Nickel Precatalysts as Enabling Tools for Catalytic Coupling Reactions

by

Eric A. Standley

B.S. Chemistry, *magna cum laude*
B.A. German, *magna cum laude*
Boise State University, 2010

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Signature of Author Signature redacted
Department of Chemistry
January 12th, 2015

Certified by Signature redacted
Timothy F. Jamison
Professor of Chemistry
Thesis Supervisor

Accepted by Signature redacted
Robert W. Field
Chairman, Department Committee on Graduate Students

This doctoral thesis has been examined by a committee in the Department of Chemistry as follows:

Professor Stephen L. Buchwald _____ Signature redacted _____
Chairman

Professor Timothy F. Jamison _____ Signature redacted _____
Thesis Supervisor

Professor Timothy M. Swager _____ Signature redacted _____

For Abby and my family

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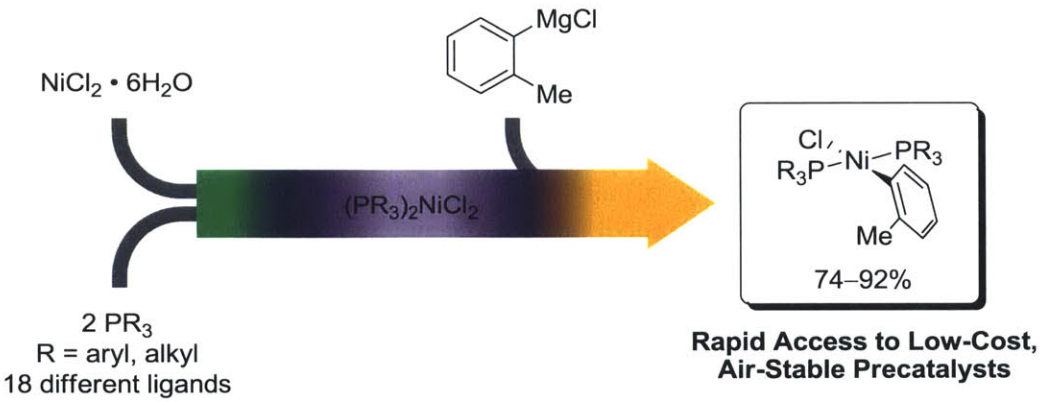
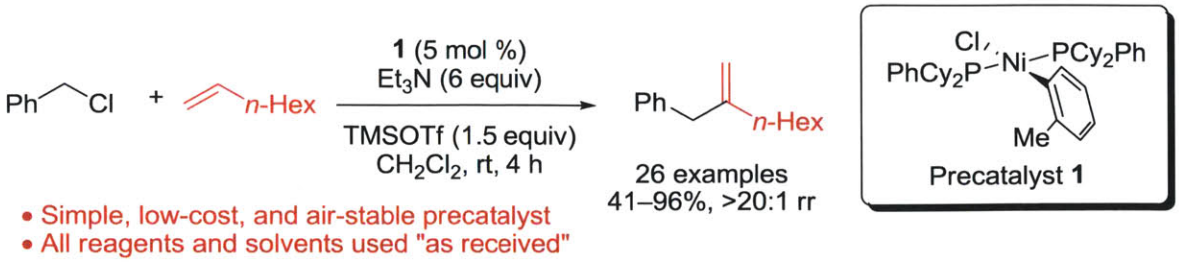
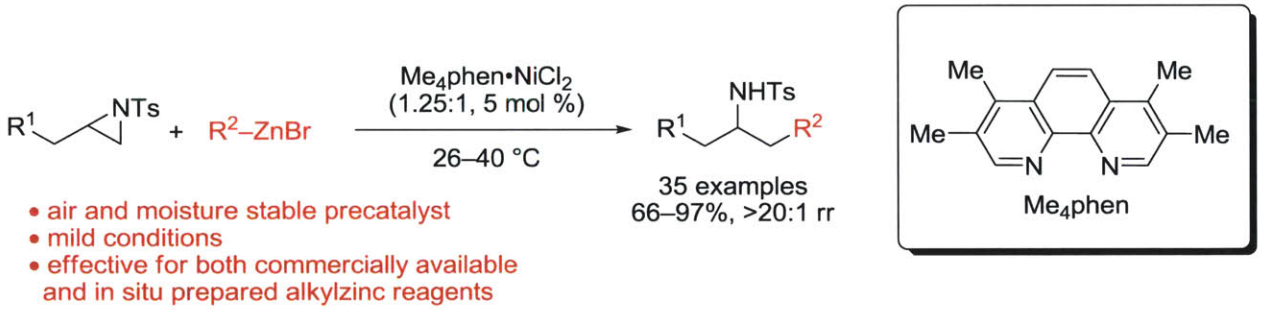
ABSTRACT



A series of air-stable nickel complexes of the form $L_2Ni(aryl)X$ (L = monodentate phosphine, X = Cl, Br) and LNi(aryl)X (L = bis-phosphine) have been synthesized and are presented as a library of precatalysts suitable for a wide variety of nickel-catalyzed transformations. These complexes are easily synthesized from low-cost $NiCl_2 \cdot 6H_2O$ or $NiBr_2 \cdot 3H_2O$ and the desired ligand followed by addition of 1 equiv of Grignard reagent. A selection of these complexes were characterized by single-crystal X-ray diffraction, and an analysis of their structural features is provided.



The air-stable nickel(II) complex *trans*-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$ was employed as a precatalyst for the Mizoroki–Heck-type, room temperature, internally selective coupling of substituted benzyl chlorides with terminal alkenes. This reaction, which employs a terminal alkene as an alkenylmetal equivalent, provides rapid, convergent access to substituted allylbenzene derivatives in high yield and with regioselectivity greater than 95:5 in nearly all cases. The reaction is operationally simple, can be carried out on the benchtop with no purification or degassing of solvents or reagents, and requires no exclusion of air or water during setup. Synthesis of the precatalyst is accomplished through a straightforward procedure that employs inexpensive, commercially available reagents, requires no purification steps, and proceeds in high yield.



The nickel-catalyzed cross-coupling of aliphatic *N*-tosylaziridines with aliphatic organozinc reagents is described. The reaction protocol displays complete regioselectivity for reaction at the less hindered C–N bond, and the products are furnished in good to excellent yield for a broad selection of substrates. An air-stable nickel(II) chloride/ligand precatalyst was also developed and employed for the reaction. In addition to increasing the activity of this catalyst system, this also greatly improves the practicality of this reaction, as the use of the very air-sensitive $Ni(cod)_2$ is avoided. Finally, mechanistic investigations, including deuterium-labeling studies, show that the reaction proceeds with overall inversion of configuration at the terminal position of the aziridine by way of aziridine ring opening by Ni (inversion), transmetallation (retention), and reductive elimination (retention).

Thesis Supervisor: Timothy F. Jamison

Title: Professor of Chemistry

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Simplifying Nickel(0) Catalysis: An Air-Stable Nickel Precatalyst for the Internally Selective Benzylation of Terminal Alkenes

Standley, E. A. and Jamison, T. F. *J. Am. Chem. Soc.* **2013**, *135*, 1585–1592. DOI: 10.1021/ja3116718. Copyright © 2013 American Chemical Society.

All synthetic work was carried out by EAS. PM carried out the single-crystal X-ray diffraction experiments, including both data collection and data analysis. PM compiled the experimental details and data tables included in the experimental section. Thermal ellipsoid plots were generated by EAS.

A Broadly Applicable Strategy for Entry into Homogeneous Nickel(0) Catalysts from Air-Stable Nickel(II) Complexes

Standley, E. A.; Smith, S. J.; Müller, P; Jamison, T. F. *Organometallics* **2014**, *33*, 2012–2018. DOI: 10.1021/om500156q. Copyright © 2014 American Chemical Society.

All synthetic work was carried out by EAS. SJS and PM carried out the single-crystal X-ray diffraction experiments, including both data collection and structure refinement. PM compiled the experimental details and data tables included in the experimental section. Thermal ellipsoid plots were generated by EAS.

Recent Advances in Homogeneous Nickel Catalysis

Tasker, S. Z.[‡]; Standley, E. A.[‡]; Jamison, T. F. *Nature* **2014**, *509*, 299–309. DOI: 10.1038/nature13274. Copyright © 2014 Nature Publishing Group.

