HYDROFUNCTIONALIZATION THROUGH ELECTROPHILIC ALKENE ACTIVATION USING CARBODICARBENE LIGANDS

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A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Chemistry

Chapel Hill
2016

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ABSTRACT

Matthew Jacob Goldfogel: Hydrofunctionalization through Electrophilic Alkene Activation Using Carbodicarbene Ligands
(Under the direction of Simon J. Meek)

Alkenes and related π-systems serve as versatile and readily available feedstocks for the synthesis of a plethora of natural products and fine chemicals. The benefits of using these ubiquitous structures has fueled industrial research into alkene functionalization and related catalysis. Industrially relevant examples include the Tsuji-Wacker oxidation, the Mizoroki-Heck reaction, and asymmetric epoxidation. Successive improvements to alkene functionalization have been accomplished through iterative design of new ligands that form increasingly active metal complexes. These organometallic complexes are particularly effective at binding alkenes in order to activate stable π-systems. One mode of activation is to bind the alkene to an electron poor metal, which withdraws electron density from the alkene, making it susceptible to attack from an external nucleophile. Known as electrophilic activation, this mechanism can be generalized for a variety of nucleophiles that allow for C-C (hydroalkylation), C-N (hydroamination), and C-O (hydroetherification) bond formation. The mechanism begins with the binding of an alkene to the electrophilic metal center. The properties of the metal center are tuned by the ligand framework, which can be used to control the reactivity of the bound alkene. Alkene binding is followed by external addition of the nucleophile to generate a metal-alkyl intermediate. The metal-alkyl bond is then protonated to form a C-H σ-bond and the product. Dissociation of the product regenerates the electrophilic metal center and closes the catalytic cycle.

The following studies will relate efforts to design organometallic catalysts for electrophilic alkene activation with the goal of promoting hydrofunctionalization reactions. Hydrofunctionalization is formally defined as a class of alkene reactions where the π-bond of the alkene is transformed into two new σ-bonds including a carbon-hydrogen bond. Such transformations have received considerable attention for their utility in forming desirable bonds with complete atom economy. The following chapters will document research into electrophilic hydrofunctionalization catalyzed by a series of new cationic metal complexes employing carbodicarbene ligands. Carbodicarbenes were not previously known as catalytically active ligands, but their unique reactivity has proved beneficial for stabilizing cationic Rh complexes.

To my family, Nancy, Gary and Aaron, for supporting me through everything I've ever accomplished and always helping me along the way. I wouldn't be who I am without your love and support.

To Michelle for sharing me with chemistry these long years and being there whenever I could escape it. You are the love of my life and source of my remaining sanity.

To my mentor Simon for teaching me everything and challenging me constantly.

To my labmates for being there every step of the way. You are all the very best kind of crazy.

ACKNOWLEDGEMENTS

A PhD may be awarded to a person, but it is truly a team effort. Assistance from the amazing people around me has contributed to every part of my graduate experience. I would like to thank you all for making this possible. I would specifically like to acknowledge my mentor and boss, Simon Meek, for teaching me most everything I know about the chemical world. You built my understanding of organic and inorganic synthesis up from nothing and I have enjoyed our debates along the way. I also wish to thank my co-conspirators Courtney Roberts and Matthew Joannou as well as my younger labmates Stephanie and Jake for building this lab from the ground up. We've been through a lot together and I couldn't ask for a better crew to share a lab with.

Not all of my time in graduate school was spent in the lab and it truly takes a community of amazing friends to celebrate successes and stick to it through the rough patches. So many of you have been instrumental in making my PhD what it is and I hope you all know how much I appreciate your friendship. I could write chapters on how each of you have helped me smile and cope. Thank you for all the game nights and late nights, the lunches and chats, for all the times you've fed me and told me to be calm and relax. You will be what I miss most of all as I move on from graduate school.

I also want to acknowledge the wonderful parents, Nancy and Gary, who've guided me every step of my life. I may have moved far away, but I always felt your support and love was close by. Thank you also to my little brother Aaron for always being excited to see me and only

gloating a little about being smarter and taller than his elder brother. Don't worry, I'll stop calling you Munchkin eventually. I also want to acknowledge my grandparents Fuzzy, Janners, Myke, John, Bob, and Wanda for making many bus rides better with a phone call and kind word whenever I most needed. I may not see as much of you as I like, but I feel incredibly close to you all.

And lastly, I want to acknowledge the person who I'm excited to spend the rest of my life with, Michelle. Thank you for always sharing me with chemistry and for putting up with the longest of long distance relationships. I love you deeply and wouldn't be sane without you. You know me better than anyone and I wouldn't have it any other way.

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LIST OF ABBREVIATIONS AND SYMBOLS

(0)	oxidation state of zero
(IV)	oxidation state of four
$[Rh(cod)Cl]_2$	chloro(1,5-cyclooctadiene)rhodium(I) dimer
$[Rh(ethylene)_2Cl]_2$	di-μ-chlorotetraethylene dirhodium(I)
°C	degrees Celsius
Å	angstrom
Ag	silver
Au	gold
BF_4	tetrafluoroborate
BINOL	1,1'-bi-2-naphthol
Bn	benzyl
Boc	tert-butoxycarbonyl
Br	bromine
Bz	benzoyl
C	carbon
Cal	calorie
CBA	cyclic bent allene
CDC	carbodicarbene
Cl	chlorine
ClO_4	perchlorate
cm	centimeter
CO	carbonyl

Cu	copper
d	doublet
DBI	Division of Biological Infrastructure
DCM	dichloromethane
dd	double of doublets
DFT	density functional theory
DIPEA	diisopropylethylamine
DMF	dimethylformamide
dr	diastereoselectivity
dt	doublet of triplets
ee	enantiomeric excess
eg	for example
ES	electrospray ionization
Et	ethyl
Et_2O	diethyl ether
EtOAc	ethyl acetate
F	fluorine
Fe	iron
GC	gas chromatography
H	hydrogen
H_2O	water
Hex	hexanes
HMDS	hexamethyldisilazide

HOMO	highest occupied molecular orbital
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
I	iodine
ie	in other words
iPrOH	isopropanol
IR	infrared
K	potassium
La	lanthanide
Li	lithium
LRMS	low resolution mass spectrometry
LUMO	lowest unoccupied molecular orbital
m	multiplet
m-	meta
Me	methyl
MeCN	acetonitrile
MeOH	methanol
MHz	megahertz
mmol	millimoles
MS	mass spectrometry
N	nitrogen
Na	sodium

$NaBAr^F_4$	tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
NH_4	ammonium
NHC	N-heterocyclic carbene
Ni	nickel
NMR	nuclear magnetic resonance
O	oxygen
o-	ortho
OAc	acetate
OMe	methoxy
OTf	triflate
P	phosphorus
p-	para
Pd	paladium
PF_6	hexafluorophosphate
Ph	phenyl
PhCl	chlorobenzene
PhH	benzene
PhMe	toluene
Pr	propyl
Pt	platinum
Q-ToF	quadrupole time of flight
Rh	rhodium
Ru	ruthenium

s	singlet
SI	supplementary information
t	triplet
TADDOL	α,α,α',α'-tetraaryl-2,2-disubstituted 1,3-dioxolane-4,5-dimethanol
TBDPS	tertbutyldiphenylsilyl
TBS	tertbutyldimethylsilyl
tBuOH	tert-butanol
THF	tetrahydrofuran
TIPS	triisopropylsilyl
Ti	titanium
TLC	thin layer chromatography
TMP	tetramethylpiperidine
TMS	trimethylsilyl
vida infra	see below
vide supra	see above
XRD	X-ray defractometer
Zn	zinc
Zr	zirconium
α	alpha
β	beta
γ	gamma
δ	delta
μ	micro

ν	frequency
π	pi
σ	sigma

CHAPTER 1: CATALYTIC HYDROAMINATION WITH CARBODICARBENE LIGATED METAL COMPLEXES[1]

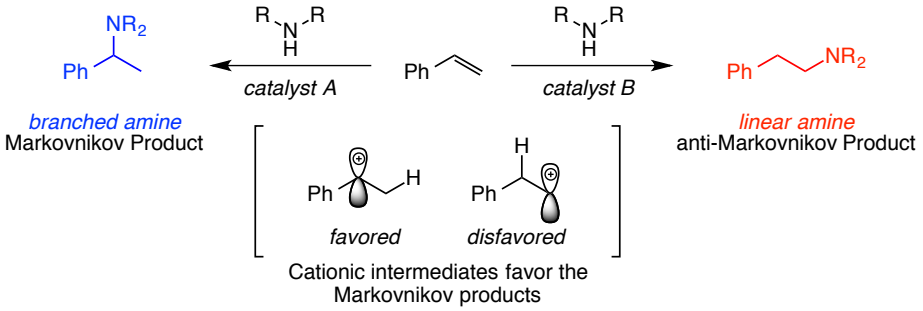
1.1: Introduction to Hydroamination

One well-studied class of alkene functionalization is hydroamination.[1–5] Hydroamination is defined as the addition of a N-H σ-bond across a C-C π-bond resulting in the formation of a new C-N and C-H bond vicinal to one another (Scheme 1.1-1). The significant interest in this reaction is in part due to the importance of carbon-nitrogen bonds in biologically active molecules, as highlighted by the rapid adoption of Buchwald-Hartwig couplings in the industrial syntheses of pharmaceuticals.[6–8] Alkene hydroamination has the potential to generate valuable C-N bonds in an atom-economical fashion, as every atom that is contained in the starting reagents is incorporated in the products. Additionally, the ready availability of alkenes and amines as starting materials allows hydroamination to rapidly transform simple compounds into complex molecules. Although a great deal of progress has been made in hydroamination, a general protocol has yet to be achieved and most catalysts are highly limited in scope.[2]

[1] A portion of this chapter appeared as a communication in the *Journal of the American Chemical Society*. The original citation is as follows: Goldfogel, M. J.; Roberts, C. C.; Meek S. J., *J. Am. Chem. Soc.*, **2014**, *136* (17), 6227–6230. Of the work discussed, C. C. Roberts was responsible for the development and synthesis of the CDC ligands (**^{Ph}CDC–H** and **^{iPr}CDC–H**), Rh complexes **^{Ph}CDC-Rh–Cl** and **^{iPr}CDC-Rh–Cl**, and development of the amine scope for the intermolecular hydroamination while M. J. Goldfogel discovered and optimized the hydroamination reactions and was responsible for the diene scope. M. V. Joannou contributed to the synthesis of the Pd complexes and solved all reported crystal structures.

Scheme 1.1-1: A general hydroamination reaction scheme.

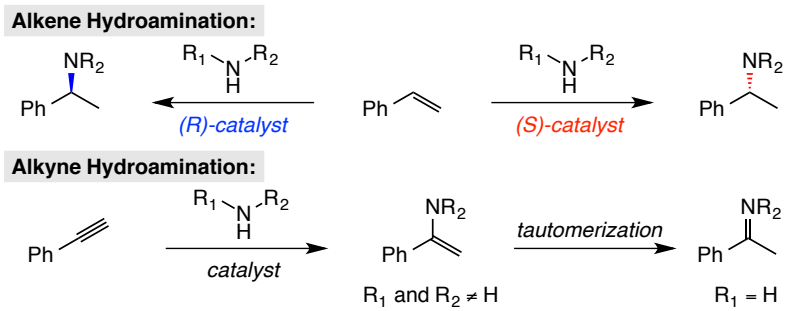
Alkene hydroamination is complicated by the regiochemistry of the C-N bond formation. Addition of the C-N bond to the more substituted alkenyl carbon provides the branched Markovnikov products, while anti-Markovnikov addition to the less substituted or terminal sp^2 carbon forms the less substituted amine (Scheme 1.1-2).[3] The Markovnikov addition is more common, as any mechanism that proceeds through a cationic intermediate will favor formation of the more substituted cationic carbon, directing addition of the nitrogen nucleophile to the same location. In 1993 anti-Markovnikov hydroamination was identified as one of the top challenges facing catalysis[9] and, despite recent catalytic examples,[10] remains a problem today. Anti-Markovnikov hydroamination has been developed utilizing such strategies as substrate bias,[11–18] hydride insertion,[19] and radical chemistry,[20–22] yet limitations still exist in scope and these methods are untested in total synthesis.



Scheme 1.1-2: Regiochemical considerations in the hydroamination of an alkene.

Stereochemical challenges further complicate many hydroamination reactions as addition to an alkene π-bond results in the formation of a stereocenter (Scheme 1.1-3).[23,24] Catalysts that can enantioselectively generate C-N bonds are particularly desirable, as many of the natural products amenable to hydroamination have specific stereochemistry.[25] Alkyne hydroamination does not form stereocenters, as the resulting carbon center is sp^2 and can tautomerize to form the imine product. This work will focus on alkene hydroamination in the interest of forming

stereogenic products through diastereo- and enantioselective transformations. The following sections will introduce several methods of alkene hydroamination to define the state-of-the-art and identify limitations that still prevent hydroamination from being adopted as a common synthetic tool.



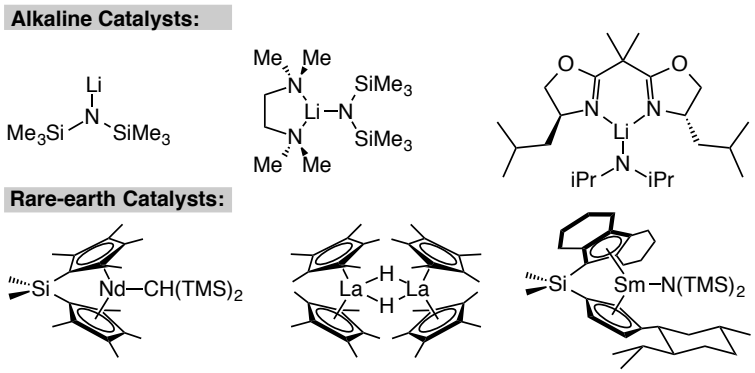
Scheme 1.1-3: Stereochemistry in hydroamination.

1.1.1: Categories of Catalytic Methods for Hydroamination

Despite its utility, mild methods for the hydroamination of alkenes are elusive. As an almost thermo-neutral process, hydroamination proceeds through an entropically disfavored transition state and consequentially high activation barrier.[2] As such, hydroamination under mild conditions necessitates the use of a catalyst. Hydroamination was initially explored with alkaline[26,3] and rare-earth metals (ie: lanthanides),[4,27] but more modern developments have introduced early transition metal[28,29] and late transition metal catalysts[5,30] which have come to dominate the literature due to their improved substrate scope, stability, and intermolecular transformations.[2] This introduction to research in the field will be organized according to the nature of catalysts used. Although this is not meant as an exhaustive review, it should provide insight into the types of catalysts that have been successful. We will briefly discuss organocatalytic methods, but organometallic catalysts will be the focus due to their greater prevalence and range of reactivity.

1.1.1.1: Alkaline and Rare-Earth Catalysts

Alkaline and rare-earth catalysts are notable for their high reactivity, boasting high turnover frequencies and reliable regioselectivity (Scheme 1.1.1-1).[4,31] Because of the reliability of these reactions, this class of catalysts is prevalent in synthetic applications of hydroamination (*vide infra,* section 1.1.3). However, alkaline and rare-earth catalysts rarely accomplish intermolecular reactions[32,33] and are highly oxygen and water sensitive.[27] These restrictions, paired with catalyst incompatibility with polar functional groups (eg: aldehydes, ketones) and acidic protons (eg: alcohols, carboxylic acids) have encouraged recent hydroamination research in alternative mild catalysts.

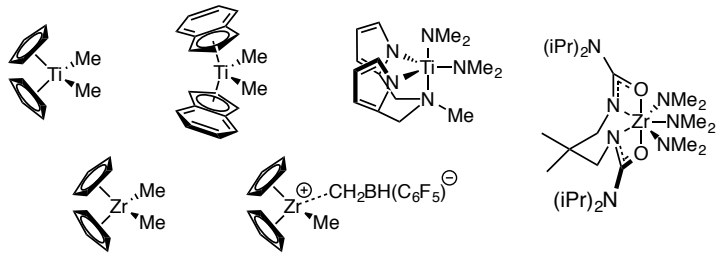


Scheme 1.1.1-1: Examples of alkaline and rare-earth hydroamination catalysts.

1.1.1.2: Early Transition Metal Catalysts:

Early transition metal catalysts have also been extensively explored for hydroamination, with the majority of research focusing on the group 4 metals Ti[34,35] and Zr[36] (Scheme 1.1.1-2). Catalysts derived from these metals have shown particular facility for alkyne and allene hydroamination, but are significantly less developed for alkenes. More recent work has shown that Ti[37,38] and Zr[29,39] can catalyze intramolecular alkene hydroamination, but intermolecular examples remain scarce.[40] These catalysts tend to be more stable than their Lanthanide

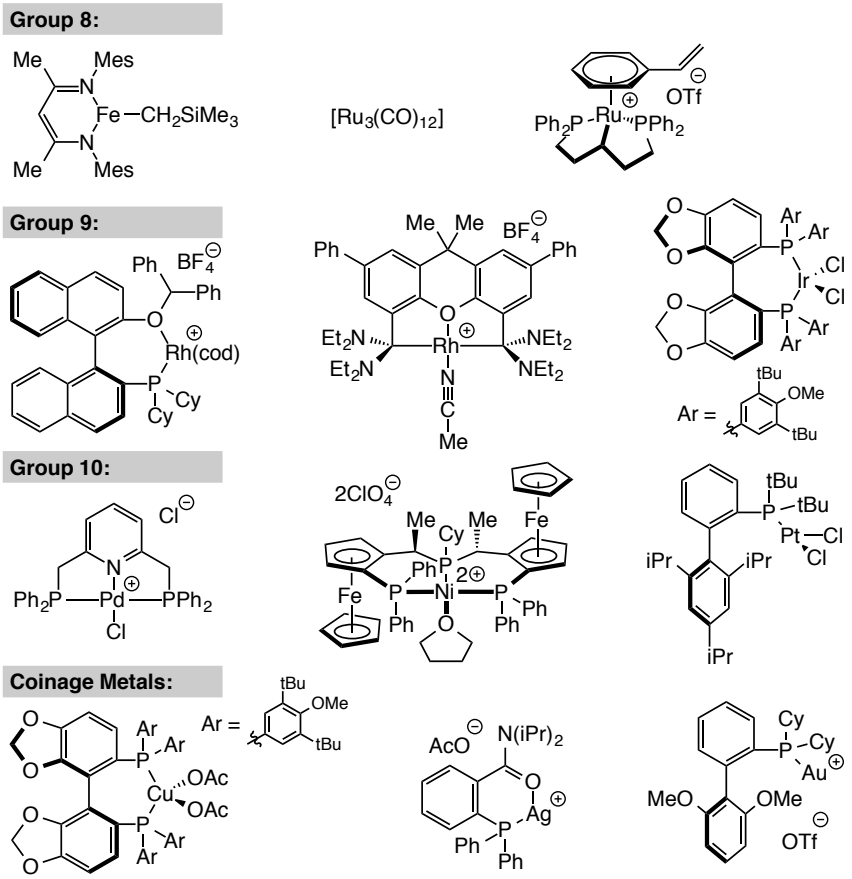
counterparts and have an accordingly greater tolerance for functional groups.[2] The amine scope is notable for reacting efficiently with congested nucleophiles (eg: secondary amines, tertbutylamine), but bulky ligands are required to react with small amines due to catalyst dimerization (*vide infra*). Overall, early transition metal hydroamination has been proven to be quite effective, but limitations still exist in: (i) the scope of alkene substrates, (ii) the availability of intermolecular reactions, and (iii) tolerance for amines of varying nucleophilicity.



Scheme 1.1.1-2: Examples of early transition metal hydroamination catalysts.

1.1.1.3: Late Transition Metal Catalysts

Many of the recent notable advances in hydroamination have come from late transition metal catalysts. Such catalysts tend to bind amines less tightly, which can allow them to overcome nucleophilic substrate limitations.[5] Because of this increased tolerance, late transition metal catalysts have become increasingly common with many examples of Ru,[41–49] Pd[50–52], Pt,[53–57] Rh,[30,58–63] and Ir[64–72] and catalysts appearing in the literature (Scheme 1.1.1-3). The coinage metals (Cu,[73–76] Ag,[77–85] Au[79,86–117]) have also been used, with both Au and Ag catalysts being the most developed for intramolecular and alkynyl reactions. Recent work with Cu has shown that hydride additions across alkenes offers an alternative, and useful, mechanism for hydroamination.[76] There are limited examples of hydroamination with other first row late transition metals (Fe,[118–122] Ni[123–130], Zn[131–142]), but these methods are still relatively unknown.



Scheme 1.1.1-3: Examples of late transition metal hydroamination catalysts.

Late transition metal catalyzed hydroamination generally benefits from a broader substrate scope than rare-earth or early transition metal methods, in part due to an increased tolerance for polar functional groups and decreased sensitivity of late transition metal complexes to oxygen and water.[1,5] Despite several notable examples of intermolecular hydroamination,[10,69,121,143,144] intramolecular examples predominate and alkene hydroamination is quite limited compared to reactions with alkynes and allenes.[2] Furthermore, hydroamination catalysts tend to catalyze the addition of only a narrow range of amine nucleophiles, as the reactivity difference between electron rich alkylamines and electron poor amines (ie: amides, ureas) prevents the development of a single catalyst that is general for most amine substrates. The progress in late transition metal catalysis is directly linked to the development of new ligand

structures and scaffolds that have allowed for the control of reactivity at the metal center. The variety of available ligands paired with the range of accessible reactivity highlights the potential of late transition metal catalysts for hydroamination.

1.1.1.4: Metal Free Methods

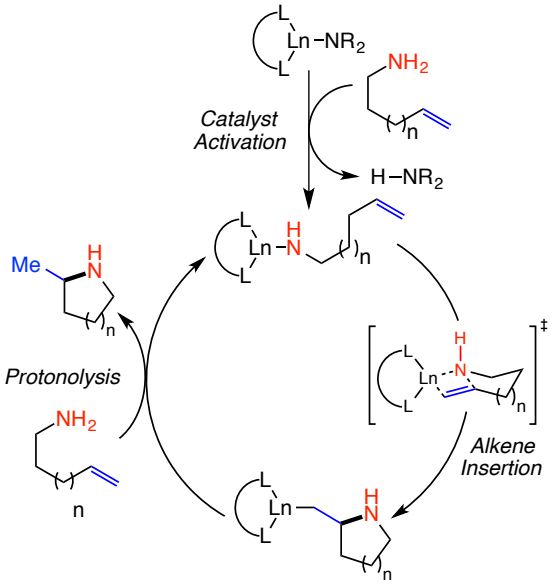
Organocatalytic hydroamination reactions have been accomplished using acids to protonate the π-system and generate cationic intermediates before amine addition.[145,146] However these reactions are generally limited by harsh reaction conditions or poor substrate scope, and are almost exclusively intramolecular.[1] This strategy is also limited mechanistically, as acid catalysts are restricted to generating Markovnikov products, since the intermediate cation is formed in the more substituted internal position. Recent advances in organocatalytic methods have overcome this limitation using photoredox catalysis to generate cation-radical intermediates that favor anti-Markovnikov addition.[147–151] Although this field is in its infancy, these new metal-free methods mark a different and intriguing approach to hydroamination.

1.1.2: Metal Catalyzed Hydroamination Mechanisms

The variety of hydroamination mechanisms posited in the literature demonstrates that the mechanism of a given reaction is highly dependent upon reaction conditions, yet general mechanisms have been identified for (i) rare-earth catalysts, (ii) early transition metal catalysts, and (iii) late transition metal catalysts. This section surveys the general mechanisms postulated for the organometallic catalyst classes discussed above. This information will be utilized in our own efforts to develop new late transition metal catalysts that can expand the synthetic utility of hydroamination reactions.

1.1.2.1: Mechanism of Catalysis with Rare-Earth Metals

Rare earth catalysts generally operate via direct nucleophilic addition or insertion of the amine into the π-system, which is usually the rate-determining step (Scheme 1.1.2-1).[27] As such, there is a great deal of similarity between alkaline and Lanthanide mechanisms of hydroamination.[152] Insertion into the π-system generates a highly basic alkyl-metal bond, which deprotonates another molecule of the amine to regenerate the active metal-amide intermediate. The high reactivity of the metal-amide intermediates is the source of the high turnover frequency and regioselectivity afforded by these catalysts.[2] However, this high reactivity also results in high catalyst sensitivity and an inability to tolerate polar functional groups that could react with the metal-amide or alkyl metal bases found in the reaction.

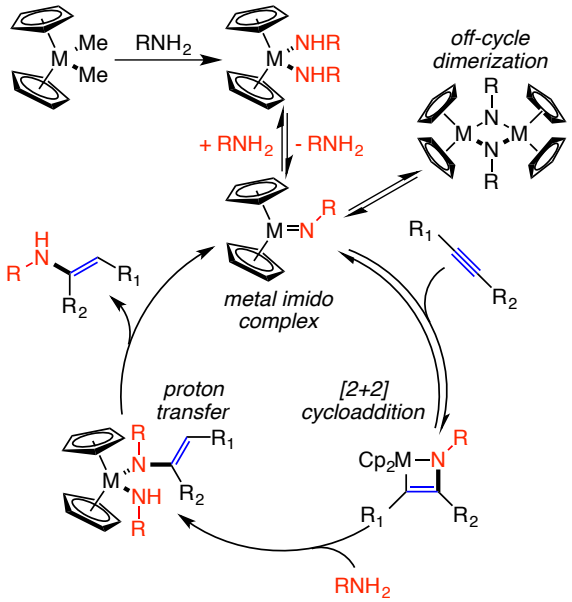


Scheme 1.1.2-1: General mechanism for hydroamination with rare-earth catalysts.

1.1.2.2: Mechanism of Catalysis with Early Transition Metals

The mechanism for hydroamination with group 4 metals has been extensively modeled and differs dramatically from other hydroamination pathways (Scheme 1.1.2-2).[153,154] The group

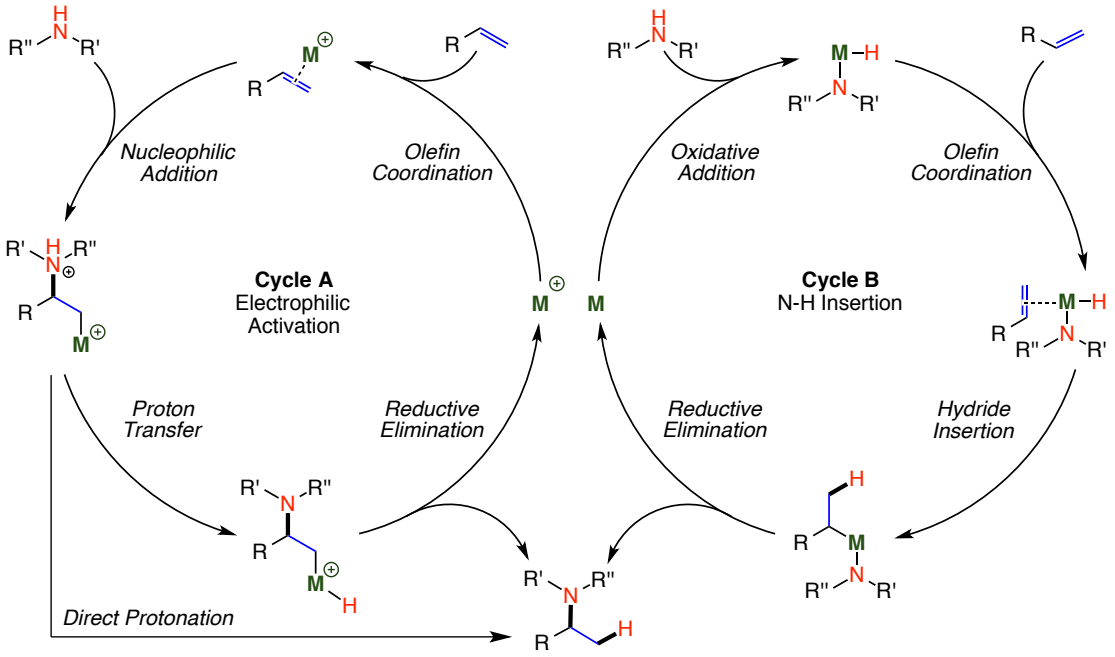
4 metal initially reacts with a basic amine to generate a catalytically active metal-imido species. C-N bond formation then occurs through a [2+2] cycloaddition between the π-systems of the metal imido and alkene in order to form a strained metalocycle. Proton transfer from another amine to break the carbon-metal and metal-nitrogen bonds follows, releasing the product and reforming the catalyst. This mechanism is complicated by dimerization of the metal imido complexes to an off-cycle intermediate. Excessive formation of this intermediate can occur if the amine is not sufficiently bulky to prevent dimer formation. It is the formation of the off-cycle dimeric intermediate that is responsible for the general favorability of bulky amine substrates over primary amines, since steric bulk disfavors the formation of the bridged metal and forces the equilibrium towards the catalytically active monomeric metal imido.[2] Smaller amine substrates can be utilized, provided ligands bound to the group 4 metal are large enough to compensate, but a specific ligand is rarely general for a large array of amine substrates.



Scheme 1.1.2-2: General mechanism for hydroamination with early transition metal catalysts.

1.1.2.3: Mechanism of Catalysis with Late Transition Metals

Much of the literature discussed above has focused on developing late transition metal catalysts, which have shown greater substrate tolerance and mechanistic flexibility. Despite the variety of mechanisms that have been proposed, catalysis with late transition metals can be broadly categorized by whether the alkene or the amine is activated (Scheme 1.1.2-3, Cycle A vs Cycle B).[2] Mechanisms that proceed via initial binding of the alkene are termed electrophilic activation, while a mechanism that occurs through activation of the amine is referred to as an N-H insertion pathway. Electrophilic activation was initially proposed for Pd and is widely accepted for many mechanisms, particularly those involving cationic metal catalysts.[155] Electrophilic catalysts operate through direct activation of the alkene by coordinating to the C-C π-system, which weakens the π-bond. This allows for external attack by the amine and subsequent formation of a metal-carbon bond. Protonation of this metal-carbon bond releases the product and regenerates the catalyst (Scheme 1.1.2-3, Cycle A).[156] The alternative N-H insertion mechanism begins with oxidative addition of the metal into the amine N-H bond,[67] or generation of a metal hydride from a stoichiometric hydride source.[157] The resulting hydride- and/or metal-amido complex can insert across the olefin forming either the C-N or C-H bond respectively.[5] The cycle is turned over by subsequent reductive elimination to release the product and regenerate the catalyst (Scheme 1.1.2-3, Cycle B). Amines with acidic N-H bonds favor the N-H insertion pathway because oxidative insertion is more facile. Variations on these mechanisms are numerous, but the focus of this thesis will be on electrophilic alkene activation because it offers a general strategy for promoting hydrofunctionalization reactions with Lewis basic nucleophiles and does not depend as heavily on the identity of the nucleophile.



Scheme 1.1.2-3: Two commonly proposed mechanisms for hydroamination with late transition metal catalysts.

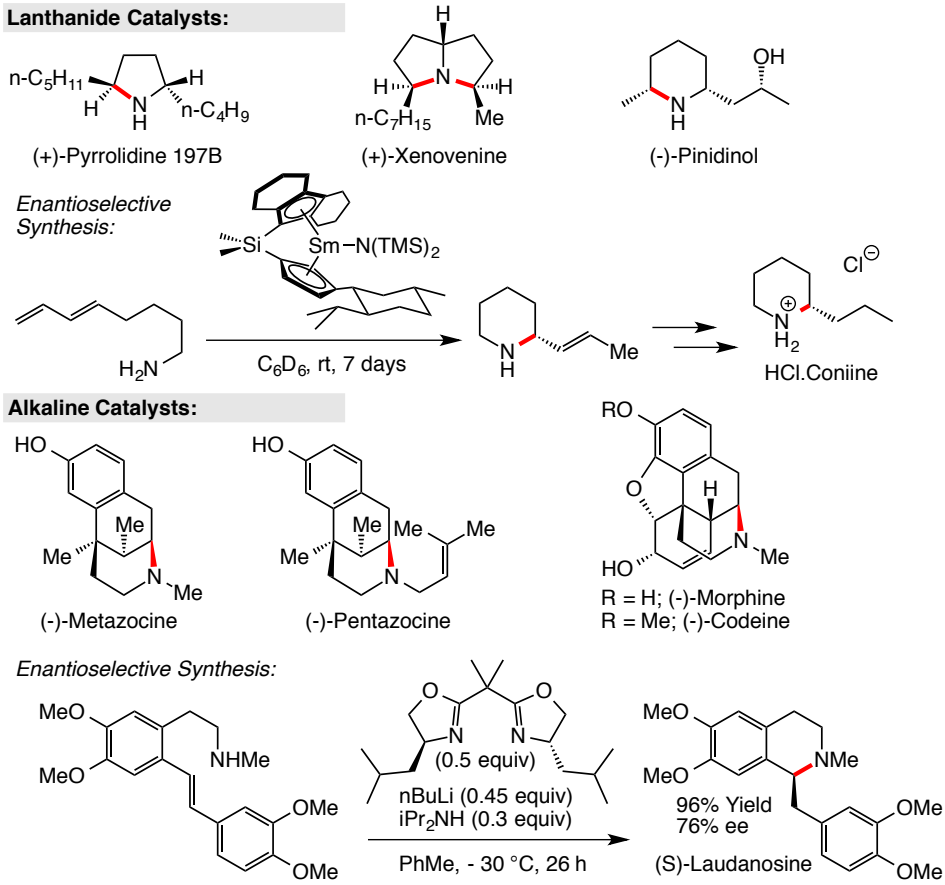
1.1.3: Hydroamination in Total Synthesis:

The use of catalytic methods in total syntheses serves as a metric for the overall utility and functional group tolerance of a reaction. Despite the prevalence of C-N bonds in natural products, and the corresponding value of forming C-N bonds with complete atom economy, hydroamination has only seen limited use in total synthesis. This is likely due to restrictions on substrate scope and the difficulty of identifying a general catalyst for a given reaction. However, several landmark examples of hydroamination in total synthesis do exist and will be discussed to enumerate the current limits of the reaction. Only stereoselective syntheses will be discussed in an effort to focus on hydroamination reactions that have the selectivity necessary to be generally applied in the synthesis of complex, stereodefined molecules.

The first application of hydroamination in natural product synthesis was by Marks *et. al.* in 1999 when they synthesized (+)-Pyrrolidine 197B and (+)-Xenovenine, which are alkaloids

produced in the mucous coating of poison dart frogs.[31] These syntheses were accomplished using organolanthanide catalysts to diastereoselectively hydroaminate allenes with a primary amine intramolecularly (Scheme 1.1.3-1: Lanthanide Catalysts). The high reactivity of organolanthanide catalysts is exemplified in the synthesis of Xenovenine as a tandem allene and alkene intramolecular cyclization could be catalyzed at temperatures as low as 45 °C. The absence of any other functional groups highlights the incompatibility of organolanthanide catalysts with Lewis basic moieties. Similar lanthanide catalysts have been subsequently used for the synthesis of (+)-Pinidinol[158] and the HCl salt of coniine.[159] The synthesis of coniine is particularly notable as one of only two examples of enantioselective hydroamination in total synthesis.

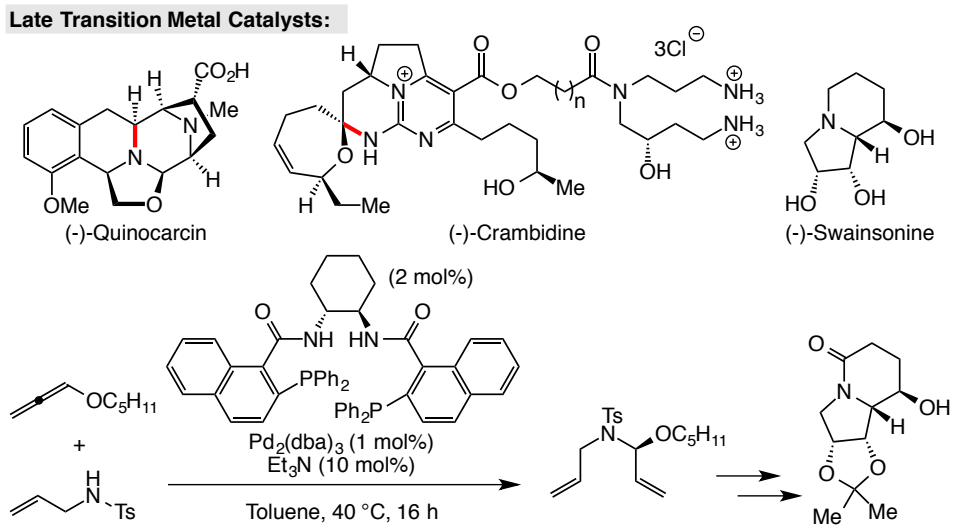
Alkaline hydroamination catalysts have seen use in total synthesis for the diastereoselective formation of pyrrolidine and piperidine rings. These methods generate lithiated amines, which have exceptional activity and selectivity. Alkaline catalysts were used in the syntheses of (-)-Codeine, (-)-Morphine,[160] (-)-Metazocine, and (-)-Pentazocine[161] by Trost *et al*. However, further extension of these methods has been dissuaded by the necessity for alkyl lithium bases, which have no tolerance for acidic protons. The synthesis of (-)-Metazocine is representative of the harsh conditions required, as the base caused *in situ* isomerization of the alkene and the only functional group tolerated was an ether (Scheme 1.1.3-1: Alkaline Catalysts). The second example of enantioselective hydroamination in synthesis was accomplished using an alkaline catalyst; a bisoxazoline ligand was paired with lithium diisopropylamine to catalyze the piperidine ring formation to synthesize (*S*)-Laudanosine with modest enantioselectivity.[162]



Scheme 1.1.3-1: Natural products synthesized stereoselectively lanthanide and alkaline catalysts for hydroamination.

More recent applications of hydroamination in synthesis have focused on late transition metal catalysts. Au,[163–167] Pd,[168] and Ag[169] have been used in the intramolecular hydroamination of sp-hybridized alkynes or allenes to form piperidine rings, and limited examples of hydroamination with less reactive sp^2-hybridized substrates are also known.[170,171] The natural products synthesized via these methods are significantly more complex and contain a variety of functional groups (Scheme 1.1.3-2). This demonstrates the increased tolerance and utility of late transition metal catalysts over their alkaline and lanthanide counterparts (Scheme 1.1.3-1: Late Transition Metal Catalysts). Particularly impressive examples include, Crambidine[164] and (-)-Quinocarcine,[165] which contain multiple fused rings and demonstrate that Au catalyzed

intramolecular hydroamination is tolerant of esters, protected alcohols, and alkenes. Most recently the formal synthesis of (-)-Swainsonine was introduced by Lim *et al*. and marks the first use of enantioselective intermolecular hydroamination in total synthesis.[172]



Scheme 1.1.3-2: Natural products synthesized stereoselectively lanthanide and alkaline catalysts for hydroamination.

The progressive increase in the complexity of natural products synthesized through hydroamination methods mirrors the progression of catalytic methods. However, these applications are still few in number and the similarities between the syntheses emphasize the limitations that still exist. Almost every reported example of asymmetric hydroamination in total synthesis has been intramolecular. Furthermore, the majority of these syntheses use reactive alkyne, or allene electrophiles and enantioselective hydroamination has only been applied three times. Using total synthesis as a metric for the maturity of a method, it is readily apparent that the limited application of hydroamination does not match the potential of this reaction as a method for forming C-N bonds. This gap between method and application can be traced to the current limitations in catalytic methods for hydroamination.

1.1.4: Current Limitations in Hydroamination

As was briefly discussed during the review of catalyst classes, efficient transition metal-catalyzed hydroamination is limited by: (i) the small scope of amines and π-systems tolerated by a given catalyst, (ii) the scarcity of intermolecular methods, and (iii) the dearth of enantioselective methods. Catalysts rarely tolerate both nucleophilic and non-nucleophilic amines[30,51] and are usually paired with sp-hybridized alkyne or allene electrophiles.[2,5] We will focus on developing methods that react with sp^2 hybridized π-systems in the interests of finding reactions that address current restrictions to substrate scope.

The nucleophilicity of the amine significantly impacts the viability of a given catalyst. Substrates containing nucleophilic amines are often plagued by product inhibition and exhibit an inverse dependence of the reaction rate on the amine concentration.[173] Nucleophilic amines are less likely to react via the N-H insertion pathway due to the stronger N-H bond (Scheme 1.1.2-3: Cycle B).[174] Similarly, electron poor amines are difficult for catalysts that favor the olefin activation pathway, as they lack the nucleophilicity necessary to add to the π* orbital of the alkene (Scheme 1.1.2-3: Cycle A). The large variance of Lewis basicity between amine nucleophiles means that most catalysts are only competent for a narrow range of amine substrates, such as alkylamines,[30] aryl amines,[142] amides,[69] or ureas.[100] A significant advance in hydroamination would be the development of a general catalyst capable of hydroamination with multiple amine classes. This could also encourage the application of hydroamination in synthesis.

The majority of organometallic hydroamination catalysts have been demonstrated with alkyne and allene substrates.[1] Reactions with alkenes are uncommon compared to these π-systems, and particularly rare with group 4 and group 11 catalysts. In the reactions that have

been demonstrated with alkenes the substrates are often strained (ie: norbornene[71]) or activated by neighboring functional groups (ie: styrenyl olefins[62] or dienes[123]). Substituted and internal alkenes still pose a major challenge to reactivity.[173]

Most hydroamination protocols have been developed with intramolecular substrates. This is particularly apparent for rare-earth[27] and early transition metal[2] catalysts, where intermolecular reactions are rare. The examples of hydroamination in the synthesis of natural products underscore this limitation, as there are currently only intramolecular examples of stereoselective hydroamination. Intramolecular transformations significantly reduce the entropic barrier of the reaction, and can be further biased towards cyclization by the incorporation of geminal substituents.[175] These limitations to substrate scope encourage the development of new catalysts and methods that can extend the viability of hydroamination as a synthetic reaction. One of the strengths of late transition metal catalysts is that they appear to be more amenable to the development of intermolecular reactions as there are examples with Cu,[19] Pd,[50] Rh,[63] and Ir[66] catalysts.

1.2: Designing a Hydroamination Catalyst

We aimed to develop a new catalyst capable of intermolecular reactions with alkenes to address systemic limitations to the field of hydroamination. To accomplish this goal, we chose to focus on late transition metal catalysts because they: (i) have been demonstrated in more intermolecular processes than other catalyst classes,[176] (ii) show greater tolerance for polar functional groups and nucleophiles,[173] and (iii) can have their reactivity tuned through judicious ligand choice.[5] Many of the recent developments in hydroamination have been facilitated by the introduction of novel ligand frameworks that unlock new reactivity profiles and suppress undesired reactions.[173] The key to developing a late transition metal catalyst will be the design

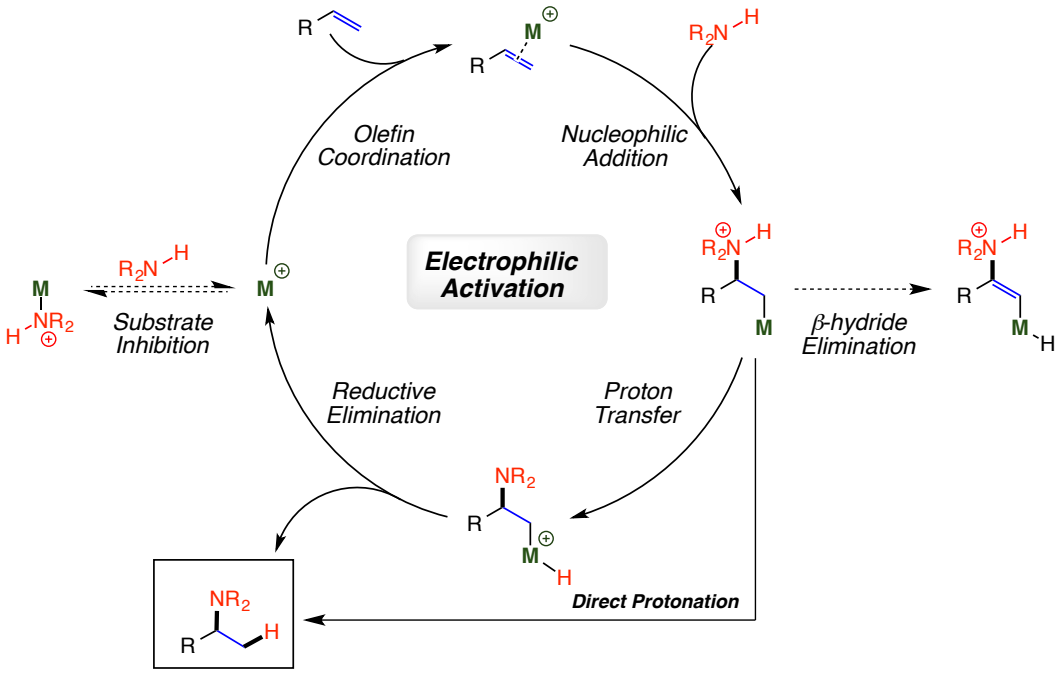
and synthesis of a new class of ligands that can control reactivity at the metal center. Known catalysts will provide the foundation for the rational design of new ligands and determine what steric and electronic traits may be beneficial to catalysis.

1.2.1: Mechanistic Approach to Catalyst Design

There are a limited number of mechanisms proposed for late transition metal catalyzed hydroamination.[2] As described above, hydroamination with late transition metals can be broadly categorized as either electrophilic activation or N-H insertion. Both have been demonstrated in alkene hydroamination, but the electrophilic activation pathway was chosen for further study in the interest of maintaining a broad nucleophile scope. Theoretically, an alkene activation mechanism could allow for the addition of any sufficiently nucleophilic Lewis base, possibly extending the developed catalysts to other hydrofunctionalization reactions (eg: hydroalkylation, hydroarylation, hydroetherification). This was particularly appealing as we hoped to develop a research program based on forming multiple types of bonds through the general activation of alkenes. Alkene activation should allow amines with varying nucleophilicity to react readily. In comparison, most N-H insertion mechanisms are restricted by the ability of the catalyst to insert into a given amine N-H bond, limiting the competent amine substrates.[5]

The general activation of an alkene by an electrophilic metal is shown in Scheme 1.2.1-1. Although simplified, this mechanism can be used to identify several key requirements for efficient alkene activation and subsequent hydroamination. The mechanism begins with binding of the alkene to an open coordination site on the metal. Only this single open coordination site is required for catalysis. Alkene binding must be competitive with binding to other Lewis basic molecules – such as amines – or the alkene will be displaced before the desired reaction can occur. This competition between alkene and amine binding is primarily responsible for the

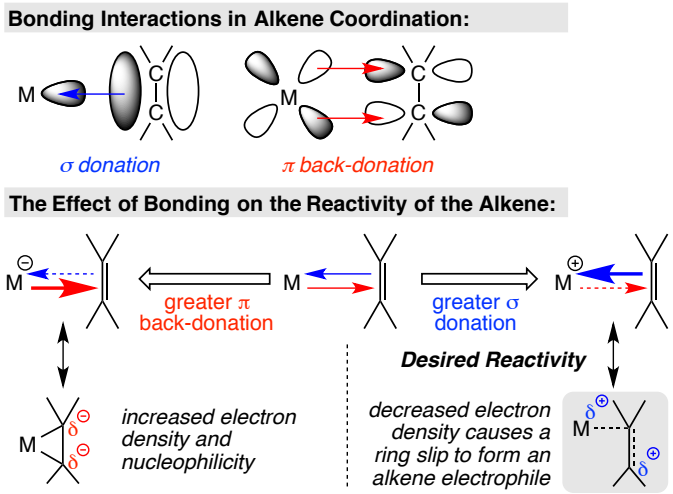
substrate inhibition that commonly limits amine scope in hydroamination. An effective ligand for general hydroamination with a variety on nucleophiles must control the steric and electronic properties at the metal center in order to encourage alkene binding.



Scheme 1.2.1-1: Working mechanism for designing a hydroamination catalyst including anticipated side reactions and off-cycle pathways.

The second step of the mechanism is external attack by a nucleophilic amine in order to generate the C-N bond and an alkyl-metal intermediate. The high activation barrier to this step requires that the alkene be sufficiently electrophilic to encourage amine addition. Coordination of the alkene to an electron poor metal can lower the activation barrier by withdrawing electron density from the alkene as predicted by the Dewar-Chatt-Dunkanson model (Scheme 1.2.1-2).[177] Alkene activation is described by Eisenstein and Hoffman as a geometric "slip" of the bound alkene to localize the LUMO on a single carbon.[156,178] The requirement for a highly electrophilic metal center suggests that cationic metal centers will be favored for alkene activation.

Additionally, computational studies predicted that the electronegativity of the metal center will impact reactivity and hypothesized that group 10 metals would be favored catalysts.[179]



Scheme 1.2.1-2: The Dewar-Chatt-Duncanson Model for alkene coordination to a late transition metal.

Unlike migratory insertion pathways, where the nucleophile initially binds to the metal before insertion can occur, electrophilic alkene activation is proposed to occur through outer sphere addition to the alkene. The catalyst only needs one open coordination site for this mechanism, encouraging bi- or tridentate ligand scaffolds that can fill unused coordination sites to prevent undesired reactivity. β-hydride elimination is a common side reaction in alkene hydroamination and forms imine products after reductive elimination. These imines can then further impede reactivity by tightly binding to the catalyst.[173] Many catalysts have only a single available coordination site to prevent β-hydride elimination, which requires a second coordination site at the metal center in order to form the metal hydride.[180] Tridentate meridonal ligands are known for preventing β-hydride elimination and are common scaffolds for group 9 and 10 hydroamination catalysts.[51,64,173]

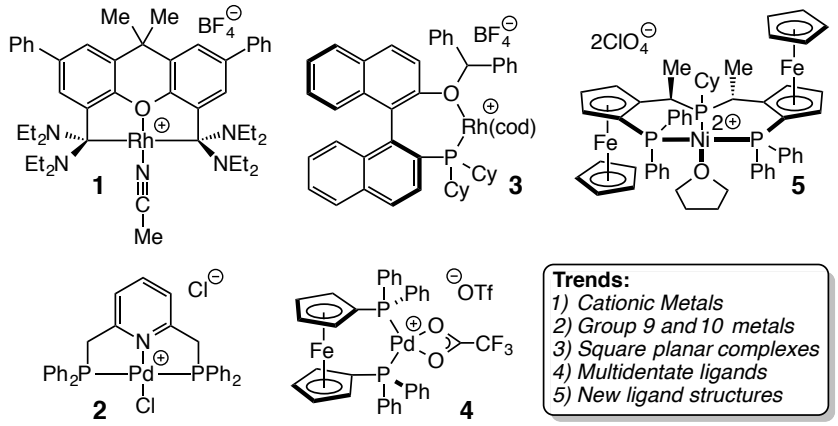
The final step of the proposed cycle is protonation of the metal-alkyl bond to form the product and regenerate the active metal catalyst with an open coordination site for alkene binding. For Rh and Ir catalysts this step is often considered to be rapid.[5] However, for Pd[181] and Au[116] catalysts this protonation can be rate-determining. This is especially apparent for Au catalysts, which have been shown to stoichiometrically generate a stable alkyl-Au complex during C-N bond formation. For many catalysts protonation at the metal is not feasible since they do not have an open coordination site. In these cases, substrate or ligand assisted protonation may allow for an intramolecular protonation of the metal-alkyl bond to generate the product.[108,181]

1.2.2: Trends in Successful Late Transition Metal Hydroamination Catalysts

Trends have begun to emerge in the catalysts that efficiently hydroaminate alkenes since the seminal work of Beller[63,182] and Hartwig.[157] DFT studies by Togni *et al*. led us to examine the group 9 and 10 metals, which were predicted to be highly effective catalysts for electrophilically activating alkenes to allow for external amine addition.[179] A series of representative catalysts are depicted in Scheme 1.2.2-1 to inform the following discussion. Examining the metals (eg: Rh,[173,183] Pd,[51,157] Ni[125]) used shows that they all have a positive charge at the metal center. This cationic nature likely assists in removing electron density from a bound alkene to weaken the C-C π-bond. The importance of a highly electrophilic metal center is demonstrated by the cationic Pd complex **2**, which was developed by Michael *et al*. and is one of the most active late transition metal catalysts.[51]

Additional trends emerge in the ligands used by effective hydroamination catalysts. Excluding Au, which favors a monodentate linear geometry, most active ligands for late transition metal catalyzed hydroamination are multidentate.[2] These tightly bound bidentate or tridentate ligands likely assist in: (i) stabilizing the positively charged metal center, (ii)

preventing inhibition, and (iii) suppressing undesired side reactions. The majority of active catalysts using group 9 and 10 metals are square planar, and have only a single open coordination site. Undesired β-hydride elimination processes will be prevented by maintaining only a single open coordination site.[173] Tridentate ligand scaffolds (ie: pincer ligands) are particularly useful in fulfilling this role and appear in many successful catalysts.[51,64,173] As discussed above, a cationic metal center is usually required for effective catalysis; this necessitates neutral L-type ligands.

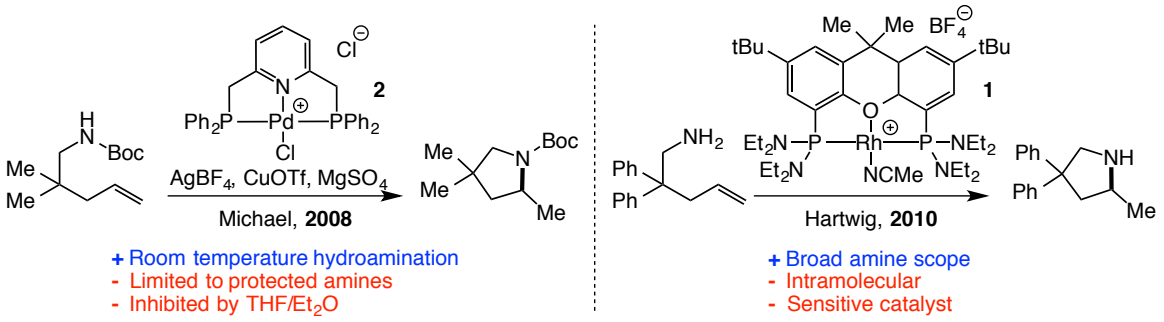


Scheme 1.2.2-1: Representative complexes used to inform catalyst design.

1.2.3: Design Goals for a Hydroamination Catalysts

The design of a catalyst was approached using the above observations and the mechanistic rationale discussed for electrophilic alkene activation. Current limitations in intermolecular processes and the amine scope in hydroamination could be overcome by improving upon the reactivity of known complexes. Two catalysts in particular proved inspirational, both for their desirable properties and notable limitations (Scheme 1.2.3-1). The first of these is the dicationic Pd complex **2** developed by Michael *et. al.*[51] At the time of its publication, this was the most active late transition metal catalyst and could efficiently catalyze intramolecular hydroamination at room temperature. Such reactivity is comparable to rare-earth

and alkaline catalysts. However, catalyst **2** also suffered from inhibition in the presence of any Lewis base; even an ethereal solvent such as diethyl ether or tetrahydrofuran completely suppressed reactivity.[181] Additionally, the reaction is restricted to intramolecular hydroamination with electron poor amides, which substantially reduces the generality of the transformation. By designing a similar complex with slightly reduced reactivity, we hoped to create a catalyst that maintained the activity of **2**, while ameliorating catalyst inhibition. This could provide a catalyst capable of intermolecular hydroamination with more electron rich amines.



Scheme 1.2.3-1: Intramolecular hydroamination reactions used as direct inspiration for designing new catalysts.

The second inspirational catalyst was the Xantphos ligated Rh complex **1** introduced by Julian and Hartwig for the formation of pyrrolidine and piperidine rings by intramolecular hydroamination.[173] Catalyst **1** serves as a counterpoint to the dicationic Pd complex discussed above, as it is notable for its general reaction scope. Intramolecular hydroamination with **1** has a broad amine scope including electron poor aryl amines, electron rich alkylamines, and primary amines. In addition, various ring sizes and polar functional groups are tolerated. The Rh(I) complex appears resistant to catalyst inhibition by strongly Lewis basic nucleophiles, yet maintains the electrophilic character necessary to efficiently activate simple alkenes. Despite the success of **1** for intramolecular reactions, intermolecular hydroamination were not reported and the catalyst rapidly decomposed at elevated temperatures due to fragmentation of the weak P-N

bonds. Development of a more stable complex could allow for higher reaction temperatures and intermolecular reactivity.

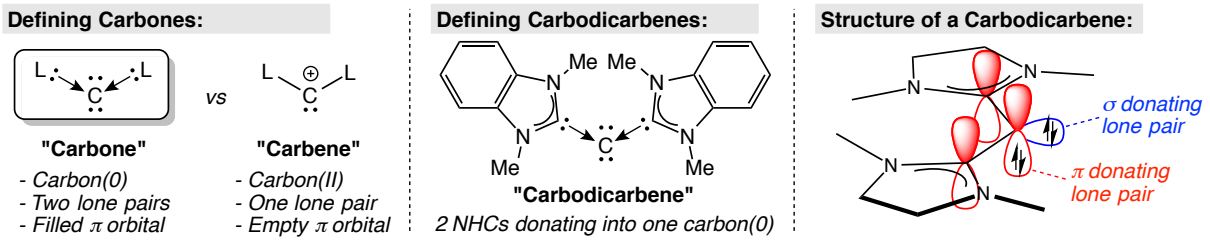
Taking these complexes as a starting point, we identified the properties expected to be beneficial to an alkene hydroamination catalyst. We reasoned that a catalyst derived from a group 9 or 10 metal would provide a flexible starting point and would need to be mono- or dicationic to be sufficiently electrophilic to promote alkene activation.[184] The limitations of catalyst **2** due to substrate inhibition encouraged the use of a highly donating set of ligands that could stabilize a cationic metal center.[180] These ligands would need to be L-type donors to maintain the cationic character at the metal center. In order to prevent β-hydride elimination, the ligand should fill three of the four available coordination sites on a square planar group 9 or 10 metal. This recommended the use of a tridentate ligand, and would have the additional benefit of incorporating a modular structure that could be used to tune the metal center through electronic and steric modifications.

A subtle trend in reports of novel catalysts is that advances in late transition metal hydroamination are usually accompanied by the introduction of a new ligand structure. Hydroamination has been thoroughly researched and most privileged ligand scaffolds have already been explored, including phosphine ligands derived from binapthyl[185] or ferocenyl backbones,[45] pincer ligands,[64] and N-heterocyclic carbenes.[186] Further screening of these known structures is unlikely to unlock new reactivity. Instead, we proposed to develop ligands that were unknown in catalysis and would therefore access entirely new chemical space. Carbodicarbenes were a class of neutral carbon donor ligands that fit this stipulation perfectly, since they had not been successfully applied to any catalytic reaction.[187] As exceptionally strong donors, we

anticipated that a ligand scaffold derived from these structures could stabilize a cationic metal center and prevent substrate inhibition.

1.2.4: Introduction to Carbodicarbene Ligands

Carbodicarbenes (CDCs) are a class of carbone ligands that were first synthesized by Bertrand[187] after being computationally predicted.[188] Carbones are defined by their central divalent carbon(0) atom, which is stabilized by a pair of donor-acceptor bonds from adjacent atoms (Scheme 1.2.4-1).[189] The zero oxidation state is present because the central atom harbors two lone pairs of electrons – one each in a σ and π orbital – making these structures both σ and π donors. This differs substantially from the more familiar carbene structure, which is defined by a central carbon(II) atom harboring a single lone pair of electrons. In contrast to the reactivity of carbones, carbenes serve as σ donors and weak π acceptors. A variety of carbones exist with various flanking donor groups, including carbodiphosphoranes[190–192] and carbodisilanes,[193] but, CDCs are specifically defined as carbones stabilized by two adjacent carbene donors. These ligands are usually N-heterocyclic carbenes (NHCs), which serve as L-type donors to stabilize the carbon(0).[187,194,195]



Scheme 1.2.4-1: Defining the reactivity and structure of carbones and carbodicarbenes.

1.2.4.1: Structure and Reactivity of Carbodicarbenes

The unusual electronic structure of CDCs is a result of the strong σ donation of the NHCs into the central carbon(0), paired with minimal π back-donation. This results in the localization

of both the HOMO and HOMO^{-1} on the central carbon. Each filled orbital manifest as a lone pairs of electrons on the central carbon. The HOMO and HOMO^{-1} occupy perpendicular σ and π orbitals, as shown by the molecular orbital calculations of Tonner and Frenking.[189,196] If the flanking donors do allow for π back-donation, then the structure changes to an sp-hybridized allene with a central carbon(IV) bound through both σ and π bonds. This related structure is termed a "bent allene," and has substantially different properties from CDCs (eqn 1).[197–199]

(eqn 1)

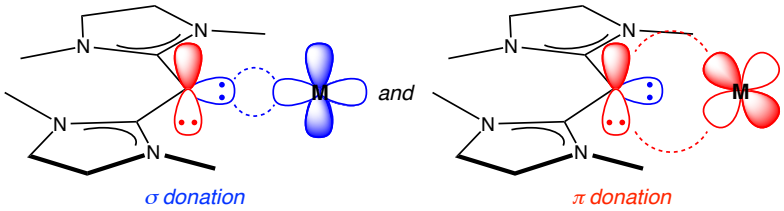
Carbodicarbene **Bent Allene**

The unique electronic nature of CDCs results in several unique structural properties, the first of which being their strongly bent bonding angles. Both calculated and experimental bonding angles for CDCs are far from linear, and range from 124° to 142°.[196,200] These angles more accurately reflect the sp^2 hybridization of the central carbon. A second property derived from the existence of the two lone pairs is that CDCs have very high first and second proton affinities.[189] The proton affinity of NHCs and CDCs was compared to illustrate this point and found that NHCs range from 40-100 kcal/mol while CDCs show values ranging from 110-200 kcal/mol.[201] These results are further demonstrated by the ready isolation of doubly protonated CDC structures.[187]

1.2.4.2: Carbodicarbenes as Ligands

The existence of two pairs of electrons on the central carbon(0) is at the core of the reactivity of CDCs and dictates their activity when binding to metals.[189] The HOMO and HOMO^{-1} of CDCs exist in orthogonal orbitals, which can bind to a metal center as both σ and π donors (Scheme 1.2.4-2). This contrasts with other neutral carbon donor ligands, such as NHCs, which behave as σ donors and weak π-acceptors. Additionally, the high electron density of the

carbon(0) suggests that CDCs are strong σ donors. This was demonstrated by Bertrand, who synthesized CDC-Rh complexes and measured their donor properties through the IR stretching frequency of a carbonyl ligand bound opposite the CDC.[187] They found a stretching frequency of 2014 cm^{-1} for the CDC-Rh complex as compared to a range of 2058-2036 cm^{-1} for similar NHC-Rh complexes. The importance of neutral carbon donor ligands has been well documented in both metathesis[202] and cross-coupling,[203] and the strong donation of NHCs has been lauded as responsible for their success in catalysis and ability to form strong metal-ligand bonds. This suggests that the strong donation of CDC ligands could be useful in the formation of catalytically active organometallic complexes. However, at the outset of this research, no examples of CDC ligands in catalysis had been reported. Furthermore, the influence of the secondary π donation on a bound metal was unknown.

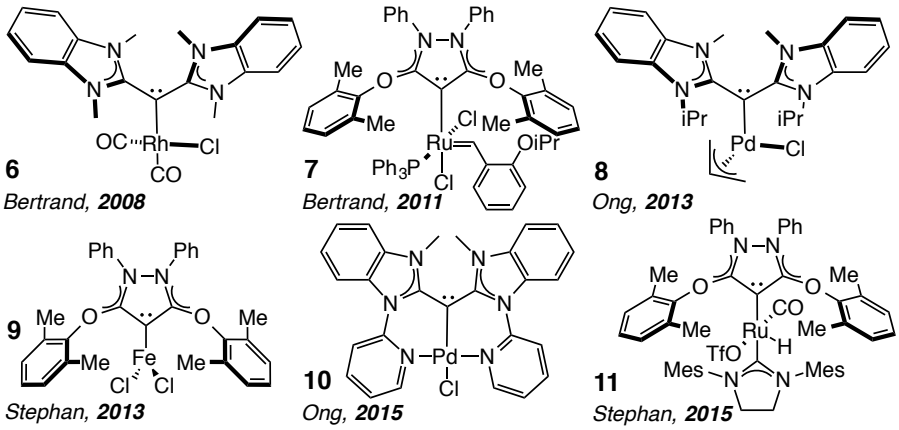


Scheme 1.2.4-2: Carbodicarbenes as ligands for late transition metals.

1.2.4.3: Metal Complexes Ligated by Carbodicarbenes

The unique structural properties of CDCs have encouraged their use as ligands for a variety of metals including Au,[194] Ru,[204,205] Rh,[187,206] Fe,[207] and Pd[208,209] (Scheme 1.2.4-3). However, these examples encompass almost all of the uses of CDCs as ligands in organometallic chemistry. CDCs were first applied in the Rh complexes developed by Bertrand in 2008 and discussed above. Since then the groups of Ong, Stephan, Fürstner and Meek[210,211] (*vide infra*) have been actively contributing to this field. Crystal structures of the formed complexes show that CDC ligands bind strongly to many metal species. Bond lengths between a C-C single and

double bond are characteristic of the central L➔C(0)🡐L motif and show that the structures are better represented as carbon(0) rather than carbon(IV). Several of these complexes have been tested for their catalytic activity, however, when this research program was begun, only complex **7** had been explored for metathesis and was found to be completely inactive.[204] Since then the Ru complex **11** has been found to be active for the hydrogenation of highly substituted alkenes[205] and Pd complex **10** has shown activity in Suzuki cross-coupling.[212] Despite these excellent examples, catalysis with CDC bound metal complexes is in its infancy.

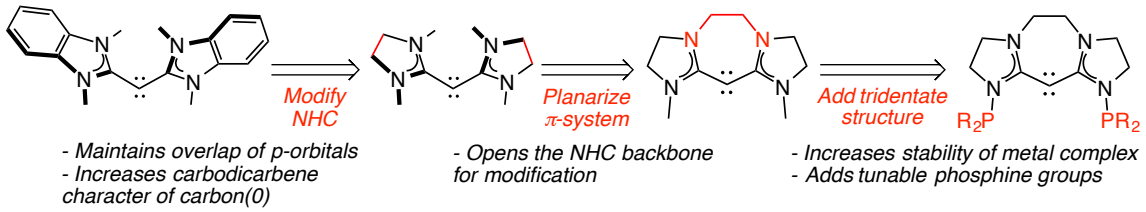


Scheme 1.2.4-3: Metal complexes that have been synthesized with carbodicarbene ligands.

1.3: Synthesis of the Carbodicarbene Ligand Scaffold

As was outlined in section 1.2.3, we hypothesized that a tridentate ligand scaffold with neutral L-type donors would be optimal for the development of an efficient hydroamination catalyst. In an effort to explore new chemical space and increase the novelty of our studies, we chose to use CDC ligands because of their strong σ donor properties and their unexplored ability to act as π donors. Using the CDC ligand developed by Bertrand[187] as a starting point, we made several modifications to improve activity (Scheme 1.2.5-1). First, we chose to use saturated NHCs, rather than the benzene backbone, to simplify the structure while opening positions that could be modified to tune the ligand properties. The next modification was to connect the two

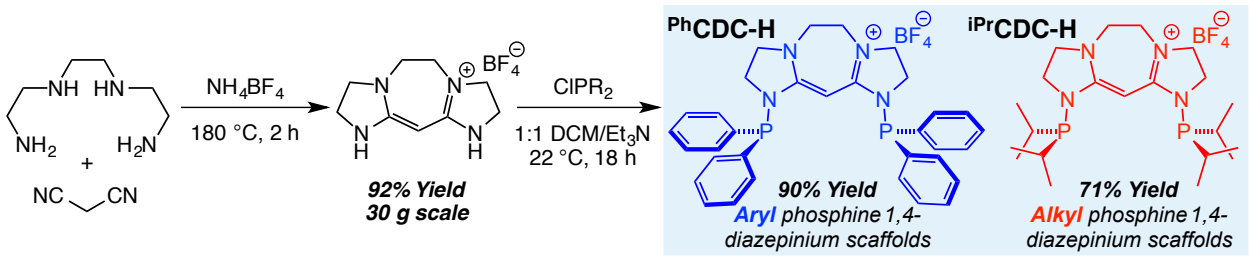
NHCs to form a cyclic diazepinium core. This serves to planarize the ligand and ensures that the filled p orbitals remain aligned and prevent back-donation from the carbon(0). Furthermore, the cyclization enforces a bent geometry to the CDC, which should increase the carbon(0) character of the central carbon. The final modification was to incorporate a tridentate scaffold as suggested by the discussion in Section 1.2.3. We chose to incorporate two phosphine ligands using P-N linkages similar to those found in the hydroamination catalyst **1** developed by Hartwig.[173] The P-N bonds promised to be more stable than those found in **1**, as each phosphine would be bound to only one inductively withdrawing nitrogen atom. Additionally, the substituents on the phosphine ligands could be modified to influence both the steric and electronic environment of the bound metal.



Scheme 1.3-1: Design of a tridentate carbodicarbene ligand scaffold.

This ligand scaffold was built from a central tricyclic diazepinium core, which had been previously synthesized in order to study its basic properties.[213] By modifying this synthesis, we were able to reliably generate the desired ligand structure on scale with good conversion (Scheme 1.2.5-2). The synthesis began with an acid catalyzed cyclization of triethylenetetramine onto malononitrile at 180 °C to yield the diazepinium core in 92% yield. This was followed by P-N bond formation via the nucleophilic addition of the diazepinium nitrogen atoms to phosphine chloride, a commercially available source of electrophilic phosphine. By changing the identity of the phosphine chloride we could efficiently synthesize the phenyl and isopropyl diazepinium ligand scaffolds on scale in high yield; **^{Ph}CDC-H** was formed in 90% yield and

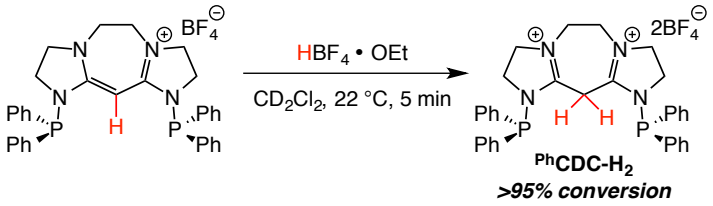
^{iPr}CDC-H in 71% yield. Both the diazepinium base and the tridentate ligand scaffolds are air and water stable and can be efficiently purified by column chromatography. Other phosphine chloride reagents were explored in an effort to generate variations to the functional groups on the phosphine; scaffolds bearing diethylamino- and tert-butyl substituents were attempted. However, scaffolds with more electron withdrawing groups (eg: $-NEt_2$) decomposed readily under ambient conditions, while larger substituents on the phosphine weakened the P-N bond – presumably due to steric clashes with the backbone – preventing the use of these structures as ligands. C. C. Roberts was responsible for exploring the diethylamino-phosphine ligand scaffold.



Scheme 1.3-2: Synthesis of achiral diazepinium ligands.

With **^{Ph}CDC-H** and **^{iPr}CDC-H** in hand, we needed to demonstrate that these complexes behaved as CDCs. This was accomplished by comparing their NMR spectra to known CDCs and by demonstrating that the diazepinium structures have a second proton affinity at the central carbon(0). The ^{13}C NMR signal of the CDC carbon(0) atoms appear as doublets of triplets in the $^{13}C\{^1H\}$ NMR spectrum: 72.98 ppm for **^{Ph}CDC-H** ($^1J_{Rh}$ = 36.0 Hz, ^1J_P = 11.7 Hz) and 73.74 ppm for **^{iPr}CDC-H** ($^1J_{Rh}$ = 36.3 Hz, ^1J_P = 10.4 Hz). These values are consistent with those previously reported[194,197] with the upfield shift indicating the electron-rich nature of the divalent carbon(0). To gain insight into the electronic nature of the ligand, we treated **^{Ph}CDC-H** with 1 equiv of $HBF_4{\cdot}OEt_2$ in CD_2Cl_2 at 22 °C, which generated the dication **^{Ph}CDC-H$_2$**. The symmetrical ^{1}H NMR confirms protonation at the central carbon, in accord with previously described

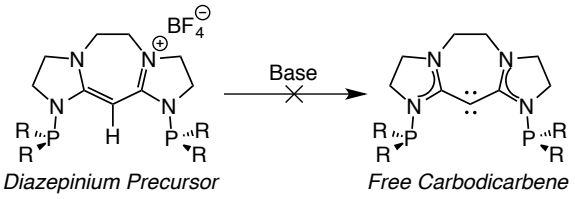
systems.[195,198] This demonstrates the presence of significant electron density at the central carbon of the diazepinium salt and supports its reactivity as a CDC with two proton affinities at the carbon(0). This exploration of the diazepinium scaffold was in large part conducted by C. C. Roberts and additional information can be found in her dissertation (Roberts, 2016).



Scheme 1.3-3: Protonation studies of the carbodicarbene ligand used to demonstrate that the HOMO and HOMO^{-1} lies on the carbon(0).

1.4: Syntheses of Carbodicarbene Ligated Metal Complexes

With syntheses of **^{Ph}CDC-H** and **^{iPr}CDC-H** in hand, we began to explore how these structures could be metallated. The diazepinium framework is not a CDC, but rather the protonated form of a CDC. It is only after deprotonation of the central proton that the CDC structure is revealed (Scheme 1.4-1). Initial efforts to directly affect this deprotonation with alkoxide, amide, or alkyl bases proved ineffective.[197] The central proton was too basic to be deprotonated by weak bases, and stronger bases reacted preferentially with the Lewis acidic phosphine substituents to break the P-N bond and quench the positive charge of the diazepinium backbone. Even bulky bases such as lithium tetramethylpiperidide or potassium bis(trimethylsilyl)amide destroyed the ligand structure before forming the free CDC.



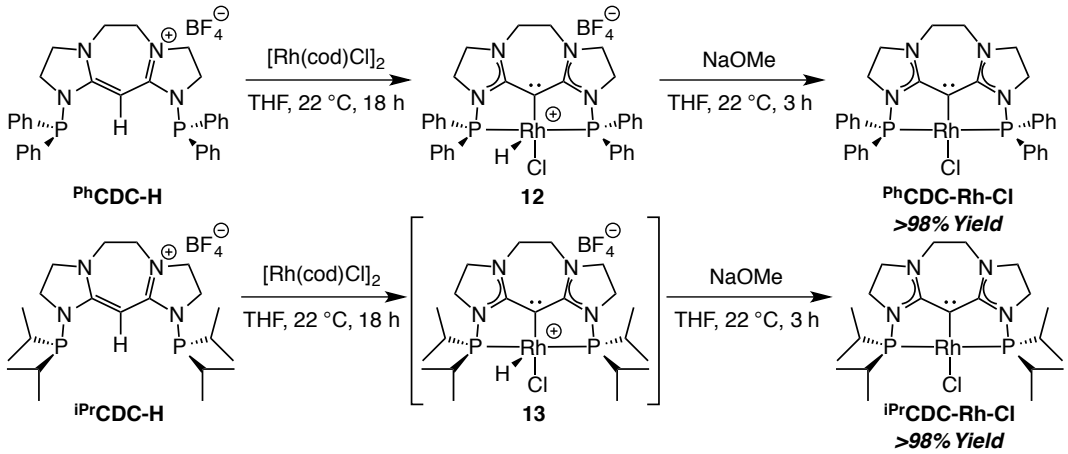
Base = NaOMe, KOtBu, nBuLi, LiTMP, KHMDS, etc.

Scheme 1.4-1: Attempts to form the free CDC ligand.

The incompatibility of the P-N bond with strongly basic conditions prevents the formation of the free CDC directly from the diazepinium salt. An alternative strategy for ligand formation is through C-H insertion into the CDC.[214] This strategy is commonly used for forming pincer complexes of second and third row metals.[215–217] We reasoned that coordination to the phosphine substituents could direct the metal to insert into the C-H bond of the carbodicarbene, generating a metal hydride. The metal hydride would then be deprotonated in a second step to generate the desired metal complex. This deprotonation is more facile than the direct strategy described above, as the metal hydride is more acidic than an alkyl hydride.

1.4.1: Synthesis and Characterization of Carbodicarbene-Rh Complexes

Using this strategy, diazepinium ligands **^{Ph}CDC-H** and **^{iPr}CDC-H** were reacted with chloro(1,5-cyclooctadiene)rhodium(I) dimer {$[Rh(cod)Cl]_2$} to generate the Rh(III)-hydride complexes **12** and **13** (Scheme 1.4.1-1). These complexes were deprotonated with an alkoxide base to provide the desired CDC-Rh(I) complexes **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** in high yields. The intermediate Rh(III)-hydride complex **12** was not fully characterized, but is stable and could be isolated. However, the analogous Rh hydride of the isopropyl phosphine ligand **13** does not form cleanly. Rh(III) complex **12** is insoluble in THF, but becomes partially soluble after deprotonation to form **^{Ph}CDC-Rh-Cl**. Both **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** are transiently stable in acetonitrile (MeCN), but may decompose in dichloromethane (DCM), as the electron rich Rh complex appears to insert into the C-Cl bonds of DCM. Additionally, extended solvation in acetonitrile can result in ligand substitution of the chloride to form an acetonitrile ligated cationic Rh(I) complex. As with the above ligand syntheses, C. C. Roberts discovered these complexes and more information can be found in her dissertation (Roberts, 2016).

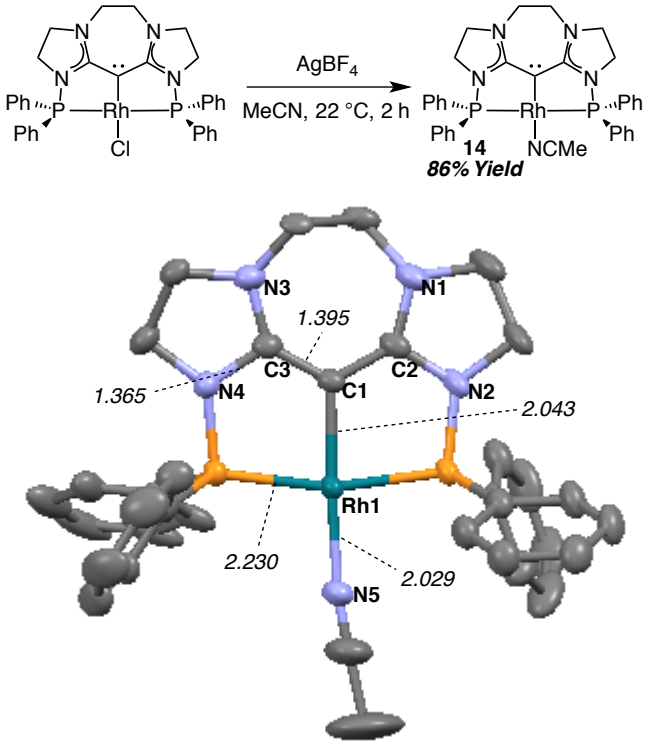


Scheme 1.4.1-1: Synthesis of CDC-Rh(I) complexes through C-H activation of the diazepinium ligand.

In order to better understand the Rh complex and the nature of the CDC ligand, we attempted to recrystallize **^{Ph}CDC-Rh-Cl** to determine its structure by X-Ray crystallography. All attempts to directly recrystallize **^{Ph}CDC-Rh-Cl** were unsuccessful; the compound oiled out, generated unsuitable crystals or, when solvated by acetonitrile, slowly under went ligand substitution. Reasoning that a cationic complex might be more amenable to recrystallization, acetonitrile ligated Rh complex **14** was synthesized by abstraction of the chloride with a Ag salt and trapping of the resulting open coordination site. X-ray quality crystals were formed through slow formation of **14** from **^{Ph}CDC-Rh-Cl** via salt metathesis with $NaBF_4$ in acetonitrile. The resulting crystal structure is shown in Scheme 1.4.1-2. M. V. Joannou was responsible for solving this crystal structure. The crystal structure shows that the CDC ligand remains almost planar. The CDC-Rh bond length is 2.043 Å and the bond lengths of the ligand indicate a CDC structure with average C3–C1 bond lengths of 1.395 Å. These bond lengths are in-between the values expected for a C-C single or double bond, demonstrating that the ligand framework does not have the structure of a bent allene.[180] The C-N bond lengths support the assignment of a CDC structure by being shorter than the C-C bonds (N2–C2 average 1.365 Å), as would be expected

for the structure of an NHC. The Rh1– N5 bond length of 2.029 Å indicates that the CDC imparts a strong trans influence on the bound acetonitrile.

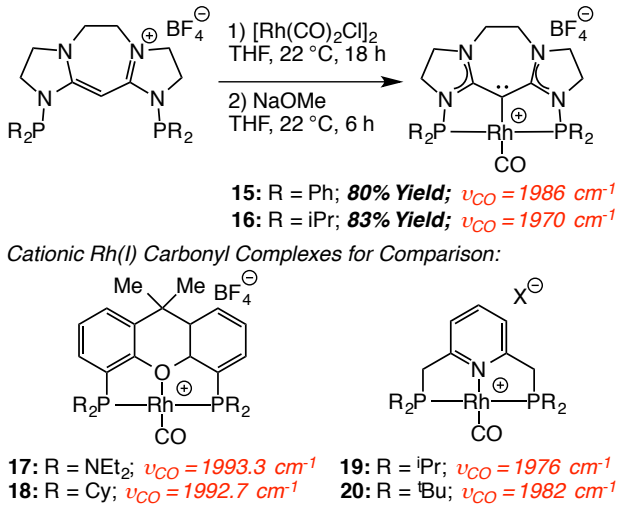
The lengthened bond of the ligand trans to the CDC suggested that the ligand scaffold is a strong σ donor but did not provide any quantitation for this property. In the interest of determining the strength of the donation from **^{Ph}CDC-H** and **^{iPr}CDC-H**, we sought to synthesize the carbonyl ligated Rh complexes **^{Ph}CDC-Rh-CO** and **^{iPr}CDC-Rh-CO** (Scheme 1.4.1-3). Bertrand demonstrated that the donor properties of a CDC ligand could be assayed by measuring the stretching frequency of a carbonyl bound trans to the CDC.[187] This value correlates to the back-donation of the Rh metal to the carbonyl providing a measurement of the relative electron density at the Rh center. The synthesis of **^{Ph}CDC-Rh-CO** and **^{iPr}CDC-Rh-CO** was accomplished using the same C-H insertion strategy utilized in the previous organometallic syntheses, but employing $[Rh(CO)_2Cl]_2$ as the Rh source. The strong interaction between Rh and a carbonyl ligand favors formation of the cationic carbonyl complex over the neutral chlorides **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** allowing for the synthesis of complex **15** and **16** in high yield.



Scheme 1.4.1-2: Crystal structure of a CDC-Rh complex.

As mentioned above, Bertrand found that a cyclic CDC donor exhibited a stretching frequency of 2014 cm^{-1} for a neutral CDC-Rh(I) complex.[187] This provides an estimate for the stretching frequency values, but not a direct comparison, as **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** are monocationic Rh(I) complexes and are expected to have substantially different electron densities at the Rh center. IR stretching frequency values for complexes **15** and **16** were found to be 1986 and 1970 cm^{-1} respectively. This suggests that **^{iPr}CDC** is a stronger donor than **^{Ph}CDC**, as expected from the inductive withdrawl of electron density from the aryl rings. A literature search provided several tridentate cationic Rh(I) complexes that could serve as reasonable comparisons to gauge the donor properties of the CDC ligands **^{Ph}CDC-H** and **^{iPr}CDC-H**.[173,218,219] These complexes are shown in Scheme 1.4.1-3 and show similar values for the IR stretching frequency as obtained for the CDC-Rh complexes. This provides evidence that the **^{Ph}CDC-H** and **^{iPr}CDC-H** ligands are strong donors, but are not substantially more donating than other tridentate

scaffolds. One particularly notable comparison is to **17**, which is the carbonyl-ligated version of the Rh catalyst **1** used in intramolecular hydroamination.[173] The lower stretching frequency of **15** and **16** compared to **1** suggests that the CDC-Rh complexes are more electrophilic than those used by Hartwig for hydroamination, although differences in the phosphine substituents do not allow for direct comparison.

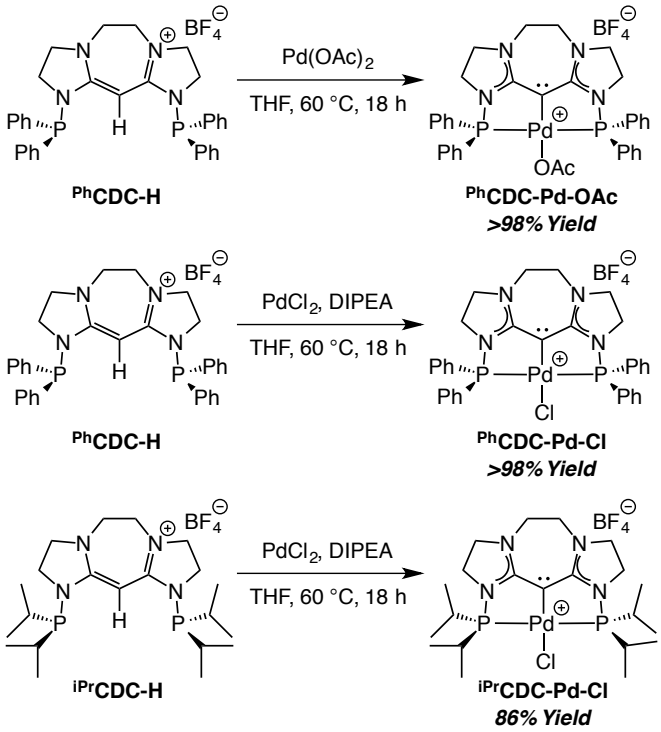


Scheme 1.4.1-3: Complexes for determining carbonyl stretching frequency.

1.4.2: Synthesis and Characterization of Carbodicarbene-Ligated Group 9 Complexes

The synthesis of Pd and Ni complexes derived from the **^{Ph}CDC-H** and **^{iPr}CDC-H** ligand scaffolds were undertaken in an effort to generate prospective group 9 catalysts. Application of the C-H insertion strategy utilized for the **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** complexes described above failed to provide the desired Pd hydride complexes, however M. V. Joannou showed that the use of $Pd(OAc)_2$ generated complex **^{Ph}CDC-Pd-OAc** at room temperature (Scheme 1.4.1-1, unpublished work). This showed that weak bases (eg: acetate) could be utilized to deprotonate the diazepinium framework if bound to the metal. This insertion likely occurs through an assisted internal deprotonation where coordination of the metal to the C-H bond allows for C-H activation.[220] The acetate ligand on complex **^{Ph}CDC-Pd-OAc** could not be reliable abstracted to

generate the cationic complex identified as necessary for hydroamination. As such, we chose to pursue the synthesis of the chloride-ligated complexes, which could be removed by abstraction with Ag to generate a cationic Pd complex and AgCl.

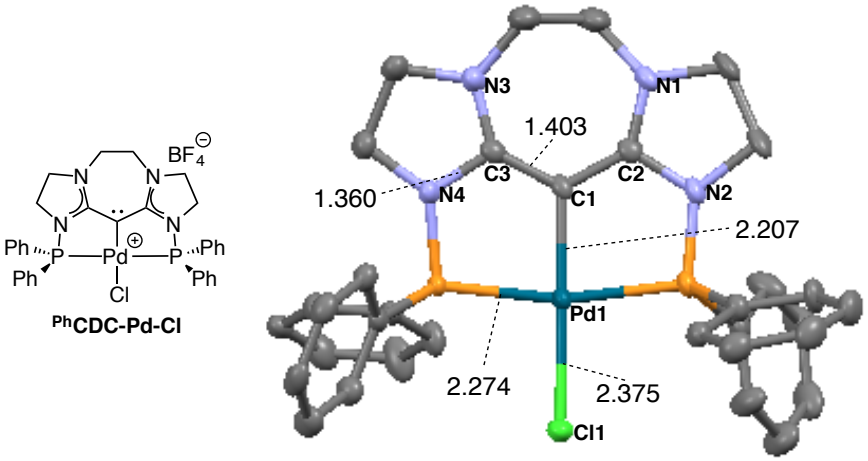


Scheme 1.4.2-1: Synthesis of CDC-Pd(II) complexes.

Heating $PdCl_2$ with the **^{Ph}CDC-H** and **^{iPr}CDC-H** ligands failed to form the Pd(II)-hydride complexes analogous to **12** and **13**. Inspired by the success of the internal deprotonation/C-H activation with $Pd(OAc)_2$, triethylamine (Et_3N) was added in the hope that it would bind to Pd and act as an internal base. Heating a solution of the appropriate ligand, $PdCl_2$ and Et_3N in THF efficiently precipitated the desired complex as a yellow powder (Scheme 1.4.1-1). However, attempts to purify this compound away from the triethyl ammonium salt byproducts proved difficult. This problem was solved by substituting diisopropylethylamine (DIPEA) for Et_3N as the ammonium byproducts of DIPEA are partially soluble in THF and could be washed away from the desired Pd complexes **^{Ph}CDC-Pd-Cl** and **^{iPr}CDC-Pd-Cl**. The reverse of this strategy

can be applied to the purification of complexes that are soluble in THF and was later used in the syntheses of chiral variants of the Pd complexes (*vide infra*).

Crystals of **^{Ph}CDC-Pd-Cl** suitable for X-ray crystallography were obtained by slow recrystallization from layering DCM and hexanes (Scheme 1.4.2-2). Although this crystal structure cannot be directly compared to the cationic Rh complex **14**, the bond lengths for the ligand scaffold are very similar. The most notable differences between the Rh and Pd complexes are the bond lengths of the C1-Pd1 (2.207 Å) and the Pd1-Cl1 (2.375 Å) bonds, both of which are substantially longer than in the cationic Rh complex. M. V. Joannou was responsible for solving the crystal structure shown in Scheme 1.4.2-2.



Scheme 1.4.2-2: Crystal structure of the ^{Ph}CDC-Pd-Cl complex.

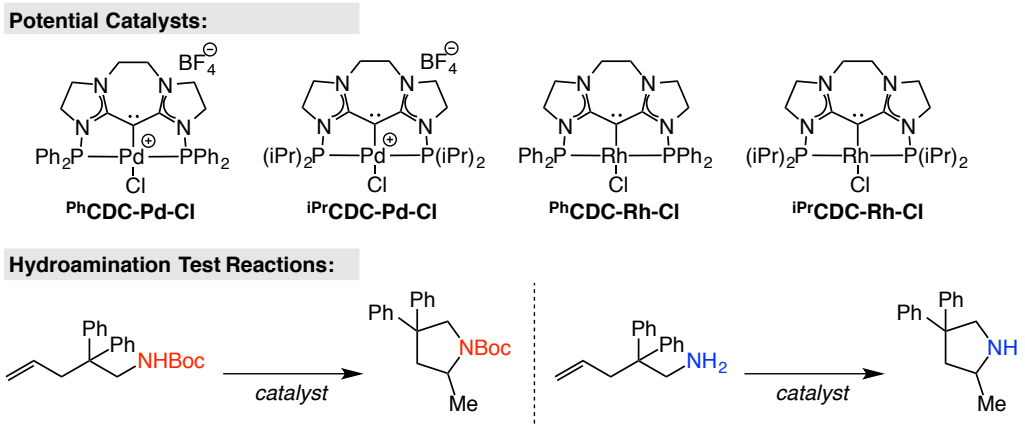
1.5: Intramolecular Hydroamination with Carbodicarbene Ligated Rh Complexes

Pd and Rh complexes derived from a tridentate carbodicarbene (CDC) ligand scaffold were successfully synthesized and characterized. These complexes demonstrated that the **^{Ph}CDC-H** and **^{iPr}CDC-H** scaffolds behave as neutral CDC donors after metallation. The next goal was to apply these new CDC-metal complexes to catalytic reactions. Prior to this work, no CDC ligated metal complex had been used as a catalyst and there was no proof that these complexes would be

catalytically active. The metal complexes described in Section 1.4 were applied to intramolecular hydroamination of unactivated terminal alkenes to validate the design principles discussed in Section 1.2 and explore how CDC donors affected the reactivity of bound metals. Intramolecular hydroamination was selected as a starting point because it is a well-studied reaction catalyzed by several late-transition metal complexes. Comparing our CDC-ligated metal complexes to known catalysts will allows us to gauge the reactivity of CDC-ligated metal complexes and determine whether they could expand the synthetic utility of hydroamination.

1.5.1: General Catalyst and Reaction Considerations

Our goal was to explore whether **^{Ph}CDC-Pd-Cl**, **^{iPr}CDC-Pd-Cl**, **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** could serve as hydroamination catalysts (Scheme 1.5.1-1). The inspiration for these organometallic compounds originated in the work of Michael[51] and Hartwig[173] for Pd and Rh, respectively. We chose to repeat the intramolecular hydroamination reactions catalyzed by **1** and **2** with our CDC-metal complexes to provide a point of comparison and gauge reactivity. There are significant differences in the expected reactivity of the CDC-Pd and CDC-Rh complexes, as they differ in both the identity and oxidation state of the metal (eg: **CDC-Pd^{II}-Cl** vs **CDC-Rh^{I}-Cl**). This difference manifests in the expected charges of the active catalysts after abstraction of the X-type chloride ligand; the Pd complexes will be dicationic in nature whereas the Rh complexes are monocationic. The reported catalysts **1** and **2** share this difference and demonstrates how it effects reactivity, as the dicationic Pd catalyst **2** reacts efficiently with electron poor amides while the monocationic Rh complex is tolerant of electron rich alkylamines. This difference prompted us to test all four CDC-metal complexes for intramolecular hydroamination with both an electron poor protected amine and with an electron rich primary amine (Scheme 1.5.1-1).



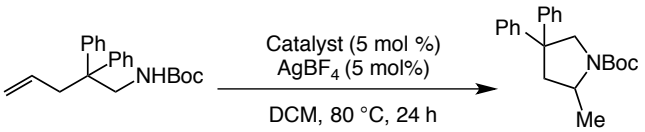
Scheme 1.5.1-1: Potential catalysts for intramolecular hydroamination and the test reactions used to gauge reactivity.

The metal complexes shown in Scheme 1.5.1-1 are stabilized by an X-type ligand and do not have an open coordination site to bind an alkene. As such, the chloride ligands needed to be abstracted in order to form the active catalysts. Ag salts were utilized as activators of the catalyst, as they are proficient in removing halides from metal complexes.[180] We considered isolating the cationic complexes directly, but decided that *in situ* catalyst activation would serve the same purpose and avoid the need for additional inorganic syntheses.

1.5.2: Intramolecular Hydroamination of Electron Poor Protected Amines

The similarity in structure between literature catalyst **2** (Scheme 1.2.2-1) and complexes **^{Ph}CDC-Pd-Cl** and **^{iPr}CDC-Pd-Cl** prompted us to begin our study of intramolecular hydroamination with the intramolecular pyrrolidine formation introduced by Michael *et. al.*[51] This reaction requires substantial activation, as the carbamate nucleophile is far less Lewis basic than an unprotected amine and the terminal alkene is unactivated by any electron-withdrawing group. The geminal-diphenyl substitution of the substrate was used to impart conformational bias towards a cyclic ring structure through the Thorpe-Ingold effect.[175] Both the CDC-Pd and CDC-Rh complexes were tested for catalytic activity using the conditions developed by Michael *et al.*,

although we only anticipated reactivity with the CDC-Pd complexes.[51] To our surprise, no reactivity was observed with any of the catalysts at 80 °C (Table 1.5.2-1). At higher temperatures thermal deprotection of the tert-butoxycarbonyl (Boc) group occurred, resulting in a background reaction and limiting the viable temperature range.



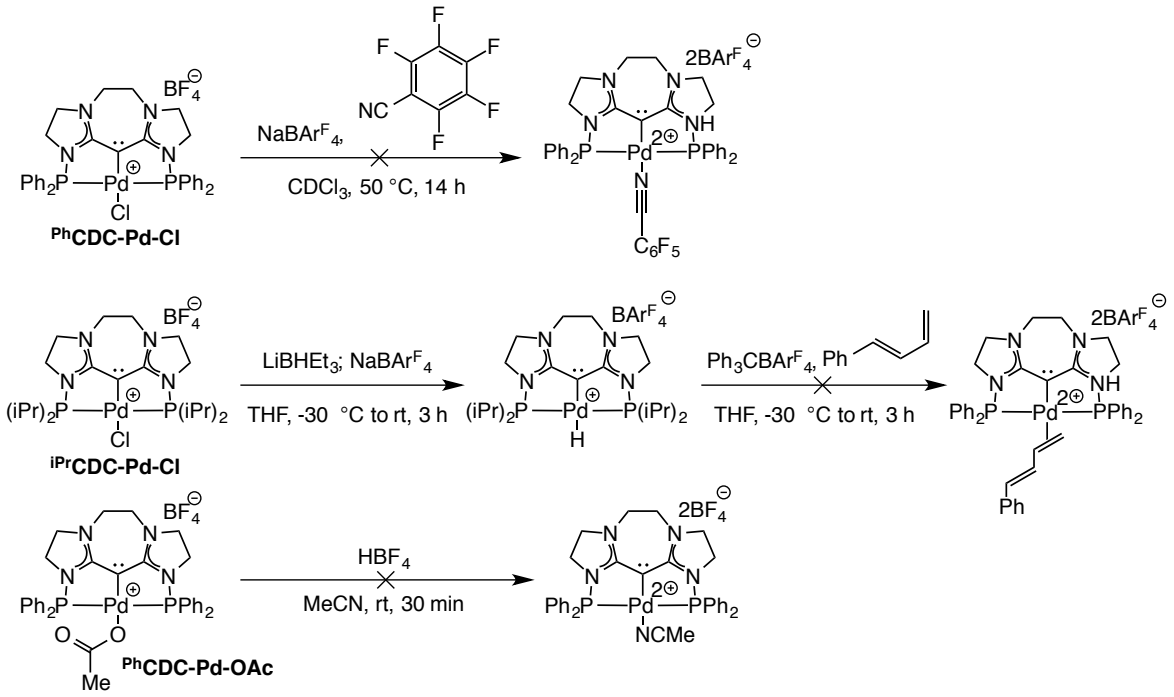
Entry	Catalyst	Yield (%)
1	^{Ph}CDC-Pd-Cl	0
2	^{iPr}CDC-Pd-Cl	0
3	^{Ph}CDC-Rh-Cl	0
4	^{iPr}CDC-Rh-Cl	0

Table 1.5.2-1: Catalyst activity screening for the intramolecular hydroamination of an electron poor amine.

Since the structure of **^{Ph}CDC-Pd-Cl** strongly resembles **2**, the reason for the inactivity of the synthesized CDC-Pd complexes was not immediately apparent. Reaction screens were run with various Ag salts (eg: $AgPF_6$, $AgClO_4$, AgOTf) and a range of solvents (eg: tetrahydrofuran, benzene, toluene, 1,2-dichloroethane) in an effort to discover conditions for catalysis, but no conversion to the desired product was observed (unpublished results). Significant isomerization of the terminal alkene to the internal position did occur, particularly at higher temperatures. Addition of $AgBF_4$ and sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ($NaBAr^F_4$) allowed for conversion to the desired product, however identical conversion were obtained in the absence of the CDC-Pd catalyst. This suggested that a naked Ag cation is capable of intramolecular hydroamination, but failed to provide any evidence of reactivity with CDC ligated complexes.

The repeated failure of CDC-Pd complexes to catalyze a reaction known to occur with similar Pd catalysts suggested that the active dicationic Pd complex was not being efficiently

formed *in situ*. The stoichiometric synthesis of a dicationic CDC-Pd complex was undertaken to resolve this question. We attempted to isolate the complex generated after abstraction of the chloride from **^{Ph}CDC-Pd-Cl** following the conditions developed by Vitagliano *et al.*[221] Ethylene was bubbled through the reaction to trap the dicationic Pd complex theoretically formed from the reaction. However, analysis by NMR spectroscopy showed that the chloride ligand was never abstracted from the complex to form the dicationic Pd species. These conditions were very similar to those used *in situ*, meaning that it is unlikely the desired dicationic complex would also have formed during the catalytic screen for intramolecular hydroamination. Several conditions were attempted to isolate the dicationic Pd complex including: (i) abstraction of the chloride with $NaBAr^F_4$ and concurrent ligand substitution with alkene or nitrile ligands; (ii) synthesis of the Pd-hydride **^{iPr}CDC-Pd-H** and abstraction of the hydride with triphenylmethyl BAr^F_4; and (iii) protonation of **^{Ph}CDC-Pd-OAc** with strong acid (Scheme 1.5.2-3, unpublished results). None of these attempts reliably produced the desired complex.



Scheme 1.5.2-3: Failed strategies for forming the dicationic CDC-Pd complexes.

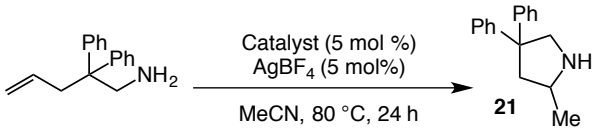
It is not clear why the formation of the dicationic Pd complex is so challenging with the diazepinium CDC backbone considering the similarities between the tridentate diazepinium ligand scaffold and that used in **2**. Based on the IR stretching frequencies discussed above (see Scheme 1.4.1-3), it is unlikely that the σ donation from the diazepinium backbone accounts for the difficulty of abstracting the chloride ligand. The carbonyl stretching frequency show that **^{Ph}CDC** and tridentate pyridine ligand should be similar donors. Therefore both should effectively stabilize the dicationic Pd complex. The most substantial difference between a pyridyl and CDC donor is the π donor properties of the second lone pair on the CDC. We hypothesize that an interaction between this lone pair and the orbitals at the metal center may account for the difficulties of ligand substitution found for the Pd complexes. Ligand substitution of a square planar d^8 metal complex proceeds via an associative mechanism that utilizes an empty metal p orbital. This orbital also aligns with the filled p orbital of the CDC $HOMO^{-1}$. We hypothesize that the CDC may fill the empty orbital necessary for associative ligand substitution, resulting in a much higher energy barrier. This explanation is purely theoretical and we do not currently have the evidence required to fully support this claim. However, the difficulty of generating the dicationic complex does explain the lack of reactivity demonstrated by the CDC-Pd complexes for intramolecular hydroamination.

1.5.3: Intramolecular Hydroamination of Electron Rich Amines

The intramolecular hydroamination of electron rich primary and secondary amines was studied in parallel to the Boc protected amines described above. The reactivity of CDC-ligated metal complexes was tested using the intramolecular formation of pyrrolidines developed by Hartwig (Scheme 1.5.3-1).[173] This reaction is similar to that described in Section 1.5.2, but employs an electron rich primary amine. The primary amine is substantially more nucleophilic,

which allows for addition to less activated π-systems and increases the likelihood that the substrate will inhibit the catalyst by outcompeting alkene coordination.[173] An efficient catalyst must be tolerant of stronger nucleophiles, as exemplified by the broad tolerance of catalyst **1** (Scheme 1.2.2-1) for polar functional groups.

An initial screen of **^{Ph}CDC-Pd-Cl**, **^{iPr}CDC-Pd-Cl**, **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** provided the first example of catalysis with a CDC-ligated metal complex (Table 1.5.3-1). Reaction with the tridentate CDC-Rh complexes produced the desired pyrrolidine in modest 32% yield with both **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl**. Product formation was accompanied by isomerization of the terminal alkene to the internal position. Both **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** provided similar conversions to the pyrrolidine **21**, but the more electron rich **^{iPr}CDC-Rh-Cl** complex was substantially more selective and efficiently suppressed the alkene isomerization side reaction. Initial optimizations were performed with the **^{Ph}CDC-Rh-Cl** complex to observe how changes in reaction conditions affected the selectivity of the reaction for hydroamination versus alkene isomerization.

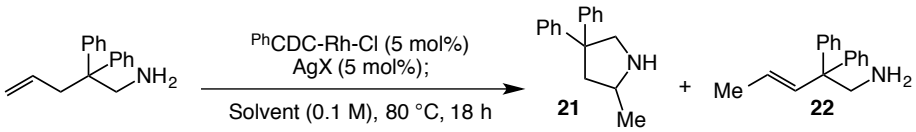


Entry	Catalyst	Yield (%)
1	^{Ph}CDC-Pd-Cl	0
2	^{iPr}CDC-Pd-Cl	0
3	^{Ph}CDC-Rh-Cl	32
4	^{iPr}CDC-Rh-Cl	32

Table 1.5.3-1: Initial catalyst screen for intramolecular hydroamination with electron rich amines.

1.5.3.1: Optimization of the Reaction Conditions

Optimization of the reaction began with a solvent screen (Table 1.5.3-2). Only acetonitrile and benzene were effective solvents for the reaction with acetonitrile proving optimal; the reaction run in acetonitrile yielded 43% of **21**, whereas the same reaction in benzene provided only 11% yield. Although formation of the pyrrolidine was suppressed in other solvents, the alkene isomerization to **22** occurred readily. Entry 6 demonstrates that the reaction is only minimally sensitive to protic conditions; a solvent mixture of acetonitrile and water provides **21** in 24% yield with 47% alkene isomerization to **22**. The presence of oxygen completely shuts down any reactivity, likely due to oxidation of the Rh(I) catalyst. Alternative Ag sources were screened, but the reaction was minimally affected by the identity of the counterion; entry 7 shows very similar reactivity with $AgPF_6$ (32% yield) compared to reaction with $AgBF_4$ (24% yield). A control reaction was performed in the absence of Ag to demonstrate that abstraction of the chloride is necessary (Entry 8); without the Ag activator no hydroamination occurred and isomerization was suppressed.

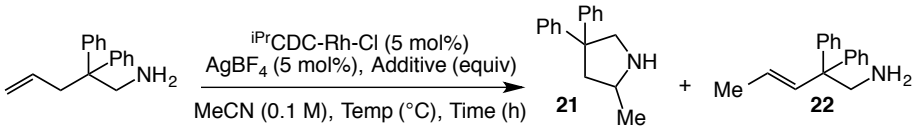


Entry	Solvent	Ag Source	Amine Yield (%)	Isomerization Yield (%)	Ratio
1	MeCN	$AgBF_4$	32	36	1:1.1
2	C_6H_6	$AgBF_4$	11	28	1:2.5
3	Dioxane	$AgBF_4$	0	4	-
4	$MeNO_2$	$AgBF_4$	0	47	-
5	tBuOH	$AgBF_4$	0	41	-
6	H_2O/MeCN (1:1)	$AgBF_4$	24	47	1:2.0
7	MeCN	$AgPF_6$	32	37	1:1.2
8	MeCN	-	0	15	-

Table 1.5.3-2: Solvent screen for the intramolecular hydroamination of a primary amine.

The results reported in Table 1.5.3-2 show that isomerization is prevalent under a variety of reaction conditions when **^{Ph}CDC-Rh-Cl** is used as a catalyst. This side reaction cannot be fully suppressed by modifying the solvent or silver source. However, the initial screen showed that the **^{iPr}CDC-Rh-Cl** complex was substantially more selective. Using this complex, further optimizations were performed to obtain high conversion to the desired hydroamination product **21** (Table 1.5.3-3).

The effect of temperature on the intramolecular hydroamination reaction was examined, and a screen from 60 to 100 °C found that 80 °C was optimal. Temperatures below 80 °C (Entries 1-2) substantially decreased conversion to **21**, whereas higher temperatures failed to increase product formation (Entries 4-5). We hypothesized that the low conversion might be due to product inhibition, since the secondary amine in the product is more basic than the primary amine in the starting material. The addition of ammonium tetrafluoroborate (NH_4BF_4) as a weak acid was explored to see if an acid additive could protonate a portion of the product and prevent inhibition. We were pleased to discover that addition of a substoichiometric quantity of the weak acid improved catalyst turnover, with 0.2 equivalents of NH_4BF_4 proving optimal and providing **21** in 56% yield (Entries 6-9). The effect of the ammonium counterion was explored (Entry 10) and demonstrated that it has a minimal effect on the reaction (55% yield). Extension of the reaction time from 18 h to 48 h provided the pyrrolidine **21** in a synthetically useful yield of 81%. The success of the ammonium additive does not necessarily prove our hypothesis that product inhibition is responsible for the modest reactivity obtained without an acid additive. Later experiments with Lewis acids as activators of the CDC ligand (see Chapter 2) have suggested that there could be a positive interaction between the ammonium and CDC lone pair of electrons that is responsible for the improved reactivity.



Entry	Temp (°C)	Additive; equiv	Time (h)	Amine Yield (%)	Isomerization Yield (%)	Ratio
1	60	-	18	12	2	6:1
2	70	-	18	11	2	6:1
3	80	-	18	32	3	11:1
4	90	-	18	30	2	15:1
5	100	-	18	27	3	9:1
6	80	NH_4BF_4; 0.1	18	52	4	13:1
7	80	NH_4BF_4; 0.2	18	56	2	28:1
8	80	NH_4BF_4; 0.5	18	48	4	12:1
9	80	NH_4BF_4; 1.0	18	32	3	11:1
10	80	NH_4PF_6; 0.2	18	55	4	14:1
11	80	NH_4BF_4; 0.2	48	81	4	20:1

Table 1.5.3-3: Survey of conditions for optimizing intramolecular hydroamination with CDC-Rh(I) catalysts.

1.5.3.2: Control Reactions

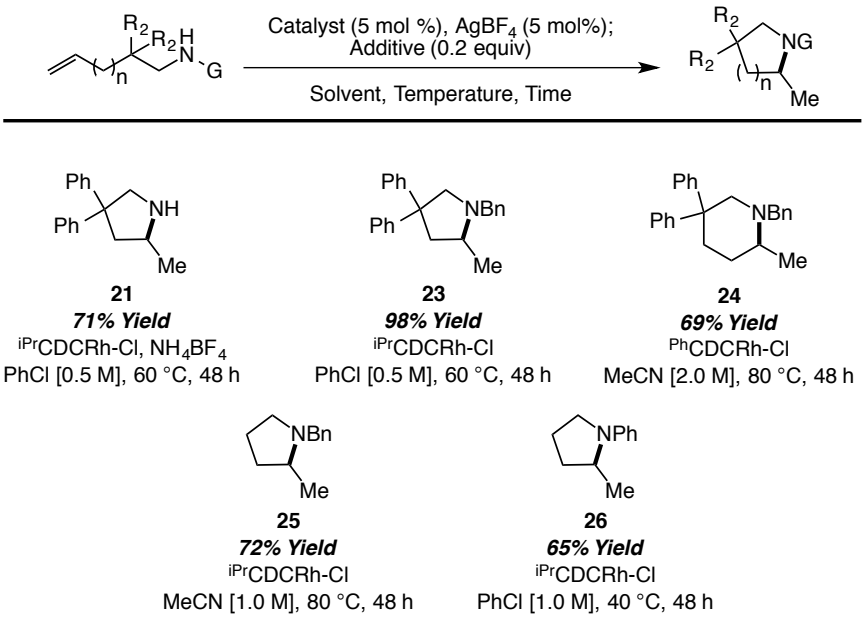
In order to demonstrate that the reaction was not acid catalyzed a series of control reactions were performed. The desired pyrrolidine was formed in 44% yield when 0.5 equivalents of lutidine was added in place of the acidic additive, which is similar to conversions obtained without any additive. If the reaction was acid catalyzed, the addition of basic lutidine would have significantly decreased reactivity. Control reactions were also performed, (i) in the absence of **^{iPr}CDC-Rh-Cl**, (ii) in the absence of the silver salt, and (iii) substituting $[Rh(cod)Cl]_2$ for the CDC-Rh complex. None of these reactions provided the pyrrolidine, demonstrating that the CDC-ligated Rh complex is vital for catalysis.

1.5.3.3: Scope of the Intramolecular Hydroamination Reaction

We sought to explore the limits of catalysis with ^{iPr}**CDC-Rh-Cl** to gauge the proficiency of our CDC-ligated metal complexes for alkene activation and determine their tolerance of Lewis basic functionality. The reaction scope was explored using the optimized conditions developed above (Scheme 1.5.3-4). During substrate screening we discovered that chlorobenzene is an excellent solvent for many substrates, allowing for high conversions at decreased temperatures. For example, **21** can be formed in 71% yield at 60 °C in chlorobenzene, but the same reaction in acetonitrile requires a temperature of 80 °C to provide **21** in 81% yield. Slower reactions favored competitive alkene isomerization, however, by tuning the solvent, concentration, and temperature, we could limit this side reaction for more challenging substrates. In the case of compound **24**, we found that the ^{Ph}**CDC-Rh-Cl** catalyst was optimal, which shows the complementary reactivity between the two CDC-Rh complexes.

Five substrates were tested to probe reactivity and are shown in Table 1.5.3-4. Changing the solvent to chlorobenzene allowed for the isolation of **21** in 71% yield at a lower temperature of 60 °C. Reaction with a secondary benzylamine (as opposed to a primary amine) improved reactivity substantially and **23** could be readily formed in 98% yield at 60 °C. The reaction efficiently catalyzes the formation of 6-membered rings as piperidine **24** is produced in 69% yield. Higher yields were obtained in this reaction by using acetonitrile as solvent because it suppressed competitive alkene isomerization, but required elevated higher temperatures. This tradeoff in reactivity versus selectivity is common across multiple substrates as reactions run in chlorobenzene generally provide higher activity whereas reactions run in acetonitrile provide greater selectivity (see Chapter 2).

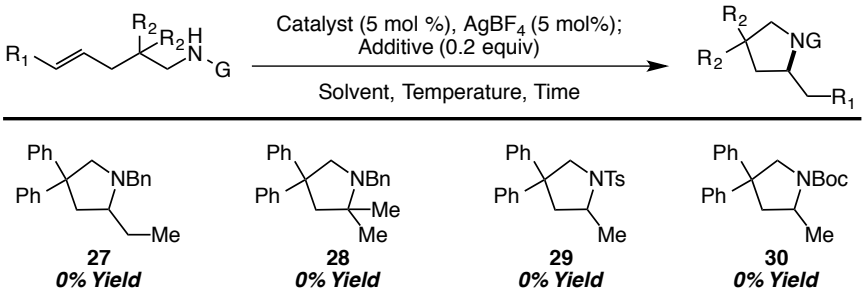
25 was synthesized in 72% yield and demonstrates that geminal substitution on the substrate is not necessary for ring closure. Alkene isomerization is more competitive without the benefits of the Thorpe-Ingold effect, but can be minimized by using acetonitrile as solvent or reducing the reaction temperature. Unexpectedly, an arylamine nucleophile efficiently reacted to form **26** in 65% yield at significantly reduced temperature (40 °C). The fact that a less basic arylamine nucleophile could be added across an alkene at lower temperatures than more basic alkylamines suggested that C-N bond formation was not limiting reaction turnover. Instead, the higher reaction temperatures are probably required to overcome catalyst inhibition or promote proton transfer. We found this highly encouraging as it implied that the CDC-Rh catalyst was efficiently activating the alkene and might be able to catalyze the addition of even weaker Lewis bases.



Scheme 1.5.3-4: Substrate scope for intramolecular hydroamination catalyzed by CDC-Rh-Cl.

In order to show the limitations of the reaction, a second table of substrates is provided that catalogs the substrates that proved inimical to reactivity (Table 1.5.3-5). These compounds show two general limitations to the substrate scope: (i) any substitution on the terminal alkene

prevents reactivity; and (ii) carbamates and sulfonamides are not effective nucleophiles. The attempted formation of **27** and **28** demonstrate the first limitation, as substitution of the alkene at the terminal or internal position is not tolerated. This limitation is likely the result of alkene substitution disfavoring coordination to the Rh catalyst, and subsequently preventing alkene activation. The limitations to the amine scope can be linked to the decreased nucleophilicity of carbamates and sulfonamides compared to alkyl- and arylamines. Attempted hydroamination with sulfonamide and carbamate nucleophiles was unsuccessful as both **29** and **30** failed to cyclize. The lack of conversion with these substrates shows the limit to amine nucleophilicity.



Scheme 1.5.3-5: Failed intramolecular hydroamination substrates.

Overall, the scope of intramolecular hydroamination with CDC-Rh complexes was very encouraging and closely mirrored the catalytic activity of **1** (Scheme 1.2.2-1), which is one of the most general late transition metal catalysts for intramolecular hydroamination (see Section 1.5.1).[173] **^{iPr}CDC-Rh-Cl** catalyzed the addition of highly electron rich secondary and primary amines – which inhibit many electrophilic metal complexes used for alkene activation – while being equally effective with comparatively electron poor arylamines. This suggested that tridentate CDC-Rh complexes could tolerate an unusually broad range of nucleophiles. Furthermore, the catalysts were sufficiently electrophilic to allow for formation of both five and six membered heterocycles without the assistance of the Thorpe-Ingold effect.[175] Intramolecular

hydroamination proved to be a useful metric for gauging the reactivity of ^{Ph}**CDC-Rh-Cl** and ^{iPr}**CDC-Rh-Cl**, but was not sufficiently unique to warrant immediate publication.

1.5.4: Summary and Outlook

This unpublished work is, to the best of our knowledge, the first example of CDCs in catalysis. The reactions described above provided proof of concept that the designed ligand scaffolds could accomplish hydroamination. Furthermore, the brief substrate scope proved to be invaluable for gauging what types of substrates could react using ^{Ph}**CDC-Rh-Cl** and ^{iPr}**CDC-Rh-Cl** as catalysts. The CDC-Rh species favor electron rich primary and secondary alkylamine nucleophiles, but were also exceptionally tolerant of less nucleophilic arylamines. This broad substrate scope was our first clue that tridentate CDC-ligated Rh complexes might have special properties for hydroamination. Our goal was to develop catalytic methods that would have direct applications in the synthesis of natural products and bioactive molecules and, although this reaction is the first example of catalysis with CDC-ligated metal complexes, there are already a number of catalysts for intramolecular hydroamination. We chose to pursue more challenging intermolecular transformations to demonstrate that these complexes have unique properties that can overcome unsolved challenges in catalysis.

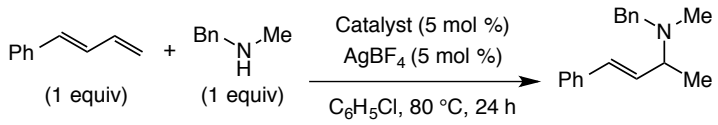
1.6: Intermolecular Hydroamination with Carbodicarbene-Ligated Rh Complexes

The results from our studies in intramolecular hydroamination were highly encouraging and hinted that carbodicarbene ligands could be used to access a broad scope of Rh catalyzed hydroamination substrates. However, our studies on the unique donor properties of these ligands would only be of interest to the synthetic community if we were able to apply CDCs to solving outstanding challenges in catalysis. Intermolecular hydroamination is substantially more

challenging than intramolecular hydroamination and comparatively few examples are known (see section 1.1.4). We chose to focus on addressing this gap in the state-of-the-art as a platform for introducing CDC catalysts to the literature. Intermolecular reactions must overcome a higher entropic barrier than intramolecular processes, and generally require more activating catalysts. Additionally, substrate inhibition is more problematic since the spatial assistance of having the alkene tethered to the amine can no longer assist in ligand substitution.[173] We began our studies by screening a variety of amine and alkene analogs in order to determine if the CDC-Rh catalysts were capable of intermolecular hydroamination. The work discussed herein was published in 2014 and marks the first reported use of CDCs in catalysis.[210]

1.6.1 Screening for Intermolecular Hydroamination

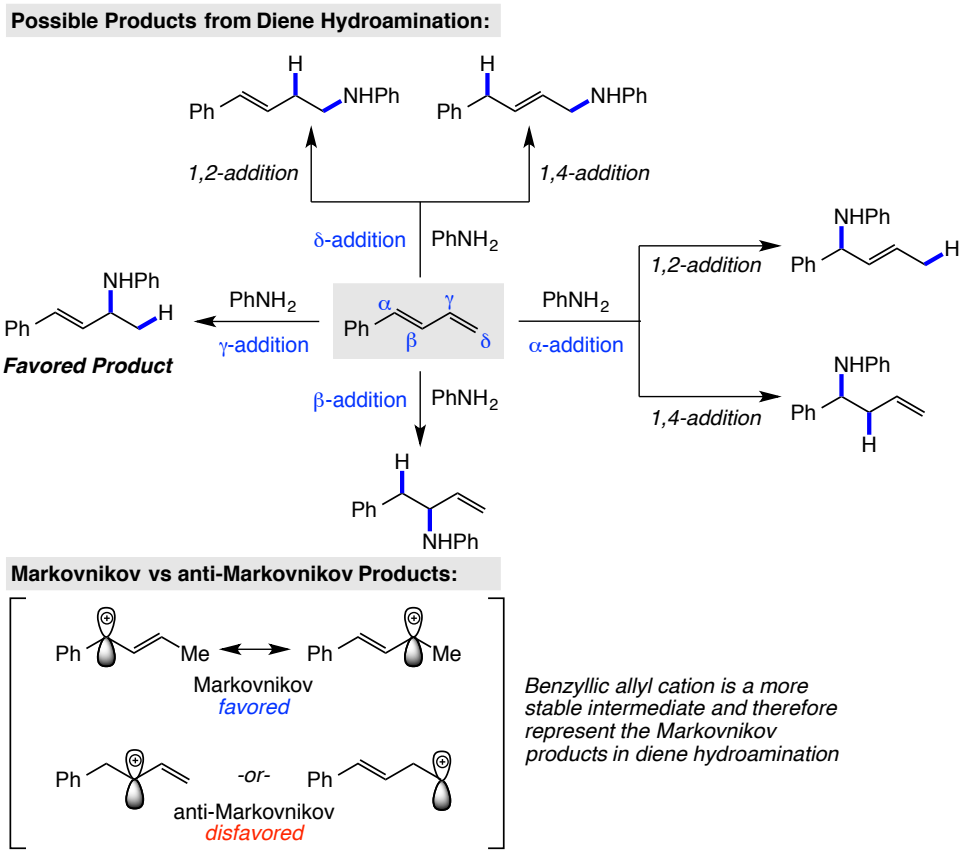
A series of intermolecular test reactions were selected based on the reactivity observed for intramolecular hydroamination with **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl**. N-methylbenzylamine was selected as a test substrate for intermolecular hydroamination because we naively hypothesized that a stronger Lewis base would require less alkene activation. We did not anticipate catalyst inhibition being an issue since our intramolecular studies proved that nucleophilic alkylamines do not irreversibly inhibit the **^{iPr}CDC-Rh-Cl** catalyst. N-methylbenzylamine was paired with several alkene-derived π-electrophiles to explore alkene electrophiles with varied reactivity. Dodecene, styrene, allylbenzene, and phenylbutadiene were tested and we were pleased to discover that the reaction between N-methylbenzylamine and phenylbutadiene proceeded at 80 °C to provide **31** in 34% yield (Scheme 1.5.1-1). This yield nearly doubled to 61% when the catalyst was switched from **^{iPr}CDC-Rh-Cl** to the more active **^{Ph}CDC-Rh-Cl** complex.



Entry	Catalyst	Yield (%)
1	^{iPr}CDC-Rh-Cl	34
2	^{Ph}CDC-Rh-Cl	61

Scheme 1.6.1-1: Discovery of intermolecular hydroamination with CDC-Rh catalysts.

Identical conditions failed to hydroaminate the other alkenes that were explored. This is indicative of the increased reactivity of dienes compared to unactivated alkenes or styrenes. Dienes are not activated alkenes, which have a heteroatom in conjugation with the π-system (eg: α,β-unsaturated ketones), but the second π-bond does provide a slight dipole moment that can help with reactivity. Additions to dienes have the added complication of variable regioselectivity (Scheme 1.6.1-2). Hydroamination with dienes can result in the Markovnikov or anti-Markovnikov products by adding to form the more stable benzylic cation or less stable terminal cation. For a mechanism that proceeds via electrophilic alkene activation, the formation of a C-N bond at the α or γ position of the alkene yields the Markovnikov products. The reaction is further complicated by alkene isomerization prior to the protonation step, which can result in the 1,2- or 1,4-addition products. The hydroamination reactions discussed here favor the formation of the γ-addition products with good selectivity. This is likely due to a combination of Markovnikov selectivity and the steric bias of the substrate favoring nucleophile approach further away from the large aryl ring.



Scheme 1.6.1-2: Describing regioselectivity in the hydroamination of a diene.

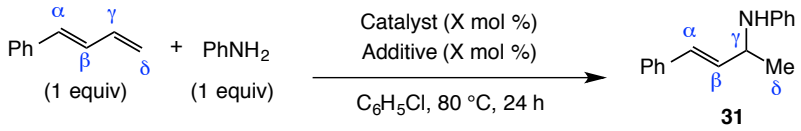
General catalytic procedures for the synthesis of functionalized, unsaturated N-containing molecules by the direct addition of amines to C–C π-bonds offer desirable, atom-economical transformations for chemical synthesis.[2,3,24,27] The catalytic intermolecular hydroamination of phenylbutadiene with alkylamines proves that CDC-Rh catalysts can accomplish this goal by forming valuable allylic amine products. Transition-metal-catalyzed intermolecular addition of amines to dienes to selectively afford allylic amines has been studied;[47,50,123,222–224] however, poor control of site selectivity and the lack of a general catalytic system capable of both aryl and alkylamine additions limit diene hydroamination.[114,159,225–227] Catalytic protocols have focused on the use of aryl and alkylamines in order to obtain high site selectivity. In the interest of filling the

gap in available methods for diene hydroamination and introducing the first example of catalysis with CDC ligands, we chose to extensively explore this transformation.[210]

1.6.2: Optimization of the Intermolecular Hydroamination of 1,3-Dienes

We began our study of diene hydroamination by optimizing the addition of aniline to 1,3-phenylbutadiene (Table 1.6.2-1). This nucleophile was selected because its decreased Lewis basicity allows for generally lower reaction temperatures. Since alkene isomerization was not a concern with phenylbutadiene, chlorobenzene was used as the solvent (as opposed to acetonitrile, see Section 1.5.3) and both **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** were tested. All of the reported results are an average of two reactions. Abstraction of the chloride was necessary for catalysis (Entries 1 and 2) both to generate a more electrophilic Rh center and to open a coordination site for alkene binding. We were pleased to discover that both **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** efficiently catalyzed the transformation providing 66% and 65% yields respectively (Entries 3 and 4). Further screening was conducted with **^{Ph}CDC-Rh-Cl**, although the yields were so similar that later substrate screens were run with both complexes to ensure the optimal catalyst was used. A screen of silver activators with various counterions showed no obvious trend between the degree of counterion dissociation and conversion to product; $AgBF_4$ provided the products in the highest yield, although $AgPF_6$ was similarly effective, providing **31** in 59% yield. We were pleased to discover that a reduction in catalyst loading from 5% to 1% produced the allylic amine in only slightly diminished yields; 1 mol% **^{Ph}CDC-Rh-Cl** yielded 59% of **31** compared to 66% with 5 mol% catalyst. This screen left us with optimal conditions that could be used as a starting point for exploring intermolecular hydroamination with various substrates. As will be discussed below, specific substrates often required modifications to the reaction conditions, but reaction

with 5 mol% ^{Ph}**CDC-Rh-Cl**, with 5 mol% $AgBF_4$ in chlorobenzene at 80 °C is a reliable starting point for most reactions.



Entry	Complex; mol %	Additive; mol %	Conv (%)	Yield (%)
1	^{Ph}**CDC-Rh-Cl**; 5	-	<2	-
2	^{iPr}**CDC-Rh-Cl**; 5	-	<2	-
3	^{Ph}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	75	66
4	^{iPr}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	73	65
5	^{Ph}**CDC-Rh-Cl**; 5	$AgPF_6$; 5	70	59
6	^{Ph}**CDC-Rh-Cl**; 5	$AgSbF_6$; 5	40	31
7	^{Ph}**CDC-Rh-Cl**; 5	AgOTf; 5	60	51
8	^{Ph}**CDC-Rh-Cl**; 1	$AgBF_4$; 1	63	59
9	**14**; 5	-	72	67
10	-	$HBF_4.OEt_2$; 5	<2	nd
11	-	$AgBF_4$; 5	<2	nd

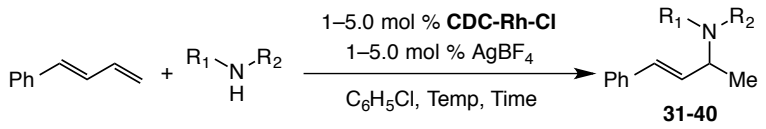
Table 1.6.2-1: Evaluation of the CDC-Rh complexes in hydroamination and optimization of the reaction conditions.

The results described above established optimal conditions for the reaction and proved that lower catalyst loadings can be tolerated with only a marginal effect on conversion. We validated our understanding of the transformation with several control reactions to establish that: (i) the active catalyst was a cationic Rh species, (ii) the reaction was not acid catalyzed, and (iii) the reaction was not silver catalyzed. Entry 9 shows that reaction with the isolated cationic CDC-Rh-acetonitrile complex provides **31** in 67% yield, which is nearly identical to the conversion found for the *in situ* generated complex. This strongly suggests that a cationic Rh species is the active catalyst, although it should be noted that the catalyst formed *in situ* is more effective at temperatures lower than 80 °C. We attribute the reactivity difference at lower temperatures to the presence of the acetonitrile, which may compete with alkene binding and require higher temperatures to dissociate from the metal. Hydrotetrafluoroboric acid etherate ($HBF_4.OEt_2$) was

added (Entry 10) to demonstrate that the reaction is not acid catalyzed. No conversion to **31** was observed and the diene was completely destroyed, presumably due to acid catalyzed polymerization. Lastly, the reaction was run without the CDC-Rh catalyst to show that the silver additive alone is incapable of catalyzing the intermolecular addition of aniline to dienes; Entry 11 shows no conversion to **31** in the absence of ^{Ph}**CDC-Rh-Cl**.

1.6.3: Amine Scope of the Intermolecular Hydroamination

With optimized conditions identified for the addition of aniline to phenylbutadiene, we set out to explore the amine scope of the transformation. C. C. Roberts, a co-author for this work, took the lead in screening these substrates and should be consulted regarding the specifics of their reactivity (Roberts, 2016). Initial screening with N-benzylmethyl amine (see Scheme 1.6.1-1) suggested that basic dialkylamines could be viable substrates for this reaction. Similarly, the optimizations described above demonstrated that arylamines could be utilized. We opted to separate our screening into the amine classes identified by these early observations, (i) electron rich alkylamines, and (ii) electron poor arylamines. A series of arylamines and alkylamines were screened with varied electronic and steric properties to demonstrate the broad scope of the reaction and encourage its use in synthesis.



Entry	Amine; Product	Complex; mol %	Temp (°C)	Time (h)	Conv (%)	Yield (%)
1	$C_6H_5NH_2$; **31**	**^{Ph}CDC-Rh-Cl**; 1	60	24	88	71
2	*p*-$CF_3C_6H_4NH_2$; **32**	**^{iPr}CDC-Rh-Cl**; 2	60	24	96	91
3	*p*-$MeOC_6H_4NH_2$; **33**	**^{iPr}CDC-Rh-Cl**; 3	60	48	68	64
4	*o*-$BrC_6H_4NH_2$; **34**	**^{Ph}CDC-Rh-Cl**; 3	50	48	86	85
5	*o*-MeC_6H_4-NH_2; **35**	**^{iPr}CDC-Rh-Cl**; 5	60	48	89	80
6	morpholine; **36**	**^{iPr}CDC-Rh-Cl**; 3	80	48	92	89
7	pyrrolidine; **37**	**^{Ph}CDC-Rh-Cl**; 5	80	48	80	75[a]
8	Bn_2NH; **38**	**^{iPr}CDC-Rh-Cl**; 2	80	48	58	56
9	Bn(Me)NH; **39**	**^{iPr}CDC-Rh-Cl**; 5	80	48	74	72
10	*n*-Pr_2NH; **40**	**^{iPr}CDC-Rh-Cl**; 5	80	48	14[b]	6

See SI for experimental details; all reactions performed under N_2 atm with 2 equiv. diene; up to >98% site-selectivity; yields of purified products are an average of two runs. [a]With 20 mol % NH_4BF_4 additive; 11% without NH_4BF_4. [b]12% conv at 100 °C.

Table 1.6.3-1: CDC-Rh-catalyzed hydroamination of phenyl-1,3-butadiene with aryl and secondary alkylamines.

The amine scope of the intermolecular hydroamination is shown in Table 1.6.3-1. These results were optimized for temperature, catalyst loading, and reaction time to provide the most efficient conversions to the products **31-35**. The types of amine substrates are split between the first 5 entries, which focus on arylamines, and the second 5 entries, which show reactions with dialkylamines. This division shows that the catalyst can efficiently react amines with highly variable nucleophilicity. Rh-complexes **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** catalyze the hydroamination of phenyl 1,3-butadiene with various aryl and alkylamines to generate allylic amines in >98% γ-selectivity. Dropping the reaction temperature from 80 °C to 60 °C gave **31** in 71% yield, which was a slight improvement over the 66% yield obtained during optimization (Table 1.6.2-1: Entry 3). The findings in entries 2 and 3 of Table 2 illustrate that allylic aryl amines with electron-withdrawing (**32**) and electron-donating (**33**) groups can be accessed with high site-selectivity; the reaction of *p*-CF_3-substituted aniline proves to be slightly more efficient providing 91% yield compared to 64% with *p*-MeO-aniline. Sterically hindered *o*-bromoaniline

and *o*-toluidine (Entries 4 and 5) require 3–5 mol % of ^{Ph}**CDC-Rh-Cl** and ^{iPr}**CDC-Rh-Cl** to generate allylic amines **34** and **35** with complete site-selectivity in 85% and 80% yield, respectively.

The CDC-Rh-Cl complexes also efficiently catalyzed reactions with alkylamines. As shown in Entries 6 and 7, cyclic alkylamines morpholine and pyrrolidine are tolerated and react to furnish allylic amines **36** (89% yield) and **37** (75% yield); however, pyrrolidine requires the use of 20 mol % ammonium tetrafluoroborate (NH_4BF_4) additive. The inclusion of this additive was inspired by our intramolecular hydroamination conditions where it appeared to assist by decreasing catalyst inhibition when strongly Lewis basic and unhindered amines were utilized. Similarly, secondary alkylamines bearing benzyl (Entries 8 and 9) and *n*-propyl (Entry 10) groups can participate in Rh-catalyzed site-selective hydroamination, albeit with varying efficiency. Dialkylamines that do not incorporate branching near the amine proceed efficiently and products **38** and **39** are isolated in 56% and 72% yields respectively. However, the reaction is less effective with nucleophiles that incorporate branching alpha to the amine; for example, diisopropylamine reacts to form compound **40** in only 6% yield. We hypothesize that the reduced reactivity of diisopropylamine is due to the more demanding sterics of the nucleophile interfering with C-N bond formation.

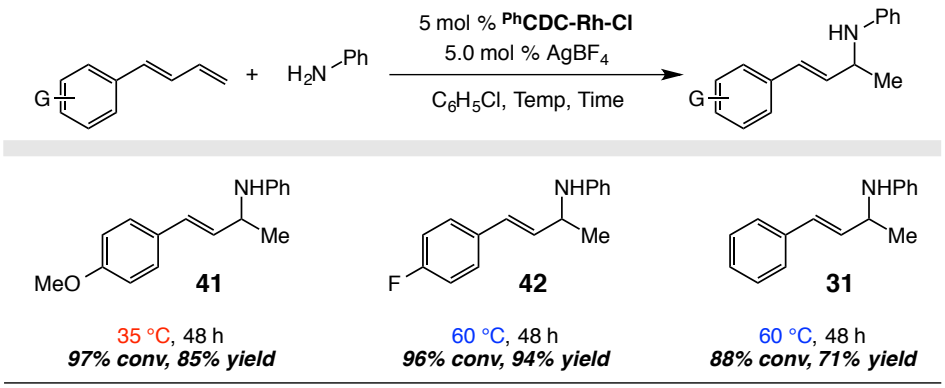
We took several general lessons from the substrate scope cataloged in Table 1.6.3-1. First, the optimal complex (^{Ph}**CDC-Rh-Cl** or ^{iPr}**CDC-Rh-Cl**) and reaction conditions in each case vary depending on the amine structure. Although the ^{Ph}**CDC-Rh-Cl** catalyst was generally more active for the intramolecular hydroamination reactions studied in Section 1.6.2, no obvious trend emerged for the intermolecular transformations. Selection of the given catalyst was almost entirely empirical, although there is some correlation between catalysis with the ^{iPr}**CDC-Rh-Cl**

complex and greater selectivity for the 1,2-addition products. Second, in general, CDC-Rh-catalyzed hydroaminations with alkylamines require higher temperatures (80 °C) to proceed compared to aryl amines (50–60 °C). This trend was also observed for intramolecular hydroamination (see Section 1.5) and we rationalize it as a result of the greater Lewis basicity of the alkylamine substrates. This increased basicity could cause tighter binding to the Rh complexes and correspondingly greater substrate inhibition, which necessitates higher temperatures to allow for ligand substitution by the alkene. Despite these minor differences between aryl- and alkylamines, the intermolecular hydroamination shows exceptional tolerance for a variety of amine nucleophiles. This is one of the strengths of this transformation, as most hydroamination reactions – especially intermolecular variants – use only a narrow range of amine nucleophiles.

1.6.4: Diene Scope of the Intermolecular Hydroamination

To further evaluate the catalytic properties of the CDC-Rh complexes, we investigated the scope of the diene component. We began by exploring how functionalization of the aryl ring of phenylbutadiene affected reaction efficiency (Scheme 1.6.4-1). When *p*-MeO-phenylbutadiene and *p*-F-phenylbutadiene were explored as substrates we discovered that the electron rich aryl ring allowed for reaction to proceed at significantly decreased temperatures; addition of aniline to *p*-MeO-substituted diene occurs at 35 °C to afford **41** in 85% yield, whereas *p*-F-substituted diene adds efficiently at 60 °C to form **42** in 94% yield. The substantial difference in reactivity between the electron rich aryl ring and the fluorinated aryl ring provides insight into the transition state of the reaction. The increased activity of the *p*-MeO-substituent derives from its ability to stabilize a transition state characterized by a buildup of positive charge. Since the unsubstituted and *p*-F-substituted products **31** and **41** respectively have similar

electronic properties, it follows that both show similar conversions at 60 °C. The mechanism of electrophilic alkene activation is expected to proceed through a positively charged transition state, which aligns with the reactivity observed for functionalized aryl dienes.

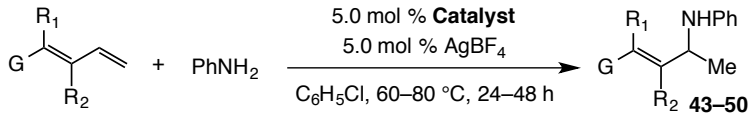


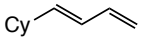
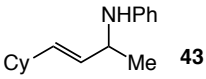
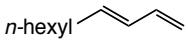
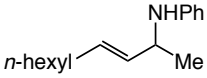
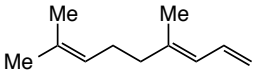
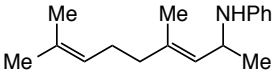
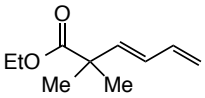
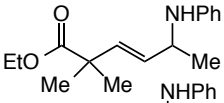
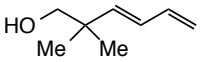
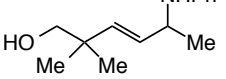
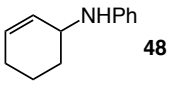
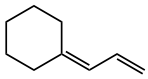
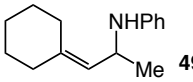
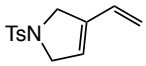
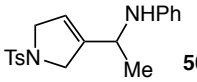
See SI for experimental details; all reactions performed under N_2; yields of purified products are an average of two runs.

Scheme 1.6.4-1: Reactivity of electronically disparate phenylbutadiene derivatives.

The Rh-catalyzed diene hydroamination reaction promoted by a pincer CDC ligand was very tolerant of a variety of alkyl diene substrates. As the representative examples in Table 1.6.4-2 indicate, Rh complexes **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** promote the hydroamination to deliver allylic amine products bearing di- or trisubstituted olefins (up to >98% γ-selectivity for most substrates). Under optimal reaction conditions (5 mol % **^{Ph}CDC-Rh-Cl** at 60 °C) cyclohexyl butadiene is efficiently converted to **43** in 89% yield (Entry 1). Alkyl substituents that lack branching undergo efficient catalytic hydroamination to generate allylic amines as mixtures of constitutional isomers; **44** (5 mol % **^{Ph}CDC-Rh-Cl**, 70 °C; Entry 2) is generated in 70% as an inseparable 3:2 mixture of γ:α addition products. The decrease in regioselectivity is a consequence of the reduction in steric bias from a branched alkane to a linear alkane. Without functionality on the terminus of the diene that sterically differentiates between the γ and α positions, intermolecular hydroamination proceeds with minimal selectivity. A limitation of the CDC-Rh catalysts is that site-selectivity is primarily controlled by the substrate rather than the

catalyst. As illustrated in Entries 3, 7, and 8, trisubstituted 1,3-dienes undergo site-selective (>98%) Rh-catalyzed hydroamination (5 mol % **^{Ph}CDC-Rh-Cl** or **^{iPr}CDC-Rh-Cl**, 80 °C, 48 h) to deliver the corresponding allylic amines in good yield: **45** (97%), **49** (77%), and **50** (69%). The Rh-catalyzed protocol is also effective for the generation of cyclic allylic amines as demonstrated by the formation **48** (Entry 6) in 96% yield. It should be noted that a number of functional groups are compatible under the relatively mild reaction conditions, including: alkenes (Entry 3), esters (Entry 4), alcohols (Entry 5), and *N*-tosyl amines (Entry 8).



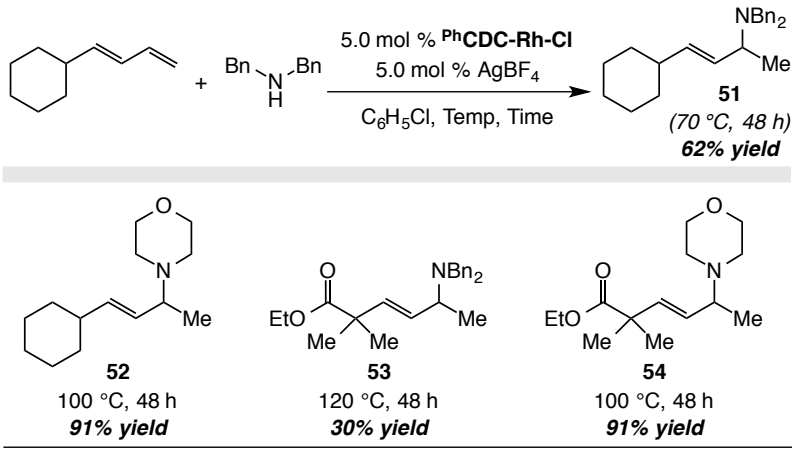
Entry	Diene	Catalyst; Temp (°C)	Product	Yield (%)
1		**^{Ph}CDC-Rh-Cl**; 60	 **43**	89
2		**^{Ph}CDC-Rh-Cl**; 70	 **44**	70[a]
3		**^{Ph}CDC-Rh-Cl**; 60	 **45**	97
4		**^{Ph}CDC-Rh-Cl**; 80	 **46**	78
5		**^{Ph}CDC-Rh-Cl**; 80	 **47**	74
6		**^{Ph}CDC-Rh-Cl**; 60	 **48**	96[b]
7		**^{Ph}CDC-Rh-Cl**; 60	 **49**	77
8		**^{iPr}CDC-Rh-Cl**; 65	 **50**	69

See SI for experimental details; all reactions performed under N_2 atm with 2 equiv. diene; up to >98% site-selectivity; yields of purified products are an average of two runs. [a]3:2 mixture of γ:α addition. [b]4 equivalents of diene were used.

Table 1.6.4-2: CDC-Rh-catalyzed hydroamination of aniline with alkyl dienes.

The four representative examples in Scheme 1.6.4-3 further underline the generality and synthetic utility of this protocol. These substrates demonstrate that amine and diene substrates

from the previous tables can be reliably paired to yield the expected products. As noted above, catalytic hydroamination with aliphatic amines generally requires higher temperatures (70–120 °C) versus aryl amines. Site-selective formation of aliphatic allylic amines **51** (62%) and **52** (91%) from dibenzyl amine and morpholine proceeds efficiently in the presence of 5 mol % **^{Ph}CDC-Rh-Cl** (70 and 100 °C). Incorporation of ester functionality is also tolerated, as catalytic hydroamination delivers **53** (120 °C, 48 h) and **54** (5 mol % **^{Ph}CDC-Rh-Cl**, 100 °C, 48 h) in modest to excellent yields (30% and 91%). These results underscore the general nature of this intermolecular reaction and this study catalogs one of the most broadly tolerant intermolecular hydroamination reactions known in the literature.[210]



See SI for experimental details; all reactions performed under N_2 atm with 2 equiv. diene; yields of purified products are an average of two runs.

Scheme 1.6.4-3: CDC-Rh-catalyzed hydroamination of varied alkyl amines with alkyl dienes.

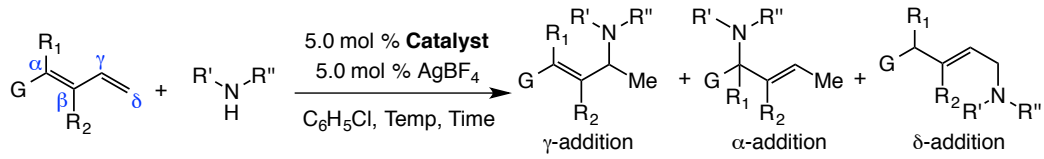
Most of the results discussed in this section were reported in 2014 when we disclosed the first use of CDC-ligands in catalysis. However, a number of substrates that provided lower conversions or yielded inseparable regioisomers were not reported. The data reported in Table 1.6.4-4 has not been published and is less likely to be of synthetic merit, however it is useful in establishing the synthetic limitations of this method and identifying whether a given substrate is likely to react with high conversion and selectivity. Limitations to both the amine scope and

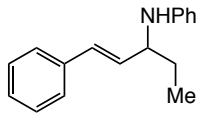
diene scope will be discussed, but data will be provided to demonstrate the limitations to the diene as it is the more nuanced reaction component. The yields reported are from single reactions and are reported as either isolated yields or as NMR yields (see SI for details).

The amine scope is separated into aryl and alkyl amines, both of which can be varied substantially without destroying the regioselectivity of the reaction. After much study, we have established that primary aryl amine nucleophiles react more efficiently than secondary aryl amines and that large *ortho* substituents can begin to decrease conversion. Electronic and steric modifications beyond that are well tolerated, albeit many require some optimization of temperature and catalyst for optimal conversions. Modifying the alkyl amine scope is significantly more challenging, as these reactions generally require higher temperatures and face competitive catalyst inhibition. Disubstituted alkyl amines react reliably provided that the alkyl functional groups are of middling sterics; benzyl and cyclic amines react readily, but branching alpha to the amine decreases conversions dramatically. Cyclic alkyl amines are particularly reliable reaction partners. Various ring sizes hydroaminate a variety of dienes with little need for optimization beyond modifying the reaction temperature.

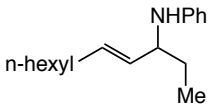
The diene scope is more complicated due to the variety of regioselective additions that can occur. Labeling the diene carbons from the most substituted terminal position shows how the amine addition can occur at the γ, α, or δ position. Addition to the later two positions is accompanied by alkene isomerization to provide the products shown in Table 1.6.4-4. Although other addition products could be imagined, no evidence of their formation has ever been found in these transformations (see Scheme 1.6.1-2). The evidence garnered from these hydroamination reactions suggests that the regioselectivity of the transformation is primarily substrate controlled; switching from the more active **^{Ph}CDC-Rh-Cl** catalyst to **^{iPr}CDC-Rh-Cl** will generally increase

the selectivity for the γ-addition, but can be overridden by minor steric changes to the substrate. The γ-product is the major product when singly substituted terminal dienes are used as reaction partners (see Tables 1.6.4-2 and 1.6.4-3). However, internal dienes show substantially decreased reactivity; **55** and **56** demonstrate that a simple aryl and alkyl internal dienes react to yield 6% and <2% respectively. We hypothesize that this decrease in reactivity is caused by the difficulty of binding an internal diene to the Rh complex. Steric clashes between an internal diene and the CDC ligand will decrease the binding affinity of Rh to the alkene, allowing for the amine nucleophile to outcompete the alkene for the open coordination site.

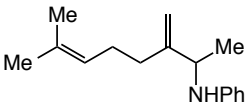




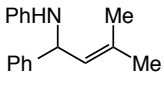
55
^{iPr}CDC-Rh-Cl
80 °C, 24 h
6% Yield
>20:1 *γ:α*



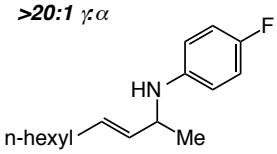
56
^{Ph}CDC-Rh-Cl
60 °C, 24 h
<2% Yield
- *γ:α*



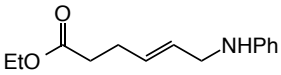
57
^{Ph}CDC-Rh-Cl
80 °C, 24 h
82% Yield
1:1 *γ:α*



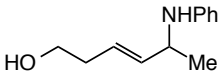
58
^{Ph}CDC-Rh-Cl
110 °C, 48 h
34% Yield
0:1 *γ:α*



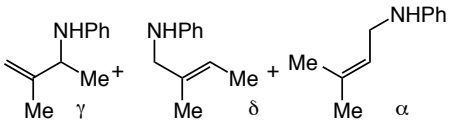
59
^{Ph}CDC-Rh-Cl
60 °C, 24 h
60% Yield
1:1 *γ:α*



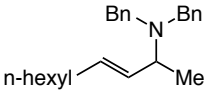
60
^{iPr}CDC-Rh-Cl
30 °C, 24 h
50% Yield
0:0:1 *γ:α:δ*



61
^{Ph}CDC-Rh-Cl
50 °C, 48 h
54% Yield
3:2 *γ:α*



62
^{iPr}CDC-Rh-Cl
60 °C, 24 h
71% Yield
2:1:1 *γ:α:δ*



63
^{iPr}CDC-Rh-Cl
60 °C, 48 h
60% Yield
1:0:1 *γ:α:δ*

See SI for experimental details; all reactions performed under N_2 atm.

Scheme 1.6.4-4: Unselective or unreactive substrates tested during the study of the intermolecular hydroamination catalyzed by CDC-Rh complexes.

The CDC-Rh catalysts are more tolerant of substitution at the α, β, and γ positions of the diene, but decreased conversions are common and regioselectivity varies dramatically. Hydroaminated products **57** and **58** demonstrate how the regioselectivity of the reaction shifts from favoring the γ-addition to preferring the α-addition as the substitution pattern of the diene progressively increases the steric congestion at the γ-carbon relative to the α-carbon. Reaction with myrcene, which is substituted at the β position, yields **57** in 82% yield as a 1:1 mixture of the γ:α regioisomers, whereas substitution at the γ position forms **58** in 34% yield with exclusive addition to the α-carbon. The regioselectivity of these hydroamination reactions can also be eroded by using: (i) electronically varied aryl amines (eg: **59**, 60% yield, 1:1 γ:α regioisomers); (ii) dienes prone to isomerization (eg: **60**, 50% yield, 0:0:1 γ:α:δ regioisomers); (iii) substrates with minimal steric bias (eg: **61**, 54% yield, 3:2 γ:α regioisomers) and (iv) highly reactive dienes (eg: **62**, 71% yield, 2:1:1 γ:α:δ regioisomers). It is particularly notable that the nucleophilicity of the amine also appears to have some impact on regioselectivity, with dialkyl amines preferring the linear substitution pattern (δ-addition), while aryl amines tend to form the branched α-addition products. This exemplified by **59** and **63**, which show comparable yields but opposite regioisomers; **63** is formed in 60% yield as a 1:0:1 ratio of the γ:α:δ isomers, while **59** (described above) reacts to give a 1:1 mixture of the γ:α products.

The inclusion of these less selective substrates provides a more nuanced understanding of the intermolecular hydroamination catalyzed by **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl**. By carefully selecting the substitution pattern of the diene, three different regioisomers can be generated. Although it would be preferable to be able to control this regioselectivity through judicious

catalyst choice rather than by varying the substrate, we believe that the reaction generates valuable products that are challenging to efficiently synthesize via other known methods.

1.6.5: Summary and Outlook

In conclusion, we have developed a tridentate carbodicarbene ligand scaffold that enables efficient Rh-catalyzed site-selective intermolecular hydroamination of 1,3-dienes compatible with both alkyl and aryl amines. The reactions described, represent the first published example of a carbodicarbene transition-metal complex that functions as an effective catalyst.[210] This work efficiently forms C-N bonds, which are ubiquitous in natural products, from readily available diene and amine starting materials. The allylic amine products incorporate an alkene that can conceivably be used as a synthetic handle to incorporate additional functionality. This method provides an unusually broad substrate scope that tolerates amines of varied nucleophilicity and 1,3-dienes with alkyl or aryl substituents. Yields are generally modest to excellent and regioselectivities are high, despite the array of different possible regioisomers. Reactions with more highly substituted dienes do begin to erode regioselectivity. Overall, this work demonstrates how CDC ligands can be used to overcome standing challenges in intermolecular hydroamination. The untapped potential of this new class of ligands has only just been identified and we expect that additional work will elucidate why the structure of the CDC is beneficial for alkene activation.

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CHAPTER 2: CARBODICARBENE-LIGATED RHODIUM COMPLEXES AS ALKENE ACTIVATION CATALYSTS FOR HYDROARYLATION[2]

2.1: Introduction

Chapter 1 of this dissertation established that Rh complexes ligated by a tridentate carbodicarbene (CDC) ligand scaffold could act as catalysts for both intramolecular and intermolecular hydroamination. Chapter 2 will chronicle our efforts to expand the utility of these catalysts beyond hydroamination to the general hydrofunctionalization of dienes. This is nominally an expansion of the nucleophile scope, but would extend the application of CDC ligands to new reaction classes under the greater umbrella of hydrofunctionalization. These reactions share a common mode of olefin activation despite forming different bonds.[1] The large variance in reactivity between nucleophile classes means that few, if any, catalysts are general for multiple classes of hydrofunctionalization.[2,3] Whereas hydroamination is defined as the addition of an N-H bond across a C-C π-system, hydrofunctionalization is more broadly categorized as the addition of any X-H bond across a C-C π-system (Scheme 2.1-1).[4] Since one can readily imagine N-H (eg: amine,[5] amide[6]), O-H (eg: alcohol,[7] acid), and C-H (eg: enol,[8] enamine,[9] aryl[10]) nucleophiles, it is apparent how hydrofunctionalization can be applied to form many desirable molecules from simple starting materials.

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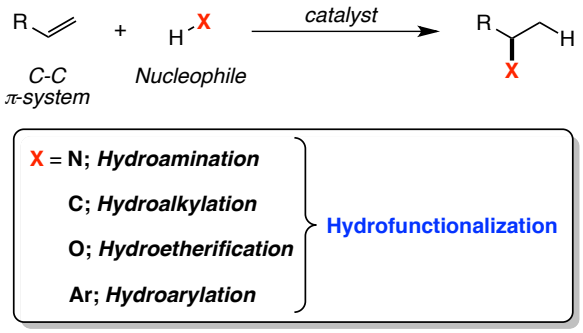
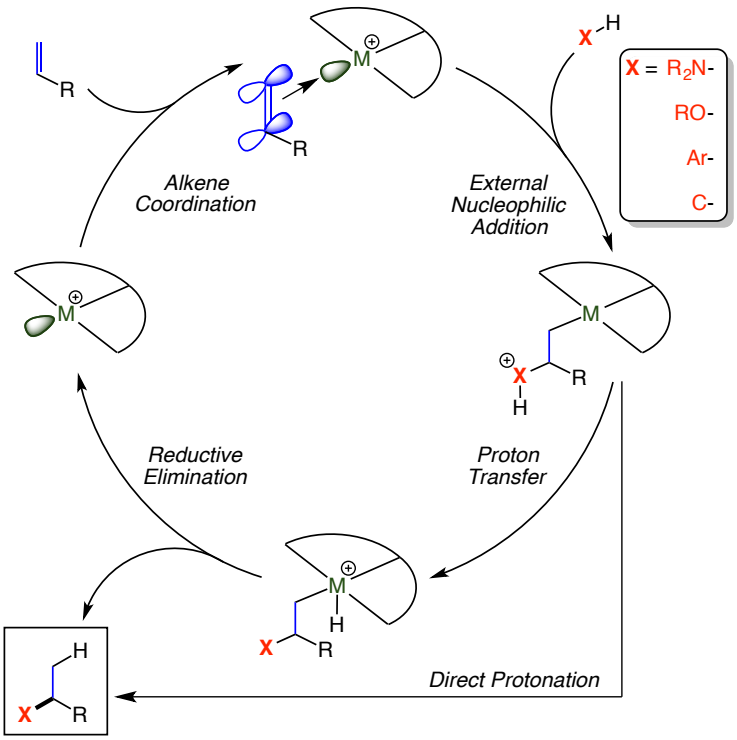
[2] A portion of this chapter appeared as a communication in the Journal of the American Chemical Society. The original citation is as follows: Roberts, C. C.; Matías, D. M.; Goldfogel, M. J.; Meek, S. J., *J. Am. Chem. Soc.* **2015**, *137*, 6488– 6491. Of the work discussed, C. C. Roberts developed and synthesized ^{Ph}**CDC-Rh–styrene**, discovered the hydroarylation reaction in addition to the Lewis acid additive effects. C. C. Roberts and D. M. Matías were responsible for the reaction development, characterization, optimization, and mechanistic studies. M. J. Goldfogel contributed to reaction development and characterization.



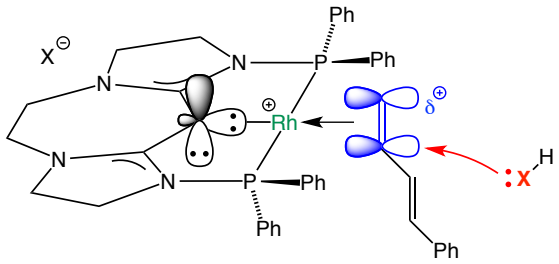
Scheme 2.1-1: Defining classes of hydrofunctionalization.

One of our initial motivations for designing alkene activation catalysts was that their mechanism is translatable to a variety of nucleophiles with minimal catalyst modification.[11] Our initial working hypothesis for the general mechanism of alkene activation is shown in Scheme 2.1-2 and depicts how a single catalytic intermediate can be applied to multiple nucleophiles. The catalyst has minimal influence on the identity of the nucleophile since addition is proposed to occur externally for a catalyst with a single coordination site.[3,12] Conceivably, a single catalyst can allow for a variety of nucleophiles with similar Lewis basicity to add to a common electrophilic intermediate.



Scheme 2.1-2: Working mechanism for alkene activation with tridentate, square-planar metal catalysts.

The anticipated restrictions on the identity of the nucleophile were that it: (i) does not outcompete the π-electrophile for binding to the catalyst, (ii) is sufficiently nucleophilic to add to the π-system, and (iii) will result in an intermediate that is sufficiently acidic to allow for proton transfer to the Rh-alkyl bond. Our studies in intermolecular hydroamination demonstrated that amines with a broad range of nucleophilicity were tolerated and that the catalyst was remarkably resilient to inhibition by Lewis basic molecules.[13] Both of these trends suggested that CDC-Rh catalysts might translate to an array of nucleophiles. We hypothesized that the diene coordinated to the cationic CDC-Rh catalyst was the relevant catalytic intermediate for promoting nucleophilic addition and began searching for a method that could utilize this proposed active species as a general electrophile (Scheme 2.1-3).



Scheme 2.1-3: Hypothetical catalytic intermediate responsible for alkene activation; it was later discovered that this model is missing a key interaction with the CDC (see Section 2.4).

2.1.1 Selecting a Hydrofunctionalization Reaction for Study

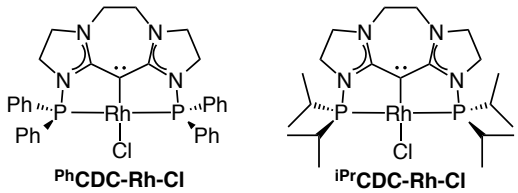
We approached the challenge of applying new nucleophiles to the proposed activated olefin intermediate by selecting a range of reactions and substrates that could be tested. This allowed us to narrow our focus to a reasonable number of substrates that were likely to succeed based on the past reactivity of **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl**. We chose to limit our screening to diene electrophiles, since initial results with hydroamination showed that these alkene derivatives are uniquely effective substrates (see Chapter 1). Furthermore, the incorporation of the second alkene provided a valuable synthetic handle for further functionalization.[14] This choice has since been validated, as expanding the alkene scope beyond dienes has been challenging. The second governing principle for selecting a test reaction was that we wanted to develop intermolecular, rather than intramolecular, transformations. Intermolecular methods are far less common in hydrofunctionalization and are substantially more flexible when applied to synthesis.[3,15] The ease of combining simple, commercially available substrates is a substantial advantage over methods that require the synthesis of a specific intramolecular substrate prior to hydrofunctionalization. This axiom was exemplified by our experience with hydroamination reactions where intramolecular substrates required multi-step syntheses prior to

data acquisition, while intermolecular processes could apply a library of diene electrophiles to rapidly screen substrates with various electronic and steric properties.

The next design decision was to select the class of nucleophiles for study. Chapter 1 demonstrated that C-N bonds could be efficiently formed using the first generation of CDC-Rh complexes, **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** (Scheme 2.1.1-2). Our goal was to develop a catalytic method for forming C-C bonds since C-C bond forming reactions are the benchmark for synthetic methods and lie at the heart of total synthesis.[1,16] Olefin substrates similar to those we have applied to hydroamination have proven to be useful starting materials in many C-C bond forming reactions, as exemplified by the venerable Heck[17] and Friedel-Crafts reactions.[18] These examples show that dienes are already utilized as molecular building blocks in fundamental synthetic methods. Hydrofunctionalization has the potential to improve upon these strategies as it can form C-C bonds with complete atom-economy while generating stereocenters enantio- and/or diastereoselectively.[1]

A brief analysis of the nucleophiles used in Friedel-Crafts and Heck reactions led us to consider arene nucleophiles for our initial hydrofunctionalization screens. The addition of an Ar-H bond across an alkene is referred to as hydroarylation and is a known subset of hydrofunctionalization.[4,12,19,20] Arenes and heterocycles are present in many, if not most, natural products and of substantial synthetic importance.[16] Additionally, arenes are readily available, reliable, and well-studied carbon nucleophiles which are often commercially available. The steric and electronic properties of arene nucleophiles are easily modifiable via the installation of pendant functional groups. Hence, arene nucleophiles can operate as a tuneable platform for probing the impact of subtle electronic and/or steric changes on the efficiency of a reaction via classical Hammett[21] and linear free-energy relationship analyses.[22,23] Developing a method for the

hydroarylation of dienes with CDC-Rh complexes to intermolecularly from C-C bonds would provide a valuable synthetic method and further demonstrate the utility of CDC ligands in catalysis.



Scheme 2.1.1-2: First generation of active CDC-Rh catalysts.

2.1.2 Hydroarylation in the Literature

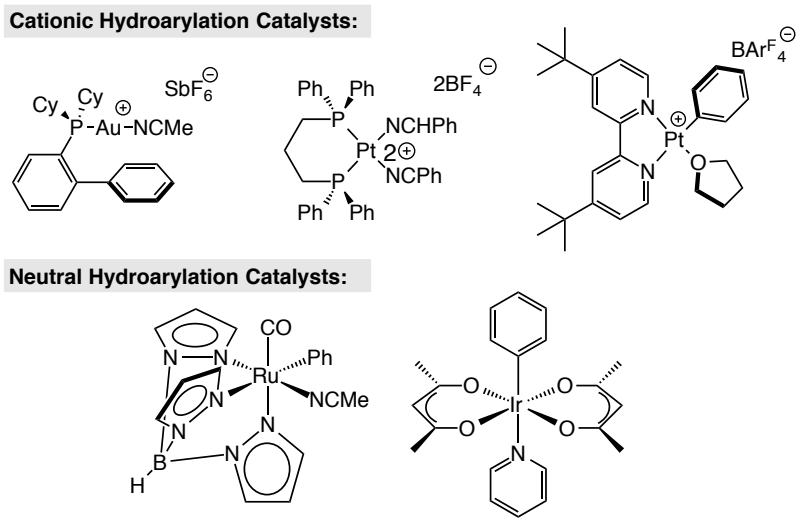
Methods for C-C bond formation via the catalytic addition of nucleophiles to olefins have been studied.[1,2,11] Hydroarylation stands out among these reactions as a highly atom-economical process involving the net C–H addition across an unsaturated C–C bond.[12,19,20] As such, hydroarylation is a potential alternative to Lewis acid catalyzed Friedel-Crafts reactions, which are often used in industrial applications.[12] Friedel-Crafts reactions are limited by selectivity and regiochemistry challenges and there is a significant need for new catalytic methods for arylation.[18,24] Hydroarylation has been studied with a variety of organic acids and metal π-acids, which operate by activating the C=C bond to render it electrophilic and susceptible to addition by arene nucleophiles.[12] Catalytic methods have been developed with Fe,[25] Ru,[26–31] Rh,[32] Pd,[33–36] Pt,[10,37–39] and Au[40–44] catalysts, although many intermolecular methods have focused on the hydroarylation of ethylene and have neglected more complex alkene substrates.[12] Intermolecular hydroarylation reactions typically proceed at elevated temperatures (70–135 °C) in the presence of a cationic Pt, [38,40,43]or Au[41,42,44] catalyst with electron-rich alkenes, and are generally inhibited by Lewis-basic functionality,[44] a problem also common to catalytic hydroamination.[3]

A significant difference between the nucleophile classes used in hydroarylation and hydroamination is that the average nucleophilicity of an arene is substantially lower than that of an amine. The high Lewis basicity of amines means there are relatively few acid catalyzed hydroamination reactions, as the addition of an acid generally results in the formation of an ammonium salt rather than protonation of the olefin to generate a carbon electrophile. This is not the case in hydroarylation reactions since many olefins have comparable Lewis basicity to arenes. As such, acid catalyzed hydroarylation reactions are more prevalent. For example, both trifluoroacetic acid[45] and Lewis acids[46,47] are known to efficiently catalyze the addition of arenes to π-electrophiles. As we develop CDC-Rh complexes for the hydroarylation of olefins we will need to demonstrate that the metal is responsible for catalysis and that the reaction is not catalyzed by adventitious acid.

2.1.2.1 Trends in Hydroarylation Catalyst Design

A number of effective hydroarylation catalysts are depicted in Scheme 2.1.2-1. Many of these catalysts, particularly the Pt[10,37,39] and Au[40,41,43,44] complexes, are cationic as was common for the electrophilic hydroamination catalysts discussed in Chapter 1. Such structures are favored because the electron paucity of the metal center assists in activating the bound alkene towards nucleophilic addition. However, hydroarylation has a substantial subset of catalysts that counter this trend and feature neutral complexes with π-acid ligands and octahedral geometries.[12] These catalyst structures tend to be favored by Ru[26,30,31] and Ir[48–52] catalysts and are an indication that the mode of activation differs from electrophilic alkene activation. Mechanistic studies have shown that these complexes hydroarylate through activation of an aryl C-H bond, followed by insertion of the resulting hydride or arene across a C-C π-system.[4] Catalytic hydroarylation with these complexes is therefore a balance between maintaining a sufficiently electron rich metal center

for oxidative addition into an aryl-H bond, while ensuring that an alkene bound to the metal center is still activated enough to promote migratory insertion.[12] This alternative mechanism is unrelated to the electrophilic alkene activation strategy proposed for our CDC-Rh complexes (see Scheme 1.1.2-3: Cycle A), which should occur through an external addition to a bound alkene rather than migratory insertion. We will focus our efforts on the olefin activation mechanism previously introduced for hydroamination as the proposed active CDC-Rh complexes are monocationic.



Scheme 2.1.2-1: Literature examples of cationic and neutral hydroarylation catalysts.

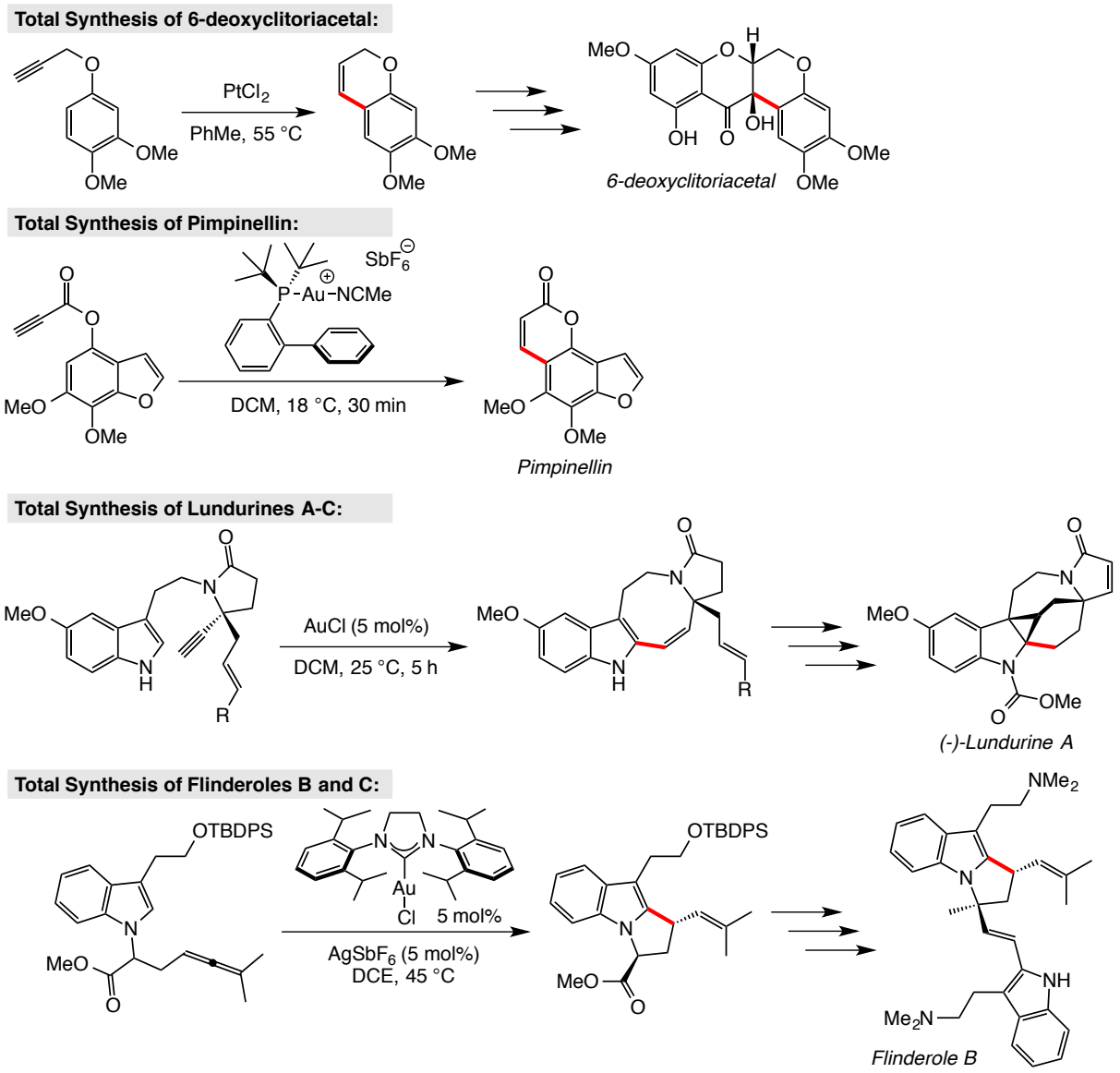
Among the cationic complexes that react through electrophilic activation, we were particularly inspired by the work of Che *et. al.,* who utilized a cationic Au catalyst formed from halide abstraction with Ag to efficiently hydroarylate styrenes, dienes, and unactivated alkenes, with indole nucleophiles.[40] At the time of our studies, this method marked the state-of-the-art for intermolecular hydroarylation under mild conditions. This same catalyst system was used to promote the addition of a range of simple arenes across styrene under mild conditions with temperatures as low as 50 °C.[42] Despite these excellent catalytic examples much of the work in this field has been intramolecular or been confined to intermolecular reactions with

ethylene.[12,26,30,51] New intermolecular and functional group tolerant methods for the general hydroarylation of π-systems would significantly improve the utility of hydroarylation as a synthetic method.

2.1.2.2 Hydroarylation in Total Synthesis

Hydroarylation has been used sparingly in total synthesis with only four relevant examples employing hydroarylation as a key step.[53–56] These synthetic examples mirror the restrictions observed for hydroamination in that: (i) only intramolecular cyclizations have been employed, and (ii) the π-electrophiles that have been used are all sp-hybridized. To our knowledge, intermolecular hydroarylation has not been used in the synthesis of a natural product. The reliability of entropically favored intramolecular reactions, paired with a lack of highly active hydroarylation catalysts, discourages intermolecular applications. The scope of the π-systems employed as electrophiles is similarly stifled. Three of the syntheses employ an alkyne electrophile, while the fourth employs an allene. As such, none of these examples use hydroarylation to generate a stereocenter enantio- or diastereoselectively.

The key steps shown in Scheme 2.1.2-2 serve to demonstrate how hydroarylation is still relatively unexplored in total synthesis. This cannot be due to the identity of the hydroarylation products as related arylation reactions (eg: Friedel-Crafts[18]) are used extensively in total synthesis.[16] We propose that it is the lack of general and reliable methods for intermolecular hydroarylation that is responsible for the scarcity of hydroarylation in synthesis. Since there are so few examples of hydroarylation in complex molecular settings, we cannot use total synthesis as a reliable metric for the specific challenges facing hydroarylation catalysts, yet the absence of examples is an indication of the relative infancy of this field. The success of these few synthetic hydroarylations highlights the impact that new catalysts could have in the literature.



Scheme 2.1.2-2: Examples of hydroarylation in total synthesis.

2.2: Discovery of Hydroarylation with Carbodicarbene-Rh Catalysts

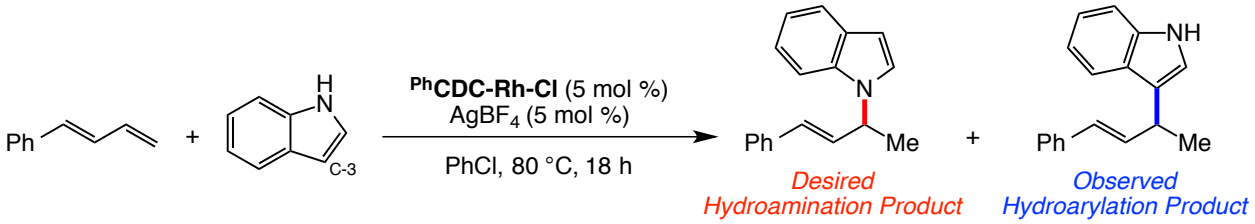
2.2.1 Screening for Catalytic Hydroarylation

Having established a framework for screening reactivity with the CDC-Rh complexes **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl**, we set out to find a specific test reaction. We chose to attempt an intermolecular reaction with diene substrates because intermolecular reactions are

underexplored and dienes displayed reactivity with CDC-Rh catalysts.[13] The reliable activity of 1,3-phenylbutadiene, paired with its selectivity for forming the 1,2-addition products with high regioselectivity, recommended its use as a trial substrate. The optimized conditions from intermolecular hydroamination reactions were appropriated as a starting point in the hope that the temperature (80 °C) and solvent (chlorobenzene) would translate between reactions proposed to occur through the same electrophilic Rh-alkene complex (Scheme 2.1-3). This left only the choice of the arene nucleophile.

During our studies intermolecular hydroamination of dienes we naively attempted to use indoles as amine nucleophiles.[57] However, indoles are more nucleophilic at the C-3 position than at the nitrogen and intermolecular hydroamination failed to provide the C-N bond.[58] Instead, high conversion was observed to the hydroarylated product (Scheme 2.2.1-1). At the time this result was shelved in favor of pursuing amination. However, a survey of the literature found that a similar addition of indole to styrenes and dienes was at the forefront of synthetic methods for hydroarylation.[40] The mild conditions and wide scope of Che's Au catalyzed hydroarylation encouraged us to explore indoles as nucleophiles for our prospective hydroarylation of dienes. As such, a general method for forming allylic indole structures would provide a valuable synthetic method since substituted indoles are found in many natural products.[59]

Indoles are strongly nucleophilic compared to simple arenes,[58] which is likely partially responsible for the exceptionally mild conditions achieved by Che.[40] According to the parameters developed by Mayr *et al.*, the relative nucleophilicity of aniline and indole differs by 7.44 units, whereas a simple arene, such as 1,3-xylene, differs by over 16.[60] As a point of comparison for understanding the range of these nucleophilicity units, an alkene and enolsilane nucleophile exhibits the same approximate difference (7 units) in nucleophilicity by the Mayr scale.

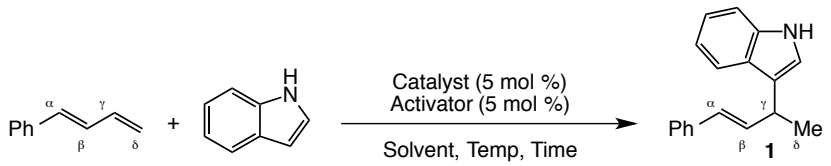


Scheme 2.2.1-1: Serendipitous observation of hydroarylation with indole.

Initial screening of indole with 1,3-phenylbutadiene immediately demonstrated that hydroarylation could be readily catalyzed by both **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** in 77% and 34% yields respectively (Table 2.2.1-1: Entries 1 and 2). **^{Ph}CDC-Rh-Cl** provided the desired product with greater selectivity for the 1,2-addition product over the 1,4-addition. No diene was returned in either reaction. The lost mass balance was ascribed to diene oligomerization, which would result in a large molecular weight oligomer lacking defined NMR signals for a specific side product.[61]

In an effort to improve upon our initial result, we ran a short optimization screen with **^{Ph}CDC-Rh-Cl** to determine how solvent, concentration, reaction temperature, and reaction time effected conversion to **1**. Decreasing the concentration proved to have little effect on the reaction, whereas increasing the concentration produced multiple products non-selectively and consumed the diene substrate; hydroarylation at 0.5 M produced **1** in 76% yield (Table 2.2.1-1: Entry 3) compared to reaction at 2.0 M which provided only 28% product (Table 2.2.1-1: Entry 4). The loss of diene to oligomerization, and the observation that increasing the concentration harmed conversion, led us to believe that the reaction conditions were excessively forcing. This proved true as dropping the temperature to 40 °C allowed us to reduce the reaction time to just 2 h while still generating **1** in 98% yield. Reducing the reaction temperature suppressed the loss of diene to oligomerization and allowed for quantitative conversion to the desired product. This result suggests that indole hydroarylation catalyzed by a CDC-Rh complex is actually more

facile than hydroamination, possibly because the indole nucleophile is less likely to cause substrate inhibition.



Entry	Catalyst; mol %	Activator; mol %	Solvent; M	Temp (°C)	Time (h)	Yield (%)
1	^{Ph}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	PhCl; 1.0	80	18	77
2	^{iPr}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	PhCl; 1.0	80	18	34
3	^{Ph}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	PhCl; 0.5	80	18	76
4	^{Ph}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	PhCl; 2.0	80	18	28
5	^{Ph}**CDC-Rh-Cl**; 1	$AgBF_4$; 1	PhCl; 1.0	80	18	78
6	^{Ph}**CDC-Rh-Cl**; 5	$AgBF_4$; 5	PhCl; 1.0	40	2	98
7	^{Ph}**CDC-Rh-Cl**; 5	-	PhCl; 1.0	80	18	0
8	-	HBF_4	PhCl; 1.0	80	18	0

Table 2.2.1-1: Initial hits for intermolecular hydroarylation with CDC-Rh complexes and optimization to obtain an efficient reaction.

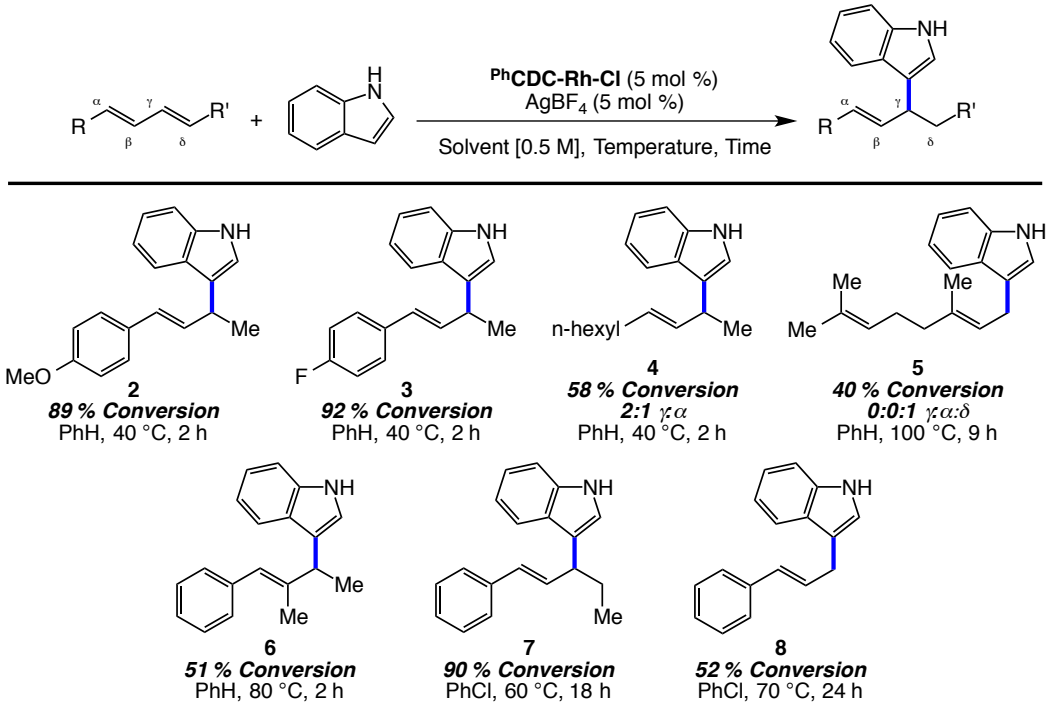
Control reactions were run to establish that the transformation is catalyzed by a cationic Rh species and not through the *in situ* formation of an acid. Generation of the proposed active Rh(I)-olefin complex shown in Scheme 2.1-3 requires catalyst initiation of ^{Ph}**CDC-Rh-Cl** through halide abstraction. As with hydroamination, the halide additive responsible for chloride abstraction was necessary for catalysis and starting materials were returned when the $AgBF_4$ salt was excluded (Table 2.2.1-1: Entry 7). To demonstrate that the formation of **1** was catalyzed by Rh rather than by an *in situ* generated acid, a reaction was performed with HBF_4 added in place of ^{Ph}**CDC-Rh-Cl**. This reaction completely consumed the added 1,3-phenylbutadiene, but failed to yield **1** (Entry 8). We have observed that diene electrophiles are sensitive to acidic conditions when heated and often decompose due to oligomerization. As such, it is unlikely that the hydroarylation of 1,3-phenylbutadiene is acid catalyzed.

2.2.2 Scope of Diene Hydroarylation Catalyzed by a Carbodicarbene-Ligated Rh Complex

Although we spent relatively little effort optimizing the **^{Ph}CDC-Rh-Cl** catalyzed hydroarylation of 1,3-phenylbutadiene, the reaction provided conversions that matched or exceeded those found by Che *et al*. for the related indole hydroarylation of sp^2-hybridized π-electrophiles.[40] It is likely that further optimization could have lowered the catalyst loading and reaction temperature further, but we opted to explore the diene scope to better understand the limits of the reaction. We theorized that the increased reactivity compared to hydroamination might be leveraged to promote reactivity with diene substrates that were previously unreactive. The reaction conditions described above were utilized with the exception that benzene was used in place of chlorobenzene.

The electronics of the diene were well tolerated and reactions proceeded efficiently with electron rich aryl dienes and halogenated aryl dienes; after just 2 h at 40 °C **2** and **3** were formed in 89% and 92% conversion, respectively (Scheme 2.2.2-1). We then explored reactions with alkyl dienes, as they had been more challenging substrates for hydroamination. We were pleased to see that reaction with a linear alkyl diene proceeded with only a minor reduction in conversion to provide **4** in 58% conversion as a 2:1 mixture of regioisomers. As observed for intermolecular hydroamination, substrates without steric bias to direct addition to the terminal alkene resulted in mixtures of the 1,2- and 1,4- addition products. This was even more pronounced in the reaction of myrcene and indole, which proceeded at 100 °C to give **5** in 40% conversion with complete selectivity for the 1,4-addition product where the indole had added to the δ-carbon of the diene. The increased sterics at both the γ- and α-positions resulted in the linear products. This suggests that indole nucleophiles may be more sensitive to steric differences than anilines.

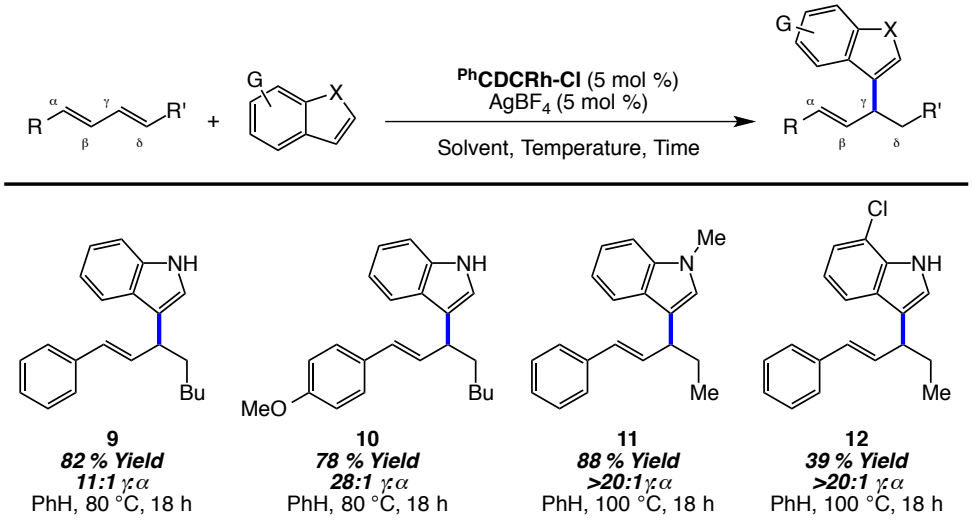
The formations of compounds **2**-**5** demonstrate that hydroarylation can occur with similar regioselectivity to hydroamination at substantially lower temperatures. The apparent increase in reactivity prompted us to explore substituted dienes that were previously unreactive with CDC-Rh catalysts (Scheme 2.2.2-1: Entries 6-8). Reactions with internal and substituted dienes were a consistent limitation to hydroamination, however, hydroarylation with indole proved more tolerant of substitution on the diene; hydroarylation of both internal dienes and 1,2-substiuted dienes proceeds in modest to high conversion providing **6** and **7** in 51% and 90% conversion. Literature examples of regioselective hydrofunctionalization of internal alkenes are rare, as the greater sterics of the π-system disfavor metal coordination to the alkene. Reaction with an allene substrate was also tolerated and **8** could be formed in 52% conversion at 70 °C. This result demonstrates the possibility that an entirely new class of sp-hybridized π-electrophiles could be utilized in CDC-Rh(I) catalyzed hydrofunctionalization, but this possibility was not explored further.



Scheme 2.2.2-1: Diene scope of the intermolecular hydroarylation catalyzed by ^{Ph}**CDC-Rh-Cl**.

We were particularly excited to observe hydroarylation with internal dienes because these substrates were unpublished by Che *et al*.[40] and are rarely tolerated in metal-catalyzed hydrofunctionalization reactions.[3,12,20] Several reactions with internal dienes were run to establish the tolerance of this method for variations to the diene and to the indole nucleophile (Scheme 2.2.2-2). Extensions of the alkyl chain on an internal diene from methyl to butyl was well tolerated and demonstrate that the identity of the internal diene can be varied without impairing conversion; **9** was formed in 82% yield as an 11:1 mixture of the γ:α regioisomers. However, the regioselectivity of the transformation does decrease as the difference in the size of the substituents on either side of the diene decreases (compare >20:1 γ:α for **7** to 11:1 γ:α for **9**). Modifications of the electronics of the internal diene could be used to recover high regioselectivity as the inclusion of the electron donating *para*-methoxy substituent substantially increased regioselectivity while only slightly decreasing conversion; **10** could be formed in 78% conversion as 28:1 mixture of the γ:α regioisomers.

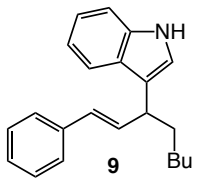
Variations in the indole nucleophile were also tolerated by the ^{Ph}**CDC-Rh-Cl** catalyzed hydroarylation of internal dienes. N-methyl substitution of indole and the inclusion of an electron withdrawing group on the arene backbone did not prevent reactivity, although higher temperatures were required; ^{Ph}**CDC-Rh-Cl** provided **11** in 88% conversion as a >20:1 mixture of γ:α regioisomers and **12** in 39% conversion as a single regioisomer. Reaction with an electron poor indole nucleophile reduced conversion, but maintained exceptionally high regioselectivity.



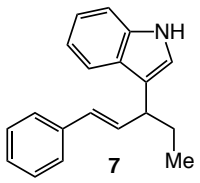
Scheme 2.2.2-2: Further explorations of the scope of hydroarylation with internal dienes.

2.2.3: Problems with Reproducibility in Carbodicarbene Catalyzed Hydroarylation

We were highly encouraged by the versatile scope of **^{Ph}CDC-Rh-Cl** catalyzed hydroarylation, however the reaction was not without difficulties and reproducibility proved to be the Achilles' heel of this method. As is shown by the examples in Scheme 2.2.3-1, reactions that were set up under theoretically identical conditions commonly resulted in conversions that varied by 20% conversion or more; **9** was formed in 98% conversion and 11:1 dr in one reaction, but 78% conversion and 9:1 dr when the reaction was repeated. These inconsistencies were especially apparent when dichloromethane (DCM) was used as a solvent; two reactions to form **7** provided 56% yield or 0% yield respectively without any change in the reaction conditions. The irreproducibility of these results meant that we were uncomfortable publishing these transformations until a solution was found.



1st Data Point:	2nd Data Point:
98 % Conversion	*78 % Conversion*
11:1 γα	*9:1 γα*
PhH, 80 °C, 18 h	PhH, 80 °C, 18 h



1st Data Point:	2nd Data Point:
56 % Conversion	*0 % Conversion*
6:1 γα	*-- γα*
DCM, 60 °C, 18 h	DCM, 60 °C, 18 h

Scheme 2.2.3-1: Irreproducibility in hydroarylation reactions catalyzed by **^{Ph}CDC-Rh-Cl**.

The source of the irreproducibility appeared to be the efficiency of the catalyst activation. The *in situ* catalyst formation was achieved by combining **^{Ph}CDC-Rh-Cl** and $AgBF_4$ in solution and allowing the reaction to stir at room temperature for 1 h prior to substrate addition. Unfortunately, neither **^{Ph}CDC-Rh-Cl** or $AgBF_4$ are completely soluble in non-polar solvents (eg: benzene) and a highly heterogeneous solution that varied in color from purple to red was generated after the 1 h catalyst formation. The reactions became homogenous after the addition of the amine when these conditions were used for intermolecular hydroamination, but the addition of indole did not have the same homogenizing effect. This difference may be rooted in the ligand properties of the nucleophiles since indole cannot bind to Rh or Ag as readily as a Lewis basic amine. Furthermore, this implied that the substrate scope might be impeded by the solubility of a nucleophile rather than the inherent reactivity. Although the *in situ* catalyst generation was previously embraced as an experimental expedience, the likelihood that it was responsible for inconsistent reactivity could not be ignored.

2.3: Developing a Cationic Carbodicarbene-Rh Complex

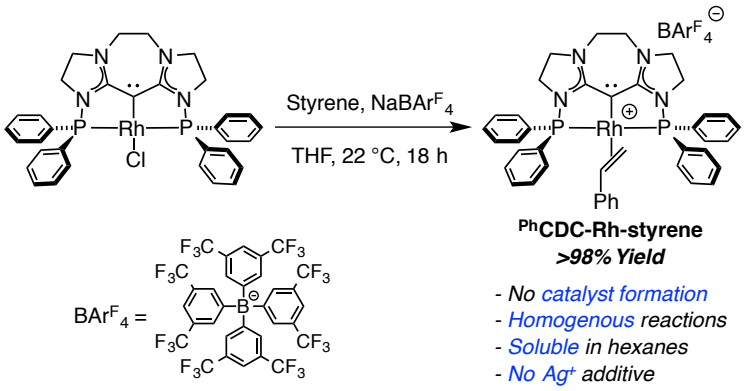
Our discovery that **^{Ph}CDC-Rh-Cl** can be used as a general catalysts for both the hydroamination and hydroarylation of dienes encouraged us to continue studying the activity of CDC-Rh(I) complexes in catalysis. However, our initial foray into hydroarylation demonstrated that the solubility of our first generation complexes was non-ideal. These complexes are

technically pre-catalysts and require activation via halide abstraction prior to catalysis. This meant that $AgBF_4$ has to be added to each reaction, which complicated the experimental procedure, introduced insoluble AgCl salts to the reaction, and resulted in inconsistent conversions and regioselectivities. The heterogeneity of the catalyst formation also limited the solvents that could be explored for hydrofunctionalization; if the solvent was not polar enough to solubilize $AgBF_4$ then catalyst formation could not occur regardless of how effective the solvent might be for the reaction itself.

Many of the drawbacks to the first generation of CDC-Rh catalysts relate to the need for *in situ* catalyst activation. Synthesizing a CDC-Rh complex that was bound by a neutral ligand rather than an X-type chloride could solve these issues. Unlike the chloride ligand, a weakly coordinating L-type donor could be displaced under the reaction conditions by a π-electrophile to provide the proposed active Rh-olefin complex (Scheme 2.1-3). This would obviate the need for catalyst formation and excise the addition of $AgBF_4$ from the experimental procedure. The solubility of the proposed monocationic CDC-Rh(I) complex could be modulated via the anionic counterion.[62] Non-coordinating anions such as tetrakis[3,5-bis(trifluoromethyl)phenyl]borate[63] (BAr^F_4) and tetrakis(pentafluoro)phenylborate[64] have previously been used to solubilize cationic metal complexes and can have significant effects on catalyst reactivity.[65,66] We proposed to synthesize cationic CDC-ligated Rh complexes that do not require catalyst activation using one of these non-coordinating counterions to increase the solubility of the catalyst relative to **^{Ph}CDC-Rh-Cl**. This was accomplished in large part due to the efforts of C. C. Roberts and additional information can be found in her related dissertation (Roberts, 2016).

We envisioned that stoichiometrically abstracting the chloride from **^{Ph}CDC-Rh-Cl** and filling the open coordination site with an L-type donor would provide the simplest synthesis of a

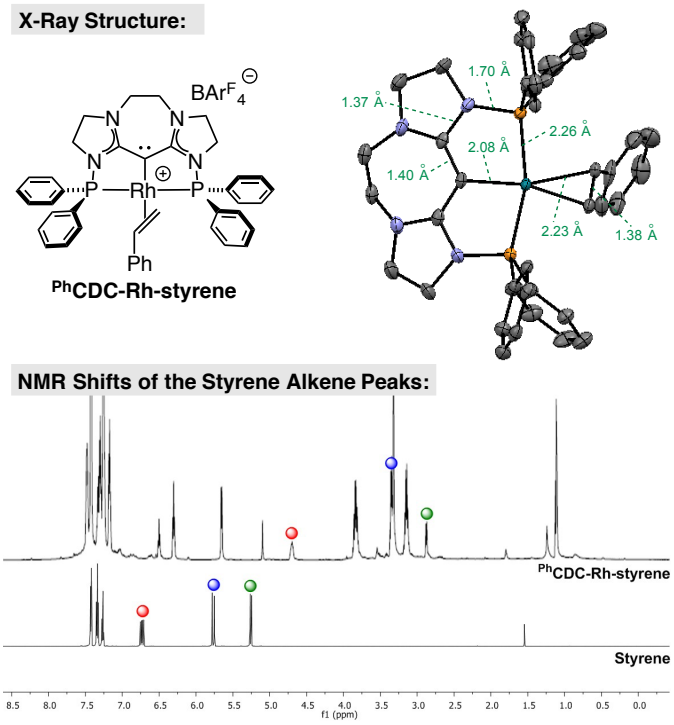
monocationic CDC-Rh(I) complex. We were confident that this strategy could form monocationic Rh complexes, as it is identical to the strategy used to make the cationic catalyst *in situ*. However, our interest in a silver free reaction meant that we needed a replacement for the $AgBF_4$ used for halide abstraction. Sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate[63] proved to be ideal as: (i) the sodium cation was able to abstract the chloride ligand from **^{Ph}CDC-Rh-Cl**, and (ii) the weakly coordinating BAr^F_4 counterion solubalized the resulting monocationic Rh complex (Scheme 2.3-1).[67] Excess styrene was added to the reaction to fill the vacated coordination site with an L-type ligand that could be readily substituted by the diene electrophile during the catalytic cycle. The NaCl byproduct from the halide abstraction could be filtered off to provide styrene-ligated complex **^{Ph}CDC-Rh-styrene** in >98% yield after extensive azeotroping to remove excess styrene. This monocationic CDC-Rh(I) complex was soluble in non-polar organic solvents, such as hexanes and diethyl ether, due to the influence of the BAr^F_4 counterion.



Scheme 2.3-1: Synthesis of **^{Ph}CDC-Rh-styrene**, the monocationic CDC-Rh complex.

To gain insight into the structure of a monocationic CDC-Rh complex, we obtained an X-ray structure of **^{Ph}CDC-Rh-styrene** (Scheme 2.3-2).[67] **^{Ph}CDC-Rh-styrene** has a square-planar structure analogous to **^{Ph}CDC-Rh-Cl** with an sp^2-hybridized central C(0)-donor bound to the Rh center with a C(0)-Rh bond length of 2.07 Å. The styrene ligand exhibits significant metal-

alkene π-back-donation demonstrated by the elongation of the styrene C=C bond from the expected 1.325 Å to 1.395 Å.[68] Additionally, the ^{1}H and ^{13}C NMR shifts for the bound styrene differ substantially from free styrene. The three protons of the alkene alkene shift from 7.34, 6.84-6.77, and 5.86-5.79 ppm in the free alkene to 4.90, 3.44 and 2.99 ppm respectively in the bound alkene. Similarly, the alkenyl ^{13}C peaks shift from 126.2 and 113.7 to 75.6 and 53.4 in the bound alkene.[69] The ligand backbone displays bond angles and lengths that are very similar to those observed for **^{Ph}CDC-Rh-Cl**, which is indicative of the CDC structure and high electron density on the central C(0). Overall, the changes in the ligand backbone from a neutral Rh complex to a monocationic Rh complex are nominal. However, the bond lengths and chemical shifts of the bound alkene indicate the strong activation of the bound π-system.

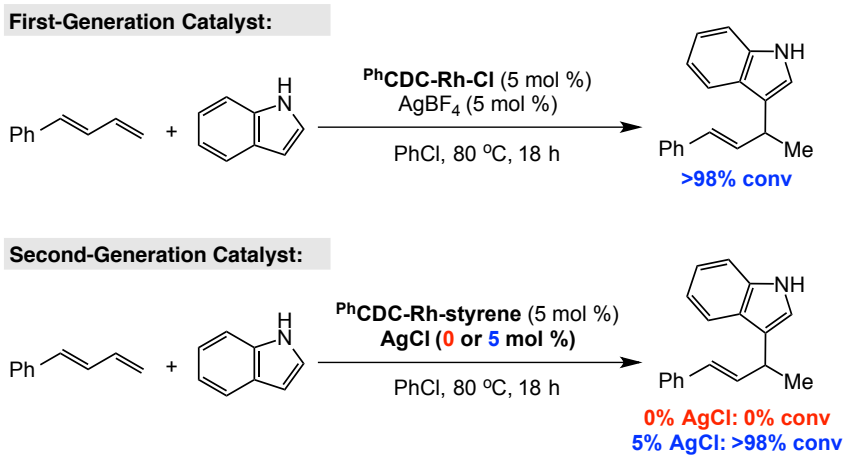


Scheme 2.3-2: Characterization of the cationic CDC-Rh complex by X-ray crystallography and NMR.

2.4: The Discovery of Lewis Acid Activation of Carbodicarbene-Ligated Rh

2.4.1: Discovery of Bimetallic Catalyst Activation

We were excited to explore the catalytic properties of the newly synthesized cationic **^{Ph}CDC-Rh-styrene** complex to determine if removing the catalyst pre-activation could improve reaction reproducibility. We began our investigations by repeating the hydroarylation of phenylbutadiene with indole using the optimized catalytic conditions identified in Section 2.2 (for the original experimental discussion see the dissertation of Roberts, 2016). However, we were surprised to discover that **^{Ph}CDC-Rh-styrene** provided little to no product under identical conditions (Scheme 2.4-1). This completely unexpected result was directly at odds with the active catalytic species we had envisioned (Scheme 2.1-3). If alkene activation was a simple as binding the olefin to a cationic Rh complex, then reactions with **^{Ph}CDC-Rh-styrene** should exhibit similar reactivity to the cationic complex generated *in situ* from **^{Ph}CDC-Rh-Cl** and $AgBF_4$. These results implied that our understanding of the active catalyst and the role of the CDC ligand were oversimplified.



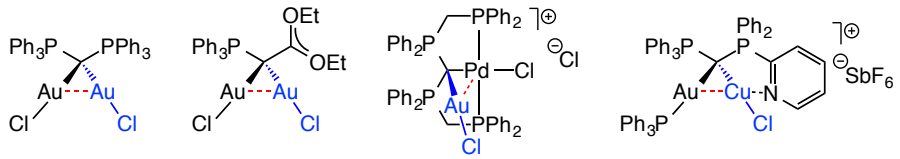
Scheme 2.4-1: Unanticipated difference in reactivity between the neutral and cationic catalysts with and without AgCl.

The unexpected difference in reactivity between **^{Ph}CDC-Rh-styrene** and **^{Ph}CDC-Rh-Cl** led us to carefully examine the differences between *in situ* catalyst formation and direct addition of a cationic Rh complex. The apparent difference in the contents of the two reactions was the presence of the Ag additive. Previously, we observed that the addition of $AgBF_4$ rapidly generated the active cationic Rh complex via halide abstraction and formation of AgCl, which could be observed as a grey/black solid precipitate forming during catalyst activation. We had presumed that this AgCl was an insoluble spectator that remained in the reaction as a byproduct and served no further purpose. However, when AgCl was added back into the reaction catalyzed by **^{Ph}CDC-Rh-styrene** we observed a complete recovery of catalytic activity. The *in situ* catalyst formation and the cationic complex displayed identical reactivity provided AgCl was present (Scheme 2.4-1).

Clearly AgCl had an important and unanticipated role in CDC-Rh(I) catalyzed hydrofunctionalization. We had continually speculated on the importance of the CDC for reactivity, but had little evidence to extrapolate from. The core of a CDC is the divalent carbon(0) supported by two L-type donor groups (see Chapter 1: Section 1.2.4).[70] Unlike their carbon(II) analogs, N-heterocyclic carbenes (NHCs), the reactivity profile of carbon(0) ligands is centered around two lone-pairs of electrons that are available for binding to Lewis acids. We were unsatisfied with the explanation that the unique activity of CDC-Rh complexes was exclusively caused by the σ-strong donation predicted for CDC ligands,[71] but did not have a solid rationale for how the second lone pair of the C(0) ligand could be assisting in catalysis. Ag is often employed as a Lewis acid[72] and we hypothesized that it could serve the same purpose in our reactions. Previous protonation experiments with strong acids demonstrated that the HOMO of the CDC-ligated metal complexes is the second lone pair of the carbon(0). It would follow

that a Lewis acid added to the reaction should bind to the same HOMO at the carbon(0). We hypothesized that his would significantly alter the donation properties of the CDC ligand and could account for the importance of the AgCl additive.

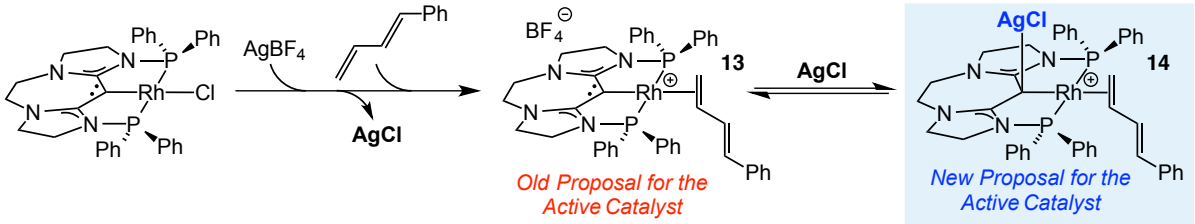
Homo- and hetero-bimetallic transition-metal complexes of carbon(0) have been reported and primarily employ CDC ligand frameworks with coinage metals (Scheme 2.4-2).[73–76] We hypothesized that binding a Lewis acid to the carbon(0), either temporarily or permanently, could electronically and sterically modify the reactivity profile of **^{Ph}CDC-Rh-styrene**.[77] The unique ability of carbon(0) ligands to simultaneously act as strong σ-donors and bind a Lewis acid through the second lone pair could account for the catalytic activity we observed. Furthermore, the use of a carbon(0) bimetallic complex as a catalysts, or the application of Lewis acids to alter catalyst reactivity by secondary binding to carbon(0) ligand, had not been previously reported and would be a worthy addition to organometallic catalysis.[78] Demonstrating the intermediacy of this interaction would significantly improve our understanding of CDC ligands and open a new strategy for tuning catalyst activity without needing to directly modify the CDC ligand itself.



Scheme 2.4-2: Examples of homo- and hetero-bimetallic transition metal complexes with two metal centers bound to a single carbon(0) donor.

This rationale allowed us to update our hypothesis for the catalytically active Rh-olefin complex responsible for general electrophilic alkene activation. Our new hypothesis for the active catalyst is shown in Scheme 2.4-3. Initial coordination of the olefin by the cationic CDC-Rh complex forms the square planar complex **13** previously discussed in Scheme 2.1-3. The lack

of reactivity observed for **^{Ph}CDC-Rh-styrene** without the addition of AgCl demonstrates that **13** it not the active catalyst. This is likely because the Rh-olefin complex is too electron rich to sufficiently weaken the π-system and catalyze external nucleophilic addition. Instead, we propose that a Lewis acid additive is bound to the available lone pair of the carbon(0) on the ligand to form **14**. This interaction between the electron rich CDC and electron poor Lewis Acid reduces the electron density at carbon(0) and occupies the filled π-orbital of the CDC. Together this reduces the donation of the CDC to Rh, resulting in a more electron-deficient Rh center and increased positive charge at the bound alkene. Thus, reversible binding of a Lewis acid to a CDC-Rh(I) complex will result in decreased electron density at Rh(I), rendering the Rh(I) more activating toward π acids. Armed with this new hypothesis, we set out to apply the cationic CDC-Rh complex to the hydroarylation of dienes in order to better understand the importance of CDC ligands in catalysis.



Scheme 2.4-3: Updated model for diene activation catalyzed by a CDC-Rh complex.

2.4.2: Summary and Outlook

The application of this bimetallic system to hydroarylation was described in a communication published in the *Journal of the American Chemical Society* in 2015 and more information can be found there.[67] To briefly summarize, these studies described a key attribute of carbon(0) donor ligands and expanded their limited use in catalysis.[79–81] We showed the potential for tuning ligand donation in CDCs through secondary binding of Lewis acids, which enabled

the use of cationic CDC-Rh-based complexes as catalysts for diene hydroarylation. Notably, simple lithium salts emerged as effective catalytic Lewis acids that could promote reactions under mild conditions for a range of heteroarenes with terminal and internal dienes. The work has been vital to our understanding of the mode of activation responsible for catalysis with CDC ligands. Furthermore, it began to reveal why the unique structure of CDCs could be vital to catalyzing diene hydrofunctionalization. As we suspected in Section 2.4, the strong donor properties of CDCs are not solely responsible for catalytic activity with Rh complexes. The second lone pair is intimately involved in a secondary activation of the complex through binding a Lewis acid additive. The resulting bimetallic catalytic intermediate **14** has become our working hypothesis for further studies with CDC-Rh(I) complexes, replacing our initial hypothesis that **13** was the active catalytic species (Scheme 2.4-3). For details on the substrate scope and characterization of the interaction between the Lewis acid and CDC-Rh catalyst, please see our published work.

2.5: Future Directions

The work discussed in this section has been instrumental in establishing our understanding of how CDC ligands operate in catalysis. The secondary activation by a Lewis acid co-catalyst was discovered entirely serendipitously and has completely changed the way we approach catalysis with CDC-Rh(I) complexes. The ability to tune the reactivity of the metal center without the need for synthesizing a different ligand structure allowed us to publish multiple papers with relatively minor modifications to the initially developed **^{Ph}CDC-Rh-Cl** complex.[13] Introduction of the **^{Ph}CDC-Rh-styrene** complex may seem like a minor change, but it has consistently improved conversions in all hydrofunctionalization reactions and allowed us to utilize non-polar solvents, such as toluene, that have since proved vital for more challenging

reactions. C-C bond formations are a benchmark among catalytic methods and the success of hydroarylation for forming C-C bonds challenged us to take a step beyond well-established indole nucleophiles. Our focus since these studies has been on discovering new carbon nucleophiles that can form more challenging sp^3-sp^3 hybridized C-C linkages. The following work will detail our success in that arena.

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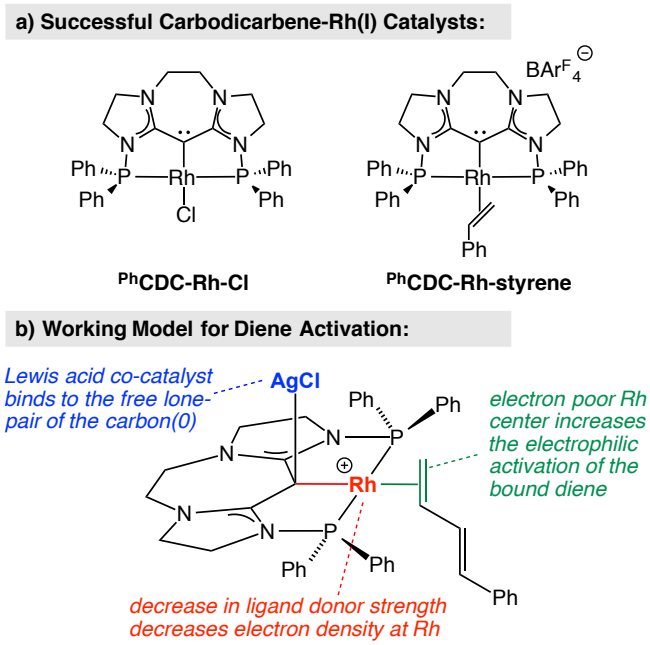
CHAPTER 3: DIENE HYDROALKYLATION WITH CATIONIC CARBODICARBENE-RHODIUM CATALYSTS[3]

3.1: Introduction

Previous work with Rh catalyzed hydroarylation explained a great deal about how tridentate carbodicarbene (CDC) ligands assist in the electrophilic activation of dienes.[1,2] The related CDC complexes **^{Ph}CDC-Rh-Cl** and **^{Ph}CDC-Rh-styrene** (Scheme 3.1-1a) proved themselves as reliable catalysts for multiple classes of hydrofunctionalization reactions including hydroamination (Chapter 1), and hydroarylation (Chapter 2). The generality of this catalyst for multiple nucleophiles implied that these reactions are accessing the same electrophilic intermediate (Scheme 3.1-1b). Our hypothesis for this activation mode was refined during the study of hydroarylation to include a bimetallic activation with two metals bound to the CDC carbon(0) center. This chapter will relate how a greater understanding of the catalytic system responsible for alkene activation was applied to expanding the scope of hydrofunctionalizations catalyzed by CDC-Rh(I) complexes to include alkyl nucleophiles.

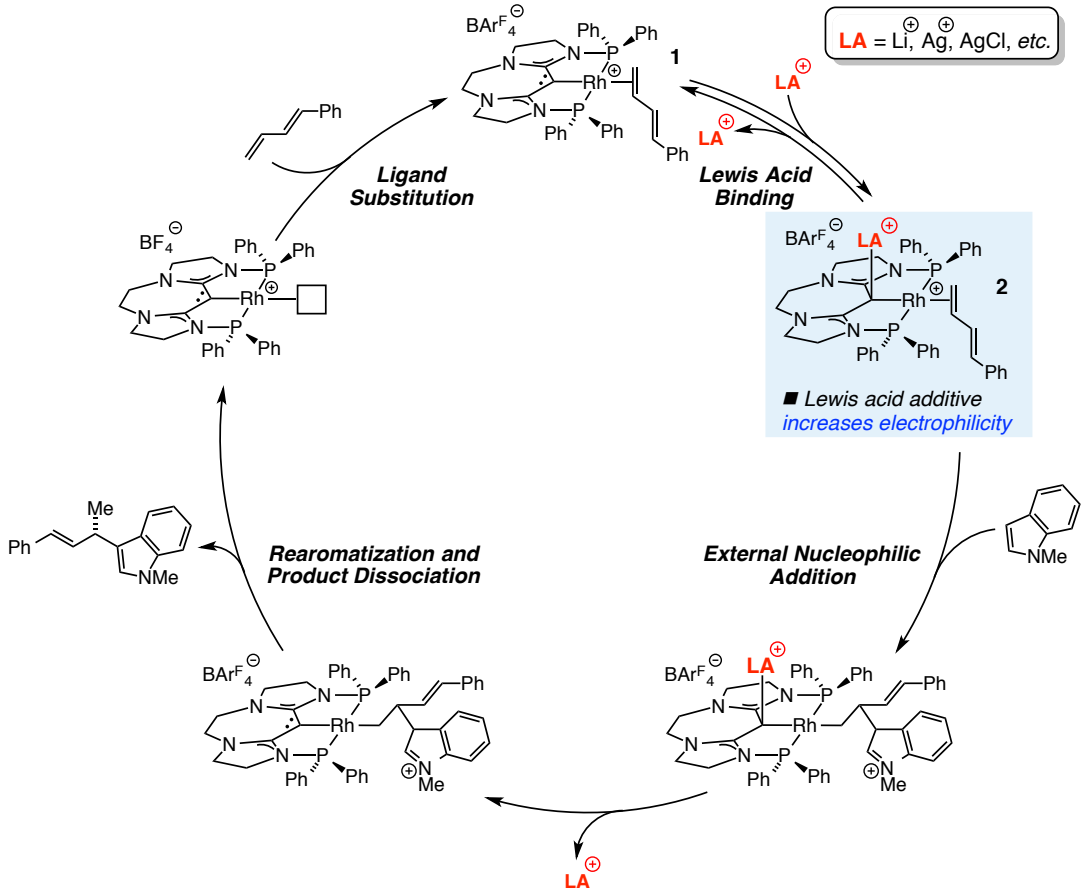
[3] A portion of this chapter appeared as a communication in *Chemical Science*. The original citation is as follows: Goldfogel, M. J.; Meek, S. J., *Chem. Sci.*, **2016**, *7*, 4079-4084.



Scheme 3.1-1: The structures of our CDC-Rh(I) complexes and the proposed activation mode for these catalysts.

The proposed mechanistic cycle is presented in Scheme 3.1-2. Past studies were directed towards the development of an electron poor catalyst capable of activating C-C π-systems towards external nucleophilic addition, yet the assumptions regarding the mechanism were challenged during the development of a catalytic method for hydroarylating dienes with indoles and related nucleophiles. Reactions failed to proceed without the addition of a Lewis acid activator that was able to bind the second lone pair of the CDC carbon(0) to form **2**. This binding temporarily reduced the electron density of the Rh metal and, subsequently, further activated the bound olefin. This activation allowed for the external addition of the nucleophile followed by dissociation of the Lewis acid prior to protonation of the Rh-alkyl bond to deliver the product and regenerate the cationic CDC-Rh(I) complex. The identity of the diene had a far greater impact on hydrofunctionalization than the nucleophile, suggesting addition to the π-system was

occurring externally and that the catalyst and Lewis base interacted in a limited fashion during the transformation.



Scheme 3.1-2: Proposed mechanism for diene hydroarylation catalyzed by a CDC-Rh(I) complex and a Lewis acid co-catalyst.

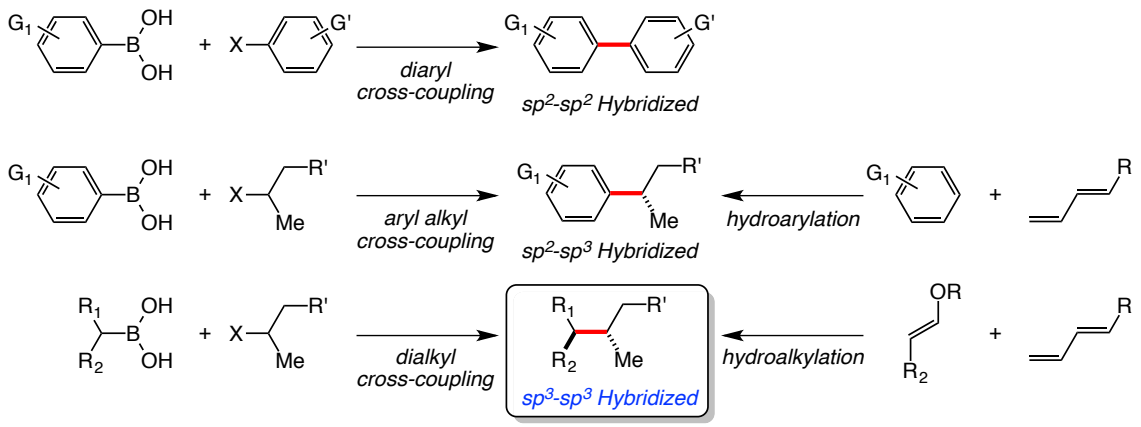
The transient nature of the secondary activation of the carbon(0) with a Lewis acid frustrated any attempts to directly observe it. Evidence pointed to the need for an equilibrium between **1** and **2** that favors **1**, as an excess of the Lewis acid harmed reactivity. The bimetallic activation mode proved to be tuneable through selection of a Lewis acidic metal with greater or lesser charge density. Li salts proved to be the most activating and allowed for hydroarylation at exceptionally low temperatures to form C-C sp^3-sp^2 hybridized linkages. The success of this

strategy prompted us to seek even more challenging bond formations to probe what nucleophiles were are tolerated by the active CDC-Rh(I)-diene intermediate **2**.

Cross-coupling has demonstrated the impact that methods for forming C-C bonds can have on the literature.[3–5] It is no exaggeration to say that the Suzuki-Miyaura cross-coupling has revolutionized chemical approaches to total synthesis and medicine.[6,7] The desire to generate similarly useful carbon frameworks in an atom-economical fashion was a significant driving force behind our desire to develop efficient hydroarylation reactions. As was discussed in Chapter 2, C-C bond forming reactions have become the benchmark for synthetic methods as chemists have highlighted the challenge of constructing the stereodefined carbon skeletons of natural products.[8,9] Our aim was to introduce a C-C bond forming reaction catalyzed by our CDC-Rh(I) complexes that would excite the organometallic and synthetic community and propel CDC ligands into the limelight by finding synthetic applications for their unique reactivity (see Chapter 1).[10]

Research in cross-coupling has progressed from forming C-C sp^2-sp^2 hybridized bonds to sp^2-sp^3 hybridized systems (Scheme 3.1.3).[3,11,12] This has been a significant challenge and spurred the development of numerous novel ligand structures and catalytic methods. Only recently has cross-coupling begun to tackle the challenge of C-C sp^3-sp^3 bonds.[13–15] A tremendous effort has been put forth by the catalytic community to solve this problem and notable professors have built their careers around it (eg: Gregory Fu[16]). Much like cross-coupling, our foray into C-C bond formation through hydroarylation could form C-C sp^3-sp^2 bonds, but left the significant challenge of forming C-C sp^3-sp^3 bonds unsolved. As such, we proposed to develop methods for the hydroalkylation of dienes using alkyl carbon nucleophiles. Such bond formations allow for the installation of adjacent stereocenters and could lead to useful diastereoselective transformations.[8]

Alkyl C-C bond formations rapidly generate molecular complexity and catalytic methods can quickly generate sterochemically dense products that map onto the complex carbon skeletons of many natural products and pharmaceutical agents.[9] Our efforts in stereoselective catalysis have been relatively unmentioned thus far, (primarily due to limited success, see Chapter 4 for more information), yet this was a significant driving force behind our desire to develop a C-C sp^3-sp^3 bond formation. For these reasons the next goal for hydrofunctionalization with CDC-Rh catalysts was the hydroalkylation of diene electrophiles.

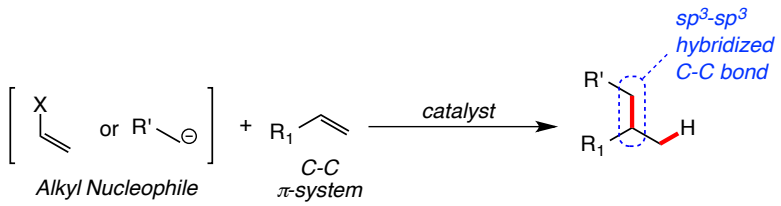


Scheme 3.1.3: Comparing cross-coupling and hydrofunctionalization for the formation of new C-C bonds.

3.1.1 Hydroalkylation in the Literature

The catalytic hydroalkylation of alkenes is a valuable, atom-economical approach for the synthesis of C–C bonds from readily available starting materials.[17] It is formally defined as the addition of an alkyl nucleophile across a C-C π-system to form a new C-C and C-H σ-bond (Scheme 3.1.1-1), which differs from hydroarylation in that the bond formed is between two sp^3-hybridized carbon atoms. The carbon nucleophiles used are usually derived from nucleophilic π-bonds of an sp^2 carbon center (ie: silyl enol ethers[18]). Hydrofunctionalization is often touted as

being an atom-economical process, however hydroalkylation can be the exception to this rule as protected enolate nucleophiles generate byproducts. For the purposes of this section, any carbon nucleophile that adds across a C-C π-system to install an adjacent C-C sp^3-sp^3 linkage and C-H bond will qualify as a hydroalkylation.



Scheme 3.1.1-1: Defining hydroalkylation as a subset of hydrofunctionalization.

3.1.1.1 Classifying Hydroalkylation Reactions by π-Electrophile

Pioneering studies have led to the development of intermolecular processes that employ styrenes,[19–21] unactivated alkenes,[22–25] allenes,[26–28] and alkynes[18,29,30,30–32] as effective substrates that can react with appropriate C-based nucleophiles. These studies will focus on diene electrophiles for the practical reason that they react efficiently with the developed CDC-Rh(I) catalysts[1,2] and because such reactions convert readily available unsaturated hydrocarbons into versatile allyl-containing building blocks. Only a limited number of catalytic intermolecular hydroalkylations of dienes have been reported, with none able to effectively promote the diastereoselective addition of C-based nucleophiles to terminal dienes. Catalytic intermolecular diene hydroalkylation was first accomplished with a Pd catalyst by Takahashi[33] and subsequent Pd catalyzed hydroalkylations have introduced a variety of enolizable nucleophiles.[34–36] These reactions selectively generate linear products via 1,4-addition with modest to excellent site-selectivity. Such reactions work well with small 2,3-substituted dienes, but are limited to methyl-substituted or cyclic substrates for 1,4-substituted dienes (e.g., cyclohexadiene).[39]

3.1.1.2 Classifying Hydroalkylation Reactions by Nucleophile

The type of carbon nucleophile employed can also be used to classify hydroalkylation reactions. The majority of carbon nucleophiles[36–38] can be categorized as enols, enolates, or organometallic reagents. Neutral enol nucleophiles form from *in situ* tautomerization of carbonyl species, either thermally[39] or with the assistance of an acidic[40] or basic[41] promoter. The equilibrium between the enol and carbonyl form must be favorable enough to generate a sufficient concentration of the π-nucleophile to react with an electrophilic π-system. The necessity of this equilibrium limits enol nucleophiles to acidic carbon atoms alpha to a carbonyl or similar π-system. Although many useful products can be formed with readily enolizable C-C π-systems, this curtails the range of nucleophiles that could be utilized. This class of carbon nucleophiles is the most prevalent in the hydroalkylation literature and has been shown with Cu,[39] Ag,[42] Au,[41,43–48] Pd,[22,23,27,28,49–54] Pt,[22,23,55] Rh,[24,25,32] Ru,[56] and Lewis acid[20,40,57–67] catalysts. It is also important to note that the majority of these methods employ 1,3-diketo or malonate nucleophiles and there is a distinct lack of nucleophile diversity in the reported literature.

Enolates are a separate class of carbon nucleophiles that are derived from the anionic form of the enol nucleophiles discussed above. These reagents are prepared by deprotonating alpha to a carbonyl and then trapping the resulting enolate through protection of the anionic oxygen, usually with a silyl group.[18,26,31,68–70] The formed silyl enol ethers can be deprotected *in situ* to form a reactive charged nucleophile either concurrently or prior to addition to the olefin. A proton source, such as an alcohol, is commonly necessary to turn over the reaction and to trap silyl byproducts. The use of enolates significantly increases the scope of carbon nucleophiles available from neutral enols since there is no need for *in situ* equilibrium between the carbonyl and enol tautomers. This has been extensively applied in Mukaiyama-Aldol[71–75] and Michael

additions,[76,77] where the variety and synthetic utility of enolate nucleophiles has been extensively demonstrated. However, far fewer hydroalkylation reactions have been studied with enolates. Examples of silyl enol ether additions to activated carbon π-systems exist (eg: additions to α,β-unsaturated carbonyls), but there are no prior examples of intermolecular enolate additions to unactivated olefins.

The final class of carbon nucleophiles utilized in hydroalkylation is organometallic reagents such as grignards and alkyl-zincs. These more reactive species behave as carbon anions rather than carbon π-nucleophiles. Although there are relatively few publications in this area, Sigman *et al*. has introduced several impressive transformations to this rapidly developing field.[78–81] The increased reactivity of organometallic reagents is both a strength and weakness of this nucleophile class, as the increased nucleophilicity can allow for difficult additions, but the reagents are unstable and must be synthesized rather than purchased. These nucleophiles also trade reactivity for atom economy as they produce metal salts as byproducts (ie: Mg^{2+} or Zn^{2+}).

3.1.1.3 Current Limitations in Hydroalkylation

Although it was discovered as early as 1972 by Takahashi,[33] relatively few methods for hydroalkylation exist. This is mirrored in the limited application of hydroalkylation in synthesis; the only synthetic use for hydroalkylation was in a formal synthesis of KRN7000.[79] Despite the advances in olefin hydroalkylation discussed above, intramolecular[41,45,49,52,82–90] examples predominate. The rarity of intermolecular transformations has been a trend common to all the classes of hydrofunctionalization reviewed in this dissertation and is likely caused by the increased entropic penalty associated with intermolecular reactions. Intermolecular processes can be more generally applied to the synthesis of natural products without the need for the preparation of specific intramolecular substrates. One of the goals of our research program is to

develop intermolecular transformations that bridge the gap between methods development and the application of hydrofunctionalization in total synthesis.

The types of nucleophiles applied to hydroalkylation reactions highlight the lack of diversity in hydroalkylation methods; the majority of examples utilize 1,3-diketone or malonate derived nucleophiles and do not stray from established enols. This is evidenced in the literature in that the number of publications that utilize enols dwarfs those with either enolate or organometallic nucleophiles. Even thermally enolizable nucleophiles other than 1,3-diketones are comparatively uncommon (ie: oxazolones,[26] oxindoles,[28] β-keto amides,[44] etc.). The development of methods for the general addition of multiple carbon π-systems would significantly expand the utility of hydroalkylation.

One of the advantages of hydroalkylation over hydroarylation is that it is capable of forming two adjacent stereocenters in a single step. Limited examples of enantioselective transformations exist for intramolecular reactions[18,31,41,43] and intermolecular reactions[26–28,91] with the majority of the work accomplished by the Trost lab. Diastereoselective transformations are more common, although few are highly diastereoselective (>90% dr).[37,44,45,47,48,68,70,87] Almost all of these diastereoselective reactions are from intramolecular cyclizations, and exhibit selectivities that vary dramatically depending on the substrate. The potential to form two stereocenters enantioselectively has attracted significant attention, but is still an unsolved challenge.

Hydroalkylation is capable of forming exceptionally useful C-C sp^3-sp^3 hybridized bonds and installing two stereocenters, however current methods are not general enough to be used in synthesis. While this reaction is often applied to the transformation of alkenes, the intermolecular hydroalkylation of dienes remains relatively unexplored. This was particularly encouraging as

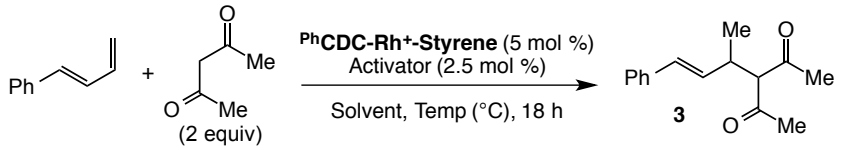
catalysis with CDC-Rh(I) complexes would be a novel addition to the field. A logical first step would be to establish that **^{Ph}CDC-Rh-styrene** could catalyze the intermolecular hydroalkylation of a diene. Starting with an intermolecular reaction would ensure that these studies will impact the field. After establishing proof-of-concept we could look towards expanding the nucleophile scope to include carbon nucleophiles with more varied functionality.

3.2 Intermolecular Diene Hydroalkylation with 1,3-Diketo Nucleophiles

This exploration of intermolecular hydroalkylation initially took direction from literature precedent with thermally enolizable 1,3-diketo nucleophiles. These nucleophiles readily enolize at room temperature without additional additives and are the most common nucleophiles employed in hydroalkylation reactions. Their use minimizes the variables that must be varied to thoroughly screen for reactivity as they form the nascent carbon nucleophile without additional additives or reagents. It was theorized that hydroalkylation catalyzed by **^{Ph}CDC-Rh-styrene** would proceed through the common catalytic intermediate **2** and that the diene electrophiles utilized in hydroamination and hydroarylation would translate between hydrofunctionalizations. Therefore, like the hydroamination and hydroarylation reactions explored in Chapters 1 and 2, the electrophilic activation of 1,3-phenylbutadiene was used for reaction screening.

The reaction conditions developed for hydroarylation were adopted as a starting point for screening intermolecular hydroalkylation with the prototypical 1,3-diketone nucleophile, 2,4-pentanedione. The loading of the activator was dropped to 2.5 mol% on the suspicion that an excess of Lewis base compared to **^{Ph}CDC-Rh-styrene** (5 mol% loading) decreased reactivity by favoring catalytic intermediate **2** over **1** (Table 3.2-1). This precaution was later proven to have little effect on the reaction (see Section 3.3). Additionally, the heavier $LiPF_6$ was substituted for $LiBF_4$ to allow for more accurate mass additions at such low loading. Previously it was observed

that lithium tetrafluoroborate ($LiBF_4$) lithium hexafluorophosphate ($LiPF_6$) reacted similarly, and that the PF_6 counteranion gave slightly improved results for many substrates.

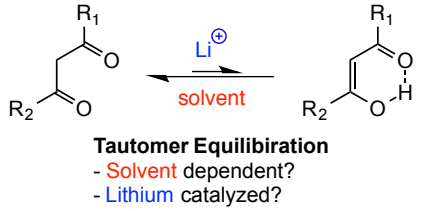


Entry	Activator; mol %	Temp (°C)	Solvent; M	NMR Yield (%)
1	$LiPF_6$; 2.5	50	PhMe; 1.0	**88**
2	$LiPF_6$; 2.5	22	PhMe; 1.0	**17**
3	AgCl; 2.5	50	PhMe; 1.0	**0**
4	$LiPF_6$; 2.5	50	Et_2O; 1.0	**53**
5	$LiPF_6$; 2.5	50	THF; 1.0	**4**
6	AgCl; 2.5	50	Et_2O; 1.0	**5**
7	$Cu(MeCN)_4$ PF_6; 2.5	50	Et_2O; 1.0	**8**
8	NH_4PF_6; 2.5	50	Et_2O; 1.0	**5**
9	$AgBF_4$; 2.5	50	Et_2O; 1.0	**0**

Table 3.2-1: Screening for the hydroalkylation of 1,3-phenylbutadiene with 2,4-pentanedione catalyzed by a cationic CDC-Rh(I) complex.

Initial screening at 50 °C in toluene observed the formation of **3** in 88% yield based on NMR spectroscopy with dimethylformamide (DMF) as an internal standard (Entry 1). This proved that hydroalkylation could be efficiently catalyzed by **^{Ph}CDC-Rh-styrene** and further studies were conducted modifying the temperature, activator and solvent. Reducing the temperature from 50 °C to room temperature (22 °C) dropped the yield to 17% (Entry 2). This suggested that the reaction occurs less readily than hydroalkylation with an indole nucleophile, which occured in quantitative yield at room temperature under similar reaction conditions (see Table 2.5.1-1). Anticipating that the reaction would behave similarly to the hydroarylation, silver chloride (AgCl) was added as an activator. Unexpectedly, the reaction failed to generate **3** and reaction with 5 mol% AgCl in the place of $LiPF_6$ gave 0% conversion (Entry 3). This result discredited the assumption that enolization would be unaffected by the Rh catalyst and/or Lewis

acid. It was hypothesized that the thermal enolization required to form the enol nucleophile might be affected by both the identity of the solvent and the activator (Scheme 3.2-2).



Scheme 3.2-2: Questioning whether the equilibrium between the keto and enol form of 2,4-pentanedione could account for the observed reactivity.

The theory that the tautomer equilibrium was effecting reactivity prompted a brief solvent screen. In diethyl ether (Et_2O) the reaction proceeded in similar conversion to toluene, but conversion was suppressed in more polar THF; reaction in Et_2O provided **3** in 53% yield (Entry 4), whereas the same conditions in THF gave only 4% yield (Entry 5). This is likely due to a decrease in nucleophilicity of the tautomer of 2,4-pentanedione in a more stabilizing polar solvent. The failure to hydroalkylate 1,3-phenylbutadiene with AgCl as an activator could also be attributed to a solubility effect where insolubility of the activator was preventing reactivity in non-polar solvents such as toluene. A series of potential Lewis acid activators was tested in Et_2O to more reliably solubilize the reaction mixtures. Using Et_2O as a solvent was not necessarily optimal for conversion, as it did not provide **3** in as high conversion as toluene, but the increased polarity should tolerate a larger range of Lewis acid activators. A screen including AgCl, tetrakis(acetonitrile)copper(I) hexafluorophosphate [$Cu(MeCN)_4PF_6$], ammonium hexafluorophosphate (NH_4PF_6), and silver tetrafluoroborate ($AgBF_4$) showed substantially decreased reactivity when compared to $LiPF_6$; reaction with AgCl, $Cu(MeCN)_4PF_6$, NH_4PF_6, and $AgBF_4$ provided **3** in 5%, 8%, 5%, and 0% respectively (Entries 6-9). Lithium has been shown to

assist in the tautomerization of ketones to enols and the success of lithium Lewis acids is tentatively attributed to this secondary activation of the 2,4-pentanedione nucleophile.[92]

With effective conditions for the hydroalkylation of 1,3-phenylbutadiene in hand, we proceeded to explore the nucleophile scope to observe how tolerant it would be of differences in the nucleophilicity of the enol (Table 3.2-3). Reaction with methyl acetoacetate proceeded to provide **4** in 71% NMR yield as a 4.5:1 mixture of the γ:α regioisomers. The reaction was only minimally diastereoselective, providing a 1.4:1 ratio of the diastereoisomers. Although the selectivity of this transformation was non-ideal, it did demonstrate that a β-keto ester could be used in place of a 1,3-diketone despite its reduced nucleophilicity. Hydroalkylation with ethyl malonate further cemented this link between enol nucleophilicity and reactivity, as the decreased nucleophilicity of a malonate resulted in the formation of **5** in only 25% yield despite an increased reaction temperature of 80 °C. Meldrum's acid, a cyclic 1,3-diketo derivative, was also tested because it has a nucleophilicity similar to diethylmalonate, but does not readily form the enol tautomer due to its cyclic structure. Reaction with Meldrum's acid failed to yield **6**, which strongly suggests that the enol form is necessary for reaction.

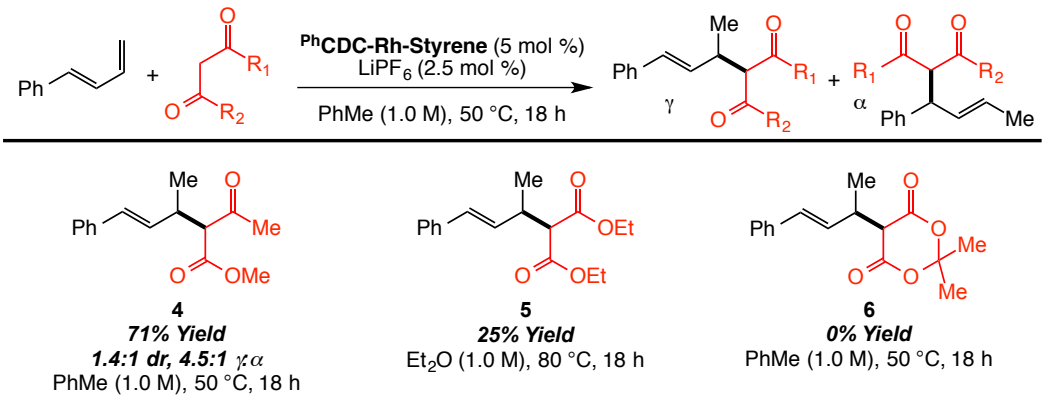


Table 3.2-3: A brief survey of the nucleophile scope for diene hydroalkylation with 1,3-diketo derivatives.

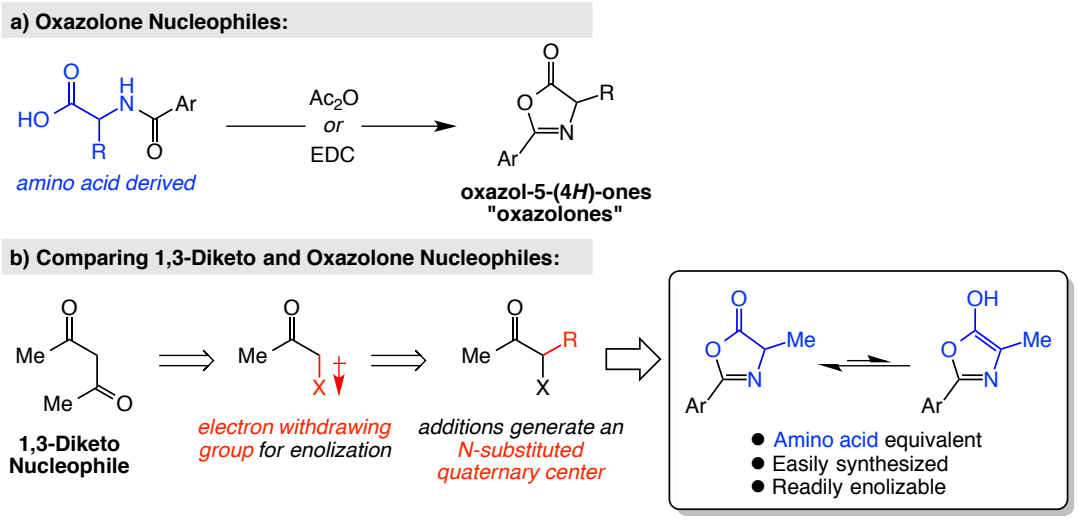
The discovery of hydroalkylation with 1,3-diketo derivatives proved that **^{Ph}CDC-Rh-styrene** could efficiently catalyze the formation of a C-C sp^3-sp^3 hybridized bond. The substrate scope further demonstrated that enol tautomers with varying nucleophilicity can serve as reaction partners. However, thermal equilibration to the enol form is necessary for catalysis as Meldrum's acid did not react with 1,3-phenylbutadiene. Furthermore, reactions that proceed through thermal tautomerization to form the active nucleophile benefit from the use of a lithium activator; this observation would prove vital to further studies where lithium Lewis acids proved vital to obtaining reactivity. Despite these encouraging results, the study of 1,3-diketone additions to dienes was discontinued as the addition of 1,3-diketo nucleophiles has been previously studied and can be accomplished with simple Brønstead acids.[40,62,64,66] It is therefore difficult to justify the need for a complex late-transition metal catalyst. However, the introduction of a highly diastereo- and/or enantioselective transformations would significantly impact this field. As such, focus was moved towards developing the addition of more challenging and synthetically applicable enolizable nucleophiles to showcase the unique reactivity of our CDC-Rh(I) catalysts.

3.3: Diastereoselective Synthesis of Vicinal Tertiary and N-Substituted Quaternary Stereogenic Centers via Intermolecular Diene Hydroalkylation

The knowledge that **^{Ph}CDC-Rh-styrene** could efficiently hydroalkylate diene electrophiles left us with the challenge of finding a class of thermally enolizable carbon nucleophiles that could be useful for the synthesis of natural products. This would increase the utility of the developed method and display the value of our CDC-Rh(I) catalysts for hydroalkylation. Amino acids are ubiquitous in biologically active molecules and this section relates a method for the installation of amino acid surrogates in order to synthesize allylic amino acid derivatives with complete atom-economy.

3.3.1: Selecting Oxazolones as Enolizable Carbon Nucleophiles

In a search of enolizable carbon nucleophiles oxazol-5-(4*H*)-ones are notable as they can enolize to form a carbon nucleophile alpha to both a carbonyl and amine functional group (Scheme 3.3.1-1a). This is functionally analogous to the enolization of an amino acid and provides the opportunity to install amino acids as C-C π-nucleophiles. These heterocyclic rings are commonly referred to as oxazolones and are notable as: (i) useful building blocks in total synthesis,[93] (ii) effective substrates for forming quaternary centers,[94] and (iii) reactive molecules for 1,3-dipolar cycloadditions[95] and ene-type reactions.[96] Oxazolones can be readily synthesized from modified amino acids through cyclization of the benzoylated amino acid under acidic conditions.[95,97] A comparison of the reactivity of 1,3-diketone nucleophiles to oxazolones shows how the cyclic imine acts to increase the acidity of the enolizable carbon similarly to the second carbonyl in a 1,3-diketone (Scheme 3.3.1-1b). This reactivity is exemplified by the low pKa of oxazolones (pKa ≈ 9) and their ability to readily enolize at mild temperatures.[98] Furthermore, oxazolones have proven to be exceptionally useful in the synthesis of unnatural and highly congested amino acids that are otherwise challenging synthetic targets.



Scheme 3.3.1: Introduction to oxazolone nucleophiles and their activity as nucleophiles.

We postulated that the catalyst controlled γ-selective addition of a prochiral enol nucleophile to 1-substituted diene would enable C(sp^3)–C(sp^3) formation and generate vicinal stereogenic centers. By applying our CDC-Rh(I) catalysts to oxazolones nucleophiles we hoped to develop a useful synthesis of allylic amino acid equivalents. Enantioselective Michael additions of 1,3-oxazol-5(4H)-ones to activated C–C π-bonds[94] has been demonstrated (aldehydes,[99] ketones,[100–103] amides,[104–106] allenoates[107]), however, additions to unactivated alkenes or dienes substrates have not been reported. Trost[108,109] and Kawatsura[110,111] have developed methods for the synthesis of allyl substituted oxazolones via metal-catalyzed allylic alkylations, but the products have different substitution patterns than our proposed hydroalkylation reactions and are not derived from diene electrophiles.

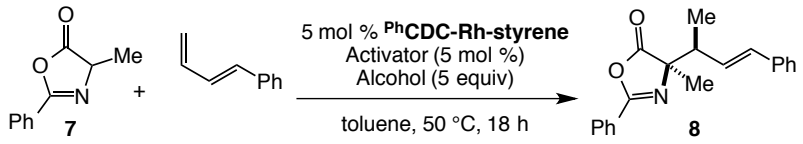
The following discussion will describe our efforts in developing a diastereoselective catalytic addition of substituted 1,3-oxazol-5(4H)-ones to 1-substituted dienes in order to generate vicinal stereogenic centers diastereoselectively. The use of substituted oxazolones has allowed for the formation of N-substituted quaternary centers that can be converted to synthetically challenging amino acid equivalents. This work was published in *Chemical Science* in 2016 (although it is currently only available as an advanced article) and chronicles our first foray into diastereoselective hydrofunctionalization.[112]

3.3.2: Discovery and Optimization of Intermolecular Diene Hydroalkylation with Oxazolone Nucleophiles

We began our search for an efficient catalytic hydroalkylation of dienes by reacting methyl-substituted oxazolone **7** with 1,3-phenylbutadiene in the presence of 5 mol % **^{Ph}CDC-Rh-styrene** and 5 mol % $LiPF_6$ activator in toluene at 50 °C (Table 3.3.2-1, Entry 1). We were encouraged to observe the formation of allylic oxazolone **8** in 17% yield and 10:1 dr (anti/syn).

A brief survey of solvents provided slightly higher yields (up to 21%), but reduced diastereoselectivities (<6:1 dr) in all cases (*vide infra*). As such, toluene was used for further optimization. A variety of Lewis acid activators were screened (Entries 2–4) and demonstrated that lithium salts were most effective; 5 mol % of AgCl and $LiBF_4$ resulted <10% conversion to **8** most likely the due to poor solubility of the metal salt in toluene. The necessity for lithium salts mirrored our earlier experience using 1,3-diketo nucleophiles in hydroalkylation and we hypothesize that the lithium cation may assist in enolization of the oxazolone. Weaker coordinating counter anions lead to dramatically improved reactivity as shown by lithium tetrakis(pentafluorophenyl)borate ($LiBAr^F_4$), which furnishes **8** in 51% yield with 18:1 dr.

We do not currently have a satisfactory explanation for the dramatic effect of the counterion on conversion and diastereoselectivity. Furthermore, the effect of the counterion on the reaction is not necessarily consistent between substrates and reaction conditions. As will be described below, some reactions are more efficient and selective with less dissociated PF_6 counterions or display little difference between PF_6^- and $BAr^F_4^-$. The preferred counterion for a given reaction could only be determined experimentally, although further studies might result in a predictive trend.



Entry	Activator; mol %	Alcohol[b]	Yield (%)[c]; dr[d]
1	$LiPF_6$; 5	-	17; 10:1
2	AgCl; 5	-	0; -
3	$LiBF_4$; 5	-	8; 4:1
4	$LiBAr^F_4$; 5	-	51; 18:1
5	$LiBAr^F_4$; 5	*i*-PrOH	50; 11:1
6	***$LiPF_6$; 5***	***i-PrOH***	***85; 19:1***
7	$LiPF_6$; 5	MeOH	26; 3:1
8	$LiPF_6$; 5	*t*-BuOH	29; 5:1
9	-	*i*-PrOH	0; -
10[e]	$LiPF_6$; 5	*i*-PrOH	0; -

[a]See SI for experimental details; all reactions performed under N_2 atm. [b]A solvent ratio of 40:1 toluene/alcohol used. [c]Yields of purified products are an average of two runs. [d]Values determined by analysis of 400 or 600 MHz ^1H NMR spectra of unpurified mixtures with hexamethyldisiloxane as an internal standard. [e]Reaction run with 2.5 mol % $[Rh(cod)Cl]_2$ and 5 mol % $NaBAr^F_4$ as catalyst.

Table 3.3.2-1: Screening for hydroalkylation of 1,3-phenylbutadiene with Me-oxazolone **7**.

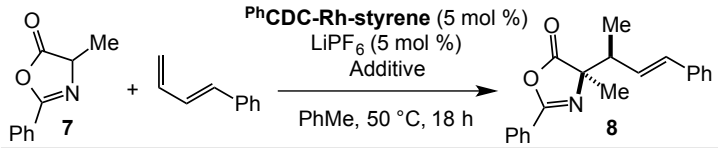
Further increase in reaction efficiency was achieved through the use of alcohol co-solvents (Entries 5–8). While addition of isopropanol (*i*-PrOH) led to no improvement in the $LiBAr^F_4$ promoted reaction (50% yield, 11:1 dr, Entry 5), treatment of **7** and 1,3-phenylbutadiene with 5 mol % **^{Ph}CDC-Rh-styrene** and 5 mol % $LiPF_6$ in toluene/*i*-PrOH 40:1 at 50 °C proved optimal, delivering **8** in 85% yield and 19:1 dr (Entry 6). Screening sterically larger and smaller alcohol co-solvents results in both decreased conversion and selectivity (Entries 7 and 8); methanol (MeOH) and tert-butanol (*t*-BuOH) afforded **8** in 26% yield (3:1 dr), and 29% yield (5:1 dr), respectively. It should be noted that MeOH as a co-solvent leads to competitive oxazolone decomposition via ring-opening. The conditions reported in Entry 6 were identified as optimal and employed in further reaction development, although $LiBAr^F_4$ was found to be optimal for certain substrates (*vide infra*). Additional control reactions run without $LiPF_6$ (Entry 9), or with 2.5 mol % $[Rh(cod)Cl]_2$ and 5 mol $NaBAr^F_4$ in place of **^{Ph}CDC-Rh-styrene** (Entry

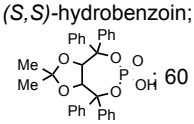
10) result in no reaction, highlighting the importance of cationic (CDC)-Rh complex **1**, in combination with a Lewis acid co-catalyst, for reactivity.

The influence of the identity of the alcohol on reaction efficiency and diastereoselectivity cannot necessarily be explained or predicted from our studies. However, a number of observations were made regarding trends in reactivity: (1) The lithium salt is required for the reaction to occur and reaction does not occur with similar Lewis acid additives. (2) Based on the difference in reaction efficiency between $LiPF_6$ and $LiBAr^F_4$ without *i*-PrOH (Table 3.3.2-1, Entries 1 and 4), it is likely that the alcohol assists in solubilizing the lithium salt. (3) The identity and presence of the alcohol additive dramatically changes the product diastereoselectivity, but a predictive trend cannot be derived from available data. To illustrate this point the addition of alcohol has the opposite effect on reactions with $LiPF_6$ as opposed to $LiBAr^F_4$; reactions that are co-catalyzed by $LiPF_6$ increase in diastereoselectivity from 10:1 to 19:1 dr upon addition of *i*-PrOH (Entries 1 and 6), whereas reactions with $LiBAr^F_4$ decrease from 18:1 dr to 11:1 dr when *i*-PrOH is added (Entries 4 and 5). This suggests that the alcohol must be participating in either hydrogen bonding with the nucleophile or in alcohol solvation of the lithium salt. (4) It is highly unlikely that the reaction is acid catalyzed, as a control reaction run in the presence of 2,6-ditert-butyl pyridine showed no deleterious effects and provided **8** in 23% NMR yield, 20:1 dr without *i*-PrOH, and 86% NMR yield, 20:1 dr with *i*-PrOH (Table 3.3.2-2, Entries 9 and 10). Similarly, this means that the alcohol cannot be acting as a Brønsted acid.

It was theorized that the alcohol was directly assisting in the formation of the active enol nucleophile through hydrogen bonding with the oxazolone. This would account for the impact of the alcohol on diastereoselectivity and explain why reactions still proceed to a lesser degree without it. Based on this theory a chiral additive was introduced in the place *i*-PrOH in the hope

of engendering an enantioselective addition through hydrogen bonding with the oxazolone to catalytically form a chiral nucleophile. These reactions were run with 60 mol% of a chiral or achiral H-bond donor to observe the effects on diastereoselectivity and enantioselectivity (Table 3.3.2-2). The increased loading of the alcohol additive improved conversion and selectivity with the achiral alcohols MeOH and *t*-BuOH, but reaction with *i*-PrOH was essentially unchanged; reaction with MeOH, *i*-PrOH, and *t*-BuOH provided **8** in 68%, 84%, and 87% NMR yields as 7:1, 19:1, and 12:1 mixtures of diastereoisomers respectively. Reaction with menthol gave a similar reaction, but failed to induce any enantioselectivity; the addition of 60 mol% menthol to the reaction provided **8** in 62% NMR yield, >20:1 dr, and 0% ee. Diol additives decreased reaction efficiency and selectivity as evidenced by the addition of (R)-BINOL and (S,S)-hydrobenzoin, which gave 56% NMR yield, 15:1 dr, 0% ee, and 53% NMR yield, 10:1 dr, 0% ee. The additions of a chiral acid and a chiral diamine were also explored, but resulted in low conversions while failing to generate **8** with any enantioselectivity; reaction with 60 mol % TADDOL-phosphoric acid gave 13% yield, 2:1 dr, 0% ee, while reaction with 10 mol% diphenylethylenediamine gave 27% yield, 18:1 dr, 0% ee. Unfortunately despite the dramatic effect on diastereoselectivity, the use of chiral alcohols, diols, or amines failed to provide an enantioselective reaction. This is not sufficient evidence to prove or disprove the role of hydrogen-bonding in oxazolone hydroalkylation, but it is highly likely that there is some benefit to enolization.



