of cycloheptenyl triflate **1.41** at 170 °C for 24 hours, only a 30% yield of styrene **1.42** was obtained (Figure 1.8a). Furthermore, vinyl triflates derived from smaller rings (5- or 6-membered) remained completely unreactive even at these elevated temperatures. Forty years later, Brewer reported an intramolecular Friedel-Crafts reaction utilizing a similar strategy as shown in Figure 1.7b.[32] Here, exposure of β-hydroxy-α-diazoketone **1.43** to one equivalent of F_{15} for 10 minutes at room temperature smoothly provided indenone **1.44** in 80% yield. This reaction proceeds through the intermediate vinyl cation **1.45**, which can ring expand to cycloheptenyl cation **1.46** and undergo subsequent trapping by the tethered aryl ring. Most recently, Bour and coworkers reported that lithium cations paired with aluminate-derived WCAs were sufficiently Lewis acidic to catalyze formation of vinyl cations

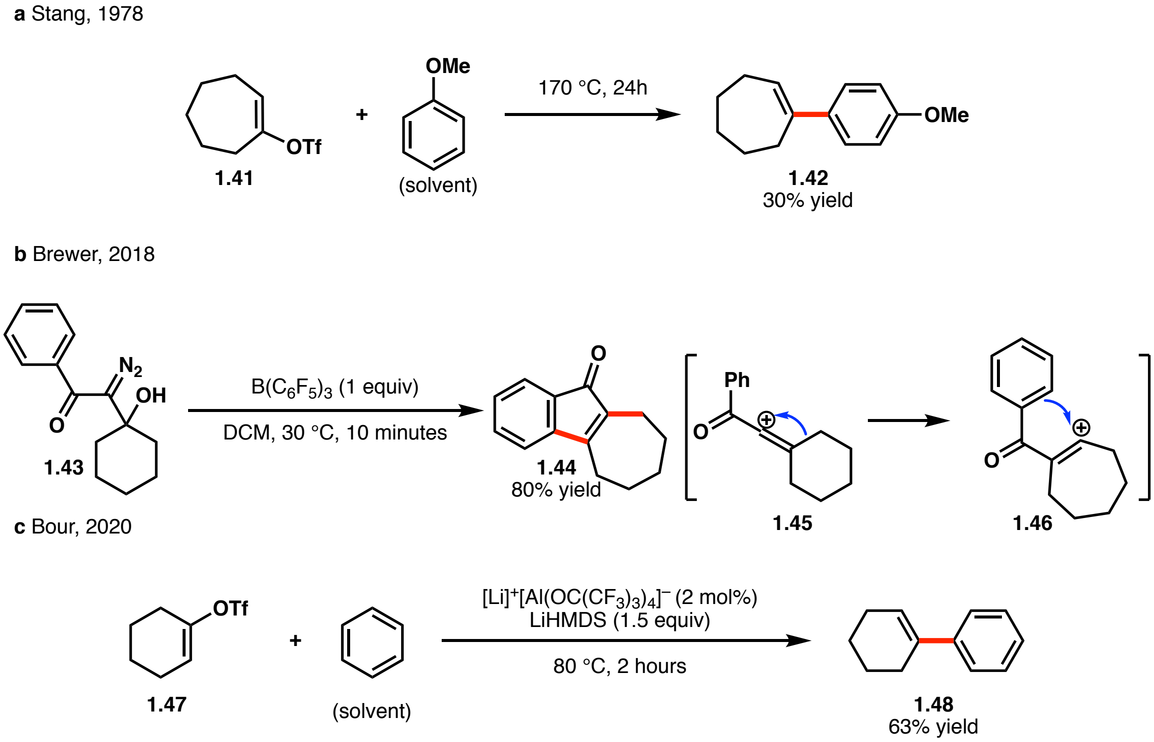


Figure 1.8 Friedel-Crafts reactions of vinyl cations

from vinyl triflates.[33] With a stoichiometric amount of LiHMDS to turnover the reaction, they were able to perform solvolytic Friedel-Crafts reactions of cyclohexenyl triflate (**1.47**) with benzene to obtain styrene **1.48** in moderate yields. Notably, this reaction proceeds at 80 °C, whereas cyclohexenyl triflate remained completely unreactive at this temperature in Stang's pioneering work even with stoichiometric BF_3 additives.[31] In their report, Bour and coworkers also demonstrated that with more easily ionizable vinyl triflates, the reaction could also be performed in pentane solvent with only 2 equivalents of arene nucleophile to obtain styrene products in moderate to good yields.

1.5 Conclusion

The work discussed in this chapter lays the framework for our own research that will be outlined in the remainder of the document. From early studies in the field of dicoordinated vinyl cations to more recent catalytic methodologies, these studies have given us a great deal of conceptual tools to work with in order to forge thoughtful hypotheses and design experiments to push the frontiers of the field. While the research shown here is nowhere close to a comprehensive overview of the field, many of the concepts highlighted in this chapter will be present as reoccurring themes in the chapters to come.

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CHAPTER TWO

Intermolecular C–H Insertion Reactivity of Aryl and Vinyl Cations Under the Catalysis of Silylium-Carborane Reagents

Brian Shao, Alex L. Bagdasarian, Stasik Popov, Hosea M. Nelson *Science*, **2017**, *355*, 1403–1407.

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2.1 Abstract

Over the past century, there have been numerous theoretical and computational studies on dicoordinated carbcocations, namely phenyl and vinyl cations. Despite this long history of study, the utility of these high-energy species in synthesis has remained limited. Most early vinyl cation investigations have been limited to intramolecular or solvolysis reactions in polar protic solvents. Aryl cations have been even more seldom used in organic methodology, and even their existence as a synthetic intermediate was not certain until recently (REF). Here, we report that sliylium-carborane reagents are Lewis acidic enough to generate both phenyl and vinyl cations in non-polar media. Furthermore, these cations are kinetically persistent enough to undergo intermolecular C–C bond forming reactions with inert alkane and arene C–H bonds. This work represents a new use for these dicoordinated cations as C–H arylation and C–H alkylation reagents under mild conditions.

2.2 Introduction

For more than a century, carbocations have played a central role in the chemical sciences, inspiring the development of broadly applied chemical reactions and a greater understanding of the fundamental properties of molecules.[1,2] Conceptually, carbocations can serve as retrons, guiding the design of retrosynthetic analyses and elucidating the selection of synthetic precursors.[3] In practice, they are equally important, as stabilized carbocations are routinely utilized in standard synthetic transformations.[4] On the other hand, carbocations that are divalent (dicoordinated carbocations), and/or not stabilized by resonance donating groups or hyperconjugation, are neither easily manipulated nor employed in routine transformations.[5] This can be observed in the case of vinyl and phenyl cations. Phenyl cations are seldom invoked as reactive intermediates and there are only a few reports that detail their generation through photolysis or thermolysis.[6–9] Vinyl cations have been studied extensively, but most reactivity studies have focused on solvolysis reactions where the reactive vinyl cation is intercepted by heteroatom-containing solvent molecules.[10–12]

2.3 Initial Generation of Aryl Cations

At the outset of this research program in our group, we were inspired by several reports from the Ozerov and Siegel groups where silylium-carborane reagents are used to perform C–F bond cleavage and to generate highly unstable vinyl cations.[13–15] The Ozerov lab managed to perform hydrodefluorinations of multiple benzylic and aliphatic alkyl fluorides **2.1** to alkanes **2.2** by using silylium carborane salts to generate carbocations (e.g. **2.3**) that can later be reduced by silanes to generate a reduced C–H product and regenerate the silylium-carborane salt (Figure 2.1a).[13] Despite the highly electron deficient nature of carbocation intermediate **2.3**, this reaction proceeded smoothly at 25 °C with extremely low catalyst loading. In 2011, Siegel and coworkers applied the same class of reagents to abstract fluorides from aryl fluorides **2.4** that then went on to do intramolecular Friedel-Crafts reactions and generate polycyclic aromatic hydrocarbons **2.5** (Figure 2.1b).[14] This reaction is believed to proceed through the highly unstable aryl cation intermediate **2.6**. Although this reaction proceeded at much more elevated temperatures (110 °C), it is still an exciting advancement in the field of aryl cation chemistry. Notably, both of these reactions proceed in non-polar media and rely on the use of the weakly coordinating nature of the carborane to impart kinetic persistence to cations **2.3** and **2.6** in order for them to undergo the desired reactivity. Carboranes and other types of WCAs seem to be the key in generating a highly Lewis acidic silylium cation, as well as generating persistent non-stabilized carbocations in solution. Despite this precedent, catalytic, intermolecular reactions of phenyl cation equivalents have been elusive.[16–19] To this end, we pursued application of phenyl cations in catalytic, intermolecular C–H functionalization reactions to forge new C–C bonds.

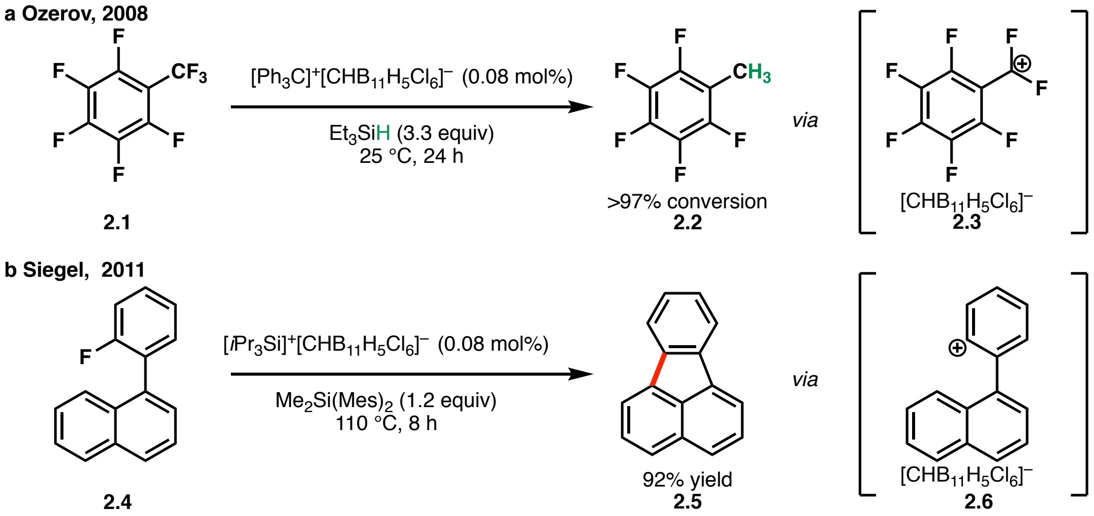


Figure 2.1 Previous reports on alkyl carbocation (a) and aryl cation (b) generation with silylium-carborane salts

2.4 C–C Bond Forming Reactions of Aryl Cations

We envisioned that β-silylated aryl fluorides (**2.7**) would be particularly well suited as phenyl cation precursors for several reasons. First, we anticipated that β-silicon stabilization would lower the barrier for fluoride abstraction and stabilize the phenyl cation **2.8**.[20–24] Finally, we hypothesized that elimination of the β-silicon group from a reactive intermediate such as arenium **2.9** could regenerate the silylium-carborane

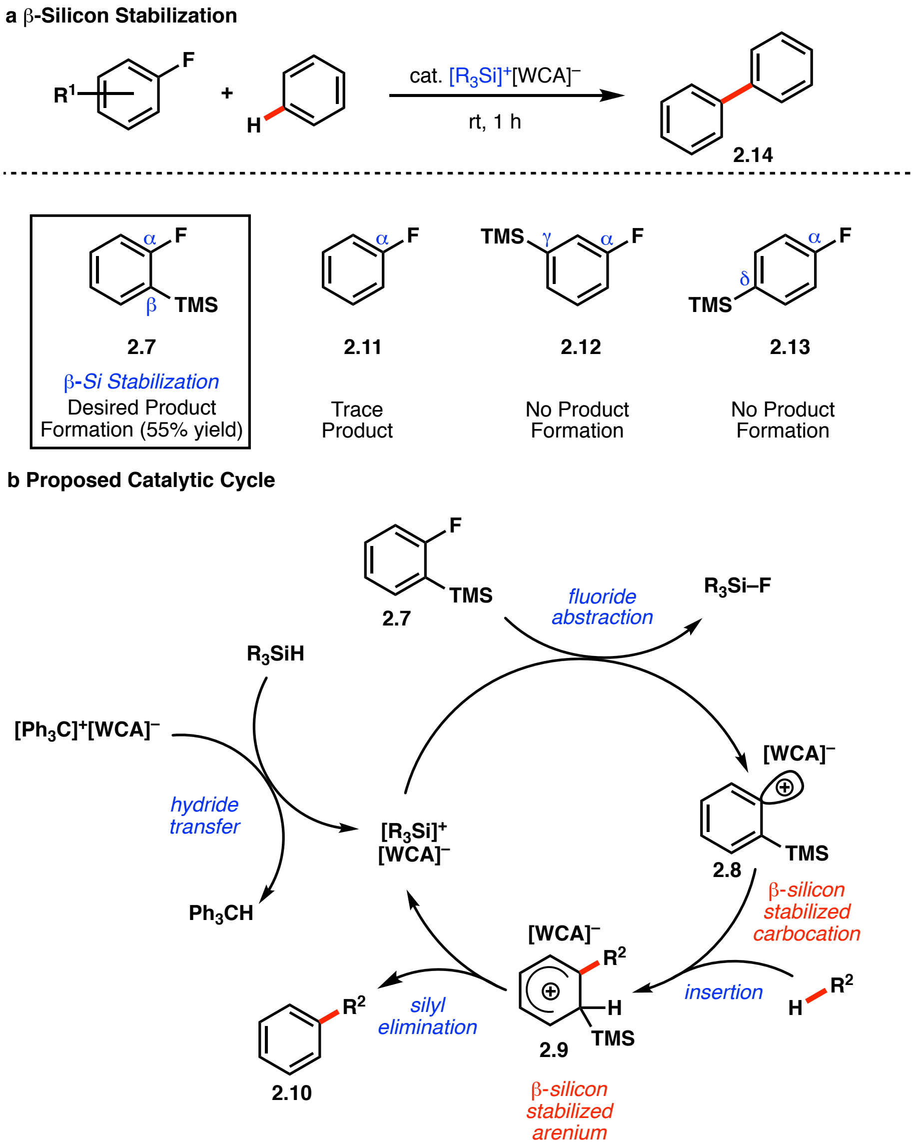
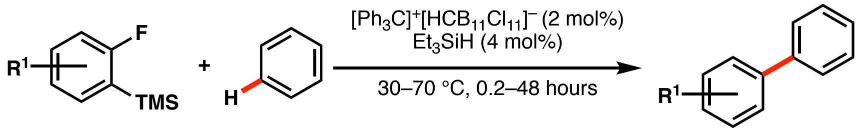


Figure 2.2 Early investigation (a) and mechanistic hypothesis (b) of aryl cation reactions

catalyst. To test this hypothesis, we exposed fluorobenzene (**2.11**) and a variety of differentially trimethylsilyl (TMS)-substituted aryl fluorides **2.7**, **2.12**, and **2.13** to a solution of catalytic amounts of silylium-carborane (generated from reduction of the triphenylmethylcarbenium-carborane salt with silane) in benzene.[25] Notably, only the *ortho*-substituted variant produces biphenyl (**2.14**) in 55% yield, while the arylfluorides remain unreactive. This reaction is hypothesized to occur through silylium-mediated fluoride abstraction to generate aryl cation **2.8**. This aryl cation can then undergo an intermolecular C–C bond-forming reaction with an alkane/arene to generate silyl-arenium complex **2.9**. This intermediate can eject a silylium group to regenerate active catalyst



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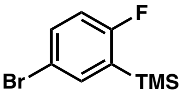
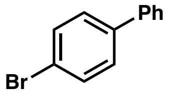
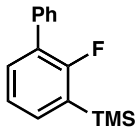
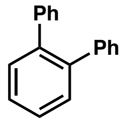
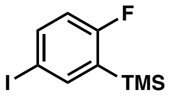
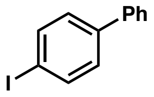
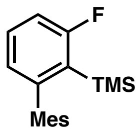
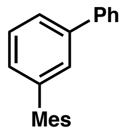
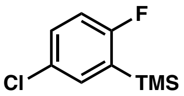
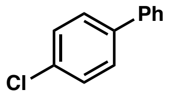
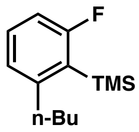
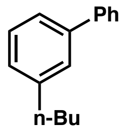
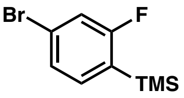
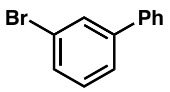
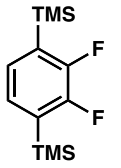
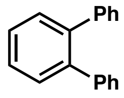
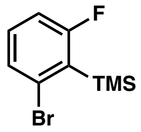
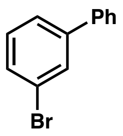
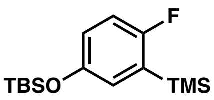
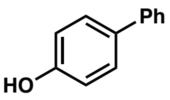
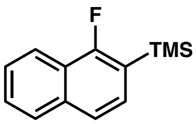
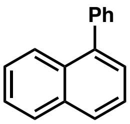
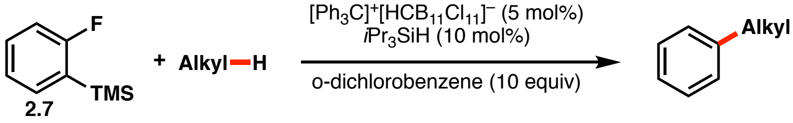
1			56	7			45
2			71	8			47
3			47	9			99
4			52	10			36
5			77	11			29
6			49				

Table 2.1 Scope of C–H arylation of arenes with aryl cations

2.15 and generate the arylated product **2.10**.

With our initial promising results that validated our mechanistic hypothesis, we decided to probe the scope of this methodology. We looked towards the synthesis of various *ortho*-silyl aryl fluorides, which could be easily accessed by directed *ortho*-lithiation of aryl fluorides followed by silylation. We were pleased to observe selective C–F functionalization in the presence of weaker carbon-halogen (C–X) bonds, which contrasts canonical cross-coupling reactivity (entries 1–4, Table 2.1). Notably, entry 5 shows that this selectivity holds true even when the resulting cation of a C–Br bond abstraction would also be β-silicon stabilized. In general, the yields for all halide substituents were moderate to good. Polycyclic aromatic fluorides (entry 6) were competent under the reaction conditions as well, as demonstrated by the formation of 1-phenylnaphthalene in 49% yield. Additionally, aryl and alkyl substitution (Table 2.1, entries 7–9) were tolerated under the reaction conditions, providing phenylated aromatics in moderate to excellent yields (45–99%). Consecutive arylation of difluorides was also possible, as demonstrated by the formation of *o*-terphenyl (entry 10), albeit in a diminished 36% yield. Introduction of a heteroatom donor (entry 11) provided a diminished 29% yield of the desired phenol derivative. Despite the low yield, we were pleased with this result given the hyper-Lewis acidic nature of the silylium cation. Usually, any compounds with Lewis basic functionalities poison the silylium-carborane catalyst through Lewis acid-base interactions, which result in no conversion.[13–15] Notably, throughout our scope studies, the new aryl group was introduced solely at the carbon that originally bore the fluorine. This resulted in a development of a formal C–H/C–F cross-coupling reaction.

Bolstered by these results, we began our investigation into the arylation of alkanes. After a brief optimization, we found that cyclohexane could be phenylated by aryl fluoride **2.7** in 41% yield after two hours at 60 °C (entry 1, Table 2.2) We were surprised to find that this alkane arylation reaction proceeded under such mild conditions, so we decided to look at other alkanes. Likewise, cyclopentane and cycloheptane underwent smooth arylation under similar conditions in 54% and 40% yield, respectively (entries 2 and 3). Switching to linear alkanes, we found that *n*-hexane underwent arylation to yield all three phenylhexane isomers in 40% overall yield (entry 4). This C–H arylation reaction displayed terminal selectivity, with an α:β:γ ratio of 5:2:1. In a similar fashion, *n*-pentane also underwent terminal-selective



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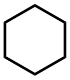
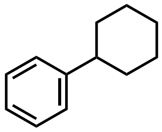
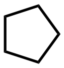
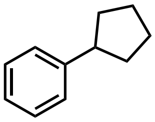
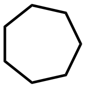
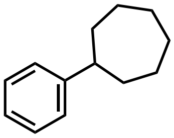
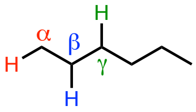
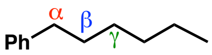
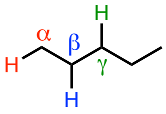
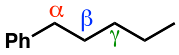
1		60		41
2		70		54
3		100		40
4		60		40 α:β:γ 26:9:5
5		60		42 α:β:γ 30:10:2

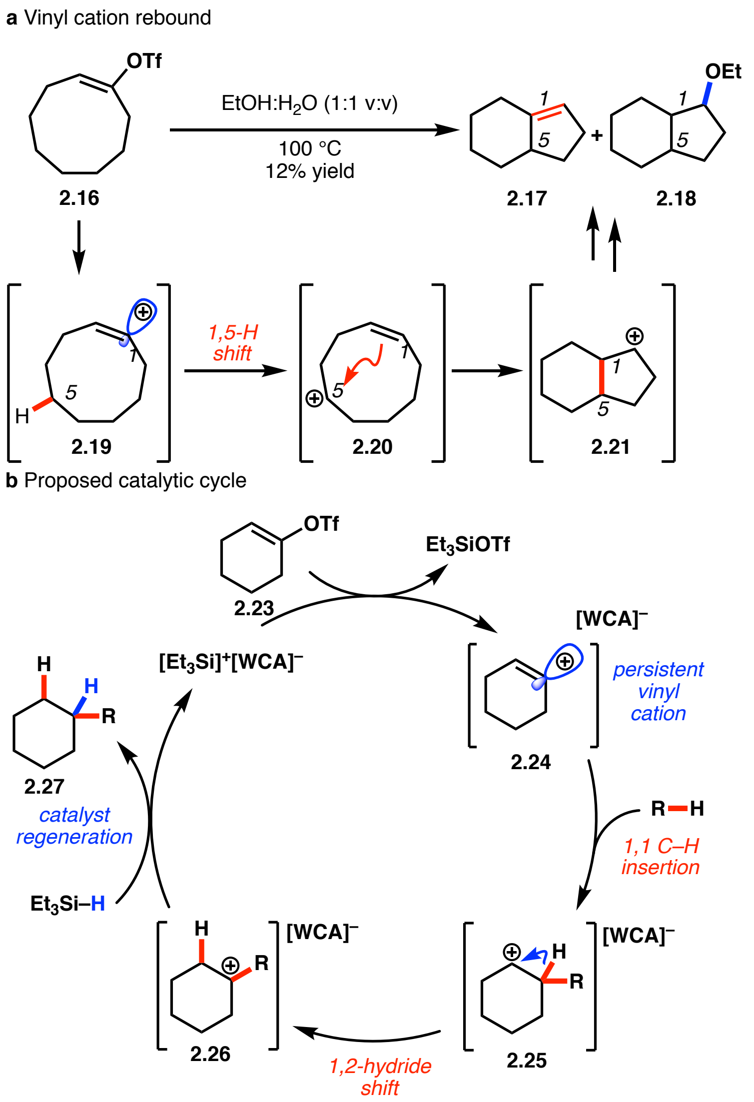
Table 2.2 C–H arylation of alkanes *via* phenyl cations

arylation to yield phenylpentane isomers in 42% yield with a 10:3:1 ratio (entry 5). This terminal selectivity might be due to the steric bulk of the TMS group next to the active cationic site. With these results in hand, we have successfully developed a catalytic intermolecular aryl cation reaction for functionalizion of inert C–H bonds.

2.5 Early Investigations into Vinyl Cations

With these successes in hand, we pondered if perhaps vinyl cations could be generated by utilizing similar silylium-carborane electrophiles with suitable vinyl cation precursors. Looking through the vinyl cation literature, vinyl triflates stood out as good candidates due to their ease of preparation (one step from ketone) and their widespread use in modern methodology.[11,26–28] Furthermore, we were intrigued by an isolated example from Hanack where solvolysis of cyclononenyl triflate (**2.16**) yielded fused ring products **2.17** and **2.18** (Figure 2.3a).[29] This mechanism was rationalized as a "carbocation rebound" mechanism where vinyl cation **2.19** was quenched *via 1,5*-hydride shift, and the neutralized alkene **2.20** attacks the newly formed alkyl carbocation.[30] This sequence forges the ring fusion of the bicyclononenyl cation **2.21** leading to products **2.17** and **2.18**. More recent efforts from Metzger and Brewer that showed vinyl cations engaging in C–C bond forming reactions empowered us to pursue this reaction development.[31–34]

Our mechanistic hypothesis was that perhaps the silylium-carborane salt could ionize a vinyl triflate **2.33** to generate a kinetically persistent vinyl cation-WCA ion pair **2.24** (Figure 2.3b). A 1,1-insertion of this reactive dicoordinated cation **2.24** into a C–H bond would lead to formation of alkyl carbocation **2.25**.[35] A *1,2*-hydride shift would lead to the more stable tertiary cation **2.26** that, upon reduction by a stoichiometric silane reagent, would generate the functionalized hydrocarbon product **2.27**, and regenerate the silylium/carborane catalyst **2.22**. In its entirety, this process would enable the direct C–H alkylation of alkanes and arenes with simple ketone derivatives.[36]



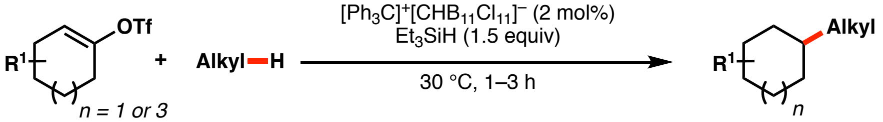
a Vinyl cation rebound

b Proposed catalytic cycle

Figure 2.3 Mechanistic hypothesis of fused ring formation (a) and our catalytic system (b)

2.6 C–H Insertion Reactions of Vinyl Cations

With our mechanistic hypothesis in hand, we initiated our studies with cyclohexenyl triflate (**2.23**). We found early success when exposure of cyclohexenyl triflate (**2.23**) to 1.5 equivalents of triethylsilane and 2 mol% $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ in anhydrous cyclohexane at 30 °C resulted in the formation of bicyclohexyl **2.28** (entry 1, Table 2.3) in 87% yield. Astounded by the remarkably mild conditions employed in this alkane alkylation reaction, we explored the scope to further elucidate potential synthetic applications and to gain mechanistic insight. Other alkane C–H bonds, such as those of cycloheptane and *n*-pentane, also reacted efficiently with the cyclohexenyl cation, albeit with poor regioselectivity in the latter case, which is contrary



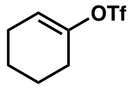
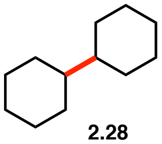
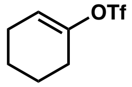
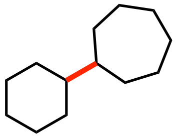
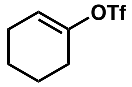
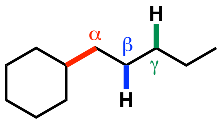
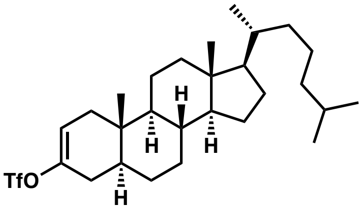
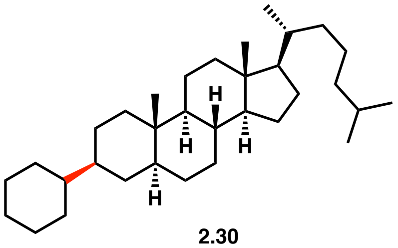
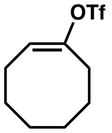
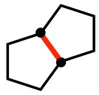
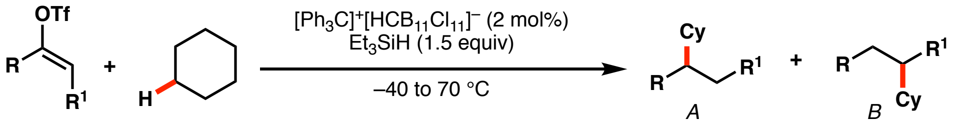
Entry	Substrate	Solvent	Product	Yield (%), Time (h)
1	 **2.23**	C_6H_{12}	 **2.28**	87, 1.5
2		C_7H_{14}		88, 2
3		n-C_5H_{12}	 21:36:11	68, 1.5
4	 **2.29**	C_6H_{12}	 **2.30**	88, 3 (15:1 *d.r.*)
5	 **2.31**	C_6H_{12}	 **2.32**	91, 1

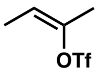
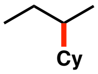
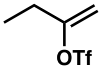
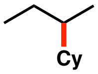
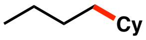
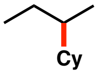
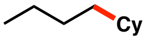
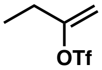
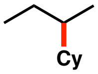
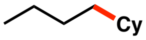
Table 2.3 C–H alkylation of alkanes

to the selectivity displayed by the related phenyl carbocation (entries 2, 3). Although cyclohexenyl triflates bearing substituents at the *2*- or *6*-positions led to complex mixtures of products, presumably due to non-productive unimolecular decompositions, other positions of the cyclohexenyl ring were tolerant of substitution.[37,38] For example, exposure of the enol triflate derived from *5*α-cholestan-*3*-one (**2.29**, entry 4) to our reaction conditions led to formation of the alkylated steroid **2.30** in 88% yield and 15:1 *d.r.* (entry 5). Analogous to the previously reported ring-contraction reactions of medium-sized cyclic vinyl triflates, exposure of cyclooctenyl triflate (**2.31**) to our optimized reaction conditions led to rapid transannular C–H insertion to yield bicyclic product **2.32** (Table 1, entry 5).[29]

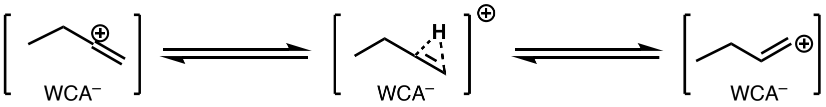
With strained cyclic vinyl cations successfully undergoing intermolecular C–H insertion, we turned our attention to acyclic vinyl cations. We wondered if the more stable *sp*-hybridized linear vinyl cations could also undergo this challenging C–H insertion reactivity. Acyclic vinyl cations have constituted the majority of previous experimental and theoretical studies of dicoordinated cations, as cyclic variants have traditionally proven difficult to generate under solvolytic conditions.[39] Subjection of butenyl triflate **2.33** to the reaction conditions led to high-yielding reductive alkylation of cyclohexane, providing *2*-cyclohexylbutane (**2.34**) in 85% yield (entry 1, Table 2.4a). The analogous reaction of triflate **2.35** gave formation of a high yielding 1:1 mixture of *1*-cyclohexylbutane (**2.34**) and *2*-cyclohexylbutane (**2.36**) (entry 2). Use of terminal triflate **2.37** (entry 3) resulted in an identical product distribution to that of entry 2, albeit requiring higher temperatures and longer reaction times due to initial formation of a primary vinyl cation. Carrying out the reaction at –40 °C in chloroform solvent allowed for more selective formation of *1*-cyclohexylbutane (**2.36**) (*ca.* 2:1) (entry 4). These product distributions can be rationalized by hydride bridging in the vinyl cation intermediate. For example, ionization of butenyl triflate **2.35** would lead to vinyl cation **2.38**, which could then form the bridged intermediate **2.39** (Table 2.4b). A minor equilibration to the less stable primary vinyl cation **2.40** could also be envisioned.

a C–H insertion reactions of acyclic vinyl cations



Entry	Substrate	Solvent	Temp. (°C)	Product	Yield (A, B) (%)
1	 **2.33** 2.5:1 *E:Z*	C_6H_{12}	30	 **2.34**	85
2	 **2.35**	C_6H_{12}	30	 +  **2.34** **2.36**	40, 39
3	 **2.37** 1:1.8 *E:Z*	C_6H_{12}	70	 +  **2.34** **2.36**	16, 19
4	 **2.35**	$CHCl_3/C_6H_{12}$	–40	 +  **2.34** **2.36**	17, 34

b Possible bridged nature of vinyl cation intermediate leading to observed product distributions



2.38 **2.39** **2.40**

Table 2.4 C–H insertion reactions of acyclic vinyl cations (a) and mechnastic insights (b)

Although we could not verify this computationally, direct insertion of this bridged species into cyclohexane is in agreement with the experimental observations made over the course of these studies.[40–42]

2.7 Reductive Friedel-Crafts Reactions of Vinyl Cations

Having established that vinyl triflates are competent vinyl cation precursors under silylium catalysis conditions and that these reactive intermediates undergo efficient *sp*^{3} C–H functionalization reactions, we sought to investigate their reactivity with arenes. It has been reported that cyclic vinyl cations are poor electrophiles in Friedel-Crafts arylation reactions.[43] We posited that the use of silylium/carborane salts would allow for mild ionization of cyclic vinyl triflates in nonpolar solvents, allowing for facile Friedel–Crafts arylation reactions. We were pleased to find that with 4 equivalents of benzene in pentane solvent, cyclohexenyl triflate (**2.23**) underwent smooth reductive arylation to yield phenylcyclohexane (**2.41**) in 79% yield in 2 hours at room temperature (Figure 2.4). While we posit that triflate abstraction is rate-limiting, we hypothesize that the product-determining step is the C–C bond forming event, with the barrier for attack by the arene π-system falling nearly 20 kcal/mol below the barrier for C–H insertion.[44] In addition to benzene, electron-poor haloarenes such as difluorobenzene and dichlorobenzene underwent smooth, C–C bond formation to yield cyclohexylated haloarenes **2.42**–**2.45** in synthetically useful yields. Likewise, electron-rich arenes, such as mesitylene were competent nucleophiles giving mesityl cyclohexane (**2.46**) in 61% yield. Cyclohexenyl triflates bearing substituents at the *4*- or *5*-positions could also be arylated (**2.47**–**2.49**), including the enol triflate derived from *5*α-cholestan-*3*-one, which yielded an arylated steroid core **2.50** in 90% yield and 8:1 *d.r.*. Various ring sizes were also competent under these reaction conditions, with cyclopentenyl triflate and cycloheptenyl triflate undergoing smooth reductive alkylation with benzene reaction partners in 64% and 71% yield, respectively (**2.51** and **2.52**). Cyclobutenyl triflate participated in this reductive

Friedel-Crafts alkylation (**2.53**), as did aromatic alkenes. The triflate derived from α-tetralone was reductively arylated in 43% yield (**2.54**), and acetophenone-derived acyclic triflates were also arylated in 51 to 77% yield (**2.55** and **2.56**). Simple acyclic vinyl triflates were competent electrophiles for arylation by both electron-poor and electron-

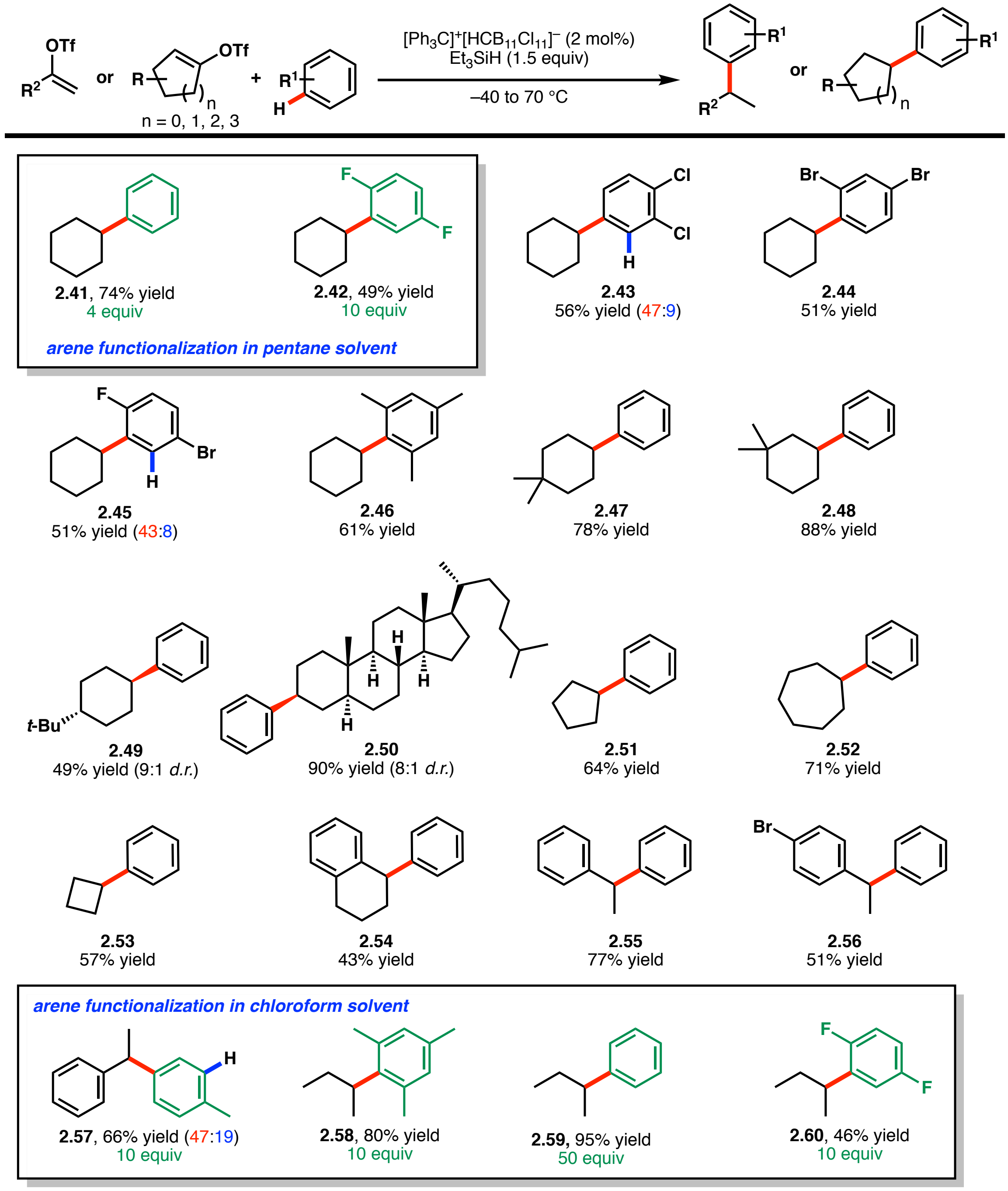


Figure 2.4 Reductive Friedel-Crafts reactions of vinyl cations

rich arenes, requiring as little as 10 equivalents of arene in chloroform solvent at –40 °C (**2.57–2.60**).

2.8 Conclusion

In conclusion we have successfully disclosed the generation and C–C bond forming reactions of aryl and vinyl cations that were formed from suitable aryl fluoride and vinyl triflate precursors, respectively, by ionization from silylium-carborane salts. The electrophilicity of the silylium as well as the kinetic persistence imparted by the WCA were paramount to the success of these reactions. These reactions were all conducted in non-polar media enabling new modes of reactivity that have remained largely elusive until now. These fundamental findings have laid the groundwork for further discoveries in this field by our own group as well as others.

2.9 Experimental Section

2.9.1 Materials and Methods

Unless otherwise stated, all reactions were performed in an MBraun glovebox under nitrogen atmosphere with < 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and allowed to cool *in vacuo* before use. All liquid substrates were either dried over CaH_2 or filtered through dry neutral aluminum oxide. Solid substrates were dried over P_2O_5. All solvents were rigorously dried before use. Benzene, *o*-dichlorobenzene, and toluene were degassed and dried in a JC Meyer solvent system and stored inside a glovebox. Cyclohexane (Sigma-Aldrich), fluorobenzene (Sigma-Aldrich), and *n*-hexane (Oakwood) were distilled over potassium. Chlorobenzene (Fisher Scientific), cycloheptane (Alfa Aesar) and *o*-difluorobenzene (Oakwood) were distilled over sodium. Cyclopentane (Matheson Cole and Bell) was filtered through dry neutral aluminum oxide. Pentane (Sigma-Aldrich) was distilled over sodium-potassium alloy. Hexafluorobenzene (Oakwood) was dried over CaH_2 and stored in a glovebox. All solvents were stored over 4 Å molecular sieves. Chloroform was dried over CaH_2 and stored in a glovebox. Triethylsilane (Oakwood) and triisopropylsilane (AK Scientific) were dried over CaH_2 and stored inside a glovebox over 4 Å molecular sieves. *Closo*-carborane anions, including $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$, were prepared according to literature procedure.[16] Butylcyclohexane and *n*-pentylcyclohexane were purchased from Alfa Aesar. $AgNO_3$-Impregnated silica gel was prepared by mixing with a solution of $AgNO_3$ (150% v/w of 10% w/v solution in acetonitrile), removing solvent under reduced pressure, and drying at 120 °C. Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230–400 mesh) was used for flash chromatography. NMR spectra were recorded on a Bruker AV-300 (^{1}H, ^{19}F), Bruker AV-400 (^{1}H, ^{13}C, ^{19}F), Bruker DRX-500 (^{1}H), and Bruker AV-500 (^{1}H, ^{13}C). ^{1}H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) and CD_2Cl_2 (5.32 ppm). Data for ^{1}H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted otherwise. GC spectra were recorded on an Agilent 6850 series GC using an Agilent HP-1 (50 m, 0.32 mm ID, 0.25 mm DF) column. GCMS spectra were recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 mm DF) column. IR Spectra were recorded on a Perkin Elmer 100 spectrometer and are reported in terms of absorption frequency (cm^{-1}). High resolution mass spectra (HR-MS) were recorded on a Waters (Micromass) GCT Premier spectrometer and are reported as follows: m/z (% relative intensity). Purification by preparative HPLC was done on an Agilent 1200 series instrument with a reverse phase Alltima C_{18} (5μ, 25 cm length, 1 cm internal diameter) column.

2.9.2 Experimental Procedures for Aryl Cations

Synthesis of substrates for ***Table 2.1*** *and* ***Figure 2.2*** *are reported in the adapted article.*

2.9.3 Aryl Insertion Reactions

2.9.3.1 Optimization Table for Aryl Insertion Reaction

In our studies, we optimized our reaction conditions for anion, silane, concentration, and temperature using **2.7** in benzene.

Anion	% Cat. Loading	Conc.	Silane	Temperature	Yield
$[HCB_{11}H_5Cl_6]$	5 mol%	0.1 M	iPr_3SiH (10 mol%)	70 °C	41%
$[HCB_{11}H_5Br_6]$	5 mol%	0.1 M	Et_3SiH (10 mol%)	70 °C	0%
$[HCB_{11}Me_5Br_6]$	5 mol%	0.1 M	Et_3SiH (10 mol%)	70 °C	0%
$[HCB_{11}Cl_{11}]$	1 mol%	0.02 M	Et_3SiH (2 mol%)	30 °C	55%
$[HCB_{11}Cl_{11}]$	2 mol%	0.1 M	Et_3SiH (4 mol%)	30 °C	49%
$[HCB_{11}Br_{11}]$	5 mol%	0.1 M	Et_3SiH (10 mol%)	30 °C	31%
$[(C_6F_5)_4B]$	5 mol%	0. 1M	Et_3SiH (10 mol%)	30 °C	27%

Table 2.5 Optimization of (2-fluorophenyl)trimethylsilane substrate in benzene.

2.9.3.2 Initial Investigation of Aryl Fluorides

Outlined below are our initial experiments evaluating the reactivity of aryl fluorides in both the presence and absence of the trimethylsilyl group (Figure 2.2a). Our experiments below support the need for an *ortho*-trimethylsilyl group for our catalytic system.

2.9.3.2.1 Fluorobenzene Control

Described below is the application of fluorobenzene using our optimized conditions.

$[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 1.1 μmol, 0.02 equiv) and triethylsilane (0.5 μL, 2.2 μmol, 0.04 equiv) were stirred in benzene (3 mL) to form a colorless solution (0.02 M) before the addition of fluorobenzene (9.5 μL, 0.054 mmol, 1 equiv). Reaction was stirred at 30 °C. After 5 days, GC-FID showed formation of biphenyl. Addition of nonane (9.7 μL, 0.054 mmol, 1 equiv) as an internal standard showed < 5% yield of biphenyl (Fig. 2.6).

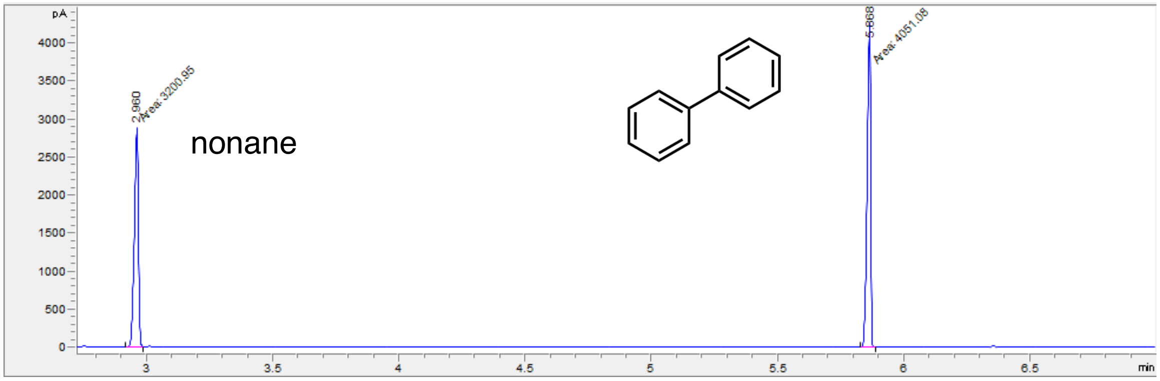


Figure 2.5 GC trace for internal standard nonane and biphenyl in 1:1 ratio.

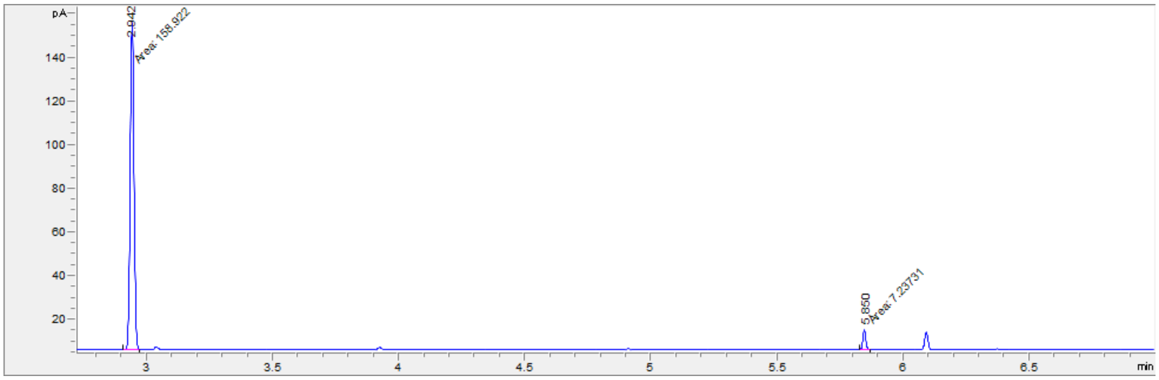


Figure 2.6 GC trace for internal standard nonane in fluorobenzene control reaction.

2.9.3.2.2 Positional Effects of the Silyl Group

Outlined below are a series of experiments probing the reactivity of our substrate in varying the position of the trimethylsilyl group relative to the aryl C–F carbon. The experiments below support the need for a trimethylsilyl group *ortho* to the aryl C–F carbon to generate the desired product in catalytic fashion.

$[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.5 mg, 3.3 μmol) and triethylsilane (1 μL, 6.6 μmol,) were stirred in benzene (1.5 mL) to form a colorless solution. This solution was partitioned equally into three separate vials before aryl fluorides **2.7**, **2.12**, and **2.13** (0.054 mmol) were added in their respective reactions. Reactions were then stirred at 30 °C for 2 hours before addition of nonane (9.7 μL, 0.054 mmol, 1 equiv) as an internal standard. As shown below, no formation of biphenyl was observed when using *meta*- or *para*-trimethylsilyl aryl fluorides (Figs. 2.9 and 2.10). The *ortho*-trimethylsilyl aryl fluoride was the only positional isomer that afforded biphenyl in 47% yield (Fig. 2.11).

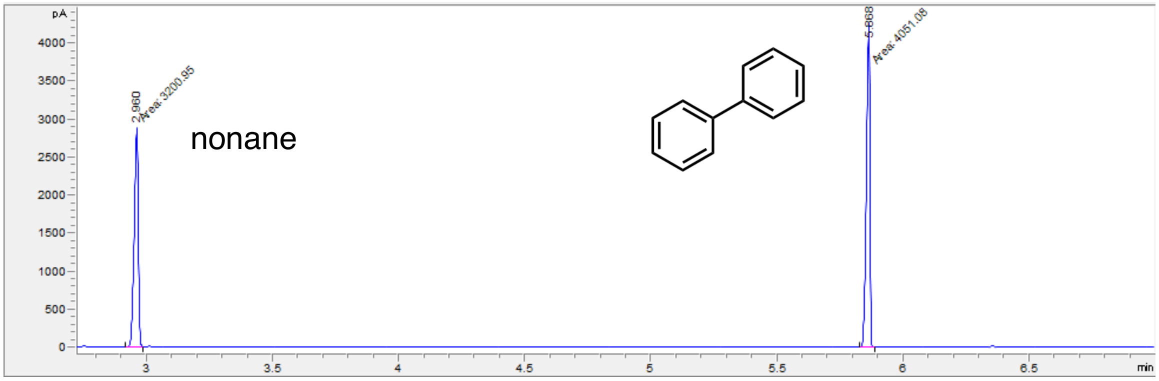


Figure 2.7 GC trace for internal standard nonane and biphenyl in 1:1 ratio.

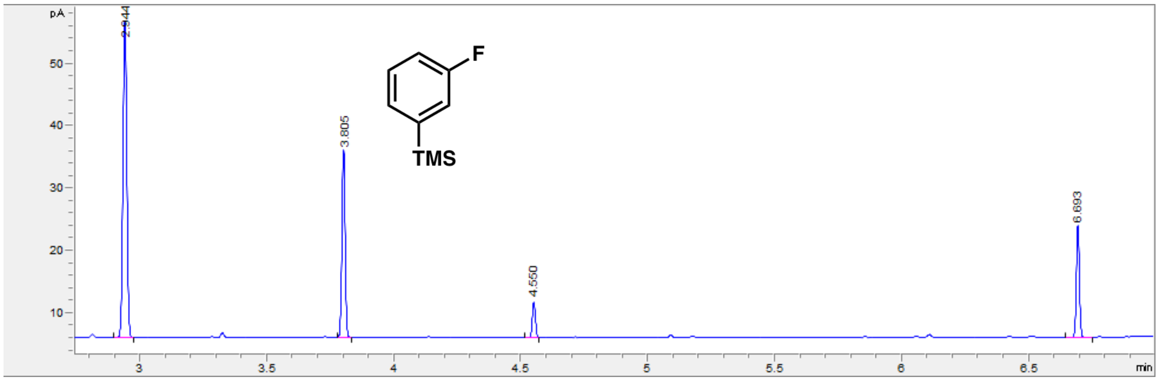


Figure 2.8 GC trace for internal standard nonane and **2.12** after 2 hour reaction time.

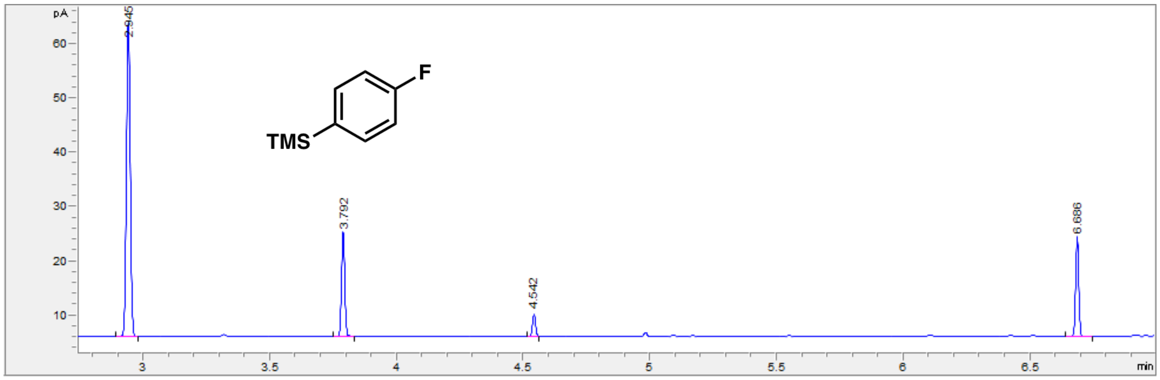


Figure 2.9 GC trace for internal standard nonane and **2.13** after 2 hour reaction time.

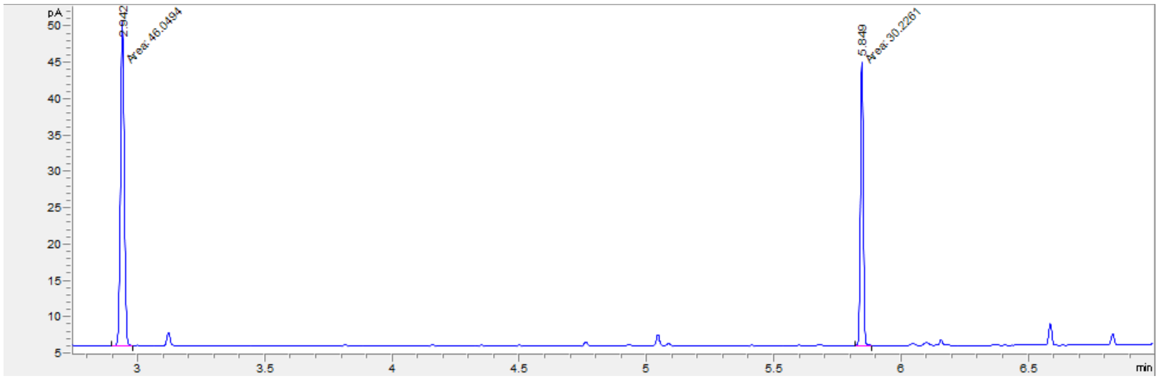
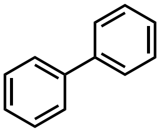


Figure 2.10 GC trace for internal standard nonane and **2.7** after 2 hour reaction time showing formation of biphenyl in 47% yield.

2.9.3.3 General Procedure for Intermolecular Aryl Insertion Reactions

$[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 1.1 μmol, 0.02 equiv) and triethylsilane (0.5 μL, 2.2 μmol, 0.04 equiv) were stirred in benzene (0.5 mL) to form a colorless solution (0.1 M) before the addition of aryl fluoride substrate (0.054 mmol, 1 equiv). Substrates were stirred between 30–70 °C for 0.2–9 hours (see individual substrates for reaction conditions). Reactions were monitored by GC-FID spectra. If previously heated, reactions were cooled to room temperature before volatiles were rotary evaporated and purified by flash column or preparatory thin layer chromatography.



Biphenyl (2.14). Synthesized according to general procedure 2.9.3.3 with a modified 1 mol% catalyst loading and 0.02 M concentration. Catalyst loading was achieved by taking 0.55 mL from a freshly prepared stock solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.5 mg) and triethylsilane (0.5 µL) in benzene (2 mL). Additional benzene was added to reach a total volume of 3 mL before aryl fluoride **2.7** (9.1 mg, 0.054 mmol, 1 equiv) was added to the colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.54 µmol, 0.01 equiv) and triethylsilane (1.1 µmol, 0.02 equiv) in benzene. Reaction was stirred at 30 °C for 1 hour to afford **2.14** in 55% yield (GC) as shown in Fig. 2.12.

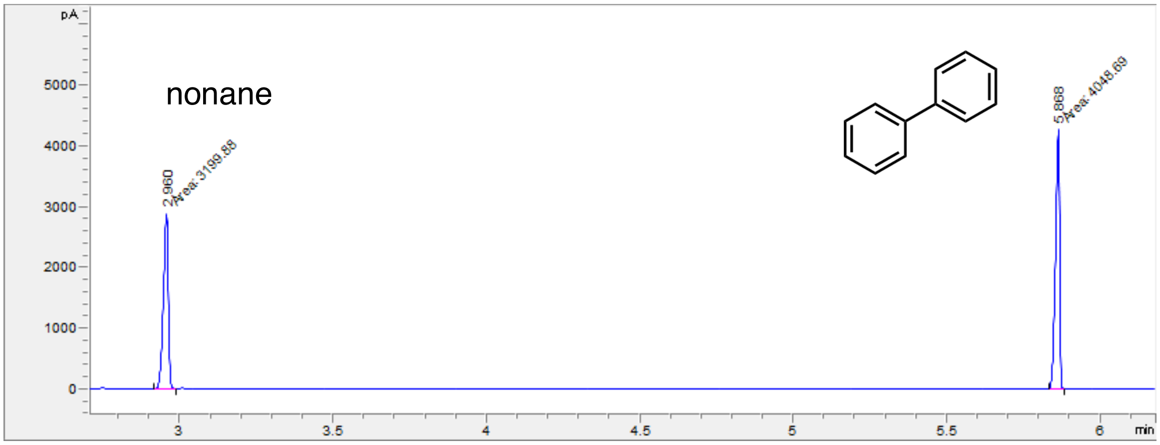


Figure 2.11 GC trace for internal standard nonane and **2.14** in 1:1 ratio.

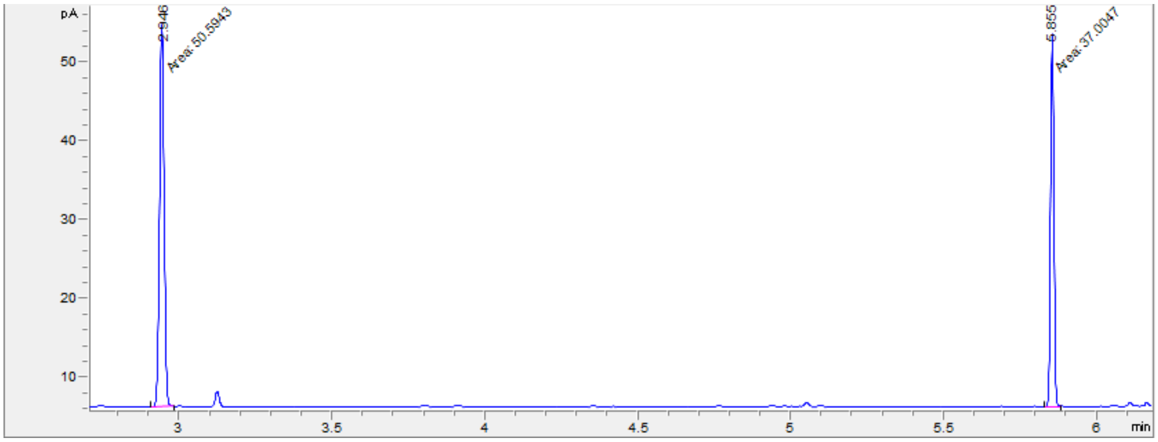


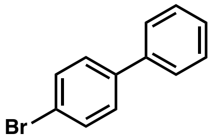
Figure 2.12 GC trace for yield shown for **2.14**.

2.9.3.4 Scope of Fluorotrimethylsilyl Arene Electrophiles

Described below is the characterization and procedure for the scope described in Table 2.1.

General Procedure

$[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 1.1 μmol, 0.02 equiv) and triethylsilane (0.5 μL, 2.2 μmol, 0.04 equiv) were stirred in benzene (0.5 mL) to form a colorless solution (0.1 M) before the addition of aryl fluoride substrate (0.054 mmol, 1 equiv). Substrates were stirred between 30–70 °C for 0.2–9 hours (see individual substrates for reaction conditions). Reactions were monitored by GC-FID spectra. If previously heated, reactions were cooled to room temperature before volatiles were rotary evaporated and purified by flash column or preparatory thin layer chromatography.



4-bromobiphenyl (2.61). 2.61 was synthesized according to general procedure described in 2.9.3.4. The corresponding aryl fluoride (13.4 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 µmol, 0.02 equiv) and triethylsilane (2.2 µmol, 0.04 equiv), and was stirred at 60 °C for 1 hour to give **2.61** in 56% yield (GC) as shown in Figure 2.14. Crude product was purified by flash column chromatography (hexanes) to give **2.61** as a white solid (5.8 mg, 46% yield). NMR Spectra match those reported in literature.[45]

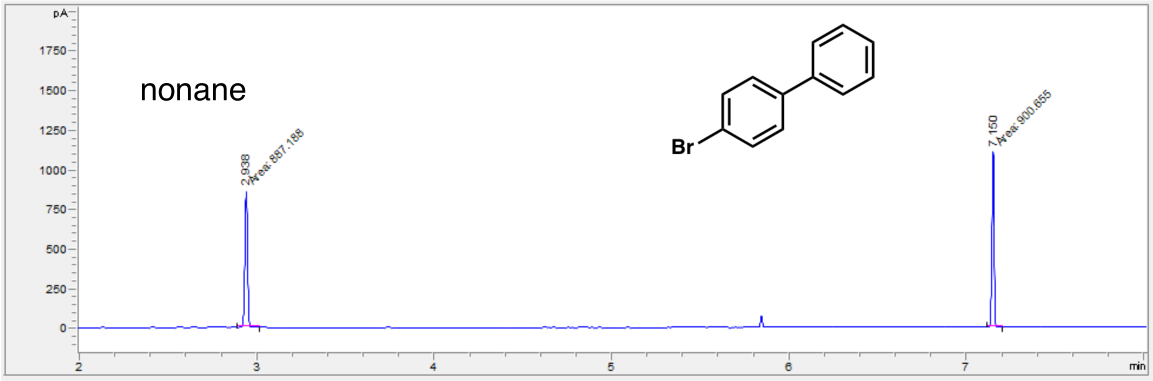


Figure 2.13 GC trace for internal standard nonane and **2.61** in 1:1 ratio.

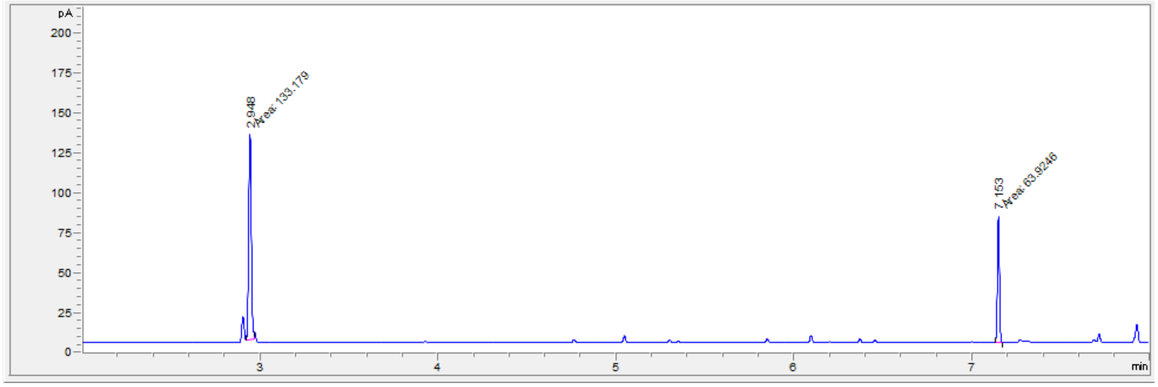
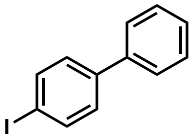
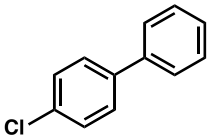


Figure 2.14 GC trace showing formation of **2.61** in 56% yield.



4-iodobiphenyl (2.62). 2.62 was synthesized according to general procedure described in 2.9.3.4. The corresponding aryl fluoride (15.9 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 μmol, 0.02 equiv) and triethylsilane (2.2 μmol, 0.04 equiv) and was stirred at 70 °C for 1 hour to give **2.62** in 71% yield (NMR). Crude product was purified by preparatory thin layer chromatography (hexanes) to give **2.62** as a white solid (7.8 mg, 52% yield). NMR Spectra match those reported in literature.[46]



4-chlorobiphenyl (2.63). 2.63 was synthesized according to general procedure described in 2.9.3.4. The corresponding aryl fluoride (11.0 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 μmol, 0.02 equiv) and triethylsilane (2.2 μmol, 0.04 equiv), and was stirred at 70 °C for 9 hours to give **2.63** in 47% yield (GC) as shown in Figure 2.16. Crude product was purified by column chromatography (hexanes) to give **2.63** as a white solid (4.1 mg, 40% yield). NMR Spectra match those reported in literature.[47]

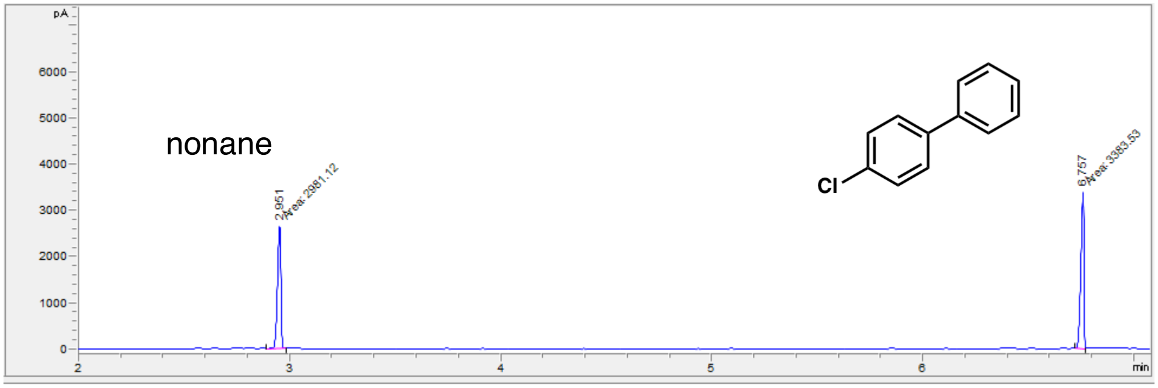


Figure 2.15 GC trace for internal standard nonane and **2.63** in 1:1 ratio.

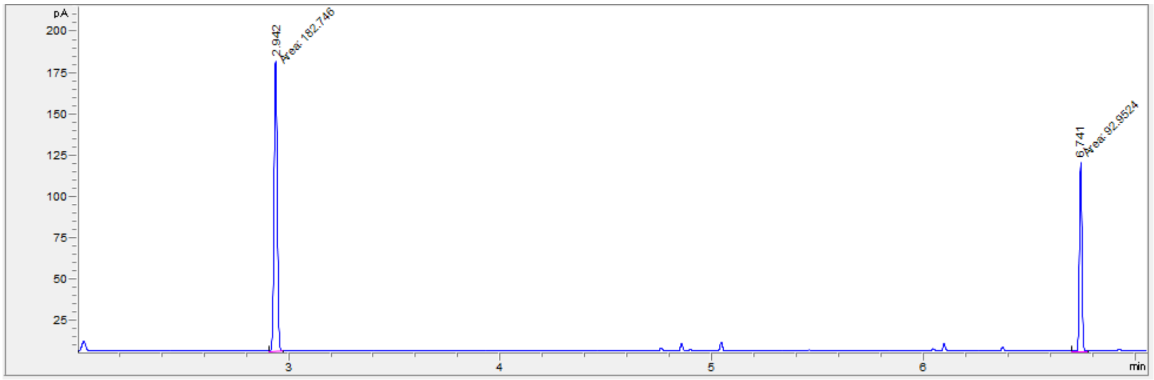
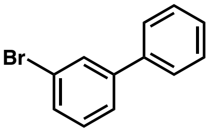


Figure 2.16 GC trace showing formation of **2.63** in 47% yield.



3-bromobiphenyl (2.64). 3-bromobiphenyl was synthesized from two different substrates according to general procedure 2.9.3.4.

For Entry 4, the corresponding aryl fluoride (13.4 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 μmol, 0.02 equiv) and triethylsilane (2.2 μmol, 0.04 equiv), and was stirred at 60 °C for 1 hour to give **2.64** in 52% yield (GC) as shown in Figure 2.18.

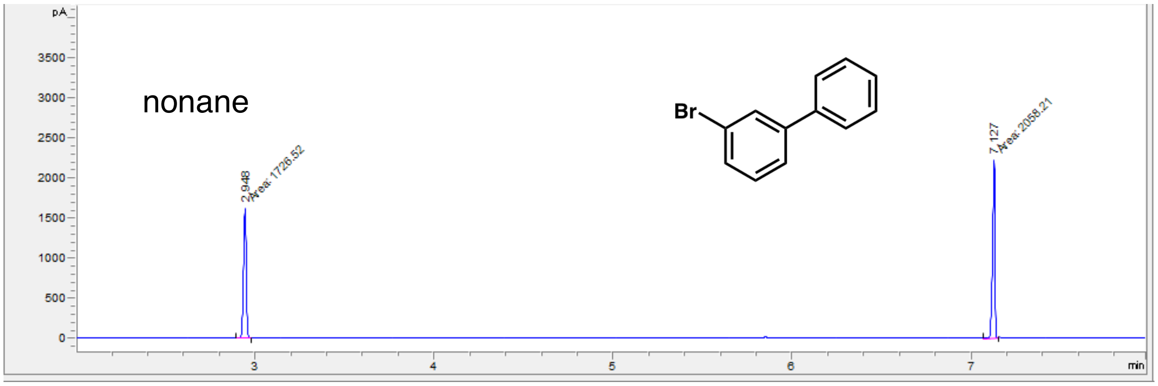


Figure 2.17 GC trace for internal standard nonane and **2.64** in 1:1 ratio.

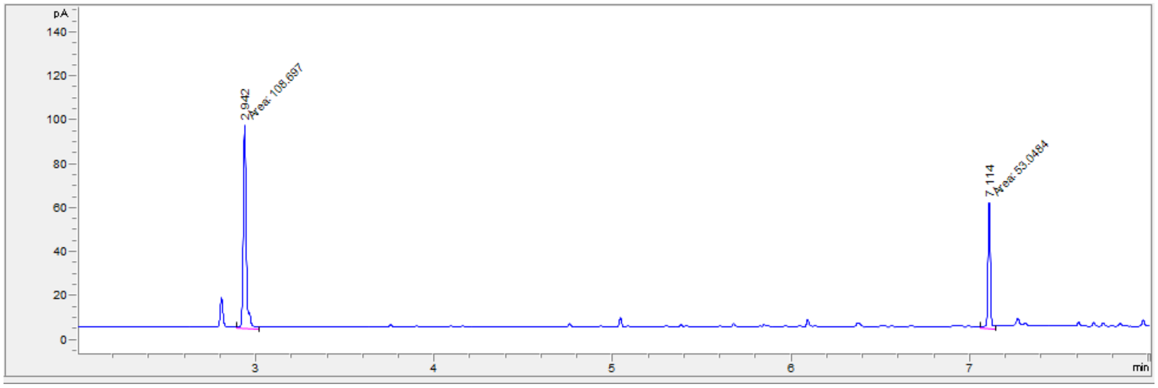


Figure 2.18 GC trace showing formation of **2.64** in 52% yield.

Similarly, the corresponding aryl fluoride (13.4 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 µmol, 0.02 equiv) and triethylsilane (2.2 µmol, 0.04 equiv) and was stirred at 60 °C for 1 hour to give **2.64** in 77% yield (GC) as shown in Figure 2.19. Crude product was purified by preparatory thin layer chromatography (hexanes) to give **2.64** as a white solid (7.4 mg, 59% yield). NMR Spectra match those reported in literature.[48]

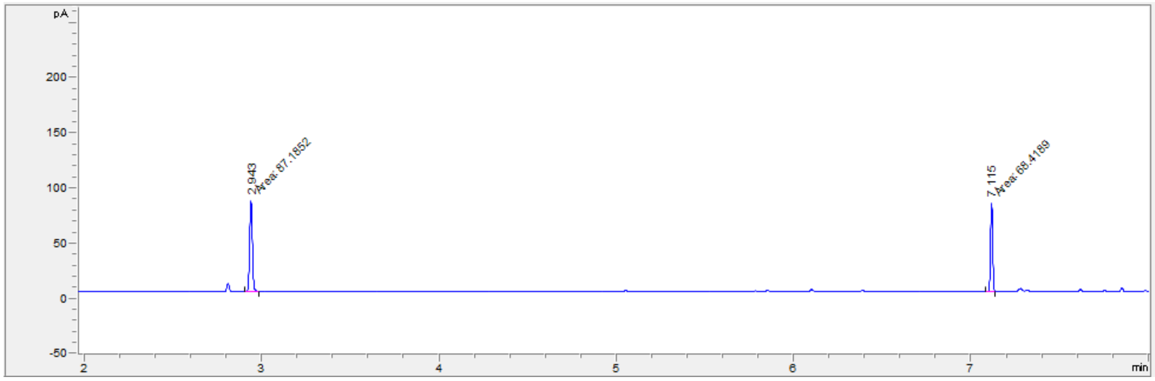
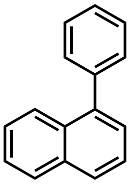
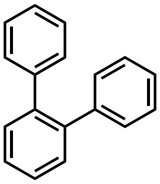


Figure 2.19 GC trace showing formation of **2.64** in 77% yield.



1-phenylnaphthalene (2.65). 2.65 was synthesized according to general procedure described in 2.9.3.4. The corresponding aryl fluoride (11.8 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 µmol, 0.02 equiv) and triethylsilane (2.2 µmol, 0.04 equiv), and was stirred at 30 °C for 1 hour. Crude product was purified by preparatory thin layer chromatography (hexanes) to give **2.65** as a colorless oil (5.4 mg, 49% yield). NMR Spectra match those reported in literature.[49]



***o*-terphenyl (2.66). 2.66** (Table 2.1 entry 7) was synthesized according to general procedure 2.9.3.4. The corresponding aryl fluoride (13.2 mg, 0.054 mmol, 1 equiv) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 µmol, 0.02 equiv) and triethylsilane (2.2 µmol, 0.04 equiv), and was stirred at 70 °C for 36 hours to give **2.66** in

45% yield (GC) as shown in Figure 2.21. Crude product was purified by flash column chromatography (hexanes) to give **2.66** as a white solid (4.4 mg, 35% yield). NMR Spectra match those reported in literature.[50] The reaction for entry 10 was performed analogously from corresponding aryl fluoride to give **2.66** in a 36% GC yield.

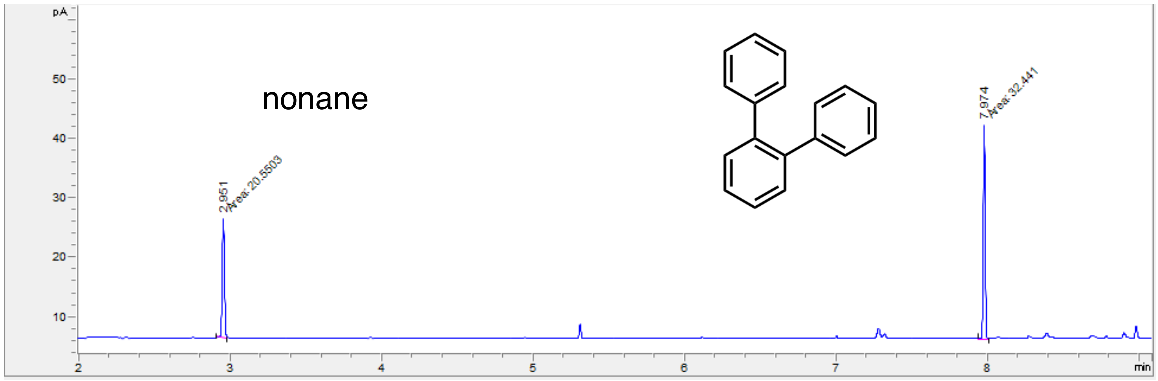


Figure 2.20 GC trace for internal standard nonane and **2.66** in 1:1 ratio.

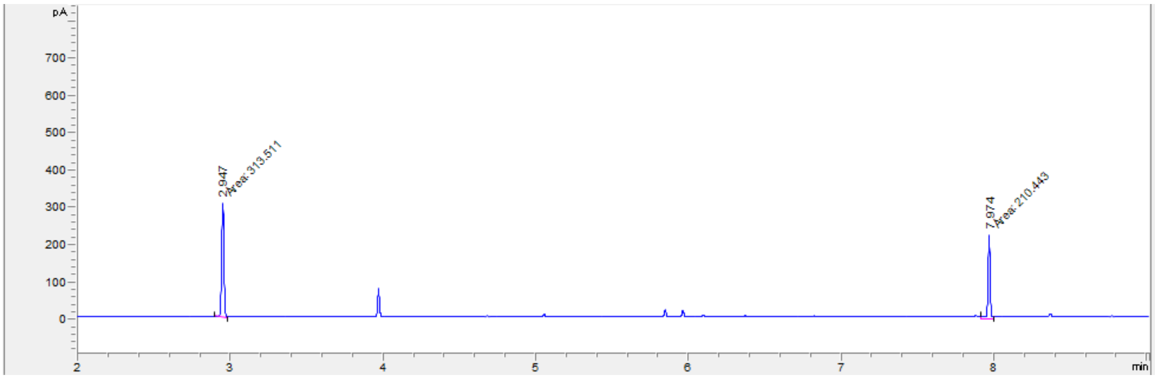
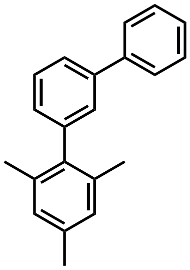


Figure 2.21 GC trace showing formation of **2.66** in 45% yield.

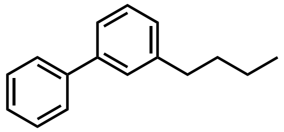


3-mesitylbiphenyl (2.67). 2.67 was synthesized according to general procedure described in 2.9.3.4. The corresponding aryl fluoride (15.5 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 μmol, 0.02 equiv) and triethylsilane (2.2 μmol, 0.04 equiv), and was stirred at 30 °C for 1 hour. Crude product was purified by flash column chromatography (9:1 pentane:dichloromethane) to give **2.67** as a colorless oil (6.9 mg, 47% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.62 (m, 2H), 7.59 (ddd, *J* = 7.8, 1.9, 1.2 Hz, 1H), 7.52–7.41 (m, 4H), 7.38–7.31 (m, 1H), 7.14 (dt, *J* = 7.5, 1.5 Hz, 1H), 6.98 (s, 2H), 2.36 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 141.1, 141.0, 138.9, 136.6, 136.0, 128.8, 128.7, 128.2, 128.1, 128.0, 127.3, 127.1, 125.2, 21.0, 20.8.

FTIR (Neat Film NaCl): 3059, 3030, 2952, 2919, 2867, 1946, 1880, 1803, 1730, 1471, 850, 757 cm^{-1}.

HR-MS (GC-CI): Calculated for $C_{21}H_{20}$: 272.1565; measured: 272.1575.

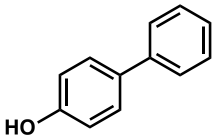


3-butylbiphenyl (2.68). 2.68 was synthesized according to general procedure described in 2.9.3.4. The corresponding aryl fluoride (12.1 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 μmol, 0.02 equiv) and triethylsilane (2.2 μmol, 0.04 equiv), and was stirred at 30 °C for 0.2 hours to give **2.68** in 99% yield (NMR). Crude product was purified by flash column chromatography (hexanes) to give **2.68** as a colorless oil (10.6 mg, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.60 (m, 2H), 7.51–7.41 (m, 4H), 7.38 (td, *J* = 7.4, 5.2 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 1H), 2.72 (t, *J* = 7.7 Hz, 2H), 1.74–1.65 (m, 2H), 1.49–1.38 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 141.5, 141.2, 128.7, 128.6, 127.4, 127.3, 127.2, 127.1, 124.5, 35.8, 33.7, 22.4, 14.0.

FTIR (Neat Film NaCl): 3059, 3029 2956, 2928, 2857, 1889, 1873, 1799, 1600, 1479, 754, 697 cm^{-1}.

HR-MS (GC-CI): Calculated for $C_{16}H_{18}$: 210.1409; measured: 210.1404.



4-hydroxybiphenyl (2.69). 2.69 was synthesized according to general procedure described in 2.9.3.4 with a slight modification. The corresponding aryl fluoride (16.1 mg, 0.054 mmol) was added to a colorless solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.1 μmol, 0.02 equiv) and triethylsilane (2.2 μmol, 0.04 equiv) and was stirred at 60 °C for 48 hours. After cooling to room temperature, the reaction was quenched with a saturated aqueous sodium bicarbonate solution. The aqueous layer was extracted with Et_2O (3 x 1 mL) and combined organic layers were rotary evaporated. Crude product was purified by flash column chromatography (4:1 hexanes:ethyl acetate) to give **2.69** as a white solid (2.3 mg, 29% yield). NMR Spectra match those reported in literature.[51]

2.9.4 Alkane Insertion Reactions

2.9.4.1 Optimization Table for Intermolecular Alkane C–H Insertion

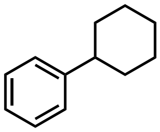
We optimized our reaction conditions for anion, silane, and additive using **2.7** in cyclohexane.

Anion (5 mol%)	Silane (10 mol%)	Additive	Time	Yield
$[HCB_{11}H_5Cl_6]$	iPr_3SiH	o-$C_6H_4Cl_2$ (10 equiv)	120 hr	32%
$[HCB_{11}Cl_{11}]$	Et_3SiH	o-$C_6H_4Cl_2$ (10 equiv)	8 hr	24%
$[HCB_{11}Cl_{11}]$	iPr_3SiH	o-$C_6H_4Cl_2$ (10 equiv)	2 hr	41%
$[HCB_{11}Cl_{11}]$	iPr_3SiH	$Me_2(Mes)_2Si$ (1 equiv)	9 hr	37%
$[HCB_{11}Cl_{11}]$	iPr_3SiH	o-$C_6H_4F_2$ (10 equiv)	2 hr	27%
$[HCB_{11}Cl_{11}]$	iPr_3SiH	none	22 hr	38%
$[(C_6F_5)_4B]$	iPr_3SiH	none	36 hr	18%

Table 2.6. Optimization of (2-fluorophenyl)trimethylsilane substrate in cyclohexane.

2.9.4.2 General Procedure for Intermolecular Alkane C–H Insertion

$[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.0 mg, 2.7 μmol, 0.05 equiv) and triisopropylsilane (1.1 μL, 5.4 μmol, 0.1 equiv) were stirred in *o*-dichlorobenzene (60 μL, 0.54 mmol, 10 equiv) to give a colorless solution. Alkane solvent (1 mL), followed by aryl fluoride **2.7** (0.054 mmol, 1 equiv), were added respectively to give a 0.05 M solution. The reaction was then heated between 60–100 °C for 1–9 hours (see individual substrates for reaction conditions). Reaction was monitored by GC-FID. After cooling to room temperature, the reaction mixture was quenched with saturated aqueous sodium bicarbonate and the organic layers were concentrated *via* rotary evaporation and purified by flash column chromatography (hexanes or pentane).



Phenylcyclohexane (Table 2.2, entry 1, 2.70). Synthesized according to general procedure 2.9.4.2. Aryl fluoride **2.7** (9.1 mg, 0.054 mmol) was added to a solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.0 mg, 2.7 µmol, 0.05 equiv), triisopropylsilane (1.1 µL, 5.4 µmol, 0.1 equiv), *o*-dichlorobenzene (60 µL, 0.54 mmol, 10 equiv), and cyclohexane (1 mL). Reaction was stirred at 60 °C for 2 hours to give **2.70** in 41% yield (GC) as shown in Figure 2.23. Crude product was purified by flash column chromatography (pentane) to give **2.70** as colorless oil. NMR Spectra match those reported in literature.[52]

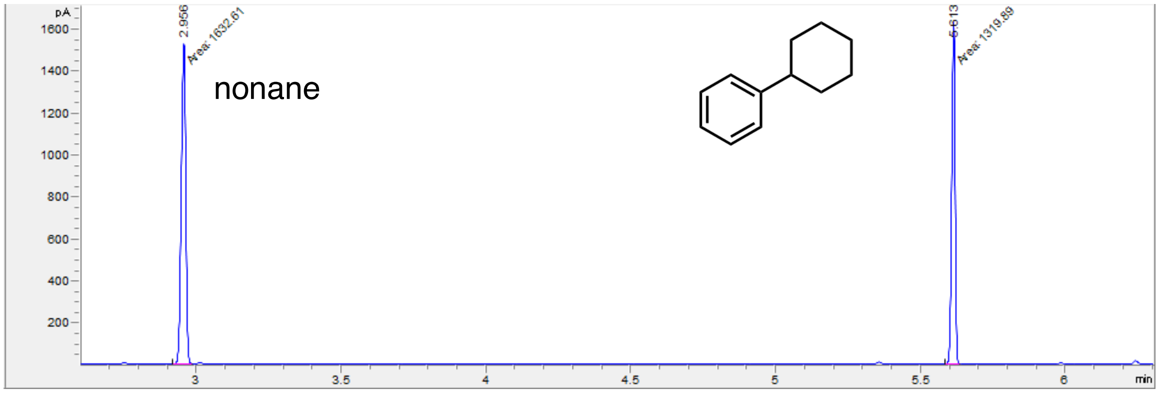


Figure 2.22 GC trace for internal standard nonane and **2.70** in 1:1 ratio.

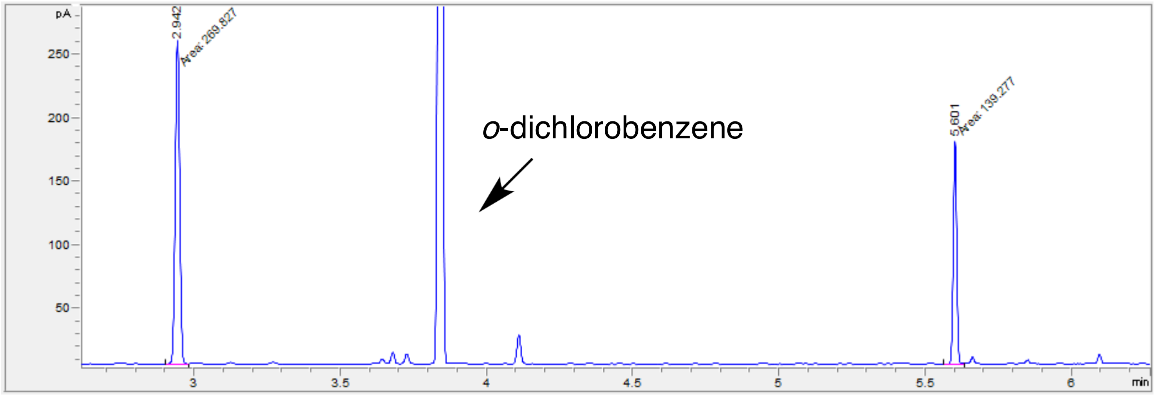
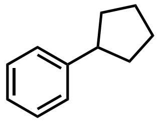
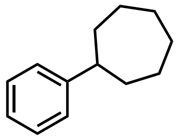


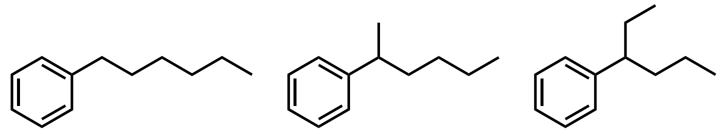
Figure 2.23 GC trace showing formation of **2.70** in 41% yield.



Phenylcyclopentane (Table 2.2, entry 2, 2.71). Synthesized according to general procedure 2.9.4.2. Aryl fluoride **2.7** (0.054 mmol, 9.1 mg) was added to a solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.0 mg, 2.7 µmol, 0.05 equiv), triisopropylsilane (1.1 µL, 5.4 µmol, 0.1 equiv), *o*-dichlorobenzene (60 µL, 0.54 mmol, 10 equiv), and cyclopentane (1 mL). Reaction was stirred at 70 °C for 1 hour to give **2.71** in 54% yield (NMR). Crude product was purified by flash column chromatography (pentane) to give **2.71** as a colorless oil. NMR Spectra match those reported in literature.[53]



Phenylcycloheptane (Table 2.2, entry 3, 2.72). Synthesized according to general procedure 2.9.4.2 excluding *o*-dichlorobenzene. Aryl fluoride **2.7** (0.054 mmol, 9.1 mg) was added to a solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.0 mg, 2.7 µmol, 0.05 equiv), triisopropylsilane (1.1 μL, 5.4 μmol, 0.1 equiv), and cycloheptane (1 mL). Reaction was heated at 100 °C for 9 hours to give **2.72** in 40% yield (NMR). Crude product was purified by flash column chromatography (hexanes) to give **2.72** as a colorless oil (3.4 mg, 36%). NMR Spectra match those reported in literature.[53]



Phenylhexane isomers (Table 2.2, entry 4, 2.73, 2.74 and 2.75). Synthesized according to general procedure 2.9.4.2. Aryl fluoride **2.7** (0.054 mmol, 9.1 mg) was added to a solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.0 mg, 2.7 μmol, 0.05 equiv), triisopropylsilane (1.1 μL, 5.4 μmol, 0.1 equiv), *o*-dichlorobenzene (60 μL, 0.54 mmol, 10 equiv), and *n*-hexane (1 mL). Reaction was heated at 60 °C for 8 hours to give phenylhexane isomers in 40% overall yield (GC) as shown in Figures 2.26, 2.28, and 2.30. Crude product was purified by flash column chromatography (hexanes) to give phenylhexane isomers as colorless oil. The error associated with the 3-phenylhexane **2.75** calibration curve was shown to be greater than the theoretical yield. Yield of 3-phenylhexane was then calculated by using 1-phenylhexane **2.73** and 2-phenylhexane **2.74** as reference, taking into account the integral ratio of 1 for all isomers shown in Figure 2.30. Calculated yields were: 1-phenylhexane **2.73** (26%) shown in Figure 2.26, 2-phenylhexane **2.74** (9%) shown in Figure 2.28, 3-phenylhexane **2.75** (5%) shown in Figure 2.30. NMR Spectra match those reported in literature.[54, 55]

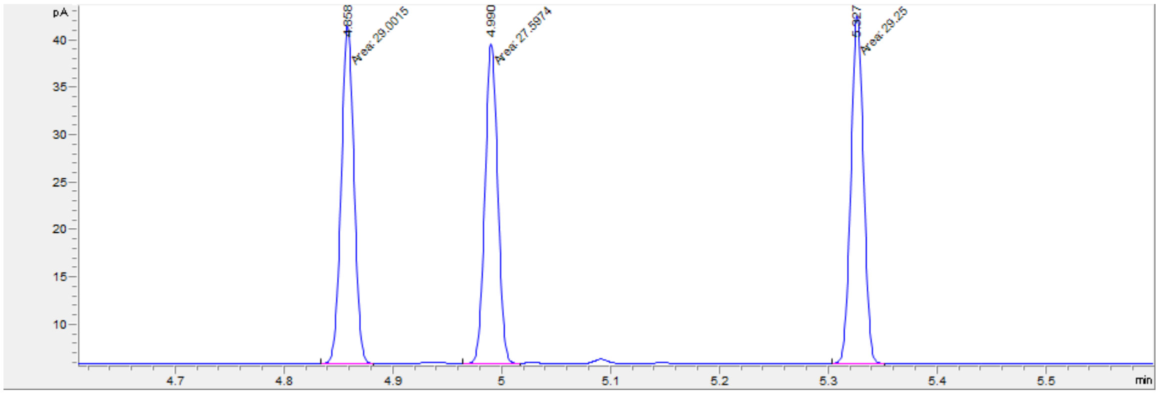


Figure 2.24 GC trace for a 1:1:1 ratio of phenylhexane isomers.

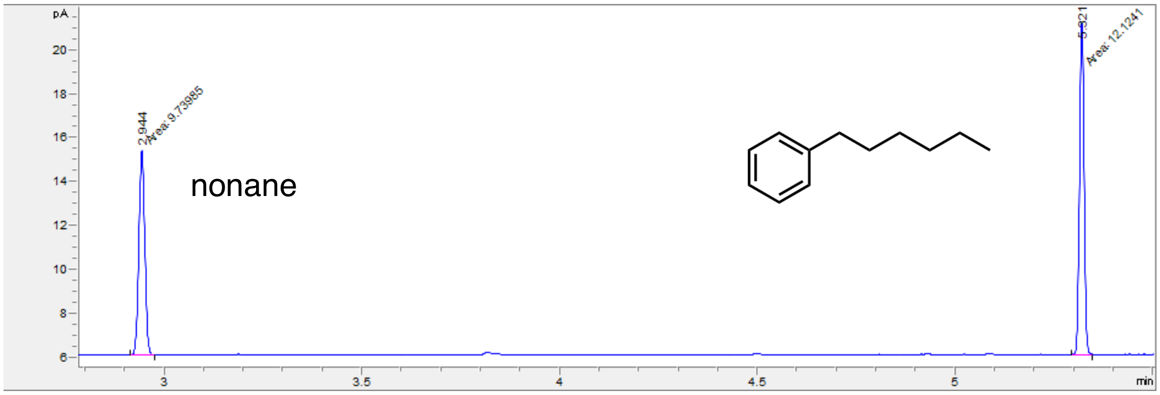


Figure 2.25 GC trace for internal standard nonane and **2.73** in 1:1 ratio.

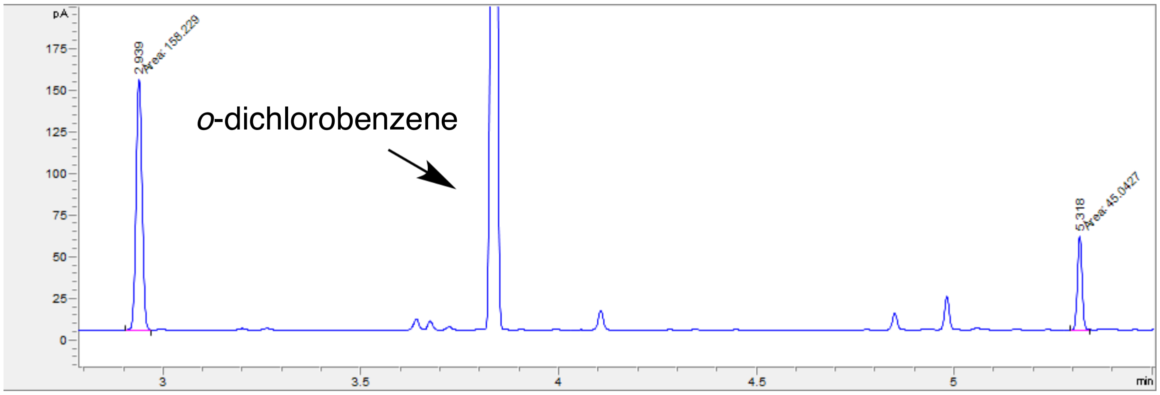


Figure 2.26 GC trace showing the formation of **2.73** from **2.7** in 26% yield.

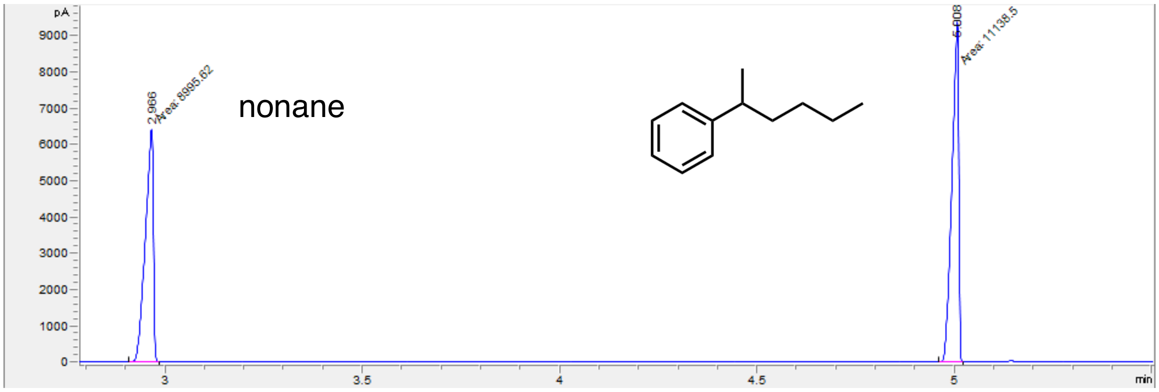


Figure 2.27 GC trace for internal standard nonane and **2.74** in 1:1 ratio.

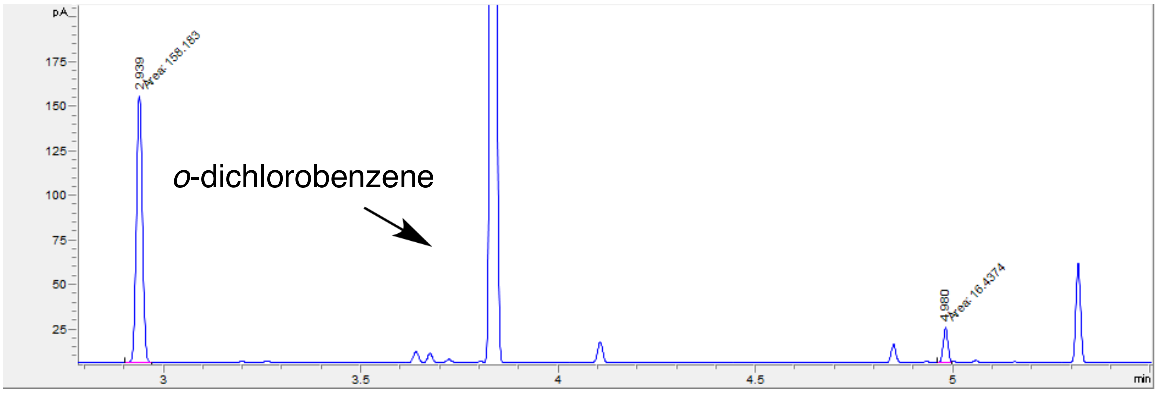


Figure 2.28 GC trace showing the formation of **2.74** from **2.7** in 9% yield.

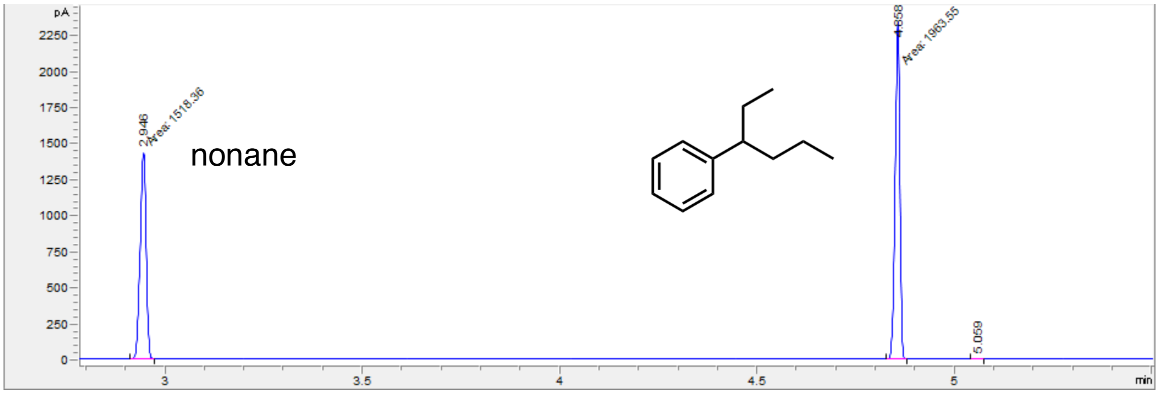


Figure 2.29 GC trace for internal standard nonane and **2.75** in 1:1 ratio.

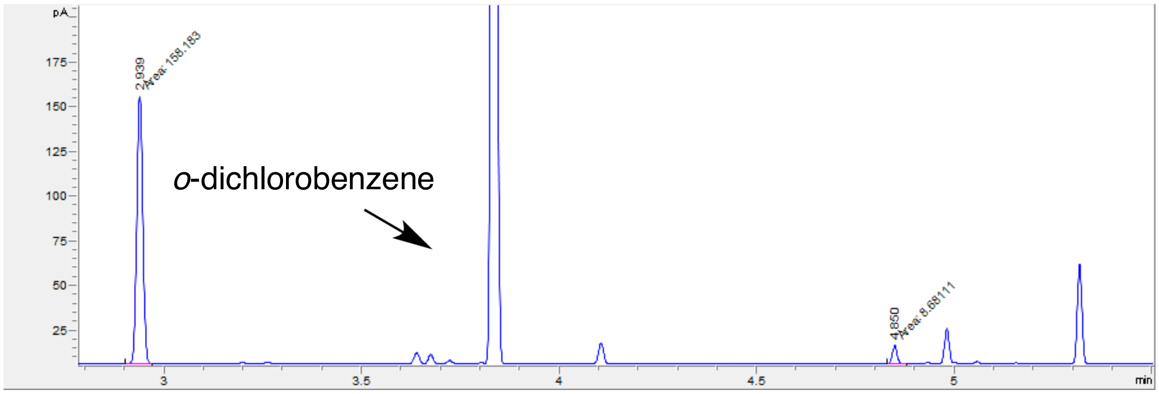
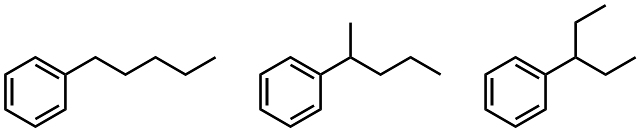


Figure 2.30 GC trace showing formation of **2.75** from **2.7**. The error associated with the 3-phenylhexane calibration curve was shown to be greater than the theoretical yield.



Phenylpentane isomers (Table 2.2, entry 5, 2.76, 2.77, and 2.78). Synthesized according to general procedure 2.9.4.2. Aryl fluoride **2.7** (0.054 mmol, 9.1 mg) was added to a solution of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (2.0 mg, 2.7 μmol, 0.05 equiv), triisopropylsilane (1.1 μL, 5.4 μmol, 0.1 equiv), *o*-dichlorobenzene (60 μL, 0.54 mmol, 10 equiv), and *n*-pentane (1 mL). Reaction was heated at 60 °C for 8 hours to give phenylpentane isomers in 42% overall yield (GC) as shown in Figures 2.33, 2.35, and 2.37. Crude product was purified by flash column chromatography (hexanes) to give phenylpentane isomers as colorless oil. Calculated GC yields were: 1-phenylpentane **2.76** (30%) shown in Figure 2.33, 2-phenylpentane **2.77** (10%) shown in Figure 2.35, 3-phenylpentane **2.78** (2%) shown in Figure 2.37. NMR Spectra match those reported in literature.[56–58]

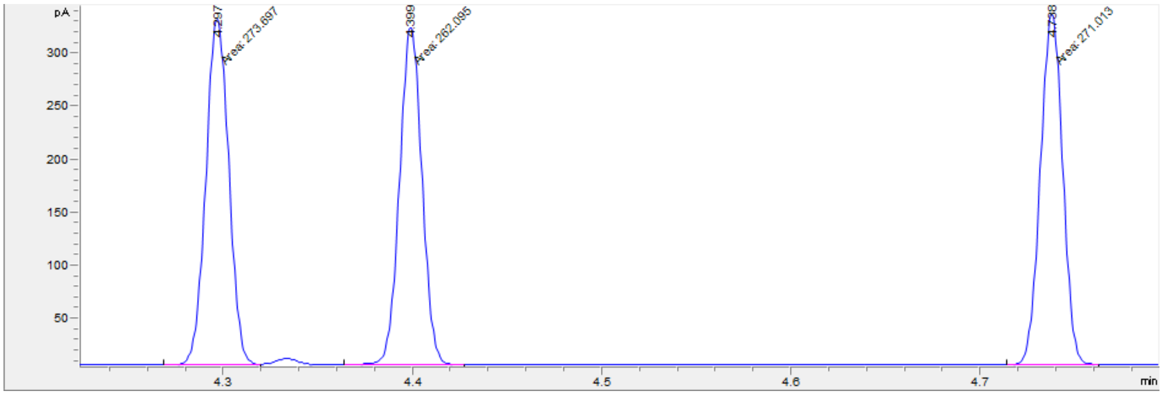


Figure 2.31 GC trace for a 1:1:1 ratio of phenylpentane isomers.

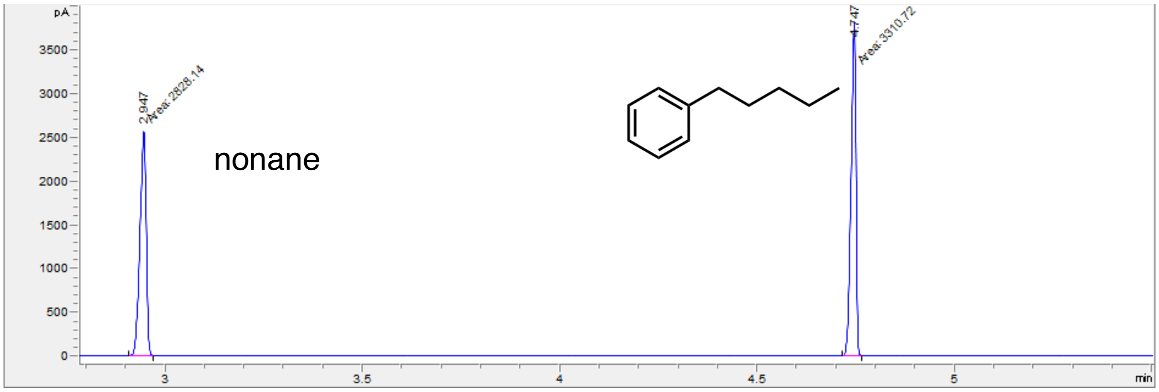


Figure 2.32 GC trace for internal standard nonane and **2.76** in 1:1 ratio.

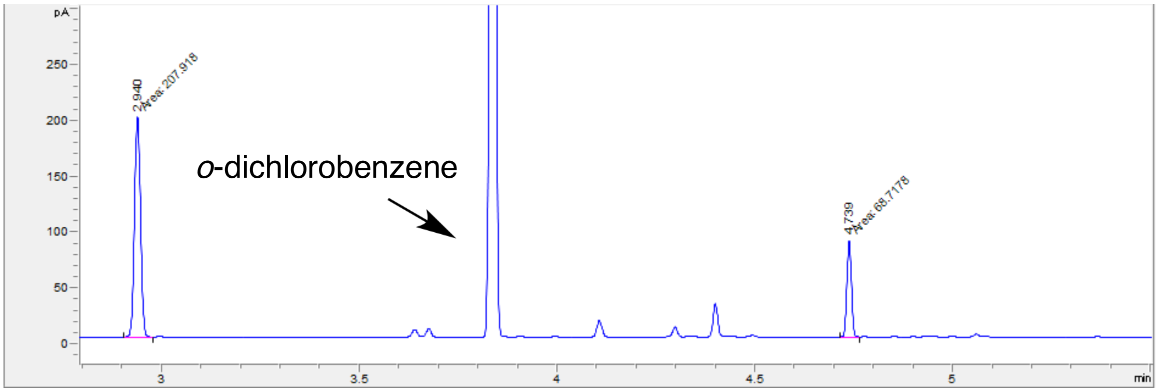


Figure 2.33 GC trace showing formation of **2.76** from **2.7** in 30% yield.

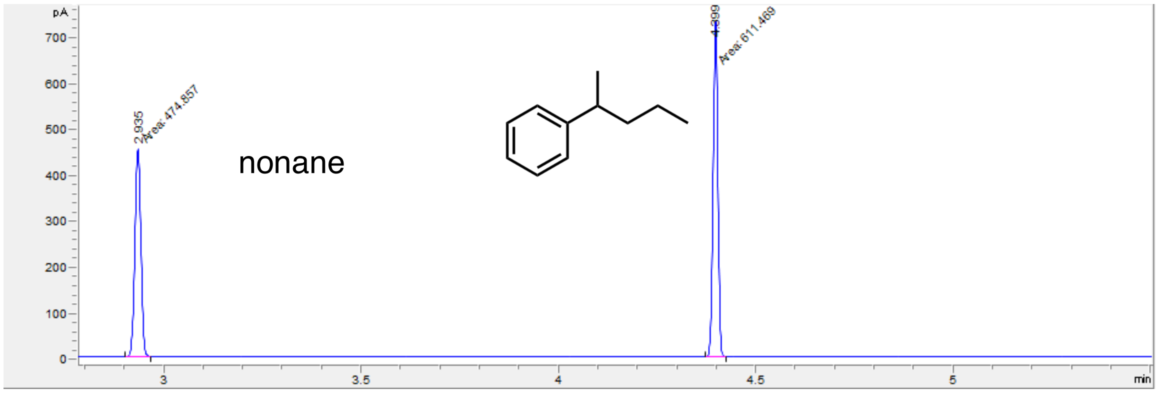


Figure 2.34 GC trace for internal standard nonane and **2.77** in 1:1 ratio.

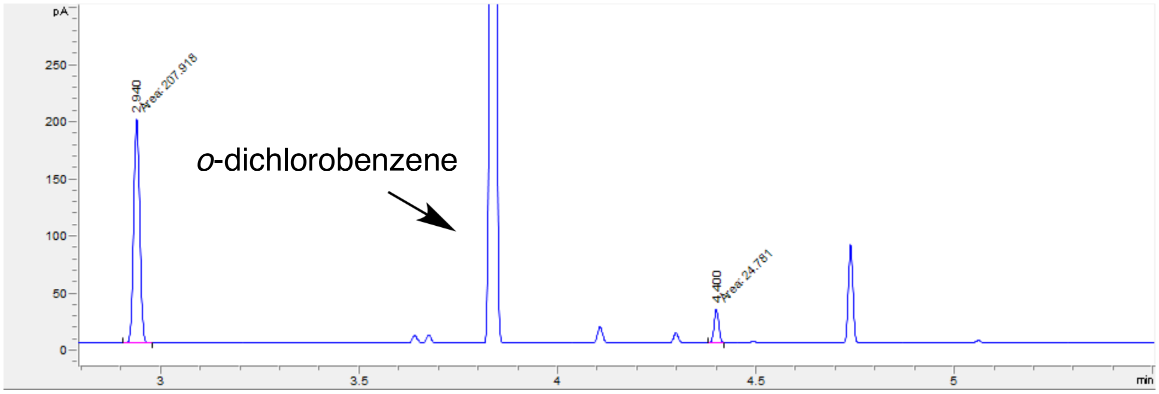


Figure 2.35 GC trace showing formation of **2.77** from **2.7** in 10% yield.

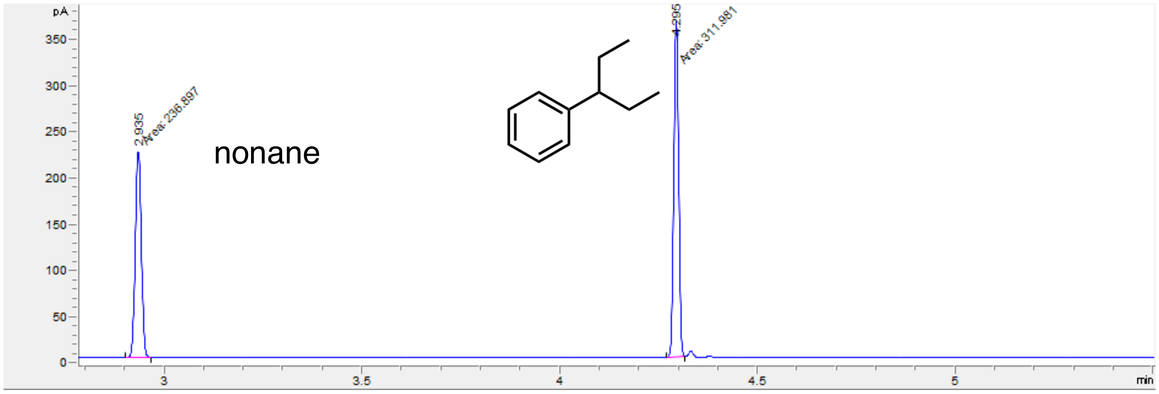


Figure 2.36 GC trace for internal standard nonane and **2.78** in 1:1 ratio.

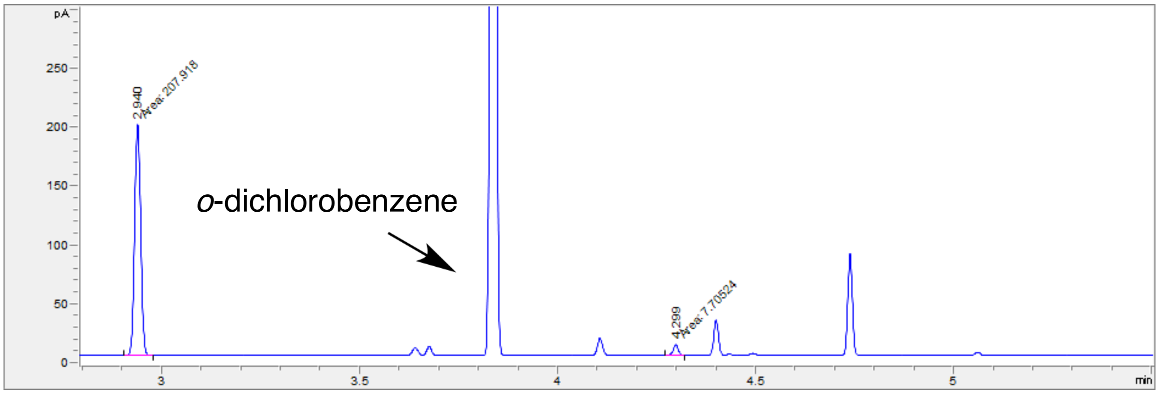
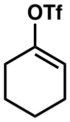


Figure 2.37 GC trace showing formation of **2.78** from **2.7** in 2% yield.

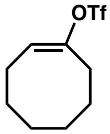
2.9.5 Experimental Procedures for Vinyl Cations

*Synthesis of substrates for **Figure 2.4** are reported in the adapted article.*

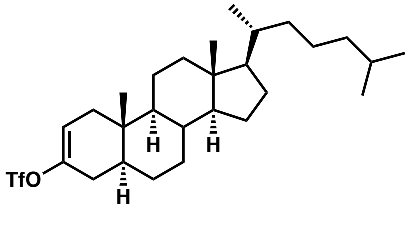
2.9.5.1 Synthesis of Vinyl Triflates



Cyclohex-1-en-1-yl trifluoromethanesulfonate (2.23). In a flame dried 1 L three-neck flask equipped with a dropping funnel, cyclohexanone (25.0 g, 255 mmol, 1.0 equiv) and freshly distilled anhydrous pyridine (22.2 g, 280 mmol, 1.1 equiv) were dissolved in anhydrous methylene chloride (400 mL). The solution was cooled to 0 °C. The dropping funnel was charged with a solution of triflic anhydride (79.0 g, 280 mmol, 1.1 equiv) in methylene chloride (160 mL). The solution was added dropwise to the reaction (~45 minutes). After addition ceased, the ice bath was removed and the reaction stirred for 16 hours. The volatiles were removed under reduced pressure and the crude material was suspended in petroleum ether and filtered. The supernatant was concentrated and the resulting oil was purified by vacuum distillation at 0.2 mmHg to give cyclohexenyl triflate (**2.23**) as colorless oil (25.8 g, 44% yield). NMR data match those reported in literature.[59]

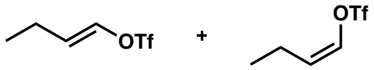


(*E*)-Cyclooct-1-en-1-yl trifluoromethanesulfonate (2.31). In a flame dried 250 mL round bottom flask, cyclooctanone (3.0 g, 23.8 mmol, 1.0 equiv) and freshly distilled 2-chloropyridine (3.0 g, 26.1 mmol, 1.1 equiv) were dissolved in anhydrous methylene chloride (90 mL). The solution was cooled to 0 °C. Triflic anhydride (8.1 g, 28.5 mmol, 1.2 equiv) was added dropwise to the solution. After addition, the ice bath was removed and the reaction stirred for 16 hours. The reaction mixture was quenched with 0.5 M aqueous HCl (200 mL). The phases were separated and the aqueous layer was extracted with methylene chloride (2 x 100 mL). The combined organics were dried over magnesium sulfate, filtered and volatiles removed under reduced pressure to give the crude material as purple oil. The product was purified by vacuum distillation (5 mmHg, 100 °C) to give triflate **(2.31)** as colorless oil (3.2 g, 51% yield). NMR data match those reported in literature.[59]



***S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)-4,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-**

yl trifluoromethanesulfonate (2.29). Synthesized from 5a-cholestan-3-one according to reported literature. NMR data match those reported in literature.[60]



(E/Z)-But-1-en-1-yl trifluoromethanesulfonate (2.37). In a flame dried 500 mL round bottom flask, butyraldehyde (6.0 g, 83.2 mmol, 1.0 equiv) and freshly distilled 2-chloropyridine (10.4 g, 91.5 mmol, 1.1 equiv) were dissolved in anhydrous methylene chloride (300 mL). The solution was cooled to 0 °C. Triflic anhydride (28.2 g, 99.8 mmol, 1.2 equiv) was added dropwise to this solution. After addition, the ice bath was removed and the reaction was stirred at room temperature overnight. The reaction was quenched with 0.5 M HCl. The phases were separated and the combined organic were dried over magnesium sulfate, filtered and volatiles removed under reduced pressure. The resulting oil was purified by vacuum distillation at 20 mmHg while heating at 60 °C to give triflate **2.37** as a brown oil (5.7 g, 30% yield). The distillate was brought into the glovebox and plugged through dry neutral alumina to afford the triflate **2.37** (1.8:1 Z:E mixture) as an off tan oil.

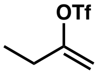
E isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53–6.48 (m, 1H), 5.82 (dt, J = 11.8, 7.2 Hz, 1H), 2.09 (pd, J = 7.2, 1.6 Hz, 2H), 1.06 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, C_6D_6) δ –74.0; ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 124.5, 118.8 (q, $^{1}J_{C\text{–}F}$ = 319 Hz), 20.3, 13.3.

Z isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53–6.48 (m, 1H), 5.27 (dt, J = 7.6, 5.6 Hz, 1H), 2.22 (pd, J = 7.6, 1.6 Hz, 2H), 1.04 (t, J = 7.6 Hz, 3H); ^{19}F NMR (376 MHz, C_6D_6)

δ –74.4; ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.9, 122.6, 118.8 (q, $^1J_{C\text{–}F}$ = 319 Hz), 17.8, 13.3.

FTIR (Neat film NaCl): 2967, 1719, 1428, 1223, 1177, 1025, 766, 636, 578, 514.

HR-MS (GCT-LIFDI): Calculated for $C_5H_7F_3O_3S$: 204.0068; measured: 204.0075.

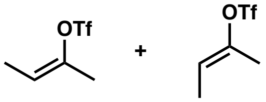


But-1-en-2-yl trifluoromethanesulfonate (2.35). To a 250 mL flame dried schlenk flask was condensed 1-butyne (5.00 g, 92.0 mmol, 1.1 equiv) at –78 °C. This was dissolved in anhydrous hexanes (92.0 mL) and the solution was warmed to –35 °C. Triflic acid (12.5 g, 83.0 mmol, 1.0 equiv) was added dropwise and the solution was allowed to slowly warm up to room temperature. After 2 hours of stirring, the reaction was quenched with saturated aqueous sodium bicarbonate (100 mL). The layers were separated and the organic layer was washed with saturated aqueous sodium bicarbonate (2 x 100 mL), dried over anhydrous potassium carbonate, filtered and volatiles removed under reduced pressure (being careful of product volatility). The crude product was purified by vacuum distillation (25 mmHg, 50 °C) to give triflate **2.35** as a colorless oil (6.3 g, 37% yield).

^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 5.34–5.11 (m, 2H), 2.44 (qt, J = 7.4, 1.0 Hz, 2H), 1.15 (t, J = 7.4 Hz, 3H); ^{19}F NMR (282 MHz, $(CD_3)_2CO$) δ –75.6; ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 158.8, 118.6 (q, $^1J_{C\text{–}F}$ = 318 Hz), 103.4, 26.8, 10.1.

FTIR (Neat film NaCl): 2986, 2950, 1670, 1415, 1249, 1202, 1138, 929, 848, 610, 506, 469.

HR-MS (GCT-LIFDI): Calculated for $C_5H_7F_3O_3S$: 204.0068; measured: 204.0065.



(*E*)-But-2-en-2-yl trifluoromethanesulfonate and **(*Z*)-but-2-en-2-yl trifluoromethanesulfonate (2.33).** In a 100 mL flame dried round bottom flask, triflate **2.35** (4.00 g, 19.6 mmol, 1 equiv) was dissolved in anhydrous methylene chloride (35 mL). Triflic acid (0.15 g, 0.98 mmol, 0.05 equiv) was added and the reaction stirred for 1 hour. The reaction was quenched with 5% aqueous sodium bicarbonate (35 mL). The layers were separated and the aqueous layer was extracted with pentane (3 x 20 mL). The volatiles were distilled off at 80 °C and then the product was purified by vacuum distillation (50 mmHg) to give triflate **2.33** as a 2.5:1 (*E:Z*) mixture of isomers (3.1 g, 78% yield).

Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31 (qd, J = 6.8, 0.8 Hz, 1H), 2.05 (br s, 3H), 1.71 (dq, J = 6.8, 1.6 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –75.0; ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 118.4 (q, $^1J_{C–F}$ = 318 Hz), 116.4, 19.6, 11.1.

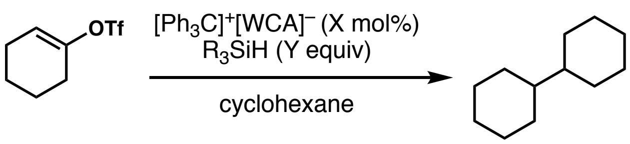
Minor Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (qd, J = 7.2, 0.8 Hz, 1H), 2.03 (br s, 3H), 1.69 (dq, J = 7.2, 1.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –74.2; ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.7, 118.6 (q, $^1J_{C–F}$ = 318 Hz), 116.8, 15.7, 11.9.

FTIR (Neat film NaCl): 2934, 1710, 1412, 1245, 1201, 1135, 936, 876, 728, 632, 468.

HR-MS (GCT-LIFDI): Calculated for $C_5H_7F_3O_3S$: 204.0068; measured: 204.0065.

2.9.5.2 Catalytic C–H Insertion Reactions

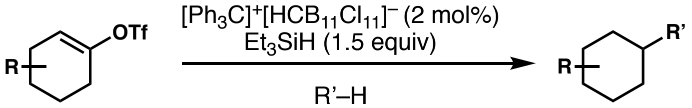
This section outlines the optimization of the reaction shown below. All yields of bicyclohexyl (**2.28**) are GC yields.



2.23 **2.28**

Anion	% Cat. Loading	Conc.	Temp.	Silane	Yield
[$HCB_{11}Cl_{11}$]	2 mol%	0.1 M	30 °C	Et_3SiH (150 mol%)	87%
[$HCB_{11}Cl_{11}$]	2 mol%	0.1 M	30 °C	iPr_3SiH (150 mol%)	68%
[$HCB_{11}Cl_{11}$]	0 mol%	0.1 M	30 °C	Et_3SiH (120 mol%)	0%
[$HCB_{11}Cl_{11}$]	2 mol%	0.1 M	30 °C	none	0%
[$HCB_{11}H_5Cl_6$]	2 mol%	0.1 M	30 °C	Et_3SiH (150 mol%)	50%
[$HCB_{11}Br_{11}$]	2 mol%	0.1 M	30 °C	Et_3SiH (150 mol%)	69%
[$B(C_6F_5)_4$]	2 mol%	0.1 M	30 °C	Et_3SiH (150 mol%)	6%

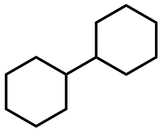
Table 2.7 Optimization of intermolecular alkylation reaction.



Scheme 2.1 General scheme for intermolecular C–H insertion reactions of vinyl triflates.

2.9.5.2.1 General Procedure

In a well-kept glovebox, H_2O, O_2 ≤ 0.5 ppm, a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.02 equiv) and this was suspended in alkane (0.1 M). Triethylsilane (1.5 equiv) along with a magnetic stirring bar were added to the mixture, and the resulting suspension stirred for 10 minutes. At this point, vinyl triflate (1.0 equiv) was added to the reaction and stirred for 0.16–12 hours at 30 °C (see substrates for specific details). Upon completion, the reaction mixture was passed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. Some substrates needed further purification by silica column chromatography (see below).



Bicyclohexyl (Table 2.3, entry 1, 2.28). Synthesized according to general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in cyclohexane (0.5 mL, 4.63 mmol). Triethylsilane (12 mL, 0.075 mmol, 1.5 equiv) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Cyclohexenyl triflate (**2.23**) (11.5 mg, 0.05 mmol, 1.0 equiv) was added to the reaction and stirred for 1.5 hours at 30 °C. Upon completion the reaction was plugged through silica and bicyclohexyl was obtained in 87% GC yield. The crude could be further purified by flash column chromatography (hexanes) to give **2.28** as colorless oil. NMR spectra match those reported in literature.[61]

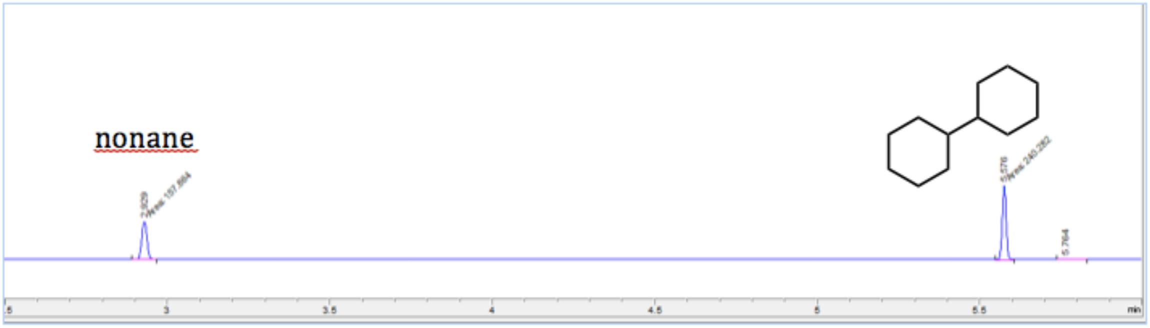


Figure 2.38 GC trace showing one to one mixture of nonane to bicyclohexyl.

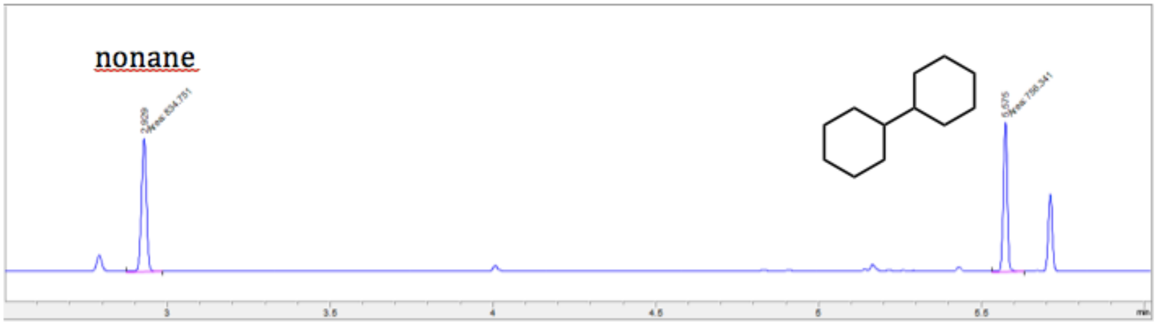
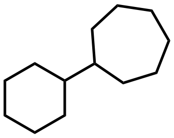


Figure 2.39 GC trace showing 87% yield of bicyclohexyl.



Cyclohexylcycloheptane (Table 2.3, entry 2, 2.79). Synthesized according to general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in cycloheptane (0.5 mL). Triethylsilane (12 mL, 0.075 mmol, 1.5 equiv) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Cyclohexenyl triflate (**2.23**) (11.5 mg, 0.05 mmol, 1 equiv) was added to the reaction and stirred for 2 hours at 30 °C. Upon completion the reaction was plugged through silica and cyclohexylcycloheptane was obtained in 88% GC yield. The crude could be further purified by flash column chromatography (hexanes) to give cyclohexylcycloheptane as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74–1.68 (m, 2H), 1.68–1.52 (m, 9H), 1.50–1.43 (m ,2H), 1.42–1.34 (m, 2H), 1.32–1.07 (m, 7H), 1.06–0.96 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 45.0, 44.9, 31.5, 30.0, 28.6, 27.6, 27.2, 27.1.

FTIR (Neat film NaCl): 2918, 2850, 2670, 1448, 1349, 1263, 972, 893, 844.

HR-MS (GCT-LIFDI): Calculated for $C_{13}H_{24}$: 180.1878; measured: 180.1881.

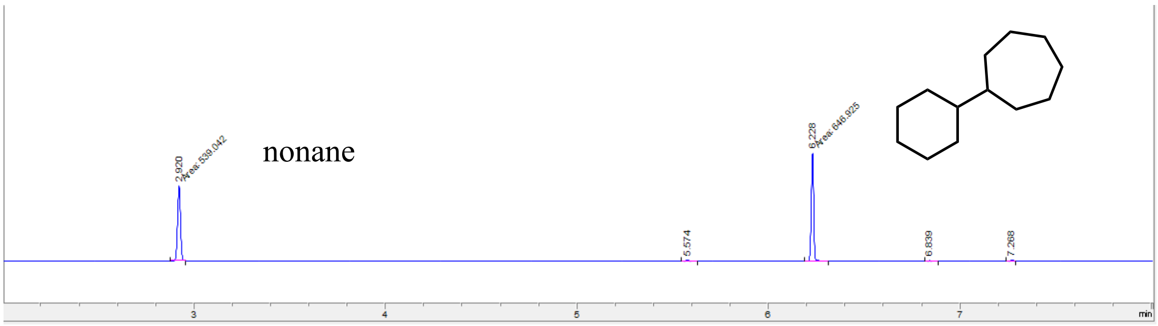


Figure 2.40 GC trace showing one to one mixture of nonane to cyclohexylcycloheptane.

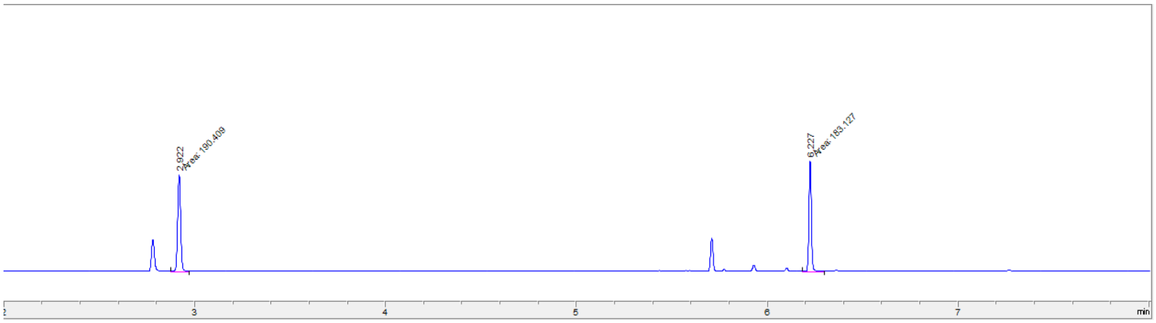


Figure 2.41 GC trace showing 88% yield of cyclohexylcycloheptane.

Pentylcyclohexane (Table 2.3, entry 3). Synthesized according to general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in pentane (0.5 mL). Triethylsilane (12 mL, 0.075 mmol, 1.5 equiv) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Cyclohexenyl triflate (**2.23**) (11.5 mg, 0.05 mmol, 1.0 equiv) was added to the reaction and it stirred for 1.5 hours at 30 °C to give 11% of 3-cyclohexylpentane, 36% of 2-cyclohexylpentane and 21% of 1-cyclohexylpentane (GC). Upon completion the reaction was passed through silica and an inseparable mixture of the three isomers were obtained as colorless oil (4.3 mg, 56%). The NMR data of this mixture matched those of the three authentic samples. For synthesis and characterization of authentic isomers, see SI of adapted paper.

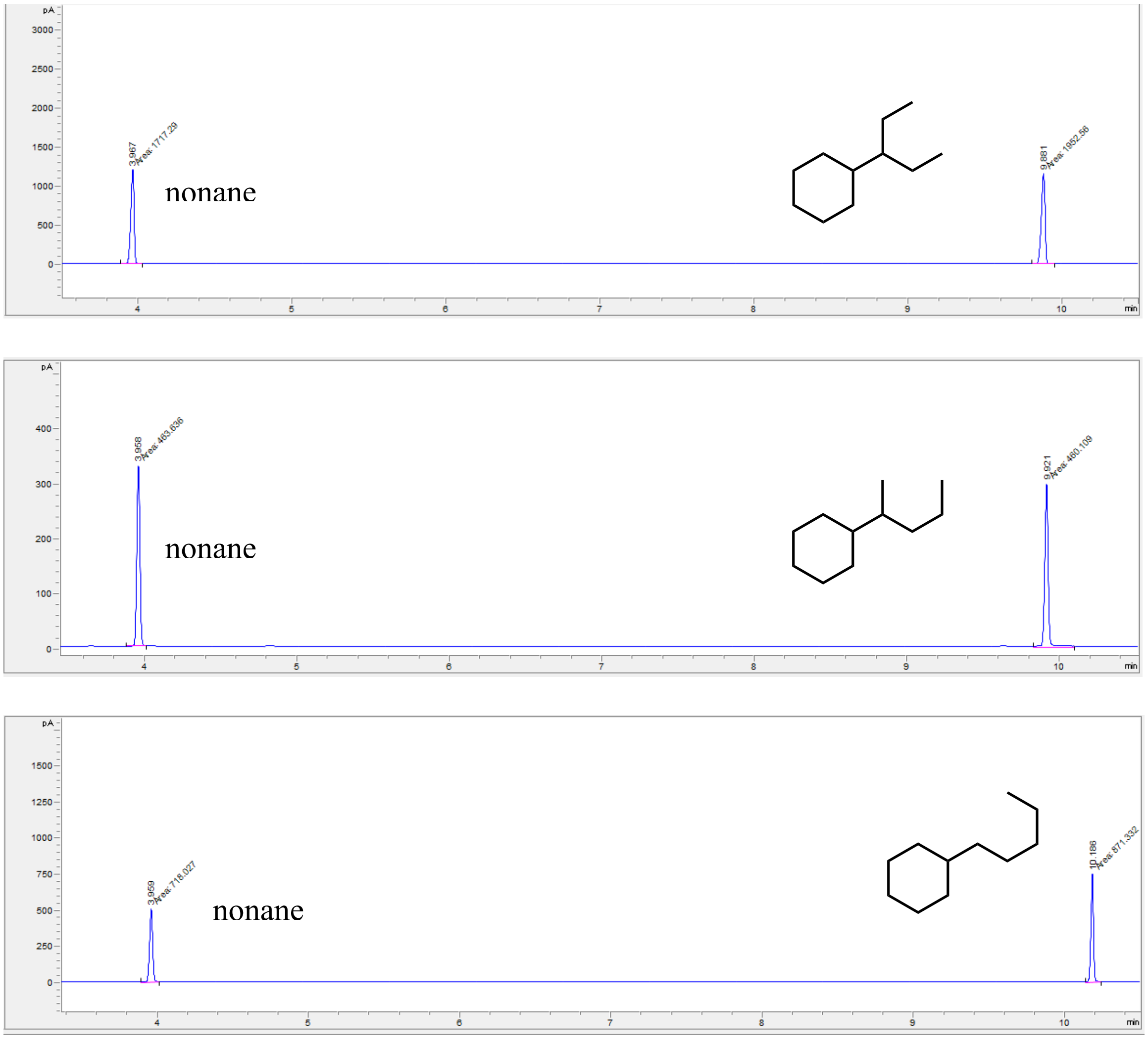


Figure 2.42 GC traces showing one to one mixture of nonane to 3-cyclohexylpentane (top), nonane to 2-cyclohexylpentane (middle), and nonane to 1-cyclohexylpentane (bottom).

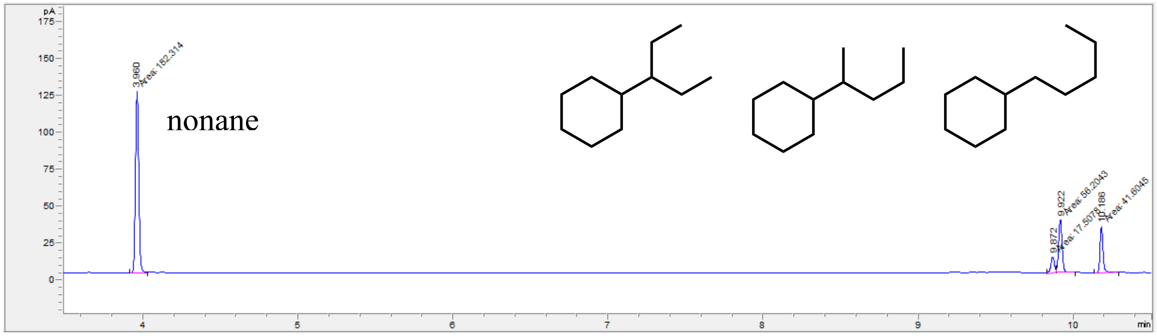
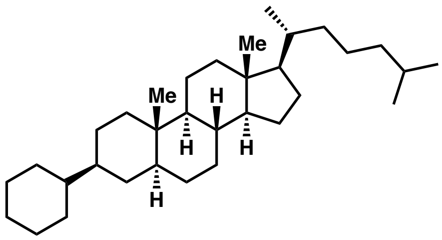


Figure 2.43 GC trace showing 11% of 3-cyclohexylpentane, 36% of 2-cyclohexylpentane and 21% of 1-cyclohexylpentane.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-Cyclohexyl-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene (Table 2.3, entry 4, 2.30). Synthesized according to general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in cyclohexane (0.5 mL, 4.63 mmol). Triethylsilane (12 mL, 0.075 mmol, 1.5 equiv) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Triflate **2.23** (26.0 mg, 0.05 mmol, 1.0 equiv) was added to the reaction and it stirred for 3 hours at 30 °C. Upon completion the reaction was passed through silica and volatiles removed under reduced pressure to give product **2.30** as a white solid (19.5 mg, 88%). GC-FID analysis showed ~15:1 d.r. In order to assign the stereochemistry of the newly formed C–C bond, the material was crystallized by vapor diffusion in the following manner: ~3 mg of the material was dissolved in a minimal amount of cyclohexane in a small crystallization tube. This was placed into a 20 mL vial of acetone and the vial was capped. After 3 days, a crystal suitable for single crystal X-ray diffraction was grown.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.79–0.66 (m, 4H), 0.83 (s, 3H), 0.96 (dd, J = 6.7, 2.3 Hz, 8H), 1.00 (d, J = 6.5 Hz, 3H), 1.37–1.04 (m, 22H), 1.49–1.37 (m, 4H), 1.69–1.56 (m, 3H), 1.85–1.70 (m, 7H), 1.95–1.86 (m, 1H), 2.05 (dt, J = 12.5, 3.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.8, 56.5, 54.9, 47.0, 43.8, 43.6, 42.8, 40.3, 39.7, 39.1, 36.4, 36.2, 36.0, 35.7, 32.6, 32.4, 30.5, 30.4, 29.4, 28.4, 28.2, 27.1, 27.0, 25.8, 24.4, 24.0, 23.0, 22.7, 21.2, 18.8, 12.5, 12.3.

FTIR (Neat film NaCl): 2917, 2848, 1446, 1383, 1172, 930, 890.

HR-MS (GCT-LIFDI): Calculated for $C_{33}H_{58}$: 454.4539; measured: 454.4536.

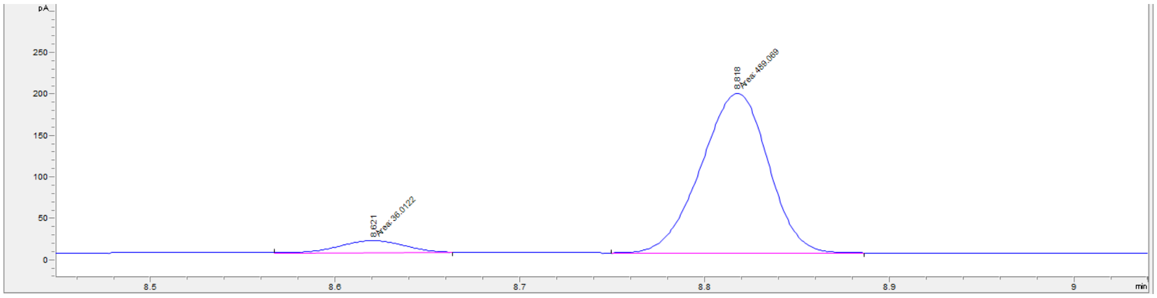


Figure 2.44 GC trace showing ~15:1 d.r. of **2.30**.

(3a,6a)-Octahydropentalene (Table 2.3, entry 5, 2.32). Synthesized according to general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was suspended in cyclohexane (0.5 mL, 4.63 mmol). Triethylsilane (12 mL, 0.075 mmol) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Cyclooctenyl triflate (**2.31)** (18.0 mg, 0.07 mmol, 1.0 equiv) was added to the reaction and it stirred for 1 hour at 30

°C. The reaction was passed through silica in the glovebox and volatiles removed under reduced pressure to give **2.32** as colorless oil (91% GC yield). NOTE: This compound is volatile. NMR spectra match those reported in literature.[62]

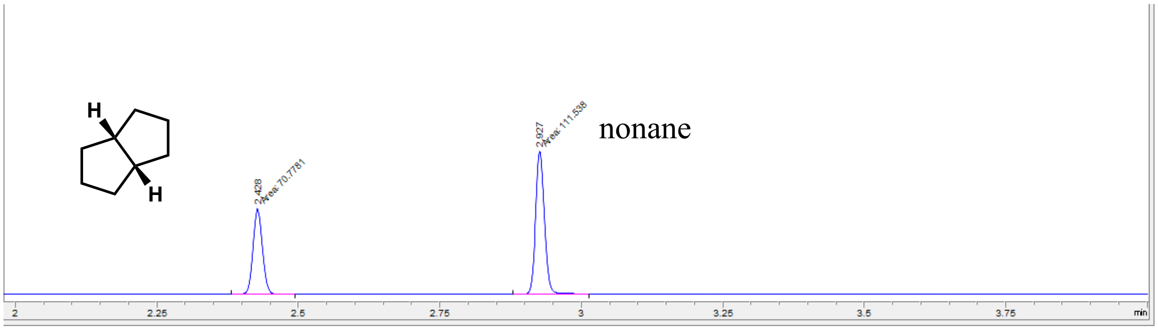


Figure 2.45 GC trace showing one to one mixture of nonane to **2.32**.

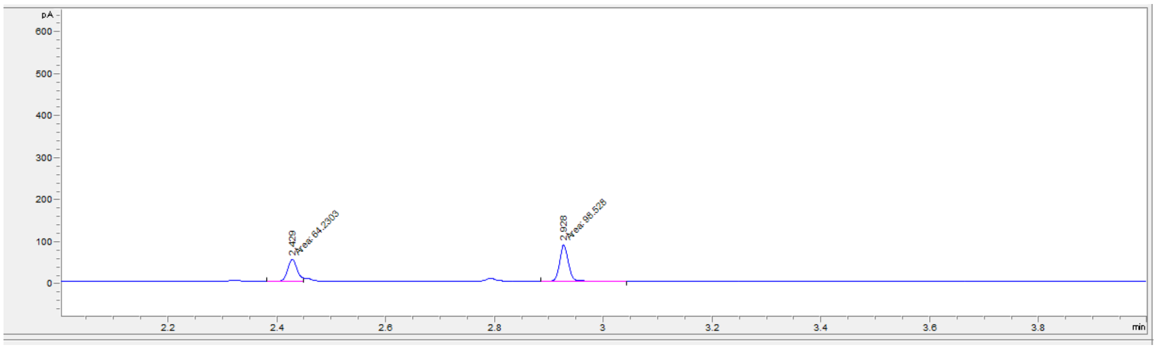
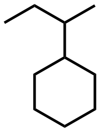


Figure 2.46 GC trace showing 91% yield of (3a, 6a)-octahydropentalene.



***sec*-Butylcyclohexane (Table 2.4, entry 1, 2.34).** Synthesized according to a modified version of general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in cyclohexane (0.5 mL, 5.63 mmol). Triisopropylsilane (15 mL, 0.075 mmol, 1.2 equiv) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Triflate **2.33** (10.2 mg, 0.05 mmol, 1.0 equiv) was added to the reaction and it stirred for 6 hours at 30 °C. Upon completion the reaction was passed through silica inside the glovebox and volatiles removed under reduced pressure. The crude product was further purified by silica column chromatography (hexanes) to give product **2.34** as colorless oil. (85% GC yield). NMR spectra match those reported in literature.[63]

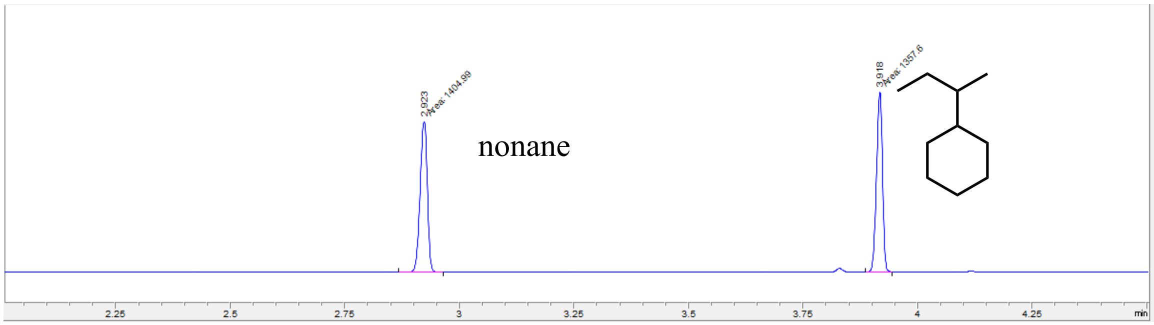


Figure 2.47 GC trace showing one to one mixture of nonane to **2.34**.

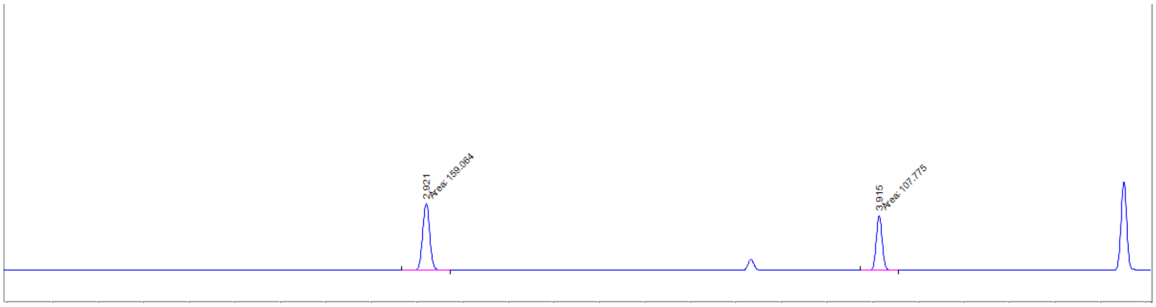
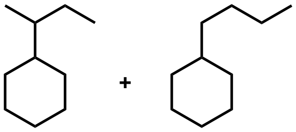


Figure 2.48 GC trace showing 85% yield of **2.34**.



Butylcyclohexane (Table 2.4, entry 2, 2.34 and 2.36). Synthesized according to a modified version of general procedure 2.9.5.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in cyclohexane (9 mL). Triflate **2.35** (10.2 mg, 0.05 mmol, 1.0 equiv) was added to the reaction along with a magnetic stir bar. A solution of triethylsilane (12 ml, 0.075 mmol, 1.5 equiv) in cyclohexane (1 mL) was added portionwise to the reaction mixture over 10 minutes (100 mL every minute). 1 hour after the last addition of silane, the reaction was passed through silica in the glovebox and volatiles removed under reduced pressure to give the ~1:1 mixture of products *s*-butylcyclohexane **2.34** and *n*-butylcyclohexane **2.36** in 40% and 39% GC yields, respectively. The NMR spectra of the mixture matched the isolated NMR of the *s*-butylcyclohexane and the NMR of the commercial *n*-butylcyclohexane.[63]

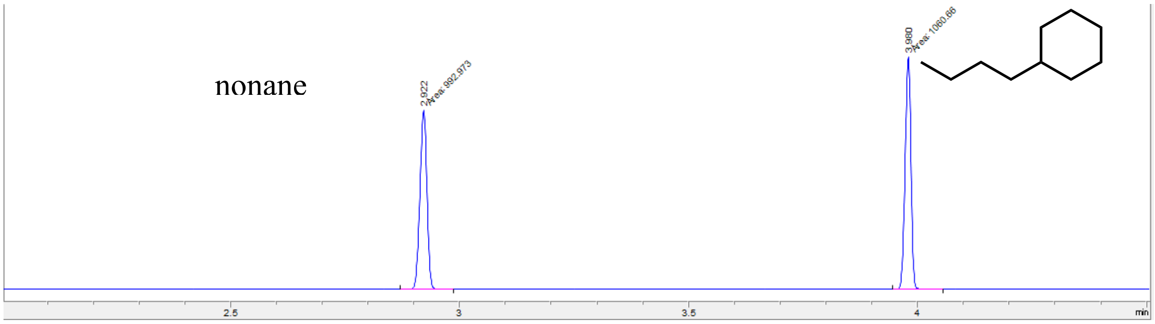


Figure 2.49 GC trace showing one to one mixture of nonane to **2.36**.

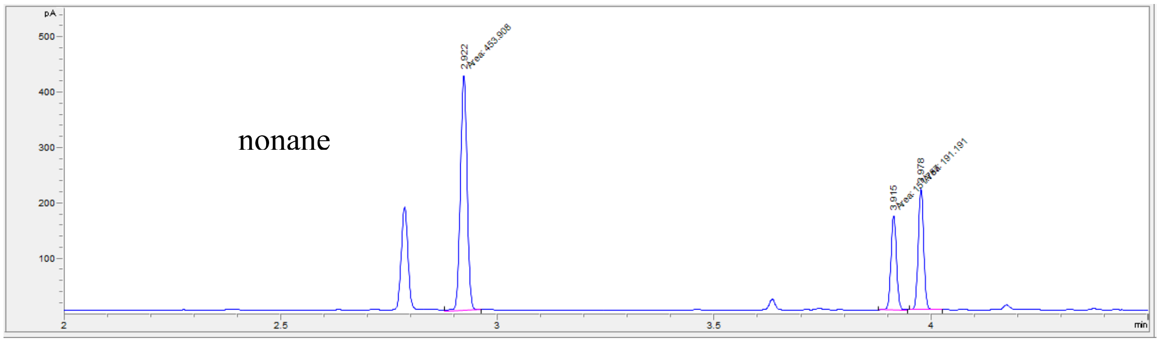


Figure 2.50 GC trace showing 40% yield of **2.34** and 39% yield of **2.36**.

Butylcyclohexane (Table 2.4, entry 3, 2.34 and 2.36). A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv) and this was suspended in cyclohexane (0.5 mL). Triisopropylsilane (11.9 mg, 0.075 mmol, 1.5 equiv) was added the reaction along with a magnetic stir bar. After stirring the reaction for 5 minutes, triflate **2.37** (10.2 mg, 0.05 mmol, 1.0 equiv) was added and the reaction was heated to 70 °C. After 10 days, the reaction was cooled to room temperature and was passed through silica in the glovebox and volatiles removed under reduced pressure to give the ~1:1 mixture of product (16% *s*-butylcyclohexane, 19% *n*-butylcyclohexane GC yield).

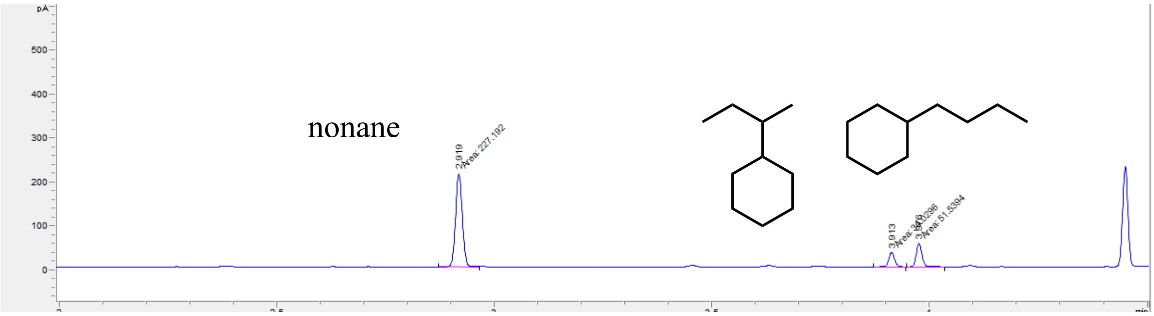
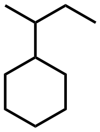
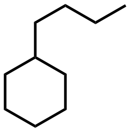


Figure 2.51 GC trace showing 16% yield of **2.34** and 19% yield of **2.36**.





Butylcyclohexane (Table 2.4, entry 4, 2.34 and 2.36). A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.9 mg, 0.0025 mmol, 0.05 equiv) and this was dissolved in chloroform (3 mL) and hexanes (3 mL). Triflate **2.35** (10.2 mg, 0.05 mmol, 1.0 equiv) was added to the solution and it was cooled to –40 °C. Triethylsilane (12 mL, 0.075 mmol, 1.5 equiv) was quickly added and the reaction was stirred at –40 °C for 12 hours to give *n*-butylcyclohexane (**2.36,** 34% GC yield) and *s*-butylcyclohexane (**2.34**, 17% GC yield).

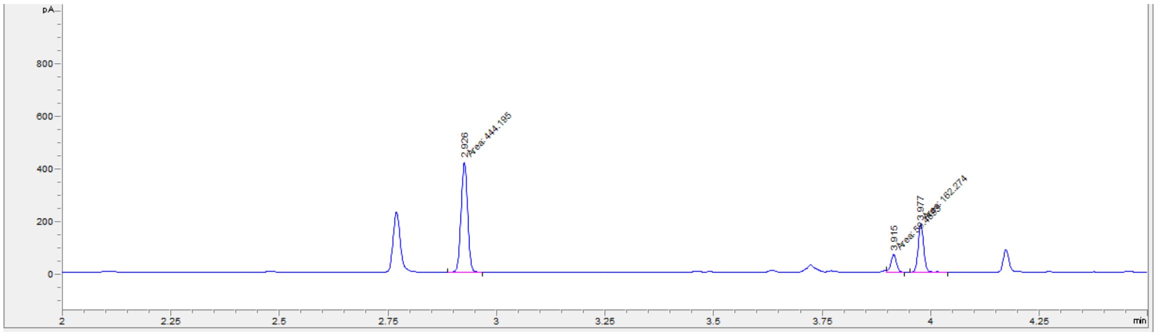
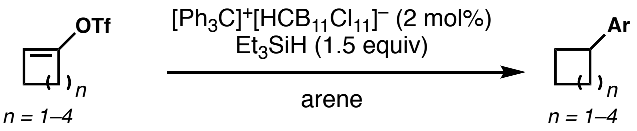


Figure 2.52 GC trace showing 17% yield of **2.34** and 34% yield of **2.36**.

2.9.5.3 Arene Alkylation Reactions

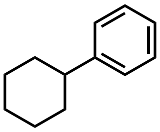
2.9.5.3.1 General Procedures for Intermolecular Reductive Friedel-Crafts Reactions.



Scheme 2.2 General reaction scheme for intermolecular reductive Friedel-Crafts reactions.

General Procedure A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.02 equiv.) and this was dissolved in arene (enough to make a 0.1 M solution of vinyl triflate). Triethylsilane (1.5 equiv.) along with a magnetic stirring bar were added to the mixture and was shaken until it turned colorless. At this point, vinyl triflate (1.0 equiv.) was added to the reaction and it stirred for 0.1–48 hours at 30–75 °C (see substrates for specific details). Upon completion, the reaction mixture was pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. Some substrates needed further purification by silica column chromatography (see below) or preparative high pressure liquid chromatography (HPLC).

General Procedure B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.02 equiv.) and this was dissolved in chloroform (enough to make a 0.1 M solution of vinyl triflate). Arene (10-50 equiv.) and vinyl triflate (1 equiv.) were added along with a magnetic stirring bar to the solution. The solution was cooled to –40 °C. At this point, silane (1.5 equiv.) was added to the reaction and it stirred at this temperature until completion (see substrates for specific details). Upon completion, the reaction mixture was pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. Some substrates needed further purification by silica column chromatography (see below) or preparative high pressure liquid chromatography (HPLC).



Phenylcyclohexane (2.41). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.002 mmol) and this was suspended in pentane (0.5 mL, 11.1 mmol). Triethylsilane (9.6 mL, 0.060 mmol), benzene (18 mL, 0.2 mmol, 4 equiv), and a magnetic stirring bar were added respectively to the mixture and stirred for 10 minutes. Cyclohexenyl triflate (**2.23**) (12.0 mg, 0.050 mmol) was added to the reaction and stirred for 2 hour at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.41** in 74% yield (GC). NMR spectra match those reported in literature.[64]

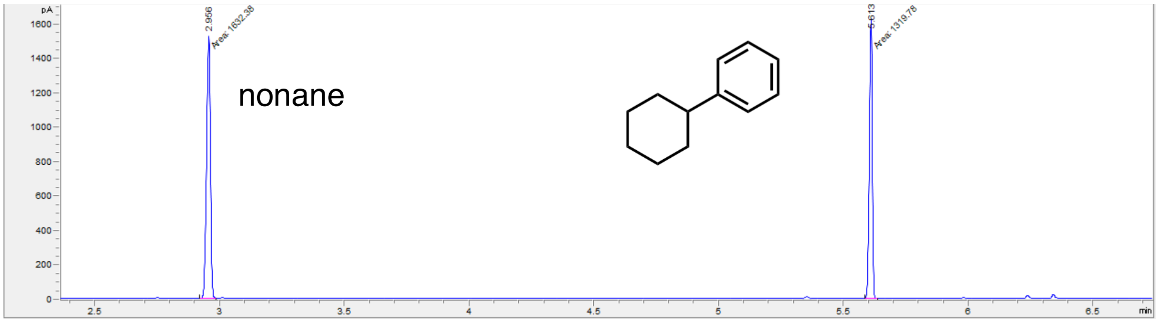


Figure 2.53 GC trace showing one to one mixture of nonane to **2.41**.

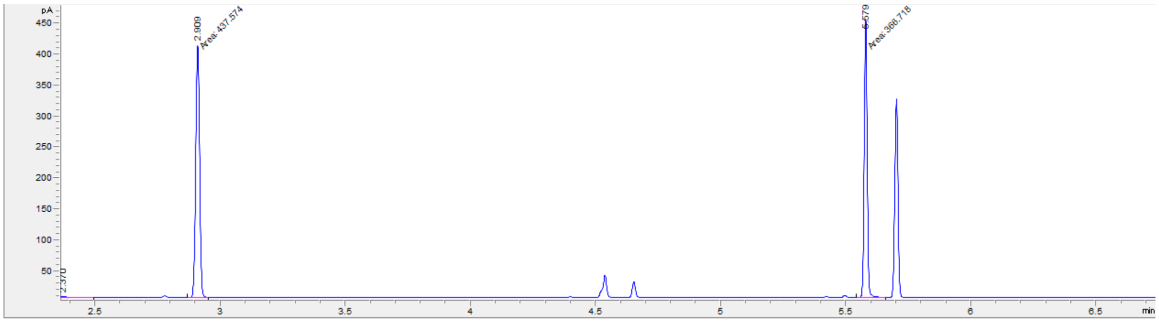
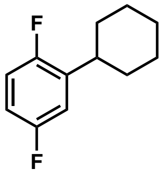


Figure 2.54 GC trace showing 74% yield of **2.41**.

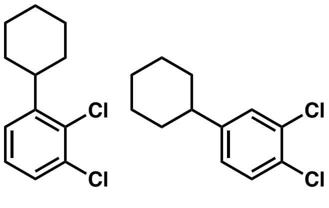


2-cyclohexyl-1,4-difluorobenzene (2.42). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (3.2 mg, 0.004 mmol) and this was suspended in pentane (0.5 mL) and 1,4-difluorobenzene (51 mL, 0.50 mmol). Triethylsilane (9.6 mL, 0.06 mmol) along with a magnetic stirring bar were added to the mixture and stirred for 10 minutes. Cyclohexenyltriflate (**2.23**) (12.0 mg, 0.05 mmol) was added to the reaction and stirred for 3 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to yield **2.42** in 49% yield (NMR). **2.42** was also synthesized as described above in 1,4-difluorobenzene solvent (0.5 mL). Crude material was purified by flash column chromatography (hexanes) to yield a colorless oil (22 mg, 56%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 – 6.88 (m, 2H), 6.83 – 6.78 (m, 1H), 2.84 (t, J = 10.8 Hz, 1H), 1.85 (br d, J = 10.5 Hz, 4H), 1.76 (br d, J = 12.9 Hz, 1H), 1.47 – 1.32 (m, 4H), 1.29 – 1.20 (m, 1H); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ –119.4 (J = 17.7 Hz), –125.7 (J = 17.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9 (dd, $^1J_{C–F}$ = 240.8 Hz, $^4J_{C–F}$ = 2.3 Hz), 156.4 (dd, ${}^1J_{C\text{–}F}$ = 239.9 Hz, ${}^4J_{C\text{–}F}$ = 2.4 Hz), 136.3 (dd, ${}^2J_{C\text{–}F}$ = 17.4 Hz, ${}^3J_{C\text{–}F}$ = 7.0 Hz), 115.9 (dd, ${}^2J_{C\text{–}F}$ = 26.2 Hz, ${}^3J_{C\text{–}F}$ = 8.7 Hz), 114.1 (dd, ${}^2J_{C\text{–}F}$ = 24.0 Hz, ${}^3J_{C\text{–}F}$ = 5.5 Hz), 113.1 (dd, ${}^2J_{C\text{–}F}$ = 24.1 Hz, ${}^3J_{C\text{–}F}$ = 8.8 Hz), 37.1, 32.9, 26.7, 26.0.

FTIR (Neat film NaCl): 2928, 2854, 1625, 1596, 1493, 1450, 1425, 1232, 1178, 866, 810, 780, 731.

HR-MS (GCT-LIFDI): Calculated for $C_{12}H_{14}F_2$: 196.1064; measured: 196.1067.



~1:5 ratio

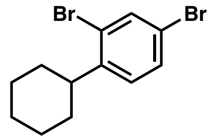
1,2-dichloro-4-cyclohexylbenzene (2.43). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (3.2 mg, 0.004 mmol) and this was suspended in 1,4-difluorobenzene (2 mL, 19.5 mmol). Triethylsilane (48 mL, 0.3 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. Cyclohexenyltriflate (**2.23**) (46.0 mg, 0.20 mmol) was added the reaction and it stirred for 1 hour at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.43** as a mixture of isomers in 47% yield (NMR) and 9% yield (NMR). Crude material was further purified *via* flash column chromatography (hexanes) to give product **2.43** (mixture of isomers) as a colorless oil.

^{1}H NMR major isomer (500 MHz, $CDCl_3$) δ 7.33 (d, J = 8.3 Hz, 1H), 7.28 (d, J = 1.9 Hz, 1H), 7.03 (dd, J = 8.3, 1.9 Hz, 1H), 2.46 (dd, J = 10.2, 7.5 Hz, 1H), 1.84 (br d, J = 12.9 Hz, 4H), 1.75 (br d, J = 12.9 Hz, 1H), 1.41 – 1.33 (m, 4H), 1.28 – 1.19 (m, 2H); ^{13}C

NMR major isomer (125 MHz, $CDCl_3$) δ 148.4, 132.2, 130.3, 129.6, 129.0, 126.5, 44.0, 34.4, 26.8, 26.1.

FTIR (Neat film NaCl): 2924, 2852, 1584, 1560, 1475, 1461, 1449, 1131, 1028, 671, 592.

HR-MS (GCT-LIFDI): Calculated for $C_{12}H_{14}Cl_2$: 228.0473; measured: 228.0473.

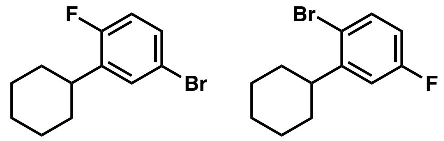


2,4-dibromo-1-cyclohexylbenzene (2.44). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was dissolved in 1,3-dibromobenzene (0.5 mL, 3.4 mmol). Triethylsilane (12 mL, 0.075 mmol) along with a magnetic stirring bar were added to the mixture and the resulting solution stirred for 10 minutes. Triflate **2.23** (12.0 mg, 0.05 mmol) was added to the reaction and stirred for 2 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.44** in 51% yield (NMR). The crude product was further purified by reverse phase HPLC (9:1 acetonitrile:water) to give pure product as a colorless oil.

^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 2.0 Hz, 2H), 7.38 (dd, J = 8.3, 2.0 Hz, 2H), 7.11 (d, J = 8.3 Hz, 1H), 2.90 (tt, J = 11.6, 3.0 Hz, 1H), 1.90 – 1.81 (m, 4H), 1.49 – 1.18 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.6, 135.1, 130.8, 128.6, 125.1, 119.7, 43.0, 33.3, 26.9, 26.2.

FTIR (Neat film NaCl): 2924, 2851, 1730, 1577, 1551, 1465, 1448, 1379, 1083, 1033, 998, 812, 779, 720, 700, 553.

HR-MS (GCT-LIFDI): Calculated for $C_{12}H_{14}Br_2$: 317.9442; measured: 317.9455.



5.4:1

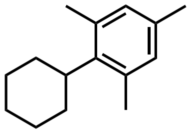
4-bromo-2-cyclohexyl-1-fluorobenzene (2.45). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was dissolved in 1,4-bromofluorobenzene (0.5 mL, 4.6 mmol). Triethylsilane (12 mL, 0.075 mmol) along with a magnetic stirring bar were added to the mixture and the resulting solution stirred for 10 minutes. Triflate **2.23** (12.0 mg, 0.05 mmol) was added to the reaction and stirred for 2 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.45** as a mixture of isomers in 43% and 8% yield (NMR), respectively. The reaction mixture was purified by reverse phase HPLC (85:15 acetonitrile:water) to give the product **2.45** and a regioisomer as a mixture (~5:1 ratio) as a colorless oil. Major isomer was assigned by looking at the ^{13}C NMR and the HSQC. By ^{13}C NMR, the carbon on the fluorine and the carbons *ortho* to the fluorine could be assigned by their large $^{1}J_{\text{C-F}}$ and $^{2}J_{\text{C-F}}$ values respectively. Of the two carbons *ortho* to the fluorine, only one of them was attached to a hydrogen, meaning that the other position was cyclohexylated.

^{1}H NMR major isomer (500 MHz, $CDCl_3$) δ 7.33 (dd, J = 6.5, 2.5 Hz, 1H), 7.25 – 7.22 (m, 1H), 6.87 (dd, J = 9.9, 8.7 Hz, 1H), 2.85 – 2.77 (m, 1H), 1.87 – 1.80 (m, 4H), 1.79 – 1.72 (m, 1H), 1.44 – 1.36 (m, 4H), 1.30 – 1.21 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ –119.4; ^{13}C NMR major isomer (125 MHz, $CDCl_3$) δ 159.8 (d, $^{1}J_{\text{C–F}}$ = 244.9

Hz), 137.0 (d, ${}^{2}J_{C\text{–}F}$ = 16.3 Hz), 130.9 (d, ${}^{3}J_{C\text{–}F}$ = 5.4 Hz), 130.0 (d, ${}^{3}J_{C\text{–}F}$ = 5.7 Hz), 117.1 (d, ${}^{2}J_{C\text{–}F}$ = 24.8 Hz), 116.7 (d, ${}^{4}J_{C\text{–}F}$ = 3.3 Hz), 37.2 (d, ${}^{3}J_{C\text{–}F}$ = 1.7 Hz, 33.0, 26.8, 26.2.

FTIR (Neat film NaCl): 2929, 2853, 1605, 1579, 1480, 1449, 1232, 1181, 1168, 1099, 1005, 869, 810, 612.

HR-MS (GCT-LIFDI): Calculated for $C_{12}H_{14}BrF$: 256.0263; measured: 256.0260.

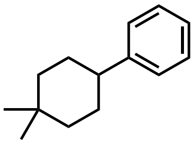


2-cyclohexyl-1,3,5-trimethylbenzene (2.46). Synthesized according to a modified procedure. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in perfluorohexanes (1.0 mL). Triethylsilane (24 mL, 0.15 mmol) and mesitylene (120 mg, 0.1 mmol) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Triflate **2.23** (24.0 mg, 0.1 mmol) was added to the reaction and stirred for 3 minutes at 30 °C. The reaction mixture was quenched with anhydrous ether inside the glovebox and then plugged through silica inside the glovebox to give the crude material as a colorless oil in 61% NMR yield. The crude was further purified by reverse phase HPLC (85:15 acetonitrile:water) to give product **2.46** as a colorless oil.