EAS, SZT, and TFJ worked together to outline the content, which was written by EAS and SZT. Revisions were carried out jointly between EAS and SZT under TFJ's guidance.

Highly Regioselective Nickel-Catalyzed Cross-Coupling of N-Tosylaziridines and Alkylzinc Reagents

Jensen, K. L.; Standley, E. A.; Jamison, T. F. *J. Am. Chem. Soc.* **2014**, *136*, 11145–11152. DOI: 10.1021/ja505823s. Copyright © 2014 American Chemical Society.

KLJ determined initial conditions for the coupling reaction and synthesized the majority of starting aziridines. Reaction optimization, screening, and scope were carried out jointly between EAS and KLJ. The precatalyst synthesis methods were devised and carried out by EAS. Organozinc reagents were mostly synthesized by KLJ. Synthesis of the deuterium-labeled substrates was carried out by EAS. NMR analysis (NOE and 2D experiments) was carried out with the assistance of Dr. Jeff Simpson (Director, MIT Department of Chemistry Instrumentation Facility) and spectra were interpreted, annotated, and tabulated by EAS. Metallacycles (azanickelacyclobutanes) were synthesized and characterized by EAS. Stoichiometric mechanistic experiments were carried out by KLJ. Sulfonamide deprotection studies were carried out by KLJ.

[‡]These authors contributed equally to this work.

Acknowledgements

"The good life is one inspired by love and guided by knowledge."
Bertrand Russell in *What I Believe*, 1925.

My experience as a graduate student turned out to be as close to the ideal experience as I imagine is possible, and it is important to me that I fully and publicly thank those people who believed in me, encouraged me, and helped me to get to where I am now.

My passion for chemistry was first nurtured by my eighth grade physical science teacher, Mrs. Stafford. Later, in high school, I was fortunate to have an incredible set of teachers who supported my love for science: Mr. Brooks (earth science), Mrs. Foss (chemistry), Mr. Slaughter (math), Mr. Hills (math and computer science), and Mr. Antonini (physics). It was with their guidance that I really began to believe that a career in science and teaching was for me, and so I owe these six mentors and teachers my deepest gratitude.

Later, my undergraduate research advisors, Prof. Don Warner and Prof. Eric Brown, both provided me with wisdom, encouragement, and patience during the years of my undergraduate education. I am particularly indebted to Don for giving me the opportunity to carry out research in his lab while I was still in high school. It takes a certain leap of faith to trust a high school student to have the maturity to carry out research, and there were times when I lacked the requisite maturity, but Don believed in me anyway. During my first six months in his lab, he and (now Dr.) Tyler Wilson introduced me to the way of synthesis and showed me why synthetic chemistry is so powerful, exciting, and valuable. Later in my career, Eric took me into his lab to study bioinorganic chemistry. Although I did not work in her laboratory, I also wish to thank Dr. Dale Russell, who taught several courses to me and further fueled my interest in analytical and instrumental techniques, especially in regard to understanding instrumental analysis methods at the deepest, physical level. That education has helped me on many occasions during my graduate career, and I imagine it will continue to serve me well.

One other extremely influential professor during my undergraduate education, whom I would also like to thank, was Prof. Beret Norman, who taught many of the German courses I took at Boise State. Thanks in part to her guidance, I ended up choosing to obtain a degree in German, which turned out to be one of the best decisions of my life. Indeed, I briefly considered going to graduate school to study Germanic linguistics before making my final decision to further peruse chemistry.

I owe my deepest thanks and gratitude to Tim for his support, guidance, advice, and friendship. The Jamison lab is an outstanding place in which to do science, and that ultimately stems from the culture that Tim has set.

During the Spring of 2010, while visiting graduate schools as a prospective student, I struggled to identify differentiating features in each of the schools that would convince me a particular school would be the right place for me. My visit to MIT in March 2010 changed that, because during that visit I met Prof. Timothy Jamison. The first day of the visit day at MIT convinced me to come here for graduate school, and that was, overwhelmingly, because of my interaction with Tim. I have never once regretted that decision.

In addition to thanking the entire Jamison group, I need to give specific thanks to several members of the lab: Dr. Chris Morten for welcoming me to the group, even before I officially joined. Prof. Dr. Ryosuke Matsubara for mentoring me when I first joined the group and for giving me my introduction to using the glovebox and handling air-sensitive nickel complexes.

Prof. Dr. Jeff Byers for his mentorship and advice. Kurt Armbrust for many years of advice, lending me his sympathetic ear, and lunches at Momogoose food truck. Toma Halkina, who, thanks to her delightful company in my lab bay, has been a huge factor in keeping me sane during marathon lab sessions. Finally, all of my colleagues over the years who also investigated nickel chemistry: Dr. Alicia Gutierrez, Dr. Wonsuk Kim, Dr. Matthew Beaver, Dr. Alba Millán Delgado, Yury Minko, Edwin Winkler, Dennis Ulsøe Nielsen, and most recently Jessica Weber, my protégé-in-the-making.

Missing from the above list of "nickel people" are Sarah Tasker and Dr. Kim Lebek Jensen. I owe both of them so much for their hard work and dedication on the projects on which we collaborated. These collaborations were scientifically fulfilling, educational, and productive. I additionally owe my gratitude to my collaborators in the MIT X-Ray facility, Dr. Peter Müller and Dr. Stacey Smith, both of whom solved numerous crystal structures for me.

One of my greatest accomplishments outside of lab, completing the 2014 Timberman 70.3 triathlon, was only possible thanks to the inspiration and support of my fellow triathletes, whom I want to thank: Beth Kelley (particularly for her and her parents' hospitality in New Hampshire), Dr. Matt Katcher, Andy McTeague, Dr. Kim Jensen, and, and Dr. Adam Brown.

Outside of the Jamison lab, a very influential mentor has been Prof. Steve Buchwald, who has also served as my thesis chair. For his guidance in this role, I am extremely grateful. Early in my graduate career, as I was first making progress with cod-free precatalysts, Steve suggested investigating the air-stable arylnickel complexes that ultimately turned into a large portion of my doctoral work. On this note, I need to give specific thanks to Dr. Georgiy Teverovskiy for providing me with helpful information and for a sample of one of the complexes for some early experiments. I also thank Nathan Park, who also worked with nickel precatalysts for amination, for his insightful discussions. I am also thankful to Prof. Tim Swager, who has served as my third thesis committee member.

A number of additional staff throughout the chemistry department also helped to make my graduate education enjoyable: Dr. Jeff Simpson, Anne Rachupka, and Li Li, all of whom I worked closely with and got to know well as a part of my duties as a DCIF Student Instrument Steward; Nancy Parkins and Sara Frenier, administrative and financial assistants, respectively; the outstanding staff of the Chemistry Education Office and Chemistry HQ, who make everything run smoothly.

So far I have thanked everyone who has guided me with knowledge, but perhaps even more importantly, I want to thank those people in my life who have inspired me with love. Throughout graduate school I have had the continual support of my wife, Abby (who, for the record, also deserves to be called out as someone who has guided me with knowledge). Abby has sacrificed her aspirations in life to be with me while I pursue mine, which has involved moving from our mutual home in Idaho to Cambridge, and now after the completion of my PhD, moving from our home in Cambridge to Germany for me to follow my dream of living and working in Germany. We don't know where we'll be after that, but we'll tackle it together, wherever it will be.

Finally, I naturally owe an immeasurable thanks to my family for their support (of all kinds) throughout graduate school and throughout my life. Mom, Dad, Grandma, Brian, Eve, Vera, Margaret, Greg, Drew, and Kirby: thank you!