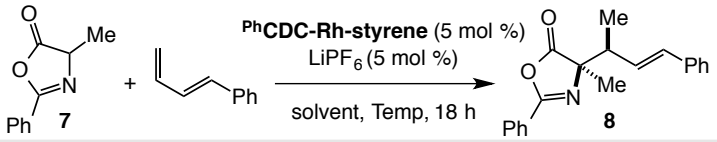
Entry[a]	Additive; mol %	NMR Yield (%)[c]; dr[b]	% ee
1	MeOH; 60	68; 7:1	-
2	iPrOH; 60	84; 19:1	-
3	tBuOH; 60	87; 12:1	-
4	Menthol; 60	62; >20:1	0
5	*(R)*-BINOL; 60	56; 15:1	0
6	*(S,S)*-hydrobenzoin; 60	53; 10:1	0
7	 ; 60	13; 2:1	0
8	(*S,S)*-diphenylethylenediamine; 10	27; 18:1	0
9	2,6-ditertbutylpyridine; 10	23; >20:1	-
10	2,6-ditertbutylpyridine; 10 iPrOH; 60	86; >20:1	-

[a]See SI for experimental details; all reactions performed under N_2 atmosphere. [b]Values determined by analysis of 500 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with trimethylsilyl ether as an internal standard. [c]NMR Yield reported for conversion to the cis- and trans-**8** products.

Table 3.3.2-2: Studies on the role of the alcohol in oxazolone hydroalkylation and attempts to develop an enantioselective transformation through stereospecific hydrogen bonding.

A substantial amount of optimization occurred prior to the discovery of the alcohol additive and could not be included in the 2016 publication. In particular, solvent and temperature screens were excised from the paper in the interest of brevity and readability. Table 3.3.2-3 shows additional optimization that was conducted during our discovery of hydroalkylation with oxazolones. The initial solvent screen for this transformation was not exceptionally informative as reactions in toluene (PhMe) proved only marginally more effective than in chlorobenzene (PhCl), THF, and dichloromethane (DCM); hydroalkylation to form **8** proceeded with 26% NMR yield in PhMe compared to 21% in PhCl, 21% in THF and 20% in DCM. Future reactions were run in toluene because it provided **8** in slightly higher conversion and had proved optimal for previous hydrofunctionalization reactions. This choice was later validated as the addition of

alcohol improves reactions in non-polar solvents, but is less beneficial in THF or DCM. Decreasing the reaction concentration appeared to substantially improve reactivity, as evidenced by Entry 5 where reaction at 0.25 M in toluene provided the desired product in 84% yield, 19:1 dr. Further decreases in the concentration decreased yield and selectivity and product **8** was formed in 38% NMR yield with 4:1 diastereoselectivity when run at a concentration of 0.125 M in toluene. The result in toluene at 0.25 M is comparable to the best results with an alcohol additive and demonstrates how individual substrates can be coaxed into providing high conversions with multiple reaction conditions. However, later studies found that reaction at 1.0 M with the alcohol additive gave more consistent results when the reaction was extended to different oxazolones and diene substrates.



Entry	Solvent; M	Temp (°C)	NMR Yield (%)[c]; dr[b]
1	PhCl; 1.0	50	21; 6:1
2	THF; 1.0	50	21; 4:1
3	DCM; 1.0	50	20; 3:1
4	PhMe; 1.0	50	26; 3:1
5	PhMe; 1.0	60	56; 7:1
6	PhMe; 1.0	80	0; -:-
7	PhMe; 0.25	50	84; 19:1
8	PhMe; 0.125	50	38; 4:1

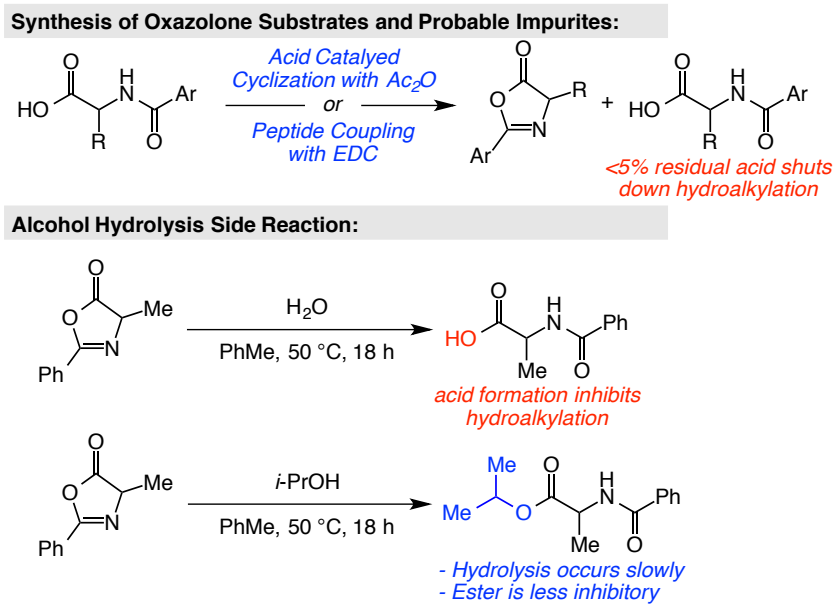
[a]See SI for experimental details; all reactions performed under N_2 atmosphere. [b]Values determined by analysis of 400 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with trimethylsilyl ether as an internal standard.

Table 3.3.2-3: Additional optimization prior to the discovery of the alcohol additive.

Modifying the reaction temperature initially looked promising as increasing from 50 °C to 60 °C resulted in a 56% NMR yield of a 7:1 mixture of diastereomers. Unfortunately this result proved inconsistent when the reaction was repeated and increasing the temperature further

completely shut down any reactivity; reaction at 80 °C did not generate any of **8**. Reexamining the reaction established that higher temperatures decomposed the oxazolone. Although it is unclear what decomposition was occurring under anhydrous conditions, it is clear that the side products generated by decomposition harmed the overall reaction and decreased reproducibility. As such, a reaction temperature of 50 °C was maintained for all further studies.

The importance of the oxazolone decomposition to the ring-opened product is mentioned above, but deserves further review to describe the eccentricities of the reaction. During the course of these screens we observed that the purity of the oxazolone substrate **7** is exceptionally important for providing an efficient reaction. A pure sample of **7** is a clear crystalline solid, but the presence of any impurity transforms this material into a semi-solid gel. Based on NMR spectroscopy and chemical intuition it is likely that the impurity in the synthesis of **7** is the uncyclized acid **9**. Free acid has previously proven to be detrimental to hydrofunctionalization reactions catalyzed by **^{Ph}CDC-Rh-styrene** (see control reactions in Chapters 1 and 2). Reactivity decreases dramatically when the oxazolone substrate is hydrolyzed through the addition of adventitious water to form the acid (Scheme 3.3.2-3). This side reaction partially explains why *i*-PrOH is the optimal alcohol additive as: (i) hydrolysis of the oxazolone is slower with larger alcohols, and (ii) the hydrolysis forms the ester rather than the more detrimental acid.

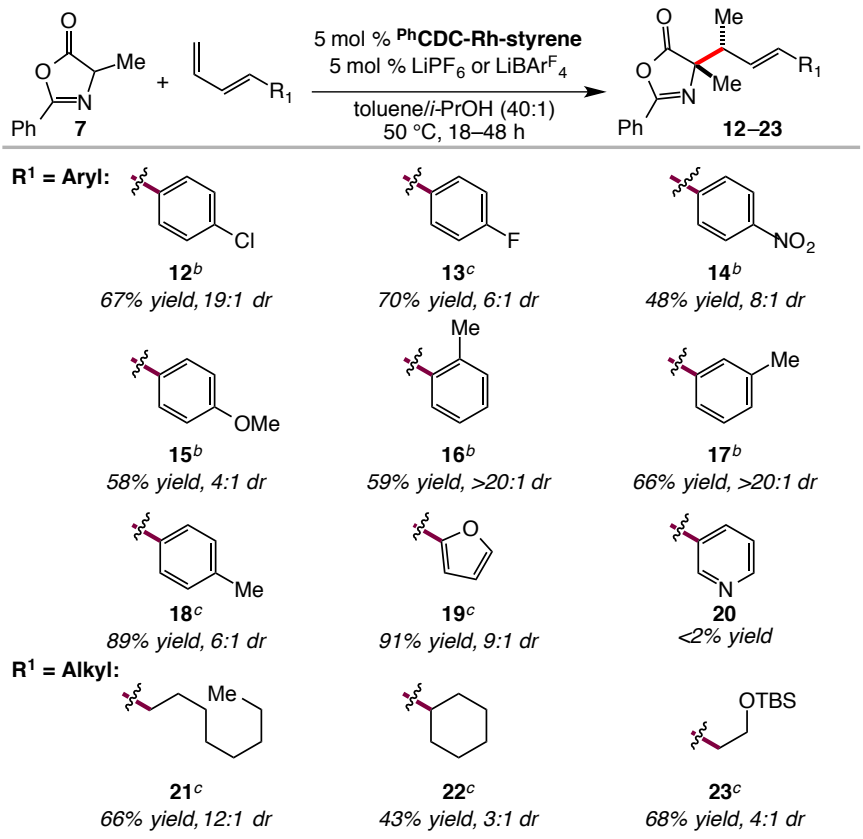


Scheme 3.3.2-4: The effect of acid impurities and oxazolone hydrolysis on reactivity.

3.3.3: Diene Scope for Intermolecular Hydroalkylation with Oxazolones

With optimized conditions in hand, we sought to explore the diene scope of the hydroalkylation with oxazolone **7**. For certain diene substrates $LiBAr^F_4$ proved to be the more effective lithium salt and was necessary to obtain good yields and selectivities. As shown in Scheme 3.3.3-1, formation of the N-substituted quaternary carbon occurs readily with modest to excellent levels of selectivity with aryl (**12**-**20**) and alkyl dienes (**21**–**23**). Electronic modifications to the aryl ring were well tolerated by the reaction. Aryl rings bearing halogens or electron withdrawing groups react with only slight decreases to yield and diastereoselectivity; *p*-Cl-, *p*-F- and *p*-NO_2-phenylbutadienes react to give **12** in 67% yield (19:1 dr), **13** in 70% yield (6:1 dr), and **14** in 48% yield (8:1 dr) respectively. Electron-rich arenes are also compatible, but result in reduced anti/syn diastereoselectivity; *p*-MeO-phenylbutadiene reacts to form **15** in 58% yield and 4:1 dr. Phenylbutadiene containing alkyl substitution at the *ortho*-, *meta*- and *para*-positions of the aryl ring are excellent substrates providing **16** in 59% yield (>20:1 dr), **17** in

66% yield (>20:1 dr), and **18** in 89% yield (6:1 dr). The high selectivity in the formation of **16** and **17** demonstrates the influence of sterics and its translation to increased diastereoselectivity in C–C bond formation with only slight decreases in yield. Dienes bearing oxygen heterocycles participate in the hydroalkylation reaction with **19** formed in 91% and in 9:1 dr; however, pyridyl groups appear to inhibit **^{Ph}CDC-Rh-styrene** as **20** does not form under the same reaction conditions. As was shown in Table 3.3.2-2, catalytic hydroalkylation of 1,3-phenylbutadiene in the presence of 10 mol % 2,6-di-tertbutylpyridine afforded **8** in 86% conv, and >20:1 dr, which indicates that Lewis basic N-heteroarenes do not inhibit hydroalkylation due to their Bronsted basicity, but rather by binding to the cationic CDC-Rh(I) catalyst.



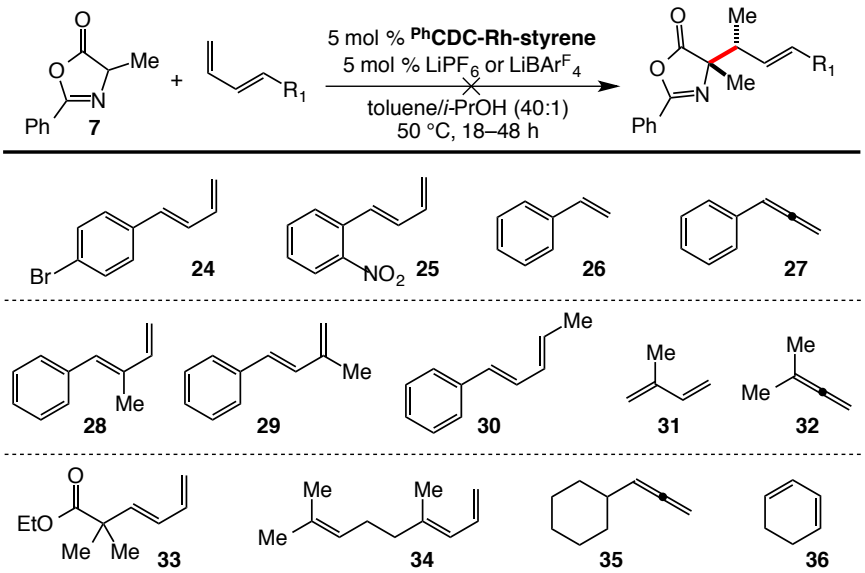
[a]See SI for experimental details; All reaction performed under N2 atmosphere; Yields of purified products are an average of two runs. [b]5 mol% of $LiPF_6$. [c]5 mol% of $LiBAr^F{}_4$.

Scheme 3.3.3-1: Scope of the diene for the CDC-Rh(I) catalyzed hydroalkylation with methyl-oxazolone **7**.

Alkyl-substituted dienes are also effective substrates and react with oxazolone **7** to produce alkenyl products **21**-**23** in good yields and selectivities (Scheme 3.3.3-1). We anticipated that the decreased size of the alkyl chain, compared to an aryl ring, would result in diminished diastereoselectivity, however, the opposite was observed; **14** was formed in high diastereoselectivity (12:1 dr) in 66% yield. The increased α-branching in cyclohexylbutadiene results in lower reactivity and diastereoselectivity, providing **15** in 43% yield and 3:1 dr. Additionally, the mild reaction conditions are tolerant of silyl ether functionality; for example homoallyl TBS ether **16** is delivered in 68% yield and 4:1 dr without silyl ether deprotection or elimination to form the conjugated diene. For some substrates lower conversions are observed due to competitive ring-opening of the oxzalone by *i*-PrOH, however, high yields can often be recovered by increasing the equivalents of the nucleophile.

Notably absent from these substrate tables are any examples of disubstituted dienes. Despite extensive screening, acceptable conversions could not be obtained for any diene that was not terminal and unsubstituted. This is likely due to the decreased binding affinity of more highly substituted π-systems for the Rh metal. A number of additional diene substrates were explored, but their decreased activity meant they were not included in our 2016 publication. The substrates shown in Scheme 3.3.3-2 were unsuitable reaction partners (<5% NMR Yield) for the addition of oxazolone **7** and, although these results are not synthetically useful, they help to establish the limitations of our hydroalkylation method. Certain electron poor aryl dienes (**24** and **25**) failed to hydroalkylate under the given reaction conditions, presumably because they proceed through a positively charged intermediate that is destabilized by an electron-withdrawing group. The failure of **24** suggests that an insertion into the aryl-bromide bond might also be occurring as the aryl-chloride reacts to form **12** without difficulty. The unsuitability of allene and alkene reaction

partners (eg: **26**, **27**, and **35**) demonstrates the importance of diene electrophiles for these reactions. Any substitution of the terminal diene completely removes any activity for hydroalkylation as evidenced by **28**-**30**. This trend also extends to alkyl dienes (eg: **31-34**) and we have yet to find any substituted diene that is capable of reacting to form the desired N-substituted quaternary center. Even cyclohexadiene **36**, which was well tolerated in the previously explored diene hydroamination (Chapter 1), failed to react.



Scheme 3.3.3-2: Diene substrates that did not react in intermolecular hydroalkylation.

To summarize the scope of diene scope of this hydroalkylation reaction, the developed method tolerates a broad range of diene electrophiles while maintaining modest to excellent diastereoselectivity. Aryl dienes can be counted on to generate the desired vicinal and fully substituted α-amino stereocenters in good yields and high diastereoselectivities. Highly electron poor dienes result in decreased conversion, whereas electron rich arene rings tend to decrease diastereoselectivity. Only dienes with functional groups that could tightly bind to the catalyst proved problematic. Alkyl dienes were also reliable reaction partners, but displayed reduced conversions and diastereoselectivities compared to aryl diene electrophiles. Highly efficient

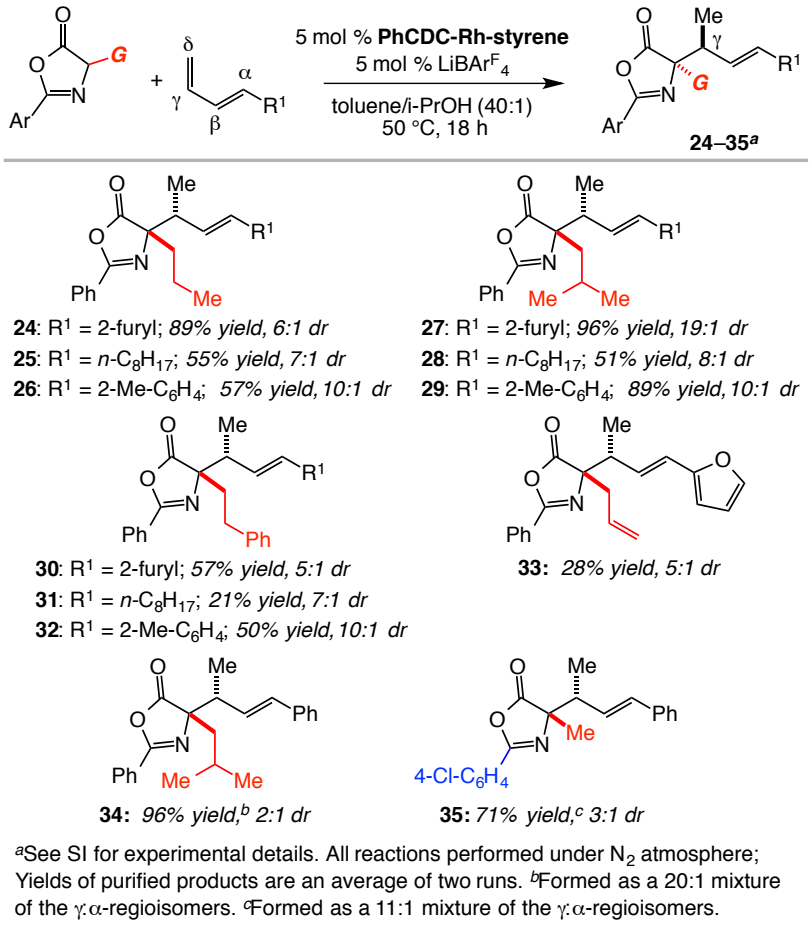
reactions cannot be reliably produced with alkyl diene substrates, but many terminal dienes do react.

3.3.4: Oxazolone Scope for the Carbodicarbene-Rh Catalyzed Intermolecular Hydroalkylation

Following our examination of the diene scope, we turned our attention towards probing the tolerance of the transformation for variations in the oxazolone nucleophile. To explore the interplay between the identity of the oxazolone substituent and diene, oxazolones were reacted with representative dienes bearing heterocyclic, alkyl and aryl motifs to afford **24**-**35** (Scheme 3.3.4-1). Extension from methyl- to *n*-propyl-substituted oxazolones (**24**–**26**) resulted in high conversions, similar to those obtained with **7**, but with lower selectivity compared to **16**, **19** and **21**; **24** was produced in 89% yield with 6:1 dr, **25** was synthesized in 55% yield with 7:1 dr, and **26** was formed in 57% yield with 10:1 dr. The lower selectivity may be a consequence of increased sterics on the α-substituent influencing the orientation of the nucleophile as it approaches the activated diene. Reactions with *sec*-butyl-substituted oxazolone demonstrate that β-branched alkyl substituents work effectively as **27**–**29** are formed in good to high yields with varying selectivity; **27** is formed in 96% yield with 19:1 dr, while **28** is synthesized in 51% yield with 8:1 dr and **29** in 89% yield with 10:1 dr. To further demonstrate that increased substitution on the oxazolone is viable, phenethyl-oxazolone was reacted to give **30**–**32**; **30** was formed in 57% yield with 5:1 dr, **31** in 21% yield with 7:1 dr and **32** in 50% yield with 10:1 dr.

The cationic catalyst ^{Ph}**CDC-Rh-styrene** is compatible with alkenes as evidenced by the successful formation of **33** in 28% yield with 5:1 dr. The reduction in yield is from competitive isomerization of the allyl group to the internal alkene, as the resulting oxazolone with an internal alkene is not a competent nucleophile. Furthermore, formation of **34** (2:1 dr) demonstrates the subtle effect that the sterics of the diene play in obtaining a selective reaction (c.f., **29**, generated

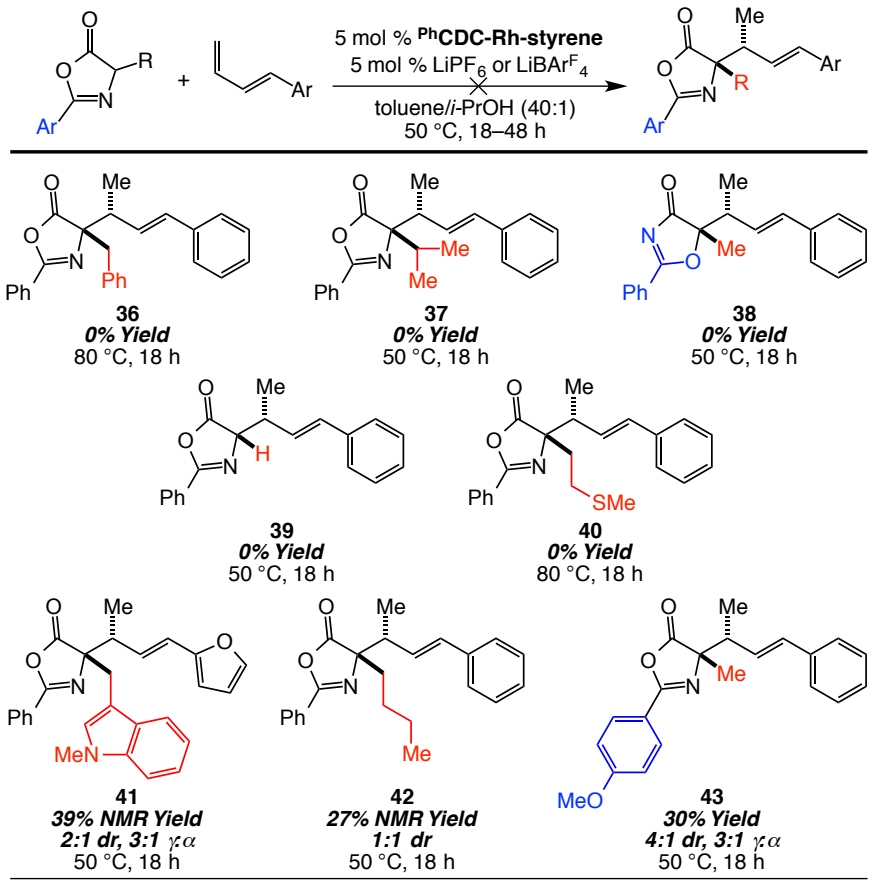
in 20:1 dr). The aryl substituent of the oxazolone could be varied, as demonstrated by the formation of **35**, but these modifications decreased selectivity and provided a mixture of regioisomers; *p*-Cl-phenyl-oxazolone reacted to provide **35** in 71% yield and 3:1 dr, however, the site-selectivity of the reaction decreased to give a 11:1 mixture of γ,δ- and α,δ-regioisomers.



Scheme 3.3.4-1: Survey of the scope of the oxazolone nucleophile used in the CDC-Rh(I) catalyzed hydroalkylation of dienes.

As with our study of the diene scope, many unsuccessful reactions could not be included in publication. Scheme 3.3.4-1 catalogs some of the oxazolone nucleophiles that proved unreactive (<10% NMR yield or poor regio- and diastereoselectivity). As mentioned above, oxazolones that are branched in the α-position of the R group (eg: **37**), or have particularly large

substituents (eg: **36**), are not effective nucleophiles. Surprisingly, an unsubstituted oxazolone also failed to react and **39** was produced in 0% yield. We suspect that changes in the enolization of the oxazolone are responsible for the failed reactivity of both **39** and modified heterocycles such as **38**. The inclusion of sulfur appears to inhibit the cationic CDC-Rh(I) catalyst as **40** was completely unreactive even at elevated temperatures. Some oxazolone nucleophiles did show low conversions for diene hydroalkylation, but were sufficiently non-selective for the desired regioisomer and/or diastereomer that they were not included in the 2016 publication. Compounds **41** and **43** could be formed in 39% and 30% yields respectively with no greater than 3:1 selectivity for the γ- over the α-regioisomers (ie: 1,2-addition versus 1,4-addition). Similarly, **42** could be formed in 27% yield, but as a 1:1 mixture of the anti/syn-diastereomers. These substrates demonstrate how modifications to the sterics and electronics of the oxazolone nucleophile can substantially impact the selectivity of diene hydroalkylation and establish some limits that we hope to improve upon in the future.

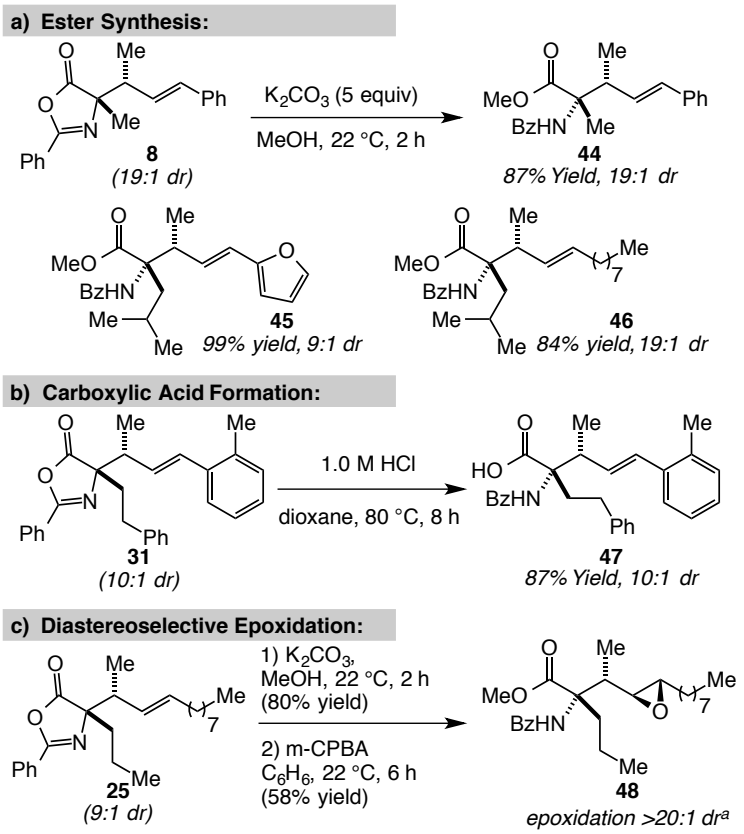


Scheme 3.3.4-2: Oxazolone nucleophiles that were not successful reaction partners due to either low conversion or poor selectivity.

3.3.5: Stereoretentive Functional Group Transformations of Allylic Oxazolone Products

One of the major weaknesses in the current applications of hydroalkylation is that there is only a single example of its use in synthesis.[79] We hoped that this method could be applied to the construction of natural products, as it is capable of incorporating an amino acid equivalent while diastereoselectively forming two vicinal stereocenters. In addition, one of these stereocenters is an N-substituted quaternary center and relates to the synthesis of unnatural amino acids. To establish the utility of the products generated through this catalytic stereoselective

hydroalkylation protocol, several transformations of the oxazolone products to other useful molecules were demonstrated (Scheme 3.3.5-1).



Scheme 3.3.5-1: Stereoretentive or selective functional group transformations of allylic oxazolone products.

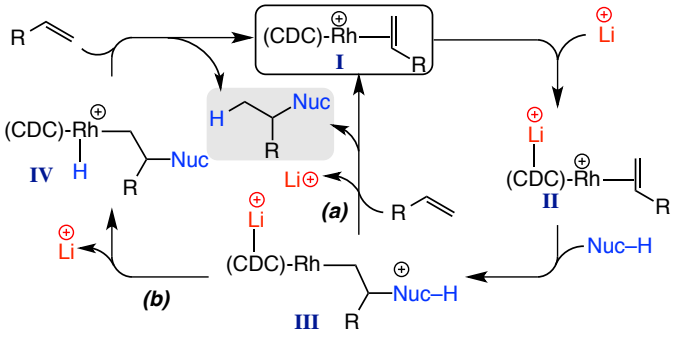
Experiments proved that oxazolone products could be readily ring opened under basic conditions to form benzoyl protected quaternary amino esters; the ring-opening of allyl-substituted oxazolone **8** with MeOH and K_2CO_3 at 22 °C delivers methyl esters **44** in 87% yield. The synthesis of **44** confirmed that this hydroalkylation method generates the *anti*-diastereomer as the major product by comparison to previously reported data.[111] Two additional α,α-disubstituted products, **27** and **28,** were converted to their corresponding methyl esters **45** and **46** in 99% and 84% yield, respectively. The oxazolone moiety could be converted to the benzoyl-protected amino acids through acid hydrolysis; the conversion of **31** to **47** with dilute HCl in

87% yield is representative. Finally, the vicinal tertiary allylic, and N-substituted quaternary stereocenters can be used to impart stereocontrol in further alkene functionalizations. In this regard, **25** (9:1 dr) was successively hydrolyzed to the methyl ester and subjected to *meta*-chloroperoxybenzoic acid (*m*-CPBA) epoxidation to form epoxide **48** in 58% yield over two steps with complete stereocontrol.[113] This diastereoselective epoxidation was based on previous literature examples that used amides as directing groups for epoxidation.[114,115] The resulting product contains four contiguous stereocenters and a versatile epoxide ring, which could be opened stereoselectively to introduce a variety of nucleophiles. Excellent examples of stereospecific ring-opening reactions with internal epoxides are known with both carbon[116–119] and nitrogen[120,121] nucleophiles and we expect that they will translate to these substrates.

3.3.6: Proposed Mechanism of Diene Hydroalkylation

The mechanism of CDC-Rh(I) catalyzed electrophilic alkene activation has been discussed throughout this dissertation, but a mechanistic cycle of CDC-Rh(I) catalyzed hydroamination or hydroarylation had not been published for lack of experimental support for our assertions. During the publication process for this work, we were asked to include our proposed mechanistic cycle (Scheme 3.3.6), which is very similar to that shown in Scheme 3.1-2 for hydroarylation. Enolization to form the carbon nucleophile is not shown, but can be translated from that shown in Scheme 3.3.1. While the specific role of the lithium salt is not yet fully determined, previous studies indicate that secondary binding to the CDC carbon (e.g., **II**) decreases electron density at the Rh center, resulting in decreased π-back donation,[2] and thus facilitating nucleophile addition (**II→III**).[122,123] Product formation and regeneration of **I** could occur via two possible pathways: (**a**) direct Rh–alkyl protonation, or (**b**) proton transfer to Rh

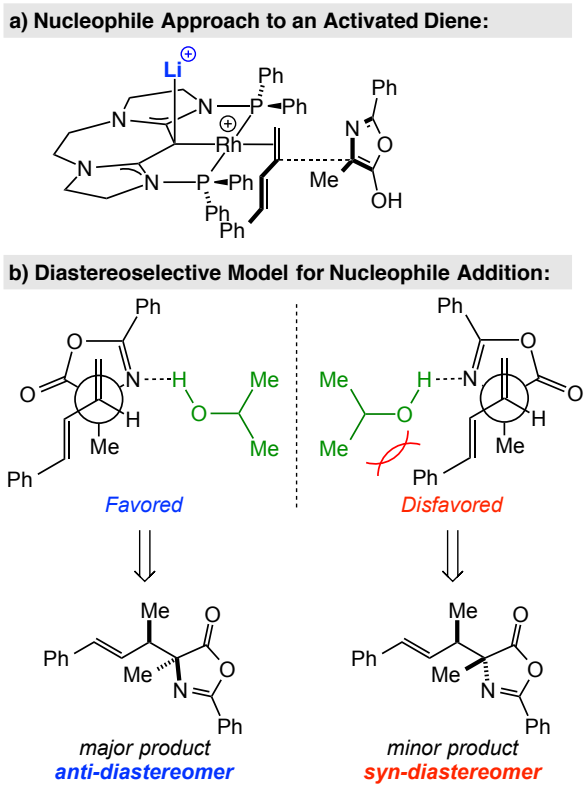
and subsequent reductive elimination. A density functional theory calculation for the related hydroamination through activation of an olefin π-system has been reported by Togni *et al* and provides precedent for this mechanistic proposal.[124]



Scheme 3.3.6-1: Proposed mechanistic cycle for the addition of oxazolones to diene electrophiles catalyzed by a CDC-Rh(I) complex.

Although the major diastereomer formed in our hydroalkylation reactions was established through association with literature precedent, a stereochemical model for the observed selectivity was not published. Based on previous experience with the regioselectivity of reactions catalyzed by CDC-Rh(I) complexes, and the dramatic effect that the identity of the substrate has on diastereocontrol, it is likely that the stereochemistry of the vicinal carbon centers is substrate—rather than catalyst—controlled. This has been further supported by unpublished experiments where modifications to the aryl phosphine substituents of the catalyst (eg: xylyl or *meta*-tolyl as compared to phenyl) proved detrimental to diastereoselectivity. The external approach of the enol form of the oxazolone nucleophile is shown in Scheme 3.3.6-2a and demonstrates how the nucleophile approaches opposite to the catalyst. This minimizes any interactions that could result in catalyst-controlled diastereoselectivity. Instead, the substituents on the diene and oxazolone will be in direct contact during the facial approach of the carbon π-systems. This approach is modeled in Scheme 3.3.6-2b and shows how the largest diene substituent is placed opposite from

the larger imine in the favored transition state model. Based on the large influence that the identity of the alcohol additive has on diastereocontrol, we propose that there is a hydrogen bonding interaction between the imine and the alcohol that further increases the relative size of the cyclic imine as opposed to the cyclic ester. Hydrogen bonding to the imine is predicted to be favored over the less nucleophilic ester. Although this model accurately accounts for the observed diastereoselectivity, there is not enough evidence to fully support these conjectures.



Scheme 3.3.6-2: Model to explain the substrate controlled diastereoselective addition of CDC-Rh(I) catalyzed diene hydroalkylation.

3.3.7: Summary and Outlook

In summary, we have demonstrated the first diastereo- and siteselective hydroalkylation of 1-substituted 1,3-dienes with oxazolone nucleophiles promoted by a cationic (CDC)-Rh catalyst. The use of a catalytic lithium salt activator, and alcohol serve to provide optimal

reactivity and good diastereoselectivity under mild conditions for a range of dienes with oxazolone nucleophiles. The resulting products contain two contiguous stereocenters and an N-substituted quaternary center. These oxazolone products can be deprotected to generate useful amino acid analogues, or exploited to impart acyclic stereocontrol in alkene epoxidation. We have also presented a mechanism for this transformation that describes how an olefin can be electrophilically activated to allow for the external addition of the carbon nucleophile, as well as a related model to account for both the selective formation of the *anti*-diastereomer and the influence of the alcohol additive on diastereoselectivity. Related studies are in progress to expand the scope of carbon-based nucleophiles and alkene electrophiles in hydroalkylation processes as well as to develop enantioselective variants of this reaction.

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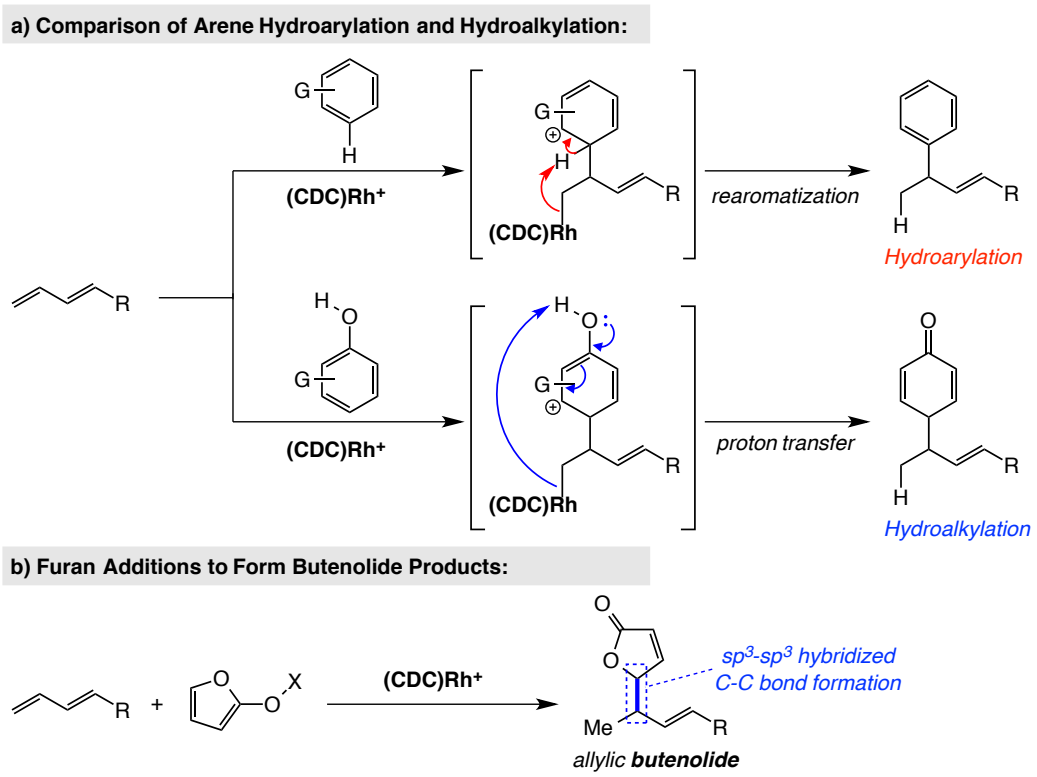
CHAPTER 4: HYDROALKYLATION WITH ENOLATE NUCLEOPHILES TO DIASTEREOSELECTIVELY GENERATE ALLYLIC BUTENOLIDE PRODUCTS[4]

4.1: Introduction

Our work with oxazolone nucleophiles introduced hydroalkylation with **^{Ph}CDC-Rh-styrene** to the organometallic and synthetic community, yet it was not the first hydroalkylation we explored. The development of enolate additions using silyl enol ether nucleophiles was attempted first, however, the facility of the oxazolone addition to dienes and the potential of the generated vicinal stereocenters led us to pursue that transformation upon its discovery. Hydroalkylation was first approached after publication of diene hydroarylation to generate allylic arenes. Interest in developing a C(sp^3)-C(sp^3) bond formation led to a search for arene nucleophile that could protonate on the arene to form a sp^3-hybridized stereocenter rather than rearomatizing to form an sp^2 hybridized stereocenter (Scheme 4.1-1). The successful addition of 2,4-dimethylpyrrole in the hydroarylation of 1,3-phenybutadiene and 1,3-cyclohexylbutadiene observed in Section 2.5 proved that heterocycles could be utilized in conjunction with cationic CDC-Rh(I) catalysts. The goal was to substitute a stable derivative of furan-2-ol as the arene nucleophile such that reaction would form the butenolide product rather than the furan. Butenolides are found in many natural products and a catalytic method for their synthesis would be a useful contribution.[1–3]

[4] The work described in this chapter is currently unpublished and is being prepared for submission. M. J. Goldfogel discovered the reaction and ran all catalytic reactions. C. C. Roberts synthesized some of the **^{Ph}CDC-Rh–styrene** complex used for initial reaction development.



Scheme 4.1-1: Hydrofunctionalization with arene nucleophiles to form C-C sp^3-sp^3 hybridized bonds.

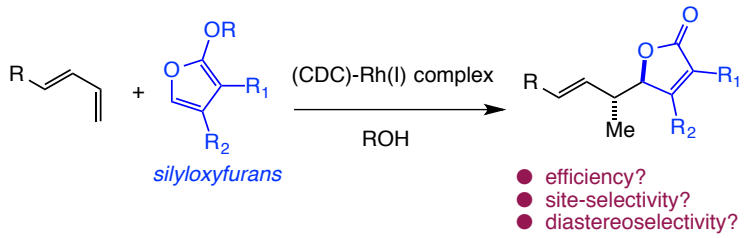
4.1.1: Literature Examples of Hydroalkylation with Silyl Enol Ethers

The direct functionalization of olefins is one of the most enabling classes of chemical transformations in organic synthesis[4–6] and benefits from the commercial availability of many olefins substrates.[7] A subgroup of these reaction types is catalytic hydroalkylation involving the net C–H addition across the unsaturated C–C double bond to form a C-C sp^3-sp^3 hybridized bond. Hydroalkylation has the potential to diastereoselectively generate vicinal stereogenic centers from carbon nucleophiles.[8] Many thermally enolizable carbon nucleophiles have been employed to catalytically generate useful C-C bonds with Cu, Ag,[9] Au,[10–16] Pd,[17–26] Pt,[17,25,27] Rh,[28–31] Ru,[32] and Lewis acid[33–45] catalysts, but comparatively few examples of hydroalkylation with organometallic[46–49] or enolate[50–55] nucleophiles exist. This is a significant limitation in current

methods for hydroalkylation as a relatively small subset of carbon nucleophiles are thermally enolizable. The importance of enolate and enolsilane carbon nucleophiles has been extensively demonstrated by the Aldol[56–59] and Mukaiyama-Aldol[60–64] reactions, but translation to hydroalkylation has lagged. A few excellent examples exist for the catalytic addition of silyl enol ethers to Michael acceptors,[65,66] but these reactions are still relatively unexplored and, to our knowledge, there are no examples of the addition of silyl enol ethers to unactivated olefins.

4.1.2: Proposed Extension to Enolate Nucleophiles for Hydroalkylation

We recently explored the use of a cationic CDC-Rh(I) catalyst for the diastereoselective hydroalkylation of dienes with thermally enolizable oxazolone nucleophiles[31] and are interested in expanding this new class of tridentate ligands to additional C-C bond forming reactions. Silyl enol ethers can act as surrogates for enolate nucleophiles and the development of a catalytic diene hydroalkylation with these structures would provide access to a much larger pool of carbon nucleophiles than is currently possible with enols; unlike thermally enolizable carbon nucleophiles, silyl enol ethers are minimally constrained by the acidity of the position alpha to the carbonyl (Scheme 4.1.2-1). Extension of CDC-Rh catalyzed hydroalkylation to include additions with silyloxyfuran nucleophiles[65] will allow for the formation of butenolides, which are common motifs in many natural products.[1–3] The proposed diastereoselective synthesis of allylic butenolide products would provide a useful synthetic method and expand the applications of underexplored carbodicarbene ligands in organometallic catalysis.



Scheme 4.1.2-1: Proposed diastereoselective hydroalkylation of 1,3-dienes with silyloxyfurans.

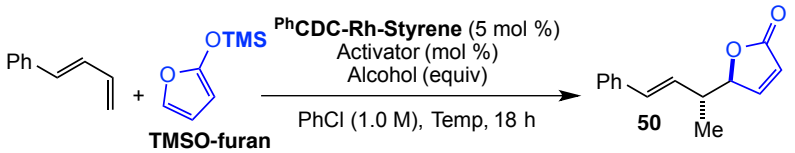
4.2: Discovery of Diene Hydroalkylation with Silyloxyfuran Nucleophiles

Previously developed reactions provided conditions for the hydrofunctionalization of diene electrophiles through a common catalytic intermediate **2** (Scheme 3.1-2), which left the challenge of selecting a furan nucleophile that would provide the desired reactivity. This transformation is nominally an enolate addition and contrasts with the enol additions of 1,3-pentandeione and oxazolones discussed in Sections 3.2 and 3.3. The previously discussed hydroalkylations relied on thermal tautomerization to generate a carbon π-nucleophile, but furanone, the parent nucleophile to the proposed furan hydroalkylation, cannot tautomerize thermally. Instead, the enolate form must be generated by deprotonation with a strong base and trapping the resulting oxyanion with a protecting group (eg: "O-X" in Scheme 4.1-1b). The majority of known enolate hydroalkylation reactions are derived from silyl protected enols that deprotect *in situ* to generate the anionic nucleophile (see Section 3.1.1.2). These literature examples were used as precedent for the application of silyl enol ethers to form allylic butenolide products from diene hydroalkylation.

4.2.1: Reaction Screening to Identify a Furan Nucleophile

As with previous screens to discover new nucleophiles for the hydroalkylation of dienes, test reaction were performed using 1,3-phenylbutadiene and **^{Ph}CDC-Rh-styrene** as catalyst. Numerous Mukaiyama-Aldol[60–64] reactions have been published that use 2-trimethylsilyloxyfuran (**TMSO-furan**) as an effective carbon nucleophile and reaction screens were run using this readily synthesized substrate (Table 4.2.1-1).[67] An alcohol additive was necessary to protonate the anticipated Rh-alkyl bond formed after furan addition in order to release the product and

regenerate the catalyst. This additive would also sequester the silyl byproducts generated from the deprotection of the **TMSO-furan** nucleophile.[68] However, we soon realized that deprotection occurred too readily at elevated temperatures with small alcohols. The reaction with 1 equivalent of MeOH and 5 mol% of $LiBF_4$ as the Lewis acid co-catalyst failed to provided **50** at 60 °C while completely consuming the **TMSO-furan** to generate furanone (Entry 1). The reaction was repeated with larger alcohols to slow the rate of desilylation, but complete deprotection was still observed over the course of the reaction; using *t*-BuOH as the alcohol additive **50** was produced in 4% NMR yield (Entry 2). Decreasing the temperature from 60 °C to 40 °C slowed the desilylation to the point that 18% **TMSO-furan** was recovered, but the conversion to **50** decreased to just 1% (Entry 3). Switching the Lewis acid co-catalyst from $LiBF_4$ to $LiBAr^F_4$ slightly improved the reaction by increasing the conversion to **50** to 10%, but the **TMSO-furan** reagent was clearly not an efficient source of the furan enolate. Despite extensive additional efforts to screen various solvents, alcohol additives, additive loadings, and temperatures, the best result obtained with **TMSO-furan** as the nucleophile is shown in Entry 5 where **50** was obtained in 12% NMR yield using sterically hindered triphenylsilanol (Ph_3SiOH) as the proton source at 40 °C.



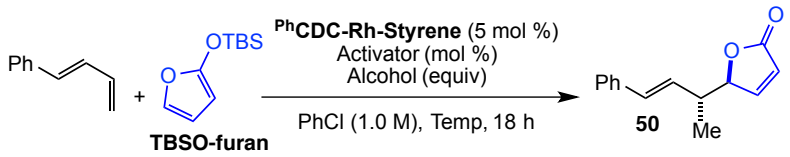
Entry	Alcohol; equiv	Activator; mol %	Temp (°C)	NMR Yield (%)
1	MeOH; 1.0	$LiBF_4$; 5.0	60	0
2	*t*-BuOH; 1.0	$LiBF_4$; 5.0	60	4
3	*t*-BuOH; 1.0	$LiBF_4$; 5.0	40	1
4	*t*-BuOH; 1.0	$LiBAr^F_4$; 5.0	60	10
5	Ph_3SiOH; 1.0	$LiBF_4$; 5.0	40	12
6	-	$LiBF_4$; 5.0	60	0

Table 4.2.1-1: Reaction screening with 2-trimethylsilyloxyfuran to yield the allylic butenolide **50**.

Despite the low conversions and complete consumption of the starting material, these results proved that hydroalkylation could be accomplished using a silyl enol ether and alcohol to generate the required enolate nucleophile *in situ*. This served as proof of concept, but we were concerned that the reaction might be occurring through a hydroarylation followed by a silyl deprotection rather than a formal addition of 2-furanolate. To test this, the reaction was run without the alcohol additive (Table 4.2.1-1). Arylation should occur readily under these conditions as the silyl deprotection is unnecessary for rearomatization to the sp^2 hybridized carbon and a similar reaction with 2,4-dimethylpyrole occurs readily.[69] No conversion to **50** was observed, which suggests that reaction is occurring through the enolate nucleophile or through concurrent addition/deprotection of the silyl enol ether (Entry 6).

The instability of **TMSO-furan** was preventing high conversions to the desired allylic butenolide products. Increasing the size of the alkyl substituents on the silanol protecting group from trimethylsilyl (TMS) to *tert*-butyldimethylsilyl (TBS) was used to improve thermal stability and decreases the rate of desilylation.[70] Initial attempts at optimizing the reaction with 2-*tert*-butyldimethylsilyloxyfuran (**TBSO-furan**) are shown in Table 4.2.1-2. A screen of alcohol additives revealed that *t*-BuOH was the most effective, although there was little difference between it and *i*-PrOH; the use of MeOH, *i*-PrOH, *t*-BuOH, and *t*-AmylOH generated in **50** in <2%, 8%, 10% and 3% respectively (Entries 1-4). The anticipated reduced rate of silyl deprotection for the more stable TBS protecting group was born out as the larger alcohols returned a portion of the **TBSO-furan** starting material. Various temperatures were screened and we observed that lower reaction temperatures decreased yields while higher temperatures had

little effect; reaction at 45 °C gave 1% **50** (Entry 5), whereas the same reaction at 80 °C gave 12% (Entry 6). The reaction at higher temperature did completely destroy the furan nucleophile, which suggests that the catalyst is loses reactivity prior to complete consumption of the **TBSO-furan** substrate. In an effort to improve catalytic activity, we screened a series of Lewis acidic co-catalysts and observed that both $LiPF_6$ and AgF were slightly more active than $LiBF_4$; catalysis with $LiPF_6$, $LiBAr^F{}_4$, AgF, and CuCl generated **50** in 12%, 0%, 12%, and <2% yields (Entries7-10). Despite finding reaction conditions that returned a portion of both the diene and furan starting materials, the reaction could not be coaxed into providing more than a single catalytic turnover.

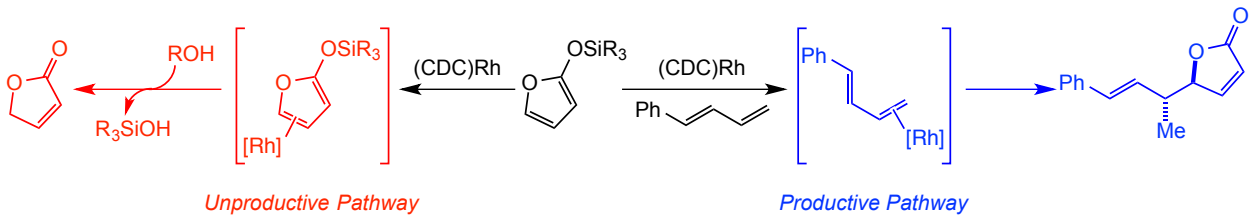


Entry	Alcohol; equiv	Temp (°C)	Activator; mol %	NMR Yield (%)
1	MeOH; 1.0	60	$LiBF_4$; 5.0	<2
2	*i*-PrOH; 1.0	60	$LiBF_4$; 5.0	8
3	*t*-BuOH; 1.0	60	$LiBF_4$; 5.0	10
4	t-AmylOH; 1.0	60	$LiBF_4$; 5.0	3
5	*t*-BuOH; 1.0	45	$LiBF_4$; 5.0	1
6	*t*-BuOH; 1.0	80	$LiBF_4$; 5.0	12
7	*t*-BuOH; 1.0	60	$LiPF_6$; 5.0	12
8	*t*-BuOH; 1.0	60	$LiBAr^F{}_4$; 5.0	0
9	*t*-BuOH; 1.0	60	AgF; 5.0	12
10	*t*-BuOH; 1.0	60	CuCl; 5.0	<2

Table 4.2.1-2: Screening the effect of modifying the alcohol additive, temperature and Lewis acid on hydroalkylation with 2-*tert*-butyldimethylsilyloxyfuran.

The continued poor conversions to **50** and the rapid deprotection of the furan to the furanone led to the conclusion that the catalyst was participating in competing pathways vying for the silyloxyfuran substrate (Scheme 4.2.1-3). The desired hydroalkylation occurs when the

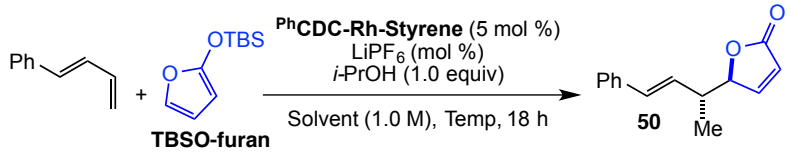
CDC-Rh(I) catalyst binds the diene and activates it towards addition by the silyl enol ether. However, if the silyloxyfuran outcompetes the diene for binding to the catalyst, the electron poor Rh center can pull electron density out of the bound furan and catalyze unproductive desilylation to furanone and silanol. Furthermore, the catalyst does not remain active throughout the reaction, as the conversion to **50** does not correlate with the amount of returned **TBSO-furan**.



Scheme 4.2.1-3: Competing catalytic pathways in the hydroalkylation of 1,3-phenylbutadiene with a silyloxyfuran nucleophile.

Additional screening was undertaken in an attempt to favor hydroalkylation over unproductive Rh-catalyzed desilylation (Table 4.2.1-4). *i*-PrOH was used because it showed comparable reactivity to *t*-BuOH (Table 4.2.1-2, Entries 2 and 3) and further optimizations with *t*-BuOH were beginning to show diminishing returns. Additionally, $LiPF_6$ was used in place of $LiBF_4$ since it showed marginally better activity and can be weighed more accurately on small scale. A series of solvents with varying polarity were screened and the reduced polarity of toluene gave improved reactivity; reaction with chlorobenzene (PhCl), benzene (PhH), toluene (PhMe), acetonitrile (MeCN), and diethyl ether (Et_2O) provided **50** in 12%, 13%, 21%, and 0%, respectively (Entries 1-5). The loading of $LiPF_6$ was reduced to 2.5% on the suspicion that an excess of Lewis acid might favor desilylation. This resulted in a modest increase in conversion to 26% yield, and 8:1 diastereoselectivity (Entry 6). The improved conversion allowed for the accurate determination of diastereoselectivity through NMR spectroscopy and we were pleased to discover that hydroalkylation was modestly selective for a single diastereoisomer. Doubling

the equivalents of **TBSO-furan** provided the best conversion to **50** in 36% yield, 10:1 dr (Entry 7).



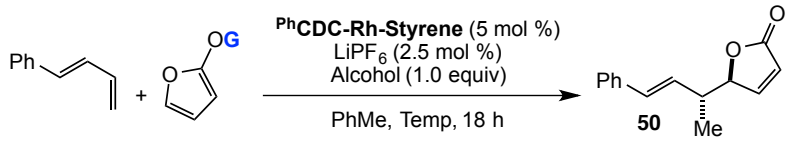
Entry	Solvent; M	Activator; mol %	NMR Yield (%)	dr
1	PhCl; 1.0	$LiPF_6$; 5.0	12	-
2	PhH; 1.0	$LiPF_6$; 5.0	13	-
3	PhMe; 1.0	$LiPF_6$; 5.0	21	-
4	MeCN; 1.0	$LiPF_6$; 5.0	0	-
5	Et_2O; 1.0	$LiPF_6$; 5.0	0	-
6	PhMe; 1.0	$LiPF_6$; 2.5	26	8:1
7[a]	PhMe; 1.0	$LiPF_6$; 2.5	36	10:1

[a]The reaction was run with two equivalents of TBSO-furan and *i*-PrOH.

Table 4.2.1-4: Searching for improved reactivity with silyloxyfuran nucleophiles by modifying solvent, Lewis base loading and the equivalents of nucleophile.

Despite the significant improvement in conversion compared to the previous reaction, options for meaningful changes to the reaction conditions were being rapidly exhausted. As such, further modifications to the silyl protecting group were explored in the hope that a different group might allow for improved reactivity. A series of protected silyloxyfuran nucleophiles were synthesized and their reactivity explored. Brief optimizations of the temperature and alcohol additive are shown in Table 4.2.1-5 and the highest conversions obtained with each protected furan nucleophile listed. Three larger silyl protecting groups, triisopropylsilyl- (TIPS), *tert*-butyldiphenylsilyl- (TBDPS), and tris(trimethylsilyl) [$Si(TMS)_3$] were synthesized and tested in hydroalkylation (Entries 1-3). TIPS proved to be the most active providing **50** in 33% NMR yield and 4:1 dr, whereas TBDPS and $Si(TMS)_3$ gave 15% and 13% yields, respectively. 2-triisopropylsilyloxyfuran (**TIPSO-furan**) was the most successful nucleophile and formed

vicinal stereocenters with modest diastereoselectivity. However, this result was eclipsed by the more stable benzoyl (Bz) protected nucleophile, which allowed for the formation of **50** in 58% yield, albeit with only 2:1 dr (Entry 5). The methyl ether proved too stable for *in situ* formation of the reactive enolate and failed to react to form **50** (Entry 5). The results presented here were used to select **TIPSO-furan** and furan-2-yl benzoate (**BzO-furan**) as the most promising enolate nucleophiles for additional screening.



Entry	G	Alcohol; equiv	Temp (°C)	NMR Yield (%)	dr
1	TIPS	MeOH; 1.0	60	33	4:1
2	TBDPS	H_2O; 1.0	80	15	-
3	$Si(TMS)_3$	H_2O; 1.0	50	13	-
4	Bz	MeOH; 1.0	60	58	2:1
5	Me	H_2O; 1.0	60	0	-

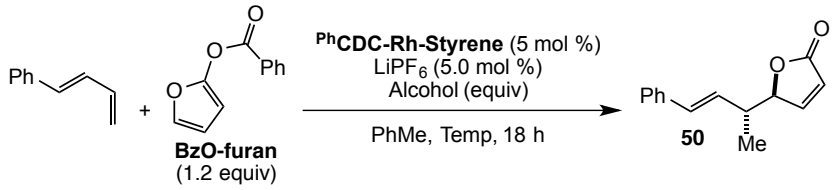
Table 4.2.1-5: Screening various protecting groups on 2-furanol as nucleophiles for hydroalkylation.

4.3: Diene Hydroalkylation with Benzoyl-Derived Furan Nucleophiles

The result with furan-2-yl benzoate (**BzO-furan**) eclipsed any previously observed conversions and offered a new manifold for optimization. However, the low diastereoselectivity provided by the reaction dramatically reduced the synthetic value and encouraged further optimization.

4.3.1: Optimization of the Addition of Benzoyl-furans to 1,3-Phenylbutadiene

Modifications to the alcohol additive and temperature were undertaken in the interest of increasing diastereoselectivity. Previously MeOH provided **50** in 58% yield as a 2:1 mixture of diastereoisomers and the same reaction with water (H_2O) resulted in a far less selective reaction and complete consumption of the **BzO-furan** substrate and diene; reaction with H_2O gave **50** in 20% yield, 1:1 dr (Table 4.3.1-1, Entry 2). Hydrolysis of the benzoyl protecting group with MeOH generates an ester byproduct, whereas hydrolysis with H_2O forms benzoic acid. The *in situ* generation of acid is extremely detrimental to diene hydrofunctionalization and can result in oligomerization side reactions (see Section 3.3.2). It is therefore necessary to use an alcohol additive that has only one available proton. Hydroalkylation of 1,3-phenylbutadiene with **BzO-furan** proceeded with *i*-PrOH and *t*-BuOH to a lesser degree than MeOH; **50** is formed in 22% yield, 5:1 dr and 23% yield, 2:1 dr with *i*-PrOH and *t*-BuOH. It is notable that *i*-PrOH did improve the diastereoselectivity of the reaction, but this was not pursued due to the poor yield.



Entry	Alcohol; equiv	Temp (°C)	NMR Yield (%)	dr
1	MeOH; 1.2	60	58	2:1
2	H_2O; 1.2	60	20	1:1
3	*i*-PrOH; 1.2	60	22	5:1
4	*t*-BuOH; 1.2	60	23	2:1
5	Menthol; 1.2	60	63	4:1
6	MeOH; 6.0	60	71	1:1
7	MeOH; 1.2	50	48	3:1

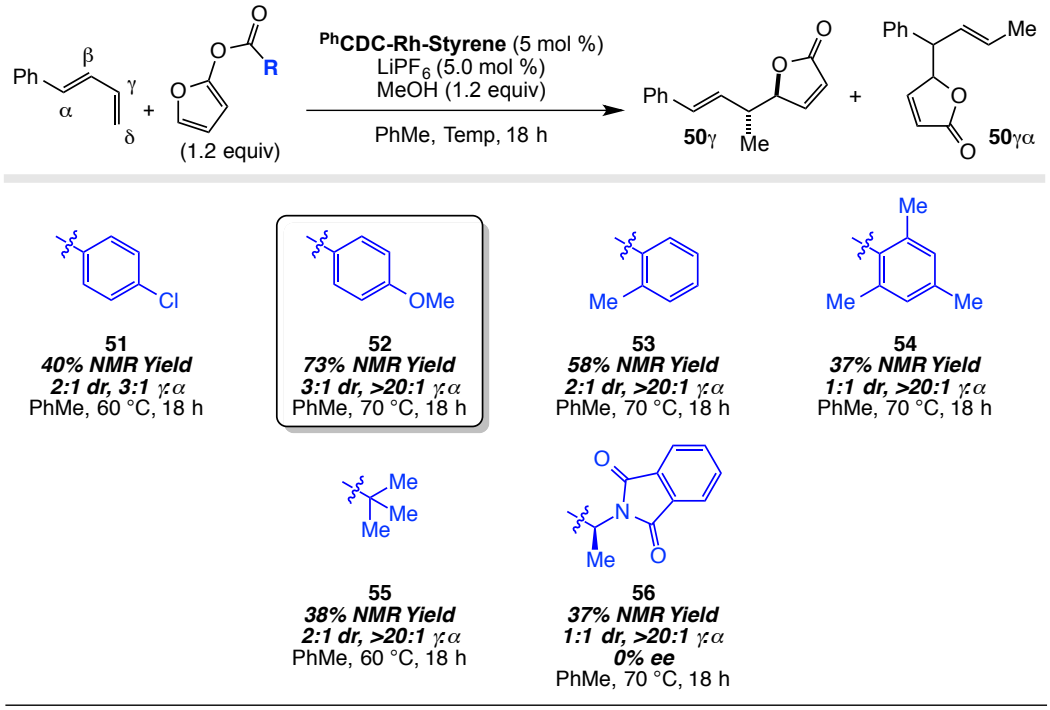
Table 4.3.1-1: Alcohol and temperature screens for benzoyl-protected furan additions to 1,3-phenylbutadiene.

Initial results with menthol were promising, yielding **50** in 63% NMR conversion and 4:1 dr, however attempts to repeat this reaction were inconsistent. This irreproducibility is ascribed to miscibility issues associated with menthol in toluene, as the heavier alcohol makes up a larger fraction of the solvent mixture. Further screening was done using MeOH for its consistency and high conversion. Increasing the equivalents of the alcohol improved converstion at the cost of diastereoselectivity; **50** was formed in 71% yield with 1:1 dr. As such, the 1:1 stoichiometry between the furan nucleophile and alcohol additive was maintained. The effect of decreasing the temperature was explored and reaction at 50 °C gave a 48% yield of **50** with 3:1 dr. This slight increase in diastereoselectivity was encouraging as it suggests modification to the reaction conditions might provide higher selectivity.

Steric and electronic modification to the benzoyl protecting group were explored to improve conversion and selectivity (Scheme 4.3.1-2, unpublished results). Electronic modifications to the aryl ring of the benzoyl group dramatically affected the selectivity of diene hydroalkylation. When the *para*-chlorobenzoyl furan **51** was used the regioselectivity of the transformation decreased and **50** was produced in 40% yield as a 3:1 mixture of the γ:α regioisomers with 2:1 dr for the γ isomer. The decreased conversion and selectivity are likely in part due to the increased rate of hydrolysis observed for **51**. The opposite was observed for the *para*-methoxybenzoyl furan **52**, which hydrolyzed slowly even at raised temperatures (70 °C) and allowed for a 73% conversion to product in 3:1 dr as a single regioisomer. This would prove to be the best reaction obtained using a benzoyl protected furan nucleophile.

Modifications to the sterics of the benzoyl protecting group proved detrimental to both the conversion and diastereoselectivity of the transformation; hydroalkylation with **53** and **54** generated **50** in 58% yield, 2:1 dr and 37% yield, 1:1 dr, respectively. Although these reactions

were completely selective for a single regioisomer, they did not improve upon the previous result with **BzO-furan** or **52**. The reactivity of acyl protecting groups was also explored and the pivlate protected furan **55** reacted to provide **50** in 38% yield as a single regioisomer in 2:1 dr. Similarly, the amino acid derived substrate **56** gave 37% yield as a 1:1 mixture of diastereomers. This substrate was tested in the hope that the enantiopure stereocenter of **56** would allow relay enantiocontrol to the newly formed vicinal stereocenters, but the reaction proceeded to provide the products in 0% ee.



Scheme 4.3.1-2: The effect of modifying the acyl protecting group on the conversion and selectivity of **PhCDC-Rh-styrene** catalyzed hydroalkylation (unpublished results).

The cationic CDC-Rh(I) catalyzed hydroalkylation of 1,3-phenylbutadiene to form **50** occurred with good conversion when **52** was used as the source of the furan nucleophile. However, the diastereoselectivity of the transformation was suboptimal and must be improved further before publication was considered. Any modifications of the protecting group failed to

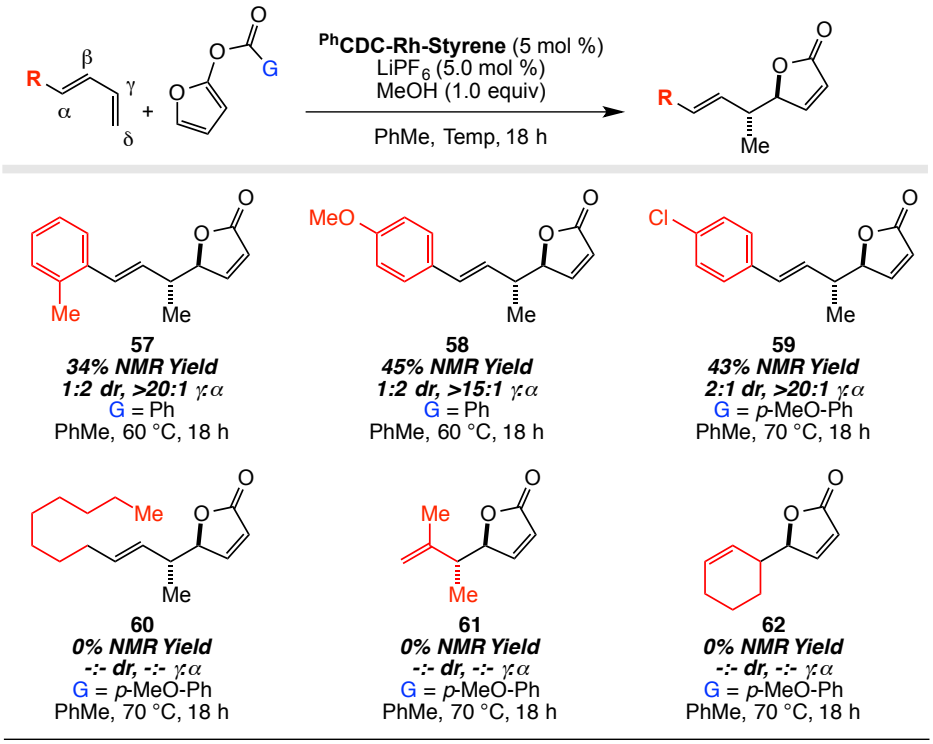
significantly improve the diastereoselectivity of the transformation, although a drop in regioselectivity was observed when an electron poor benzoyl group was employed. We opted to briefly explore the substrate scope to observe how the efficiency and selectivity of the reaction adapted to electronic and steric modifications of the diene.

4.3.2: Reaction Scope of Diene Hydroalkylation with Benzoyl-Furan Nucleophiles

The enolate hydroalkylation of terminal dienes with furan nucleophiles forms valuable allylic butenolide natural products and generates vicinal stereocenters. The diastereoselectivity of hydroalkylation with oxazolone nucleophiles was one of the strengths of that method (see Section 3.3), but additions with benzoyl furans proved far less selective. The lackluster diastereoselectivity obtained with **BzO-furan** and **52** for **50** was troubling, but other diene electrophiles might be more selective and provide a better understanding of the transformation. As such, a simple substrate scope was tested to observe how aryl and alkyl dienes with various functional groups would behave with the **^{Ph}CDC-Rh-styrene** catalyst.

The preliminary substrate scope shows how **BzO-furan** and **52** react with aryl and alkyl dienes (Scheme 4.3.2-1, unpublished results). Substrate **57** demonstrated that the selectivity of the reaction could not be easily predicted. During studies on the addition of oxazolones to dienes, the inclusion of a methyl group in the *ortho*-position of the aryl diene had improved region- and diastereocontrol. However, this did not translate to enolate hydroalkylation as **57** was formed in 34% yield as a 1:2 mixture of diastereomers. Minor changes to the diene significantly decreased conversion and NMR analysis of the hydroalkylation of 2-methyl-1,3-phenylbutadiene showed that the reaction generated the opposite diastereomer compared to previous reactions forming **50** (see Supporting Info). Similar stereoselectivity was obtained in the formation of **58**, which was synthesized in 45% yield as a similar 1:2 mixture of diastereomers. To further confuse the

situation, hydroalkylation formed **59** with the same major diastereomer as **50** in 43% NMR yield and 2:1 dr. These diastereoselectivities were independent of the identity of the benzoyl protecting group (ie: Ph versus *p*-MeO-Ph). Further attempts to explore the scope of alkyl dienes, such as **60**, **61**, and **62**, failed to provide any of the allylic butenolide products



Scheme 4.3.2-1: Diene scope of CDC-Rh(I) catalyzed hydroalkylation with benzoyl furan nucleophiles (unpublished results).

The substrate scope of the addition of benzoyl furans to dienes was explored as a method for vetting the reactivity and selectivity of our optimized reaction conditions. Overall, the reaction was not sufficiently tolerant of modifications to the diene substrate scope. Any changes to the diene resulted in reduced conversion and diastereoselectivity. Diastereoselectivity did not improve beyond a 2:1 ratio of products and the favored diastereomer appeared to be substrate specific. In order for this reaction to be synthetically useful, higher selectivities would need to be

obtained and a model for predicting the favored diastereoisomer developed. To solve these challenges we began to explore modifications to the **^{Ph}CDC-Rh-styrene** catalyst.

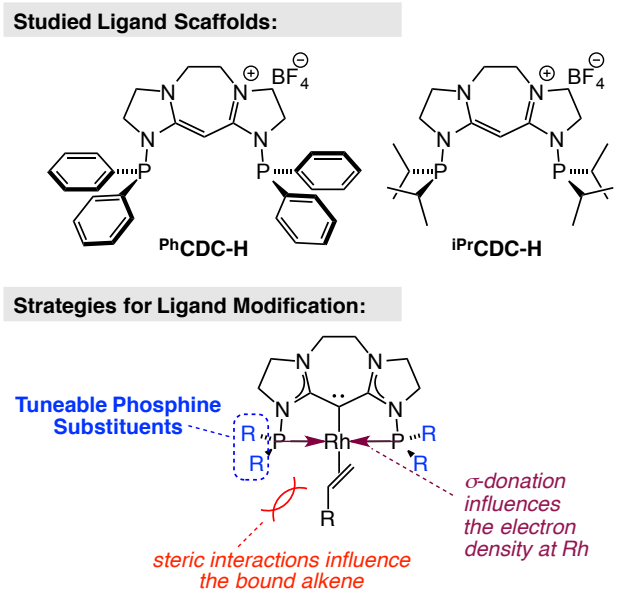
4.4: Synthesis of Sterically and Electronically Modified CDC-Rh(I) Catalysts

The results of our experiments with benzoyl- and silyloxyfuran proved that the addition of enolates to dienes could be catalyzed by **^{Ph}CDC-Rh-styrene** to generate C-C sp^3-sp^3 hybridized bonds and generate allylic butenolide products. These compounds are relevant to the synthesis of many natural products that incorporate butenolides.[1–3] However, the efficiency and stereoselectivity obtained with **^{Ph}CDC-Rh-styrene** as a catalyst was insufficient for publication and initial optimization of the reaction conditions failed to overcome these challenges. Modifying the catalyst to improve reactivity and selectivity could solve problems with this potentially useful transformation. The process of developing electronically and sterically modified catalysts was begun as soon as the diazepinium ligand scaffolds were discovered, but this was the first instance where it was necessary to move a reaction beyond proof-of-concept.

4.4.1: Goals for Synthetic Modifications to the Carbodicarbene Ligand Scaffold

The diazepinium ligand scaffold used in the **^{Ph}CDC-Rh-styrene** complex was designed to be modular with the phosphine substituents serving as handles for tuning the steric and electronic properties of the ligand (Scheme 4.4.1-1). Such modifications had not been necessary up to this point and, despite many ligand syntheses (*vida infra*), catalyst modifications had not improved catalytic activity. Hence, ligand syntheses beyond **^{Ph}CDC-H** and **^{iPr}CDC-H** have not been discussed for the previously developed hydrofunctionalizations. The phosphine substituents provide excellent sites for catalyst modification as these groups are adjacent to the reactive metal center and can provide substantial steric control over any bound olefins. Furthermore, the

electron-withdrawing or donating properties of these substituents can influence the electron density of the phosphine ligands. This directly impacts the σ-donation from the phosphine ligands to the Rh metal and, subsequently, the electron density at the metal center. Since its application in hydroamination (see Chapter 1), **^{iPr}CDC-H** consistently exhibited reduced activity compared to **^{Ph}CDC-H**. As such, more effort was spent developing ligand modifications that incorporate aryl phosphine substituents rather than alkyl phosphines under the assumption that this trend would remain valid for the modified catalyst structures. The carbon backbone of the diazepinium scaffold offers several sites for catalyst modification, however these positions are pro-chiral and would complicate the development an achiral catalyst for a diastereoselective, rather than enantioselective, reaction.



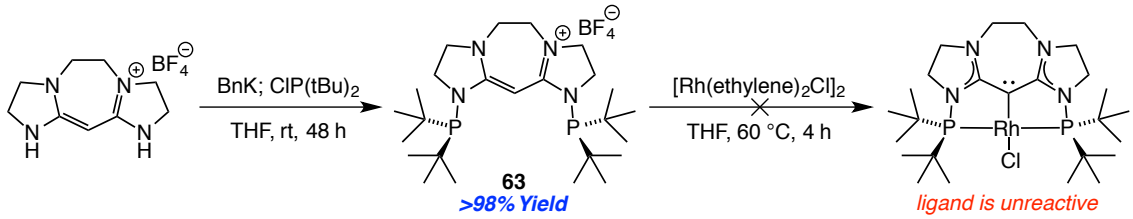
Scheme 4.4.1-1: Strategies for tuning the activity of the diazepinium ligand scaffold.

During many ligand syntheses several trends have become apparent: (i) Electron rich aryl phosphine substituents tend to result in more stable ligand scaffolds. This is likely due to the increased bond strength of the P-N bond when the phosphine has a greater electron density. (ii) The installation of electron poor phosphines commonly requires forcing reaction conditions with

anionic nucleophiles, whereas more electron rich phosphines benefit from using uncharged nucleophiles. (iii) Large alkyl substituents or the inclusion of any *ortho*-substituents prevents the tridentate scaffold from coordinating to the metal center. (iv) The more electron poor CDC-Rh complexes are often unstable to small alkoxide bases, but can usually tolerate highly hindered bases that cannot reach the occluded phosphine atoms. We will begin our discussion with several failed syntheses that reveal many of the challenges in forming modified diazepinium ligands.

4.4.2: Early Attempts at Synthesizing Modified Ligand Scaffolds with Increased Sterics

Some of the earliest efforts in ligand synthesis were made during the study of intramolecular hydroamination with **^{iPr}CDC-Rh-Cl**. It was proposed that a ligand bearing a more hindered alkyl phosphine could assist in preventing catalyst inhibition from tightly bound amine nucleophiles. The di-*tert*-butyl phosphine analogue of **^{iPr}CDC-H** could be readily synthesized using a strong base to form the doubly deprotonated diazepinium anion (Scheme 4.4.2-1). Benzyl potassium (BnK) was particularly useful as a titrating base; the color change from bright red to a dull white heterogeneous mixture in THF signaled that the potassium amide of the diazepinium backbone was formed. These forcing conditions proved necessary in the synthesis of **63**, and many other ligands, as the large size of *tert*-butyl substituents prevented the formation of the P-N bonds with neutral bases (ie: triethylamine). The necessity for forcing conditions was a prelude to the challenges encountered metallating **63**. Reactions in refluxing THF failed to form the tridentate Rh complex, instead returning unreacted **63**. Refluxing in toluene also failed to accomplish the desired metallation and the ligand was abandoned.

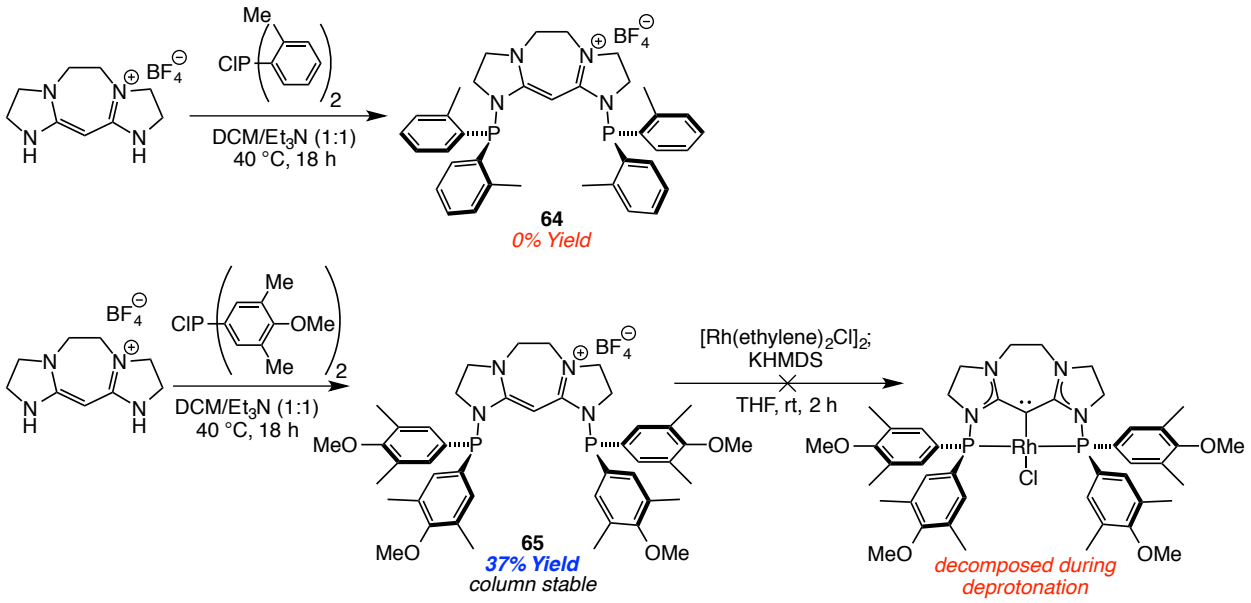


Scheme 4.4.2-1: Attempted synthesis of a *tert*-butyl phosphine substituted CDC-Rh complex.

The attempted metallation of **63** exemplifies the reluctance of sterically encumbered phosphine substituents to bind to Rh. The importance of sterics in these ligand syntheses is further evidenced in the attempted formation of **64** and **65**. The increased sterics of an *ortho*-tolyl group prevented the formation of the P-N bond in **64**, which demonstrates how increasing the size of the aryl substituents can destabilize the ligand structure (Scheme 4.4.2-2). The failed reactivity of *ortho*-substituted arenes is a general limitation for the phosphine substituents.

The synthesis of **65** shows how sterics can affect metallation with hindered phosphine substituents (Scheme 4.4.2-2). **65** could be synthesized analogously to **^{Ph}CDC-H** in a modest 37% yield after purification by column chromatography. Many electron rich aryl phosphines are stable to silica gel chromatography, which greatly simplifies their synthesis. The reduced yield is indicative of partial conversion to the bis-phosphorylated ligand. This is commonly observed for more challenging P-N bond formations where it is common to obtain the product as a mixture with the mono-phosphorylated diazepine. This can be partially ameliorated by increasing the equivalents of phosphine chloride in the reaction. The influence of the increased steric contributions of the trisubstituted arenes in **65** was not observed until the attempted formation of the corresponding CDC-Rh complex. The increased congestion of the Rh complex weakens the P-N bonds of the ligand and causes **65** to decompose upon addition of KHMDS. Although hindered bases are usually tolerated by CDC-Rh(I) complexes, any steric or electronic effects that reduce the strength of the P-N bond decrease the stability of the catalyst. The catalyst

formation with **65** is indicative of later syntheses as combining the diazepinium ligand with a source of Rh allows for partial formation of the octahedral Rh-hydride. Decomposition only occurs when base is used to convert the complex from Rh(III) to square planar Rh(I).



Scheme 4.4.2-2: Additional examples of syntheses where the sterics of the phosphine substituents prevented ligand and/or complex formation.

The attempted synthesis of **65** serves is an excellent example of how the substitution pattern and electronics of the phosphine substituents effect catalyst formation. The electron rich arene assists in the initial formation of the P-N bond and allows for purification using column chromatography. As such, **65** can be readily synthesized despite being a trisubstituted arene. However, its subsequent use as a ligand is prevented by sterics and results in fragmentation of the P-N bond.

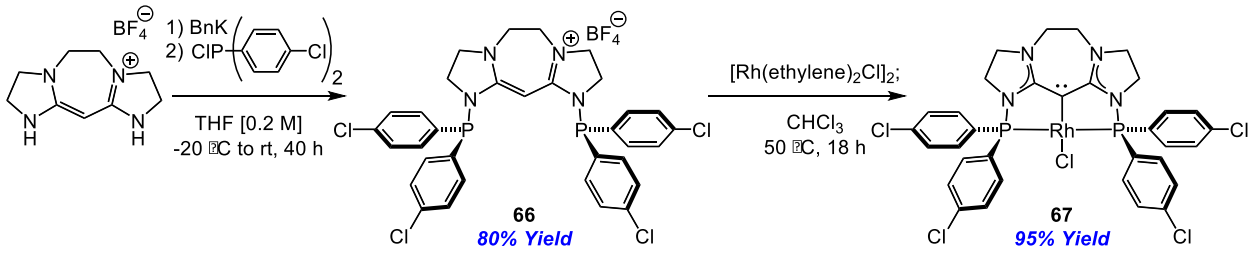
4.4.3: Synthesis of Achiral CDC-Rh(I) Complexes with Modified Phosphine Substituents

One of the goals of developing new catalysts was to increase the reactivity of the CDC-Rh(I) complexes. It was predicted that a more electron poor Rh center would increase the

activation of a bound π-system. Complexes with more electropositive Rh centers could be synthesized by installing electronegative functional groups on the phosphines, which would reduce the electron density of the phosphorus atoms, reduce σ-donation to the Rh center, and weaken the P-N bonds. Several electron poor Rh complexes were synthesized using this strategy, but the reduced electron density at the Rh center had unintended consequences on complex synthesis; the insertion into the diazepinium C-H bond proved more challenging with less electron rich Rh centers. This is presumably due to the increased activation barrier for oxidative addition in electron poor metal complexes.[71] Increasing the reaction temperature for the formation of the Rh-hydride could often solve this issue.

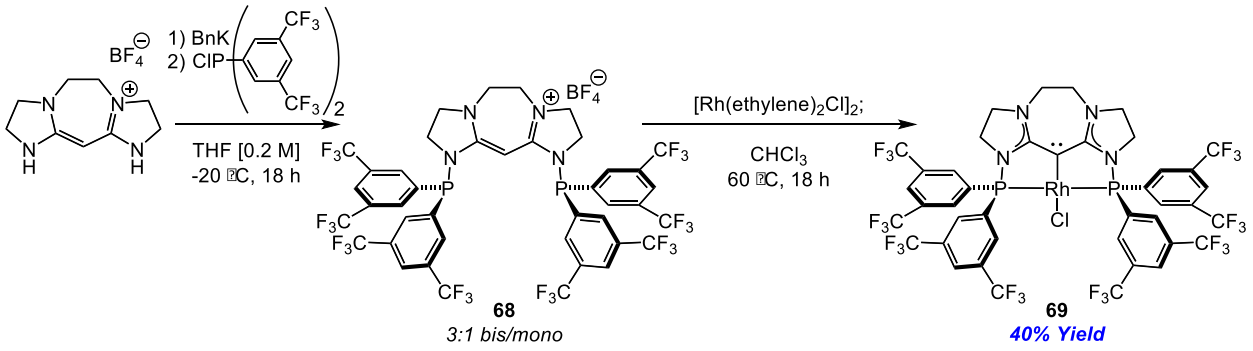
The synthesis of the *para*-chlorophenylphosphine substituted diazepinium scaffold **66** could be accomplished through the anionic method developed during the formation of **63** (Scheme 4.4.3-1). Deprotonation of the diazepinium salt with BnK at room temperature generated the amide anion, which efficiently added to bis(4-chlorophenyl)chlorophosphine at -20 °C to generate **66** in 80% yield. The purification of ligands synthesized through this method is challenging, as they are not stable to aqueous conditions or column chromatography. Purification can often be accomplished using solvent washes and/or triturations, but it is not uncommon for the ligands synthesized via these methods to be slightly contaminated with the mono-phosphine products formed from incomplete phosphorylation. Formation of the CDC-Rh complex **67** required elevated temperatures (50 °C) and the use of di-μ-chlorotetraethylene dirhodium(I) ($[Rh(ethylene)_2Cl]_2$), when substitution of the cyclooctadiene ligand of chloro(1,5-cyclooctadiene)rhodium(I) dimer ($[Rh(cod)Cl]_2$) proved challenging with the less electron rich phosphine ligands of **67**. The addition of a basic additive to deprotonate the Rh-hydride proved unnecessary as the product was formed without additional base after heating at 50 °C. This

appears to be common to the synthesis of electron poor CDC-Rh complexes (*vide infra*). $[Rh(ethylene)_2Cl]_2$ has proven to be a more reliable source of Rh for metallations of modified diazepinium ligand scaffolds.



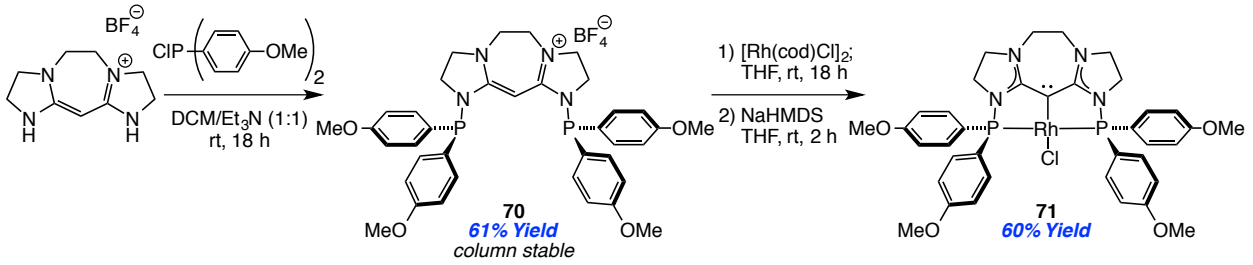
Scheme 4.4.3-1: Synthesis of the *para*-chlorophenylphosphine derivative of the CDC-Rh(I) complex.

The 3,5-bis(trifluoromethyl)phenylphosphine derived ligand **68** could be synthesized in a manner similar to **66**, but in lower yield and purity (Scheme 4.4.3-2). The more electron withdrawing bis(trifluoromethyl) substituents decreased the efficiency of the P-N bond formation and reduced the stability of **68**. The ligand could only be formed as a 3:1 mixture of the desired bis-phosphine **68** and the mono-phosphine. Additionally, the reduced stability of the P-N bond meant that **68** must be stored at -20 °C and used immediately. Metallation could be accomplished to form slightly impure **69** in 40% yield and, curiously, did not require the addition of a base to deprotonate the hydride and form the square planar Rh(I) complex. The decreased electron density at the Rh center appears to increase the acidity of the Rh-hydride to the point that it either eliminates spontaneously as HBF_4 or is deprotonated by an adventitious base (ie: decomposed diazepinium impurities).



Scheme 4.4.3-2: Synthesis of the 3,5-bis(trifluoromethyl)phenylphosphine derivative of the CDC-Rh(I) complex.

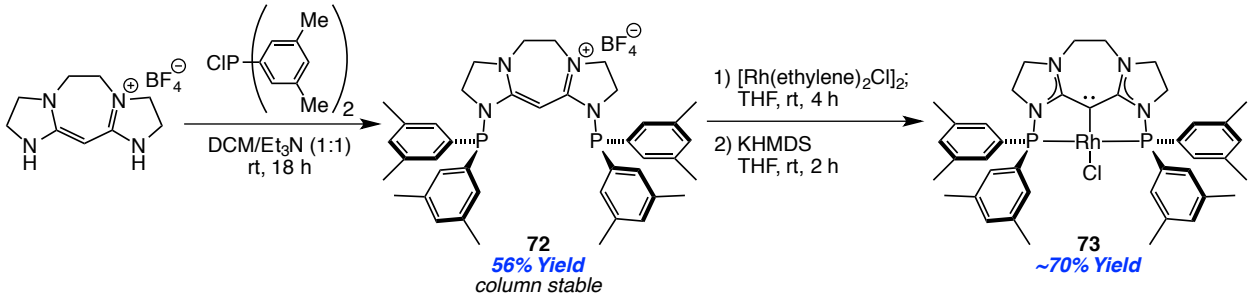
In order to have a point of comparison for the electron poor CDC-Rh complexes **67** and **69**, a ligand with an electron donating methoxy-substituent was synthesized (Scheme 4.4.3-3). The electron rich ligand **70** proved to be stable to column chromatography and was isolated in 61% yield using the neutral P-N bond synthesis developed for **^{Ph}CDC-H**. The synthesis of the **^{Ph}CDC-Rh-Cl** complex translated to **71**, which was formed in 60% yield by combining **70** and $[Rh(cod)Cl]_2$ in THF at room temperature and deprotonating the resulting Rh-hydride with the hindered amine base sodium hexamethyldisilazide (NaHMDS).



Scheme 4.4.3-3: Synthesis of the *para*-methoxyphenylphosphine derivative of the CDC-Rh(I) complex.

With several examples of electronically modified achiral CDC-Rh(I) complexes in hand, there was renewed interest in synthesizing a catalyst that differed from **^{Ph}CDC-Rh-Cl** sterically rather than electronically. The attempted synthesis of a complex derived from **65** showed that

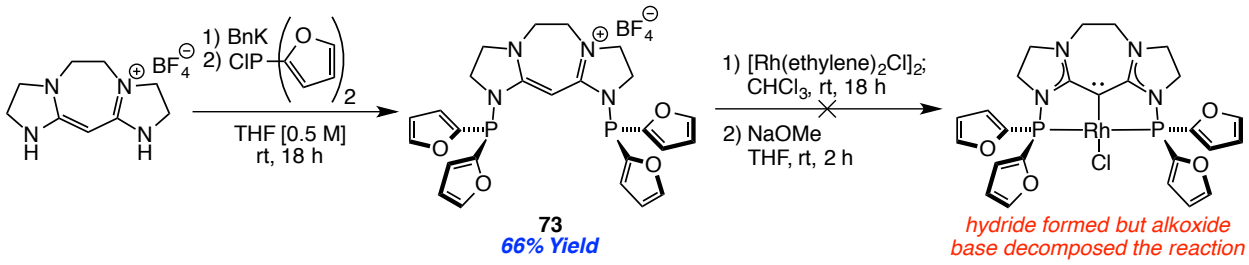
this could be challenging, however, the successful synthesis of **69** proved that *meta*-substitution could be incorporated into the phosphine substituents without preventing complex formation. Diazepinium salt **72** was synthesized in 56% yield after purification by column chromatography using the neutral P-N bond formation method (Scheme 4.4.3-4). This ligand could be applied to Rh to generate **73** in approximately 70% yield with a small amount of an unknown impurity. The complex could not be further purified due to its increased solubility in non-polar solvents and was used in catalytic reactions as formed.



Scheme 4.4.3-4: Synthesis of the *3,5*-dimethylphenylphosphine derivative of the CDC-Rh(I) complex.

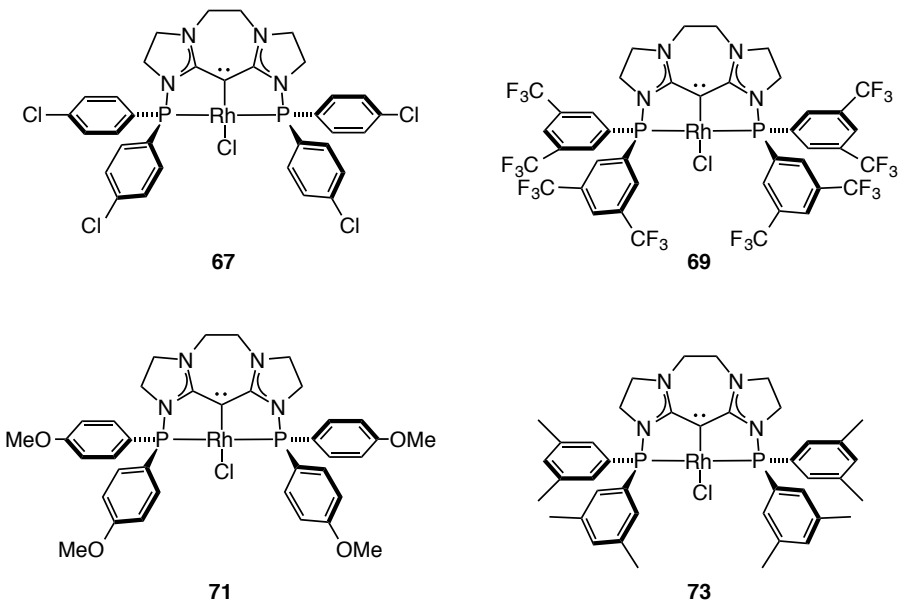
The last achiral complex synthesis attempted employed heterocyclic furyl- rather than phenyl substituents (Scheme 4.4.3-5). Furan rings are both smaller and more electron withdrawing than phenyl rings. Since the steric contributions of a phenyl ring cannot be reduced without modifying the arene structure, furylphosphine was selected as a counterpoint to the larger substituted arenes with the reasoning that a reduction in sterics might prevent clashes between the bound diene and/or approaching nucleophile. **73** was readily synthesized in 66% yield using the anionic method developed for installing P-N bonds to electron poor phosphine atoms. The combination of $[Rh(ethylene)_2Cl]_2$ and **73** in chloroform was observed by NMR spectroscopy to form the Rh-hydride, however, when sodium methoxide (NaOMe) was added the complex decomposed completely. It is possible that a more hindered base (eg: KHMDS)

might allow for deprotonation of the Rh-hydride complex, but this synthesis was not pursued further due to time constraints and poor catalytic results with other electron poor catalysts (*vide infra*).



Scheme 4.4.3-5: Attempted synthesis of the furylphosphine derivative of the CDC-Rh(I) complex.

In summary, four new achiral CDC-Rh(I) complexes were synthesized that incorporate steric and electronic variations in the structure of ^{Ph}**CDC-Rh-Cl** (Scheme 4.4.3-6). Challenges in ligand and complex stability were encountered throughout the synthesis of **67**, **69**, **71**, and **73** that necessitated the development of improved conditions for the formation of the P-N bond and for the metallation with Rh. These studies are an important component of our understanding of the behavior of diazepinium derived CDC ligands and demonstrate how the electronics and sterics of the phosphine effect the complexes formed. These catalysts have since been applied to many catalytic hydrofunctionalizations, but only a few of will be discussed in this dissertation. Despite the promise of these new structures, none of them have proven to be more useful than the parent ^{Ph}**CDC-Rh-Cl** for catalysis.



Scheme 4.4.3-6: Structures of successfully synthesized CDC-Rh(I) complexes with differentially substituted aryl phosphines.

4.5: Applications of Modified CDC-Rh(I) Complexes to the Hydroalkylation of Dienes

The purpose of our efforts in catalyst synthesis was to develop a solution to the poor selectivity and reactivity observed in the hydroalkylation of dienes with benzoyl-furan nucleophiles. This went hand-in-hand with the broader goal of creating a library of CDC-Rh(I) complexes that could be applied to a myriad of hydrofunctionalization reactions and applied to reactions outside the purvey of olefin activation. A challenge in applying the new complexes to catalytic reactions is that they are formally pre-catalysts. Two chapters of this dissertation elapsed before catalyst activation of **^{Ph}CDC-Rh-Cl** with $AgBF_4$ could be fully explained. It would be naïve to assume that the catalyst formations of the complexes described in Section 4.4 are identical to that of **^{Ph}CDC-Rh-Cl**. Furthermore, this approach does not include the fact that recent reactions utilize the cationic **^{Ph}CDC-Rh-styrene** complex. Despite these complications, the most direct way to learn more about these modified CDC complexes is to apply them to

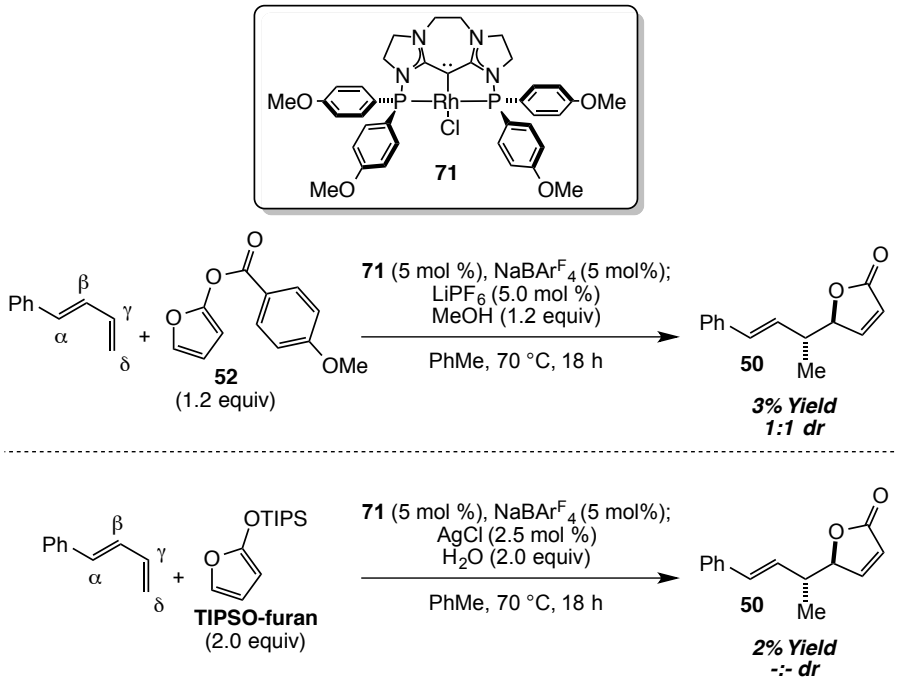
reactions and observe their catalytic activity. As such, the hydroalkylation of 1,3-phenylbutadiene with **BzO-furan** will serve as a testing ground for these new complexes. Additional reactions (eg: hydroarylation, hydroamination, enol hydroalkylation) have also been explored, but will only be discussed in passing as we focus on solving the challenge presented by enolate hydroalkylation.

4.5.1: Screening Electronically Modified CDC-Rh(I) Complexes for the Formation of Allylic Butenolides

The *in situ* catalyst formation for the complexes shown in Scheme 4.4.3-6 was adapted from the synthesis of **^{Ph}CDC-Rh-styrene** using $NaBAr^F_4$ and a diene substrate. The reactivity differences between **^{Ph}CDC-Rh-Cl** and **^{Ph}CDC-Rh-styrene** have proven that the cationic complex is more reactive than the first generation in many respects. In theory this forms the cationic CDC-Rh(I) complexes *in* situ as $NaBAr^F_4$ strips the chloride and allow for the desired diene to bind the metal center. However, we were unable to validate that catalyst formation was occurring efficiently in all cases due to time constraints and minor impurities in the modified CDC-Rh(I) complexes. As such, the reactivity of these complexes is judged solely from the conversions obtained in catalytic hydrofunctionalizations.

One of the major challenges in the furan hydroalkylations described above (*vide supra*) is that the decomposition of the nucleophile is competitive with the rate of product formation. It was hypothesized that increasing the electron density at the Rh center would reduce the rate of desilylation through electrophilic activation of the furan while maintaining an electropositive metal center capable of activating a bound olefin. Hydroalkylation of 1,3-phenylbutadiene was explored with both **52** and **TIPSO-furan** to validate or disprove this hypothesis. Catalyst formation with **71** was accomplished by stirring with $NaBAr^F_4$ and 1,3-phenylbutadiene to form

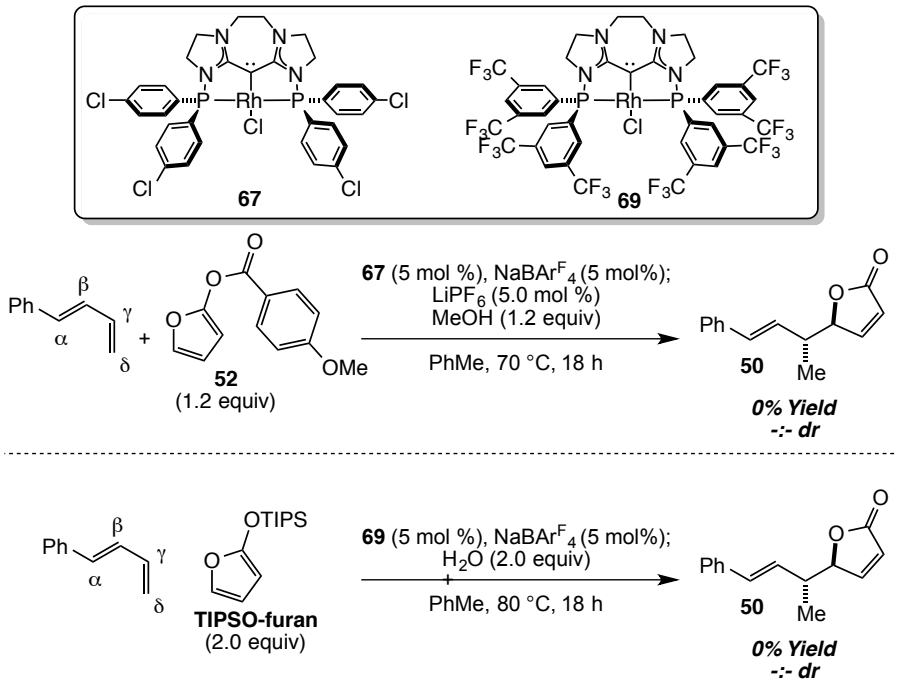
the catalytic intermediate analogous to **1**. Reaction at 70 °C with **52** generated **50** in 3% yield, whereas reaction at 50 °C with **TIPSO-furan** gave a 2% yield (Scheme 4.5.1-1, unpublished results). In both of these reactions a portion of the furan starting material was returned, which validated the hypothesis that a less electropositive Rh center would decrease desilylation. However, the rate of product formation was decreased to an even greater extent and **71** proved to be a poor catalyst for the diene hydroalkylation.



Scheme 4.5.1-1: Enolate hydroalkylations catalyzed by **71** (unpublished results).

The evident failure of an electron rich variant of the CDC-Rh(I) catalysts suggested that a solution to the observed reactivity problems might lie in an electron poor catalyst such as **67** or **69**. These catalysts were applied to the formation of allylic butenolide **50** using **52** and **TIPSO-furan**, but no reactivity was observed (Scheme 4.5.1-2, unpublished results). Furthermore, the starting materials were completely consumed, indicating the relative increase in electrophilicity of the Rh center compared to **^{Ph}CDC-Rh-styrene**. This could explain the failure of these catalysts as the byproducts generated from the desilylation likely inhibit catalysis (see Section

4.6). Alternatively, the poor reactivity exhibited by **67** and **69** may be indicative of incomplete catalyst activation, since the chloride ligand will be more difficult to abstract from an electron poor Rh complex. Although these results were in no way optimized, the complete lack of reactivity for reactions that previously generated **50** in modest to good conversions led us to seek a catalyst that could improve the diastereoselectivity of the transformation while maintaining the activity observed with **52** and **^{Ph}CDC-Rh-styrene**.



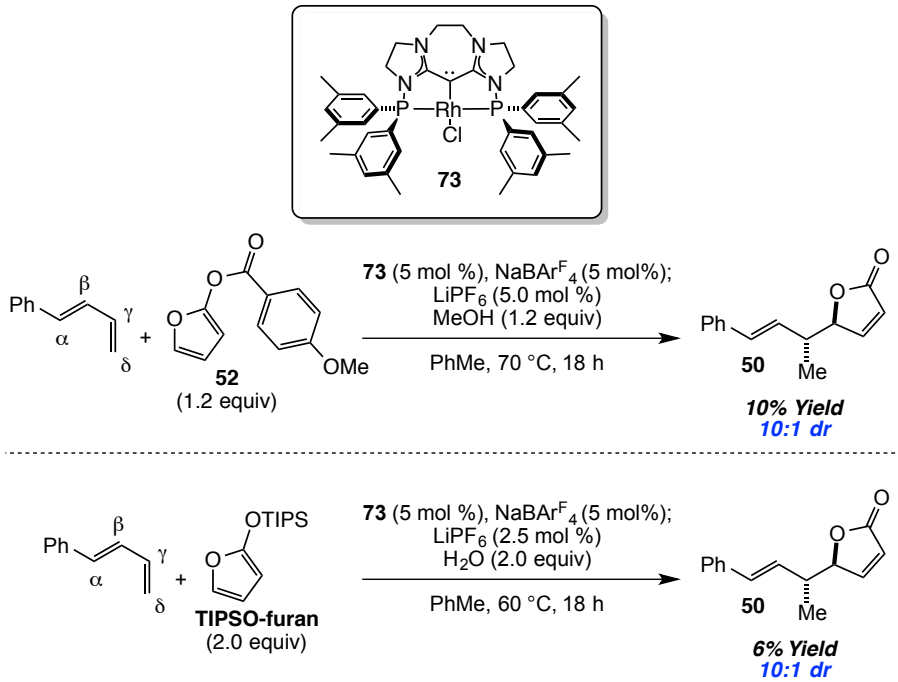
Scheme 4.5.1-2: Enolate hydroalkylations catalyzed by **67** and **69** (unpublished results).

4.5.2: Screening Sterically Modified CDC-Rh(I) Complexes for the Formation of Allylic Butenolides

The poor reactivity observed with both electron rich and electron poor phosphine substituents suggested that the electronics of the **^{Ph}CDC-Rh** complexes are close to optimal for hydroalkylation. As such, modified catalysts that incorporated phosphine substituents with minimal electronic differences were likely candidates for further catalyst modification. It is unlikely that the reactivity of the cationic CDC-Rh(I) catalyst could be substantially improved

without electronic modifications, but the selectivity of the hydroalkylation could be addressed through steric modifications to the aryl phosphine substituents. The poor diastereo- and regioselectivity of the hydroalkylation with **BzO-furan** was the primary issue preventing its application in synthesis, since a synthetically useful conversion of 73% was previously obtained. Of the newly synthesized CDC-Rh complexes, **73** should differ in electronics only slightly from catalysts derived from **^{Ph}CDC-H**. However, the steric contribution of the methyl substituents should significantly impact the binding of the olefin and approach of the nucleophile during C-C bond formation.

Hydroalkylation catalyzed by **73** was tested with both **52** and **TIPSO-furan** to determine how the inclusion of *meta*-methyl substituents on the arene rings affected diastereoselectivity (Scheme 4.5.2-1, unpublished results). Hydroalkylation of 1,3-phenylbutadiene with **52** at 70 °C generated the butenolide **50** in 10% yield as a 10:1 mixture of diastereoisomers. The dramatic improvement in diastereoselectivity demonstrates that the sterics on the phosphine substituents can be used to control selectivity, but at significant cost to conversion. The same reaction with **^{Ph}CDC-Rh-styrene** generated **50** in 73% yield, which demonstrates how minor changes to the catalyst and reaction conditions can dramatically reduce activity. A similar reaction with **TIPSO-furan** using 2.5 mol% $LiPF_6$ at 60 °C generated **50** in 6% yield and 10:1 dr. This result reinforces the above reaction as the catalyst allows for the most diastereoselective transformation observed with an enolate nucleophile, yet shows extremely poor conversion to product. Furthermore, neither reaction returned the furan starting materials, suggesting that the catalyst does not remain active in solution.



Scheme 4.5.2-1: Enolate hydroalkylations catalyzed by **73** (unpublished results).

The improved diastereoselectivity obtained with reactions catalyzed by **73** is strong evidence for the versatility of the diazepinium ligand framework, but every ligand modification explored resulted in decreased reactivity. Our results prove that more stereoselective catalysts can be developed using the tridentate ligand framework, however, the loss in reactivity was too great to justify the use of **73** over **^{Ph}CDC-Rh-styrene**. Preliminary efforts were undertaken to synthesize the styrene complex of **73**, but were not pursued as we opted to seek alternative solutions to the challenges posed by enolate hydroalkylation.

These studies proved that the CDC ligands derived from the diazepinium scaffold can be tuned by simple modifications to the phosphine substituents. Modified ligands can be synthesized in only two-steps from readily available materials and have been successfully applied to Rh and several other late transition metals. The application of these ligands to enolate hydroalkylation provided insight into their synthesis and, more importantly, into the reactivity engendered from changes to the electronics and sterics of the ligand. Although diversification of

the diazepinium scaffold is not currently an active vein of research in our laboratory, we hope that these studies assist in the application of these unique CDC ligands to new organometallic complexes and catalytic reactions. We are excited to see what future uses are found for these tridentate ligand scaffolds.

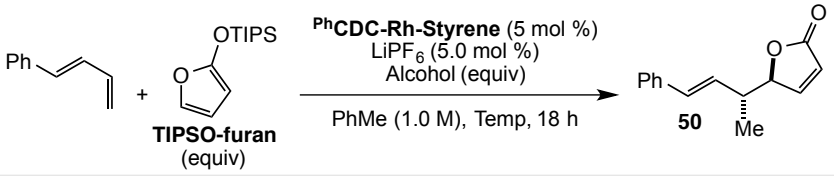
4.6: Revisiting the Additions of Silyloxyfurans to 1,3-Phenylbutadiene

The continued failure to improve the reactivity of diene hydroalkylation with benzoyl-protected furans suggested that that enolate source might be suboptimal for the formation of the desired allylic butenolide products. As stated previously, the low diastereoselectivity was the greatest issue with benzoyl-furan nucleophiles and could not be reliable improved via optimization of the reaction conditions or selection of the alcohol additive. Only catalyst modification allowed for improved diastereoselectivity, but could only be accomplished in 10% conversion. Examination of past reactions for the most diastereoselective results showed that silyl-protected furan nucleophiles generally provided selectivities ranging from 4:1 to 8:1 dr. **TIPSO-furan** was previously passed over in favor of **52** due to the higher conversion with that enolate equivalent, however, the importance of diastereoselectivity led us to return to **TIPSO-furan** as a possible solution to our selectivity problems. The goal was to improve reaction conversion while maintaining the 4:1 diastereoselectivity shown in Scheme 4.2.1-5.

4.6.1: Diene Hydroalkylation with Triisopropylsilyloxyfuran

Preliminary optimizations of hydroalkylation with **TIPSO-furan** were performed to determine how the reaction responded to changes in the alcohol additive, temperature and equivalents of the nucleophile (Table 4.6.1-1, unpublished results). The initial result with MeOH at 60 °C gave **50** in 33% NMR yield to a 4:1 mixture of diastereomers (Entry 1). Increasing the

equivalents of alcohol reduced conversion slightly to 24%, but did not affect the diastereoselectivity (Entry 2). When the reaction temperature was reduced to 50 °C both the yield and diastereoselectivity improved and **50** was synthesized in 35% yield, 5:1 dr (Entry 3). This result was particularly informative as it also returned 11% of the **TIPSO-furan** starting material, suggesting that higher conversions might be possible. However, when the equivalents of **TIPSO-furan** added to the reaction was doubled, **50** was only formed in 41% NMR yield with approximately the same amount of returned **TIPSO-furan** (Entry 4). The fact that conversion to product improved by only slightly while consuming an additional equivalent of the furan strongly indicated that the reaction conditions were too forcing and resulted in catalyst deactivation. Reaction with a 2:1 ratio of furan to alcohol failed to generate any product, which suggests that desilylation in the absence of an alcohol destroys the catalyst. Lastly, the use of a smaller alcohol H_2O decreased diastereoselectivity to 4:1 while providing **50** in 42% yield.

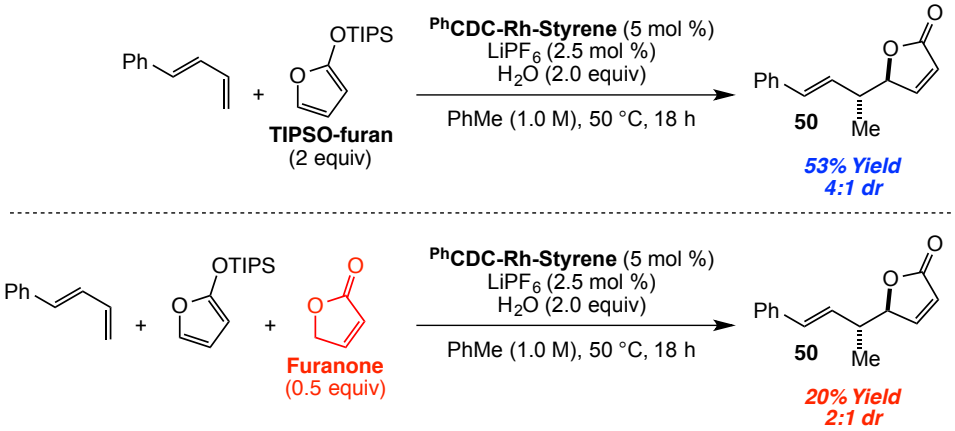


Entry	Equiv Furan	Alcohol; equiv	Temp (°C)	NMR Yield (%)	dr
1	1.0	MeOH; 1.0	60	33	4:1
2	1.0	MeOH; 2.0	60	24	4:1
3	1.0	MeOH; 1.0	50	35	5:1
4	1.0	MeOH; 2.0	60	41	5:1
5	2.0	MeOH; 1.0	60	0	-
6	2.0	H_2O; 2.0	60	42	4:1

Table 4.6.1-1: Screen of reaction conditions for the hydroalkylation of 1,3-phenylbutadiene with **TIPSO-furan** (unpublished results).

Results from initial investigation of hydroalkylation with **TIPSO-furan** as the enolate source did not reach the high conversions obtained with the benzoyl derivative **52**. The limited

effect of adding more furan indicated that the catalyst was being inhibited as the reaction progressed (Table 4.6.1-1, Entry 1 vs 2, unpublished results). This could indicate that product inhibition favored desilylation over hydroalkylation. Product inhibition could also stem from the byproducts of desilylation, furanone and triisopropylsilanol. We suspected that furanone might bind to the CDC-Rh(I) complex. This would explain why conversion did not significantly increase with higher equivalents of silyloxyfuran, as catalyst deactivation would occur before the excess nucleophile could react with the electrophilically activated diene. An experiment was run with and without the addition of furanone to observe how its presence affected reactivity (Scheme 4.6.1-2). The reaction with H_2O at 50 °C generated **50** in 53% yield and 4:1 dr, but the identical conditions with the addition of 0.5 equivalents of furanone formed **50** in only 20% yield and 2:1 dr. These results clearly demonstrated that the byproducts of desilylation were inhibiting the catalyst.



Scheme 4.6.1-2: Control reaction demonstrating the inhibitory effect of furanone on hydroalkylation with **TIPSO-furan** (unpublished results).

The discovery of the harmful effects of furanone on reactivity led us to the conclusion that we needed to explore reaction conditions that would result in as little desilylation as possible. The rate of reaction did not matter significantly provided that the ratio of product

formation to desilylation was kept as high as possible. Previous experiments demonstrated that larger alcohol additives slowed desilylation of silyloxyfuran. Similarly, lower temperatures and reduced concentrations of the furan nucleophile should encourage catalyst association with the diene rather than the furan. These insights were used to begin developing a useful catalytic method for the intermolecular hydroalkylation of dienes to generate allylic butenolide products diastereoselectively.

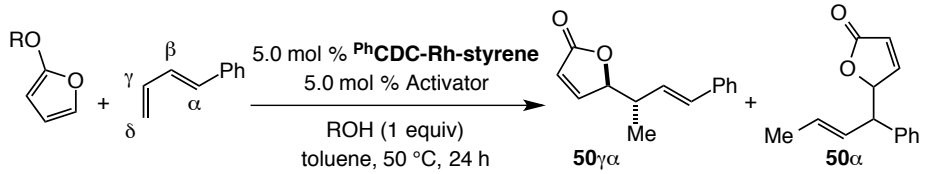
4.7: Diastereoselective Synthesis of Substituted 2-Butanones through Carbodicarbene-Rh Catalyzed Additions of Silyloxyfurans

In the following section we present our preliminary efforts towards the development of a diastereoselective synthesis of 2-allyl-butanones through the CDC-Rh catalyzed hydroalkylation of dienes with silyl enol ethers. This work will be accomplished through electrophilic activation of bound C-C π-systems and represent the first hydroalkylation of unactivated olefins with silyl enol ethers. The reactions generate allylic butenolides in up to 95% yield, 5:1 dr and >20:1 regioselectivity using 5 mol% of a CDC-Rh(I) catalyst and 5 mol% $LiPF_6$ as a co-catalyst. It is our goal to have this work published in the near future as a follow-up to the recent disclosure of hydroalkylation with oxazolones.

4.7.1: Optimization of Carbodicarbene-Rh Catalyzed Diene Hydroalkylation with Silyloxyfurans

The search for an efficient hydroalkylation of terminal diene electrophiles with silyloxyfuran nucleophiles began by exploring the effect of the silyl protecting group on reactions catalyzed by 5 mol% **^{Ph}CDC-Rh-styrene** and 5 mol% of $LiPF_6$ as a Lewis acid for catalyst activation (Table 4.7.1-1).[69] Reactions were run with silyloxyfurans protected with trimethyl-, *tert*-butyldimethyl-, tris(trimethylsilyl)-, and triisopropylsilyl groups at 50 °C with 1

equivalent of water as a proton source and silyl scavenger. Trimethylsilyloxyfuran hydrolyzed readily under the reaction conditions to generate furanone and failed to provide any of the desired product **50** (Entry 1). The more stable silyl protecting groups *tert*-butyldimethyl-, tris(trimethylsilyl)-, and triisopropylsilyl provided **50** in 29% yield, 5:1 dr, 16% yield, 3:1 dr and 29% yield, 5:1 dr, respectively (Entries 2-4, dr refers to the γ-regioisomer). The butenolide product **50** was generated as a 5:1 mixture of the γ- and α-regioisomers when *tert*-butyldimethyloxyfuran and triisopropylsilyloxyfuran were used, but in a 2:1 ratio with the tris(trimethylsilyl)silyloxyfuran nucleophile. As such, reaction with **TIPSO-furan** generated the desired product in the highest conversion and with the greatest diastereo- and regioselectivity and this nucleophile was used for all further screening.



Entry	R	Alcohol	Activator	Yield (%)	dr	γ:α
1	$SiMe_3$	H_2O	$LiPF_6$	0	-:-	-
2	Si(*t*-Bu)Me_2	H_2O	$LiPF_6$	29	5:1	5:1
3	$Si(SiMe)_3$	H_2O	$LiPF_6$	16	3:1	2:1
4	Si(*i*-Pr)$_3$	H_2O	$LiPF_6$	29	4:1	5:1
5	Si(*i*-Pr)$_3$	H_2O	AgCl	21	3:1	3:1
6	Si(*i*-Pr)$_3$	H_2O	$LiBAr^F{}_4$	20	4:1	5:1
7	Si(*i*-Pr)$_3$	MeOH	$LiPF_6$	36	4:1	5:1
8	Si(*i*-Pr)$_3$	*i*-PrOH	$LiPF_6$	41	4:1	6:1
9[c]	Si(*i*-Pr)$_3$	*i*-PrOH	$LiPF_6$	68	3:1	5:1
10[c,d]	Si(*i*-Pr)$_3$	*i*-PrOH	$LiPF_6$	0	-	-

[a]See SI for experimental details. All reactions performed under N_2 atm. Yields of purified products are an average of two runs. [b]Values determined by analysis of 400 or 600 MHz ^1H NMR spectra of unpurified mixtures with hexamethyldisiloxane as an internal standard.; [c]Reactions run with four equivalents of *i*-PrOH and furan, added in four aliquots over three hours. [d]Control reaction run with $[Rh(cod)Cl]_2$ as catalyst with 5 mol % $AgBF_4$.

Table 4.7.1-1: Survey of conditions for the addition of silyloxyfurans to 1,3-phenylbutadiene using a cationic CDC-Rh(I) catalyst.

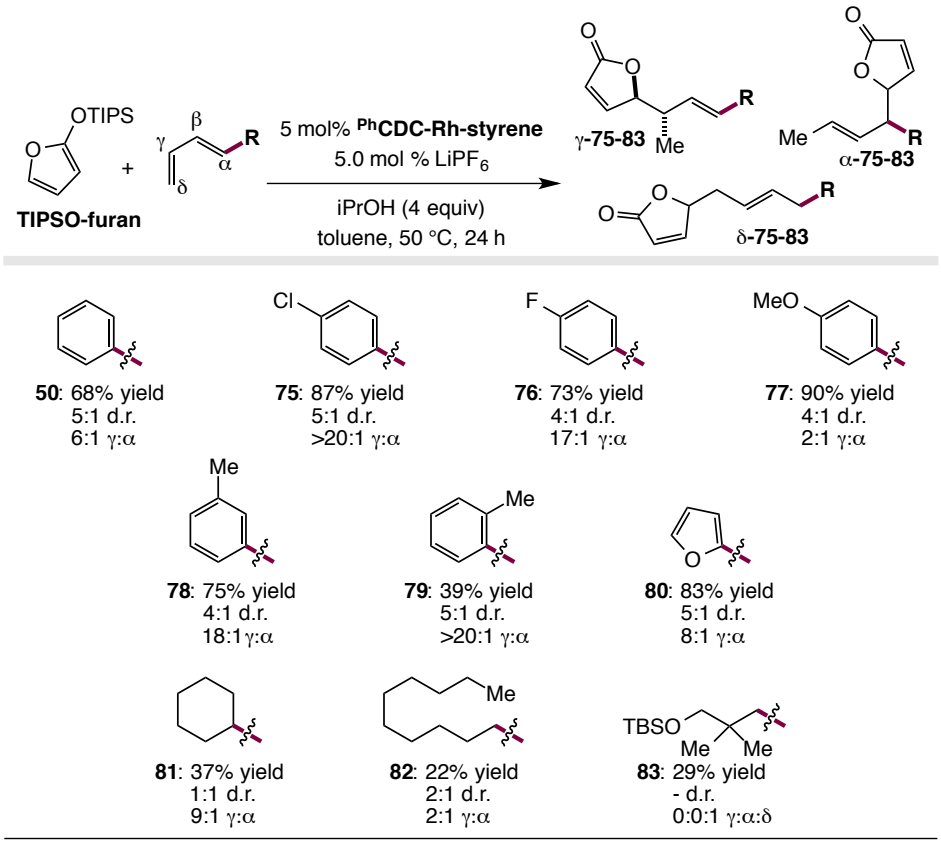
A brief survey of Lewis acid activators showed that $LiPF_6$ was optimal for the reaction; hydroalkylation with 5 mol% AgCl generated **50** in 21% yield as a 3:1 mixture of the γ:α regioisomers with 3:1 dr for the major product (Entry 5), whereas 5 mol% $LiBAr^F_4$ gave **50** in 20% yield as a 5:1 mixture of the γ:α regioisomers with 4:1 dr (Entry 6). During these screens we observed that the majority of **TIPSO-furan** was being hydrolyzed under the reaction conditions to form furanone. In an effort to disfavor this undesired side reaction a series of larger alcohols were screened and *i*-PrOH proved optimal; reaction with MeOH provided **50** in 36% yield as a 5:1 mixture of the γ:α regioisomers with 4:1 dr of the major product (Entry 7), while *i*-PrOH gave 41% yield, 6:1 regioselectivity, and 4:1 dr (Entry 8). The conversion to product was improved by an excess of **TIPSO-furan** in four separate aliquots over the course of 4 hours to limit the concentration of the silyloxyfuran and further discourage hydrolysis; increasing the substrate loading to 4 equivalents of **TIPSO-furan** generated **50** in 68% yield, 5:1 regioselectivity, and 3:1 dr (Entry 9). These conditions proved to be optimal for hydroalkylation to form allylic butenolide products. A control reaction was performed with 2.5 mol% $[Rh(cod)Cl]_2$ instead of **^{Ph}CDC-Rh-styrene** to demonstrate the importance of the CDC ligand for obtaining any reactivity and failed to yield **50** (Entry 10).

Although they are unlikely to be included in the final publication, many of the previous reaction screens with silyloxyfuran nucleophiles were instrumental in developing the reaction conditions used here. In particular, the solvent, concentration and reaction temperatures were all derived from previous studies reacting silyl enol ethers with 1,3-phenylbutadiene. These results succeed in matching the conversion obtained with **BzO-furan** and significantly exceed the diastereoselectivities obtained with benzoyl protected furan nucleophiles. However, the

regioselectivity of the transformation is non-ideal and provides an opportunity for improving this reaction further.

4.7.2: Exploring the Diene Scope for Hydroalkylation with Silyloxyfuran

Having established a set of reaction conditions for the efficient hydroalkylation of 1,3-phenylbutadiene with **TIPSO-furan**, we began to explore the diene scope of the transformation (Scheme 4.7.2-1). The reaction proved exceptionally tolerant of modifications to the electronics of the aryl diene and both electron poor and electron rich aryl dienes reacted with higher conversions than those obtained for 1,3-phenylbutadiene. Electron poor *p*-chloro-1,3-phenylbutadiene reacted to yield **75** in 87% yield and 5:1 dr as a single regioisomer and reaction with *p*-fluoro-1,3-phenylbutadiene was similarly successful resulting in **76** in 73% yield, as a 17:1 mixture of the γ:α-regioisomers with 4:1 dr for the major product. Dienes with electron donating groups provided even higher yields, but significantly reduced regioselectivities; *p*-methoxy-1,3-phenylbutadiene reacted to form **77** in 90% yield and 4:1 dr, but with only a 2:1 selectivity for the γ-addition over the α-addition product. We were pleased to observe that substitution of the aryl ring in the *meta*- and *ortho*-positions is well tolerated and significantly improves regioselectivity while maintain diastereoselectivity; the *meta*-methyl substituted product **78** is generated in 75% yield, 4:1 dr, and 18:1 γ:α selectivity, while the *ortho*-methyl derivative **79** is provided in 39% yield and 5:1 dr as a single regioisomer. Heterocyclic arenes can also serve as good reaction partners as **80** can be formed in 83% yield and 5:1 dr as an 8:1 mixture of regioisomers.



Scheme 4.7.2-1: Diene scope for the CDC-Rh(I) catalyzed formation of allylic butenolides.

Although aryl dienes generally provide higher conversions to the allylic butenolide products, alkyl dienes also react to generate the desired products in modest yields. An alkyl diene substrate with branching at the position alpha to the olefin reacted to form **81** in 37% yield as a 9:1 mixture of the γ:α-regioisomers, but showed no diastereoselectivity. Poor diastereoselectivity is observed for all alkyl diene substrates explored thus far. Hydroalkylation with 1,3-dodecadiene reacted to form **82** in 22% yield, 2:1 dr and 2:1 γ:α regioselectivity demonstrating that linear dienes can be used as substrates, although an alkene isomerization side reaction to the unreactive internal dienes is competitive with product formation. This can be mitigated by reducing the reaction concentration. When a gem-dimethyl substituted diene was employed as a substrate we were surprised to observe the formation of a third regioisomer where the silyloxyfuran added to the terminus of the diene; the δ-addition product **83** was formed in 29% yield as a single

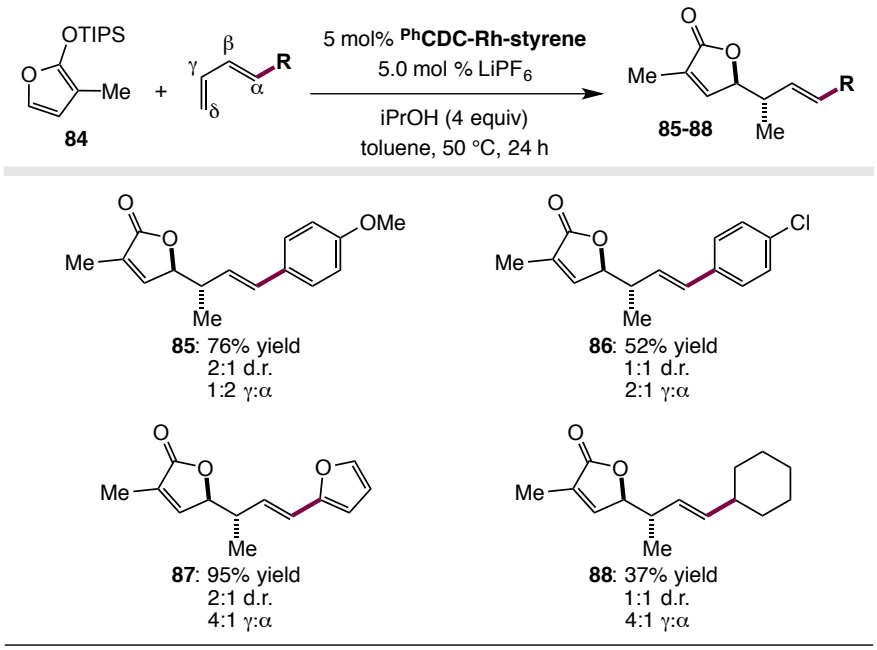
regioisomer. Overall, reactions with alkyl dienes are far less efficient than with aryl dienes. This is likely due to arene stabilization of a cationic transition-state during the transformation. Despite this, alkyl dienes do react and can be used to form valuable 2-allyl-butanones.

4.7.3: Preliminary Studies of the Silyloxyfuran Scope of Diene Hydroalkylation

Our explorations of the diene scope were followed by studies to determine how tolerant the reaction is of various substituted furan nucleophiles. Many of the triisopropylsilyl-protected furan nucleophiles of interest have not been previously synthesized. These substrates have proven unexpectedly challenging to purify due to decomposition on silica gel and thermal instability preventing distillation. As such, only triisopropyl((3-methylfuran-2-yl)oxy)silane has been synthesized tested as an alternative furan nucleophile for CDC-Rh(I) catalyzed hydroalkylation, although further efforts are in progress.

Hydroalkylation translates very effectively to form butanone products with substitution adjacent to the carbonyl (Scheme 4.7.3-1). In reactions with methyl-substituted **84** conversions are comparable to yields obtained with **TIPSO-furan** although diastereo- and regioselectivity drops precipitously. **84** reacted with electron rich aryl dienes efficiently generating **85** in 76% yield and 2:1 dr; however, the regioselectivity of the reaction switched to favoring the α-addition product over the typical γ-addition in a 1:2 ratio. This suggests that it may be possible to favor different substitution patterns for individual substrates with modifications to the reaction conditions. Reaction with electron poor aryl dienes was similarly effective providing **86** in slightly reduced yield and minimal selectivity; the generation of **86** was accomplished in 52% yield with 1:1 dr and 2:1 γ:α regioselectivity. Heterocyclic arenes were well tolerated for reaction with substituted silyloxyfuran **84** and **87** can be synthesized in exceptionally high 95% yield as a 2:1 mixture of diastereomers and 4:1 selectivity for the γ- over the α-addition

products. Lastly, cylcohexyl-1,3-butadiene reacted to provide **88** in higher conversions than observed for reaction with **TIPSO-furan** and with similar selectivities; **88** was formed in 37% yield as a 4:1 mixture of the γ:α regioisomers with no diastereoselectivity. It is not currently clear why the region- and stereoselectivity decreases so dramatically when **84** is employed as a nucleophile, but we were encouraged to observe minimal decrease in yield compared to the unsubstituted silyloxyfuran nucleophile.



Scheme 4.7.3-1: Expanding hydroalkylation to 3-methyl-silyloxyfuran **84** with substituted aryl and alkyl dienes.

4.7.4 Summary and Outlook

The work presented in this section is entirely unpublished and we are racing to finish the substrate scope and improve upon the current selectivity of the transformation. Work is ongoing to expand the nucleophile scope for they hydroalkylation of diene electrophiles. Before publication the reactivity of 3- and 4-substituted furans will be explored as well as how different heterocycles (eg: thiophene and pyrrole) behave as silyl enol ether nucleophiles. The identity of

the major diastereomer also must be determined before publication as we are currently unsure whether the *syn*- or *anti*-diastereomer is formed preferentially. This will be accomplished by recrystallization to generate a diastereomerically pure sample and then X-ray crystallography to characterize the stereocenters present in the molecule. We believe that the products formed from this transformation have potential applications to the synthesis of several natural products and that the organometallic community will be interested in this new chapter in the reactivity of cationic CDC-Rh(I) catalysts.

4.8: Hydroalkylation Synopsis and the Directions of Future Studies

This chapter has been exclusively dedicated to hydroalkylation reactions that can efficiently form C-C sp^3-sp^3 hybridized bonds. This vein of research is the only non-enantioselective transformations that we are actively pursuing. This is certainly subject to change, but it demonstrates just how useful these bond formations are. The knowledge gleaned from hydroamination and hydroarylation reactions catalyzed by CDC-ligated Rh complexes was necessary to address the challenges presented by both enol and enolate nucleophiles. In many ways this chemistry is only possible as the culmination of our non-enantioselective hydrofunctionalization studies. Although these reactions are not enantioselective, they were able to introduce diastereoselectivity with CDC-Rh(I) catalysts and show how substrate control can provide highly useful allylic products from the hydroalkylation of dienes.

Future work will be directed towards the completion of the silyloxyfuran addition to diene electrophiles as well as expansion to new enol (eg: oxindoles) and enolate (eg: acyclic silyl enol ethers) nucleophiles. The current limitation of electrophilic alkene activation with CDC-Rh(I) complexes to dienes will also be addressed. We are very interested in moving towards the activation of styrenes and unactivated alkenes. Even within diene electrophiles there is a great

deal of work to be done in the hydrofunctionalization of substituted dienes as current methods are largely restricted to terminal unsubstituted olefins. Olefin hydrofunctionalization continues to be a vibrant area of research in our laboratory and we expect that the synthesis of new catalyst and reaction manifolds will open up many new catalytic transformations catalyzed by CDC-ligated late-transition metals

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CHAPTER 5: ENANTIOSELECTIVE HYDROFUNCTIONALIZATION WITH CARBODICARBENE-RHODIUM CATALYSTS[5]

5.1: Introduction

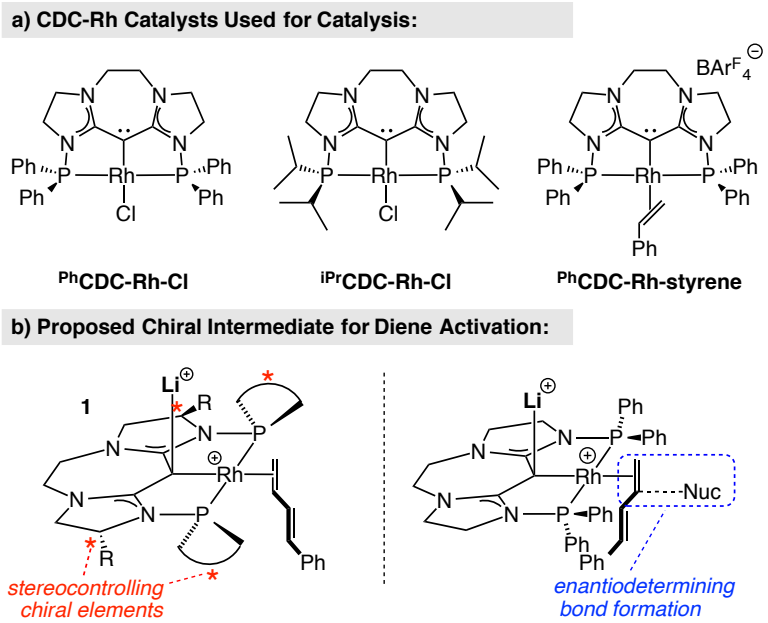
We have worked to develop methods for stereoselective catalysis from the initiation of our studies in hydrofunctionalization[1] with carbodicarbene (CDC) bound Rh complexes. The importance of enantioselective catalysis is evidenced by the 2001 Nobel prize awarded to Sharpless, Noyori and Knowles for their work in catalytic asymmetric epoxidation, and in the subsequent impact of this reaction on organometallic catalysis,[2–4] industrial syntheses,[5] and the construction of natural products.[6–8] In the preceding chapters a number of achiral or diastereoselective transformations were introduced that allow for the addition of amine[9] (hydroamination), aryl[10] (hydroarylation), enol[11] (hydroalkylation) nucleophiles across diene π-systems. These transformations would be of far greater utility if they could be accomplished enantioselectivly, as the stereoselective construction of new bonds is one of the greatest challenges in catalysis.[12–14] A core goal of our studies in CDC-Rh catalyzed hydrofunctionalization is to develop enantioselective functionalizations of olefins that can be applied to the stereoselective synthesis of complex biologically active molecules.

The common thread throughout these studies is the unique class of CDC-Rh(I) complexes developed for the electrophilic activation of olefins. Catalytic methods for enantioselective

[5] The work discussed in this chapter is unpublished. Of the work discussed, C. C. Roberts was responsible for the synthesis and development of valine-derived chiral CDC ligand **29** and complex **32c**. C. C. Roberts was responsible for the synthesis, design, and development of CBA ligand **35**, and corresponding Rh (**38**), Pd (**39**), and Pt (**40**) complexes. M. J. Goldfogel developed the remaining chiral CDC ligands and catalysts and explored enantioselective hydroalkylation with CBA-Rh(I) complexes.

hydrofunctionalization will be accomplished by the inclusion of chirality into one of the achiral methods discussed in the preceding chapters. Reactions with CDC-Rh(I) catalysts have proven surprisingly general for the activation of π-systems towards the external addition of a nucleophile and, although the olefin source is thus far limited to dienes, these achiral methods developed would have a significant impact on the field if made enantioselective. Our achiral methods offer a rich array of reactions that can serve as the focus of new enantioselective strategies.

The previous achiral studies were accomplished with three catalysts, **^{Ph}CDC-Rh-Cl**, **^{iPr}CDC-Rh-Cl**, and **^{Ph}CDC-Rh-styrene**, and are proposed to occur through a common electrophilic intermediate **1** (Scheme 5.1-1). Intermediate **1** shows how a diene bound to a cationic Rh center can be activated with the assistance of a Lewis acid co-catalyst towards the external addition of a Lewis base. If this common intermediate **1** could be modified to include a chiral element then we hypothesized that the stereoselectivity of the enantiodetermining bond formation could be controlled. Pursuit of this impactful and elusive goal has been threaded through the past five years of research in CDC-Rh catalyzed hydrofunctionalization. This chapter will catalog our attempts to develop a catalytic system that incorporates chirality to impart stereoselectivity to the hydrofunctionalization of dienes.



Scheme 5.1-1: CDC-Rh(I) complexes used in catalysis and the proposed catalytic intermediate responsible for diene activation.

5.1.1: Introduction to Enantioselective Hydrofunctionalization

Enantioselective hydrofunctionalization is a varied field of research with many published methods that can be subdivided by the type of hydrofunctionalization achieved (ie: hydroamination vs hydroarylation). Examples of enantioselective catalysis will be discussed for each class of hydrofunctionalization that we have published an achiral method for. This brief review is intended to define the state-of-the-art for enantioselective hydrofunctionalization and provide context for our own efforts. Many of these enantioselective methods for hydroamination,[15–17] hydroarylation,[14,18,19] and hydroalkylation[20] have inspired our studies. Some broad trends are consistent between these transformations, as (i) enantioselective methods for intramolecular hydrofunctionalization are far more common than the intermolecular counterparts, (ii) reactions with unactivated alkenes are very challenging, and (iii)

functionalizations using sp-hybridized olefin sources predominate due to their increased reactivity.

5.1.1.1: Enantioselective Hydroamination

Enantioselective hydroamination is the most developed stereoselective hydrofunctionalization with numerous intramolecular examples and a growing number of intermolecular transformations. Hartwig[21–23] and Marks[24,25] first introduced enantioselective inter- and intramolecular hydroamination, respectively, in the early 2000's. Although no new methods for intermolecular hydroamination were disclosed until 2008, methods for the intramolecular hydroamination of unactivated alkenes proliferated rapidly. Although intramolecular hydroamination is by no means a solved problem, it has been thoroughly studied and reviewed.[15–17] Numerous publications with early transition metals[26–36] (primarily Zr and Ti), rare-earth catalysts,[24,25,37–59] late transition metals[60,60–66] (Pd, Rh, and Ir), Lewis acids,[67–70] amide bases,[71] and coinage metals[72–87] (Au, and Cu) have been reported with modest to excellent enantioselectivities. There have also been three applications of enantioselective hydroamination in total synthesis.[88–90] Despite these successes, the scope of intramolecular hydroamination remains limited, as substrates often require geminal functionalization to bias the substrates for cyclization or exhibited low enantioselectivities ranging from 30 to 70% ee. In addition, few catalysts are tolerant of more than a single class of amines (ie: secondary amines vs amides).

Intermolecular hydroamination is not as well developed, but recent efforts with Cu-hydride catalysts have been highly successful and dramatically impacted the field.[91–100] The mechanism of these reactions is discussed in Chapter 1 as the electronic reverse of the electrophilic activation invoked for CDC-Rh catalysts; reactions catalyzed by Cu-hydride transform the alkene into the nucleophile by generating an alkyl Cu species via hydride insertion

across the olefin π-system. The alkyl Cu nucleophile can then transmetallate with an electrophilic source of nitrogen and reductively eliminate to form the C-N bond. As such, Cu catalyzed reactions utilize electrophilic nitrogen sources, which are often complementary to the products obtained through electrophilic olefin activation.

Prior to the discovery of Cu catalyzed hydroamination, studies by the Hartwig lab utilized late transition metals to catalyze the addition of amines through electrophilic mechanisms.[21–23] These reactions operate similarly to the proposed mechanism for CDC-Rh complexes. Later publications have primarily employed late transition metal catalysts such as Pd,[101] Rh,[102–105] Ir,[106–108] and Au.[109–111] Unlike intramolecular catalysis, relatively few rare-earth[112,113] and early transition metal catalysts[114,115] are known. In addition although limited examples of metal-free organocatalysts have been demonstrated.[116–118] Many of the reported methods for intermolecular hydroamination require sp-hybridized olefins[102–105,109,111,118] or alkenes activated through ring strain.[106] As such, the limitations of enantioselective hydroamination mirror those discussed for achiral catalysts in Chapter 1.1: (i) intermolecular methods are rare compared to their intramolecular counterparts, (ii) the olefin scope rarely includes unactivated alkene substrates, and (iii) the olefin electrophiles are often limited to more reactive sp-hybridized π-systems.

5.1.1.2: Enantioselective Hydroarylation

Methods for the enantioselective hydroarylation of olefins are significantly less common than those for hydroamination. Only a handful of inter-[119–129] or intramolecular[130–133] hydroarylations have been reported, although the difficulty in separating a hydroarylation reaction from a Friedel-Crafts arylation, reductive Heck coupling, or aryl-cross coupling does blur the boundaries of classification. Enantioselective hydroarylation has been accomplished with a handful late transition metal catalysts (Ir,[121–126] Rh,[127–129,132,133] Pt,[131] and Au,[120,130]) and a

single acid catalyst.[119] The olefin scope of these reactions is exceptionally limited and current methods for enantioselective hydroarylation are unlikely to be used over established Friedel-Crafts[134] and cross-coupling[135] methods. Most intermolecular reactions require norbornene derived olefins that are activated by ring strain.[121,122,124,126,127] The development of new methods could address this gap in the literature and allow for the construction of important stereoselective molecules from readily available olefin substrates and nucleophilic arene partners.

5.1.1.3: Enantioselective Hydroalkylation

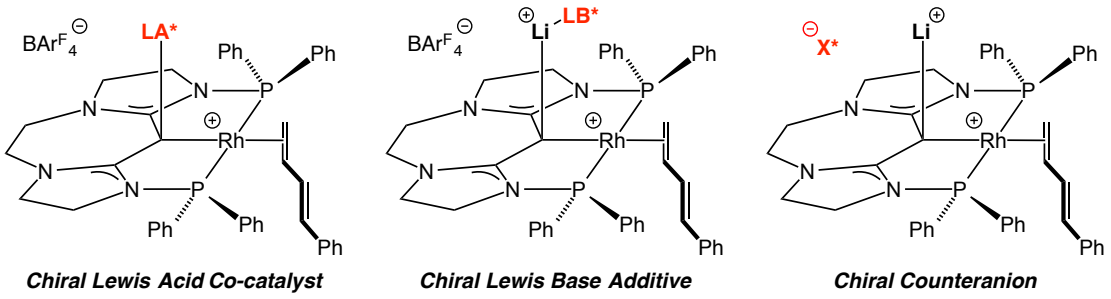
The difficulties and limitations to achiral hydroalkylation were discussed in Chapter 3 and highlight that this is a challenging class of reactions. It follows that this category of olefin functionalization has the fewest published enantioselective methods. Several contributions to enantioselective hydroarylation were made in the Trost lab and utilize Pd catalysts to intermolecularly pair thermally enolizable nucleophiles with allene electrophiles.[136–138] Since these seminal publications, Toste[139,140] and Boutier[141] *et al*. have contributed three intramolecular Pd catalyzed transformations. The remaining examples of enantioselective hydroarylation are catalyzed by Au[142] and Rh[143] complexes that allow for efficient intra- and intermolecular additions, respectively. Enol nucleophiles are more commonly employed over enolates (eg: silyl enol ethers); of the eight reported examples only two use enolate nucleophiles.[139,140] Unlike hydroarylation, there are few reactions that can generate the products obtained from these hydroarylation reactions.

Many strategies for imparting enantiocontrol have been applied to olefin hydrofunctionalization and could be adapted to our achiral CDC-ligated Rh catalysts. The most common strategy is to use a chiral ligand directly bound to the metal to control the stereochemical environment of the bond-forming step. For electrophilic activation mechanisms

this is usually the external addition of the nucleophile to a specific face of the π-electrophile (see Scheme 5.1-1b). An alternative strategy is to incorporate a chiral additive or counterion which can form acomplex with the catalyst during the rate determining transition state.[78,144] The chiral additive can then control the stereochemical environment without being directly bound to the metal. Both strategies will be explored as possible methods for imparting stereocontrol to hydrofunctionalization reactions catalyzed by CDC-Rh(I) complexes.

5.2: Enantiocontrol with Chiral Additives

A strategy for developing an enantioselective version of a known achiral reaction is to find a chiral additive that will form a strong interaction with the catalytic intermediate responsible for stereodifferentiation.[144] The additive can then provide chirality without requiring major changes to a successful achiral catalyst. For the purposes of the CDC-Rh(I) catalysts we envisioned that enantiocontrol could be translated through: (i) a chiral Lewis acid additive that would bind the Lewis basic lone pair of the CDC, (ii) a chiral Lewis base that would coordinate to the bimetallic catalyst system, or (iii) a chiral counteranion that formed a tight ion-pair with the cationic CDC-Rh(I) catalyst (Scheme 5.2-1). These methods were explored for a variety of hydrofunctionalization reactions and demonstrate that it is challenging to impart enantioselectivity through a transient association between an active catalyst and additive.



Scheme 5.2-1: Strategies for enantiocontrol with chiral additives.

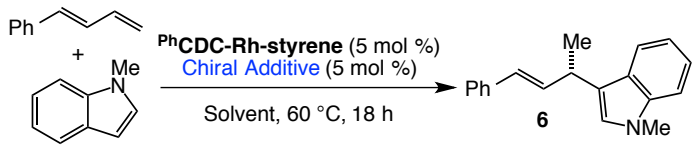
5.2.1: Hydrofunctionalization with Chiral Lewis Acids

When the importance of the Lewis acid additive was discovered during the development of diene hydroarylation it appeared to be an ideal opportunity to incorporate a chiral element into the stereodetermining catalytic intermediate. Catalysis requires a bimetallic intermediate **1** where the Lewis acid is directly bound to the ligand. We hypothesized that a chiral Lewis acid additive would control stereoselectivity at the Rh center.[144] This could allow for enantioinduction without the need for any modifications to the CDC-Rh(I) complexes themselves. This is experimentally expedient, as it does not require any additional catalyst synthesis, and minimizes the likelihood that catalyst modification will dramatic decreases in conversion or regioselectivity, as seen when the phosphine substituents of **^{Ph}CDC-Rh-Cl** were modified (see Section 3.6).

A series of Lewis acid additives were selected based on previous results that suggested the carbon(0) of the CDC could associate with proton sources through hydrogen bonding (see Chapter 2). Coordination of the free lone pair of the CDC decreases the donation from the ligand to Rh and thereby increases the relative electrophilicity of the complex. Since studies with **^{Ph}CDC-Rh-styrene** demonstrated that catalysis does not occur without a Lewis acid additive (eg: AgCl), we anticipated that product formation through an achiral background reaction would be minimal. Protic Lewis acids with a variety of pKas were selected to provide a range of co-catalysts.

The ligand protonation studies published as part of the achiral hydroarylation[10] demonstrated that the CDC could associate with a proton source. This suggested that TADDOL and BINOL derived chiral phosphoric acids **2** and **3** could impart enantioselectivity to reactions catalyzed by **^{Ph}CDC-Rh-styrene**. Hydroalkylation of 1,3-phenylbutadiene with 1-methylindole was selected as a test reaction because **6** was one of the most reliable achiral substrates, and

because a racemic trace could be readily obtained. Reactions with **2** as the Lewis acid additive generated **6** in very high conversion in both toluene (PhMe) and chlorobenzene (PhCl), but only as racemic mixtures (Table 5.2.1-1: Entries 1 and 2). Solvation effects were predicted to have a large impact on the association between the Lewis acid and the catalyst, yet the change in solvent had little effect on the reaction. Use of **3** as the acidic additive dramatically decreased conversion to **6** and failed to provide any enantioselectivity.



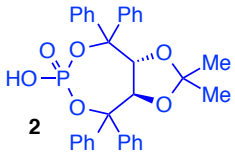
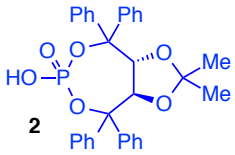
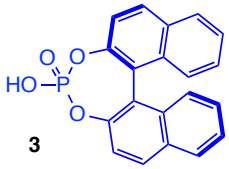
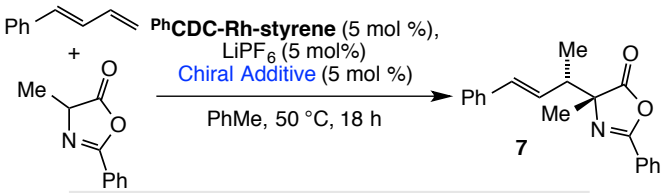
Entry	Chiral Additive	Solvent; M	Yield (%)	%ee
1	 **2**	PhCl; 1.0	92	2
2	 **2**	THF; 1.0	91	1
3	 **3**	PhCl; 1.0	10	0

Table 5.2.1-1: Survey of chiral phosphoric acid additives for diene hydroarylation.

We hypothesized that the poor enantioselectivity with phosphoric acid additives could be due to dissociation of the proton from the chiral phosphate (ie: proton transfer vs hydrogen bonding). This could prevent the spatial association of the stereodetermining element and ligand. The use of alcohols with substantially higher pKa values would favor hydrogen bonding over deprotonation. This theory was tested for the hydroalkylation of 1,3-phenylbutadiene with 4-methyl-2-phenyloxazol-5(4*H*)-one with a series of chiral alcohols, acids, and amines. These

results were published as an addendum to our achiral method (see Section 3.3).[11] The alcohol proved to have no effect on the enantioselectivity of the transformation despite possible interactions with the oxazolone nucleophile, or associations with the CDC ligand (Table 5.2.1-2). Both the phosphoric acid **2** and the amine **5** resulted in reduced conversions to the allylic oxazolone **7**, whereas the alcohols **4**, **5**, and *(R)*-BINOL generated **7** in similar conversions. Unfortunately none of these additives imparted any enantioselectivity to the transformation.



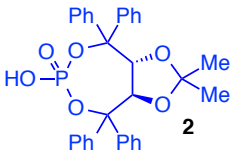
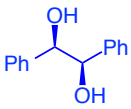
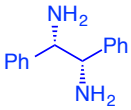
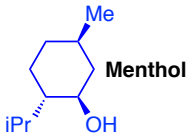
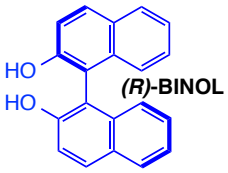
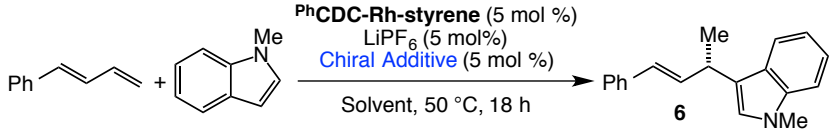
Entry	Chiral Additive	Yield (%)	%ee
1	 **2**	13	0
2	 **4**	53	0
3	 **5**	27	0
4	 **Menthol**	62	0
5	 ***(R)*-BINOL**	56	0

Table 5.2.1-2: Survey of protic chiral additives for the hydroalkylation of 1,3-phenylbutadiene (see Section 3.3).

5.2.2: Hydroarylation with Chiral Lewis Bases

The apparent failure of Lewis acid additives suggested that hydrogen-bonding with the carbon(0) was incapable of controlling enantioselectivity. An alternative approach is to use a chiral Lewis base to tightly bind known Li co-catalysts (see Chapter 2).[145] Protected cinchona bases **8** and **9** were selected for their strong Lewis basicity and tested as additives for the hydroarylation of 1,3-phenylbutadiene. Protection of the cinchonidine was necessary to minimize inhibition of the Rh catalyst. We theorized that these nitrogen bases would tightly associate with cationic Li and be positioned near the site of stereoinduction when the active catalytic intermediate **1** was formed (Scheme 5.2-1). As anticipated, the addition of Lewis bases **8** and **9** reduced conversion to **6** (Table 5.1-1). This is likely due to catalyst inhibition caused by either association of the Lewis base with the **^{Ph}CDC-Rh-styrene** complex or competition between the Lewis base and the the CDC carbon(0) for the Li co-catalyst. The allylic arene 6 was obtained in too low conversion to allow for clean isolation and determination of %ee The significant reduction in conversion prompted us to abandon this strategy for stereoinduction.



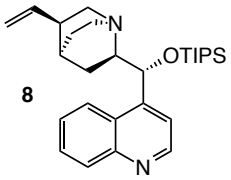
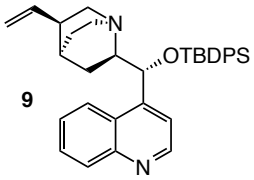
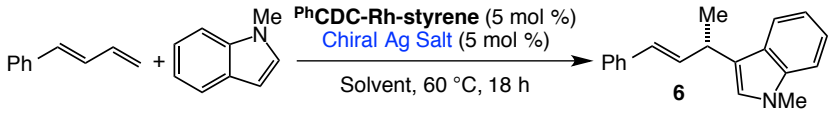
Entry	Chiral Additive	Solvent; M	Yield (%)
1	 **8**	Et_2O; 0.7	6
2	 **9**	Et_2O; 0.7	2

Table 5.2.2-1: Survey of Lewis basic additives for stereoinduction in diene hydroarylation.

5.2.3: Hydroarylation with Chiral Counterions

A different tactic for stereoinduction with chiral additives was required in response to the lack of stereoselectivity obtained with Lewis acidic and basic additives. Chiral counterions have been shown to control the stereoselectivity of a variety of catalytic transformations with cationic metal complexes[146,147] and the active catalyst **^{Ph}CDC-Rh-styrene** is an achiral cationic complex. Substitution of the achiral BAr^F_4 anion for a chiral phosphate could result in a tightly bound ion pair capable of inducing stereocontrol in a CDC-Rh(I) catalyzed reaction. Furthermore, the chiral counterion could be derived from the Lewis acid additive, minimizing both the number of additives required in the reaction and the spectator ions present in solution.

The use of TADDOL and BINOL derived Ag salts **11** and **12** were explored for the hydroarylation of 1,3-phenylbutadiene with 1-methylindole (Table 5.2.3-1). The Ag cation provided the Lewis acid necessary for the generation of the active bimetallic catalyst **1** while the phosphoric acid anion was added to pair with the Rh cation. Reaction in PhCl and PhMe proceeded to generate **6** in 95% and 93% yields respectively when **11** was used as an additive (Entries 1 and 2). However, none enantioselectivity was obtained as **6** was formed in a racemic mixture with both solvents. Surprisingly, reaction with **12** failed to generate the product (Entry 3). It is not clear why a BINOL derived anion is detrimental to reactivity, but this trend was also observed for reactions with BINOL derived acid **3** (Table 5.2.1-1).



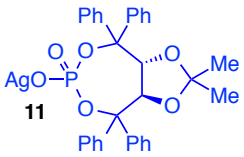
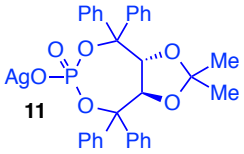
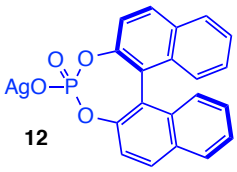
Entry	Chiral Ag Salt	Solvent; M	Yield (%)	%ee
1	 **11**	PhCl; 1.0	95	1
2	 **11**	THF; 1.0	93	2
3	 **12**	PhCl; 1.0	0	-

Table 5.2.3-1: Attempted enantioselective hydroarylation with chiral counterions.

The control of enantioselectivity through the addition of chiral additives was reevaluated after three separate strategies failed to engender enantioselectivity in hydroarylation or hydroalkylation. Both Lewis acidic and basic additives failed to impact the enantioselectivity of the transformation, although the Lewis acidic additives did allow for high conversions to product. The use of chiral counterions met with similarly limited success. We concluded that the association between the chiral additives and the CDC-Rh catalyst was either too weak to transfer stereochemical control, or the chiral additives were too spatially removed from the site of bond formation to influence enantioselectivity. These challenges could be better addressed by the inclusion of chiral centers on the CDC ligand itself.

5.3: Enantioselective Hydrofunctionalization Controlled by P-Stereogenic Carbodicarbene Ligands

The conclusion that chiral additives were unable to control enantioselectivity in hydrofunctionalization reactions with CDC-Rh(I) complexes led us to consider synthetic

modifications to the tridentate ligand structure. As discussed in Section 3.5, the phosphine substituents on the diazepinium backbone are ideal locations for modifying the electronic and steric properties of the ligand. This comes with the caveat that most modifications to the phosphine substituents in Section 3.5 resulted in substantially reduced catalyst activity. Tridentate ligands with chiral phosphine substituents are known and have been used in highly enantioselective catalysis.[148–152] We theorized that the application of such ligands to Rh could allow provide highly enantioselective methods for electrophilic olefin activation. Ligand modifications incorporating P-stereogenic phosphines directly bound to the metal center place the stereodetermining elements in close proximity to the site of bond formation and should allow for efficient stereoinduction.

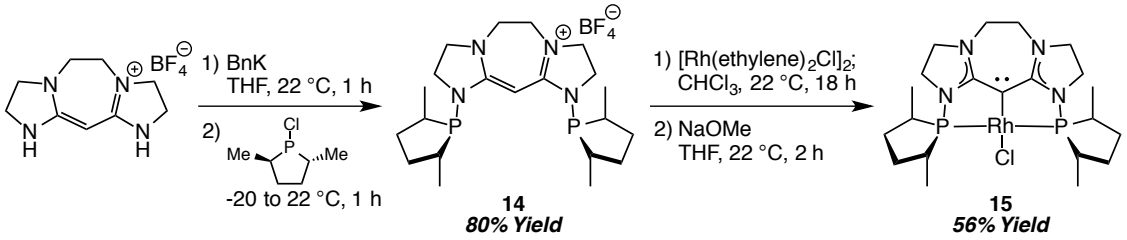
5.3.1: Synthesis of P-Stereogenic CDC-Rh(I) Complexes

The phosphine substituents are the logical location for catalyst modification, as they are the last motifs installed before metallation. The synthesis of achiral diazepinium ligand with modified phosphine substituents demonstrated the general nature of the P-N bond formation (see Section 3.5). The installation of P-stereogenic phosphines will be accomplished analogously using chiral phosphorus chloride reagents akin to the choloro-phosphines used in the synthesis of achiral diazepinium scaffolds (ie: chlorodiphenylphosphine and chlorodiisopropylphosphine). Unlike achiral chloro-phosphines, which can be synthesized readily from the desired aryl Grignard, chiral phosphine reagents must be synthesized from a stereodefined chiral center. A literature search revealed two notable chlorophosphine compounds that met these requirements and had previously been synthesized: 2,5-dimethylphospholane[153] and BINEPINE.[154]

5.3.1.1: Synthesis of Carbodicarbene Ligands Incorporating 2,5-Dimethylphospholane

The synthesis of P-stereogenic CDC ligands requires P-stereogenic chlorophosphine reagents. DuPhos ligands are well known in the literature as privileged structures for enantioselective catalysis derived from 5-membered phospholanes.[155–157] The 5-membered ring is substituted at the 2,5-positions to generate a C_2-symmetric P-stereogenic phosphine. Application of a Duphos-derived carbodicarbene to a Rh metal center will significantly alter the electronics of the formed CDC-Rh(I) complex compared to the aryl substituted CDC ligands that have proven the most general for hydrofunctionalization. However, our work with hydroamination has demonstrated that CDCs incorporating alkyl phosphines can be equally efficient catalysts.

The literature synthesis of phosphine chloride **13**[158] was undertaken and the resulting reagent used to form the P-stereogenic diazepinium salt **14** via the anionic P-N bond formation first described in Section 3.5 (Scheme 5.3.1.1-1). The CDC precursor **14** was then metallated with di-μ-chlorotetraethylene dirhodium(I) ($[Rh(ethylene)_2Cl]_2$) and the resulting hydride deprotonated to form the CDC-Rh(I) complex **15** in 56% yield. This catalyst formation proceeded very similarly to the synthesis of the achiral complexes with modified arene substituents, further demonstrating the variety of CDC complexes that can be rapidly synthesized using these methods.

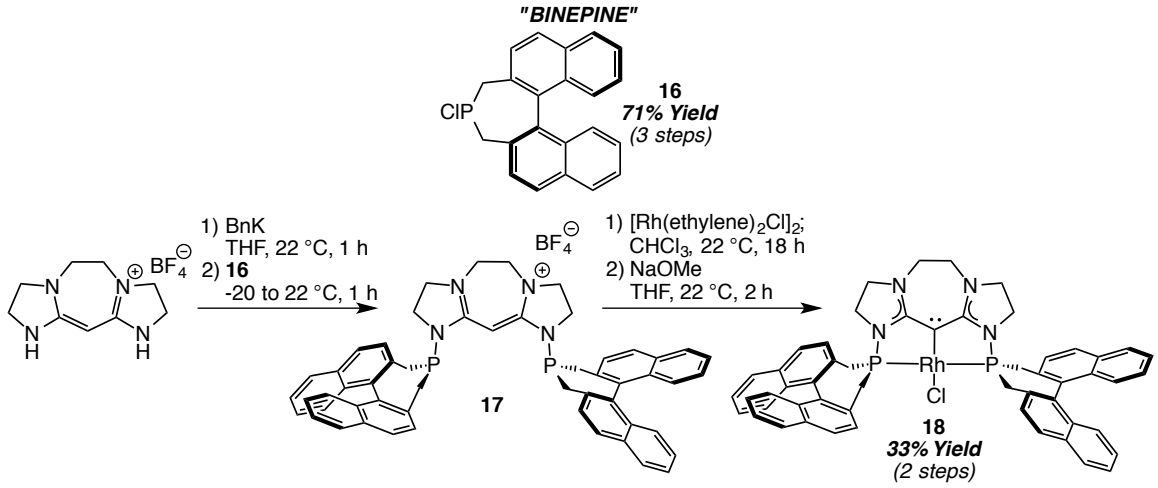


Scheme 5.3.1.1-1: Synthesis of chiral a CDC-Rh(I) complex incorporating P-stereogenic 2,5-dimethylphospholanes.

5.3.1.2: Synthesis of BINEPINE Derived Carbodicarbene Ligands

A second class of P-stereogenic phosphorus ligands was selected to compliment the Duphos derived Rh complex **15**. P-stereogenic phosphines derived from a chiral binapthyl moiety have been used sparingly in the literature as enantioselective ligands.[152,159–161] Termed BINEPINES,[154] these seven membered heterocyclic structures can be employed as monodentate[160] phosphine ligands or incorporated into multidentate ligands.[159] The chloro-BINEPINE **16** has been used as an electrophilic source of BINEPINE and its synthesis is known.[162] We reasoned that the binapthyl structure of BINEPINE would be significantly different both sterically and electronically from 2,5-dimethylphospholane to provide a substantially different P-stereogenic catalyst.

The synthesis of **16** proved challenging as the reaction of the alkyl-lithium species and following hydrochloric acid addition are highly sensitive to minimal changes in the reaction conditions (Scheme 5.3.1.2-1). Many of the steps in this synthesis are extremely sensitive to air and moisture and utilize malodorous pyrophoric reagents and it proved beneficial to minimize purification and characterization throughout the synthesis. **16** was effectively formed and applied to the synthesis of the diazepinium ligand **17** without purification. Metallation of the impure material with $[Rh(ethylene)_2Cl]_2$ generate **18** in 33% yield over two steps. The resulting tan solid could be purified through subsequent washes and triturations to provide the CDC-Rh(I) complex cleanly.



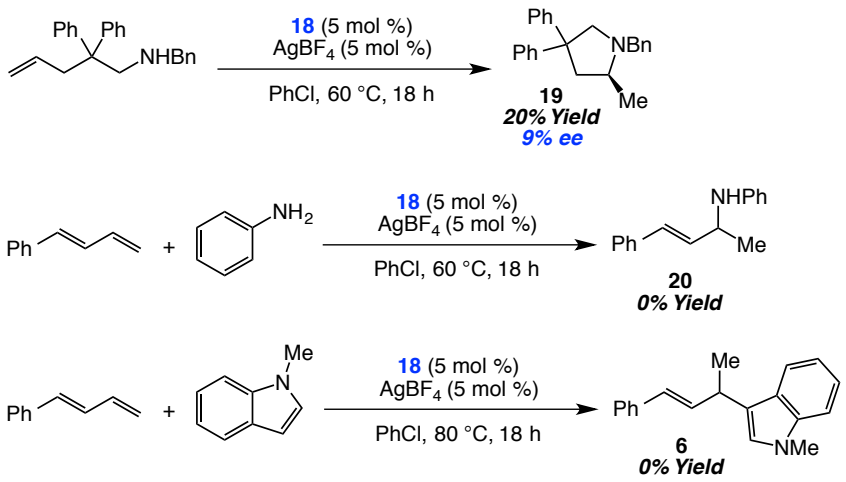
Scheme 5.3.1.2-1: Synthesis of chiral a CDC-Rh(I) complex incorporating P-stereogenic BINEPINE.

5.3.2: Enantioselective Hydrofunctionalization Catalyzed by P-Stereogenic CDC-Rh(I) Complexes

With the P-stereogenic CDC-Rh(I) complexes **15** and **18** in hand, we proceeded to test their catalytic activity and enantioselectivity in hydroamination and hydroarylation reactions. Both complexes contain alkyl-phosphine substituents on the phosphorus atoms, which suggested that their reactivity would most closely mimic the achiral **^{iPr}CDC-Rh-Cl** complex. This directed focus towards reaction screens of hydroamination as the **^{iPr}CDC-Rh-Cl** complex was optimal for intramolecular reactions and showed comparable reactivity for intermolecular additions across dienes (see Chapter 1). Hydroarylation was included to gauge whether a P-stereogenic complex would react substantially differently from its achiral counterpart.

Intramolecular hydroamination has been widely used as a metric for the enantioselectivity of chiral catalysts (see Section 5.1). We selected *N*-benzyl-2,2-diphenylpent-4-en-1-amine as a test substrate for its exceptional conversion with **^{iPr}CDC-Rh-Cl** as the catalyst. The reaction catalyzed by the P-stereogenic BINEPINE complex **18** generated the desired

cyclized product **19** in 20% yield and 9% ee (Scheme 5.3.2-1). This result was exceptionally encouraging in spite of the low enantioselectivity as it is the first example of enantioselectivity with a chiral CDC-Rh(I) complex. It serves as proof of concept that the chirality of the P-stereogenic phosphines can directly influence the bond formation in an electrophilic alkene activation mechanism catalyzed by a tridentate CDC-ligated metal. However, the reaction did generate the product in substantially reduced yield compared to an identical transformation with **^{iPr}CDC-Rh-Cl** (20% versus 98% yield).

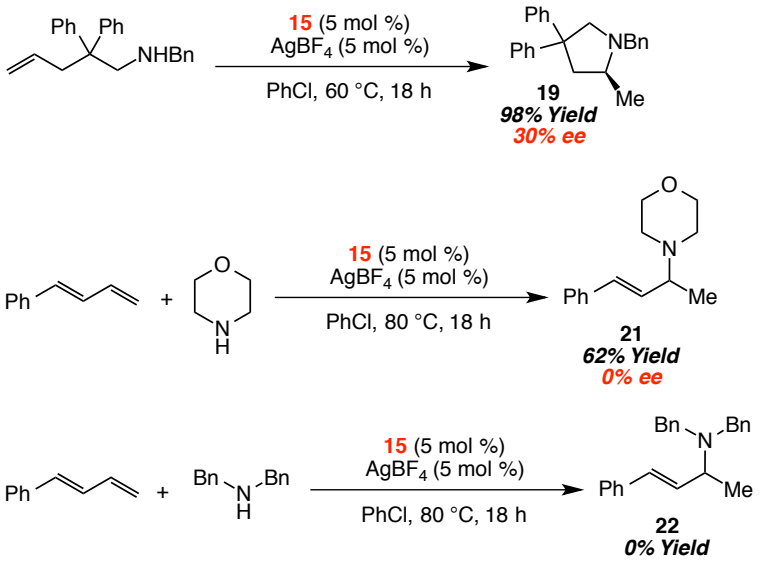


Scheme 5.3.2-1: Screening for enantioselectivity with hydroamination and hydroarylation reactions catalyzed by BINEPINE-derived **18**.

Following the result for intramolecular hydroamination, the same catalyst **18** was tested for intermolecular hydroamination and hydroarylation. Despite previous results showing that the achiral complex **^{iPr}CDC-Rh-Cl** could catalyze both reactions, no conversion to the desired products **20** or **6** was observed (Scheme 5.3.2-2). A common trend in all the catalyst modifications studied is that modification of the phosphine substituents result in substantially lower catalytic activity. Although it is highly unlikely that this is a universal axiom, it does hamper the application of chiral CDC-Rh(I) complexes to hydrofunctionalization. On the basis

of this low conversion and the minimal enantioselectivity obtained in the formation of **19**, further studies with the catalyst **18** were discontinued in favor of exploring alternative P-stereogenic CDC-Rh(I) complexes.

Intramolecular hydroamination with **18** provided proof of concept for the viability of enantioselective olefin activation with P-stereogenic complexes. We hoped that the smaller DuPhos-related catalyst **15** would further improve upon the 9% enantiomeric excess (ee) obtained with **18**, as the stereocenters are positioned closer to the phosphine. This would hypothetically allow for better relay of stereochemistry to the chiral pocket where the exigent olefin was bound. This theory was tested using both intra- and intermolecular hydroamination with the assumption that the intramolecular reaction would proceed more readily and that catalysts with alkyl-phosphine substituents were better suited for amination over arylation. Reaction to form **19** catalyzed by 5 mol% **15** with 5 mol% $AgBF_4$ proceeded in quantitative conversion (98%) and 30% ee. This result was a substantial improvement in both reactivity and selectivity over the BINEPINE catalyst **18** and suggests that a less hindered catalyst improves reactivity. Additionally, it lends circumstantial support for the hypothesis that the close proximity of the chiral stereocenters is beneficial to enantioselectivity.



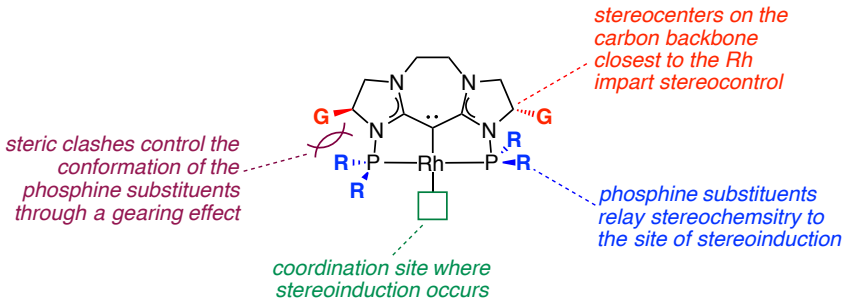
Scheme 5.3.2-2: Screening for enantioselectivity with hydroamination reactions catalyzed by DuPhos-related complex **15**.

Further studies were undertaken to determine if the improved results with **15** could translate to an intermolecular transformation. Intermolecular hydroamination with morpholine at the elevated temperature of 80 °C generated **21** in 62% yield, but without any enantioselectivity. More troubling, reaction with dibenzylamine failed to generate **22**, suggesting that, although **15** was more active than **18**, its activity is still substantially reduced compared to the achiral **^{iPr}CDC-Rh-Cl** complex (see Chapter 1). The lack of reactivity for intermolecular hydroamination with a diene substrate can be rationalized based on the increased conformational flexibility associated with an intermolecular process. Unlike intramolecular hydroamination where the nucleophilic amine is tethered to the alkene substrate, intermolecular hydroamination has no conformational bias and enantioselectivity must be controlled through which face of the alkene is bound to the Rh-center. Unfortunately, the vinylogous diene π-system of the diene appears to place the large phenyl substituent outside of the influence of the P-stereogenic phosphines.

Despite the improvements to both conversion and enantioselectivity obtained with the DuPhos-related complex **15**, it seemed unlikely that further modifications to the phosphine substituents would be able to improve enantioselectivity without incurring a commensurate cost in reactivity. The steric and electronic properties of the phosphine substituents on the achiral catalysts **^{Ph}CDC-Rh-Cl** and **^{iPr}CDC-Rh-Cl** appear to be well tuned for accomplishing the hydrofunctionalizations discussed in the preceding chapters. Thus, we decided that a different strategy that did not modify the phosphine substituents would be necessary in order to develop a catalyst capable of efficient and enantioselective diene hydrofunctionalization.

5.4: Enantioselective Hydrofunctionalization with Chiral Carbodicarbene-Rh Complexes Derived from Chiral Diazepinium Ligands

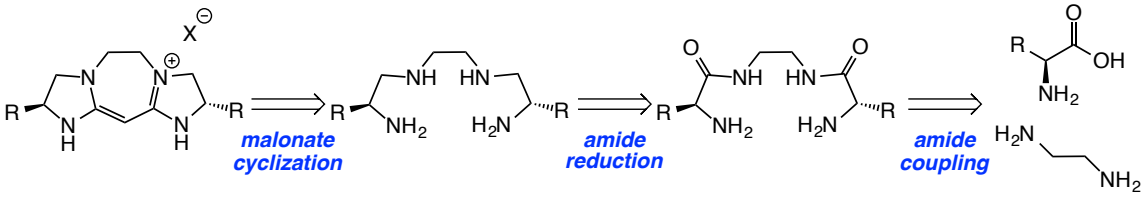
The catalyst modifications discussed prior to this section avoided changes to the carbon backbone of the diazepinium scaffold in the interest of limiting ligand synthesis. However, we did not hesitate to explore multistep ligand syntheses in the hope of providing a highly reactive and enantioselective CDC-Rh(I) catalyst. Our approach to generating chiral diazepinium ligands was to install stereocenters adjacent to the secondary nitrogen atoms (Scheme 5.4-1). These locations were selected for their proximity to the binding pocket of the CDC ligand, and we hypothesized that the stereocenters could relay chiral information to the open coordination site on Rh through interactions with the phosphine substituents. This relay could occur through a "gearing effect" where the phosphine substituents were locked in the lowest energy conformation by interactions with the chiral stereocenters. C_2-symmetric ligands were selected to simplify the synthesis of the proposed chiral diazepinium salts.



Scheme 5.4-1: Design philosophy for a chiral CDC-Rh(I) complex constructed from a chiral diazepinium ligand.

5.4.1: Retrosynthetic Analysis of the Chiral Diazepinium Core

A brief retrosynthesis is presented to summarize the synthetic route used for constructing the chiral diazepinium salts (Scheme 5.4.1-1). The malonate cyclization developed by Schwesinger[163] forms 4 σ-bonds in a single step and was selected as the most efficient method for forming the diazepinium ring. This disconnection led to a chiral tetra-amine structure with stereocenters in the positions alpha to the terminal amines. The C_2-symmetry of the tetra-amine allows for instillation of both stereocenters through amide coupling with diethylenediamine followed by hydride reduction from the amide to the amine. Commercially available amino acids could then be utilized as inexpensive sources of enantiopure chiral molecules.

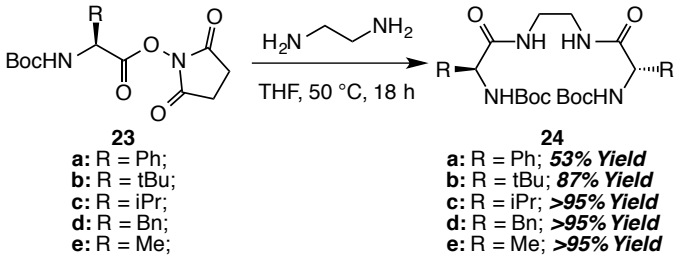


Scheme 5.4.1-1: Retrosynthetic analysis of the chiral diazepinium salts.

5.4.2: Synthesis of Chiral Diazepinium Salts

The synthetic route to the chiral diazepinium ligand precursor appeared straightforward. A variety of amino acids were selected to supply a range of sterics including (a) phenylglycine

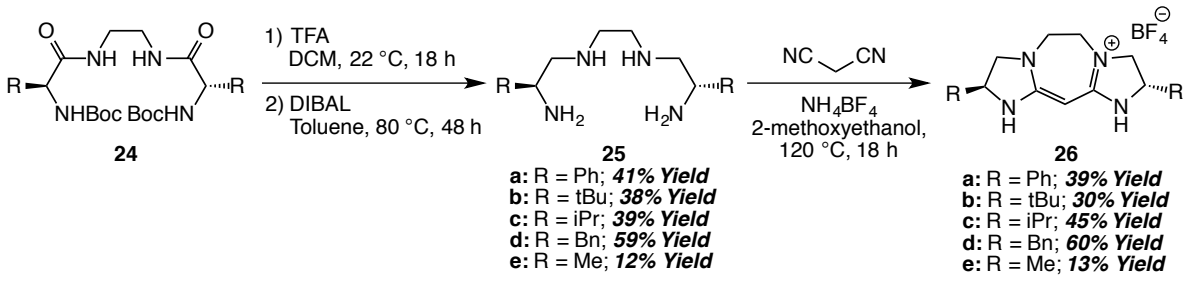
(R = Ph), (b) *tert*-leucine (R = tBu), (c) valine (R = iPr), (d) phenylalanine (R = Bn), and (e) alanine (R = Me) (Scheme 5.4.2-1). The amide coupling required protection of the nitrogen and activation of the carboxylic acid with N-hydroxysuccinimide as initial attempts at directly coupling amino acids with ethylenediamine proved inconsistent between amino acids. Heating the commercially available protected amino acid-succinimides **23** with ethylenediamine formed the desired diamides **24** in good to quantitative yields; substitution of the succinimide provided **24a-e** in 53% (R = Ph), 87% (R = tBu), >95% (R = iPr), >95% (R = Bn), and >95% yields (R = Me). The synthesis of the valine-derived scaffold is reported in the dissertation of C. C. Roberts (Roberts, 2016).



Scheme 5.4.2-1: Formation of the diamide backbones for the diazepinium ligand synthesis.

The Boc-protected amides **24** were deprotected with trifluoroacetic acid (TFA) before being reduced to the amines. Reactions with diisobutylaluminum hydride (DIBAL) generated **25a-e** in low to modest yields over two steps; **26a-e** were formed in 41% (R = Ph), 38% (R = tBu), 39% (R = iPr), 59% (R = Bn), and 12% yields (R = Me), respectively. This reduction proved to be a weakness in the diazepinium syntheses with generally poor yields and challenging purifications. Furthermore, concerns over epimerization with phenylglycine-derived **25a** under the basic reduction conditions led to the discontinuation of this substrate. Despite minor setbacks, products were obtained for each reduction and syntheses could continue. Cyclization with malononitrile generated the desired diazepinium salts **26** in modest yields. Variations in the

polarity of the chiral diazepinium salts required changes in solvent compared to cyclizations to form the achiral diazepinium salt and higher boiling point solvents proved challenging to remove. Cyclization of **25** gave 39% (R = Ph), 30% (R = tBu), 45% (R = iPr), 60% (R = Bn), and 13% yields (R = Me) for **26a-e** respectively.



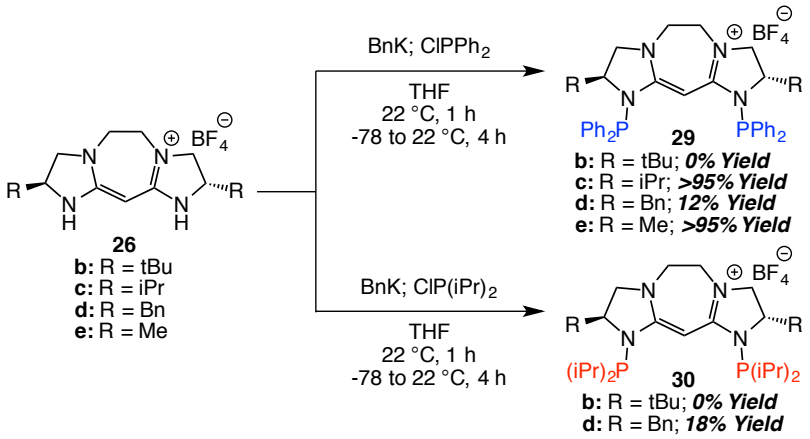
Scheme 5.4.2-2: Deprotection, reduction and cyclization steps in the synthesis of chiral diazepinium ligand precursors.

5.4.3: Synthesis of Chiral Diazepinium Tridentate Ligands

The syntheses described above provided the necessary chiral diazepinium salts **26**. Instillation of the P-N bonds and subsequent metallation of the tridentate ligands was accomplished using synthetic methods adapted from synthesis of the P-stereogenic CDC-Rh(I) complexes (see Section 5.3). The anticipated gearing effect responsible for enantiocontrol was predicted to be highly dependent on both the identity of the R group and the phosphine substituents. As such, syntheses of the chiral tridentate scaffolds incorporating both phenyl and isopropyl substituents were attempted in analogy to the achiral **^{Ph}CDC-H** and **^{iPr}CDC-H** ligand structures.

Phosphorylation with the chiral diazepinium salts **26** proved substantially more challenging than the achiral systems. As was observed during attempts to incorporate large phosphine substituents, the P-N bond is weakened by steric clashes between the phosphine substituents and diazepinium backbone (see Section 3.5). Large R groups destabilize the thermal

stability of the P-N bond and can prevent its formation. This is evidenced in the attempted synthesis of **29b**; reaction with chlorophosphine reagents using the anionic P-N bond formation developed in Section 3.5 failed to generate the desired product (Scheme 5.4.3-1). Few of the ligands represented in Scheme 5.4.3-1 are stable to column chromatography and purifications must be done using triturations and solvent washes. In spite of these obstacles, syntheses of **29** and **30** with smaller R groups were accomplished in varying yields. Reactions with chlorodiphenylphosphine ($ClPPh_2$) proceeded to form the P-N bond of **29c**, **29d**, and **29e** in >95%, 12% and >95% yields, respectively. The benzyl substituent in **26d** significantly inhibits P-N bond formation, likely because the extended aryl ring clashes with the phosphine substituents. The instability of these compounds often prevents isolation of **29** in high purity, and partial conversion to the mono-phosphorylated diazepine are common.

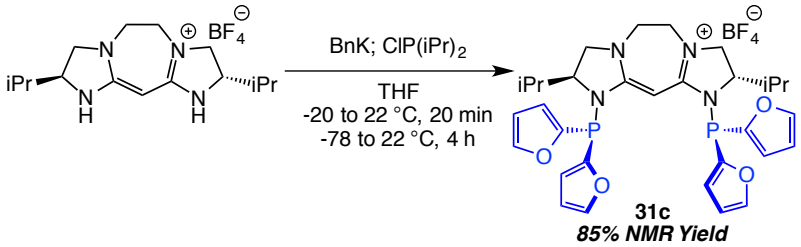


Scheme 5.4.3-1: Phosphorylation of the diazepinium salt to form the tridentate ligand precursor **27**.

Reaction with chlorodiisopropylphosphine [$ClP(iPr)_2$] proceeded reluctantly and the phosphorylation of **26** generated **30d** in 18% yield (Scheme 5.4.3-1). We do not fully understand what causes the poor conversion to the phosphorylated product with isopropyl phosphine substituents. The factors governing these reactions are complex and yields depend on the relative

conversion to the mono- and bis-phosphorylated products. Furthermore, the identity of the non-polar R group substantially changes the solubility of chiral diazepinium salts compared to their achiral counterparts, which can complicate isolation or reduce reactivity.

The detrimental effect of sterics on the stability of diazepinium ligands suggested that smaller phosphine substituents might lead to more robust ligands. Phosphorylation of **26c** with chlorodifurylphosphine was explored to test this hypothesis, as the furyl substituent is sterically less demanding than phenyl (Scheme 5.4.3-2). The result was formation of **31c** in 85% conversion as a 10:1 mixture of the bis- and mono-phosphorylated products. Although we did not have time to pursue alternative phosphine substituents further, this demonstrates that it is possible to further tune the interplay between the sterics of the diazepinium backbone and phosphine by modifying multiple components of the ligand simultaneously.



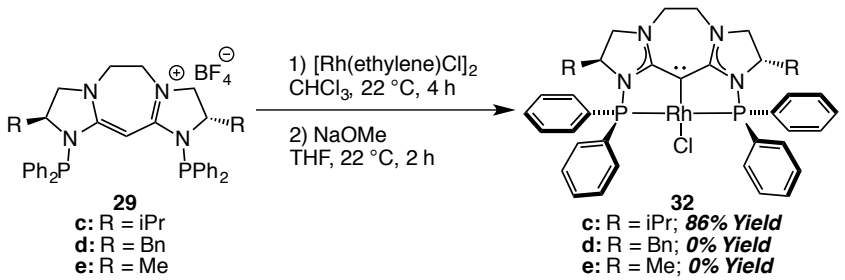
Scheme 5.4.3-2: Ligands formed from simultaneous modifications to the diazepinium skeleton and phosphine substituents.

5.4.4: Metallation of Chiral Diazepinium Ligands

The previous section illustrated the successful synthesis of 5 new chiral diazepinium ligand structures: phenylphosphines **29c-e**, isopropylphosphine **30d**, and furylphosphine **31c**. Without a clear method for predicting the reactivity or selectivity likely to be exhibited by CDC-Rh(I) complexes formed from these ligands, we opted to explore metallating each ligand to

determine their activity experimentally. C. C. Roberts developed the valine-derived CDC-Rh(I) complex and the synthesis can be found in the related dissertation (Roberts, 2016).

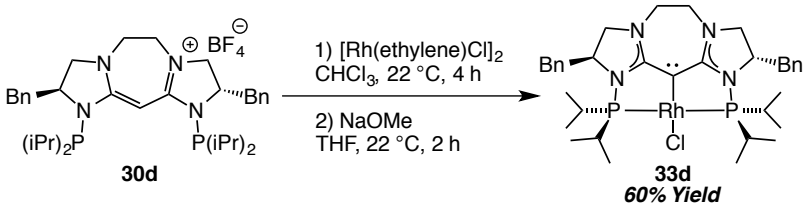
The first attempted metallations were with the phenylphosphine diazepinium salts **29c-e**. The optimal conditions developed from Section 3.5 with $[Rh(ethylene)_2Cl]_2$ were applied to the synthesis of complexes **32c-e** (Scheme 5.4.4-1). The valine derived CDC-Rh(I) complex **32c** was formed efficiently in 86% yield using these conditions. However, neither the phenylalanine or alanine variants generated the metallated complexes cleanly. The failure to form **32d** can be explained by the larger steric influence of the benzyl substituent, as this interaction was previously observed to weaken the P-N bond of **29d** resulting in poor conversion (Scheme 5.4.3-1). Metallation appears to further constrain the molecule and increases the limitations imposed by large R groups and phosphines. Alternative reaction temperatures, bases, and solvents were explored but did not improve the reaction. The failure to form **32e** was more surprising. The methyl substituent is smaller than the isopropyl found in **32c** and the sterics of the R group do not explain the poor metallation. The alanine-derived substrates proved problematic in nearly every synthetic step, but there is currently no satisfactory explanation for the challenges associated with their synthesis.



Scheme 5.4.4-1: Synthesis of chiral CDC-Rh(I) complexes with phenyl phosphine substituents.

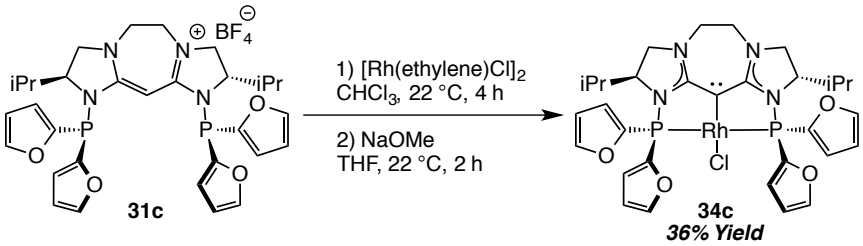
The synthesis of chiral CDC-Rh(I) complexes containing isopropyl phosphine substituents was also explored. Metallation with $[Rh(ethylene)_2Cl]_2$ provided the phenylalanine

derived CDC-Rh(I) complex **33d** in 60% yield. This suggests that isopropyl phosphine substituents are less sterically demanding than phenyl, as the analogous complex **32d** with phenylphosphines could not be formed. This theory has since been supported by catalytic experiments showing enantioselectivity with the larger phenyl phosphine substituents exclusively (*vide infra*).



Scheme 5.4.4-2: Synthesis of chiral CDC-Rh(I) complexes with isopropyl phosphine substituents.

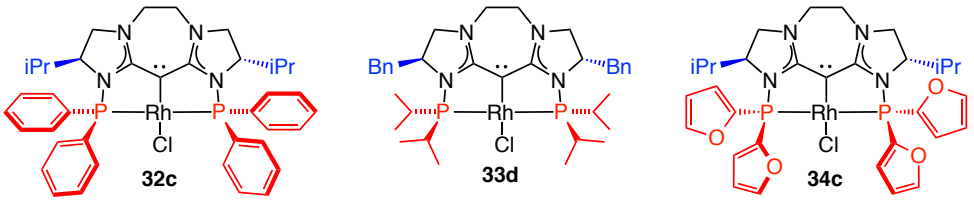
The last chiral diazepinium ligand synthesized was the furylphosphine **31c**. The smaller furyl substituents were predicted to improve the metallation, but the electron withdrawing nature could weaken σ-donation from the phosphorus atoms counteract this effect. Metallation of **31c** occurred readily using the reaction conditions described above with $[Rh(ethylene)_2Cl]_2$ and generated **34c** in 36% yield. Although the yield is low, it provided enough material to test **34c** as a hydrofunctionalization catalyst.



Scheme 5.4.4-3: Synthesis of chiral CDC-Rh(I) complexes with furyl phosphine substituents.

5.4.5: Surveying Enantioselectivity with Chiral CDC-Rh(I) Complexes

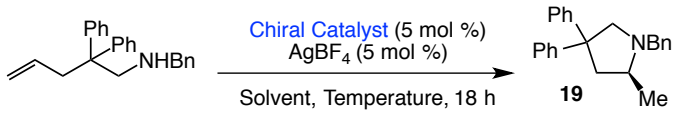
Synthetic efforts provided the thee chiral CDC-Rh(I) complexes shown in Scheme 5.4.5-1. Although we had hoped to have a wider range of chiral catalysts to determine trends between ligand properties and catalysis, we were eager to explore the catalytic activity of these complexes. Hydroamination and hydroarylation were used as the primary test reactions for surveying the reactivity and selectivity of each chiral complex.



Scheme 5.4.5-1: Chiral CDC-Rh(I) complexes successfully synthesized and used applied to hydrofunctionalization reactions.

5.4.5.1: Enantioselective Intramolecular Hydroamination

Intramolecular hydroamination was used as the flagship reaction for testing enantioselectivity with the new chiral CDC-Rh(I) complexes because catalysts consistently react efficiently with these substrates. Table 5.4.5.1-1 summarizes the surveyed catalysts and conditions for enantioselective hydroamination. A survey of all three chiral CDC-Rh(I) complexes shown in Scheme 5.4.5.1 demonstrated that only **33d** and **32c** catalyzed the formation of **19** in 56% (Entry 2) and 40% NMR yield (Entry 3), respectively. Reaction with **33d** required the higher reaction temperature of 80 °C. When the products were analyzed for enantioselectivity the valine scaffold paired with phenyl phosphine substituents provided 17% ee (Entry 3), while products formed from **33d** were racemic. Both of these catalysts were screened with PhCl as solvent in an attempt to improve enantioselectivity, but both catalyst failed to catalyze the formation of **19** unless MeCN was used as the solvent (Entries 4 and 5).



Entry	Chiral Catalyst	Solvent; M	Temp (°C)	NMR Yield (%)	% ee
1	**34c**	MeCN; 1.0	60	0	**0**
2	**33d**	MeCN; 1.0	80	56	**0**
3	**32c**	MeCN; 1.0	60	40	**17**
4	**33d**	PhCl; 1.0	60	0	**0**
5	**32c**	PhCl; 1.0	60	0	**0**

Table 5.4.5.1-1: Surveying enantioselective intramolecular hydroamination with chiral CDC-Rh(I) complexes.

This reaction screen proved that the chiral stereocenters in the diazepinium framework could control enantioselectivity. However, catalyst reactivity decreased dramatically compared to achiral **^{iPr}CDC-Rh-Cl** and the enantioselectivities obtained were far from synthetically useful. These results mirrored those found with P-stereogenic chiral CDC-Rh(I) catalysts. Intermolecular hydroamination reactions were also explored by C. C. Roberts with **32c** and results can be found in the relevant dissertation (Roberts, 2016). These reactions further supported the trends in reactivity and enantioselectivity found for intramolecular hydroamination, as the only enantioselective result was obtained with very low conversion and enantioselectivity; dibenzylamine and 1,3-phenylbutadiene were combined in 5% yield and 22% ee using **32c** as the catalyst.

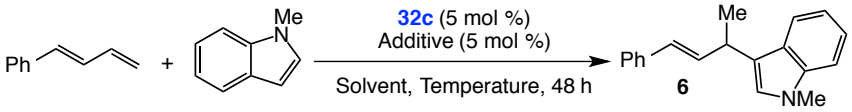
The results from intra- and intermolecular hydroamination show that **32c** is the only chiral complex that can control enantioselectivity through a chiral CDC backbone. We suspect that this is because of the large spatial separation between the stereocenters and the site of bond-formation. **32c** contains the largest phosphine substituents of the three screened chiral CDC-Rh(I) complexes, which may explain its higher enantioselectivity compared to **33d**. Attempts at

the synthesis of larger complexes resulted in the decomposition of the P-N bond. Similarly, electronic modifications to the ligand scaffold did not appear promising, as evidenced by the complete lack of catalysis obtained with furylphosphine-substituted **34c**. From these results we concluded that **32c** was the most enantioselective chiral diazepinium catalyst that we could access.

5.4.5.2: Enantioselective Intermolecular Hydroarylation

More enantioselective reactions are often obtained at lower temperatures. This prompted us to use intermolecular hydroarylation as as a test reaction with chiral CDC-Rh(I) complexes as achiral intermolecular hydroarylation was catalyzed at lower temperatures than any other hydrofunctionalization explored with CDC-Rh(I) complexes (see Chapter 2). The results from both intra- and intermolecular hydroamination succinctly demonstrated that **32c** was the only complex likely to impart enantioselectivity, therefore reaction screens focused on it exclusively.

Hydroarylation of 1,3-phenylbutadiene with 1-methylindole at 60 °C in benzene (PhH) catalyzed by 5 mol% of **32c** and $AgBF_4$ provided **6** in 22% yield and 23% ee (Table 5.4.5.2-1: Entry 1). This result was further improved by changing the solvent from PhH to PhCl and increasing the reaction temperature to 60 °C; **6** was formed in 50% yield and 29% ee (Entry 2). This result marks the highest yield and enantioselectivity obtained for any intermolecular reaction with the first generation of CDC-Rh(I) complexes. Further attempts at optimizing the Lewis acid additive failed to improve the selectivity of the transformation and reaction with 5 mol% $NaBAr^F_4$ and 5 mol% of a neutral Lewis acid, such as CuCl or AgF, generated **6** in 54% yield, 7% ee and 26% yield, 5% ee, respectively (Entries 3-4). In spite of these enantioselective results, catalysis with **32c** proved too low yielding and selective to warrant further study.



Entry	Solvent; M	Temp (°C)	Additive; mol%	NMR Yield (%)	% ee
1	PhH; 1.0	50	$AgBF_4$; 5	22	23
2	PhCl; 1.0	60	$AgBF_4$; 5	50	29
3[a]	PhCl; 1.0	60	CuCl; 5	54	7
4[a]	PhCl; 1.0	60	AgF; 5	26	5

[a] Reaction run with 5 mol% $NaBAr^F{}_4$ to generate the cationic CDC-Rh(I) catalyst.

Table 5.4.5.2-1: Enantioselective intermolecular hydroarylation catalyzed by **32c**.

We were pleased to observe that a chiral CDC-Rh(I) catalyst could be general for hydroamination and hydroarylation, but the modest yields and low enantioselectivities provided by **32c** could not be overcome. It was apparent that none of the CDC-Rh(I) complexes that could be synthesized from chiral diazepinium ligands could provide the general reactivity observed for the achiral **^{Ph}CDC-Rh-styrene** complex. The catalyst modifications proved too detrimental to conversion while only providing modest levels of enantioselectivity. After four years of research, we were forced to come to the conclusion that the ligand design for achiral catalysts was unlikely to be optimal for an enantioselective transformation.

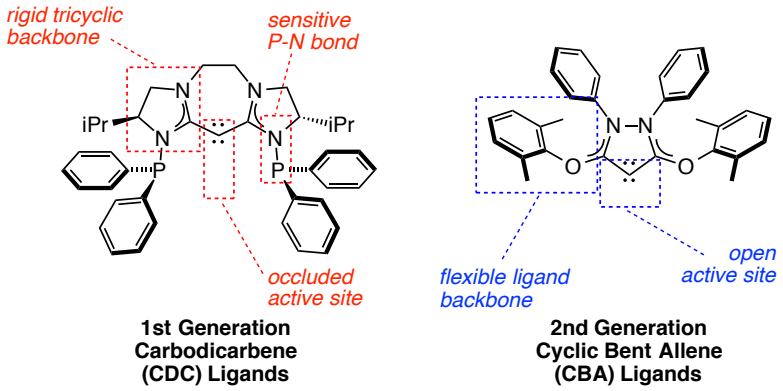
5.5: Enantioselective Hydrofunctionalization with a Chiral Tridentate Cyclic Bent Allene

Studies with chiral CDC-Rh(I) complexes showed that a general catalyst for enantioselective hydrofunctionalization could be developed, but that the ligand framework adopted from the achiral transformations was unsuitable to the task. This conclusion came from the observation that a single catalyst **32c** was able to engender similar enantioselectivity for both hydroamination and hydroarylation. This further suggests that the proposed electrophilic intermediate **1** (Scheme 5.1-1) will allow for a single ligand structure to translate to multiple enantioselective catalytic reactions. These positive results were marred by the poor reactivity and

selectivity obtained using chiral variants of the diazepinium ligand. The poor reactivity could be rationalized by the active site of the CDC-Rh(I) complex being too hindered to accommodate additional steric restrictions from chiral elements. We hypothesized that a more flexible ligand structure would allow for a more reactive catalyst. Additionally, the poor enantioselectivity suggested that the sites of stereoinduction were too far removed from the stereodetermining bond formation. A more stereoselective catalyst should be achieved by constructing a ligand that more effectively encapsulated the catalyst active site. These hypotheses led to the design of a second-generation of carbodicarbene-derived ligands.

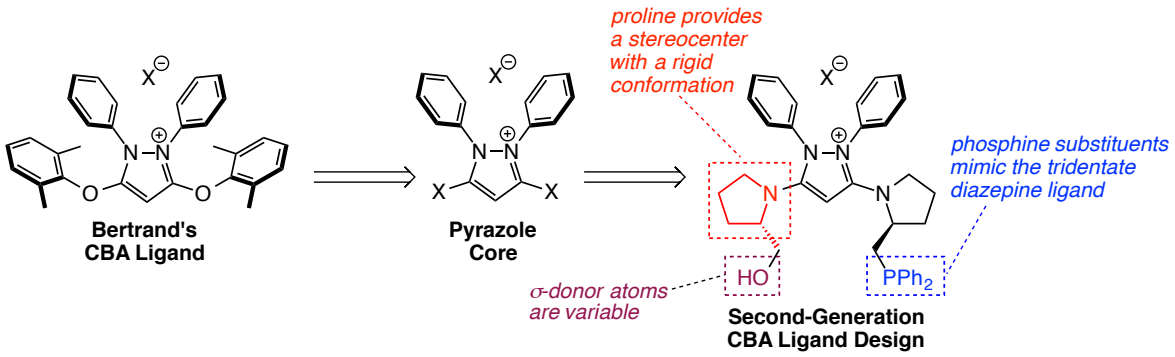
5.5.1: Designing a Second Generation Chiral Carbodicarbene Catalyst

The unique reactivity of the carbon(0) found in a carbodicarbene ligand allowed for efficient achiral hydrofunctionalization and would benefit from further study. We wanted to continue exploring these structures by incorporating a carbon(0) donors into the second-generation ligand and maintain a narrative between the first- and second-generation ligands. The design and initial synthesis of these ligands was accomplished by C. C. Roberts and details are in the related dissertation (Roberts, 2016). Reexamination of the carbodicarbene literature highlighted a cyclic bent allene (CBA) ligand developed by Bertrand as a starting points for developing a new carbon(0) catalyst (Scheme 5.5.1-1).[164] CBAs retain much of the σ- and π-donation of CDCs, but lack the rigid tricyclic structure of the diazepinium framework. Arguments can be made whether the CBA core is a true CDC or a bent allene,[165] but recent studies by Stephan *et al*. have shown that these structures are strong σ-donors[166] and can form catalytically active Ru complexes.[167] This literature precedent encouraged applications of the CBA core to enantioselective catalysis.



Scheme 5.5.1-1: Comparing the structure of CDC and CBA ligands.

The most readily modifiable sites of the CBA framework are the alcohol substituents on either side of the pyrazole core. The donor properties of the CBA ligand were designed to mimic the CDC framework in order to allow for a similar mode of olefin activation. As such, the ligand was designed from a tridentate ligand framework composed of phosphorus-carbon-phosphorus (P-C-P) donors flanking a central carbodicarbene (see Chapter 1). Replacing the 2,6-dimethylphenol substituents on the pyrazole provides allows the installation of stereocenters for enantiocontrol (Scheme 5.5.1-2). We elected to use amino acids as a chiral pool by deriving the pyrazole substituents from proline. Proline was selected because its cyclic structure strikes a balance between the rigidity of a tricylic CDC and the conformational restrictions needed to define a chiral pocket. The ligand design was completed by incorporating diphenylphosphine substituents analogous to those used for ^{Ph}**CDC-Rh-styrene** complex.



Scheme 5.5.1-2: Ligand design of a chiral tridentate CBA incorporating two phosphine donors.

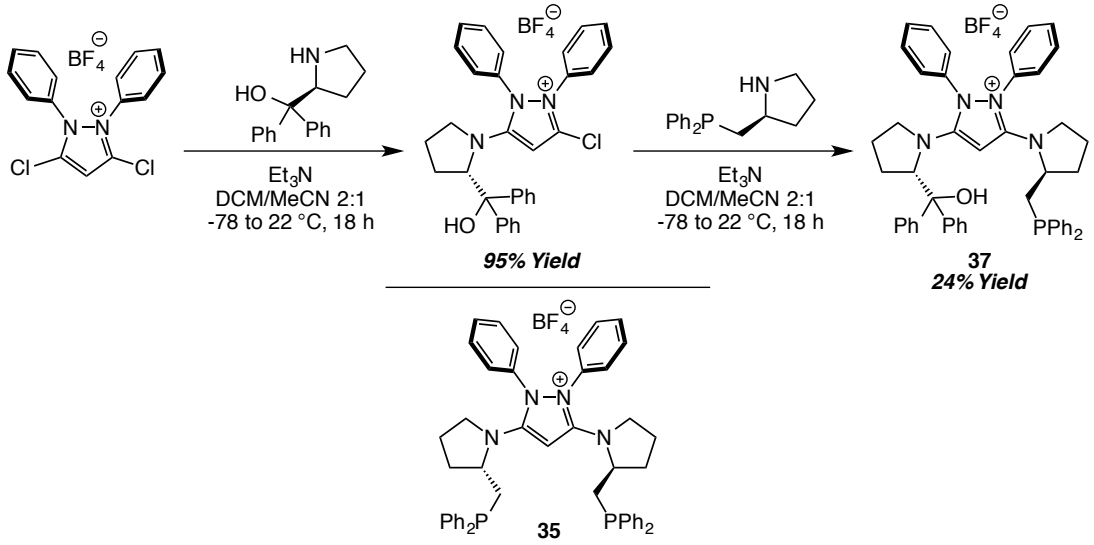
The CBA framework will also accommodate structures that are not C_2-symmetric. This includes ligand structures beyond P-C-P donors that could incorporate X-type ligands (eg: O-C-P). Changes to the donor atoms are particularly intriguing as they allow access to oxidation states that were not previously possible with the CDC structure. This could lend itself to the synthesis of organometallic complexes with Pd(II) and Pt(II). Early studies of group 8 metals (Pd and Ni) showed that the dicationic complexes could not be readily formed through halide abstraction (see Chapter 1). However, the opportunity to incorporate X-type donors into the tridentate ligand framework can allow for the synthesis of monocationic Pd and Ni complexes that may electrophilically active olefins.

5.5.2: Synthesis of the Second-Generation Cyclic Bent Complexes

Having established the design of chiral CBA ligands, effort was directed towards synthesizing the proposed structures. The initial synthesis of the proline-derived CBA ligand **35** and corresponding CBA-Rh(I) complex **36** can be found in the dissertation of C. C. Roberts (Roberts, 2106). The following discussion will focus on development of a tridentate O-C-P ligand **37**.

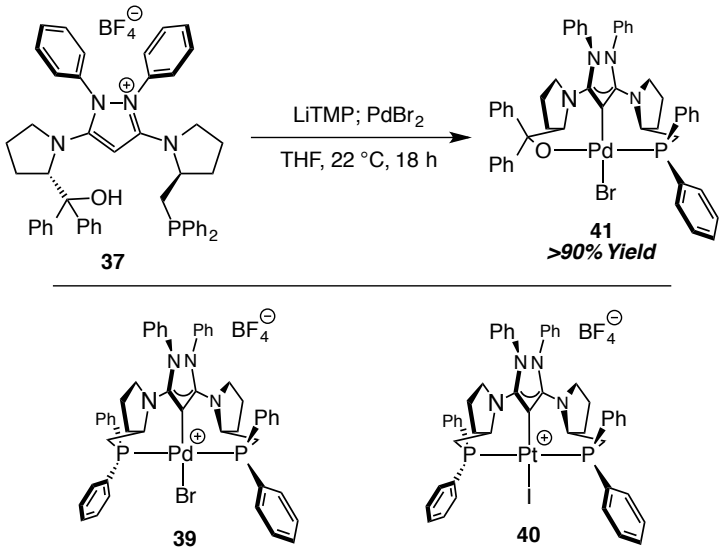
The synthesis of a dissymmetric pyrazole can be accomplished by adding a single equivalent of a less reactive amine followed by reaction with a second amine using more forcing conditions (Scheme 5.5.2-1). This interrupted pyrazole substitution allows for the synthesis of the O-C-P CBA **37** in 23% yield over two steps. The ligand scaffold is amenable to further diversification on both the phosphine substituents and the amino acids used as sources of chirality. Furthermore, the electronics of the carbon(0) donor can be modified by installing

electron donating or electron withdrawing substituents on the aryl rings bound to the 1- and 2-positions of the pyrazole. Work is ongoing to develop variants of **36** and **37**.



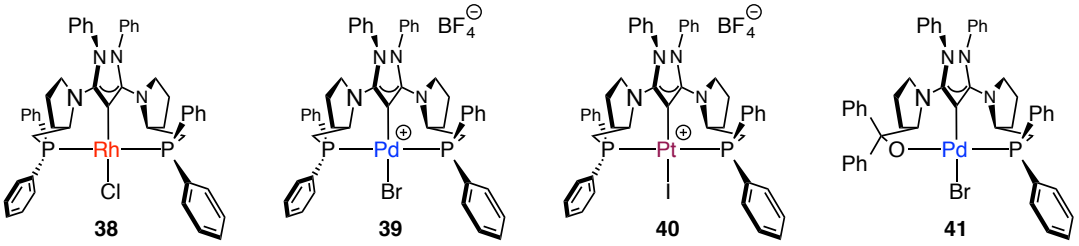
Scheme 5.5.2-1: CBA ligand syntheses.

With ligands **35** and **37** in hand, we explored various metallation procedures. This was spearheaded by C. C. Roberts and for the synthesis of the CBA-Rh(I) complex **38** (Scheme 5.5.3-1) please see the corresponding dissertation (Roberts, 2016). Metallations proceeded analogously to those developed for CDC-ligated complexes except that an internal base was used to assist with deprotonating the C-H bond to form the carbon(0) ligand.[164] Metallation of the O-C-P CBA ligand **37** required full deprotonation prior to addition of the metal complex. The Pd complex **41** could be formed in >90% yield by stirring **37** with LiTMP in THF, presumably to deprotonate both the oxygen and carbon(0), and then adding $PdBr_2$.



Scheme 5.5.2-2: Metallation of CBA ligands to form complexes with Pd and Pt.

The synthesis of the CBA carbon(0) scaffold and associated metal complexes was only begun in the last few months prior to this dissertation, yet the ease of synthesizing these structures – and our experience with carbon(0)-ligated metal complexes – has allowed for the rapid isolation of four new metal complexes **38**, **39**, **40**, and **41** (Scheme 5.5.2-3). These complexes are derived from two basic ligands and the synthesis of sterically and electronically modified variants are currently in progress. Although our previous efforts with group 8 metals had been fruitless (see Chapter 1), we hoped that the new catalyst structure would expand the available hydrofunctionalization catalysts beyond Rh.

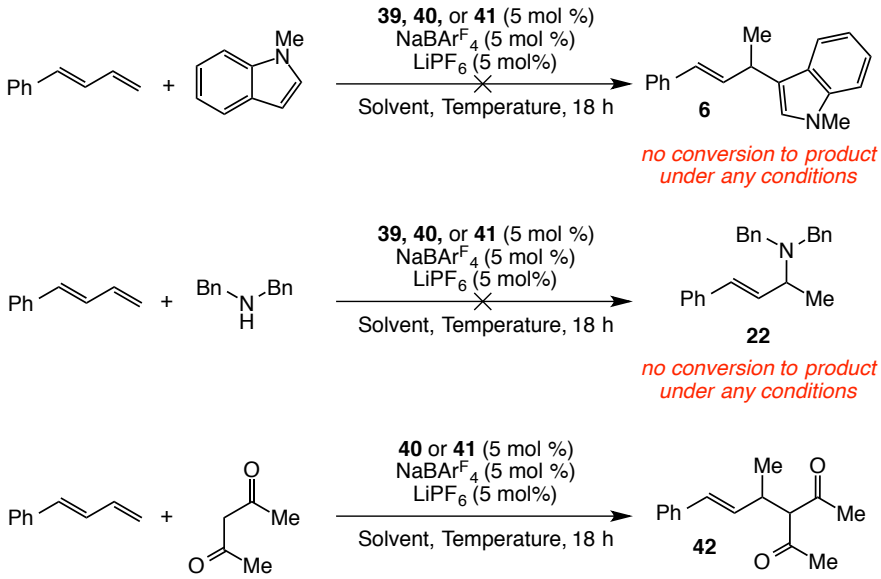


Scheme 5.5.2-3: Newly prepared CBA-ligated metal complexes.

5.5.3: Enantioselective Hydrofunctionalization Catalyzed by Cyclic Bent Allene-Ligated Metal Complexes

Our primary interest was to assay the reactivity and enantioselectivity of CBA-ligated metal complexes for the hydrofunctionalization of olefins. As with the chiral complexes developed in Section 5.4, this was accomplished by surveying these complexes as catalysts for hydroamination, hydroarylation, and hydroalkylation using the reaction conditions developed for achiral transformations. Studies are ongoing and only the most successful will be discussed here.

The group 8 metal complexes proved reluctant catalysts for intermolecular hydrofunctionalization. Test reactions pairing 1,3-phenylbutadiene and 1-methylindole or dibenzylamine failed to generate the desired products (Scheme 5.5.3-1). Results were similar for hydroalkylation with oxazolone and silyloxyfuran nucleophiles, however, reaction with 2,4-pentanedione proceeded to generate **42** with complex **40** and **41** in 45% and 13% NMR yields, respectively. These compounds were assayed by chiral HPLC to find that the products were formed in 9% and 3% ee. The diene was completely consumed during the course of the reaction. The difficulty of applying carbon(0) ligated group 8 complexes to hydrofunctionalization has appeared in both our studies with CDC and CBA ligands. As such, we turned our focus towards the more promising Rh analogues in the hope that reactivity would directly translate between the first- and second-generation complexes.



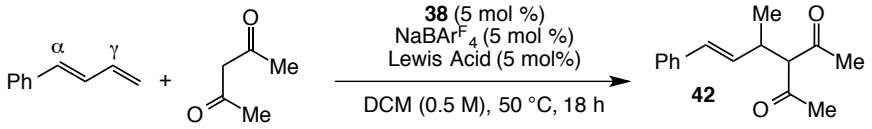
Entry	Catalyst	Solvent; M	Temp (°C)	Yield (%)	%ee
1	**40**	THF; 0.5	22	45	9
2	**41**	Et_2O; 0.5	50	13	3

Scheme 5.5.3-1: Surveying reactivity with CBA complexes of group 8 metals.

Results with the CBA-Rh(I) complex **38** are more encouraging. Catalytic activity has been observed for intermolecular hydroamination and hydroarylation with excellent enantioselectivity (see Roberts, 2016) and the complex appears to be general for multiple reaction classes. Efforts were made to extend the catalytic activity of complex **38** to hydroalkylation as enantioselective reactions with carbon nucleophiles are underexplored (see Section 5.1). Additionally, there was interest in publishing hydroalkylation with malonate-derived carbon nucleophiles (see Chapter 3), but these studies would only be impactful if they could be accomplished enantioselectively.

A survey of Lewis acid activators was performed to gauge the reactivity and selectivity of **38** using DCM as the solvent based on initial screens with intermolecular hydroarylation. Reactions with Li salts gave variable results and generated **42** as a mixture of the γ- and α-additions regioisomers (Table 5.5.3-2). Yields and enantioselectivities were modest, but the

regioselectivity of the transformation was unexpectedly poor; hydroalkylation with **38** and $LiBAr^F_4$, gave 67% yield, 22% ee and 1:1 γ:α selectivity, while $LiBF_4$ gave 53% yield, 0% ee and 3:1 γ:α selectivity, and $LiPF_6$ gave 34% yield, -8% ee and 2:1 γ:α selectivity. The Li counterion had a modest effect on the yields and regioselectivities obtained with **38**, but proved vital to controlling the enantioselectivity of the transformation. The identity of the Li counterion could switch which enantiomer was favored in the catalytic reaction. Additional Lewis acids derived from metal salts other than Li were screened to find that reactions with CuCl, AuCl, and AgCl provided **42** in 26% yield, 2:1 γ:α selectivity, -23% ee; 16% yield, 1:1 γ:α selectivity, -13% ee; and 32% yield, 2:1 γ:α selectivity, 0% ee, respectively. This further emphasized the importance of the Lewis acid for determining enantioselectivity. We do not currently have an explanation for this surprising effect. Overall, this screen demonstrated that **38** could serve as an effective catalyst for hydroalkylation and has the potential to control enantioselectivity.

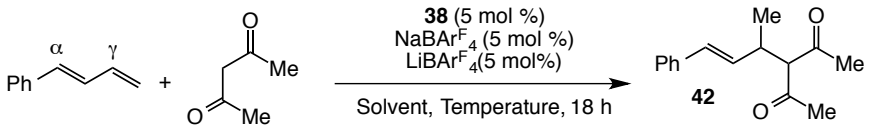


Entry	Lewis Acid; mol%	Yield (%)	γ:α	%ee
1	$LiBAr^F_4$; 5	67	1:1	22
2	$LiBF_4$; 5	53	3:1	0
3	$LiPF_6$; 5	34	2:1	-8
4	CuCl; 5	26	2:1	-23
5	AuCl; 5	16	1:1	-13
6	AgCl; 5	32	2:1	0

Table 5.5.3-2: Screening Lewis acids for the enantioselective hydroalkylation of 1,3-phenylbutadiene with 2,4-pentanedione.

The large variation in reactivity and selectivity obtained with relatively minor changes to the Lewis acid suggested that further optimization might substantially improve the reaction (Table 5.5.3-3). Various solvents were explored to determine their effect on hydroalkylation, but

none superseded the conversion and enantioselectivity obtained with DCM (Entry 1). Hydroalkylation proceeded with reduced yields when Et_2O, PhCl and PhMe were used as solvents, but reaction in chloroform ($CHCl_3$) failed to generate **42** (Entries 2-5). The enantioselectivities were diminished compared to Entry 1 and DCM was adopted as the optimal solvent. Lowering the reaction temperature failed to improve enantioselectivity and reaction at 22 °C gave **42** in 15% yield, 2:1 regioselectivity and 10% ee. Next, the effect of concentration was examined and we were pleased to discover that decreasing the solvent concentration from 0.5 M to 0.1 M and 0.05 M provided enantioselectivities of 50% and 55% ee, respectively (Entries 7 and 8). These higher enantioselectivities were accompanied by reductions in conversion and increases in regioselectivity; reaction at 0.1 M gave 45% yield to a 2:1 mixture of regioisomers, whereas 0.05 M gave 33% yield as a 5:1 mixture of isomers. Increasing the loading of the diene electrophile to two equivalents provided the best enantioselectivity obtained to date, as **42** was formed in 31% yield, 2:1 γ:α selectivity and 60% ee (Entry 9).



Entry	Solvent; M	Temp (°C)	Yield (%)	γ:α	%ee
1	DCM; 0,5	50	67	1:1	22
2	Et_2O; 0.5	50	40	2:1	<5
3	PhCl; 0.5	50	34	2:1	15
4	$CHCl_3$; 0.5	50	0	-	-
5	PhMe; 0.5	50	50	2:1	9
6	DCM; 0.5	22	15	2:1	10
7	DCM; 0.1	50	45	2:1	50
8	DCM; 0.05	50	33	5:1	55
9[a]	DCM; 0.05	50	31	2:1	60

[a] Reaction was run with 2 equiv of 1,3-phenylbutadiene.

Table 5.5.3-3: Optimization of the solvent, concentration and temperature for enantioselective intermolecular diene hydroalkylation with 2,4-pentanedione.

These results are extremely encouraging and obtained with less effort compared to the development of enantioselective CDC-Rh(I) complexes. The second-generation CBA ligand appears to be far more amenable to enantioselective transformations, although it does suffer from decreased regioselectivity and activity when compared to similar reactions with **^{Ph}CDC-Rh-styrene** (see Chapter 3). Efforts are ongoing and we are excited to delve into this new vein of research. We anticipate this ligand being the foundation for future studies on catalytic hydrofunctionalization with carbon(0)-ligated metal complexes.

5.5.4: Summary and Outlook

All signs point towards the CBA ligands being the future of catalysis within the Meek group. Years of exploring chiral ligands and additives with the diazepinium CDC framework gave interesting – but ultimately disappointing – yields and selectivities for various hydrofunctionalization reactions. In comparison, research with CBAs has provided the highest enantioselectivities known with a carbon(0) ligand. We anticipate that the first publication of an enantioselective carbon(0) ligand will further improve our understanding of these tridentate CBA Rh complexes. Further efforts in enantioselective catalysis with CDC-Rh(I) complexes have been discontinued for the time being, but it is the author's hope that future applications will arise for the developed chiral diazepinium ligands.

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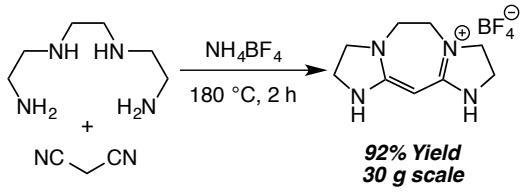
APPENDIX 1: SUPPORTING INFORMATION FOR CHAPTER 1

■ **General:** All reactions were carried out in flame or oven (140 ºC) dried glassware that had been cooled under vacuum. Unless otherwise stated, all reactions were carried out under an inert N_2 atmosphere. All reagents were purged or sparged with N_2 for 20 min prior to distillation or use. All solid reagents were dried by azeotropic distillation with benzene three times prior to use. Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer or a ASI ReactIR 1000, Model: 001-1002 for air sensitive rhodium carbonyl complexes. Mass spectra were obtained using a Micromass Quattro-II triple quadrupole mass spectrometer in combination with an Advion NanoMate chip-based electrospray sample introduction system and nozzle for low-res or Waters Q-ToF Ultima Tandem Quadrupole/Time-of-Flight Instrument UE521 at University of Illinois at Urbana Champaign for high-res or Waters Q-ToF Xevo Tandem Quadrupole/Time-of-Flight Instrument. The Q-Tof Ultima mass spectrometer was purchased in part with a grant from the National Science Foundation, Division of Biological Infrastructure (DBI-0100085). All samples were prepared in MeOH or MeCN for metal complexes. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker model DRX 400 or a Bruker AVANCE III 600 CryoProbe (^{1}H NMR at 400 MHz or 600 MHz, ^{13}C NMR at 100 or 150 MHz, ^{31}P NMR at 160 or 243 MHz and ^{19}F NMR at 376 or 564 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CDCl_3$ at 7.26 ppm, CD_2Cl_2 at 5.30 ppm, C_6D_6 at 7.16 ppm, CD_3CN at 1.94 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, C_6D_6 at 128.4 ppm, CD_3CN at 1.31 ppm). NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, septetd = septet of doublets, m = multiplet, bs = broad singlet, bm = broad multiplet), and

coupling constants (Hz). X-ray diffraction studies were conducted on a Bruker-AXS SMART APEXII diffractometer. Crystals were selected and mounted using Paratone oil on a MiteGen Mylar tip.

■ **Solvents:** Solvents were purged with argon and purified under a positive pressure of dry argon by a SG Waters purification system: dichloromethane (EMD Millipore) and THF (EMD Millipore) were passed through activated alumina columns. Chlorobenzene (Alfa Aesar) was dried over K_2CO_3, distilled under vacuum and stored over activated 5 Å molecular sieves in a dry box.

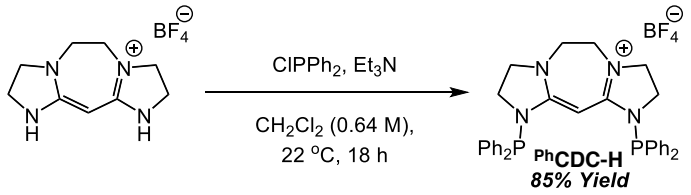
Section 1.3: Synthesis of the Carbodicarbene Ligand Scaffold



Synthesis of the Diazepinium Base

A 1 L three-neck flask was charged with reagent grade triethylenetetramine (26.6 mL, 177 mmol) and fitted with a condenser and addition funnel. The flask was evacuated and backfilled with N_2 before undried, solvent grade methanol (52 mL) and 2-methoxyethoxy ethanol (65 mL) were added after being sparged for 30 minutes with N_2. The reaction was heated to 50 °C and ammonium tetrafluoroborate (56.8 g, 542 mmol) added quickly in one large portion. The reaction was heated to 75 °C and malononitrile (10.3 g, 156 mmol) added to the addition funnel as a solution in N_2 sparged MeOH (27 mL). The solution of malononitrile was added dropwise over 10 minutes and the reaction fitted with a Claisen head and distillation flask while maintaining a N_2 atmosphere. The solution was heated to 180 °C for 3 h causing the MeOH to be distilled off. The reaction was then cooled to 100 °C and butylamine (15.7 mL, 159 mmol) added

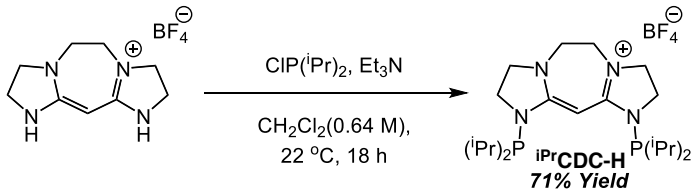
before the reaction was allowed to stand overnight at -20 °C as a yellow powder crashed out of solution. The solid was isolated by filtration and extensive washing with iPrOH, followed by purification by silica gel column chromatography (7:3 DCM:Hexanes) to yield a sticky yellow powder. Further washing of this powder with iPrOH removed residual 2-methoxyethoxy ethanol to yield a free flowing yellow crystalline powder (26 g, 144 mmol, 92% yield). This powder was dried by heating in a drying pistol with refluxing iPrOH with P_2O_5 to trap volatilized moisture.



Synthesis of ^{Ph}CDC-H

A 250 mL round-bottom flask with a stir bar was charged with diazepinium salt 3 (2.00 g, 7.52 mmol), sealed with a septum and purged with nitrogen. Dichloromethane (12.0 mL, [ ] = 0.640 M) and triethylamine (12.0 mL, 860 mmol) were added via syringe and the solution was allowed to stir for 5 min. To the yellow heterogenous solution, chlorodiphenylphosphine (4.05 mL, 22.6 mmol) was added via syringe and the reaction was allowed to stir at 22 ºC for 18 h. The reaction was triturated with diethyl ether (100 mL) and filtered to isolate a yellow solid. The yellow solid was purified by SiO_2 column chromatography (20:1 to 9:1 CH_2Cl_2/MeOH). After concentrating the solution to a solid, the resulting yellow residue was dissolved in benzene (5 mL) before being triturated with toluene (150 mL) to produce a white powder which was filtered off (4.10 g, 6.39 mmol 85% yield). Excess water was removed by azeotropic distillation with benzene (3 x 3 mL). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.41 (20H, m), 6.17 (1H, t, J = 7.3 Hz), 3.80 (4H, s), 3.77 (4H, t, J = 8.8 Hz), 3.34 (4H, t, J = 8.8 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 163.90 (d, J = 19.2 Hz),

132.98 (d, J = 9.2 Hz), 132.50 (d, J = 17.0 Hz), 130.43, 129.18 (d, J = 5.4 Hz), 62.21 (t, J = 26.4 Hz), 50.92, 47.52, 44.40 (d, J = 7.3 Hz). **^{31}P NMR** (243 MHz, $CDCl_3$): δ 41.4. **^{19}F NMR** (376 MHz): δ -153.33 (d, J = 19.8 Hz). IR (ν/cm^{-1}): 3057 (w), 2891 (w), 1594 (w), 1557 (s), 1524 (s), 1508 (w), 1478 (m), 1436 (m), 1312 (w), 1292 (m), 1227 (m), 1161 (w), 1097 (w), 1054 (s). HRMS (ES$^+$) $[M+H]^+$ calcd for $C_{33}H_{33}N_4P_2^+$ 547.2175, found: 547.2172.

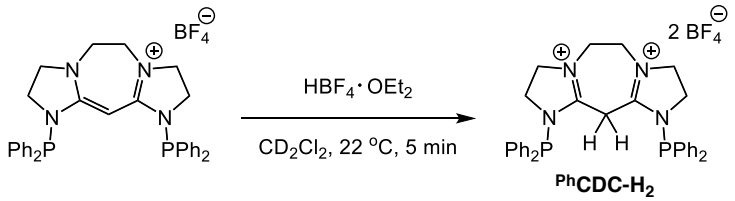


Synthesis of ^{iPr}CDC-H

A 250 mL round-bottom flask with a stir bar was charged with diazepinium salt 3[11] (2.00 g, 7.52 mmol), sealed with a septum and purged with nitrogen. Dichloromethane (12.0 mL, [ ] = 0.640 M) and triethylamine (12.0 mL, 860 mmol) were added via syringe and the solution was allowed to stir for 5 min. To the yellow heterogeneous solution, chlorodiisopropylphosphine (3.6 mL, 22.6 mmol) was added via syringe and the reaction was allowed to stir at 22 °C for 18 h. The reaction was filtered through a pad of Celite® which was washed with dichloromethane (100 mL). The filtrate was concentrated and purified by SiO_2 column chromatography (30:1 CH_2Cl_2/MeOH). The resulting off-white solid was dissolved in a minimal amount of dichloromethane and triturated with hexanes to produce a white powdery solid which was filtered off (2.65 g, 71% yield). Excess water was removed by azeotropic distillation with benzene (3 x 3 mL).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.70 (^{1}H, t, J = 7.0 Hz), 3.73 (4H, m), 3.65, (4H, s), 3.59 (4H, m), 2.08 (4H, septd, J = 7.0, 1.6 Hz), 1.11 (12H, dd, J = 16.8, 7.0 Hz), 1.03 (12H, dd, J = 12.5,

7.0 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 165.04 (d, *J* = 21.3 Hz), 63.63 (t, *J* = 29.7 Hz), 51.13, 47.27, 44.55, 25.11 (d, *J* = 15.1 Hz), 19.21 (d, *J* = 19.21 Hz), 18.80 (d, *J* = 22.9 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$): δ 63.24. **^{19}F NMR** (376 MHz): δ -153.64 (d, *J* = 18.8 Hz). IR (ν/cm^{-1}): 2952 (m), 2924 (w), 2867 (m), 1557 (s), 1523 (m), 1507 (w), 1457 (w), 1436 (w), 1386 (m), 1291 (m), 1227 (m), 1163 (w), 1053 (s). HRMS (ES$^+$) $[M+H]^+$ calcd for $C_{21}H_{41}N_4P_2^+$ 411.2801, found: 411.2799.

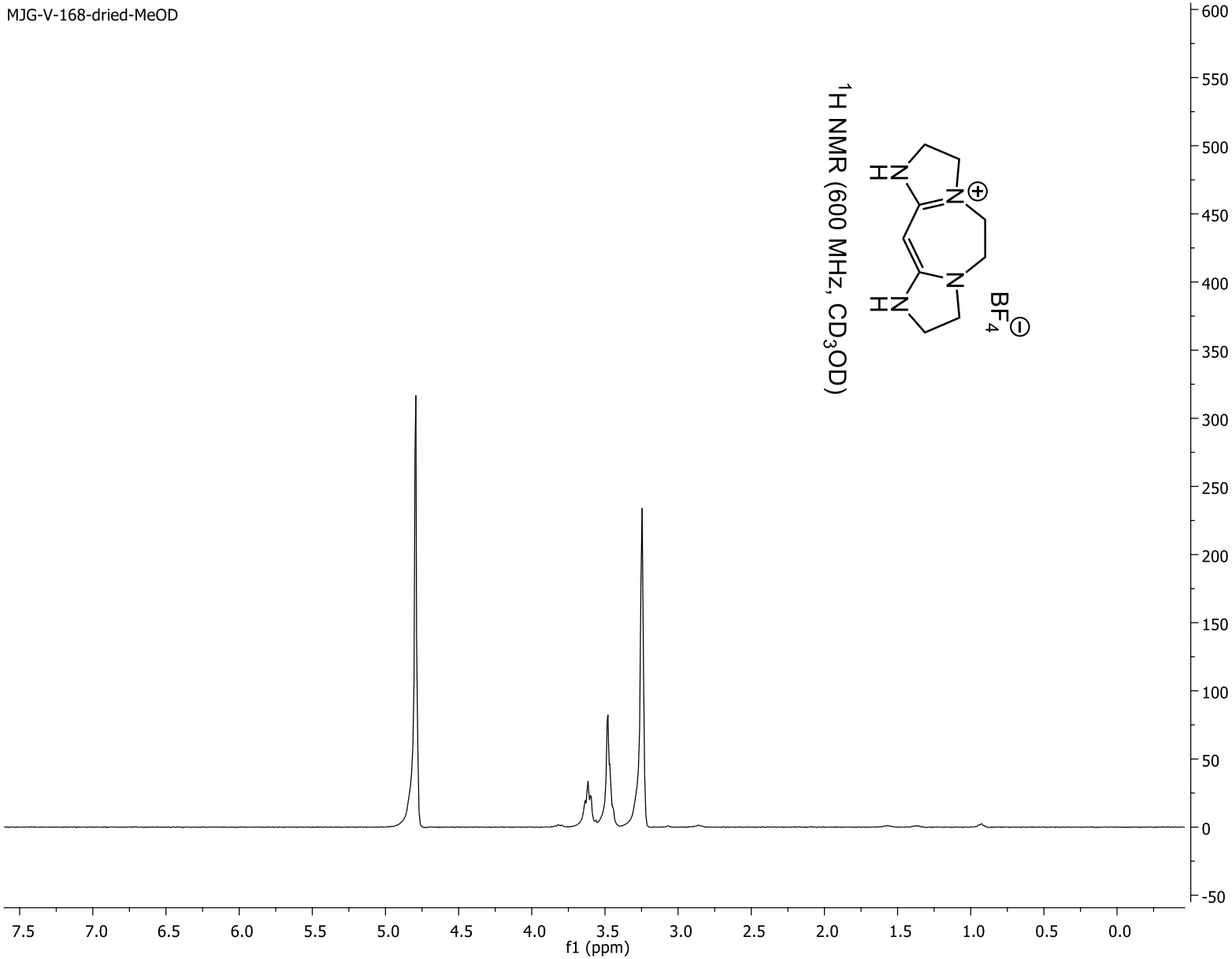


Synthesis of Dicationic ^{Ph}CDC-H_2

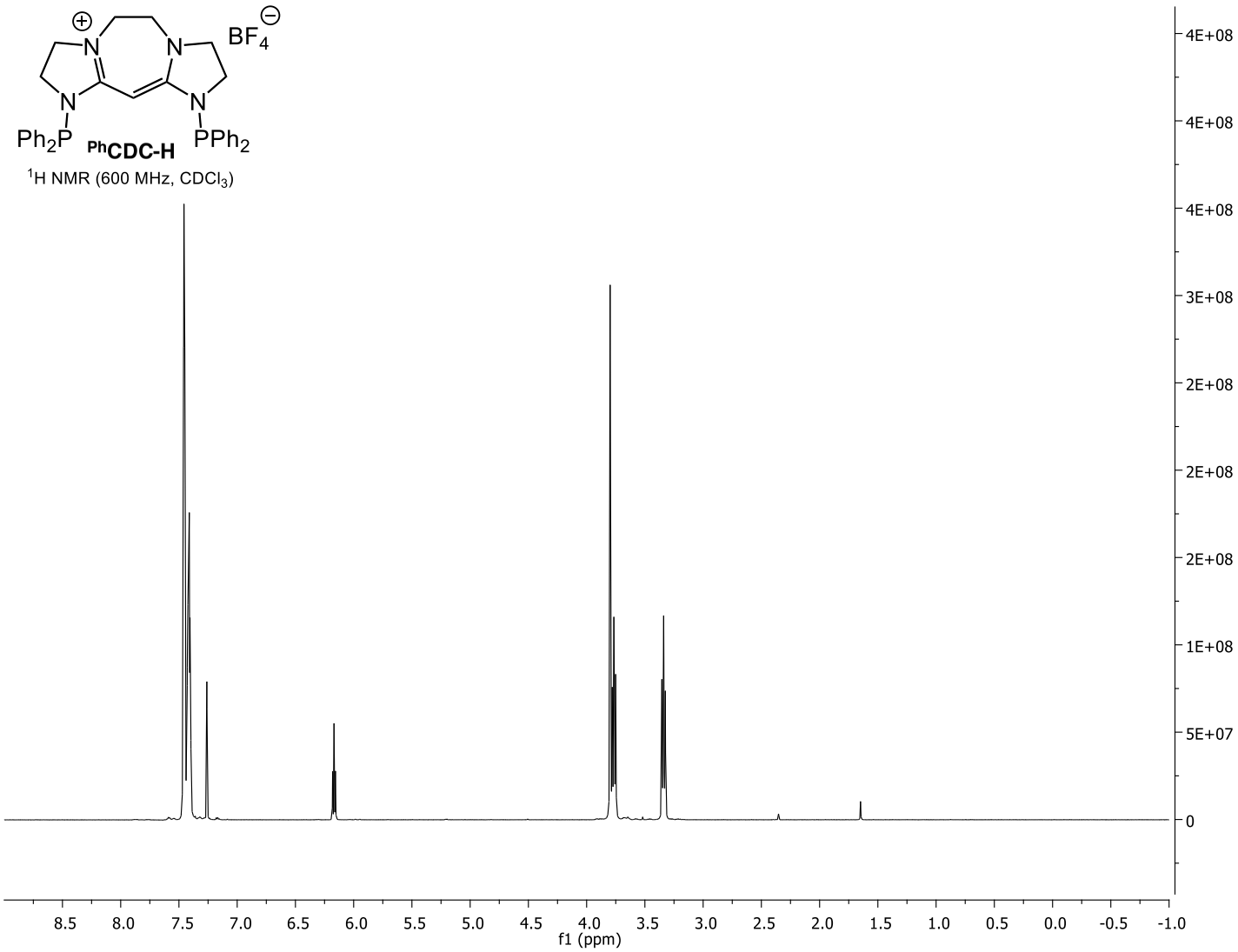
In an N_2 filled dry box, an 8-mL vial was charged with 4 (10.0 mg, 0.016 mmol) and CD_2Cl_2 (0.25 mL). The solution was transferred to an NMR tube and the vial was washed with CD_2Cl_2 (2 x 0.25 mL). The tube was capped with a septum-lined lid and brought outside the dry box. Tetrafluoroboric acid (5.1 μL, 0.019 mmol) was added via syringe, which resulted in an immediate color change from pale yellow to almost colorless, and the tube was shaken for 5 min before being analyzed.

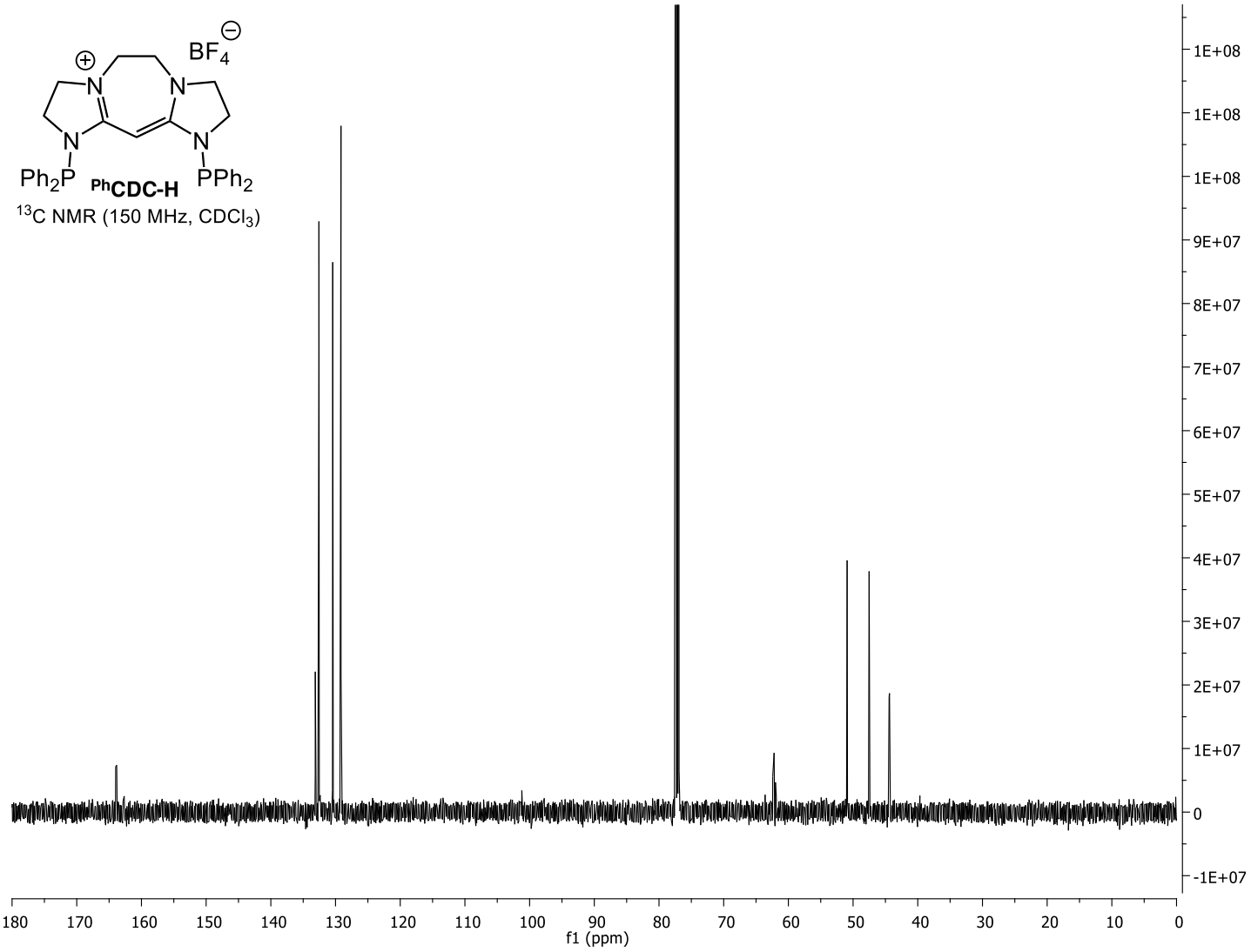
^{1}H NMR (600 MHz, CD_2Cl_2): δ 7.44-7.7.52 (m, 20H), 5.36 (t, *J* = 4.9 Hz), 4.05-4.09 (m, 8H), 3.64 (t, 4H, *J* = 10.9 Hz).