^{1}H NMR (500 MHz, 57 °C, $CDCl_3$) δ 6.79 (s, 2H), 3.02 – 2.94 (m, 1H), 2.37 (s, 6H), 2.23 (s, 3H), 1.96 – 1.85 (m, 3H), 1.77 (br d, J = 12.3 Hz, 1H), 1.68 (br d, J = 13.1 Hz, 1H), 1.44 – 1.26 (m, 4H); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (s, 2H), 2.97 (tt, J = 12.4, 3.3 Hz, 1H), 2.51 – 2.29 (m, 6H), 2.24 (s, 3H), 1.96 – 1.83 (m, 4H), 1.80–1.74 (m, 1H), 1.71 – 1.65 (m, 2H), 1.45 – 1.23 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 136.3, 134.9, 131.3, 129.4, 41.4, 30.7, 27.9, 26.6, 21.8, 20.7.

FTIR (Neat film NaCl): 2924, 2851, 1612, 1483, 1448, 1369, 1261, 1025, 849, 572.

HR-MS (GCT-LIFDI): Calculated for $C_{15}H_{22}$: 202.1721; measured: 202.1727.

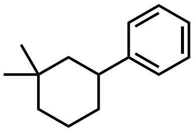


4,4-Dimethylcyclohexyl)benzene (2.47). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in benzene (1 mL, 11.2 mmol). Triethylsilane (24 μL, 0.15 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. The corresponding triflate (25.8 mg, 0.10 mmol) was added to the reaction and stirred for 1.5 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give **2.47** in 78% yield (NMR). The crude product was further purified by flash column chromatography (hexanes) to give **2.47** as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.25 – 7.22 (m, 2H), 7.20 – 7.16 (m, 1H), 2.42 (tt, *J* = 11.9, 4.0 Hz, 1H), 1.73 – 1.59 (m, 4H), 1.53 – 1.47 (m, 2H), 1.34 (td, *J* = 13.1, 4.1 Hz, 2H), 0.98 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 128.3, 126.9, 125.8, 44.5, 39.7, 33.2, 30.2, 29.8, 24.2.

FTIR (Neat film NaCl): 3062, 3027, 2923, 2861, 2843, 1740, 1602, 1471, 1451, 1385, 1364, 753, 697, 532.

HR-MS (GCT-LIFDI): Calculated for $C_{14}H_{20}$: 188.1565; measured: 188.1572.

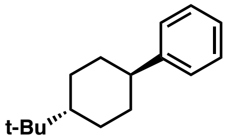


(3,3-Dimethylcyclohexyl)benzene (2.48). Synthesized according to general procedure A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was suspended in benzene (0.5 mL, 5.6 mmol). Triethylsilane (12 μL, 0.075 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. The corresponding triflate (12.9 mg, 0.05 mmol) was added to the reaction and stirred for 1.5 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give **2.48** in 88% yield (NMR). The crude product was further purified by flash column chromatography (hexanes) to give **2.48** as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.20 (m, 2H), 7.20 – 7.15 (m, 1H), 2.70 (tt, *J* = 12.5, 3.4 Hz, 1H), 1.91 – 1.84 (m, 1H), 1.71 – 1.52 (m, 3H), 1.46 – 1.41 (m, 1H), 1.36 – 1.26 (m, 2H), 1.19 (td, *J* = 13.2, 4.4 Hz, 1H), 1.01 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 128.4, 127.1, 125.9, 47.7, 40.1, 39.0, 34.2, 33.6, 31.4, 24.8, 22.9.

FTIR (Neat film NaCl): 3062, 3027, 2922, 2862, 2844, 1602, 1493, 1471, 1451, 1385, 1363, 756, 697, 538, 525.

HR-MS (GCT-LIFDI): Calculated for $C_{14}H_{20}$: 188.1565; measured: 188.1571.

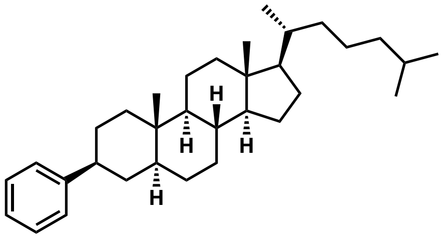


***anti*-4-(*tert*-Butyl)cyclohexyl)benzene (2.49).** Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in benzene (1 mL, 11.2 mmol). Triethylsilane (24 mL, 0.15 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. The corresponding triflate (29.0 mg, 0.10 mmol) was added to the reaction and stirred for 10 minutes at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give **2.49** as a mixture of diastereomers (44% NMR yield of *trans*, 5% NMR yield of *cis*).[65] The crude product was further purified by reverse phase prep HPLC (95:5 acetonitrile/water) to give the *trans* product **2.49** as a colorless oil (7.5 mg, 35%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.23 – 7.20 (m, 2H), 7.20 – 7.16 (m, 1H), 2.45 (tt, *J* = 12.2, 3.5 Hz, 1H), 1.99 – 1.87 (m, 4H), 1.45 (qd, *J* = 12.5, 2.6 Hz, 2H), 1.21 – 1.05 (m, 3H), 0.89 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 128.4, 127.0, 125.9, 47.92, 44.7, 34.9, 32.6, 27.9, 27.8.

FTIR (Neat film NaCl): 3061, 3027, 2937, 2921, 2855, 1602, 1493, 1479, 1448, 1364, 1232, 895, 755, 697, 532.

HR-MS (GCT-LIFDI): Calculated for $C_{16}H_{24}$: 216.1878; measured: 216.1889.

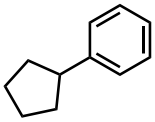


(3*S*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-3-phenylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene (2.50). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was suspended in benzene (0.5 mL, 5.6 mmol). Triethylsilane (12 mL, 0.075 mmol) along with a magnetic stirring bar were added to the mixture and the resulting suspension stirred for 10 minutes. Triflate **2.29** (26.0 mg, 0.05 mmol) was added to the reaction and stirred for 2 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.50** as a diastereomeric mixture in 79% and 11% yield (NMR) of the major and minor diastereomers, respectively. The crude mixture was purified *via* silica column chromatography (hexanes) to give an inseparable mixture of diastereomers as a white solid (18.5 mg, 85% of mixture). Assignment of major isomer was based on key cross-peaks in ^{1}H COSY and ^{1}H NOESY spectroscopy experiments. From the major benzylic proton, adjacent protons were identified at 1.47 ppm and 1.72 ppm through COSY. The same peaks were observed in NOESY in addition to two peaks at 1.08 ppm and 1.26 ppm corresponding to 1,3-diaxial interactions of the benzylic proton. Through 2D HSQC and HMBC experiments, the cross-peak at 1.26 ppm was determined to be the *trans*-decalin proton.

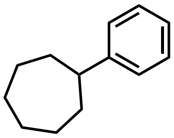
Major Isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.27 – 7.24 (m, 2H), 7.22 – 7.18 (m, 1H), 2.58 (tt, *J* = 11.5, 5.0 Hz, 1H), 2.02 (dt, *J* = 12.5, 3.4 Hz, 1H), 1.90 – 1.80 (m, 2H), 1.77 – 1.66 (m, 3H), 1.65 – 1.58 (m, 2H), 1.56 – 1.46 (m, 3H), 1.43 – 1.25 (m, 9H), 1.23 – 1.00 (m, 11H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 2.3 Hz, 3H), 0.90 (s, 3H), 0.89 (d, *J* = 2.3 Hz, 3H), 0.77 – 0.71 (m, 1H), 0.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 128.4, 127.0, 125.9, 56.8, 56.5, 54.8, 47.2, 45.0, 42.8, 39.7, 39.1, 36.8, 36.4, 36.0, 35.9, 35.7, 30.0, 28.2, 24.0, 23.0, 22.7, 18.9, 12.7, 12.3.

FTIR (Neat film NaCl): 3070, 3023, 2926, 2846, 1466, 1381, 757, 696, 513.

HR-MS (GCT-LIFDI): Calculated for $C_{33}H_{52}$: 448.4069; measured: 448.4058.

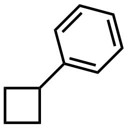


Phenylcyclopentane (2.51). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in benzene (1 mL, 11.2 mmol). Triethylsilane (24 mL, 0.15 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. Cyclopentenyl triflate (22.0 mg, 0.10 mmol) was added to the reaction and stirred for 6 days at 70 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give phenylcyclopentane (**2.51**) in 64% yield (NMR). The crude product was further purified by flash column chromatography (hexanes) to give phenylcyclopentane as a colorless oil (7.6 mg, 52%). NMR spectra match those reported in literature.[64]

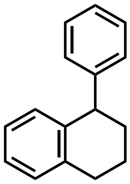


Phenylcycloheptane (2.52). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in benzene (1 mL, 11.2 mmol). Triethylsilane (24 mL, 0.15 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. Cycloheptenyl triflate (24.0 mg, 0.10 mmol) was added to the reaction and stirred for 1.5

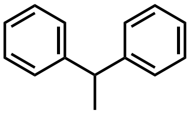
hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.52** in 71% yield (NMR) with ~10% yield of (cyclohexylmethyl)benzene as a small inseparable side product. NMR data match those reported in literature.[64, 66]



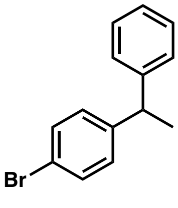
Phenylcyclobutane (2.53). Synthesized according to a modified general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was dissolved in benzene (10 mL, 112 mmol). Triisopropylsilane (15 mL, 0.075 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. Cyclobutenyl triflate (10.0 mg, 0.05 mmol) was added to the reaction and stirred for 0.5 hours at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.53** in 57% yield (NMR). The crude product was purified *via* silica column chromatography (hexanes) to give phenylcyclobutane as a colorless oil. NMR data match those reported in literature.[67]



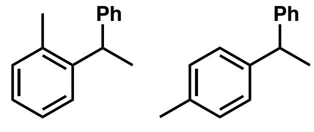
1-phenyl-1,2,3,4-tetrahydronaphthalene (2.54). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in benzene (1 mL, 11.2 mmol). Triethylsilane (24 mL, 0.15 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. The corresponding triflate (28.0 mg, 0.10 mmol) was added to the reaction and stirred for 2 days at 60 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.54** in 43% yield (NMR). Crude material was purified by flash column chromatography (hexanes) to give product **2.54** as a colorless oil (8.6 mg, 41.3%). NMR spectra match those reported in literature.[68]



1,1-Diphenylethane (2.55). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was suspended in benzene (1 mL, 11.2 mmol). Triethylsilane (24 ,mL, 0.15 mmol) along with a magnetic stirring bar were added to the mixture and stirred until colorless. The corresponding triflate (29.0 mg, 0.10 mmol) was added to the reaction and stirred for 1 hour at 30 °C. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give triflate **2.55** in 77% yield (NMR). Crude material was further purified *via* flash column chromatography (hexanes) to give product **2.55** as a colorless oil (12.2 mg, 67%). NMR spectra match those reported in literature.[68]

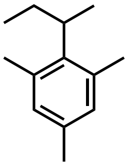


1-bromo-4-(1-phenylethyl)benzene (2.56). Synthesized according to general procedure 2.9.5.3.1A. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv.) and this was dissolved in benzene (0.5 mL). Triethylsilane (7.0 mg, 0.060 mmol, 1.2 equiv.) and 1-(4-bromophenyl)vinyl trifluoromethanesulfonate (10.2 mg, 0.05 mmol) were added along with a magnetic stirring bar to the solution and stirred for 2 hours. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure to give product **2.56** in 51% yield (NMR) as a colorless oil. NMR spectra match those reported in literature.[69]



19:47

1-methyl-4-(1-phenylethyl)benzene (2.57). Synthesized according to general procedure 2.9.5.3.1B. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was dissolved in chloroform (1 mL). Toluene (92 mg, 1 mmol) and 1-phenylvinyl trifluoromethanesulfonate (25.2 mg, 0.1 mmol) were added along with a magnetic stirring bar to the solution. The solution was cooled to –40 °C. At this point, triethylsilane (17.4 mg, 0.15 mmol) was added to the reaction and stirred at –40 °C for 1 hour. The reaction mixture was warmed to room temperature and was plugged through silica in the glovebox and volatiles removed under reduced pressure. The crude material was purified by flash column chromatography (hexanes) to give an inseparable mixture of products **2.57** in 47% and 19% yield, *para* and *ortho* isomers, respectively, as a colorless oil. NMR spectra match those reported in literature.[70, 71]

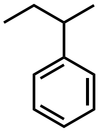


2-(*sec*-butyl)-1,3,5-trimethylbenzene (2.58). Synthesized according to general procedure 2.9.5.3.1B. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was dissolved in chloroform (1 mL). Mesitylene (120 mg, 1 mmol) and but-1-en-2-yl trifluoromethanesulfonate (**2.35**) (20.4 mg, 0.1 mmol) were added along with a magnetic stirring bar to the solution. The solution was cooled to –40 °C. At this point, triethylsilane (17.4 mg, 0.15 mmol) was added to the reaction and it stirred at –-40 °C for 1 hour. The reaction mixture was warmed to room temperature and pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. The crude material was purified by flash column chromatography (hexanes) to give **2.58** as a colorless oil (80% NMR yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 2H), 3.14 (sex, *J* = 7.5 Hz, 1H), 2.32 (br s, 6H), 2.26 (s, 3H), 1.83 – 1.67 (m, 2H), 1.30 (d, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 136.4, 134.8, 131.2, 129.6, 36.7, 28.4, 21.7, 20.8, 19.0, 13.3.

FTIR (Neat film NaCl): 2962, 2926, 2872, 1612, 1455, 1377, 850, 578.

HR-MS (GCT-LIFDI): Calculated for $C_{13}H_{20}$: 176.1565; measured: 176.1572.



***sec*-butylbenzene (2.59).** Synthesized according to a modified general procedure 2.9.5.3.1B. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.02 equiv.) and this was dissolved in chloroform (0.4 mL). Benzene (195 mg, 2.5 mmol, 50 equiv.) and but-1-en-2-yl trifluoromethanesulfonate (**2.35**) (10.2 mg, 0.05 mmol) were added along with a magnetic stirring bar to the solution. Triisopropylsilane (11.9 mg, 0.075 mmol, 1.5 equiv.) was added dropwise to the reaction and stirred for 1 hour. The reaction was plugged through silica in the glovebox and volatiles removed under reduced pressure. The solution was brought out and volatiles removed under reduced pressure) to give product **2.59** in 95% yield (GC) as a colorless oil. NMR spectra match those reported in literature.[72]

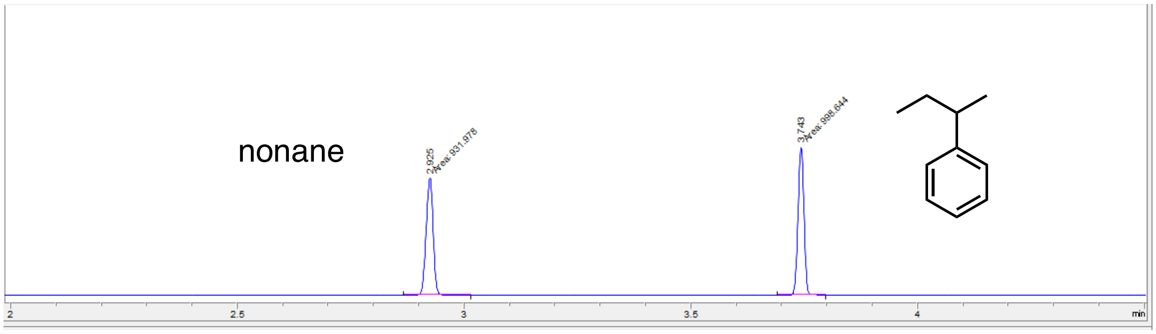


Figure. 2.55 GC trace of a 1:1 mixture of nonane to *s*-butylbenzene.

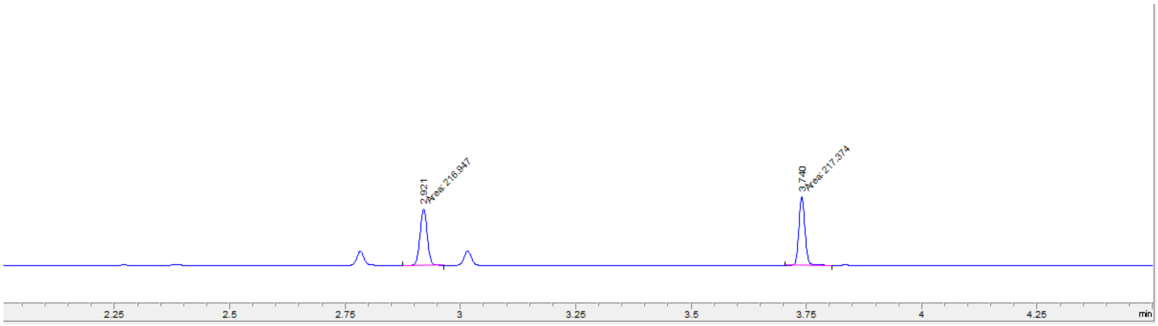
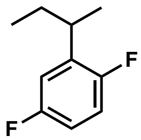


Figure 2.56 GC trace showing a 95% yield of *s*-butylbenzene.



2-(*sec*-butyl)-1,4-difluorobenzene (2.60). Synthesized according to general procedure 2.9.5.3.1B. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.6 mg, 0.002 mmol) and this was dissolved in chloroform (1 mL). 1,4-Difluorobenzene (114 mg, 1 mmol) and but-1-en-2-yl trifluoromethanesulfonate (**2.35**) (20.4 mg, 0.1 mmol) were added along with a magnetic stirring bar to the solution. The solution was cooled to –40 °C. At this point, triisopropylsilane (23.8 mg, 0.15 mmol) was added to the reaction and it stirred at –40 °C for 3 hours. The reaction mixture was warmed to room temparature and pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. The crude material was further purified by flash column chromatography (petroleum ether) with silver nitrate impregnated silica gel as a stationary phase to give product **2.60** as a colorless oil (46% NMR yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (td, J = 9.2, 4.6 Hz, 1H), 6.88 (ddd, J = 12.8, 6.2, 3.4 Hz, 1H), 6.85 – 6.79 (m, 1H), 3.00 – 2.93 (sex, J = 7.0, 2H), 1.60 (sex, J = 7.0 Hz, 2H), 1.22 (d, J = 7.0 Hz, 3H), 0.84 (t, J = 7.0, 3H); ^{19}F {^{1}H} NMR (282 MHz, $CDCl_3$) δ –119.5 (d, J = 17.8 Hz), –125.2 (d, J = 17.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9 (d, $^1J_{C\text{–}F}$ = 241.0 Hz), 156.7 (d, $^1J_{C\text{–}F}$ = 239.8 Hz), 136.0 (dd, $^2J_{C\text{–}F}$ = 17.5 Hz, $^3J_{C\text{–}F}$ = 6.9 Hz), 116.1 (dd, $^2J_{C\text{–}F}$ = 26.3 Hz, $^3J_{C\text{–}F}$ = 8.7 Hz), 114.2 (dd, $^2J_{C\text{–}F}$ = 13.8 Hz, $^3J_{C\text{–}F}$ = 5.6 Hz), 113.3 (dd, $^2J_{C\text{–}F}$ = 24.1 Hz, $^3J_{C\text{–}F}$ = 8.8 Hz), 34.1, 29.8, 20.4, 12.0.

FTIR (Neat film NaCl): 2963, 2931, 2875, 1596, 1496, 1464, 1415, 1380, 1180, 1165, 870, 810, 758, 731.

HR-MS (GCT-LIFDI): Calculated for $C_{10}H_{12}F_2$: 170.0907; measured: 170.0905.

2.10 Spectra Relevant to Chapter Two:

Intermolecular C–H Insertion Reactivity of Aryl and Vinyl Cations Under the Catalysis of Silylium-Carborane Reagents.

Brian Shao, Alex L. Bagdasarian, Stasik Popov, Hosea M. Nelson *Science*, **2017**, *355*, 1403–1407.

Stasik Popov, Brian Shao, Alex L. Bagdasarian, Tyler R. Benton, Luyi Zou, Zhongyue Yang, K. N. Houk, Hosea M. Nelson *Science*, **2018**, *361*, 381–387.

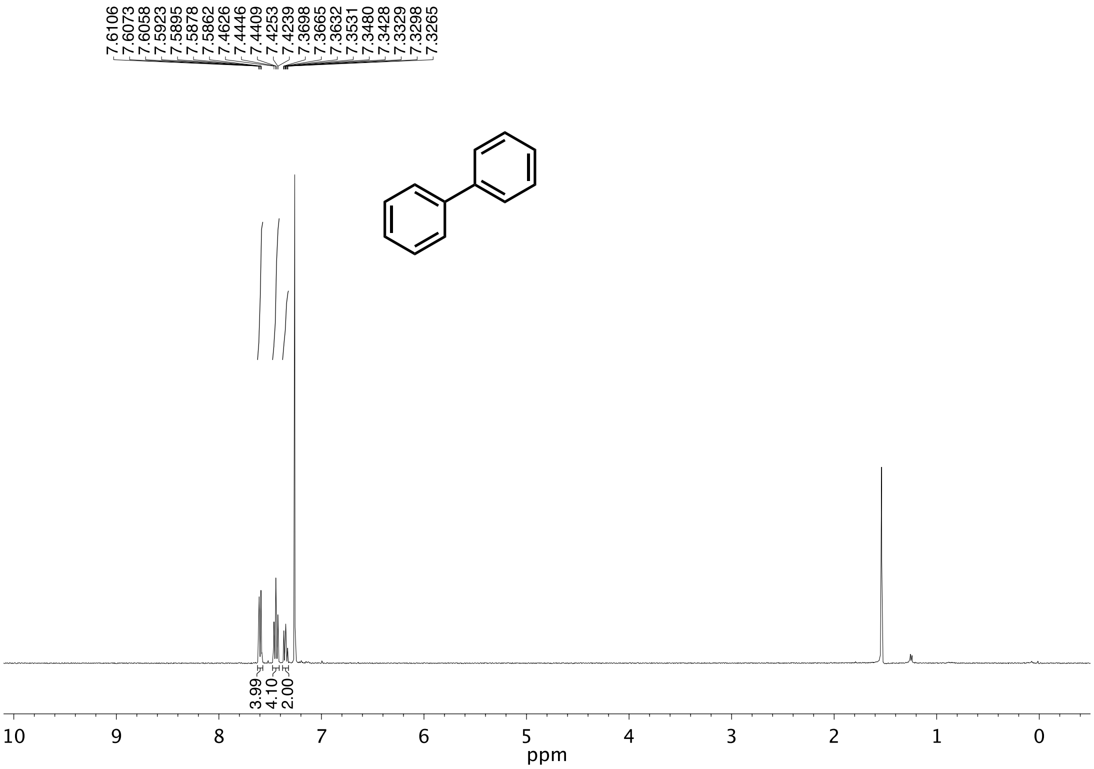


Figure 2.57 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.14**.

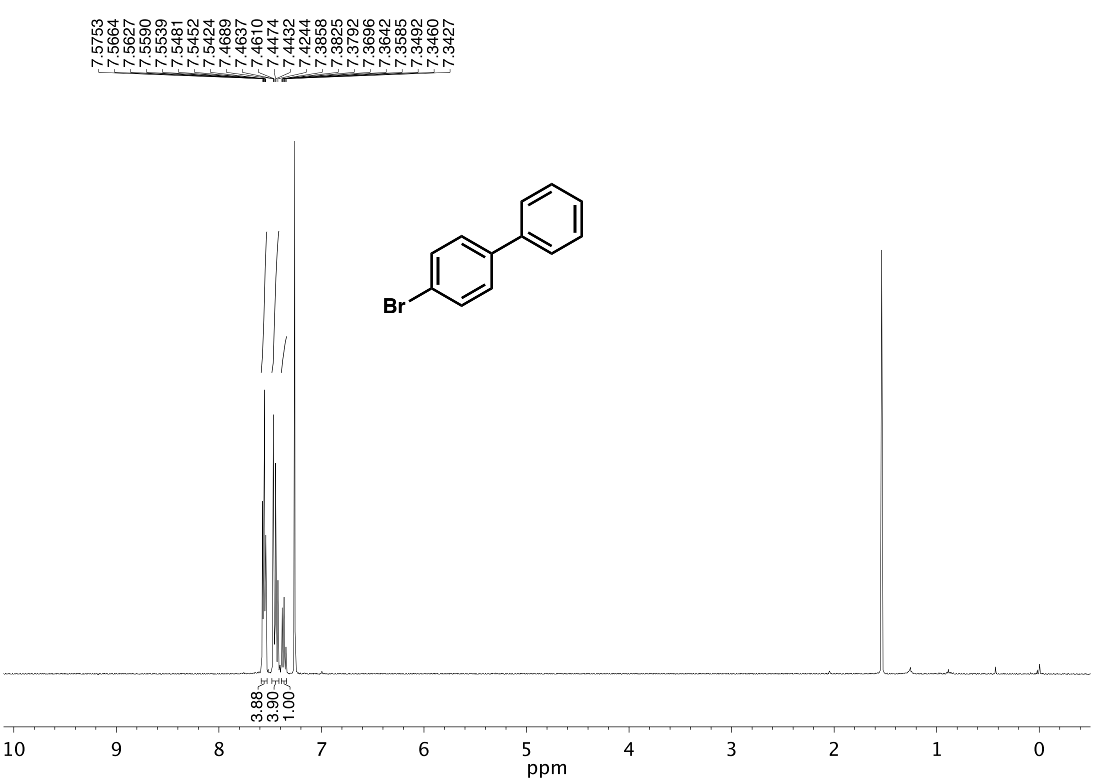


Figure 2.58 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.61**.

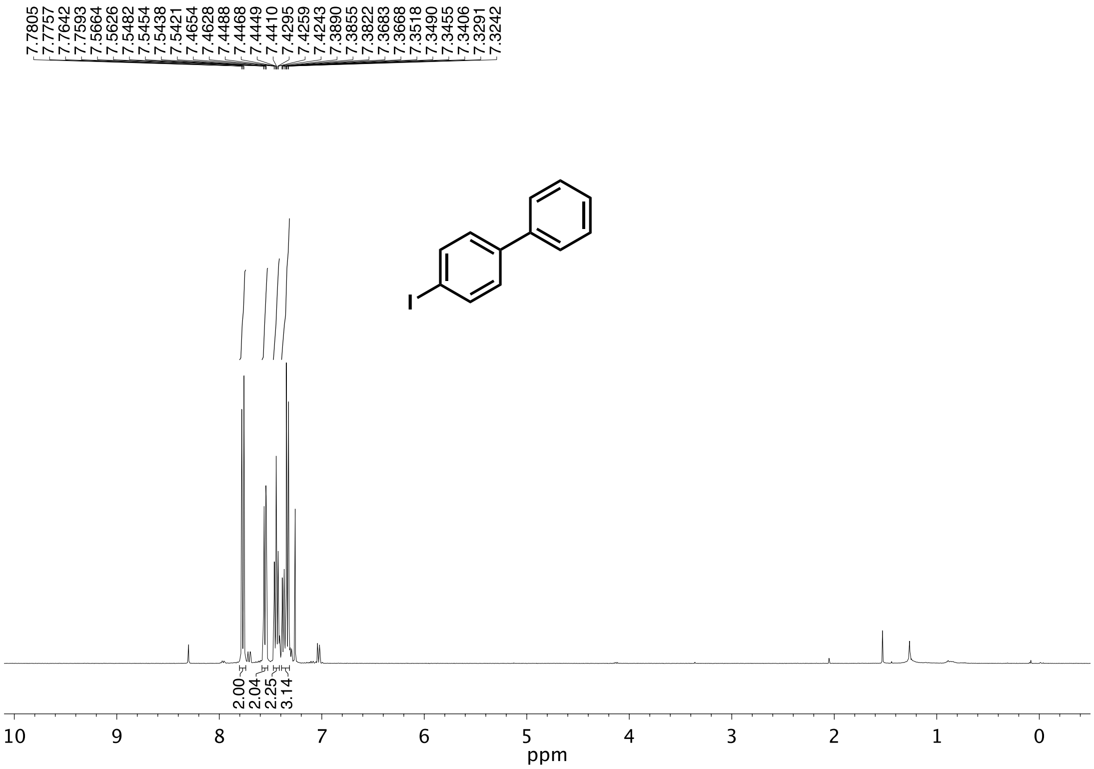


Figure 2.59 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.62**

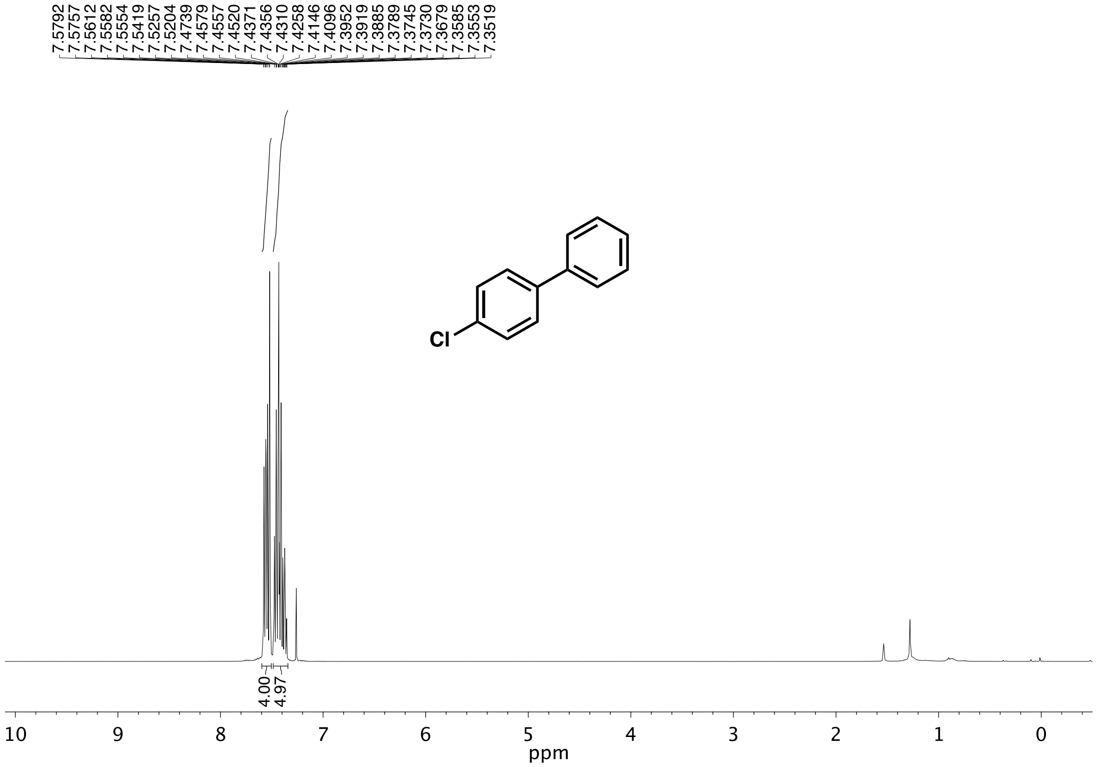


Figure 2.60 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.63**.

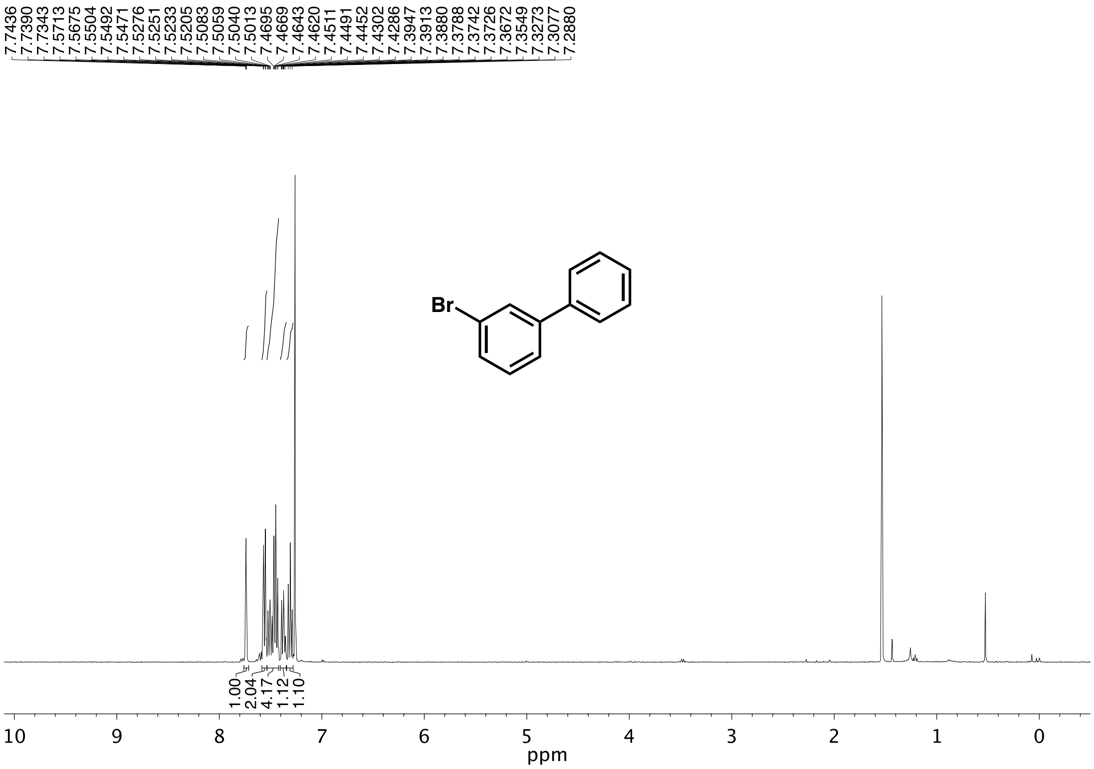


Figure 2.61 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.64**.

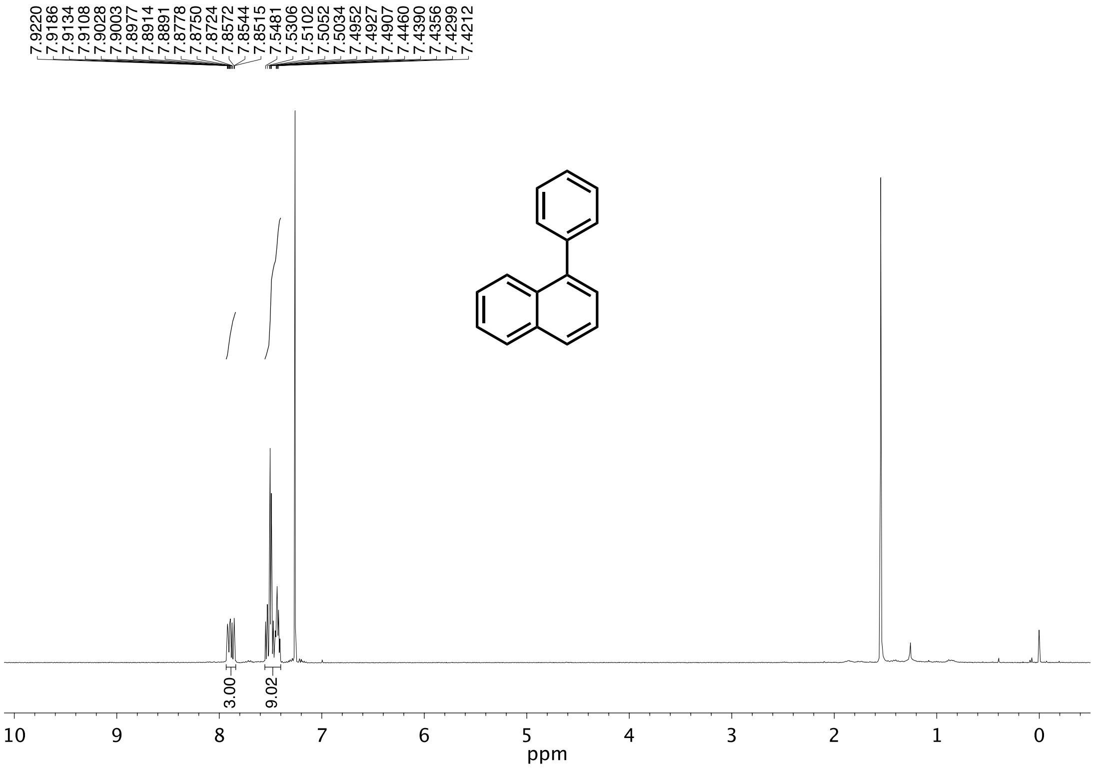


Figure 2.62 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.65**.

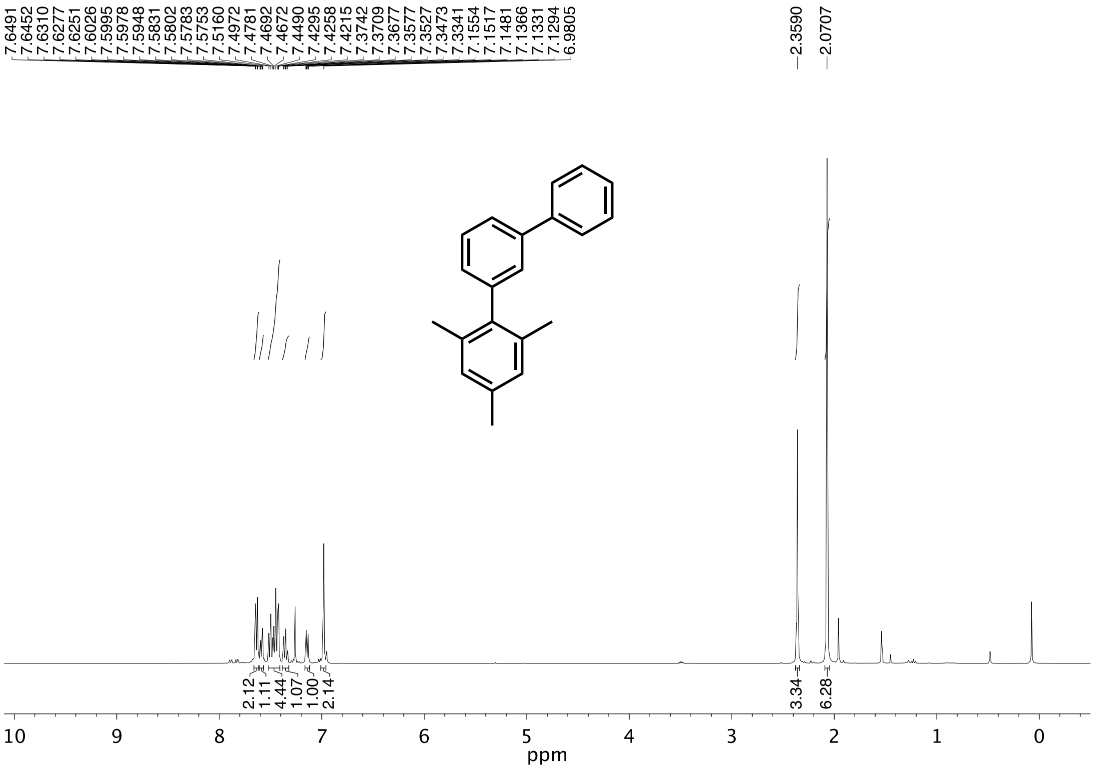


Figure 2.63 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2.67**.

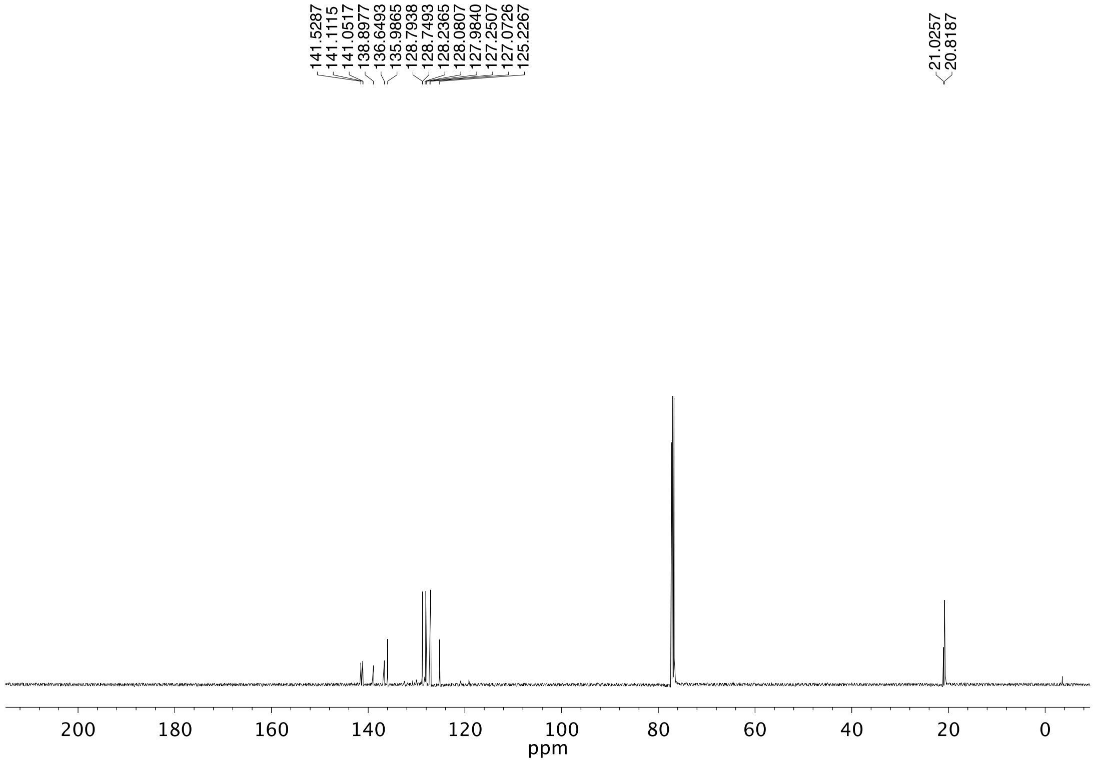


Figure 2.64 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **2.67**.

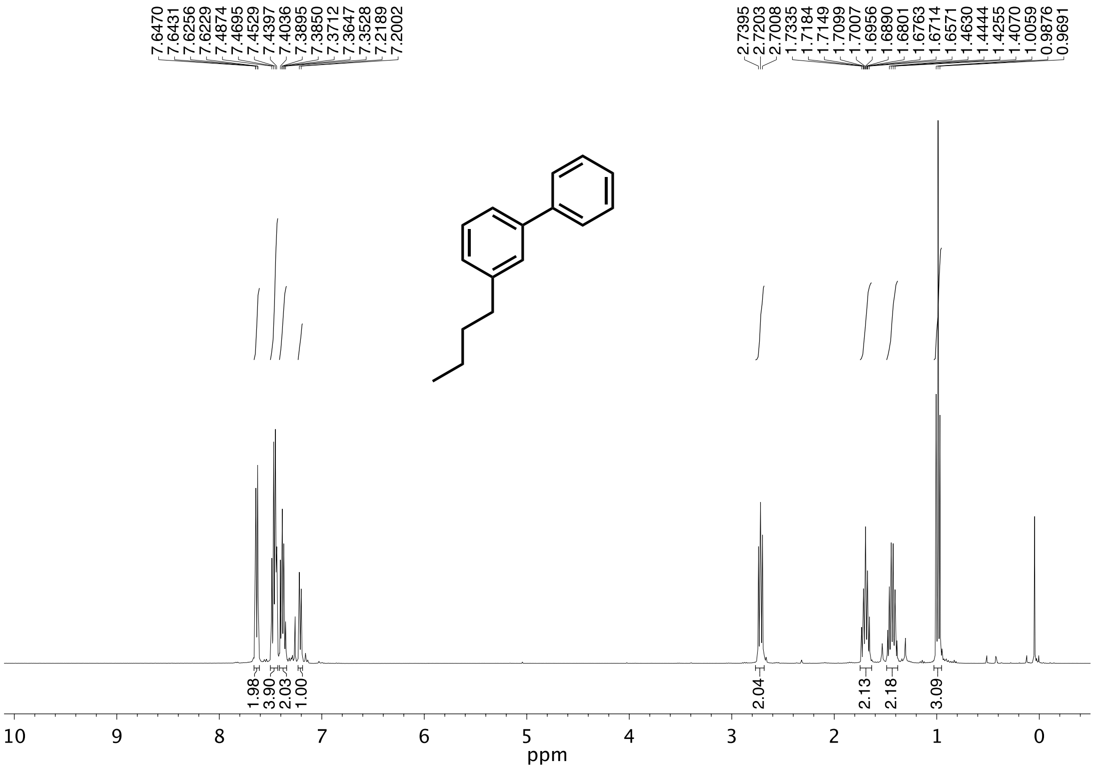


Figure 2.65 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **2.68**.

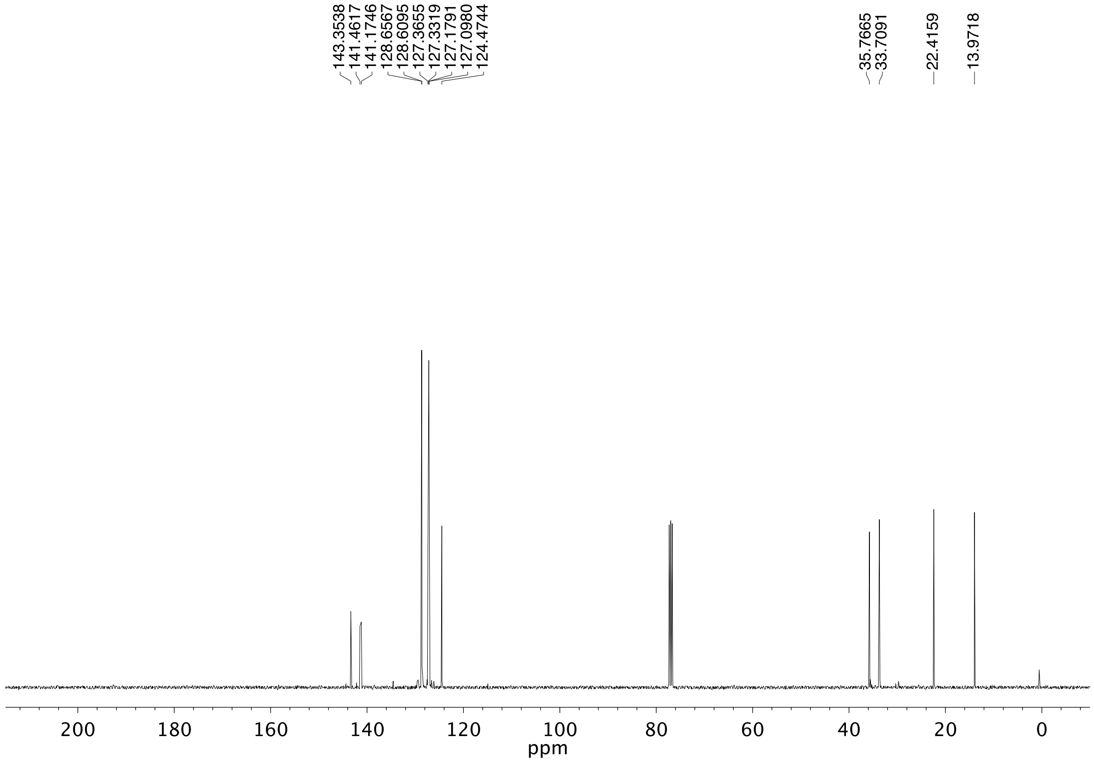


Figure 2.66 ^{13}C NMR (100 MHz, CDCl$_3$) of compound **2.68**.

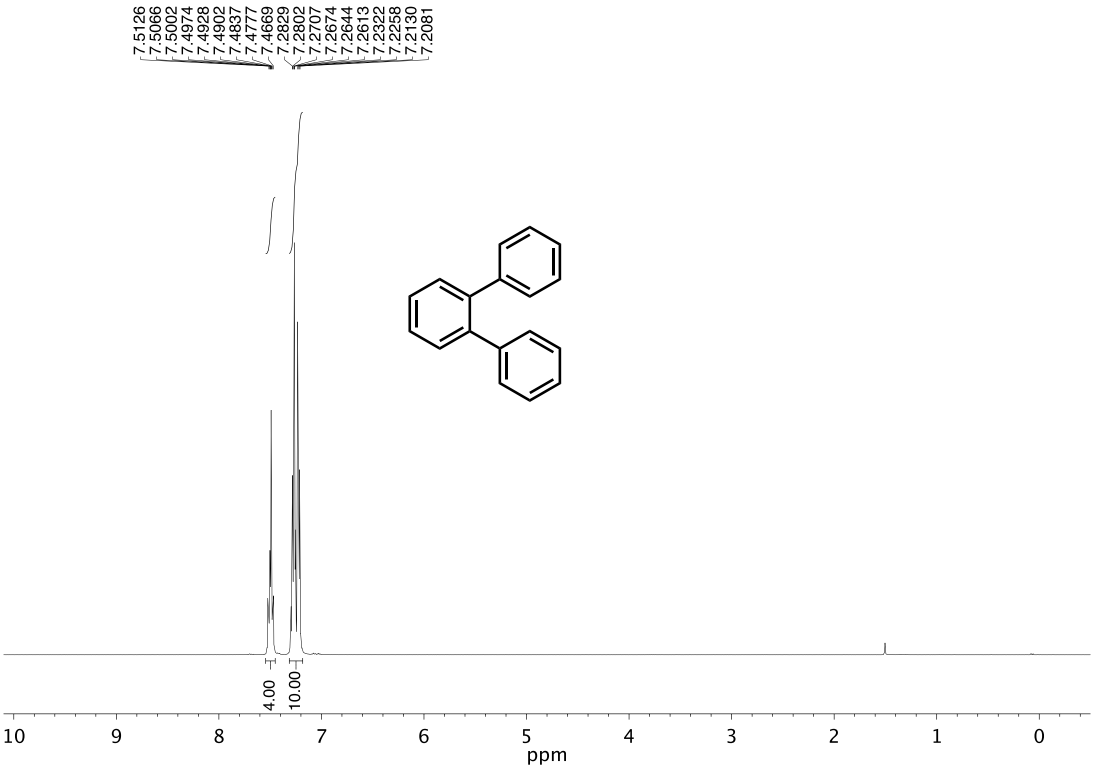


Figure 2.67 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2.66**.

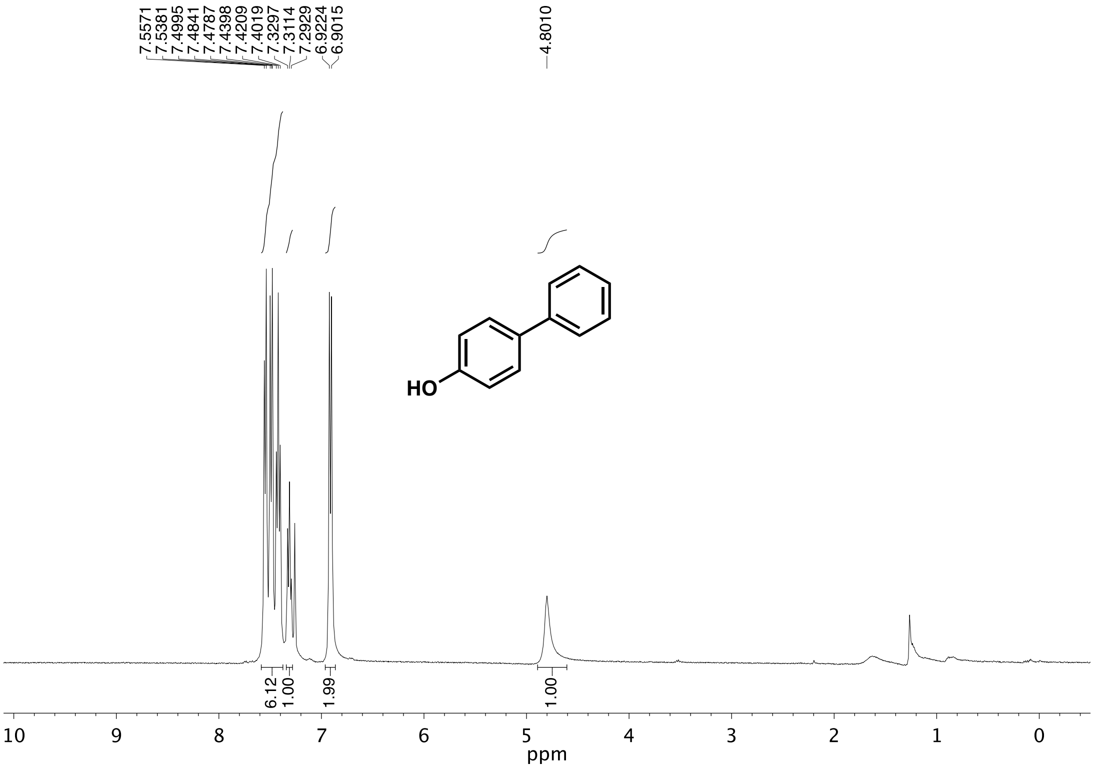


Figure 2.68 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2.69**.

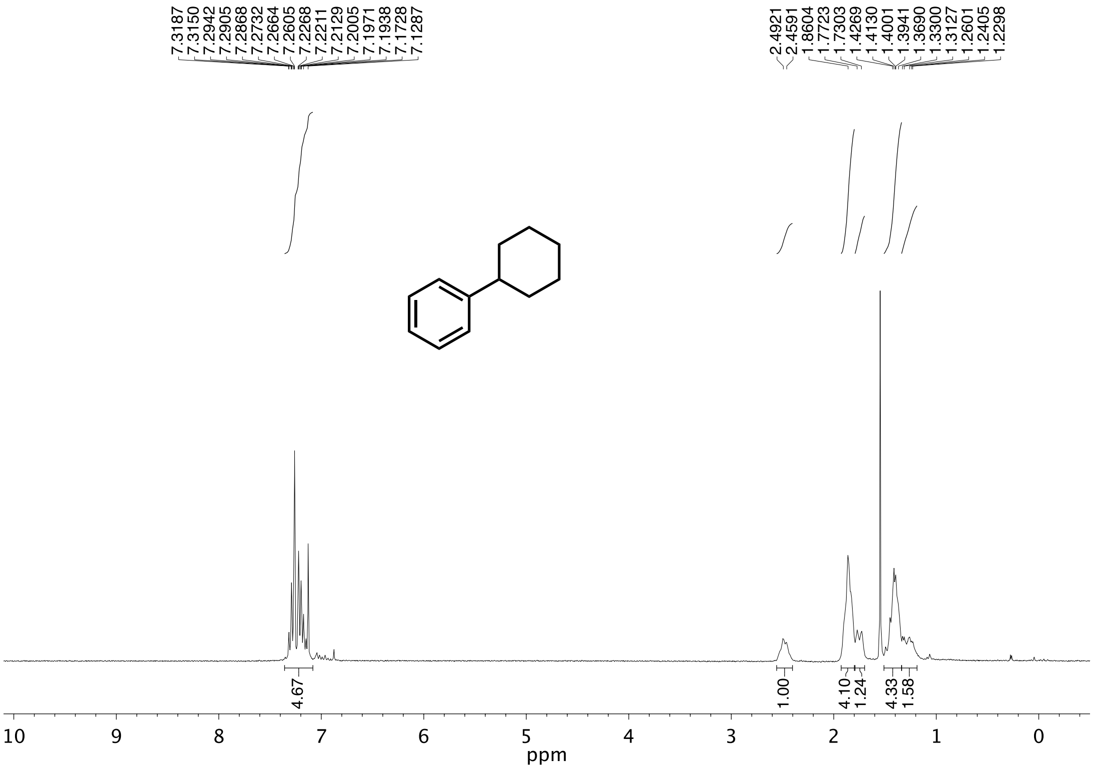


Figure 2.69 ^{1}H NMR (500 MHz, CDCl$_3$) of **2.70**.

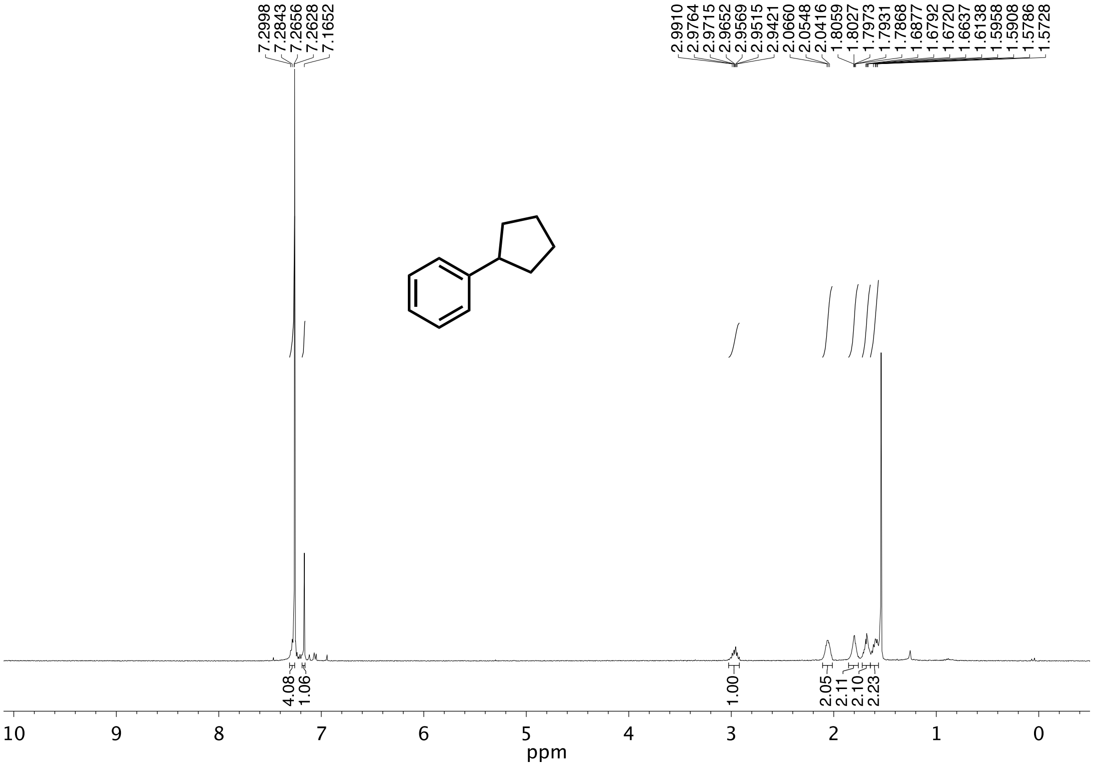


Figure 2.70 ^{1}H NMR (500 MHz, CDCl$_3$) of **2.71**.

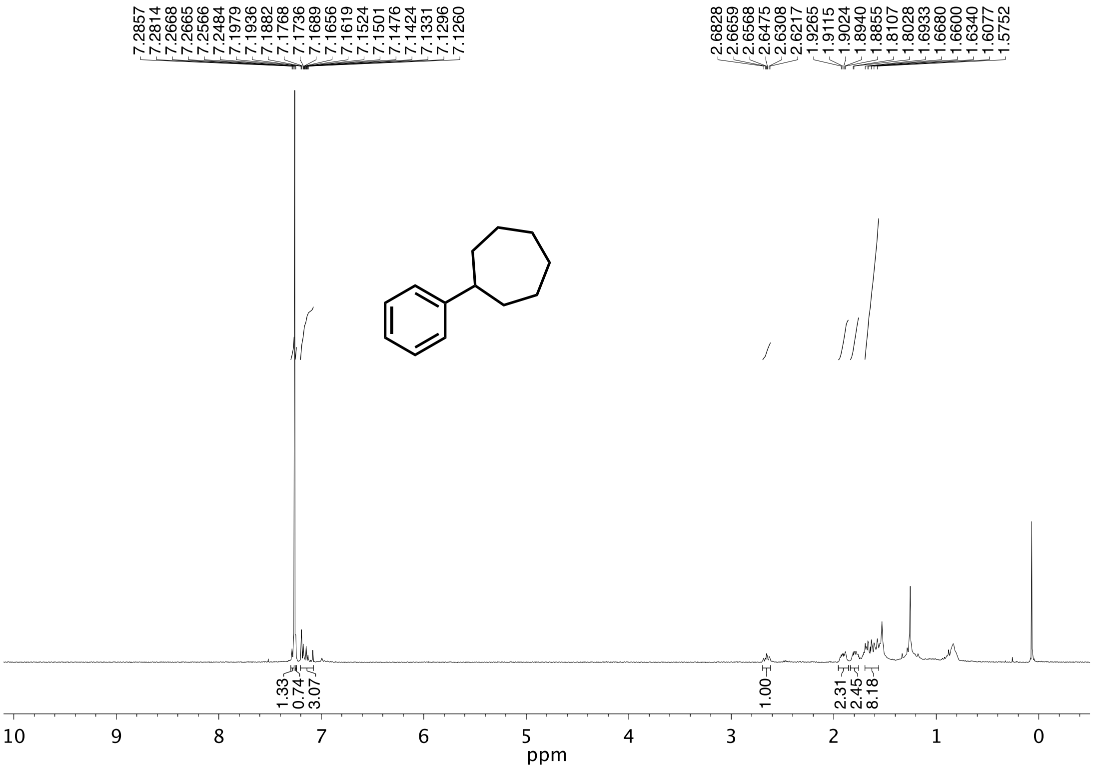


Figure 2.71 ^{1}H NMR (500 MHz, $CDCl_3$) of **2.72**.

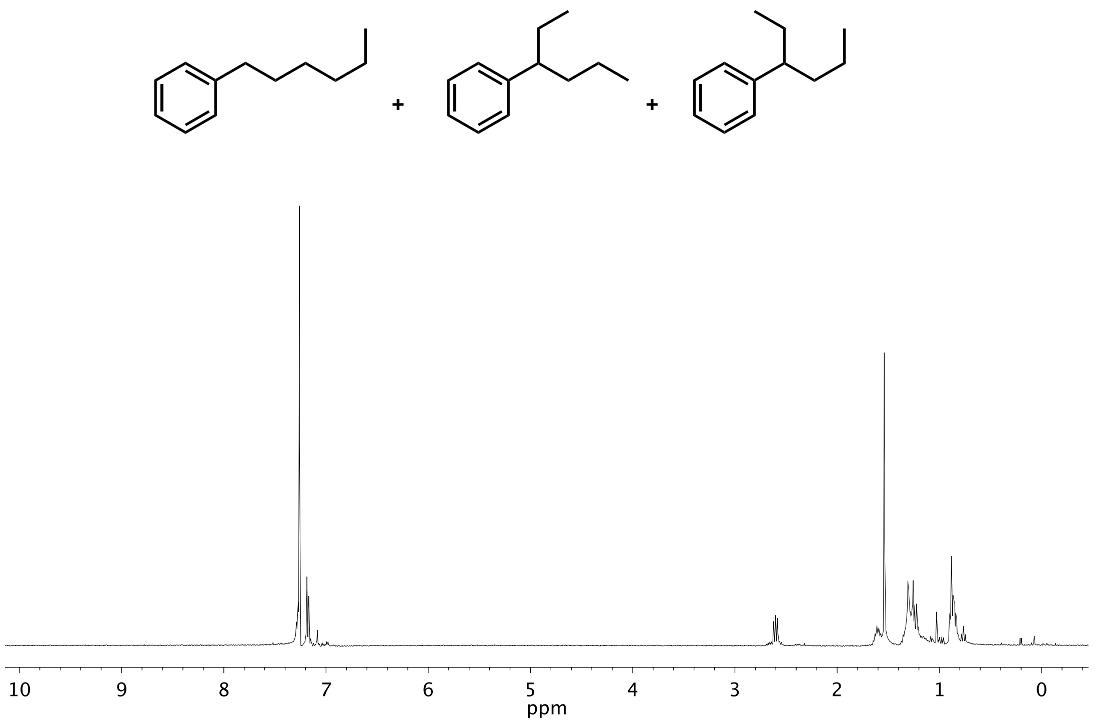


Figure 2.72 ^{1}H NMR (500 MHz, $CDCl_3$) of **2.73, 2.74** and **2.75**.

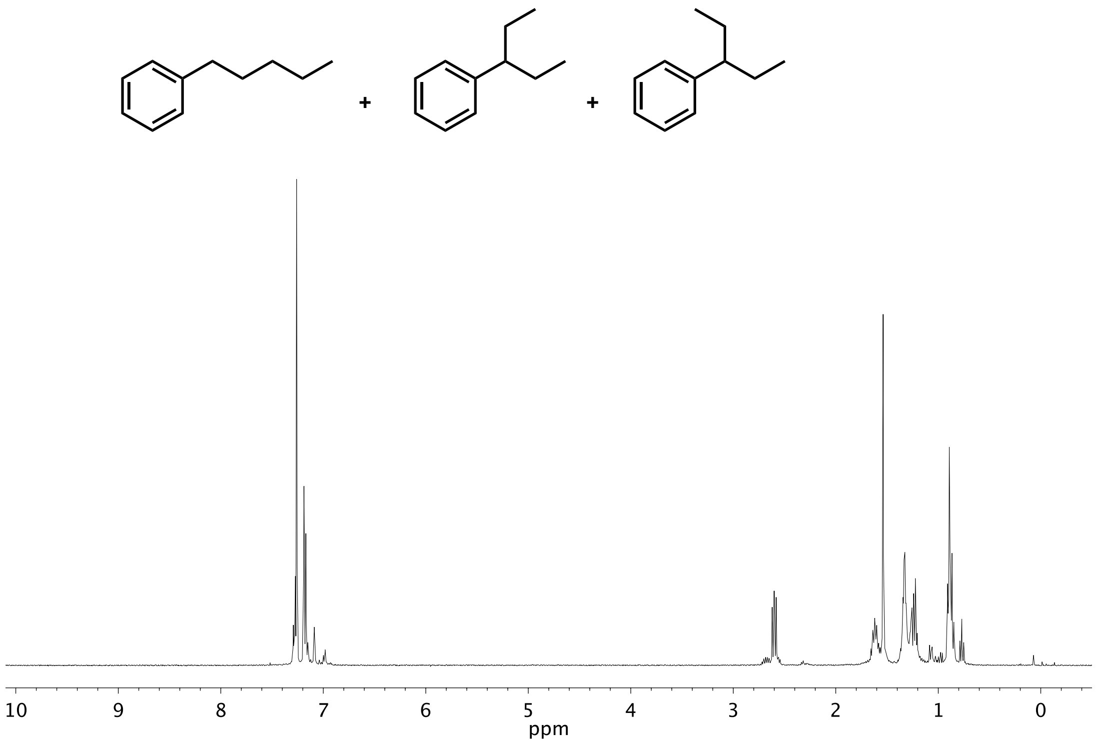


Figure 2.73 ^{1}H NMR (500 MHz, $CDCl_3$) of **2.76**, **2.77**, and **2.78**.

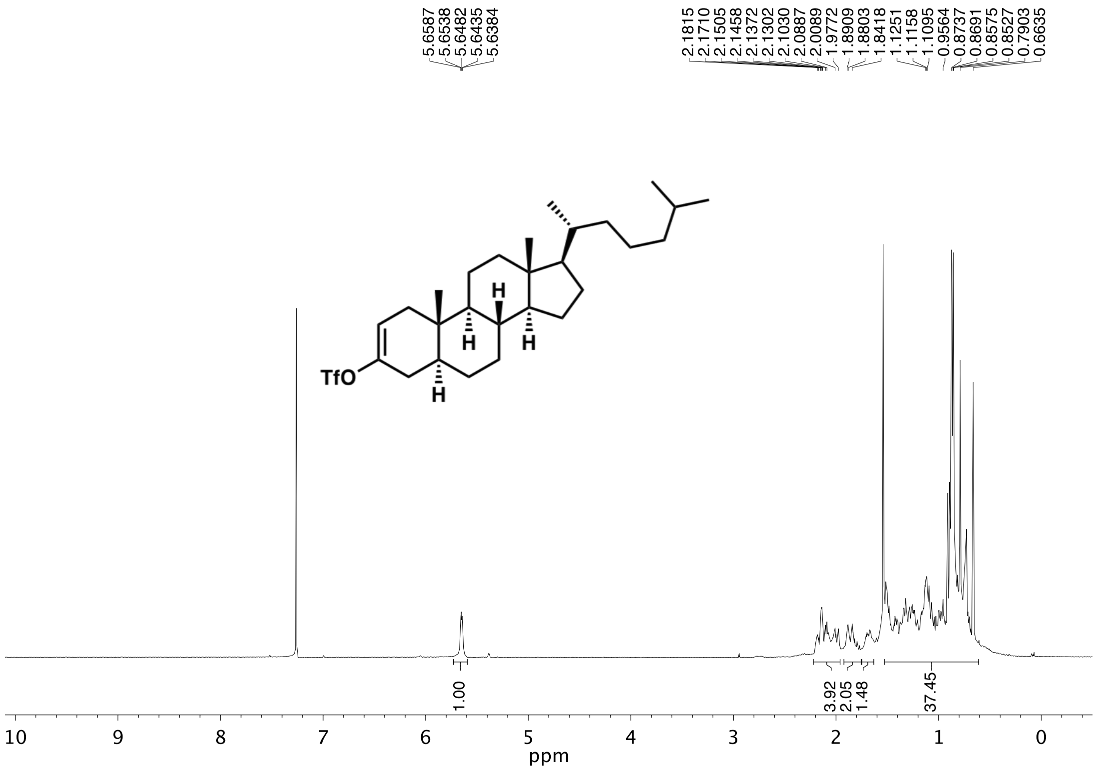


Figure 2.74 ^{1}H NMR (500 MHz, $CDCl_3$) of **2.29**.

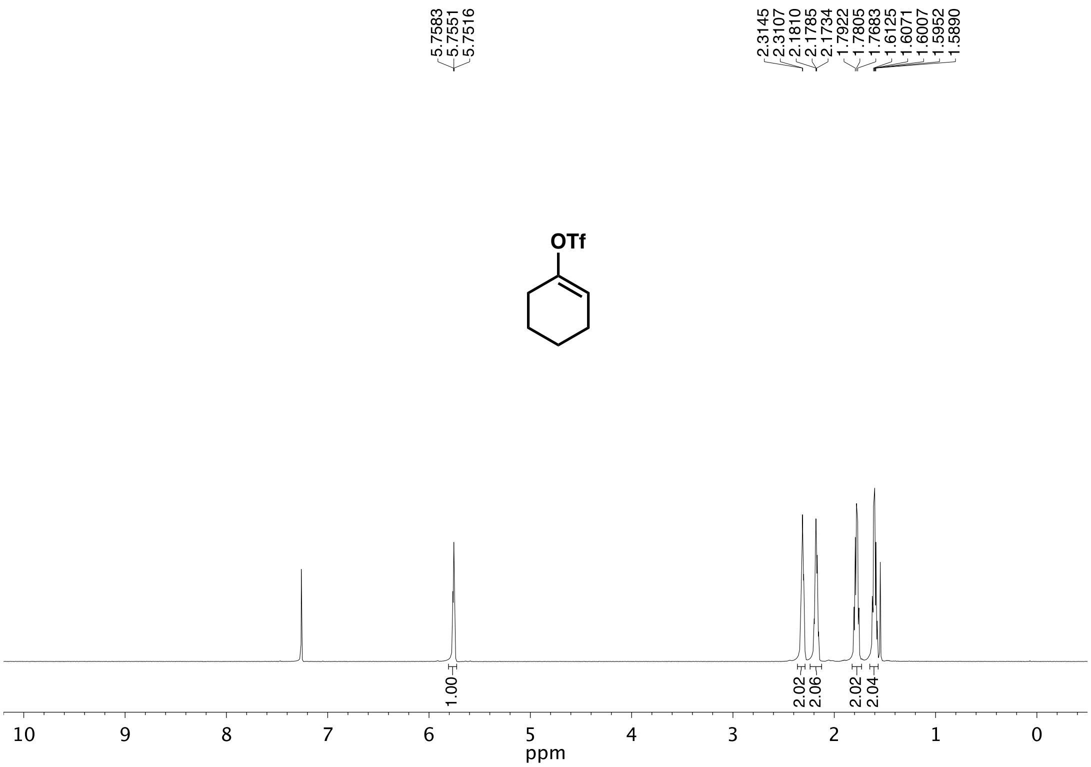


Figure 2.75 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.23**.

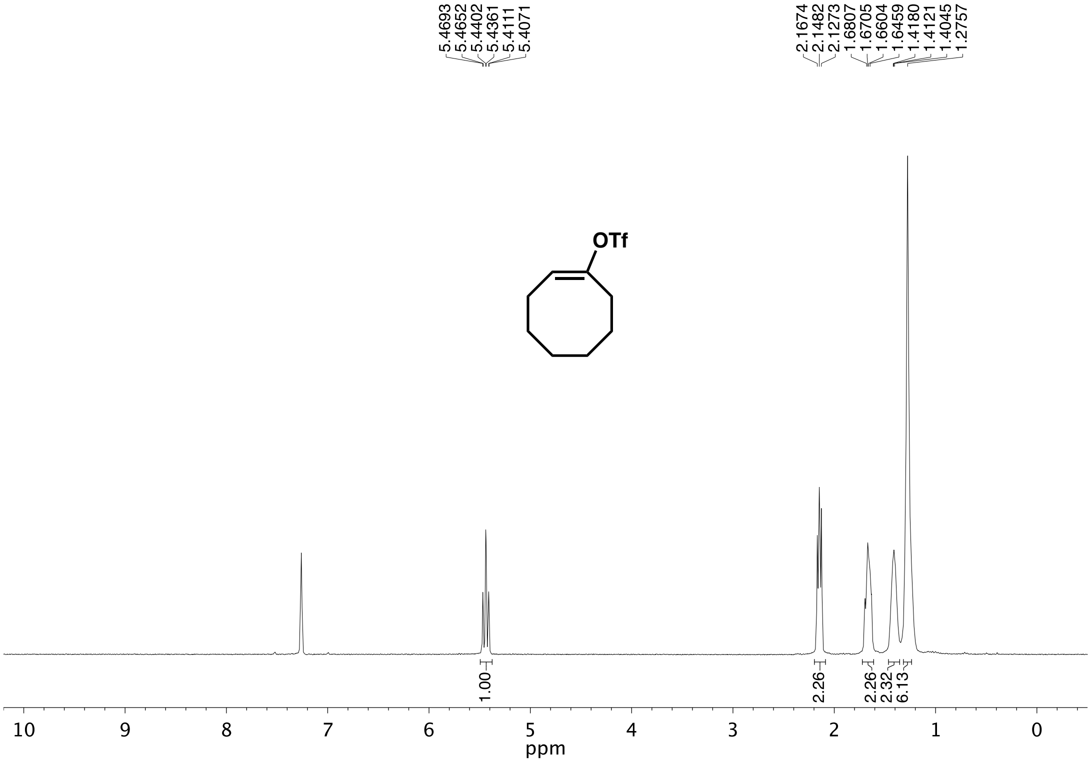


Figure 2.76 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.31**.

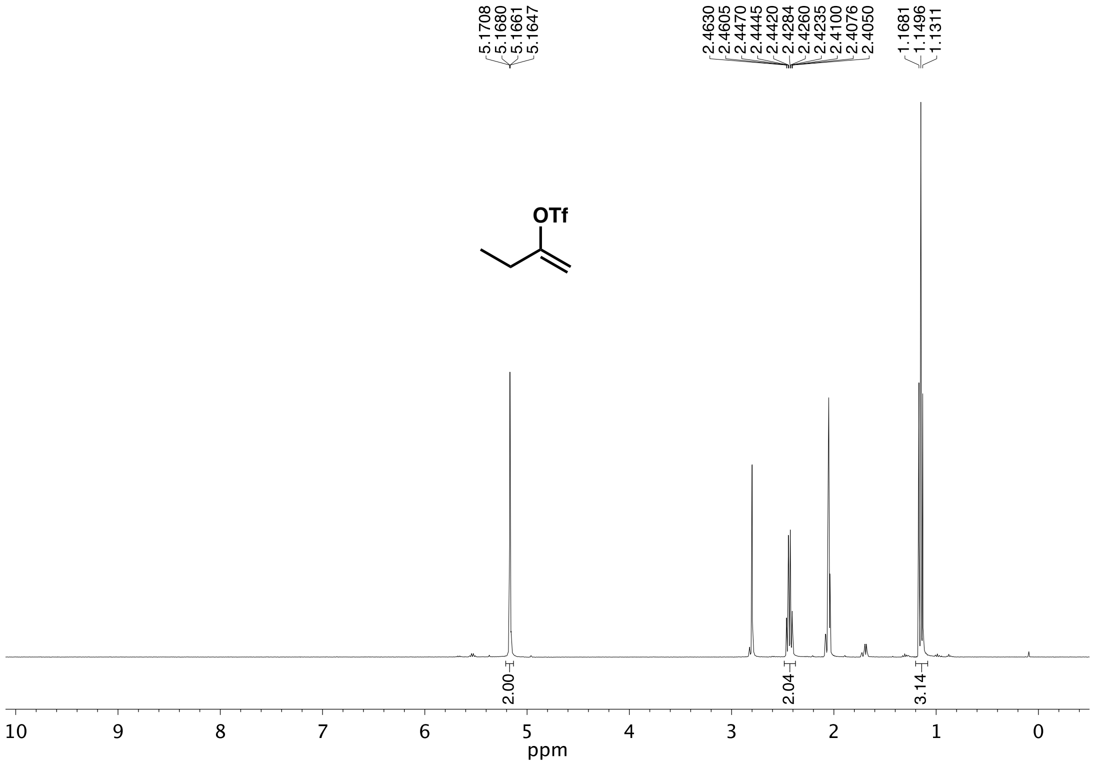


Figure 2.77 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.35**.

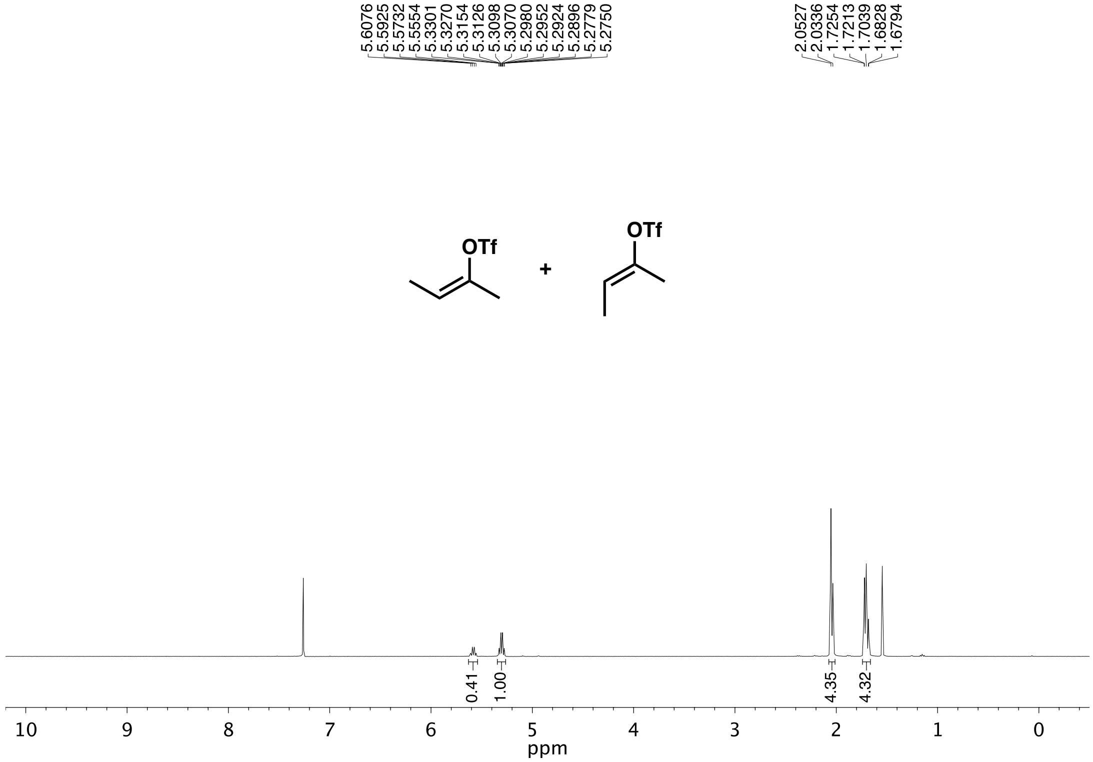


Figure 2.78 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.33**.

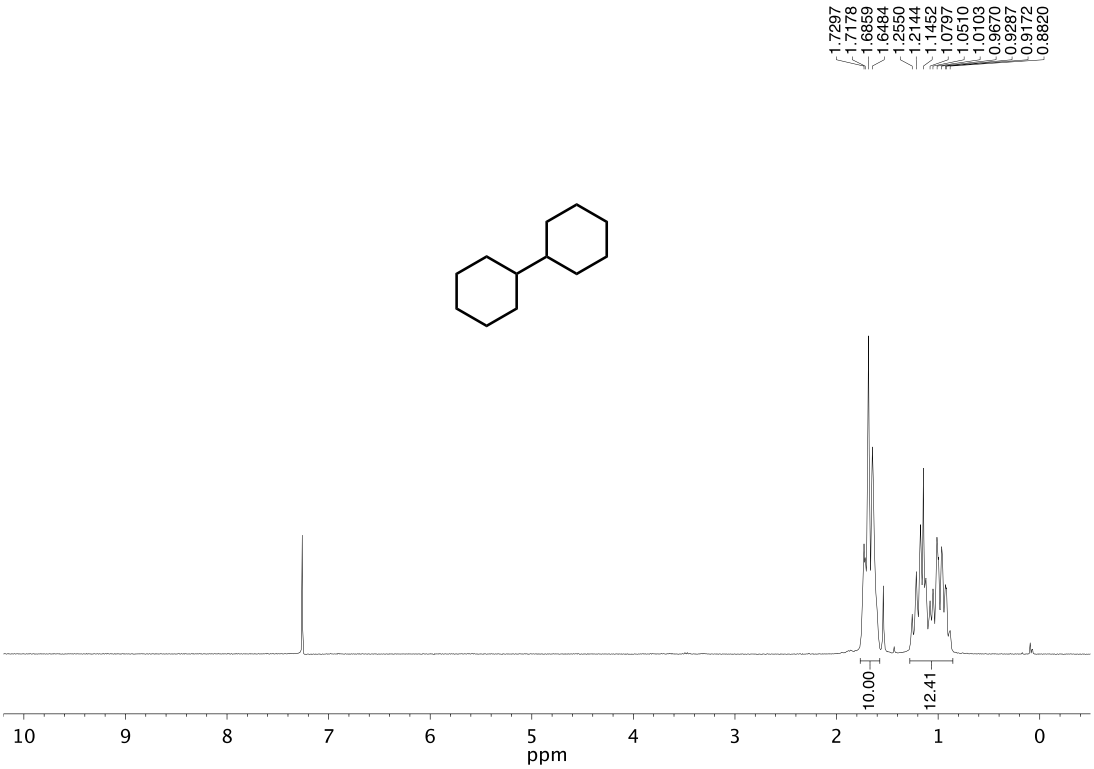


Figure 2.79 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.28**.

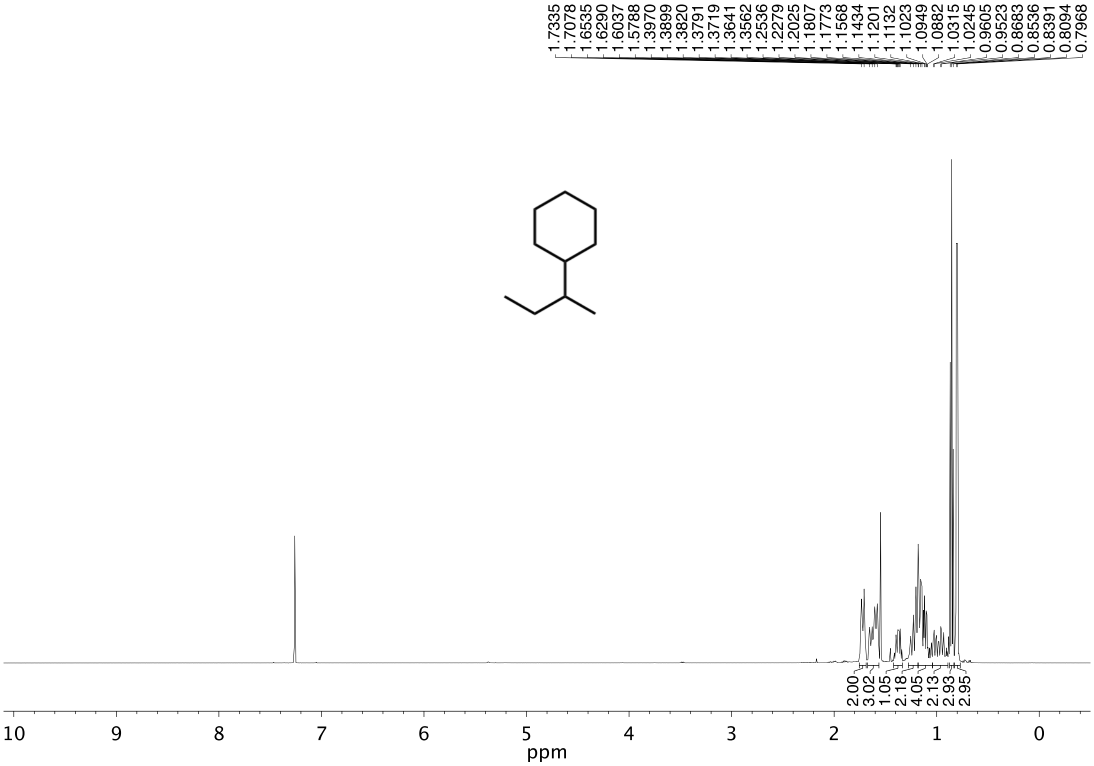


Figure 2.80 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.34**.

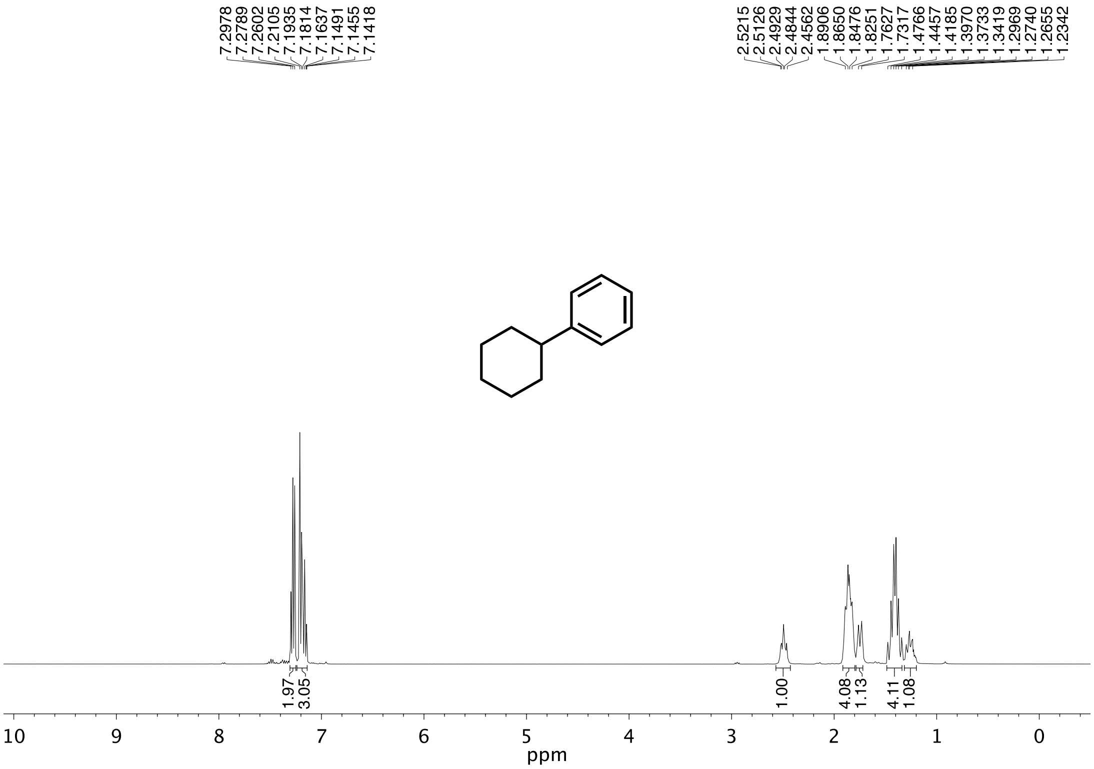


Figure 2.81 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.41**.

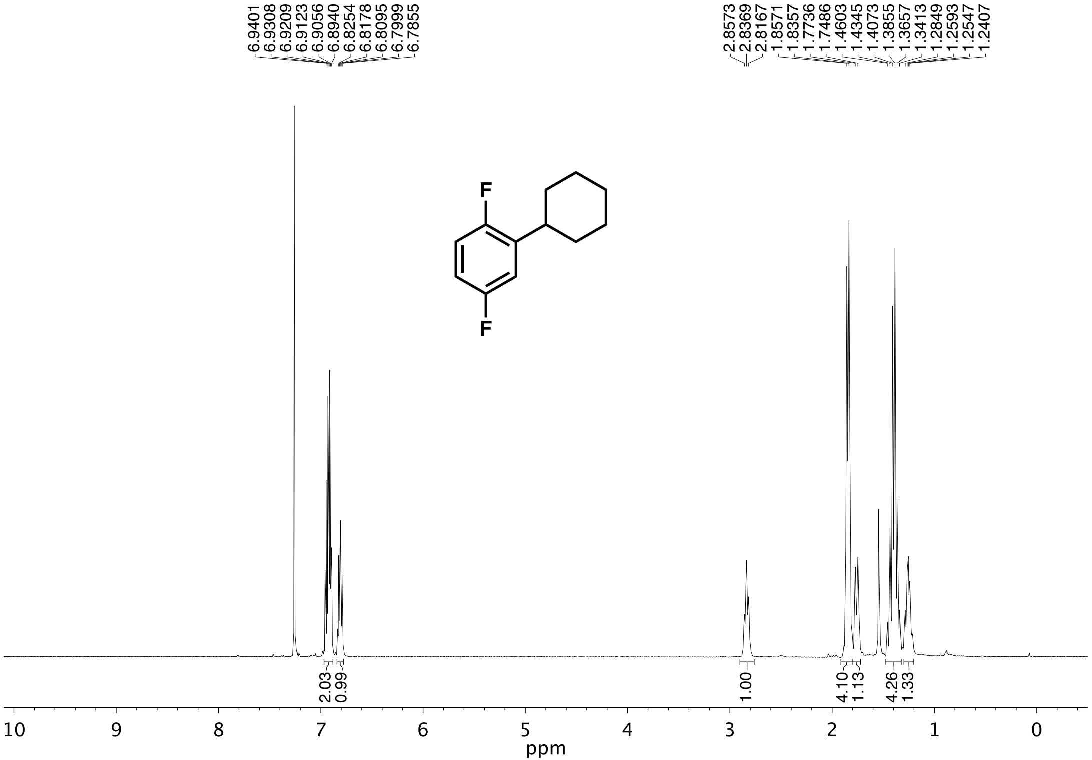


Figure 2.82 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.42**.

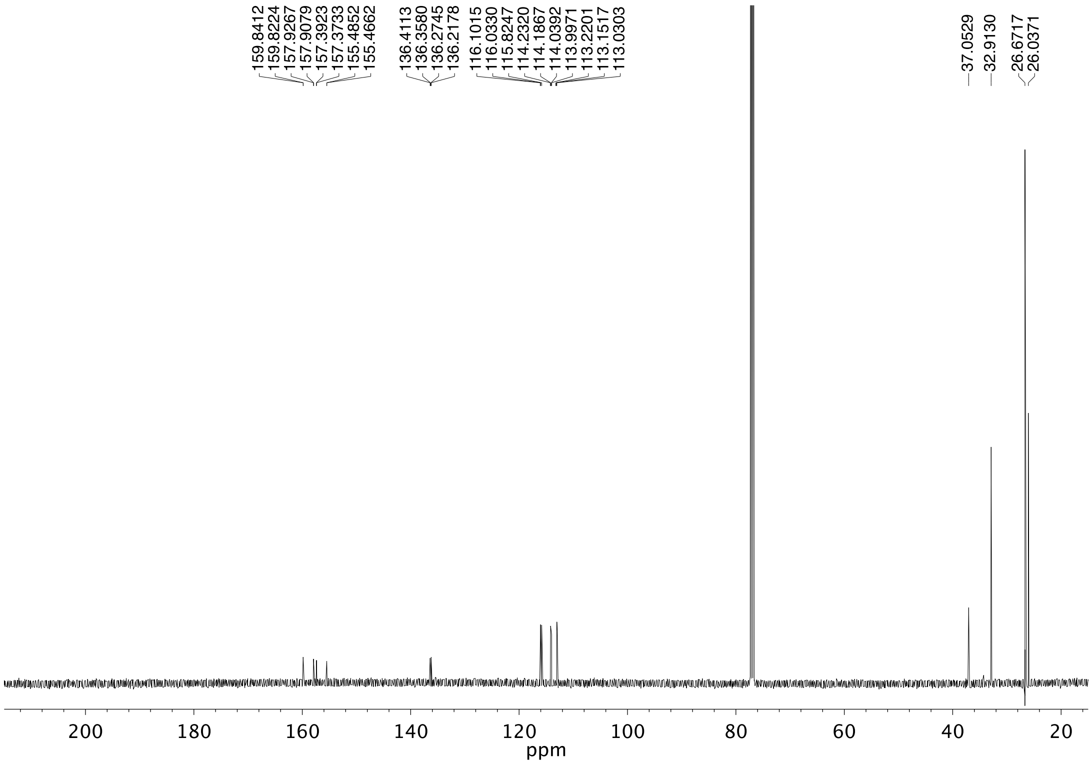


Figure 2.83 ^{13}C NMR (100 MHz, $CDCl_3$) of **2.42**.

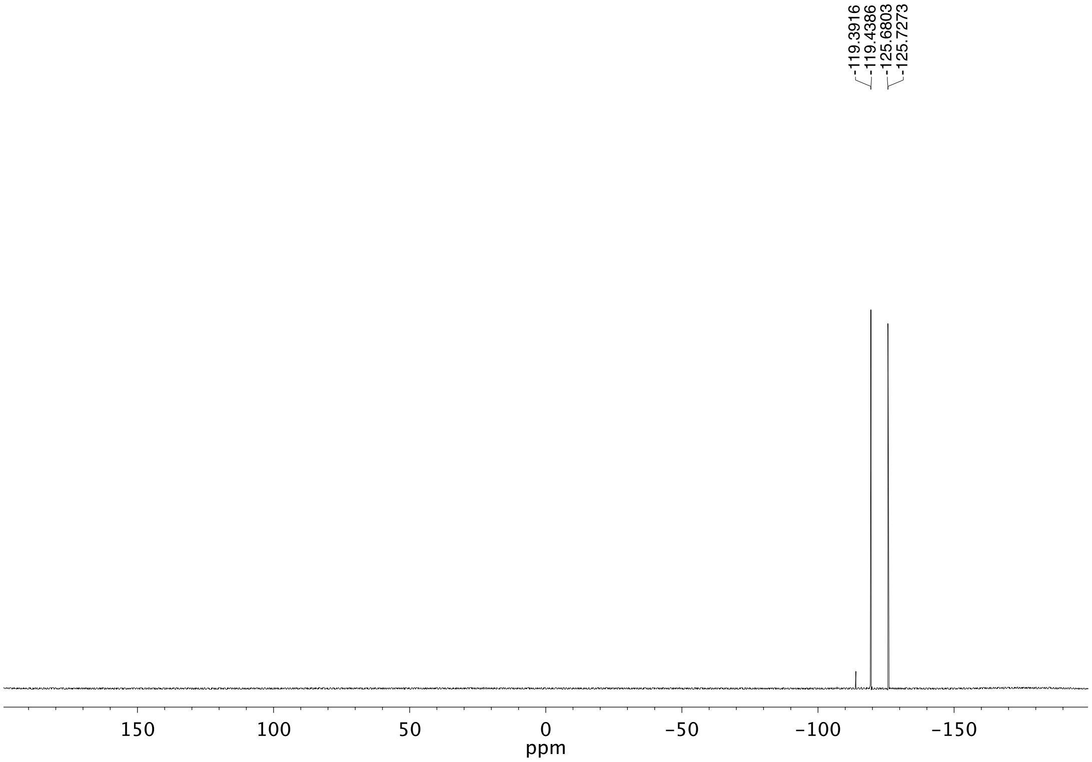


Figure 2.84 ^{19}F NMR (282 MHz, $CDCl_3$) of **2.42**.

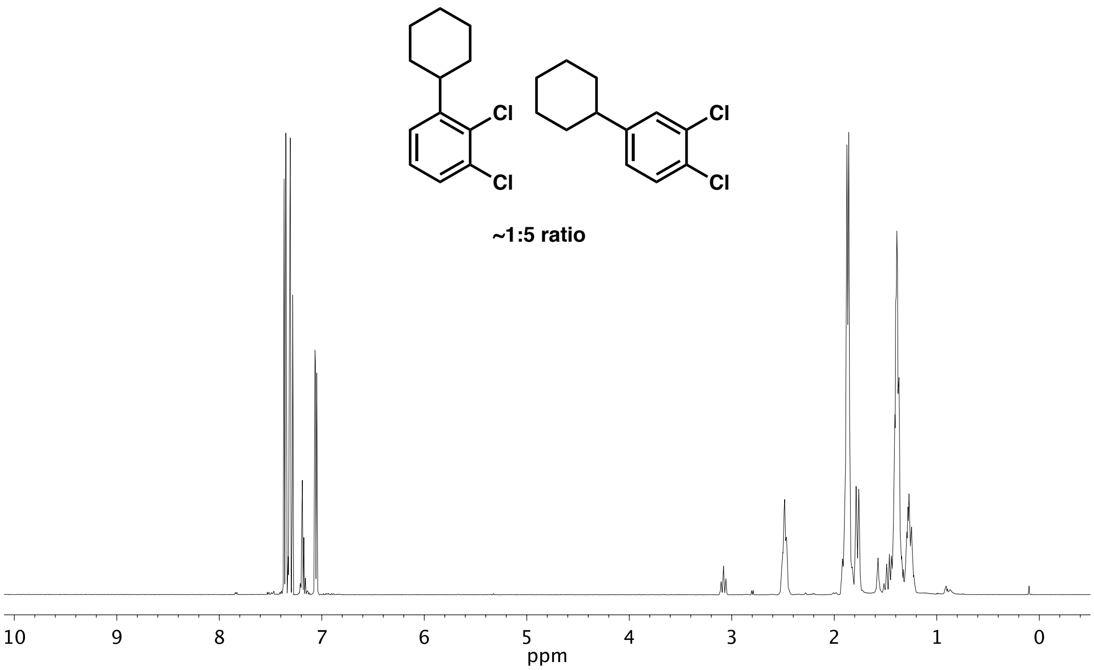


Figure 2.85 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.43**.

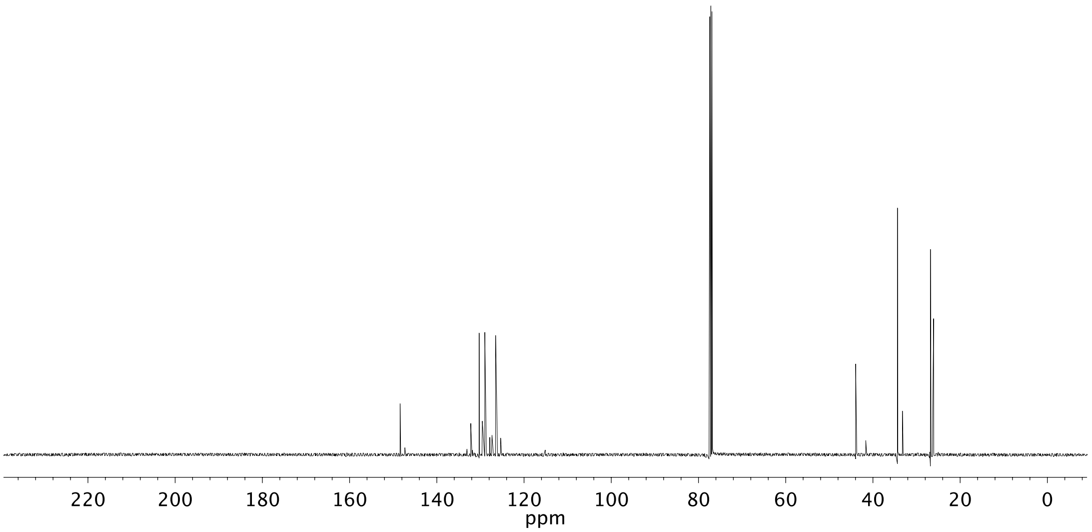


Figure 2.86 ^{13}C NMR (100 MHz, CDCl$_3$) of **2.43**.

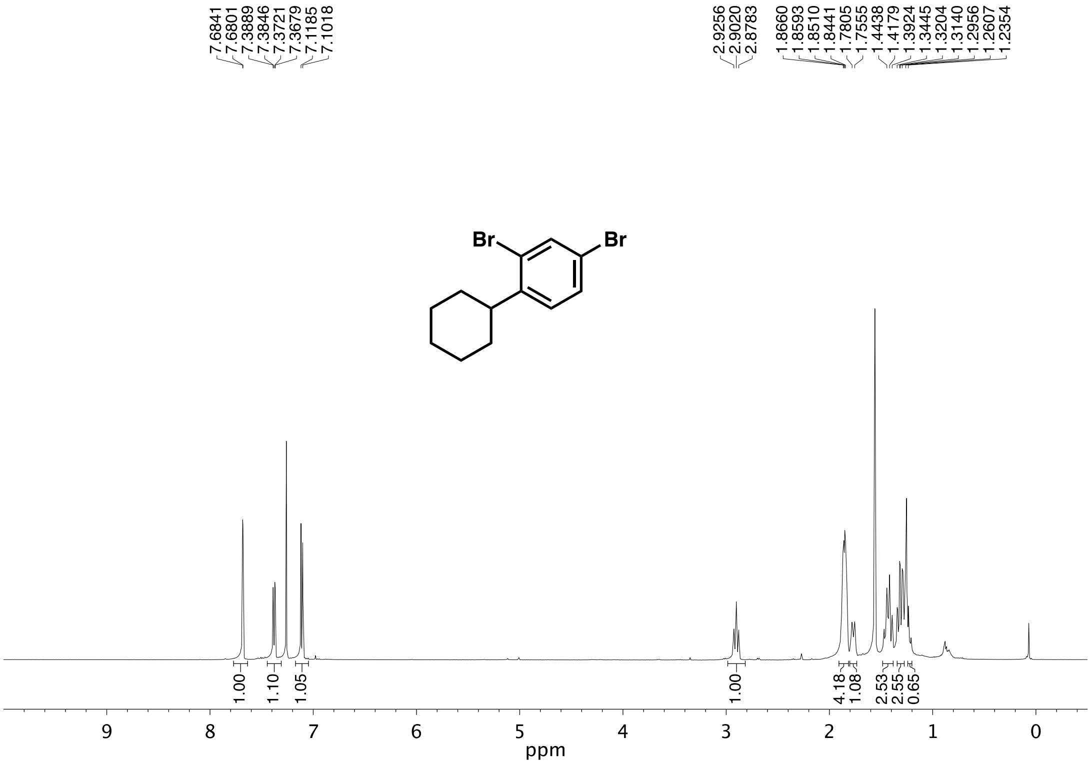


Figure 2.87 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.44**.

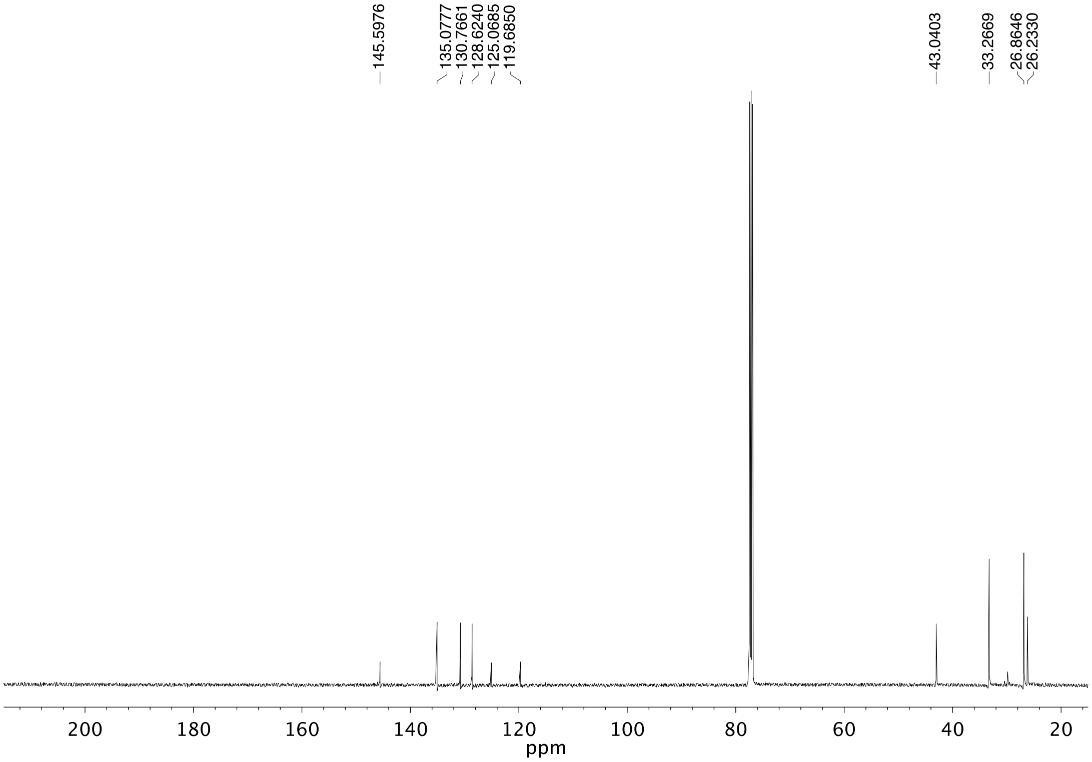


Figure 2.88 ^{13}C NMR (100 MHz, $CDCl_3$) of **2.44**.

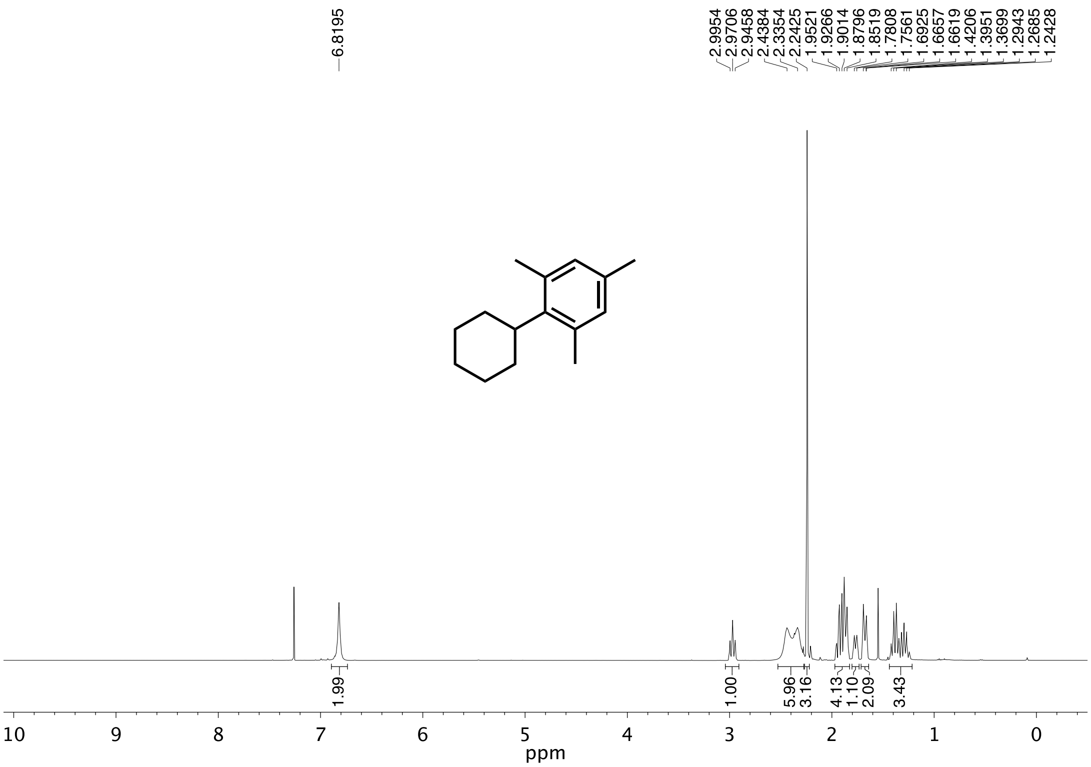


Figure 2.89 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.46**.

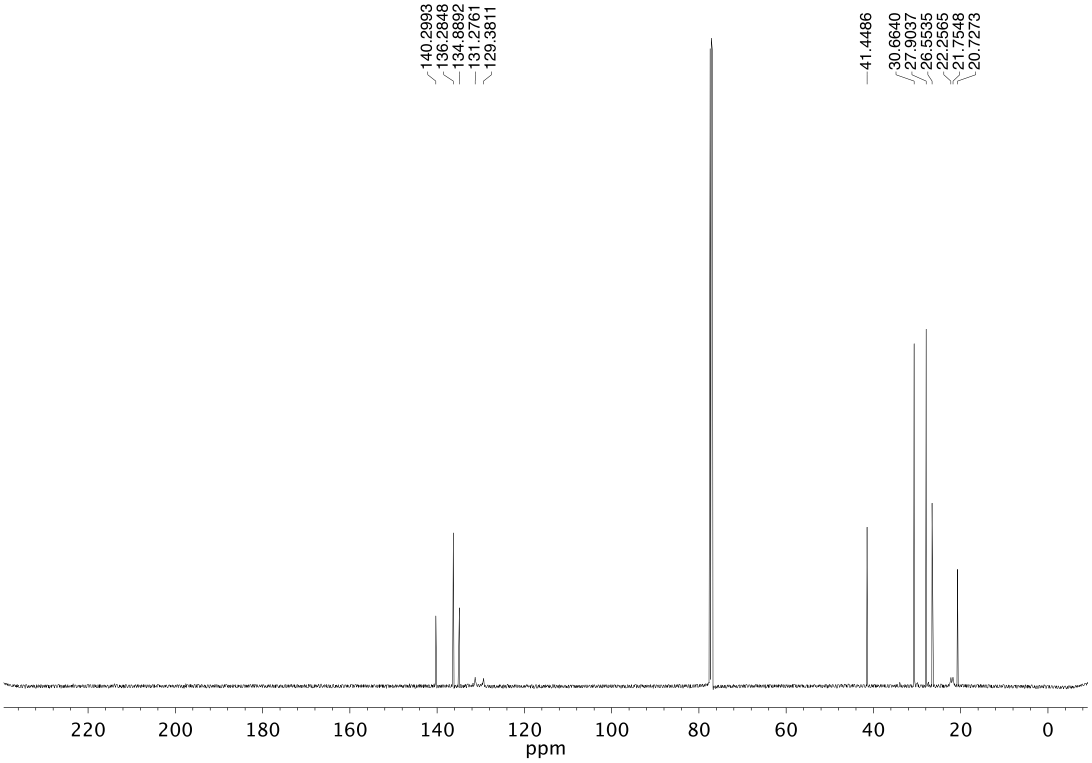


Figure 2.90 ^{13}C NMR (100 MHz, CDCl$_3$) of **2.46**.

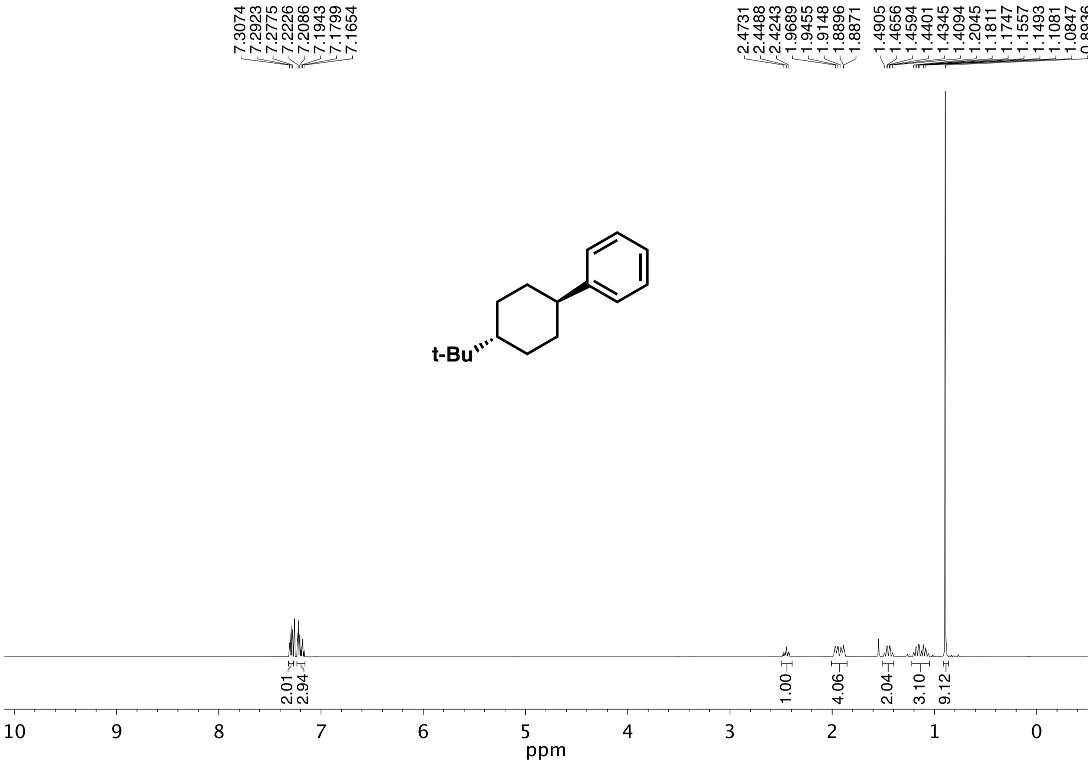


Figure 2.91 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.49**.

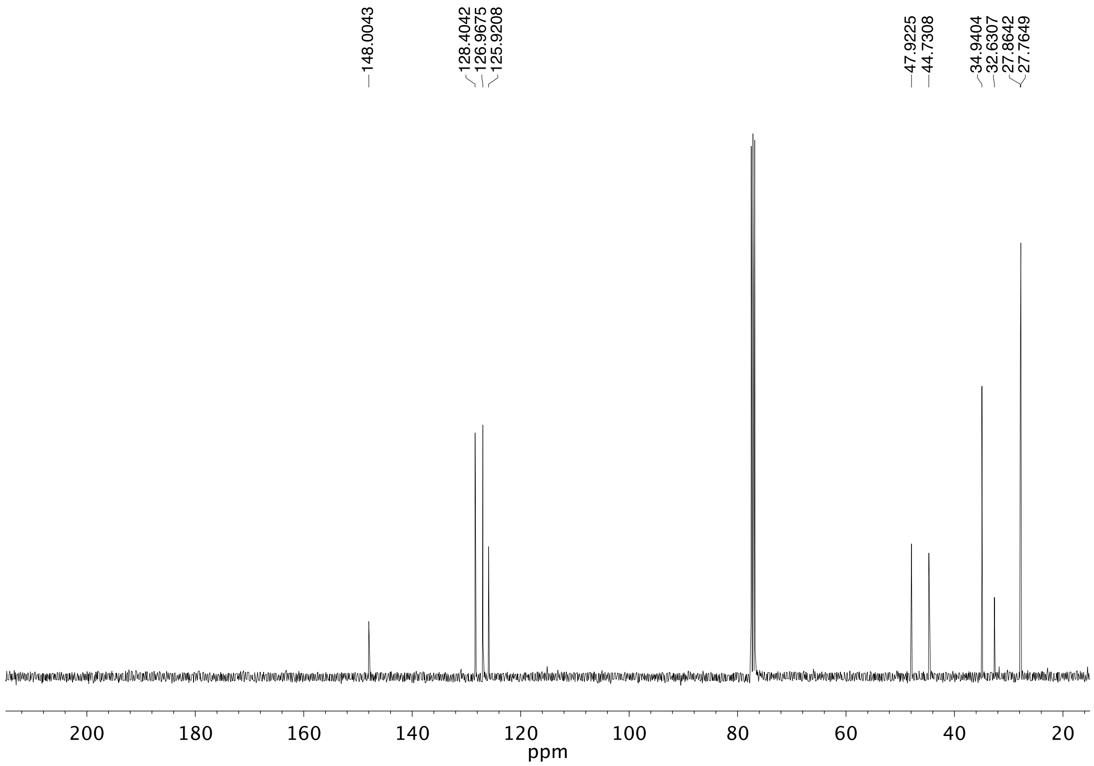


Figure 2.92 ^{13}C NMR (100 MHz, $CDCl_3$) of **2.49**.

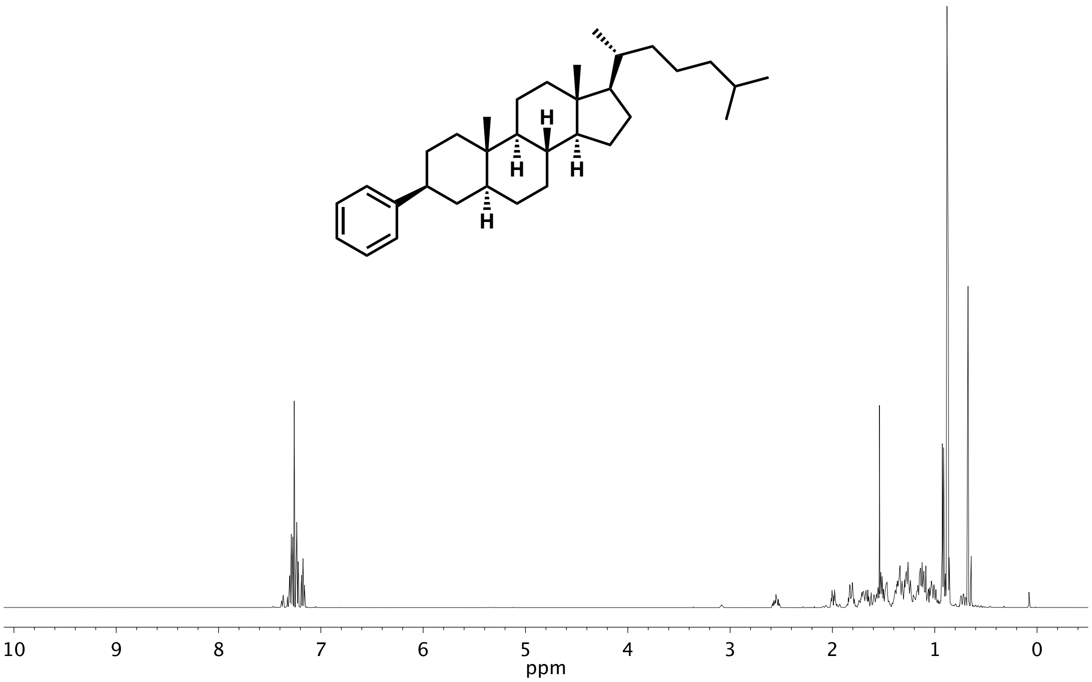


Figure 2.93 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.50**.

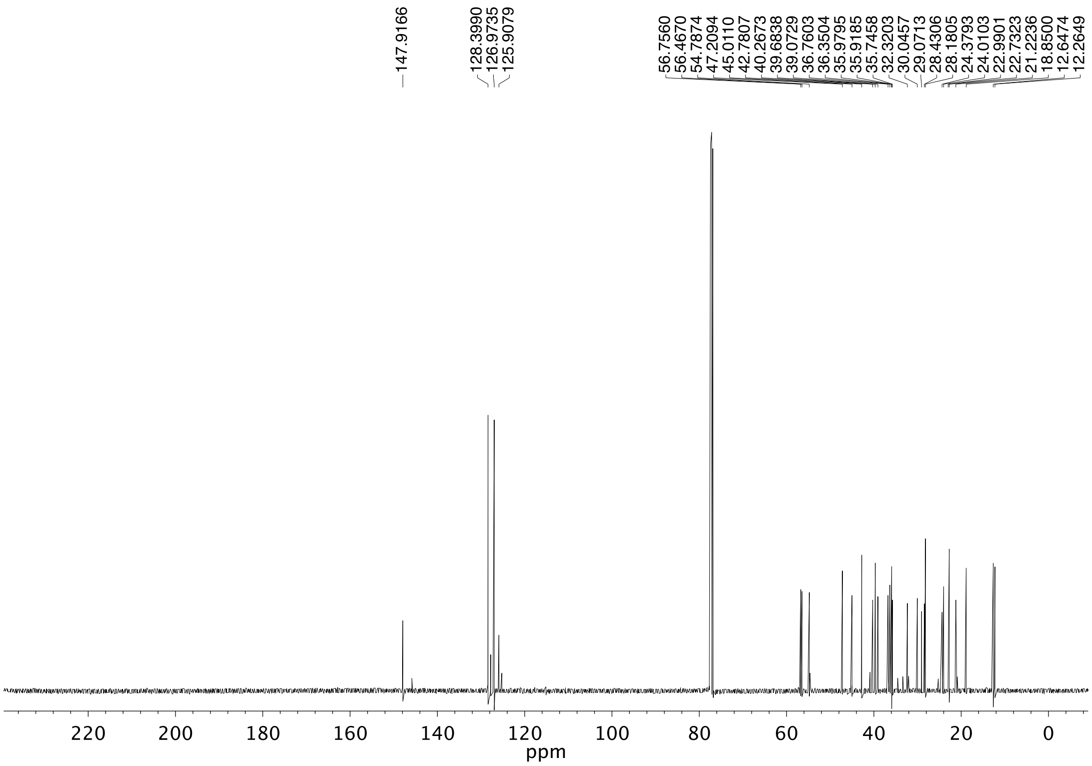


Figure 2.94 ^{13}C NMR (100 MHz, CDCl$_3$) of **2.50**.

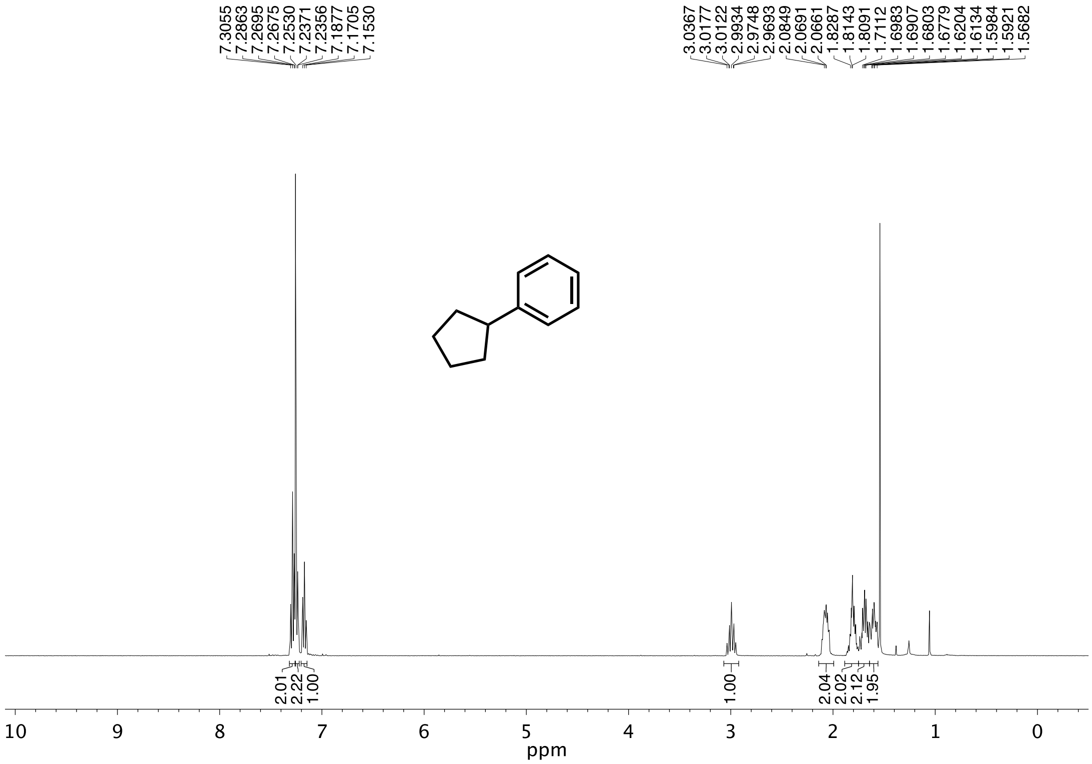


Figure 2.95 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.51**.

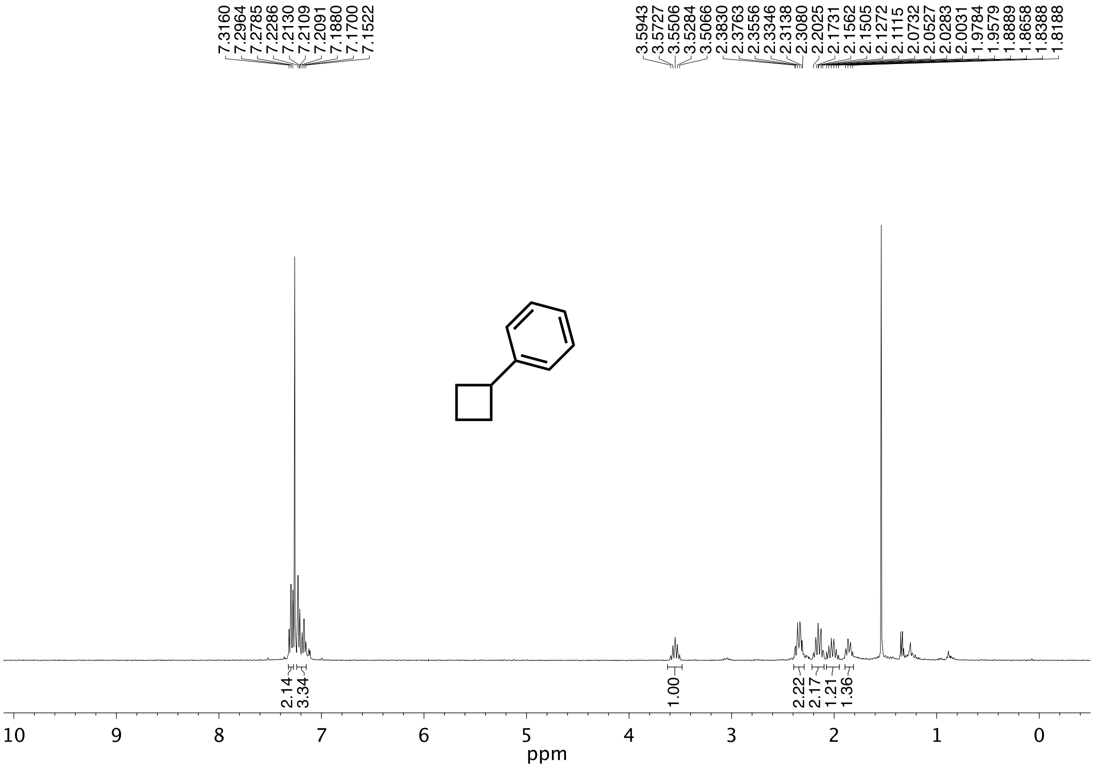


Figure 2.96. ^{1}H NMR (400 MHz, CDCl$_3$) of **2.53**.

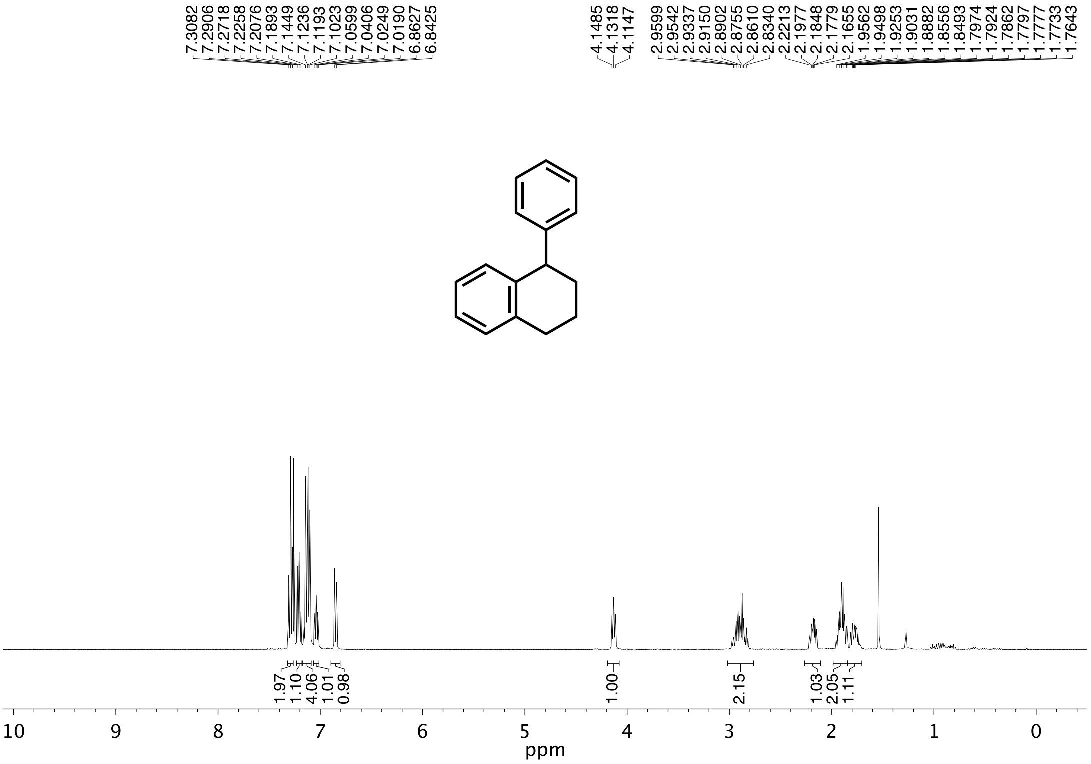


Figure 2.97 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.54**.

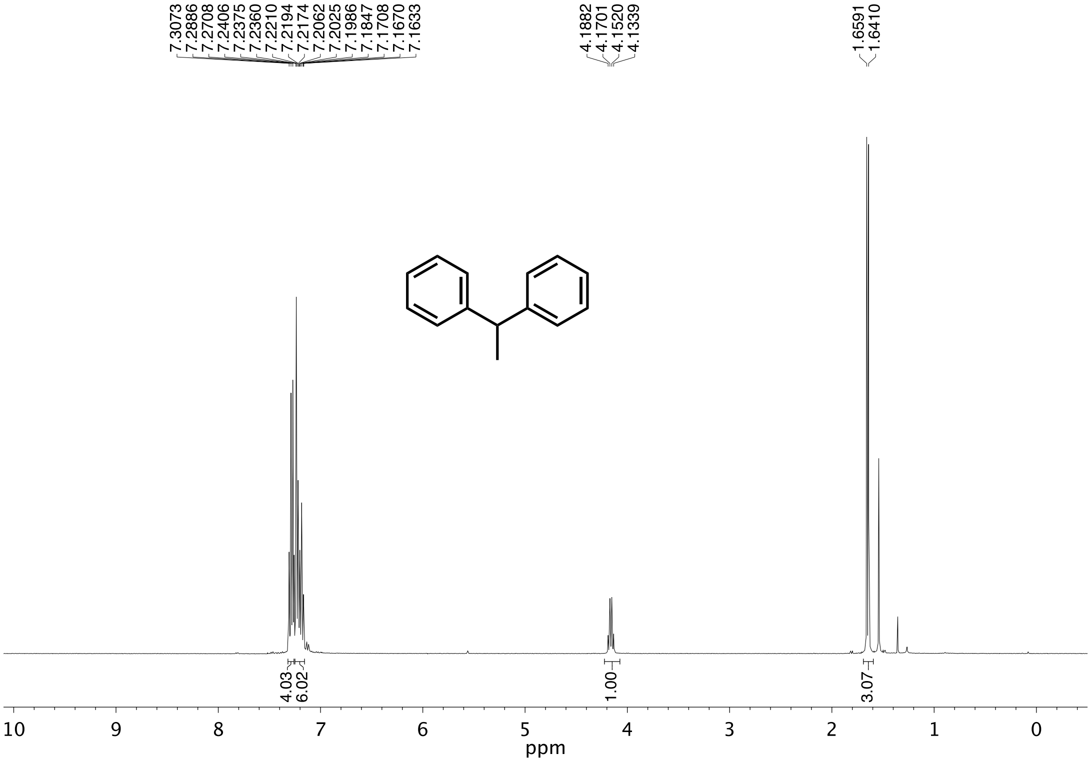


Figure 2.98 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.55**.

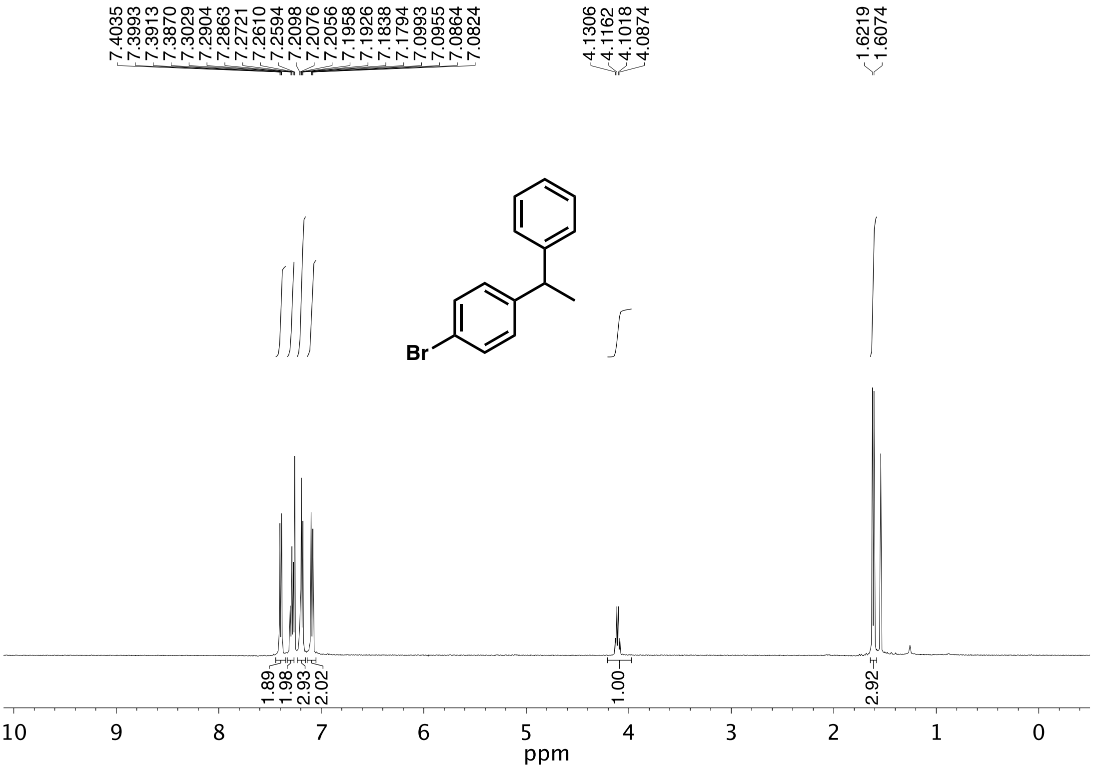


Figure 2.99 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.56**.

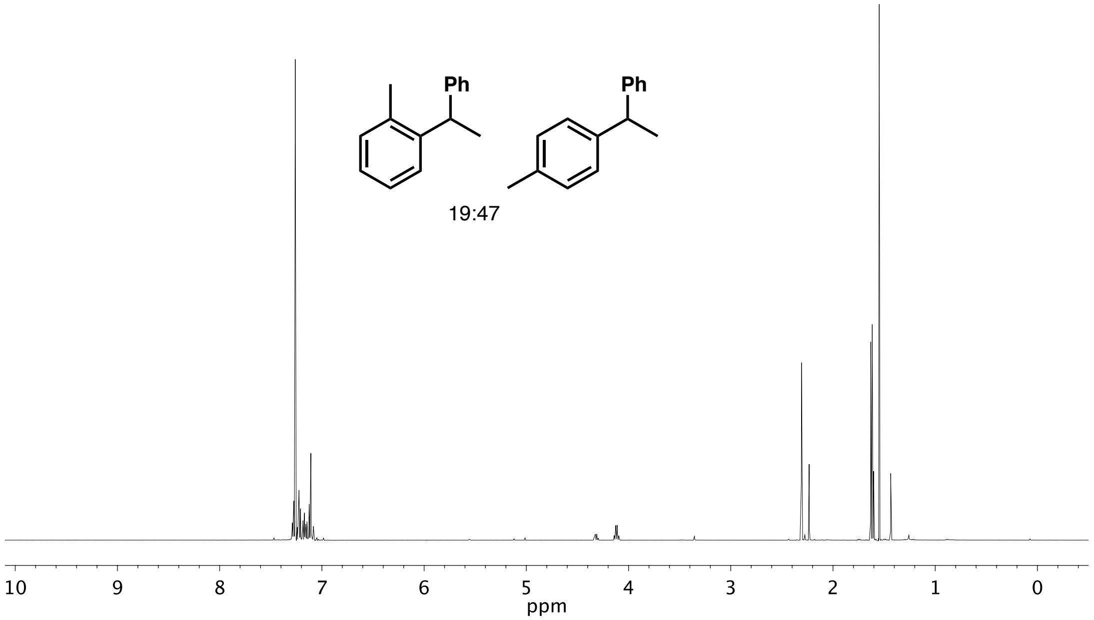


Figure 2.100 ^{1}H NMR (400 MHz, $CDCl_3$) of **2.57**.

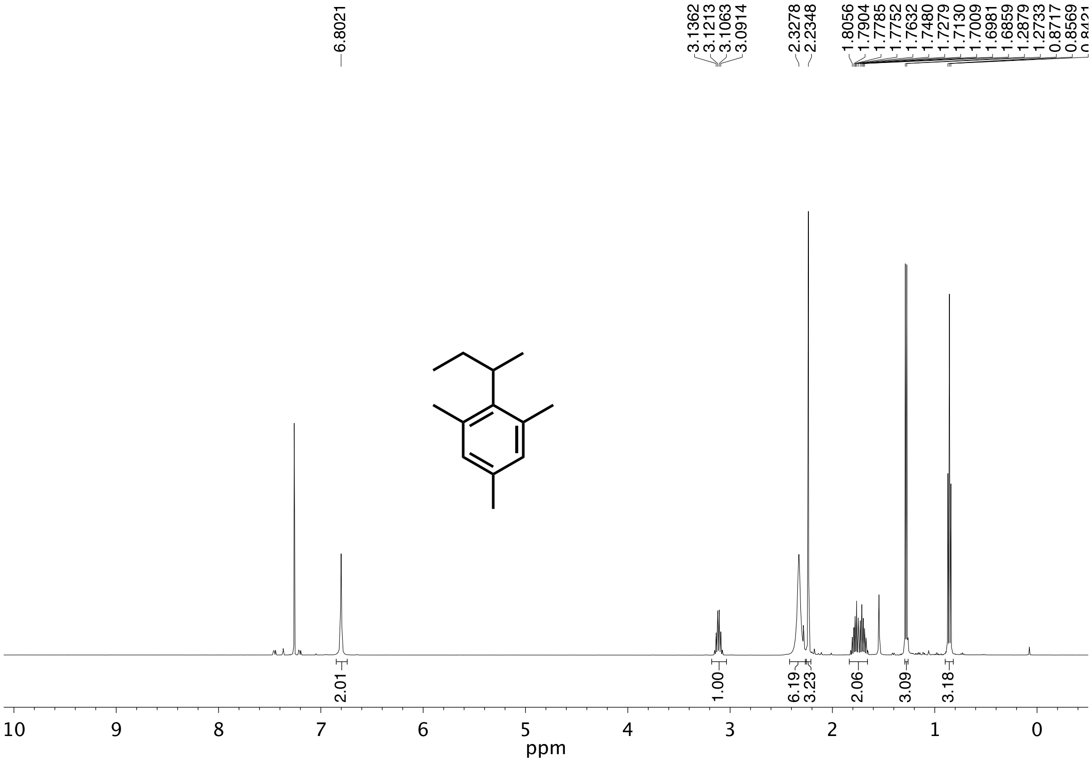


Figure 2.101. ^{1}H NMR (400 MHz, CDCl$_3$) of **2.58**.

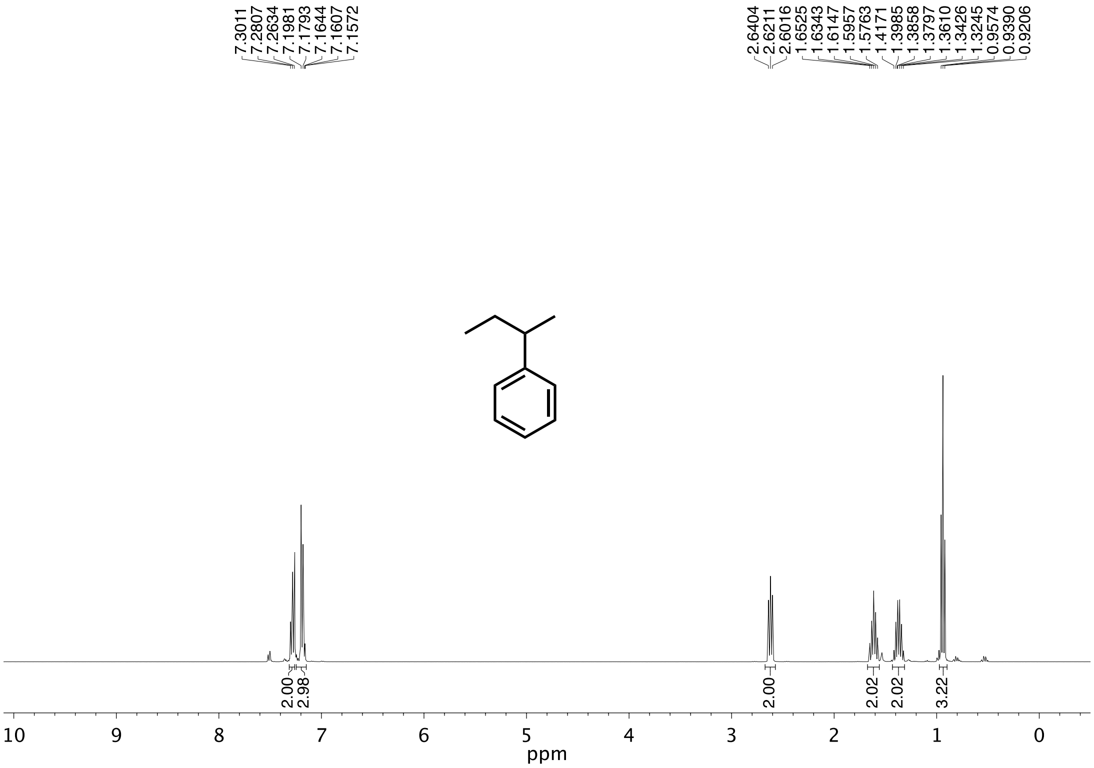


Figure 2.102 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.59**.

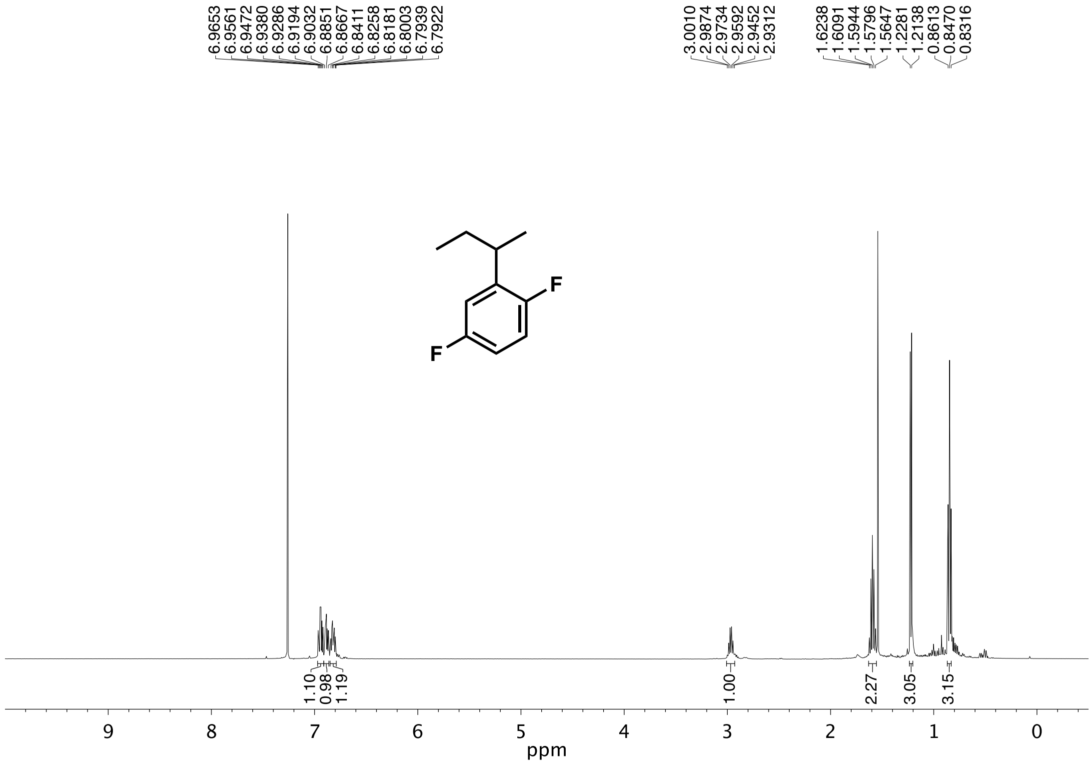


Figure 2.103 ^{1}H NMR (400 MHz, CDCl$_3$) of **2.60**.

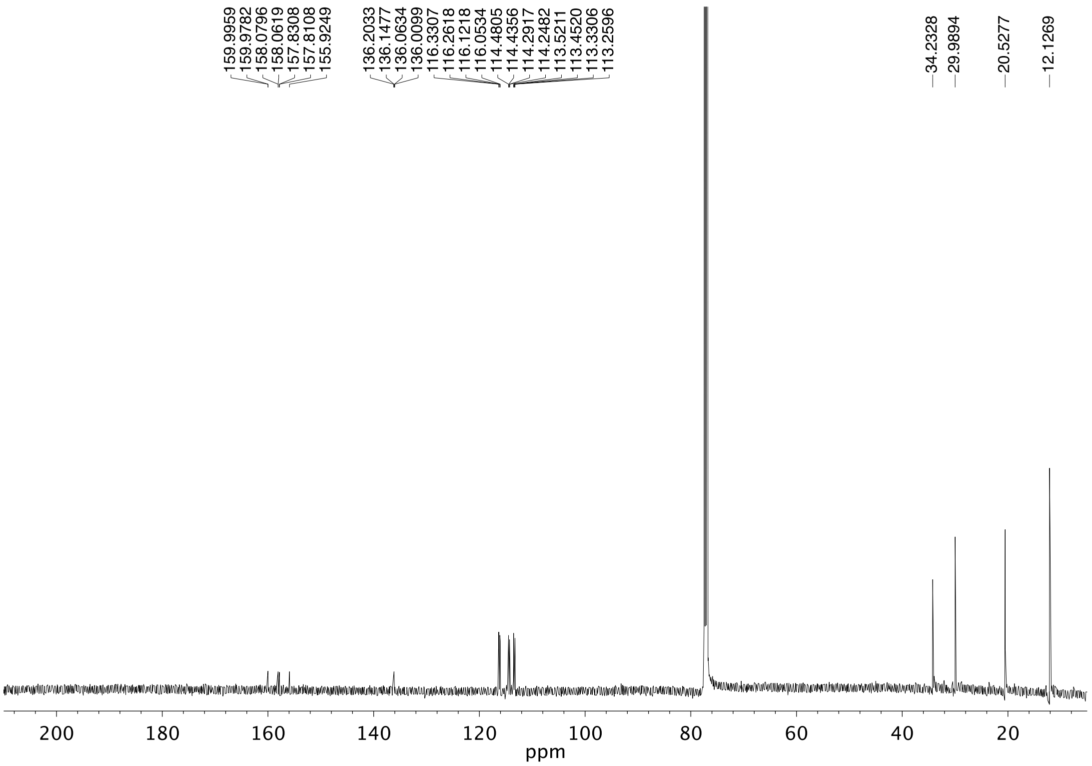


Figure 2.104. ^{13}C NMR (125 MHz, CDCl$_3$) of **2.60**.

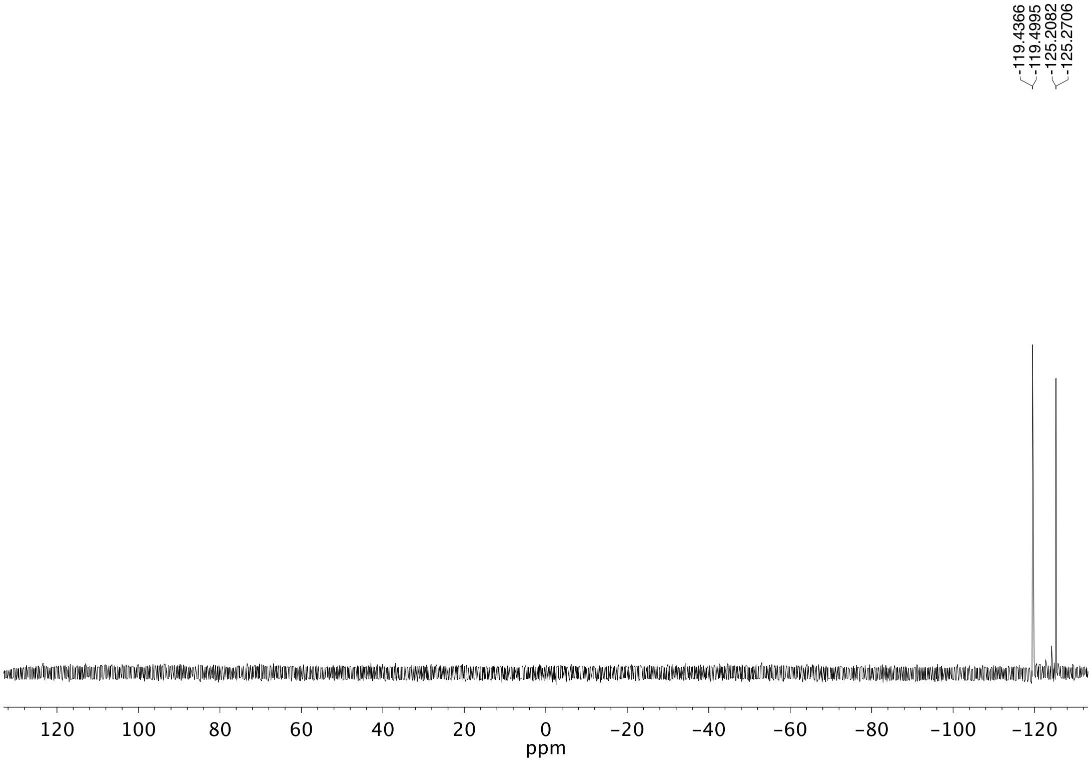


Figure 2.105 ^{19}F NMR (282 MHz, $CDCl_3$) of **2.60**.

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CHAPTER THREE

Lithium Lewis Acid Generation of Vinyl Cations and their Intramolecular C–H Insertion and Intermolecular Friedel-Crafts Reactions

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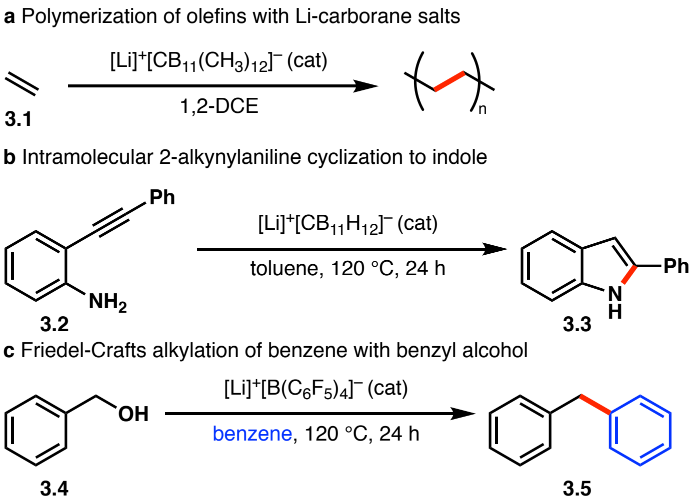
3.1 Abstract

Here we report the surprising discovery that high-energy vinyl carbocations can be generated under strongly basic conditions, and that they engage in intramolecular sp^3 C–H insertion reactions in the presence of catalytic quantities of commercially available electron deficient borate salts or easily accessible, benchtop stable 3,5-bistrifluoromethylphenyl urea species. This approach relies on the unconventional combination of lithium hexamethyldisilazide base and triphenylmethylium tetrakis(pentafluorophenyl)borate (TrF_{20}) or urea catalyst. These reagents form a catalytically active lithium species that is Lewis acidic enough to ionize strong C–O bonds. This enables the application of vinyl cation C–H insertion reactions to heteroatom-containing substrates, and expands upon the synthetic utility of vinyl cation C–C bond forming reactions.

3.2 Introduction

Through a multitude of both synthetic and experimental studies, carbocations have played a large role in the development of modern organic chemistry.[1,2] Such species, which contain an electron deficient, positively charged carbon center, are typically generated under Brønsted acidic or Lewis acidic conditions.[3–5] This mode of generation is popular for all different types of carbocations, including vinyl cations.[6–8] While Brønsted acidic and highly oxidizing "magic acid," and potent electrophiles, like silylium ions, are useful in generating such reactive carbocations for the conversion of hydrocarbons, they hinder the application of these strategies in the syntheses of heteroatom-rich complex molecules, such as those utilized for materials and pharmaceuticals.[8–10] These limitations were evident in our own studies as well (see Chapter 2). In order to overcome these challenges, we desired to find a mode of ionization that did not rely on the hyper-electrophilic silylium ion.


a Polymerization of olefins with Li-carborane salts

b Intramolecular 2-alkynylaniline cyclization to indole

c Friedel-Crafts alkylation of benzene with benzyl alcohol

Figure 3.1 Previous application of Li-Lewis acids for cation generation

We were inspired by work from Michl and Uchiyama that showed how lithium cations were powerful enough Lewis acids to activate alkenes, alkynes and alcohols.[11–13] Michl was able to apply Li-carborane salts to promote electrophilic radical polymerizations of simple olefins **3.1** (Figure 3.1a).[11] Uchiyama and coworkers showed that Li-carborane salts are strong π-acids and can promote Larock type cyclization of 2-alkynylanilines **3.2** to give indole products **3.3** (Figure 3.1b).[13] Furthermore, they also showed that lithium tetrakis(pentafluorophenyl)borate (LiF_{20}) could abstract a hydroxide group from benzyl alcohol (**3.4**) and the ensuing benzylic cation could undergo Friedel-Crafts trapping by benzene to give diphenylmethane (**3.5**) (Figure 3.1c).

3.3 Transannular C–H Insertion of Cyclooctenyl Triflates Under Basic Conditions

To evaluate this hypothesis, we investigated cyclooctenyl triflates (e.g. **3.6**, Figure 3.2a) that undergo facile ionization by silylium cations to form vinyl carbocations.[8] These cations subsequently engage in transannular C–H insertion reactions to generate bicyclooctane product **3.7** in excellent yield (Figure 3.2b). We postulated that nucleophilic attack of a lithium base on $[Ph_3C]^+[WCA]^-$ would yield the active $[Li]^+[WCA]^-$ catalyst (Figure 3.2a). Catalyst-mediated triflate abstraction would then afford vinyl cation **3.8**, which would undergo transannular C–H insertion to form bicyclic secondary cation **3.9**. Importantly, we envisioned that deprotonation of this cation by a lithium base would generate the desired alkene products **3.10** and concomitantly

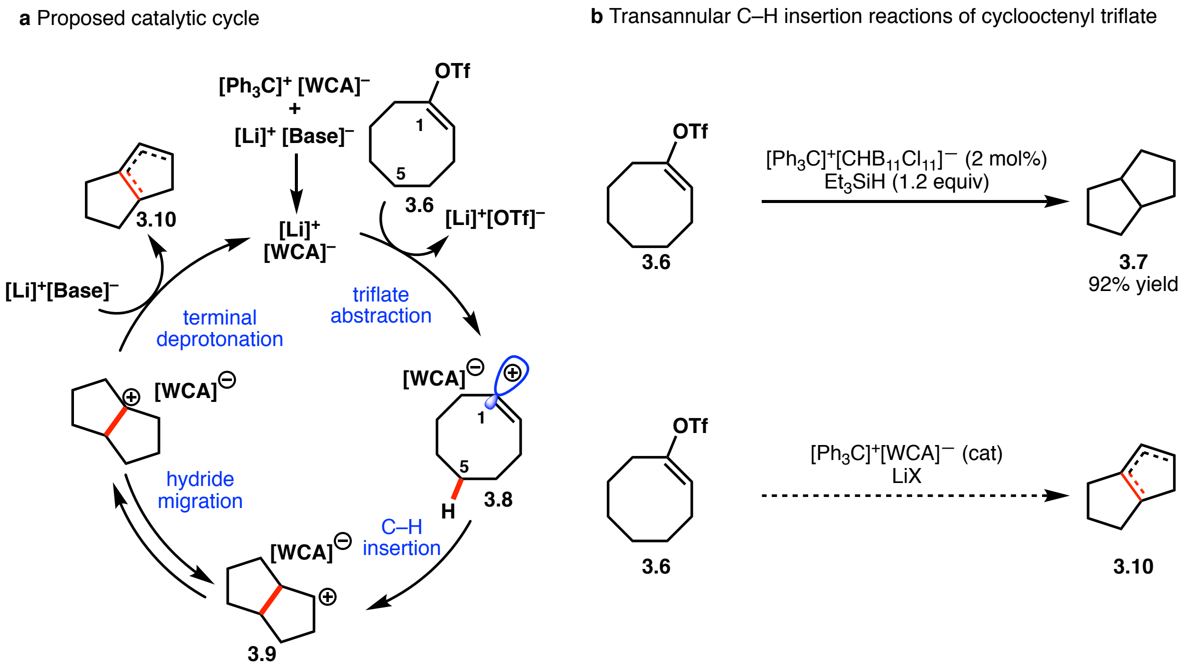
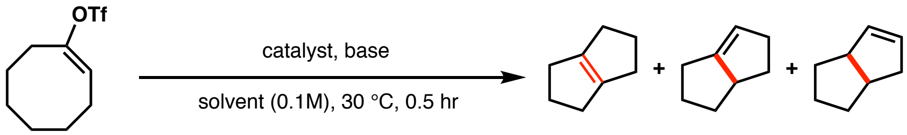


Figure 3.2 Mechanistic hypothesis of Li-WCA vinyl cation reactions (a) and reactions of cyclooctenyl triflate (b)

regenerate the active $[Li]^+[WCA]^-$ catalyst.

In early attempts, we looked at several lithium bases, trityl-WCA catalysts, and general reaction parameters in order to find a good catalytic platform. We were gratified to find that using a catalytic amount (5 mol%) of $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ and 1.5 equivalents of LiHMDS base in *o*-difluorobenzene (*o*-DFB) solvent produced a mixture of bicyclooctene products **3.10** in a combined yield of 90% (Table 3.1, entry 1). Remarkably, deleterious nucleophilic quenching or elimination products were not observed despite the utilization of the highly basic hexamethyldisilazide anion in the presence of a high-energy, reactive vinyl cation intermediate. Chlorinated solvents, which are traditionally unstable under silylium catalysis, were also competent media for these reactions, albeit providing the products in lower yield (Entry 2).[14] Pleasingly, commercially available $[Ph_3C]^+[B(C_6F_5)_4]^-$ was superior in this reaction, providing the bicyclooctene products **3.10** in 98% yield in 30 minutes at room temperature, obviating the need for the less accessible $[HCB_{11}Cl_{11}]^-$ anion (Entry 3). Without catalyst, or without lithium ions, the reaction failed to yield any insertion products (Entries 4–6). Notably, $[Li]^+[B(C_6F_5)_4]^-$ could also be utilized instead of using a trityl precatalyst, although this salt is not commercial (entry 7). Moreover, unlike silylium-mediated reductive coupling conditions, here we generate olefinic products that can be further functionalized.[15,16]



3.6 **3.10**

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

Table 3.1 Optimization table for transannular C–H insertion

With optimized conditions in hand, we desired to evaluate the scope of this reaction. Specifically, we sought to validate our hypothesis that the use of Li^+ ions would improve the substrate compatibility of vinyl cation reactions. To this end, silyl ether-containing cyclooctenyl triflate **3.11** was synthesized and exposed to slightly modified Li-WCA conditions to yield silyl enol ether products **3.12** in 92% overall yield (Figure 3.3a). Furthermore, my colleagues have synthesized and optimized the conditions for transannular insertion reactions of 3-arylcyclooctenyl triflates **3.13** to give predominantly bicyclic styrene products **3.14** in a 48–97% total yield of olefin isomers (Figure 3.3b).[17] These reactions allowed us to expand our scope to substrates containing silyl ether, morpholine, thioether, and anisole functional groups.

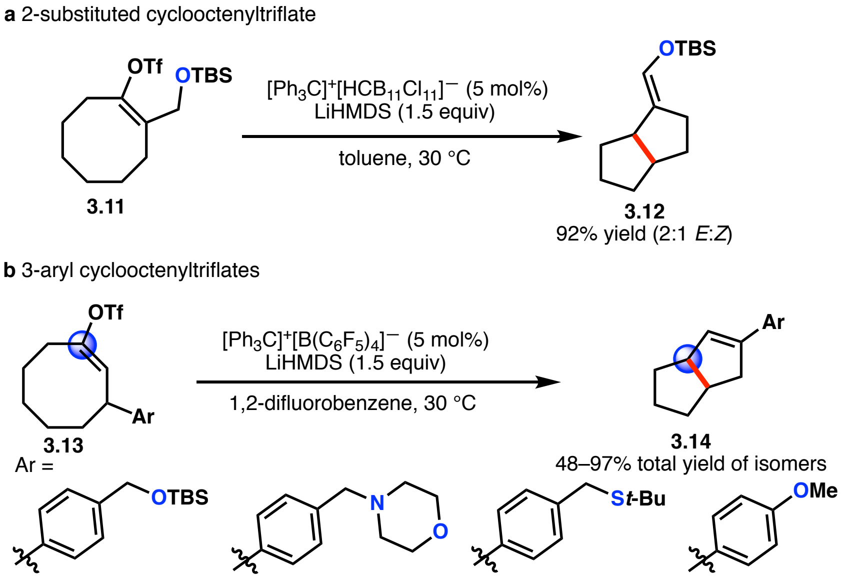


Figure 3.3 Cyclooctenyl triflate scope in the Li-WCA catalyzed C–H insertion reactions of vinyl cations

3.4 Intramolecular C–H Insertion Annulation Reactions Under Basic Conditions

While my colleagues were developing the transannular C–H insertion reactions of cyclooctenyl triflates, I pondered if the scope of this C–H insertion chemistry could be expanded to annulation reactions. To this end, alkylated benzosuberone-derived triflates **3.15** with tethered alkyl chains stood out as potential candidates for several reasons: 1) The 7-membered ring triflate would have a low barrier for vinyl cation formation, 2) the possibility of insertion into 1° carbon C–H bonds could be probed and, 3) the potential for intramolecular, not just transannular C–H insertion could be investigated.[18] Furthermore, the vinyl carbocation intermediates **3.16** derived from these vinyl triflates (**3.15**) are unable to undergo deprotonation/elimination reactions to yield undesired alkyne/allene products (Figure 3.4).[19] Gratifyingly, upon exposure to 10 mol% of $[Ph_3C]^+[B(C_6F_5)_4]^-$ and 1.1 equivalents of LiHMDS, propylbenzoxepinyl triflate afforded tricycle **3.17** in 84% yield (3.3:1 isomer ratio) after two hours (Figure 3.4). Further, 2-substituted pinacol boronic ester and anisole benzosuberone derivatives were successfully converted to their corresponding tricyclic styrene products **3.18** and **3.19** in 68% and 48% yield respectively. C–H insertion into a benzylic 2° C–H bond was also possible, offering styrene **3.20** in 76% yield in 3.3:1 *d.r.* Protected aniline-containing triflate also reacted smoothly to give tricycle **3.21** in 66% yield. Similarly, *meta*-halogenated benzosuberonyl triflates provided the desired styrene products (**3.22** and **3.23**) in 72% and 82% yield. Functionalization at other

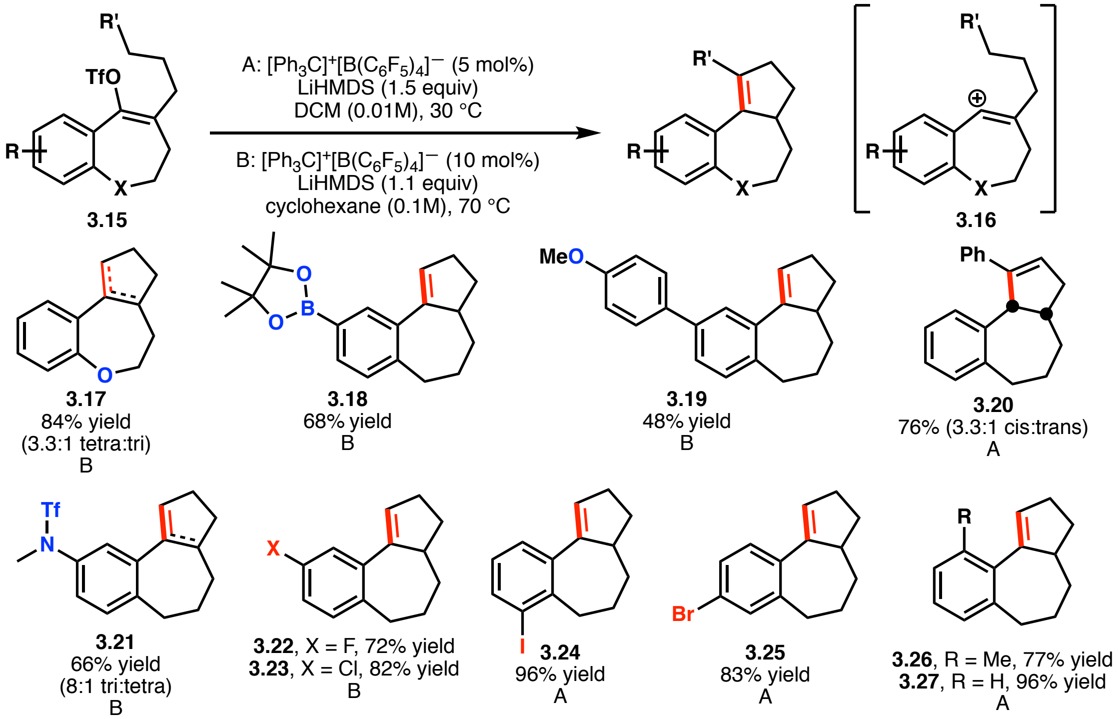


Figure 3.4 Alkylated benzosuberone triflate C–H annulation scope

positions of the fused aryl system afforded tricyclic styrene products (**3.24-3.27**) in good to excellent yields (77–96%). These examples not only further highlight the vastly improved heteroatom compatibility of these conditions, but also demonstrate the C–H insertion reactivity of benzylic vinyl cations into 1° as well as 2° C–H bonds.

3.5 Urea-Catalyzed Vinyl Carbocation Formation

While we were really excited about the newfound substrate tolerance of the LiF_{20} system outlined above, we sought out new catalysts for this transformation that have more tunable groups on them than on the F_{20} anion. The end goal for this research program is to find a catalytic system that can be tuned to give C–H insertion products chemoselectively or ultimately, enantioselectively. To this end, we looked towards hydrogen-bonding catalysts, such as thioureas. These readily available and highly tunable scaffolds have found success in promoting the formation of cationic intermediates.[20–23] Specifically, we were inspired by Reisman, Doyle, and Jacobsen's use of thioureas to generate resonance-stabilized tricoordinate carbocations that engage in highly-selective bond-forming processes.[24] The same group later showed that squaramides, combined with trimethylsilyl triflate (TMSOTf), enhance the electrophilicity of the silicon center *via* triflate binding.[25] Building upon these reports, we posited that hydrogen-bonding catalysts could perhaps ionize vinyl triflates to generate vinyl cations.