Table of Contents

Abbreviations

2-mesityl	1,3,5-trimethylphenyl
Ac	acetyl
anis	methoxyphenyl
ATR	attenuated total reflectance
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
Boc	*t*-butyloxycarbonyl
bpy	2,2'-bipyridine
Bz	benzoyl
CAN	ceric ammonium molybdate
cod	1,5-cyclooctadiene
Cp	cyclopentadienyl
DART	direct analysis in real time
dba	dibenzylideneacetone
DCE	1,2-dichloroethane
dcpf	1,1'-bis(dicyclohexylphosphino)ferrocene
DEAD	diethyl azodicarboxylate
DIBAL	diisobutylaluminum hydride
DMA	*N*,*N*-dimethylacetamide
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1'-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
dr	diastereomeric ratio
equiv	equivalent
er	enantiomeric ratio
ESI	electrospray ionization
FT	Fourier transform
GC	gas chromatography
GC/MS	gas chromatography/mass spectrometry
Hex	hexyl
ICR	ion cyclotron resonance (type of mass spectrometer)
IR	infrared (spectroscopy)
*m*CPBA	*meta*-chloroperbenzoic acid
Me_4phen	3,4,7,8-tetramethyl-1,10-phenanthroline
MHR	Mizoroki–Heck reaction

MSD	mass spectrometric detector
nd	not detected
NMR	nuclear magnetic resonance (spectroscopy)
Ns	4-nitrophenylsulfonyl
OAc	acetate
OMs	methanesulfonate
OTf	trifluoromethanesulfonate
OTs	4-methylphenylsulfonate
Ph	phenyl
phen	1,10-phenanthroline
PhMe	toluene
Phth	phthaloyl
Piv	pivaloyl; trimethylacetyl
PMA	phosphomolybdic acid
PMB	*para*-methoxybenzyl
PTC	phase-transfer catalyst
pyphos	2-[2-(diphenylphosphino)ethyl]pyridine
rr	regioratio
rt	room temperature; 22 ± 4 °C
TBS	*tert*-butyldimethylsilyl
TBSOTf	*tert*-butyldimethylsilyl triflate
t-Bu-Xantphos	9,9-dimethyl-4,5-bis(di-*t*-butylphosphino)xanthene
TEA	triethylamine
TES	triethylsilyl
TESOTf	triethylsilyl triflate
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin-layer chromatography
TMS	trimethylsilyl
TMSOTf	trimethylsilyl triflate
tolyl	methylphenyl
Ts	tosyl; 4-(methyl)phenylsulfonyl
USP	United States Pharmacopeia
Xantphos	9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene

Preface

Nickel's Place in Modern Transition Metal Catalysis

To the uninitiated, nickel might seem like just the impoverished younger sibling of palladium in the field of transition metal catalysis. After all, the use of palladium-catalyzed cross-coupling reactions has soared over the past half-century and palladium is presently the de facto standard metal for virtually all cross-coupling reactions. Palladium catalysis was honored with the 2010 Nobel Prize in Chemistry, and its use is ubiquitous in applications that range from natural product synthesis to drug discovery to manufacturing. Nickel lies just above palladium in the periodic table, and as a group 10 metal, it can readily perform many of the same elementary reactions as palladium or platinum. Because of these commonalities, nickel is often viewed solely as a low-cost replacement catalyst for cross-coupling reactions. However, this common misconception is clearly refuted by the numerous and diverse nickel catalyzed reactions reported in the literature. Indeed, homogeneous nickel catalysis is currently experiencing a renaissance.

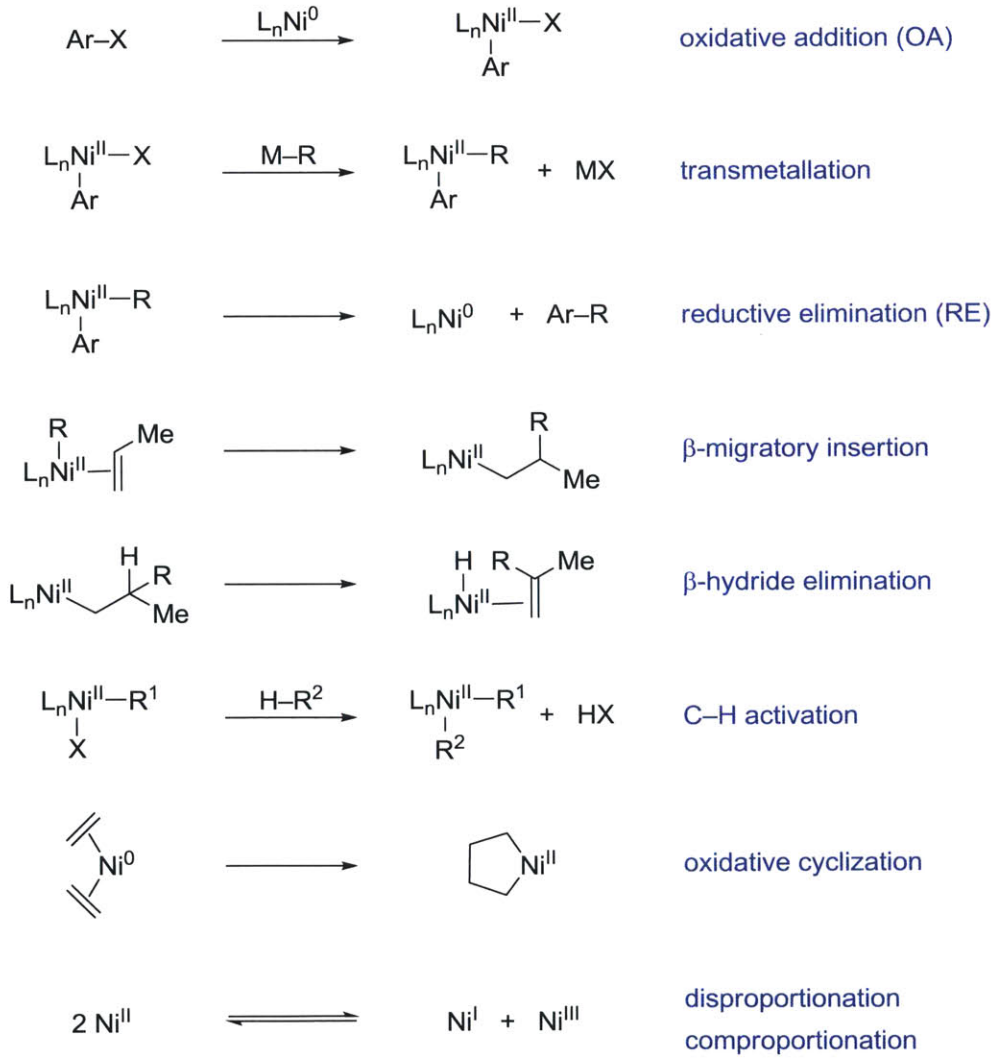
Recent developments in organonickel chemistry illustrate how the intrinsic properties of nickel have enabled its use as an effective catalyst for many intriguing, valuable and difficult transformations. Nickel was first isolated in 1751; its name is derived from the German Kupfernickel, the name given to a nickel ore originally believed by miners to contain copper, but which did not yield copper on extraction (hence use of Nickel, a mischievous demon). Historically, the use of nickel in organometallic reactions pre-dates many other examples of transition metal catalysis.[1,2] In the 1890s, Mond observed one of the unusual reactivity patterns of nickel: elemental nickel and CO reacted at room temperature to form an extremely toxic, low-boiling liquid, subsequently identified as $Ni(CO)_4$. This process, now termed the Mond process, can be used to purify the metal and indeed is presently used to make nickel metal of extraordinarily high purity. Shortly thereafter, Sabatier performed the first hydrogenation of ethylene using nickel, for which he was awarded the 1912 Nobel Prize in Chemistry.

The modern era of nickel catalysis arguably began with Wilke, one of the most prominent and prolific early contributors to organonickel chemistry.[1] Wilke made seminal contributions to the understanding of the structure and reactivity of nickel complexes, including the synthesis of $Ni(cod)_2$, a ubiquitous source of complexed zerovalent nickel that is still in widespread use today. Beginning in the 1970s, nickel found extensive use both for cross-coupling and for reactions of alkenes and alkynes, such as nucleophilic allylation, oligomerization, cycloisomerization, and reductive coupling. Numerous excellent books and general reviews of

organonickel chemistry have been written,[1,2] as well as of specific transformations (for example, reductive coupling[3] and cross-coupling[4]).

Scheme 1. Mechanism and Elementary Steps[a]

Nickel	Palladium
-1 **0** **+1** **+2** **+3** +4	**0** +1 **+2** +3 **+4**
Smaller atomic radius	Larger atomic radius
Less electronegative	More electronegative
Harder	Softer
Facile oxidative addition	Facile reductive elimination
Facile β-migratory insertion	Facile β-hydride elimination
Radical pathways more accessible	



[a]The oxidation states shown are illustrative and not necessarily inclusive, i.e. for oxidative addition, Ni(0) is shown oxidatively adding to an aryl halide and increasing in oxidation state to Ni(II), but Ni(I) could theoretically undergo the same process to end at a Ni(III) species. Likewise, for disproportionation, two Ni(I) could disproportionate to Ni(0) and Ni(II).