MJG-V-168-dried-MeOD



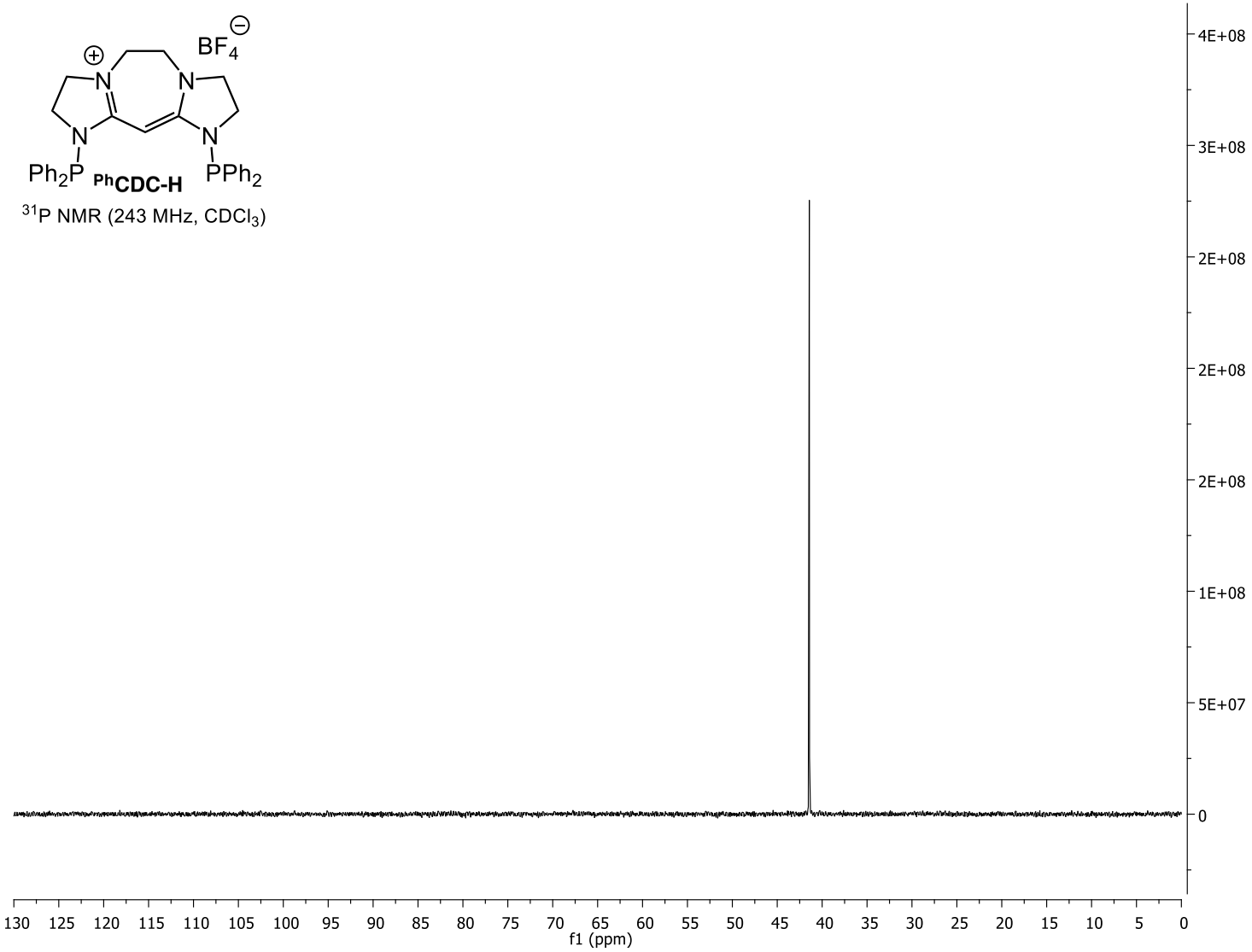
^{1}H NMR (600 MHz, CD_3OD)


BF4
Ph2P
PhCDC-H
PPh2
1H NMR (600 MHz, CDCl3)
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


BF4
N
N
N
N
Ph2P
PPh2
PhCDC-H
13C NMR (150 MHz, CDCl3)
1E+08
1E+08
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
-1E+07
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

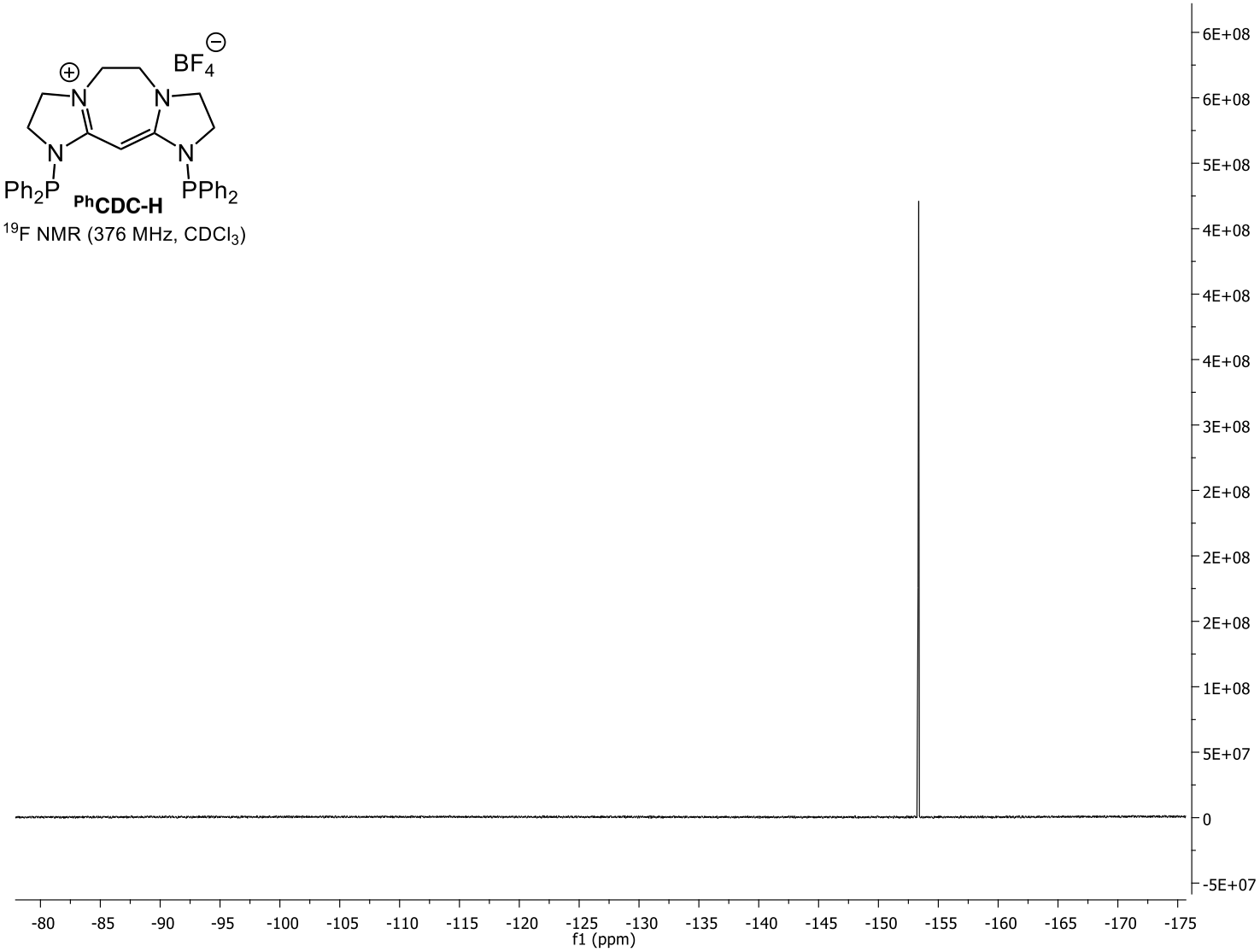
PhCDC-H

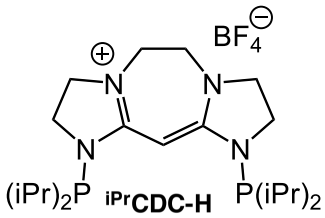
^{31}P NMR (243 MHz, $CDCl_3$)



^{Ph}CDC-H

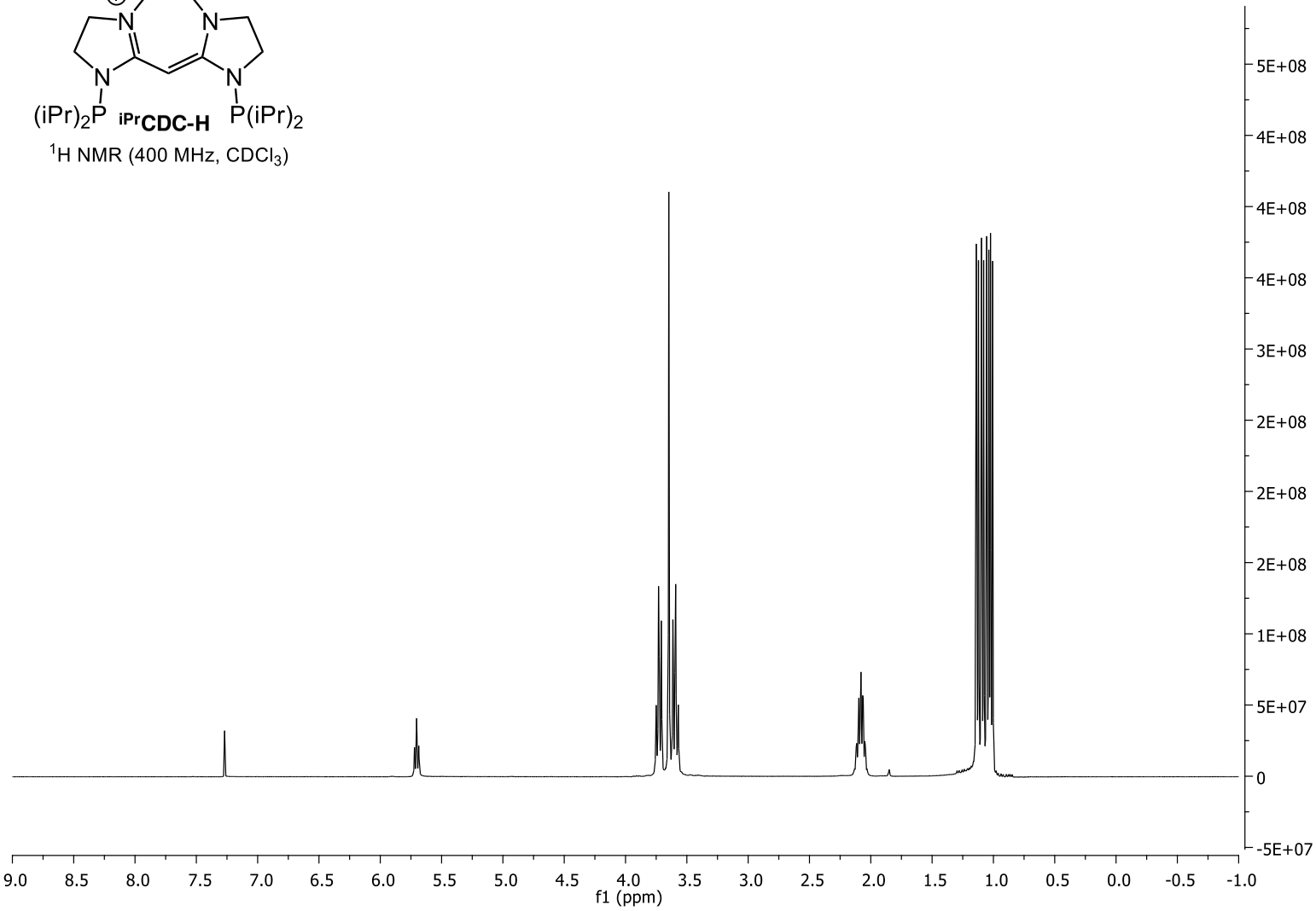
^{19}F NMR (376 MHz, $CDCl_3$)





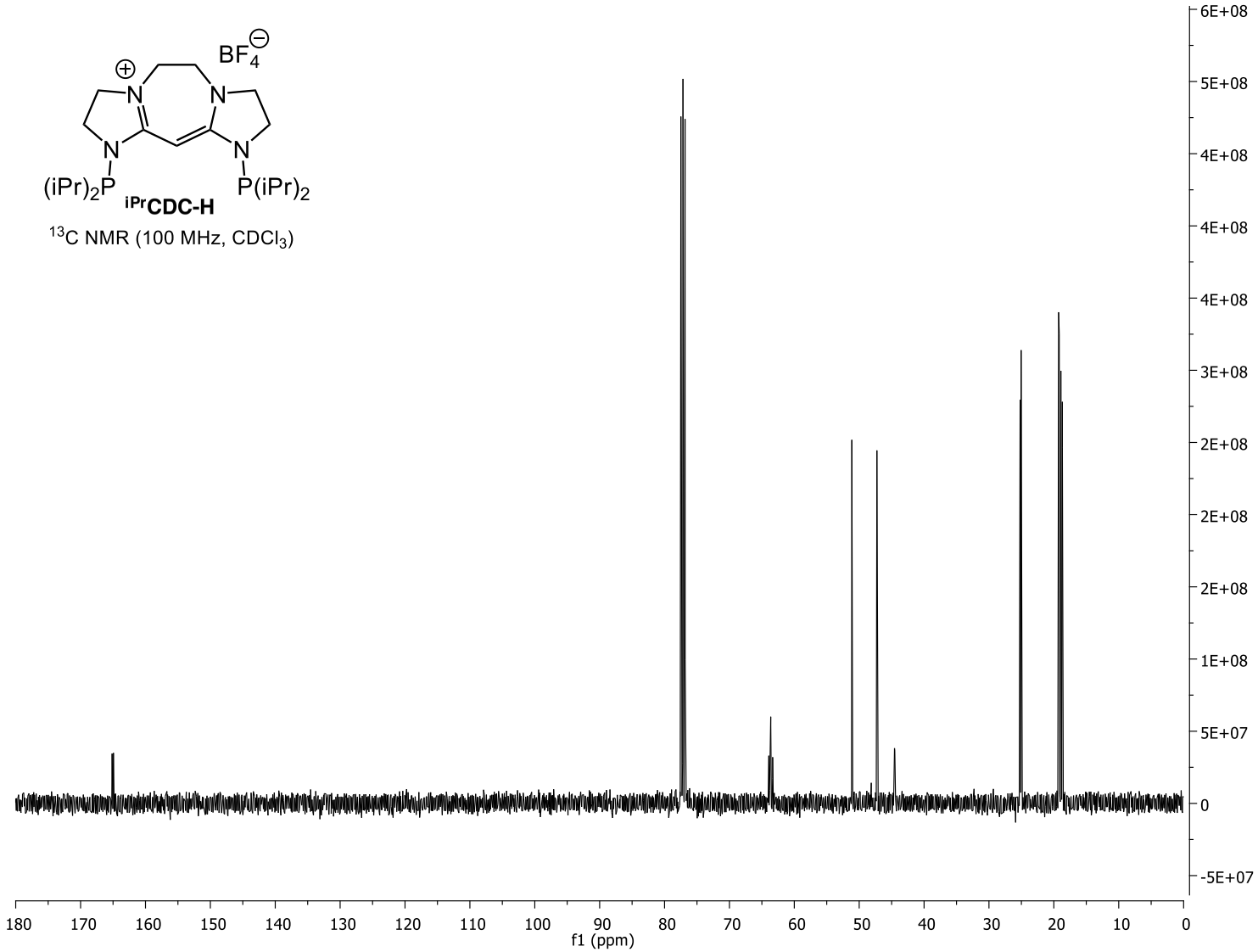
iPrCDC-H

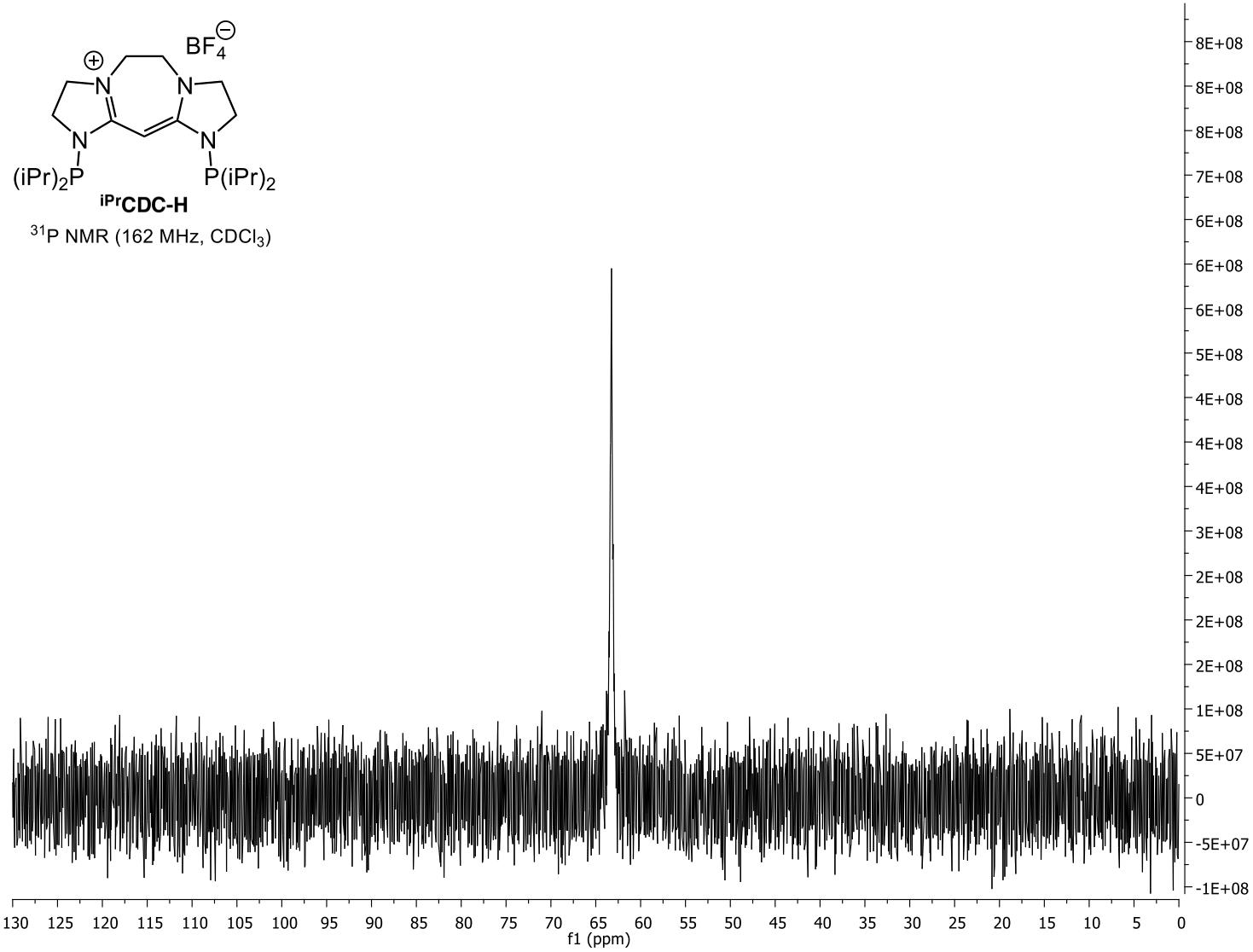
^{1}H NMR (400 MHz, $CDCl_3$)



iPrCDC-H

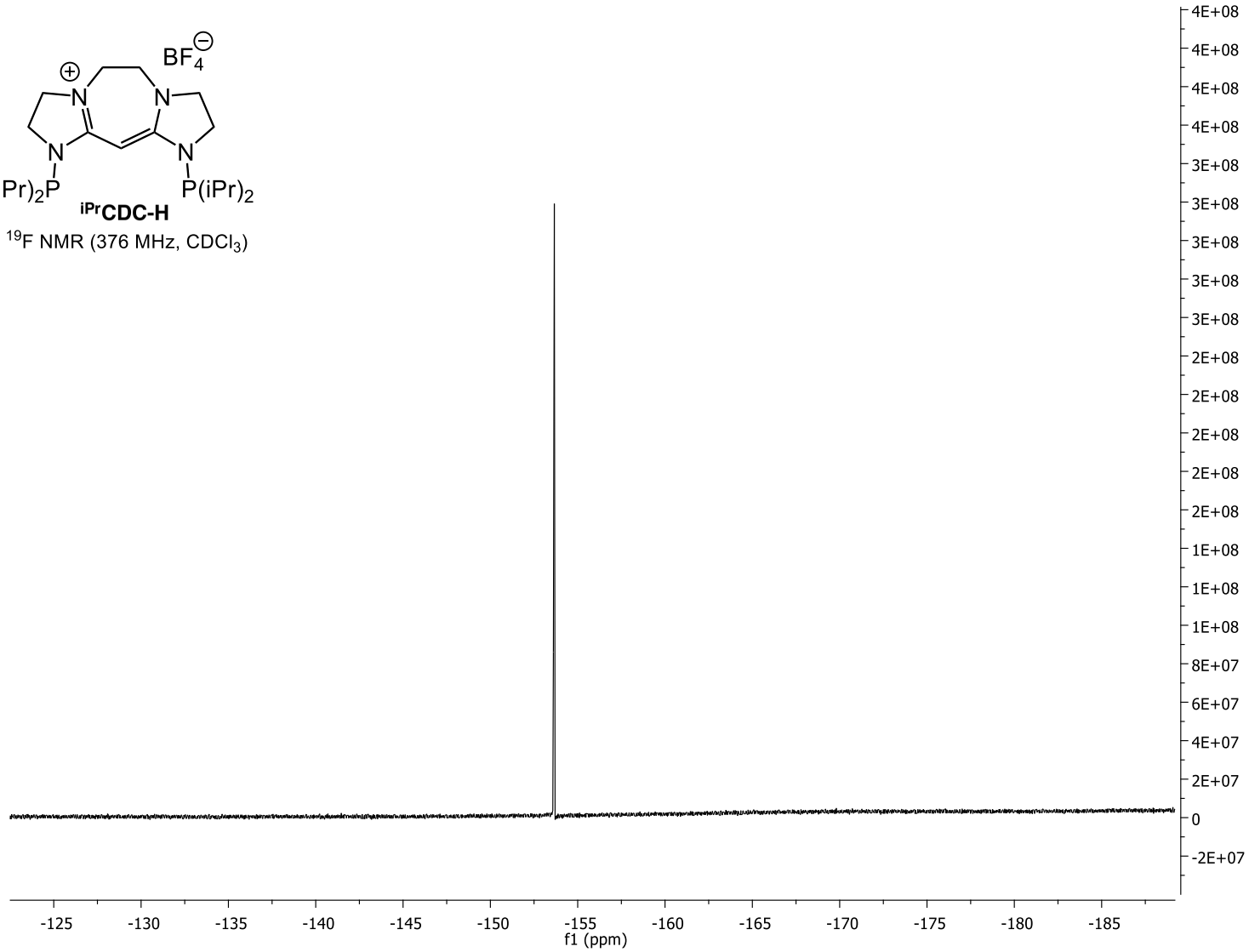
^{13}C NMR (100 MHz, $CDCl_3$)




BF4
N
N
N
N
(iPr)2P
P(iPr)2
iPrCDC-H
31P NMR (162 MHz, CDCl3)
8E+08
8E+08
8E+08
7E+08
6E+08
6E+08
6E+08
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
-1E+08
130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

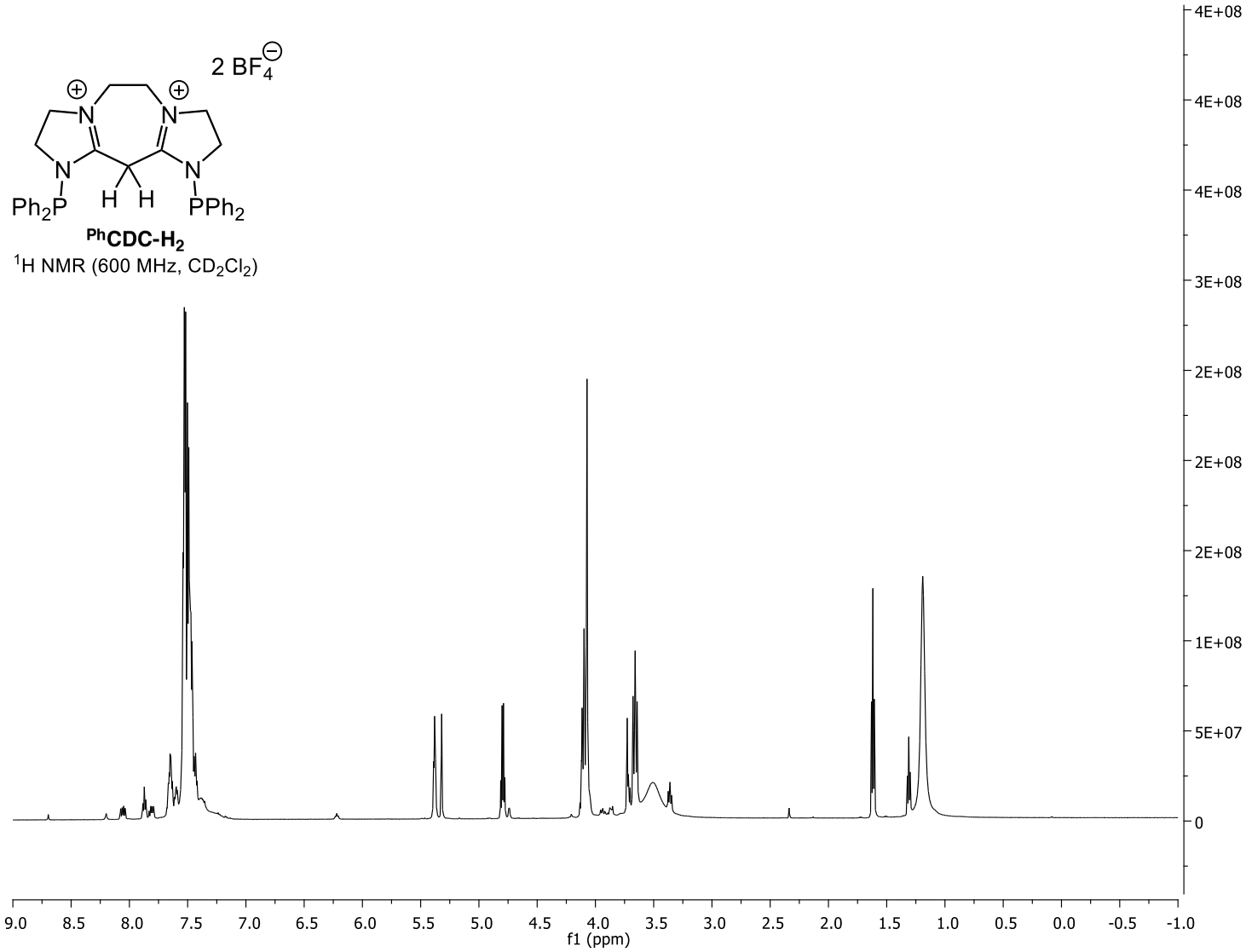
iPrCDC-H

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



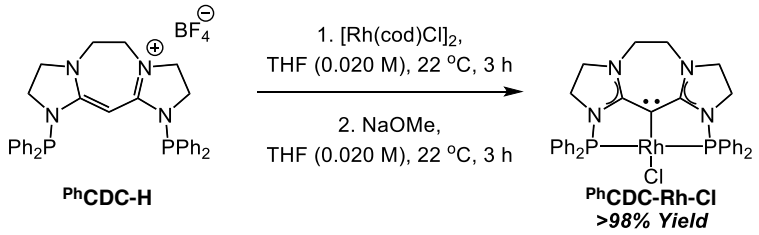
^{Ph}CDC-H$_2$

^{1}H NMR (600 MHz, CD_2Cl_2)



Section 1.4: Syntheses of Carbodicarbene Ligated Metal Complexes

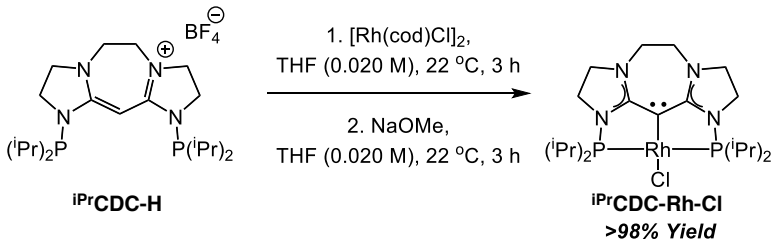
■ **General procedure for the preparation of CDC-Rh(I)Cl complexes ^{Ph}CDC-Rh-Cl and ^{iPr}CDC-Rh-Cl:** In an N_2 filled dry box, a 20-mL scintillation vial with a stir bar was charged with CDC-H BF_4 salt (1.0 equiv) and chloro(1,5-cyclooctadiene)rhodium(I) dimer (0.50 equiv). Tetrahydrofuran was added, the vial capped, and the resulting mixture was allowed to stir for 3 h at 22 °C. The solution was concentrated *in vacuo*. Residual 1,5-cyclooctadiene was removed by azeotropic distillation with benzene (3 x 1 mL). Sodium methoxide (1.0 equiv) and THF were added to the reaction vial. The resulting heterogeneous mixture was allowed to stir for 3 h at 22 °C.



Synthesis of ^{Ph}CDC-Rh-Cl

Following the general procedure for the preparation of CDC-Rh(I)-Cl complexes, **^{Ph}CDC-H BF_4** (258 mg, 0.406 mmol) and chloro(1,5-cyclooctadiene)rhodium(I) dimer (100 mg, 0.203 mmol) were solvated with THF (10 mL, [ ] = 0.020 M). After concentration, NaOMe (21.9 mg, 0.406 mmol) was added and solvated with THF (10 mL, [ ] = 0.020 M). After reaction was complete, acetonitrile (4.0 mL) was added to the solution, which was then filtered through a pad of Celite®. The Celite® pad was washed with a 1:1 mixture of THF:MeCN (5 mL) to dissolve the solid. The resulting filtrate was concentrated to afford orange solid **^{Ph}CDC-Rh-Cl** in >98% yield (282 mg, 0.412 mmol).

^{1}H NMR (600 MHz, CD_3CN): δ 7.65-7.68 (8H, m), 7.50-7.56 (12H, m), 4.01 (4H, t, *J* = 8.1 Hz), 3.45 (4H, s), 3.30 (4H, t, *J* = 8.3 Hz). **^{13}C NMR** (150 MHz, CD_3CN): δ 173.11 (td, *J* = 18.1, 1.3 Hz), 134.61, (t, *J* = 17.0 Hz), 133.15 (t, *J* = 6.8 Hz), 131.70, 129.82 (t, *J* = 3.8 Hz), 72.98 (dt, *J* = 29.9, 9.7 Hz), 58.88, 47.32, 42.24. **^{31}P NMR** (243 MHz, CD_3CN): δ 79.20 (d, *J* = 170.4 Hz). HRMS (ES+) $[M–Cl]^+$ calcd for $C_{33}H_{32}N_4P_2Rh^+$ 649.1157, found: 649.1155. When formic acid was added to neutral complex **6** the protonated N_2 adduct was formed. HRMS (ES^+) $[M+H+N_2]^+$ calcd for $C_{33}H_{33}N_6P_2RhCl^+$ 713.0985, found: 713.1317.

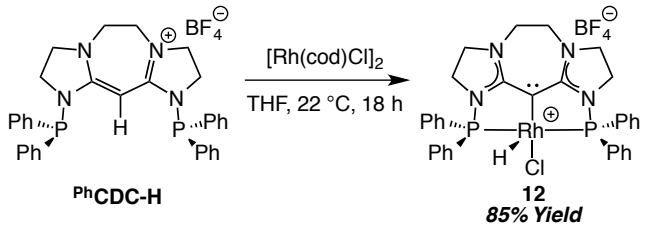


Synthesis of ^{iPr}CDC-Rh-Cl

Following the general procedure for the preparation of CDC-Rh(I)-Cl complexes, **^{iPr}CDC-H BF_4** (100 mg, 0.201 mmol) and chloro(1,5-cyclooctadiene)rhodium(I) dimer (49.5 mg, 0.100 mmol) were solvated with THF (5.0 mL, [ ] = 0.020]. After concentration, NaOMe (10.9 mg, 0.201 mmol) was added and solvated with THF (5 mL, [ ] = 0.020 M). The resulting yellow powder was filtered through a pad of Celite® and washed with THF (4 x 1 mL). The yellow solid was dissolved off the Celite® pad using acetonitrile (5 mL) and concentrated *in vacuo* to afford **^{iPr}CDC-Rh-Cl** in >98% yield (110 mg, 0.201 mmol) as a canary yellow powder.

^{1}H NMR (600 MHz, CD_3CN): δ 3.88 (4H, t, *J* = 8.2 Hz), 3.42 (4H, t, *J* = 8.2 Hz), 3.31 (4H, s), 2.29 (4H, septetd, *J* = 7.0, 1.0 Hz), 1.27 (12H, m), 1.20 (12H, m). **^{13}C NMR** (150 MHz, CD_3CN): δ 173.95 (t, *J* = 15.1 Hz), 73.76 (dt, *J* = 30.1, 8.7 Hz), 58.69, 47.40, 42.66, 27.91 (t, *J* = 8.1 Hz),

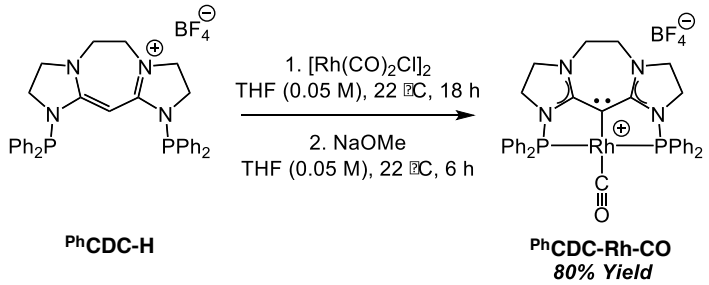
19.37, 18.89 (t, J = 4.4 Hz). **^{31}P NMR** (162 MHz, CD_3CN): 110.44 (d, J = 167.1 Hz). HRMS (ES^+) $[M–Cl]^+$ calcd for $C_{21}H_{40}N_4P_2Rh^+$ 513.1783, found: 513.1795.



Synthesis of ^{Ph}CDC-Rh-HCl (12)

In an N_2 filled dry box, a 20 mL scintillation vial equipped with a stir bar was charged with **^{Ph}CDC-H** (103 mg, 0.162 mmol) and $[Rh(cod)Cl]_2$ (40 mg, 0.0811 mmol) before being solvated with THF (3 mL). The reaction was allowed to stir at room temperature for 18 h during which time a yellow precipitate crashed out of solution. The reaction was filtered through a plug of celite® and washed with excess THF (3 x 2 mL) until the flowthrough had no yellow color. The product was then dissolved off the column with MeCN and the solution concentrated to yield **12** as a yellow powder (106.6 mg, 0.138 mmol), 85% yield). This powder was dried on high vacuum for several hours to remove residual THF.

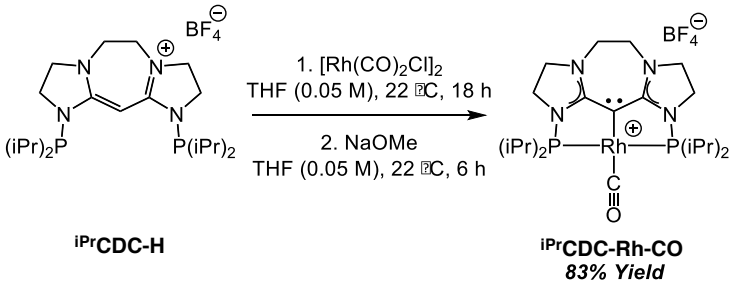
^{1}H NMR (600 MHz, Acetonitrile-d_3) δ 7.98 (dtd, J = 7.7, 6.1, 1.4 Hz, 4H), 7.66 (t, J = 7.4 Hz, 2H), 7.62 – 7.55 (m, 8H), 7.55 – 7.49 (m, 6H), 4.14 (td, J = 9.7, 8.4 Hz, 2H), 3.95 (td, J = 9.8, 5.6 Hz, 2H), 3.68 (td, J = 9.8, 5.7 Hz, 2H), 3.54 – 3.43 (m, 4H), 3.27 (q, J = 9.7 Hz, 2H), -16.32 (dt, J = 19.3, 9.8 Hz, 1H). **^{13}C NMR** (151 MHz, Acetonitrile-d_3) δ 169.23 (t, J = 18.6 Hz), 162.68, 134.85 (t, J = 8.4 Hz), 132.51, 131.32 (t, J = 6.7 Hz), 131.07 (d, J = 4.6 Hz), 130.89, 129.11, 128.85 (t, J = 5.7 Hz), 128.56 (t, J = 4.9 Hz), 67.29, 57.71, 57.36, 46.33, 42.32, 25.25.



Synthesis of ^{Ph}CDC-Rh-CO

In an N_2 filled dry box, an 8-mL vial with a stir bar was charged with ^{Ph}**CDC-H** (16.3 mg, 0.026 mmol) and dicarbonylchlororhodium(I) dimer (5.0 mg, 0.013 mmol), and tetrahydrofuran (0.50 mL, [ ] = 0.050 M). The vial was capped and the resulting mixture was allowed to stir for 18 h at 22 °C. The resulting solution was concentrated to afford a yellow powder. To this solid, NaOMe (1.4 mg, 0.026 mmol) was added followed by tetrahydrofuran (0.50 mL, [ ] = 0.05 M). The yellow heterogeneous solution was allowed to stir for 6 h at 22 °C. The solution was concentrated *in vacuo*, dissolved in $CHCl_3$ (1 mL), and filtered through a cotton plug, which was washed with $CHCl_3$ (2 x 1 mL). The filtrate was concentrated *in vacuo* to afford ^{Ph}**CDC-Rh-CO** in 80% yield (15.8 mg, 0.021 mmol) as a burnt yellow powder.

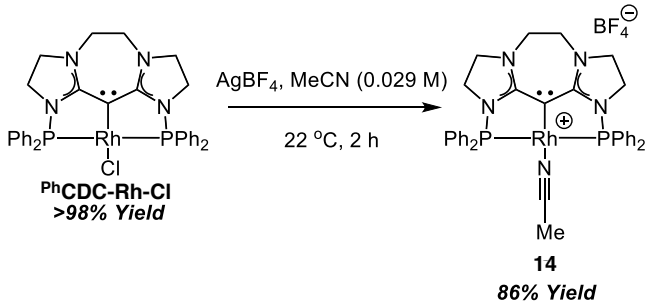
^{1}**H NMR** (600 MHz, CD_3CN): δ 7.67-7.70 (8H, m), 7.52-7.57 (4H, m), 7.50-7.54 (8H, m), 4.19 (4H, t, *J* = 8.4 Hz), 3.65 (4H, s), 3.36 (4H, t, *J* = 14.4 Hz). ^{13}**C NMR** (150 MHz, CD_3CN): δ 194.6 (dt, *J* = 57.2, 12.7 Hz), 174.4 (t, *J* = 21.6 Hz), 133.4 (t, *J* = 7.9 Hz), 132.9, 132.2, (t, *J* = 27.1 Hz), 130.2, (t, *J* = 5.4 Hz), 86.4 (dt, *J* = 28.1, 11.0 Hz), 59.5, 47.2, 42.4. ^{31}**P NMR** (162 MHz, CD_3CN): δ 87.99 (d, *J* = 103.6 Hz). IR (ν/cm^{-1}) (CH_2Cl_2): 1986 (ν_{CO}), 1537 (m), 1475 (w), 1375 (w), 1267 (w). HRMS (ES+) $[M\text{-}CO]^+$ calcd for $C_{34}H_{32}N_4OP_2Rh^+$ 677.1101, found: 677.1809.



Synthesis of ^{iPr}CDC-Rh-CO

In an N_2 filled dry box, an 8-mL vial with a stir bar was charged with **^{iPr}CDC-Rh-Cl** (13.0 mg, 0.026 mmol) and dicarbonylchlororhodium(I) dimer (5.0 mg, 0.013 mmol), and tetrahydrofuran (0.50 mL, [ ] = 0.050 M). The vial was capped, and the resulting mixture was allowed to stir for 18 h at 22 °C. The resulting solution was concentrated to afford a yellow powder. To this solid, NaOMe (1.4 mg, 0.026 mmol) was added followed by tetrahydrofuran (0.50 mL, [ ] = 0.05 M). The yellow heterogeneous solution was allowed to stir for 6 h at 22 °C. The solution was concentrated *in vacuo* to afford **^{iPr}CDC-Rh-CO** in 83% yield (16.5 mg, 0.0216 mmol) as a canary yellow powder.

^{1}H NMR (600 MHz, $CDCl_3$): δ 4.11 (4H, t, *J* = 8.52 Hz), 3.55 (4H, t, *J* = 8.52 Hz), 3.53 (4H, s), 2.38 (4H, m), 1.28-1.32 (12H, m), 1.2-1.24 (12H, m). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 195.36 (dt, *J* = 34.5, 19.0 Hz), 174.15 (t, *J* = 19.1 Hz), 85.16 (dt, *J* = 19.0, 9.3 Hz), 58.24, 46.37, 42.26, 27.31 (t, *J* = 12.3 Hz), 18.95, 18.73 (t, *J* = 4.3 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$): δ 119.97 (d, *J* = 98.8 Hz). IR (ν/cm^{-1}) (CH_2Cl_2): 2966 (w), 2885 (w), 1970 (ν_{CO}), 1529 (m), 1475 (w), 1375 (w), 1182 (w), 1055 (s). HRMS (ES+) $[M\text{-}CO]^+$ calcd for $C_{22}H_{40}N_4OP_2Rh^+$ 541.1727, found: 541.1715.



Synthesis of cationic ^{Ph}CDC-Rh-MeCN BF_4 (14)

An 8-mL amber vial equipped with a stir bar was charged with **^{Ph}CDC-Rh-Cl** (40.0 mg, 0.0584 mmol) and $AgBF_4$ (17.1 mg, 0.0876 mmol). Acetonitrile (2.0 mL, [ ] = 0.029) was added to the vial and the heterogeneous solution was allowed to stir for 2 h at 22 °C. The resulting solution was filtered through a pad of Celite® and concentrated to afford **14** (39.0 mg, 0.0502 mmol, 86% yield) as a dark orange powder. X-ray quality crystals of **14** were grown from a slow salt metathesis of **^{Ph}CDC-Rh-Cl** and $NaBF_4$ in a 5:1 mixture of benzene:MeCN.

^{1}H NMR (600 MHz, CD_3CN): δ 7.75-7.78 (12H, m), 7.68-7.70 (8H, m), 4.31 (4H, t, *J* = 8.5 Hz), 3.78-3.80 (8H, m). **^{13}C NMR** (150 MHz, CD_3CN): δ 168.67 (t, *J* = 16.6 Hz), 134.75, 133.60 (t, *J* = 7.1 Hz), 130.94 (t, *J* = 5.8 Hz), 125.40, (t, *J* = 29.8 Hz), 58.29, 56.33 (dt, *J* = 28.1, 4.5 Hz), 47.51, 44.55. **^{31}P NMR** (162 MHz, CD_3CN): 67.63 (d, *J* = 58.4 Hz). **^{19}F NMR** (376 MHz): δ -152.24 (d, *J* = 20.0 Hz). HRMS (ES^+) $[M+H]^+$ calcd for $C_{35}H_{35}N_5P_2Rh^+$ 690.1423, found: 690.1435.

Crystal Structure Data for ^{Ph}CDC-Rh-MeCN

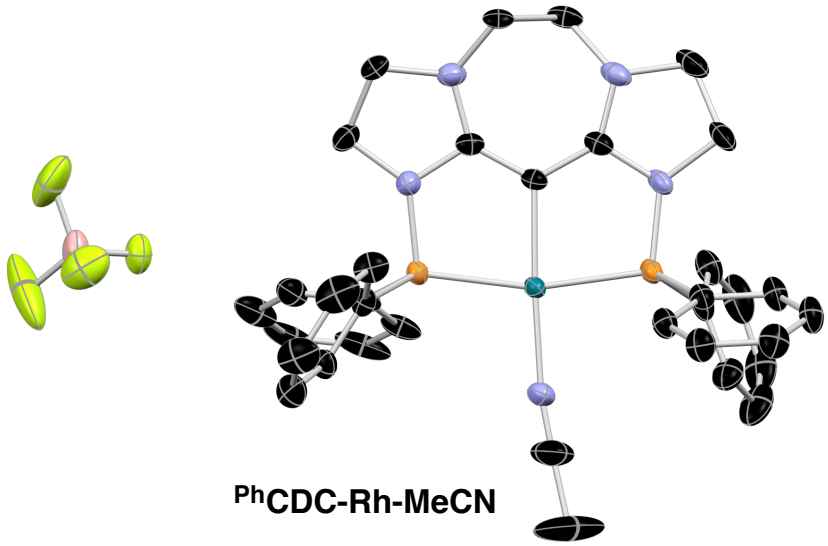


Table 2. Crystal structure data for ^{Ph}**CDC-Rh-MeCN**

Identification code	x1312005_0m_p21onc
Empirical formula	C47 H44 B F4 N5 P2 Rh
Formula weight	930.53
Temperature	100 K
Wavelength	1.54178
Crystal system	monoclinic
Space group	P 21/c
Unit cell dimensions	a = 17.0682(4) Å α= 90
	b = 16.9409(4) Å β= 110.952(1)
	c = 17.3070(5) Å γ = 90
Volume	4673.5(2)
Z	4
Density (calculated)	1.322 Mg/m3
Absorption coefficient	4.041 (mm-1)
F(000)	1908
Crystal size	0.086 x 0.124 x 0.279
Theta range for data collection	77.10-2.77
Index ranges	Hmax = 20, kmax = 20, lmax = 20
Reflections collected	43697
Independent reflections	8846
Completeness to theta	99.5
Max. and min. transmission	0.2815, 0.6907
Refinement method	XS least squares
Goodness-of-fit on F2 0	1.2983

Final R indices [I>2sigma(I)]	R1 = 0.0477, wR2 = 0.1542
R indices (all data)	R1 = 0.0435, wR2 = 0.1542
Extinction coefficient	na

Table 3. Bond lengths (Å) for ^{Ph}**CDC-Rh-MeCN**

Number	Atom 1	Atom 2	Length
1	Rh1	P1	2.2301(8)
2	Rh1	P2	2.2400(7)
3	Rh1	N5	2.027(3)
4	Rh1	C1	2.043(2)
5	P1	N4	1.699(2)
6	P1	C16	1.814(3)
7	P1	C10	1.817(4)
8	P2	N1	1.704(2)
9	P2	C28	1.819(3)
10	P2	C22	1.817(4)
11	N1	C3	1.379(4)
12	N1	C7	1.465(3)
13	N2	C3	1.359(3)
14	N2	C9	1.458(7)
15	N2	C6	1.539(7)
16	N3	C2	1.352(4)
17	N3	C5	1.465(5)
18	N3	C8	1.516(9)
19	N4	C2	1.374(4)
20	N4	C4	1.469(4)
21	N5	C34	1.132(5)
22	C16	C21	1.387(4)
23	C16	C17	1.379(5)
24	C25	H25	0.950(7)
25	C25	C24	1.366(9)
26	C25	C26	1.372(8)
27	C32	H32	0.950(4)
28	C32	C31	1.372(7)
29	C32	C33	1.378(7)
30	C31	H31	0.949(3)
31	C31	C30	1.399(5)
32	C18	H18	0.950(5)
33	C18	C19	1.374(6)

34	C18	C17	1.397(6)
35	C24	H24	0.950(5)
36	C24	C23	1.380(9)
37	C19	H19	0.950(5)
38	C19	C20	1.365(7)
39	C20	H20	0.950(4)
40	C20	C21	1.389(5)
41	C34	C35	1.468(9)
42	C33	H33	0.950(6)
43	C33	C29	1.393(6)
44	C26	H26	0.951(5)
45	C26	C27	1.405(9)
46	C35	H35A	0.981(8)
47	C35	H35B	0.980(9)
48	C35	H35C	0.98(1)
49	C28	C30	1.390(4)
50	C28	C29	1.393(5)
51	C15	H15	0.950(3)
52	C15	C10	1.396(5)
53	C15	C14	1.386(5)
54	C22	C27	1.379(5)
55	C22	C23	1.397(4)
56	C1	C2	1.398(4)
57	C1	C3	1.387(4)
58	C10	C11	1.394(4)
59	C11	H11	0.950(3)
60	C11	C12	1.384(5)
61	C30	H30	0.949(4)
62	C27	H27	0.950(4)
63	C23	H23	0.950(5)
64	C29	H29	0.950(3)
65	C13	H13	0.949(4)
66	C13	C12	1.389(5)
67	C13	C14	1.388(5)
68	C12	H12	0.949(3)
69	C14	H14	0.950(3)
70	C21	H21	0.950(5)
71	C4	H4A	0.991(3)
72	C4	H4B	0.990(4)
73	C4	C5	1.517(5)
74	C5	H5A	0.990(4)
75	C5	H5B	0.990(4)
76	C17	H17	0.950(3)

77	C7	H15A	0.989(3)
78	C7	H15B	0.991(4)
79	C7	C6	1.511(8)
80	C8	H1WA	0.99(1)
81	C8	H1WB	0.989(9)
82	C8	C9	1.58(1)
83	C9	H1XA	0.989(7)
84	C9	H1XB	0.990(5)
85	C6	H1YA	0.990(8)
86	C6	H1YB	0.988(6)
87	C45	H45	0.949(6)
88	C45	C46	1.39(1)
89	C45	C44	1.390(8)
90	C46	H46	0.950(6)
91	C46	C47	1.390(9)
92	C47	H47	0.950(3)
93	C47	C42	1.391(8)
94	C42	H42	0.949(5)
95	C42	C43	1.389(7)
96	C43	H43	0.951(5)
97	C43	C44	1.390(8)
98	C44	H44	0.950(4)
99	C40	H40	0.950(7)
100	C40	C39	1.402(9)
101	C40	C41	1.37(1)
102	C37	H37	0.950(7)
103	C37	C38	1.34(1)
104	C37	C36	1.379(8)
105	C39	H39	0.950(6)
106	C39	C38	1.31(1)
107	C41	H41	0.950(6)
108	C41	C36	1.294(9)
109	C38	H38	0.950(6)
110	C36	H36	0.951(6)
111	F1	B7	1.380(5)
112	F2	B7	1.355(7)
113	F3	B7	1.401(5)
114	F4	B7	1.339(9)

Table 4. Bond angles (º) for **^{Ph}CDC-Rh-MeCN**

Number	Atom 1	Atom 2	Atom 3	Angle

1	P1	Rh1	P2	165.13(3)
2	P1	Rh1	N5	94.44(8)
3	P1	Rh1	C1	82.49(8)
4	P2	Rh1	N5	100.42(8)
5	P2	Rh1	C1	82.65(8)
6	N5	Rh1	C1	176.9(1)
7	Rh1	P1	N4	103.4(1)
8	Rh1	P1	C16	117.4(1)
9	Rh1	P1	C10	120.4(1)
10	N4	P1	C16	103.9(1)
11	N4	P1	C10	106.4(1)
12	C16	P1	C10	103.7(1)
13	Rh1	P2	N1	102.69(9)
14	Rh1	P2	C28	119.3(1)
15	Rh1	P2	C22	121.7(1)
16	N1	P2	C28	103.1(1)
17	N1	P2	C22	104.2(1)
18	C28	P2	C22	103.2(1)
19	P2	N1	C3	116.6(2)
20	P2	N1	C7	131.8(2)
21	C3	N1	C7	111.5(2)
22	C3	N2	C9	122.9(3)
23	C3	N2	C6	108.9(3)
24	C9	N2	C6	113.8(4)
25	C2	N3	C5	111.7(3)
26	C2	N3	C8	122.7(4)
27	C5	N3	C8	120.1(4)
28	P1	N4	C2	116.3(2)
29	P1	N4	C4	131.1(2)
30	C2	N4	C4	111.5(3)
31	Rh1	N5	C34	172.4(3)
32	P1	C16	C21	119.3(3)
33	P1	C16	C17	120.5(2)
34	C21	C16	C17	119.5(3)
35	H25	C25	C24	119.6(6)
36	H25	C25	C26	119.7(6)
37	C24	C25	C26	120.7(5)
38	H32	C32	C31	119.6(4)
39	H32	C32	C33	119.7(5)
40	C31	C32	C33	120.7(4)
41	C32	C31	H31	120.3(4)
42	C32	C31	C30	119.2(3)
43	H31	C31	C30	120.4(3)

44	H18	C18	C19	119.9(5)
45	H18	C18	C17	119.9(5)
46	C19	C18	C17	120.2(4)
47	C25	C24	H24	120.0(6)
48	C25	C24	C23	119.9(5)
49	H24	C24	C23	120.0(5)
50	C18	C19	H19	120.1(5)
51	C18	C19	C20	119.7(5)
52	H19	C19	C20	120.2(5)
53	C19	C20	H20	119.5(5)
54	C19	C20	C21	121.0(4)
55	H20	C20	C21	119.5(4)
56	N5	C34	C35	178.1(6)
57	C32	C33	H33	119.8(5)
58	C32	C33	C29	120.4(4)
59	H33	C33	C29	119.9(5)
60	C25	C26	H26	120.0(6)
61	C25	C26	C27	120.0(5)
62	H26	C26	C27	120.0(5)
63	C34	C35	H35A	109.4(7)
64	C34	C35	H35B	109.6(7)
65	C34	C35	H35C	109.5(7)
66	H35A	C35	H35B	109.4(8)
67	H35A	C35	H35C	109.4(8)
68	H35B	C35	H35C	109.5(8)
69	P2	C28	C30	121.6(2)
70	P2	C28	C29	118.8(2)
71	C30	C28	C29	119.0(3)
72	H15	C15	C10	119.5(3)
73	H15	C15	C14	119.7(3)
74	C10	C15	C14	120.8(3)
75	P2	C22	C27	117.9(3)
76	P2	C22	C23	122.7(3)
77	C27	C22	C23	119.4(3)
78	Rh1	C1	C2	118.7(2)
79	Rh1	C1	C3	118.9(2)
80	C2	C1	C3	122.4(3)
81	P1	C10	C15	122.9(2)
82	P1	C10	C11	118.3(2)
83	C15	C10	C11	118.8(3)
84	C10	C11	H11	119.7(3)
85	C10	C11	C12	120.6(3)
86	H11	C11	C12	119.7(3)

87	C31	C30	C28	120.9(3)
88	C31	C30	H30	119.6(3)
89	C28	C30	H30	119.5(3)
90	N3	C2	N4	108.1(3)
91	N3	C2	C1	132.9(3)
92	N4	C2	C1	119.0(3)
93	C26	C27	C22	119.5(4)
94	C26	C27	H27	120.2(4)
95	C22	C27	H27	120.3(4)
96	C24	C23	C22	120.5(4)
97	C24	C23	H23	119.8(4)
98	C22	C23	H23	119.8(4)
99	C33	C29	C28	119.8(3)
100	C33	C29	H29	120.1(4)
101	C28	C29	H29	120.0(3)
102	N1	C3	N2	107.6(2)
103	N1	C3	C1	119.0(3)
104	N2	C3	C1	133.4(3)
105	H13	C13	C12	120.0(3)
106	H13	C13	C14	120.0(3)
107	C12	C13	C14	120.0(3)
108	C11	C12	C13	120.1(3)
109	C11	C12	H12	119.9(3)
110	C13	C12	H12	119.9(3)
111	C15	C14	C13	119.8(3)
112	C15	C14	H14	120.1(3)
113	C13	C14	H14	120.1(3)
114	C16	C21	C20	119.6(4)
115	C16	C21	H21	120.2(4)
116	C20	C21	H21	120.2(4)
117	N4	C4	H4A	111.3(3)
118	N4	C4	H4B	111.3(3)
119	N4	C4	C5	102.3(3)
120	H4A	C4	H4B	109.2(3)
121	H4A	C4	C5	111.3(3)
122	H4B	C4	C5	111.4(3)
123	N3	C5	C4	103.3(3)
124	N3	C5	H5A	111.1(3)
125	N3	C5	H5B	111.0(3)
126	C4	C5	H5A	111.1(3)
127	C4	C5	H5B	111.1(3)
128	H5A	C5	H5B	109.1(4)
129	C16	C17	C18	120.0(3)

130	C16	C17	H17	120.0(3)
131	C18	C17	H17	120.1(4)
132	N1	C7	H15A	111.2(3)
133	N1	C7	H15B	111.2(3)
134	N1	C7	C6	102.7(3)
135	H15A	C7	H15B	109.2(3)
136	H15A	C7	C6	111.3(4)
137	H15B	C7	C6	111.1(4)
138	N3	C8	H1WA	109.9(7)
139	N3	C8	H1WB	110.0(7)
140	N3	C8	C9	108.6(6)
141	H1WA	C8	H1WB	108.4(9)
142	H1WA	C8	C9	109.9(7)
143	H1WB	C8	C9	110.0(7)
144	N2	C9	C8	107.9(5)
145	N2	C9	H1XA	110.1(5)
146	N2	C9	H1XB	110.1(5)
147	C8	C9	H1XA	110.1(6)
148	C8	C9	H1XB	110.1(6)
149	H1XA	C9	H1XB	108.5(6)
150	N2	C6	C7	99.5(4)
151	N2	C6	H1YA	111.8(6)
152	N2	C6	H1YB	111.9(6)
153	C7	C6	H1YA	111.8(6)
154	C7	C6	H1YB	111.9(6)
155	H1YA	C6	H1YB	109.6(6)
156	H45	C45	C46	120.0(6)
157	H45	C45	C44	120.1(6)
158	C46	C45	C44	119.9(6)
159	C45	C46	H46	120.0(6)
160	C45	C46	C47	120.0(5)
161	H46	C46	C47	120.0(5)
162	C46	C47	H47	120.0(5)
163	C46	C47	C42	120.0(4)
164	H47	C47	C42	120.0(4)
165	C47	C42	H42	119.9(4)
166	C47	C42	C43	120.0(4)
167	H42	C42	C43	120.1(5)
168	C42	C43	H43	120.0(5)
169	C42	C43	C44	120.0(5)
170	H43	C43	C44	120.0(5)
171	C45	C44	C43	120.0(5)
172	C45	C44	H44	119.9(6)

173	C43	C44	H44	120.0(5)
174	H40	C40	C39	121.2(7)
175	H40	C40	C41	121.3(7)
176	C39	C40	C41	117.5(6)
177	H37	C37	C38	120.3(7)
178	H37	C37	C36	120.3(6)
179	C38	C37	C36	119.4(6)
180	C40	C39	H39	120.3(6)
181	C40	C39	C38	119.2(6)
182	H39	C39	C38	120.5(6)
183	C40	C41	H41	119.2(7)
184	C40	C41	C36	121.7(6)
185	H41	C41	C36	119.1(7)
186	C37	C38	C39	121.5(7)
187	C37	C38	H38	119.2(7)
188	C39	C38	H38	119.3(7)
189	C37	C36	C41	120.0(6)
190	C37	C36	H36	120.0(5)
191	C41	C36	H36	120.0(6)
192	F1	B7	F2	111.5(4)
193	F1	B7	F3	108.0(4)
194	F1	B7	F4	111.2(4)
195	F2	B7	F3	105.4(4)
196	F2	B7	F4	112.0(5)
197	F3	B7	F4	108.4(4)

Table 5. Torsion angles (°) for **^{Ph}CDC-Rh-MeCN**

Number	Atom 1	Atom 2	Atom 3	Atom 4	Torsion
1	P2	Rh1	P1	N4	-5.4(2)
2	P2	Rh1	P1	C16	-119.1(1)
3	P2	Rh1	P1	C10	113.0(2)
4	N5	Rh1	P1	N4	177.0(1)
5	N5	Rh1	P1	C16	63.3(1)
6	N5	Rh1	P1	C10	-64.6(1)
7	C1	Rh1	P1	N4	-3.4(1)
8	C1	Rh1	P1	C16	-117.1(1)
9	C1	Rh1	P1	C10	115.0(1)
10	P1	Rh1	P2	N1	-1.2(2)
11	P1	Rh1	P2	C28	-114.3(1)
12	P1	Rh1	P2	C22	114.7(2)
13	N5	Rh1	P2	N1	176.4(1)

14	N5	Rh1	P2	C28	63.3(1)
15	N5	Rh1	P2	C22	-67.7(1)
16	C1	Rh1	P2	N1	-3.2(1)
17	C1	Rh1	P2	C28	-116.3(1)
18	C1	Rh1	P2	C22	112.7(1)
19	P1	Rh1	N5	C34	10(3)
20	P2	Rh1	N5	C34	-169(3)
21	C1	Rh1	N5	C34	3(4)
22	P1	Rh1	C1	C2	2.3(2)
23	P1	Rh1	C1	C3	-177.1(2)
24	P2	Rh1	C1	C2	-178.3(2)
25	P2	Rh1	C1	C3	2.3(2)
26	N5	Rh1	C1	C2	9(2)
27	N5	Rh1	C1	C3	-170(2)
28	Rh1	P1	N4	C2	4.8(2)
29	Rh1	P1	N4	C4	172.0(3)
30	C16	P1	N4	C2	127.9(2)
31	C16	P1	N4	C4	-64.9(3)
32	C10	P1	N4	C2	-123.0(2)
33	C10	P1	N4	C4	44.2(3)
34	Rh1	P1	C16	C21	-88.7(3)
35	Rh1	P1	C16	C17	81.6(3)
36	N4	P1	C16	C21	157.9(3)
37	N4	P1	C16	C17	-31.8(3)
38	C10	P1	C16	C21	46.9(3)
39	C10	P1	C16	C17	-142.9(3)
40	Rh1	P1	C10	C15	174.7(2)
41	Rh1	P1	C10	C11	-4.3(3)
42	N4	P1	C10	C15	-68.4(3)
43	N4	P1	C10	C11	112.6(3)
44	C16	P1	C10	C15	40.8(3)
45	C16	P1	C10	C11	-138.2(3)
46	Rh1	P2	N1	C3	4.2(2)
47	Rh1	P2	N1	C7	179.6(3)
48	C28	P2	N1	C3	128.8(2)
49	C28	P2	N1	C7	-55.8(3)
50	C22	P2	N1	C3	-123.6(2)
51	C22	P2	N1	C7	51.8(3)
52	Rh1	P2	C28	C30	-103.8(3)
53	Rh1	P2	C28	C29	67.1(3)
54	N1	P2	C28	C30	143.2(3)
55	N1	P2	C28	C29	-45.9(3)
56	C22	P2	C28	C30	34.9(3)

57	C22	P2	C28	C29	-154.2(3)
58	Rh1	P2	C22	C27	-2.7(3)
59	Rh1	P2	C22	C23	179.1(2)
60	N1	P2	C22	C27	112.4(3)
61	N1	P2	C22	C23	-65.9(3)
62	C28	P2	C22	C27	-140.1(3)
63	C28	P2	C22	C23	41.6(3)
64	P2	N1	C3	N2	177.4(2)
65	P2	N1	C3	C1	-3.0(4)
66	C7	N1	C3	N2	1.1(3)
67	C7	N1	C3	C1	-179.3(3)
68	P2	N1	C7	H15A	45.0(4)
69	P2	N1	C7	H15B	-76.9(4)
70	P2	N1	C7	C6	164.2(3)
71	C3	N1	C7	H15A	-139.4(3)
72	C3	N1	C7	H15B	98.6(3)
73	C3	N1	C7	C6	-20.3(4)
74	C9	N2	C3	N1	155.7(4)
75	C9	N2	C3	C1	-23.9(6)
76	C6	N2	C3	N1	18.8(4)
77	C6	N2	C3	C1	-160.8(4)
78	C3	N2	C9	C8	64.4(6)
79	C3	N2	C9	H1XA	-55.7(6)
80	C3	N2	C9	H1XB	-175.3(4)
81	C6	N2	C9	C8	-160.5(5)
82	C6	N2	C9	H1XA	79.3(6)
83	C6	N2	C9	H1XB	-40.3(7)
84	C3	N2	C6	C7	-30.0(5)
85	C3	N2	C6	H1YA	88.2(6)
86	C3	N2	C6	H1YB	-148.4(5)
87	C9	N2	C6	C7	-171.2(4)
88	C9	N2	C6	H1YA	-53.0(7)
89	C9	N2	C6	H1YB	70.4(7)
90	C5	N3	C2	N4	6.2(4)
91	C5	N3	C2	C1	-174.8(3)
92	C8	N3	C2	N4	160.0(5)
93	C8	N3	C2	C1	-21.0(7)
94	C2	N3	C5	C4	-15.0(4)
95	C2	N3	C5	H5A	-134.2(3)
96	C2	N3	C5	H5B	104.2(4)
97	C8	N3	C5	C4	-169.5(5)
98	C8	N3	C5	H5A	71.3(6)
99	C8	N3	C5	H5B	-50.4(6)

100	C2	N3	C8	H1WA	-59.7(9)
101	C2	N3	C8	H1WB	-178.9(5)
102	C2	N3	C8	C9	60.6(7)
103	C5	N3	C8	H1WA	92.0(8)
104	C5	N3	C8	H1WB	-27.2(9)
105	C5	N3	C8	C9	-147.7(5)
106	P1	N4	C2	N3	175.5(2)
107	P1	N4	C2	C1	-3.6(4)
108	C4	N4	C2	N3	5.9(3)
109	C4	N4	C2	C1	-173.3(3)
110	P1	N4	C4	H4A	58.7(4)
111	P1	N4	C4	H4B	-63.3(4)
112	P1	N4	C4	C5	177.7(2)
113	C2	N4	C4	H4A	-133.6(3)
114	C2	N4	C4	H4B	104.4(3)
115	C2	N4	C4	C5	-14.6(3)
116	Rh1	N5	C34	C35	24(19)
117	P1	C16	C21	C20	168.6(3)
118	P1	C16	C21	H21	-11.5(5)
119	C17	C16	C21	C20	-1.8(6)
120	C17	C16	C21	H21	178.2(4)
121	P1	C16	C17	C18	-169.2(3)
122	P1	C16	C17	H17	10.8(5)
123	C21	C16	C17	C18	1.1(5)
124	C21	C16	C17	H17	-179.0(3)
125	H25	C25	C24	H24	-0.1(9)
126	H25	C25	C24	C23	179.9(5)
127	C26	C25	C24	H24	180.0(6)
128	C26	C25	C24	C23	-0.0(9)
129	H25	C25	C26	H26	1.0(9)
130	H25	C25	C26	C27	-179.1(5)
131	C24	C25	C26	H26	-179.1(6)
132	C24	C25	C26	C27	0.9(8)
133	H32	C32	C31	H31	0.1(7)
134	H32	C32	C31	C30	-179.9(4)
135	C33	C32	C31	H31	-179.9(4)
136	C33	C32	C31	C30	0.1(6)
137	H32	C32	C33	H33	-0.8(8)
138	H32	C32	C33	C29	179.4(4)
139	C31	C32	C33	H33	179.2(5)
140	C31	C32	C33	C29	-0.7(7)
141	C32	C31	C30	C28	0.0(5)
142	C32	C31	C30	H30	180.0(4)

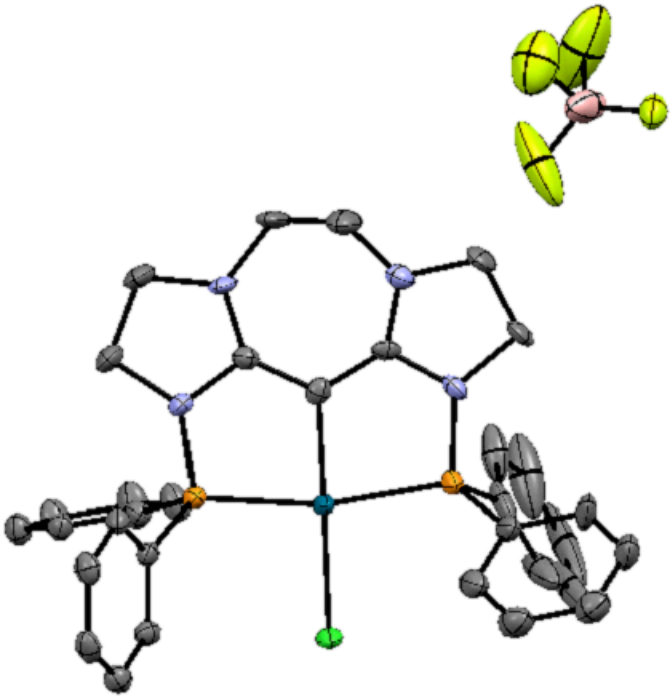
143	H31	C31	C30	C28	-179.9(3)
144	H31	C31	C30	H30	-0.0(6)
145	H18	C18	C19	H19	-2.4(9)
146	H18	C18	C19	C20	177.6(5)
147	C17	C18	C19	H19	177.7(5)
148	C17	C18	C19	C20	-2.3(7)
149	H18	C18	C17	C16	-178.9(4)
150	H18	C18	C17	H17	1.2(7)
151	C19	C18	C17	C16	1.0(7)
152	C19	C18	C17	H17	-179.0(4)
153	C25	C24	C23	C22	-0.3(7)
154	C25	C24	C23	H23	179.7(5)
155	H24	C24	C23	C22	179.7(5)
156	H24	C24	C23	H23	-0.3(8)
157	C18	C19	C20	H20	-178.3(5)
158	C18	C19	C20	C21	1.6(7)
159	H19	C19	C20	H20	1.7(8)
160	H19	C19	C20	C21	-178.4(5)
161	C19	C20	C21	C16	0.4(7)
162	C19	C20	C21	H21	-179.5(4)
163	H20	C20	C21	C16	-179.7(4)
164	H20	C20	C21	H21	0.4(7)
165	N5	C34	C35	H35A	-72(18)
166	N5	C34	C35	H35B	168(17)
167	N5	C34	C35	H35C	48(18)
168	C32	C33	C29	C28	1.0(6)
169	C32	C33	C29	H29	-179.0(4)
170	H33	C33	C29	C28	-178.8(4)
171	H33	C33	C29	H29	1.1(7)
172	C25	C26	C27	C22	-1.4(7)
173	C25	C26	C27	H27	178.6(5)
174	H26	C26	C27	C22	178.6(5)
175	H26	C26	C27	H27	-1.4(8)
176	P2	C28	C30	C31	171.2(3)
177	P2	C28	C30	H30	-8.7(5)
178	C29	C28	C30	C31	0.3(5)
179	C29	C28	C30	H30	-179.6(3)
180	P2	C28	C29	C33	-172.0(3)
181	P2	C28	C29	H29	8.0(5)
182	C30	C28	C29	C33	-0.8(5)
183	C30	C28	C29	H29	179.2(3)
184	H15	C15	C10	P1	0.3(5)
185	H15	C15	C10	C11	179.3(3)

186	C14	C15	C10	P1	-179.6(3)
187	C14	C15	C10	C11	-0.5(5)
188	H15	C15	C14	C13	-178.8(3)
189	H15	C15	C14	H14	1.2(6)
190	C10	C15	C14	C13	1.1(5)
191	C10	C15	C14	H14	-179.0(3)
192	P2	C22	C27	C26	-177.3(3)
193	P2	C22	C27	H27	2.7(5)
194	C23	C22	C27	C26	1.1(6)
195	C23	C22	C27	H27	-179.0(4)
196	P2	C22	C23	C24	178.0(4)
197	P2	C22	C23	H23	-2.0(5)
198	C27	C22	C23	C24	-0.2(6)
199	C27	C22	C23	H23	179.8(4)
200	Rh1	C1	C2	N3	-178.7(3)
201	Rh1	C1	C2	N4	0.2(4)
202	C3	C1	C2	N3	0.7(5)
203	C3	C1	C2	N4	179.6(3)
204	Rh1	C1	C3	N1	-0.3(4)
205	Rh1	C1	C3	N2	179.3(3)
206	C2	C1	C3	N1	-179.6(3)
207	C2	C1	C3	N2	-0.1(5)
208	P1	C10	C11	H11	-1.0(5)
209	P1	C10	C11	C12	179.0(3)
210	C15	C10	C11	H11	179.9(3)
211	C15	C10	C11	C12	-0.1(5)
212	C10	C11	C12	C13	0.1(5)
213	C10	C11	C12	H12	-179.8(3)
214	H11	C11	C12	C13	-179.9(3)
215	H11	C11	C12	H12	0.2(6)
216	H13	C13	C12	C11	-179.5(3)
217	H13	C13	C12	H12	0.3(6)
218	C14	C13	C12	C11	0.4(5)
219	C14	C13	C12	H12	-179.7(3)
220	H13	C13	C14	C15	178.9(3)
221	H13	C13	C14	H14	-1.0(6)
222	C12	C13	C14	C15	-1.0(5)
223	C12	C13	C14	H14	179.0(3)
224	N4	C4	C5	N3	16.8(3)
225	N4	C4	C5	H5A	136.0(3)
226	N4	C4	C5	H5B	-102.3(4)
227	H4A	C4	C5	N3	135.8(3)
228	H4A	C4	C5	H5A	-105.0(4)

229	H4A	C4	C5	H5B	16.6(5)
230	H4B	C4	C5	N3	-102.1(3)
231	H4B	C4	C5	H5A	17.0(5)
232	H4B	C4	C5	H5B	138.7(3)
233	N1	C7	C6	N2	28.3(4)
234	N1	C7	C6	H1YA	-90.0(6)
235	N1	C7	C6	H1YB	146.7(5)
236	H15A	C7	C6	N2	147.4(3)
237	H15A	C7	C6	H1YA	29.1(7)
238	H15A	C7	C6	H1YB	-94.2(6)
239	H15B	C7	C6	N2	-90.7(4)
240	H15B	C7	C6	H1YA	151.0(5)
241	H15B	C7	C6	H1YB	27.7(7)
242	N3	C8	C9	N2	-81.5(6)
243	N3	C8	C9	H1XA	38.7(8)
244	N3	C8	C9	H1XB	158.2(6)
245	H1WA	C8	C9	N2	38.8(9)
246	H1WA	C8	C9	H1XA	159.0(7)
247	H1WA	C8	C9	H1XB	-81.5(9)
248	H1WB	C8	C9	N2	158.1(6)
249	H1WB	C8	C9	H1XA	-81.7(9)
250	H1WB	C8	C9	H1XB	38(1)
251	H45	C45	C46	H46	0(1)
252	H45	C45	C46	C47	-180.0(6)
253	C44	C45	C46	H46	-180.0(6)
254	C44	C45	C46	C47	-0.2(9)
255	H45	C45	C44	C43	179.9(6)
256	H45	C45	C44	H44	-0(1)
257	C46	C45	C44	C43	0.1(9)
258	C46	C45	C44	H44	-179.9(6)
259	C45	C46	C47	H47	180.0(5)
260	C45	C46	C47	C42	0.1(8)
261	H46	C46	C47	H47	-0.2(9)
262	H46	C46	C47	C42	180.0(5)
263	C46	C47	C42	H42	179.9(5)
264	C46	C47	C42	C43	-0.0(7)
265	H47	C47	C42	H42	0.1(8)
266	H47	C47	C42	C43	-179.9(5)
267	C47	C42	C43	H43	-179.9(5)
268	C47	C42	C43	C44	-0.0(7)
269	H42	C42	C43	H43	0.2(8)
270	H42	C42	C43	C44	-179.9(5)
271	C42	C43	C44	C45	0.0(8)

272	C42	C43	C44	H44	-180.0(5)
273	H43	C43	C44	C45	179.9(5)
274	H43	C43	C44	H44	-0.1(9)
275	H40	C40	C39	H39	-10(1)
276	H40	C40	C39	C38	170.3(7)
277	C41	C40	C39	H39	170.3(6)
278	C41	C40	C39	C38	-10(1)
279	H40	C40	C41	H41	6(1)
280	H40	C40	C41	C36	-173.6(7)
281	C39	C40	C41	H41	-173.7(6)
282	C39	C40	C41	C36	6(1)
283	H37	C37	C38	C39	176.7(7)
284	H37	C37	C38	H38	-3(1)
285	C36	C37	C38	C39	-3(1)
286	C36	C37	C38	H38	176.7(6)
287	H37	C37	C36	C41	179.6(6)
288	H37	C37	C36	H36	-0(1)
289	C38	C37	C36	C41	-0(1)
290	C38	C37	C36	H36	179.8(6)
291	C40	C39	C38	C37	8(1)
292	C40	C39	C38	H38	-171.8(6)
293	H39	C39	C38	C37	-171.6(7)
294	H39	C39	C38	H38	8(1)
295	C40	C41	C36	C37	-2(1)
296	C40	C41	C36	H36	178.6(6)
297	H41	C41	C36	C37	178.5(6)
298	H41	C41	C36	H36	-1(1)

Crystal Structure Data for ^{Ph}CDC-Pd-Cl



Identification code	phcdcpdcl_2_0m
Empirical formula	C35 H33.78 B Cl7 F4.50 N4 P2 Pd
Formula weight	1023.24
Temperature	100 K
Wavelength	1.54178
Crystal system	triclinic
Space group	P -1
Unit cell dimensions	a = 10.4744(2) Å α= 110.1005(11)
	b = 18.9611(4) Å β= 94.9400(12)
	c = 22.0214(4) Å γ = 93.4040(12)
Volume	4073.4
Z	4
Density (calculated)	1.669 Mg/m3
Absorption coefficient	9.111 (mm-1)
Theta range for data collection	66.754-2.493
Reflections collected	14098
Independent reflections	11759
Max. and min. transmission	0.7437, 0.2931
Refinement method	XS least squares
Goodness-of-fit on F2 0	1.296

Table of Bond Lengths for ^{Ph}**CDC-Pd-Cl**

Number	Atom1	Atom2	Bond Length
1	Pd1	P1	2.274(1)
2	Pd1	P2	2.271(1)
3	Pd1	Cl1	2.375(1)
4	Pd1	C1	2.027(4)
5	P1	N1	1.703(4)
6	P1	C22	1.810(5)
7	P1	C10	1.799(6)
8	P2	N4	1.690(4)
9	P2	C28	1.814(6)
10	P2	C16	1.805(5)
11	C1	C2	1.403(6)
12	C1	C3	1.399(6)
13	N1	C2	1.380(5)
14	N1	C4	1.473(7)
15	N4	C9	1.464(5)
16	N4	C3	1.372(6)
17	C22	C27	1.403(8)
18	C22	C23	1.400(7)
19	C28	C29	1.394(8)
20	C28	C33	1.383(7)
21	N2	C2	1.334(6)
22	N2	C6	1.475(7)
23	N2	C5	1.474(6)
24	C27	H27	0.949(5)
25	C27	C26	1.378(9)
26	C9	H9A	0.991(6)
27	C9	H9B	0.990(6)
28	C9	C8	1.523(7)
29	C3	N3	1.352(5)
30	C32	H32	0.951(6)
31	C32	C33	1.384(9)
32	C32	C31	1.394(8)
33	C4	H4A	0.989(5)
34	C4	H4B	0.991(7)
35	C4	C5	1.519(8)
36	C16	C21	1.389(8)
37	C16	C17	1.389(6)
38	N3	C8	1.463(6)
39	N3	C7	1.476(7)
40	C8	H8A	0.989(5)

41	C8	H8B	0.990(6)
42	C10	C15	1.377(7)
43	C10	C11	1.393(9)
44	C29	H29	0.951(5)
45	C29	C30	1.400(8)
46	C33	H33	0.950(6)
47	C30	H30	0.950(6)
48	C30	C31	1.374(7)
49	C31	H31	0.950(6)
50	C18	H18	0.951(4)
51	C18	C17	1.393(8)
52	C18	C19	1.376(8)
53	C26	H26	0.951(6)
54	C26	C25	1.392(8)
55	C21	H21	0.949(5)
56	C21	C20	1.39(1)
57	C7	H7A	0.991(7)
58	C7	H7B	0.990(5)
59	C7	C6	1.483(7)
60	C15	H15	0.952(7)
61	C15	C14	1.377(8)
62	C25	H25	0.950(7)
63	C25	C24	1.380(9)
64	C6	H6A	0.991(7)
65	C6	H6B	0.989(5)
66	C23	H23	0.950(6)
67	C23	C24	1.379(9)
68	C13	H13	0.949(6)
69	C13	C14	1.37(1)
70	C13	C12	1.371(9)
71	C17	H17	0.951(6)
72	C19	H19	0.952(7)
73	C19	C20	1.395(8)
74	C5	H5A	0.990(6)
75	C5	H5B	0.989(7)
76	C24	H24	0.951(6)
77	C14	H14	0.950(6)
78	C20	H20	0.951(6)
79	C12	H12	0.949(7)
80	C12	C11	1.388(8)
81	C11	H11	0.950(5)
82	Pd2	P3	2.262(1)
83	Pd2	Cl2	2.362(1)

84	Pd2	P4	2.272(1)
85	Pd2	C34	2.009(5)
86	P3	N5	1.679(4)
87	P3	C43	1.788(6)
88	P3	C49	1.799(5)
89	P4	N8	1.680(4)
90	P4	C55	1.804(7)
91	P4	C61	1.799(7)
92	C34	C36	1.388(6)
93	C34	C35	1.407(7)
94	N5	C35	1.387(5)
95	N5	C37	1.476(7)
96	N8	C42	1.487(5)
97	N8	C36	1.381(6)
98	C42	H42A	0.989(6)
99	C42	H42B	0.990(5)
100	C42	C41	1.522(8)
101	C36	N7	1.341(5)
102	N7	C41	1.456(5)
103	N7	C40	1.444(7)
104	N6	C35	1.336(6)
105	N6	C38	1.442(7)
106	N6	C39	1.463(6)
107	C44	H44	0.949(6)
108	C44	C43	1.392(6)
109	C44	C45	1.380(8)
110	C43	C48	1.403(8)
111	C45	H45	0.951(5)
112	C45	C46	1.383(8)
113	C48	H48	0.951(5)
114	C48	C47	1.395(8)
115	C49	C54	1.390(6)
116	C49	C50	1.393(9)
117	C37	H37A	0.989(6)
118	C37	H37B	0.989(7)
119	C37	C38	1.519(7)
120	C46	H46	0.950(6)
121	C46	C47	1.378(7)
122	C38	H38A	0.991(7)
123	C38	H38B	0.990(6)
124	C54	H54	0.950(6)
125	C54	C53	1.394(7)
126	C51	H51	0.949(6)

127	C51	C50	1.39(1)
128	C51	C52	1.384(7)
129	C53	H53	0.951(4)
130	C53	C52	1.369(9)
131	C41	H41A	0.990(5)
132	C41	H41B	0.990(6)
133	C55	C60	1.402(8)
134	C55	C56	1.390(8)
135	C60	H60	0.950(6)
136	C60	C59	1.38(1)
137	C47	H47	0.950(6)
138	C50	H50	0.950(5)
139	C61	C66	1.39(1)
140	C61	C62	1.39(1)
141	C52	H52	0.949(7)
142	C40	H40A	0.990(5)
143	C40	H40B	0.991(8)
144	C40	C39	1.476(9)
145	C39	H39A	0.990(6)
146	C39	H39B	0.990(8)
147	C56	H56	0.948(5)
148	C56	C57	1.383(9)
149	C66	H66	0.950(8)
150	C66	C1B	1.41(1)
151	C59	H59	0.950(5)
152	C59	C58	1.384(8)
153	C62	H62	0.951(9)
154	C62	C1A	1.40(1)
155	C57	H57	0.950(5)
156	C57	C58	1.379(7)
157	C58	H58	0.952(7)
158	C1A	H1A	0.95(1)
159	C1A	C1C	1.31(2)
160	C1B	H1B	0.95(1)
161	C1B	C1C	1.39(2)
162	C1C	H1C	0.95(1)
163	C67	H67	1.001(5)
164	C67	Cl12	1.764(6)
165	C67	Cl14	1.760(6)
166	C67	Cl13	1.759(6)
167	Cl5	C69	1.789(9)
168	Cl4	C69	1.71(1)
169	C69	H69	1.000(7)

170	C69	Cl6	1.745(9)
171	F2F	B1	1.376(9)
172	F14	B1	1.356(9)
173	F2	B1	1.36(1)
174	F3	B1	1.36(1)
175	Cl8	C70	1.762(8)
176	Cl7	C70	1.739(8)
177	C70	H70	1.000(6)
178	C70	Cl9	1.759(7)
179	Cl10	C68	1.71(1)
180	Cl11	C68	1.83(1)
181	Cl15	C68	1.77(1)
182	C68	H68	1.000(9)
183	F4	B2	1.30(1)
184	F1	B2	1.340(9)
185	F5	B2	1.56(1)
186	F6	B2	1.35(1)
187	B2	F7	1.72(2)

Table of Bond Angles for ^{Ph}**CDC-Pd-Cl**

Number	Atom1	Atom2	Atom3	Angle
1	P1	Pd1	P2	166.70(5)
2	P1	Pd1	Cl1	97.73(5)
3	P1	Pd1	C1	83.4(1)
4	P2	Pd1	Cl1	95.51(4)
5	P2	Pd1	C1	83.4(1)
6	Cl1	Pd1	C1	178.8(1)
7	Pd1	P1	N1	101.5(2)
8	Pd1	P1	C22	118.6(2)
9	Pd1	P1	C10	117.6(2)
10	N1	P1	C22	106.1(2)
11	N1	P1	C10	107.0(2)
12	C22	P1	C10	104.9(2)
13	Pd1	P2	N4	101.2(1)
14	Pd1	P2	C28	121.3(2)
15	Pd1	P2	C16	117.3(2)
16	N4	P2	C28	104.7(2)
17	N4	P2	C16	106.2(2)

18	C28	P2	C16	104.5(2)
19	Pd1	C1	C2	118.2(3)
20	Pd1	C1	C3	117.5(3)
21	C2	C1	C3	124.3(4)
22	P1	N1	C2	117.1(3)
23	P1	N1	C4	130.4(4)
24	C2	N1	C4	110.9(4)
25	P2	N4	C9	130.0(3)
26	P2	N4	C3	117.2(3)
27	C9	N4	C3	110.6(4)
28	P1	C22	C27	119.0(4)
29	P1	C22	C23	121.4(4)
30	C27	C22	C23	119.6(5)
31	P2	C28	C29	120.7(4)
32	P2	C28	C33	119.0(4)
33	C29	C28	C33	120.0(5)
34	C2	N2	C6	124.2(4)
35	C2	N2	C5	111.2(4)
36	C6	N2	C5	119.9(4)
37	C22	C27	H27	120.3(5)
38	C22	C27	C26	119.6(5)
39	H27	C27	C26	120.1(5)
40	N4	C9	H9A	111.2(4)
41	N4	C9	H9B	111.4(4)
42	N4	C9	C8	102.2(4)
43	H9A	C9	H9B	109.3(5)
44	H9A	C9	C8	111.3(4)
45	H9B	C9	C8	111.4(5)
46	C1	C2	N1	119.6(4)
47	C1	C2	N2	131.4(4)
48	N1	C2	N2	109.0(4)
49	C1	C3	N4	120.1(4)
50	C1	C3	N3	131.7(4)
51	N4	C3	N3	108.2(4)
52	H32	C32	C33	120.8(6)
53	H32	C32	C31	120.7(6)
54	C33	C32	C31	118.5(5)
55	N1	C4	H4A	111.4(5)
56	N1	C4	H4B	111.4(5)
57	N1	C4	C5	101.8(4)
58	H4A	C4	H4B	109.3(6)
59	H4A	C4	C5	111.4(5)
60	H4B	C4	C5	111.4(5)

61	P2	C16	C21	119.4(4)
62	P2	C16	C17	121.4(4)
63	C21	C16	C17	119.2(5)
64	C3	N3	C8	111.5(4)
65	C3	N3	C7	123.9(4)
66	C8	N3	C7	117.4(4)
67	C9	C8	N3	101.8(4)
68	C9	C8	H8A	111.5(5)
69	C9	C8	H8B	111.4(5)
70	N3	C8	H8A	111.4(4)
71	N3	C8	H8B	111.4(4)
72	H8A	C8	H8B	109.2(5)
73	P1	C10	C15	117.7(4)
74	P1	C10	C11	124.1(4)
75	C15	C10	C11	118.0(5)
76	C28	C29	H29	120.6(5)
77	C28	C29	C30	118.7(5)
78	H29	C29	C30	120.7(5)
79	C28	C33	C32	121.3(5)
80	C28	C33	H33	119.3(6)
81	C32	C33	H33	119.4(6)
82	C29	C30	H30	119.8(5)
83	C29	C30	C31	120.5(5)
84	H30	C30	C31	119.7(5)
85	C32	C31	C30	120.9(5)
86	C32	C31	H31	119.5(5)
87	C30	C31	H31	119.5(5)
88	H18	C18	C17	120.4(5)
89	H18	C18	C19	120.4(5)
90	C17	C18	C19	119.2(5)
91	C27	C26	H26	119.8(6)
92	C27	C26	C25	120.4(5)
93	H26	C26	C25	119.8(6)
94	C16	C21	H21	119.9(6)
95	C16	C21	C20	120.2(5)
96	H21	C21	C20	119.9(6)
97	N3	C7	H7A	109.2(5)
98	N3	C7	H7B	109.2(5)
99	N3	C7	C6	112.1(5)
100	H7A	C7	H7B	107.9(5)
101	H7A	C7	C6	109.2(5)
102	H7B	C7	C6	109.2(5)
103	C10	C15	H15	119.2(6)

104	C10	C15	C14	121.5(6)
105	H15	C15	C14	119.3(6)
106	C26	C25	H25	120.0(6)
107	C26	C25	C24	120.0(5)
108	H25	C25	C24	120.0(6)
109	N2	C6	C7	114.9(5)
110	N2	C6	H6A	108.5(5)
111	N2	C6	H6B	108.6(5)
112	C7	C6	H6A	108.5(5)
113	C7	C6	H6B	108.5(5)
114	H6A	C6	H6B	107.6(5)
115	C22	C23	H23	120.0(5)
116	C22	C23	C24	119.9(5)
117	H23	C23	C24	120.0(5)
118	H13	C13	C14	120.0(6)
119	H13	C13	C12	120.0(6)
120	C14	C13	C12	120.0(6)
121	C16	C17	C18	121.0(5)
122	C16	C17	H17	119.4(5)
123	C18	C17	H17	119.6(5)
124	C18	C19	H19	119.8(6)
125	C18	C19	C20	120.5(6)
126	H19	C19	C20	119.7(6)
127	N2	C5	C4	103.4(4)
128	N2	C5	H5A	111.1(5)
129	N2	C5	H5B	111.1(5)
130	C4	C5	H5A	111.0(5)
131	C4	C5	H5B	111.1(5)
132	H5A	C5	H5B	109.1(6)
133	C25	C24	C23	120.4(6)
134	C25	C24	H24	119.7(6)
135	C23	C24	H24	119.9(6)
136	C15	C14	C13	119.9(6)
137	C15	C14	H14	120.1(6)
138	C13	C14	H14	120.0(6)
139	C21	C20	C19	119.9(6)
140	C21	C20	H20	120.0(6)
141	C19	C20	H20	120.2(6)
142	C13	C12	H12	119.9(7)
143	C13	C12	C11	120.0(6)
144	H12	C12	C11	120.1(7)
145	C10	C11	C12	120.5(5)
146	C10	C11	H11	119.7(6)

147	C12	C11	H11	119.8(6)
148	P3	Pd2	Cl2	96.03(5)
149	P3	Pd2	P4	166.89(5)
150	P3	Pd2	C34	83.5(1)
151	Cl2	Pd2	P4	97.05(5)
152	Cl2	Pd2	C34	178.4(2)
153	P4	Pd2	C34	83.4(1)
154	Pd2	P3	N5	102.0(1)
155	Pd2	P3	C43	118.1(2)
156	Pd2	P3	C49	117.5(2)
157	N5	P3	C43	107.5(2)
158	N5	P3	C49	104.0(2)
159	C43	P3	C49	106.2(2)
160	Pd2	P4	N8	101.2(2)
161	Pd2	P4	C55	116.8(2)
162	Pd2	P4	C61	118.2(2)
163	N8	P4	C55	108.5(2)
164	N8	P4	C61	106.8(3)
165	C55	P4	C61	104.7(3)
166	Pd2	C34	C36	118.4(4)
167	Pd2	C34	C35	117.9(4)
168	C36	C34	C35	123.7(5)
169	P3	N5	C35	116.6(3)
170	P3	N5	C37	130.6(4)
171	C35	N5	C37	110.6(4)
172	P4	N8	C42	131.2(3)
173	P4	N8	C36	117.4(3)
174	C42	N8	C36	111.2(4)
175	N8	C42	H42A	111.3(4)
176	N8	C42	H42B	111.3(4)
177	N8	C42	C41	102.3(4)
178	H42A	C42	H42B	109.1(5)
179	H42A	C42	C41	111.3(5)
180	H42B	C42	C41	111.3(5)
181	C34	C36	N8	119.5(4)
182	C34	C36	N7	131.4(5)
183	N8	C36	N7	109.1(4)
184	C36	N7	C41	112.2(4)
185	C36	N7	C40	125.5(4)
186	C41	N7	C40	121.8(4)
187	C35	N6	C38	112.8(4)
188	C35	N6	C39	124.2(4)
189	C38	N6	C39	121.8(4)

190	C34	C35	N5	119.4(4)
191	C34	C35	N6	131.7(5)
192	N5	C35	N6	108.8(4)
193	H44	C44	C43	119.3(5)
194	H44	C44	C45	119.2(5)
195	C43	C44	C45	121.5(4)
196	P3	C43	C44	118.4(4)
197	P3	C43	C48	123.0(4)
198	C44	C43	C48	118.4(4)
199	C44	C45	H45	120.1(5)
200	C44	C45	C46	119.9(5)
201	H45	C45	C46	120.0(5)
202	C43	C48	H48	120.2(5)
203	C43	C48	C47	119.6(5)
204	H48	C48	C47	120.2(5)
205	P3	C49	C54	122.4(4)
206	P3	C49	C50	118.0(4)
207	C54	C49	C50	119.3(5)
208	N5	C37	H37A	111.1(5)
209	N5	C37	H37B	111.1(5)
210	N5	C37	C38	103.0(4)
211	H37A	C37	H37B	109.2(6)
212	H37A	C37	C38	111.1(5)
213	H37B	C37	C38	111.2(5)
214	C45	C46	H46	120.1(5)
215	C45	C46	C47	119.8(5)
216	H46	C46	C47	120.1(5)
217	N6	C38	C37	104.6(5)
218	N6	C38	H38A	110.8(5)
219	N6	C38	H38B	110.9(5)
220	C37	C38	H38A	110.8(5)
221	C37	C38	H38B	110.8(5)
222	H38A	C38	H38B	108.9(6)
223	C49	C54	H54	119.8(5)
224	C49	C54	C53	120.2(5)
225	H54	C54	C53	120.0(5)
226	H51	C51	C50	120.1(6)
227	H51	C51	C52	120.1(6)
228	C50	C51	C52	119.8(6)
229	C54	C53	H53	120.2(5)
230	C54	C53	C52	119.9(5)
231	H53	C53	C52	120.0(5)
232	C42	C41	N7	105.0(4)

233	C42	C41	H41A	110.8(4)
234	C42	C41	H41B	110.7(4)
235	N7	C41	H41A	110.8(4)
236	N7	C41	H41B	110.7(4)
237	H41A	C41	H41B	108.9(5)
238	P4	C55	C60	122.2(5)
239	P4	C55	C56	118.7(4)
240	C60	C55	C56	119.0(5)
241	C55	C60	H60	120.2(6)
242	C55	C60	C59	119.7(6)
243	H60	C60	C59	120.1(6)
244	C48	C47	C46	120.8(5)
245	C48	C47	H47	119.6(5)
246	C46	C47	H47	119.5(5)
247	C49	C50	C51	120.2(5)
248	C49	C50	H50	119.9(6)
249	C51	C50	H50	119.9(6)
250	P4	C61	C66	120.0(5)
251	P4	C61	C62	119.9(5)
252	C66	C61	C62	119.6(6)
253	C51	C52	C53	120.7(5)
254	C51	C52	H52	119.7(6)
255	C53	C52	H52	119.6(6)
256	N7	C40	H40A	108.7(5)
257	N7	C40	H40B	108.7(5)
258	N7	C40	C39	114.1(5)
259	H40A	C40	H40B	107.5(6)
260	H40A	C40	C39	108.8(6)
261	H40B	C40	C39	108.8(6)
262	N6	C39	C40	113.9(5)
263	N6	C39	H39A	108.8(5)
264	N6	C39	H39B	108.8(5)
265	C40	C39	H39A	108.8(6)
266	C40	C39	H39B	108.8(6)
267	H39A	C39	H39B	107.7(6)
268	C55	C56	H56	119.7(6)
269	C55	C56	C57	120.6(5)
270	H56	C56	C57	119.7(6)
271	C61	C66	H66	120.5(7)
272	C61	C66	C1B	118.9(7)
273	H66	C66	C1B	120.6(8)
274	C60	C59	H59	119.5(6)
275	C60	C59	C58	121.0(6)

276	H59	C59	C58	119.5(6)
277	C61	C62	H62	121.0(7)
278	C61	C62	C1A	117.8(8)
279	H62	C62	C1A	121.2(8)
280	C56	C57	H57	119.7(6)
281	C56	C57	C58	120.4(5)
282	H57	C57	C58	119.8(6)
283	C59	C58	C57	119.4(5)
284	C59	C58	H58	120.3(6)
285	C57	C58	H58	120.3(6)
286	C62	C1A	H1A	118(1)
287	C62	C1A	C1C	125(1)
288	H1A	C1A	C1C	118(1)
289	C66	C1B	H1B	119(1)
290	C66	C1B	C1C	121(1)
291	H1B	C1B	C1C	119(1)
292	C1A	C1C	C1B	118(1)
293	C1A	C1C	H1C	121(1)
294	C1B	C1C	H1C	121(1)
295	H67	C67	Cl12	108.6(4)
296	H67	C67	Cl14	108.5(4)
297	H67	C67	Cl13	108.6(4)
298	Cl12	C67	Cl14	110.0(3)
299	Cl12	C67	Cl13	110.4(3)
300	Cl14	C67	Cl13	110.7(3)
301	Cl5	C69	Cl4	109.0(5)
302	Cl5	C69	H69	108.0(6)
303	Cl5	C69	Cl6	110.4(5)
304	Cl4	C69	H69	108.1(7)
305	Cl4	C69	Cl6	113.1(5)
306	H69	C69	Cl6	108.0(6)
307	F2F	B1	F14	107.7(6)
308	F2F	B1	F2	108.0(7)
309	F2F	B1	F3	111.1(7)
310	F14	B1	F2	112.6(6)
311	F14	B1	F3	108.4(7)
312	F2	B1	F3	109.2(7)
313	Cl8	C70	Cl7	109.6(4)
314	Cl8	C70	H70	108.7(5)
315	Cl8	C70	Cl9	110.3(4)
316	Cl7	C70	H70	108.7(5)
317	Cl7	C70	Cl9	110.7(4)
318	H70	C70	Cl9	108.7(5)

319	Cl10	C68	Cl11	107.7(6)
320	Cl10	C68	Cl15	115.1(6)
321	Cl10	C68	H68	109.0(8)
322	Cl11	C68	Cl15	107.0(6)
323	Cl11	C68	H68	109.0(8)
324	Cl15	C68	H68	108.9(8)
325	F4	B2	F1	115.5(8)
326	F4	B2	F5	86.6(7)
327	F4	B2	F6	131.4(9)
328	F4	B2	F7	86.7(7)
329	F1	B2	F5	102.2(7)
330	F1	B2	F6	112.1(8)
331	F1	B2	F7	96.7(7)
332	F5	B2	F6	92.7(7)
333	F5	B2	F7	161.0(8)
334	F6	B2	F7	78.6(7)

Table of Torsion Angles for **PhCDC-Pd-Cl**

Number	Atom1	Atom2	Atom3	Atom4	Torsion
1	P2	Pd1	P1	N1	2.1(3)
2	P2	Pd1	P1	C22	117.7(3)
3	P2	Pd1	P1	C10	-114.2(3)
4	Cl1	Pd1	P1	N1	176.3(2)
5	Cl1	Pd1	P1	C22	-68.1(2)
6	Cl1	Pd1	P1	C10	60.0(2)
7	C1	Pd1	P1	N1	-3.3(2)
8	C1	Pd1	P1	C22	112.4(2)
9	C1	Pd1	P1	C10	-119.5(2)
10	P1	Pd1	P2	N4	-11.4(3)
11	P1	Pd1	P2	C28	-126.4(3)
12	P1	Pd1	P2	C16	103.5(3)
13	Cl1	Pd1	P2	N4	174.3(1)
14	Cl1	Pd1	P2	C28	59.3(2)
15	Cl1	Pd1	P2	C16	-70.7(2)
16	C1	Pd1	P2	N4	-6.1(2)
17	C1	Pd1	P2	C28	-121.1(2)
18	C1	Pd1	P2	C16	108.8(2)
19	P1	Pd1	C1	C2	1.7(4)
20	P1	Pd1	C1	C3	-176.8(4)
21	P2	Pd1	C1	C2	-177.1(4)
22	P2	Pd1	C1	C3	4.5(4)

23	Cl1	Pd1	C1	C2	-155(7)
24	Cl1	Pd1	C1	C3	26(7)
25	Pd1	P1	N1	C2	5.1(4)
26	Pd1	P1	N1	C4	169.1(4)
27	C22	P1	N1	C2	-119.5(4)
28	C22	P1	N1	C4	44.5(5)
29	C10	P1	N1	C2	128.9(4)
30	C10	P1	N1	C4	-67.1(5)
31	Pd1	P1	C22	C27	0.1(5)
32	Pd1	P1	C22	C23	-176.5(4)
33	N1	P1	C22	C27	113.3(4)
34	N1	P1	C22	C23	-63.3(5)
35	C10	P1	C22	C27	-133.7(4)
36	C10	P1	C22	C23	49.7(5)
37	Pd1	P1	C10	C15	-74.3(5)
38	Pd1	P1	C10	C11	102.0(5)
39	N1	P1	C10	C15	172.5(4)
40	N1	P1	C10	C11	-11.2(5)
41	C22	P1	C10	C15	60.0(5)
42	C22	P1	C10	C11	-123.6(5)
43	Pd1	P2	N4	C9	169.6(4)
44	Pd1	P2	N4	C3	8.0(4)
45	C28	P2	N4	C9	-63.6(5)
46	C28	P2	N4	C3	134.9(4)
47	C16	P2	N4	C9	46.6(5)
48	C16	P2	N4	C3	-115.0(4)
49	Pd1	P2	C28	C29	84.2(4)
50	Pd1	P2	C28	C33	-90.9(4)
51	N4	P2	C28	C29	-29.0(5)
52	N4	P2	C28	C33	155.9(4)
53	C16	P2	C28	C29	-140.4(4)
54	C16	P2	C28	C33	44.5(5)
55	Pd1	P2	C16	C21	-2.7(5)
56	Pd1	P2	C16	C17	179.8(3)
57	N4	P2	C16	C21	109.4(4)
58	N4	P2	C16	C17	-68.1(4)
59	C28	P2	C16	C21	-140.3(4)
60	C28	P2	C16	C17	42.2(5)
61	Pd1	C1	C2	N1	1.2(6)
62	Pd1	C1	C2	N2	-177.3(4)
63	C3	C1	C2	N1	179.5(5)
64	C3	C1	C2	N2	1.0(9)

65	Pd1	C1	C3	N4	-0.5(6)
66	Pd1	C1	C3	N3	-178.9(4)
67	C2	C1	C3	N4	-178.8(4)
68	C2	C1	C3	N3	2.8(9)
69	P1	N1	C2	C1	-4.6(6)
70	P1	N1	C2	N2	174.2(3)
71	C4	N1	C2	C1	-171.6(4)
72	C4	N1	C2	N2	7.2(6)
73	P1	N1	C4	H4A	59.8(7)
74	P1	N1	C4	H4B	-62.5(7)
75	P1	N1	C4	C5	178.7(4)
76	C2	N1	C4	H4A	-135.4(5)
77	C2	N1	C4	H4B	102.3(5)
78	C2	N1	C4	C5	-16.5(5)
79	P2	N4	C9	H9A	58.7(6)
80	P2	N4	C9	H9B	-63.4(6)
81	P2	N4	C9	C8	177.6(3)
82	C3	N4	C9	H9A	-138.8(4)
83	C3	N4	C9	H9B	99.1(5)
84	C3	N4	C9	C8	-19.9(5)
85	P2	N4	C3	C1	-5.8(6)
86	P2	N4	C3	N3	172.9(3)
87	C9	N4	C3	C1	-170.8(4)
88	C9	N4	C3	N3	7.9(5)
89	P1	C22	C27	H27	4.4(7)
90	P1	C22	C27	C26	-175.5(4)
91	C23	C22	C27	H27	-178.9(5)
92	C23	C22	C27	C26	1.2(8)
93	P1	C22	C23	H23	-5.6(7)
94	P1	C22	C23	C24	174.3(4)
95	C27	C22	C23	H23	177.8(5)
96	C27	C22	C23	C24	-2.2(8)
97	P2	C28	C29	H29	5.4(7)
98	P2	C28	C29	C30	-174.4(4)
99	C33	C28	C29	H29	-179.6(5)
100	C33	C28	C29	C30	0.6(7)
101	P2	C28	C33	C32	174.9(5)
102	P2	C28	C33	H33	-4.9(8)
103	C29	C28	C33	C32	-0.1(8)
104	C29	C28	C33	H33	180.0(5)
105	C6	N2	C2	C1	-19.7(8)
106	C6	N2	C2	N1	161.7(4)

107	C5	N2	C2	C1	-175.3(5)
108	C5	N2	C2	N1	6.1(6)
109	C2	N2	C6	C7	56.0(7)
110	C2	N2	C6	H6A	-65.6(7)
111	C2	N2	C6	H6B	177.7(5)
112	C5	N2	C6	C7	-150.4(5)
113	C5	N2	C6	H6A	88.0(6)
114	C5	N2	C6	H6B	-28.7(7)
115	C2	N2	C5	C4	-16.1(6)
116	C2	N2	C5	H5A	-135.3(5)
117	C2	N2	C5	H5B	103.1(5)
118	C6	N2	C5	C4	-172.9(4)
119	C6	N2	C5	H5A	68.0(7)
120	C6	N2	C5	H5B	-53.6(7)
121	C22	C27	C26	H26	-178.6(5)
122	C22	C27	C26	C25	1.3(8)
123	H27	C27	C26	H26	1.4(9)
124	H27	C27	C26	C25	-178.6(5)
125	N4	C9	C8	N3	22.9(5)
126	N4	C9	C8	H8A	141.8(4)
127	N4	C9	C8	H8B	-95.9(5)
128	H9A	C9	C8	N3	141.7(4)
129	H9A	C9	C8	H8A	-99.4(5)
130	H9A	C9	C8	H8B	22.9(7)
131	H9B	C9	C8	N3	-96.1(5)
132	H9B	C9	C8	H8A	22.8(7)
133	H9B	C9	C8	H8B	145.1(5)
134	C1	C3	N3	C8	-172.9(5)
135	C1	C3	N3	C7	-23.6(8)
136	N4	C3	N3	C8	8.6(5)
137	N4	C3	N3	C7	157.9(4)
138	H32	C32	C33	C28	179.6(6)
139	H32	C32	C33	H33	-0(1)
140	C31	C32	C33	C28	-0.4(9)
141	C31	C32	C33	H33	179.5(6)
142	H32	C32	C31	C30	-179.6(6)
143	H32	C32	C31	H31	0.4(9)
144	C33	C32	C31	C30	0.4(8)
145	C33	C32	C31	H31	-179.5(5)
146	N1	C4	C5	N2	18.5(5)
147	N1	C4	C5	H5A	137.7(5)
148	N1	C4	C5	H5B	-100.7(5)

149	H4A	C4	C5	N2	137.4(5)
150	H4A	C4	C5	H5A	-103.4(6)
151	H4A	C4	C5	H5B	18.1(8)
152	H4B	C4	C5	N2	-100.3(6)
153	H4B	C4	C5	H5A	18.9(7)
154	H4B	C4	C5	H5B	140.5(5)
155	P2	C16	C21	H21	1.1(8)
156	P2	C16	C21	C20	-178.8(4)
157	C17	C16	C21	H21	178.7(5)
158	C17	C16	C21	C20	-1.3(8)
159	P2	C16	C17	C18	178.3(4)
160	P2	C16	C17	H17	-1.8(7)
161	C21	C16	C17	C18	0.8(8)
162	C21	C16	C17	H17	-179.3(5)
163	C3	N3	C8	C9	-20.3(5)
164	C3	N3	C8	H8A	-139.2(5)
165	C3	N3	C8	H8B	98.5(5)
166	C7	N3	C8	C9	-171.8(4)
167	C7	N3	C8	H8A	69.3(6)
168	C7	N3	C8	H8B	-53.0(6)
169	C3	N3	C7	H7A	-63.4(7)
170	C3	N3	C7	H7B	178.8(5)
171	C3	N3	C7	C6	57.7(7)
172	C8	N3	C7	H7A	84.2(6)
173	C8	N3	C7	H7B	-33.5(7)
174	C8	N3	C7	C6	-154.7(5)
175	P1	C10	C15	H15	-6.0(8)
176	P1	C10	C15	C14	174.1(5)
177	C11	C10	C15	H15	177.5(6)
178	C11	C10	C15	C14	-2.5(9)
179	P1	C10	C11	C12	-174.7(5)
180	P1	C10	C11	H11	5.3(8)
181	C15	C10	C11	C12	1.6(9)
182	C15	C10	C11	H11	-178.4(6)
183	C28	C29	C30	H30	179.6(5)
184	C28	C29	C30	C31	-0.6(8)
185	H29	C29	C30	H30	-0.1(8)
186	H29	C29	C30	C31	179.7(5)
187	C29	C30	C31	C32	0.1(8)
188	C29	C30	C31	H31	-180.0(5)
189	H30	C30	C31	C32	179.9(5)
190	H30	C30	C31	H31	-0.2(8)

191	H18	C18	C17	C16	179.8(5)
192	H18	C18	C17	H17	-0.1(8)
193	C19	C18	C17	C16	-0.3(8)
194	C19	C18	C17	H17	179.8(5)
195	H18	C18	C19	H19	0.2(9)
196	H18	C18	C19	C20	-179.9(5)
197	C17	C18	C19	H19	-179.8(5)
198	C17	C18	C19	C20	0.2(9)
199	C27	C26	C25	H25	177.2(6)
200	C27	C26	C25	C24	-2.7(9)
201	H26	C26	C25	H25	-3(1)
202	H26	C26	C25	C24	177.2(6)
203	C16	C21	C20	C19	1.2(9)
204	C16	C21	C20	H20	-178.8(6)
205	H21	C21	C20	C19	-178.8(6)
206	H21	C21	C20	H20	1(1)
207	N3	C7	C6	N2	-73.5(6)
208	N3	C7	C6	H6A	48.1(7)
209	N3	C7	C6	H6B	164.7(5)
210	H7A	C7	C6	N2	47.6(7)
211	H7A	C7	C6	H6A	169.2(5)
212	H7A	C7	C6	H6B	-74.2(7)
213	H7B	C7	C6	N2	165.3(5)
214	H7B	C7	C6	H6A	-73.1(7)
215	H7B	C7	C6	H6B	43.5(7)
216	C10	C15	C14	C13	2.3(9)
217	C10	C15	C14	H14	-177.5(6)
218	H15	C15	C14	C13	-177.6(6)
219	H15	C15	C14	H14	3(1)
220	C26	C25	C24	C23	1.6(9)
221	C26	C25	C24	H24	-178.2(6)
222	H25	C25	C24	C23	-178.3(6)
223	H25	C25	C24	H24	2(1)
224	C22	C23	C24	C25	0.8(9)
225	C22	C23	C24	H24	-179.3(5)
226	H23	C23	C24	C25	-179.2(5)
227	H23	C23	C24	H24	0.6(9)
228	H13	C13	C14	C15	178.6(6)
229	H13	C13	C14	H14	-2(1)
230	C12	C13	C14	C15	-1(1)
231	C12	C13	C14	H14	178.6(6)
232	H13	C13	C12	H12	0(1)

233	H13	C13	C12	C11	-179.5(6)
234	C14	C13	C12	H12	-179.7(6)
235	C14	C13	C12	C11	0(1)
236	C18	C19	C20	C21	-0.7(9)
237	C18	C19	C20	H20	179.3(6)
238	H19	C19	C20	C21	179.3(6)
239	H19	C19	C20	H20	-1(1)
240	C13	C12	C11	C10	-1(1)
241	C13	C12	C11	H11	179.4(6)
242	H12	C12	C11	C10	179.5(6)
243	H12	C12	C11	H11	-0(1)
244	Cl2	Pd2	P3	N5	179.2(2)
245	Cl2	Pd2	P3	C43	61.6(2)
246	Cl2	Pd2	P3	C49	-67.9(2)
247	P4	Pd2	P3	N5	2.6(3)
248	P4	Pd2	P3	C43	-115.0(3)
249	P4	Pd2	P3	C49	115.5(3)
250	C34	Pd2	P3	N5	-2.3(2)
251	C34	Pd2	P3	C43	-119.9(2)
252	C34	Pd2	P3	C49	110.6(2)
253	P3	Pd2	P4	N8	-6.8(3)
254	P3	Pd2	P4	C55	110.7(3)
255	P3	Pd2	P4	C61	-122.9(3)
256	Cl2	Pd2	P4	N8	176.6(2)
257	Cl2	Pd2	P4	C55	-65.9(2)
258	Cl2	Pd2	P4	C61	60.5(2)
259	C34	Pd2	P4	N8	-1.9(2)
260	C34	Pd2	P4	C55	115.6(3)
261	C34	Pd2	P4	C61	-118.0(3)
262	P3	Pd2	C34	C36	178.9(4)
263	P3	Pd2	C34	C35	-1.7(4)
264	Cl2	Pd2	C34	C36	-107(5)
265	Cl2	Pd2	C34	C35	72(6)
266	P4	Pd2	C34	C36	0.1(4)
267	P4	Pd2	C34	C35	179.4(4)
268	Pd2	P3	N5	C35	6.4(4)
269	Pd2	P3	N5	C37	168.1(4)
270	C43	P3	N5	C35	131.4(4)
271	C43	P3	N5	C37	-66.9(5)
272	C49	P3	N5	C35	-116.2(4)
273	C49	P3	N5	C37	45.5(5)
274	Pd2	P3	C43	C44	-69.0(4)

275	Pd2	P3	C43	C48	105.9(4)
276	N5	P3	C43	C44	176.4(4)
277	N5	P3	C43	C48	-8.7(5)
278	C49	P3	C43	C44	65.5(4)
279	C49	P3	C43	C48	-119.6(4)
280	Pd2	P3	C49	C54	165.9(4)
281	Pd2	P3	C49	C50	-20.8(5)
282	N5	P3	C49	C54	-82.3(4)
283	N5	P3	C49	C50	91.0(4)
284	C43	P3	C49	C54	31.0(5)
285	C43	P3	C49	C50	-155.7(4)
286	Pd2	P4	N8	C42	179.2(4)
287	Pd2	P4	N8	C36	3.9(4)
288	C55	P4	N8	C42	55.8(5)
289	C55	P4	N8	C36	-119.5(4)
290	C61	P4	N8	C42	-56.6(5)
291	C61	P4	N8	C36	128.1(4)
292	Pd2	P4	C55	C60	-172.8(4)
293	Pd2	P4	C55	C56	10.5(5)
294	N8	P4	C55	C60	-59.3(6)
295	N8	P4	C55	C56	124.0(5)
296	C61	P4	C55	C60	54.5(6)
297	C61	P4	C55	C56	-122.2(5)
298	Pd2	P4	C61	C66	73.4(6)
299	Pd2	P4	C61	C62	-99.3(6)
300	N8	P4	C61	C66	-39.7(6)
301	N8	P4	C61	C62	147.7(5)
302	C55	P4	C61	C66	-154.7(5)
303	C55	P4	C61	C62	32.7(6)
304	Pd2	C34	C36	N8	2.5(6)
305	Pd2	C34	C36	N7	-175.1(4)
306	C35	C34	C36	N8	-176.8(5)
307	C35	C34	C36	N7	5.6(9)
308	Pd2	C34	C35	N5	6.6(6)
309	Pd2	C34	C35	N6	-169.8(4)
310	C36	C34	C35	N5	-174.1(5)
311	C36	C34	C35	N6	9.5(9)
312	P3	N5	C35	C34	-8.9(6)
313	P3	N5	C35	N6	168.3(3)
314	C37	N5	C35	C34	-174.1(4)
315	C37	N5	C35	N6	3.1(6)
316	P3	N5	C37	H37A	77.1(6)

317	P3	N5	C37	H37B	-44.7(7)
318	P3	N5	C37	C38	-163.8(4)
319	C35	N5	C37	H37A	-120.3(5)
320	C35	N5	C37	H37B	117.9(5)
321	C35	N5	C37	C38	-1.3(6)
322	P4	N8	C42	H42A	69.3(6)
323	P4	N8	C42	H42B	-52.6(6)
324	P4	N8	C42	C41	-171.6(4)
325	C36	N8	C42	H42A	-115.1(5)
326	C36	N8	C42	H42B	122.9(5)
327	C36	N8	C42	C41	3.9(5)
328	P4	N8	C36	C34	-4.5(6)
329	P4	N8	C36	N7	173.6(3)
330	C42	N8	C36	C34	179.3(4)
331	C42	N8	C36	N7	-2.6(5)
332	N8	C42	C41	N7	-3.7(5)
333	N8	C42	C41	H41A	116.0(5)
334	N8	C42	C41	H41B	-123.2(5)
335	H42A	C42	C41	N7	115.4(5)
336	H42A	C42	C41	H41A	-125.0(5)
337	H42A	C42	C41	H41B	-4.1(7)
338	H42B	C42	C41	N7	-122.7(5)
339	H42B	C42	C41	H41A	-3.1(7)
340	H42B	C42	C41	H41B	117.8(5)
341	C34	C36	N7	C41	177.8(5)
342	C34	C36	N7	C40	6.0(9)
343	N8	C36	N7	C41	-0.0(6)
344	N8	C36	N7	C40	-171.9(5)
345	C36	N7	C41	C42	2.5(5)
346	C36	N7	C41	H41A	-117.1(5)
347	C36	N7	C41	H41B	122.0(5)
348	C40	N7	C41	C42	174.7(5)
349	C40	N7	C41	H41A	55.1(7)
350	C40	N7	C41	H41B	-65.8(6)
351	C36	N7	C40	H40A	-171.1(5)
352	C36	N7	C40	H40B	72.1(7)
353	C36	N7	C40	C39	-49.5(8)
354	C41	N7	C40	H40A	17.8(8)
355	C41	N7	C40	H40B	-99.0(6)
356	C41	N7	C40	C39	139.4(5)
357	C38	N6	C35	C34	172.9(5)
358	C38	N6	C35	N5	-3.7(6)

359	C39	N6	C35	C34	5.5(9)
360	C39	N6	C35	N5	-171.2(5)
361	C35	N6	C38	C37	2.8(6)
362	C35	N6	C38	H38A	-116.6(5)
363	C35	N6	C38	H38B	122.3(5)
364	C39	N6	C38	C37	170.6(5)
365	C39	N6	C38	H38A	51.2(7)
366	C39	N6	C38	H38B	-69.9(7)
367	C35	N6	C39	C40	-51.0(7)
368	C35	N6	C39	H39A	-172.4(5)
369	C35	N6	C39	H39B	70.5(7)
370	C38	N6	C39	C40	142.6(5)
371	C38	N6	C39	H39A	21.2(8)
372	C38	N6	C39	H39B	-95.9(6)
373	H44	C44	C43	P3	-4.3(7)
374	H44	C44	C43	C48	-179.4(5)
375	C45	C44	C43	P3	175.5(4)
376	C45	C44	C43	C48	0.4(7)
377	H44	C44	C45	H45	-0.6(8)
378	H44	C44	C45	C46	179.3(5)
379	C43	C44	C45	H45	179.5(5)
380	C43	C44	C45	C46	-0.5(8)
381	P3	C43	C48	H48	4.4(7)
382	P3	C43	C48	C47	-175.4(4)
383	C44	C43	C48	H48	179.3(5)
384	C44	C43	C48	C47	-0.5(7)
385	C44	C45	C46	H46	-179.3(5)
386	C44	C45	C46	C47	0.8(8)
387	H45	C45	C46	H46	0.7(8)
388	H45	C45	C46	C47	-179.3(5)
389	C43	C48	C47	C46	0.8(8)
390	C43	C48	C47	H47	-179.2(5)
391	H48	C48	C47	C46	-179.1(5)
392	H48	C48	C47	H47	1.0(8)
393	P3	C49	C54	H54	-7.4(7)
394	P3	C49	C54	C53	172.6(4)
395	C50	C49	C54	H54	179.4(5)
396	C50	C49	C54	C53	-0.6(8)
397	P3	C49	C50	C51	-173.2(4)
398	P3	C49	C50	H50	6.9(8)
399	C54	C49	C50	C51	0.4(8)
400	C54	C49	C50	H50	-179.5(5)

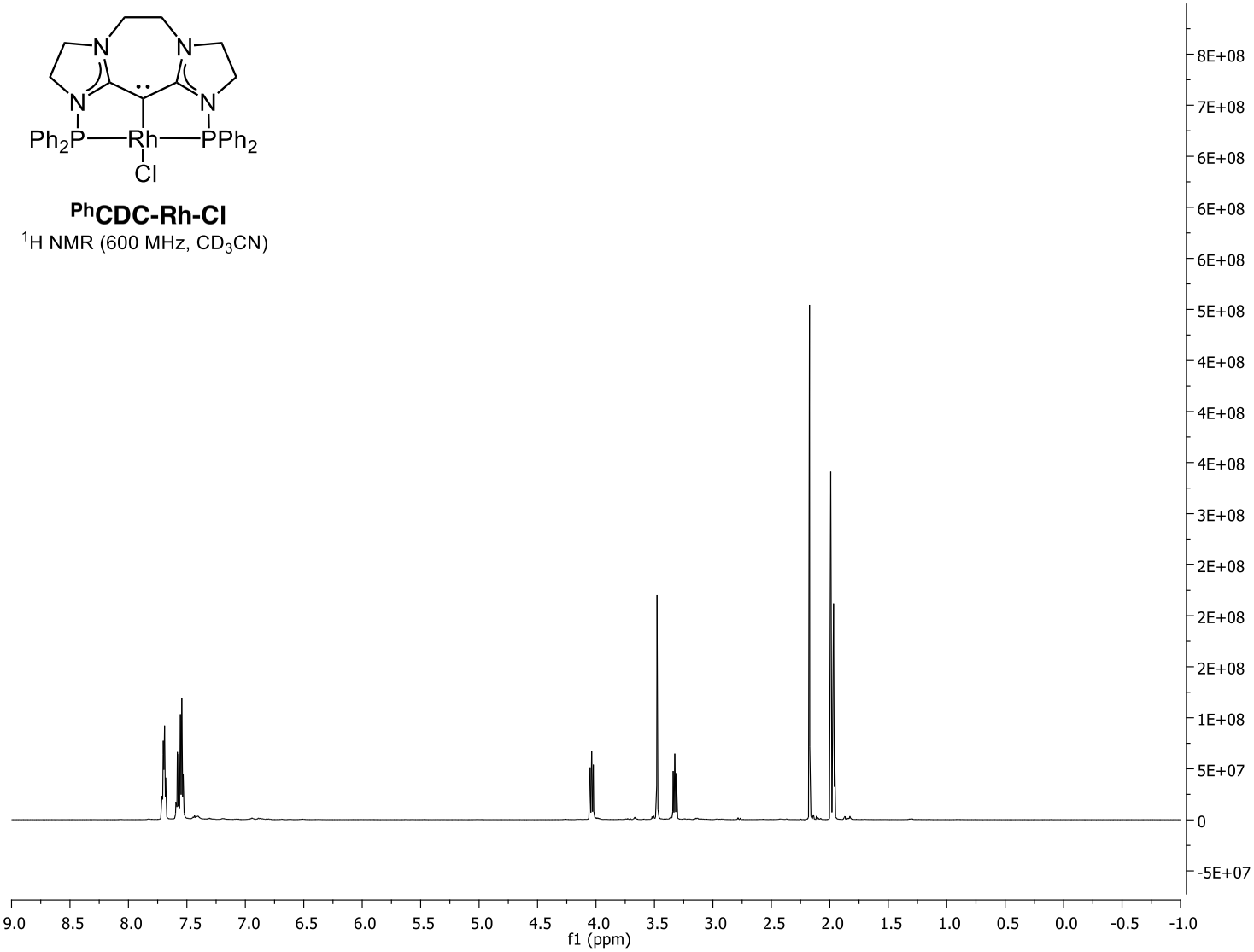
401	N5	C37	C38	N6	-0.8(5)
402	N5	C37	C38	H38A	118.6(5)
403	N5	C37	C38	H38B	-120.4(5)
404	H37A	C37	C38	N6	118.2(5)
405	H37A	C37	C38	H38A	-122.4(6)
406	H37A	C37	C38	H38B	-1.3(8)
407	H37B	C37	C38	N6	-119.9(5)
408	H37B	C37	C38	H38A	-0.5(8)
409	H37B	C37	C38	H38B	120.6(6)
410	C45	C46	C47	C48	-0.9(8)
411	C45	C46	C47	H47	179.1(5)
412	H46	C46	C47	C48	179.1(5)
413	H46	C46	C47	H47	-0.9(8)
414	C49	C54	C53	H53	-179.5(5)
415	C49	C54	C53	C52	0.5(8)
416	H54	C54	C53	H53	0.4(8)
417	H54	C54	C53	C52	-179.5(5)
418	H51	C51	C50	C49	180.0(6)
419	H51	C51	C50	H50	-0(1)
420	C52	C51	C50	C49	0.0(9)
421	C52	C51	C50	H50	179.9(6)
422	H51	C51	C52	C53	179.9(6)
423	H51	C51	C52	H52	-0(1)
424	C50	C51	C52	C53	-0.1(9)
425	C50	C51	C52	H52	179.9(6)
426	C54	C53	C52	C51	-0.1(8)
427	C54	C53	C52	H52	179.8(5)
428	H53	C53	C52	C51	179.9(5)
429	H53	C53	C52	H52	-0.1(9)
430	P4	C55	C60	H60	3.0(9)
431	P4	C55	C60	C59	-177.0(5)
432	C56	C55	C60	H60	179.7(6)
433	C56	C55	C60	C59	-0.3(9)
434	P4	C55	C56	H56	-3.3(8)
435	P4	C55	C56	C57	176.7(5)
436	C60	C55	C56	H56	179.9(6)
437	C60	C55	C56	C57	-0.1(9)
438	C55	C60	C59	H59	-179.3(6)
439	C55	C60	C59	C58	0.7(9)
440	H60	C60	C59	H59	1(1)
441	H60	C60	C59	C58	-179.3(6)
442	P4	C61	C66	H66	9(1)

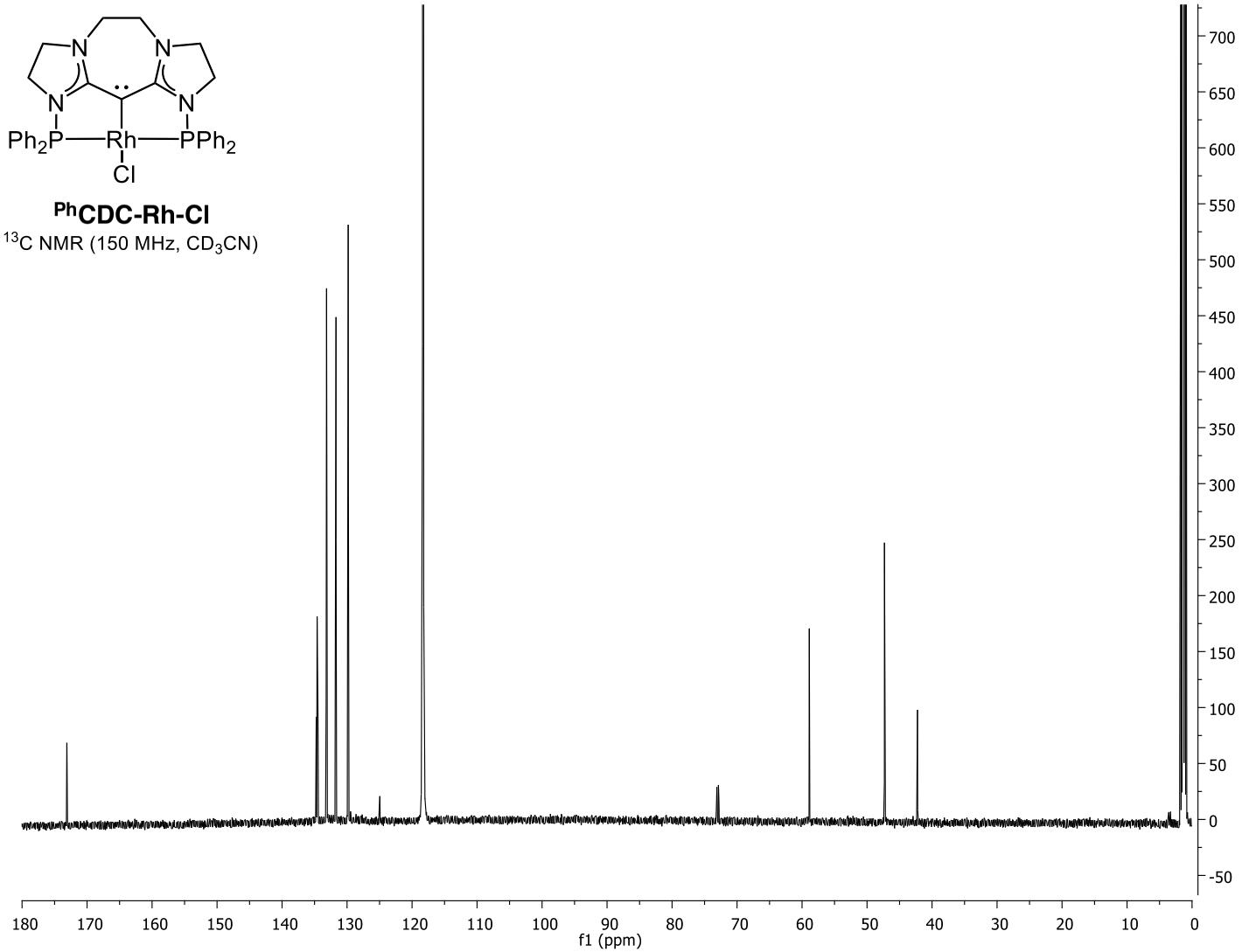
443	P4	C61	C66	C1B	-170.8(7)
444	C62	C61	C66	H66	-178.2(7)
445	C62	C61	C66	C1B	2(1)
446	P4	C61	C62	H62	-10(1)
447	P4	C61	C62	C1A	169.9(7)
448	C66	C61	C62	H62	177.2(7)
449	C66	C61	C62	C1A	-3(1)
450	N7	C40	C39	N6	74.3(7)
451	N7	C40	C39	H39A	-164.2(5)
452	N7	C40	C39	H39B	-47.1(7)
453	H40A	C40	C39	N6	-164.1(5)
454	H40A	C40	C39	H39A	-42.6(8)
455	H40A	C40	C39	H39B	74.5(7)
456	H40B	C40	C39	N6	-47.2(7)
457	H40B	C40	C39	H39A	74.2(7)
458	H40B	C40	C39	H39B	-168.7(6)
459	C55	C56	C57	H57	-179.8(6)
460	C55	C56	C57	C58	0.1(9)
461	H56	C56	C57	H57	0(1)
462	H56	C56	C57	C58	-179.9(6)
463	C61	C66	C1B	H1B	179.2(9)
464	C61	C66	C1B	C1C	-1(1)
465	H66	C66	C1B	H1B	-1(2)
466	H66	C66	C1B	C1C	179(1)
467	C60	C59	C58	C57	-0.7(9)
468	C60	C59	C58	H58	179.5(6)
469	H59	C59	C58	C57	179.4(6)
470	H59	C59	C58	H58	-1(1)
471	C61	C62	C1A	H1A	-177.2(9)
472	C61	C62	C1A	C1C	3(2)
473	H62	C62	C1A	H1A	3(2)
474	H62	C62	C1A	C1C	-177(1)
475	C56	C57	C58	C59	0.3(9)
476	C56	C57	C58	H58	-179.9(6)
477	H57	C57	C58	C59	-179.8(6)
478	H57	C57	C58	H58	0(1)
479	C62	C1A	C1C	C1B	-2(2)
480	C62	C1A	C1C	H1C	178(1)
481	H1A	C1A	C1C	C1B	178(1)
482	H1A	C1A	C1C	H1C	-2(2)
483	C66	C1B	C1C	C1A	1(2)
484	C66	C1B	C1C	H1C	-179(1)

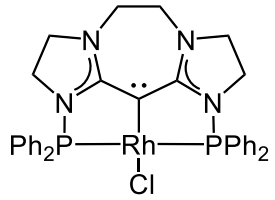
485	H1B	C1B	C1C	C1A	-179(1)
486	H1B	C1B	C1C	H1C	1(2)

^{Ph}CDC-Rh-Cl

^{1}H NMR (600 MHz, CD_3CN)

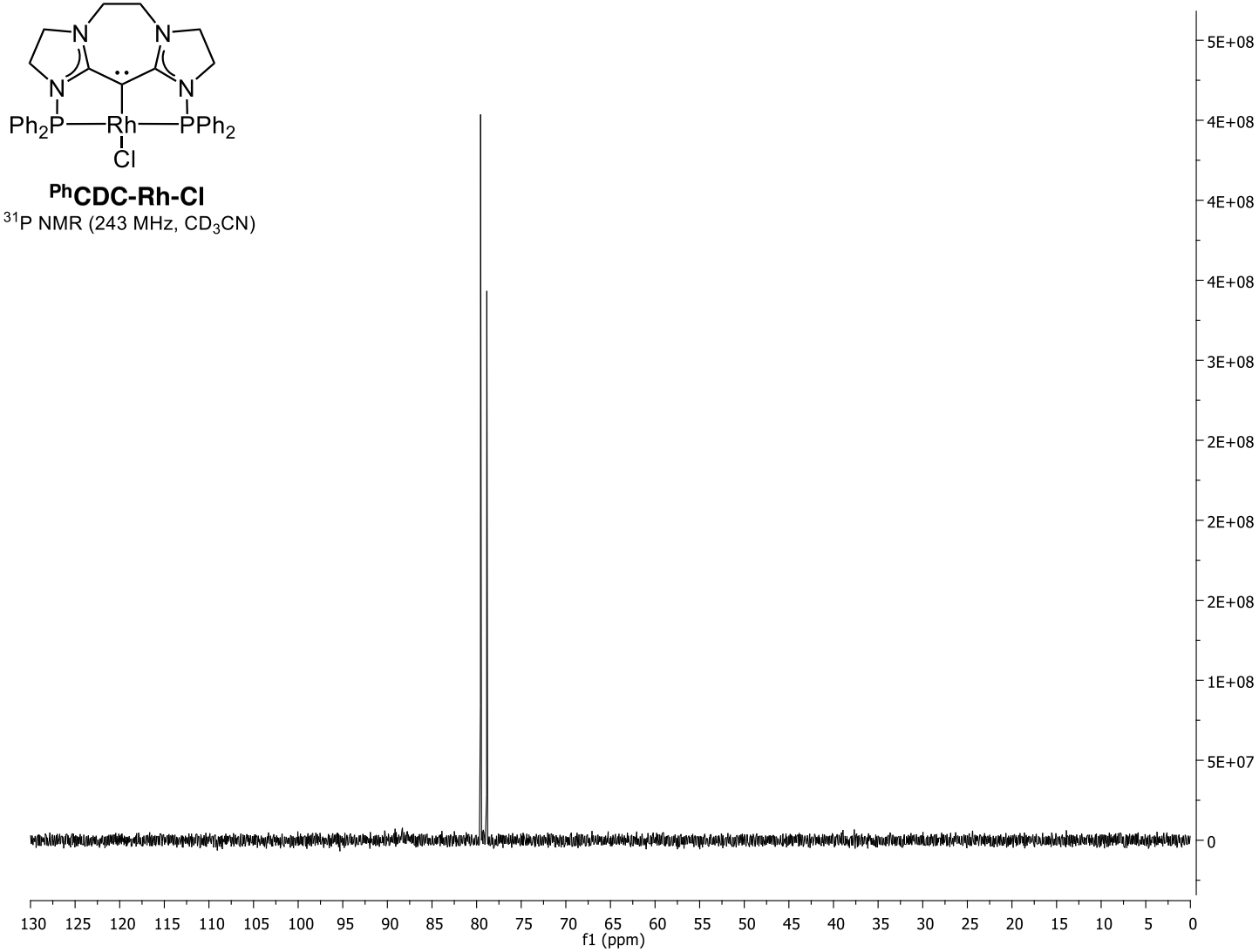



N
N
N
N
Ph2P
Rh
PPh2
Cl
PhCDC-Rh-Cl
13C NMR (150 MHz, CD3CN)
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



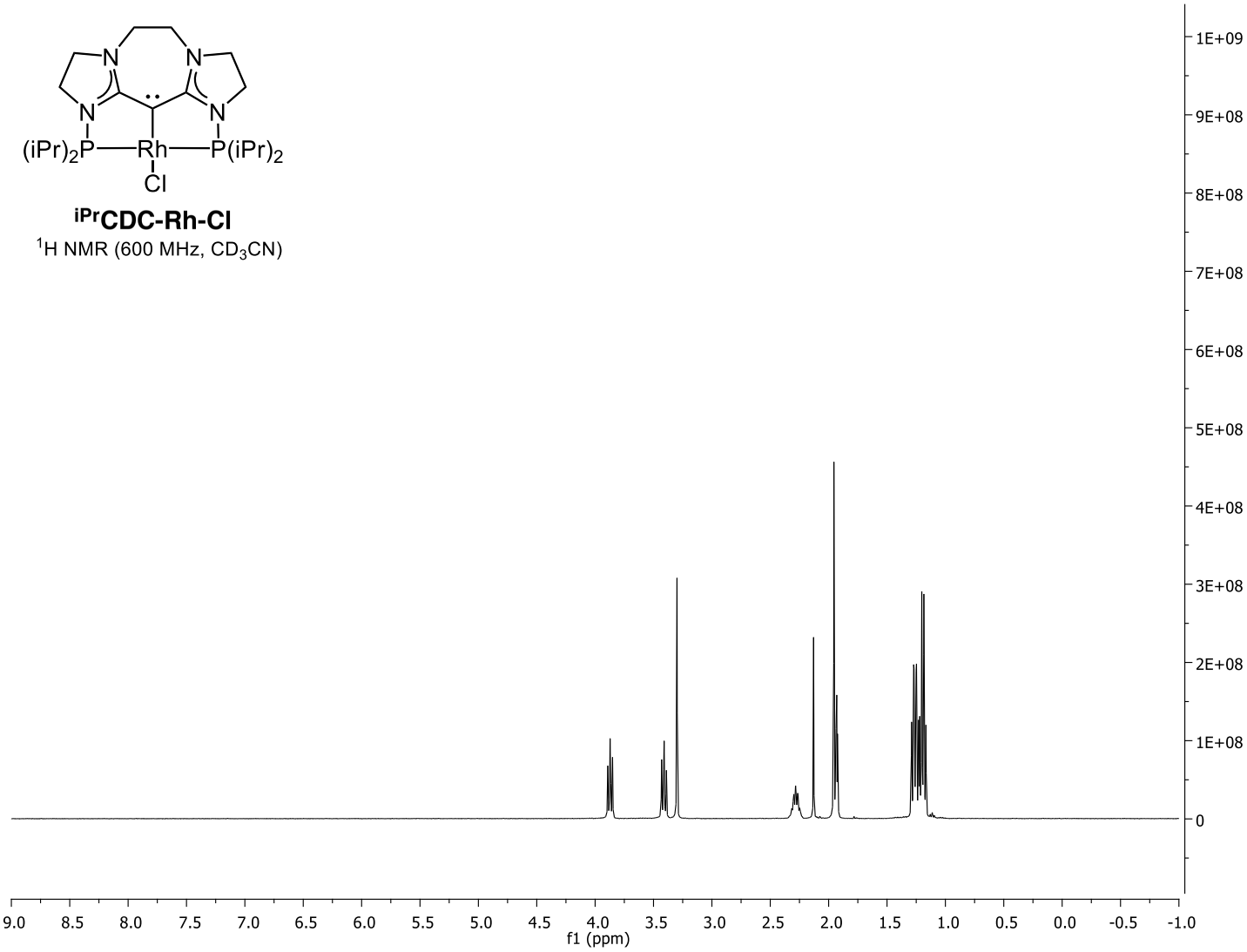
^{Ph}CDC-Rh-Cl

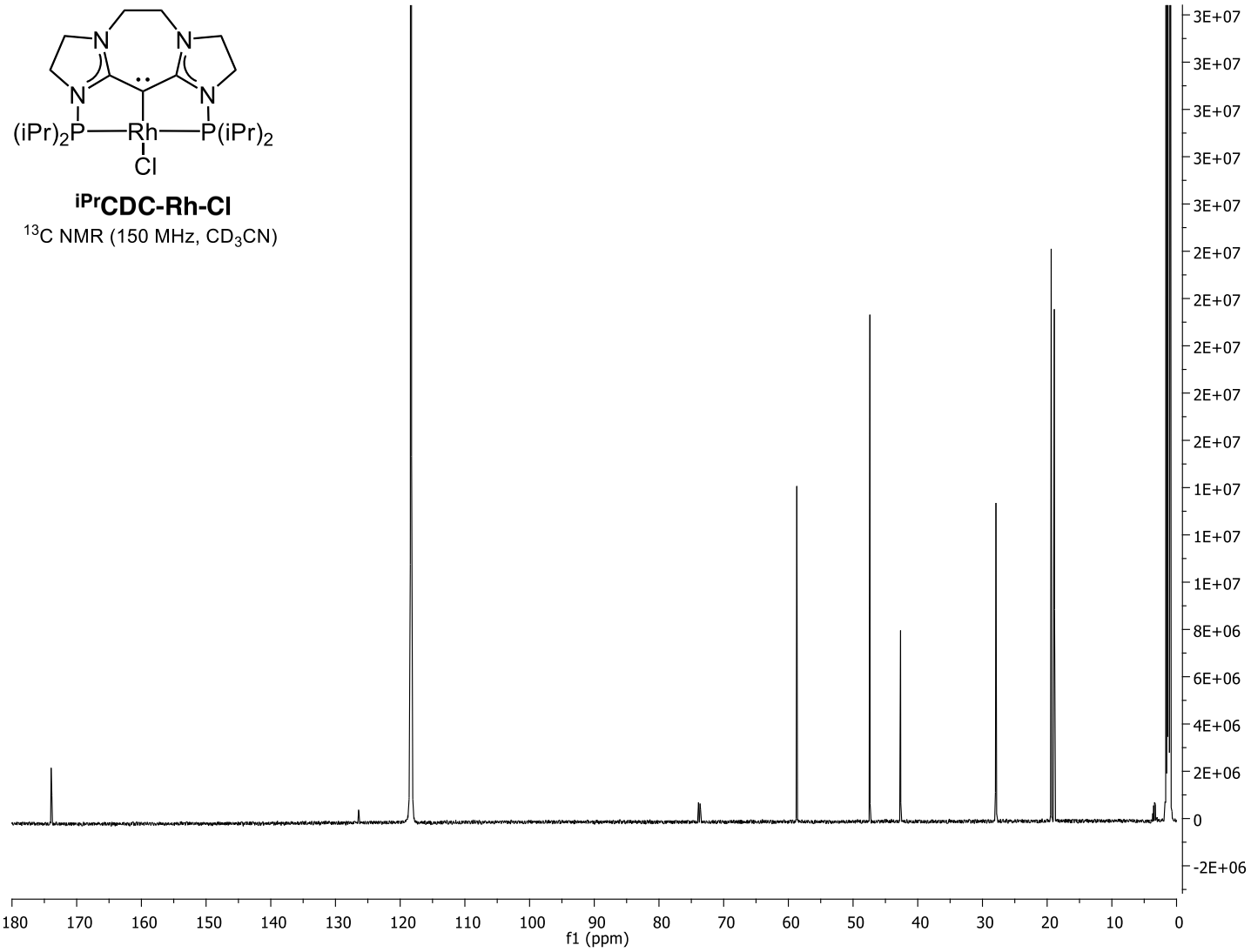
^{31}P NMR (243 MHz, CD_3CN)

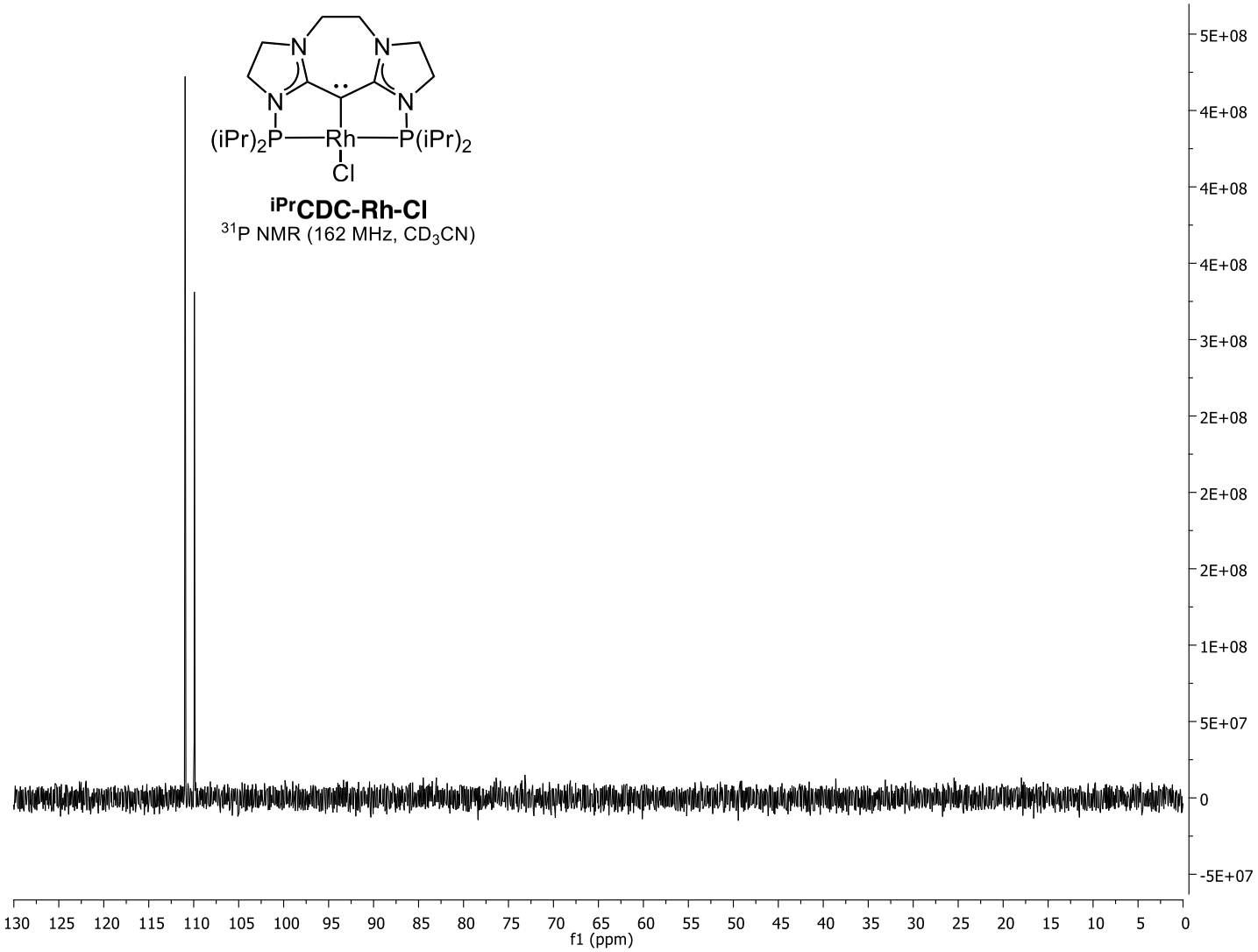


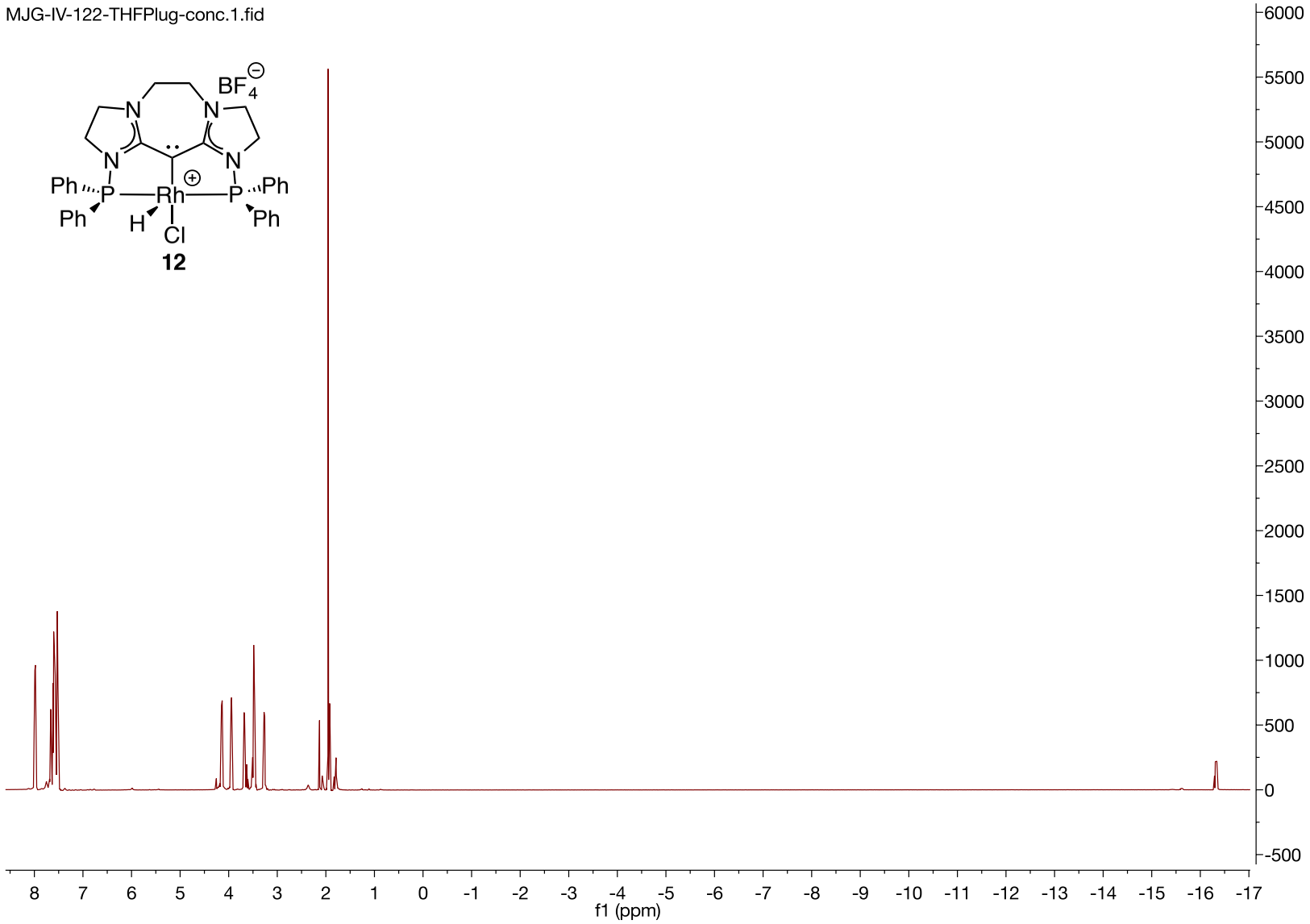
^{iPr}CDC-Rh-Cl

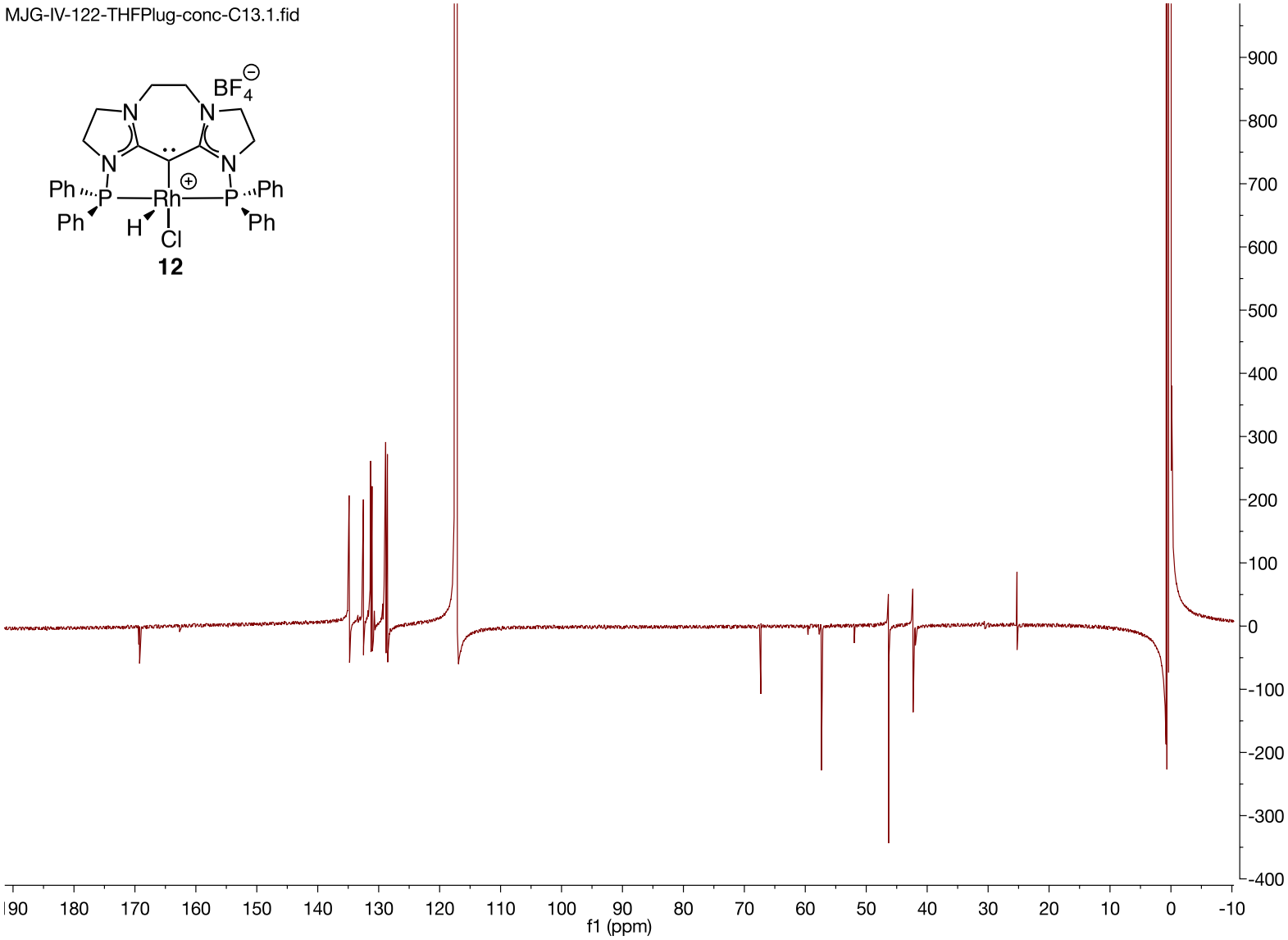
^{1}H NMR (600 MHz, CD_3CN)

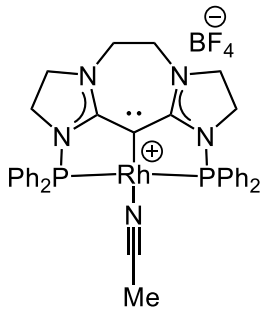



N
N
N
N
(iPr)2P
Rh
P(iPr)2
Cl
iPrCDC-Rh-Cl
13C NMR (150 MHz, CD3CN)
3E+07
2E+07
1E+07
8E+06
6E+06
4E+06
2E+06
0
-2E+06
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


N
N
N
N
(iPr)2P
Rh
P(iPr)2
Cl
iPrCDC-Rh-Cl
31P NMR (162 MHz, CD3CN)
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

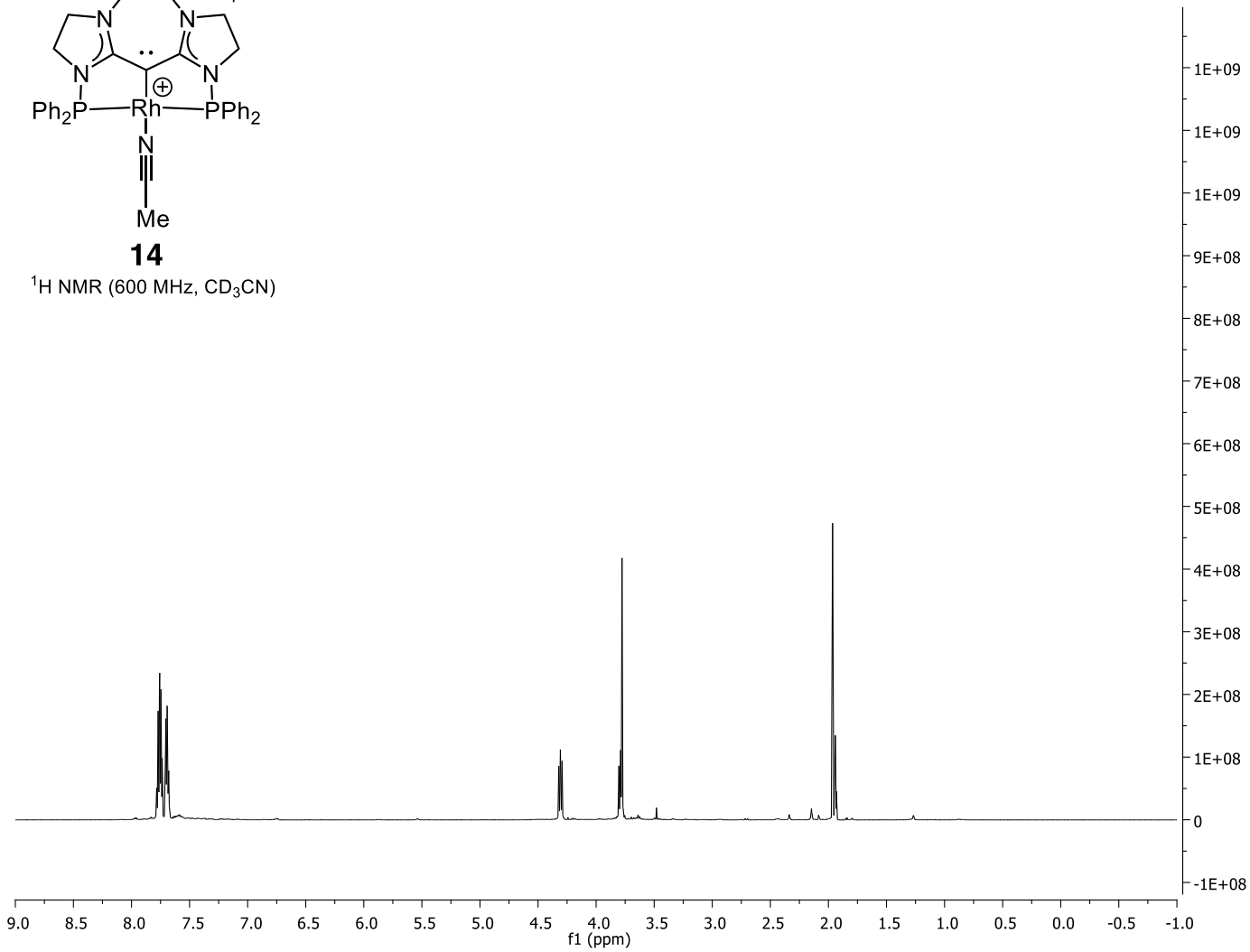

MJG-IV-122-THFPlug-conc.1.fid
BF4
N
N
N
N
Ph
P
Rh
P
Ph
Ph
H
Cl
Ph
Ph
12
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
8 7 6 5 4 3 2 1 0 -1 -2 -3 -4 -5 -6 -7 -8 -9 -10 -11 -12 -13 -14 -15 -16 -17
f1 (ppm)

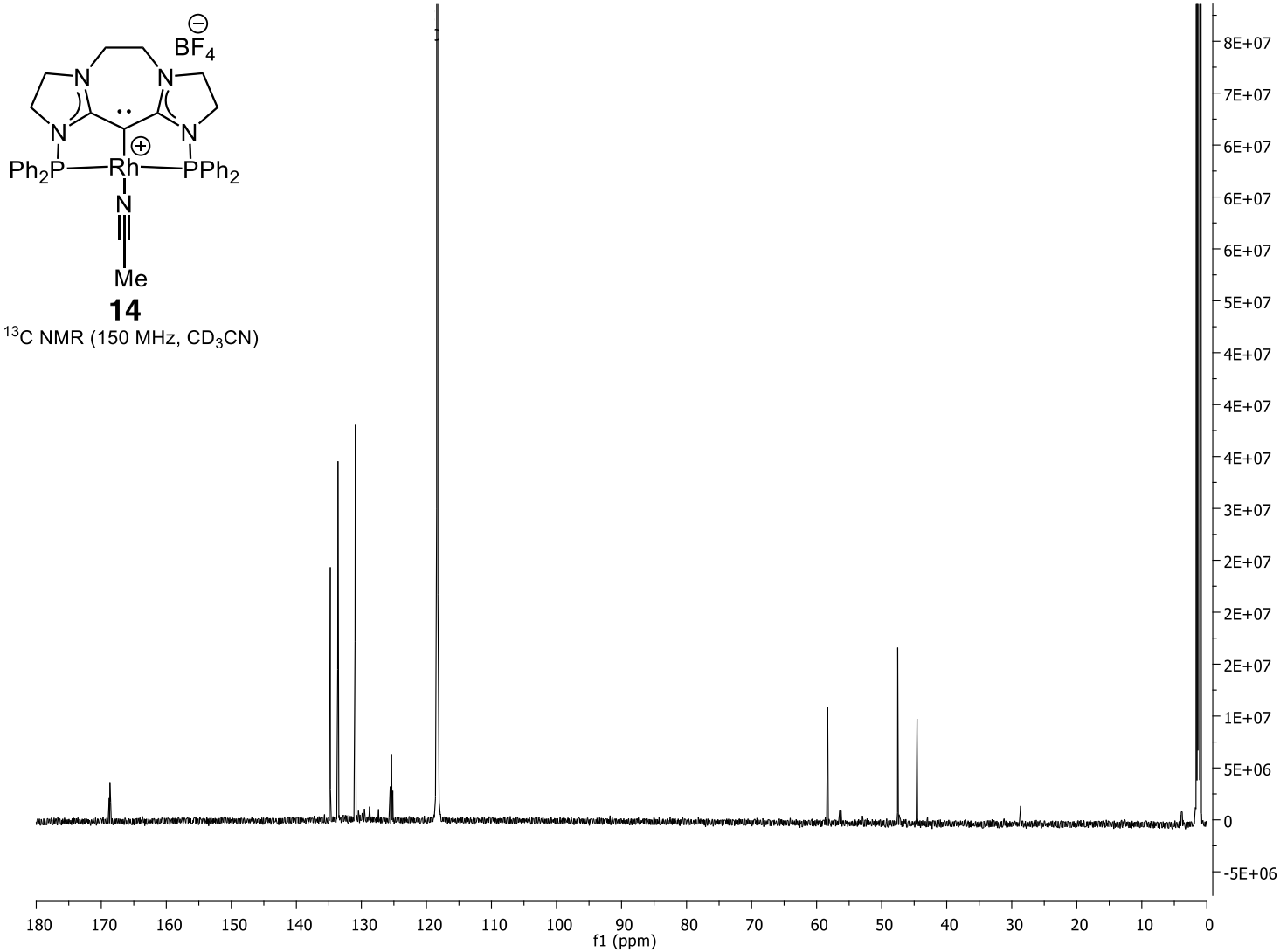

MJG-IV-122-THFPlug-conc-C13.1.fid
BF4
N
N
N
N
Ph
P
Rh
P
Ph
Ph
H
Cl
Ph
12
900
800
700
600
500
400
300
200
100
0
-100
-200
-300
-400
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

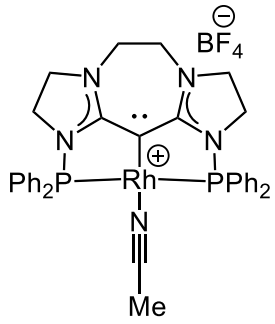


14

^{1}H NMR (600 MHz, CD_3CN)

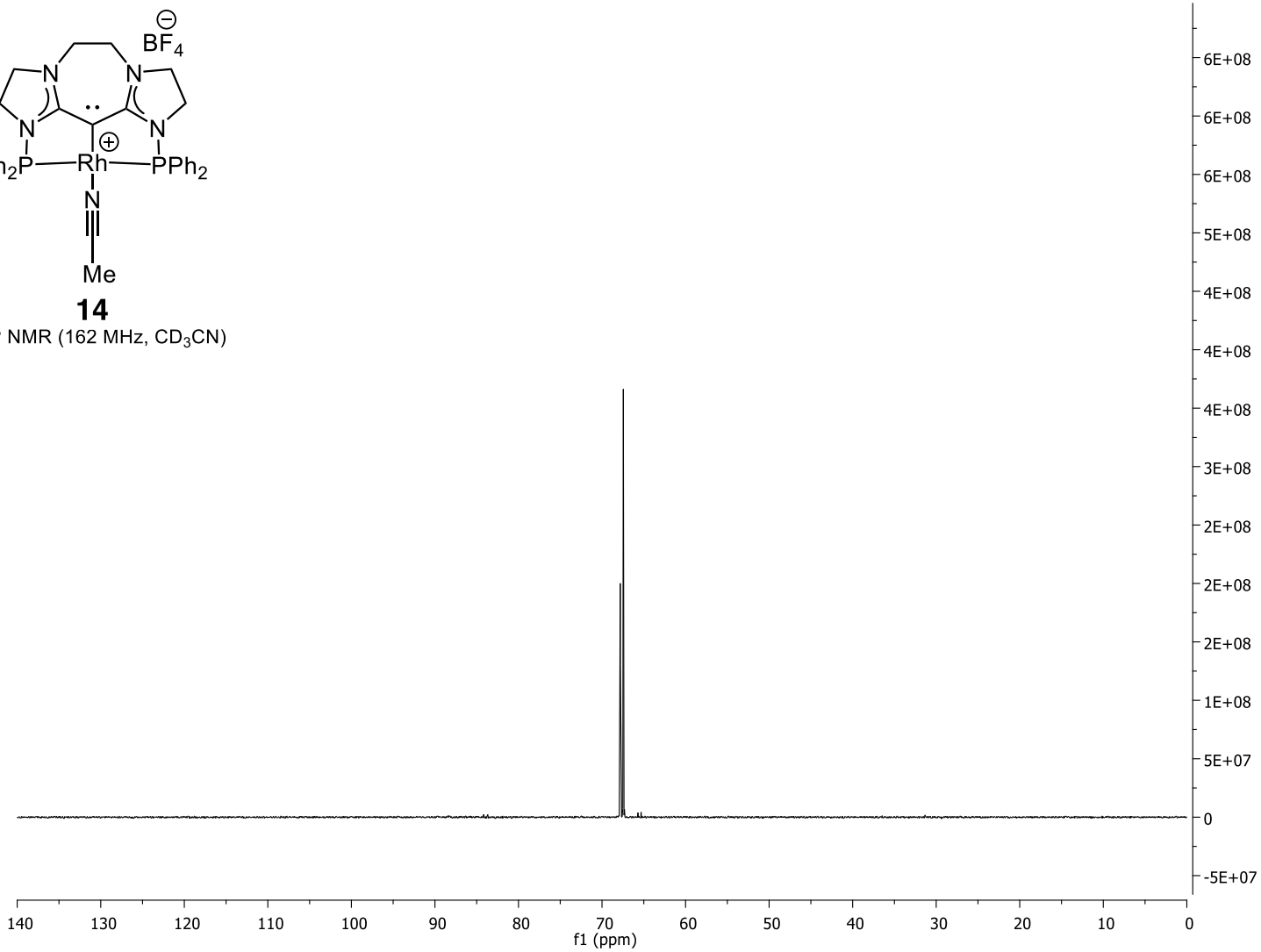


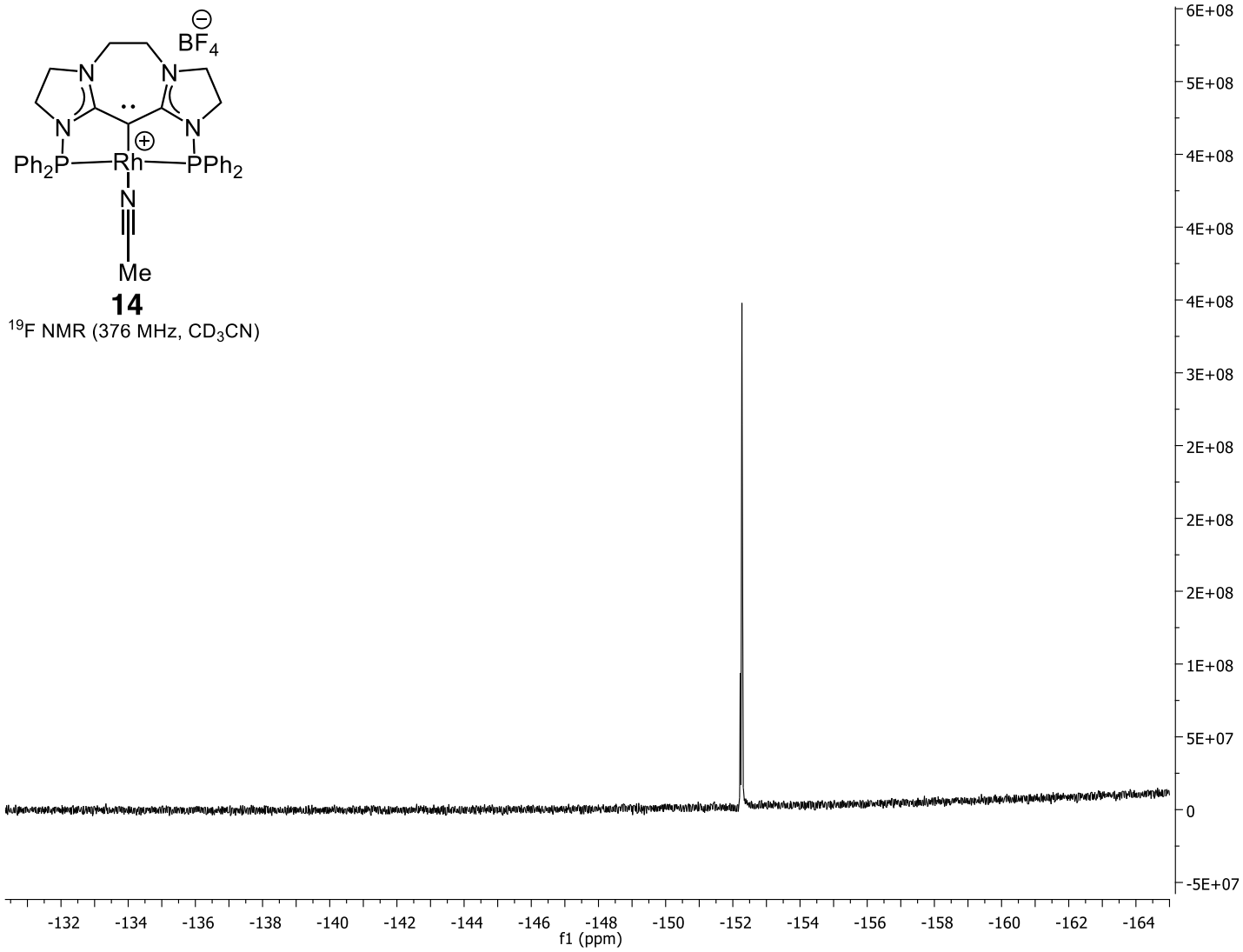

BF4
N
N
N
N
Ph2P
Rh
PPh2
N
Me
14
13C NMR (150 MHz, CD3CN)
8E+07
7E+07
6E+07
6E+07
6E+07
5E+07
4E+07
4E+07
4E+07
3E+07
2E+07
2E+07
2E+07
1E+07
5E+06
0
-5E+06
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



14

^{31}P NMR (162 MHz, CD_3CN)

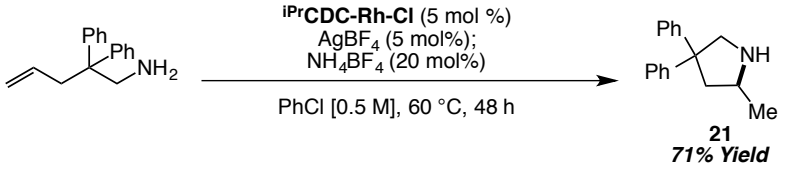



BF4
N
N
N
N
Ph2P
Rh
PPh2
N
Me
14
19F NMR (376 MHz, CD3CN)
6E+08
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
-132
-134
-136
-138
-140
-142
-144
-146
-148
-150
-152
-154
-156
-158
-160
-162
-164
f1 (ppm)

Section 1.5: Intramolecular Hydroamination with Carbodicarbene Ligated Rh Complexes

■ General procedure for Intramolecular Hydroamination Catalyzed by CDC-metal Complexes

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the appropriate CDC-metal complex (0.005 mmol, 5 mol%) and silver salt (0.005 mmol, 5 mol%). The solids were solvated with the listed solvent and allowed to stir at room temperature for >20 minutes. The intramolecular amine substrate (0.1 mmol) was added to the reaction, followed by the addition of an additive if appropriate, and the vial was capped with a Teflon® lined lid or septum cap, taped with electrical tape and brought outside the dry box. Any volatile liquids (eg: $HBF_4.OEt_2$) were added via syringe through the Teflon® septa under an atmosphere of N_2. The reaction was allowed to warm to the appropriate temperature and stir for 18 to 48 h as appropriate. The reaction was allowed to cool and an aliquot was taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solvent evaporated before the products were purified by SiO_2 column chromatography.

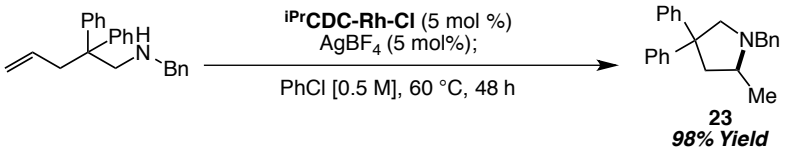


Synthesis of 2-methyl-4,4-diphenylpyrrolidine (21)

Following the general procedure for (CDC)-Rh-catalyzed intramolecular hydroamination, 2,2-diphenylpent-4-en-1-amine (23.7 mg, 0.100 mmol) was added to a solution of **^{iPr}CDC-Rh-Cl** (2.7 mg, 0.0050 mmol) and $AgBF_4$ (1.2 mg, 0.005 mmol) in chlorobenzene (200 μL, [ ] = 0.50 M). Ammonium tetrafluoroborate (2.1 mg , 0.02 mmol) was added to the solution and the

reaction was sealed and allowed to stir at 60 °C for 48 h. The reaction was concentrated and the resulting oil was purified by SiO_2 column chromatography (20:1 DCM/MeOH) to afford **21** (16.9 mg, 0.071 mmol, 71% yield) as a colorless oil.

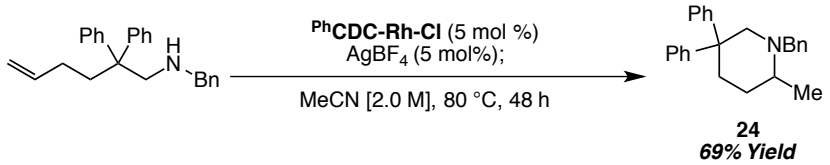
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 6H), 7.25 – 7.20 (m, 2H), 7.19 – 7.14 (m, 2H), 3.71 (d, *J* = 11.5 Hz, 1H), 3.51 – 3.45 (m, 1H), 3.43 – 3.32 (m, 1H), 2.75 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.06 (dd, *J* = 12.6, 9.3 Hz, 1H), 1.22 (d, *J* = 6.4 Hz, 3H).



Synthesis of 1-benzyl-2-methyl-4,4-diphenylpyrrolidine (23)

Following the general procedure for (CDC)-Rh-catalyzed intramolecular hydroamination, N-benzyl-2,2-diphenylpent-4-en-1-amine (32.7 mg, 0.100 mmol) was added to a solution of **^{iPr}CDC-Rh-Cl** (2.7 mg, 0.0050 mmol) and $AgBF_4$ (1.2 mg, 0.005 mmol) in chlorobenzene (200 μL, [ ] = 0.50 M). The reaction was sealed and allowed to stir at 60 °C for 48 h. The reaction was concentrated and the resulting oil was purified by SiO_2 column chromatography (20:1 Hex/EtOAc) to afford **23** (32.0 mg, 0.098 mmol, 98% yield) as a colorless oil.

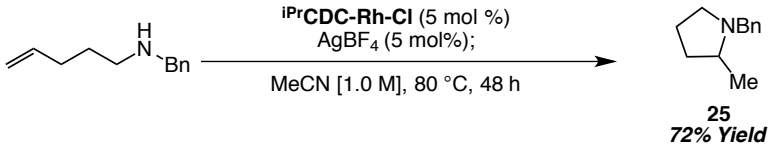
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.33 (dd, *J* = 17.8, 10.8 Hz, 2H), 7.30 – 7.23 (m, 5H), 7.23 – 7.15 (m, 5H), 7.11 (dd, *J* = 19.2, 12.1 Hz, 1H), 4.10 (d, *J* = 13.2 Hz, 1H), 3.65 (d, *J* = 9.9 Hz, 1H), 3.27 (d, *J* = 13.2 Hz, 1H), 2.93 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.89 – 2.82 (m, 1H), 2.80 (d, *J* = 9.9 Hz, 1H), 2.22 (dd, *J* = 12.6, 8.0 Hz, 1H), 1.18 (d, *J* = 5.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.67, 148.76, 140.12, 128.62, 128.23, 128.15, 127.84, 127.46, 127.27, 126.79, 125.81, 125.42, 66.46, 59.68, 58.03, 52.54, 48.02, 19.54.



Synthesis of 1-benzyl-2-methyl-5,5-diphenylpiperidine (24)

Following the general procedure for (CDC)-Rh-catalyzed intramolecular hydroamination, N-benzyl-2,2-diphenylhex-5-en-1-amine (34.2 mg, 0.100 mmol) was added to a solution of **^{iPr}CDC-Rh-Cl** (2.7 mg, 0.0050 mmol) and $AgBF_4$ (1.2 mg, 0.005 mmol) in acetonitrile (50 μL, [ ] = 2.0 M). The reaction was sealed and allowed to stir at 80 °C for 48 h. The reaction was concentrated and the resulting oil was purified by SiO_2 column chromatography (40:1 Hex/EtOAc) to afford **24** (23.6 mg, 0.069 mmol, 69% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 4H), 7.30 – 7.26 (m, 1H), 7.22 – 7.14 (m, 6H), 7.13 – 7.06 (m, 4H), 4.05 (d, *J* = 13.3 Hz, 1H), 3.35 (d, *J* = 12.2 Hz, 1H), 3.13 (d, *J* = 13.3 Hz, 1H), 2.50 – 2.43 (m, 2H), 2.41 (d, *J* = 12.2 Hz, 1H), 2.21 – 2.13 (m, 1H), 1.62 (ddt, *J* = 8.9, 6.7, 3.5 Hz, 1H), 1.40 – 1.32 (m, 1H), 1.13 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.59, 146.75, 139.46, 129.51, 128.48, 128.02, 127.95, 127.62, 127.06, 126.89, 125.65, 125.30, 77.24, 77.02, 76.81, 60.94, 58.90, 56.13, 46.54, 34.22, 30.99.

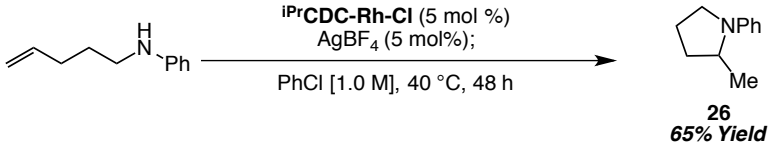


Synthesis of 1-benzyl-2-methylpyrrolidine (25)

Following the general procedure for (CDC)-Rh-catalyzed intramolecular hydroamination, N-benzylpent-4-en-1-amine (17.5 mg, 0.100 mmol) was added to a solution of **^{iPr}CDC-Rh-Cl** (2.7 mg, 0.0050 mmol) and $AgBF_4$ (1.2 mg, 0.005 mmol) in acetonitrile (100 μL, [ ] = 2.0 M). The

reaction was sealed and allowed to stir at 80 °C for 48 h. The reaction was concentrated and the resulting oil was purified by SiO_2 column chromatography (20:1 Hex/EtOAc) to afford **25** (12.6 mg, 0.072 mmol, 72% yield) as a colorless oil.

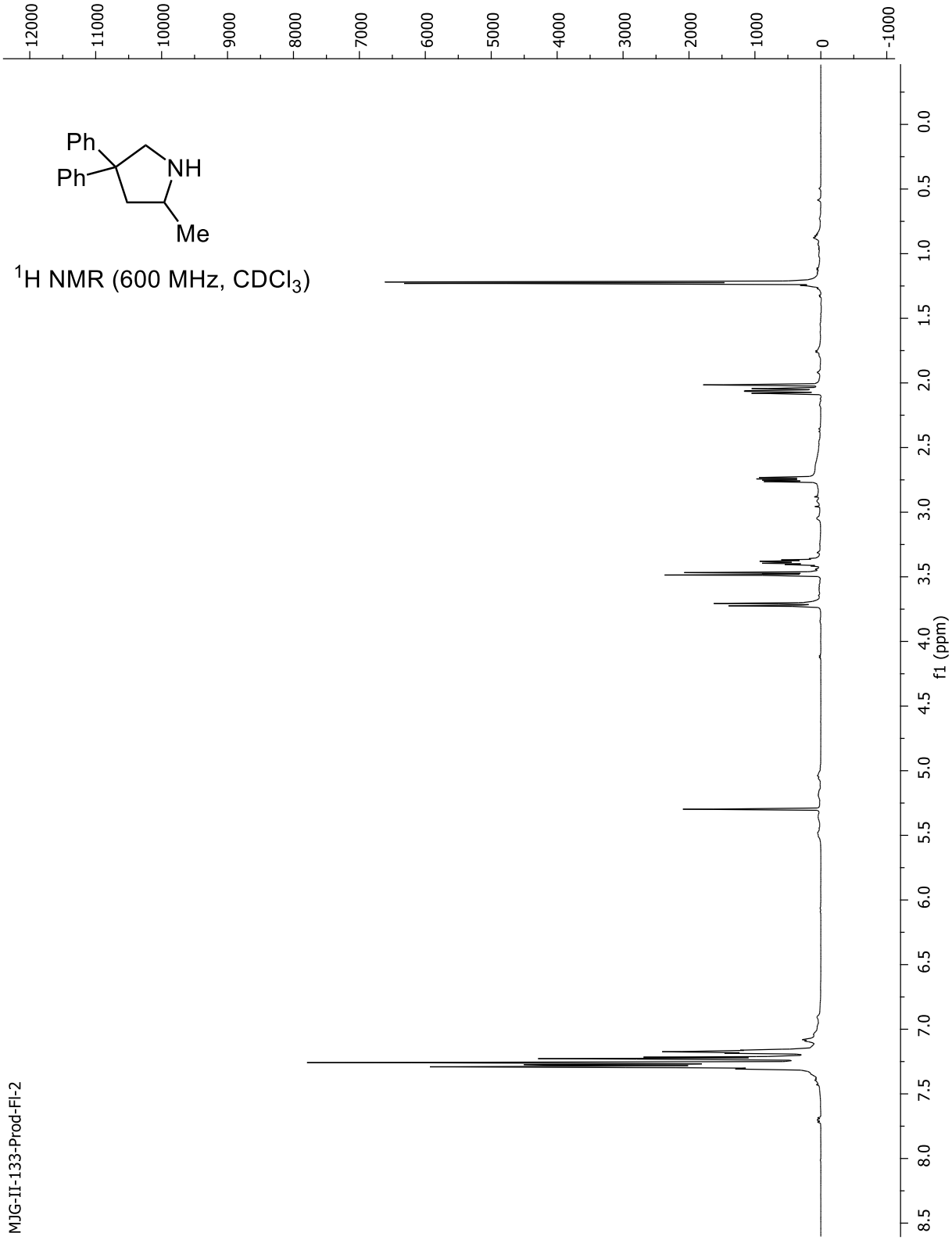
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 7.25 – 7.20 (m, 1H), 4.02 (d, *J* = 12.8 Hz, 1H), 3.14 (d, *J* = 12.8 Hz, 1H), 2.93 – 2.83 (m, 1H), 2.44 – 2.32 (m, 1H), 2.10 (q, *J* = 9.0 Hz, 1H), 1.98 – 1.84 (m, 1H), 1.76 – 1.54 (m, 2H), 1.51 – 1.40 (m, 1H), 1.17 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 129.12, 129.09, 128.15, 126.78, 59.63, 58.35, 54.04, 32.72, 21.47, 19.14.

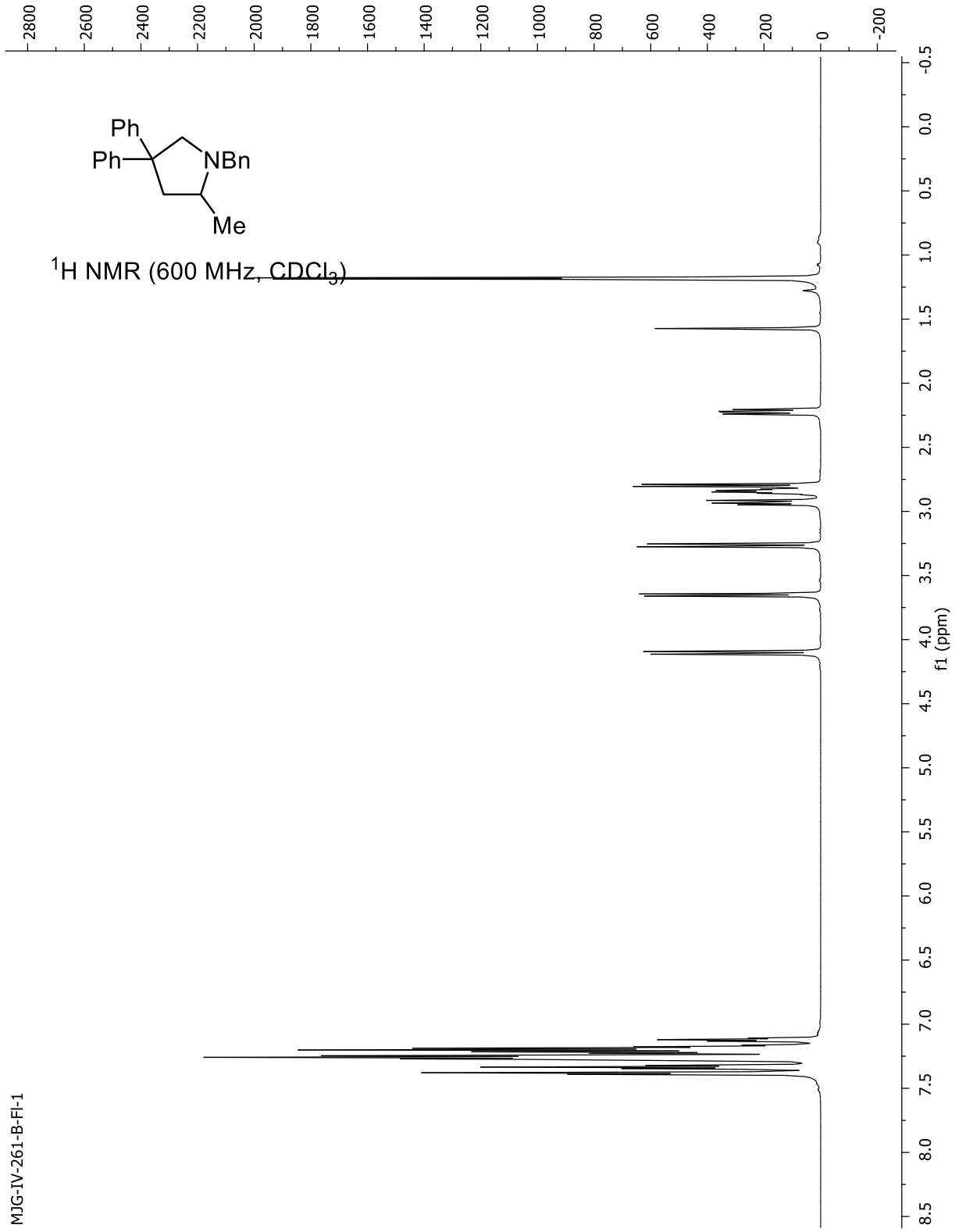


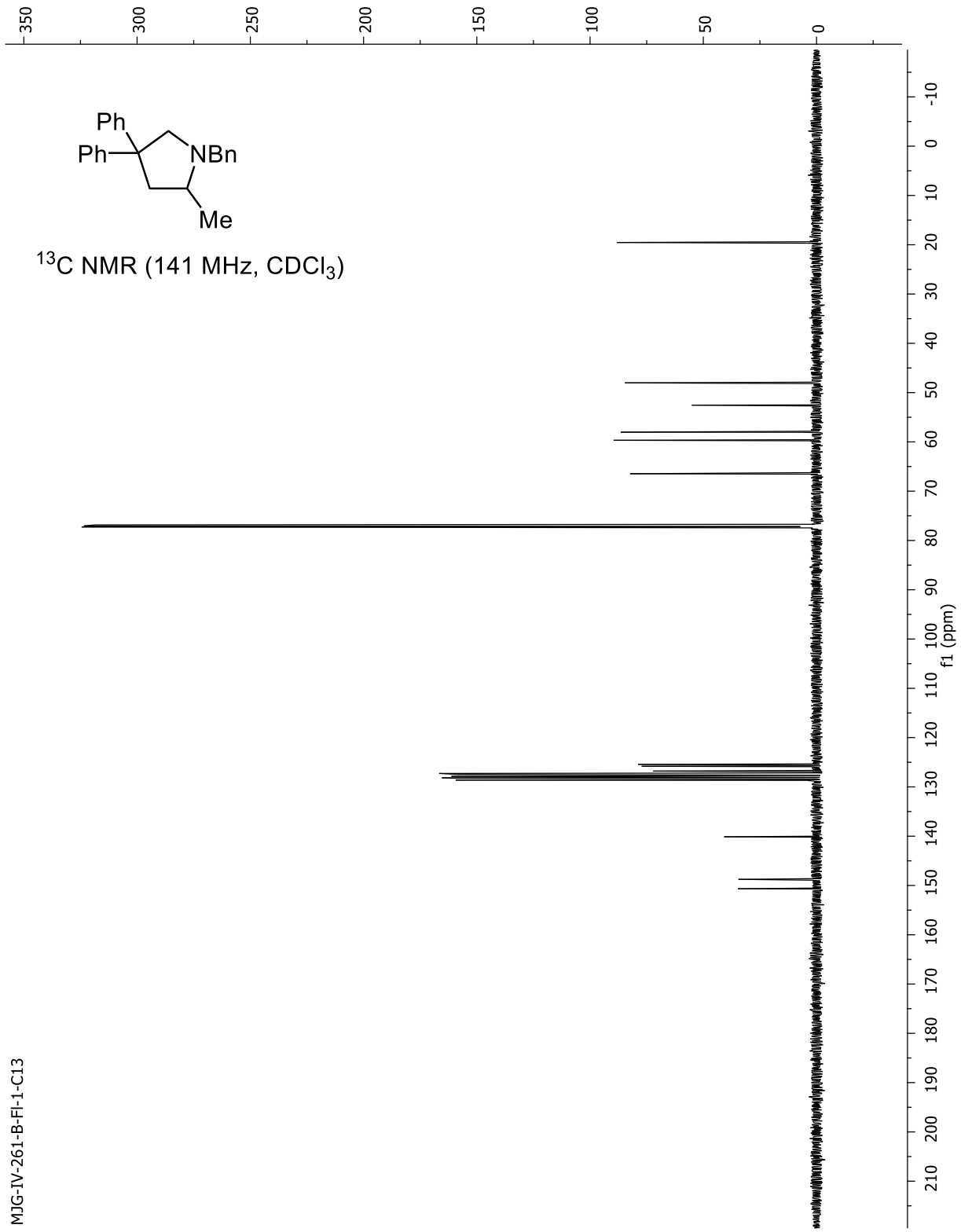
Synthesis of 2-methyl-1-phenylpyrrolidine (26)

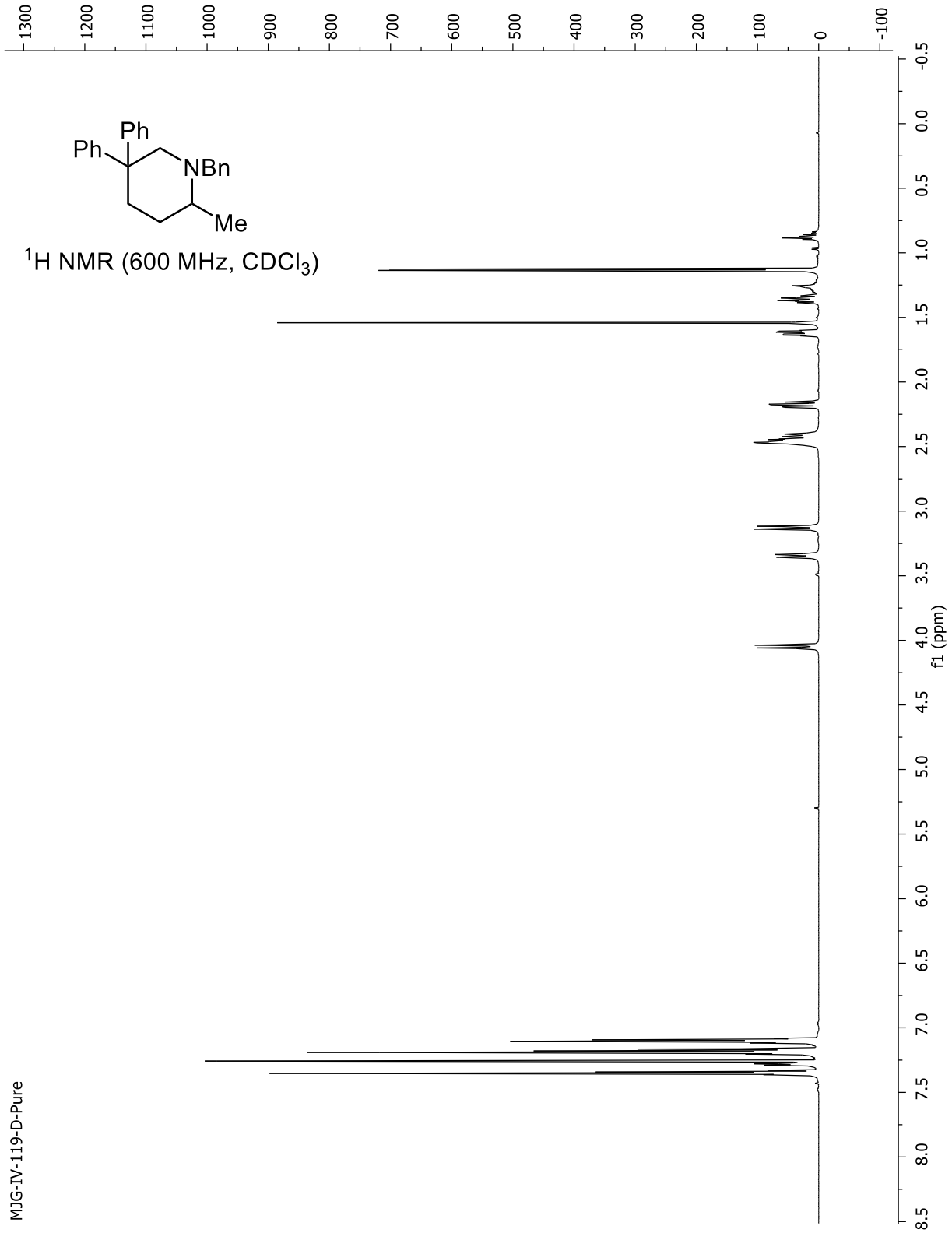
Following the general procedure for (CDC)-Rh-catalyzed intramolecular hydroamination, N-(pent-4-en-1-yl)aniline (17.5 mg, 0.100 mmol) was added to a solution of **^{iPr}CDC-Rh-Cl** (2.7 mg, 0.0050 mmol) and $AgBF_4$ (1.2 mg, 0.005 mmol) in acetonitrile (100 μL, [ ] = 2.0 M). The reaction was sealed and allowed to stir at 80 °C for 48 h. The reaction was concentrated and the resulting oil was purified by SiO_2 column chromatography (20:1 Hex/EtOAc) to afford **26** (12.6 mg, 0.072 mmol, 72% yield) as a colorless oil.

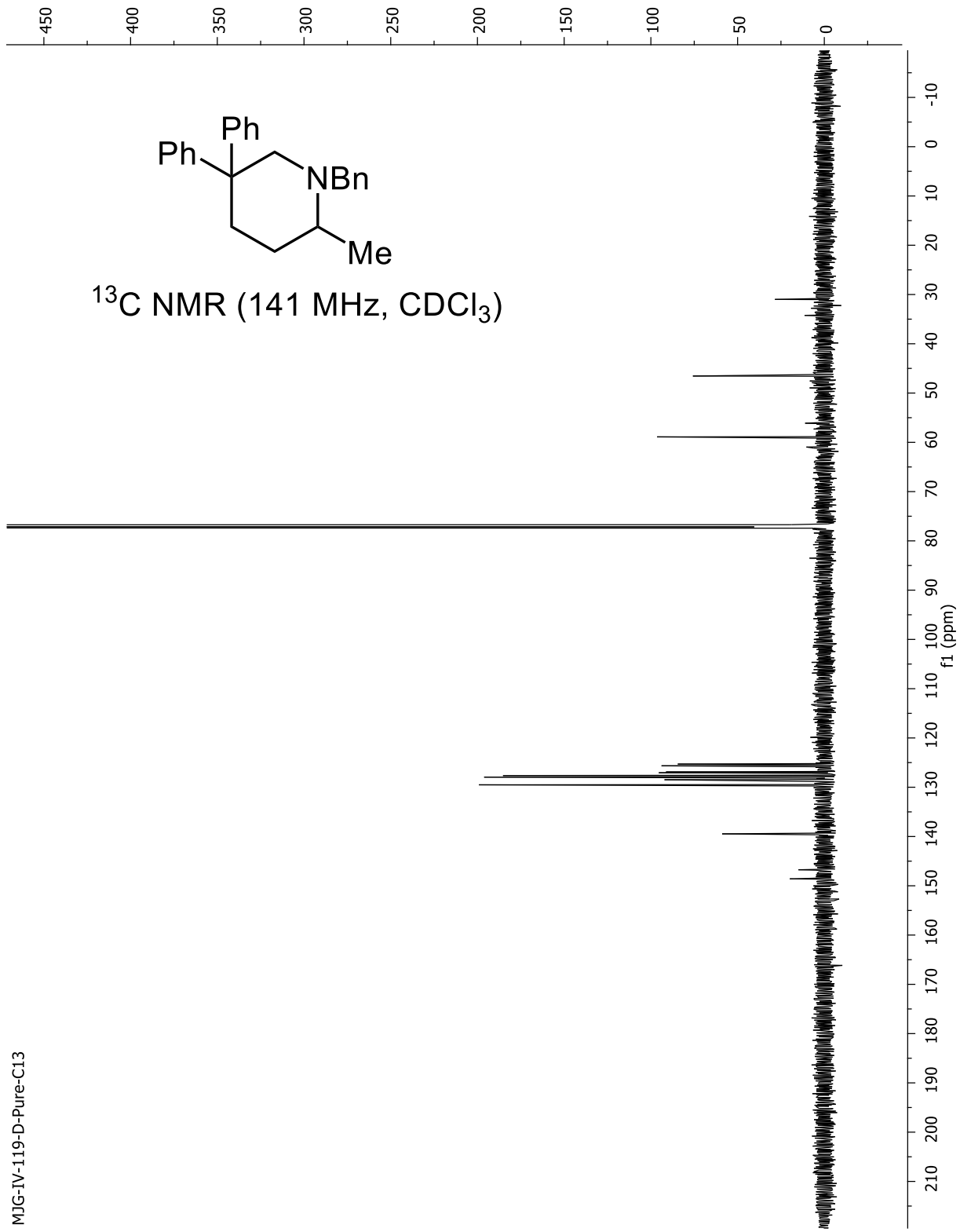
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 7.9 Hz, 2H), 3.91 – 3.83 (m, 1H), 3.44 – 3.39 (m, 1H), 3.19 – 3.11 (m, 1H), 2.13 – 2.00 (m, 2H), 2.00 – 1.92 (m, 1H), 1.72 – 1.67 (m, 1H), 1.17 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.23, 129.17, 129.15, 115.11, 111.75, 111.73, 53.58, 48.14, 33.11, 23.29, 19.37.

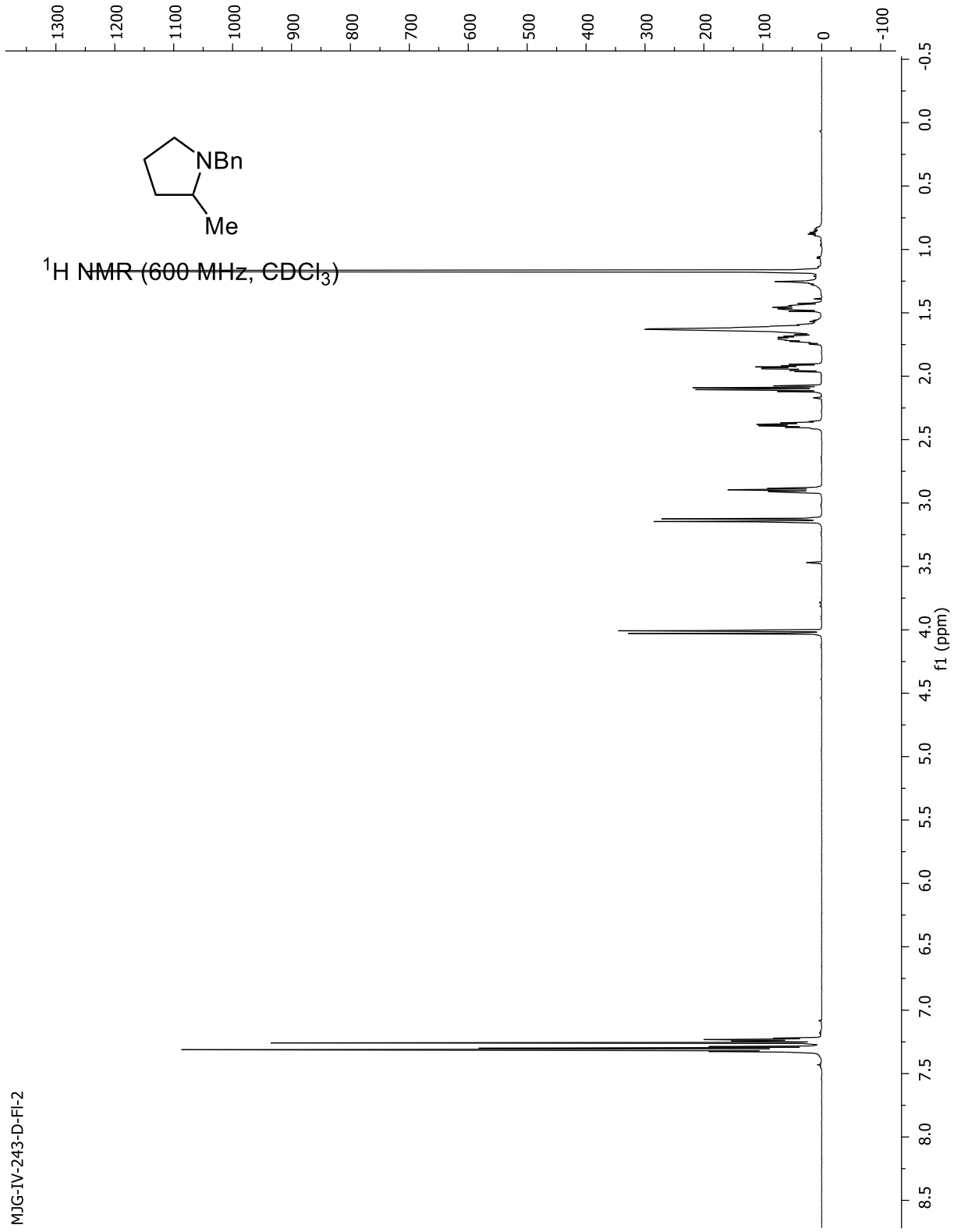

Ph
Ph
NH
Me
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-II-133-Prod-Fl-2
f1 (ppm)

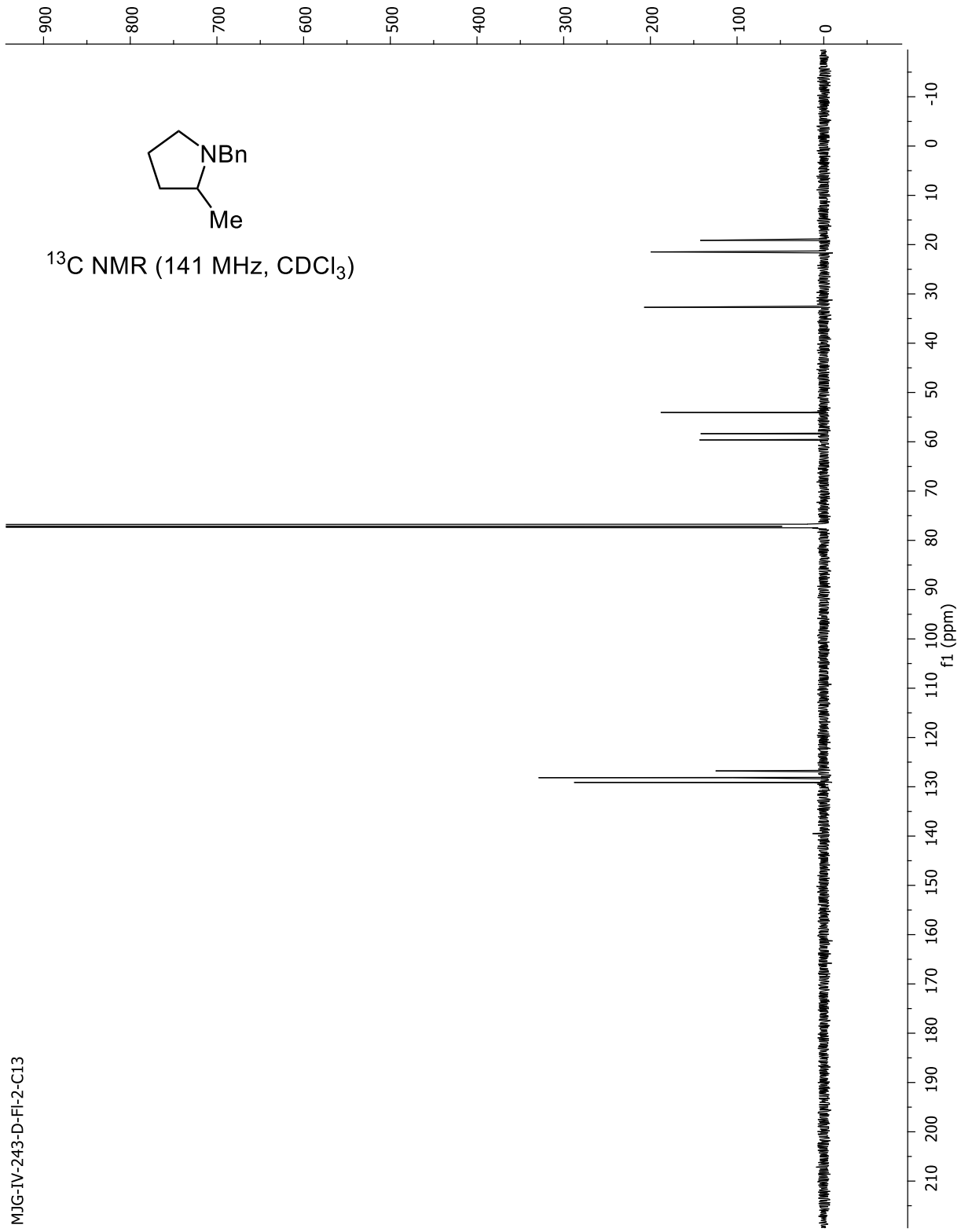

Ph
Ph
NBn
Me
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-IV-261-B-Fl-1
f1 (ppm)

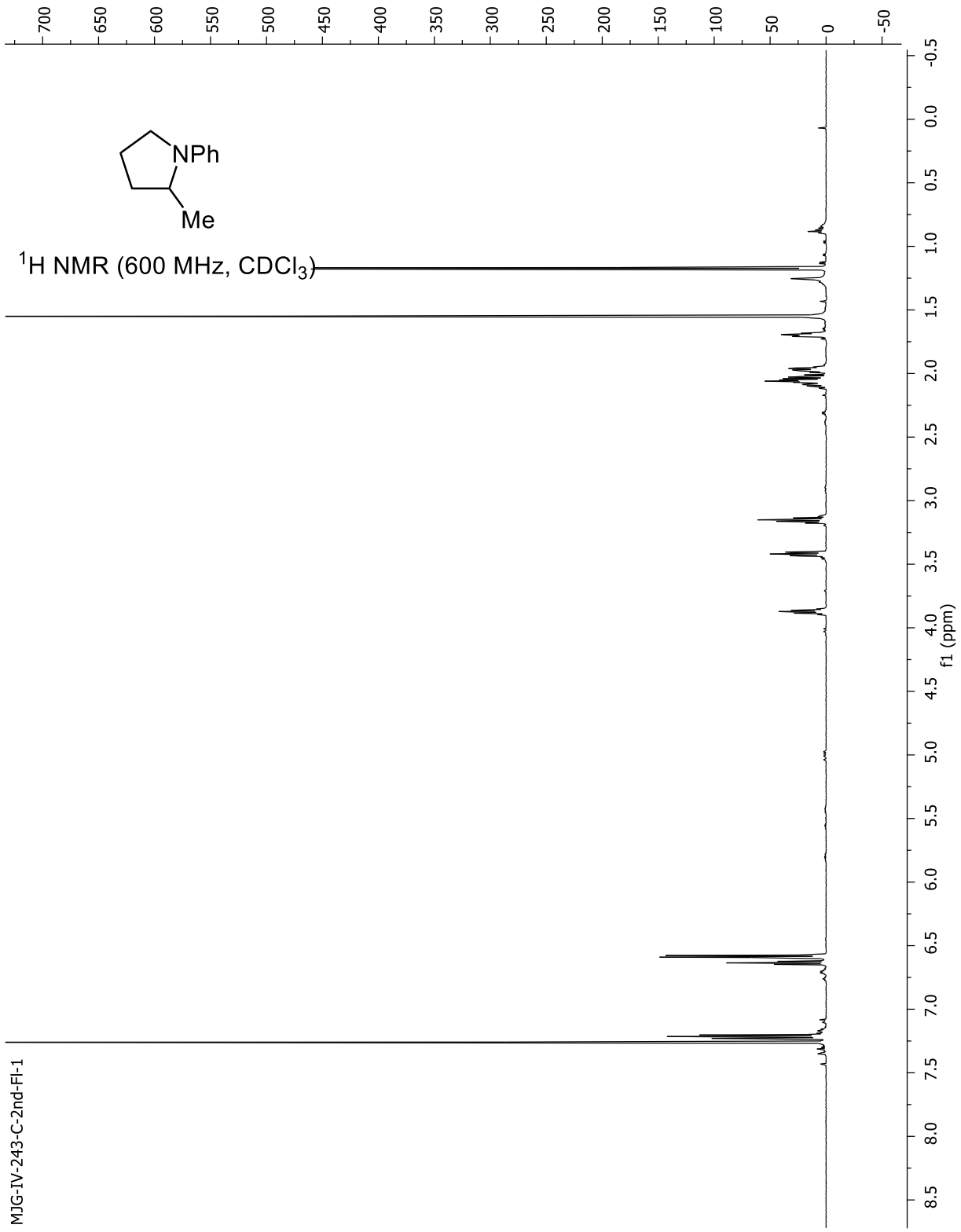

Ph
Ph
NBn
Me
^{13}C NMR (141 MHz, $CDCl_3$)
MJG-IV-261-B-Fl-1-C13
f1 (ppm)

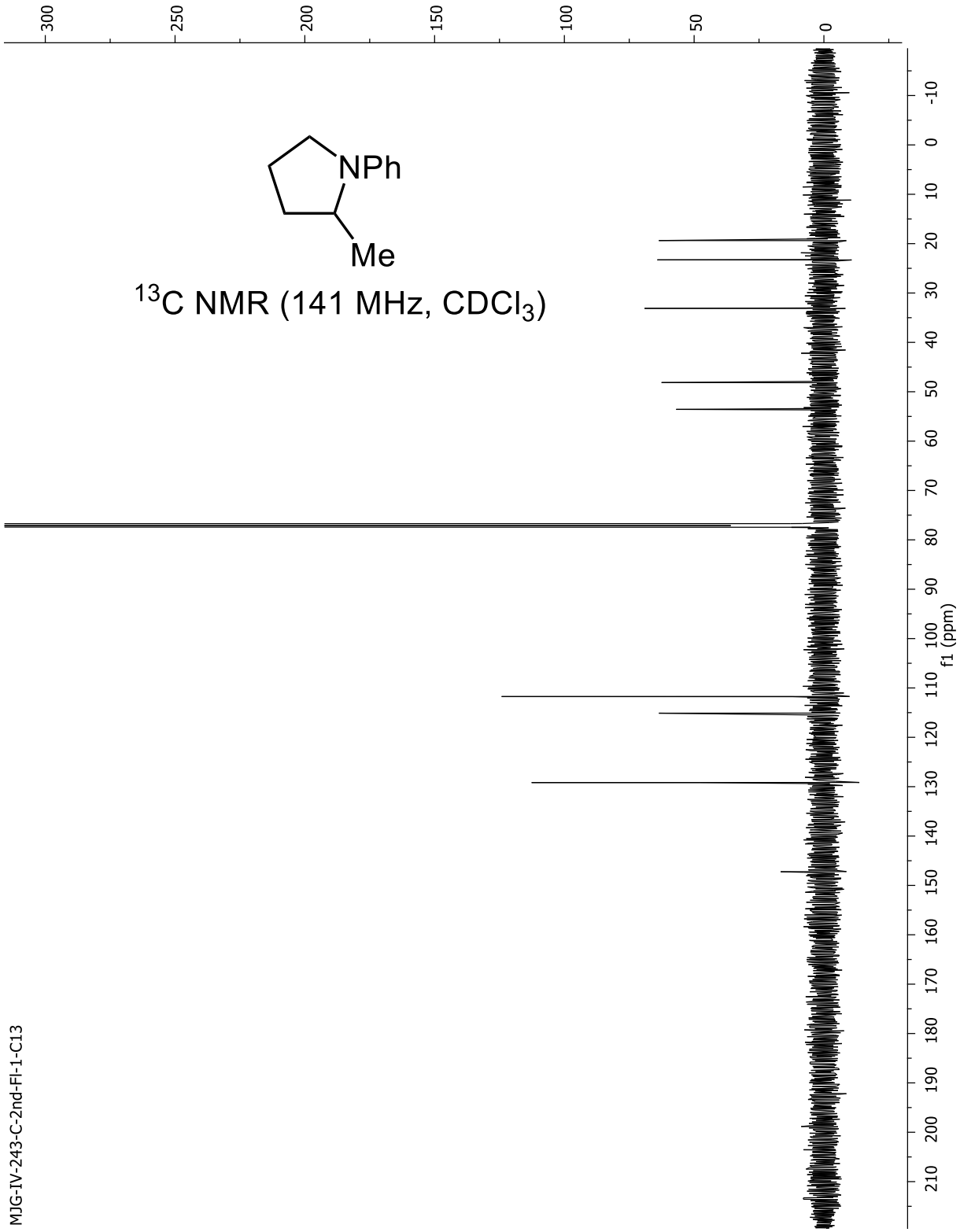

Ph
Ph
NBn
Me
1H NMR (600 MHz, CDCl3)
MJG-IV-119-D-Pure
f1 (ppm)


Ph
Ph
NBn
Me
^{13}C NMR (141 MHz, $CDCl_3$)
MJG-IV-119-D-Pure-C13
f1 (ppm)


NBn
Me
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-IV-243-D-FI-2
f1 (ppm)


NBn
Me
^{13}C NMR (141 MHz, $CDCl_3$)
MJG-IV-243-D-Fl-2-C13
f1 (ppm)


NPh
Me
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-IV-243-C-2nd-Fl-1
f1 (ppm)


NPh
Me
^{13}C NMR (141 MHz, $CDCl_3$)
MJG-IV-243-C-2nd-Fl-1-C13
f1 (ppm)

Section 1.6: Intermolecular Hydroamination with Carbodicarbene-Ligated Rh Complexes

■ **Reagents:**

Acetonitrile – d_3 was purchased from Cambridge Isotope Labs, dried over CaH_2 and stored in a dry box over activated 4 Å molecular sieves.

$AgNO_3$ Doped Silica Gel was prepared as a 1% mixture by weight as described in the literature.[10]

Aniline was purchased from Aldrich, dried on CaH_2, distilled under vacuum, and stored in a dry box freezer at -30ºC.

***p*-Anisidine** was purchased from Alfa Aesar, dried over $CaCl_2$, distilled under vacuum, and stored in a dry box.

Benzylmethylamine was purchased from Alfa Aesar, dried over K_2CO_3, distilled under vacuum, and stored in a dry box.

2-Bromoaniline was purchased from Alfa Aesar, dried over $CaCl_2$, distilled under vacuum, and stored in a dry box.

Chlorobenzene was dried over K_2CO_3, distilled under vacuum and stored over activated 5 Å molecular sieves in a dry box.

Chloroform – d_1 was purchased from Cambridge Isotope Labs, dried over CaH_2 and stored in a dry box over activated 4 Å molecular sieves.

Chloro(1,5-cyclooctadiene)rhodium(I) dimer was purchased from Pressure Chemicals, stored in a dry box and used as received.

Chlorodiisopropyl phosphine was purchased from Acros Organics and used as received.

Chlorodiphenylphosphine was purchased from Alfa Aesar and used as received.

Cyclohexa-1,3-diene was purchased from Alfa Aesar and was distilled and stored under N_2 at -20 °C.

Dichloromethane – d_2 was purchased from Cambridge Isotope Labs, dried over CaH_2 and stored in a dry box over activated 4 Å molecular sieves.

Dibenzyl amine was purchased from Alfa Aesar, passed through a plug of alumina onto activated 5 Å molecular sieves for 24 h and transferred to a vial in a dry box.

Di-*n*-propyl amine was purchased from Aldrich, dried over KOH, and distilled under reduced pressure and stored in a dry box.

Morpholine was purchased from Alfa Aesar, dried over KOH, distilled under reduced pressure and stored in a dry box.

Pyrrolidine was purchased from Alfa Aesar, dried over Na, distilled under reduced pressure and stored in a dry box.

Silver tetrafluoroborate was purchased from Strem, stored in a dry box, and used without further purification.

4-(Trifluoromethyl)aniline was purchased from Alfa Aesar, distilled over CaH_2, and stored in at -30 ºC in a dry box freezer.

Sodium methoxide was purchased from Strem, stored in a dry box, and used as received.

o-Toluidine was purchased from Alfa Aesar, dried over CaH_2, distilled under vacuum, and stored in a dry box.

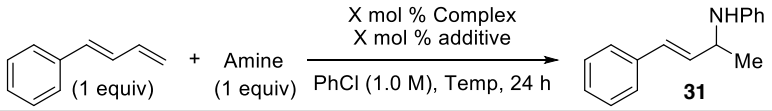
Tetrafluoroboric acid was purchased from Alfa Aesar and used as received.

Triethylamine was purchased from Fisher and dried over CaH_2 and distilled immediately prior to use.

■ **General procedure for the (CDC)-Rh-catalyzed hydroaminations of phenyl 1,3-butadiene in SI Tables 1 and 2.**

In an N_2 filled dry box, an 8-mL vial equipped with a stir bar was charged with the appropriate (CDC)-RhCl complex and silver salt. Chlorobenzene was added via syringe, the vial was capped and the mixture allowed to stir for 1 h at 22 °C. Reactions that did not require the addition of (CDC)-RhCl were also allowed to stir for 1 h at 22 ºC for consistency. Aniline was added via syringe, followed by addition of the phenyl 1,3-butadiene. The vial was capped with a Teflon® lined lid or septum cap, taped with electrical tape and brought outside the dry box. Any volatile acids ($HBF_4.OEt_2$ and HCl-dioxane) were added via syringe through the Teflon® septa under an atmosphere of N_2. The reaction was allowed to warm to the appropriate temperature and stir for 24 h. The reaction was allowed to cool and an aliquot was taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The remaining solvent was removed *in vacuo*. The products were purified by SiO_2 column chromatography.

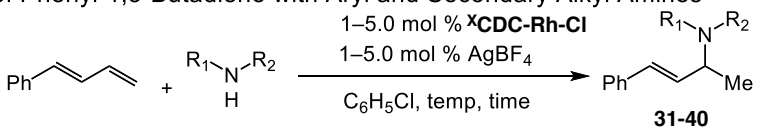
Table 1. Control reactions



Entry	Complex; mol %	Additive; mol %	Amine	Temp (°C)	Conv of Diene (%)	Conv to Product (%)[1]	Isolated Yield (%)
1	^{Ph}PCP-Rh-Cl; 5	-	aniline	80	**5**	**<2**	**-**
2	^{iPr}PCP-Rh-Cl; 5	-	aniline	80	**4**	**<2**	**-**
3	^{Ph}PCP-Rh-Cl; 5	$AgBF_4$; 5	aniline	80	**85**	**75**	**67**
4	^{iPr}PCP-Rh-Cl; 5	$AgBF_4$; 5	aniline	80	**81**	**73**	**65**
5	^{Ph}PCP-Rh-Cl; 5	$AgPF_6$; 5	aniline	80	**81**	**68**	**59**
6	^{Ph}PCP-Rh-Cl; 5	$AgSbF_6$; 5	aniline	80	**91**	**40**	**31**
7	^{Ph}PCP-Rh-Cl; 5	AgOTf; 5	aniline	80	**87**	**60**	**51**
8	^{Ph}PCP-Rh-Cl; 5	$AgBF_4$; 5, HBF_4; 20	aniline	80	**96**	**30**	**-**
9	^{Ph}PCP-Rh-Cl; 1	$AgBF_4$; 1	aniline	80	**83**	**62**	**59**
10	-	HBF_4; 5	aniline	80	**12**	**<2**	**-**
11	-	HCl; 50	aniline	80	**27**	**<2**	**-**
12	-	HCl; 50	aniline	120	**75**	**<2**	**-**
13	-	$AgBF_4$; 5	aniline	80	**12**	**<2**	**-**
14	-	NH_4BF_4; 20	aniline	80	**12**	**<2**	**-**
15	-	NH_4BF_4; 20	pyrrolidine	80	**31**	**<2**	**-**

All reactions were run according to the procedure outlined above. 1) The conversion to product is based off of an NMR conversion with an internal standard of DMF.

Table 2. Initial catalyst screen for (CDC)-Rh-Catalyzed Hydroaminations of Phenyl-1,3-Butadiene with Aryl and Secondary Alkyl Amines[a]

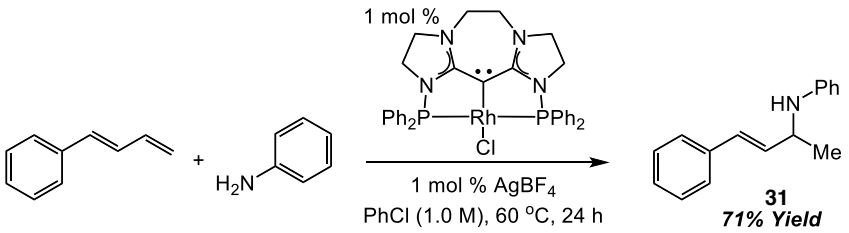


entry	amine; product	complex; mol %	temp (°C)	time (h)	conv (%)[b]
1	$C_6H_5NH_2$; **31**	**Ph**; 1	60	24	88
2	$C_6H_5NH_2$; **31**	**iPr**; 1	60	48	73
3	*p*-$CF_3C_6H_4NH_2$; **32**	**Ph**; 2	60	48	42
4	*p*-$CF_3C_6H_4NH_2$; **32**	**iPr**; 2	60	24	96
5	*p*-$MeOC_6H_4NH_2$; **33**	**Ph**; 2	60	48	38
6	*p*-$MeOC_6H_4NH_2$; **33**	**iPr**; 3	60	48	68
7	*o*-$BrC_6H_4NH_2$; **34**	**Ph**; 3	50	48	86
8	*o*-$BrC_6H_4NH_2$; **34**	**iPr**; 2	50	24	39
9	*o*-MeC_6H_4-NH_2; **35**	**Ph**; 5	60	48	55
10	*o*-MeC_6H_4-NH_2; **35**	**iPr**; 5	60	48	89
11	morpholine; **36**	**Ph**; 3	80	48	90
12	morpholine; **36**	**iPr**; 3	80	48	92
13	pyrrolidine; **37**	**Ph**; 5	80	48	80
14	pyrrolidine; **37**	**iPr**; 5	80	48	<2
15	Bn_2NH; **38**	**Ph**; 2	90	48	10
16	Bn_2NH; **38**	**iPr**; 2	80	24	58
17	Bn(Me)NH; **39**	**Ph**; 5	80	36	61
18	Bn(Me)NH; **39**	**iPr**; 5	80	48	74
19	*n*-Pr_2NH; **40**	**Ph**; 5	80	48	14
20	*n*-Pr_2NH; **40**	**iPr**; 5	80	48	13

a. All reactions performed under N_2 atm; >98% site selectivity in all cases, see optimized reactions for concentrations and diene equivalents. b. Values determined by analysis of 400 or 600 MHz ^1H NMR spectra of unpurified mixtures.

■ **General procedure for Rh-catalyzed hydroaminations in Tables 1.6.2-1 and 1.6.3-1:** In an N_2 filled dry box, an 8-mL vial equipped with a stir bar was charged with (CDC)-Rh-Cl, $AgBF_4$, and chlorobenzene. The vial was capped and the mixture allowed to stir at 22 °C for 1 h, to generate a heterogeneous, purple or blue solution. The appropriate amine was added via syringe (or weighed into the vial) followed by the 1,3-diene. The vial was capped with a Teflon® lined lid, sealed with electrical tape, brought outside the dry box, and heated to the indicated temperature for the appropriate amount of time. The reaction was allowed to cool to 22 °C, and

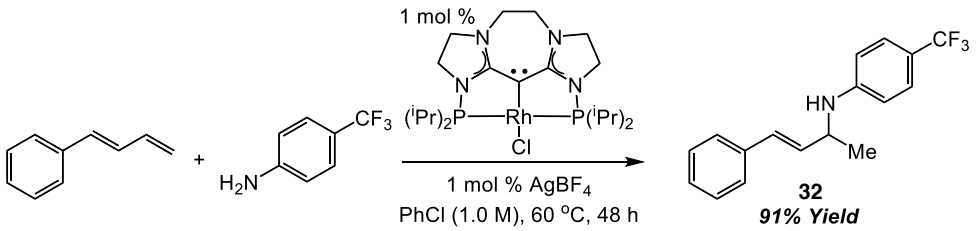
an aliquot was taken to determine the conversion by ^{1}H NMR using an internal DMF standard. The remaining solvent was removed *in vacuo*. The products were purified by SiO_2 column chromatography to give isolated yields.



Synthesis of *(E)*-N-(4-phenylbut-3-en-2-yl)aniline (31)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and phenyl 1,3-butadiene (26.0 mg, 0.200 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (1.4 mg, 0.0020 mmol) and $AgBF_4$ (0.4 mg, 0.0020 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 24 h. The resulting oil was purified by SiO_2 column chromatography (20:1 Hex/Et_2O) to afford **31** (31.3 mg, 0.142 mmol, 71% yield) as a colorless oil.

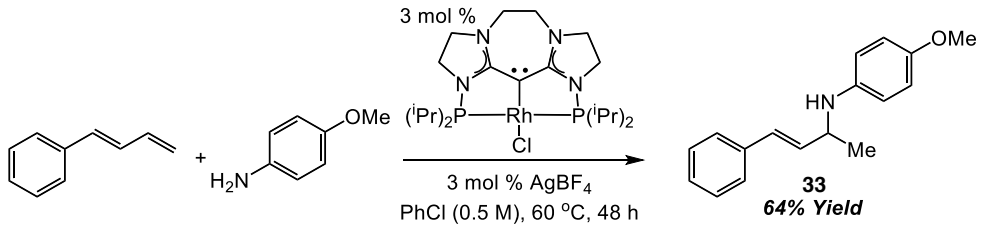
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 (2H, d, *J* = 7.4 Hz), 7.30 (2H, t, *J* = 7.6 Hz), 7.22 (1H, t, *J* = 7.3 Hz), 7.17 (2H, t, *J* = 8.0 Hz), 6.69 (1H t, *J* = 7.3 Hz), 6.66 (2H, d, *J* = 7.9 Hz), 6.58 (1H, d, *J* = 16.0 Hz), 6.22 (1H, dd, *J* = 15.9, 5.9 Hz), 4.14-4.17 (1H, m), 3.72 (1H, bs), 1.41 (3H, d, *J* = 6.6 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 147.53, 137.09, 133.31, 129.39, 129.34, 128.65, 127.49, 126.45, 117.46, 113.50, 50.98, 22.25. IR (ν/cm^{-1}): 3412 (br, m), 3081 (w), 3056 (w), 3023 (m), 2968 (m), 2926 (w), 2867 (w), 1602 (s), 1506 (s), 1456 (w), 1429 (w), 1317 (m), 1257 (m), 1178 (m), 1156 (w). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{16}H_{18}N^+$ 224.14, found: 224.04.



Synthesis of *(E)*-N-(4-phenylbut-3-en-2-yl)-4-(trifluoromethyl)aniline (32)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, 4-(trifluoromethyl)aniline (32.2 mg, 0.200 mmol) and phenyl 1,3-butadiene (31.2 mg, 0.240 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (1.4 mg, 0.0020 mmol) and $AgBF_4$ (0.4 mg, 0.0020 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M) and the reaction allowed to stir at 60 ºC for 48 h. The resulting oil was purified by SiO_2 column chromatography (10:1 Hex/EtOAc) to afford **32** (53.0 mg, 0.182 mmol, 91% yield) as a colorless oil.

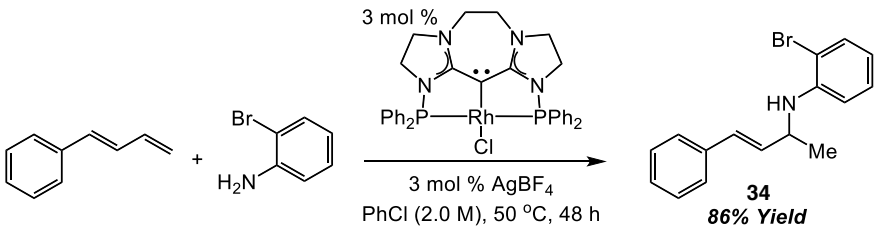
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 (2H, d, *J* = 8.4 Hz), 7.38 (2H, dd, *J* = 8.2, 1.2 Hz), 7.33 (2H, t, *J* = 7.8 Hz) 7.25 (1H, tt, *J* = 7.2, 1.8 Hz), 6.66 (2H, d, *J* = 8.4 Hz), 6.58 (1H, d, *J* = 6.2 Hz), 6.20 (1H, dd, *J* = 15.9, 5.7 Hz), 4.19-4.22 (1H, m), 4.1 (1H, bs) 1.45 (3H, d, *J* = 6.6 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 149.75, 131.95, 129.72, 128.56, 127.57, 126.52 (q, *J* = 2.5 Hz), 126.32, 124.97 (q, *J* = 223.8 Hz), 118.68 (q, *J* = 27.5 Hz), 112.38, 50.53, 21.91. ^{19}F NMR (564 MHz, $CDCl_3$): δ 60.89. IR (ν/cm^{-1}): 3418 (br, s), 3083 (w), 3062 (w), 3027 (m), 2973 (m), 2928 (m), 2871 (m), 1616 (s), 1531 (s), 1491 (w), 1327 (s), 1266 (m), 1188 (m), 1159 (m), 1110 (s). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{17}H_{17}NF_3^+$ 292.13, found: 292.06.



Synthesis of *(E)*-4-methoxy-N-(4-phenylbut-3-en-2-yl)aniline (33)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, 4-methoxyaniline (24.6 mg, 0.200 mmol) and phenyl 1,3-butadiene (26.0 mg, 0.200 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (3.3 mg, 0.0060 mmol) and $AgBF_4$ (1.2 mg, 0.0062 mmol) in chlorobenzene (400 μL, [ ] = 0.500 M), and the reaction allowed to stir at 60 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (10:1 Hex/EtOAc) to afford **33** (32.5 mg, 0.128 mmol, 64% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 (2H, dd, *J* = 8.1, 1.2 Hz), 7.31 (2H, t, *J* = 7.8 Hz), 7.23 (1H, tt, *J* = 7.2, 1.2 Hz), 6.77-6.80 (2H, m), 6.63-6.66 (2H, m), 6.58 (1H, d, *J* = 15.6 Hz), 6.23 (1H, dd, *J* = 16.2, 6.0 Hz), 4.07-4.10 (1H, m), 3.75 (3H, s), 1.40 (3H, d, *J* = 6.6 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 152.04, 141.56, 136.98, 133.53, 129.19, 128.47, 127.27, 126.26, 114.89, 114.76, 55.72, 51.80, 22.09. IR (ν/cm^{-1}): 3396 (br, m), 3059 (w), 3025 (m), 2964 (m), 2928 (m), 2831 (m), 1502 (s), 1448 (m), 1291 (m), 1234 (s), 1177 (m), 1038 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{17}H_{20}NO^+$ 254.15, found: 254.05.

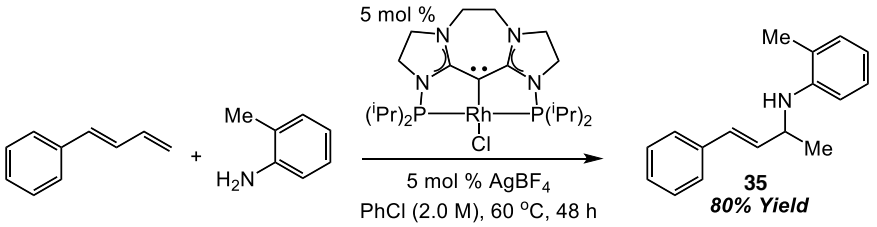


Synthesis of *(E)*-2-bromo-N-(4-phenylbut-3-en-2-yl)aniline (34)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, 2-bromoaniline (34.4 mg, 0.200 mmol) and phenyl 1,3-butadiene (39.0 mg, 0.300 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (4.1 mg, 0.0059 mmol) and $AgBF_4$ (1.2 mg, 0.0062 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 50 °C for 48 h. The resulting oil was

purified by SiO_2 column chromatography (15:1 Hex/Et_2O) to afford **34** (51.2 mg, 0.172 mmol, 86% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (1H, dd, *J* = 7.9, 1.4 Hz), 7.35-7.37 (2H, m), 7.30 (2H, t, *J* = 7.3 Hz), 7.22 (1H, tt, *J* = 6.9, 2.0 Hz), 7.13 (1H, td, *J* = 7.7, 1.3 Hz), 6.69 (1H, dd, *J* = 8.2, 1.1 Hz), 6.53-6.58 (2H, m), 6.21 (1H, dd, *J* = 15.9, 5.9 Hz), 4.41 (1H, bd, *J* = 6.1 Hz), 4.15-4.20 (1H, m), 1.47 (3H, d, *J* = 6.6 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.15, 136.78, 132.47, 132.34, 129.54, 128.53, 128.39, 127.46, 126.36, 117.72, 112.45, 109.72, 50.98, 22.14. IR (ν/cm^{-1}): 3409 (br, m), 3060 (w), 3025 (m), 2967 (m), 2922 (m), 2867 (w), 1595 (s), 1504 (s), 1459 (m), 1426 (m), 1319 (s), 1165 (m), 1018 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{16}H_{17}BrN^+$ 302.05, found: 302.00.

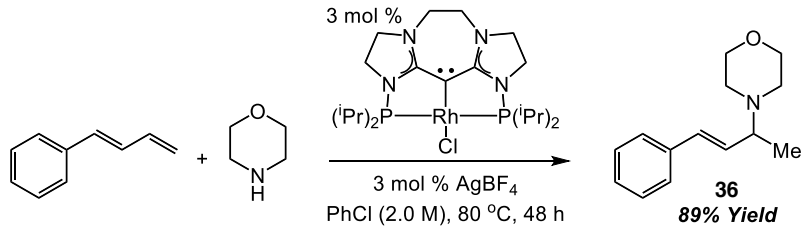


Synthesis of *(E)*-2-methyl-N-(4-phenylbut-3-en-2-yl)aniline (35)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, *o*-toluidine (21.4 mg, 0.200 mmol) and phenyl 1,3-butadiene (39.0 mg, 0.300 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (5.5 mg, 0.010 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 60 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (15:1 Hex/Et_2O) to afford **35** (38.0 mg, 0.160 mmol, 80% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 (2H, d, *J* = 7.2 Hz), 7.30 (2H, t, *J* = 7.2 Hz), 7.22 (1H, t, *J* = 7.8 Hz), 6.66 (2H, m), 6.58 (1H, d, *J* = 16.2 Hz), 6.25 (1H, dd, *J* = 16.2, 6.0 Hz), 4.20 (1H, bm),

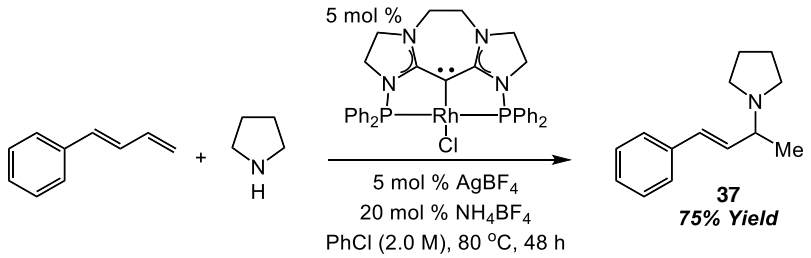
3.26 (1H, s), 2.19 (3H, s), 1.46 (3H, d, J = 7.2 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 145.47, 137.14, 133.51, 130.23, 129.37, 128.65, 127.48, 127.24, 126.48, 121.84, 116.99, 110.97, 50.85, 22.45, 17.77. IR (ν/cm^{-1}): 3429 (br, m), 3056 (w), 3024 (m), 2967 (m), 2924 (m), 2861 (w), 1605 (s), 1585 (m), 1510 (s), 1477 (w), 1445 (w), 1371 (m), 1314 (m), 1259 (m), 1163 (m), 1050 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{17}H_{20}N^+$ 238.16, found: 238.13.



Synthesis of *(E)*-4-(4-phenylbut-3-en-2-yl)morpholine (36)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, morpholine (17.4 mg, 0.200 mmol) and phenyl 1,3-butadiene (39.0 mg, 0.300 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (3.5 mg, 0.0064 mmol) and $AgBF_4$ (1.2 mg, 0.0062 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 80 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 CH_2Cl_2:MeOH) to afford **36** (38.8 mg, 0.178 mmol, 89% yield) as a yellow oil.

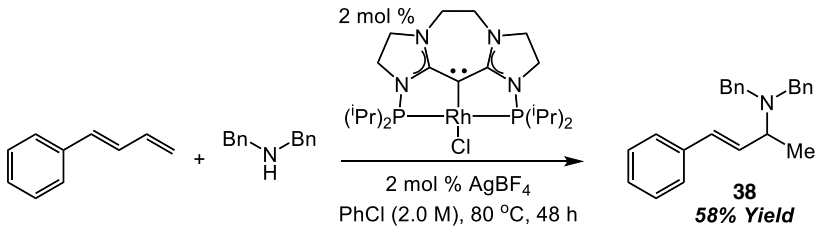
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 (2H, d, J = 7.2 Hz), 7.31 (2H, t, J = 7.8 Hz), 7.23 (1H, t, J = 7.2 Hz), 6.46 (1H, d, J = 16.2 Hz), 6.17 (1H, dd, J = 15.9, 8.1 Hz), 3.74 (4H, t, J = 6.6 Hz), 3.01-3.04 (1H, m), 2.57 (4H, bt, J = 5.1Hz), 1.26 (3H, d, J = 6.6 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 137.04, 132.27, 131.36, 128.72, 127.61, 126.40, 67.36, 63.27, 50.92, 17.90. IR (ν/cm^{-1}): 3058 (w), 3025 (m), 2961 (s), 2891 (w), 2852 (m), 2806 (m), 2755 (w), 2687 (w), 1494 (m), 1448 (m), 1315 (w), 1266 (m), 1142 (w), 1119 (s), 1069 (w), 1040 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{14}H_{20}NO^+$ 218.15, found: 218.01.



Synthesis of *(E)*-1-(4-phenylbut-3-en-2-yl)pyrrolidine (37)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, pyrrolidine (14.2 mg, 0.200 mmol), phenyl 1,3-butadiene (52.1 mg, 0.400 mmol) and NH_4BF_4 (4.2 mg, 0.040 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 80 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (50:1 CH_2Cl_2/MeOH) to afford **37** (30.2 mg, 0.150 mmol, 75% yield) as a colorless oil.

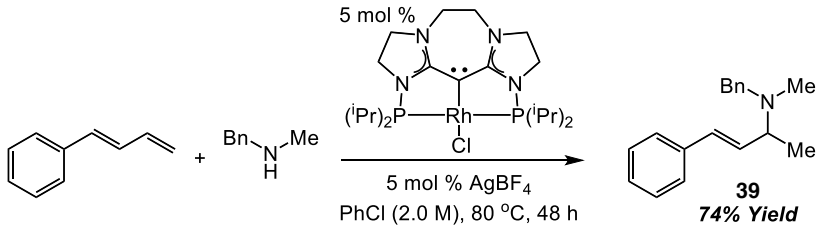
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 (2H, d, *J* = 7.3 Hz), 7.29 (2H, t, *J* = 7.7 Hz), 7.21 (1H, t, *J* = 7.3 Hz), 6.47 (1H, d, *J* = 15.8 Hz), 6.24 (1H, dd, *J* = 15.8, 8.5 Hz), 2.90-2.92 (1H, m), 2.56-2.61 (4H, m), 1.77-1.82 (4H, m), 1.3 (3H, d, *J* = 6.5 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 137.33, 134.07, 129.86, 128.70, 127.44, 126.41, 63.26, 52.40, 23.50, 21.16. IR (ν/cm^{-1}): 3057 (w), 3025 (m), 2968 (s), 2929 (w), 2873 (m), 2781 (s), 1495 (m), 1457 (m), 1370 (w), 1311 (m), 1167 (m), 1139 (m), 1070 (m), 1025 (m). LRMS (ES$^+$) [M+H]$^+$ calcd for $C_{14}H_{20}N^+$ 202.16, found: 202.13.



Synthesis of *(E)*-N,N-dibenzyl-4-phenylbut-3-en-2-amine (38)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, dibenzylamine (39.4 mg, 0.200 mmol) and phenyl 1,3-butadiene (52.0 mg, 0.400 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (2.2 mg, 0.0040 mmol) and $AgBF_4$ (0.80 mg, 0.0041mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 80 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (5:1 Hex/EtOAc) to afford **38** (38.2 mg, 0.116 mmol, 58% yield) as a colorless oil.

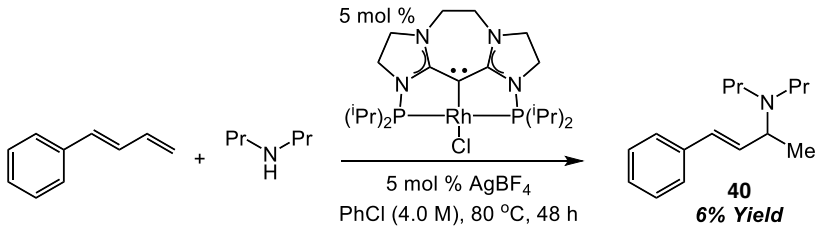
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41-7.44 (6H, m), 7.32-7.36 (6H, m), 6.46 (1H, d, *J* = 16.1 Hz), 6.34 (1H, dd, *J* = 13.5, 6.7 Hz), 3.73 (2H, d, *J* = 14.0 Hz), 3.62 (2H, d, *J* = 13.9 Hz), 3.49-3.52 (1H, m), 1.32 (3H, d, *J* = 6.7 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 140.58, 137.30, 131.64, 130.93, 128.53, 128.51, 128.17, 127.25, 126.67, 126.25, 54.53, 53.64, 15.80. IR (ν/cm^{-1}): 3061 (w), 3025 (m), 2967 (m), 2928 (m), 2799 (m), 1601 (m), 1494 (m), 1451 (m), 1366 (m), 1144 (m), 1057 (m), 1024 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{24}H_{26}N^+$ 328.21, found: 328.17.



Synthesis of *(E)*-N-benzyl-N-methyl-4-phenylbut-3-en-2-amine (39)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, benzylmethylamine (24.2 mg, 0.200 mmol) and phenyl 1,3-butadiene (39.0 mg, 0.300 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (5.5 mg, 0.010 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 80 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (10:1 Hex/EtOAc to 100% EtOAc) to afford **39** (37.0 mg, 0.148 mmol, 74% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 (2H, d, *J* = 7.2 Hz), 7.32-7.37 (6H, m), 7.23-7.27 (2H, m), 6.49 (1H, d, *J* = 16.2 Hz), 6.33 (1H, dd, *J* = 16.2, 7.2 Hz), 3.67 (1H, d, *J* = 13.2 Hz), 3.53 (1H, d, *J* = 13.2 Hz), 3.37-3.40 (1H, m), 2.24 (3H, s), 1.32 (3H, d, *J* = 6.6Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 140.06, 137.40, 132.25, 130.89, 129.00, 128.68, 128.35, 127.41, 126.91, 126.40, 60.52, 58.39, 38.06, 17.11. IR (ν/cm^{-1}): 3082 (w), 3060 (w), 3026 (m), 2970 (s), 2932 (w), 2876 (w), 2839 (m), 2788 (s), 1601 (m), 1494 (m), 1450 (s), 1368 (m), 1311 (m), 1209 (w), 1156 (w), 1129 (w), 1073 (m), 1027 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{18}H_{22}N^+$ 252.17, found: 252.07.

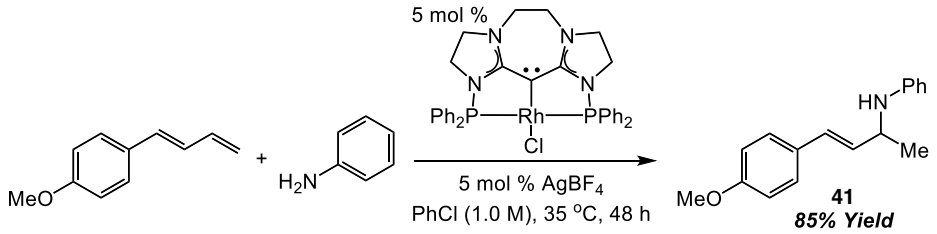


Synthesis of *(E)*-4-phenyl-*N*,*N*-dipropylbut-3-en-2-amine (40)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, di-*n*-propyl amine (20.2 mg, 0.200 mmol) and phenyl 1,3-butadiene (39.0 mg, 0.300 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (5.5 mg, 0.010 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (50 μL, [ ] = 4.00 M), and the reaction allowed to stir at 80 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (100% CH_2Cl_2 to 20:1 CH_2Cl_2:MeOH) to afford **40** (2.7 mg, 0.012 mmol, 6% yield) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (2H, d, *J* = 9.1 Hz), 7.32-7.37 (3H, m), 6.74 (1H, d, *J* = 15.9 Hz), 6.26 (1H, dd, *J* = 15.9, 8.5 Hz), 4.10-4.17 (1H, m), 3.09-3.11 (4H, m), 1.82 (4H, quintet, *J* = 8.2 Hz), 1.60 (3H, d, *J* = 6.7 Hz), 0.99 (6H, t, *J* = 7.3 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 138.03, 134.83, 129.35, 129.00, 127.18, 121.68, 62.89, 53.04, 18.24, 16.19, 11.2. IR

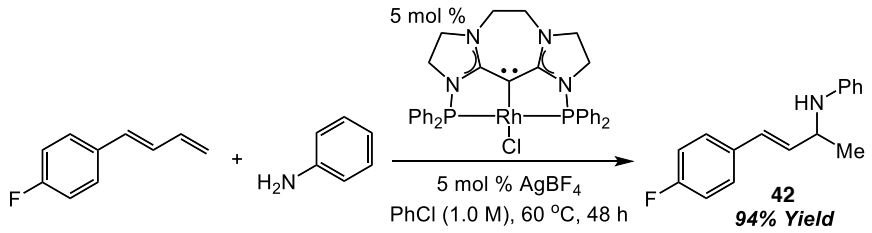
(ν/cm^{-1}): 3140 (br, m), 2972 (m), 2932 (m), 2883 (w), 2852 (w), 1652 (m), 1457 (m), 1061 (s). LRMS (ES$^+$) [M+H]$^+$ calcd for $C_{16}H_{26}N^+$ 232.21, found: 232.18.



Synthesis of *(E)*-N-(4-(4-methoxyphenyl)but-3-en-2-yl)aniline (41)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (64.1 mg, 0.400 mmol) were added to a solution of ^{Ph}**CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 35 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 Hex/Et_2O) to afford **41** (43.1 mg, 0.170 mmol, 85% yield) as a light yellow solid.

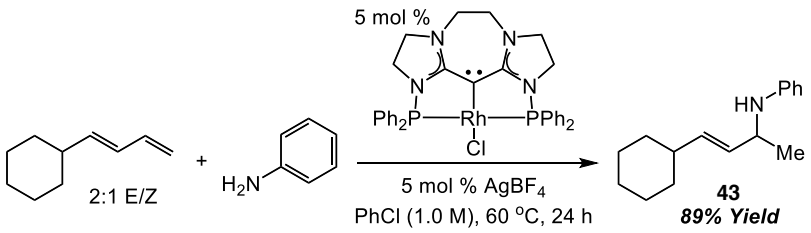
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 (2H, d, *J* = 8.7 Hz), 7.17 (2H, t, *J* = 8.0 Hz), 6.85 (2H, d, *J* = 8.7 Hz), 6.70 (1H, t, *J* = 7.3 Hz), 6.66 (2H, d, *J* = 7.6), 6.53 (1H, d, *J* = 15.8), 6.09 (1H, dd, *J* = 15.9, 5.9), 4.13-4.16 (1H, m), 3.81 (3H, s), 3.72 (1H, bs), 1.41 (3H, d, *J* = 6.6 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.98, 147.42, 130.95, 129.72, 129.14, 128.63, 127.41, 117.22, 113.88, 113.35, 55.25, 50.83, 22.12. IR (ν/cm^{-1}): 3407 (br, m), 3052 (w), 3021 (w), 2967 (m), 2922 (m), 2865 (w), 1602 (s), 1507 (s), 1316 (m), 1227 (s), 1157 (m). LRMS (ES$^+$) [M+H]$^+$ calcd for $C_{17}H_{19}NO^+$ 254.15, found: 254.11.



Synthesis of *(E)*-N-(4-(4-fluorophenyl)but-3-en-2-yl)aniline (42)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-1-(buta-1,3-diene-1-yl)-4-fluorobenzene (59.3 mg, 0.400 mmol) were added to a solution of ^{Ph}**CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography with a layer of 1% (by weight) $AgNO_3$ doped silica gel (20:1 Hex/EtOAc) to afford **42** (45.4 mg, 0.188 mmol, 94% yield) as a light yellow solid.

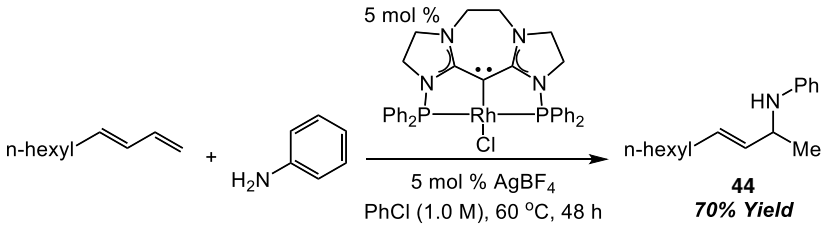
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (2H, m), 7.16 (2H, t, *J* = 7.9 Hz), 6.98 (2H, t, *J* = 8.7 Hz), 6.69 (1H, t, *J* = 7.2 Hz), 6.64 (2H, d, *J* = 7.6 Hz), 6.53 (1H, d, *J* = 15.9 Hz), 6.13 (1H, dd, *J* = 15.9, 5.8 Hz), 4.13 (1H, m, *J* = 6.2 Hz), 3.72 (1H, bs), 1.4 (1H, d, *J* = 6.6 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 147.35, 133.12, 132.91, 132.89, 129.23, 128.10, 127.82, 127.77, 117.38, 115.47, 115.32, 113.35, 50.79, 22.13. IR (ν/cm^{-1}): 3407 (br, m), 3052 (w), 3021 (w), 2967 (m), 2922 (m), 2865 (w), 1602 (s), 1507 (s), 1316 (m), 1227 (s), 1157 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{16}H_{17}FN^+$ 242.13, found: 242.14.



Synthesis of *(E)*-N-(4-cyclohexylbut-3-en-2-yl)aniline (43)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and buta-1,3-dien-1-ylcyclohexane (54.5 mg, 0.400 mmol, 2:1 mixture of *E*/*Z* isomers) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 24 h. The resulting oil was purified by SiO_2 column chromatography (100% hexanes) to afford an 88:12 mixture of **43** and an unidentifiable constitutional isomer (40.8 mg, 0.178 mmol, 89% combined yield) as a clear oil.

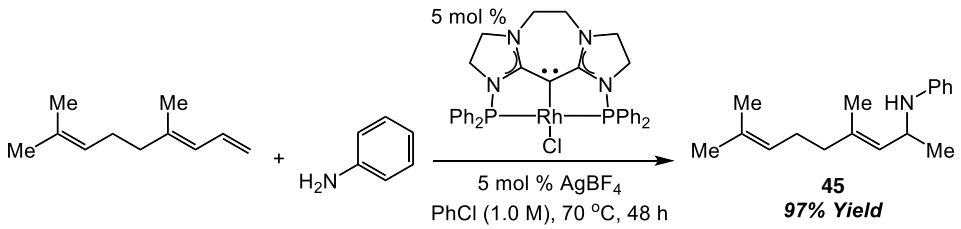
Data is reported for the major product *(E)*-N-(4-cyclohexylbut-3-en-2-yl)aniline. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.17 (2H, t, *J* = 7.8 Hz), 6.69 (1H, t, *J* = 7.3 Hz), 6.63 (2H, d, *J* = 8.2 Hz), 5.61 (1H, dd, *J* = 15.5, 6.7 Hz), 5.39 (1H, dd, *J* = 15.6, 6.0 Hz), 3.94-3.97 (1H, m), 3.61 (1H, bs), 1.98-1.93 (1H, m), 1.78-1.65 (6H, m), 1.30 (2H, d, *J* = 6.6 Hz), 1.28-1.26 (1H, m), 1.21-1.15 (1H, m), 1.12-1.06 (2H, m). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 147.54, 136.43, 130.32, 113.39, 50.59, 40.27, 32.90, 26.04, 22.04. IR (ν/cm^{-1}): 3405 (br, m), 3048 (w), 3017 (w), 2923 (s), 2850 (s), 1601 (s), 1503 (s), 1448 (m), 1318 (m), 1254 (w), 1179 (w). LRMS (ES$^+$) [M+H]$^+$ calcd for $C_{16}H_{24}N^+$ 230.19, found: 230.11.



Synthesis of *(E)*-N-(dec-3-en-2-yl)aniline and *(E)*-N-(dec-2-en-4-yl)aniline (44) Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-deca-1,3-diene (55.3 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg,

0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 Hex/Et_2O) to afford **44** (32.4 mg, 0.140 mmol, 70% combined yield, 3:2 β/δ isomers) as a clear oil.

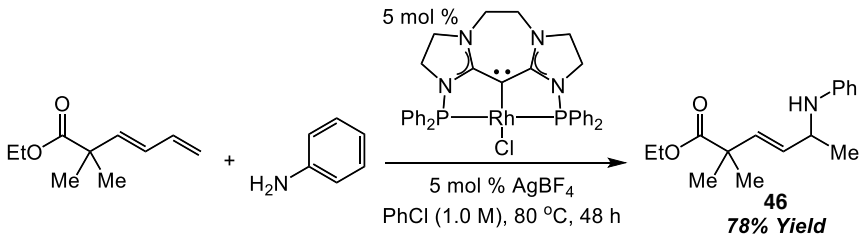
Reported as a 3:2 mixture of *(E)-N*-(dec-3-en-2-yl)aniline and *(E)-N*-(dec-2-en-4-yl)aniline: The regio-isomers were characterized by ^{1}H COSY NMR (spectra included). **^{1}H NMR** (400 MHz, $CDCl_3$): δ [*N*-(dec-3-en-2-yl)aniline: 7.15 (2H, t, *J* = 7.9 Hz), 6.67 (1H, m), 6.60 (2H, t, *J* = 7.5 Hz), 5.62 (1H, td, *J* = 15.4, 7.0 Hz), 5.41 (1H, dd, *J* = 15.4, 6.0 Hz), 3.90-3.97 (1H, m), 3.59 (1H, bs), 2.02 (2H, q, *J* = 7.1 Hz), 1.27-1.39 (8H, m) 1.29 (3H, d, *J* = 6.6 Hz), 0.88 (3H, t, *J* = 7.1 Hz)], [*(E)-N*-(dec-2-en-4-yl)aniline: 7.15 (2H, t, *J* = 7.9 Hz), 6.67 (1H, m), 6.60 (2H, t, *J* = 7.5 Hz), 5.62 (1H, td, *J* = 15.4, 7.0 Hz), 5.33 (1H, ddd, *J* = 15.3, 6.6, 1.4 Hz), 3.69-3.75 (1H, m), 3.59 (1H, bs), 1.45-1.64 (2H, m), 1.68 (3H, d, *J* = 6.4 Hz), 1.27-1.39 (8H, m), 0.88 (3H, t, *J* = 6.6 Hz)]. **^{13}C NMR** (100 MHz, $CDCl_3$): δ [Reported as a mixture of *N*-(dec-3-en-2-yl)aniline and *(E)*-N-(dec-2-en-4-yl)aniline: 147.76, 147.54, 133.16, 132.91, 130.66, 129.05, 125.89, 117.00, 116.81, 113.38, 113.20, 55.30, 50.51, 36.22, 32.19, 31.68, 29.23, 28.74, 25.94, 22.60, 22.09, 17.70, 14.07]. IR (ν/cm^{-1}): 3410 (br, m), 3053 (w), 3021 (w), 2956 (m), 2926 (s), 2855 (s), 1601 (s), 1504 (s), 1457 (m), 1428 (w), 1374 (w), 1318 (m), 1253 (m), 1179 (w), 1154 (w). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{16}H_{26}N^+$ 232.21, found: 232.18.



Synthesis of *(E)*-N-(4,8-dimethylnona-3,7-dien-2-yl)aniline (45)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-4,8-dimethylnona-1,3,7-triene (60.1 mg, 0.400 mmol, 92:8 *E*/*Z*) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 70 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 Hex/Et_2O) to afford **45** (47.2 mg, 0.194 mmol, 97% yield, 92:8 *E*/*Z*) as a clear oil.