We began proof-of-concept studies in the context of the C–H insertion reactions of propylated benzosuberonyl triflate **3.28**, since we saw great success with this substrate in the context of Li-WCA systems (Figure 3.5). After some optimization, we found that both the presence of a lithium base *<u>and</u>* a hydrogen-bonding catalyst is necessary for this transformation to take place.[26] Other key findings included that the 3,5-bisCF_3 substituents are key to the

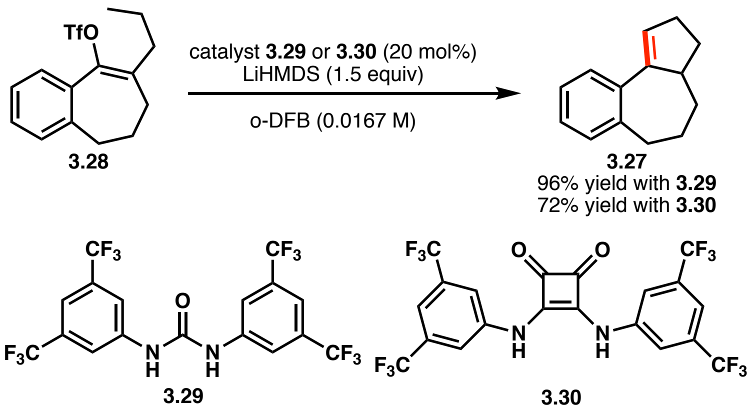


Figure 3.5 Optimized conditions for C–H insertion with hydrogen-bonding catalysts

reactivity of these catalysts. Under these conditions, both the urea **3.29** and squareamide **3.30** catalysts furnished the desired C–H insertion product **3.27** in good yield. Notably, the 96% yield obtained with urea is the same as the yield we saw with the LiF_{20} catalytic system (Figure 3.4).

To further develop the scope of this reaction, urea-catalyzed Friedel-Crafts reactions of vinyl triflates were explored. Here, we decided to use the optimized reaction conditions from the above insertion chemistry as a starting point. I found a large scope of both triflates and arenes to be tolerant of this transformation. A silylated pyrrole gave moderate selectivity for vinylation of the C3 position (Figure 3.6a, **3.31**).[27] Electron deficient vinyl triflates were tolerated, reacting with anisoles and xylenes in moderate to good yields (52–76%, **3.32–3.34**). The trifluoromethylated vinyl triflate also reacted with benzene or a bromobenzene derivative yielding vinylated arenes in high yields (**3.35**, **3.36**). More electron rich aromatic nucleophiles, such as dimethoxybenzene, underwent smooth coupling with a variety of halogenated vinyl triflates in good yields (**3.37–3.39**). There was minimal decrease in efficiency when performing the reaction on 1-gram scale with the iodinated vinyl triflate, giving styrene **3.39** in 64% yield. Furthermore, cyclooctenyl triflate **3.6** was observed to undergo a transannular C–H insertion, Friedel-Crafts cascade with 4-methylanisole giving alkylated arene **3.40** in 57% yield (Figure

3.6b). Here, two C–C bonds, a 5,5-fused ring system, and a quaternary carbon center were all forged in a single step. Notably, all of the reactions

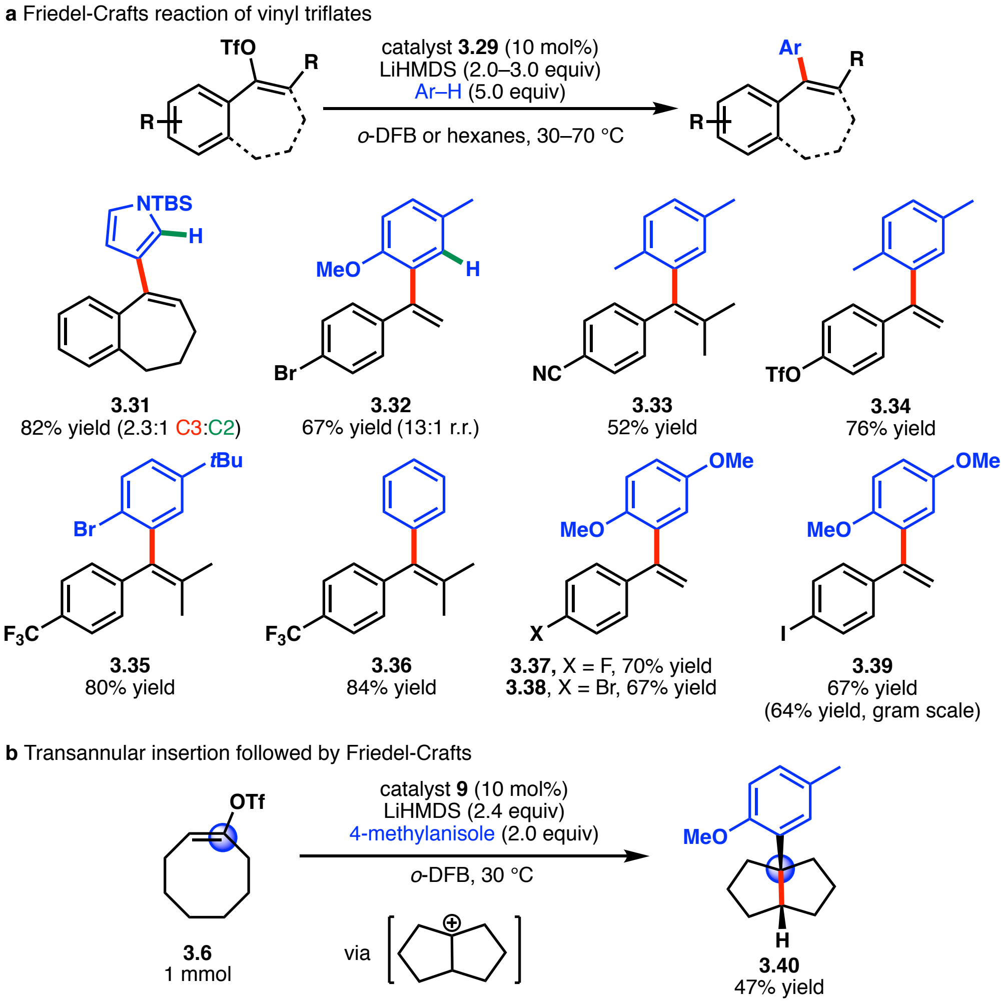


Figure 3.6 Li-urea catalyzed Friedel-Crafts reactions

outlined in Figure 3.6 were performed on the bench and required neither scrupulous drying of substrates nor catalysts. This is one advantage of this Li-urea system over all previous examples. All of the reactions done previously in this chapter and in Chapter 2 were performed in the glovebox. Furthermore, when comparing these reactions to the Friedel-Crafts reactions in Figure 2.4, we can see that the substrate tolerance is much broader than with silylium-carborane catalysis.

After developing the intermolecular Friedel-Crafts chemistry, I assisted my colleagues in designing and synthesizing some substrates for intramolecular C–H insertion reactions. Here, we targeted tetrasubstituted acyclic vinyl triflates that had relatively low ionization barriers and that could not eliminate to alkyne/allene products (Figure 3.7a).[19] We then sought to validate our hypothesis that these readily accessible organocatalysts were able to tolerate various functional groups in the context of vinyl cation C–H insertion reactions. To explore the functional group tolerance, a variety of alkylated styrenyl triflates were prepared (Figure 3.7). We were quite pleased to find that a substrate bearing a pyridine substituent was competent in this transformation, yielding cyclopentenyl pyridine **3.41** in 61 % yield. Substrates bearing electron-withdrawing substituents, however, resulted in products with poor olefin isomer ratios. Upon further optimization, we discovered that utilization of LiH allowed for high yielding reactions with excellent olefin selectivity for these substrates (**3.42–3.44**). Moreover LiO*t*Bu was also a competent base for this transformation, allowing for formation of dihydrofuran **3.45** in 61

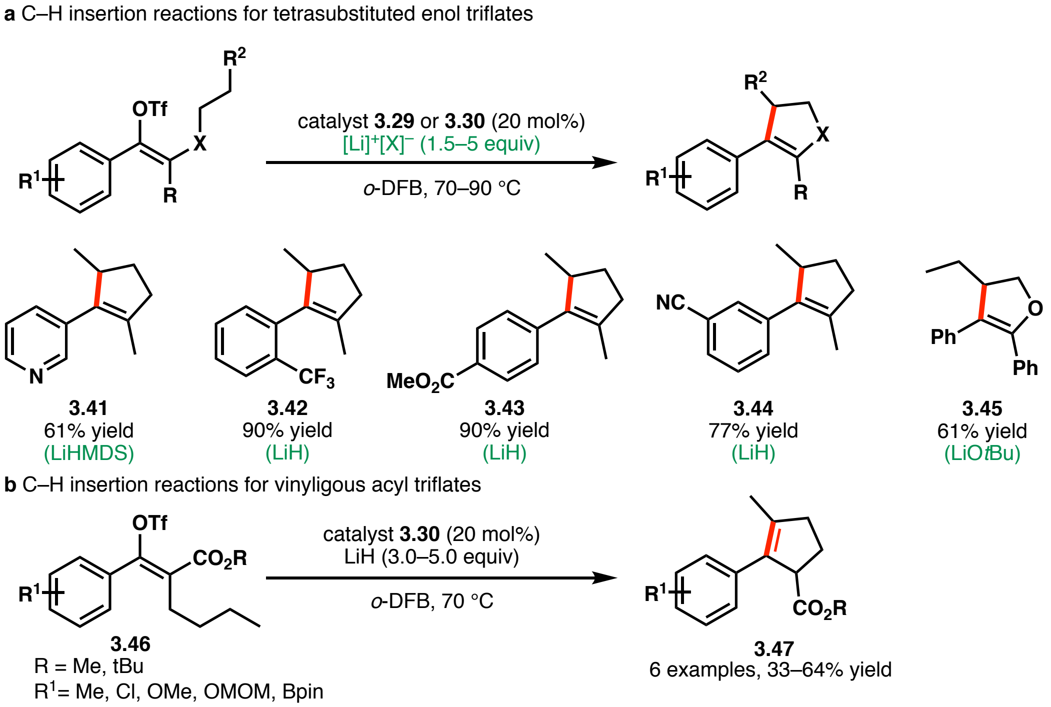


Figure 3.7 Li-urea catalyzed intramolecular C–H insertion reactions of vinyl triflates

% yield, *via* insertion into an ether tether**.** To the best of our knowledge, this example showcases the first heterocycle synthesis from a C–H insertion reaction of a vinyl cation. Furthermore, my colleagues have also demonstrated that vinyligous acyl triflates **3.46** (easily made from the corresponding β-ketoester) can undergo moderate yielding C–H insertion reactions using similar conditions (with LiH instead of LiHMDS) to give non-conjugated enoate product **3.47** in 33–64% yield.

3.6 Mechanistic Studies

With our scope studies in hand, we began our investigation into the mechanistic underpinnings of this transformation. Several experiments were conducted to support our proposed reaction pathway. Because hexamethyldisilazane has been previously used as a silyl transfer reagent, we sought to discount the formation of silylium intermediates.[28] To this end, we showed that these reactions work with a stoichiometric amount of what is believed to be the active catalyst in system: LiF_{20} and Li-urea (Figure 3.8a, 3.8b). In the event, subjecting propylatedbenzosuberonyl triflate **3.28** to a stoichiometric amount of LiF_{20} led to full consumption of the vinyl triflate and formation of LiOTf. Furthermore, fully reduced tricyclic product **3.48** was observed as one component in a mixture of organic products with varying degrees of unsaturation (Figure 3.8a). Exposure of vinyligous acyl triflate **3.49** to a stoichiometric amount of Li-urea **3.50** (synthesized from deprotonation of parent urea **3.29**) led to a similar result wherein full consumption of starting material was observed as well as formation of LiOTf and enoate **3.51** in 22% yield (Figure 3.8b). To confirm the intermediacy of a vinyl cation species in our system

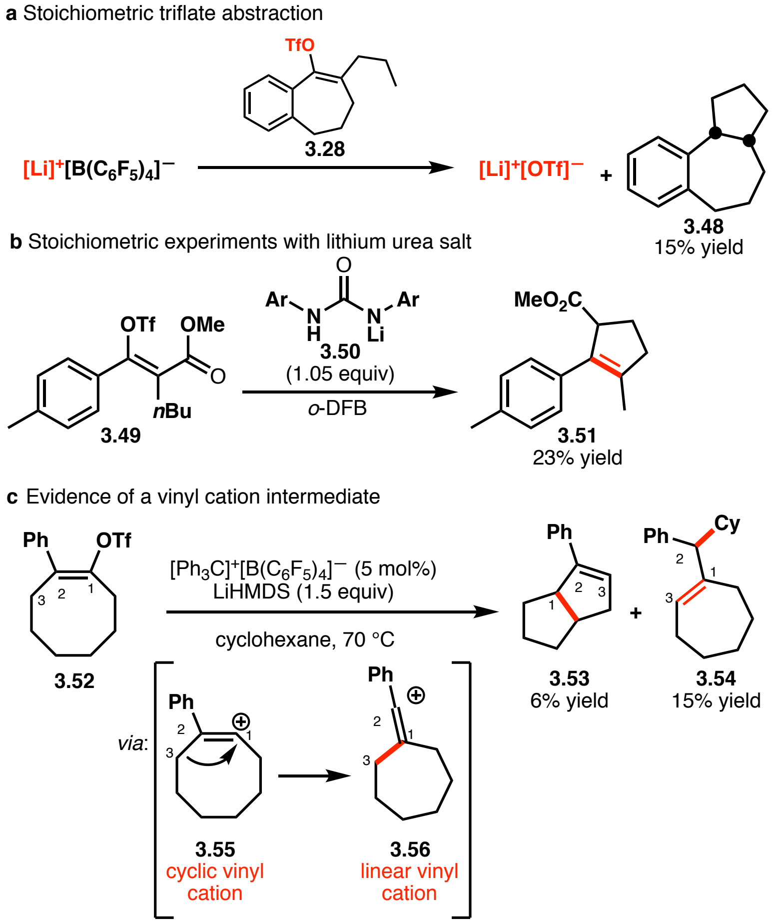


Figure 3.8 Mechanistic studies probing vinyl cation generation under basic conditions

despite the strongly basic conditions, we synthesized 2-phenyl vinyl triflate **3.52**, as 2-substituted cyclic vinyl cations have been previously reported to undergo ring-contractive rearrangement to exocyclic vinyl cations (Figure 3.8c).[29] Under the reaction conditions, we were pleased to observe formation of ring-contracted product **3.54** and transannular insertion product **3.53**. The cycloheptene derivative **3.54** is a result of C–H insertion into cyclohexane from the ring-contracted exocyclic vinyl cation **3.56**. We have also done some mechanistic studies to investigate the concerted *vs.* stepwise nature of the C–H insertion event, but the results suggested that this is highly substrate dependent. For example, we found that in the case of benzosuberonyl triflates, a concerted C–H insertion is more likely, while for vinyligous acyl triflates a stepwise "rebound" mechanism is proposed.[30,31]

3.7 Conclusion

In conclusion, we showed that it is possible to generate kinetically persistent vinyl carbocations in highly basic media. Importantly, this catalytic regime represents a new strategy in synthetic chemistry where lithium bases can be utilized to fuel $[\mathrm{Li}]^+[\mathrm{WCA}]^-$ catalyzed, intramolecular C–H insertion reactions of carbocations. We have also developed a newfound utility for widespread hydrogen-bonding catalysts such as ureas and squareamides. This study highlights the power of main group-catalyzed and organocatalyzed C–H functionalization reactions in a field dominated by transition metal-based systems. The easily accessible catalysts, simple reaction protocols described above, and the vastly improved functional group compatibility render this strategy an attractive approach to build complex molecules through the intermediacy of vinyl cations.

3.8 Experimental Section

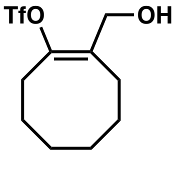
3.8.1 Materials and Methods

Unless otherwise stated, all reactions were performed in an MBraun glovebox under nitrogen atmosphere with ≤ 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and dried *in vacuo* before use. All liquid substrates were either dried over CaH_2 or filtered through dry neutral aluminum oxide. Solid substrates were dried over P_2O_5. All solvents were rigorously dried before use. Benzene, *o*-dichlorobenzene, and toluene were degassed and dried in a JC Meyer solvent system and stored inside a glovebox. Cyclohexane, fluorobenzene, and *n*-hexane were distilled over potassium. Chlorobenzene was distilled over sodium. *o*-Difluorobenzene was distilled over CaH_2. Pentane was distilled over sodium-potassium alloy. Chloroform was dried over CaH_2 and stored in a glovebox. Triethylsilane and triisopropylsilane were dried over sodium and stored inside a glovebox. *Closo*-Carborane catalysts were prepared according to literature procedure.[32] $[Li]^+[B(C_6F_5)_4]^-$ and $[K]^+[B(C_6F_5)_4]^-$ salts were synthesized according to literature procedure.[33] Hydrogen-bonding catalysts were prepared according to original or modified literature procedures.[34] Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. $AgNO_3$-Impregnated silica gel was prepared by mixing with a solution of $AgNO_3$ (150% v/w of 10% w/v solution in acetonitrile), removing solvent under reduced pressure, and drying at 120 °C. NMR spectra were recorded on a Bruker AV-300 (^1H, ^{19}F), Bruker AV-400 (^1H, ^{13}C, ^{19}F), Bruker DRX-500 (^1H), and Bruker AV-500 (^1H, ^{13}C). ^1H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^1H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted otherwise. GC spectra were recorded on an Agilent 6850 series GC using an Agilent HP-1 (50 m, 0.32 mm ID, 0.25 mm DF) column. GCMS spectra were recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 mm DF) column interface at room temperature. IR Spectra were record on a Perkin Elmer 100 spectrometer and are reported in terms of frequency absorption (cm^{-1}). High resolution mass spectra (HR-MS) were recorded on a Waters (Micromass) GCT Premier spectrometer, a Waters (Micromass) LCT Premier, or an Agilent GC EI-MS, and are reported as follows: m/z (% relative intensity). Purification by preparative HPLC was done on an Agilent 1200 series instrument with a reverse phase Alltima C_{18} (5m, 25 cm length, 1 cm internal diameter) column.

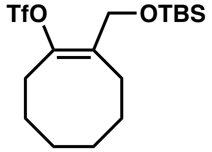
3.8.2 Experimental Procedures for LiF_{20} Catalysis

*Spectra for substrates in **Figure 3.4** are reported in the adapted article. Full synthetic procedures for substrates in **Figure 3.4** are reported in the adapted article. Synthesis and spectra of substrates and products for **Figure 3.3b** are reported in the adapated article. Synthesis of triflate **3.6** is reported in Chapter 2.*

3.8.2.1 Preparation of Vinyl Triflate Substrates



(*Z*)-2-(hydroxymethyl)cyclooct-1-en-1-yl trifluoromethanesulfonate (3.57). Synthesized according to known procedures. Spectral data match those reported in the literature.[35]



(*Z*)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)cyclooct-1-en-1-yl trifluoromethanesulfonate (3.11). In a 10 mL roundbottom flask, imidazole (809 mg, 11.9 mmol, 2.5 equiv.) and alcohol **3.57** (1.37 g, 4.75 mmol, 1 equiv.) were dissolved in anhydrous dimethylformamide (1.37 mL). TBSCl (860 mg, 5.70 mmol, 1.2 equiv.) was added and the reaction was stirred for 24h at room temperature. The reaction was diluted with water (10 mL) and the product was extracted out of the aqueous layer with diethyl ether (3 x 10 mL). The organics were washed with water (5 x 20 mL) followed by brine (1 x 20 mL), dried over magnesium sulfate, filtered and concentrated to give crude product as colorless oil. The crude was purified by silica flash column chromatography (100% hexanes to 5% ethyl acetate in hexanes) to give **3.11** as a colorless oil (1.29 g, 67%).

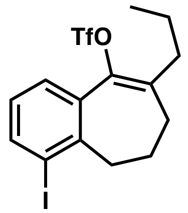
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.27 (s, 2H), 2.52 – 2.45 (m, 2H), 2.37 – 2.28 (m, 2H), 1.73 – 1.64 (m, 4H), 1.57 – 1.50 (m, 4H), 0.90 (s, 9H), 0.07 (s, 6H).

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

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

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

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



4-iodo-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.58).
In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (436 mg, 4.11 mmol, 3 equiv.) in anhydrous methylene chloride (14 mL). To this suspension was added corresponding ketone (450 mg, 1.37 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (426 mg, 1.51 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction wasn't done, triflic anhydride (426 mg, 1.51 mmol, 1.10 equiv.) and sodium carbonate (436 mg, 4.11 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (15 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as brown oil. The crude product was purified by silica flash column chromatography (25% dichloromethane in hexanes) to give pure vinyl triflate **3.58** as a yellow oil (298 mg, 47%).

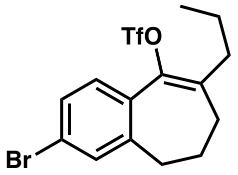
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.82 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.34 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 2.94 (t, *J* = 7.0 Hz, 2H), 2.56 – 2.28 (m, 2H), 2.19 (p, *J* = 7.2 Hz, 2H), 1.89 (t, *J* = 7.2 Hz, 2H), 1.65 – 1.55 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 143.2, 139.8, 139.0, 136.6, 134.9, 127.6, 126.6, 118.3 (q, $^{1}J_{C–F}$ = 320.3 Hz), 100.5, 36.6, 34.1, 33.3, 28.2, 21.3, 14.1.

^{19}F NMR (376 MHz, CDCl$_3$) δ –74.2.

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

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



3-bromo-8-propyl-6,7-dihydro-5H-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.59). In a flame dried 100 mL roundbottom flask, sodium carbonate (628 mg, 5.90 mmol, 3.00 equiv.) was suspended in anhydrous methylene chloride (18 mL). To this suspension, corresponding ketone (0.556 g, 2.00 mmol, 1.00 equiv.) was added, and the reaction was cooled to 0 °C. Triflic anhydride (400 µL, 2.4 mmol, 1.20 equiv.) was added dropwise and the reaction was allowed to warm to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete additional triflic anhydride (400 µL, 2.4 mmol, 1.20 equiv.) and sodium carbonate (628 mg, 5.90 mmol, 3.00 equiv.) were added. Upon completion by TLC, the reaction was quenched with 50 mL of saturated aqueous sodium bicarbonate solution. The crude product was then extracted with diethyl ether (3 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered, and then concentrated to give the crude compound. The crude product was purified by silica flash chromatography (100% hexanes to 1% ethyl acetate in hexanes) to give pure vinyl triflate **3.59** as a white solid (628 mg, 77%).

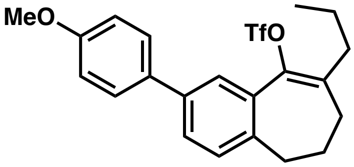
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 2H), 7.24 (d, *J* = 8.2 Hz, 1H), 2.66 (t, *J* = 7.2 Hz, 2H), 2.42 – 2.30 (m, 2H), 2.19 (p, *J* = 7.2 Hz, 2H), 1.92 (t, *J* = 7.2 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.01 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 143.0, 138.7, 136.4, 132.8, 131.9, 129.4, 128.0, 123.0, 118.3 (q, $^1J_{C\text{–}F}$ = 320.1 Hz), 34.2, 34.1, 31.5, 28.1, 21.3, 14.1.

^{19}F NMR (282 MHz, CDCl$_3$) δ –74.2.

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

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



2-(4-methoxyphenyl)-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.60). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (188 mg, 1.77 mmol, 3 equiv.) in anhydrous methylene chloride (7 mL). To this suspension was added corresponding ketone (182 mg, 0.59 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (183 mg, 0.65 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride (183 mg, 0.65 mmol, 1.10 equiv.) and sodium carbonate (188 mg, 1.77 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 10 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as brown oil. The crude product was purified by silica flash column chromatography (5% diethyl ether in hexanes) to give pure vinyl triflate **3.60** as colorless oil (75 mg, 29%).

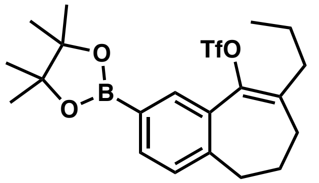
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.56 (d, *J* = 2.2 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.46 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 2.72 (t, *J* = 7.1 Hz, 2H), 2.41 (dd, *J* = 8.7, 6.9 Hz, 2H), 2.21 (p, *J* = 7.2 Hz, 2H), 1.97 (t, *J* = 7.2 Hz, 2H), 1.60 (sex, *J* = 8.0 Hz, 2H), 1.03 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 159.2, 139.7, 139.3, 138.9, 135.7, 134.1, 133.0, 129.4, 127.9, 127.3, 124.78, 118.4 (q, $^1J_{C\text{–}F}$ = 320.3 Hz), 114.3, 55.3, 34.2, 34.1, 31.2, 28.2, 21.3, 14.1.

^{19}F NMR (376 MHz, CDCl$_3$) δ –74.2.

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

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



8-propyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.61). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (213 mg, 2.01 mmol, 3 equiv.) in anhydrous methylene chloride (7 mL). To this suspension was added corresponding ketone (220 mg, 0.67 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (208 mg, 0.74 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, an additional batch of triflic anhydride anhydride (208 mg, 0.74 mmol, 1.10 equiv.) and sodium carbonate (213 mg, 2.01 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 10 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as red oil. The crude product was purified by silica flash column chromatography (5% diethyl ether in hexanes) to give pure vinyl triflate **3.61** as yellow oil (160 mg, 52%).

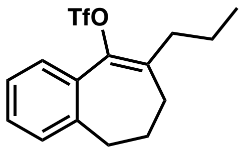
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.70 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 2.70 (t, *J* = 7.1 Hz, 2H), 2.48 – 2.30 (m, 2H), 2.19 (p, *J* = 7.2 Hz, 2H), 1.90 (t, *J* = 7.2 Hz, 2H), 1.58 (sex, *J* = 7.6 Hz, 2H), 1.34 (s, 12H), 1.01 (t, *J* = 7.3 Hz, 3H).

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

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

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

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



8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.28). In a flame dried 100 mL round bottom flask was suspended sodium carbonate (563 mg, 5.31 mmol, 3 equiv.) in anhydrous methylene chloride (16 mL). To this suspension was added corresponding ketone (358 mg, 1.77 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (549 mg, 1.95 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (549 mg, 1.95 mmol, 1.10 equiv.) and sodium carbonate (563 mg, 5.31 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 30 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark red oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **3.28** as yellow oil (540 mg, 91%).

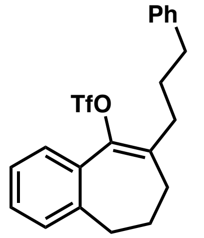
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 1H), 7.31 – 7.26 (m, 2H), 7.23 (dt, J = 4.6, 3.2 Hz, 1H), 2.70 (t, J = 7.1 Hz, 2H), 2.43 – 2.34 (m, 2H), 2.20 (p, J = 7.2 Hz, 2H), 1.93 (t, J = 7.2 Hz, 2H), 1.65 – 1.55 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H).

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

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

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

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



8-(3-phenylpropyl)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.63). In a flame dried 100 mL round bottom flask was suspended sodium carbonate (857 mg, 8.08 mmol, 3 equiv.) in anhydrous methylene chloride (25 mL). To this suspension was added corresponding ketone (750 mg, 2.69 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (836 mg, 2.96 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (836 mg, 2.96 mmol, 1.10 equiv.) and sodium carbonate (857 mg, 8.08 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as a dark red oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **3.63** as a yellow oil (880 mg, 80%).

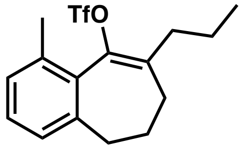
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 1H), 7.33 – 7.26 (m, 4H), 7.24 – 7.17 (m, 4H), 2.70 (dt, J = 13.8, 7.5 Hz, 4H), 2.52 – 2.40 (m, 2H), 2.19 (p, J = 7.1 Hz, 2H), 1.98 – 1.83 (m, 4H).

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

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

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

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



1-methyl-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.64).

In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (572 mg, 5.39 mmol, 3 equiv.) in anhydrous methylene chloride (15 mL). To this suspension was added ketone corresponding ketone (389 mg, 1.80 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (558 mg, 1.98 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (558 mg, 1.98 mmol, 1.10 equiv.) and sodium carbonate (572 mg, 5.39 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark brown oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **3.64** as a yellow oil (437 mg, 70%).

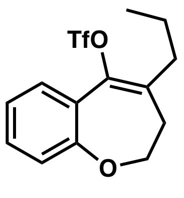
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 7.04 (d, J = 7.4 Hz, 1H), 2.84 (td, J = 13.1, 7.8 Hz, 1H), 2.67 – 2.52 (m, 1H), 2.50 – 2.36 (m, 2H), 2.33 (s, 3H), 2.16 (tt, J = 13.0, 6.8 Hz, 1H), 2.07 – 1.93 (m, 2H), 1.85 – 1.54 (m, 3H), 1.03 (t, J = 7.3 Hz, 3H).

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

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

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

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



4-propyl-2,3-dihydrobenzo[*b*]oxepin-5-yl trifluoromethanesulfonate (3.65). In a flame dried 100 mL roundbottom flask, sodium carbonate (1.37 g, 12.9 mmol, 3.00 equiv.) was suspended in anhydrous methylene chloride (40 mL). To this suspension, corresponding ketone (880 mg, 4.31 mmol, 1.00 equiv.) was added, and the reaction was cooled to 0 °C. Triflic anhydride (1.34 g, 4.74 mmol, 1.20 equiv.) was added dropwise and the reaction was allowed to warm to room temperature. The reaction was monitored by TLC and every 12 hours that the reaction was not complete additional triflic anhydride (1.34 g, 4.74 mmol, 1.20 equiv.) and sodium carbonate (1.37 g, 12.9 mmol, 3.00 equiv.) was added. Upon completion by TLC, the reaction was quenched with 70 mL of aqueous sodium bicarbonate solution. The layers were separated and the crude product was then extracted out of the aqueous layer with diethyl ether (3 x 70 mL). The combined organic layers were dried over magnesium sulfate, filtered, and then concentrated to give the crude compound. The crude was purified by silica flash chromatography (20% dichloromethane in hexanes) to give pure vinyl triflate **3.65** as a yellow oil (510 mg, 31%).

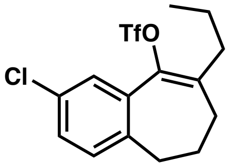
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.9 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 1H), 4.50 (td, *J* = 6.2, 1.9 Hz, 2H), 2.40 (dtd, *J* = 12.6, 6.9, 6.2, 2.0 Hz, 4H), 1.64 – 1.57 (m, 2H), 1.01 (t, *J* = 7.4, 3H).

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

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

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

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



2-Chloro-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.66). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (255 mg, 2.40 mmol, 3 equiv.) in anhydrous methylene chloride (7.5 mL). To this suspension was added corresponding ketone (190 mg, 0.80 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (249 mg, 0.88 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not done, additional triflic anhydride (249 mg, 0.88 mmol, 1.10 equiv.) and sodium carbonate (255 mg, 2.40 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (20 mL). The layers were separated and the product was extracted with diethyl ether (3 x 20 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as a brown oil. The crude product was purified by silica flash column chromatography (5% dichloromethane in hexanes) to give pure vinyl triflate **3.66** as a yellow oil (140 mg, 47%).

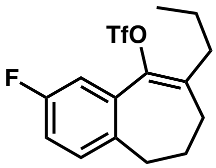
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 2.2 Hz, 1H), 7.24 (dd, J = 8.1, 2.2 Hz, 1H), 7.16 (d, J = 8.1 Hz, 1H), 2.66 (t, J = 7.2 Hz, 2H), 2.46 – 2.30 (m, 2H), 2.18 (p, J = 7.2 Hz, 2H), 1.93 (t, J = 7.2 Hz, 2H), 1.71 – 1.57 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H)

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

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

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

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



2-fluoro-8-propyl-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.67). In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (296 mg, 2.79 mmol, 3 equiv.) in anhydrous methylene chloride (8 mL). To this suspension was added corresponding ketone (205 mg, 0.93 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (289 mg, 1.02 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (289 mg, 1.02 mmol, 1.10 equiv.) and sodium carbonate (296 mg, 2.79 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with methylene chloride (3 x 10 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark green oil. The crude product was purified by silica flash column chromatography (15% dichloromethane in hexanes) to give pure vinyl triflate **3.67** as yellow oil (162 mg, 49%).

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

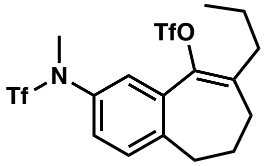
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2 (d, $^1J_{C-F}$ = 244.9 Hz), 138.6 (d, $^4J_{C-F}$ = 2.6 Hz), 136.9, 136.6 (d, $^4J_{C-F}$ = 3.3 Hz), 135.4 (d, $^3J_{C-F}$ = 7.8 Hz), 130.4 (d, $^3J_{C-F}$ = 8.0 Hz), 118.3 (q, $^1J_{C-F}$ =

320.1 Hz), 116.0 (d, $^2J_{C\text{–}F}$ = 21.2 Hz), 113.3 (d, $^2J_{C\text{–}F}$ = 22.7 Hz), 34.2, 34.1, 30.9, 28.1, 21.3, 14.1.

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

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

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



8-propyl-2-((1,1,1-trifluoro-*N*-methylmethyl)sulfonamido)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.68).

In a flame dried 100 mL roundbottom flask was suspended sodium carbonate (350 mg, 3.30 mmol, 3 equiv.) in anhydrous methylene chloride (10 mL). To this suspension was added corresponding ketone (400 mg, 1.10 mmol, 1.00 equiv.) and the reaction was cooled to 0 °C. Triflic anhydride (342 mg, 1.21 mmol, 1.10 equiv.) was added dropwise at 0 °C and the reaction was allowed to warm up to r.t. The reaction was monitored by TLC and every 12 hours that the reaction was not complete, additional triflic anhydride anhydride (342 mg, 1.21 mmol, 1.10 equiv.) and sodium carbonate (350 mg, 3.30 mmol, 3 equiv.) were added. Upon completion of the reaction by TLC, the reaction was quenched with water (10 mL). The layers were separated and the product was extracted with methylene chloride (3 x 15 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated to give the crude material as dark brown oil. The crude product was purified by silica flash column chromatography (2% ethyl acetate in hexanes) to give pure vinyl triflate **3.68** as a white solid (363 mg, 67%).

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

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

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

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

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

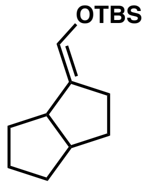
3.8.2.2 C–H Insertion Reactions Fueled by LiHMDS Base

3.8.2.2.1 General Procedure for C–H Insertion Reactions

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

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

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



(*E/Z*)-*tert*-butyl((hexahydropentalen-1(2*H*)-ylidene)methoxy)dimethylsilane (3.12E and 3.12Z). In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[CHB_{11}Cl_{11}]^-$ (7.6 mg, 0.010 mmol, 0.05 equiv.) and this was dissolved in toluene (0.4 mL). Lithium hexamethyldisilazide (50.1 mg, 0.30 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the solution. The solution was stirred for 4 minutes at 30 °C. Vinyl triflate **3.11** (80.4 mg, 0.20 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 12 hours. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and filtered. The supernatant was concentrated to give crude product as orange oil (60% NMR yield of major olefin isomer **3.12E**, 32% minor olefin isomer **3.12Z**). The crude was then purified by silica flash column chromatography (1% ethyl acetate in hexanes**)** to give the major (*E*)–isomer **3.12E** as colorless oil. Assignment of the major isomer was based on key cross peaks in ^{1}H NOESY experiments. Through HSQC and COSY experiments it was determined that the proton at 2.86 ppm was the tertiary allylic ring fusion proton and that the CH_2 protons adjacent to that CH showed up at 1.46 and 1.33. There were key NOEs present between the olefinic proton at 6.25 and the tertiary allylic proton at 2.86 as well as one of the protons on the aforementioned CH_2 leading to the assignment of the (*E*)–isomer.

The minor (*Z*)–isomer was found to be unstable on SiO2, so the crude reaction mixture could be purified by flash column chromatography on triethylamine treated silica gel (0.1:99.9 NEt_3:hexanes) to give pure **3.12Z** as colorless oil. The olefin geometry of this isomer was assigned based on key cross peaks in ^{1}H NOESY experiments. There were key NOEs present between the olefinic proton and the protons on the allylic methylene carbon. This lead to assignment of the minor compound as the (*Z*)–isomer.

Characterization of 3.12E

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

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

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

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

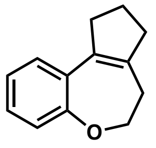
Characterization of 3.12Z

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

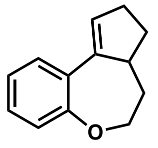
^{13}C NMR (126 MHz, C_6D_6) δ 130.8, 129.8, 44.5, 44.4, 34.2, 33.6, 32.8, 29.2, 27.7, 25.9, 18.4, –5.1, –5.2.

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

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



3.17a



3.17b

7,8,9,10-tetrahydro-6*H*-benzo[*b*]cyclopenta[*d*]oxepine (3.17). Synthesized according to a modified version of general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (4.6 mg, 0.005 mmol, 0.10 equiv.) and this was suspended in cyclohexane (0.5 mL). Lithium hexamethyldisilazide (5.02 mg, 0.028 mmol, 0.6 equiv.) was added along with a magnetic stirring bar to the suspension. Vinyl triflate **3.65** (16.8 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was heated to 70 °C for 60 minutes. The reaction mixture was cooled to room temperature and then another batch of LiHMDS (4.30 mg, 0.022 mmol, 0.5 equiv.) was added and the reaction was heated to 70 °C for an additional hour. The reaction was then cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.17a** as brown oil (66% NMR yield.). The crude was then purified by silica column chromatography on silver nitrate treated silica (2% ethyl acetate in hexanes) to give product **3.17a** as colorless oil. The remaining material was further purified *via* silica flash column chromatography on silver nitrate impregnated silica (10% benzene in hexanes) to give the minor trisubstituted isomer **3.17b** as colorless oil.

Characterization of 3.17a

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

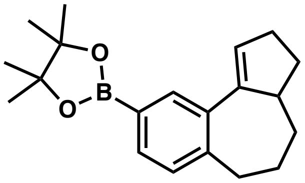
^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 140.7, 131.3, 128.9, 127.2, 127.0, 122.6, 120.1, 69.5, 39.9, 36.9, 34.7, 21.6.

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

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

Characterization of 3.17b

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



2-(2,3,3a,4,5,6-hexahydrobenzo[*e*]azulen-9-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.18). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.25 mL). Lithium hexamethyldisilazide (4.6 mg, 0.033 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.61** (11.5 mg, 0.025 mmol, 1 equiv.) was added to the reaction and it was subsequently stirred for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. The reaction was quenched with saturated aqueous ammonium chloride and extracted with diethyl ether. The combined organics were filtered through a pad of silica gel and concentrated to give crude tricyclic compound **3.18** as a yellow oil (68% NMR yield). The crude was then purified by flash silver nitrate impregnated silica gel chromatography (2% ethyl acetate in hexanes) to give pure product **3.18** as a colorless oil.

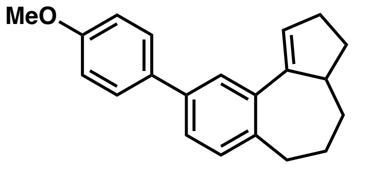
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 1H), 5.79 (s, 1H), 2.84 (dd, *J* = 14.6, 7.8 Hz, 1H), 2.71 – 2.60 (m, 2H), 2.54 (dt, *J* = 16.9, 8.3 Hz, 1H), 2.39 – 2.29 (m, 1H), 2.28 – 2.16 (m, 1H), 2.05 – 1.87 (m, 2H), 1.65 – 1.58 (m, 1H), 1.55 – 1.52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

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

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

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

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



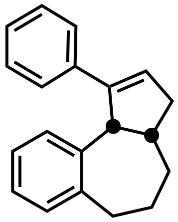
9-(4-methoxyphenyl)-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (3.19). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (4.3 mg, 0.0047 mmol, 0.10 equiv.) and this was suspended in cyclohexane (0.47 mL). Lithium hexamethyldisilazide (8.65 mg, 0.052 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. Vinyl triflate **3.60** (20.7 mg, 0.047 mmol, 1 equiv.) was added to the reaction and it was heated to 70 °C for 10 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.19** as brown oil (48% NMR yield*,* 44% solated yield on 0.1 mmol scale). The crude was then purified by silica column chromatography on silver nitrate treated silica (5% ethyl acetate in hexanes) to give product **3.19** as a white solid.

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

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

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

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



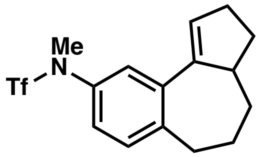
1-phenyl-3,3a,4,5,6,10b-hexahydrobenzo[*e*]azulene (3.20). Synthesized according to general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (5.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C and then cooled to –40 °C. Vinyl triflate **3.63** (20.5 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at –40 °C for 30 minutes. The reaction mixture was warmed to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.20** as a yellow oil (61% NMR yield). The crude was purified first by flash silica gel column chromatography (hexanes) to give product **3.20** as a mixture of diastereomers. This mixture was further purified by HPLC to give the major *cis*-ring fused product **3.20** as a white solid. Assignment of the major *cis* product was determined by key cross peaks in ^1H NOESY experiments. HSQC and ^1H COSY experiments led to the assignment of the tertiary allylic benzylic proton to be at 4.50 ppm and the other tertiary proton to be at 2.09 ppm. Further, the two diastereotopic CH_2 benzylic protons on the seven membered ring were assigned to be at 3.15

ppm and 2.79 ppm. The allylic benzylic proton showed key NOE interactions with the other ring tertiary CH proton as well as one of the diastereotopic benzylic protons at 3.15 ppm. The other diasteretopic benzylic proton at 2.79 ppm showed an NOE with the neighboring aromatic CH doublet at 6.5 ppm. These NOE interactions lead to the assignment of the product as the *cis* fused product.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.0 Hz, 3H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.12 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.00 (td, *J* = 7.3, 1.4 Hz, 1H), 6.88 (dd, *J* = 8.2, 6.9 Hz, 1H), 6.22 (q, *J* = 2.4 Hz, 1H), 4.50 (d, *J* = 9.2 Hz, 1H), 3.15 (t, *J* = 13.6 Hz, 1H), 2.79 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.71 – 2.63 (m, 1H), 2.25 – 2.17 (m, 2H), 2.14 – 2.04 (m, 2H), 1.86 (qd, *J* = 12.9, 4.0 Hz, 1H), 1.46 – 1.37 (m, 1H).

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

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



1,1,1-trifluoro-*N*-(2,3,3a,4,5,6-hexahydrobenzo[*e*]azulen-9-yl)-*N*-methylmethanesulfonamide (3.21). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.7 mg, 0.003 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.3 mL). Lithium hexamethyldisilazide (6.8 mg, 0.045 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.68** (12.4

mg, 0.03 mmol, 1.0 equiv.) was added to the reaction and it was subsequently heated to 70 °C for 3 hours. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.21** as a yellow oil (51% NMR yield). The crude was then purified by silver impregnated silica flash column chromatography (1% ethyl acetate in hexanes) to give pure product **3.21** as a colorless oil.

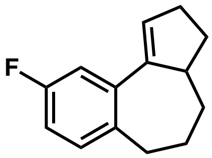
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 2.1 Hz, 1H), 7.14 – 7.05 (m, 2H), 5.85 – 5.69 (m, 1H), 3.45 (s, 3H), 2.86 (dd, *J* = 14.7, 8.0 Hz, 1H), 2.72 – 2.66 (m, 1H), 2.66 – 2.49 (m, 2H), 2.41 – 2.34 (m, 1H), 2.31 – 2.20 (m, 1H), 2.03 – 1.95 (m, 1H), 1.94 – 1.86 (m, 1H), 1.67 – 1.60 (m, 1H), 1.57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

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

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

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

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



9-Fluoro-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (3.22). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.7 mg, 0.003 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.3 mL). Lithium hexamethyldisilazide (5.5 mg, 0.033 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.67** (10.6 mg, 0.03 mmol, 1.0 equiv.) was added to the reaction and it was subsequently heated to 70 °C for 10 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.22** as a yellow oil (72% NMR yield). The crude was then purified by silica flash column chromatography (hexanes) to give pure product **3.22** as a colorless oil.

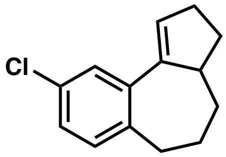
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.01 (dd, *J* = 8.3, 5.9 Hz, 1H), 6.96 (dd, *J* = 9.9, 2.8 Hz, 1H), 6.79 (td, *J* = 8.4, 2.8 Hz, 1H), 5.77 (q, *J* = 2.2 Hz, 1H), 2.81 (dd, *J* = 14.6, 8.4 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.63 – 2.49 (m, 2H), 2.41 – 2.32 (m, 1H), 2.25 (dddd, *J* = 12.6, 9.5, 8.6, 7.3 Hz, 1H), 2.06 – 1.94 (m, 1H), 1.90 (dtdd, *J* = 10.3, 5.1, 3.5, 2.0 Hz, 1H), 1.62 (ddt, *J* = 12.5, 8.7, 3.7 Hz, 1H), 1.57 – 1.50 (m, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 161.08 (d, *J* = 243.1 Hz), 148.94 (d, *J* = 1.8 Hz), 140.82 (d, *J* = 7.6 Hz), 136.56, 130.59 (d, *J* = 8.1 Hz), 128.59, 114.99 (d, *J* = 21.1 Hz), 112.95 (d, *J* = 20.5 Hz), 46.86, 36.97, 35.97, 32.69, 31.19, 26.87.

^{19}F NMR (282 MHz, CDCl$_3$) δ –118.7.

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

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



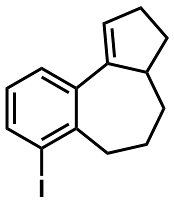
9-Chloro-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (3.23). Synthesized according to general procedure 3.8.2.2.1B. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.1 equiv.) and this was suspended in cyclohexane (0.25 mL). Lithium hexamethyldisilazide (4.6 mg, 0.033 mmol, 1.1 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.66** (9.2 mg, 0.025 mmol, 1 equiv.) was added to the reaction and it was subsequently heated to 70 °C for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.23** as a yellow oil (82% NMR yield). The crude was then purified by silica flash column chromatography (hexanes) to give pure product **3.23** as a colorless oil.

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

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

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

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



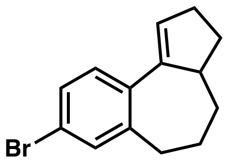
7-iodo-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (3.24). Synthesized according to general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (9.2 mg, 0.010 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (5.0 mL). Lithium hexamethyldisilazide (50.2 mg, 0.30 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the solution. Vinyl triflate **3.58** (92.1 mg, 0.20 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude product as brown oil (96% NMR yield). The crude was then purified by silica flash column chromatography (hexanes) to give product **3.24** as a colorless oil (55.9 mg, 90% yield).

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

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

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

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



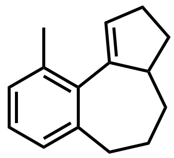
8-bromo-2,3,3a,4,5,6-hexahydrobenzo[e]azulene (3.25). Synthesized according to general procedure 3.8.2.2.1A. In a well-kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.). This was suspended in methylene chloride (3.2 mL) and stirred for 5 minutes at 30 °C. Vinyl triflate **3.59** (20.7 mg, 0.05 mmol, 1.0 equiv.) was added to the reaction and the reaction was stirred for 15 minutes. The reaction was brought outside the glovebox and was passed through a pad of silica with diethyl ether and concentrated to give crude tricyclic compound **3.25** as a yellow oil (77% NMR yield). The crude was then purified by silica flash chromatography (hexanes) to give pure product **3.25** as colorless oil.

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

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

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

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



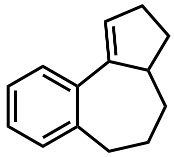
10-methyl-2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (3.26). Synthesized according to general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (3.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.64** (17.4 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and passed through silica and concentrated to give crude tricyclic compound **3.26** as a yellow oil (77% NMR yield, 60% isolated yield on 0.1 mmol scale). The crude was then purified by flash silver impregnated silica gel column chromatography (hexanes) to give pure product **3.26** as a colorless oil.

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

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

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

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



2,3,3a,4,5,6-hexahydrobenzo[*e*]azulene (3.27). Synthesized according to a modified general procedure 3.8.2.2.1A. In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.9 mg, 0.0025 mmol, 0.05 equiv.) and this was dissolved in methylene chloride (5.0 mL). Lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.28** (16.7 mg, 0.05 mmol, 1 equiv.) was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was cooled to room temperature and brought outside the glovebox. It was quenched by addition of diethyl ether and pass through silica and concentrated to give crude tricyclic compound **3.27** as a yellow oil (96% NMR yield, 90% isolated yield on 0.2 mmol scale). The crude was then purified by silica flash column chromatography (hexanes) to give pure product **3.27** as a colorless oil.

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

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

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

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

3.8.3 Experimental Procedures for Li-urea Catalysis

3.8.3.1 Catalyst Synthesis

Synthesis of catalysts ***3.29*** *and* ***3.30*** *is reported in the adapted article.*

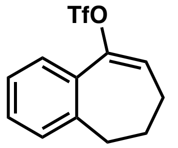
3.8.3.2 Vinyl Triflate Synthesis

For synthesis of ketone precursors for vinyl triflates in ***Figure 3.6****,* ***Figure 3.7****, and* ***Figure 3.8*** *see adapted articles. Spectral data for these precursors and vinyl triflates are also reported in the adapted article.*

3.8.3.2.1 General Procedure

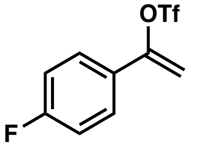
A: In a flame dried roundbottom flask, the starting ketone (1 equiv) was dissolved in THF to make a 0.413 M solution and this was cooled to –78 °C. To this solution was added a solution of NaHMDS (1.5 equiv, 1M solution in THF). This was warmed up to –40 °C for one hour before being cooled back down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

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



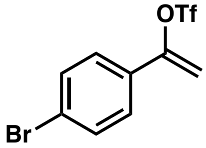
6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (3.69).

Synthesized according to known procedures. Spectral data match those reported in the literature.[36]



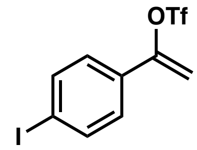
1-(4-fluorophenyl)vinyl trifluoromethanesulfonate (3.70).

Synthesized according to general procedure 3.8.3.2.1B starting from 4-fluoroacetophenone. Triflate **3.70** (600 mg, 2.22 mmol) was obtained as a yellow oil in 6% yield. NMR data matched those reported in the literature.[37]



1-(4-bromophenyl)vinyl trifluoromethanesulfonate (3.71).

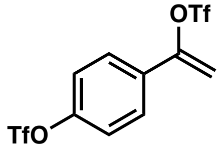
Synthesized according to general procedure 3.8.3.2.1B starting from 4-bromoacetophenone. Triflate **3.71** (4.20 g, 13.0 mmol) was obtained as a yellow oil in 42% yield. NMR data matched those reported in the literature.[37]



1-(4-iodophenyl)vinyl trifluoromethanesulfonate (3.72).

Synthesized according to general procedure 3.8.3.2.1B starting from 4-iodoacetophenone.

Triflate **3.72** (4.77 g, 12.6 mmol) was obtained as an orange oil in 61% yield. NMR data matched those reported in the literature.[37]



1-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)vinyl trifluoromethanesulfonate (3.73).

Synthesized according to general procedure 3.8.3.2.1B starting from 4-(((trifluoromethyl)sulfonyl)oxy)acetophenone. Triflate **3.73** (1.50 g, 3.7 mmol) was obtained as a yellow oil in 29% yield.

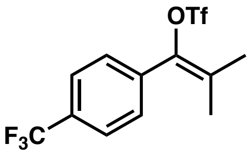
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.9 Hz, 2H), 7.35 (d, *J* = 8.9 Hz, 2H), 5.66 (d, *J* = 4.2 Hz, 1H), 5.49 (d, *J* = 4.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.5, 150.4, 132.4, 127.4, 122.0, 118.6 (q, *J* = 349.0 Hz), 118.5 (q, $^{1}J_{C\text{–}F}$ = 292.3 Hz), 106.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ –72.7, –73.6.

FTIR (Neat film NaCl): 3002, 2928, 2867, 1619, 1416, 1326, 1212, 1138, 1067, 967, 858, 615.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{12}H_{10}F_6O_3S$ 348.0255; Found 348.0252.



2-methyl-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl trifluoromethanesulfonate (3.74)

Synthesized according to general procedure 3.8.3.2.1A starting from 2-methyl-1-(4-(trifluoromethyl)phenyl)propan-1-one. Triflate **3.74** (220 mg, 1.80 mmol) was obtained as a colorless oil in 35% yield. Chromatography was performed using 5% ether/hexanes as a solvent system on silica gel.

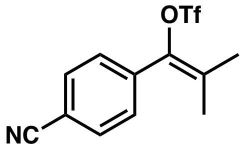
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.66 (d, J = 7.6 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 2.02 (s, 3H), 1.82 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 140.0, 136.2, 131.2 (q, $^2J_{C\text{–}F}$ = 32.8 Hz), 130.0, 129.9, 125.4 (q, $^3J_{C\text{–}F}$ = 3.8 Hz), 123.7 (q, $^1J_{C\text{–}F}$ = 272.5 Hz), 118.1 (q, $^1J_{C\text{–}F}$ = 320.2 Hz), 20.2, 19.1.

^{19}F NMR (282 MHz, CDCl$_3$) δ –180.0, –191.7.

FTIR (Neat film NaCl): 3002, 2928, 2867, 1619, 1416, 1326, 1212, 1138, 1067, 967, 858, 615.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{12}H_{10}F_6O_3S$: 348.0255; Found 348.0252.



1-(4-cyanophenyl)-2-methylprop-1-en-1-yl trifluoromethanesulfonate (3.75)

Synthesized according to general procedure 3.8.3.2.1A starting from 4-isobutyrlbenzonitrile. Column chromatography was performed using 85:14.9:0.1 hexane:ethyl acetate:triethylamine. Product **3.75** was obtained as colorless oil (660 mg, 6.1 mmol, 36%).

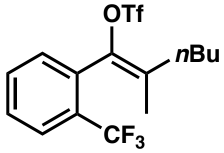
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.69 (d, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 7.6 Hz, 2H), 2.03 (s, 3H), 1.83 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 139. 4, 137.2, 132.2, 130.8, 130.1, 118.1, 118.1 (q, $^1J_{C–F}$ = 320.7 Hz), 113.1, 20.2, 19.2.

^{19}F NMR (376 MHz, CDCl$_3$) δ –74.5.

FTIR (Neat film NaCl): 3067, 3000, 2952, 2865, 2231, 1608, 1504, 1412, 1242, 1206, 1138, 1081, 957, 855, 617, 595.

HR-MS (EI-MS m/z: [M]+ Calc'd for $C_{12}H_{10}F_3NO_3S$ 305.0333; Found 305.0331.



2-Methyl-1-(2-(trifluoromethyl)phenyl)hex-1-en-1-yl trifluoromethanesulfonate (3.8:1 *Z*:*E* isomers) (3.76).

Synthesized according to general procedure 3.8.3.2.1A starting from 2-methyl-1-(2-(trifluoromethyl)phenyl)hexan-1-one. Column chromatography was performed using 95:5:0.1 hexane:diethyl ether:triethylamine. **3.76** was obtained as colorless oil and as a 3.8:1 mixture of *Z*:*E* isomers (260 mg, 1.8 mmol, 36%). The major isomer was determined by observing an NOE between the allylic methyl peak at 1.57 with aromatic protons.

NMR Data for Major Isomer:

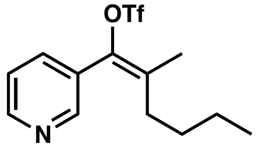
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.74 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.59 (td, *J* = 7.4, 1.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.53 – 7.48 (m, 1H), 2.46 (ddd, *J* = 13.4, 9.1, 7.0 Hz, 1H), 2.30 (ddd, *J* = 13.4, 8.9, 6.4 Hz, 1H), 1.57 (s, 3H), 1.55 – 1.49 (m, 2H), 1.48 – 1.36 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 137.2, 135.1, 133.9, 131.8, 130.1, 130.1 (q, $^2J_{C–F}$ = 20.5 Hz), 126.56 (q, $^3J_{C–F}$ = 4.9 Hz), 123.5 (q, $^1J_{C–F}$ = 273.8 Hz), 118.0 (q, $^1J_{C–F}$ = 319.9 Hz), 31.7, 29.0, 22.5, 17.9, 13.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ -61.1, -75.3.

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

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



(*E*)-2-methyl-1-(pyridin-3-yl)hex-1-en-1-yl trifluoromethanesulfonate (3.77).

Synthesized according to general procedure 3.8.3.2.1A starting from 2-methyl-1-(pyridin-3-yl)hexan-1-one. Purified by column chromatography (first with 20% ether/hexanes and then 8% acetone/hexanes) to afford pure triflate **3.77** as yellow oil (530 mg, 26%).

Assignment of the *E* configuration of this substrate was based on key cross peaks in ^{1}H NOESY experiments. There were key NOEs present between the two aromatic protons of pyridine (7.68, 8.61 ppm) and the allylic CH$_2$ protons (2.03-2.09 ppm). This led to the assignment of the (*E*)-isomer.

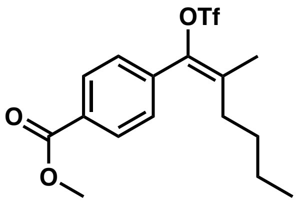
^{1}H NMR (500 MHz, CDCl$_3$) δ 8.63 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.61 (d, *J* = 2.0 Hz, 1H), 7.68 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.35 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H), 2.09 – 2.03 (m, 2H), 2.00 (s, 3H), 1.50 – 1.40 (m, 2H), 1.24 (hex, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 150.4, 150.3, 139.0, 137.0, 134.8, 128.9, 123.2, 118.1 (q, $^1J_{C\text{–}F}$ = 320.1 Hz), 33.1, 29.9, 22.3, 16.5, 13.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ –74.7.

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

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



Methyl (*E*)-4-(2-methyl-1-(((trifluoromethyl)sulfonyl)oxy)hex-1-en-1-yl)benzoate (3.78)

Synthesized according to general procedure 3.8.3.2.1A starting from corresponding ketone. To a 25 mL round bottom flask was added corresponding ketone (130 mg, 0.52 mmol, 1 equiv) as a solution in dry THF (1mL). This flask was cooled to –78 ºC, and to it was added a solution of NaHMDS (144 mg, 0.79 mmol, 1.5 equiv) as a solution in dry THF (5 mL) drop wise. This solution was allowed to stir for 30 minutes at –78 ºC. To the reaction was added 1,1,1-trifluoro-N-phenyl-N-((trifluoromethyl)sulfonyl)methanesulfonamide (206 mg, 0.58 mmol, 1.1 equiv) as a solution in dry THF (2 mL). The reaction was allowed to warm to room temperature and stir for 8h. The reaction was concentrated and suspended in 1:1 ether:hexanes (15 mL) and filtered. The solids were washed with cold 1:5 ether:hexanes. The filtrate was concentrated and purified by flash column chromatography (8% ether:hexanes) to give **3.78** as a clear oil (50 mg, 25% yield).

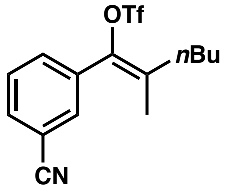
^{1}H NMR (300 MHz, CDCl$_3$) δ 8.07 (d, J = 7.9 Hz, 2H), 7.44 (d, J = 7.6 Hz, 2H), 3.94 (s, 3H), 2.07 (t, J = 7.8 Hz, 2 H), 1.98 (s, 3H), 1.45 (p, J = 8.0, 7.5 Hz, 2H), 1.23 (q, J = 7.3 Hz, 2H), 0.83 (t, J = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 166.7, 141.3, 137.3, 133.9, 131.1, 129.9, 129.8, 118.3 (q, $^{1}J_{C–F}$ = 320.2 Hz),52.6, 33.4, 30.2, 22.6, 16.8, 14.1.

^{19}F NMR (282 MHz, CDCl$_3$) δ -74.66.

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

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



(*Z*)-1-(3-Cyanophenyl)-2-methylhex-1-en-1-yl trifluoromethanesulfonate (3.79). Synthesized according to general procedure 3.8.3.2.1A starting from corresponding ketone. To a round bottom flask was added corresponding ketone (220 mg, 1.0 mmol, 1 equiv) as a solution in dry THF (2.5 mL). This flask was cooled to –78 ºC, and to it was added a solution of NaHMDS (281 mg, 1.5 mmol, 1.5 equiv) as a solution in dry THF (2 mL) drop wise. This solution was allowed to stir for 30 minutes at –78 ºC. To the reaction was added 1,1,1-trifluoro-N-phenyl-N-((trifluoromethyl)sulfonyl)methanesulfonamide (365 mg, 1.0 mmol, 1.0 equiv) as a solution in dry THF (0.6 mL). The reaction was allowed to warm to room temperature and stir overnight.

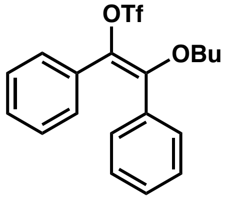
The reaction was then cooled to –78 °C and was quenched by addition of MeOH in EtOAc (10% *v/v*). The solution was allowed to warm to room temperature and the combined organics were washed with water and brine. The organic layer was then dried over $MgSO_4$, filtered and concentrated. The crude material was concentrated and purified by flash column chromatography (2.5% ether:hexanes) to give **3.79** as a clear oil (310 mg, 87% yield).

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

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

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

HRMS (CI-MS) m/z: [M]+ Calc'd for $C_{15}H_{16}F_3NO_3S$ 347.0803; Found 347.0797. FTIR (Neat Film NaCl): 2960, 2932, 2864, 2233, 1412, 1244, 1207, 1139, 983, 903, 844, 592 cm^{-1}.



(*Z*)-2-Butoxy-1,2-diphenylvinyl trifluoromethanesulfonate (3.80). Synthesized according to general procedure 3.8.3.2.1A starting from known butoxy benzoin derivative. To a flame dried flask was added NaHMDS (1.08 g, 5.9 mmol, 1.5 equiv) and anhydrous THF 20 ml, then cool the solution to –78 °C. 2-butoxy-1,2-diphenylethan-1-one (1.09 g, 3.9 mmol, 1 equiv) in 10 ml THF was added dropwise. Stir the solution at –78 °C for 30min and then warm up to 0 °C and keep at 0 °C for 30 min. 1,1,1-trifluoro-N-phenyl-N-((trifluoromethyl)sulfonyl)methanesulfonamide (1.55 g, 4.3 mmol, 1.1 equiv) in 10 ml THF was added after the solution was cooled to –78 °C then warm up slowly to room temperature. Reaction was quenched with 10 ml 1:5 methanol/ethyl actetate after 1 hour stirring at room temperature. The solvent was evaporated and the crude was purified by flash column chromatography (1% ether:hexanes) to give **3.80** as white solid (920 mg, 59% yield).

*Note: Vinyl triflate **3.80** was found to be unstable for long term storage on benchtop and should be stored in a glovebox freezer at – 40 °C after purification in order to maintain purity.

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

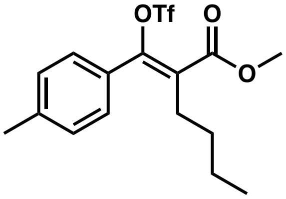
^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.38 – 7.33 (m, 2H), 7.30 – 7.25 (m, 2H), 7.25 – 7.17 (m, 6H), 4.59 (dd, *J* = 9.8, 8.8 Hz, 1H), 4.23 (dd, *J* = 8.8, 7.0 Hz, 1H), 3.49 (dddd, *J* = 10.3, 8.9, 6.9, 3.5 Hz, 1H), 1.61 (dqd, *J* = 13.7, 7.6, 3.5 Hz, 1H), 1.45 – 1.35 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H).

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

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

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

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



Methyl (*Z*)-2-(*p*-tolyl(((trifluoromethyl)sulfonyl)oxy)methylene)hexanoate (3.49)

To a 3-neck flask equipped with a reflux condenser and a stir bar was added NaH (170 mg, 60% *w/w*, 4.35 mmol, 1.8 equiv) followed by dry toluene (20 mL). To this was added dropwise corresponding ketone(600 mg, 2.4 mmol, 1 equiv). This was heated to 85 ºC for 1.5 hours. The reaction mixture was then cooled to 0 ºC and trifluoromethanesulfonic anhydride (0.57 mL, 3.4 mmol, 1.5 equiv). This was allowed to stir at 0 ºC for 1h, and then warmed to r.t. overnight. The reaction was diluted with ether (15 mL), followed by addition of satd. aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with ether (3 x 20 mL). The organic layer was dried with Na_2CO_3, filtered, and concentrated. The crude oil was purified by column chromatography (6% ether:hexanes) to give **3.49** as a yellow oil (600 mg, 65% yield).

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

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

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

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

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

3.8.3.3 Li-urea Catalyzed Friedel–Crafts Reactions.

In this section we outline reactions done in ***Figure 3.6***.

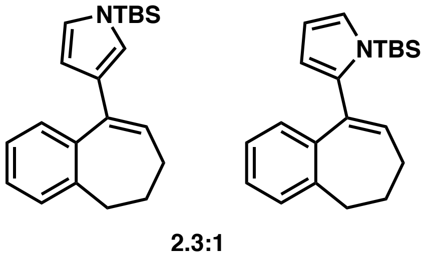
3.8.3.3.1 General procedure for hydrogen-bond donor catalyzed reactions performed outside of glovebox.

To an oven dried 2-dram vial with a magnetic stir bar was added catalyst (0.1 equiv, 0.02 mmol). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. Solvent (1.4 mL) was added followed by LiHMDS (0.3 mmol, 1.5 equiv, 0.6 mL of 0.5 M solution in reaction solvent). To this was added arene (1.0–2.0 mmol, 5–10 equiv) and allowed to prestir for 5 minutes. Substrate (0.2 mmol, 1.0 equiv) was added through the septum and the reaction was allowed to stir at r.t. For reactions conducted at elevated temperature, the septum was quickly replaced with a PTFE lined cap under a stream of argon and further sealed with electrical tape. The reaction progress was closely monitored by TLC and/or GC. If a reaction started to stall, an extra equivalent of LiHMDS (0.2 mmol, 1.0 equiv, 0.4 mL of 0.5 M solution in reaction solvent) was added. Upon completion of reaction, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography to give the pure product.

*Solutions of LiHMDS in 1,2-difluorobenzene have a limited storage lifetime due to slow nucleophilic aromatic substitution reaction of LiHMDS with 1,2-difluorobenzene.

**depending on quality of LiHMDS solution and airfree technique, slightly more LiHMDS may be required to drive a reaction to full conversion.

***hexanes was obtained directly from solvent system and 1,2-difluorobenzene was distilled over CaH_2 prior to performing reaction, but arene and substrate were used without careful drying.



1-(*tert*-Butyldimethylsilyl)-3-(6,7-dihydro-5*H*-benzo[7]annulen-9-yl)-1*H*-pyrrole (3.31a) and 1-(*tert*-butyldimethylsilyl)-2-(6,7-dihydro-5*H*-benzo[7]annulen-9-yl)-1*H*-pyrrole (3.31b)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.6 mg, 0.02 mmol, 0.10 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. Hexanes (1.4 mL) was added followed by LiHMDS (0.30 mmol, 0.6 mL of 0.5M solution in hexanes, 1.5 equiv). This was allowed to prestir for 5 minutes. *N*-TBSPyrrole (363 mg, 2.0 mmol, 10 equiv) was added followed by benzosuberonyl triflate **3.69** (58.5 mg, 0.2 mmol, 1.0 equiv) through the septum. The septum was replaced with a PTFE cap and sealed with electrical tape under a flow of argon. The reaction was stirred at 50 °C for 12 hours. At this point LiHMDS (0.20 mmol, 0.4 mL of 0.5M solution in hexanes, 1.0 equiv) was added and reaction stirred for additional 24 hours. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as orange oil. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give product as a mix of isomers (2.3:1 C3:C2) as colorless oil (52.8 mg, 82%, 0.16 mmol). The isomers were further separated by silica flash chromatography (15% benzene/hexanes) to give analytically pure samples of both major and minor isomers.

The major isomer was assigned by using NOESY, COSY, and HSQC NMR experiments. The methyl groups of the TBS (0.89 and 0.34 ppm) exhibited NOE's with 2 distinct protons on the pyrrole ring suggesting that neither of the C2 positions were functionalized. Another observation was made that in general the C2 peaks are more downfield than the C3 peaks in these mono-substituted pyrrole compounds. In the major isomer the three pyrrole protons are at 6.75, 6.58, and 6.39 ppm whereas in the minor they are located at 6.77, 6.22, and 6.05 ppm.

Major isomer **(3.31a)**:

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.35 – 7.32 (m, 1H), 7.27 – 7.23 (m, 1H), 7.23 – 7.19 (m, 2H), 6.75 (dd, *J* = 2.8, 2.1 Hz, 1H), 6.58 (t, *J* = 1.8 Hz, 1H), 6.39 (dd, *J* = 2.7, 1.4 Hz, 1H), 6.36 (t, *J* = 7.4 Hz, 1H), 2.62 (t, *J* = 7.0 Hz, 2H), 2.13 (p, *J* = 7.1 Hz, 2H), 1.88 (q, *J* = 7.2 Hz, 2H), 0.89 (s, 9H), 0.39 (s, 6H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 141.9, 140.8, 136.8, 128.6, 128.5, 127.9, 126.7, 125.6, 124.5, 122.6, 122.4, 109.4, 35.4, 32.3, 25.7, 24.7, 18.1, –5.7.

FTIR (Neat film NaCl): 3121, 3096, 3055, 3020, 2928, 2900, 2855, 1616, 1479, 1471, 1258, 1112, 1094, 837, 807, 787, 748, 681, 661.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{21}H_{29}NSi$ 323.2069; Found 323.2061.

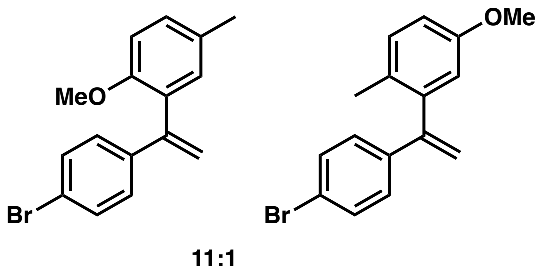
Minor isomer **(3.31b)**:

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.19 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.13 (td, *J* = 7.4, 1.6 Hz, 1H), 7.08 (td, *J* = 7.5, 1.6 Hz, 1H), 6.84 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.77 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.26 (t, *J* = 6.5 Hz, 1H), 6.22 (t, *J* = 3.0 Hz, 1H), 6.06 (dd, *J* = 3.1, 1.5 Hz, 1H), 2.74 (t, *J* = 6.5 Hz, 2H), 2.17 (pd, *J* = 6.2, 2.8 Hz, 2H), 2.13 – 2.01 (m, 2H), 0.84 (s, 9H), 0.12 (s, 6H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 142.0, 141.2, 141.0, 136.7, 132.6, 129.3, 128.9, 126.7, 126.3, 125.8, 114.6, 109.8, 34.3, 33.9, 27.3, 26.6, 19.2, –3.6.

FTIR (Neat film NaCl): 3096, 3063, 3017, 2929, 2857, 1471, 1462, 1404, 1257, 1140, 1063, 839, 809, 788, 721.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{21}H_{29}NSi$ 323.2069; Found 323.2060.



2-(1-(4-Bromophenyl)vinyl)-1-methoxy-4-methylbenzene (3.32a) and 2-(1-(4-bromophenyl)vinyl)-4-methoxy-1-methylbenzene (3.32b)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 3,4-bis((3,5-bis(trifluoromethyl)phenyl)amino)cyclobut-3-ene-1,2-dione **3.30** (10.7 mg, 0.02 mmol, 0.10 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. Hexanes (1.4 mL) was added followed by LiHMDS (0.30 mmol, 0.6 mL of 0.5 M solution in hexanes, 1.5 equiv). Next, 4-methylanisole (122 mg, 0.20 mmol, 5 equiv) was added to the reaction. This was allowed to prestir for 5 minutes. 1-(4-bromophenyl)-2-methylprop-1-en-1-yl trifluoromethanesulfonate (66.2 mg, 0.2 mmol, 1.0 equiv) was added through the septum. The reaction was allowed to stir for 12 hours. At this point, more LiHMDS (0.2 mmol, 1.0 equiv, 0.4 mL of 0.5 M solution in hexanes) was added. Reaction stirred for an additional 4 hours at which point it was complete. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as orange oil. The crude material was purified by silica flash chromatography (3% ethyl acetate/hexanes) to give a 13:1 mixture of isomers as yellow oil (40.6 mg, 67%, 0.134 mmol). To separate the isomers, a small portion of the mixture was purified by reverse phase preparative HPLC (95:5 MeCN:water) to give a pure sample of the major isomer and a ca. 90% pure sample of the minor isomer for characterization. The major isomer was assigned by observing key NOE's between aryl protons on the anisole with the tolyl peak and the methoxy peak. Notably, protons at 7.14 ppm and 7.05 ppm had NOE's with the tolyl peak at 2.32 ppm, while the proton at 6.81 ppm had an NOE with the methoxy peak at 3.61 ppm. This lead to assigning the major isomer with substitution *ortho* to the OMe peak.

Major isomer **(3.32a)**:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.14 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 5.69 (d, *J* = 1.2 Hz, 1H), 5.33 (m, *J* = 1.2 Hz, 1H), 3.61 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 146.2, 140.1, 131.8, 131.0, 130.2, 129.9, 129.5, 128.0, 121.1, 115.7, 111.2, 55.7, 20.4.

FTIR (Neat film NaCl): 3088, 3020, 3000, 2924, 1495, 1487, 1243, 1009, 902, 834, 744.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{15}BrO$ 302.0306; Found 302.0303

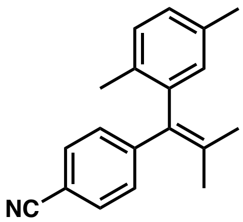
Minor isomer **(3.32b)**:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.81 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.77 (d, *J* = 2.9 Hz, 1H), 5.75 (s, 1H), 5.22 (s, 1H), 3.80 (s, 3H), 1.95 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 148.4, 141.9, 139.2, 131.4, 131.1, 131. 0, 128.1, 121.6, 115.5, 115.3, 113.0, 55.3, 19.1.

FTIR (Neat film NaCl): 3090, 2994, 2953, 2924, 2850, 1610, 1488, 1236, 1074, 1040, 1009, 904, 835, 802.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{15}BrO$ 302.0306; Found 302.0302



4-(1-(2,5-Dimethylphenyl)-2-methylprop-1-en-1-yl)benzonitrile (3.33)

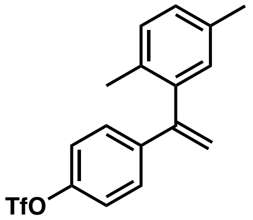
Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.7 mg, 0.02 mmol, 0.10 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. 1,2-Difluorobenzene (1.4 mL) was added followed by LiHMDS (0.30 mmol, 0.6 mL of 0.5 M solution in 1,2-difluorobenzene, 1.5 equiv). Next, *para*-xylenes (106 mg, 0.2 mmol, 5 equiv) was added to the reaction. This was allowed to prestir for 5 minutes. 1-(4-cyanophenyl)-2-methylprop-1-en-1-yl trifluoromethanesulfonate **3.75** (61.1 mg, 0.2 mmol, 1.0 equiv) was added through the septum. The septum was replaced with a PTFE cap under a stream of argon and the reaction was heated to 70 °C for 16 hours. At this point, more LiHMDS (0.2 mmol, 1.0 equiv, 0.4 mL of 0.5 M solution in 1,2-difluorobenzene) was added. Reaction stirred for an additional 10 hours at which point it was complete. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as orange oil. The crude material was purified by silica flash chromatography (5% ether/hexanes) to give pure product **3.33** as yellow oil (27.2 mg, 52%, 0.104 mmol).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 1.9 Hz, 1H), 6.88 (d, *J* = 1.9 Hz, 1H), 2.29 (s, 3H), 2.07 (s, 3H), 1.88 (s, 3H), 1.64 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 147.0, 141.4, 135.1, 134.8, 133.9, 132.9, 131.6, 130.6, 130.2, 130.1, 127.8, 119.2, 109.4, 22.6, 21.7, 20.9, 19.2.

FTIR (Neat film NaCl): 3037, 2985, 2922, 2858, 2227, 1603, 1500, 1438, 851, 816.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{19}H_{19}N$ 261.1518; Found 261.1513



4-(1-(2,5-Dimethylphenyl)vinyl)phenyl trifluoromethanesulfonate (3.34)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.6 mg, 0.02 mmol, 0.10 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. *para*-Xylene (1.4 mL) was added followed by LiHMDS (0.30 mmol, 0.6 mL of 0.5M solution in *para*-xylene, 1.5 equiv). This was allowed to prestir for 5 minutes. 1-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)vinyl trifluoromethanesulfonate **3.73** (80.1 mg, 0.2 mmol, 1.0 equiv) was added through the septum. The reaction was stirred at r.t. for 12 hours. At this point LiHMDS (0.20 mmol, 0.4 mL of 0.5M solution in *para*-xylene, 1.0 equiv) was added and reaction stirred for additional 4 hours. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as orange solid. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give product **3.34** as colorless oil (53.8 mg, 76%, 0.15 mmol).

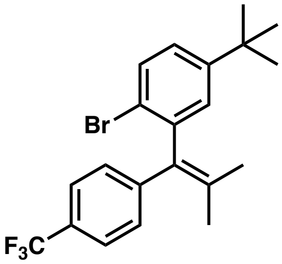
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34 (d, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 1.3 Hz, 2H), 7.01 (s, 1H), 5.77 (d, *J* = 1.3 Hz, 1H), 5.27 (d, *J* = 1.3 Hz, 1H), 2.34 (s, 3H), 1.99 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 148.8, 147.9, 141.1, 140.5, 135.4, 132.7, 130.6, 130.2, 128.6, 128.2, 121.2, 118.7 (q, $^1J_{C\text{–}F}$ = 320.8 Hz), 116.4, 20. 9, 19.6.

^{19}F NMR (376 MHz, CDCl$_3$) δ –72.8.

FTIR (Neat film NaCl): 3092, 3016, 2925, 2861, 1615, 1499, 1425, 1250, 1210, 1140, 886, 848, 607.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{17}H_{15}F_3O_3S$ 356.0694; Found 356.0692.



1-Bromo-4-(*tert*-butyl)-2-(2-methyl-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl)benzene (3.35)

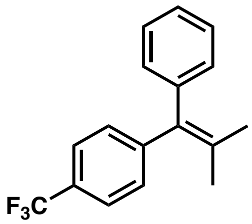
Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (10.7 mg, 0.02 mmol, 0.10 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. Hexanes (1.4 mL) was added followed by LiHMDS (0.30 mmol, 0.6 mL of 0.5 M solution in hexanes, 1.5 equiv). Next, 4-*tert*butylbromobenzene (213 mg, 1.0 mmol, 5 equiv) was added to the reaction. This was allowed to prestir for 5 minutes. 2-methyl-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl trifluoromethanesulfonate **3.74** (69.7 mg, 0.2 mmol, 1.0 equiv) was added through the septum. The septum was replaced with a PTFE cap under a stream of argon and the reaction was heated to 50 °C for 4 hours. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as orange oil. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give product as yellow oil (65.9 mg, 80%, 0.16 mmol). The major isomer was assigned using key interactions from the 1H-1H NOESY. Notably, the methyl peaks of the *t*-Butyl (1.30 ppm) had NOE's with two peaks in the aromatic region at 7.22 and 7.14 which is suggestive of the isomer depicted

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 8.0, 2H), 7.22 (d, *J* = 2.5 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.6 Hz, 1H), 1.87 (s, 3H), 1.65 (s, 3H), 1.30 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7, 144.9, 142.5, 135.0, 134.6, 132.3, 129.9, 128.5, 128.1 (q, $^2J_{C–F}$ = 32.2 Hz), 125.6, 124.7 (q, $^3J_{C–F}$ = 3.8 Hz), 124.3 (q, $^1J_{C–F}$ = 272.3 Hz), 120.9, 34.6, 31.3, 22.5, 21.6.

FTIR (Neat film NaCl): 3053, 2965, 2909, 2870, 1614, 1463, 1322, 1163, 1108, 1066, 830, 820.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{22}H_{22}BrF_3$: 410.0857; Found 410.0856.



1-(2-methyl-1-phenylprop-1-en-1-yl)-4-(trifluoromethyl)benzene (3.36)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (4.8 mg, 0.01 mmol, 0.10 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. Hexanes (0.7 mL) was added followed by LiHMDS (0.15 mmol, 0.3 mL of 0.5 M solution in hexanes, 1.5 equiv). Next, benzene (39 mg, 0.5 mmol, 5 equiv) was added to the reaction. This was allowed to prestir for 5 minutes. 2-methyl-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl trifluoromethanesulfonate **3.74** (34.8 mg, 0.1 mmol, 1.0 equiv) was added through the septum. The reaction was stirred at r.t. for 12 hours. At this point LiHMDS (0.10 mmol, 0.2 mL of 0.5M solution in hexanes, 1.0 equiv) was added and reaction stirred for additional 4 hours. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as yellow oil. The crude material was purified by silica flash chromatography (2% ether/hexanes) to give product **3.36** as colorless oil (23.1 mg, 84%, 0.84 mmol).

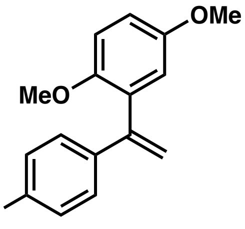
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.32 – 7.28 (m, 2H), 7.28 – 7.25 (m, 2H), 7.24 – 7.20 (m, 1H), 7.15 – 7.10 (m, 2H), 1.83 (s, 3H), 1.82 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.0, 142.5, 136.0, 132.6, 130.1, 129.8, 128.1 (q, $^{2}J_{C–F}$ = 31.5 Hz), 128.0, 126.4, 124.8 (q, $^{3}J_{C–F}$ = 3.8 Hz), 124.3 (q, $^{1}J_{C–F}$ = 248.6), 22.5 (d, *J* = 14.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ –62.3.

FTIR (Neat film NaCl): 3050, 3027, 2988, 2928, 2861, 1616, 1493, 1325, 1164, 1124, 1069, 759.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{17}H_{15}F_3$ 276.1126; Found 276.1124.



2-(1-(4-fluorophenyl)vinyl)-1,4-dimethoxybenzene (3.37)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.7 mg, 0.02 mmol, 0.10 equiv) and 1,4-dimethoxybenzene (138.0 mg, 1.0 mmol, 5.0 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. 1,2-Difluorobenzene (1.5 mL) was added followed by LiHMDS (0.24 mmol, 0.48 mL of 0.5 M solution in 1,2-difluorobenzene, 1.2 equiv). This was allowed to prestir for 5 minutes. 1-(4-fluorophenyl)vinyl trifluoromethanesulfonate **3.70** (54.0 mg, 0.2 mmol, 1.0 equiv) was added through the septum and the reaction was allowed to stir at r.t for 6 hours. At this point, more LiHMDS (0.16 mmol, 0.8 equiv, 0.32 mL of 0.5 M solution in 1,2-difluorobenzene) was added. Reaction stirred for an additional 12 hours at which point it was complete. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as a yellow solid. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give a mixture of product with some leftover 1,4-dimethoxybenzene. This was heated under reduced pressure (50 °C, 0.2 mmHg) to remove residual dimethoxybenzene and afford pure product **3.37** as a yellow oil (35.9 mg, 70%, 0.14 mmol)

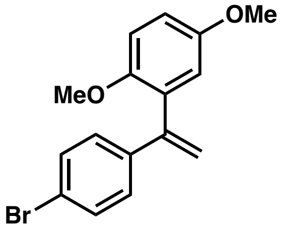
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34 – 7.21 (m, 2H), 6.98 – 6.93 (m, 2H), 6.90 – 6.80 (m, 3H), 5.65 (d, *J* = 1.3 Hz, 1H), 5.30 (d, *J* = 1.3 Hz, 1H), 3.79 (s, 3H), 3.58 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 162.27 (d, $^1J_{C\text{–}F}$ = 246.1 Hz), 153.59, 151.22, 145.91, 136.95 (d, $^4J_{C\text{–}F}$ = 3.1 Hz), 131.89, 127.95 (d, $^3J_{C\text{–}F}$ = 8.1 Hz), 117.04, 115.23, 114.83 (d, $^2J_{C\text{–}F}$ = 21.4 Hz), 113.46, 112.66, 56.36, 55.73.

^{19}F NMR (376 MHz, CDCl$_3$) δ –115.4.

FTIR (Neat film NaCl): 3046, 2999, 2936, 2833, 1602, 1582, 1507, 1491, 1464, 1422, 1298, 1218, 1045, 1025, 841.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{15}FO_2$ 218.1056; Found 218.0153



2-(1-(4-bromophenyl)vinyl)-1,4-dimethoxybenzene (3.38)

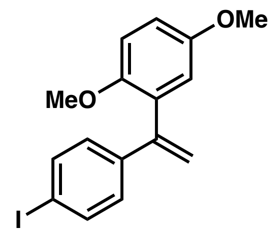
Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.7 mg, 0.02 mmol, 0.10 equiv) and 1,4-dimethoxybenzene (138.0 mg, 1.0 mmol, 5.0 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. 1,2-Difluorobenzene (1.5 mL) was added followed by LiHMDS (0.24 mmol, 0.48 mL of 0.5 M solution in 1,2-difluorobenzene, 1.2 equiv). This was allowed to prestir for 5 minutes. 1-(4-bromophenyl)vinyl trifluoromethanesulfonate **3.71** (66.2 mg, 0.2 mmol, 1.0 equiv) was added through the septum and the reaction was allowed to stir at r.t for 6 hours. At this point, more LiHMDS (0.16 mmol, 0.8 equiv, 0.32 mL of 0.5 M solution in 1,2-difluorobenzene) was added. Reaction stirred for an additional 12 hours at which point it was complete. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as a yellow solid. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give a mixture of product with some leftover 1,4-dimethoxybenzene. This was heated under reduced pressure (100 °C, 0.2 mmHg) to remove residual dimethoxybenzene and afford pure product **3.38** as a yellow oil (43.8 mg, 67%, 0.134 mmol)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42 – 7.35 (m, 2H), 7.21 – 7.13 (m, 2H), 6.91 – 6.78 (m, 3H), 5.70 (d, *J* = 1.2 Hz, 1H), 5.34 (d, *J* = 1.2 Hz, 1H), 3.79 (s, 3H), 3.58 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 153.6, 151.2, 146.0, 139.8, 131.5, 131.1, 128. 0, 121.3, 117.1, 116.0, 113.6, 112.6, 56.3, 55.7.

FTIR (Neat film NaCl): 3088, 2997, 2933, 2832, 1611, 1583, 1490, 1463, 1421, 1217, 1045, 1038, 904, 834, 806.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{15}BrO_2$ 318.0255; Found 318.0248



2-(1-(4-iodophenyl)vinyl)-1,4-dimethoxybenzene (3.39)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To an oven dried 2-dram vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29**

(9.7 mg, 0.02 mmol, 0.10 equiv) and 1,4-dimethoxybenzene (138.0 mg, 1.0 mmol, 5.0 equiv). The 2-dram vial was covered with a septum and vacuum/backfill three times and left under nitrogen. 1,2-Difluorobenzene (1.5 mL) was added followed by LiHMDS (0.24 mmol, 0.48 mL of 0.5 M solution in 1,2-difluorobenzene, 1.2 equiv). This was allowed to prestir for 5 minutes. 1-(4-iodophenyl)vinyl trifluoromethanesulfonate **3.72** (66.2 mg, 0.2 mmol, 1.0 equiv) was added through the septum and the reaction was allowed to stir at r.t for 6 hours. At this point, more LiHMDS (0.16 mmol, 0.8 equiv, 0.32 mL of 0.5 M solution in 1,2-difluorobenzene) was added. Reaction stirred for an additional 12 hours at which point it was complete. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as a yellow solid. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give a mixture of product with some leftover 1,4-dimethoxybenzene. This was heated under reduced pressure (100 °C, 0.2 mmHg) to remove residual dimethoxybenzene and afford pure product **3.39** as a yellow oil (48.9 mg, 67%, 0.134 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.51 (m, 2H), 7.06 – 6.99 (m, 2H), 6.93 – 6.78 (m, 3H), 5.70 (d, *J* = 1.2 Hz, 1H), 5.33 (d, *J* = 1.2 Hz, 1H), 3.79 (s, 3H), 3.58 (s, 3H).

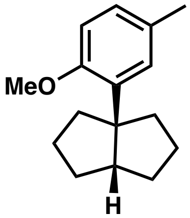
^{13}C NMR (126 MHz, $CDCl_3$) δ 153.6, 151.2, 146.1, 140.4, 137.1, 131.4, 128.3, 117.1, 116.0, 113.6, 112.6, 92.9, 56.3, 55.7.

FTIR (Neat film NaCl): 3086, 2996, 2933, 2831, 1610, 1582, 1492, 1462, 1421, 1268, 1219, 1045, 1004, 841, 756.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{15}IO_2$ 366.0117; Found 366.0114

Gram scale reaction procedure

To a flame dried 100 mL schlenk flask with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (145 mg, 0.3 mmol, 0.10 equiv) and 1,4-dimethoxybenzene (2070 mg, 15.0 mmol, 5.0 equiv). 1,2-difluorobenzene (23 mL) was added followed by LiHMDS (3.60 mmol, 7.2 mL of 0.5 M solution in 1,2-difluorobenzene, 1.2 equiv). This was allowed to prestir for 5 minutes. 1-(4-iodophenyl)vinyl trifluoromethanesulfonate **3.72** (1.13 g, 3.0 mmol, 1.0 equiv) was added through the septum and the reaction was allowed to stir at r.t for 4.5 hours. At this point, more LiHMDS (3.0 mmol, 1.0 equiv, 6.0 mL of 0.5 M solution in difluorobenzene) was added. Reaction stirred for an additional 12 hours at which point it was complete. The reaction was diluted with ether (ca. 2 mL) and pushed through a pad of silica. This was concentrated to give the crude material as a yellow solid. The crude material was purified by silica flash chromatography (3% ether/hexanes) to give a mixture of product with some leftover 1,4-dimethoxybenzene. This was heated under reduced pressure (100 °C, 0.2 mmHg) to remove residual dimethoxybenzene and afford pure product **3.39** as a yellow oil (701 mg, 64%, 1.91 mmol).



(*cis*)-3a-(2-Methoxy-5-methylphenyl)octahydropentalene (3.40)

Synthesized according to a slightly modified general procedure 3.8.3.3.1. To a flame dried 25 mL schlenk flask with a magnetic stir bar was added 3,4-bis((3,5-bis(trifluoromethyl)phenyl)amino)cyclobut-3-ene-1,2-dione **3.30** (53.6 mg, 0.1 mmol, 0.10 equiv). LiHMDS (1.20 mmol, 2.4 mL of 0.5M solution in 1,2-difluorobenzene, 1.2 equiv) was added to the flask. This was allowed to prestir for 5 minutes. *4*-methylanisole (244 mg, 2.0

mmol, 2 equiv) was added followed by cyclooctenyl triflate **3.6** (258.3 mg, 1.0 mmol, 1.0 equiv) through the septum. The reaction was stirred at room temperature for 14 hours. At this point LiHMDS (1.20 mmol, 2.4 mL of 0.5M solution in 1,2-difluorobenzene, 1.2 equiv) was added and reaction stirred for additional 48 hours. Nonane (150 μL) was added to acquire a GC yield (57%). The reaction was diluted with ether (10 mL) and water (10 mL). The layers were separated and the aqueous was extracted with ether (2 x 10 mL). Combined organics dried over magnesium sulfate, filtered and concentrated to give crude product as orange oil. The crude material was heated to 70 °C under reduced pressure to remove residual *4*-methylanisole. The remaining material was purified by silica flash chromatography (3% ether/hexanes) to give bicycle **3.40** as colorless oil (107 mg, 47%, yield, 0.47 mmol). The major regioisomer/Friedel-Crafts isomer was determined by performing 2D NMR experiments: NOESY, COSY, HSQC, and HMBC. First, on HSQC it was evident that there was only one tertiary carbon peak (47.5 ppm on carbon NMR and 2.83 on proton NMR) which was suggestive that the product was arylated at the ring fusion position. In order to assign the correct Friedel-Crafts isomer, the aromatic protons were analyzed for NOE's with the tolyl peak or methoxy peak. The protons at 7.08 and 6.97 had NOE's with the tolyl peak at 2.29 whereas the proton at 6.78 had an NOE with the methoxy protons at 3.79. Taken together, this suggested that the arene was functionalized *ortho* to the methoxy as drawn.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 2.2 Hz, 1H), 6.97 (dd, *J* = 2.2, 0.8 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 3.79 (s, 3H), 2.83 (tt, *J* = 8.8, 4.7 Hz, 1H), 2.29 (d, *J* = 0.7 Hz, 3H), 1.99 – 1.91 (m, 4H), 1.90 – 1.84 (m, 2H), 1.70 – 1.60 (m, 2H), 1.54 – 1.46 (m, 2H), 1.40 – 1.34 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 138.3, 128.7, 126.9, 126.6, 111.6, 57.2, 55.2, 47.6, 40.5, 34.2, 25.8, 20.9.

FTIR (Neat film NaCl): 3111, 2937, 2862, 2831, 1606, 1585, 1495, 1464, 1450, 1291, 1236, 1226, 1180, 1034, 803, 735.

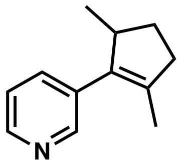
HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{22}O$: 230.1671; Found 230.1671.

3.8.3.4 Li-urea Catalyzed Intramolecular C–H Insertion Reactions.

In this section we outline reactions done in ***Figure 3.7a***.

3.8.3.4.1 General Procedure

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with the urea catalyst **3.29** (2.4 mg, 0.01 mmol, 0.2 equiv) and LiH (1.0 mg, 0.25 mmol, 5 equiv) followed by dry 1,2-difluorobenzene (1.5 mL). To this was added vinyl triflate (0.050 mmol, 1 equiv) and heated to 70 ºC until reaction was completed as monitored by GC-FID or TLC. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography to yield cyclopentene product.



3-(2,5-Dimethylcyclopent-1-en-1-yl)pyridine (3.41).

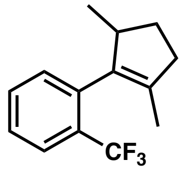
Synthesized according to a slightly modified general procedure 3.8.3.4.1. To a 20 mL vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.6 mg, 0.02 mmol, 0.20 equiv). LiHMDS (56.5 mg, 0.34 mmol, 3.4 equiv) was added followed by cyclohexane (6 mL). After a five minute prestir, vinyl triflate **3.77** (32.3 mg, 0.10 mmol, 1 equiv) was added. The reaction was heated to 70 °C. After 4 hours, the reaction was cooled to room temperature and removed from the glovebox. The reaction was concentrated and then suspended in ether and pushed through a pad of silica. This was concentrated to give crude product as dark solid (80% NMR yield). This was purified by silica flash column chromatography (1% MeOH/DCM) and then another flash column chromatography (1:25:175 triethylamine:ethyl acetate:hexanes). This gave cyclopentyl product **3.41** as colorless oil (10.6 mg, 61% yield, 0.061 mmol).

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

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

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

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



1-(2,5-Dimethylcyclopent-1-en-1-yl)-2-(trifluoromethyl)benzene (3.42).

Synthesized according to general procedure 3.8.3.4.1. To a 20 mL vial with a magnetic stir bar was added 1,3-bis(3,5-bis(trifluoromethyl)phenyl)urea **3.29** (9.6 mg, 0.02 mmol, 0.20 equiv). LiH (2.9 mg, 0.30 mmol, 3.0 equiv) was added followed by 1,2-difluorobenzene (6 mL). After a five minute prestir, vinyl triflate **3.76** (39.0 mg, 0.10 mmol, 1 equiv) was added. The reaction was heated to 70 °C. After 2 hours, the reaction was cooled to room temperature and removed from the glovebox. The reaction was concentrated and then suspended in ether and pushed through a pad of silica. This was concentrated to give crude product as yellow solid. This was purified by silica flash column chromatography (3% ether/hexanes) to give cyclopentenyl product **3.42** as colorless oil (21.6 mg, 90% yield, 0.90 mmol).

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

Major Rotamer

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

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

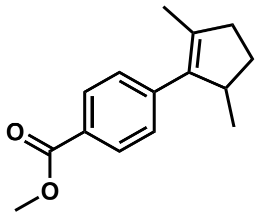
^{19}F NMR (376 MHz, $CDCl_3$) δ –61.7.

VT NMR (70 °C)

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

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

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



Methyl 4-(2,5-dimethylcyclopent-1-en-1-yl)benzoate (3.43)

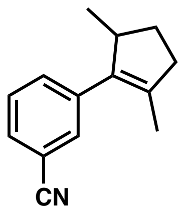
Synthesized according to a modified general procedure 3.8.3.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with the urea catalyst **3.29** (2.4 mg, 0.005 mmol, 0.2 equiv) and LiH (0.6 mg, 0.075 mmol, 3 equiv) followed by dry 1,2-difluorobenzene (1.5 mL). To this was added **3.78** (9.5 mg, 0.025 mmol, 1 equiv) and heated to 70 ºC for 6 hours. The reaction vial was removed from the glove box and plugged through silica gel with ether and concentrated. The crude oil was purified by flash column chromatography (4% acetone:hexanes) to yield cyclopentene **3.43** as a clear oil (5.2 mg, 90% yield).

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

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

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

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



3-(2,5-Dimethylcyclopent-1-en-1-yl)benzonitrile (3.44).

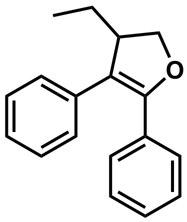
Synthesized according to general procedure 3.8.3.4.1. In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with the urea catalyst **3.29** (4.8 mg, 0.01 mmol, 0.2 equiv) and LiH (2.0 mg, 0.25 mmol, 5 equiv) followed by dry 1,2-difluorobenzene (3.0 mL). To this was added **3.79** (17.4 mg, 0.050 mmol, 1 equiv) and heated to 70 ºC for 24 hrs. The reaction vial was removed from the glove box, diluted with ether and plugged through silica gel with dichloromethane and concentrated. The crude oil was purified by flash column chromatography (2% ether:hexanes) to yield olefin **3.44** as a clear oil (7.6 mg, 77% yield).

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

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

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

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



3-Ethyl-4,5-diphenyl-2,3-dihydrofuran (3.45).

Synthesized according to a slightly modified general procedure 3.8.3.4.1. To an 1-dram vial with a magnetic stir bar in the glove box was added LiOtBu (9.0 mg, 0.11 mmol, 1.5 equiv), 3,4-bis((3,5-bis(trifluoromethyl)phenyl)amino) cyclobut-3-ene-1,2-dione **3.30** (8.0 mg, 0.015 mmol, 0.2 equiv), 1.5 ml DCE, and 0.1 ml hexanes. This was allowed to prestir at room temperature for 1 hour. Then triflate **3.80** (30.0 mg, 0.075 mmol, 1 equiv) was added. The reaction was heated to 70 °C for 12 hours then 90 °C for another 12 hours. The reaction was diluted with ether and pushed through a pad of silica. The crude material was purified by silica flash chromatography (3% acetone/hexanes) to give pure dihydrofuran **3.45** as colorless oil (11.5 mg, 61%, 0.046 mmol).

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

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

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

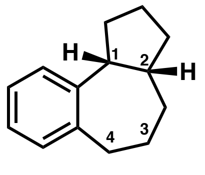
HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{18}H_{18}O$ 250.1358; Found 250.1354

3.8.4 Mechanistic Studies

This section describes the experiments in ***Figure 3.8.***

3.8.4.1 Stoichiometric LiF_{20} Experiment

In a In a well-kept glovebox, (H_2O, $O_2 \leq 0.5$ ppm), a J. Young tube was charged with $[Li]^+[B(C_6F_5)_4]^-$ (18.1 mg, 0.0026 mmol, 1.05 equiv.) and suspended in dry $CDCl_3$ (0.5 mL). Vinyl triflate **3.28** (8.3 mg, 0.025 mmol, 1.0 equiv.) was added to the reaction and the reaction was shaken by hand for 10 minutes. At this point, ^1H and ^{19}F NMR spectra were acquired indicating incomplete reaction. The reaction was shaken by hand for an additional 80 minutes and another ^1H and ^{19}F NMR spectra were acquired. At this point, full consumption of starting material was observed. The reaction was poured into D_2O (0.8 mL) and the layers were separated. The aqueous layer was analyzed by ^{19}F NMR and LiOTf was observed. The organic layer had many products, but HRMS data was suggestive that intermolecular hydride transfer was occurring to quench the incipient cations resulting in insertion products with varying degrees of unsaturation. One such product was **3.48** which was identified in 15% NMR yield from the crude reaction mixture.



(Preparation of authentic sample of reduced product)

(3a*R*,10b*R*)-1,2,3,3a,4,5,6,10b-octahydrobenzo[*e*]azulene (3.48). In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.0030 mmol, 0.02 equiv.) and this was suspended in cyclohexane (1.5 mL). Triethylsilane (36 μL, 0.225 mmol, 1.5 equiv.) was added along with a magnetic stirring bar to the suspension. The suspension was stirred for 5 minutes at 30 °C. Vinyl triflate **3.28** (16.7 mg, 0.05 mmol, 1 equiv.)

was added to the reaction and it was stirred at 30 °C for 15 minutes. The reaction mixture was passed through a plug of silica with hexanes in the glovebox. The resulting solution was brought outside of the glovebox and concentrated to give crude tricyclic compound **3.48** in 76% NMR yield. The crude was then purified by silica flash column chromatography (hexanes) to give pure product **3.48** as a colorless oil. Assignment of the major *cis*-diastereomer was done using 2D NMR experiments: ^{13}C–^{1}H HSQC, ^{1}H–^{1}H COSY and ^{1}H–^{1}H NOESY. Three key NOE interactions were observed. The interaction between the protons on C1 and C2, the interaction between the proton on C1 with one of the protons on C4, and lastly, the proton of C2 with the protons on C3.

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

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

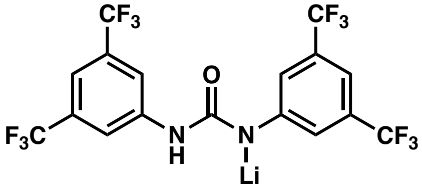
FTIR (Neat film NaCl): 3063, 3016, 2926, 2855, 1685, 1487, 1451, 1378, 1258, 1047, 764, 751, 714 cm^{-1}.

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

3.8.4.2 Stoichiometric Li-urea Experiment

3.8.4.2.1 Preparation of Lithium-urea

In this section, the synthesis of the mono-lithiated urea catalyst is described. This is simply performed by a mono-deprotonation of the parent urea with a sufficiently strong base.



lithium (3,5-bis(trifluoromethyl)phenyl)((3,5-bis(trifluoromethyl)phenyl) carbamoyl)amide (3.50)

In a well kept glovebox, urea **3.29** (1.26 g, 2.6 mmol, 1 equiv) and LiHMDS (435 mg, 2.6 mmol, 1 equiv) were weighed out into a 250 mL schlenk. This was brought outside the glovebox and 60 mL of anhydrous benzene were added. The reaction mixture was heated to 70 °C for 14 hours. This was cooled down to r.t. and then solvents were removed on the schlenk line. The flask was cycled back into the glovebox and the residue was suspended in hexanes and filtered inside the glovebox. This was washed with extra hexanes to yield a white solid. After evaporation of residual hexanes under reduced pressure, obtained the lithium salt **3.50** as a white powder (950 mg, 75% yield).

This solid was characterized by ^{1}H, ^{13}C, ^{19}F and ^{7}Li NMR as shown below.

Notably, this compound has different solubility properties than the parent urea **4** and is readily soluble in 1,2-difluorobenzene. The spectra were recorded in anhydrous d3-acetonitrile (distilled over CaH_2) and NMR samples were prepared in J Young tubes inside the glovebox. Some residual benzene is observed which was not able to be removed even under reduced pressure.

^{1}H NMR (500 MHz, CD_3CN) δ 7.94 (s, 4H), 7.29 (s, 2H), 7.12 (s, 1H).

^{13}C NMR (126 MHz, CD_3CN) δ 159.1, 148.7, 131.8 (q, $^{2}J_{C\text{–}F}$ = 32.4 Hz), 129.3, 124.9 (q, $^{1}J_{C\text{–}F}$ = 271.7 Hz), 112.87.

^{19}F NMR (282 MHz, CD_3CN) δ -63.5

^{7}Li NMR (194 MHz, CD_3CN) δ -1.88

3.8.4.2.2 Stoichiometric C–H Insertion with Li-urea

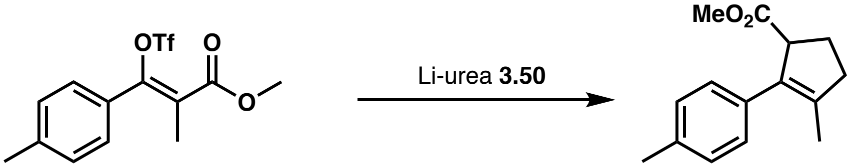


Figure 3.9 Stoichiometric Li-Urea experiment

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with Li-urea **3.50** (25.7 mg, 0.0525 mmol, 1.05 equiv) and dissolved in dry 1,2-difluorobenzene (3 mL). To this was added vinyl triflate **3.49** (19.0 mg, 0.0500 mmol, 1 equiv) and stirred at 30 °C for 1.5 hours. The reaction vial was removed from the glove box and to it was added ~1 mL of D_2O and the biphasic mixture was stirred for 5 minutes. The layers were separated and the aqueous D_2O layer was analyzed by NMR to see LiOTf. The organic layer was concentrated and analyzed by proton NMR with 3 μL of nitromethane to obtain a 23% NMR yield of cyclopentene product **3.51**. For characterization data of **3.51** see the adapted article.

*Notably, the reaction started out fully homogeneous, but became cloudy after completion. This is further evidence of formation of LiOTf (insoluble in 1,2-DFB) during the reaction.

3.8.4.3 Vinyl Cation Rearrangment Experiment

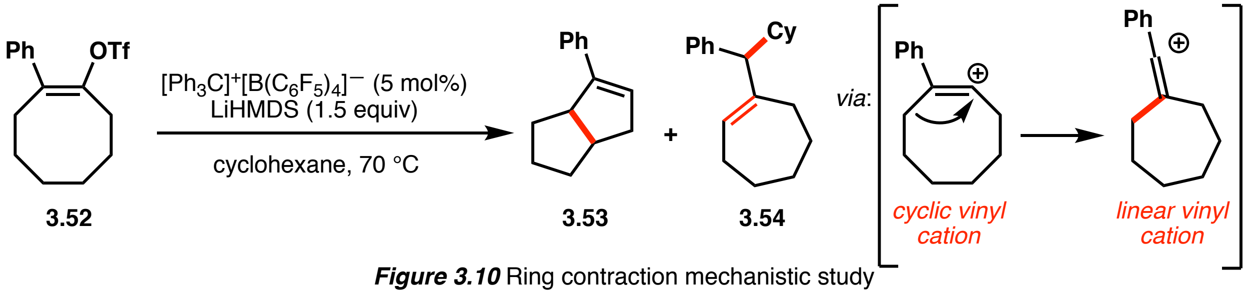


Figure 3.10 Ring contraction mechanistic study

1-(cyclohexyl(phenyl)methyl)cyclohept-1-ene and **6-phenyl-1,2,3,3a,4,6a-hexahydropentalene (3.53 and 3.54).** Synthesized according to general procedure B. In a well-kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (2.3 mg, 0.0025 mmol, 0.05 equiv.) and lithium hexamethyldisilazide (12.5 mg, 0.075 mmol, 1.5 equiv.). This was suspended in cyclohexane (0.5 mL) and stirred for 5 minutes at 30 °C. Vinyl triflate **3.52** (16.7 mg, 0.05 mmol, 1.0 equiv.) was added to the reaction and the reaction was stirred for 5 minutes at 70 °C. The reaction was cooled to room temperature and brought outside the glovebox and was passed through a pad of silica with diethyl ether and concentrated to give crude bicyclic compound **3.53** and ring contracted cyclohexylated product **3.54** as yellow solid (6% NMR yield of transannular product **3.53**, 15% NMR yield of cyclohexylated product **3.54**). The crude was then purified by silica flash chromatography (hexanes) to give pure cyclohexylated product **3.54** as a white solid. The transannular insertion product was further purified by preparative reverse phase HPLC (10% water in acetonitrile) to give bicycle **3.53** as a colorless oil.

Characterization of bicycle 3.53:

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

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

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

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

Characterization of cyclohexyl adduct 3.54:

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

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

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

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

3.9 Spectra Relevant to Chapter Three:

Lithium Lewis Acid Generation of Vinyl Cations and Their Intramolecular C–H Insertion and Intermolecular Friedel-Crafts Reactions

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

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

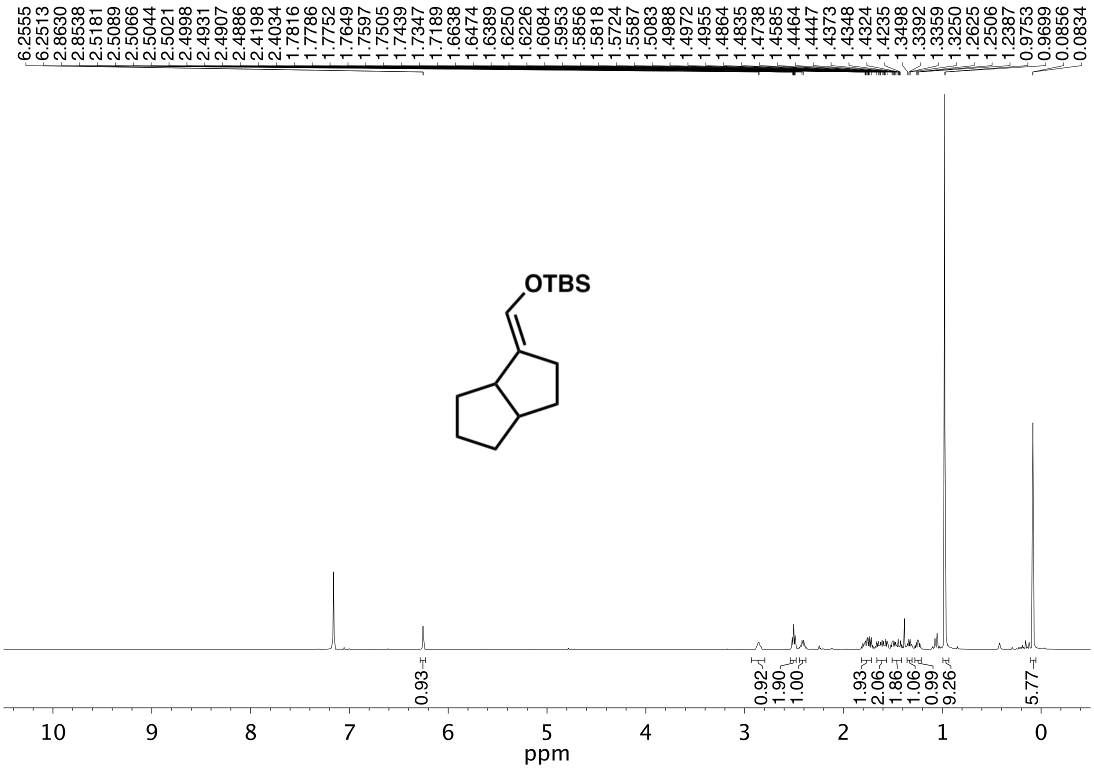


Figure 3.11 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.12E**.

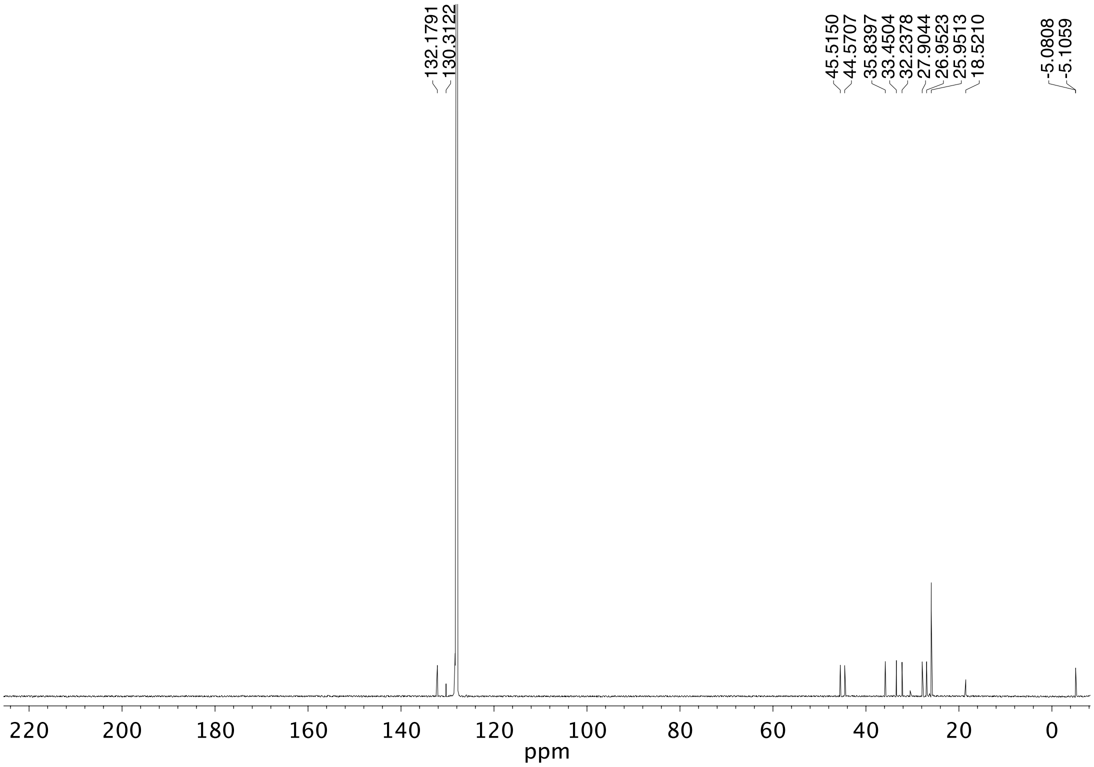


Figure 3.12 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.12E**.

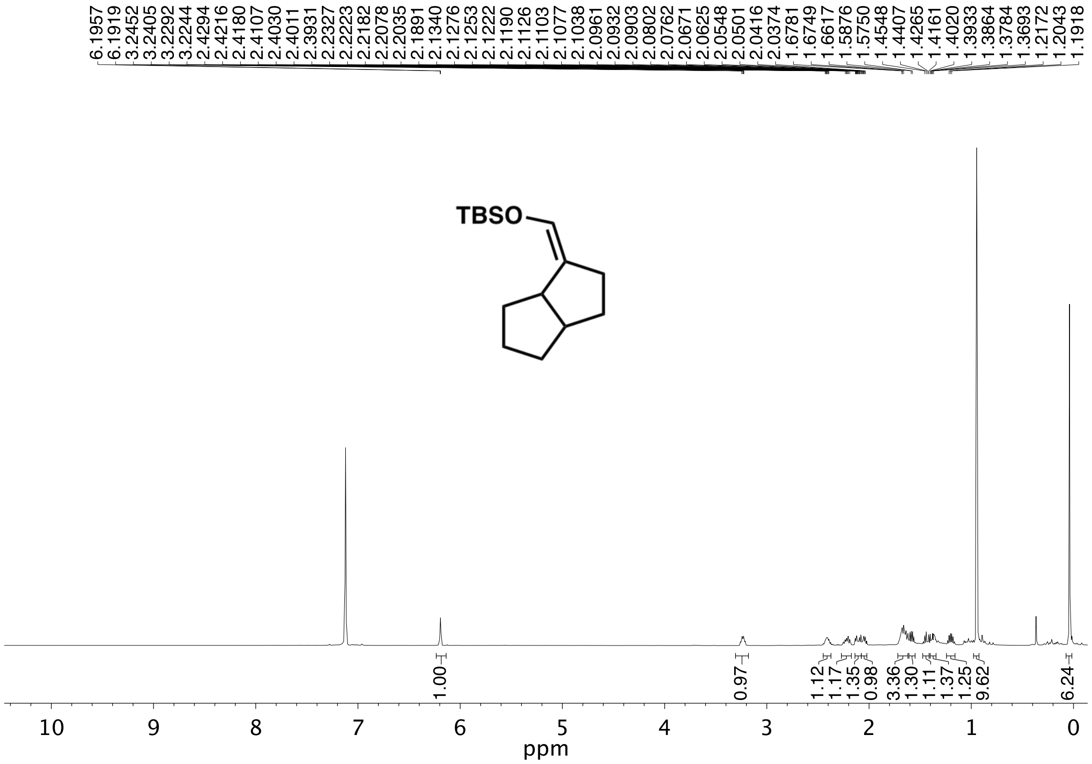


Figure 3.13 ^{1}H NMR (500 MHz, C_6D_6) of compound **3.12Z**.

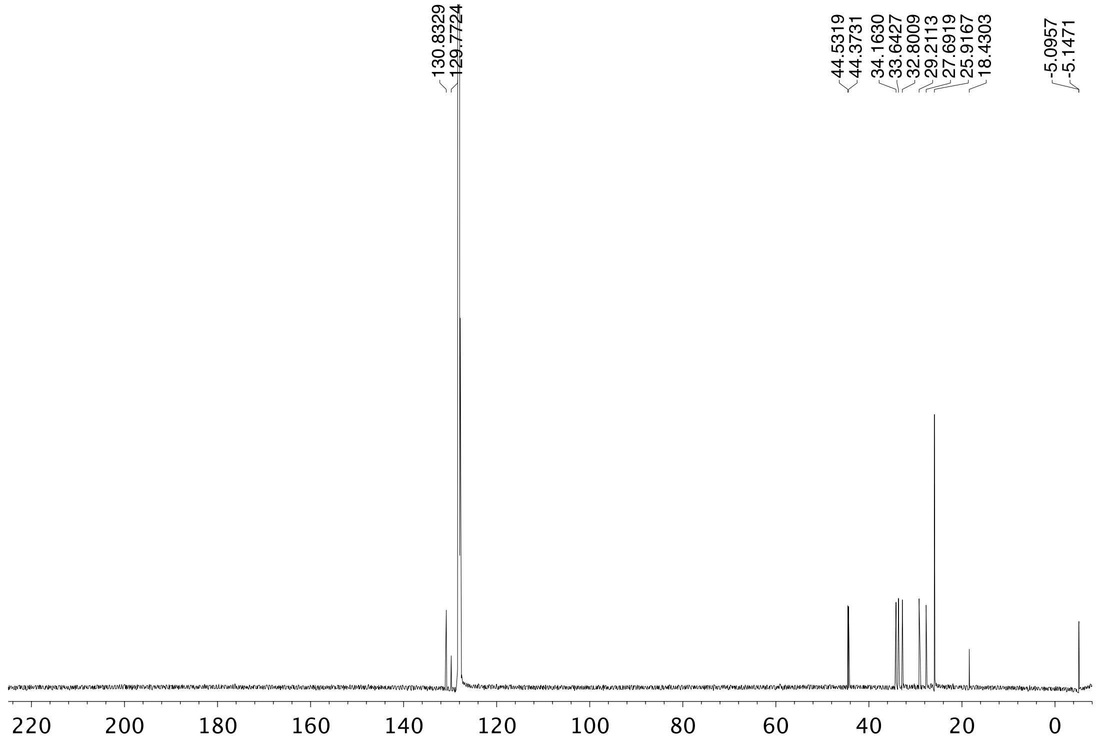


Figure 3.14 ^{13}C NMR (126 MHz, C_6D_6) of compound **3.12Z**.

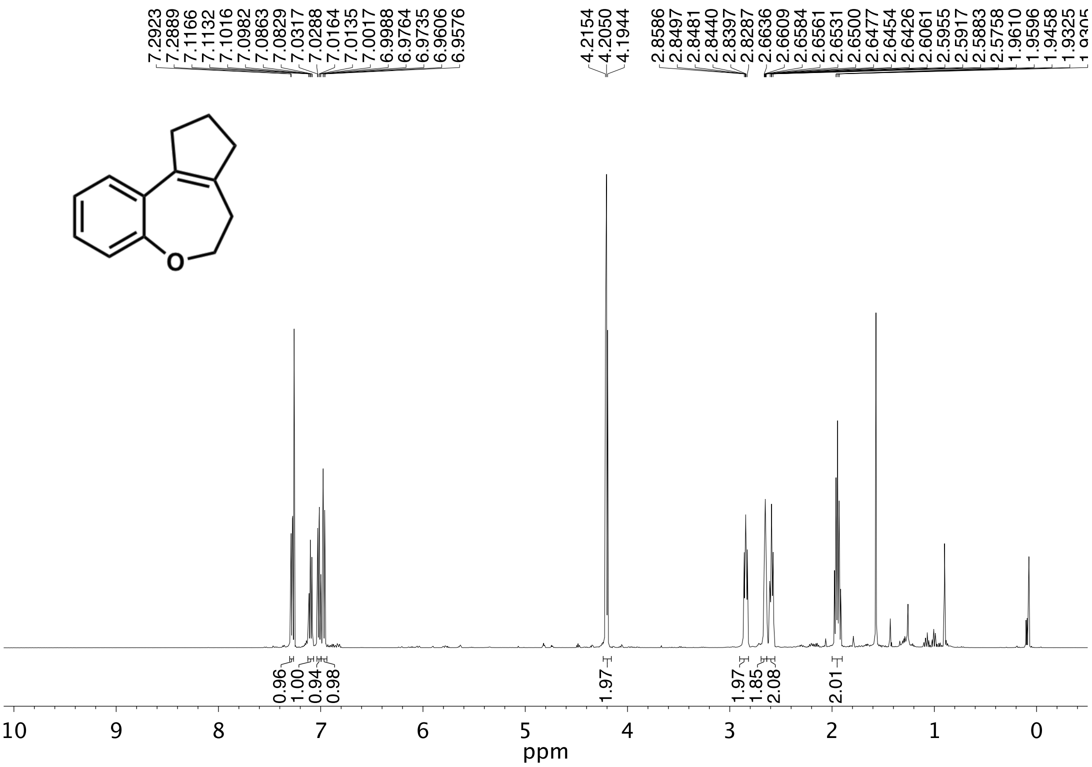


Figure 3.15 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.17a**.

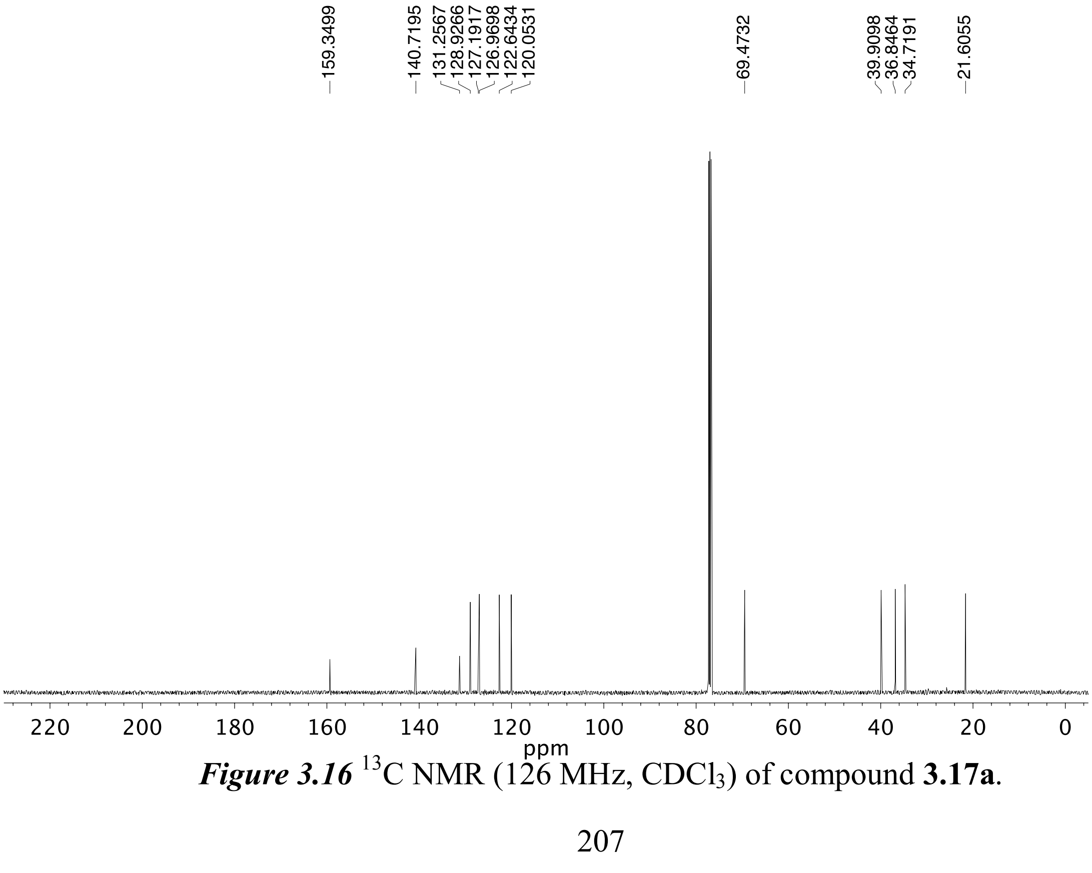


Figure 3.16 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.17a**.

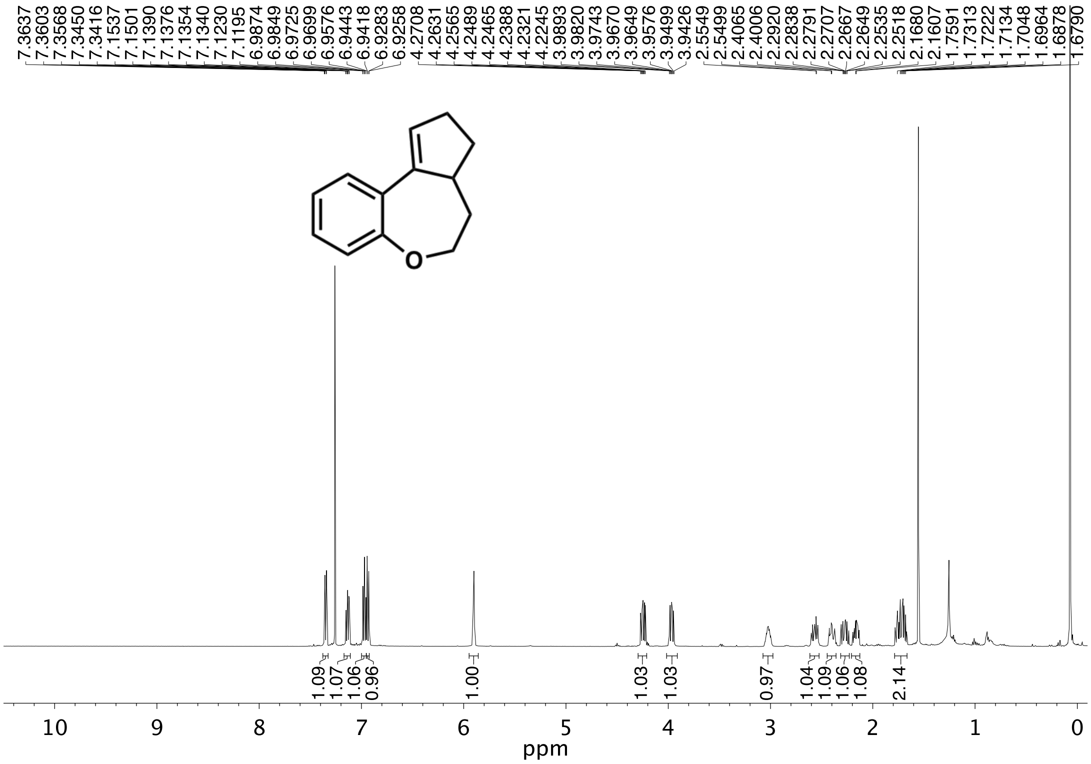


Figure 3.17 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.17b**

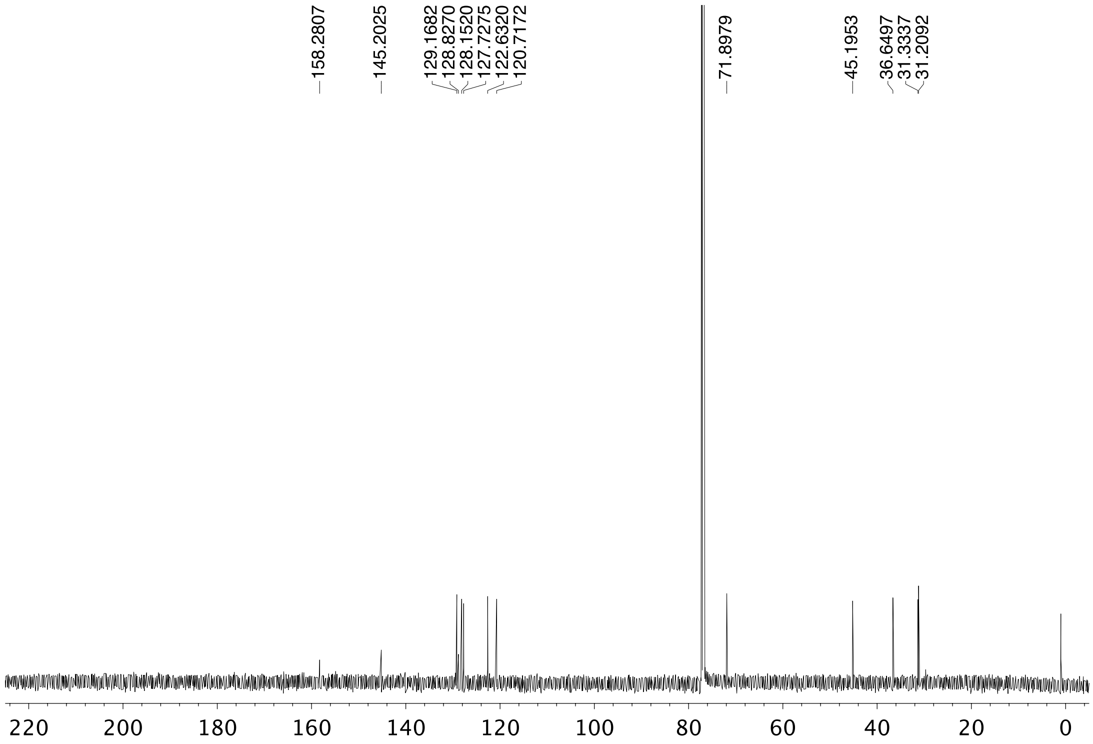


Figure 3.18 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **2.63**.

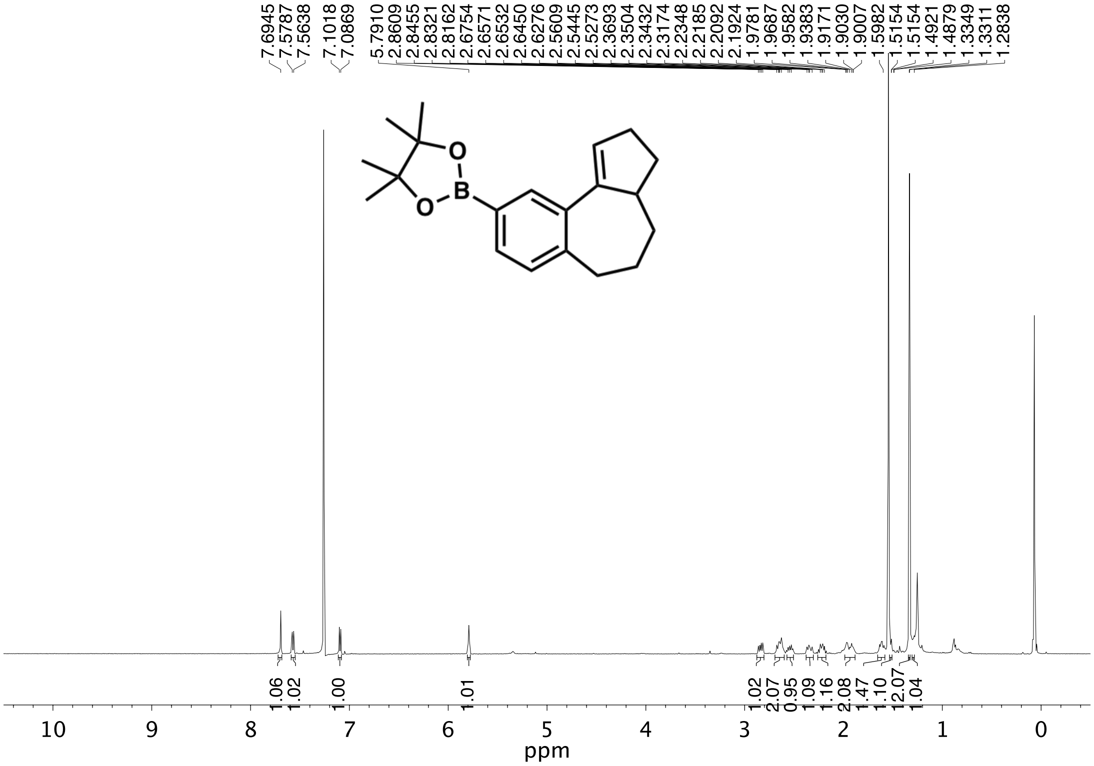


Figure 3.19 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.18**

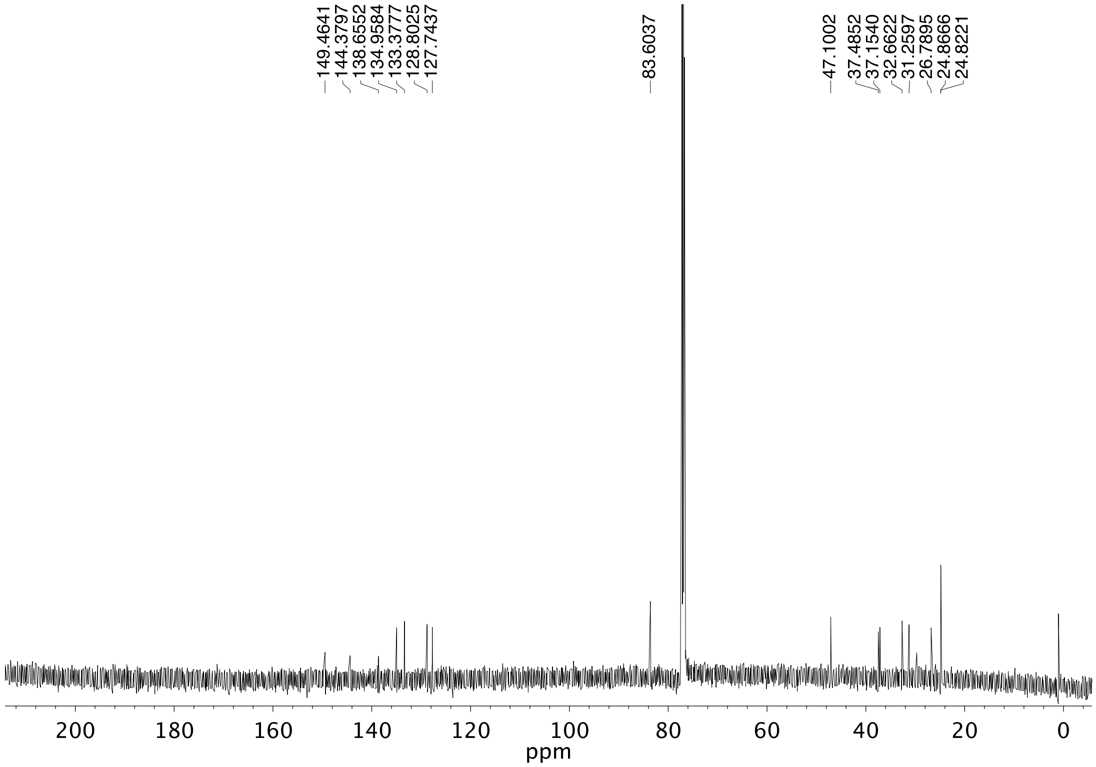


Figure 3.20 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.18**.

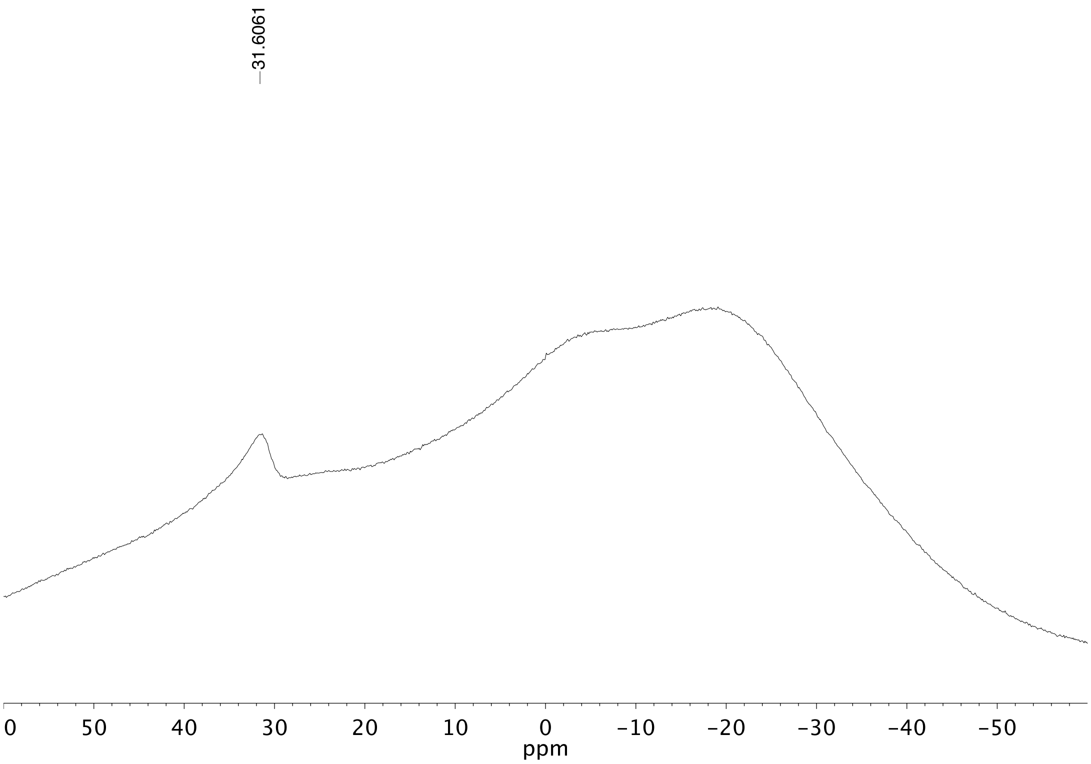


Figure 3.21 ^{11}B NMR (128 MHz, CDCl$_3$) of compound **3.18**

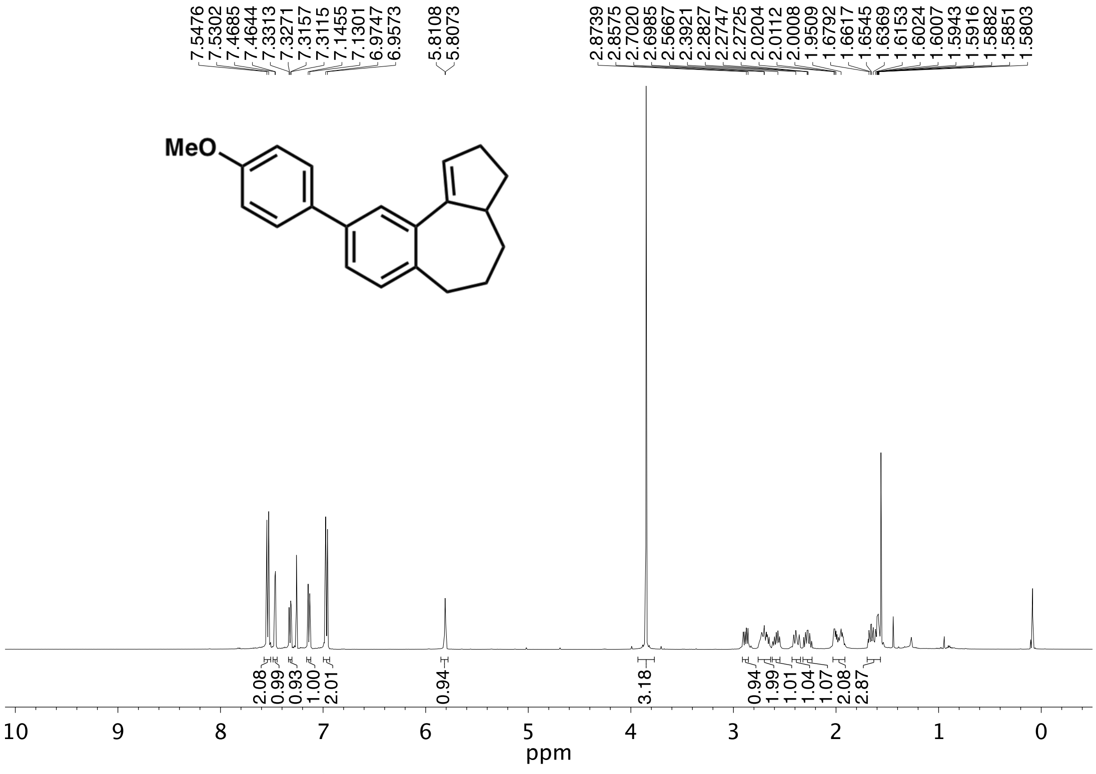


Figure 3.22 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.19**.

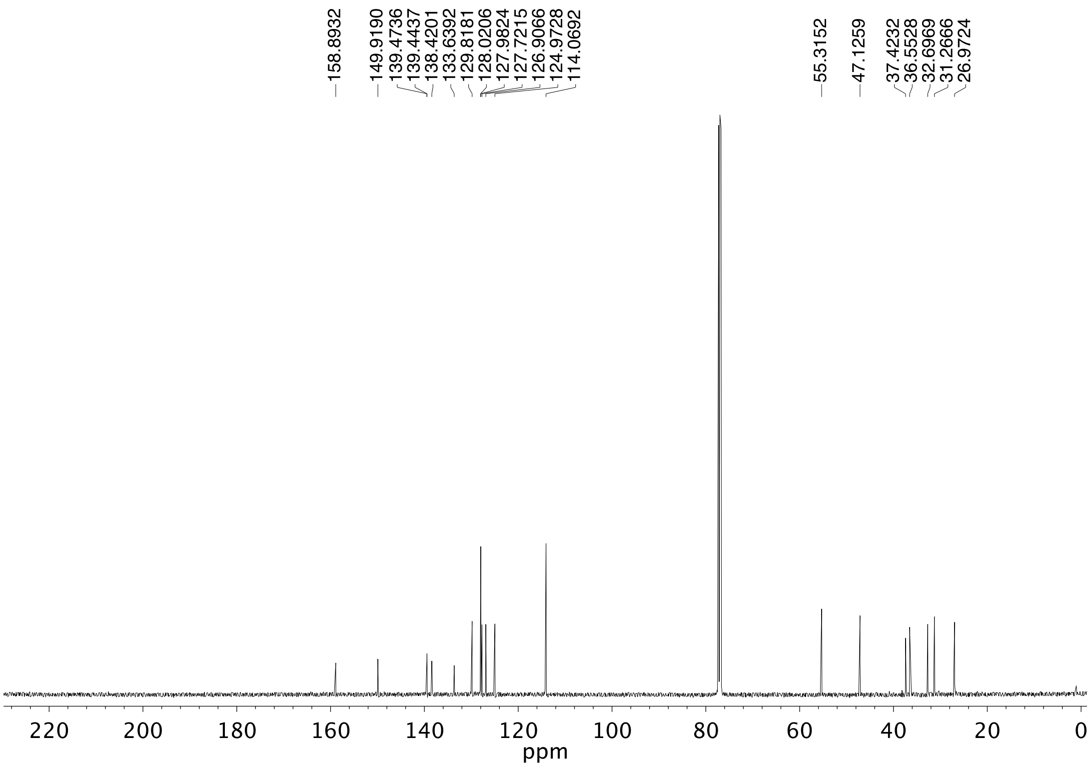


Figure 3.23 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.19**.

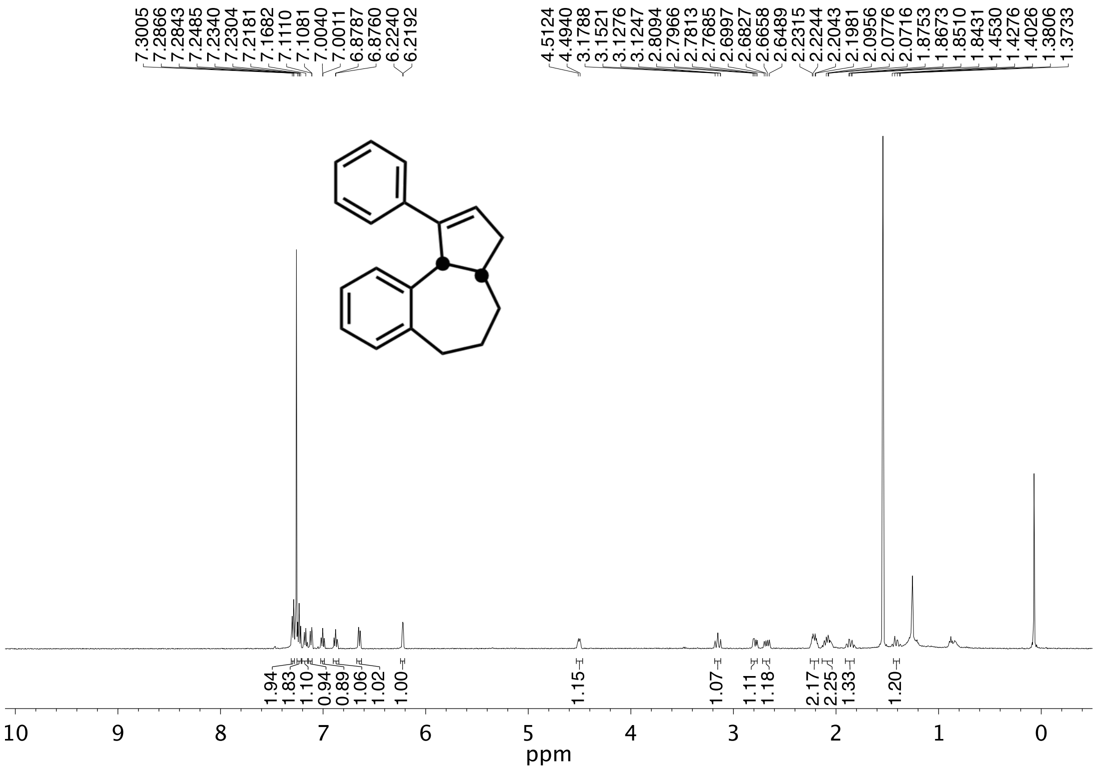


Figure 3.24 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.20**.

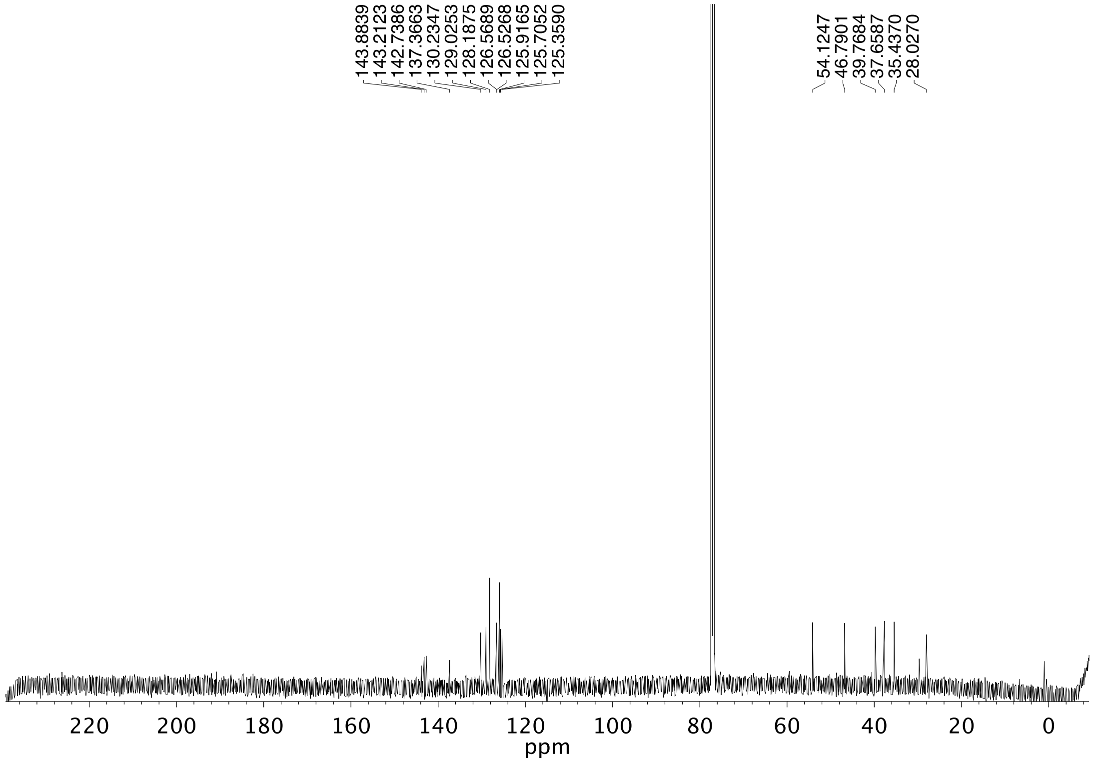


Figure 3.25 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.20**

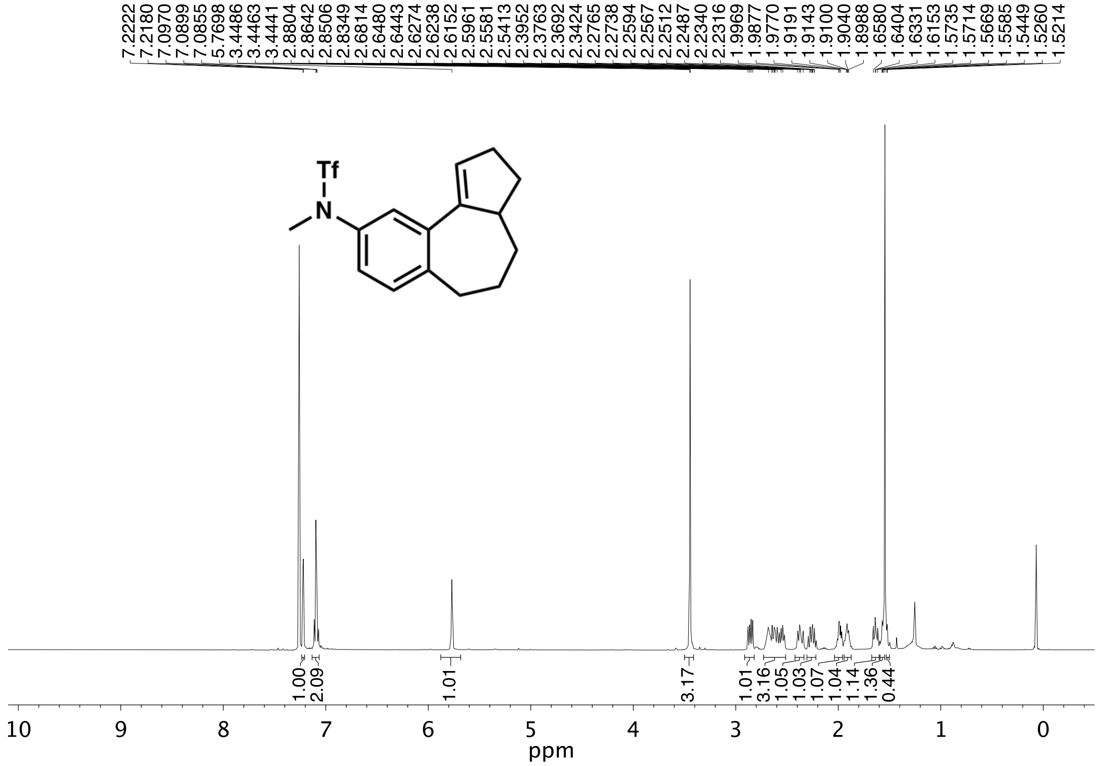


Figure 3.26 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.21**.

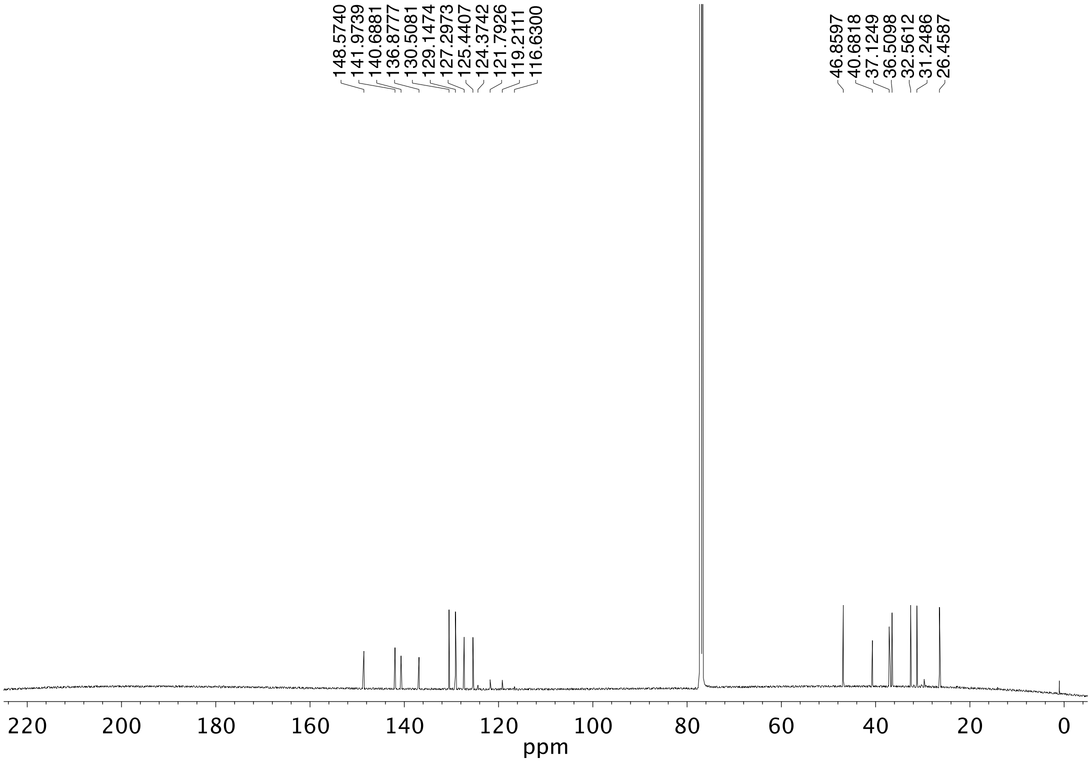


Figure 3.27 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.21**.

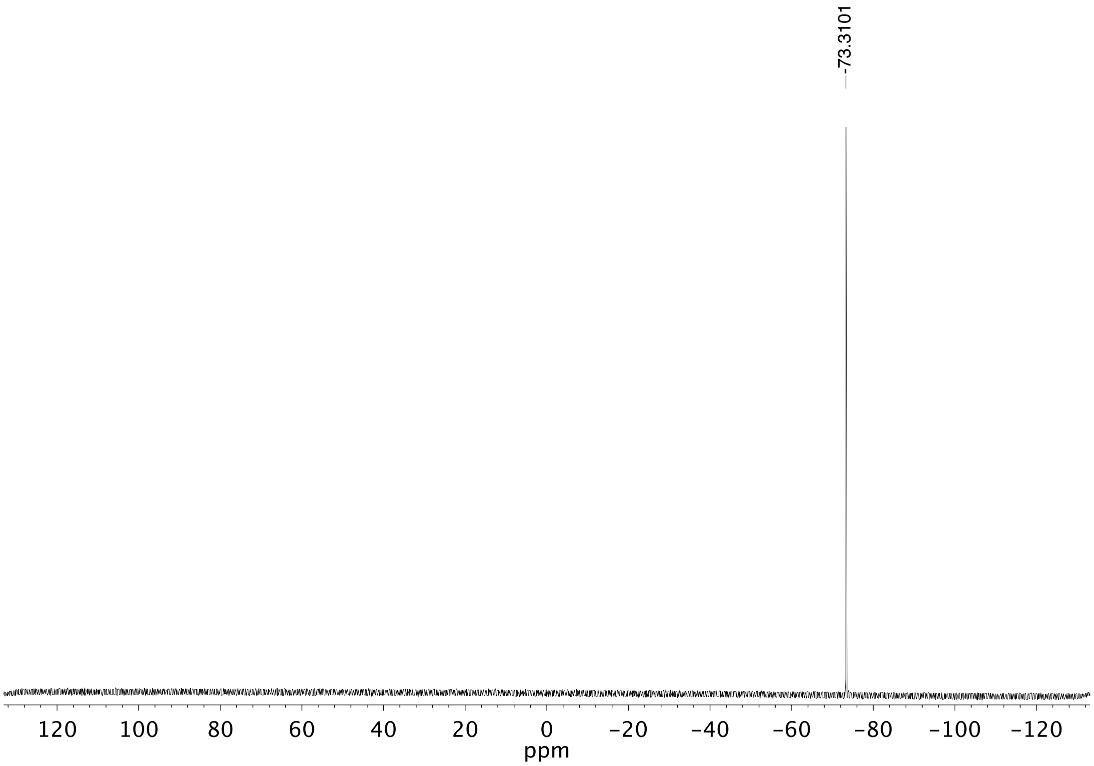


Figure 3.28 ^{19}F NMR (282 MHz, CDCl$_3$) of compound **3.21**.

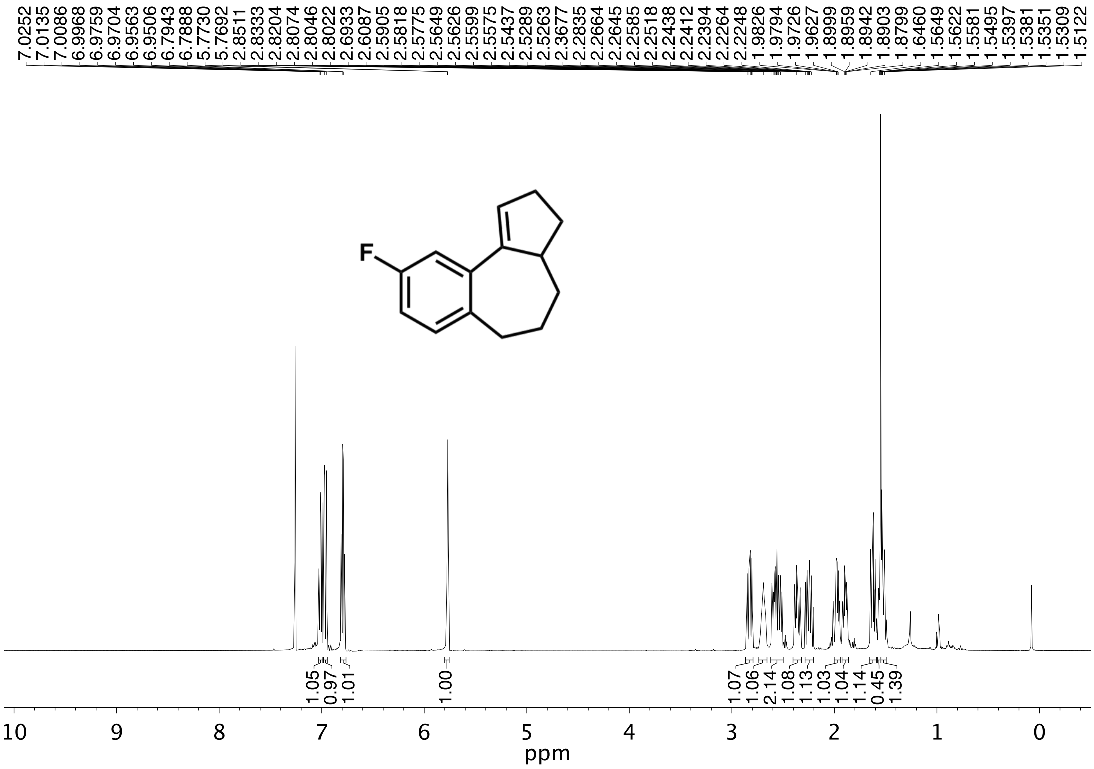


Figure 3.29 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.22**.

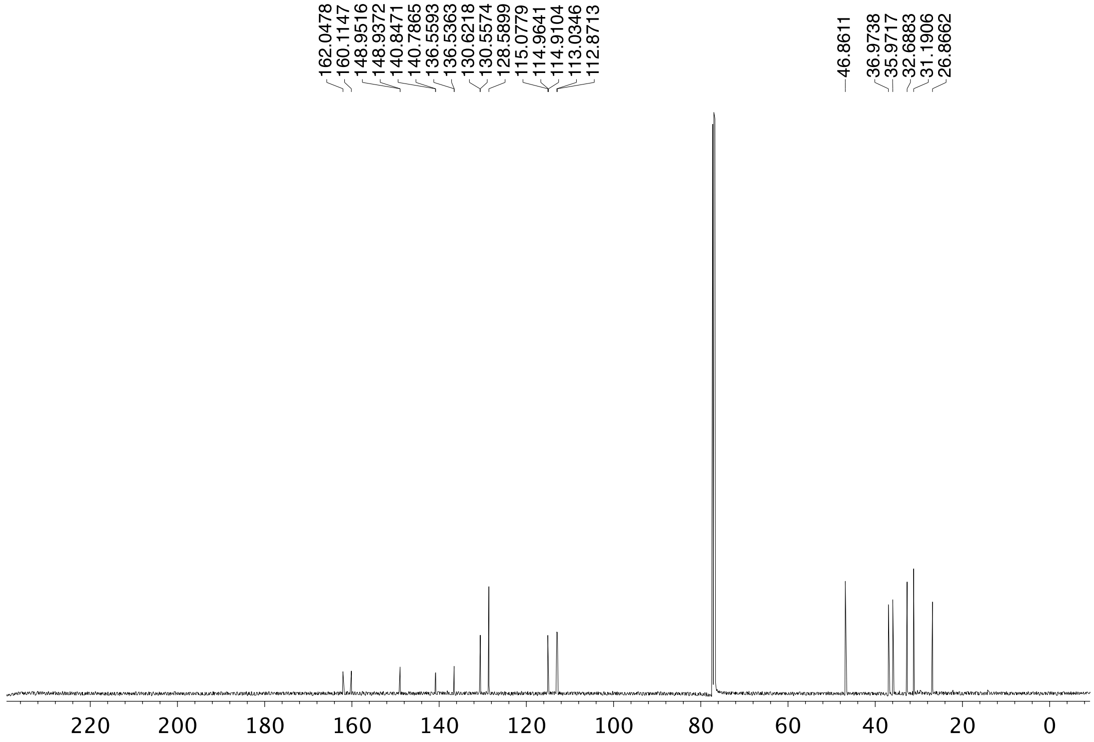


Figure 3.30 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.22**.

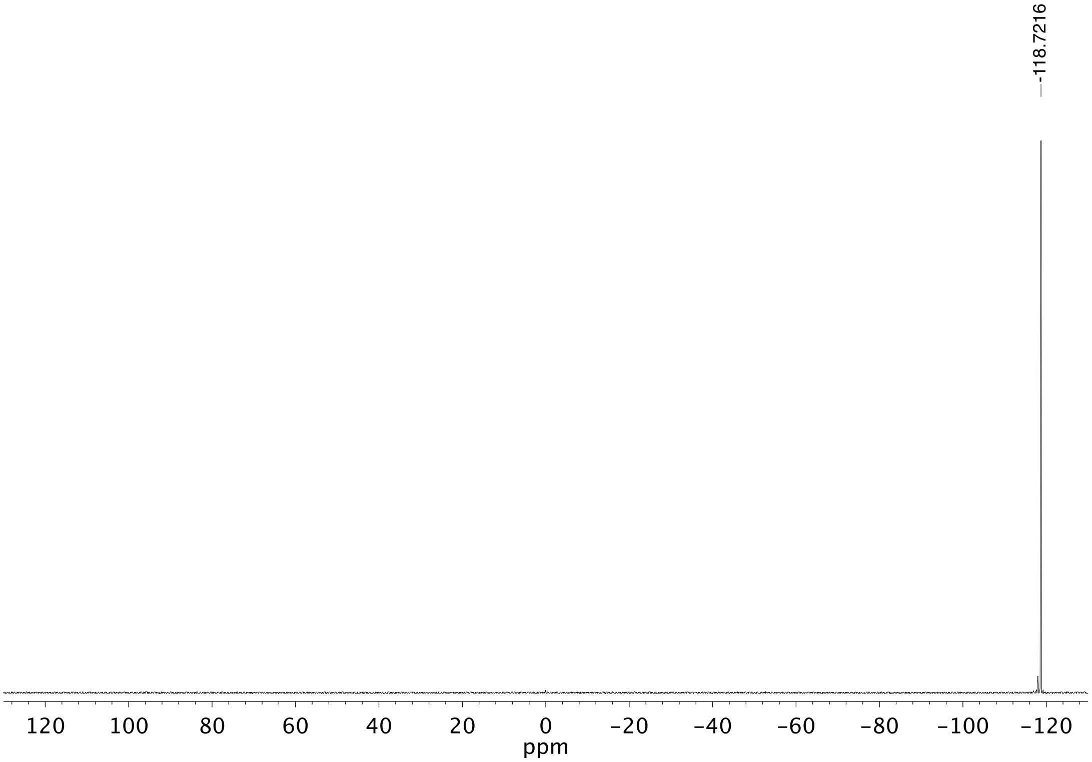


Figure 3.31 ^{19}F NMR (282 MHz, CDCl$_3$) of compound **3.22**.

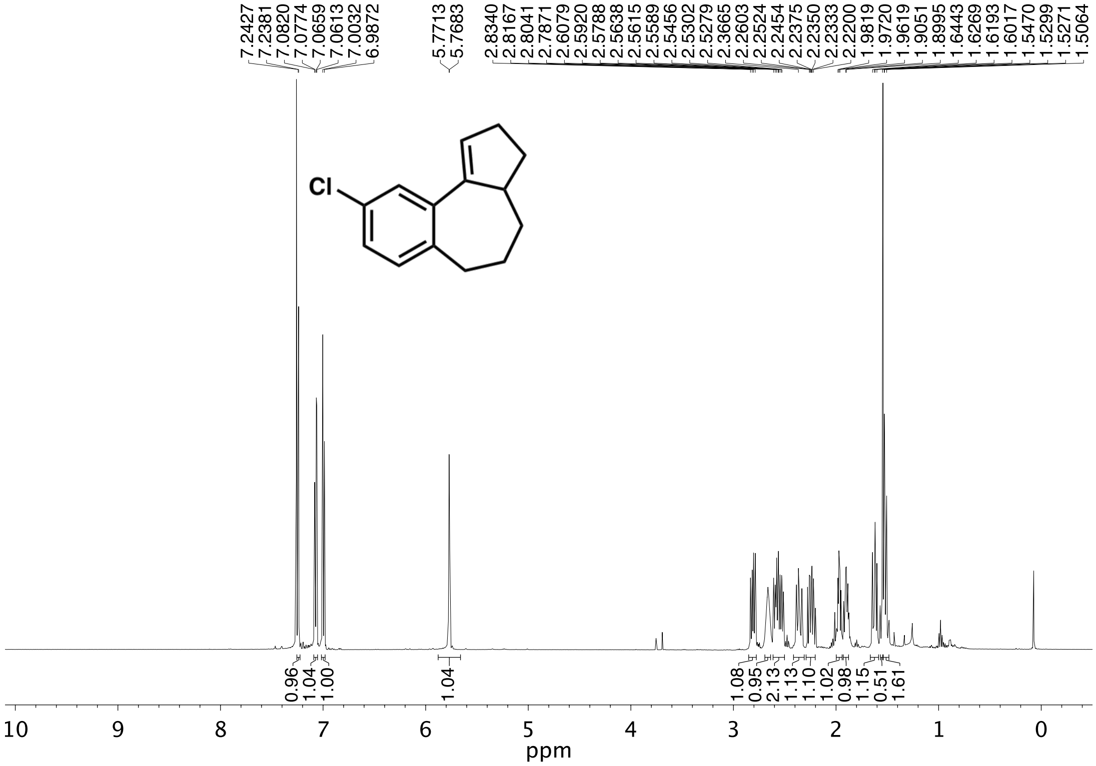


Figure 3.32 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.23**.