To set the context for the work to be described in this thesis, a survey of nickel's characteristic modes of reactivity, particularly in regard to some of the elementary steps of transition metal catalysis (Scheme 1) is needed. Nickel is a relatively electropositive late transition metal. Therefore, oxidative addition,[5] which results in loss of electron density around nickel, tends to occur quite readily (though, conversely, reductive elimination is correspondingly more difficult).[6] This facile oxidative addition allows for the use of cross-coupling electrophiles that would be considerably less reactive under palladium catalysis, such as phenol derivatives,[7,8,9] aromatic nitriles[10] or even aryl fluorides.[11] Nickel also has a number of readily available oxidation states commonly invoked in catalysis. The majority of palladium-catalyzed reactions are based on a Pd(0)/Pd(II) catalytic cycle, and most often proceed through polar (that is, non-radical) mechanisms. Likewise, Ni(0)/Ni(II) catalytic cycles are widespread, but the easy accessibility of Ni(I) and Ni(III) oxidation states allows different modes of reactivity and radical mechanisms. As a result, many transformations are based on Ni(I)/Ni(III), Ni(0)/Ni(II)/Ni(I), or even cycles in which nickel remains in the Ni(I) state for the entire catalytic cycle.[12] Many nickel complexes have long been known as privileged catalysts for reactions of alkenes and alkynes, such as oligomerization[13] and reductive coupling. Nickel readily donates *d*-electrons to π-acceptors, so olefin bonding is generally strong.[14] β-Hydride elimination tends to be slower with nickel relative to palladium; specifically, the energy barrier to Ni–C bond rotation prior to β-hydride elimination is often significantly higher for nickel than comparable palladium species.[15] Finally, there are a few more obvious differences between nickel and its group 10 counterparts. Practically speaking, the cost of nickel in its elemental form is roughly 2 000 times lower than palladium and 10 000 times lower than platinum on a mole-for-mole basis, though the price of commonly used nickel sources for catalysis can be less favorable. As a first-row transition metal, nickel has a small atomic radius, and Ni–ligand bond lengths are often relatively short.[16]

Numerous researchers have contributed tremendously to the understanding of the chemical behavior of nickel at a fundamental level, and these contributions have enabled the development of an enormous range of innovative reactions. In line with this progression, it has been my aim throughout my doctoral work to enable innovative reactions by developing innovative tools to further advance nickel catalysis.

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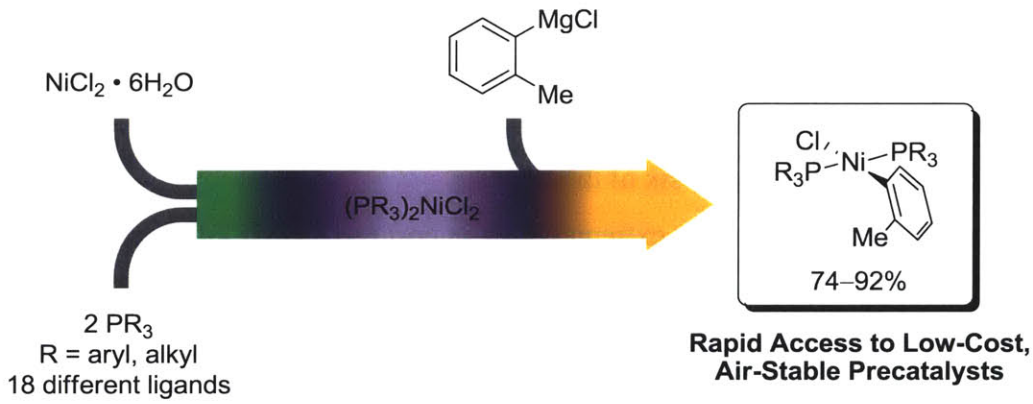
Chapter 1

Air-Stable Nickel Precatalysts for Organic Synthesis

Abstract



A series of air-stable nickel complexes of the form $L_2Ni(aryl)X$ (L = monodentate phosphine, X = Cl, Br) and LNi(aryl)X (L = bis-phosphine) have been synthesized and are presented as a library of precatalysts suitable for a wide variety of nickel-catalyzed transformations. These complexes are easily synthesized from low-cost $NiCl_2 \cdot 6H_2O$ or $NiBr_2 \cdot 3H_2O$ and the desired ligand followed by addition of 1 equiv of Grignard reagent. A selection of these complexes were characterized by single-crystal X-ray diffraction, and an analysis of their structural features is provided.

Introduction

Homogeneous nickel catalysis has continued to develop in recent years as a powerful set of tools for the construction of a wide variety of carbon–carbon and carbon–heteroatom bonds.[1] Nickel, a base metal, is a low-cost, versatile, and attractive metal for use in catalytic transformations. Arguably the greatest barrier to the wider adoption of homogeneous nickel catalysis for synthesis, however, is the difficulty and cost of synthesizing and handling nickel(0) sources and the phosphines often used in conjunction with such complexes. It is for this reason we aim to further develop nickel(II)-based precatalysts, as this would greatly increase the accessibility of homogeneous nickel catalysis in both academic as well as industrial settings.

Ideally, these precatalysts would (1) be indefinitely air stable, (2) have a low molecular weight, (3) produce highly active catalysts, (4) be simple to synthesize from low-cost materials, (5) be readily activated under a variety of conditions without producing interfering byproducts of activation, and (6) be applicable to virtually any nickel-catalyzed transformation. Precatalysts possessing many or all of these qualities would greatly add to the value of new as well as previously established nickel catalyzed transformations, though it is unlikely that any one approach would be able to satisfy all six of these tenets.

Although nickel metal itself is extremely low in cost (~15 USD/kg at commodity prices), the cost of nickel(0) sources such as $Ni(cod)_2$ easily exceeds 20 000 USD/kg, which often weakens the economic argument for using nickel in catalytic transformations. Indeed, $Ni(cod)_2$ is only marginally less expensive than comparable palladium(0) sources such as $Pd_2(dba)_3$ on a mole-for-mole basis, despite the fact that palladium metal is far more expensive than nickel metal.[2] Taken in conjunction with the fact that a high catalyst loading of nickel is often required (5–20 mol %), there is little economic incentive to use nickel in place of precious metals such as palladium unless cheaper sources of nickel can be used. Regardless of cost and ease of use issues, however, any comparison between nickel and precious metals (particularly palladium) should recognize that nickel has demonstrated valuable and unique reactivity and behavior, which enables an entirely different set of chemical transformations.[1]

The use of precatalysts in transition-metal catalysis is not a new idea: indeed, $Pd(OAc)_2$ has been in use as a precursor to Pd(0) species for close to 50 years,[3] although the concept of the single-component, discrete precatalyst is a somewhat newer development.[4] Several groups (most prominently Nolan,[5] Buchwald,[6] Organ,[7] but also many others) have greatly advanced the

ubiquity of precatalysts in organic synthesis, with much of the effort focused on palladium catalysts for cross couplings, amination, and related transformations.[8] Likewise, though by far less established than those for palladium-catalyzed reactions, single-component nickel precatalysts are not new, with the most frequently employed being complexes such as $(PPh_3)_2NiCl_2$.[9] Though air stable, these precatalysts are usually limited to activation by nucleophilic organometallic reagents, and as such, they must often be preactivated by addition of an exogenous reductant.[10] Such a strategy has been shown to be effective in many instances, but it is neither an ideal nor a universal solution.