Data for the *E* isomer is reported. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.15 (2H, dt, *J* = 7.0, 1.7 Hz), 6.67 (1H, dt, *J* = 7.3, 0.9 Hz), 6.58 (2H, dd, *J* = 8.5, 0.9 Hz), 5.05-5.07 (2H, m), 4.14 (1H, m), 3.57 (1H, s), 1.98-2.09 (4H, m), 1.73 (3H, d, *J* = 1.2 Hz), 1.66 (3H, d, *J* = 0.8 Hz), 1.59 (3H, s), 1.25 (3H, d, *J* = 6.5 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 147.79, 136.12, 131.53, 129.59, 129.11, 124.00, 117.03, 113.30, 47.25, 39.43, 26.39, 25.69, 22.01, 17.72, 16.38. IR (ν/cm^{-1}): 3406 (br, m), 3052 (w), 2966 (s), 2924 (s), 2859 (w), 1602 (s), 1502 (s), 1443 (m), 1424 (m), 1378 (m), 1318 (m), 1254 (m), 1150 (m), 1105 (m), 1072 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{17}H_{26}N^+$ 244.21, found: 244.09.

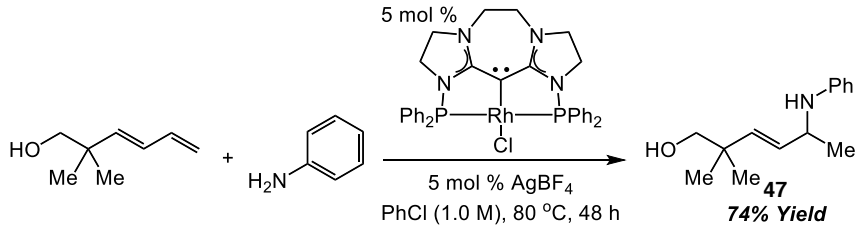


Synthesis of *(E)*-ethyl 2,2-dimethyl-5-(phenylamino)hex-3-enoate (46)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-ethyl-2,2-dimethylhexa-3,5-dienoate (67.3 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 80 °C for 48 h. The

resulting oil was purified by SiO_2 column chromatography with a layer of 1% (by weight) $AgNO_3$ doped silica (20:1 Hex/Et_2O) to afford **46** (40.8 mg, 0.156 mmol, 78% yield) as a clear oil.

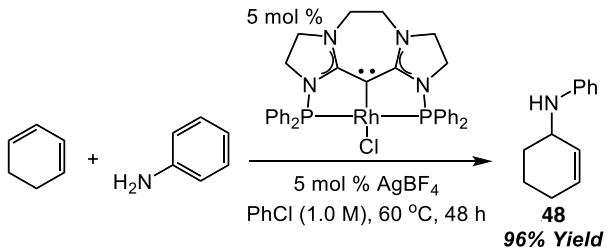
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.13 (2H, t, *J* = 7.8 Hz), 6.67 (1H, t, *J* = 7.2 Hz), 6.59 (2H, d, *J* = 7.7 Hz), 5.83 (1H, dd, *J* = 15.7, 0.5 Hz), 5.47 (1H, dd, *J* = 15.7, 5.9 Hz), 4.08 (2H, q, *J* = 7.1 Hz), 3.95-3.98 (1H, m), 1.29 (3H, d, *J* = 6.5 Hz), 1.27 (6H, s), 1.2 (3H, t, *J* = 7.1 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 176.46, 147.35, 134.73, 131.39, 129.07, 117.31, 113.55, 60.63, 50.76, 43.82, 25.01, 21.99, 14.13. IR (ν/cm^{-1}): 3399 (br, m), 2977 (w), 2933 (s), 2874 (m), 1726 (s), 1603 (s), 1503 (s), 1318 (m), 1254 (m), 1144 (s), 1027 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{16}H_{24}NO_2^+$ 262.18, found: 262.13.



Synthesis of *(E)*-2,2-dimethyl-5-(phenylamino)hex-3-en-1-ol (47)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-2,2-dimethylhexa-3,5-dien-1-ol (50.5 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.099 mmol) and $AgBF_4$ (1.9 mg, 0.098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 80 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography with a layer of 1% (by weight) $AgNO_3$ doped silica (10:1 Hex/Et_2O) to afford **47** (32.5 mg, 0.148 mmol, 74% yield) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16 (2H, dt, *J* = 7.0, 1.6 Hz), 6.69 (1H, dt, *J* = 7.3, 0.9 Hz), 6.59 (2H, dd, *J* = 8.5, 0.9 Hz), 5.54 (1H, dd, *J* = 15.8, 0.9 Hz), 5.39 (1H, dd, *J* = 15.8, 6.3 Hz), 3.96-3.99 (1H, m), 3.58 (1H, bs), 3.25 (2H, dd, *J* = 14.2, 10.6 Hz), 1.31 (3H, d, *J* = 6.6 Hz), 0.98 (6H, d, *J* = 4.0 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 147.37, 136.92, 132.10, 129.15, 117.47, 113.73, 71.54, 51.02, 38.29, 23.92, 23.57, 22.21. IR (ν/cm^{-1}): 3360 (br, s), 2959 (s), 2926 (s), 2869 (m), 1743 (s), 1602 (s), 1503 (s), 1461 (m), 1374 (m), 1319 (m), 1254 (m), 1155 (m), 1041 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{14}H_{22}NO^+$ 220.17, found: 220.11.

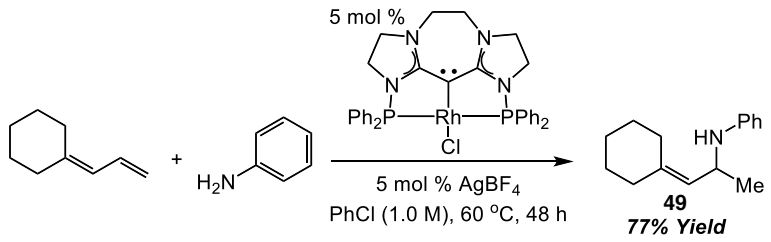


Synthesis of *N*-(cyclohex-2-en-1-yl)aniline (48)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and cyclohexa-1,3-diene (64.1 mg, 0.800 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 Hex/Et_2O) to afford **48** (33.3 mg, 0.192 mmol, 96% yield) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.17 (2H, dt, *J* = 7.0, 1.6 Hz), 6.69 (1H, t, *J* = 7.1 Hz), 6.62 (2H, d, *J* = 5.0 Hz), 5.84-5.87 (1H, m), 5.75-5.77 (1H, m), 4.00 (1H, bs), 3.63 (1H, bs), 1.99-2.09 (2H, m), 1.89-1.93 (1H, m), 1.69-1.75 (1H, m), 1.60-1.67 (2H, m). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 147.20, 130.15, 129.33, 128.59, 117.14, 113.23, 47.86, 28.90, 25.18, 19.67. IR (ν/cm^{-1}): 3404

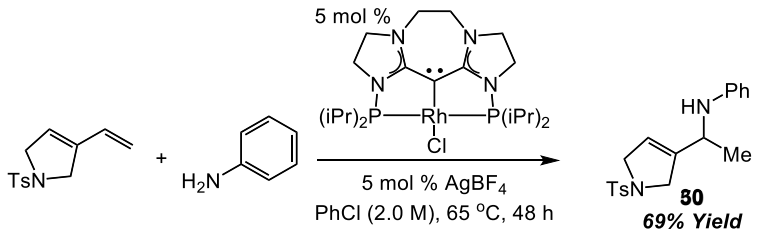
(br, m), 3083 (w), 3050 (w), 3021 (m), 2925 (s), 2859 (m), 2360 (w), 1603 (s), 1558 (s), 1504 (m), 1429 (m), 1309 (m), 1257 (m), 1179 (w), 1102 (m). LRMS (ES^+) $[M+H]^+$ calcd for $C_{12}H_{16}N^+$174.13, found: 174.05.



Synthesis of *N*-(1-cyclohexylidenepropan-2-yl)aniline (49)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and allylidenecylohexane (48.9 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 Hex/Et_2O) to afford **49** (33.2 mg, 0.154 mmol, 77% yield) as colorless oil.

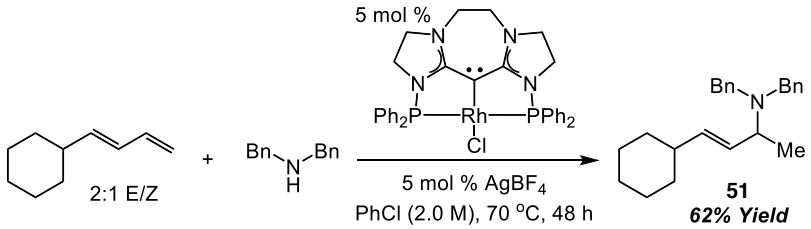
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (2H, dt, *J* = 8.0, 2.1 Hz), 6.66 (2H, t, *J* = 7.3 Hz), 6.59 (2H, dd, *J* = 8.6, 1.0 Hz), 4.99 (3H, d, *J* = 8.4 Hz), 4.17-4.24 (1H, m), 3.57 (1H, bs), 2.20-2.28 (2H, m), 2.04-2.07 (2H, m), 1.48-1.61 (6H, bm), 1.25 (3H, d, *J* = 6.5 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 140.68, 129.09, 126.20, 117.02, 113.36, 46.36, 36.92, 29.27, 28.51, 27.78, 26.78, 22.60. IR (ν/cm^{-1}): 3405 (br, m), 3083 (w), 3050 (w), 3018 (w), 2926 (s), 2852 (s), 1666 (w), 1601 (s), 1503 (s), 1447 (m), 1374 (w), 1317 (m), 1253 (w), 1179 (w), 1154 (w), 1111 (w), 1074 (w), 1029 (w). LRMS (ES^+) $[M+K]^+$ calcd for $C_{15}H_{21}NK^+$ 254.13, found: 254.03.



Synthesis of *N*-(1-(1-tosyl-2,5-dihydro-1H-pyrrol-3-yl)ethyl)aniline (50)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and 1-tosyl-3-vinyl-2,5-dihydro-1H-pyrrole (99.7 mg, 0.400 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (5.5 mg, 0.010 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 65 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (20:1 to 100% Et_2O) to afford **50** (47.1mg, 0.138 mmol, 69% yield) as a light yellow oil.

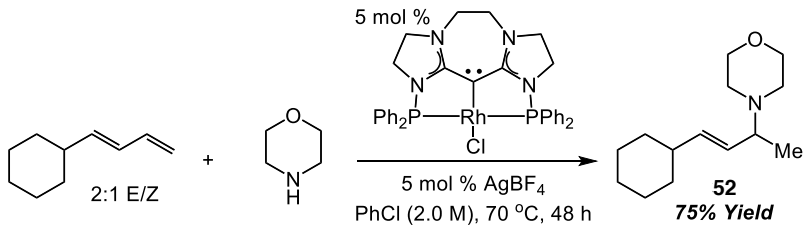
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66 (2H, d, *J* = 8.2 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 7.09 (2H, t, *J* = 7.9 Hz), 6.69 (1H, t, *J* = 7.3 Hz), 6.45 (2H, d, *J* = 7.9 Hz), 5.48-5.49 (1H, m), 4.03-4.18 (4H, m), 4.00 (1H, m), 3.52 (1H, bs), 2.43 (3H, m), 1.29 (2H, d, *J* = 6.7 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 146.72, 143.34, 142.50, 134.09, 129.71, 129.19, 127.33, 119.30, 117.73, 113.06, 55.04, 54.32, 47.84, 21.51, 20.57. IR (ν/cm^{-1}): 3391 (br, m), 3052 (w), 3019 (w), 2962 (w), 2923 (m), 2859 (m), 1602 (s), 1506 (s), 1338 (s), 1254 (m), 1162 (s), 1099 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{19}H_{23}N_2O_2S^+$ 343.15, found: 343.14



Synthesis of *(E)*-N,N-dibenzyl-4-cyclohexylbut-3-en-2-amine (51)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, dibenzylamine (39.5 mg, 0.200 mmol) and buta-1,3-dien-1-ylcyclohexane (54.5 mg, 0.400 mmol, 2:1 *E*/*Z*) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 70 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography with a layer of 1% (by weight) $AgNO_3$ doped silica (20:1 Hex/Et_2O) to afford **51** (41.4 mg, 0.124 mmol, 62% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (4H, d, *J* = 7.4 Hz), 7.28 (4H, t, *J* = 7.5 Hz), 7.20 (2H, t, *J* = 7.2 Hz), 5.39-5.47 (2H, m), 3.62 (2H, d, *J* = 13.9 Hz), 3.48 (2H, d, *J* = 13.9 Hz), 3.21-3.24 (1H, m), 1.95-2.00 (1H, m), 1.66-1.75 (4H, m), 1.64-1.66 (1H, m), 1.25-1.33 (3H, m), 1.15 (2H, d, *J* = 6.7 Hz), 1.05-1.18 (2H, m). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 140.94, 138.41, 128.57, 128.09, 127.99, 126.54, 54.50, 53.45, 40.78, 33.39, 33.31, 26.23, 26.10, 16.16. IR (ν/cm^{-1}): 3063 (w), 3026 (m), 2963 (w), 2923 (s), 2850 (m), 2796 (w), 1494 (w), 1450 (m), 1376 (m), 1147 (w), 1073 (w), 1028 (w). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{24}H_{32}N^+$ 334.25, found: 334.21.

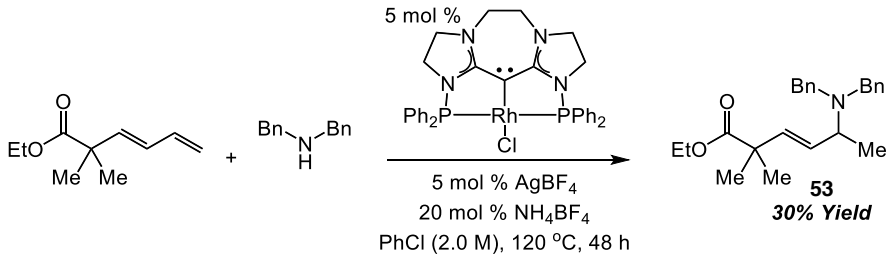


Synthesis of *(E)*-4-(4-cyclohexylbut-3-en-2-yl)morpholine (52)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, morpholine (17.4 mg, 0.200 mmol) and buta-1,3-dien-1-ylcyclohexane (54.5 mg, 0.400 mmol, 2:1 *E*/*Z*) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 90 °C for 48 h. The

resulting oil was purified by SiO_2 column chromatography (3:1 Hex/Et_2O) to afford a 89:11 mixture of **52** and an unidentifiable constitutional isomer (33.5 mg, 0.150 mmol, 75% combined yield) as a clear oil.

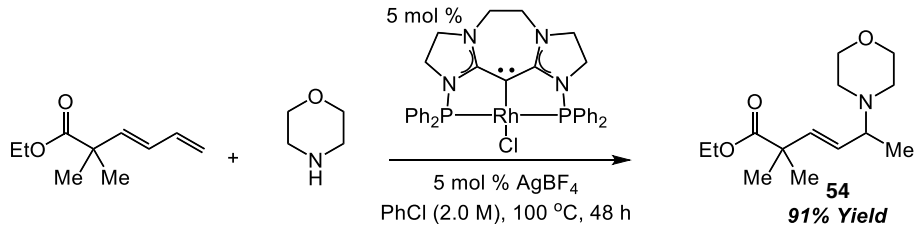
Data is reported for the major product *(E)*-4-(4-cyclohexylbut-3-en-2-yl)morpholine. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.45 (1H, dd, *J* = 15.5, 6.5 Hz), 5.28 (1H, ddd, *J* = 15.5, 8.2, 1.2 Hz), 3.69-3.71 (4H, m), 2.74-2.78 (1H, m), 2.41-2.53 (4H, m), 1.90-1.95 (1H, m), 1.67-1.71 (4H, m), 1.60-1.65 (1H, m), 1.23-1.30 (2H, m), 1.13-1.18 (1H, m), 1.13 (3H, d, *J* = 6.5 Hz), 1.01-1.09 (2H, m). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 138.52, 128.92, 67.22, 62.89, 50.52, 40.41, 33.04, 32.97, 26.14, 25.98, 18.06. IR (ν/cm^{-1}): 2958 (w), 2924 (s), 2851 (s), 2802 (m), 1448 (m), 1265 (m) 1245 (w), 1198 (s). LRMS (ES$^+$) [M+H]$^+$ calcd for $C_{24}H_{32}N^+$ 224.20, found: 224.16.



Synthesis of *(E)*-ethyl 5-(dibenzylamino)-2,2-dimethylhex-3-enoate (53)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, dibenzylamine (19.7 mg, 0.100 mmol), *(E)*-ethyl 2,2-dimethylhexa-3,5-dienoate (33.6 mg, 0.200 mmol) and NH_4BF_4 (2.1 mg, 0.02 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.0050 mmol) and $AgBF_4$ (1.0 mg, 0.0051 mmol) in chlorobenzene (50 μL, [ ] = 2.0 M), and the reaction allowed to stir at 120 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (100:1 Hex/Et_2O) to afford **53** (11.0 mg, 0.030 mmol, 30% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 (4H, d, *J* = 7.1 Hz), 7.30 (4H, t, *J* = 3.6 Hz), 7.20 (2H, t, *J* = 7.2 Hz), 5.69 (1H, dd, *J* = 15.9, 1.0 Hz), 5.56 (1H, dd, *J* = 15.9, 6.7 Hz), 4.12 (2H, q, *J* = 7.1 Hz), 3.63 (1H, d, *J* = 13.9 Hz), 3.47 (1H, d, *J* = 13.9 Hz), 3.25-3.35 (1H, m), 1.30 (6H, d, *J* = 16.4 Hz), 1.22 (3H, t, *J* = 7.1 Hz), 1.17 (3H, d, *J* = 6.8 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 176.68, 140.66, 136.39, 129.29, 128.56, 128.14, 126.65, 60.64, 54.40, 53.50, 44.11, 25.38, 25.10, 15.88, 14.20. IR (ν/cm^{-1}): 3061 (w), 3027 (w), 2965 (m), 2927 (m), 2866 (w), 2801 (w), 1731 (s), 1495 (w), 1455 (m), 1363 (m), 1249 (m), 1143 (s), 1029 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{24}H_{31}NO_2^+$ 366.24, found: 366.22.



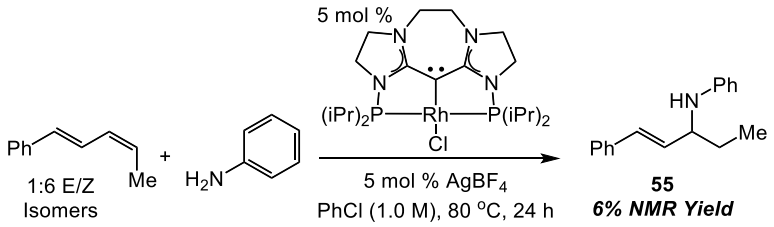
Synthesis of *(E)*-ethyl 2,2-dimethyl-5-morpholinohex-3-enoate (54)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, morpholine (17.0 mg, 0.200 mmol) and *(E)*-ethyl 2,2-dimethylhexa-3,5-dienoate (67.3 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (100 μL, [ ] = 2.00 M), and the reaction allowed to stir at 100 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (10:1 Hex/Et_2O) to afford **54** (46.5 mg, 0.182 mmol, 91% yield) as a clear oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.73 (1H, dd, *J* = 15.7, 0.5 Hz), 5.43 (1H, dd, *J* = 15.8, 8.3 Hz), 4.11 (2H, q, *J* = 6.1 Hz), 3.71 (4H, t, *J* = 4.7 Hz), 2.82-2.85 (1H, m), 2.45-2.52 (4H, m), 1.29 (6H, d, *J* = 5.8 Hz), 1.23 (3H, t, *J* = 7.1 Hz), 1.15 (3H, d, *J* = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.46, 136.59, 130.30, 67.23, 62.71, 60.63, 50.60, 44.04, 25.11, 17.90, 14.15. IR

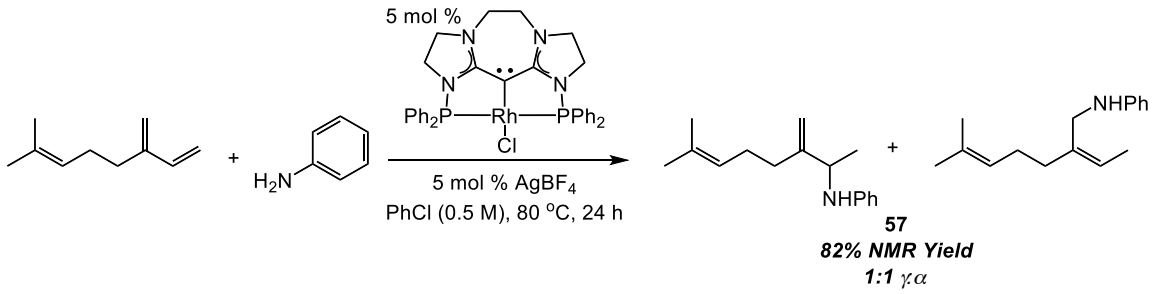
(ν/cm^{-1}): 2975 (s), 2852 (m), 2805 (m), 1731 (s), 1558 (w), 1541 (w), 1507 (w), 1457 (m), 1226 (br, m), 1144 (s), 1119 (m), 1029 (m). LRMS (ES$^+$) $[M+H]^+$ calcd for $C_{14}H_{26}NO_3^+$ 256.19, found: 256.07.

The following data was not characterized for publication and is unpublished work. As such, values are not an average of two experiments and some compounds are not completely characterized.



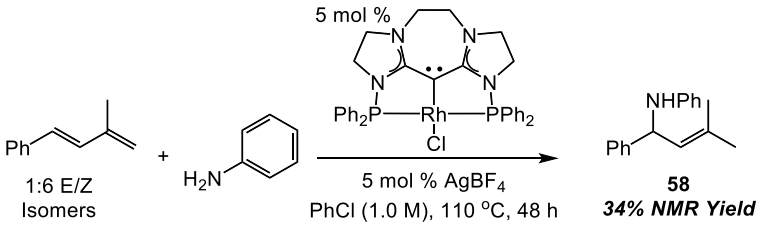
Synthesis of *(E)*-N-(1-phenylpent-1-en-3-yl)aniline (55)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and a 6:1 mixture of (*(1E,3Z)*-penta-1,3-dien-1-yl)benzene and ((1E,3E)-penta-1,3-dien-1-yl)benzene (28.8 mg, 0.200 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 80 °C for 24 h. The crude reaction was assayed by NMR spectroscopy to determine an NMR conversion to **55** of 6% compared to 20 μL of DMF used as an internal standard.



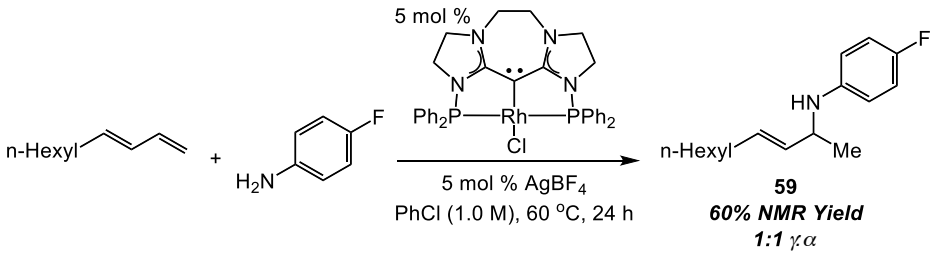
Synthesis of N-(7-methyl-3-methyleneoct-6-en-2-yl)aniline (57)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and myrcene (54.5 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (400 μL, [ ] = 0.50 M), and the reaction allowed to stir at 80 °C for 24 h. The crude reaction was assayed by NMR spectroscopy to determine an NMR conversion compared to 20 μL of DMF used as an internal standard. The reaction produced 82% of **57** as a 1:1 mixture of N-(7-methyl-3-methyleneoct-6-en-2-yl)aniline and (*Z*)-N-(2-ethylidene-6-methylhept-5-en-1-yl)aniline.



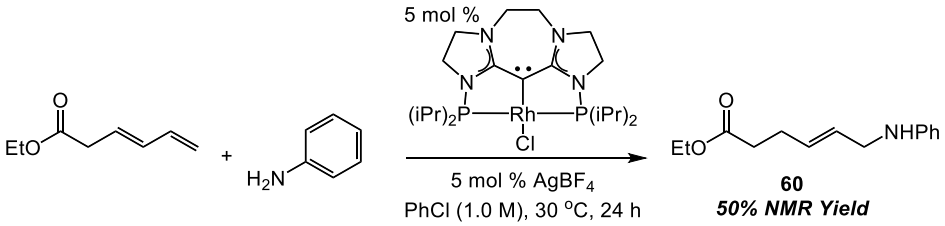
Synthesis of N-(3-methyl-1-phenylbut-2-en-1-yl)aniline (58)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and (E)-(3-methylbuta-1,3-dien-1-yl)benzene (57.7 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 110 °C for 48 h. The resulting oil was purified by SiO_2 column chromatography (10:1 Hex/Et_2O) to afford **58** (16.1 mg, 0.068 mmol, 34% yield) as a clear oil.



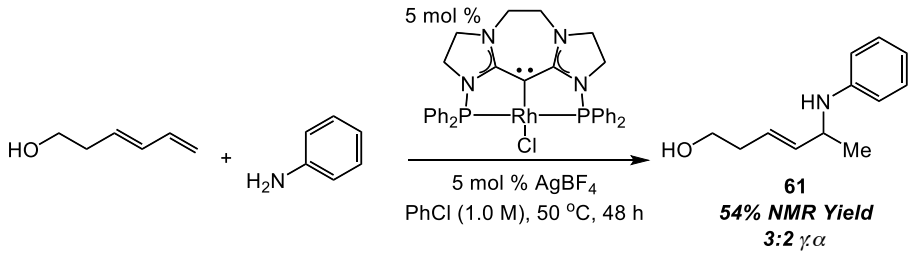
Synthesis of (*E*)-N-(dec-3-en-2-yl)-4-fluoroaniline (59)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and *(E)*-deca-1,3-diene (55.3 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 24 h. The crude reaction was assayed by NMR spectroscopy to determine an NMR conversion compared to 20 μL of DMF used as an internal standard. The reaction produced 60% of **59** as a 1:1 mixture of (E)-N-(dec-3-en-2-yl)-4-fluoroaniline and (E)-N-(dec-2-en-4-yl)-4-fluoroaniline.



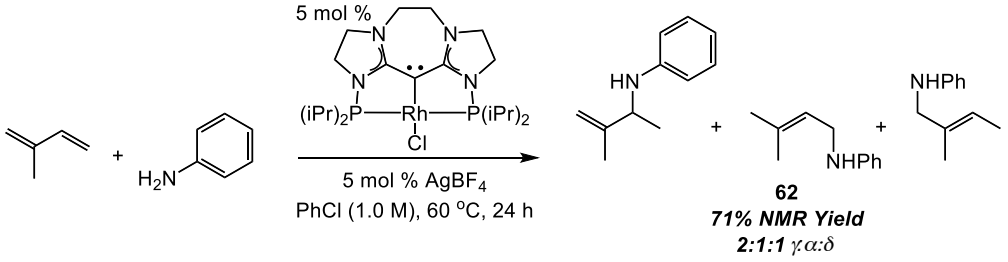
Synthesis of ethyl (*E*)-6-(phenylamino)hex-4-enoate (60)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and ethyl (*E*)-hexa-3,5-dienoate (42.1 mg, 0.300 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 30 °C for 24 h. The crude reaction was assayed by NMR spectroscopy to determine an NMR conversion to **60** of 50% compared to 20 μL of DMF used as an internal standard.



Synthesis of (*E*)-5-(phenylamino)hex-3-en-1-ol (61)

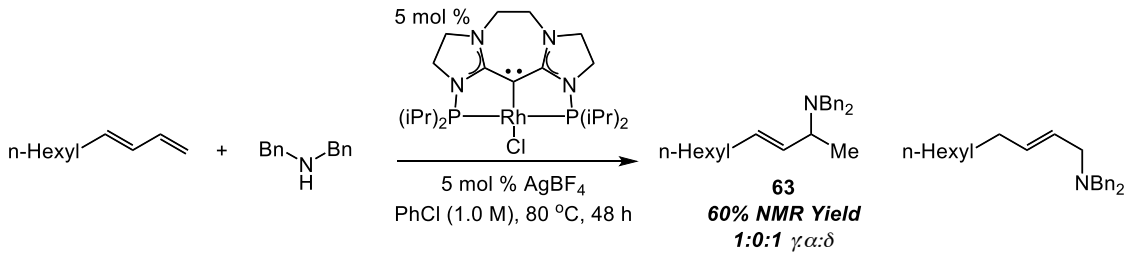
Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and (*E*)-hexa-3,5-dien-1-ol (39.3 mg, 0.400 mmol) were added to a solution of **^{Ph}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 50 °C for 48 h. The crude reaction was assayed by NMR spectroscopy to determine an NMR conversion compared to 20 μL of DMF used as an internal standard. The reaction produced 54% of **61** as a 3:2 mixture of (*E*)-5-(phenylamino)hex-3-en-1-ol and (*E*)-3-(phenylamino)hex-4-en-1-ol.



Synthesis of N-(3-methylbut-3-en-2-yl)aniline (62)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (18.6 mg, 0.200 mmol) and isoprene (200 μL, 2.00 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (200 μL, [ ] = 1.00 M), and the reaction allowed to stir at 60 °C for 48 h. The crude reaction was assayed by NMR

spectroscopy to determine an NMR conversion compared to 20 μL of DMF used as an internal standard. The reaction produced 71% of **62** as a 2:1:1 mixture of N-(3-methylbut-3-en-2-yl)aniline, N-(3-methylbut-2-en-1-yl)aniline, and (E)-N-(2-methylbut-2-en-1-yl)aniline.

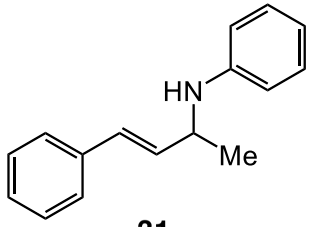


Synthesis of (*E*)-N,N-dibenzyldec-3-en-2-amine (63)

Following the general procedure for (CDC)-Rh-catalyzed hydroamination, aniline (9.5 mg, 0.050 mmol) and *(E)*-deca-1,3-diene (13.8 mg, 0.100 mmol) were added to a solution of **^{iPr}CDC-Rh-Cl** (6.8 mg, 0.0099 mmol) and $AgBF_4$ (1.9 mg, 0.0098 mmol) in chlorobenzene (50 μL, [ ] = 1.00 M), and the reaction allowed to stir at 80 °C for 48 h. The crude reaction was assayed by NMR spectroscopy to determine an NMR conversion compared to 20 μL of DMF used as an internal standard. The reaction produced 60% of **63** as a 1:1 mixture of (*E*)-N,N-dibenzyldec-3-en-2-amine and (*E*)-N,N-dibenzyldec-2-en-1-amine.

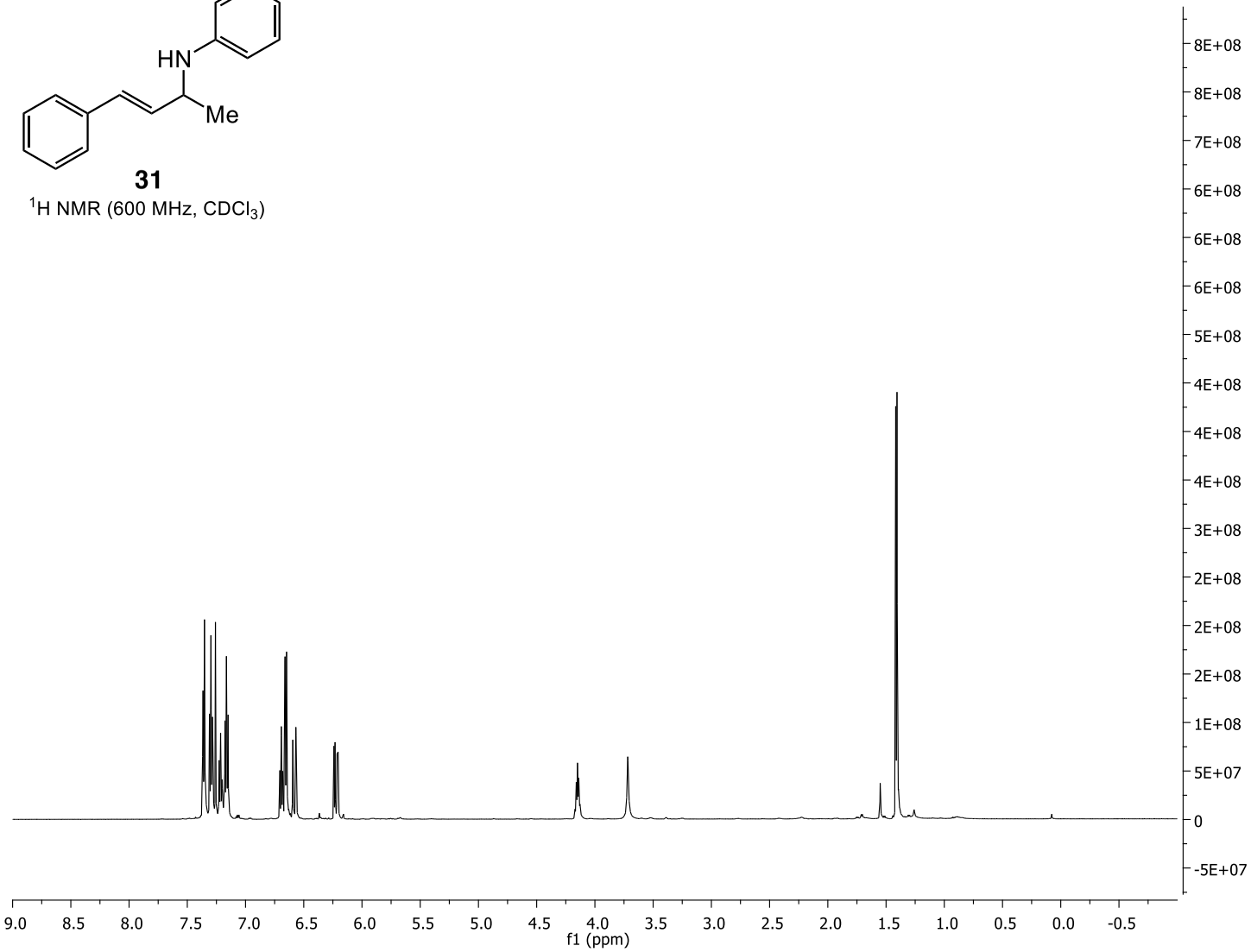
NMR Data for (*E*)-N,N-dibenzyldec-3-en-2-amine: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.2 Hz, 4H), 7.28 (t, *J* = 7.6 Hz, 4H), 7.20 (t, *J* = 7.3 Hz, 2H), 5.52 – 5.40 (m, 2H), 3.63 (d, *J* = 14.0 Hz, 2H), 3.49 (d, *J* = 14.0 Hz, 2H), 3.23 (p, *J* = 6.7 Hz, 1H), 2.09 – 2.01 (m, 2H), 1.41 – 1.22 (m, 8H), 1.15 (d, *J* = 6.8 Hz, 3H), 0.92 – 0.85 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.06, 132.53, 130.91, 128.68, 128.66, 128.49, 128.23, 128.22, 126.69, 54.65, 53.62, 32.75, 31.87, 29.71, 28.98, 22.81, 16.28, 14.26. NMR Data for (*E*)-N,N-dibenzyldec-2-en-1-amine: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.4 Hz, 4H), 7.29 (dd, *J* = 15.7, 8.0 Hz, 4H), 7.22 (t, *J* =

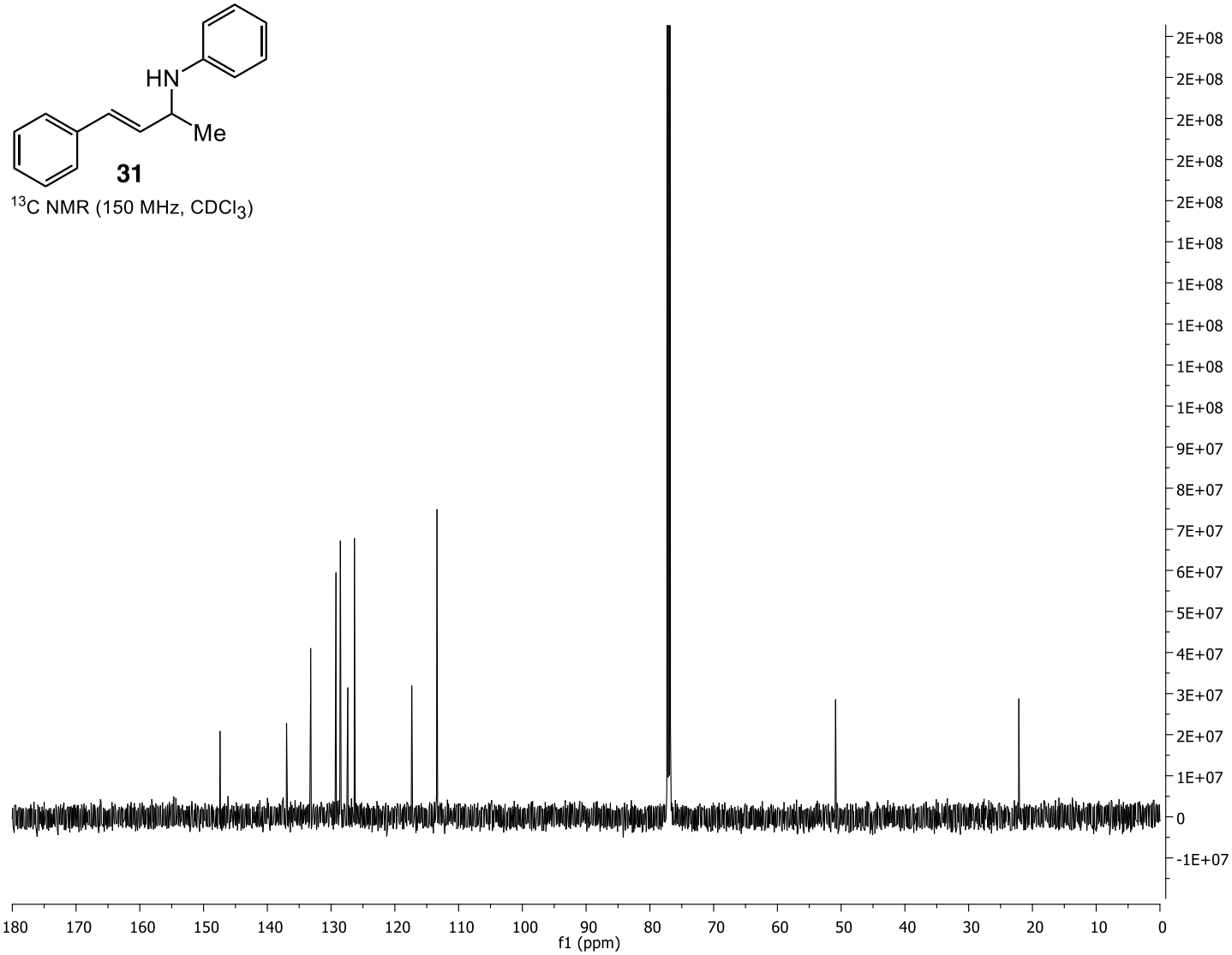
7.3 Hz, 2H), 5.64 – 5.42 (m, 2H), 3.56 (s, 3H), 3.00 (d, J = 6.2 Hz, 2H), 2.06 – 1.97 (m, 2H), 1.40 – 1.17 (m, 8H), 0.90 – 0.82 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.06, 134.41, 128.94, 128.27, 127.18, 126.85, 57.76, 55.68, 32.61, 32.00, 29.54, 29.30, 29.28, 22.81, 14.25.



31

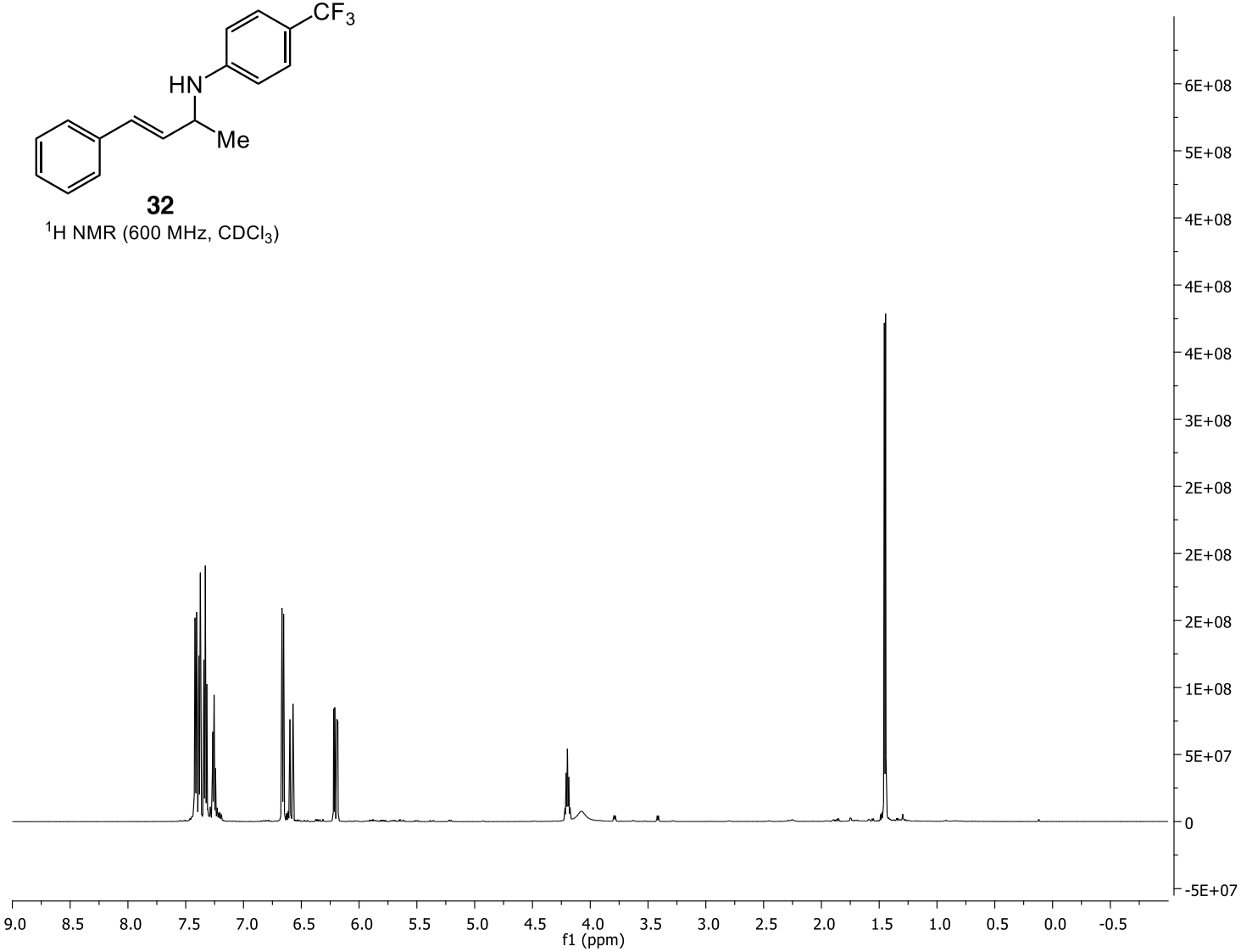
^{1}H NMR (600 MHz, $CDCl_3$)

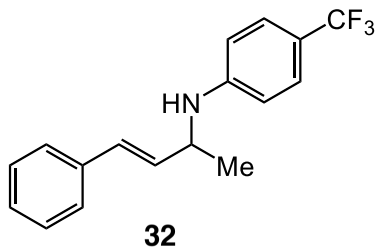



HN
Me
31
13C NMR (150 MHz, CDCl3)
2E+08
2E+08
2E+08
2E+08
2E+08
1E+08
1E+08
1E+08
1E+08
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
-1E+07
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

32

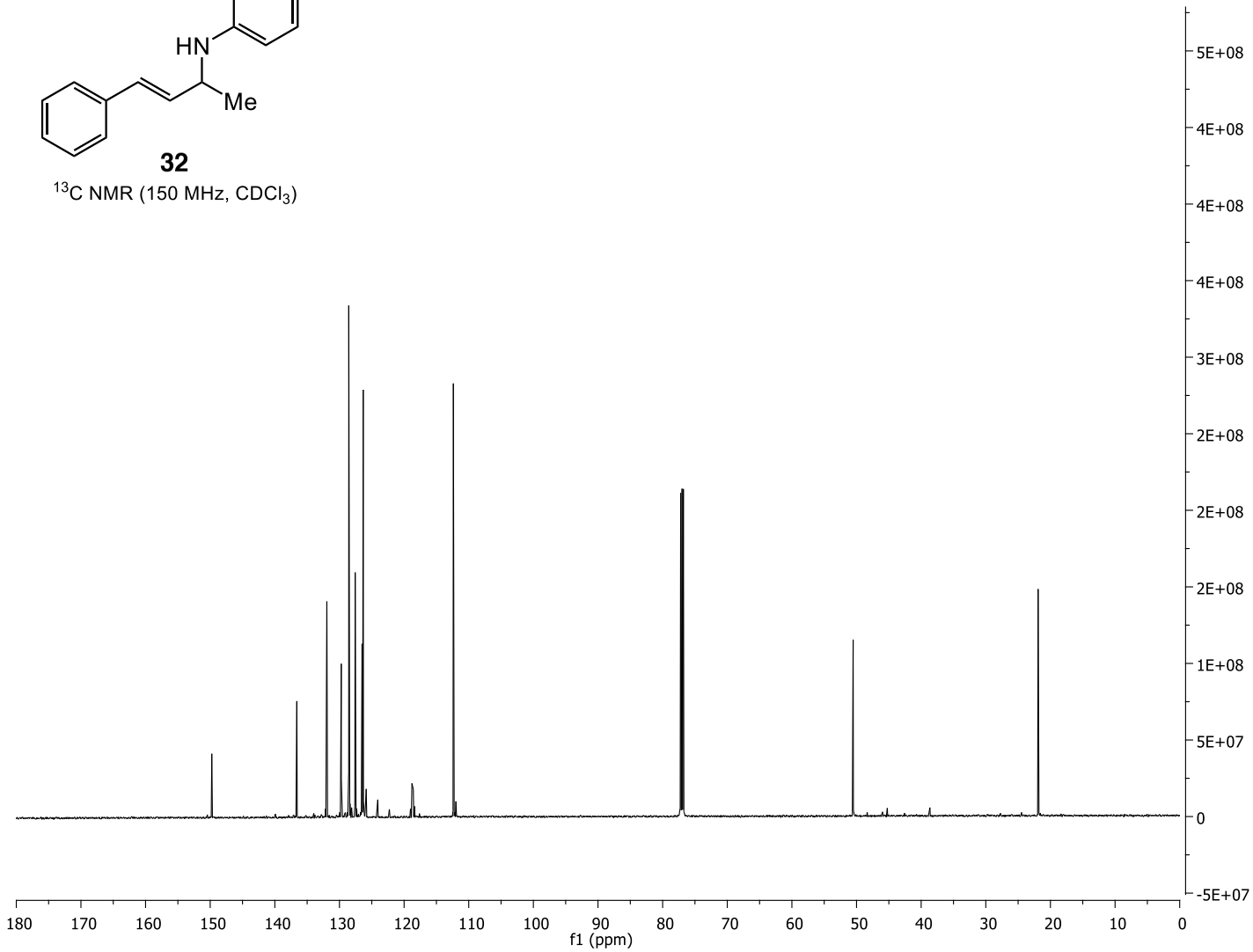
^{1}H NMR (600 MHz, $CDCl_3$)

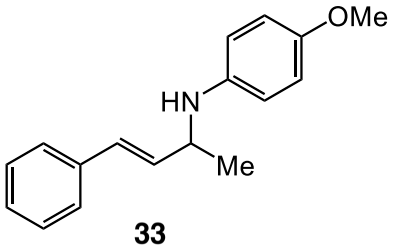




32

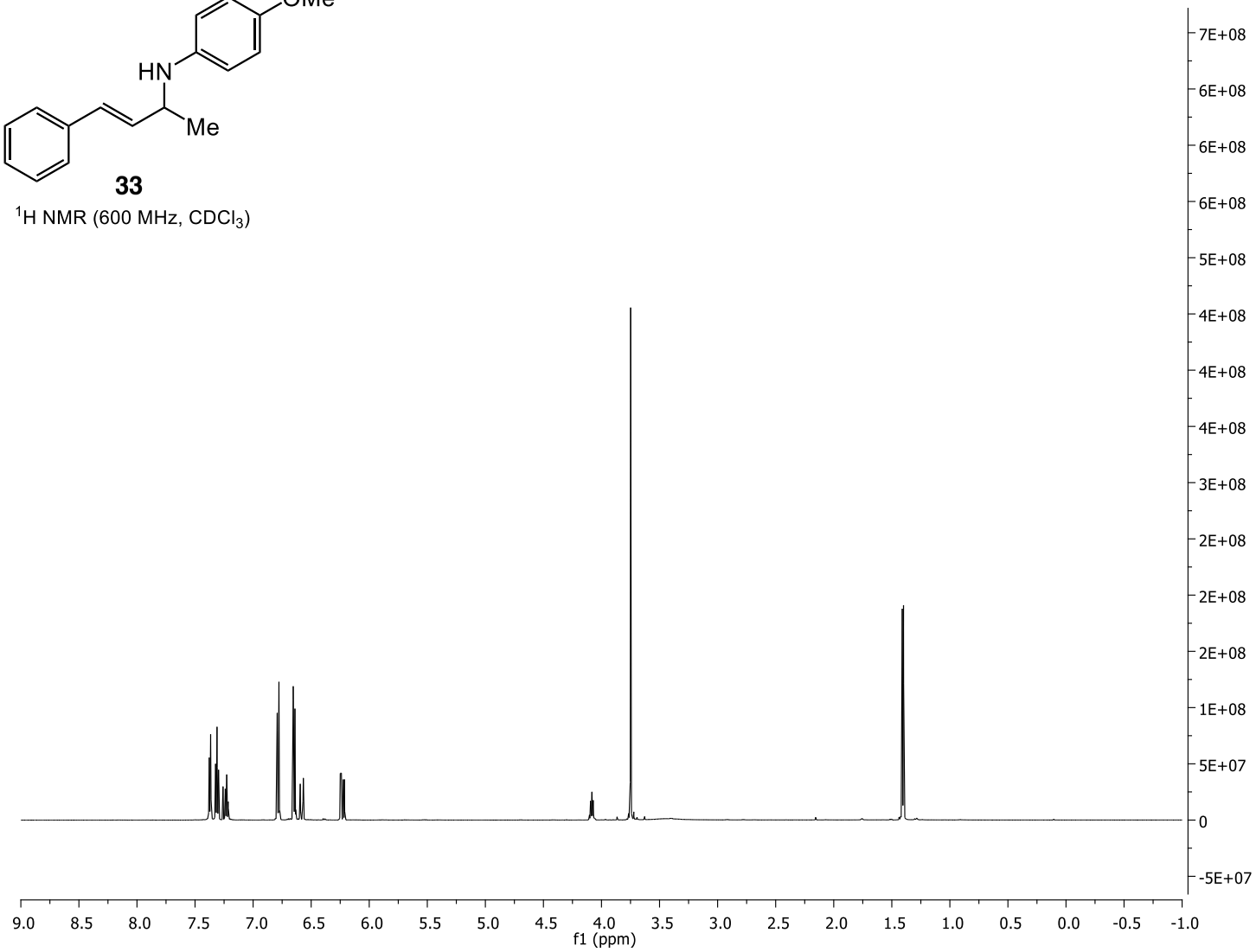
^{13}C NMR (150 MHz, $CDCl_3$)

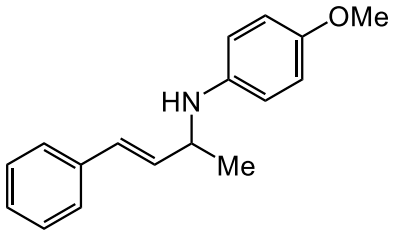




33

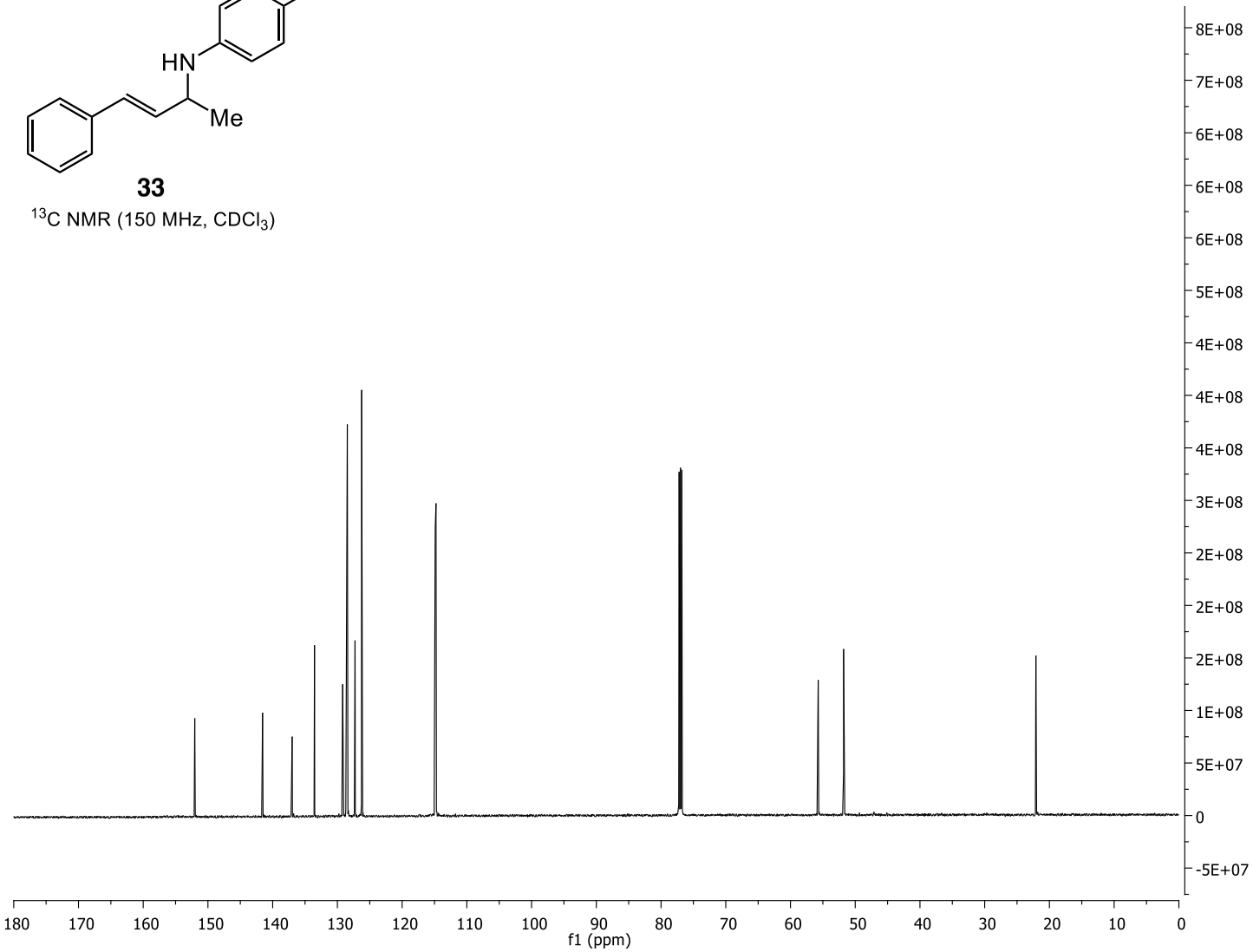
^{1}H NMR (600 MHz, $CDCl_3$)





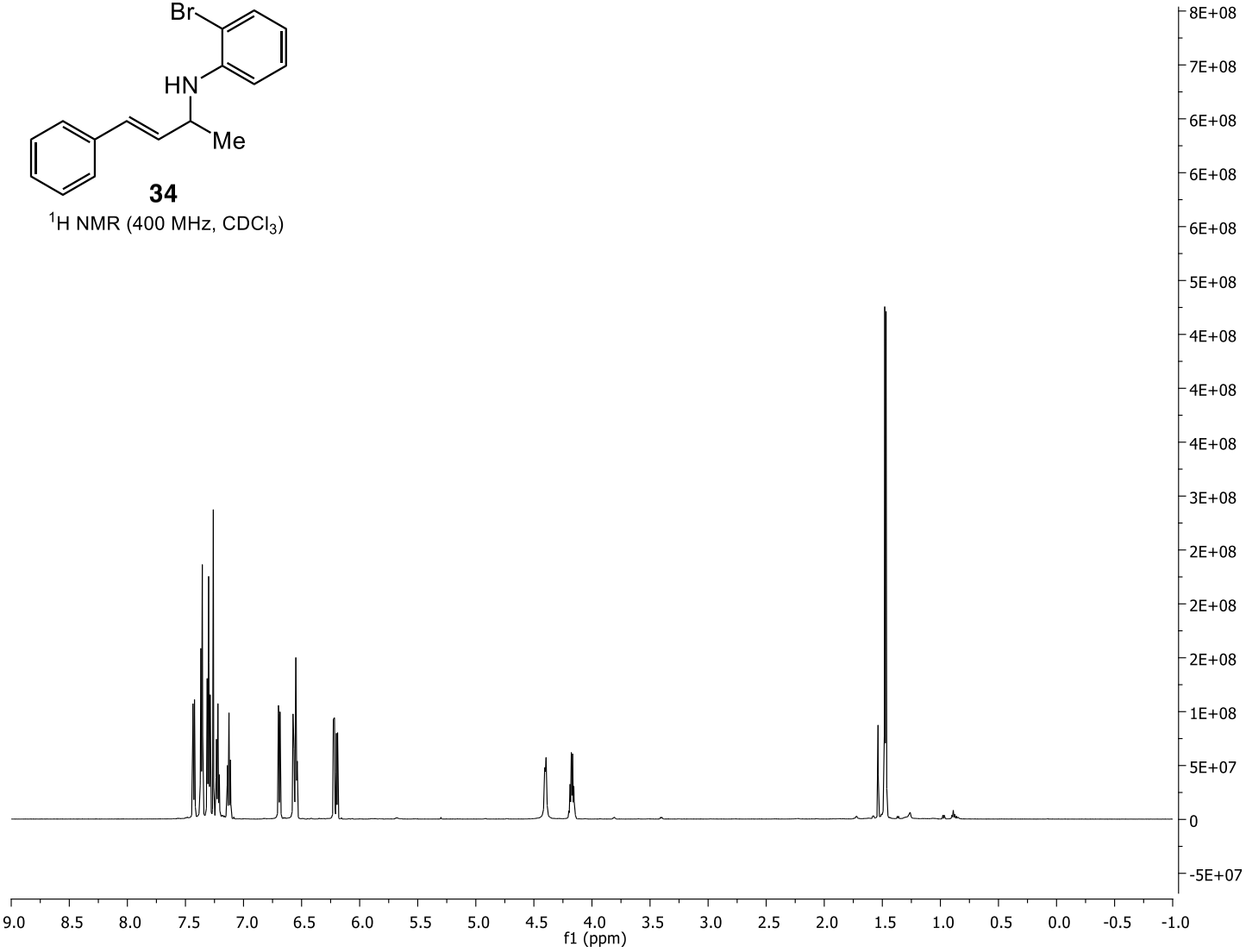
33

^{13}C NMR (150 MHz, $CDCl_3$)



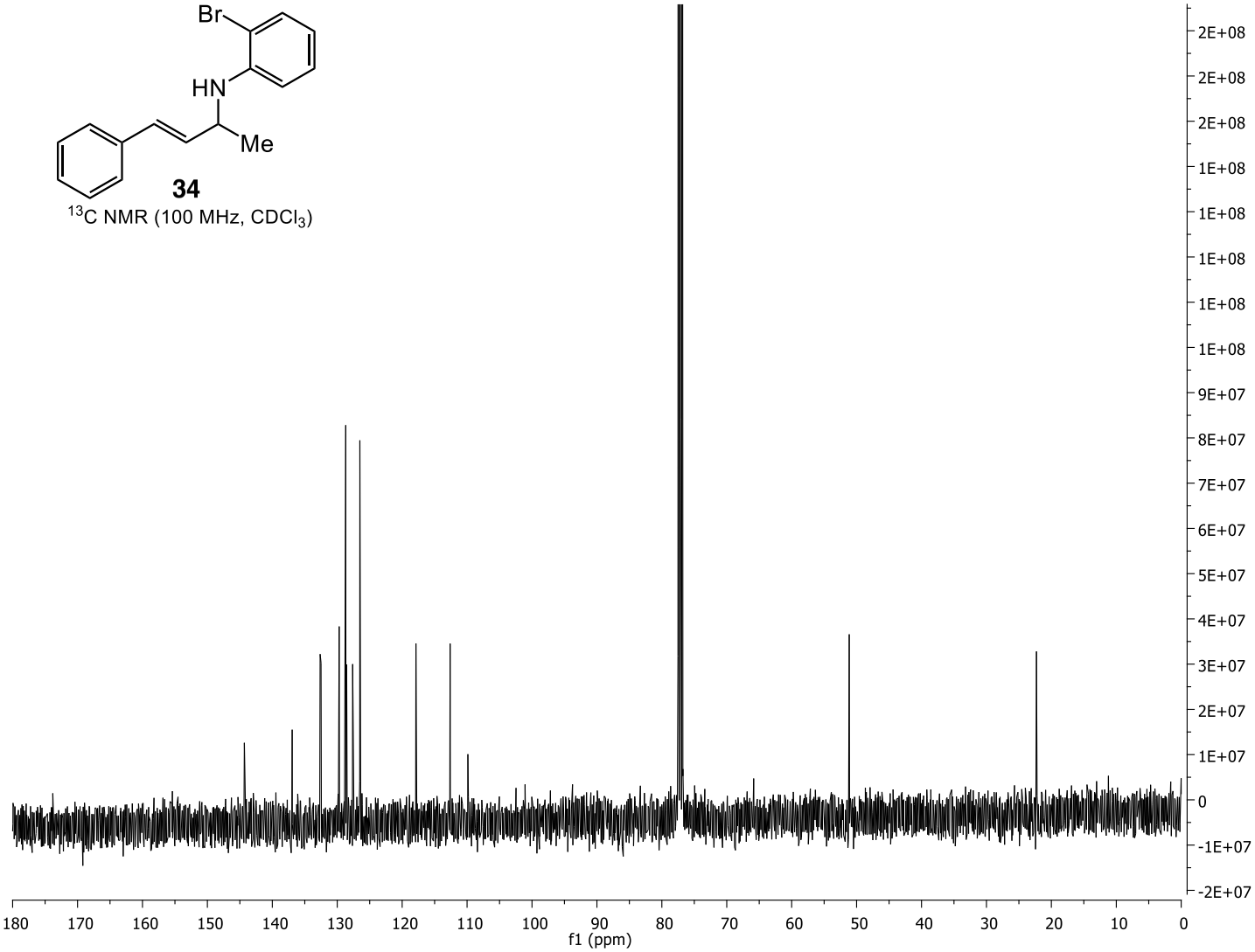
34

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



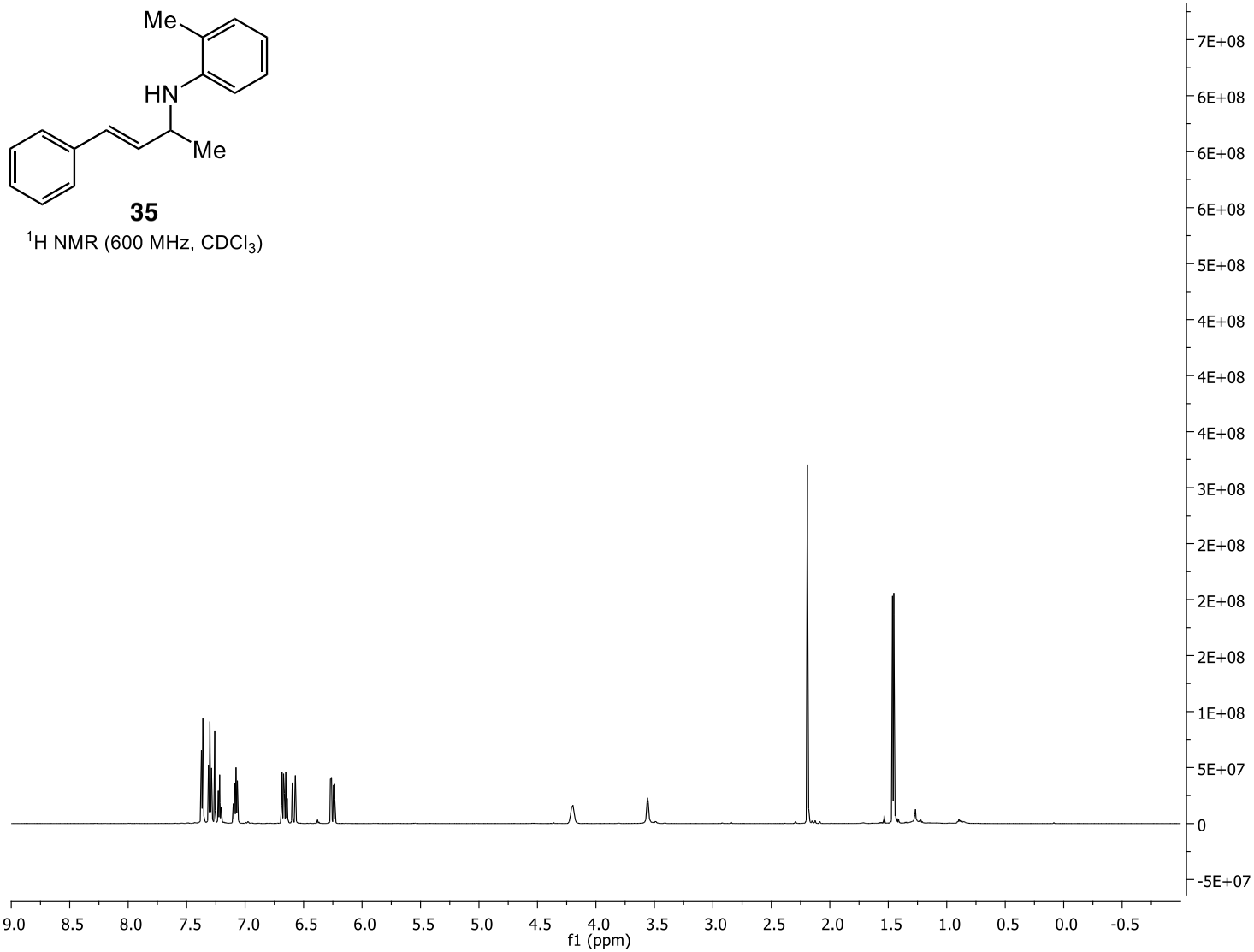
34

^{13}C NMR (100 MHz, $CDCl_3$)



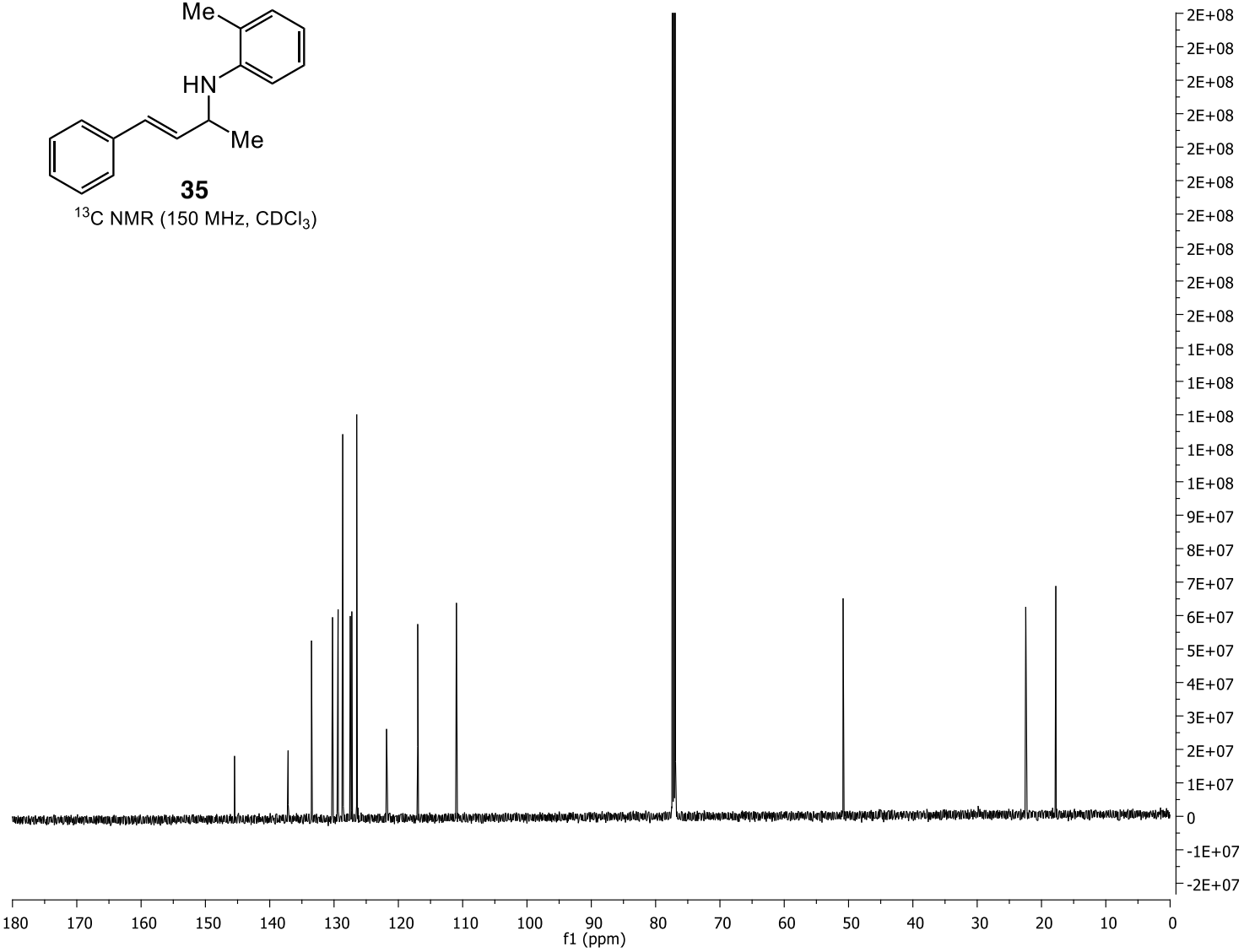
35

^{1}H NMR (600 MHz, $CDCl_3$)



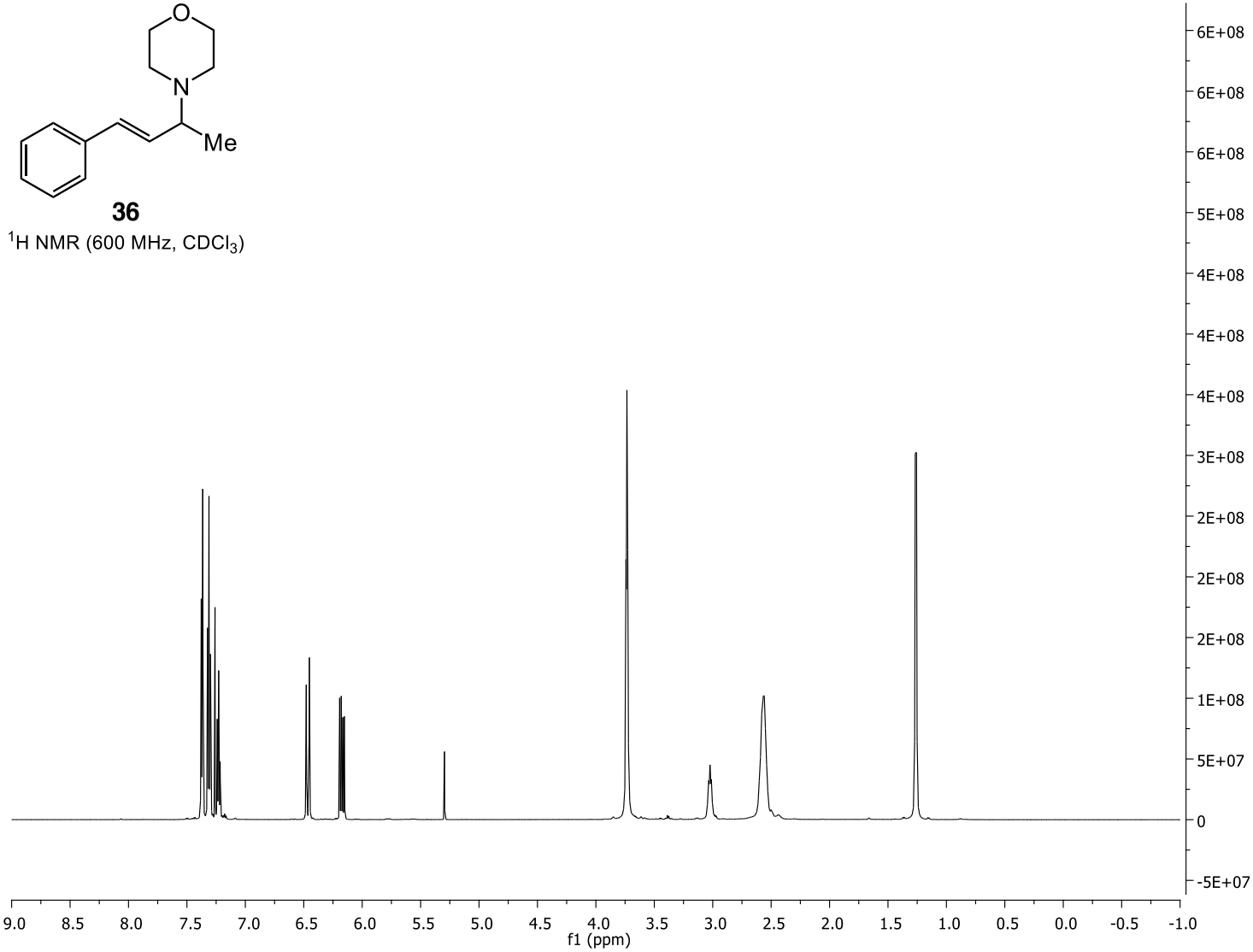
35

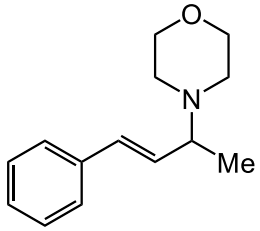
^{13}C NMR (150 MHz, $CDCl_3$)



36

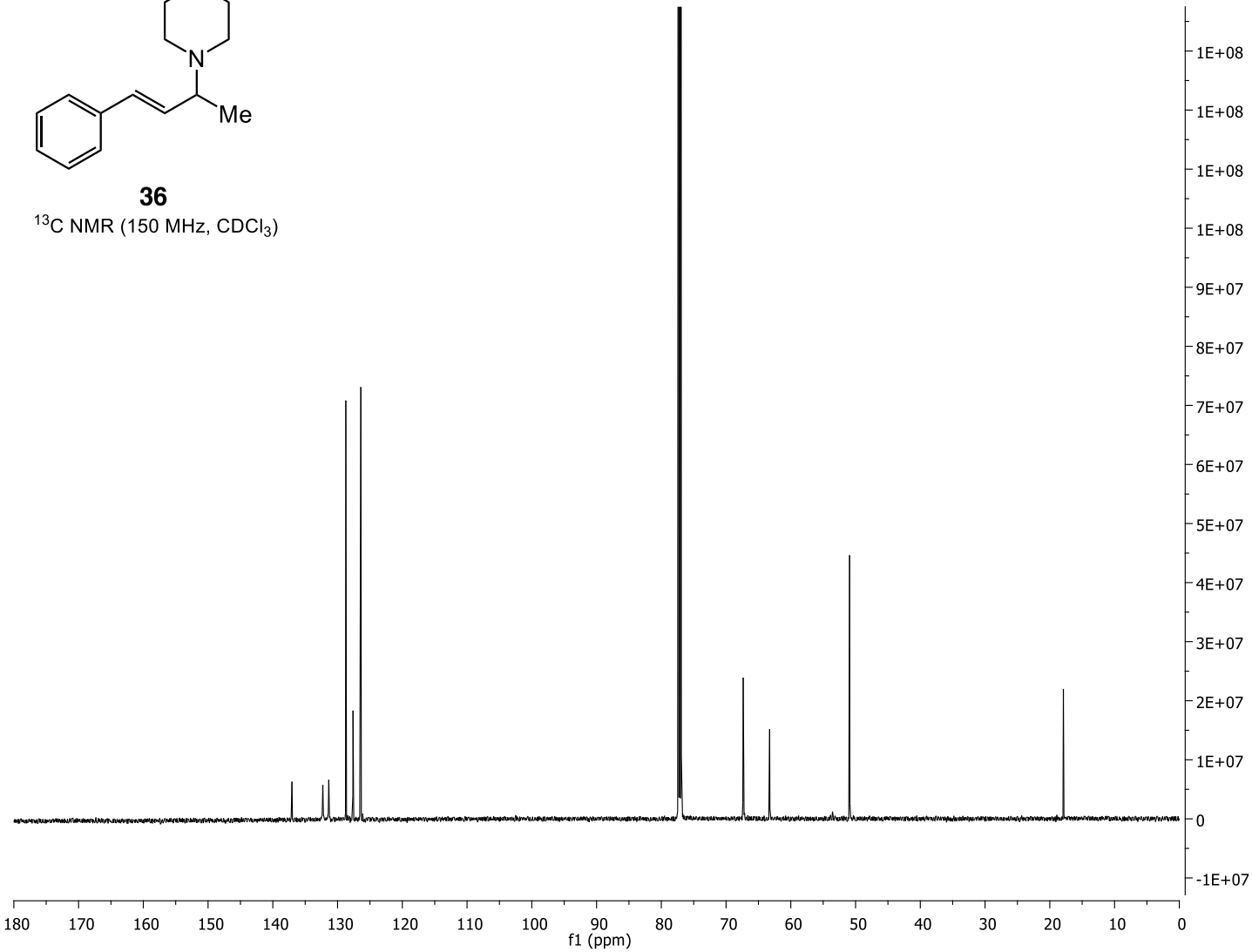
^{1}H NMR (600 MHz, $CDCl_3$)





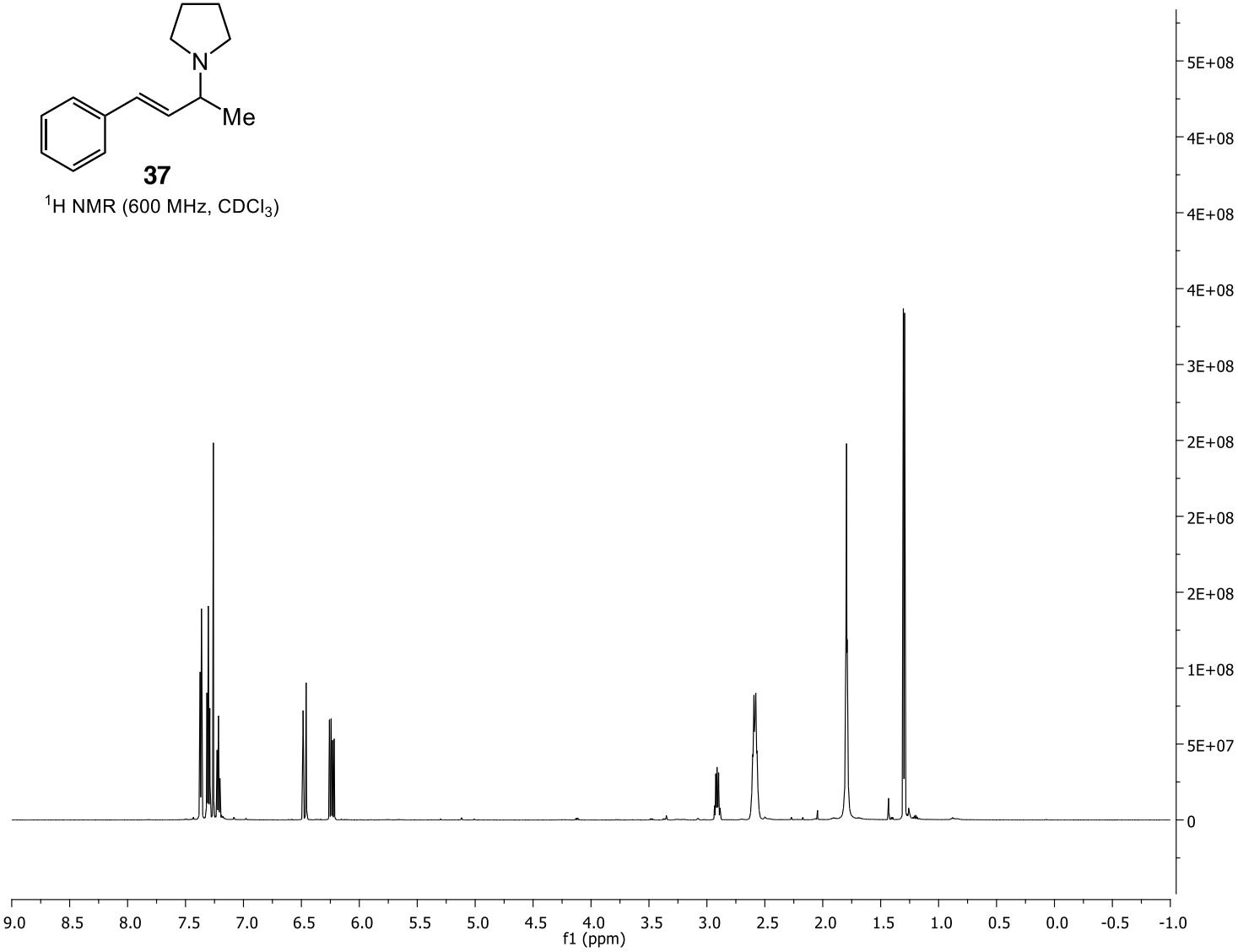
36

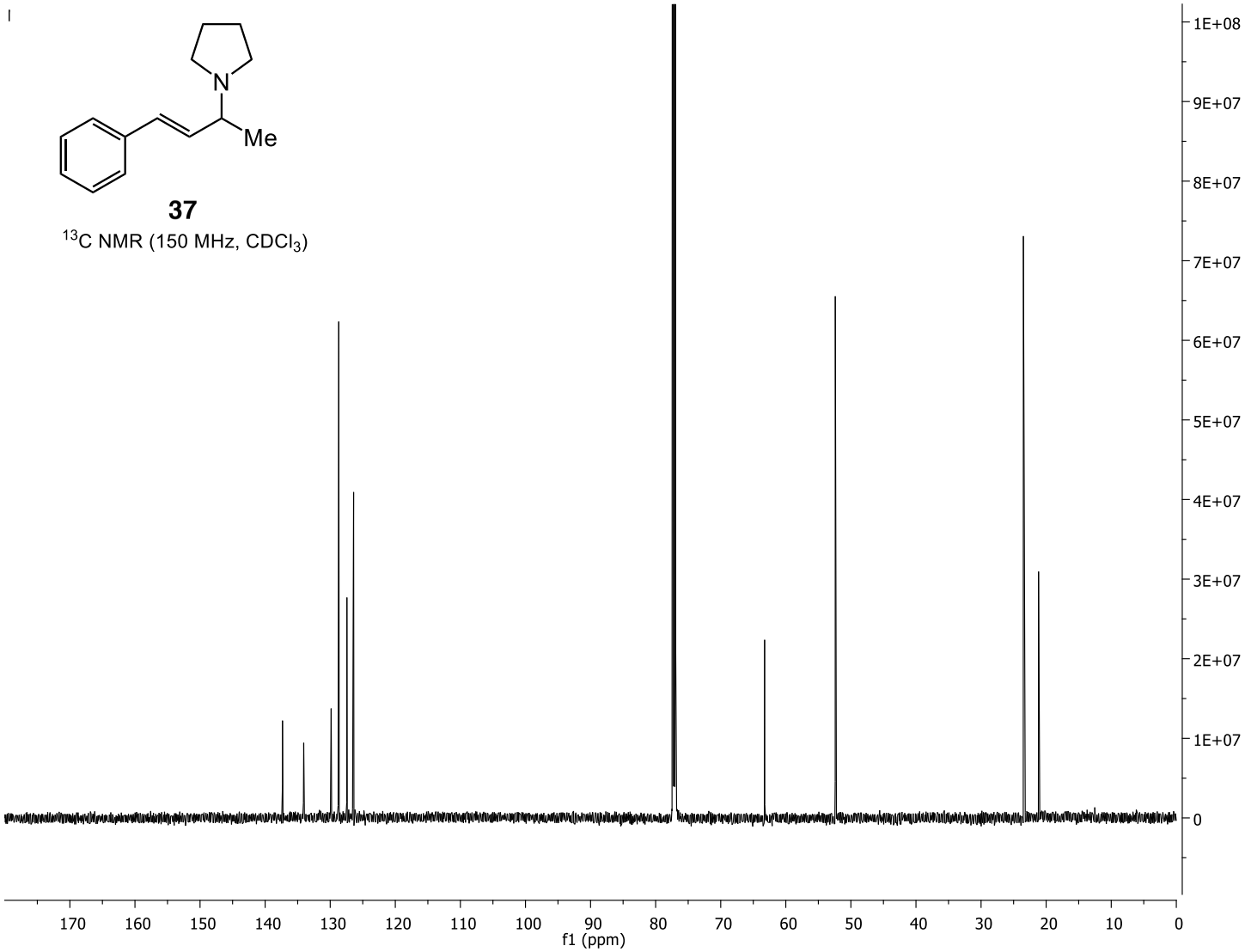
^{13}C NMR (150 MHz, $CDCl_3$)



37

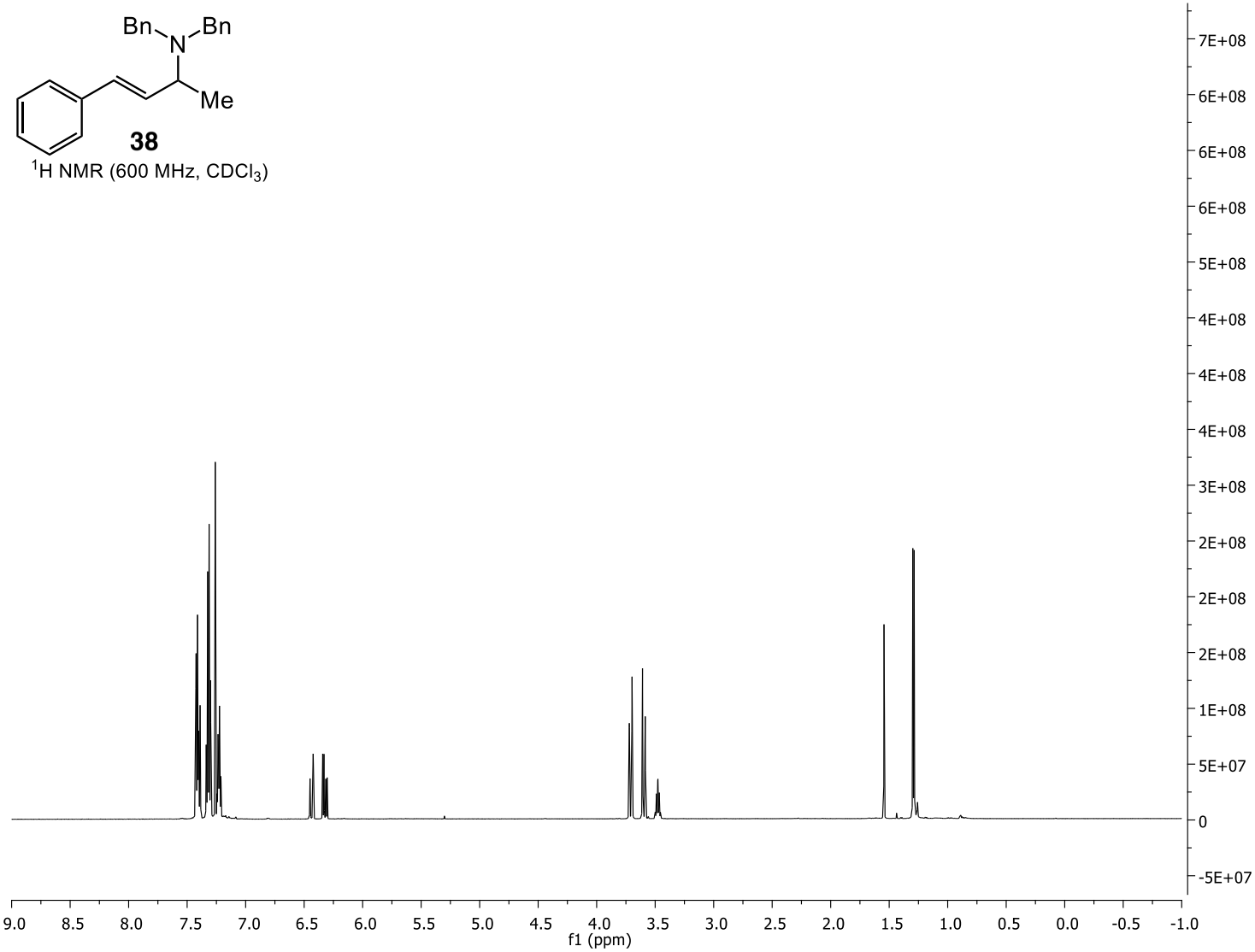
^{1}H NMR (600 MHz, $CDCl_3$)




N
Me
37
13C NMR (150 MHz, CDCl3)
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

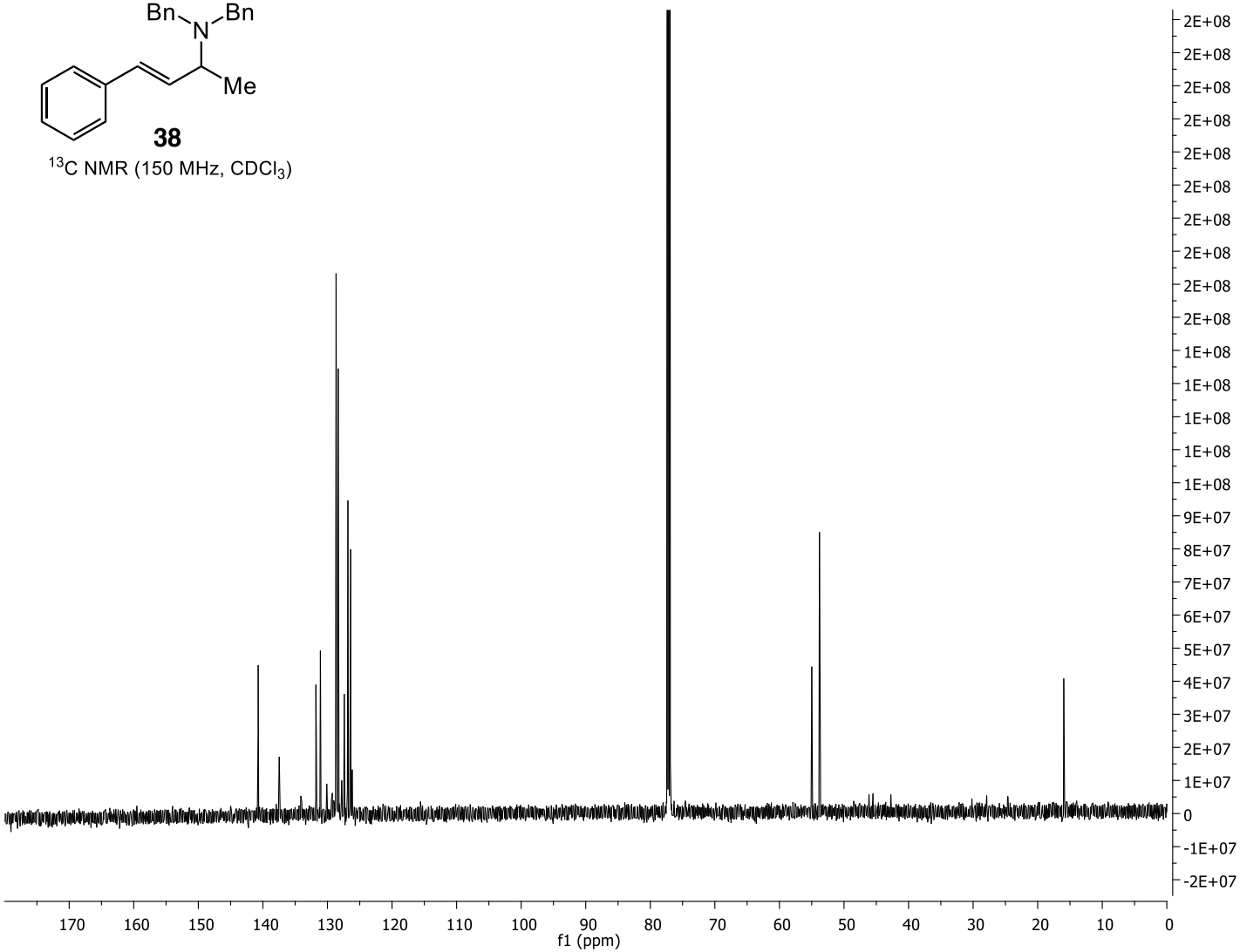
38

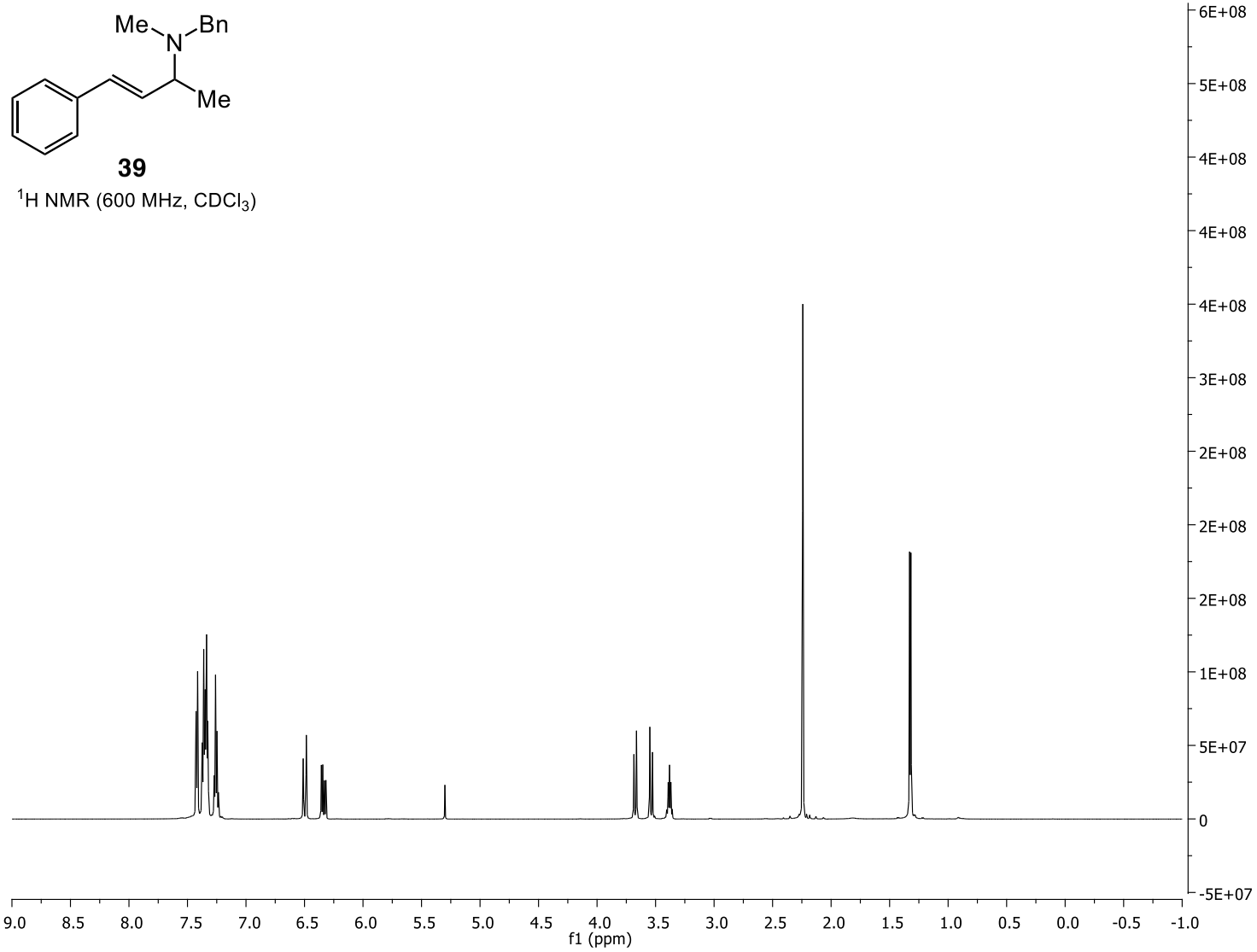
^{1}H NMR (600 MHz, $CDCl_3$)



38

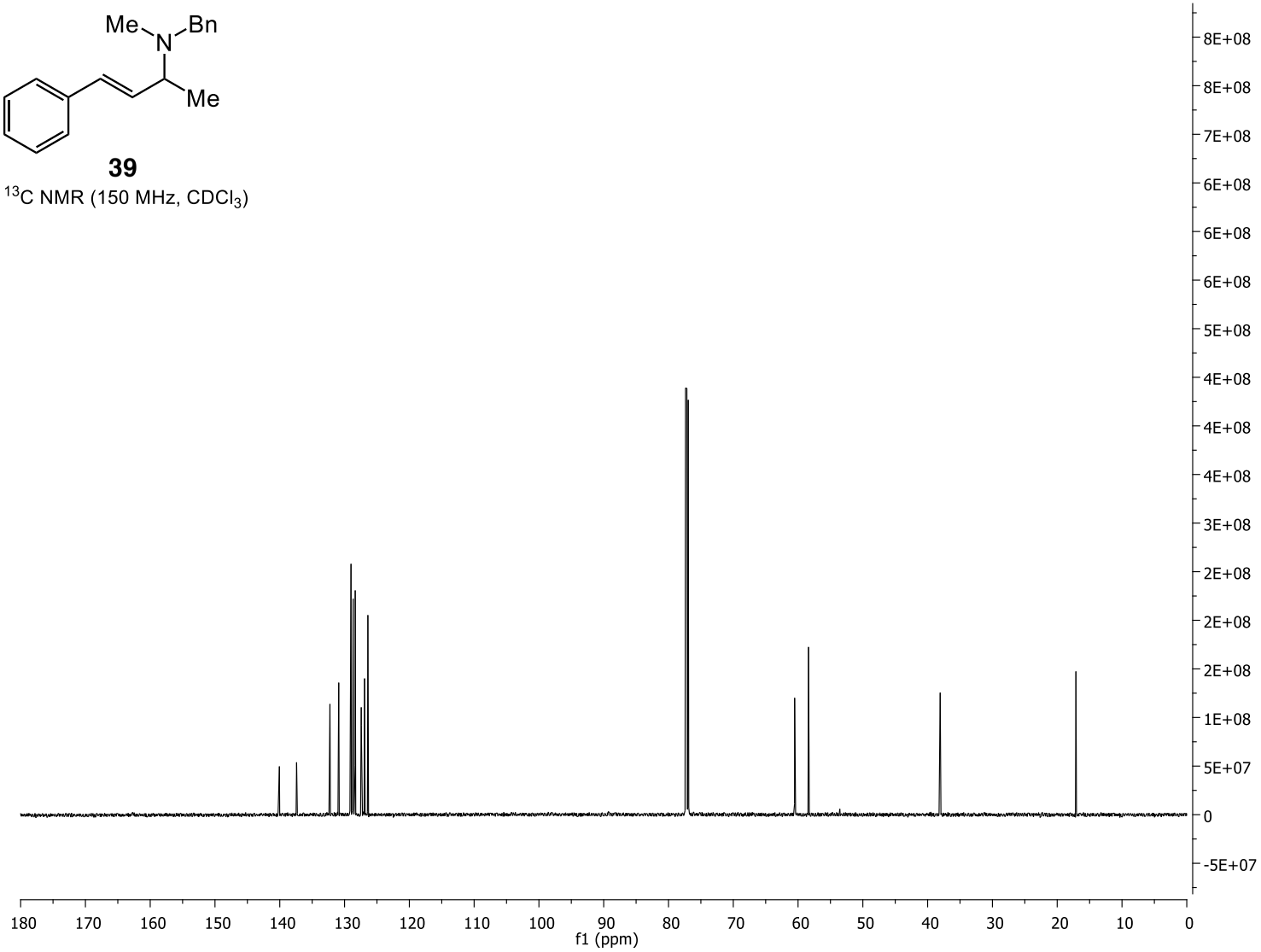
^{13}C NMR (150 MHz, $CDCl_3$)




Me
N
Bn
Me
39
1H NMR (600 MHz, CDCl3)
6E+08
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

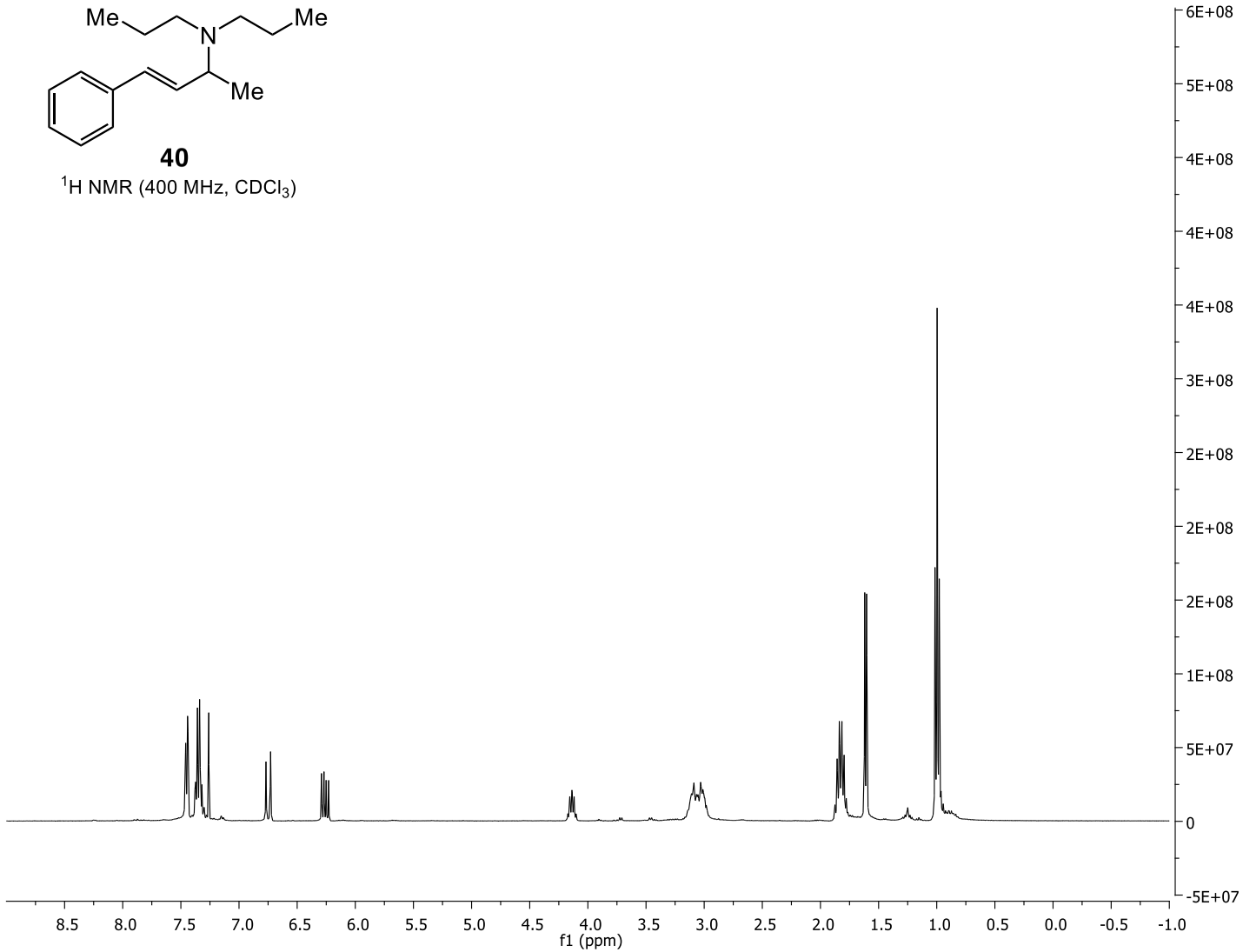
39

^{13}C NMR (150 MHz, $CDCl_3$)



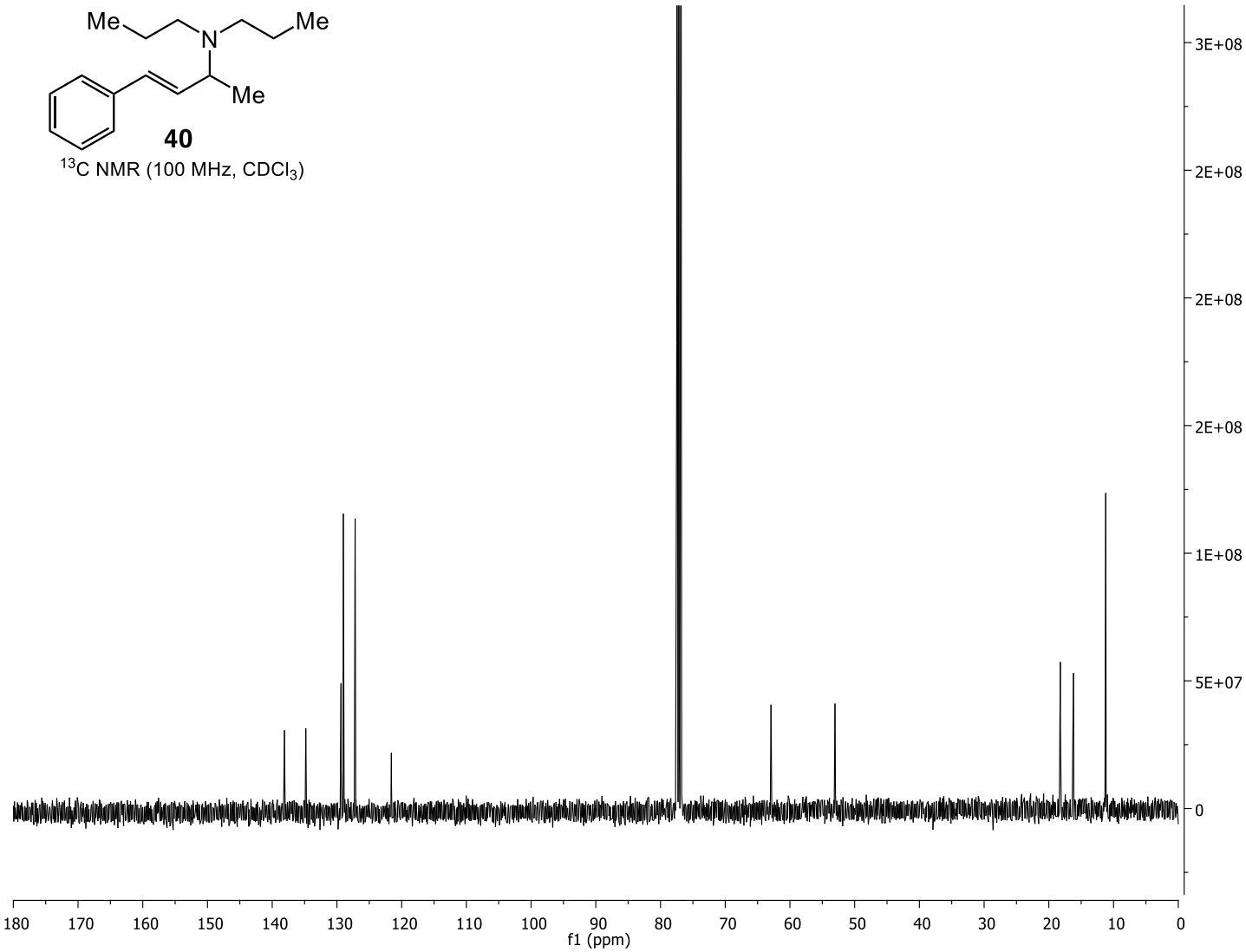
40

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



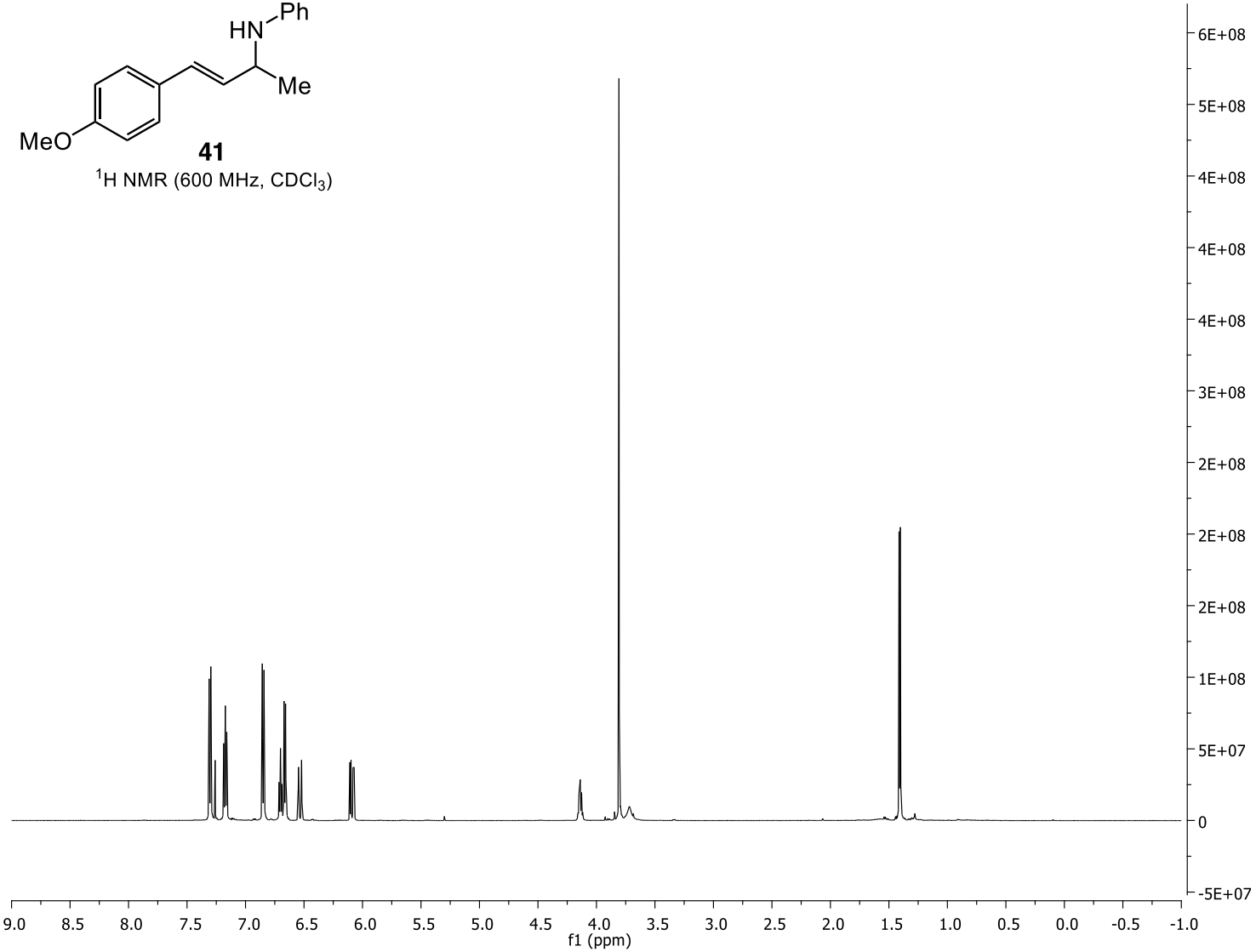
40

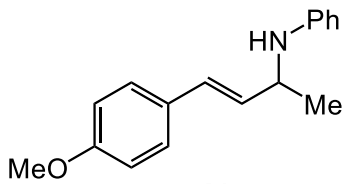
^{13}C NMR (100 MHz, $CDCl_3$)



41

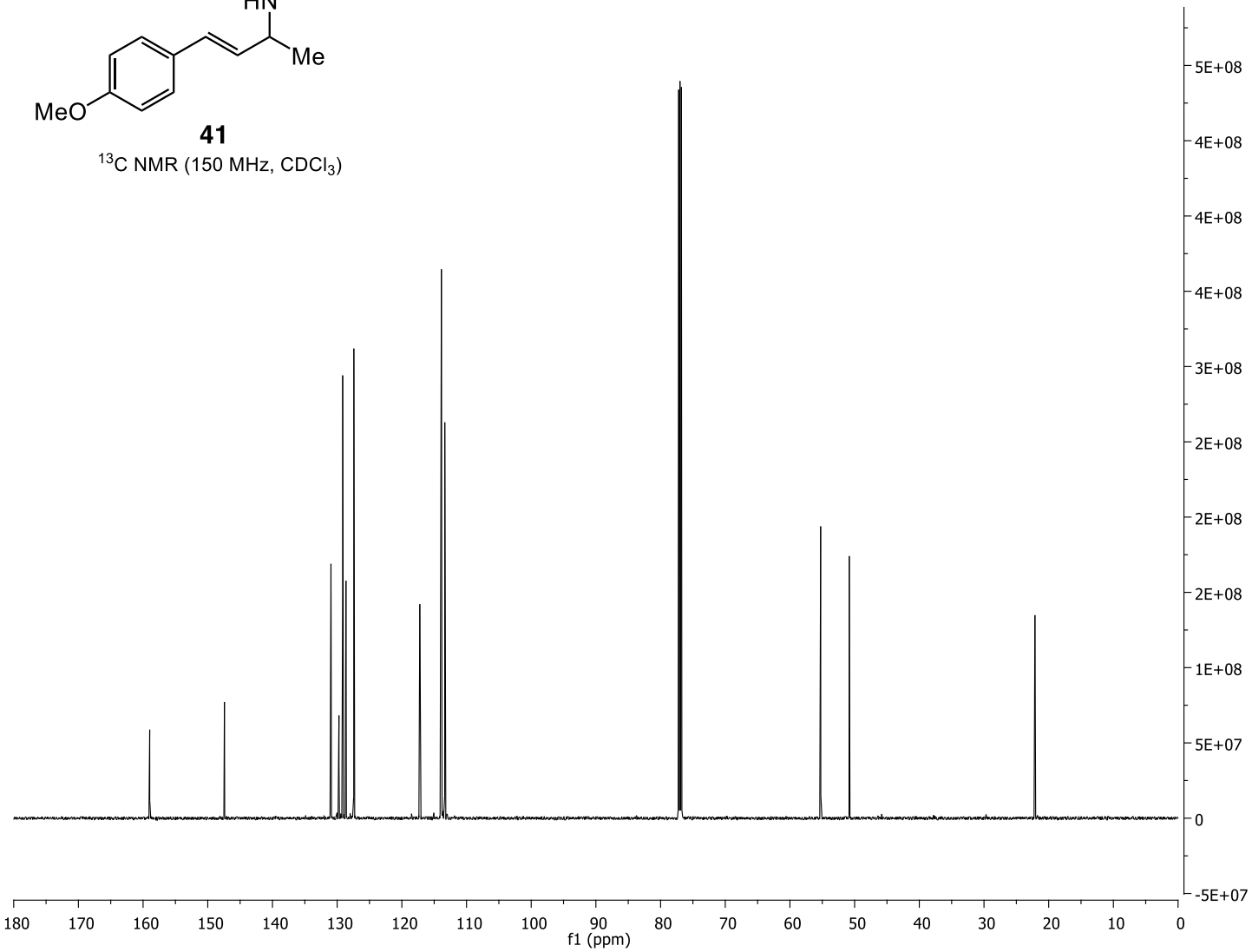
^{1}H NMR (600 MHz, $CDCl_3$)

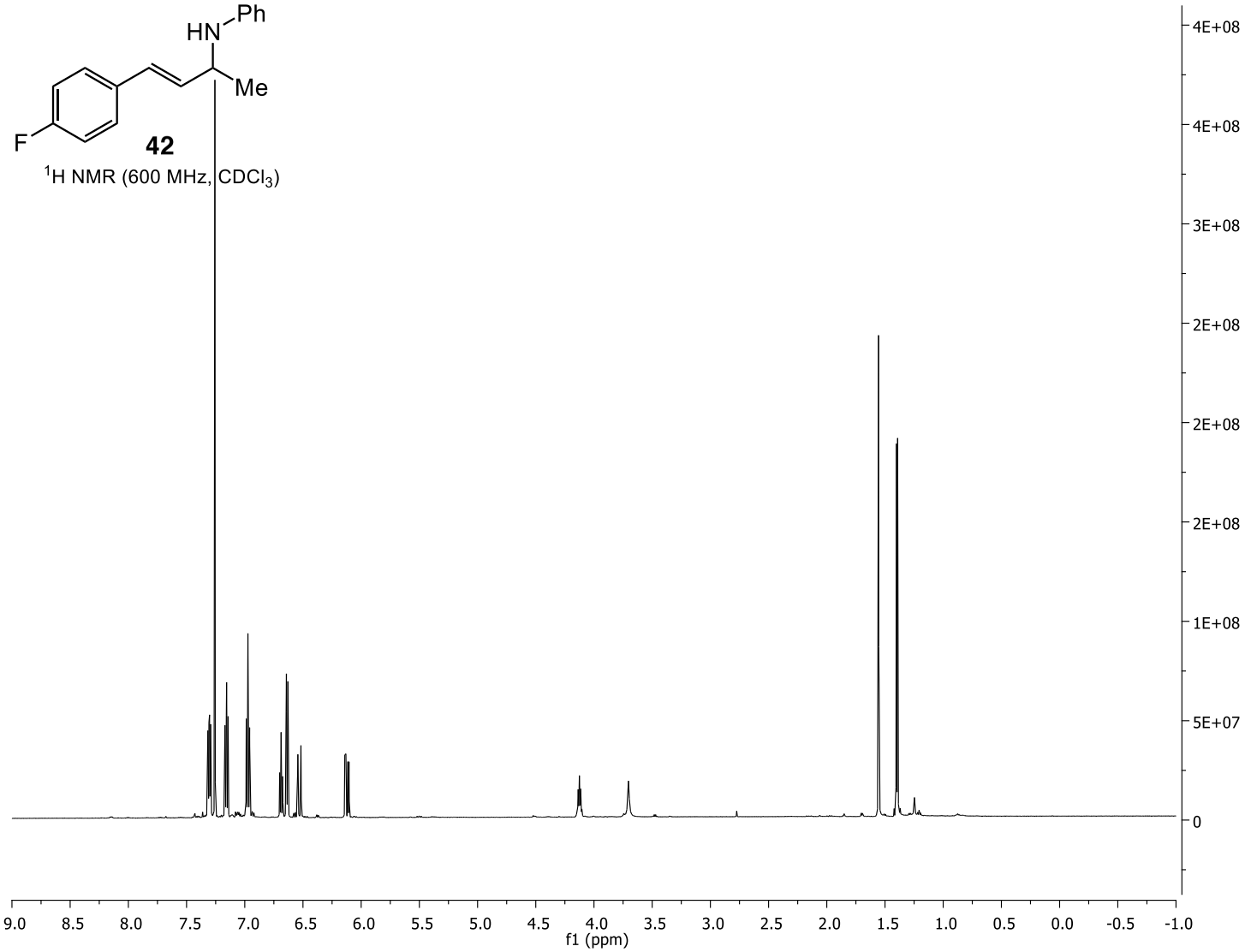


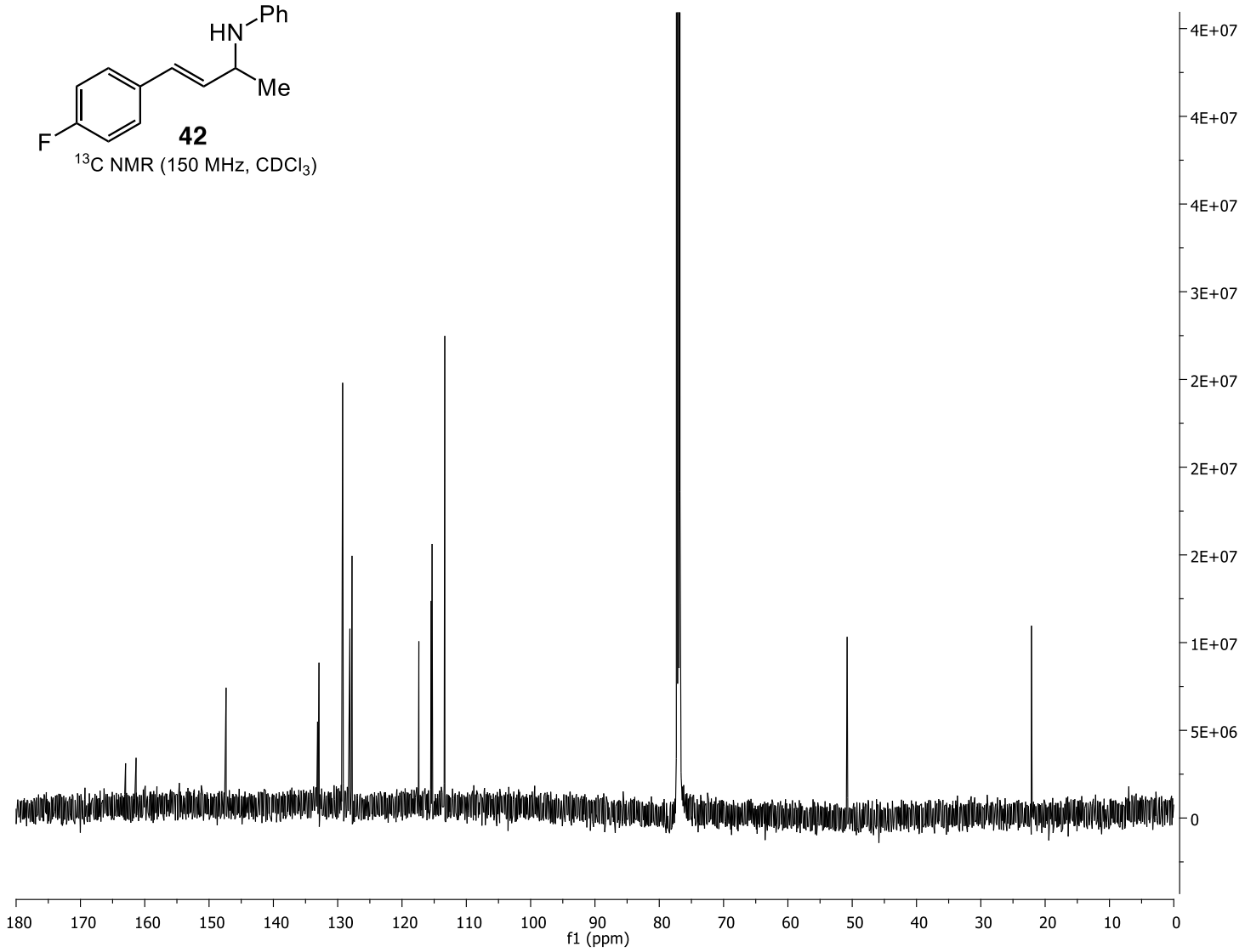


41

^{13}C NMR (150 MHz, $CDCl_3$)

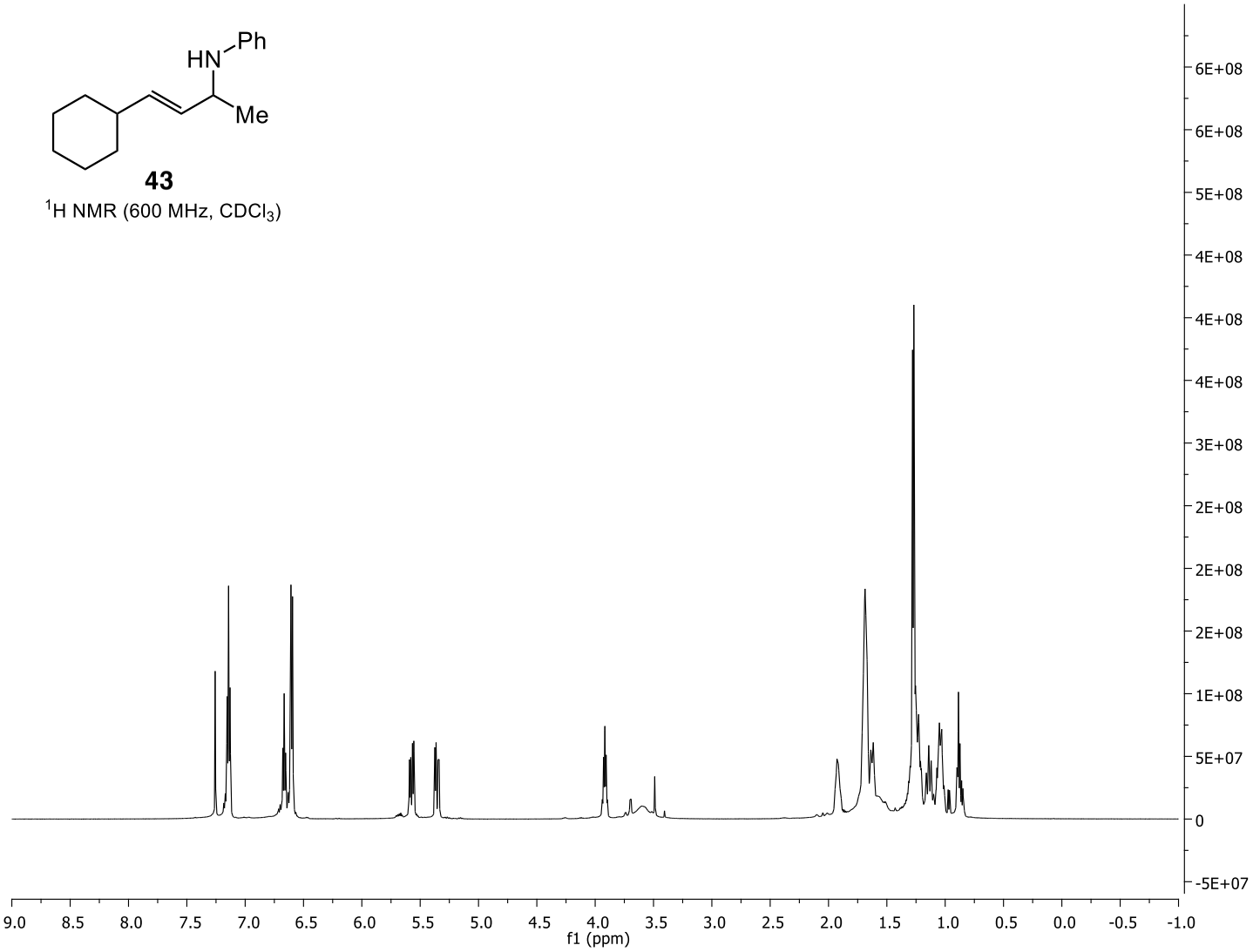



HN
Ph
Me
F
42
^{1}H NMR (600 MHz, $CDCl_3$)
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


HN
Ph
Me
F
42
13C NMR (150 MHz, CDCl3)
4E+07
4E+07
4E+07
3E+07
2E+07
2E+07
2E+07
1E+07
5E+06
0
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

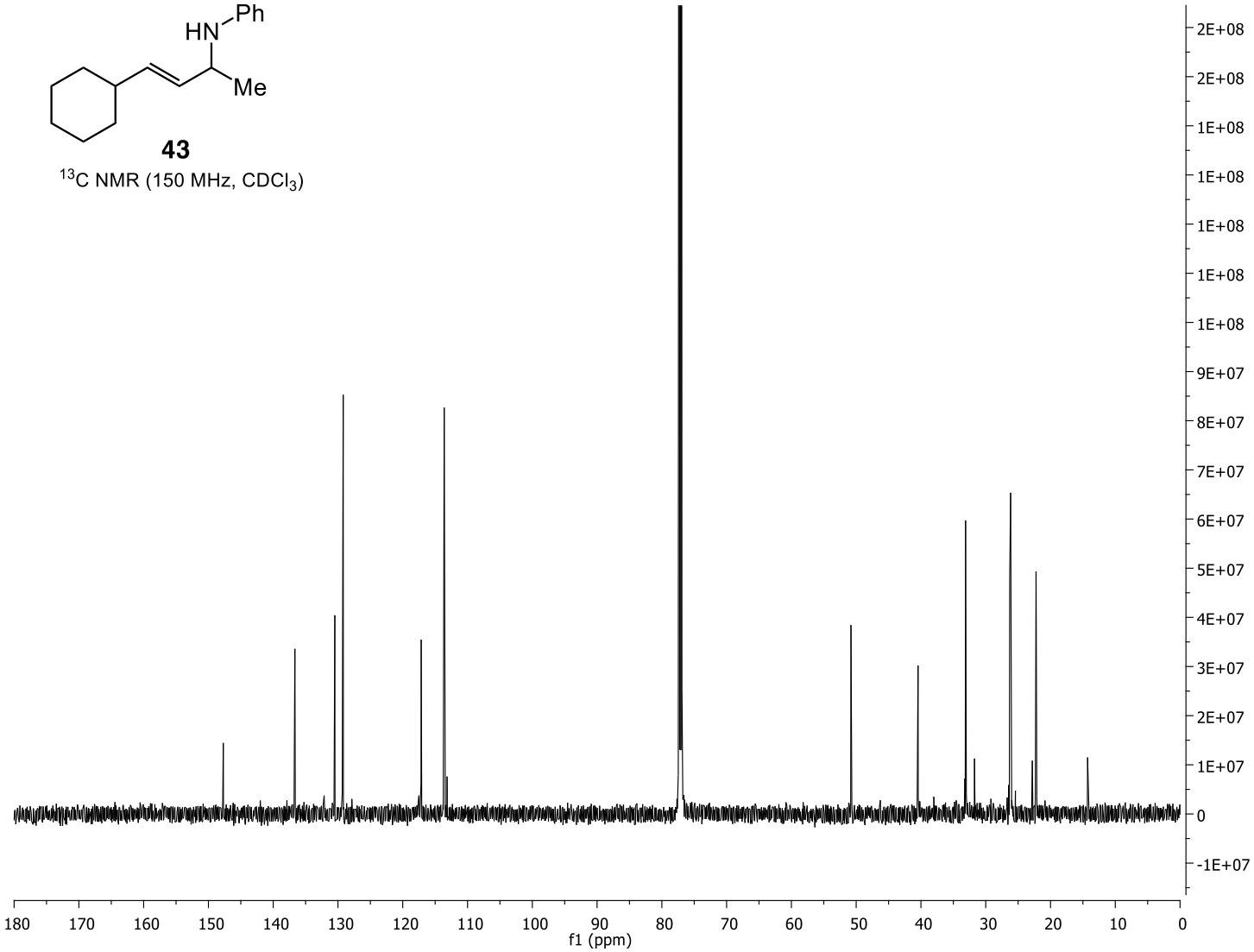
43

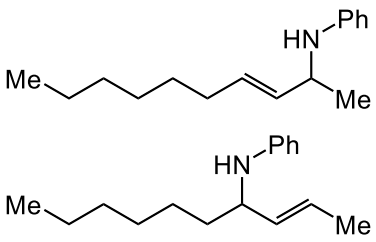
^{1}H NMR (600 MHz, $CDCl_3$)



43

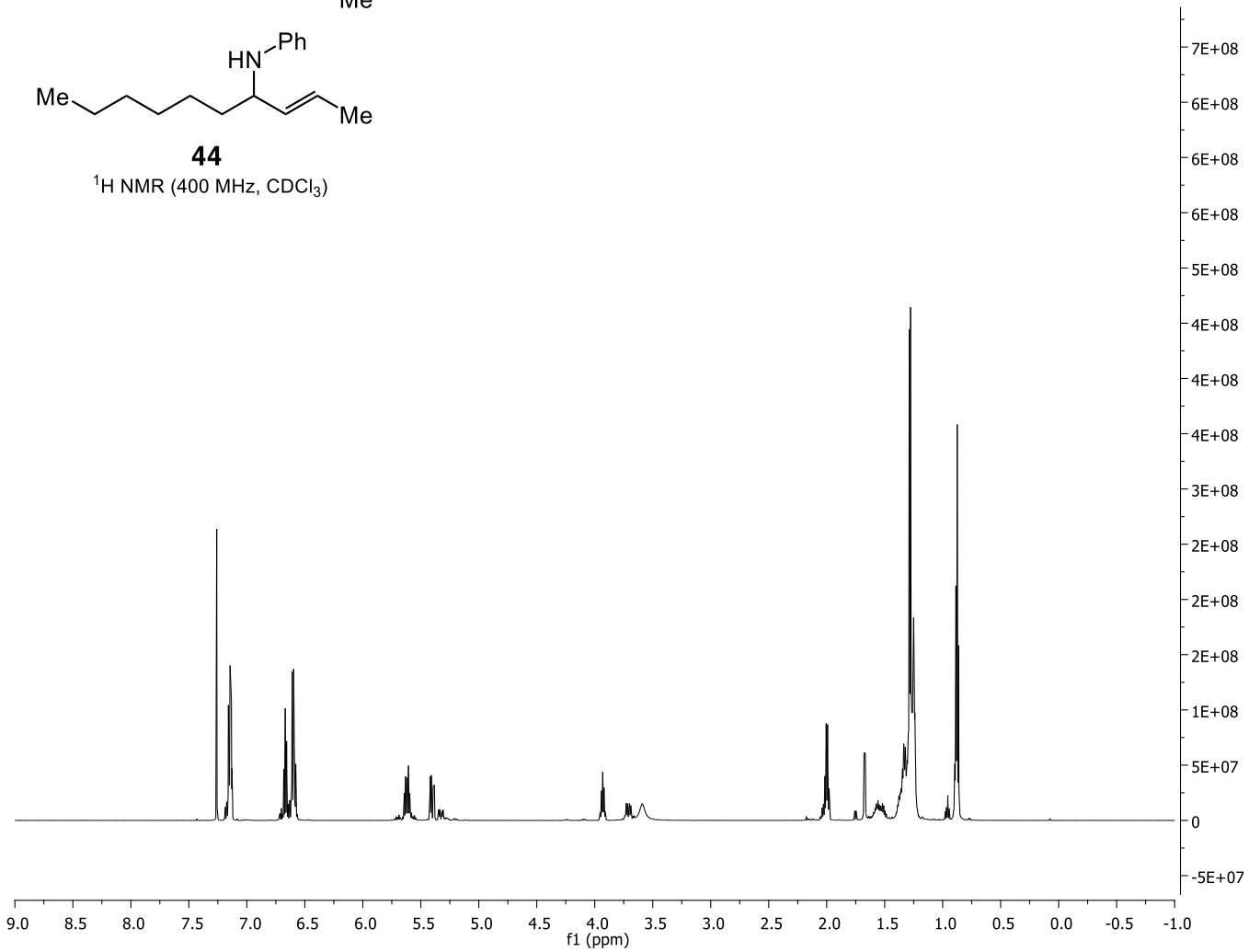
^{13}C NMR (150 MHz, $CDCl_3$)

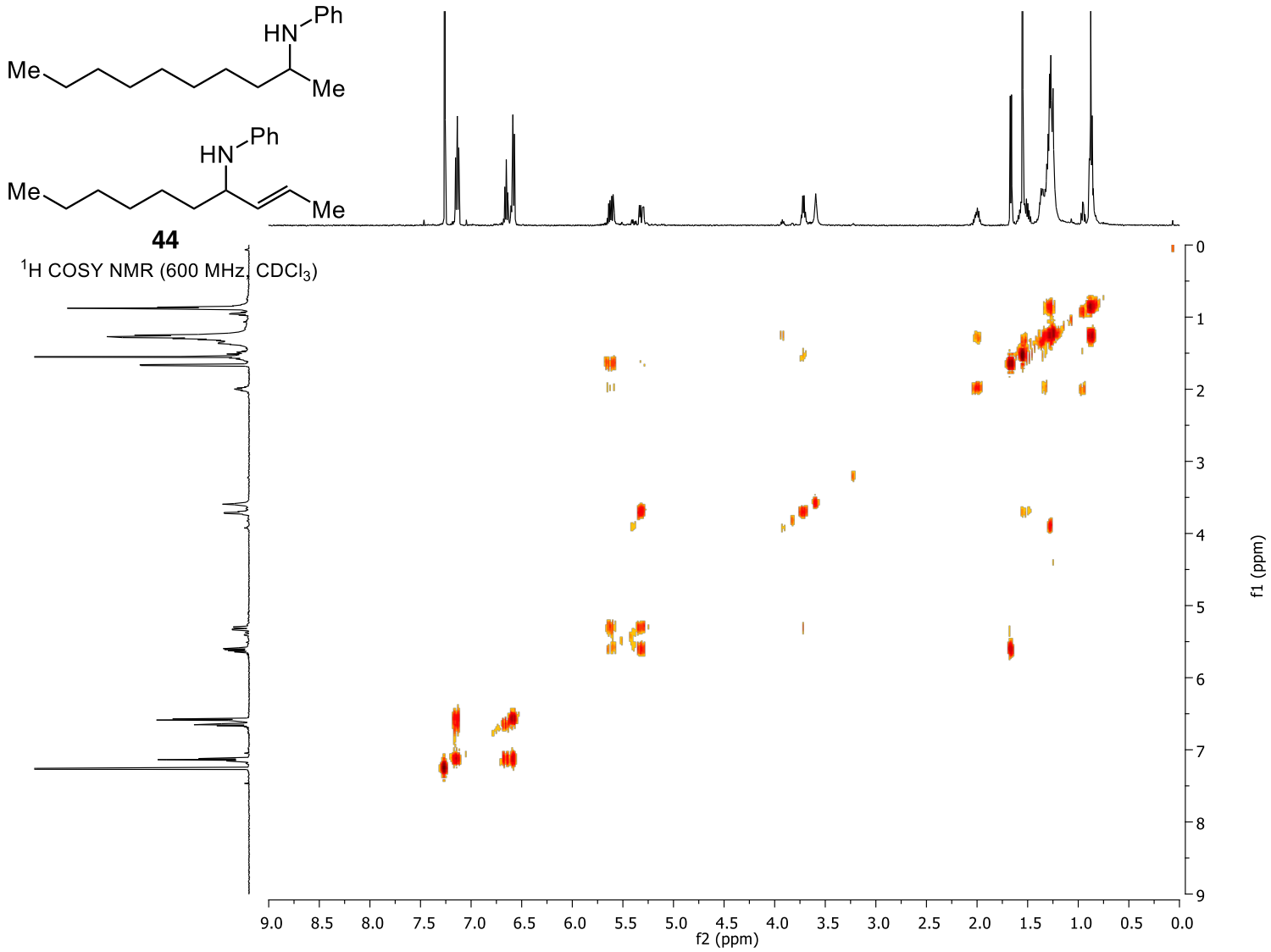


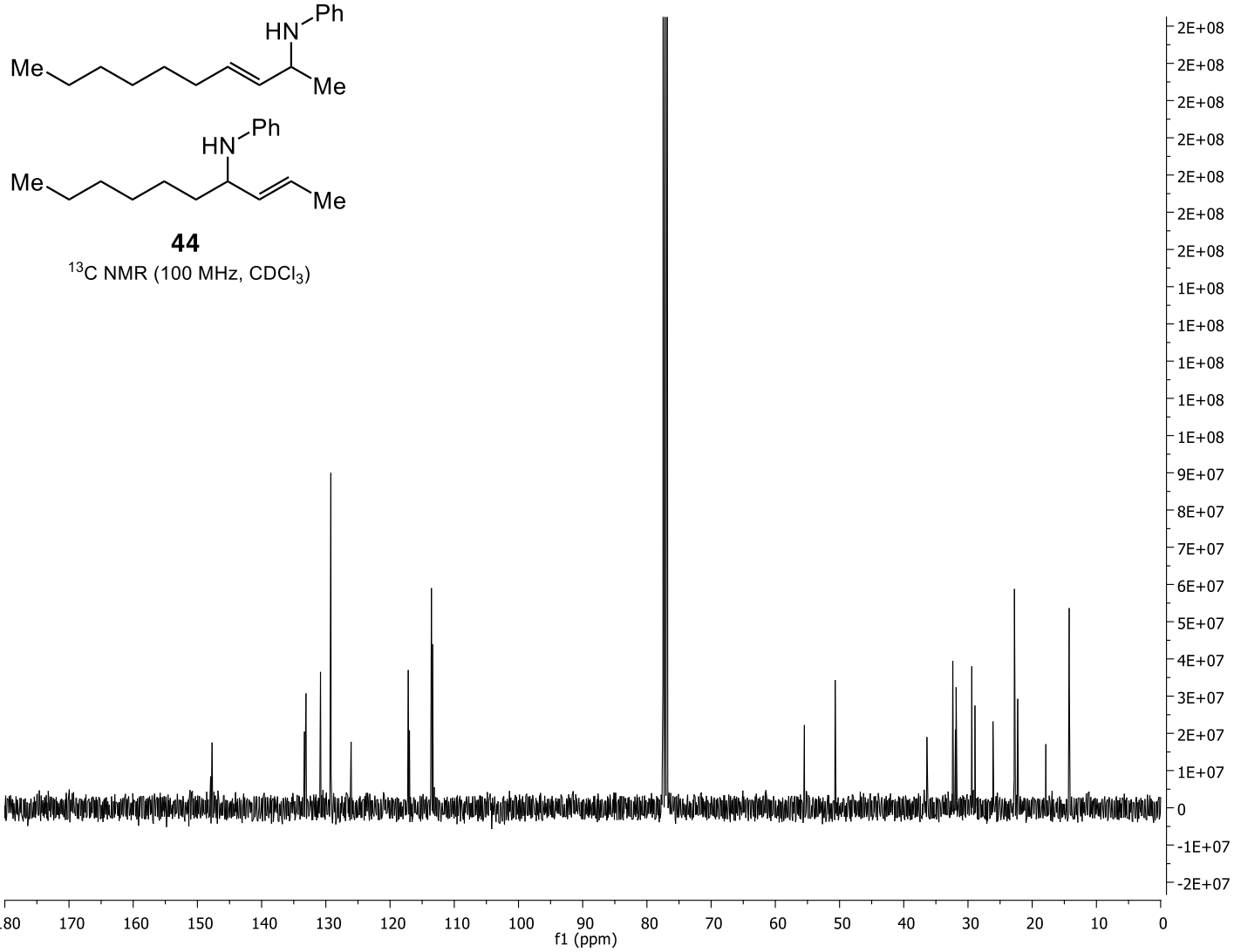


44

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




Me
HN
Ph
Me
Me
HN
Ph
Me
Me
44
^{1}H COSY NMR (600 MHz, $CDCl_3$)
f2 (ppm)
f1 (ppm)

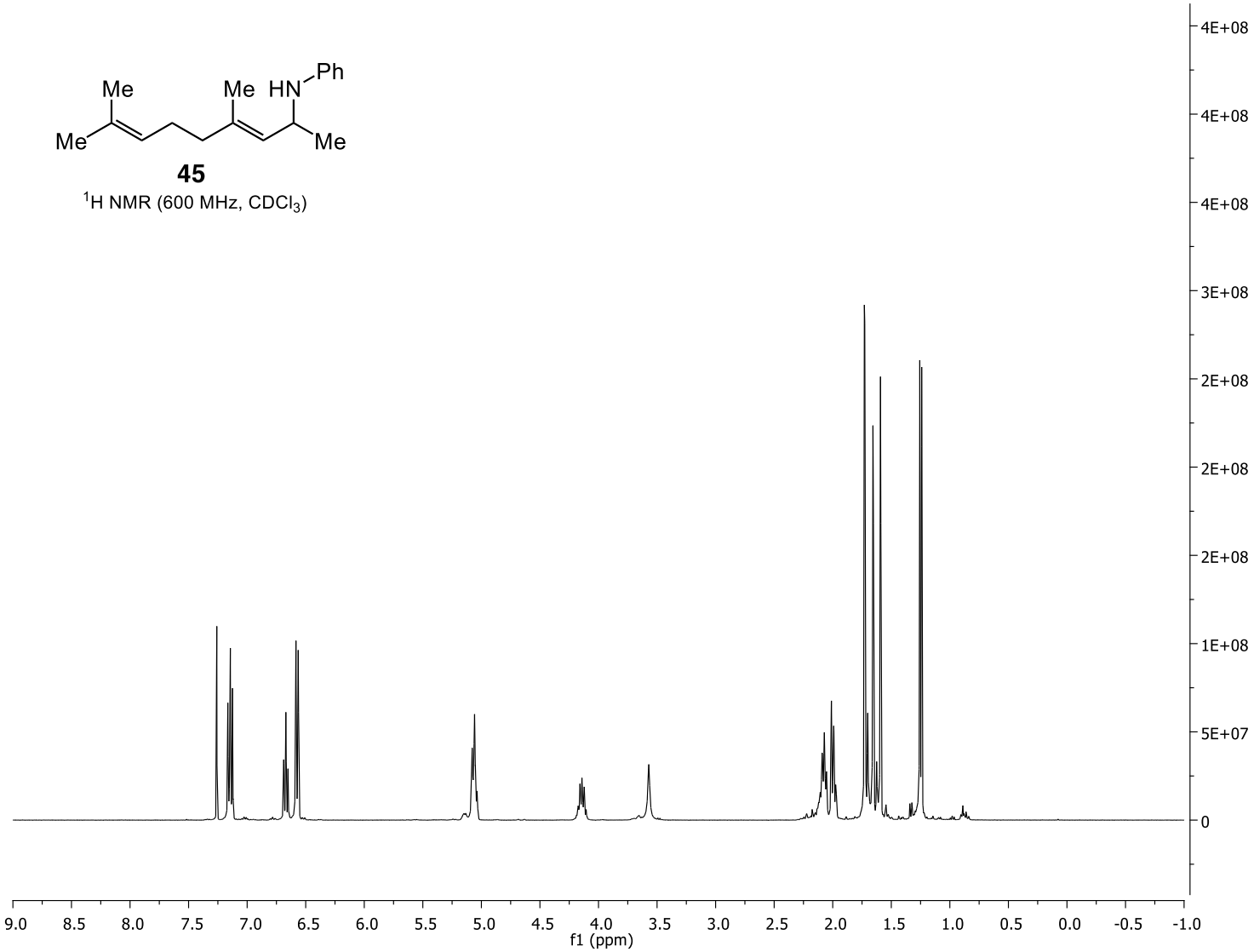


44

^{13}C NMR (100 MHz, $CDCl_3$)

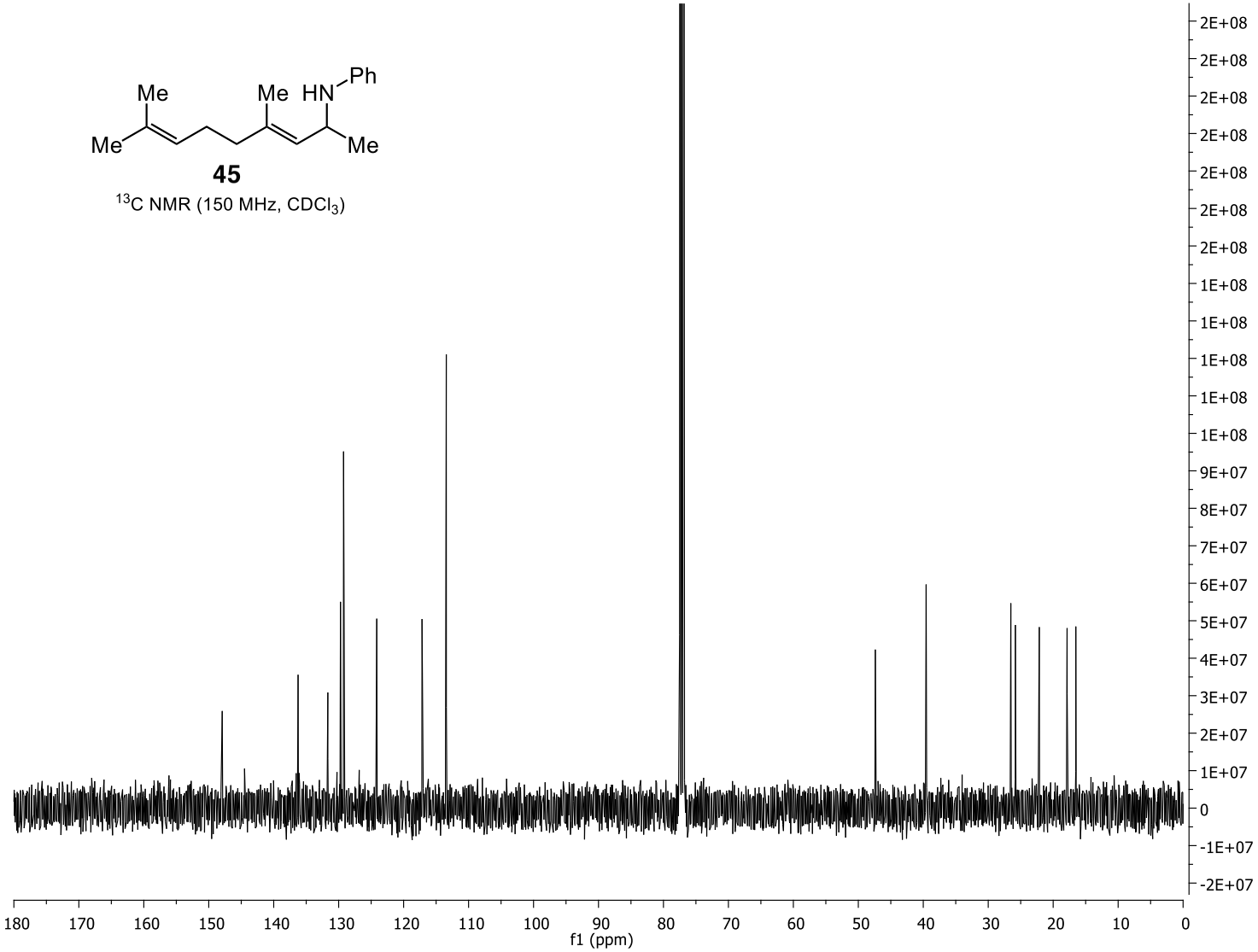
45

^{1}H NMR (600 MHz, $CDCl_3$)



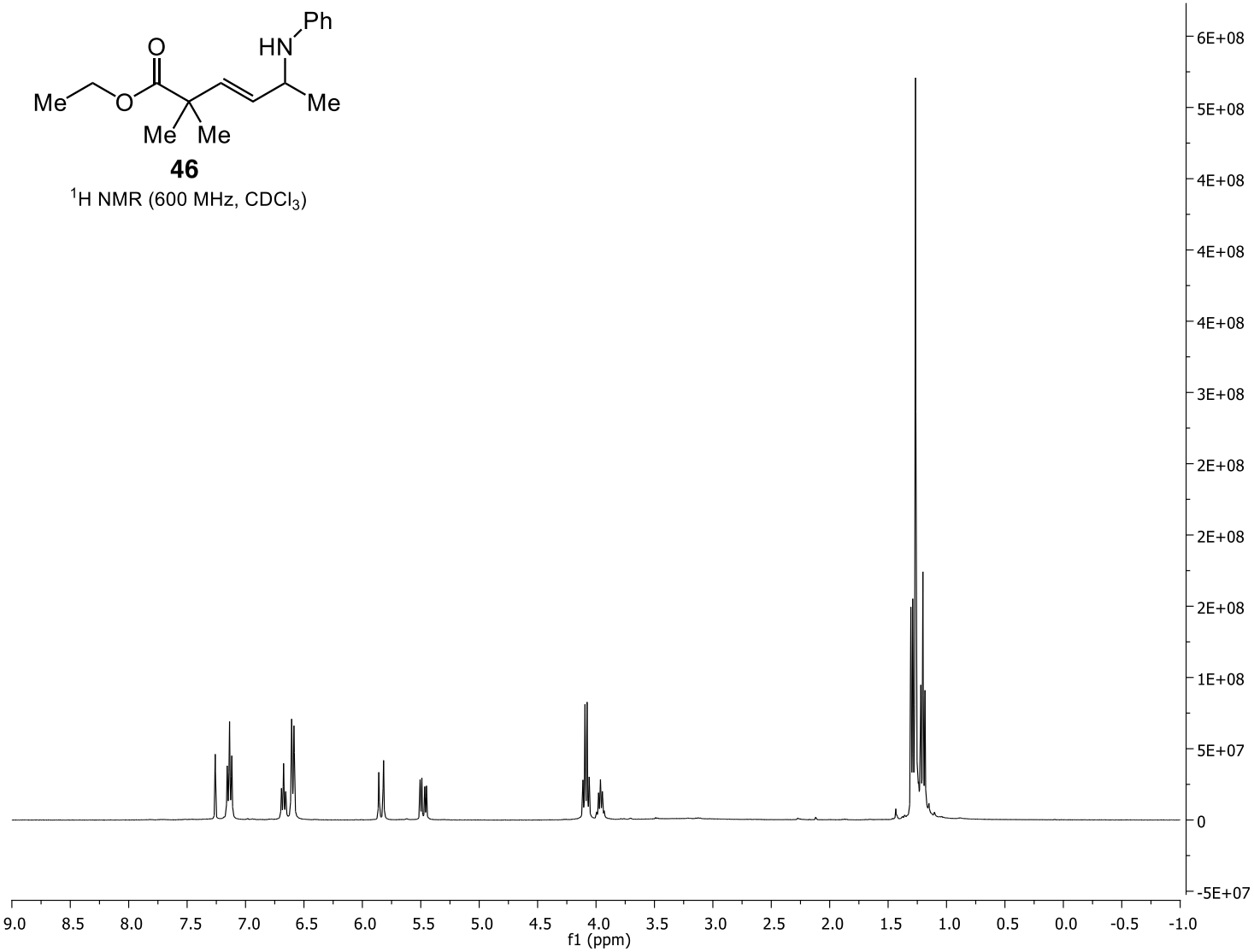
45

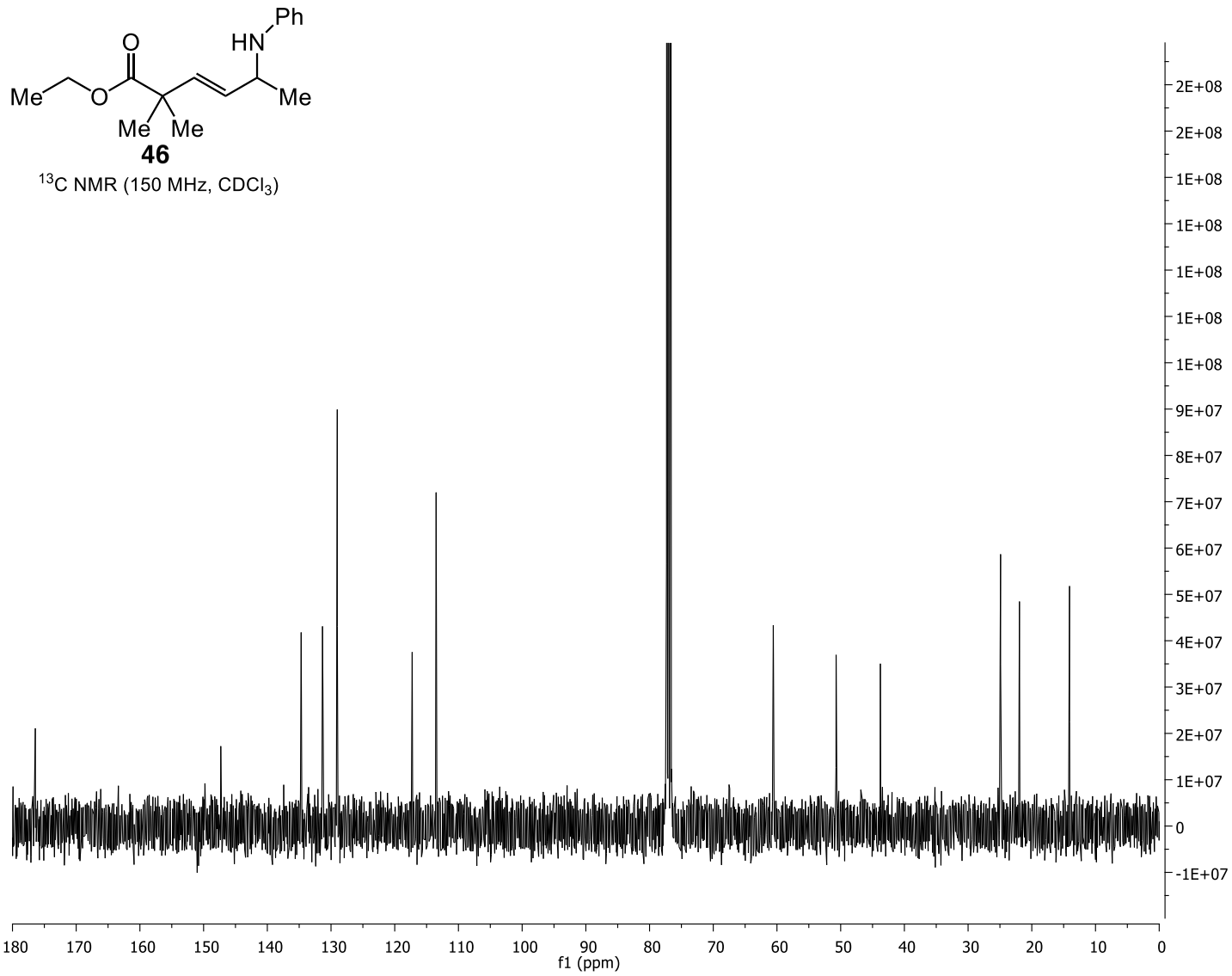
^{13}C NMR (150 MHz, $CDCl_3$)



46

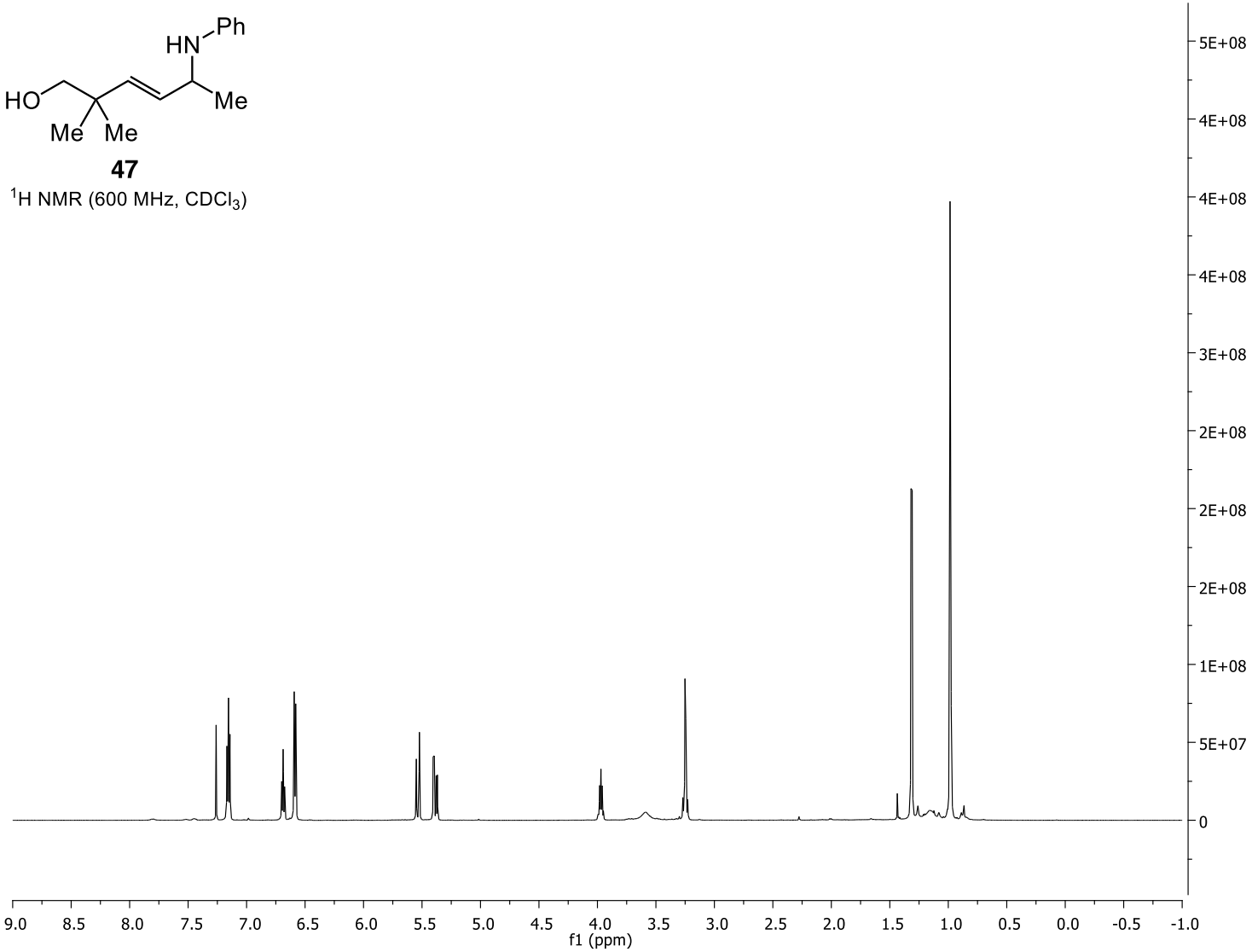
^{1}H NMR (600 MHz, $CDCl_3$)




Ph
HN
O
Me
O
Me
Me
Me
46
13C NMR (150 MHz, CDCl3)
2E+08
2E+08
1E+08
1E+08
1E+08
1E+08
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
-1E+07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

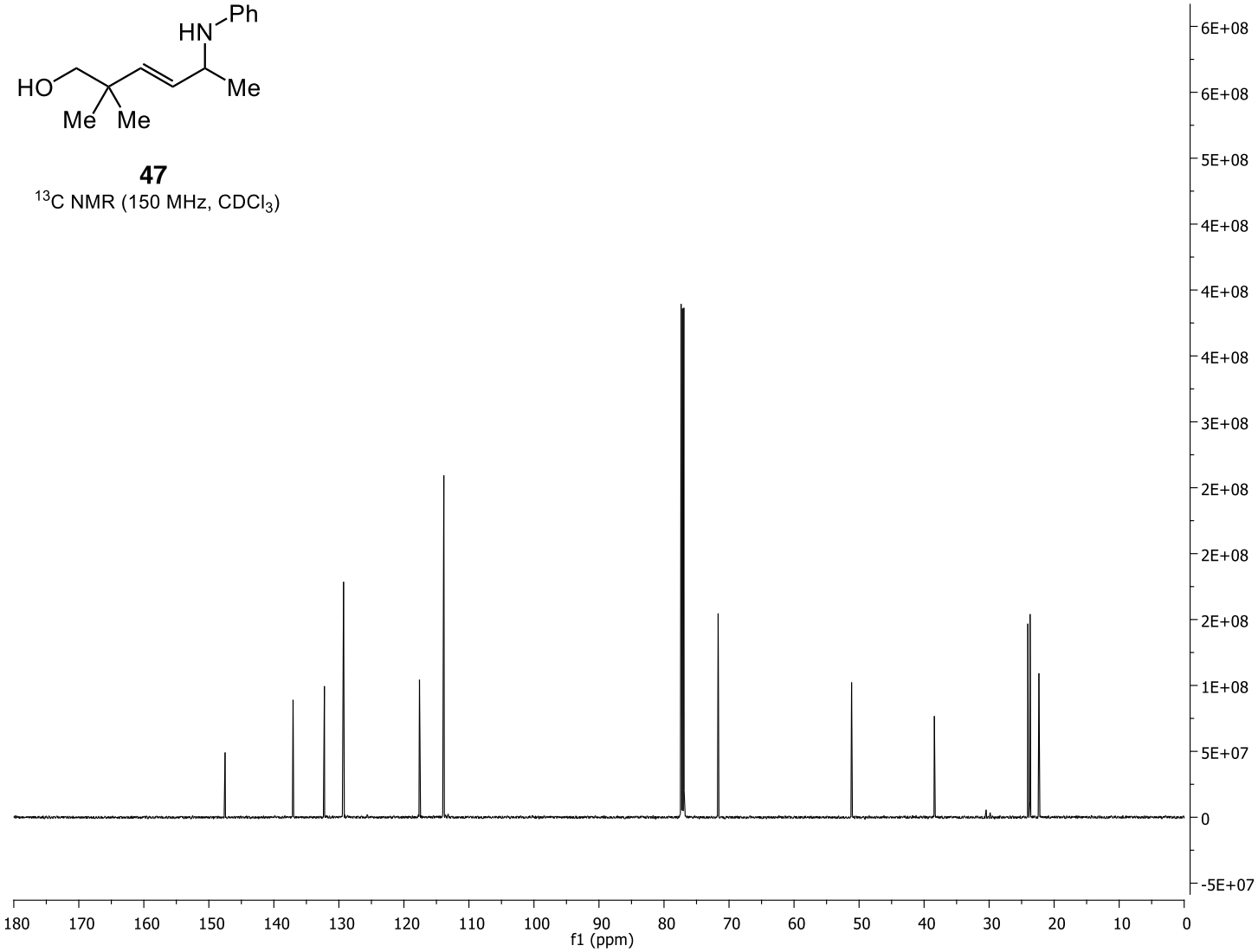
47

^{1}H NMR (600 MHz, $CDCl_3$)



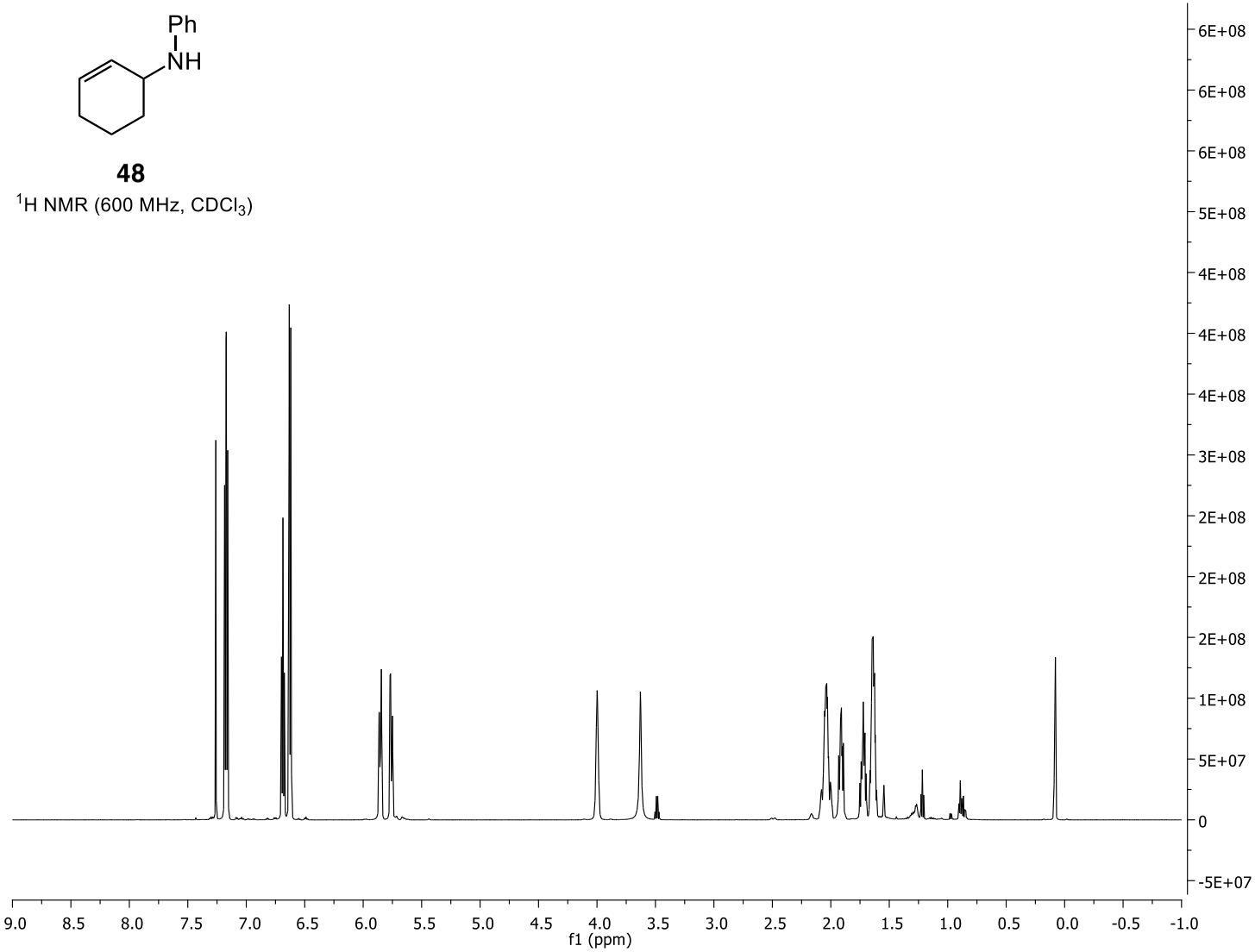
47

^{13}C NMR (150 MHz, $CDCl_3$)



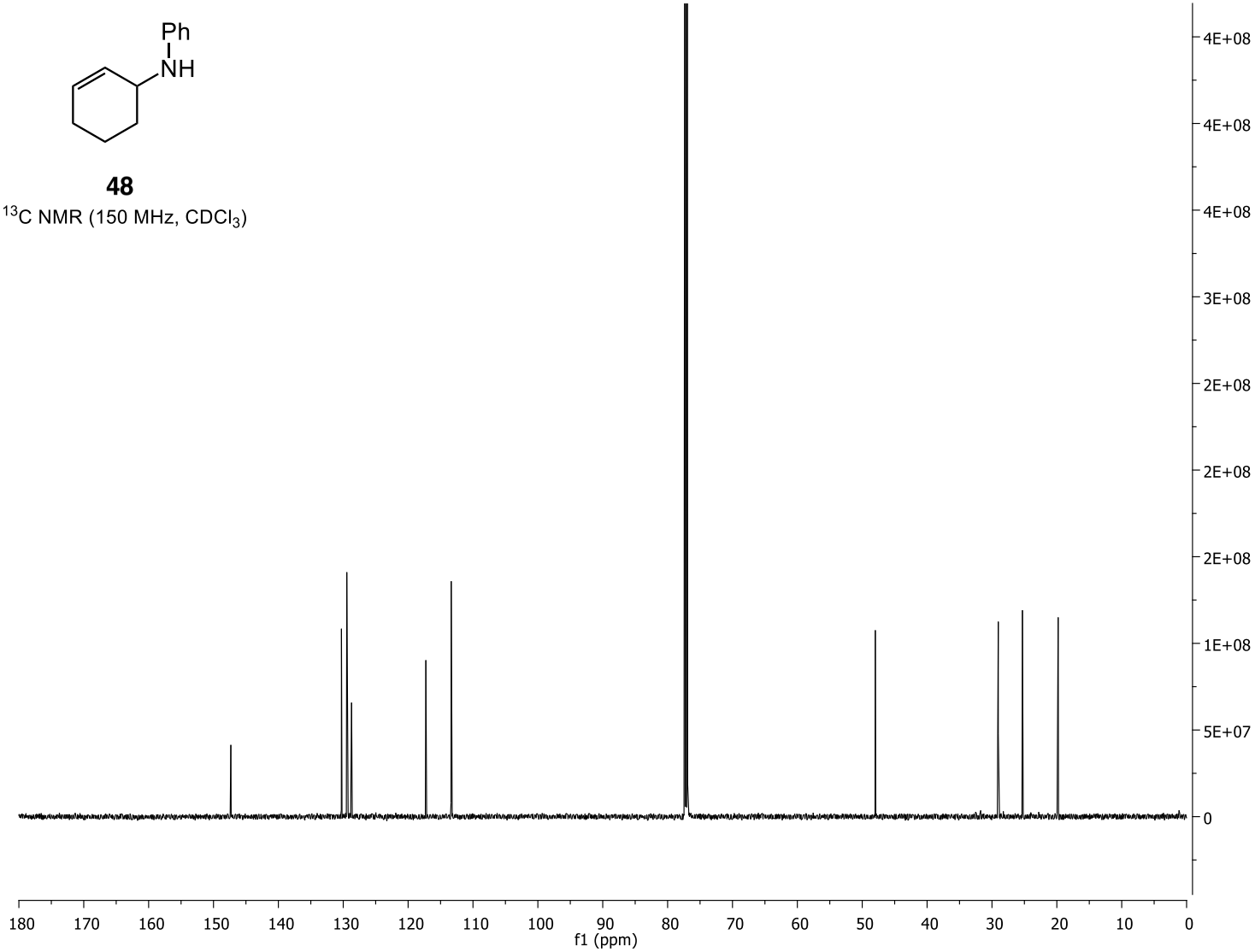
48

^{1}H NMR (600 MHz, $CDCl_3$)



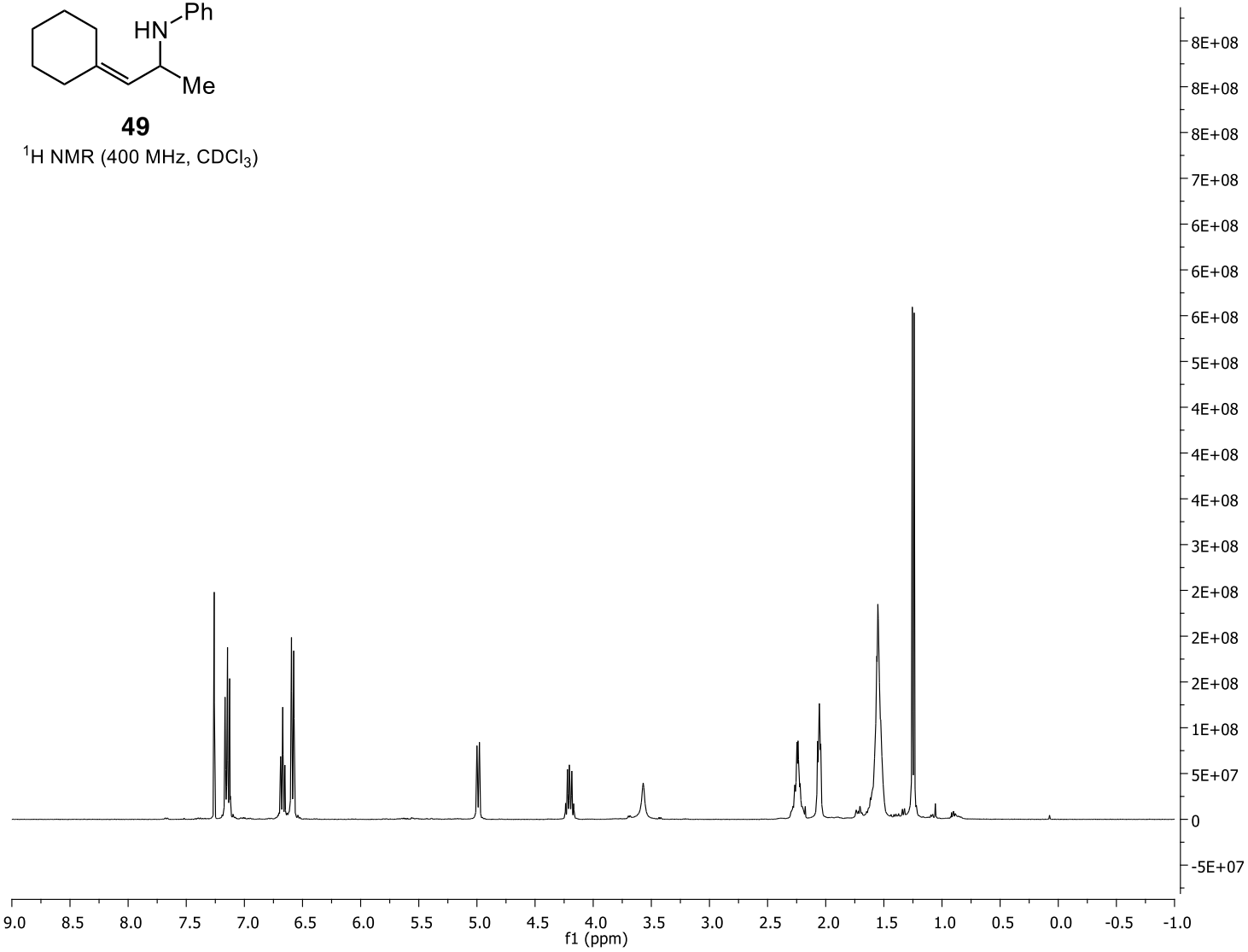
48

^{13}C NMR (150 MHz, $CDCl_3$)



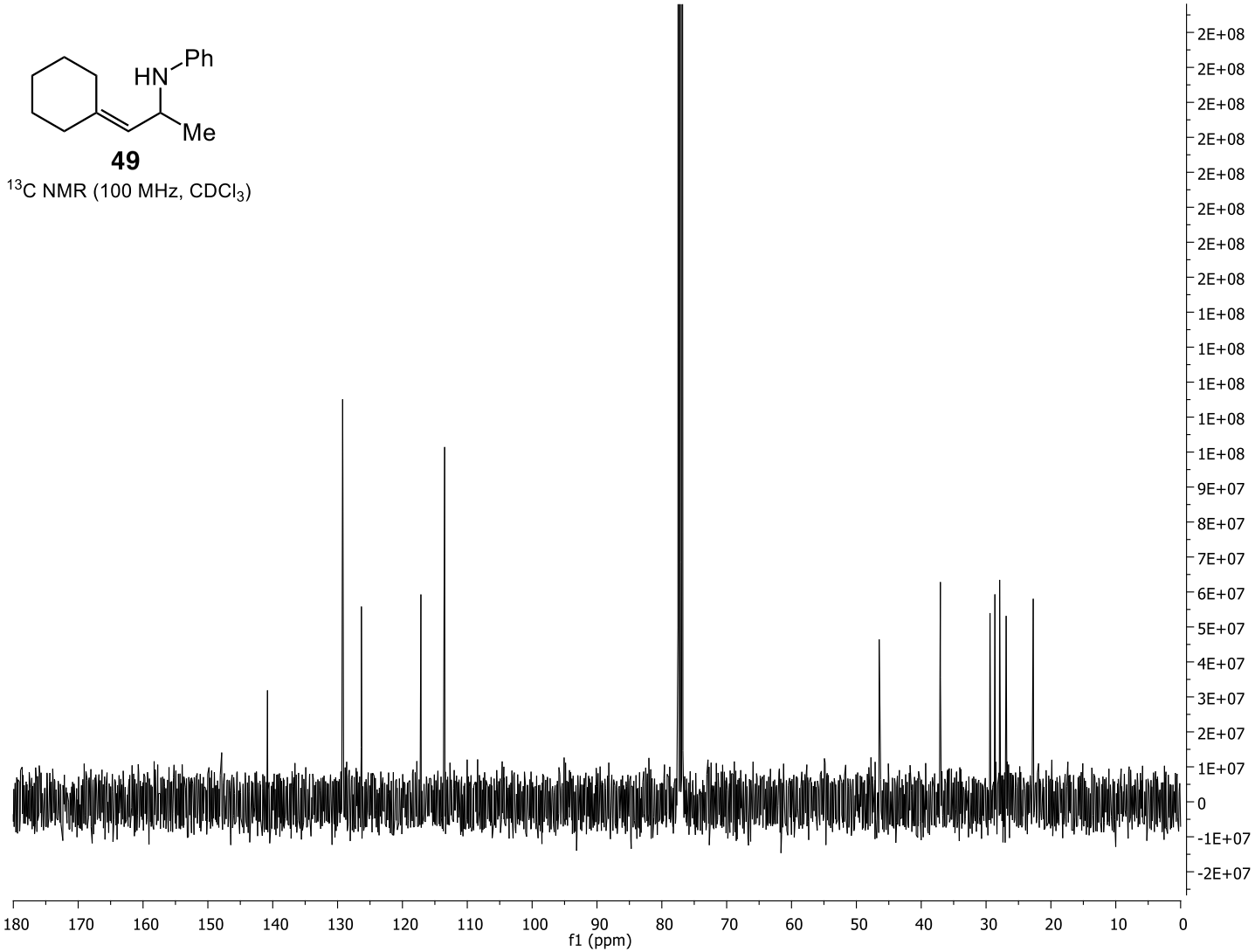
49

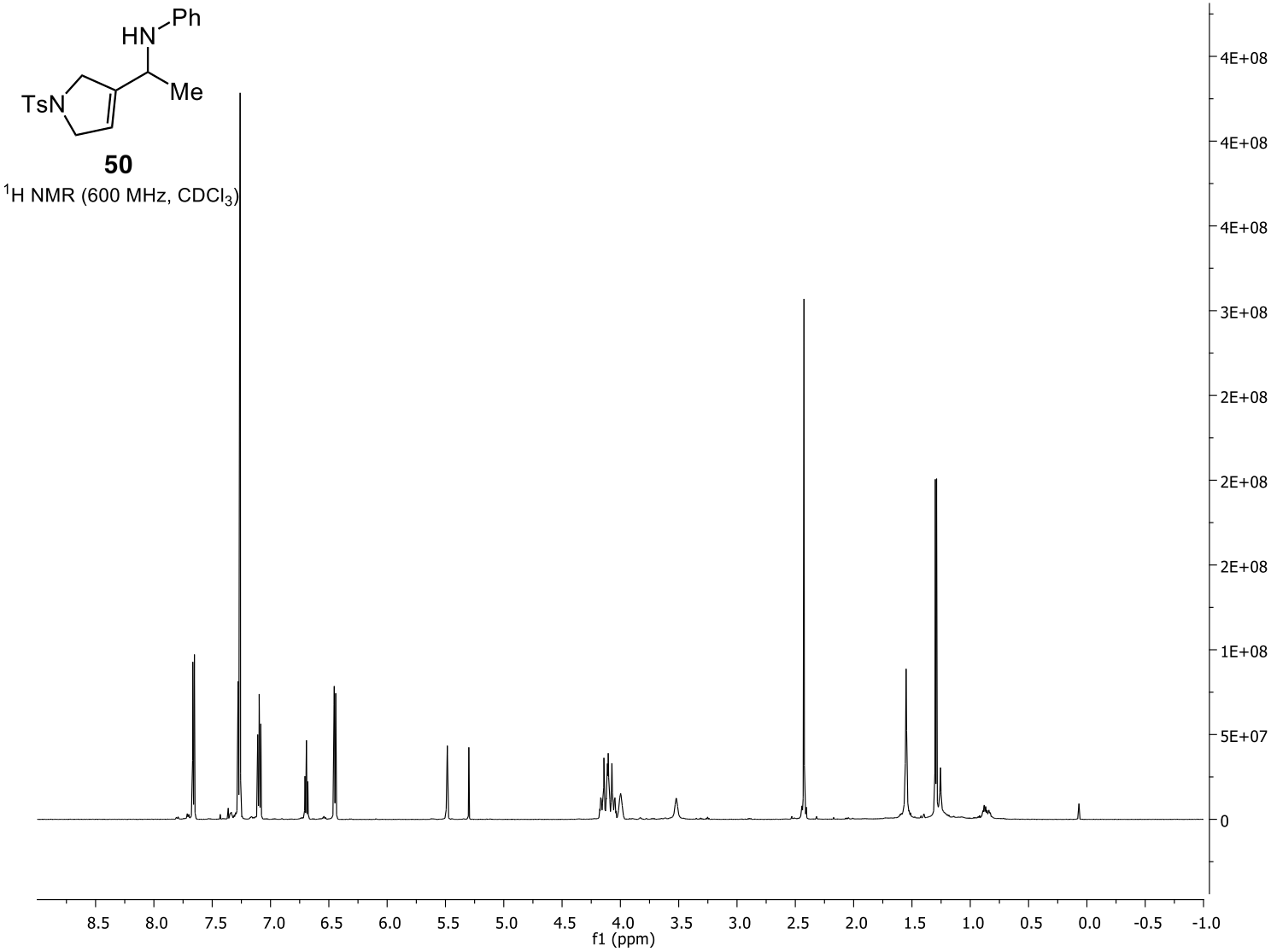
^{1}H NMR (400 MHz, $CDCl_3$)



49

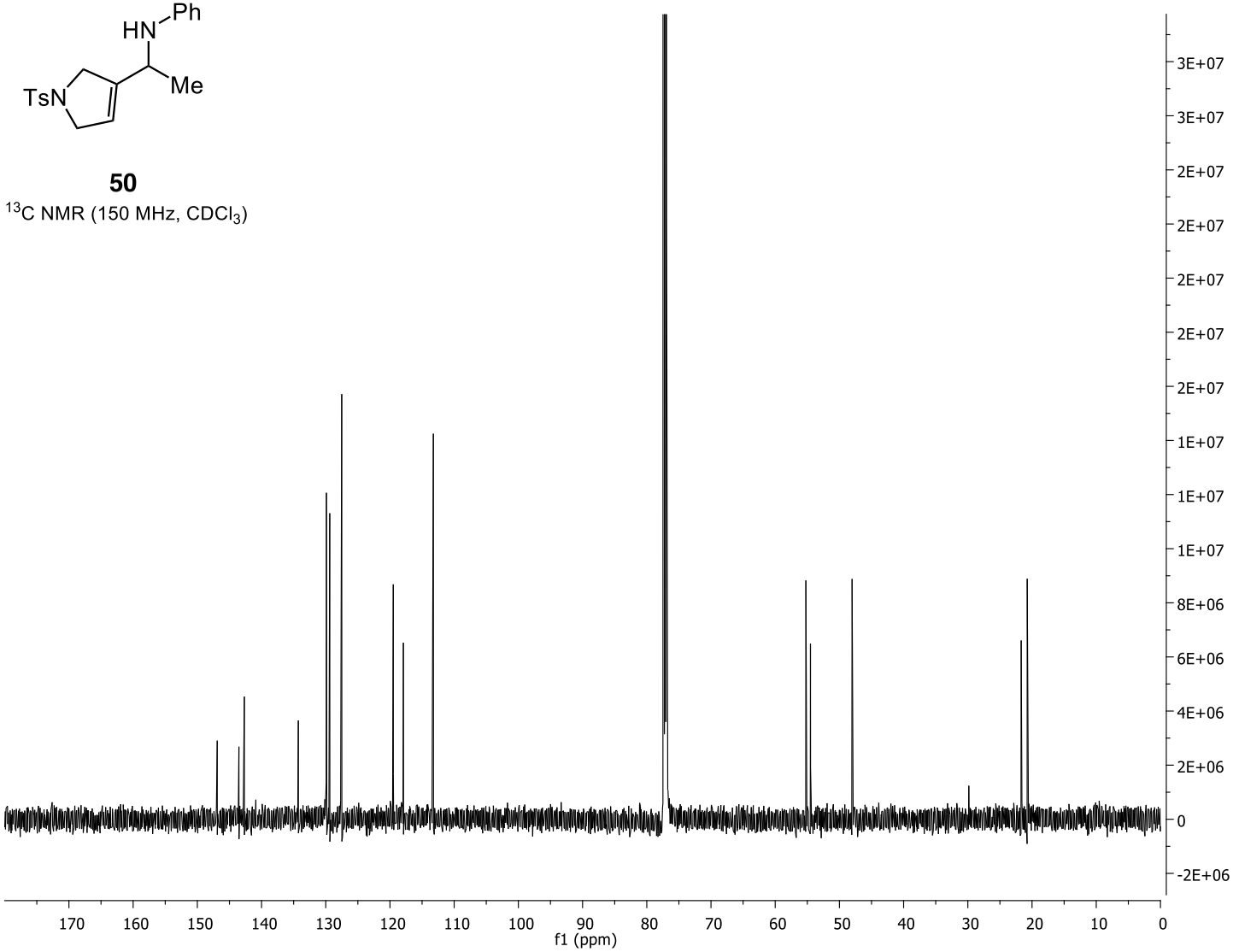
^{13}C NMR (100 MHz, $CDCl_3$)




HN
Ph
Me
TsN
50
1H NMR (600 MHz, CDCl3)
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

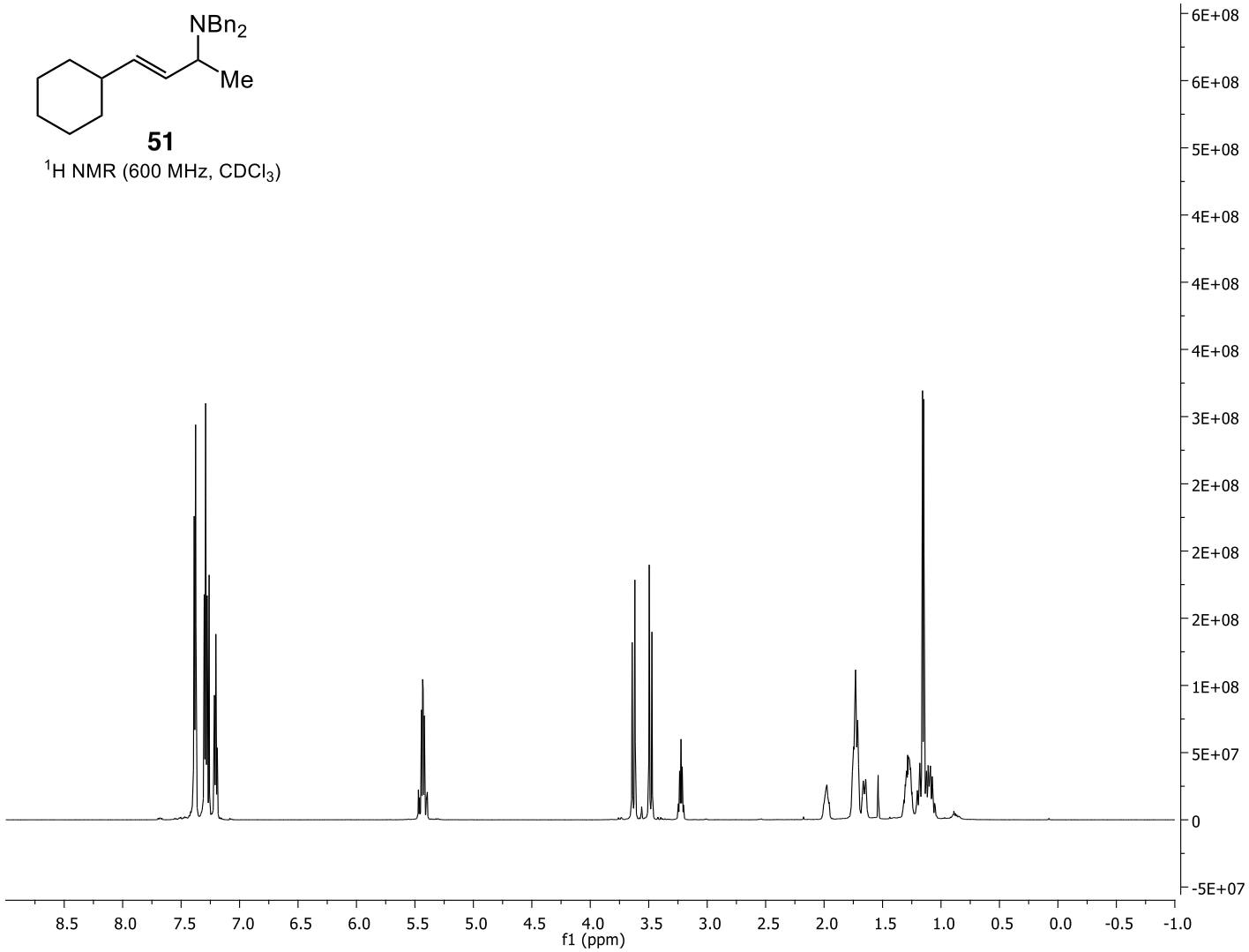
50

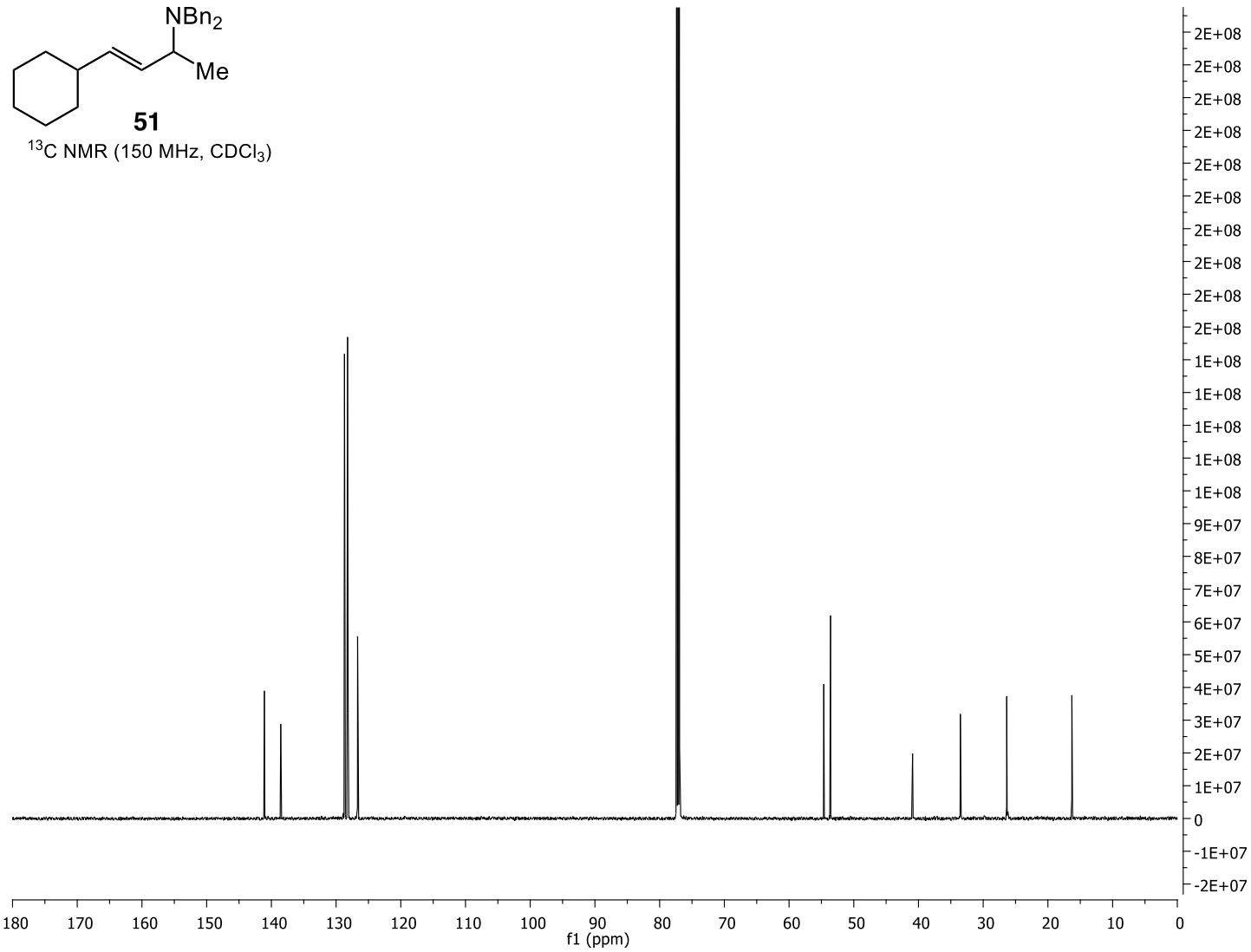
^{13}C NMR (150 MHz, $CDCl_3$)



51

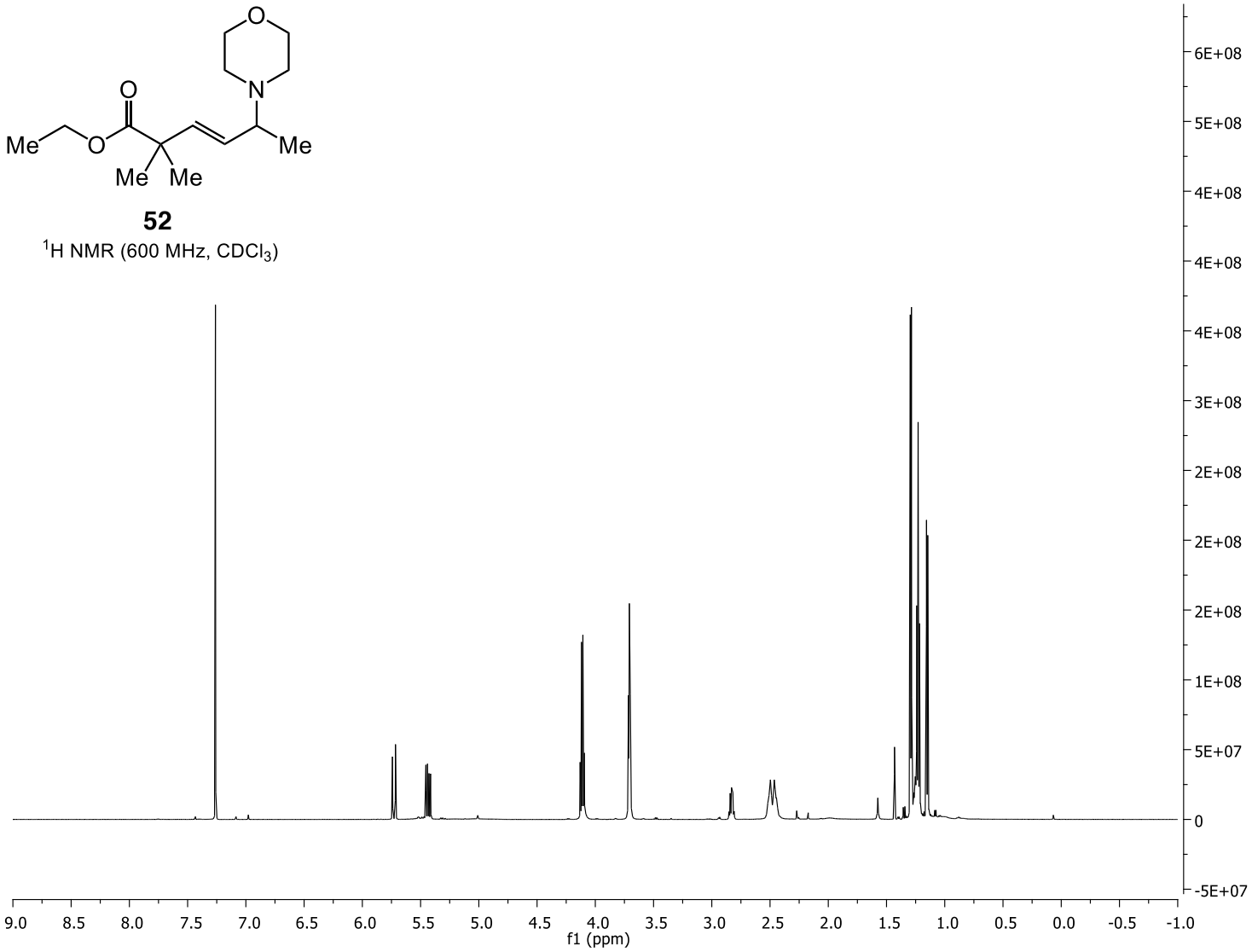
^{1}H NMR (600 MHz, $CDCl_3$)

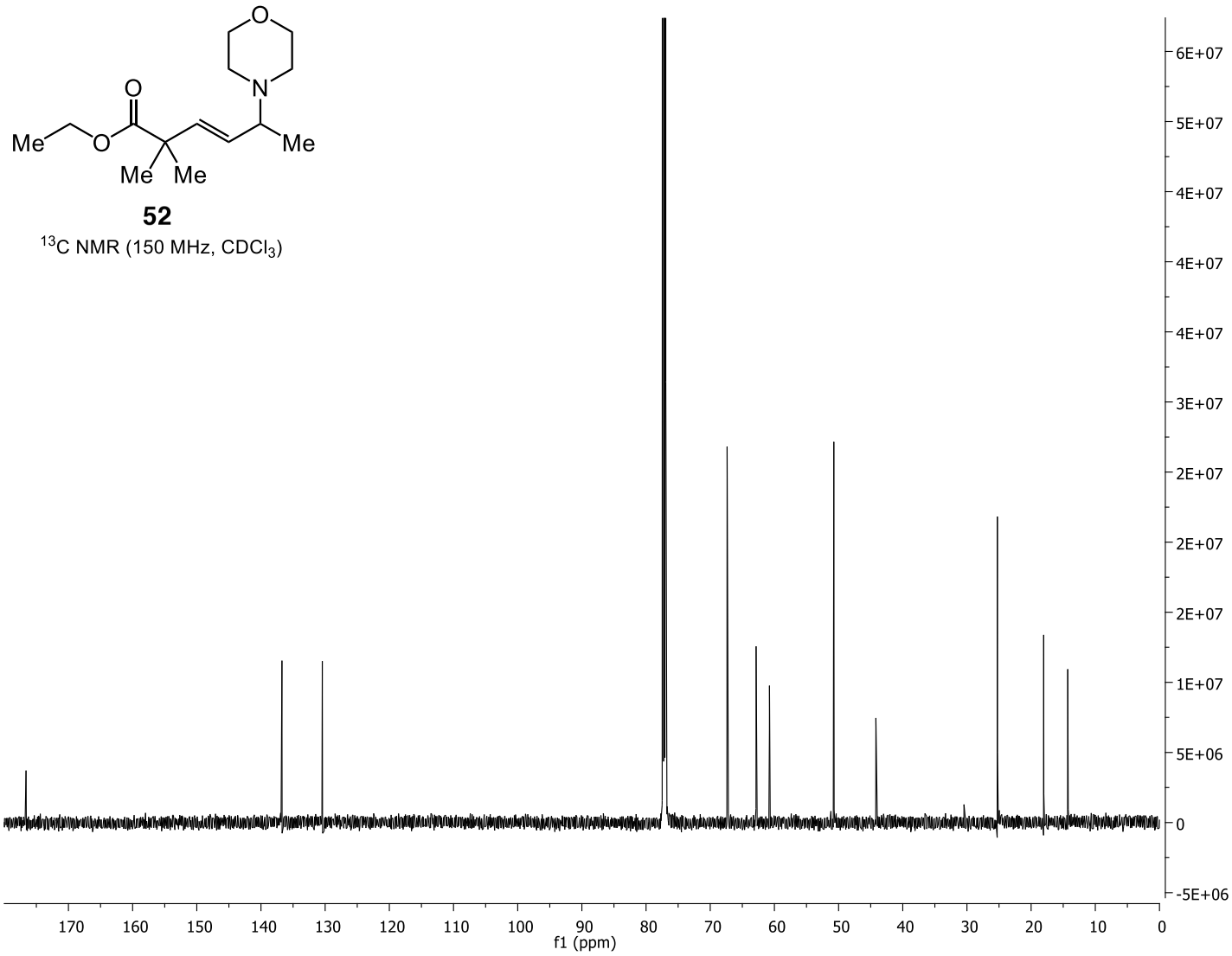



NBn2
Me
51
13C NMR (150 MHz, CDCl3)
f1 (ppm)

52

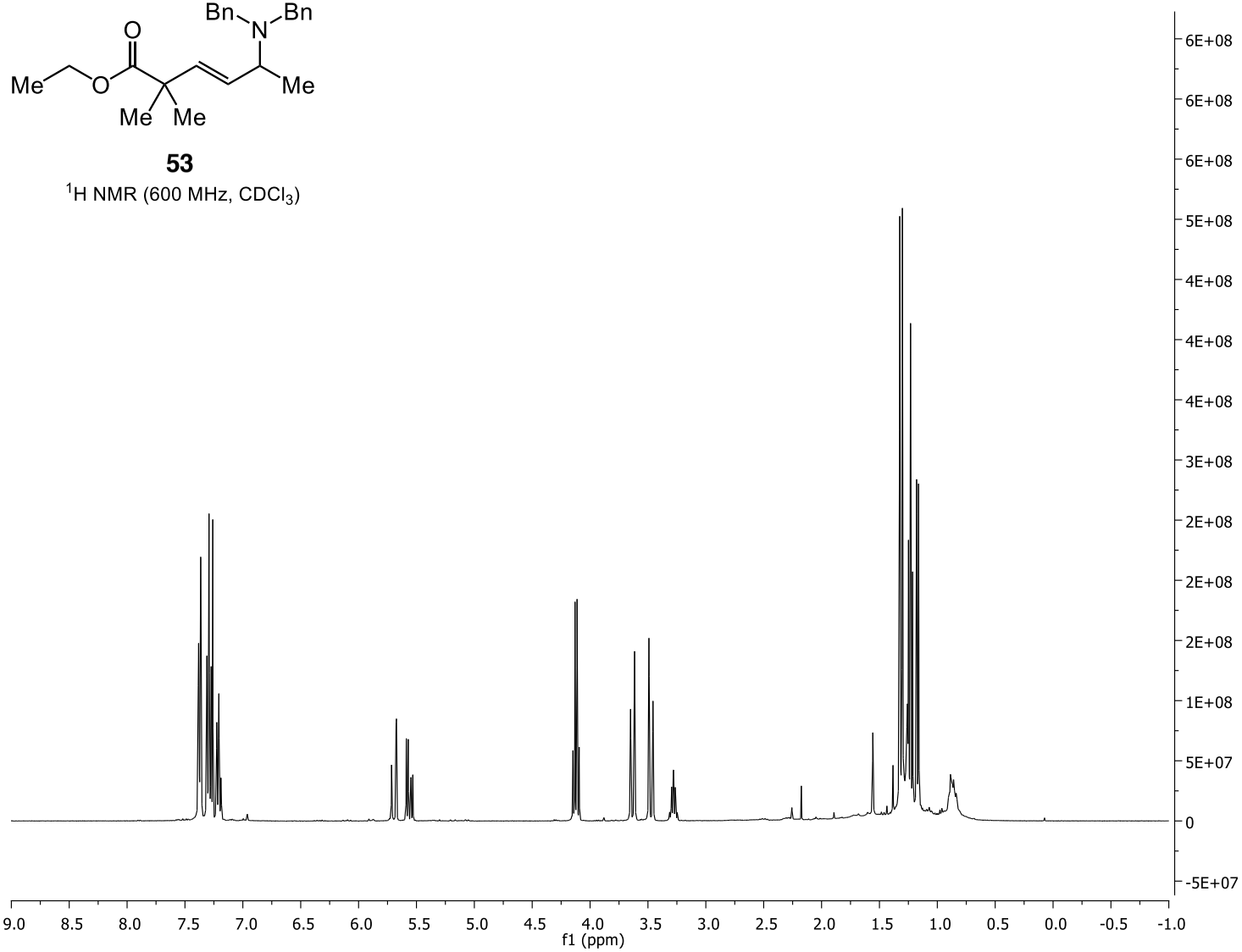
^{1}H NMR (600 MHz, $CDCl_3$)

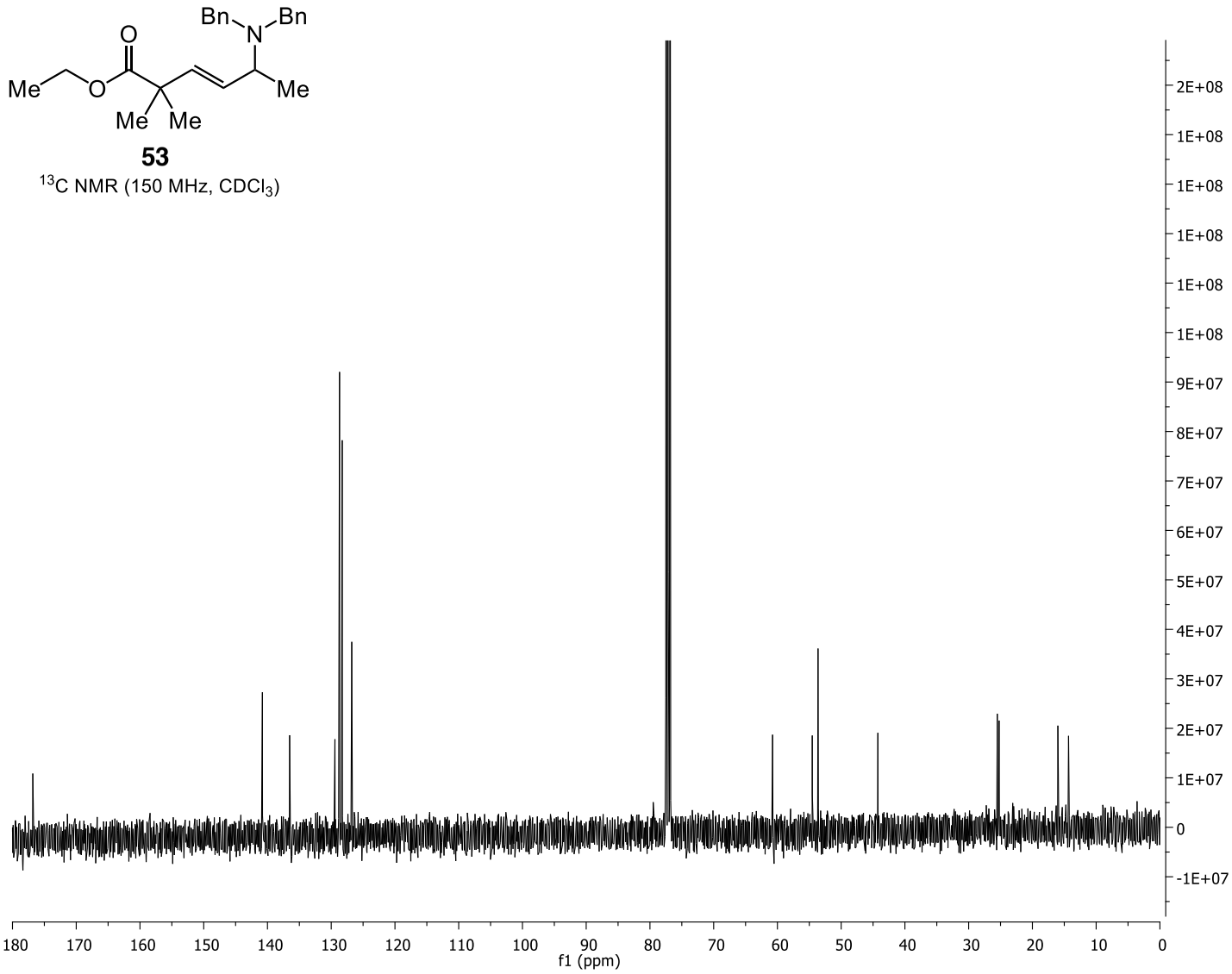


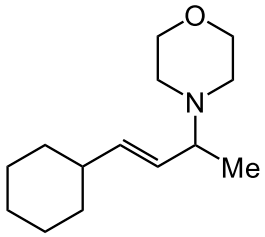

O
N
O
Me
O
Me
Me
Me
52
13C NMR (150 MHz, CDCl3)
6E+07
5E+07
4E+07
4E+07
4E+07
3E+07
2E+07
2E+07
2E+07
1E+07
5E+06
0
-5E+06
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

53

^{1}H NMR (600 MHz, $CDCl_3$)

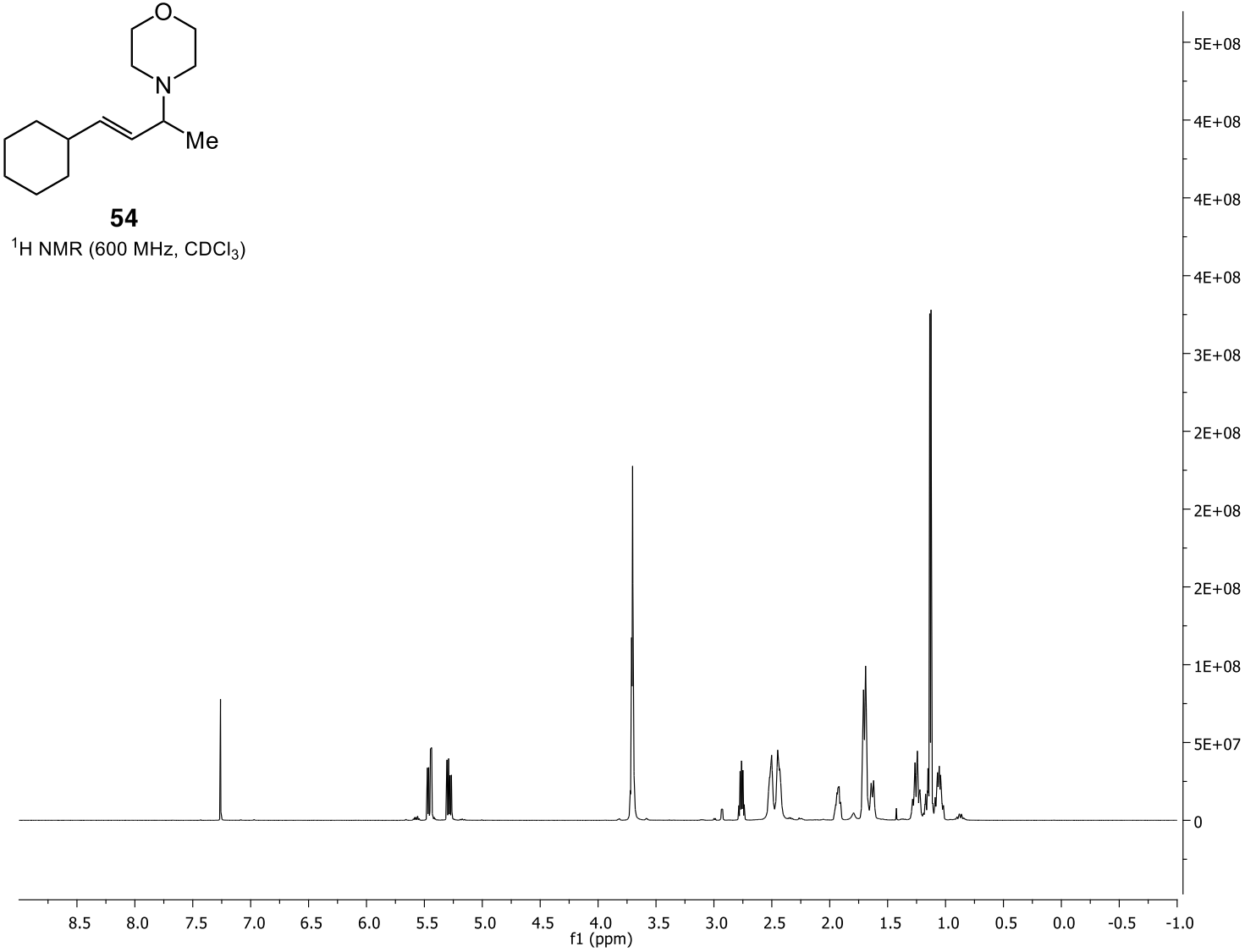



Bn
Bn
N
O
Me
O
Me
Me
Me
53
13C NMR (150 MHz, CDCl3)
2E+08
1E+08
1E+08
1E+08
1E+08
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
-1E+07
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



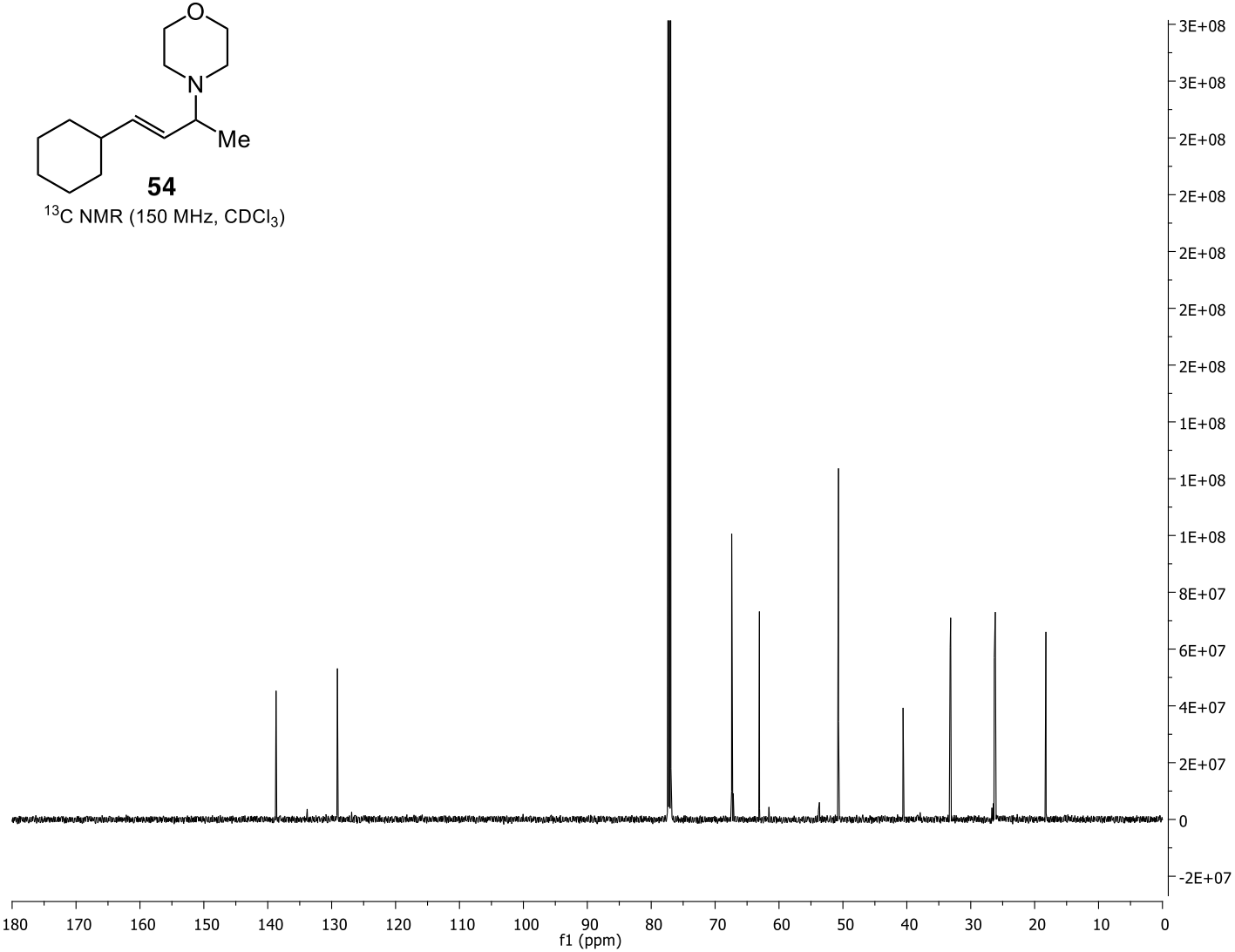
54

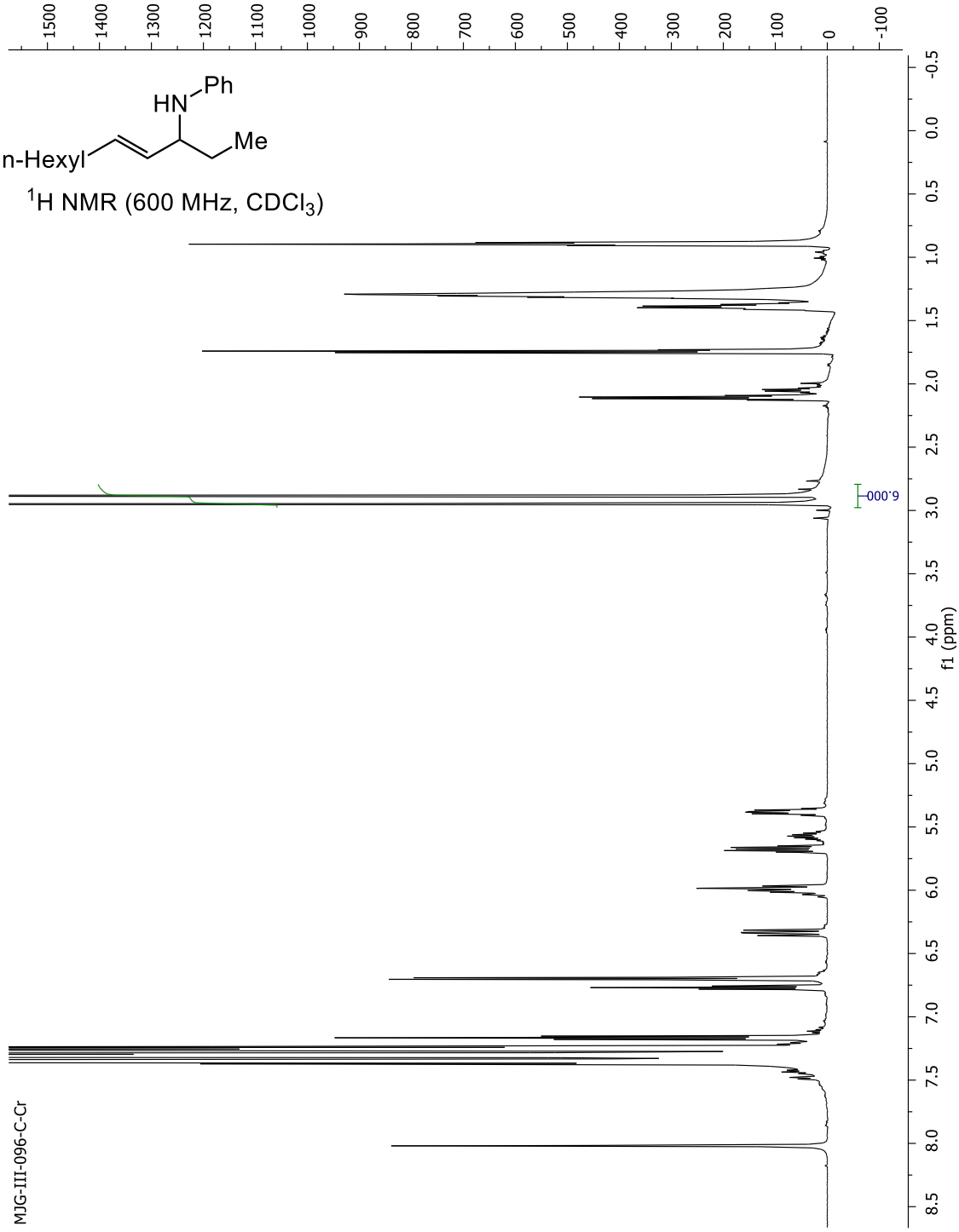
^{1}H NMR (600 MHz, $CDCl_3$)

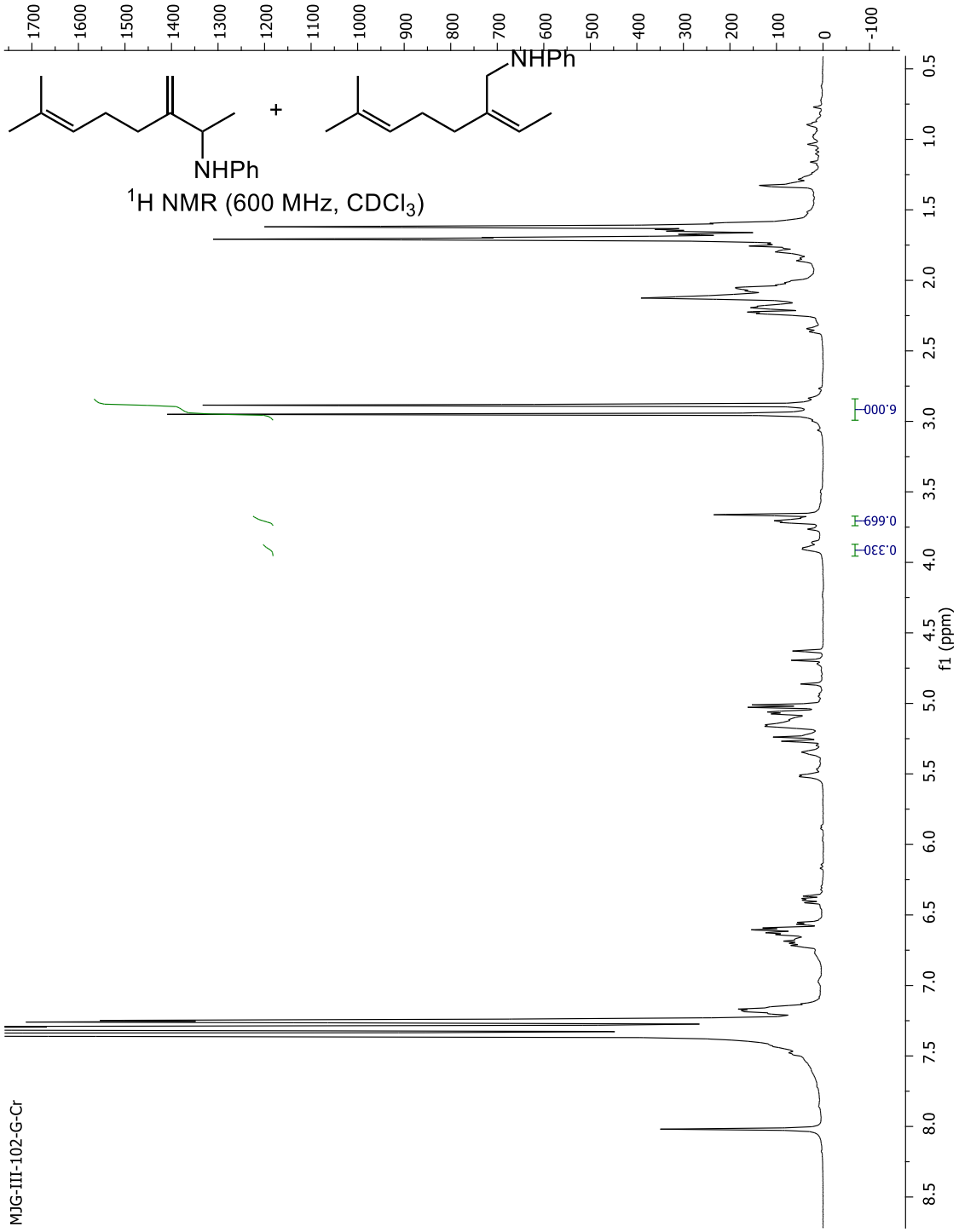


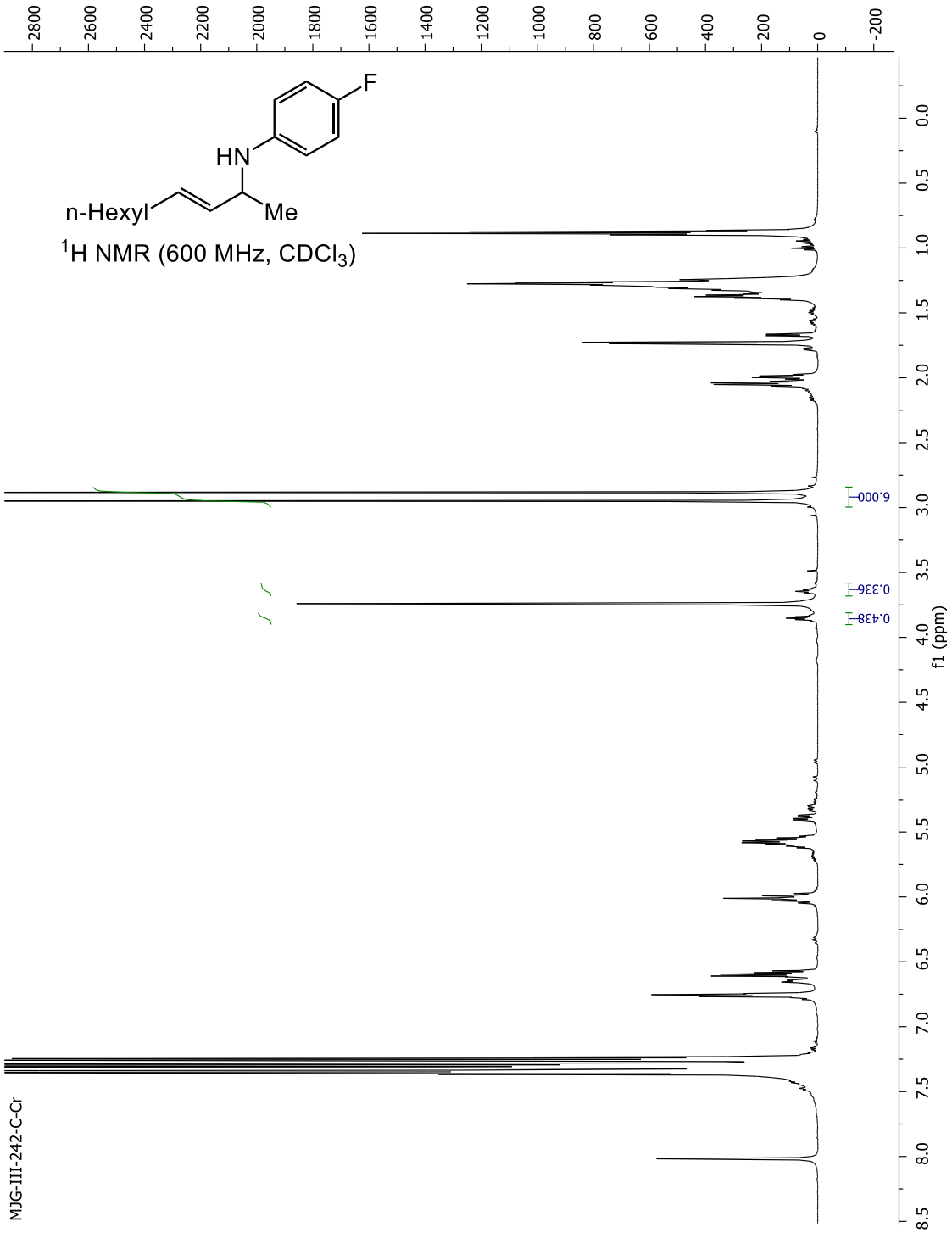
54

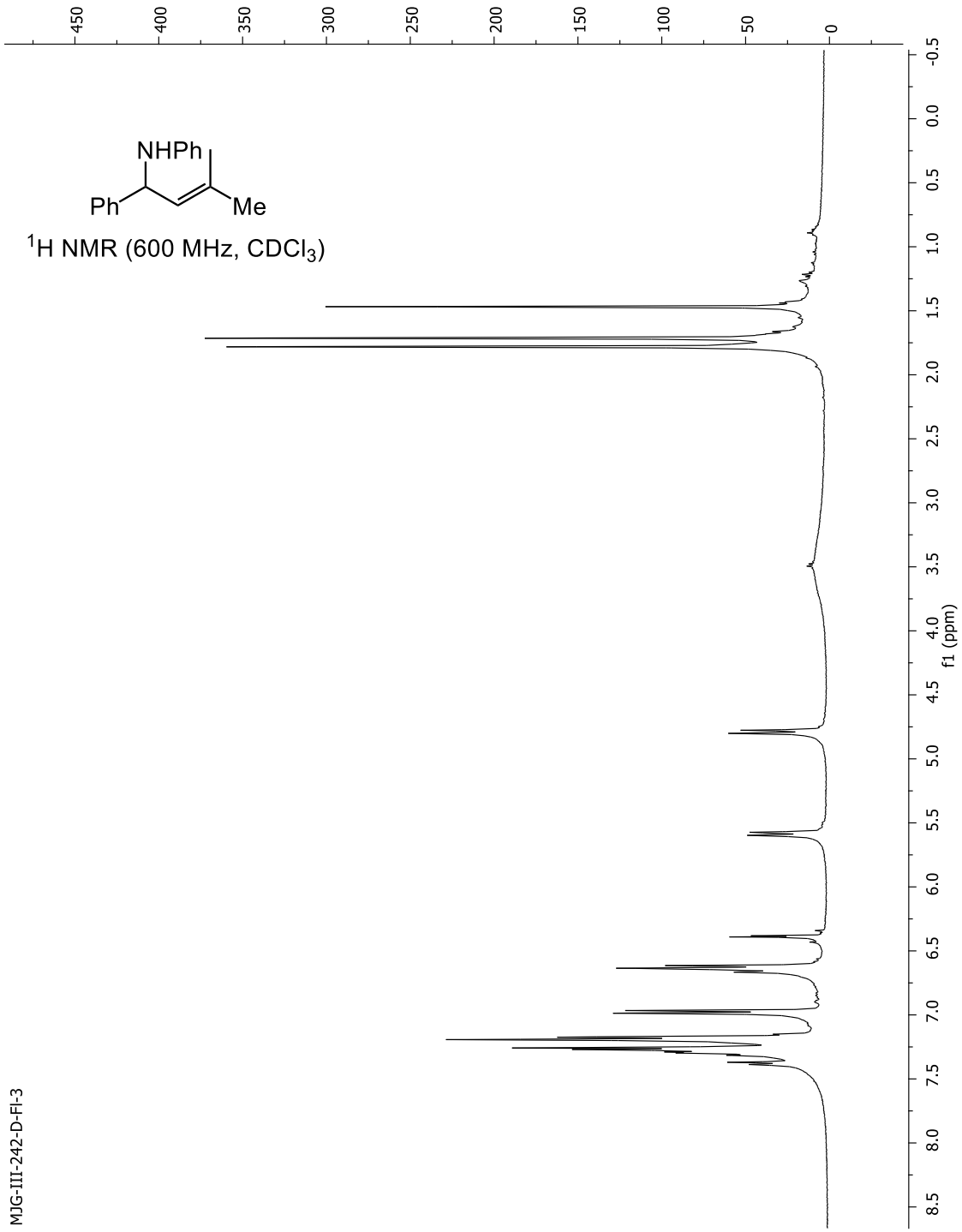
^{13}C NMR (150 MHz, $CDCl_3$)

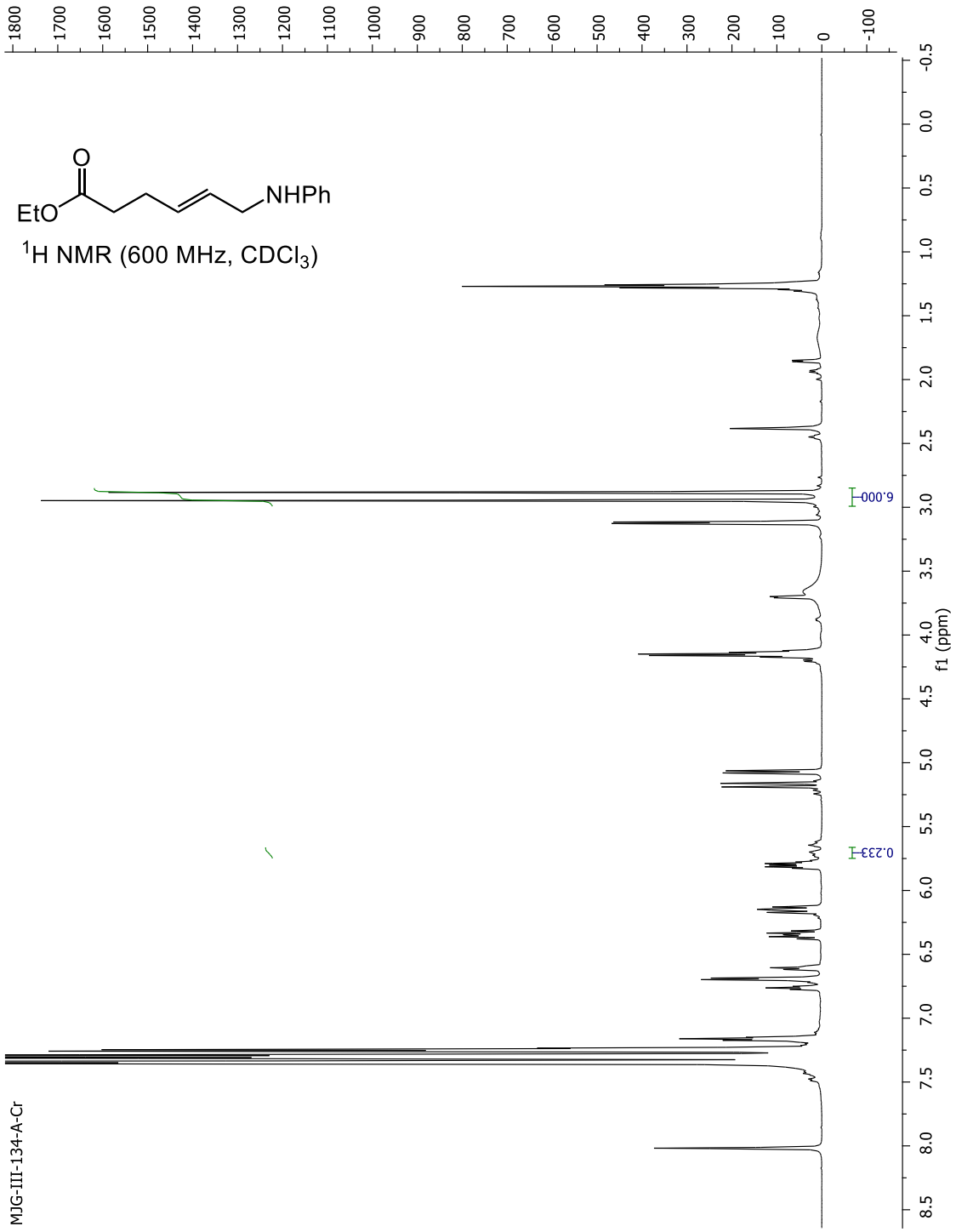


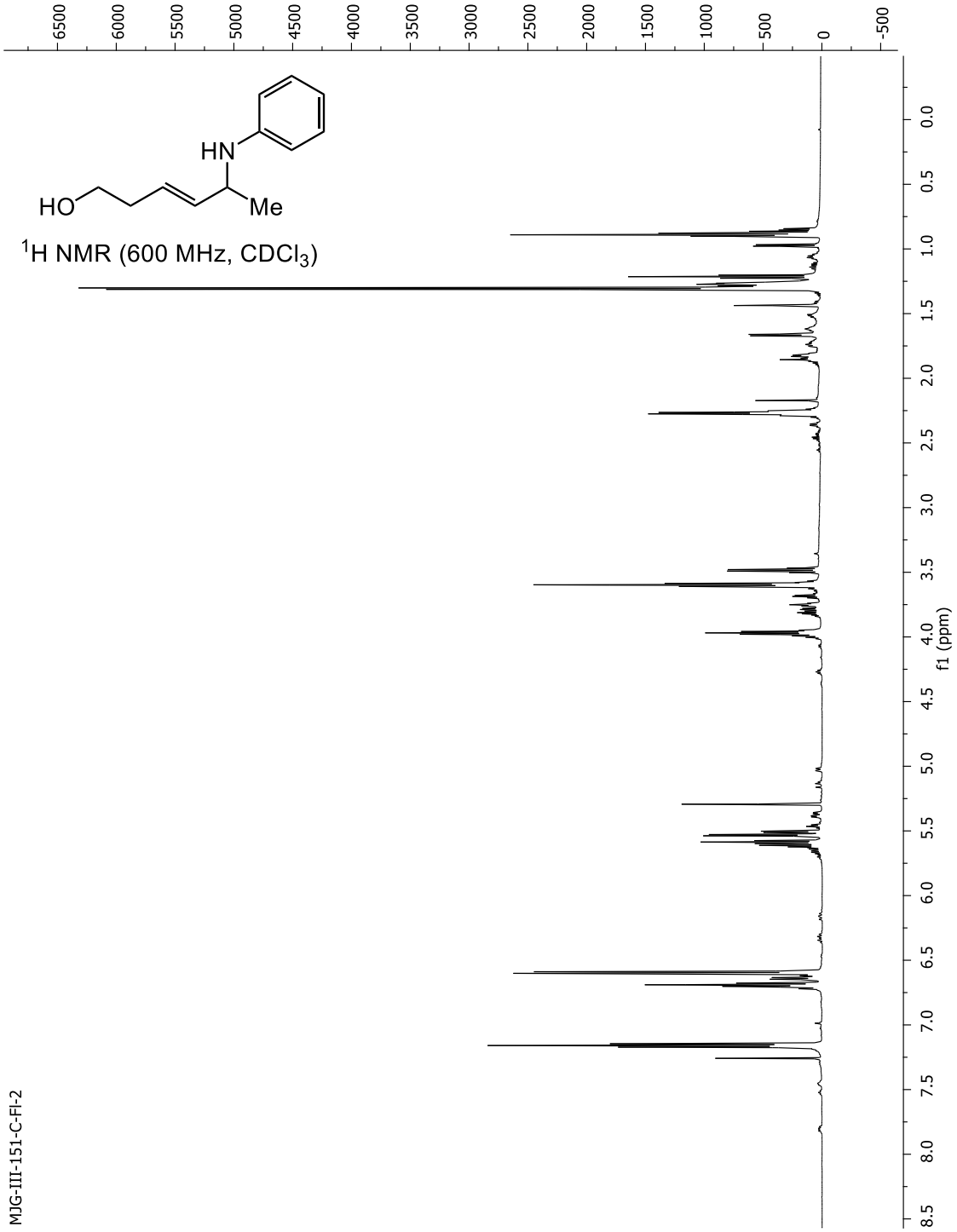

n-Hexyl
HN
Ph
Me
^{1}H NMR (600 MHz, $CDCl_3$)
6.000
f1 (ppm)
MJG-III-096-C-Cr

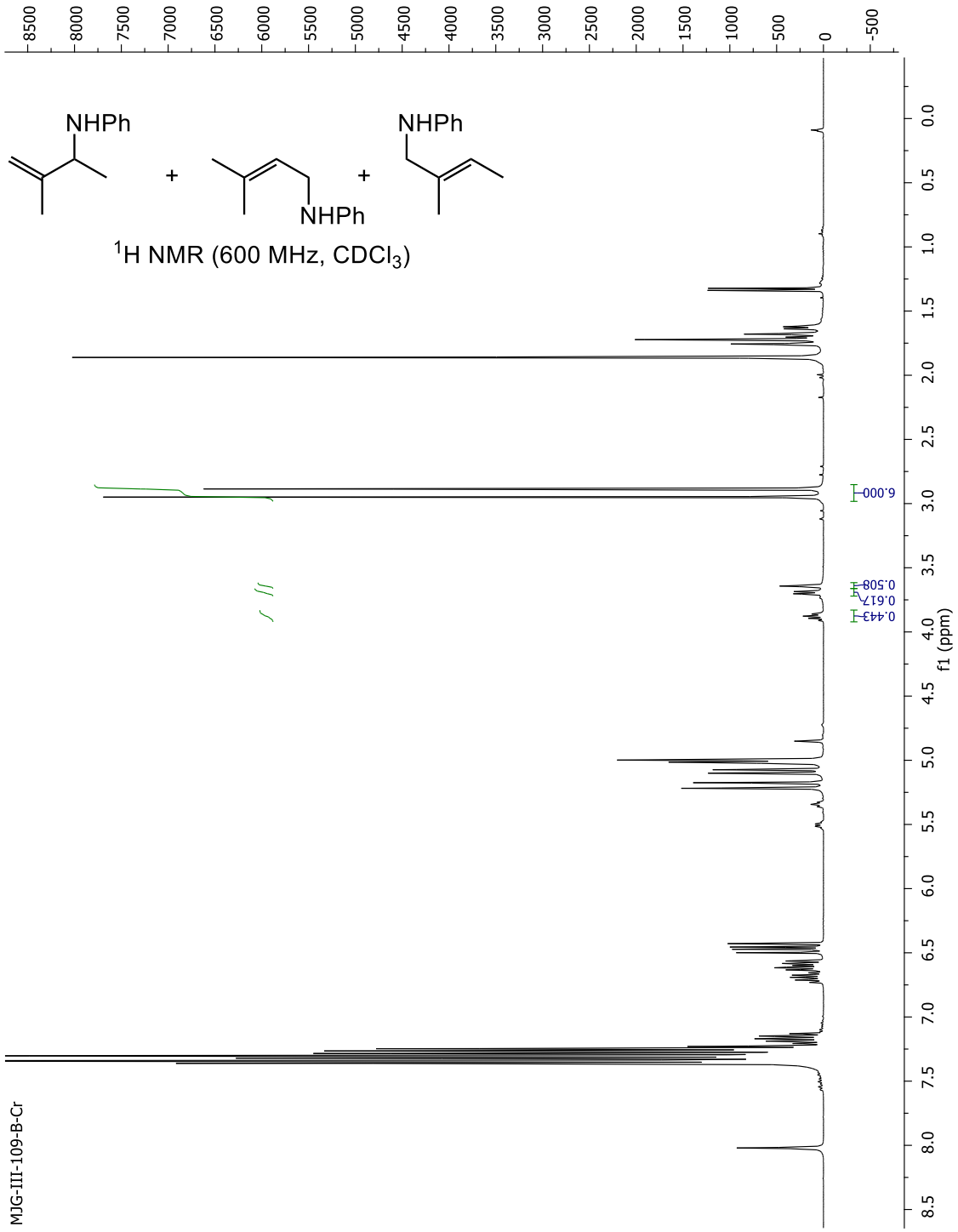

NHPh
+
NHPh
^{1}H NMR (600 MHz, $CDCl_3$)
6.000
0.669
0.330
f1 (ppm)
MJG-III-102-G-Cr

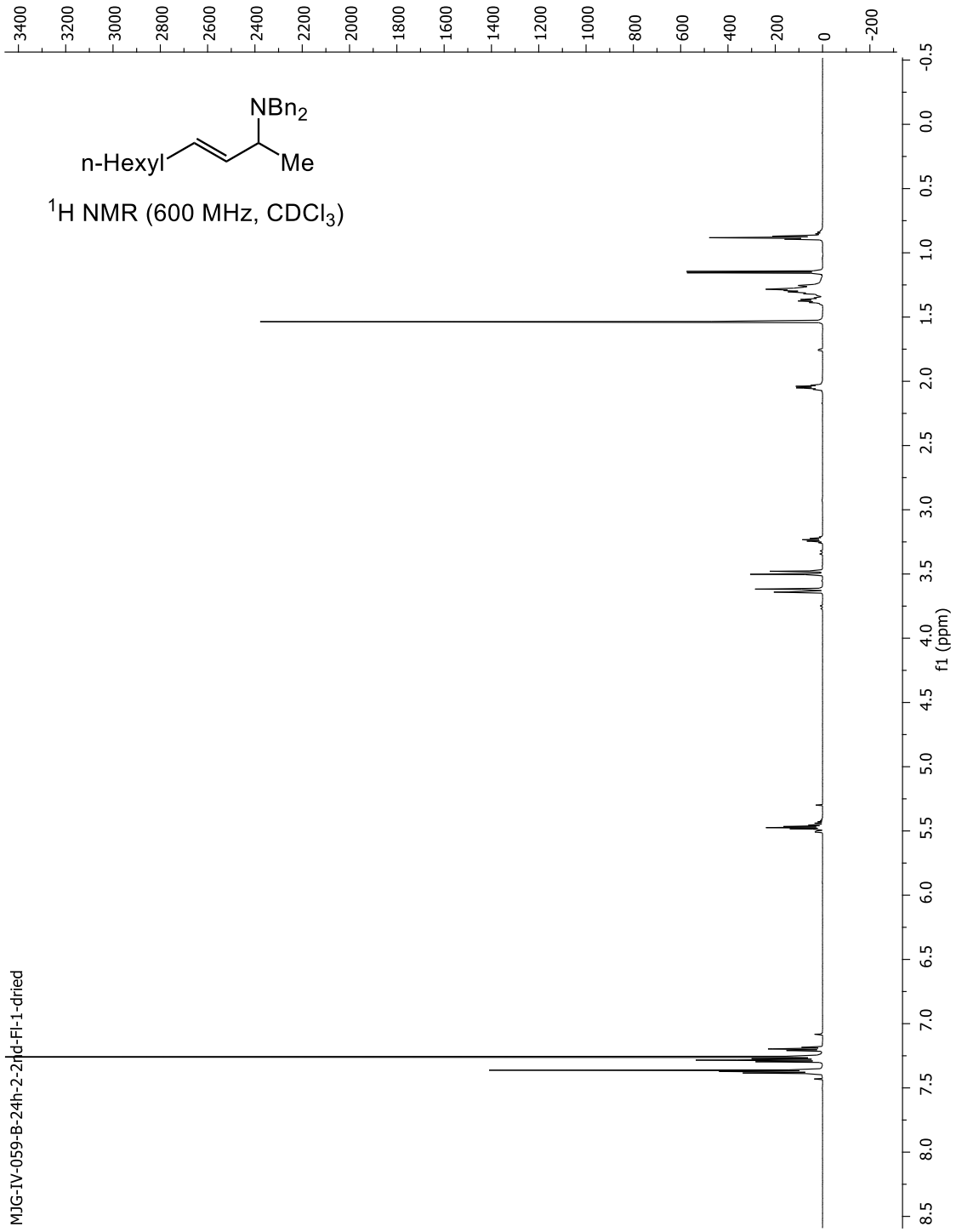

F
HN
n-Hexyl
Me
^{1}H NMR (600 MHz, $CDCl_3$)
6.000
0.336
0.438
f1 (ppm)
MJG-III-242-C-Cr

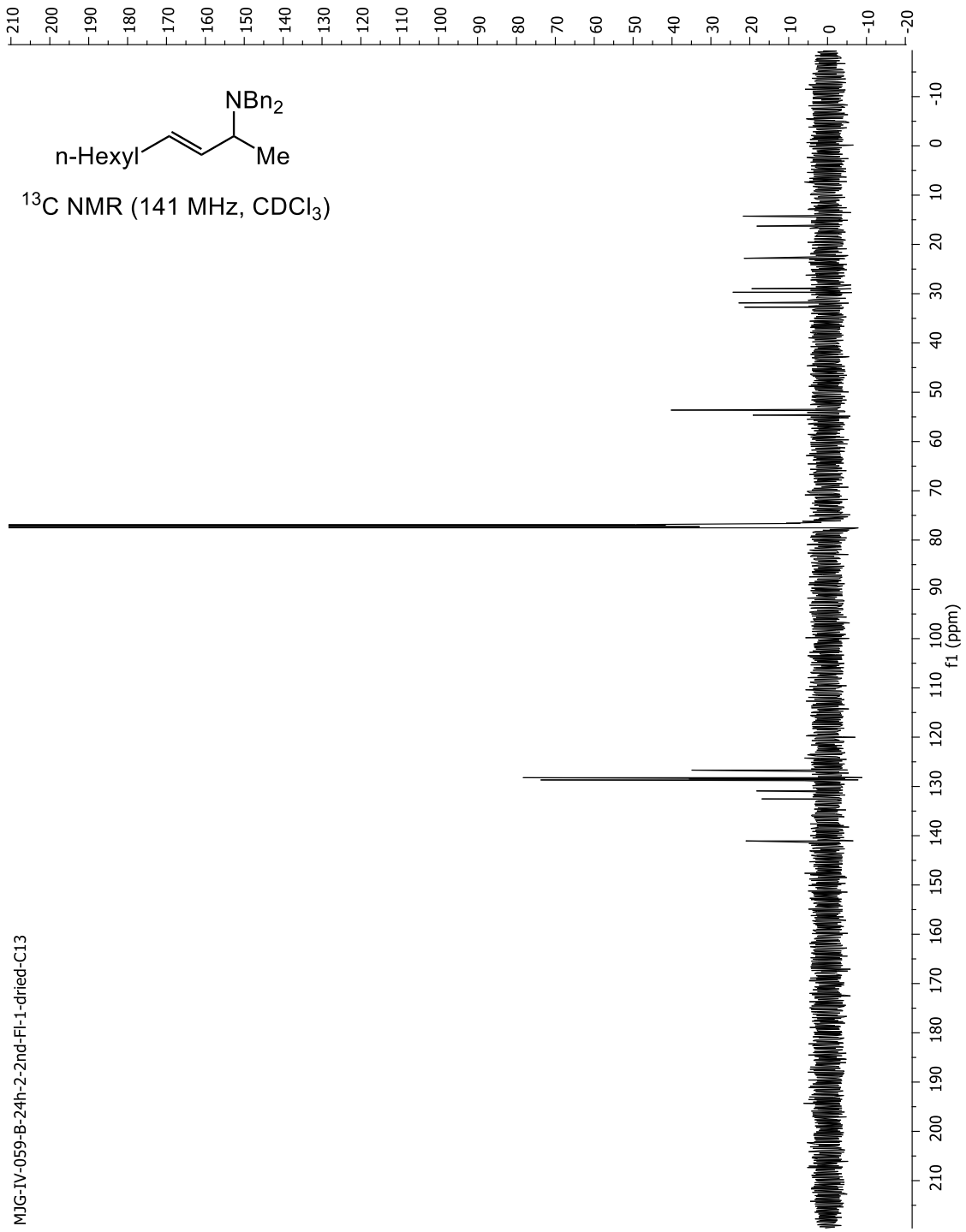

NHPh
Ph
Me
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-III-242-D-FI-3
f1 (ppm)

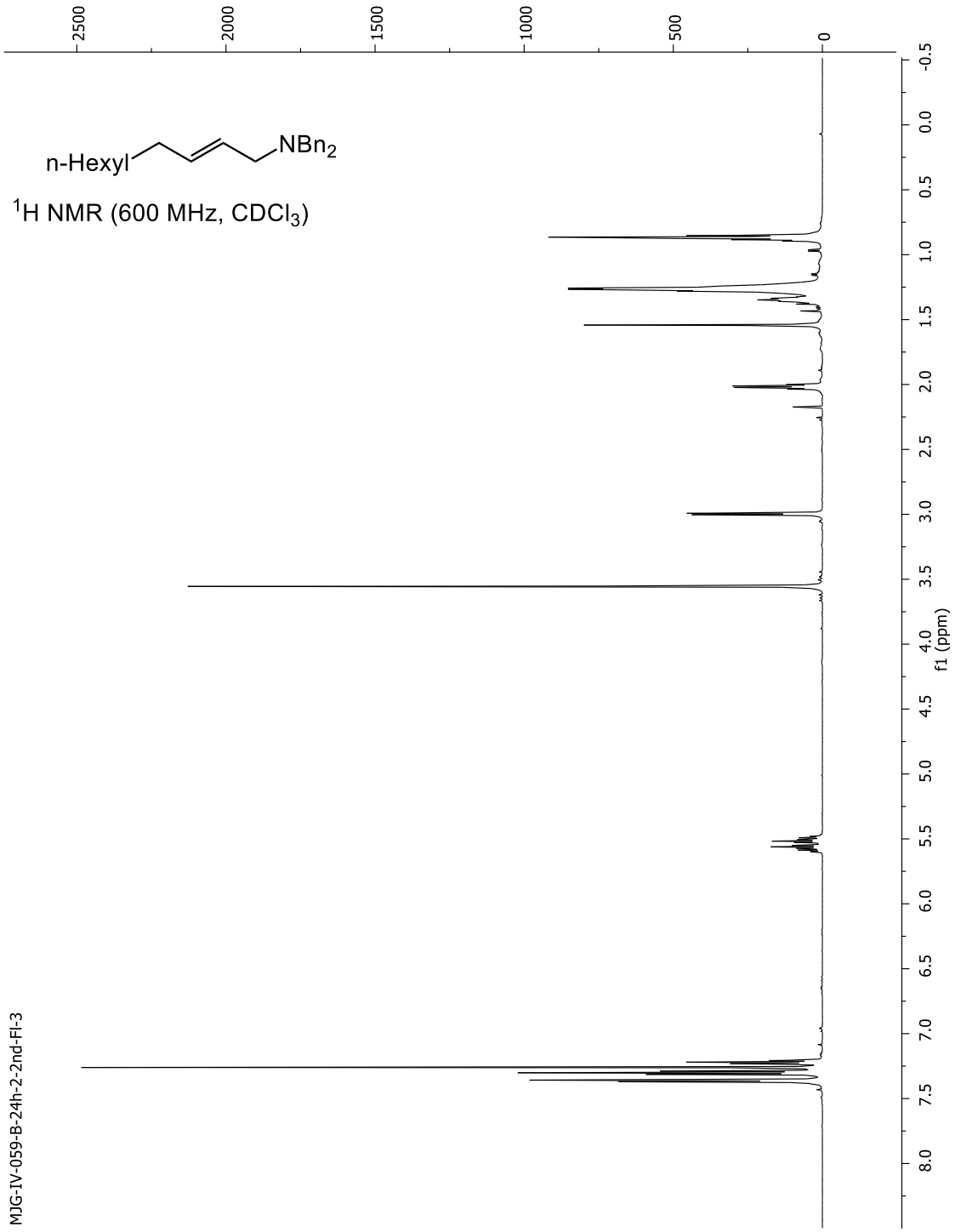

EtO
O
NHPh
1H NMR (600 MHz, CDCl3)
MJG-III-134-A-Cr
6.000
0.233
f1 (ppm)

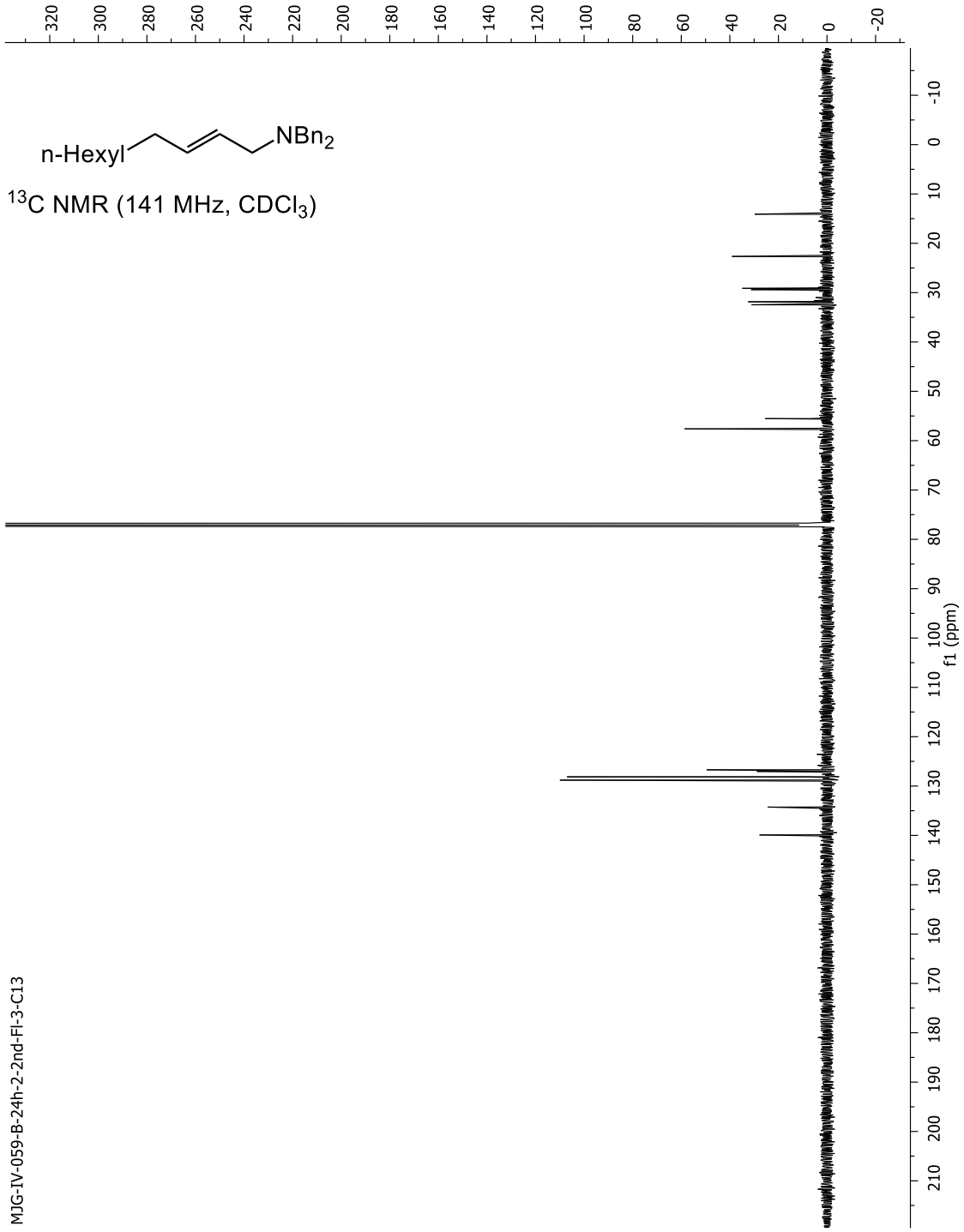

HN
HO
Me
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-III-151-C-FI-2
f1 (ppm)


NHPh
+
NHPh
+
NHPh
^{1}H NMR (600 MHz, $CDCl_3$)
MJG-III-109-B-Cr
6.000
0.443
0.617
0.508
f1 (ppm)


NBn2
n-Hexyl
Me
1H NMR (600 MHz, CDCl3)
MJG-IV-059-B-24h-2-2nd-FI-1-dried
f1 (ppm)


NBn2
n-Hexyl
Me
13C NMR (141 MHz, CDCl3)
MJG-IV-059-B-24h-2-2nd-FI-1-dried-C13
f1 (ppm)


n-Hexyl
NBn2
1H NMR (600 MHz, CDCl3)
MJG-IV-059-B-24h-2-2nd-FI-3
f1 (ppm)


n-Hexyl
NBn2
13C NMR (141 MHz, CDCl3)
MJG-IV-059-B-24h-2-2nd-FI-3-C13
f1 (ppm)

APPENDIX 2: SUPPORTING INFORMATION FOR CHAPTER 2

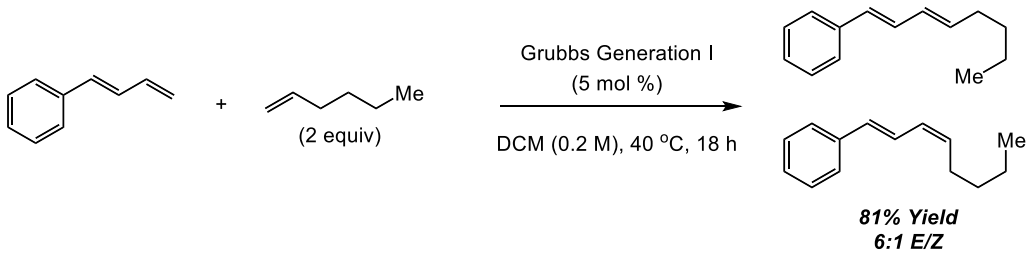
■ **General:** All reactions were carried out in flame or oven (140 °C) dried glassware that had been cooled under vacuum. Unless otherwise stated, all reactions were carried out under an inert N_2 atmosphere. All reagents were purged or sparged with N_2 for 20 min prior to distillation or use. All solid reagents were dried by azeotropic distillation with benzene three times prior to use. Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer or a ASI ReactIR 1000, Model: 001-1002 for air sensitive rhodium carbonyl complexes. Mass spectra were obtained using a Thermo LTqFT mass spectrometer with electrospray ionization and external calibration. All samples were prepared in MeOH, MeCN or $CHCl_3$ for metal complexes. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker model DRX 400 or a Bruker AVANCE III 600 CryoProbe (^{1}H NMR at 400 MHz or 600 MHz, ^{13}C NMR at 100 or 151 MHz, ^{31}P NMR at 160 or 243 MHz and ^{19}F NMR at 376 or 564 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: Chloroform-d at 7.26 ppm, CD_2Cl_2 at 5.32 ppm, CD_3CN at 1.94 ppm; ^{13}C NMR: Chloroform-d at 77.16 ppm, CD_2Cl_2 at 53.84 ppm, CD_3CN at 1.32 ppm). NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet, bs = broad singlet, bm = broad multiplet, etc.), and coupling constants (Hz). X-ray diffraction studies were conducted on a Bruker-AXS SMART APEXII diffractometer. Crystals were selected and mounted using Paratone oil on a MiteGen Mylar tip.