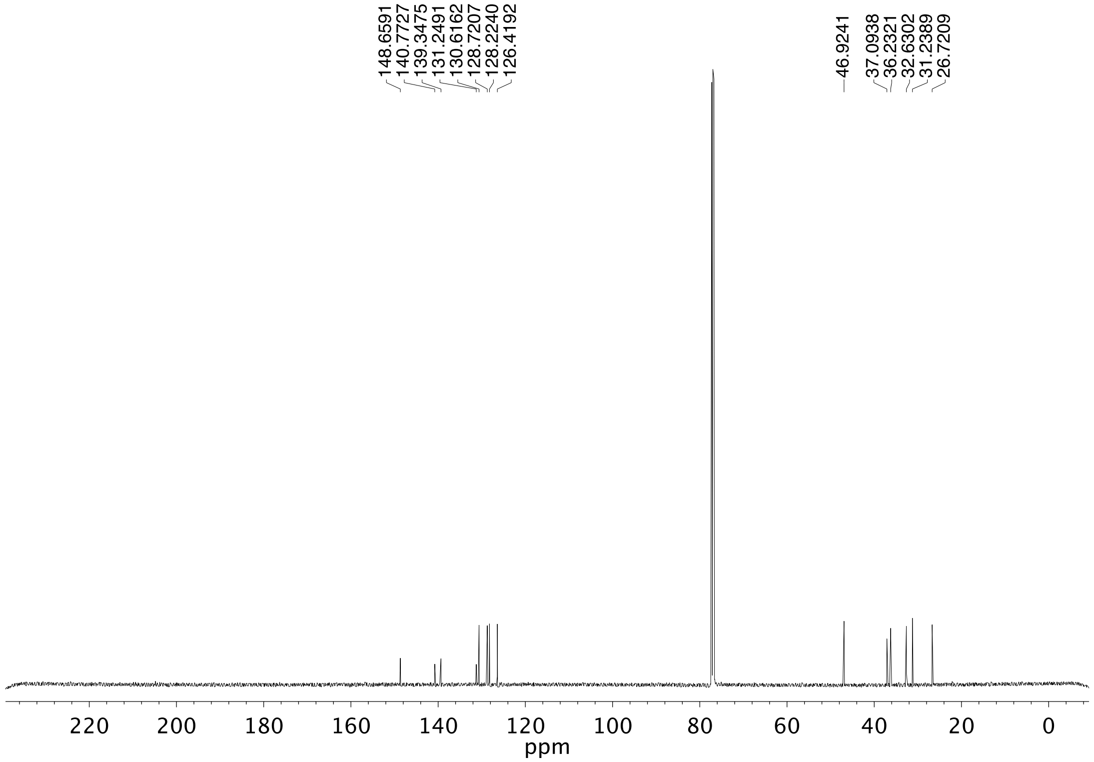


Figure 3.33 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.23**.

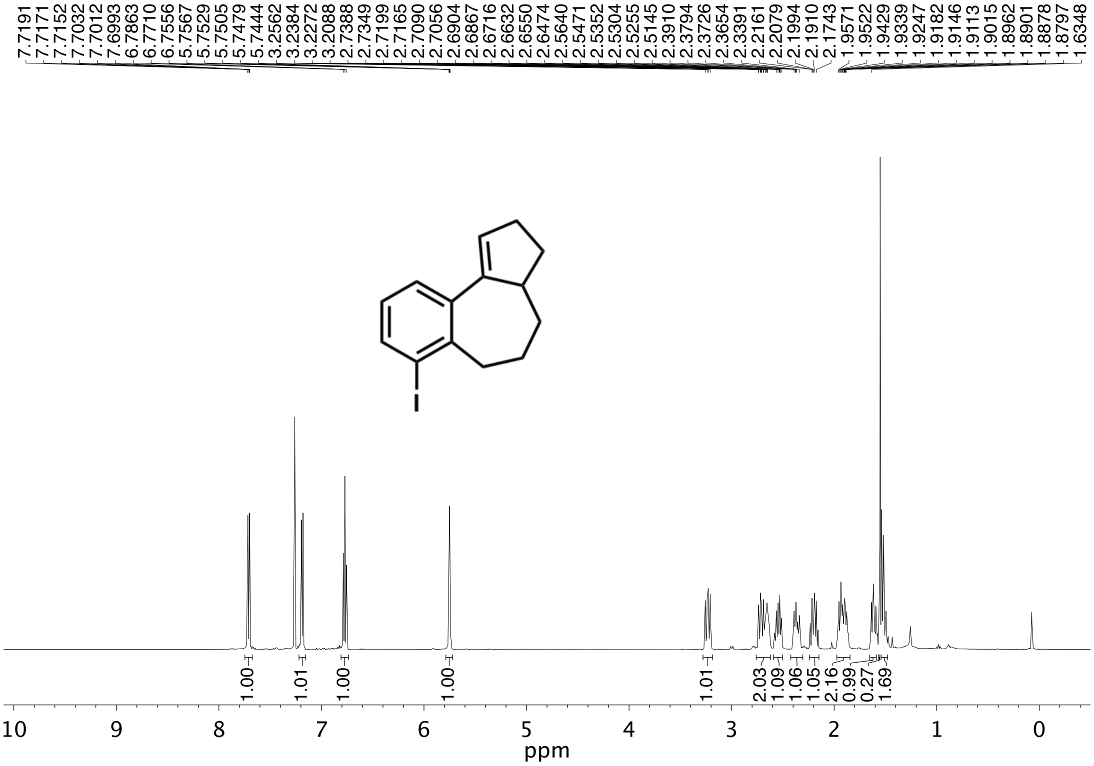


Figure 3.34 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.24**.

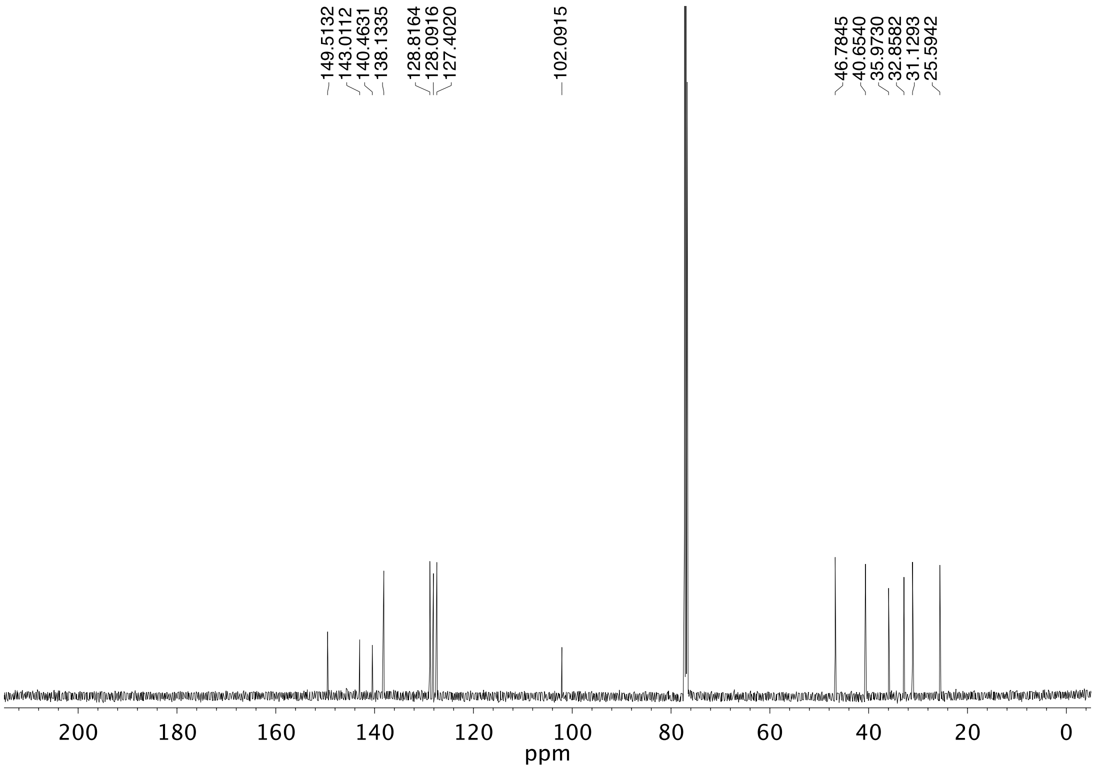


Figure 3.35 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.24**.

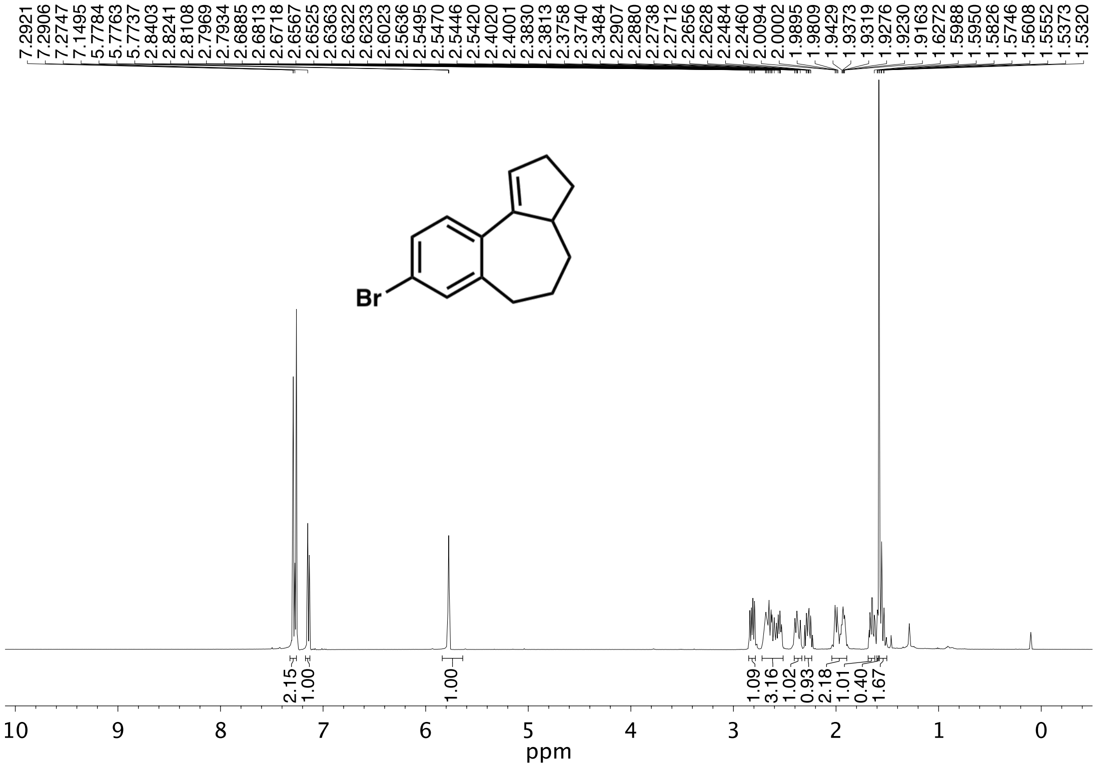


Figure 3.36 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.25**.

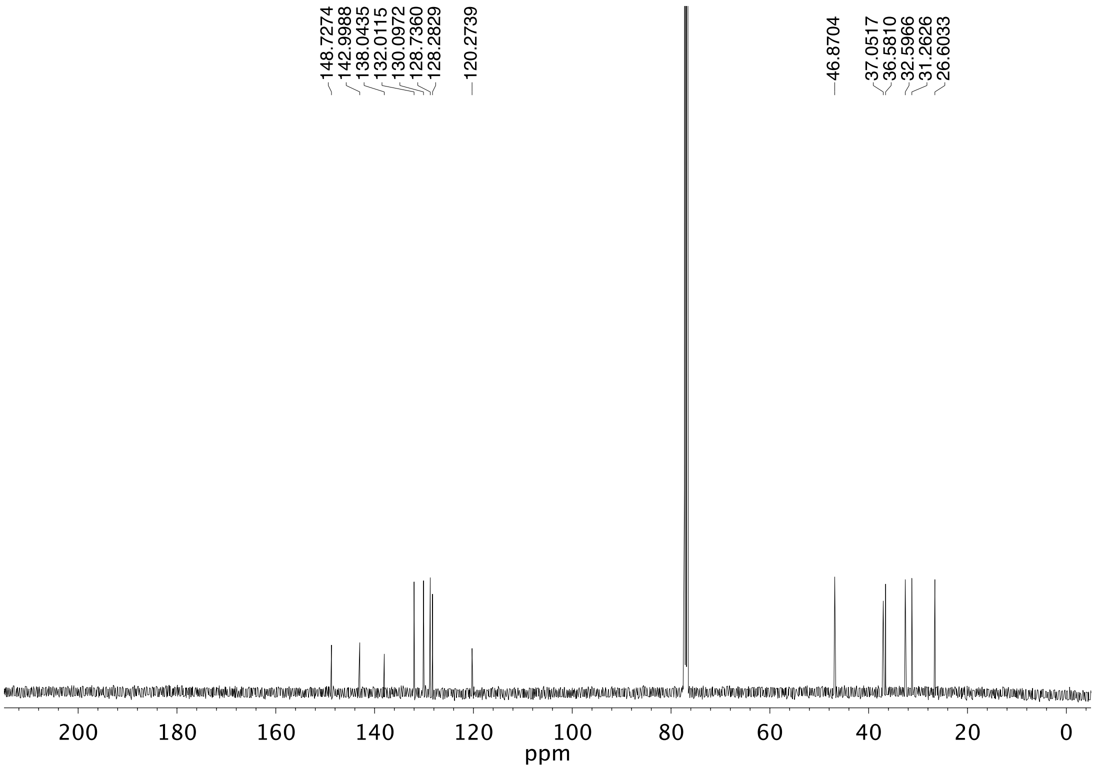


Figure 3.37 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.25**.

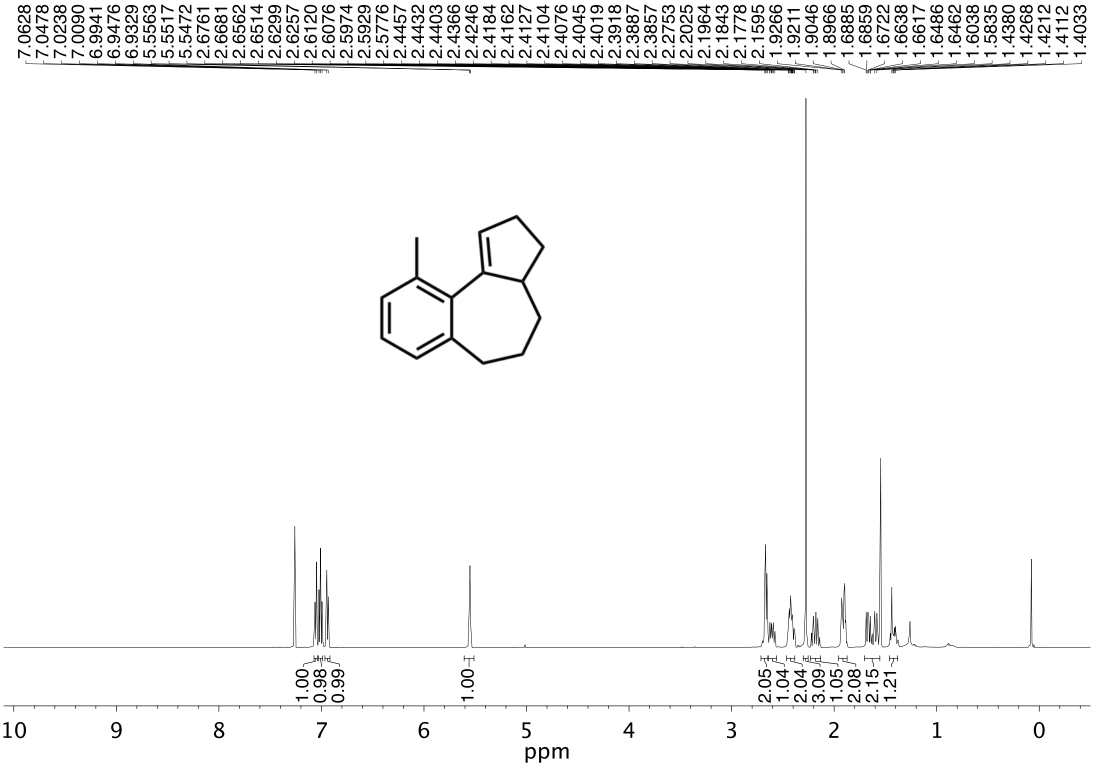


Figure 3.38 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.26**.

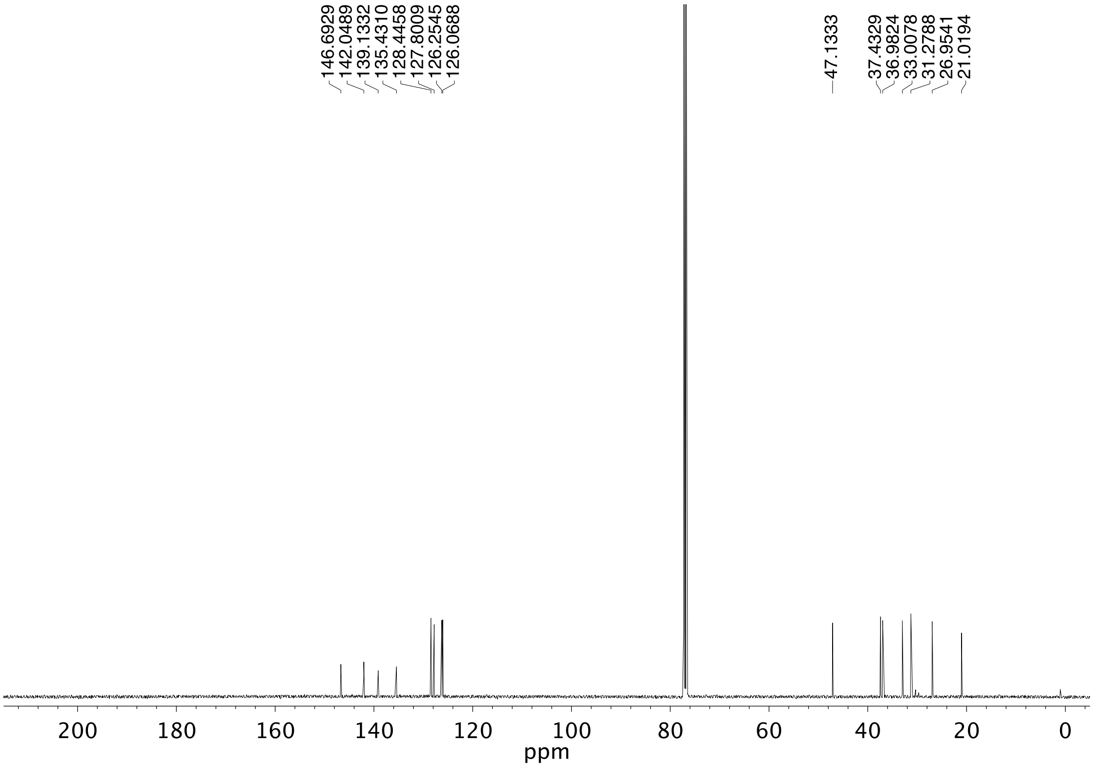


Figure 3.39 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.26**.

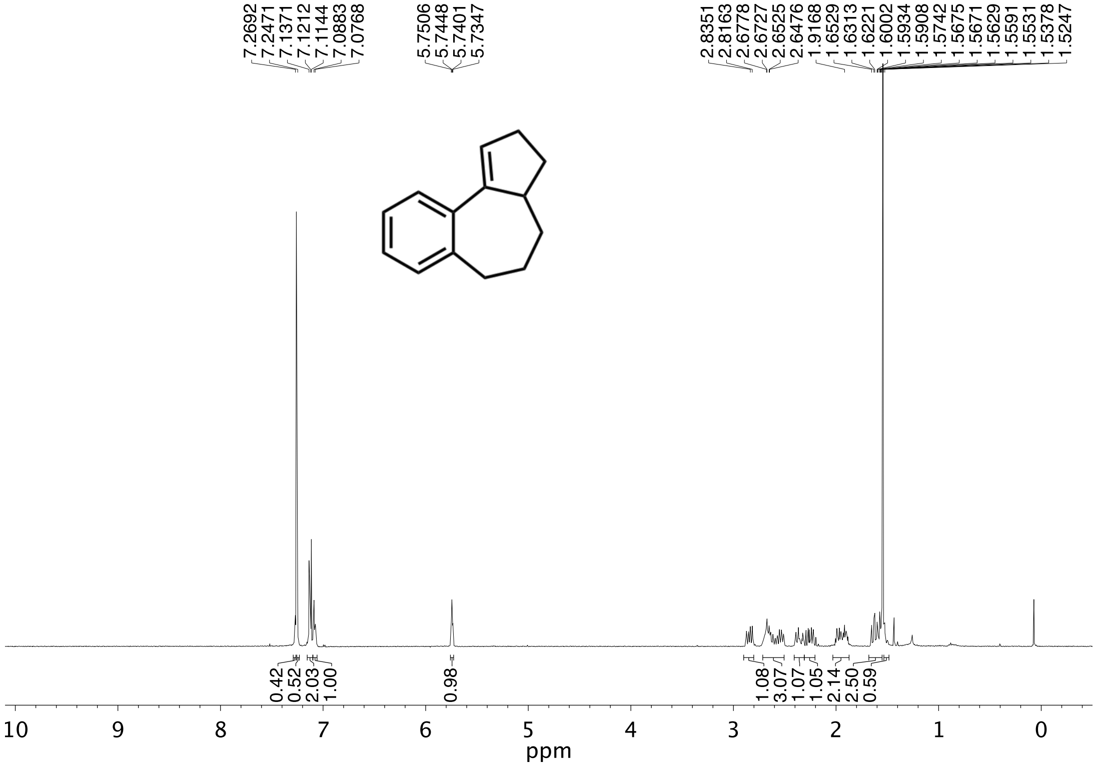


Figure 3.40 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.27**.

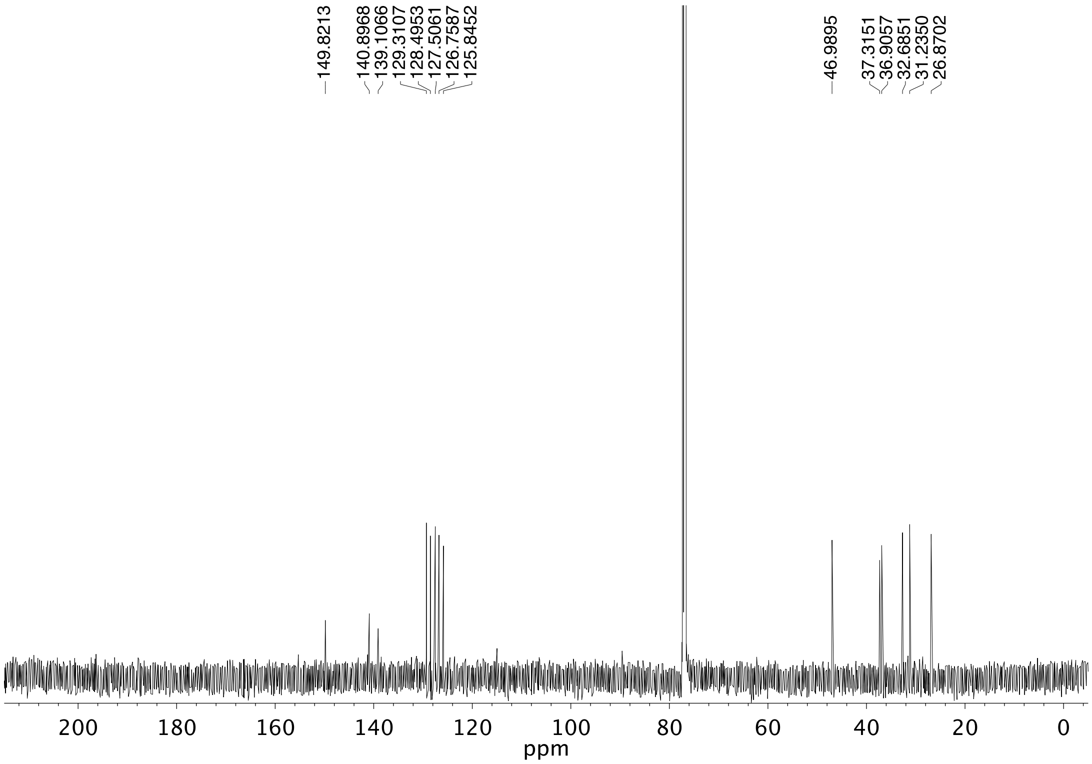


Figure 3.41 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.27**.

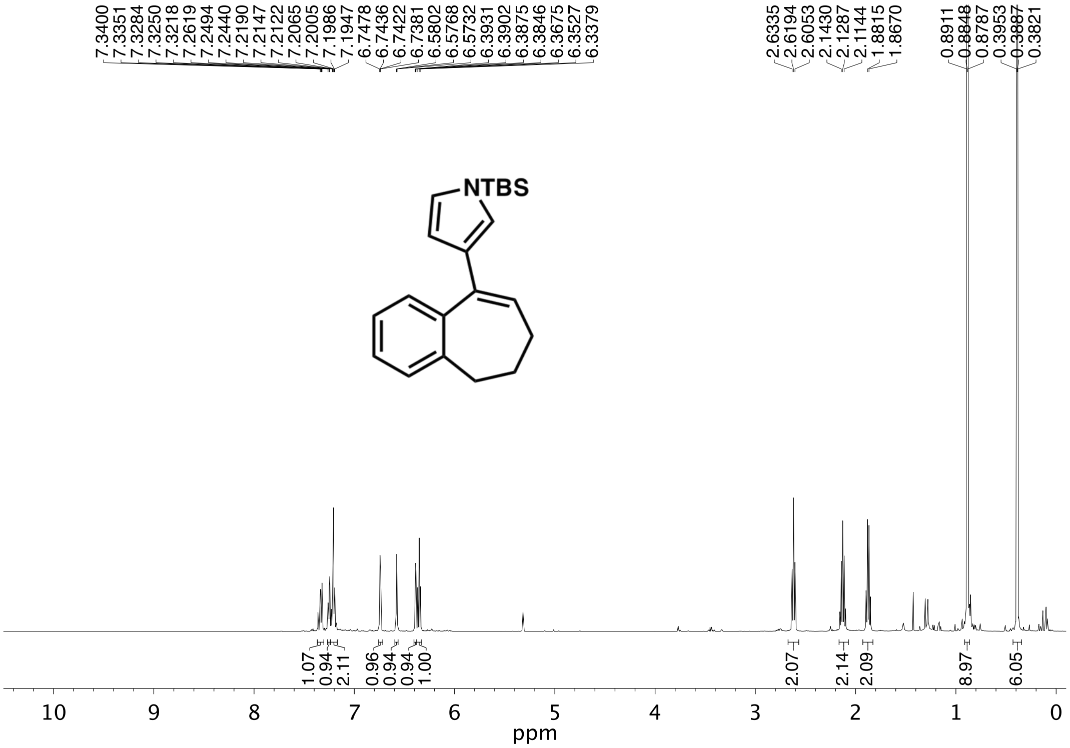


Figure 3.42 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.31a**.

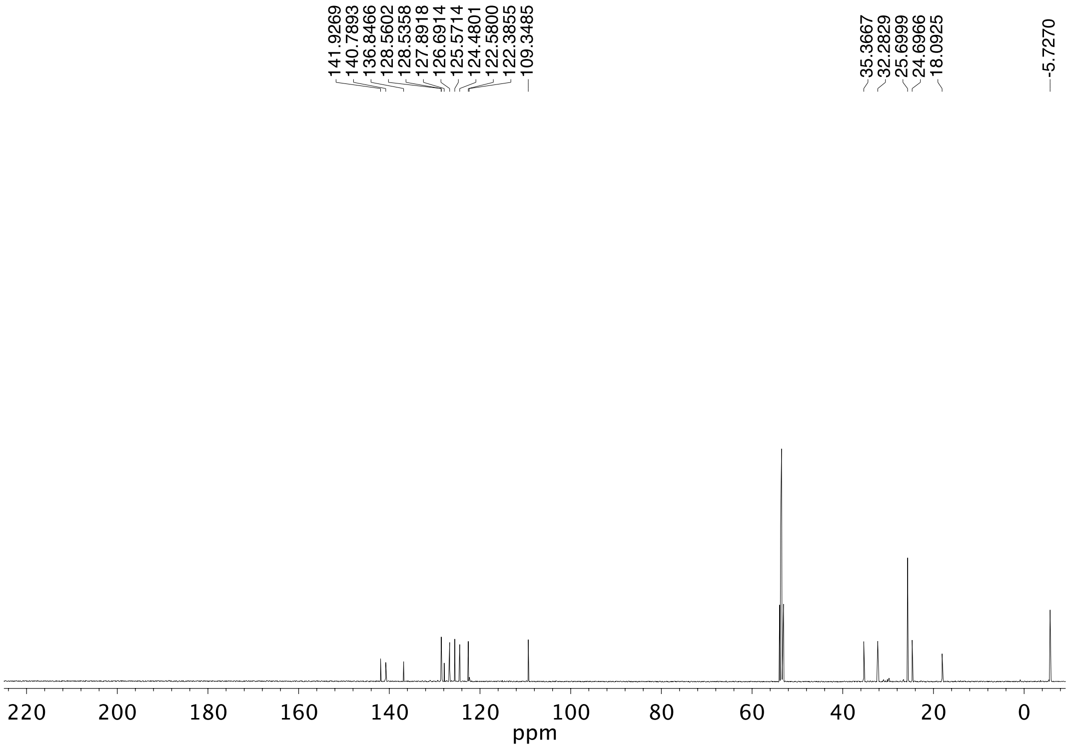


Figure 3.43 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.31a**.

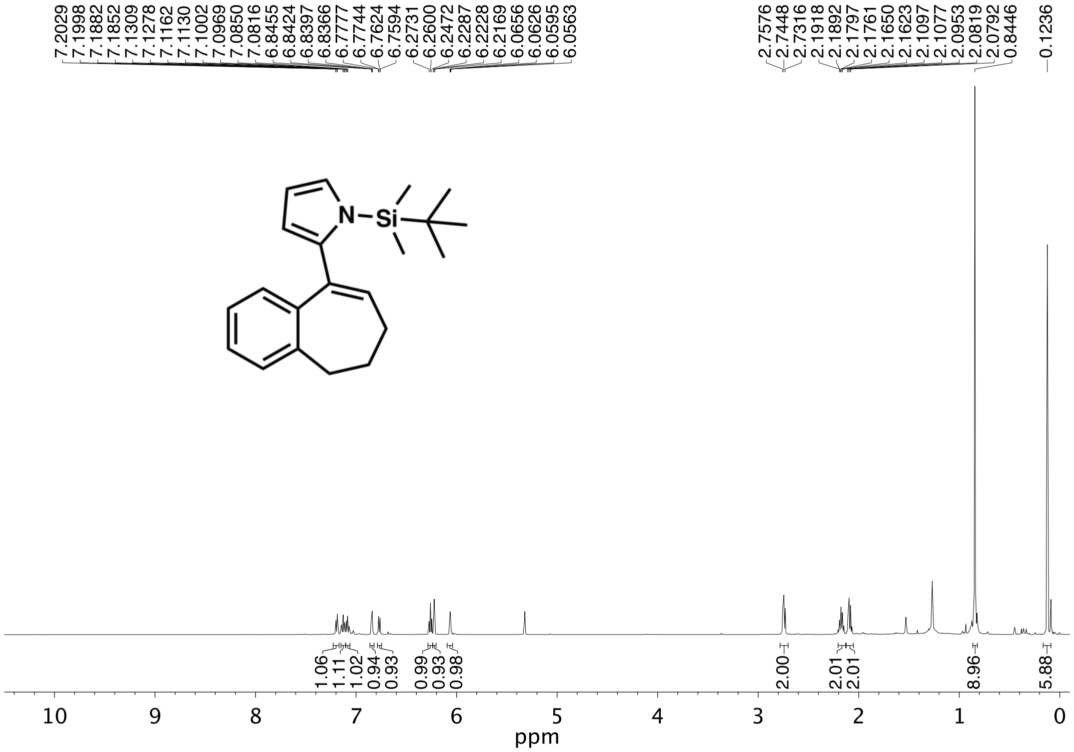


Figure 3.44 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.31b**.

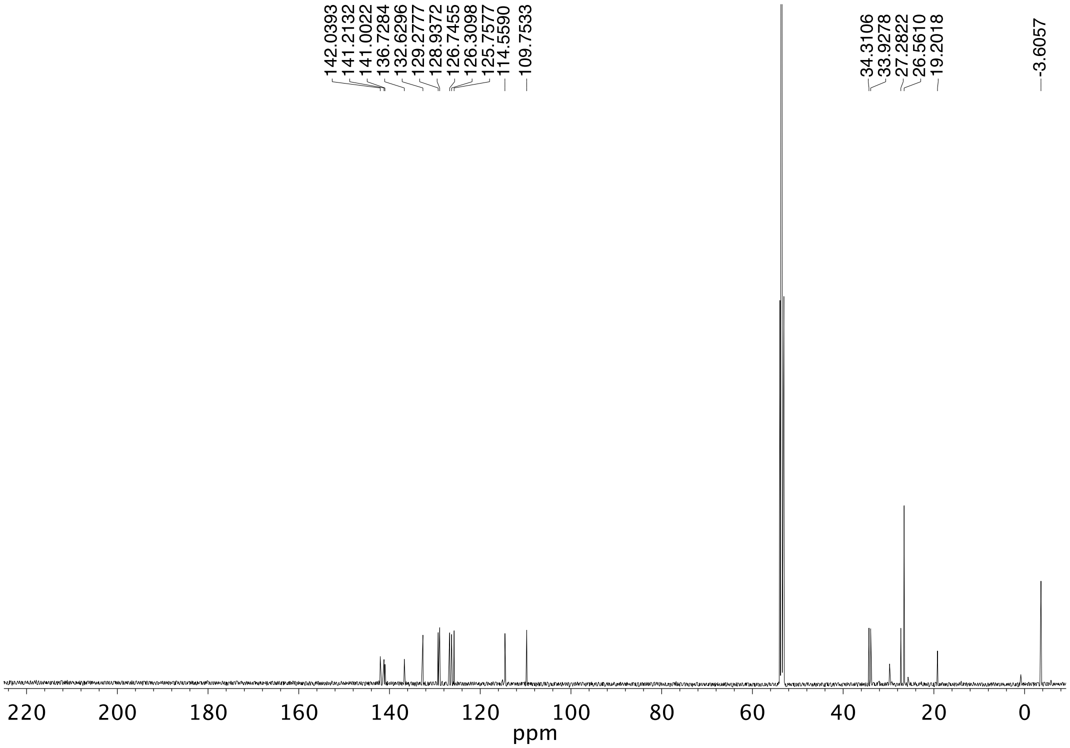


Figure 3.45 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.31b**.

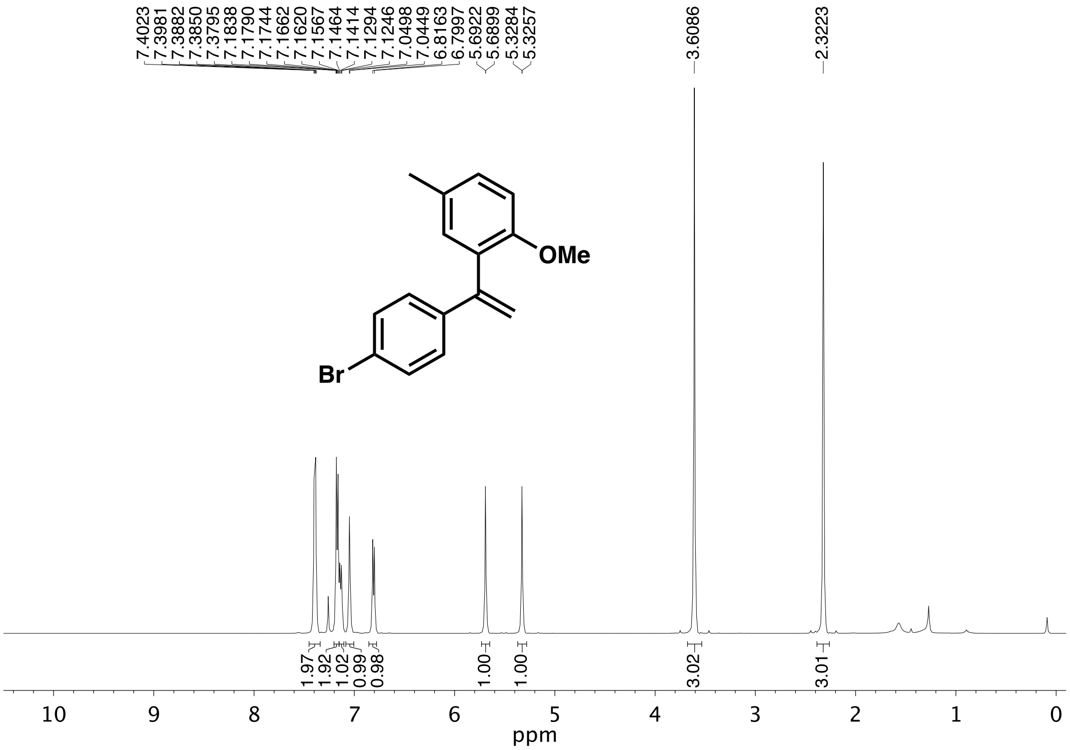


Figure 3.46 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.32a**.

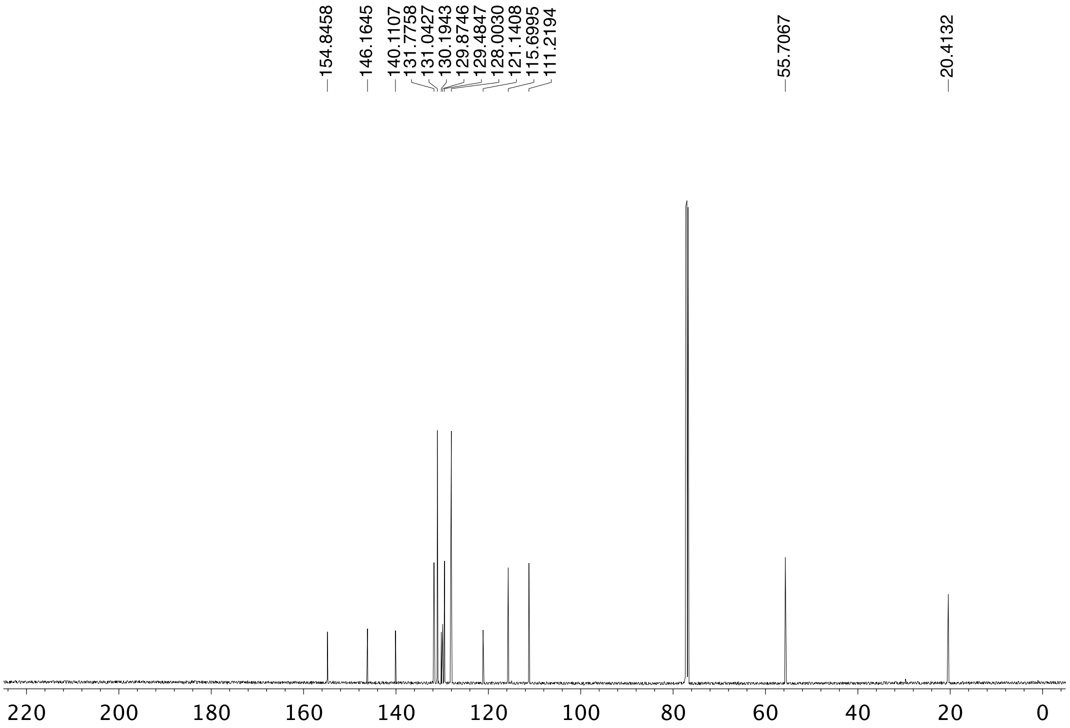


Figure 3.47 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.32a**

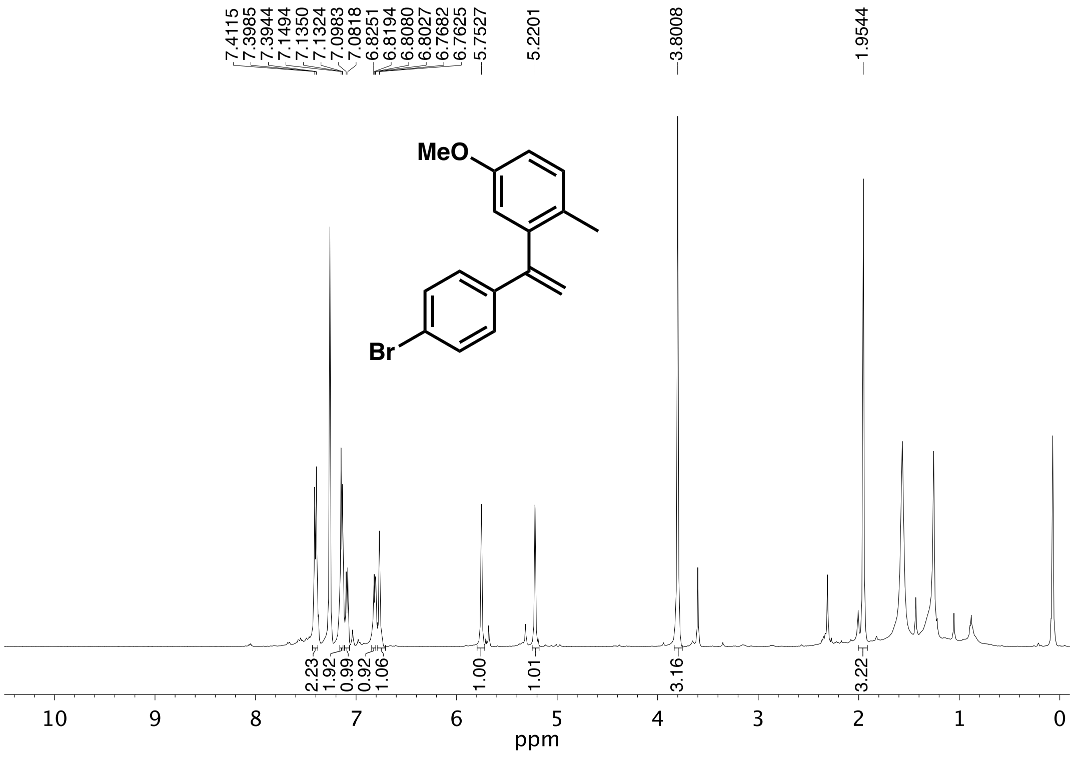


Figure 3.48 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.32b**.

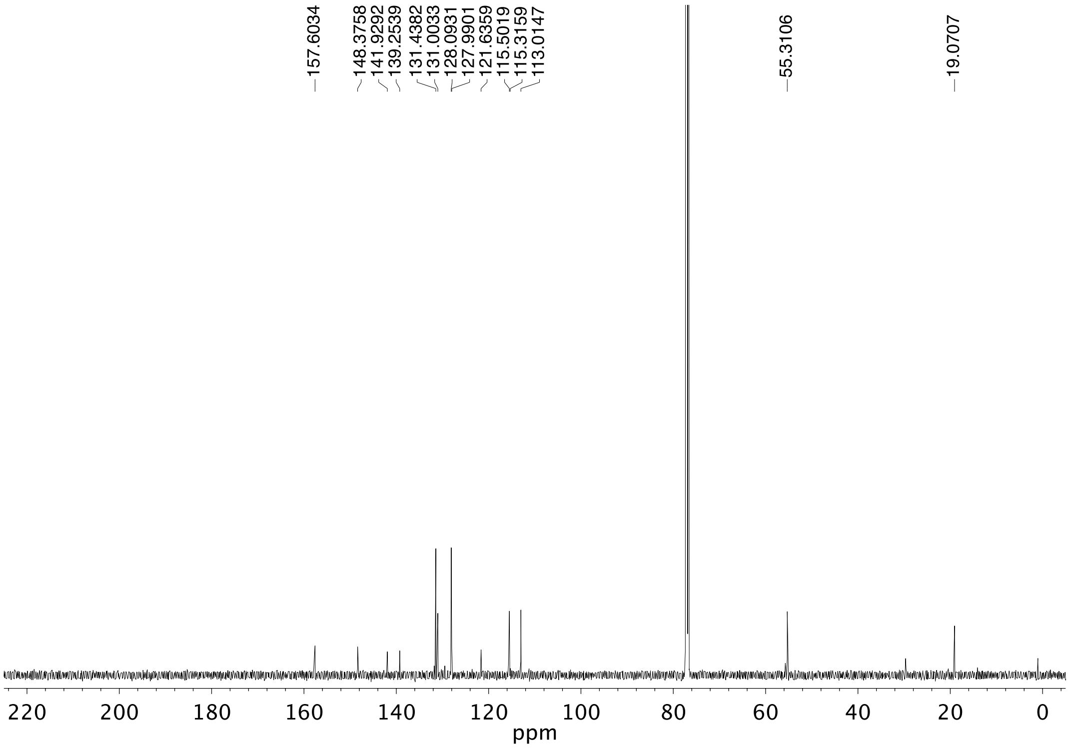


Figure 3.49 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.32b**.

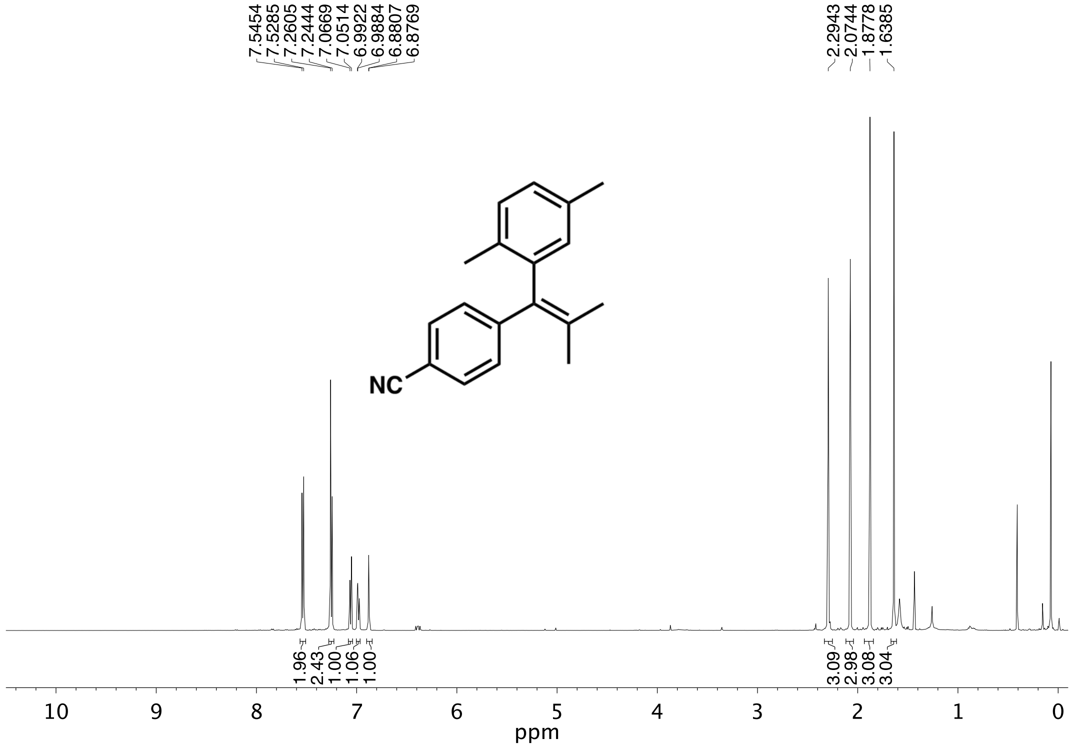


Figure 3.50 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.33**.

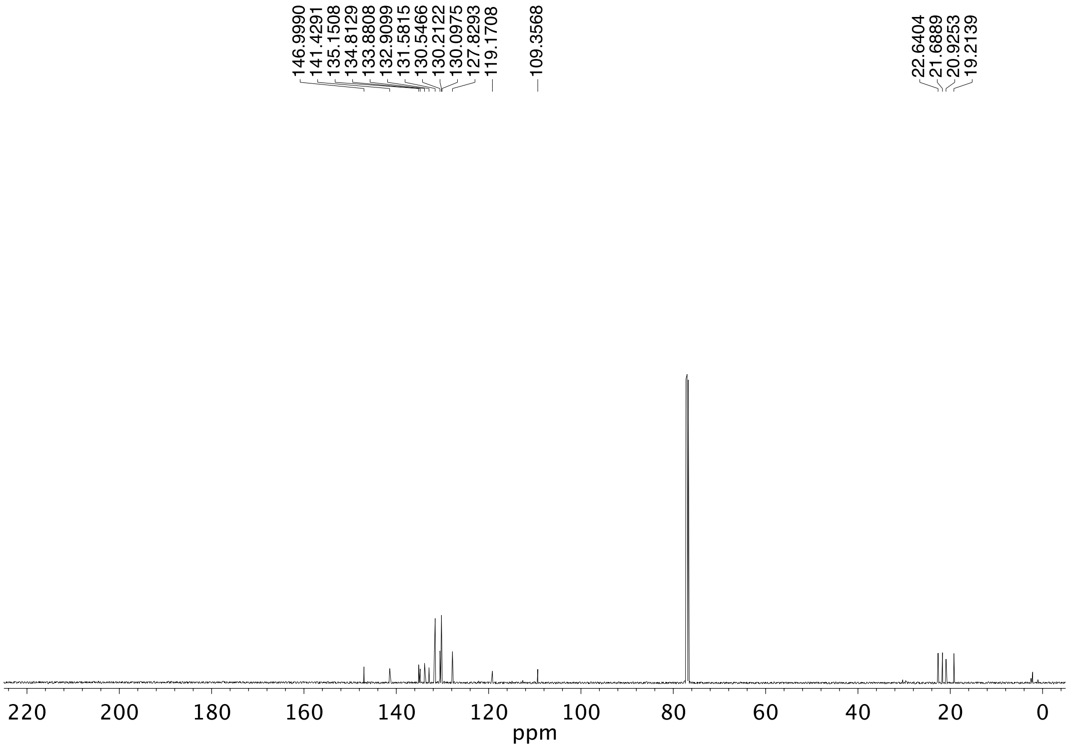


Figure 3.51 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.33**.

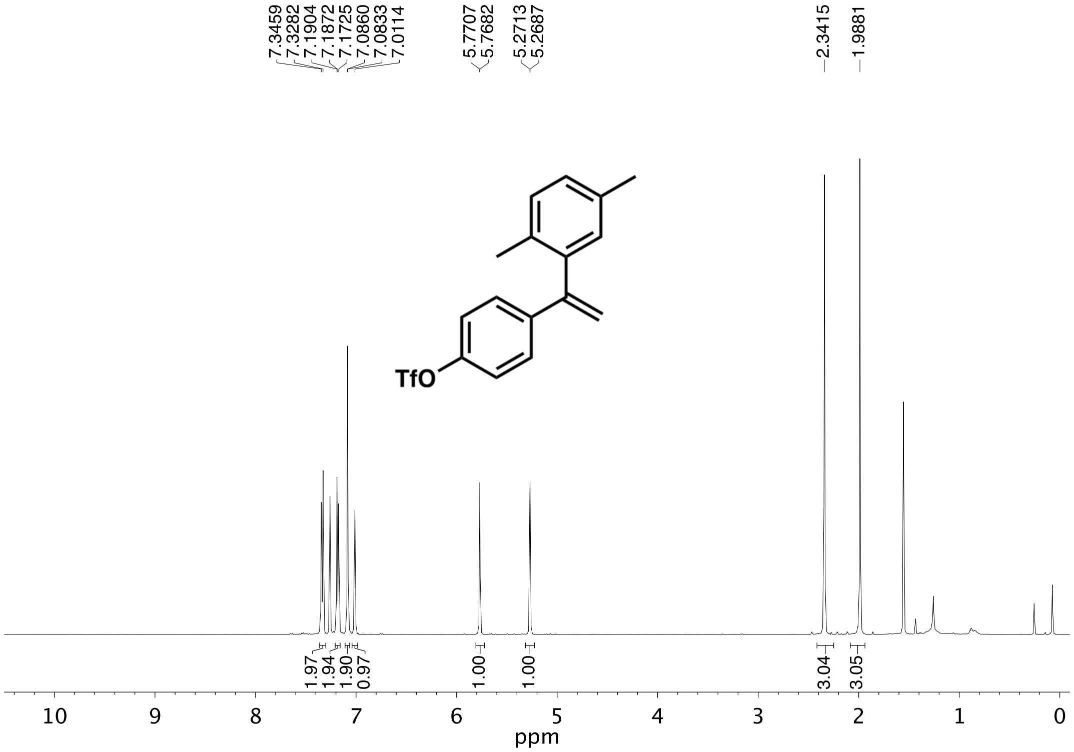


Figure 3.52 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.34**.

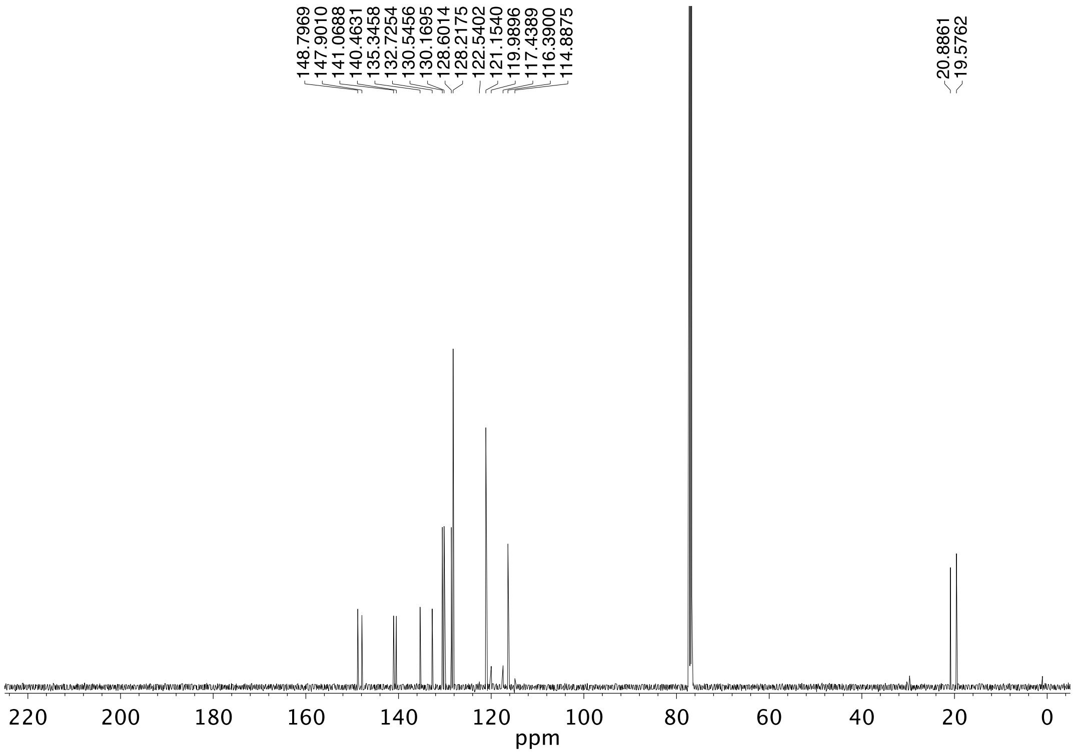


Figure 3.53 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.34**.

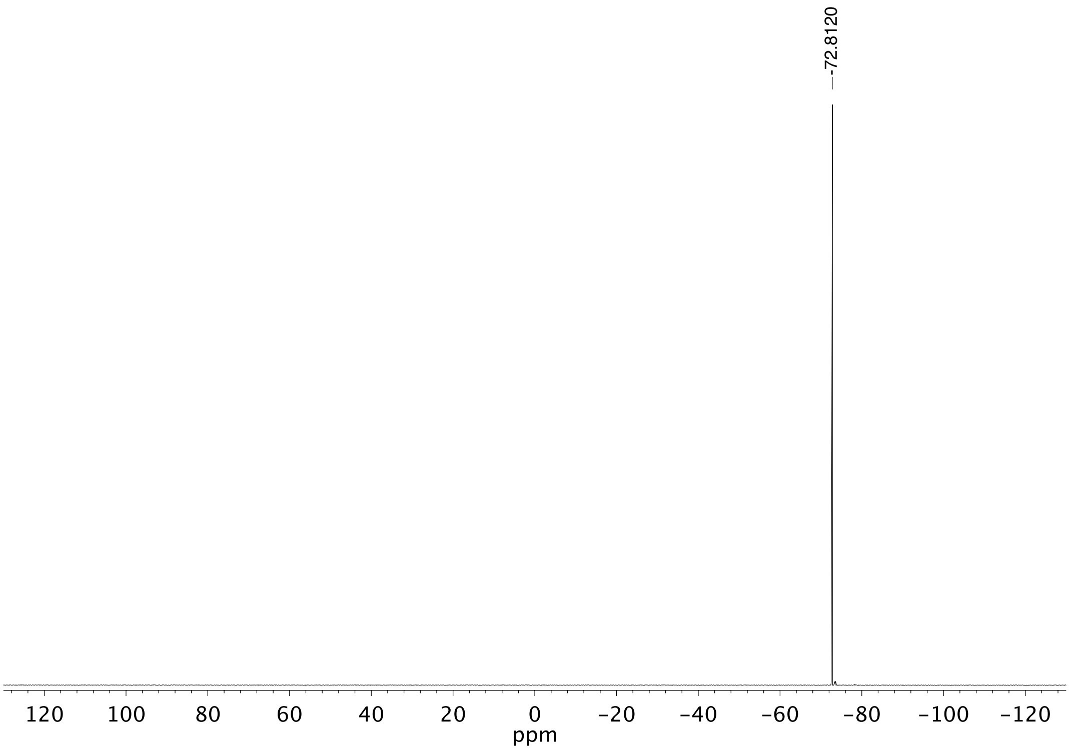


Figure 3.54 ^{19}F NMR (376 MHz, $CDCl_3$) of compound **3.34**.

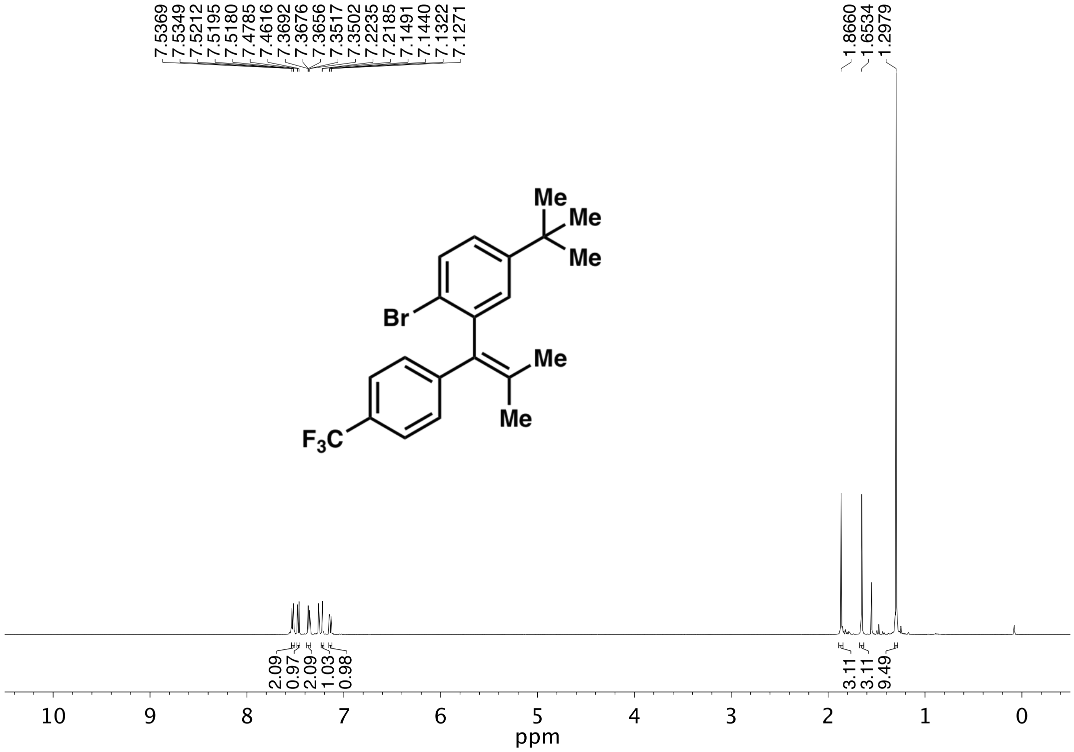


Figure 3.55 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.35**.

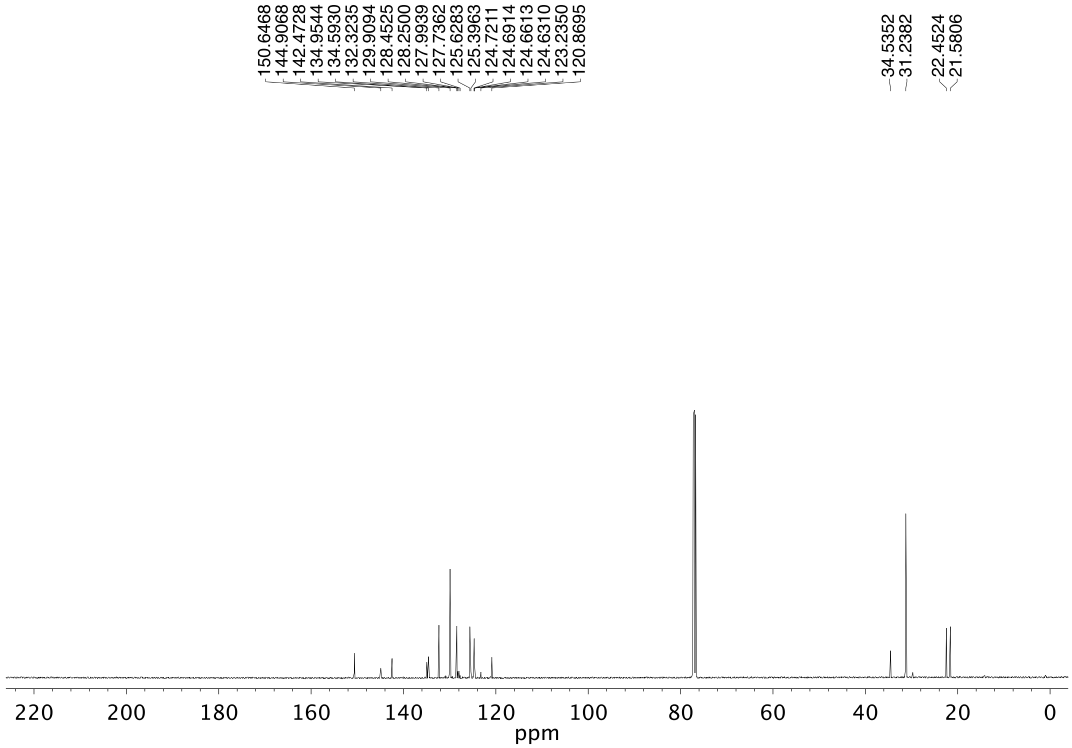


Figure 3.56 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.35**.

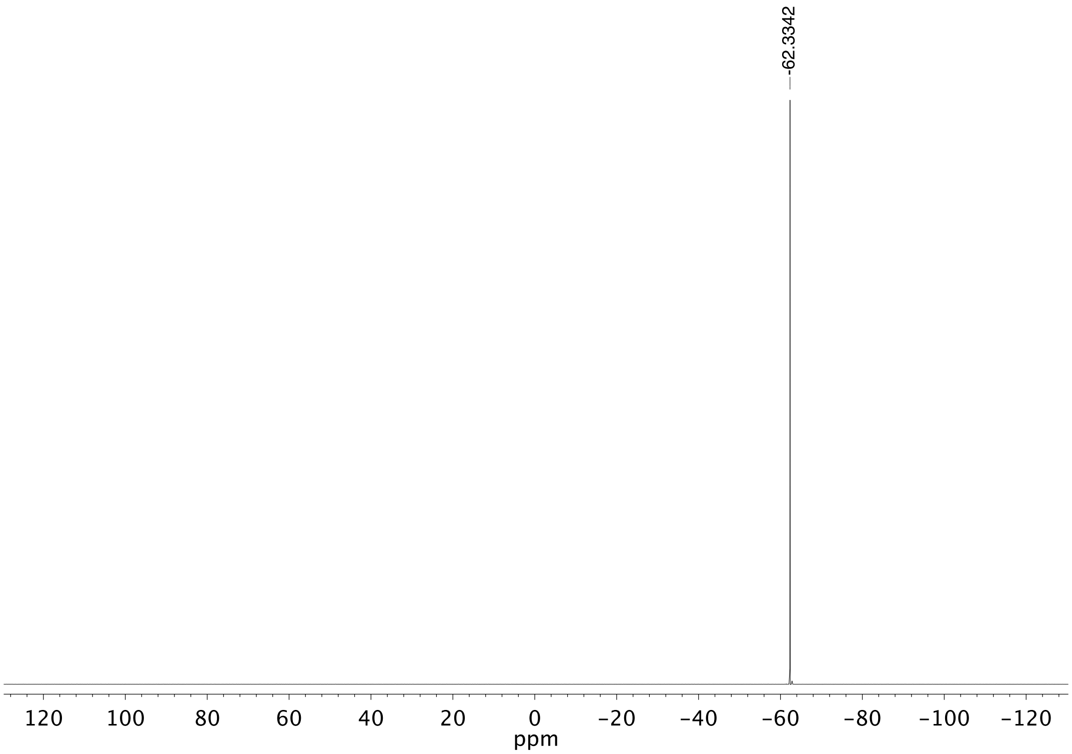


Figure 3.57 ^{19}F NMR (376 MHz, CDCl$_3$) of compound **3.35**.

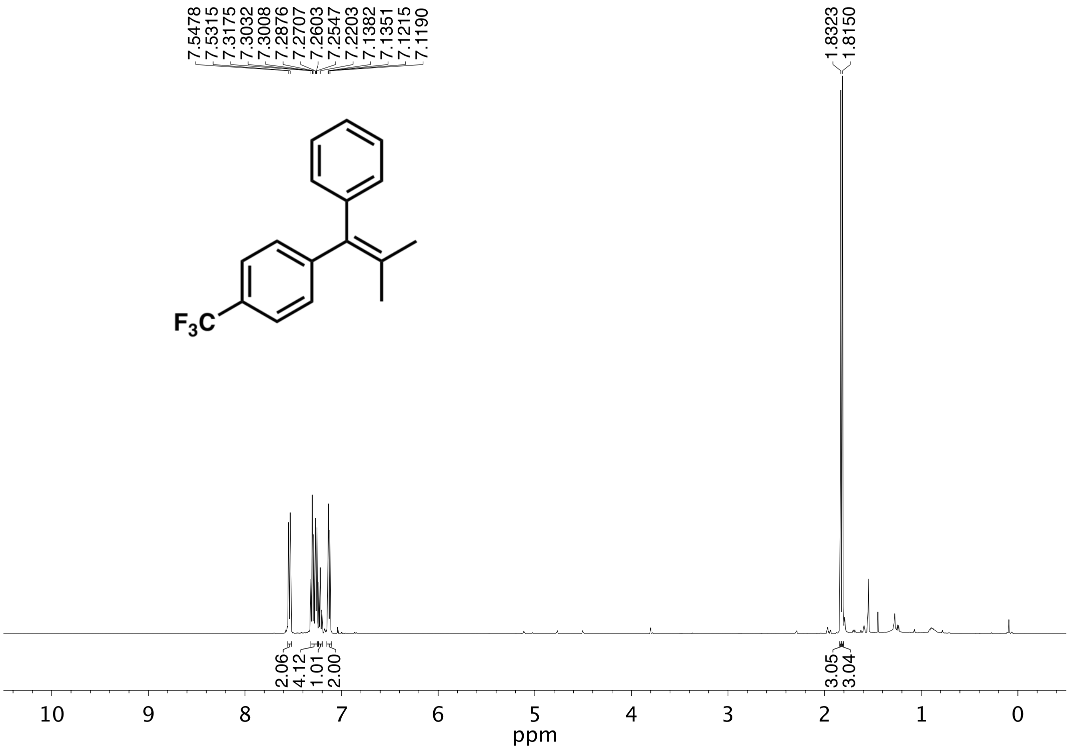


Figure 3.58 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.36**.

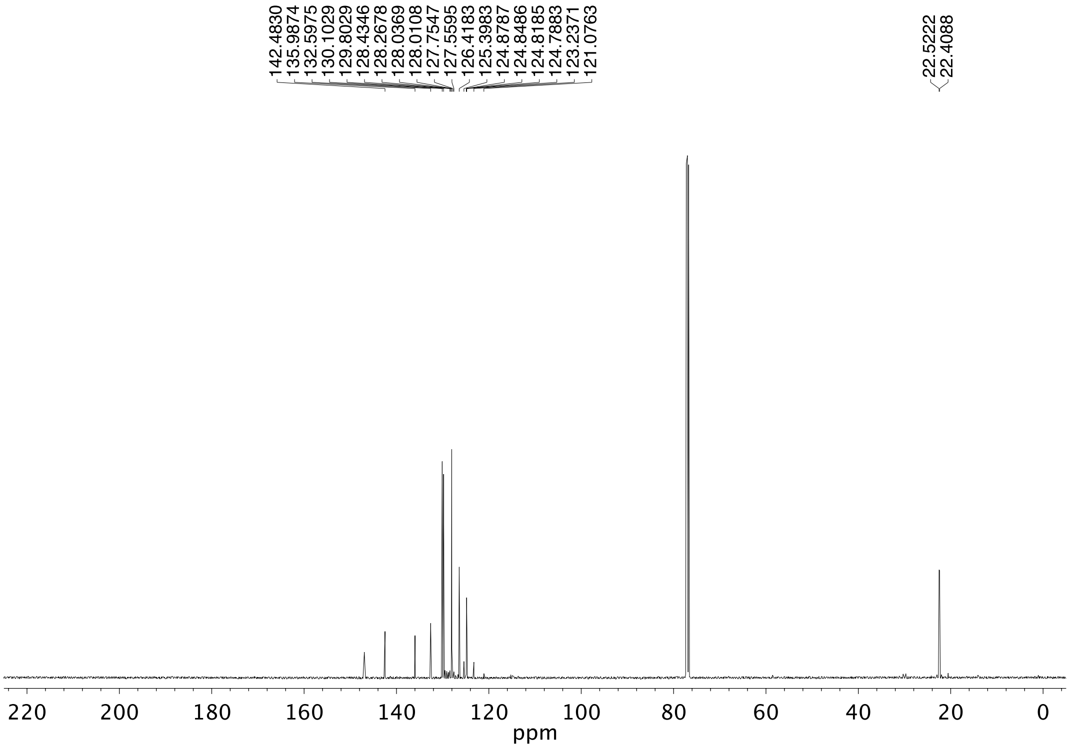


Figure 3.59 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.36**.

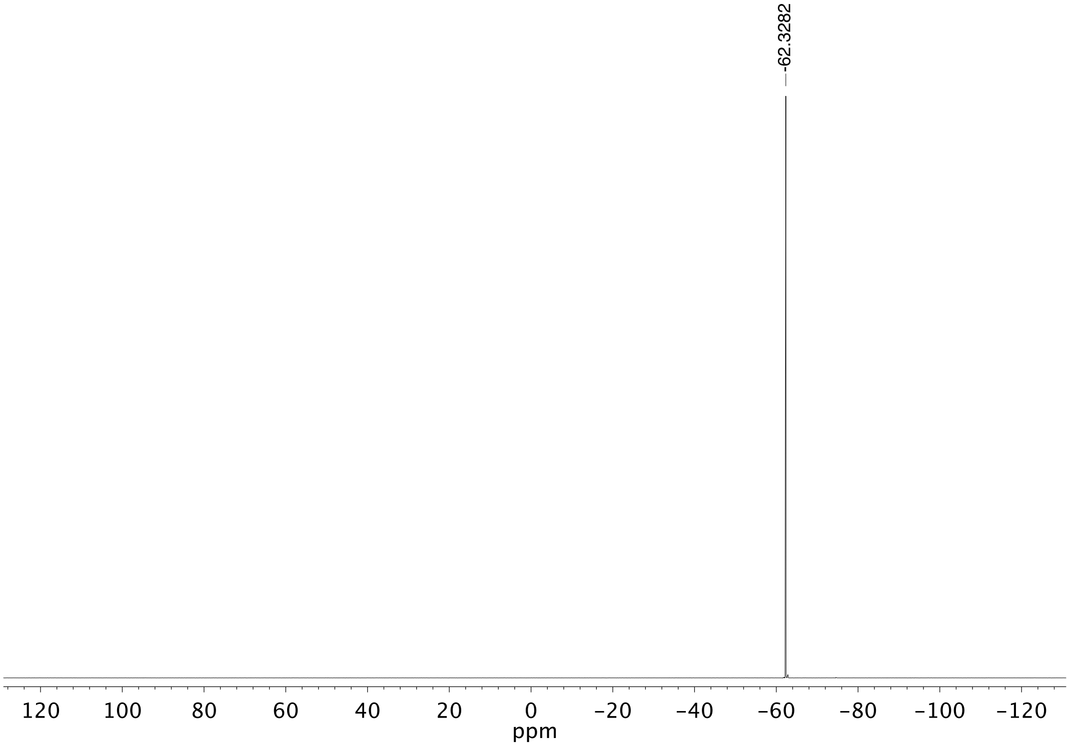


Figure 3.60 ^{19}F NMR (376 MHz, CDCl$_3$) of compound **3.36**.

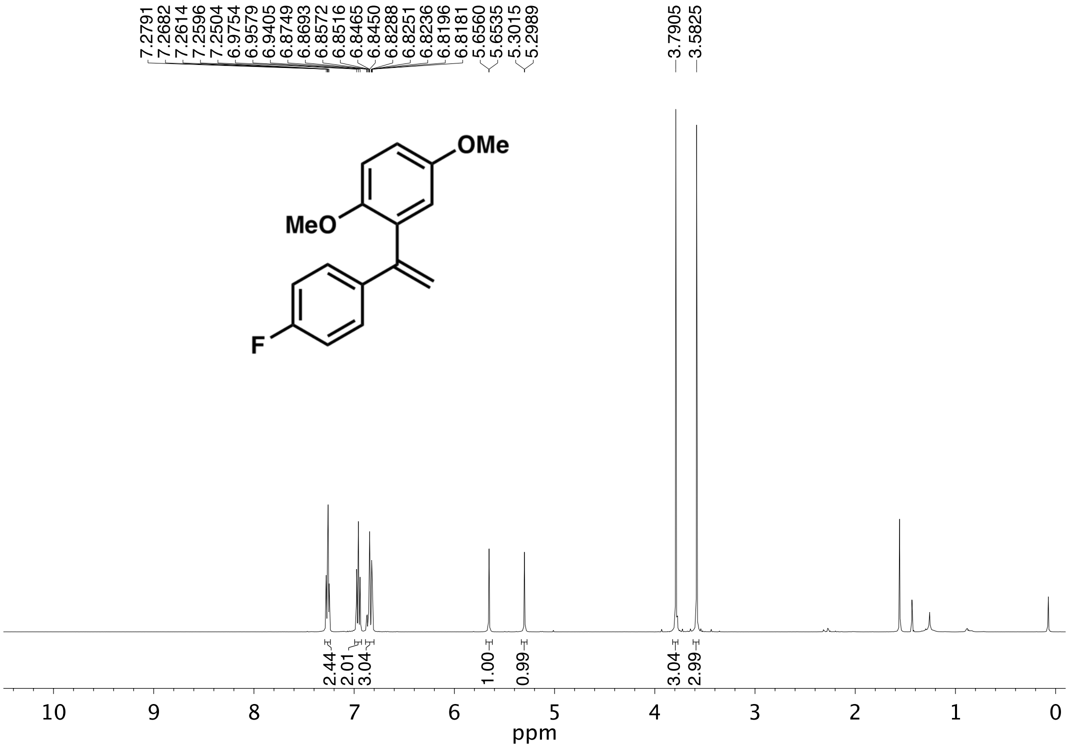


Figure 3.61 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.37**.

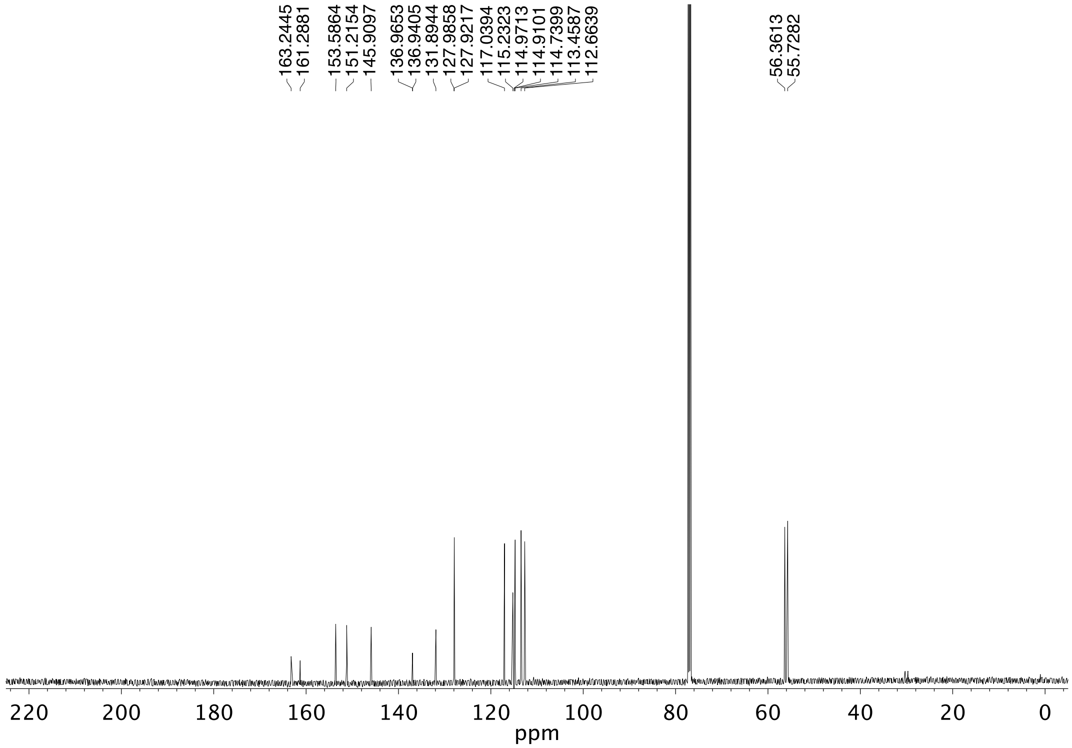


Figure 3.62 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.37**.

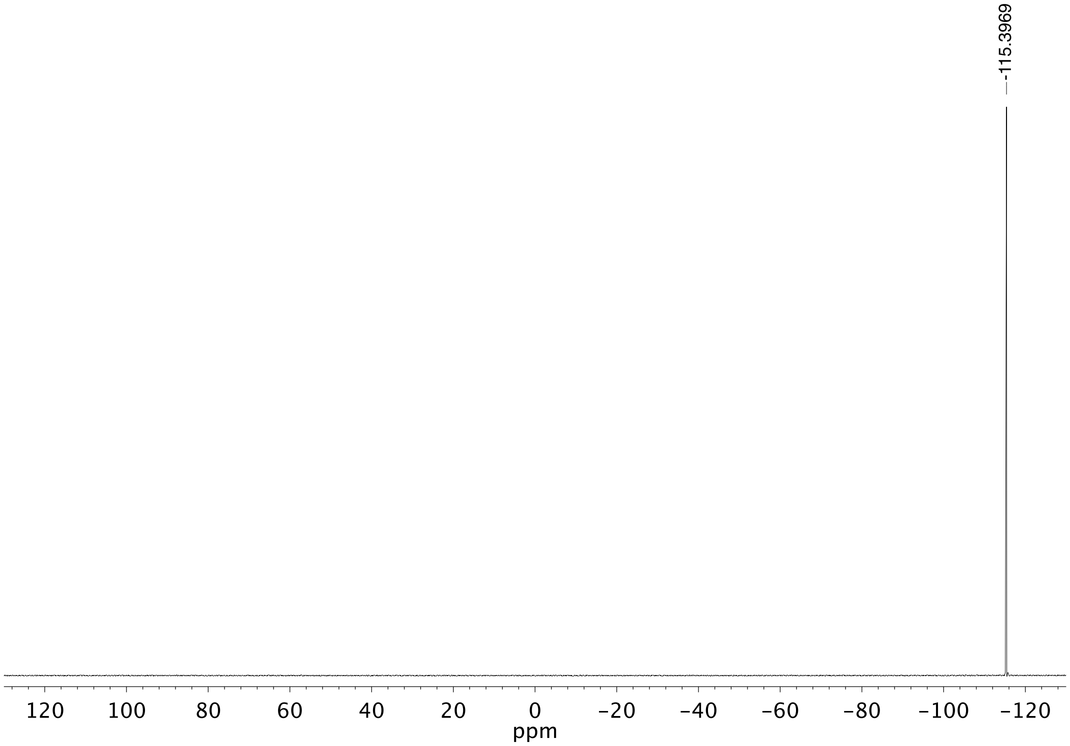


Figure 3.63 ^{19}F NMR (376 MHz, CDCl$_3$) of compound **3.37**.

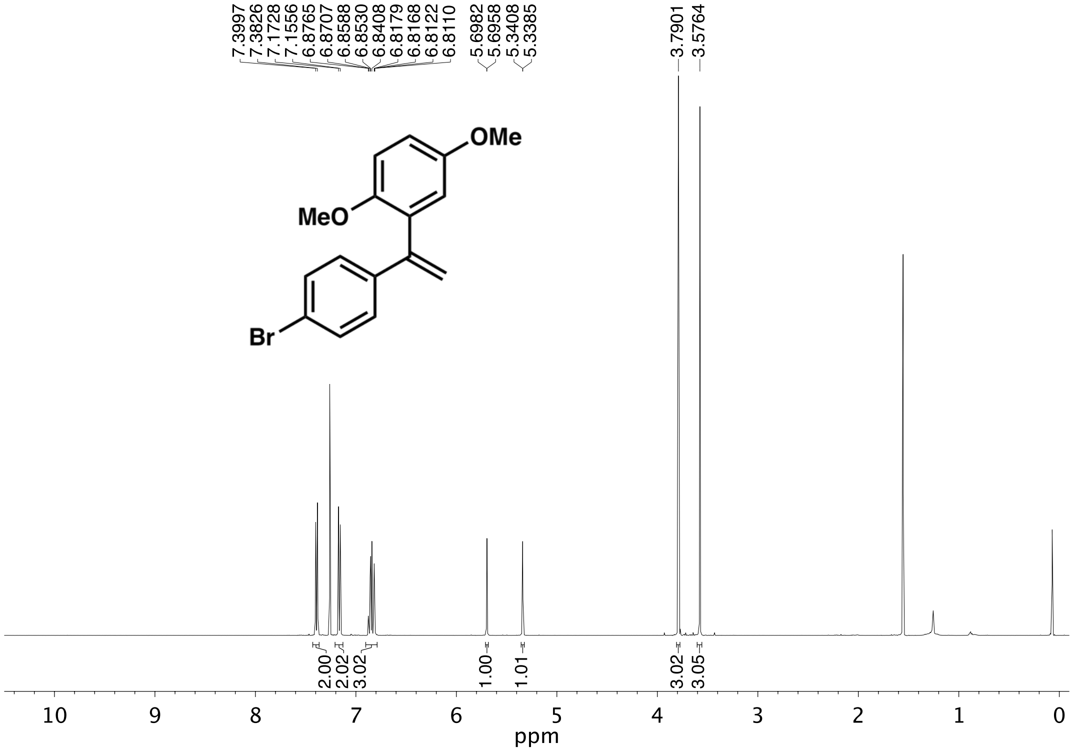


Figure 3.64 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.38**.

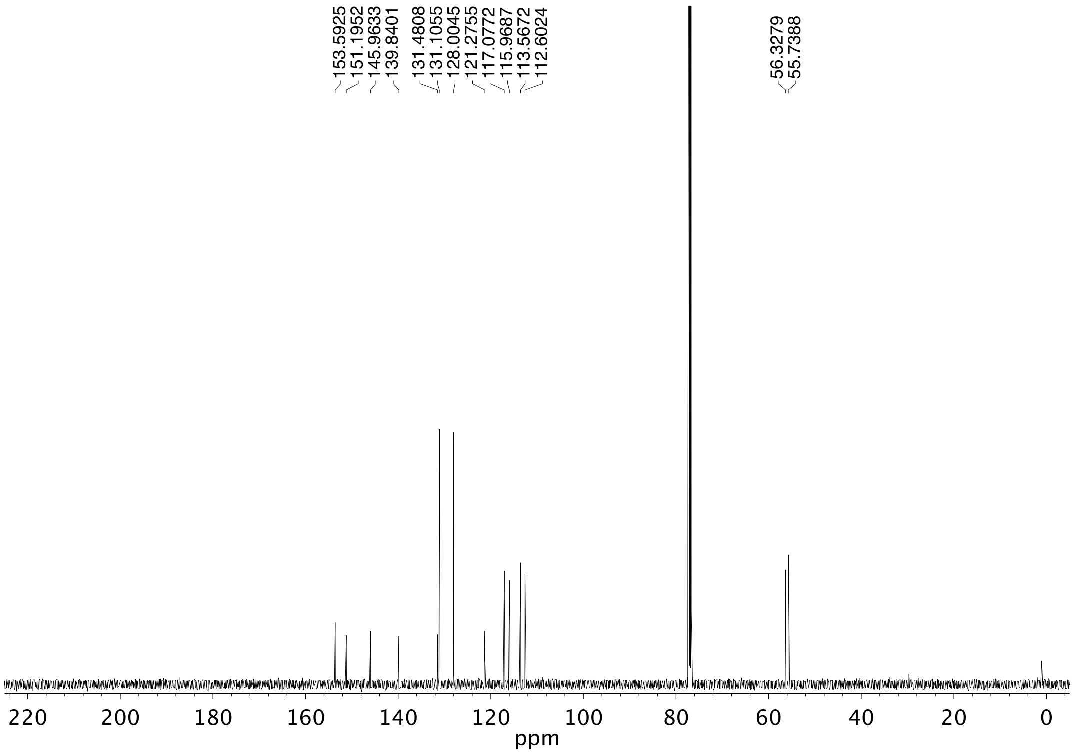


Figure 3.65 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.38**.

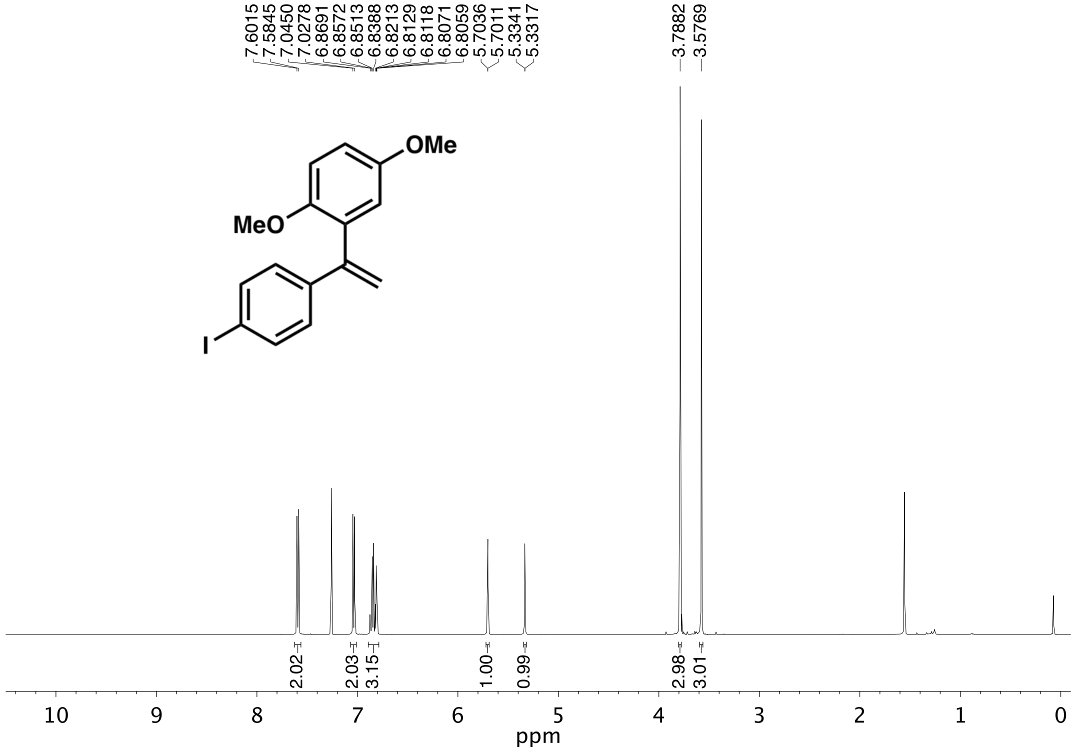


Figure 3.66 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.39**.

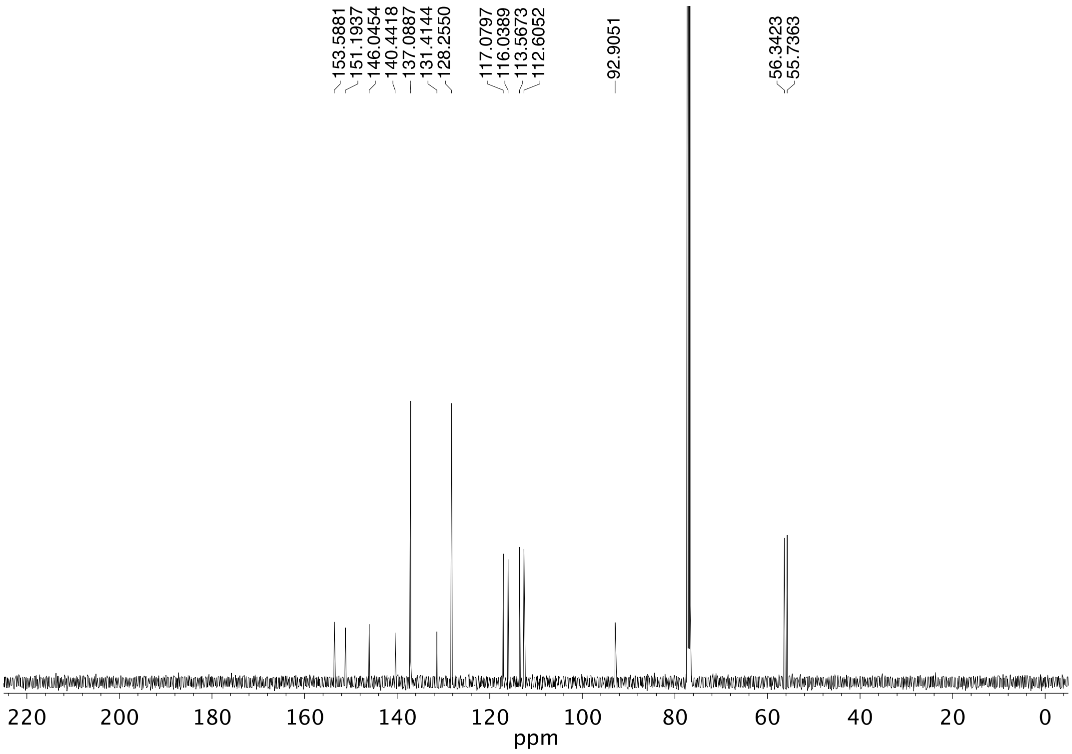


Figure 3.67 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.39**.

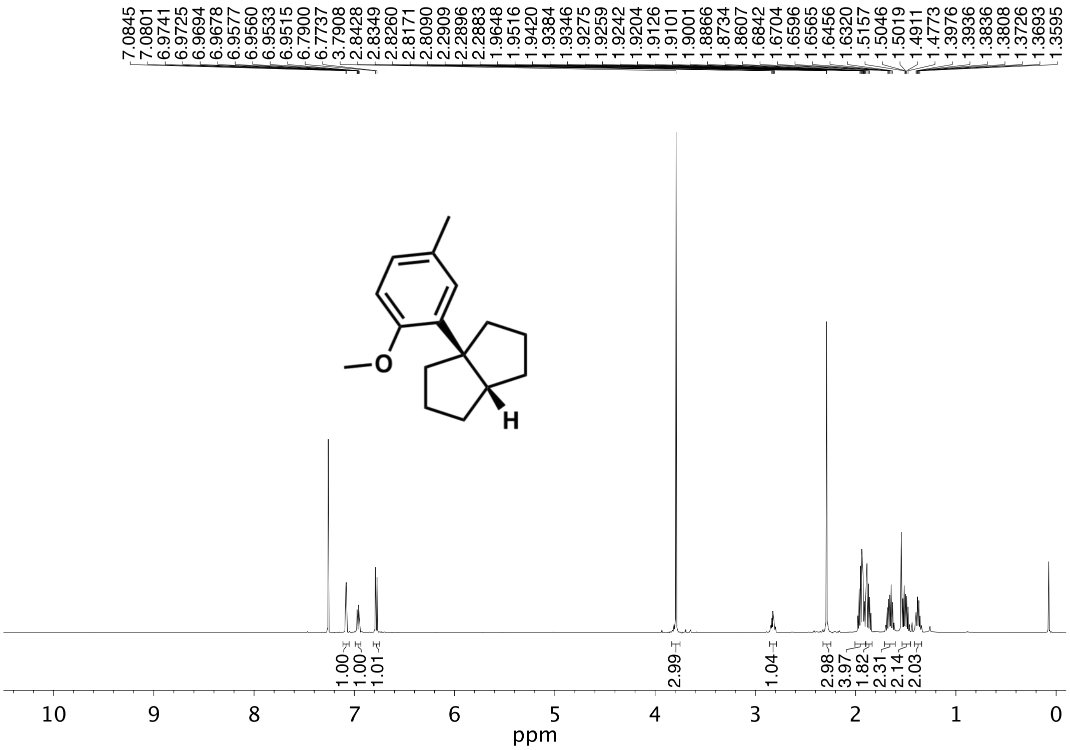


Figure 3.68 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.40**.

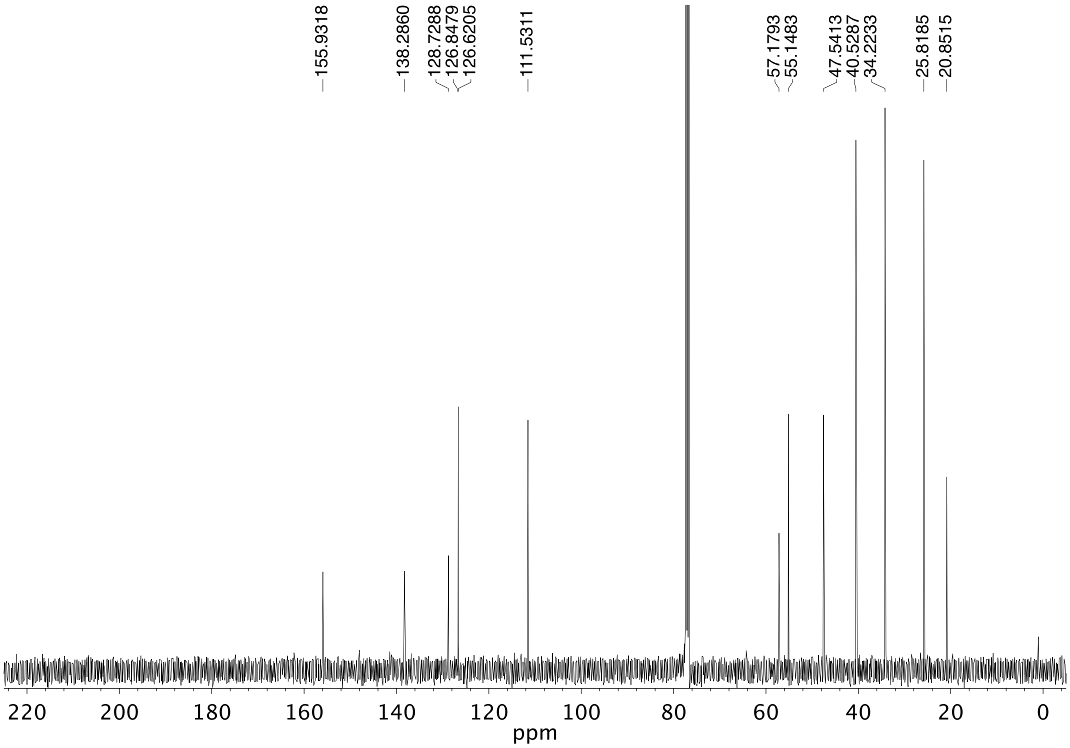


Figure 3.69 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.40**.

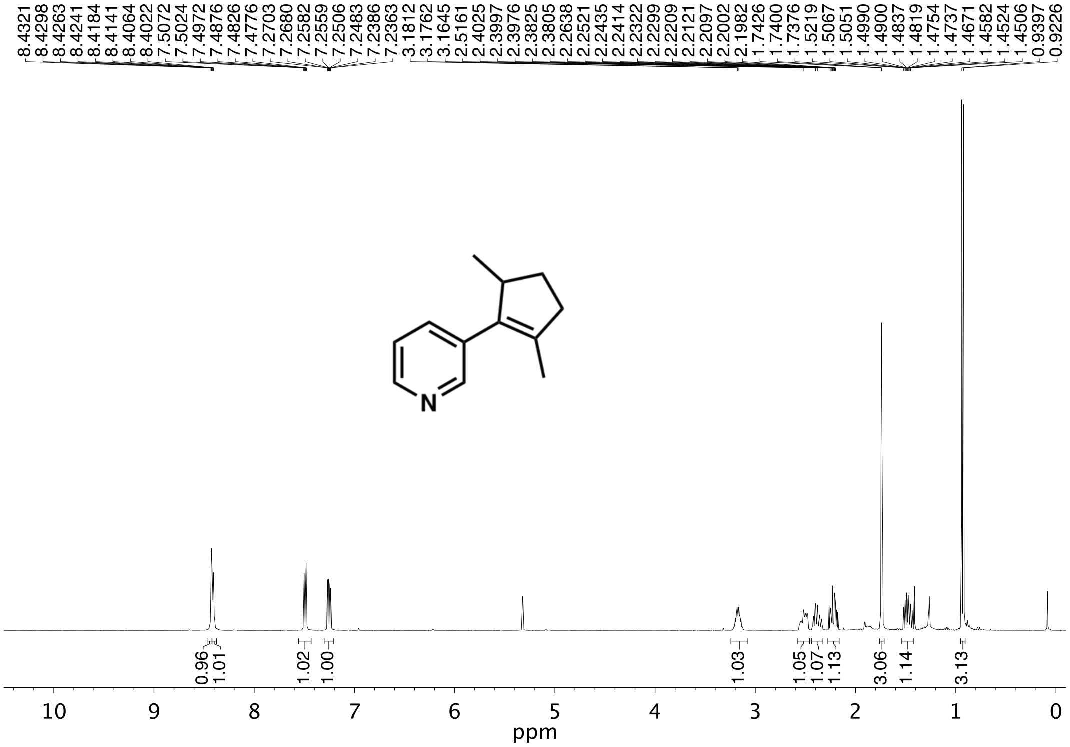


Figure 3.70 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.41**.

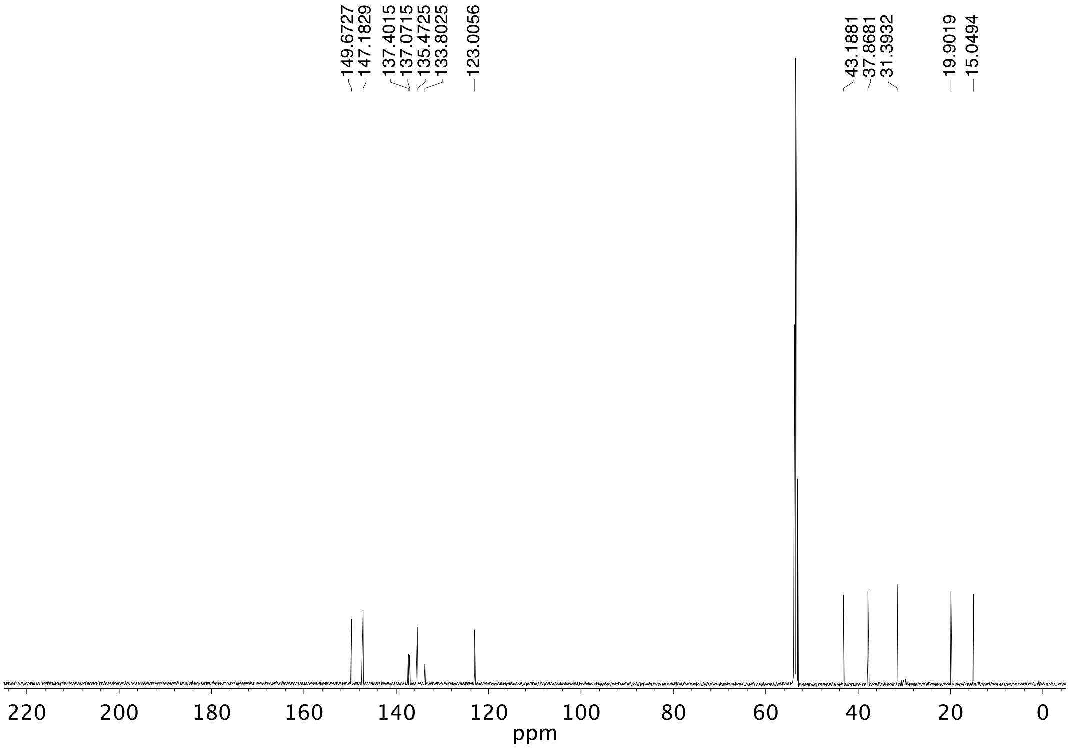


Figure 3.71 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.41**.

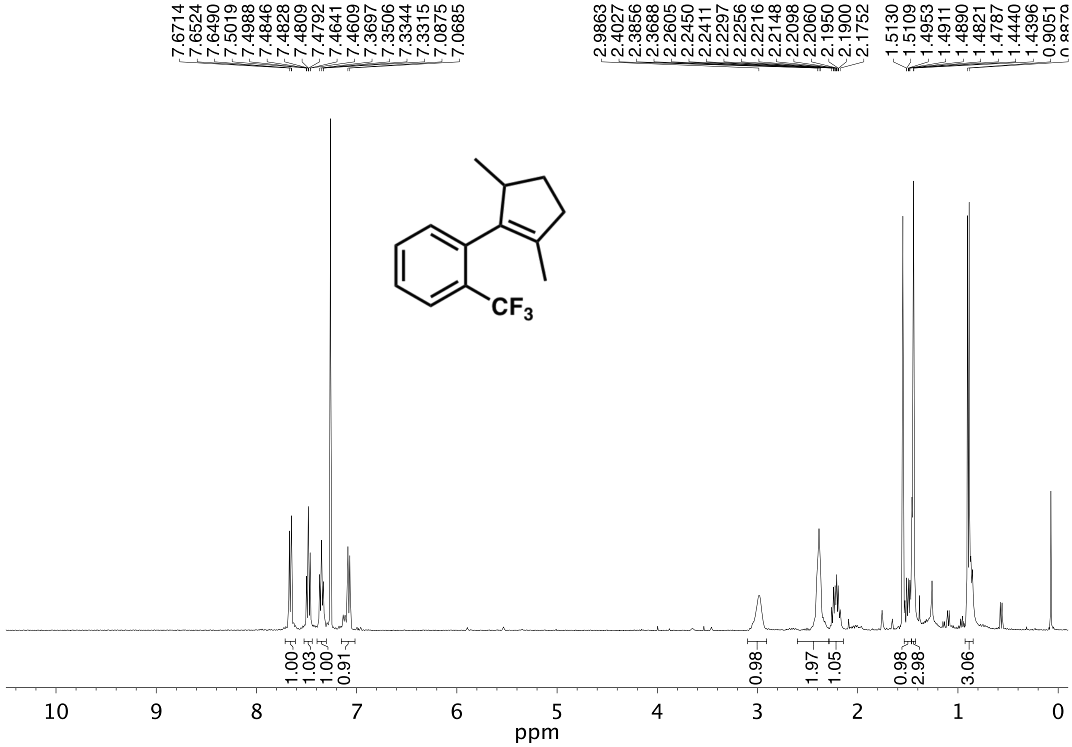


Figure 3.72 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.42**.

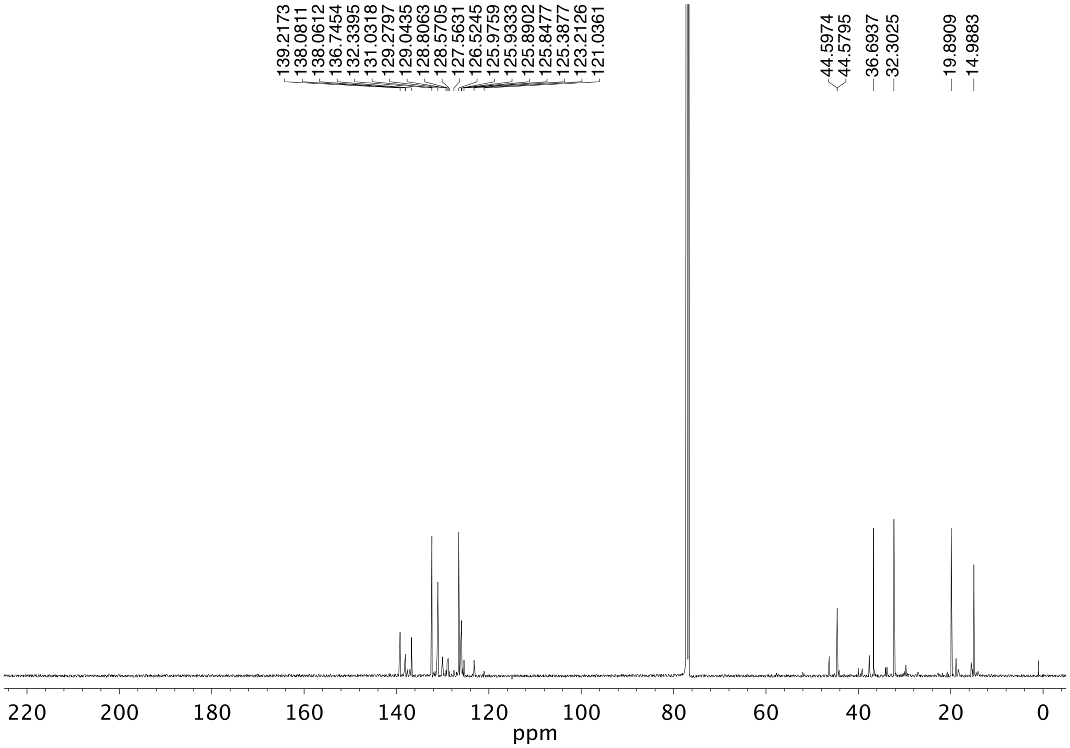


Figure 3.73 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.42**.

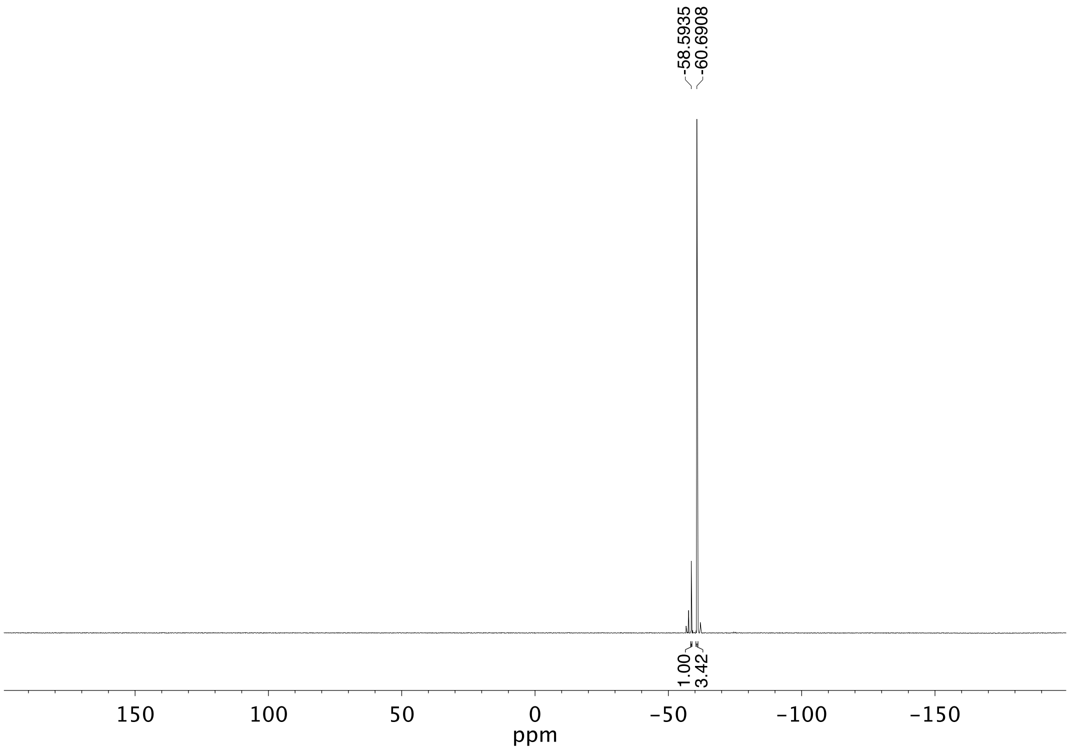


Figure 3.74 ^{19}F NMR (376 MHz, $CDCl_3$) of compound **3.42**.

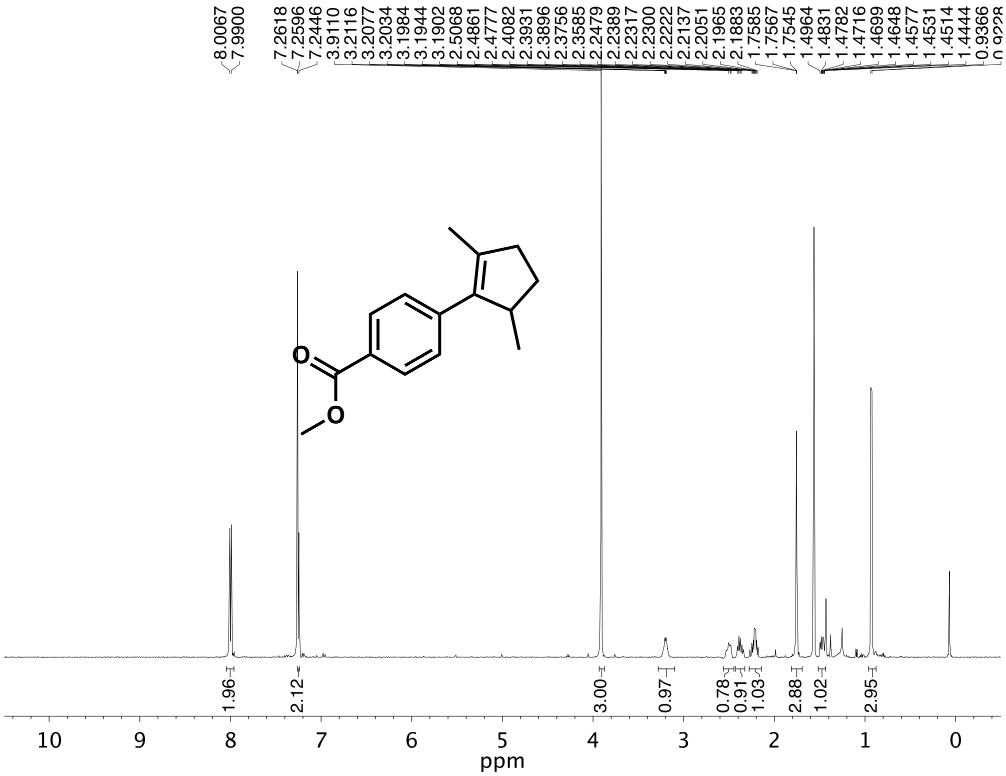


Figure 3.75 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.43**.

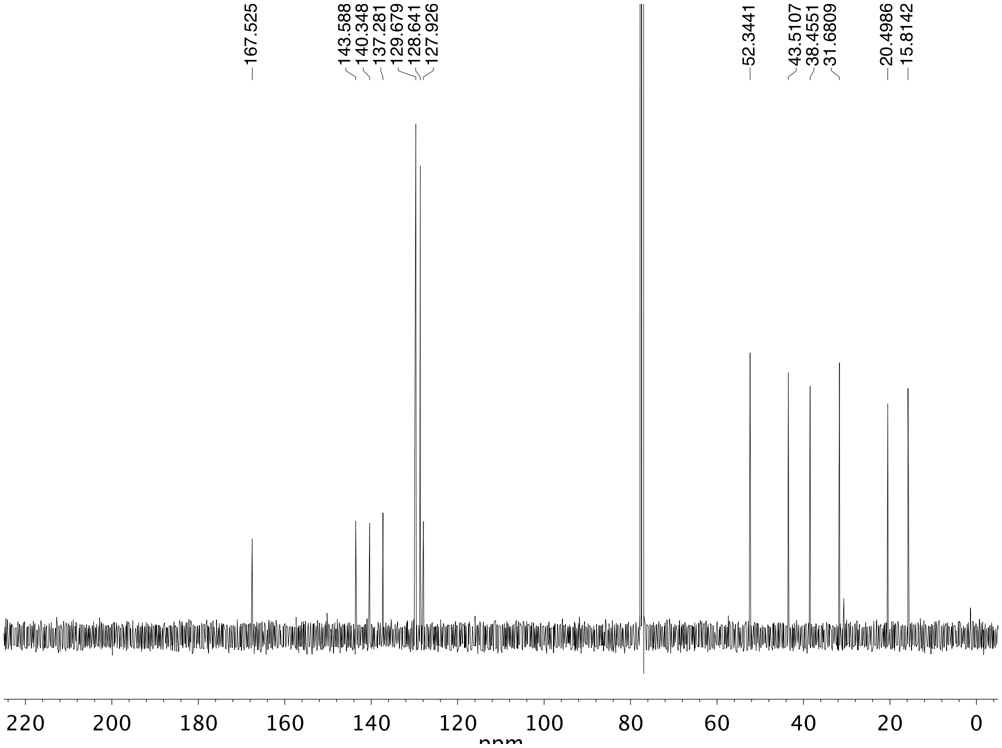


Figure 3.76 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.43**.

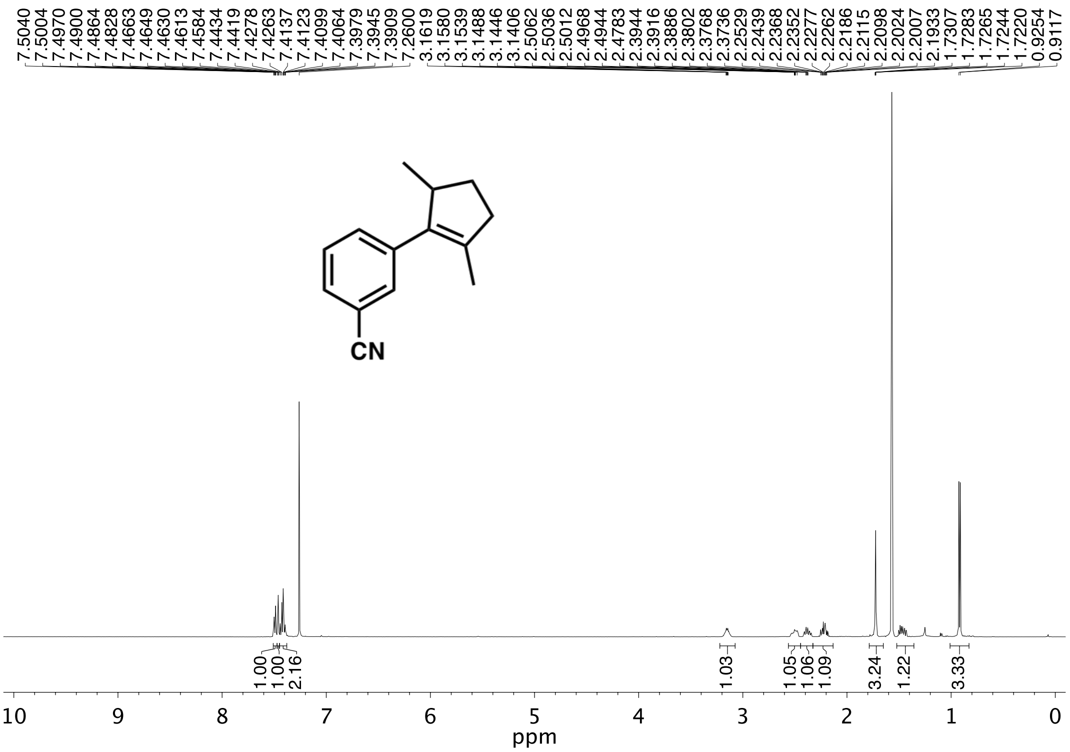


Figure 3.77 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.44**.

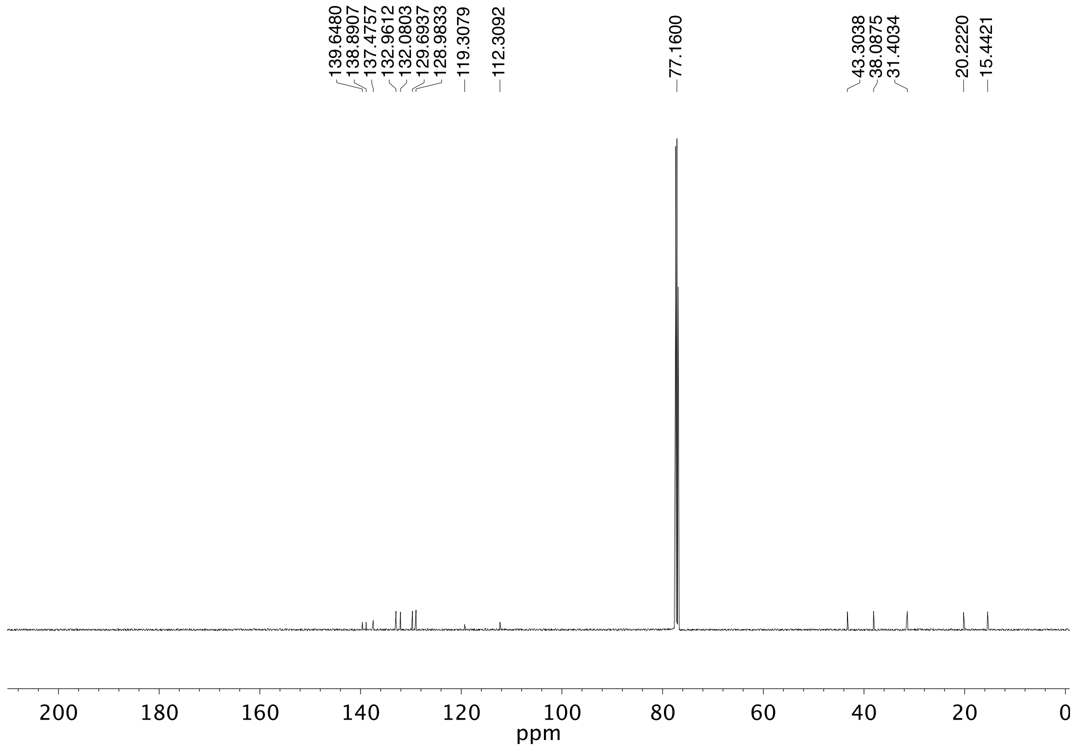


Figure 3.78 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.44**.

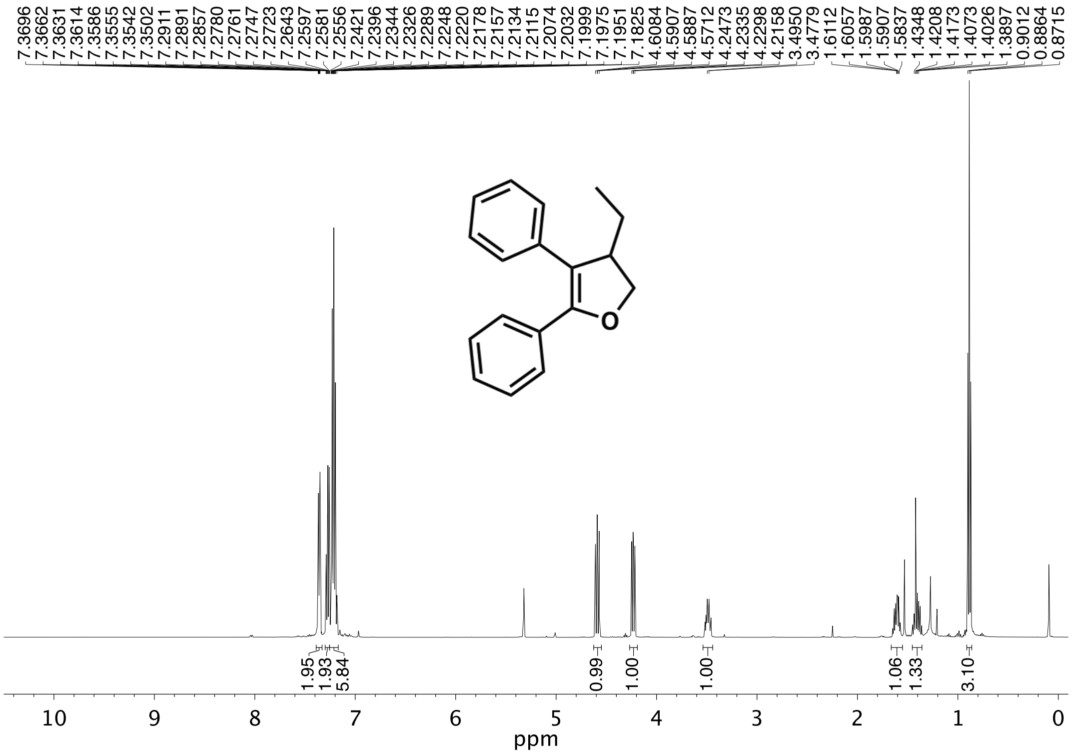


Figure 3.79 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.45**.

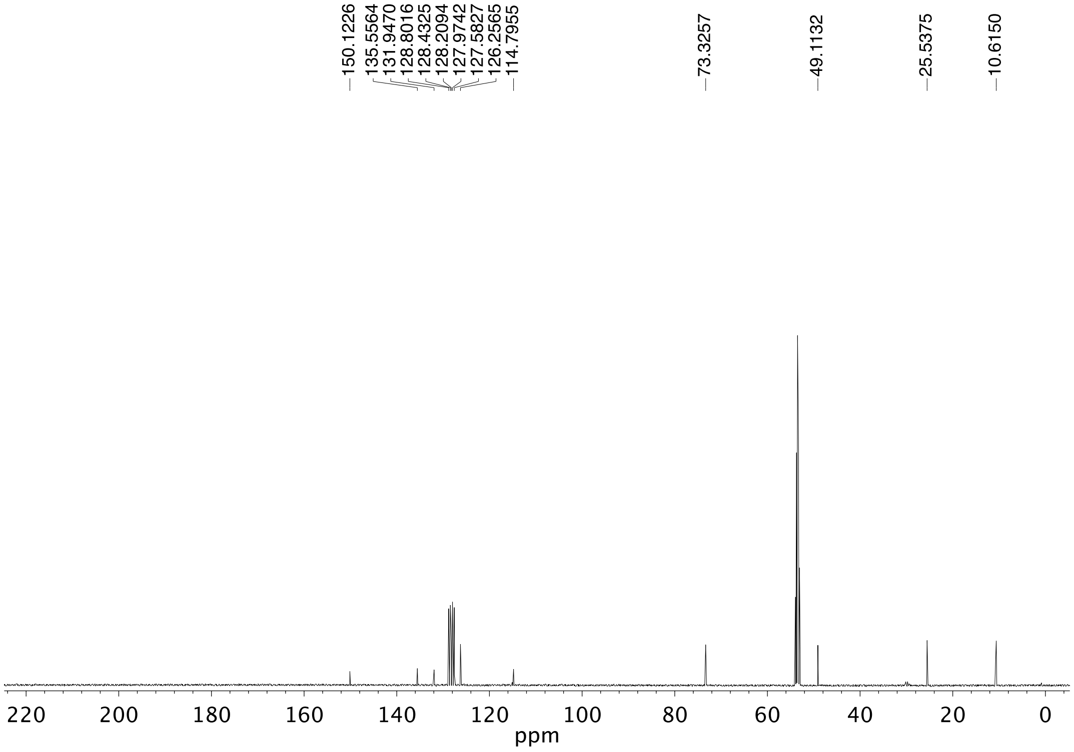


Figure 3.80 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.45**.

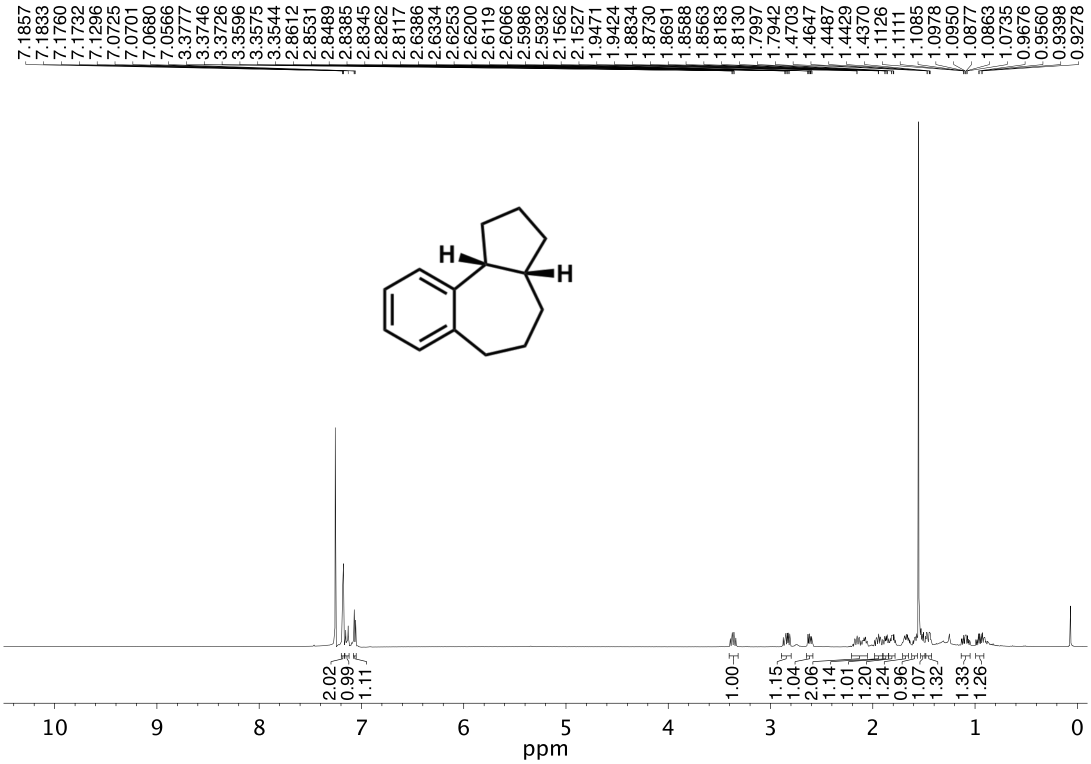


Figure 3.81 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.48**.

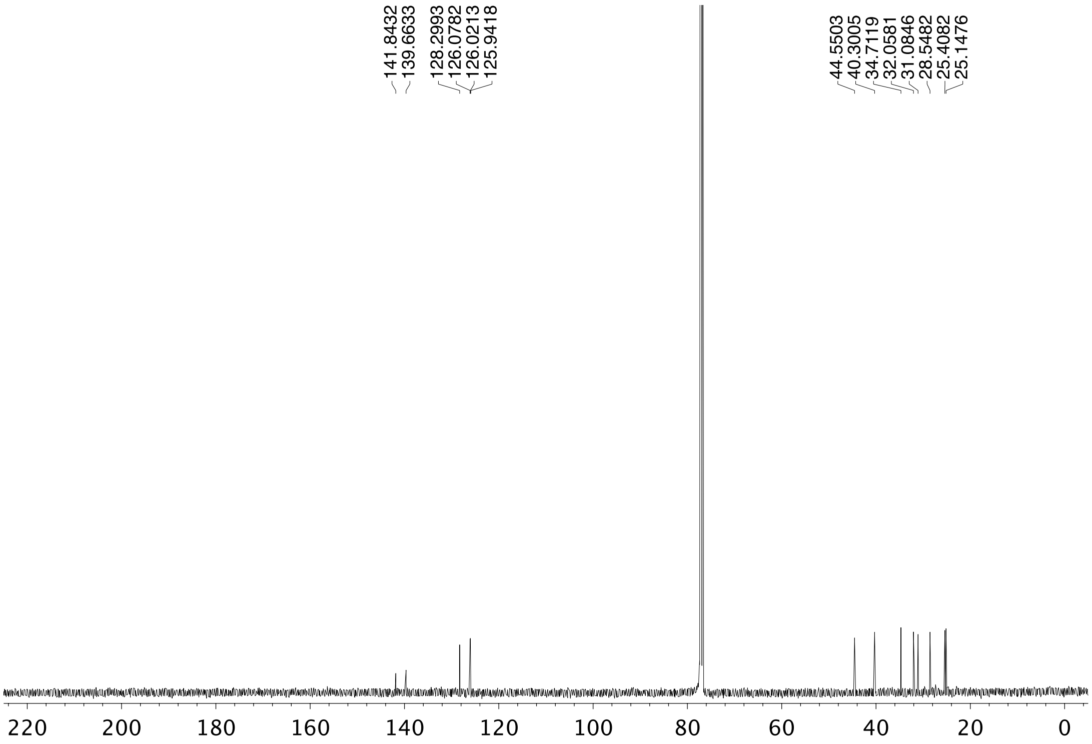


Figure 3.82 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.48**.

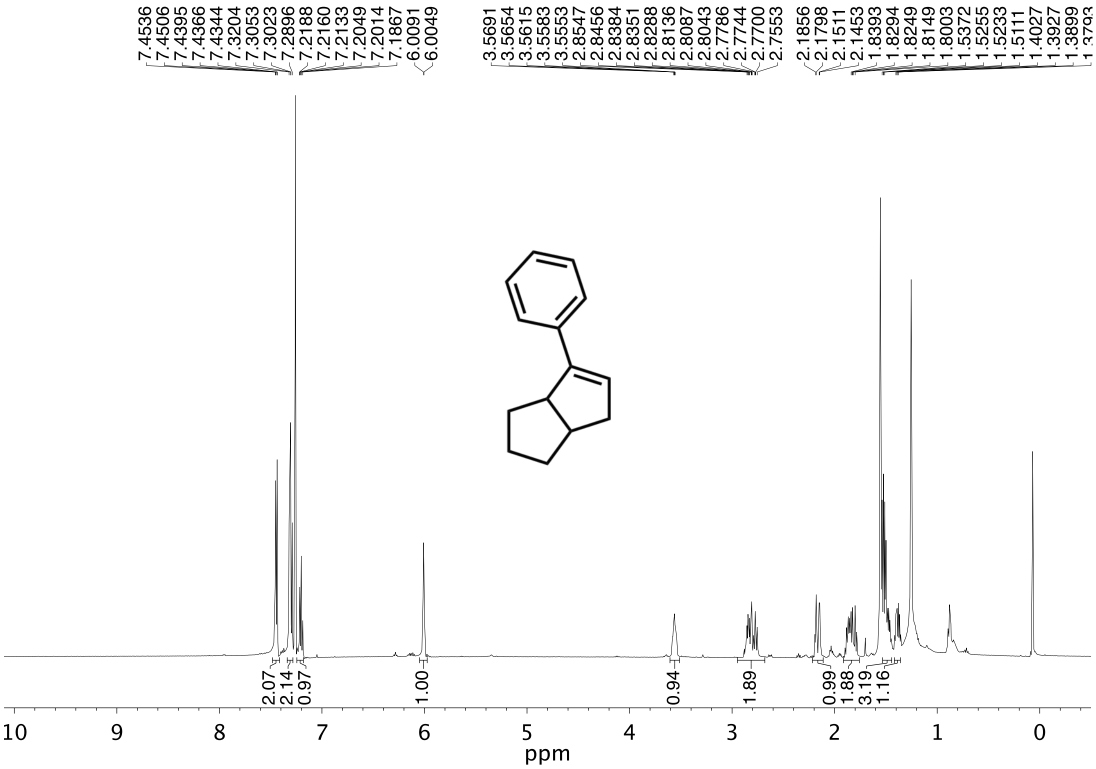


Figure 3.83 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **3.53**.

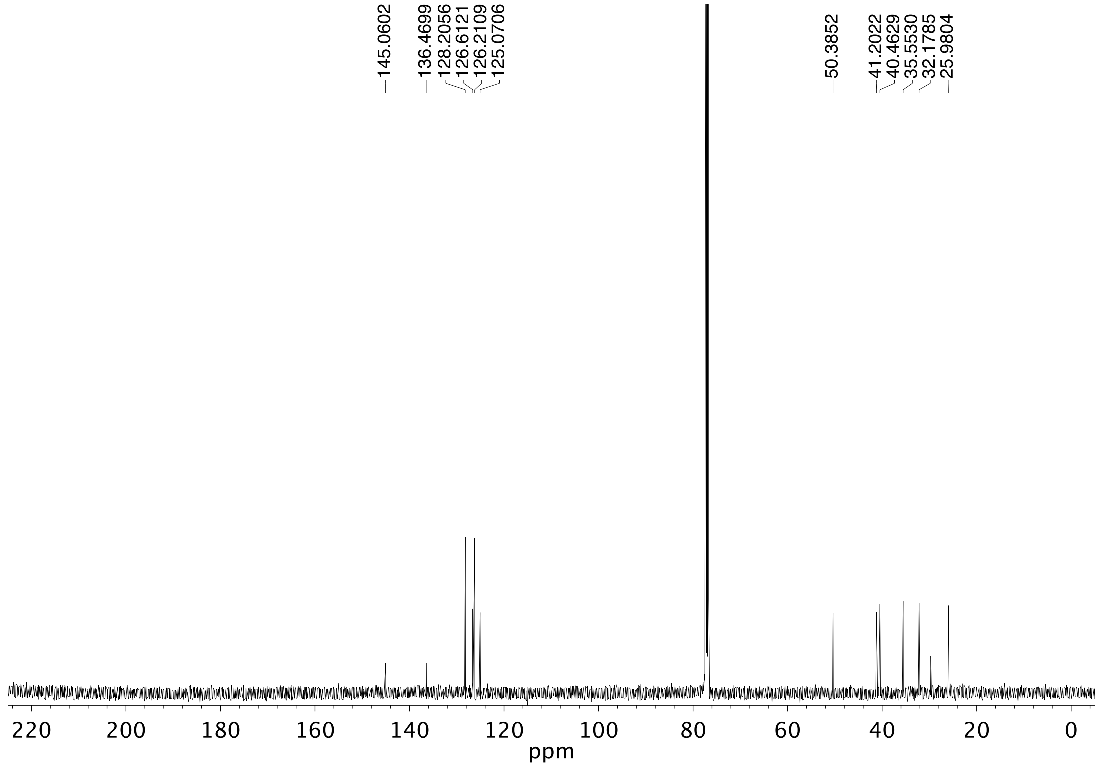


Figure 3.84 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **3.53**.

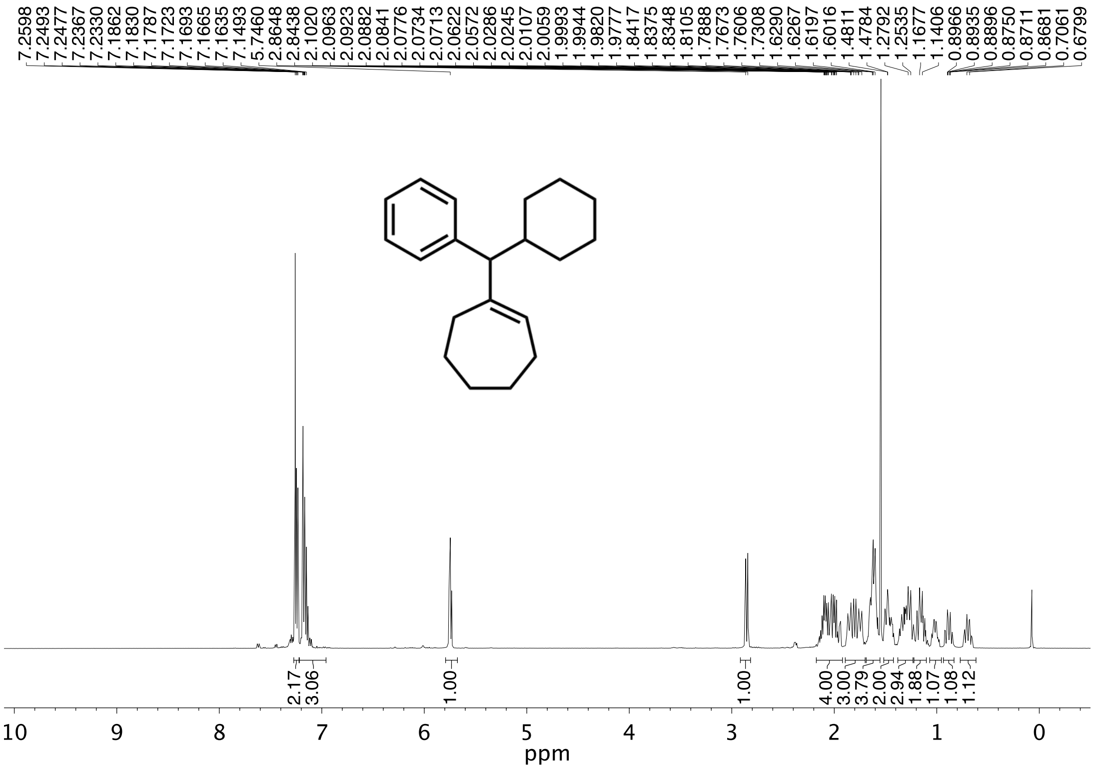


Figure 3.85 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **3.54**.

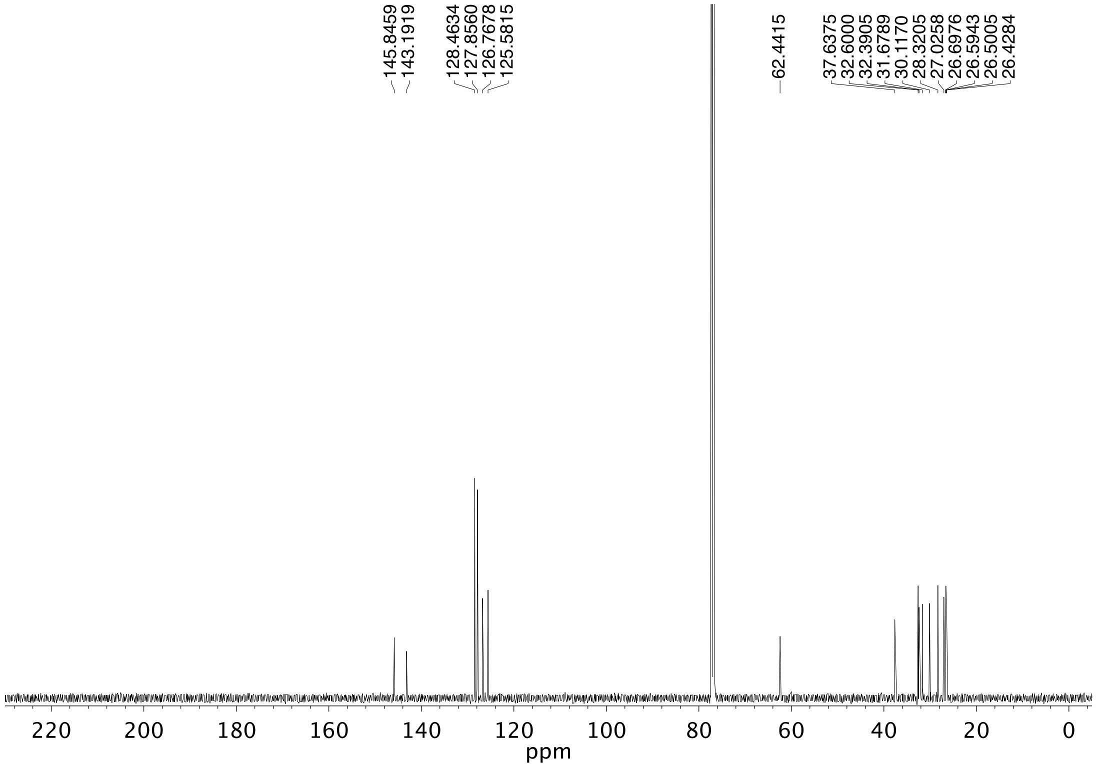


Figure 3.86 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **3.54**.

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(18) See Chapter 5.3 for discussion of vinyl cation ionization

(19) See Chapter 5.6 and Figure 5.9 for discussion on elimination reactions

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CHAPTER FOUR

Vinyl Tosylates as Vinyl Cation Precursors Enable Broad Heterocycle Synthesis, as well as Intermolecular Trapping by Carbon and Oxygen Based Nucleophiles

(Unpublished Work)

Zhenqi Zhao, Chloe G. Williams, Stasik Popov, Lee Joon Kim, Jonathan Wong, and Hosea M. Nelson

4.1 Abstract

During the course of our research on vinyl cation chemistry, it has remained difficult to add functionality due to the instability of the vinyl triflate substrates (REF see chapter 5). Due to this substrate instability, we sought to investigate a new vinyl sulfonate to be utilized as a vinyl cation precursor. We found that vinyl tosylates could be ionized under the catalysis of Li-WCA salts to generate vinyl cation intermediates. Concurrently with these exciting results, we present several new intermolecular vinyl cation reactions, which include an intermolecular vinyl ether synthesis, allylation of vinyl cations as well as α-vinylation of silyl ketene acetals through vinyl cation intermediates. We also report on an intramolecular Friedel-Crafts methodology that allows facile access to medium-sized rings in a catalytic fashion.

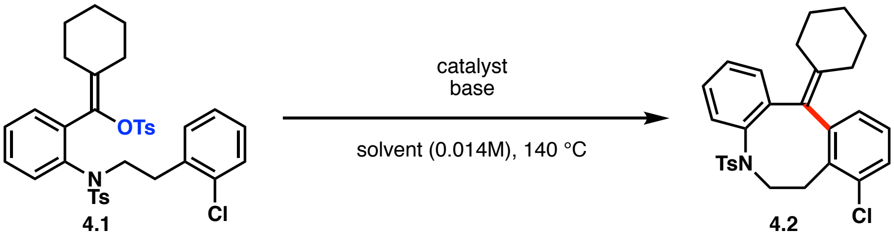
4.2 Introduction

Triflates, which have been initially developed to be excellent leaving groups, are considered to be "pseudohalides" and have found many applications in cross-coupling and other transition-metal catalyzed processes.[1–5] However, because of their excellent leaving group-ability, alkyl triflates and even some vinyl triflates can be unstable and readily decompose upon isolation attempts.[6] In our efforts to bring C–C bond forming vinyl cation chemistry from a fundamental study to an applicable methodology[7,8], we sought a robust vinyl cation precursor that could enable us access to previously unavailable substrate classes. Here, we demonstrate that a tosylate group is a competent leaving group, and vinyl cations can be readily generated from vinyl tosylates[9] under Li-WCA conditions. Changing the leaving group-ability of the vinyl sulfonate precursor would not only allow us to access a wider class of substrates, but also grant us tunable substrate design based on the electronics of the starting material (triflate for electron-deficient substrate, tosylate for electron-rich substrate).

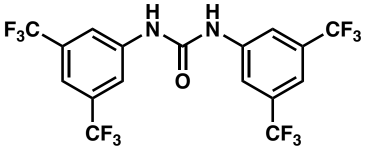
In addition to expanding the scope of available vinyl cation precursors, we seek to develop new methodologies that possess good chemoselectivity to deliver single products in high yields and easy isolation. C–H functionalization reactions of alkanes have often yielded complex product mixtures derived from the plethora of C–H bonds available.[10-12] Furthermore, some of the previously developed strained cyclic vinyl cations undergo unimolecular rearrangements often yielding product mixtures.[13] Here, we report several new classes of vinyl cation reactions that can forge new C–C and C–O bonds in an intermolecular fashion with complete chemoselectivity analogous to that found in transition-metal cross-coupling. Specifically, we find that allyl silanes, silyl ketene acetals (SKAs) and methyl ethers can all trap the incipient vinyl cation intermediate and lead to chemoselective product formation. Furthermore, we leverage the high energy of the vinyl cation intermediate to forge C–C bonds through intramolecular Friedel-Crafts reactions to furnish medium-sized ring products (8–10 membered), despite the high energetic cost associated with making these rings[14–16].

4.3 Initial Results and Optimization of Intramolecular Friedel-Crafts

Initial studies into medium-sized ring formation began with the conversion of vinyl tosylate **4.1** to dihydro-dibenzazocine **4.2** (Table 4.1). We started by surveying a suspension of LiF_{20} **4.4** (10 mol%) with LiH (5 equiv) in different solvents. Due to the high ionization barrier of the vinyl tosylate, we needed to use high boiling solvents at



entry	*catalyst*	*catalyst loading*	*base (equiv)*	*solvent*	*yield*
1	**4.4**	10 mol%	LiH (5)	o-DCB	74%
2	**4.4**	10 mol%	LiH (5)	mesitylene	50%
3	**4.4**	10 mol%	LiH (5)	DMF	0%
4	**4.4**	10 mol%	LiH (5)	o-DFB (90 °C)	0%
5	**4.4**	5 mol%	LiH (5)	o-DCB	49%
6	**4.4**	20 mol%	LiH (5)	o-DCB	71%
7	**4.4**	10 mol%	LiHMDS (1.5)	o-DCB	21%
8	**4.3**	10 mol%	LiHMDS (1.5)	o-DCB	0%
9	**4.3**	10 mol%	LiH (5)	o-DCB	19%
10	**4.4**	10 mol%	none	o-DCB	40%
11	**none**	0 mol%	LiH (5)	o-DCB	0%



4.3

$[Li]^+[B(C_6F_5)_4]^-$

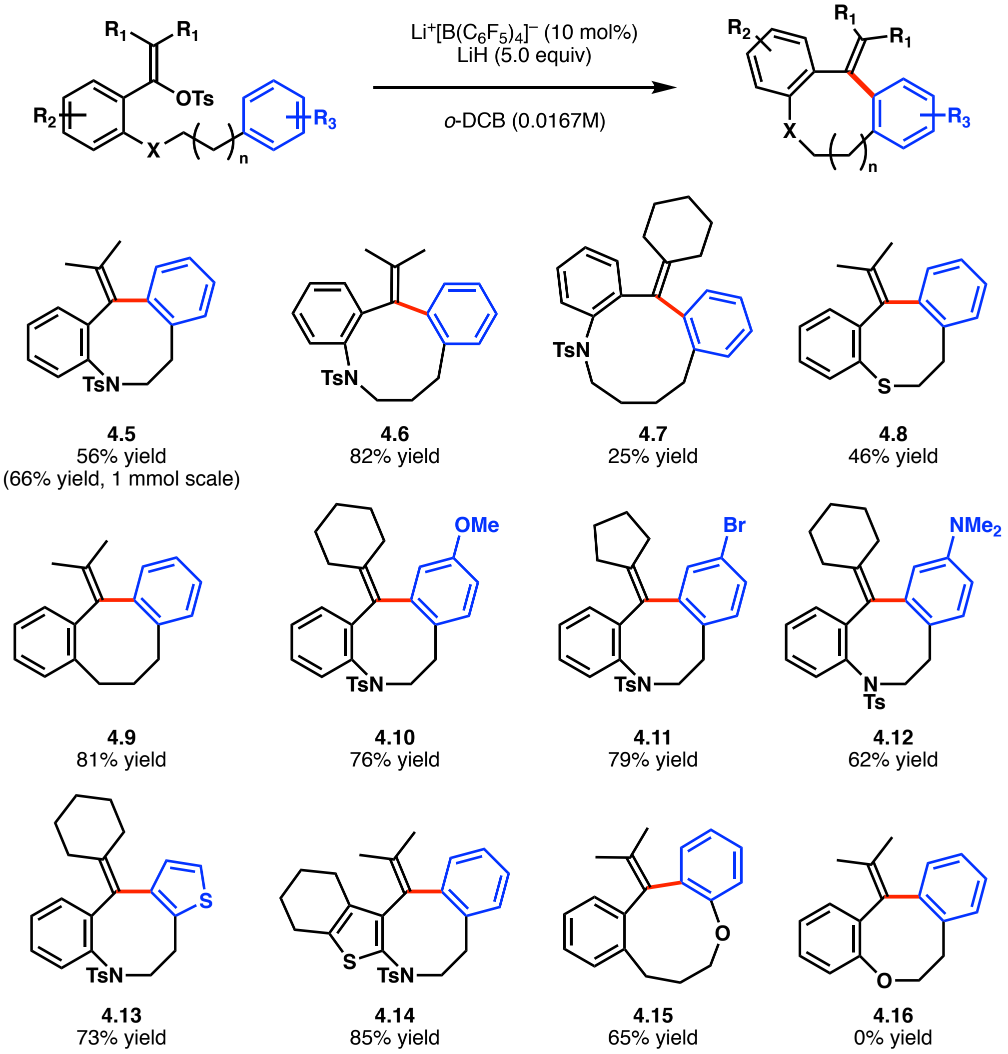
4.4

Table 4.1. *Optimization table for intramolecular Friedel-Crafts*

140 °C and obtained a 74% yield of desired product **4.2** with 1,2-DCB and a 50% yield with mesitylene (entries 1–2, Table 4.1). DMF did not give any desired product likely due to its high polarity/nucleophilicity (entry 3). 1,2-DFB also provided diminished results, likely due to limitations in reaction temperature (entry 4). Decreasing catalyst loading to 5 mol% gave a lower 49% yield (entry 5) while increased loading did not have a positive impact on the reaction (entry 6). Using LiHMDS as base gave a lower 21% yield (entry 7). Furthermore, using our previously developed urea catalyst **4.3**[7] with either LiHMDS or LiH resulted in poor yields (entries 8 and 9). Additionally, we found that the addition of base was important, as the reaction performed poorly when base was excluded giving only 40% yield of the desired product **4.2** (entry 10). Lastly, the reaction failed to make any product in the absence of catalyst (entry 11).

4.4 Scope of intramolecular Friedel-Crafts

With optimized conditions in hand for this transformation, we wanted to explore the scope of medium-sized rings that can be forged with this catalytic reaction. First, we looked at the scope of ring sizes that we could make with this reaction. Eight-membered ring formation was facile, leading to dibenzazocine **4.5** in a 56% yield (Figure 4.1). We found this reaction to be scalable, with the same conditions affording product **4.5** in a 66% yield on 1 mmol scale. Nine-membered ring formation also proceeded smoothly, furnishing dibenzazonine **4.6** in an 82% yield under identical conditions. Ten-membered ring synthesis proved more challenging, with Friedel-Crafts product **4.7** being obtained in only 25% yield. The majority of the mass balance of this reaction was unreacted starting material as well as a small amount of intramolecular C–H insertion products. Heating at higher temperatures or for longer periods of time failed to improve the yield of this product. Replacement of the protected nitrogen with a sulfur atom in the chain was well tolerated, leading to thioether **4.8** in a 46% yield. This reaction manifold can also be applied to construct carbocycles as demonstrated by the synthesis of cyclooctane **4.9** in 81% yield. Substitution on the aryl ring was also tolerated with anisole, bromobenzene and dimethylaniline derivatives forging benzazocine product **4.10**, **4.11**, and **4.12** in 62–79% yield. Furthermore, heterocycles could be used either as the nucleophile (blue) or on the parent aryl group (black) connected to the enol tosylate



4.5
56% yield
(66% yield, 1 mmol scale)

4.6
82% yield

4.7
25% yield

4.8
46% yield

4.9
81% yield

4.10
76% yield

4.11
79% yield

4.12
62% yield

4.13
73% yield

4.14
85% yield

4.15
65% yield

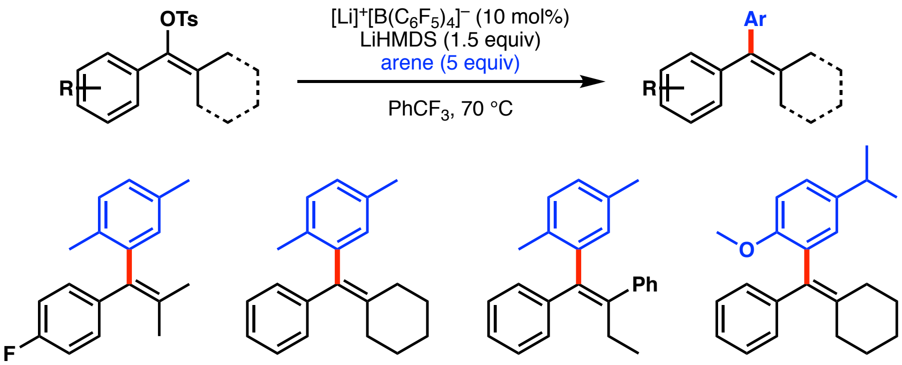
4.16
0% yield

Figure 4.1. Scope of lithium-catalyzed medium size ring synthesis

as demonstrated by the thiophene products **4.13** and **4.14** produced in 73% and 85% yields from their respective tosylate precursors. Lastly, substitution in the chain of the ring conjugated to the C–H donor arene was also tolerated giving phenylether **4.15** in 65% yield. Unfortunately, oxygen substitution was not tolerated when conjugated to the vinyl tosylate, as demonstrated by the lack of ether **4.16** formation from its tosylate precursor. This is hypothesized to be due to higher electron-donating ability of the oxygen as compared to a sulfonamide, sulfur or carbon substituent, leading to significant stabilization of the vinyl cation, making this reaction too sluggish.[17]

4.5 Intermolecular C–C Bond Forming Reactions of Vinyl Tosylates

During the course of our medium-sized ring formation studies, we have successfully demonstrated that vinyl tosylates are good vinyl cation precursors and allow for a larger scope of stable enol sulfonates to be synthesized. We wanted to explore these tosylates for a wider array of C–C bond forming reactions. First we started by looking at intermolecular Friedel-Crafts reactions using stoichiometric amounts of arene nucleophiles in trifluorotoluene solvent. These reactions generally proceeded in good yields similar to those obtained with vinyl triflate precursors.[7] Fluoro-substituted vinyl tosylate reacted with five equivalents of *p*-xylene in the presence of catalytic LiF_{20} to yield diarylalkene **4.17** in 87% yield (Figure 4.2). Unlike the intramolecular Friedel-Crafts reactions, we found LiHMDS to be more effective as the stoichiometric base instead of LiH. Under the same conditions, both cyclohexyl substituted vinyl tosylate as well as a diarylvinyl tosylate yielded styrene product **4.18** and **4.19** in 75% and 82% yields respectively. Using 4-isopropylanisole as a nucleophile led to generation of the



4.17 87% yield **4.18** 75% yield **4.19** 82% yield (*3:1 Z:E*) **4.20** 80% yield

Figure 4.2 Intermolecular Friedel-Crafts reactions of vinyl tosylates.

tetrasubstituted olefin **4.20** as a single isomer in 80% isolated yield. Notably, the vinyl triflate analogs of the three vinyl tosylates employed in this study have been previously found to be unstable, further demonstrating the complementary nature of the tosylate leaving group.

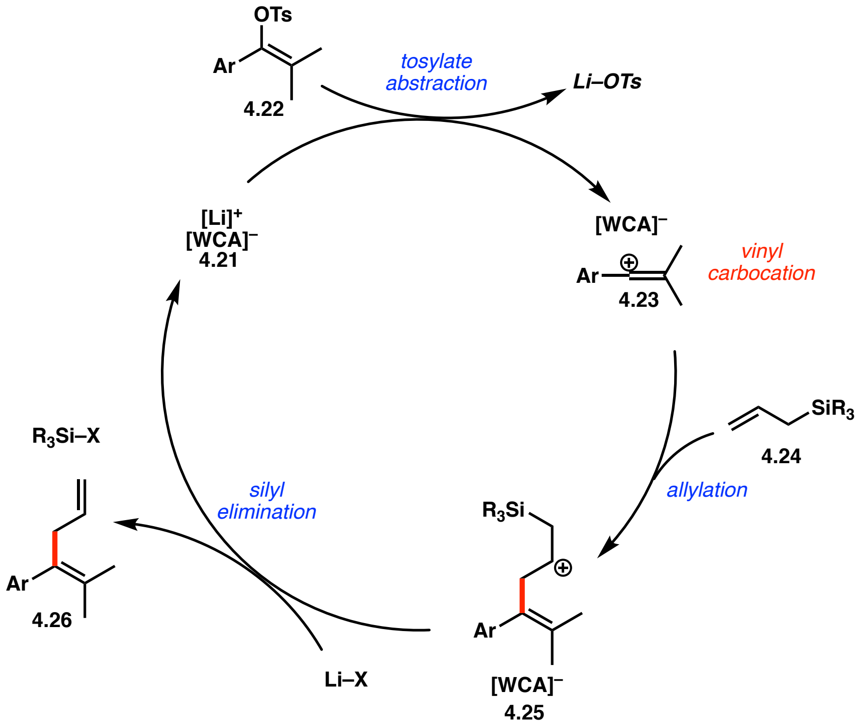


Figure 4.3 Mechanistic hypothesis for allylation of vinyl cations

Empowered by our Friedel-Crafts successes, we sought to further investigate the reactivity of these vinyl tosylates. We hypothesized that perhaps vinyl cation allylation reactions could be achieved using an allyl silane reagent analogous to a Sakurai allylation.[18–21] Our mechanistic hypothesis was that upon generation of vinyl cation **4.23** *via* ionization of vinyl tosylate **4.22** with Li-Lewis acid **4.21**, nucleophilic attack by allylsilane **4.24** would generate a β-silicon stabilized carbocation **4.25** (Figure 4.3). This species can then be attacked by a Li-salt to generate the allylated product **4.26** and concomitantly regenerate Li-WCA species **4.21** along with a silyl adduct. We were pleased to see that these reactions proceeded smoothly to forge new C–C bonds and give allylated products after some minor optimization. Reaction of arylvinyl tosylates with an excess of allyltrimethylsilane furnished allylated products **4.27–4.29** in 84%–97% yield (Figure 4.4). Using differentially substituted methallylsilanes yielded β-methallyl styrene **4.30** in 77% yield or the branched products **4.31** and **4.32** in 60% and 81% yield respectively. These efforts

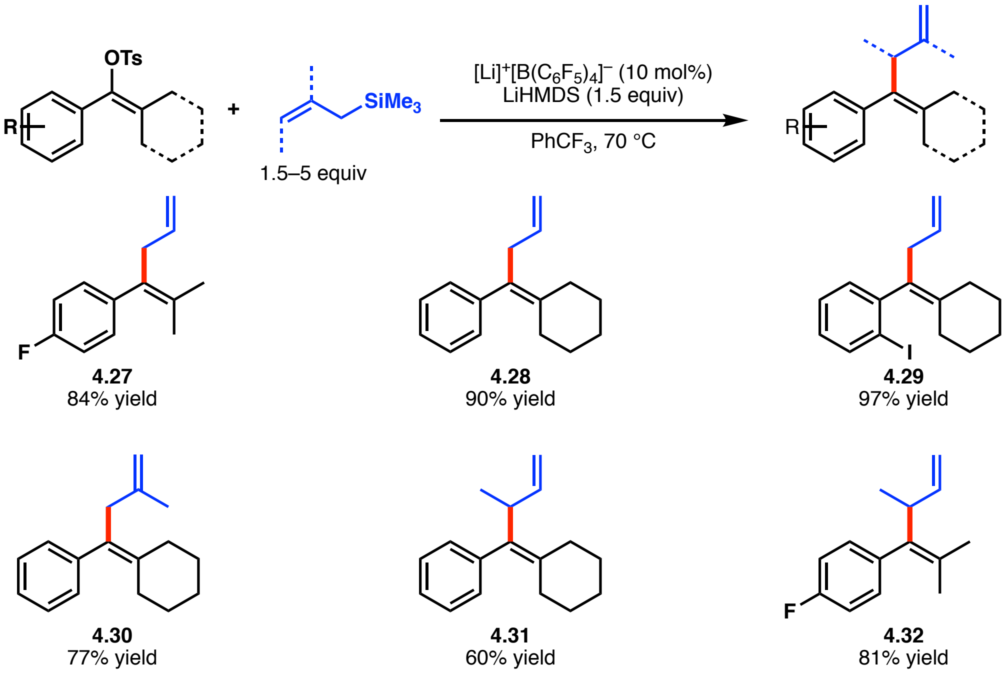
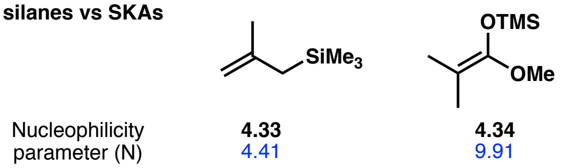


Figure 4.4 Intermolecular allylation reactions of vinyl tosylates.

present an alternative to classic transition metal-catalyzed allylations of vinyl sulfonates or vinyl halides.[22–24]

After developing the successful Sakurai-type allylation reaction, we decided to investigate if we could use other common "soft" carbon nucleophiles to trap the vinyl carbocation intermediates. Based on work by Mayr and coworkers[17], we saw that silyl ketene acetals (SKAs) have a nucleophilicity parameter even greater than that of allyl silanes (Figure 4.5a). After a brief optimization of several reaction parameters, we found that this reaction works best under base-free conditions in electron-deficient arene solvents. The proposed mechanism for this base-free reaction is believed to proceed

a Nucleophilicity of allyl silanes vs SKAs



b Proposed catalytic cycle

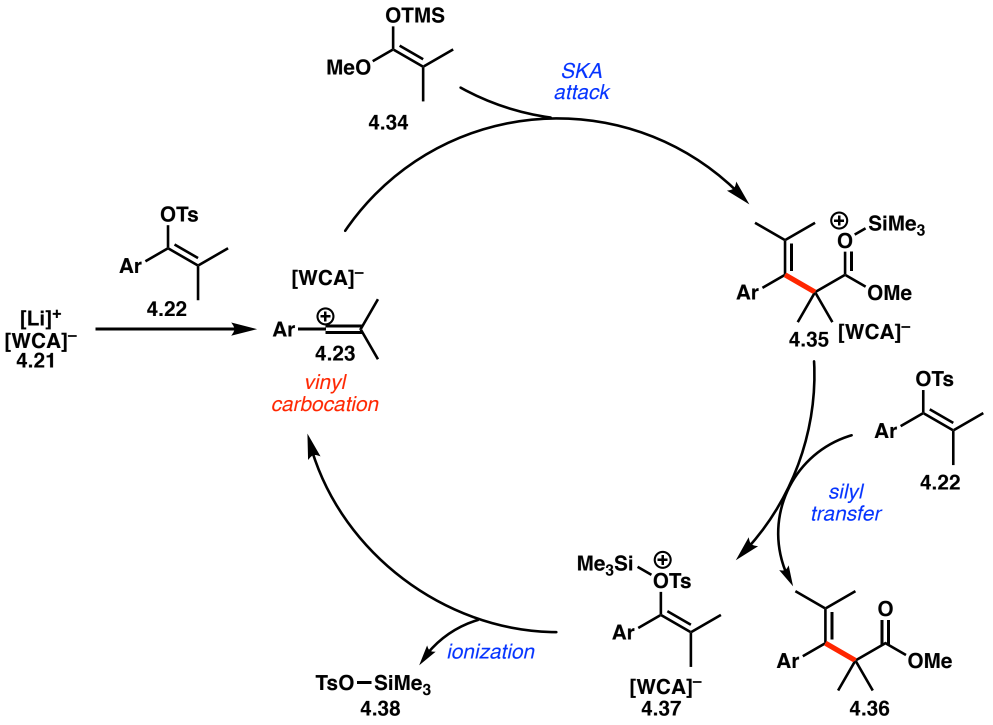


Figure 4.5 Mechanistic hypothesis for α-vinylation of silyl ketene acetals with vinyl cations

through a "silyl-transfer" type mechanism similar to a Mukaiyama-Aldol reaction (Figure 4.5b).[25,26] Here, the first ionization step is performed by the Li-WCA **4.21** to generate vinyl cation **4.23**, which can then be trapped by the SKA **4.34** to give the silyl oxocarbenium **4.35**. This adduct can transfer its silyl group to another tosylate and liberate ester product **4.36**. The ensuing silyl complex **4.37** can heterolyze to give vinyl cation **4.23**, generating an equivalent of trimethylsilyl tosylate **4.38**.

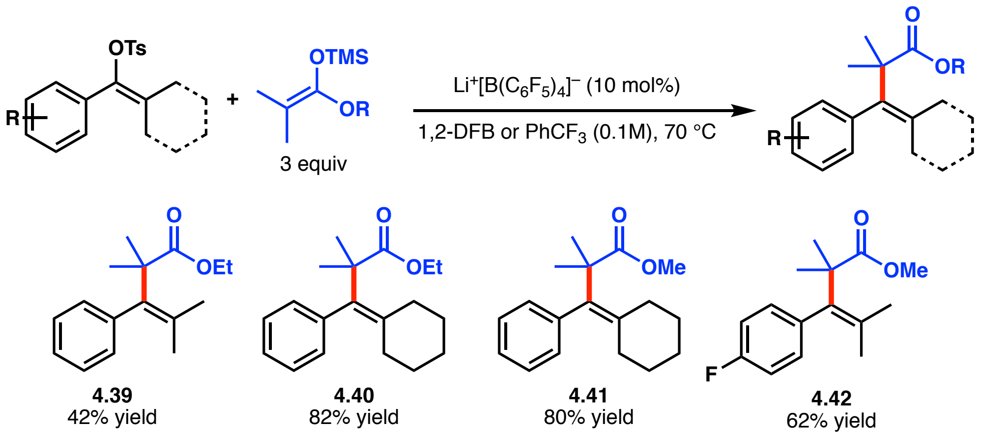


Figure 4.6 Synthesis of α-vinylated esters from SKAs attacking vinyl cations

With successful optimization efforts completed, we decided to briefly survey the scope of this reaction with different SKAs and vinyl tosylates. From our current studies, fully substituted SKAs seemed optimal for this reaction. This yielded ester products that have a quaternary carbon center with a tetrasubstiuted olefin on two adjacent carbons. Despite the sterically congested nature of these products, they were able to be synthesized with only 3 equivalents of SKA. With an ethyl ester derived SKA, the α-vinylated products **4.39** and **4.40** were obtained in 42% and 82% yields respectively (Figure 4.6). Using a methyl ester derived SKA, methyl ester products **4.41** and **4.42** were obtained in a slightly diminished 80% and 62% yields respectively. The scope of this reaction is still being explored, but these initial results are promising examples of delivering sterically encumbered and synthetically useful products under simple conditions.

4.6 C–O Bond Forming Reactions of Vinyl Tosylates

Early vinyl cation studies focused on solvolysis of vinyl triflates or other precursors in aqueous ethanol to generate ketones or vinyl ethers through trapping by solvent.[27,28] We wanted to see if catalytic C–O bond formation was possible under non-solvolytic conditions using our knowledge from working in the area of vinyl cations for several years. To this end, we attempted to mimic some of the reactions presented in this chapter by simply replacing the carbon-based nucleophile with an oxygen nucleophile. We decided to look at a model system similar to that of our intramolecular Friedel-Crafts reactions. In the event, vinyl tosylate **4.43** was synthesized and exposed to the same conditions as highlighted in section **4.4**. We were pleased to see the formation of cyclic vinyl ether **4.44** in 92% yield upon exposure of the tosylate precursor to a suspension of LiF_{20} and LiH in 1,2-DCB (Figure 4.7). Furthermore, upon synthesizing diarylvinyl tosylate **4.45** and employing conditions from section **4.5**, we saw facile formation of benzofuran **4.46** in 88% yield.[29] Both of these reactions are believed to involve the attack of the methyl ether oxygen onto the intermediate vinyl cation followed by the loss of a methyl group to the arene solvent or the lithium base. Notably, this benzofuran contained substitution both at *C2* and *C3*, which can be difficult to achieve under traditional Larock synthesis conditions.[30]

After observing intramolecular reactivity from methyl ethers attacking vinyl cations, we pondered if perhaps adding an external methyl ether would facilitate

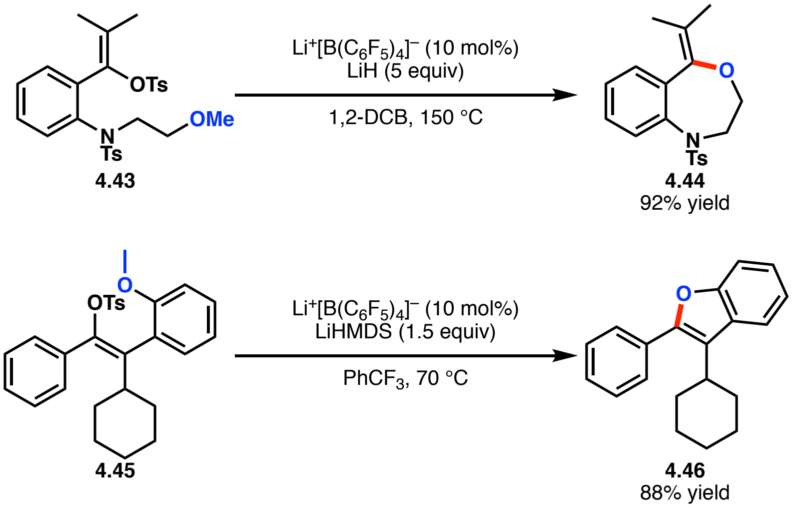


Figure 4.7 Intramolecular C–O bond formation of vinyl cations

intermolecular vinyl ether synthesis in a similar mechanistic fashion. To this end, several methyl ethers were synthesized and explored for reactions with vinyl tosylates using the previously developed conditions. In the event, we found that 1-methoxycyclohexene was a competent nucleophile delivering divinyl ether **4.47** in 77% yield (Figure 4.8). Simple dialkyl ethers such as methyloctyl ether were also competent as octylvinyl ethers **4.48** and **4.49** were synthesized in 65% and 41% yields respectively under these conditions. Notably, these reactions work in non-polar media with a stoichiometric amount of nucleophile (5 equiv); a far cry from the early solvolytic studies done by the giants of the field.