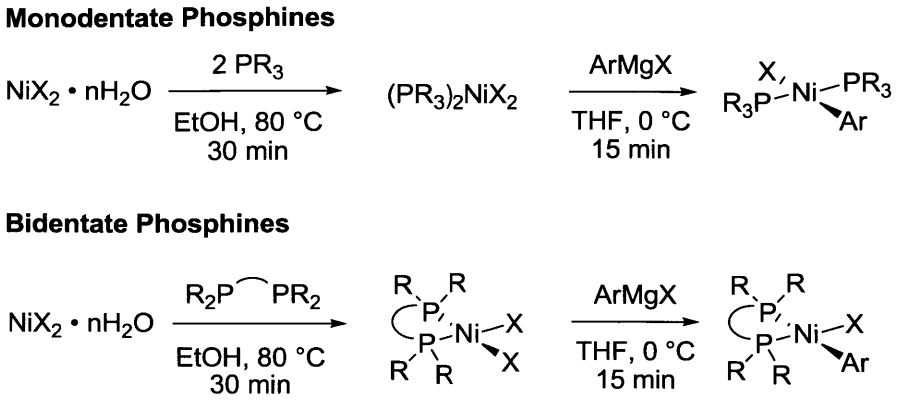
Complexes such as *trans*-$(PPh_3)_2$Ni(1-naphthyl)Cl have been known to be air-stable since 1960, when they were first reported by Chatt and Shaw,[11] but these complexes were not utilized in catalytic transformations until many years later. Relatively few phosphine ligands have been used to prepare such complexes for use in catalysis,[12,13,14] although several new types of nickel precatalysts with varying degrees of air stability have also been developed in recent years.[15]

During the development of *trans*-$(PCy_2Ph)_2$Ni(*o*-tolyl)Cl for use in the coupling reaction of benzyl chlorides with alkenes,[16] it became apparent that such complexes could be used for numerous nickel-catalyzed transformations, since these precatalysts can be activated by nucleophilic reagents (RMgX, RZnX, R_3B, R_3SiH—by a transmetallation/reductive elimination sequence) as well as electrophilic reagents (R_3SiOTf—by a Lewis acid induced Ni to Ni transmetallation followed by reductive elimination of a biaryl). Members of this class have been shown to possess significantly enhanced catalytic activity in comparison to the combination of $Ni(cod)_2$ and the corresponding phosphine ligand due to the absence of cod, which is known to hinder catalysis in some instances.[17]

Synthesis of Precatalysts

Synthesis of the precatalyst complexes is straightforward (see Scheme 1): $NiCl_2 \cdot 6H_2O$ and the desired mono- or bidentate phosphine are combined in ethanol and briefly refluxed, after which the L_2NiCl_2 complex is isolated by a simple vacuum filtration on a sintered-glass frit.

Scheme 1. General Procedure for Synthesis of Precatalysts[a]



[a]X = Cl or Br. R = alkyl or aryl. Ar = o-tolyl, 2-mesityl, (2,4,6-triisopropyl)phenyl, (2,6-dimethoxy)phenyl

After it is dried under vacuum to remove residual solvent, the complex is redissolved in THF or CH_2Cl_2 and 1 equiv of Grignard reagent (*o*-tolylmagnesium chloride, 2-mesitylmagnesium bromide, or similar) is added. Removal of the solvent with the aid of a rotary evaporator followed by the addition of methanol precipitates the complex and dissolves the magnesium chloride or bromide; isolation by vacuum filtration on a glass frit followed by washing with the appropriate solvent yields the complex. No further purification of the powder obtained this way is necessary, though recrystallization can be carried out if desired.

At present, we have prepared more than 20 such complexes, with the most significant examples shown in Table 1. The selection of ligands is intended to encompass a variety of mono and bidentate phosphines commonly used in organic synthesis, as well as a number of less frequently employed ligands. Many of the ligands in the latter category, particularly the low molecular-weight, liquid phosphines, find less frequent use in organic synthesis at least in part because they are difficult to synthesize and handle safely and because they are expensive to purchase due to the high cost of shipping pyrophoric and/or highly flammable goods. Triethylphosphine (**10**), dimethylphenylphosphine (**8**, **9**), tricyclopentylphosphine (**5**), tri-*n*-butylphosphine (**11**), and tribenzylphosphine (**6**) all undergo reactions with air ranging from vigorous to violent, yet the precatalysts derived from each of these ligands are completely stable to oxygen in the solid phase and can be stored in air indefinitely.

Table 1. Nickel-Phosphine Complexes Synthesized[a]

Entry	Ligand	Halide	Geometry	Aryl group	Isolated yield (%)		
					L_nNiX_2	$L_nNi(Ar)X$	overall
Monodentate Ligands							
1	PPh_3	Cl	*trans*	*o*-tolyl	91	89	81
2	$PCyPh_2$	Cl	*trans*	*o*-tolyl	92	81	75
3	PCy_2Ph	Cl	*trans*	*o*-tolyl	95	88	84
4	PCy_3	Cl	*trans*	*o*-tolyl	97	87	84
5	$PCyp_3$	Cl	*trans*	*o*-tolyl	99	90	89
6	PBn_3	Cl	*trans*	*o*-tolyl	96	90	86
7	PPh_2Me	Cl	*trans*	*o*-tolyl	99	81	80
8	PMe_2Ph	Br	*trans*	[2,4,6-(*i*-Pr)$_3$]Ph	95	83	79
9	PMe_2Ph	Br	*trans*	[2,6-(OMe)]Ph	95	87	83
10	PEt_3	Br	*trans*	2-mesityl	95	88	84
11	P(*n*-Bu)$_3$	Br	*trans*	2-mesityl	89	90	80
Bidentate Ligands							
12	dppe	Cl	*cis*	*o*-tolyl	98	84	82
13	dppp	Br	*cis*	2-mesityl	89	85	76
14	dppb	Br	*trans*	2-mesityl	96	86	83
15	(*S*)-(−)-BINAP	Cl	*cis*	*o*-tolyl	94	97	91
16	dppf	Cl	*cis*	*o*-tolyl	97	95	92
17	dcpf	Cl	*trans*	*o*-tolyl	98	83	81
18	Xantphos	Cl	*trans*	*o*-tolyl	86	92	79
19	pyphos	Cl	*cis*	*o*-tolyl	90	82	74

[a]All complexes were synthesized according to the method shown in Scheme 1. Isolated yield is of material that was not recrystallized after synthesis, but that provided acceptable CH(N) analysis as a test of purity.

In some instances, the complexes containing the *o*-tolyl moiety were not adequately stable to allow isolation in good yield and/or did not form air-stable complexes. For example, *trans*-$(PEt_3)_2Ni$(*o*-tolyl)Cl can be isolated in good yield (>90%); however, upon standing in air for several days, it begins to show clear signs of decomposition. A solution to this problem was found by increasing the steric bulk of the aryl group on nickel, which is hypothesized to further shield nickel from associative substitution.

To synthesize these complexes with more substituted aryl groups, the phosphine was condensed with $NiBr_2 \cdot 3H_2O$ to yield the corresponding L_2NiBr_2 complex, which was then treated with commercially available 2-mesitylmagnesium bromide.[18] In this way, several complexes which had proven elusive could be synthesized to form stable precatalysts. In the case of tri-*n*-butylphosphine, *trans*-(P*n*-$Bu_3)_2$Ni(*o*-tolyl)Cl was found to be a liquid at room temperature that could not be stored for more than a few days, whereas *trans*-(P*n*-$Bu_3)_2$Ni(2-mesityl)Br (**11**) is an indefinitely stable solid.

Additionally, [dppp]Ni(*o*-tolyl)Cl and [dppb]Ni(*o*-tolyl)Cl are difficult to synthesize in good yield and purity using this method. In both instances, the addition of a second equiv of *o*-tolylmagnesium chloride takes place very readily (which lowers the yield and purity of the isolated product) and neither complex is very stable to methanol, leading to a loss of yield during workup and purification. In both instances, however, changing the aryl group from *o*-tolyl to 2-mesityl solved this problem, allowing isolation of *cis*-[dppp]Ni(2-mesityl)Br (**13**) and *trans*-[dppb]Ni(2-mesityl)Br (**14**). It should be noted, however, that these complexes containing the *o*-tolyl ligand can be synthesized by ligand metathesis starting from *trans*-$(PPh_3)_2$Ni(*o*-tolyl)Cl (**1**), indicating they are indeed stable complexes.[13b]

Unfortunately, the switch from *o*-tolyl to 2-mesityl did not enable isolation of a stable complex in one instance: PMe_2Ph. Neither the *o*-tolyl nor the 2-mesityl complexes were stable under ambient conditions or in the presence of alcohols. Because PMe_2Ph represents the least sterically demanding phosphine used in this study, it is perhaps unsurprising that its complex is in turn the most sensitive to nucleophilic attack by water or alcohols, since nickel is less shielded. As before, increasing the steric hindrance around nickel provided the solution. Reaction of *trans*-$(PMe_2Ph)_2NiBr_2$ with 2,4,6-triisopropylphenylmagnesium bromide[19] gave *trans*-$(PMe_2Ph)_2$Ni(2,4,6-triisopropylphenyl)Br (**8**) in 83% yield. This complex, in stark contrast to the corresponding *o*-tolyl and 2-mesityl complexes, demonstrates absolutely no air or water sensitivity. However, due to the concern that activation of this precatalyst may be slow because of the extreme hindrance provided by the isopropyl groups at the 2- and 6-positions of the aryl ring, a precatalyst incorporating a 2,6-dimethoxyphenyl substituent (**9**) was also prepared and found to be air stable. This method is marginally less convenient, as it requires the in situ preparation of 2,6-dimethoxyphenyllithium from 1,3-dimethoxybenzene and *n*-BuLi.