■ **Solvents:** Solvents were purged with argon and purified under a positive pressure of dry argon by a SG Waters purification system: dichloromethane (EMD Millipore), diethyl ether (EMD

Millipore, hexanes (EMD Millipore), benzene (EMD Millipore), and THF (EMD Millipore) were passed through activated alumina columns. Chloroform – d_1 and Dichloromethane – d_2 were purchased from Cambridge Isotope Labs, distilled over CaH_2 and stored in a dry box over activated 4 Å molecular sieves.

Section 2.2: Discovery of Hydroarylation with Carbodicarbene-Rh Catalysts

■ **Procedures for the preparation of internal diene substrates:**

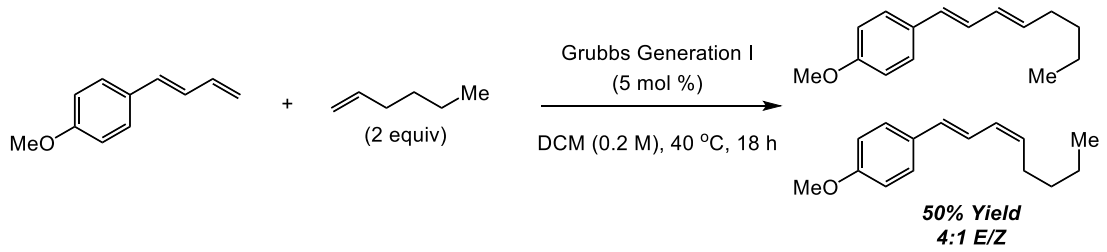


Synthesis of ((1E,3E)-octa-1,3-dien-1-yl)benzene and ((1E,3Z)-octa-1,3-dien-1-yl)benzene

Grubb's 1st generation catalyst (71 mg, 0.087 mmol, 5 mol%) was weighed into an oven dried 8 mL vial or 50 mL flask equipped with a stir bar which was then capped using a Teflon lined lid. The vial was purged with N2 for 10 min then charged with dichloromethane ([ ] = 0.20). N_2 sparged 1-hexene (0.43 mL, 3.46 mmol) was added via syringe followed by 1,3-phenylbutadiene (255 μL, 1.73 mmol). The reaction was allowed to warm to 40 °C and stir for 18 h. The reaction was plugged through a plug of silica gel using hexanes then concentrated. The residue was purified by column chromatography using 100% hexanes to provide the product in 81% yield.

Isolated as a 6:1 mixture of ((1E,3E)-octa-1,3-dien-1-yl)benzene and ((1E,3Z)-octa-1,3-dien-1-yl)benzene. **^{1}H NMR** (600 MHz, $CDCl_3$): δ [((1E,3E)-octa-1,3-dien-1-yl)benzene: 7.38 (2H, d, J = 7.6 Hz), 7.29 (2H, t, J = 7.4 Hz), 7.19 (1H, t, J = 7.0 Hz), 6.76 (1H, dd, J = 15.5, 10.6 Hz), 6.44 (1H, d, J = 15.7 Hz), 6.21 (1H, dd, J = 15.8, 9.8 Hz), 5.83 (1H, td, J = 15.2, 7.3 Hz), 2.13-2.17 (2H, m), 1.30-1.43 (4H, m), 0.91 (3H, t, J = 7.3 Hz)], [((1E,3Z)-octa-1,3-dien-1-yl)benzene: 7.42

(2H, d, J = 7.4 Hz), 7.30-7.33 (2H, m), 7.19-7.22 (1H, m), 7.07 (1H, dd, J = 14.6, 12.1 Hz), 6.53 (2H, d, J = 15.5 Hz), 6.14-6.20 (1H, m), 5.52-5.56 (1H, m), 2.28-2.31 (2H, m) 1.30-1.43 (4H, m), 0.91 (3H, t, J = 7.3 Hz)]. **^{13}C NMR** (150 MHz, $CDCl_3$): δ [((1E,3E)-octa-1,3-dien-1-yl)benzene: 137.70, 136.03, 130.47, 129.89, 129.49, 128.54, 127.05, 126.11, 32.56, 31.47, 22.27], [((1E,3Z)-octa-1,3-dien-1-yl)benzene: 133.39, 131.91, 128.66, 128.57, 127.31, 126.31, 126.12, 124.51, 31.88, 27.73, 22.36].



Synthesis of 1-methoxy-4-((1E,3E)-octa-1,3-dien-1-yl)benzene and 1-methoxy-4-((1E,3Z)-octa-1,3-dien-1-yl)benzene

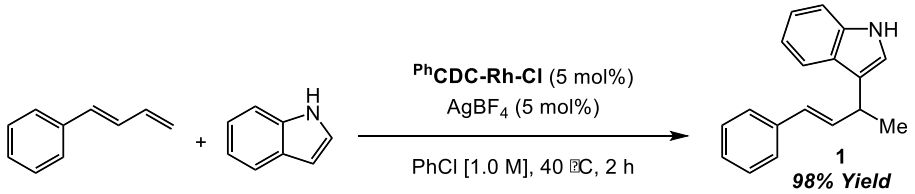
Grubb's 1st generation catalyst (64.2 mg, 0.078 mmol, 5 mol%) was weighed into an oven dried 8 mL vial or 50 mL flask equipped with a stir bar which was then capped using a Teflon lined lid. The vial was purged with N2 for 10 min then charged with dichloromethane ([ ] = 0.20). N_2 sparged 1-hexene (390 μL, 3.12 mmol) was added via syringe followed by (E)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (250 mg, 1.56 mmol). The reaction was allowed to warm to 40 °C and stir for 18 h. The reaction was plugged through a plug of silica gel using hexanes then concentrated. The residue was purified by column chromatography using 20:1 Hex/Et_2O to provide the product in 50% yield.

Isolated as a 4:1 mixture of 1-methoxy-4-((1E,3E)-octa-1,3-dien-1-yl)benzene and 1-methoxy-4-((1E,3Z)-octa-1,3-dien-1-yl)benzene. **^{1}H NMR** (600 MHz, $CDCl_3$): δ [1-methoxy-4-((1E,3E)-octa-1,3-dien-1-yl)benzene: 7.32 (2H, d, J = 8.6 Hz), 6.85-6.88 (2H, m), 6.64 (1H, dd, J = 15.6,

10.3 Hz), 6.41 (1H, d, J = 15.7 Hz), 6.19 (1H, dd, J = 24.1, 1.5 Hz), 5.76-5.81 (1H, m), 3.81 (3H, s), 2.15 (2H, q, J = 7.2 Hz), 1.33-1.45 (4H, m), 0.92 (3H, t, J = 7.2 Hz)], [1-methoxy-4-((1E,3Z)-octa-1,3-dien-1-yl)benzene: 7.35 (2H, d, J = 8.6 Hz), 6.93 (1H, dd, J = 15.6, 11.1 Hz), 6.86-6.88 (2H, m), 6.47 (2H, d, J = 15.5 Hz), 6.11-6.17, (1H, m), 5.46-5.48 (1H, m), 3.81 (3H, s), 2.30 (2H, q, J = 7.1 Hz), 1.33-1.45 (4H, m), 0.94 (3H, m)]. **^{13}C NMR** (150 MHz, $CDCl_3$): δ Reported as a mixture of 1-methoxy-4-((1E,3E)-octa-1,3-dien-1-yl)benzene and 1-methoxy-4-((1E,3Z)-octa-1,3-dien-1-yl)benzene: 159.06, 158.86, 134.82, 132.23, 131.45, 130.61, 130.54, 129.43, 128.81, 127.53, 127.49, 127.27, 122.61, 114.04, 114.01, 55.29, 32.54, 31.92, 31.55, 27.69, 22.36, 22.26, 13.96.

■ General procedure for Intermolecular Hydroarylation Catalyzed by CDC-Rh-Cl Complexes

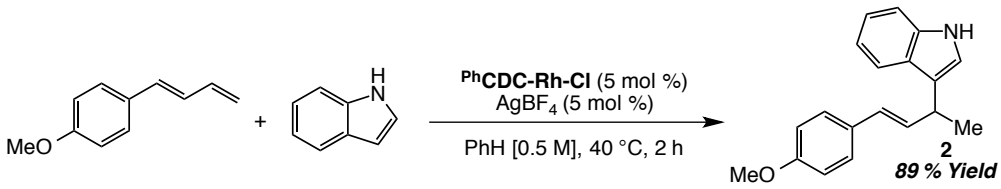
In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the appropriate amount of CDC-Rh complex and an equal mol% of $AgBF_4$ when appropriate. The solids were solvated with the listed solvent and allowed to stir at room temperature for 1 hour sealed. The appropriate indole (0.1 mmol) was added to the reaction, followed shortly by the addition of the listed diene (0.1 mmol), and the vial was capped with a Teflon® lined lid or septum cap, taped with electrical tape and brought outside the dry box. Any volatile liquids (eg: $HBF_4.OEt_2$) were added via syringe through the Teflon® septa under an atmosphere of N_2. The reaction was allowed to warm to the appropriate temperature and stir for 18 to 48 h as appropriate. The reaction was allowed to cool and an aliquot was taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solvent evaporated before the products were purified by SiO_2 column chromatography.



Synthesis of (*E*)-3-(4-phenylbut-3-en-2-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (12.9 mg, 0.110 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.0050 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.0050 mmol, 5 mol%) in chlorobenzene (100 μL, [ ] = 1.0 M). The reaction was mixed and (*E*)-buta-1,3-dien-1-ylbenzene (13.0 mg, 0.100 mmol) was added. The reaction was sealed and allowed to stir at 40 °C for 2 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO2 column chromatography (25:1 Pentane/EtOAc) to afford **1** (24.2 mg, 0.098 mmol, 98% Yield) as a colorless oil.

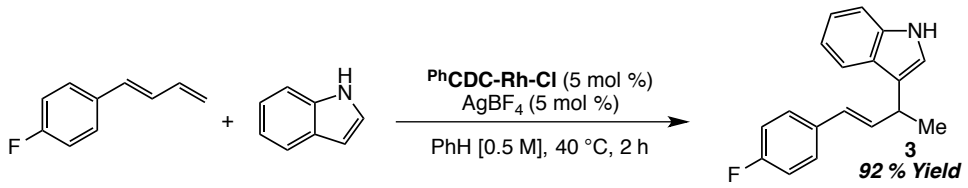
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.42 – 7.33 (m, 3H), 7.33 – 7.27 (m, 3H), 7.23 – 7.15 (m, 2H), 7.10 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.03 (dd, *J* = 2.5, 0.9 Hz, 1H), 3.95 (p, *J* = 6.9 Hz, 1H), 1.58 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.93, 136.71, 135.57, 128.58, 128.32, 127.02, 126.95, 126.29, 122.13, 120.63, 120.53, 119.78, 119.40, 111.25, 34.40, 20.84. IR (ν/cm-1): 3025 (s), 2962 (s), 1492 (s), 1456 (s), 1417 (s), 1337 (s), 1221 (w), 1095 (w) MS (ES+) [M+H]+ calcd for $C_{18}H_{18}N$+ 248.14, found: 248.18.



Synthesis of (*E*)-3-(4-(4-methoxyphenyl)but-3-en-2-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (5.9 mg, 0.05 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (1.7 mg, 0.0025 mmol, 5 mol%) and $AgBF_4$ (0.5 mg, 0.0025 mmol, 5 mol%) in benzene (100 μL, [ ] = 0.50 M). The reaction was mixed and (*E*)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (8.0 mg, 0.05 mmol) was added. The reaction was sealed and allowed to stir at 40 °C for 2 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **2** (12.3 mg, 0.0445 mmol, 89% yield) as a yellow oil.

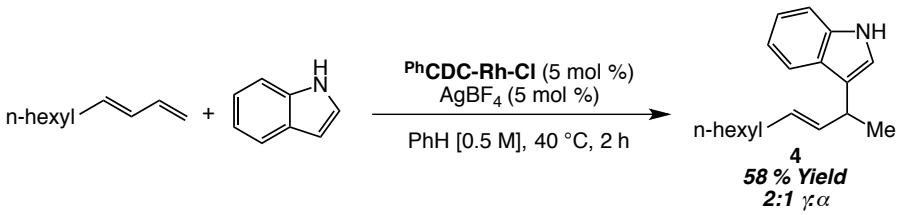
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (1H, bs), 7.68 (1H, d, J = 7.9 Hz), 7.37 (1H, m), 7.29 (2H, m), 7.18 (1H, t, J = 7.3 Hz), 7.08 (1H, t, J = 7.3 Hz), 7.03 (1H, d, J = 2.0 Hz), 6.82 (2H, m), 6.45 (1H, d, J = 15.8 Hz), 6.32 (1H, dd, J = 15.8, 7.0 Hz), 3.91 (1H, m), 3.79 (3H, s), 1.55 (3H, d, J = 6.8 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.70, 136.58, 133.34, 130.62, 127.54, 127.22, 126.85, 121.96, 120.76, 120.35, 119.69, 119.22, 113.87, 111.09, 55.30, 34.22, 20.82.



Synthesis of (*E*)-3-(4-(4-fluorophenyl)but-3-en-2-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (5.9 mg, 0.05 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (1.7 mg, 0.0025 mmol, 5 mol%) and $AgBF_4$ (0.5 mg, 0.0025 mmol, 5 mol%) in benzene (100 μL, [ ] = 0.50 M). The reaction was mixed and (*E*)-1-(buta-1,3-dien-1-yl)-4-fluorobenzene (7.4 mg, 0.05 mmol) was added. The reaction was sealed and allowed to stir at 40 °C for 2 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **3** (12.2 mg, 0.046 mmol, 92% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (1H, bs), 7.66 (1H, d, J = 7.9 Hz), 7.37 (1H, d, J = 8.2 Hz), 7.30 (2H, m), 7.19 (1H, t, J = 7.4 Hz), 7.09 (1H, t, J = 7.5 Hz), 7.03 (1H, d, J = 2.2 Hz), 6.96 (2H, m), 6.46 (1H, d, J = 15.9 Hz), 6.37 (1H, q, J = 7.7 Hz), 3.93 (1H, m), 1.56 (3H, d, J = 7.0 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.93 (d, J = 243 Hz), 136.58, 135.22, 135.20, 133.92, 127.57, 127.52, 127.02, 126.78, 122.04, 120.39, 119.59, 119.29, 115.34, 115.20, 111.15, 34.22, 20.68. ^{19}F NMR (376 MHz): δ -115.76.

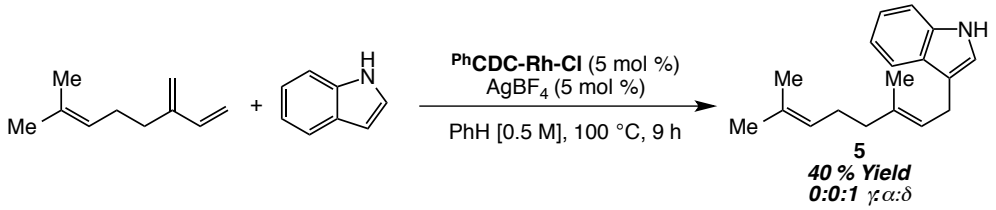


Synthesis of (*E*)-3-(dec-3-en-2-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (5.9 mg, 0.05 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (1.7 mg, 0.0025 mmol, 5 mol%) and $AgBF_4$ (0.5 mg, 0.0025 mmol, 5 mol%) in benzene (100 μL, [ ] = 0.50 M). The reaction was

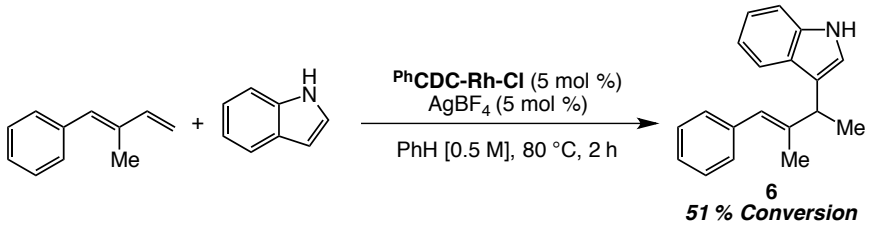
mixed and (*E*)-deca-1,3-diene (6.9 mg, 0.05 mmol) was added. The reaction was sealed and allowed to stir at 40 °C for 2 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **4** (7.4 mg, 0.029 mmol, 58% yield) as a colorless oil.

Isolated as a 2:1 mixture of the γ:α regioisomers (*E*)-3-(dec-3-en-2-yl)-1*H*-indole and (*E*)-3-(dec-2-en-4-yl)-1*H*-indole. (*E*)-3-(dec-3-en-2-yl)-1*H*-indole: [**^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.91 (bs, 1H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 5.65 (dd, *J* = 15.4, 6.8 Hz, 1H), 5.59 – 5.52 (m, 1H), 3.72 (p, *J* = 6.8 Hz, 1H), 2.02 (q, *J* = 7.0 Hz, 2H), 1.45 (d, *J* = 6.8 Hz, 2H), 1.37 – 1.27 (m, 8H), 0.93 – 0.82 (m, 3H).] (*E*)-3-(dec-2-en-4-yl)-1*H*-indole: [**^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.91 (bs, 1H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.26 (s, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 5.62 (dd, *J* = 17.8, 7.3 Hz, 1H), 5.57 – 5.49 (m, 1H), 3.52 – 3.46 (m, 1H), 1.87 – 1.80 (m, 1H), 1.77 – 1.69 (m, 1H), 1.67 (d, *J* = 6.2 Hz, 3H), 1.37 – 1.27 (m, 8H), 0.92 – 0.83 (m, 3H).] **^{13}C NMR** (151 MHz, $CDCl_3$) δ 136.59, 136.53, 135.13, 134.86, 128.99, 126.91, 126.86, 124.11, 121.85, 121.82, 121.39, 120.33, 120.31, 120.07, 119.77, 119.70, 119.02, 119.01, 111.08, 111.05, 40.18, 35.40, 33.97, 32.51, 31.89, 31.77, 29.58, 29.38, 28.89, 27.72, 22.71, 22.66, 20.99, 17.90, 14.12, 14.12.



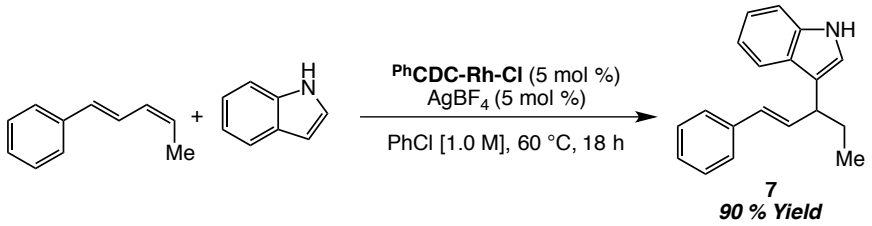
Synthesis of (*E*)-3-(3,7-dimethylocta-2,6-dien-1-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (5.9 mg, 0.05 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (1.7 mg, 0.0025 mmol, 5 mol%) and $AgBF_4$ (0.5 mg, 0.0025 mmol, 5 mol%) in benzene (100 μL, [ ] = 0.50 M). The reaction was mixed and myrcene (10.2 mg, 0.075 mmol) was added. The reaction was sealed and allowed to stir at 100 °C for 9 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard, which showed a 40% conversion to (*E*)-3-(3,7-dimethylocta-2,6-dien-1-yl)-1*H*-indole. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford impure **5** as a colorless oil.



Synthesis of (*E*)-3-(3-methyl-4-phenylbut-3-en-2-yl)-1*H*-indole

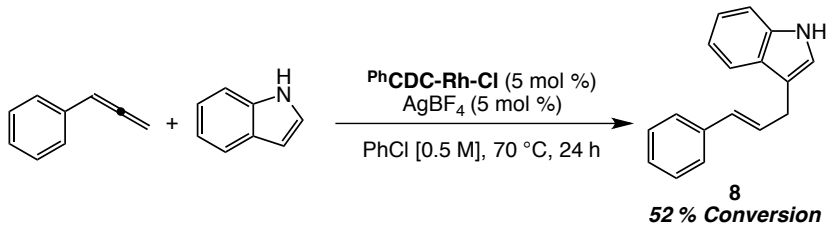
Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (5.9 mg, 0.05 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (1.7 mg, 0.0025 mmol, 5 mol%) and $AgBF_4$ (0.5 mg, 0.0025 mmol, 5 mol%) in benzene (100 μL, [ ] = 0.50 M). The reaction was mixed and (*E*)-(2-methylbuta-1,3-dien-1-yl)benzene (7.2 mg, 0.05 mmol) was added. The reaction was sealed and allowed to stir at 80 °C for 2 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard, which showed a 40% conversion to (*E*)-3-(3-methyl-4-phenylbut-3-en-2-yl)-1*H*-indole. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford impure **6** as a colorless oil.



Synthesis of (*E*)-3-(1-phenylpent-1-en-3-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (11.7 mg, 0.1 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) in chlorobenzene (100 μL, [ ] = 1.0 M). The reaction was mixed and (1*E*-penta-1,3-dien-1-yl)benzene (17.3 mg, 0.12 mmol, mixture of 3*E*/*Z* isomers) was added. The reaction was sealed and allowed to stir at 60 °C for 18 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (50:1 Hex/Et_2O) to afford **7** (23.5 mg, 0.09 mmol, 90% yield) as a colorless oil.

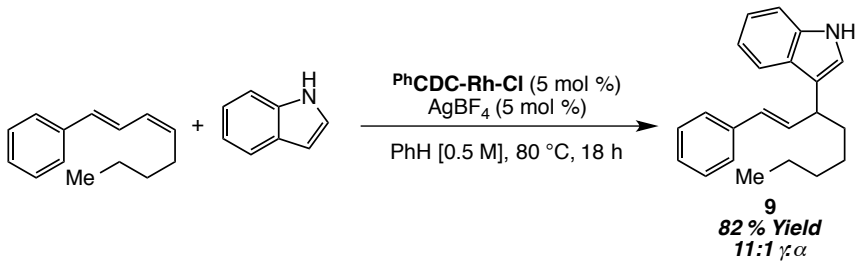
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (bs, 1H), 7.67 (t, *J* = 10.6 Hz, 1H), 7.36 (t, *J* = 8.2 Hz, 3H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.18 (dd, *J* = 12.2, 7.0 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.04 (s, 1H), 6.50 (d, *J* = 15.8 Hz, 1H), 6.40 (dd, *J* = 15.8, 7.8 Hz, 1H), 3.64 (q, *J* = 7.4 Hz, 1H), 2.01 (dp, *J* = 14.2, 7.1 Hz, 1H), 1.95 – 1.83 (m, 1H), 1.00 (t, *J* = 7.3 Hz, 3H).



Synthesis of 3-cinnamyl-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (11.7 mg, 0.1 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) in benzene (200 μL, [ ] = 0.50 M). The reaction was mixed and (propa-1,2-dien-1-yl)benzene (11.6 mg, 0.1 mmol) was added. The reaction was sealed and allowed to stir at 70 °C for 24 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **8** (12.1 mg, 0.052 mmol, 52% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (bs, 1H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 3H), 7.28 (t, *J* = 7.0 Hz, 2H), 7.21 – 7.16 (m, 2H), 7.11 – 7.07 (m, 1H), 7.03 (d, *J* = 2.2 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.46 (dd, *J* = 15.9, 6.4 Hz, 1H), 3.94 (p, *J* = 6.9 Hz, 1H), 1.57 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.78, 136.56, 135.42, 128.44, 128.18, 126.87, 126.81, 126.14, 121.99, 120.50, 120.38, 119.64, 119.25, 111.10, 34.27, 20.70.

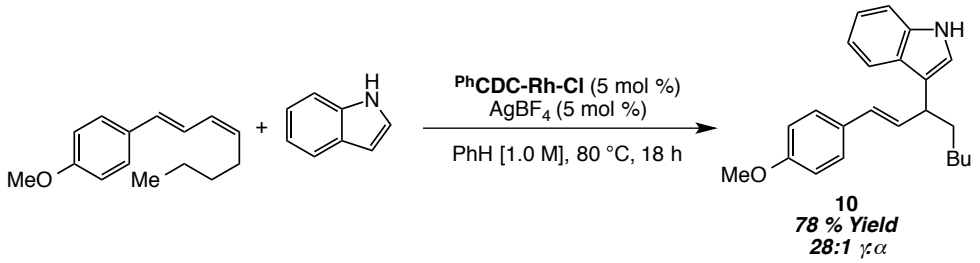


Synthesis of (*E*)-3-(1-phenyloct-1-en-3-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (11.7 mg, 0.1 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.005 mmol, 5 mol%)

and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) in benzene (200 μL, [ ] = 0.50 M). The reaction was mixed and (1*E*-octa-1,3-dien-1-yl)benzene (11.6 mg, 0.1 mmol, mixture of 3*E*/*Z* isomers) was added. The reaction was sealed and allowed to stir at 80 °C for 18 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **9** (24.8 mg, 0.082 mmol, 82% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (bs, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.36 (m, 3H), 7.33 – 7.28 (m, 2H), 7.24 – 7.16 (m, 2H), 7.15 – 7.10 (m, 1H), 7.03 (t, *J* = 2.9 Hz, 1H), 6.52 (d, *J* = 15.8 Hz, 1H), 6.43 (dd, *J* = 15.8, 7.8 Hz, 1H), 3.76 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.03 – 1.95 (m, 1H), 1.92 – 1.83 (m, 1H), 1.52 – 1.18 (m, 6H), 0.93 – 0.88 (m, 3H).

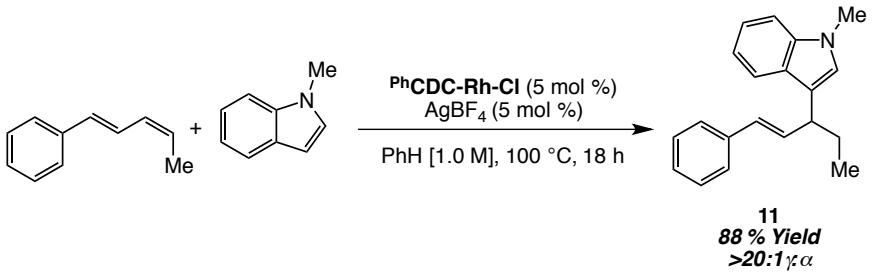


Synthesis of (*E*)-3-(1-(4-methoxyphenyl)oct-1-en-3-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, indole (11.7 mg, 0.1 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) in benzene (100 μL, [ ] = 1.0 M). The reaction was mixed and 1-methoxy-4-(1*E*-octa-1,3-dien-1-yl)benzene (26.0 mg, 0.12 mmol, mixture of 3*E*/*Z* isomers) was added. The reaction was sealed and allowed to stir at 80 °C for 18 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an

internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **10** (26.1 mg, 0.078 mmol, 78% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (bs, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.21 – 7.16 (m, 1H), 7.11 – 7.06 (m, 1H), 7.03 (d, *J* = 2.2 Hz, 1H), 6.84 – 6.80 (m, 2H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.26 (dd, *J* = 15.8, 7.9 Hz, 1H), 3.79 (s, *J* = 3.1 Hz, 3H), 3.70 (q, *J* = 7.6 Hz, 1H), 2.00 – 1.90 (m, 1H), 1.89 – 1.79 (m, 1H), 1.50 – 1.19 (m, 6H), 0.87 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.66, 136.54, 132.36, 130.70, 128.38, 127.21, 126.96, 121.90, 120.60, 119.70, 119.17, 113.85, 111.10, 55.31, 40.45, 35.32, 31.95, 27.49, 22.67, 14.16.

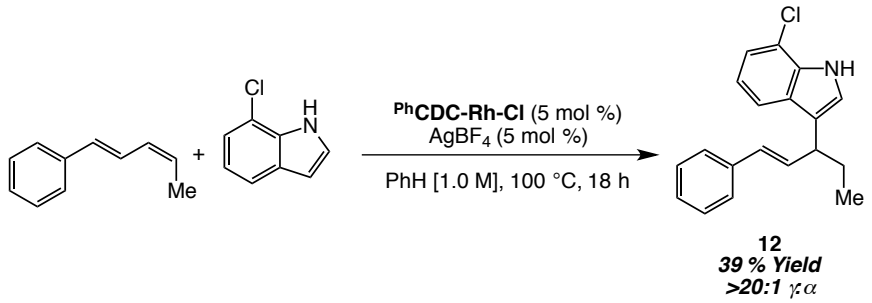


Synthesis of (*E*)-1-methyl-3-(1-phenylpent-1-en-3-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, 1-methyl-1*H*-indole (13.2 mg, 0.1 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) in benzene (100 μL, [ ] = 1.0 M). The reaction was mixed and (1*E*-penta-1,3-dien-1-yl)benzene (17.3 mg, 0.12 mmol, mixture of 3*E*/*Z* isomers) was added. The reaction was sealed and allowed to stir at 100 °C for 18 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting

oil was purified by SiO_2 column chromatography (50:1 Hex/Et_2O) to afford **11** (24.2 mg, 0.088 mmol, 88% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.33 – 7.25 (m, 7H), 7.22 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.20 – 7.15 (m, 1H), 7.11 – 7.04 (m, 1H), 6.89 (s, 1H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.40 (dd, *J* = 15.8, 7.8 Hz, 1H), 3.77 (s, 3H), 3.63 (m, 1H), 1.99 (dt, *J* = 13.9, 7.0 Hz, 1H), 1.88 (dt, *J* = 13.3, 7.5 Hz, 1H), 1.00 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.35, 134.45, 129.21, 128.55, 127.47, 126.95, 126.26, 125.72, 121.60, 119.83, 118.75, 117.75, 109.33, 42.37, 32.81, 28.40, 12.62. IR (ν/cm-1): 2958 (m), 2871 (m), 1471 (m), 1374 (m), 1326 (s), 1333 (m). MS (ES+) [M+H]+ calcd for C20H22N+ 276.17, found: 276.09.

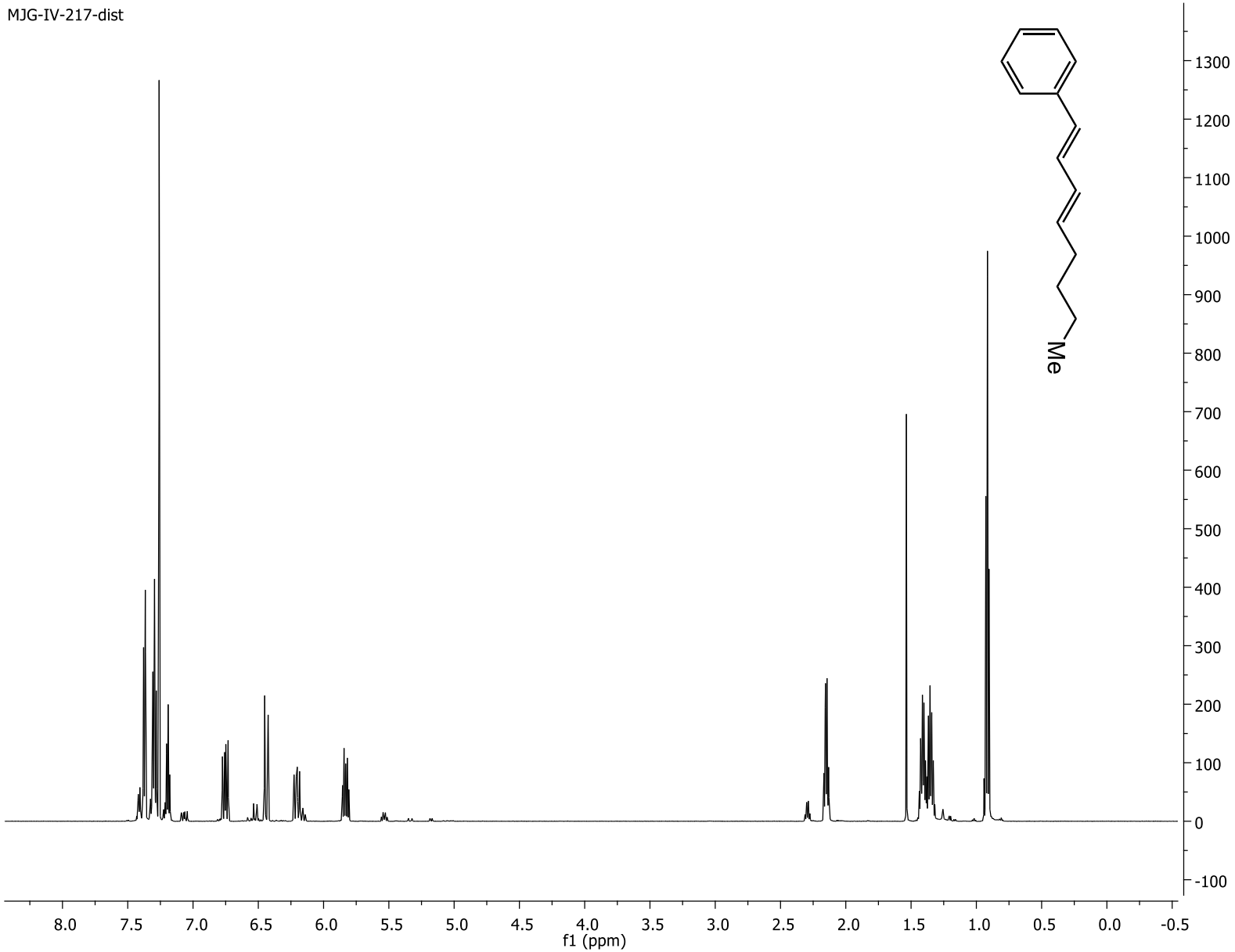


Synthesis (*E*)-7-chloro-3-(1-phenylpent-1-en-3-yl)-1*H*-indole

Following the general procedure for CDC-Rh-Cl catalyzed intermolecular hydroarylation, 7-chloro-1*H*-indole (15.2 mg, 0.1 mmol) was added to a solution of **^{Ph}CDC-Rh-Cl** (3.4 mg, 0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) in benzene (100 μL, [ ] = 1.0 M). The reaction was mixed and (1*E*-penta-1,3-dien-1-yl)benzene (17.3 mg, 0.12 mmol, mixture of 3*E*/*Z* isomers) was added. The reaction was sealed and allowed to stir at 100 °C for 18 h before being allowed to cool and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting

oil was purified by SiO_2 column chromatography (40:1 Hex/Et_2O) to afford **12** (11.5 mg, 0.039 mmol, 39% yield) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 2H), 7.29 (dt, *J* = 13.3, 7.8 Hz, 2H), 7.22 – 7.17 (m, 2H), 7.10 (t, *J* = 4.1 Hz, 1H), 7.05 – 6.99 (m, 1H), 6.49 (d, *J* = 15.9 Hz, 1H), 6.38 (dd, *J* = 15.8, 7.7 Hz, 1H), 3.63 (q, *J* = 7.4 Hz, 1H), 2.06 – 1.96 (m, 1H), 1.95 – 1.84 (m, 1H), 1.00 (t, *J* = 7.4 Hz, 3H).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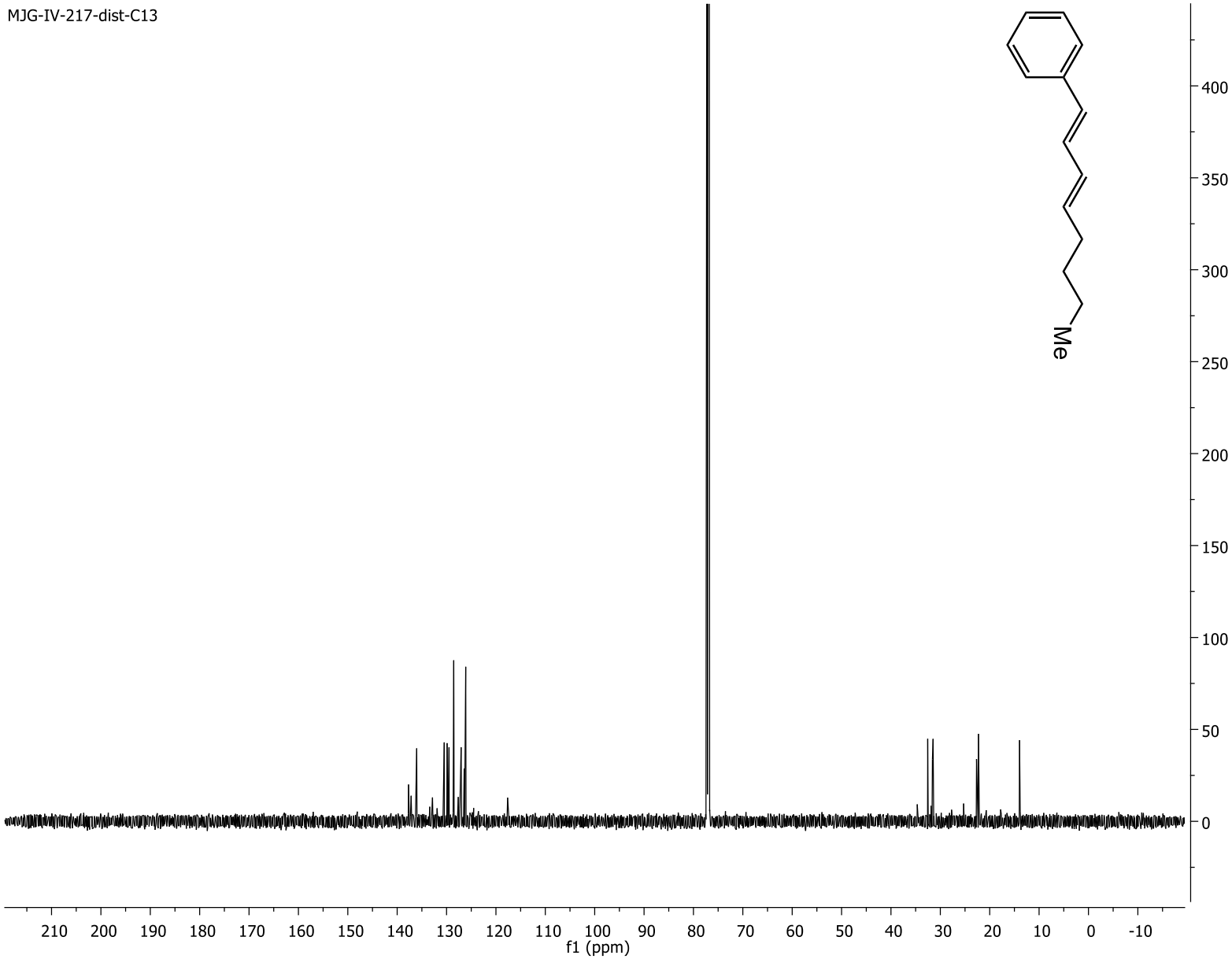
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100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f1 (ppm)
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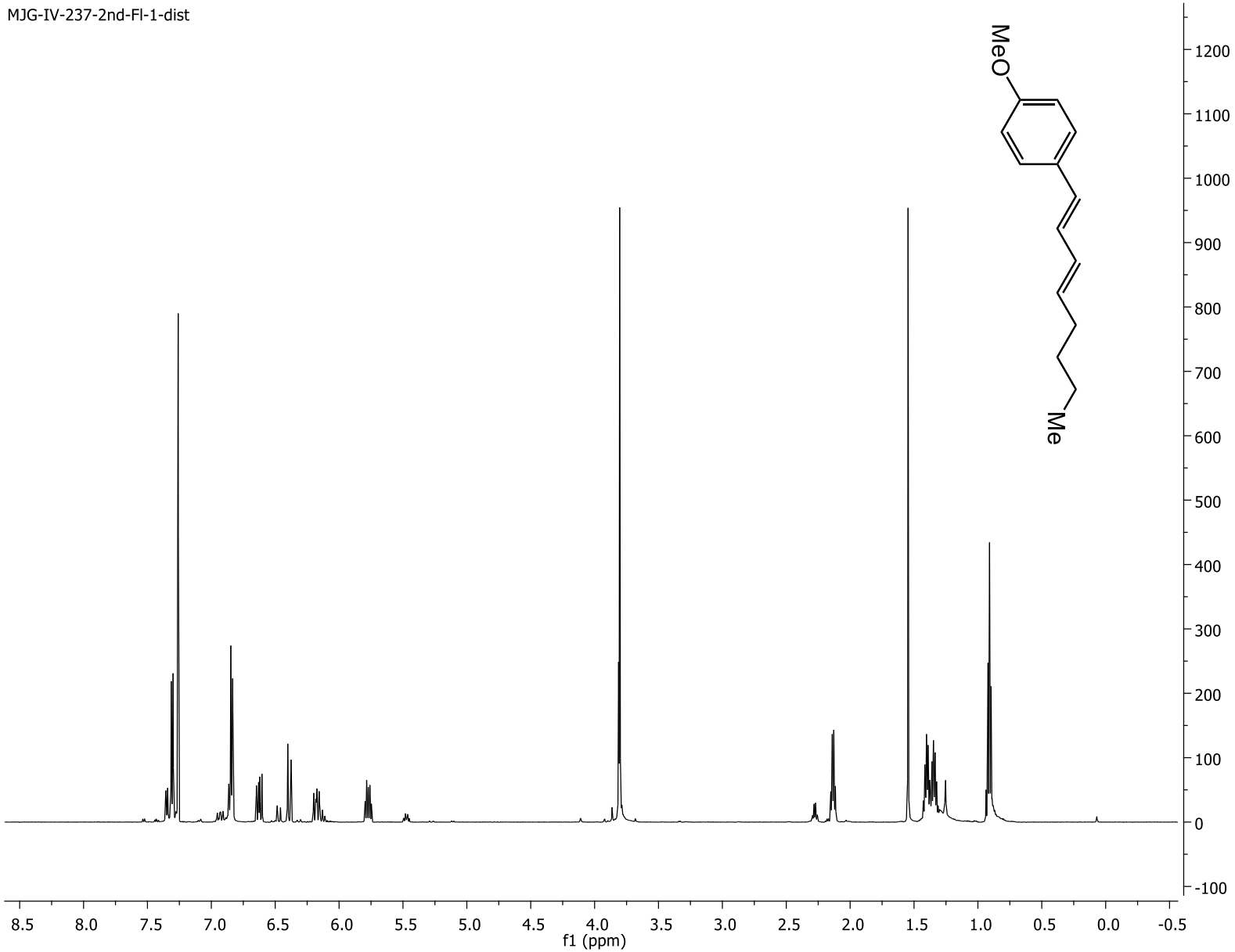
0 50 100 150 200 250 300 350 400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Me
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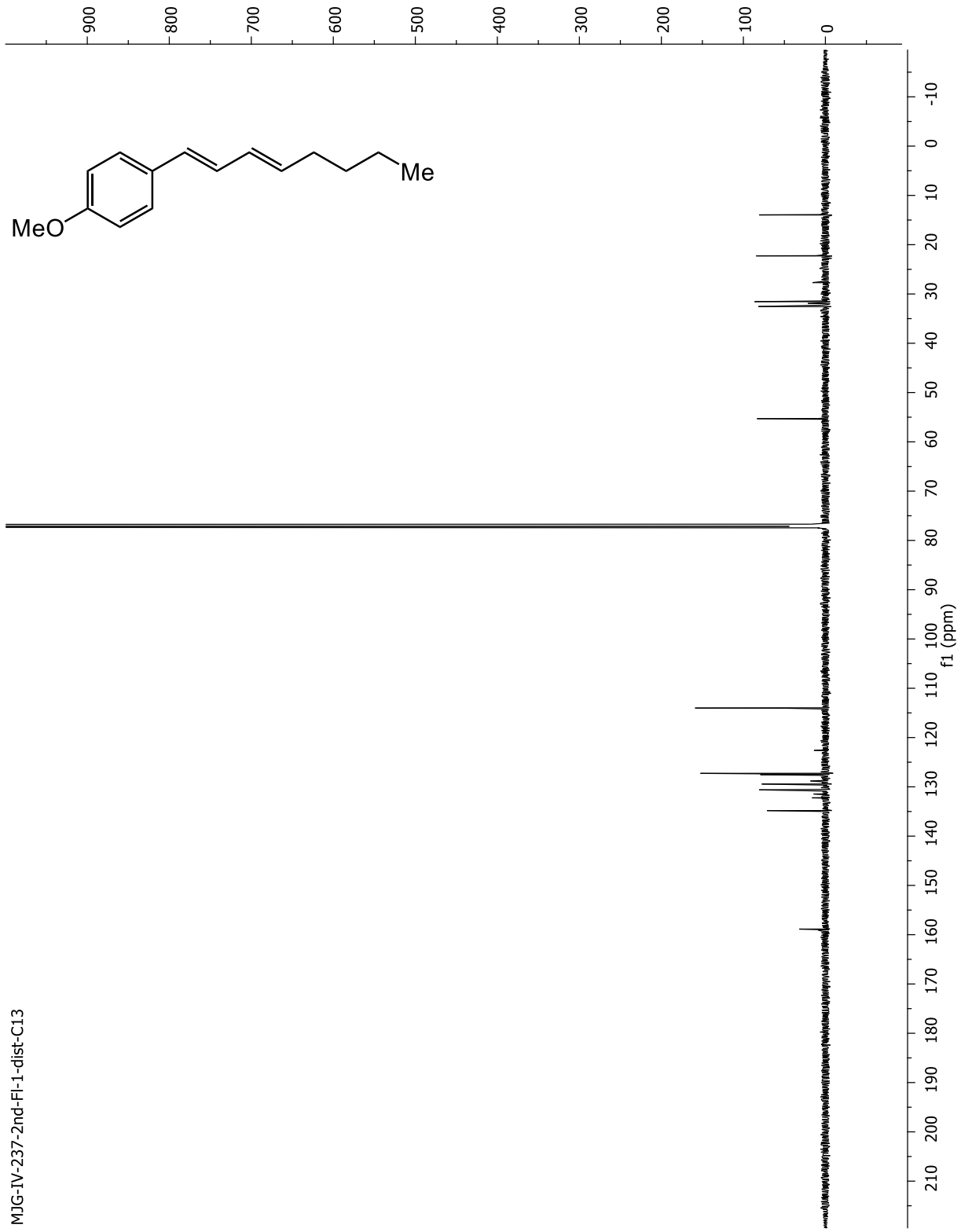
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100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Me
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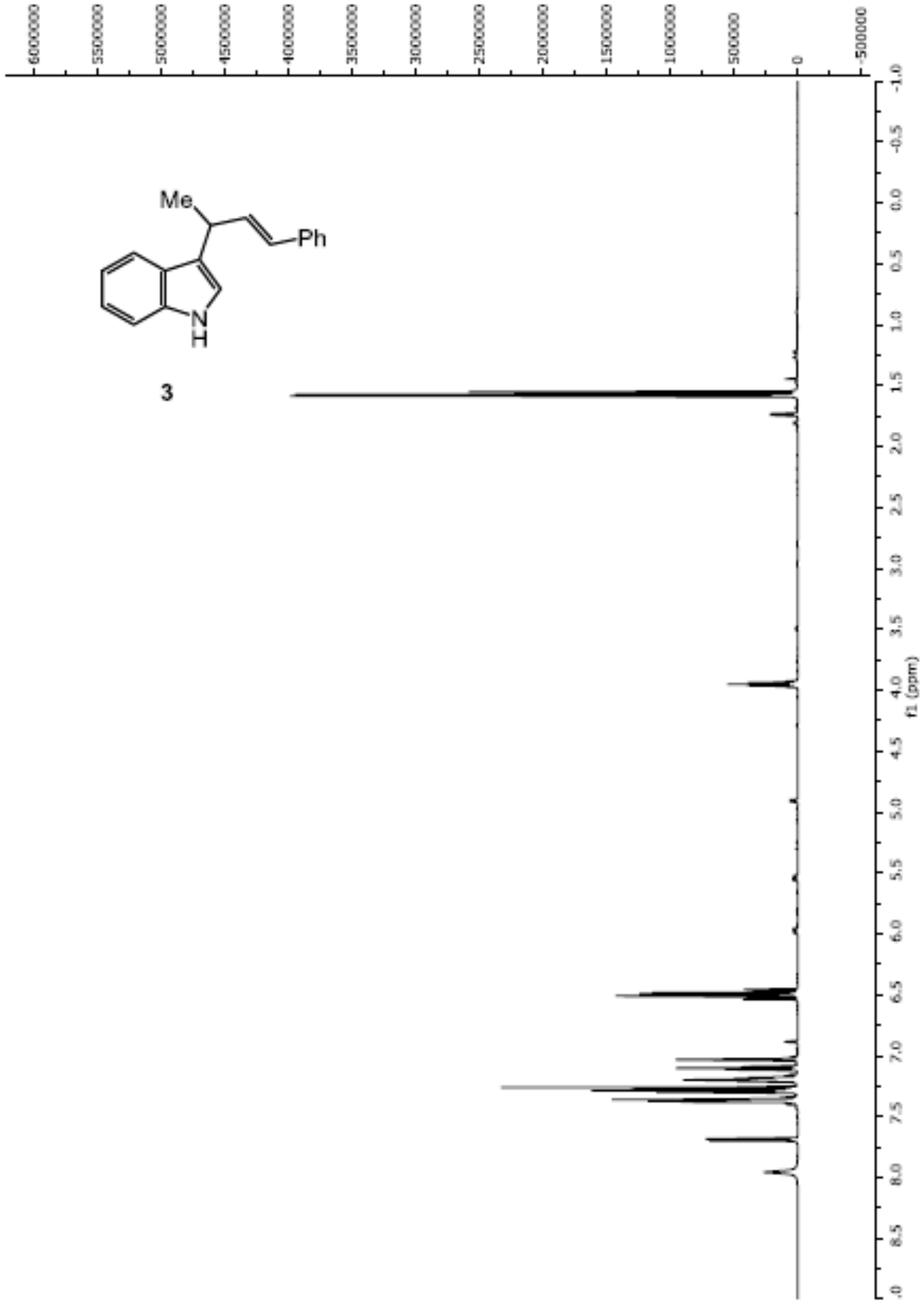
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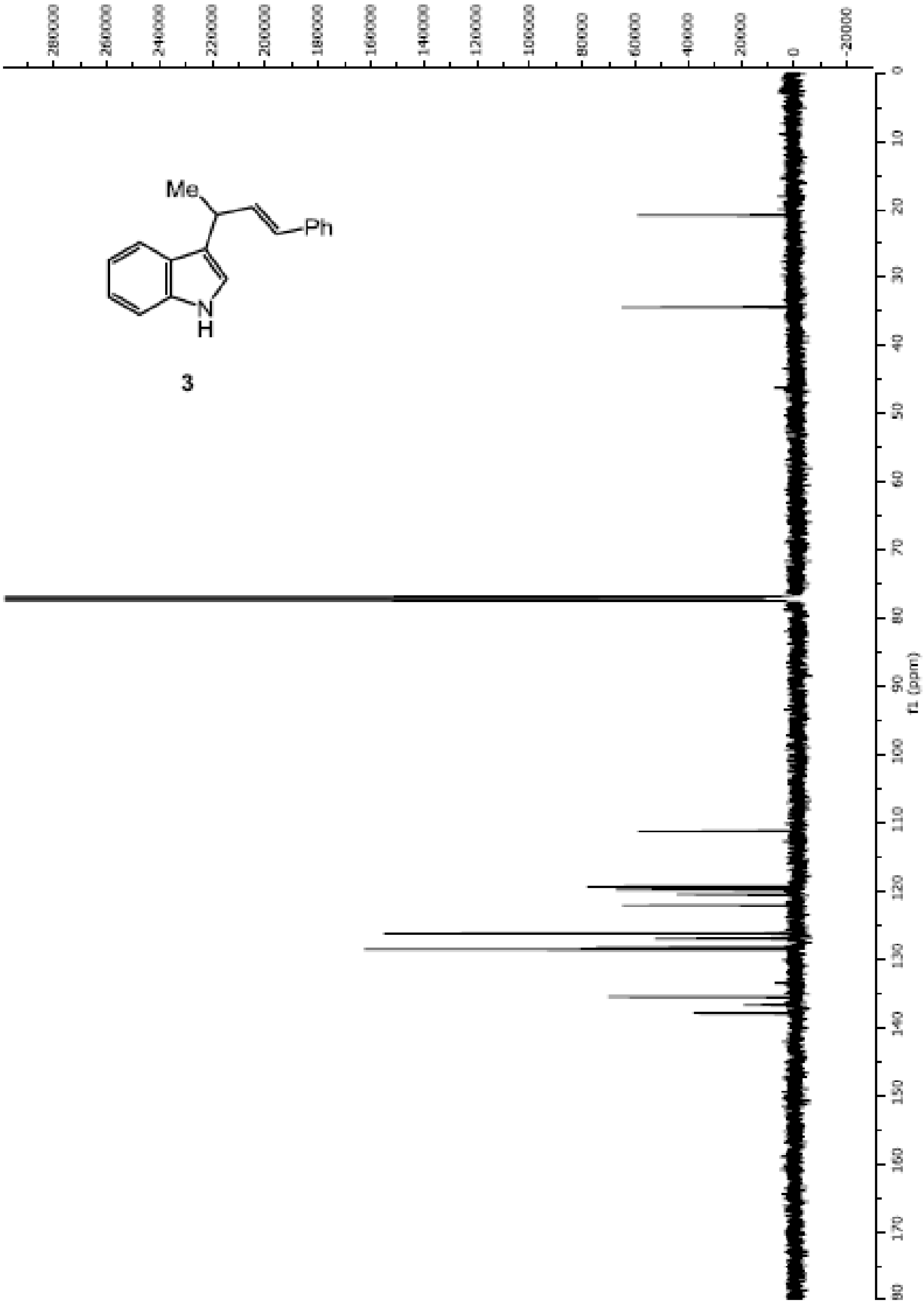
Ph
N
H
3
f1 (ppm)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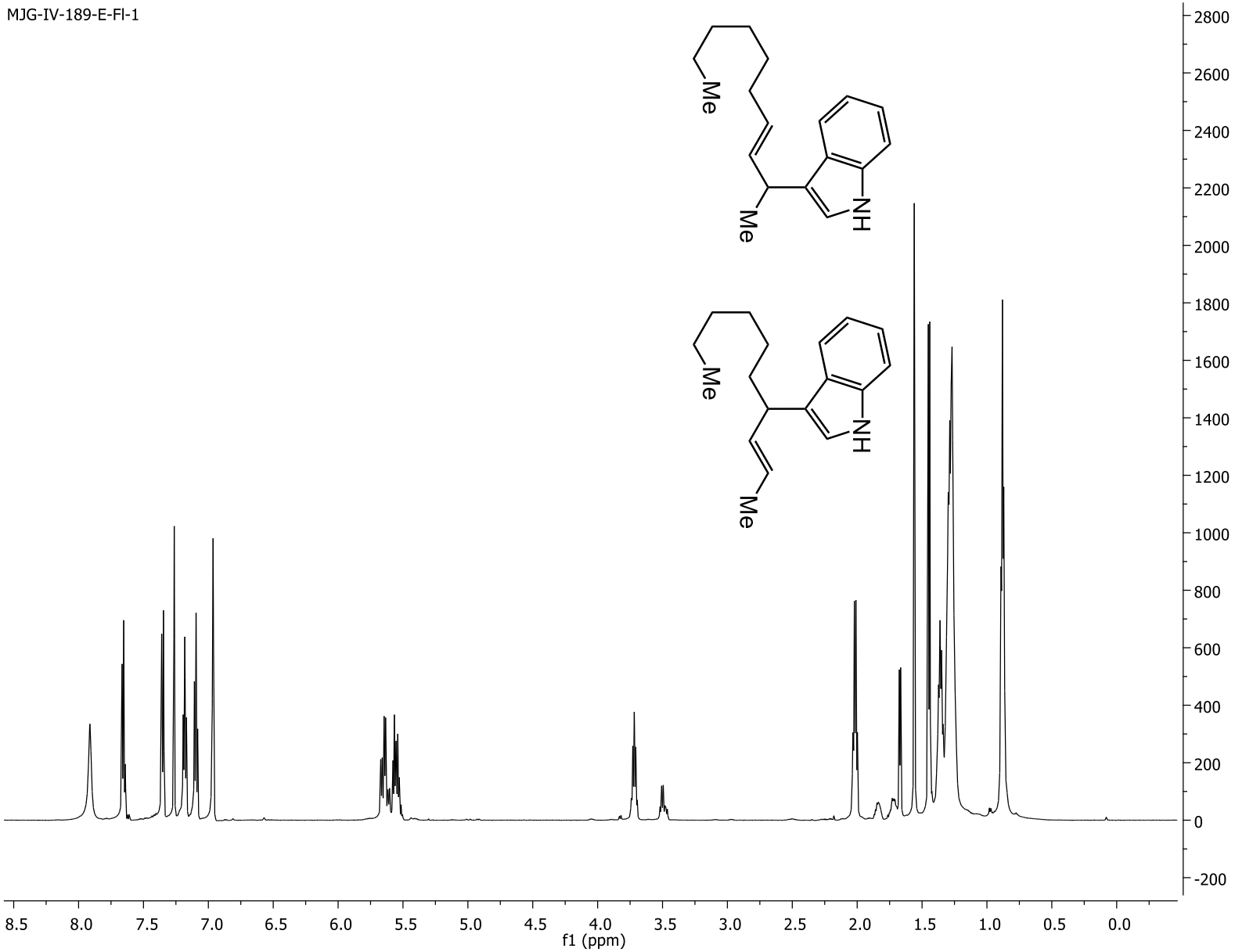
Ph
N
H
3
f1 (ppm)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Me
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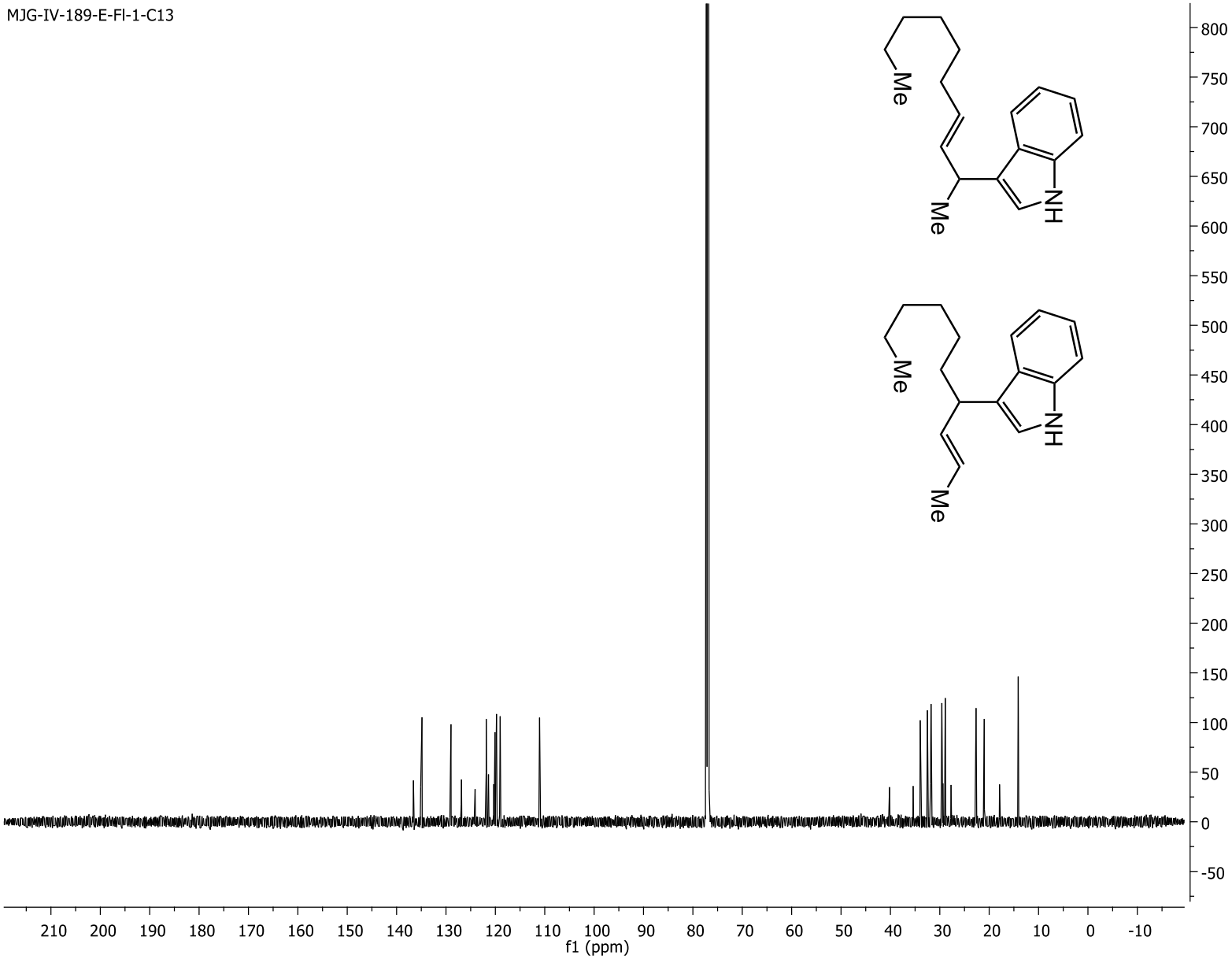
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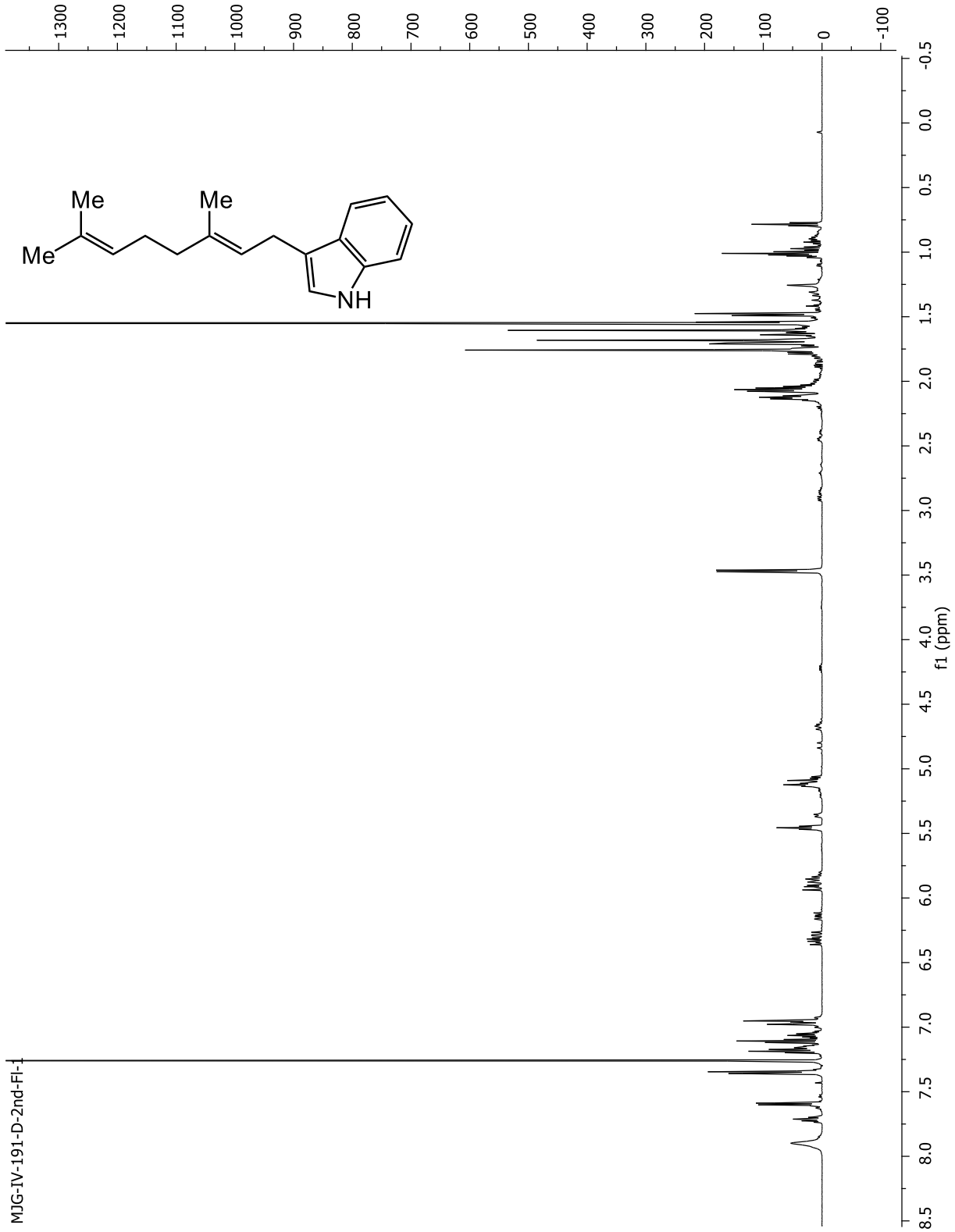
Me
NH
Me
Me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Me
Me
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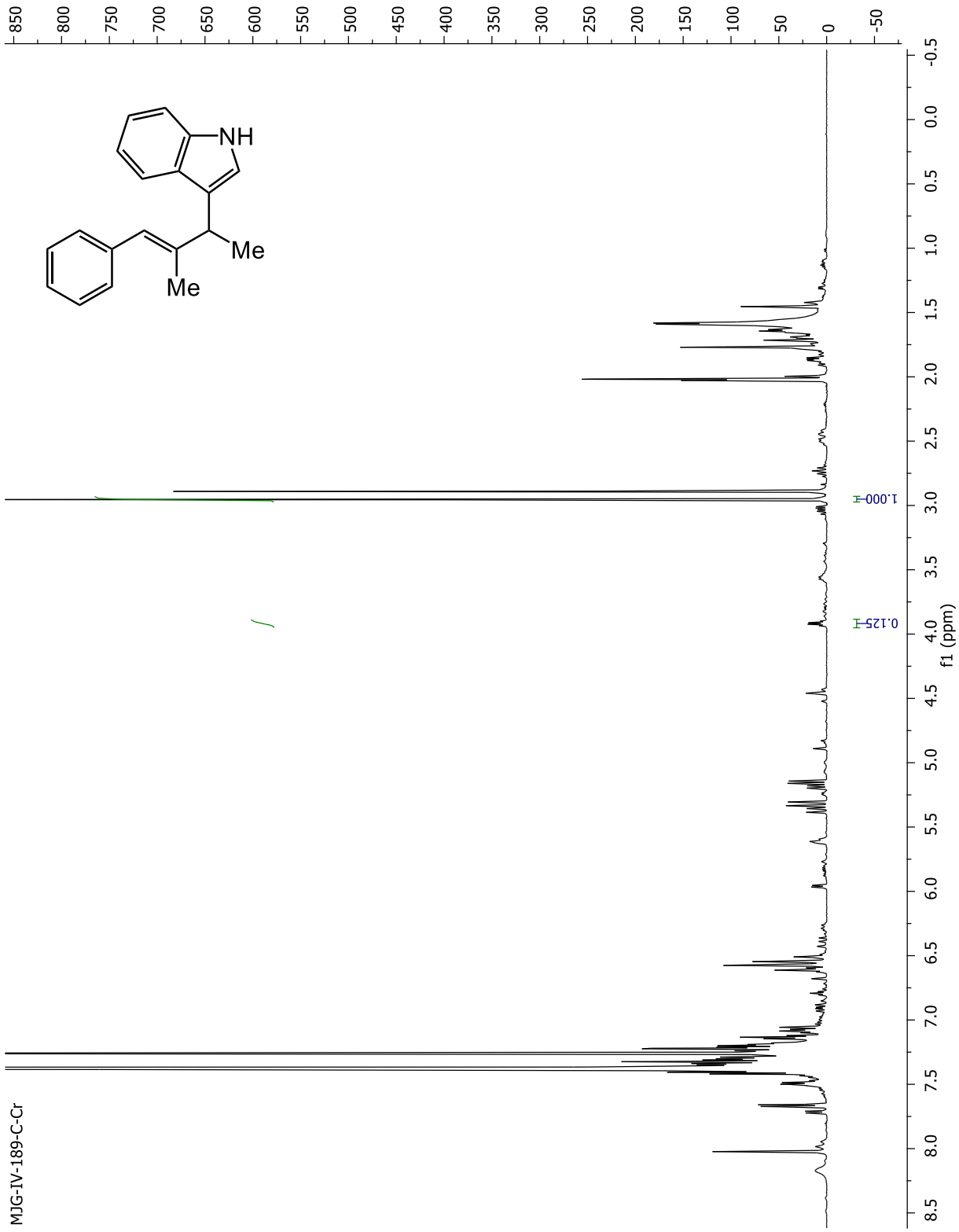
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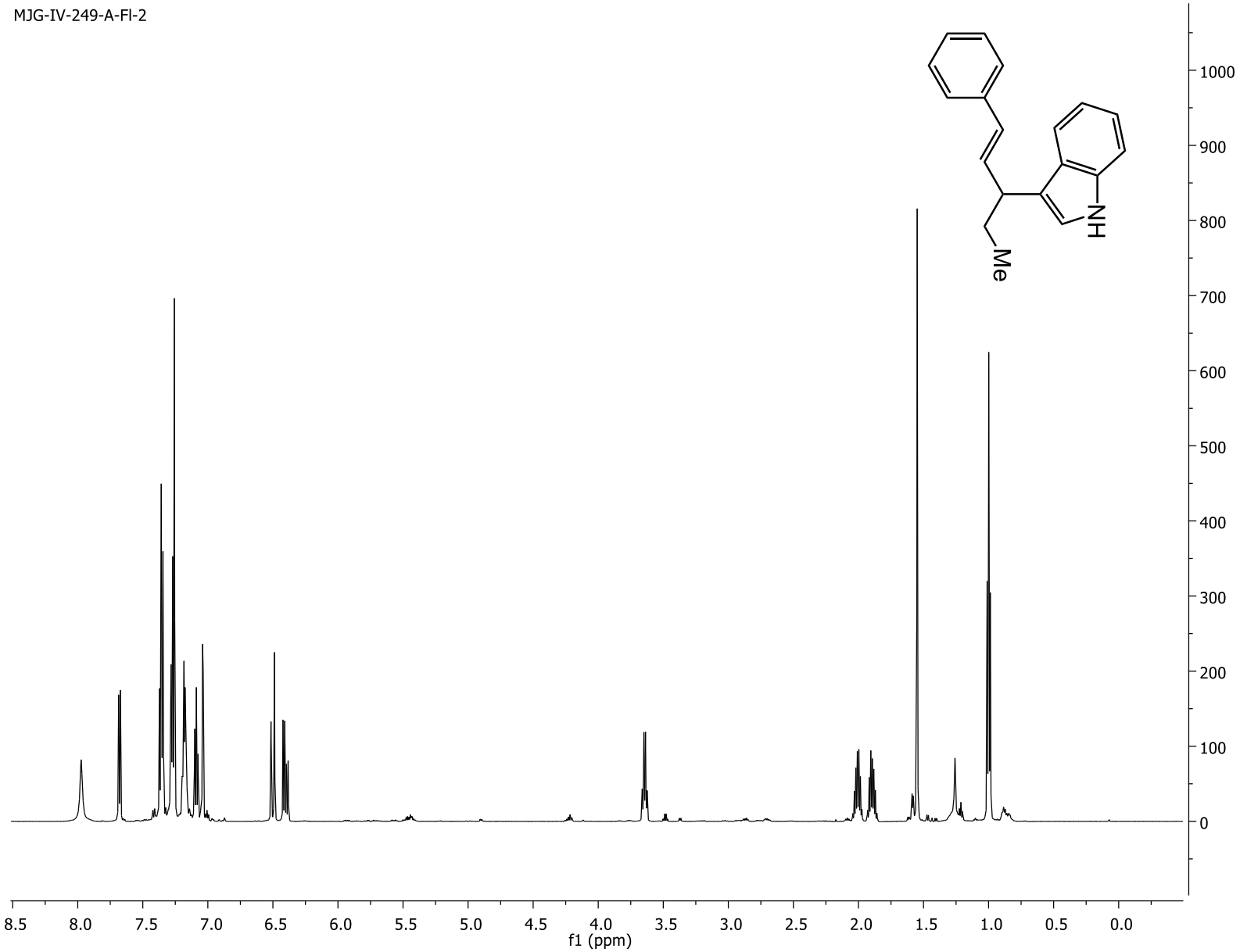
Me
Me
1.000
0.125
f1 (ppm)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700
600
500
400
300
200
100
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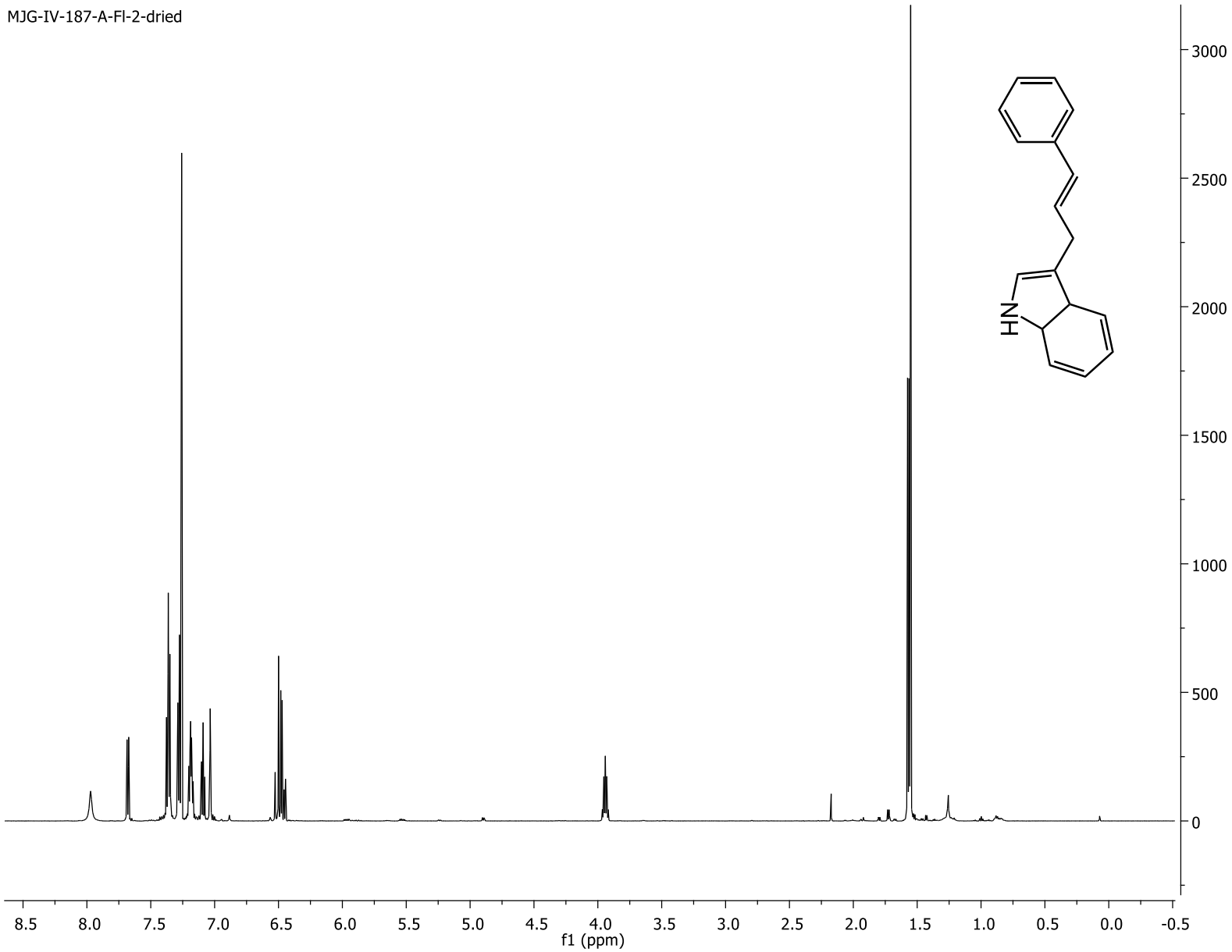
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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2500
2000
1500
1000
500
0
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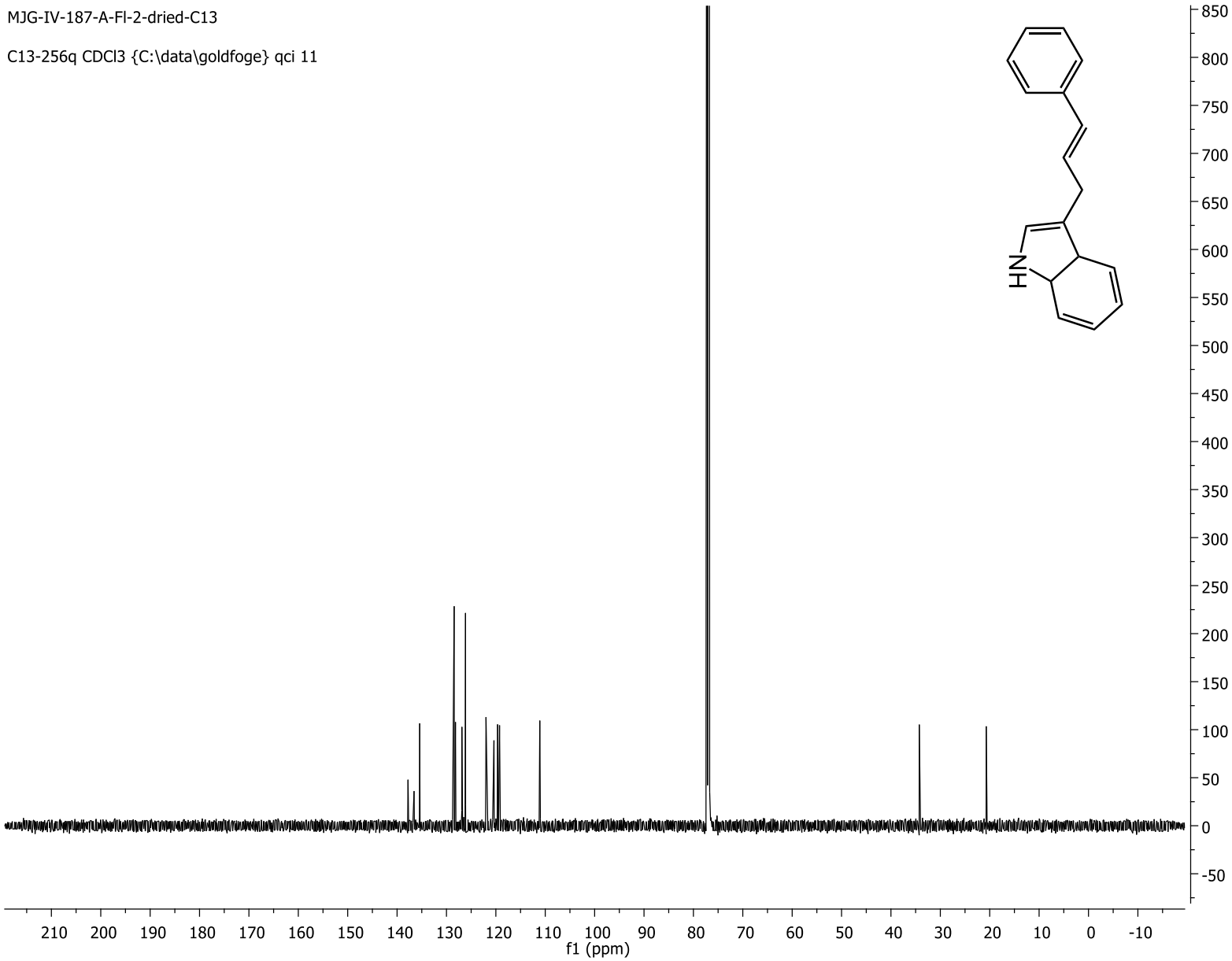
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
N
H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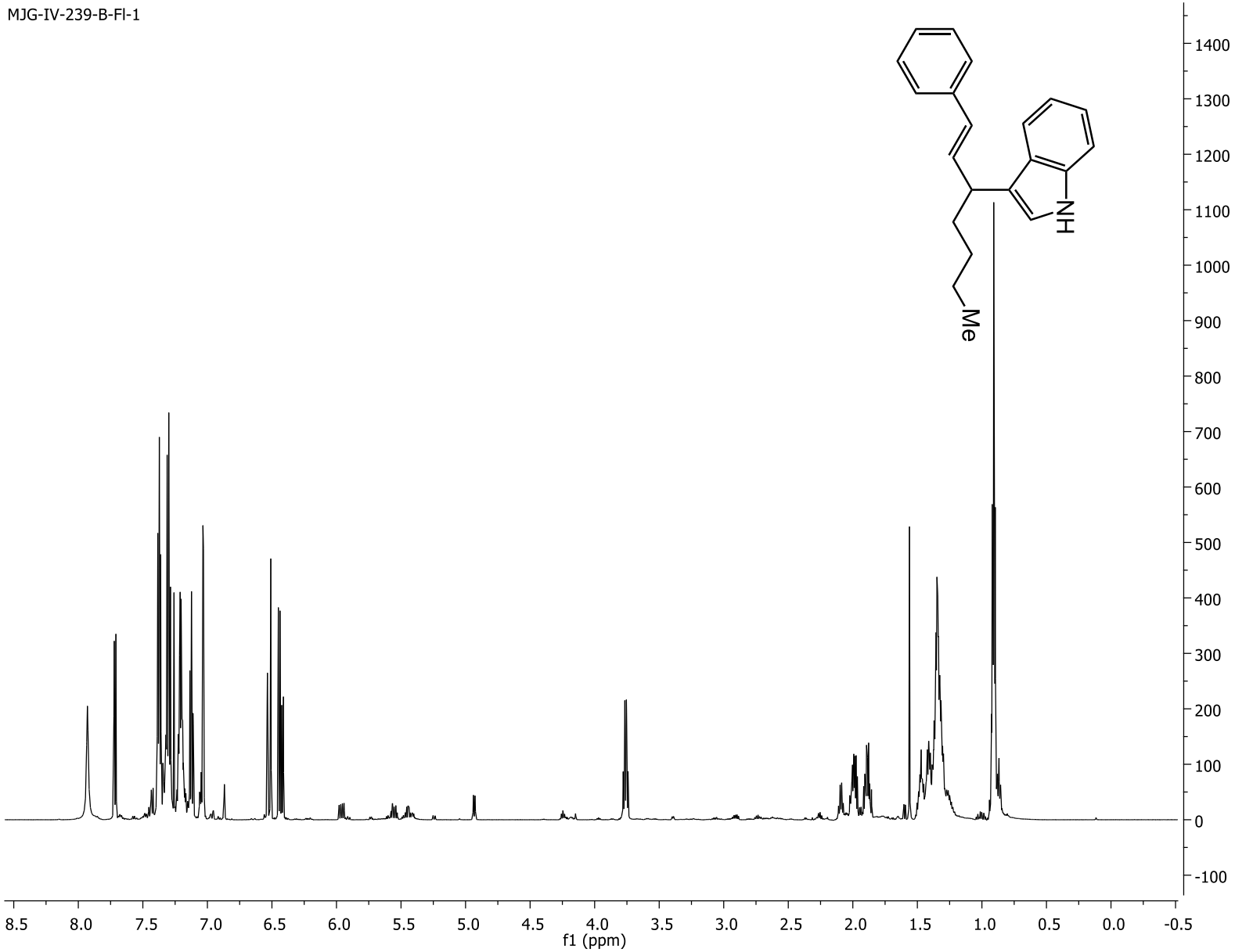
C13-256q CDCl3 {C:\data\goldfoge} qci 11
HN
f1 (ppm)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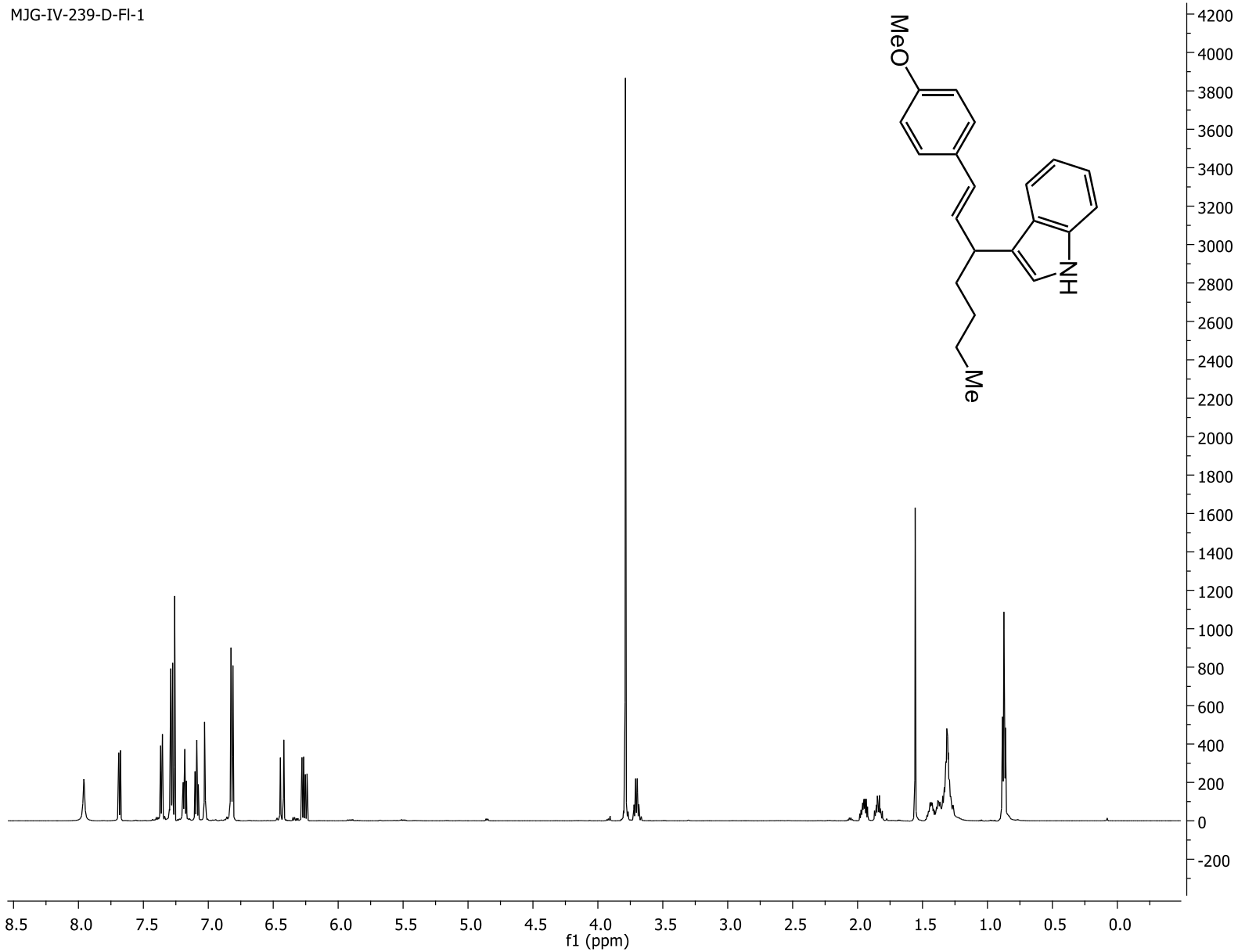
Me
NH
f1 (ppm)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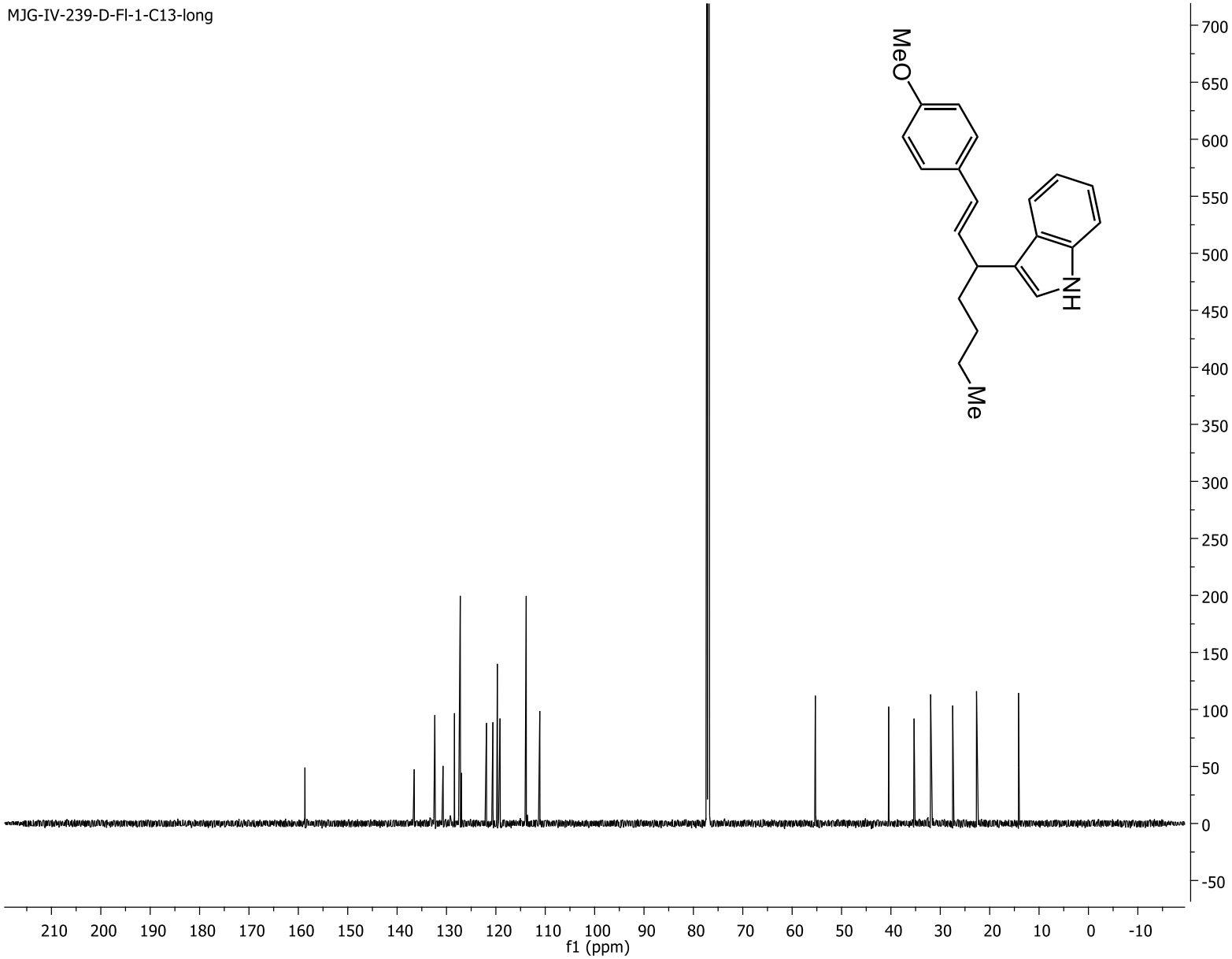
MeO
NH
Me
f1 (ppm)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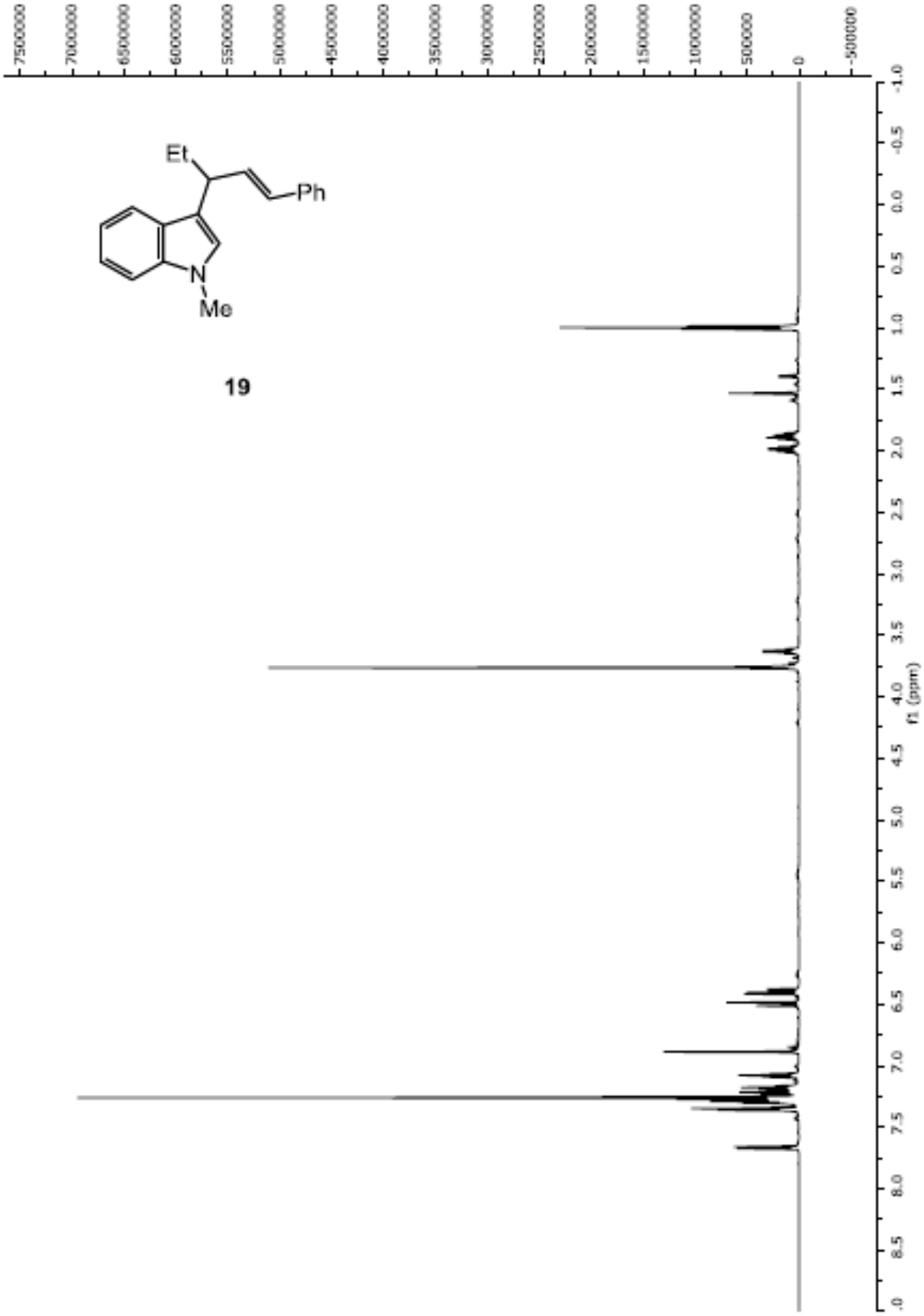
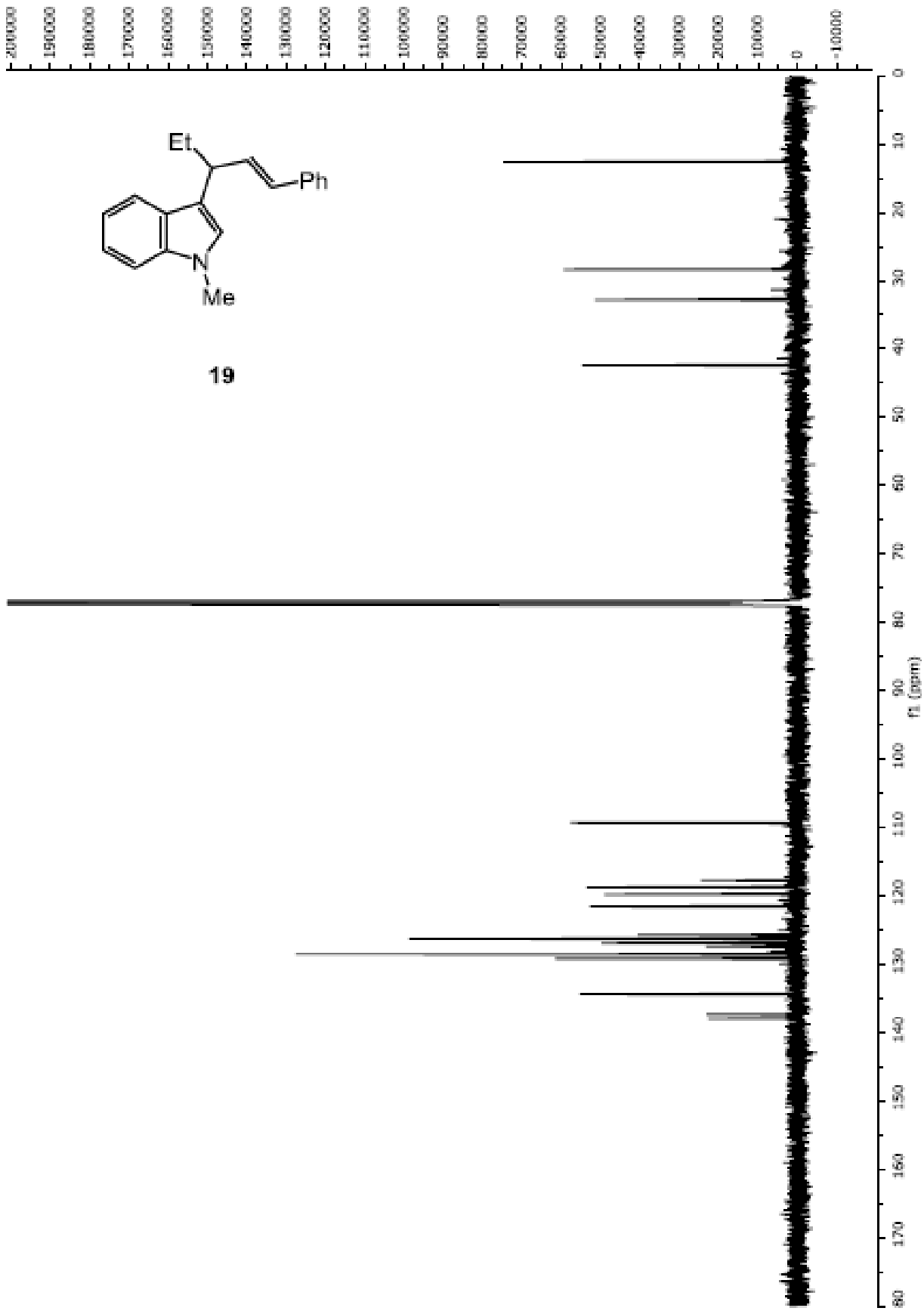
MeO
HN
Me
f1 (ppm)


Et
Ph
N
Me
19
f1 (ppm)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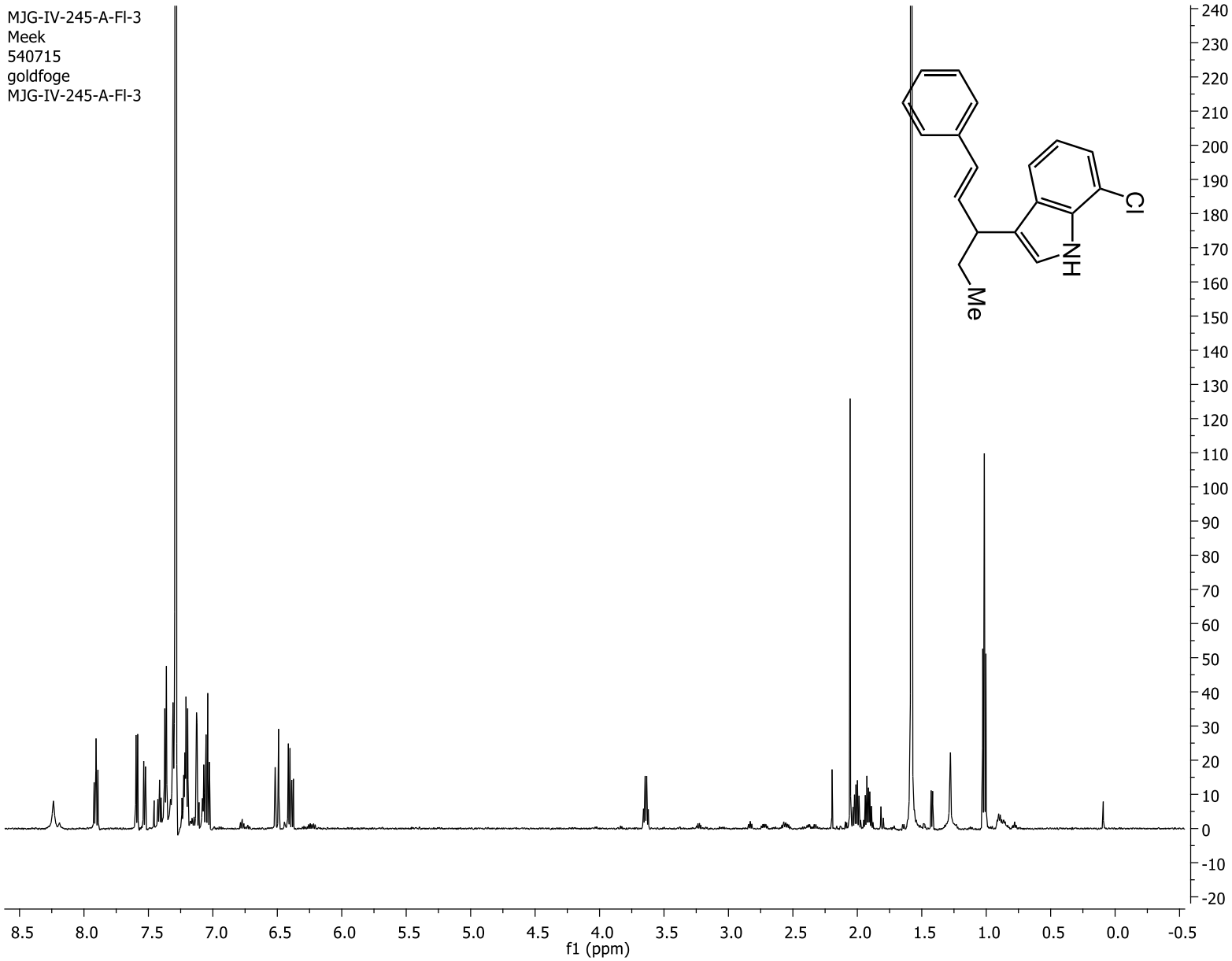
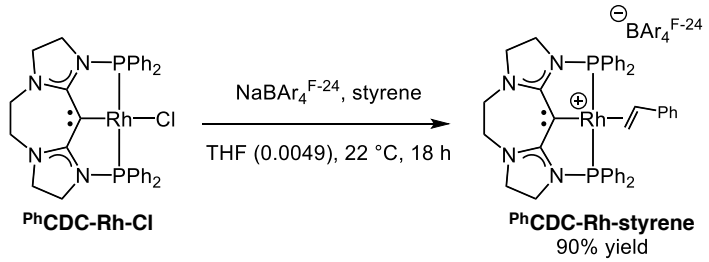
Ph
N
Me
19
f1 (ppm)


MJG-IV-245-A-Fl-3
Meek
540715
goldfoge
MJG-IV-245-A-Fl-3
Cl
NH
Me
f1 (ppm)

Section 2.3: Developing a Cationic Carbodicarbene-Rh Complex

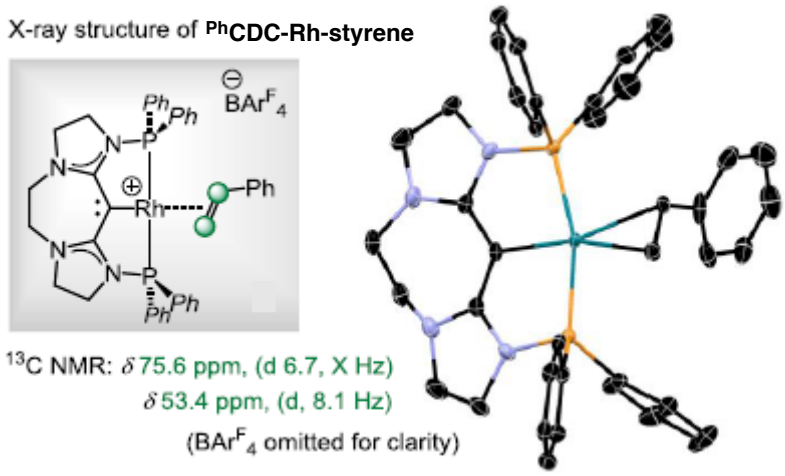


Synthesis of ^{Ph}CDC-Rh-styrene BAr_4^{F-24} complex

In an N_2 filled dry box, a 20-mL scintillation vial with a stir bar was charged with **^{Ph}CDC-Rh-Cl** (540 mg, 0.788 mmol, 1.0 equiv) and $NaBAr_4^{F-24}$ (733 mg, 0.827 mmol, 1.05 equiv) Tetrahydrofuran (16 mL, [ ] = 0.049 M) was added followed by the addition of styrene (0.451 mL, 3.94 mmol, 5.0 equiv) via syringe. The vial was capped and the resulting dark orange mixture was allowed to stir for 18 h at 22 °C. After the reaction was complete, the NaCl precipitate was allowed to settle and the solution was filtered through a Celite® pad followed by washing with 5 mL of THF. The orange solution was concentrated and more THF (2.0 mL) was added to remove excess styrene. The solvent was removed *in vacuo* and two more aliquots of THF (2.0 mL) and 1 aliquot (2.0 mL) of ether were added to repeat this process. The tacky dark orange solid on the side of the vial was crushed into a powder via spatula and left to dry *in vacuo* for 6 h. The dark orange powder was isolated in 90% yield (1.15 g, 0.709 mmol). **^{1}H NMR** (600 MHz, Methylene Chloride-d_2) δ 7.81-7.73 (m, 12H), 7.69 – 7.55 (m, 16H), 7.49 (t, J = 7.5 Hz, 4H), 6.79 (t, J = 7.4 Hz, 1H), 6.58 (t, J = 7.6 Hz, 2H), 5.90 (d, J = 7.7 Hz, 2H), 4.90 (td, J = 8.1, 4.1 Hz, 1H), 4.06 – 3.94 (m, 4H), 3.44 (m, 5H), 3.27 (m, 4H), 2.99 (d, J = 8.2 Hz, 1H). **^{13}C NMR** (151 MHz, Methylene Chloride-d_2) δ 172.82 (t, J = 21.3 Hz), 162.17 (m), 140.89, 135.22, 133.38 (dt, J = 60.1, 7.5 Hz), 131.97 (d, J = 47.2 Hz), 130.70 (td, J = 22.3, 13.1 Hz), 129.48 (dt, J = 19.8, 9.9 Hz), 129.19 (m), 128.45, 127.72, 126.38, 125.92, 125.57, 124.11, 122.31, 117.94 (q, J

= 4.2 Hz), 83.76 (dt, J = 34.3, 11.4 Hz), 75.62 (d, J = 6.7 Hz), 58.75, 53.38 (d, J = 8.1 Hz), 46.85, 41.38. **^{31}P NMR** (243 MHz, Methylene Chloride-d_2) δ 86.47 (d, J = 164.3 Hz). HRMS (ES+) $[M]^+$ calcd for $C_{41}H_{40}N_4P_2Rh^+$ 753.18 , found: 753.09.

Crystal Structure Data for ^{Ph}CDC-Rh-styrene



Empirical formula	C75 H52 B F24 N4 P2 Rh
Formula weight	1640.87
Temperature	100K
Wavelength	0.71073
Crystal system	triclinic
Space group	P-1
Unit cell dimensions	a = 14.5732(5) Å α= 72.9946(16)
	a = 14.5732(5) Å α= 72.9946(16)
	b = 16.2543(6) Å β= 69.1536(17)
	c = 16.4636(6) Å γ = 78.1710(16)
Volume	3462.92
Z	2
Density (calculated)	1.548 g/cm-1
Absorption coefficient	0.406 (mm-1)
F(000)	1624.5
Crystal size	0.193 x 0.238 x 0.283
Theta max	70.15
Index ranges	Hmax = 17, kmax = 19, lmax = 20
Reflections collected	13181
Independent reflections	12784
Completeness to theta	97

Max. and min. transmission	0.663, 0.753
Refinement method	XS least squares
Goodness-of-fit on F2 0	1.019
R indices	R1 = 0.0336, wR2 = 0.1139

Table S3. Bond lengths (Å) for ^{Ph}**CDC-Rh-styrene**

Number	Atom1	Atom2	Length
1	Rh1	P2	2.2637(6)
2	Rh1	P1	2.2601(5)
3	Rh1	C1	2.075(2)
4	Rh1	C40	2.233(3)
5	Rh1	C41	2.201(3)
6	P2	N1	1.707(2)
7	P2	C10	1.821(2)
8	P2	C16	1.822(2)
9	P1	N2	1.704(2)
10	P1	C22	1.820(3)
11	P1	C28	1.821(2)
12	C1	C2	1.404(3)
13	C1	C3	1.391(3)
14	N3	C2	1.348(3)
15	N3	C8	1.453(3)
16	N3	C5	1.442(4)
17	N2	C3	1.369(3)
18	N2	C7	1.470(3)
19	C2	N1	1.369(3)
20	N1	C4	1.461(4)
21	C3	N4	1.354(3)
22	N4	C6	1.468(3)
23	N4	C9	1.454(4)
24	C22	C23	1.397(3)
25	C22	C27	1.401(3)
26	C10	C11	1.405(3)
27	C10	C15	1.398(4)
28	C6	H6A	0.99
29	C6	H6B	0.99
30	C6	C7	1.521(5)
31	C11	H11	0.95
32	C11	C12	1.385(3)
33	C23	H23	0.949
34	C23	C24	1.394(4)
35	C15	H15	0.951
36	C15	C14	1.392(3)
37	C14	H14	0.95
38	C14	C13	1.387(3)

39	C13	H13	0.95
40	C13	C12	1.393(4)
41	C12	H12	0.951
42	C26	H26	0.95
43	C26	C27	1.388(4)
44	C26	C25	1.390(3)
45	C27	H27	0.95
46	C29	H29	0.95
47	C29	C28	1.388(4)
48	C29	C30	1.390(3)
49	C28	C33	1.395(4)
50	C33	H33	0.95
51	C33	C32	1.388(3)
52	C30	H30	0.95
53	C30	C31	1.381(4)
54	C24	H24	0.95
55	C24	C25	1.384(3)
56	C25	H25	0.95
57	C31	H31	0.95
58	C31	C32	1.381(5)
59	C32	H32	0.95
60	C4	H4A	0.989
61	C4	H4B	0.99
62	C4	C5	1.513(4)
63	C9	H9A	0.99
64	C9	H9B	0.99
65	C9	C8	1.513(3)
66	C8	H8A	0.991
67	C8	H8B	0.99
68	C7	H7A	0.99
69	C7	H7B	0.99
70	C16	C17	1.392(3)
71	C16	C21	1.400(4)
72	C17	H17	0.95
73	C17	C18	1.394(4)
74	C21	H21	0.95
75	C21	C20	1.388(4)
76	C19	H19	0.95
77	C19	C18	1.365(5)
78	C19	C20	1.390(4)
79	C18	H18	0.95
80	C20	H20	0.951
81	C34	C40	1.495(4)
82	C34	C35	1.375(4)
83	C34	C39	1.388(4)
84	C40	H40	1
85	C40	C41	1.381(5)
86	C35	H35	0.95
87	C35	C36	1.377(5)

88	C41	H41A	0.95
89	C41	H41B	0.95
90	C36	H36	0.949
91	C36	C37	1.382(5)
92	C39	H39	0.95
93	C39	C38	1.377(4)
94	C38	H38	0.951
95	C38	C37	1.361(4)
96	C37	H37	0.949
97	C5	H5A	0.99
98	C5	H5B	0.991
99	F20	C58	1.339(3)
100	F24	C59	1.321(3)
101	F22	C59	1.336(4)
102	F23	C59	1.343(3)
103	C57	H57	0.95
104	C57	C56	1.395(3)
105	C57	C52	1.401(3)
106	C54	C53	1.396(3)
107	C54	C55	1.383(3)
108	C54	C58	1.494(3)
109	C53	H53	0.95
110	C53	C52	1.405(3)
111	C56	C55	1.381(3)
112	C56	C59	1.505(3)
113	C55	H55	0.95
114	C52	B1	1.648(3)
115	F21	C58	1.329(4)
116	F19	C58	1.358(3)
117	B1	C44	1.641(3)
118	B1	C60	1.640(4)
119	B1	C68	1.647(3)
120	C44	C49	1.391(3)
121	C44	C45	1.404(3)
122	C60	C61	1.400(3)
123	C60	C65	1.397(3)
124	C68	C73	1.399(3)
125	C68	C69	1.403(3)
126	C73	H73	0.95
127	C73	C72	1.398(3)
128	C62	C61	1.388(4)
129	C62	C63	1.394(3)
130	C62	C66	1.486(4)
131	C71	H71	0.95
132	C71	C72	1.377(3)
133	C71	C70	1.390(3)
134	C69	H69	0.951
135	C69	C70	1.396(3)
136	C74	C70	1.501(3)

137	C74	F1	1.38(2)
138	C74	F2	1.340(9)
139	C74	F3	1.31(1)
140	C61	H61	0.95
141	C72	C75	1.499(3)
142	C65	H65	0.949
143	C65	C64	1.395(4)
144	C63	H63	0.95
145	C63	C64	1.376(5)
146	C64	C67	1.513(4)
147	F5	C75	1.340(4)
148	F4	C75	1.332(3)
149	F6	C75	1.327(4)
150	F15	C66	1.328(4)
151	C66	F13	1.355(3)
152	C66	F14	1.315(3)
153	C67	F18	1.28(1)
154	C67	F16	1.36(1)
155	C67	F17	1.31(1)
156	C49	H49	0.95
157	C49	C48	1.392(4)
158	C45	H45	0.95
159	C45	C46	1.390(4)
160	C48	C47	1.384(3)
161	C48	C50	1.498(4)
162	C46	C47	1.388(4)
163	C46	C51	1.501(3)
164	C47	H47	0.951
165	C51	F10	1.336(4)
166	C51	F11	1.347(3)
167	C51	F12	1.317(4)
168	F7	C50	1.39(2)
169	F8	C50	1.38(2)
170	F9	C50	1.22(2)

Table S4. Bond angles (°) for **^{Ph}CDC-Rh-styrene**

Number	Atom1	Atom2	Atom3	Angle
1	P2	Rh1	P1	162.95(2)
2	P2	Rh1	C1	81.46(6)
3	P2	Rh1	C40	82.70(8)
4	P2	Rh1	C41	112.96(8)
5	P1	Rh1	C1	81.65(6)
6	P1	Rh1	C40	114.30(8)
7	P1	Rh1	C41	83.51(8)
8	C1	Rh1	C40	159.8(1)
9	C1	Rh1	C41	163.7(1)

10	C40	Rh1	C41	36.3(1)
11	Rh1	P2	N1	103.37(7)
12	Rh1	P2	C10	118.04(8)
13	Rh1	P2	C16	123.63(8)
14	N1	P2	C10	102.4(1)
15	N1	P2	C16	100.8(1)
16	C10	P2	C16	105.0(1)
17	Rh1	P1	N2	103.01(7)
18	Rh1	P1	C22	123.85(8)
19	Rh1	P1	C28	119.51(8)
20	N2	P1	C22	103.6(1)
21	N2	P1	C28	100.9(1)
22	C22	P1	C28	102.5(1)
23	Rh1	C1	C2	119.3(2)
24	Rh1	C1	C3	118.9(2)
25	C2	C1	C3	121.7(2)
26	C2	N3	C8	126.6(2)
27	C2	N3	C5	112.1(2)
28	C8	N3	C5	121.0(2)
29	P1	N2	C3	117.2(2)
30	P1	N2	C7	131.3(2)
31	C3	N2	C7	111.5(2)
32	C1	C2	N3	133.2(2)
33	C1	C2	N1	118.6(2)
34	N3	C2	N1	108.2(2)
35	P2	N1	C2	117.1(2)
36	P2	N1	C4	130.8(2)
37	C2	N1	C4	111.7(2)
38	C1	C3	N2	118.9(2)
39	C1	C3	N4	132.6(2)
40	N2	C3	N4	108.5(2)
41	C3	N4	C6	110.2(2)
42	C3	N4	C9	121.8(2)
43	C6	N4	C9	118.4(2)
44	P1	C22	C23	119.7(2)
45	P1	C22	C27	121.1(2)
46	C23	C22	C27	119.1(2)
47	P2	C10	C11	122.5(2)
48	P2	C10	C15	118.4(2)
49	C11	C10	C15	118.8(2)
50	N4	C6	H6A	111.2
51	N4	C6	H6B	111.1
52	N4	C6	C7	103.0(2)
53	H6A	C6	H6B	109.2
54	H6A	C6	C7	111.2
55	H6B	C6	C7	111.2
56	C10	C11	H11	119.9
57	C10	C11	C12	120.2(2)
58	H11	C11	C12	119.9

59	C22	C23	H23	119.9
60	C22	C23	C24	120.2(2)
61	H23	C23	C24	119.9
62	C10	C15	H15	119.7
63	C10	C15	C14	120.6(2)
64	H15	C15	C14	119.7
65	C15	C14	H14	120
66	C15	C14	C13	120.0(2)
67	H14	C14	C13	120.1
68	C14	C13	H13	120
69	C14	C13	C12	119.9(2)
70	H13	C13	C12	120
71	C11	C12	C13	120.4(2)
72	C11	C12	H12	119.8
73	C13	C12	H12	119.8
74	H26	C26	C27	119.9
75	H26	C26	C25	119.9
76	C27	C26	C25	120.2(2)
77	C22	C27	C26	120.3(2)
78	C22	C27	H27	119.8
79	C26	C27	H27	119.8
80	H29	C29	C28	119.9
81	H29	C29	C30	119.8
82	C28	C29	C30	120.3(2)
83	P1	C28	C29	121.9(2)
84	P1	C28	C33	118.9(2)
85	C29	C28	C33	119.1(2)
86	C28	C33	H33	119.8
87	C28	C33	C32	120.3(2)
88	H33	C33	C32	119.9
89	C29	C30	H30	119.9
90	C29	C30	C31	120.2(3)
91	H30	C30	C31	119.9
92	C23	C24	H24	119.8
93	C23	C24	C25	120.3(2)
94	H24	C24	C25	119.9
95	C26	C25	C24	119.9(2)
96	C26	C25	H25	120.1
97	C24	C25	H25	120
98	C30	C31	H31	119.9
99	C30	C31	C32	120.0(3)
100	H31	C31	C32	120
101	C33	C32	C31	120.1(3)
102	C33	C32	H32	119.9
103	C31	C32	H32	120
104	N1	C4	H4A	111.2
105	N1	C4	H4B	111.2
106	N1	C4	C5	102.7(2)
107	H4A	C4	H4B	109.2

108	H4A	C4	C5	111.2
109	H4B	C4	C5	111.2
110	N4	C9	H9A	109.2
111	N4	C9	H9B	109.3
112	N4	C9	C8	112.0(2)
113	H9A	C9	H9B	107.9
114	H9A	C9	C8	109.2
115	H9B	C9	C8	109.2
116	N3	C8	C9	113.1(2)
117	N3	C8	H8A	109
118	N3	C8	H8B	109
119	C9	C8	H8A	108.9
120	C9	C8	H8B	108.9
121	H8A	C8	H8B	107.8
122	N2	C7	C6	101.5(2)
123	N2	C7	H7A	111.5
124	N2	C7	H7B	111.4
125	C6	C7	H7A	111.5
126	C6	C7	H7B	111.5
127	H7A	C7	H7B	109.3
128	P2	C16	C17	123.7(2)
129	P2	C16	C21	116.9(2)
130	C17	C16	C21	119.3(2)
131	C16	C17	H17	120.1
132	C16	C17	C18	119.8(2)
133	H17	C17	C18	120.1
134	C16	C21	H21	119.9
135	C16	C21	C20	120.0(3)
136	H21	C21	C20	120.1
137	H19	C19	C18	119.9
138	H19	C19	C20	119.9
139	C18	C19	C20	120.2(3)
140	C17	C18	C19	120.7(3)
141	C17	C18	H18	119.6
142	C19	C18	H18	119.7
143	C21	C20	C19	120.0(3)
144	C21	C20	H20	119.9
145	C19	C20	H20	120.1
146	C40	C34	C35	113.2(3)
147	C40	C34	C39	128.1(3)
148	C35	C34	C39	118.6(3)
149	Rh1	C40	C34	109.8(2)
150	Rh1	C40	H40	115.5
151	Rh1	C40	C41	70.6(2)
152	C34	C40	H40	115.5
153	C34	C40	C41	121.6(3)
154	H40	C40	C41	115.5
155	C34	C35	H35	119.7
156	C34	C35	C36	120.7(3)

157	H35	C35	C36	119.6
158	Rh1	C41	C40	73.1(2)
159	Rh1	C41	H41A	108.4
160	Rh1	C41	H41B	88.5
161	C40	C41	H41A	120.1
162	C40	C41	H41B	120
163	H41A	C41	H41B	120
164	C35	C36	H36	119.9
165	C35	C36	C37	120.3(4)
166	H36	C36	C37	119.9
167	C34	C39	H39	119.9
168	C34	C39	C38	120.3(3)
169	H39	C39	C38	119.9
170	C39	C38	H38	119.6
171	C39	C38	C37	120.9(3)
172	H38	C38	C37	119.5
173	C36	C37	C38	119.2(3)
174	C36	C37	H37	120.4
175	C38	C37	H37	120.4
176	N3	C5	C4	104.2(2)
177	N3	C5	H5A	110.9
178	N3	C5	H5B	110.9
179	C4	C5	H5A	110.9
180	C4	C5	H5B	111
181	H5A	C5	H5B	108.9
182	H57	C57	C56	119
183	H57	C57	C52	119.1
184	C56	C57	C52	121.9(2)
185	C53	C54	C55	120.8(2)
186	C53	C54	C58	119.1(2)
187	C55	C54	C58	120.0(2)
188	C54	C53	H53	118.9
189	C54	C53	C52	122.2(2)
190	H53	C53	C52	118.9
191	C57	C56	C55	121.2(2)
192	C57	C56	C59	120.0(2)
193	C55	C56	C59	118.8(2)
194	C54	C55	C56	118.2(2)
195	C54	C55	H55	120.9
196	C56	C55	H55	120.9
197	C57	C52	C53	115.7(2)
198	C57	C52	B1	123.1(2)
199	C53	C52	B1	121.0(2)
200	F20	C58	C54	113.3(2)
201	F20	C58	F21	107.1(2)
202	F20	C58	F19	106.1(2)
203	C54	C58	F21	113.7(2)
204	C54	C58	F19	110.4(2)
205	F21	C58	F19	105.6(2)

206	C52	B1	C44	105.8(2)
207	C52	B1	C60	112.4(2)
208	C52	B1	C68	113.9(2)
209	C44	B1	C60	111.2(2)
210	C44	B1	C68	111.0(2)
211	C60	B1	C68	102.7(2)
212	F24	C59	F22	106.3(2)
213	F24	C59	F23	106.6(2)
214	F24	C59	C56	112.4(2)
215	F22	C59	F23	106.9(2)
216	F22	C59	C56	112.0(2)
217	F23	C59	C56	112.3(2)
218	B1	C44	C49	122.5(2)
219	B1	C44	C45	121.6(2)
220	C49	C44	C45	115.8(2)
221	B1	C60	C61	121.2(2)
222	B1	C60	C65	122.7(2)
223	C61	C60	C65	115.8(2)
224	B1	C68	C73	119.7(2)
225	B1	C68	C69	123.9(2)
226	C73	C68	C69	116.1(2)
227	C68	C73	H73	118.9
228	C68	C73	C72	122.1(2)
229	H73	C73	C72	119
230	C61	C62	C63	120.5(2)
231	C61	C62	C66	121.5(2)
232	C63	C62	C66	117.9(2)
233	H71	C71	C72	120.9
234	H71	C71	C70	121
235	C72	C71	C70	118.1(2)
236	C68	C69	H69	119.2
237	C68	C69	C70	121.6(2)
238	H69	C69	C70	119.2
239	C70	C74	F1	113.2(5)
240	C70	C74	F2	111.7(5)
241	C70	C74	F3	111.5(5)
242	F1	C74	F2	103.4(7)
243	F1	C74	F3	111.4(7)
244	F2	C74	F3	105.2(7)
245	C60	C61	C62	122.3(2)
246	C60	C61	H61	118.9
247	C62	C61	H61	118.8
248	C73	C72	C71	120.9(2)
249	C73	C72	C75	118.3(2)
250	C71	C72	C75	120.7(2)
251	C71	C70	C69	121.1(2)
252	C71	C70	C74	119.1(2)
253	C69	C70	C74	119.8(2)
254	C60	C65	H65	118.9

255	C60	C65	C64	122.2(2)
256	H65	C65	C64	118.9
257	C62	C63	H63	120.9
258	C62	C63	C64	118.2(3)
259	H63	C63	C64	120.9
260	C65	C64	C63	120.9(3)
261	C65	C64	C67	119.1(3)
262	C63	C64	C67	120.0(3)
263	C72	C75	F5	111.8(2)
264	C72	C75	F4	113.0(2)
265	C72	C75	F6	112.9(2)
266	F5	C75	F4	106.1(2)
267	F5	C75	F6	105.5(2)
268	F4	C75	F6	107.0(2)
269	C62	C66	F15	113.0(2)
270	C62	C66	F13	112.6(2)
271	C62	C66	F14	114.0(3)
272	F15	C66	F13	105.1(2)
273	F15	C66	F14	108.0(3)
274	F13	C66	F14	103.4(3)
275	C64	C67	F18	113.6(6)
276	C64	C67	F16	109.2(5)
277	C64	C67	F17	111.1(5)
278	F18	C67	F16	108.7(7)
279	F18	C67	F17	109.4(7)
280	F16	C67	F17	104.4(6)
281	C44	C49	H49	118.8
282	C44	C49	C48	122.4(2)
283	H49	C49	C48	118.8
284	C44	C45	H45	119.1
285	C44	C45	C46	121.9(2)
286	H45	C45	C46	119
287	C49	C48	C47	121.0(2)
288	C49	C48	C50	118.5(2)
289	C47	C48	C50	120.4(2)
290	C45	C46	C47	121.2(2)
291	C45	C46	C51	118.9(2)
292	C47	C46	C51	119.9(2)
293	C48	C47	C46	117.6(2)
294	C48	C47	H47	121.2
295	C46	C47	H47	121.2
296	C46	C51	F10	112.9(2)
297	C46	C51	F11	111.8(2)
298	C46	C51	F12	112.7(2)
299	F10	C51	F11	105.4(2)
300	F10	C51	F12	106.9(2)
301	F11	C51	F12	106.6(2)
302	C48	C50	F7	110.2(8)
303	C48	C50	F8	112.4(7)

304	C48	C50	F9	113(1)
305	F7	C50	F8	99(1)
306	F7	C50	F9	113(1)
307	F8	C50	F9	109(1)

Table S5. Torsion angles (°) for **^{Ph}CDC-Rh-styrene**

Number	Atom1	Atom2	Atom3	Atom4	Torsion
1	P1	Rh1	P2	N1	-10.2(1)
2	P1	Rh1	P2	C10	102.0(1)
3	P1	Rh1	P2	C16	-123.1(1)
4	C1	Rh1	P2	N1	-2.17(9)
5	C1	Rh1	P2	C10	110.0(1)
6	C1	Rh1	P2	C16	-115.1(1)
7	C40	Rh1	P2	N1	165.2(1)
8	C40	Rh1	P2	C10	-82.7(1)
9	C40	Rh1	P2	C16	52.3(1)
10	C41	Rh1	P2	N1	-174.3(1)
11	C41	Rh1	P2	C10	-62.2(1)
12	C41	Rh1	P2	C16	72.8(1)
13	P2	Rh1	P1	N2	10.9(1)
14	P2	Rh1	P1	C22	-105.5(1)
15	P2	Rh1	P1	C28	121.6(1)
16	C1	Rh1	P1	N2	2.91(9)
17	C1	Rh1	P1	C22	-113.5(1)
18	C1	Rh1	P1	C28	113.6(1)
19	C40	Rh1	P1	N2	-164.0(1)
20	C40	Rh1	P1	C22	79.5(1)
21	C40	Rh1	P1	C28	-53.3(1)
22	C41	Rh1	P1	N2	176.2(1)
23	C41	Rh1	P1	C22	59.8(1)
24	C41	Rh1	P1	C28	-73.0(1)
25	P2	Rh1	C1	C2	0.1(2)
26	P2	Rh1	C1	C3	177.3(2)
27	P1	Rh1	C1	C2	177.7(2)
28	P1	Rh1	C1	C3	-5.0(2)
29	C40	Rh1	C1	C2	-38.8(4)
30	C40	Rh1	C1	C3	138.5(3)
31	C41	Rh1	C1	C2	153.4(3)
32	C41	Rh1	C1	C3	-29.3(4)
33	P2	Rh1	C40	C34	-95.4(2)
34	P2	Rh1	C40	H40	37.3
35	P2	Rh1	C40	C41	147.0(2)
36	P1	Rh1	C40	C34	83.1(2)
37	P1	Rh1	C40	H40	-144.2
38	P1	Rh1	C40	C41	-34.5(2)
39	C1	Rh1	C40	C34	-56.7(4)

40	C1	Rh1	C40	H40	76
41	C1	Rh1	C40	C41	-174.3(2)
42	C41	Rh1	C40	C34	117.6(3)
43	C41	Rh1	C40	H40	-109.7
44	P2	Rh1	C41	C40	-35.9(2)
45	P2	Rh1	C41	H41A	-152.7
46	P2	Rh1	C41	H41B	86.1
47	P1	Rh1	C41	C40	148.7(2)
48	P1	Rh1	C41	H41A	31.9
49	P1	Rh1	C41	H41B	-89.3
50	C1	Rh1	C41	C40	172.9(3)
51	C1	Rh1	C41	H41A	56.1
52	C1	Rh1	C41	H41B	-65.1
53	C40	Rh1	C41	H41A	-116.8
54	C40	Rh1	C41	H41B	122
55	Rh1	P2	N1	C2	4.5(2)
56	Rh1	P2	N1	C4	176.7(2)
57	C10	P2	N1	C2	-118.7(2)
58	C10	P2	N1	C4	53.6(2)
59	C16	P2	N1	C2	133.1(2)
60	C16	P2	N1	C4	-54.6(2)
61	Rh1	P2	C10	C11	-175.0(2)
62	Rh1	P2	C10	C15	-1.2(2)
63	N1	P2	C10	C11	-62.3(2)
64	N1	P2	C10	C15	111.4(2)
65	C16	P2	C10	C11	42.6(2)
66	C16	P2	C10	C15	-143.7(2)
67	Rh1	P2	C16	C17	-113.6(2)
68	Rh1	P2	C16	C21	62.8(2)
69	N1	P2	C16	C17	132.3(2)
70	N1	P2	C16	C21	-51.3(2)
71	C10	P2	C16	C17	26.2(2)
72	C10	P2	C16	C21	-157.4(2)
73	Rh1	P1	N2	C3	-1.1(2)
74	Rh1	P1	N2	C7	177.2(2)
75	C22	P1	N2	C3	129.0(2)
76	C22	P1	N2	C7	-52.8(2)
77	C28	P1	N2	C3	-125.1(2)
78	C28	P1	N2	C7	53.1(2)
79	Rh1	P1	C22	C23	1.8(2)
80	Rh1	P1	C22	C27	177.6(2)
81	N2	P1	C22	C23	-114.3(2)
82	N2	P1	C22	C27	61.4(2)
83	C28	P1	C22	C23	141.0(2)
84	C28	P1	C22	C27	-43.3(2)
85	Rh1	P1	C28	C29	102.5(2)
86	Rh1	P1	C28	C33	-72.8(2)
87	N2	P1	C28	C29	-145.6(2)
88	N2	P1	C28	C33	39.1(2)

89	C22	P1	C28	C29	-38.9(2)
90	C22	P1	C28	C33	145.8(2)
91	Rh1	C1	C2	N3	-176.3(2)
92	Rh1	C1	C2	N1	2.8(3)
93	C3	C1	C2	N3	6.5(4)
94	C3	C1	C2	N1	-174.3(2)
95	Rh1	C1	C3	N2	6.0(3)
96	Rh1	C1	C3	N4	-173.1(2)
97	C2	C1	C3	N2	-176.9(2)
98	C2	C1	C3	N4	4.1(4)
99	C8	N3	C2	C1	-0.3(4)
100	C8	N3	C2	N1	-179.6(2)
101	C5	N3	C2	C1	-174.8(3)
102	C5	N3	C2	N1	5.9(3)
103	C2	N3	C8	C9	-40.6(3)
104	C2	N3	C8	H8A	-161.9
105	C2	N3	C8	H8B	80.7
106	C5	N3	C8	C9	133.5(3)
107	C5	N3	C8	H8A	12.2
108	C5	N3	C8	H8B	-105.2
109	C2	N3	C5	C4	-9.7(3)
110	C2	N3	C5	H5A	-129.1
111	C2	N3	C5	H5B	109.8
112	C8	N3	C5	C4	175.5(2)
113	C8	N3	C5	H5A	56
114	C8	N3	C5	H5B	-65.1
115	P1	N2	C3	C1	-2.9(3)
116	P1	N2	C3	N4	176.4(2)
117	C7	N2	C3	C1	178.6(2)
118	C7	N2	C3	N4	-2.1(3)
119	P1	N2	C7	C6	-162.7(2)
120	P1	N2	C7	H7A	78.5
121	P1	N2	C7	H7B	-44
122	C3	N2	C7	C6	15.6(3)
123	C3	N2	C7	H7A	-103.2
124	C3	N2	C7	H7B	134.3
125	C1	C2	N1	P2	-5.0(3)
126	C1	C2	N1	C4	-178.7(2)
127	N3	C2	N1	P2	174.4(2)
128	N3	C2	N1	C4	0.7(3)
129	P2	N1	C4	H4A	62
130	P2	N1	C4	H4B	-59.9
131	P2	N1	C4	C5	-178.9(2)
132	C2	N1	C4	H4A	-125.4
133	C2	N1	C4	H4B	112.7
134	C2	N1	C4	C5	-6.3(3)
135	C1	C3	N4	C6	165.8(3)
136	C1	C3	N4	C9	20.3(4)
137	N2	C3	N4	C6	-13.3(3)

138	N2	C3	N4	C9	-158.8(2)
139	C3	N4	C6	H6A	-96.6
140	C3	N4	C6	H6B	141.6
141	C3	N4	C6	C7	22.5(3)
142	C9	N4	C6	H6A	50.2
143	C9	N4	C6	H6B	-71.6
144	C9	N4	C6	C7	169.3(2)
145	C3	N4	C9	H9A	174.4
146	C3	N4	C9	H9B	56.6
147	C3	N4	C9	C8	-64.5(3)
148	C6	N4	C9	H9A	31.6
149	C6	N4	C9	H9B	-86.2
150	C6	N4	C9	C8	152.7(2)
151	P1	C22	C23	H23	-3.9
152	P1	C22	C23	C24	176.1(2)
153	C27	C22	C23	H23	-179.8
154	C27	C22	C23	C24	0.2(3)
155	P1	C22	C27	C26	-175.2(2)
156	P1	C22	C27	H27	4.8
157	C23	C22	C27	C26	0.6(4)
158	C23	C22	C27	H27	-179.5
159	P2	C10	C11	H11	-7.5
160	P2	C10	C11	C12	172.5(2)
161	C15	C10	C11	H11	178.8
162	C15	C10	C11	C12	-1.2(3)
163	P2	C10	C15	H15	6.7
164	P2	C10	C15	C14	-173.3(2)
165	C11	C10	C15	H15	-179.3
166	C11	C10	C15	C14	0.7(3)
167	N4	C6	C7	N2	-21.7(3)
168	N4	C6	C7	H7A	97.1
169	N4	C6	C7	H7B	-140.4
170	H6A	C6	C7	N2	97.4
171	H6A	C6	C7	H7A	-143.8
172	H6A	C6	C7	H7B	-21.3
173	H6B	C6	C7	N2	-140.7
174	H6B	C6	C7	H7A	-21.9
175	H6B	C6	C7	H7B	100.5
176	C10	C11	C12	C13	0.2(4)
177	C10	C11	C12	H12	-179.8
178	H11	C11	C12	C13	-179.8
179	H11	C11	C12	H12	0.2
180	C22	C23	C24	H24	178.9
181	C22	C23	C24	C25	-1.1(4)
182	H23	C23	C24	H24	-1.1
183	H23	C23	C24	C25	178.9
184	C10	C15	C14	H14	-179.3
185	C10	C15	C14	C13	0.7(4)
186	H15	C15	C14	H14	0.7

187	H15	C15	C14	C13	-179.3
188	C15	C14	C13	H13	178.3
189	C15	C14	C13	C12	-1.7(4)
190	H14	C14	C13	H13	-1.7
191	H14	C14	C13	C12	178.3
192	C14	C13	C12	C11	1.2(4)
193	C14	C13	C12	H12	-178.7
194	H13	C13	C12	C11	-178.8
195	H13	C13	C12	H12	1.3
196	H26	C26	C27	C22	179.5
197	H26	C26	C27	H27	-0.4
198	C25	C26	C27	C22	-0.5(4)
199	C25	C26	C27	H27	179.5
200	H26	C26	C25	C24	179.6
201	H26	C26	C25	H25	-0.4
202	C27	C26	C25	C24	-0.4(4)
203	C27	C26	C25	H25	179.7
204	H29	C29	C28	P1	4.7
205	H29	C29	C28	C33	179.9
206	C30	C29	C28	P1	-175.3(2)
207	C30	C29	C28	C33	-0.0(4)
208	H29	C29	C30	H30	0
209	H29	C29	C30	C31	180
210	C28	C29	C30	H30	179.9
211	C28	C29	C30	C31	-0.1(4)
212	P1	C28	C33	H33	-4.2
213	P1	C28	C33	C32	175.7(2)
214	C29	C28	C33	H33	-179.7
215	C29	C28	C33	C32	0.3(4)
216	C28	C33	C32	C31	-0.5(4)
217	C28	C33	C32	H32	179.5
218	H33	C33	C32	C31	179.5
219	H33	C33	C32	H32	-0.5
220	C29	C30	C31	H31	179.9
221	C29	C30	C31	C32	-0.1(4)
222	H30	C30	C31	H31	-0.1
223	H30	C30	C31	C32	179.9
224	C23	C24	C25	C26	1.2(4)
225	C23	C24	C25	H25	-178.9
226	H24	C24	C25	C26	-178.9
227	H24	C24	C25	H25	1.1
228	C30	C31	C32	C33	0.4(4)
229	C30	C31	C32	H32	-179.6
230	H31	C31	C32	C33	-179.6
231	H31	C31	C32	H32	0.4
232	N1	C4	C5	N3	9.1(3)
233	N1	C4	C5	H5A	128.5
234	N1	C4	C5	H5B	-110.3
235	H4A	C4	C5	N3	128.2

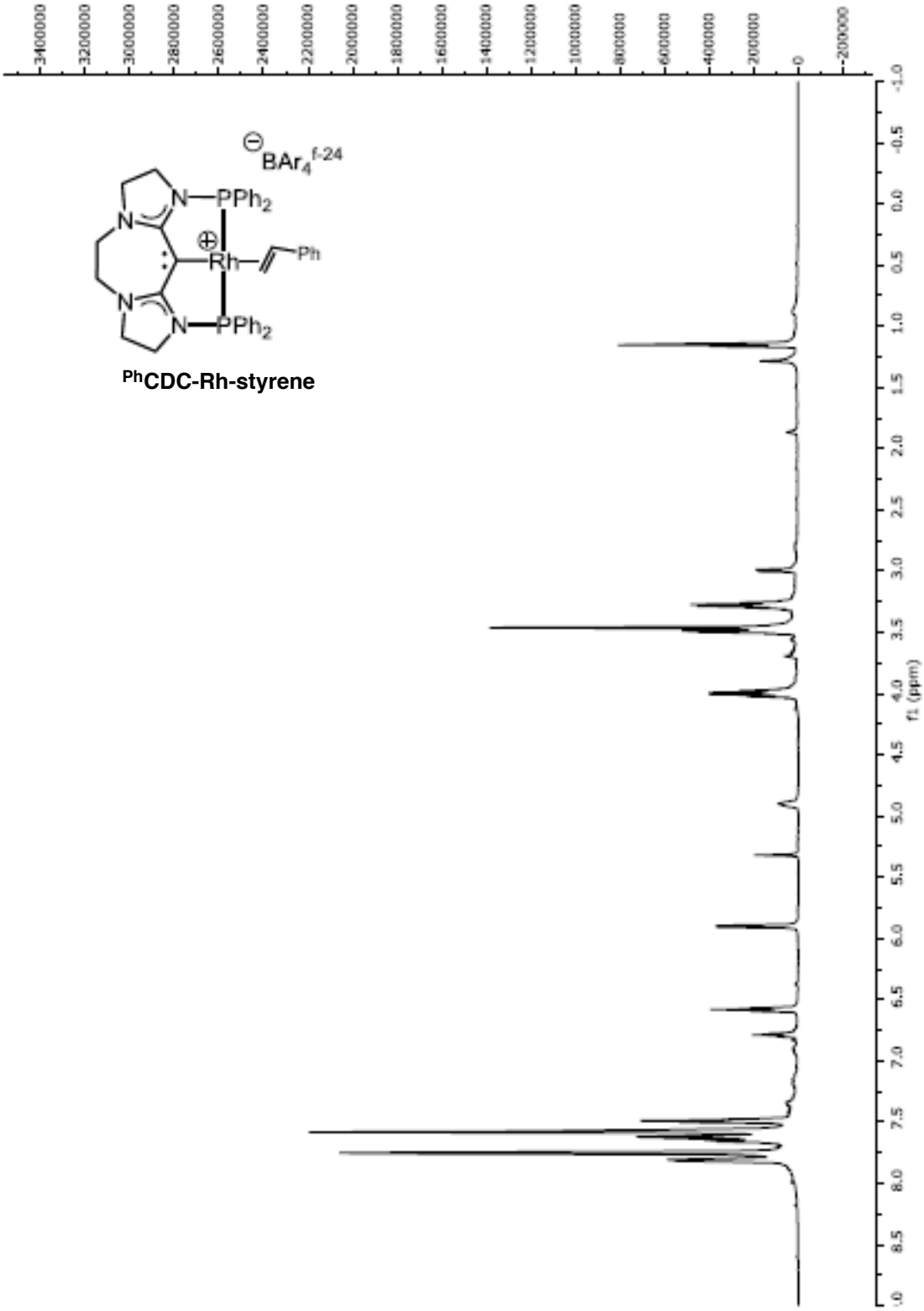
236	H4A	C4	C5	H5A	-112.4
237	H4A	C4	C5	H5B	8.7
238	H4B	C4	C5	N3	-109.9
239	H4B	C4	C5	H5A	9.6
240	H4B	C4	C5	H5B	130.7
241	N4	C9	C8	N3	74.7(3)
242	N4	C9	C8	H8A	-164
243	N4	C9	C8	H8B	-46.7
244	H9A	C9	C8	N3	-164.3
245	H9A	C9	C8	H8A	-42.9
246	H9A	C9	C8	H8B	74.4
247	H9B	C9	C8	N3	-46.5
248	H9B	C9	C8	H8A	74.8
249	H9B	C9	C8	H8B	-167.8
250	P2	C16	C17	H17	-3.1
251	P2	C16	C17	C18	176.9(2)
252	C21	C16	C17	H17	-179.4
253	C21	C16	C17	C18	0.6(4)
254	P2	C16	C21	H21	2.3
255	P2	C16	C21	C20	-177.7(2)
256	C17	C16	C21	H21	178.9
257	C17	C16	C21	C20	-1.1(4)
258	C16	C17	C18	C19	0.3(4)
259	C16	C17	C18	H18	-179.6
260	H17	C17	C18	C19	-179.7
261	H17	C17	C18	H18	0.4
262	C16	C21	C20	C19	0.7(4)
263	C16	C21	C20	H20	-179.4
264	H21	C21	C20	C19	-179.3
265	H21	C21	C20	H20	0.6
266	H19	C19	C18	C17	179.1
267	H19	C19	C18	H18	-1
268	C20	C19	C18	C17	-0.7(5)
269	C20	C19	C18	H18	179.2
270	H19	C19	C20	C21	-179.6
271	H19	C19	C20	H20	0.5
272	C18	C19	C20	C21	0.2(5)
273	C18	C19	C20	H20	-179.7
274	C35	C34	C40	Rh1	132.8(2)
275	C35	C34	C40	H40	0.1
276	C35	C34	C40	C41	-148.3(3)
277	C39	C34	C40	Rh1	-47.5(4)
278	C39	C34	C40	H40	179.8
279	C39	C34	C40	C41	31.4(5)
280	C40	C34	C35	H35	0.6
281	C40	C34	C35	C36	-179.3(3)
282	C39	C34	C35	H35	-179.1
283	C39	C34	C35	C36	0.9(5)
284	C40	C34	C39	H39	-0.5

285	C40	C34	C39	C38	179.5(3)
286	C35	C34	C39	H39	179.2
287	C35	C34	C39	C38	-0.9(4)
288	Rh1	C40	C41	H41A	101.9
289	Rh1	C40	C41	H41B	-78.1
290	C34	C40	C41	Rh1	-101.9(3)
291	C34	C40	C41	H41A	0
292	C34	C40	C41	H41B	-179.9
293	H40	C40	C41	Rh1	109.7
294	H40	C40	C41	H41A	-148.4
295	H40	C40	C41	H41B	31.6
296	C34	C35	C36	H36	179.5
297	C34	C35	C36	C37	-0.4(6)
298	H35	C35	C36	H36	-0.5
299	H35	C35	C36	C37	179.6
300	C35	C36	C37	C38	-0.2(5)
301	C35	C36	C37	H37	179.9
302	H36	C36	C37	C38	179.9
303	H36	C36	C37	H37	0
304	C34	C39	C38	H38	-179.6
305	C34	C39	C38	C37	0.3(5)
306	H39	C39	C38	H38	0.4
307	H39	C39	C38	C37	-179.8
308	C39	C38	C37	C36	0.3(5)
309	C39	C38	C37	H37	-179.8
310	H38	C38	C37	C36	-179.9
311	H38	C38	C37	H37	0
312	H57	C57	C56	C55	-177.5
313	H57	C57	C56	C59	0.7
314	C52	C57	C56	C55	2.4(4)
315	C52	C57	C56	C59	-179.3(2)
316	H57	C57	C52	C53	177
317	H57	C57	C52	B1	2.7
318	C56	C57	C52	C53	-3.0(3)
319	C56	C57	C52	B1	-177.2(2)
320	C55	C54	C53	H53	-179.5
321	C55	C54	C53	C52	0.5(3)
322	C58	C54	C53	H53	4.8
323	C58	C54	C53	C52	-175.2(2)
324	C53	C54	C55	C56	-1.2(3)
325	C53	C54	C55	H55	178.8
326	C58	C54	C55	C56	174.5(2)
327	C58	C54	C55	H55	-5.6
328	C53	C54	C58	F20	-165.1(2)
329	C53	C54	C58	F21	-42.5(3)
330	C53	C54	C58	F19	76.0(3)
331	C55	C54	C58	F20	19.1(3)
332	C55	C54	C58	F21	141.8(2)
333	C55	C54	C58	F19	-99.7(3)

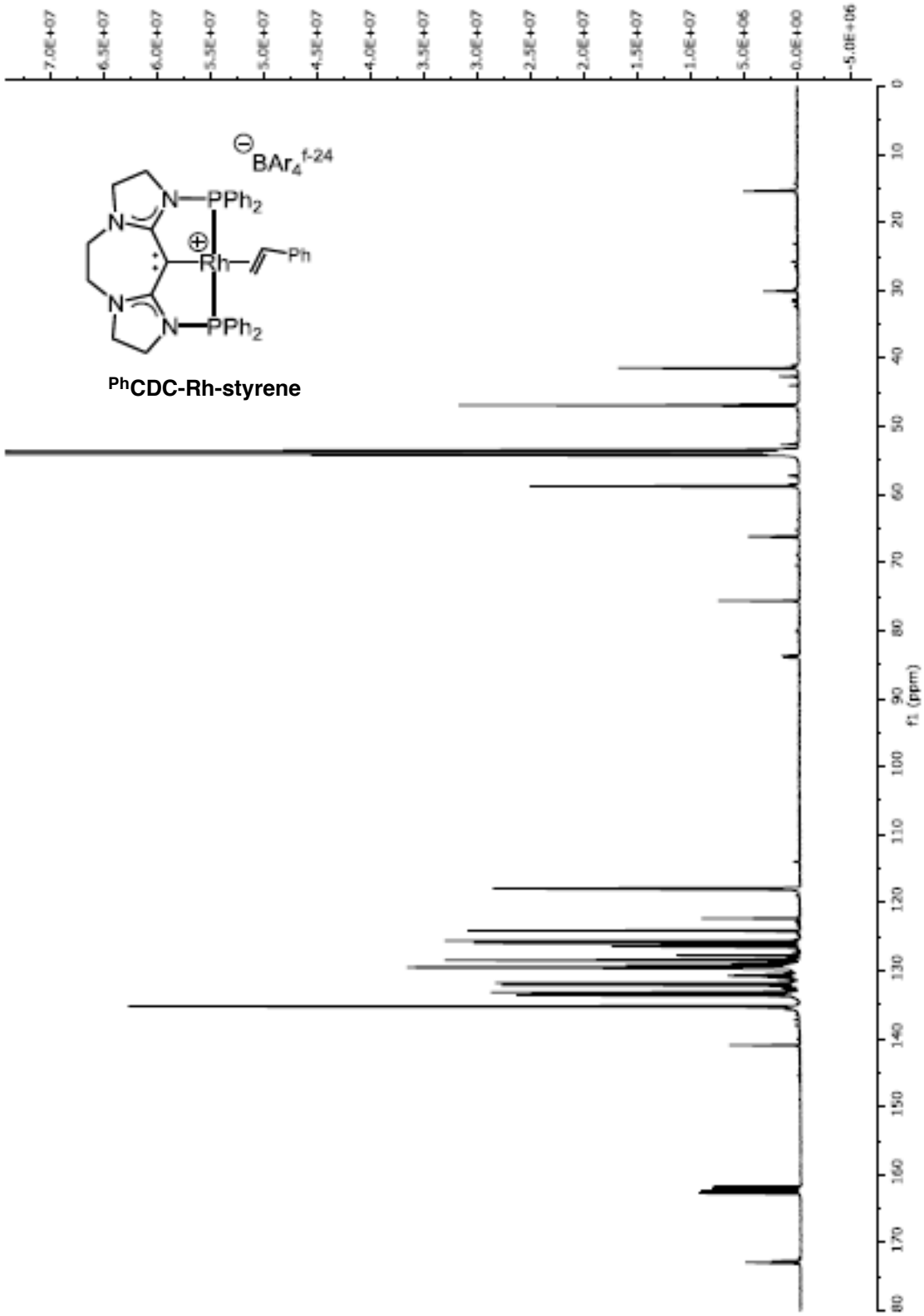
334	C54	C53	C52	C57	1.5(3)
335	C54	C53	C52	B1	175.9(2)
336	H53	C53	C52	C57	-178.4
337	H53	C53	C52	B1	-4.1
338	C57	C56	C55	C54	-0.2(3)
339	C57	C56	C55	H55	179.8
340	C59	C56	C55	C54	-178.5(2)
341	C59	C56	C55	H55	1.5
342	C57	C56	C59	F24	36.4(3)
343	C57	C56	C59	F22	-83.1(3)
344	C57	C56	C59	F23	156.6(2)
345	C55	C56	C59	F24	-145.2(2)
346	C55	C56	C59	F22	95.2(3)
347	C55	C56	C59	F23	-25.0(3)
348	C57	C52	B1	C44	86.0(2)
349	C57	C52	B1	C60	-152.5(2)
350	C57	C52	B1	C68	-36.2(3)
351	C53	C52	B1	C44	-87.9(2)
352	C53	C52	B1	C60	33.6(3)
353	C53	C52	B1	C68	149.9(2)
354	C52	B1	C44	C49	-93.5(2)
355	C52	B1	C44	C45	82.6(2)
356	C60	B1	C44	C49	144.2(2)
357	C60	B1	C44	C45	-39.7(3)
358	C68	B1	C44	C49	30.5(3)
359	C68	B1	C44	C45	-153.4(2)
360	C52	B1	C60	C61	39.6(3)
361	C52	B1	C60	C65	-147.3(2)
362	C44	B1	C60	C61	158.0(2)
363	C44	B1	C60	C65	-28.9(3)
364	C68	B1	C60	C61	-83.2(2)
365	C68	B1	C60	C65	89.9(2)
366	C52	B1	C68	C73	163.9(2)
367	C52	B1	C68	C69	-23.3(3)
368	C44	B1	C68	C73	44.6(3)
369	C44	B1	C68	C69	-142.5(2)
370	C60	B1	C68	C73	-74.3(2)
371	C60	B1	C68	C69	98.5(2)
372	B1	C44	C49	H49	-2.9
373	B1	C44	C49	C48	177.2(2)
374	C45	C44	C49	H49	-179.2
375	C45	C44	C49	C48	0.9(3)
376	B1	C44	C45	H45	2.2
377	B1	C44	C45	C46	-177.8(2)
378	C49	C44	C45	H45	178.5
379	C49	C44	C45	C46	-1.5(3)
380	B1	C60	C61	C62	174.6(2)
381	B1	C60	C61	H61	-5.3
382	C65	C60	C61	C62	1.0(3)

383	C65	C60	C61	H61	-178.9
384	B1	C60	C65	H65	5.7
385	B1	C60	C65	C64	-174.2(2)
386	C61	C60	C65	H65	179.2
387	C61	C60	C65	C64	-0.8(3)
388	B1	C68	C73	H73	-7
389	B1	C68	C73	C72	173.0(2)
390	C69	C68	C73	H73	179.7
391	C69	C68	C73	C72	-0.4(3)
392	B1	C68	C69	H69	6
393	B1	C68	C69	C70	-174.0(2)
394	C73	C68	C69	H69	179.1
395	C73	C68	C69	C70	-0.9(3)
396	C68	C73	C72	C71	1.2(4)
397	C68	C73	C72	C75	179.6(2)
398	H73	C73	C72	C71	-178.8
399	H73	C73	C72	C75	-0.4
400	C63	C62	C61	C60	-1.0(4)
401	C63	C62	C61	H61	179
402	C66	C62	C61	C60	176.7(2)
403	C66	C62	C61	H61	-3.3
404	C61	C62	C63	H63	-179.5
405	C61	C62	C63	C64	0.5(4)
406	C66	C62	C63	H63	2.8
407	C66	C62	C63	C64	-177.2(3)
408	C61	C62	C66	F15	128.1(3)
409	C61	C62	C66	F13	-113.0(3)
410	C61	C62	C66	F14	4.4(4)
411	C63	C62	C66	F15	-54.1(3)
412	C63	C62	C66	F13	64.8(3)
413	C63	C62	C66	F14	-177.9(3)
414	H71	C71	C72	C73	179.1
415	H71	C71	C72	C75	0.8
416	C70	C71	C72	C73	-0.8(4)
417	C70	C71	C72	C75	-179.2(2)
418	H71	C71	C70	C69	179.6
419	H71	C71	C70	C74	-3.1
420	C72	C71	C70	C69	-0.5(4)
421	C72	C71	C70	C74	176.9(2)
422	C68	C69	C70	C71	1.4(4)
423	C68	C69	C70	C74	-175.9(2)
424	H69	C69	C70	C71	-178.7
425	H69	C69	C70	C74	4
426	F1	C74	C70	C71	-78.3(6)
427	F1	C74	C70	C69	99.1(6)
428	F2	C74	C70	C71	165.6(6)
429	F2	C74	C70	C69	-17.1(6)
430	F3	C74	C70	C71	48.2(5)
431	F3	C74	C70	C69	-134.4(5)

432	C73	C72	C75	F5	-62.7(3)
433	C73	C72	C75	F4	177.7(2)
434	C73	C72	C75	F6	56.2(3)
435	C71	C72	C75	F5	115.7(3)
436	C71	C72	C75	F4	-3.9(4)
437	C71	C72	C75	F6	-125.5(3)
438	C60	C65	C64	C63	0.4(4)
439	C60	C65	C64	C67	178.7(3)
440	H65	C65	C64	C63	-179.5
441	H65	C65	C64	C67	-1.3
442	C62	C63	C64	C65	-0.3(4)
443	C62	C63	C64	C67	-178.5(3)
444	H63	C63	C64	C65	179.7
445	H63	C63	C64	C67	1.5
446	C65	C64	C67	F18	35.3(7)
447	C65	C64	C67	F16	-86.2(5)
448	C65	C64	C67	F17	159.2(5)
449	C63	C64	C67	F18	-146.4(6)
450	C63	C64	C67	F16	92.1(5)
451	C63	C64	C67	F17	-22.6(6)
452	C44	C49	C48	C47	0.2(4)
453	C44	C49	C48	C50	-179.2(2)
454	H49	C49	C48	C47	-179.7
455	H49	C49	C48	C50	0.9
456	C44	C45	C46	C47	1.0(4)
457	C44	C45	C46	C51	-176.9(2)
458	H45	C45	C46	C47	-179
459	H45	C45	C46	C51	3.1
460	C49	C48	C47	C46	-0.7(4)
461	C49	C48	C47	H47	179.3
462	C50	C48	C47	C46	178.6(2)
463	C50	C48	C47	H47	-1.4
464	C49	C48	C50	F7	61.5(9)
465	C49	C48	C50	F8	171.0(7)
466	C49	C48	C50	F9	-65(1)
467	C47	C48	C50	F7	-117.8(8)
468	C47	C48	C50	F8	-8.4(8)
469	C47	C48	C50	F9	115(1)
470	C45	C46	C47	C48	0.1(4)
471	C45	C46	C47	H47	-179.9
472	C51	C46	C47	C48	178.0(2)
473	C51	C46	C47	H47	-2
474	C45	C46	C51	F10	-163.9(2)
475	C45	C46	C51	F11	-45.2(3)
476	C45	C46	C51	F12	74.8(3)
477	C47	C46	C51	F10	18.1(4)
478	C47	C46	C51	F11	136.8(2)
479	C47	C46	C51	F12	-103.1(3)



^{Ph}CDC-Rh-styrene


BAr4f-24
N
PPh2
Rh
Ph
PhCDC-Rh-styrene
f1 (ppm)

APPENDIX 3: SUPPORTING INFORMATION FOR CHAPTER 3

■ **General:** All reactions were carried out in flame or oven (140 °C) dried glassware that had been cooled under vacuum. Unless otherwise stated, all reactions were carried out under an inert N_2 atmosphere. All reagents were purged or sparged with N_2 for 20 min prior to distillation or use. All solid reagents were dried by azeotropic distillation with benzene three times prior to use. Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer or a ASI ReactIR 1000, Model: 001-1002 for air sensitive rhodium carbonyl complexes. Mass spectra were obtained using a Thermo LTqFT mass spectrometer with electrospray ionization and external calibration. All samples were prepared in MeOH, MeCN or $CHCl_3$ for metal complexes. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker model DRX 400 or a Bruker AVANCE III 600 CryoProbe (^{1}H NMR at 400 MHz or 600 MHz, ^{13}C NMR at 100 or 151 MHz, ^{31}P NMR at 160 or 243 MHz and ^{19}F NMR at 376 or 564 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: Chloroform-d at 7.26 ppm, CD_2Cl_2 at 5.32 ppm, CD_3CN at 1.94 ppm; ^{13}C NMR: Chloroform-d at 77.16 ppm, CD_2Cl_2 at 53.84 ppm, CD_3CN at 1.32 ppm). NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet, bs = broad singlet, bm = broad multiplet, etc.), and coupling constants (Hz). X-ray diffraction studies were conducted on a Bruker-AXS SMART APEXII diffractometer. Crystals were selected and mounted using Paratone oil on a MiteGen Mylar tip.

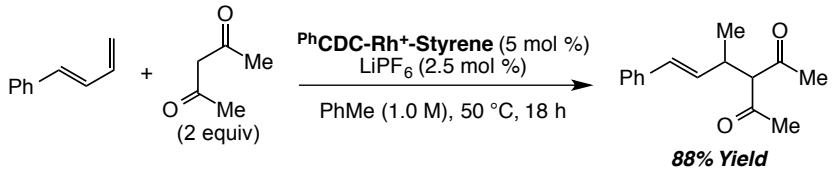
■ **Solvents:** Solvents were purged with argon and purified under a positive pressure of dry argon by a SG Waters purification system: dichloromethane (EMD Millipore), diethyl ether (EMD

Millipore, hexanes (EMD Millipore), benzene (EMD Millipore), and THF (EMD Millipore) were passed through activated alumina columns. Chloroform – d_1 and Dichloromethane – d_2 were purchased from Cambridge Isotope Labs, distilled over CaH_2 and stored in a dry box over activated 4 Å molecular sieves.

Section 3.2: Intermolecular Diene Hydroalkylation with 1,3-Diketo Nucleophiles

■ **General Procedure for Intermolecular Hydroalkylation with 2,4-pentanedione Catalyzed by CDC-Rh-styrene**

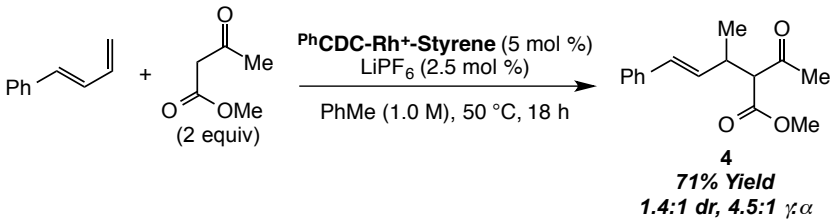
In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the **^{Ph}CDC-Rh-styrene** complex (8.1 mg, 0.005 mmol, 5 mol%), the appropriate Lewis acid activator (0.0025 mmol, 2.5 mol%), and 1,3-phenylbutadiene (13.0 mg, 0.10 mmol). The reagents were solvated with the listed solvent and the reaction was sealed with a Teflon® lined septum cap before being allowed to stir at room temperature for 1 hour. Any additional additives were added before the vial was taped with electrical tape and the reactions brought outside the dry box. A vial of 2,4-pentanedione (20.5 μL, 0.20 mmol) was sparged with N_2 for a minimum of 10 minutes before being added via syringe. The reaction was allowed to warm to the appropriate temperature and stir for 18 h before being allowed to cool to room temperature and an aliquot was taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solvent evaporated before the products were purified by SiO_2 column chromatography.



Synthesis of (*E*)-3-(4-phenylbut-3-en-2-yl)pentane-2,4-dione

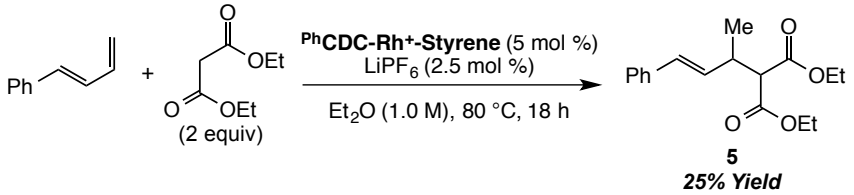
Following the general procedure for CDC-Rh-styrene catalyzed intermolecular hydroalkylation, (*E*)-buta-1,3-dien-1-ylbenzene (13.0 mg, 0.10 mmol) was added to a solution of **^{Ph}CDC-Rh-styrene** (8.1 mg, 0.0050 mmol, 5 mol%) and $LiPF_6$ (0.4 mg, 0.0025 mmol, 2.5 mol%) in toluene (100 μL, [ ] = 1.0 M). The reaction was sealed and allowed to stir for 1 hour before being removed from the dry box. Outside the dry box N_2 sparged 2,4-pentanedione (20.5 μL, 0.20 mmol) was added via syringe under N_2 and the reaction sealed and allowed to stir at 50 °C for 18 h. The reaction was cooled and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO2 column chromatography (20:1 Hexanes/Et_2O) to afford **3** as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 4H), 7.24 – 7.20 (m, 1H), 6.44 (d, *J* = 15.8 Hz, 1H), 5.99 (dd, *J* = 15.8, 8.6 Hz, 1H), 3.69 (d, *J* = 10.4 Hz, 1H), 3.25 – 3.16 (m, 1H), 2.23 (s, 3H), 2.13 (s, 3H), 1.08 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.62, 203.53, 136.77, 130.97, 130.95, 128.58, 127.59, 126.24, 75.65, 37.90, 30.04, 29.75, 18.88.



Synthesis of methyl (*E*)-2-acetyl-3-methyl-5-phenylpent-4-enoate

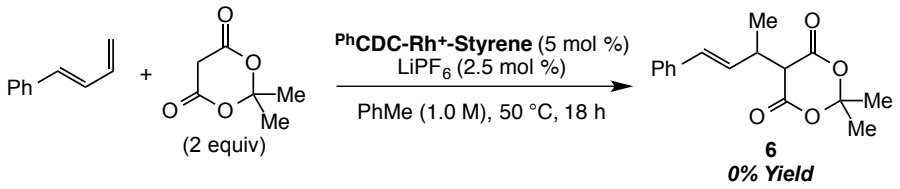
Following the general procedure for CDC-Rh-styrene catalyzed intermolecular hydroalkylation, (*E*)-buta-1,3-dien-1-ylbenzene (13.0 mg, 0.10 mmol) was added to a solution of **^{Ph}CDC-Rh-styrene** (8.1 mg, 0.0050 mmol, 5 mol%) and $LiPF_6$ (0.4 mg, 0.0025 mmol, 2.5 mol%) in toluene (100 μL, [ ] = 1.0 M). The reaction was sealed and allowed to stir for 1 hour before being removed from the dry box. Outside the dry box N_2 sparged methyl 3-oxobutanoate (21.5 μL, 0.20 mmol) was added via syringe under N_2 and the reaction sealed and allowed to stir at 50 °C for 18 h. The reaction was cooled and an aliquot taken, which showed that methyl (*E*)-2-acetyl-3-methyl-5-phenylpent-4-enoate (71% NMR yield, 1.4:1 dr, 4.5:1 γ:α isomer) was formed by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated.



Synthesis of diethyl (*E*)-2-(4-phenylbut-3-en-2-yl)malonate

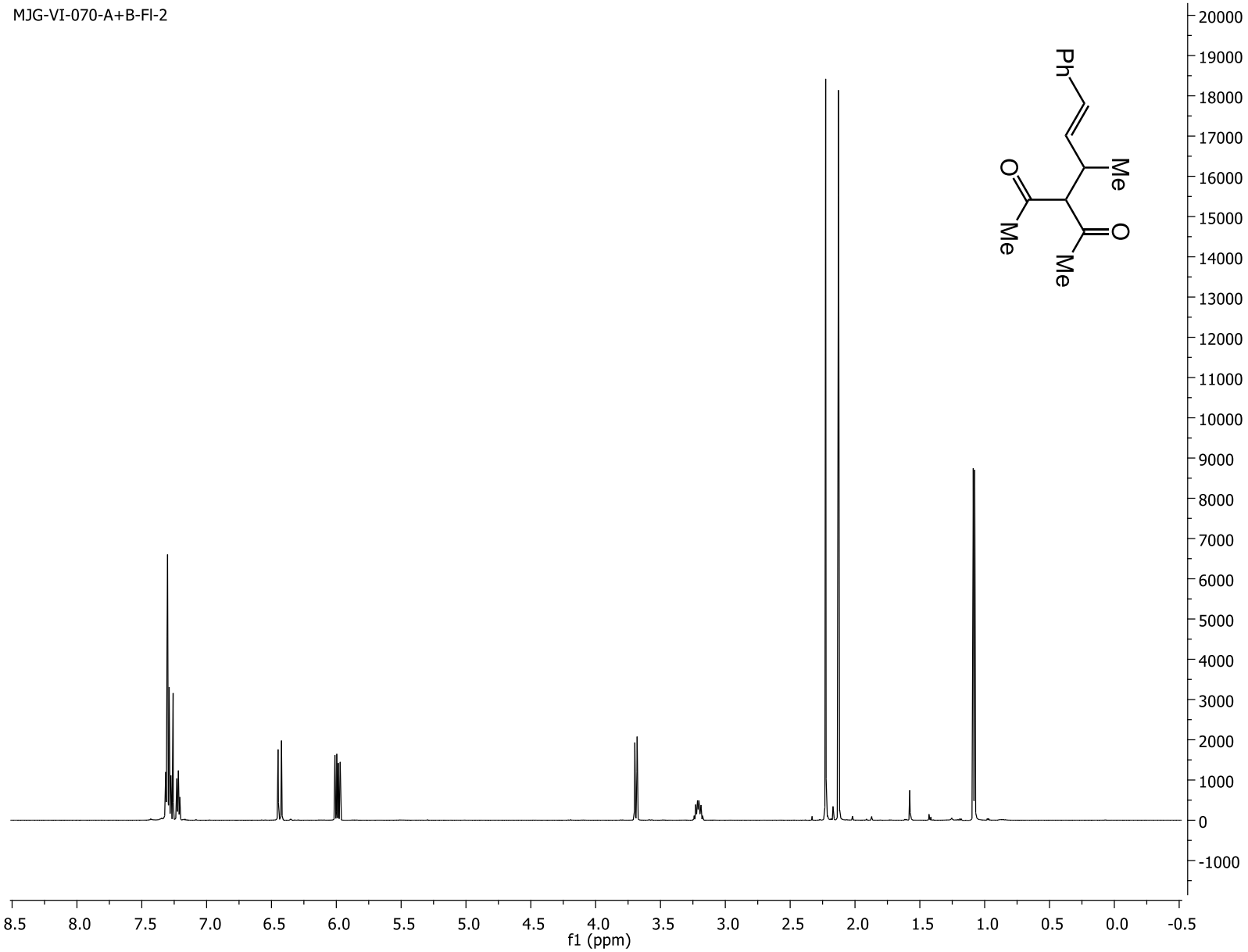
Following the general procedure for CDC-Rh-styrene catalyzed intermolecular hydroalkylation, (*E*)-buta-1,3-dien-1-ylbenzene (13.0 mg, 0.10 mmol) was added to a solution of **^{Ph}CDC-Rh-styrene** (8.1 mg, 0.0050 mmol, 5 mol%) and $LiPF_6$ (0.8 mg, 0.005 mmol, 5.0 mol%) in diethyl ether (100 μL, [ ] = 1.0 M). The reaction was sealed and allowed to stir for 1 hour before being removed from the dry box. Outside the dry box N_2 sparged diethyl malonate (31 μL, 0.20 mmol) was added via syringe under N_2 and the reaction sealed and allowed to stir at 80 °C for 18 h. The reaction was cooled and an aliquot taken, which showed that diethyl (*E*)-2-(4-phenylbut-3-en-2-

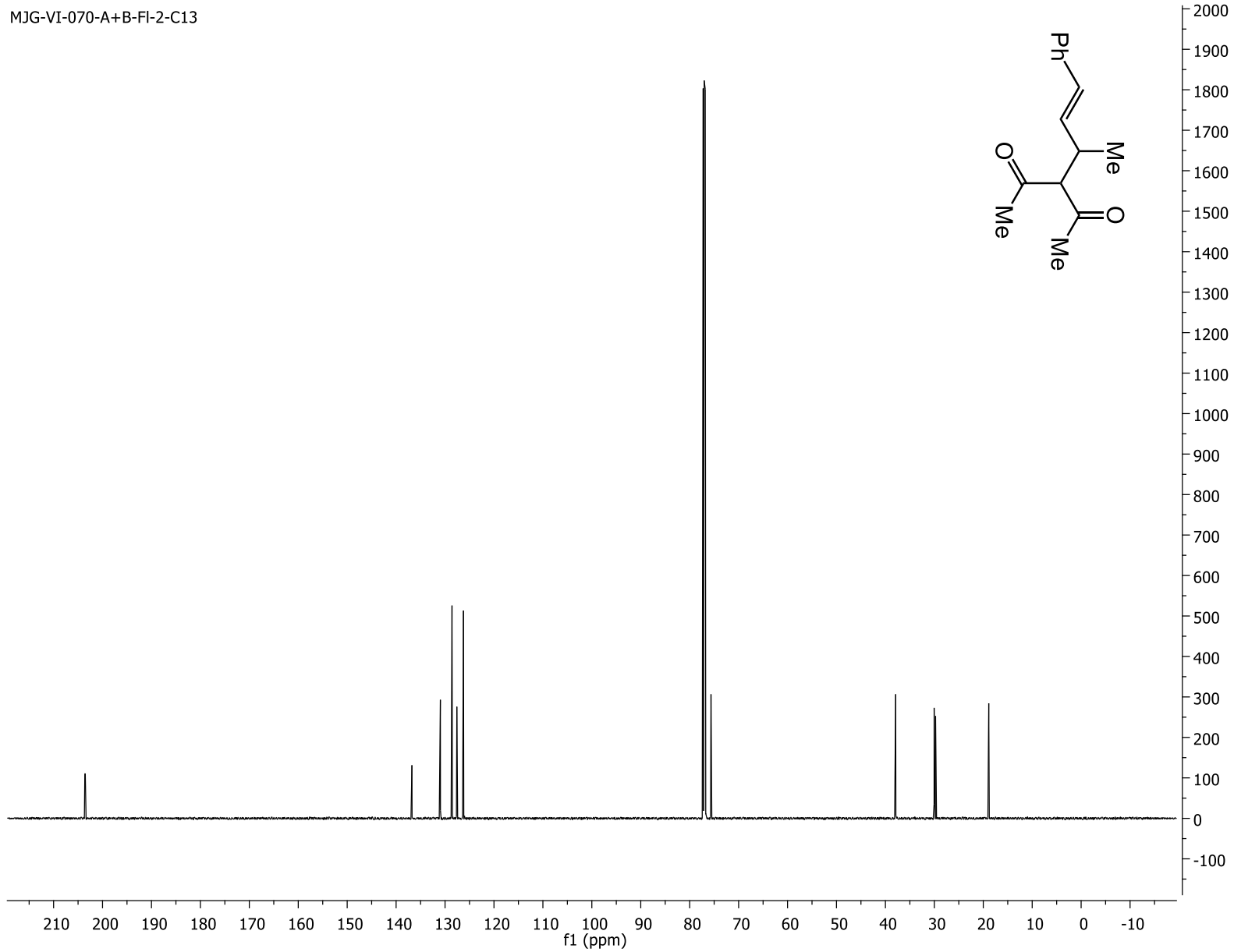
yl)malonate (25% NMR yield) was formed by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated.

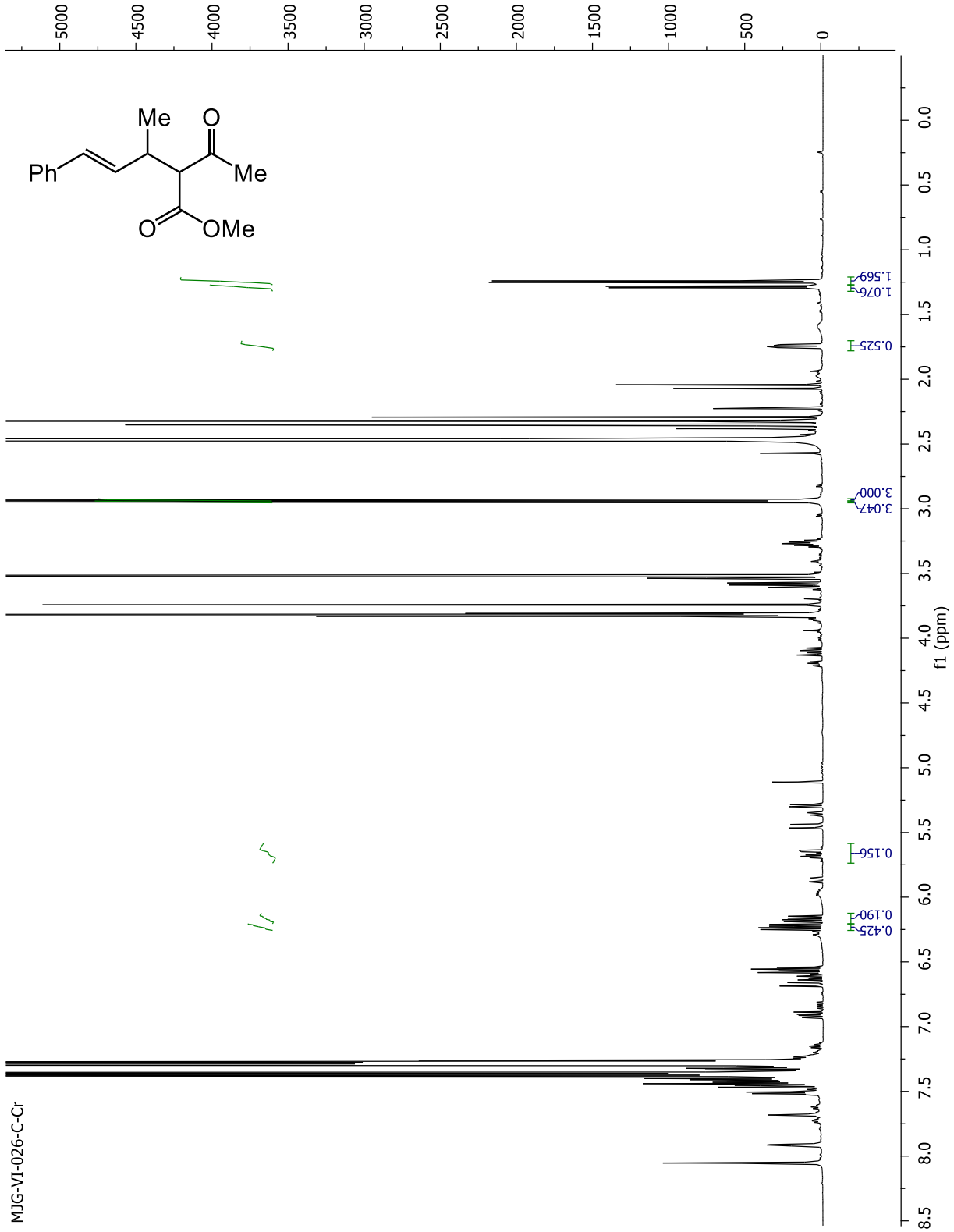


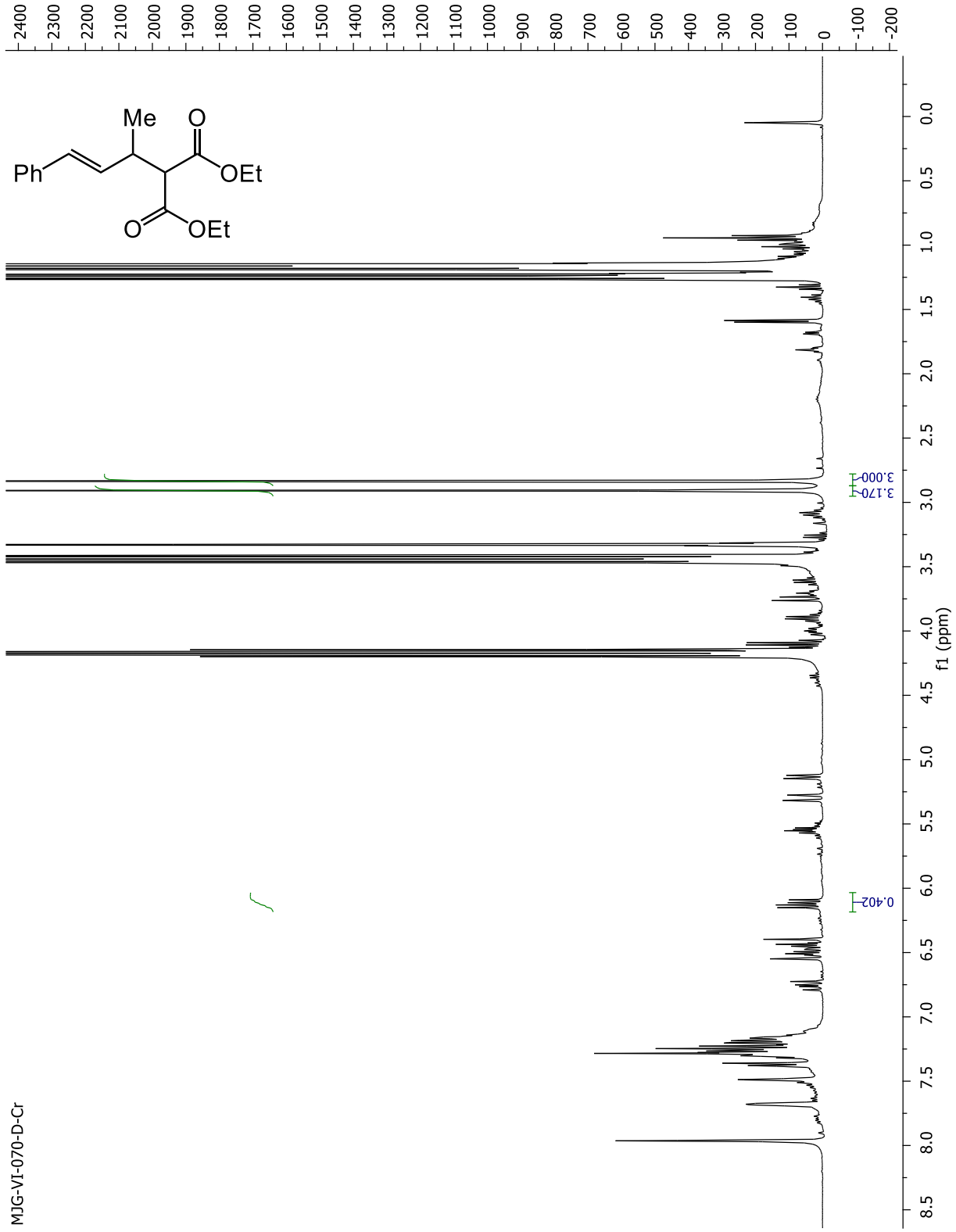
Synthesis of (*E*)-2,2-dimethyl-5-(4-phenylbut-3-en-2-yl)-1,3-dioxane-4,6-dione

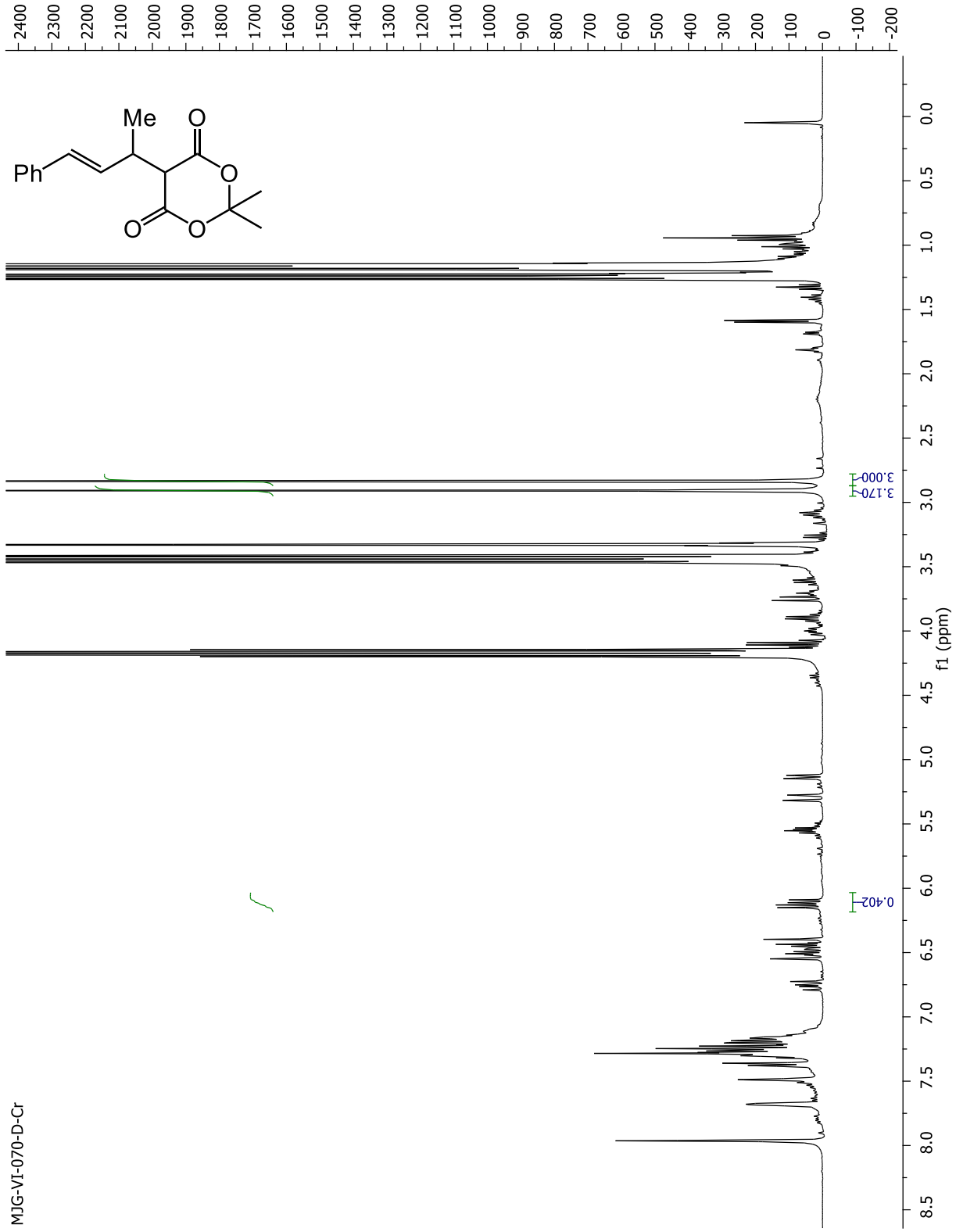
Following the general procedure for CDC-Rh-styrene catalyzed intermolecular hydroalkylation, (*E*)-buta-1,3-dien-1-ylbenzene (13.0 mg, 0.10 mmol) was added to a solution of **^{Ph}CDC-Rh-styrene** (8.1 mg, 0.0050 mmol, 5 mol%) and $LiPF_6$ (0.4 mg, 0.0025 mmol, 2.5 mol%) in toluene (100 μL, [ ] = 1.0 M). The reaction was sealed and allowed to stir for 1 hour before being removed from the dry box. Outside the dry box N_2 sparged 2,2-dimethyl-1,3-dioxane-4,6-dione (28.8 mg, 0.20 mmol) was added via syringe under N_2 and the reaction sealed and allowed to stir at 50 °C for 18 h. The reaction was cooled and an aliquot taken to determine the conversion by ^{1}H NMR (0% NMR yield) using DMF as an internal standard.


MJG-VI-070-A+B-Fl-2
Ph
Me
O
Me
O
Me
f1 (ppm)


MJG-VI-070-A+B-Fl-2-C13
Ph
Me
O
Me
O
Me
f1 (ppm)


MJG-VI-026-C-Cr
Ph
Me
O
Me
O
OMe
f1 (ppm)
1.569
1.076
0.525
3.047
3.000
0.156
0.425
0.190


Me
O
Ph
OEt
O
OEt
MJG-VI-070-D-Cr
3.000
3.170
0.402
f1 (ppm)


Me
O
Ph
O
O
O
MJG-VI-070-D-Cr
3.000
3.170
0.402
f1 (ppm)

Section 3.3: Diastereoselective Synthesis of Vicinal Tertiary and N-Substituted Quaternary Stereogenic Centers via Intermolecular Diene Hydroalkylation

- **Reagents:**

(R)-(+)-1,1'-Bi(2-napthol) was purchased from Chem Impex, dried by azeotropic distillation with benzene, stored in a dry box and used without further purification.

Chloro(1,5-cyclooctadiene)rhodium(I) dimer was purchased from Pressure Chemicals, stored in a dry box and used as received.

(S,S)-1,2-Diphenylethylenediamine was purchased from Ivy Chemicals, dried by azeotropic distillation with benzene, stored in a dry box and used without further purification.

Hexamethyldisiloxane was purchased from Sigma Aldrich, stored over 4Å molecular sieves, and used without further purification.

(S,S)-Hydrobenzoin was purchased from Sigma Aldrich, dried by azeotropic distillation with benzene, stored in a dry box and used without further purification.

Isopropanol was purchased from Fischer Scientific, distilled over CaH_2, stored in a flask over 4Å molecular sieves and sparged with N_2 before use.

Lithium tetrafluoroborate was purchased from Sigma Aldrich, stored in the dry box after overnight heating over P_2O_5 under vacuum and used without further purification.

Lithium hexafluorophosphate was purchased from Sigma Aldrich, stored in the dry box and used as received.

Lithium tetrakis(pentafluorophenyl)borate - ethyl ether complex was purchased from Boulder Scientific, stored in a dry box, and used as received.

m-Chloroperoxybenzoic acid was purchased from Alfa-Aesar as 50-55% purity by weight and used as received without further pufication.

Methanol was purchased from Fischer Scientific, distilled over CaH_2, stored in a flask over 4Å molecular sieves and sparged with N_2 before use.

Menthol was purchased from Sigma Aldrich, dried by azeotropic distillation with benzene, stored in a dry box and used without further purification.

Potassium carbonate was purchased from Fischer Scientific and used as received.

Silver chloride was purchased from Strem, stored in a dry box, and used without further purification.

Silver tetrafluoroborate was purchased from Strem, stored in a dry box, and used without further purification.

Sodium methoxide was purchased from Strem, stored in a dry box, and used without further purification.

Styrene was purchased from Alfa Aesar, distilled over CaH_2, and stored at – 20 ^{o}C in a dry box.

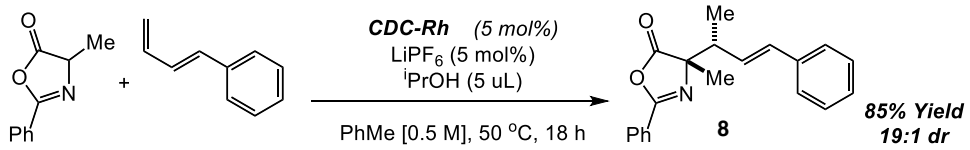
t-Butanol was purchased from Sigma Aldrich, distilled over CaH_2, stored in a flask over 4Å molecular sieves and melted before use.

The following substrates were prepared according to literature method or a modified literature method and matched reported characterization data: (E)-phenyl-1,3-butadiene,[125] (E)/(Z)-2-methyl-phenyl-1,3-butadiene,[126] (E)/(Z)-3-methyl-phenyl-1,3-butadiene,[126] (E)/(Z)-4-methyl-phenyl-1,3-butadiene,[126] (E)/(Z)-1-buta-1,3-dien-1-ylcylohexane,[126] (E)-4-methoxy-phenyl-1,3-butadiene,[126] (E)/(Z)-2-nitro-phenyl-1,3-butadiene,[126] (E)/(Z)-4-chloro-phenyl-1,3-butadiene,[127] (E)/(Z)-4-fluoro-phenyl-1,3-butadiene,[127] (E)-2-(buta-1,3-dien-1-yl)furan,[126] (E)-tert-butyl(hexa-3,5-dien-1-yloxy)dimethylsilane,[128] (E)-dodeca-1,3-diene,[129] 4-methyl-2-phenyloxazol-5(4H)-one,[130] 2-phenyl-4-propyloxazol-5(4H)-one,[131] 4-isobutyl-2-phenyloxazol-5(4H)-one,[132] 4-

phenethyl-2-phenyloxazol-5(4H)-one,[131] 4-allyl-2-phenyloxazol-5(4H)-one,[133] 2-(4-chlorophenyl)-4-methyloxazol-5(4H)-one,[130] sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate,[134] complex **^{Ph}CDC-Rh-Cl,**[1] complex **^{Ph}CDC-Rh-styrene**,[135] and (R,R)-TADDOL-P(O)OH[136]**.**

■ **General procedure for the (CDC)-Rh(I) catalyzed hydroalkylation of dienes with oxazalones in Tables 3.3.2-1, 3.3.2-2, 3.3.2-3, 3.3.3-1, 3.3.4-1:**

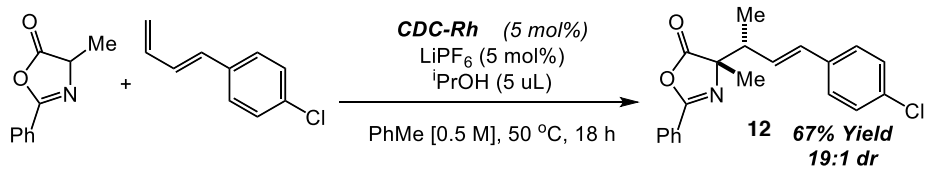
In a N_2 filled glove box, an 8 mL reaction vial with a stir bar was charged with (CDC)-Rh(I)styrene $BAr^F{}_4$, the appropriate additive and the listed diene. The appropriate solvent was added by syringe, the reaction vial capped with a Teflon® lined septum cap and the reaction allowed to stir at 22 °C for 10 minutes. The cap was removed and the nucleophile was added directly to the solution as a solid or as a liquid via syringe. The reaction was resealed with the septum cap, the lid secured with electrical tape to ensure a tight seal, and the reaction removed from the glove box. Outside the glove box, a vial of alcohol was sparged for 10 minutes with N_2 and added to the reaction via syringe under an atmosphere of N_2. The reaction was allowed to stir at the appropriate temperature for the listed time before being cooled to room temperature, unsealed, and 5 μL of hexamethyldisiloxane added as an internal standard. The solution was diluted with $CDCl_3$ and analyzed by NMR spectroscopy to determine the conversion and diastereoselectivity. The NMR sample was recombined with the reaction and the solvents removed in vacuo before being purified by SiO_2 gel chromatography. Products eluted with similar retention times in the following order: 1) the 1,4-addition products, 2) the anti-1,2-addition products, and 3) the syn-1,2-addition products.



Synthesis of 4-methyl-2-phenyl-4-(E-4-phenylbut-3-en-2-yl)oxazol-5(4H)-one (8).

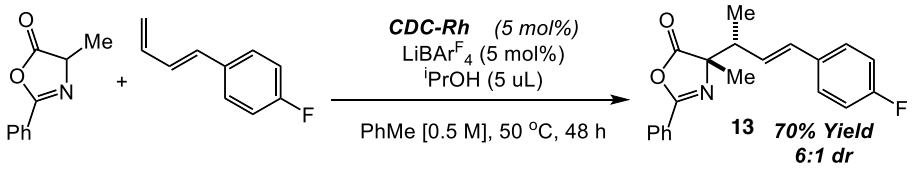
Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and phenylbutadiene (13.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 19:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **8** (26.0 mg, 0.085 mmol, 85% yield, >20:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 2H), 7.61 – 7.55 (m, 1H), 7.51-7.48 (m, 2H), 7.40 (d, J = 7.3 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.23 (t, J = 7.3 Hz, 1H), 6.53 (d, J = 15.9 Hz, 1H), 6.25 (dd, J = 15.9, 9.3 Hz, 1H), 2.80 (dq, J = 13.7, 6.9 Hz, 1H), 1.50 (s, 3H), 1.05 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.0, 160.1, 137.0, 132.8, 132.7, 129.3, 128.8, 128.5, 128.0, 127.5, 126.4, 125.9, 72.5, 45.1, 22.7, 15.8. **IR** (ν/cm^{-1}): 3060 (w), 3028 (w), 2973 (m), 2930 (m), 2872 (w), 1821 (s), 1654 (s), 1494 (w), 1450 (m), 1320 (w), 1291 (m), 1173 (m), 1001 (s), 969 (w), 889 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{20}H_{20}NO_2^+$ 306.1489, found: 306.1488.



Synthesis of 4-(E-4-(4-chlorophenyl)but-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (12). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and p-chloro-phenylbutadiene (16.5 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 19:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **12** (22.8 mg, 0.067 mmol, 67% yield, 19:1 dr) as a colorless oil. The product was isolated with less than 5% of the inseparable 1,4-addition product.

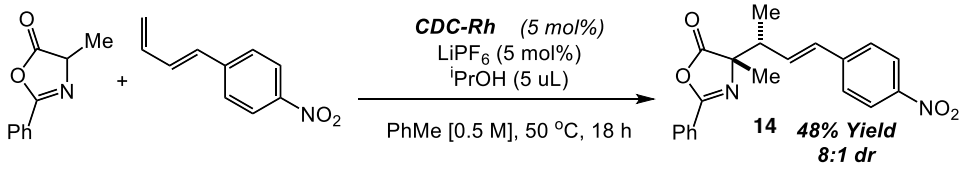
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.02 (m, 2H), 7.61 – 7.56 (m, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 6.49 (d, J = 15.9 Hz, 1H), 6.22 (dd, J = 15.9, 9.3 Hz, 1H), 2.79 (dq, J = 13.7, 6.8 Hz, 1H), 1.49 (s, 3H), 1.05 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.9, 160.4, 135.6, 132.9, 131.7, 130.2, 129.0, 128.8, 128.2, 127.7, 125.9, 72.5, 45.1, 22.8, 15.9. **IR** (ν/cm^{-1}): 2972 (m), 2930 (m), 1820 (s), 1654 (s), 1492 (m), 1451 (m), 1320 (w), 1291 (m), 1173 (m), 1091 (m), 1001 (s), 971 (w), 890 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{20}H_{19}ClNO_2^+$ 340.1099, found: 340.1099.



Synthesis of 4-(E-4-(4-fluorophenyl)but-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (13). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and p-fluoro-phenylbutadiene (29.6 mg, 0.200 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (17.5 mg, 0.100 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 9:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **13** (22.6 mg, 0.070 mmol, 70% yield, 6:1 dr) as a colorless oil. The product was isolated with less than 5% of the inseparable 1,4-addition product.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.36 (dd, J = 8.6, 5.5 Hz, 2H), 7.00 (t, J = 8.6 Hz, 2H), 6.49 (d, J = 15.9 Hz, 1H), 6.16 (dd, J = 15.9, 9.3 Hz, 1H), 2.79 (td, J = 13.7, 6.8 Hz, 1H), 1.50 (s, 3H), 1.04 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.9, 160.2, 132.7, 131.6 129.0, 128.8, 128.0, 127.9, 127.8, 126.4, 125.9, 115.4 (d, J = 21.5 Hz) 72.4, 45.0, 22.7, 15.8. **IR** (ν/cm^{-1}): 2974 (m), 2930 (m), 1821 (s),

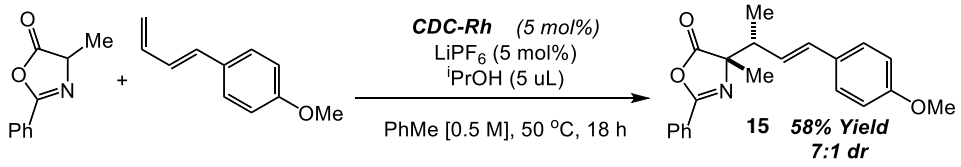
1783 (m), 1654 (s), 1603 (w), 1508 (s), 1451 (m), 1291 (m), 1229 (m), 1158 (m), 1001 (s), 970 (w), 890 (m), 819 (m). **HRMS** (ES^+) $[M–H]^+$ calcd for $C_{20}H_{19}FNO_2^+$ 324.1394, found: 324.1395.



Synthesis of 4-(E-4-(4-nitrophenyl)but-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (7). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and p-nitro-phenylbutadiene (17.5 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 8:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **14** (16.8 mg, 0.048 mmol, 48% yield, 8:1 dr) as a light yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 8.06 – 8.01 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.54 – 7.48 (m, 4H), 6.61 (d, J = 15.9 Hz, 1H), 6.46 (dd, J = 15.9, 9.2 Hz, 1H), 2.86 (dq, J = 13.7, 6.8 Hz, 1H), 1.51 (s, 3H), 1.08 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.6, 160.6, 147.1, 143.5, 134.7, 133.0, 131.1, 129.0, 128.2, 127.1, 125.9, 124.2, 72.3, 45.2, 22.8, 15.7. **IR** (ν/cm^{-1}): 3062 (w), 2975 (m), 2932 (m), 2851 (w), 1822 (s), 1653 (s), 1596 (m), 1519 (s),

1456 (m), 1342 (s), 1290 (w), 1174 (m), 1002 (m), 891 (m). **HRMS** (ES^+) $[M–H]^+$ calcd for $C_{20}H_{19}N_2O_4^+$ 351.1339, found: 351.1338.

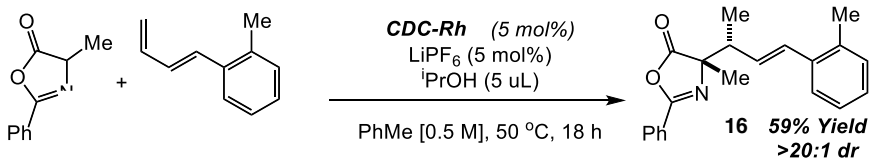


Synthesis of 4-(E-4-(4-methoxyphenyl)but-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (15).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and p-methoxy-phenylbutadiene (16.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 4:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **15** (19.4 mg, 0.058 mmol, 58% yield, 7:1 dr) as a colorless oil.

anti-Diastereomer (major): [**^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.03 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 6.47 (d, J = 15.8 Hz, 1H), 6.09 (dd, J = 15.8, 9.3 Hz, 1H), 3.80 (s, 3H), 2.82 – 2.72 (m, 1H), 1.49 (s, 3H), 1.03 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.1, 160.1, 159.1, 132.7, 132.2,

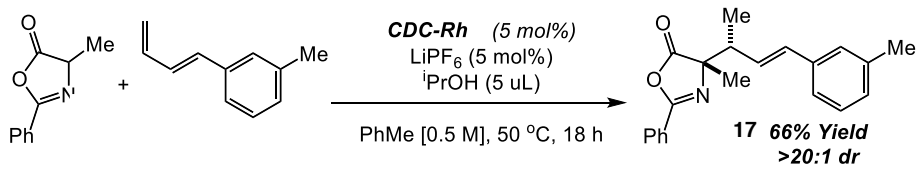
129.8, 128.8, 128.0, 127.5, 127.0, 125.9, 113.9, 72.5, 55.3, 45.1, 22.7, 15.9.] **syn-Diastereomer (minor):** [^{1}**H NMR** (600 MHz, $CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 2H), 7.59 – 7.53 (m, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 6.82 (d, J = 8.7 Hz, 2H), 6.28 (d, J = 15.9 Hz, 1H), 5.73 (dd, J = 16.0, 8.4 Hz, 1H), 3.80 (s, J = 6.8 Hz, 3H), 3.12 – 3.07 (m, 1H), 2.22 (s, 3H), 1.07 (d, J = 6.9 Hz, 3H).] **IR** (ν/cm^{-1}): 3062 (w), 3033 (w), 2972 (m), 2933 (m), 2836 (m), 1820 (s), 1782 (m), 1654 (s), 1607 (m), 1511 (s), 1450 (m), 1297 (m), 1250 (s), 1175 (m), 1033 (m), 1001 (s), 969 (m), 889 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{21}H_{22}NO_3^+$ 336.1594, found: 336.1593.



Synthesis of 4-methyl-2-phenyl-4-(E-4-(o-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (16).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and o-methyl-phenylbutadiene (14.4 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a >20:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **16** (18.8 mg, 0.059 mmol, 59% yield, >20:1 dr) as a colorless oil.

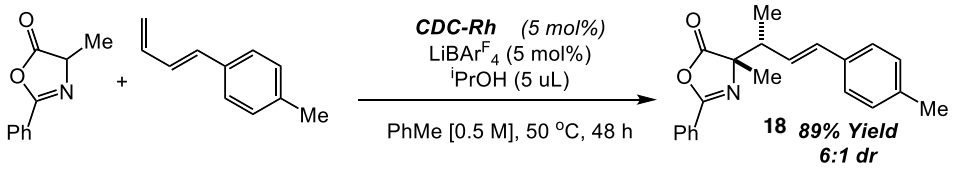
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.62 – 7.53 (m, 1H), 7.51 – 7.47 (m, 2H), 7.46 – 7.39 (m, 1H), 7.20 – 7.04 (m, 3H), 6.74 (d, J = 15.7 Hz, 1H), 6.08 (dd, J = 15.7, 9.3 Hz, 1H), 2.83 (dq, J = 13.7, 6.9 Hz, 1H), 2.32 (s, 3H), 1.52 (s, 3H), 1.09 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 181.0, 160.2, 136.4, 135.4, 132.8, 131.0, 130.9, 130.3, 128.9, 128.1, 127.6, 126.2, 126.1, 126.0, 72.5, 45.4, 22.8, 19.9, 15.9. **IR** (ν/cm^{-1}): 3062 (w), 3022 (w), 2973 (m), 2930 (m), 2872 (w), 1821 (s), 1653 (s), 1451 (m), 1320 (w), 1291 (m), 1173 (m), 1001 (s), 970 (w), 889 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{21}H_{22}NO_2^+$ 320.1645, found: 320.1645.



Synthesis of 4-methyl-2-phenyl-4-(E-4-(m-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (17).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and m-methyl-phenylbutadiene (14.4 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a >20:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **17** (21.1 mg, 0.066 mmol, 66% yield, 20:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 – 7.98 (m, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.23-7.20 (m, 3H), 7.05 – 7.04 (m, 1H), 6.50 (d, J = 15.8 Hz, 1H), 6.23 (dd, J = 15.8, 9.3 Hz, 1H), 2.81 – 2.77 (m, 1H), 2.35 (s, 3H), 1.50 (s, 3H), 1.04 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.0, 160.1, 138.1, 136.9, 132.9, 132.7, 129.1, 128.8, 128.4, 128.3, 128.0, 127.0, 125.9, 123.61, 72.5, 45.1, 22.7, 21.4, 15.9. **IR** (ν/cm^{-1}): 3060 (w), 3030 (m), 2974 (m), 2930 (m), 2872 (w), 1821 (s), 1653 (s), 1494 (m), 1451 (m), 1375 (m), 1292 (m), 1174 (m), 1093 (m), 1001 (s), 970 (w), 888 (s). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{21}H_{22}NO_2^+$ 320.1645, found: 320.1644.

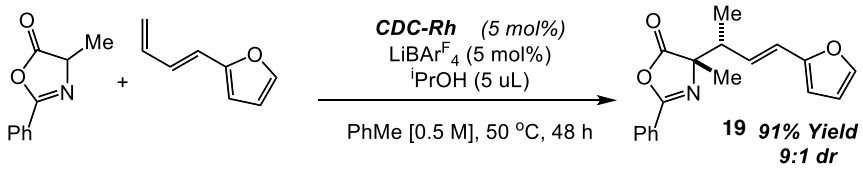


Synthesis of 4-methyl-2-phenyl-4-(E-4-(p-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (18).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiBAr^F_4$ (3.4 mg, 0.005 mmol), and p-methyl-phenylbutadiene (28.8 mg, 0.200 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (17.5 mg, 0.100 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 6:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1

Hex/Et_2O) to afford **18** (28.4 mg, 0.089 mmol, 89% yield, 6:1 dr) as a colorless oil. The product was isolated with 5% of the inseparable 1,4-addition product.

anti-Diastereomer (major): [^{1}**H NMR** (500 MHz, $CDCl_3$) δ 8.05 – 8.02 (m, 2H), 7.59 – 7.56 (m, 1H), 7.51 – 7.48 (m, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 6.50 (d, J = 15.8 Hz, 1H), 6.18 (dd, J = 15.8, 9.3 Hz, 1H), 2.83 – 2.72 (m, 1H), 2.33 (m, 3H), 1.49 (s, 3H), 1.03 (d, J = 6.8 Hz, 3H).] **syn-Diastereomer (minor):** [^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, J = 7.1 Hz, 2H), 7.41 – 7.32 (m, 3H), 7.17 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 6.30 (d, J = 15.9 Hz, 1H), 5.82 (dd, J = 15.9, 8.4 Hz, 1H), 3.15 – 3.06 (m, 1H), 2.32 (s, 3H), 2.22 (s, 3H), 1.07 (d, J = 6.9 Hz, 3H).] ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 181.2, 165.6, 160.2, 159.9, 137.7, 137.6, 137.5, 134.3, 134.2, 134.0, 132.8, 132.8, 129.4, 129.4, 128.9, 128.8, 128.4, 128.3, 128.1, 126.5, 126.4, 126.3, 126.2, 126.1, 109.3, 72.6, 47.0, 45.3, 22.8, 21.3, 16.0, 15.3, 14.0. **IR** (ν/cm^{-1}): 3026 (w), 2974 (m), 2930 (m), 2873 (w), 1820 (s), 1783 (m), 1653 (s), 1513 (m), 1451 (m), 1291 (m), 1173 (m), 1001 (s), 971 (m), 889 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{21}H_{22}NO_2^+$ 320.1645, found: 320.1646.

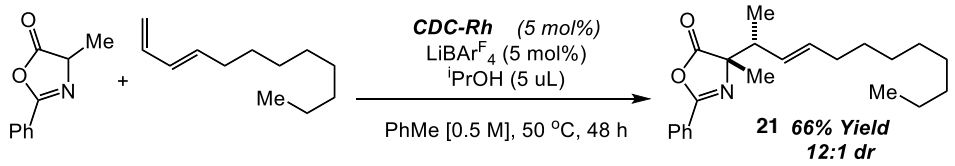


Synthesis of 4-(E-4-(furan-2-yl)but-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (19).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 2-(buta-1,3-dien-1-yl)furan (24.0 mg, 0.200 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (17.5 mg, 0.100 mmol) was added. The reaction was sealed with a

Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 9:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **19** (26.9 mg, 0.091 mmol, 91% yield, 9:1 dr) as a colorless oil.

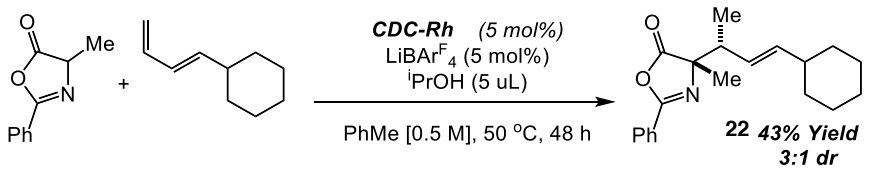
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 2H), 7.61 – 7.56 (m, 1H), 7.53 – 7.46 (m, 2H), 7.38 – 7.32 (m, 1H), 6.39 – 6.33 (m, 2H), 6.23 (d, J = 3.3 Hz, 1H), 6.20 (dd, J = 16.0, 9.4 Hz, 1H), 2.77 – 2.72 (m, 1H), 1.50 (s, 3H), 1.03 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.1, 160.3, 152.6, 142.0, 132.8, 128.9, 128.2, 128.2, 126.0, 121.3, 111.4, 107.7, 72.6, 44.9, 22.8, 15.9. **IR** (ν/cm^{-1}): 3062 (w), 2976 (m), 2933 (w), 2874 (w), 1820 (s), 1655 (s), 1451 (m), 1291 (m), 1173 (m), 1002 (s), 887 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{18}H_{19}NO_3^+$ 296.1287, found: 296.1282.



Synthesis of 4-(E-dodec-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (21).

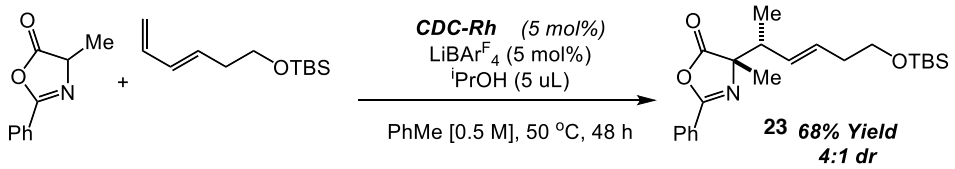
Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 1,3-dodecadiene (33.3 mg, 0.200 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (17.5 mg, 0.100 mmol) was added. The reaction was sealed with a

Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 12:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (100% Hex to 20:1 Hex/Et_2O) to afford **21** (22.5 mg, 0.066 mmol, 66% yield, 12:1 dr) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.61 – 7.54 (m, 1H), 7.50 – 7.47 (m, 2H), 5.58 (dt, J = 13.8, 7.9 Hz, 1H), 5.40 (dd, J = 15.3, 9.1 Hz, 1H), 2.58 (dq, J = 13.8, 6.9 Hz, 1H), 2.02 – 1.99 (m, 2H), 1.47 (s, 3H), 1.34 – 1.17 (m, 12H), 0.98 (d, J = 6.9 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.0, 159.8, 134.4, 132.6, 129.0, 128.7, 127.9, 126.0, 72.3, 44.6, 32.6, 31.9, 29.4, 29.4, 29.3, 29.1, 22.7, 22.4, 15.6, 14.1. **IR** (ν/cm^{-1}): 3063 (w), 3033 (w), 2957 (w), 2926 (s), 2854 (m), 1822 (s), 1654 (s), 1452 (m), 1321 (w), 1292 (m), 1175 (m), 1000 (s), 972 (w), 886 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{22}H_{32}NO_2^+$ 342.2428, found: 342.2428.



Synthesis of 4-(E-4-cyclohexylbut-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (22). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and cyclohexylbutadiene (27.2 mg, 0.200 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-

2-phenyloxazol-5(4H)-one (17.5 mg, 0.100 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 3:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (100% Hex to 20:1 Hex/Et_2O) to afford **22** (13.3 mg, 0.043 mmol, 43% yield, 6:1 dr) as a colorless oil. **anti-Diastereomer (major):** [^{1}**H NMR** (600 MHz, $CDCl_3$) δ 8.00 – 7.98 (m, 2H), 7.58 – 7.54 (m, 1H), 7.50 – 7.45 (m, 2H), 5.51 (dd, J = 15.0, 6.9 Hz, 1H), 5.33 (ddd, J = 15.4, 9.1, 1.1 Hz, 1H), 2.57 – 2.51 (m, 1H), 1.95 – 1.90 (m, 1H), 1.67 – 1.56 (m, 6H), 1.45 (s, 3H), 1.28 – 1.13 (m, 2H), 1.07 – 0.98 (m, 2H), 0.96 (d, J = 6.8 Hz, 3H). ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 181.2, 159.9, 140.4, 132.7, 128.9, 128.1, 128.0, 126.6, 126.2, 72.5, 44.8, 40.8, 33.2, 33.1, 26.3, 26.1, 22.4, 15.8.] **syn-Diastereomer (minor):** [^{1}**H NMR** (600 MHz, $CDCl_3$) δ 8.01 – 7.98 (m, 2H), 7.58 – 7.54 (m, 1H), 7.50 – 7.46 (m, 2H), 5.48 (dd, J = 14.5, 6.9 Hz, 1H), 5.23 (ddd, J = 15.4, 9.0, 1.1 Hz, 1H), 2.57 – 2.51 (m, 1H), 1.88 – 1.81 (m, 1H), 1.69 – 1.54 (m, 6H), 1.47 (s, 3H), 1.27 – 1.13 (m, 2H), 1.11 (d, J = 6.9 Hz, 3H), 1.09 – 0.98 (m, 2H). ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 180.7, 159.9, 140.1, 132.7, 128.9, 128.1, 128.0, 126.4, 126.2, 73.1, 44.5, 40.6, 33.2, 33.0, 26.2, 26.0, 22.1, 15.1.] **IR** (ν/cm^{-1}): 2973 (w), 2925 (s), 2851 (m), 1822 (s), 1653 (s), 1508 (s), 1457 (m), 1291 (m), 1228 (m), 1158 (m), 1001 (s), 890 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{20}H_{25}NO_2^+$ 312.1964, found: 312.1958.

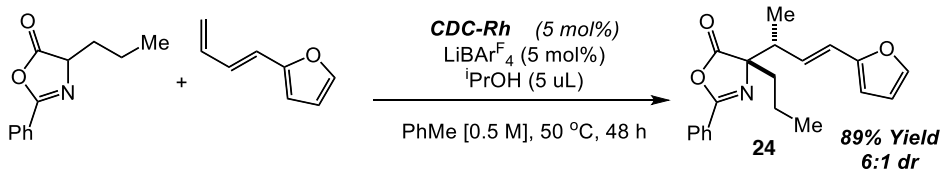


Synthesis of 4-(E-6-((tert-butyldimethylsilyl)oxy)hex-3-en-2-yl)-4-methyl-2-phenyloxazol-5(4H)-one (23).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and tert-butyl(hexa-3,5-dien-1-yloxy)dimethylsilane (42.5 mg, 0.200 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (17.5 mg, 0.100 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 4:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (100% Hex to 20:1 Hex/Et_2O) to afford **23** (26.4 mg, 0.068 mmol, 68% yield, 4:1 dr) as a colorless oil.

anti-Diastereomer (major): [**^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.02 – 7.99 (m, 2H), 7.60 – 7.53 (m, 1H), 7.51 – 7.46 (m, 2H), 5.64 – 5.56 (m, 1H), 5.48 (dd, J = 15.4, 9.0 Hz, 1H), 3.58 (t, J = 6.8 Hz, 2H), 2.68 – 2.50 (m, 1H), 2.30 – 2.20 (m, 2H), 1.46 (s, 3H), 0.96 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.2, 160.0, 132.8, 131.2, 130.6, 128.9, 128.1, 126.1, 72.4, 63.1, 44.8, 36.3, 26.1, 22.6, 18.5, 15.8, -5.1.] **syn-Diastereomer (minor):** [**^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.01 – 7.98 (m, 2H), 7.60 – 7.53 (m, 1H), 7.51 – 7.46

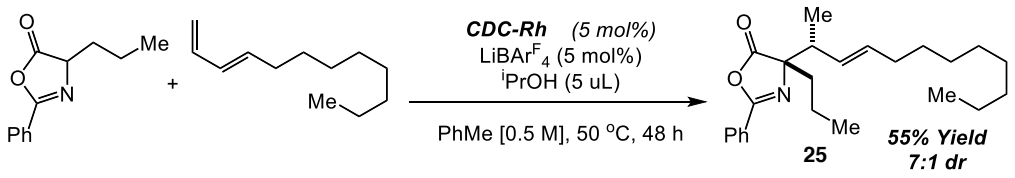
(m, 2H), 5.61 – 5.53 (m, 1H), 5.38 (dd, J = 15.4, 9.0 Hz, 1H), 3.56 – 3.52 (m, 2H), 2.68 – 2.50 (m, 1H), 2.19 – 2.15 (m, 2H), 1.48 (s, 3H), 1.11 (d, J = 6.9 Hz, 3H), 0.85 (s, 9H), 0.00 (s, 3H), 0.00 (s, 3H).] **IR** (ν/cm^{-1}): 2954 (m), 2929 (s), 2857 (m), 1823 (s), 1653 (s), 1452 (m), 1292 (m), 1255 (m), 1174 (m), 1099 (s), 1002 (s), 886 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{22}H_{34}NO_{3Si}^+$ 388.2308, found: 388.2302.



Synthesis of 4-(E-4-(furan-2-yl)but-3-en-2-yl)-2-phenyl-4-propyloxazol-5(4H)-one (24). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 2-(buta-1,3-dien-1-yl)furan (12.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 2-phenyl-4-propyloxazol-5(4H)-one (30.5 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 6:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1 Hex/Et_2O) to afford **24** (28.8 mg, 0.089 mmol, 89% yield, 6:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 2H), 7.60 – 7.56 (m, 1H), 7.52 – 7.48 (m, 2H), 7.34 (d, J = 1.5 Hz, 1H), 6.37 (dd, J = 3.3, 1.8 Hz, 1H), 6.34 (d, J = 15.9 Hz, 1H), 6.24 – 6.18 (m,

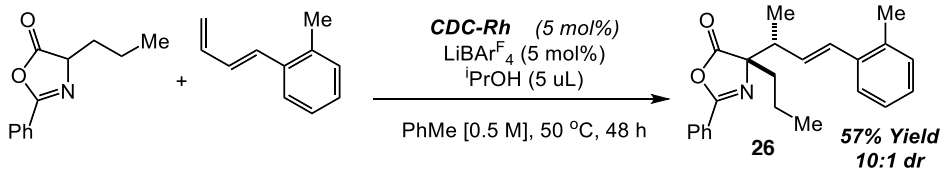
2H), 2.76 (dq, J = 9.1, 6.8 Hz, 1H), 2.00 – 1.92 (m, 1H), 1.84 – 1.76 (m, 1H), 1.27 – 1.16 (m, 1H), 1.16 – 1.07 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.7, 160.4, 152.6, 141.9, 132.8, 128.9, 128.5, 128.2, 125.9, 120.9, 111.4, 107.6, 76.9, 44.7, 38.3, 17.4, 16.0, 14.0. **IR** (ν/cm^{-1}): 3446 (br, w), 2964 (s), 2933 (m), 2874 (m), 1811 (s), 1653 (s), 1493 (m), 1452 (m), 1320 (m), 1293 (m), 1163 (m), 1020 (m), 944 (m), 883 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{20}H_{22}NO_3^+$ 324.1600, found: 324.1610.



Synthesis of 4-(E-dodec-3-en-2-yl)-2-phenyl-4-propyloxazol-5(4H)-one (25).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 1,3-dodecadiene (16.6 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 2-phenyl-4-propyloxazol-5(4H)-one (30.5 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 7:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (100% Hex to 40:1 Hex/Et_2O) to afford **25** (20.3 mg, 0.055 mmol, 55% yield, 7:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 2H), 7.61 – 7.53 (m, 1H), 7.50 – 7.47 (m, J = 7.5, 4.1, 2.5 Hz, 2H), 5.59 – 5.50 (m, 1H), 5.42 – 5.37 (m, 1H), 2.65 – 2.53 (m, 1H), 2.02 – 1.98 (m, 2H), 1.95 – 1.88 (m, 1H), 1.78 (ddd, J = 13.7, 12.1, 4.8 Hz, 1H), 1.35 – 1.16 (m, 13H), 1.17 – 1.05 (m, 1H), 0.95 (d, J = 6.9 Hz, 3H), 0.87 (t, J = 7.2 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.8, 160.1, 134.1, 132.7, 129.4, 128.9, 128.1, 126.1, 76.7, 44.5, 38.1, 32.7, 32.0, 29.6, 29.5, 29.4, 29.3, 22.8, 17.5, 15.9, 14.3, 14.1. **IR** (ν/cm^{-1}): 2960 (m), 2926 (s), 2873 (w), 2854 (m), 1812 (s), 1654 (s), 1452 (m), 1321 (m), 1293 (m), 1165 (w), 1040 (m), 1020 (m), 942 (m), 881 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{24}H_{36}NO_2^+$ 370.2746, found: 370.2751.

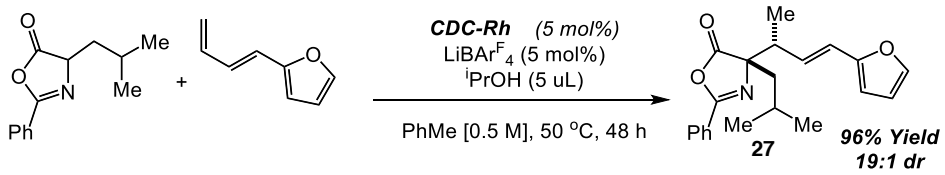


Synthesis of 2-phenyl-4-propyl-4-(E-4-(o-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (26).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and o-methyl-phenylbutadiene (14.4 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 2-phenyl-4-propyloxazol-5(4H)-one (30.5 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 10:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1

Hex/Et_2O) to afford **26** (19.8 mg, 0.057 mmol, 57% yield, 10:1 dr) as a colorless oil. The product was isolated with less than 5% of the inseparable 1,4-addition product.

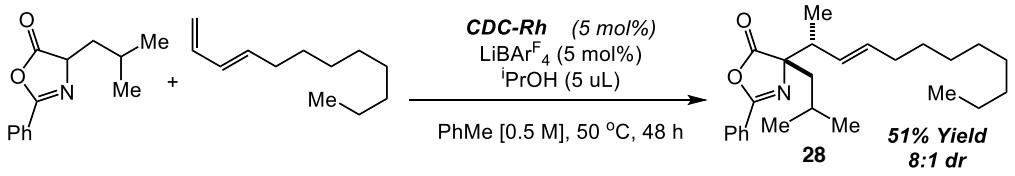
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 2H), 7.61 – 7.55 (m, 1H), 7.52 – 7.47 (m, 2H), 7.48 – 7.43 (m, 1H), 7.20 – 7.12 (m, 3H), 6.72 (d, J = 15.7 Hz, 1H), 6.10 (dd, J = 15.7, 9.4 Hz, 1H), 2.85 (dq, J = 9.1, 6.8 Hz, 1H), 2.61 – 2.47 (m, 1H), 2.32 (s, 3H), 1.96 (ddd, J = 13.5, 12.4, 4.6 Hz, 1H), 1.85 (ddd, J = 13.7, 12.1, 4.9 Hz, 1H), 1.77 – 1.63 (m, 1H), 1.29 – 1.10 (m, 2H), 1.06 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.71, 160.31, 136.32, 135.38, 132.78, 131.14, 130.50, 130.34, 128.92, 128.12, 127.52, 126.19, 125.95, 125.93, 76.75, 45.16, 38.34, 19.94, 17.44, 16.00, 14.04. **IR** (ν/cm^{-1}): 3062 (w), 3022 (w), 2963 (s), 2932 (w), 2874 (m), 1812 (s), 1782 (m), 1653 (s), 1456 (m), 1292 (m), 1162 (m), 1020 (m), 944 (m), 882 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{23}H_{26}NO_2^+$ 348.1964, found: 348.1971.



Synthesis of 4-(E-4-(furan-2-yl)but-3-en-2-yl)-4-isobutyl-2-phenyloxazol-5(4H)-one (27). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 2-(buta-1,3-dien-1-yl)furan (12.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-isobutyl-2-phenyloxazol-5(4H)-one (32.6 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The

reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 19:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1 Hex/Et_2O) to afford **27** (32.4 mg, 0.096 mmol, 96% yield, 19:1 dr) as a colorless oil.

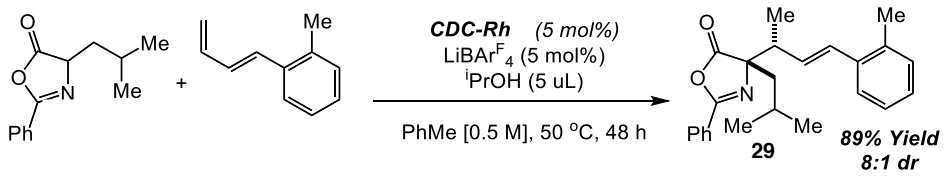
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 2H), 7.61 – 7.56 (m, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.34 (d, J = 1.5 Hz, 1H), 6.36 (dd, J = 3.2, 1.8 Hz, 1H), 6.31 (d, J = 15.9 Hz, 1H), 6.22 (d, J = 3.2 Hz, 1H), 6.16 (dd, J = 15.9, 9.3 Hz, 1H), 2.71 (dq, J = 9.1, 6.8 Hz, 1H), 2.05 (dd, J = 14.2, 5.8 Hz, 1H), 1.76 (dd, J = 14.2, 6.9 Hz, 1H), 1.56 – 1.47 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.84 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.2, 160.1, 152.6, 141.9, 132.8, 128.9, 128.5, 128.1, 126.0, 121.1, 111.4, 107.6, 76.1, 45.9, 44.8, 25.2, 24.2, 23.4, 15.6. **IR** (ν/cm^{-1}): 2961 (s), 2934 (w), 2908 (w), 2873 (m), 1812 (s), 1653 (s), 1456 (m), 1319 (w), 1291 (m), 1153 (m), 1022 (m), 961 (m), 882 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{21}H_{24}NO_3^+$ 338.1756, found: 338.1763.



Synthesis of 4-(E-dodec-3-en-2-yl)-4-isobutyl-2-phenyloxazol-5(4H)-one (28).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 1,3-dodecadiene (16.6 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-isobutyl-2-phenyloxazol-5(4H)-one (32.6 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged

isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 8:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (100% Hex to 40:1 Hex/Et_2O) to afford **28** (19.6 mg, 0.051 mmol, 51% yield, 8:1 dr) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 2H), 7.60 – 7.55 (m, 1H), 7.51 – 7.48 (m, 2H), 5.57 – 5.46 (m, 1H), 5.37 – 5.29 (m, 1H), 2.58 – 2.53 (m, 1H), 2.07 – 1.99 (m, 1H), 1.99 – 1.92 (m, 2H), 1.80 – 1.64 (m, 1H), 1.61 – 1.46 (m, 1H), 1.33 – 1.13 (m, 13H), 0.97 (d, J = 6.8 Hz, 2H), 0.89 – 0.83 (m, 6H), 0.82 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.3, 159.7, 134.5, 132.6, 129.3, 128.9, 128.0, 126.2, 75.9, 45.7, 44.6, 32.7, 32.0, 29.6, 29.5, 29.4, 29.2, 25.2, 24.3, 23.2, 22.8, 15.4, 14.3. **IR** (ν/cm^{-1}): 2957 (m), 2925 (s), 2871 (w), 2854 (m), 1813 (s), 1654 (s), 1452 (m), 1320 (w), 1292 (m), 1160 (w), 1023 (m), 954 (m), 881 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{25}H_{38}NO_2^+$ 384.2903, found: 384.2905.

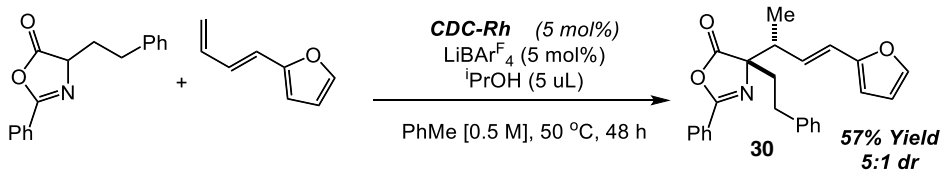


Synthesis of 4-isobutyl-2-phenyl-4-(E-4-(o-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (29).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and o-methyl-phenylbutadiene (14.4 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-isobutyl-2-phenyloxazol-5(4H)-one (32.6 mg, 0.150 mmol) was added. The reaction was sealed with a

Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 10:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1 Hex/Et_2O) to afford **29** (32.2 mg, 0.089 mmol, 89% yield, 8:1 dr) as a colorless oil. The product was isolated with less than 5% of the inseparable 1,4-addition product.

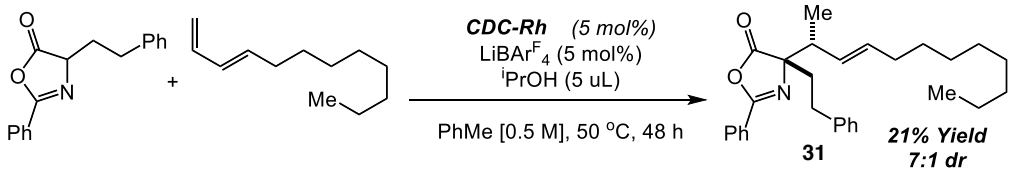
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.60 – 7.55 (m, 1H), 7.51 – 7.48 (m, 2H), 7.45 – 7.40 (m, 1H), 7.18 – 7.10 (m, 3H), 6.69 (d, J = 15.7 Hz, 1H), 6.05 (dd, J = 15.7, 9.4 Hz, 1H), 2.80 (dq, J = 13.6, 6.8 Hz, 1H), 2.30 (s, 3H), 2.07 (dd, J = 14.2, 5.7 Hz, 1H), 1.81 (dd, J = 14.2, 7.0 Hz, 1H), 1.58 – 1.51 (m, 1H), 1.07 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.2, 160.0, 136.4, 135.4, 132.7, 131.2, 130.8, 130.3, 128.9, 128.1, 127.5, 126.2, 126.1, 126.0, 76.0, 46.3, 44.8, 25.2, 24.2, 23.4, 19.9, 15.6. **IR** (ν/cm^{-1}): 3062 (w), 3021 (w), 2960 (s), 2872 (m), 1812 (s), 1781 (m), 1653 (s), 1452 (m), 1292 (m), 1159 (m), 1023 (m), 956 (m), 882 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{24}H_{28}NO_2^+$ 362.2120, found: 362.2123.



Synthesis of 4-(E-4-(furan-2-yl)but-3-en-2-yl)-4-phenethyl-2-phenyloxazol-5(4H)-one (30). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and 2-

(buta-1,3-dien-1-yl)furan (12.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-phenethyl-2-phenyloxazol-5(4H)-one (39.8 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 5:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1 Hex/Et_2O) to afford **30** (22.0 mg, 0.057 mmol, 57% yield, >20:1 dr) as a colorless oil.

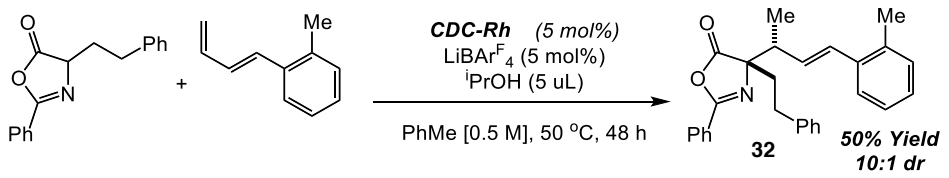
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 – 8.04 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 1.3 Hz, 1H), 7.22 (t, J = 7.5 Hz, 2H), 7.15 (t, J = 7.4 Hz, 1H), 7.12 (d, J = 7.1 Hz, 2H), 6.35 (dd, J = 3.2, 1.8 Hz, 1H), 6.31 (d, J = 15.9 Hz, 1H), 6.24 – 6.17 (m, 2H), 2.80 (dq, J = 13.6, 6.8 Hz, 1H), 2.53 – 2.48 (m, 1H), 2.42 – 2.37 (m, 1H), 2.32 – 2.27 (m, 1H), 2.16 – 2.11 (m, 1H), 1.04 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.5, 160.8, 152.5, 141.9, 140.6, 132.9, 129.0, 128.6, 128.6, 128.2, 128.2, 126.3, 125.8, 121.1, 111.4, 107.8, 76.6, 44.9, 38.1, 30.6, 16.0. **IR** (ν/cm^{-1}): 3063 (w), 3029 (m), 2966 (m), 2929 (m), 2873 (w), 1816 (s), 1653 (s), 1455 (m), 1320 (w), 1292 (m), 1059 (w), 997 (m), 877 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{25}H_{24}NO_3^+$ 386.1756, found: 386.1761.



Synthesis of 4-(E-dodec-3-en-2-yl)-4-phenethyl-2-phenyloxazol-5(4H)-one (31).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiBAr^F_4$ (3.4 mg, 0.005 mmol), and 1,3-dodecadiene (16.6 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-phenethyl-2-phenyloxazol-5(4H)-one (39.8 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 7:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (100% Hex to 40:1 Hex/Et_2O) to afford **31** (9.1 mg, 0.021 mmol, 21% yield, 8:1 dr) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 7.5 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 7.13 (d, J = 7.1 Hz, 2H), 5.59 – 5.50 (m, 1H), 5.40 (dd, J = 15.3, 9.1 Hz, 1H), 2.65 (dq, J = 13.8, 6.9 Hz, 1H), 2.56 – 2.50 (m, 1H), 2.43 – 2.37 (m, 1H), 2.31 – 2.22 (m, 1H), 2.16 – 2.09 (m, 1H), 1.98 (q, J = 6.8 Hz, 2H), 1.33 – 1.14 (m, 12H), 0.98 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.5, 160.4, 140.9, 134.4, 132.8, 129.6, 129.1, 128.9, 128.6, 128.1, 126.3, 126.0, 76.4, 44.5, 37.8, 32.7, 32.1, 30.5, 29.6, 29.5, 29.4, 29.3, 22.8, 15.8, 14.3. **IR** (ν/cm^{-1}): 3437 (br, m), 2957 (w), 2925 (s), 2854 (m), 1818 (s), 1653 (s), 1455 (m), 1321 (w), 1292 (m), 1059 (m), 995 (m), 877 (m). **HRMS** (ES^+) $[M–H]^+$ calcd for $C_{29}H_{38}NO_2^+$ 432.2903, found: 432.2906.

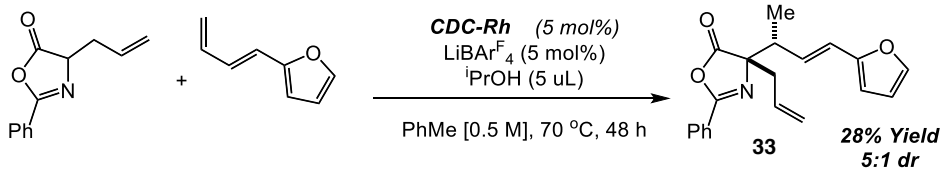


Synthesis of 4-phenethyl-2-phenyl-4-(E-4-(o-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (32).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiBAr^F_4$ (3.4 mg, 0.005 mmol), and o-methyl-phenylbutadiene (14.4 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-phenethyl-2-phenyloxazol-5(4H)-one (39.8 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 μL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 10:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1 Hex/Et_2O) to afford **32** (20.5 mg, 0.050 mmol, 50% yield, 10:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 – 8.05 (m, 2H), 7.62 – 7.58 (m, 1H), 7.53 – 7.50 (m, 2H), 7.47 – 7.43 (m, 1H), 7.24 – 7.21 (m, 2H), 7.18 – 7.09 (m, 6H), 6.71 (d, J = 15.7 Hz, 1H), 6.11 (dd, J = 15.7, 9.4 Hz, 1H), 2.94 – 2.85 (m, 1H), 2.58 – 2.50 (m, 1H), 2.46 – 7.41 (m, 1H), 2.34 – 2.29 (m, 1H), 2.28 (s, 3H), 2.23 – 2.15 (m, 1H), 1.09 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.4, 160.7, 140.6, 136.2, 135.4, 132.9, 130.8, 130.7, 130.4, 129.0, 128.6, 128.5, 128.2, 127.6, 126.3, 126.2, 125.9, 125.9, 76.4, 45.2, 38.0, 30.5, 19.9, 16.0. **IR** (ν/cm^{-1}): 3062 (w), 3027 (m), 2967 (m), 2929 (m), 2866 (w), 1816 (s), 1653 (s), 1496 (w), 1456 (m), 1292 (m), 1118

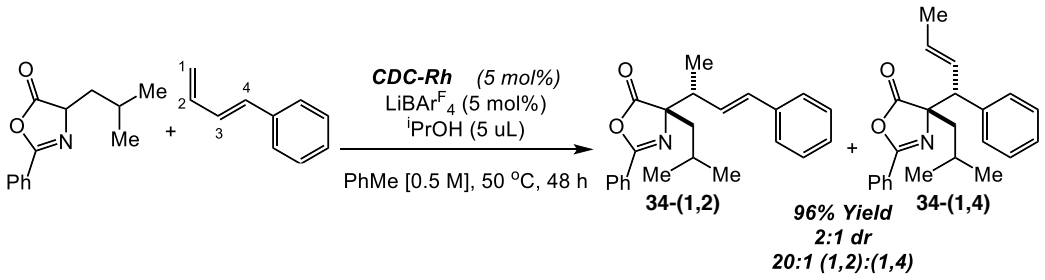
(m), 1058 (m), 996 (s), 877 (m). **HRMS** (ES^+) $[M–H]^+$ calcd for $C_{28}H_{28}NO_2^+$ 410.2121, found: 410.2124.



Synthesis of 4-(E-4-(furan-2-yl)but-3-en-2-yl)-4-phenethyl-2-phenyloxazol-5(4H)-one (33). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiBAr^F_4$ (3.4 mg, 0.005 mmol), and 2-(buta-1,3-dien-1-yl)furan (12.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-allyl-2-phenyloxazol-5(4H)-one (30.2 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 70 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 5:1 mixture of the anti:syn diastereomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (40:1 Hex/Et_2O) to afford **33** (9.0 mg, 0.028 mmol, 28% yield, 9:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 – 8.03 (m, 2H), 7.62 – 7.57 (m, 1H), 7.51 – 7.48 (m, 2H), 7.35 (d, J = 1.5 Hz, 1H), 6.39 – 6.32 (m, 2H), 6.25 – 6.19 (m, 2H), 5.60 – 5.53 (m, 1H), 5.14 (d, J = 17.0, 1H), 5.06 (d, J = 10.2 Hz, 1H), 2.80 (dq, J = 9.2, 6.9 Hz, 1H), 2.75 (dd, J = 13.7, 6.4 Hz, 1H), 2.53 (dd, J = 13.8, 8.3 Hz, 1H), 1.02 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.9, 160.5, 152.5, 142.0, 132.8, 131.0, 128.9, 128.2, 128.2, 125.9, 121.2, 120.7, 111.4, 107.8,

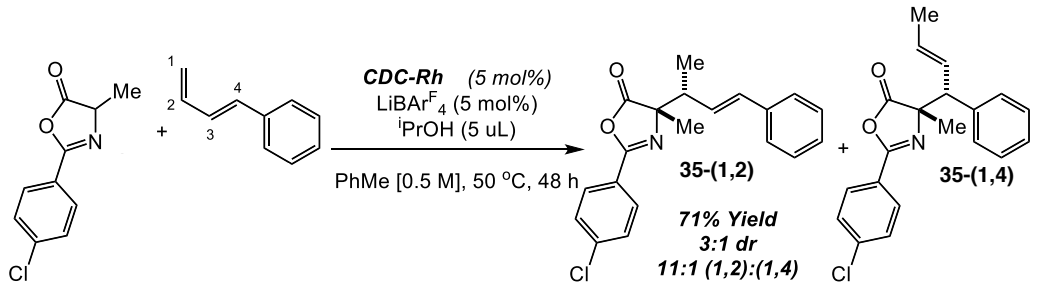
44.3, 40.5, 16.0. **IR** (ν/cm^{-1}): 2968 (m), 2927 (m), 1815 (s), 1654 (s), 1451 (m), 1322 (m), 1292 (m), 1152 (w), 1055 (m), 998 (m), 964 (m), 927 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{20}H_{20}NO_3^+$ 322.1443, found: 322.1438.