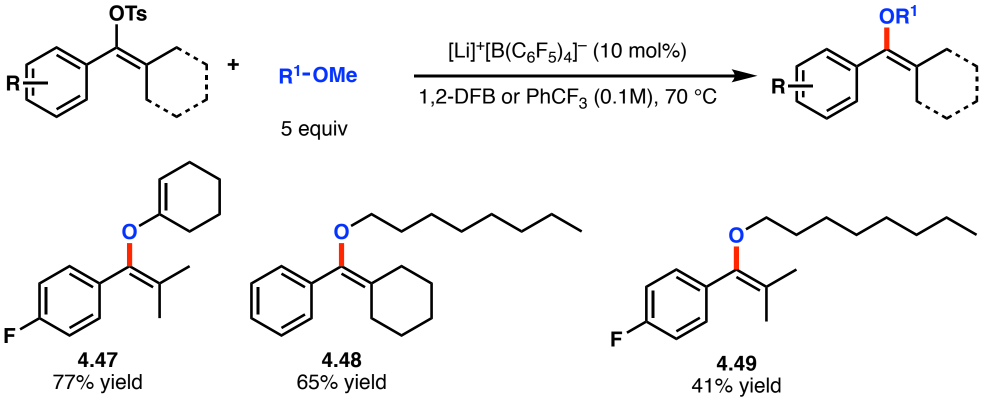


Figure 4.8 Synthesis of vinyl ethers through C–O bond forming reactions

4.7 Conclusion

In conclusion, we have discovered that vinyl tosylates are competent vinyl cation precursors under Li-WCA conditions and can generate similar vinyl cation-WCA ion pairs as seen in our previous reports. We have shown that these precursors have enhanced stability compared to their vinyl triflate/nonaflate counterparts and thus broaden the scope of the methodology. In addition to demonstrating several intermolecular Friedel-Crafts reactions analogous to those reported in chapter 3, we have developed a simple methodology to catalytically access medium-sized rings through an intramolecular Friedel-Crafts reaction. Furthermore, we have expanded the range of nucleophiles that are competent in “trapping” vinyl cations to include allyl silanes, silyl ketene acetals as well as methyl ethers, resulting in new intermolecular C–C and C–O bond forming methodologies that can deliver useful products with simple Li-WCA catalysts.

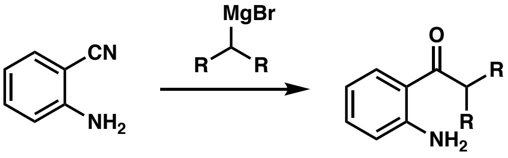
4.8 Experimental Section

4.8.1 Materials and Methods

Unless otherwise stated, all reactions were performed in a VAC glovebox under nitrogen atmosphere with ≤ 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and dried *in vacuo* before use. All liquid substrates were rigorously dried before use. Ethyl ether, tetrahydrofuran, dichloromethane, dimethylformamide, toluene, 1,2-dichloroebenzene, and hexanes were degassed and dried in a JC Meyer solvent system. Acetonitrile, triethylamine, and pyridine were distilled over calcium hydride. Solid substrates were dried over P_2O_5. $[Li]^+[B(C_6F_5)_4]^-$ salts were synthesized according to literature procedure.[31] Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. NMR spectra were recorded on a Bruker AV-300 (^{1}H, ^{13}C, ^{19}F), AV-400 (^{1}H, ^{13}C, ^{19}F), Bruker DRX-500 (^{1}H, ^{13}C), and Bruker AV-500 (^{1}H, ^{13}C). ^{1}H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^{1}H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, tt = triplet of triplet, quint = quintet, sept = septet, m = multiplet. ^{13}C NMR spectra are reported relative to $CDCl_3$ (77.0 ppm) unless noted otherwise. GC spectra were recorded on an Agilent 6850 series GC using an Agilent HP-1 (50 m, 0.32 mm ID, 0.25 μm DF) column. GCMS spectra were recorded on a Shimadzu GCMS-QP2010 using a Restek XTI-5 (50 m, 0.25 mm ID, 0.25 μm DF) column interface at room temperature. IR Spectra were record on a Perkin Elmer 100 spectrometer and are reported in terms of frequency absorption (cm^{-1}). High resolution mass spectra (HR-MS) were recorded on a Waters (Micromass) GCT Premier spectrometer, a Waters (Micromass) LCT Premier, an Agilent GC EI-MS, and are reported as follows: m/z (% relative intensity). Purification by preparative HPLC was done on an Agilent 1200 series instrument with a reverse phase Alltima C_{18} (5m, 25 cm length, 1 cm internal diameter) column.

4.8.2 Experimental Procedures

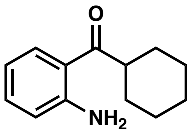
4.8.2.1 Synthesis of Vinyl Tosylates



Scheme 4.1 Representative scheme for the reaction between Grignard reagent and aryl nitrile.

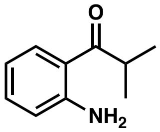
4.8.2.1.1 General Procedure for Reaction Between Grignard and Aryl Nitriles

Magnesium (3.0 equiv) was put into a flame-dried three-neck flask equipped with a condenser. THF was then added into the flask to generate a 1M solution for the following alkyl bromide. Alkyl bromide (1.0 equiv) was added slowly into the flask to keep the solution under gentle reflux. After the formation of the Grignard reagent, cooled the solution down to 0 °C and 1 M solution of 2-aminobenzonitrile (3.0 equiv) in THF was added dropwise. The reaction was run overnight. After this the reaction was quenched with water and concentrated hydrochloric acid to make the pH down to 1. Then it was extracted with ethyl ether three times. The combined organic phase was washed with saturated sodium bicarbonate solution and brine. It was dried with magnesium sulfate, filtered, and concentrated to give the crude product. The crude product was purified *via* flash column chromatography to give the product.



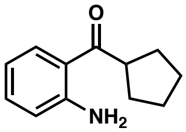
(2-aminophenyl)(cyclohexyl)methanone (4.50).

Synthesized according to general procedure **4.8.2.2** starting from 25.4 mmol of 2-aminobenzonitrile. Crude product was purified *via* flash column chromatography using 20% ethyl ether in hexanes to give the product as a yellow solid (2.51 g, 48.6% yield). Spectral data matched those reported in the literature.[32]



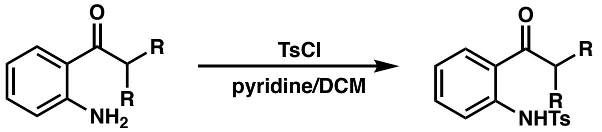
1-(2-aminophenyl)-2-methylpropan-1-one (4.51).

Synthesized according to general procedure **4.8.2.2** starting from 42.3 mmol of 2-aminobenzonitrile. Crude product was purified *via* flash column chromatography using 10% ethyl ether in hexanes to give the product as a yellow solid (5.45 g, 78.9% yield). Spectral data matched those reported in the literature.[33]



(2-aminophenyl)(cyclopentyl)methanone (4.52).

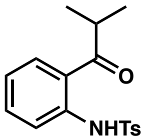
Synthesized according to general procedure **4.8.2.2** starting from 78.28 mmol of 2-aminobenzonitrile. Crude product was purified *via* flash column chromatography using 10% ethyl ether in hexanes to give the product as a white solid (13.32 g, 88.8% yield). Spectral data matched those reported in the literature.[33]



Scheme 4.2 Representative scheme for the N-tosylation of anilines

4.8.2.1.2 General Procedure for N-Tosylation of Anilines

To a flame dried roundbottom flask was added aniline (1.0 equiv) followed by DCM (13.0 equiv) and pyridine (7.0 equiv). This was cooled to 0 °C and then tosyl chloride (1.42 equiv) was added. The reaction was warmed up to room temperature and stirred for 16 hours. The reaction was diluted with additional DCM (~15 equiv) and water. The layers were separated and the aqueous later was extracted twice more with DCM. The combined organics were washed 1M aqueous HCl, water and brine in that order and the dried over magnesium sulfate, filtered and concentrated. The crude product was purified by flash column chromatography to give pure material as a white solid.



***N*-(2-isobutyrylphenyl)-4-methylbenzenesulfonamide (4.53).**

Synthesized according to general procedure 4.8.2.1.2 starting from 24.5 mmol of the corresponding aniline **4.51**. Crude product was purified *via* flash column chromatography using 30% ethyl acetate in hexanes to give sulfonamide **4.53** as a white solid (5.15 g, 66% yield). Spectral data matched those reported in the literature.[33]

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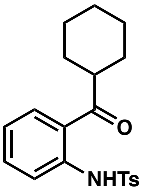
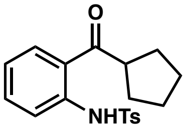


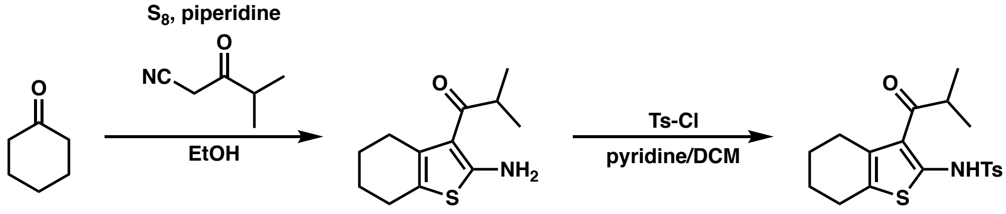
***N*-(2-(cyclohexanecarbonyl)phenyl)-4-methylbenzenesulfonamide (4.54).**

Synthesized according to general procedure 4.8.2.1.2 starting from 73.3 mmol of the corresponding aniline **4.50**. Crude product was purified *via* flash column chromatography using 20% ethyl acetate in hexanes to give sulfonamide **4.54** as a white solid (26.2 g, 80% yield). Spectral data matched those reported in the literature.[33]

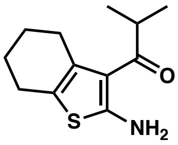


***N*-(2-(cyclopentanecarbonyl)phenyl)-4-methylbenzenesulfonamide (4.55).**

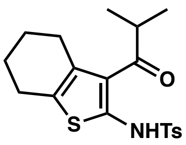
Synthesized according to general procedure 4.8.2.1.2 starting from 62.51 mmol of the corresponding aniline **4.52**. Crude product was purified *via* flash column chromatography using 20% ethyl acetate in hexanes to give sulfonamide **4.55** as a white solid (10.43 g, 48.59% yield). Spectral data matched those reported in the literature .[34]



Scheme 4.3 Gewald synthesis of thiophene ketone **4.57**



1-(2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophen-3-yl)-2-methylpropan-1-one (4.56). Cyclohexanone (1.25 g, 12.7 mmol, 1.0 equiv) was added to a 100 mL schlenk followed by α-cyano isopropyl ketone (1.70 g, 15.3 mmol, 1.2 equiv) and this was dissolved in ethanol (20 mL). To this solution was added S_8 (3.92 g, 15.3 mmol, 1.2 equiv) and piperidine (1.30 g, 15.3 mmol, 1.2 equiv). The reaction vessel was sealed and heated to 65 °C for 48 hours. Upon completion, the reaction was cooled to r.t. and poured onto ice. After the ice melted, the resultant suspension was filtered and washed with water followed by pentane. The light yellow solid (2.54 g, ca. 89%) was dried under vacuum and carried forward to the next step without further purification.

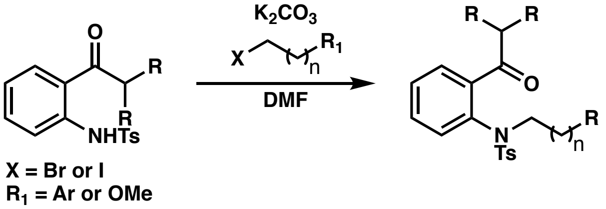


***N*-(3-isobutyryl-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-4-methylbenzenesulfonamide (4.57).**

Synthesized from the crude material (2.54 g) from the previous step according to a slightly modified general procedure 2 using 26 equiv of DCM instead of 13 equiv. The crude product was purified by flash column chromatography using 30% ether/hexanes to give roughly a 7:1 mixture of desired sulfonamide **4.57** to di-tosylated sulfonamide (2.80 g, ca. 60% yield desired). This was carried forward without additional purification. Representative ^{1}H NMR shifts of desired product shown below.

^{1}H NMR (300 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 3.12 (sept, *J* = 6.7 Hz, 1H), 2.74 – 2.59 (m, 4H), 2.38 (s, 3H), 1.82 – 1.72 (m, 4H), 0.99 (d, *J* = 6.7 Hz, 6H).

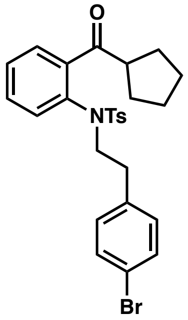
HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{19}H_{23}NO_3S_2Na$ 400.1017; Found 400.1015.



Scheme 4.4 Representative scheme for alkylation of sulfonamides

4.8.2.1.3 General Procedure for N-Alkylation of Sulfonamides.

To an oven dried 20 mL scintillation vial was added sulfonamide (1.0 equiv) followed by DMF (to yield a 1M solution). To the solution was added and potassium carbonate (2.0 equiv) and alkyl iodide (2.0 equiv) under a stream of N_2. The vial was sealed and heated to 100 °C for 24h. The reaction mixture was cooled to rt, diluted with water and ether. The layers were separated and the aqueous layer was extracted with ether (3x). The combined organics were washed with water (3x) and brine (1x) then dried over $MgSO_4$, filtered and concentrated to give crude product. The crude product was purified by flash column chromatography.



N-(4-bromophenethyl)-N-(2-(cyclopentanecarbonyl)phenyl)-4-methylbenzenesulfonamide (4.58).

Synthesized according to general procedure 4.8.2.1.3 starting from 2.91 mmol of the corresponding sulfonamide **4.55** and 5.82 mmol of 1-bromo-4-(2-bromoethyl)benzene. Crude product was purified via flash column chromatography using 40% ether in hexanes to give sulfonamide **4.58** as a white powder (1.06g, 69% yield).

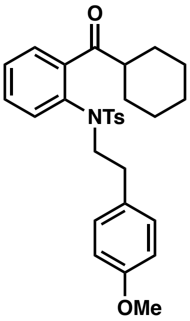
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) δ 7.59 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 6.4 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 2H), 6.84 (d, *J* = 7.9 Hz, 1H), 3.77 (br s, 2H), 3.63 (quint, *J* = 8.0 Hz, 1H), 2.86 (br s, 2H), 2.42 (s, 3H), 1.93 (br s, 4H), 1.76 (m, 2H), 1.62 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) δ 206.2, 143.3, 142.3, 137.4, 136.7, 136.1, 131.4, 130.4, 130.2, 129.2, 129.0, 128.7, 127.9, 127.8, 120.2, 53.1, 50.3, 34.3, 30.3, 26.1, 21.2.

FTIR (Neat film NaCl): 3064, 3028, 2952, 2867, 1690, 1595, 1488, 1440, 1348, 1159, 572

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{27}H_{28}BrNO_3SNa$ 548.0871; Found 548.0877.



N-(2-(cyclohexanecarbonyl)phenyl)-N-(4-methoxyphenethyl)-4-methylbenzenesulfonamide (4.59).

Synthesized according to general procedure 4.8.2.1.3 starting from 2.86 mmol of the corresponding sulfonamide **4.54** and 5.72 mmol of 1-(2-iodoethyl)-4-methoxybenzene. Crude product was purified via flash column chromatography using 40% ether in hexanes to give sulfonamide **4.59** as a white powder (1.22 g, 86.7% yield).

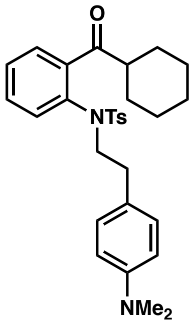
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) δ 7.54 (m, 3H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 6.99 (d, *J* = 7.4 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.78 (d, *J* = 6.9 Hz, 2H), 3.76 (s, 3H), 3.75 (br s, 2H), 3.36 (m, 1H), 2.81 (br s, 2H), 2.41 (s, 3H), 2.01 (br s, 2H), 1.83 (m, 2H), 1.69 (m, 1H), 1.36 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) δ 206.6, 158.4, 143.4, 141.9, 136.9, 136.0, 130.3, 129.4, 129.2, 129.1, 128.3, 127.9, 127.8, 114.1, 55.1, 53.6, 49.2, 33.9, 29.0, 25.9, 25.7, 21.2.

FTIR (Neat film NaCl): 3032, 2930, 2853, 1691, 1513, 1350, 1248, 1162, 578

HR-MS (ESI-MS) m/z: [M+H]+ Calc'd for $C_{29}H_{34}NO_4S$ 492.2209; Found 492.2229.



N-(2-(cyclohexanecarbonyl)phenyl)-N-(4-(dimethylamino)phenethyl)-4-methylbenzene sulfonamide (4.60).

Synthesized according to general procedure 4.8.2.1.3 starting from 2.41 mmol of the corresponding sulfonamide **4.54** and 4.82 mmol of 4-(2-bromoethyl)-N,N-dimethylaniline. Crude product was purified via flash column chromatography using 20% ethyl acetate in hexanes to give sulfonamide **4.60** as a white powder (0.50 g, 41% yield).

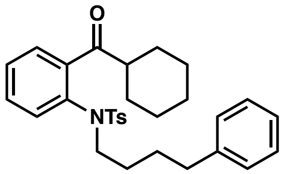
*NMR had poor resolution at room temperature, so NMRs are reported below at 60 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 60 °C) δ 7.56 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.36 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.32 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 2H), 3.73 (br s, 2H), 3.40 (tt, *J* = 11.2, 3.4 Hz, 1H), 2.90 (s, 6H), 2.77 (m, 2H), 2.41 (s, 3H), 2.01 (br s, 2H), 1.83 (d, *J* = 12.6 Hz, 2H), 1.70 (d, *J* = 12.5 Hz, 1H), 1.46 (br s, 2H), 1.37 (m, 2H), 1.28 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.4, 149.4, 143.7, 141.9, 136.8, 134.7, 130.7, 129.7, 129.4, 129.4, 128.5, 128.1, 128.1, 127.1, 113.0, 53.4, 49.2, 40.8, 33.8, 29.7, 28.6, 26.0, 21.6.

FTIR (Neat film NaCl): 2925, 2854, 1691, 1522, 1350, 1163, 1033, 577

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{30}H_{36}N_2O_3SNa$ 527.2344; Found 527.2333.



N-(2-(cyclohexanecarbonyl)phenyl)-4-methyl-N-(4-phenylbutyl)benzenesulfonamide (4.61).

Synthesized according to general procedure 4.8.2.1.3 starting from 3.00 mmol of the corresponding sulfonamide **4.54** and 6.00 mmol of (4-iodobutyl)benzene. Crude product was purified via flash column chromatography using 40% ethyl ether in hexanes to give sulfonamide **4.54** as a white powder (1.16 g, 79.0% yield).

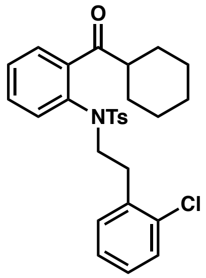
*NMR had poor resolution at room temperature, so ^{13}C NMR is reported below at 50 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, J = 7.6 Hz, 1H), 7.46 (ddd, J = 8.3, 1.8, 1.8 Hz, 2H), 7.35 (ddd, J = 7.4, 7.4, 1.3 Hz, 1H), 7.28 (ddd, J = 7.8, 7.8, 1,8 Hz, 1H), 7.23 (m, 3H), 7.16 (m, 2H), 7.09 (d, J = 6.8 Hz, 2H), 6.68 (dd, J = 7.9, 1.3 Hz, 1H), 3.67 (br s, 1H), 3.36 (tt, J = 11.4, 3.4 Hz, 1H), 3.33 (m, 1H), 2.55 (t, J = 7.4 Hz, 2H), 2.42 (s, 3H), 2.07 (br s, 1H), 1.83-1.18 (m, 13H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.1, 145.5, 143.5, 142.0, 141.8, 136.9, 135.7, 130.4, 129.4, 129.3, 128.3, 128.1, 128.0, 127.9, 125.7, 51.8, 49.2, 35.3, 29.1, 28.5, 27.7, 26.0, 25.8, 21.4.

FTIR (Neat film NaCl): 3062, 3026, 2929, 2855, 1689, 1596, 1495, 1450, 1350, 1162, 700, 661, 577, 545.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{30}H_{35}NO_3SNa$ 512.2235; Found 512.2233.



N-(2-chlorophenethyl)-N-(2-(cyclohexanecarbonyl)phenyl)-4-methylbenzenesulfonamide (4.62).

Synthesized according to general procedure 4.8.2.1.3 starting from 1.50 mmol of the corresponding sulfonamide **4.54** and 6.00 mmol of 1-(2-bromoethyl)-2-chlorobenzene. Crude product was purified via flash column chromatography using 25% ethyl ether in hexanes to give sulfonamide **4.62** as a white powder (0.50 g, 67% yield).

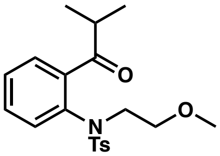
*NMR had poor resolution at room temperature, so ^{13}C NMR is reported below at 50 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.39 (ddd, *J* = 7.5, 7.5, 1.3 Hz, 1H), 7.33 (ddd, *J* = 7.8, 7.8, 1.8 Hz, 1H), 7.29 (m, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.17 (m, 3H), 6.78 (dd, *J* = 7.9, 1.2 Hz, 1H), 3.95 (m, 1H), 3.49 (m, 1H), 3.42 (tt, *J* = 10.8, 3.4 Hz, 1H), 3.10 (m, 1H), 2.94 (m, 1H), 2.41 (s, 3H), 2.11 (m, 1H), 1.94-1.56 (m, 5H), 1.46-1.22 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.8, 143.6, 141.8, 136.8, 136.0, 135.5, 134.2, 131.0, 130.6, 129.5, 129.4, 129.3, 128.2, 128.1, 128.0, 127.0, 51.3, 49.3, 32.8, 29.2, 26.0, 25.9, 21.4.

FTIR (Neat film NaCl): 3065, 2928, 2853, 1690, 1596, 1444, 1351, 1159, 1092, 580

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{28}H_{30}ClNO_3SNa$ 518.1533; Found 518.1528.



N-(2-isobutyrylphenyl)-N-(2-methoxyethyl)-4-methylbenzenesulfonamide (4.63).

Synthesized according to general procedure 4.8.2.1.3 starting from 7.88 mmol of the corresponding sulfonamide **4.53** and 11.8 mmol of 1-iodo-2-methoxyethane. Crude product was purified *via* flash column chromatography using 40% ether in hexanes to give sulfonamide **4.63** as a yellow oil (2.40 g, 81% yield).

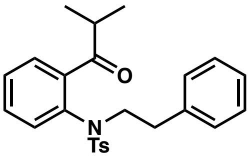
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) δ 7.48 (d, *J* = 7.6 Hz, 1H), 7.42 (br s, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.72 (s, 1H), 3.72 (br s, 2H), 3.57 (sept, *J* = 6.9 Hz, 1H), 3.42 (s, 2H), 3.10 (s, 3H), 2.32 (s, 3H), 1.14 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) δ 207.0, 143.3, 141.2, 136.9, 135.6, 130.4, 129.0, 128.9, 128.6, 127.8, 127.1, 69.7, 57.9, 51.1, 38.6, 18.7.

FTIR (Neat film NaCl): 3067, 2972, 2930, 2873, 1692, 1596, 1445, 1349, 1164, 1117, 981, 657, 577.

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{20}H_{26}NO_4S$ 376.1583; Found 376.1581.



N-(2-isobutyrylphenyl)-4-methyl-N-phenethylbenzenesulfonamide (4.64).

Synthesized according to general procedure 4.8.2.1.3 starting from 6.30 mmol of the corresponding sulfonamide **4.53** and 9.45 mmol of (2-iodoethyl)benzene. Crude product was purified *via* flash column chromatography using 30% ether in hexanes to give sulfonamide **4.64** as a white solid (1.70 g, 64% yield).

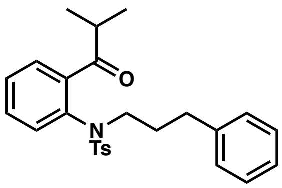
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 7.3 Hz, 4H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 2H), 6.85 (d, *J* = 7.7 Hz, 1H), 3.82 (s, 2H), 3.58 (sept, *J* = 6.9 Hz, 1H), 2.90 (s, 2H), 2.40 (s, 3H), 1.24 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) δ 207.2, 143.6, 141.6, 138.2, 137.0, 135.7, 130.6, 129.3, 129.2, 128.5, 128.4, 128.0, 127.9, 126.4, 53.3, 39.2, 34.8, 31.4, 18.8.

FTIR (Neat film NaCl): 2924, 1693, 1596, 1455, 1349, 1163, 1093, 1056, 1033, 1017, 815, 688, 579.

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{25}H_{28}NO_3S$ 422.1790; Found 422.1790.



***N*-(2-isobutyrylphenyl)-4-methyl-*N*-(3-phenylpropyl)benzenesulfonamide (4.65).**

Synthesized according to general procedure 4.8.2.1.3 starting from 6.30 mmol of the corresponding sulfonamide **4.53** and 9.45 mmol of (3-iodopropyl)benzene. Crude product was purified *via* flash column chromatography using 30% ether in hexanes to give sulfonamide **4.65** as a white solid (2.60 g, 95% yield).

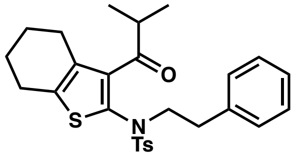
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) δ 7.55 (d, *J* = 7.5 Hz, 1H), 7.49 (s, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 4H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.09 (d, J = 7.3 Hz, 2H), 6.79 (s, 1H), 3.64 – 3.55 (m, 3H), 2.59 (t, J = 7.5 Hz, 2H), 2.41 (s, 3H), 1.98 – 1.85 (m, 2H), 1.24 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) δ 207.4, 143.5, 141.7, 141.0, 137.2, 135.8, 130.5, 129.3, 129.2, 128.3, 128.2, 128.0, 127.9, 125.9, 51.6, 39.3, 33.1, 29.5, 21.3, 18.8.

FTIR (Neat film NaCl): 3063, 3027, 2971, 2932, 2871, 1694, 1596, 1348, 1161, 980, 700, 658, 576.

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{26}H_{30}NO_3S$ 436.1946; Found 436.1946.



***N*-(3-isobutyryl-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-4-methyl-*N*-phenethylbenzenesulfonamide (4.66).**

Synthesized according to general procedure 4.8.2.1.3 starting from 7.42 mmol of the corresponding sulfonamide **4.57** (7:1 mixture) and 11.1 mmol of (2-iodoethyl)benzene. Crude product was purified *via* flash column chromatography using 20% ether in hexanes and then recrystallization from boiling DCM/hexanes (1:1) to give sulfonamide **4.66** as yellow crystalline solid (1.35 g, 38% yield).

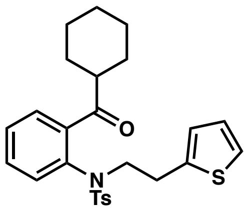
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) δ 7.55 (d, J = 8.3 Hz, 2H), 7.30 – 7.21 (m, 5H), 7.20 – 7.15 (d, J = 8.3 Hz, 2H), 4.15 – 3.21 (br s, 2H), 3.55 (quint, J = 6.9 Hz, 1H), 2.92 (t, J = 8.5 Hz, 2H), 2.71 – 2.51 (br s, 2H), 2.64 (t, J = 6.1 Hz, 2H), 2.42 (s, 3H), 1.94 – 1.68 (m, 4H), 1.13 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) δ 204.4, 144.3, 140.0, 137.9, 137.5, 134.4 (d, *J* = 2.9 Hz), 133.1, 129.5, 128.7, 128.6, 128.4, 126.7, 54.6, 39.4, 34.9, 25.2, 25.1, 22.9, 22.4, 21.6.

FTIR (Neat film NaCl): 3206, 3029, 2931, 2868, 1685, 1597, 1560, 1454, 1356, 1167, 1091, 1059, 662, 575.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{27}H_{31}NO_3S_2Na$ 504.1643; Found 504.1660.



N-(2-(cyclohexanecarbonyl)phenyl)-4-methyl-N-(2-(thiophen-2-yl)ethyl)benzenesulfonamide (4.67).

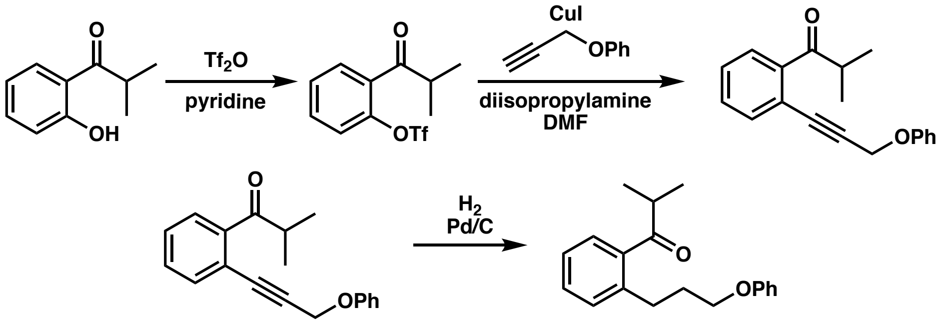
Synthesized according to general procedure 4.8.2.1.3 starting from 4.20 mmol of the corresponding sulfonamide **4.54** and 6.30 mmol of 2-(2-iodoethyl)thiophene. Crude product was purified *via* flash column chromatography using 15% ether in hexanes to give sulfonamide **4.67** as a white solid (0.80 g, 40% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.59 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.39 (td, *J* = 7.5, 1.2 Hz, 1H), 7.34 (td, *J* = 7.7, 1.7 Hz, 1H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.10 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.88 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.76 – 6.73 (m, 2H), 4.04 (br s, 1H), 3.60 (br s, 1H), 3.35 (tt, *J* = 11.4, 3.4 Hz 1H), 3.25 (br s, 1H), 3.00 (br s, 1H), 2.41 (s, 3H), 2.10 (br s, 1H), 1.92 (br s, 1H), 1.87 – 1.77 (m, 2H), 1.69 (d, *J* = 12.5 Hz, 1H), 1.63 – 1.53 (m, 1H), 1.41 – 1.18 (m, 4H).

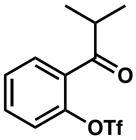
^{13}C NMR (151 MHz, CDCl$_3$) δ 206.8, 143.7, 141.4, 140.0, 136.5, 134.6, 130.8, 129.4, 129.3, 128.2, 127.8, 127.7, 126.8, 125.2, 123.7, 53.1, 49.0, 28.8, 25.8, 21.4.

FTIR (Neat film NaCl): 3068, 2929, 1854, 1690, 1596, 1444, 1350, 1162, 1092, 907, 728.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{26}H_{29}NO_3S_2Na$ 490.1487; Found 490.1496.

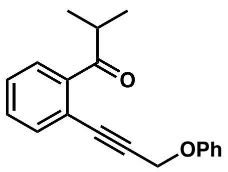


Scheme 4.5 Scheme for synthesis of ketone **4.70**



2-isobutyrylphenyl trifluoromethanesulfonate (4.68).

1-(2-Hydroxyphenyl)-2-methylpropan-1-one (9.60 g, 58.5 mmol, 1.0 equiv) was dissolved in pyridine (58.0 mL, 720 mmol, 12.0 equiv) and cooled to 0 °C. Triflic anhydride (19.8 g, 70.2 mmol, 1.2 equiv) was added dropwise. The reaction was warmed up to rt and stirred for 12h. Ethyl acetate (150 mL) was added to the reaction it was washed with aqueous $CuSO_4$ (50 mL x 4) and brine (100 mL x 1). The organic layer was dried over $MgSO_4$, filtered and concentrated to give crude aryl triflate. Crude material was purified by silica flash column chromatography using 5% ethyl acetate in hexanes to give pure aryl triflate as yellow oil **4.68** (12.9 g, 75% yield). Spectral data match those reported in the literature.[36]



2-methyl-1-(2-(3-phenoxyprop-1-yn-1-yl)phenyl)propan-1-one (4.69).

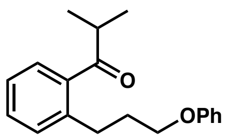
Copper iodide (6.43 mg, 0.034 mmol, 0.01 equiv) and palladium tetrakis (39.0 mg, 0.034 mmol, 0.01 equiv) were added to a schlenk flask and vacuum/backfilled three times. This was dissolved in DMF (12 mL) and added diisopropylamine (1.02 g, 10.1 mmol, 3 equiv) aryl triflate **4.68** (1.00 g, 3.38 mmol, 1.0 equiv) and (prop-2-yn-1-yloxy)benzene (1.34 g, 10.1 mmol, 3.0 equiv). The resulting solution was heated to 80 °C for 16 hours. The reaction was cooled to r.t and diluted with 30 mL of H_2O. This was then extracted with diethyl ether (3 x 40 mL). The combined organics were washed with 1M aqueous HCl (50 mL), water (50 mL) and brine (50 mL). Afterwards, the organic layer was dried over $MgSO_4$, filtered and concentrated to give crude alkyne. This was purified by silica flash column chromatography using 3% ether in hexanes to give desired product **4.69** as an orange oil (540 mg, 58% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 2H), 7.42 – 7.35 (m, 2H), 7.34 – 7.30 (m, 2H), 7.01 (ddd, *J* = 9.1, 7.0, 0.9 Hz, 3H), 4.94 (s, 2H), 3.53 (sept, *J* = 6.9 Hz, 1H), 1.09 (d, *J* = 6.9, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.0, 157.6, 141.9, 133.8, 130.3, 129.5, 128.6, 127.7, 121.5, 119.9, 114.9, 88.7, 85.4, 56.4, 38.9, 18.4.

FTIR (Neat film NaCl): 3063, 2971, 2932, 2871, 1691, 1598, 1589, 1494, 1211, 1033, 752, 590.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{19}H_{18}O_2$ 278.1307; Found 278.1307.



2-methyl-1-(2-(3-phenoxypropyl)phenyl)propan-1-one (4.70).

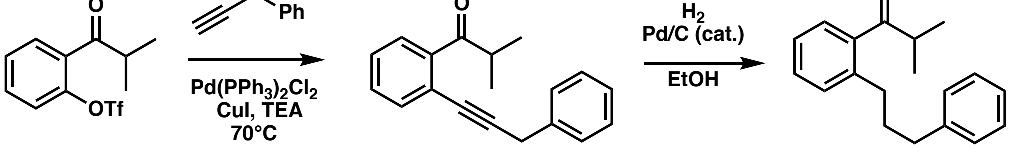
To a 25 mL roundbottom flask was added 10% Pd/C (70.4 mg, 0.066 mmol, 0.034 equiv) and suspended in 8 mL of ethanol. To this was added alkyne **4.69** (540 mg, 1.94 mmol, 1.0 equiv) and the reaction was sparged with hydrogen gas for 10 minutes. After the sparging, a new hydrogen balloon was attached and reaction stirred for 18 hours. At this point, the reaction was filtered through celite and concentrated. The crude material was purified by a short silica plug with 5% ether in hexanes to give pure ketone **4.70** as a light yellow oil (230 mg, 1.94 mmol, 42% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.53 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.38 (td, *J* = 7.5, 1.3 Hz, 1H), 7.33 – 7.19 (m, 4H), 6.94 (td, *J* = 7.3, 1.1 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.00 (t, *J* = 6.2 Hz, 2H), 3.36 (sept, *J* = 6.9 Hz, 1H), 2.96 – 2.79 (m, 2H), 2.26 – 1.97 (m, 2H), 1.18 (d, *J* = 6.9 Hz, 6H).

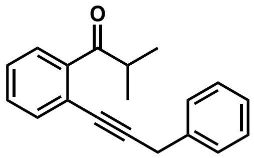
^{13}C NMR (151 MHz, CDCl$_3$) δ 209.3, 158.9, 141.1, 138.6, 130.9, 130.7, 129.4, 127.6, 125.8, 120.5, 114.5, 67.0, 38.9, 31.3, 30.2, 18.7.

FTIR (Neat film NaCl): 3067, 2930, 2869, 1686, 1599, 1497, 1469, 1243, 1037, 976, 751, 591.

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{19}H_{23}O_2$ 283.1698; Found 283.1700.



Scheme 4.6 Scheme for synthesis of ketone **4.72**



2-methyl-1-(2-(3-phenylprop-1-yn-1-yl)phenyl)propan-1-one (4.71).

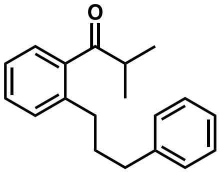
Ph(PPh$_3$)$_2$Cl$_2$ (237 mg, 0.337 mmol) and CuI (64.2 mg, 0.337 mmol) were added into a flame-dried Schlenk flask. Triethylamine (46 mL) and aryl triflate **4.68** (2.00 g, 6.74 mmol) were then added under nitrogen atmosphere. And at last prop-2-yn-1-ylbenzene (2.52 mL, 20.2 mmol) was added and the reaction was heated at 70 °C overnight. The reaction was cooled down to room temperature and quenched with saturated ammonium chloride solution. The mixture was extracted with ethyl acetate three times, and the combined organic phase was washed with water two times and brine. It was dried with magnesium sulfate, filtered and concentrated to give the crude product. The crude product was purified via flash column chromatography using 10% ethyl ether in hexanes to give the product **4.71** as an oil (0.62 g, 35% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.46 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.37 (m, 6H), 7.26 (tt, *J* = 7.8, 1.6 Hz, 1H), 3.85 (s, 2H), 3.62 (sept, *J* = 6.9 Hz, 1H), 1.12 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 208.9, 142.2, 136.3, 133.5, 130.2, 128.6, 128.0, 127.8, 127.6, 126.8, 121.2, 92.7, 81.0, 39.1, 26.0, 18.5.

FTIR (Neat film NaCl): 3386, 3063, 3030, 2972, 2932, 2873, 2199, 1768, 1690, 1593, 1454, 1214, 980, 757, 698.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{19}H_{18}ONa$ 285.1255; Found 285.1243.



2-methyl-1-(2-(3-phenylpropyl)phenyl)propan-1-one (4.72).

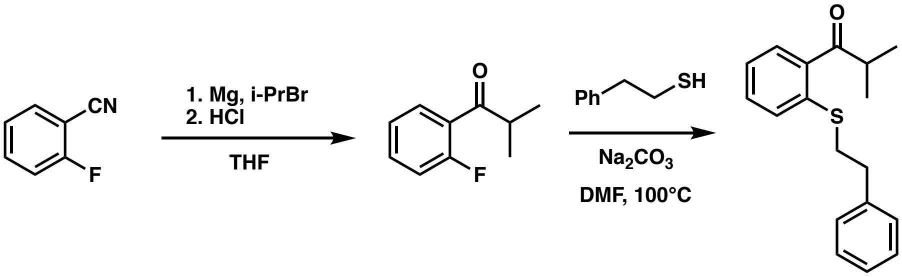
Alkyne **4.71** (0.750 g, 2.86 mmol) was dissolved in ethanol (50 mL). Pd/C (0.103 g, 0.0972 mmol, 10% Pd) was then added. Hydrogen gas was blown into the solution for a while and the reaction was run under hydrogen atmosphere (1 atm) overnight. The reaction solution was filtered through celite and concentrated to give the crude product. The crude product was purified by flash chromatography with 4% ether in hexanes to give the product **4.72** (0.63 g, 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.8 Hz, 1H), 7.36 (t, *J* = 7.0 Hz, 1H), 7.31-7.21 (m, 4H), 7.21-7.14 (m, 3H), 3.30 (sept, *J* = 6.9 Hz, 1H), 2.76 (m, 2H), 2.68 (t, *J* = 7.8 Hz, 2H), 1.93 (m, 2H), 1.16 (d, *J* = 6.9 Hz, 6H).

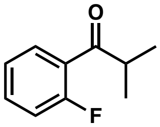
^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6, 142.3, 141.7, 138.8, 130.7, 130.5, 128.5, 128.3, 127.4, 125.8, 125.7, 39.1, 35.9, 33.5, 33.4, 18.7.

FTIR (Neat film NaCl): 3062, 3026, 2969, 2931, 2869, 1686, 1454, 1221, 976, 745, 633.

HR-MS (ESI-MS) m/z: [M+H]+ Calc'd for $C_{19}H_{23}O$ 267.1749; Found 267.1750.

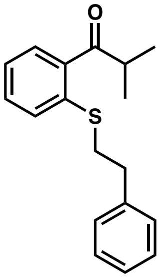


Scheme 4.7 Scheme for synthesis of ketone **4.74**



1-(2-fluorophenyl)-2-methylpropan-1-one (4.73).

Magnesium (0.602 g, 24.8 mmol) was put into a flame-dried three-neck flask equipped with a condenser. THF (24 mL) was then added into the flask. 2-bromopropane (2.33 mL, 24.8 mmol) was added slowly into the flask to keep the solution under gentle reflux. After the formation of the Grignard reagent, cooled the solution down to 0 °C and 2-fluorobenzonitrile (2.21 g, 20.6 mmol) in THF (20 mL) was added dropwise. The reaction was run overnight. After this the reaction was quenched with water and concentrated hydrochloric acid to make the pH down to 1. Then it was extracted with ethyl ether three times. The combined organic phase was washed with saturated sodium bicarbonate solution and brine. It was dried with magnesium sulfate, filtered, and concentrated to give the crude product. The crude product was purified via flash column chromatography using 2% ethyl acetate in hexanes to give the product **4.73** as an oil (1.35 g, 39.3% yield). Spectral data matched those reported in the literature.[36]



2-methyl-1-(2-(phenethylthio)phenyl)propan-1-one (4.74).

2-phenylethane-1-thiol (1.91 mL, 14.2 mmol), aryl fluoride **4.73** (1.18 g, 7.10 mmol), sodium carbonate (3.01 g, 28.4 mmol) and DMF (7 mL) was added to a flask. The solution was heated at 100 °C overnight. After this, ethyl acetate and water was added into the solution. After the separation, the organic phase was washed with water three times and then washed with brine. The organic phase was dried with sodium sulfate and concentrated to give the crude product. The crude product was purified with flash column chromatography with 2% ethyl acetate in hexanes to give the product **4.74** as a pale-yellow oil (0.53 g, 26% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.7 Hz, 1H), 7.41 (m, 2H), 7.30 (m, 2H), 7.22 (m, 4H), 3.44 (sept, *J* = 6.8 Hz, 1H), 3.15 (m, 2H), 2.94 (m, 2H), 1.20 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.3, 140.3, 138.3, 137.9, 131.2, 128.9, 128.6, 128.5, 128.1, 126.5, 124.8, 38.2, 35.0, 34.9, 18.8.

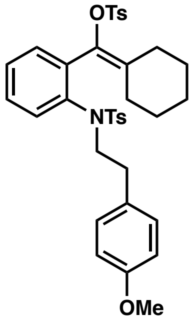
FTIR (Neat film NaCl): 3061, 3027, 2969, 2930, 2870, 1691, 1585, 1454, 1431, 1214, 1075, 974, 738, 697.

HR-MS (CI-MS) m/z: [M+H]+ Calc’d for $C_{18}H_{21}OS$ 285.1313; Found 285.1323.

4.8.2.1.4 General Procedure for Tosylation of Ketones

A: The corresponding ketone (1 equiv) was dissolved in THF (0.33 M solution) and cooled to 0 °C. To this was added a solution of potassium *tert*-butoxide (1.5 equiv) in THF (1.0 M solution). This was stirred 1.5 hours and then tosic anhydride (1.5 equiv) was added and the reaction was warmed up to rt. After 4 hours, the reaction mixture (generally a thick slurry) was diluted with ethyl acetate. This was washed with water (x1) and brine (x1) then dried over $MgSO_4$, filtered and concentrated to give crude vinyl tosylate. This was purified by flash column chromatography to give pure vinyl tosylate.

B: Followed established literature procedure.[37] Inside a glovebox, LiHMDS (2.0 equiv) was dissolved in dry toluene (0.9 M) inside a roundbottomflask which was then removed from the glovebox. To this was added distilled *N,N*-dimethylethylamine (DMEA, 2.0 equiv) and a 1M solution of ketone (1.0 equiv) in dry toluene. After stirring for 20 minutes, a 0.4 M solution of tosic anhydride (2.0 equiv) in DCM was added and this was stirred for one hour at room temperature. The reaction was then diluted with diethyl ether and 0.25 M aqueous NaOH. The layers were separated and the aqueous was extracted with diethyl ether (x3). The combined organics were washed with brine, dried over $MgSO_4$, filtered and conc to give crude vinyl tosylate. This was purified by flash column chromatography to give pure vinyl tosylate.



cyclohexylidene(2-((*N*-(4-methoxyphenethyl)-4-methylphenyl)sulfonamido)phenyl)methyl 4-methylbenzenesulfonate (4.75).

Synthesized according to general procedure 4.8.2.1.4B starting from 1.18 mmol of the corresponding ketone **4.59**. Crude product was purified via flash column chromatography using 40% ether in hexanes to give vinyl tosylate **4.75** as a white solid (0.43 g, 56% yield).

*NMR had poor resolution at room temperature, so NMRs are reported below at 50 °C.

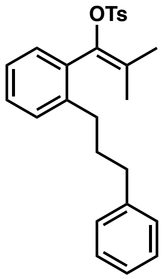
^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.67 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.43 (br s, 1H), 7.31 (m, 2H), 7.26 (d, *J* = 6.6 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.96 (br s, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 3.76 (s, 3H), 3.59 (ddd, *J* =

13.2, 5.5, 5.5 Hz, 1H), 3.38 (ddd, *J* = 12.2, 5.0, 5.0 Hz, 1H), 2.66 (ddd, *J* = 12.8, 5.4, 5.4 Hz, 1H), 2.44 (m, 2H), 2.43 (s, 3H), 2.31 (s, 3H), 2.29 (m, 1H), 2.12 (m, 1H), 2.03 (m, 1H), 1.67 (m, 2H), 1.54 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$, 50 °C) δ 158.1, 144.2, 143.2, 139.2, 136.6, 136.5, 135.5, 134.4, 133.5, 130.5, 129.4, 129.3, 129.2, 129.1, 128.1, 127.9, 127.6, 113.8, 55.1, 53.0, 33.5, 30.4, 28.5, 26.8, 26.6, 26.1, 21.3, 21.2.

FTIR (Neat film NaCl): 3029, 2971, 2928, 2855, 1611, 1597, 1512, 1364, 1175, 1157, 788, 656, 570, 552.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{36}H_{39}NO_6S_2Na$ 668.2117; Found 668.2093.



2-methyl-1-(2-(3-phenylpropyl)phenyl)prop-1-en-1-yl 4-methylbenzenesulfonate (4.76).

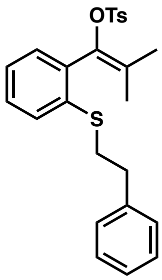
Synthesized according to general procedure 4.8.2.1.4B starting from 2.37 mmol of the corresponding ketone **4.72**. Crude product was purified via flash column chromatography using 20% ethyl acetate in hexanes to give vinyl tosylate **4.76** as a white solid (0.32 g, 32% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.19 (m, 2H), 7.15 (m, 1H), 7.11 (d, *J* = 6.8 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.97 (t, *J* = 6.2 Hz, 1H), 2.57 (m, 1H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.34 (m, 1H), 2.29 (s, 3H), 1.93 (s, 3H), 1.68 (quint, *J* = 8.0 Hz, 2H), 1.57 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 143.9, 142.3, 142.0, 140.9, 134.5, 132.6, 132.3, 129.1, 128.8, 128.4, 128.3, 127.6, 127.0, 125.7, 125.2, 35.7, 32.6, 32.0, 21.5, 19.9, 18.4.

FTIR (Neat film NaCl): 3065, 3026, 2922, 2859, 1599, 1496, 1453, 1367, 1081, 990, 823, 810.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{26}H_{28}O_3SNa$ 443.1657; Found 443.1649.



2-methyl-1-(2-(phenethylthio)phenyl)prop-1-en-1-yl 4-methylbenzenesulfonate (4.77).

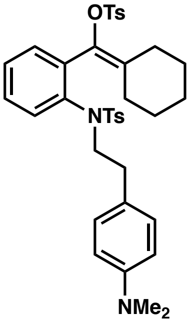
Synthesized according to general procedure 4.8.2.1.4B starting from 1.20 mmol of the corresponding ketone **4.74**. Crude product was purified via flash column chromatography using 40% ether in hexanes to give vinyl tosylate **4.77** as a pale yellow oil (0.29 g, 55% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.29 (m, 2H), 7.23 (m, 2H), 7.16 (m, 3H), 7.07 (m, 2H), 7.02 (d, *J* = 7.7 Hz, 2H), 2.97 (m, 2H), 2.79 (m, 2H), 2.29 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 143.9, 140.3, 139.6, 137.7, 134.4, 133.5, 132.6, 129.1, 129.0, 128.6, 128.4, 128.2, 127.8, 127.3, 126.5, 124.8, 35.4, 34.2, 21.5, 19.9, 18.4.

FTIR (Neat film NaCl): 3062, 3032, 2918, 2856, 1598, 1496, 1454, 1364, 1176, 1086, 1071, 990, 823, 809, 792.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{25}H_{26}O_3S_2Na$ 461.1221; Found 461.1209.



cyclohexylidene(2-((*N*-(4-(dimethylamino)phenethyl)-4-methylphenyl)sulfonamido)phenyl) methyl 4-methylbenzenesulfonate (4.78).

Synthesized according to general procedure 4.8.2.1.4B starting from 0.67 mmol of the corresponding ketone **4.60**. Crude product was purified via flash column chromatography using 50% ether in hexanes with 5% triethylamine to give vinyl tosylate **4.78** as a white solid (0.18 g, 41% yield).

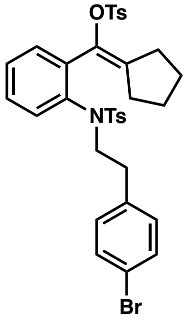
*NMR had poor resolution at room temperature, so ^{1}H NMR is reported below at 70 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) δ 7.69 (d, *J* = 7.7 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.43 (br s, 1H), 7.29 (m, 2H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 6.6 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 2H), 3.56 (m, 1H), 3.39 (m, 1H), 2.90 (s, 6H), 2.61 (m, 1H), 2.49 (m, 1H), 2.43 (s, 3H), 2.40 (m, 1H), 2.31 (s, 3H), 2.28 (m, 1H), 2.11 (m, 1H), 2.04 (m, 1H), 1.69 (br s, 2H), 1.59 (br s, 2H), 1.50 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 144.2, 143.4, 139.2, 136.7, 136.2, 135.5, 134.2, 133.6, 129.4, 129.4, 129.4, 129.3, 128.7, 128.3, 128.1, 127.8, 126.4, 125.5, 112.8, 53.2, 40.8, 33.4, 30.6, 28.7, 27.0, 26.7, 26.2, 21.6, 21.6.

FTIR (Neat film NaCl): 3032, 2929, 2857, 1616, 1597, 1522, 1445, 1352, 1188, 1176, 1161, 1093, 807, 789, 572, 555.

HR-MS (ESI-MS) m/z: [M+H]+ Calc'd for $C_{37}H_{43}N_2O_5S_2$ 659.2614; Found 659.2619.



(2-((*N*-(4-bromophenethyl)-4-methylphenyl)sulfonamido)phenyl)(cyclopentylidene)methyl 4-methylbenzenesulfonate (4.79).

Synthesized according to general procedure 4.8.2.1.4B starting from 1.75 mmol of the corresponding ketone **4.58**. Crude product was purified via flash column chromatography using 40% ether in hexanes to give vinyl tosylate **4.79** as a white solid (0.72 g, 61% yield).

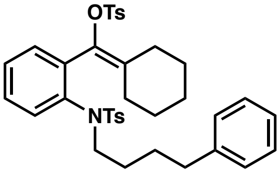
*NMR had poor resolution at room temperature, so NMRs are reported below at 70 °C.

^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) δ 7.63 (m, 4H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.31 (m, 4H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 2H), 3.54 (m, 2H), 2.63 (m, 3H), 2.43 (s, 3H), 2.35 (s, 3H), 2.26 (m, 3H), 1.65 (br s, 4H).

^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) δ 144.3, 143.3, 141.9, 138.5, 137.6, 136.6, 135.2, 133.2, 131.3, 130.3, 130.2, 130.1, 129.3, 129.2, 129.1, 129.0, 128.0, 128.0, 127.9, 120.0, 52.7, 33.9, 30.8, 30.1, 26.2, 25.8, 21.2, 21.2.

FTIR (Neat film NaCl): 3070, 3032, 2957, 2869, 1597, 1488, 1352, 1189, 1176, 1160, 806, 788, 659, 572, 553.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{34}H_{34}BrNO_5S_2Na$ 702.0959; Found 702.0975.



cyclohexylidene(2-((4-methyl-*N*-(4-phenylbutyl)phenyl)sulfonamido)phenyl)methyl 4-methylbenzenesulfonate (4.80).

Synthesized according to general procedure 4.8.2.1.4A starting from 2.23 mmol of the corresponding ketone **4.61**. Crude product was purified via flash column chromatography using 12% acetone in hexanes to give vinyl tosylate **4.80** as a white solid (0.75 g, 52% yield).

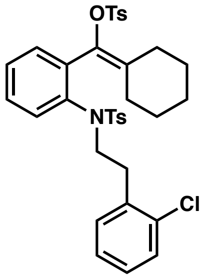
*NMR had poor resolution at room temperature, so NMRs are reported below at 55 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 55 °C) δ 7.65 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.37 (m, 1H), 7.28-7.21 (m, 6H), 7.16 (m, 1H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 6.8 Hz, 2H), 6.95 (m, 1H), 3.32 (m, 2H), 2.42 (m, 3H), 2.41 (s, 3H), 2.33 (s, 3H), 2.25 (m, 1H), 2.05 (m, 1H), 1.98 (m, 1H), 1.65 (m, 2H), 1.56-1.39 (m, 5H), 1.36-1.28 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$, 55 °C) δ 144.3, 143.2, 142.1, 139.2, 137.3, 136.5, 136.3, 135.7, 134.6, 133.6, 129.8, 129.3, 129.3, 129.2, 128.2, 128.2, 128.1, 128.1, 127.6, 125.7, 51.4, 35.2, 30.5, 28.6, 28.5, 27.5, 27.0, 26.7, 26.2, 21.4, 21.4.

FTIR (Neat film NaCl): 3027, 2926, 2854, 1598, 1486, 1447, 1364, 1188, 1176, 1158, 1093, 789, 571.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{37}H_{41}NO_5S_2Na$ 666.2324; Found 666.2312.



(2-((*N*-(2-chlorophenethyl)-4-methylphenyl)sulfonamido)phenyl) (cyclohexylidene)methyl-4-methylbenzenesulfonate (4.1).

Synthesized according to general procedure 4.8.2.1.4A starting from 2.96 mmol of the corresponding ketone **4.62**. Crude product was purified via flash column chromatography using benzene to give vinyl tosylate **4.1** as a white solid (0.66 g, 34% yield).

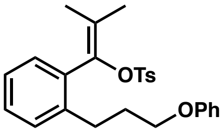
*NMR had poor resolution at room temperature, so ^{1}H NMR is reported below at 70 °C and ^{13}C NMR is reported below at 50 °C.

^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) δ 7.71 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.44 (br s, 1H), 7.31 (m, 2H), 7.25 (m, 3H), 7.09 (m, 2H), 7.04 (d, *J* = 7.8 Hz, 3H), 6.97 (m, 1H), 3.60 (m, 1H), 3.44 (m, 1H), 2.79 (m, 1H), 2.59 (m, 1H), 2.49 (m, 1H), 2.43 (s, 3H), 2.32 (m, 1H), 2.26 (s, 3H), 2.10 (m, 2H), 1.68 (br s, 2H), 1.59 (br s, 2H), 1.51 (br s, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 144.4, 143.4, 139.0, 136.8, 136.39, 136.36, 135.6, 134.5, 134.1, 133.6, 130.9, 129.4, 129.3, 128.4, 128.0, 127.79, 127.76, 126.8, 50.8, 32.3, 30.6, 28.7, 27.0, 26.7, 26.2, 21.4, 21.3.

FTIR (Neat film NaCl): 3066, 2973, 2928, 2855, 1597, 1475, 1444, 1356, 1176, 1160, 656, 571, 552.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{35}H_{36}ClNO_5S_2Na$ 672.1621; Found 672.1607.



2-methyl-1-(2-(3-phenoxypropyl)phenyl)prop-1-en-1-yl 4-methylbenzenesulfonate (4.81).

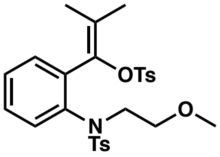
Synthesized according to general procedure 4.8.2.1.4B starting from 0.82 mmol of the corresponding ketone **4.70**. Crude product was purified *via* flash column chromatography using 30% ether in hexanes to give vinyl tosylate **4.81** as a white solid (90 mg, 25% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.31 – 7.24 (m, 1H), 7.23 – 7.19 (m, 1H), 7.16 (td, *J* = 7.5, 1.6 Hz, 1H), 7.09 (td, *J* = 7.5, 1.4 Hz, 1H), 7.01 (t, *J* = 8.0 Hz, 3H), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 2H), 3.87 – 3.79 (m, 2H), 2.77 – 2.65 (m, 1H), 2.51 – 2.40 (m, 1H), 2.31 (s, 3H), 1.91 (s, 3H), 1.90 – 1.83 (m, 2H), 1.55 (s, 3H), 1.55 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 158.9, 143.9, 141.1, 140.7, 134.5, 132.7, 132.3, 129.4, 129.1, 128.9, 128.8, 127.5, 127.2, 125.4, 120.5, 114.4, 66.8, 29.7, 29.1, 21.5, 19.8, 18.3.

FTIR (Neat film NaCl): 3065, 2923, 2870, 1600, 1497, 1367, 1245, 1177, 1080, 1037, 990.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{26}H_{28}O_4SNa$ 459.1606; Found 459.1619.



1-(2-((*N*-(2-methoxyethyl)-4-methylphenyl)sulfonamido)phenyl)-2-methylprop-1-en-1-yl 4-methylbenzenesulfonate (4.43).

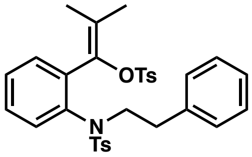
Synthesized according to general procedure 4.8.2.1.4A starting from 6.39 mmol of the corresponding ketone **4.63**. Crude product was purified *via* flash column chromatography using 40% ethyl acetate in hexanes to give vinyl tosylate **4.43** as a yellow solid (1.75 g, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.53 (m, 4H), 7.41 – 7.37 (m, 1H), 7.33 – 7.21 (m, 4H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 7.7 Hz, 1H), 3.52 (t, *J* = 6.8 Hz, 2H), 3.37 – 3.28 (m, 1H), 3.25 – 3.14 (m, 1H), 3.12 (s, 3H), 2.41 (s, 3H), 2.37 (s, 3H), 1.72 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.57, 143.27, 138.65, 138.10, 136.38, 134.01, 133.62, 130.08, 129.93, 129.41, 129.28, 129.15, 128.20, 127.95, 69.28, 58.30, 50.21, 21.53, 21.49, 20.31, 18.53.

FTIR (Neat film NaCl): 3072, 2986, 2923, 2882, 2815, 1597, 1486, 1360, 1176, 1160, 810, 792, 725.

HR-MS (ESI-MS) m/z: [M+H]+ Calc'd for $C_{27}H_{32}NO_6S_2$ 530.1671; Found 530.1678.



2-methyl-1-(2-((4-methyl-*N*-phenethylphenyl)sulfonamido)phenyl)prop-1-en-1-yl 4-methylbenzenesulfonate (4.82).

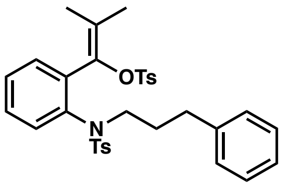
Synthesized according to general procedure 4.8.2.1.4A starting from 4.03 mmol of the corresponding ketone **4.64**. Crude product was purified *via* flash column chromatography using 25% diethyl ether in hexanes to give vinyl tosylate **4.82** as a yellow solid (0.76 g, 33% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65 – 7.59 (m, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.44 (m, 1H), 7.38 – 7.29 (m, 2H), 7.29 – 7.23 (m, 2H), 7.23 – 7.14 (m, 3H), 7.07 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 6.5 Hz, 3H), 3.60 (d, *J* = 10.9 Hz, 1H), 3.36 (td, *J* = 13.0, 4.9 Hz, 1H), 2.73 (td, *J* = 12.7, 5.3 Hz, 1H), 2.48 (td, *J* = 12.7, 4.8 Hz, 1H), 2.42 (s, 3H), 2.29 (s, 3H), 1.81 (s, 3H), 1.65 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 144.5, 143.5, 139.0, 138.5, 137.9, 136.1, 134.1, 133.8, 130.2, 129.5, 129.4, 129.1, 128.6, 128.3, 128.2, 127.9, 126.3, 53.1, 34.5, 21.6, 21.5, 20.4, 18.69.

FTIR (Neat film NaCl): 3064, 3028, 2921, 1598, 1487, 1446, 1352, 1305, 1190, 1177, 1161, 1093, 1083, 814.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{32}H_{33}NO_5S_2Na$ 598.1698; Found 598.1689.



2-methyl-1-(2-((4-methyl-*N*-(3-phenylpropyl)phenyl)sulfonamido)phenyl)prop-1-en-1-yl 4-methylbenzenesulfonate (4.83).

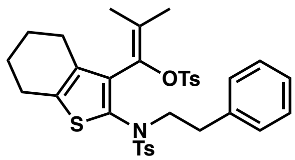
Synthesized according to general procedure 4.8.2.1.4A starting from 5.97 mmol of the corresponding ketone **4.65**. Crude product was purified *via* flash column chromatography using 25% diethyl ether in hexanes to give vinyl tosylate **4.83** as a yellow solid (1.10 g, 31% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.53 (app d, *J* = 8.2 Hz, 4H), 7.40 (s, 1H), 7.31 – 7.21 (m, 6H), 7.20 – 7.15 (m, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 6.9 Hz, 2H), 6.92 (s, 1H), 3.41 – 3.18 (m, 2H), 2.42 (s, 3H), 2.36 (t, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.80 (s, 3H), 1.76 – 1.65 (m, 2H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 144. 5, 143.3, 140.9, 138.9, 138.0, 136.4, 134.1, 133.6, 129.9, 129.6, 129.3, 129.28, 129.26, 128.23, 128.21, 127.96, 127.91, 127.7, 125.8, 51.0, 32.9, 29.1, 21.5, 21.4, 20.3, 18.6.

FTIR (Neat film NaCl): 3063, 3027, 2971, 2932, 2871, 1694, 1596, 1495, 1348, 1161, 980, 700, 658, 576.

HR-MS (ESI-MS) m/z: [M+H]+ Calc'd for $C_{33}H_{36}NO_5S_2$ 590.2035; Found 590.2061.



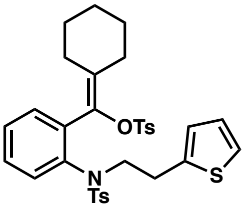
2-methyl-1-(2-((4-methyl-*N*-phenethylphenyl)sulfonamido)-4,5,6,7-tetrahydrobenzo[*b*]thiophen-3-yl)prop-1-en-1-yl 4-methylbenzenesulfonate (4.84). Synthesized according to a slightly modified general procedure 4.8.2.1.4B starting from 2.80 mmol of the corresponding ketone **4.66**. Followed procedure with exception that 10 mL of PhME was used for ketone solution and 14 mL DCM used for tosic anhydride due to poor solubility of ketone. Crude product was purified *via* flash column chromatography using 20% diethyl ether in hexanes to give vinyl tosylate **4.84** as a white solid (390 mg, 22% yield).

^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) δ 7.69 (d, *J* = 7.9 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.19 (m, 7.7 Hz, 4H), 7.17 (app q, *J* = 7.0 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 7.4 Hz, 2H), 3.65 (td, *J* = 12.8, 12.4, 5.4 Hz, 1H), 3.50 (td, *J* = 12.7, 5.0 Hz, 1H), 2.86 (dd, *J* = 16.4, 5.5 Hz, 1H), 2.80 – 2.61 (m, 4H), 2.45 – 2.35 (m, 1H), 2.41 (s, 3H), 2.33 (s, 3H), 1.98 – 1.81 (m, 4H), 1.79 (s, 3H), 1.61 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) δ 144.3, 143.5, 138.6, 136.8, 136.7, 135.2, 134.7, 134.6, 133.1, 131.1, 129.5, 129.5, 129.4, 128.7, 128.4, 128.3, 127.8, 127.4, 126.3, 54.2, 34.8, 25.4, 25.0, 23.5, 22.8, 21.4, 21.3, 20.0, 18.5.

FTIR (Neat film NaCl): 3199, 3063, 3028, 2932, 2858, 1598, 1453, 1351, 1176, 1162, 1092, 1059, 813, 661, 580, 547.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{34}H_{37}NO_5S_3Na$ 658.1732; Found 658.1712.



cyclohexylidene(2-((4-methyl-*N*-(2-(thiophen-2-yl)ethyl)phenyl)sulfonamido)phenyl)methyl 4-methylbenzenesulfonate (4.85).

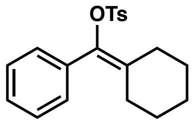
Synthesized according to general procedure 4.8.2.1.4A starting from 1.18 mmol of the corresponding ketone **4.67**. Crude product was purified *via* flash column chromatography using 30% diethyl ether in hexanes to give vinyl tosylate **4.85** as a yellow solid (490 mg, 67% yield).

^{1}H NMR (500 MHz, $CDCl_3$, 55 °C) δ 7.67 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.35 – 7.23 (m, 5H), 7.15 – 7.04 (m, 2H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.86 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.60 (dd, *J* = 3.5, 1.2 Hz, 1H), 3.65 (ddd, *J* = 13.7, 12.0, 5.3 Hz, 1H), 3.46 (ddd, *J* = 13.8, 12.0, 5.0 Hz, 1H), 2.95 (ddd, *J* = 14.5, 12.2, 5.3 Hz, 1H), 2.75 (ddd, *J* = 14.5, 11.9, 4.9 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.43 (s, 3H), 2.31 (s, 3H), 2.37 – 2.25 (m, 1H), 2.15 – 1.98 (m, 2H), 1.76 – 1.64 (m, 2H), 1.62 – 1.46 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$, 55 °C) δ 144.4, 143.6, 140.8, 139.3, 136.8, 136.5, 135.6, 134.5, 133.7, 129.5, 129.4, 129.2, 128.3, 128.0, 127.9, 126.8, 125.0, 123.5, 52.9, 30.6, 28.7, 27.0, 26.8, 26.3, 21.5.

FTIR (Neat film NaCl): 2930, 2925, 2856, 1492, 1356, 1175, 1093, 802, 573.

HR-MS (ESI-MS) m/z: $[M+NH_4]+$ Calc'd for $C_{33}H_{39}N_2O_5S_3$ 639.2021; Found 639.2044.



cyclohexylidene(phenyl)methyl 4-methylbenzenesulfonate (4.86).

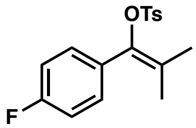
Synthesized according to general procedure 4.8.2.1.4A starting from 10.6 mmol of cyclohexylphenylketone. Crude product was purified *via* flash column chromatography using 1:5:94 triethylamine:ethyl acetate:hexanes to give vinyl tosylate **4.86** as a white solid (1.01 g, 28% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.13 (dt, *J* = 4.5, 0.9 Hz, 5H), 7.09 – 7.04 (m, 2H), 2.40 (dd, *J* = 6.9, 5.0 Hz, 2H), 2.34 (s, 3H), 2.17 (dd, *J* = 6.8, 5.0 Hz, 2H), 1.65 – 1.46 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 138.6, 134.4, 133.7, 133.5, 129.6, 129.1, 127.9, 127.8, 127.7, 29.9, 28.8, 27.7, 27.1, 26.2, 21.5.

FTIR (Neat film NaCl): 3057, 2929, 2854, 1599, 1446, 1368, 1187, 1176, 1002, 786, 700, 555.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{20}H_{22}O_3S$ 342.1290; Found 342.1294.



1-(4-fluorophenyl)-2-methylprop-1-en-1-yl 4-methylbenzenesulfonate (4.87).

Synthesized according to general procedure 4.8.2.1.4A starting from 18.1 mmol of 1-(4-fluorophenyl)-2-methylpropan-1-one. Crude product was purified *via* flash column chromatography using 7% ether/hexanes to give vinyl tosylate **4.87** as a white solid (3.83 g, 66% yield).

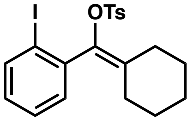
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46 (d, *J* = 8.3 Hz, 2H), 7.17 – 7.06 (m, 4H), 6.83 (t, *J* = 8.7 Hz, 2H), 2.36 (s, 3H), 1.88 (s, 3H), 1.73 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 162.2 (d, $^1J_{C\text{–}F}$ = 248.1 Hz), 144.4, 140.1, 134.3, 131.3 (d, $^3J_{C\text{–}F}$ = 8.3 Hz), 130.0 (d, $^4J_{C\text{–}F}$ = 3.2 Hz), 129.2, 127.8, 126.7, 114.7 (d, $^2J_{C\text{–}F}$ = 21.6 Hz), 21.5, 19.9, 19.0.

^{19}F NMR (376 MHz, CDCl$_3$) δ -112.9.

FTIR (Neat film NaCl): 3069, 2994, 2920, 2861, 1601, 1508, 1366, 1189, 1177, 1082, 995, 844, 784, 669.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{17}H_{17}FO_3S$ 320.0883; Found 320.0883.



cyclohexylidene(2-iodophenyl)methyl 4-methylbenzenesulfonate (4.88).

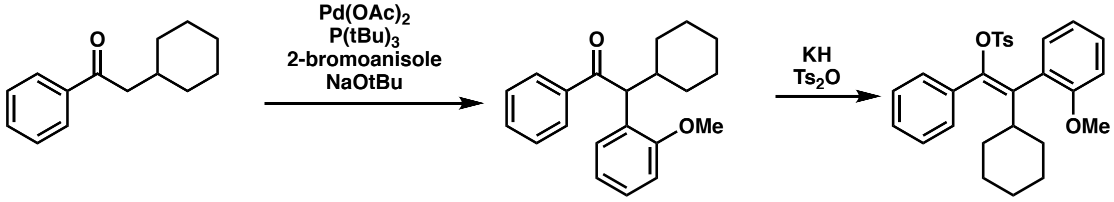
Synthesized according to general procedure 4.8.2.1.4A starting from 7.96 mmol of cyclohexyl(2-iodophenyl)methanone. Crude product was purified *via* flash column chromatography using 15% ether/hexanes and then recrystallized from diethyl ether to give vinyl tosylate **4.88** as a white solid (3.05 g, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.22 (dtd, *J* = 15.9, 8.7, 8.0, 6.4 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.87 (td, *J* = 7.6, 1.9 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.38 (dd, *J* = 7.8, 5.2 Hz, 1H), 2.32 (s, 3H), 1.92 (t, *J* = 5.7 Hz, 2H), 1.65 (q, *J* = 6.0 Hz, 2H), 1.59 – 1.46 (m, 4H).

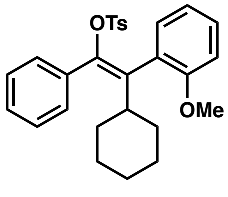
^{13}C NMR (126 MHz, , $CDCl_3$) δ 143.9, 139.1, 138.9, 138.5, 135.1, 134.4, 132.8, 129.6, 129.0, 127.6, 127.3, 99.9, 30.1, 28.3, 27.4, 26.9, 26.2, 21.5.

FTIR (Neat film NaCl): 3064, 2927, 2853, 1598, 1460, 1448, 1431, 1364, 1307, 1257, 1232, 1209, 1188, 1175, 1117, 1095, 1051, 1018, 1002, 979, 827.

HR-MS (EI-MS) m/z: [M+Na]+ Calc'd for: 491.0154 Observed: 491.0143



Scheme 4.8 Scheme for synthesis of tosylate **4.45**



(*Z*)-2-cyclohexyl-2-(2-methoxyphenyl)-1-phenylvinyl-4-methylbenzenesulfonate (4.45).

Inside a glovebox, $Pd(OAc)_2$ (30.0 mg, 0.134 mmol, 0.05 equiv), NaOtBu (385 mg, 4.01 mmol, 1.5 equiv) and tri-*tert*-butylphosphine (27.0 mg, 0.134 mmol, 0.05 equiv) were weighed into a dry schlenk flask. This was removed from the glovebox and the solids were suspended in THF (3.0 mL). 2-Bromoanisole (500 mg, 2.67 mmol, 1 equiv) and 2-cyclohexylacetophenone (595 mg, 2.94 mmol, 1.1 equiv) were sequentially added *via* syringe. The reaction was heated for 16 hours at 80 °C. The reaction was quenched by addition of 1M HCl (10 mL) and diethyl ether (10 mL). The layers were separated and the aqueous layer extracted twice more with ether. Organics washed with brine, dried over MgSO4, filtered and concentrated to give crude product. This was purified using silica flash column chromatrography (7% acetone/hexanes) to give product as a viscous yellow oil with some minor impurities (490 mg, ca. 59% yield). This was taken forward to the tosylation step without further purification.

To a flame dried Schlenk flask was added KH (1.04 g, 7.78 mmol, 5 equiv, 30% w/w in mineral oil) followed by THF (3.5 mL). To this was added a solution of ketone (480 mg, 1.56 mmol, 1.0 equiv) in THF (2 mL). This was heated to 75 °C for 16 hours. At this point, the reaction mixture was cooled to rt and Ts_2O (762 mg, 2.33 mmol, 1.5 equiv) was added. The reaction was stirred at rt for an additional 5 hours before being quenched with water. The product was extracted from the aqueous phase with ether (3 x 25 mL). Combined organics washed with brine, dried over MgSO4, filtered and concentrated to give crude product. Product was purified by silica flash column chromatography (10-15% ether/hexanes) to give pure tosylate **4.45** as white solid (160 mg, 22%). The Major isomer was determined by NOE experiments where an interaction between the cyclohexyl methine C–H and the protons on the phenyl ring can be observed.

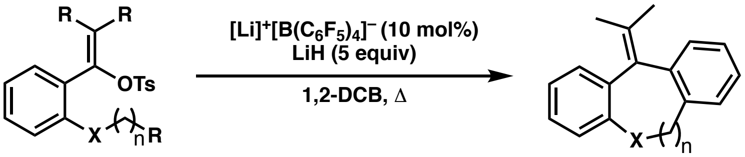
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.38 (m, 2H), 7.31 – 7.28 (m, 4H), 7.08 (d, *J* = 8.2 Hz, 2H), 7.00 (dd, *J* = 7.4, 1.8 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.94 – 6.88 (m, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 3.75 (s, 3H), 2.55 – 2.41 (m, 1H), 2.33 (s, 3H), 1.80 (d, *J* = 12.9 Hz, 1H), 1.69 (d, *J* = 13.0 Hz, 2H), 1.49 (d, *J* = 16.2 Hz, 2H), 1.34 (dd, *J* = 12.5, 3.4 Hz, 1H), 1.22 – 1.13 (m, 1H), 1.09 – 1.01 (m, 1H), 0.95 – 0.79 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 143.5, 142.2, 135.2, 134.7, 134.1, 130.8, 129.7, 128.9, 128.5, 128.3, 127.9, 127.5, 125.2, 119.6, 110.8, 55.6, 41.3, 32.1, 30.2, 26.2, 26.0, 25.7, 21.5.

FTIR (Neat film NaCl): 3062, 3029, 2929, 2853, 1598, 1493, 1371, 1189, 1177, 1003, 980, 824, 778, 698.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{28}H_{30}O_4SNa$ 485.1762; Found 485.1765.

4.8.2.2 Intramolecular Friedel-Crafts reactions

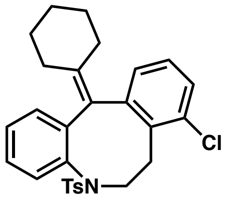


Scheme 4.9 Representative Scheme for Friedel-Crafts reactions portrayed in ***Figure 4.1***

In this section, procedures and characterization for the compounds in ***Figure 4.1*** are described.

4.8.2.2.1 General Procedure for Intramolecular Friedel-Crafts Reactions

In the glovebox, lithium tetrakis(pentafluorophenyl)borate (0.1 equiv), lithium hydride (5.0 equiv), and vinyl tosylate (1.0 equiv) were dissolved into 1,2-dichlorobenzene to generate a 0.0143 M solution for the vinyl tosylate. The reaction was heated under 140 °C overnight. The reaction solution was directly purified via flash column chromatography using hexanes to get rid of 1,2-dichlorobenzene and then ethyl acetate to flush the remaining products off the column. Then the crude product was purified *via* flash column chromatography again to get the pure product.



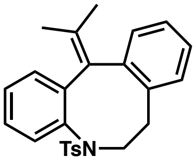
8-chloro-12-cyclohexylidene-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*]azocine (4.2). Synthesized according to general procedure 4.8.2.2.1 starting from 0.231 mmol of the corresponding vinyl tosylate **4.1**. Crude product was purified via flash column chromatography using 10% ethyl ether in hexanes to give the product **4.2** as a white powder (0.080 g, 73% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.85 (d, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.25 (m, 2H), 7.18 (m, 1H), 7.08 (m, 3H), 6.90 (d, *J* = 8.0 Hz, 1H), 4.31 (dd, *J* = 15.3, 6.9 Hz, 1H), 3.56 (dd, *J* = 14.9, 6.9 Hz, 1H), 3.36 (dd, *J* = 15.1, 9.4 Hz, 1H), 2.80 (dd, *J* = 15.3, 9.4 Hz, 1H), 2.46 (s, 3H), 2.21 (m, 2H), 2.06 (m, 2H), 1.87 (m, 1H), 1.57 (m, 5H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 146.1, 145.4, 143.2, 140.5, 139.4, 139.2, 136.7, 133.9, 130.1, 130.0, 129.8, 128.7, 128.1, 127.8, 127.7, 127.6, 127.4, 127.3, 50.3, 33.7, 31.8, 31.5, 28.1, 27.8, 26.5, 21.6.

FTIR (Neat film NaCl): 3062, 2925, 2852, 1560, 1482, 1446, 1349, 1158, 1092, 569.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{28}H_{28}ClNO_2SNa$ 500.1427; Found 500.1436.



12-(propan-2-ylidene)-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*]azocine (4.5).

Synthesized according to general procedure 4.8.2.2.1 at 140 °C for 36 hours starting from 0.050 mmol of the corresponding vinyl tosylate **4.82**. Crude product was purified *via* flash column chromatography using a gradient of 1-15% diethyl ether in hexanes to give arene **4.5** as white solid (11.3 mg, 56% yield).

Performing the reaction on a 1 mmol scale of **4.82** in a Schlenk heating at 140 °C outside the glovebox gave arene **4.5** as a white solid (265 mg, 66% yield)

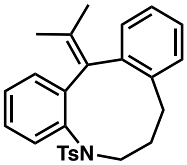
*NMR had poor resolution at room temperature, so NMR spectra are reported below at 75 °C.

^{1}H NMR (500 MHz, DMSO-d_6, 75 °C) δ 7.72 (d, J = 7.9 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.30 (dd, J = 7.5, 1.7 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.18 – 7.05 (m, 5H), 7.00 (d, J = 8.0 Hz, 1H), 4.26 – 4.06 (br s, 2H), 2.95 (br s, 5H), 2.40 (s, 3H), 1.69 (s, 3H), 1.56 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6, 75 °C) δ 143.7, 143.5, 139.7, 138.9, 138.7, 134.5, 131.6, 130.5, 130.3, 128.9, 128.4, 127.8, 127.7, 127.3, 127.2, 51.5 (br s), 37.5 (br s), 21.9, 21.4, 21.1.

FTIR (Neat film NaCl): 3065, 2955, 2923, 2854, 1738, 1599, 1484, 1447, 1348, 1325, 1159, 1092, 1020, 813, 717, 568, 549.

HR-MS (CI-MS) m/z: [M]+ Calc’d for $C_{25}H_{25}NO_2S$ 403.1606; Found 403.1620.



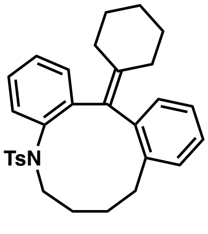
13-(propan-2-ylidene)-5-tosyl-6,7,8,13-tetrahydro-5*H*-dibenzo[*b*,*e*]azonine (4.6). Synthesized according to general procedure 4.8.2.2.1 at 140 °C for 36 hours starting from 0.050 mmol of the corresponding vinyl tosylate **4.83**. Crude product was purified *via* flash column chromatography using a gradient of 1-15% diethyl ether in hexanes to give arene **4.6** as white solid (17.1 mg, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 1H), 7.20 – 7.05 (m, 5H), 6.98 (dd, *J* = 14.7, 7.6 Hz, 2H), 4.11 – 3.93 (m, 1H), 3.52 – 3.25 (m, 2H), 2.74 – 2.55 (m, 1H), 2.14 (dt, *J* = 10.2, 5.6 Hz, 1H), 1.73 (s, 3H), 1.70 – 1.66 (m, 1H), 1.60 (s, 3H).

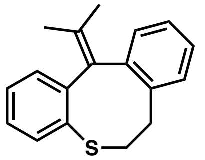
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 142.4, 139.6, 137.5, 132.8, 131.7, 131.0, 129.1, 128.8, 127.9, 126.8, 125.9, 123.9, 122.3, 73.7, 31.6, 29.6, 21.4, 21.1.

FTIR (Neat film NaCl): 3062, 2973, 2920, 2859, 1597, 1483, 1445, 1350, 1161, 1083, 814, 754, 697.

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{26}H_{28}NO_2S$ 418.1841; Found 418.1840.

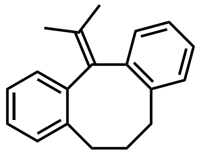


14-cyclohexylidene-5-tosyl-5,6,7,8,9,14-hexahydrodibenzo[*b*,*e*]azecine (4.7). Synthesized according to general procedure 4.8.2.2.1 starting from 0.100 mmol of the corresponding vinyl tosylate **4.80**. Crude product was obtained in 25% NMR yield after first column to get rid of 1,2-DCB. This was then was purified via flash column chromatography using 10% ethyl ether in hexanes to give the product **4.7** in 25% NMR yield.



12-(propan-2-ylidene)-7,12-dihydro-6H-dibenzo[*b,e*]thiocine (4.8).

Synthesized according to general procedure 4.8.2.2.1 starting from 0.100 mmol of the corresponding vinyl tosylate **4.77**. Crude product was purified via flash column chromatography using 5% ethyl ether in hexanes to give the product **4.8** as an oil in 46% NMR yield.



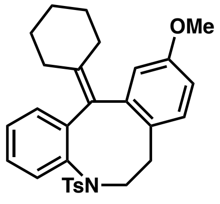
12-(propan-2-ylidene)-5,6,7,12-tetrahydrodibenzo[*a,d*][8]annulene (4.9).

Synthesized according to general procedure 4.8.2.2.1 starting from 0.250 mmol of the corresponding vinyl tosylate **4.76**. Crude product was purified via flash column chromatography using 5% ethyl ether in hexanes to give the product **4.9** as a white powder (50 mg, 81% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.20 – 7.01 (m, 8H), 2.87 (app d, *J* = 55.2 Hz, 4H), 2.26 (br s, 1H), 1.65 (s, 6H), 1.55 – 1.39 (m, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 144.3, 140.7, 136.9, 129.7, 128.8, 127.9, 126.5, 126.4, 37.9 (br), 29.1 (br), 20.7.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{19}H_{20}$ 248.1565; Found 248.1562.



12-cyclohexylidene-10-methoxy-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*]azocine (4.10).

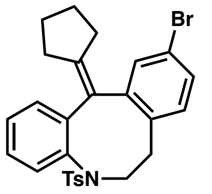
Synthesized according to general procedure 4.8.2.2.1 starting from 0.050 mmol of the corresponding vinyl tosylate **4.75**. Crude product was purified via flash column chromatography using 10% ethyl ether in hexanes to give the product **4.10** as a white powder (0.018 g, 76% yield).

*NMR had poor resolution at room temperature, so NMRs are reported below at 75 °C in DMSO-*d*6.

^{1}H NMR (500 MHz, DMSO-*d*6, 75 °C) δ 7.73 (d, *J* = 7.6 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.23 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.12 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.68 (s, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 4.41 (br s, 1H), 3.68 (s, 3H), 3.21 (br s, 1H), 2.75 (br s, 1H), 2.48 (m, 1H), 2.41 (s, 3H), 2.16-2.02 (m, 2H), 2.02-1.90 (m, 2H), 1.74 (br s, 1H), 1.58-1.44 (m, 5H).

^{13}C NMR (126 MHz, DMSO-*d*6, 75°C) δ 158.6, 143.6, 139.9, 139.0, 138.9, 131.4, 131.2, 131.1, 130.4, 130.2, 128.4, 127.8, 127.6, 114.8, 112.3, 55.6, 52.0, 36.9, 31.7, 31.3, 27.9, 27.6, 26.5, 21.4.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{29}H_{31}NO_3SNa$ 496.1922; Found 496.1930.



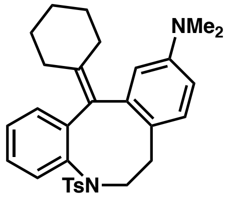
10-bromo-12-cyclopentylidene-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*]azocine (4.11). Synthesized according to general procedure 4.8.2.2.1 starting from 0.050 mmol of the corresponding vinyl tosylate **4.79**. Crude product was purified via flash column chromatography using 10% ethyl ether in hexanes to give the product **4.11** as a white powder (0.020 g, 79% yield).

*NMR had poor resolution at room temperature, so NMRs are reported below at 75 °C in DMSO-*d*6.

^{1}H NMR (500 MHz, DMSO-*d*6, 75 °C) δ 7.73 – 7.59 (m, 2H), 7.38 (dd, *J* = 7.6, 1.7 Hz, 3H), 7.33 (s, 1H), 7.28 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.15 (td, *J* = 7.7, 1.6 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 2H), 3.82 (br s, 2H), 2.99 (br s, 2H), 2.39 (s, 3H), 2.23 (br s, 2H), 2.00 (br s, 2H), 1.64 (app s, 4H). **CH2 next to nitrogen is very broad and hard to see/integrate

^{13}C NMR (126 MHz, DMSO-*d*6, 75 °C) δ 142.9, 138.9, 132.1, 130.5, 129.68, 129.4, 129.2, 128.9, 127.2, 126.8, 119.3, 50.5 (br), 35.9 (br), 30.8, 30.6, 29.6, 25.6, 25.5, 20.6.

HR-MS (ESI-MS) m/z: [M+Na]$^{+}$ Calc'd for $C_{27}H_{26}BrNO_{2}SNa$ 530.0765; Found 530.0781.



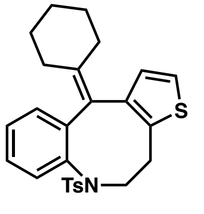
12-cyclohexylidene-N,N-dimethyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*]azocin-10-amine (4.12).

Synthesized according to general procedure 4.8.2.2.1 starting from 0.050 mmol of the corresponding vinyl tosylate **4.78**. Crude product was purified via flash column chromatography using 10% ethyl ether in hexanes to give the product **4.12** as a white powder (0.015 g, 62% yield).

*NMR had poor resolution at room temperature, so NMRs are reported below at 75 °C in DMSO-*d*6.

^{1}H NMR (500 MHz, DMSO-d_6, 75 °C) δ 7.75 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 7.8 Hz, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.9 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.88 (dd, J = 8.3, 2.5 Hz, 1H), 6.56 – 6.35 (m, 2H), 4.19 – 4.09 (m, 1H), 3.20 (d, J = 12.0 Hz, 1H), 2.83 (d, J = 2.7 Hz, 7H), 2.74 – 2.64 (m, 1H), 2.42 (d, J = 2.8 Hz, 3H), 2.18 – 1.92 (m, 4H), 1.59 – 1.45 (m, 6H).

^{13}C NMR (126 MHz, DMSO-d_6, 75 °C) δ 149.2, 142.7, 139.0, 138.3, 137.5, 131.13, 130.1, 129.5, 129.4, 127.5, 126.7, 125.9, 112.2, 110.5, 51.5 (br), 36.0 (br), 30.9, 30.5, 27.2, 26.8, 25.7, 20.5.



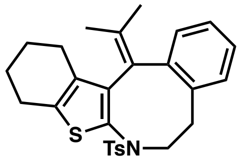
11-cyclohexylidene-6-tosyl-4,5,6,11-tetrahydrobenzo[*b*]thieno[3,2-*e*]azocine (4.13).

Synthesized according to general procedure 4.8.2.2.1 at 140 °C for 20 hours starting from 0.050 mmol of the corresponding vinyl tosylate **4.85**. Crude product was purified *via* flash column chromatography using a gradient of 0-30% diethyl ether in hexanes to give arene **4.13** as white solid (16.5 mg, 73% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.20 (m, 2H), 7.14 – 7.04 (m, 1H), 6.92 (d, *J* = 5.1 Hz, 1H), 6.88 – 6.82 (m, 1H), 6.77 (d, *J* = 5.1 Hz, 1H), 4.15 (ddd, *J* = 14.5, 5.5, 2.1 Hz, 1H), 3.48 (ddd, *J* = 15.8, 10.5, 2.1 Hz, 1H), 2.98 (dd, *J* = 14.4, 10.3 Hz, 1H), 2.81 (dd, *J* = 15.7, 5.3 Hz, 1H), 2.46 (s, 3H), 2.27 – 2.14 (m, 3H), 2.12 (dd, *J* = 8.4, 4.4 Hz, 1H), 1.87 – 1.79 (m, 1H), 1.73 – 1.65 (m, 1H), 1.63 – 1.48 (m, 4H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 145.9, 143.2, 142.0, 141.0, 139.3, 138.4, 135.0, 130.3, 130.2, 129.6, 128.6, 128.1, 127.6, 127.4, 125.5, 120.8, 51.4, 32.0, 31.6, 31.1, 28.4, 27.9, 26.6, 21.5.

FTIR (Neat film NaCl): 3062, 2921, 2851, 1598, 1483, 1343, 1157, 1094, 864, 737, 726, 661.



13-(propan-2-ylidene)-7-tosyl-5,6,7,9,10,11,12,13-octahydrobenzo[*e*]benzo[4,5]thieno[2,3-*b*]azocine (4.14).

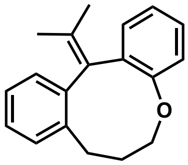
Synthesized according to general procedure 4.8.2.2.1 at 120 °C for 20 hours starting from 0.050 mmol of the corresponding vinyl tosylate **4.84**. Crude product was purified *via* flash column chromatography using a gradient of 1-20% diethyl ether in hexanes to give arene **4.14** as white solid (19.6 mg, 85% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.21 – 7.04 (m, 4H), 4.26 (dd, *J* = 15.1, 7.1 Hz, 1H), 3.41 (dd, *J* = 15.0, 9.7 Hz, 1H), 3.00 – 2.71 (m, 2H), 2.71 – 2.47 (m, 4H), 2.44 (s, 3H), 1.86 – 1.79 (m, 2H), 1.75 (s, 3H), 1.75 – 1.67 (m, 2H), 1.60 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 143.4, 143.1, 139.1, 137.8, 134.8, 133.7, 132.9, 132.7, 130.4, 129.6, 128.9, 128.39, 127.6, 126.8, 126.7, 51.7, 38.9, 25.1, 25.0, 23.3, 22.7, 21.6, 21.3, 21.0.

FTIR (Neat film NaCl): 3059, 2986, 2929, 2857, 2843, 1484, 1441, 1341, 1159, 1091, 731, 659, 545.

HR-MS (ESI-MS) m/z: [M+Na]+ Calc'd for $C_{27}H_{29}NO_2S_2Na$ 486.1537; Found 486.1538.



13-(propan-2-ylidene)-6,7,8,13-tetrahydrodibenzo[*b*,*e*]oxonine (4.15).

Synthesized according to general procedure 4.8.2.2.1 at 140 °C for 48 hours starting from 0.050 mmol of the corresponding vinyl tosylate **4.81**. Crude product was purified *via* flash column chromatography using a gradient of 0-4% diethyl ether in hexanes to give arene **4.15** as colorless oil (8.6 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 5.7 Hz, 1H), 7.20 – 7.05 (m, 5H), 6.98 (dd, *J* = 14.7, 7.6 Hz, 2H), 4.05 – 3.98 (m, 1H), 3.45 – 3.31 (m, 2H), 2.66 (d, *J* = 12.9 Hz, 1H), 2.14 (tt, *J* = 9.8, 4.1 Hz, 1H), 1.73 (s, 3H), 1.72 – 1.65 (m, 1H), 1.60 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 142.3, 139.6, 137.5, 132.7, 131.7, 131.0, 129.1, 128.8, 127.9, 126.7, 125.9, 123.9, 122.3, 73.6, 31.6, 29.5, 21.4, 21.0.

FTIR (Neat film NaCl): 3062, 3017, 2923, 2857, 1598, 1570, 1483, 1445, 1380, 1238, 1061, 754, 741, 630.

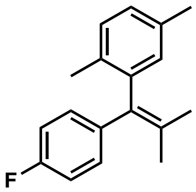
HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{19}H_{20}O$ 264.1514; Found 264.1512.

4.8.2.3 Intermolecular Friedel-Crafts reactions

In this section, the procedures and characterization data for reactions in ***Figure 4.2*** *are highlighted.*

4.8.2.3.1 General Procedure

Inside a well-kept glovebox, to an oven dried dram vial with a magnetic stir bar was added LiF_{20} (16.5 mg, 0.02 mmol, 0.1 equiv). To this was added LiHMDS (50.2 mg, 0.3 mmol, 1.5 equiv). To this was added trifluorotoluene (2 mL), and arene (5 equiv) and allowed to prestir for 5 minutes. Substrate (0.2 mmol, 1.0 equiv) was added and the reaction was allowed to stir at specified temperature. Upon completion of reaction, the reaction mixture was removed from the glovebox and diluted with ether. This was pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography to give the pure product.



2-(1-(4-fluorophenyl)-2-methylprop-1-en-1-yl)-1,4-dimethylbenzene (4.17)

Synthesized according to general procedure 4.8.2.3.1 from 0.20 mmol of vinyl tosylate **4.87** and *p*-xylene. Heated for 3 hours at 70 °C. Crude product was purified via silica column chromatography (0.5% ether/hexanes) to give product **4.17** as a colorless oil (44.0 mg, 87% yield).

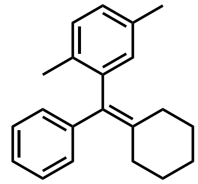
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.19 – 7.12 (m, 2H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.00 – 6.90 (m, 4H), 2.32 (s, 3H), 2.13 (s, 3H), 1.88 (s, 3H), 1.64 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 161.0 (d, $^1J_{C\text{–}F}$ = 244.7 Hz), 142.6, 138.1 (d, $^4J_{C\text{–}F}$ = 3.4 Hz), 134.9 ($^2J_{C\text{–}F}$, *J* = 17.4 Hz), 132.8, 131.3, 130.9 (d, $^3J_{C\text{–}F}$ = 7.7 Hz), 130.4, 129.9, 127.3, 114.5 (d, *J* = 21.0 Hz), 22.4, 21.6, 20.9, 19.2.

^{19}F NMR (376 MHz, CDCl$_3$) δ -116.9.

FTIR (Neat film NaCl): 3040, 2985, 2920, 2858, 1600, 1504, 1447, 1221, 846, 809, 517

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{18}H_{19}F$ 254.1471; Found 254.1477.



2-(cyclohexylidene(phenyl)methyl)-1,4-dimethylbenzene (4.18)

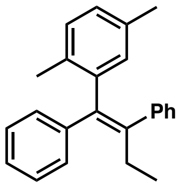
Synthesized according to general procedure 4.8.2.3.1 from 0.20 mmol of vinyl tosylate **4.86** and *p*-xylene. Heated for 3 hours at 70 °C. Crude product was purified via silica column chromatography (hexanes) to give product **4.18** as a colorless oil (41.7 mg, 75% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.26 (td, *J* = 7.1, 1.6 Hz, 2H), 7.19 – 7.13 (m, 3H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.96 (dd, *J* = 5.7, 2.1 Hz, 2H), 2.40 – 2.33 (m, 2H), 2.31 (s, 3H), 2.14 (s, 3H), 2.06 – 2.00 (m, 2H), 1.74 – 1.48 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 141.8, 138.9, 134.7, 133.2, 132.9, 130.5, 129.7, 127.7, 127.2, 125.8, 32.6, 31.5, 28.7, 28.3, 26.8, 21.0, 19.4.

FTIR (Neat film NaCl): 3077, 3054, 2920, 1598, 1493, 1442, 1178, 804, 730, 691.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{21}H_{24}$ 276.1878; Found 276.1875.



(*Z*)-(1-(2,5-dimethylphenyl)but-1-ene-1,2-diyl)dibenzene (4.19)

Synthesized according to general procedure 4.8.2.3.1 from 0.20 mmol of corresponding vinyl tosylate[37] and *p*-xylene. Heated for 3 hours at 70 °C. Crude product was purified via silica column chromatography (0.5% ether/hexanes) to give product **4.19** as a yellow oil (51.1 mg, 82% yield) as a *3:1 Z:E* ratio of olefin isomers. These isomers could be separated by semi-preparative reverse phase HPLC (90:10 MeCN:water) to give analytically pure samples of each isomer.

Characterization data of major isomer **4.19Z**:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.29 – 7.20 (m, 3H), 7.18 – 7.00 (m, 5H), 6.89 – 6.65 (m, 3H), 2.59 (s, 2H), 2.13 (d, J = 0.8 Hz, 3H), 2.01 (s, 3H), 1.01 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6, 142.5, 142.4, 142.2, 138.2, 134.1, 132.7, 131.9, 129.6, 129.1, 128.9, 127.9, 127.4, 127.0, 126.3, 126.0, 27.9, 20.8, 19.8, 13.9.

FTIR (Neat film NaCl): 3077, 3054, 3018, 2960, 2922, 1598, 1493, 1441, 698.

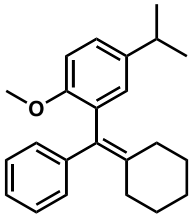
HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{24}H_{24}$ 312.1878; Found 312.1882.

Characterization data of minor isomer **4.19E**:

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.22 – 7.07 (m, 7H), 7.04 – 6.94 (m, 4H), 6.92 – 6.85 (m, 2H), 2.37 (s, 3H), 2.34 – 2.24 (m, 2H), 2.15 (s, 3H), 0.84 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 142.3, 141.9, 141.5, 137.8, 134.8, 132.8, 130.3, 130.4, 130.1, 129.7, 127.8, 127.6, 127.2, 126.2, 125.3, 29.1, 21.1, 19.4, 12.8.

FTIR (Neat film NaCl): 3078, 3054, 3016, 2964, 2923, 2871, 1597, 1492, 1442, 807, 759, 696.



2-(cyclohexylidene(phenyl)methyl)-4-isopropyl-1-methoxybenzene (4.20)

Synthesized according to general procedure 4.8.2.3.1 from 0.20 mmol of vinyl tosylate **4.86** and *4*-isopropylanisole. Heated for 15 hours at 70 °C. Purified by silica flash column chromatography (0.1:5.0:94.9 triethylamine:benzene:hexanes) to give pure product **4.20** as colorless oil (51.3 mg, 80% yield).

^{1}H NMR (500 MHz, CD$_2$Cl$_2$) δ 7.30 – 7.24 (m, 2H), 7.22 – 7.20 (m, 2H), 7.19 – 7.15 (m, 1H), 7.09 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.00 (d, *J* = 2.4 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 3.69 (s, 3H), 2.86 (hept, *J* = 6.9 Hz, 1H), 2.27 (tdd, *J* = 13.3, 9.4, 4.8 Hz, 2H), 2.07 (dtdd, *J* = 16.3, 12.7, 7.5, 4.3 Hz, 2H), 1.74 – 1.55 (m, 6H), 1.24 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (126 MHz, CD$_2$Cl$_2$) δ 155.0, 142.9, 140.7, 139.4, 132.1, 130.7, 129.4, 129.1, 127.6, 125.7, 125.2, 111.2, 55.6, 33.2, 32.6, 31.6, 28.6, 28.3, 26.9, 24., 23.9.

FTIR (Neat film NaCl): 3078, 3053, 2957, 2923, 2851, 2883, 1600, 1493, 1242, 1031, 699.

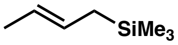
HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{23}H_{28}O$ 320.2140; Found 320.2147.

4.8.2.4 Intermolecular allylation reactions

*In this section, the procedures and characterization data for reactions in **Figure 4.4** are highlighted.*

4.8.2.4.1 Synthesis of allyl silanes

Allyltrimethylsilane and Methallyltrimethylsilane were purchased from Sigma Aldrich.

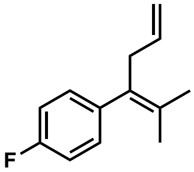


(*E*)-but-2-en-1-yltrimethylsilane (4.89)

(*E)*-Crotyltrimethylsilane was synthesized according to literature procedures.
Spectral data matched those reported in the literature.[38]

4.8.2.4.2 General procedure for allylation

Inside a well-kept glovebox, to an oven dried dram vial with a magnetic stir bar was added LiF_{20} (16.5 mg, 0.02 mmol, 0.1 equiv). To this was added LiHMDS (50.2 mg, 0.3 mmol, 1.5 equiv). To this was added trifluorotoluene (2 mL), and allylsilane (1.5–3 equiv). Substrate (0.2 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 70 °C for 12 hours. Upon completion of reaction, the reaction mixture was removed from the glovebox and diluted with ether. This was pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography to give the pure product.



1-fluoro-4-(2-methylhexa-2,5-dien-3-yl)benzene (4.27)

Synthesized according to general procedure 4.8.2.4.2 from vinyl tosylate **4.86** and allyltrimethylsilane**.** Purified by silica flash column chromatography (hexanes) to give pure product **4.27** as colorless oil (32.0 mg, 84% yield).

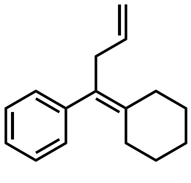
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.10 – 7.02 (m, 2H), 7.03 – 6.92 (m, 2H), 5.72 (ddt, *J* = 16.6, 10.2, 6.3 Hz, 1H), 5.02 – 4.94 (m, 1H), 4.93 (t, *J* = 1.6 Hz, 1H), 3.12 – 3.03 (m, 2H), 1.81 (s, 3H), 1.58 (s, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 161.32 (d, $^1J_{C–F}$ = 244.0 Hz), 139.89 (d, $^4J_{C–F}$ = 3.3 Hz), 135.91, 131.45, 130.50 (d, $^3J_{C–F}$ = 7.7 Hz), 129.78, 114.99, 114.79 (d, $^2J_{C–F}$ = 21.1 Hz), 39.27, 22.32, 20.39.

^{19}F NMR (282 MHz, CDCl$_3$) δ -117.26.

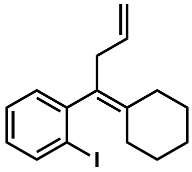
FTIR (Neat film NaCl): 3079, 2987, 2910, 2860, 1889, 1601, 1507, 1221, 1157, 912, 836, 550.

HR-MS (CI-MS) m/z: [M]+ Calc’d for $C_{13}H_{15}F$ 190.1158; Found 190.1161.



(1-cyclohexylidenebut-3-en-1-yl)benzene (4.28)

Synthesized according to general procedure 4.8.2.4.2 from 0.20 mmol of vinyl tosylate **4.86** and allyltrimethylsilane. Purified by silica flash column chromatography (hexanes) to give pure product **4.28** as colorless oil (38.5 mg, 90% yield). Spectral data matched thos reported in the literature.[39]



1-(1-cyclohexylidenebut-3-en-1-yl)-2-iodobenzene (4.29)

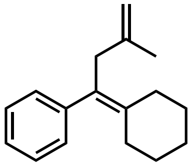
Synthesized according to general procedure 4.8.2.4.2 from 0.20 mmol of vinyl tosylate **4.88** and allyltrimethylsilane. Purified by silica flash column chromatography (hexanes) to give pure product **4.29** as colorless oil (66.0 mg, 97% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 (dd, J = 7.9, 1.2 Hz, 1H), 7.30 – 7.22 (m, 1H), 7.00 (dd, J = 7.6, 1.8 Hz, 1H), 6.90 (td, J = 7.6, 1.7 Hz, 1H), 5.80 – 5.71 (m, 1H), 4.98 – 4.90 (m, 2H), 3.33 (ddd, J = 15.1, 6.1, 1.7 Hz, 1H), 2.75 (dd, J = 15.2, 7.1 Hz, 1H), 2.39 – 2.27 (m, 2H), 1.80 (dd, J = 7.3, 4.8 Hz, 2H), 1.76 – 1.64 (m, 1H), 1.64 – 1.51 (m, 4H), 1.45 – 1.33 (m, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 148.0, 138.8, 138.2, 135.9, 131.7, 130.2, 127.7, 127.6, 115.0, 100.6, 37.4, 32.2, 30.0, 27.8, 27.7, 26.8.

FTIR (Neat film NaCl): 3074, 3058, 2922, 2851, 2663, 1914, 1831, 1459, 1445, 1427, 1012, 991, 909, 737.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{16}H_{19}I$ 338.0531; Found 338.0534.

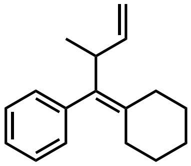


(1-cyclohexylidene-3-methylbut-3-en-1-yl)benzene (4.30)

Synthesized according to general procedure 4.8.2.4.2 from vinyl tosylate **4.86** and methyallyltrimethylsilane. Purified by silica flash column chromatography (hexanes) to give pure product **4.30** as colorless oil (35.0 mg, 77% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 1H), 7.25 – 7.23 (m, 1H), 7.21 – 7.14 (m, 1H), 7.12 – 7.07 (m, 2H), 4.74 – 4.62 (m, 2H), 3.05 (s, 2H), 2.30 – 2.22 (m, 2H), 2.09 – 2.00 (m, 2H), 1.69 (d, J = 0.6 Hz, 3H), 1.64 – 1.55 (m, 4H), 1.52 – 1.42 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2, 143.7, 138.2, 129.3, 129.0, 127.9, 125.9, 111.0, 42.4, 32.3, 31.1, 28.7, 28.4, 27.0, 23.0.



(1-cyclohexylidene-2-methylbut-3-en-1-yl)benzene (4.31)

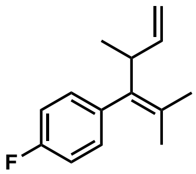
Synthesized according to general procedure 4.8.2.4.2 from vinyl tosylate **4.86** and silane **4.89**. Purified by silica flash column chromatography (hexanes) to give pure product **4.31** as colorless oil (27.0 mg, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 2H), 7.24 – 7.14 (m, 1H), 7.06 – 6.90 (m, 2H), 5.77 (ddd, *J* = 17.0, 10.2, 6.3 Hz, 1H), 4.98 – 4.89 (m, 2H), 3.63 (tt, *J* = 6.8, 1.6 Hz, 1H), 2.35 (td, *J* = 5.7, 3.0 Hz, 2H), 1.83 – 1.77 (m, 2H), 1.65 – 1.59 (m, 2H), 1.58 – 1.52 (m, 2H), 1.44 – 1.34 (m, 2H), 0.95 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.09, 141.42, 136.42, 134.89, 130.02, 127.56, 125.88, 112.48, 38.96, 32.92, 30.31, 28.67, 28.66, 27.15, 18.96.

FTIR (Neat film NaCl): 3055, 3076, 3018, 2966, 2922, 2851, 2663, 1942, 1873, 1820, 1632, 1449, 1442, 1071, 997, 908, 1724, 701

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{17}H_{22}$ 226.1721; Found 226.1722.



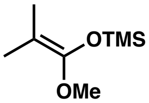
1-(2,4-dimethylhexa-2,5-dien-3-yl)-4-fluorobenzene (4.32)

Synthesized according to a modified general procedure 4.8.2.4.2 from vinyl tosylate **4.86** and silane **4.87** using 1,2-DFB as solvent instead of trifluorotoluene. Reaction finished after 3 hours at 70 °C. Purified by silica flash column chromatography (pentane) to give pure product **4.30** as colorless oil (33.3 mg, 81% yield).

4.8.2.5 Trapping vinyl cations with silyl ketene acetals (SKAs)

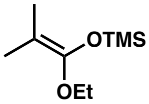
In this section, the procedures and characterization data for reactions in ***Figure 4.6*** *are highlighted.*

4.8.2.5.1 Synthesis of silyl ketene acetals



((1-Methoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane (4.90)

Synthesized according to literature procedures. Spectral data matched those reported in the literature.[40]

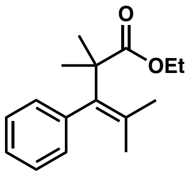


((1-Ethoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane (4.91)

Synthesized according to literature procedures. Spectral data matched those reported in the literature.[41]

4.8.2.5.2 General procedure

Inside a well-kept glovebox, to an oven dried dram vial with a magnetic stir bar was added LiF_{20} (16.5 mg, 0.02 mmol, 0.1 equiv). To this was added trifluorotoluene (2 mL), and SKA (3 equiv). Substrate (0.2 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 70 °C for 12 hours. Upon completion of reaction, the reaction mixture was removed from the glovebox and diluted with ether containing a small amount of triethylamine. This was pushed through a plug of triethylamine treated silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography on triethylamine treated silica gel to give the pure product.

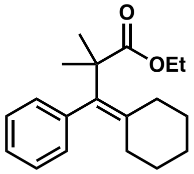


Ethyl 2,2,4-trimethyl-3-phenylpent-3-enoate (4.39)

Synthesized according to general procedure 4.8.2.5.2 from corresponding vinyl tosylate and SKA **4.91**. Purified by silica flash column chromatography (0.1:3:96.9 triethylamine:diethyl ether:hexanes) to give pure product **4.39** as colorless oil (35.0 mg, 77% yield).

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.20 (m, 1H), 7.08 – 7.01 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.67 (s, 3H), 1.36 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.16 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 179.2, 142.7, 138.7, 130.1, 129.5, 128.0, 126.1, 60.7, 45.9, 27.6, 23.9, 20.9, 14.4.

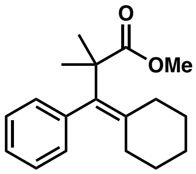


Ethyl 3-cyclohexylidene-2,2-dimethyl-3-phenylpropanoate (4.40)

Synthesized according to general procedure 4.8.2.5.2 from vinyl tosylate **4.86** and SKA **4.91**. Purified by silica flash column chromatography (0.1:3:96.9 triethylamine:diethyl ether:hexanes) to give pure product **4.40** as colorless oil (47.0 mg, 82% yield).

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.33 – 7.26 (m, 2H), 7.25 – 7.20 (m, 1H), 7.10 – 7.00 (m, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.11 (m, 2H), 1.78 – 1.66 (m, 2H), 1.58 – 1.45 (m, 4H), 1.42 – 1.34 (q, *J* = 6.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.15 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 179.5, 142.3, 138.2, 135.8, 129.5, 127.9, 126.1, 60.7, 45.6, 33.8, 31.3, 28.4, 28.1, 27.6, 26.8, 14.4.



Methyl 3-cyclohexylidene-2,2-dimethyl-3-phenylpropanoate (4.41)

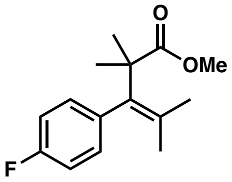
Synthesized according to general procedure 4.8.2.5.2 from vinyl tosylate **4.86** and SKA **4.90**. Purified by silica flash column chromatography (0.1:5:94.9 triethylamine:diethyl ether:hexanes) to give pure product **4.41** as colorless oil (43.5 mg, 80% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.33 – 7.26 (m, 2H), 7.24 – 7.16 (m, 1H), 7.13 – 6.95 (m, 2H), 3.73 (s, 3H), 2.09 –2.07 (m, 2H), 1.74 – 1.68 (m, 2H), 1.57 – 1.44 (m, 4H), 1.40 – 1.32 (m, 2H), 1.15 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 180.1, 142.1, 138.3, 135.6, 129.5, 127.9, 126.1, 52.2, 45.6, 33.8, 31.2, 28.4, 28.0, 27.6, 26.8.

FTIR (Neat film NaCl): 3054, 3018, 2974, 2924, 2852, 1728, 1457, 1443, 1249, 1137, 1129, 774, 761, 703,

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{18}H_{25}O_2$ 273.1855; Found 273.1846.



Methyl 3-(4-fluorophenyl)-2,2,4-trimethylpent-3-enoate (4.42)

Synthesized according to general procedure 4.8.2.5.2 from vinyl tosylate **4.87** and SKA **4.90**. Purified by silica flash column chromatography (0.1:3:96.9 triethylamine:diethyl ether:hexanes) to give pure product **4.42** as colorless oil (21.0 mg, 42% yield).

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.04 – 6.96 (m, 4H), 3.73 (s, 3H), 1.65 (s, 3H), 1.36 (s, 3H), 1.15 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 179.6, 161.5 (d, $^1J_{C\text{–}F}$ = 244.2 Hz), 138.3 (d, $^4J_{C\text{–}F}$ = 3.4 Hz), 137.6, 131.1, 131.0 (d, $^3J_{C\text{–}F}$ = 7.6 Hz), 114.9 (d, $^2J_{C\text{–}F}$ = 21.0 Hz), 52.3, 45.9, 27.6, 23.9, 20.7.

^{19}F NMR (282 MHz, CDCl$_3$) δ -116.94.

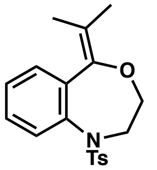
FTIR (Neat film NaCl): 2976, 2948, 2873, 1731, 1601, 1506, 1251, 1220, 1138, 844, 584, 337

HR-MS (CI-MS) m/z: [M+H]+ Calc'd for $C_{15}H_{20}FO_2$ 251.1447; Found 251.1445.

4.8.2.6 Vinyl ether synthesis

In this section, the procedures and characterization data for reactions in ***Figure 4.7*** *and* ***Figure 4.8*** *are highlighted.*

4.8.2.6.1 Intramolecular vinyl ether synthesis



5-(propan-2-ylidene)-1-tosyl-1,2,3,5-tetrahydrobenzo[*e*][1,4]oxazepane (4.44).

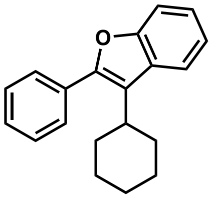
Synthesized according to general procedure 4.8.2.2.1 at 160 °C for 36 hours starting from 0.050 mmol of the corresponding vinyl tosylate **4.43**. Crude product was purified *via* flash column chromatography using a gradient of 1-30% diethyl ether in hexanes to give arene **4.44** as white solid (15.8 mg, 92% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.60 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.35 (td, *J* = 7.7, 1.7 Hz, 1H), 7.26 (td, *J* = 7.7, 1.7 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.13 (dd, *J* = 7.5, 1.7 Hz, 1H), 3.85 (br s, 2H), 3.78 (t, *J* = 4.7 Hz, 2H), 2.38 (s, 3H), 1.44 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 145.6, 142.9, 137.7, 135.8, 133.5, 131.6, 130.9, 129.2, 128.8, 127.5, 127.3, 65.0, 50.5, 21.4, 20.1, 16.7.

FTIR (Neat film NaCl): 3065, 2922, 2856, 1598, 1483, 1448, 1345, 1156, 1088, 677, 657, 546.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{19}H_{21}NO_3S$ 343.1242; Found 343.1234.



3-cyclohexyl-2-phenylbenzofuran (4.46)

Inside a well-kept glovebox, to an oven dried dram vial with a magnetic stir bar was added LiF$_{20}$ (8.3 mg, 0.01 mmol, 0.1 equiv). To this was added trifluorotoluene (1 mL), Vinyl tosylate **4.45** (46.3 mg, 0.1 mmol, 1.0 equiv) was added and the reaction was heated to 70 °C for 5 hours. The reaction mixture was removed from the glovebox and diluted with ether. This was pushed through a plug silica gel in a pipette and concentrated to give the crude material. The crude material was purified by silica flash chromatography (2% ether/hexanes) give the pure product **4.46** as a white solid (24.4 mg, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.79 (m, 1H), 7.73 – 7.68 (m, 2H), 7.57 – 7.48 (m, 3H), 7.46 – 7.40 (m, 1H), 7.30 (ddd, *J* = 8.3, 7.2, 1.4 Hz, 1H), 7.26 – 7.21 (m, 1H), 3.10 (tt, *J* = 12.2, 3.5 Hz, 1H), 2.10 – 1.99 (m, 2H), 1.97 – 1.78 (m, 5H), 1.54 – 1.35 (m, 3H).

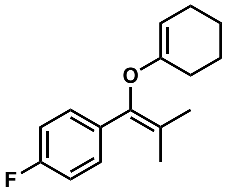
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.47, 150.35, 131.47, 128.84, 128.56, 128.23, 127.95, 123.81, 121.88, 121.58, 121.02, 111.32, 35.95, 32.32, 26.80, 26.20.

FTIR (Neat film NaCl): 3085, 3062, 2926, 2852, 1598, 1454, 1369, 1257, 1138, 744, 696.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{20}H_{20}O$ 276.1514; Found 276.1509.

4.8.2.6.2 General procedure for intermolecular vinyl ether synthesis

Inside a well-kept glovebox, to an oven dried dram vial with a magnetic stir bar was added LiF_{20} (16.5 mg, 0.02 mmol, 0.1 equiv). To this was added LiHMDS (50.2 mg, 0.30 mmol, 1.5 equiv), trifluorotoluene (2 mL), and methyl ether (5 equiv). Substrate (0.2 mmol, 1.0 equiv) was added and the reaction was allowed to stir at specified temperature. Upon completion of reaction, the reaction mixture was removed from the glovebox and diluted with ether containing a small amount of triethylamine. This was pushed through a plug of triethylamine treated silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography on triethylamine treated silica gel to give the pure product.



1-(1-(Cyclohex-1-en-1-yloxy)-2-methylprop-1-en-1-yl)-4-fluorobenzene (4.47)

Synthesized according to general procedure 4.8.2.6.2 from 0.20 mmol of vinyl tosylate **4.87** and 1-methoxycyclohex-1-ene. Crude was purified on silica flash column chromatography (0.3:1:98.7 triethylamine:diethyl ether:hexanes) to give pure product **4.47** as colorless oil (37.8 mg, 77% yield).

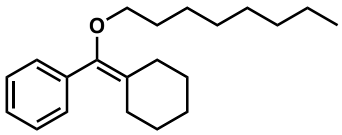
^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.34 (dd, *J* = 8.7, 5.7 Hz, 2H), 7.01 (t, *J* = 8.8 Hz, 2H), 4.65 (ddt, *J* = 4.1, 2.8, 1.4 Hz, 1H), 2.07 (ddt, *J* = 6.5, 4.5, 1.8 Hz, 2H), 1.89 (dp, *J* = 6.2, 2.0 Hz, 2H), 1.78 (s, 3H), 1.75 (s, 3H), 1.65 – 1.59 (m, 2H), 1.51 – 1.40 (m, 2H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 161.8 (d, $^1J_{C–F}$ = 245.6 Hz), 152.1, 142.5, 132.9 (d, $^4J_{C–F}$ = 3.3 Hz), 130.7 (d, $^3J_{C–F}$ = 7.9 Hz), 120.4, 114.5 (d, $^2J_{C–F}$ = 21.4 Hz), 98.8, 27.4, 23.4, 22.9, 22.5, 19.6, 18.1.

^{19}F NMR (282 MHz, CD_2Cl_2) δ -115.5.

FTIR (Neat film NaCl): 3057, 2988, 2929, 2859, 2842, 1673, 1603, 1507, 1224, 1149, 1136, 840, 789.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{16}H_{19}FO$ 246.1420; Found 246.1412



1-Fluoro-4-(2-methyl-1-(octyloxy)prop-1-en-1-yl)benzene (4.48)

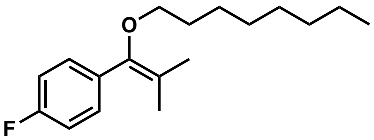
Synthesized according to a modified general procedure 4.8.2.6.2 from 0.20 mmol of vinyl tosylate **4.86** and methyloctylether where 1,2-DFB was used as solvent instead of trifluorotoluene. Purified crude by silica flash column chromatography (0.2% triethylamine/hexanes) to give pure product **4.48** as a yellow oil (38.8 mg, 65% yield).

δ ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.37 – 7.27 (m, 4H), 7.25 (app s, 1H), 3.35 (t, *J* = 6.6 Hz, 2H), 2.42 (dd, *J* = 6.9, 4.7 Hz, 2H), 2.19 – 2.00 (m, 2H), 1.54 (tdt, *J* = 22.6, 12.0, 5.0 Hz, 8H), 1.35 – 1.20 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz CDCl$_3$) δ 145.5, 136.0, 129.6, 127.8, 127.3, 123.8, 69.4, 31.8, 29.9, 29.8, 29.4, 29.2, 28.2, 27.8, 27.6, 26.9, 26.0, 22.6, 14.1.

FTIR (Neat film NaCl): 2955, 2925, 2856, 1669, 1602, 1506, 1224, 1154, 1142, 841, 812.

HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{21}H_{32}O$ 300.2453; Found 300.2456



(Cyclohexylidene(octyloxy)methyl)benzene (4.49)

Synthesized according to a modified general procedure 4.8.2.6.2 from 0.20 mmol of vinyl tosylate **4.87** and methyloctylether where 1,2-DFB was used as solvent instead of trifluorotoluene. Purified by silica flash column chromatography (0.5:1:98.5 triethylamine:diethyl ether:hexanes) to give pure product **4.49** as a yellow oil (22.8 mg, 41% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.30 – 7.27 (m, 2H), 7.02 (dd, *J* = 9.7, 7.8 Hz, 2H), 3.35 (t, *J* = 6.6 Hz, 2H), 1.83 (s, 3H), 1.63 (s, 3H), 1.58 – 1.51 (m, 2H), 1.35 – 1.20 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 161.9 (d, $^{1}J_{C\text{–}F}$ = 246.2 Hz), 146.9, 132.1 (d, $^{4}J_{C\text{–}F}$ = 3.4 Hz), 131.1 (d, $^{3}J_{C\text{–}F}$ = 8.0 Hz), 115.9, 114.8 (d, $^{2}J_{C\text{–}F}$ = 21.3 Hz), 69.4, 31.8, 29.8, 29.4, 29.2, 26.1, 22.6, 19.7, 17.7, 14.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -114.63.

FTIR (Neat film NaCl): 3057, 3021, 2954, 2922, 2852, 1662, 1599, 1444, 1211, 1121, 775, 700.

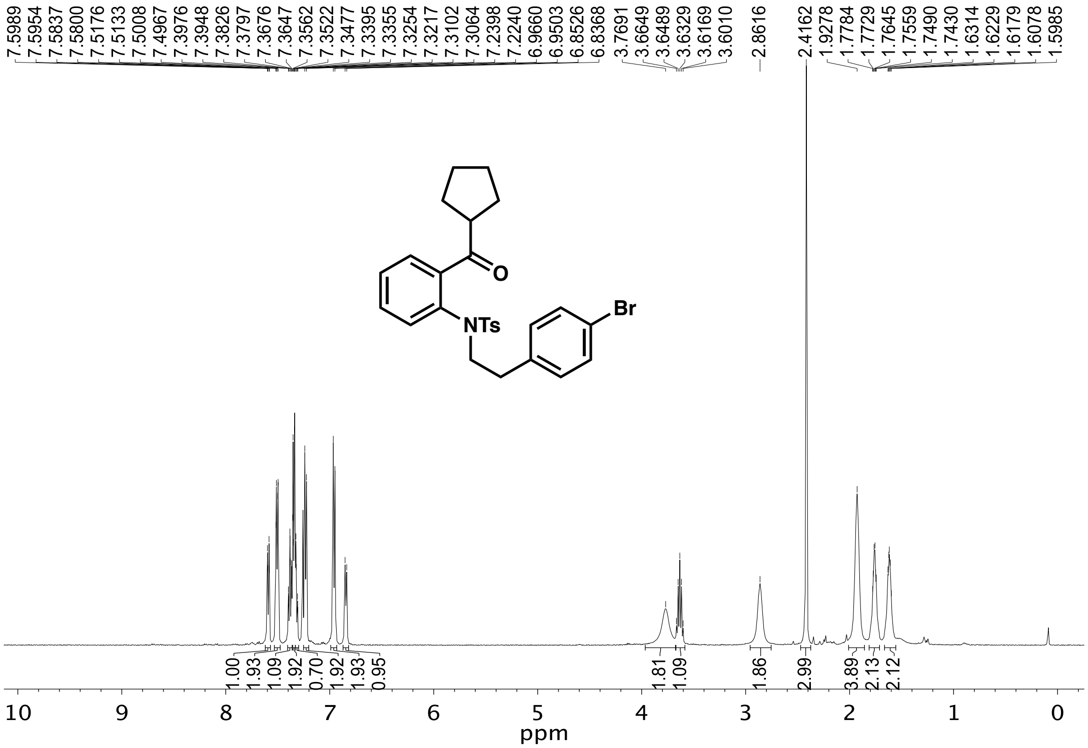
HR-MS (CI-MS) m/z: [M]+ Calc'd for $C_{18}H_{27}FO$ 278.2046; Found 278.2046.

4.9 Spectra Relevant to Chapter Four:

Vinyl Tosylates as Vinyl Cation Precursors Enable Broad Heterocycle Synthesis, as well as Intermolecular Trapping by Carbon and Oxygen Based Nucleophiles

(Unpublished Work)

Zhenqi Zhao, Chloe G. Williams, Stasik Popov, Lee Joon Kim, Jonathan Wong, and Hosea M. Nelson



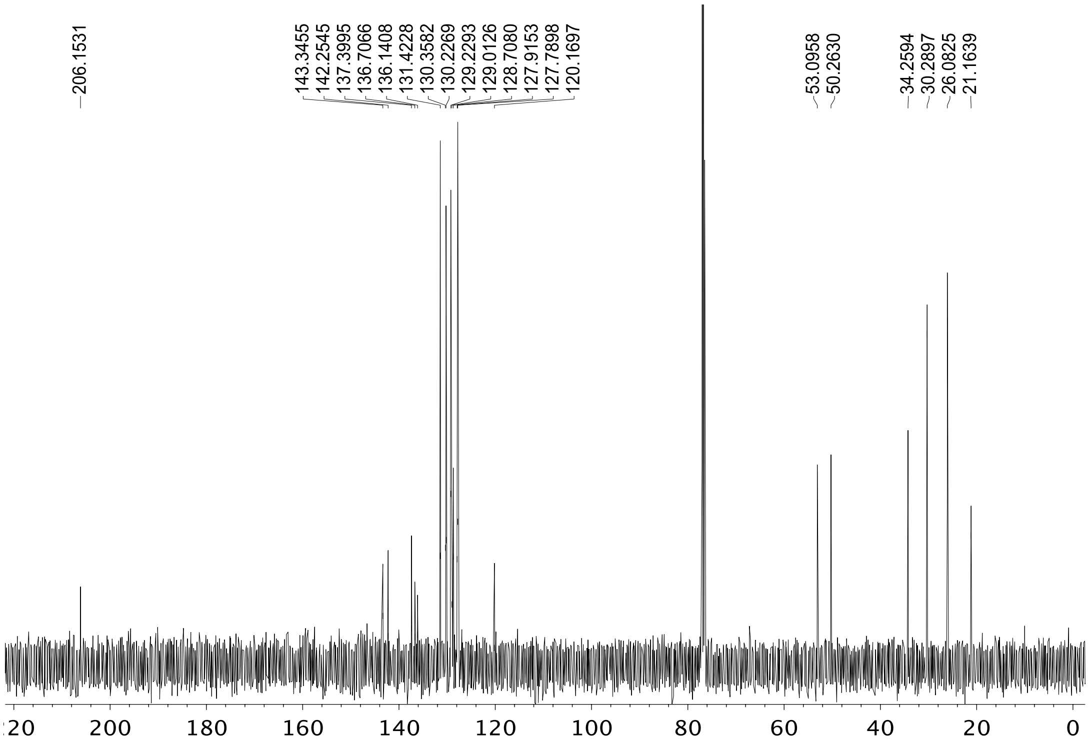


Figure 4.10 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.58**.

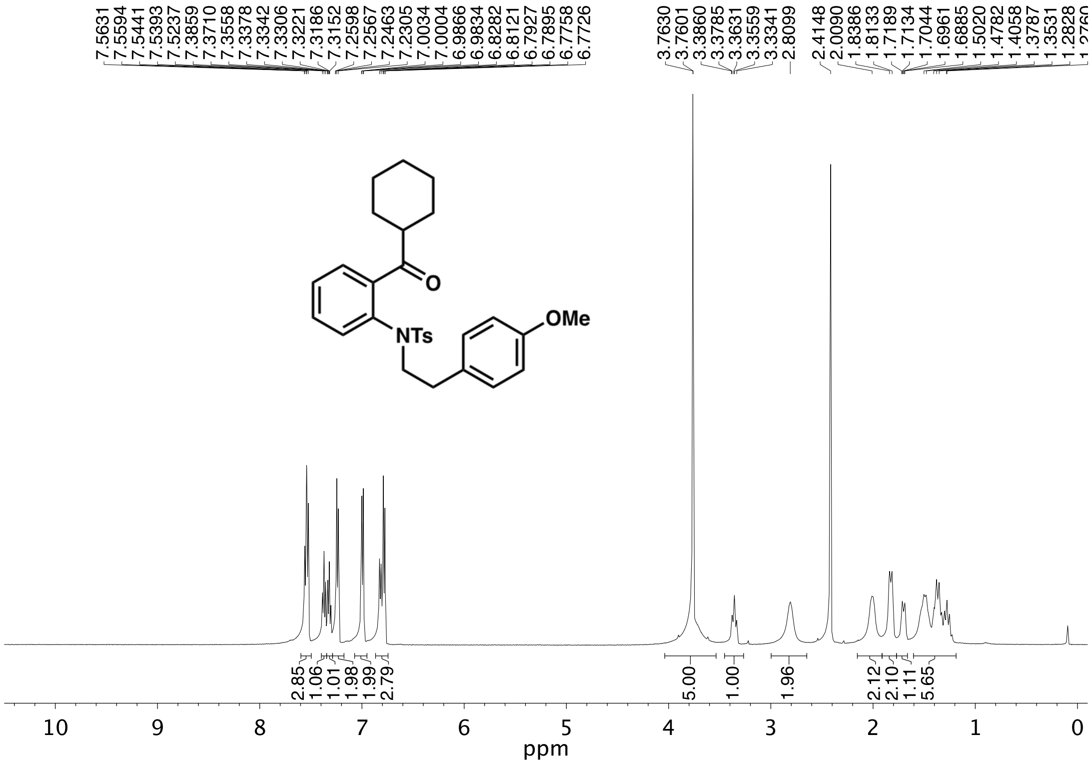


Figure 4.11 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.59**.

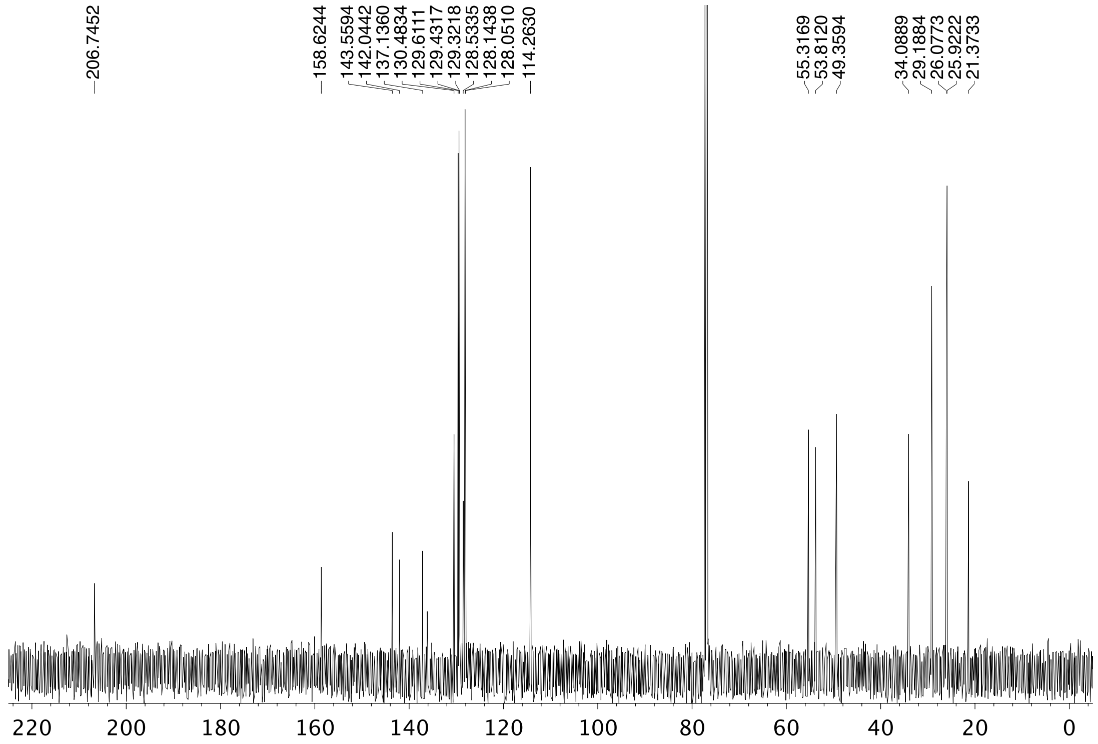


Figure 4.12 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.59**.

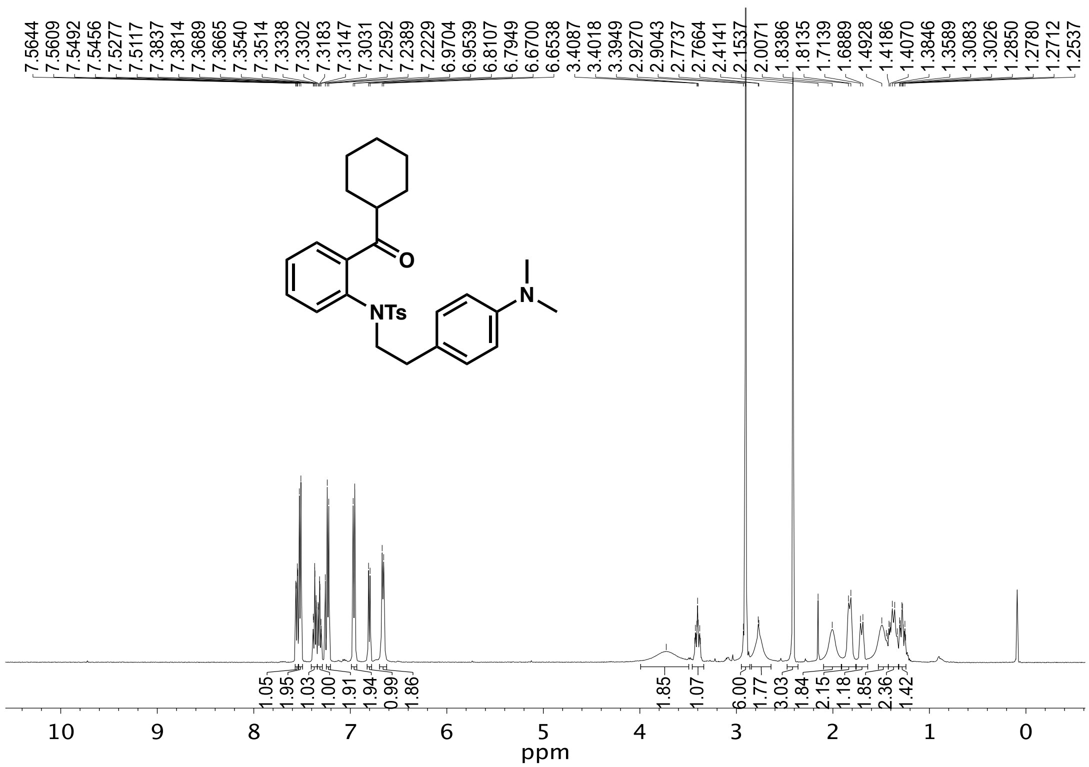


Figure 4.13 ^{1}H NMR (500 MHz, CDCl$_3$, 60 °C) of compound **4.60**.

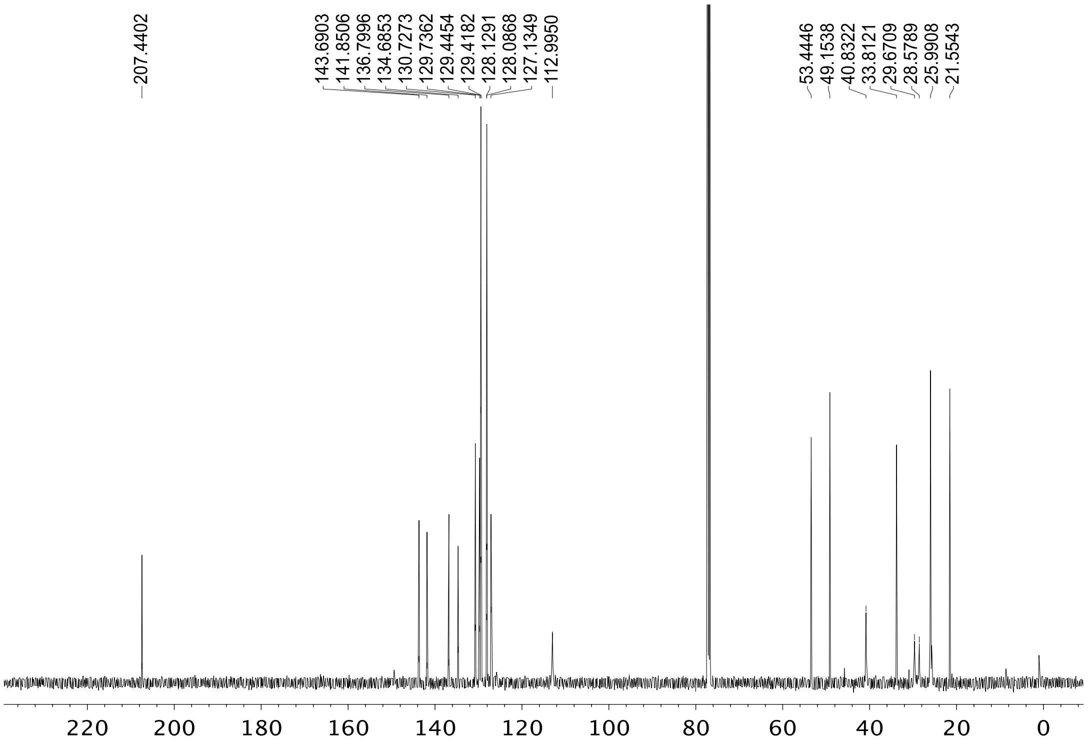


Figure 4.14 ^{13}C NMR (126 MHz, CDCl$_3$, 60 °C) of compound **4.60**.

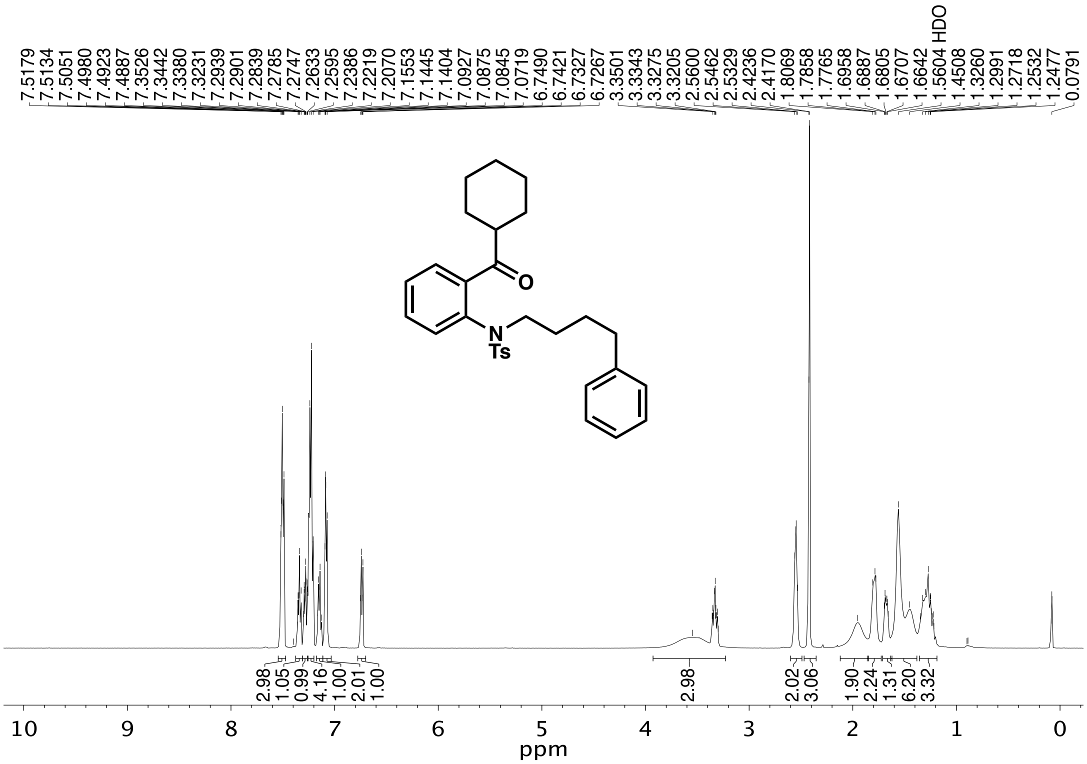


Figure 4.15 ^{1}H NMR (500 MHz, CDCl$_3$, 50 °C) of compound **4.61**.

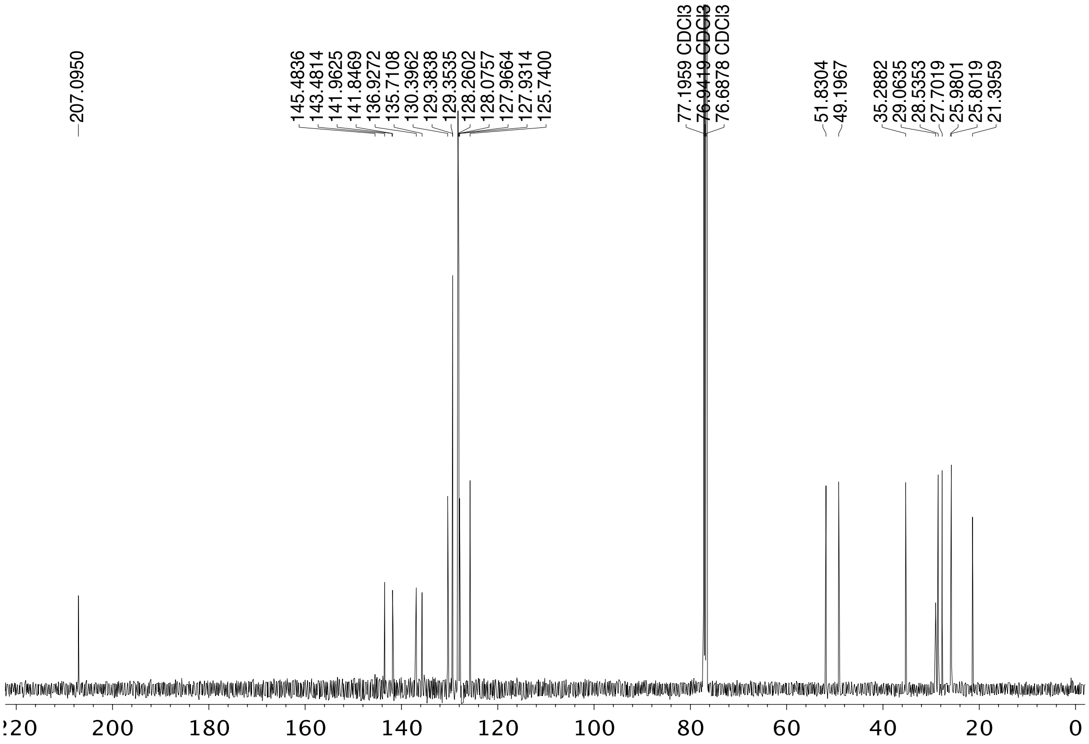


Figure 4.16 ^{13}C NMR (126 MHz, CDCl$_3$, 50 °C) of compound **4.61**.

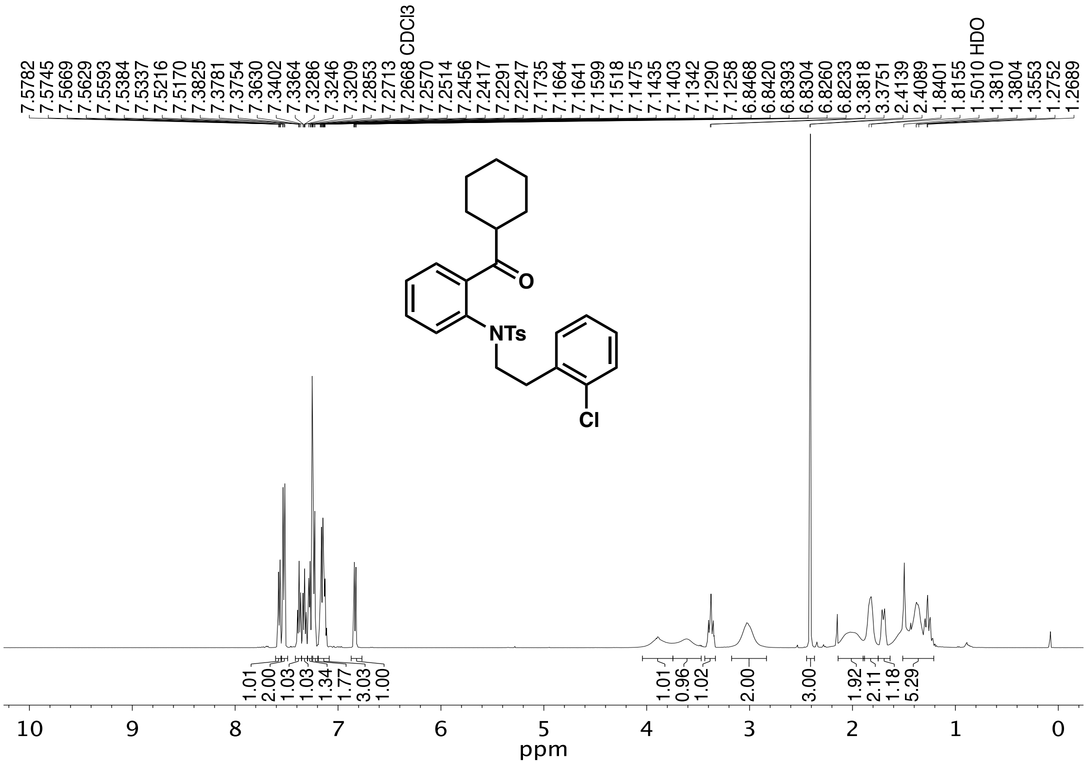


Figure 4.17 ^{1}H NMR (500 MHz, CDCl$_3$, 50 °C) of compound **4.62**.

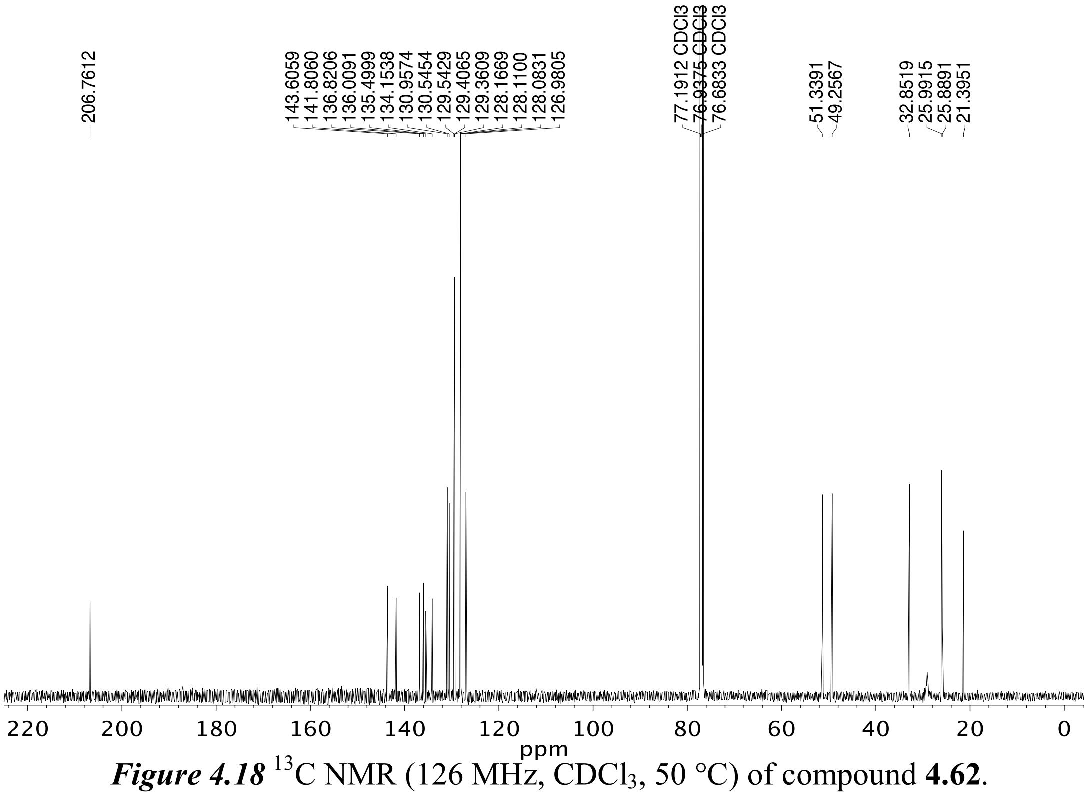


Figure 4.18 ^{13}C NMR (126 MHz, CDCl$_3$, 50 °C) of compound **4.62**.

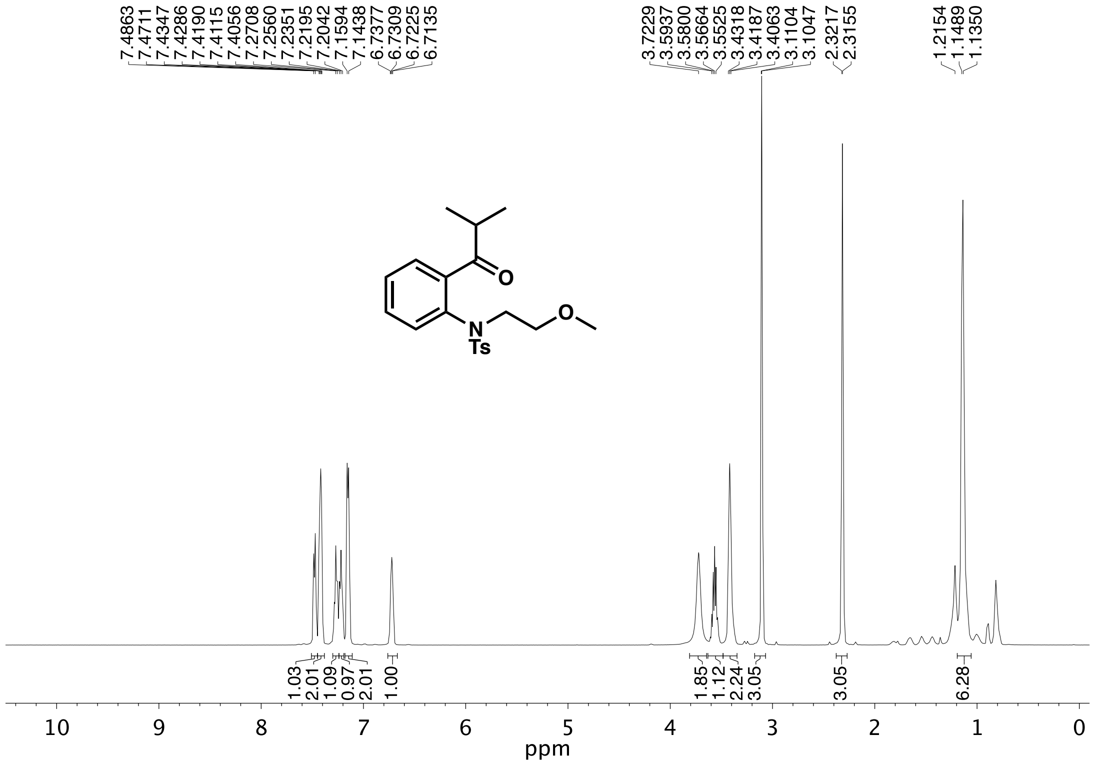


Figure 4.19 ^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) of compound **4.63**.

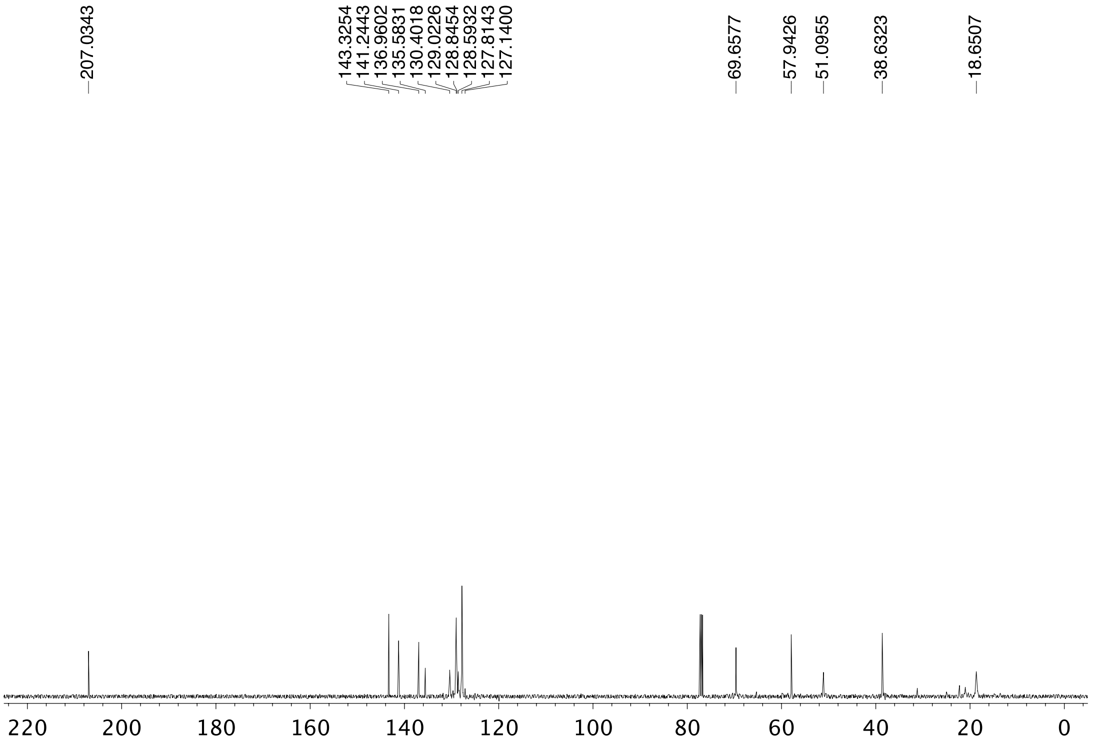


Figure 4.20 ^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) of compound **4.63**.

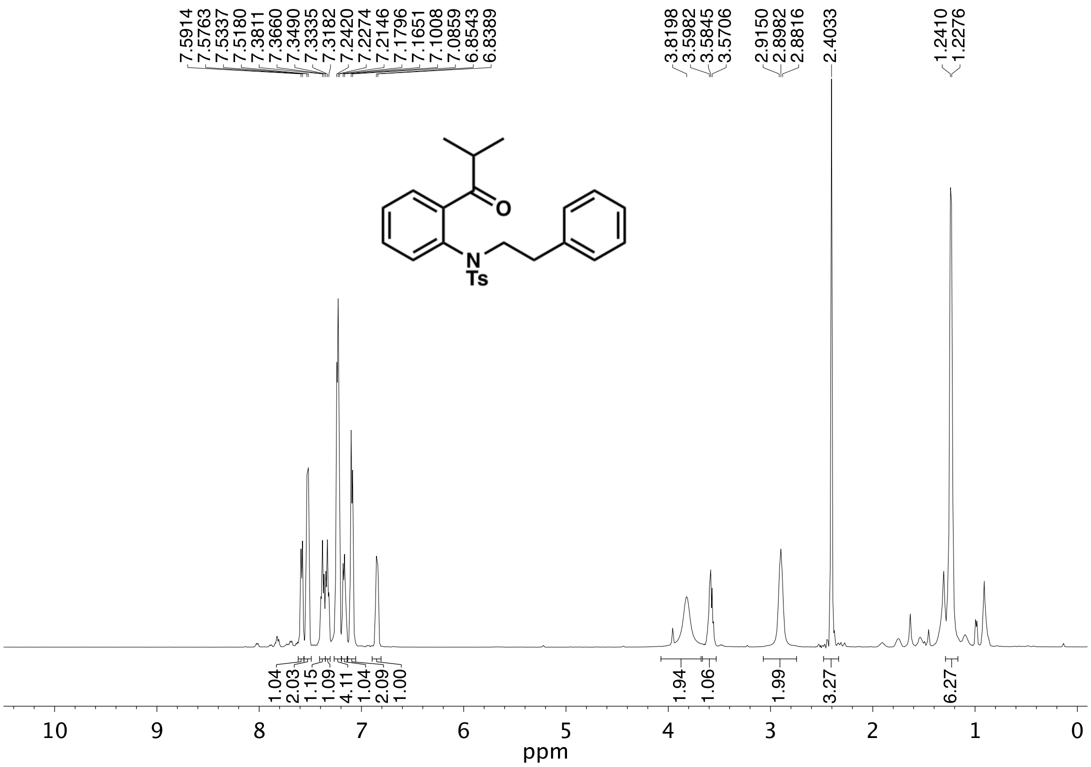


Figure 4.21 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.64**.

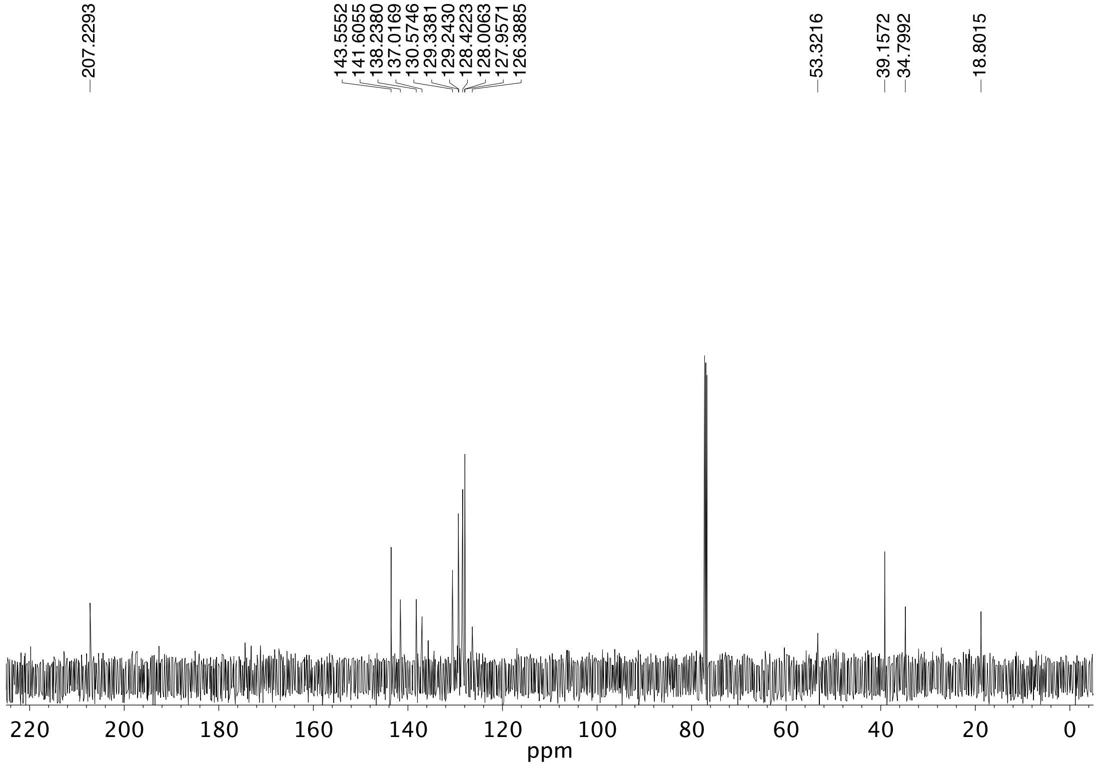


Figure 4.22 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.64**.

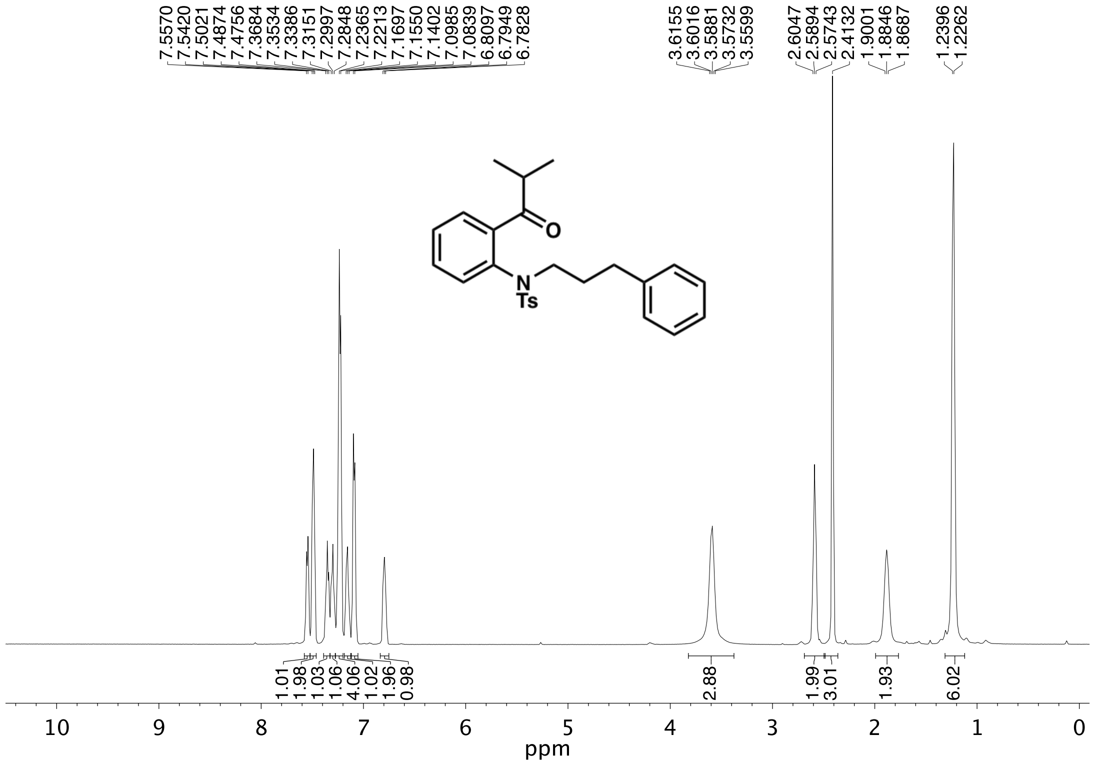


Figure 4.23 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.65**.

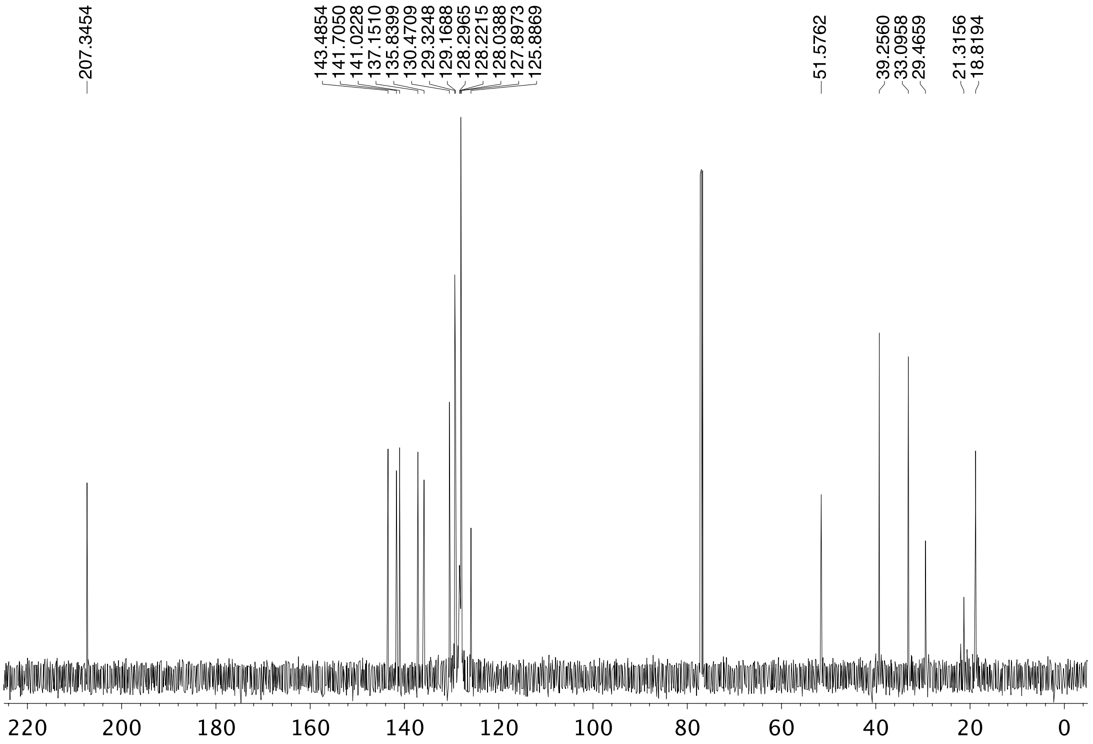


Figure 4.24 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.65**.

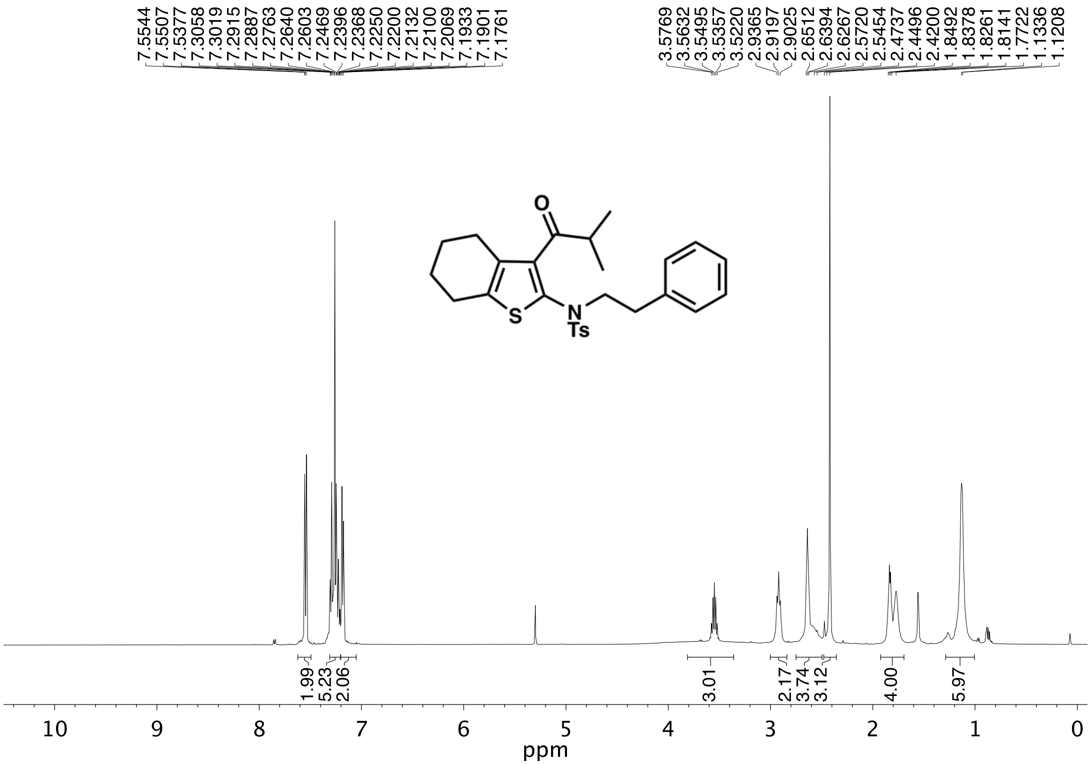


Figure 4.25 ^{1}H NMR (500 MHz, $CDCl_3$, 70 °C) of compound **4.66**.