As the numerous entries in Table 1 demonstrate, complexes of this type can be made from a wide range of phosphines, including electron-rich and electron-poor as well as sterically demanding and undemanding phosphines. However, a number of phosphines were not able to be successfully incorporated into these types of complexes. Those ligands fall into two categories: electron-poor, sterically hindered P(*p*-F-C_6H_4)$_3$, P(*o*-tolyl)$_3$, and P(*o*-anis)$_3$) and extremely sterically hindered phosphines, regardless of their electronic nature (P(*t*-Bu)$_3$,[20] *t*-Bu-Xantphos, and 1,2-bis((di-*tert*-butylphosphino)methyl)benzene). In all instances, the required L_2NiX_2 or $LNiX_2$ complexes did not form, precluding attempts to synthesize the corresponding arylnickel complexes by this synthetic route.

Structural Analysis of Complexes

Although our principal interest in these complexes is their catalytic activity, it is also important to understand their structural features, geometry, and bonding, as this may afford deeper insight that would enable further development of new complexes, types of precatalysts, or alternative modes of activation.

The complexes strongly favor a square-planar arrangement, and whether the two phosphorus atoms are in a *cis* or *trans* arrangement at nickel is readily discerned from inspection of each complex's ^{31}P NMR spectrum. Complexes derived from monodentate phosphines were universally found to adopt a *trans* geometry, as indicated by the presence of only one singlet in the ^{31}P NMR spectrum. This arrangement presumably results from the minimization of steric interaction between the ligands on nickel, and the magnitude of the steric repulsion is evidently large enough to overwhelm any thermodynamic trans effects that might favor a *cis* arrangement.[21]

Conversely, complexes derived from bidentate phosphines were more often observed to adopt a *cis* arrangement, but several counterexamples were also seen. The preferred arrangement appears to depend on the bite angle of the ligand, its rigidity, and the identity of the substituents on phosphorus. For example, the complex derived from dppf (**16**) exists only as the *cis*, square planar isomer in solution, whereas the closely related dcpf (**17**) adopts a distorted *trans*, square planar geometry, as illustrated in its single-crystal X-ray structure and in its ^{31}P NMR spectrum. In this instance, the change from phenyl groups to cyclohexyl groups on phosphorus is enough to

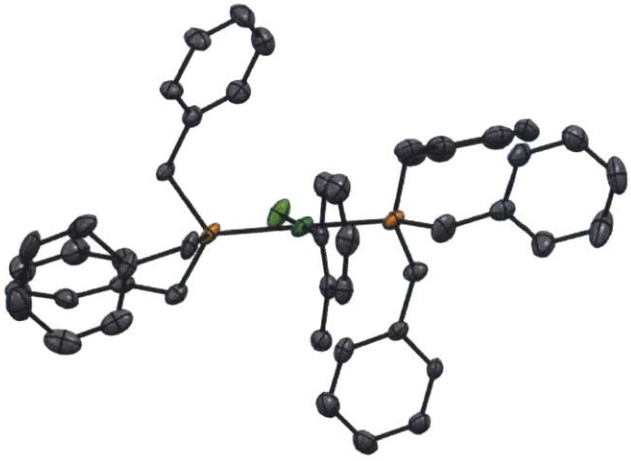
alter the preferred geometry, despite the fact that both complexes are built on the same ferrocene scaffold.

A selection of these precatalysts have been characterized by single-crystal X-ray diffraction (Figure 1). Crystal structures were determined following established procedures,[22] and complete details are given in the Experimental Section. Complexes derived from PBn_3 and PMe_2Ph both adopt nearly ideal *trans*, square planar structures and are, for the most part, structurally unremarkable. Complex **15** (derived from (*S*)-BINAP) adopts a nearly ideal square planar structure with a *cis* arrangement, yielding a dihedral angle of 73.24(3)° between the two naphthalene rings of BINAP. The most interesting feature of this complex, though, is the fact that it forms diastereomers due to the two possible arrangements of the *o*-tolyl group. These diastereomers are both crystallographically and spectroscopically (^1H and ^{31}P NMR) observable, suggesting that interconversion is either slow or does not take place at any appreciable rate near room temperature.

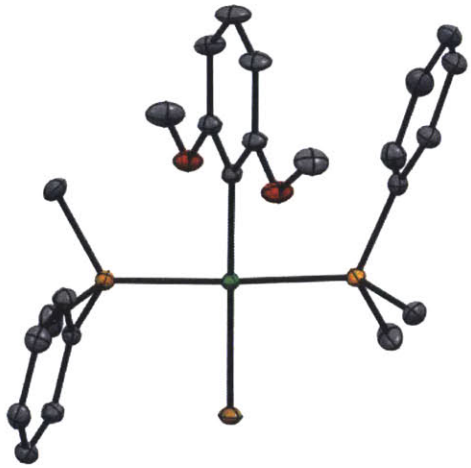
The complex derived from dcpf (**17**) is another interesting case; its ^{31}P NMR spectrum exhibits one singlet, despite the fact that it is a bidentate phosphine. Single-crystal X-ray diffraction analysis showed a geometry at nickel that is best described as square planar, but with significant distortion toward tetrahedral.[23] For example, the P(1)–Ni–P(2) bond angle is ca. 145°, well shy of the ideal 180°. However, the P(1)–Ni–Cl and P(2)–Ni–Cl bond angles are 91.264(13) and 91.642(13)°, very close to the ideal 90° for a square plane. The sum of the bond angles at nickel is 370.69°; ideal square planar structures would sum to 360°, whereas ideal tetrahedral structures would correspond to ca. 438°. Therefore, it is appropriate to describe the two phosphorus atoms as *trans* to one another.

Complex **18** (derived from Xantphos) adopts a distorted square-pyramidal geometry in the solid state. The oxygen atom of the ligand occupies the apical position and the two phosphorus atoms are in equatorial positions *trans* to each other. In solution, two isomers are observed by ^1H and ^{31}P NMR, the second perhaps being the true square-planar isomer without oxygen coordinated at nickel.

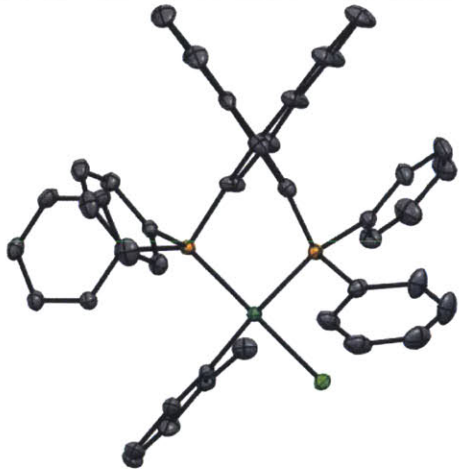
Figure 1. Single-Crystal X-Ray Diffraction Analysis of Nickel Complexes[a]



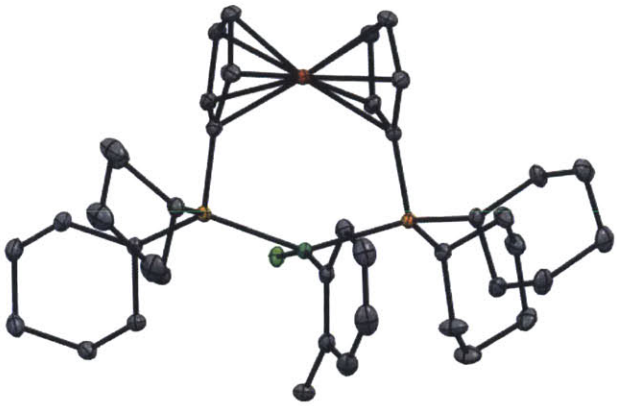
PBn_3 (**6**)