Synthesis of 4-isobutyl-2-phenyl-4-(E-4-phenylbut-3-en-2-yl)oxazol-5(4H)-one (34).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and phenylbutadiene (13.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-isobutyl-2-phenyloxazol-5(4H)-one (32.6 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 2:1 mixture of the anti:syn diastereomers and a 20:1 mixture of the (1,2):(1,4) regioisomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **34** (33.4 mg, 0.0960 mmol, 96% yield, 2:1 dr, 19:1 (1,2):(1,4)) as a colorless oil.

anti-Diastereomer (major): [^{1}**H NMR** (600 MHz, $CDCl_3$) δ 8.05 – 8.04 (m, 2H), 7.60 – 7.56 (m, 1H), 7.52 – 7.49 (m, 2H), 7.39 – 7.37 (m, 2H), 7.32 – 7.30 (m, 2H), 7.25 – 7.21 (m, 1H), 6.49 (d, J = 15.9 Hz, 1H), 6.21 (dd, J = 15.9, 9.3 Hz, 1H), 2.77 (dq, J = 9.1, 6.8 Hz, 1H), 2.43 (dd, J = 7.0, 4.3 Hz, 1H), 2.05 (dd, J = 14.2, 5.8 Hz, 1H), 1.78 (dd, J = 14.2, 6.9 Hz, 1H), 1.55 – 1.49 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.83 (t, J = 7.0 Hz, 6H).] **syn-Diastereomer (minor):** [^{1}**H NMR** (600 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 2H), 7.60 – 7.57 (m, 1H), 7.51 – 7.49 (m, 2H), 7.39 – 7.36 (m, 2H), 7.28 – 7.23 (m, 2H), 7.23 – 7.18 (m, 1H), 6.35 (d, J = 15.9 Hz, 1H), 5.91 (dd, J = 15.9, 8.5 Hz, 1H), 3.18 – 3.11 (m, 1H), 2.43 (dd, J = 7.0, 4.3 Hz, 1H), 2.15 – 2.08 (m, 1H), 2.04 (dd, J = 14.2, 5.8 Hz, 1H), 1.77 (dd, J = 14.3, 6.8 Hz, 1H), 1.09 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 6.7 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H).] **(1,4)-Regioisomer (minor):** [^{1}**H NMR** (600 MHz, $CDCl_3$) δ 7.99 – 7.96 (m, 2H), 7.56 – 7.54 (m, 1H), 7.50 – 7.46 (m, 2H), 7.38 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.23 – 7.18 (m, 1H), 5.69 – 5.58 (m, 2H), 3.61 (d, J = 8.9 Hz, 1H), 2.49 (dd, J = 7.0, 2.0 Hz, 1H), 2.24 – 2.16 (m, 1H), 1.68 (dd, J = 14.3, 5.9 Hz, 1H), 1.60 (d, J = 5.1 Hz, 3H), 0.78 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H).] ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 181.1, 165.5, 162.2, 159.9, 138.0, 137.0, 136.8, 133.8, 132.6, 129.7, 129.1, 128.8, 128.7, 128.5, 128.5, 128.3, 128.0, 127.6, 127.5, 127.3, 126.5, 126.4, 126.3, 125.9, 109.2, 76.0, 47.0, 46.0, 44.7, 36.5, 26.3, 25.1, 24.1, 23.3, 22.6, 22.4, 15.5, 15.2. **IR** (ν/cm^{-1}): 3028 (w), 2960 (s), 2934 (w), 2872 (m), 1812 (s), 1781 (m), 1653 (s), 1495 (m), 1450 (m), 1320 (w), 1292 (m), 1158 (m), 1023 (w), 960 (s), 882 (m). **HRMS** (ES^+) $[M–H]^+$ calcd for $C_{23}H_{26}NO_2^+$ 348.1964, found: 348.1958.



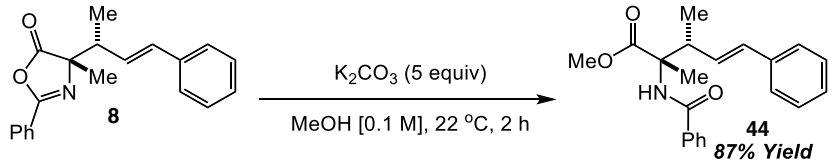
Synthesis of 2-(4-chlorophenyl)-4-methyl-4-(E-4-phenylbut-3-en-2-yl)oxazol-5(4H)-one (35). Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), LiBAr$^F_4$ (3.4 mg, 0.005 mmol), and phenylbutadiene (13.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 µL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 2-(4-chlorophenyl)-4-methyloxazol-5(4H)-one (31.4 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (5 µL) was added and the reaction allowed to stir at 50 °C for 48 h. The reaction was cooled to room temperature and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy as a 3:1 mixture of the anti:syn diastereomers and a 11:1 mixture of the (1,2):(1,4) regioisomers. The NMR sample was recombined with the reaction and the solvents removed in vacuo. The resulting oil was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O to 10:1 Hex/Et_2O) to afford **35** (24.1 mg, 0.0710 mmol, 71% yield, 3:1 dr, 11:1 (1,2):(1,4)) as a colorless oil.

anti-Diastereomer (major): [**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 – 7.95 (m, 2H), 7.51 – 7.44 (m, 2H), 7.42 – 7.37 (m, 2H), 7.33 – 7.30 (m, 2H), 7.29 – 7.22 (m, 1H), 6.53 (d, J = 15.9 Hz, 1H), 6.22 (dd, J = 15.9, 9.3 Hz, 1H), 2.80 (dq, J = 13.7, 6.9 Hz, 1H), 1.50 (s, 3H), 1.04 (d, J = 6.8 Hz, 3H).] **syn-Diastereomer (minor):** [**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 – 7.95 (m, 2H), 7.51 – 7.44 (m, 2H), 7.42 – 7.37 (m, 2H), 7.34 – 7.30 (m, 2H), 7.26 – 7.20 (m, 1H), 6.33 (d, J = 16.0

Hz, 1H), 5.88 (dd, J = 16.0, 8.4 Hz, 1H), 3.12 – 2.98 (m, 1H), 1.59 (s, 3H), 1.07 (d, J = 6.9 Hz, 3H).] **(1,4)-Regioisomer (minor): [^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.90 (m, 2H), 7.84 – 7.77 (m, 2H), 7.44 – 7.41 (m, 2H), 7.34 - 7.27 (m, 1H), 7.14 - 7.12 (m, 2H), 5.78 – 5.57 (m, 2H), 3.66 (d, J = 9.8 Hz, 1H), 2.24 (s, 3H), 1.76 (dd, J = 6.4, 1.5 Hz, 3H).] **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.0, 165.5, 163.2, 161.6, 160.3, 160.0, 137.6, 133.2, 133.1, 132.9, 132.8, 131.7, 129.1, 129.1, 128.9, 128.9, 128.5, 128.1, 127.9 (dd, J = 20.7, 8.0 Hz), 127.1, 127.1, 126.6, 126.0, 115.6 (dd, J = 21.6, 10.7 Hz), 109.2, 72.5, 47.0, 45.1, 22.8, 15.9, 15.1, 14.0. **IR** (ν/cm^{-1}): 3028 (m), 2976 (m), 2933 (m), 2873 (w), 1823 (m), 1783 (s), 1653 (m), 1490 (m), 1403 (w), 1311 (m), 1171 (m), 1092 (m), 1000 (m), 967 (m), 840 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{20}H_{19}ClNO_2^+$ 340.1104, found: 340.1099.

■ **General procedure for hydrolysis of oxazolone products in Table 3.3.5-1 (44-48):**

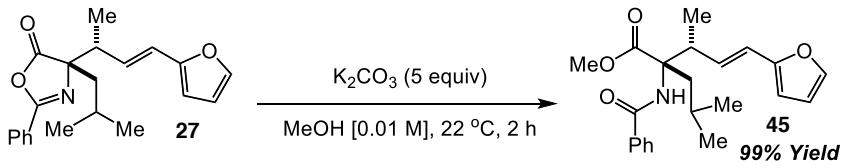
An 8 mL reaction vial with a stir bar was charged with the oxazolone and potassium carbonate with no effort to exclude oxygen or water. The reaction was solvated with wet methanol and the headspace purged with N_2 for 5 minutes. The reaction was sealed and allowed to stir at room temperature for a minimum of 2 hours before being concentrated by rotary evaporation to remove the solvent. The resulting powder was purified by SiO_2 gel chromatography to yield the hydrolyzed product.



Synthesis of methyl (E)-2-benzamido-2,3-dimethyl-5-phenylpent-4-enoate (44).

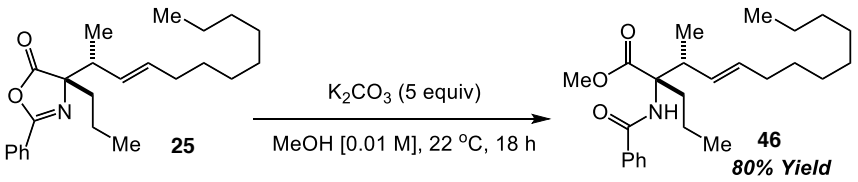
Following the general procedure for hydrolysis, 4-methyl-2-phenyl-4-(*(E)*-4-phenylbut-3-en-2-yl)oxazol-5(4H)-one (12.1 mg, 0.0396 mmol, 19:1 dr) and K_2CO_3 (27.4 mg, 0.198 mmol, 5 equiv) were solvated in methanol (400 µL) and allowed to stir at 22 °C for 2 h. The solution was concentrated to an off white solid which was purified by SiO_2 gel column chromatography (10:1 Hex/Et_2O) to afford **44** (11.1 mg, 0.0344 mmol, 87% yield, 20:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 – 7.70 (m, 2H), 7.48 – 7.45 (m, 1H), 7.39 – 7.37 (m, 2H), 7.37 – 7.33 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 6.84 (s, 1H), 6.52 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 9.3 Hz, 1H), 3.79 (s, 3H), 3.00 (dq, *J* = 14.0, 7.0 Hz, 1H), 1.80 (s, 3H), 1.22 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.5, 166.9, 136.9, 134.8, 132.6, 131.7, 130.3, 128.7, 128.7, 127.8, 127.0, 126.5, 62.8, 52.6, 45.3, 20.8, 15.9. **IR** (ν/cm^{-1}): 3410 (br, m), 3334 (br, m), 3027 (m), 2975 (m), 2949 (m), 1739 (s), 1653 (s), 1521 (s), 1488 (m), 1373 (m), 1263 (m), 1127 (m), 970 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{21}H_{24}NO_3^+$ 338.1756, found: 338.1750.



Synthesis of methyl *(E)*-2-benzamido-5-(furan-2-yl)-2-isobutyl-3-methylpent-4-enoate (45). Following the general procedure for hydrolysis, 4-*((E)*-4-(furan-2-yl)but-3-en-2-yl)-4-isobutyl-2-phenyloxazol-5(4H)-one (8.5 mg, 0.025 mmol, 9:1 dr) and K_2CO_3 (17.4 mg, 0.126 mmol, 5 equiv) were solvated in methanol (2 mL) and allowed to stir at 22 °C for 2 h. The solution was concentrated to an off white solid which was purified by SiO_2 gel column chromatography (10:1 Hex/Et_2O) to afford **45** (8.3 mg, 0.0248 mmol, 89% yield, >20:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.74 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37 (s, 1H), 7.28 (d, *J* = 1.2 Hz, 1H), 6.30 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.18 (d, *J* = 15.7 Hz, 1H), 6.07 (d, *J* = 3.2 Hz, 1H), 5.94 (dd, *J* = 15.7, 9.1 Hz, 1H), 3.84 (s, 3H), 3.57 – 3.49 (m, 1H), 2.73 (dd, *J* = 14.1, 4.3 Hz, 1H), 1.95 (dd, *J* = 14.0, 9.0 Hz, 1H), 1.68 – 1.55 (m, 1H), 1.21 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.77 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.5, 166.6, 152.7, 141.8, 135.6, 131.5, 129.3, 128.7, 127.0, 120.4, 111.2, 107.4, 67.2, 52.7, 43.1, 41.0, 25.2, 24.3, 22.0, 15.8. **IR** (ν/cm^{-1}): 3413 (w), 2962 (s), 2923 (m), 2866 (w), 1731 (m), 1669 (s), 1508 (m), 1488 (w), 1260 (s), 1095 (br, s), 1021 (br, s), 799 (s). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{22}H_{28}NO_4^+$ 370.2018, found: 370.2013.

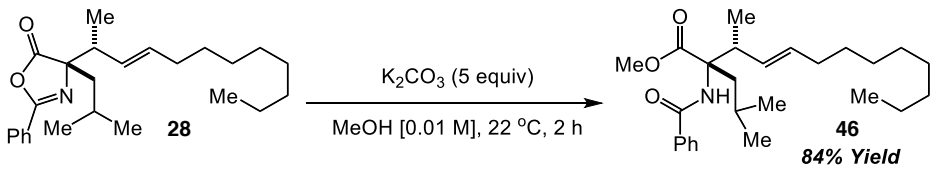


Synthesis of methyl methyl (*E*)-2-benzamido-3-methyl-2-propyltridec-4-enoate (46).

Following the general procedure for hydrolysis, 4-((*E*)-dodec-3-en-2-yl)-2-phenyl-4-propyloxazol-5(4H)-one (17.1 mg, 0.0463 mmol, 9:1 dr) and K_2CO_3 (320 mg, 2.31 mmol, 5 equiv) were solvated in methanol (4 mL) and allowed to stir at 22 °C for 18 h. The solution was concentrated to an off white solid which was purified by SiO_2 gel column chromatography (5:1 Hex/Et_2O) to afford **46** (14.9 mg, 0.0371 mmol, 80% yield, 9:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 – 7.75 (m, 2H), 7.50 – 7.47 (m, 1H), 7.44 – 7.41 (m, 2H), 7.09 (s, 1H), 5.51 – 5.43 (m, 1H), 5.26 (dd, *J* = 15.2, 9.1 Hz, 1H), 3.79 (s, 3H), 3.12 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.54 (ddd, *J* = 13.8, 12.1, 4.6 Hz, 1H), 2.10 (ddd, *J* = 13.8, 12.1, 4.5 Hz, 1H), 1.96 – 1.92 (m, 2H), 1.38 – 1.14 (m, 14H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H), 0.87

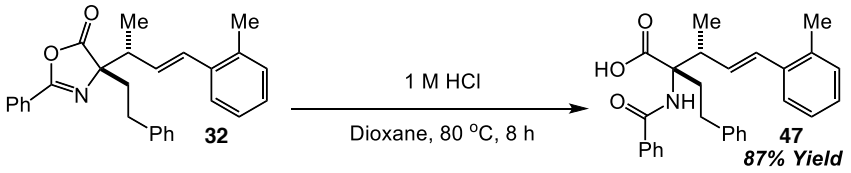
(t, J = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.02, 166.20, 135.41, 133.46, 131.48, 130.64, 128.66, 126.95, 67.31, 52.61, 42.29, 34.06, 32.68, 32.03, 29.68, 29.59, 29.39, 29.24, 22.81, 17.96, 16.05, 14.27, 14.25. **IR** (ν/cm^{-1}): 3415 (m), 2956 (m), 2925 (s), 2854 (m), 1730 (s), 1669 (s), 1515 (m), 1486 (w), 1232 (m), 971 (w). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{25}H_{39}NO_3^+$ 402.3008, found: 402.3006.



Synthesis of methyl *(E)*-2-benzamido-2-isobutyl-3-methyltridec-4-enoate (46).

Following the general procedure for hydrolysis, 4-(*(E)*-dodec-3-en-2-yl)-4-isobutyl-2-phenyloxazol-5(4H)-one (9.2 mg, 0.024 mmol, 11:1 dr) and K_2CO_3 (16.6 mg, 0.120 mmol, 5 equiv) were solvated in methanol (2 mL) and allowed to stir at 22 °C for 2 h. The solution was concentrated to an off white solid which was purified by SiO_2 gel column chromatography (20:1 Hex/Et_2O) to afford **46** (8.4 mg, 0.020 mmol, 84% yield, 10:1 dr) as a colorless oil.

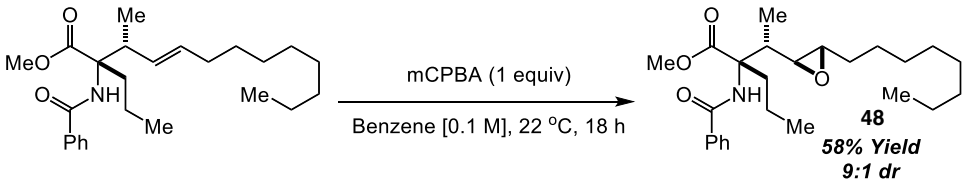
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.75 (m, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.29 (s, 1H), 5.45 – 5.39 (m, 1H), 5.17 (dd, J = 15.2, 9.0 Hz, 1H), 3.80 (s, 3H), 3.31 – 3.25 (m, 1H), 2.63 (dd, J = 14.1, 4.2 Hz, 1H), 1.96 (dd, J = 14.1, 9.0 Hz, 1H), 1.92 – 1.89 (m, 2H), 1.64-1.59 (m, 1H), 1.28 – 1.13 (br m, 12H), 1.10 (d, J = 7.0 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.7, 166.3, 135.7, 133.4, 131.4, 130.4, 128.7, 126.9, 66.9, 52.5, 42.7, 40.8, 32.7, 32.0, 29.6, 29.6, 29.4, 29.2, 25.1, 24.4, 22.8, 22.1, 15.9, 14.3. **IR** (ν/cm^{-1}): 3416 (br, s), 2955 (m), 2925 (s), 2854 (m), 1726 (m), 1669 (s), 1514 (m), 1485 (m), 1366 (m), 1235 (m), 970 (w). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{26}H_{42}NO_3^+$ 416.3165, found: 416.3160.



Synthesis of (*E*)-2-benzamido-3-methyl-2-phenethyl-5-(o-tolyl)pent-4-enoic acid (47).

To an 8 mL vial was added 4-phenethyl-2-phenyl-4-(*E*-4-(o-tolyl)but-3-en-2-yl)oxazol-5(4H)-one (6.4 mg, 0.016 mmol, 10:1 dr), dioxane (1 mL) and 1M HCl (1 mL). The reaction was sealed with a septum cap and the headspace flushed with N_2 before being heated to 80 °C. The reaction was allowed to stir at 80°C for 8 h before being cooled to room temperature and extracted three times with EtOAc (1 mL). The organic layers were dried with Na_2SO_4 and filtered before being concentrated. The resulting oil was dried by rotoray evaporation with additional chloroform to remove residual dioxane to yield **47** as a clear film (5.9 mg, 0.014 mmol, 87% yield, >20:1 dr). The product required no further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 – 7.75 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.39 – 7.38 (m, 1H), 7.24 (d, *J* = 7.4 Hz, 2H), 7.20 (d, *J* = 7.0 Hz, 2H), 7.18 – 7.14 (m, 2H), 7.13 – 7.09 (m, 2H), 7.08 – 7.06 (m, 1H), 6.66 (d, *J* = 15.5 Hz, 1H), 6.00 (dd, *J* = 15.5, 9.3 Hz, 1H), 3.51 (dq, *J* = 14.0, 7.0 Hz, 1H), 3.06 – 2.97 (m, 1H), 2.75 – 2.67 (m, 1H), 2.56 – 2.47 (m, 2H), 2.16 (s, 3H), 1.29 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.1, 167.3, 141.3, 136.3, 135.4, 134.7, 132.0, 131.6, 130.6, 130.3, 128.9, 128.8, 128.6, 127.6, 127.0, 126.2, 126.2, 126.1, 67.8, 43.2, 34.3, 31.2, 19.8, 15.9. **IR** (ν/cm^{-1}): 3384 (br, m), 3220 (br, m), 3062 (w), 3027 (m), 2972 (m), 2930 (m), 2561 (br, m), 1715 (s), 1625 (s), 1523 (s), 1488 (m), 1455 (w), 1231 (m), 1192 (m), 1122 (w), 967 (m), 909 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{25}H_{40}NO_4^+$ 428.2226, found: 428.2237.



Synthesis of methyl 2-benzamido-2-(1-(3-octyloxiran-2-yl)ethyl)pentanoate (48).

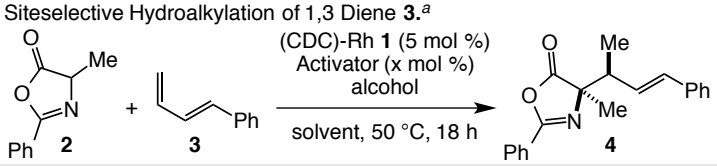
To an 8 mL vial was added 4-(*(E)*-dodec-3-en-2-yl)-2-phenyl-4-propyloxazol-5(4H)-one (8.9 mg, 0.022 mmol, 9:1 dr) and *meta*-chloroperoxybenzoic acid 50-55% by weight (7.6 mg, 0.22 mmol, 1 equiv). The headspace was flushed with N_2 and the reaction solvated with dry benzene (500 µL), the reaction sealed and allowed to stir at 22 °C for 18 h. The solution was concentrated to an oily solid which was purified by SiO_2 gel column chromatography (8:1 Hex/EtOAc to 4:1 Hex/EtOAc) to afford **48** (5.4 mg, 0.013 mmol, 58% yield, 9:1 dr) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.79 (m, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 1H), 3.85 (s, 3H), 2.86 (ddd, *J* = 13.5, 12.0, 4.6 Hz, 1H), 2.82 – 2.80 (m, 1H), 2.72 (dd, *J* = 7.8, 2.2 Hz, 1H), 2.39 (dt, *J* = 14.5, 7.1 Hz, 1H), 1.93 – 1.86 (m, 1H), 1.55 – 1.50 (m, 1H), 1.47 – 1.38 (m, 1H), 1.38 – 1.15 (m, 14H), 1.07 (d, *J* = 7.0 Hz, 3H), 1.00 – 0.94 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.6, 166.2, 135.1, 131.8, 128.8, 127.0, 67.2, 60.0, 59.8, 53.3, 42.8, 34.3, 32.2, 32.0, 29.6, 29.6, 29.3, 26.0, 22.8, 18.0, 14.3, 14.1, 12.6. **IR** (ν/cm^{-1}): 3410 (br, m), 2960 (w), 2928 (s), 2855 (m), 1732 (s), 1671 (s), 1518 (s), 1487 (m), 1271 (w), 1234 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{25}H_{40}NO_4^+$ 418.2957, found: 418.2951.

■ **General procedure for exploring the effect of the alcohol additive on hydroalkylation Table 6:**

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with oxazalones, PhCDC-Rh-styrene (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and phenylbutadiene (13.0 mg, 0.100 mmol) were combined in the glove box, solvated with toluene (200 μL, 0.5 M) and allowed to stir at 22 °C for 10 minutes. To this solution, 4-methyl-2-phenyloxazol-5(4H)-one (26.3 mg, 0.150 mmol) was added. The reaction was sealed with a Teflon® septum cap and removed from the glove box. To this reaction the appropriate alcohol additive was added either: 1) Inside the glove [eg: menthol (9.4 mg, 0.06 mmol), (R)-BINOL (17.0 mg, 0.060 mmol), TADDOL-P(O)OH (31.7 mg, 0.060 mmol), (S,S)-hydrobenzoin (12.9 mg, 0.060 mmol) or (S,S)-diphenylethylenediamine (12.7 mg, 0.060 mmol)], or 2) Outside the glove box via syringe after sparging the alcohol with N_2 [eg: methanol (2.4 μL, 0.060 mmol), isopropanol (4.6 μL, 0.060 mmol), *tert*-butanol (5.7 μL, 0.060 mmol)]. The reaction were allowed to stir at 50 °C for 18 h. The reaction was cooled to room temperature and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and both the conversion and diastereoselectivity analyzed by NMR spectroscopy. Reactions with a chiral additive were purified by by SiO_2 gel column chromatography (20:1 Hex/Et2O) before being assayed on an Agilent 1220 LC System with a Daicel ChiralPak IA column (99:1 Hexanes/Isopropanol, 1 mL/min, 210 nm).

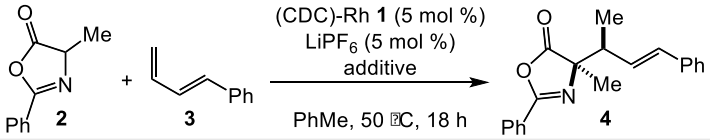
Table 1. Survey of Conditions for (CDC)-Rh-Catalyzed Diastereo- and Siteselective Hydroalkylation of 1,3 Diene **3.**[a]

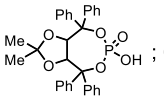


entry	activator; mol %	solvent	alcohol[d]	yield (%)[c]; dr[b]
1	AgCl; 5	PhMe	-	0; -
2	$LiBF_4$; 5	PhMe	-	8; 4:1
3	$LiPF_6$; 5	PhMe	-	17; 10:1
4	$LiPF_6$; 5	PhCl	-	21; 6:1
5	$LiPF_6$; 5	THF	-	21; 4:1
6	$LiPF_6$; 5	DCM	-	20; 3:1
7	$LiPF_6$; 5	PhMe	MeOH	26; 3:1
8	***$LiPF_6$; 5***	***PhMe***	***^{i}PrOH***	***85; 19:1***
9	$LiPF_6$; 5	PhMe	^{t}BuOH	29; 5:1
10[e]	$LiPF_6$; 5	PhMe	^{i}PrOH	0; -

[a]All reactions performed under N_2 atm. [b]Values determined by analysis of 400 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with trimethylsilyl ether as an internal standard. [c]Yields of purified products are an average of two runs. [d]A solvent ratio of 40:1 PhMe:alcohol used. [e]Reaction run with $[Rh(cod)Cl]_2$ as catalyst with $NaBAr^F{}_4$ additive.

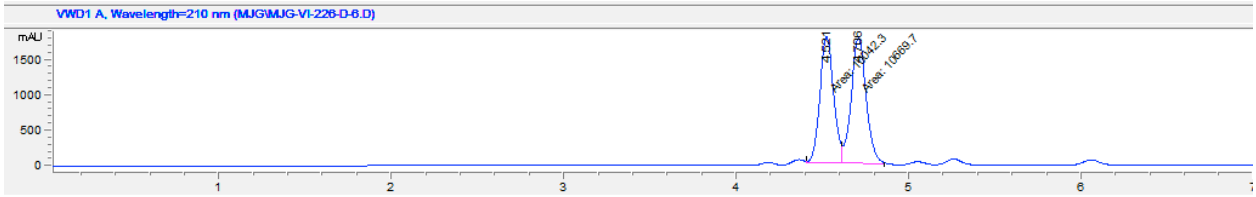
Table 6. Exploring the Influence of the Alcohol on Reaction Efficiency and Selectivity.



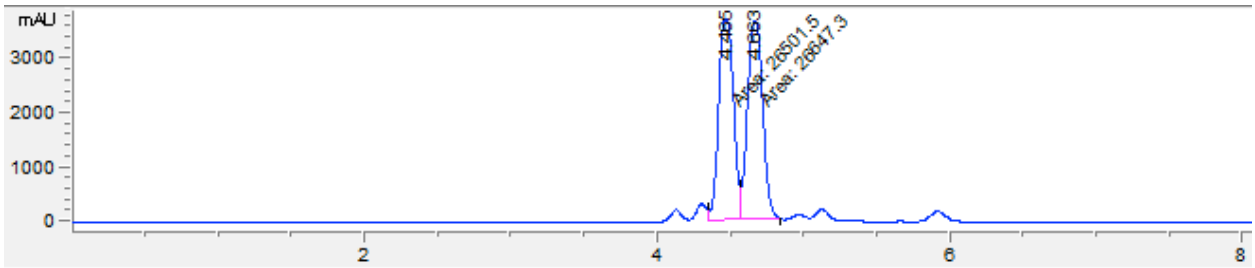
entry	additive; mol %	NMR Yield (%)[a]; dr[b]	% ee
1	MeOH; 60	68; 7:1	-
2	iPrOH; 60	84; 19:1	-
3	tBuOH; 60	87; 12:1	-
4	Menthol; 60	62; >20:1	0
5	*(R)*-BINOL; 60	56; 15:1	0
6	*(S,S)*-hydrobenzoin; 60	53; 10:1	0
7	 ; 60	13; 2:1	0
8	(*S,S)*-diphenylethylenediamine; 10	27; 18:1	0

[a]Values determined by analysis of 500 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with trimethylsilyl ether as an internal standard. [b]NMR Yield reported for conversion to the *cis*- and *trans*-**4** products.

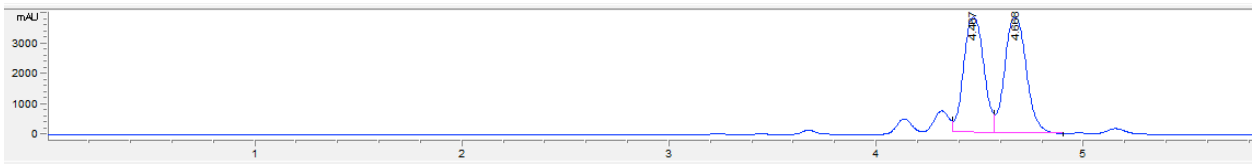
Racemic Trace:



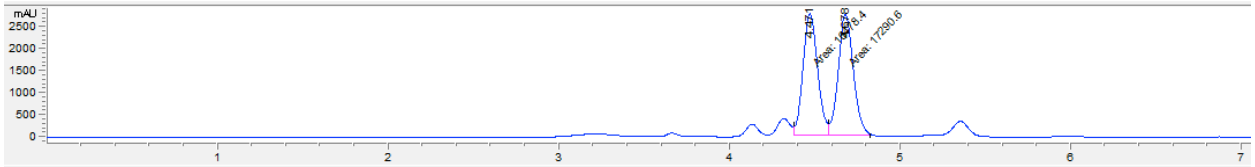
Menthol:



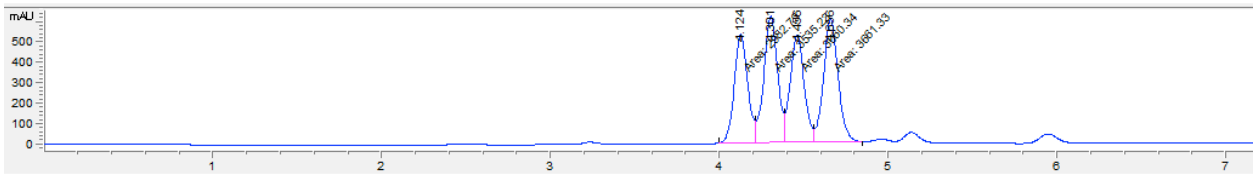
***(R)*-BINOL:**



***(S,S)*-hydrobenzoin:**

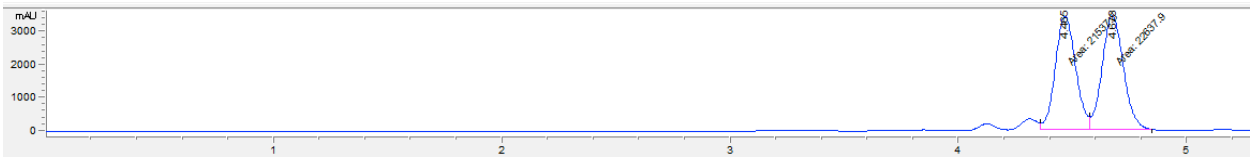


***(R,R)*-TADDOL-P(O)OH:**

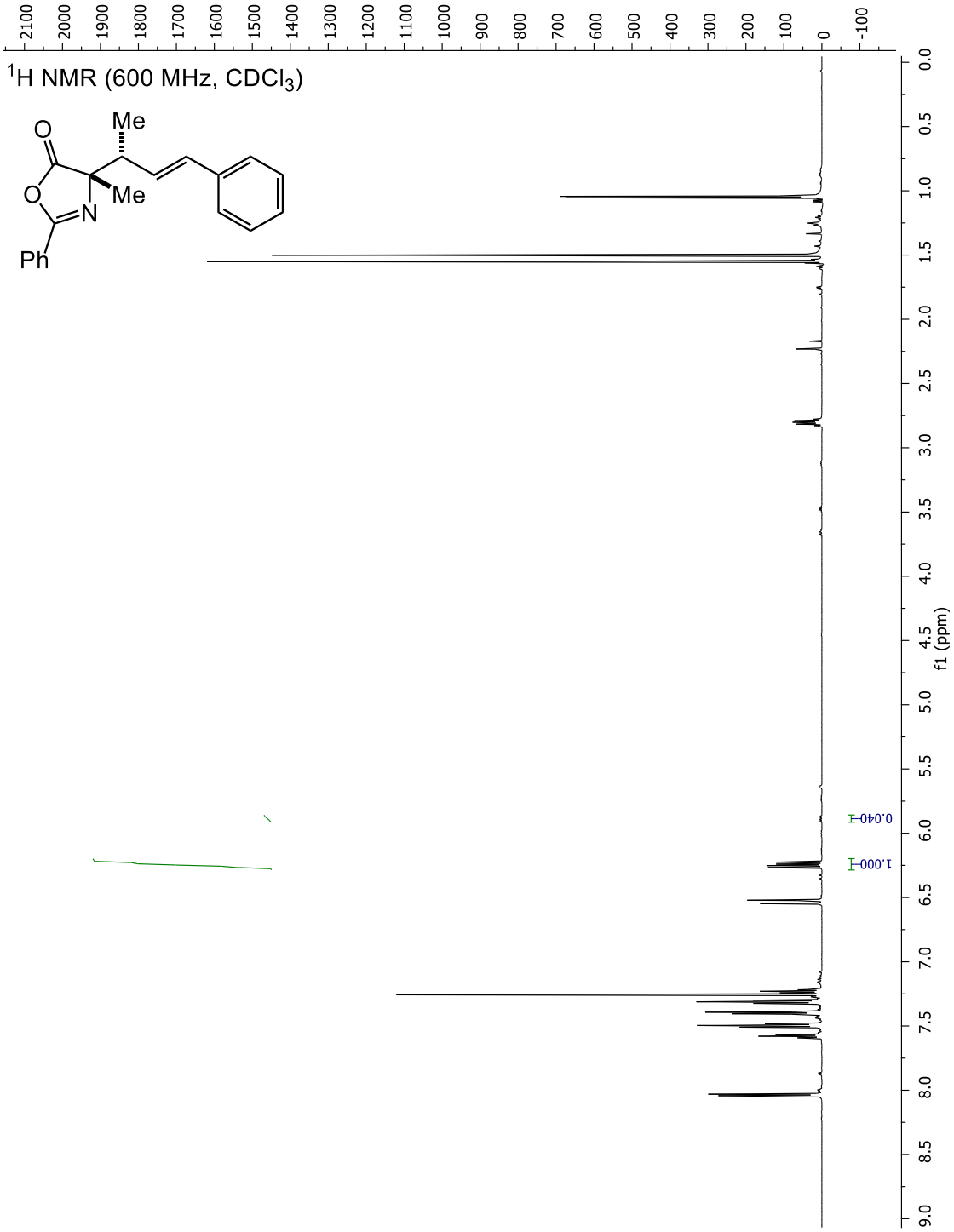


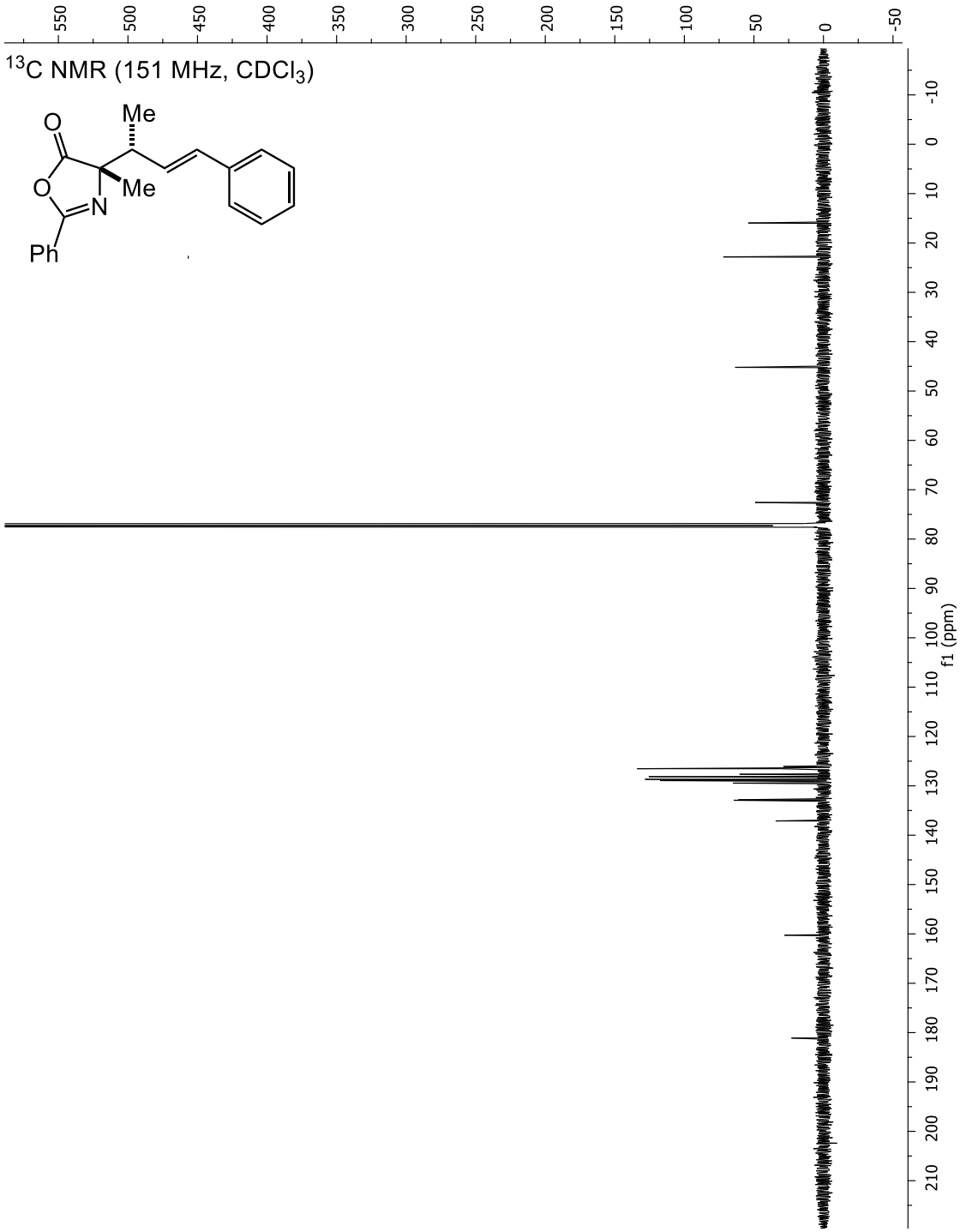
Note: Purification resulted in a 1:1 mixture of diastereomers. Both the *syn* and *anti* diastereomers show no significant enantioselectivity.

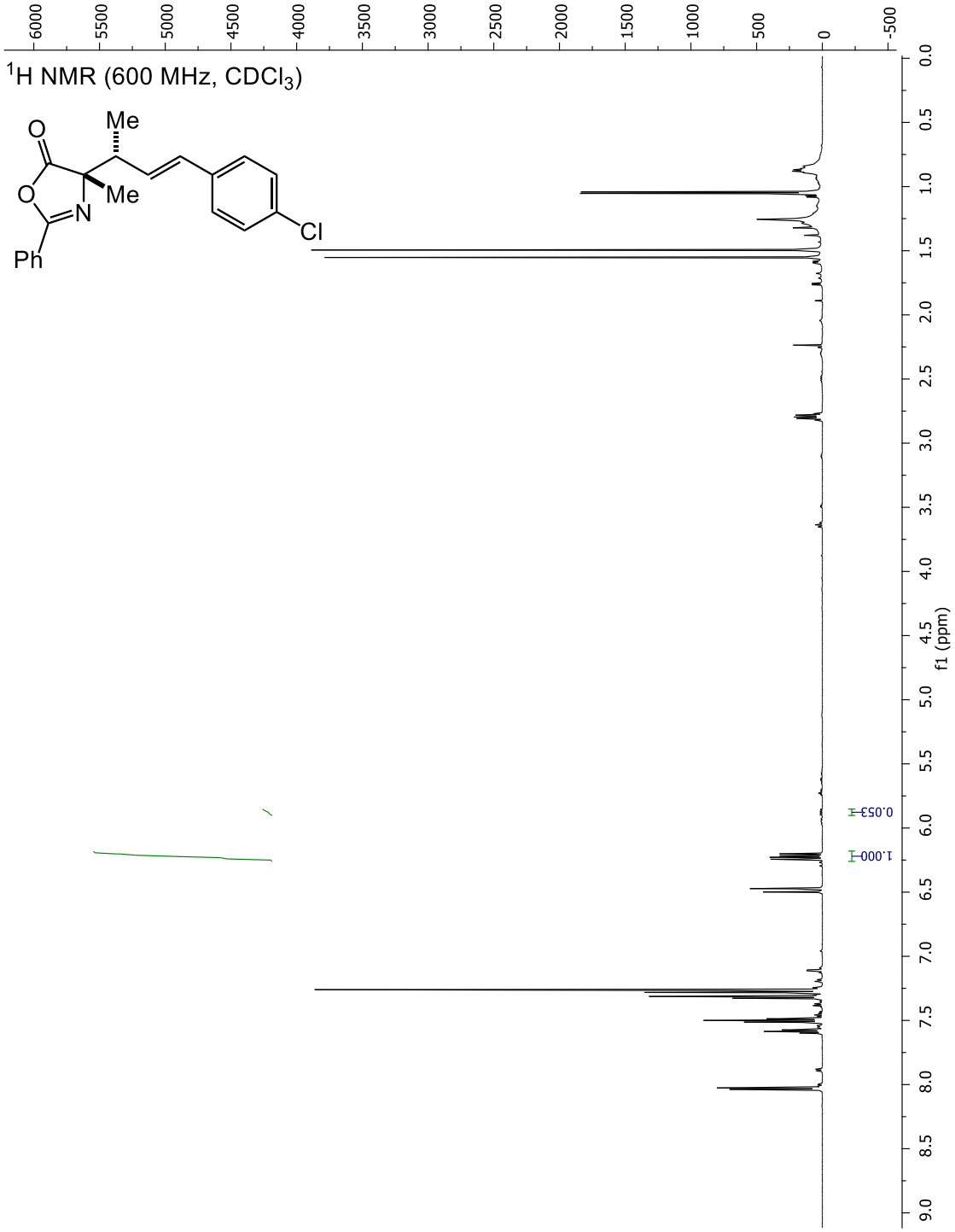
***(S,S)*-diphenylethylenediamine:**

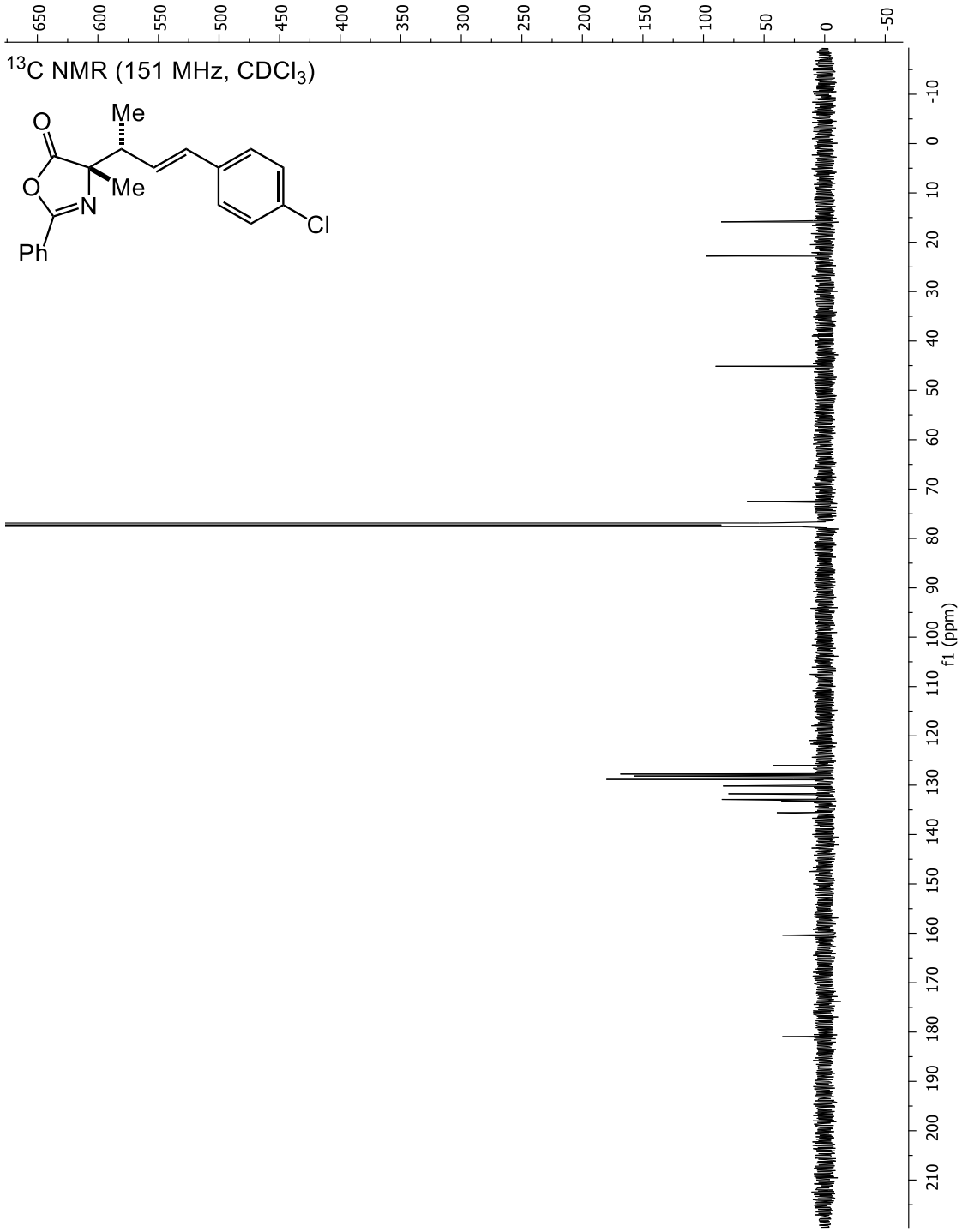


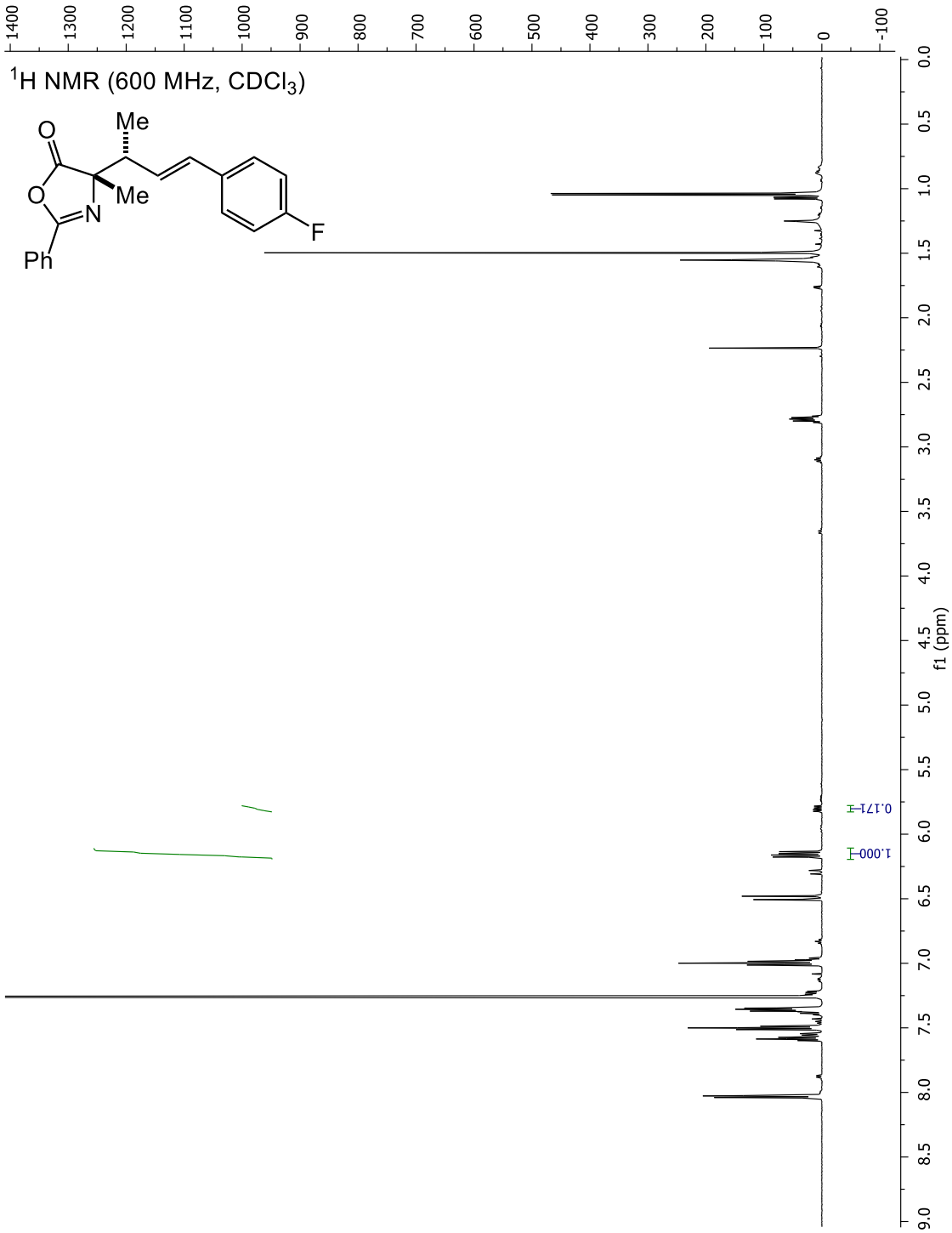
^{1}H NMR (600 MHz, $CDCl_3$)



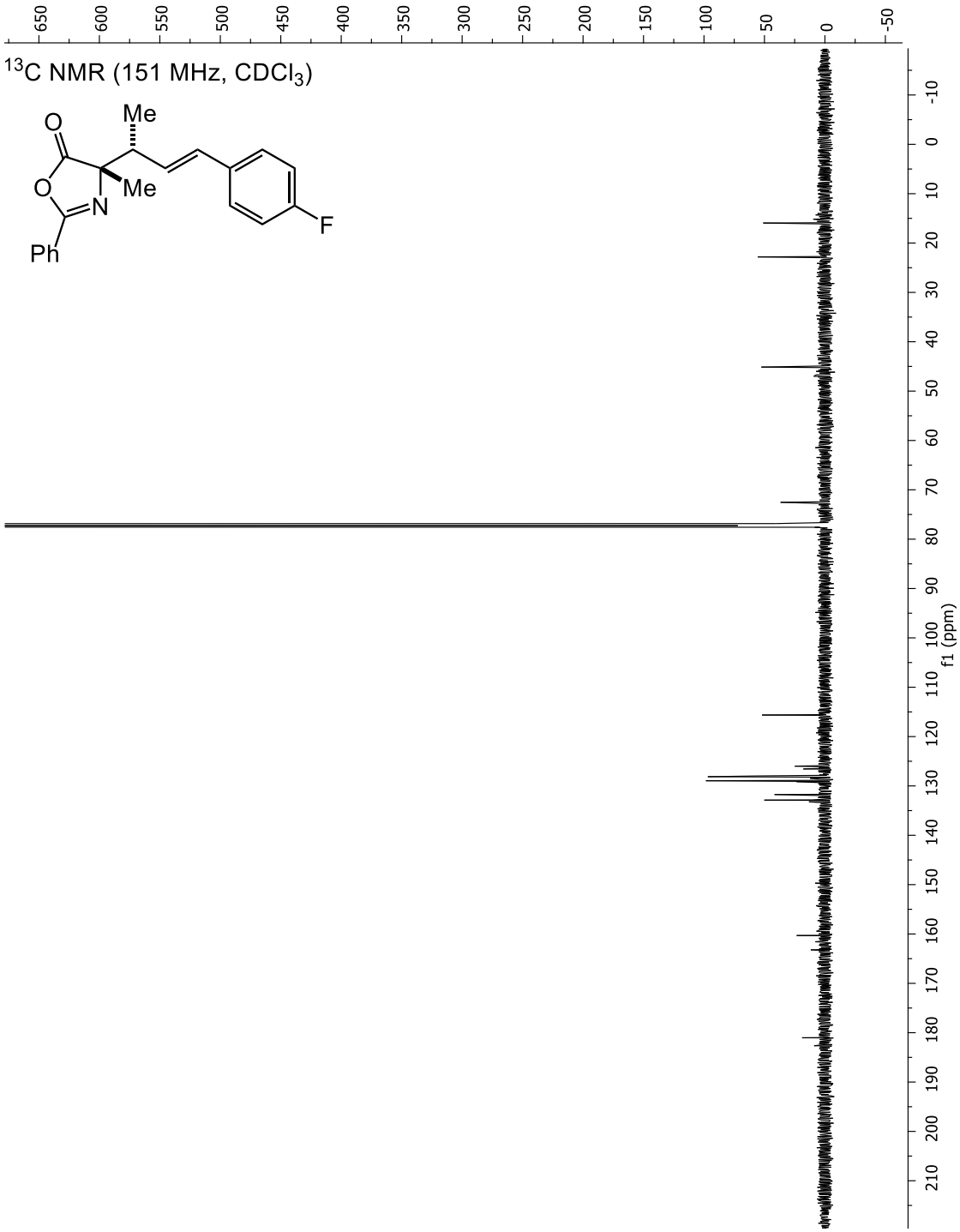

^{13}C NMR (151 MHz, $CDCl_3$)
O
Me
O
Me
N
Ph
f1 (ppm)


1H NMR (600 MHz, CDCl3)
O
Me
O
Me
N
Ph
Cl
0.053
1.000
f1 (ppm)

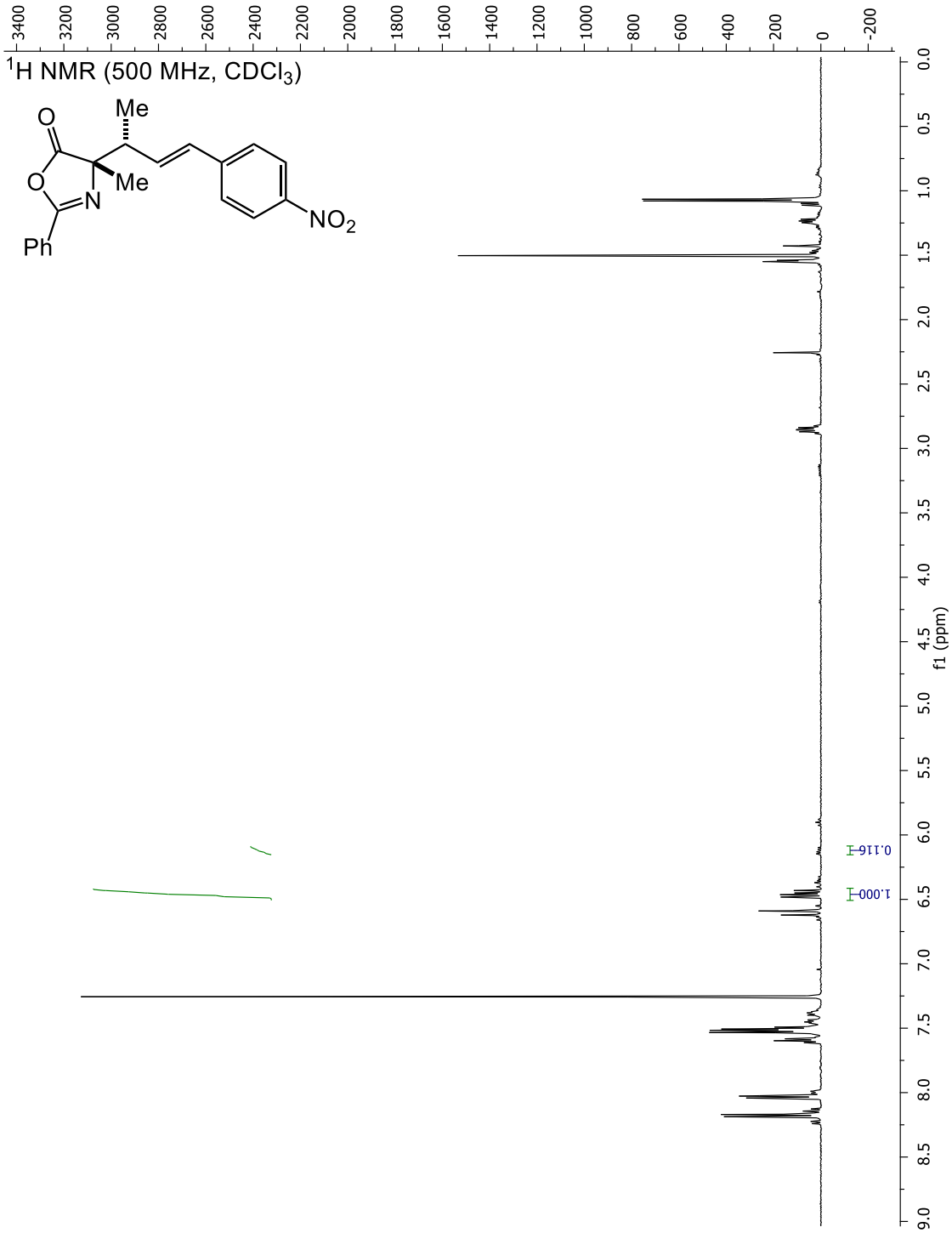

13C NMR (151 MHz, CDCl3)
O
Me
O
Me
N
Ph
Cl
f1 (ppm)


1H NMR (600 MHz, CDCl3)
O
Me
O
Me
N
Ph
F
0.171
1.000
f1 (ppm)

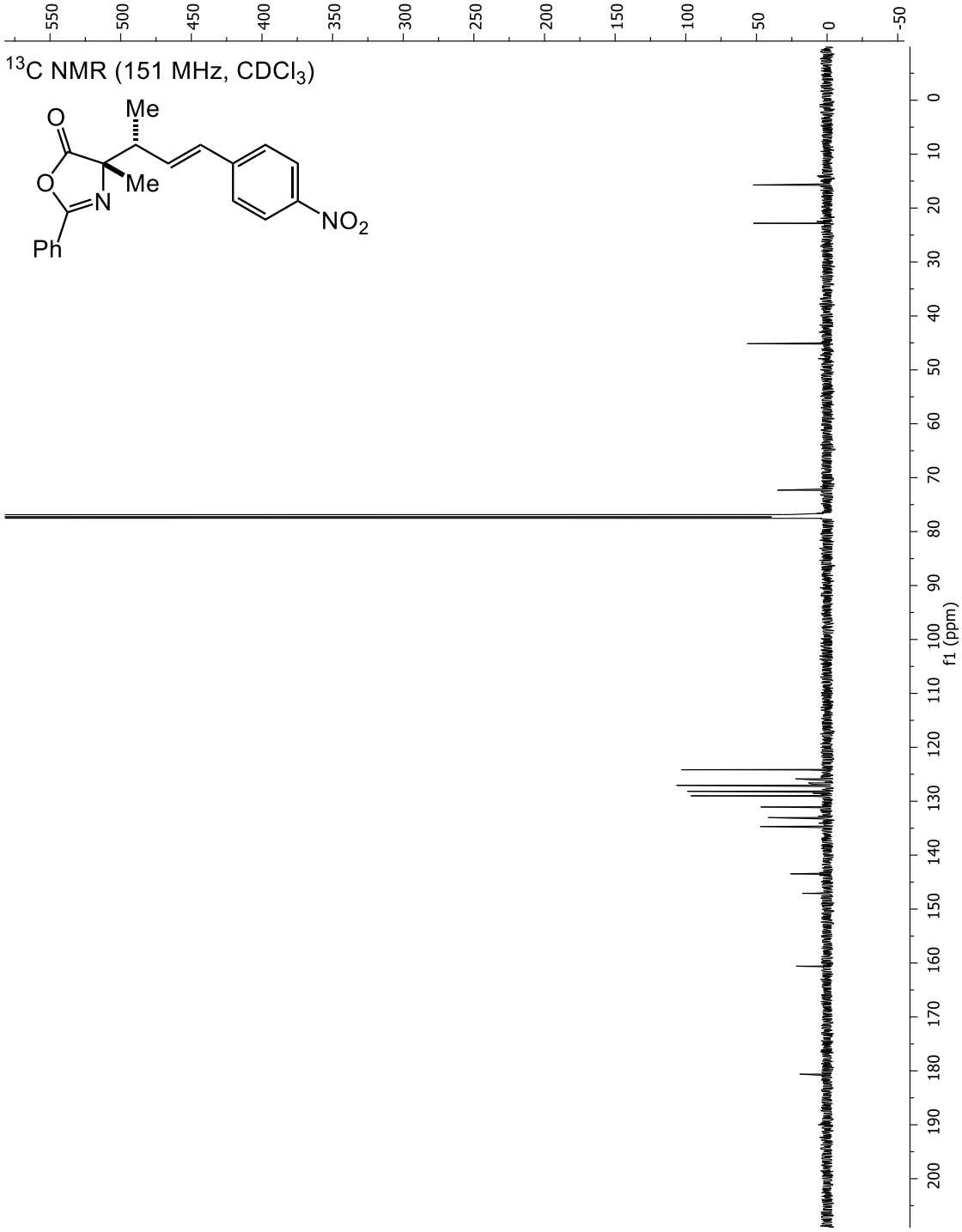
^{13}C NMR (151 MHz, $CDCl_3$)

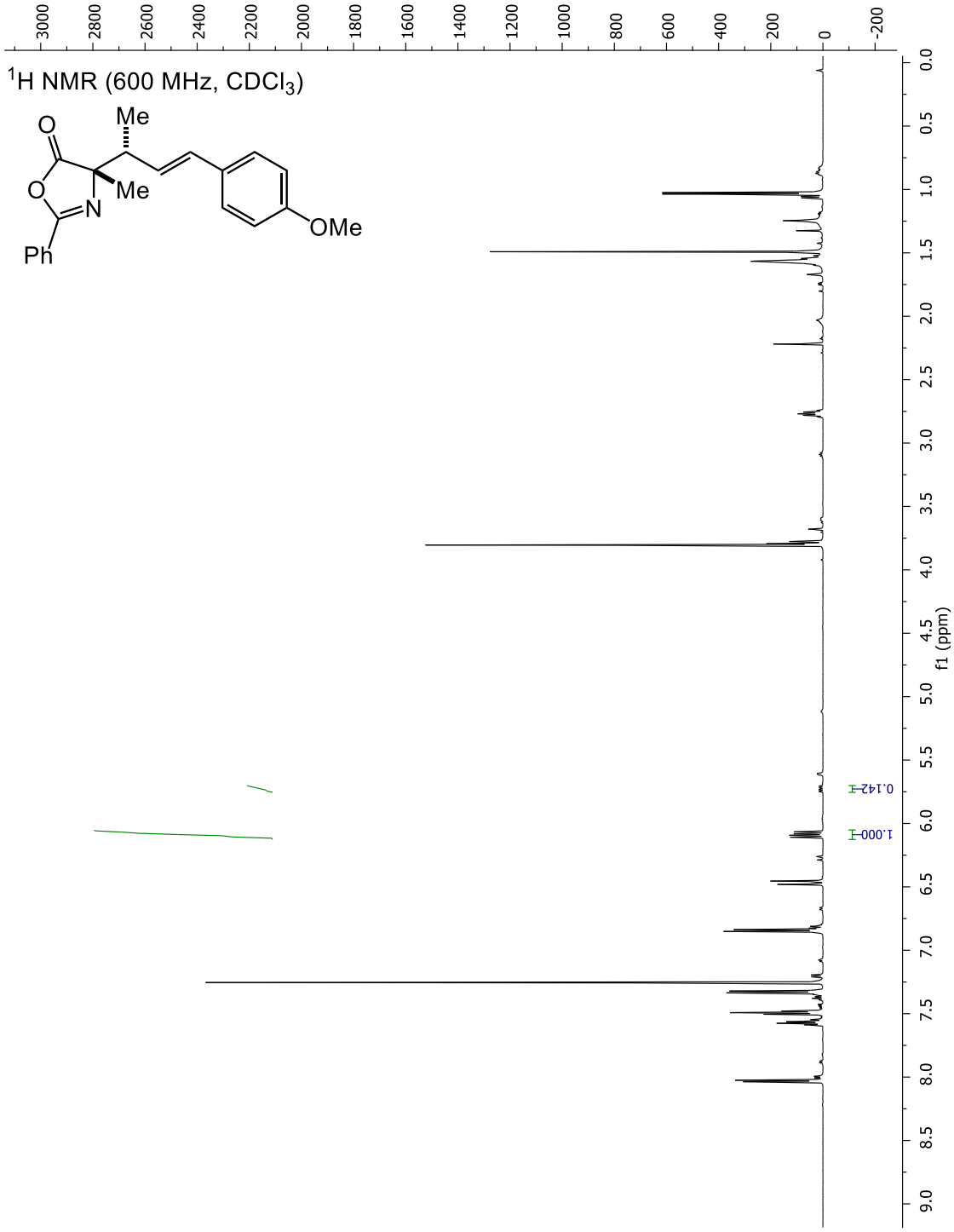


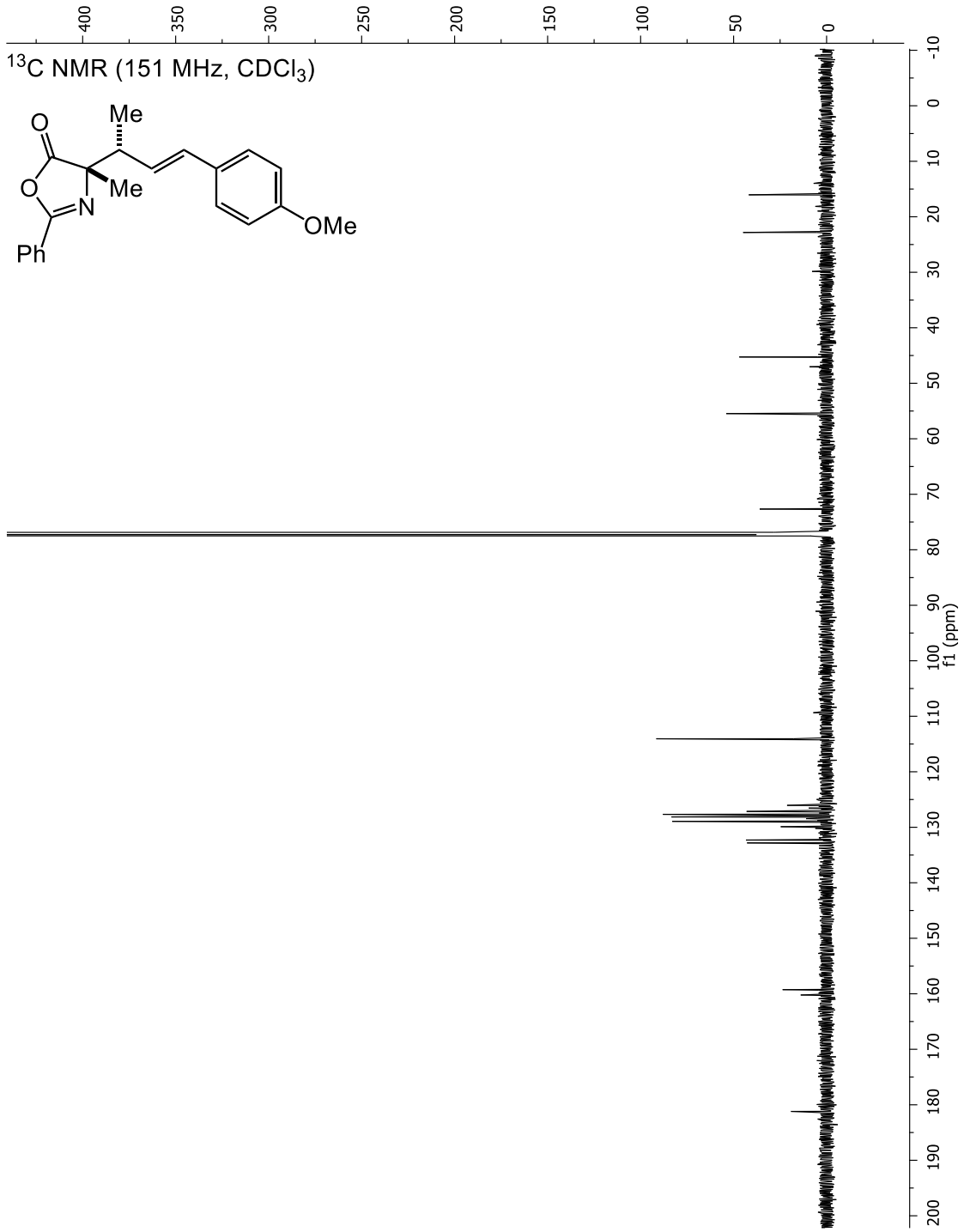
^{1}H NMR (500 MHz, $CDCl_3$)

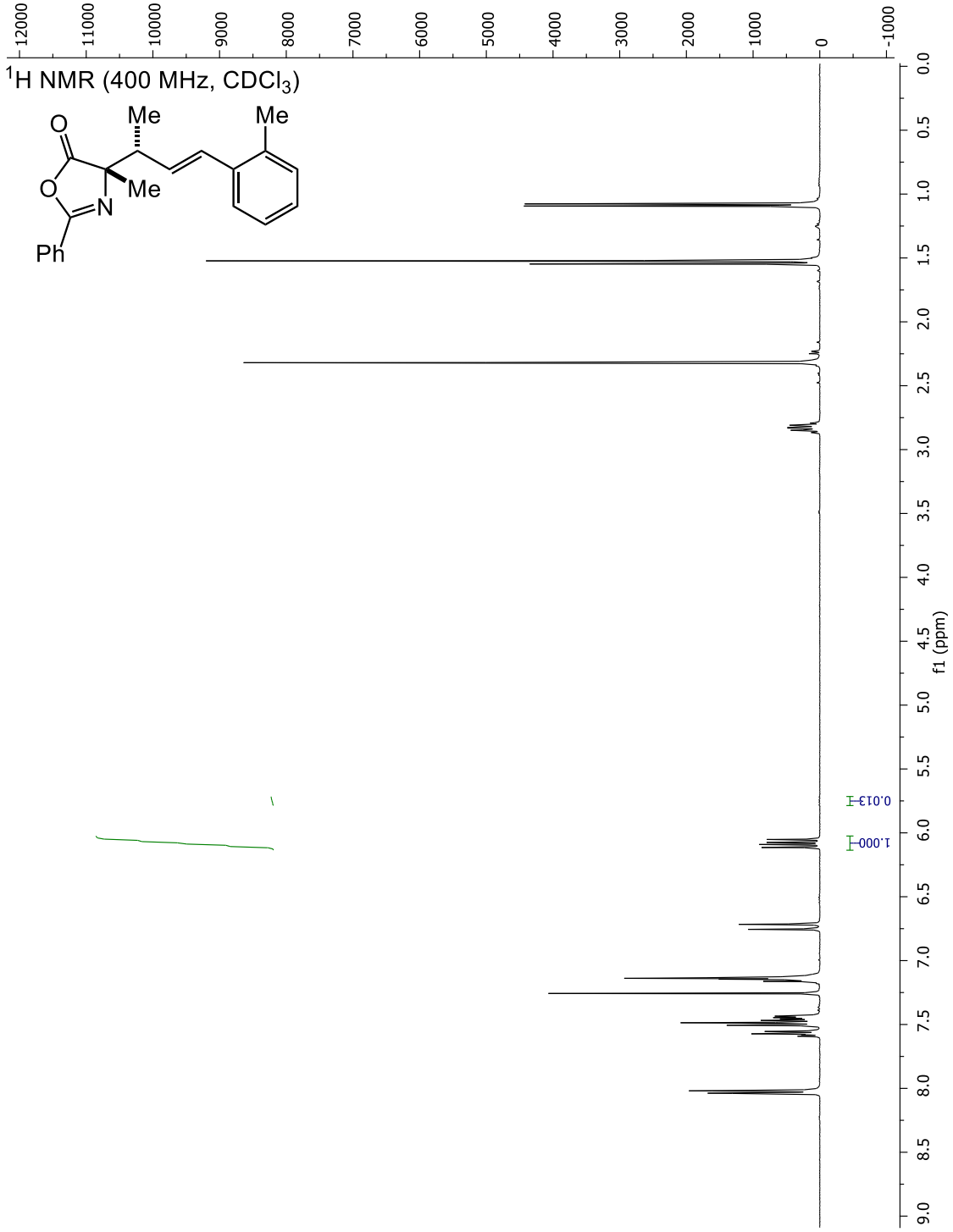


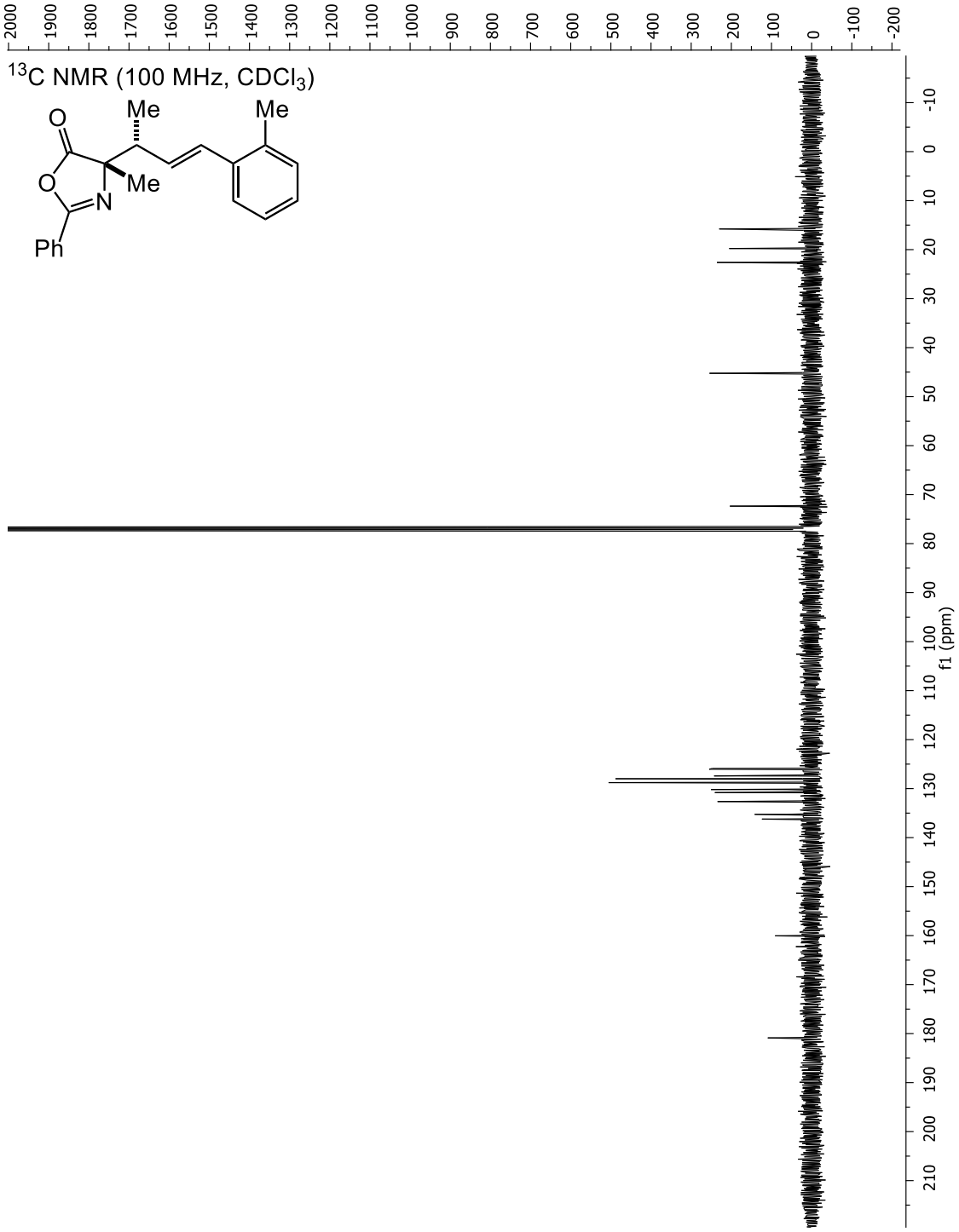
^{13}C NMR (151 MHz, $CDCl_3$)



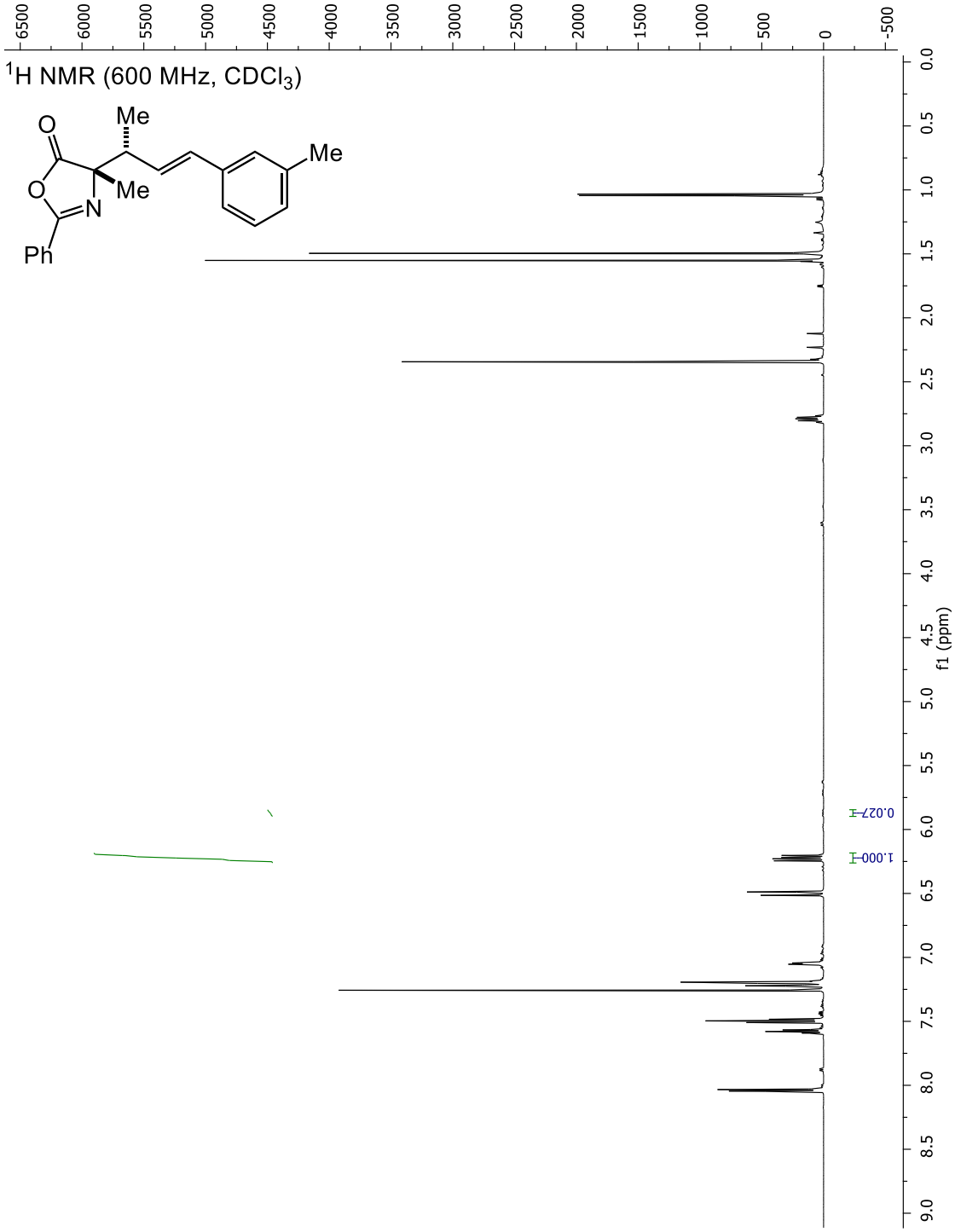

1H NMR (600 MHz, CDCl3)
Me
O
O
Me
N
Ph
OMe
1.000
0.142
f1 (ppm)

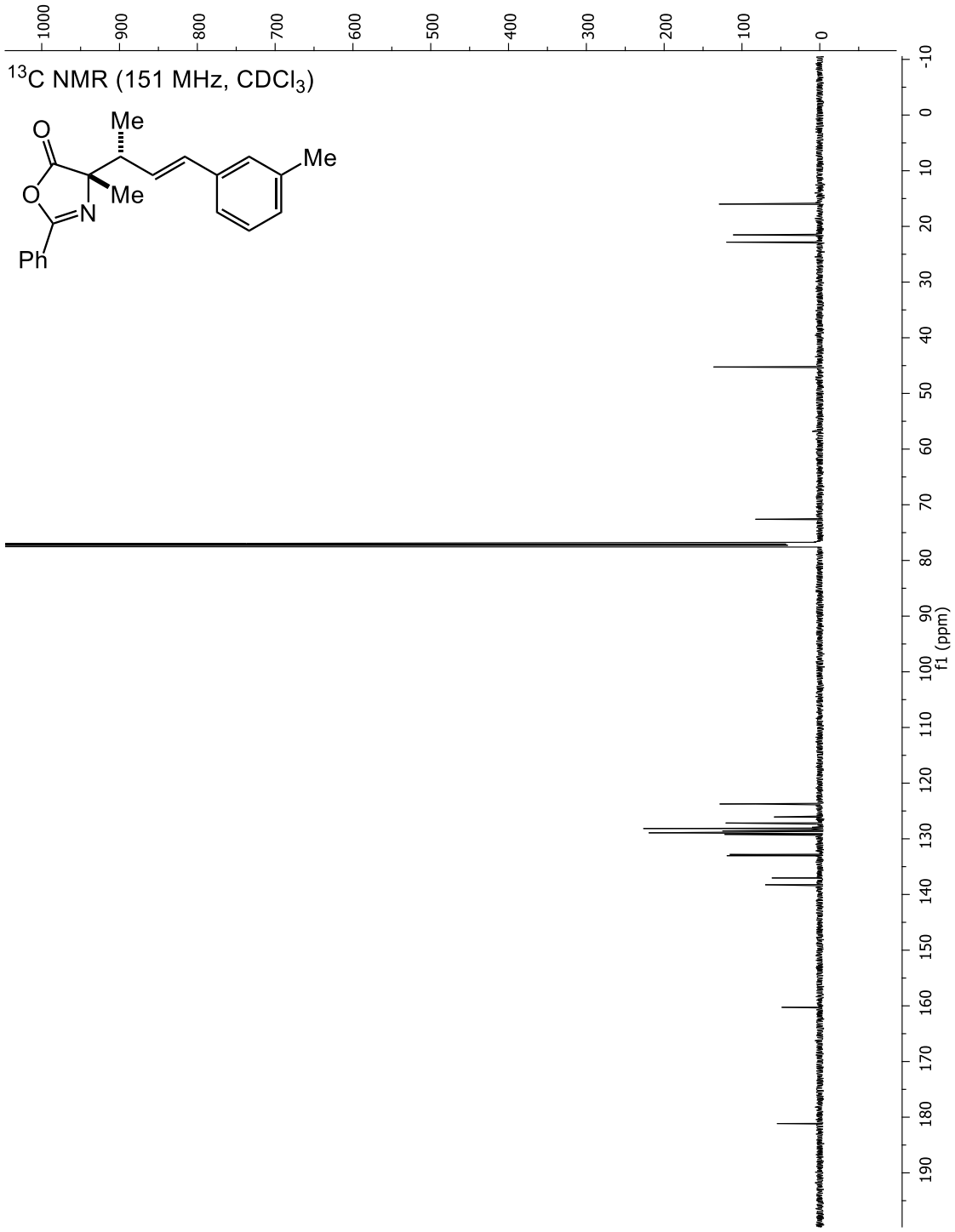

13C NMR (151 MHz, CDCl3)
O
Me
O
Me
N
Ph
OMe
f1 (ppm)

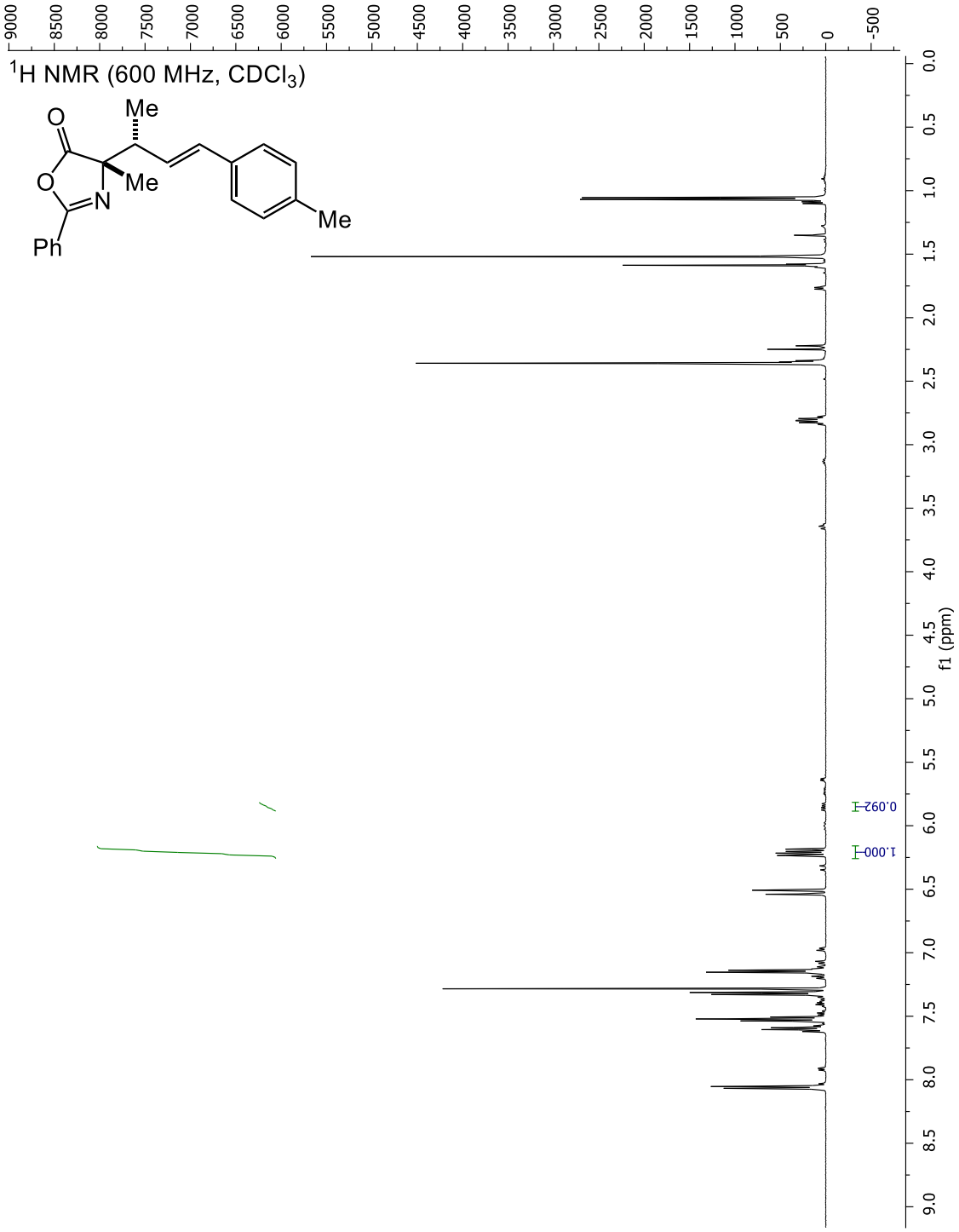

1H NMR (400 MHz, CDCl3)
O
Me
Me
O
Me
N
Ph
0.013
1.000
f1 (ppm)

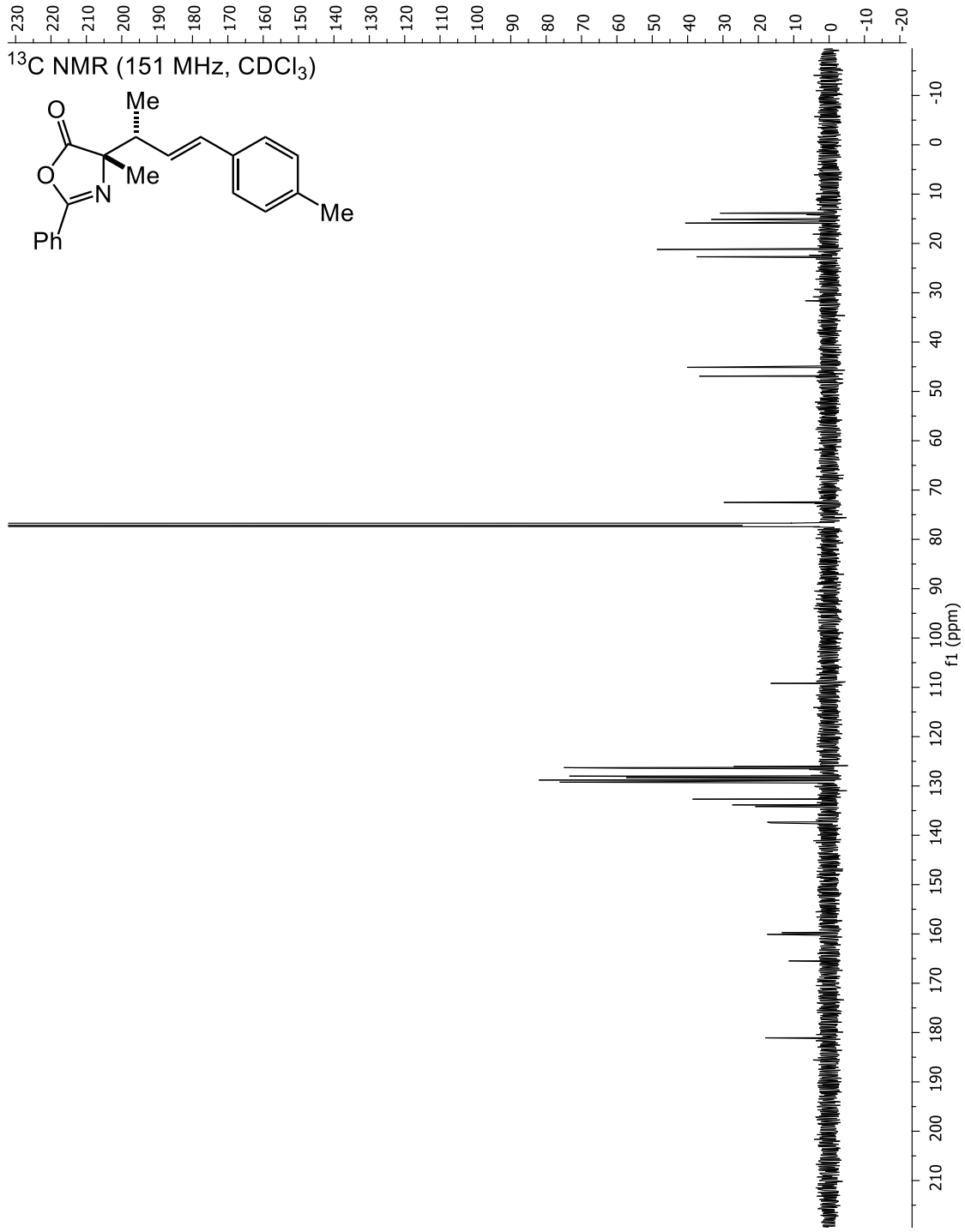

13C NMR (100 MHz, CDCl3)
O
Me
Me
O
Me
N
Ph
f1 (ppm)

^{1}H NMR (600 MHz, $CDCl_3$)

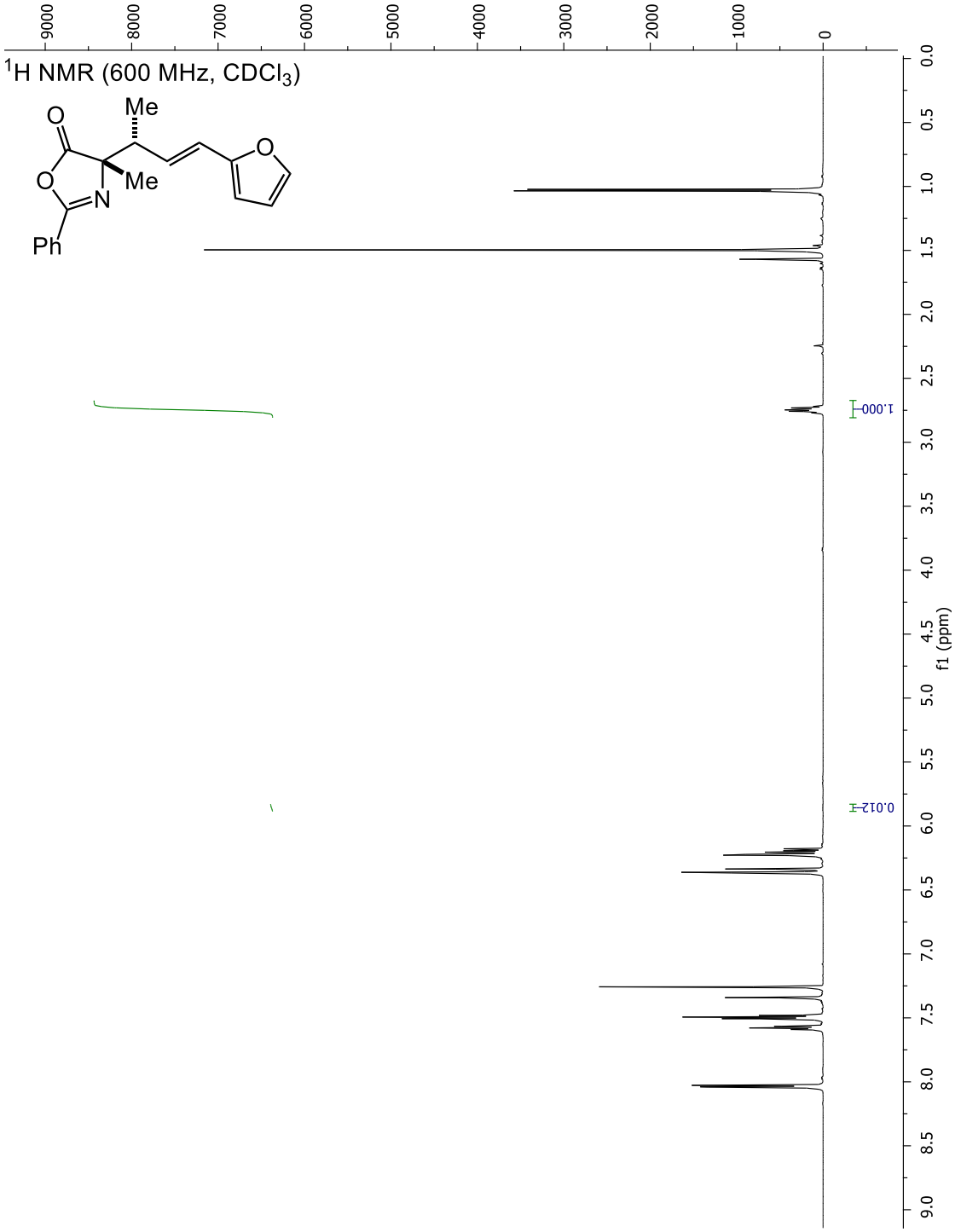


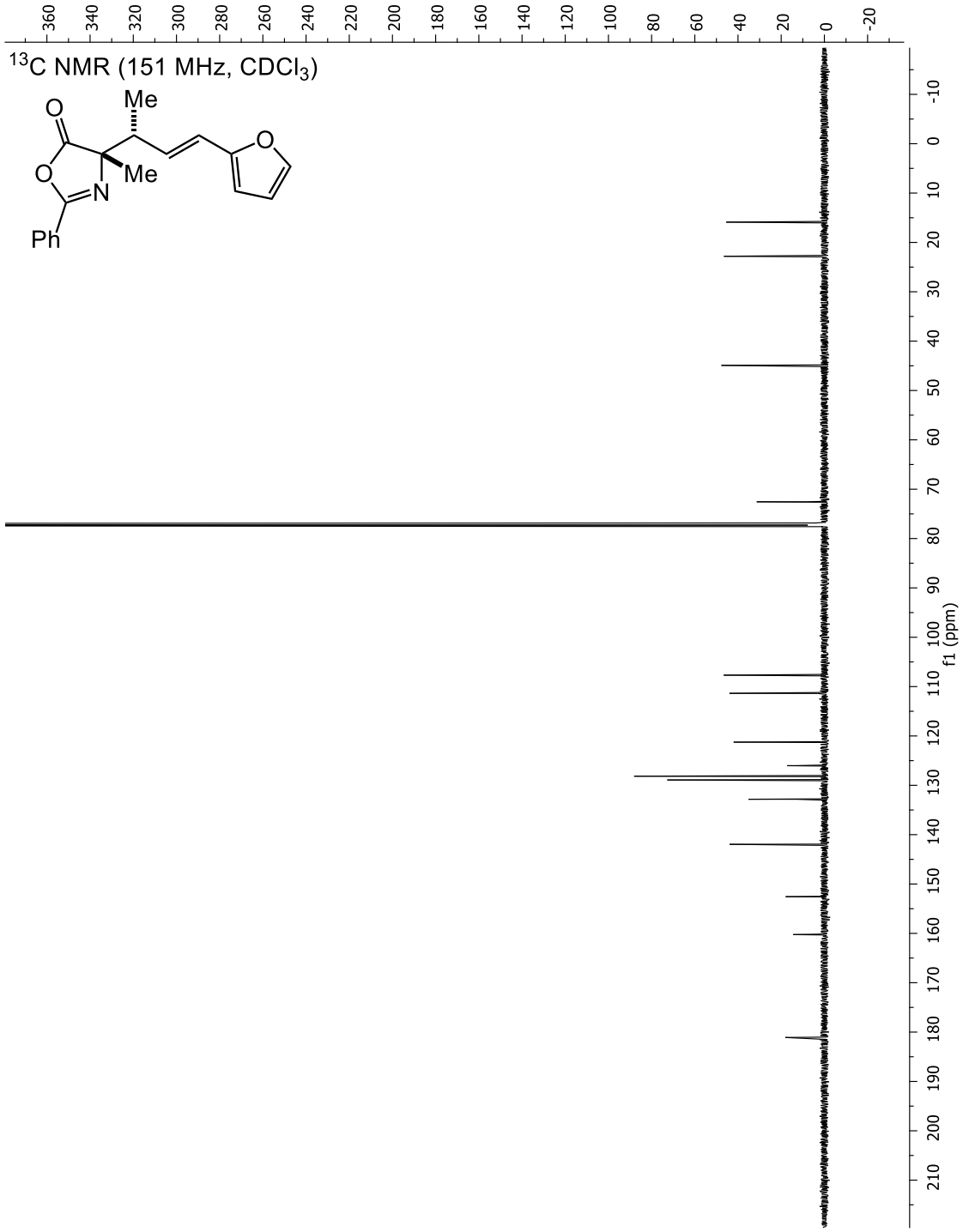

13C NMR (151 MHz, CDCl3)
O
Me
Me
O
N
Me
Ph
f1 (ppm)

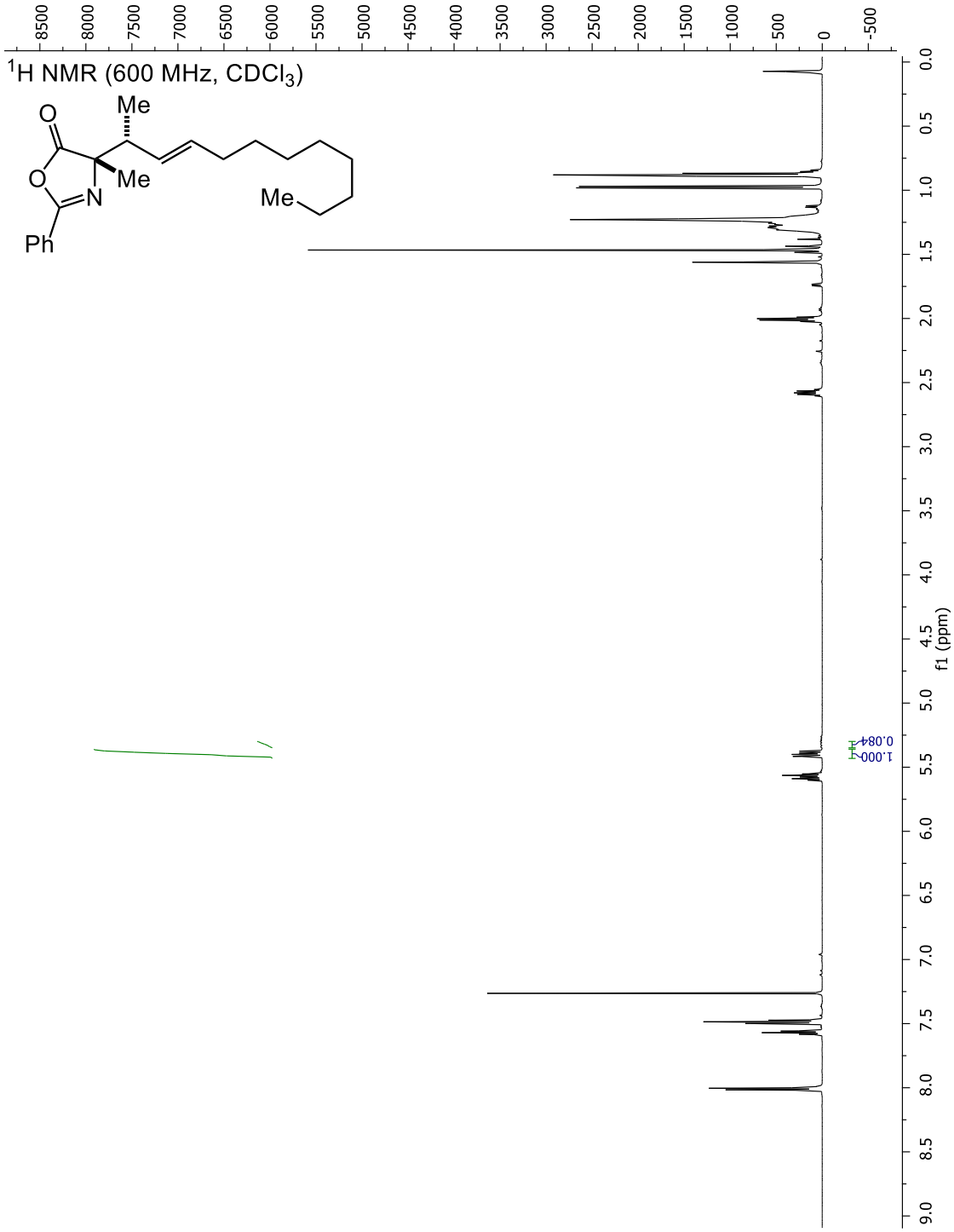

1H NMR (600 MHz, CDCl3)
O
Me
O
Me
N
Ph
Me
1.000
0.092
f1 (ppm)

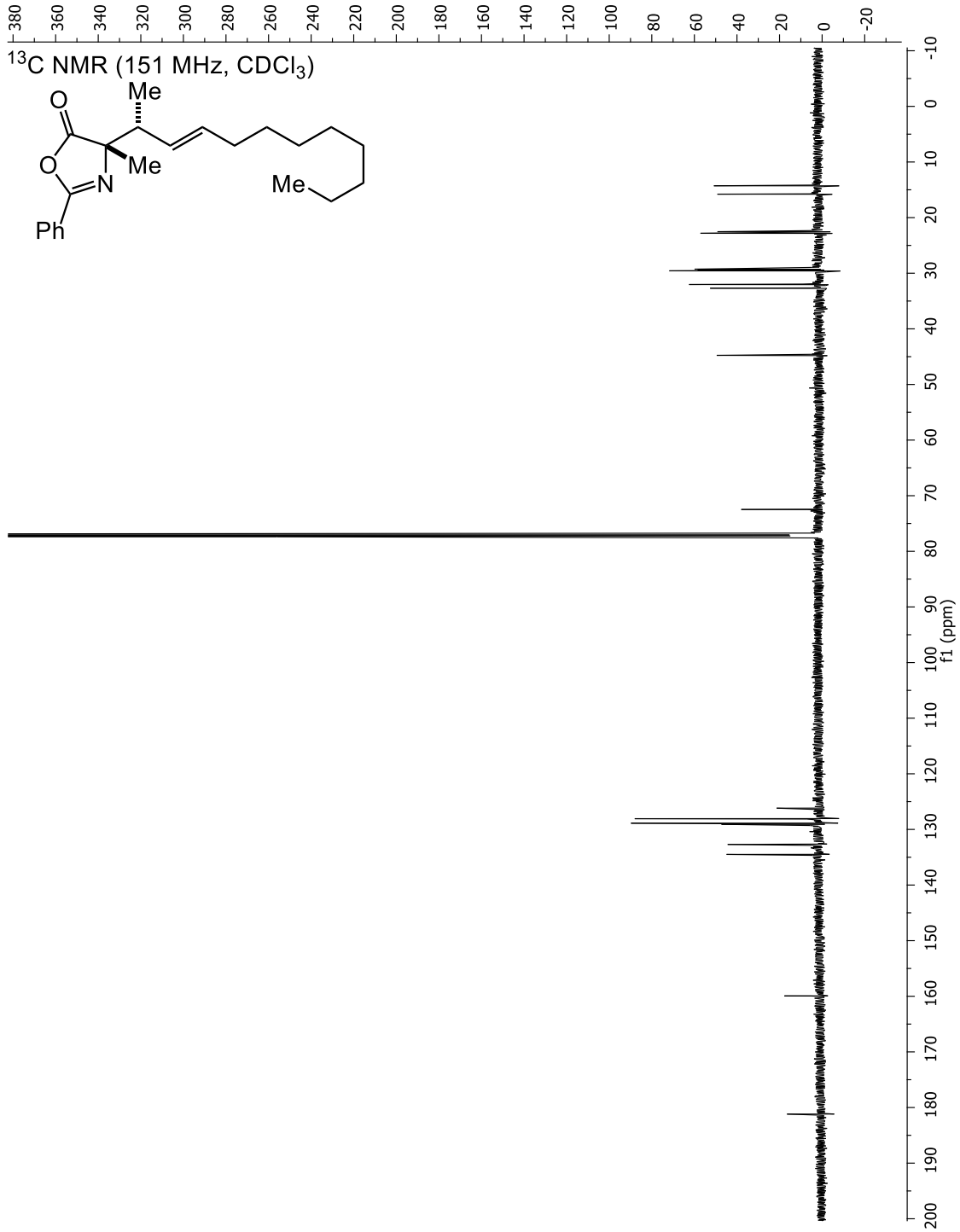

13C NMR (151 MHz, CDCl3)
O
Me
O
Me
N
Ph
Me
f1 (ppm)

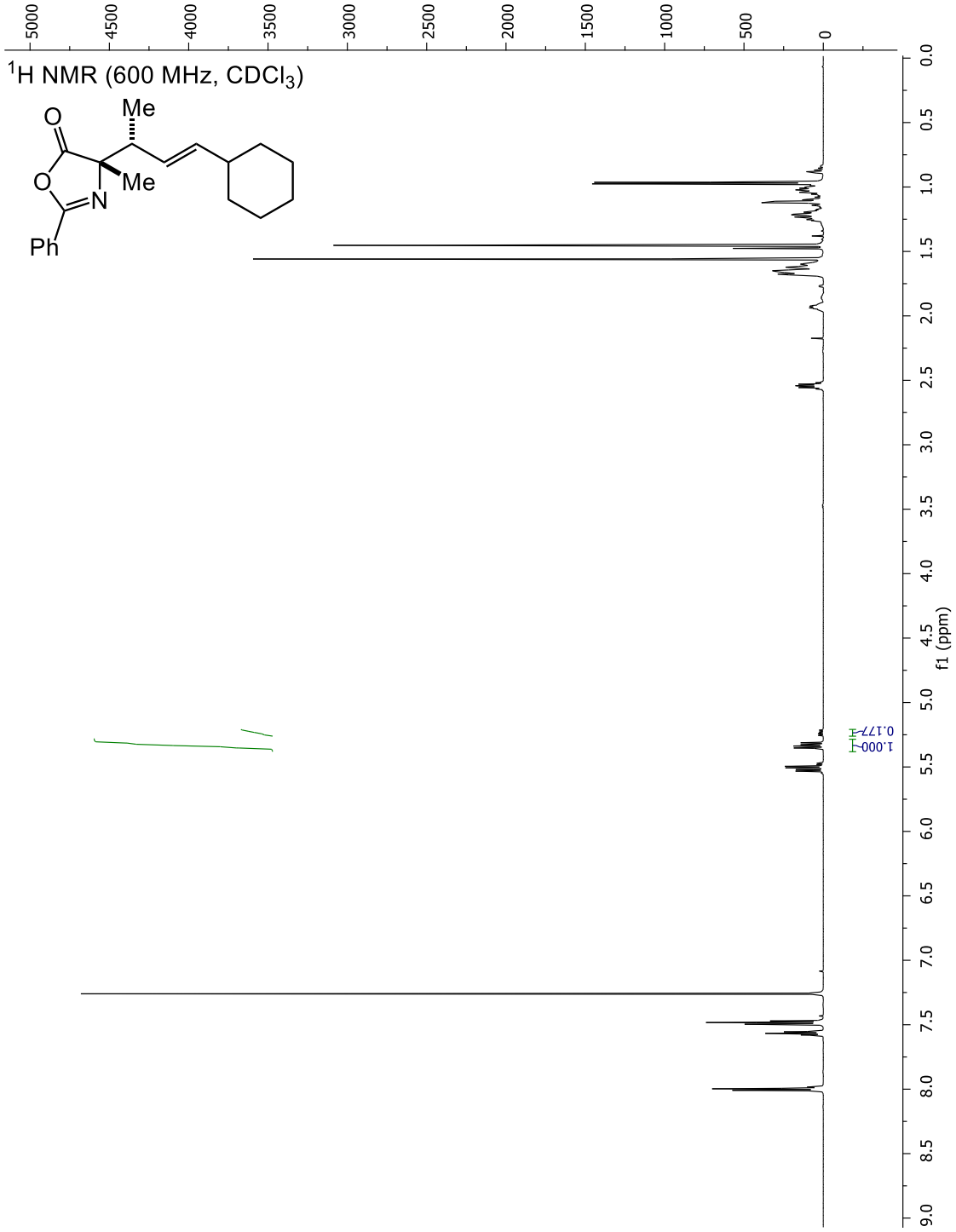
^{1}H NMR (600 MHz, $CDCl_3$)

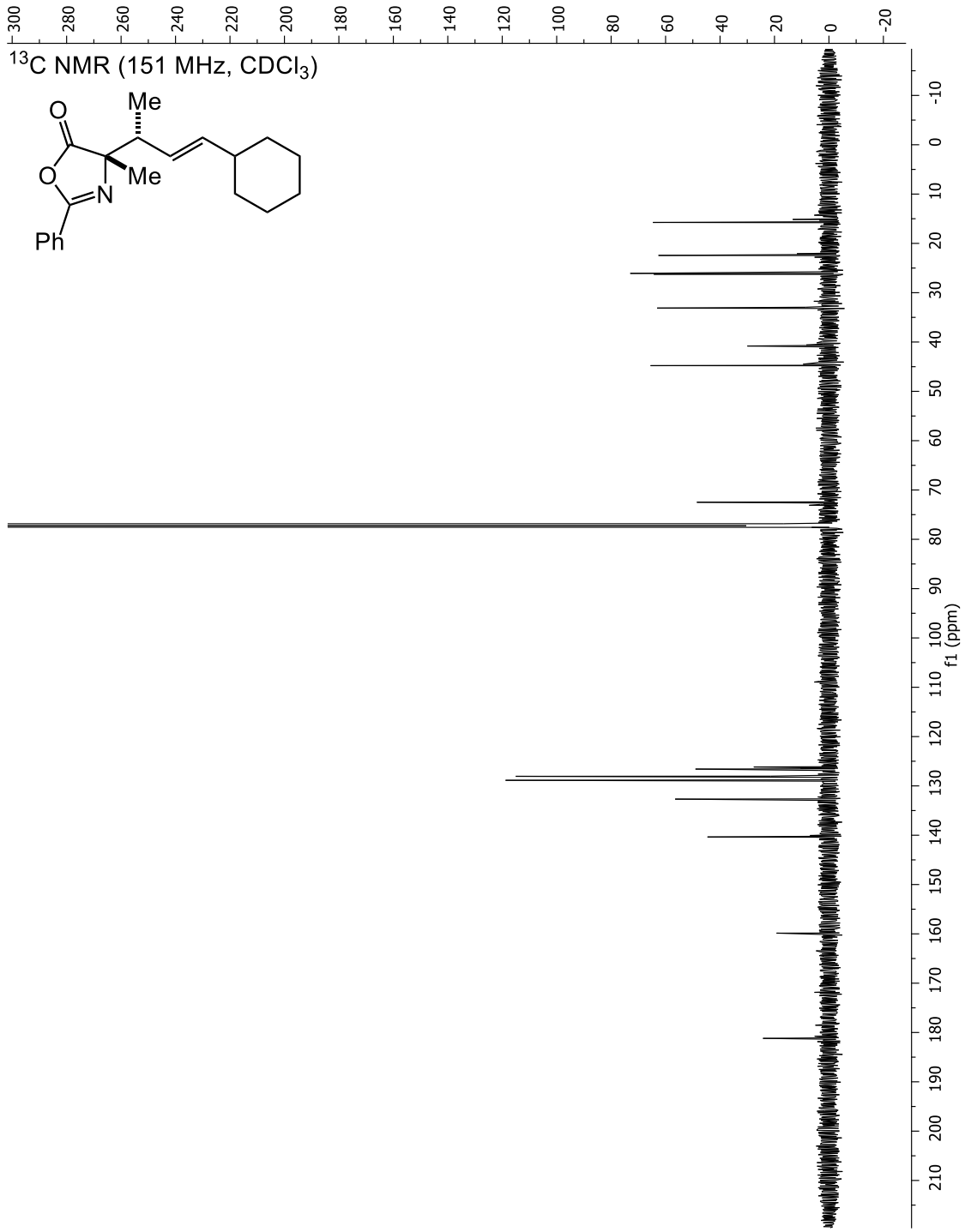


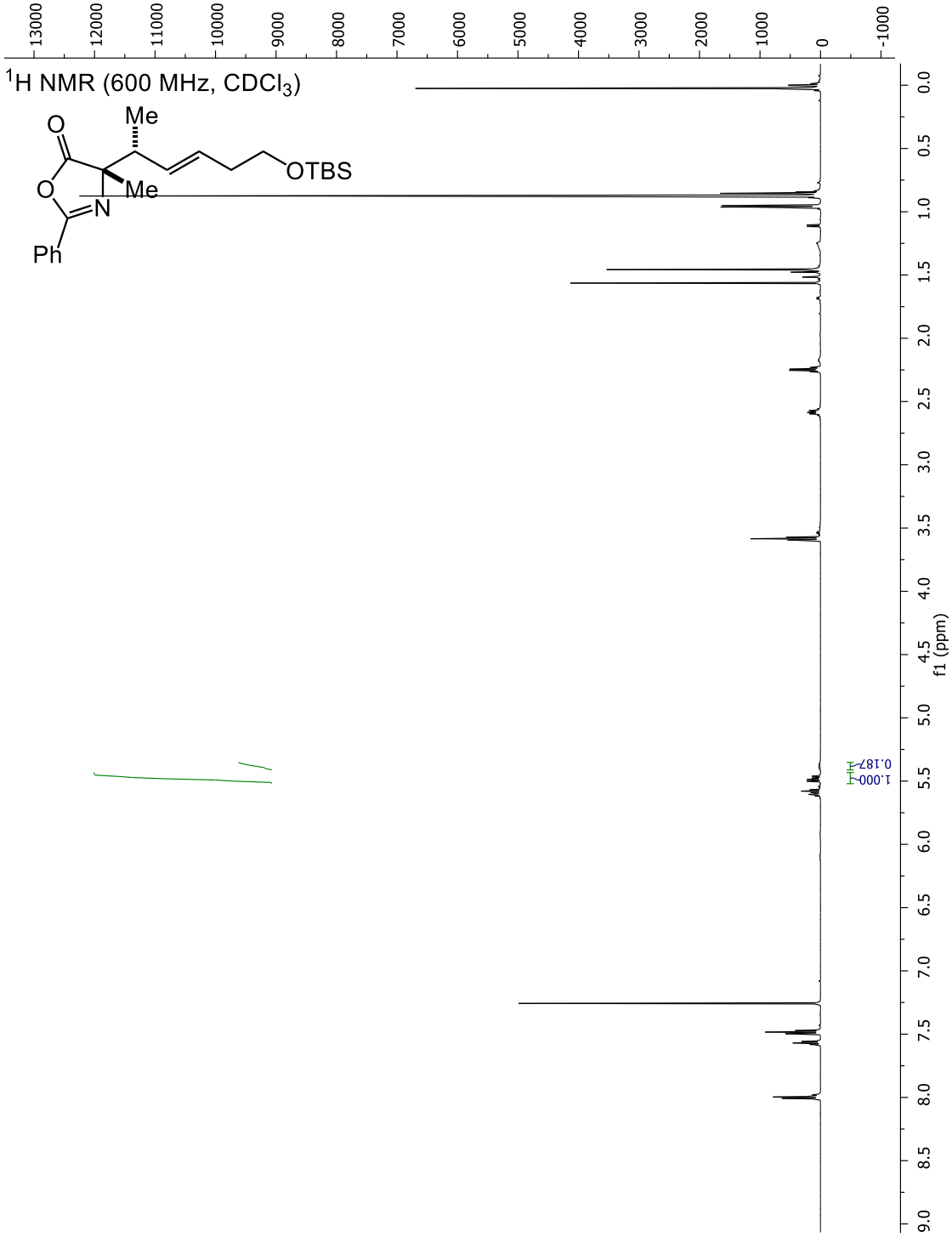

13C NMR (151 MHz, CDCl3)
O
Me
O
Me
N
Ph
O
f1 (ppm)

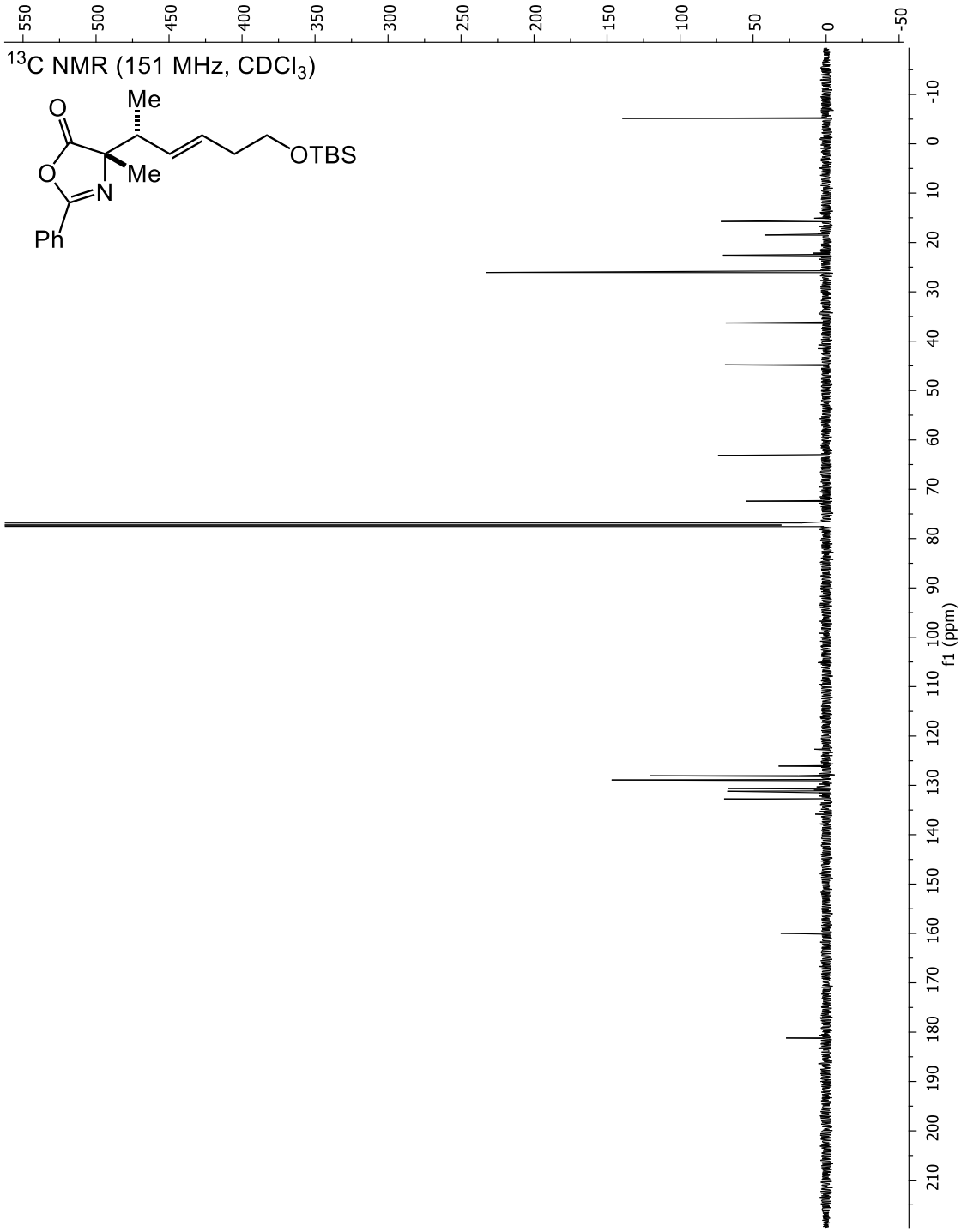

1H NMR (600 MHz, CDCl3)
Me
O
O
Me
N
Me
Ph
f1 (ppm)
1.000
0.084

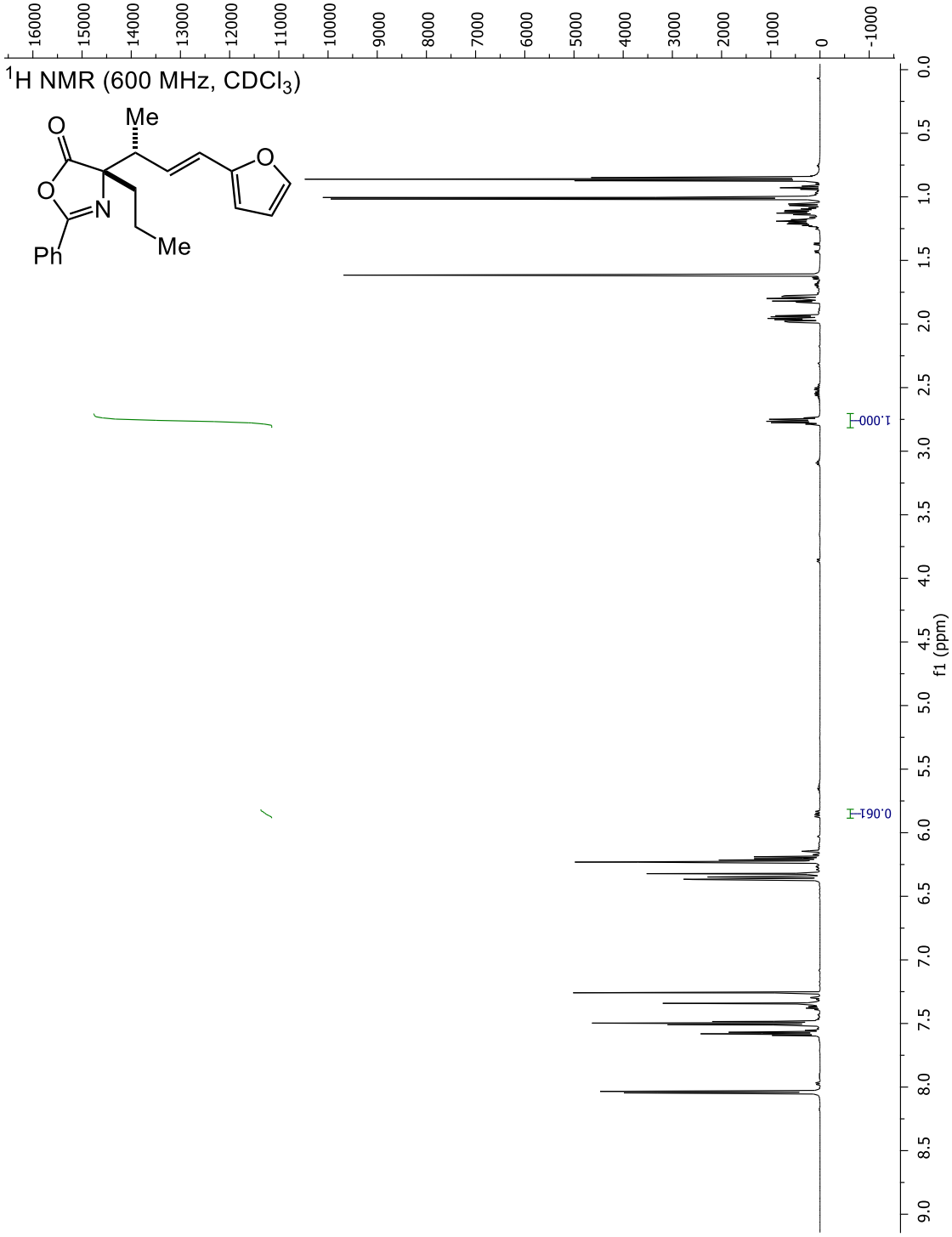

13C NMR (151 MHz, CDCl3)
O
Me
O
Me
N
Me
Ph
f1 (ppm)


1H NMR (600 MHz, CDCl3)
Me
O
O
Me
N
Ph
1.000
0.177
f1 (ppm)

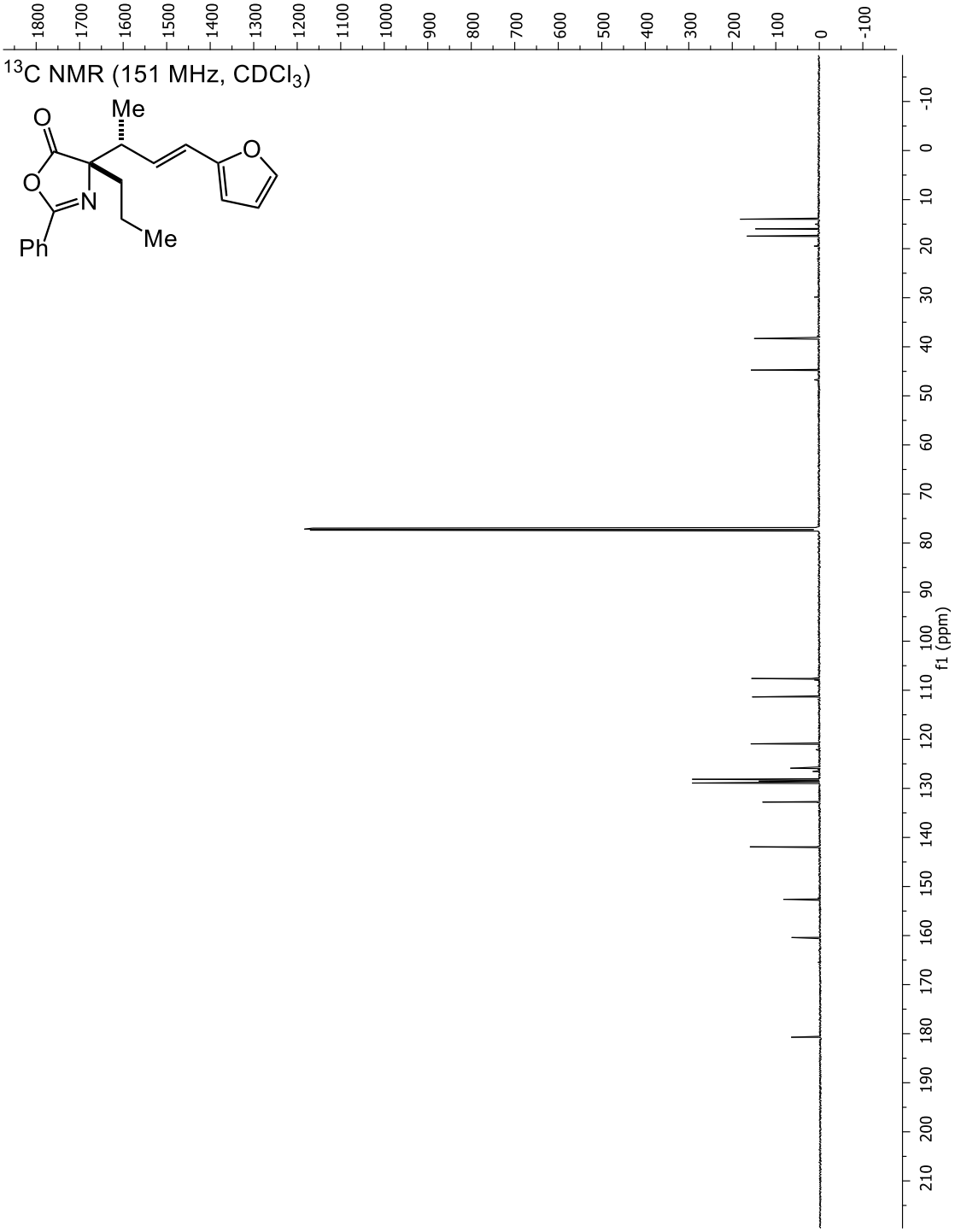

13C NMR (151 MHz, CDCl3)
Me
O
O
Me
N
Ph
f1 (ppm)

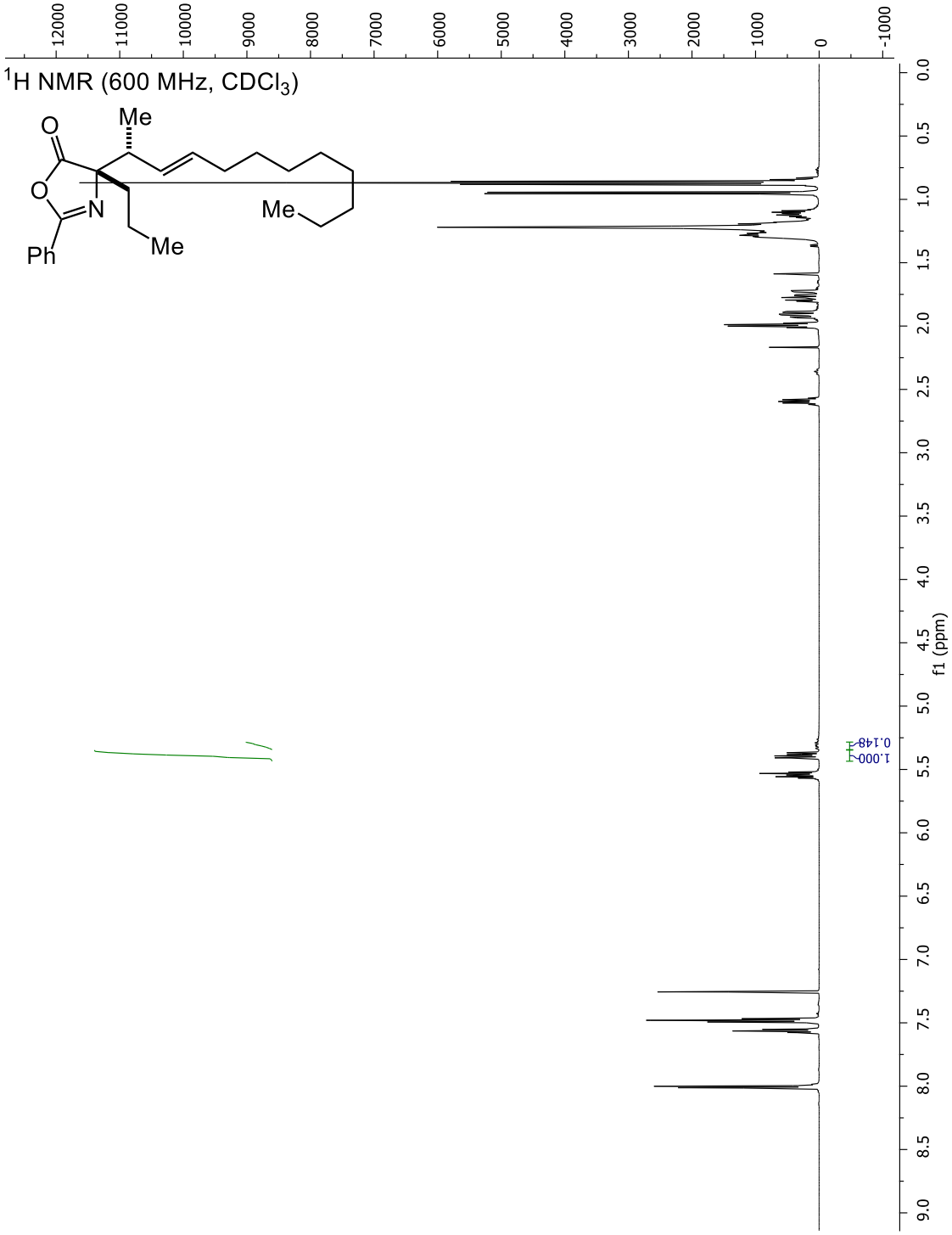

1H NMR (600 MHz, CDCl3)
Me
O
OTBS
O
Me
N
Ph
f1 (ppm)
1.000
0.187

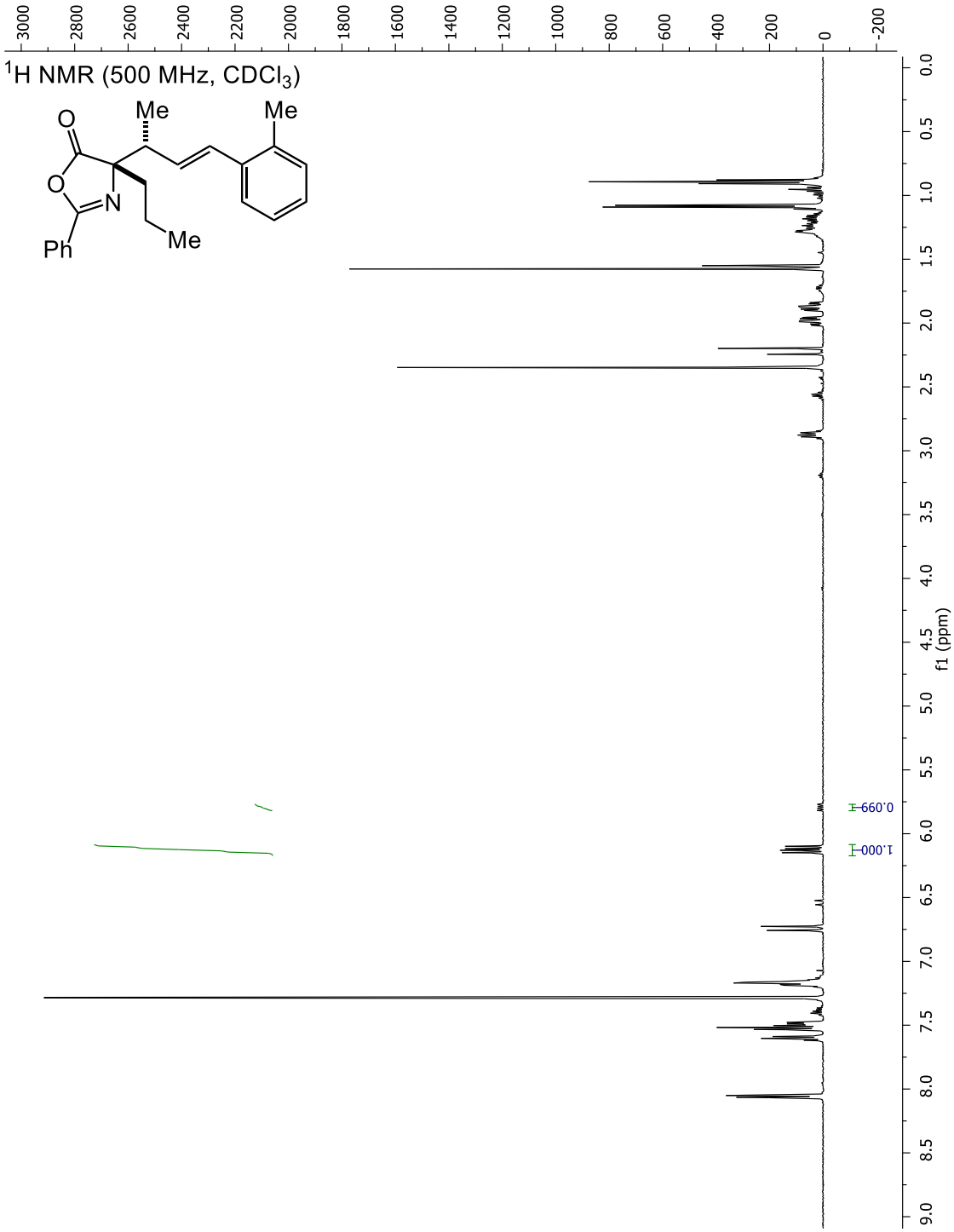

13C NMR (151 MHz, CDCl3)
O
Me
O
Me
N
OTBS
Ph
f1 (ppm)


1H NMR (600 MHz, CDCl3)
Me
O
O
N
Ph
Me
O
1.000
0.061
f1 (ppm)

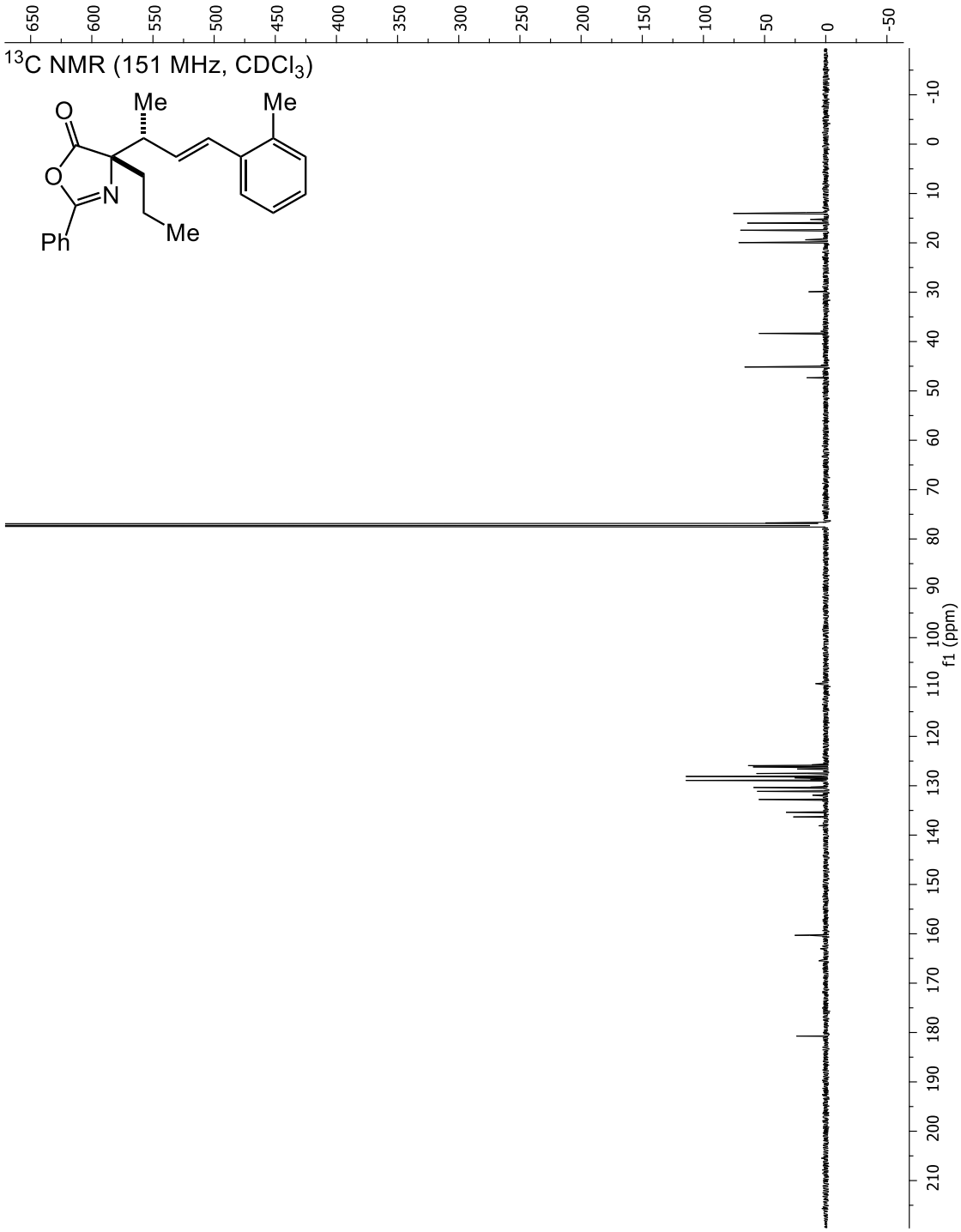
^{13}C NMR (151 MHz, $CDCl_3$)

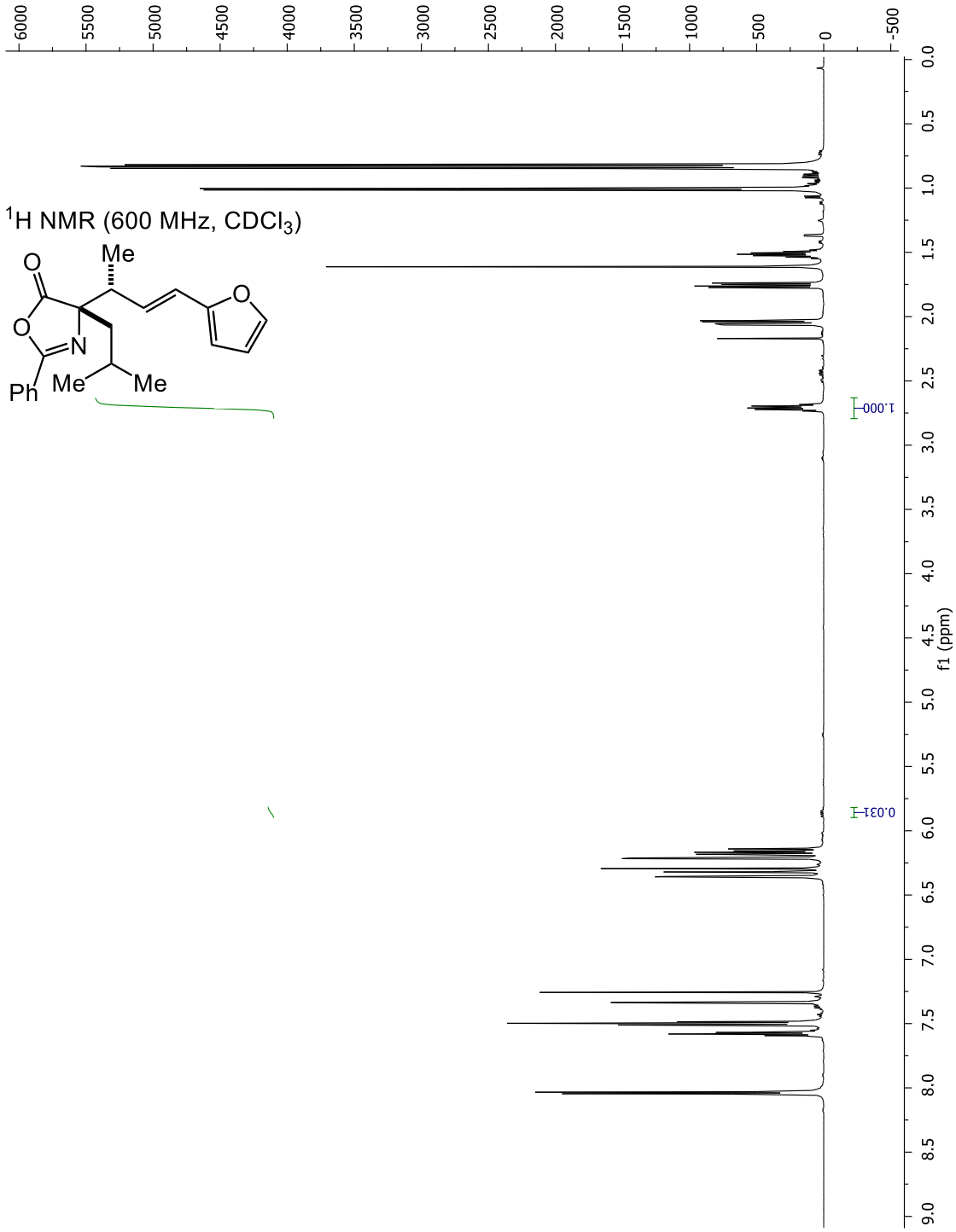


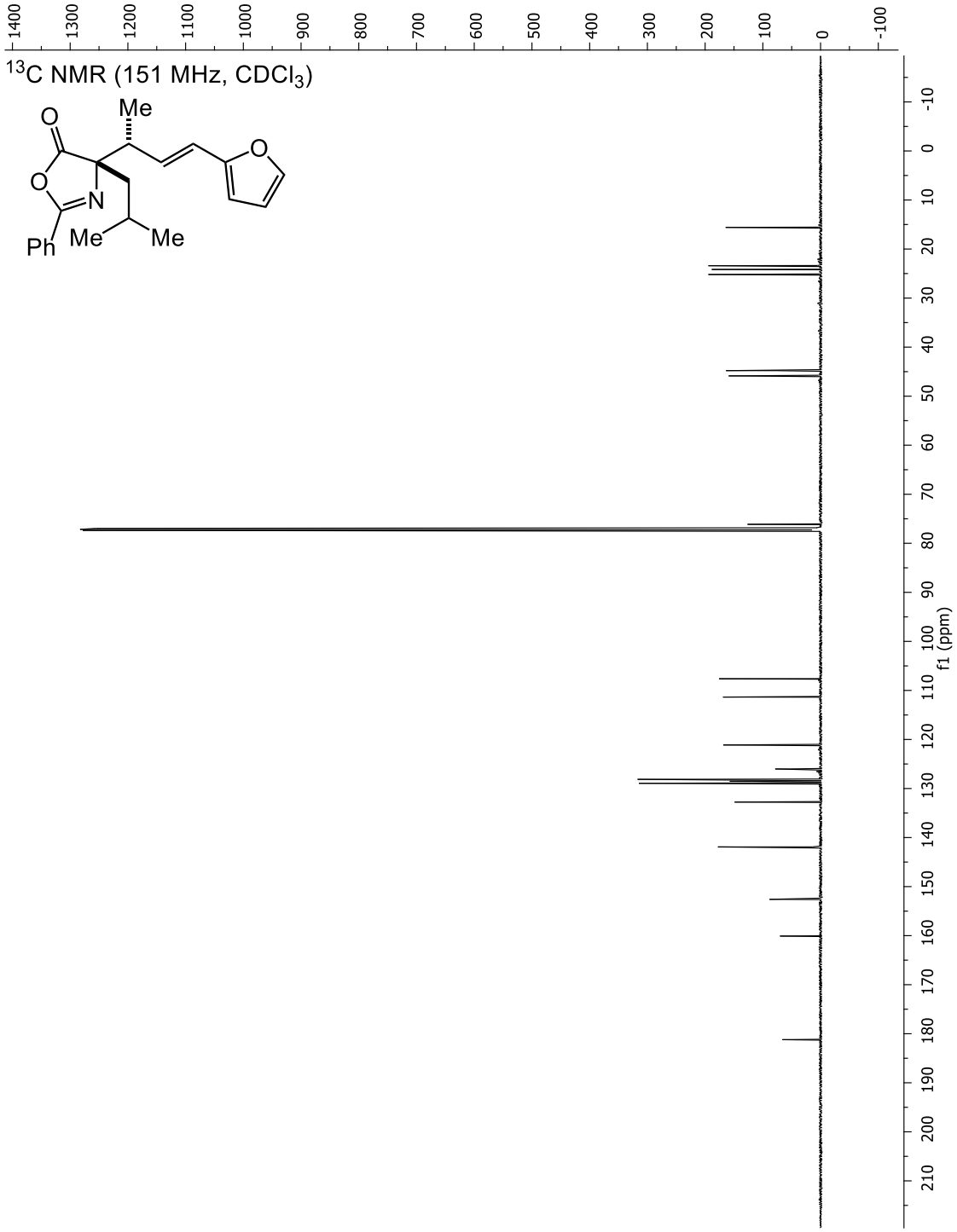

1H NMR (600 MHz, CDCl3)
O
Me
O
N
Me
Ph
Me
1.000
0.148
f1 (ppm)

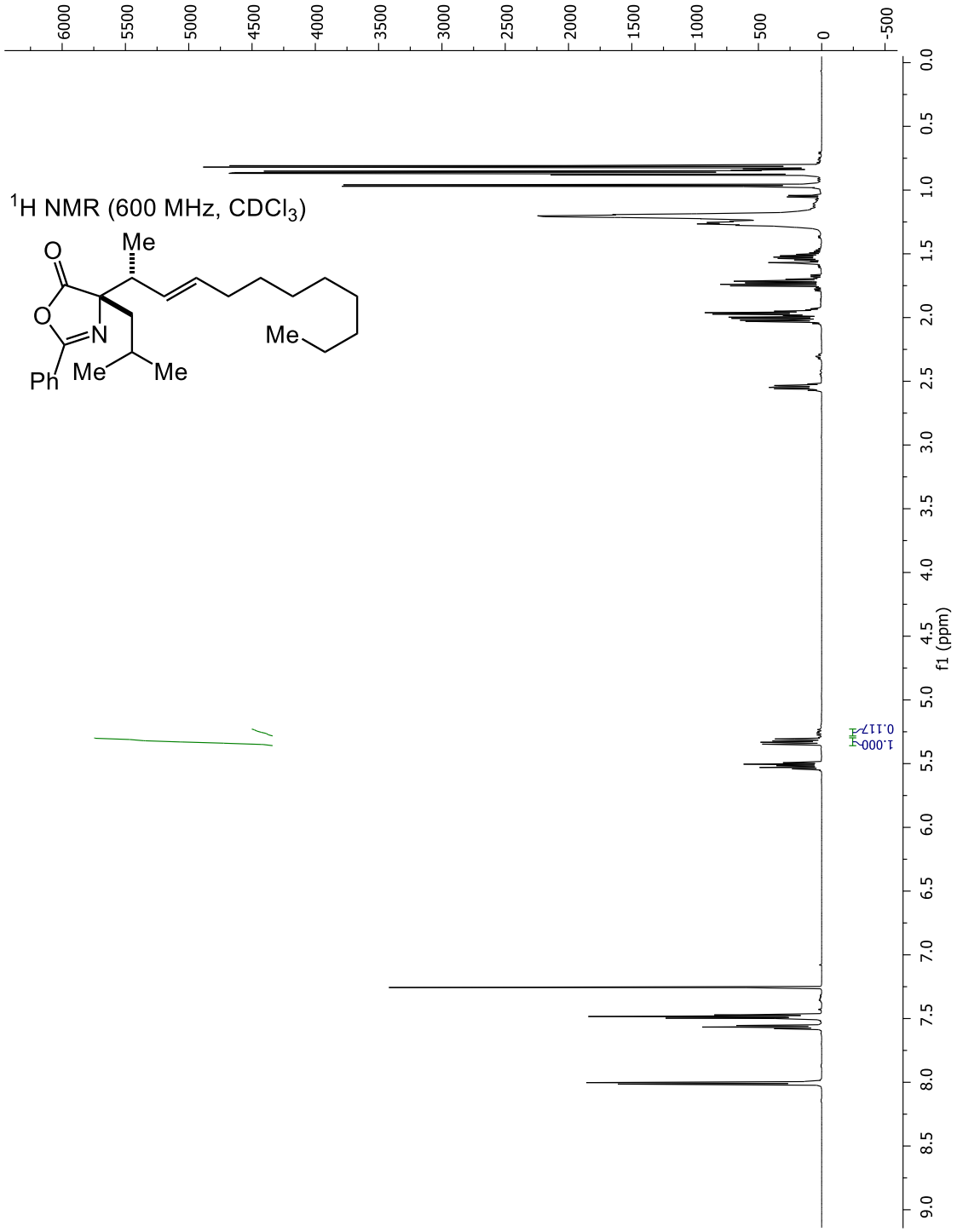

1H NMR (500 MHz, CDCl3)
O
Me
Me
O
N
Ph
Me
1.000
0.660
f1 (ppm)

^{13}C NMR (151 MHz, $CDCl_3$)

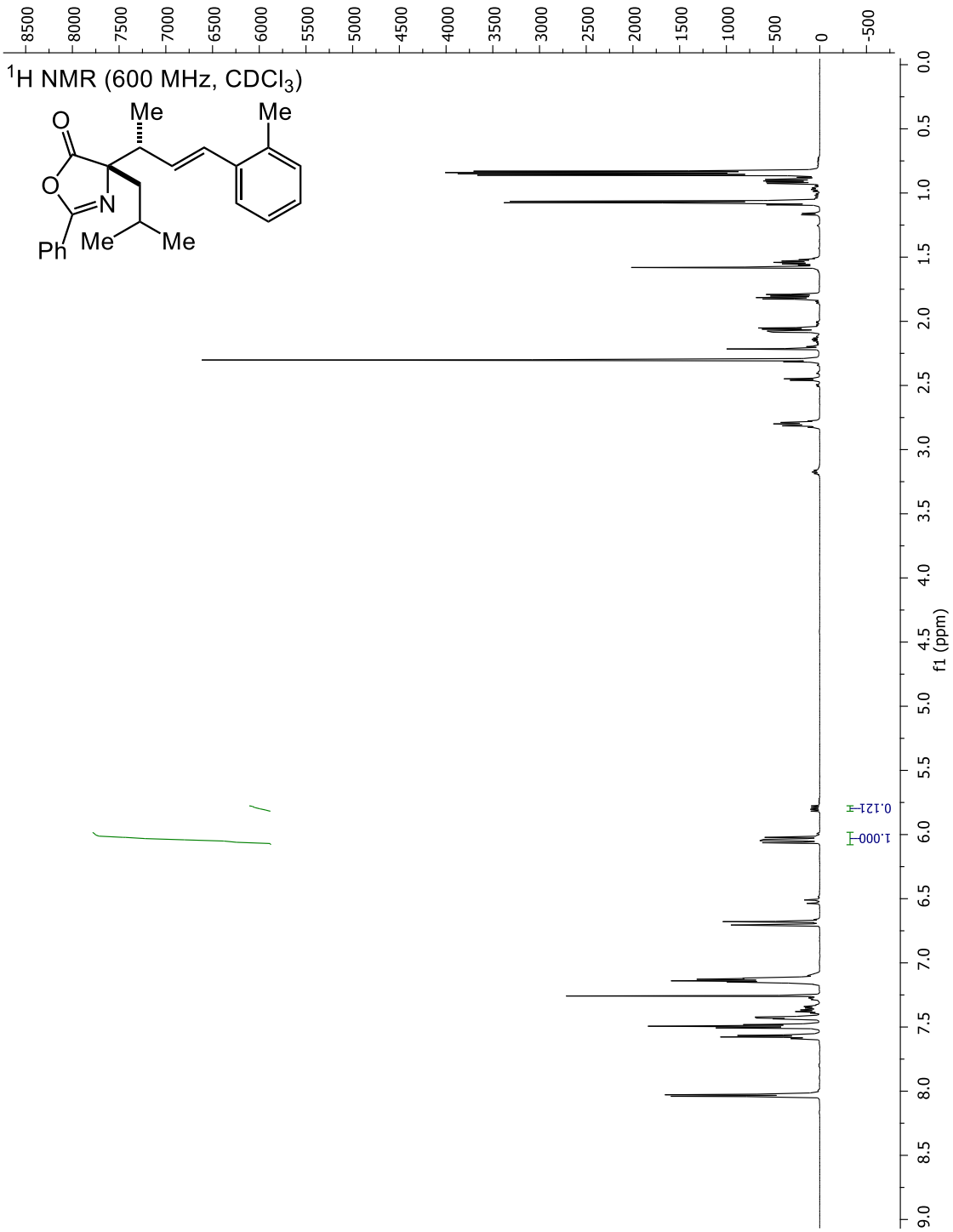



1H NMR (600 MHz, CDCl3)
Me
O
O
N
Ph
Me
Me
O
1.000
0.031
f1 (ppm)

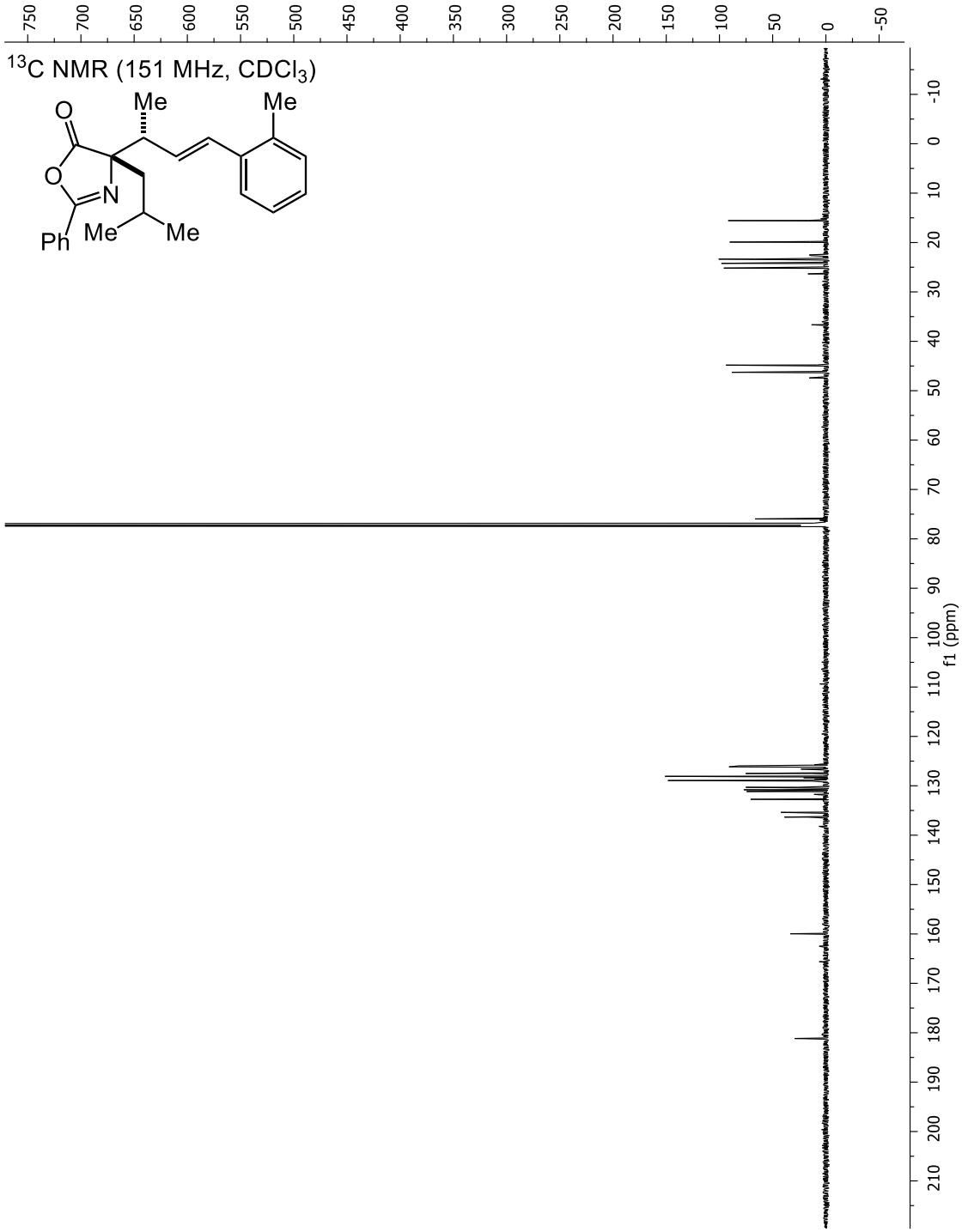

13C NMR (151 MHz, CDCl3)
O
Me
O
O
N
Ph
Me
Me
f1 (ppm)

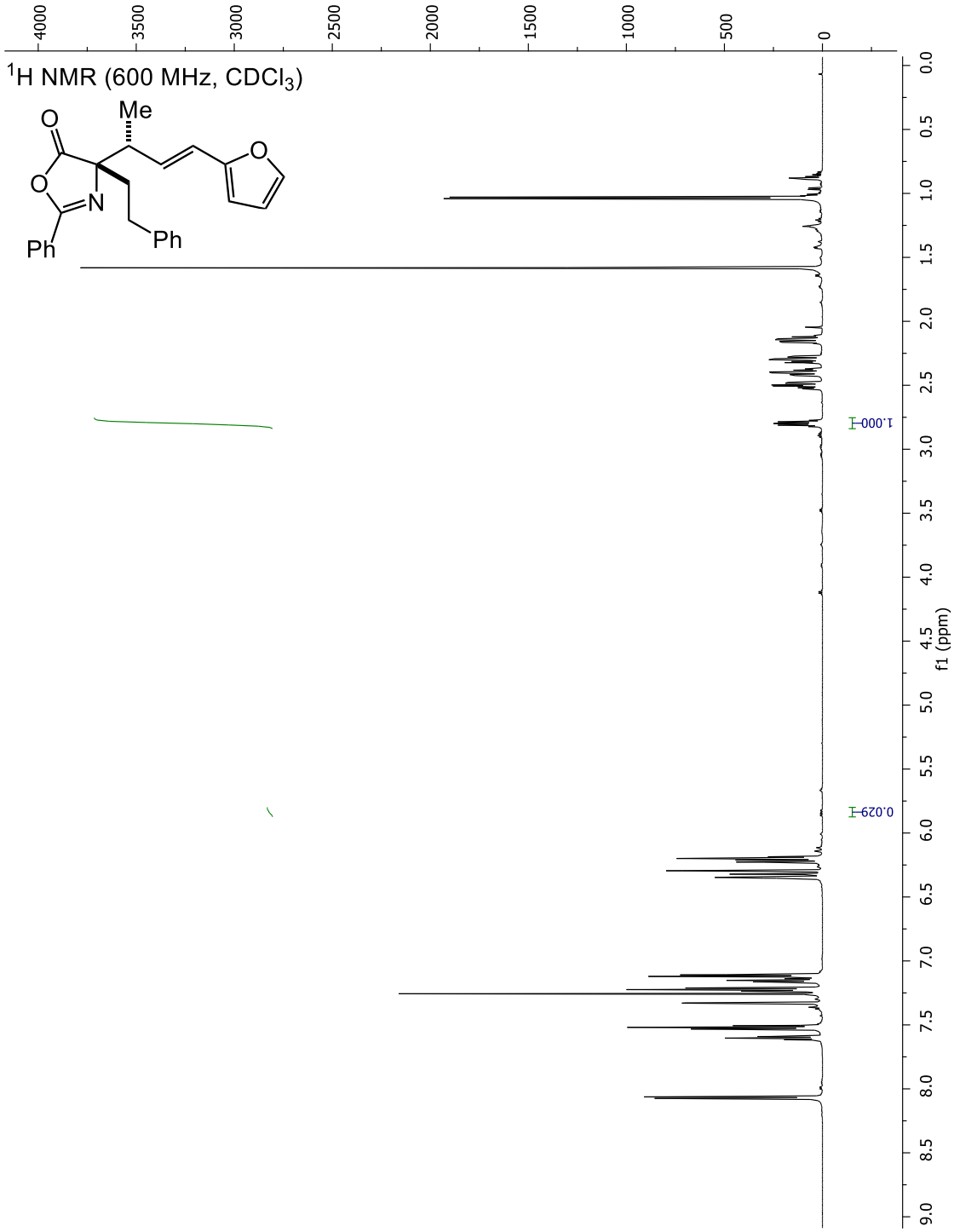

1H NMR (600 MHz, CDCl3)
Me
O
O
N
Ph
Me
Me
Me
1.000
0.117
f1 (ppm)

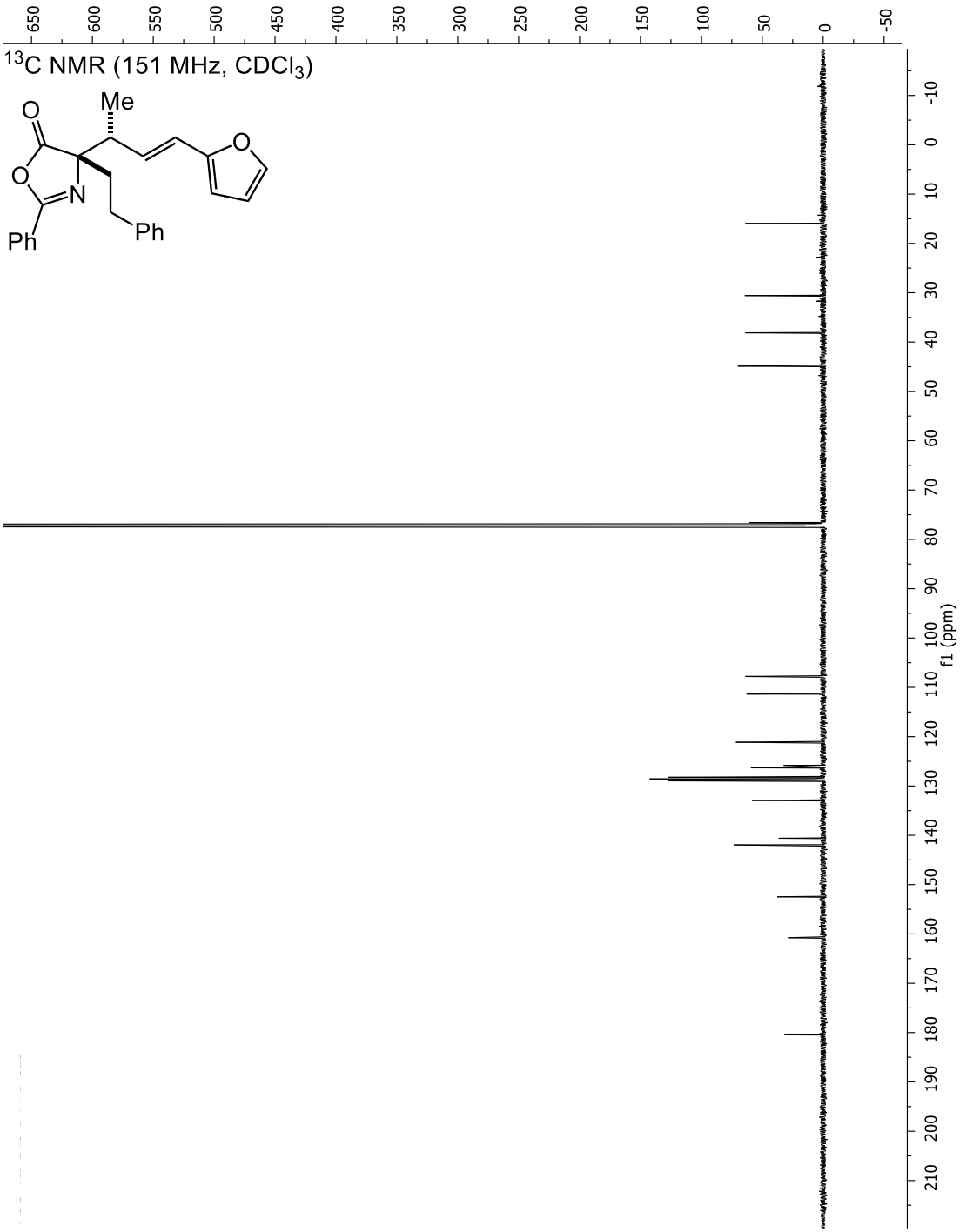

13C NMR (151 MHz, CDCl3)
Me
O
O
N
Ph
Me
Me
Me
f1 (ppm)


1H NMR (600 MHz, CDCl3)
O
Me
Me
O
N
Ph
Me
Me
1.000
0.121
f1 (ppm)

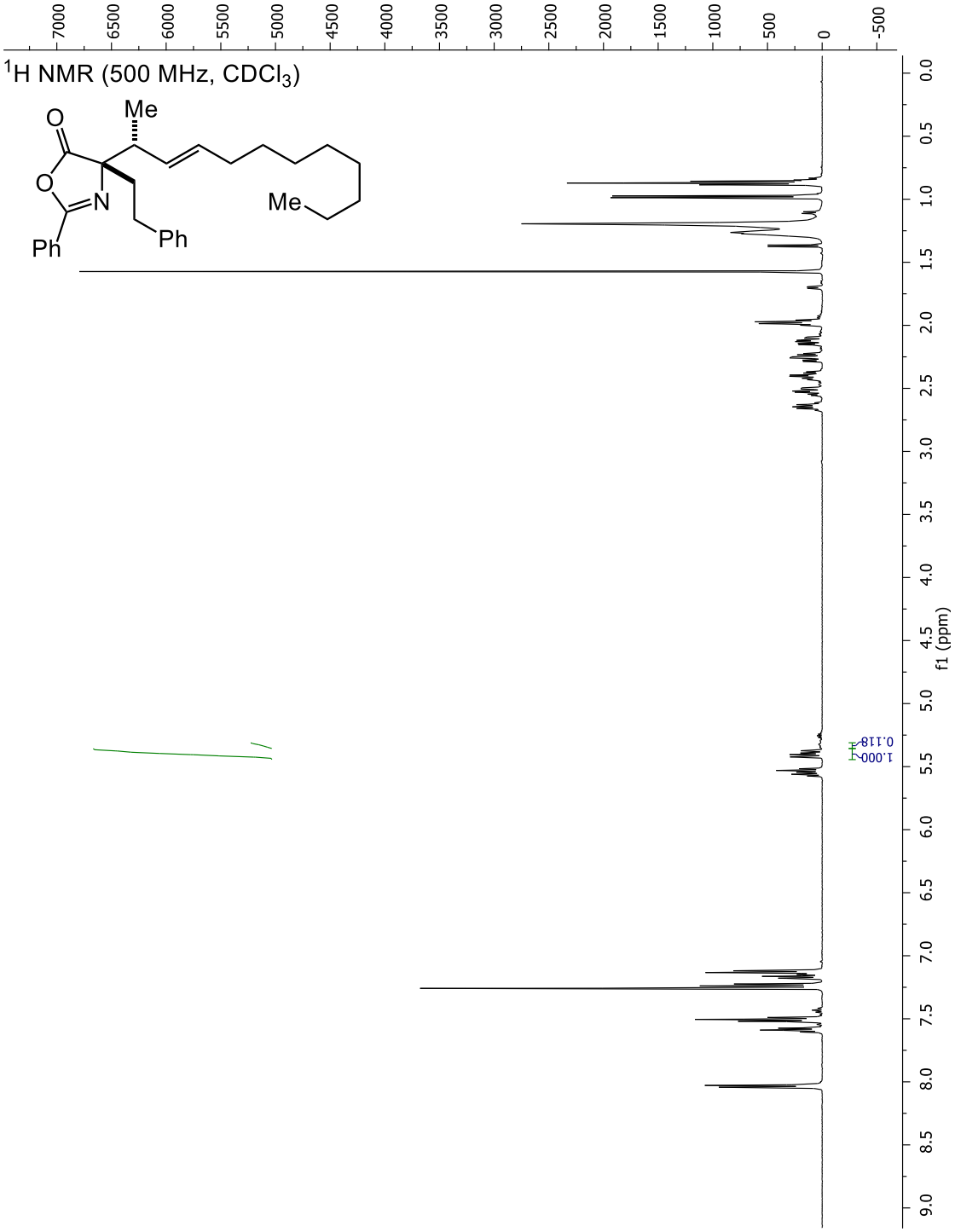
^{13}C NMR (151 MHz, $CDCl_3$)



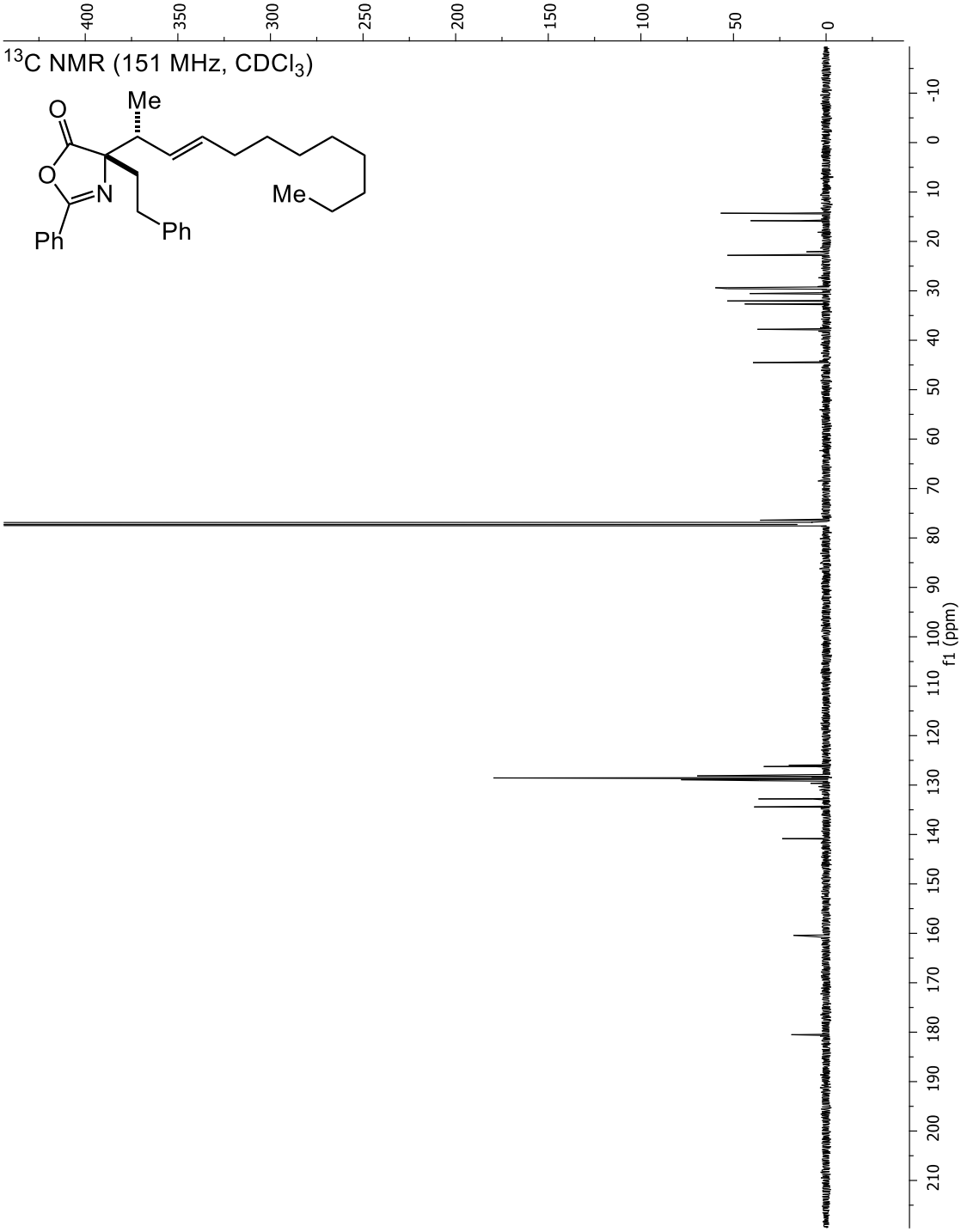

1H NMR (600 MHz, CDCl3)
Me
O
O
N
Ph
Ph
O
1.000
0.029
f1 (ppm)


13C NMR (151 MHz, CDCl3)
Me
O
O
N
Ph
Ph
O
f1 (ppm)

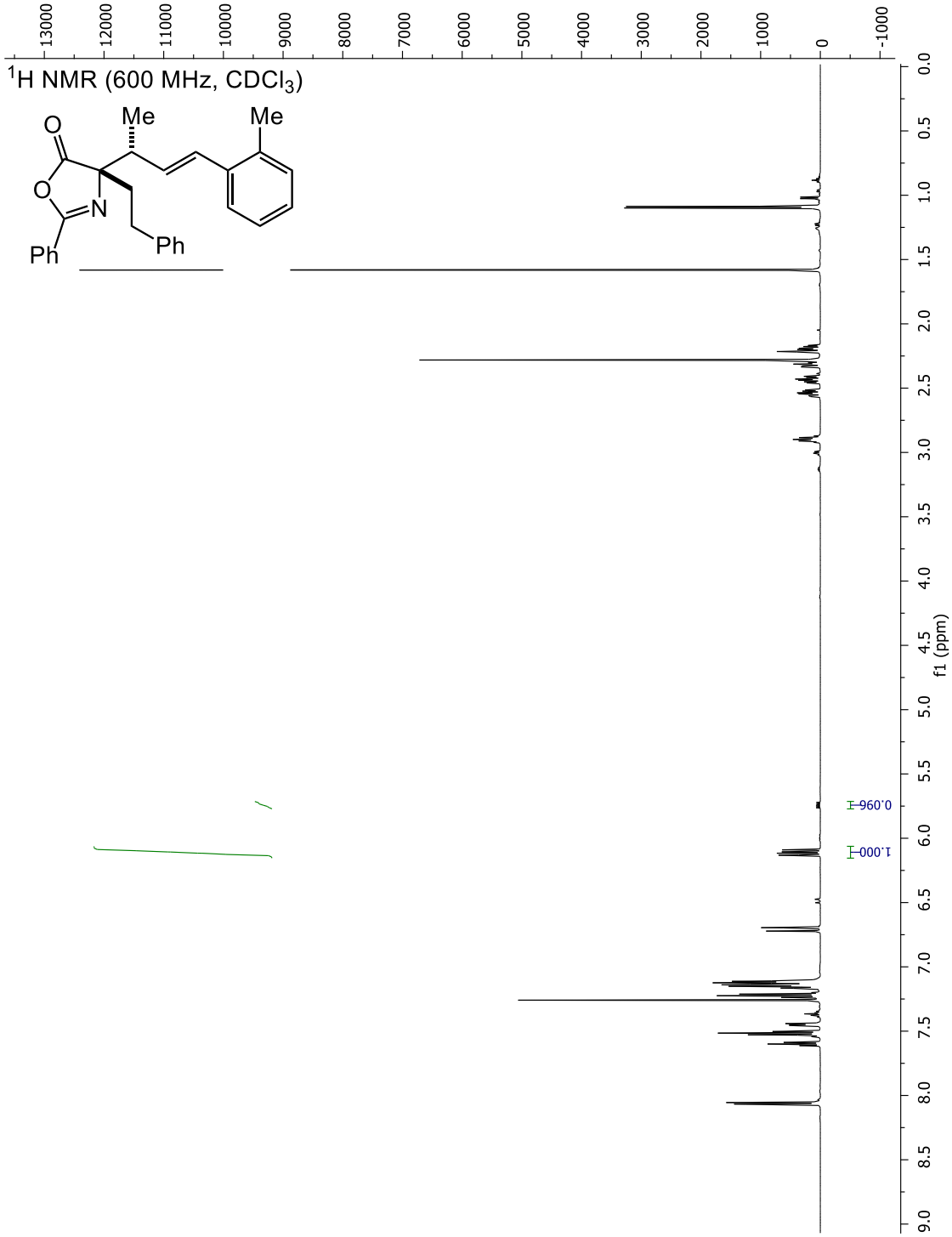
^{1}H NMR (500 MHz, $CDCl_3$)



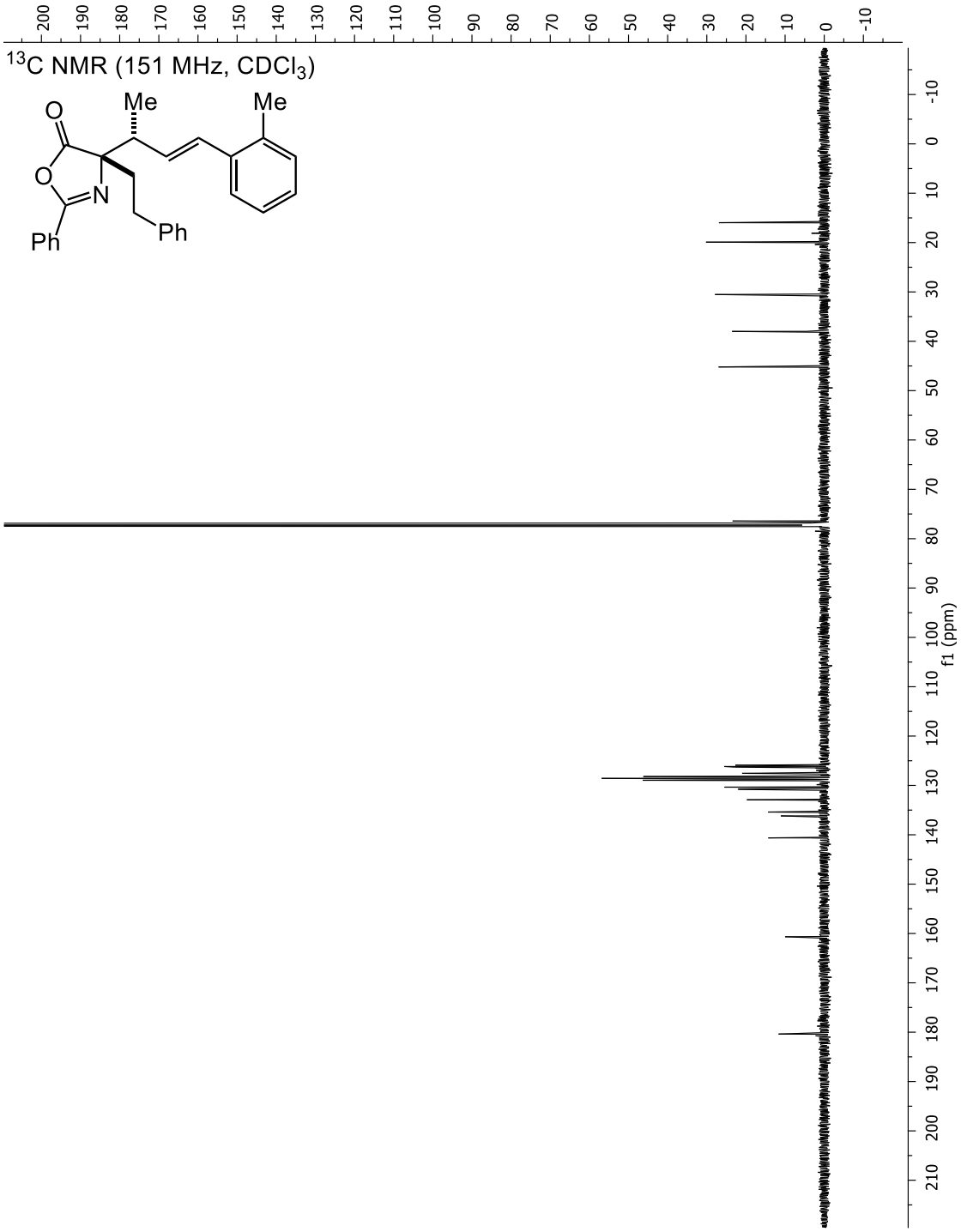
^{13}C NMR (151 MHz, $CDCl_3$)

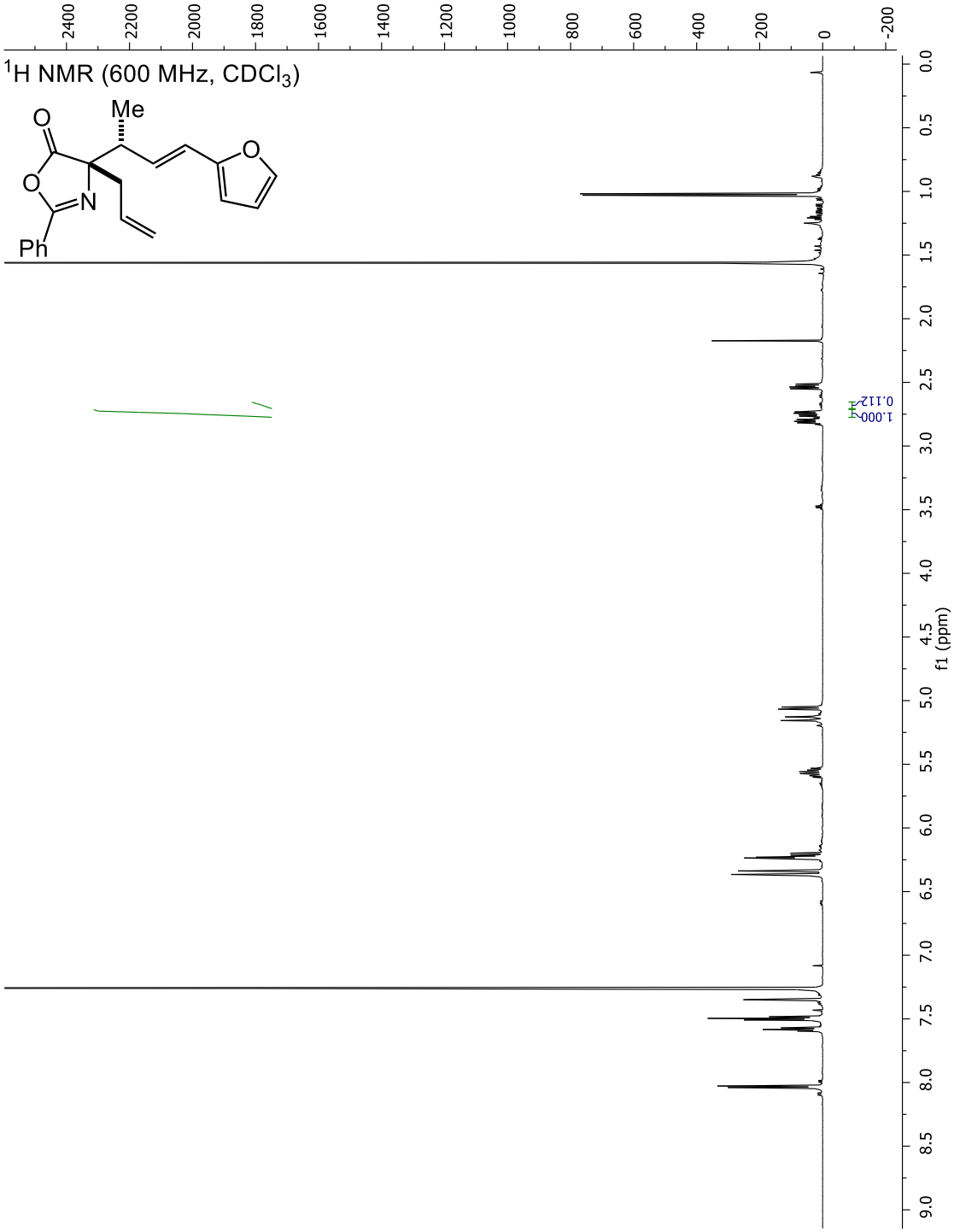


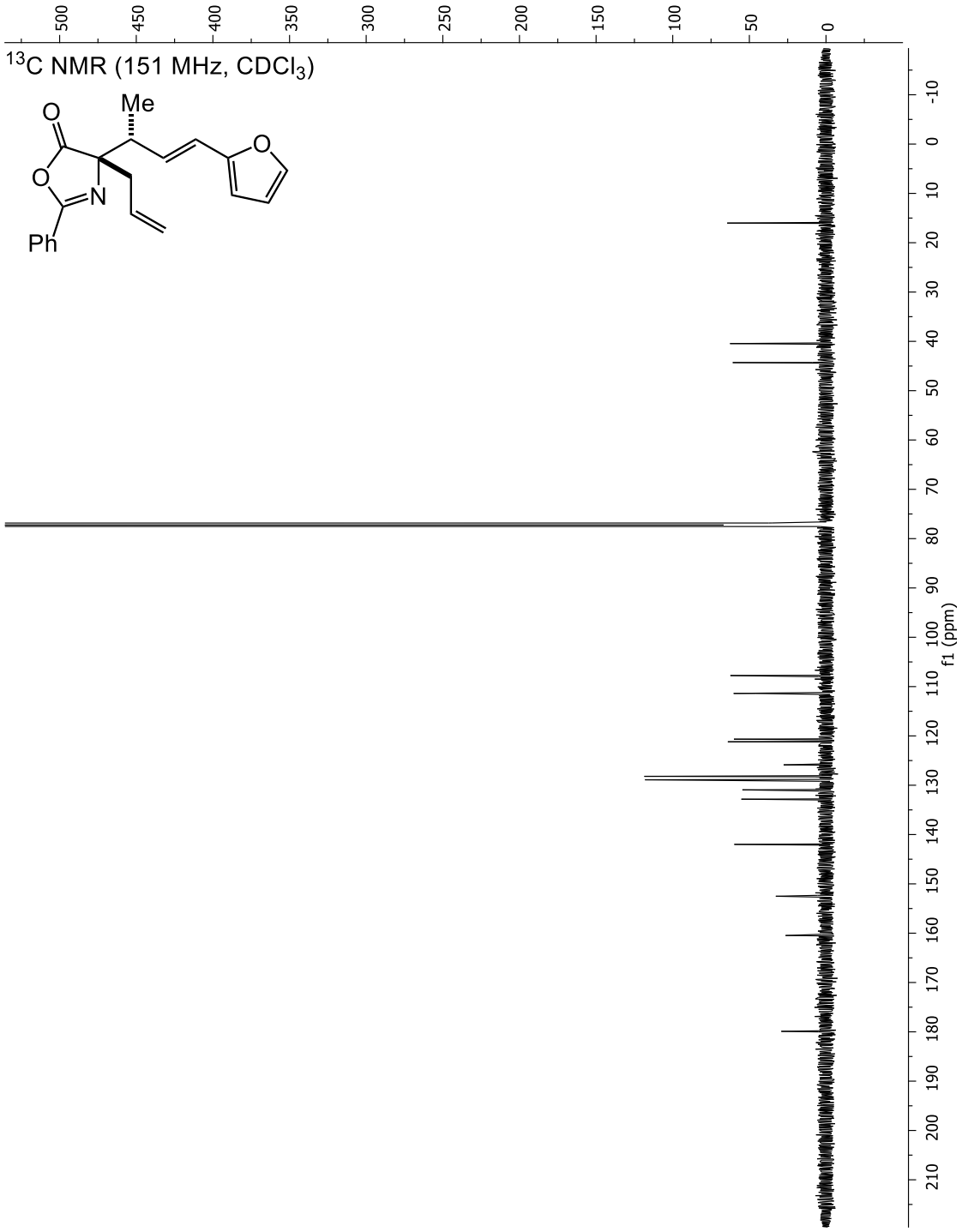
^{1}H NMR (600 MHz, $CDCl_3$)

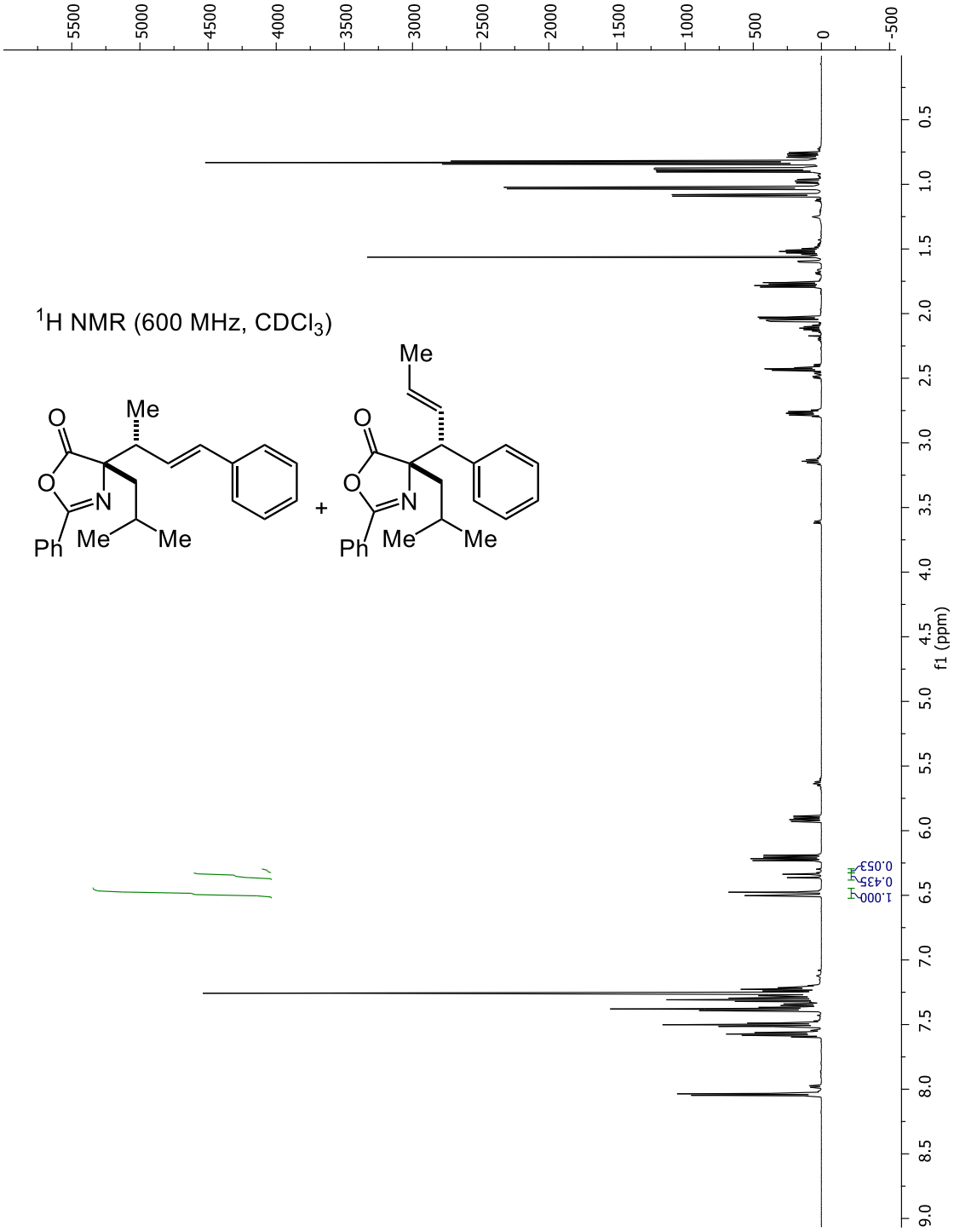


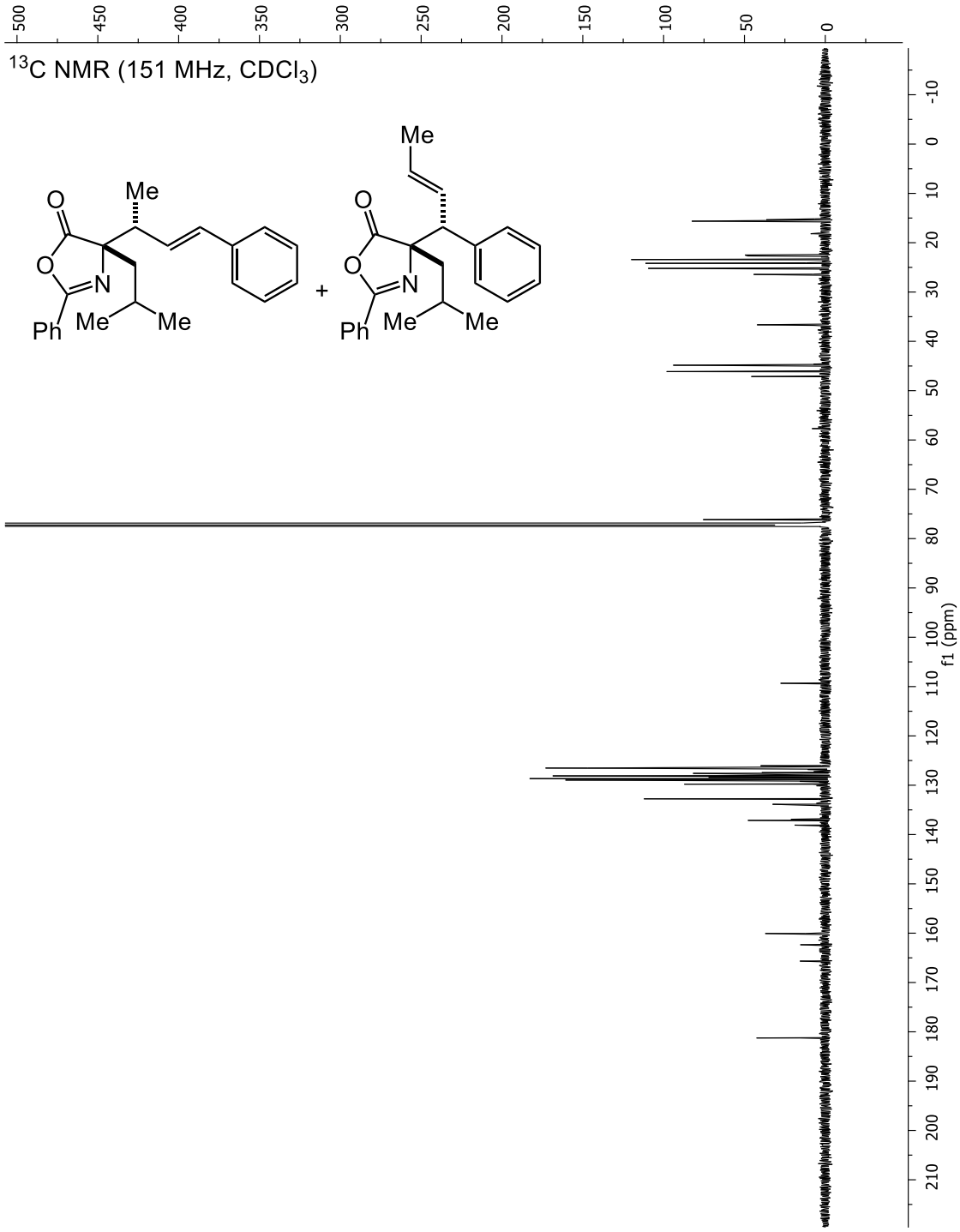
^{13}C NMR (151 MHz, $CDCl_3$)



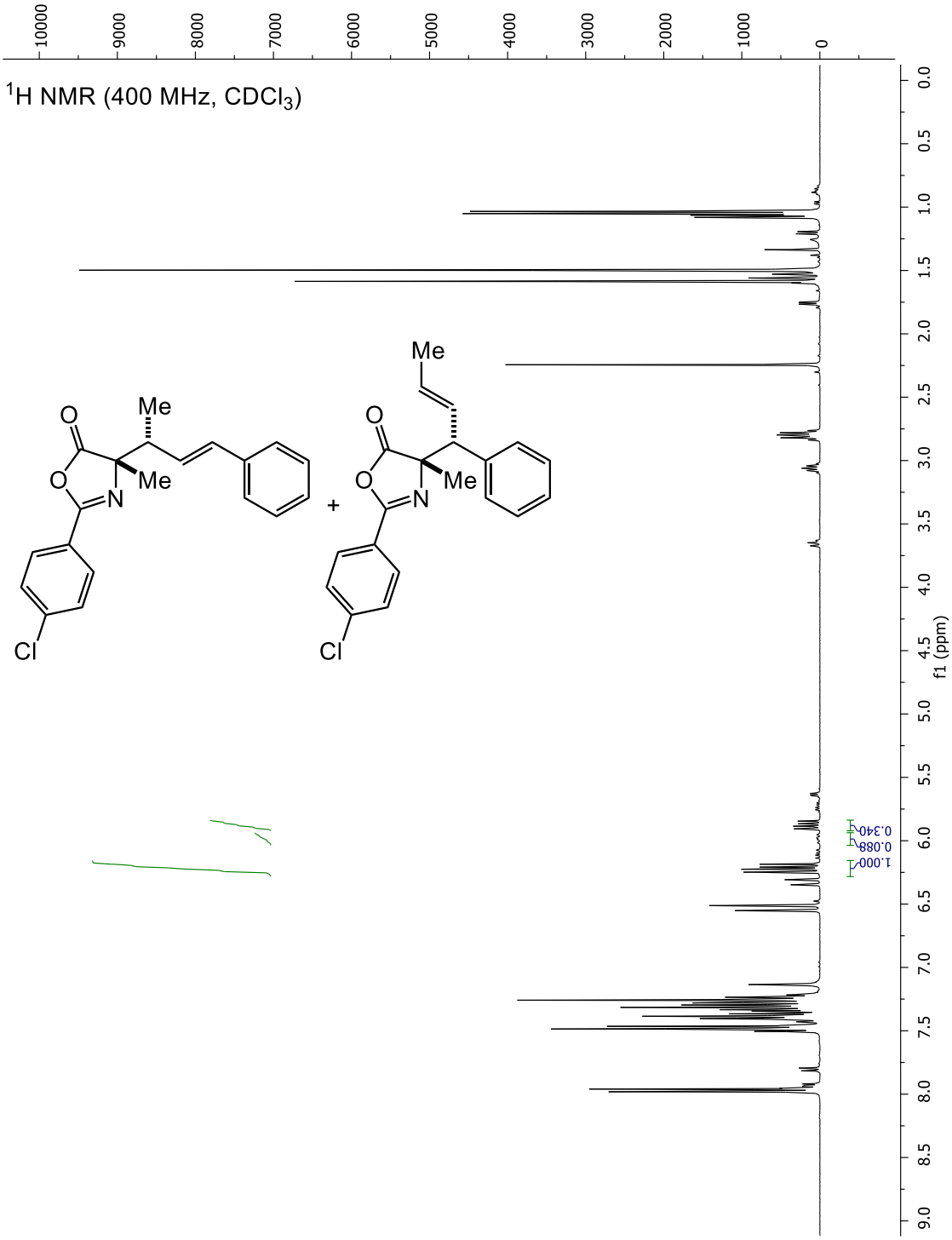

1H NMR (600 MHz, CDCl3)
Me
O
O
N
Ph
O
1.000
0.112
f1 (ppm)

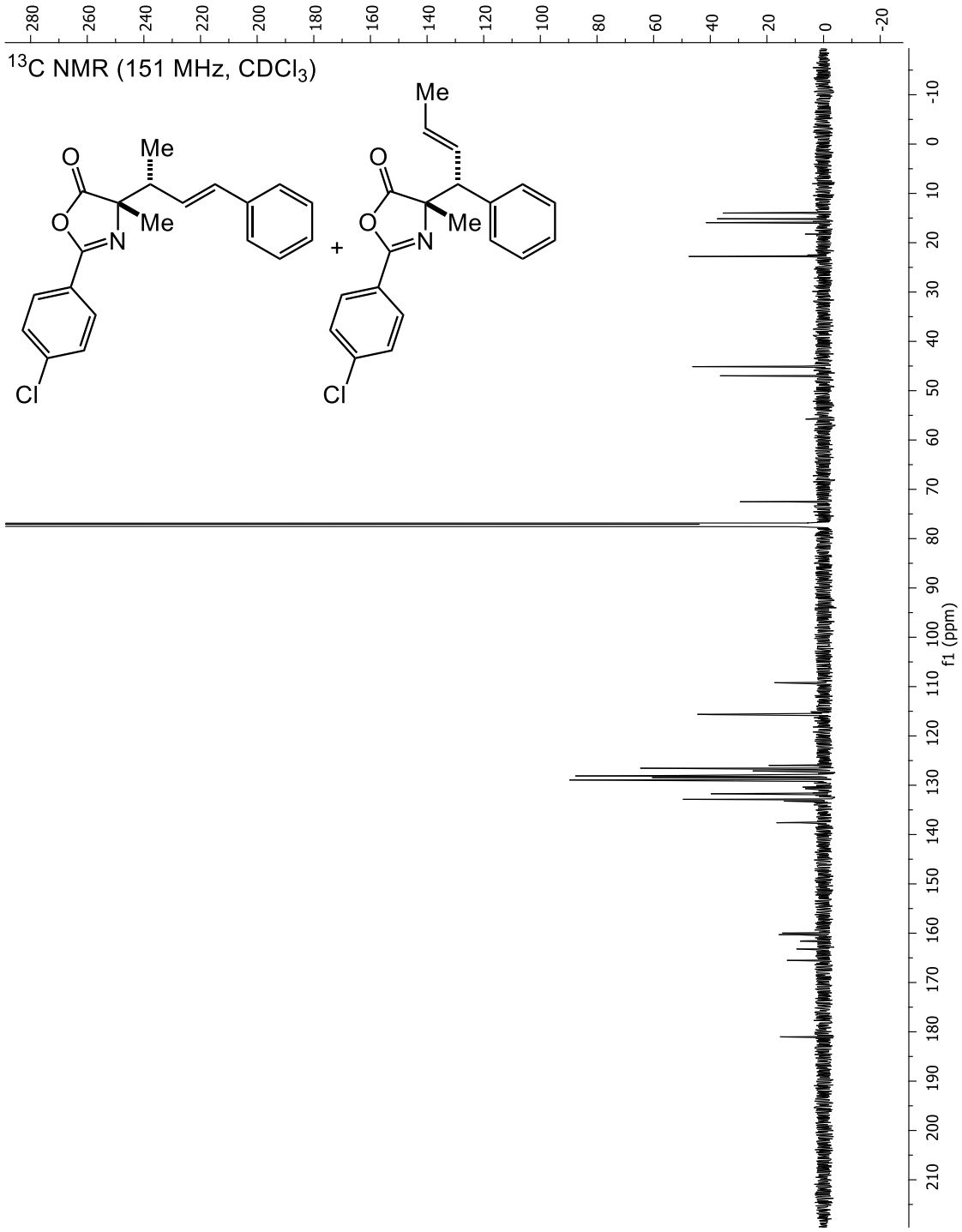

13C NMR (151 MHz, CDCl3)
Me
O
O
N
Ph
O
f1 (ppm)

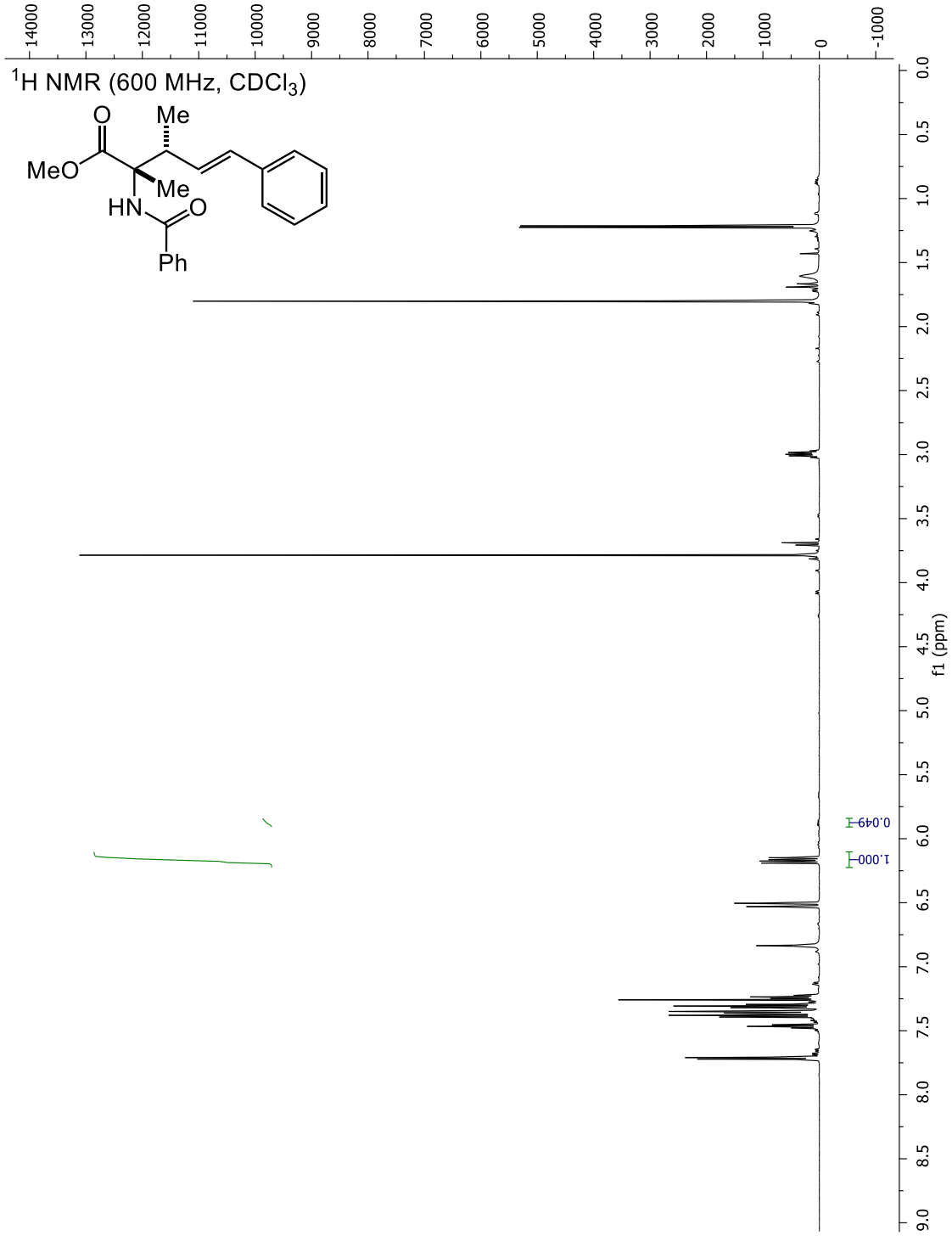

1H NMR (600 MHz, CDCl3)
Me
O
O
N
Ph
Me
Me
+
Me
O
O
N
Ph
Me
Me
1.000
0.435
0.053
f1 (ppm)

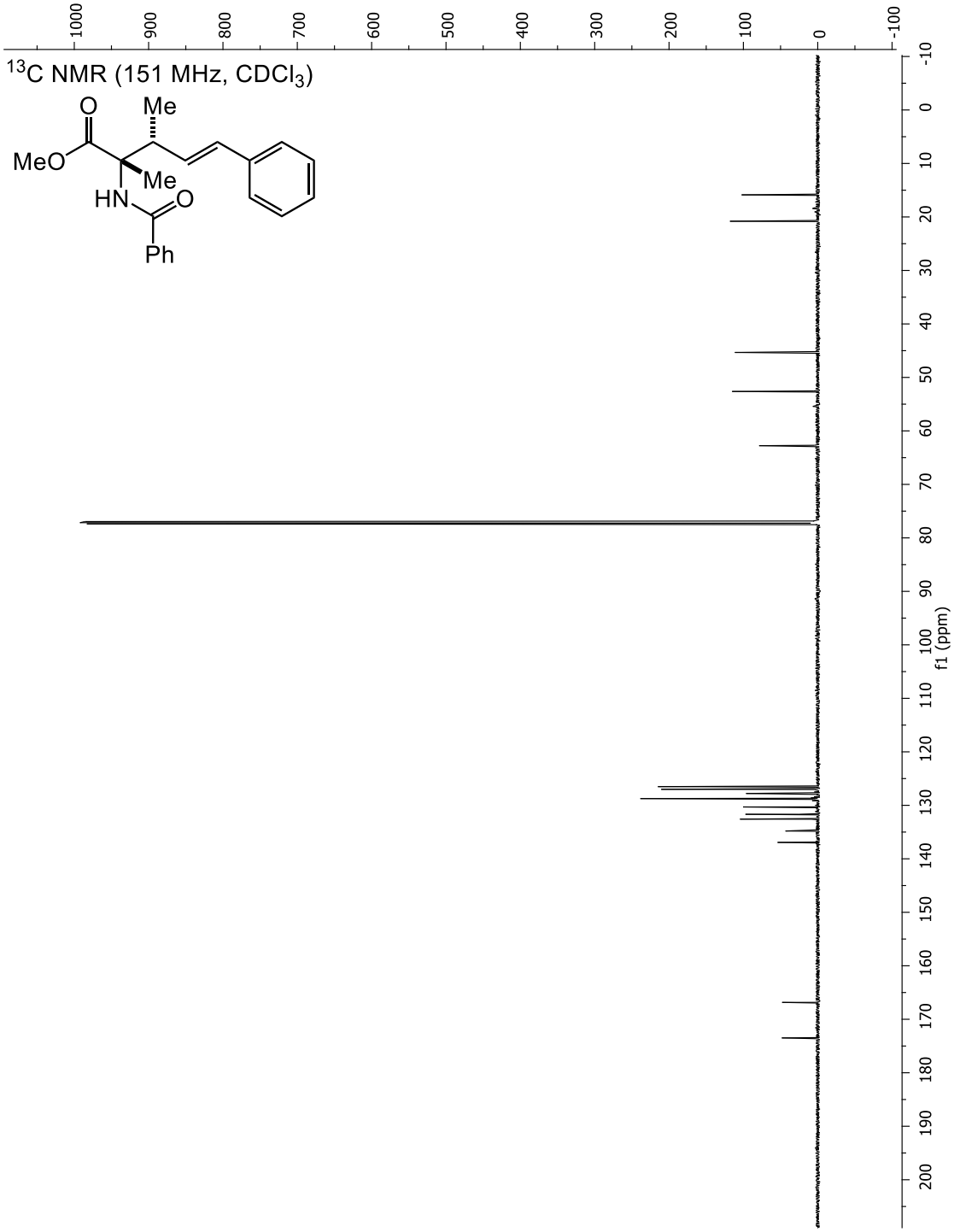

13C NMR (151 MHz, CDCl3)
f1 (ppm)

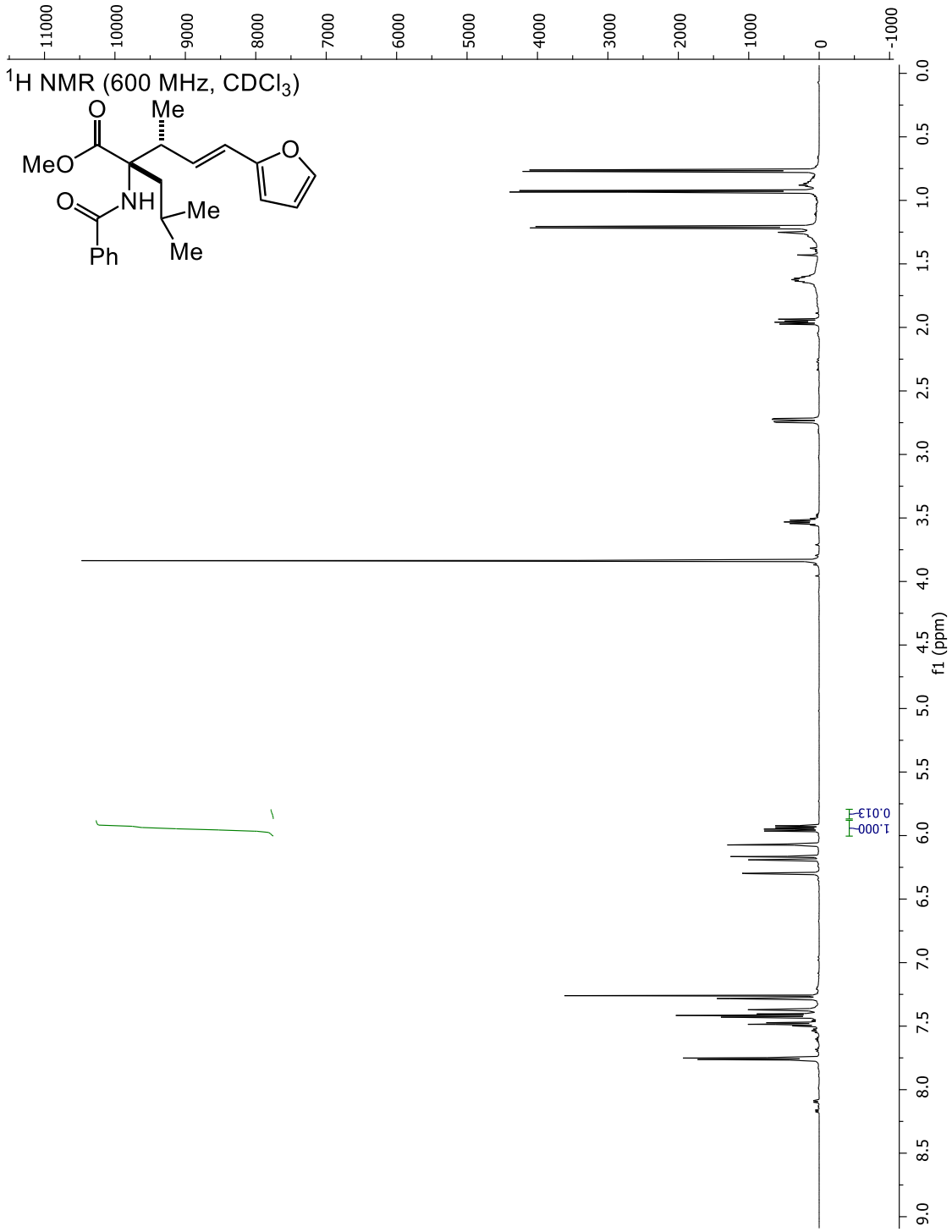
^{1}H NMR (400 MHz, $CDCl_3$)

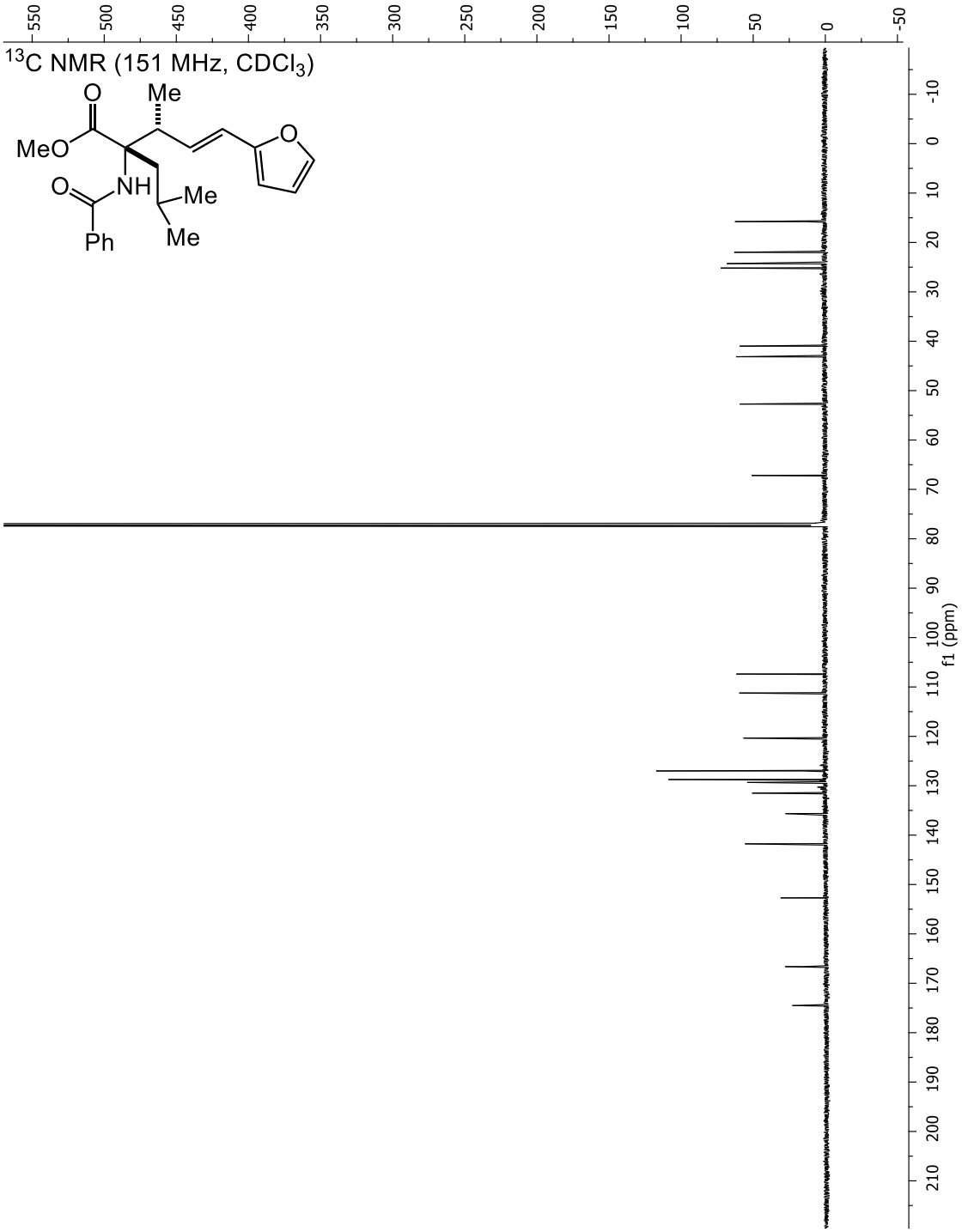



^{13}C NMR (151 MHz, $CDCl_3$)
Me
O
O
N
Me
Me
Cl
+
Me
O
O
N
Me
Cl
f1 (ppm)

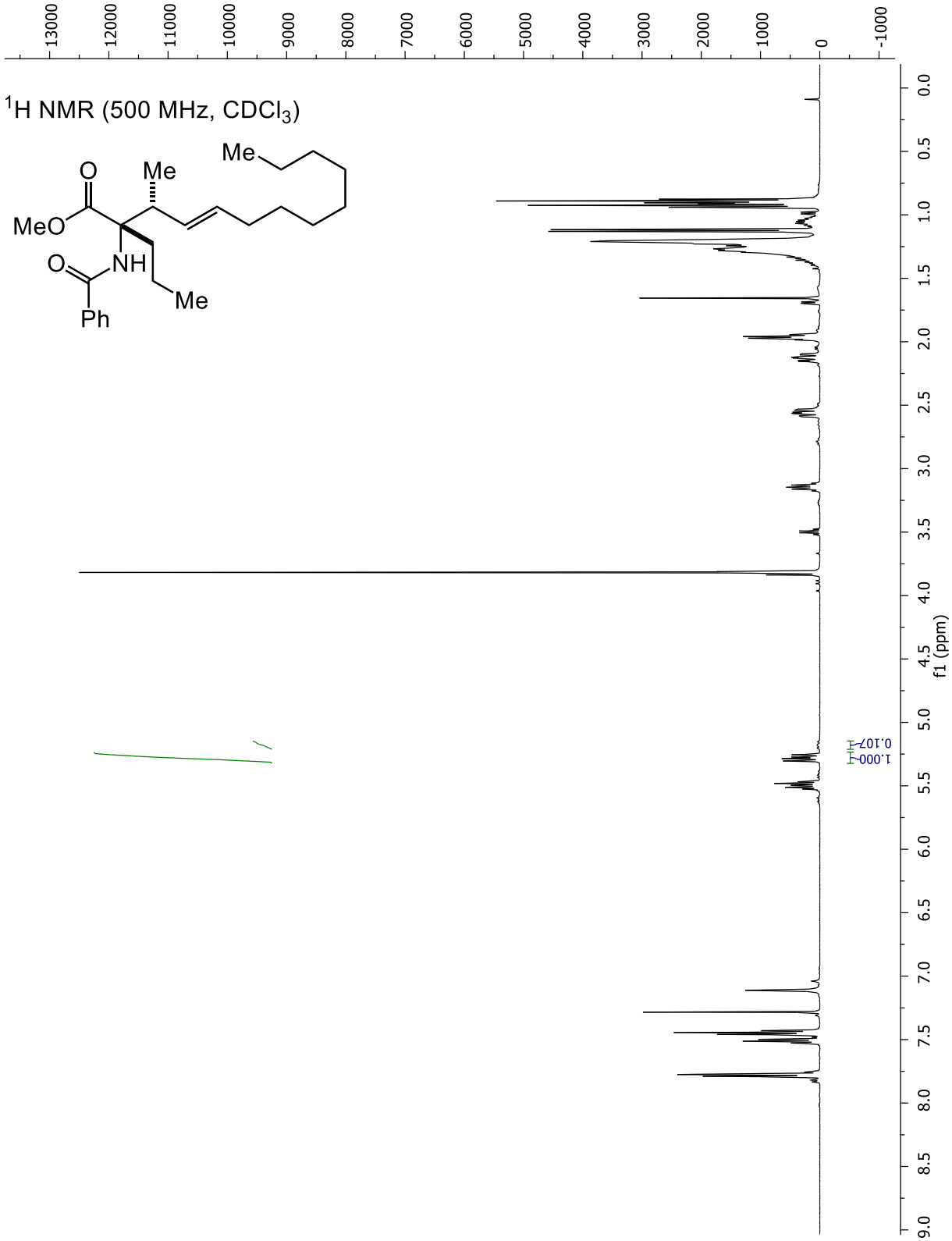

1H NMR (600 MHz, CDCl3)
O
Me
MeO
Me
HN
O
Ph
f1 (ppm)
1.000
0.049

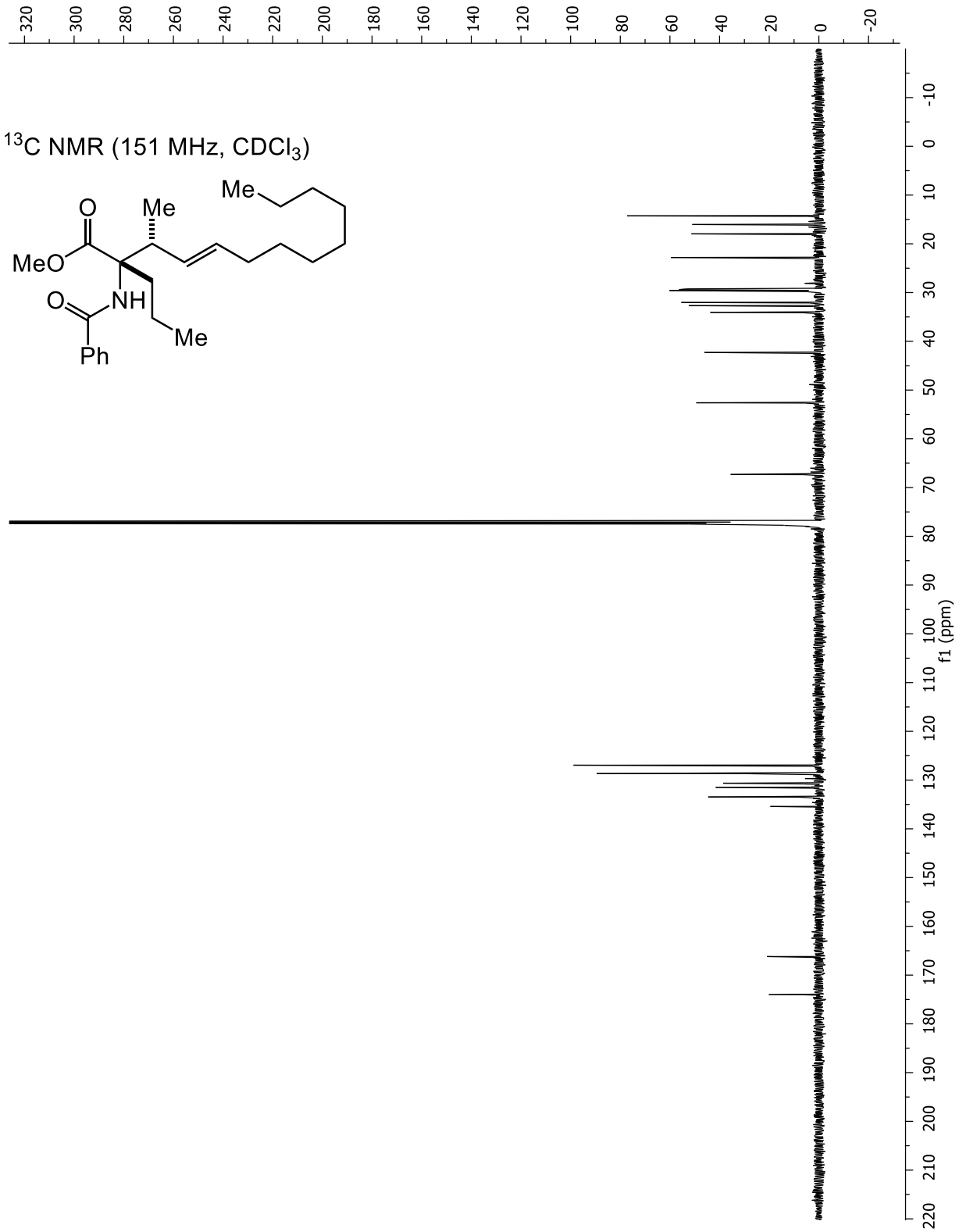

13C NMR (151 MHz, CDCl3)
O
Me
MeO
Me
HN
O
Ph
f1 (ppm)

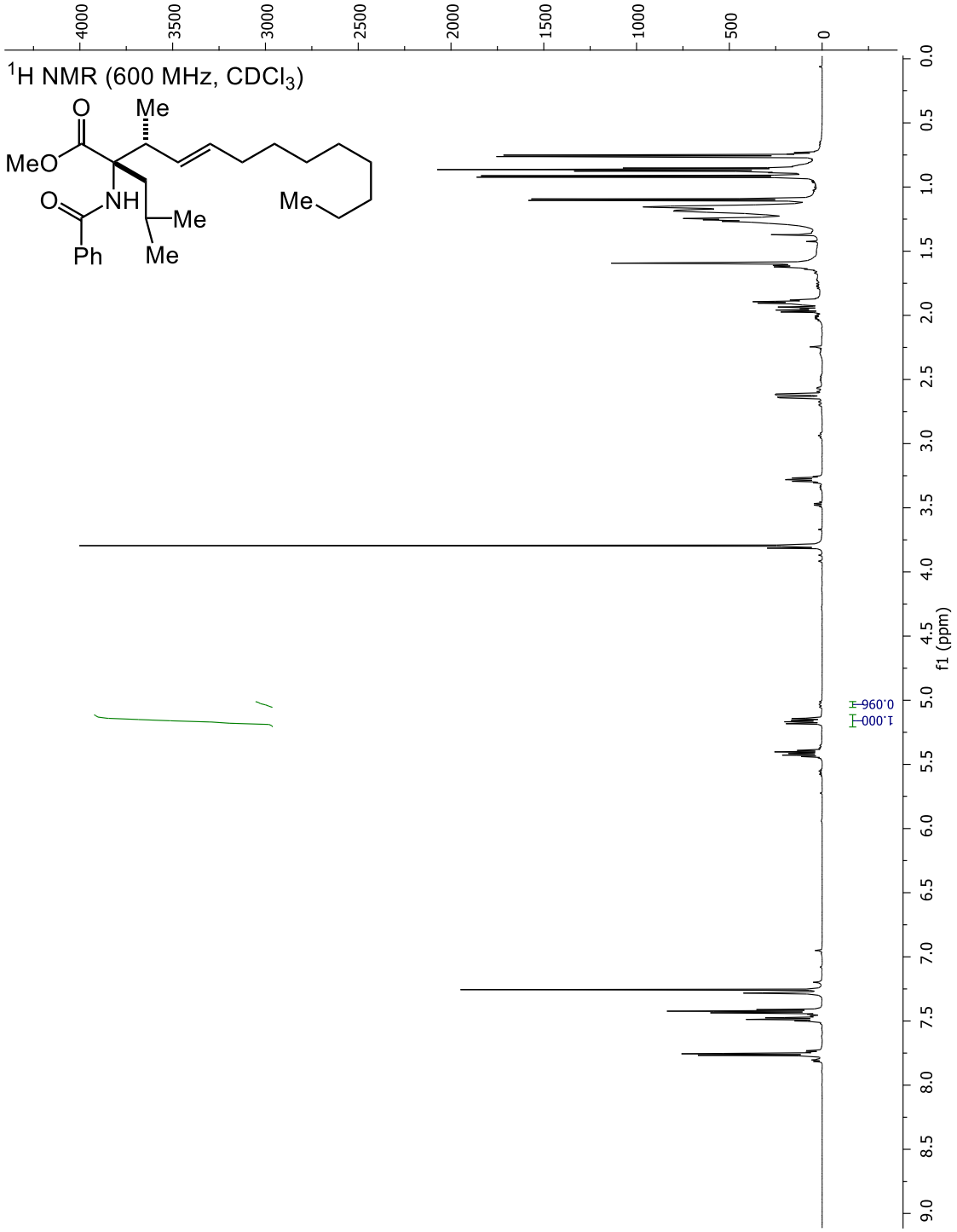

1H NMR (600 MHz, CDCl3)
MeO
O
Me
O
NH
Me
Me
O
Ph
f1 (ppm)
1.000
0.013

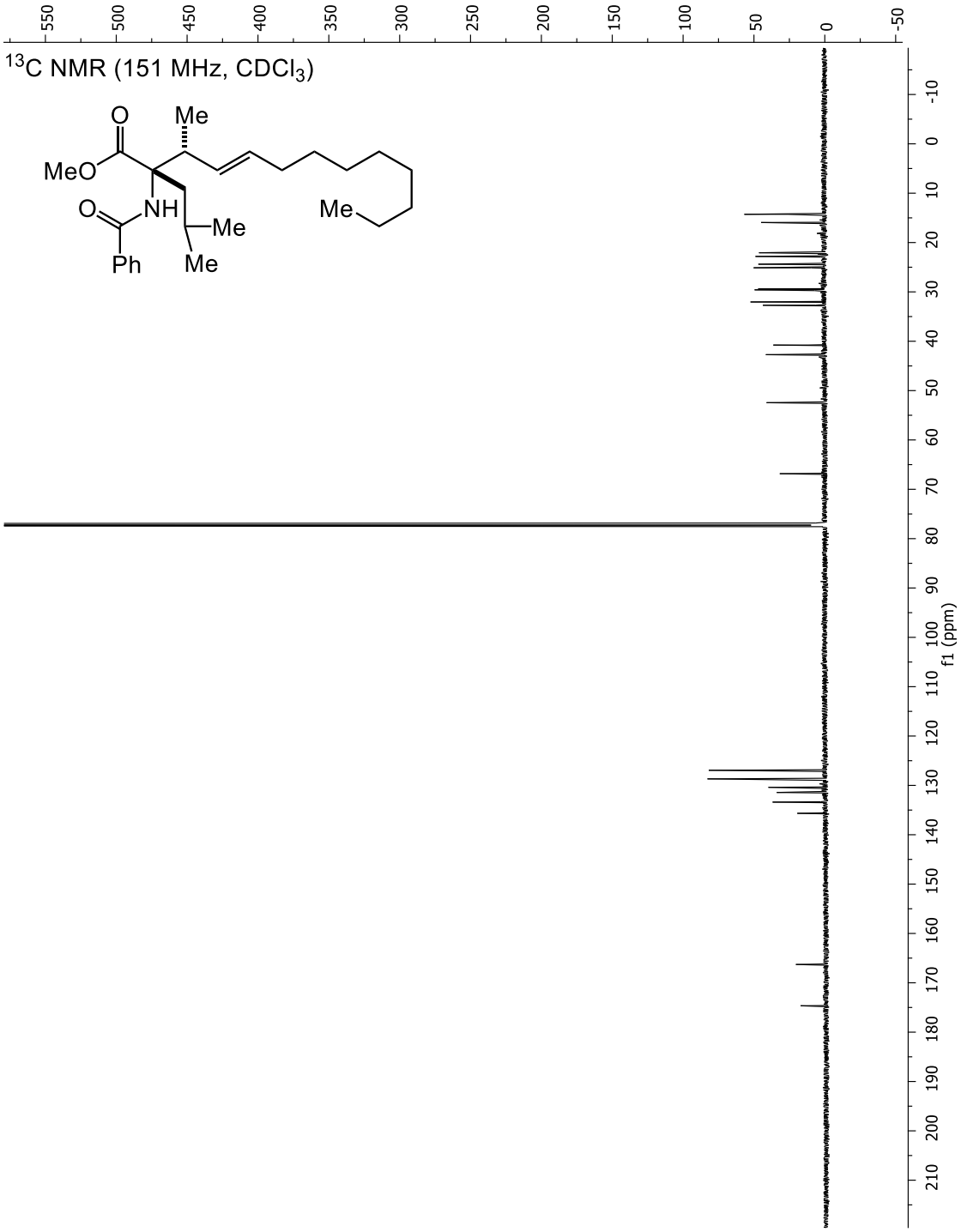

13C NMR (151 MHz, CDCl3)
O
Me
MeO
O
NH
Me
O
Ph
Me
f1 (ppm)

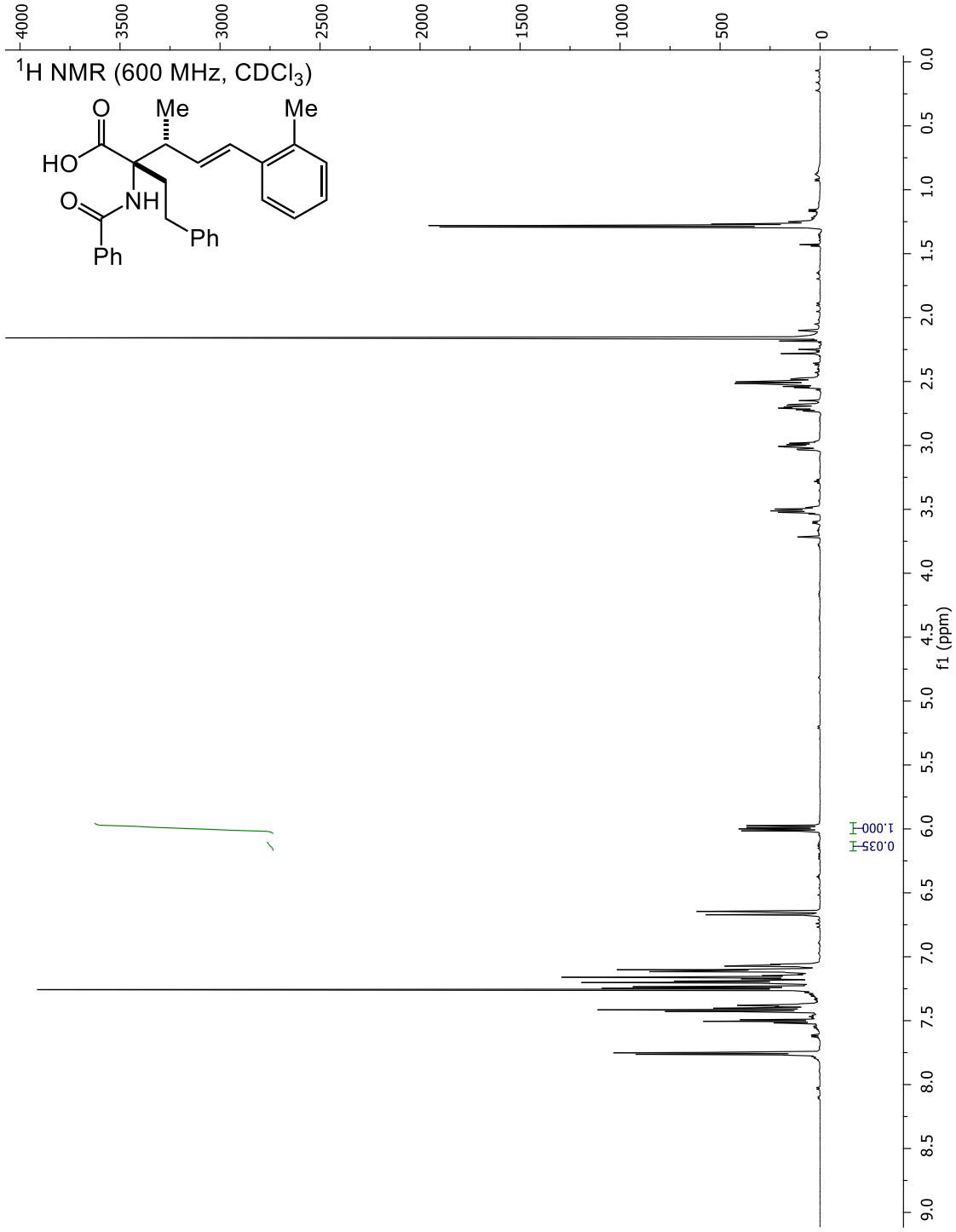
^{1}H NMR (500 MHz, $CDCl_3$)




13C NMR (151 MHz, CDCl3)
O
Me
Me
MeO
O
NH
Me
Ph
f1 (ppm)


1H NMR (600 MHz, CDCl3)
O
Me
MeO
O
NH
Me
Me
Ph
Me
Me
4000
3500
3000
2500
2000
1500
1000
500
0
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
f1 (ppm)
0.960
1.000


13C NMR (151 MHz, CDCl3)
O
Me
MeO
O
NH
Me
Me
Ph
Me
f1 (ppm)


1H NMR (600 MHz, CDCl3)
O
Me
Me
HO
O
NH
Ph
Ph
4000
3500
3000
2500
2000
1500
1000
500
0
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
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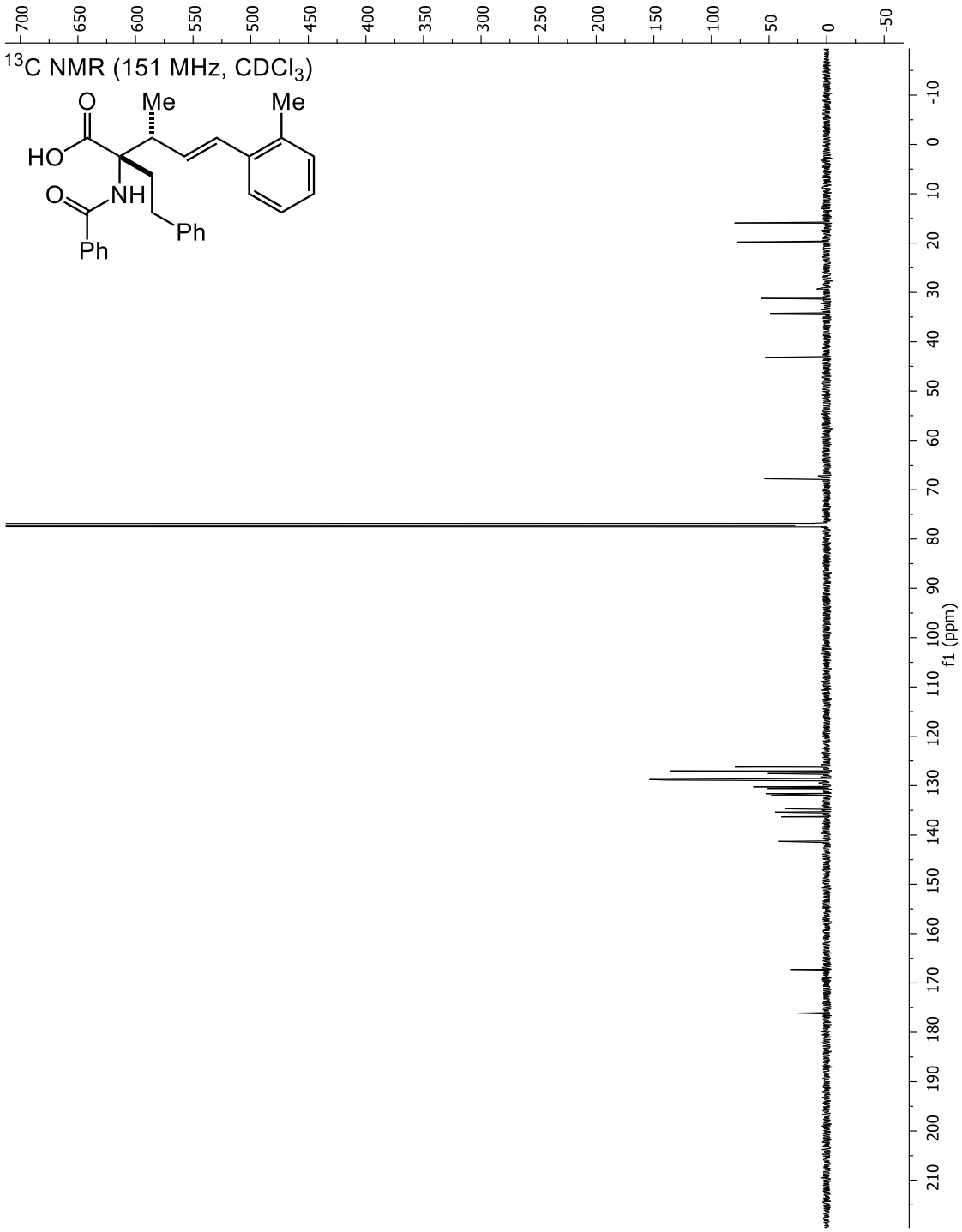
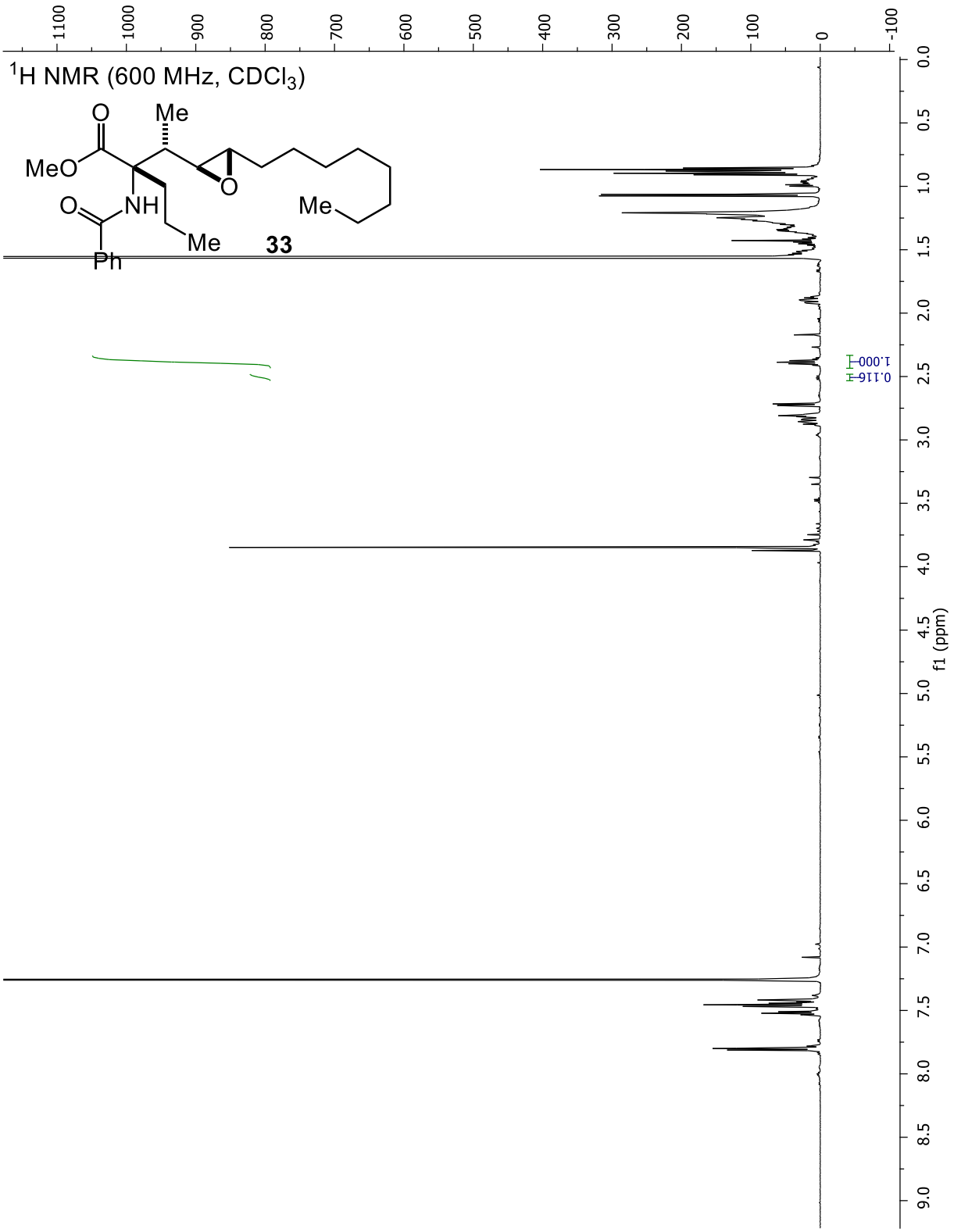
8.5
9.0
f1 (ppm)
1.000
0.035


13C NMR (151 MHz, CDCl3)
O
Me
Me
HO
O
NH
Ph
Ph
f1 (ppm)


1H NMR (600 MHz, CDCl3)
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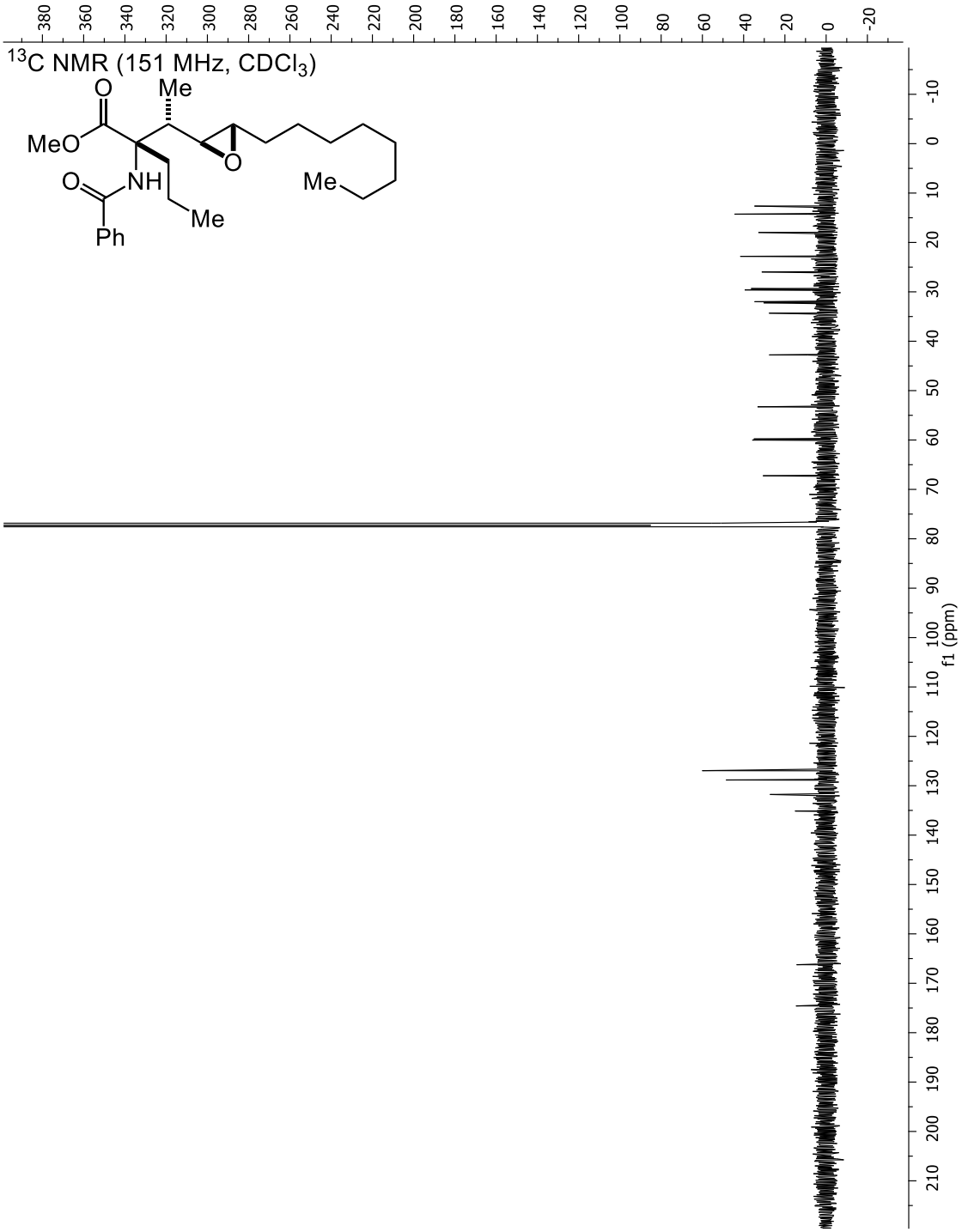
Me
MeO
O
NH
O
Me
Me
Ph
33
1.000
0.116
f1 (ppm)

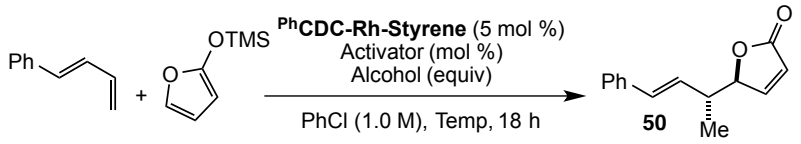

13C NMR (151 MHz, CDCl3)
O
Me
MeO
O
NH
Me
O
Me
Ph
f1 (ppm)

APPENDIX 4: SUPPORTING INFORMATION FOR CHAPTER 4

■ **General:** All reactions were carried out in flame or oven (140 ^{o}C) dried glassware that had been cooled under vacuum. Unless otherwise stated, all reactions were carried out under an inert N_2 atmosphere. All reagents were purged or sparged with N_2 for 20 min prior to distillation or use. All solid reagents were dried by azeotropic distillation with benzene twice prior to use. Mass spectra were obtained using a Thermo LTqFT mass spectrometer with electrospray ionization and external calibration. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker model DRX 400, a Bruker model AVANCE III 500, or a Bruker AVANCE III 600 CryoProbe (^{1}H NMR at 400 MHz, 500 MHz or 600 MHz, ^{13}C NMR at 100 or 151 MHz, ^{31}P NMR at 160 or 243 MHz and ^{19}F NMR at 376 or 564 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CDCl_3$ at 7.26 ppm, CD_2Cl_2 at 5.32 ppm, CD_3CN at 1.94 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, CD_2Cl_2 at 53.84 ppm, CD_3CN at 1.32 ppm). NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet, bs = broad singlet, bm = broad multiplet, etc.), and coupling constants (Hz).