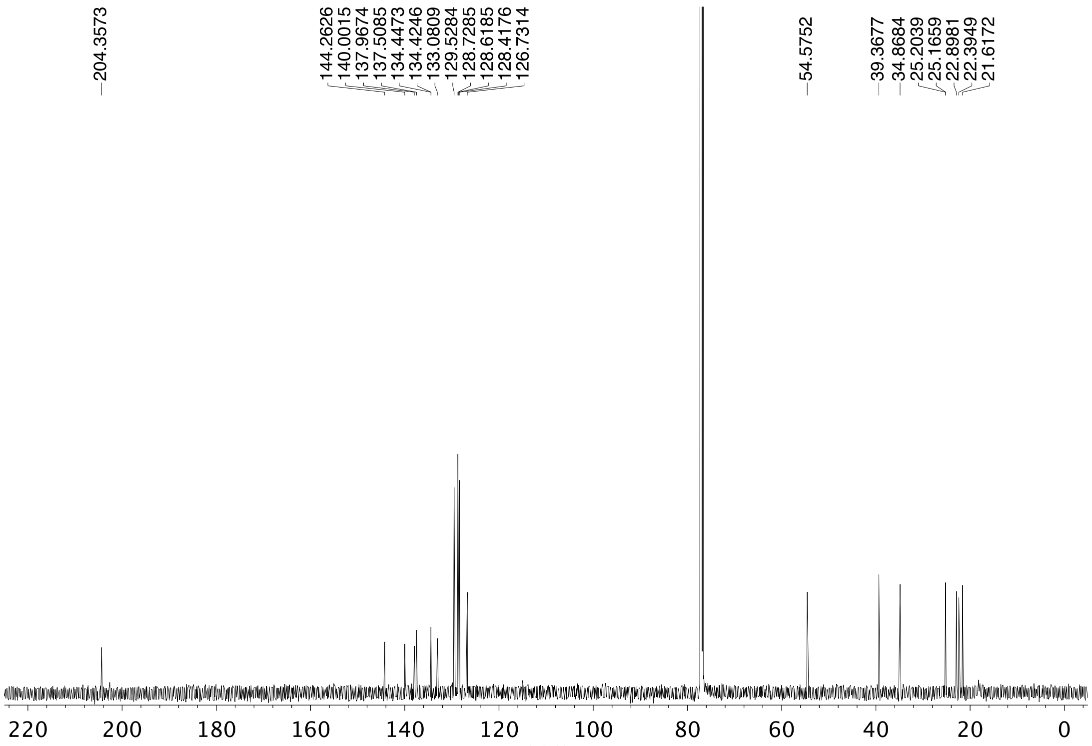


Figure 4.26 ^{13}C NMR (126 MHz, $CDCl_3$, 70 °C) of compound **4.66**.

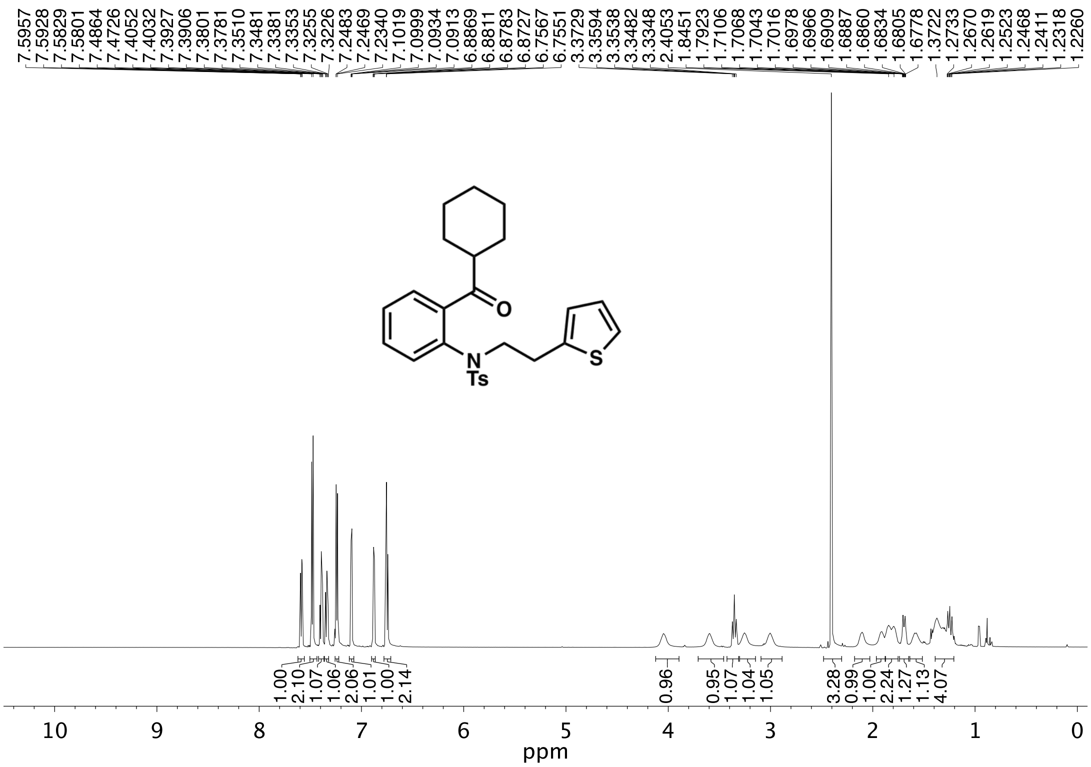


Figure 4.27 ^{1}H NMR (600 MHz, CDCl$_3$) of compound **4.67**.

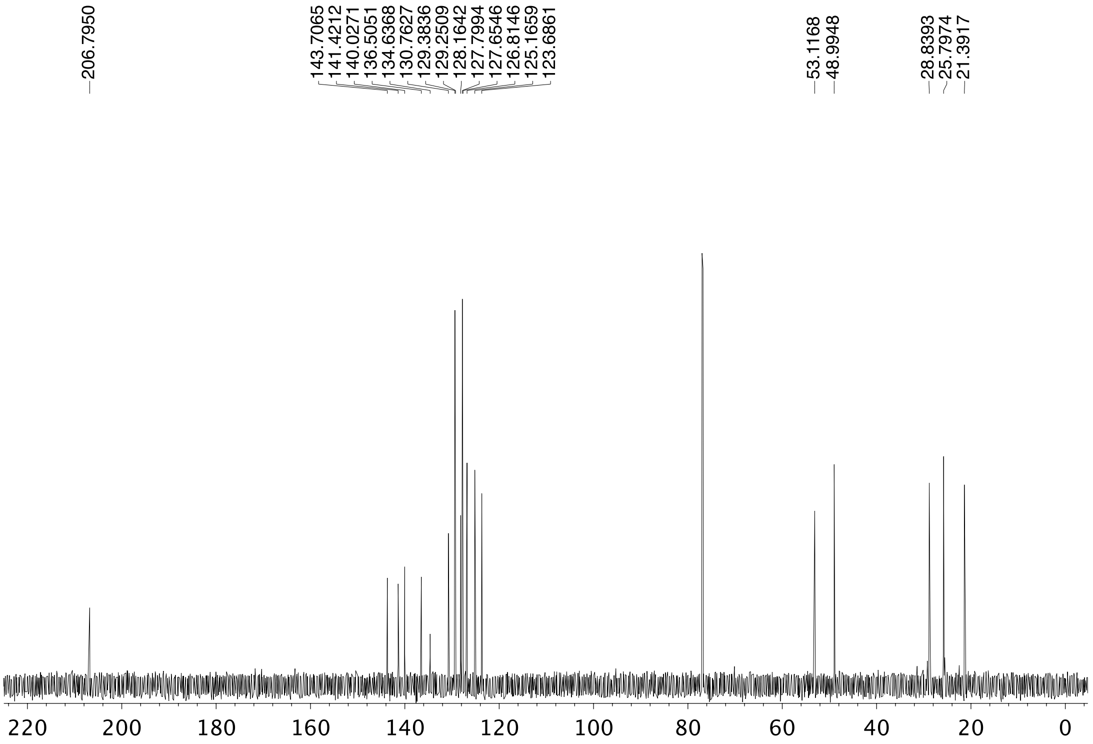


Figure 4.28 ^{13}C NMR (151 MHz, CDCl$_3$) of compound **4.67**.

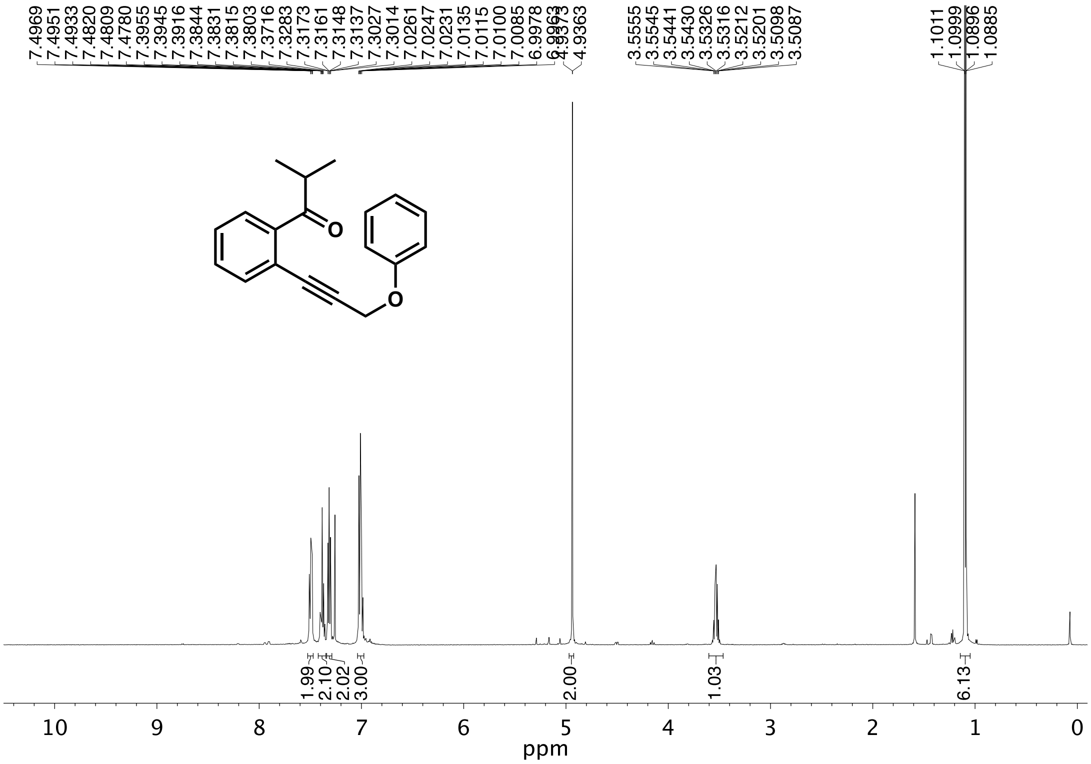


Figure 4.29 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **4.69**.

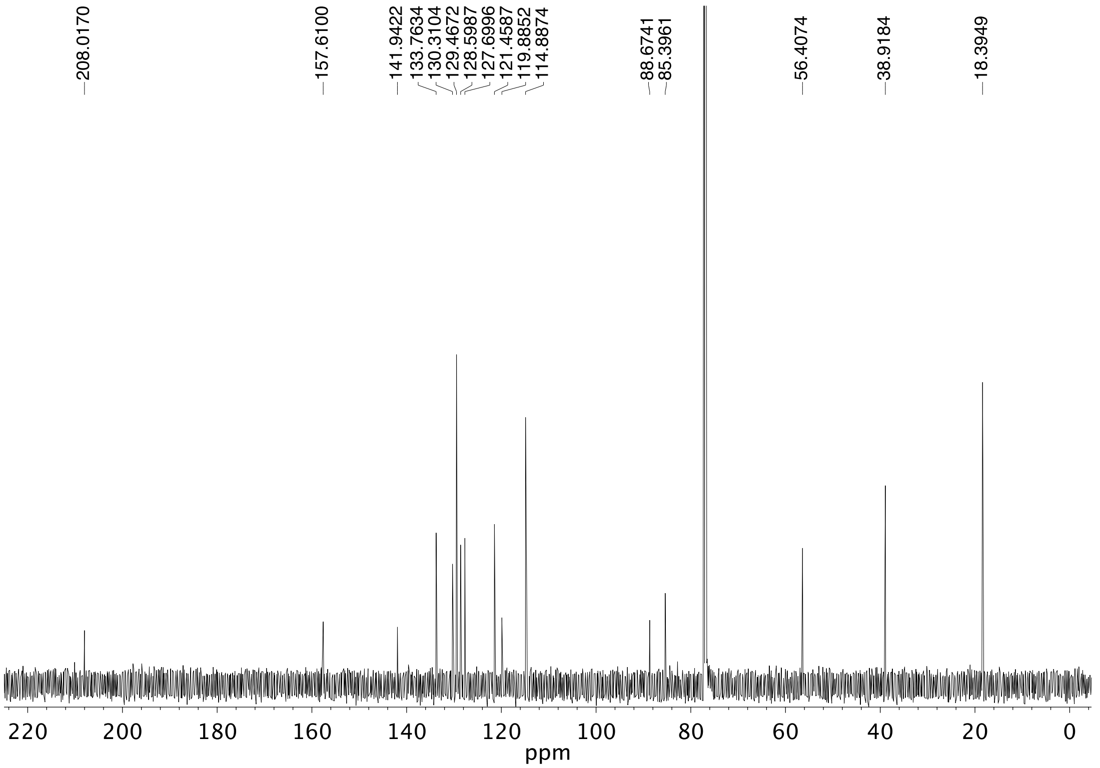


Figure 4.30 ^{13}C NMR (151 MHz, $CDCl_3$) of compound **4.69**.

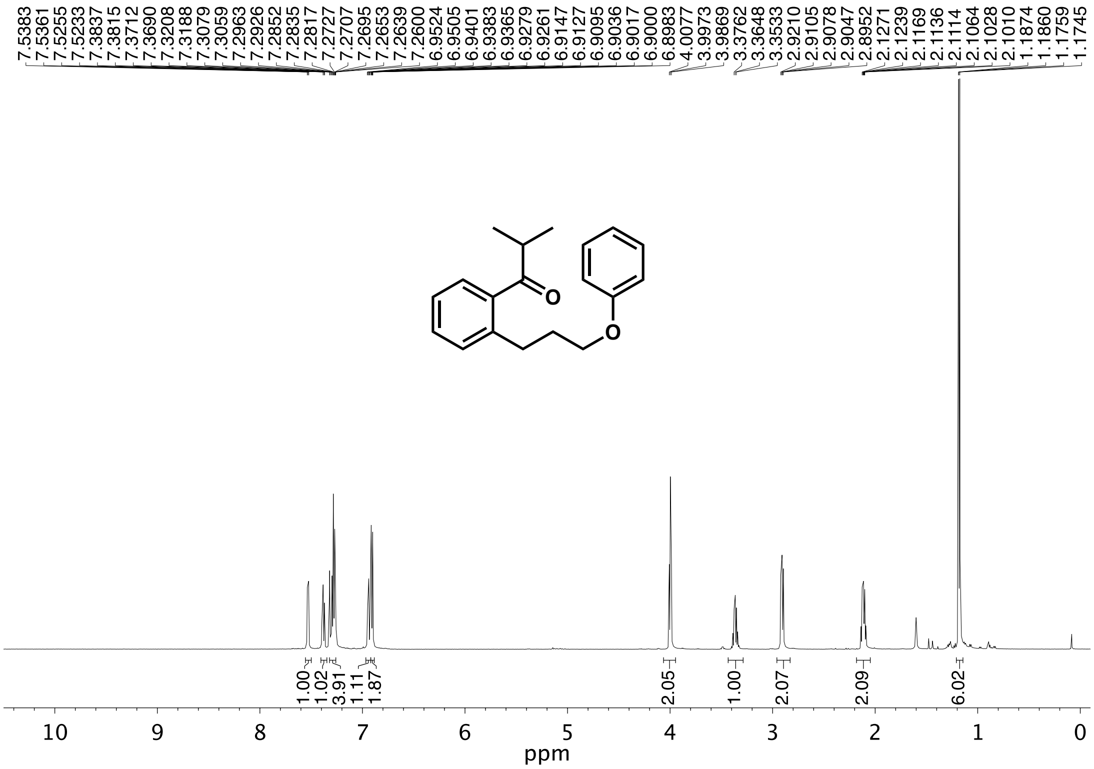


Figure 4.31 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **4.70**.

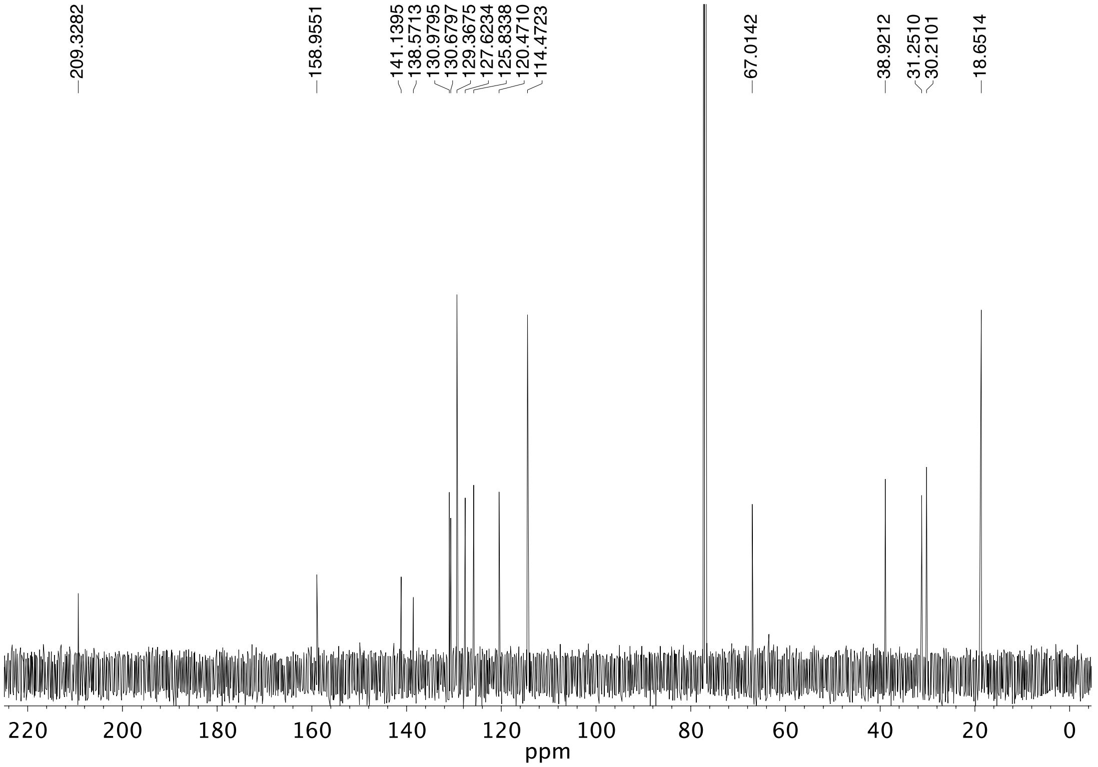


Figure 4.32 ^{13}C NMR (151 MHz, $CDCl_3$) of compound **4.70**.

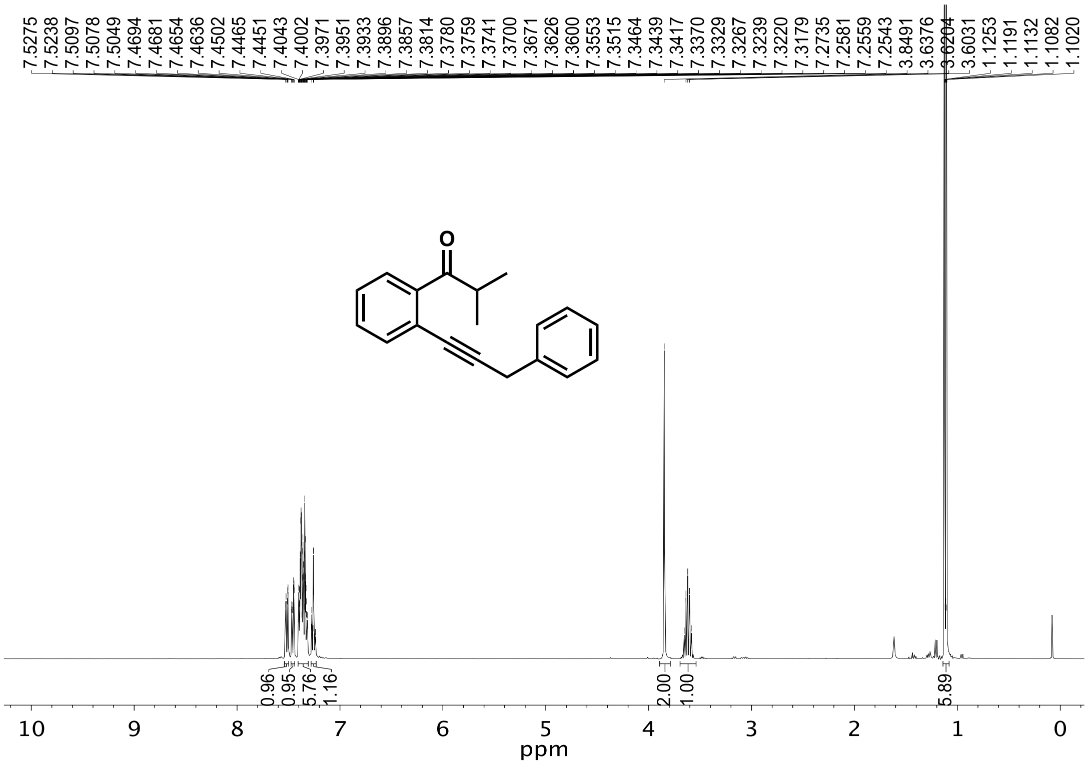


Figure 4.33 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.71**.

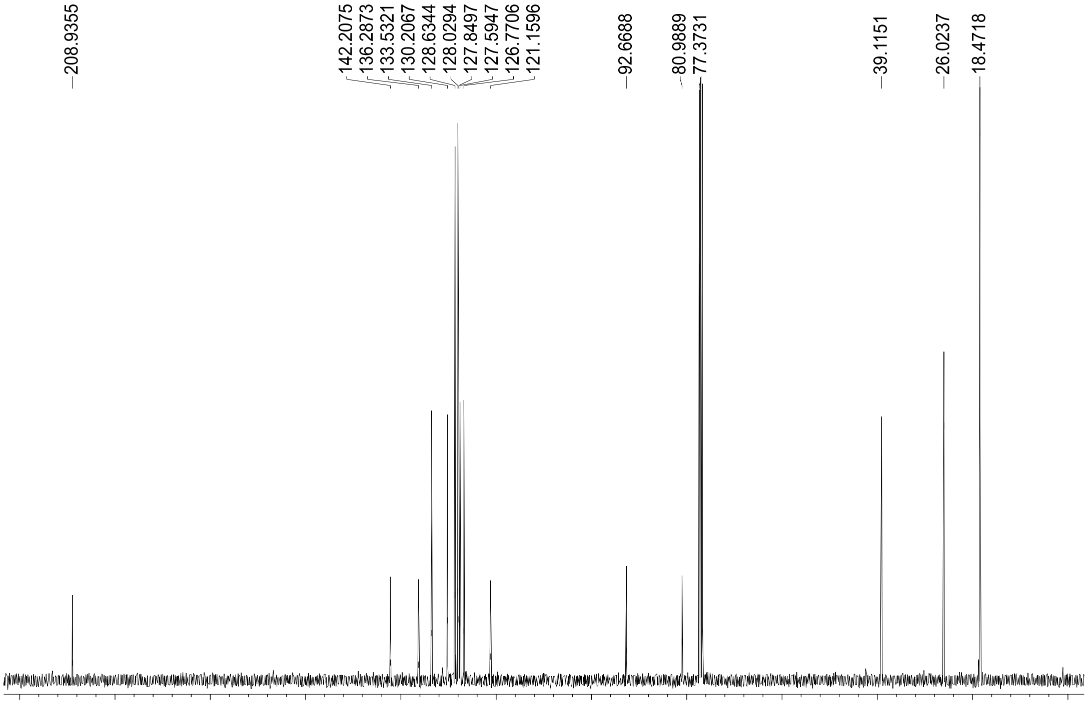


Figure 4.34 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **4.72**.

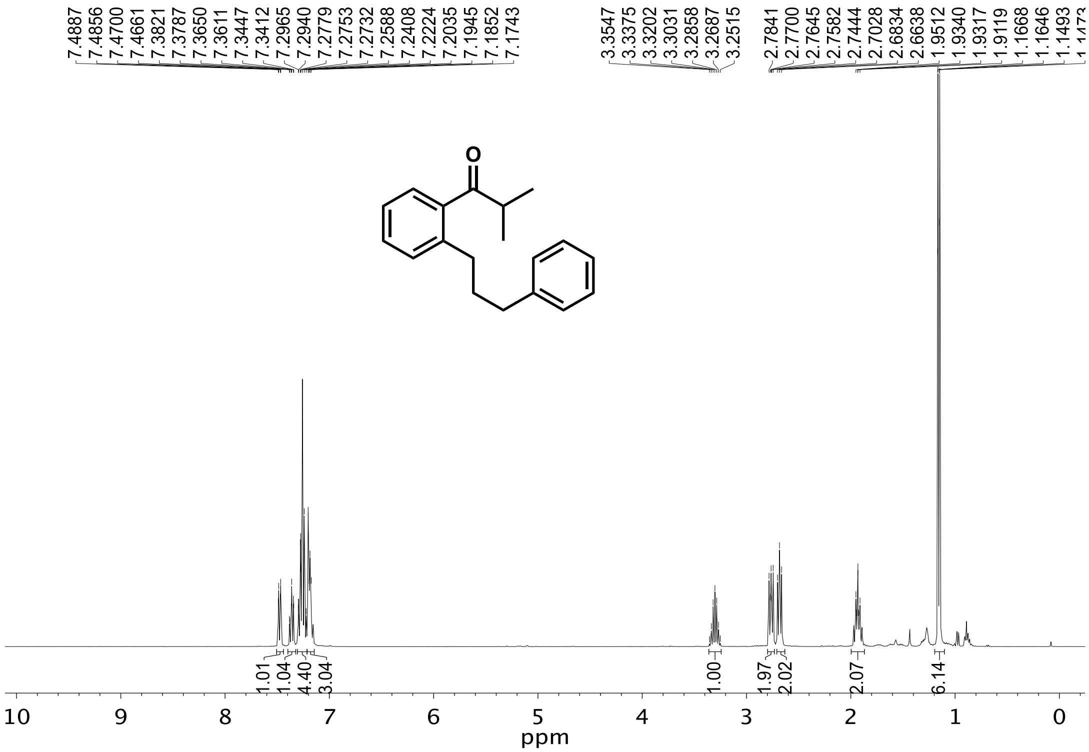


Figure 4.35 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.72**.

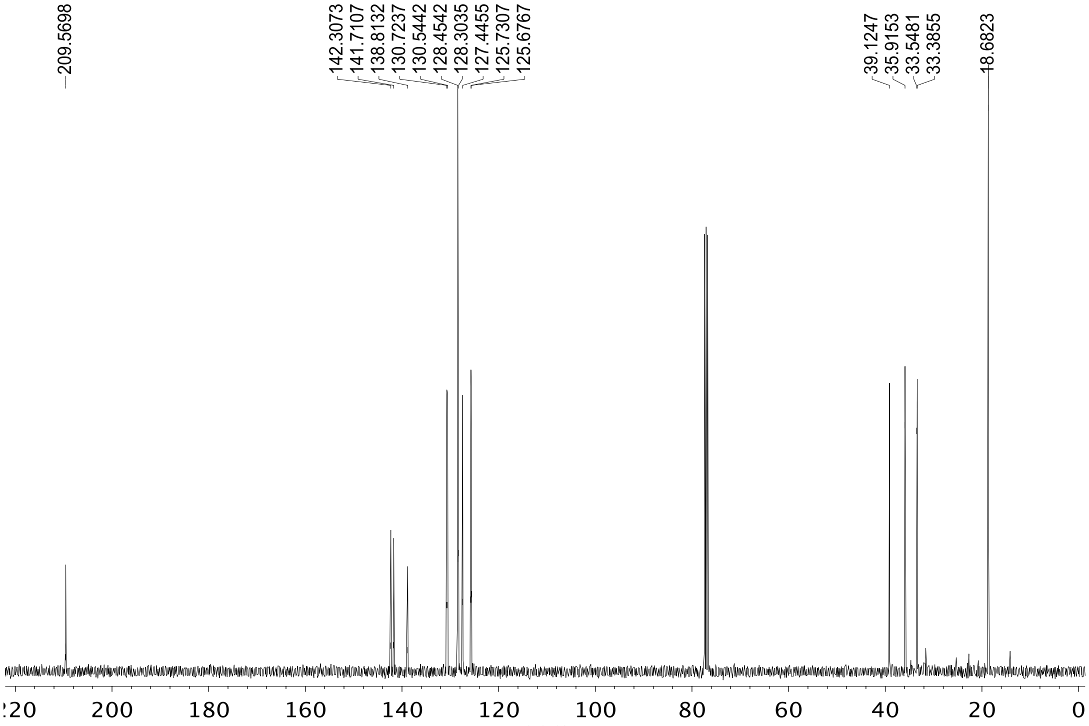


Figure 4.36 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.72**.

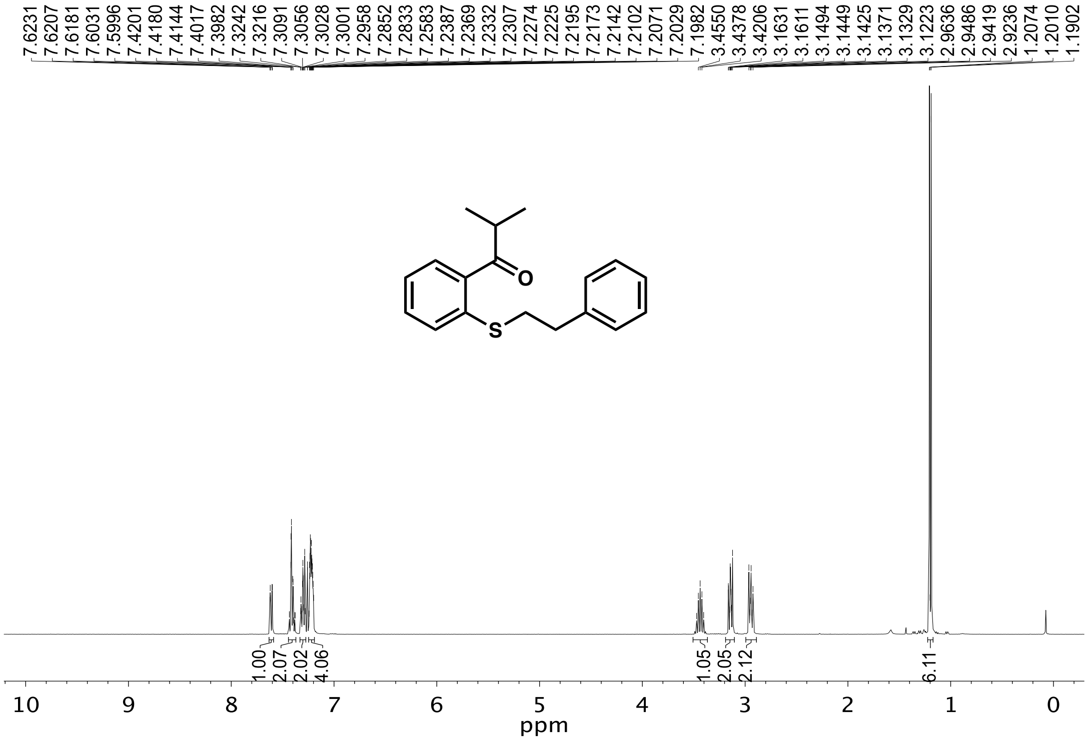


Figure 4.37 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.74**.

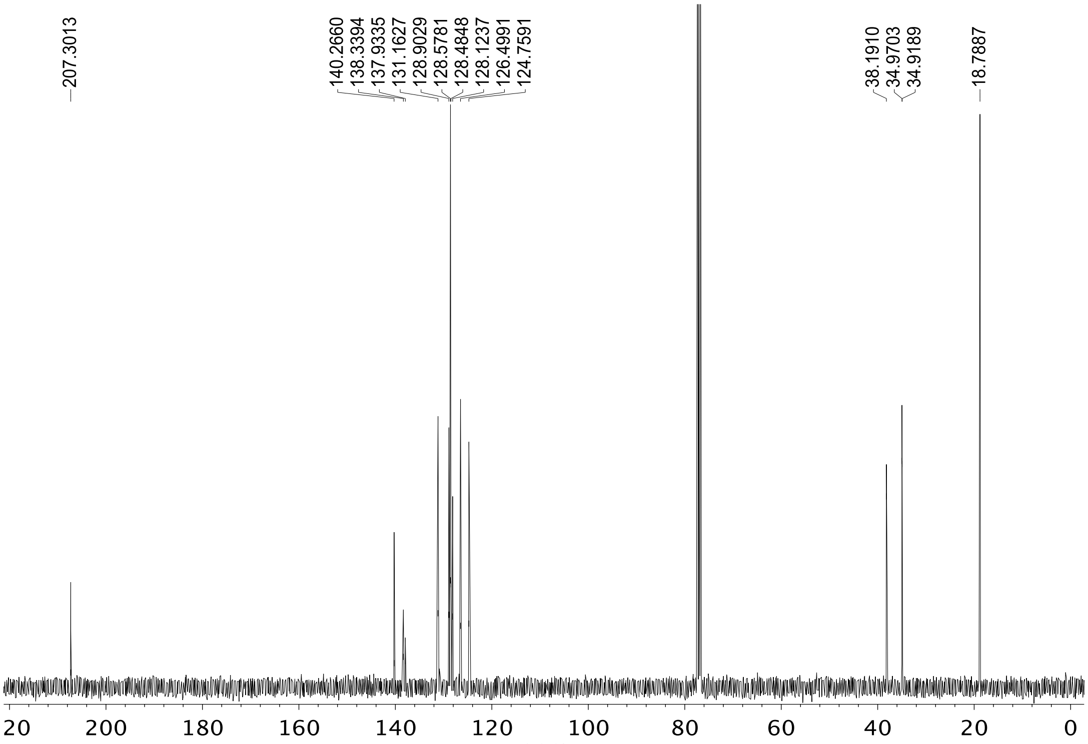


Figure 4.38 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.74**.

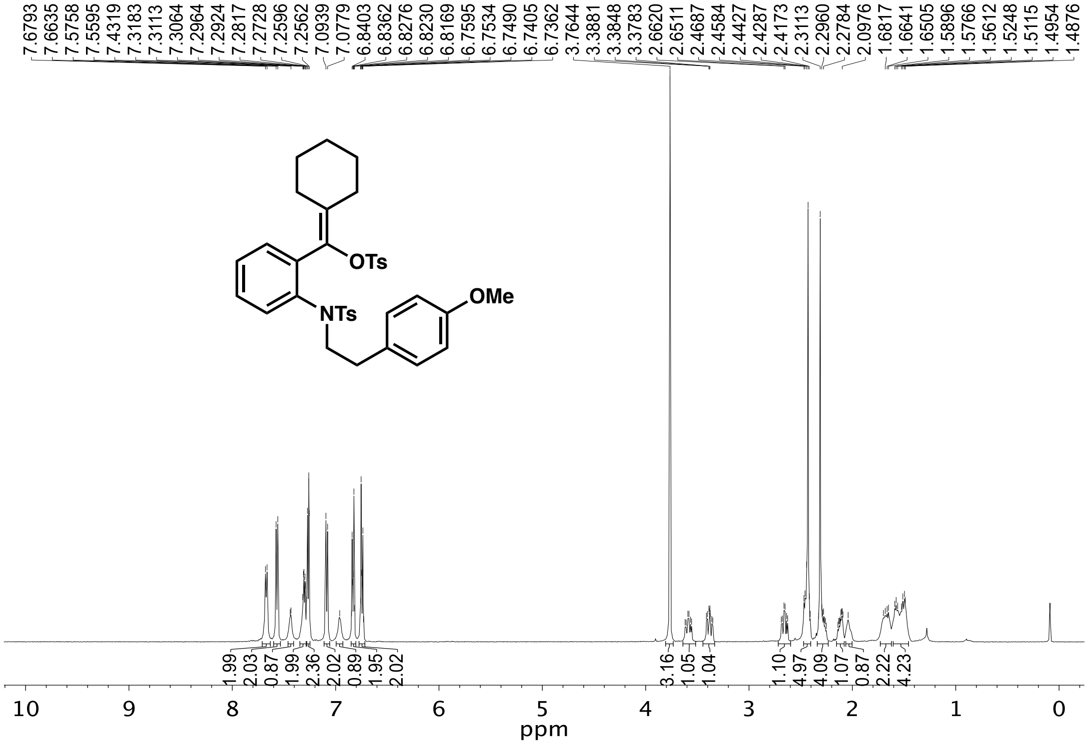


Figure 4.39 ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) of compound **4.75**

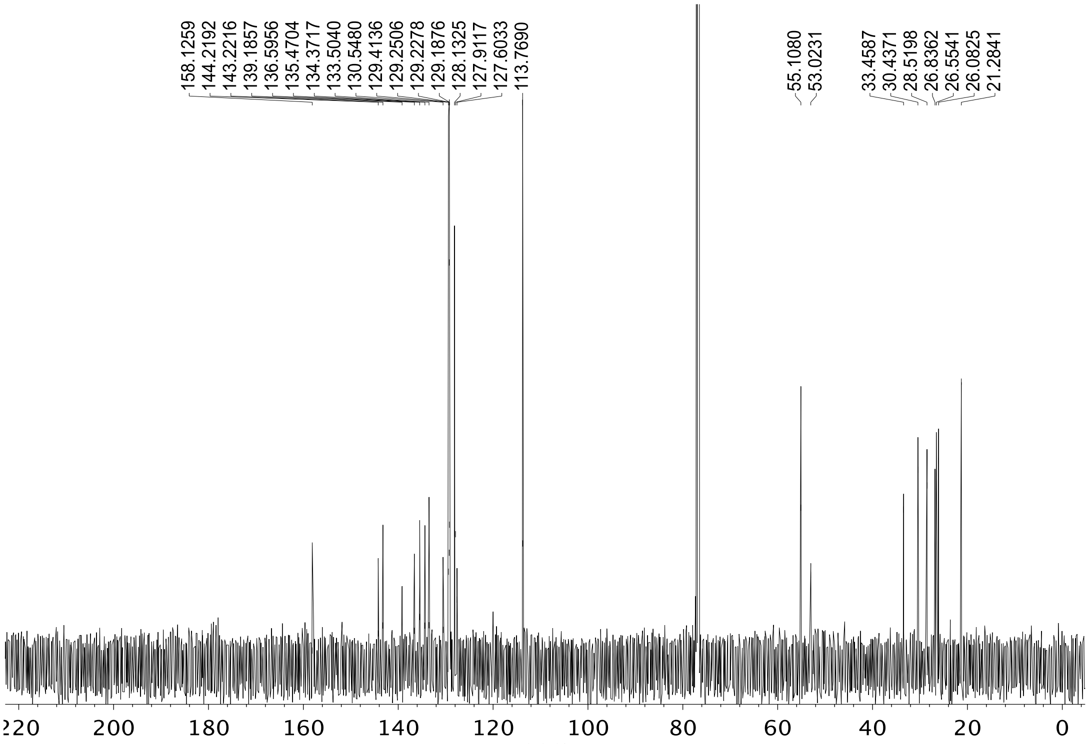


Figure 4.40 ^{13}C NMR (126 MHz, $CDCl_3$, 50 °C) of compound **4.75**.

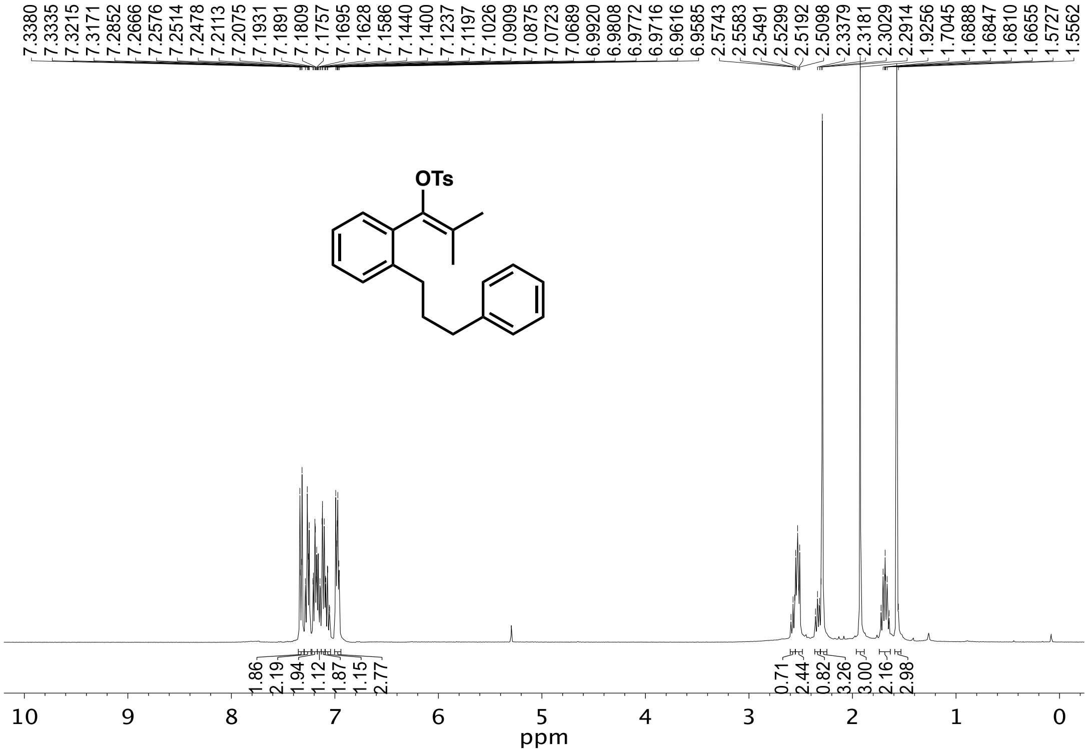


Figure 4.41 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.76**.

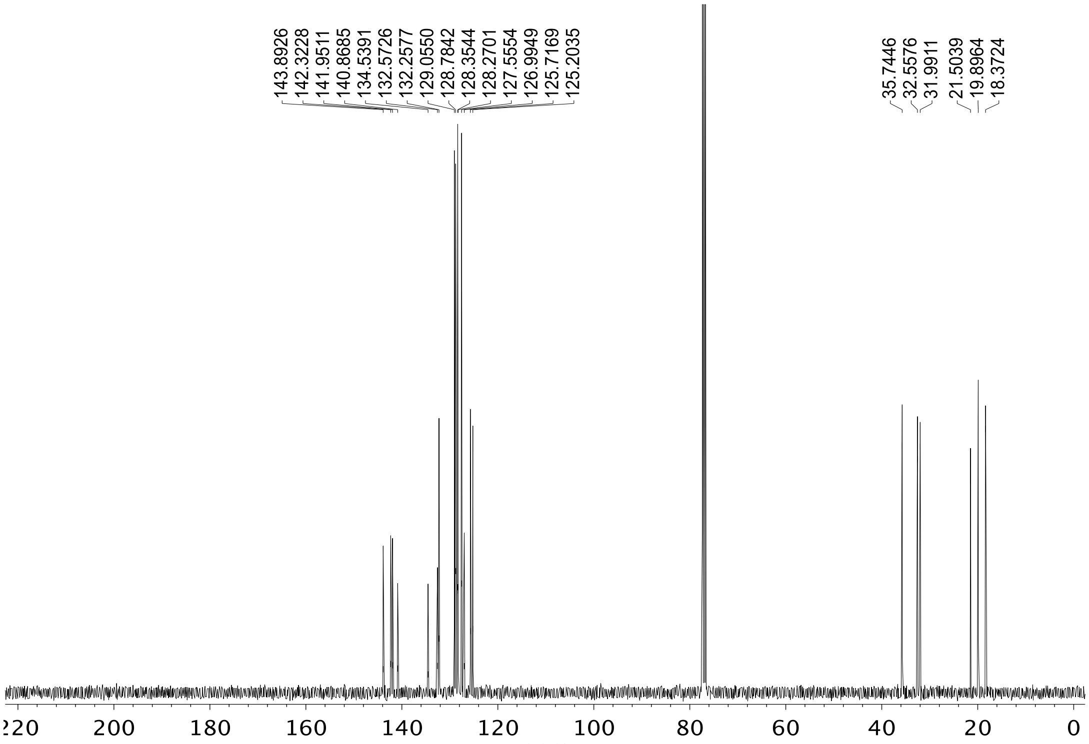


Figure 4.42 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.76**.

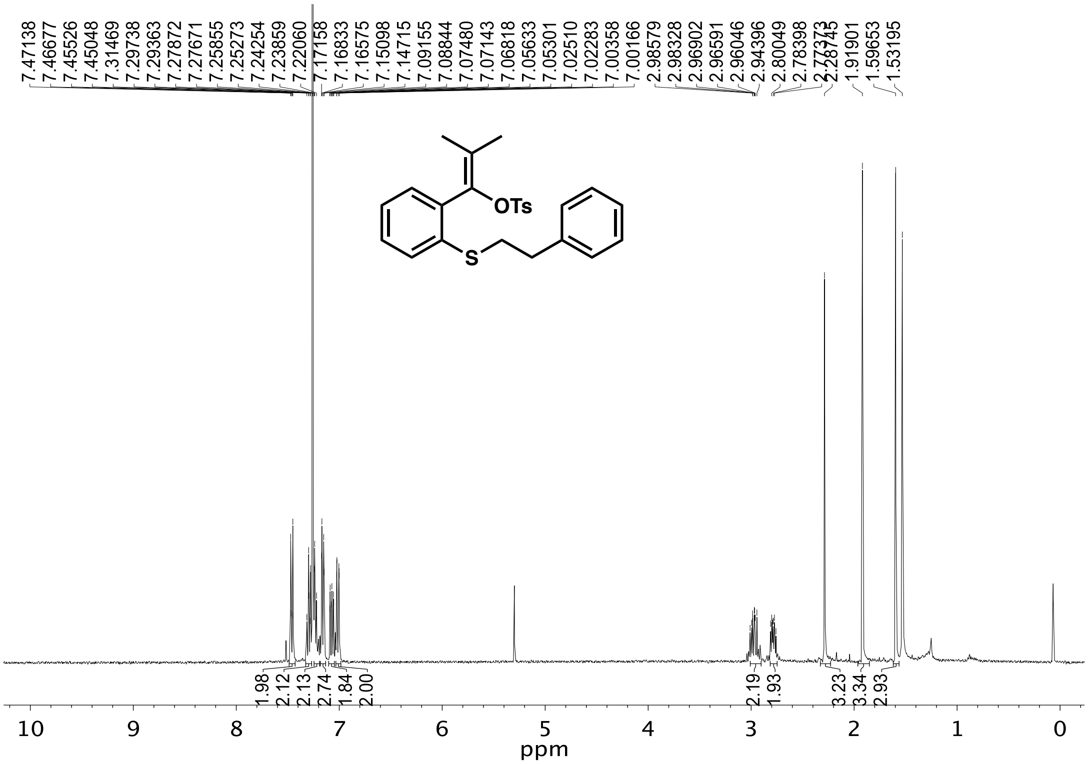


Figure 4.43 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.77**.

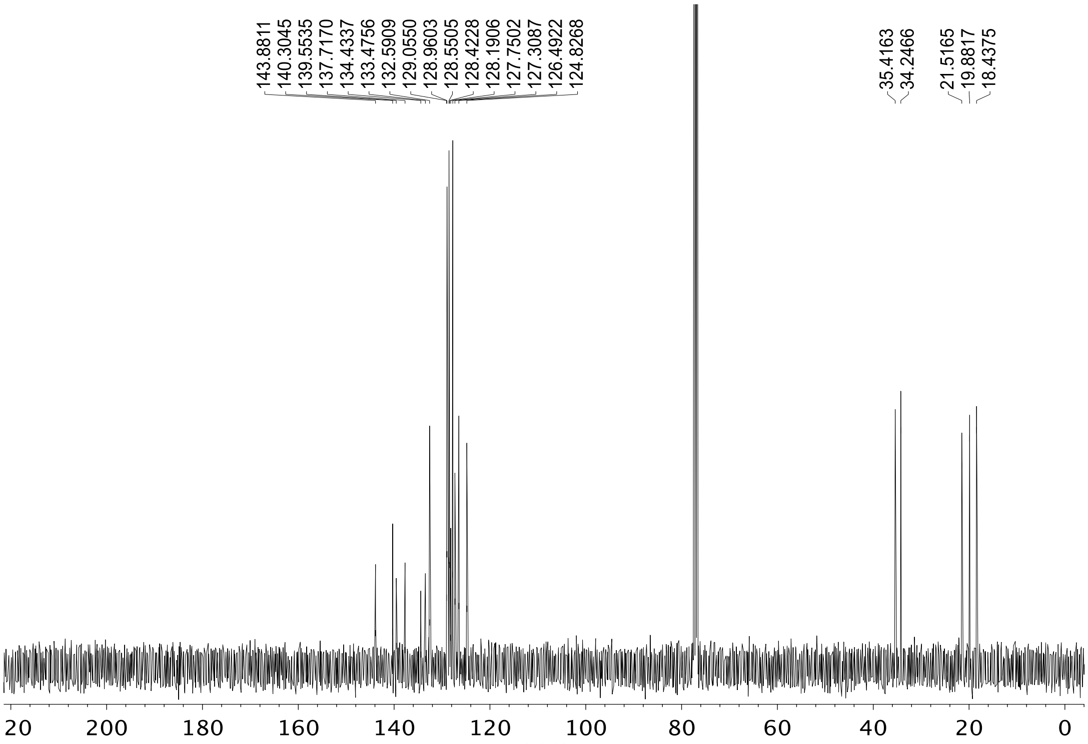


Figure 4.44 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **4.77**.

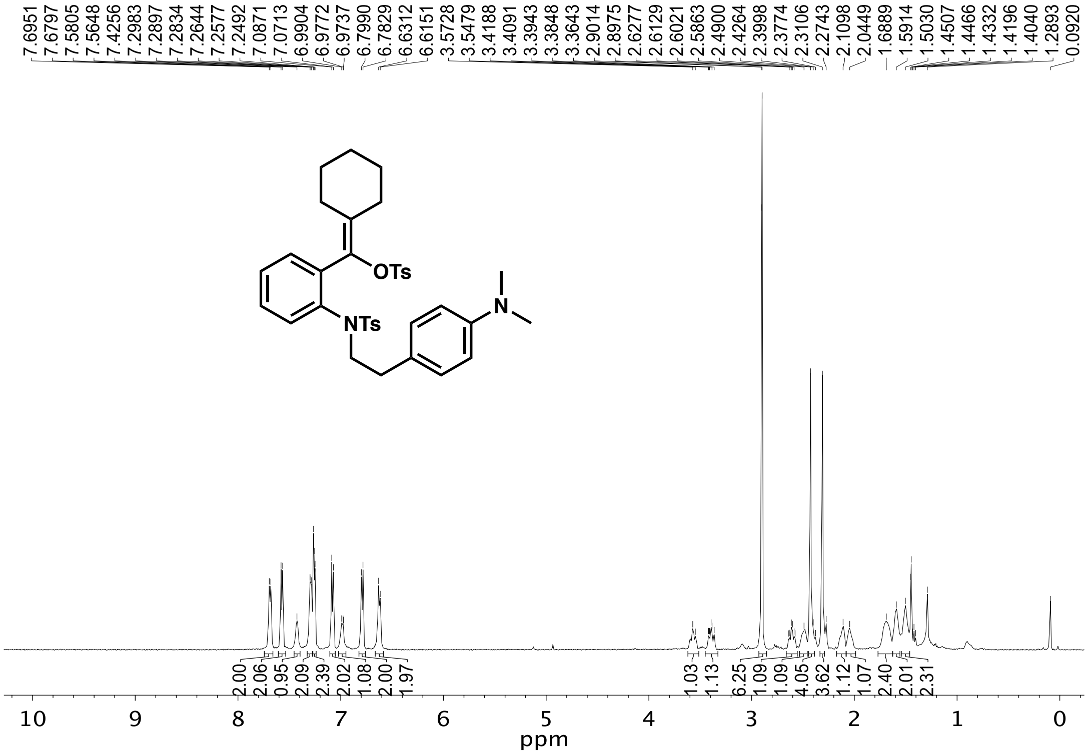


Figure 4.45 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.78**

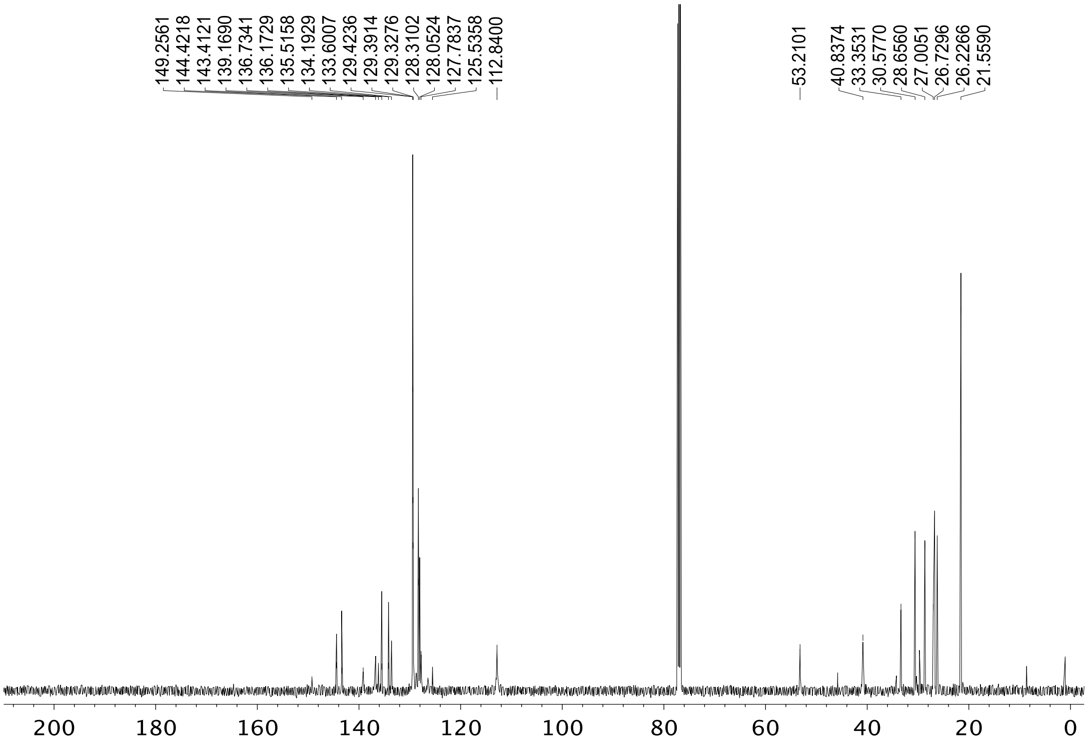


Figure 4.46 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.78**.

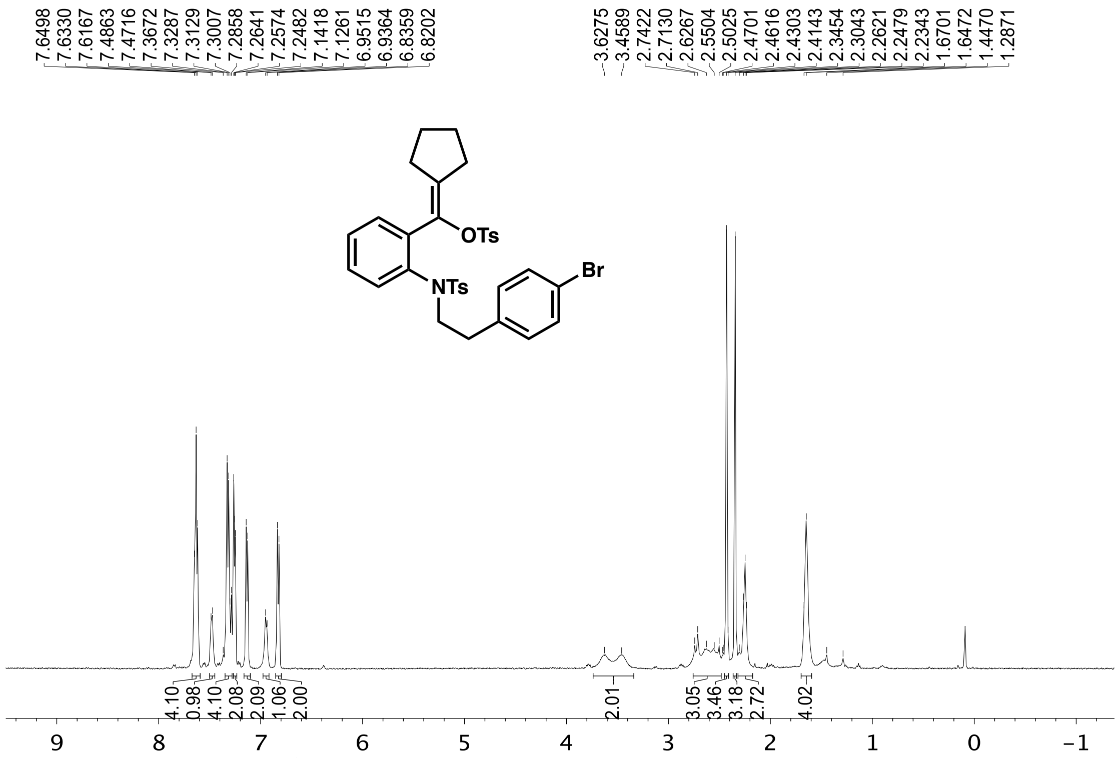


Figure 4.47 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.79**

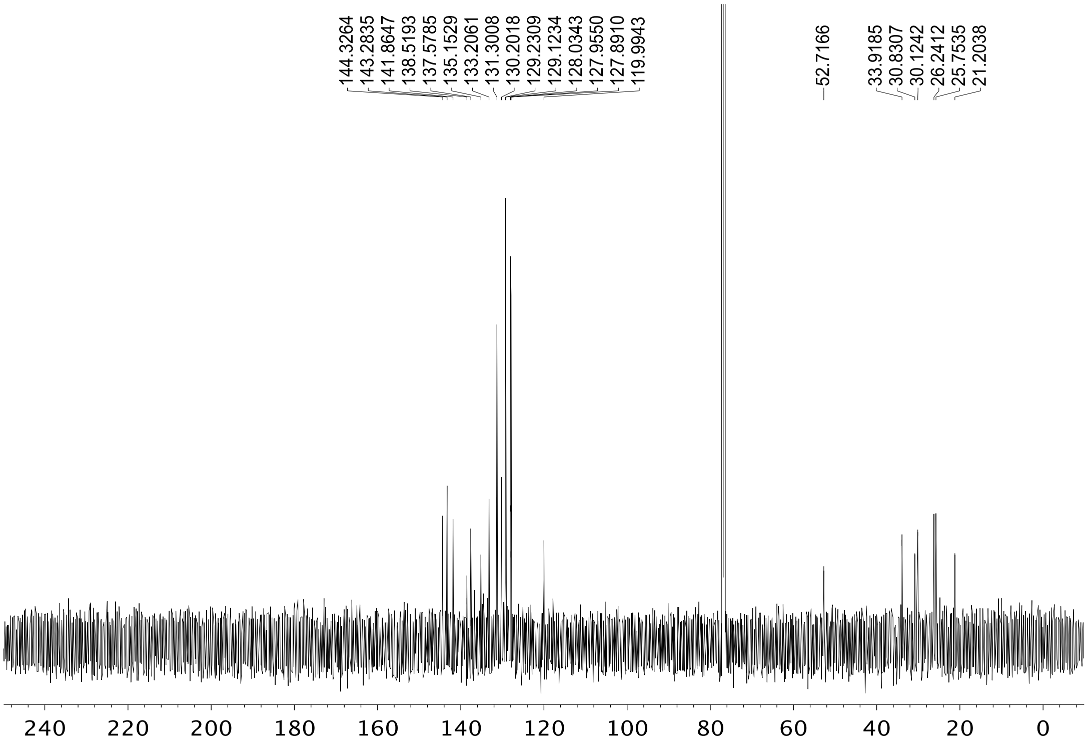


Figure 4.48 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.79**.

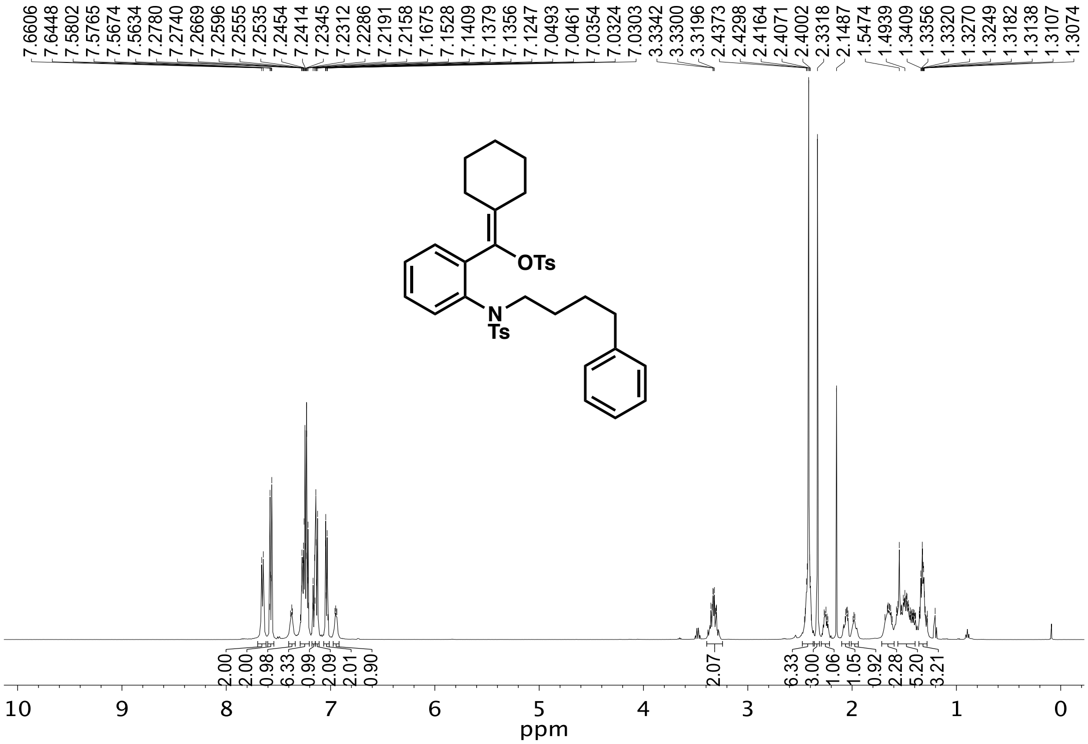


Figure 4.49 ^{1}H NMR (500 MHz, CDCl$_3$, 55 °C) of compound **4.80**

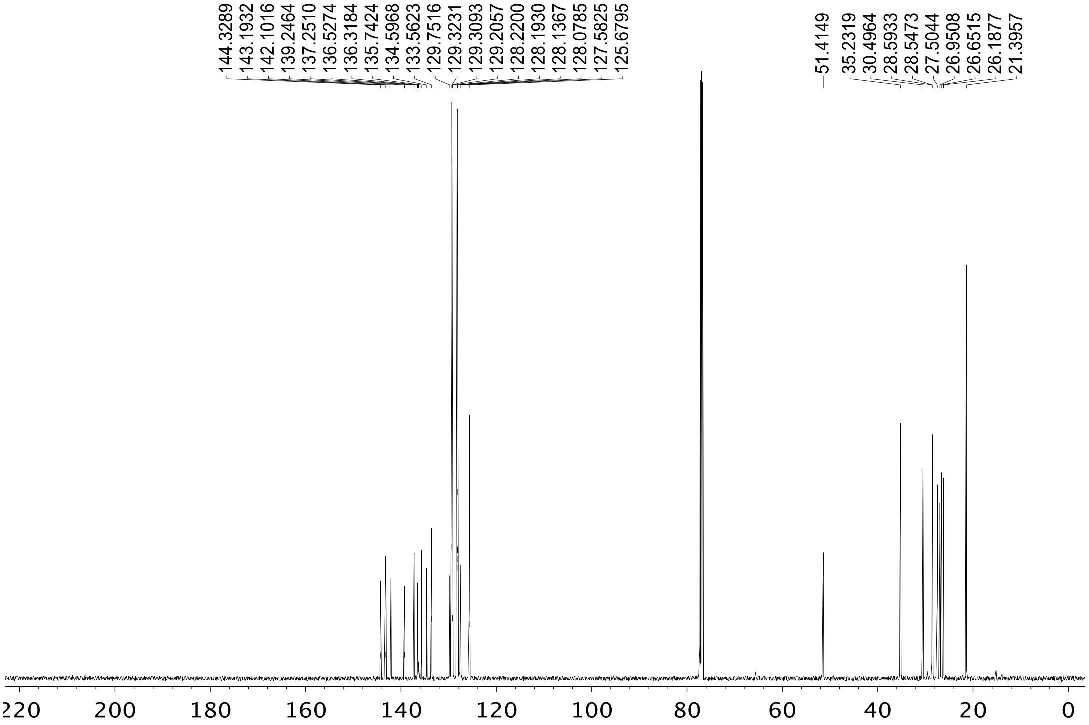


Figure 4.50 ^{13}C NMR (126 MHz, CDCl$_3$, 55 °C) of compound **4.80**.

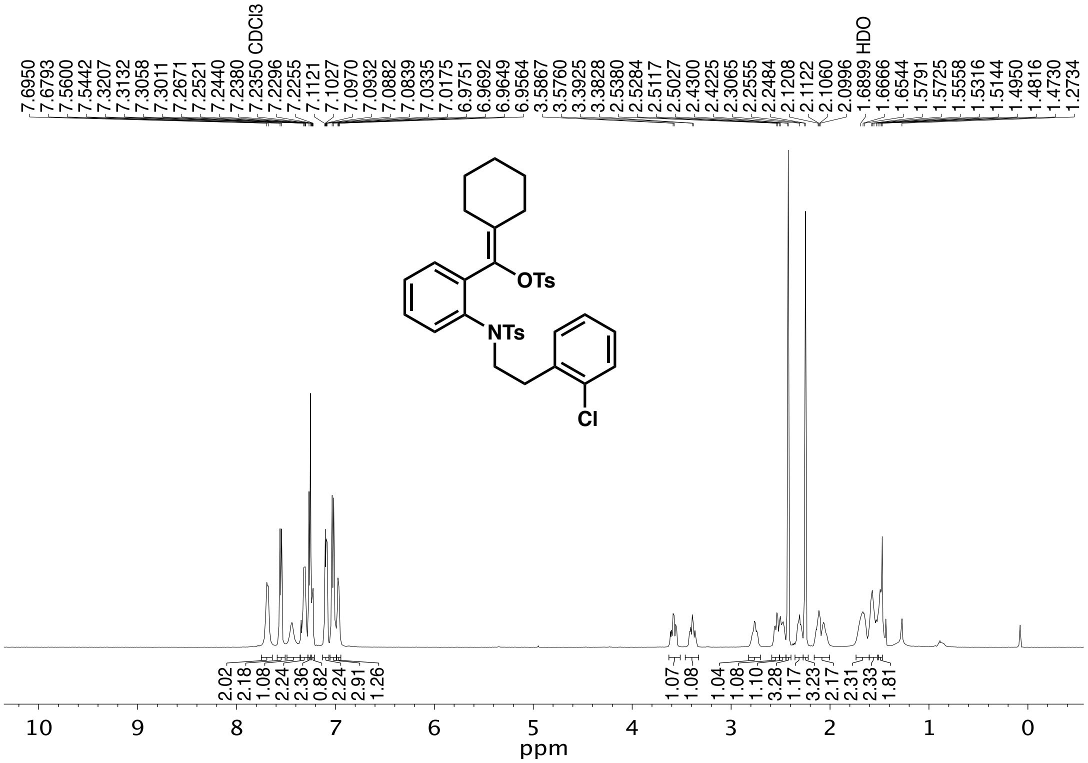


Figure 4.51 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.1**

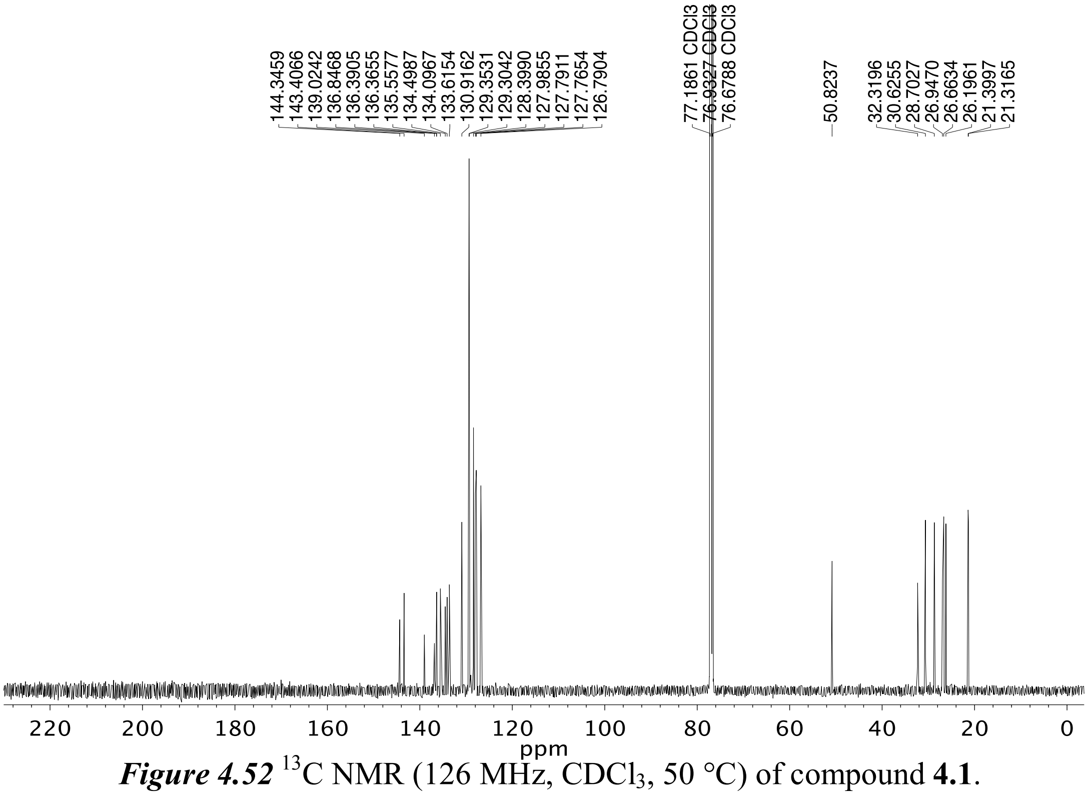


Figure 4.52 ^{13}C NMR (126 MHz, CDCl$_3$, 50 °C) of compound **4.1**.

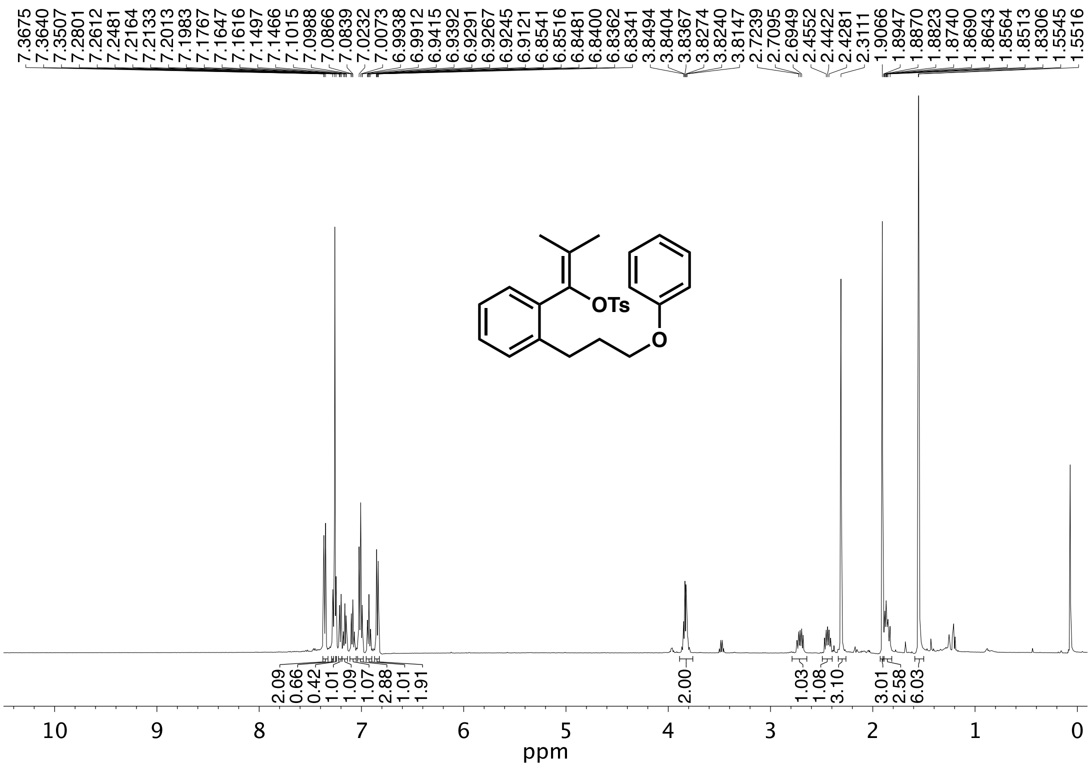


Figure 4.53 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.81**

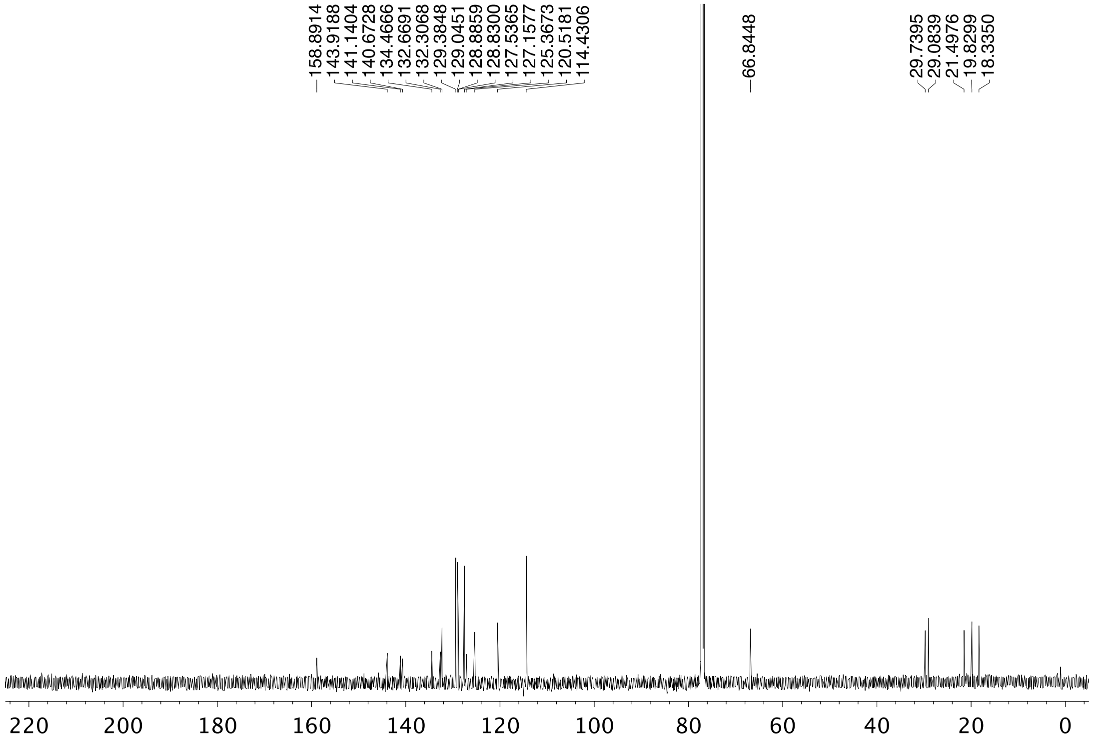


Figure 4.54 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.81**.

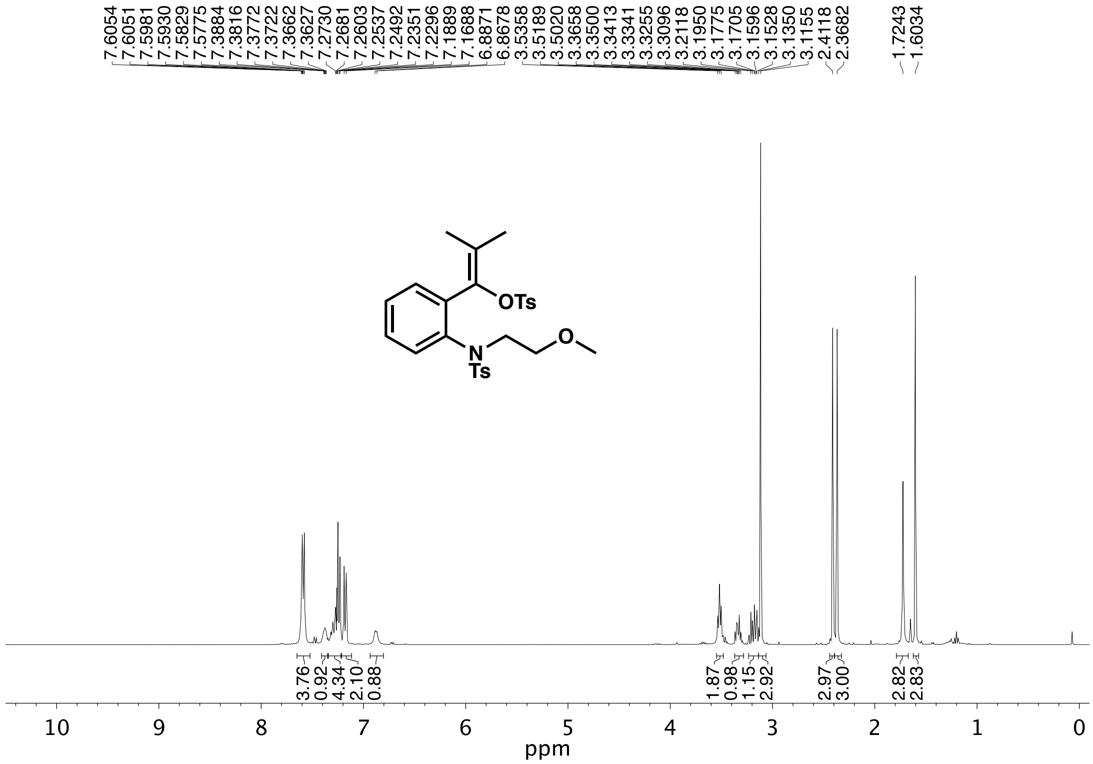


Figure 4.55 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.43**

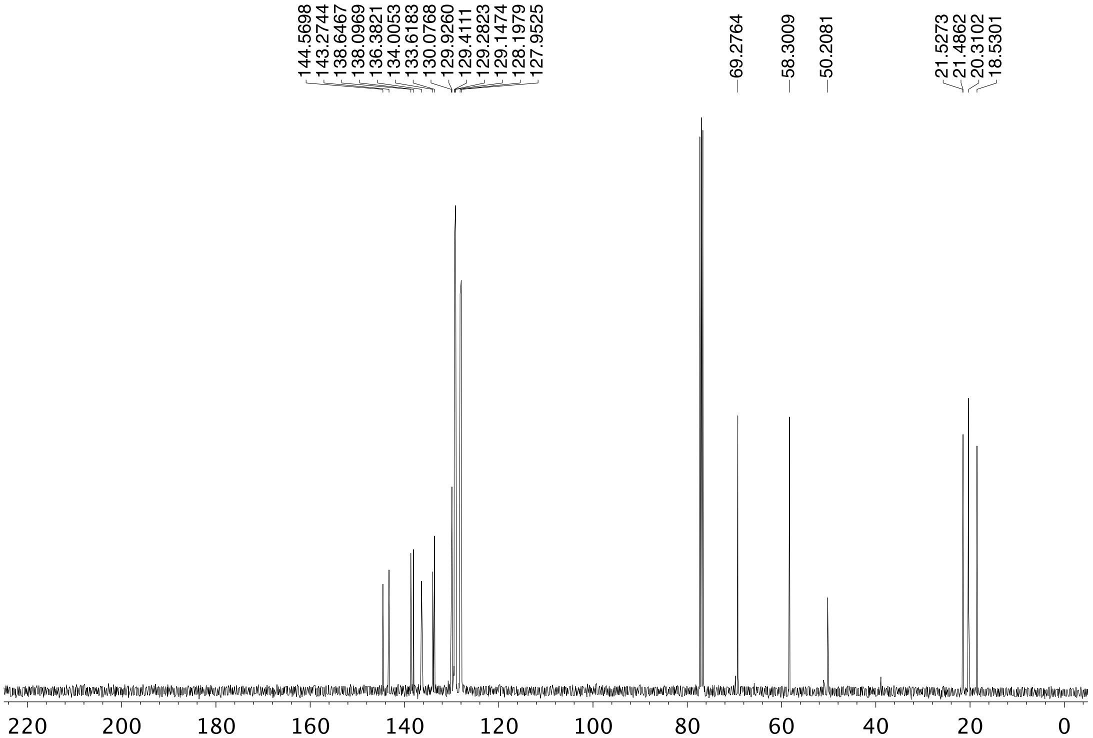


Figure 4.56 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.43**.

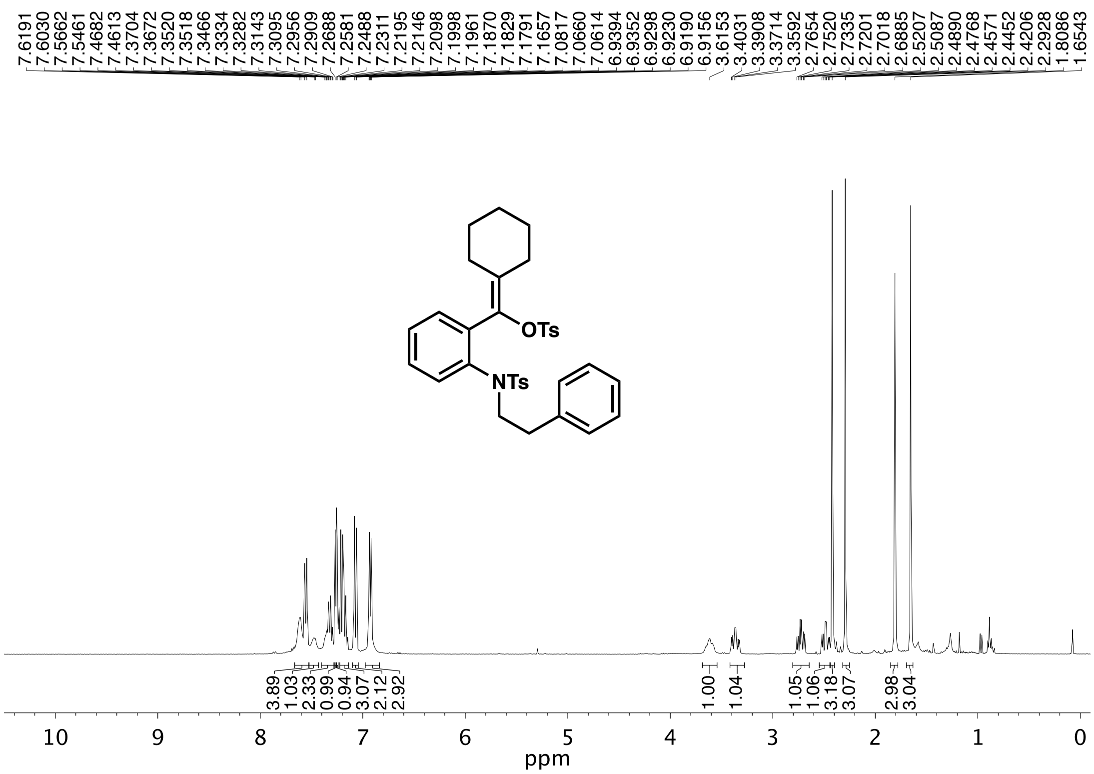


Figure 4.57 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.82**

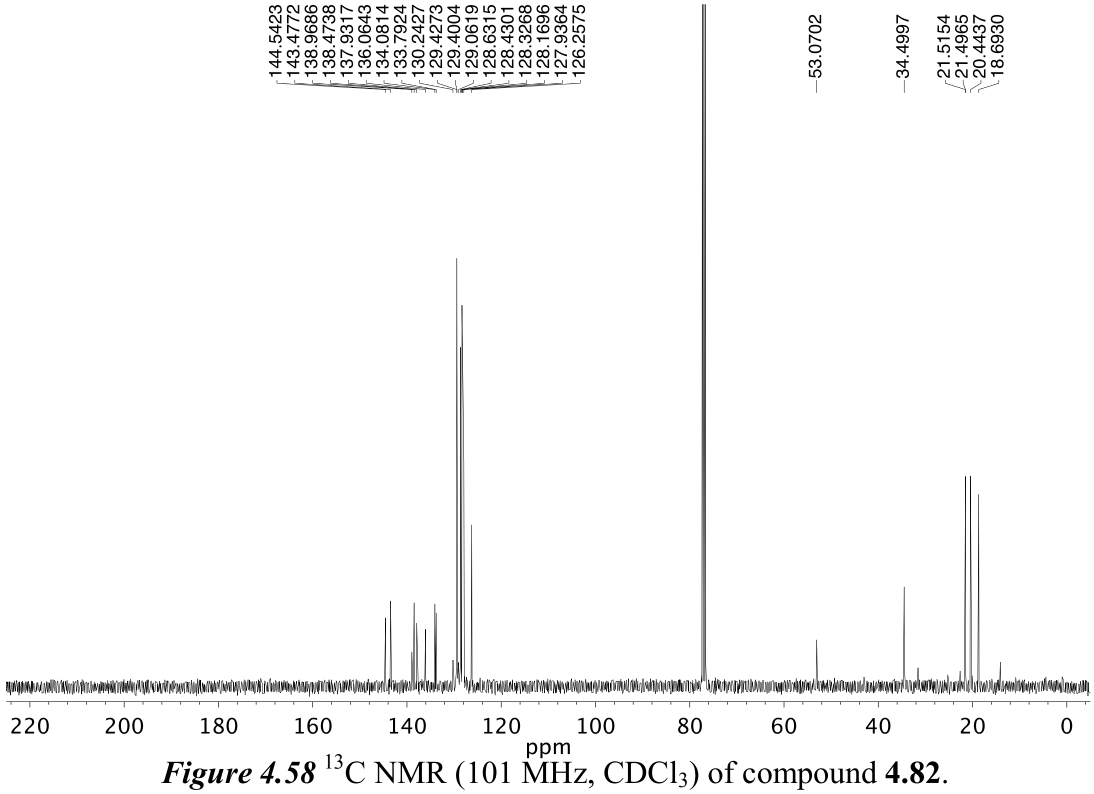


Figure 4.58 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.82**.

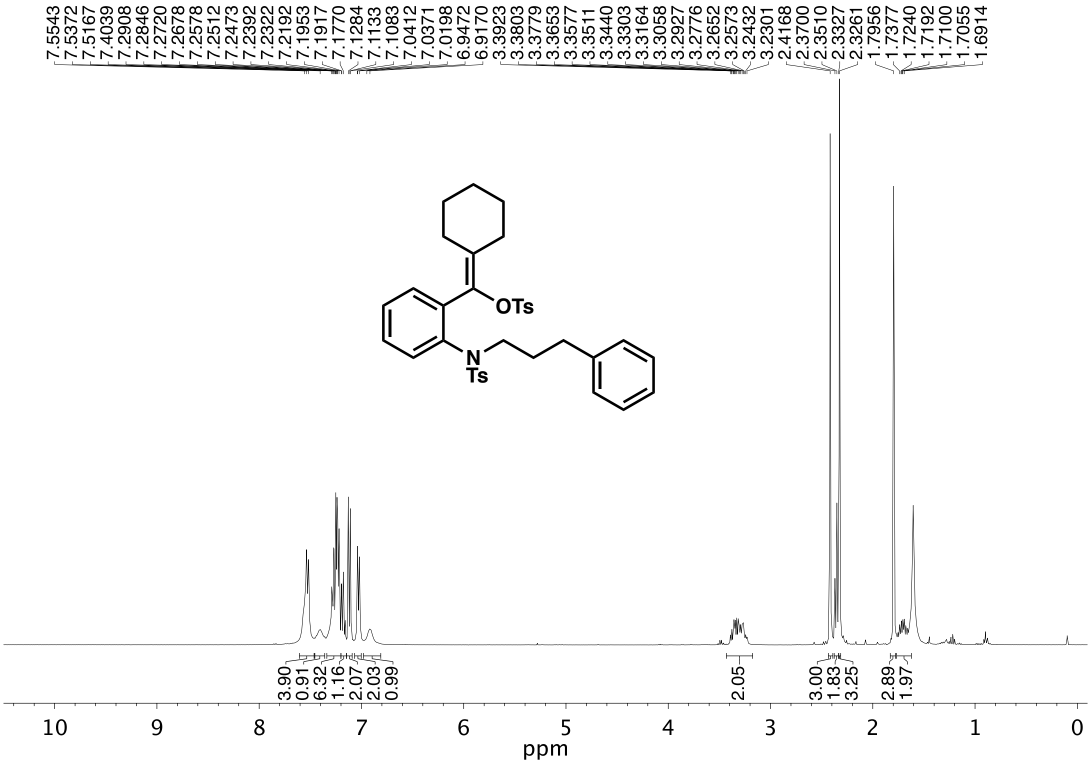


Figure 4.59 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.83**

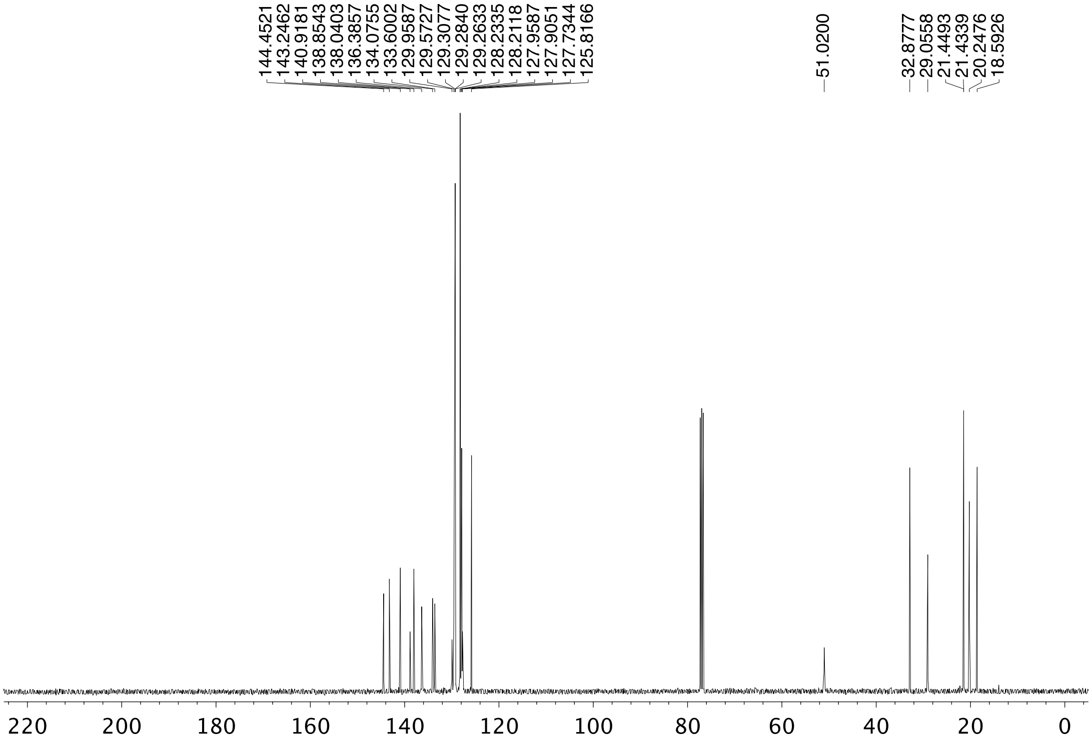


Figure 4.60 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.83**.

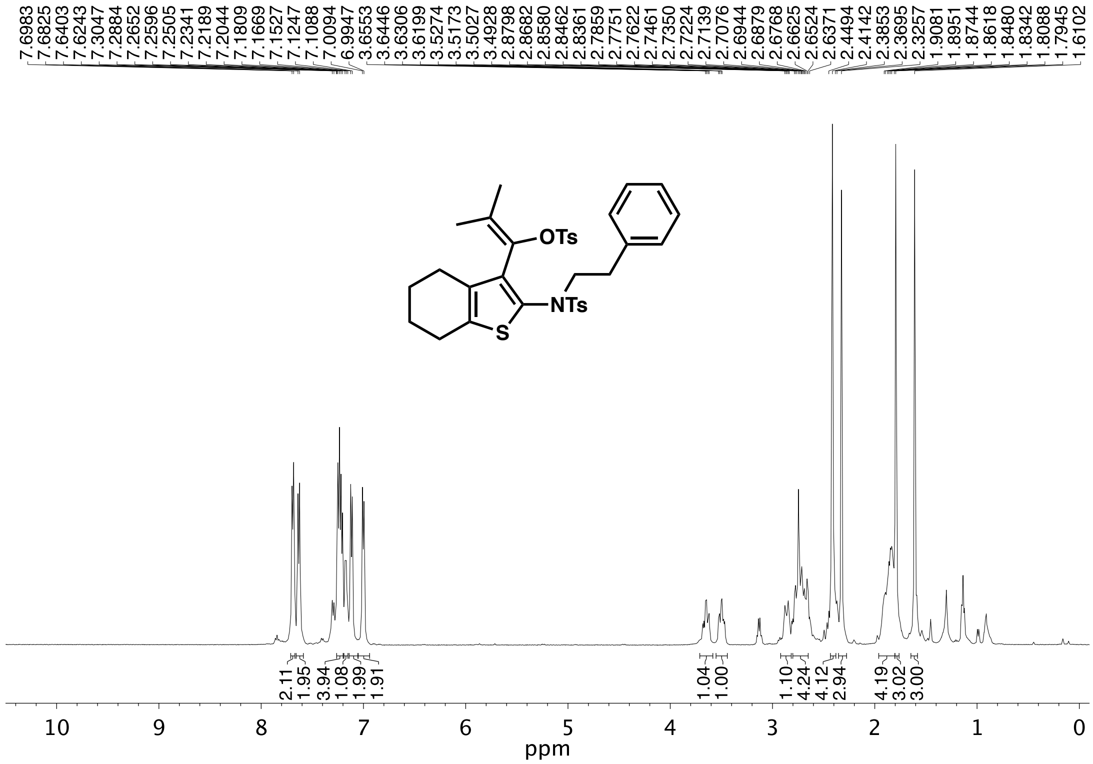


Figure 4.61 ^{1}H NMR (500 MHz, CDCl$_3$, 70 °C) of compound **4.84**

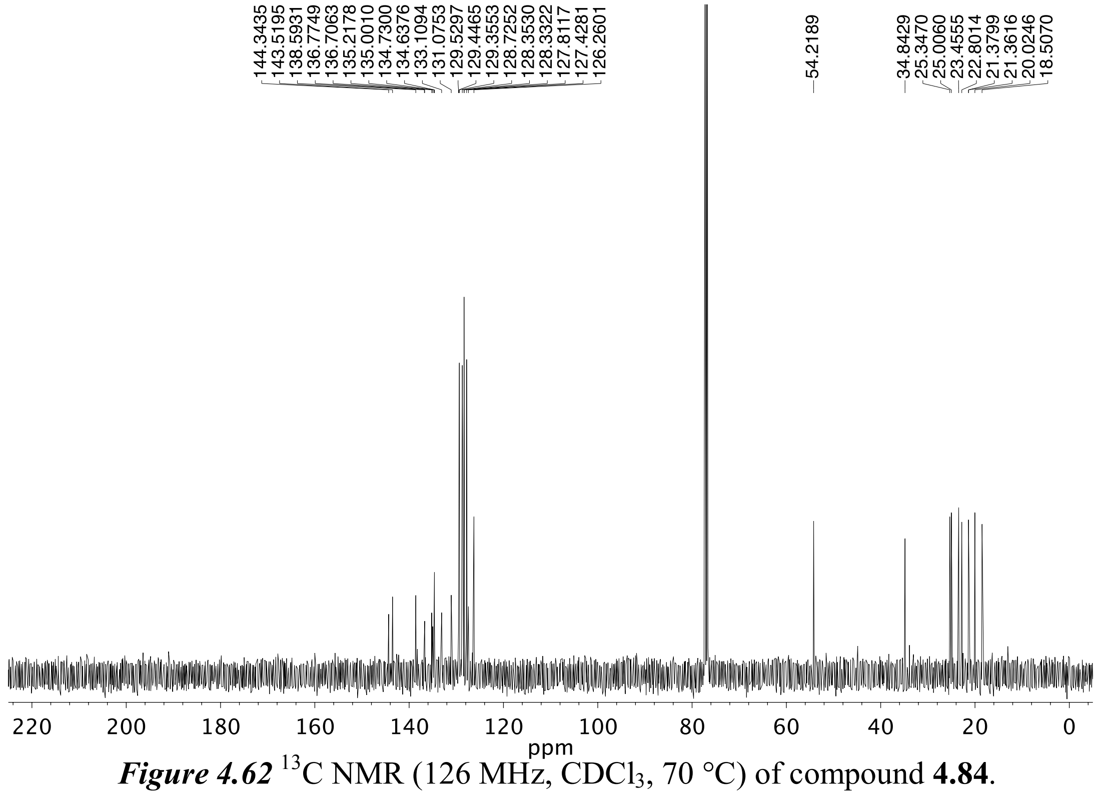


Figure 4.62 ^{13}C NMR (126 MHz, CDCl$_3$, 70 °C) of compound **4.84**.

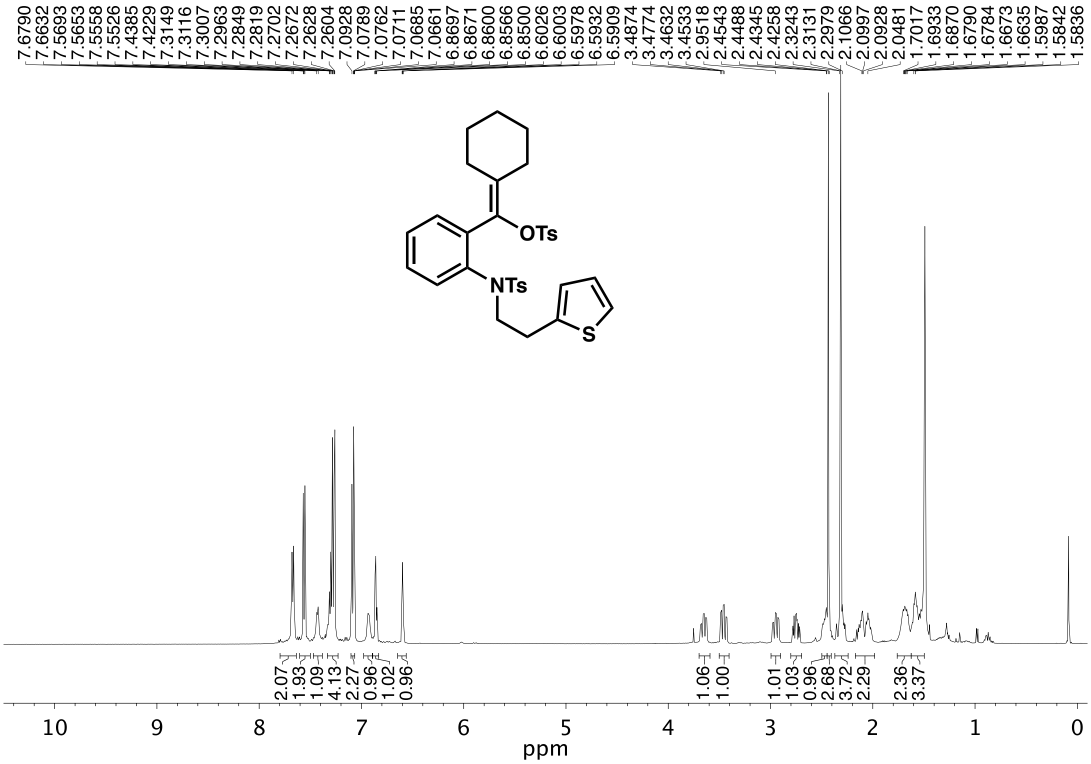


Figure 4.63 ^{1}H NMR (500 MHz, CDCl$_3$, 55 °C) of compound **4.85**

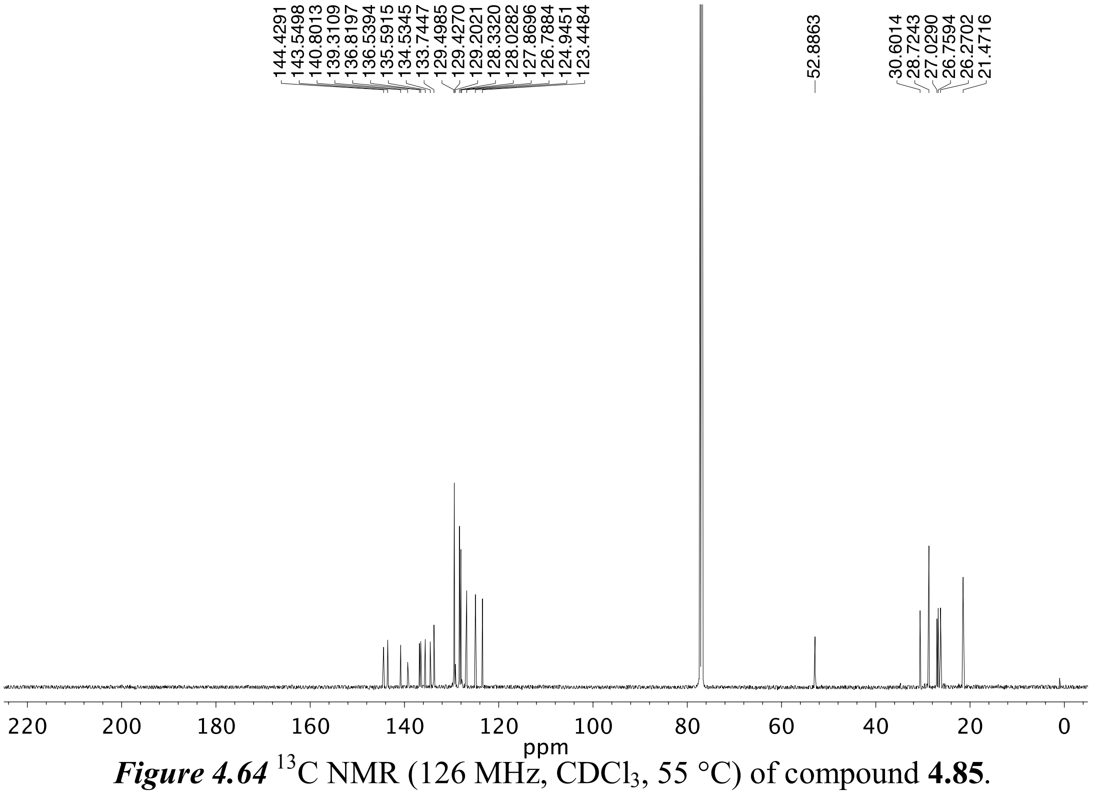


Figure 4.64 ^{13}C NMR (126 MHz, CDCl$_3$, 55 °C) of compound **4.85**.

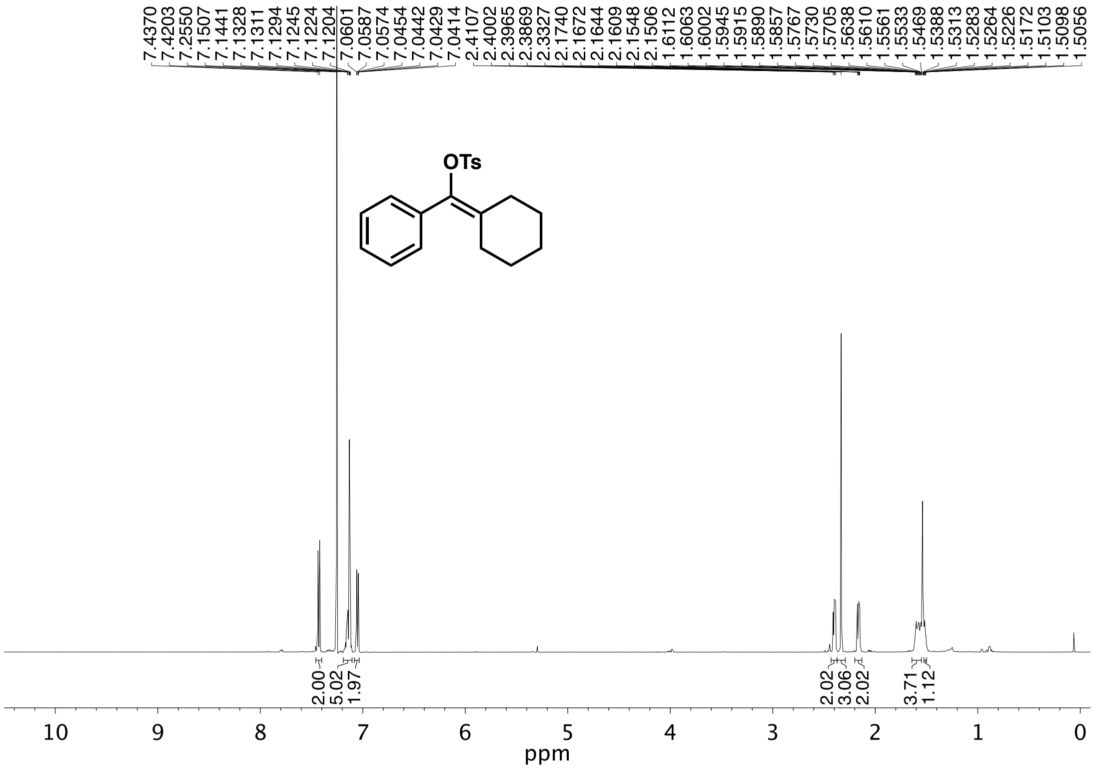


Figure 4.65 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.86**

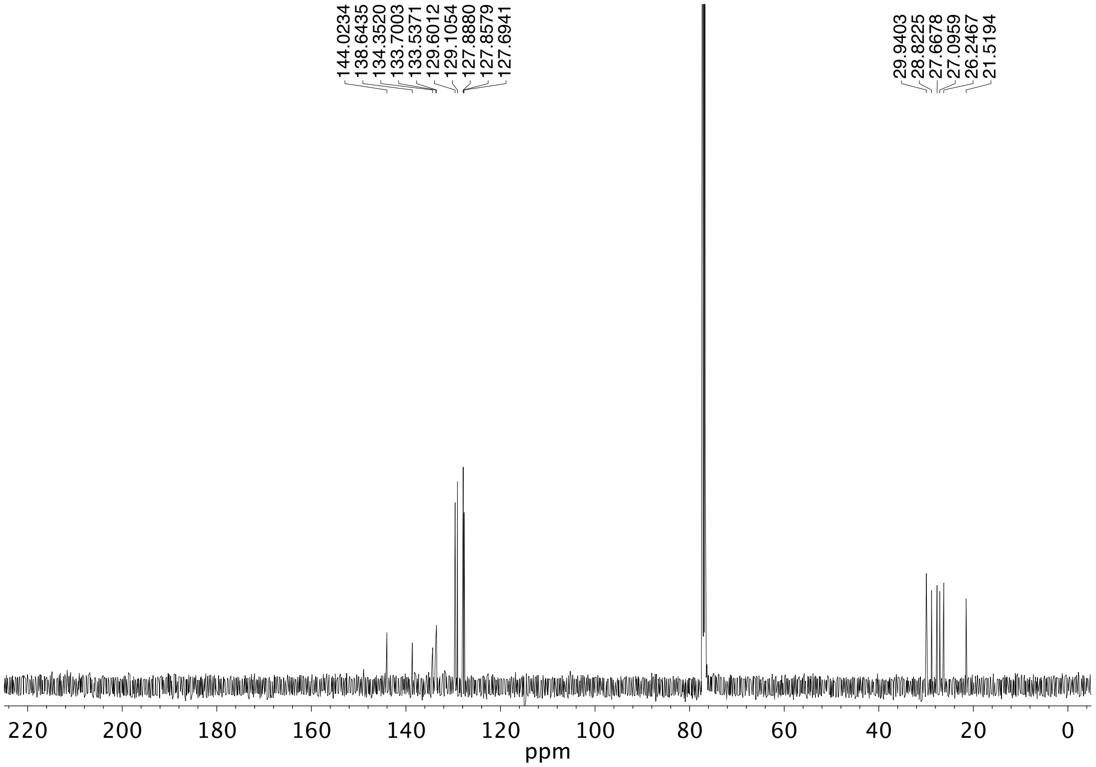


Figure 4.66 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.86**.

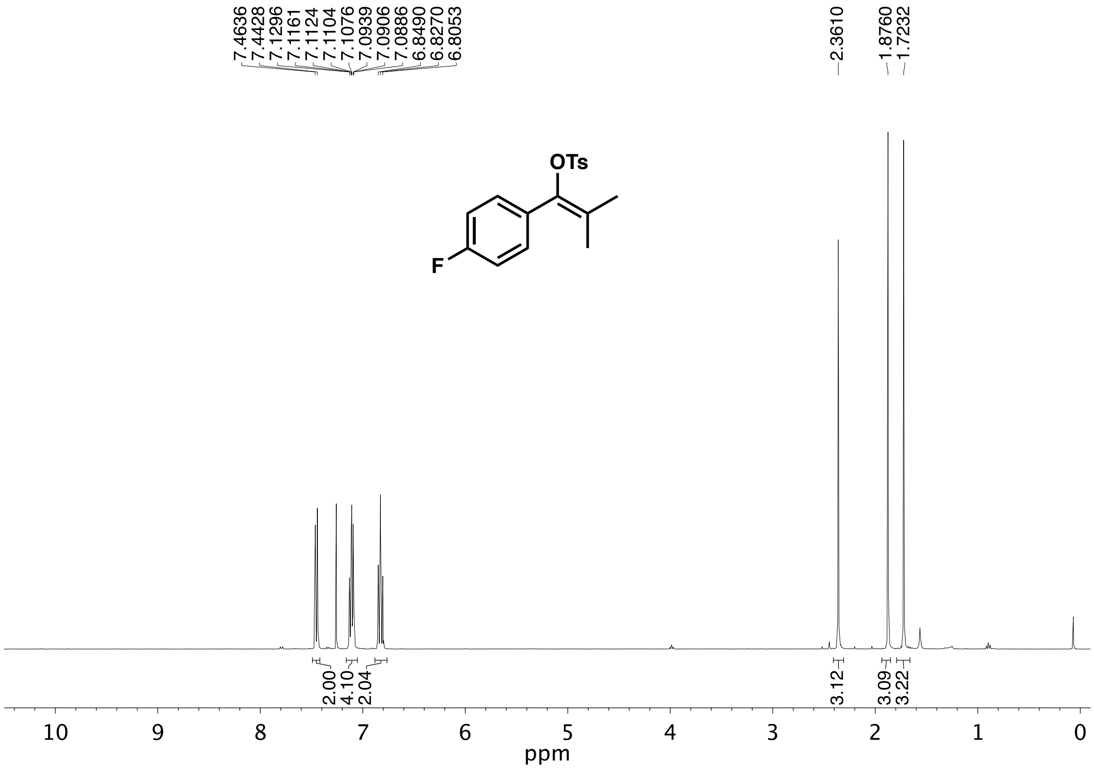


Figure 4.67 ^{1}H NMR (400 MHz, $CDCl_3$, 70 °C) of compound **4.87**.

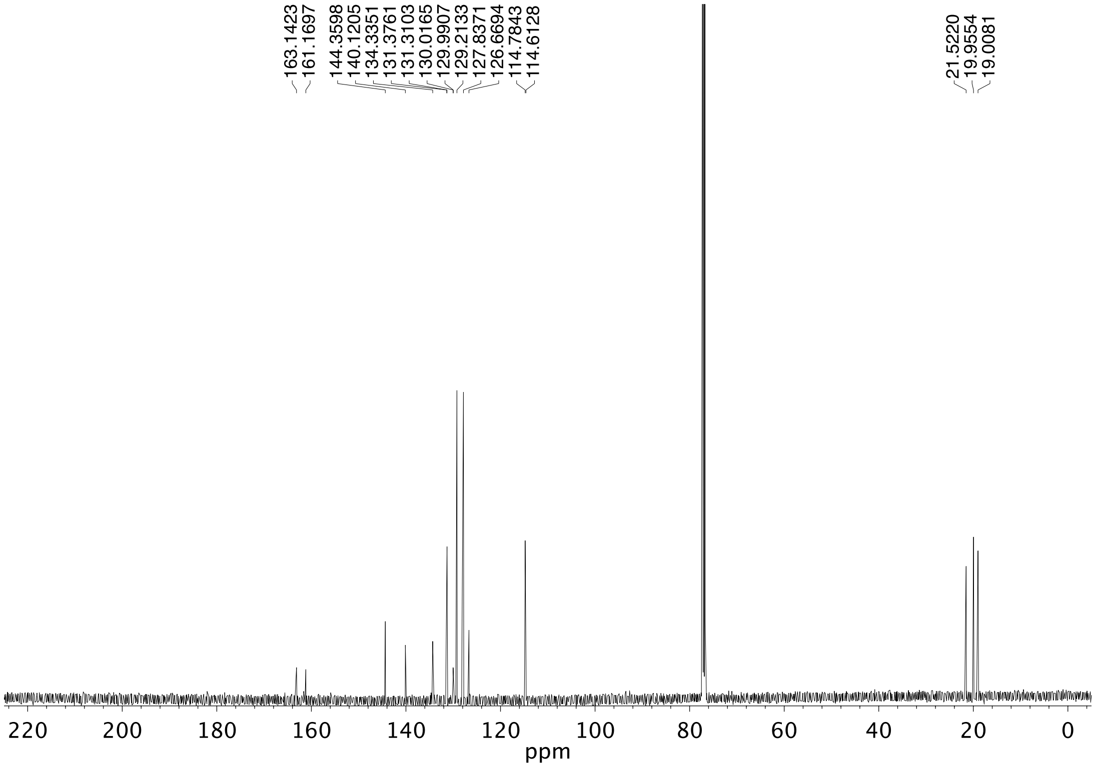


Figure 4.68 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.87**.

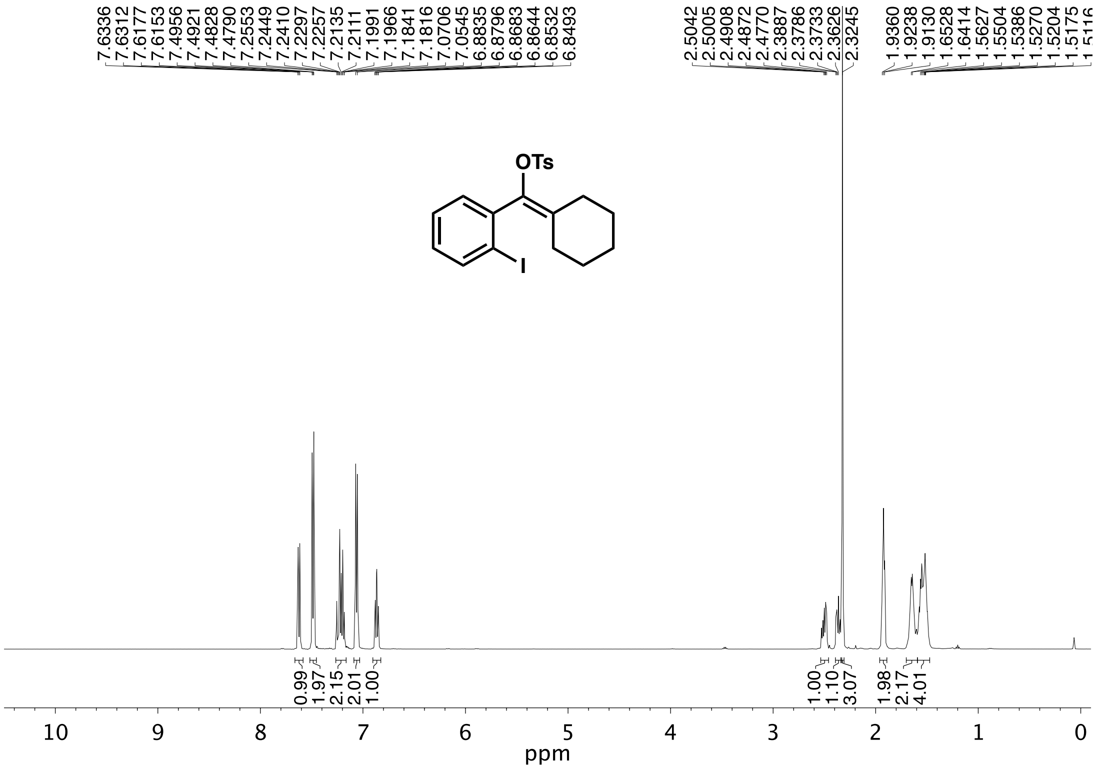


Figure 4.69 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.88**.

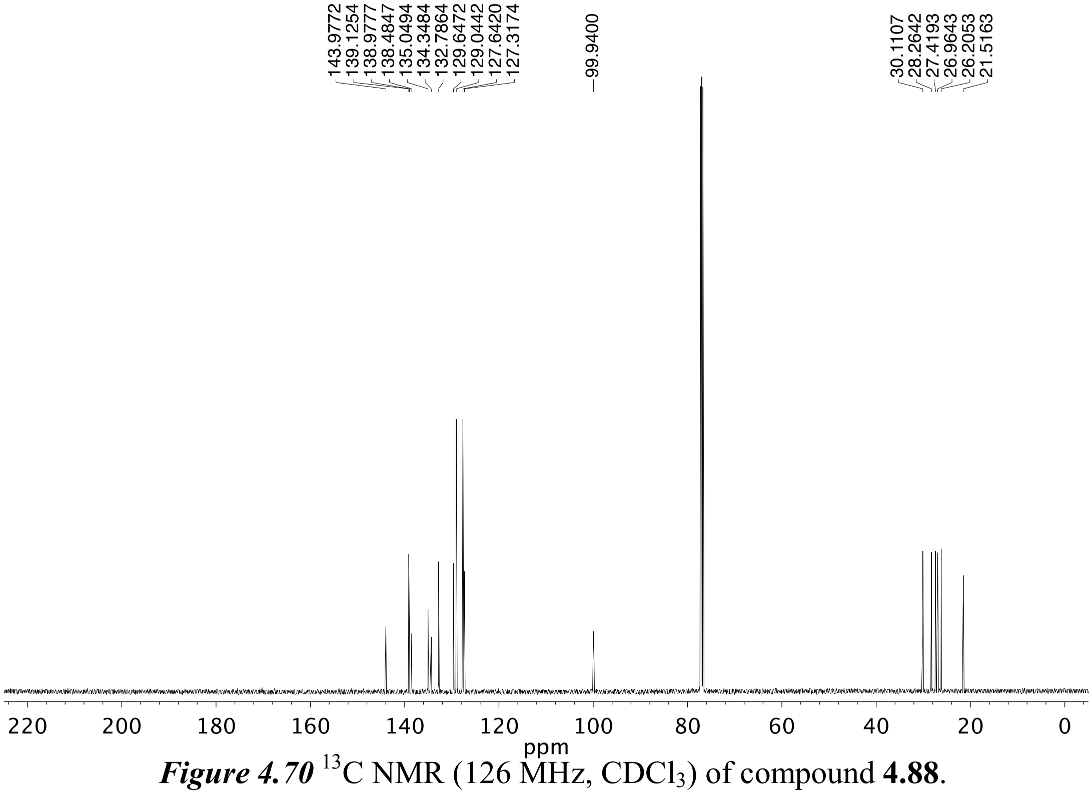


Figure 4.70 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.88**.

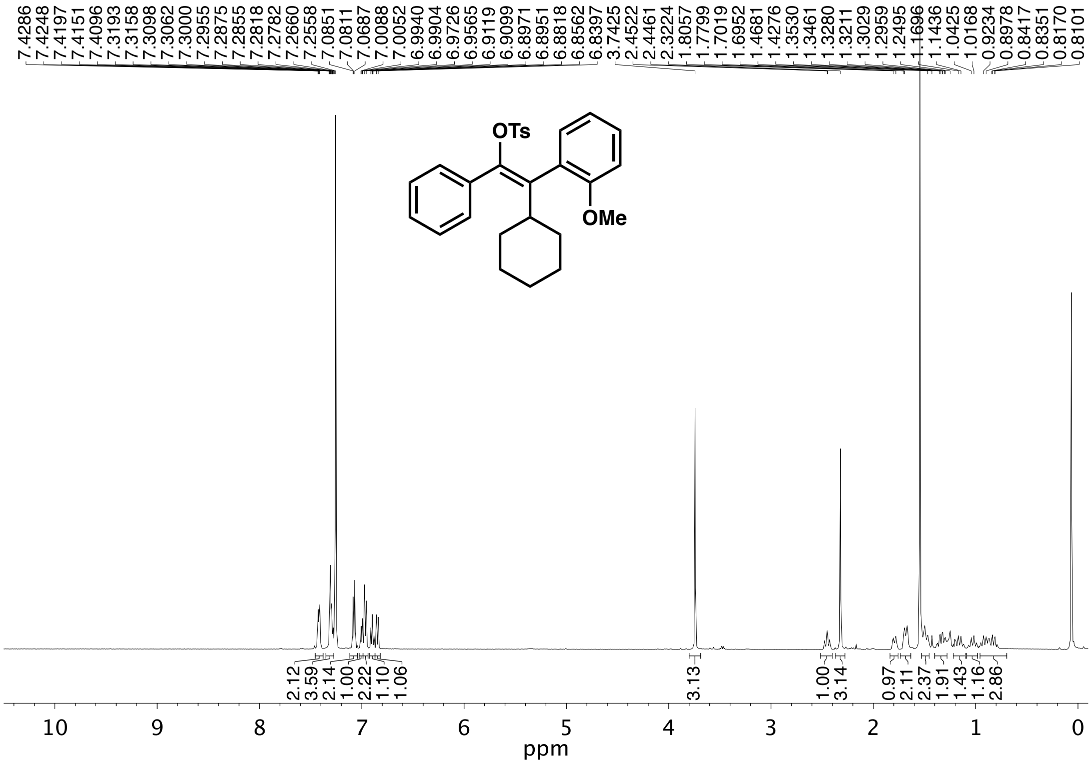


Figure 4.71 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.45**.

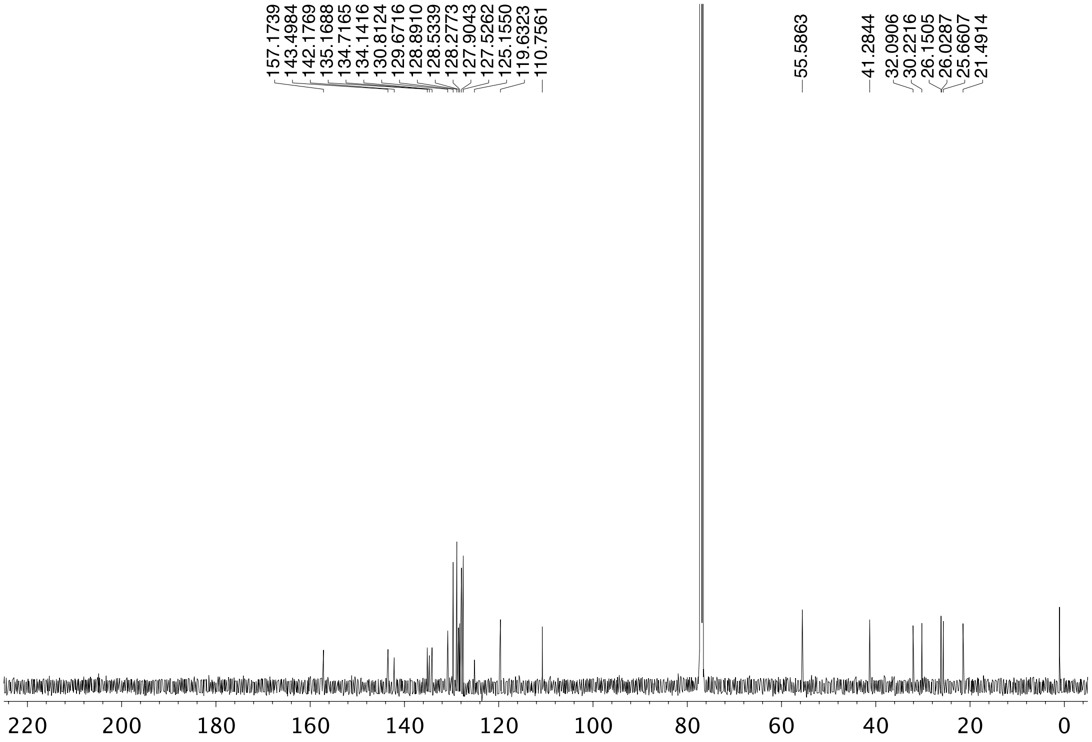


Figure 4.72 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.45**.

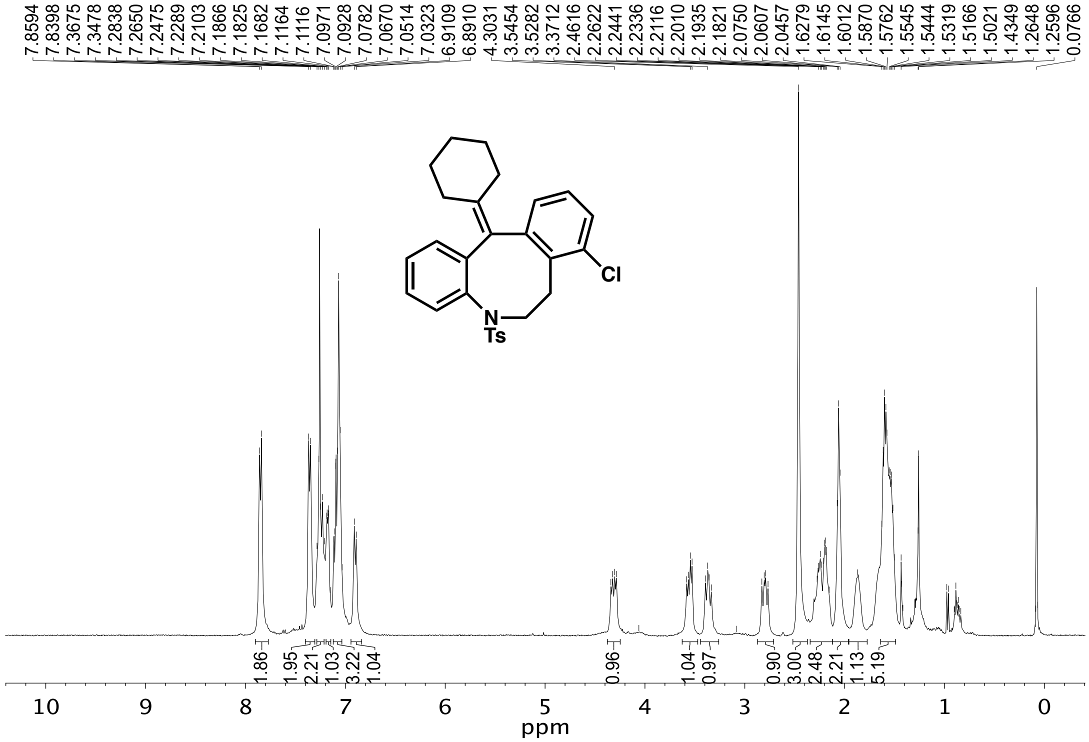


Figure 4.73 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.2**.

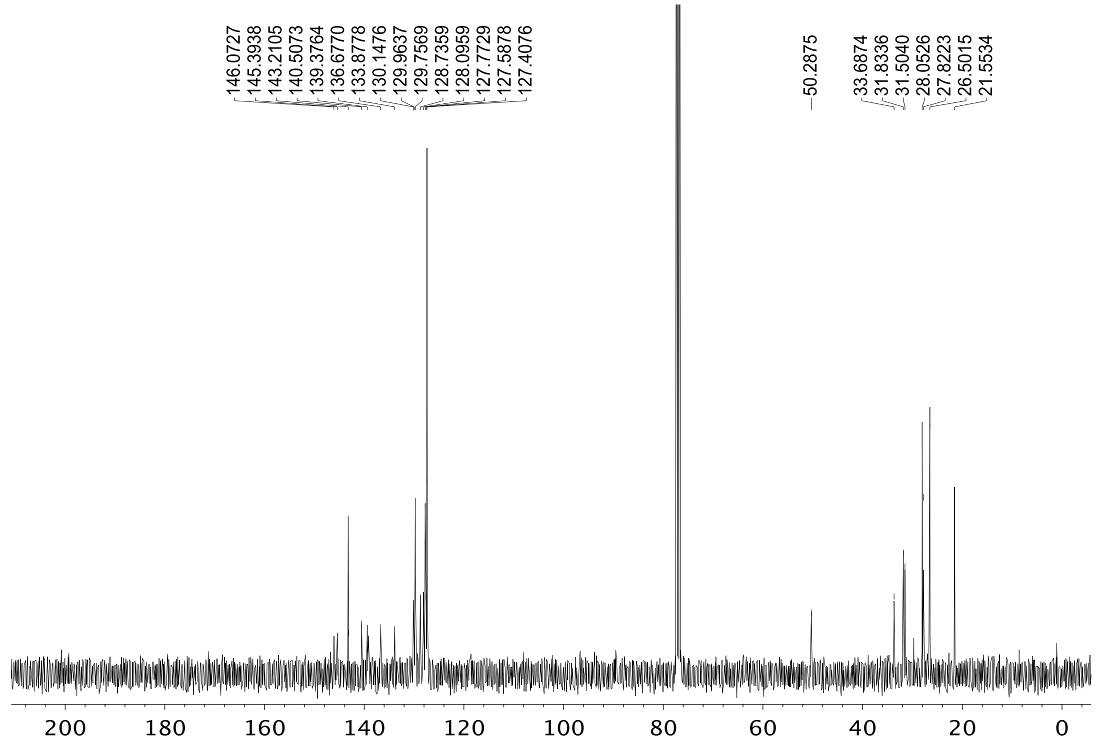


Figure 4.74 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **4.2**.

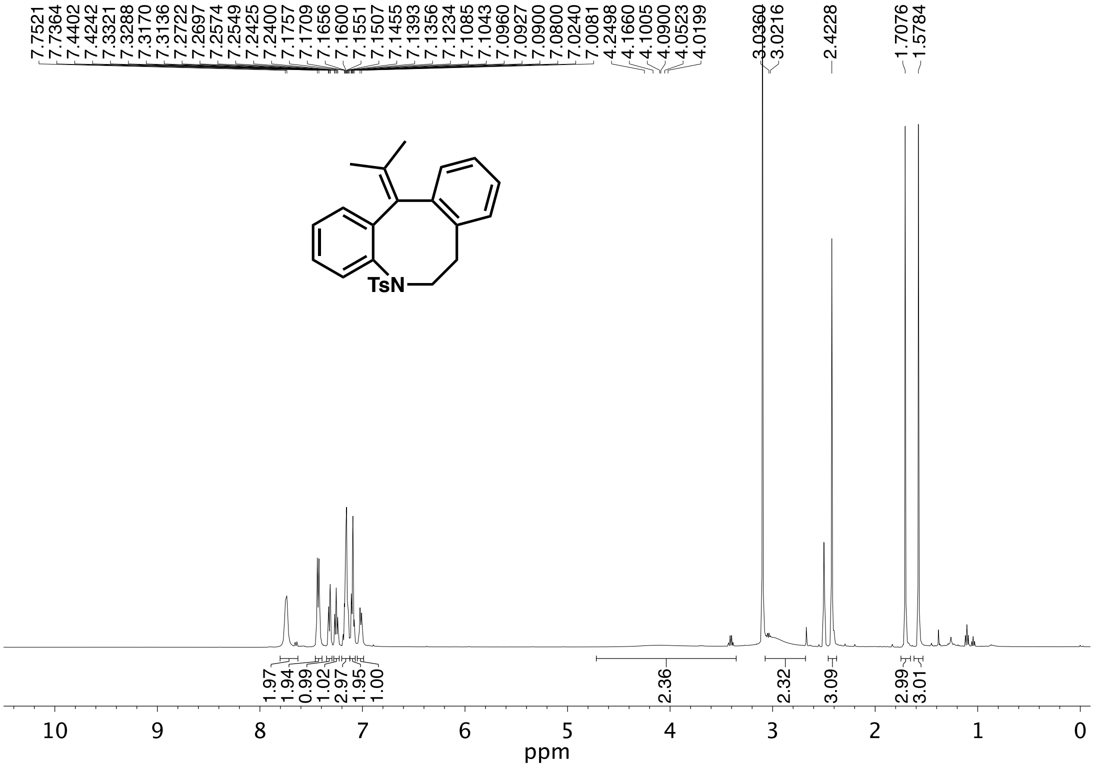


Figure 4.75 ^{1}H NMR (500 MHz, DMSO-d_6, 75 °C) of compound **4.5**.

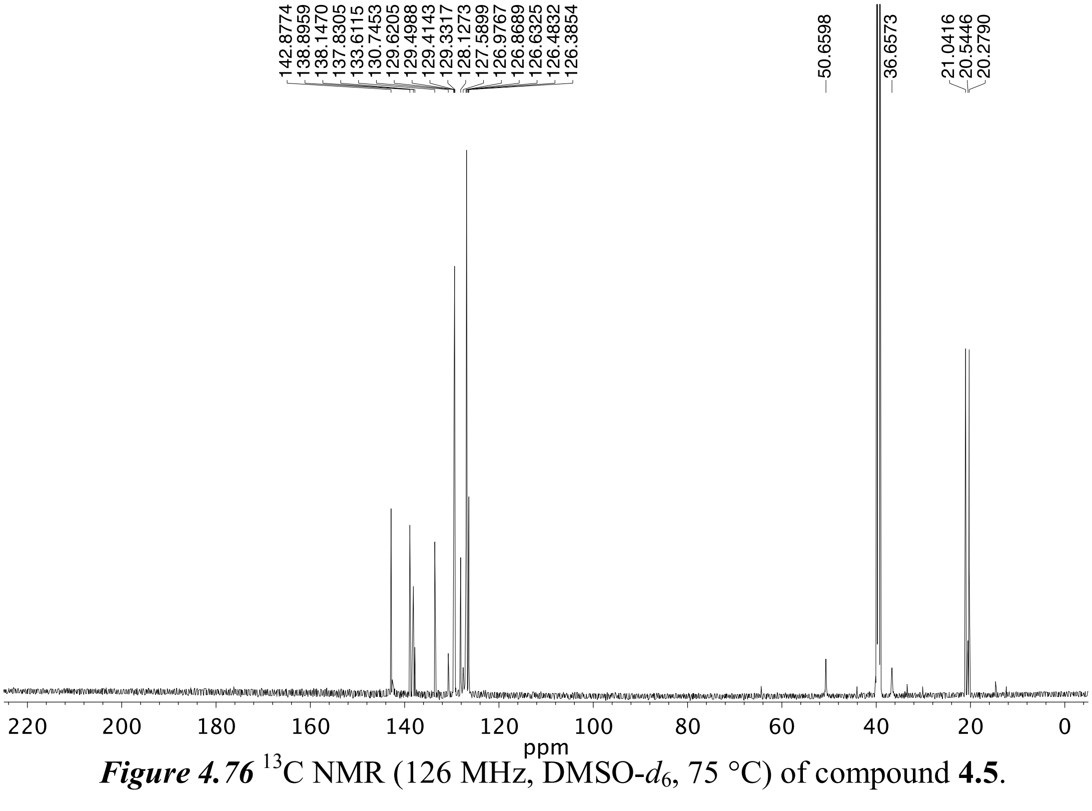


Figure 4.76 ^{13}C NMR (126 MHz, DMSO-d_6, 75 °C) of compound **4.5**.

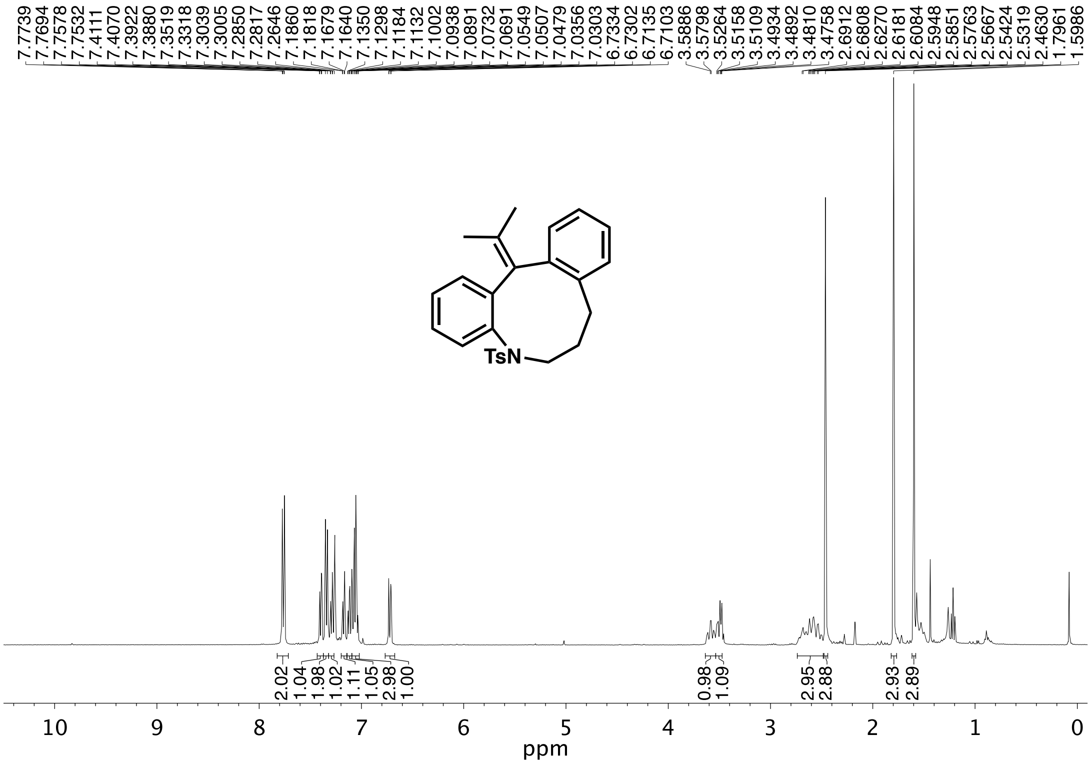


Figure 4.77 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.6**.

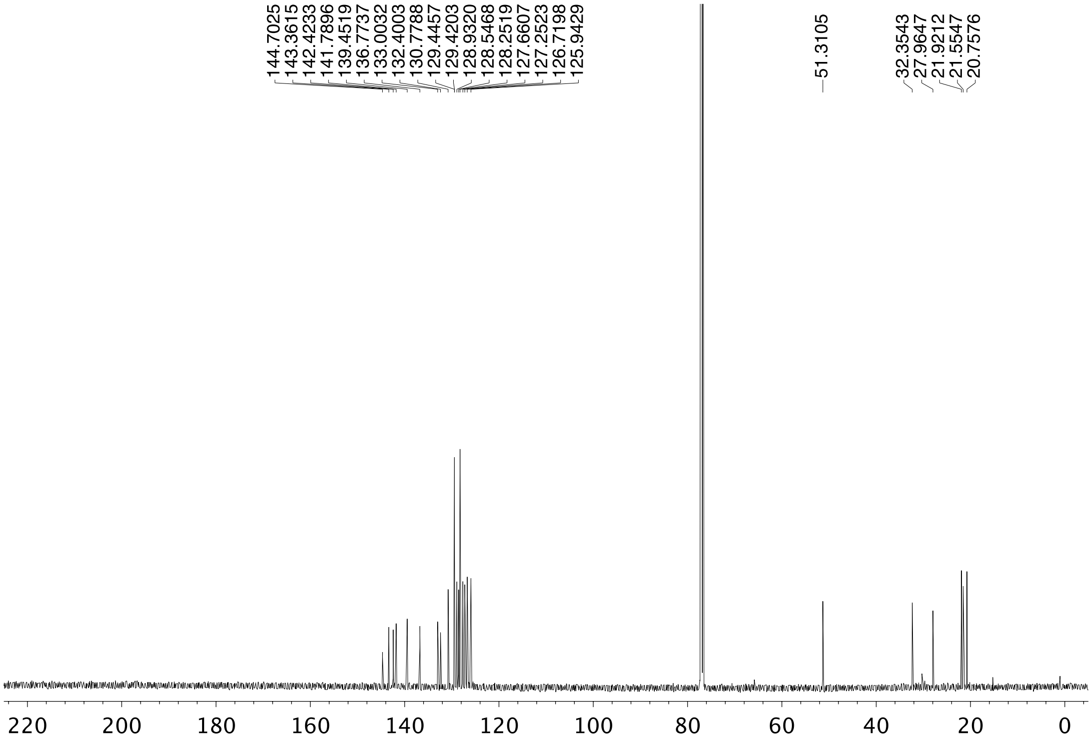


Figure 4.78 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.6**.

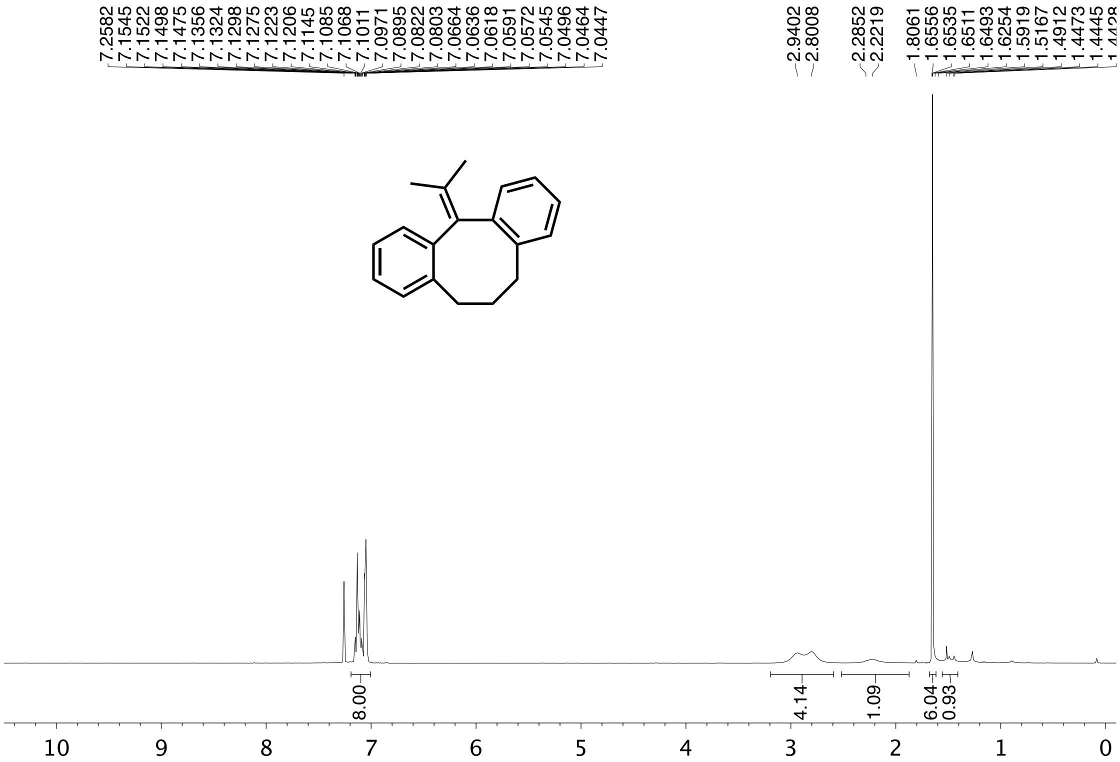


Figure 4.79 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.9**.

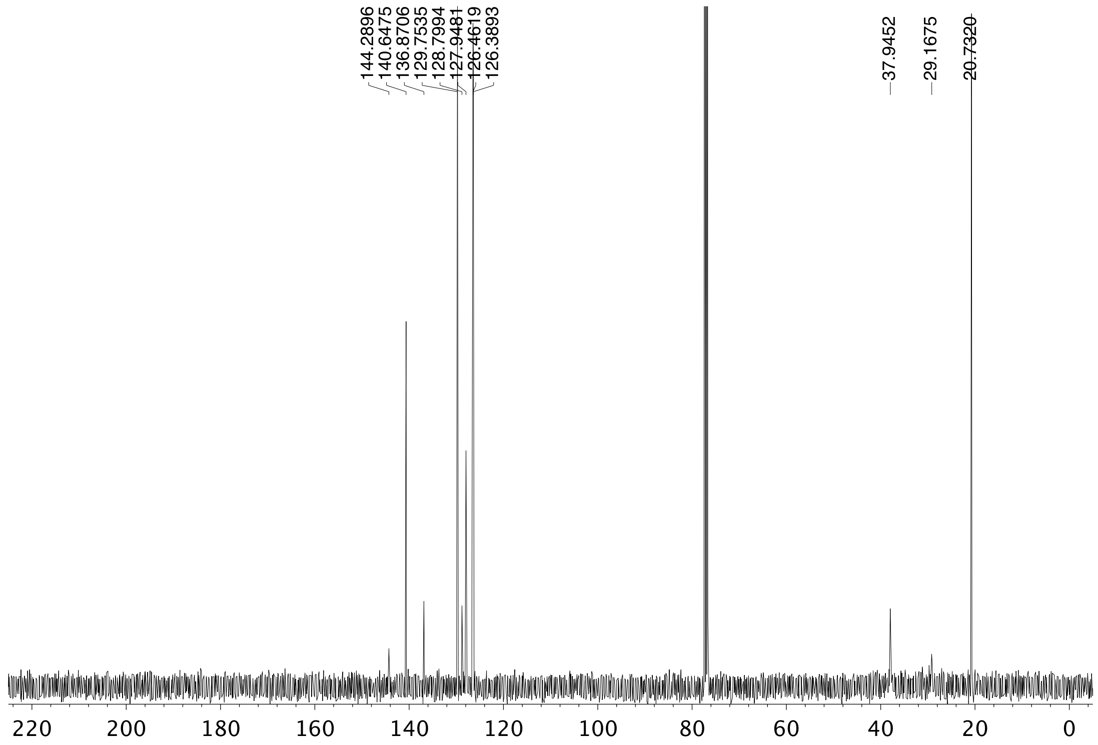


Figure 4.80 ^{13}C NMR (101 MHz, CDCl$_3$) of compound **4.9**.

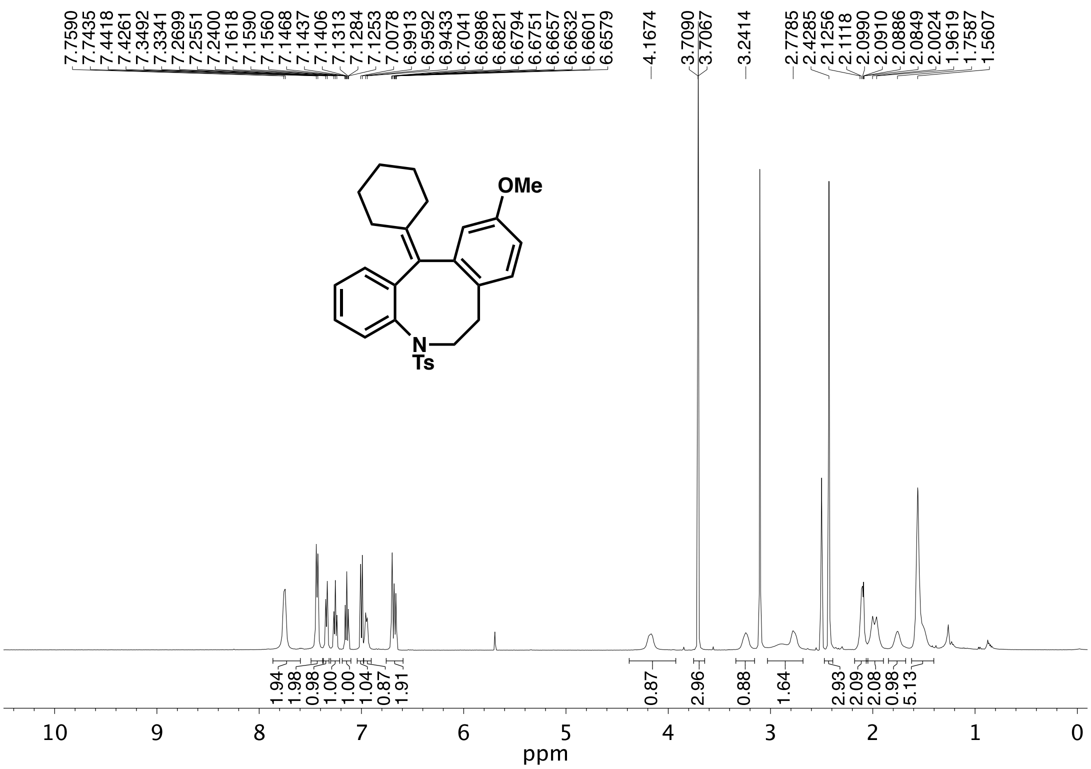


Figure 4.81 ^{1}H NMR (500 MHz, DMSO-d_6, 75 °C) of compound **4.10**.

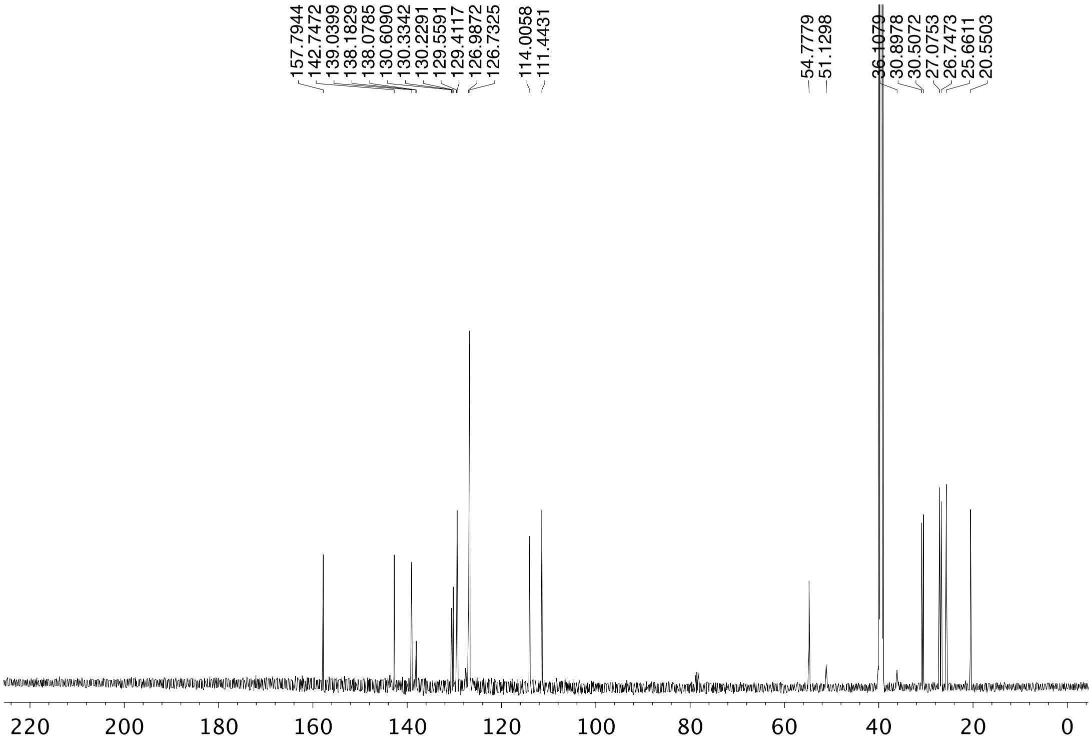


Figure 4.82 ^{13}C NMR (126 MHz, DMSO-d_6, 75 °C) of compound **4.10**.

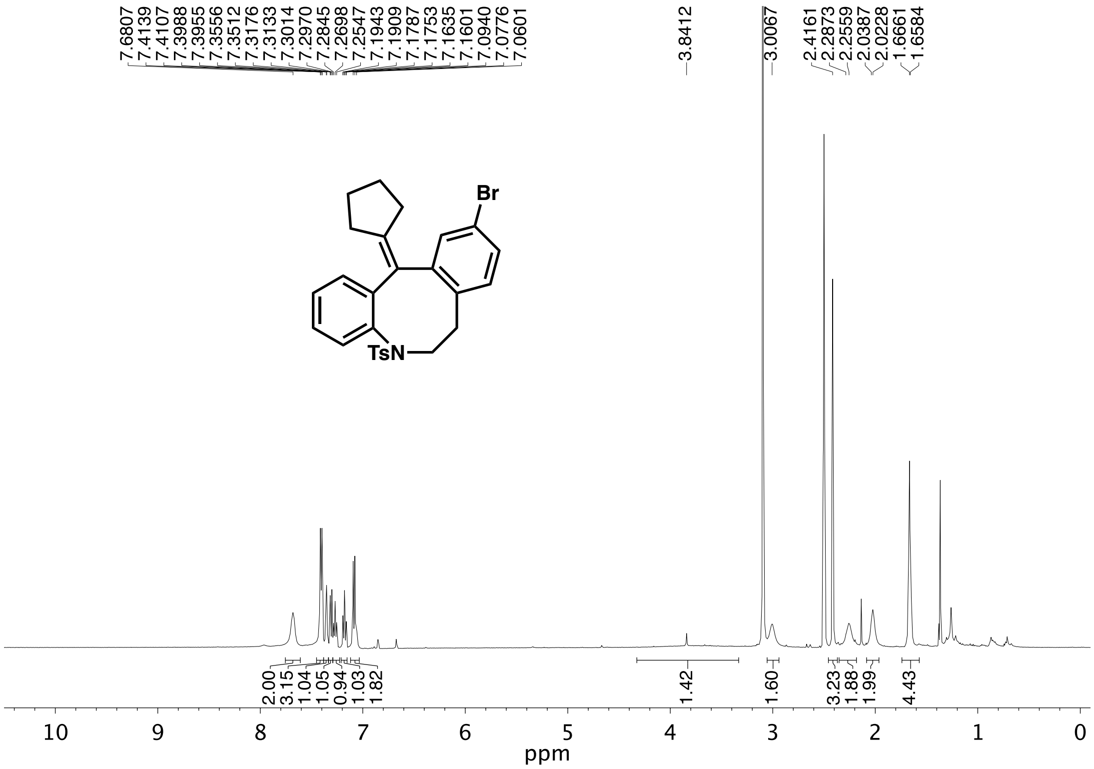


Figure 4.83 ^{1}H NMR (500 MHz, DMSO-d_6, 75 °C) of compound **4.11**.

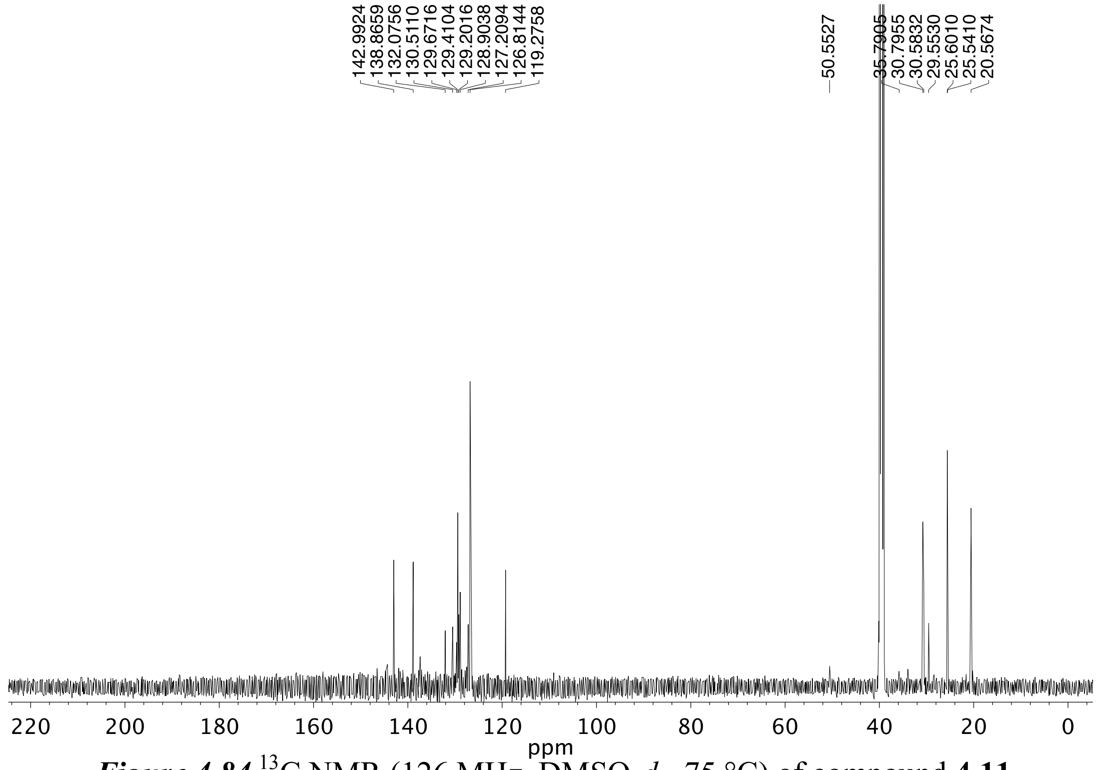


Figure 4.84 ^{13}C NMR (126 MHz, DMSO-d_6, 75 °C) of compound **4.11**.

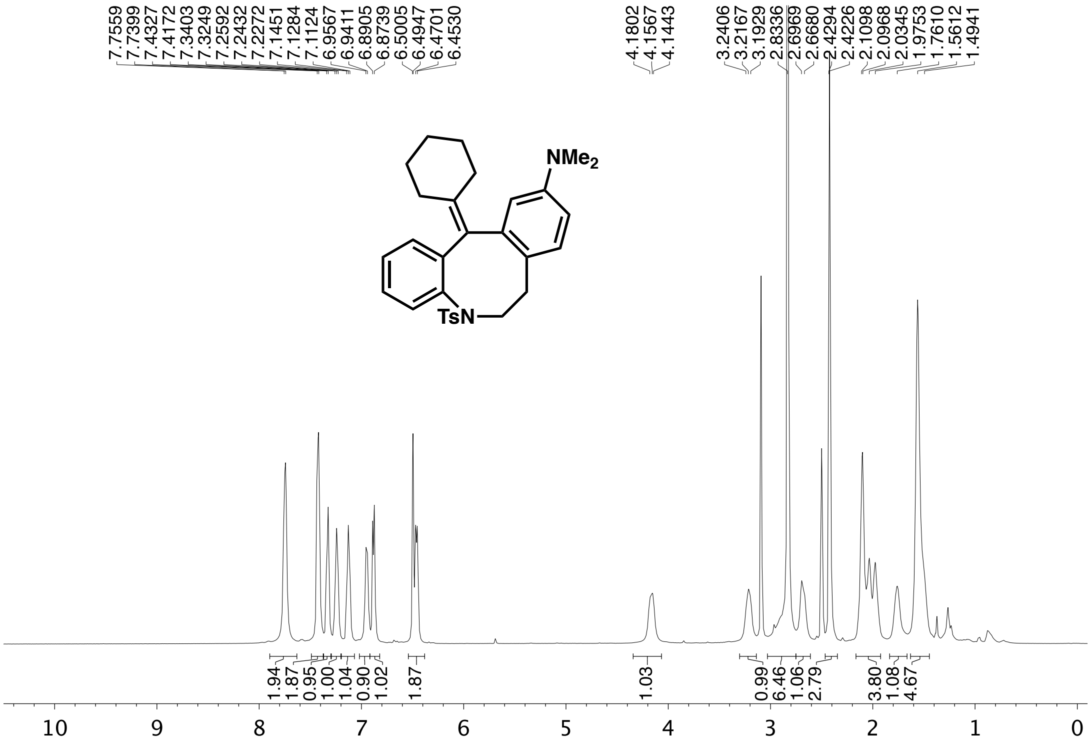


Figure 4.85 ^{1}H NMR (500 MHz, DMSO-d_6, 75 °C) of compound **4.12**.

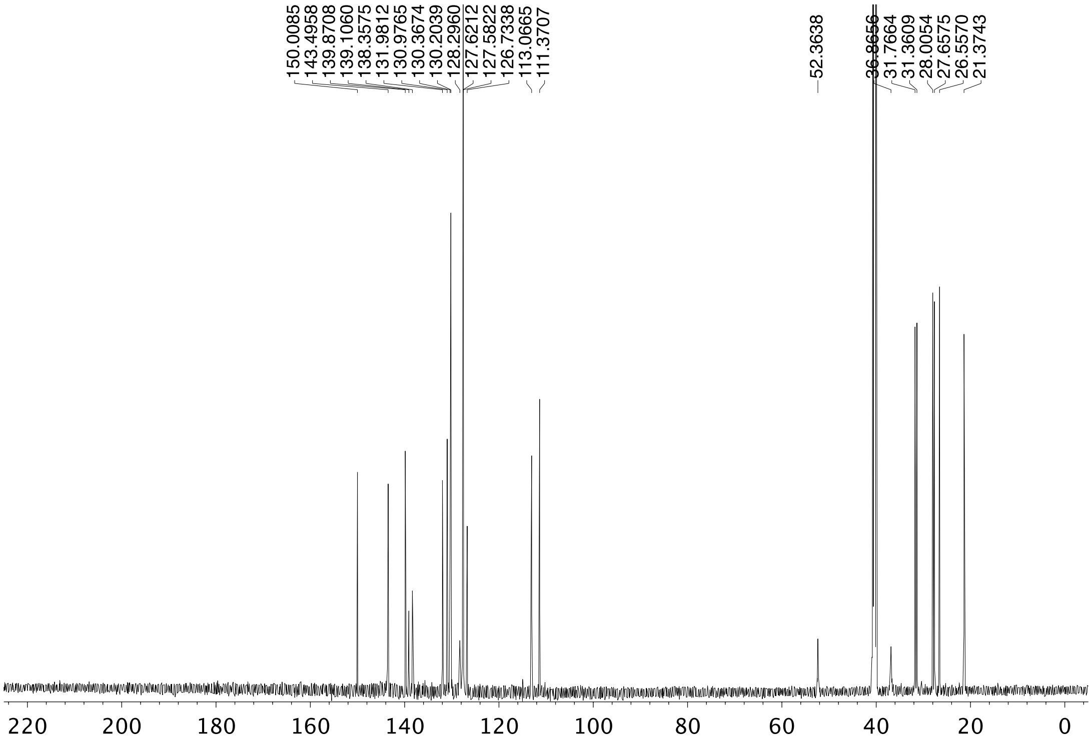


Figure 4.86 ^{13}C NMR (126 MHz, DMSO-d_6, 70 °C) of compound **4.12**.

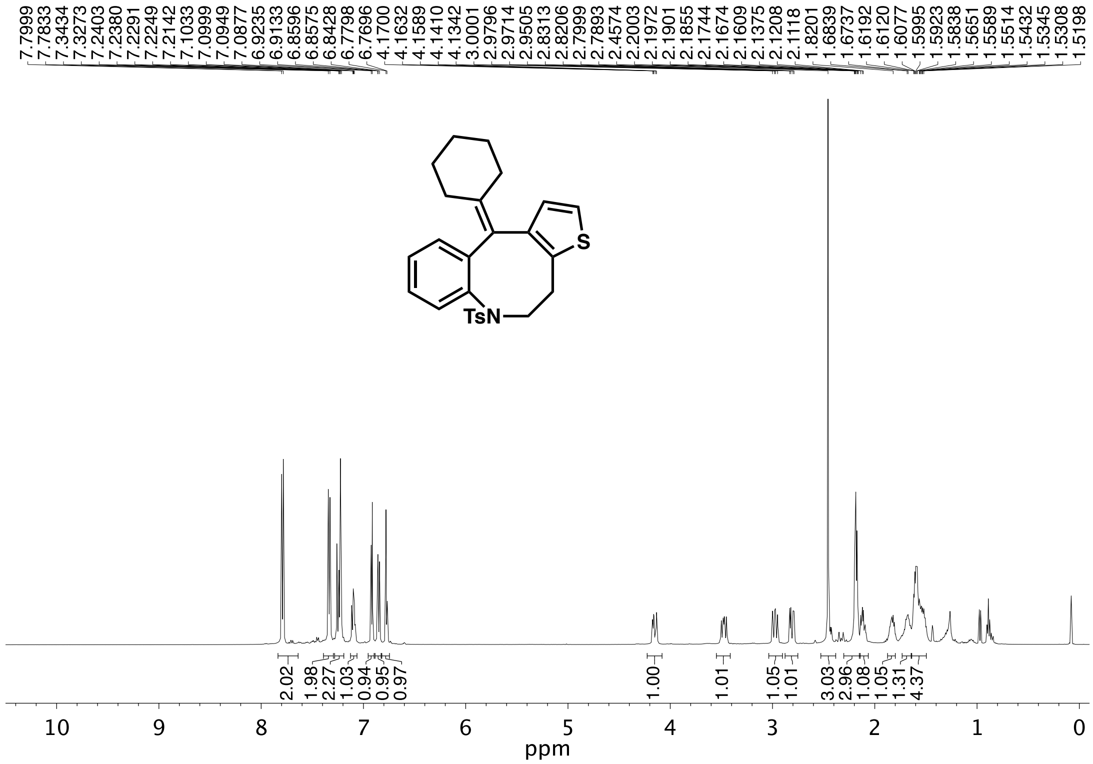


Figure 4.87 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.13**.

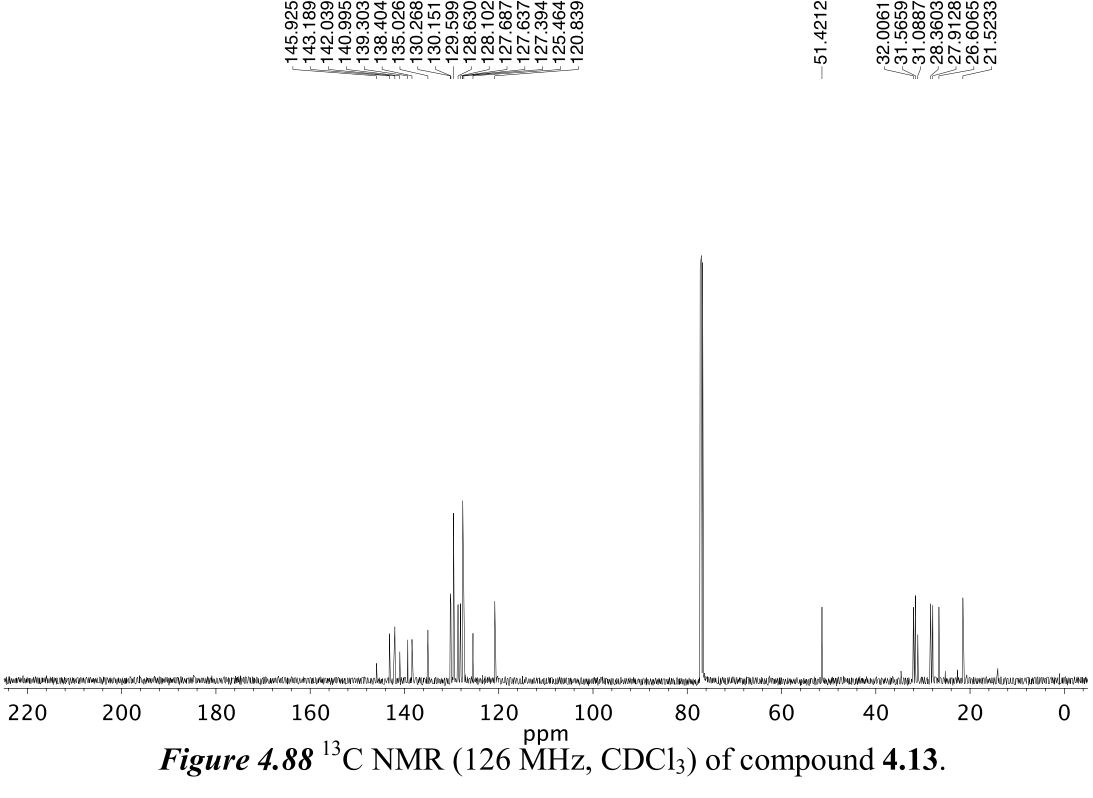


Figure 4.88 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.13**.