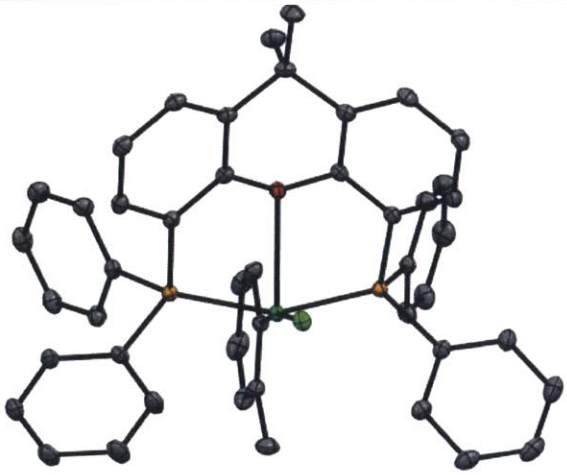
PMe_2Ph (**9**)



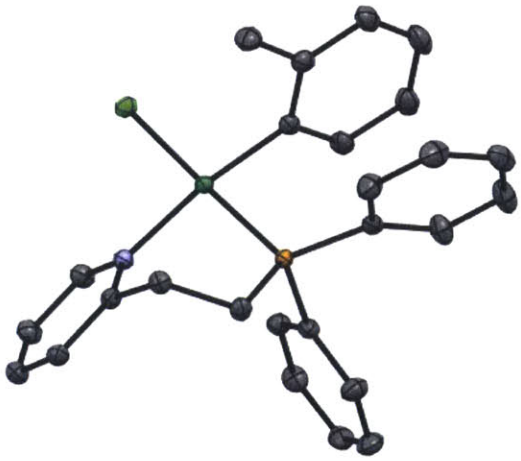
(*S*)-BINAP (**15**)



dcpf (**17**)



Xantphos (**18**)



pyphos (**19**)

[a]Thermal ellipsoids are drawn at the 50% probability level, and hydrogen atoms are not included. Disorder of the *o*-tolyl ligand (**6**, **15**, **18**, **19**) and solvent molecules of crystallization (**6**, **15**, **17**, **18**) are not shown.

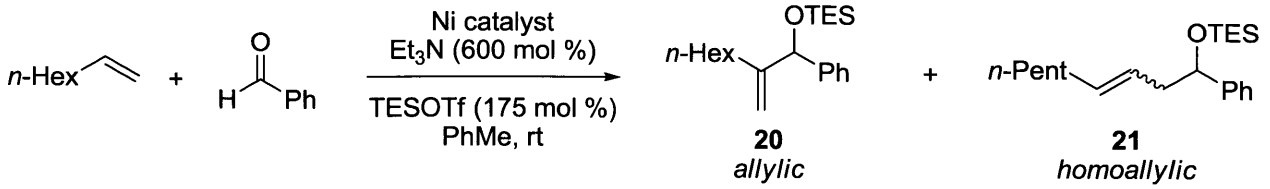
Pyphos (**19**), being an unsymmetrical, bidentate ligand, can form at least two structural isomers—chloride could be *trans* to either phosphorus or to nitrogen. The ^{31}P NMR spectrum shows only one, sharp singlet, which suggests that one isomer is dominant in solution. Single-crystal X-ray diffraction analysis showed **19** to adopt a square-planar structure with chlorine *trans* to phosphorus. This geometrical arrangement presumably indicates that the thermodynamic trans effect dominates the ground-state conformation, rather than any potential steric interaction between the diphenylphosphino moiety and the *o*-tolyl ligand.

Evaluation of Precatalysts in the Ni-catalyzed Carbonyl-Ene Reaction

To demonstrate the utility and advantages these precatalysts present over other means of entry into nickel(0), we have used the nickel-catalyzed carbonyl-ene reaction, which couples a terminal alkene (or ethylene), an aldehyde, and a silyl triflate to form allylic or homoallyic silyl ethers (Table 2).[24] Preliminary experiments demonstrated that catalysts **3** (PCy_2Ph) and **1** (PPh_3) were indeed catalytically competent and provided the desired allylic (**20**) and homoallylic (**21**) products, respectively. In both instances, the selectivity and yields were observed to be comparable to those of reactions using $Ni(cod)_2$. However, the rate was observed to be higher than when cod is present—reaction following studies demonstrated that the reaction reaches completion in ca. 18 h, rather than the 36–48 h required when using $Ni(cod)_2$ as the nickel source.

A comprehensive screen of precatalysts **1**–**19** was carried out to demonstrate the ease with which screening of ligands can be accomplished (Table 2). The use of these single-component, air-stable precatalysts reduces the effort involved to an exercise which can be carried out on the benchtop with no exclusion of air during setup of the reactions. This approach, while convenient, may however not be applicable in all instances, as it is necessary to have already synthesized the desired precatalysts. For researchers frequently involved in screening of nickel-catalyzed reactions, however, such an approach could be valuable.

Table 2. Screening of the Ni-catalyzed Carbonyl-Ene Reaction[a]



Entry	Ligand	Ni Source	Yield (%)			Ratio
			20	21	combined	20:21
1	PPh_3	**1**	7	81	88	8 : 92
1a	PPh_3	$Ni(cod)_2$	6	78	84	7 : 93
2	$PCyPh_2$	**2**	17	56	73	23 : 77
3	PCy_2Ph	**3**	54	20	74	73 : 27
3a	PCy_2Ph	$Ni(cod)_2$	52	21	73	71 : 29
4	PCy_3	**4**	18	2	20	90 : 10
5	$PCyp_3$	**5**	1	nd	1	–
6	PBn_3	**6**	1	2	3	33 : 67
7	PPh_2Me	**7**	nd	nd	–	–
8	PMe_2Ph	**8**	nd	nd	–	–
9	PMe_2Ph	**9**	nd	nd	–	–
10	PEt_3	**10**	nd	nd	–	–
11	$P(n\text{-}Bu)_3$	**11**	nd	nd	–	–
12	dppe	**12**	nd	2	2	–
13	dppp	**13**	nd	2	2	–
14	dppb	**14**	nd	nd	–	–
15	(*S*)-BINAP	**15**	nd	7	7	–
16	dppf	**16**	nd	nd	–	–
17	dcpf	**17**	nd	nd	–	–
18	Xantphos	**18**	nd	nd	–	–
19	pyphos	**19**	nd	6	6	–

[a]Yields determined by gas chromatography calibrated against an internal standard of *n*-dodecane. A listed yield of nd indicates the target product was not formed in a detectable amount.

Conclusion

In summary, we have synthesized and characterized 19 air-stable Ni(II) complexes derived from a range of mono- and bidentate phosphine ligands commonly used in synthesis. These complexes are accessed from low-cost $NiCl_2 \cdot 6H_2O$ rather than from an expensive and air-sensitive Ni(0) source such as $Ni(cod)_2$. These complexes can function as precatalysts for a range of nickel-catalyzed reactions, as they are readily converted to Ni(0) phosphine complexes by treatment with reagents such as RMgX, RZnX, R_3B, RLi, R_3SiH, and R_3SiOTf among others, allowing their convenient use in Ni(0)-catalyzed reactions. Many of these reactions, which previously employed $Ni(cod)_2$ as the Ni(0) source and thus required the use of a glovebox or glovebag, can now be carried out with no exclusion of air or water during setup, which greatly facilitates the use of nickel catalysis as a tool for synthesis. These benefits have been demonstrated in the context of the nickel-catalyzed carbonyl-ene reaction, where the use of a precatalyst provided a significant rate enhancement for the target reaction while maintaining selectivity equivalent to that of reactions catalyzed by $Ni(cod)_2$.