■ **Solvents:** Solvents were purged with argon and purified under a positive pressure of dry argon by a SG Waters purification system: dichloromethane (EMD Millipore), diethyl ether (EMD Millipore), hexanes (EMD Millipore), benzene (EMD Millipore), and THF (EMD Millipore) were passed through activated alumina columns. $CDCl_3$ and CD_2Cl_2 were purchased from Cambridge Isotope Labs, distilled over CaH_2 and stored in a dry box over activated 4 Å molecular sieves.

Section 4.2: Hydroalkylation with Enolate Nucleophiles to Diastereoselectively Generate Allylic Butenolide Products



■ **General screening Conditions for Forming 5-(*E*-4-phenylbut-3-en-2-yl)furan-2(5*H*)-one in Table 4.2.1-1, 4.2.1-2, 4.2.1-4, 4.2.1-5, 4.2.2-1 and 4.2.2-2.**

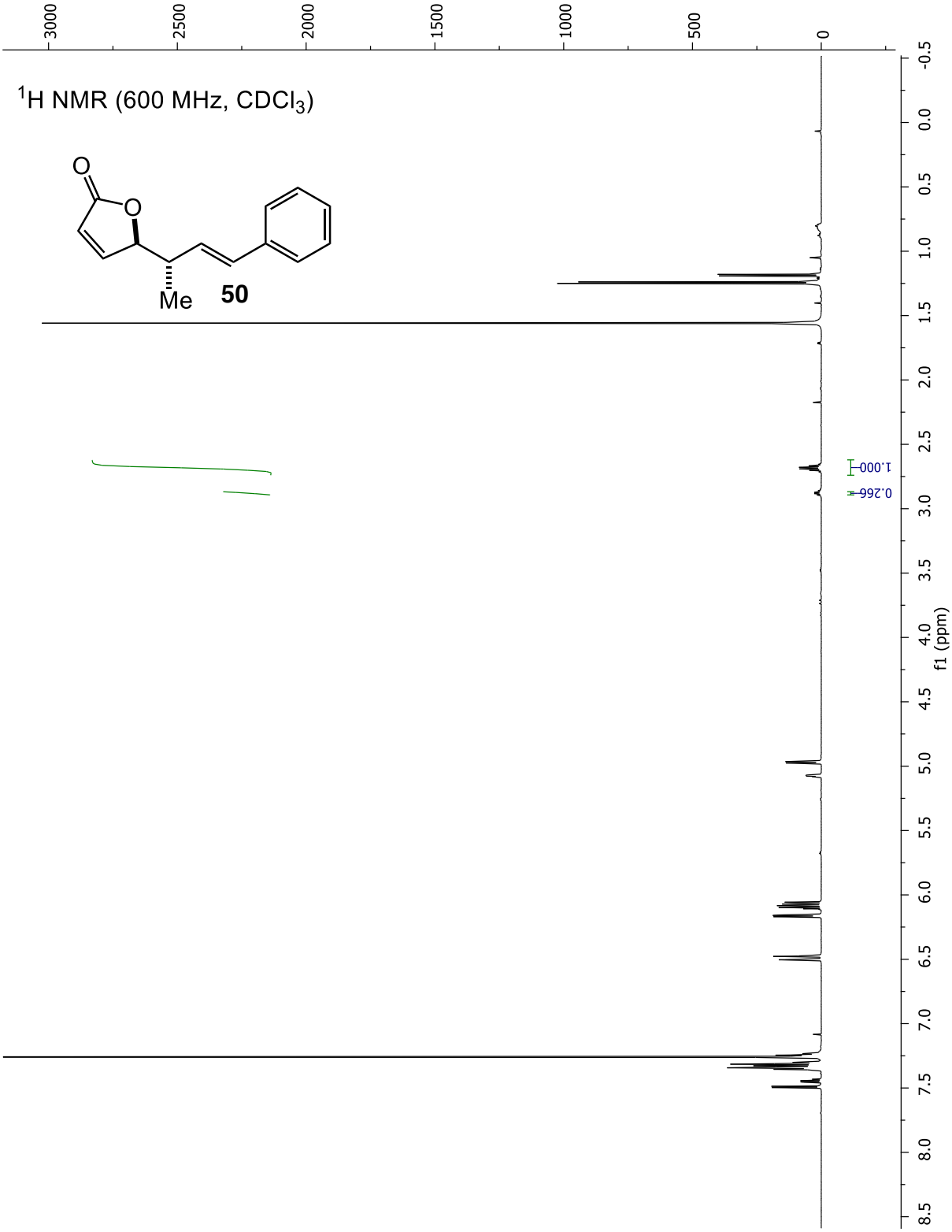
In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the **^{Ph}CDC-Rh-styrene** complex (8.1 mg, 0.005 mmol, 5 mol%), the appropriate amount of the listed Lewis acid activator, and 1,3-phenylbutadiene (13.0 mg, 0.10 mmol). The reagents were solvated with the listed solvent and the reaction sealed with a Teflon® lined septum cap before being allowed to stir at room temperature for <1 hour and removed from the dry box. A vial of the listed furan nucleophile was sparged with N_2 for a minimum of 10 minutes before the appropriate amount was added via syringe. The listed alcohol was sparged with N_2 for more than 10 minutes before being added via syringe. The reaction was allowed to warm to the appropriate temperature and stir for 18 h before being allowed to cool to 22 °C and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solvent evaporated before the product was purified by SiO_2 column chromatography to yield **50** as a colorless oil.

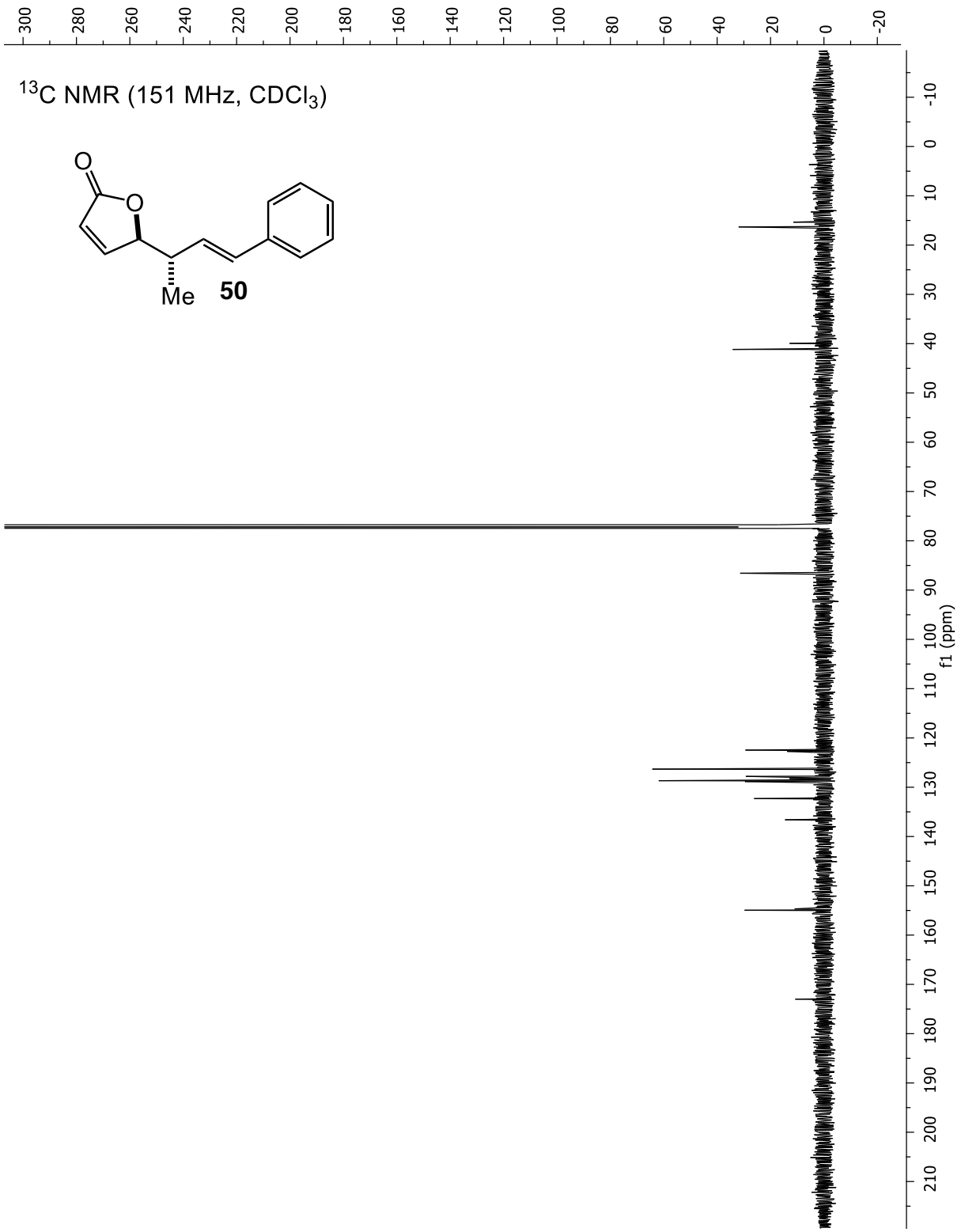
^{1}H NMR (600 MHz, CDCl3) δ 7.49 (dd, *J* = 5.7, 1.5 Hz, 1H), 7.38 – 7.29 (m, 4H), 7.26 – 7.22 (m, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.16 (dd, *J* = 5.8, 2.0 Hz, 1H), 6.08 (dd, *J* = 15.9, 8.4 Hz, 1H), 4.97 (dt, *J* = 6.7, 1.7 Hz, 1H), 2.72 – 2.65 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151

MHz, $CDCl_3$) δ 173.1, 173.1, 155.1, 154.8, 136.7, 136.7, 132.4, 132.4, 128.9, 128.8, 128.8, 128.3, 127.9, 127.9, 126.4, 126.4, 122.8, 122.6, 86.7, 86.6, 41.3, 40.0, 16.4, 15.5.

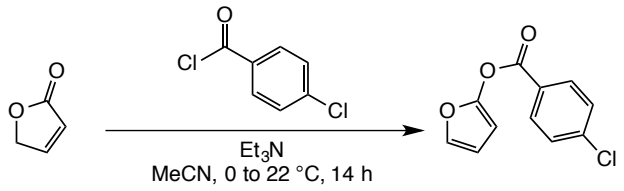
^{1}H NMR (600 MHz, $CDCl_3$)

50




13C NMR (151 MHz, CDCl3)
O
O
Me
50
f1 (ppm)

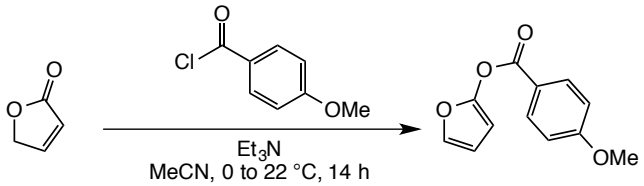
Section 4.3: Diene Hydroalkylation with Benzoyl-Derived Furan Nucleophiles



Synthesis of furan-2-yl 4-chlorobenzoate

A vial was charged with furanone (1.0 g, 11.9 mmol) and solvated with acetonitrile (4 mL, benchtop) before dry triethylamine (1.7 mL, 12.5 mmol) was added and the reaction sealed with a septa and the headspace purged with N_2. The reaction was cooled to 0 °C and 4-chlorobenzoyl chloride (1.6 mL, 12.5 mmol) added via syringe under N_2. The brown solution was warmed to room temperature and allowed to stir for 14 h during which time a white precipitate formed. The reaction was filtered and the solid rinsed with Et_2O before the organic layers were combined and washed with a saturated solution of aqueous $NaHCO_3$, water and brine. The resulting solution was dried with Na_2SO_4, filtered, and concentrated to a brown oil that was purified by SiO_2 gel chromatography (10:1 Hex/Et_2O) to yield furan-2-yl 4-chlorobenzoate as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.09 (m, 2H), 7.54 – 7.44 (m, 2H), 7.12 (dd, J = 2.1, 1.0 Hz, 1H), 6.42 (dd, J = 3.3, 2.2 Hz, 1H), 6.04 (dd, J = 3.3, 1.0 Hz, 1H).

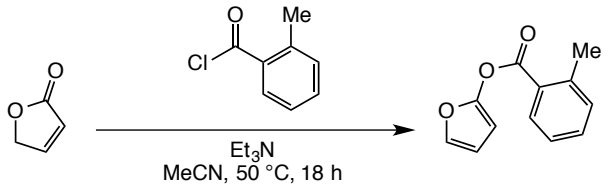


Synthesis of furan-2-yl 4-methoxybenzoate

A vial was charged with furanone (1.0 g, 11.9 mmol) and solvated with acetonitrile (4 mL, benchtop) before dry triethylamine (1.7 mL, 12.5 mmol) was added and the reaction sealed with

a septa and the headspace purged with N_2. The reaction was cooled to 0 °C and 4-methoxybenzoyl chloride (2.1 mL, 12.5 mmol) added via syringe under N_2. The brown solution was warmed to room temperature and allowed to stir for 14 h during which time a white precipitate formed. The reaction was filtered and the solid rinsed with Et_2O before the organic layers were combined and washed with a saturated solution of aqueous $NaHCO_3$, water and brine. The resulting solution was dried with Na_2SO_4, filtered, and concentrated to a brown oil that was purified by SiO_2 gel chromatography (10:1 Hex/Et_2O) to yield furan-2-yl 4-methoxybenzoate as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.07 (m, 2H), 7.11 (dd, J = 2.1, 1.1 Hz, 1H), 7.04 – 6.93 (m, 2H), 6.41 (dd, J = 3.3, 2.2 Hz, 1H), 6.00 (dd, J = 3.3, 1.1 Hz, 1H), 3.90 (s, 3H).

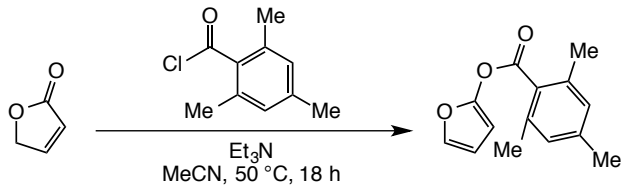


Synthesis of furan-2-yl 2-methylbenzoate

A vial was charged with furanone (500 mg, 5.95 mmol) and solvated with acetonitrile (5 mL, benchtop) before dry triethylamine (870 μL, 6.24 mmol) was added and the reaction sealed with a septa and the headspace purged with N_2. 2-methylbenzoyl chloride (770 μL, 5.95 mmol) was added at room temperature via syringe under N_2. The brown solution was warmed to 50 °C and allowed to stir for 18 h during which time a white precipitate formed. The reaction was filtered and the solid rinsed with Et_2O before the organic layers were combined and washed with a saturated solution of aqueous $NaHCO_3$, water and brine. The resulting solution was dried with

Na_2SO_4, filtered, and concentrated to a brown oil that was purified by SiO_2 gel chromatography (10:1 Hex/Et_2O) to yield furan-2-yl 2-methylbenzoate as a yellow oil.

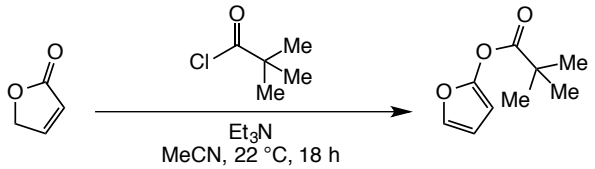
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 – 8.10 (m, 1H), 7.56 – 7.43 (m, 1H), 7.32 (t, *J* = 6.9 Hz, 2H), 7.13 (dd, *J* = 2.1, 1.1 Hz, 1H), 6.42 (dd, *J* = 3.3, 2.2 Hz, 1H), 6.00 (dd, *J* = 3.3, 1.0 Hz, 1H), 2.67 (s, 3H).



Synthesis of furan-2-yl 2,4,6-trimethylbenzoate

A vial was charged with furanone (500 mg, 5.95 mmol) and solvated with acetonitrile (5 mL, benchtop) before dry triethylamine (870 μL, 6.24 mmol) was added and the reaction sealed with a septa and the headspace purged with N_2. 2,4,6-trimethylbenzoyl chloride (990 μL, 5.95 mmol) was added at room temperature via syringe under N_2. The brown solution was warmed to 50 °C and allowed to stir for 18 h during which time a white precipitate formed. The reaction was filtered and the solid rinsed with Et_2O before the organic layers were combined and washed with a saturated solution of aqueous $NaHCO_3$, water and brine. The resulting solution was dried with Na_2SO_4, filtered, and concentrated to a brown oil that was purified by SiO_2 gel chromatography (10:1 Hex/Et_2O) to yield furan-2-yl 2,4,6-trimethylbenzoate as a yellow oil.

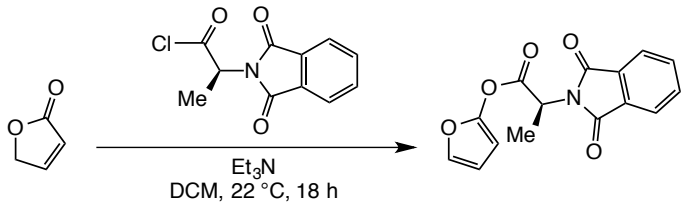
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 2.1, 1.1 Hz, 1H), 6.92 (s, 2H), 6.42 (dd, *J* = 3.3, 2.2 Hz, 1H), 6.03 (dd, *J* = 3.3, 1.1 Hz, 1H), 2.43 (s, 6H), 2.32 (s, *J* = 8.5 Hz, 3H).



Synthesis of furan-2-yl 2,4,6-trimethylbenzoate

A vial was charged with furanone (500 mg, 5.95 mmol) and solvated with acetonitrile (2 mL, benchtop) before dry triethylamine (870 μL, 6.24 mmol) was added and the reaction sealed with a septa and the headspace purged with N_2. pivaloyl chloride (730 μL, 5.95 mmol) was added at room temperature via syringe under N_2. The brown solution was allowed to stir for 18 h during which time a white precipitate formed. The reaction was filtered and the solid rinsed with Et_2O before the organic layers were combined and washed with a saturated solution of aqueous $NaHCO_3$, water and brine. The resulting solution was dried with Na_2SO_4, filtered, and concentrated to a brown oil that was purified by SiO_2 gel chromatography (10:1 Hex/Et_2O) to yield furan-2-yl pivalate as a clear oil. Characterization matched that reported in *J. Med. Chem.*, **2005**, *48* (8), 2822.

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.05 (dd, J = 2.1, 1.1 Hz, 1H), 6.36 (dd, J = 3.3, 2.2 Hz, 1H), 5.86 (dd, J = 3.3, 1.0 Hz, 1H), 1.34 (s, 9H).

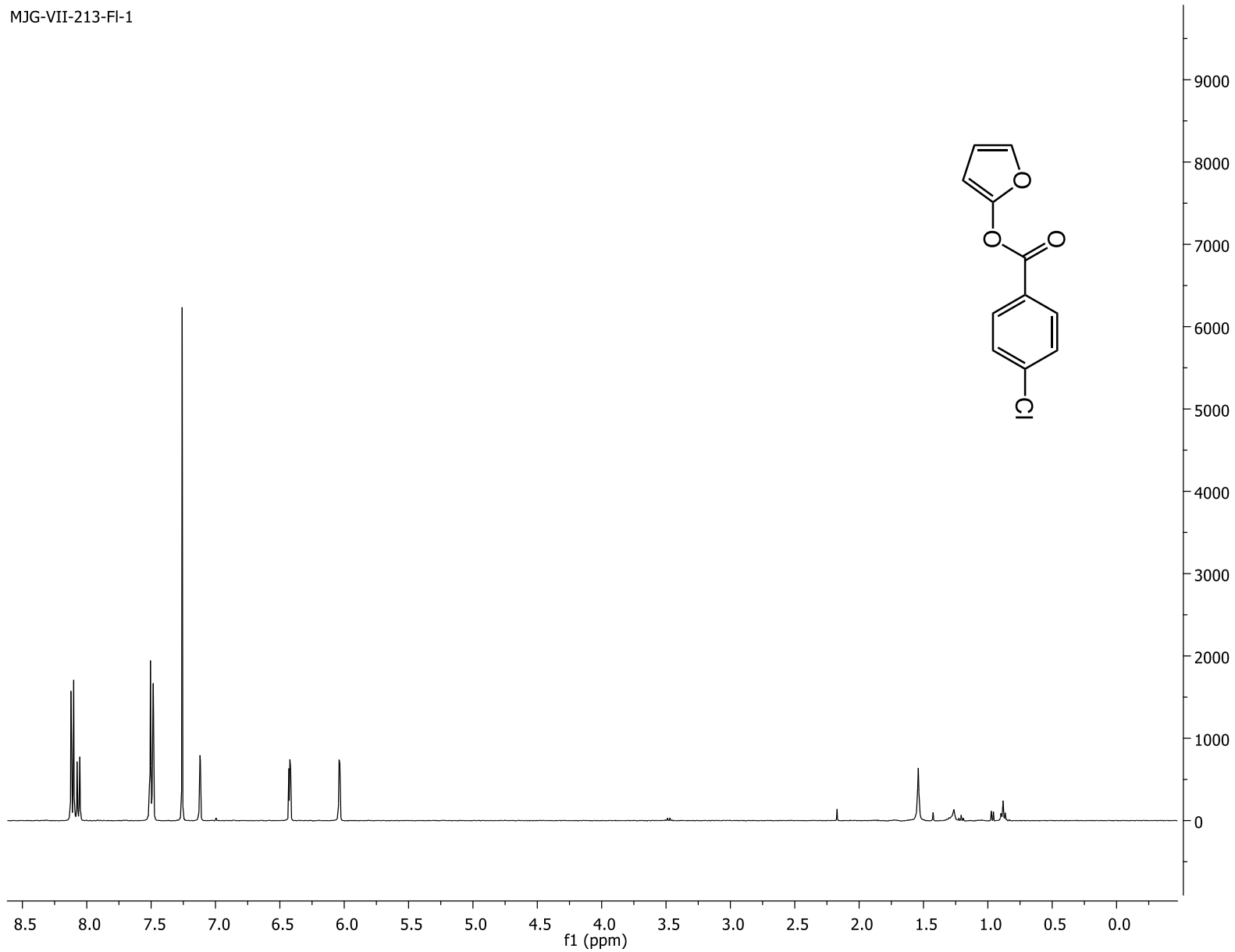


Synthesis of furan-2-yl (*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoate

A vial was charged with furanone (250 mg, 2.97 mmol) and solvated with dry dichloromethane (6 mL) before dry triethylamine (456 μL, 3.27 mmol) was added and the reaction sealed with a

septa and the headspace purged with N_2. (*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl chloride (706 μL, 2.97 mmol) was added at room temperature via syringe under N_2. The brown solution was allowed to stir for 18 h during which time a white precipitate formed. The reaction was filtered and the solid rinsed with Et_2O and the resulting solution was dried with Na_2SO_4, filtered, and concentrated to a red oil that was purified by SiO_2 gel chromatography (10:1 Hex/Et_2O) to yield furan-2-yl pivalate as a yellow crystalline solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.84 (m, H), 7.82 – 7.69 (m, 2H), 7.02 (dd, *J* = 2.1, 1.1 Hz, 1H), 6.33 (dd, *J* = 3.3, 2.2 Hz, 1H), 5.92 (dd, *J* = 3.3, 1.1 Hz, 1H), 5.21 (q, *J* = 7.3 Hz, 1H), 1.78 (d, *J* = 7.3 Hz, 3H).


MJG-VII-213-Fl-1
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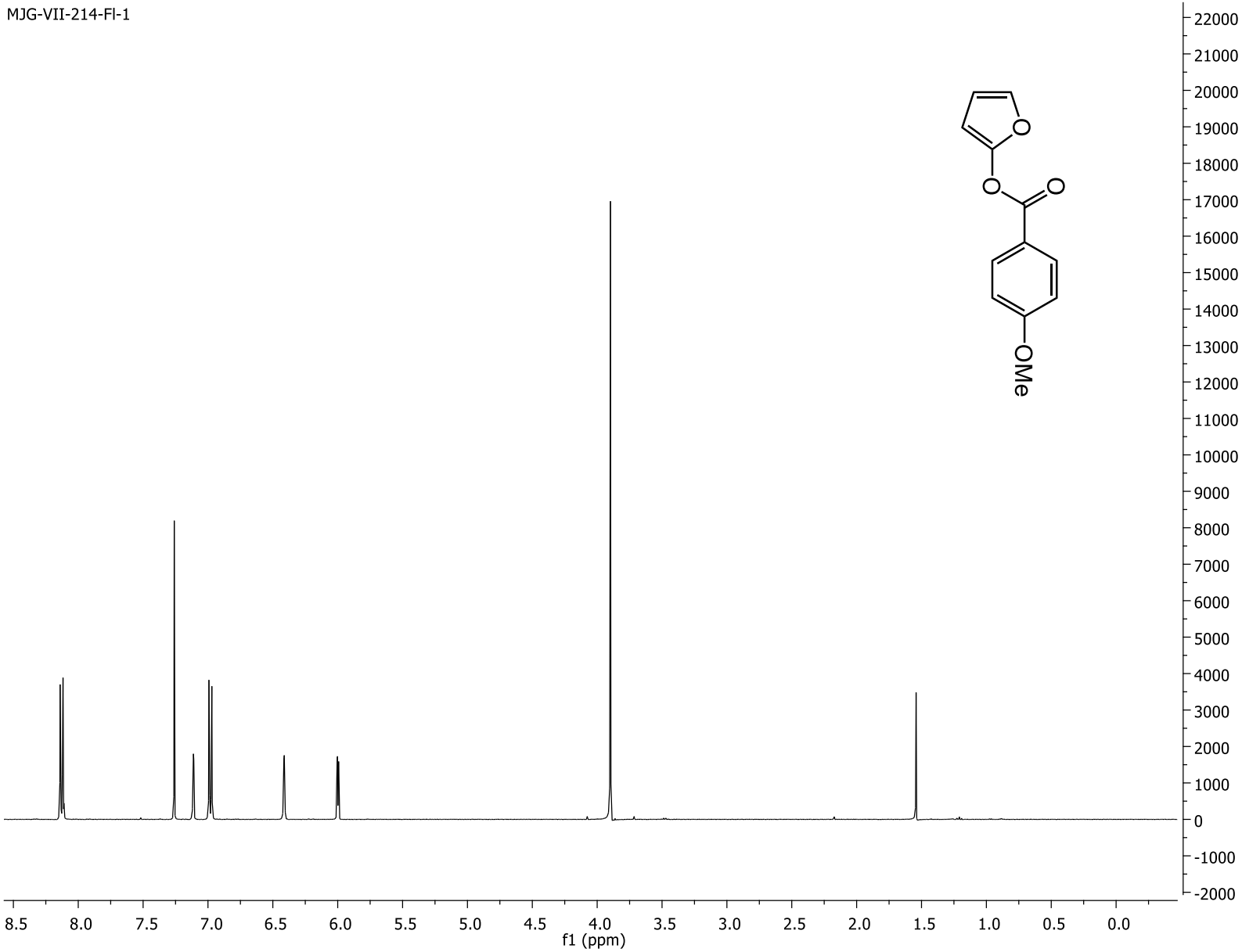
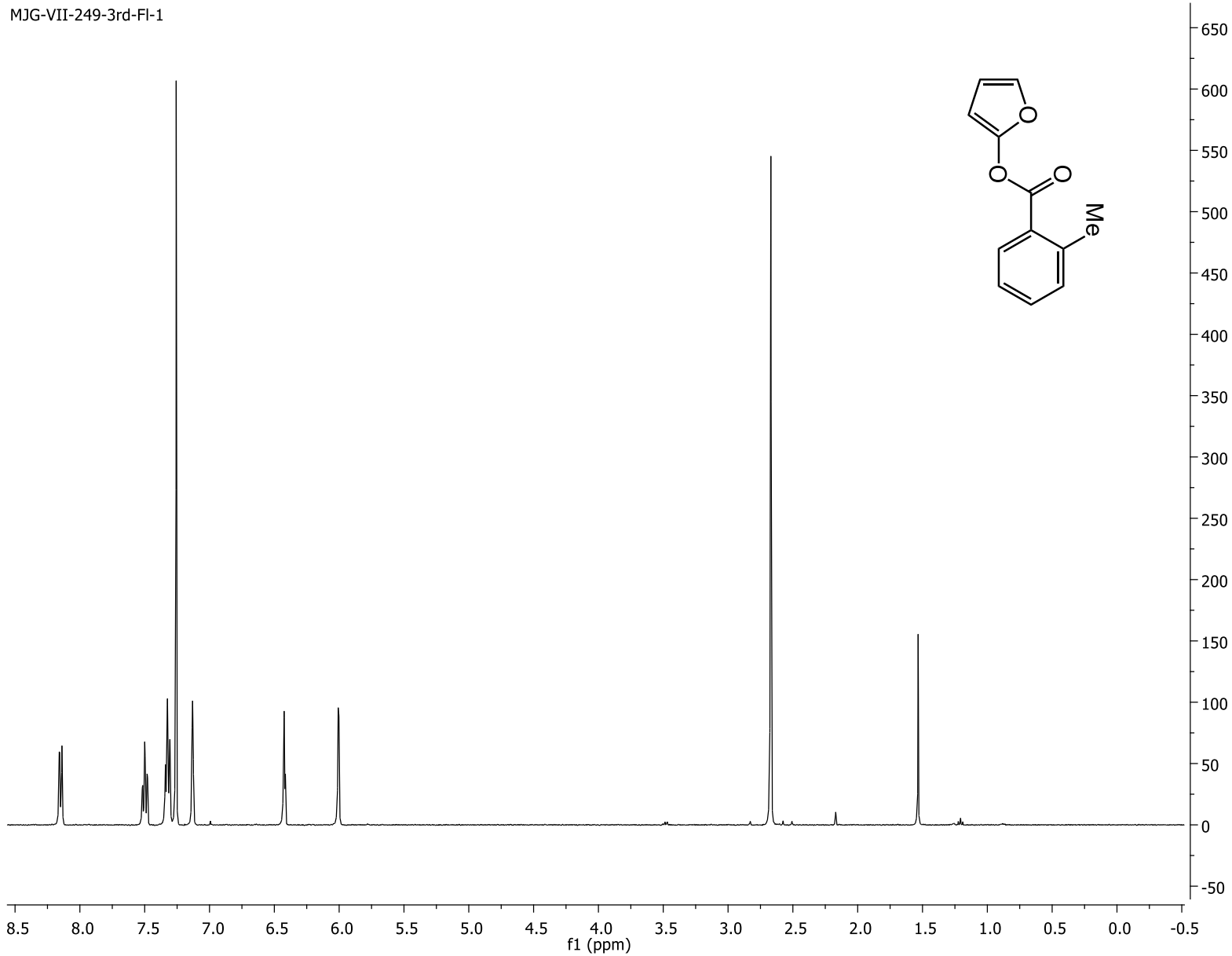
8000
7000
6000
5000
4000
3000
2000
1000
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
O
O
Cl


MJG-VII-214-Fl-1
OMe
f1 (ppm)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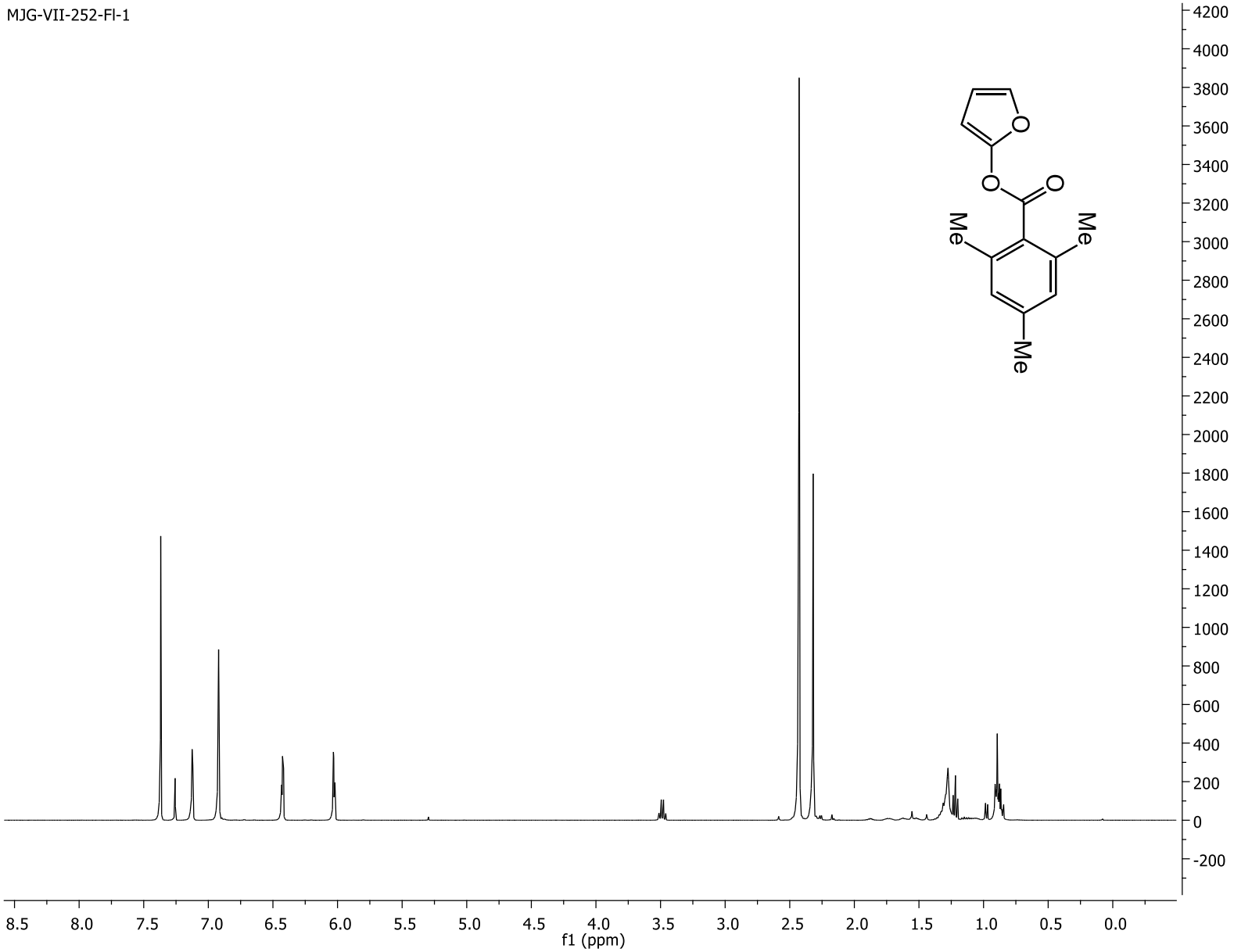
Me
f1 (ppm)


MJG-VII-252-Fl-1
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
4200
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
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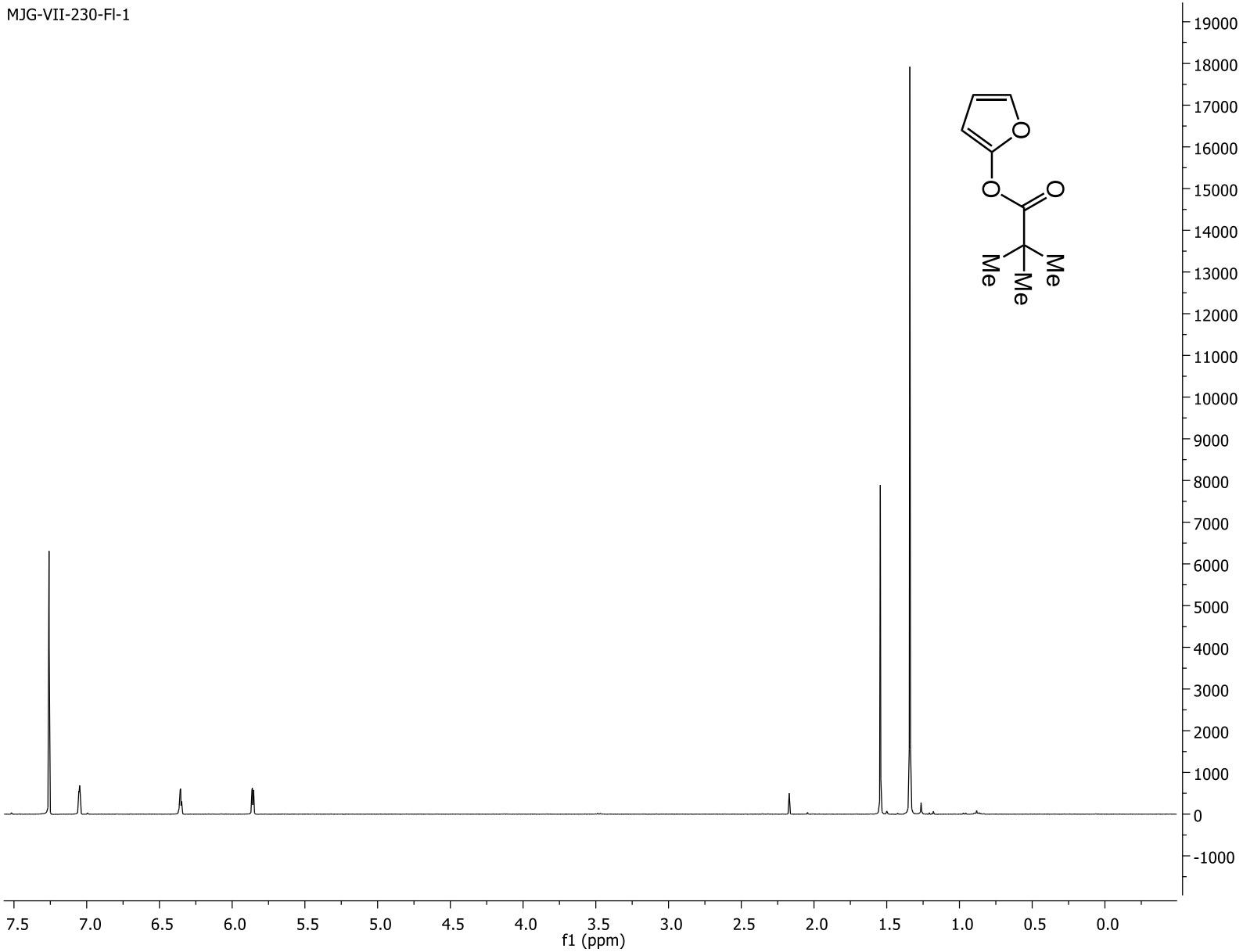
200
0
-200
O
O
O
Me
Me
Me


MJG-VII-230-Fl-1
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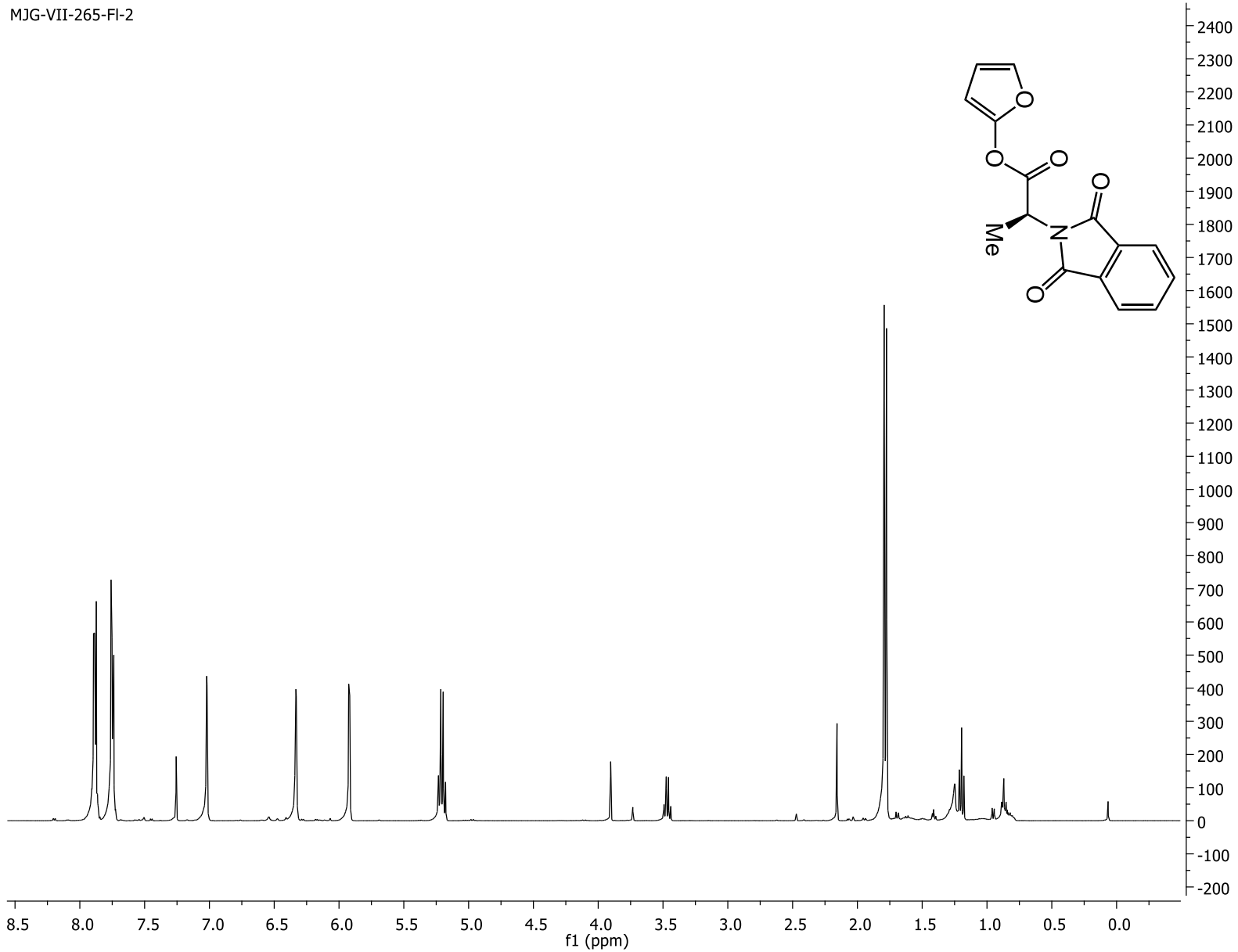
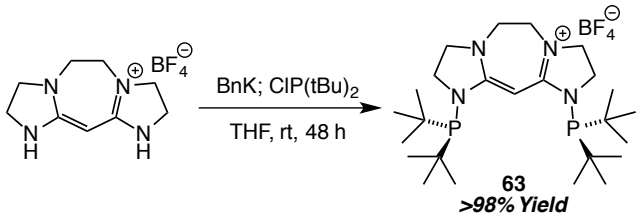
O
Me
Me
Me
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


MJG-VII-265-Fl-2
f1 (ppm)
Me

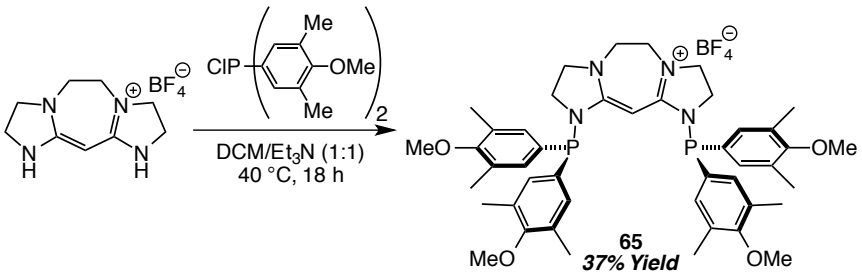
Section 4.4: Synthesizing Sterically and Electronically Modified CDC-Rh(I) Catalysts



Synthesis of 63

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (50 mg, 0.188 mmol), and benzyl potassium (61.3 mg, 0.47 mmol). The reagents were solvated with THF (1 mL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at room temperature for 1 hour. To the resulting white suspension was added di-*tert*-butylchlorophosphine (107 μL, 0.564 mmol) and the reaction was allowed to stir for 48 h. The product was triturated with hexanes and filtered through a Celite® plug before being recovered by dissolving off the plug with MeCN. The solution was concentrated to yield **63** (102 mg, 0.184 mmol, 98% yield) as an off-white powder.

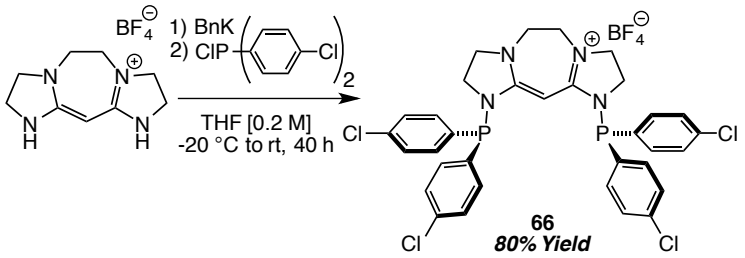
^{1}H NMR (400 MHz, CD_3CN) δ 6.12 (t, *J* = 8.3 Hz, 1H), 3.92 (t, *J* = 8.4 Hz, 4H), 3.64 (t, *J* = 8.4 Hz, 4H), 3.56 (s, 4H), 1.26 (d, *J* = 12.8 Hz, 36H). **^{31}P NMR** (162 MHz, CD_3CN) δ 80.69.



Synthesis of 65

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (50 mg, 0.0752 mmol), and bis(3,5-di-*tert*-butyl-4-methoxyphenyl)chlorophosphine (76 mg, 0.226 mmol). The reagents were solvated with DCM (0.5 mL) and the reaction sealed with a Teflon® lined septa cap before being removed from the dry box. Dry triethylamine (0.5 mL) was added via syringe under N_2 and the reaction allowed to stir at 40 °C for 18 h. The reaction was cooled and concentrated before being passed through a Celite® plug with benchtop benzene. The flowthrough was concentrated and purified by SiO_2 gel chromatography (100:1 DCM/iPrOH) to provide 65 (24.3 mg, 0.0278 mmol, 37% yield) as an off-white solid foam.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, *J* = 7.9 Hz, 8H), 6.12 (td, *J* = 7.4, 3.1 Hz, 1H), 3.80 – 3.73 (m, 12H), 3.73 – 3.64 (m, 8H), 3.34 (dd, *J* = 20.7, 12.4 Hz, 4H), 2.28 (s, *J* = 3.5 Hz, 12H), 1.19 (d, *J* = 6.1 Hz, 12H).

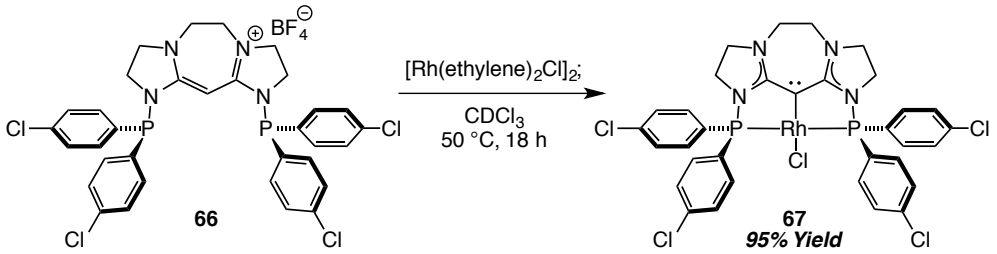


Synthesis of 66

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (60 mg, 0.226 mmol), and benzyl potassium (58.8 mg, 0.451 mmol). The reagents were solvated with THF (1.1 mL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at room temperature for 1 hour. To the resulting white suspension was added bis(4-

chlorophenyl)chlorophosphine (196 μL, 0.677 mmol) at -20 °C and the reaction allowed to stand in the dry box freezer at -20 °C for 40 h. The reaction was concentrated to dryness and then resolvated in minimal DCM before being triturated with excess hexanes. The suspension was filtered through a Celite® plug and washed with excess hexanes before being reisolated by solvation in DCM. The solution was concentrated to yield **66** (140 mg, 0.181 mmol, 80% yield) as a yellow foaming solid that was used crude without further purification.

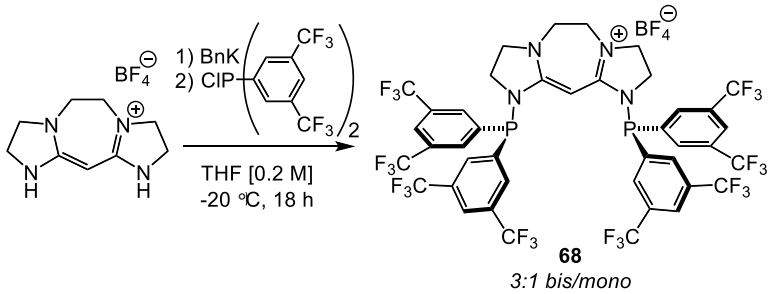
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 16H), 5.91 (bs, 1H), 3.65 – 3.58 (m, 4H), 3.44 – 3.34 (m, 4H), 3.26 (bs, 4H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 39.07.



Synthesis of 67

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **66** (32.7 mg, 0.0423 mmol), and $[Rh(ethylene)Cl]_2$ (8.2 mg, 0.0212 mmol). The reagents were solvated with $CDCl_3$ (400 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at 22 °C for 5 hours. The solution was transferred to an NMR tube and analyzed by NMR spectroscopy before being returned to the dry box and heated to 50 °C for 18 h. The reaction was cooled and concentrated to dryness before being resolvated in minimal DCM and triturated with excess hexanes. The suspension was filtered through a Celite® plug and washed with excess hexanes before being reisolated by solvation in DCM. The solution was concentrated to yield **67** (33.1 mg, 0.0402 mmol, 98% yield) as a tan powder that was used crude without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 8H), 7.37 (d, *J* = 8.0 Hz, 8H), 4.18 – 3.99 (m, 4H), 3.83 – 3.66 (m, 4H), 3.55 (s, *J* = 12.5 Hz, 4H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 69.94 (d, *J* = 107.1 Hz).

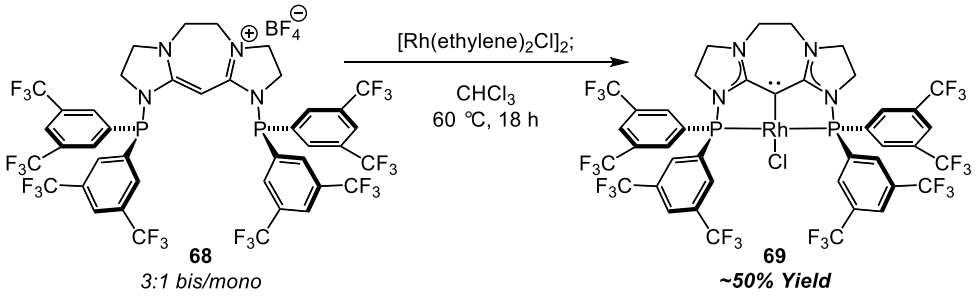


Synthesis of 68

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (10 mg, 0.0376 mmol), and benzyl potassium (9.8 mg, 0.0752 mmol). The reagents were solvated with THF (188 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at room temperature for 1 hour. To the resulting white suspension was added bis(4-chlorophenyl)chlorophosphine (56 mg, 0.113 mmol) at -20 °C and the reaction allowed to stand in the dry box freezer at -20 °C for 40 h. The reaction was concentrated to dryness and then resolvated in minimal $CHCl_3$ before being triturated with excess hexanes. The solvent was pipetted off and the remaining white powder dried under vacuum to yield **68** as a 3:1 mixture of the bis- and mono-phosphorylated products. This material was used crude without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 16.4 Hz, 8H), 7.90 – 7.78 (m, 8H), 6.05 (t, *J* = 7.3 Hz, 1H), 5.66 (d, *J* = 6.4 Hz, 1H, characteristic peak of the mono-phosphorylated impurity), 4.02

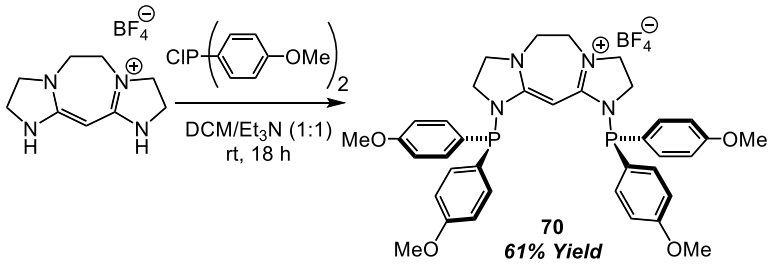
– 3.86 (m, 4H), 3.83 – 3.65 (m, 4H), 3.39 (t, J = 8.3 Hz, 4H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 37.75.



Synthesis of 69

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with impure **68** (33 mg, 0.0376 mmol), and $[Rh(ethylene)Cl]_2$ (5.5 mg, 0.0141 mmol). The reagents were solvated with $CHCl_3$ (200 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at 22 °C for 3 hours and then heated to 60 °C and allowed to stir for 18 h. The solution was cooled to room temperature, concentrated and analyzed by NMR spectroscopy before being returned to the dry box. The NMR sample was triturated with excess hexanes and the suspension filtered through a Celite® plug to remove any soluble phosphine impurities. The product was reisolated by dissolving in $CHCl_3$ and concentrating to yield **69** (7.0 mg, 0.0113 mmol, 40% yield) as a tan powder that was used crude without further purification.

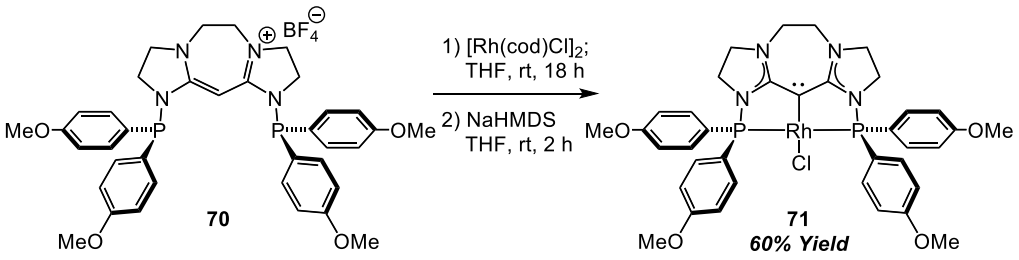
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (t, J = 5.1 Hz, 8H), 8.02 (s, J = 13.0 Hz, 4H), 4.26 (t, J = 8.1 Hz, 4H), 3.79 (d, J = 12.8 Hz, 8H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 71.14 (d, J = 110.8 Hz).



Synthesis of 70

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (39.4 mg, 0.148 mmol), and bis(4-methoxyphenyl)chlorophosphine (104 mg, 0.371 mmol). The reagents were solvated with DCM (0.5 mL) and the reaction sealed with a Teflon® lined septa cap before being removed from the dry box. Dry triethylamine (0.5 mL) was added via syringe under N_2 and the reaction allowed to stir at 22 °C for 18 h. The reaction was concentrated and purified by SiO_2 gel chromatography (100:1 DCM/iPrOH) to provide **70** (68 mg, 0.0903 mmol, 61% yield) as an off-white solid foam. The product was azeotroped with benzene to remove water before being used.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 8.0 Hz, 8H), 6.94 (dd, J = 15.8, 6.0 Hz, 8H), 6.11 (t, J = 7.4 Hz, 1H), 3.83 (s, 12H), 3.76 – 3.62 (m, 8H), 3.32 (t, J = 8.7 Hz, 4H).



Synthesis of 71

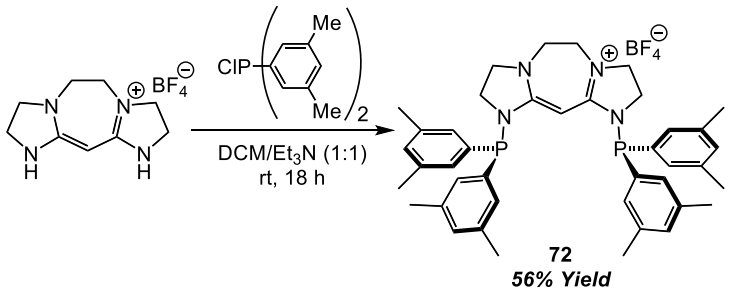
In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **70** (20 mg, 0.0265 mmol), and $[Rh(cod)Cl]_2$ (6.5 mg, 0.0133 mmol). The reagents were solvated with THF (1 mL) and the

reaction sealed with a Teflon® lined cap before being allowed to stir at 22 °C for 18 hours before being concentrated and analyzed by NMR spectroscopy to observe the Rh-hydride intermediate. The NMR sample was reisolated by concentration to generate a tan powder (10 mg, 0.0124 mmol, 47% yield).

^{1}H NMR (600 MHz, CD_3CN) δ 7.89 (dd, *J* = 12.9, 6.0 Hz, 4H), 7.46 (dt, *J* = 16.1, 7.9 Hz, 4H), 7.10 (d, *J* = 8.3 Hz, 4H), 7.04 (d, *J* = 8.2 Hz, 4H), 4.09 (dd, *J* = 18.4, 9.3 Hz, 2H), 3.91 (dt, *J* = 9.7, 6.2 Hz, 2H), 3.86 (d, *J* = 11.0 Hz, 6H), 3.84 – 3.77 (m, 6H), 3.65 – 3.60 (m, 4H), 3.50 – 3.40 (m, 2H), 3.29 – 3.18 (m, 2H), -16.46 – -16.67 (m, 1H).

A vial was charged with a portion of the Rh-hydride intermediate (5.0 mg, 0.0056 mmol) and NaHMDS (1.0 mg, 0.0056 mmol) before being solvated with THF (400 μL). The solution was allowed to stir at 22 °C for 2 h before being concentrated and plugged through Celite® with excess THF to provide an orange solution. The solution was concentrated to provide **71** (2.7 mg, 0.0159 mmol, 60% yield) as a red/tan powder.

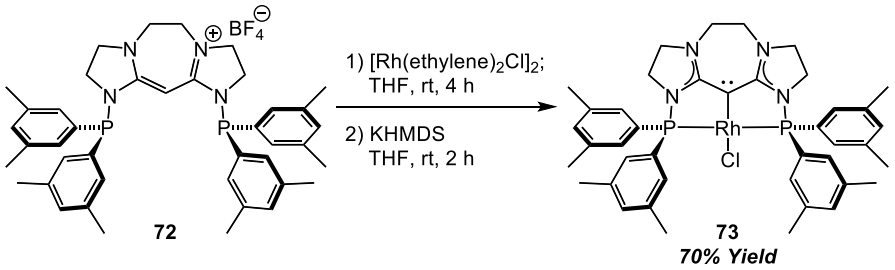
^{1}H NMR (400 MHz, CD_3CN) δ 7.62 – 7.52 (m, 8H), 7.02 (d, *J* = 8.5 Hz, 8H), 4.00 – 3.90 (m, 4H), 3.82 (s, 12H), 3.39 (d, *J* = 6.3 Hz, 4H), 3.23 (dd, *J* = 16.5, 8.6 Hz, 4H). **^{31}P NMR** (162 MHz, CD_3CN) δ 77.87 (dd, *J* = 248.7, 91.7 Hz).



Synthesis of 72

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (20 mg, 0.0752 mmol), and bis(3,5-dimethylphenyl)chlorophosphine (52 mg, 0.188 mmol). The reagents were solvated with DCM (0.5 mL) and the reaction sealed with a Teflon® lined septa cap before being removed from the dry box. Dry triethylamine (0.5 mL) was added via syringe under N_2 and the reaction allowed to stir at 22 °C for 18 h. The reaction was concentrated and purified by SiO_2 gel chromatography (100:1 DCM/iPrOH) to provide **72** (60 mg, 0.0421 mmol, 56% yield) as an off-white solid foam. The product was azeotroped with benzene to remove water before being used.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 4H), 7.13 – 7.04 (m, 4H), 7.00 (d, J = 8.2 Hz, 4H), 6.15 (t, J = 7.4 Hz, 1H), 3.78 (s, 4H), 3.77 – 3.69 (m, 4H), 3.36 (t, J = 8.7 Hz, 4H), 2.32 (s, J = 10.1 Hz, 24H).



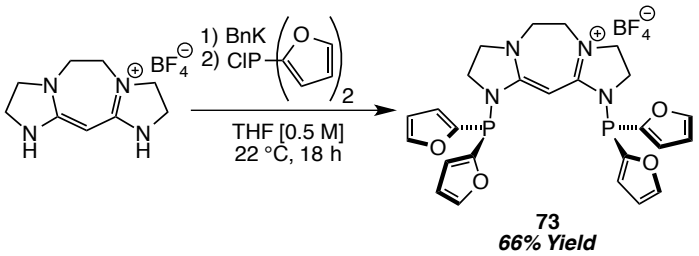
Synthesis of 73

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **72** (50 mg, 0.0704 mmol), and $[Rh(ethylene)Cl]_2$ (13.7 mg, 0.0352 mmol). The reagents were solvated with THF (200 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at 22 °C for 4 hours before being concentrated and analyzed by NMR spectroscopy to observe the Rh-hydride intermediate. The NMR sample was reisolated by concentration to generate a tan powder.

^{1}H NMR (600 MHz, CD_3CN) δ 7.63 (t, *J* = 6.1 Hz, 4H), 7.37 – 7.30 (m, 4H), 7.25 – 7.16 (m, 4H), 4.16 (q, *J* = 9.4 Hz, 1H), 4.00 – 3.90 (m, 2H), 3.75 – 3.61 (m, 2H), 3.58 – 3.46 (m, 4H), 3.30 (q, *J* = 9.6 Hz, 2H), 2.41 (d, *J* = 9.7 Hz, 3H), 2.34 (d, *J* = 4.6 Hz, 3H), 2.11 (s, 6H), -16.35 (dt, *J* = 19.1, 9.6 Hz, 1H).

The impure Rh-hydride intermediate was azeotroped twice with benzene before KHMDS (14.0 mg, 0.0704 mmol) was added and the solids solvated with THF (400 μL) to generate a deep red solution. The solution was allowed to stir at 22 °C for 2 h before being diluted with diethyl ether and plugged through Celite® to provide a red solution. The solution was concentrated to provide **73** (39.3 mg, 0.0493 mmol, 70% yield) as a tan powder.

^{1}H NMR (400 MHz, CD_3CN) δ 7.29 (t, *J* = 5.5 Hz, 8H), 7.21 (s, 4H), 4.07 – 3.99 (m, 4H), 3.46 (d, *J* = 6.0 Hz, 4H), 3.37 – 3.29 (m, 4H), 2.36 (s, 24H). **^{31}P NMR** (162 MHz, CD_3CN) δ 79.38 (dd, *J* = 220.7, 68.0 Hz).

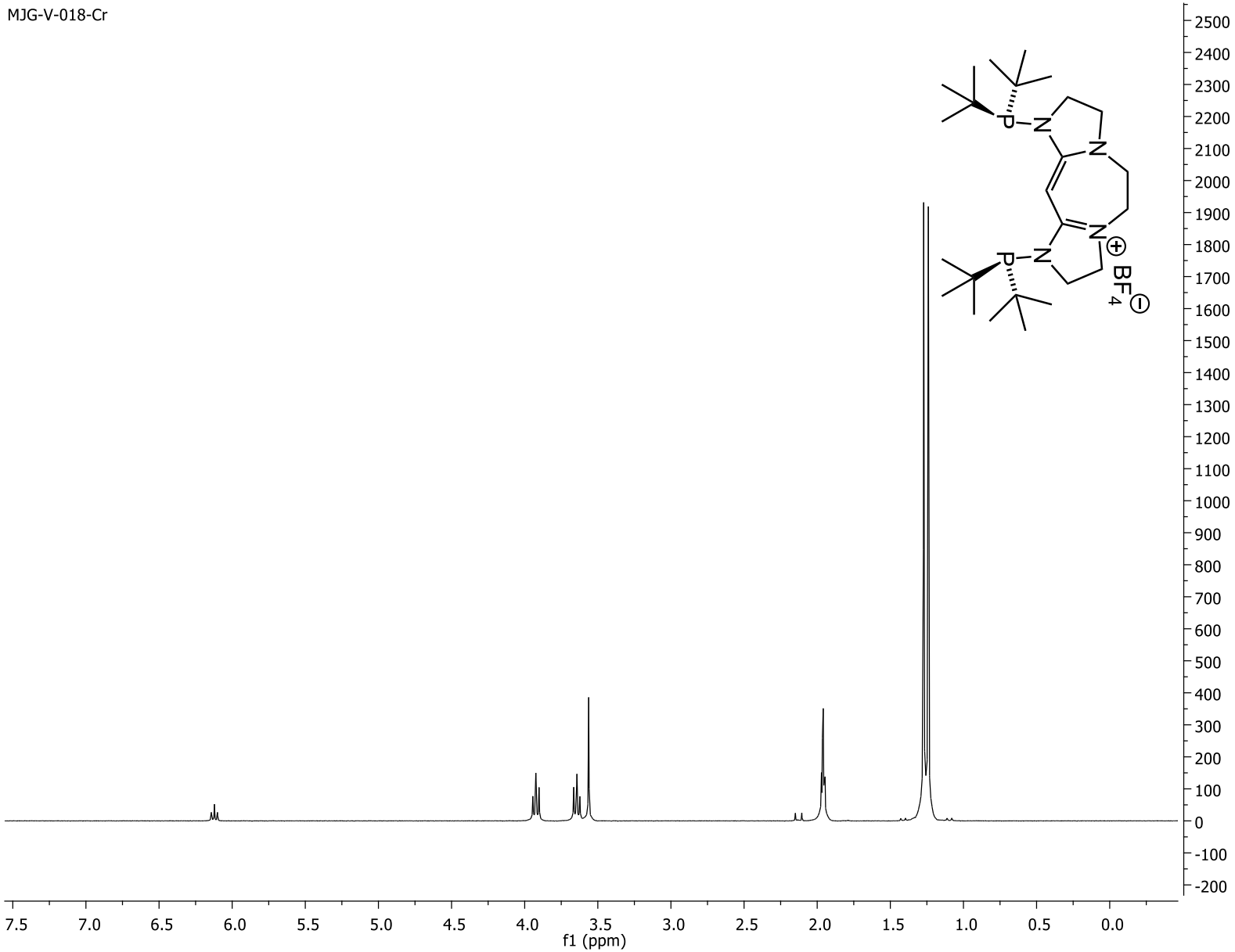


Synthesis of 73

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (40 mg, 0.150 mmol), and benzyl potassium (39.2 mg, 0.301 mmol). The reagents were solvated with THF (300 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at room temperature for 1 hour. To the resulting white suspension was added bis(2-furyl)chlorophosphine

(58.6 μL, 0.376 mmol) at 22 °C and the reaction allowed to stir for 40 h. The reaction was concentrated to dryness and resolvated in minimal THF before being triturated with excess hexanes. The liquid was pipeted off leaving a tan solid that was dried to yield impure **73** (57.2 mg, 0.099 mmol, 66% yield) as a yellow foaming solid that was used crude without further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 – 7.59 (m, 4H), 7.08 – 6.87 (m, 4H), 6.63 – 6.31 (m, 4H), 5.91 (t, J = 7.0 Hz, 1H), 3.79 – 3.68 (m, 12H).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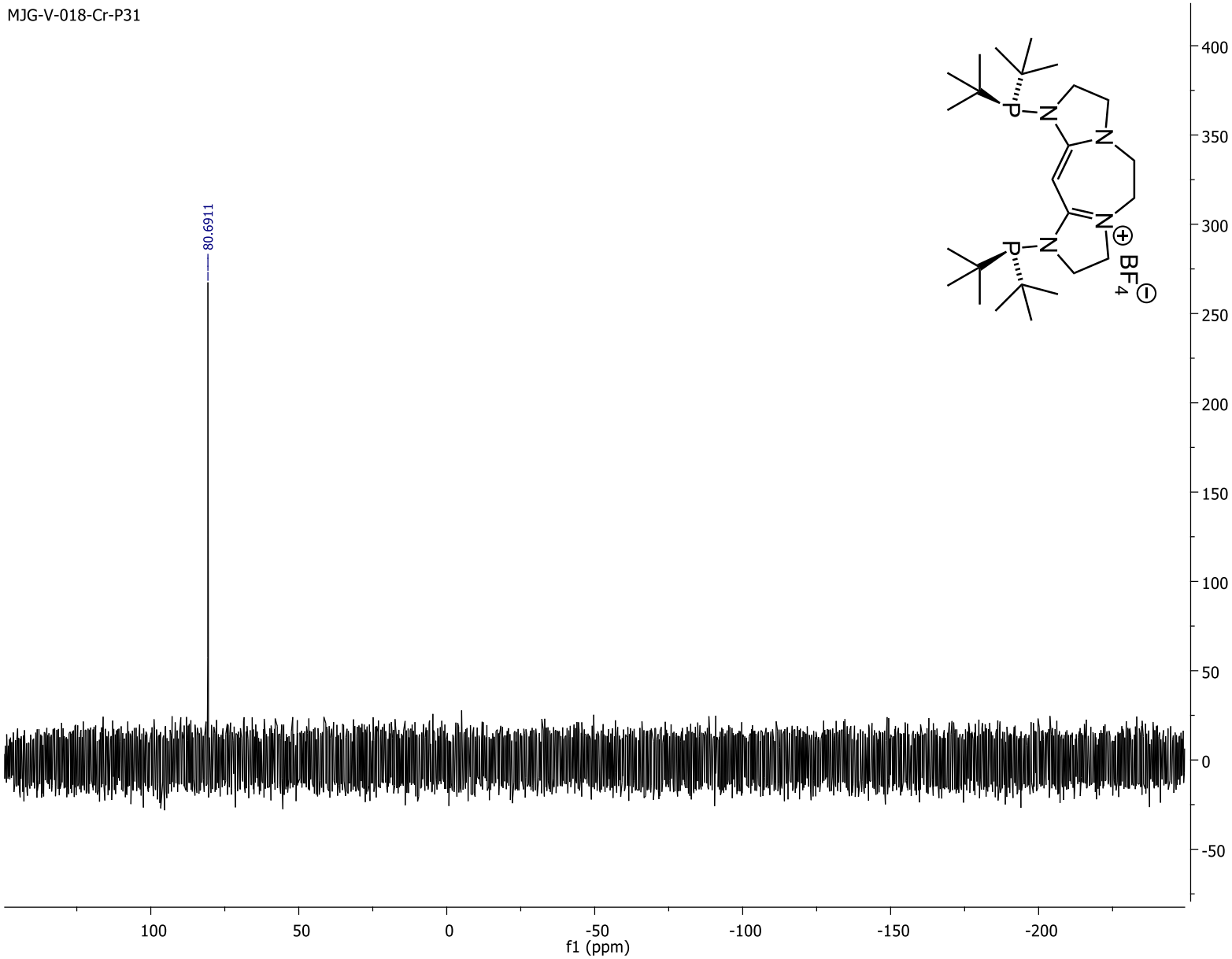
f1 (ppm)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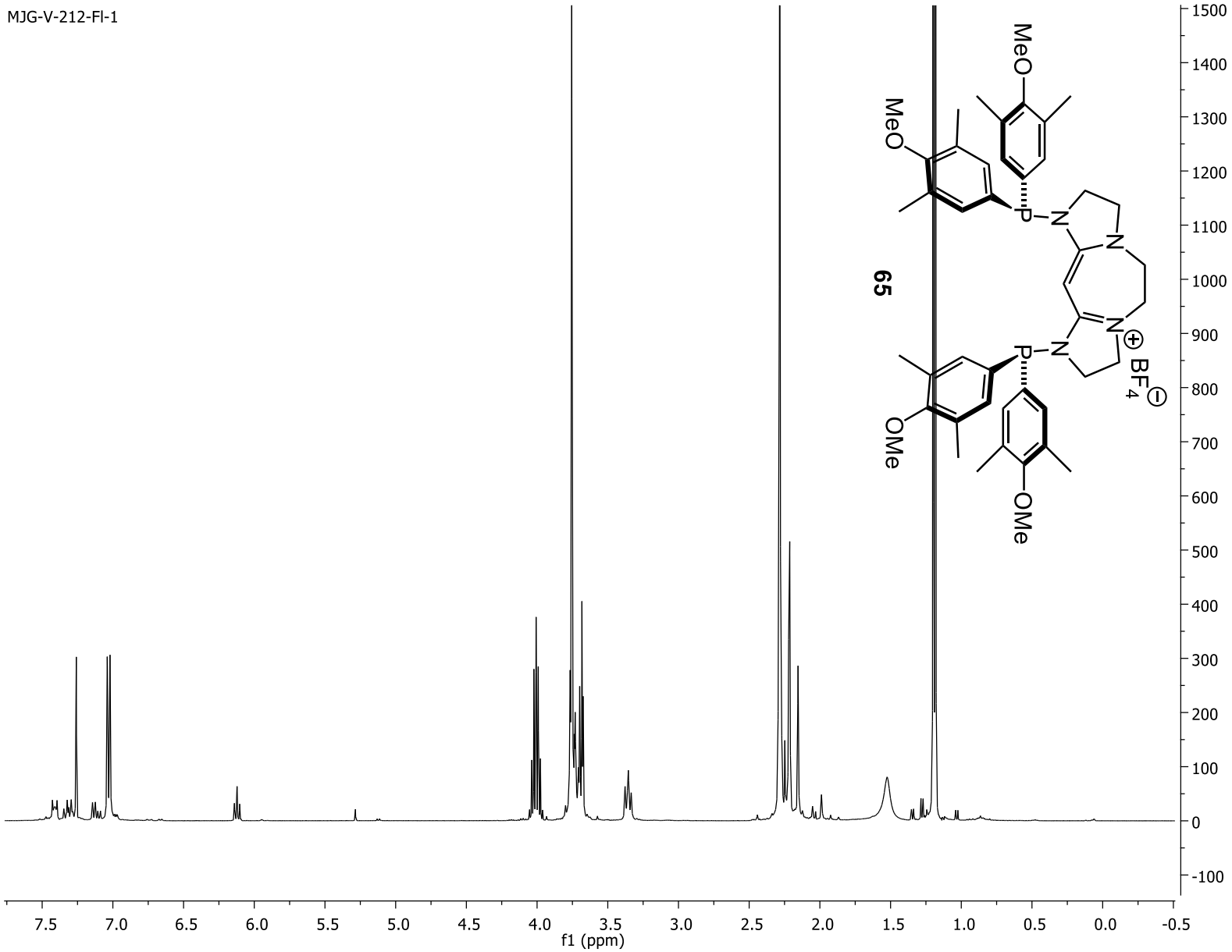
-150
-200
400
350
300
250
200
150
100
50
0
-50


MJG-V-212-Fl-1
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MeO
OMe
MeO
OMe
P
P
N
N
N
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BF4
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1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
7.5
7.0
6.5
6.0
5.5
5.0
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2.5
2.0
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0.5
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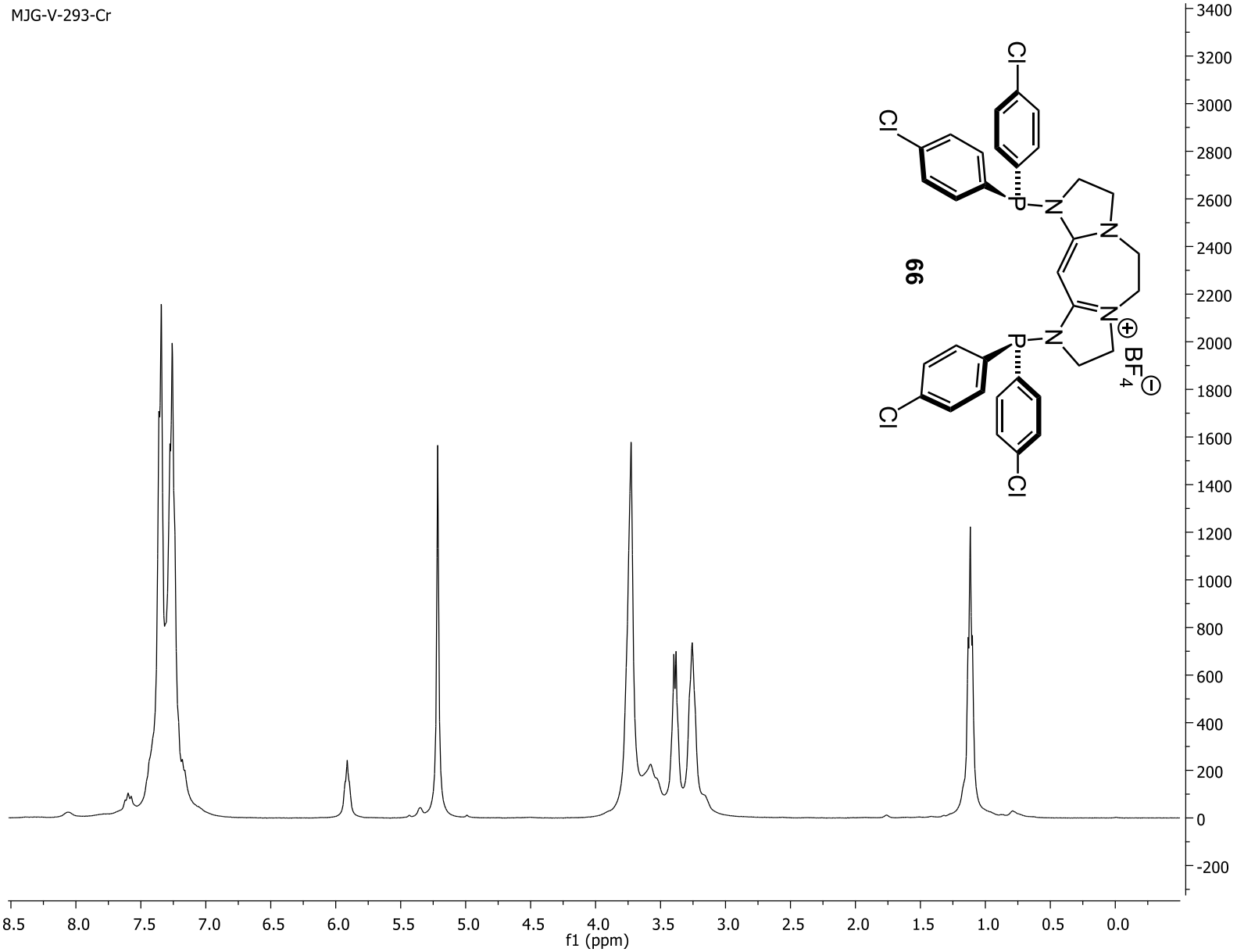
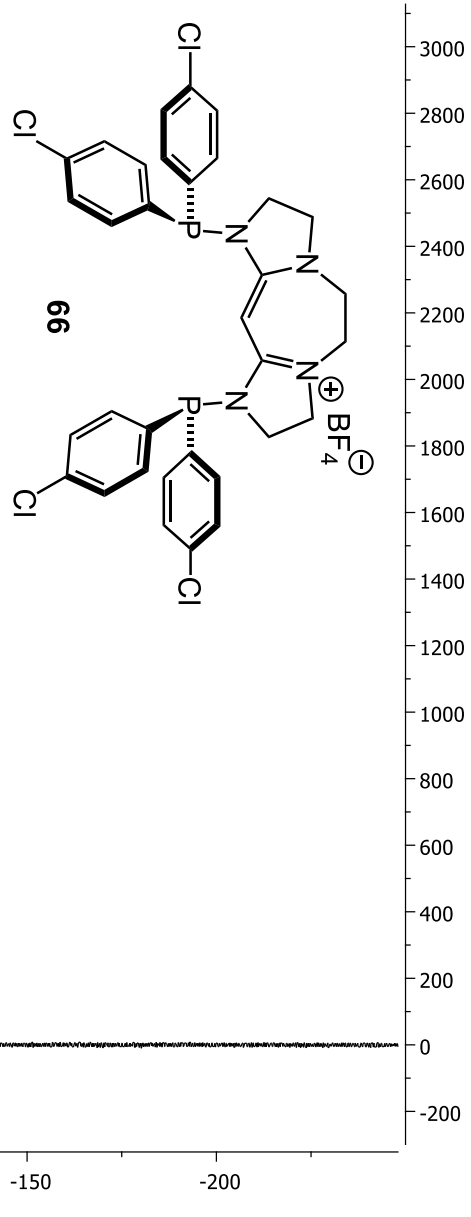
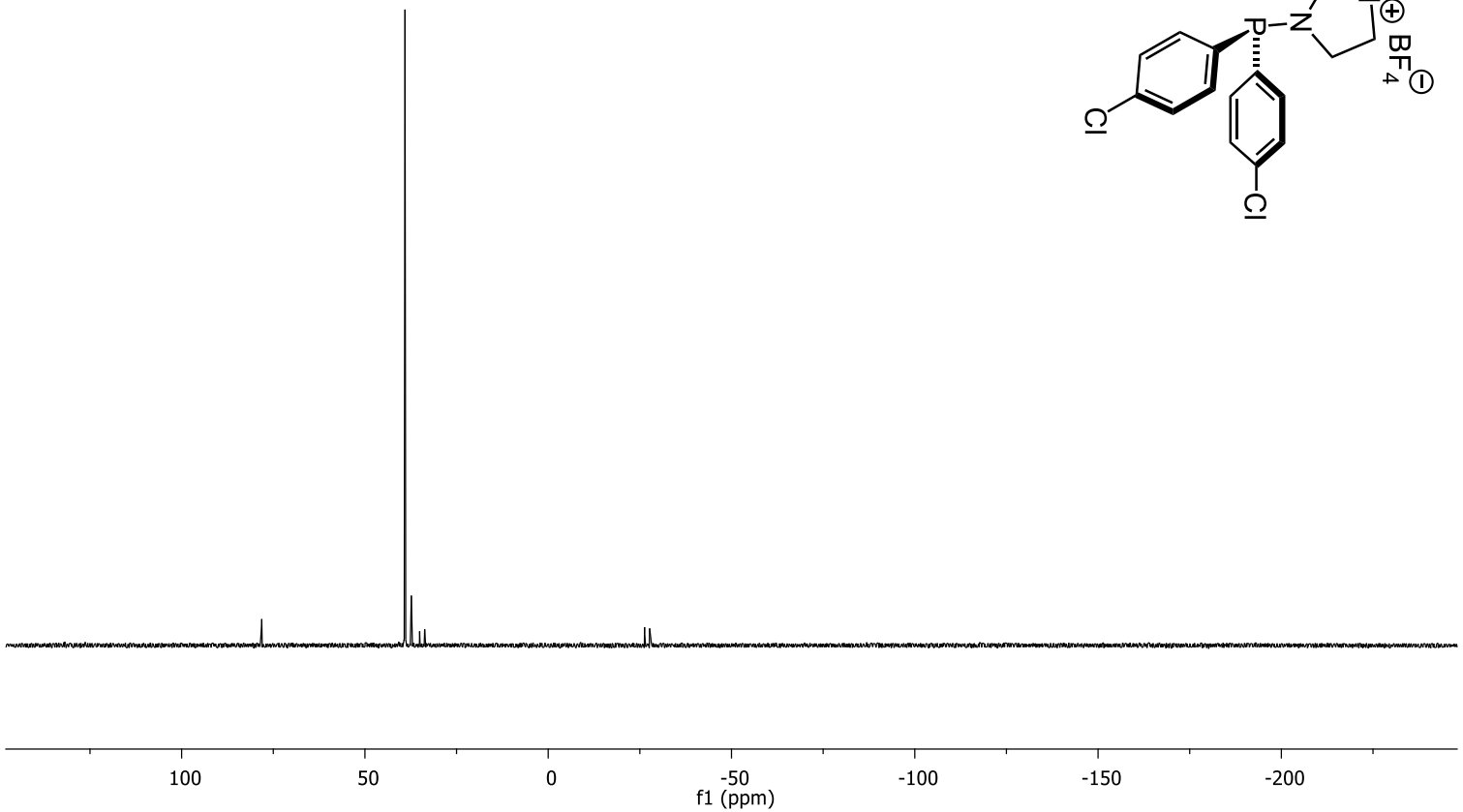
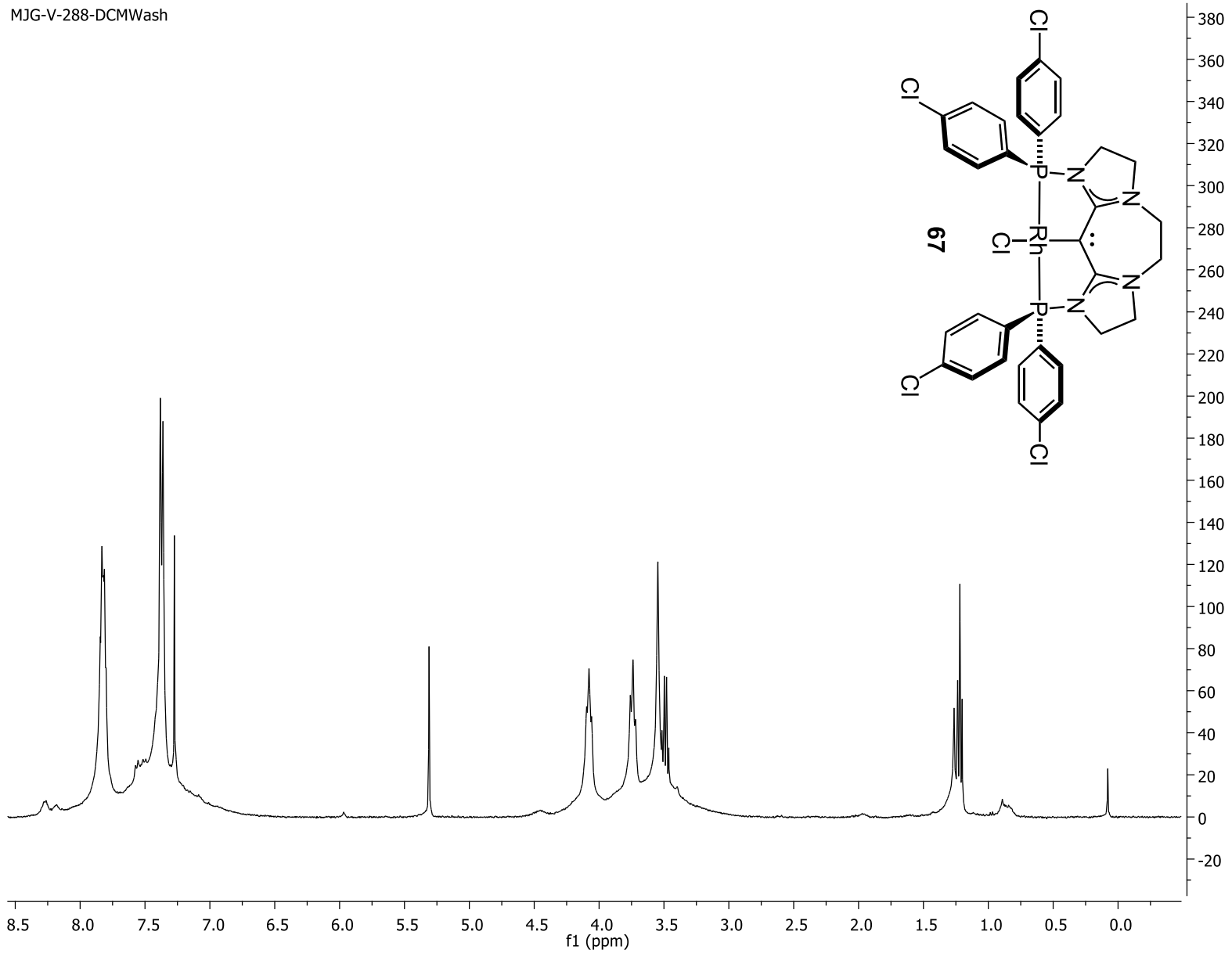
f1 (ppm)


MJG-V-293-Cr
f1 (ppm)
66

MJG-V-293-Cr-P31



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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
380
360
340
320
300
280
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180
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140
120
100
80
60
40
20
0
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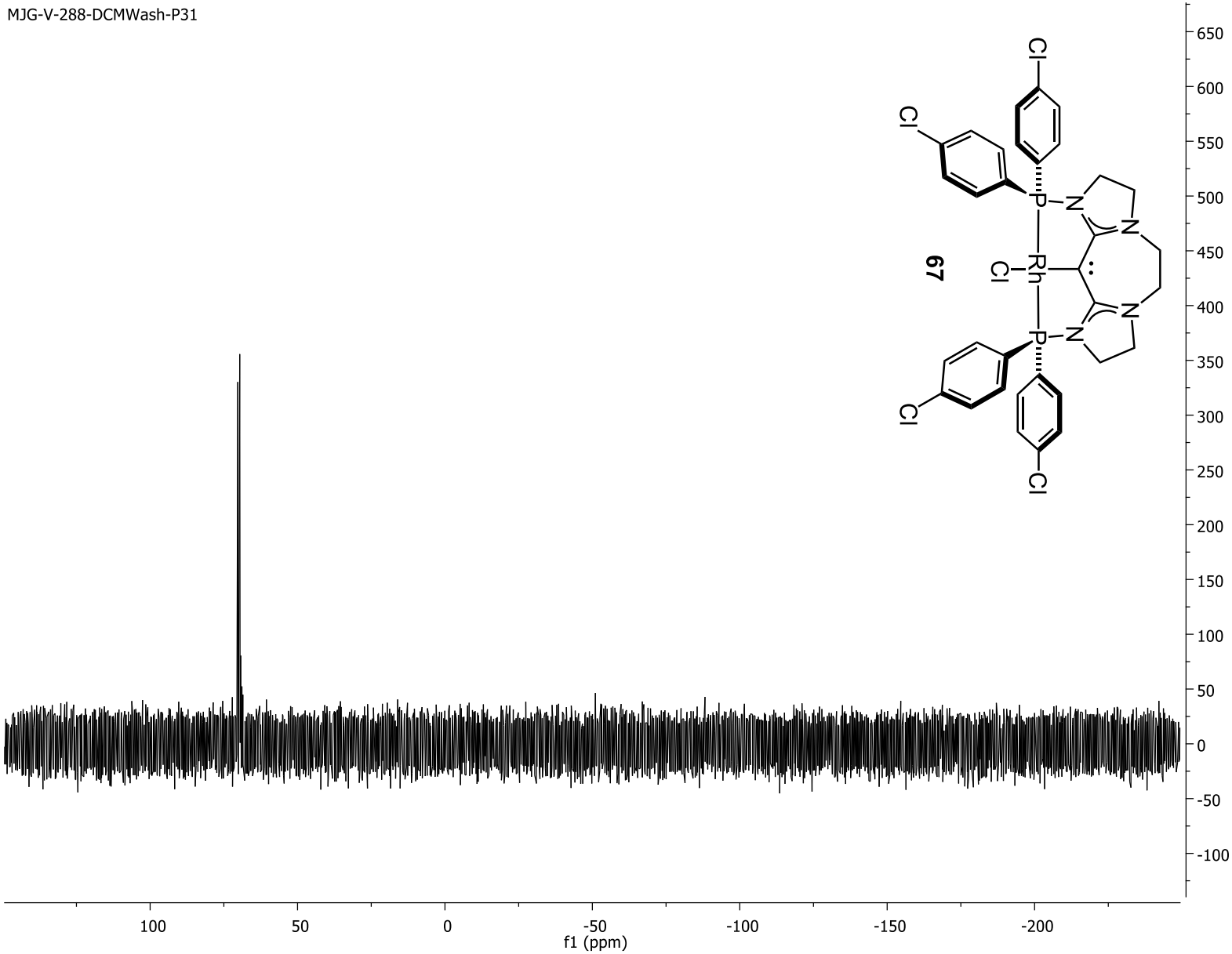
67
Cl
Rh
P
N


MJG-V-288-DCMWash-P31
f1 (ppm)
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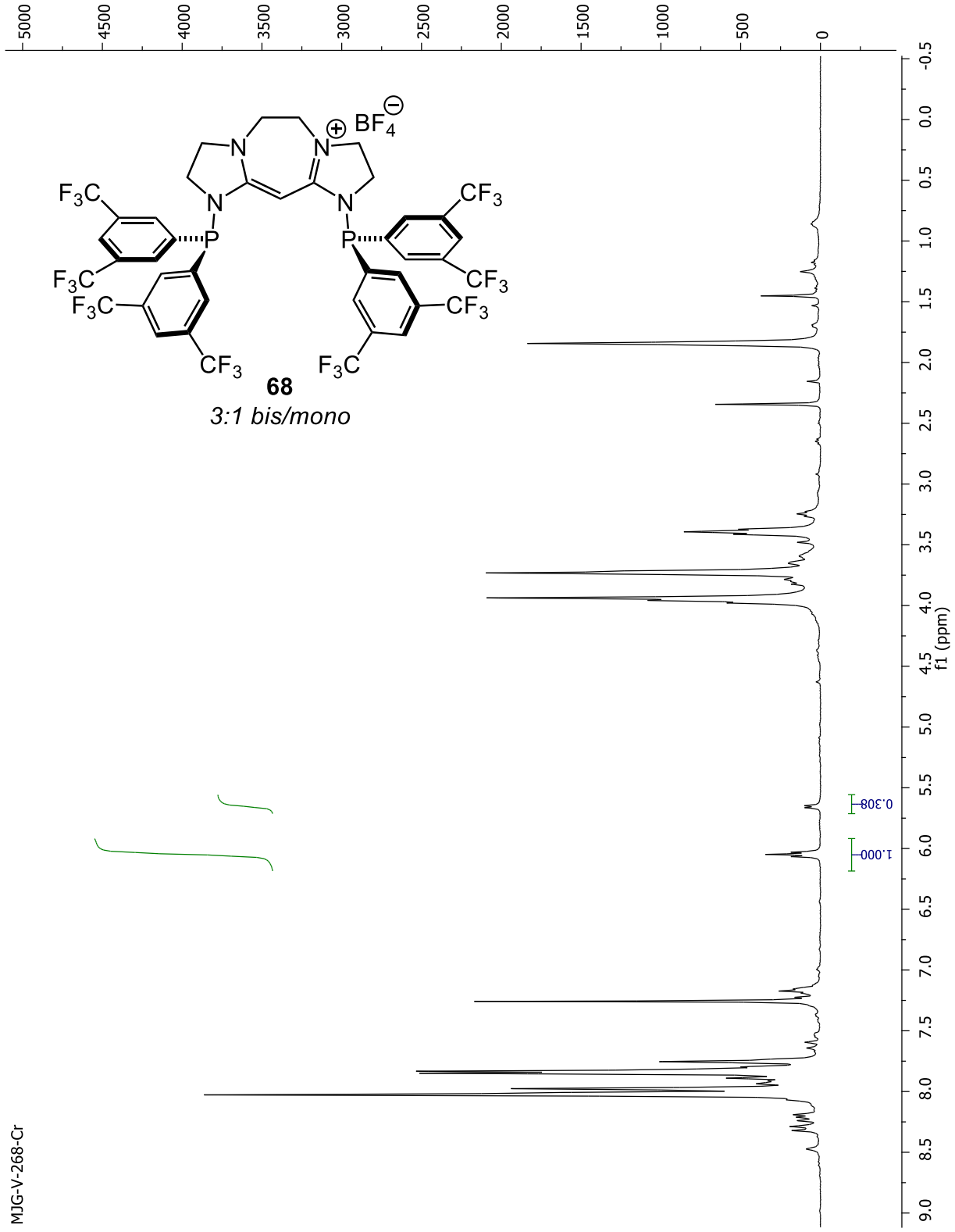
-100
-150
-200
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
-100
67
Cl
Rh
P
N


68
3:1 bis/mono
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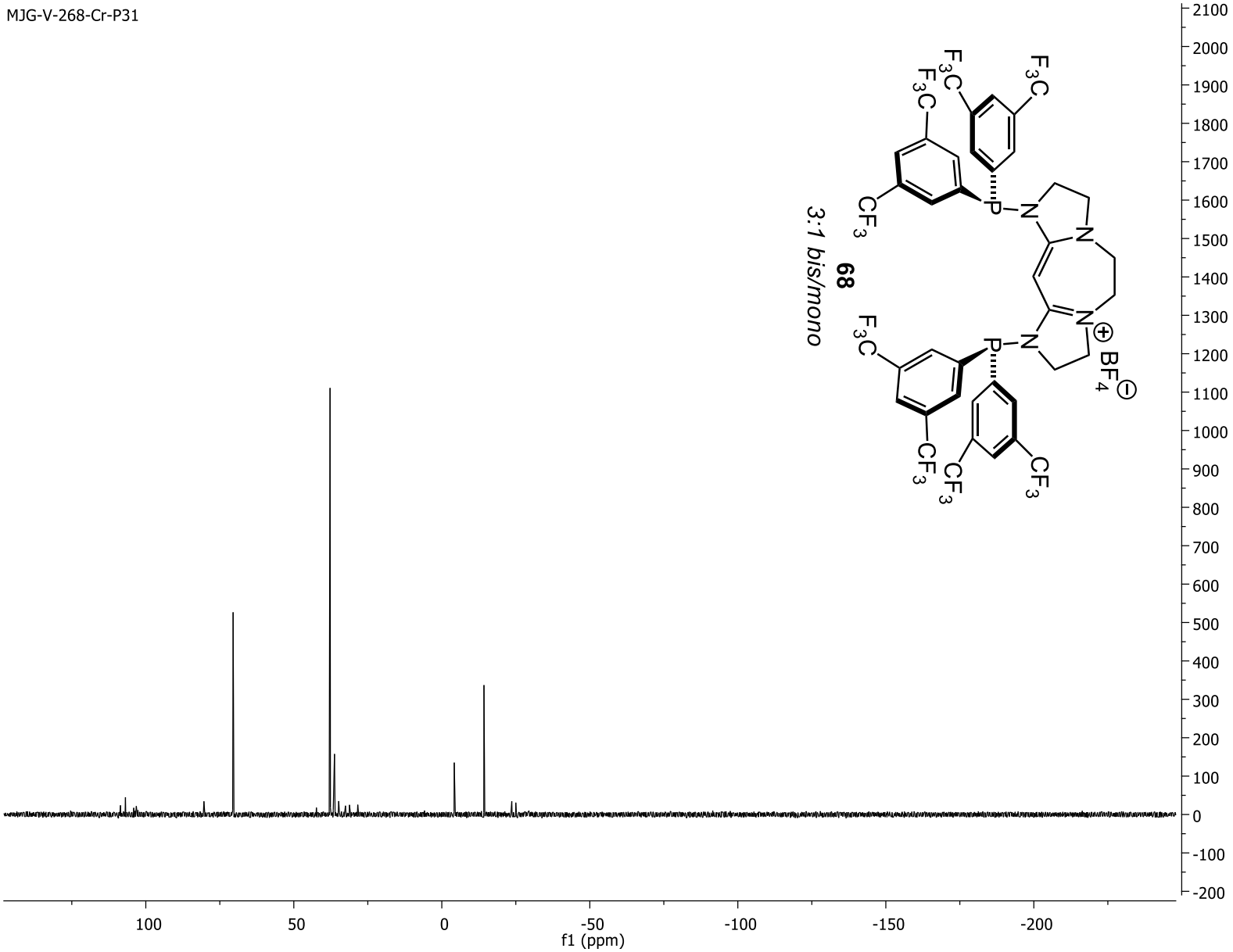
0.308

MJG-V-268-Cr-P31

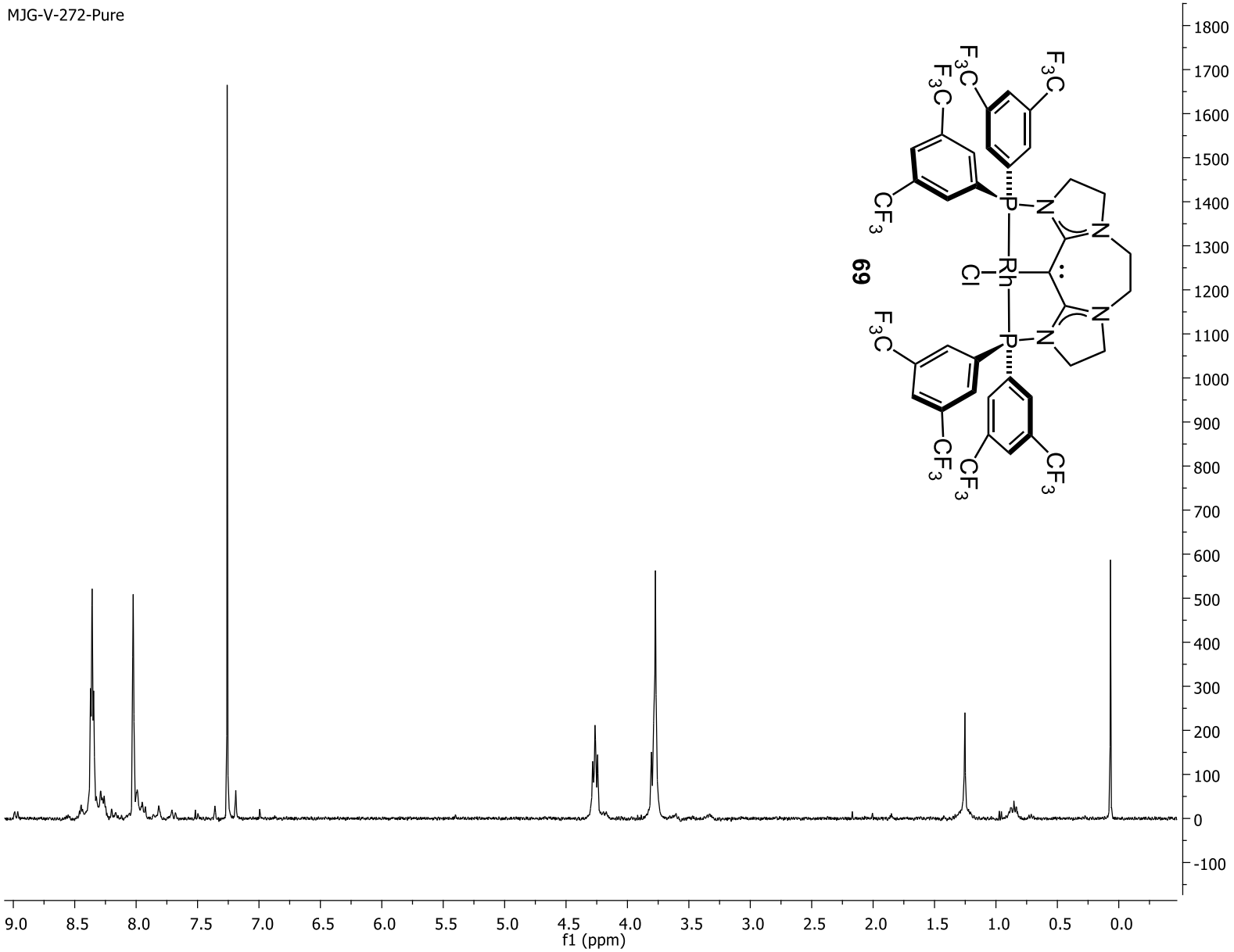


68

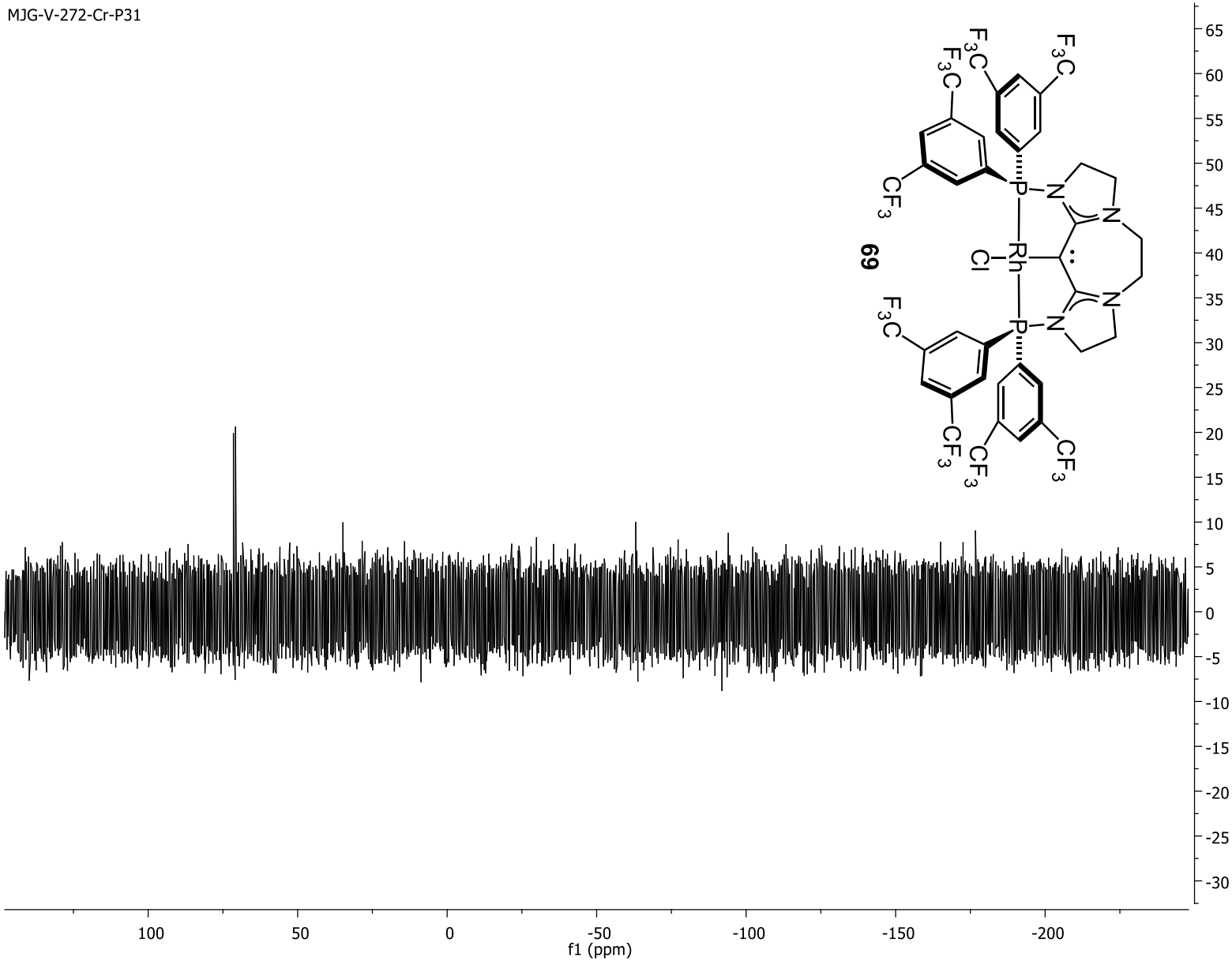
3:1 bis/mono

MJG-V-272-Pure

69

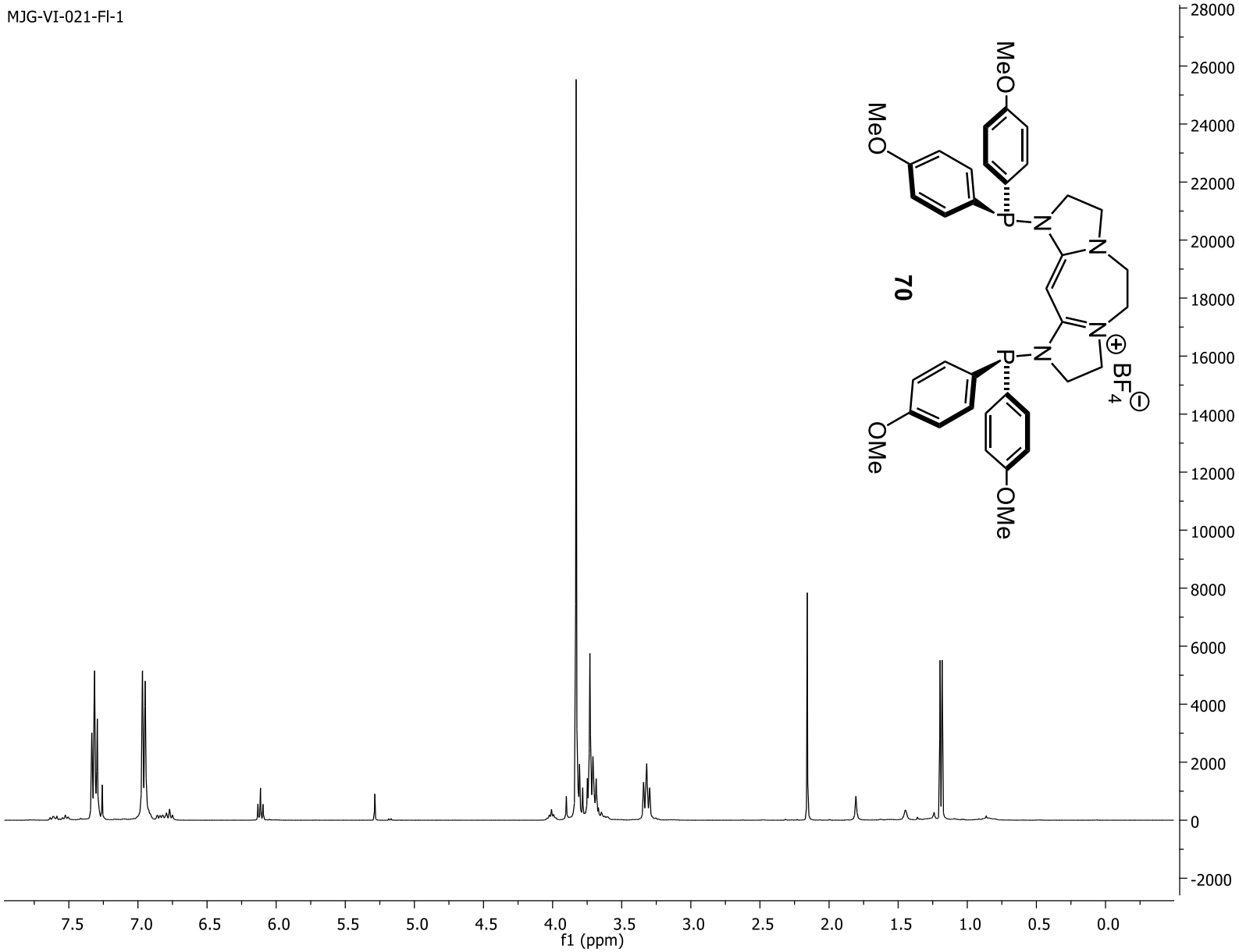


MJG-V-272-Cr-P31

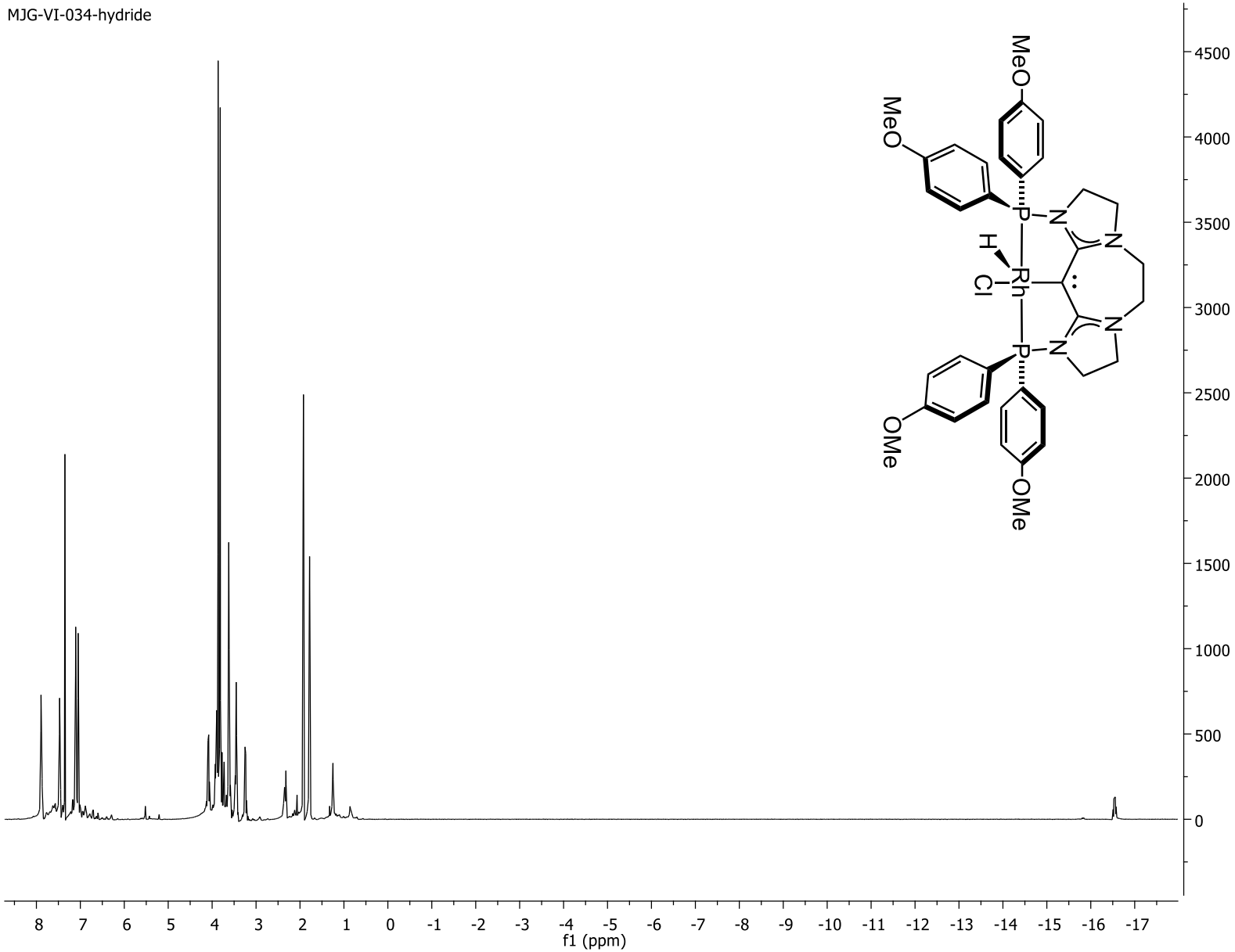


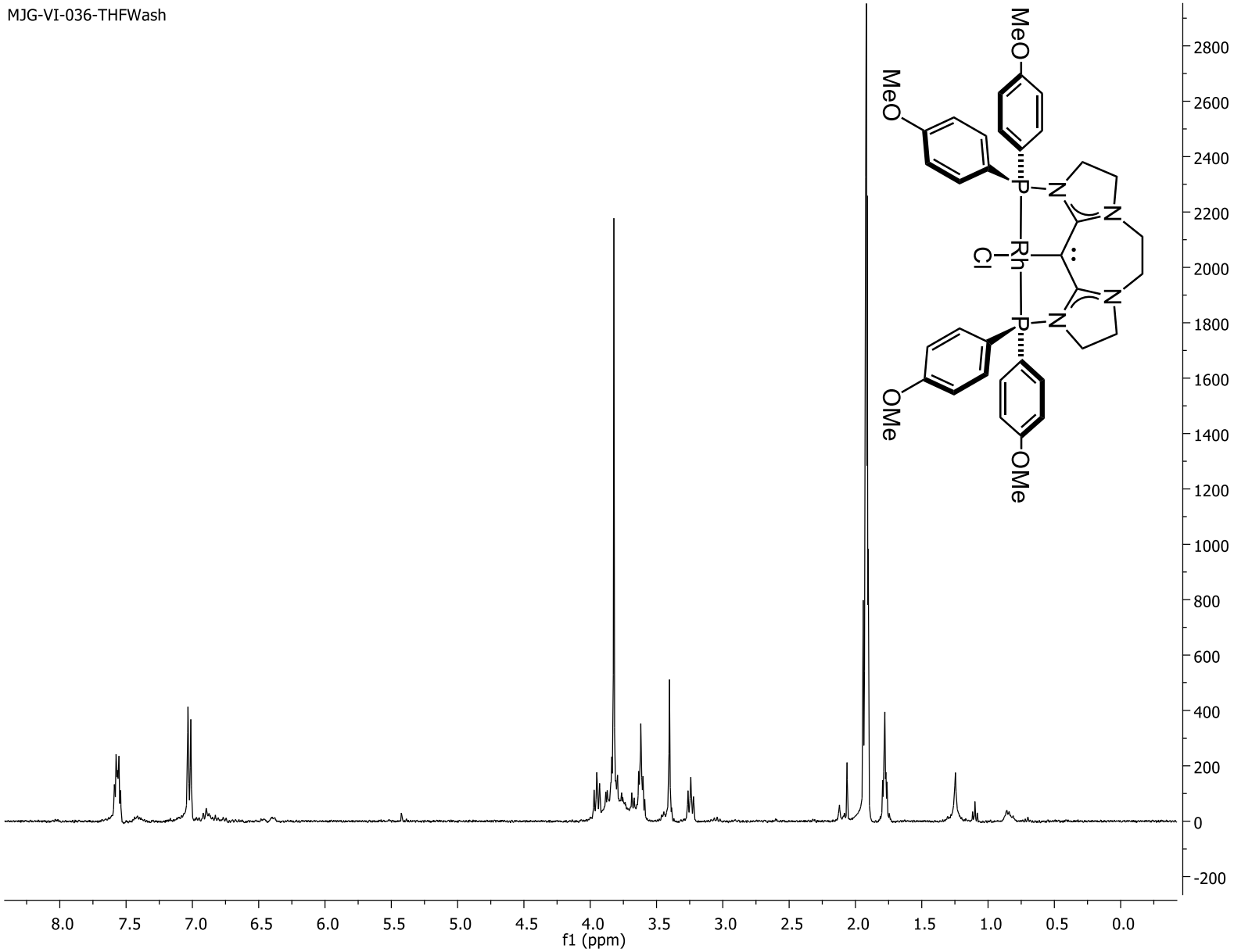
MJG-VI-021-Fl-1

70



MJG-VI-034-hydride

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6.5
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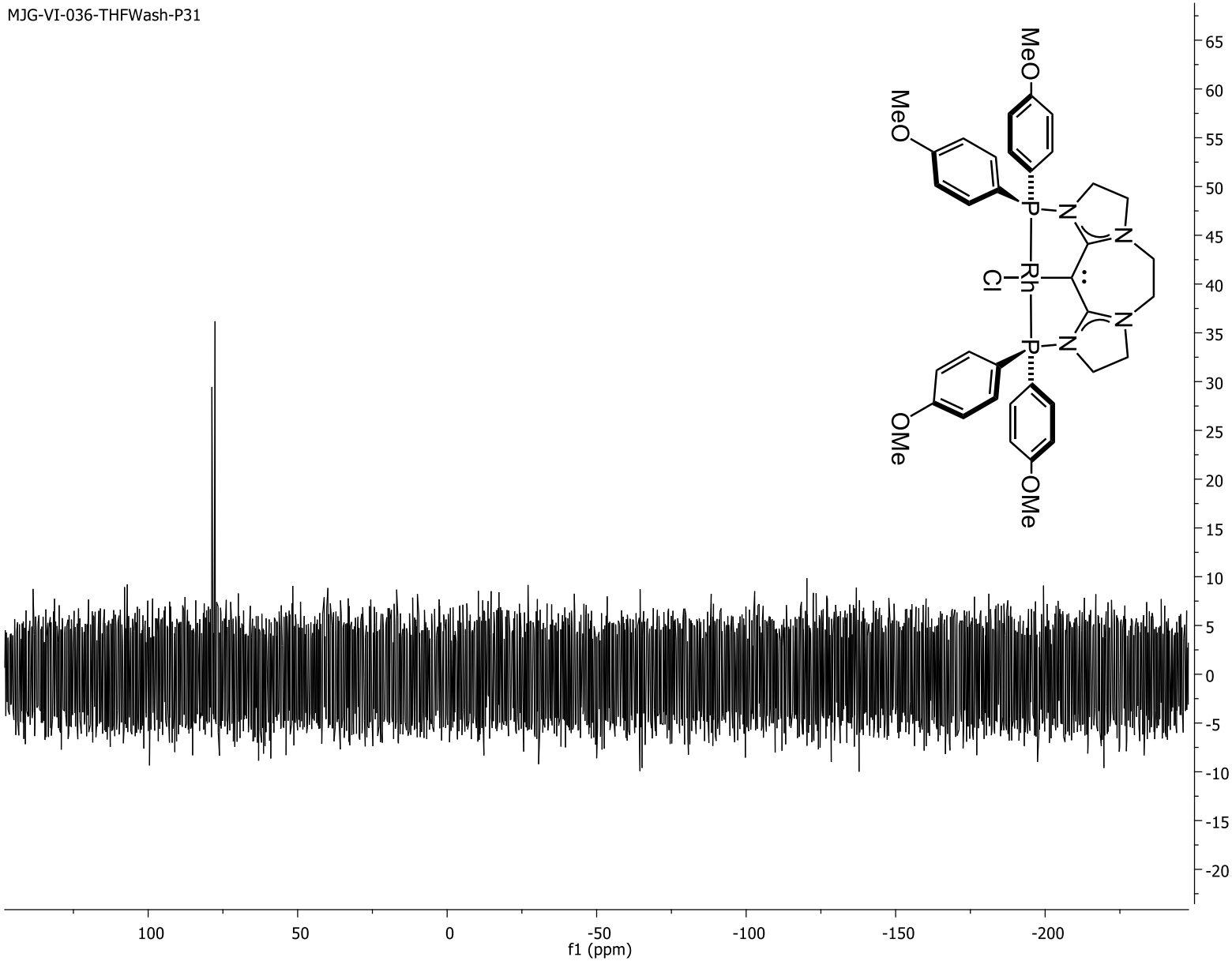
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
MeO
MeO
OMe
OMe
P
P
Rh
Cl
N
N
N
N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0
-50
-100
-150
-200
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
MeO
MeO
P
Rh
Cl
P
N
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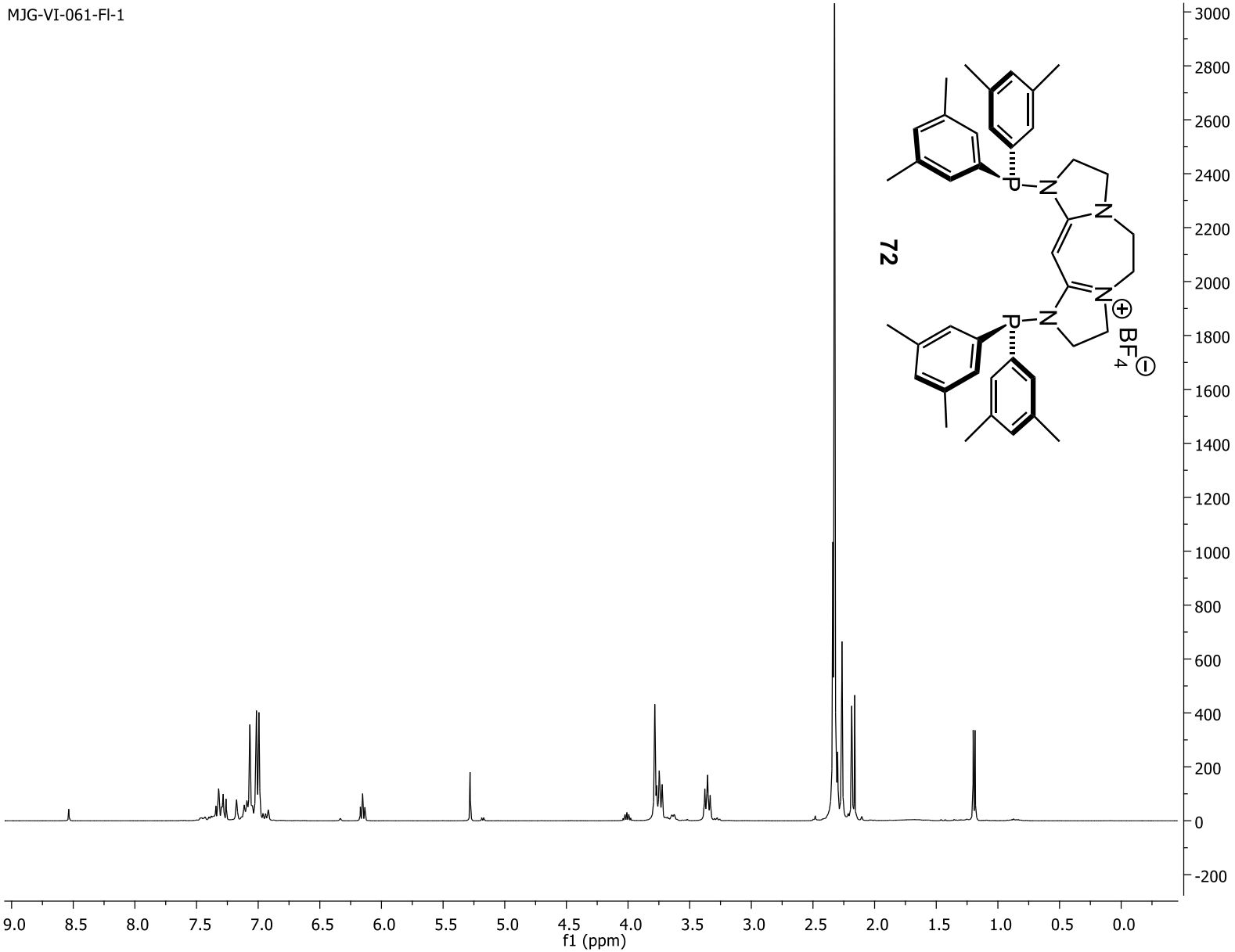
N
OMe
OMe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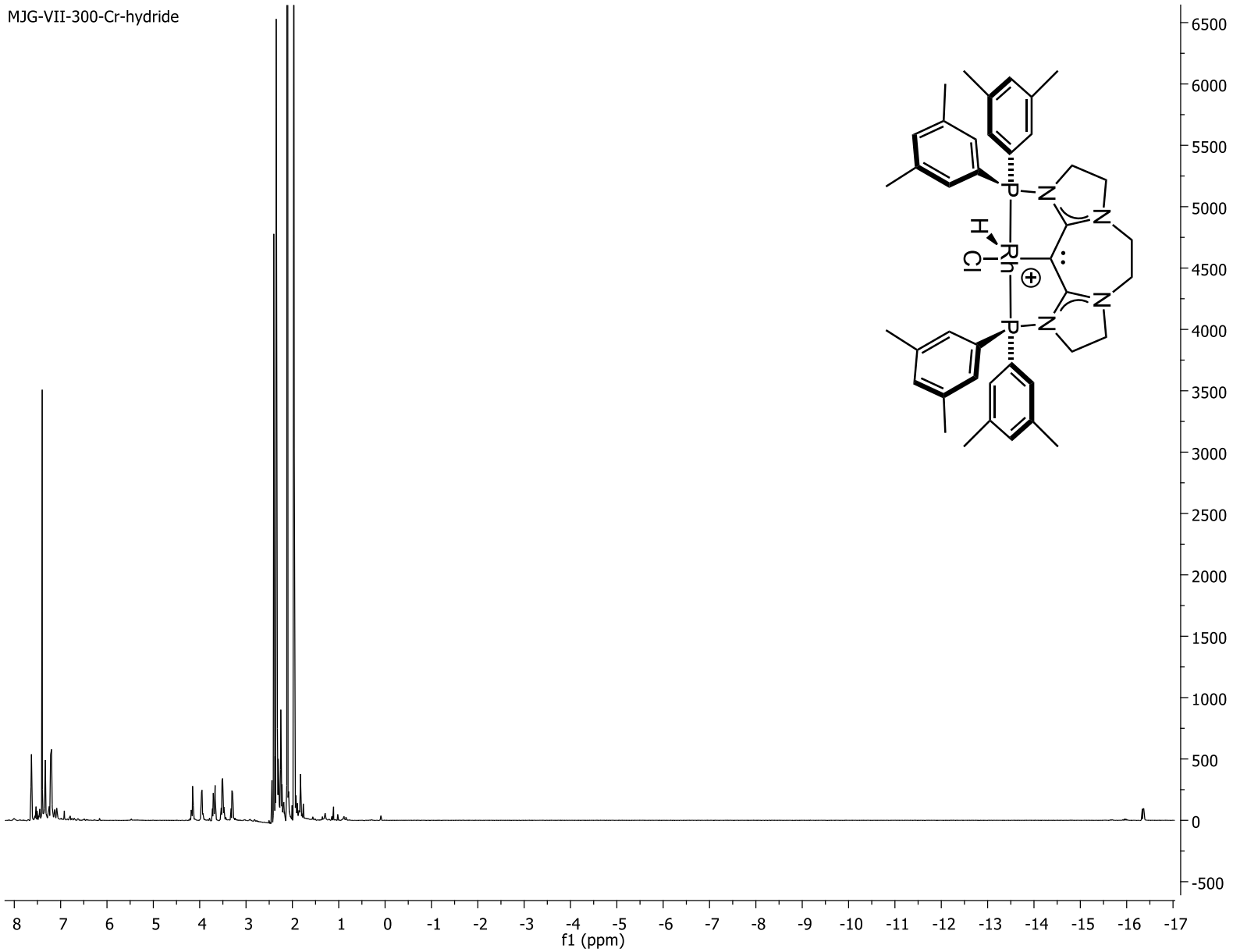
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200

P
N
N
N
P
N
BF4

72


MJG-VII-300-Cr-hydride
f1 (ppm)
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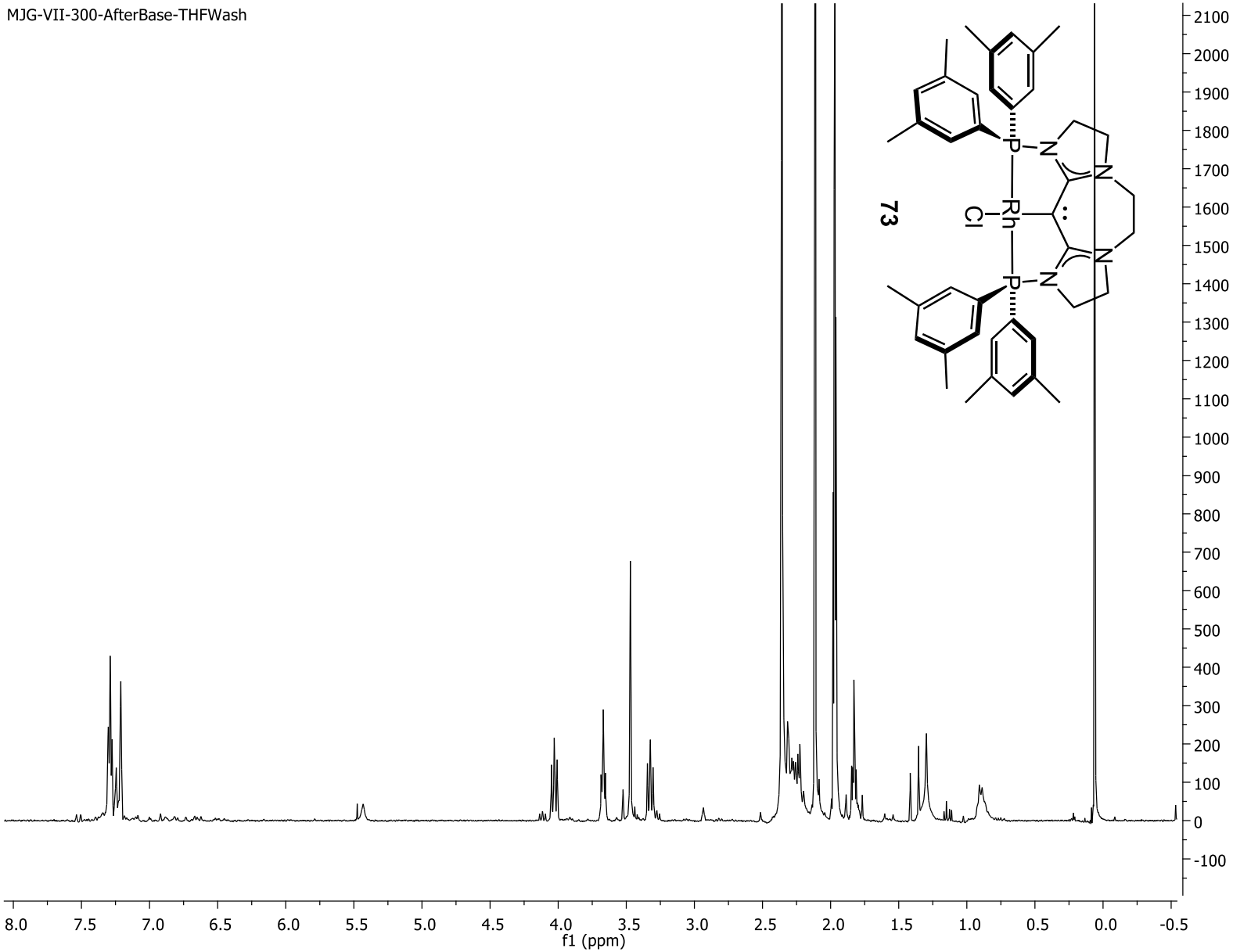
P
N
N
H
Rh
Cl
:
N
P
N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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
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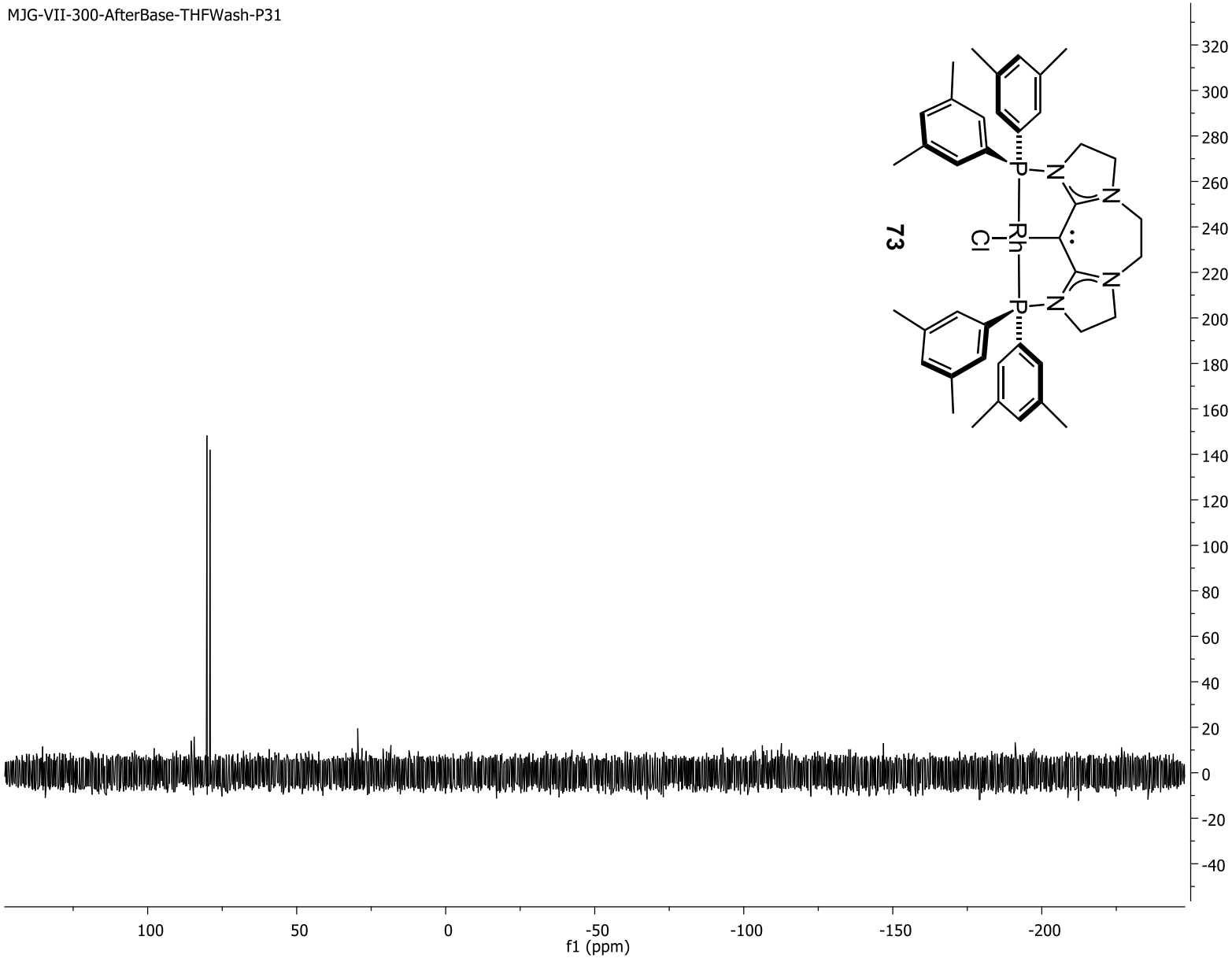
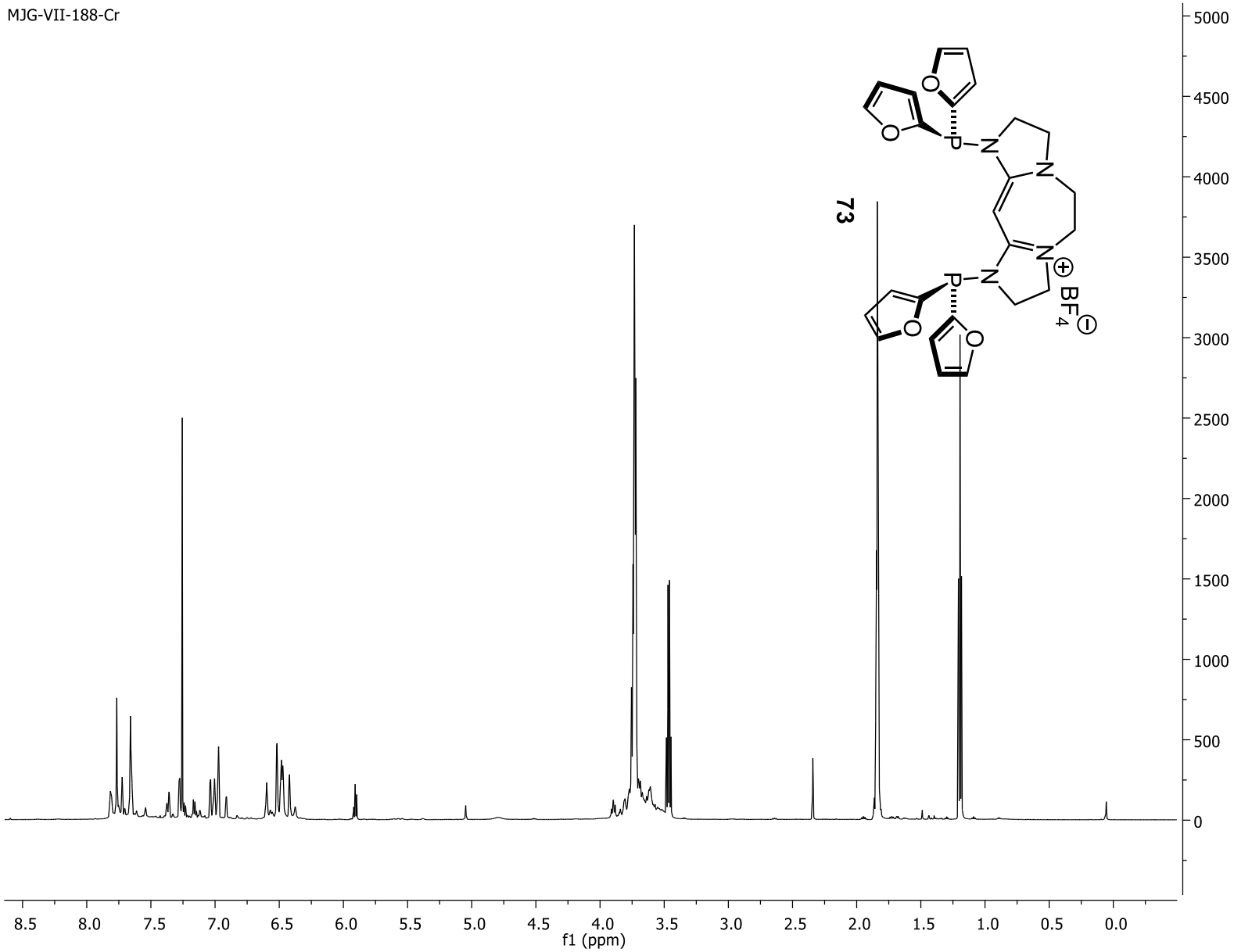
73
P
Rh
Cl
N
N
N
N
P

MJG-VII-300-AfterBase-THFWash-P31

73




MJG-VII-188-Cr
73
f1 (ppm)

Section 4.5: Applications of Modified CDC-Rh(I) Complexes to the Hydroalkylation of Dienes

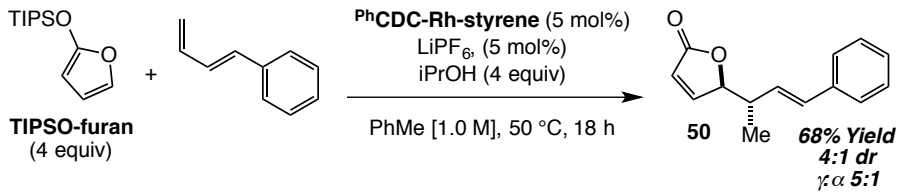
■ **General screening Conditions for Forming 5-(*E*-4-phenylbut-3-en-2-yl)furan-2(5*H*)-one with Modified CDC-Rh(I) Complexes in Scheme 4.5.1-1, 4.5.1-2, and 4.5.2-1.**

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the listed catalyst complex (0.005 mmol, 5 mol%), the appropriate amount of the listed Lewis acid activator, and 1,3-phenylbutadiene (13.0 mg, 0.10 mmol). The reagents were solvated with the listed solvent and the reaction sealed with a Teflon® lined septum cap before being allowed to stir at room temperature for <1 hour and removed from the dry box. A vial of the listed furan nucleophile was sparged with N_2 for a minimum of 10 minutes before the appropriate amount was added via syringe. The listed alcohol was sparged with N_2 for more than 10 minutes before being added via syringe. The reaction was allowed to warm to the appropriate temperature and stir for 18 h before being allowed to cool to 22 °C and an aliquot taken to determine the conversion by ^{1}H NMR using hexamethyldisiloxane as an internal standard. The NMR sample was recovered and the solvent evaporated before the product was purified by SiO_2 column chromatography to yield **50** as a colorless oil.

See Section 4.2 for characterization of **50**.

Section 4.7: Diastereoselective Synthesis of Substituted 2-Butanones through Carbodicarbene-Rh Catalyzed Additions of Silyloxyfurans

■ **Procedure and characterization for the CDC-Rh(I) catalyzed hydroalkylation of dienes with silyloxyfurans:**

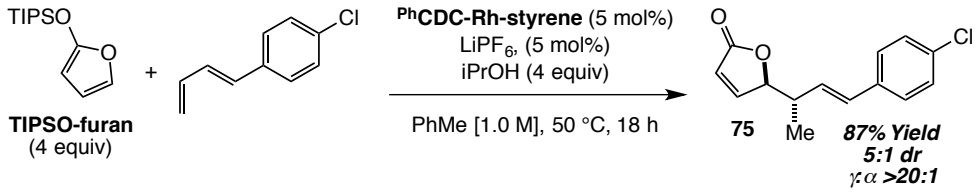


Synthesis of 5-(*E*-4-phenylbut-3-en-2-yl)furan-2(5H)-one (50).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and 1,3-phenylbutadiene (13.0 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 µL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 µL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 µL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **50** (14.6 mg, 0.068 mmol, 68% yield, 4:1 dr, 5:1 γ:α regioselectivity) as a colorless oil.

^{1}H NMR (600 MHz, CDCl3) δ 7.49 (dd, *J* = 5.7, 1.5 Hz, 1H), 7.38 – 7.29 (m, 4H), 7.26 – 7.22 (m, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.16 (dd, *J* = 5.8, 2.0 Hz, 1H), 6.08 (dd, *J* = 15.9, 8.4 Hz, 1H), 4.97 (dt, *J* = 6.7, 1.7 Hz, 1H), 2.72 – 2.65 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151

MHz, $CDCl_3$) δ 173.1, 173.1, 155.1, 154.8, 136.7, 136.7, 132.4, 132.4, 128.9, 128.8, 128.8, 128.3, 127.9, 127.9, 126.4, 126.4, 122.8, 122.6, 86.7, 86.6, 41.3, 40.0, 16.4, 15.5.

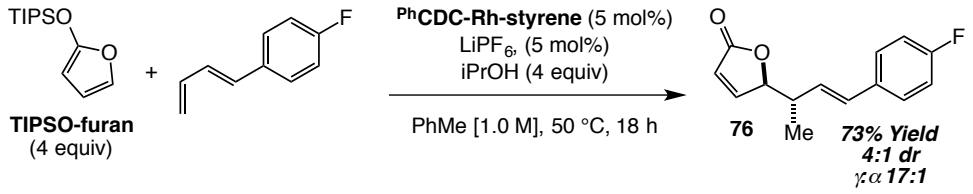


Synthesis of 5-(*E*-4-(4-chlorophenyl)but-3-en-2-yl)furan-2(5H)-one (75).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-1-(buta-1,3-dien-1-yl)-4-chlorobenzene (16.5 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 μL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography

(5:1 Hex/EtOAc) to afford **75** (21.6 mg, 0.087 mmol, 87% yield, 5:1 dr, >20:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 5.7, 0.7 Hz, 2H), 7.33 (s, 2H), 6.37 – 6.36 (m, 1H), 6.30 (d, *J* = 15.8 Hz, 1H), 6.21 (d, *J* = 3.3 Hz, 1H), 6.00 (dd, *J* = 15.8, 8.4 Hz, 1H), 4.94 – 4.93 (m, 1H), 2.67 – 2.59 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 3H).**]** ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 (d, *J* = 5.7 Hz, 2H), 7.33 (s, 2H), 6.37 – 6.35 (m, 1H), 6.30 (d, *J* = 15.9 Hz, 1H), 6.21 (d, *J* = 3.3 Hz, 1H), 6.04 (dd, *J* = 16.5, 8.2 Hz, 1H), 5.06 – 5.05 (m, 1H), 2.89 – 2.81 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H).**]** **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 173.0, 154.9, 154.5, 152.2, 152.1, 142.0, 142.0, 127.3, 126.9, 122.8, 122.5, 120.7, 120.6, 111.4, 111.4, 108.1, 108.0, 86.5, 86.2, 41.0, 39.6, 16.4, 14.8. **IR** (ν/cm^{-1}): 2971 (m), 2930 (m), 2873 (w), 1749 (s), 1653 (m), 1507 (m), 1162 (m), 1091 (m), 1013 (m), 983 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{14}H_{14}ClO_2^+$ 249.0682, found: 249.06778.



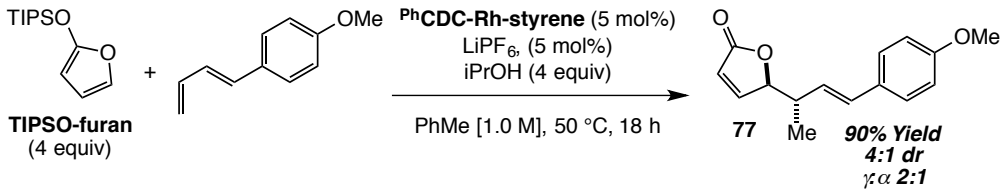
Synthesis of 5-(*E*-4-(4-fluorophenyl)but-3-en-2-yl)furan-2(5H)-one (76).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-1-(buta-1,3-dien-1-yl)-4-fluorobenzene (14.8 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 μL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the

glove box (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **76** (17.0 mg, 0.073 mmol, 73% yield, 4:1 dr, 17:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 5.8, 1.5 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.03 – 6.96 (m, 2H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.16 (dt, *J* = 6.6, 3.3 Hz, 1H), 5.98 (dd, *J* = 15.9, 8.3 Hz, 1H), 4.98 – 4.97 (m, 1H), 2.74 – 2.64 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.9, 162.4 (d, *J* = 247.0 Hz), 154.8, 132.8, 131.1, 128.6 (d, *J* = 2.2 Hz), 127.8 (d, *J* = 8.1 Hz), 122.5, 115.5 (d, *J* = 21.6 Hz), 86.5, 40.93, 16.09.**]** ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 5.8, 1.5 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.05 – 6.99 (m, 2H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.19 – 6.18 (m, 1H), 6.02 (dd, *J* = 16.7, 8.3 Hz, 1H), 5.09 – 5.06 (m, 1H), 2.90 – 2.82 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 161.9 (d, *J* = 246.0 Hz) 154.7, 132.8, 131.0 (d, *J* = 9.3 Hz), 129.6 (d, *J* = 8.0 Hz), 128.0 (d, *J* = 2.2 Hz), 122.7, 115.6 (d, *J* = 21.4 Hz), 86.4, 40.0, 15.5.**]** ***α*-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 5.8, 1.5 Hz, 1H), 7.27 (dd, *J* = 5.8, 1.5 Hz, 2H), 7.05 – 6.99 (m, 2H), 6.08 (dd, *J* = 5.8, 2.0 Hz, 1H), 5.74 – 5.58 (m, 2H), 5.27

– 5.24 (m, 1H), 3.64 (t, J = 6.7 Hz, 1H), 1.74 (d, J = 5.2 Hz, 3H).] **α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.24 – 7.22 (m, 1H), 7.05 – 6.99 (m, 2H), 6.11 (dd, J = 5.7, 2.0 Hz, 1H), 5.75 – 5.58 (m, 2H), 5.24 – 5.21 (m, 1H), 3.57 (t, J = 7.0 Hz, 1H), 1.72 (d, J = 6.4 Hz, 3H).] **IR** (ν/cm^{-1}): 3080 (w), 3039 (w), 2971 (m), 2932 (m), 1749 (s), 1602 (m), 1508 (s), 1227 (m), 1160 (m), 1094 (m), 1016 (m), 970 (m), 897 (m). **HRMS** (ES$^+$) [M–Na]$^+$ calcd for $C_{14}H_{13}FO_2Na^+$ 255.0797, found: 255.0795.

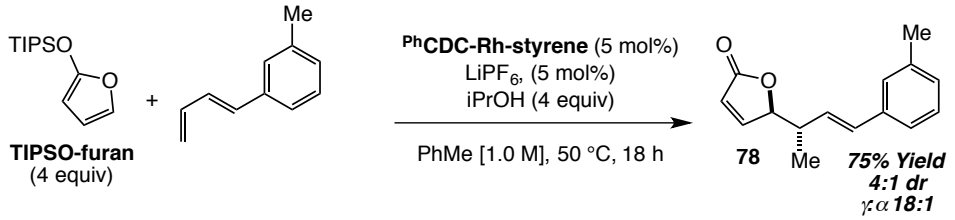


Synthesis of 5-(*E*-4-(4-methoxyphenyl)but-3-en-2-yl)furan-2(5H)-one (77).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (16.0 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 µL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 µL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 µL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 µL of

hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **77** (22.0 mg, 0.090 mmol, 90% yield, 4:1 dr, 2:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 5.7, 1.4 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.15 (dd, *J* = 5.7, 2.1 Hz, 1H), 5.92 (dd, *J* = 15.8, 8.4 Hz, 1H), 4.96 – 4.95 (m, 1H), 3.81 (s, *J* = 1.1 Hz, 3H), 2.68 – 2.60 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.1, 159.3, 155.1, 131.7, 129.4, 127.5, 126.6, 122.4, 114.0, 86.8, 55.4, 41.2, 16.5.**] *syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 5.8, 1.4 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.15 (dd, *J* = 5.1, 3.0 Hz, 1H), 5.94 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.07 – 5.06 (m, 1H), 3.78 (s, 3H), 2.89 – 2.81 (m, 1H), 1.16 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.1, 158.7, 154.8, 131.6, 129.1, 127.8, 126.0, 122.7, 114.1, 86.6, 55.4, 39.9, 15.4.**] α-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 5.8, 1.4 Hz, 2H), 7.14 – 7.13 (m, 2H), 6.86 – 6.82 (m, 1H), 6.07 – 6.02 (m, 1H), 5.73 – 5.55 (m, 2H), 5.23 – 5.22 (m, 1H), 3.79 (d, *J* = 2.6 Hz, 3H), 3.62 (t, *J* = 6.5 Hz, 1H), 1.71 (d, *J* = 4.9 Hz, 3H).**] α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.23 (dd, *J* = 5.7, 1.4 Hz, 2H), 6.89 – 6.84 (m, 1H), 6.07 – 6.05 (m, 1H), 5.75 – 5.53 (m, 1H), 5.20 – 5.17 (m, 2H), 3.80 (s, *J* = 1.1 Hz, 3H), 3.46 (t, *J* = 7.3 Hz, 1H), 1.69 (d, *J* = 7.8 Hz, 3H).**] IR** (ν/cm^{-1}): 2966 (m), 2926 (m), 2839 (w), 1749 (s), 1607 (m), 1508 (m), 1250 (m), 1163 (m), 1033 (m), 968 (w). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{15}H_{17}O_3^+$ 245.1178, found: 245.1180.

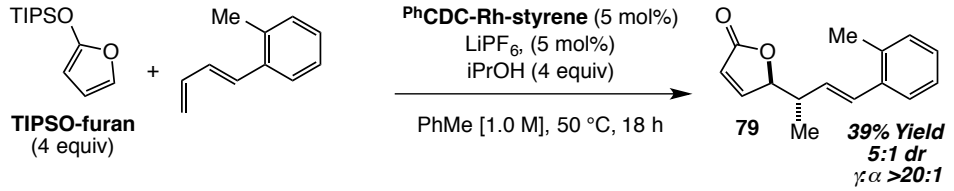


Synthesis of 5-(*E*-4-(m-tolyl)but-3-en-2-yl)furan-2(5H)-one (78).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), (*E*)-1-(buta-1,3-dien-1-yl)-3-methylbenzene (14.4 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 μL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **78** (17.2 mg, 0.075 mmol, 75% yield, 4:1 dr, 18:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 5.7, 1.4 Hz, 1H), 7.24 – 7.11 (m, 3H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.16 (dd, *J* = 5.7, 2.0 Hz,

1H), 6.06 (dd, J = 15.9, 8.4 Hz, 1H), 4.97 – 4.96 (m, 1H), 2.71 – 2.61 (m, 1H), 2.34 (s, 3H), 1.24 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 155.0, 138.2, 136.5, 132.3, 128.6, 128.6, 128.6, 127.0, 123.5, 122.4, 86.6, 41.2, 21.4, 16.4.] ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.45 (dd, J = 5.7, 1.5 Hz, 1H), 7.24 – 7.11 (m, 3H), 7.02 (d, J = 8.8 Hz, 1H), 6.46 (d, J = 15.9 Hz, 1H), 6.16 (dd, J = 5.7, 2.0 Hz, 1H), 6.07 (dd, J = 15.9, 7.7 Hz, 1H), 5.08 – 5.07 (m, 1H), 2.92 – 2.83 (m, 1H), 1.18 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.1, 154.7, 138.2, 136.5, 132.3, 128.6, 128.6, 128.0, 126.9, 123.5, 122.7, 86.5, 39.9, 21.4, 15.3.] **IR** (ν/cm^{-1}): 3024 (m), 2970 (s), 2926 (m), 2873 (w), 1756 (s), 1603 (m), 1456 (m), 1339 (m), 1161 (s), 1088 (m), 969 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{15}H_{17}O_2^+$ 229.1229, found: 229.1234.

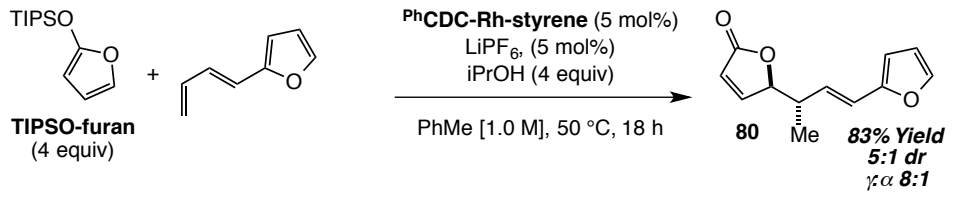


Synthesis of 5-(*E*-4-(*o*-tolyl)but-3-en-2-yl)furan-2(5H)-one (79).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), (*E*)-1-(buta-1,3-dien-1-yl)-2-methylbenzene (14.4 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 µL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 µL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-

yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **79** (8.9 mg, 0.039 mmol, 39% yield, 5:1 dr, >20:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 5.8, 1.4 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.21 – 7.15 (m, 3H), 6.72 (d, *J* = 15.7 Hz, 1H), 6.19 (dd, *J* = 5.7, 1.9 Hz, 1H), 5.94 (dd, *J* = 15.7, 8.4 Hz, 1H), 5.01 – 5.00 (m, 1H), 2.79 – 2.71 (m, 1H), 2.35 (s, 3H), 1.28 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 154.8, 135.8, 135.4, 130.4, 130.3, 130.2, 127.7, 126.2, 125.6, 122.5, 86.6, 41.3, 19.9, 16.5.**]** ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 5.8, 1.4 Hz, 1H), 7.40 – 7.37 (m, 1H), 7.22 – 7.13 (m, 3H), 6.72 (d, *J* = 15.8 Hz, 1H), 6.22 – 6.17 (m, 1H), 5.96 (dd, *J* = 16.2, 8.1 Hz, 1H), 5.12 – 5.11 (m, 1H), 2.97 – 2.89 (m, 1H), 2.35 (s, 3H), 1.22 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.1, 154.7, 135.9, 135.3, 130.4, 130.3, 130.3, 129.7, 126.2, 125.7, 122.7, 86.5, 40.1, 19.8, 15.5.**] IR** (ν/cm^{-1}): 3020 (w), 2970 (m), 2930 (m), 1750 (s), 1457 (m), 1162 (m), 1087 (m), 1016 (m), 969 (m), 896 (m). **HRMS** (ES$^+$) [M–Na]$^+$ calcd for $C_{15}H_{16}O_2Na^+$ 251.1048, found: 251.1046.

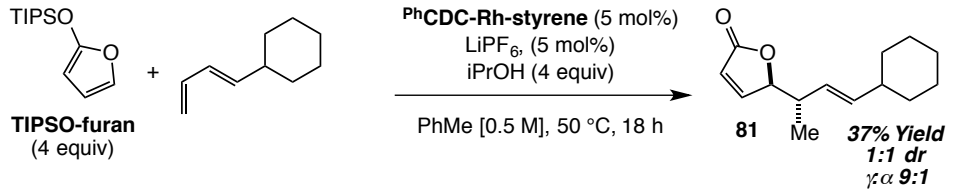


Synthesis of 5-(*E*-4-(furan-2-yl)but-3-en-2-yl)furan-2(5H)-one (80).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-2-(buta-1,3-dien-1-yl)furan (12.0 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (200 µL, 0.5 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 µL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 µL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 µL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 µL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **80** (17.0 mg, 0.083 mmol, 83% yield, 5:1 dr, 8:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 5.7, 1.2 Hz, 1H), 7.28 – 7.24 (m, 3H), 6.43 (d, *J* = 15.9 Hz, 1H), 6.16 (dd, *J* = 5.7, 1.9 Hz, 1H), 6.04 (dd, *J* = 15.9, 8.3

Hz, 1H), 5.00 – 4.94 (m, 1H), 2.76 – 2.63 (m, 1H), 1.21 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 154.8, 135.2, 133.5, 131.2, 129.6, 128.9, 127.6, 122.7, 86.5, 41.0, 16.1.**]** ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 (dd, J = 5.8, 1.2 Hz, 1H), 7.31 – 7.25 (m, 2H), 7.14 (d, J = 8.4 Hz, 1H), 6.42 (d, J = 15.9 Hz, 1H), 6.16 – 6.15 (m, 1H), 6.09 – 6.02 (m, 1H), 5.04 (dd, J = 3.5, 1.7 Hz, 1H), 2.85 – 2.80 (m, 1H), 1.18 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 154.7, 135.2, 133.5, 131.2, 129.6, 129.1, 129.0, 122.8, 85.4, 40.1, 15.6.**] α-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 (dd, J = 5.7, 1.3 Hz, 1H), 7.30 – 7.26 (m, 2H), 7.16 (d, J = 8.4 Hz, 1H), 6.10 – 6.07 (m, 1H), 5.75 – 5.52 (m, 2H), 5.21 (d, J = 6.3 Hz, 1H), 3.58 (t, J = 6.9 Hz, 1H), 1.71 (d, J = 5.4 Hz, 3H).**] α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 (dd, J = 5.7, 1.3 Hz, 1H), 7.30 – 7.26 (m, 2H), 7.16 (d, J = 8.4 Hz, 1H), 6.10 – 6.07 (m, 1H), 5.75 – 5.52 (m, 2H), 5.19 (d, J = 6.4 Hz, 1H), 3.53 (t, J = 6.9 Hz, 1H), 1.69 (d, J = 6.1 Hz, 3H).**] IR** (ν/cm^{-1}): 3118 (br, w), 2971 (m), 2927 (m), 2871 (w), 1749 (s), 1653 (m), 1521 (m), 1164 (m), 1089 (m), 1013 (m), 984 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{12}H_{13}O_3^+$ 205.0865, found: 205.0862.

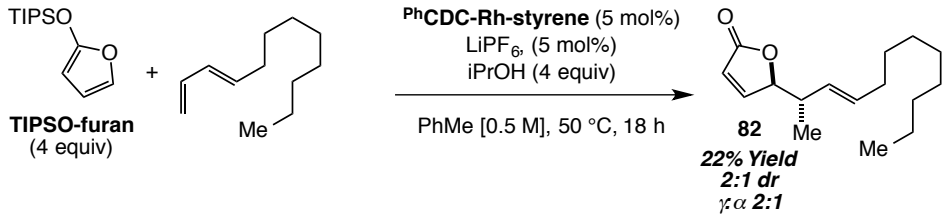


Synthesis of 5-(*E*-4-cyclohexylbut-3-en-2-yl)furan-2(5H)-one (81).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), (*E*)-buta-1,3-dien-1-ylcyclohexane (13.6 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (200 µL, 0.5 M). The reaction was sealed with a Teflon® septum cap and removed

from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **81** (8.2 mg, 0.037 mmol, 37% yield, 1:1 dr, 9:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 5.7, 1.4 Hz, 1H), 6.13-6.11 (m, 1H), 5.51 – 5.45 (m, 1H), 5.26 – 5.17 (m, 1H), 4.83 – 4.82 (m, 1H), 2.45 – 2.37 (m, 1H), 1.91 (m, 1H), 1.74 – 1.60 (m, 6H), 1.30 – 1.18 (m, 4H), 1.12 (d, *J* = 6.8 Hz, 3H).] ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 5.8, 1.4 Hz, 1H), 6.13-6.11 (m, 1H), 5.51 – 5.45 (m, 1H), 5.26 – 5.17 (m, 1H), 4.97 – 4.96 (m, 1H), 2.68 – 2.62 (m, 1H), 1.91 (m, 1H), 1.74 – 1.60 (m, 6H), 1.30 – 1.18 (m, 4H), 1.02 (d, *J* = 6.9 Hz, 3H).] **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.4, 173.3 155.3, 155.0, 139.8, 139.6, 126.4, 125.8, 122.5, 122.3, 87.1, 86.9, 40.9, 40.8, 40.8, 39.3, 33.2, 33.2, 33.1, 33.1, 26.2, 26.1, 16.8, 15.3. **IR** (ν/cm^{-1}): 2925 (s), 2851 (m), 1758 (s), 1457 (m), 1161 (m), 1086 (m), 1016 (m), 971 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{14}H_{21}O_2^+$ 221.1542, found: 221.1539.

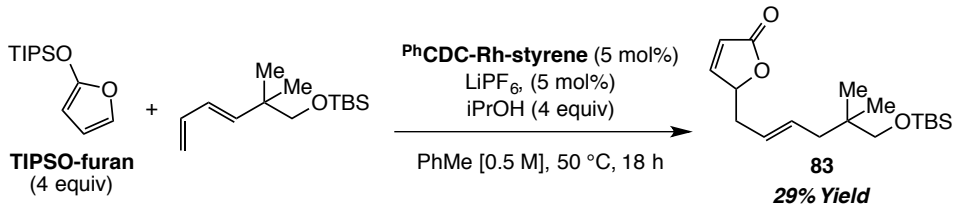


Synthesis of 5-(*E*-dodec-3-en-2-yl)furan-2(5H)-one (82).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), (*E*)-1,3-dodecadiene (16.6 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (200 μL, 0.5 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (10:1 Hex/EtOAc) to afford **82** (5.5 mg, 0.022 mmol, 22% yield, 2:1 dr, 2:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 1H), 6.16 – 6.06 (m, 1H), 5.58 – 5.48 (m, 1H), 5.25 (dd, *J* = 16.2, 9.0 Hz, 1H), 4.82 (d, *J* = 7.0 Hz, 1H), 2.46 –

2.38 (m, 1H), 1.98 (q, J = 7.0 Hz, 2H), 1.38 – 1.19 (m, 12H), 1.12 (d, J = 6.8 Hz, 3H), 0.89 – 0.85 (m, 3H).] ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 1H), 7.40 – 7.33 (m, 1H), 6.15 – 6.07 (m, 1H), 5.58 – 5.47 (m, 1H), 5.31 – 5.25 (m, 1H), 4.85 (d, J = 7.3 Hz, 1H), 2.70 – 2.62 (m, 1H), 1.98 (q, J = 7.0 Hz, 2H), 1.37 – 1.17 (m, 12H), 1.02 (d, J = 6.9 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H).] **α-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 1H), 7.41 – 7.33 (m, 1H), 6.16 – 6.06 (m, 1H), 5.10 (dddd, J = 32.1, 30.4, 13.1, 7.7 Hz, 1H), 4.96 (dt, J = 4.6, 1.5 Hz, 1H), 1.98 (q, J = 7.0 Hz, 2H), 2.28 – 2.18 (m, 1H), 1.68 (dd, J = 6.5, 1.5 Hz, 3H), 1.37 – 1.17 (m, 12H), 0.87 (t, J = 7.0 Hz, 3H).] **α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 1H), 7.41 – 7.33 (m, 1H), 6.16 – 6.06 (m, 1H), 5.10 (dddd, J = 32.1, 30.4, 13.1, 7.7 Hz, 1H), 5.02 – 4.98 (m, 1H), 1.98 (q, J = 7.0 Hz, 3H), 1.65 (dd, J = 6.5, 1.5 Hz, 3H), 1.37 – 1.17 (m, 12H), 0.87 (t, J = 7.0 Hz, 3H).] **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.4, 173.2, 173.2, 173.2, 155.5, 155.4, 155.2, 154.9, 133.8, 133.6, 129.8, 129.5, 128.8, 128.6, 128.2, 128.1, 122.5, 122.1, 122.1, 122.0, 86.9, 86.7, 86.2, 86.2, 46.9, 45.5, 40.8, 39.3, 36.7, 36.5, 36.2, 35.7, 32.6, 32.5, 31.9, 31.9, 31.1, 30.4, 29.5, 29.5, 29.5, 29.4, 29.3, 29.3, 29.2, 29.1, 27.2, 26.9, 22.7, 22.7, 18.1, 18.0, 16.7, 15.2, 14.2, 14.2. **IR** (ν/cm^{-1}): 2956 (w), 2926 (s), 2855 (m), 1758 (s), 1457 (m), 1160 (m), 1093 (m), 1017 (m), 970. **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{16}H_{27}O_2^+$ 251.2011, found: 251.2010.

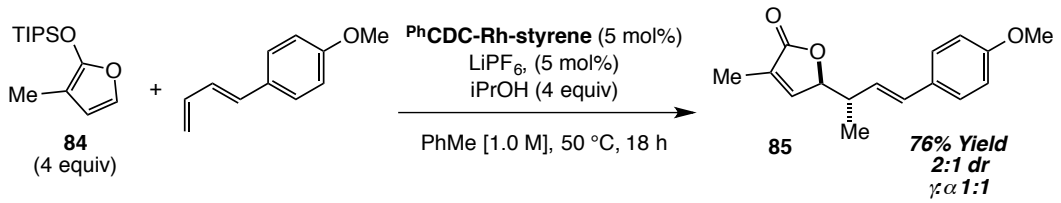


Synthesis of 5-(*E*-6-((tert-butyldimethylsilyl)oxy)-5,5-dimethylhex-3-en-2-yl)furan-2(5H)-one (83).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), (*E*)-tert-butyl((2,2-dimethylhexa-3,5-dien-1-yl)oxy)dimethylsilane (24.0 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (200 μL, 0.5 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of (furan-2-yloxy)triisopropylsilane (25 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x25 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **83** (9.4 mg, 0.029 mmol, 29% yield, 0:0:1 γ:α:δ regioselectivity) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 5.7, 1.3 Hz, 1H), 6.15 (dd, *J* = 5.7, 1.9 Hz, 1H), 5.67 – 5.55 (m, 1H), 5.41 – 5.30 (m, 1H), 5.11 – 5.02 (m, 1H), 3.22 (s, *J* = 9.7 Hz, 2H), 2.61 – 2.51 (m, 1H), 2.49 – 2.38 (m, 1H), 1.96 (d, *J* = 7.6 Hz, 2H), 0.91 (s, 9H), 0.82 (s, 6H), 0.04 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.0, 156.0, 132.8, 124.4, 122.0, 83.0, 71.3, 41.7, 36.4, 35.7, 25.9, 23.9, 23.9, 18.3, -5.5. **IR** (ν/cm^{-1}): 2955 (s), 2929 (m), 2856 (m), 1759 (s), 1472 (m), 2352

(m), 1161 (m), 1100 (s), 852 (m). **HRMS** (ES^+) $[M–Na]^+$ calcd for $C_{18}H_{32}O_3SiNa^+$ 347.2018, found: 347.2023.

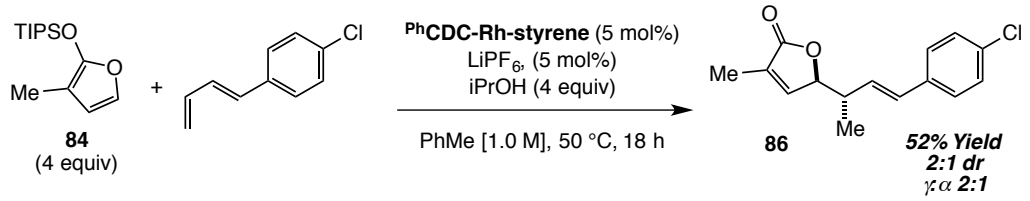


Synthesis of 5-(*E*-4-(4-methoxyphenyl)but-3-en-2-yl)-3-methylfuran-2(5H)-one (85).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (16.0 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 μL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x28 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography

(5:1 Hex/EtOAc) to afford **85** (19.6 mg, 0.076 mmol, 76% yield, 2:1 dr, 1:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 – 7.29 (m, 1H), 7.05 – 7.02 (m, 2H), 6.83 (dd, *J* = 4.9, 3.4 Hz, 2H), 6.44 (d, *J* = 15.9 Hz, 1H), 5.95 (dd, *J* = 15.8, 8.4 Hz, 1H), 4.83 – 4.79 (m, 1H), 3.83 (s, 3H), 2.65 – 2.49 (m, 1H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H).**] *syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 1H), 7.11 – 7.09 (m, 2H), 7.07 – 7.05 (m, 2H), 6.44 (d, *J* = 15.9 Hz, 1H), 5.97 (dd, *J* = 15.9, 7.7 Hz, 1H), 4.93 – 4.90 (m, 1H), 3.83 (s, 3H), 2.85 – 2.76 (m, 1H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H).**] α-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32 – 7.29 (m, 1H), 7.15 (dd, *J* = 8.6, 1.1 Hz, 2H), 6.91 – 6.85 (m, 2H), 5.75 – 5.69 (m, 1H), 5.69 – 5.62 (m, 1H), 5.10 – 5.03 (m, 1H), 3.82 (s, 3H), 3.58 – 3.53 (m, 1H), 1.87 (dt, *J* = 3.6, 1.8 Hz, 3H), 1.73 – 1.72 (m, 3H).**] α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 1H), 7.15 (dd, *J* = 8.6, 1.1 Hz, 2H), 6.91 – 6.85 (m, 2H), 5.69 – 5.63 (m, 1H), 5.61 – 5.51 (m, 1H), 5.10 – 5.03 (m, 1H), 3.81 (s, 3H), 3.40 (t, *J* = 7.5 Hz, 1H), 1.87 (dt, *J* = 3.6, 1.8 Hz, 3H), 1.71 (dd, *J* = 7.0, 0.6 Hz, 3H).**] ^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.3, 174.3, 174.2, 174.1, 159.3, 159.2, 158.7, 158.6, 147.8, 147.6, 147.2, 147.1, 131.5, 131.4, 131.3, 131.2, 131.1, 131.0, 130.7, 130.7, 129.6, 129.5, 129.4, 129.2, 129.2, 129.1, 129.0, 128.7, 128.1, 127.4, 127.1, 126.6, 114.1, 114.0, 114.0, 113.8, 84.5, 84.3, 83.8, 83.6, 55.4, 55.3, 55.3, 55.3, 51.9, 51.5, 41.5, 40.1, 18.2, 18.1, 16.5, 15.2, 10.8, 10.8, 10.7, 10.7. **IR** (ν/cm^{-1}): 3502 (br, m), 2962 (m), 2933 (m), 2837 (w), 1758 (s), 1609 (m), 1513 (m), 1455 (m), 1301 (m), 1251 (s), 1179 (m), 1096 (m), 1034 (m), 971 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{16}H_{19}O_3^+$ 259.1334, found: 259.1329.

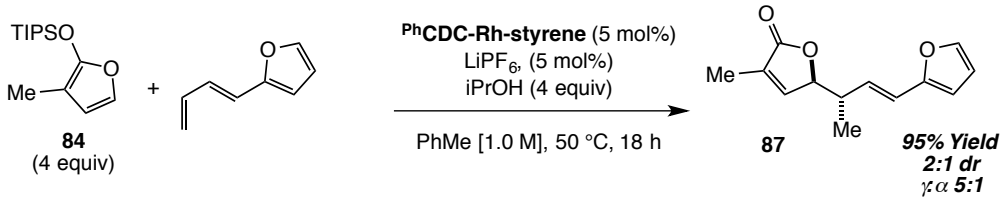


Synthesis of 5-(*E*-4-(4-chlorophenyl)but-3-en-2-yl)-3-methylfuran-2(5H)-one (86).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-1-(buta-1,3-dien-1-yl)-4-chlorobenzene (16.5 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (100 μL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x28 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **86** (13.7 mg, 0.052 mmol, 52% yield, 2:1 dr, 2:1 γ:α regioselectivity) as a colorless oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.20 – 7.14 (m, 2H), 7.08 (dd, *J* = 6.3, 4.8 Hz, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.08 (dd, *J* = 15.9, 8.3 Hz,

1H), 4.87 – 4.80 (m, 1H), 2.69 – 2.59 (m, 1H), 1.60 (s, 3H), 1.22 (d, J = 6.8 Hz, 3H).] ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H), 7.21 – 7.14 (m, 2H), 7.07 – 7.05 (m, 1H), 6.44 (d, J = 15.9 Hz, 1H), 6.10 (dd, J = 15.9, 7.6 Hz, 1H), 4.95 – 4.88 (m, 1H), 2.85 – 2.72 (m, 1H), 1.95 (dd, J = 3.4, 1.6 Hz, 3H), 1.17 (dd, J = 15.2, 6.8 Hz, 3H).] **α-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.21 – 7.14 (m, 2H), 7.05 – 7.02 (m, 1H), 5.73 – 5.50 (m, 2H), 5.11 – 5.04 (m, 1H), 3.53 (t, J = 7.0 Hz, 1H), 1.91 – 1.86 (m, 3H), 1.74 (d, J = 5.2 Hz, 3H).] **α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.21 – 7.14 (m, 2H), 6.86 – 6.82 (m, 1H), 5.73 – 5.50 (m, 1H), 5.11 – 5.04 (m, 2H), 3.48 (t, J = 7.2 Hz, 1H), 1.91 – 1.86 (m, 3H), 1.71 (d, J = 6.3 Hz, 3H).] **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.1, 174.1, 174.0, 173.9, 147.2, 147.1, 146.9, 146.9, 138.0, 137.7, 135.3, 135.2, 133.3, 133.2, 133.1, 133.0, 131.3, 131.2, 131.1, 131.0, 130.8, 130.7, 130.0, 129.6, 129.6, 129.5, 128.9, 128.8, 128.8, 127.9, 127.7, 127.5, 84.1, 84.1, 83.3, 83.1, 51.9, 51.9, 41.2, 40.2, 18.2, 18.0, 16.0, 15.3, 10.8, 10.8, 10.7, 10.7.] **^{13}C NMR** (151 MHz, $CDCl_3$) δ **IR** (ν/cm^{-1}): 2969 (m), 2926 (m), 1758 (s), 1491 (m), 1339 (m), 1092 (m), 1049 (m), 976 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{15}H_{16}ClO_2^+$ 262.0389, found: 263.0833.



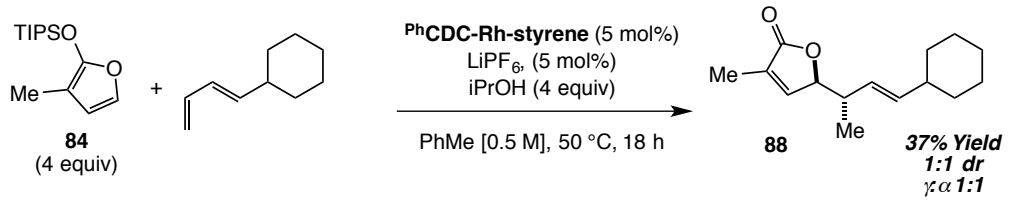
Synthesis of 5-(*E*-4-(furan-2-yl)but-3-en-2-yl)-3-methylfuran-2(5H)-one (87).

Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-2-(buta-1,3-dien-1-yl)furan (12.2 mg, 0.100 mmol) were combined in the glove box, and

solvated with toluene (100 μL, 1.0 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x28 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **87** (20.7 mg, 0.095 mmol, 95% yield, 2:1 dr, 5:1 γ:α regioselectivity) as a yellow oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 (t, *J* = 4.9 Hz, 1H), 7.12 – 7.08 (m, 1H), 6.38 (dt, *J* = 3.2, 2.1 Hz, 1H), 6.31 (d, *J* = 15.8 Hz, 1H), 6.22 (d, *J* = 3.0 Hz, 1H), 6.02 (dd, *J* = 15.9, 8.4 Hz, 1H), 4.81 – 4.75 (m, 1H), 2.60 – 2.51 (m, 1H), 1.97 – 1.92 (m, 3H), 1.23 (d, *J* = 6.8 Hz, 3H).] ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 (t, *J* = 4.9 Hz, 1H), 7.12 – 7.09 (m, 1H), 6.40 – 6.36 (m, 1H), 6.31 (d, *J* = 15.9 Hz, 1H), 6.22 (d, *J* = 3.0 Hz, 1H), 6.07 (dd, *J* = 15.9, 7.5 Hz, 1H), 4.92 – 4.89 (m, 1H), 2.85 – 2.74 (m, 1H), 1.96 – 1.93 (m, 3H), 1.12 (d, *J* = 6.9 Hz, 3H).] **α-Regioisomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 1H), 7.07 – 7.05 (m, 1H), 6.35 – 6.33 (m, 1H), 6.16 (dd, *J* = 3.2, 0.6 Hz, 1H), 5.73 – 5.57 (m, 2H), 5.17 – 5.13 (m, 1H), 3.83 (dd, *J* = 8.7, 5.5 Hz, 1H), 1.91 (t, *J* = 1.8 Hz, 3H),

1.73 (d, J = 5.4 Hz, 3H).] **α-Regioisomer (minor): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.36 (m, 1H), 6.97 – 6.94 (m, 1H), 6.35 – 6.33 (m, 1H), 6.16 (dd, J = 3.2, 0.6 Hz, 1H), 5.71 – 5.59 (m, 1H), 5.46 – 5.40 (m, 1H), 5.10 (dq, J = 8.6, 1.8 Hz, 1H), 3.64 (t, J = 6.8 Hz, 1H), 1.90 (t, J = 1.8 Hz, 3H), 1.71 (dd, J = 6.5, 1.5 Hz, 3H).] **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.2, 174.2, 174.0, 174.0, 152.6, 152.6, 152.3, 152.2, 147.3, 147.3, 146.8, 146.7, 141.9, 141.9, 141.9, 141.8, 131.3, 131.2, 131.2, 130.8, 130.8, 130.3, 127.8, 127.5, 125.5, 124.3, 120.5, 120.3, 111.3, 111.3, 110.4, 110.4, 107.9, 107.7, 107.2, 107.0, 84.2, 84.0, 82.1, 81.7, 46.2, 45.8, 41.2, 39.8, 18.1, 17.6, 16.4, 14.7, 10.8, 10.8, 10.7, 10.7. **IR** (ν/cm^{-1}): 3117 (m), 2969 (m), 2927 (m), 2973 (w), 1758 (s), 1660 (m), 1456 (m), 1339 (m), 1256 (m), 1208 (m), 1150 (m), 1095 (m), 1013 (m), 977 (m). **HRMS** (ES$^+$) [M–H]$^+$ calcd for $C_{13}H_{15}O_3^+$ 219.1021, found: 219.1018.



Synthesis of 5-(*E*-4-cyclohexylbut-3-en-2-yl)-3-methylfuran-2(5H)-one (88).

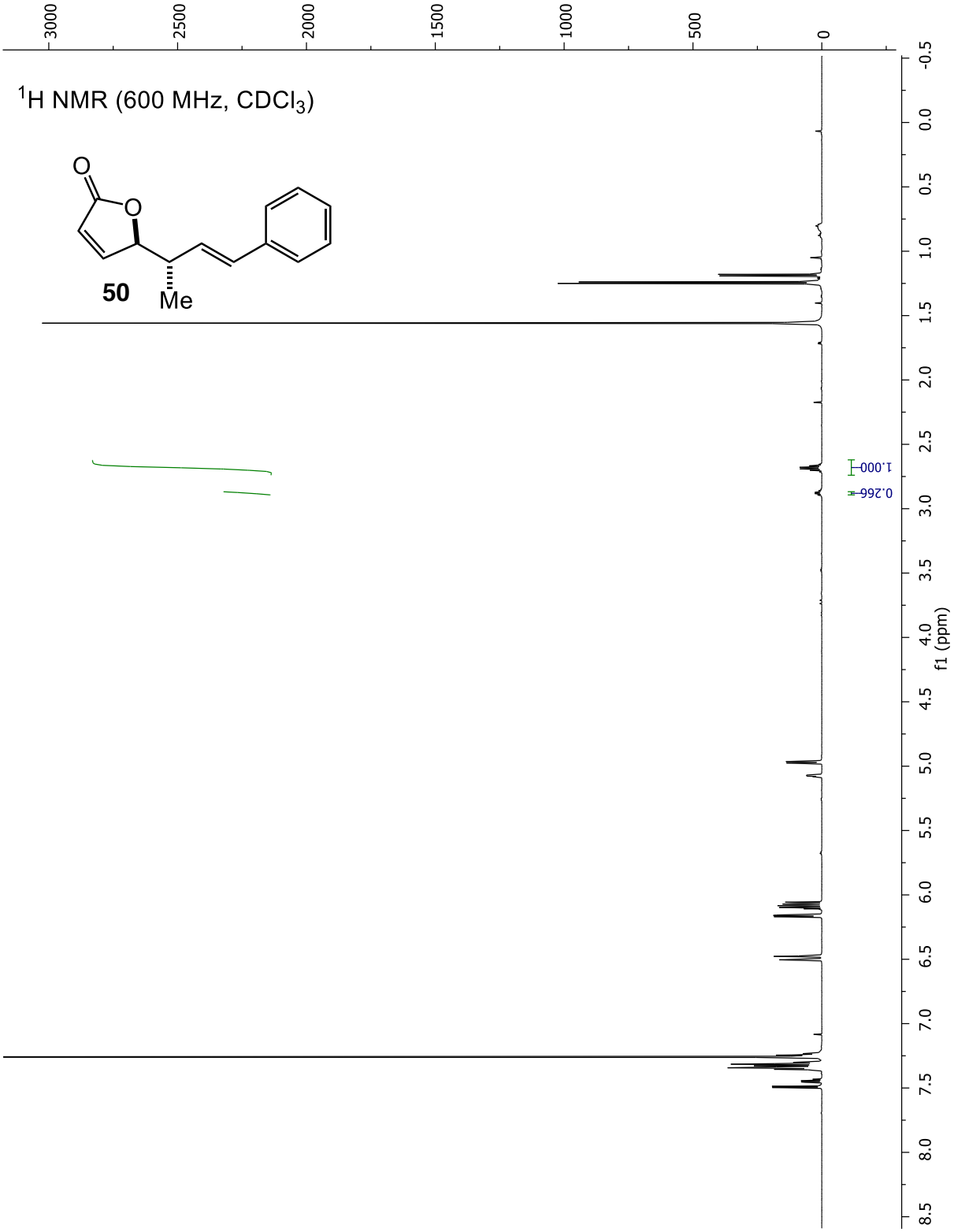
Following the general procedure for the Rh(I) catalyzed hydroalkylation of dienes with silyl enol ethers, CDC-Rh(I)-styrene $BAr^F{}_4$ **1** (8.1 mg, 0.005 mmol), $LiPF_6$ (0.8 mg, 0.005 mmol), and (*E*)-buta-1,3-dien-1-ylcyclohexane (13.6 mg, 0.100 mmol) were combined in the glove box, and solvated with toluene (200 μL, 0.5 M). The reaction was sealed with a Teflon® septum cap and removed from the glove box. Outside the glove box, N_2 sparged isopropanol (30.6 μL, 0.4 mmol) was added via syringe and the sealed reaction pumped back into the glove box. Inside the glove box triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction via syringe and the solution allowed to stir at 50 °C for 1 h. A second aliquot of

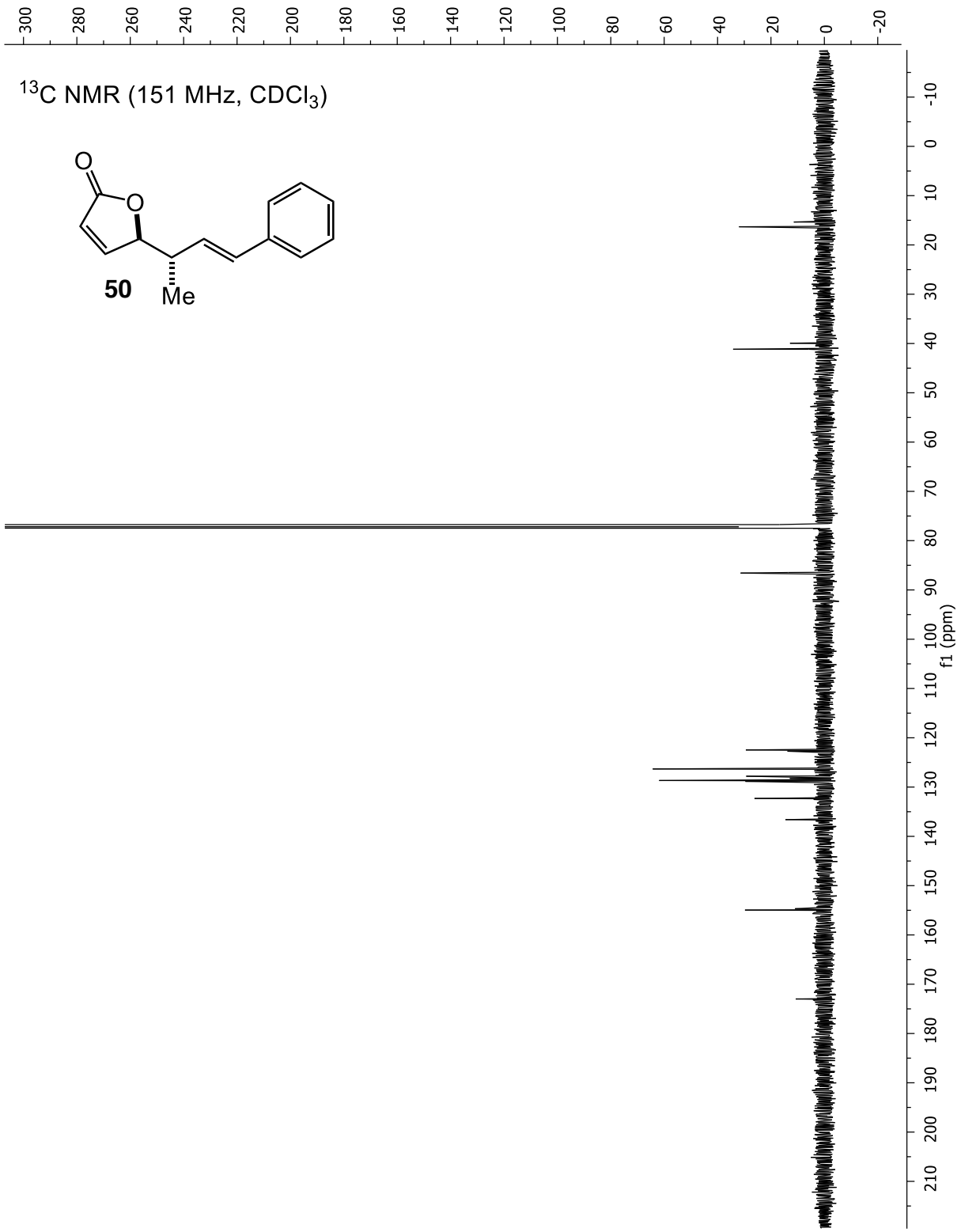
triisopropyl((3-methylfuran-2-yl)oxy)silane (28 μL, 0.1 mmol) was added to the sealed reaction at 50 °C via syringe and the reaction allowed to stir for an additional hour. This aliquot addition was repeated twice more (2x28 μL) on the hour before the reaction was allowed to stir at 50 °C for 18 h. The reaction was removed from the glove box, cooled to room temperature, and 5 μL of hexamethyldisiloxane added as an internal standard. The reaction was diluted with $CDCl_3$ and analyzed by NMR spectroscopy. The NMR sample was recombined with the reaction and the solvents removed *in vacuo*. The resulting oil was purified by SiO_2 gel column chromatography (5:1 Hex/EtOAc) to afford **88** (8.7 mg, 0.037 mmol, 37% yield, 1:1 dr, 1:1 γ:α regioselectivity) as a yellow oil.

***anti*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.01 – 6.97 (m, 1H), 5.53 – 5.43 (m, 1H), 5.29 – 5.18 (m, 1H), 4.72 – 4.65 (m, 1H), 2.42 – 2.30 (m, 1H), 1.93 (s, *J* = 5.7 Hz, 3H), 1.95 – 1.89 (m, 1H), 1.77 – 1.63 (m, 6H), 1.33 – 1.19 (m, 4H), 1.16 – 1.05 (m, 3H).**]** ***syn*-Diastereomer (major): [^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.06 – 7.02 (m, 1H), 5.53 – 5.43 (m, 1H), 5.29 – 5.17 (m, 1H), 4.84 – 4.79 (m, 1H), 2.64 – 2.56 (m, 1H), 2.20 (s, 3H), 1.95 – 1.87 (m, 1H), 1.76 – 1.62 (m, 6H), 1.32 – 1.20 (m, 4H), 1.13 – 1.05 (m, 3H).**]** **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.61, 174.45, 174.37, 151.90, 148.43, 147.58, 147.29, 139.65, 139.30, 139.15, 134.28, 130.78, 130.50, 126.64, 126.09, 123.44, 110.90, 91.93, 84.67, 84.53, 80.74, 66.59, 40.91, 40.68, 40.63, 39.42, 39.13, 37.74, 36.52, 33.06, 33.00, 32.96, 31.00, 28.88, 28.07, 26.54, 26.32, 26.12, 25.97, 17.72, 17.57, 16.66, 15.20, 12.32, 12.27, 10.72, 10.68, 8.47. **IR** (ν/cm^{-1}): 2925 (s), 2867 (m), 1761 (s), 1661 (m), 1457 (m), 1267 (m), 1093 (w), 1025 (m), 975 (m), 884 (m). **HRMS** (ES$^+$) $[M–H]^+$ calcd for $C_{15}H_{23}O_2^+$ 235.1698, found: 235.1695.

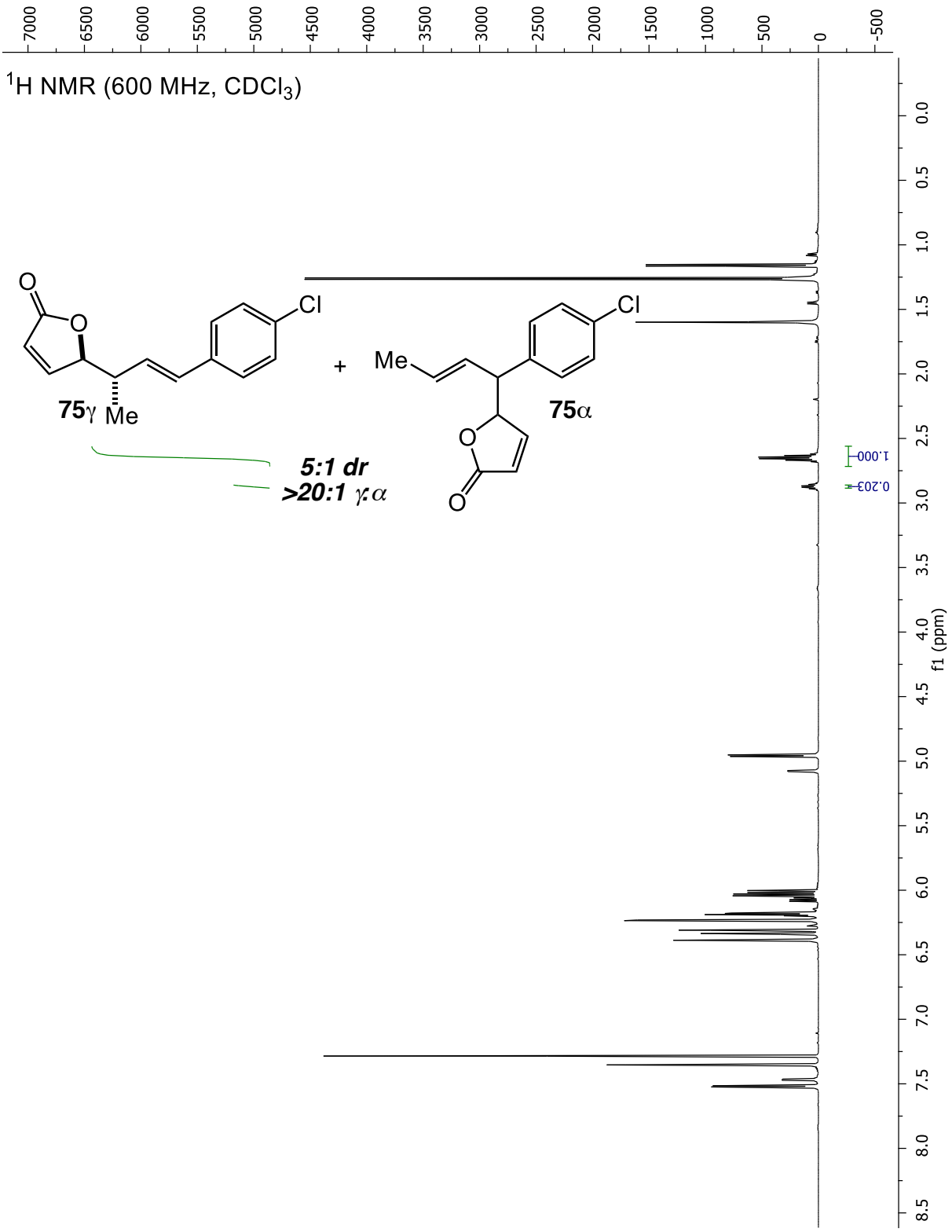
^{1}H NMR (600 MHz, $CDCl_3$)

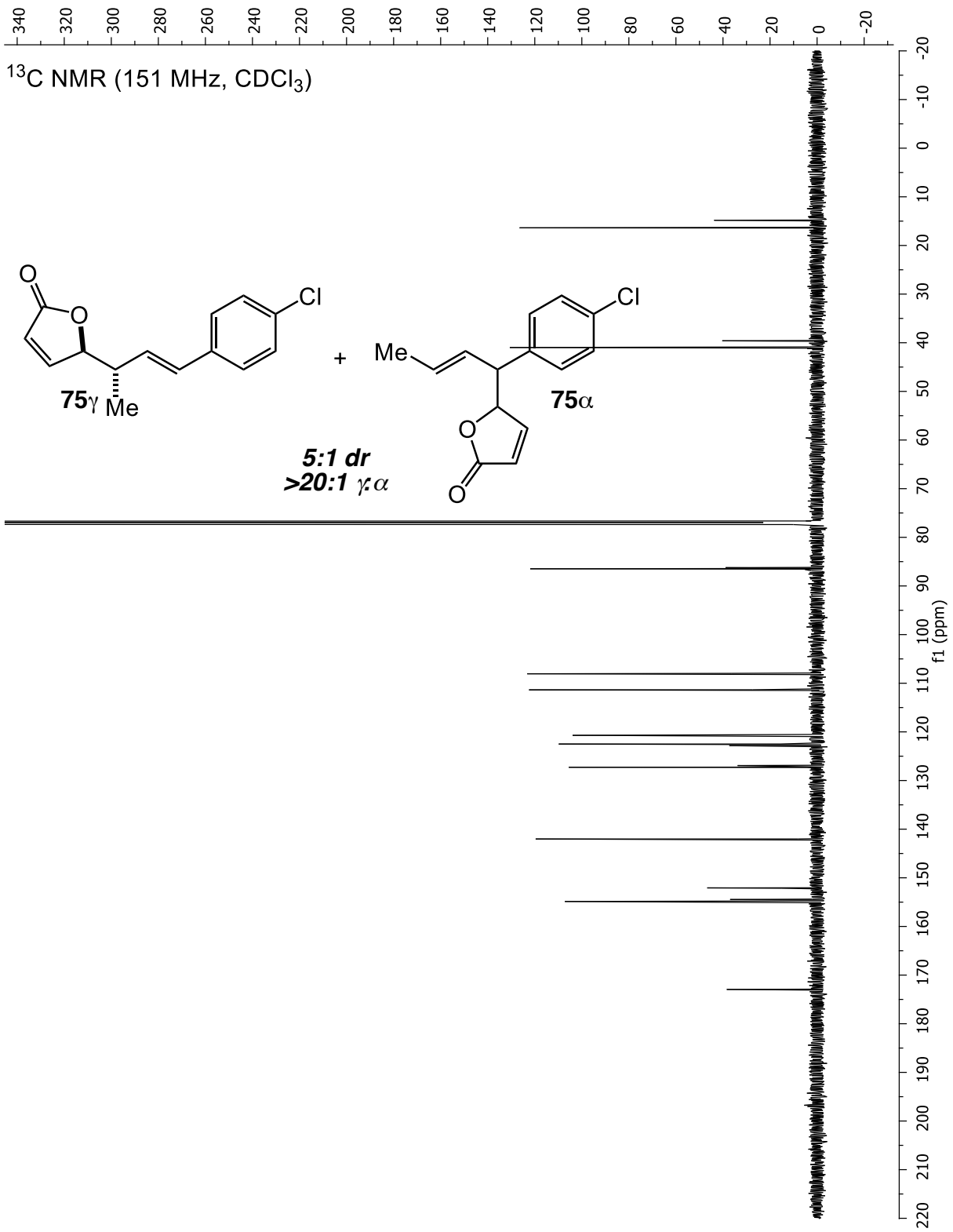
50

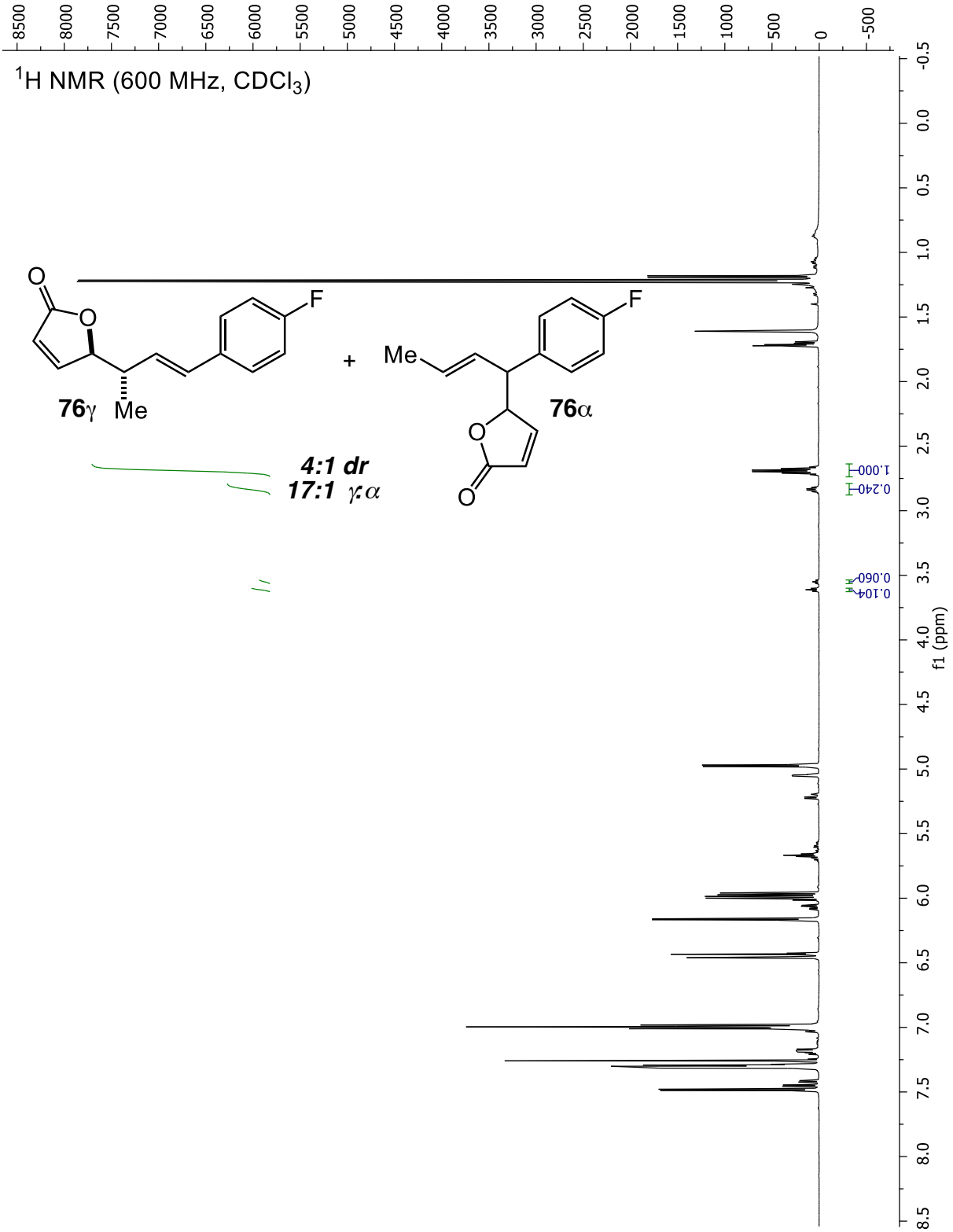



13C NMR (151 MHz, CDCl3)
O
O
50
Me
f1 (ppm)

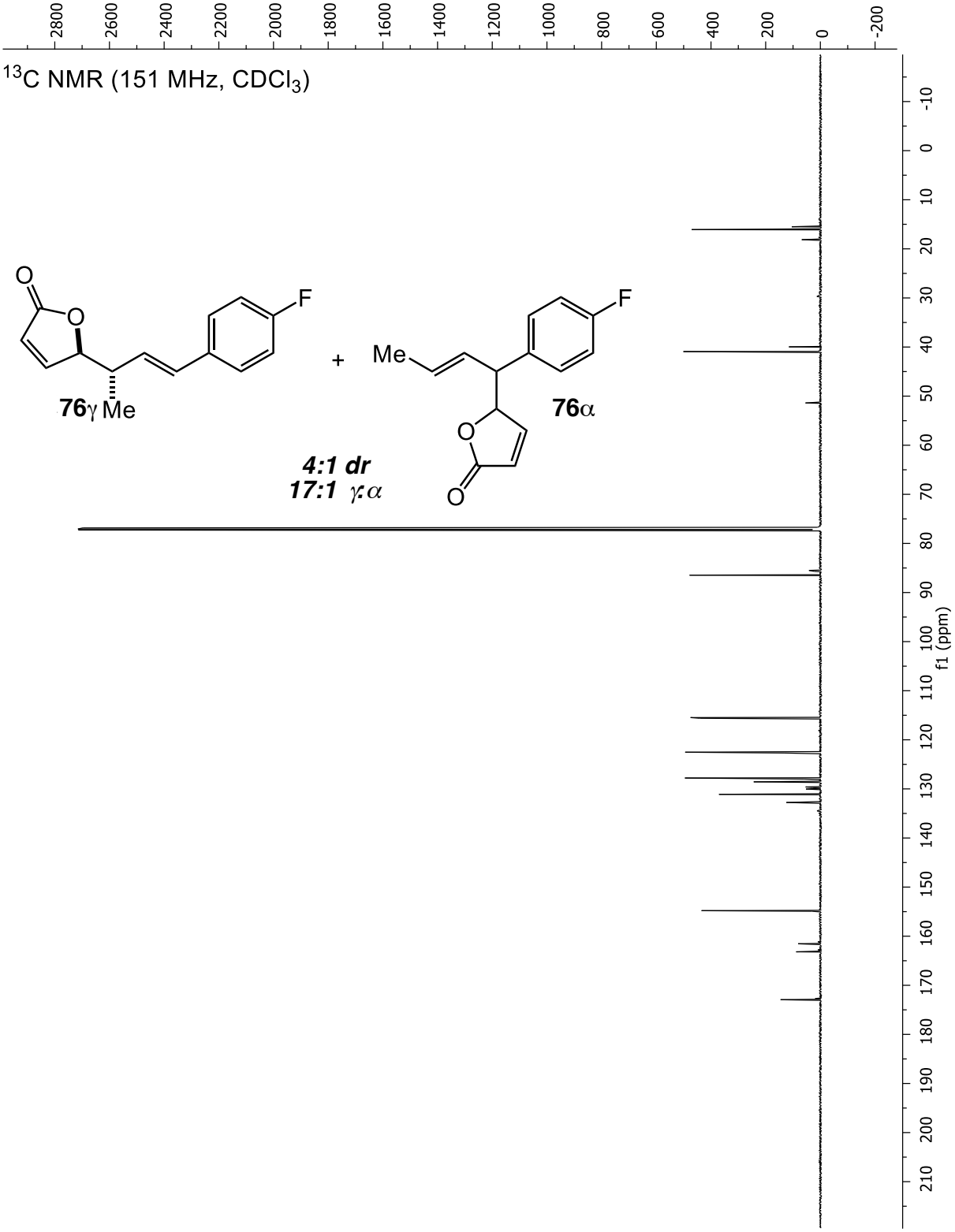
^{1}H NMR (600 MHz, $CDCl_3$)

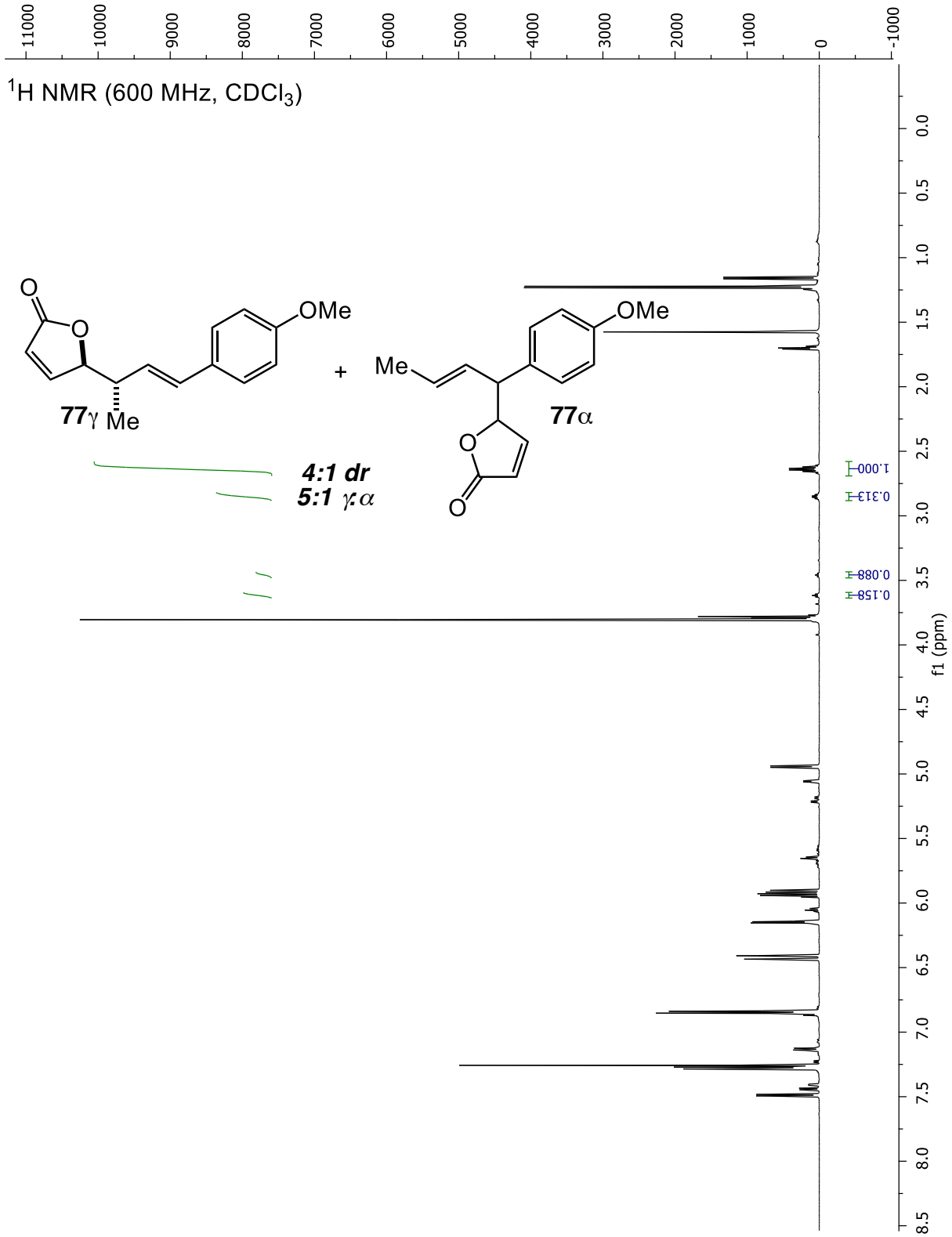



^{13}C NMR (151 MHz, $CDCl_3$)
75γ
Me
Cl
+
Me
Cl
75α
5:1 dr
>20:1 γ:α
f1 (ppm)

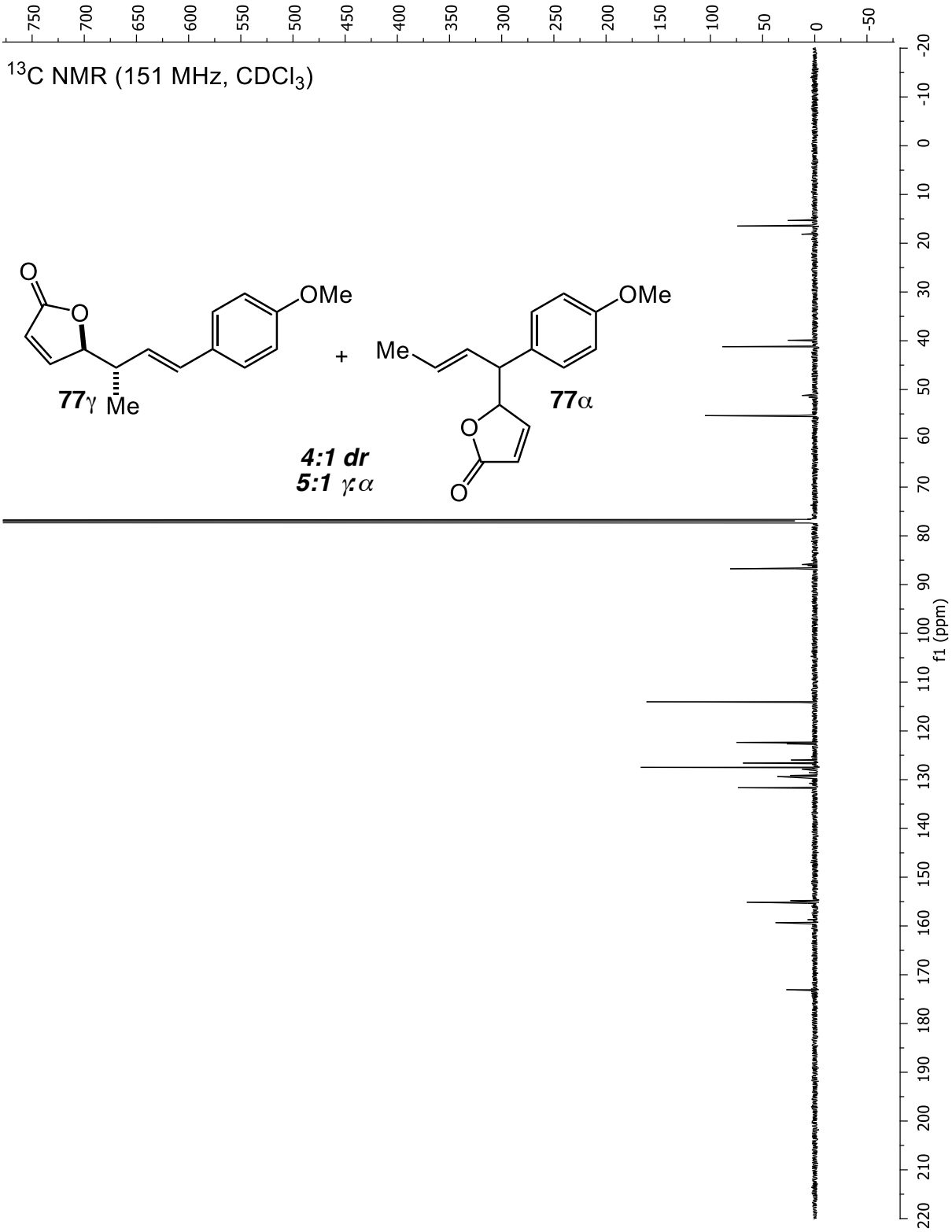

1H NMR (600 MHz, CDCl3)
76γ
Me
+
Me
76α
4:1 dr
17:1 γ:α
1.000
0.240
0.104
0.060
f1 (ppm)

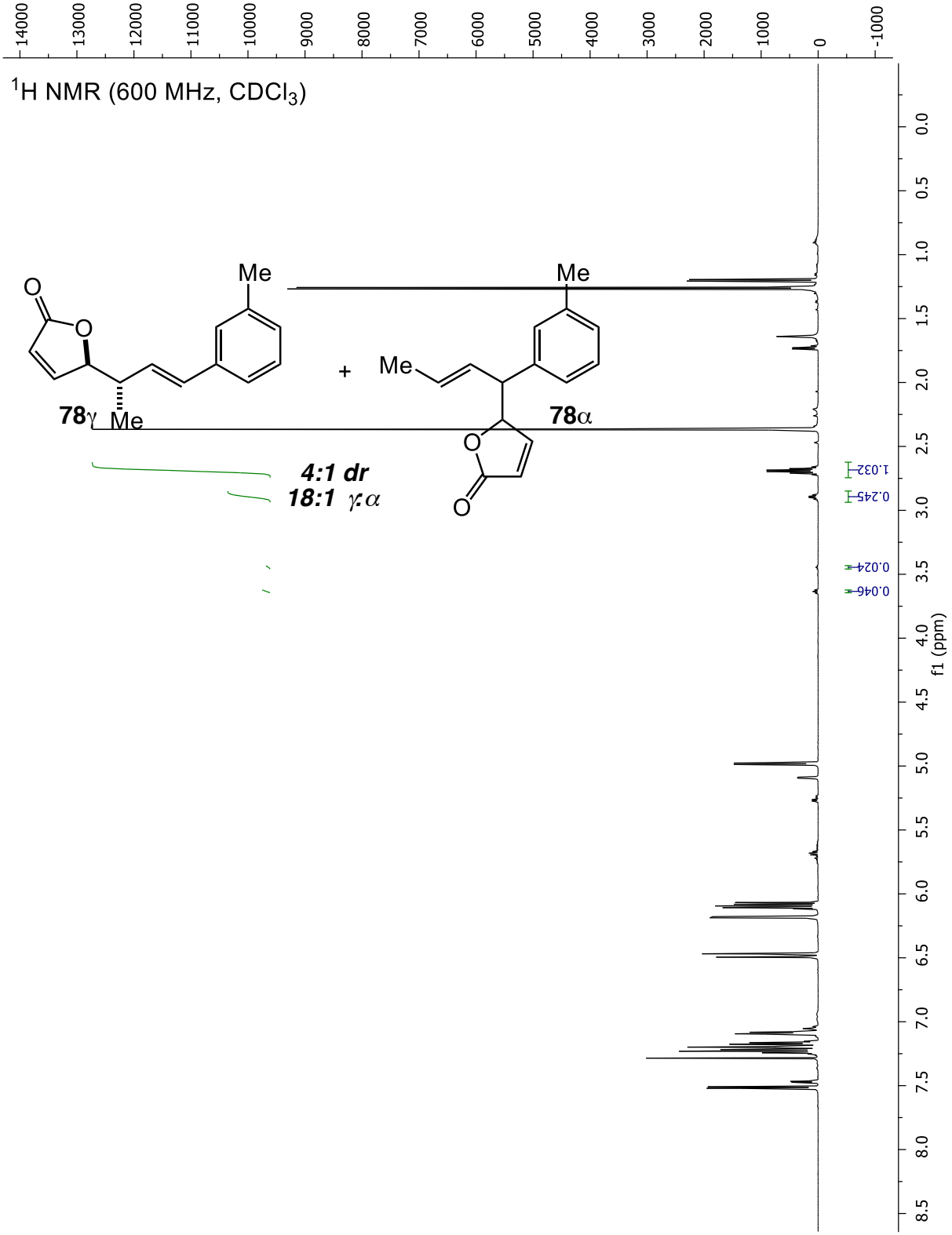
^{13}C NMR (151 MHz, $CDCl_3$)

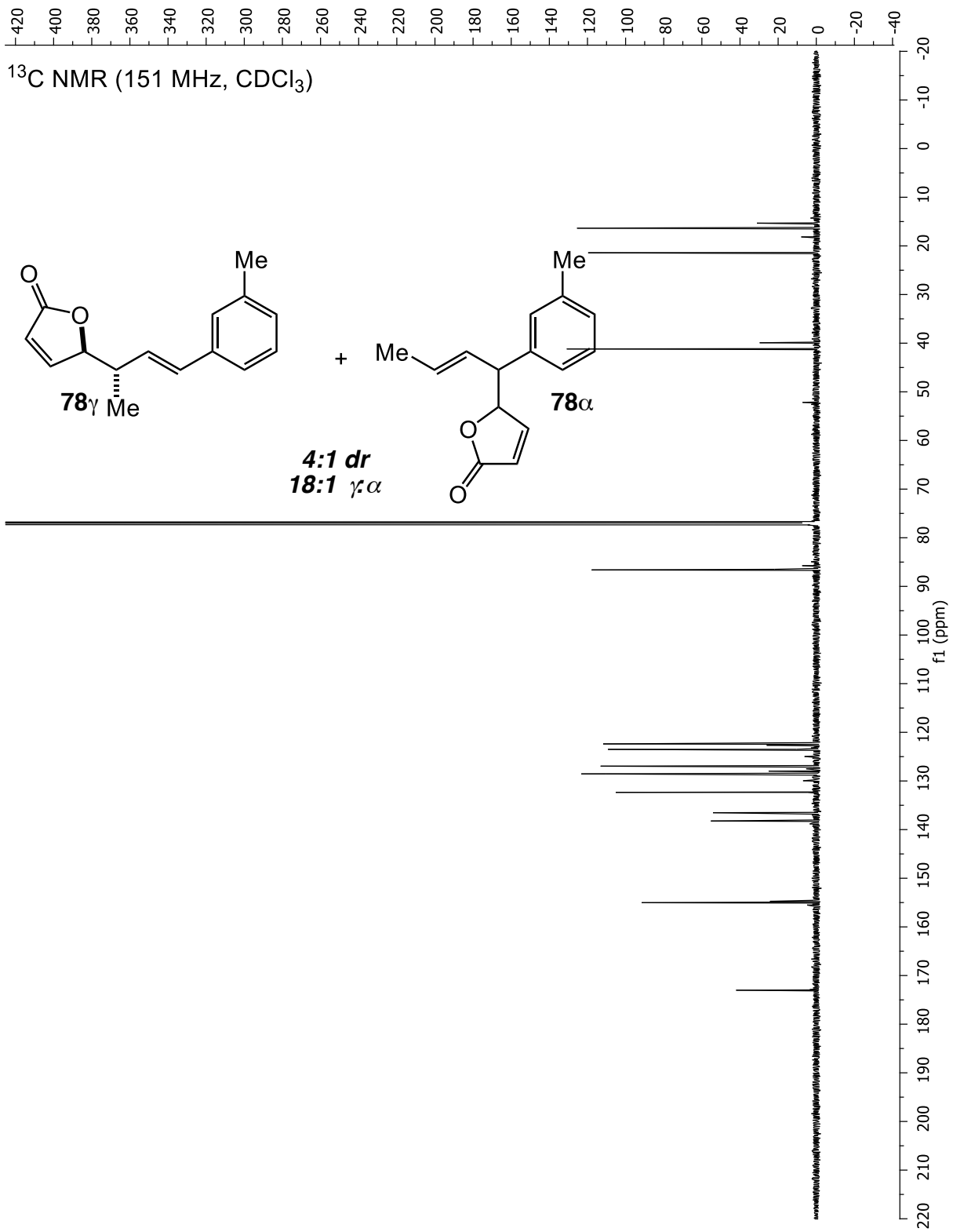


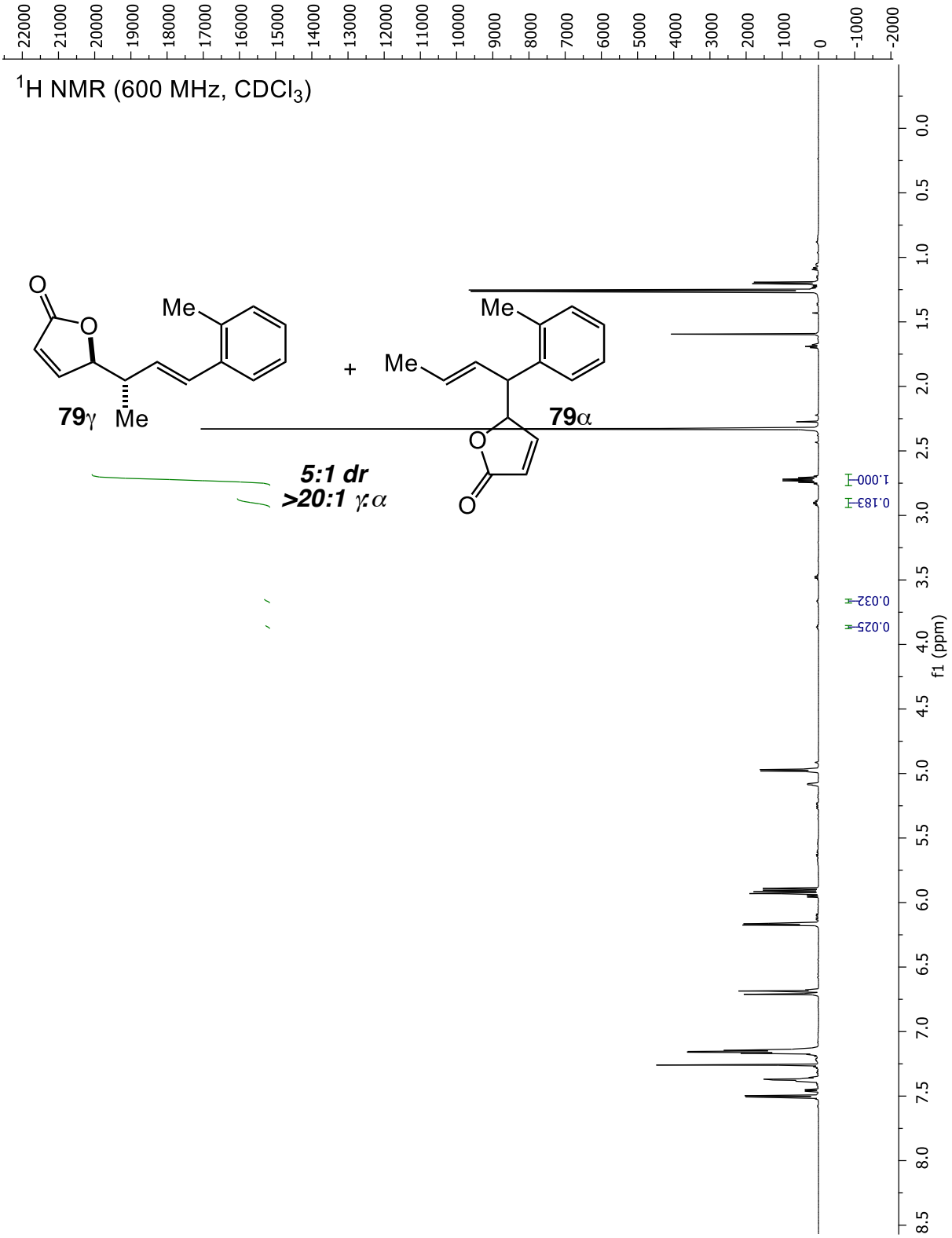

1H NMR (600 MHz, CDCl3)
OMe
Me
77γ
77α
4:1 dr
5:1 γ:α
1.000
0.313
0.088
0.158
f1 (ppm)

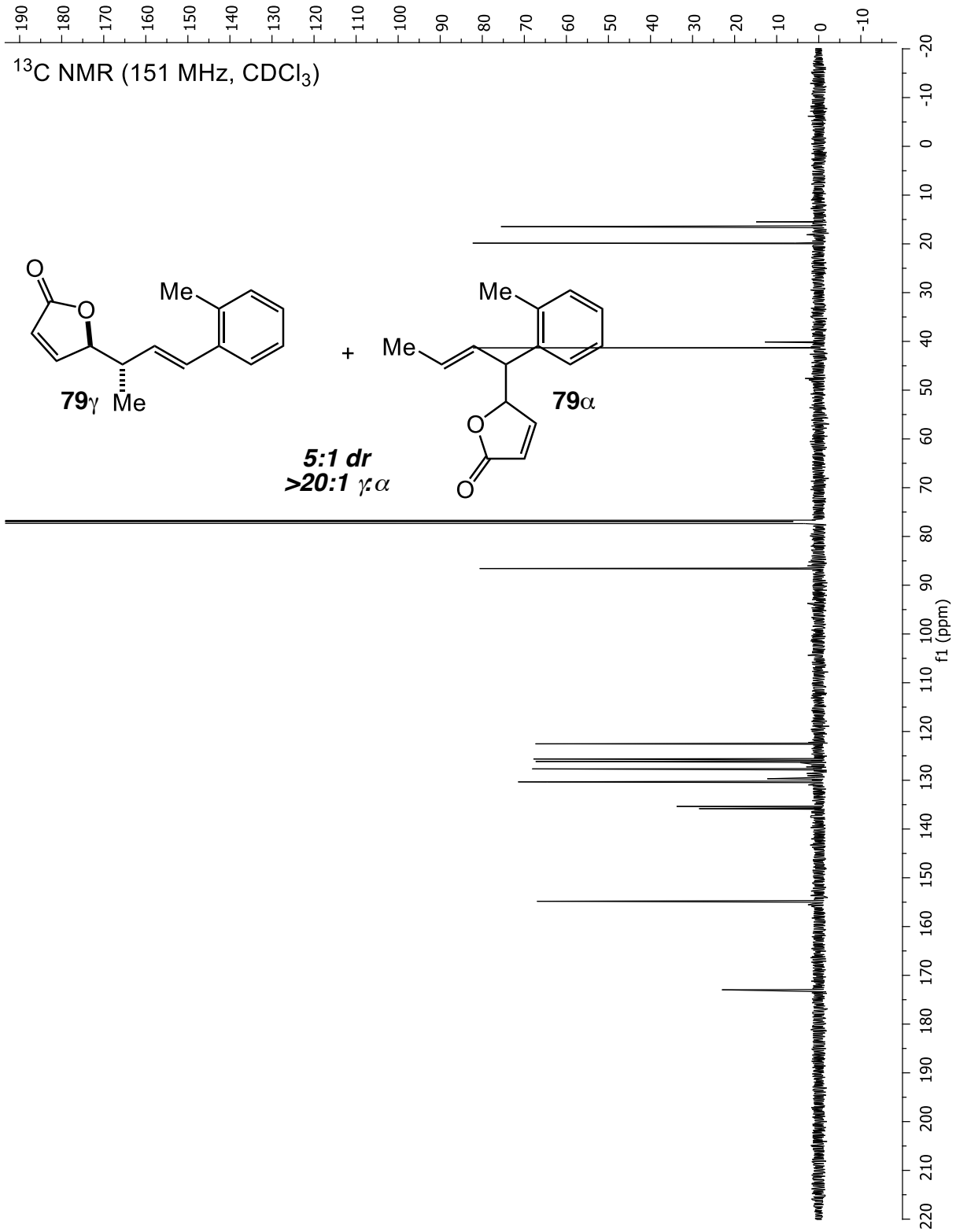
^{13}C NMR (151 MHz, $CDCl_3$)




1H NMR (600 MHz, CDCl3)
Me
Me
+
Me
78γ
Me
78α
4:1 dr
18:1 γ:α
1.032
0.245
0.024
0.046
f1 (ppm)


13C NMR (151 MHz, CDCl3)
Me
O
O
78γ Me
+
Me
Me
78α
O
O
4:1 dr
18:1 γ:α
f1 (ppm)


1H NMR (600 MHz, CDCl3)
79γ
79α
5:1 dr
>20:1 γ:α
f1 (ppm)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79γ
79α
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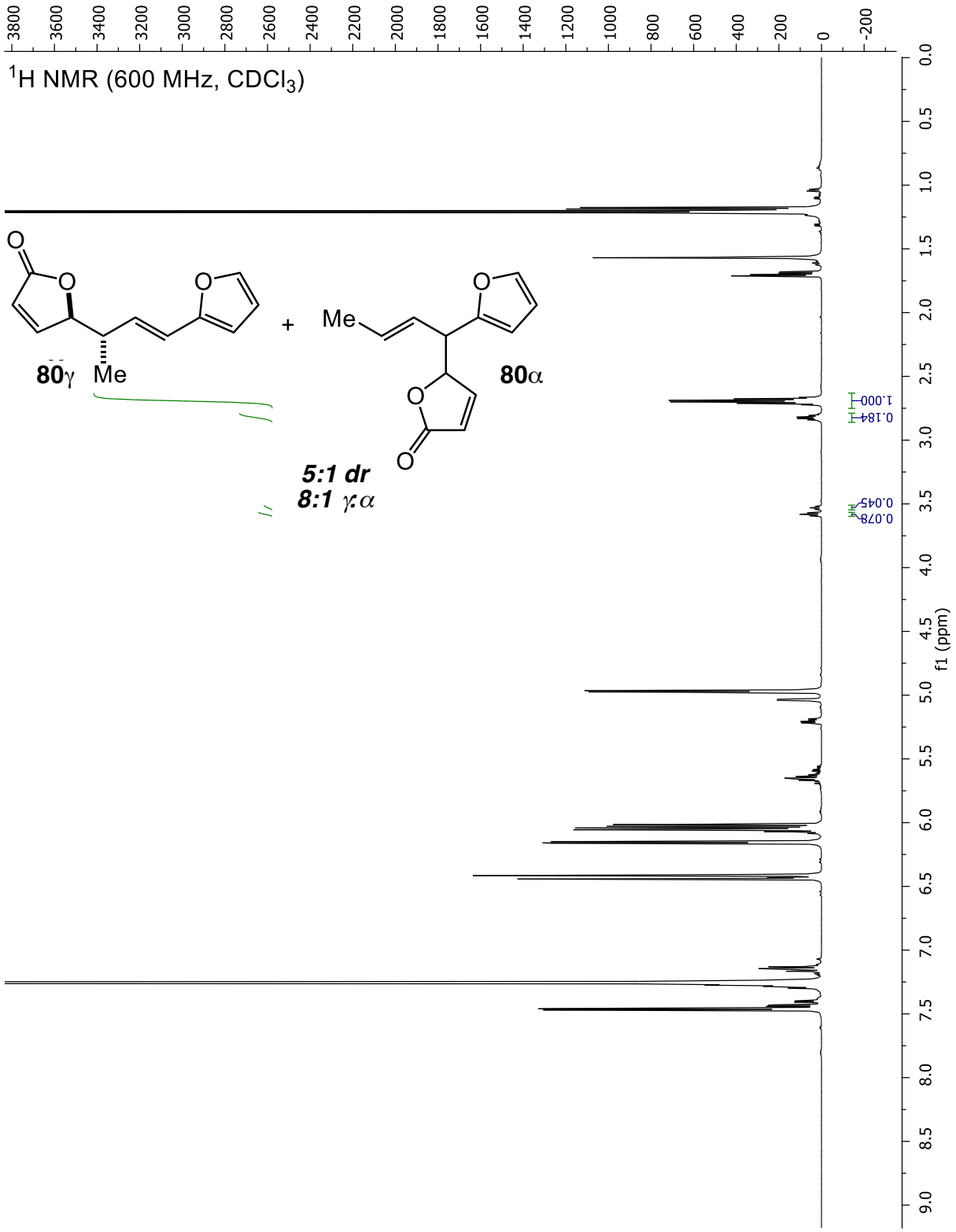
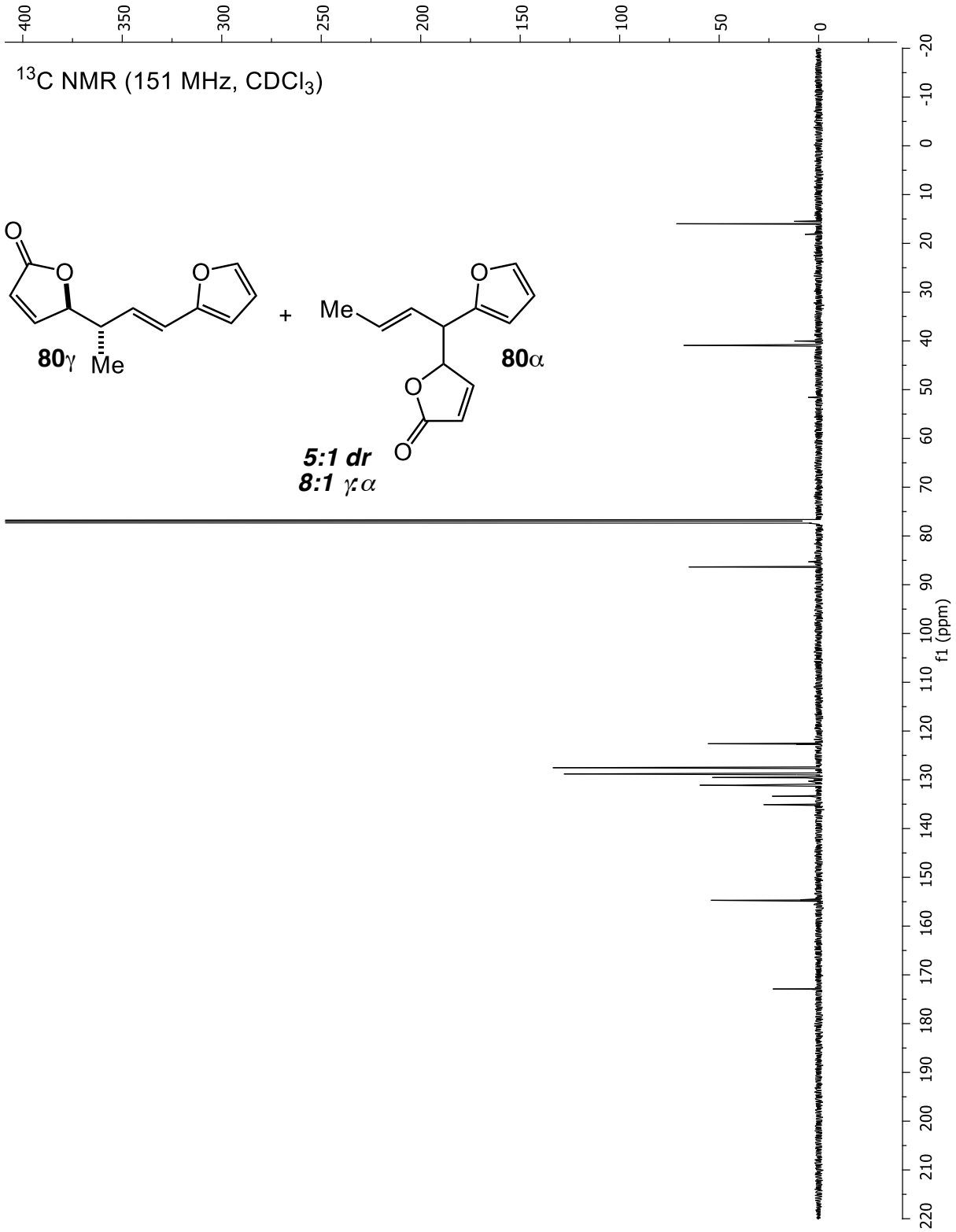
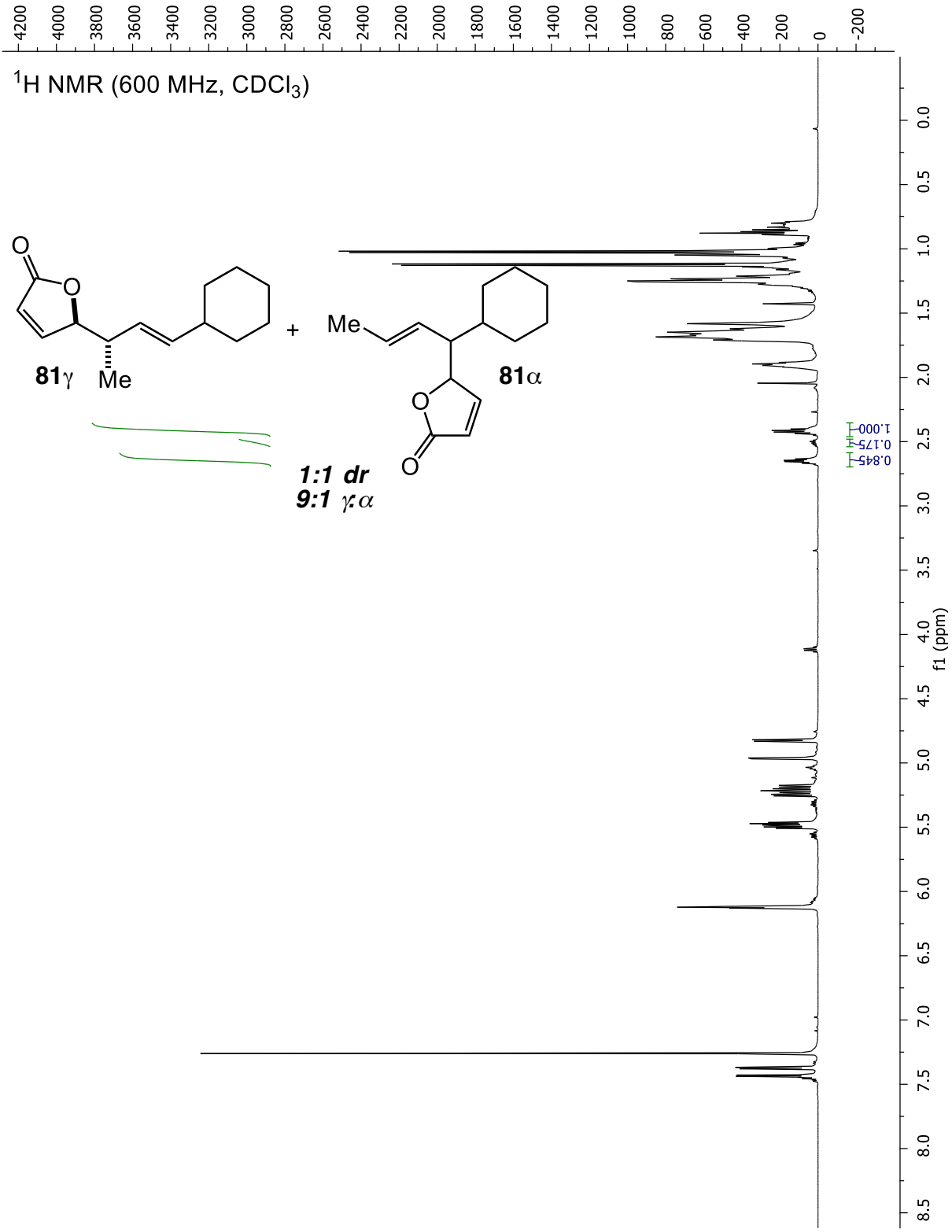
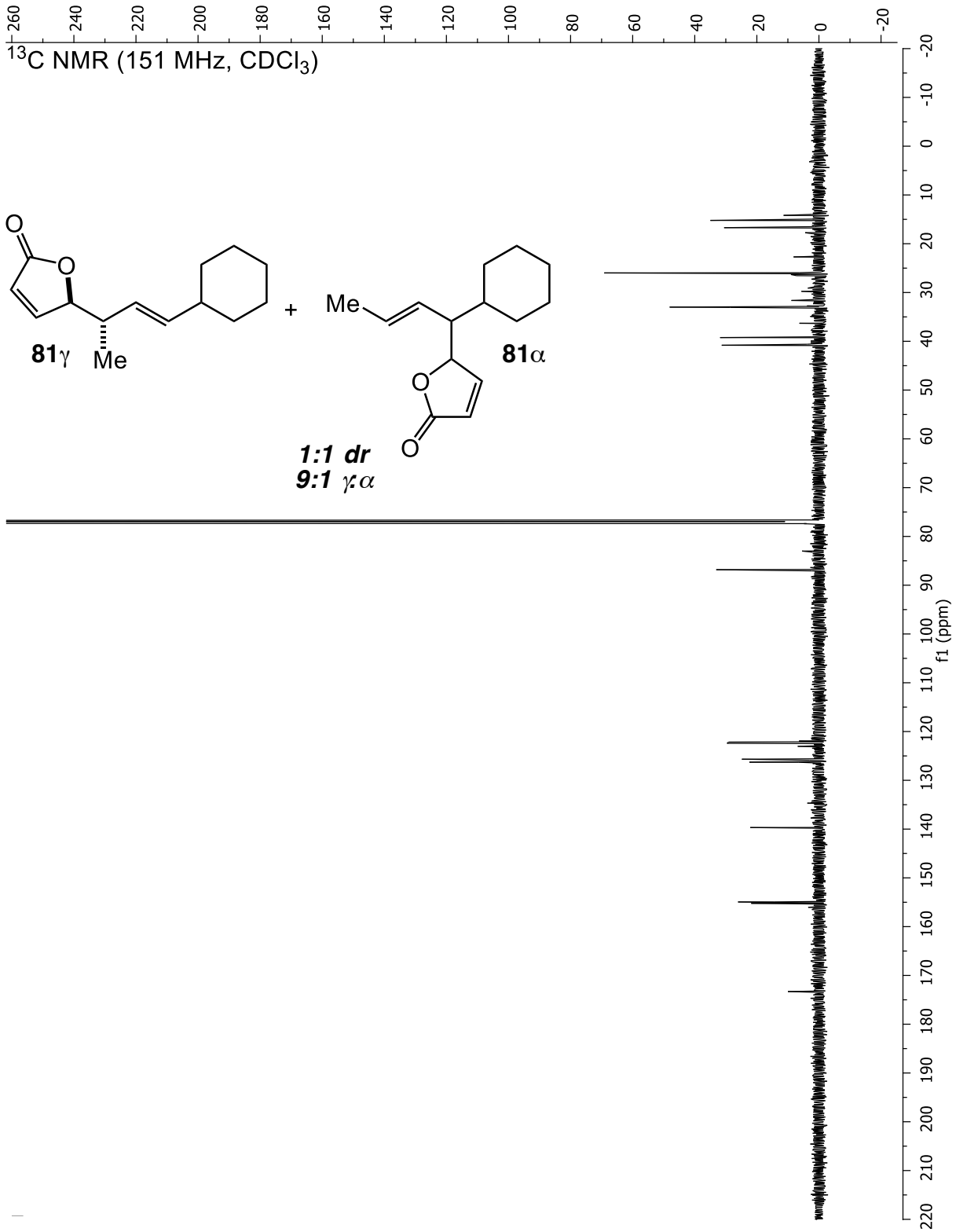
>20:1 γ:α
f1 (ppm)


1H NMR (600 MHz, CDCl3)
80γ
Me
+
Me
80α
5:1 dr
8:1 γ:α
1.000
0.184
0.078
0.045
f1 (ppm)


13C NMR (151 MHz, CDCl3)
80γ
Me
+
Me
80α
5:1 dr
8:1 γ:α
f1 (ppm)

^{1}H NMR (600 MHz, $CDCl_3$)

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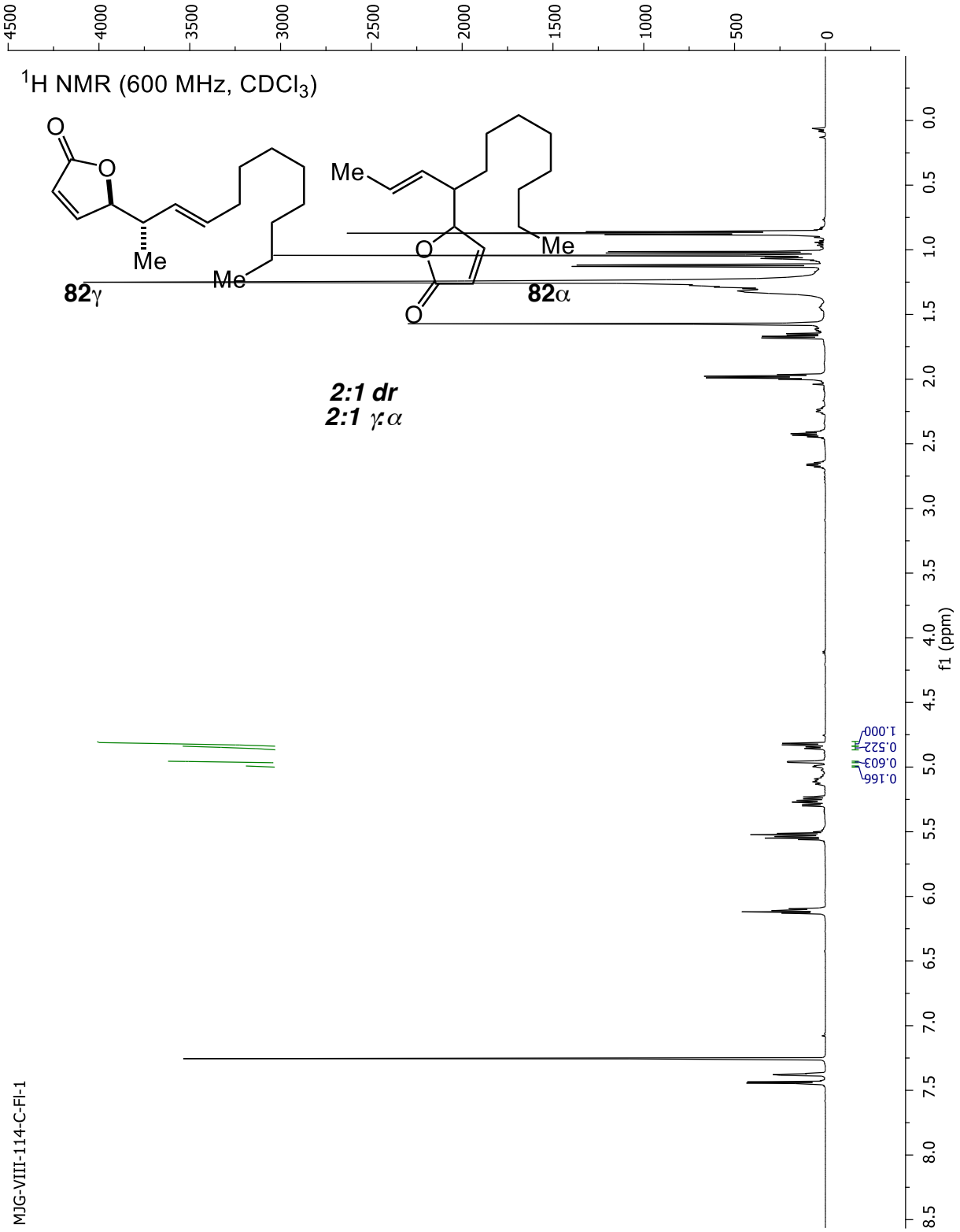
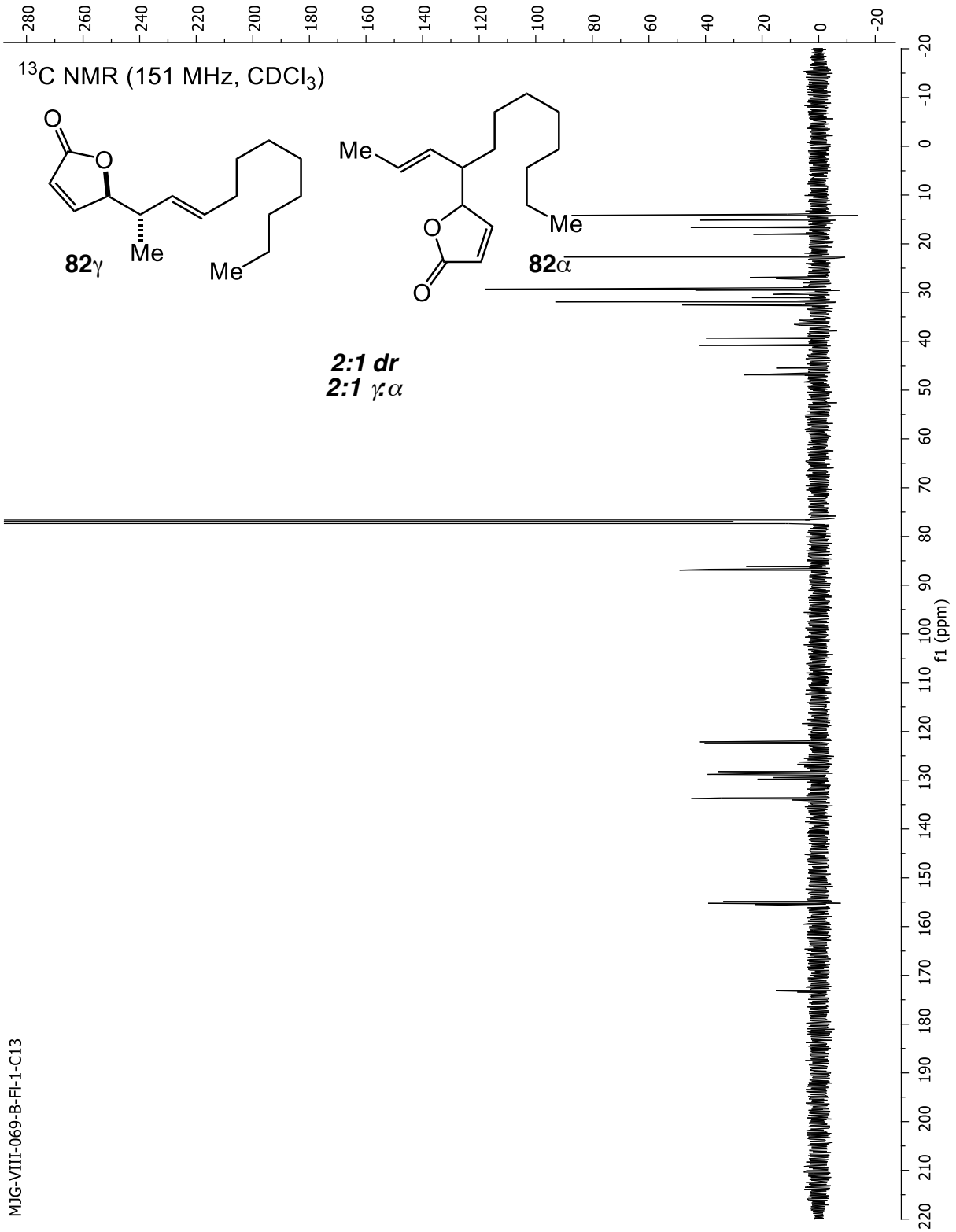
81γ
Me
+
Me
81α
1:1 dr
9:1 γ:α
f1 (ppm)