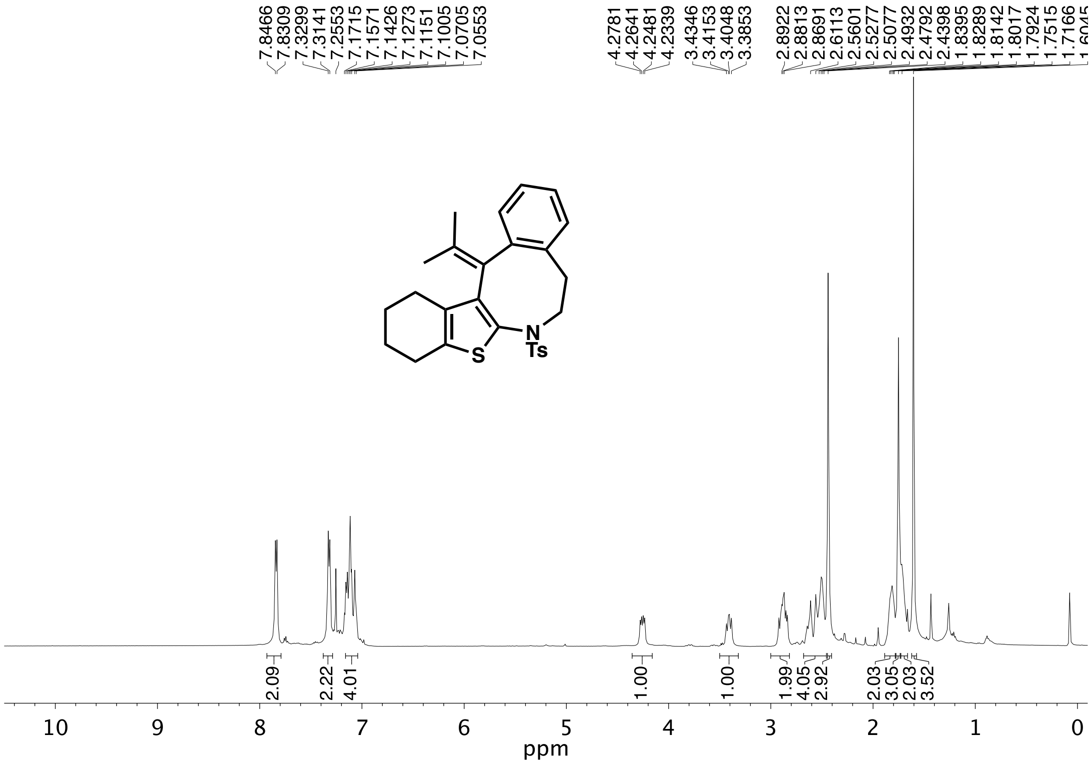


Figure 4.89 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.14**.

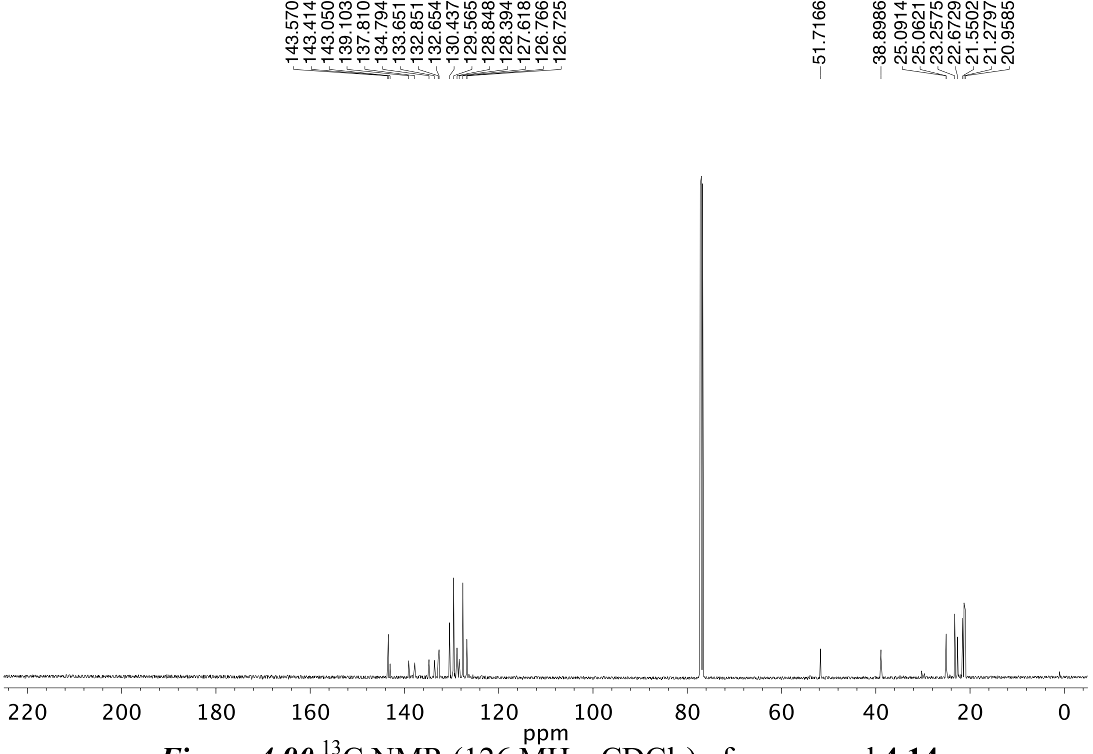


Figure 4.90 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.14**.

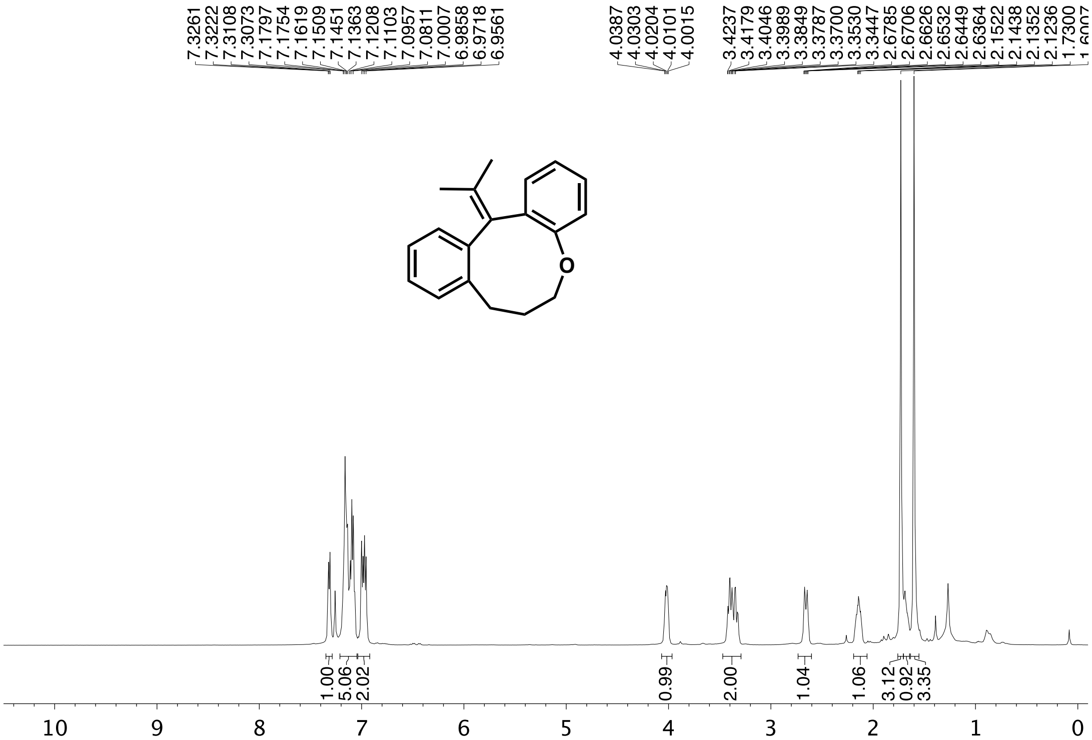


Figure 4.91 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.15**.

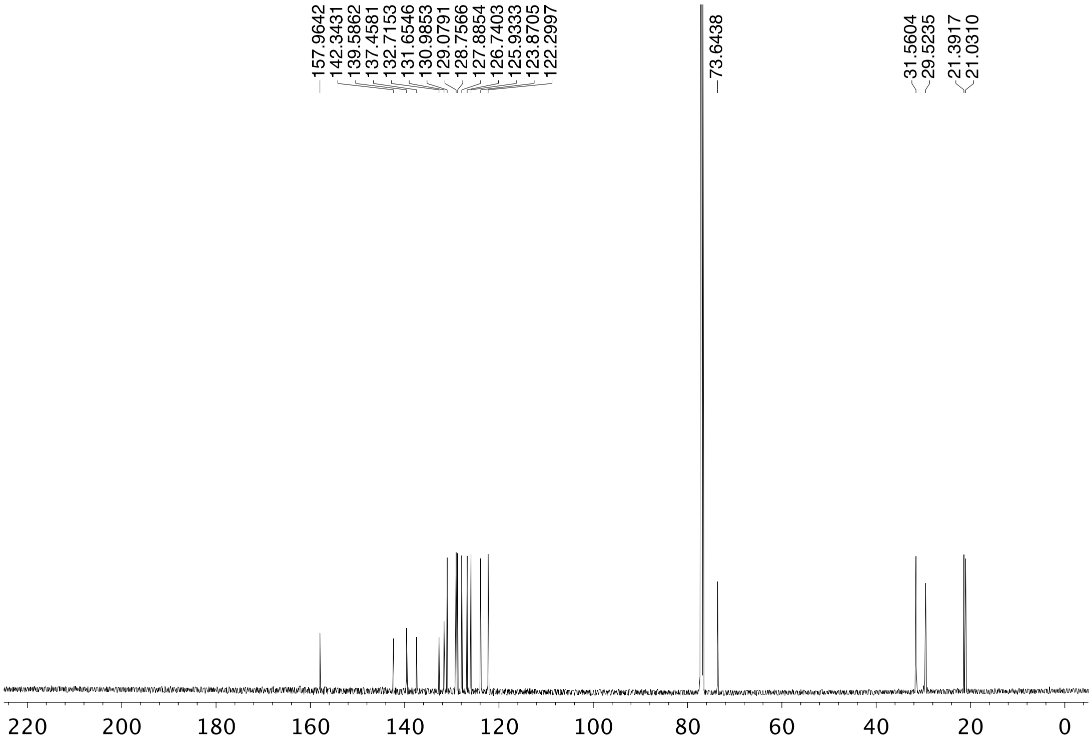


Figure 4.92 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.15**.

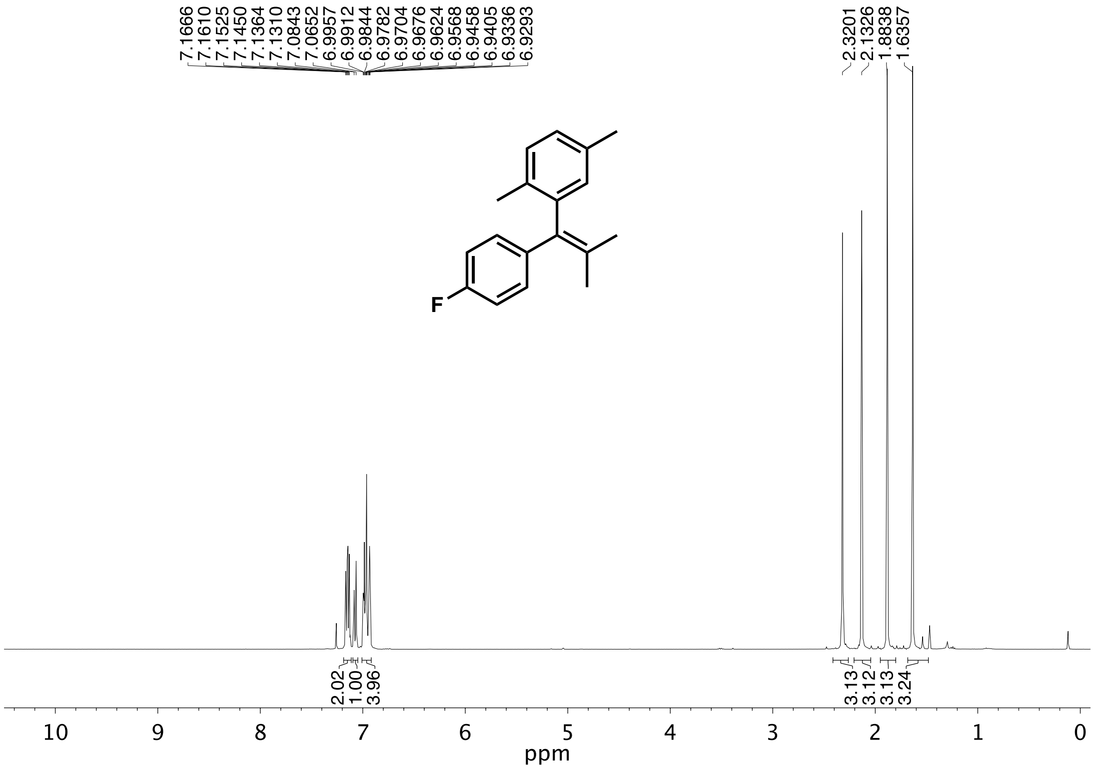


Figure 4.93 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.17**.

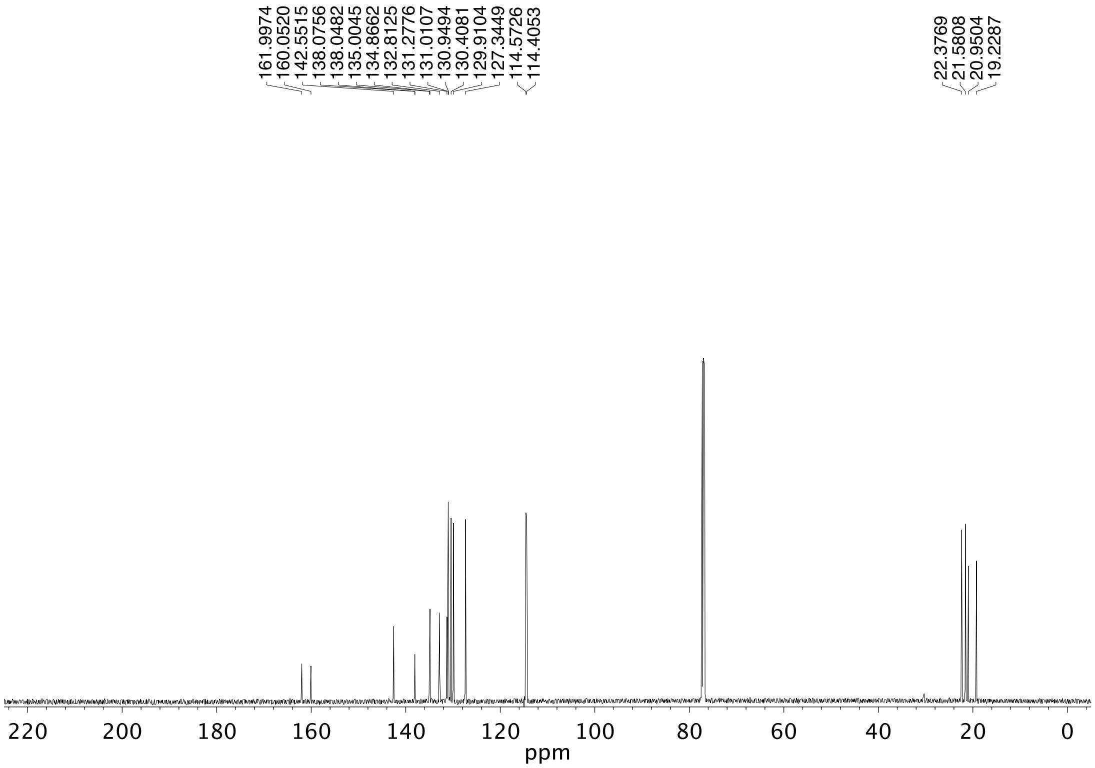


Figure 4.94^{13}C NMR (126 MHz, $CDCl_3$) of compound **4.17**.

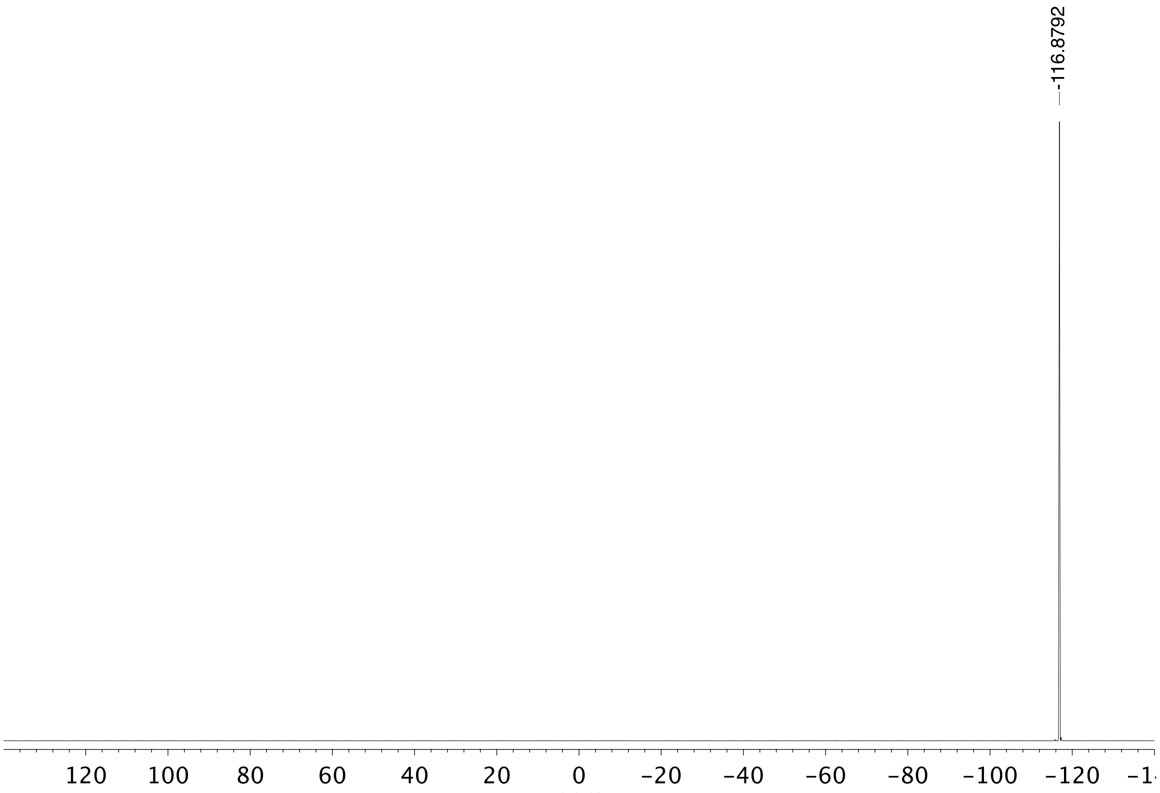


Figure 4.95 ^{19}F NMR (376 MHz, CDCl$_3$) of compound **4.17**.

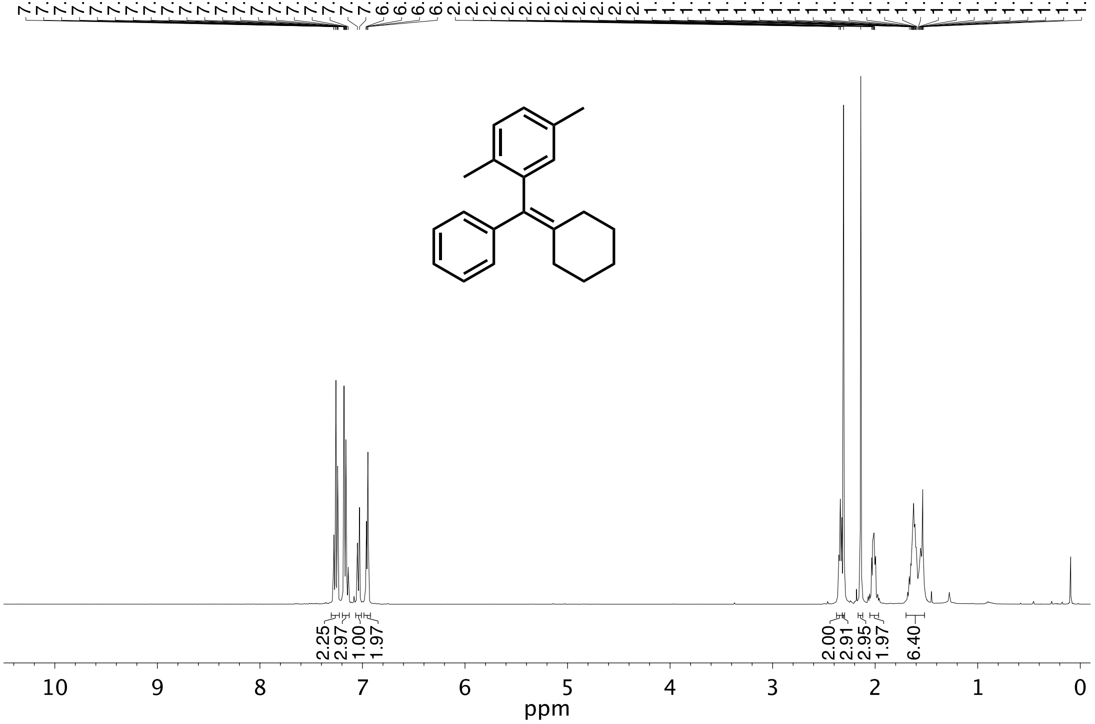


Figure 4.96 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.18**.

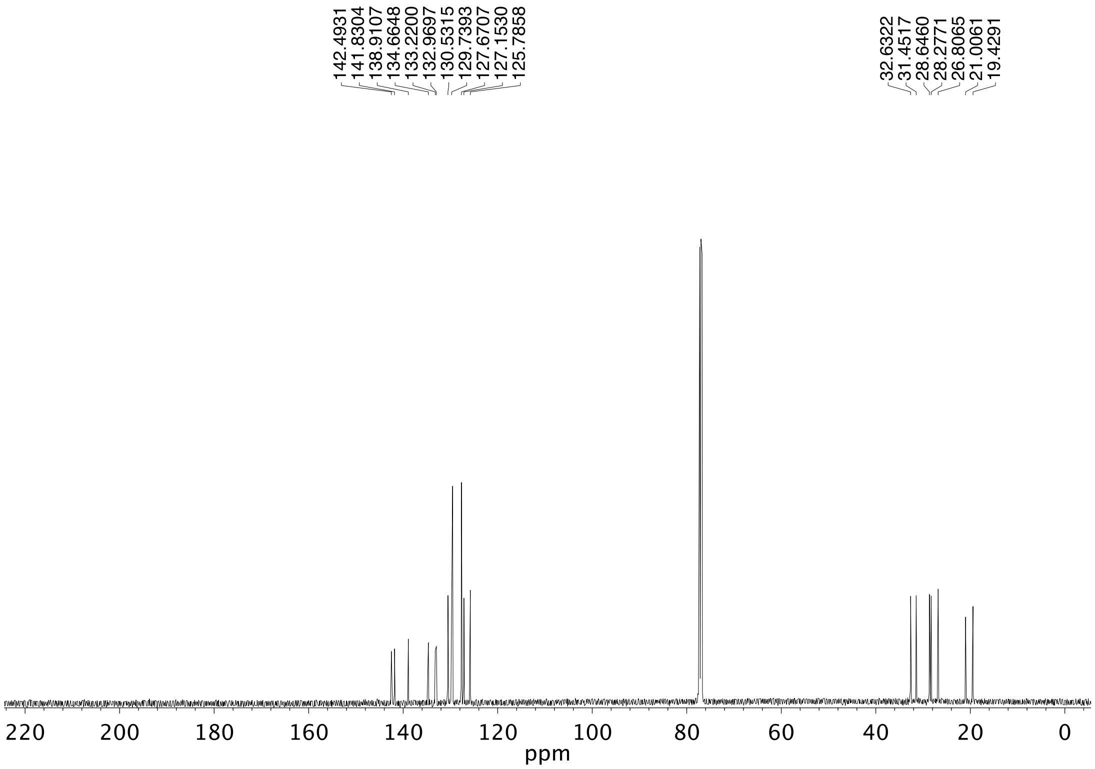


Figure 4.97 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.18**.

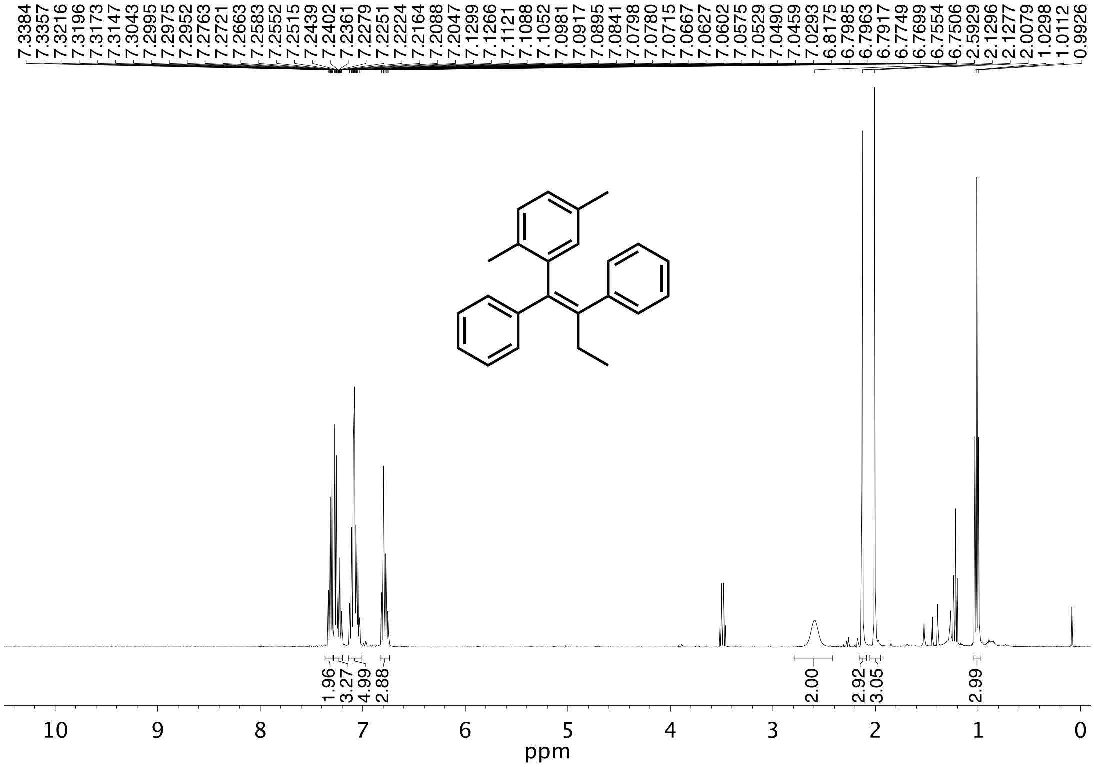


Figure 4.98 ^{1}H NMR (400 MHz, CDCl$_3$) of compound **4.19Z**.

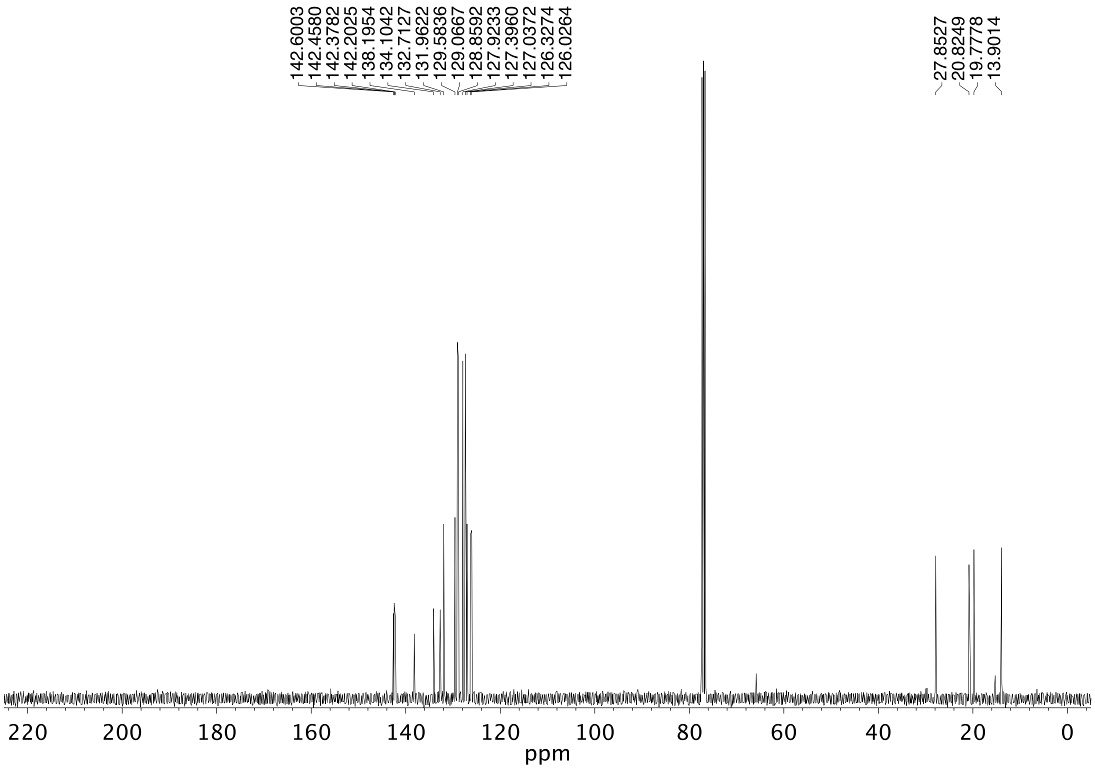


Figure 4.99 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **4.19Z**.

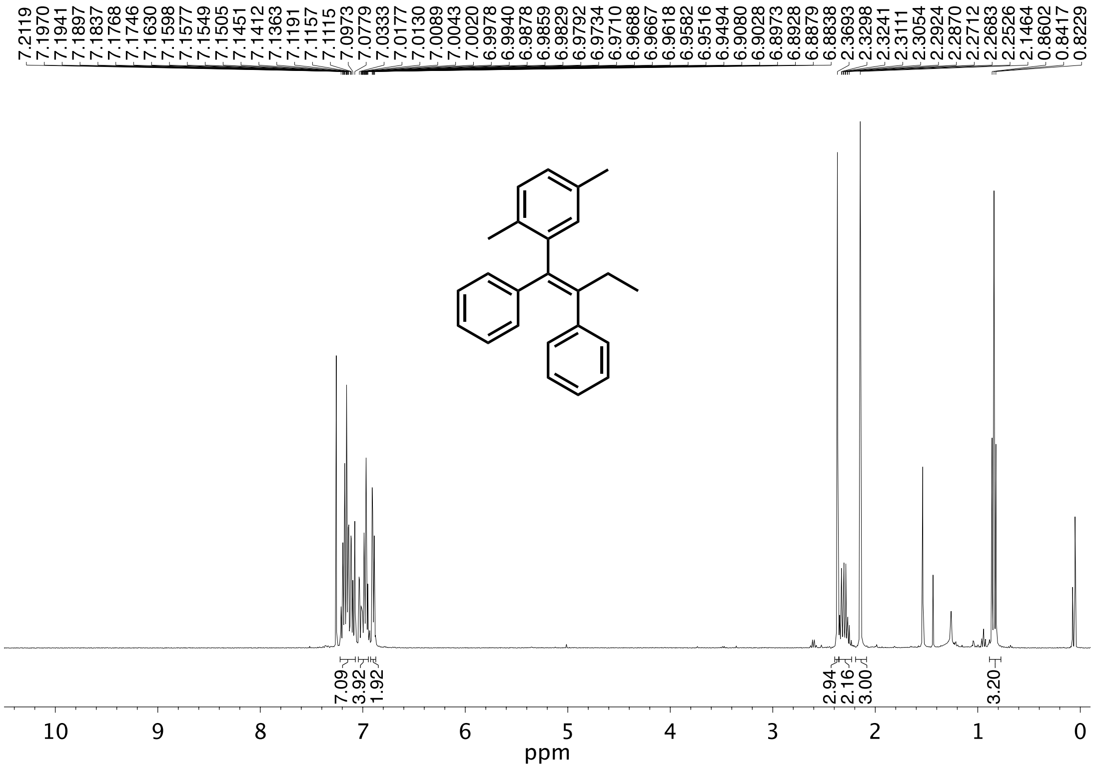


Figure 4.100 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.19E**.

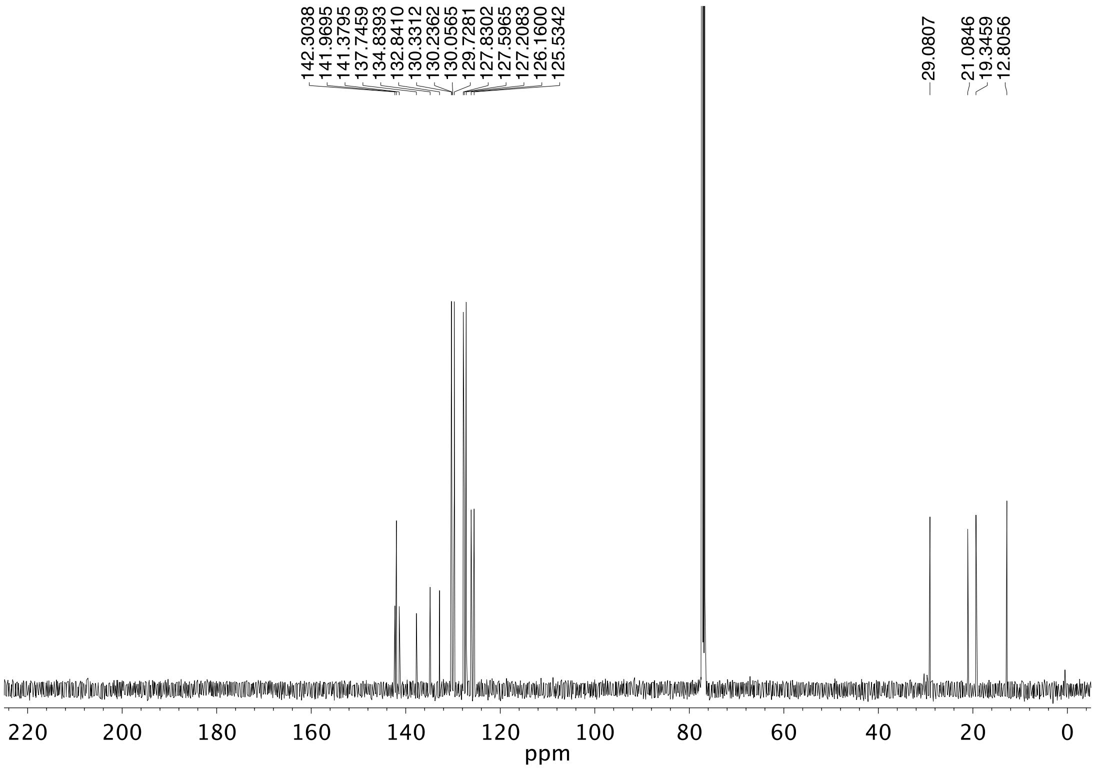


Figure 4.101 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.19E**.

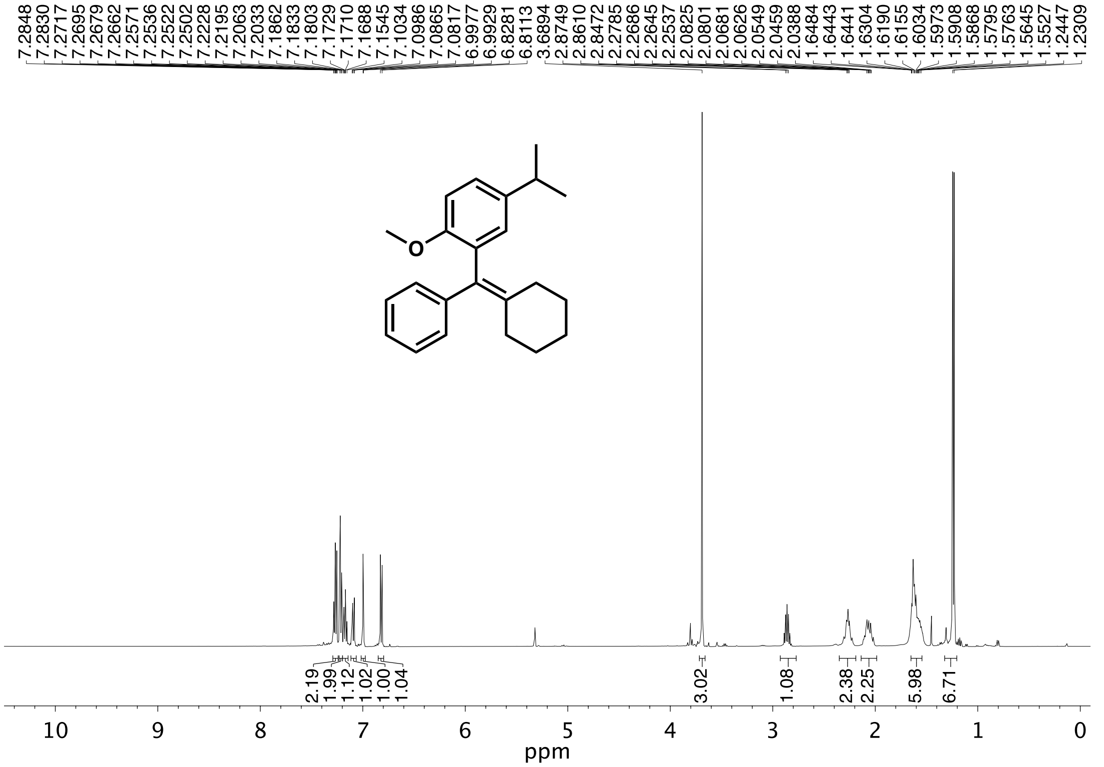


Figure 4.102 ^{1}H NMR (500 MHz, CD$_2$Cl$_2$) of compound **4.20**.

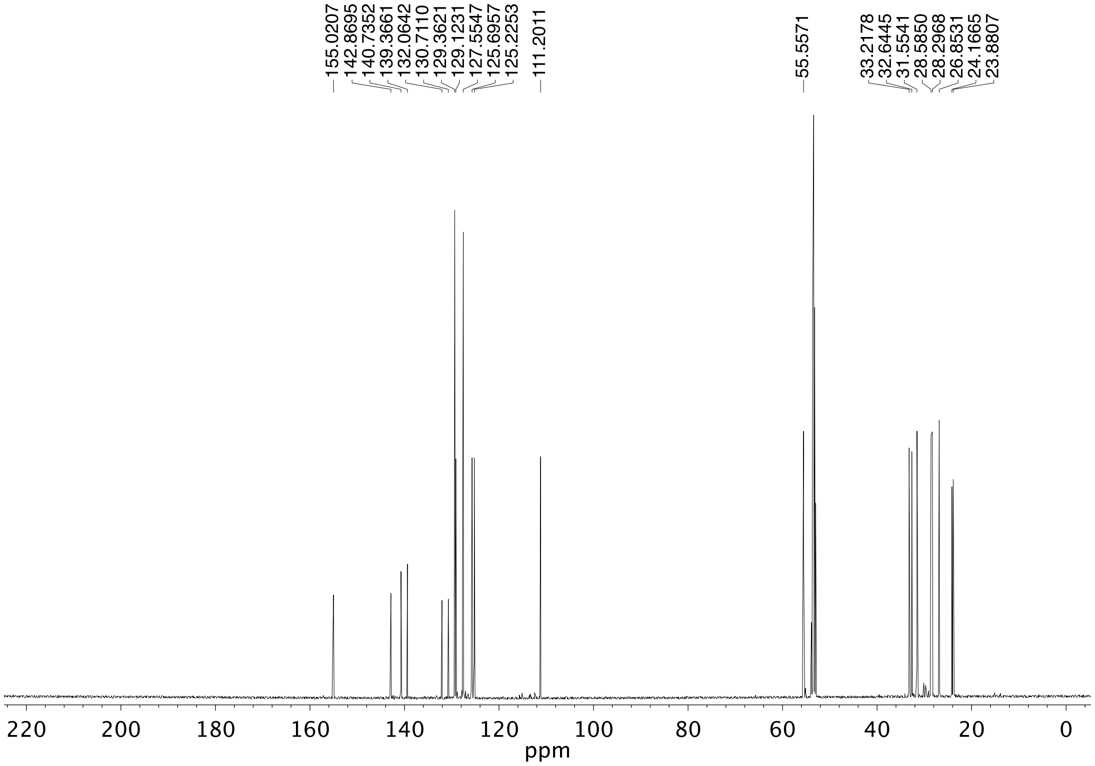


Figure 4.103 ^{13}C NMR (126 MHz, CD_2Cl_2) of compound **4.20**.

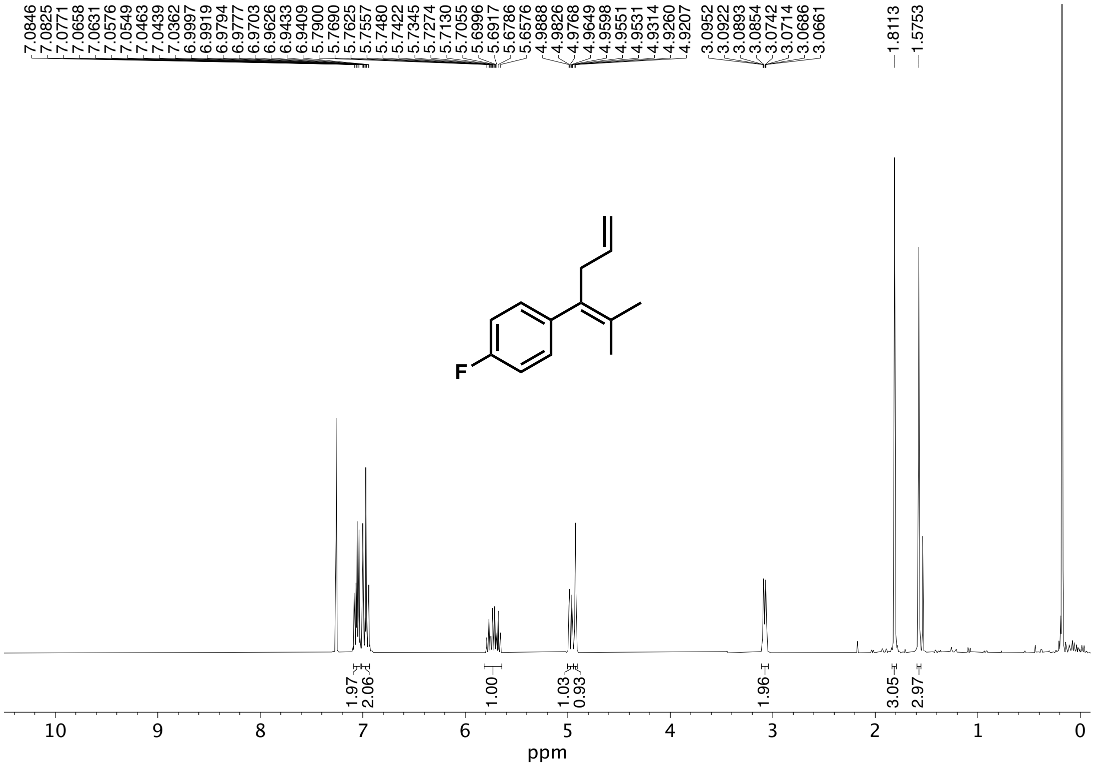


Figure 4.104 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4.27**.

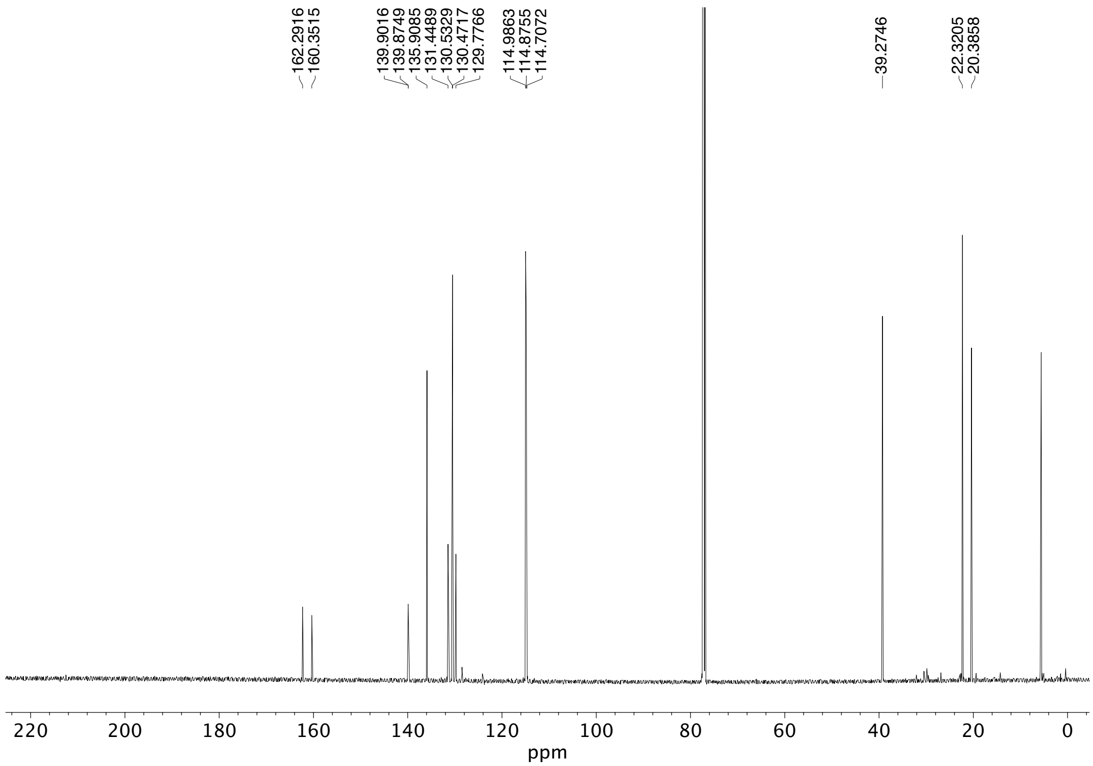


Figure 4.105 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.27**.

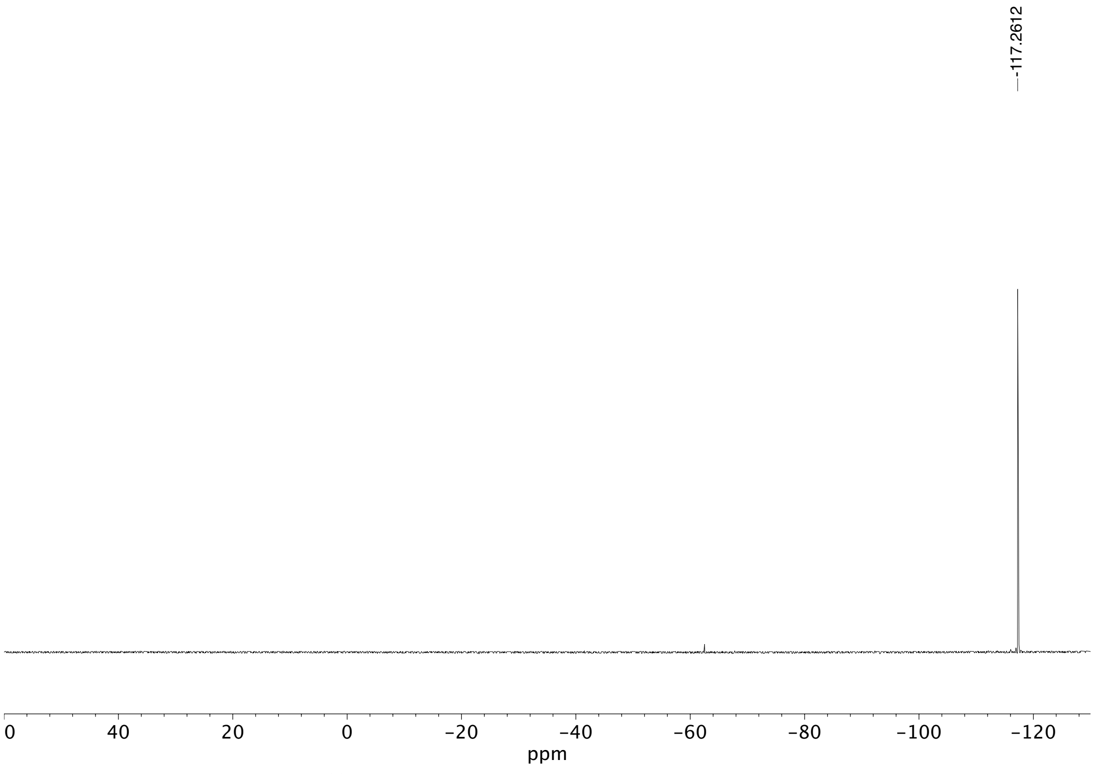


Figure 4.106 ^{19}F NMR (282 MHz, CDCl$_3$) of compound **4.27**.

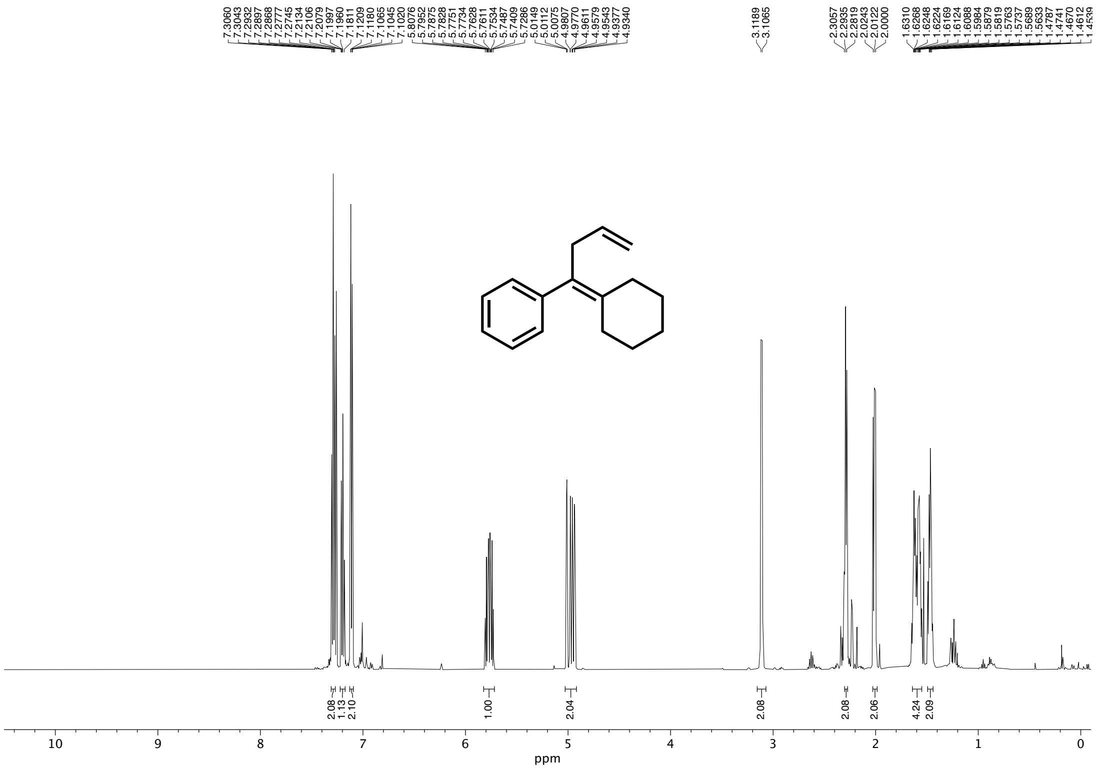


Figure 4.107 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4.28**.

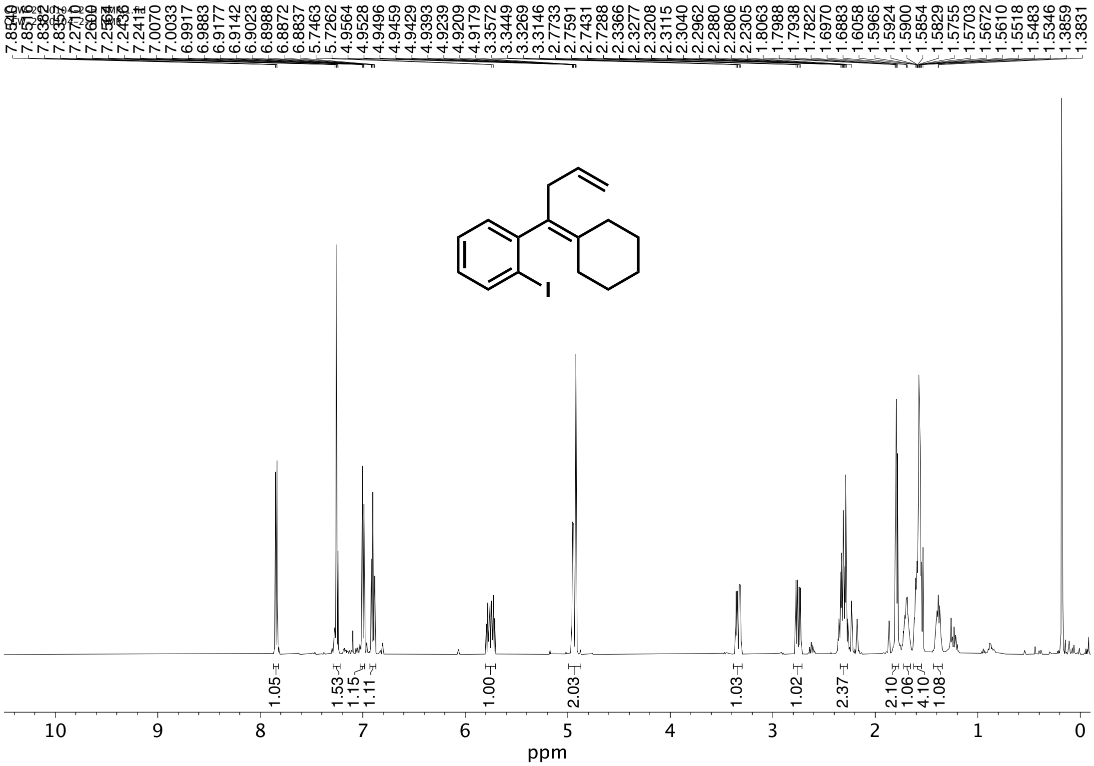


Figure 4.108 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4.29**.

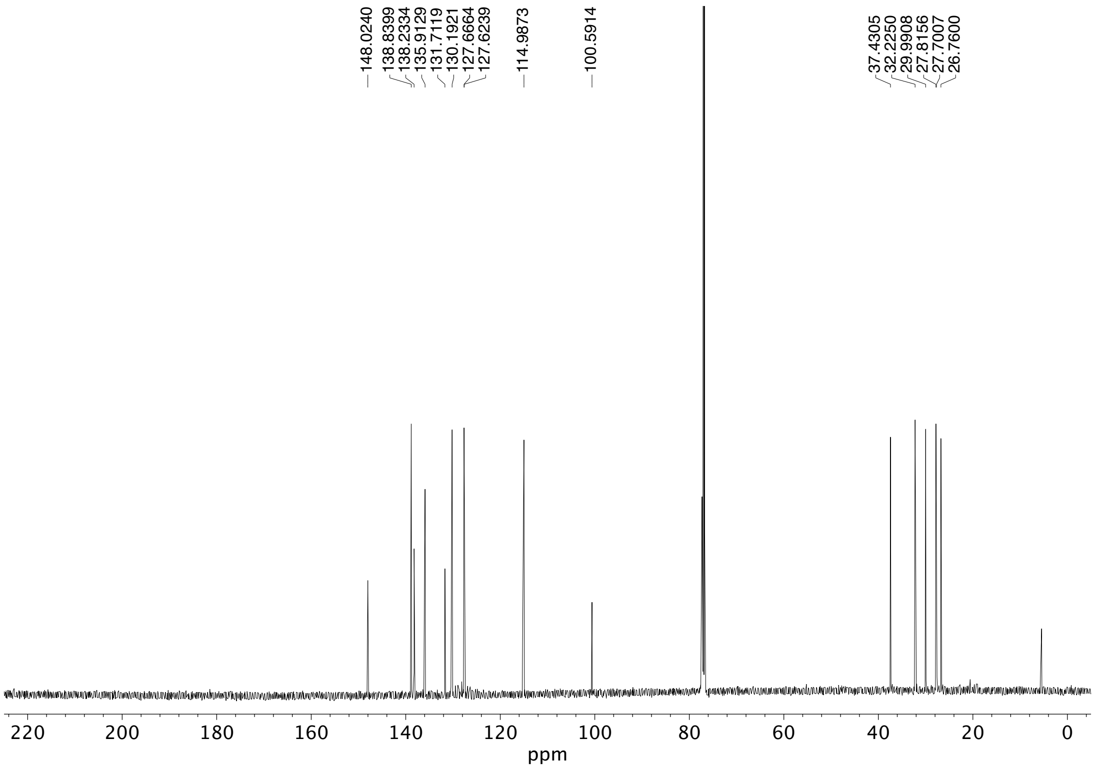


Figure 4.109 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.29**.

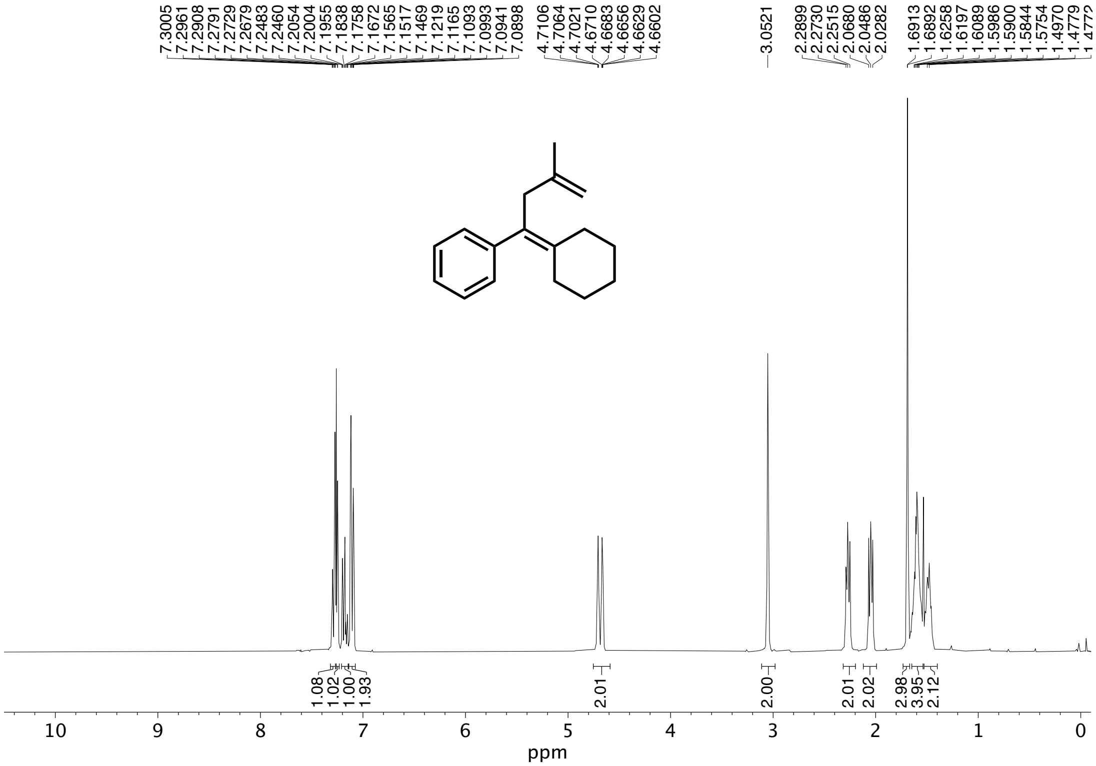


Figure 4.110 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.30**.

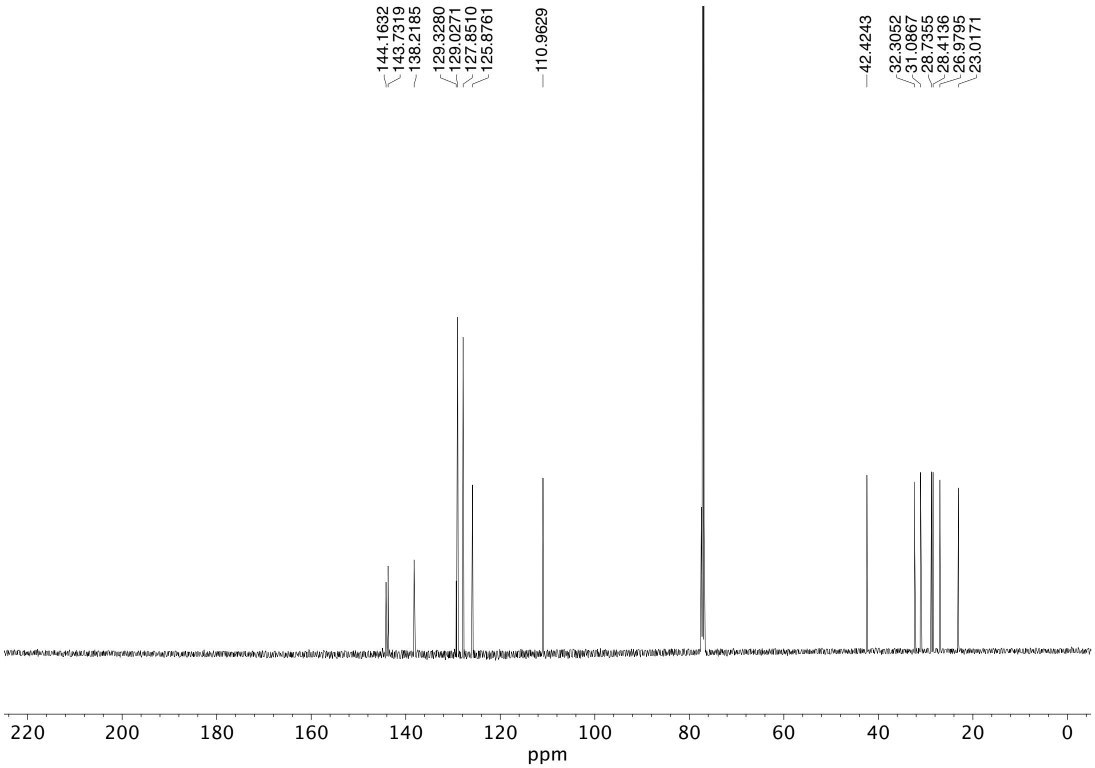
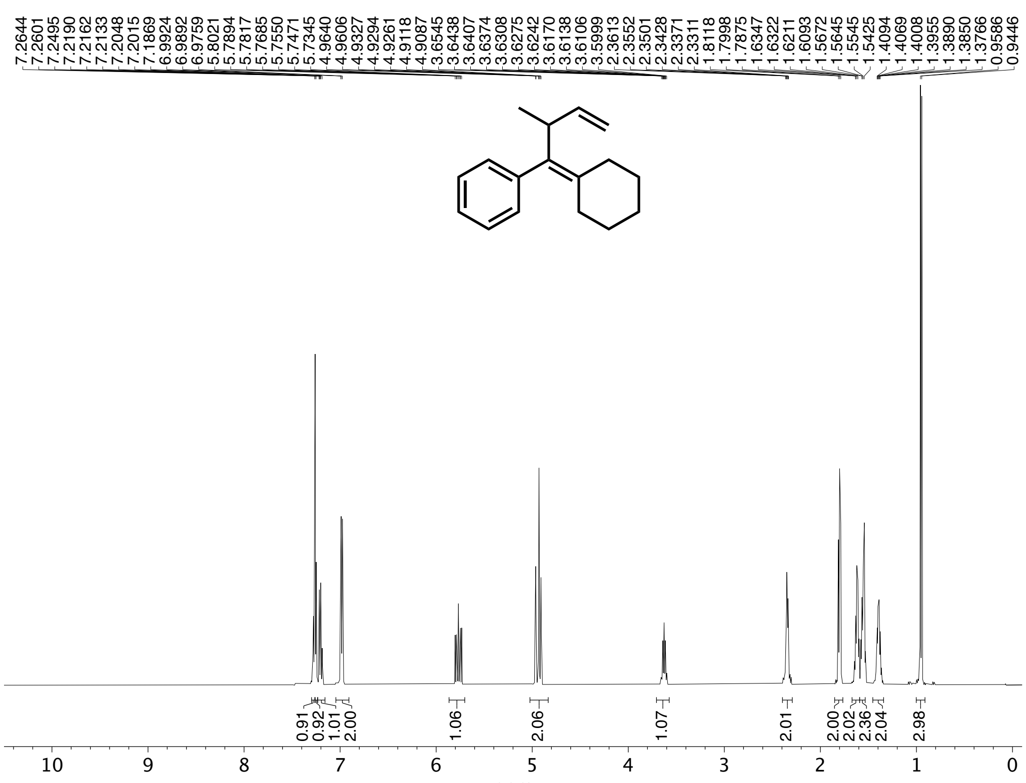


Figure 4.111 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.30**.



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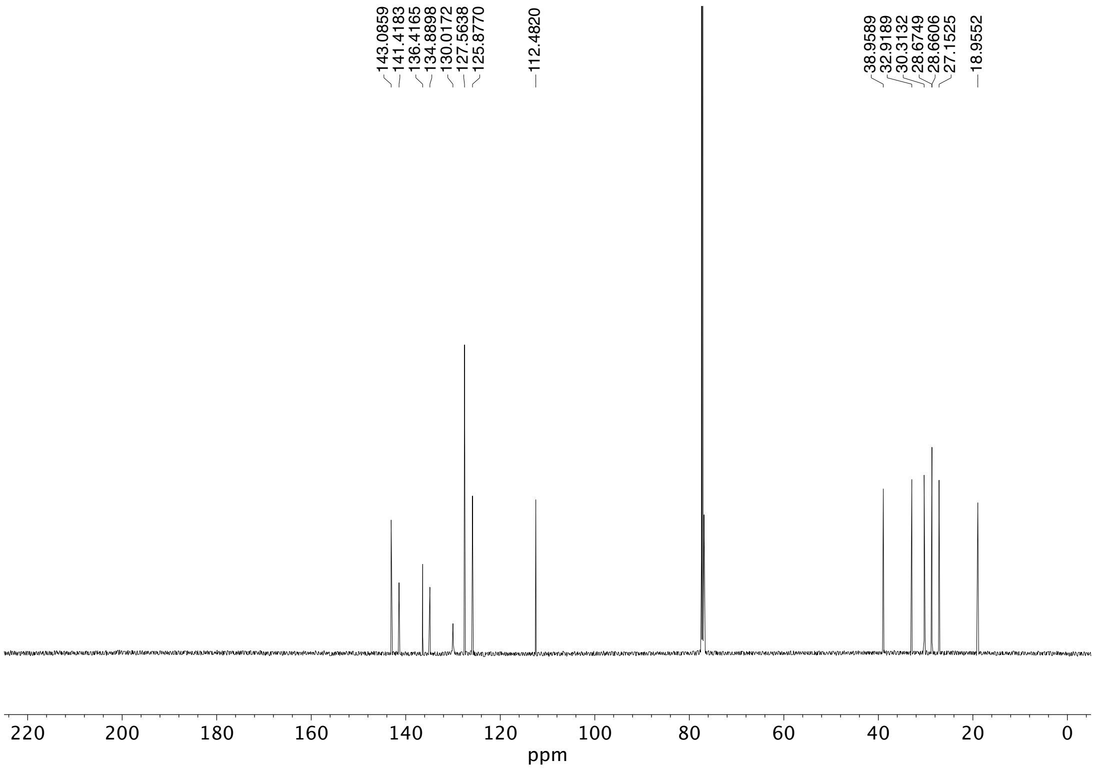

Figure 4.113 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.31**.

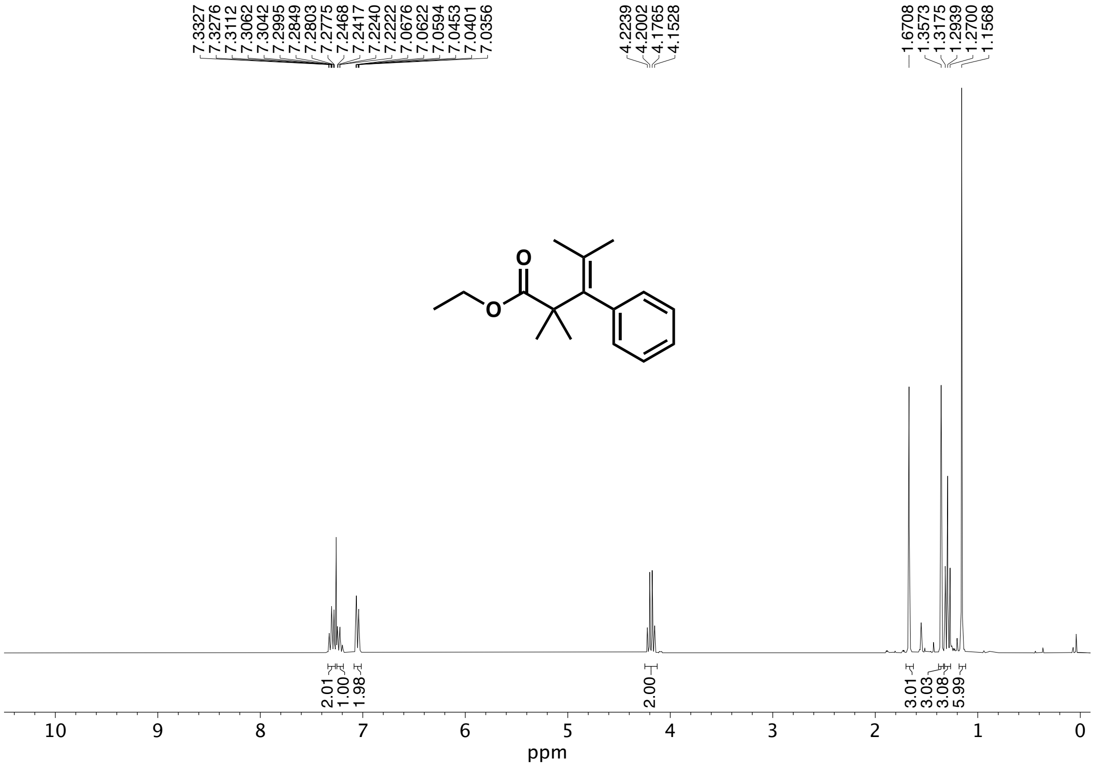

Figure 4.114 ^{1}H NMR (300 MHz, CDCl$_3$) of compound **4.39**.

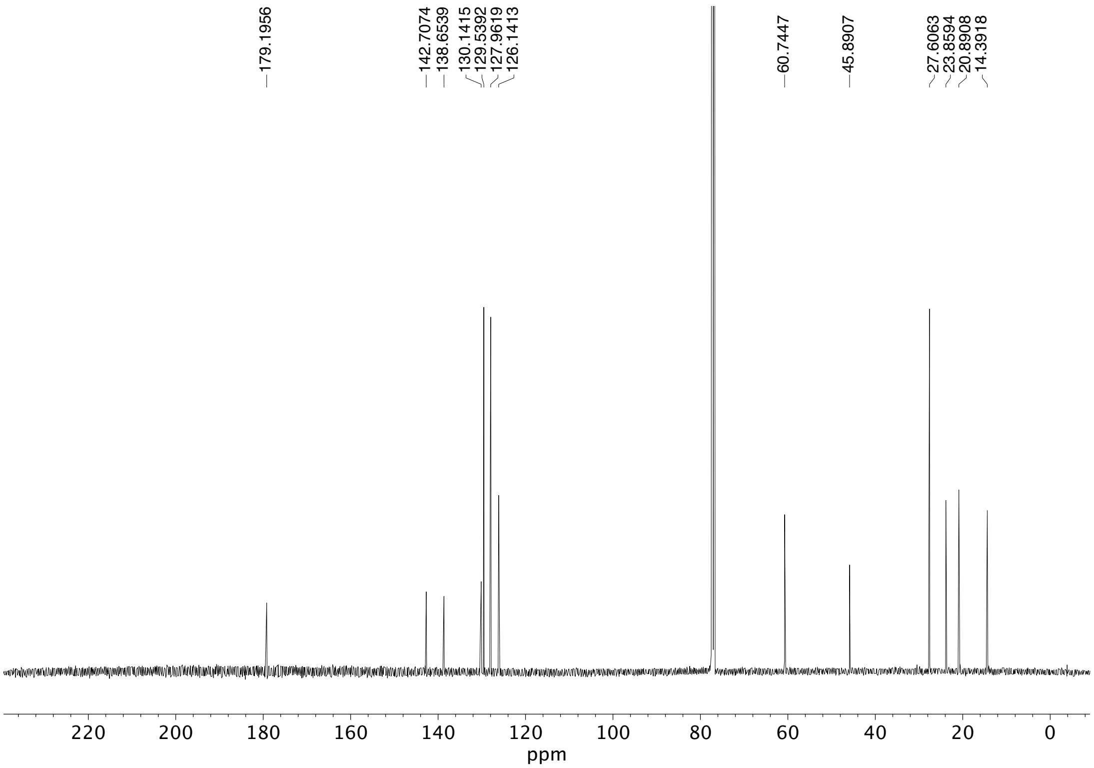

Figure 4.115 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.39**.

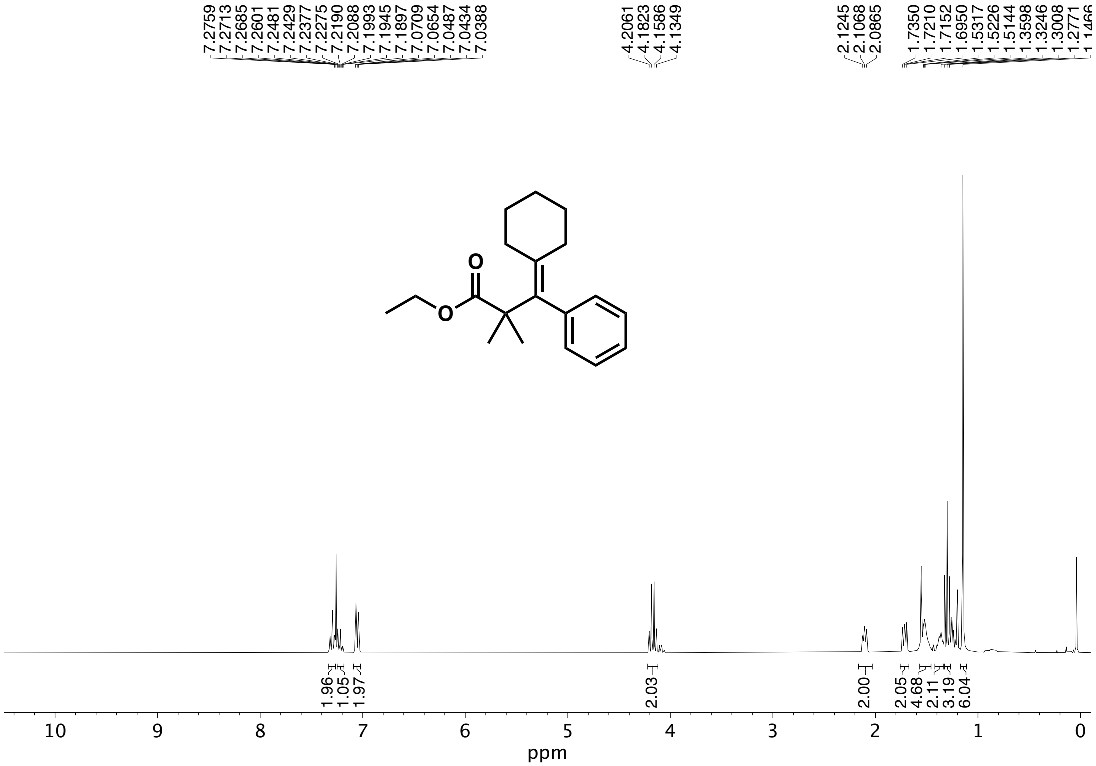

Figure 4.116 ^{1}H NMR (300 MHz, CDCl$_3$) of compound **4.40**.

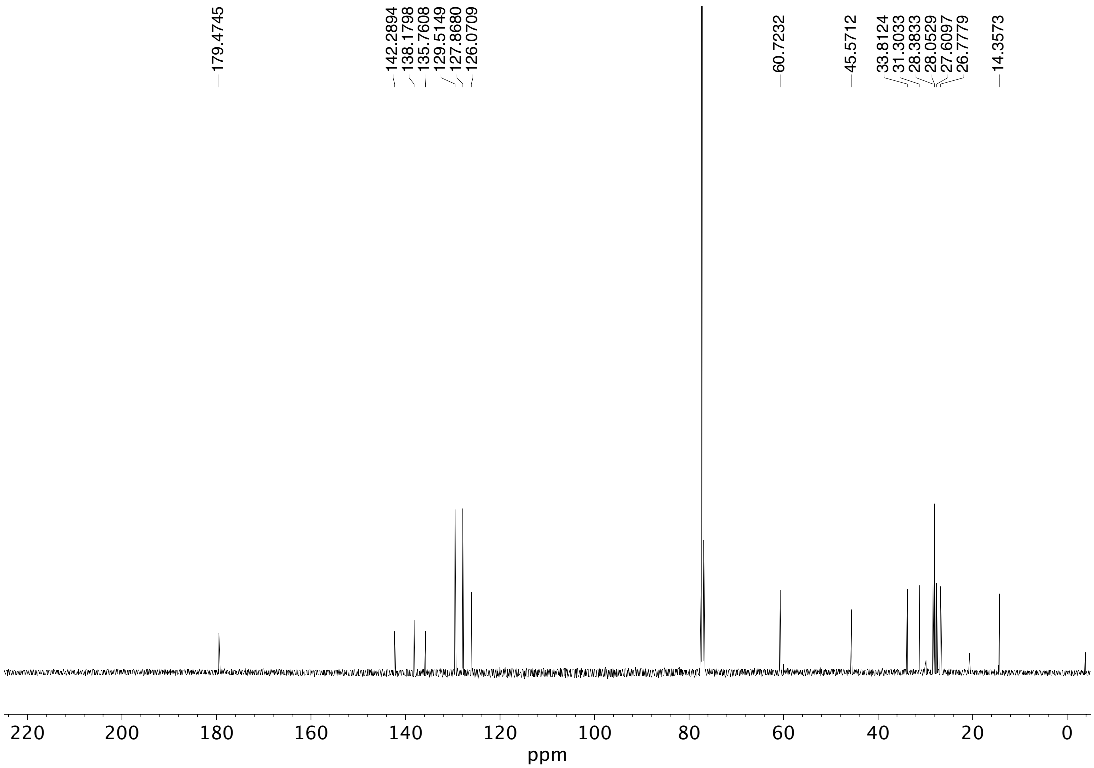

Figure 4.117 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.40**.

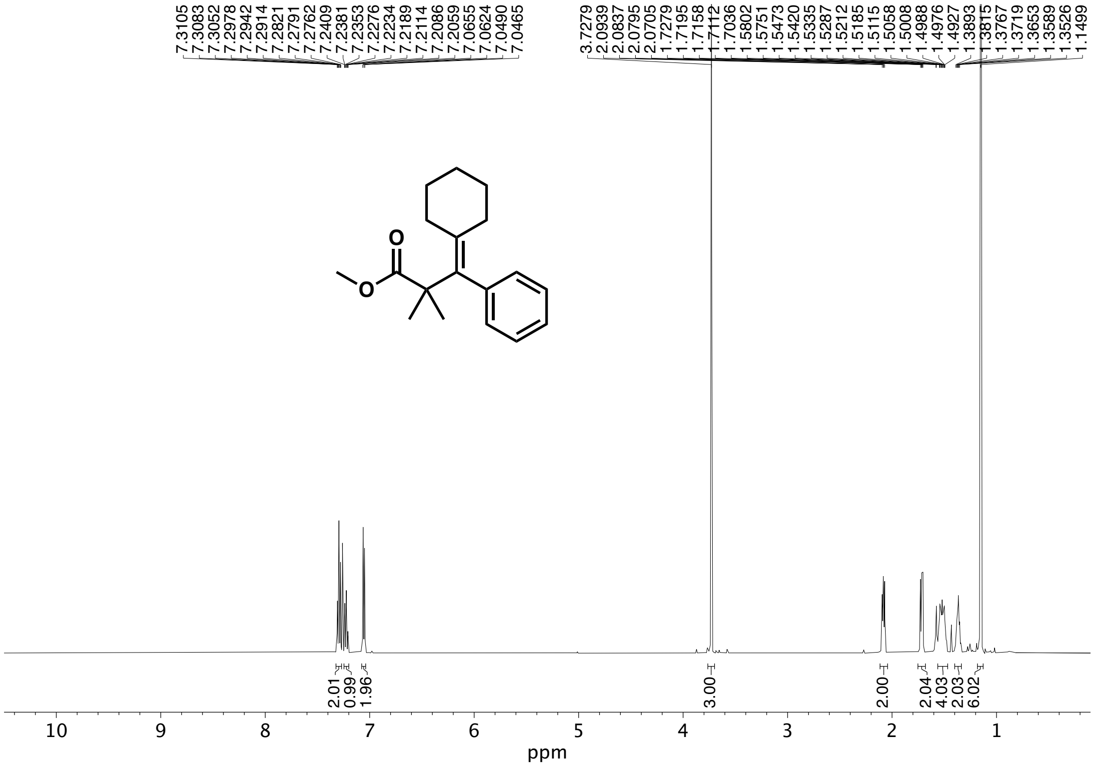

Figure 4.118 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.41**.

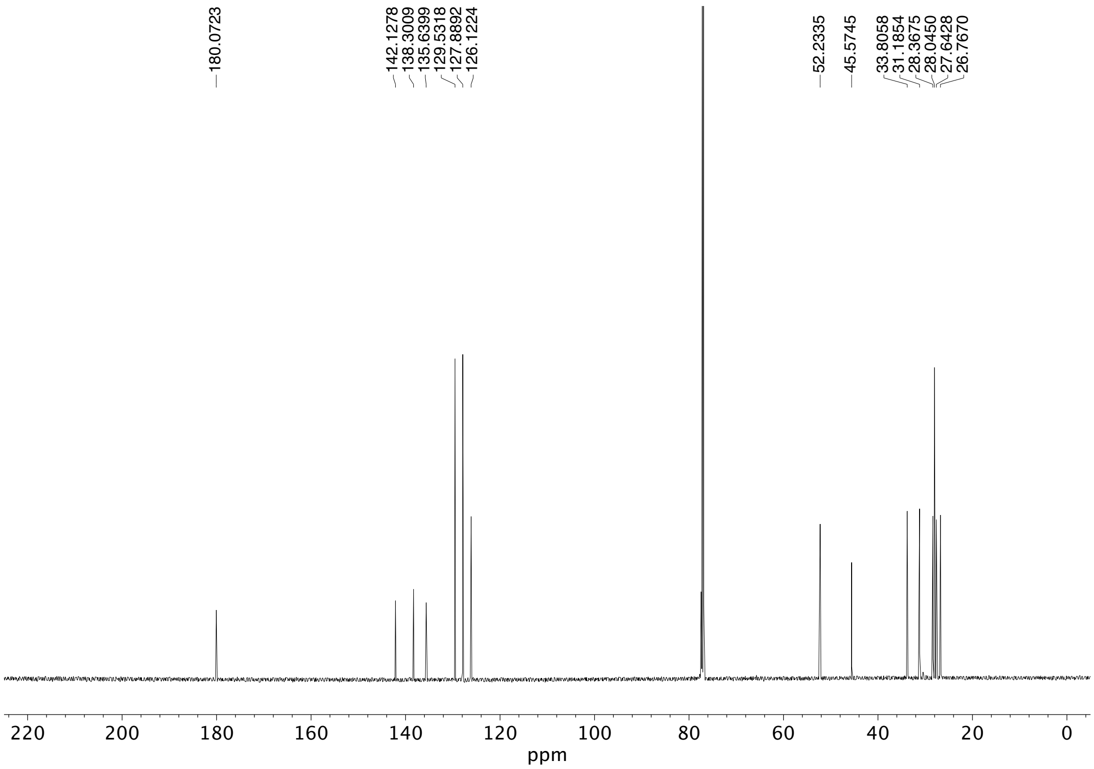

Figure 4.119 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.41**.

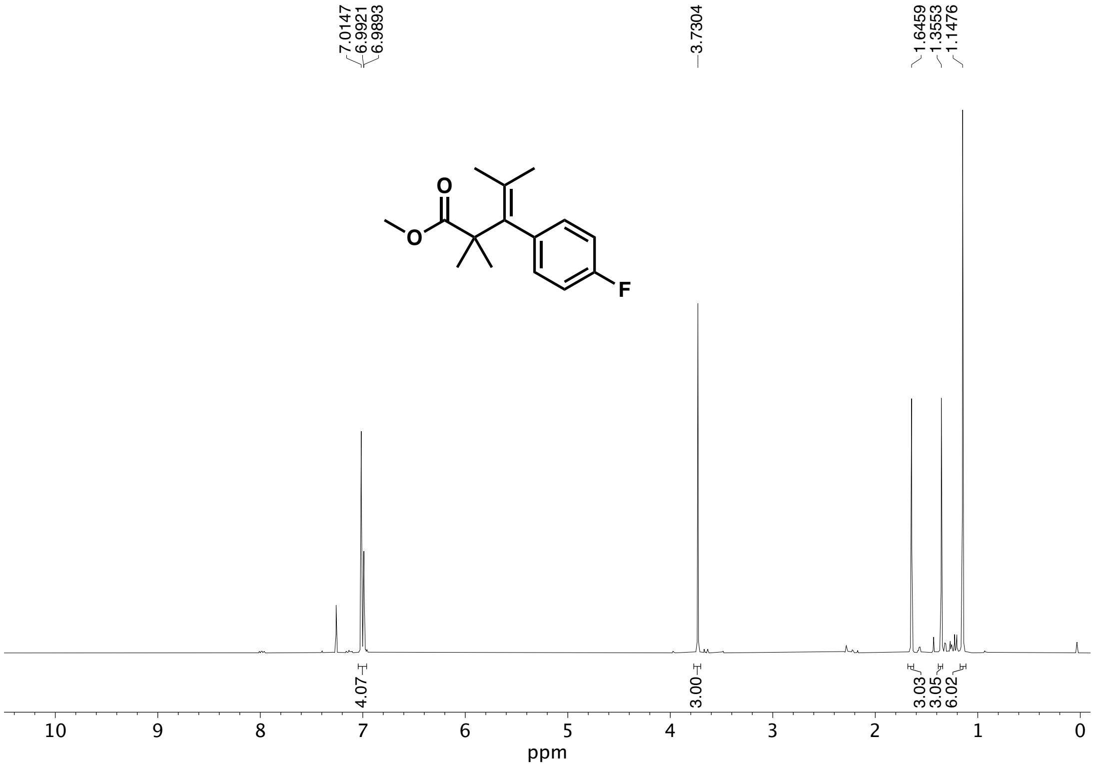

Figure 4.120 ^{1}H NMR (300 MHz, CDCl$_3$) of compound **4.42**.

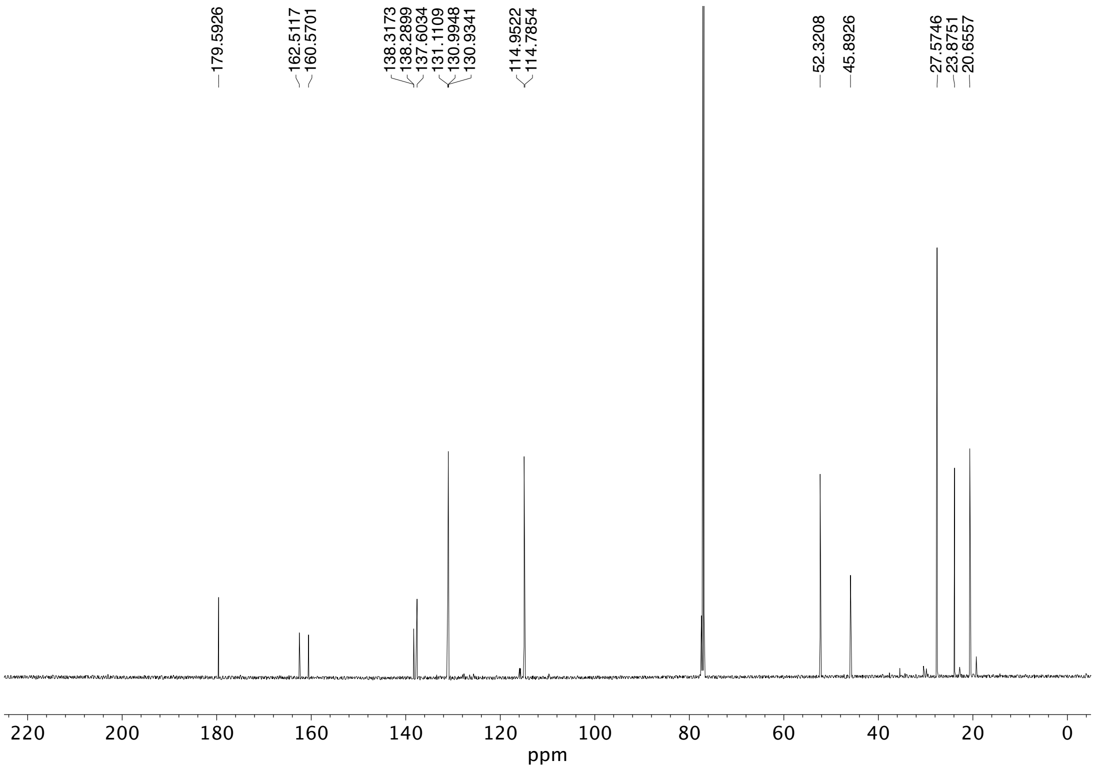

Figure 4.121 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.42**.

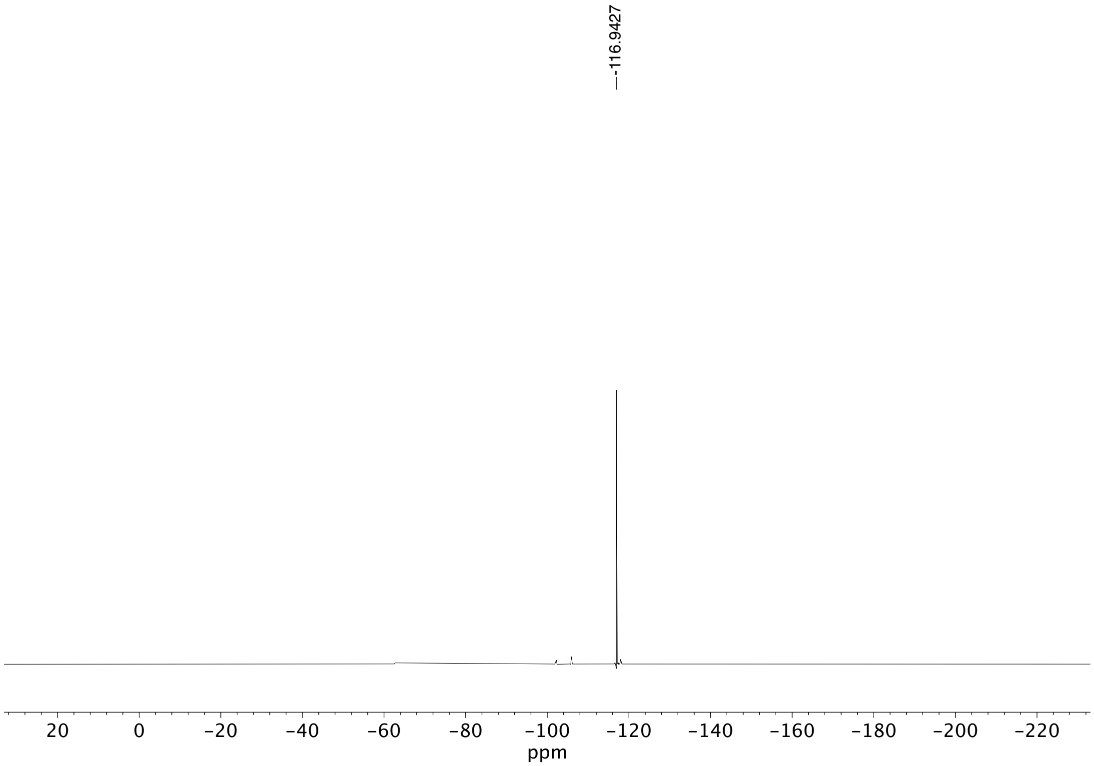

Figure 4.122 ^{19}F NMR (282 MHz, CDCl$_3$) of compound **4.42**.

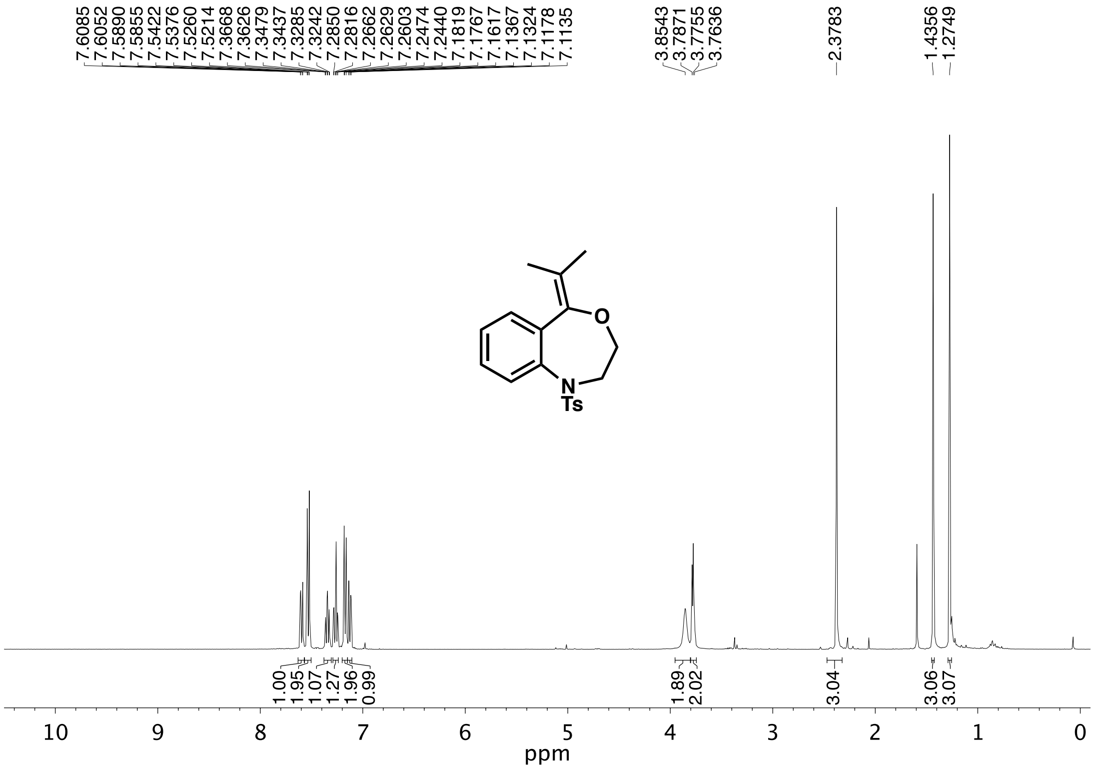

Figure 4.123 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.44**.

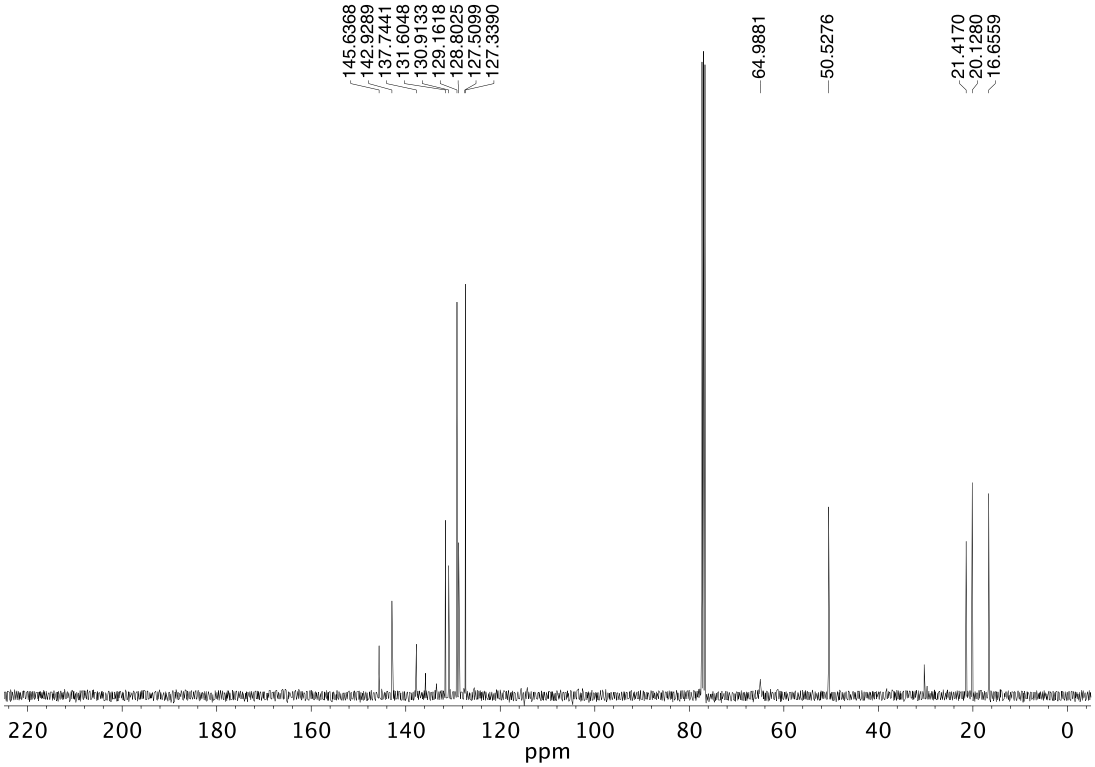

Figure 4.124 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **4.44**.

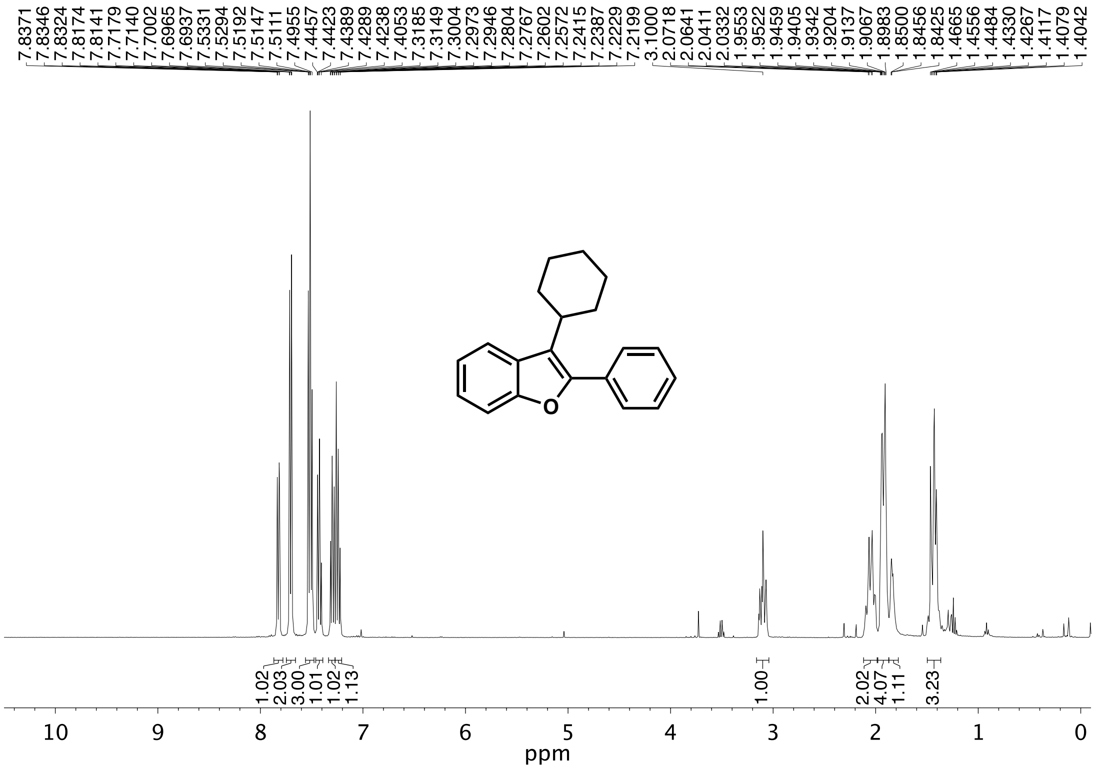

Figure 4.125 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4.46**.

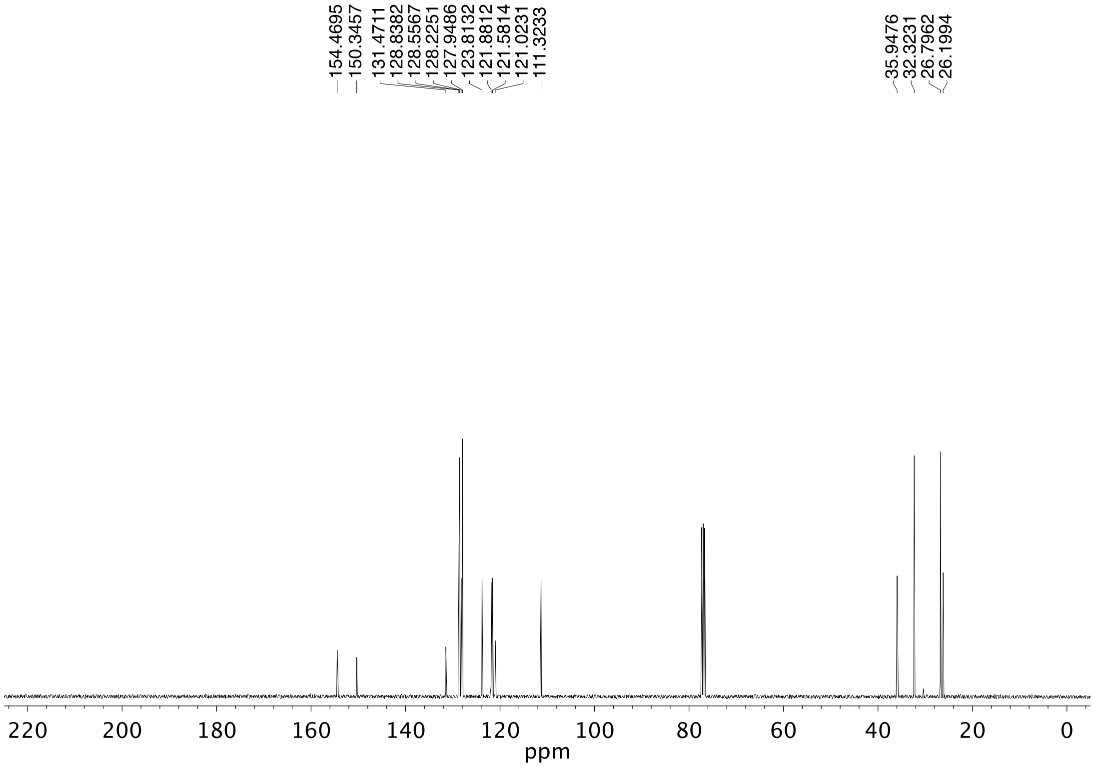

Figure 4.126 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **4.46**.

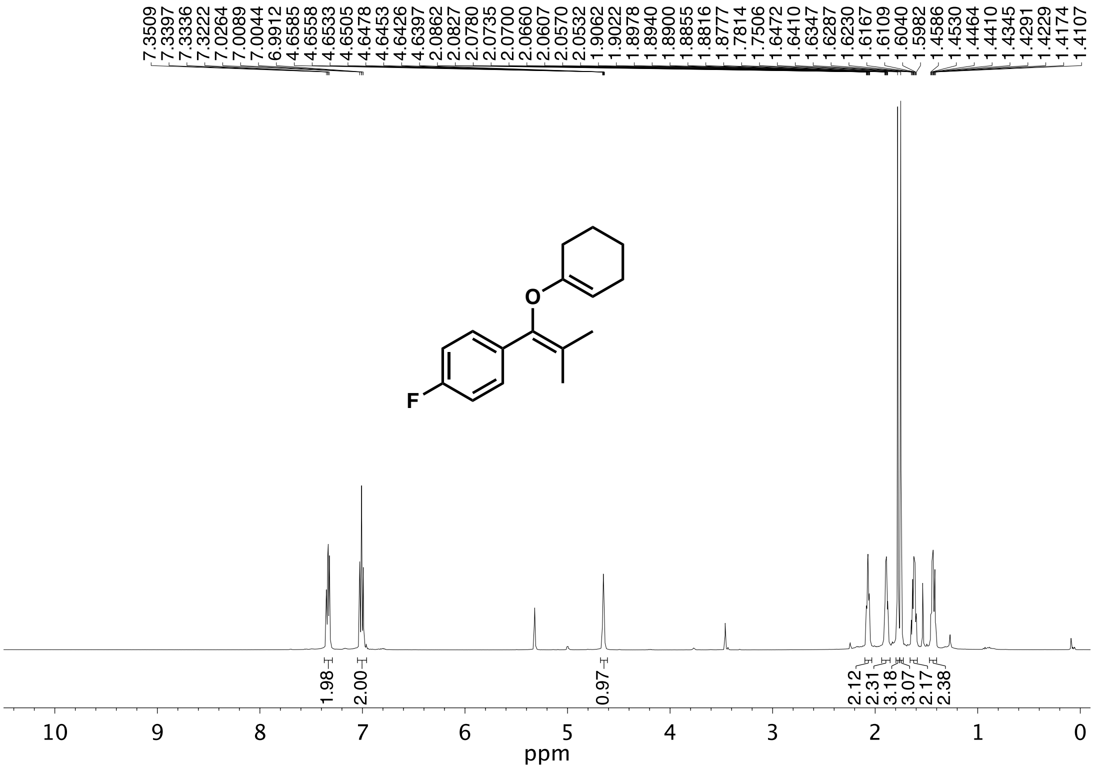

Figure 4.127 ^{1}H NMR (500 MHz, CD_2Cl_2) of compound **4.47**.

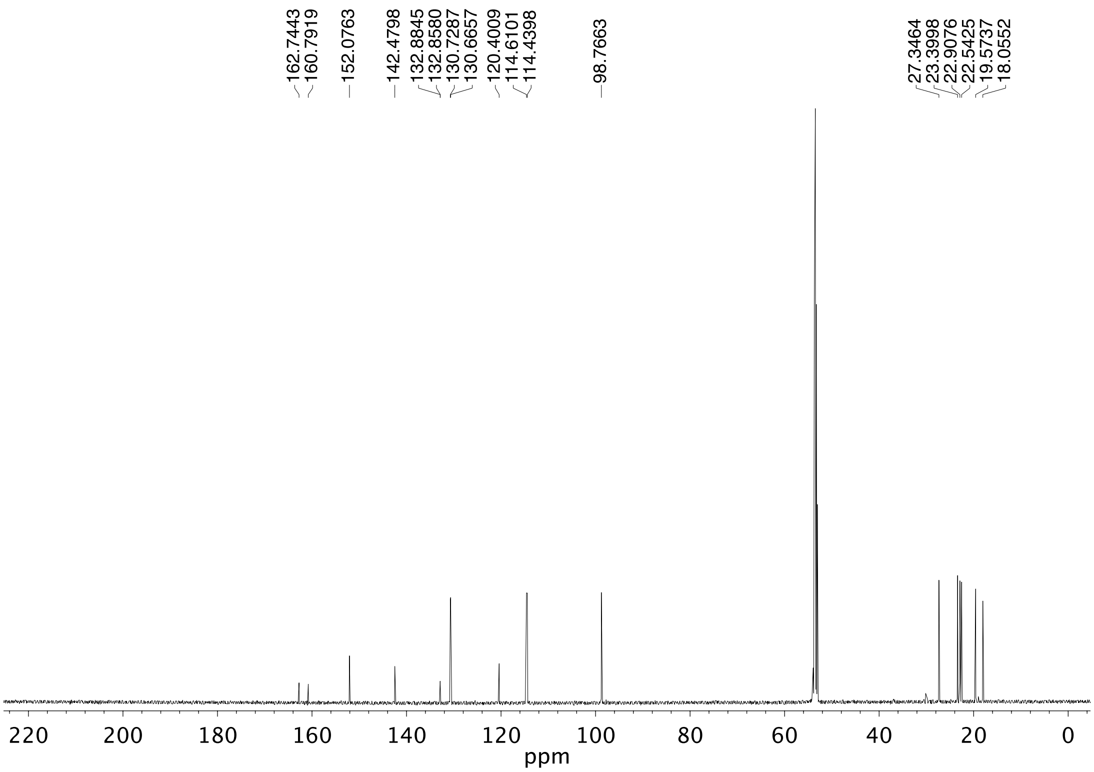

Figure 4.128 ^{13}C NMR (126 MHz, CD_2Cl_2) of compound **4.47**.

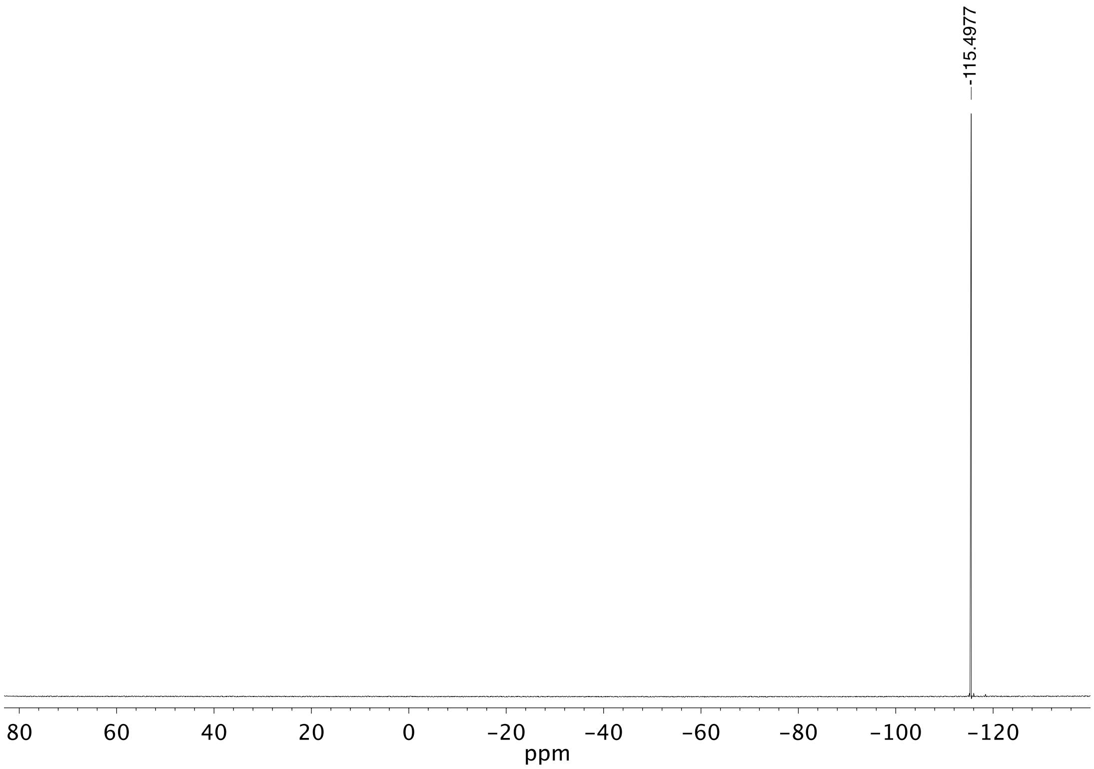

Figure 4.129 ^{19}F NMR (282 MHz, CD_2Cl_2) of compound **4.47**.

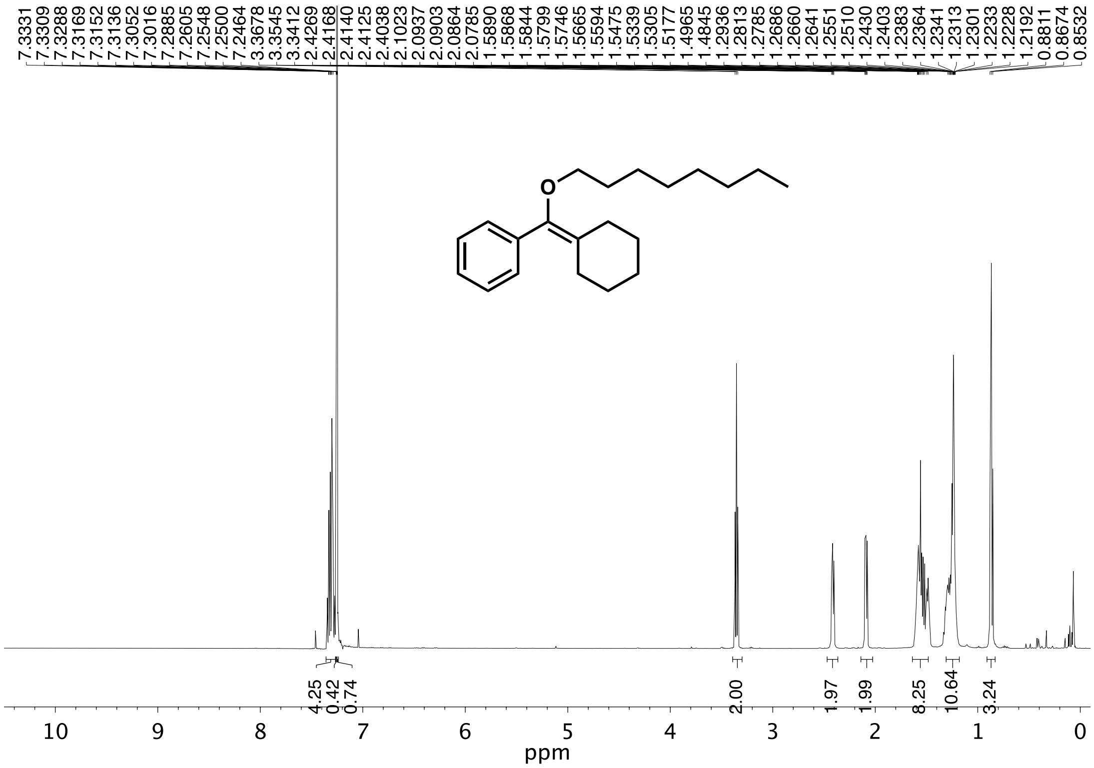

Figure 4.130 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4.48**.

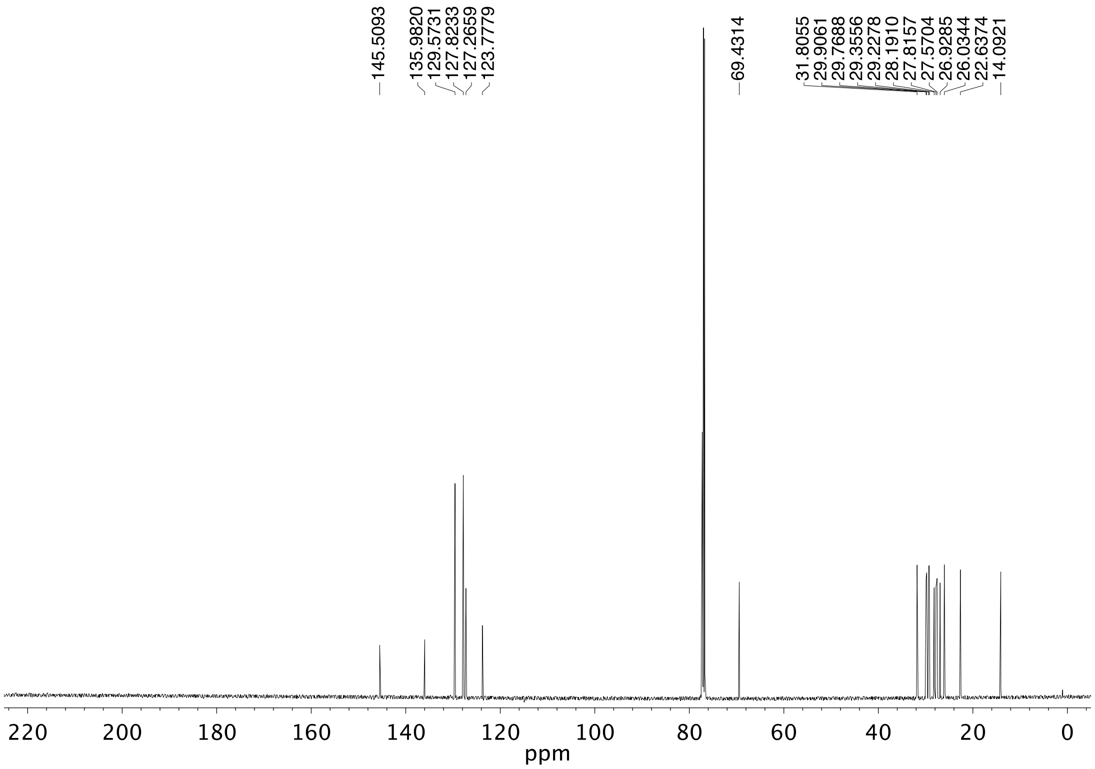

Figure 4.131 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.48**.

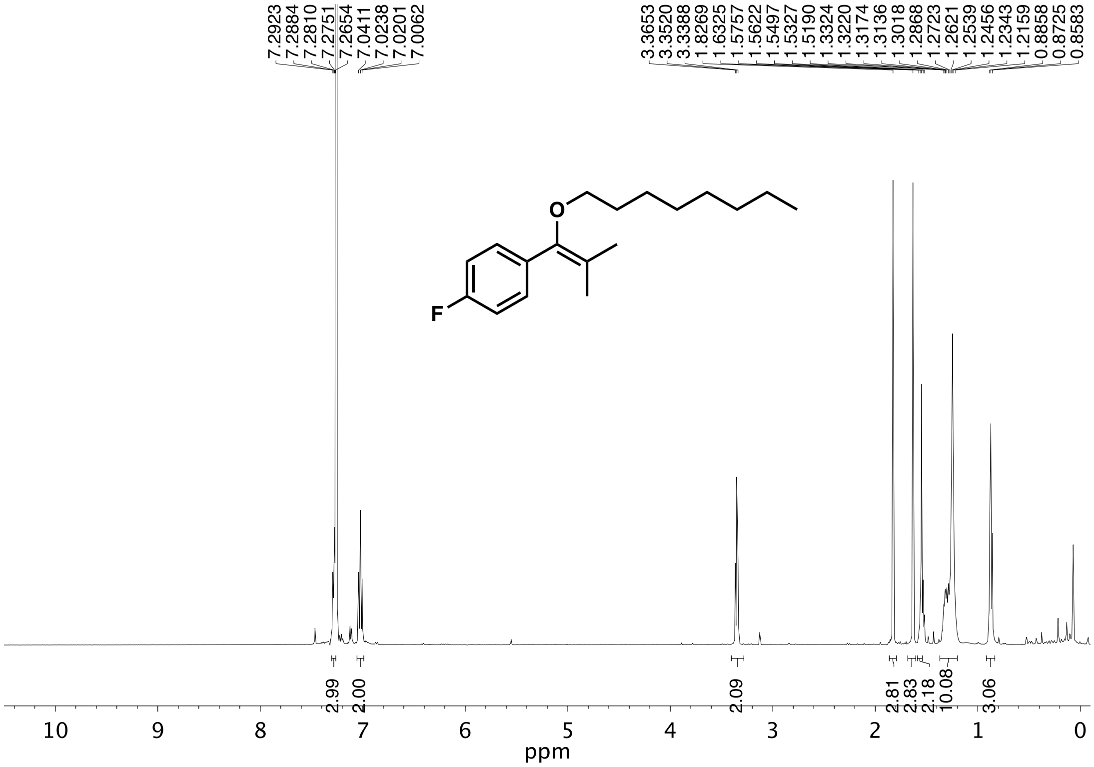

Figure 4.132 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **4.49**.

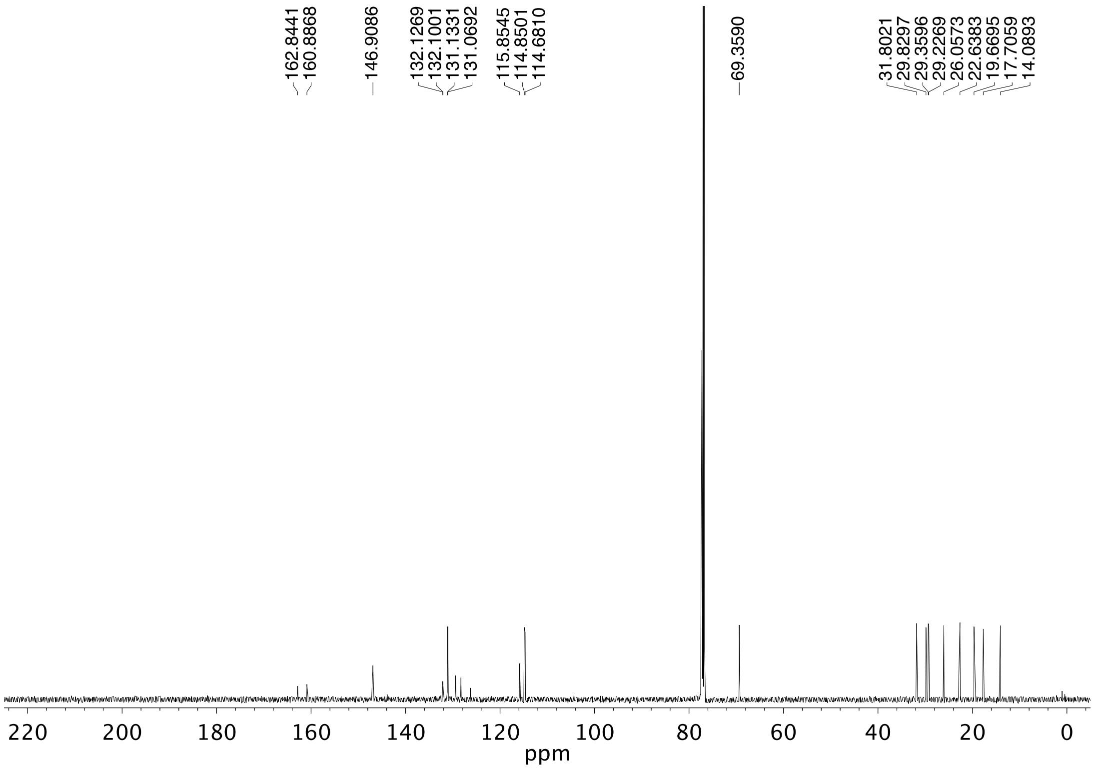

Figure 4.133 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **4.49**.

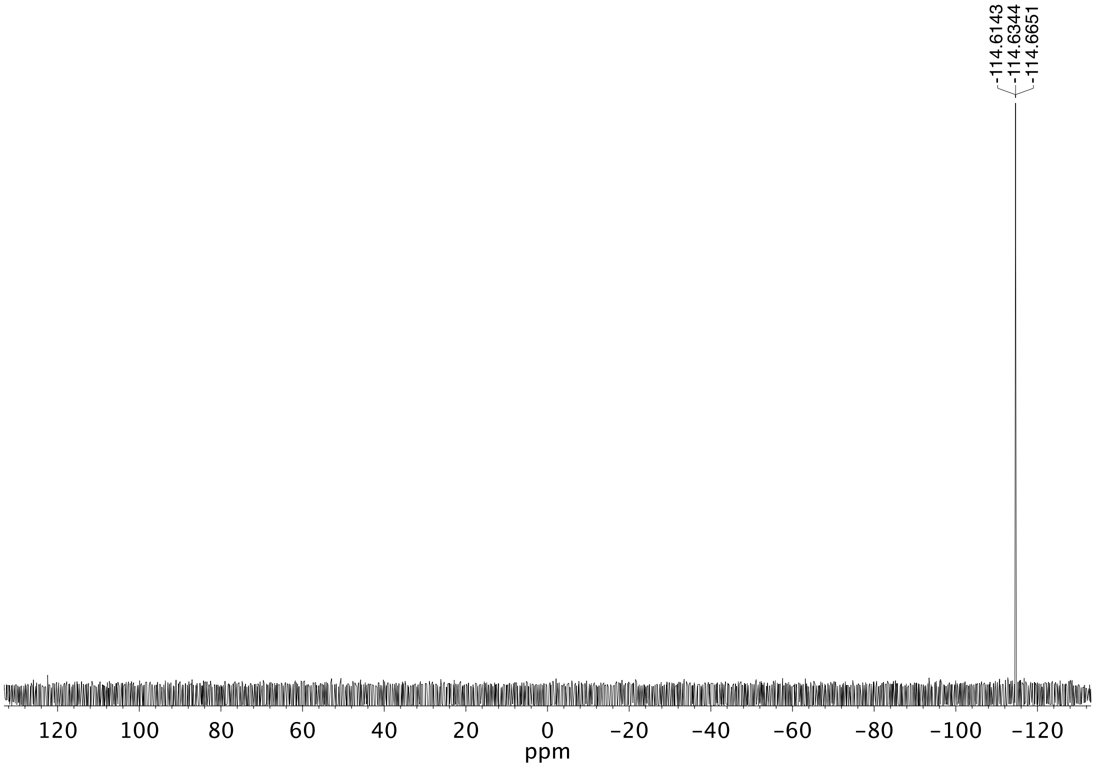

Figure 4.134 ^{19}F NMR (282 MHz, CDCl$_3$) of compound **4.49**.

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CHAPTER FIVE

Catalytic Carbon–Carbon Bond Forming Reactions of Vinyl Cations: A Field Guide

(Unpublished Work)

Stasik Popov, Benjamin Wigman, Jonathan Wong, Kendall N. Houk and Hosea M. Nelson

5.1 Abstract

Over the course of multiple years of vinyl cation research focused on C–C bond forming reactions, there have been many trials and tribulations; these include but are not limited to unstable vinyl cation precursors, unreactive vinyl cation precursors, and vinyl cation precursors that rearrange or go through non-productive unimolecular pathways upon ionization. Furthermore, we have seen cases where different catalytic systems are better suited for different types of vinyl triflates. This chapter aims to summarize some of our key findings/observations in order to aid the practicing organic chemist in utilizing some of our developed methodology as a useful disconnection in a retrosynthetic analysis.

5.2 Introduction

Since our initial discovery of the reactivity of aryl cations in 2016, our lab has studied the fundamental reactivity of dicoordinate carbocations with aliphatic and aromatic C–H bonds.[1–5] These reactive species exhibit exquisite reactivity, as they are able to engage unactivated C–H bonds to forge new C–C bonds. This newfound reactivity presented a promising synthetic method for C–C bond formation using earth abundant main group catalysts. Initially, we looked at silylium-carborane reagents (Chapter 2) for vinyl cation generation and ensuing reactivity (Figure 5.1a).[3] More recently, efforts have been focused on broadening the synthetic utility of this methodology. This led to the development of Li-WCA

(LiF_{20})[2] or Li-urea[1] (Chapter 3) catalysts in order to achieve C–C bond forming reactions of vinyl cations (Figure 5.1bc). While these efforts are described in more detail along with their respective mechanisms (Figures 2.3 and 3.2) in Chapter 2 and 3, the purpose of this study is to further highlight the advantages and disadvantages of the different catalytic systems and serve as an aid to the practicing organic chemist who might desire to utilize vinyl cations as a synthon in a retrosynthesis.

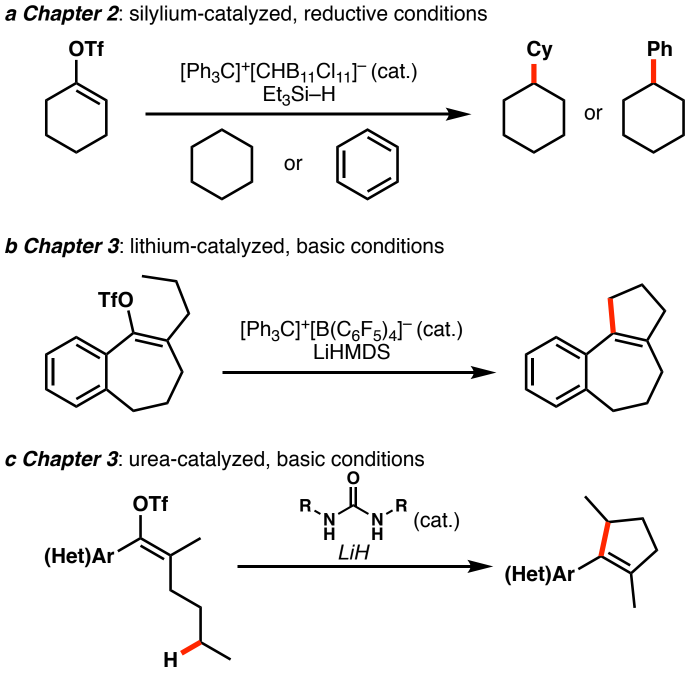


Figure 5.1 Summary of the silylium (a) and lithium (b,c) based systems for C–C bond forming reactions of vinyl cations

This study represents an amalgamation of observations and insight obtained by performing these reactions over multiple years in addition to new, carefully designed experiments and computations to tease out the advantages and limitations of several catalytic systems. First, an in depth discussion of several features of vinyl cations and their precursors are discussed. The reactivity of vinyl cations with different nucleophilic C–H bond donors is presented and analyzed. After this analysis, we discuss the advantages and disadvantages of the silylium-WCA and the Li-WCA/Li-urea systems and how to choose which one to use.

5.3 Geometrical and Strain Effects on Vinyl Cation Stability

Vinyl cations are similar to allenes in that they prefer to adopt an *sp*-hybridized linear geometry in order to keep the positive charge inside an empty p orbital.[6,7] It has been well precedented in early solvolytic studies that acyclic vinyl sulfonates as well as those derived from medium/large-sized cycloalkanones underwent solvolysis much faster than their smaller ring counterparts (Figure 5.2).[8] For example, cyclopentenyl nonaflate (**5.2**) undergoes solvolysis to cyclopentenyl cation **5.6** in aqueous ethanol twenty times slower than its cyclohexenyl counterpart (**5.3** to **5.7**).[9] On the other hand, cyclohexenyl cation (**5.7**) generation is 13000 times slower than that of cycloheptenyl cation (**5.8**). This is due to the fact that smaller ring sizes make the bond angle of the vinyl cation smaller and more deviated from linearity (180°). One exception to this rule is cyclobutenyl cation (**5.5**), which exhibits non-classical character, giving it additional stability.[10,11] Barring this exception, acyclic/linear vinyl cations are generally much more stable and easier to generate than their cyclic counterparts.

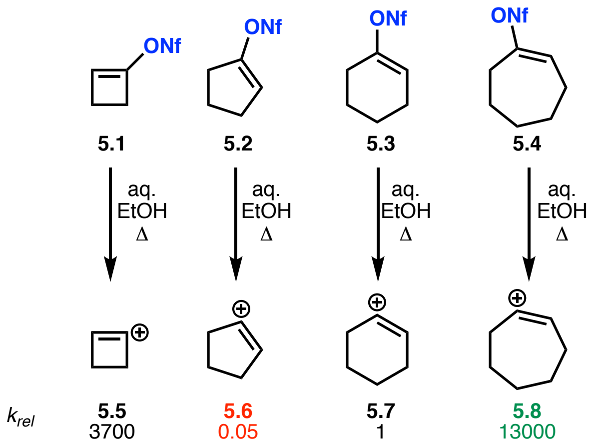
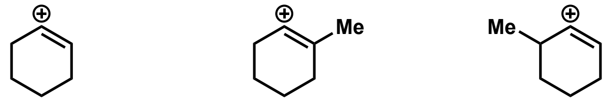


Figure 5.2 Relative ionization rates of different cyclic nonaflates

5.4 Substituent Effects on Vinyl Cations

While ring size has a large effect on the ionization barrier of a vinyl triflate, we have also observed that adding substituents on the alkene of the vinyl triflate can also have profound effects on both the ionization barrier as well as the reactivity of the generated vinyl cations.[12,13] In some cases, substitution can yield unimolecular rearrangements, which can generate product mixtures and obviate synthetically useful C–C bond forming reactions regardless of the catalytic system chosen.

We have noticed several types of substrates that react in a different manner than the expected C–H insertion or Friedel-Crafts pathways. In our 2018 report[3], we noted that 2- or 6-substituted cyclohexenyl triflates never led to successful insertion products, likely as a result of intramolecular decomposition pathways. Here, we looked at two possible methyl substitution patterns of the parent cyclohexenyl cation: the 2- and 6- methyl substitutent. Substitution at either position gave a great degree of stabilization to the vinyl cation, likely due to the electron-rich nature of the methyl group (Figure 5.3). Furthermore, these groups likely have a steric buttressing effect that promote ionization of the leaving group from the vinyl halide/pseudohalide precursor.[12] 6-Methyl cyclohexenyl cation (**5.10**) is almost 14 kcal/mol less uphill from its vinyl triflate precursor than the parent cyclohexenyl cation (**5.7**), while 2-methylcyclohexenyl cation (**5.9**) is around 4 kcal/mol less uphill than the parent system **5.7**. These cations have been studied in the past in solvolytic reactions in polar protic media and have been observed to undergo various unimolecular rearrangements.[12,14] Later in the chapter, we will revisit these substitution patterns and how these cations react under catalytic WCA conditions in nonpolar media (see Chapter 5.7).



5.7 22.4 kcal/mol

5.9 18.7 kcal/mol

5.10 8.7 kcal/mol

Figure 5.3 Substituted and unsubstituted vinyl cation relative energies
Values reported are ΔG relative to the vinyl triflate precursor

5.5 C–H Donor Effects

While the ring size of the vinyl cation precursor seems to be one of the predominant features that determines the success or failure of a vinyl cation C–C bond forming reaction, the identity of the nucleophilic partner can play a large role as well. There have been two main classes of C–H bond donors that undergo these types of reactions: alkane C–H bonds and arene C–H bonds. In general, we have observed that Friedel-Crafts type reactions have a broader scope than alkane C–H insertion reactions both in silylium and lithium-based systems.[1,3] This occurs for a few reasons. First, benzene and other arene solvents often provide a better degree of solubility in all of our catalytic systems than alkane solvents do. Secondly, arene solvents can likely stabilize the vinyl cation through cation-π interactions, which might lead to a lower ionization barrier.[15] Lastly, the key C–C bond-forming event is often much more facile with arenes than with alkanes. Arenes often proceed through a Friedel-Crafts mechanism followed by rearrangement whereas alkanes proceed through a direct C–H insertion. Figure 5.4 depicts a sample computational study looking at cyclohexenyl cation (**5.7**) performing a C–C bond forming reaction with benzene or pentane.[16] For the C–H insertion reaction with pentane, there is a 5.3 kcal/mol transition state energy for the key C–C bond forming event leading to the alkylated cation **5.11**. On the other hand, Friedel-Crafts with benzene proceeds as a barrierless, highly exothermic event, leading to Wheland intermediate **5.12**, which rapidly rearomatizes to give benzylic cation **5.13**. Experimentally, we can often perform Friedel-Crafts reactions with stoichiometric amounts of arenes in alkane solvents due to this discrepancy.[1,3]

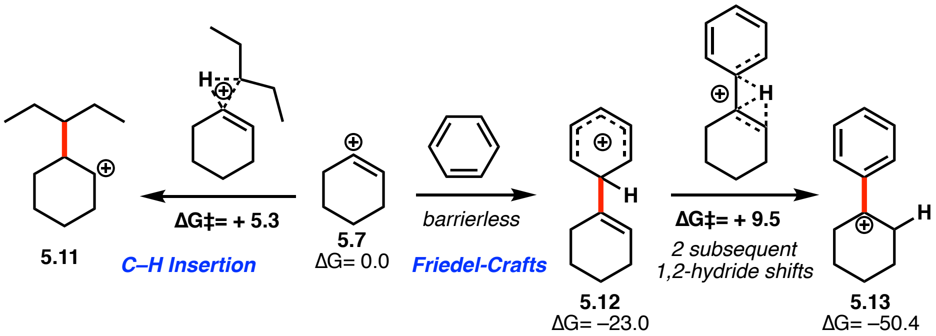


Figure 5.4 *C–H Insertion vs Friedel-Crafts pathways of cyclohexenyl cation*

5.6 Vinyl Triflate Stability

Lastly, we wanted to highlight the inherent instability of certain vinyl triflates that can hamper retrosynthetic planning. Over the years, we have attempted to synthesize a variety of substrates that are unstable to purification on silica gel and often decompose during distillations due to their thermal instability. We found that cyclic vinyl triflates (5–8 membered) exhibited good stability for purification and storage. Acyclic vinyl triflates derived from simple aliphatic ketones were silica stable, but needed to be stored in a freezer for long-term storage they would undergo slight decomposition and discoloration over time (colorless to yellow/orange). Initially, we were attracted to converting acetophenone derivatives to vinyl triflates, as these would yield 1,1-diarylalkane or 1,1-diarylalkene scaffolds after performing intermolecular Friedel-Crafts reactions.[1,3,17,18] We observed, however, when subjecting electron-neutral or electron-rich acetophenone derivatives to common triflating conditions, the ensuing vinyl triflates were incredibly unstable, especially to silica gel chromatography. The parent acetophenone triflate **5.15** could only be purified by vacuum distillation at low temperatures, because upon excessive heating it violently decomposed into a black tar.[16] Furthermore, even upon storage at – 30 °C in a glovebox freezer, discoloration was observed over time. Even the halogenated acetophenones (like **5.16**) yielded relatively unstable vinyl triflates that were often used without column chromatography to avoid decomposition.[19] These substrates are more easily accessible depending on the electron withdrawing nature of the arene (Figure 5.5). For example, trifluoromethylsubstituted arylvinyl triflate **5.17** is column stable and can be stored indefinitely in the freezer. One example of an unstable vinyl triflate is the *p*-butoxyacetophenone derivative **5.14**, which was clearly observed in the crude reaction mixture by ^{1}H NMR but was never recovered after attempted chromatographic purification.

As mentioned in Chapter 4, one way to overcome this issue is to synthesize vinyl tosylates for more electron-rich systems where the vinyl triflate might be unstable.

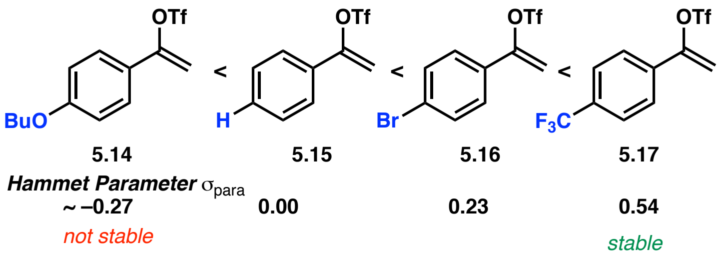


Figure 5.5 Vinyl triflate stability correlated to Hammett parameters

This concludes the broad overview of various features of the vinyl cation electrophiles and the C–H donor nucleophiles that will permeate through the reactions shown later in this chapter.

5.7 C–C Bond Forming Reactions of Vinyl Cations Under Silylium Conditions

Silylium-WCA salts are among the strongest Lewis acids known in chemistry. They have been used to generate a variety of unstable cationic intermediates both catalytically and stoichiometrically.[20-24] Here we will look at the reaction that our lab developed (Chapter 2) and how it applies to a variety of systems.[3] First, we will look at intermolecular Friedel-Crafts using benzene as solvent. These reactions are chosen as a model case study for two reasons: 1) the reagents commonly used in these reactions are soluble in benzene and 2) there are no chemoselectivity issues as there are with substituted arenes.

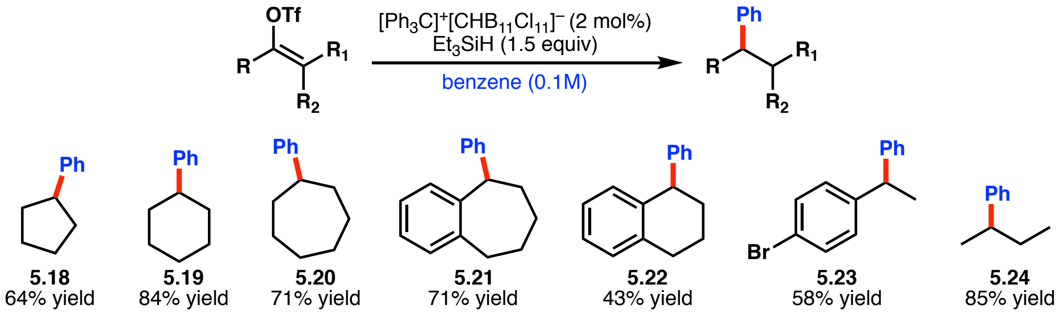
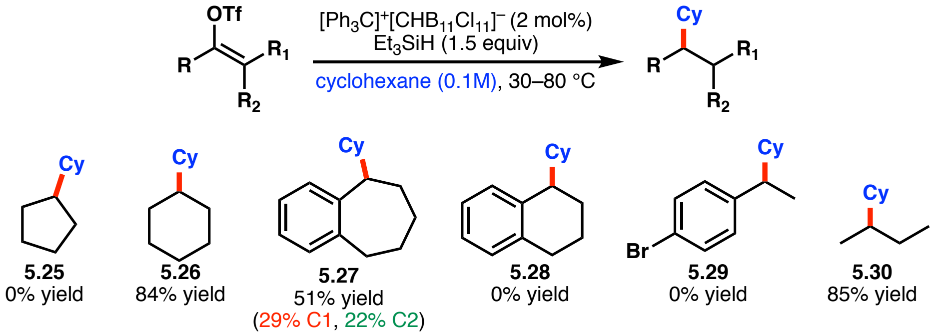


Figure 5.6 Silylium-catalyzed Friedel-Crafts reactions of vinyl triflates

Five, six, and seven-membered ring-bearing vinyl triflates were all ionized smoothly and yielded the corresponding phenylcycloalkanes **5.18**–**5.20** in 64%, 84%, and 74% yield respectively. However, cyclopentenyl triflate required 6 days of heating at 70 °C in order to go to full conversion whereas the reaction with cyclohexenyl triflate went to completion after 2 hours at 30 °C. Under identical conditions, cycloheptenyl triflate was converted to phenylcycloheptane almost instantly at 30 °C. Cyclooctenyl triflate was omitted in this study because of its propensity to undergo rapid intramolecular transannular C–H insertion.[2,3] We also explored bicyclic systems. To this end, the α-suberone and α-tetralone derived vinyl triflates were reacted with the silylium conditions in benzene solvent to yield phenylated products **5.21** and **5.22** in 43% and 71% yield respectively. Here, similar effects were observed where the smaller tetralone-derived system required heating for 2 days at 60 °C, whereas the suberonyl system only required one hour at 30 °C. Notably, when comparing the tetralone and cyclohexanone-derived vinyl triflates, it is clear that the cyclohexenyl triflate ionizes more easily despite the expected resonance stabilization from the aryl ring. This is likely due to the strain imposed by the fused benzene ring, which prevents the vinyl cation-bearing carbon from distorting closer to linearity. Lastly, acyclic vinyl triflates were explored: 4-bromophenylvinyl triflate and butenyl triflate yielded the phenylated alkanes **5.23** and **5.24** in 58% and 85% yield respectively after one hour at 30 °C. Notably, this chemistry can even work at –40 °C in chloroform solvent with benzene as a stoichiometric additive (5–10 equiv).[3] In conclusion, the silylium-WCA system can be utilized for Friedel-Crafts reactions of any ring size system (as long as there are no heteroatoms).

Next, we decided to survey the same substrates for intermolecular C–H insertion reactions with cyclohexane. After performing reactions with differentially substituted vinyl triflates under the previously optimized intermolecular cyclohexane insertion conditions, we saw that a much narrower range of substrates were competent for this reaction compared to that of intermolecular Friedel-Crafts. We observed successful insertion with cyclohexenyl triflate, benzosuberonyl triflate, and butenyl triflate to yield cyclohexylated adducts **5.26**, **5.27**, and **5.30** in 84%, 51%, and 85% yield, respectively (Figure 5.7). On the other hand, all other triflates failed to yield any C–H insertion products **5.25**, **5.28**, or **5.29**.



5.25 0% yield

5.26 84% yield

5.27 51% yield (29% C1, 22% C2)

5.28 0% yield

5.29 0% yield

5.30 85% yield

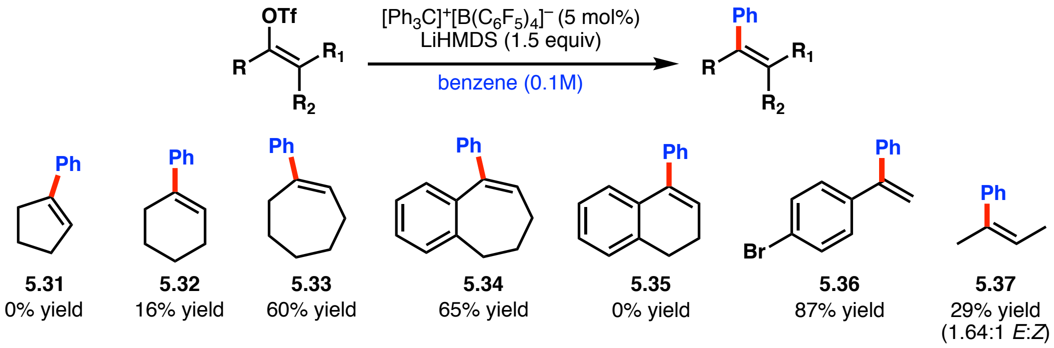
Figure 5.7 Silylium-catalyzed C–H insertion reactions of vinyl triflates

Looking at the substrates that failed to deliver any product, we can see that they fall into two distinct categories. First, vinyl triflates that would yield extremely unstable vinyl cations, such as cyclopentenyl triflate, are likely too hard to ionize in cyclohexane solvent due to lack of any stabilizing solvent-cation interactions, in contrast to the cation-π interactions that benzene can provide.[15] The second category of unsuccessful substrates is that which yields stable vinyl cations, such as the precursor to **5.29**. These cations are likely too stable to undergo productive insertion and, while they are ionized under these reaction conditions, they yield unidentified decomposition products instead. Mayr and coworkers investigated highly stabilized vinyl carbocations that were sluggish to react even with relatively strong nucleophiles.[25] Perhaps in these systems, the barrier to break the C–H bond of cyclohexane is just too disfavored. In these systems, there seems to be a good middle ground where the vinyl triflates precursors can not be too hard to ionize, but also should not yield vinyl cations too stable to undergo productive insertion reactions.

In conclusion, silylium-WCA-mediated reactions are effective for all ring sizes explored here (5-8) for intermolecular Friedel-Crafts reactions and can also perform C–H insertion reactions with some acyclic substrates as well as 6- or 7-membered cyclic vinyl cations. One big drawback is that this system has poor heteroatom compatibility as has been demonstrated in various reports, including those from our group.[3,5,20,21] In general, hydrocarbon substituents as well as some halides are tolerated under this catalytic manifold, but no Lewis basic groups.

5.8 C–C Bond Forming Reactions of Vinyl Cations Under Lithium Conditions

In this section, we investigate the limitations of the Li-WCA system. This system has proven to be much more heteroatom compatible[2], but the ionizing power of this system is less than that of silylium due to the decreased Lewis acidity when compared to silylium. We again start this investigation with intermolecular solvolytic Friedel-Crafts reactions in benzene. It is important to note that throughout our experiments, Li-urea/LiF$_{20}$ systems showed very similar reactivity and ionization power for various vinyl triflates. For clarity, we will mainly focus on LiF$_{20}$ in this discussion, but these trends also hold true for the Li-urea system.



5.31 0% yield

5.32 16% yield

5.33 60% yield

5.34 65% yield

5.35 0% yield

5.36 87% yield

5.37 29% yield (1.64:1 *E*:*Z*)

Figure 5.8 Lithium-catalyzed Friedel-Crafts reactions of vinyl triflates

First, looking at simple cycloalkenyl triflates, we observed that smaller rings had more difficulty ionizing with the five-, six- and seven-membered ring vinyl triflates yielding styrenes **5.31–5.33** in 0%, 16% and 60% yield respectively. These three results not only demonstrate the correlation of ring size with reactivity of vinyl triflates, but also the marked difference in ionizing power between the silylium-WCA conditions and the Li-WCA conditions. Moving on to bicyclic systems, the tetralone derived vinyl triflate failed to yield any arylated product **5.35** even at elevated temperatures, while the benzosuberonyl derivative gave styrene **5.34** in 65% yield after two hours at 70 °C. Lastly, exposure of acyclic vinyl triflates to these conditions gave styrenes **5.36** and **5.37** in 87% and 29% yield respectively. Notably, these reactions reached full conversion at room temperature in under a day in both cases (2 hours and 20 hours respectively for **5.36** and **5.37**). The low yield of styrene **5.36** can be attributed to alkyne and allene formation from deprotonation of the intermediate vinyl cation. This elimination pathway often plagues these basic conditions, and in order to get high yielding reactions with acyclic substrates, fully substituted vinyl triflates must be used. In general the lithium-WCA system works reliably for large ring sizes (7+) as well as acyclic systems in terms of ionization.

Given the improved heteroatom compatibility of the Li-WCA system, we wanted to explore more synthetically relevant Friedel-Crafts reactions, where arenes were used stoichiometrically instead of as solvent. To this end, we decided to investigate the transformation of styrenyl triflate **5.16** to diarylalkane **5.38** under lithium-mediated conditions with *p*-xylene as the reaction partner. Starting off, a variety of solvents were explored using 5 equivalents of *p*-xylene as a reaction partner (Figure 5.9). Here, as previously mentioned, we observed that the arene nucleophile outcompetes cyclohexane as the solvent (75% yield). Additionally, other electron-poor arenes were used as solvents with no deleterious nucleophilic attack. *o*-Dichlorobenzene and *o*-difluorobenzene yielded alkene **5.38** in 34 and 80% yield respectively. Trifluorotoluene proved to be the optimal solvent, giving nearly quantitative yield (95%) with 5 equivalents of the arene nucleophile. Dichloromethane performed modestly, yielding the product in 45% yield; 49% of the starting material remained likely due to the decomposition of LiHMDS base with solvent over time. Generally, electron poor arenes, alkanes, and halogenated solvents are suitable solvents for these reactions, with arenes performing the best. Other common polar solvents such as acetonitrile and THF yield no product, presumably due to poisoning/coordination of the Lewis basic solvents to the Lewis acidic lithium center. Using the optimal solvent trifluorotoluene, we attempted to perform the reaction using only one or two equivalents of *p*-xylene, which furnished the product in 35% and 52% yield respectively. While these reactions performed well with electron-rich arene reaction partners, using an electron deficient arene such as trifluorotoluene failed to yield any styrene product **5.39** even when the arene was used as solvent. This is again due to the troublesome elimination pathway that is favorable under these basic conditions and the major product was found to be 4-bromophenylacetylene (**5.40**). However, synthesis and ensuing reaction of dimethyl vinyl triflate **5.41** under identical conditions furnish the tetrasubstituted olefin product **5.42** in 83% yield as a single isomer.[26] This underscores the importance of substitution to prevent the alkyne formation pathway. Despite this limitation, this method to allows facile access sterically hindered, tetrasubstituted olefins.

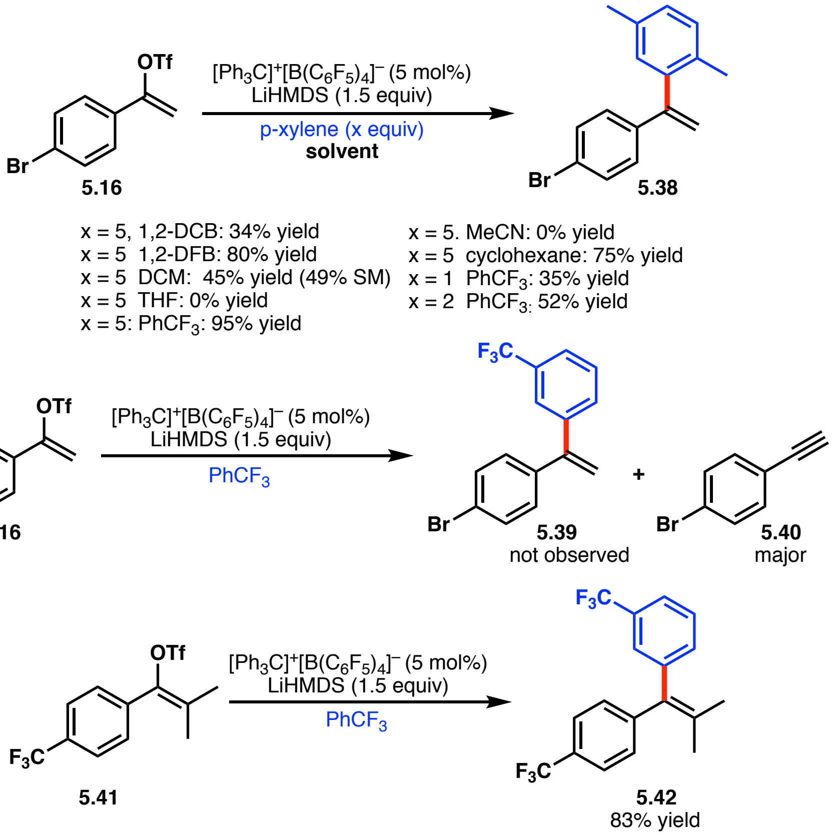
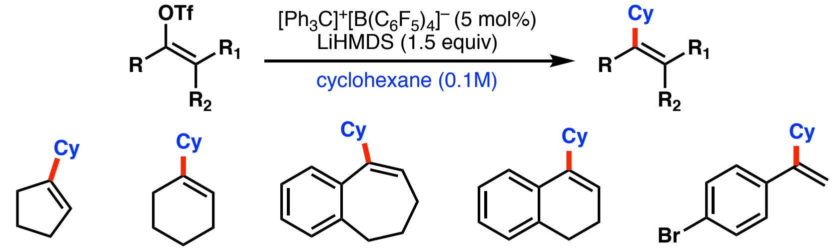


Figure 5.9 Further studies on intermolecular Friedel-Crafts reactions of vinyl triflates under Li-WCA conditions



5.43 0% yield

5.44 0% yield

5.45 21% yield

5.46 0% yield

5.47 0% yield

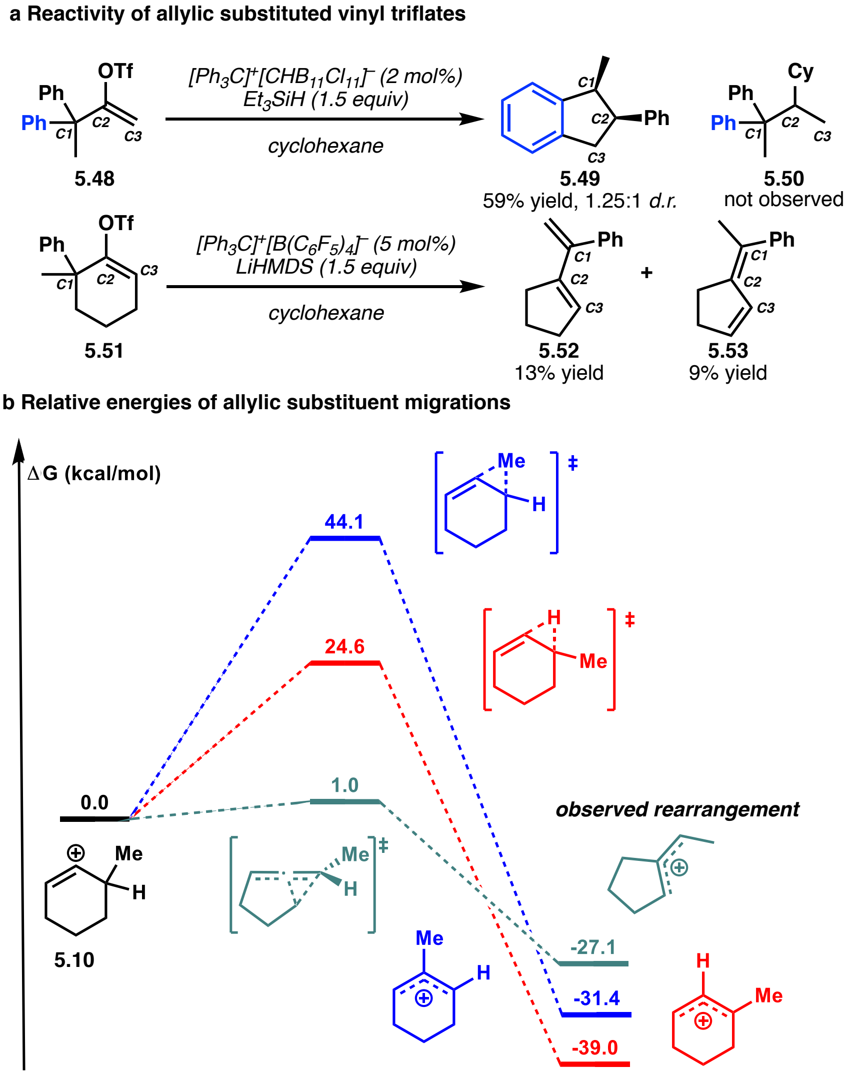
Figure 5.10 Lithium-catalyzed intermolecular C–H insertion reactions of vinyl triflates

Next, we exposed several vinyl triflates to the previously optimized LiF_{20} conditions. In the case of benzosuberonyl triflate, intermolecular C–H insertion with cyclohexane was observed giving styrene **5.45** in 21% yield (Figure 5.9). In the case of cyclopentenyl triflate, cyclohexenyl, and tetralone-derived triflate, no cyclohexylation was observed even after heating > 120 °C for extended periods of time. 4-Bromoacetophenone derived vinyl triflate failed to deliver any desired product under these conditions; only 4-bromoacetylene (**5.40**) was observed, likely due to deprotonation of the vinyl cation by LiHMDS. Overall, we found that intermolecular C–H insertion was very limited with the Li-WCA catalytic system. These results are not surprising since the ionizing power of the Li-WCA has already been shown to be weaker than that of silylium-WCA, and for acyclic substrates, the deprotonation of the vinyl cation intermediate to yield alkyne/allene type products largely outcompetes intermolecular alkane C–H insertion.

In conclusion, the Li-WCA system has its advantages in its improved heteroatom compatibility (see Chapter 3 for more details) and in non-solvolytic Friedel-Crafts reactions; however, intermolecular C–H insertion remains highly challenging in this system. Furthermore, this system is largely incapable in generating strained vinyl cations (ring size < 7) and works best for medium-sized ring systems as well as substituted acyclic systems in which alkyne formation is disfavored or impossible.

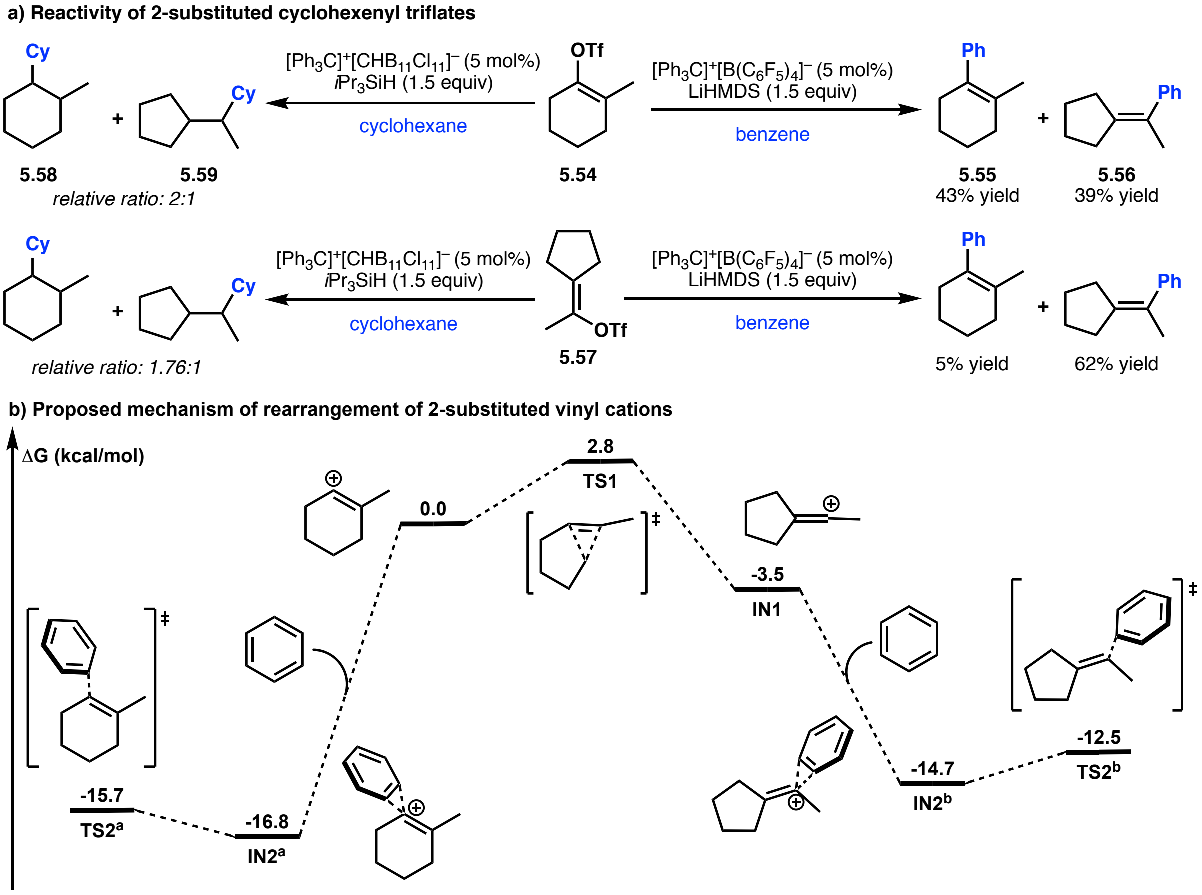
5.9 Vinyl Cation Rearrangement Reactions

After gaining some new insights into our catalytic systems, we wanted to revisit some of the substituted cyclic vinyl cations and see how they would react under WCA catalysis in non-polar media. First, we explored the reactivity of allylic substituents adjacent to the triflate. Exposure of acyclic vinyl triflate **5.48**, bearing two phenyl groups and a methyl group next to the triflate, to standard silylium conditions in cyclohexane yielded the substituted indane products **5.49** in 59% yield. No detectable amount of the expected cyclohexylated insertion product **5.50** was observed (Figure 5.10a). Additionally, a similar type of reactivity was observed under the lithium-catalyzed conditions utilizing allylically substituted vinyl


a Reactivity of allylic substituted vinyl triflates

b Relative energies of allylic substituent migrations

Figure 5.11 Computational and experimental studies of vinyl triflates bearing allylic substituents triflate **5.51**. Rather than the expected cyclohexylated product, ring contraction products **5.52** and **5.53** were observed in 15% and 8% yield, respectively. To gain mechanistic insight into this reaction pathway, we performed computational studies (Figure 5.10b). We believed that these products were being generated by allylic group migrations. A model system was chosen, starting with methylated cyclohexenyl cation **5.10**. Methyl migration (blue) was observed to be the most energetically costly transoformation, with a transition state energy of 44.1 kcal/mol. In comparison, hydride migration (red) had a transition state barrier of 24.6 kcal/mol and the most facile pathway was found to be ring contraction (green), with a barrier of only 1.0 kcal/mol.


a) Reactivity of 2-substituted cyclohexenyl triflates

b) Proposed mechanism of rearrangement of 2-substituted vinyl cations

Figure 5.12 Mechanistic studies of 2-substituted vinyl triflates. Experimental studies (a) and computational investigations (b).

Next, we investigated 2-substituted cyclic vinyl triflates, as these substrates have been previously reported to undergo ring contraction reactions.[12] Interestingly, exposure of 2-methylcyclohexenyl triflate **5.54** to standard LiF_{20} conditions in benzene solvent yielded styrene products **5.55** and **5.56** in 43% and 39% yield, respectively (Figure 5.11a). Observation of cyclohexene **5.55** is surprising given the much greater stability of acyclic vinyl cations compared to cyclohexenyl cations. Subjecting the exocyclic vinyl triflate **5.57** to identical reaction conditions yielded products **5.55** and **5.56** in 5% and 62% yield**.** Although the yield of the cyclohexene product is much lower in this case, it still suggests that equilibration to the seemingly less stable cyclohexenyl cation *via* ring expansion is occuring. Performing intermolecular C–H insertion into cyclohexane solvent under reductive silylium-WCA conditions yields a diastereomeric mixture of methylbicyclohexyl **5.58** and trialkylmethane **5.59** in a 2:1 or 1.76:1 ratio depending on which enol triflate was used as the starting material. The very similar product distribution can perhaps be rationalized by the relatively slow alkane C–C bond forming step compared to that of benzene, which might allow the system to freely equilibrate between the cyclohexenyl cation and the ring contracted acyclic cation **IN1** (Figure 5.11B). The product distribution can be considered an outcome of Curtin-Hammett kinetics.

We also performed calculations on the 2-substituted vinyl cation arylation pathway to probe these product distributions. Computationally, we did indeed observe that the acyclic ring contracted vinyl cation **IN1** was more stable than the parent cyclohexenyl cation **5.9** by 3.5 kcal/mol (Figure 5.11b). However, an energy barrier of 2.8 kcal/mol existed to achieve this ring contraction, whereas coordination of benzene solvent to the vinyl cation was an enthalpically barrierless transformation, **IN2**[a]. This may explain the discrepancy between the observed and expected product ratio in these transformations. Additionally the low barrier of interconversion between ring contracted exocyclic cation **IN1** and cyclohexenyl cation **5.9** can also explain how starting from the cyclopentenyl triflate **5.58** still yields some of the cyclohexenyl-trapped product **5.55** or **5.58**. Lastly, during exploration of these reactions, we observed that these 2- or 6- substituted cyclic substrates tend to ionize much more easily than the non-substituted cyclohexenyl triflate as predicted computationally (Figure 5.3).

5.10 Conclusion

The user guide presented in this chapter is geared for synthetic chemists both in academic and industrial settings who are looking to construct C–C bonds *via* C–H insertion or Friedel-Crafts chemistry of vinyl cations. Specifically, for those planning syntheses with limited personal experience of vinyl cation generation and reactivity, we hope that this field guide will highlight some limitations and successes of different catalytic systems that will save both time and resources by offering a good starting point for optimizations and a better guide for retrosynthetic analysis. Additionally, we hope that the new experiments/computations presented herein shed light on the precise nature of the rearrangements of differentially substituted vinyl cations as a whole.

5.11 Experimental Section

5.11.1 Materials and Methods

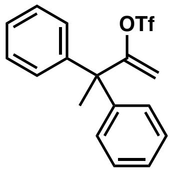
Unless otherwise stated, all reactions were performed in an MBraun glovebox under nitrogen atmosphere with ≤ 0.5 ppm O_2 levels. All glassware and stir-bars were dried in a 160 °C oven for at least 12 hours and dried *in vacuo* before use. All liquid substrates were either dried over CaH_2 or filtered through dry neutral aluminum oxide. Solid substrates were dried over P_2O_5. All solvents were rigorously dried before use. Benzene, *o*-dichlorobenzene, and toluene were degassed and dried in a JC Meyer solvent system and stored inside a glovebox. Cyclohexane, fluorobenzene, and *n*-hexane were distilled over potassium. Chlorobenzene was distilled over sodium. *o*-Difluorobenzene was distilled over CaH_2. Pentane was distilled over sodium-potassium alloy. Chloroform was dried over CaH_2 and stored in a glovebox. Triethylsilane and triisopropylsilane were dried over sodium and stored inside a glovebox. *Closo*-Carborane catalysts were prepared according to literature procedure.[24] $[Li]^+[B(C_6F_5)_4]^-$ and $[K]^+[B(C_6F_5)_4]^-$ salts were synthesized according to literature procedure.[27] Preparatory thin layer chromatography (TLC) was performed using Millipore silica gel 60 F_{254} pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. SiliaFlash P60 silica gel (230-400 mesh) was used for flash chromatography. $AgNO_3$-Impregnated silica gel was prepared by mixing with a solution of $AgNO_3$ (150% v/w of 10% w/v solution in acetonitrile), removing solvent under reduced pressure, and drying at 120 °C. NMR spectra were recorded on a Bruker AV-300 (^1H, ^{19}F), Bruker AV-400 (^1H, ^{13}C, ^{19}F), Bruker DRX-500 (^1H), and Bruker AV-500 (^1H, ^{13}C). ^1H NMR spectra are reported relative to $CDCl_3$ (7.26 ppm) unless noted otherwise. Data for ^1H NMR spectra are as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicities are as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet. ^{13}C NMR spectra are reported relative to

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

5.11.2 Experimental Procedures

5.11.2.1 Preparation of Vinyl Triflate Substrates

The synthesis and spectra of vinyl trifate precursors to the compounds shown in ***Figures 5.6–5.10*** *is reported in Chapter 2 and Chapter 3 as well as a report from our group.*[3]



3,3-diphenylbut-1-en-2-yl trifluoromethanesulfonate (5.48)

3,3-Diphenylbutan-2-one (750 mg, 3.34 mmol, 1 equiv) was dissolved in anhydrous DCM (10 mL). 2-chloropyridine (418 mg, 3.68 mmol, 1.1 equiv) was added and the solution was cooled to 0 °C. To this was added triflic anhydride (1.13 g, 4.10 mmol, 1.2 equiv). The resulting solution was allowed to warm up to room temperature and stir until for 12 hours. The reaction was quenched by adding water (30 mL) and diethyl ether (30 mL). The layers were separated and the aqueous layer was extracted twice more with ether (2 x 30 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated to give crude product. Purified by silica flash column chromatography (0.2% triethylamine in hexanes) to give product **5.48** as a yellow oil (130 mg, 11% yield).