1H NMR (600 MHz, CDCl3)
82γ
82α
2:1 dr
2:1 γ:α
MJG-VIII-114-C-FI-1
f1 (ppm)
0.166
0.603
0.522
1.000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82γ
82α
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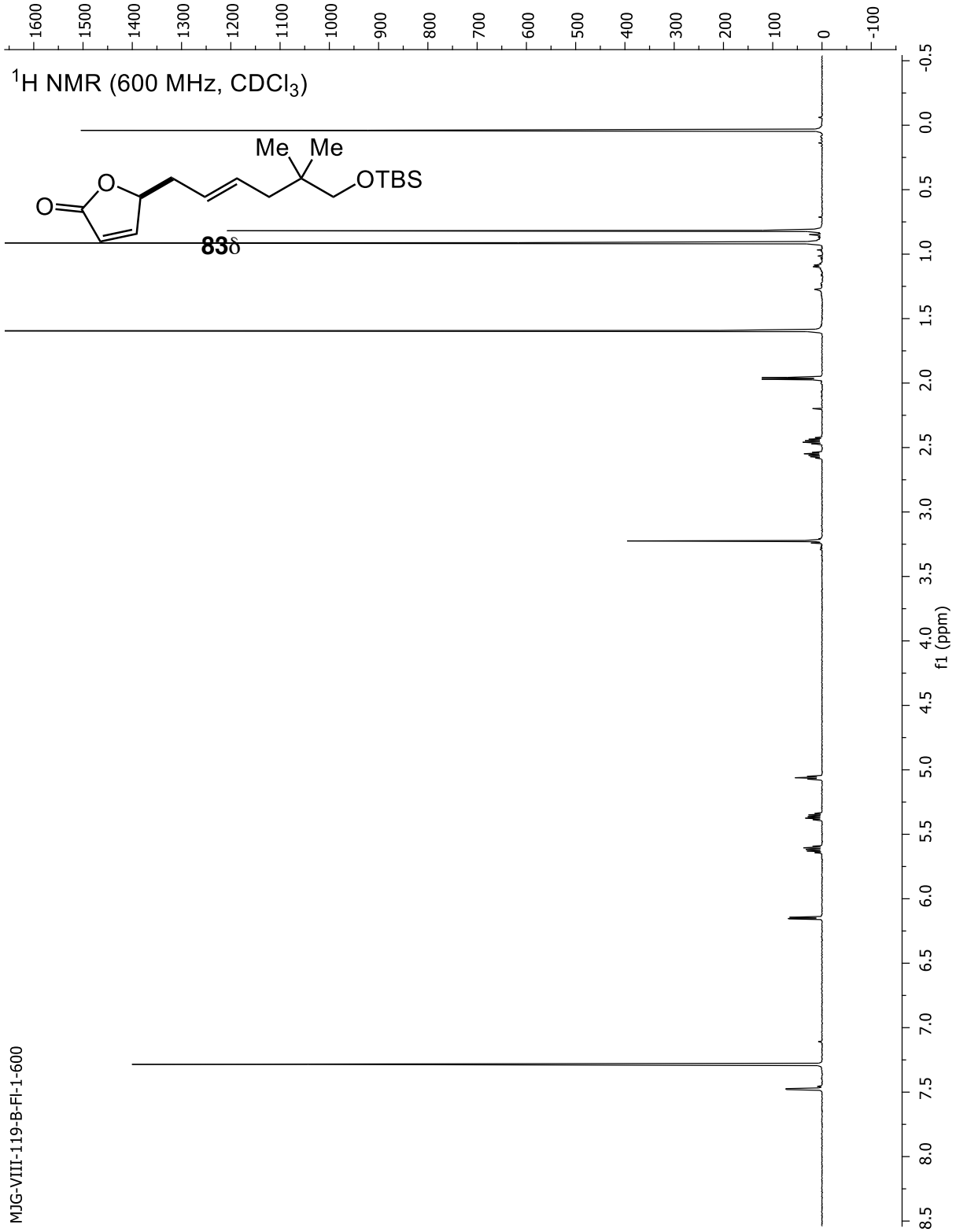
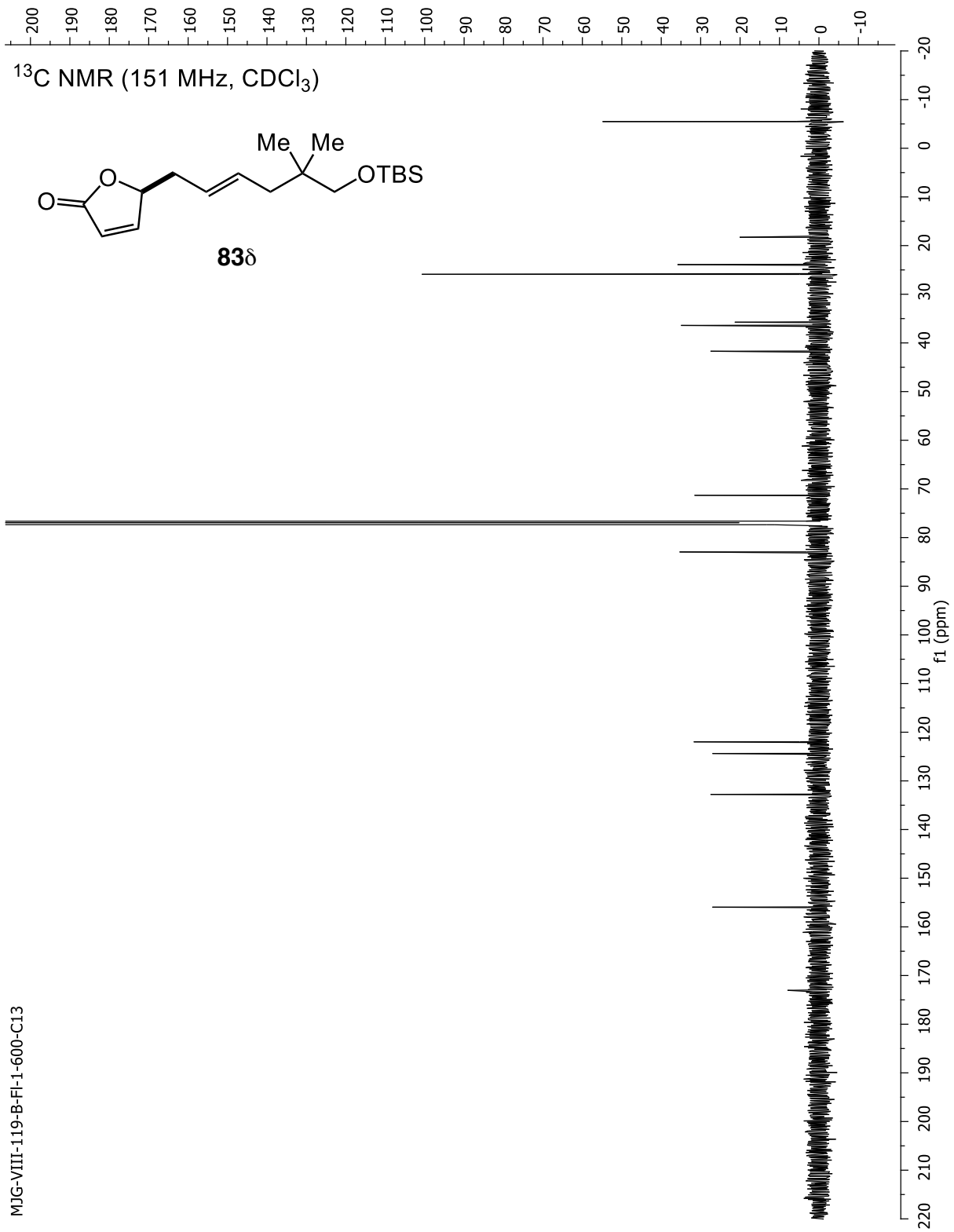
2:1 γ:α
f1 (ppm)
MJG-VIII-069-B-FI-1-C13


1H NMR (600 MHz, CDCl3)
Me Me
OTBS
O
O
83δ
MJG-VIII-119-B-FI-1-600
f1 (ppm)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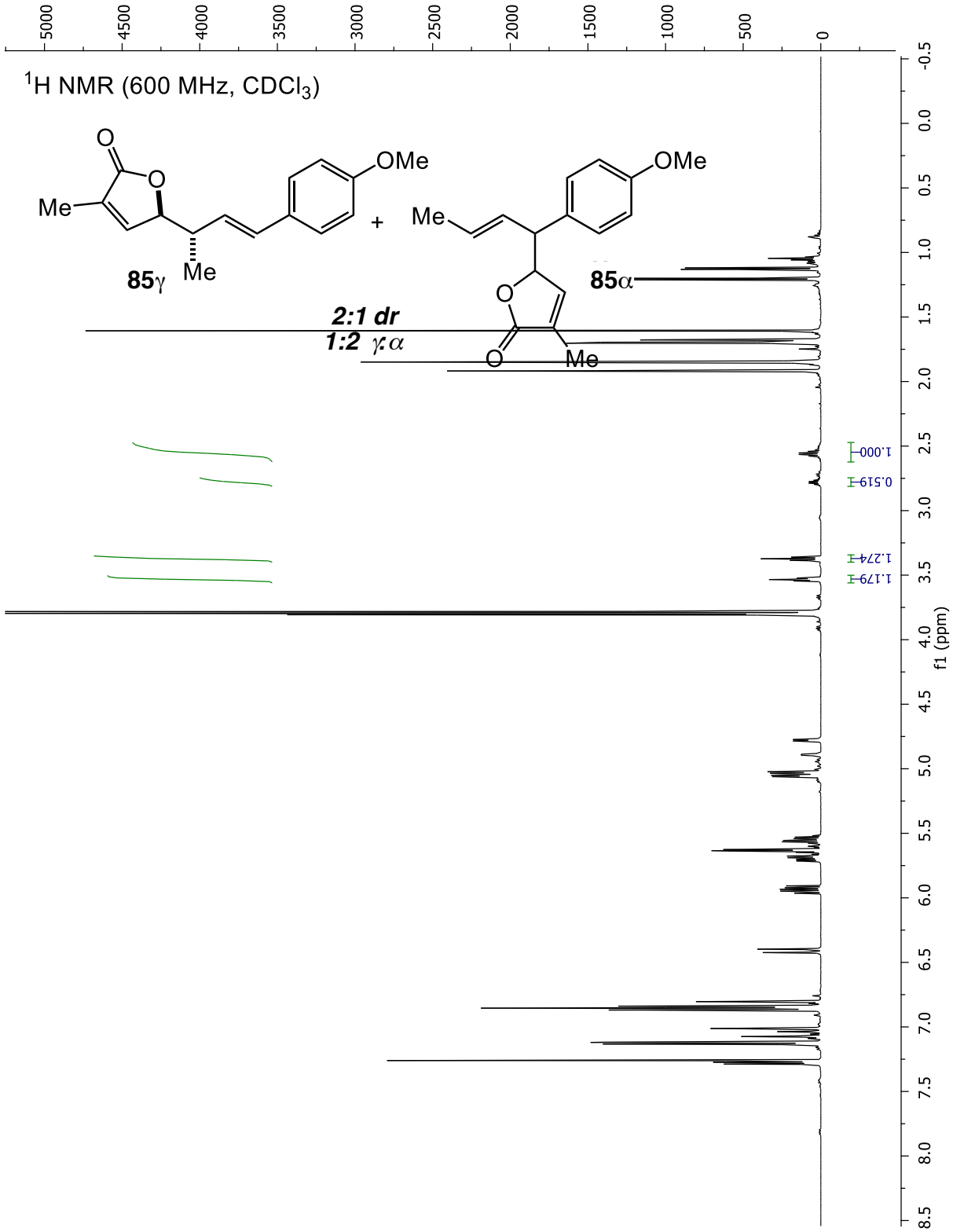
Me
Me
OTBS
O
O
83δ
MJG-VIII-119-B-Fl-1-600-C13
f1 (ppm)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85γ
85α
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1:2 γ:α
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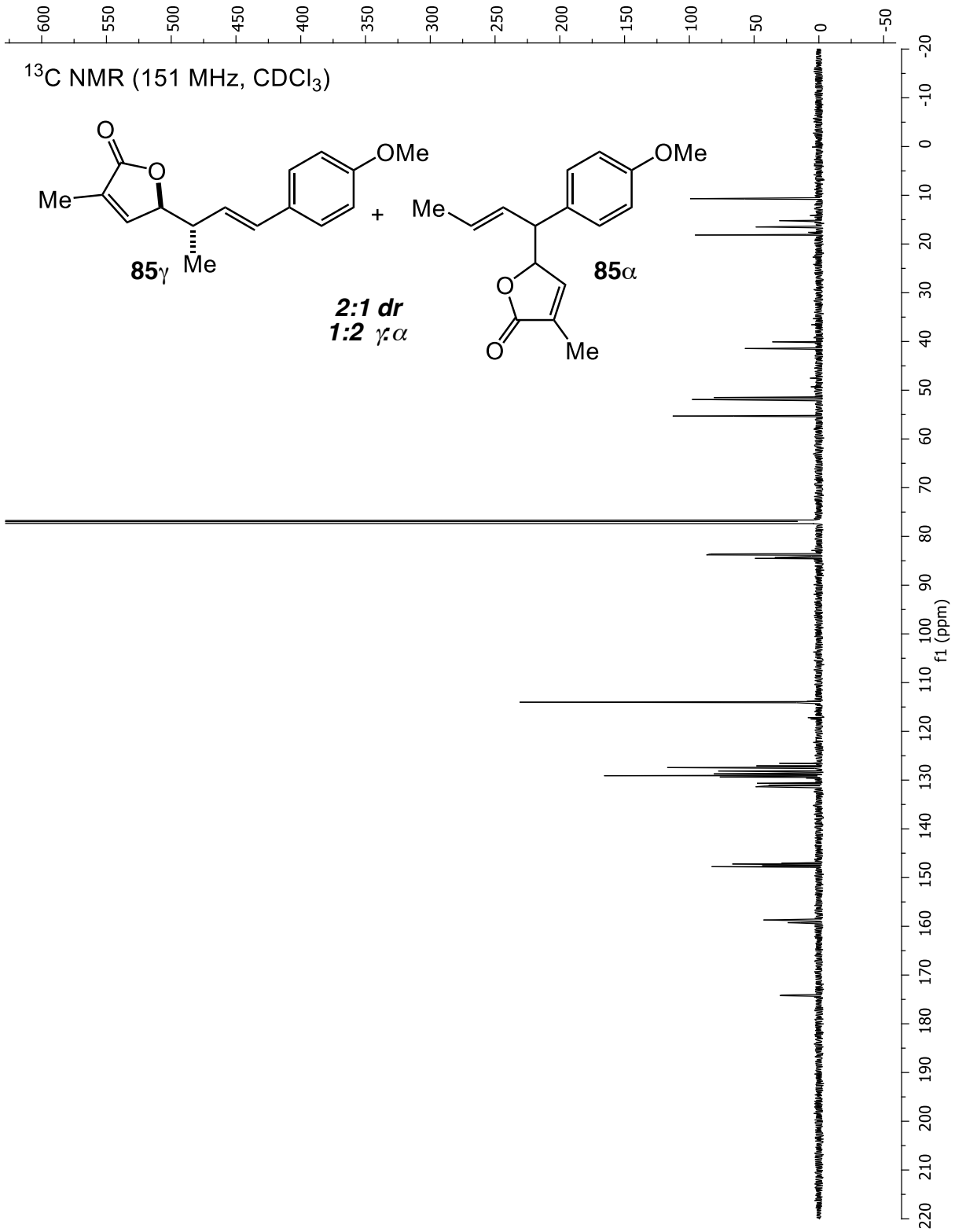
0.519
1.274
1.179
f1 (ppm)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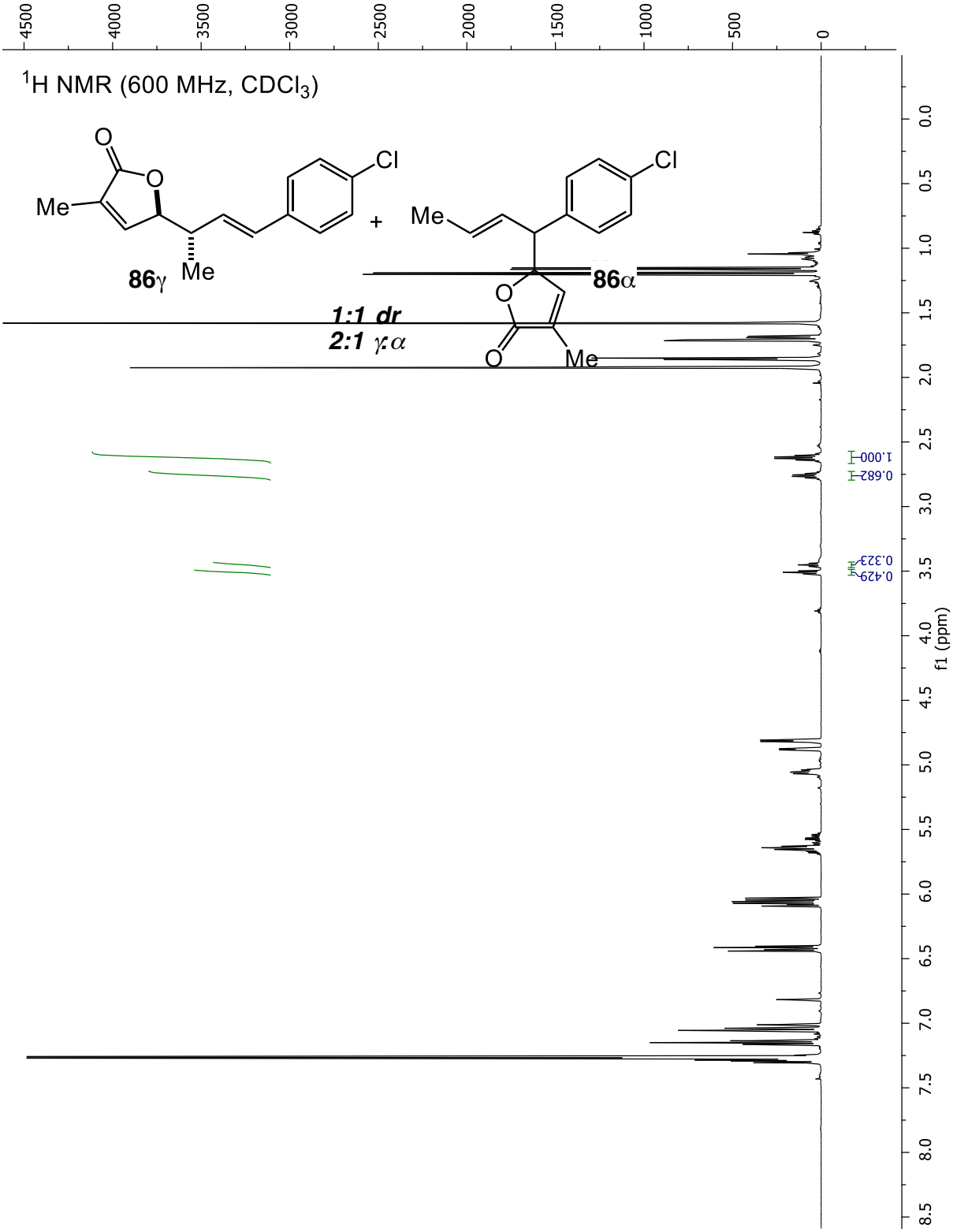
85γ
85α
2:1 dr
1:2 γ:α
f1 (ppm)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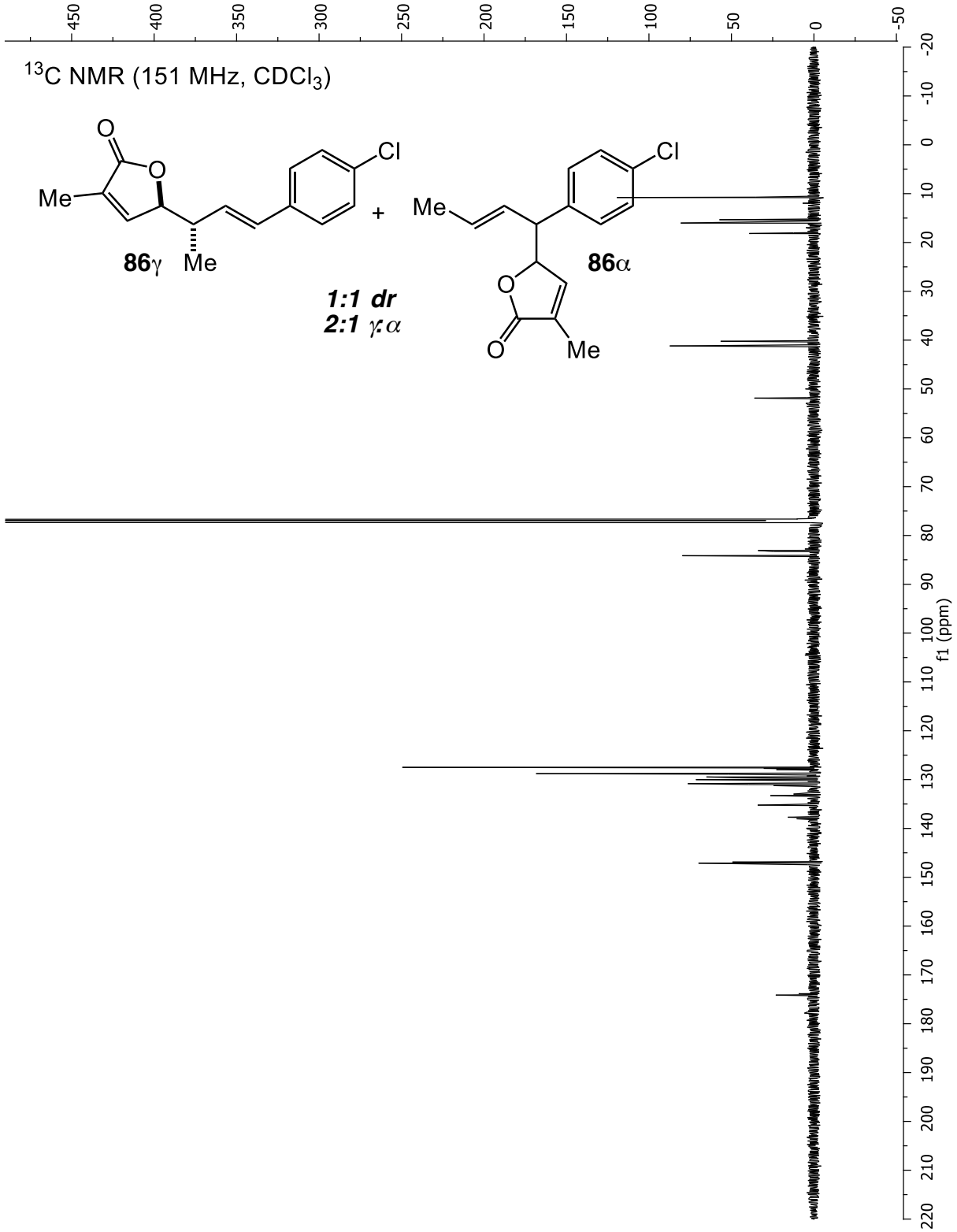
86γ
86α
1:1 dr
2:1 γ:α
1.000
0.682
0.429
0.323
f1 (ppm)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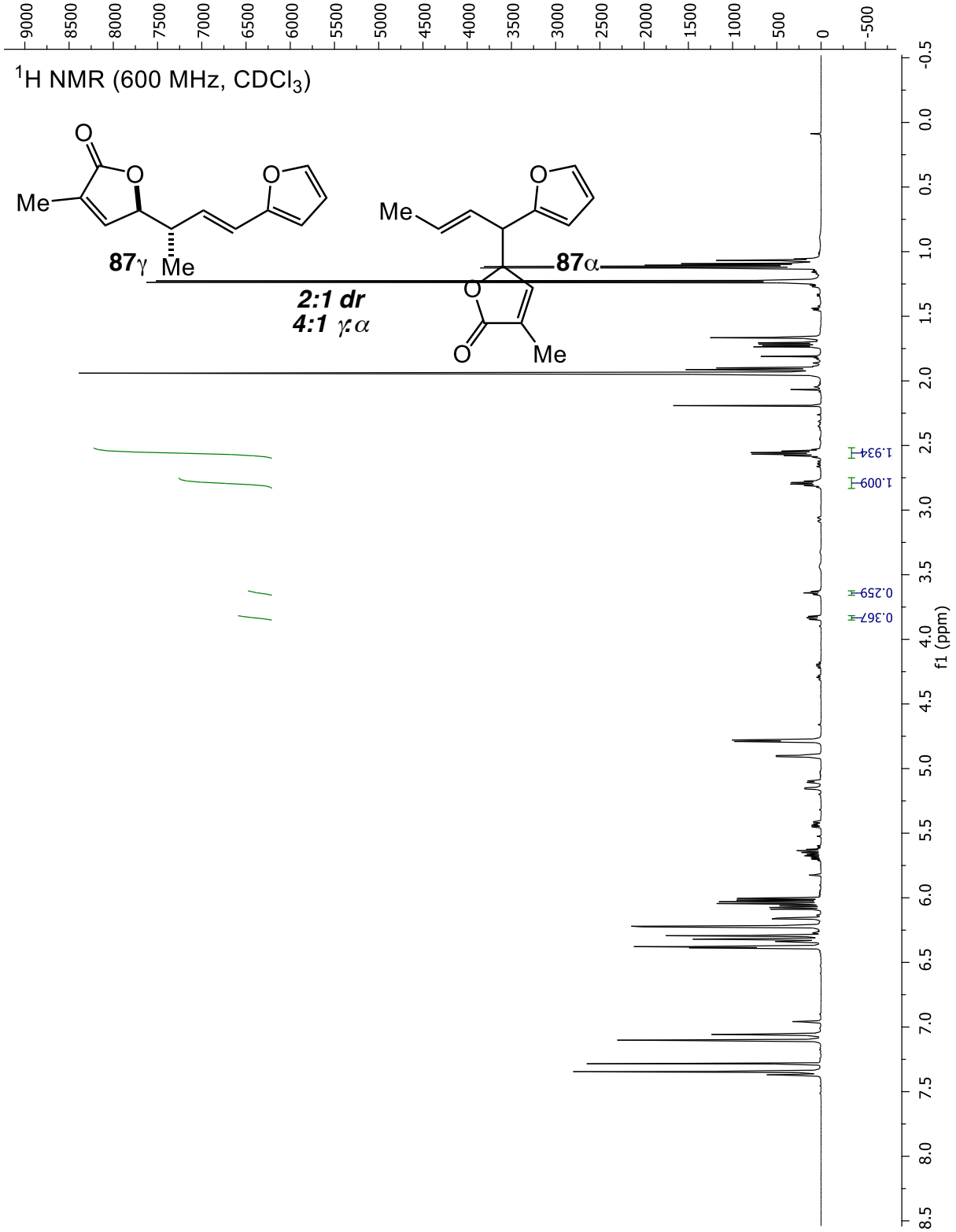
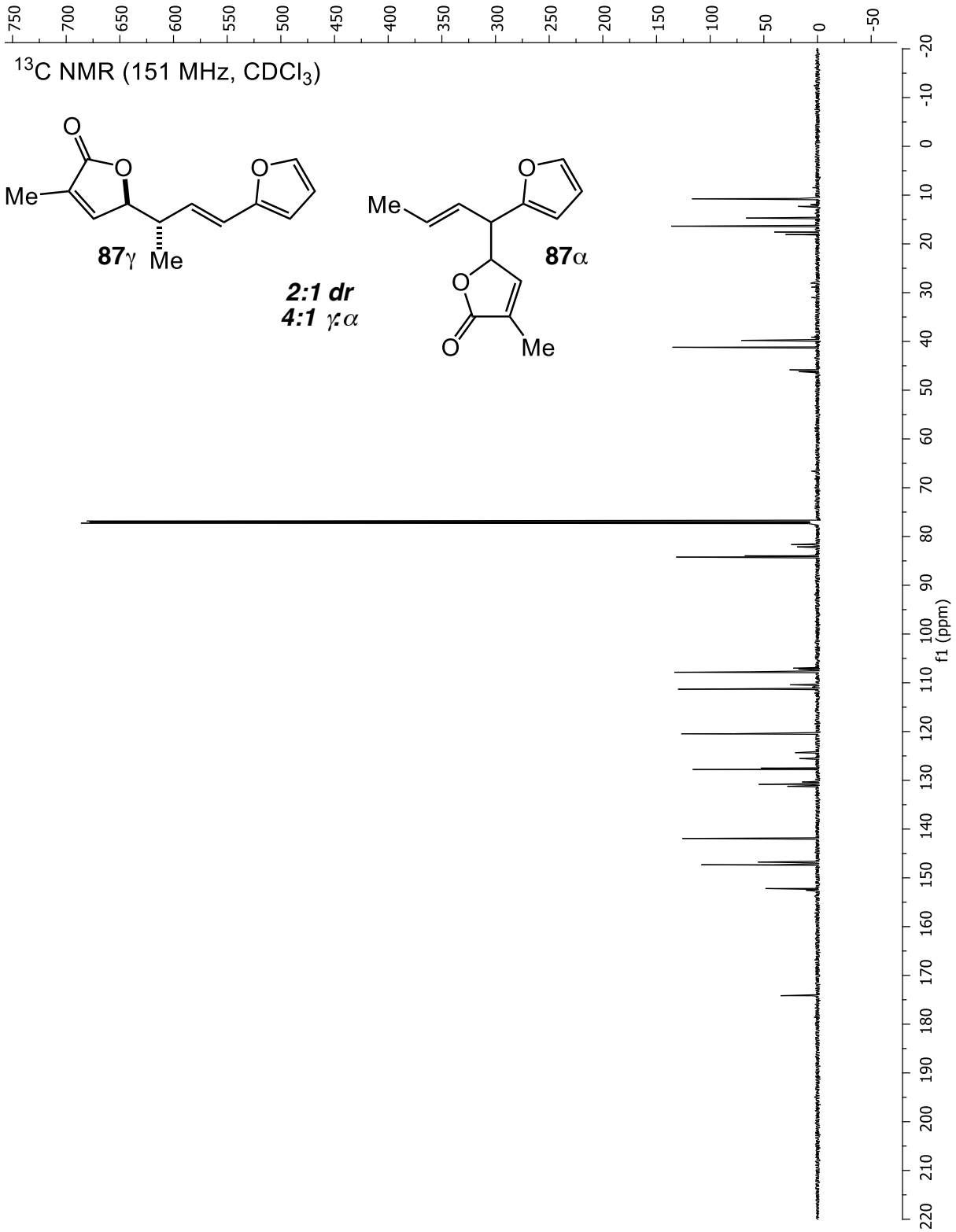
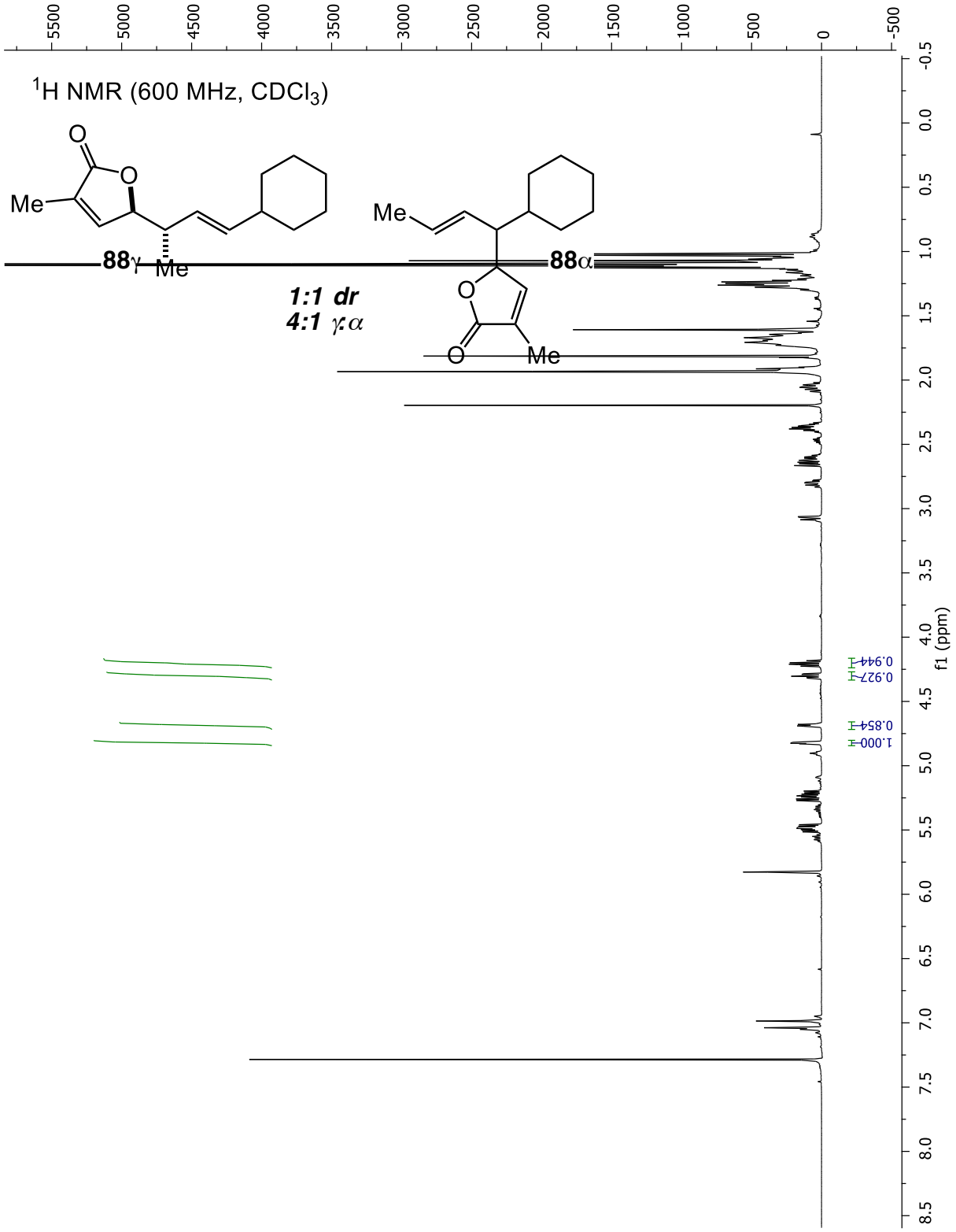
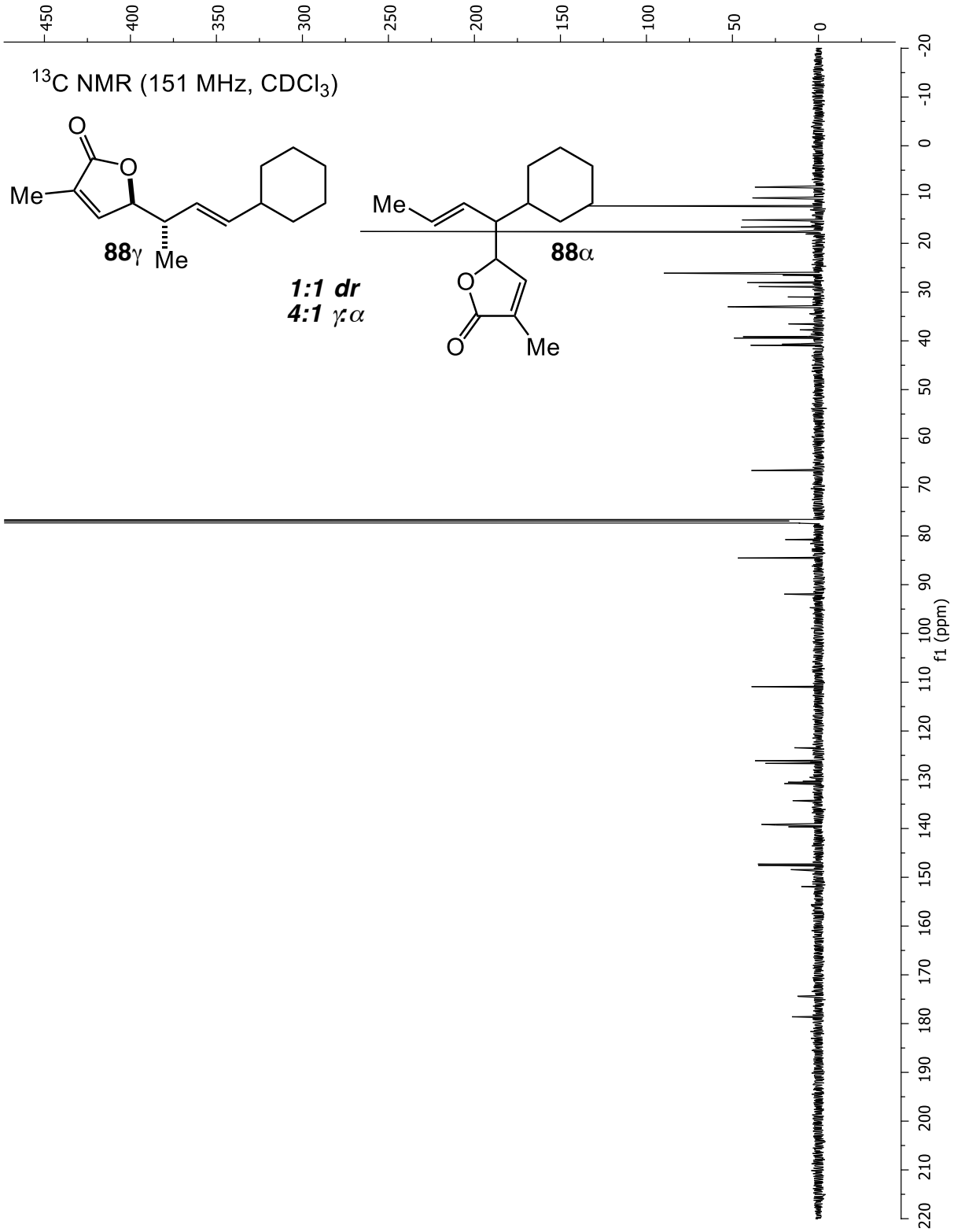
86γ
86α
1:1 dr
2:1 γ:α
f1 (ppm)


1H NMR (600 MHz, CDCl3)
87γ
87α
2:1 dr
4:1 γ:α
Me
O
f1 (ppm)
1.934
1.009
0.259
0.367


^{13}C NMR (151 MHz, $CDCl_3$)
87γ
87α
2:1 dr
4:1 γ:α
f1 (ppm)


1H NMR (600 MHz, CDCl3)
88γ
88α
1:1 dr
4:1 γ:α
Me
O
f1 (ppm)
1.000
0.854
0.927
0.944


13C NMR (151 MHz, CDCl3)
88γ
88α
1:1 dr
4:1 γ:α
f1 (ppm)

APPENDIX 5: SUPPORTING INFORMATION FOR CHAPTER 5

Section 5.2: Enantiocontrol with Chiral Additives

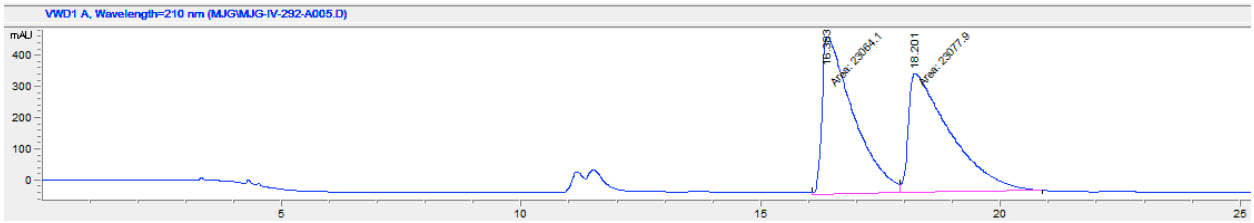
■ **General Procedure for Enantioselective Intermolecular Hydroarylation with 1,3-Pentanedione and 1-Methylindole Using Chiral Additives (Table 5.2.1-1, 5.2.2-1, and 5.2.3-1)**

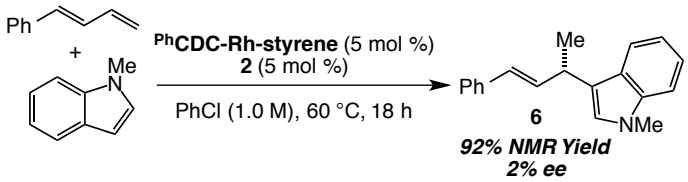
In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the **^{Ph}CDC-Rh-styrene** complex (4.1 mg, 0.0025 mmol, 5 mol%), the appropriate amount of the listed lewis acid and/or chiral additive, and 1,3-phenylbutadiene (6.5 mg, 0.05 mmol). The reagents were solvated with the listed solvent (50 μL, [ ] = 1.0 M) and the reaction was sealed with a Teflon® lined septum cap before being allowed to stir at room temperature for 1 hour. 1-methylindole (6.6 mg, 0.05 mmol) was added to the reaction and the vial sealed with black electrical tape before being removed from the glovebox. The reaction was heated to 60 °C and allowed to stir for 18 hours before being allowed to cool to room temperature and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solvent evaporated before the products were purified by SiO_2 column chromatography. A pure sample was then assayed on an Agilent 1220 LC System with a Daicel ChiralPak IA column (100% Hexanes, 1 mL/min, 210 nm).

^{1}H NMR (600 MHz, $CHCl_3$-*d*) δ 7.67 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.33 – 7.26 (m, 4H), 7.22 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.09 (ddd, *J* = 7.9, 6.9, 1.1 Hz, 1H), 6.88 (d, *J* = 0.8 Hz, 1H), 6.56 – 6.43 (m, 2H), 3.94 (m, 1H), 3.77 (s, 3H), 1.56 (d, *J* = 7.0 Hz, 4H). **^{13}C NMR** (151 MHz, $CHCl_3$-*d*) δ 137.95, 137.39, 135.72, 128.58, 128.15, 127.30, 126.99, 126.27, 125.43, 121.67, 119.82, 119.03, 118.81, 109.34, 34.35, 32.79, 20.99. IR (ν/cm^{-1}):

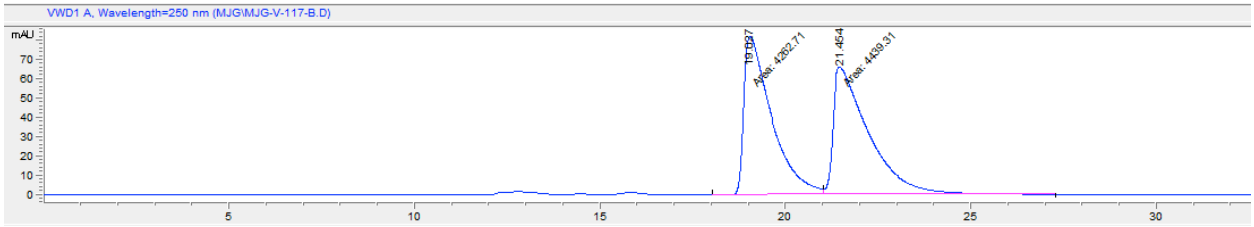
2925 (m), 2870 (s), 1472 (m), 1374 (w), 1328 (w), 1134 (s). MS (ES$^+$) $[M+H]^+$ calcd for $C_{19}H_{20}N^+$ 262.16, found: 262.00.

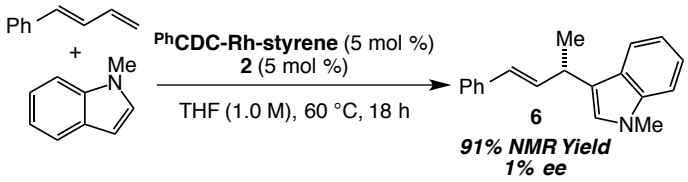
Racemic Trace:



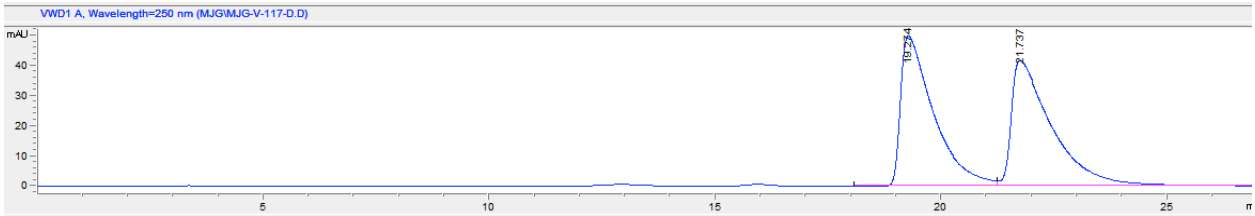


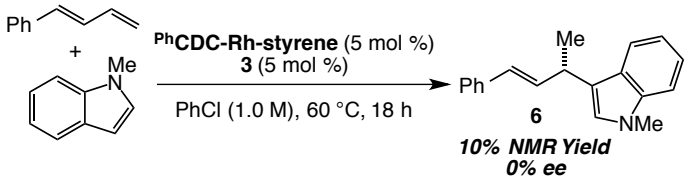
Chiral Trace:





Chiral Trace:





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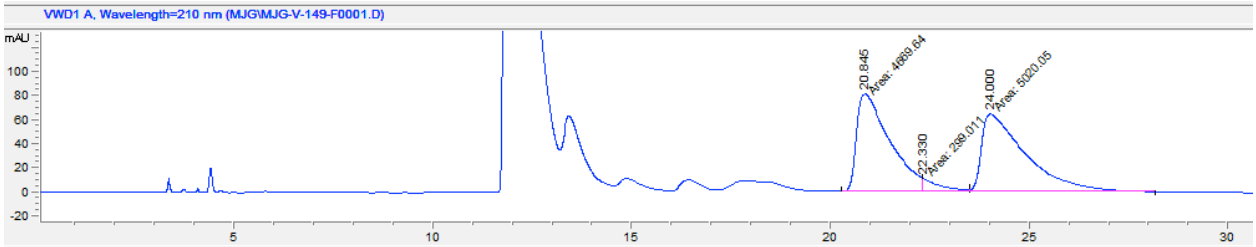

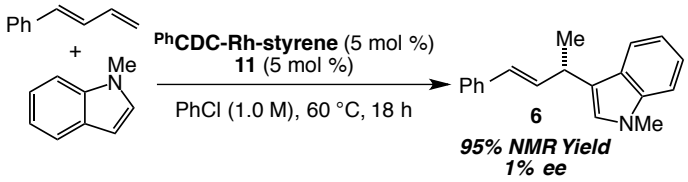

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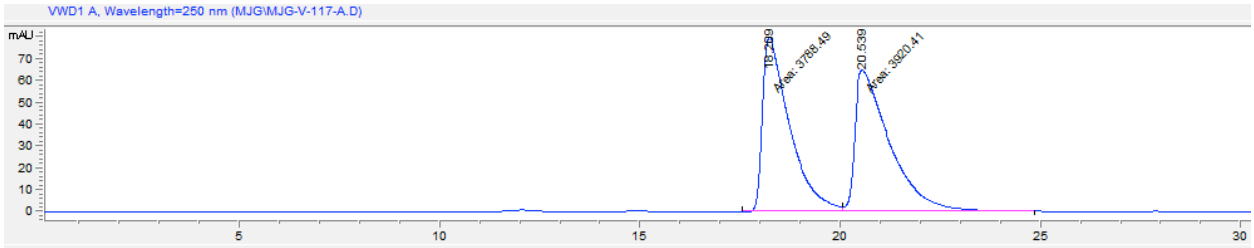

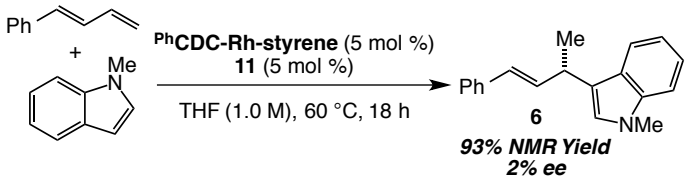

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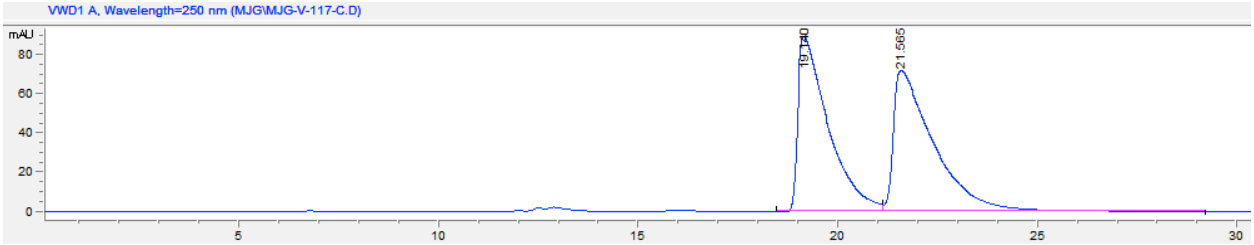
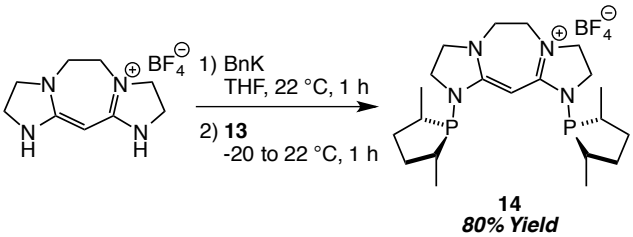


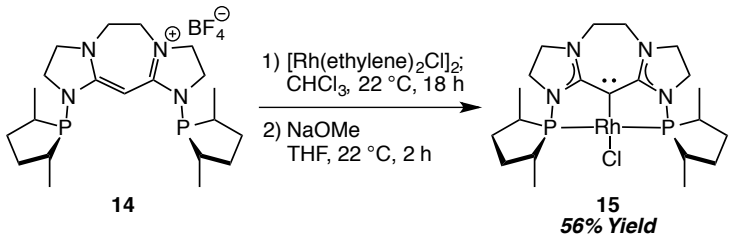
Section 5.3: Enantioselective Hydrofunctionalization Controlled by P-Stereogenic Carbodicarbene Ligands



Synthesis of 14

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (10 mg, 0.0376 mmol), and benzyl potassium (9.8 mg, 0.0752 mmol). The reagents were solvated with THF (1 mL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at room temperature for 1 hour. To the resulting white suspension was added (2*R*,5*R*)-1-chloro-2,5-dimethylphospholane (17 mg, 0.113 mmol) at -20 °C and the reaction allowed to stir a 22 °C for 1 h. The reaction was triturated with excess hexanes to generate a precipitate which was isolated by washing with hexanes and pipetting off the solvent. The precipitate was characterized by NMR spectroscopy, recovered, and dried to yield **14** (14.9 mg, 0.0301 mmol, 80% yield) as an impure mixture of the bis- and mono-phosphine (5:1), which was used without further purification.

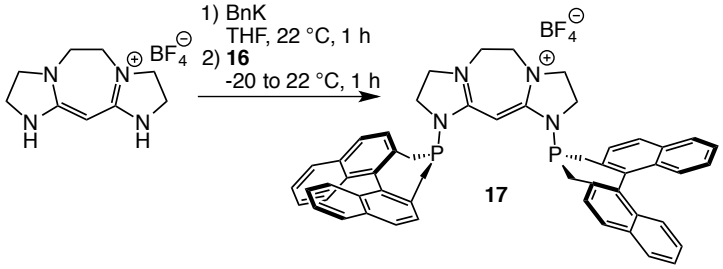
^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.84 (t, *J* = 7.5 Hz, 1H), 3.91 – 3.70 (m, 8H), 3.69 – 3.43 (m, 4H), 2.59 – 2.43 (m, 2H), 2.38 – 2.20 (m, 2H), 2.21 – 1.90 (m, 4H), 1.61 – 1.44 (m, 2H), 1.33 (dd, *J* = 20.3, 7.3 Hz, 6H), 1.30 – 1.17 (m, 2H), 1.17 (dd, *J* = 11.2, 7.1 Hz, 6H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 69.53.



Synthesis of 15

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **14** (22.8 mg, 0.0461 mmol), and $[Rh(ethylene)Cl]_2$ (9.0 mg, 0.0231 mmol). The reagents were solvated with $CDCl_3$ (600 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at 22 °C for 18 hours. The soluble material was transferred to a second vial and the remaining solid rinsed with excess $CHCl_3$ and also transferred. The solution was concentrated and sodium methoxide (2.5 mg, 0.0461 mmol) added before the solids were resolvated in THF (600 μL) and allowed to stir at 22 °C for 2 hours. The reaction precipitated a dark red/brown solid, which was isolated by filtration through a celite® plug using excess THF to rinse the solid. The product was then reisolated by dissolving off the plug with DCM and the resulting solution concentrated to yield **15** (14.2 mg, 0.0258 mmol, 56% yield) as a brown powder.

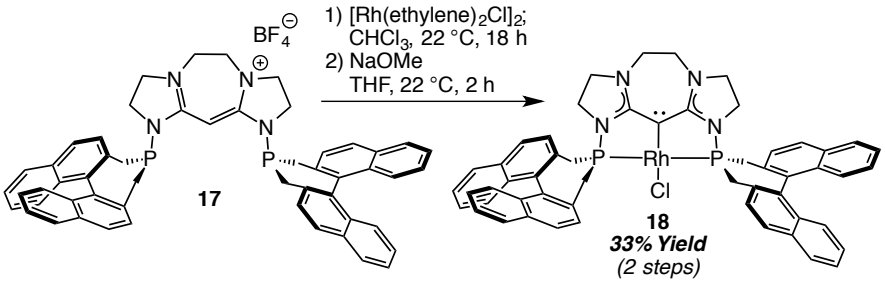
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.06 – 3.87 (m, 4H), 3.79 (dd, *J* = 19.7, 10.7 Hz, 2H), 3.66 – 3.33 (m, 6H), 3.20 (bd, *J* = 7.7 Hz, 2H), 2.80 (bs, 2H), 2.38 – 2.23 (m, 2H), 2.15 (dd, *J* = 13.6, 6.4 Hz, 2H), 1.76 (dt, *J* = 16.7, 7.6 Hz, 6H), 1.67 – 1.45 (m, 4H), 1.48 – 1.34 (m, 6H). **^{31}P NMR** (202 MHz, $CDCl_3$) δ ^{31}P NMR (202 MHz, $CDCl_3$) δ 104.13 (d, *J* = 103.8 Hz).



Synthesis of 17

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with 1,2,3,5,6,8,9,10-octahydrodiimidazo[1,2-d:2',1'-g][1,4]diazepin-4-ium tetrafluoroborate (4.0 mg, 0.0150 mmol), and benzyl potassium (4.9 mg, 0.0376 mmol). The reagents were solvated with THF (200 μL) and the reaction sealed with a Teflon® lined cap before being allowed to stir at room temperature for 1 hour. To the resulting white suspension was added (11b*R*)-4-chloro-4,5-dihydro-3*H*-dinaphtho[2,1-*c*:1',2'-*e*]phosphepine (13.0 mg, 0.0376 mmol) at -20 °C and the reaction allowed to stand for 10 minutes before being triturated with hexanes. The solvent was pipeted off and the solid resolvated with $CHCl_3$, triturated again with hexanes and the solvent removed by pipet. The remaining solid was dried in vaccuo and characterized by NMR spectroscopy. The NMR sample was recovered and dried to yield **17** as an impure mixture of the bis- and mono-phosphine (2.5:1), which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ Diagnostic peak for **17:** 5.71 (t, *J* = 7.1 Hz, 1H); Diagnostic peak for mono-phosphorylated: 5.29 (d, *J* = 6.0 Hz, 1H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ Diagnostic peak for **17**: 51.69; Diagnostic peak for 50.06.

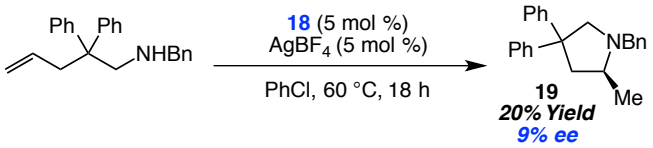


Synthesis of 18

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **17** (19.0 mg, 0.0214 mmol), and $[Rh(ethylene)Cl]_2$ (4.2 mg, 0.0107 mmol). The reagents were solvated with $CDCl_3$ (400 μL) at -20 °C and the reaction allowed to stand for 1 h at 22 °C sealed with a Teflon® lined cap. The solution was concentrated and sodium methoxide (1.2 mg, 0.0214 mmol) added before the solids were resolvated in THF (400 μL) and allowed to stir at 22 °C for 1 hour. The solution concentrated to yield **18** (6.6 mg, 0.00706 mmol, 33% yield) as a brown powder.

^{1}H NMR (400 MHz, $CDCl_3$) δ Diagnostic peak for hydride in **18**: -19.29 (dt, J = 28.9, 14.4 Hz, 1H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 100.60 (dd, J = 566.6, 117.8 Hz).

■ General Procedure for Surveying Enantioselectivity with CDC-Rh(I) Catalyst 18 (Scheme 5.3.2-1)



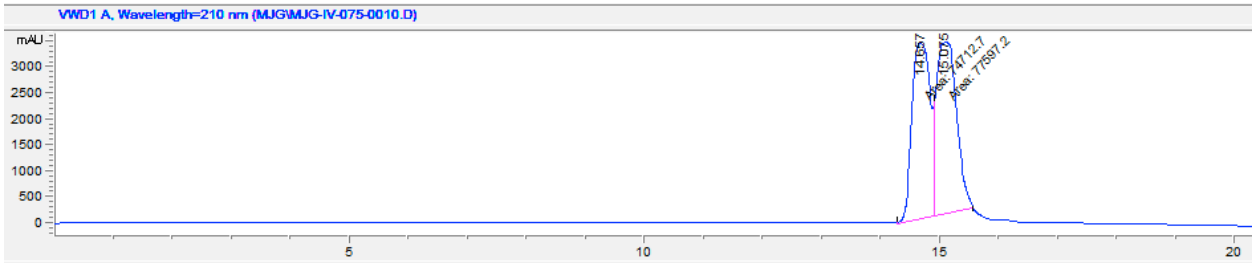
Synthesis of 19 Catalyzed by CDC-Rh(I) Complex 18

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **18** (4.7 mg, 0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) before being solvated with chlorobenzene (100 μL, [ ] = 1.0 M). The brown heterogeneous solution was allowed to stir at room temperature for 1 hour before *N*-benzyl-2,2-diphenylpent-4-en-1-amine (32.7 mg, 0.1 mmol) was added. The

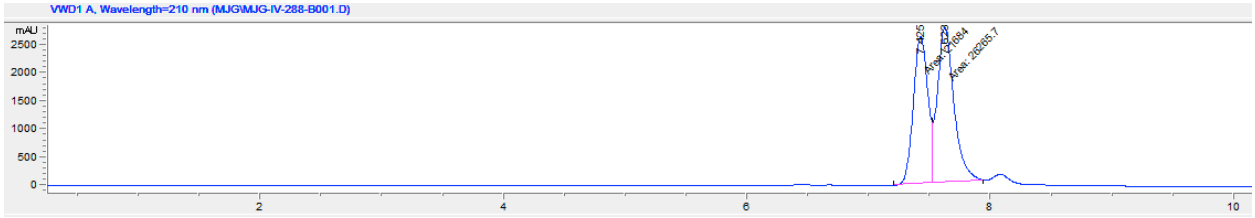
reaction was sealed with a Teflon® lined lid, taped with electrical tape and removed from the glove box before being heated to 60 °C for 18 h. The reaction was cooled and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (50:1 Hexanes/Et_2O) to afford **19** (6.5 mg, 0.02 mmol, 20% yield) as a colorless oil. A pure sample was assayed on an Agilent 1220 LC System with a Daicel ChiralPak IA column (99:1 Hexanes/Isopropanol, 0.5 mL/min, 210 nm) to find that the product was formed in 9% ee.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.33 (dd, *J* = 17.8, 10.8 Hz, 2H), 7.30 – 7.23 (m, 5H), 7.23 – 7.15 (m, 5H), 7.11 (dd, *J* = 19.2, 12.1 Hz, 1H), 4.10 (d, *J* = 13.2 Hz, 1H), 3.65 (d, *J* = 9.9 Hz, 1H), 3.27 (d, *J* = 13.2 Hz, 1H), 2.93 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.89 – 2.82 (m, 1H), 2.80 (d, *J* = 9.9 Hz, 1H), 2.22 (dd, *J* = 12.6, 8.0 Hz, 1H), 1.18 (d, *J* = 5.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.67, 148.76, 140.12, 128.62, 128.23, 128.15, 127.84, 127.46, 127.27, 126.79, 125.81, 125.42, 66.46, 59.68, 58.03, 52.54, 48.02, 19.54.

Racemic Trace:



Chiral Trace:

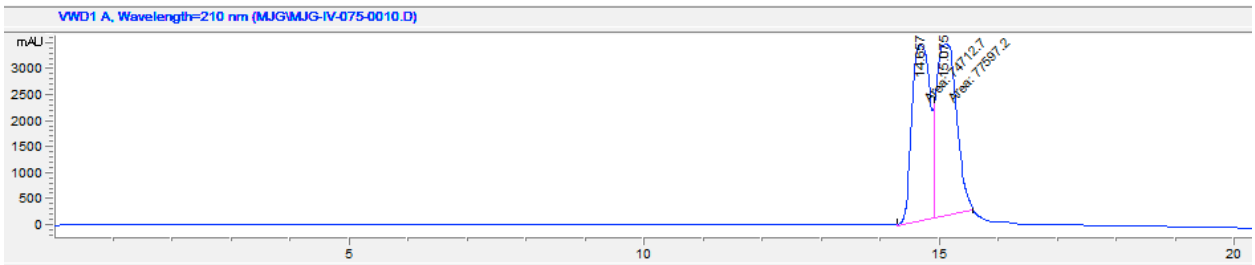


■ **General Procedure for Surveying Enantioselectivity with CDC-Rh(I) Catalyst 15 (Scheme 5.3.2-2)**

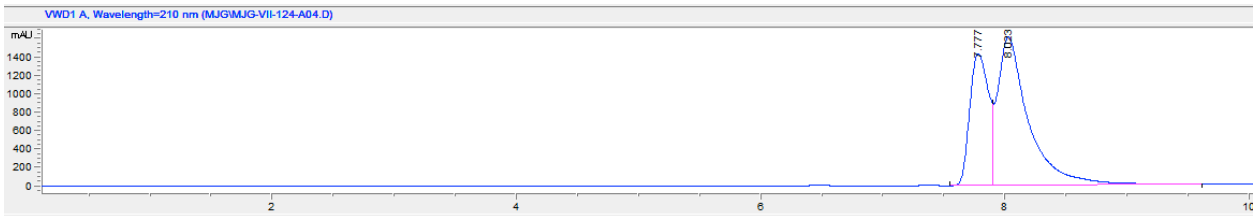
Synthesis of 19 Catalyzed by CDC-Rh(I) Complex 15

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **15** (4.7 mg, 0.00863 mmol, 5 mol%) and $AgBF_4$ (1.7 mg, 0.00863 mmol, 5 mol%) before being solvated with chlorobenzene (350 μL, [ ] = 0.5 M). The brown heterogeneous solution was allowed to stir at room temperature for 1 hour before *N*-benzyl-2,2-diphenylpent-4-en-1-amine (32.7 mg, 0.1 mmol) was added. The reaction was sealed with a Teflon® lined lid, taped with electrical tape and removed from the glove box before being heated to 60 °C for 48 h. The reaction was cooled and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (50:1 Hexanes/Et_2O) to afford **19** (32.1 mg, 0.098 mmol, 98% yield) as a colorless oil. A pure sample was assayed on an Agilent 1220 LC System with a Daicel ChiralPak IA column (99:1 Hexanes/Isopropanol, 0.5 mL/min, 210 nm) to find that the product was formed in 30% ee.

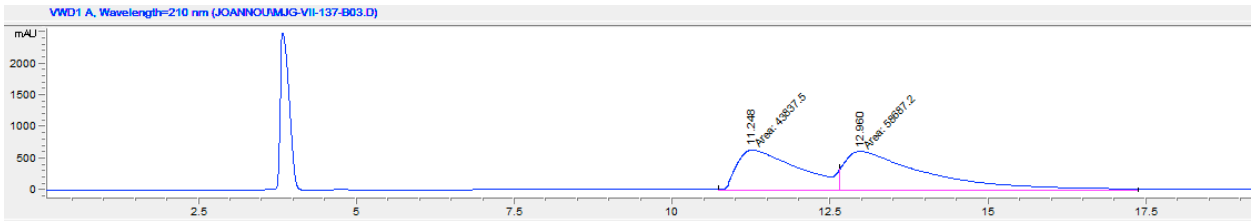
Racemic Trace:

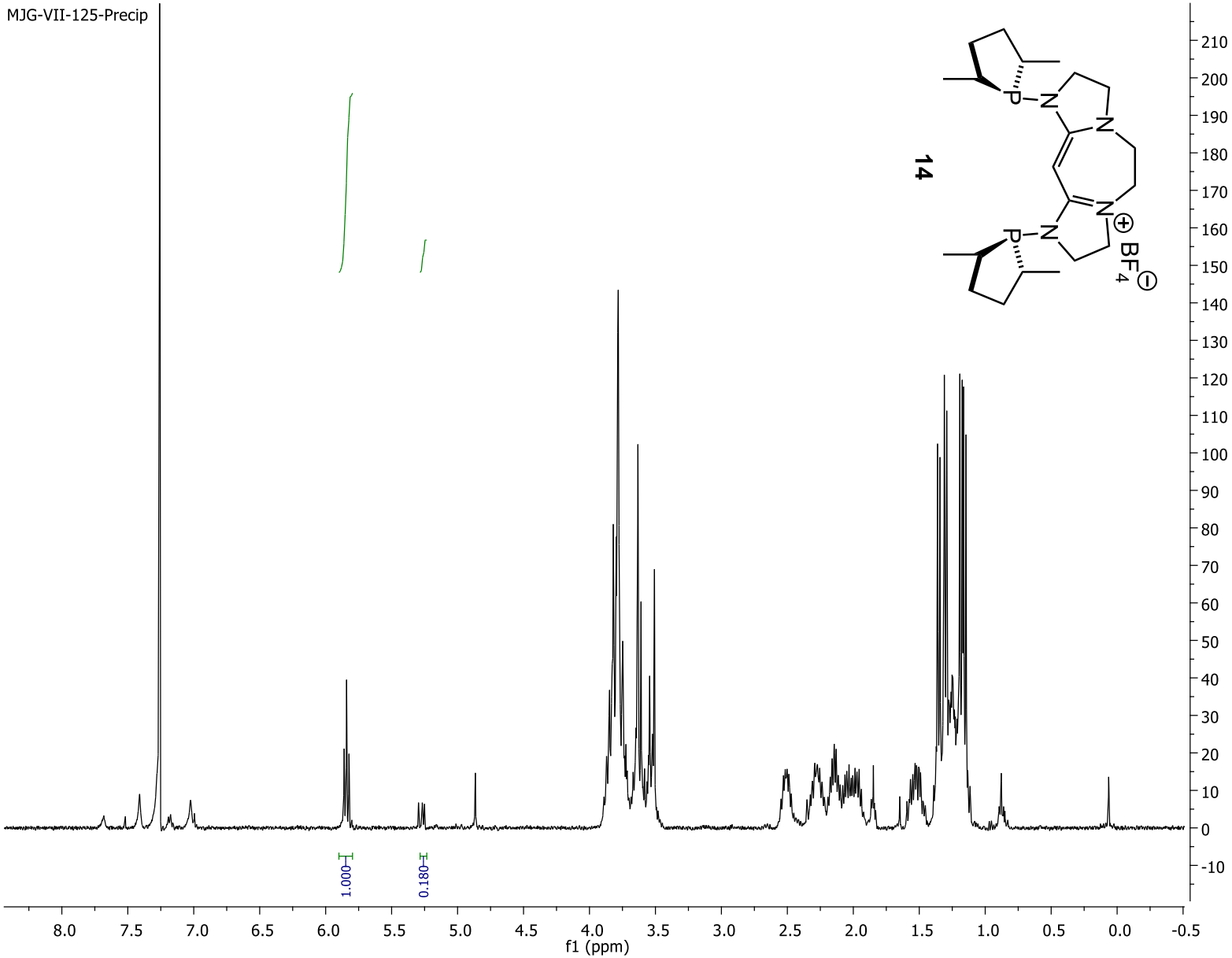


Chiral Trace:



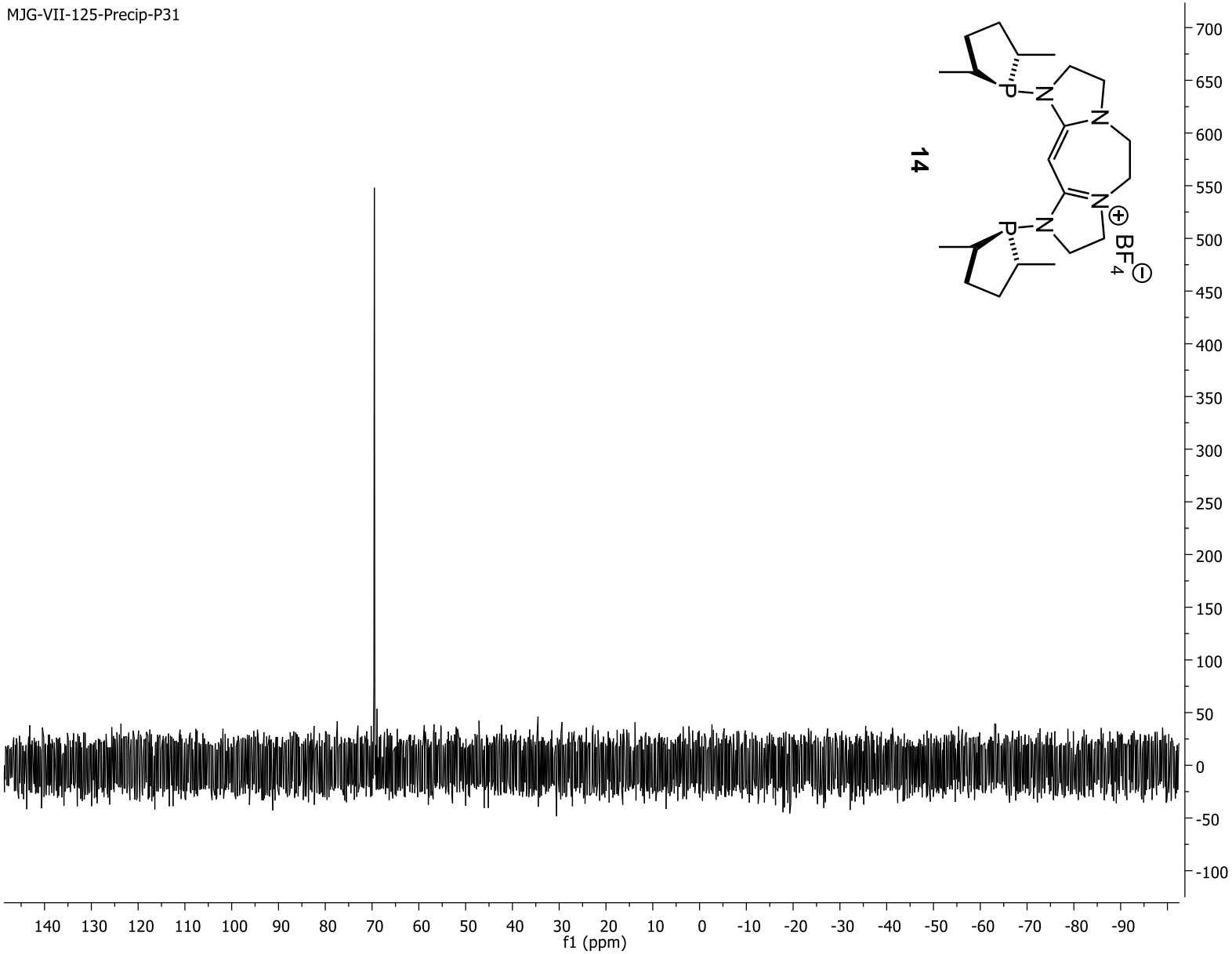
Chiral Trace:

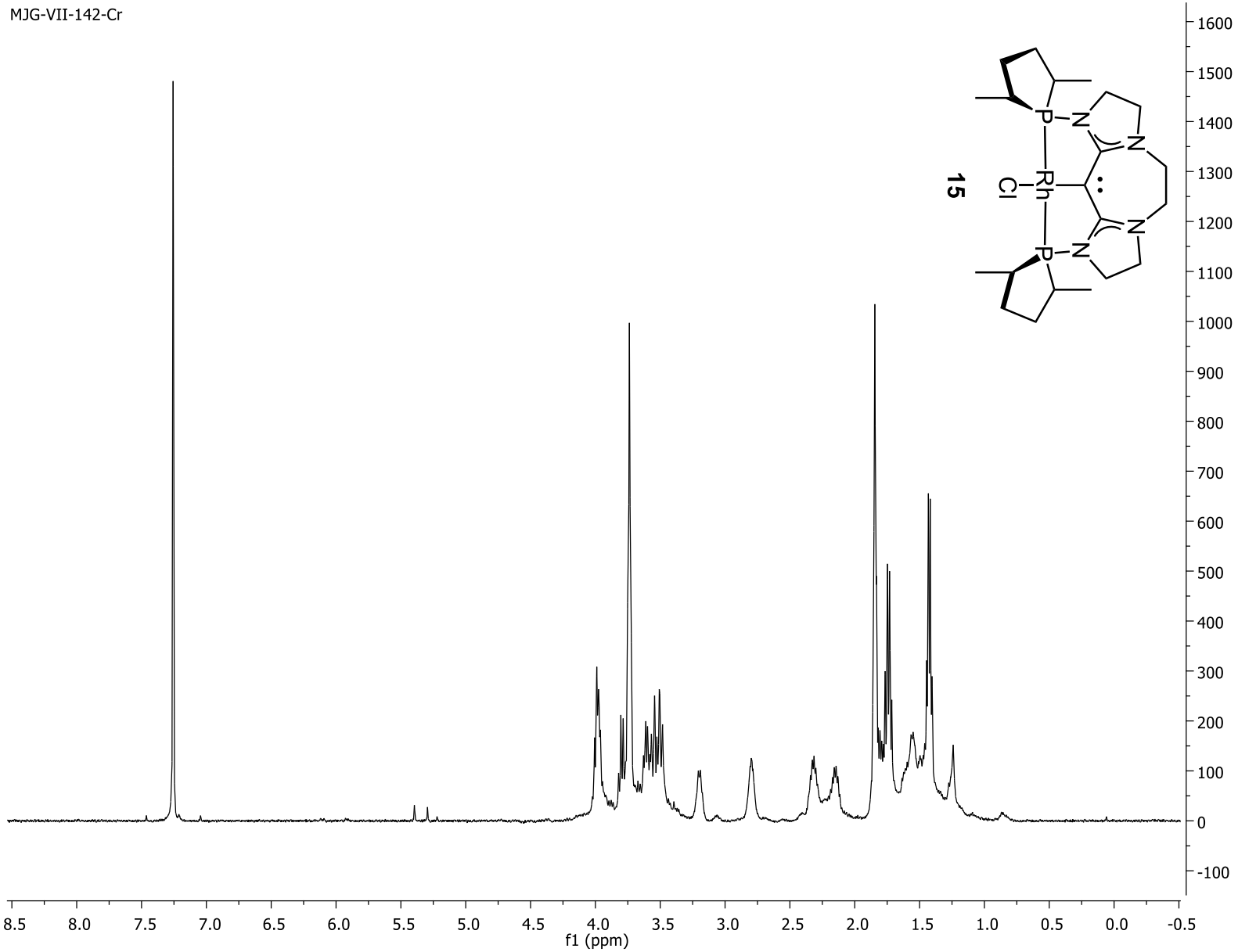



MJG-VII-125-Precip
1.000
0.180
f1 (ppm)
14

MJG-VII-125-Precip-P31

14

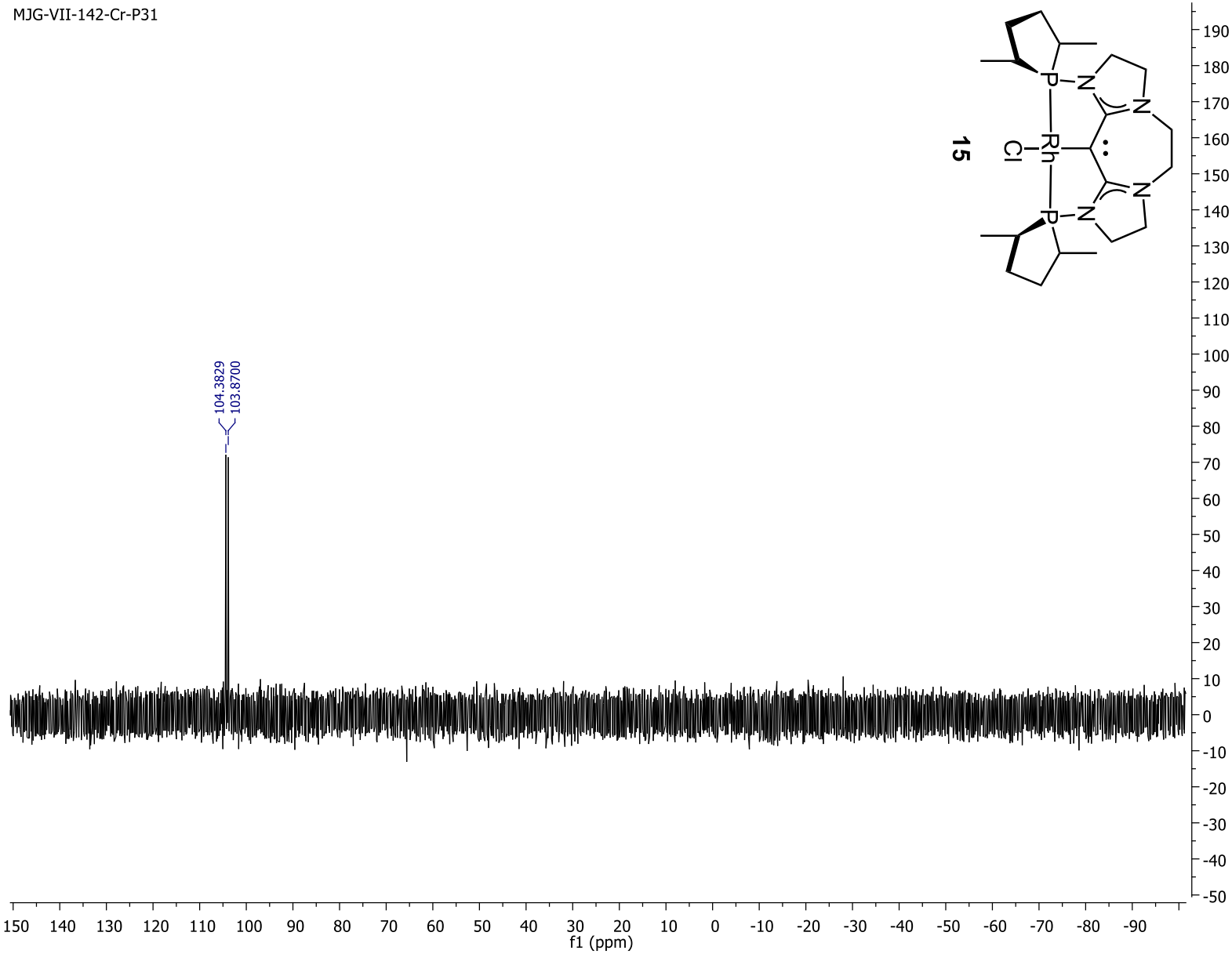


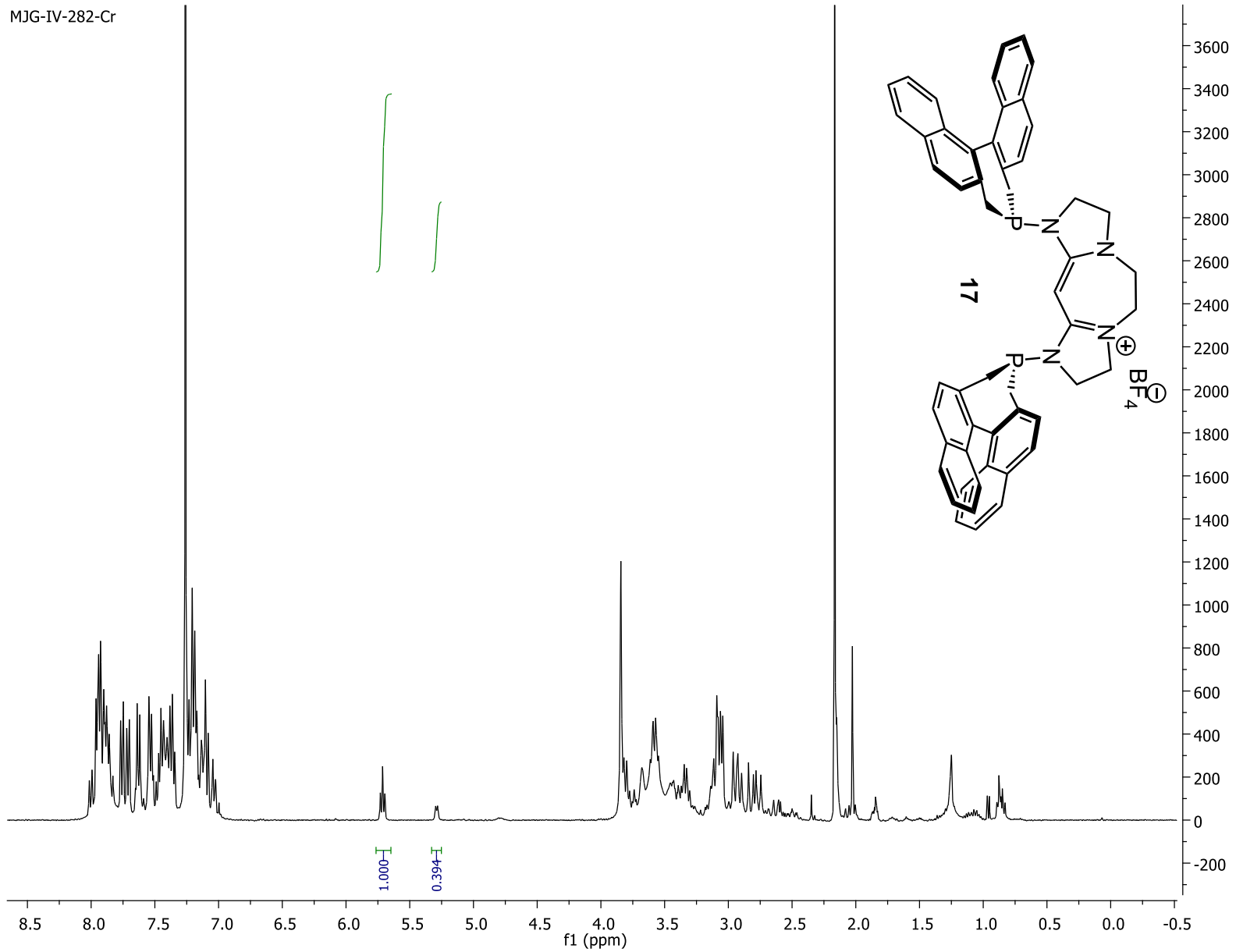

MJG-VII-142-Cr
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

15

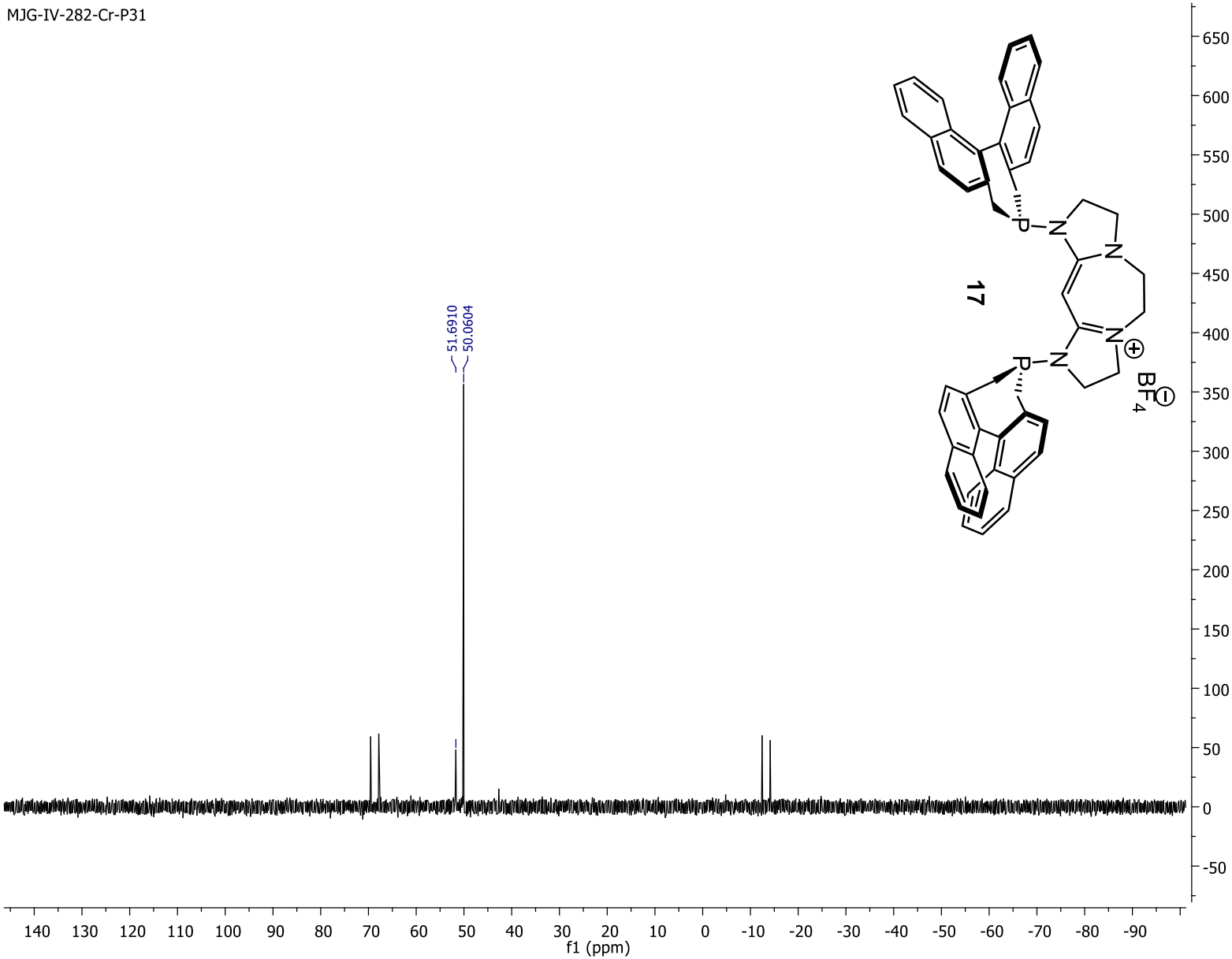
MJG-VII-142-Cr-P31

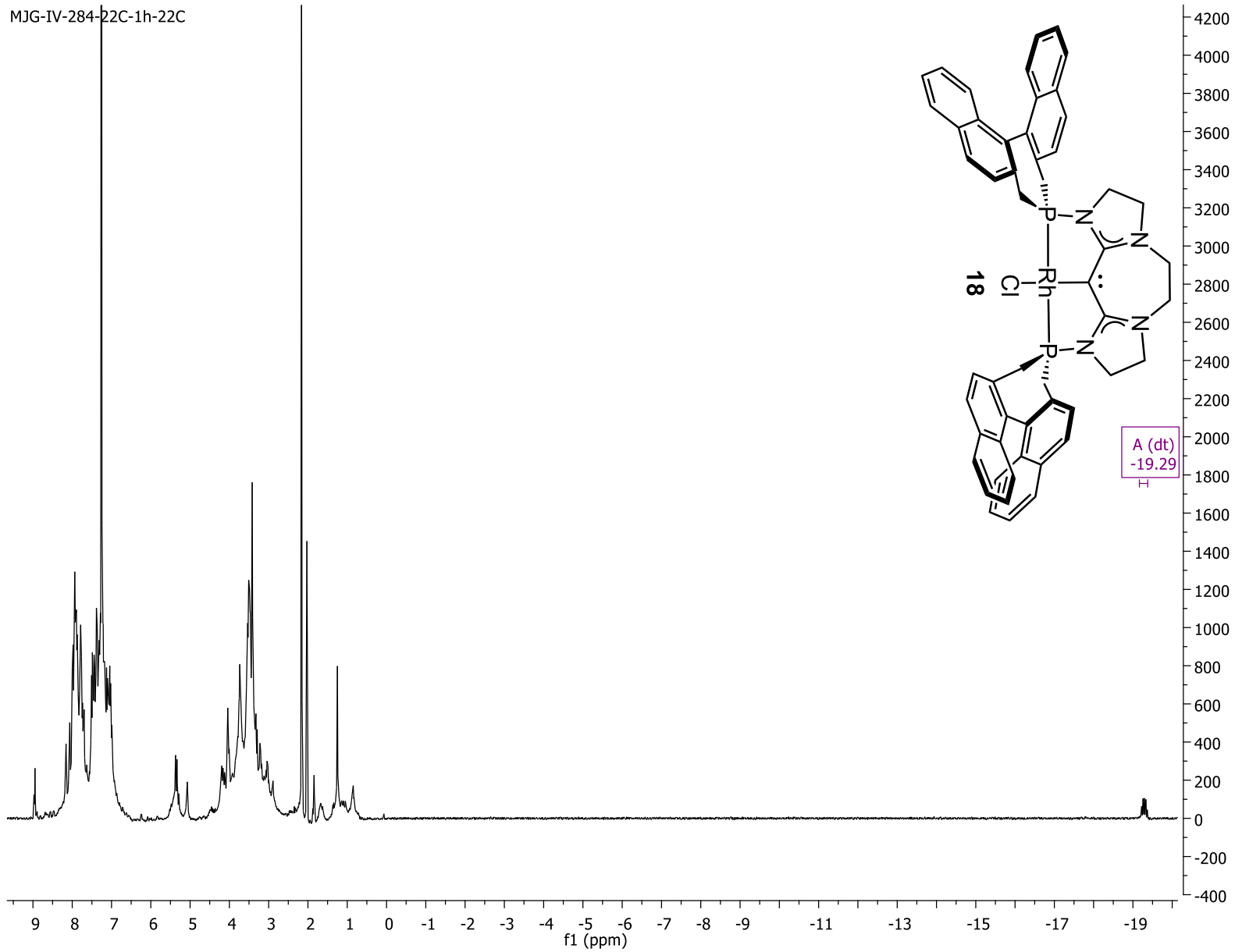
15



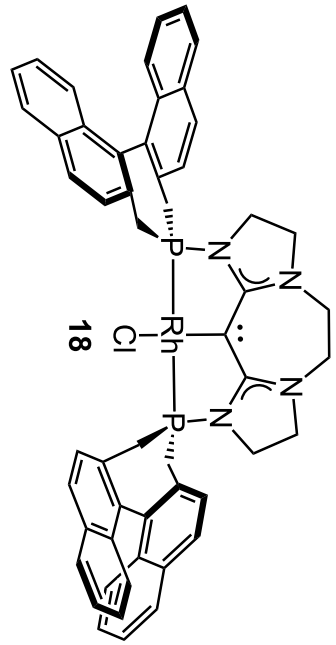

MJG-IV-282-Cr
17
1.000
0.394
f1 (ppm)

MJG-IV-282-Cr-P31

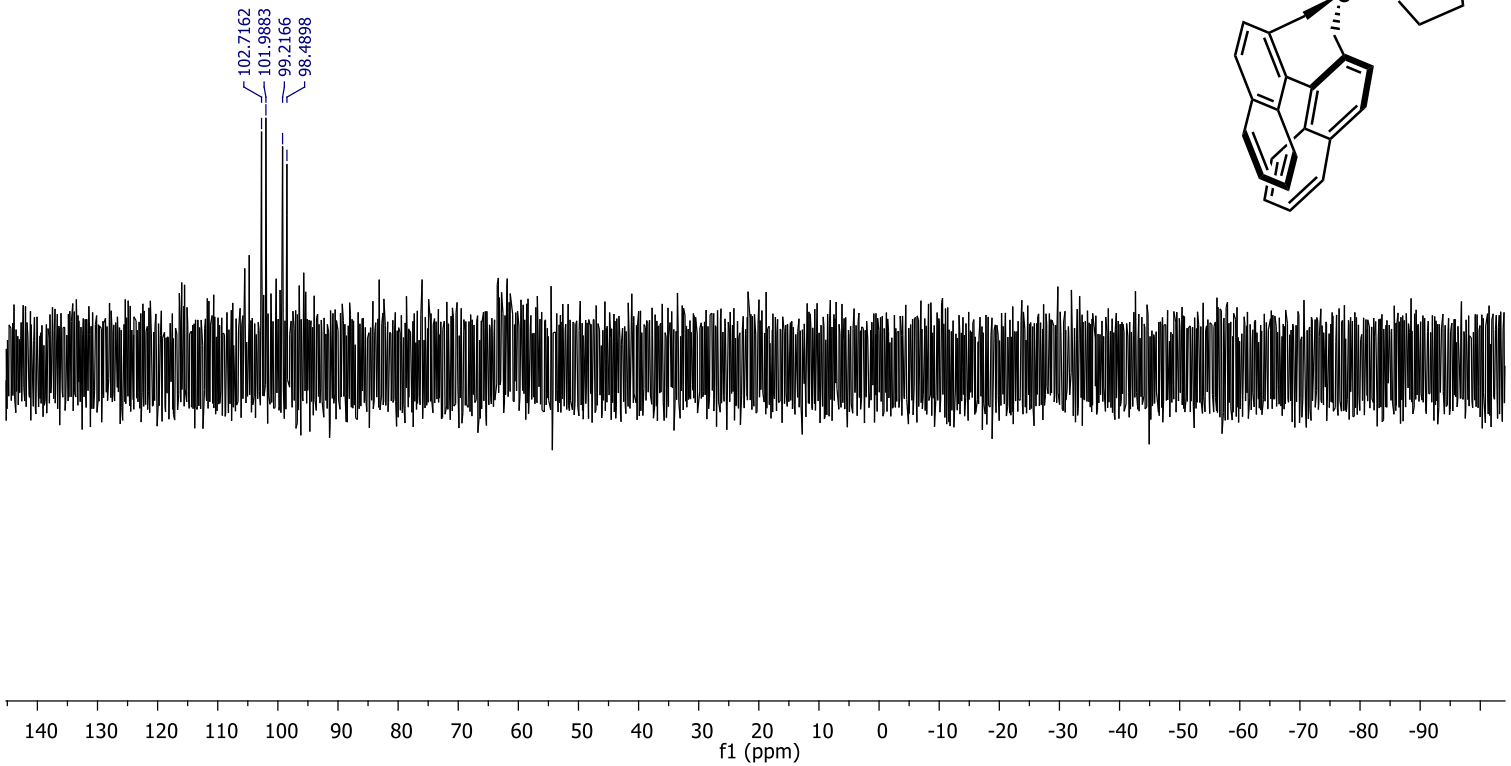



MJG-IV-284-22C-1h-22C
A (dt)
-19.29
H
f1 (ppm)
18

MJG-IV-284-22C-1h-22C-P31



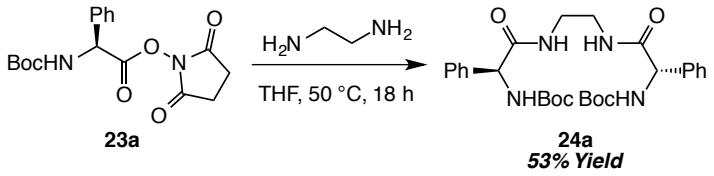
18



Section 5.4: Enantioselective Hydrofunctionalization with Chiral Carbodicarbene-Rh Complexes Derived from Chiral Diazepinium Ligands

■ **General Procedures for Amide Formation with Diethylenediamine to Form 24 (Scheme 5.4.2-1)**

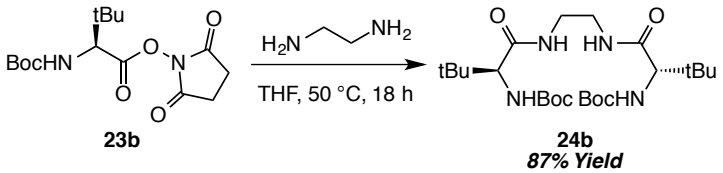
A flask was charged with the listed Boc-protected amino-succinimide, the flask evacuated then backfilled with N_2 and the solid solvated with THF before being cooled to 0 °C. To the cool solution was added ethylenediamine and the reaction was warmed to the listed temperature and allowed to stir for 48 h before being cooled and concentrated. The resulting solid was purified by SiO_2 gel chromatography to yield the expected diamide **24**. Characterization data was matched to that reported in the literature or analyzed by analogy to known compounds.



Synthesis of 24a

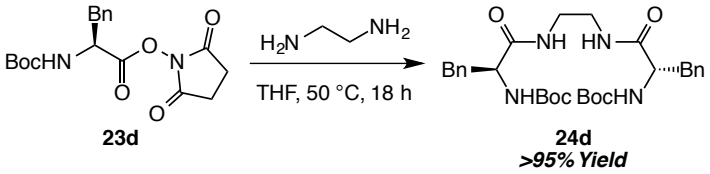
24a was synthesized according to the general procedure for amide formation and the resulting solid was purified by SiO_2 gel chromatography (9:1 DCM/MeOH) to yield **24a** (4.1 g, 7.8 mmol, 53% yield) as an off-white powder. Characterization matched those reported in *Dalton Trans*., 2012, **41**, 6764-6776.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 2.5 Hz, 10H), 6.46 (d, J = 47.5 Hz, 1H), 6.21 (d, J = 55.3 Hz, 1H), 5.70 (d, J = 16.0 Hz, 2H), 5.01 (d, J = 47.0 Hz, 2H), 3.62 – 3.05 (m, 4H), 1.42 (s, 18H).



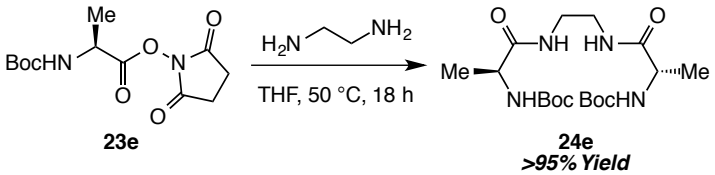
Synthesis of 24b

24b was synthesized according to the general procedure for amide formation and the resulting solid was purified by SiO_2 gel chromatography (6:1 Hex/EtOAc) to yield **24b** (265 g, 0.55 mmol, 93% yield) as an off-white powder. This material was used without further characterization, but was characterized in later steps.



Synthesis of 24d

24d was synthesized according to the general procedure for amide formation and purified by extraction from brine with DCM and EtOAc to generate **24d** (10.7 g, 9.0 mmol, 64% yield). Characterization matched that reported in *Tetrahedron Letters,* **2008,** *49*, 5746–5750.



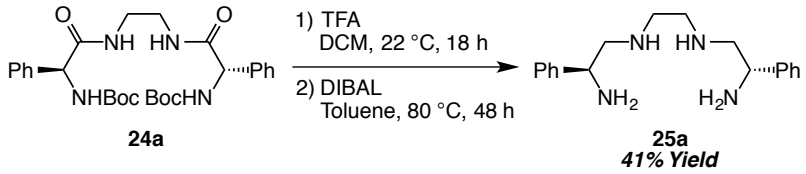
Synthesis of 24e

24e was synthesized according to the general procedure for amide formation and the resulting solid was purified by SiO_2 gel chromatography (9:1 DCM/MeOH) to yield **24e** (3.9 g, 9.7 mmol, 95% yield) as an off-white powder. Characterization matched that reported in United States

Patent: 5461176 - Processes for preparing bis-naphthalimides containing amino-acid derived linkers. 5461176, October 24, 1995.

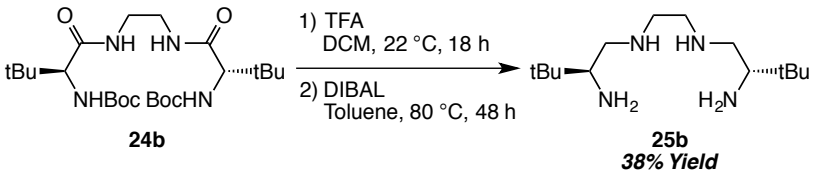
■ General Procedures for Deprotection and Reduction to Form 25 (Scheme 5.4.2-2)

A flask was charged with the listed diamide **24** and solvated with an equal volume of DCM and trifluoroacetic acid (12 equiv). The solution was allowed to stir at room temperature with a N_2 inlet and outlet needle for 18 h. During this stir, the solvent and trifluoroacetic acid was blown off. The remaining material was dried by rotary evaporation, basified with a 1M solution of sodium hydroxide and extracted with DCM. The organic layers were concentrated and used in the following step without further purification. A flask was charged with the crude material from the deprotection, evacuated and backfilled with N_2. The material was suspended in toluene and the reaction cooled to 0 °C before a 1M solution of diisobutylaluminum hydride (6 equiv) was added. The solution was heated to 80 °C and allowed to stir for 18 h before being cooled and quenched with 2M sodium hydroxide and sat. Rochelle's salt. The solution was extracted with DCM and the organic layers concentrated. The resulting semi-solid was purified by SiO_2 gel chromatography to provide the tetramine **25**.



Synthesis of 25a

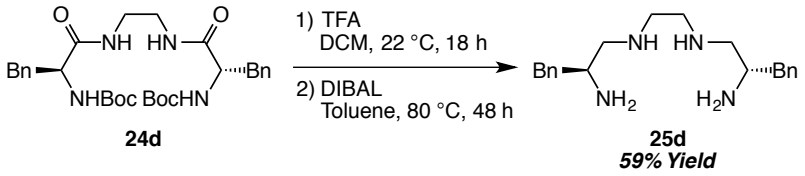
25a was synthesized according to the general procedure for amide formation and the resulting semi-solid was purified by SiO_2 gel chromatography (9:1 DCM/MeOH with 1% NH_4OH) to provide **25a** (95 mg, 0.32 mmol, 44% yield) as a yellow oil.



Synthesis of 25b

25b was synthesized according to the general procedure for amide formation and the resulting oil was purified by SiO_2 gel chromatography (9:1 DCM/MeOH with 1% NH_4OH) to provide **25b** (14 mg, 0.049 mmol, 38% yield) as a clear oil.

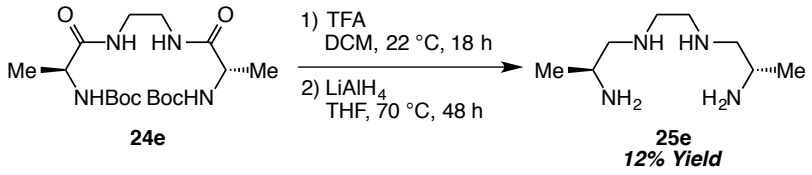
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 – 2.74 (m, 4H), 2.74 – 2.54 (m, 2H), 2.54 – 2.38 (m, 2H), 2.24 (t, J = 11.0 Hz, 2H), 1.78 (d, J = 51.3 Hz, 6H), 0.88 (s, 18H).



Synthesis of 25d

25d was synthesized according to the general procedure for amide formation and the resulting oil was purified by SiO_2 gel chromatography (9:1 DCM/MeOH with 1% NH_4OH) to provide **25d** (539 mg, 1.65 mmol, 59% yield) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, J = 6.2 Hz, 6H), 7.24 – 7.13 (m, 4H), 3.09 (ddd, J = 13.0, 8.6, 4.4 Hz, 2H), 2.91 – 2.65 (m, 8H), 2.60 – 2.36 (m, 4H), 1.29 (s, 4H).



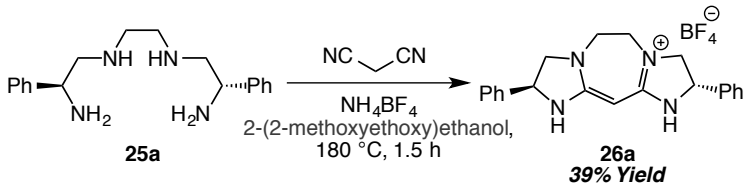
Synthesis of 25e

25e was synthesized according to the general procedure for amide formation and the resulting semi-solid was purified by distillation (<1 torr, >150 °C) to provide **25e** (225 mg, 1.22 mmol, 12% yield) as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.62 – 3.57 (m, 2H), 3.02 – 2.91 (m, 2H), 2.80 – 2.62 (m, 2H), 2.59 (dd, *J* = 11.7, 4.2 Hz, 2H), 2.36 (dd, *J* = 11.6, 8.5 Hz, 2H), 1.67 (dt, *J* = 11.1, 5.5 Hz, 2H), 1.57 (dt, *J* = 12.6, 6.1 Hz, 2H), 1.05 (d, *J* = 6.4 Hz, 6H).

■ General Procedures for Cyclization to Form 26 (Scheme 5.4.2-2)

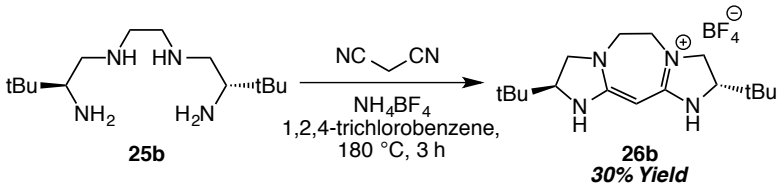
A flask fitted with a reflux condenser was charged with tetramine **25** (1 equiv), NH_4BF_4 (10 equiv), and malononitrile (2-4 equiv) before being evacuated and backfilled with N_2. The solids were solvated with the listed solvent and the solution heated to the listed temperature while stirring for the appropriate duration. The reaction was cooled and concentrated to remove residual ammonia. The remaining solution was triturated with Et_2O and the solution removed repeatedly (3x) to remove the remaining solvent. The resulting sludge was purified by SiO_2 gel chromatography to yield **26**.



Synthesis of 26a

26a was synthesized according to the general procedure for amide formation and the resulting yellow precipitate was purified by SiO_2 gel chromatography (8:1 DCM/MeOH with 1% NH_4OH) to yield **26a** (11 mg, 0.026 mmol, 39% yield) as a yellow solid.

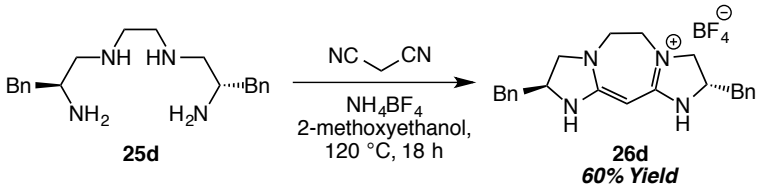
^{1}H NMR (400 MHz, MeOD) δ 7.43 – 7.27 (m, 10H), 5.02 – 4.93 (m, 2H), 4.86 (s, 1H), 4.18 – 4.07 (m, 2H), 3.65 (t, *J* = 4.9 Hz, 2H), 3.63 – 3.58 (m, 2H), 3.55 (dt, *J* = 4.2, 3.1 Hz, 2H).



Synthesis of 26b

26b was synthesized according to the general procedure for amide formation and the resulting yellow precipitate was purified by SiO_2 gel chromatography (10:1 DCM/MeOH with 1% NH_4OH) to yield **26b** (3 mg, 0.008 mmol, 30% yield) as an off-white solid.

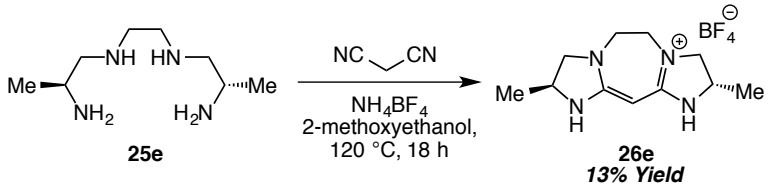
^{1}H NMR (600 MHz, $CDCl_3$) δ 4.88 (s, 1H), 3.67 – 3.55 (m, 2H), 3.49 (s, 4H), 3.46 (d, *J* = 2.2 Hz, 2H), 3.41 – 3.33 (m, 2H), 0.90 (s, 18H).



Synthesis of 26d

26d was synthesized according to the general procedure for amide formation and the resulting white precipitate was purified by SiO_2 gel chromatography (10:1 DCM/MeOH with 1% NH_4OH) to yield **26d** (51 mg, 0.114 mmol, 60% yield) as an off-white solid.

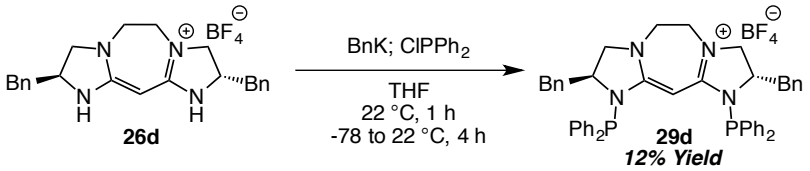
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.20 (m, 6H), 7.16 (d, *J* = 6.9 Hz, 4H), 5.99 (s, 2H), 4.37 (s, 1H), 4.18 – 3.95 (m, 2H), 3.60 (t, *J* = 9.2 Hz, 2H), 3.44 – 3.33 (m, 2H), 3.30 (s, *J* = 5.8 Hz, 4H), 2.83 (ddd, *J* = 20.6, 13.6, 6.5 Hz, 4H).



Synthesis of 26e

26e was synthesized according to the general procedure for amide formation and the resulting yellow precipitate was purified by SiO_2 gel chromatography (10:1 DCM/MeOH with 1% NH_4OH) to yield **26e** (55.6 mg, 0.189 mmol, 13% yield) as a solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (s, 2H), 5.30 (s, 1H), 4.08 – 3.93 (m, 2H), 3.76 (t, *J* = 8.9 Hz, 2H), 3.49 (d, *J* = 5.1 Hz, 4H), 3.27 – 3.18 (m, 2H), 1.30 (dt, *J* = 15.1, 7.2 Hz, 6H).

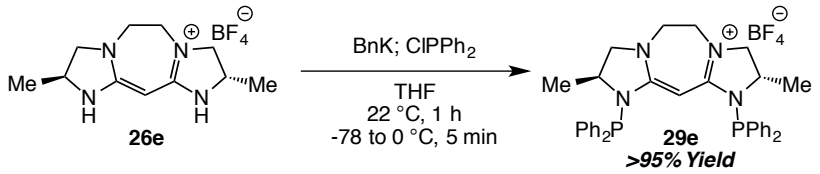


Synthesis of 29d

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **26d** (20 mg, 0.0448 mmol), and benzyl potassium (11.7 mg, 0.0896 mmol). The reagents were solvated with THF (1 mL) and the reaction sealed with a Teflon® lined septa cap before being allowed to stir at room temperature for 1 hour before being removed from the dry box. Outside the dry box chlorodiphenylphosphine (15.2 μL, 0.0896 mmol) was added under N_2 via syringe at -78 °C and the reaction allowed to stir at room temperature for 4 hours before being triturated with hexanes. The solvent was removed by syringe without exposure to oxygen or water and the orange solid dried under high vacuum. The product was purified by SiO_2 gel chromatography with attempts to

minimize O_2 and H_2O exposure to provide **29d** (4 mg, 0.0054 mmol, 12% yield) as an impure mixture.

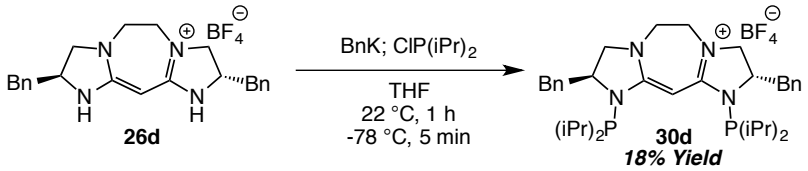
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.03 (m, 30H), 5.67 (t, *J* = 5.9 Hz, 1H), 4.03 (s, 2H), 3.87 – 3.74 (m, 2H), 3.42 (d, *J* = 9.8 Hz, 4H), 3.32 (t, *J* = 13.9 Hz, 2H), 2.25 – 1.97 (m, 4H).



Synthesis of 29e

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **26e** (5.0 mg, 0.0170 mmol), and benzyl potassium (4.4 mg, 0.0340 mmol). The reagents were solvated with THF (200 μL) and the reaction sealed with a Teflon® lined septa cap before being allowed to stir at room temperature for 1 hour before being removed from the dry box. Outside the dry box chlorodiphenylphosphine (12.2 μL, 0.0680 mmol) was added under N_2 via syringe at -78 °C and the reaction allowed to stir at 0 °C for 5 minutes before being triturated with Et_2O. The solvent was removed by syringe without exposure to oxygen or water and the orange solid dried under high vacuum and returned to the dry box. NMR analysis showed that the reaction had cleanly generated **29e** (4.9 mg, 0.0167 mmol, >95% yield).

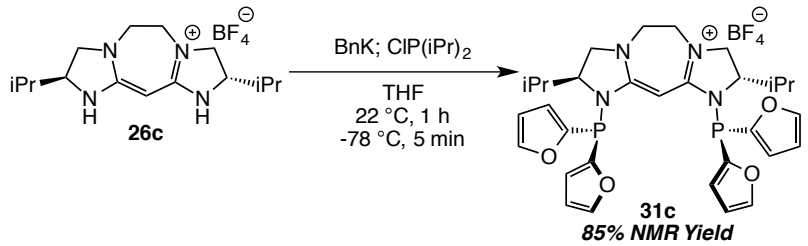
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 16.1, 7.8 Hz, 12H), 7.35 (t, *J* = 18.6 Hz, 8H), 5.49 (t, *J* = 5.5 Hz, 1H), 4.14 (dd, *J* = 16.1, 6.0 Hz, 4H), 3.95 (d, *J* = 13.7 Hz, 2H), 3.86 (s, 2H), 3.41 (dd, *J* = 10.3, 3.1 Hz, 2H), 0.78 (d, *J* = 6.3 Hz, 6H).



Synthesis of 30d

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **26d** (30 mg, 0.0672 mmol), and benzyl potassium (17.5 mg, 0.134 mmol). The reagents were solvated with THF (1 mL) and the reaction sealed with a Teflon® lined septa cap before being allowed to stir at room temperature for 1 hour before being removed from the dry box. Outside the dry box chlorodiisopropylphosphine (21.4 μL, 0.134 mmol) was added under N_2 via syringe at -78 °C and allowed to stir for 5 minutes before being triturated with hexanes. The solvent was removed by syringe without exposure to oxygen or water. The trituration and solvent removal was repeated twice before the resulting tan solid dried under high vacuum and returned to the dry box. NMR analysis showed that the reaction had generated **30d** (8.2 mg, 0.0121 mmol, 18% yield) as the majority of the sample. This material was used without further purification.

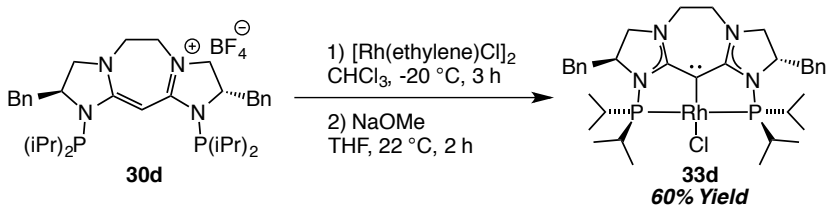
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (dd, J = 17.6, 10.2 Hz, 4H), 7.19 (d, J = 7.0 Hz, 6H), 5.15 (s, 1H), 4.03 (bs, 2H), 3.90 (d, J = 12.3 Hz, 2H), 3.82 – 3.63 (m, 4H), 3.51 (d, J = 8.0 Hz, 2H), 3.20 (bs, 2H), 2.69 (bs, 2H), 2.48 (s, 2H), 1.30 – 1.11 (m, 24H). **^{31}P NMR** (243 MHz, $CDCl_3$) δ 55.68.



Synthesis of 31c (Scheme 5.4.3-2)

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **26c** (10 mg, 0.0286 mmol), and benzyl potassium (7.4 mg, 0.0571 mmol). The reagents were solvated with THF (300 L) and the reaction sealed with a Teflon® lined septa cap before being allowed to stir at room temperature for 1 hour before being removed from the dry box. Outside the dry box chlorodifurylphosphine (8.9 μL, 0.0571 mmol) was added under N_2 via syringe at -78 °C and allowed to stir for 5 minutes before being triturated with hexanes. The solvent was removed by syringe without exposure to oxygen or water. The trituration and solvent removal was repeated twice before the resulting tan solid dried under high vacuum and returned to the dry box. NMR analysis showed that the reaction had generated **31c** (16.5 mg, 0.0243 mmol, 85% yield) as a 10:1 mixture of the bis- and mono-phosphorylated products. This material was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dt, *J* = 18.0, 4.3 Hz, 4H), 7.02 (dd, *J* = 12.1, 3.1 Hz, 4H), 6.61 – 6.50 (m, 4H), 5.80 (t, *J* = 5.4 Hz, 1H), 4.04 – 3.87 (m, 4H), 3.75 (dd, *J* = 20.5, 10.6 Hz, 2H), 3.72 – 3.62 (m, 2H), 3.53 – 3.38 (m, 2H), 1.76 – 1.57 (m, 2H), 0.80 – 0.69 (m, 6H), 0.58 (d, *J* = 6.8 Hz, 6H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ -9.24.

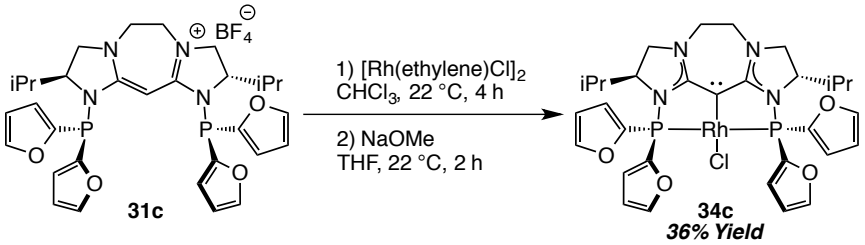


Synthesis of 33d

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **30d** (8.0 mg, 0.0118 mmol), and $[Rh(ethylene)Cl]_2$ (2.3 mg, 0.00589 mmol). The reagents were solvated with $CDCl_3$ (500 μL) at -20 °C and the reaction allowed to stir for 3 h at -20 °C sealed with a Teflon® lined cap.

The solution was concentrated and sodium methoxide (0.6 mg, 0.012 mmol) added before the solids were resolvated in THF (400 μL) and allowed to stir at 22 °C for 2 hour. The solution was concentrated and redissolved in DCM before being plugged through Celite® and reconcentrated to yield **33d** (5.2 mg, 0.0071 mmol, 60% yield) as a tan solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 6H), 7.24 (dd, *J* = 10.1, 7.5 Hz, 4H), 4.10 – 4.00 (m, 2H), 3.92 – 3.84 (m, 2H), 3.52 (dd, *J* = 13.9, 7.1 Hz, 2H), 3.48 (d, *J* = 9.4 Hz, 2H), 3.23 (q, *J* = 11.5 Hz, 4H), 3.13 (t, *J* = 11.4 Hz, 2H), 2.99 (qd, *J* = 14.2, 6.5 Hz, 4H), 1.97 (dd, *J* = 16.9, 9.2 Hz, 6H), 1.68 (dd, *J* = 16.0, 8.4 Hz, 6H), 1.61 (dd, *J* = 12.6, 6.2 Hz, 6H), 1.56 (dd, *J* = 15.1, 7.5 Hz, 6H). **^{31}P NMR** (243 MHz, $CDCl_3$) δ 90.91 (d, *J* = 101.4 Hz).



Synthesis of 34c (Scheme 5.4.4-3)

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **31c** (19.4 mg, 0.0286 mmol), and $[Rh(ethylene)Cl]_2$ (5.6 mg, 0.0143 mmol). The reagents were solvated with $CHCl_3$ (1 mL) and the reaction allowed to stir for 2 h at 22 °C sealed with a Teflon® lined cap. The solution was concentrated and sodium methoxide (1.5 mg, 0.0143 mmol) added before the solids were resolvated in THF (1 mL) and allowed to stir at 22 °C for 2 hour. The THF solution was filtered through a plug of Celite® and the product reisolated by dissolving off the plug with DCM and concentrating to yield **34c** (7.6 mg, 0.0103 mmol, 36% yield) as a tan solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 66.2, 42.1 Hz, 8H), 6.63 (d, *J* = 91.3 Hz, 4H), 4.14 (d, *J* = 15.6 Hz, 2H), 3.81 (d, *J* = 11.9 Hz, 4H), 3.58 (s, 4H), 1.03 – 0.47 (m, 14H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 37.15 (d, *J* = 114.4 Hz).

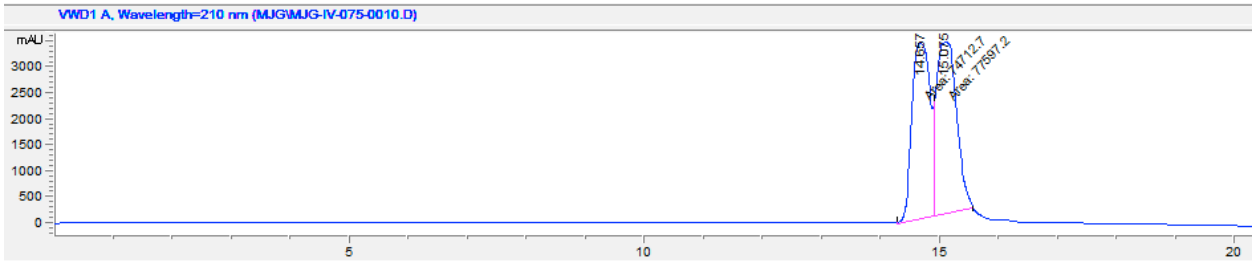
■ **General Procedure for Surveying Intramolecular Hydroamination with Chiral Diazepinium CDC-Rh(I) Catalysts (Table 5.4.5.1-1)**

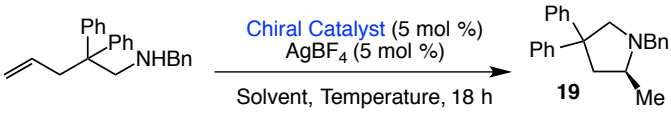
In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with the listed chiral CDC-Rh(I) complex (0.005 mmol, 5 mol%) and $AgBF_4$ (1.0 mg, 0.005 mmol, 5 mol%) before being solvated with the listed solvent (100 μL, [ ] = 1.0 M). The solution was allowed to stir at room temperature for 1 hour before *N*-benzyl-2,2-diphenylpent-4-en-1-amine (32.7 mg, 0.1 mmol) was added. The reaction was sealed with a Teflon® lined lid, taped with electrical tape and removed from the glove box before being heated to 60 °C for 18 h. The reaction was cooled and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solution concentrated. The resulting oil was purified by SiO_2 column chromatography (50:1 Hexanes/Et_2O) to afford the listed yield of **19** as a colorless oil. A pure sample was assayed on an Agilent 1220 LC System with a Daicel ChiralPak IA column (99:1 Hexanes/Isopropanol, 0.5 mL/min, 210 nm) to find that the product was formed in the listed enantiomeric excess.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.33 (dd, *J* = 17.8, 10.8 Hz, 2H), 7.30 – 7.23 (m, 5H), 7.23 – 7.15 (m, 5H), 7.11 (dd, *J* = 19.2, 12.1 Hz, 1H), 4.10 (d, *J* = 13.2 Hz, 1H), 3.65 (d, *J* = 9.9 Hz, 1H), 3.27 (d, *J* = 13.2 Hz, 1H), 2.93 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.89 – 2.82 (m, 1H), 2.80 (d, *J* = 9.9 Hz, 1H), 2.22 (dd, *J* = 12.6, 8.0 Hz, 1H), 1.18 (d, *J* = 5.6 Hz, 3H). **^{13}C**

NMR (151 MHz, $CDCl_3$) δ 150.67, 148.76, 140.12, 128.62, 128.23, 128.15, 127.84, 127.46, 127.27, 126.79, 125.81, 125.42, 66.46, 59.68, 58.03, 52.54, 48.02, 19.54.

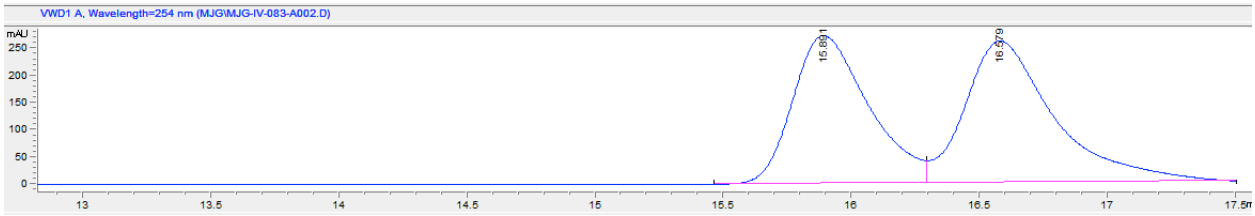
Chiral Trace:



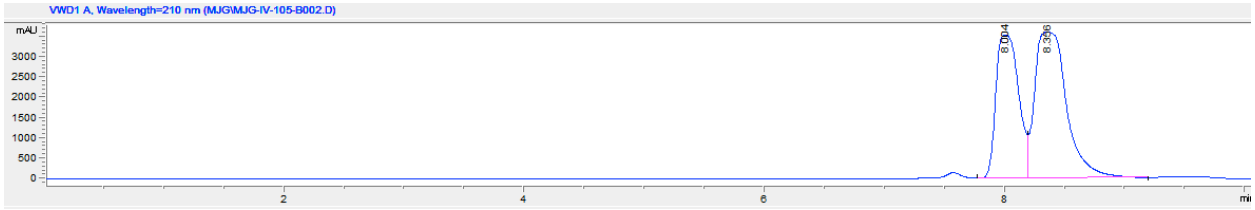


Entry	Chiral Catalyst	Solvent; M	Temp (°C)	NMR Yield (%)	% ee
1	34c	MeCN; 1.0	60	0	**0**
2	33d	MeCN; 1.0	80	56	**0**
3	32c	MeCN; 1.0	60	40	**17**
4	33d	PhCl; 1.0	60	0	**0**
5	32c	PhCl; 1.0	60	0	**0**

Entry 3: Catalyst 33d, MeCN, 80 °C



Entry 4: Catalyst 32c, MeCN, 60 °C

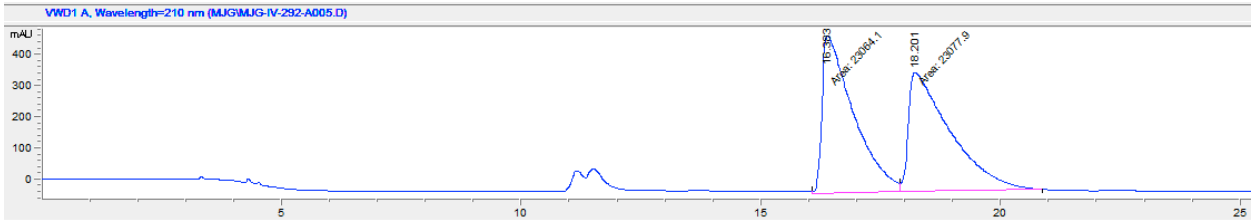


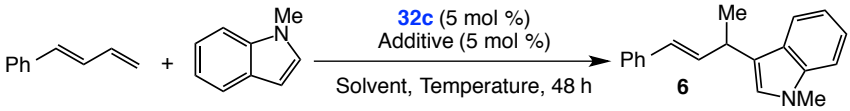
■ **General Procedure for Surveying Intermolecular Hydroarylation with Chiral Diazepinium CDC-Rh(I) Catalyst 32c (Table 5.4.5.2-1)**

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **32c** (1.9 mg, 0.0025 mmol, 5 mol%), the appropriate chiral additive (0.0025 mmol, 5.0 mol%), and $NaBAr^F_4$ (2.2 mg, 0.0025 mmol, 5 mol%) when appropriate, and 1,3-phenylbutadiene (6.5 mg, 0.05 mmol). The reagents were solvated with the listed solvent (50 μL, [ ] = 1.0 M) and the reaction was sealed with a Teflon® lined septum cap before being allowed to stir at room temperature for 1 hour. 1-methylindole (6.6 mg, 0.05 mmol) was added to the reaction and the vial sealed with black electrical tape before being removed from the glovebox. The reaction was heated to 60 °C and allowed to stir for 18 hours before being allowed to cool to room temperature and an aliquot taken to determine the conversion by ^{1}H NMR using DMF as an internal standard. The NMR sample was recovered and the solvent evaporated before the products were purified by SiO_2 column chromatography (100:1 Hex/Et_2O) to provide **6** in the listed yeild. A pure sample was then assayed on an Agilent 1220 LC System with a Daicel ChiralPak IA column (100% Hexanes, 1 mL/min, 210 nm) to determine the listed enantiomeric excess.

^{1}H NMR (600 MHz, $CHCl_3$-*d*) δ 7.67 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.33 – 7.26 (m, 4H), 7.22 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.09 (ddd, *J* = 7.9, 6.9, 1.1 Hz, 1H), 6.88 (d, *J* = 0.8 Hz, 1H), 6.56 – 6.43 (m, 2H), 3.94 (m, 1H), 3.77 (s, 3H), 1.56 (d, *J* = 7.0 Hz, 4H). **^{13}C NMR** (151 MHz, $CHCl_3$-*d*) δ 137.95, 137.39, 135.72, 128.58, 128.15, 127.30, 126.99, 126.27, 125.43, 121.67, 119.82, 119.03, 118.81, 109.34, 34.35, 32.79, 20.99. IR (ν/cm^{-1}): 2925 (m), 2870 (s), 1472 (m), 1374 (w), 1328 (w), 1134 (s). MS (ES$^+$) $[M+H]^+$ calcd for $C_{19}H_{20}N^+$ 262.16, found: 262.00.

Racemic Trace:

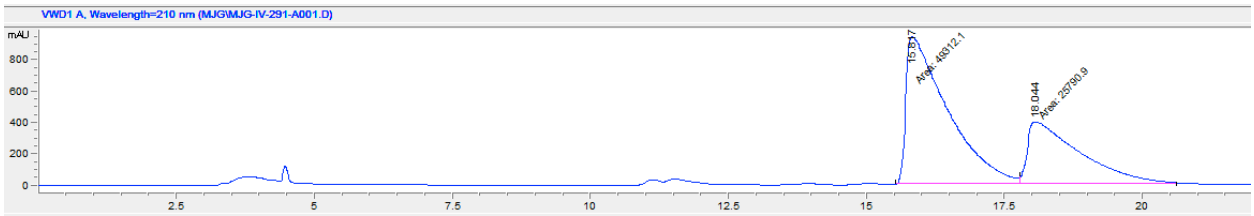




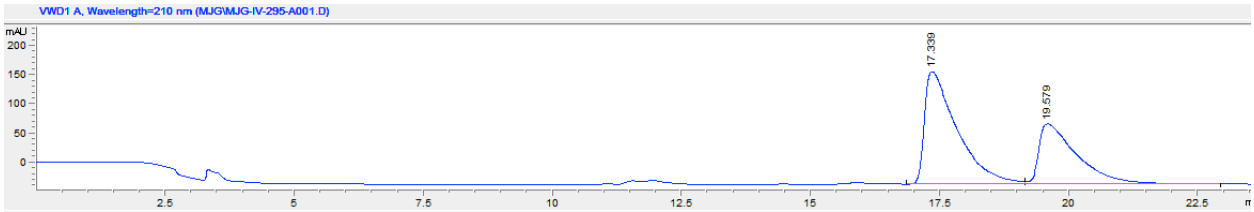
Entry	Solvent; M	Temp (°C)	Additive; mol%	NMR Yield (%)	% ee
1	PhH; 1.0	50	$AgBF_4$; 5	22	23
2	PhCl; 1.0	60	$AgBF_4$; 5	50	29
3[a]	PhCl; 1.0	60	CuCl; 5	54	7
4[a]	PhCl; 1.0	60	AgF; 5	26	5

[a] Reaction run with 5 mol% $NaBAr^F{}_4$ to generate the cationic CDC-Rh(I) catalyst.

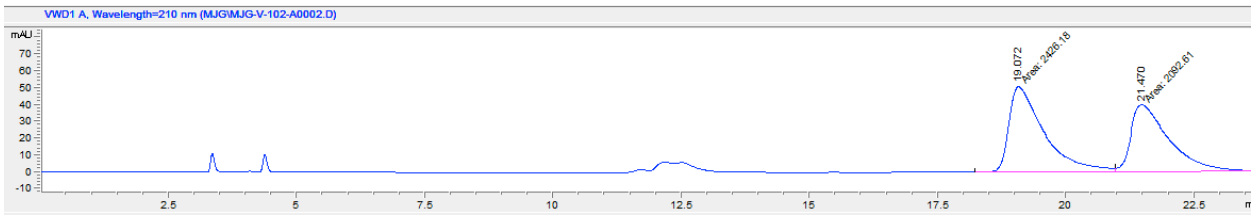
Entry 1: Toluene, 50 °C, $AgBF_4$



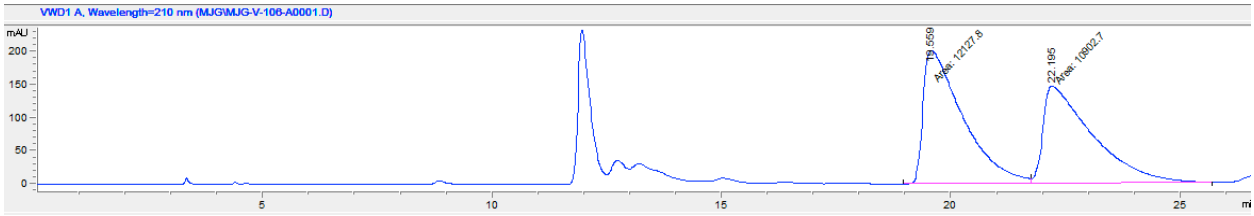
Entry 2: Chlorobenzene, 60 °C, $AgBF_4$

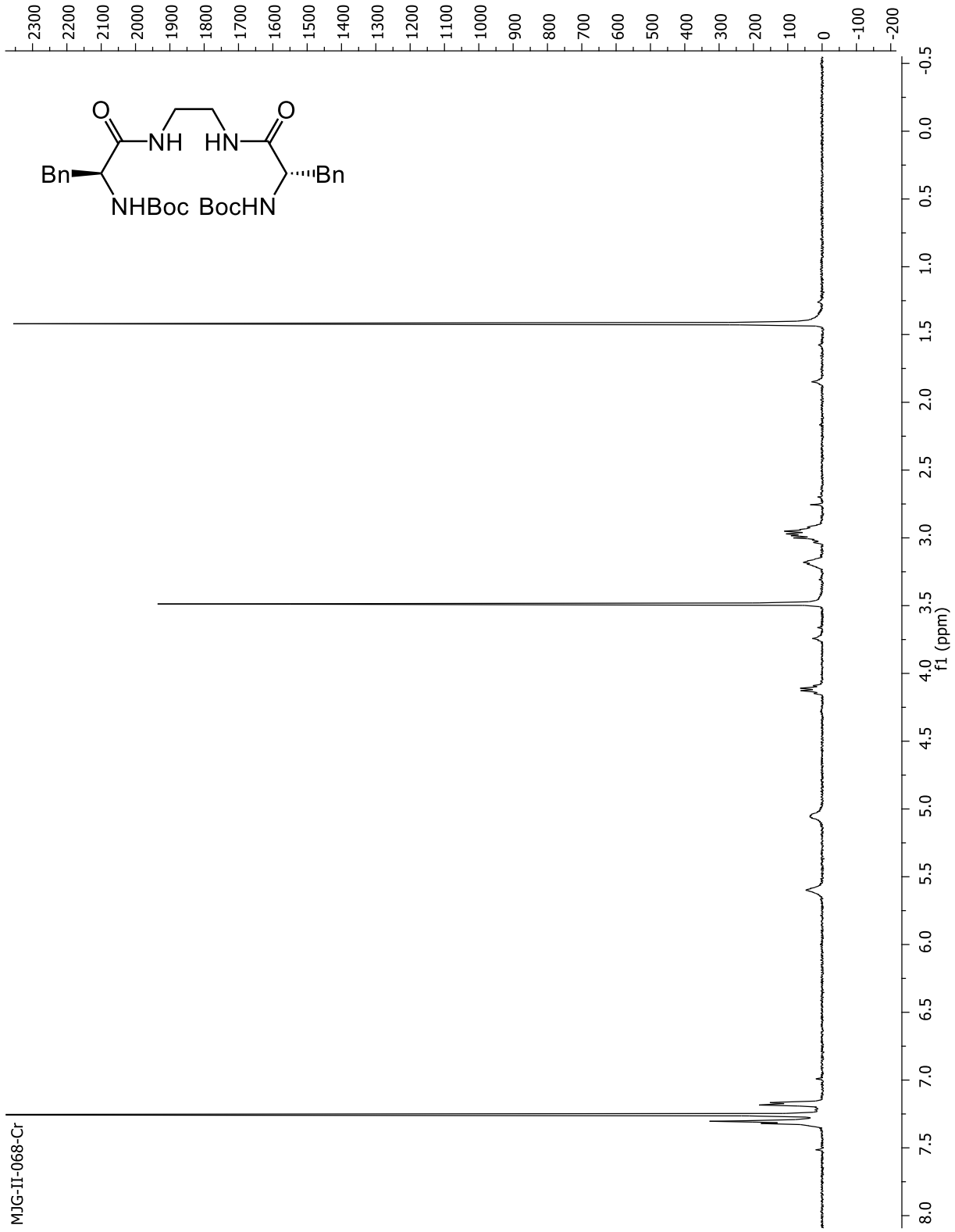


Entry 3: Chlorobenzene, 60 °C, CuCl



Entry 4: Chlorobenzene, 60 °C, AgF

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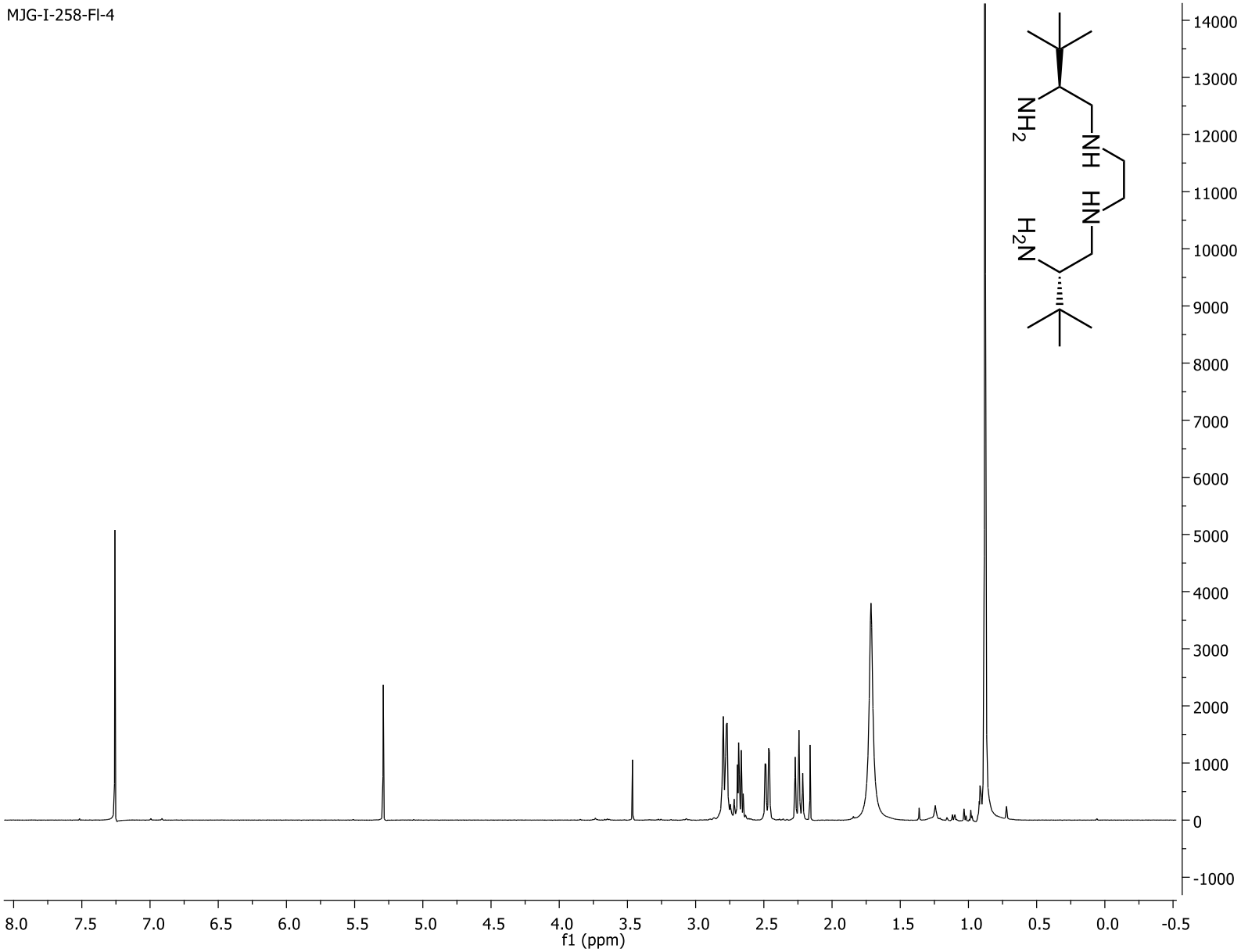
HN
O
Bn
Bn
NHBoc
BocHN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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
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13000
12000
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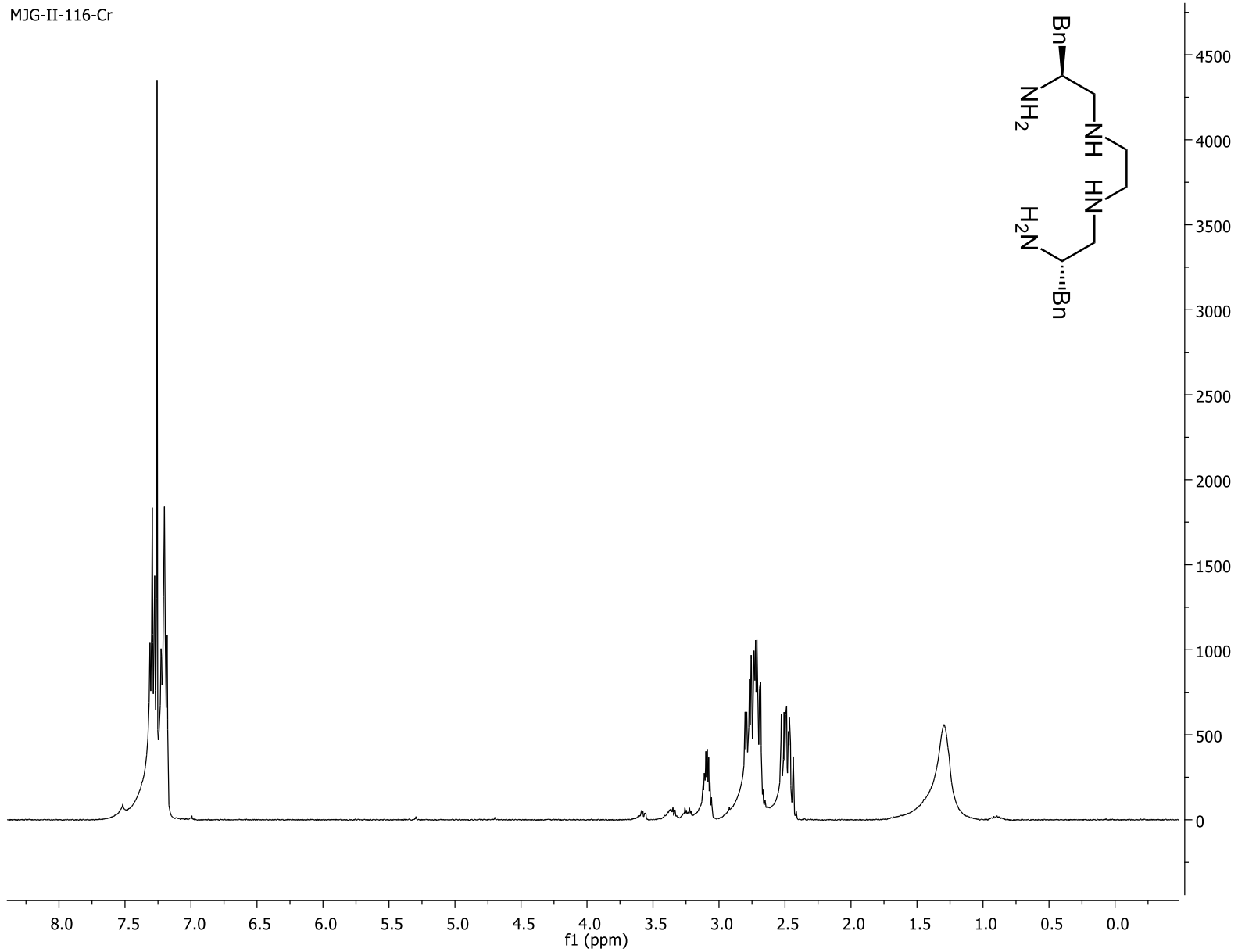
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
NH2
NH
HN
H2N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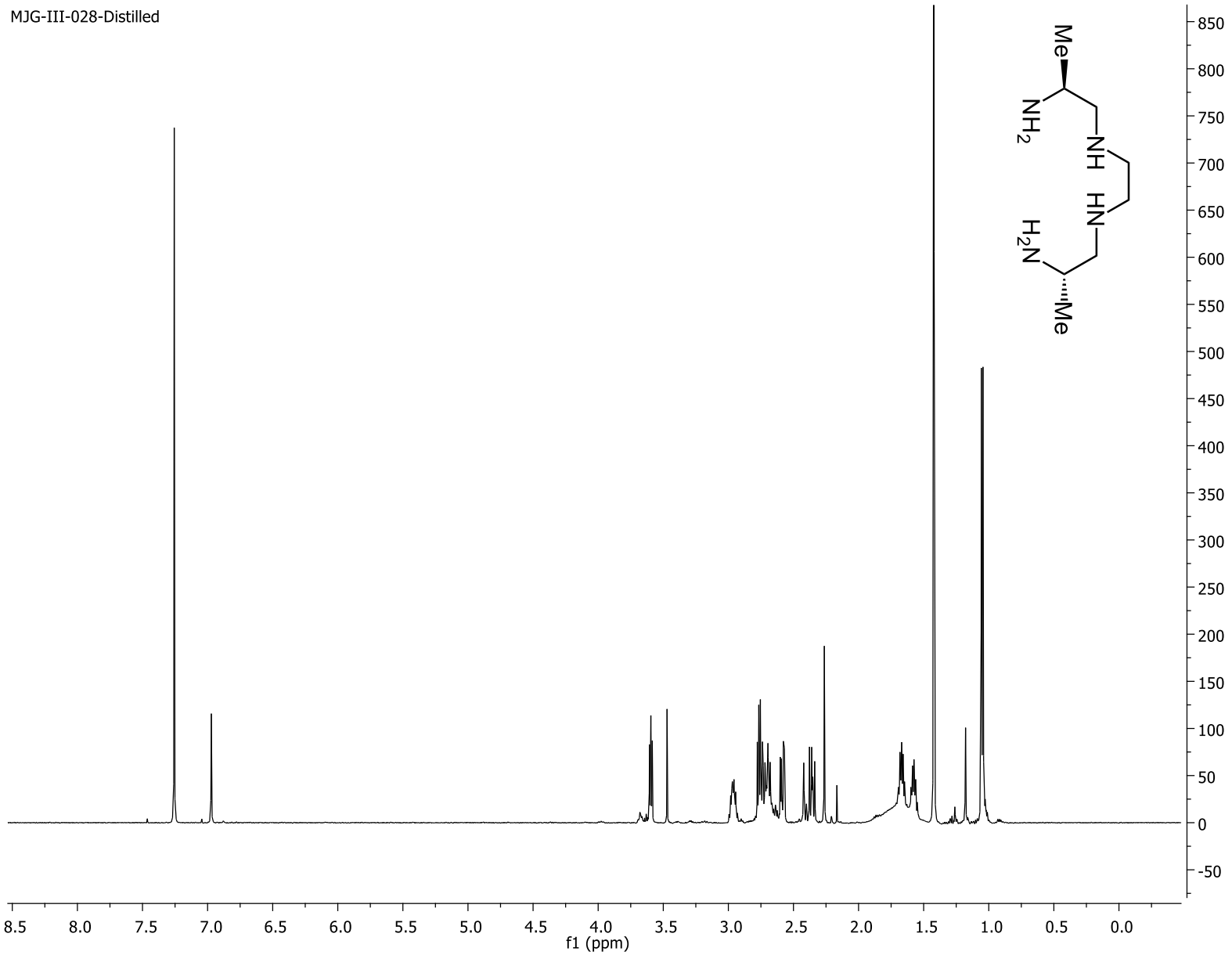
3000
2500
2000
1500
1000
500
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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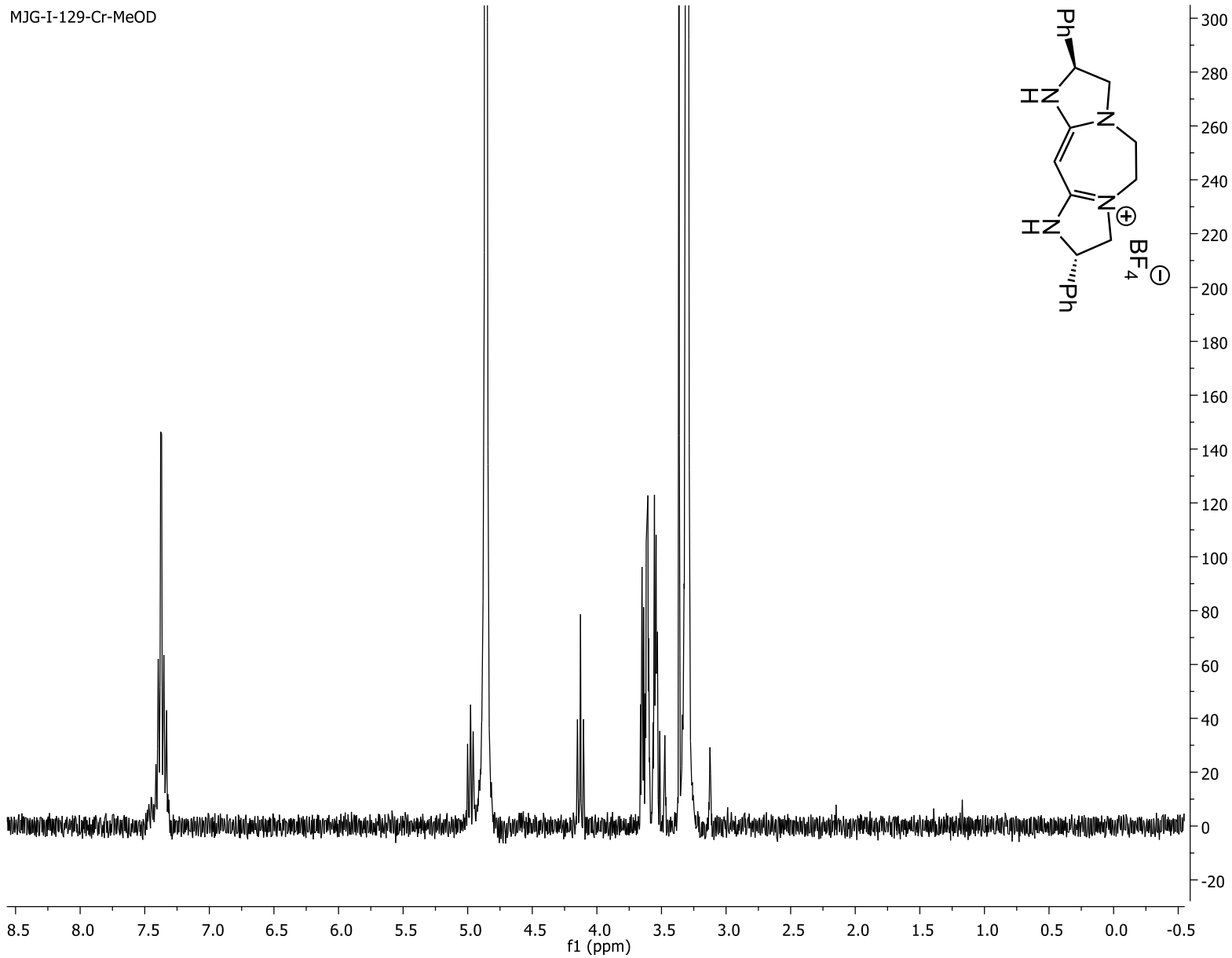
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
Me
NH2
NH
HN
H2N
Me


MJG-I-129-Cr-MeOD
f1 (ppm)
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
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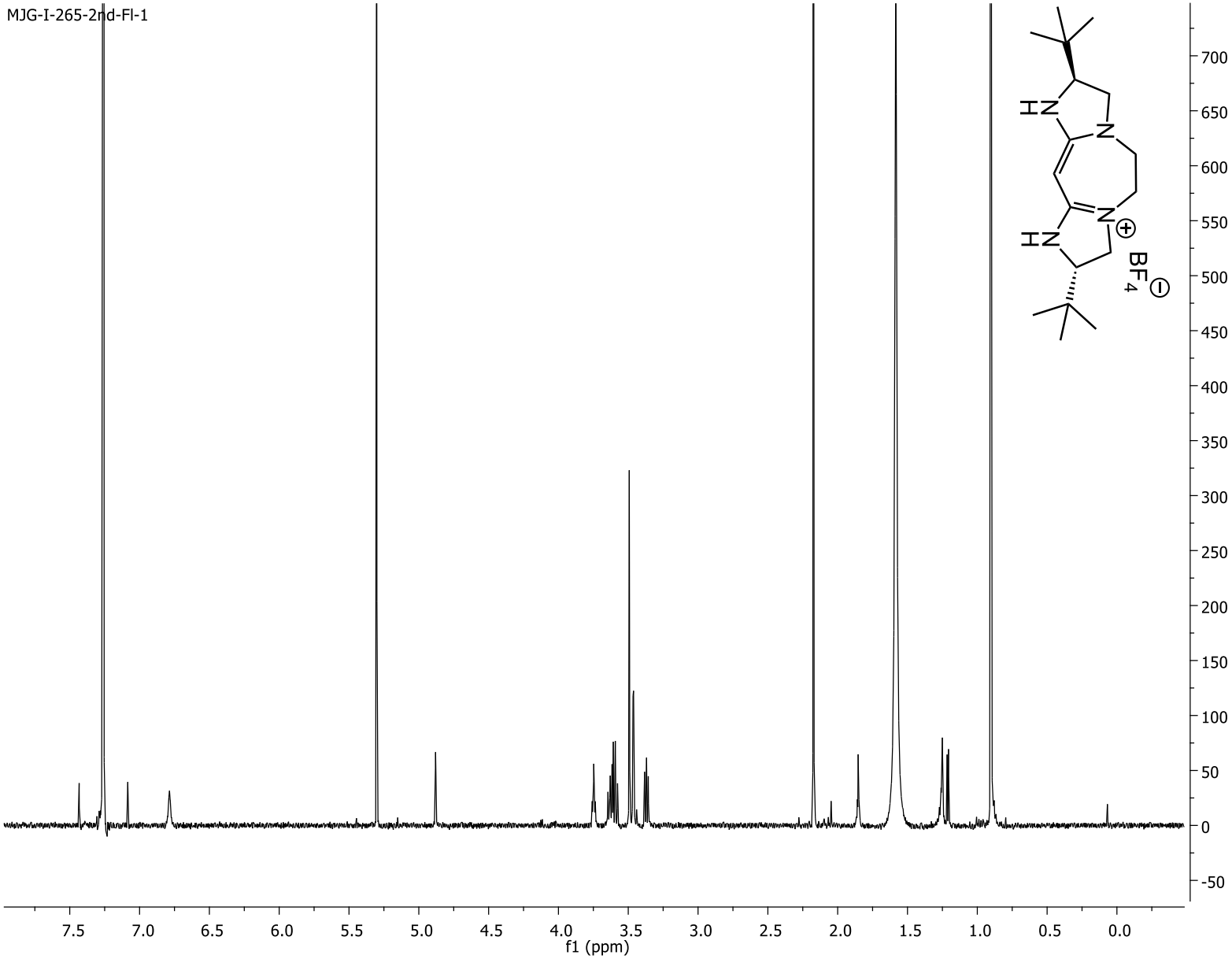
Ph
H
N
N
N
H
Ph
BF4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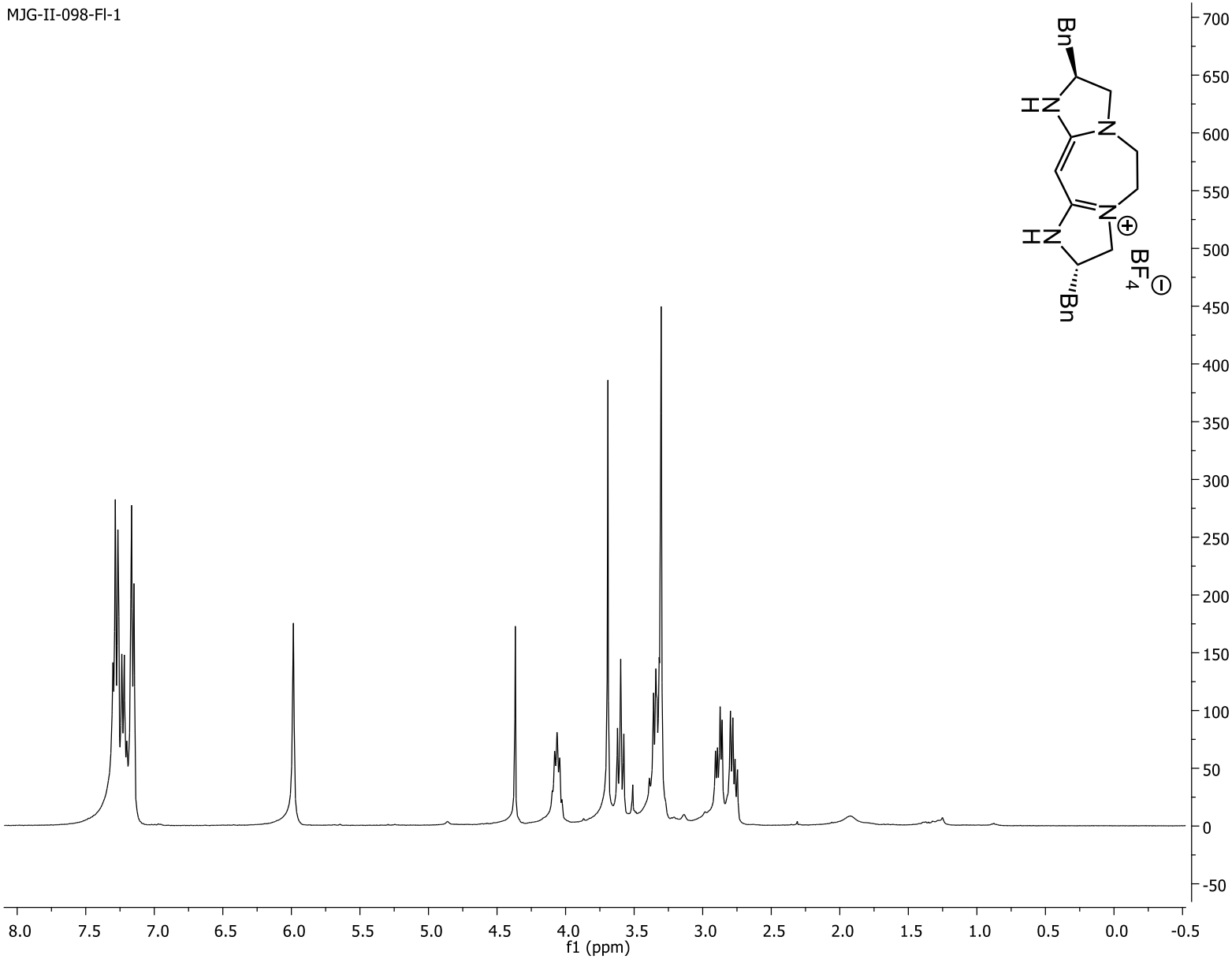
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
H
N
N
H
N
BF4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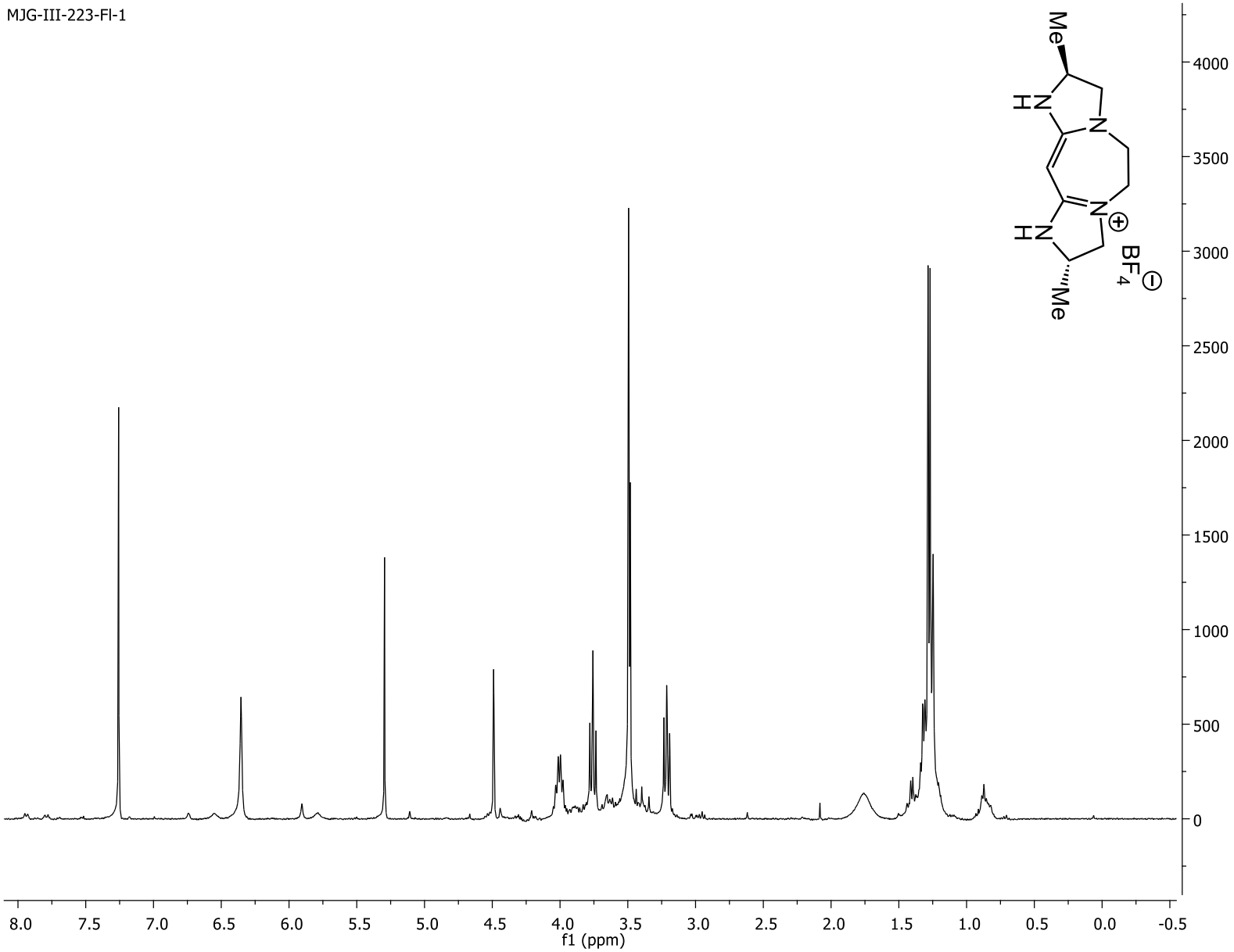
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
Bn
H
N
N
N
H
Bn
BF4


MJG-III-223-Fl-1
f1 (ppm)
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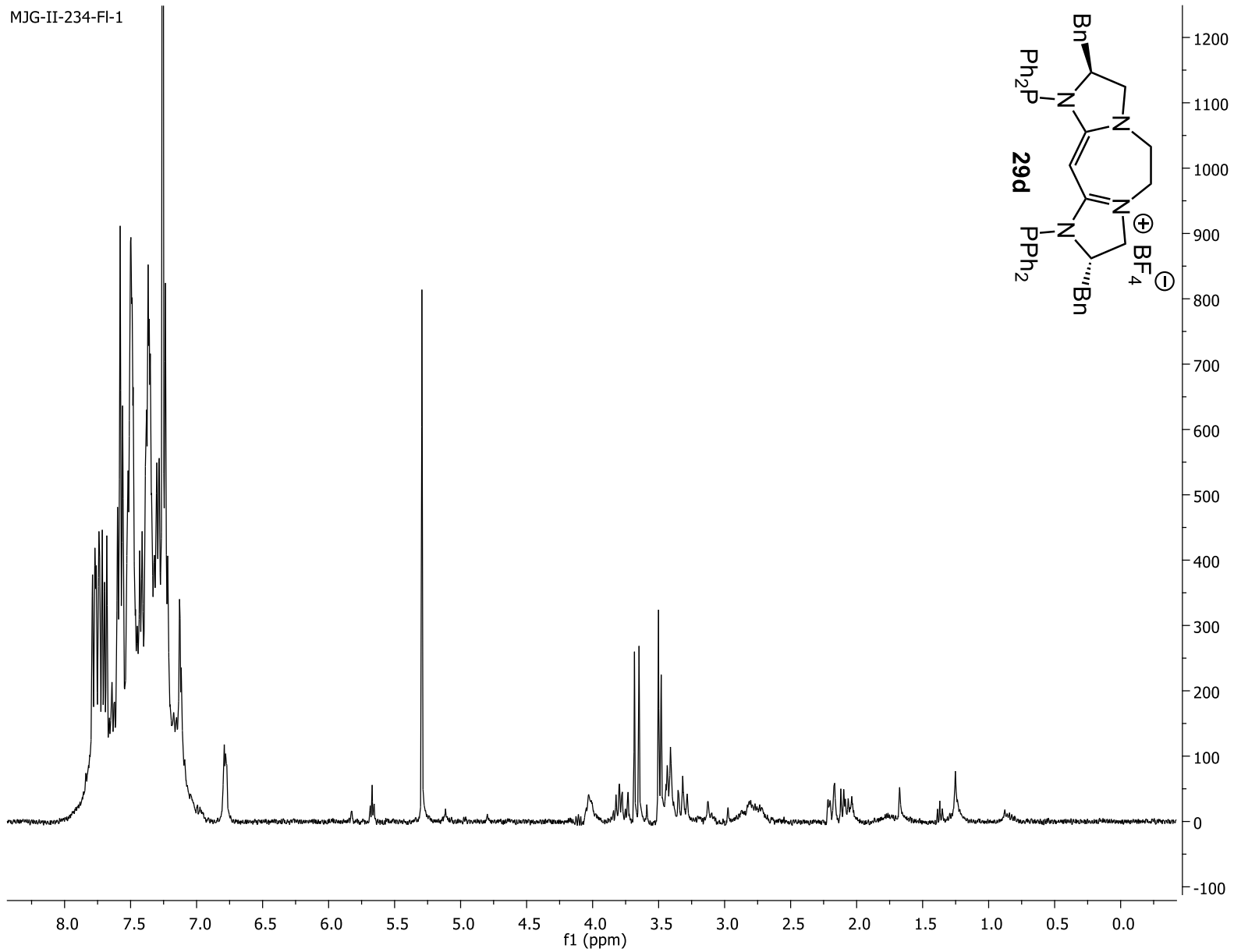
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
4000
3500
3000
2500
2000
1500
1000
500
0
Me
H
N
N
N
H
Me
BF4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f1 (ppm)
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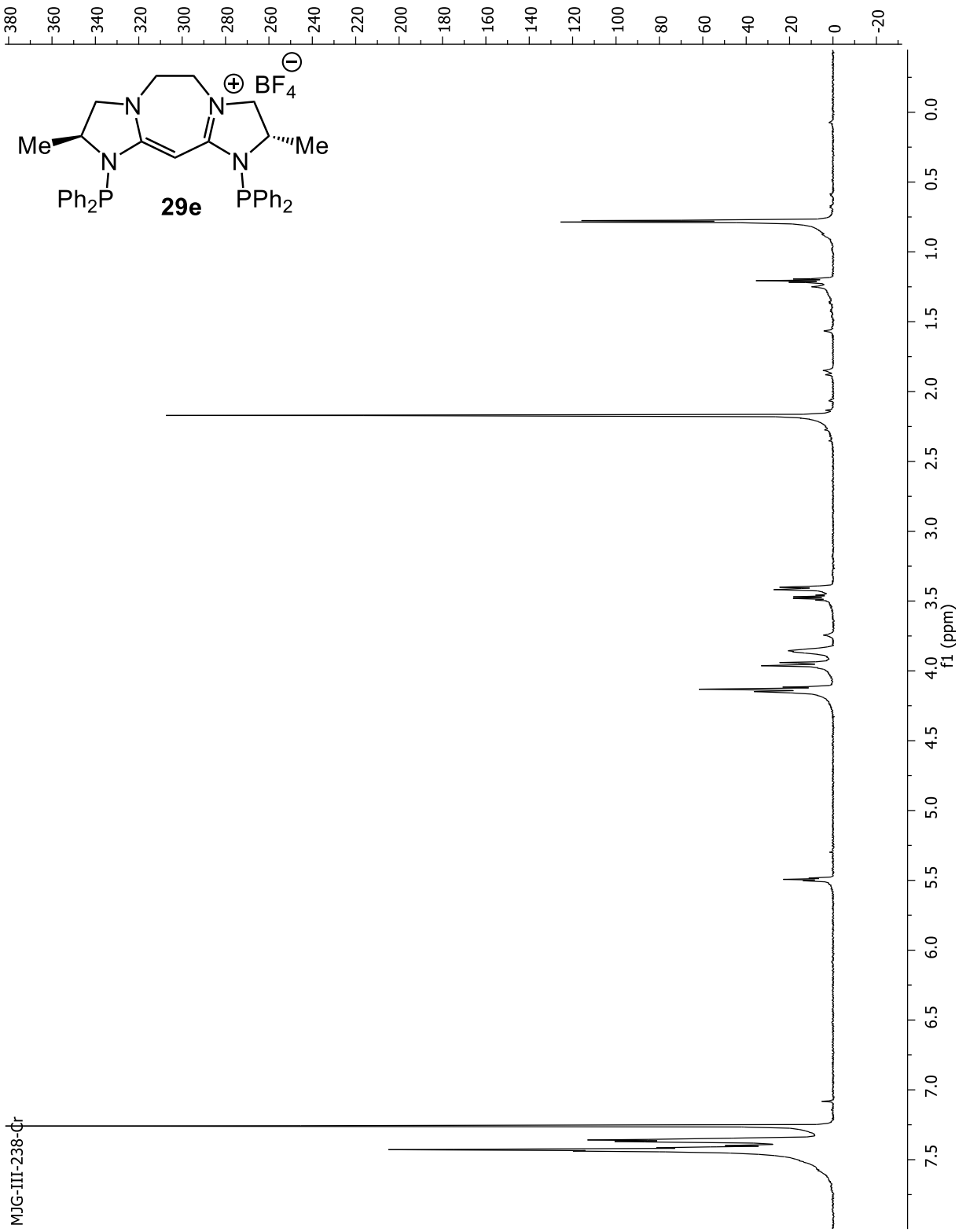
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
29d
Bn
Ph2P
N
N
N
N
PPh2
Bn
BF4


MJG-III-238-Cr
f1 (ppm)
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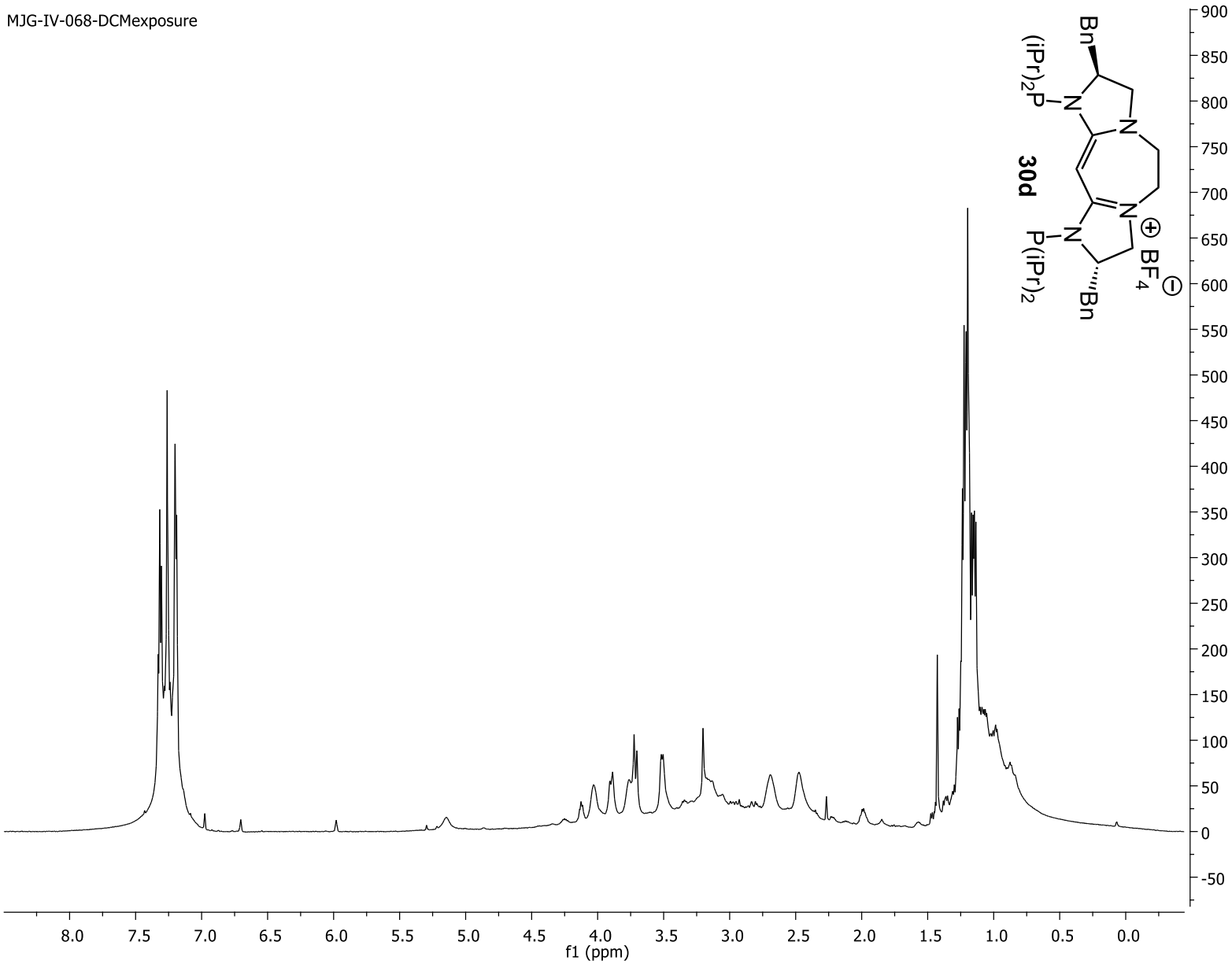
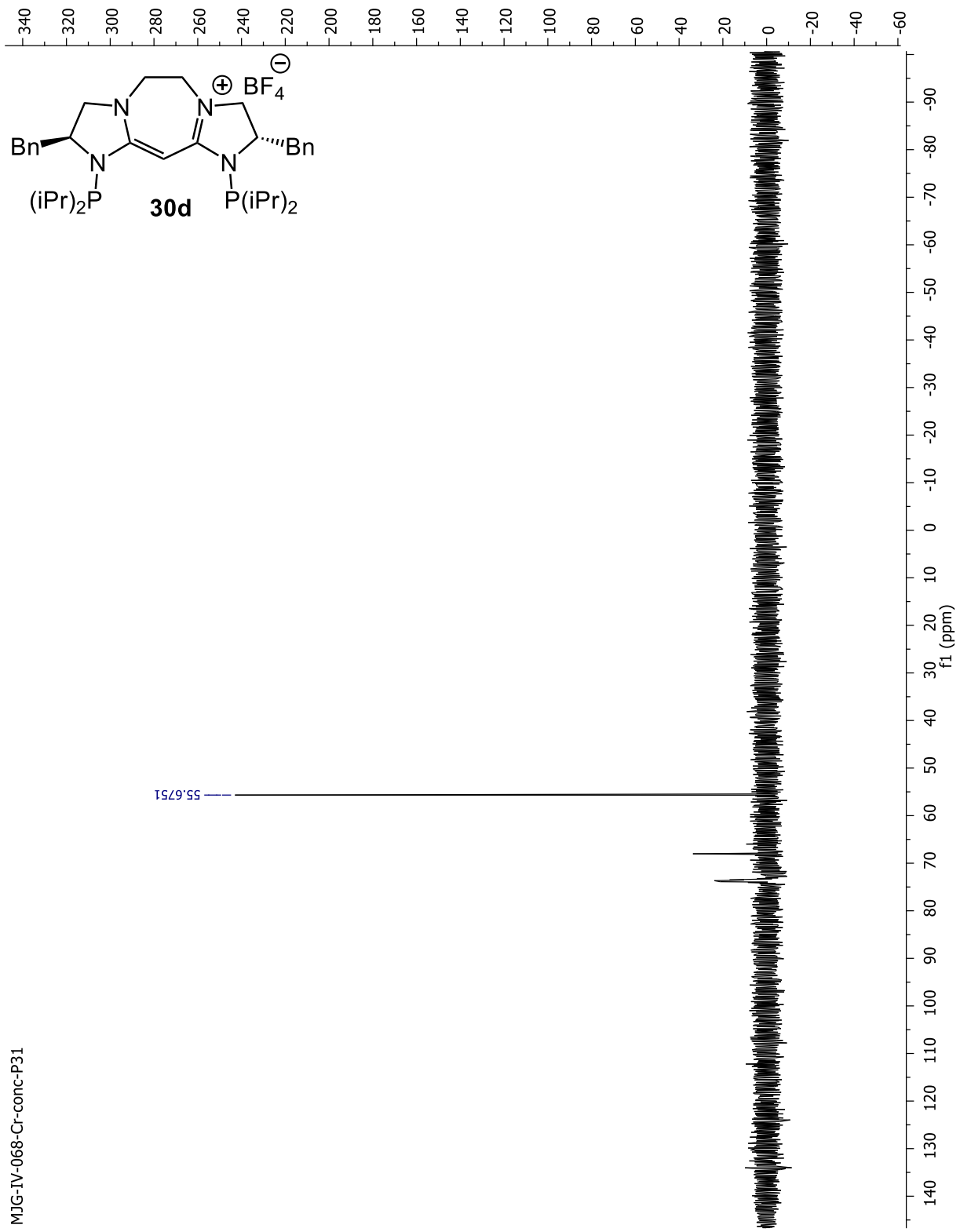
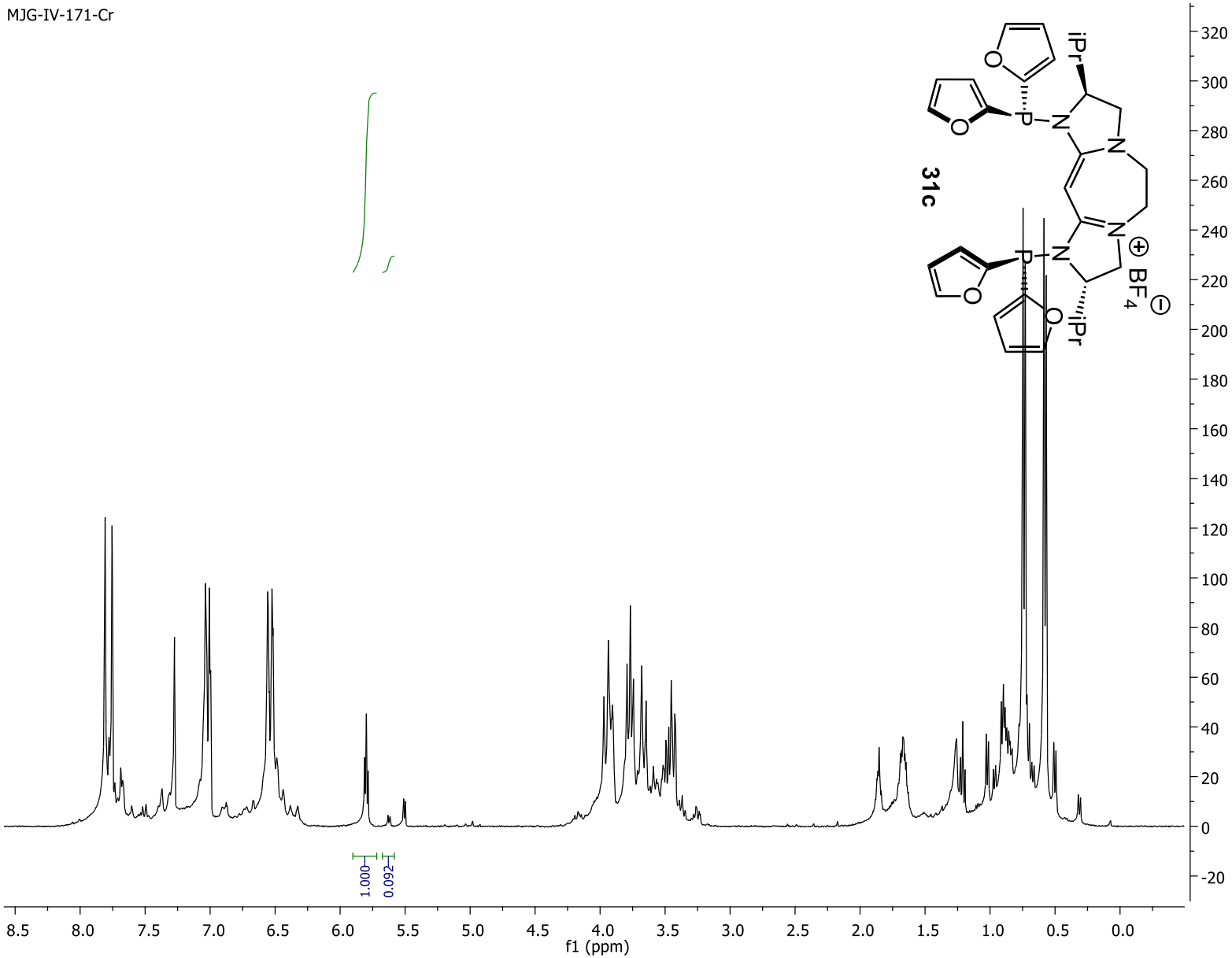
Me
Me
Ph2P
PPh2
BF4

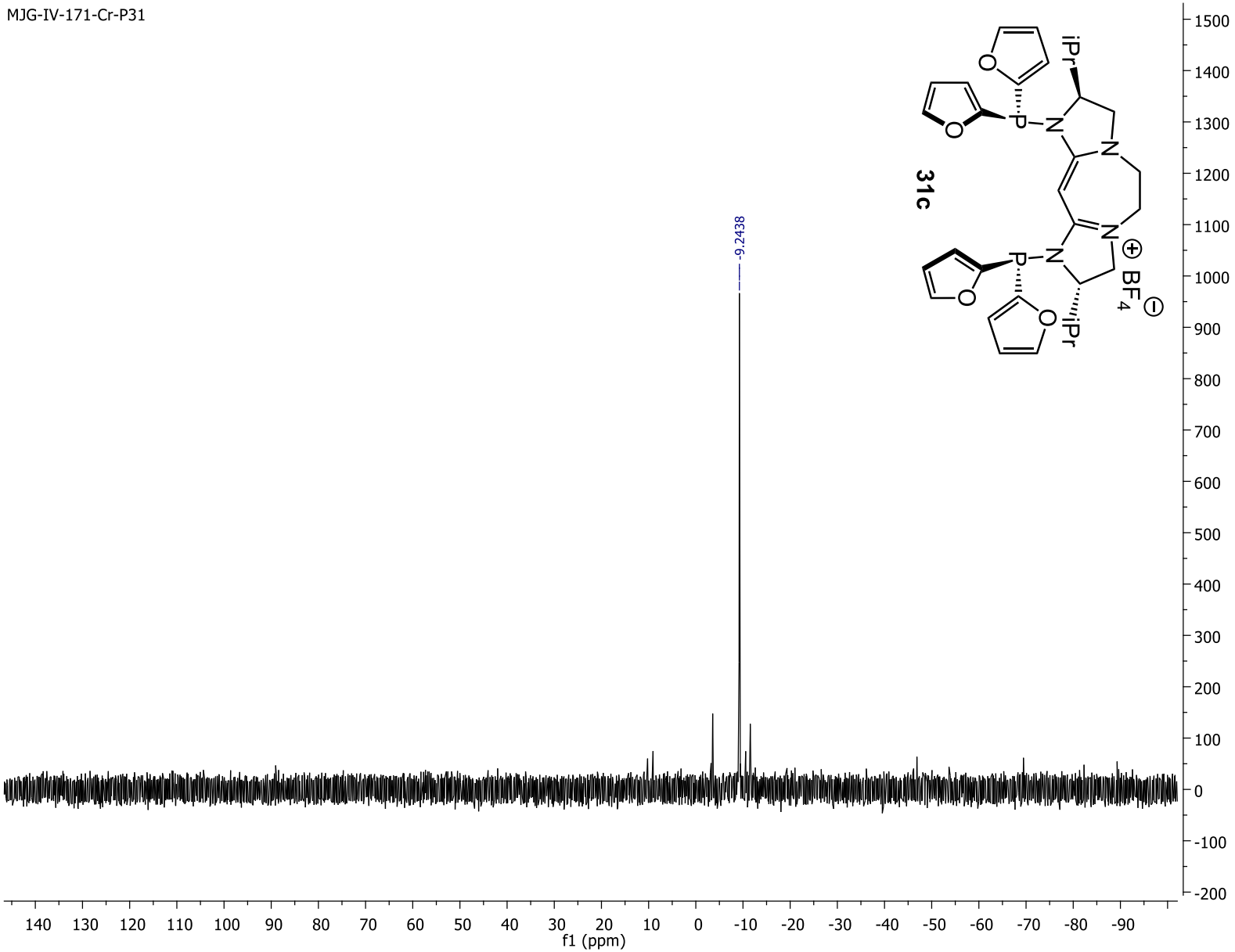

MJG-IV-068-DCMexposure
30d
f1 (ppm)

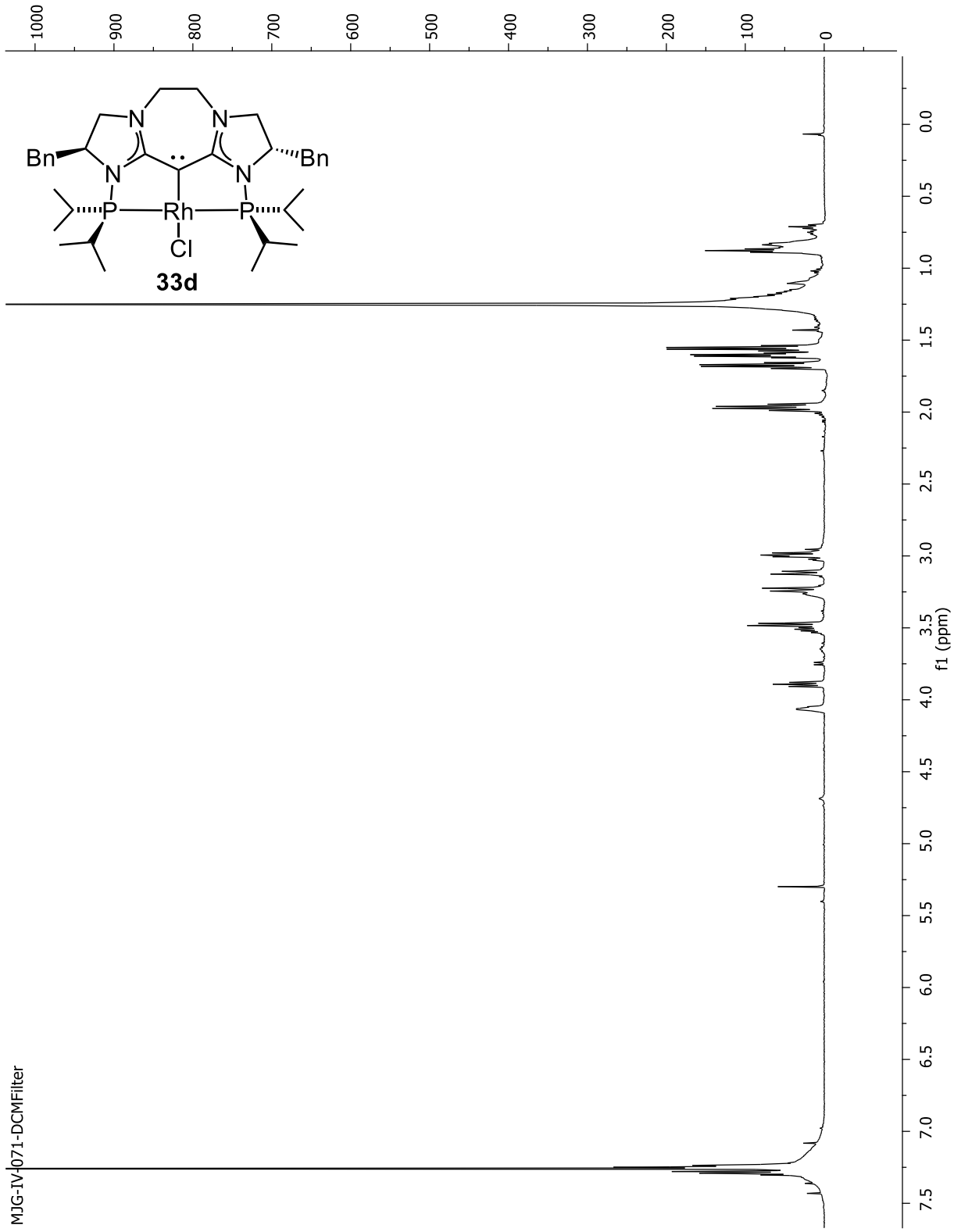

Bn
N
N
N
N
Bn
(iPr)2P
P(iPr)2
BF4
30d
55.6751
f1 (ppm)
MJG-IV-068-Cr-conc-P31

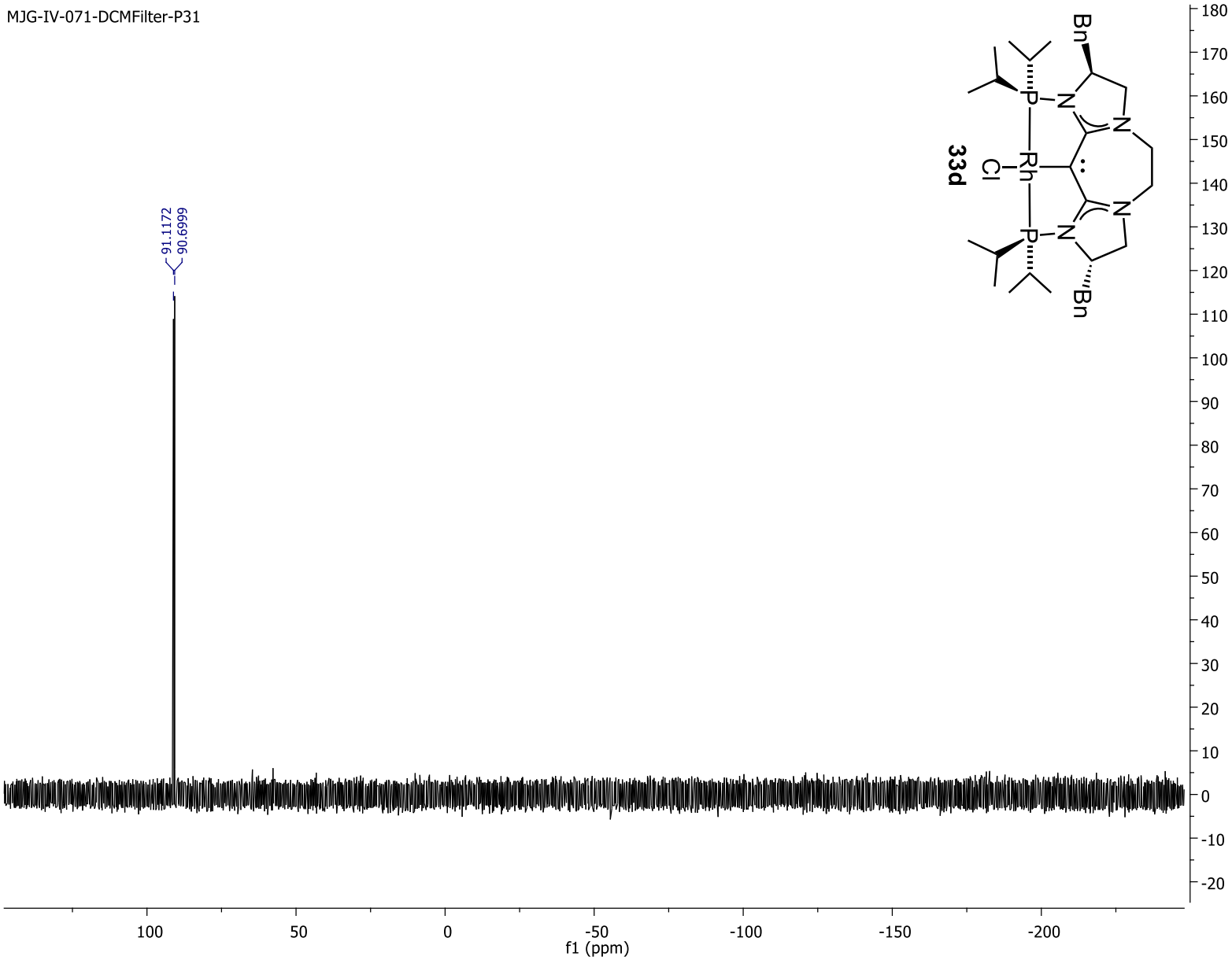
MJG-IV-171-Cr

31c




MJG-IV-171-Cr-P31
-9.2438
f1 (ppm)
31c


33d
Bn
Bn
N
N
N
N
P
Rh
P
Cl
MJG-IV-071-DCMFilter
f1 (ppm)


MJG-IV-071-DCMFilter-P31
91.1172
90.6999
f1 (ppm)
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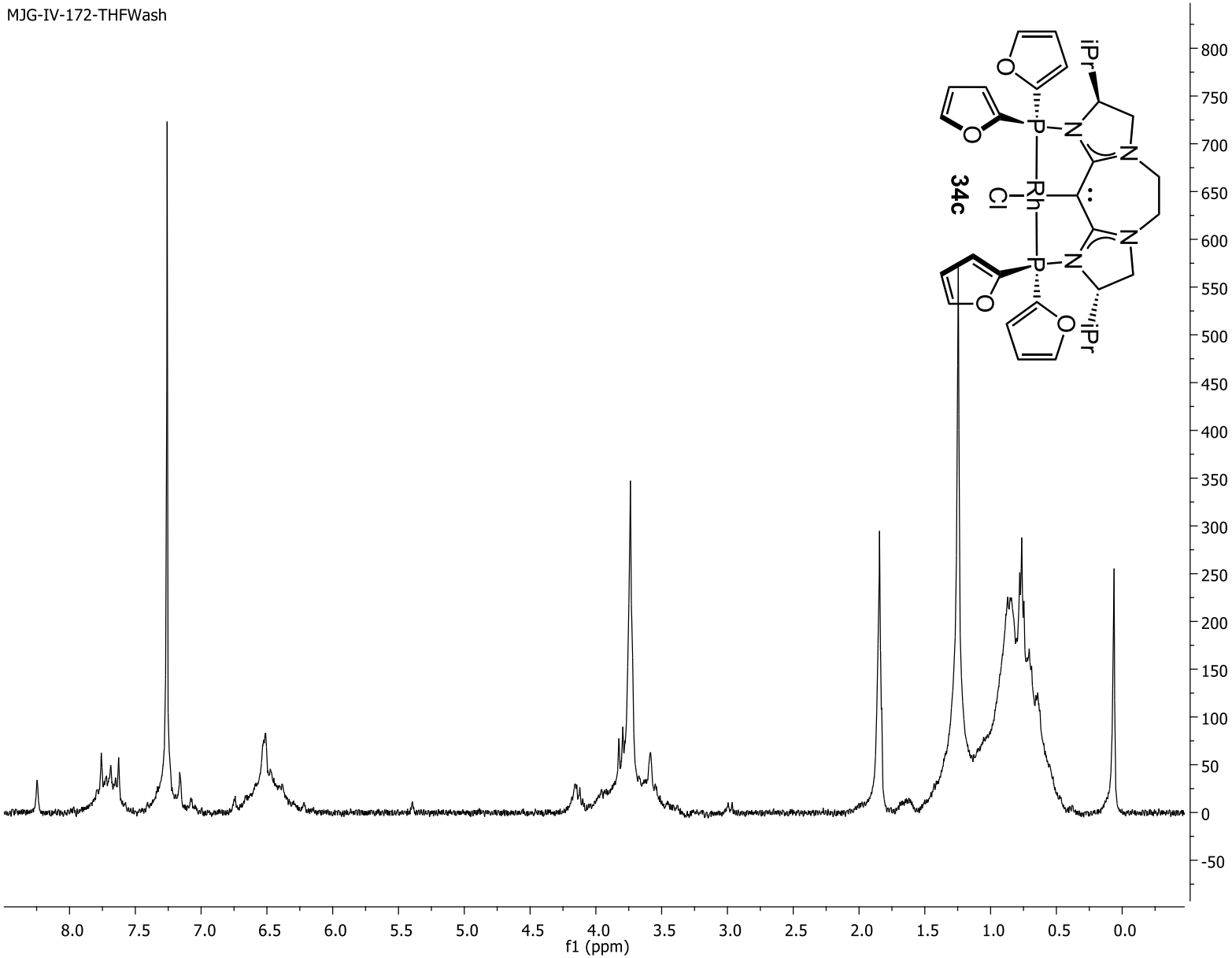
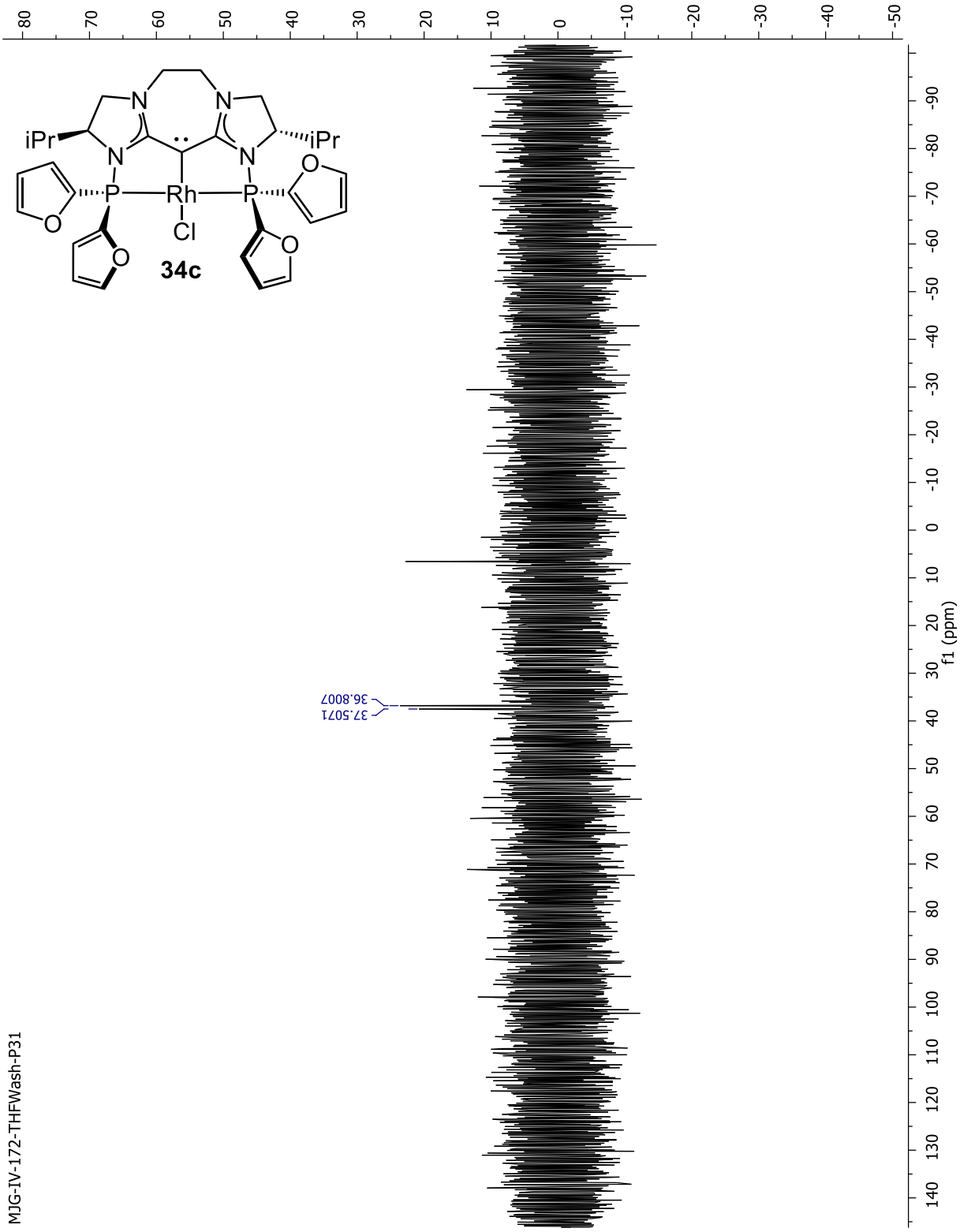
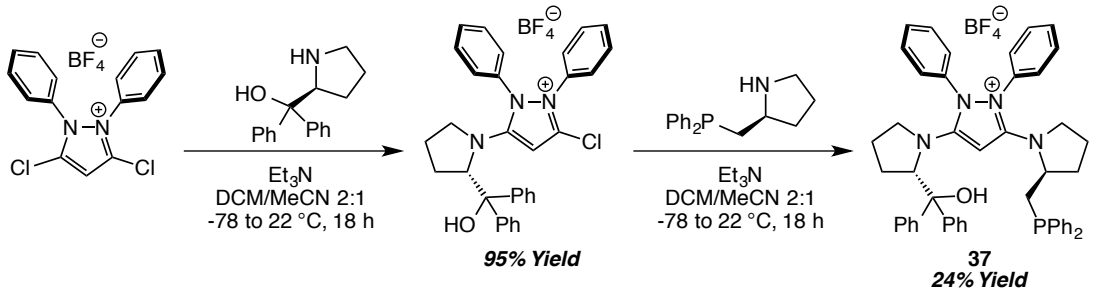
50
0
-50
-100
-150
-200
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Bn
Bn
N
N
N
N
P
P
Rh
Cl
33d


MJG-IV-172-THFWash
f1 (ppm)
34c


MJG-IV-172-THFWash-P31
34c
iPr
iPr
N
N
N
N
P
Rh
P
Cl
O
O
O
O
37.5071
36.8007
f1 (ppm)

Section 5.5: Enantioselective Hydrofunctionalization with a Chiral Tridentate Cyclic Bent Allene



Synthesis of 37

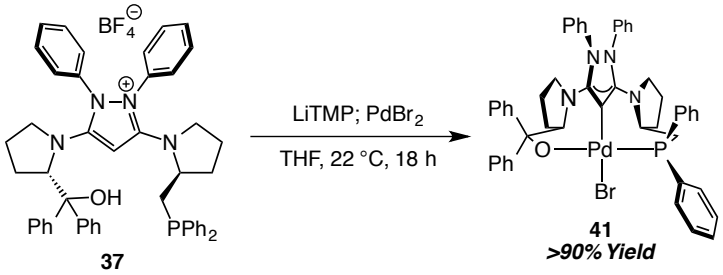
A dry flask with a stir bar was charged with 3,5-dichloro-1,2-diphenyl-1*H*-pyrazol-2-ium tetrafluoroborate (200 mg, 0.531 mmol) and (*S*)-diphenyl(pyrrolidin-2-yl)methanol (135 mg, 0.531 mmol) before being evacuated and backfilled with N_2. The reaction was solvated with dry DCM (4 mL) and benchtop MeCN (2 mL) before dry triethylamine (370 µL, 2.65 mmol) was added and the reaction allowed to stir at 22 °C for 18 h. The reaction was concentrated and the resulting solid purified by SiO_2 gel chromatography (40:1 $CHCl_3$/iPrOH to yield (*S*)-3-chloro-5-(2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-1,2-diphenyl-1*H*-pyrazol-2-ium tetrafluoroborate (301 mg, 0.504 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.24 (m, 20H), 6.11 (s, 1H), 5.08 (dd, *J* = 8.7, 2.2 Hz, 1H), 3.38 – 3.21 (m, 1H), 2.98 (bs, 1H), 2.60 – 2.36 (m, 1H), 2.04 – 1.89 (m, 1H), 1.79 (ddq, *J* = 17.6, 8.8, 4.3 Hz, 1H), 1.40 – 1.28 (m, 1H).

A dry 20 mL vial with a stir bar was charged with (*S*)-3-chloro-5-(2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-1,2-diphenyl-1*H*-pyrazol-2-ium tetrafluoroborate (100 mg, 0.168 mmol) and (*S*)-2-((diphenylphosphanyl)methyl)pyrrolidine (45.2 mg, 0.168 mmol) before being evacuated and backfilled with N_2. The reaction was solvated with dry DCM (4 mL) and benchtop MeCN (2 mL) before dry triethylamine (118 µL, 0.842 mmol) was added and the

reaction sealed under N_2. The reaction was heated to 80 °C and allowed to stir for 18 h before being cooled to room temperature, concentrated, and the resulting solid purified by SiO_2 gel chromatography (40:1 DCM/iPrOH to yield **37** (34 mg, 0.0403 mmol, 24% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.12 (m, 28H), 6.95 (t, *J* = 12.0 Hz, 2H), 6.85 (s, 2H), 4.81 (d, *J* = 6.7 Hz, 1H), 4.70 (s, 1H), 3.46 (s, 1H), 3.23 (tt, *J* = 18.4, 9.2 Hz, 1H), 3.13 (d, *J* = 16.0 Hz, 1H), 2.63 (d, *J* = 14.4 Hz, 3H), 2.36 (td, *J* = 17.9, 8.8 Hz, 1H), 2.11 (dt, *J* = 18.9, 9.5 Hz, 1H), 2.07 – 1.89 (m, 2H), 1.83 (dt, *J* = 17.0, 8.9 Hz, 5H), 1.55 – 1.41 (m, 1H). **^{31}P NMR** (162 MHz, $CDCl_3$) δ -23.50.



Synthesis of 41

An 8 mL vial with a stir bar in the dry box was charged with **37** (20 mg, 0.0242 mmol), and LiTMP (7.1 mg, 0.0484 mmol) before being solvated with THF (200 μL) and allowed to stir at 22 °C for 30 minutes. $PdBr_2$ (6.4 mg, 0.0242 mmol) was added to the solution and the reaction allowed to stir at 22 °C for 18 h. The reaction was triturated with Et_2O and plugged through Celite with excess Et_2O before being recovered by redissolving off the plug with THF. The THF solution was concentrated to provide **41** (22.2 mg, 0.0240 mmol, 99% yield).

^{1}H NMR (500 MHz, CD_3CN) δ 7.90 (d, *J* = 36.4 Hz, 2H), 7.77 (s, 2H), 7.57 (dd, *J* = 46.5, 21.3 Hz, 8H), 7.41 (s, 6H), 7.27 (dd, *J* = 28.6, 21.5 Hz, 6H), 7.12 – 6.98 (m, 6H), 5.84 (d, *J* = 44.1 Hz, 1H), 5.52 (d, *J* = 43.1 Hz, 1H), 3.22 – 2.94 (m, 4H), 2.83 (d, *J* = 12.7 Hz, 1H), 2.41 (d, *J* = 31.0

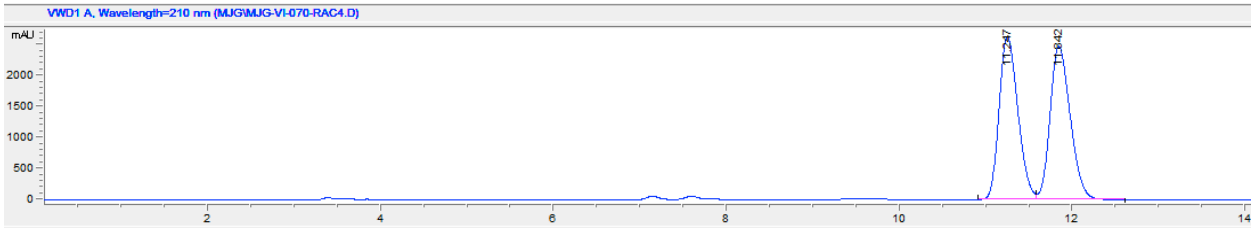
Hz, 1H), 2.31 (s, 1H), 2.24 (d, J = 3.9 Hz, 2H), 1.68 (dd, J = 15.6, 8.4 Hz, 2H), 1.32 (d, J = 21.2 Hz, 1H), 1.21 – 0.99 (m, 2H). **^{31}P NMR** (202 MHz, CD_3CN) δ 28.54.

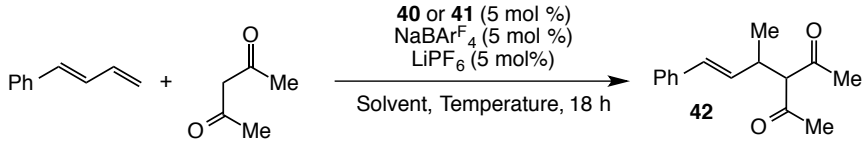
■ **General Procedure for Surveying Hydroalkylation with Chiral CBA Complexes 40, and 41 (Scheme 5.5.3-1)**

In a N_2 filled dry box, an 8 mL vial with a stir bar was charged with **38**, **40**, or **41** (0.005 mmol, 5 mol%), the listed Lewis acid (0.005 mmol, 5.0 mol%), $NaBAr^F_4$ (4.4 mg, 0.005 mmol, 5 mol%), and 1,3-phenylbutadiene (13 mg, 0.1 mmol). The reagents were solvated with the listed solvent (200 μL, [ ] = 0.5 M) and the reaction was sealed with a Teflon® lined septum cap before being removed from the dry box and allowed to stir at room temperature for 10 minutes. Outside the dry box sparged 2,4-pentanedione (10 mg, 0.1 mmol) was added under N_2 via syringe. The reaction was heated to 50 °C and allowed to stir for 18 hours before being allowed to cool to room temperature and an aliquot taken to determine the conversion by ^{1}H NMR using hexamethyldisiloxane as an internal standard. The NMR sample was recovered and the solvent evaporated before the products were purified by SiO_2 column chromatography (4:1 Hex/Et_2O) to provide **42** in the listed yield. A pure sample was then assayed on an Agilent 1220 LC System with a Daicel ChiralPak IC column (98:2 Hexanes/isopropanol, 1 mL/min, 210 nm) to determine the listed enantiomeric excess.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 4H), 7.24 – 7.20 (m, 1H), 6.44 (d, J = 15.8 Hz, 1H), 5.99 (dd, J = 15.8, 8.6 Hz, 1H), 3.69 (d, J = 10.4 Hz, 1H), 3.25 – 3.16 (m, 1H), 2.23 (s, 3H), 2.13 (s, 3H), 1.08 (d, J = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.62, 203.53, 136.77, 130.97, 130.95, 128.58, 127.59, 126.24, 75.65, 37.90, 30.04, 29.75, 18.88.

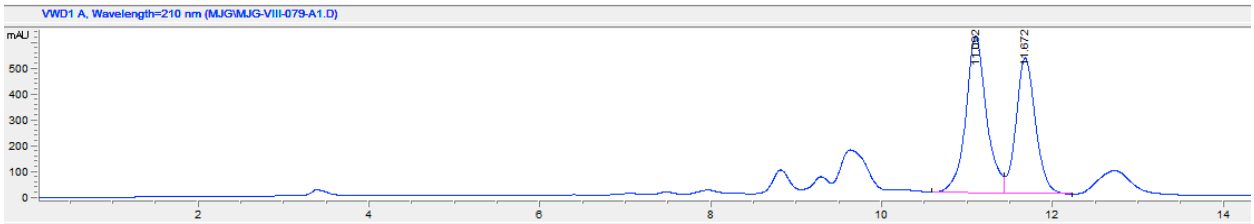
Racemic Trace:



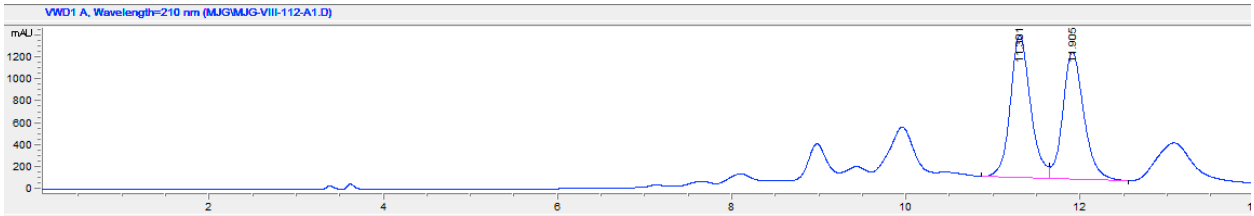


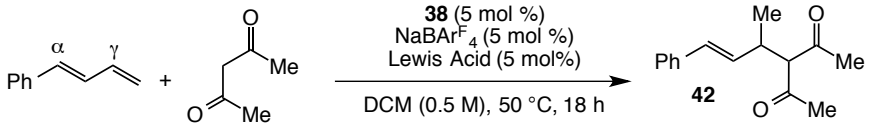
Entry	Catalyst	Solvent; M	Temp (°C)	Yield (%)	%ee
1	**40**	THF; 0.5	22	45	9
2	**41**	Et_2O; 0.5	50	13	3

Entry 1: Catalyst 40, THF, 22 °C



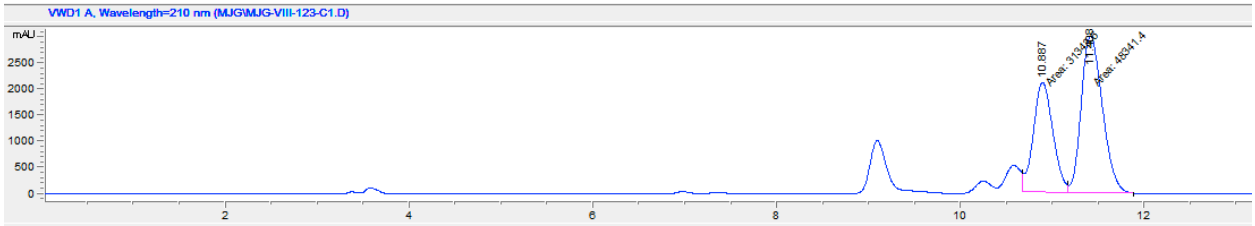
Entry 2: Catalyst 41, Et_2O, 50 °C



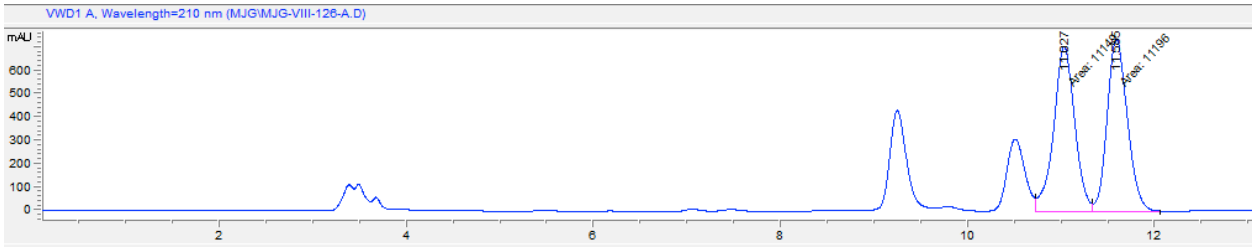


Entry	Lewis Acid; mol%	Yield (%)	γ:α	%ee
1	$LiBAr^F{}_4$; 5	67	1:1	22
2	$LiBF_4$; 5	53	3:1	0
3	$LiPF_6$; 5	34	2:1	-8
4	CuCl; 5	26	2:1	-23
5	AuCl; 5	16	1:1	-13
6	AgCl; 5	32	2:1	0

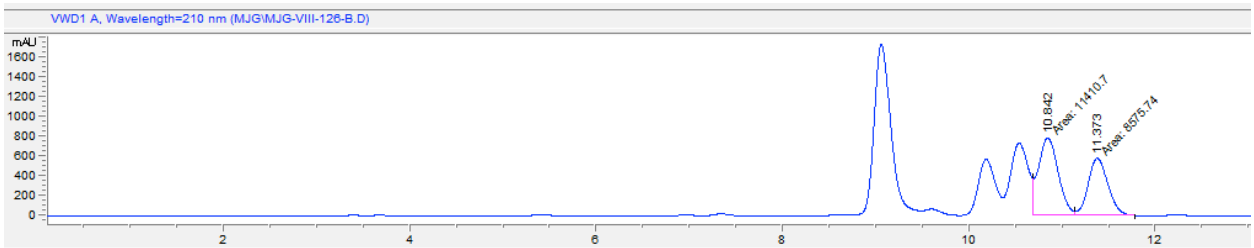
Entry 1: Catalyst 38, $LiBAr^F{}_4$



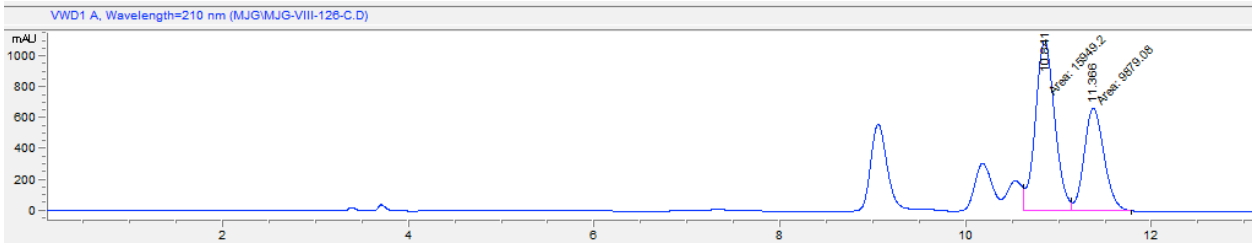
Entry 2: Catalyst 38, $LiBF_4$



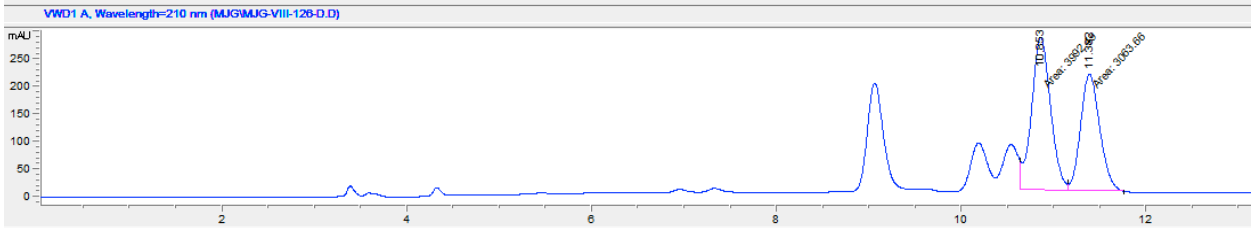
Entry 3: Catalyst 38, $LiPF_6$



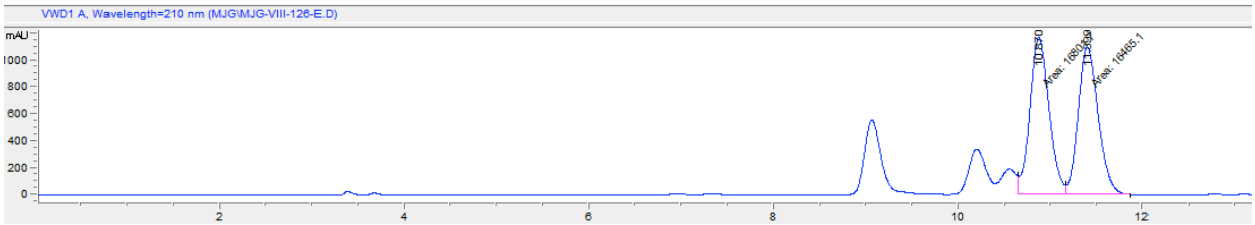
Entry 4: Catalyst 38, CuCl

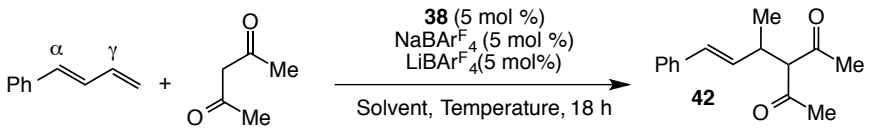


Entry 5: Catalyst 38, AuCl



Entry 6: Catalyst 38, AgCl

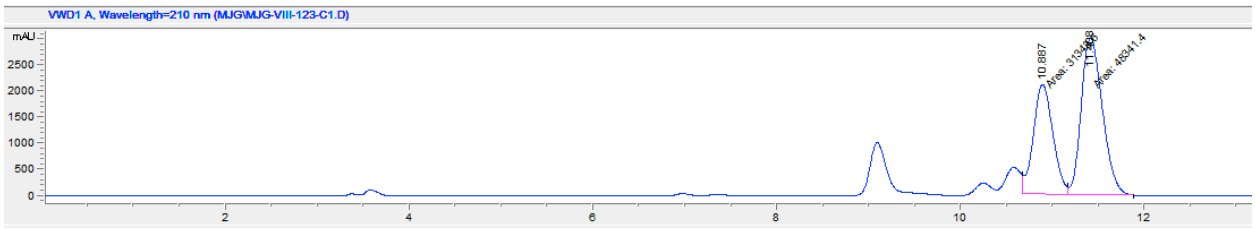




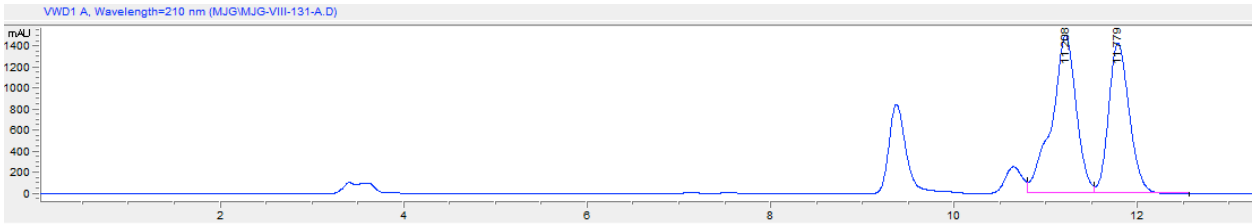
Entry	Solvent; M	Temp (°C)	Yield (%)	γ:α	%ee
1	DCM; 0,5	50	67	1:1	22
2	Et_2O; 0.5	50	40	2:1	<5
3	PhCl; 0.5	50	34	2:1	15
4	$CHCl_3$; 0.5	50	0	-	-
5	PhMe; 0.5	50	50	2:1	9
6	DCM; 0.5	22	15	2:1	10
7	DCM; 0.1	50	45	2:1	50
8	DCM; 0.05	50	33	5:1	55
9[a]	DCM; 0.05	50	31	2:1	60

[a] Reaction was run with 2 equiv of 1,3-phenylbutadiene.

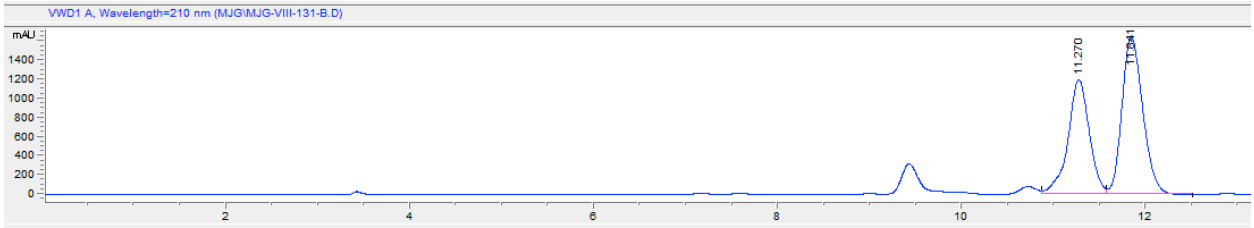
Entry 1: Catalyst 38, DCM; 0.5 M, 50 °C



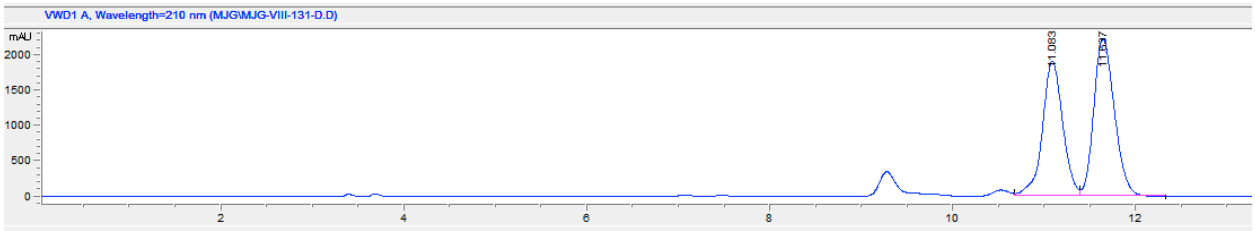
Entry 2: Catalyst 38, Et_2O; 0.5 M, 50 °C



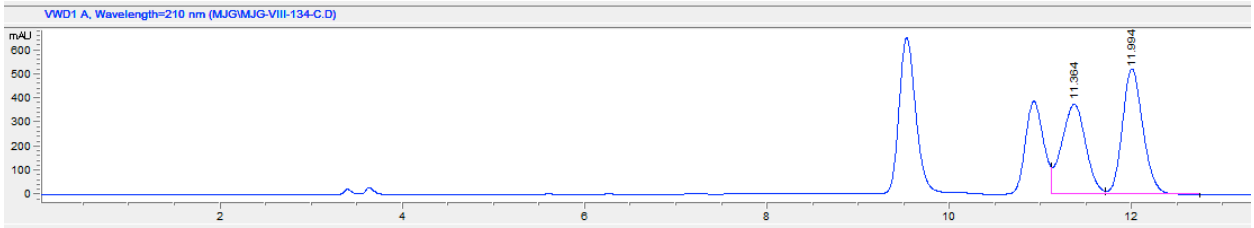
Entry 3: Catalyst 38, PhCl; 0.5 M, 50 °C



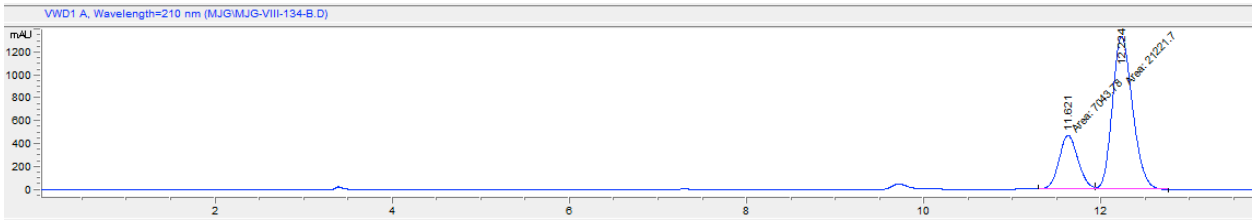
Entry 5: Catalyst 38, PhMe; 0.5 M, 50 °C



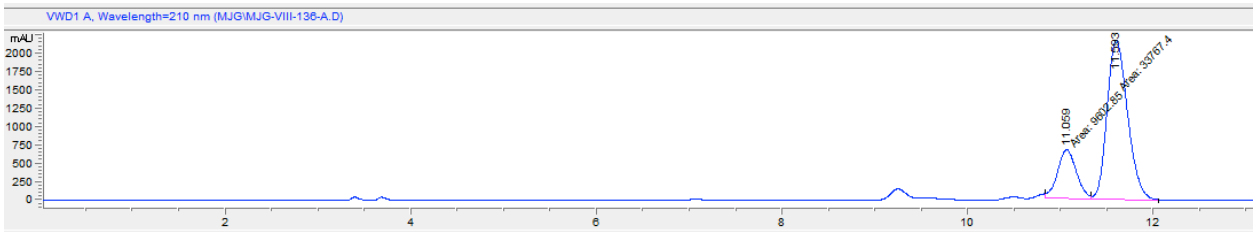
Entry 6: Catalyst 38, DCM; 0.5 M, 22 °C



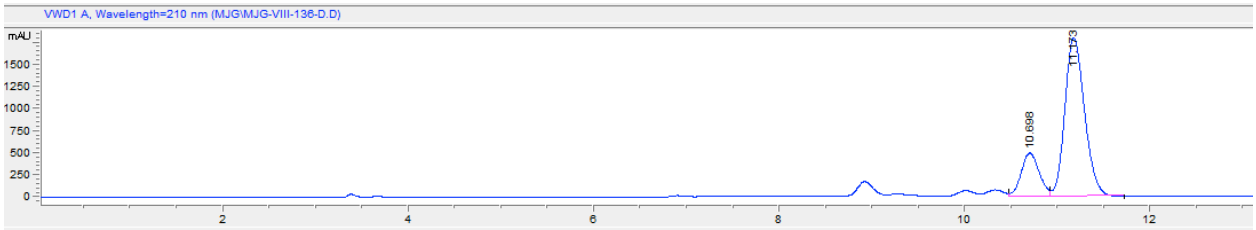
Entry 7: Catalyst 38, DCM; 0.1 M, 50 °C

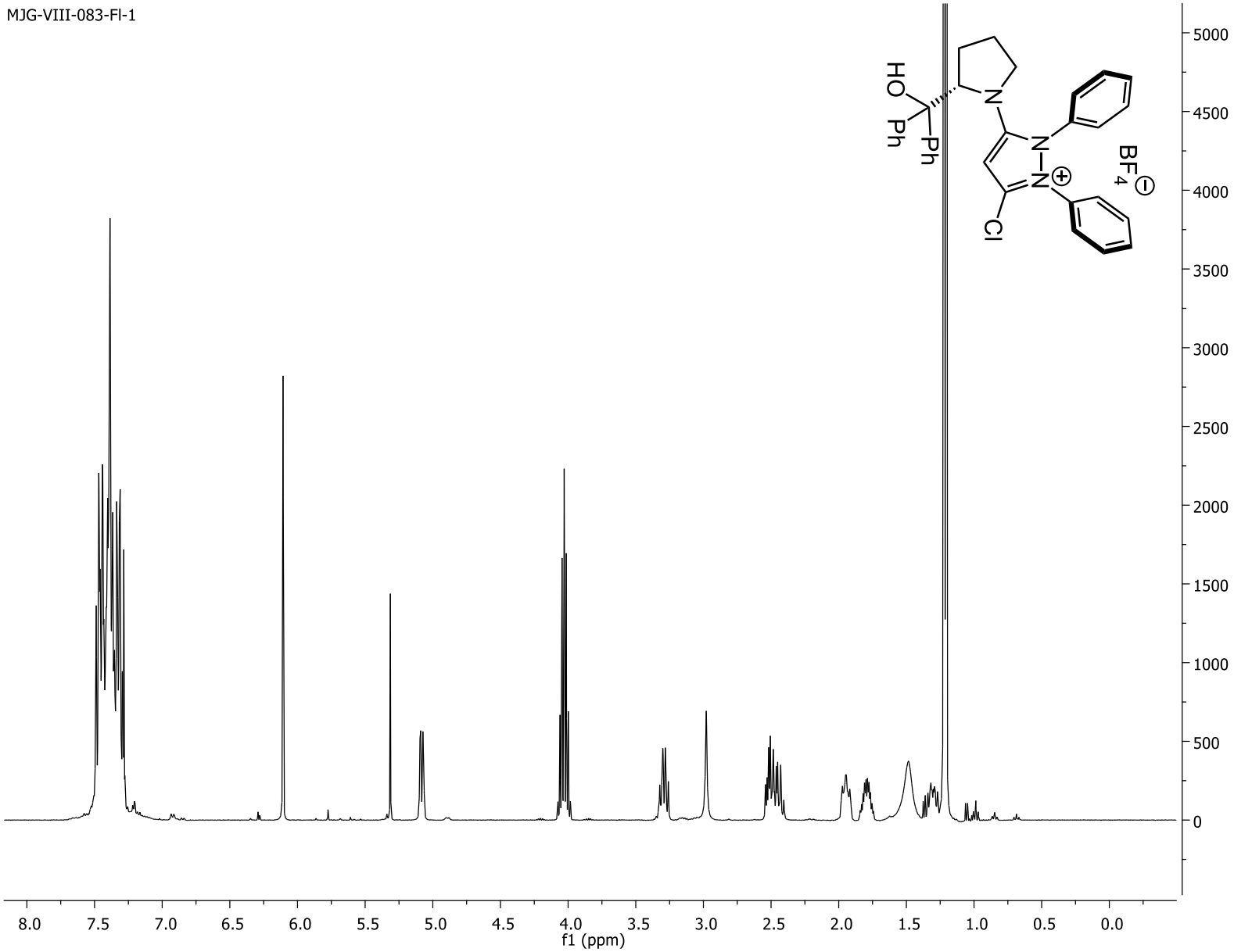


Entry 8: Catalyst 38, DCM; 0.05 M, 50 °C



Entry 9: Catalyst 38, DCM; 0.05 M, 50 °C, 2 equivalents 1,3-phenylbutadiene




MJG-VIII-083-Fl-1
f1 (ppm)
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5000
4500
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3500
3000
2500
2000
1500
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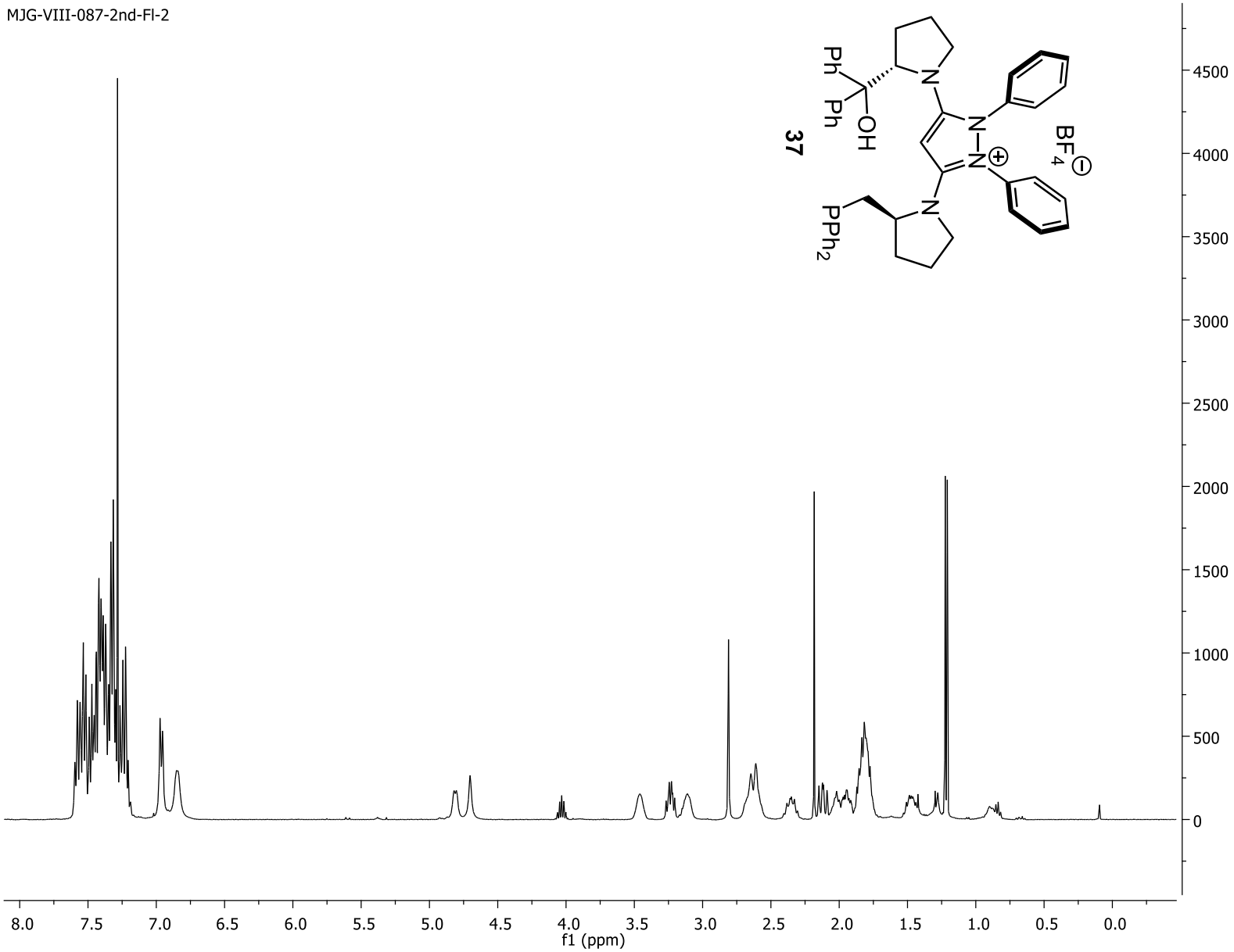
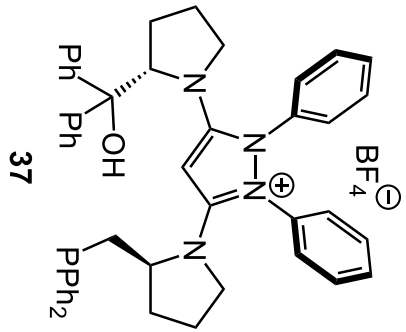
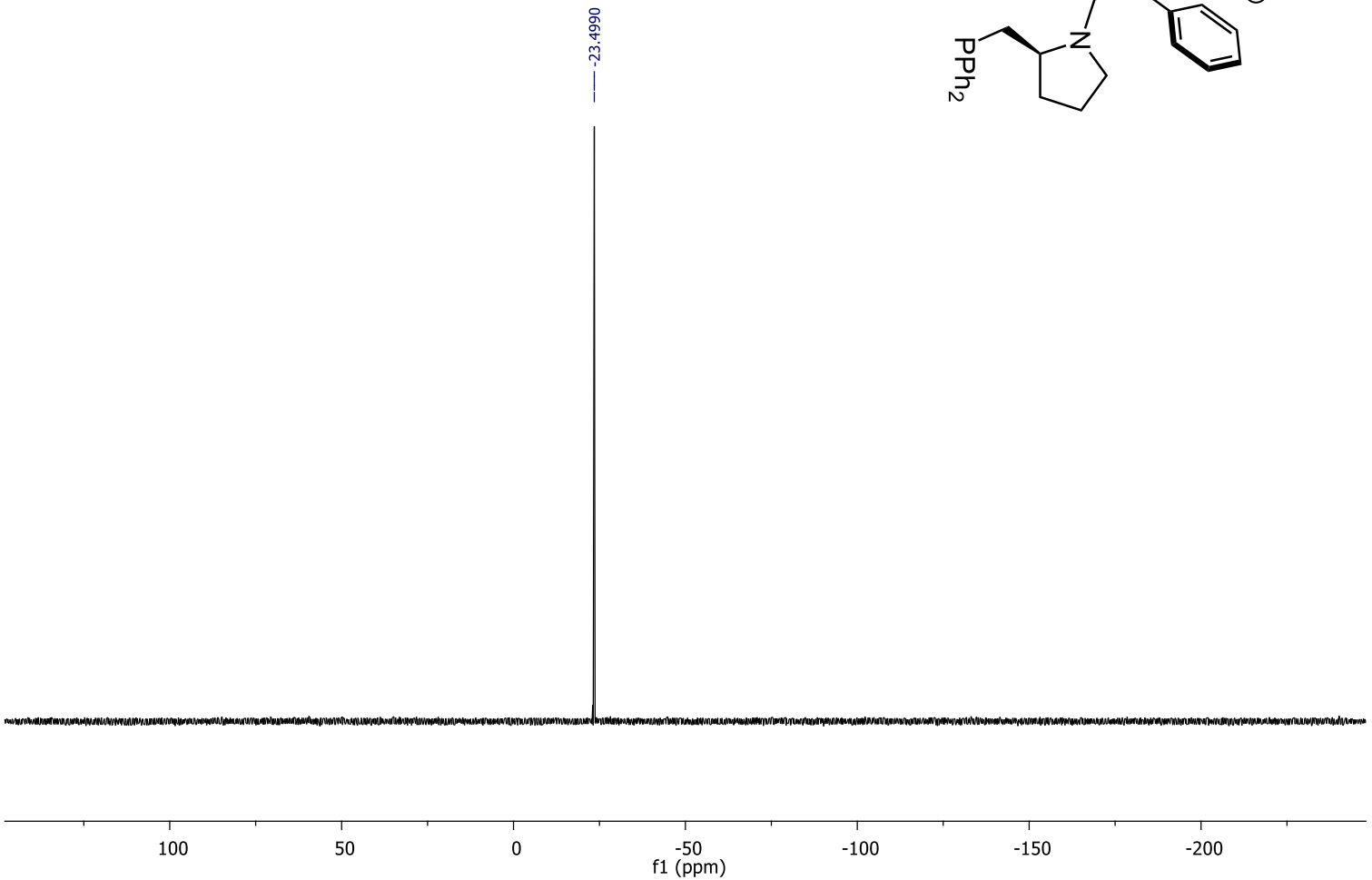
500
0
N
N
N
Cl
BF4
HO
Ph
Ph

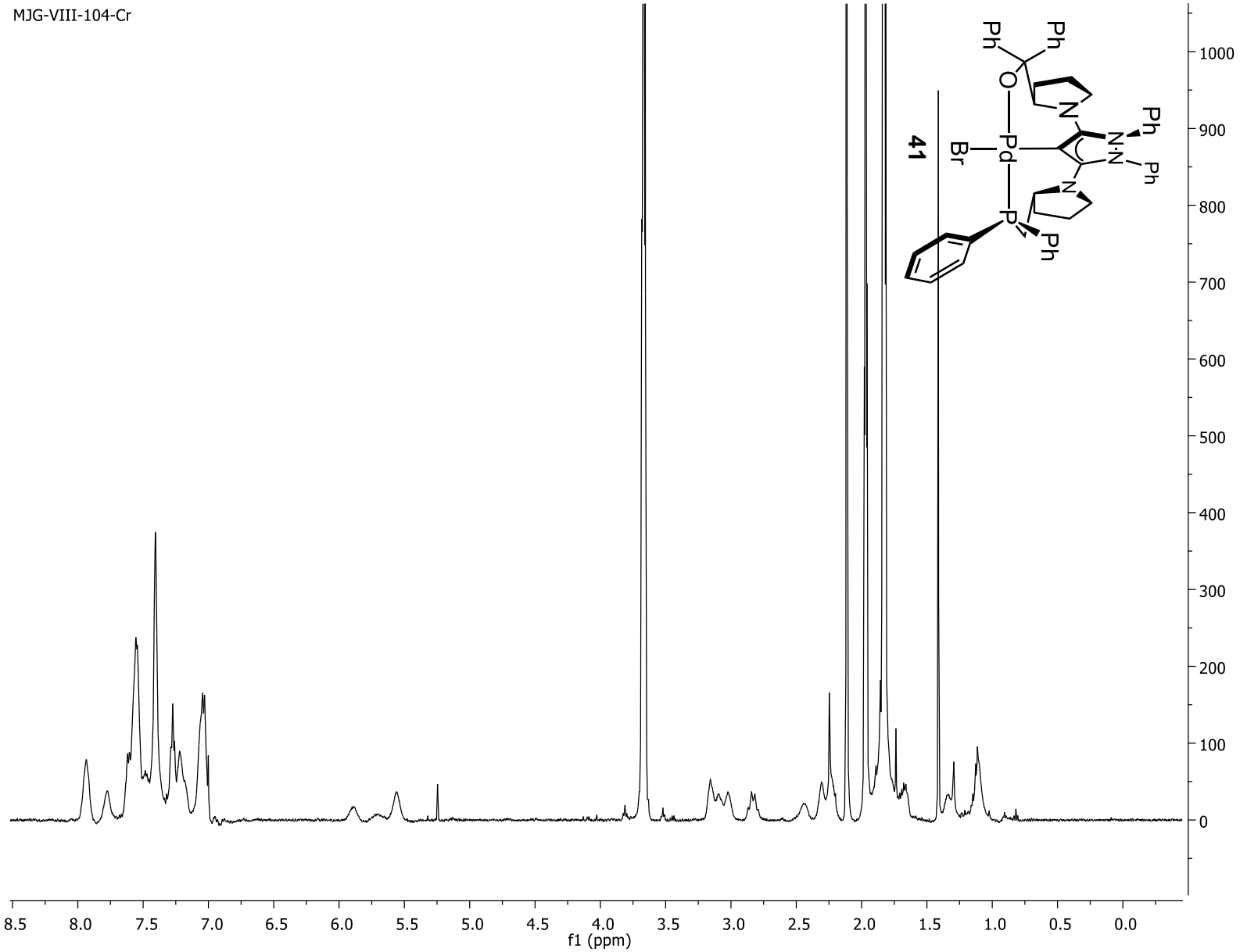

MJG-VIII-087-2nd-Fl-2
37
f1 (ppm)

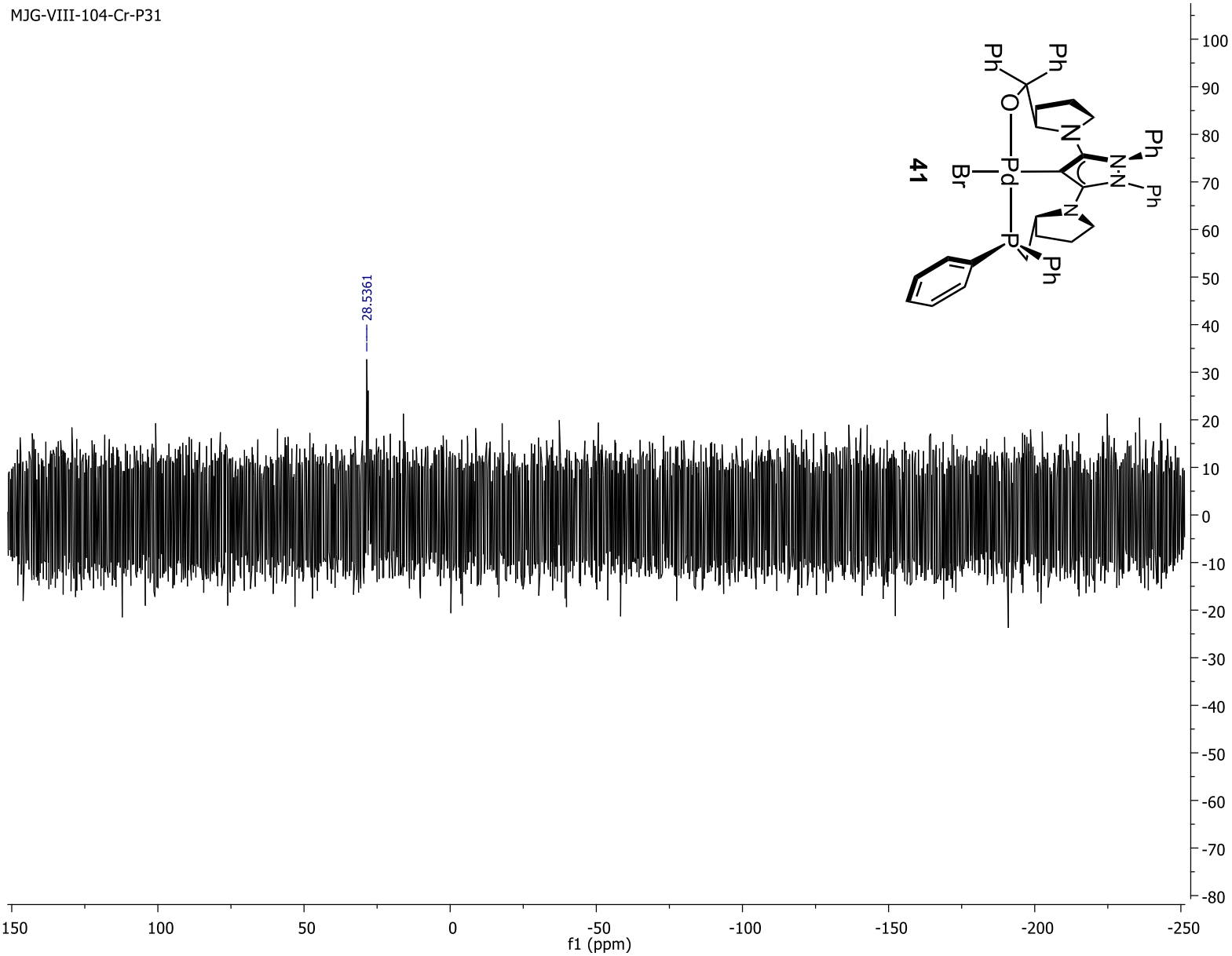
MJG-VIII-087-2nd-Fl-2-P31



37




MJG-VIII-104-Cr
41
f1 (ppm)


MJG-VIII-104-Cr-P31
28.5361
f1 (ppm)
41