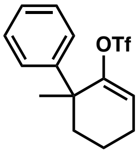
^1H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 4H), 7.33 – 7.29 (m, 2H), 7.29 – 7.26 (m, 4H), 5.44 (d, J = 4.2 Hz, 1H), 4.86 (d, J = 4.3 Hz, 1H), 2.04 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.9, 143.5, 128.3, 128.1, 127.2, 118.2 (q, $^1J_{C\text{–}F}$ = 319.8 Hz), 105.2, 53.4, 26.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ –74.7.

FTIR (Neat film NaCl): 3061, 3026, 2991, 2927, 1653, 1600, 1494, 1446, 1417, 1405, 1377, 1251, 1208, 1156, 1139, 1095, 1065, 1028, 930, 880, 848, 792, 759, 719, 699.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{17}H_{15}F_3O_3S$ 356.0694; Found 356.0682.



1-methyl-1,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl trifluoromethanesulfonate (5.51).

In a flame dried roundbottom flask, the 2-methyl-2-phenylcyclohexanone (1.16 g, 6.16 mmol, 1 equiv) was dissolved in THF (13 mL) and cooled to –78 °C. To this solution was added a solution of LiHMDS (1.16 g, 6.93 mmol, 1.12 equiv) in THF (4 mL). This was stirred for 45 minutes at –78 °C. Finally, a solution of $PhNTf_2$ (2.34 g, 6.55 mmol, 1.06 equiv) in THF (6 mL) was added dropwise and the reaction was allowed to warm up to r.t overnight. After the reaction was done, it was concentrated and then to it was added brine (30 mL) and ethyl acetate (30 mL). Layers were separated and aqueous was extracted twice more with ethyl acetate (2 x 30 mL). Combined organics were dried over MgSO4, filtered and concentrated to yield crude as orange oil. The crude was purified by flash column chromatography

(0.2:4.8:95 triethylamine:ether:hexanes) to give the pure vinyl triflate **5.51** as colorless oil (1.63 g, 83% yield).

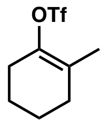
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 – 7.32 (m, 4H), 7.26 – 7.22 (m, 1H), 6.00 (td, J = 4.1, 1.7 Hz, 1H), 2.30 (ddt, J = 7.0, 4.9, 2.8 Hz, 2H), 2.00 (ddd, J = 13.3, 6.6, 2.8 Hz, 1H), 1.93 – 1.83 (m, 1H), 1.61 (d, J = 1.8 Hz, 3H), 1.60 – 1.55 (m, 1H), 1.51 – 1.40 (m, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 153.1, 144.5, 128.3, 126.6, 126.3, 118.3, 118.2 (q, $^1J_{C\text{–}F}$ = 319.5 Hz), 43.6, 41.4, 24.9, 24.7, 17.9.

^{19}F NMR (282 MHz, CDCl$_3$) δ –74.9.

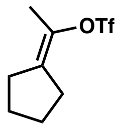
FTIR (Neat film NaCl): 3062, 3028, 2979, 2942, 2881, 1601, 1583, 1496, 1458, 1446, 1410, 1248, 1203, 1138, 1032, 1012, 950, 916, 888, 835, 780, 762, 700.

HR-MS (ESI-MS) m/z: [M+NH$_4$]+ Calc'd for $C_{14}H_{19}NF_3O_3S$ 338.1038; Found 338.1029.



2-methylcyclohex-1-en-1-yl trifluoromethanesulfonate (5.54)

Synthesized according to literature procedures. Spectral data matched those reported in the literature.[28]



1-cyclopentylideneethyl trifluoromethanesulfonate (5.57)

1-cyclopentylethan-1-one (1000 mg, 8.92 mmol, 1 equiv) was dissolved in anhydrous DCM (27 mL). 2-chloropyridine (1.11 g, 9.81 mmol, 1.1 equiv) was added and the solution was cooled to 0 °C. To this was added triflic anhydride (3.02 g, 10.7 mmol, 1.2 equiv). The resulting solution was allowed to warm up to room temperature and stir until for 12 hours.

The reaction was quenched by adding saturated aqueous $NaHCO_3$ (50 mL) and diethyl ether (50 mL). The layers were separated and the aqueous layer was extracted twice more with ether (2 x 50 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated to give crude product. Purified by silica flash column chromatography (0.2:2.8:97 triethylamine:diethyl ether:hexanes) to give product **5.57** as a colorless oil (725 mg, 33% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (t, J = 7.5 Hz, 2H), 2.29 (t, J = 7.4 Hz, 2H), 2.02 (s, 3H), 1.72 (dq, J = 18.5, 7.2 Hz, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.6, 135.9, 118.4 (q, $^1J_{C\text{–}F}$ = 319.4 Hz), 30.1, 29.9, 26.7, 26.4, 17.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ –75.2.

FTIR (Neat film NaCl): 2953, 2866, 1721, 1451, 1421, 1212, 1144.

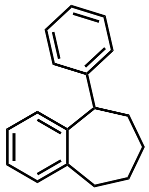
HR-MS (ESI-MS) m/z: $[M]^+$ Calc'd for $C_8H_{11}F_3O_3S$ 244.0381; Found 244.0388.

5.11.2.2 Intermolecular Friedel-Crafts reactions with silylium-carborane

*This section outlines procedures used for **Figure 5.6**. Spectral data and procedures for compounds **5.18–5.20**, **5.22**, and **5.24** are reported in the experimental section of Chapter 2.*

5.11.2.2.1 General Procedure

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.02 equiv.) and this was dissolved in benzene (enough to make a 0.1 M solution of vinyl triflate). Triethylsilane (1.5 equiv.) along with a magnetic stirring bar were added to the mixture and was shaken until it turned colorless. At this point, vinyl triflate (1.0 equiv.) was added to the reaction and it stirred for 0.1–48 hours at 30–75 °C (see substrates for specific details). Upon completion, the reaction mixture was pushed through a short plug of silica gel. Volatiles were removed under reduced pressure. Some substrates needed further purification by silica column chromatography (see below) or preparative high pressure liquid chromatography (HPLC).



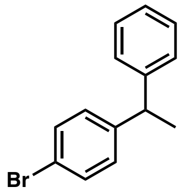
5-phenyl-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene (5.21)

Synthesized according to general procedure 5.11.2.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (1.53 mg, 0.002 mmol) and this was dissolved in benzene (1.0 mL). Triethylsilane (17.4 mg, 0.150 mmol) and a magnetic stirring bar were added respectively to the mixture and stirred for 10 minutes. Corresponding vinyl triflate (29.2 mg, 0.100 mmol, 1 equiv) was added to the reaction and stirred for 1 hour at 30 °C. The reaction was removed from the glovebox plugged through silica with ether. Volatiles were removed under reduced pressure to give product **5.21** in 71% NMR yield. Purified crude product by silica flash column chromatography (1.5% ether/hexanes) and then further purified by reverse phase semi-preparative HPLC (98:2 MeCN:water) to give compound **5.21** as colorless oil. *This sample still has a small amount of impurity remaining.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.23 (m, 2H), 7.21 – 7.17 (m, 2H), 7.17 – 7.13 (m, 1H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 4.28 (d, *J* = 10.0 Hz, 1H), 2.93 (dd, *J* = 14.1, 10.5 Hz, 1H), 2.78 (dd, *J* = 14.2, 8.3 Hz, 1H), 2.22 – 2.07 (m, 2H), 2.04 – 1.98 (m, 1H), 1.91 – 1.78 (m, 2H), 1.60 – 1.51 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.29, 144.70, 142.88, 129.59, 128.49, 128.40, 128.37, 128.25, 126.07, 125.95, 49.79, 36.45, 33.92, 30.01, 27.79.

HR-MS (EI-MS) m/z: $[M]^+$ Calc'd for $C_{17}H_{18}$ 222.1409; Found 222.1415.



1-bromo-4-(1-phenylethyl)benzene (5.23).

Synthesized according to general procedure 5.11.2.2.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol) and this was dissolved in benzene (0.5 mL). Triethylsilane (8.7 mg, 0.0750 mmol) and a magnetic stirring bar were added respectively to the mixture and stirred for 10 minutes. Corresponding vinyl triflate **5.16** (16.6 mg, 0.050 mmol, 1 equiv) was added to the reaction and stirred for 1 hour at 30 °C. The reaction was plugged through silica in the glovebox with hexanes. Volatiles were removed under reduced pressure to give product **5.23** in 74% NMR yield. Purified crude product by silica flash column chromatography (hexanes) to give pure compound **5.23**.

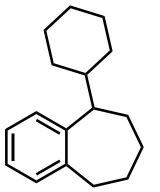
NMR spectra match those reported in literature.[29]

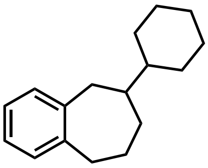
5.11.2.3 Intermolecular C–H insertion reactions with silylium-carborane

*This section outlines procedures used for **Figure 5.7**. Spectral data and procedures for compounds **5.26** and **5.30** are reported in the experimental section of Chapter 2. All 0% yielding reactions did not show any product by GC-MS or crude NMR when following general procedure below with appropriate vinyl triflate precursor.*

5.11.2.3.1 General Procedure

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.05 equiv) and this was suspended in cyclohexane (enough to make a 0.1 M solution of vinyl triflate). Triethylsilane (1.5 equiv) along with a magnetic stirring bar were added to the mixture and was shaken until it turned colorless. At this point, vinyl triflate (1.0 equiv) was added to the reaction and it stirred at 30–75 °C (see substrates for specific details). Upon completion, the reaction mixture was pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. Some substrates needed further purification by silica column chromatography (see below) or preparative high pressure liquid chromatography (HPLC).


5.27a


5.27b

5-cyclohexyl-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene (5.27a) and 6-cyclohexyl-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene (5.27b)

Synthesized according to general procedure 5.11.2.3.1. A dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (3.8 mg, 0.005 mmol) and this was dissolved in benzene (0.5 mL). Triethylsilane (17.4 mg, 0.150 mmol) and a magnetic stirring bar were added respectively to the mixture and stirred for 10 minutes. Corresponding vinyl triflate (29.2 mg, 0.10 mmol, 1 equiv) was added to the reaction and stirred for 0.5 hours at 30 °C. The reaction removed from the glovebox and plugged through silica with ether. Volatiles were removed under reduced pressure to give products **5.27a** and **5.27b** in 29% and 22% NMR yield respectively. Purified crude product by silica flash column chromatography (hexanes) to give a mixture of isomers **5.27a** and **5.27b**. Separation of regioisomers was performed with semi-preparative HPLC (95:5 MeCN:water) to give pure **5.27a** and **5.27b** as colorless oils.

Characterization for **5.27a**

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.13 – 6.96 (m, 4H), 3.03 – 2.93 (t, *J* = 13.0 Hz, 1H), 2.66 (dd, *J* = 14.5, 6.4 Hz, 1H), 2.45 (td, *J* = 6.9, 6.5, 3.4 Hz, 1H), 2.07 – 1.96 (m, 2H), 1.96 – 1.86 (m, 2H), 1.83 – 1.70 (m, 3H), 1.66 – 1.52 (m, 3H), 1.48 – 1.36 (m, 1H), 1.25 (ddd, *J* = 29.6, 14.7, 8.1 Hz, 2H), 1.17 – 1.06 (m, 2H), 0.96 – 0.84 (m, 1H), 0.79 (dd, *J* = 12.0, 3.3 Hz, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 145.1, 141.9, 130.8, 130.1, 125.7, 125.4, 53.1, 36.5, 32.8, 31.1, 29.1, 28.4, 26.6, 26.5, 26.1.

FTIR (Neat film NaCl): 3059, 3014, 2920, 2850, 2669, 1490, 1447, 1368, 1318, 1266, 1211, 1188, 1159, 1106, 1080, 1033, 977, 939, 756, 746, 549.

HR-MS (ESI-MS) m/z: [M]$^+$ Calc'd for $C_{17}H_{24}$ 228.1878; Found 228.1876.

Characterization for **5.27b**

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.16 – 7.12 (m, 4H), 2.91 – 2.75 (m, 3H), 2.70 (d, *J* = 14.1 Hz, 1H), 2.01 – 1.95 (m, 1H), 1.94 – 1.88 (m, 1H), 1.85 – 1.62 (m, 6H), 1.51 – 1.41 (m, 1H), 1.40 – 1.18 (m, 6H), 1.16 – 1.07 (m, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 143.2, 142.4, 129.1, 128.7, 125.9, 125.8, 43.8, 40.2, 36.4, 35.5, 29.7, 27.4, 26.85, 26.83, 26.80.

FTIR (Neat film NaCl): 3062, 3016, 2919, 2849, 1603, 1493, 1449, 1351, 1050, 927, 909, 894, 749, 734, 726.

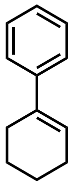
HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{17}H_{24}$ 228.1878; Found 228.1873.

5.11.2.4 Intermolecular Friedel-Crafts reactions with LiF_{20}

This section outlines procedures used for ***Figure 5.8*** *and* ***5.9****. 0% yielding reactions (****5.31*** *and* ***5.35****) did not show any formation of desired product by NMR or GC-MS.*

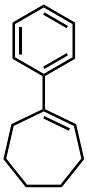
5.11.2.4.1 General Procedure

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF$_{20}$ (0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). Vinyl triflate (0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 30–80 °C. The reaction progress was closely monitored by TLC and/or GC. Upon completion of reaction, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography to give the pure product.



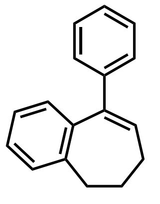
1-phenylcyclohex-1-ene (5.32)

Synthesized according to general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF$_{20}$ (0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). cyclohexenyl triflate (11.5 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 80 °C for 24 hours. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the **5.32** in 16% NMR yield. The crude material was purified by silica flash chromatography (hexanes) to give the pure product **5.32** as colorless oil. Spectral data matched those reported in the literature.[30]



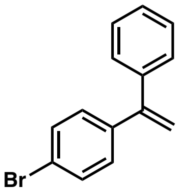
1-phenylcyclohept-1-ene (5.33)

Synthesized according to general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF$_{20}$ (0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). cycloheptenyl triflate (12.2 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 50 °C for 2 hours. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the **5.33** in 60% NMR yield. The crude material was purified by silica flash chromatography (hexanes) to give the pure product **5.33** as colorless oil. This material also contained ~4% 1-benzylcyclohex-1-ene from a vinyl cation rearrangement. Spectral data matched those reported in the literature.[30]



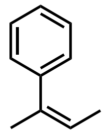
9-phenyl-6,7-dihydro-5*H*-benzo[7]annulene (5.34)

Synthesized according to general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF$_{20}$ (0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). benzosuberonyl triflate (14.6 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 70 °C for 2 hours. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the **5.34** in 65% NMR yield. The crude material was purified by silica flash chromatography (1% ether/hexanes) to give the pure product **5.34** as colorless oil. Spectral data matched those reported in the literature.[31]



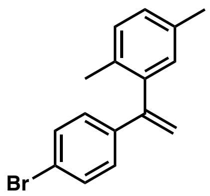
1-bromo-4-(1-phenylvinyl)benzene (5.35)

Synthesized according to general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF_{20} (0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). Vinyl triflate **5.16** (16.6 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 30 °C for 2 hours. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give product **5.35** in 87% NMR yield. The crude material was purified by silica flash chromatography (hexanes) to give the pure product **5.35** as colorless oil. Spectral data matched those reported in the literature.[32]



(*Z*)-but-2-en-2-ylbenzene (5.36)

Synthesized according to general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF_{20} (0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). But-2-en-2-yl triflate (10.2 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 30 °C for 20 hours. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give product **5.36** in 29% NMR yield (18:11 *E:Z*). These compounds were somewhat volatile, so no further purification or attempts to separate isomers was performed. Spectral data matched those reported in the literature.[33]



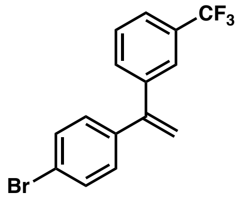
2-(1-(4-bromophenyl)vinyl)-1,4-dimethylbenzene (5.38)

Synthesized according to a modified general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with Trityl-F_{20} (0.05 equiv, 0.0025 mmol). Solvent (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv) and *p*-xylene (26.5 mg, 0.250 mmol, 5 equiv). Vinyl triflate **5.16** (16.6 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 30 °C until the reaction stopped progressing as seen by GC-FID. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give product **5.38** in XX% NMR yield (varies with solvent, see ***Figure 5.9***). The crude product was purified by silica flash column chromatography (hexanes) to give pure product **5.38** as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 7.08 (d, *J* = 1.2 Hz, 2H), 7.03 (s, 1H), 5.75 (d, *J* = 1.3 Hz, 1H), 5.21 (d, *J* = 1.3 Hz, 1H), 2.35 (s, 3H), 2.00 (s, 3H).

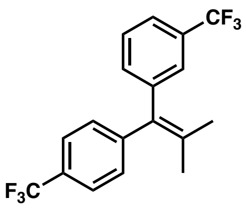
^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 140.8, 139.6, 135.2, 132.8, 131.4, 130.6, 130.1, 128.4, 128.1, 121.5, 115.2, 20.9, 19.6.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{16}H_{15}Br$ 286.0357; Found 286.0353.



1-(1-(4-bromophenyl)vinyl)-3-(trifluoromethyl)benzene (5.39)

Attempted to be synthesized according to general procedure 5.11.2.4.1 starting with vinyl triflate **5.16** and using trifluorotoluene as solvent yielded no **5.39** as product. Only 4-bromophenylacetlyene **5.40** was observed in the GC-FID and crude NMR.



1-(2-methyl-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl)-3-(trifluoromethyl)benzene (5.42)

Synthesized according to a modified general procedure 5.11.2.4.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF_{20} (0.05 equiv, 0.0025 mmol). Trifluorotoluene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). Vinyl triflate **5.41** (17.4 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 30 °C for 2 hours. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give product **5.42** in 83% NMR yield. The crude material was purified by silica flash chromatography (hexanes) to give the pure product **5.35** as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.28 (d, J = 7.6 Hz, 1H), 7.24 (d, J = 8.1 Hz, 2H), 1.82 (s, 3H), 1.81 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.1, 143.1, 134.8, 134.2, 133.2, 130.5 (q, $^2J_{C\text{–}F}$ = 32.3 Hz), 130.1, 128.6 (q, $^2J_{C\text{–}F}$ = 32.3 Hz), 128.6, 126.4 (q, J = 3.7 Hz), 125.1 (q, $^1J_{C\text{–}F}$ = 3.8 Hz), 124.2 (q, $^1J_{C\text{–}F}$ = 273.2 Hz), 124.1 (q, $^1J_{C\text{–}F}$ = 273.2 Hz), 123.3 (q, $^1J_{C\text{–}F}$ = 3.9 Hz), 22.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4, -62.5.

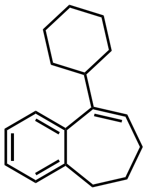
HR-MS (EI-MS) m/z: $[M]^+$ Calc'd for $C_{18}H_{14}F_6$ 344.1000; Found 344.1012.

5.11.2.5 Intermolecular C–H insertion reactions with LiF_{20}

*This section outlines procedures used for **Figure 5.9**. All 0% yielding reactions did not show any product by GC-MS or crude NMR when following general procedure below with appropriate vinyl triflate precursor.*

5.11.2.5.1 General Procedure

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF_{20} (0.05 equiv, 0.0025 mmol). Cyclohexane (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). Vinyl triflate (0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 30–80 °C. The reaction progress was closely monitored by TLC and/or GC. Upon completion of reaction, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material. The crude material was purified by silica flash chromatography to give the pure product.



9-cyclohexyl-6,7-dihydro-5*H*-benzo[7]annulene (5.45)

Synthesized according to a modified general procedure 5.11.2.5.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF_{20} (2.3 mg, 0.05 equiv, 0.0025 mmol). Cyclohexane (2.0 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). benzosuberonyl triflate (14.6 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 70 °C for 1 hour. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material in 21% NMR yield. The crude material was purified by silica flash chromatography (hexanes) to give product **5.45**.

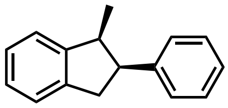
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 2H), 7.19 – 7.12 (m, 2H), 5.84 (td, *J* = 7.3, 1.4 Hz, 1H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.37 (t, *J* = 11.5 Hz, 1H), 2.02 (p, *J* = 7.1 Hz, 2H), 1.81 – 1.71 (m, 5H), 1.69 (d, *J* = 13.1 Hz, 1H), 1.37 – 1.09 (m, 6H).

^{13}C NMR (500 MHz, $CDCl_3$) δ 147.1, 141.9, 141.4, 128.4, 126.2, 125.9, 125.8, 122.1, 43.5, 34.5, 33.0, 32.0, 26.9, 26.6, 24.2.

HR-MS (EI-MS) m/z: $[M]^+$ Calc'd for $C_{17}H_{22}$ 226.1721; Found 226.1711.

5.11.2.6 Vinyl Cation Rearrangement Reactions

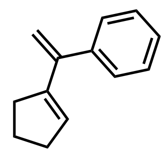
In this section, procedures and data pertinent to ***Figures 5.10*** *and* ***5.11*** *are shown.*

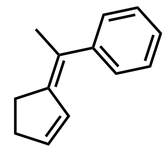


1.25:1 d.r.

(1*S*,2*S*)-1-methyl-2-phenyl-2,3-dihydro-1*H*-indene (5.49)

In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.05 equiv) and this was suspended in cyclohexane (0.5 mL). Triethylsilane (1.5 equiv) along with a magnetic stirring bar were added to the mixture and was shaken until it turned colorless. At this point, vinyl triflate **5.48** (17.8 mg, 0.050 mmol, 1.0 equiv) was added to the reaction and it stirred at 60 °C for 12 hours. Upon completion, the reaction mixture was pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure. Reaction was purified by silica flash chromatography (hexanes) to give **5.49** as a colorless oil (6.1 mg, 59% yield.). This was a 1.25:1 mixture of diastereomers of the *cis* and *trans* indanes. Spectral data for the mixture matched reported spectral data for pure diastereomers.[34,35]


5.52


5.53

(1-(cyclopent-1-en-1-yl)vinyl)benzene (5.52) and (*Z*)-(1-(cyclopent-2-en-1-ylidene)ethyl)benzene (5.53)

Synthesized according to a modified general procedure 5.11.2.5.1. In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with TritylF_{20} (2.3 mg, 0.05 equiv, 0.0025 mmol). Benzene (0.5 mL) was added followed by LiHMDS (12.5 mg, 0.075 mmol, 1.5 equiv). Triflate **5.51** (16.0 mg, 0.050 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 70 °C for 1 hour. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material in 13% and 9% NMR yield of **5.52** and **5.53** respectively. The crude material was purified by silica flash chromatography (hexanes) to give pure product **5.52** and pure product **5.53** as colorless oils.

Characterization data for **5.52**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 5H), 5.58 (d, *J* = 5.9 Hz, 1H), 5.16 (d, *J* = 5.8 Hz, 1H), 5.08 (d, *J* = 5.8 Hz, 1H), 2.60 (d, *J* = 7.6 Hz, 3H), 2.44 (d, *J* = 7.5 Hz, 3H), 1.99 (q, *J* = 7.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 143.5, 142.2, 131.4, 128.5, 127.8, 127.1, 113.6, 33.5, 32.9, 23.3.

FTIR (Neat film NaCl): 3079, 3056, 3023, 2951, 2926, 2867, 2844, 1619, 1588, 1572, 1493, 1464, 1311, 1027, 957, 886, 828, 772, 698.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{13}H_{14}$ 170.1096; Found 170.1099.

Characterization data for **5.53**

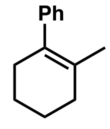
10:1 mix of Z:E isomers. Major Isomer reported below

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.6 Hz, 3H), 7.27 – 7.22 (m, 3H), 7.21 – 7.17 (m, 1H), 6.35 – 6.29 (m, 1H), 6.13 – 6.01 (m, 1H), 2.64 – 2.60 (m, 2H), 2.59 – 2.55 (m, 2H), 2.05 (s, 3H).

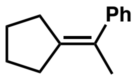
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2, 143.7, 137.7, 132.2, 128.1, 127.9, 125.9, 124.9, 31.9, 28.6, 21.0.

FTIR (Neat film NaCl): 3076, 3054, 3022, 2923, 2846, 1598, 1572, 1492, 1442, 1375, 1260, 1142, 1080, 1062.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{13}H_{14}$ 170.1096; Found 170.1094.



5.55



5.56

6-methyl-2,3,4,5-tetrahydro-1,1'-biphenyl (5.55) and (1-cyclopentylideneethyl)benzene (5.56)

*(From vinyl triflate **5.54**).* Synthesized according to a modified general procedure 5.11.2.5.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF_{20} (4.6 mg, 0.05 equiv, 0.005 mmol). Benzene (1.0 mL) was added followed by LiHMDS (25.1 mg, 0.150 mmol, 1.5 equiv). Triflate **5.54** (24.4 mg, 0.100 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 80 °C for 1 hour. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material in 43% and 39% NMR yield of **5.55** and **5.56** respectively. These compounds were unable to be separated by neither silica column chromatography nor reverse phase HPLC.

*(From vinyl triflate **5.57**)*. Synthesized according to a modified general procedure 5.11.2.5.1. In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with TritylF$_{20}$ (4.6 mg, 0.05 equiv, 0.005 mmol). Benzene (1.0 mL) was added followed by LiHMDS (25.1 mg, 0.150 mmol, 1.5 equiv). Triflate **5.57** (24.4 mg, 0.100 mmol, 1.0 equiv) was added and the reaction was allowed to stir at 80 °C for 15 minutes. At this point, the mixture was diluted with ether and pushed through a plug of silica gel in a pipette. This was concentrated to give the crude material in 5% and 62% NMR yield of **5.55** and **5.56** respectively. Crude material was purified by flash column chromatography to give a small amount of pure **5.56** for characterization.

Characterization of **5.56**

*Material contains ~5% of the disubstituted olefin isomer as well.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.24 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.22 – 7.17 (m, 1H), 2.37 (ddq, *J* = 7.3, 5.8, 1.5 Hz, 2H), 2.26 (ddq, *J* = 8.7, 5.2, 1.8 Hz, 2H), 2.01 (p, *J* = 1.7 Hz, 3H), 1.74 (p, *J* = 7.0 Hz, 2H), 1.61 (p, *J* = 7.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.9, 140.3, 127.8, 127.7, 126.2, 125.6, 32.6, 31.5, 27.4, 26.4, 20.9.

FTIR (Neat film NaCl): 3055, 3021, 2951, 2936, 2834, 1598, 1492, 1375, 1279, 1230, 1130, 1061, 1048, 1026, 951, 761.

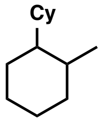
HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{13}H_{16}$ 172.1252; Found 172.1248.

Because we could not purify **5.55** from the reaction mixtures, an authentic sample was prepared *via* a Suzuki coupling. In a 2 dram vial were combined Pd(dppf)Cl_2 (8.99 mg, 0.012 mmol, 0.06 equiv), KF (35.7 mg, 0.614 mmol, 3 equiv) and phenylboronic acid (27.5 mg, 0.225 mmol, 1.1 equiv). To this was added dry, degassed THF (1 mL) and vinyl triflate **5.54** (50.0 mg, 0.205 mmol, 1.0 equiv). The vial was sealed and heated at 45 °C for 2 days. At this point, the reaction was plugged through silica with ether and concentrated to give crude product. The crude was purified by silica flash colum chromatography to give pure **5.55** as colorless oil (8.5 mg, 24% yield). Notably, the spectral data for this pure sample matched with crude spectral data for experiments outlined above.

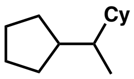
Characterization of **5.56**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 2.30 – 2.18 (m, 2H), 2.07 (s, 1H), 1.74 – 1.65 (m, 3H), 1.55 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.4, 132.3, 129.1, 128.4, 127.9, 125.8, 31.9, 31.6, 23.5, 23.1, 20.7.



5.58



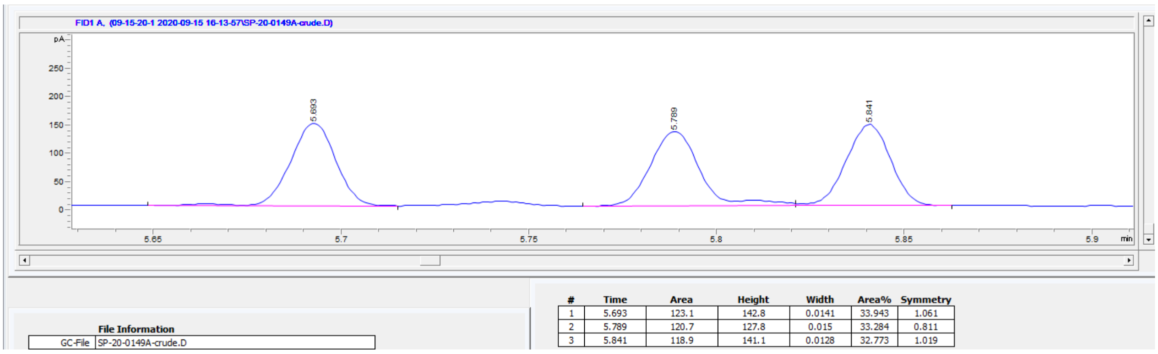
5.59

2-methyl-1,1'-bi(cyclohexane) (5.58) and (1-cyclopentylethyl)cyclohexane (5.59)

**Reactions were performed with triisopropylsilane in place of triethylsilane in order to make GC-FID analysis easier.

(From vinyl triflate ***5.54****).* In a well kept glovebox, (H_2O, O_2 < 0.5 ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.05 equiv) and this was suspended in cyclohexane (0.5 mL). Triisopropylsilane (11.9 mg, 0.075 mmol, 1.5 equiv) along with a magnetic stirring bar were added to the mixture and was shaken until it turned colorless. At this point, vinyl triflate **5.54** (12.2 mg, 0.050 mmol, 1.0 equiv) was added to the reaction and it stirred at 30 °C for 12 hours. Upon completion, the reaction mixture was pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure to give a mixture of **5.59** and the diastereoemers of **5.58** as a colorless oil (7.9 mg, 87% yield.). These compounds could not be separated from each other. GC overlays of this reaction, the next reaction and authentic

samples will be shown below. GC-FID shows a relative ratio of 2:1 for **5.58**:**5.59** (area of both diastereomers of **5.58** were added) and an equivalent extinction coefficient for all three compounds is assumed.



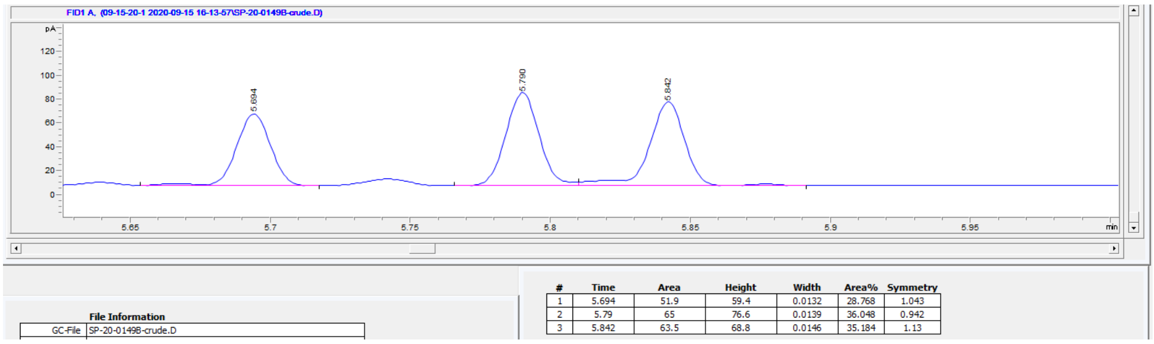
File Information

GC-File	SP-20-0149A-crude.D

#	Time	Area	Height	Width	Area%	Symmetry
1	5.693	123.1	142.8	0.0141	33.943	1.061
2	5.789	120.7	127.8	0.015	33.284	0.811
3	5.841	118.9	141.1	0.0128	32.773	1.019

Figure 5.13 GC FID spectrum of crude reaction mixture showing ~2:1 ratio of **5.58** (left and right) : **5.59** (middle)

(From vinyl triflate 5.57). In a well kept glovebox, (H_2O, $O_2 < 0.5$ ppm), a dram vial was charged with $[Ph_3C]^+[HCB_{11}Cl_{11}]^-$ (0.8 mg, 0.001 mmol, 0.05 equiv) and this was suspended in cyclohexane (0.5 mL). Triisopropylsilane (11.9 mg, 0.075 mmol, 1.5 equiv) along with a magnetic stirring bar were added to the mixture and was shaken until it turned colorless. At this point, vinyl triflate **5.54** (12.2 mg, 0.050 mmol, 1.0 equiv) was added to the reaction and it stirred at 30 °C for 12 hours. Upon completion, the reaction mixture was pushed through a short plug of silica gel inside the glovebox and washed with hexanes. The solution was brought out and volatiles removed under reduced pressure to give a mixture of **5.59** and the diastereoemers of **5.58** as a colorless oil (6.9 mg, 77% yield.). These compounds could not be separated from each other. GC overlays of this reaction, the next reaction and authentic samples will be shown below. GC-FID shows a relative ratio of 1.76:1 for **5.58**:**5.59** (area of both diastereomers of **5.58** were added) and an equivalent extinction coefficient for all three compounds is assumed.

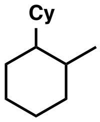


File Information

GC-File	SP-20-0149B-crude.D

#	Time	Area	Height	Width	Area%	Symmetry
1	5.694	51.9	59.4	0.0132	28.768	1.043
2	5.79	65	76.6	0.0139	36.048	0.942
3	5.842	63.5	68.8	0.0146	35.184	1.13

Figure 5.14 GC FID spectrum of crude reaction mixture showing ~1.76:1 ratio of **5.58** (left and right) : **5.59** (middle)



2-methyl-1,1'-bi(cyclohexane) (5.58)

Because this compound could not be purified from the reaction mixtures above, an authentic sample was prepared. Magnesium (1.716 g, 70.6 mmol, 2 equiv) was added to a to a to a 500 mL 3-neck flask equipped with a reflux condenser. This was suspended in ether (140 mL) and bromocyclohexane (6.91 g, 42.4 mmol, 1.2 equiv) was slowly added. Solution was initiated with heat gun (Turns cloudy upon initiation) and stirred for 2 hours at room temperature. Reaction was cooled to 0 and 2-methylcyclohexanone (3.96 g, 35.3 mmol, 1 equiv) in ether (25 mL) was added dropwise 30 minutes *via* addition funnel. Upon full addition, the ice bath was removed and reaction stirred overnight at room temperature. Reaction was quenched with sat. NH_4Cl (100 mL). The layers were separated and aqueous was extracted with ether (3 x 100 mL). Combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated to give crude alcohol. This was purified by silica flash column chromatography (5% ether/hexane to 15% ether/hexane) to give pure alcohol as a mixture of diastereomers (2.20 g, 32% yield, ca. 5:1 *d.r.*)

To a 100 mL roundbottom flask was added triphenylsilane (3.50 g, 13.4 mmol, 1.2 equiv) and dissolved in DCM (48 mL). The alcohol (2.20 g, 11.2 mmol, 1 equiv) was added followed by trifluoroacetic acid (7.67 g, 67.2 mmol, 6 equiv) and the reaction was stirred at room temperature for 48 hours. At this point, potassium carbonate (10.84 g) was added and the reaction mixture was filtered and concentrated. Crude reaction mixture was purified by silica flash column chromatography using $AgNO_3$ impregnated silica gel (hexanes) to give pure **5.58** as a colorless oil (1.10 g, 54% yield, ca. 1.25:1 *d.r.*)

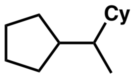
Diagnostic peaks: one isomer ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 6.5 Hz, 3H)

other isomer ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (d, J = 7.2 Hz, 3H).

Carbon peaks for both isomers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 49.8, 45.9, 39.4, 38.5, 36.5, 34.1, 34.0, 32.0, 31.1, 30.4, 28.5, 27.4, 27.22, 27.13, 27.10, 26.84, 26.80, 26.63, 26.61, 26.4, 23.8, 20.6, 20.1, 12.0.

FTIR (Neat film NaCl): 2919, 2850, 2669, 1446, 1377, 1348, 1311, 1266, 1176, 1065, 1032, 1012, 981, 892, 849.

HR-MS (EI-MS) m/z: $[M]^+$ Calc'd for $C_{13}H_{24}$ 180.1878; Found 180.1887.



5.59

(1-cyclopentylethyl)cyclohexane (5.59)

Because this compound could not be purified from the reaction mixtures above, an authentic sample was prepared. Magnesium (743 mg, 30.6 mmol, 2 equiv) was added to a to a 500 mL 3-neck flask equipped with a reflux condenser. This was suspended in ether (62 mL) and bromocyclohexane (2.99 g, 18.4 mmol, 1.2 equiv) was slowly added. Solution was initiated with heat gun (Turns cloudy upon initiation) and stirred for 2 hours at room temperature. Reaction was cooled to 0 and 1-cyclopentylethan-1-one (1.72 g, 15.3 mmol, 1 equiv) in ether

(15 mL) was added dropwise 30 minutes *via* addition funnel. Upon full addition, the ice bath was removed and reaction stirred overnight at room temperature. Reaction was quenched with sat. NH_4Cl (40 mL). The layers were separated and aqueous was extracted with ether (3 x 40 mL). Combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated to give crude alcohol. This was purified by silica flash column chromatography (5% ether/hexane to 15% ether/hexane) to give pure alcohol as colorless oil (330 mg, 11% yield)

To a 25 mL roundbottom flask was added triphenylsilane (525 mg, 2.02 mmol, 1.2 equiv) and dissolved in DCM (7.3 mL). The alcohol (330 mg, 1.68 mmol, 1 equiv) was added followed by trifluoroacetic acid (1.15 g, 10.1 mmol, 6 equiv) and the reaction was stirred at room temperature for 48 hours. At this point, potassium carbonate (1.63 g) was added and the reaction mixture was filtered and concentrated. Crude reaction mixture was purified by silica flash column chromatography using $AgNO_3$ impregnated silica gel (hexanes) to give pure **5.59** as a colorless oil (145 mg, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.79 – 1.69 (m, 4H), 1.69 – 1.63 (m, 2H), 1.62 – 1.55 (m, 3H), 1.54 – 1.41 (m, 3H), 1.41 – 1.34 (m, 1H), 1.25 (dt, *J* = 12.5, 3.3 Hz, 1H), 1.22 – 1.02 (m, 6H), 0.94 (qd, *J* = 12.4, 3.5 Hz, 1H), 0.78 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 44.1, 43.9, 41.2, 32.2, 31.3, 31.1, 27.2, 27.0, 26.9, 26.8, 25.3, 25.2.

FTIR (Neat film NaCl): 2922, 2867, 2851, 2667, 1448, 1379, 1349, 1318, 1293, 1264, 1172, 1154, 1054, 1034, 999, 890, 506.

HR-MS (EI-MS) m/z: [M]+ Calc'd for $C_{13}H_{24}$ 180.1878; Found 180.1874.

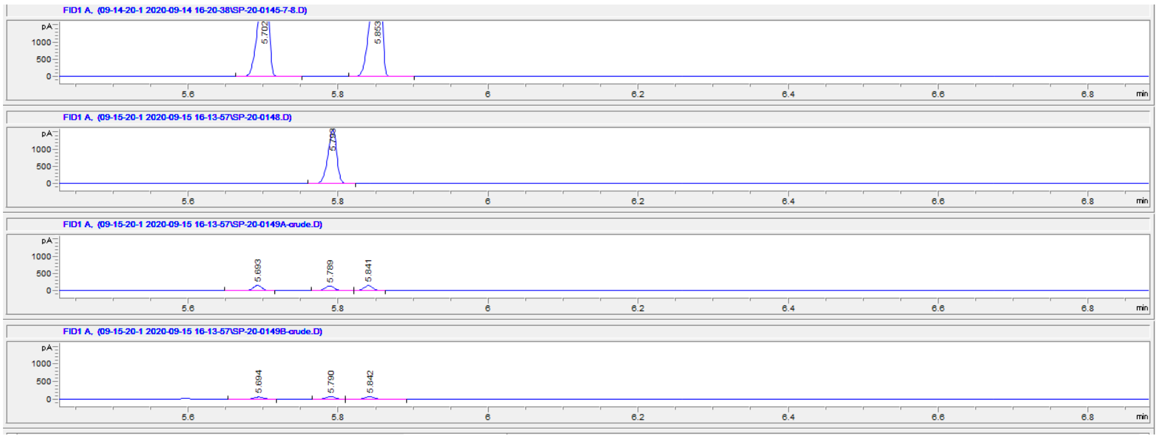


Figure 5.15 GC FID spectrum of crude reaction mixture showing overlay of authentic **5.58** (top), authentic **5.59** (2nd), and reaction mixtures from mechanistic studies (bottom spectra)

5.11.3 Computational Methods

5.11.3.1 General computational methods

All calculations were carried out with the Gaussian 16[36] software package. Geometries, Hirshfeld charges, molecular orbitals, and energies of ground states and transition states were calculated with the ωB97X-D[37] functional and the 6-311+G(d,p) basis set. A CPCM[38] implicit solvent model in benzene. Frequency calculations were carried out at the same level of theory to ensure that stationary points were truly minima or saddle points on the potential energy surface. Intrinsic reaction coordinate (IRC) calculations were carried out at this level of theory to confirm all transition states connected reactants and products. Conformational searches were carried out using the CREST conformer-rotamer ensemble sampling tool[39], version 2.7.1 with XTB version 6.2 RC2 (SAW190805)[40].

5.11.3.2 Computed Energies

Structure	**E**(benzene)	**ΔG**(benzene)	**G**(benzene)	**ΔH**(benzene)	**H**(benzene)	**Imaginary Frequency**
cyclohexenyl-Tf	-1604.55038	0.223545	-1604.326836	0.302283	-1604.248098	
cyclohexenyl-cation	-233.727802	0.104736	-233.623066	0.140212	-233.587589	
6-sub-Tf	-1643.867363	0.253457	-1643.613906	0.331883	-1643.535479	
6-sub-cation	-273.061978	0.129847	-272.932131	0.169466	-272.892512	
2-sub-Tf	-1643.872889	0.25352	-1643.619368	0.331761	-1643.541128	
2-sub-cation	-273.052173	0.130712	-272.921462	0.170417	-272.881756	
TS-contraction	-273.06187	0.131253	-272.930617	0.169243	-272.892628	-77.984

cont-allylic	-273.10613	0.130781	-272.975349	0.169995	-272.936135	
TS-6-hydride-shift	-273.018741	0.125856	-272.892886	0.165004	-272.853738	-1071.226
6-methyl-allylic	-273.127673	0.13347	-272.994203	0.171214	-272.956459	
TS-6-methyl-shift	-272.991523	0.129674	-272.861849	0.167713	-272.823811	-321.053
1-methyl-allylic	-273.114294	0.1321	-272.982194	0.170516	-272.943777	
benzene	-232.222753	0.073635	-232.149119	0.106384	-232.116369	
TS1	-273.047101	0.130119	-272.916982	0.169459	-272.877642	-190.036
IN1	-273.054903	0.127843	-272.92706	0.1692	-272.885703	
IN2[a]	-505.328554	0.231148	-505.097406	0.280839	-505.047715	
IN2[b]	-505.324053	0.230046	-505.094008	0.280077	-505.043976	
TS2[a]	-505.326209	0.230625	-505.095584	0.27972	-505.046489	-32.837
TS2[b]	-505.319301	0.228734	-505.090567	0.278902	-505.040399	-31.653

5.11.3.3 Cartesian Coordinates

cyclohexenyl-Tf

C	4.131056	-0.026330	0.851973
H	4.341455	0.735461	0.093974
H	4.745042	0.208134	1.723249
C	4.482628	-1.406438	0.297467
H	5.549810	-1.463560	0.074726
H	4.274421	-2.166335	1.058772
C	3.675372	-1.721020	-0.963888
C	2.223230	-1.366027	-0.811076
C	1.826521	-0.581122	0.174250
C	2.649542	0.052925	1.242292
H	2.465679	-0.461747	2.192022
H	2.349538	1.094250	1.385809
O	0.398856	-0.339123	0.343135
S	-0.432669	0.549652	-0.632701
O	-0.055381	0.479186	-2.003293
O	-1.838486	0.231657	-0.260595
Si	-2.817605	-1.254239	0.275652
C	-2.659998	-1.172883	2.113069
H	-3.057341	-0.233518	2.504236
H	-1.618810	-1.276188	2.427353
H	-3.229933	-1.991962	2.562877
C	-4.465765	-0.818795	-0.424727
H	-4.832838	0.126203	-0.018199
H	-4.427803	-0.744983	-1.513785
H	-5.186315	-1.600233	-0.163459
C	-1.939796	-2.665580	-0.535873
H	-1.878294	-2.534971	-1.619194
H	-2.501663	-3.585768	-0.346246
H	-0.934128	-2.804702	-0.131898
C	-0.238676	2.312157	0.018261
F	-1.095359	3.071890	-0.615462
F	-0.476162	2.305855	1.308528
F	0.997184	2.685521	-0.226932
H	1.508396	-1.765129	-1.521969
H	3.753009	-2.781492	-1.217614
H	4.073372	-1.173008	-1.826238

cyclohexenyl-cation

C	0.920588	0.933050	0.297451
C	-0.446815	1.222889	-0.305383
C	-1.501529	0.209000	0.131127
H	-2.391259	0.249076	-0.498302
H	-1.806647	0.338971	1.172513
C	-0.917368	-1.227080	0.015429
C	0.349434	-1.148288	-0.050055
C	1.588774	-0.530723	-0.116846

H	2.297065	-0.773150	0.673387
H	2.034594	-0.490541	-1.109108
H	-1.542630	-2.109734	-0.003427
H	-0.377367	1.235128	-1.396131
H	-0.749615	2.224534	0.008650
H	0.896175	0.947388	1.386516
H	1.681183	1.625240	-0.064427

6-sub-Tf

C	3.722532	-0.348172	-0.915950
C	4.019547	0.630089	0.217882
C	3.563758	0.070090	1.566195
C	2.206874	-0.565355	1.482557
C	1.657304	-0.831469	0.310359
C	2.219980	-0.641735	-1.063366
C	1.973742	-1.850771	-1.970232
H	2.461622	-1.684764	-2.932807
H	0.911420	-2.015453	-2.156224
H	2.392040	-2.759214	-1.528702
H	1.729987	0.231382	-1.515599
O	0.334606	-1.462362	0.314527
S	-0.913105	-0.593326	0.599889
O	-1.155334	-0.279589	1.970677
O	-0.888200	0.557205	-0.361294
Si	-0.976306	2.404496	-0.278780
C	-2.327796	2.739950	0.934073
H	-3.266511	2.273784	0.624633
H	-2.072580	2.391352	1.937055
H	-2.495049	3.820466	0.986432
C	0.726997	2.867374	0.269292
H	0.792662	3.956726	0.354501
H	0.974360	2.441671	1.244966
H	1.473677	2.544915	-0.459796
C	-1.367292	2.757091	-2.046367
H	-2.324419	2.317938	-2.336435
H	-0.587692	2.374967	-2.709366
H	-1.434513	3.839503	-2.193716
C	-2.231584	-1.744272	-0.106451
F	-2.179424	-2.875603	0.548080
F	-3.384121	-1.142369	0.077234
F	-1.994561	-1.920793	-1.382601
H	1.685524	-0.817006	2.400080
H	3.540879	0.854664	2.327811
H	4.270514	-0.684163	1.931665
H	5.087866	0.852171	0.253337
H	3.507736	1.579224	0.026933
H	4.097511	0.036258	-1.867234

H	4.242942	-1.294229	-0.726490

6-methyl-cation

C	-1.286832	-0.245892	0.500316
C	-0.143790	-0.967308	0.292858
C	1.059417	-1.301336	-0.009052
H	1.393183	-2.326540	-0.121533
C	1.968273	-0.091315	-0.191926
C	1.039168	1.104589	-0.385169
C	-0.128736	1.050215	0.589340
H	0.188918	1.075526	1.630211
H	-0.850330	1.843349	0.388135
H	0.666189	1.124438	-1.412050
H	1.564814	2.046690	-0.211823
H	2.626400	-0.252193	-1.046723
H	2.593728	0.003920	0.700740
C	-2.306116	-0.073598	-0.602805
H	-1.826937	0.060784	-1.573300
H	-2.940856	0.786608	-0.385472
H	-2.939496	-0.962002	-0.643985
H	-1.683923	-0.252707	1.514422

2-methyl-Tf

C	-3.204657	1.512372	-1.457591
H	-3.720594	2.322030	-0.931507
H	-3.337419	1.686438	-2.526828
C	-3.805979	0.172184	-1.043727
H	-4.858329	0.120574	-1.330017
H	-3.292375	-0.635701	-1.576071
C	-3.675595	-0.044023	0.463100
C	-2.313239	0.304037	1.016856
C	-1.489436	1.002927	0.248401
C	-1.712919	1.562886	-1.114351
H	-1.129252	0.994905	-1.849391
H	-1.346135	2.592682	-1.142921
O	-0.197863	1.389631	0.812845
S	1.085383	0.532062	0.666403
O	1.683302	0.204273	1.916731
O	0.797230	-0.572062	-0.297739
Si	0.661156	-2.414924	-0.397735
C	0.974755	-2.994646	1.328071
H	0.227088	-2.616587	2.029226
H	1.966330	-2.704051	1.681737
H	0.920721	-4.088067	1.342163
C	-1.075812	-2.598493	-0.995805
H	-1.791104	-2.239748	-0.252458
H	-1.285406	-3.656145	-1.183916
H	-1.231547	-2.053677	-1.929752

C	1.983961	-2.793193	-1.626152
H	1.995945	-3.868764	-1.828263
H	1.807992	-2.275826	-2.572012
H	2.969128	-2.511967	-1.246768
C	2.207619	1.672807	-0.329429
F	1.602368	1.971380	-1.455642
F	2.430680	2.747506	0.384337
F	3.321736	1.017194	-0.559490
C	-2.016582	-0.159193	2.409867
H	-1.096884	0.256847	2.819211
H	-1.952873	-1.251806	2.435312
H	-2.842888	0.121512	3.068370
H	-3.898224	-1.084229	0.723857
H	-4.413573	0.562079	1.002880

2-methyl-cation

C	-1.837895	0.040648	0.308030
C	-1.078185	1.210302	-0.302122
C	0.385850	1.234564	0.124629
H	0.514243	1.531628	1.168508
H	0.976648	1.898231	-0.510051
C	1.087347	-0.178063	0.005230
C	0.114214	-0.987065	-0.065031
C	-1.223294	-1.402271	-0.119764
H	-1.558867	-1.695445	-1.114029
H	-1.515548	-2.117215	0.649153
C	2.575239	-0.277141	0.012365
H	2.967731	0.237622	-0.866578
H	2.957969	0.225630	0.902464
H	2.904790	-1.313280	0.006699
H	-1.554891	2.142502	0.009361
H	-1.140824	1.166762	-1.392664
H	-2.873260	-0.000315	-0.030420
H	-1.817650	0.078031	1.397527

TS-contraction

C	-1.373309	-0.239729	0.501791
C	-0.181532	-0.852830	0.315806
C	0.998501	-1.285221	-0.002189
H	1.218473	-2.341420	-0.106825
C	2.004903	-0.177255	-0.204164
C	1.143688	1.072243	-0.381267
C	-0.038407	1.018073	0.581508
H	0.243732	1.045654	1.631992
H	-0.764286	1.799614	0.357525
H	0.778046	1.135699	-1.408558
H	1.690672	1.993529	-0.166879
H	2.637065	-0.379664	-1.069768

H	2.655779	-0.115787	0.673902
C	-2.361033	-0.032616	-0.611680
H	-1.873233	-0.005044	-1.585667
H	-2.930900	0.882954	-0.448501
H	-3.061574	-0.872098	-0.595417
H	-1.750639	-0.159436	1.519365

cont-allylic

C	-1.629438	-0.590514	-0.002902
C	-0.287545	-0.272103	-0.055431
C	0.181878	1.029155	-0.034274
H	-0.445977	1.913802	-0.013595
C	1.646793	1.075170	-0.079581
C	2.091971	-0.365838	0.233810
C	0.877276	-1.239971	-0.138506
H	0.959348	-1.620188	-1.161468
H	0.754294	-2.097852	0.523199
H	2.302223	-0.450286	1.302233
H	2.993951	-0.647589	-0.306714
H	2.067669	1.859685	0.554984
H	1.900669	1.375789	-1.112595
C	-2.770855	0.323778	0.068379
H	-2.519107	1.382021	0.042260
H	-3.337356	0.096964	0.981337
H	-3.457188	0.081024	-0.752693
H	-1.879021	-1.651441	-0.005913

TS-6-hydride-shift

C	1.839402	0.014194	-0.417508
H	2.172843	-0.104619	-1.449355
H	2.738410	0.145981	0.192823
C	0.882929	1.230676	-0.270826
H	0.453190	1.479178	-1.244431
H	1.471618	2.095001	0.042417
C	-0.278045	1.035714	0.738353
H	-0.952767	1.892843	0.734481
H	0.096986	0.890956	1.752360
C	1.216353	-1.265171	0.154354
H	1.787719	-2.000931	0.703204
C	-1.026664	-0.215667	0.237998
C	-0.078529	-1.170305	0.050815
H	-1.047966	-1.181020	1.094497
C	-2.343612	-0.125849	-0.469044
H	-3.103030	0.295995	0.190447
H	-2.215510	0.557757	-1.313847
H	-2.672494	-1.092702	-0.847449

6-methyl-allylic

C	1.896374	0.100079	0.159241

H	2.147712	0.042377	1.233239
H	2.853420	0.261257	-0.343923
C	1.192918	-1.163434	-0.319292
H	1.740516	-2.051058	-0.002726
H	1.173281	-1.167002	-1.413801
C	-0.236104	-1.214242	0.207078
H	-0.248160	-1.380240	1.299232
H	-0.806318	-2.047164	-0.212328
C	1.055678	1.302407	0.014979
H	1.547159	2.271515	0.047100
C	-0.985725	0.049749	0.015838
C	-0.308287	1.268459	-0.109049
H	-0.872694	2.187307	-0.213435
C	-2.455023	-0.004370	-0.007190
H	-2.734231	-0.360921	-1.011250
H	-2.834880	-0.752874	0.693211
H	-2.924798	0.964913	0.155055

TS-6-methyl-shift

C	1.168572	-1.065569	0.411549
H	2.087186	-1.644387	0.355099
H	0.660999	-1.249847	1.355867
C	1.531371	0.500241	0.282803
H	2.276548	0.594104	-0.506852
H	2.027347	0.754636	1.221350
C	0.364233	1.480612	0.015282
H	0.654682	2.208506	-0.751279
H	0.122561	2.070974	0.903246
C	0.321959	-1.098701	-0.779242
H	0.804576	-1.186140	-1.750487
C	-0.928249	0.855399	-0.473471
C	-0.893309	-0.493158	-0.749249
C	-1.740172	-0.424686	0.727525
H	-1.471048	-1.424035	1.066639
H	-1.492616	0.258225	1.543441
H	-2.793155	-0.374075	0.468181
H	-1.823515	1.467203	-0.516385

1-methyl-allylic

C	-1.162759	-1.248211	-0.154748
H	-1.484882	-2.159943	0.358702
H	-1.413659	-1.434388	-1.215376
C	-1.844262	-0.000072	0.386730
H	-1.773945	-0.000086	1.478261
H	-2.903555	-0.000120	0.131191
C	-1.162879	1.248147	-0.154718
H	-1.485055	2.159813	0.358820
H	-1.413860	1.434378	-1.215313

C	0.303759	-1.171191	-0.111030
H	0.853246	-2.098611	-0.265177
C	0.303662	1.171281	-0.111048
C	1.033086	0.000086	0.029365
C	2.531467	0.000013	0.135561
H	2.961366	0.885643	-0.335068
H	2.833509	-0.001469	1.186017
H	2.961378	-0.884318	-0.337530
H	0.853007	2.098779	-0.265211

Benzene

C	-1.140911	-0.796733	0.000001
C	0.119601	-1.386411	-0.000018
C	1.260460	-0.589688	0.000018
C	1.140876	0.796783	-0.000002
C	-0.119540	1.386416	-0.000015
C	-1.260486	0.589634	0.000013
H	-2.029934	-1.417685	0.000000
H	0.212705	-2.466815	-0.000013
H	2.242738	-1.049100	0.000016
H	2.029980	1.417619	0.000004
H	-0.212781	2.466808	-0.000015
H	-2.242705	1.049169	0.000023

TS1

C	-2.044643	-0.075215	0.225634
C	-1.267913	1.118461	-0.314030
C	0.164015	1.062331	0.219477
H	0.237977	1.237221	1.290137
H	0.815097	1.724197	-0.349464
C	1.354299	-0.334903	-0.030229
C	0.212614	-0.784116	-0.031504
C	-1.154697	-1.302179	-0.079016
H	-1.337797	-1.696878	-1.081186
H	-1.277095	-2.110820	0.642504
C	2.782210	-0.050941	-0.014648
H	3.061469	0.562889	-0.872467
H	3.056762	0.461734	0.908975
H	3.314824	-1.002209	-0.064787
H	-1.688095	2.075115	0.005922
H	-1.250167	1.109778	-1.406507
H	-3.027101	-0.177845	-0.232567
H	-2.181185	0.016188	1.305334

IN1

C	1.918673	-0.715384	-0.262575
C	1.920920	0.720422	0.248499
C	0.530505	1.252536	-0.126700
H	0.172353	2.073215	0.492610

H	0.490501	1.558253	-1.175122
C	-0.358119	-0.000889	0.005864
C	-1.621710	-0.026529	0.002431
C	-3.035854	-0.014226	-0.004016
H	-3.469688	-0.353406	0.938744
H	-3.462883	-0.503290	-0.881735
H	-3.269098	1.065336	-0.093707
C	0.538600	-1.253181	0.141524
H	0.177587	-2.085448	-0.460191
H	0.516645	-1.542619	1.195085
H	2.702527	1.336854	-0.196863
H	2.048880	0.740856	1.333834
H	2.710512	-1.329811	0.167465
H	2.024574	-0.736437	-1.350290

IN2[a]

C	-0.262101	0.174380	0.108153
C	-2.753774	0.156503	-0.094087
H	-3.078180	0.283513	-1.138320
H	-3.485733	0.715613	0.497440
C	-2.731796	-1.320887	0.274051
H	-3.643892	-1.797189	-0.089799
H	-2.726503	-1.429536	1.363525
C	-1.491445	-1.983018	-0.308472
H	-1.494873	-1.891294	-1.400685
H	-1.474900	-3.049549	-0.076701
C	-0.237375	-1.328926	0.262598
H	0.645010	-1.751179	-0.216707
H	-0.150393	-1.560563	1.329698
C	-1.439620	0.872072	-0.014247
C	1.969741	0.073555	-1.441789
C	2.854301	-0.638709	-0.700099
C	2.879177	-0.538245	0.733098
C	2.013897	0.268220	1.384731
C	1.019069	1.039088	0.649733
C	1.032739	0.951490	-0.797633
H	1.984819	0.035709	-2.523222
H	3.584864	-1.269857	-1.192361
H	3.627892	-1.093216	1.284919
H	2.057244	0.385884	2.460153
H	0.673344	1.947992	1.124678
H	0.586592	1.731849	-1.395767
C	-1.558620	2.358020	-0.047889
H	-1.815113	2.686393	0.967576
H	-0.665476	2.899199	-0.353617
H	-2.389860	2.654980	-0.689697

IN2[b]

C	-3.622715	0.495297	0.186235
C	-3.375181	-0.956479	-0.231262
C	-1.921132	-1.197532	0.196191
H	-1.430891	-2.034019	-0.305421
H	-1.886373	-1.417029	1.275134
C	0.102134	0.393276	-0.011178
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C	-2.290127	1.186531	-0.129075
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C	0.587610	1.811760	-0.125519
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H	-4.063475	-1.663897	0.230000
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H	2.229312	-0.611471	-2.466687
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H	4.198495	0.438398	1.204541
H	2.230118	-0.221787	2.515868

TS2[a]

C	1.677217	-1.907686	-0.548185
C	2.889984	-1.266462	0.114898
C	2.881164	0.237928	-0.128460
H	3.199752	0.458344	-1.155906
H	3.605581	0.741089	0.520435
C	1.533493	0.893770	0.073586
C	0.432817	0.144072	0.208579
C	0.393583	-1.355567	0.065521
H	0.226749	-1.804279	1.054050
H	-0.463721	-1.652863	-0.548293
C	1.588618	2.392945	0.134988
H	1.988497	2.708593	1.104480
H	2.279198	2.765695	-0.625676
H	0.632643	2.893981	-0.018422
H	3.817735	-1.697190	-0.267520

H	2.864140	-1.466753	1.191992
H	1.695125	-2.994098	-0.437793
H	1.691276	-1.692123	-1.622533
C	-3.185125	-0.557956	-0.467576
C	-2.495257	0.289465	-1.337607
C	-1.458857	1.039884	-0.840114
C	-0.964560	0.843654	0.520435
C	-1.787211	-0.003832	1.388576
C	-2.856992	-0.685782	0.900210
H	-4.021043	-1.132218	-0.854097
H	-2.800957	0.373611	-2.371928
H	-0.934056	1.749418	-1.469539
H	-0.724908	1.781629	1.025741
H	-1.495725	-0.093559	2.429194
H	-3.453527	-1.325879	1.536708

TS2^b

C	-3.789593	0.349518	0.096051
C	-3.417622	-1.134802	0.074134
C	-1.938745	-1.142018	0.488598
H	-1.401095	-2.011773	0.101974
H	-1.854380	-1.166752	1.583285
C	-0.112847	0.556378	-0.042539
C	-1.390466	0.176733	-0.021816
C	-2.548968	1.037417	-0.489081
H	-2.450749	2.080435	-0.184434
H	-2.588464	1.019042	-1.585212
C	0.404612	1.854394	-0.592417
H	1.275982	1.699496	-1.236550
H	-0.356733	2.353289	-1.190697
H	0.708442	2.536342	0.209043
H	-3.517610	-1.527389	-0.942722
H	-4.039021	-1.747066	0.728590
H	-3.944725	0.679938	1.128182
H	-4.697982	0.573790	-0.464302
C	0.983583	-0.432874	0.517104
C	1.490991	-1.127122	-0.667321
C	2.778172	-0.959257	-1.100287
C	3.653814	-0.192824	-0.320088
C	3.270941	0.412227	0.893888
C	1.980745	0.291410	1.310870
H	0.438742	-1.126645	1.169888
H	0.788633	-1.734264	-1.227854
H	3.128941	-1.420851	-2.013786
H	4.677419	-0.068700	-0.659214
H	3.999158	0.966637	1.470930

5.12 Spectra Relevant to Chapter Five:

Catalytic Carbon–Carbon Bond Forming Reactions of Vinyl Cations: A Field Guide

(Unpublished Work)

Stasik Popov, Benjamin Wigman, Jonathan Wong, Kendall N. Houk and Hosea M. Nelson

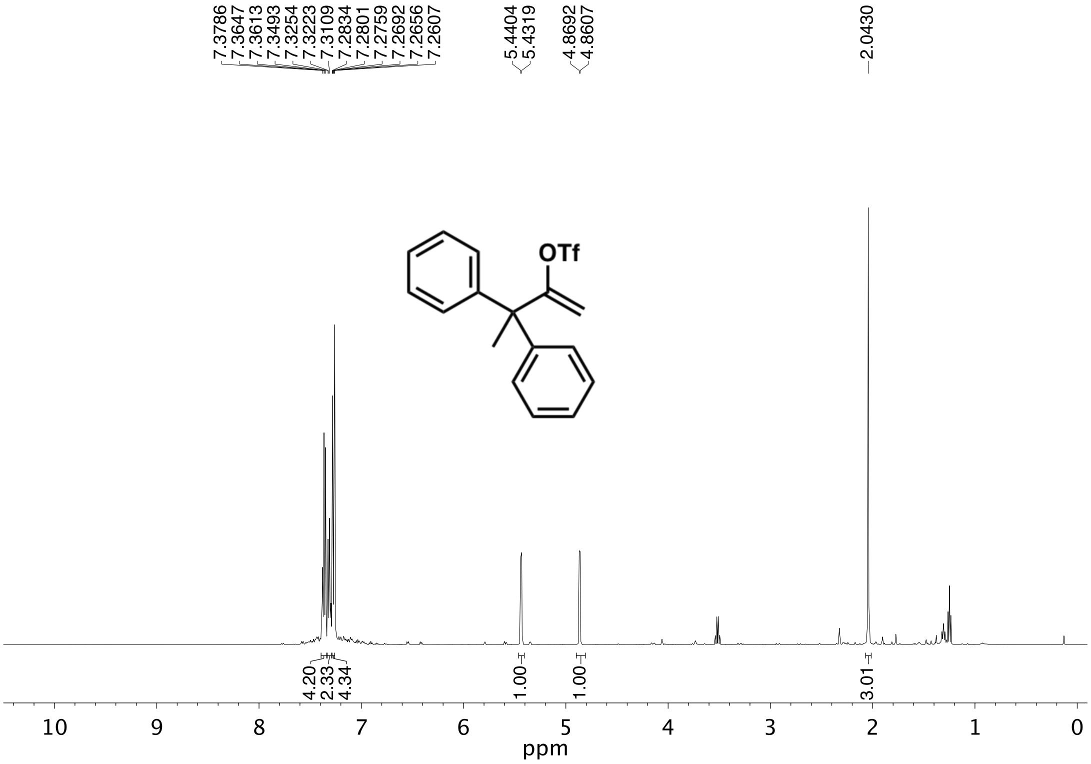

Figure 5.16 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.48**.

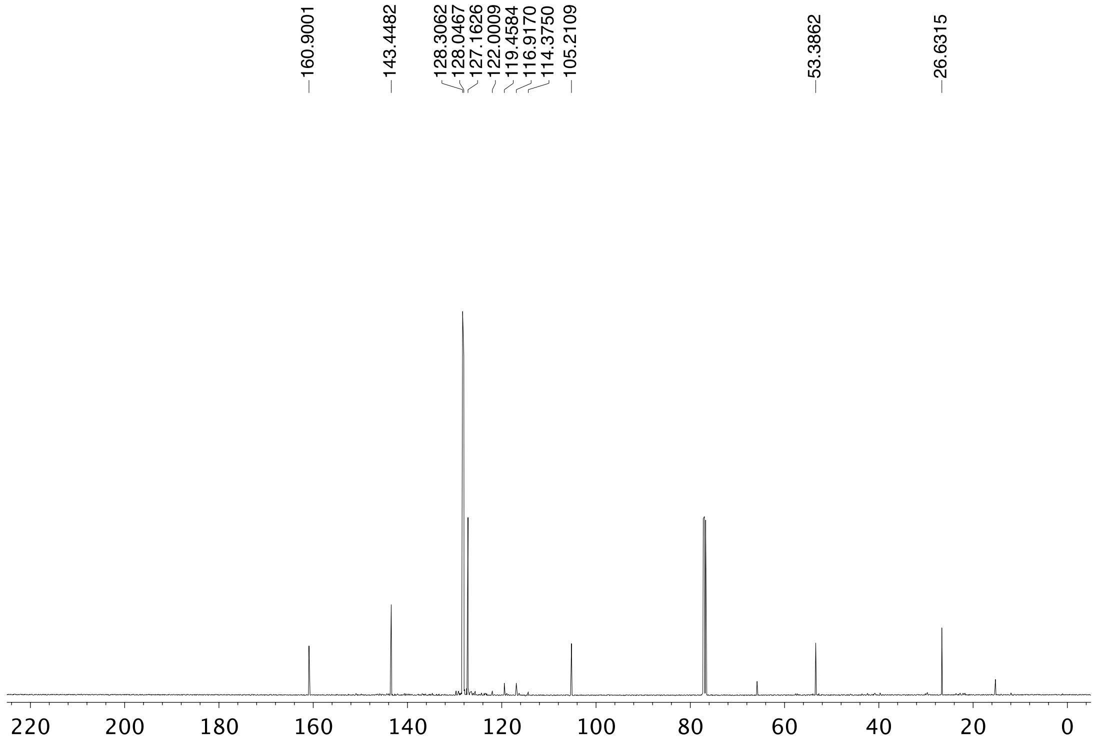

Figure 5.17 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.48**.

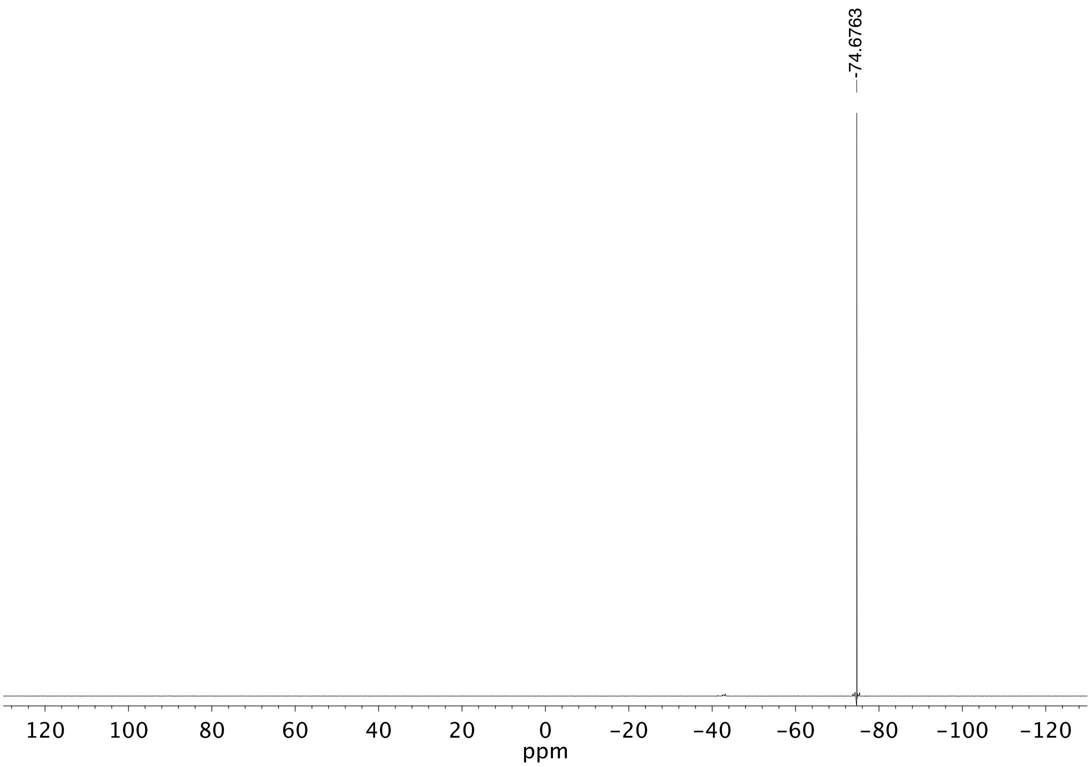

Figure 5.18 ^{19}F NMR (282 MHz, CDCl$_3$) of compound **5.48**.

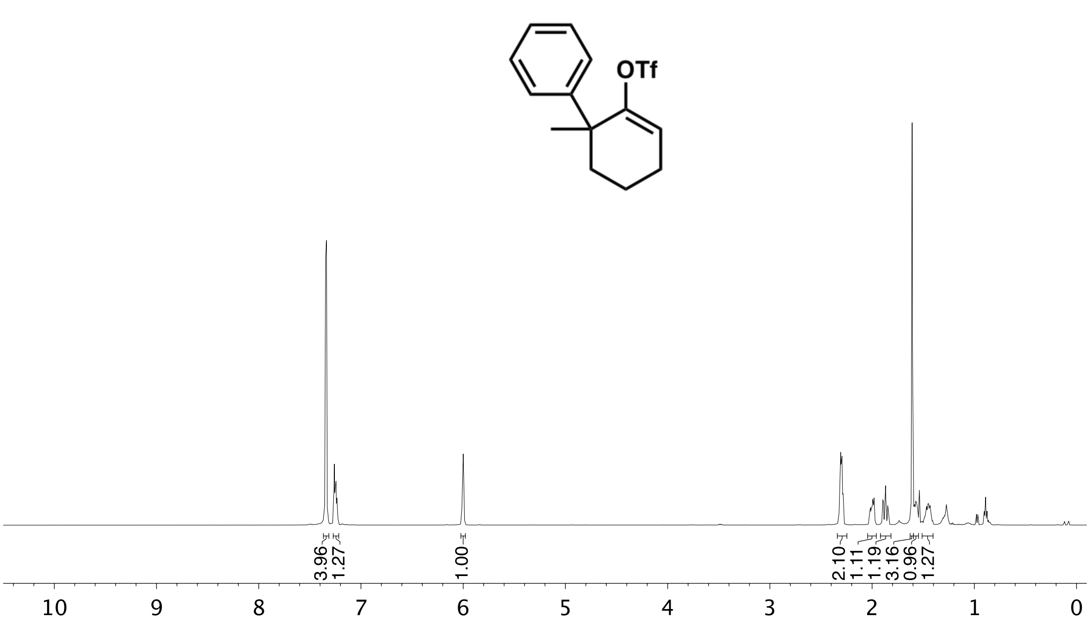

Figure 5.19 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.51**.

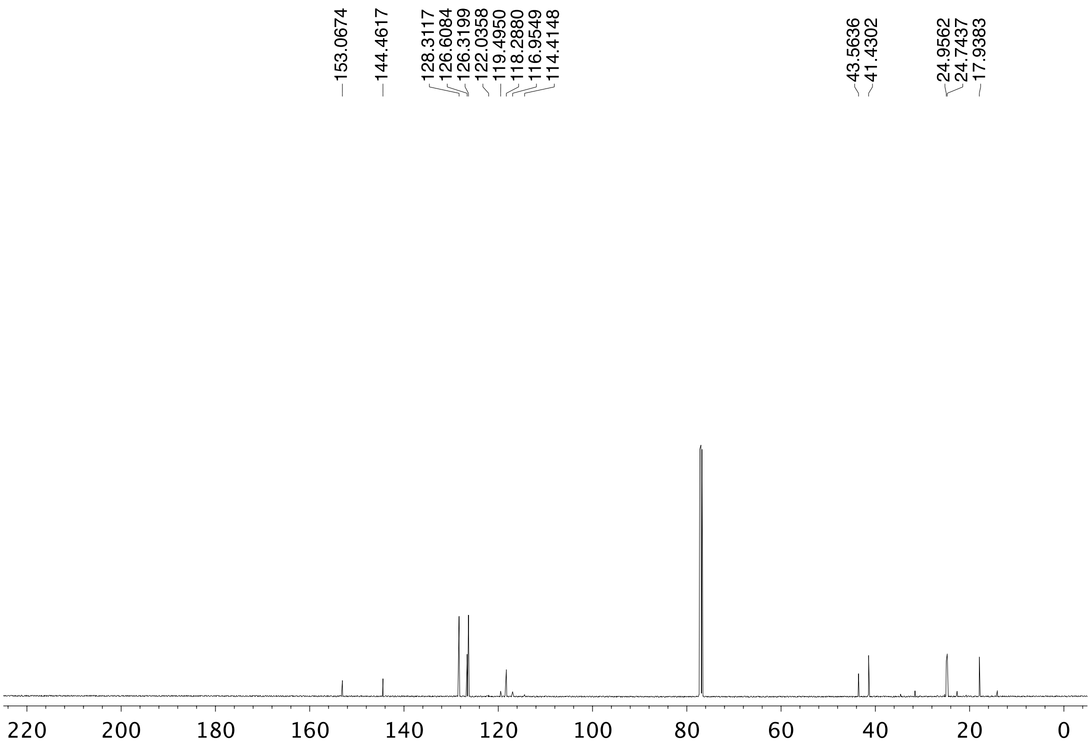

Figure 5.20 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **5.51**.

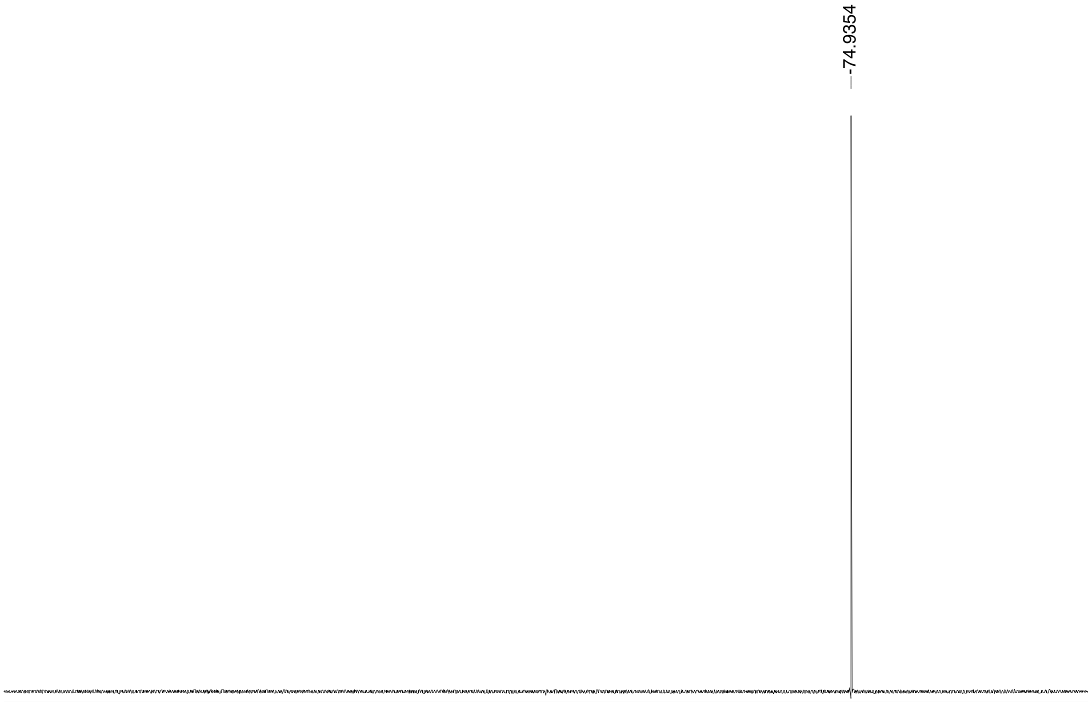

Figure 5.21 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.51**.

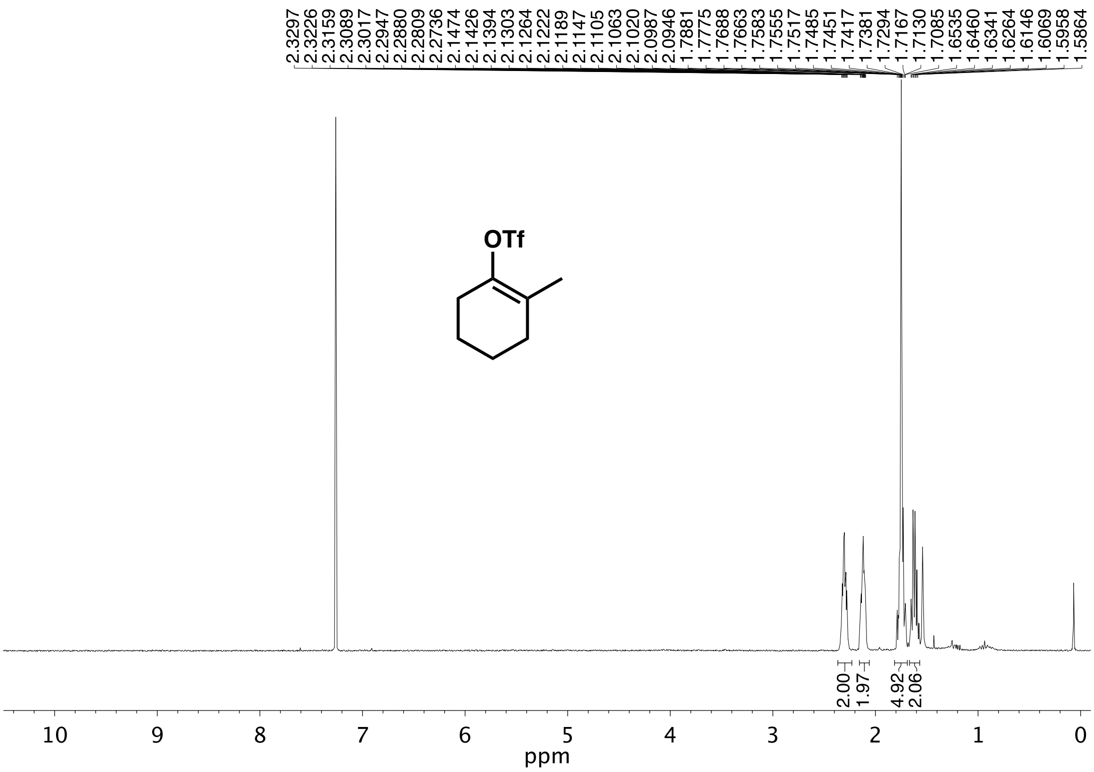

Figure 5.22 ^{1}H NMR (300 MHz, CDCl$_3$) of compound **5.54**.

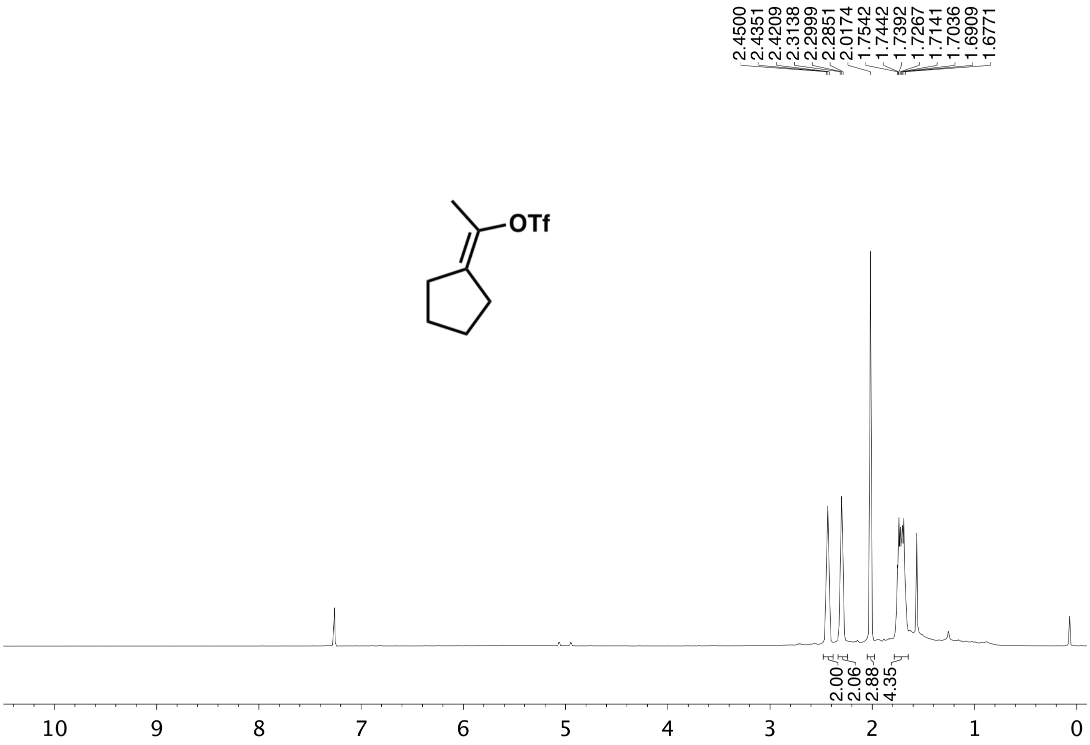

Figure 5.23 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.57**.

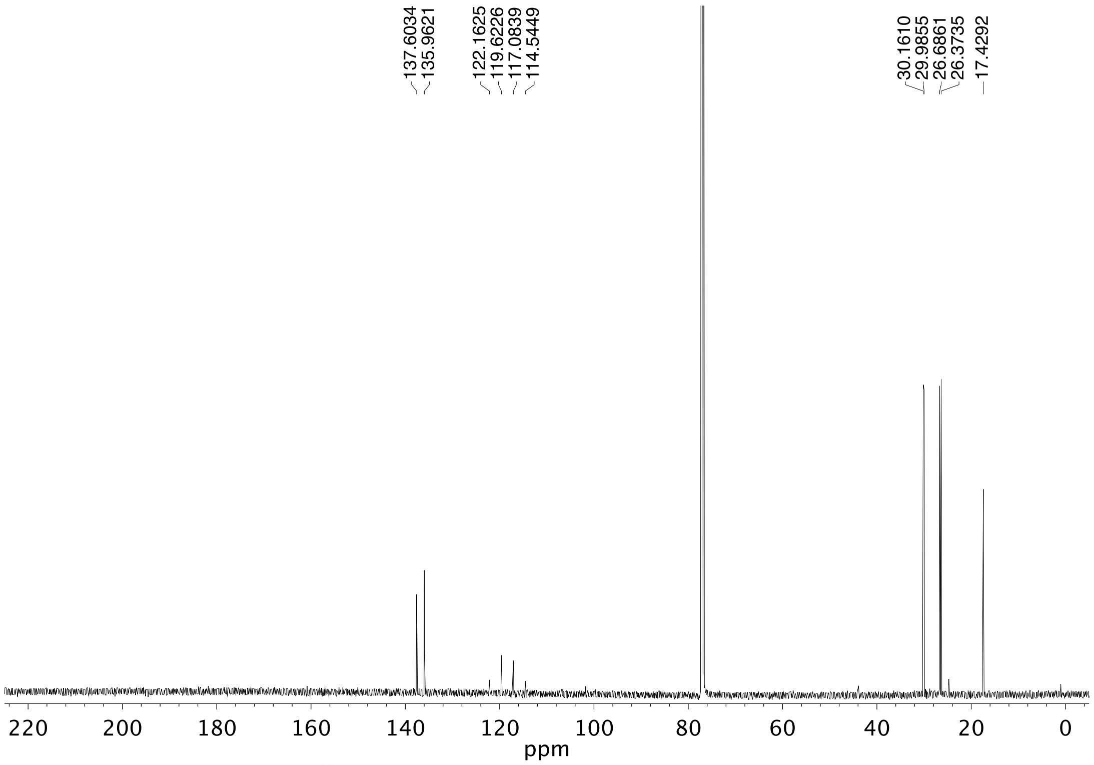

Figure 5.24 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **5.57**.

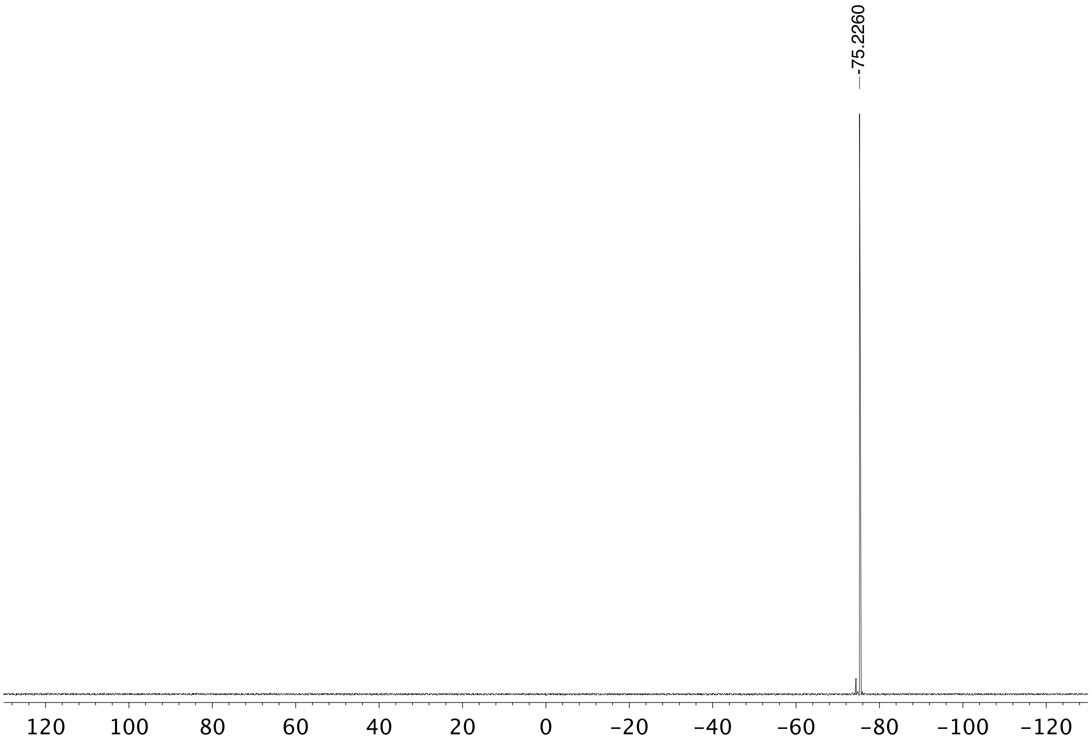

Figure 5.25 ^{19}F NMR (282 MHz, $CDCl_3$) of compound **5.57**.

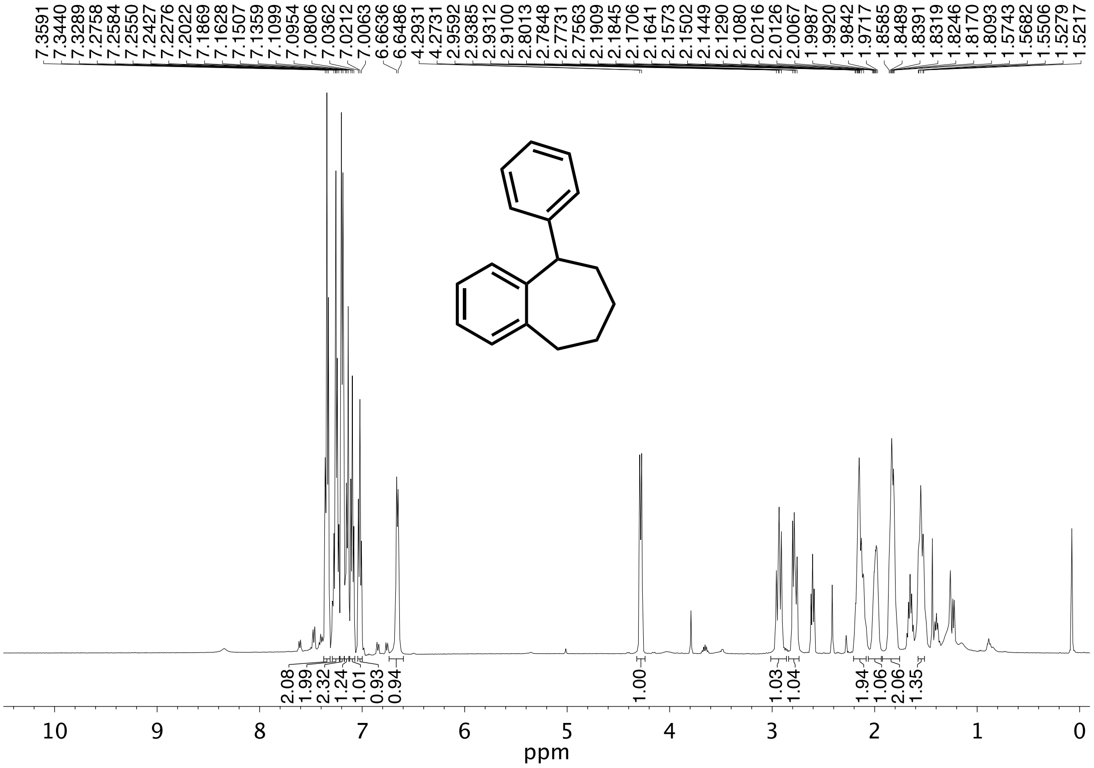

Figure 5.26 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.21**.

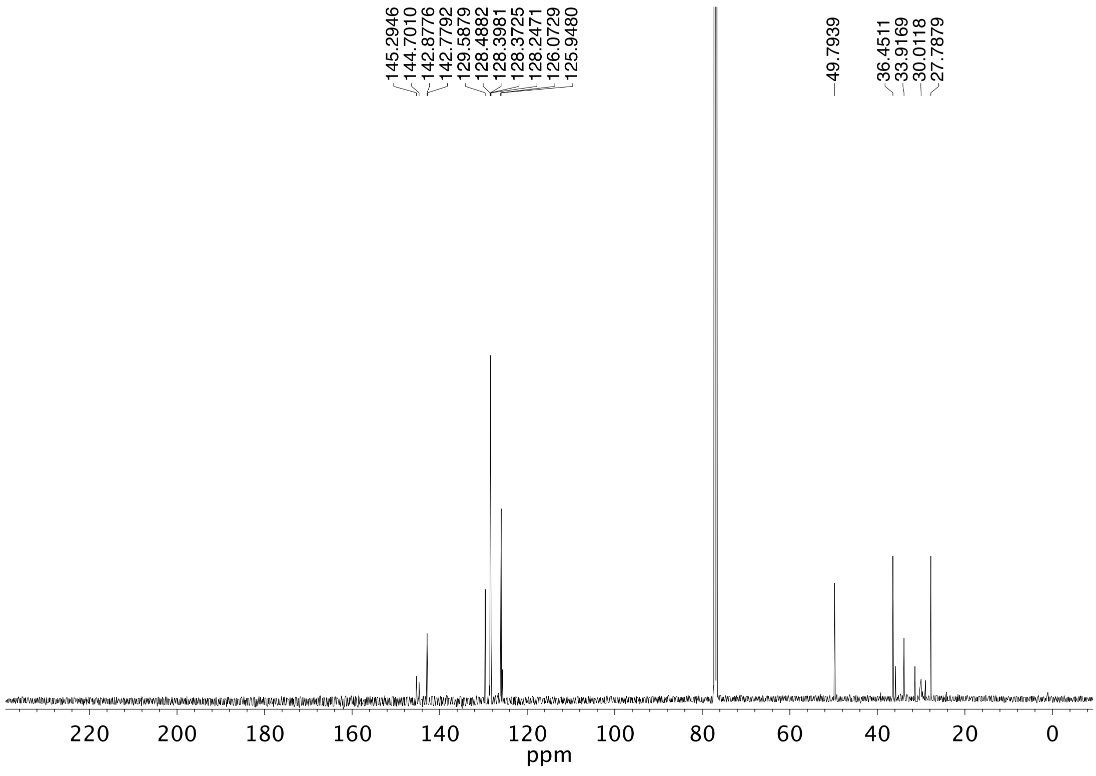

Figure 5.27 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.21**.

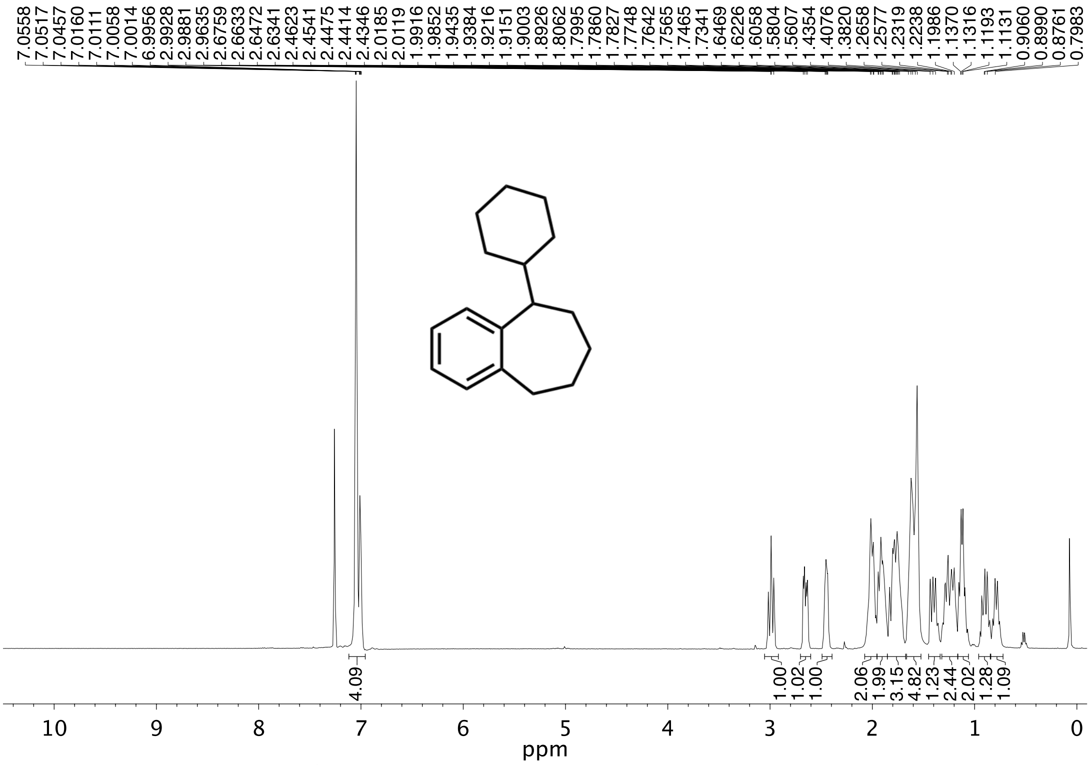

Figure 5.28 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.27a**.

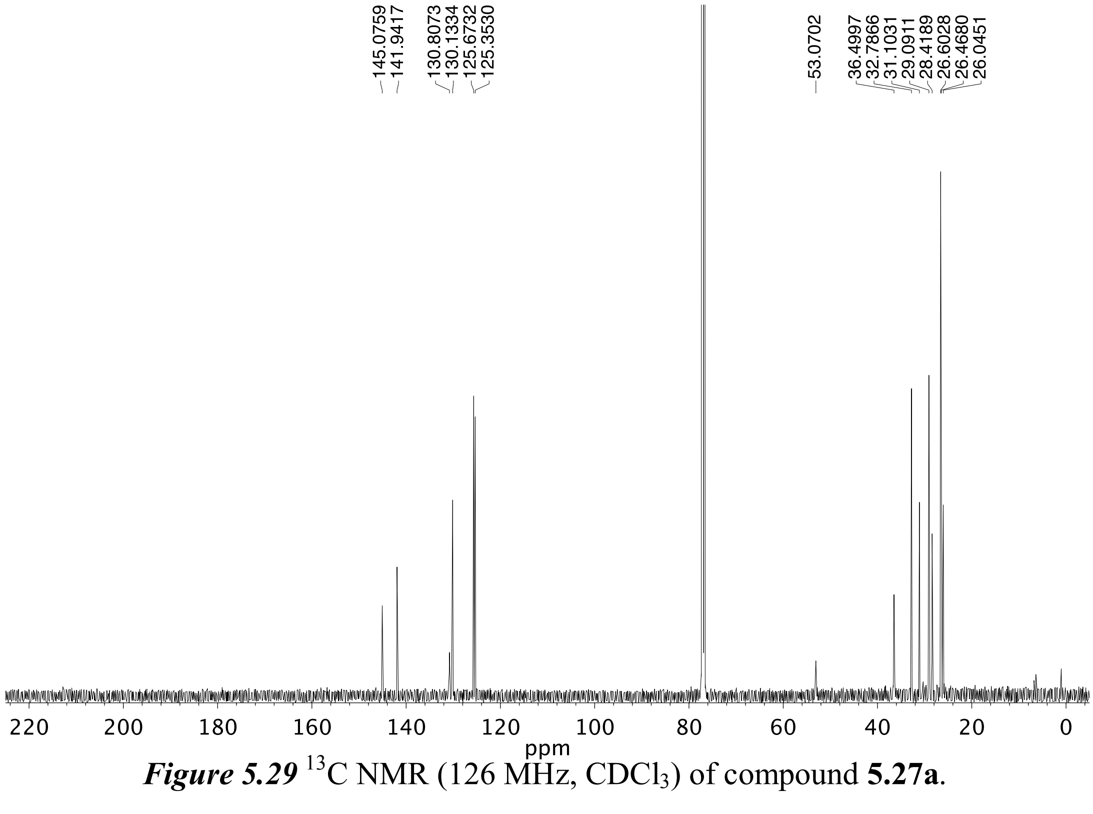

Figure 5.29 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.27a**.

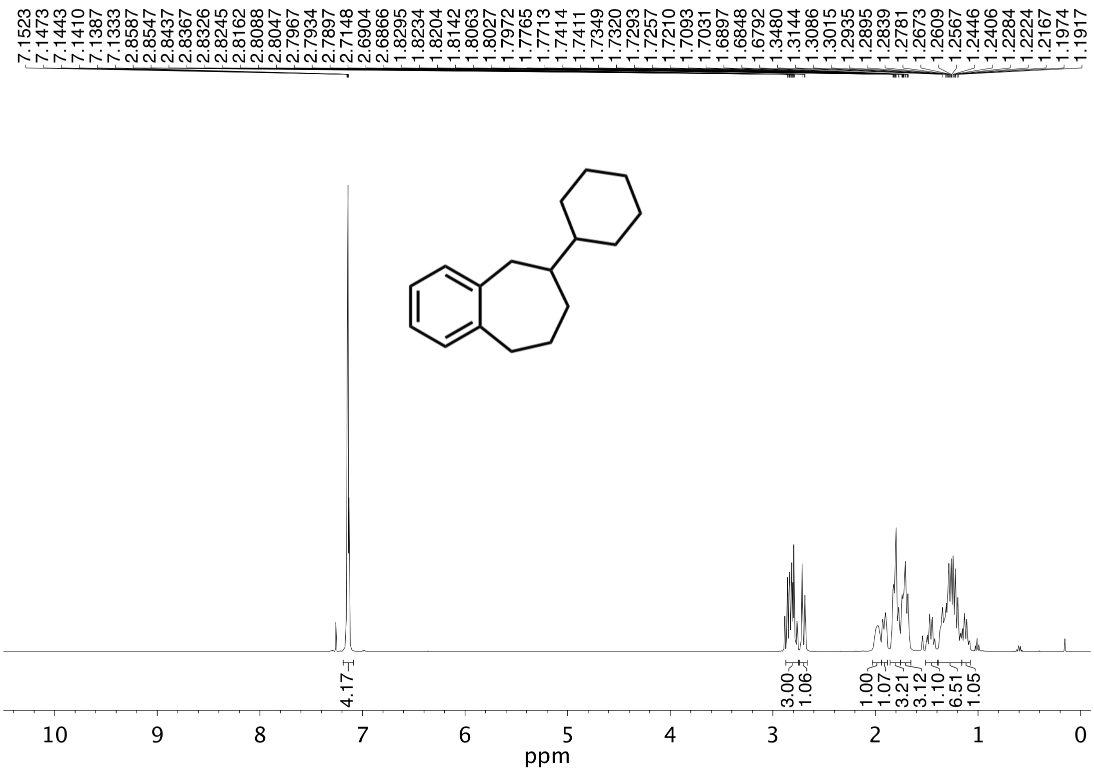

Figure 5.30 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.27b**.

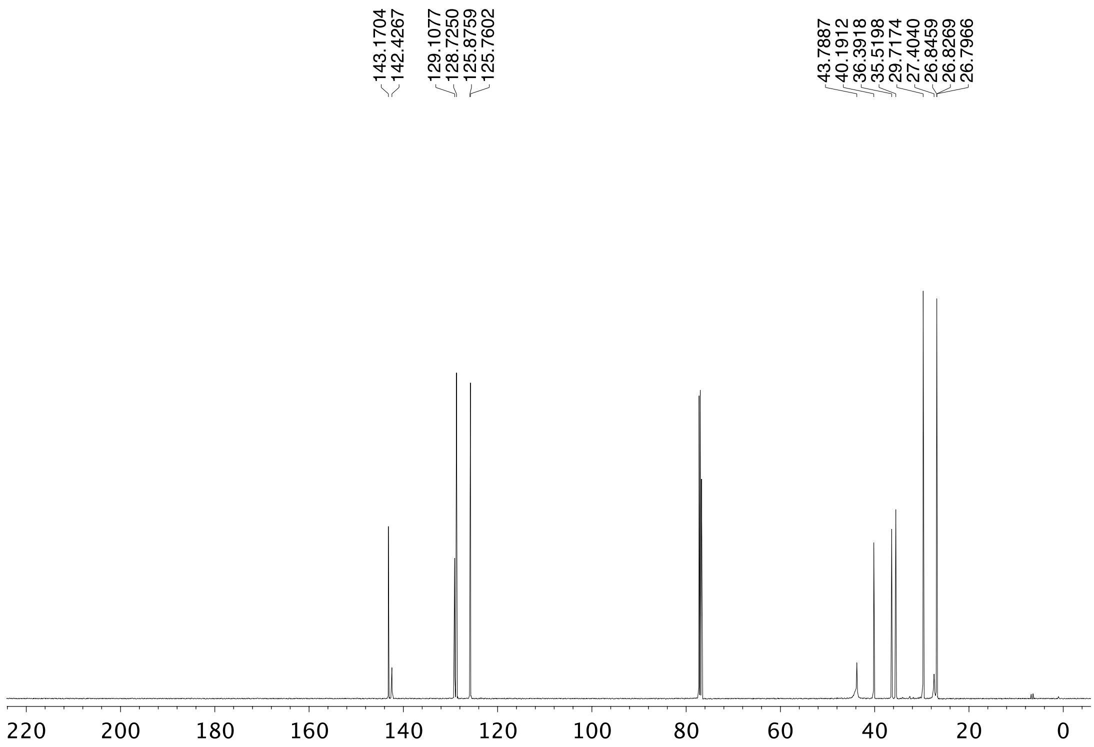

Figure 5.31 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.27b**.

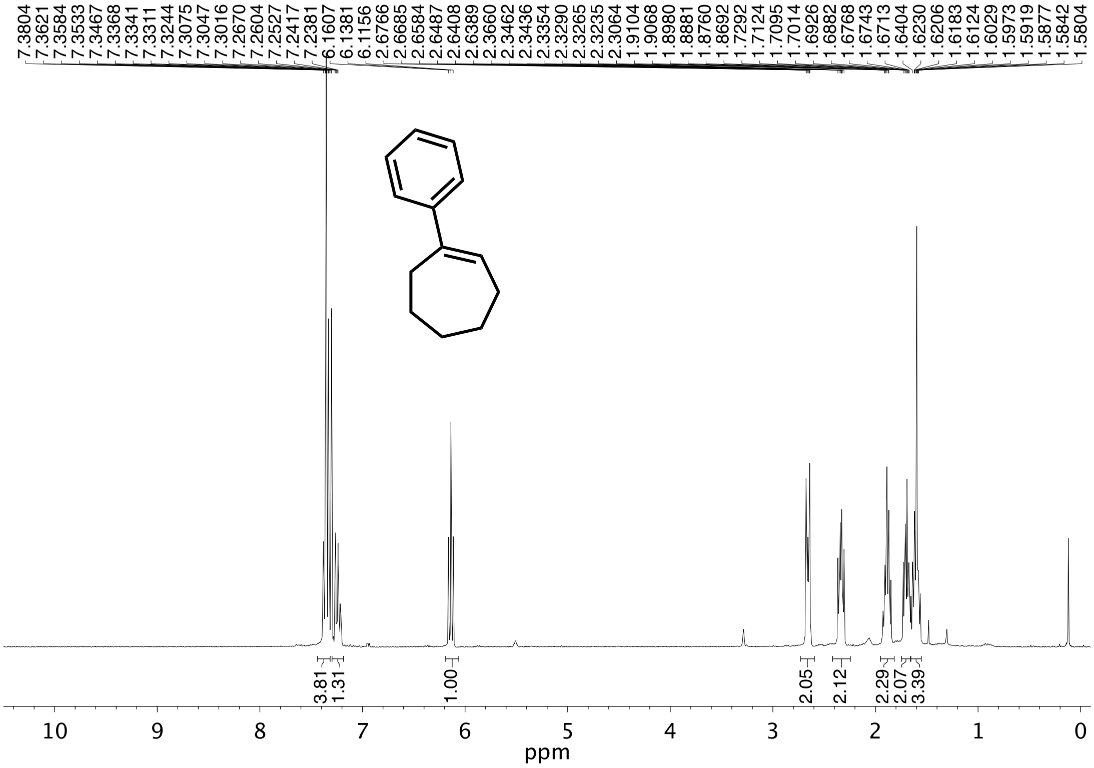

Figure 5.32 ^{1}H NMR (300 MHz, CDCl$_3$) of compound **5.33**.

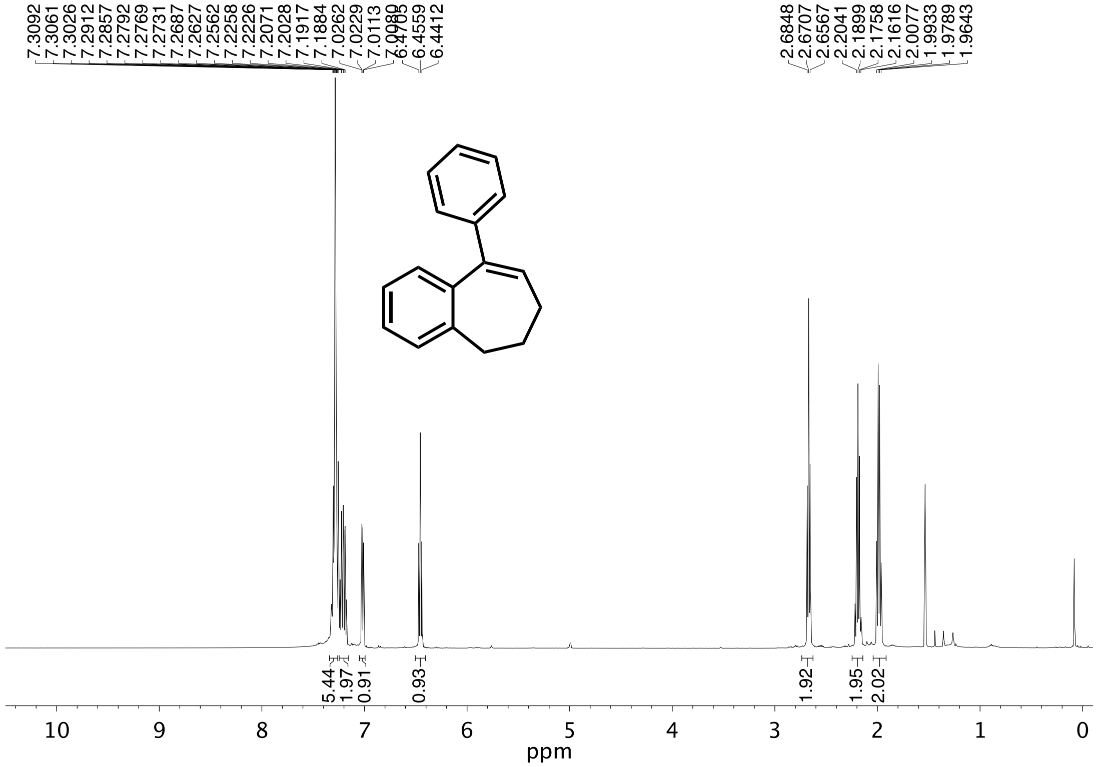

Figure 5.33 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.34**.

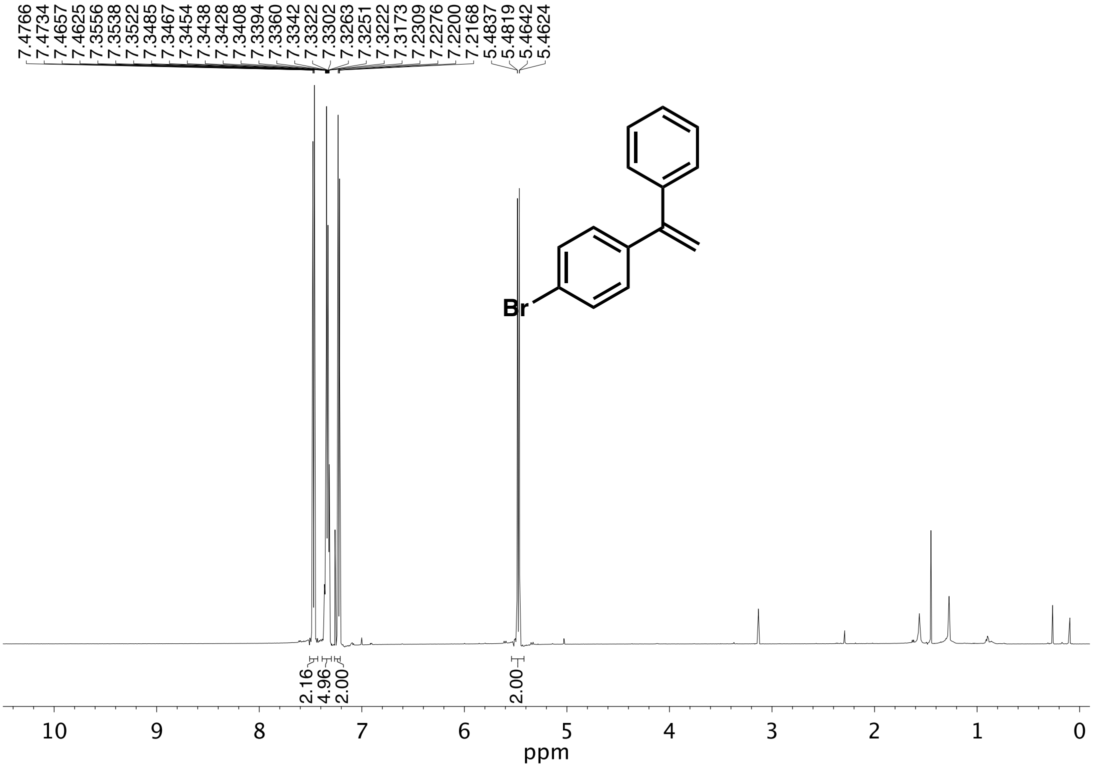

Figure 5.34 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **5.35**.

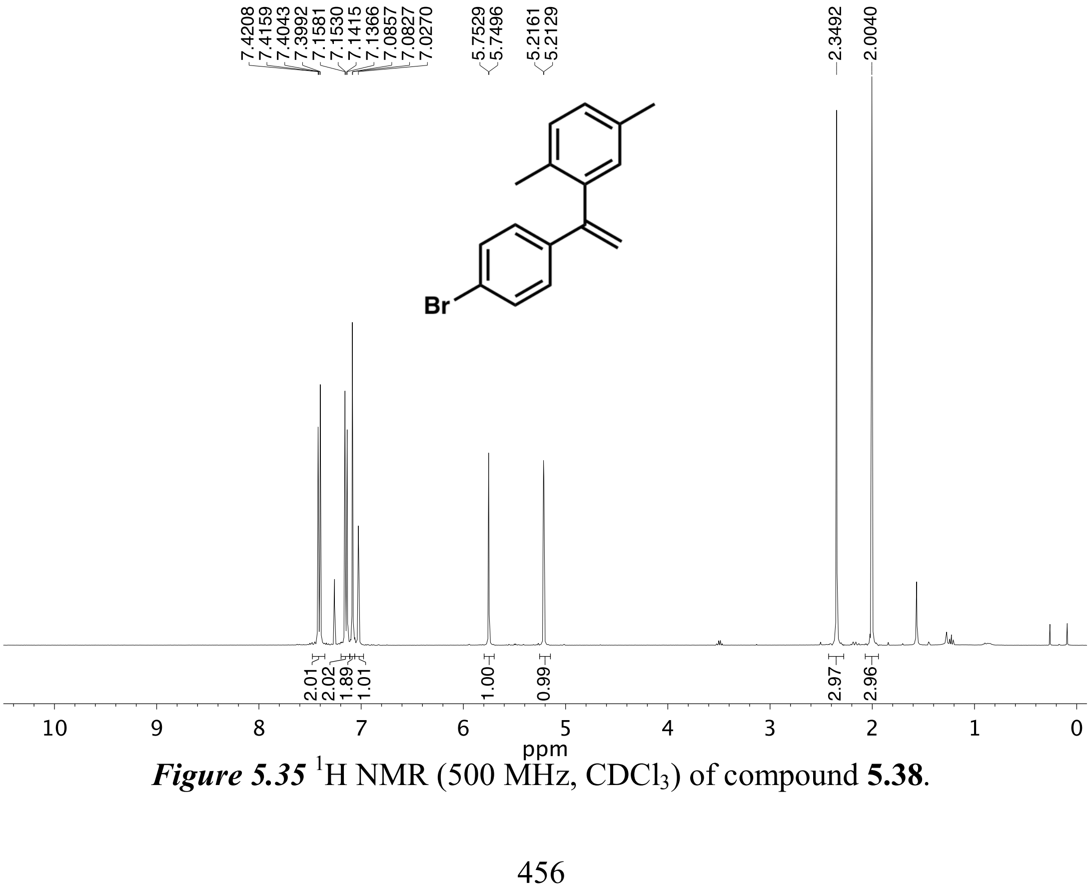

Figure 5.35 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5.38**.

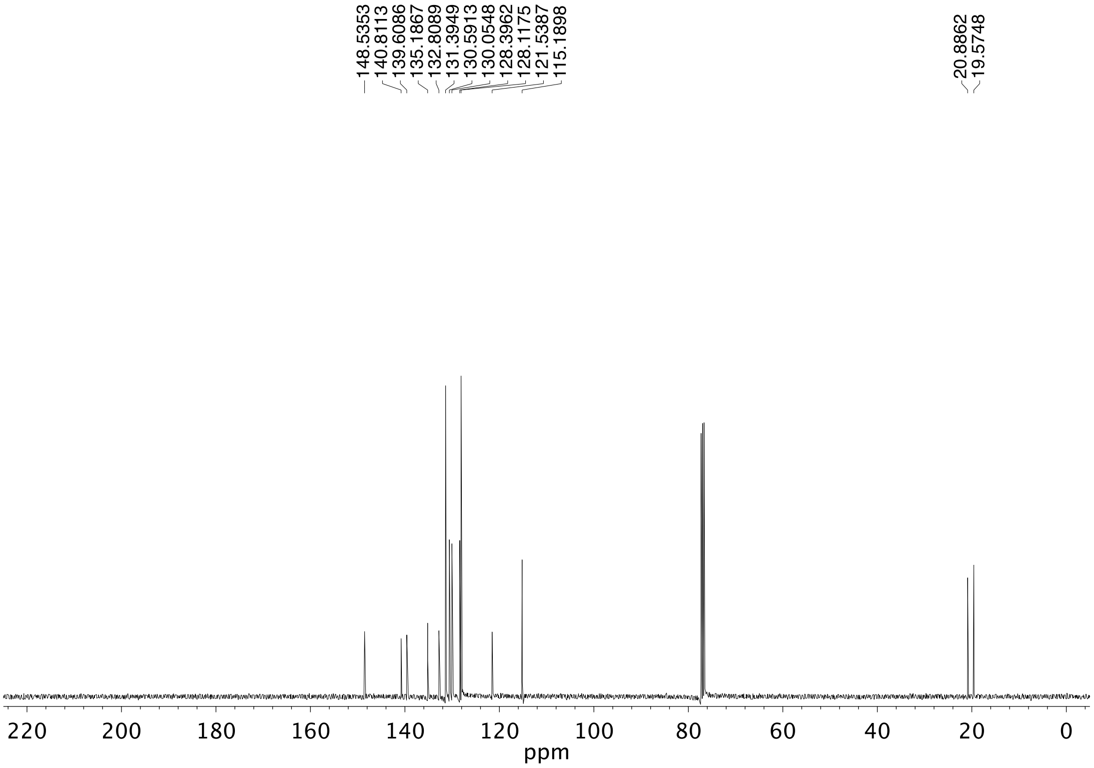

Figure 5.36 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **5.38**.

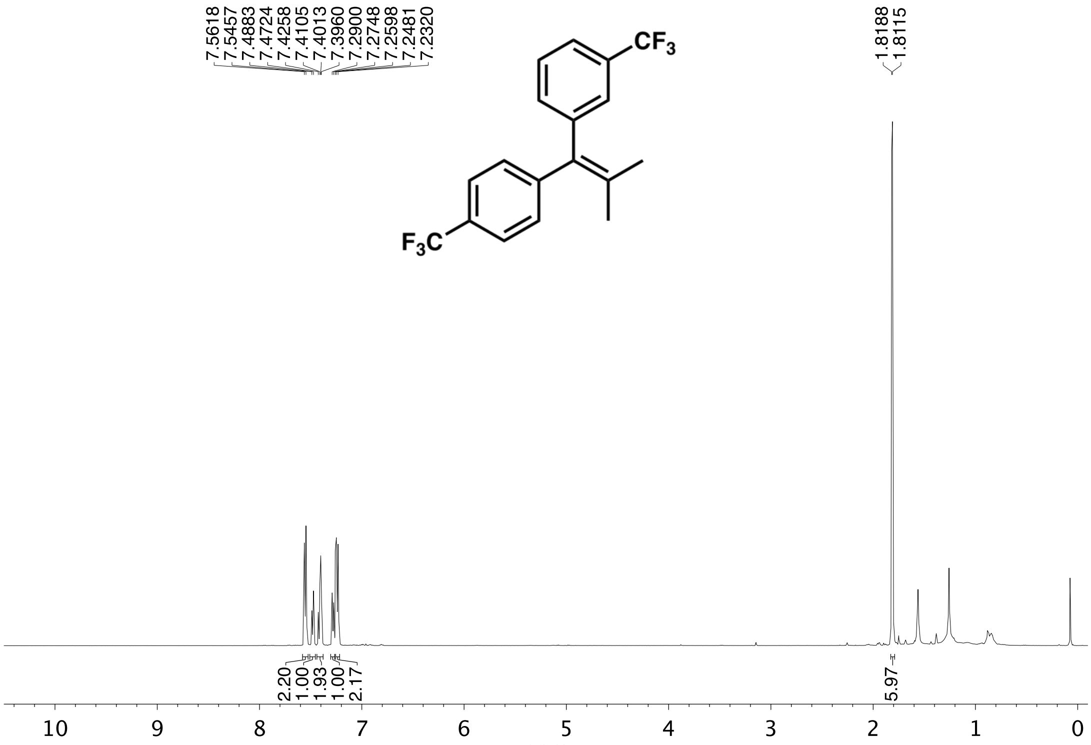

Figure 5.37 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5.42**.

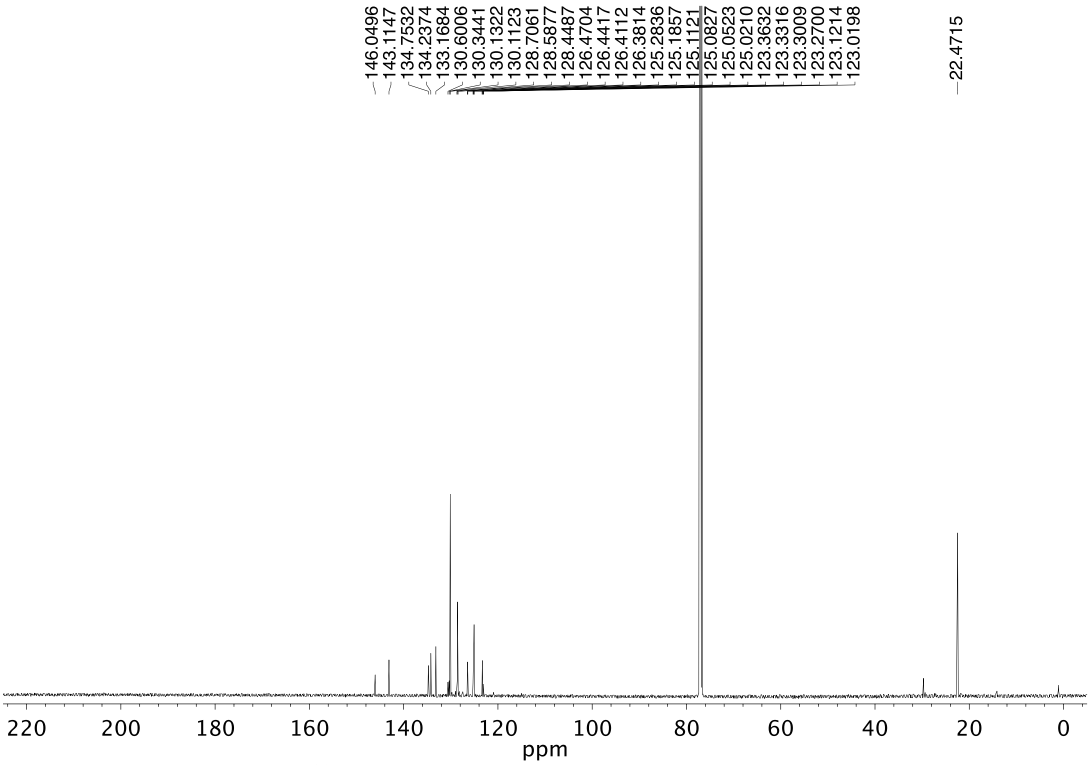

Figure 5.38^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.42**.

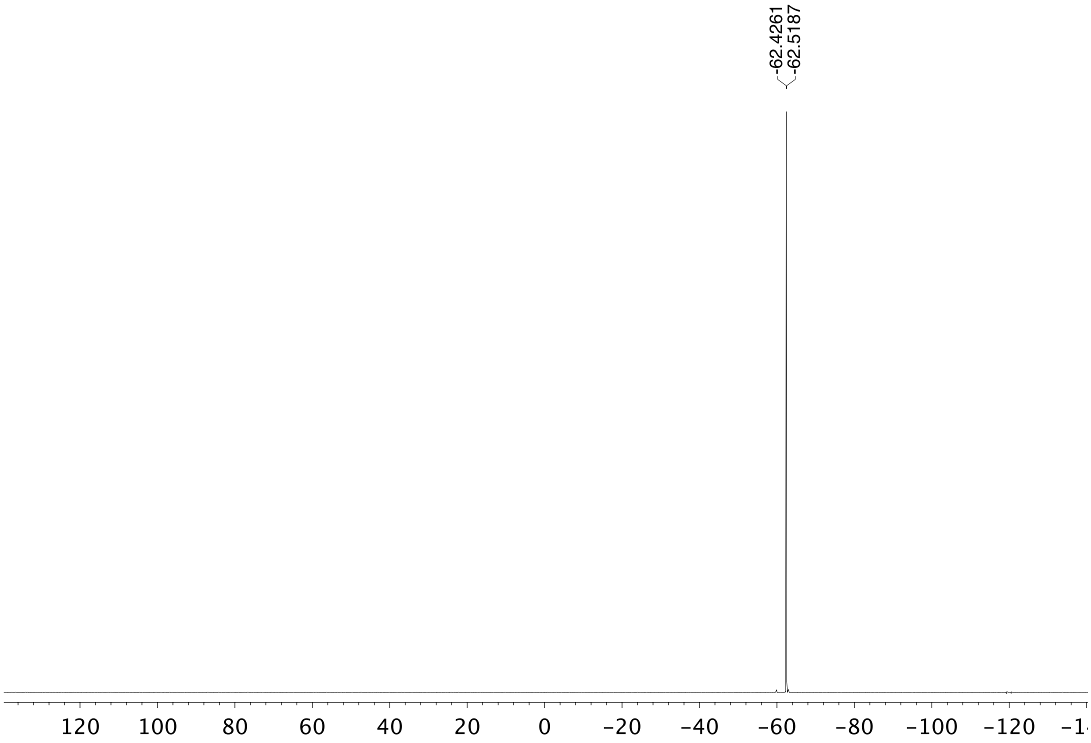

Figure 5.39^{19}F NMR (282 MHz, CDCl$_3$) of compound **5.42**.

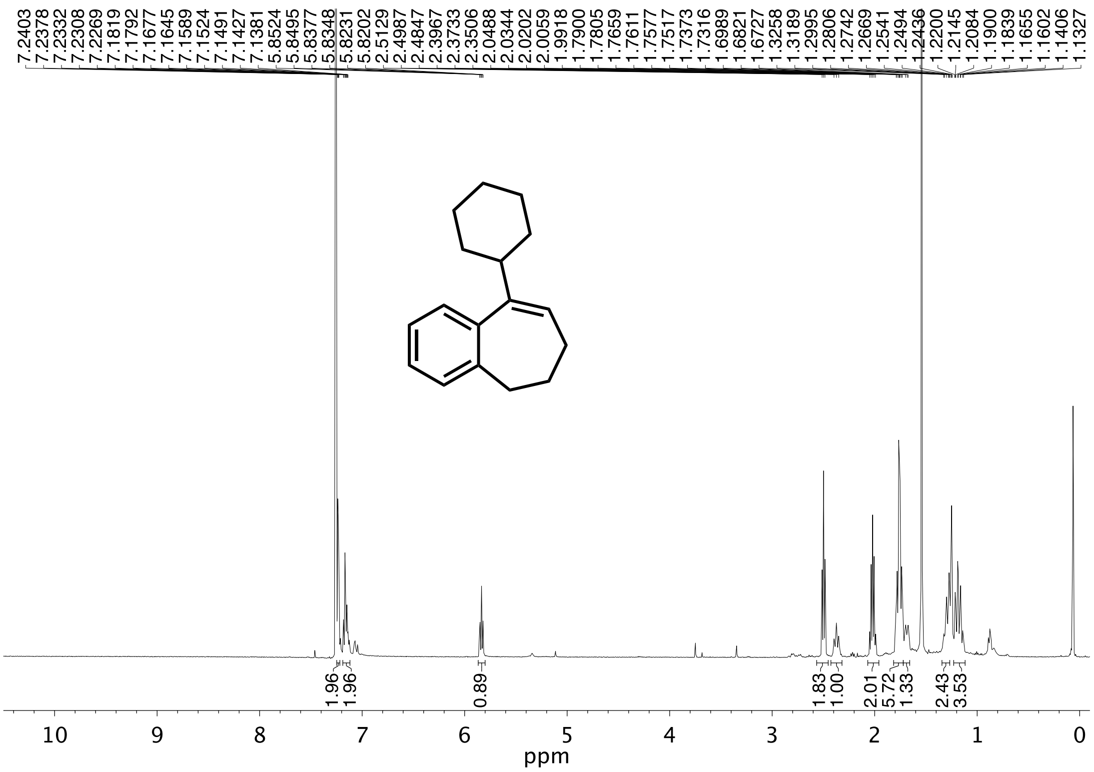

Figure 5.40 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5.45**.

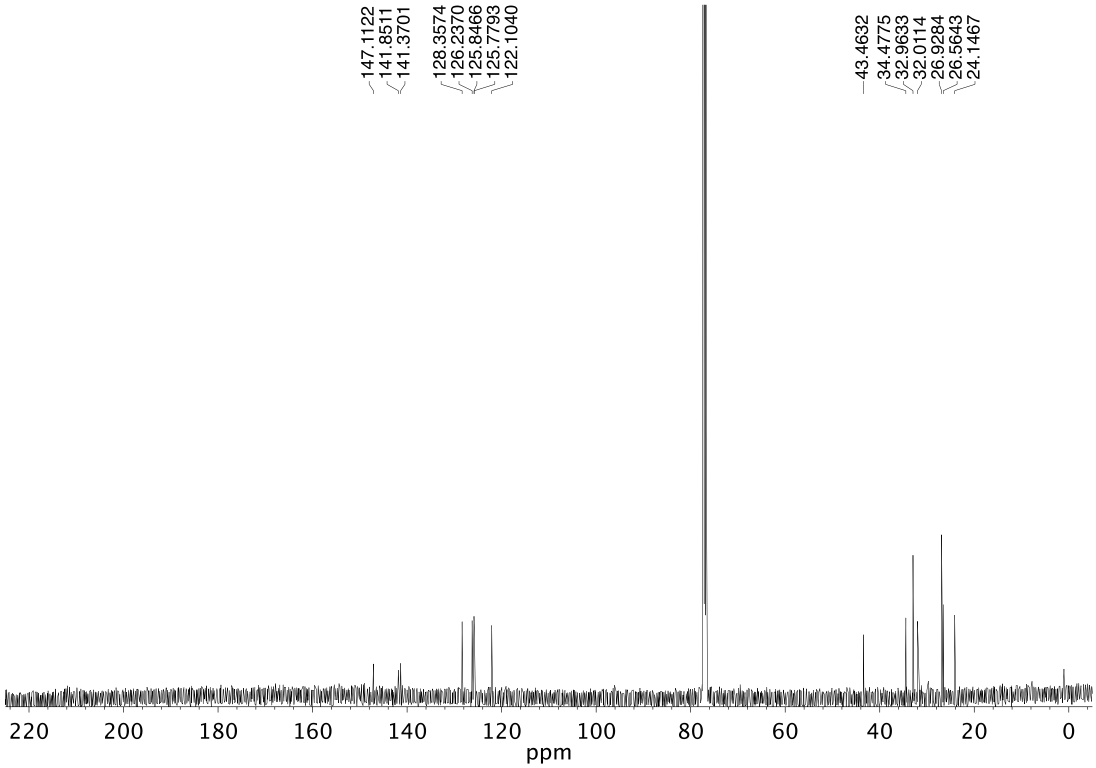

Figure 5.41 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **5.45**.

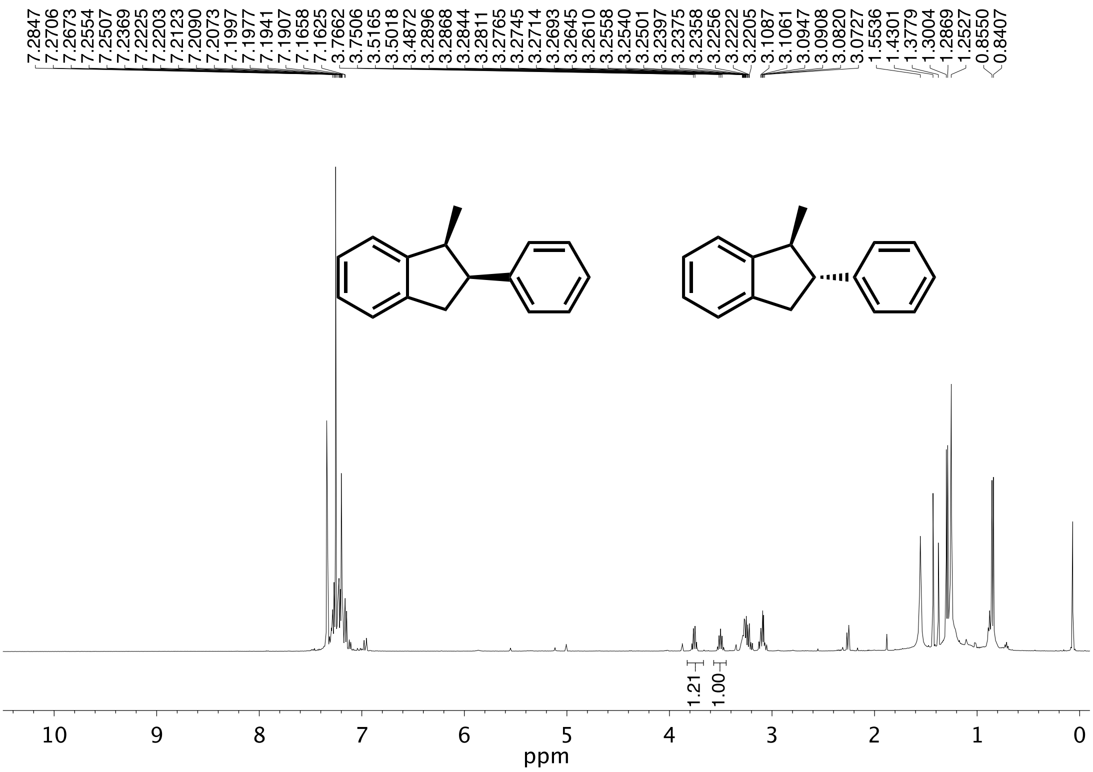

Figure 5.42 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.49**.

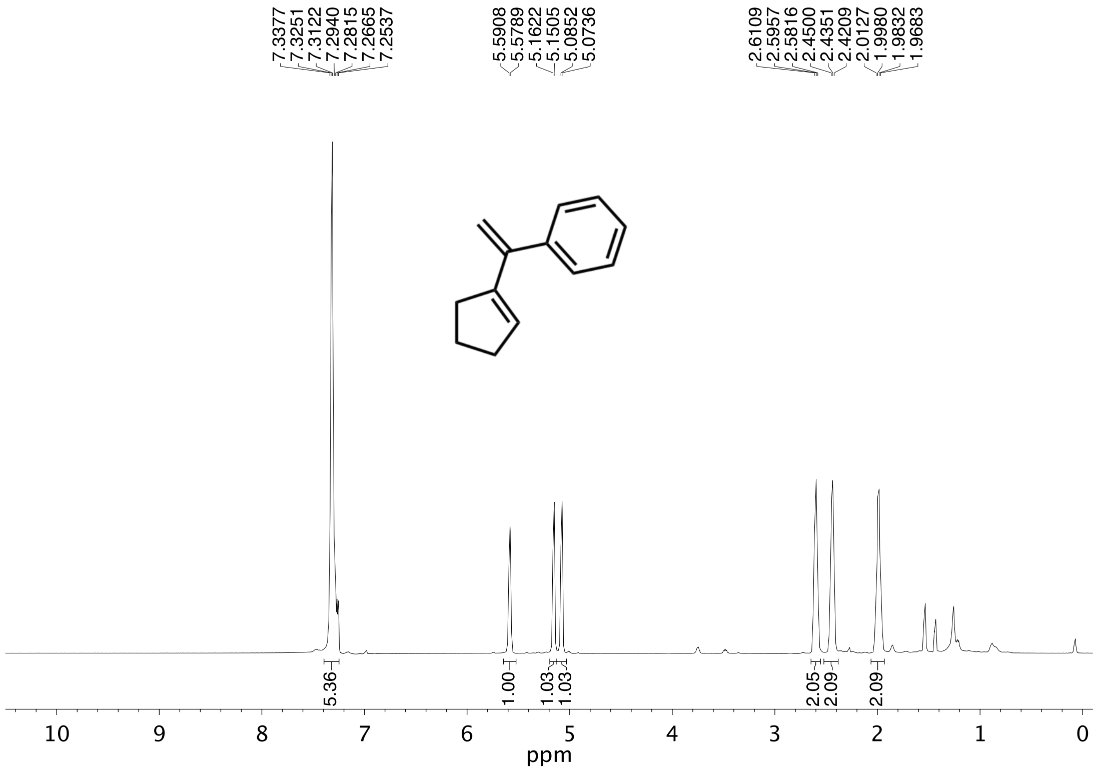

Figure 5.43 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.52**.

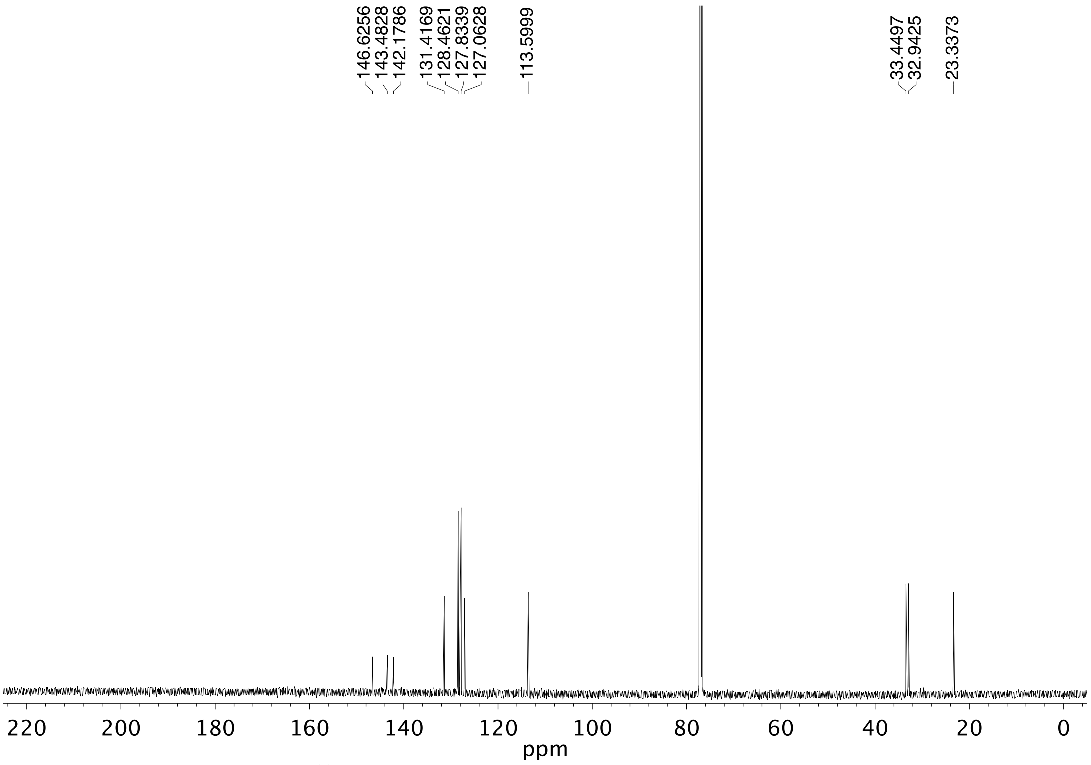

Figure 5.44 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.52**.

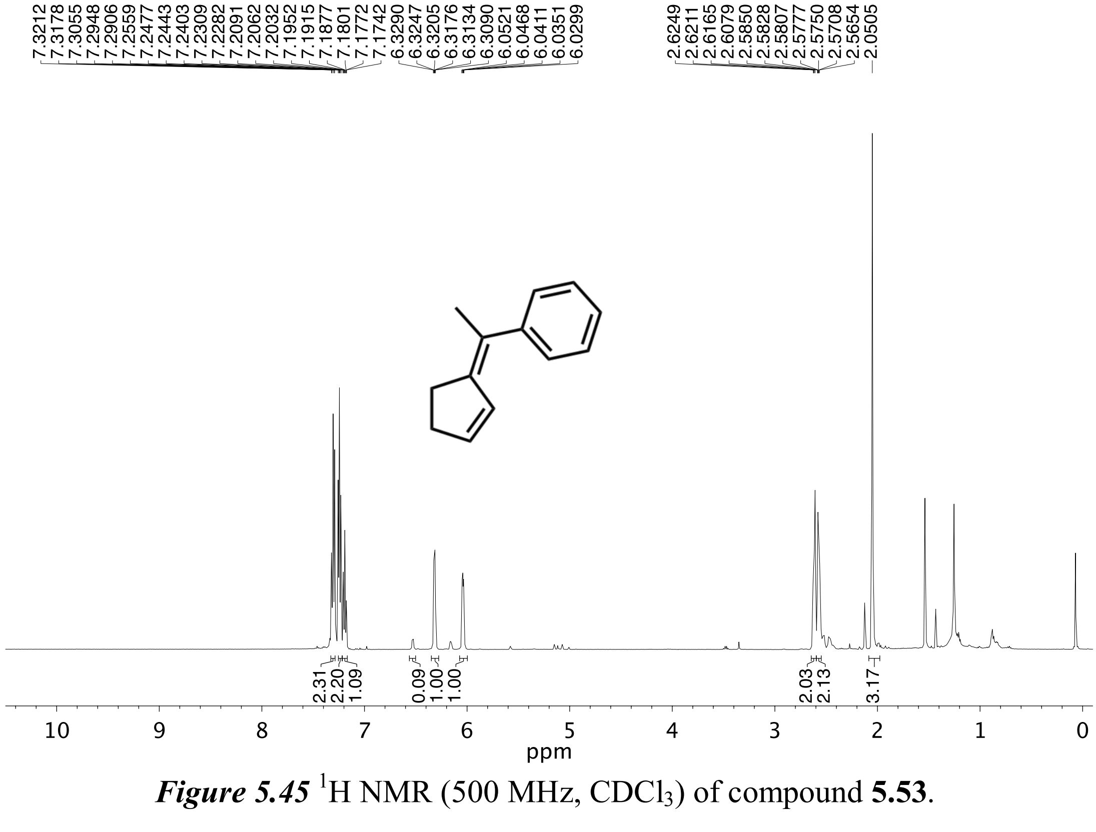

Figure 5.45 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.53**.

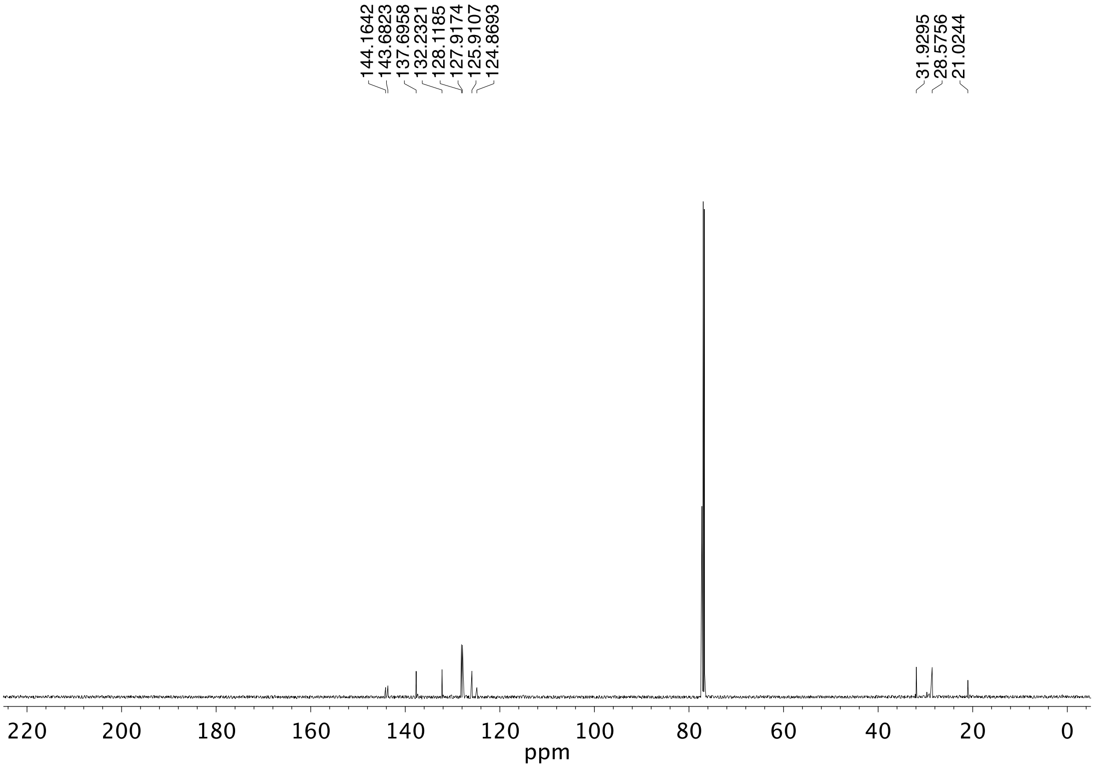

Figure 5.46 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **5.53**.

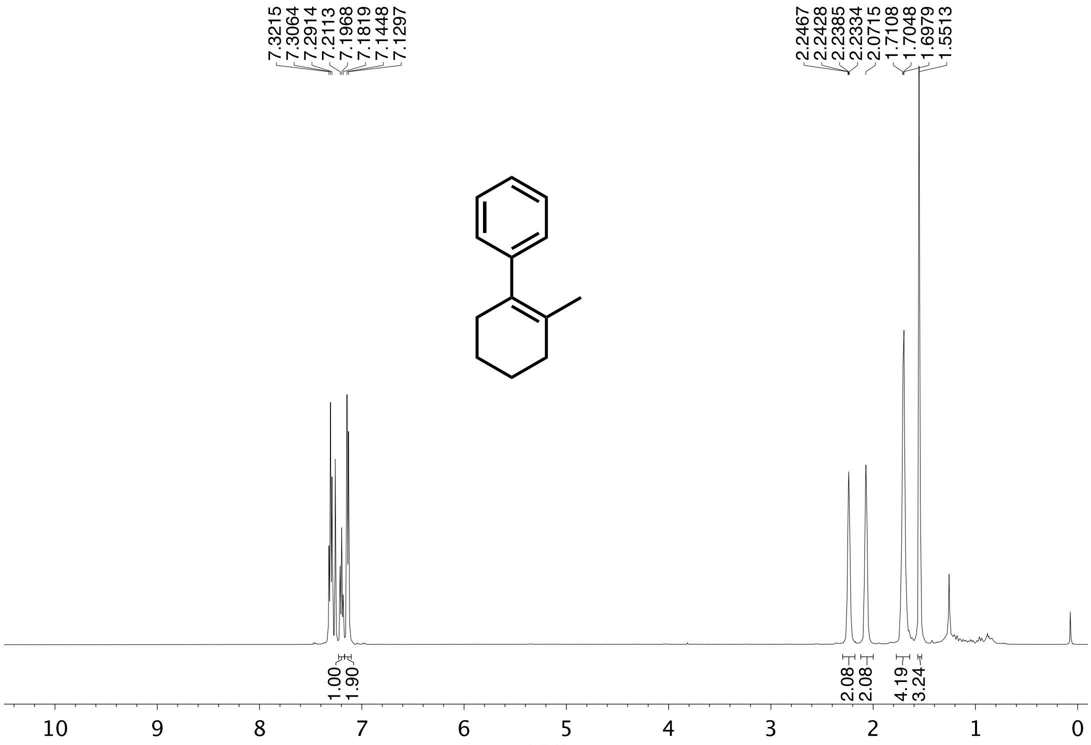

Figure 5.47 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5.55**.

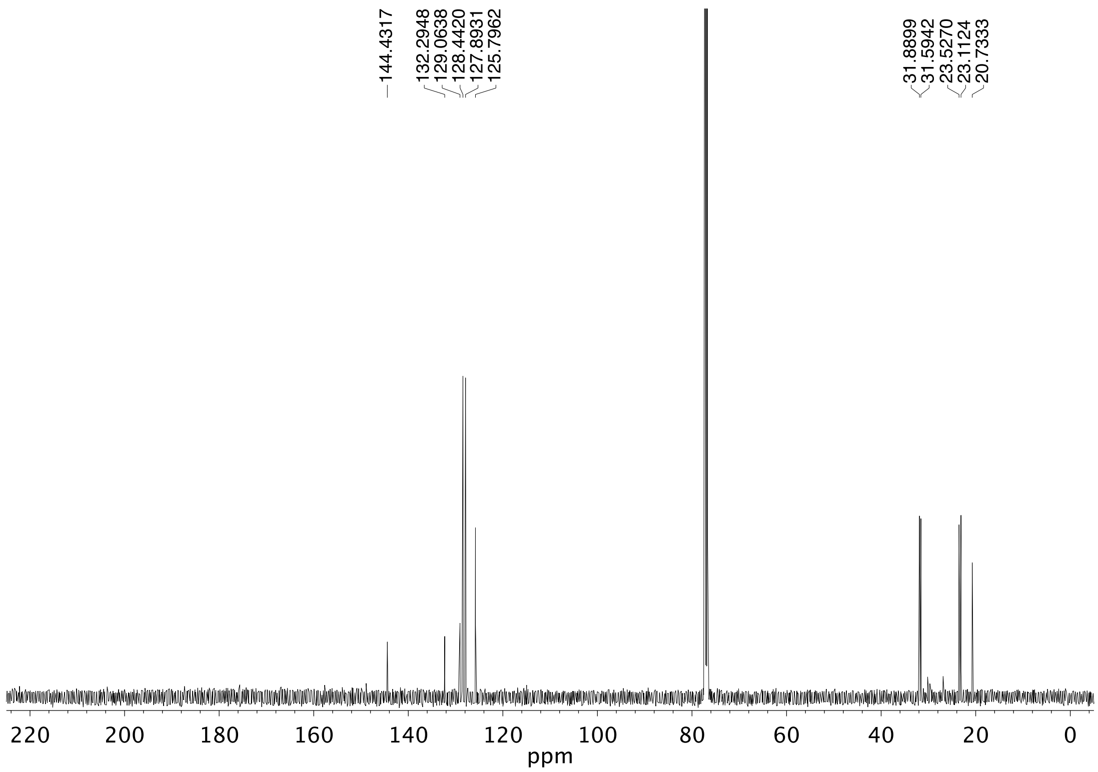

Figure 5.48 ^{13}C NMR (126 MHz, $CDCl_3$) of compound **5.55**.

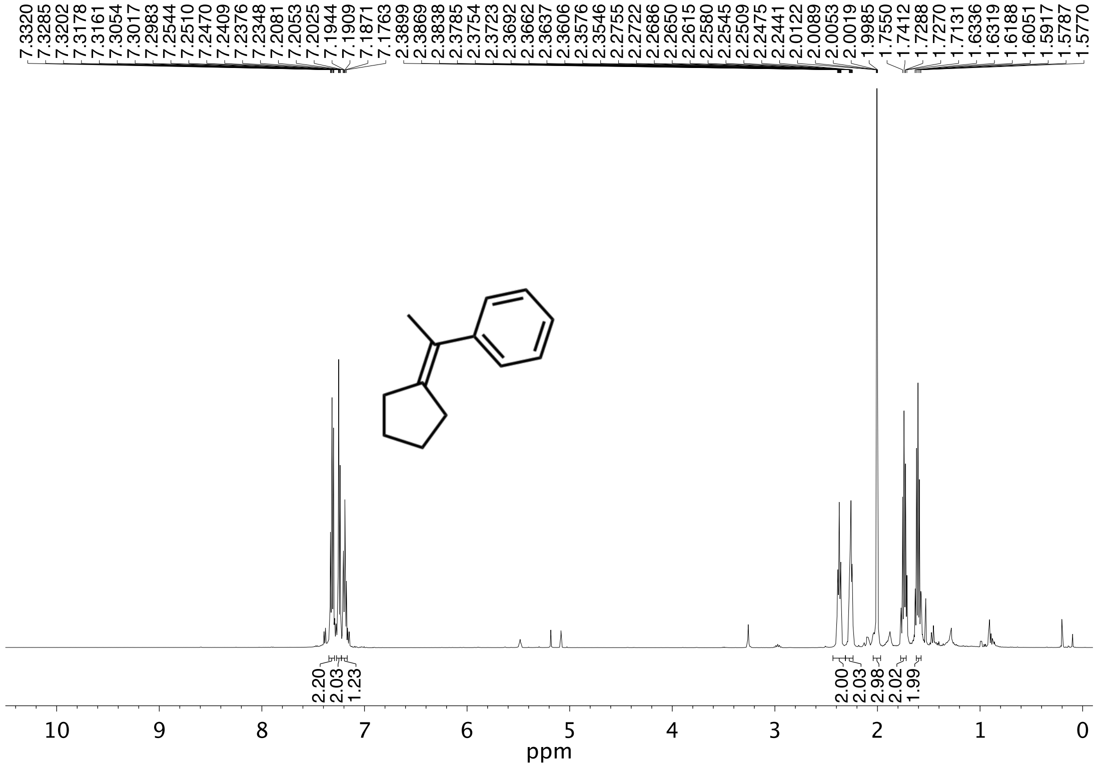

Figure 5.49 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5.56**.

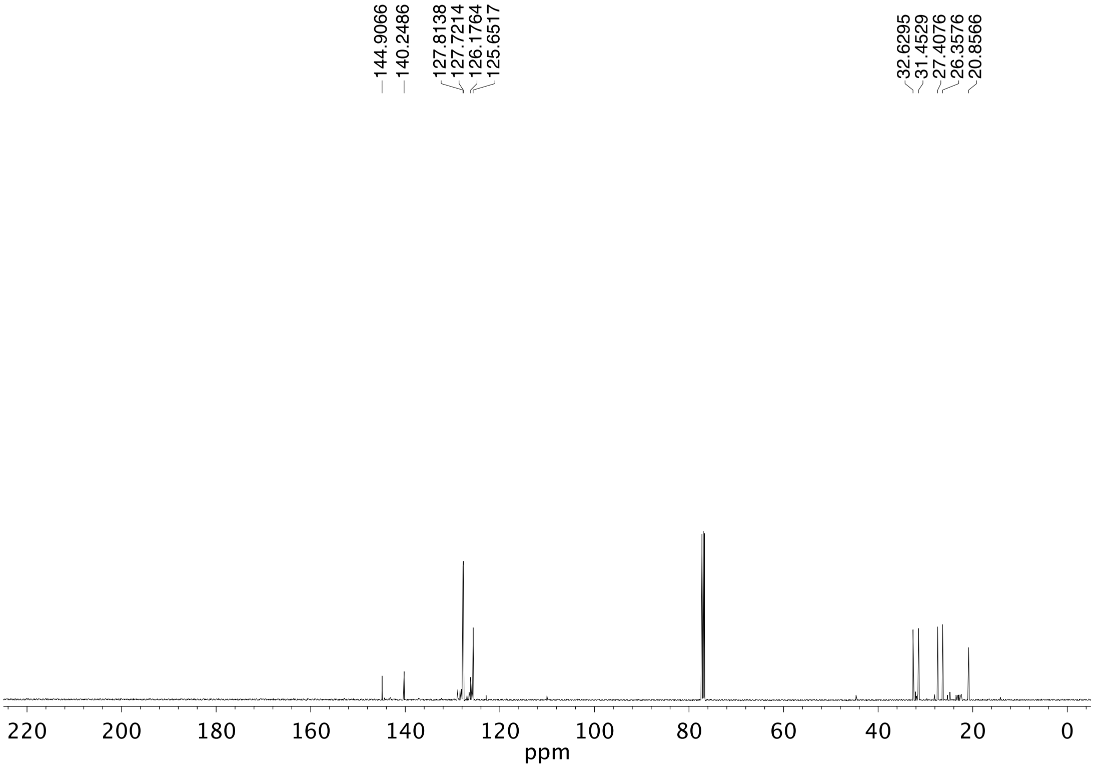

Figure 5.50 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.56**.

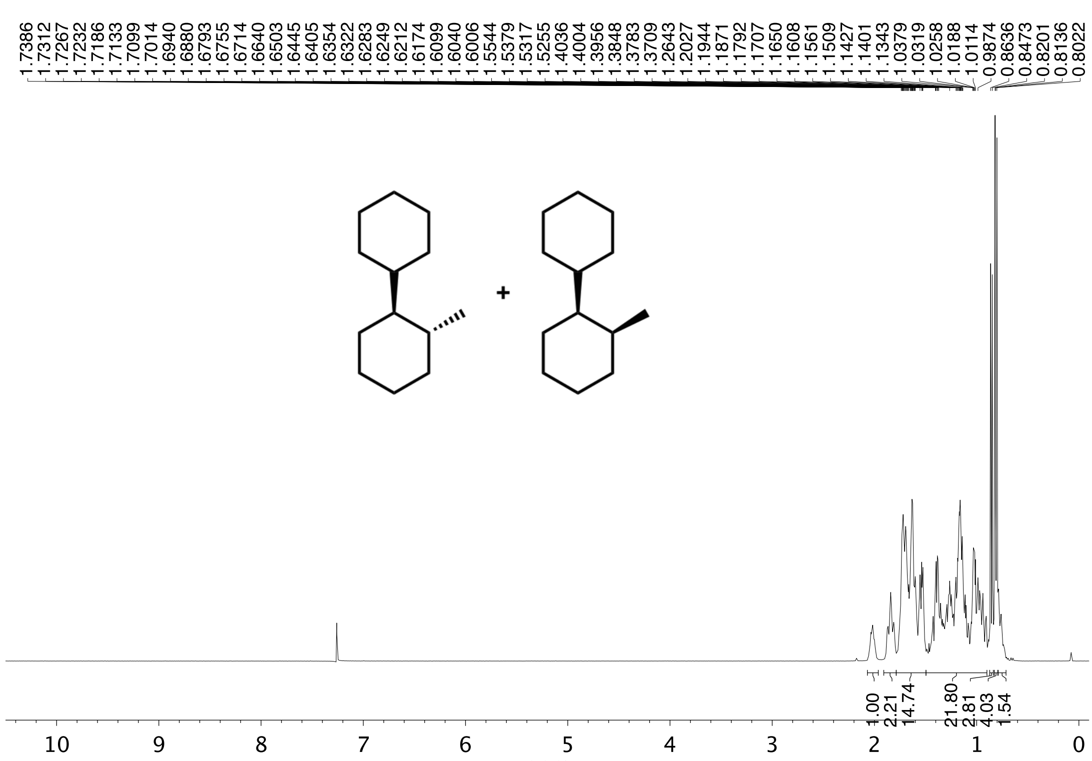

Figure 5.51 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.58**.

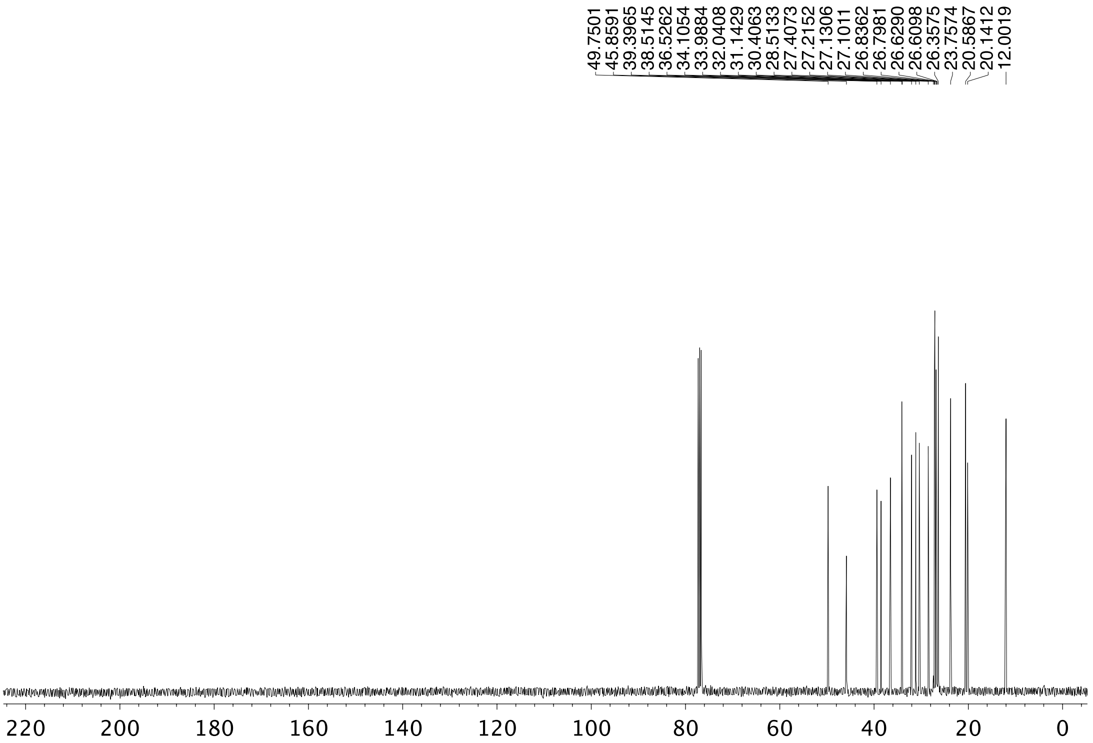

Figure 5.52 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.58**.

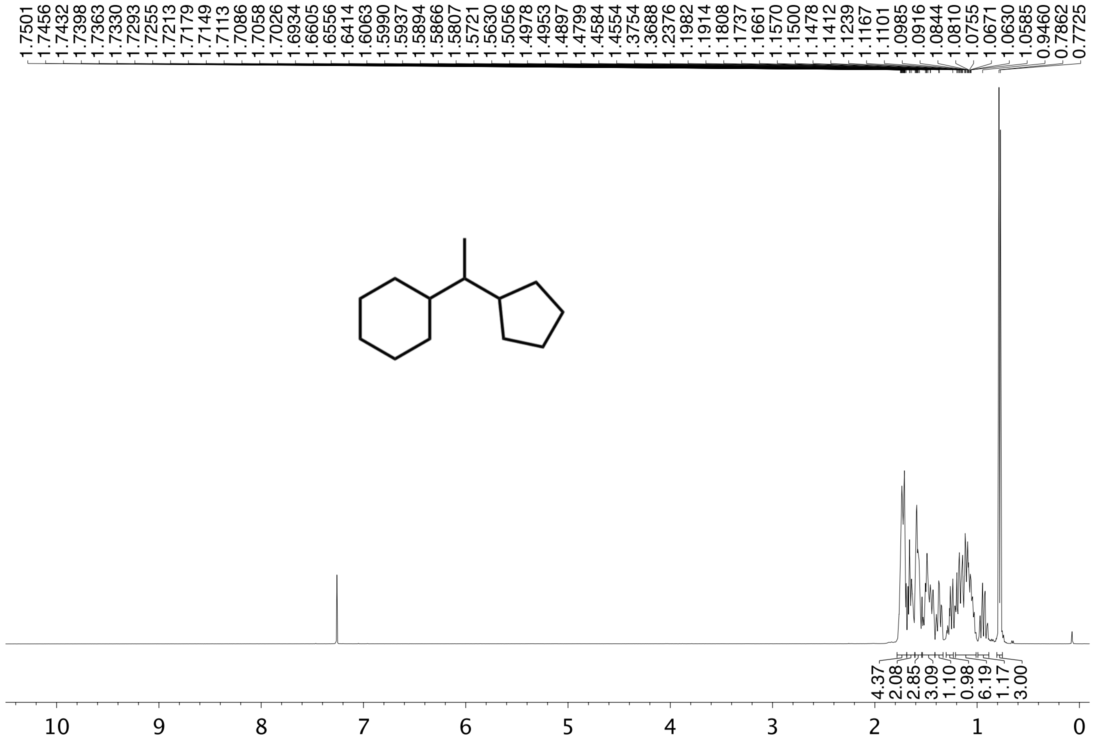

Figure 5.53 ^{1}H NMR (500 MHz, CDCl$_3$) of compound **5.59**.

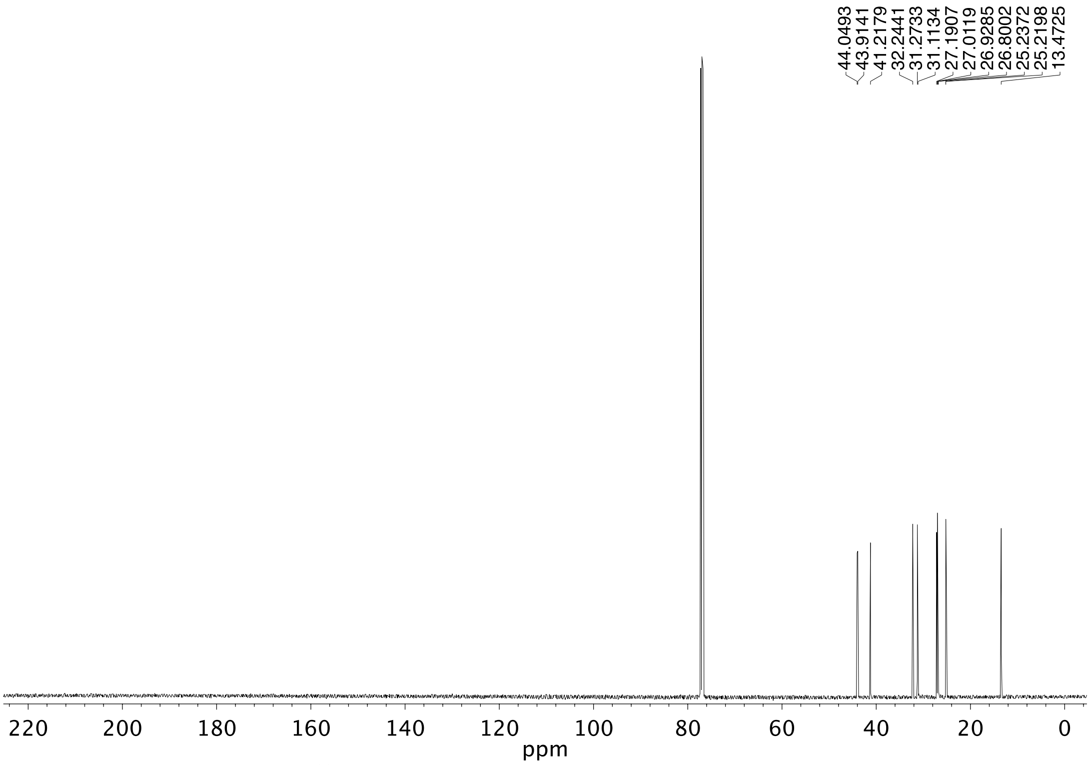

Figure 5.54 ^{13}C NMR (126 MHz, CDCl$_3$) of compound **5.59**.

5.13 Notes and References

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