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(12) For a selection of some recent examples, see: (a) Chen, C.; Yang, L.-M. *Tetrahedron Lett.* **2007**, *48*, 2427–2430. (b) Gao, C.; Yang, L. *J. Org. Chem.* **2008**, *73*, 1624–1627. (c) Zhou, L.; Feng, X.; He, R.; Bao, M. *J. Coord. Chem.* **2009**, *62*, 2824–2831. (d) Fan, X.-H.; Yang, L.-M. *Eur. J. Org. Chem.* **2010**, *2010*, 2457–2460. (e) Fan, X.-H.; Yang, L.-M. *Eur. J. Org. Chem.* **2011**, *2011*, 1467–1471. (f) Zhang, N.; Hoffman, D. J.; Gutsche, N.; Gupta, J.; Percec, V. *J. Org. Chem.* **2012**, *77*, 5956–5964. (g) Leowanawat, P.; Zhang, N.; Safi, M.; Hoffman, D. J.; Fryberger, M. C.; George, A.; Percec, V. *J. Org. Chem.* **2012**, *77*, 2885–2892. (h) Park, N. H.; Teverovskiy, G.; Buchwald, S. L. *Org. Lett.* **2014**, *16*, 220–223. (i) Jezorek, R. L.; Zhang, N.; Leowanawat, P.; Bunner, M. H.; Gutsche, N.; Pesti, A. K. R.; Olsen, J. T.; Percec, V. *Org. Lett.* **2014**, Article ASAP, DOI: 10.1021/ol503061c.

(13) For the use of these precatalysts for cross-coupling polymerization, see: (a) Miyakoshi, R.; Yokoyama, A.; Yokozawa, T. *J. Am. Chem. Soc.* **2005**, *127*, 17542–17547. (b) Bronstein, H. A.; Luscombe, C. K. *J. Am. Chem. Soc.* **2009**, *131*, 12894–12895.

(14) McNeil and co-workers have carried out detailed studies into use of this type of precatalyst for the synthesis of poly(thiophene) and related polymers: (a) Lanni, E. L.; McNeil, A. J. *J. Am. Chem. Soc.* **2009**, *131*, 16573–16579. (b) Lanni, E. L.; McNeil, A. J. *Macromolecules* **2010**, *43*, 8039–8044. (c) Lanni, E. L.; Locke, J. R.; Gleave, C. M.; McNeil, A. J. *Macromolecules* **2011**, *44*, 5136–5145. (d) Lee, S. R.; Bryan, Z. J.; Wagner, A. M.; McNeil, A. J. *Chem. Sci.* **2012**, *3*, 1562. (e) Lee, S. R.; Bloom, J. W. G.; Wheeler, S. E.; McNeil, A. J. *Dalton Trans.* **2013**, *42*, 4218–4222. (f) Bryan, Z. J.; McNeil, A. J. *Chem. Sci.* **2013**, *4*, 1620–1624. (g) Bryan, Z. J.; McNeil, A. J. *Macromolecules* **2013**, *46*, 8395–8405.

(15) (a) Iglesias, M. J.; Blandez, J. F.; Fructos, M. R.; Prieto, A.; Álvarez, E.; Belderrain, T. R.; Nicasio, M. C. *Organometallics* **2012**, *31*, 6312–6316. (b) Ge, S.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2012**, *51*, 12837–12841. (c) Ge, S.; Green, R. a; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 1617–1627. See also ref 17a.

(16) See Chapter 2. The original work was reported in Standley, E. A.; Jamison, T. F. *J. Am. Chem. Soc.* **2013**, *135*, 1585–1592.

(17) (a) Ge, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 16330–16333. (b) For a detailed report examining the role of dba in zerovalent palladium catalysis, see: Amatore, C.; Jutand, A.; Khalil, F.; M'Barki, M. A.; Mottier, L. *Organometallics* **1993**, *12*, 3168–3178.

(18) The change from chloride to bromide is merely for convenience, since 2-mesitylmagnesium bromide is commercially available, while the chloride is not. The identity of the halogen does not appear to alter the behavior of the complexes as precatalysts, save perhaps the fact that some of the bromide complexes are more soluble in organic solvents than their chloride counterparts.

(19) This particular Grignard reagent was selected for the isopropyl groups at the 2- and 6-positions, with the isopropyl group in the 4-position not expected to play a role in the complex's stability. This reagent is commercially available as a 0.5 M solution in THF.

(20) It is known, for example, that P(*t*-Bu)$_3$ reacts with $NiBr_2$ in ethanol to form [P(*t*-Bu)$_3$NiBr$_3$]$^-$ [HP(*t*-Bu)$_3$]$^+$. See: Alyea, E. C.; Costin, A.; Ferguson, G.; Fey, G. T.; Goel, R. G.; Restivo, R. J. *J. Chem. Soc., Dalton Trans.* **1975**, 1294–1298.

(21) Quagliano, J. V.; Schubert, L. *Chem. Rev.* **1952**, *50*, 201–260.

(22) Müller, P. *Crystallogr. Rev.* **2009**, *15*, 57–83.

(23) This deviation in geometry is also likely to be the reason this complex is red, as opposed to the normal bright yellow.

(24) (a) Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2005**, *127*, 14194–14195. (b) Ho, C.-Y.; Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 5362–5363. (c) Ng, S.-S.; Ho, C.-Y.; Jamison, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 11513–11528.

Chapter 1

Air-Stable Nickel Precatalysts for Organic Synthesis

Experimental Section

Materials, Methods, and General Considerations

Dichloromethane, THF, and acetonitrile were degassed by sparging with nitrogen and dried by passage through a column of activated alumina. Ethanol (200 proof, <0.1% water) and *n*-butanol (99.9%) were roughly degassed by sparging with nitrogen and were not further dried prior to use. Methanol (>99.8%, <0.1% water) was used as received. Manipulation of all air-sensitive reagents was carried out in a glovebox filled with dry nitrogen. Bis(1,5-cyclooctadiene)nickel(0)[1] was purchased from Strem Chemicals (Newburyport, MA) and stored at –30 °C in a glovebox. All other chemicals were purchased from Sigma-Aldrich (Milwaukee, WI), Alfa Aesar (Ward Hill, MA), TCI America (Portland, OR), or Oakwood Products, Inc. (West Columbia, SC).

Melting points were determined on an electrothermal apparatus using glass capillaries open to air except where specified. The material used for the determinations was not recrystallized, but was ground to a fine powder using a metal spatula before analysis.

NMR spectra were obtained in $CDCl_3$ (99.8% atom D), C_6D_6 (99.5% atom D), or CD_2Cl_2 (99.9% atom D) purchased from Cambridge Isotope Laboratories (Andover, MA). ^1H NMR spectra were obtained at 300 or 500 MHz), ^{13}C NMR spectra (when taken[2]) were obtained at 126 MHz with ^1H decoupling, and ^{31}P NMR spectra were obtained at 121 or at 202 MHz with ^1H decoupling. Chemical shifts (^1H and ^{13}C) are reported in parts per million relative to TMS (δ = 0.00 ppm) and were referenced to the residual solvent peak (^1H, $CDCl_3$ 7.26 ppm, C_6D_6 7.16 ppm, CD_2Cl_2 5.32 ppm; ^{13}C, $CDCl_3$ 77.16 ppm, C_6D_6 128.06 ppm, CD_2Cl_2 53.84 ppm)[3]; ^{31}P NMR spectra are reported in parts per million relative to an external standard of 85% phosphoric acid (δ=0.00 ppm). The following designations are used to describe multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), br (broad), app (apparent).

IR spectra were obtained on an FT-IR spectrometer equipped with an ATR accessory. Intensities are reported relative to the most intense peak of the spectrum and are defined as

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[1] The physical appearance of the bis(1,5-cyclooctadiene)nickel(0) used for all experiments was bright yellow-orange and crystalline, with block-shaped crystals ca. 0.4–0.8 mm on each side. Samples appearing as dull yellow powder, yellow-gray powder, or any sample with visible black spots (nickel) may give poor results, as these conditions all indicate at least some level of decomposition.

[2] ^{13}C NMR spectra were not acquired for five compounds due either to inadequate stability in solution or extremely low solubility in suitable solvents.

[3] Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176–2179.

follows: w (weak, intensity between 0% and 33.3%), medium (m, between 33.3% and 66.6%), and strong (s, between 66.6% and 100%).

Thin-layer chromatography was carried out on EMD Millipore 60 F_{254} glass-backed plates (250 μm coating thickness) and spots were visualized using UV light, basic potassium permanganate, ethanolic phosphomolybdic acid (PMA), or ceric ammonium nitrate (CAN) stains. Column chromatography was carried out on an automated flash column chromatography system using pre-packed columns (silica gel, 50 μm average particle size).

Gas chromatography (GC) was performed on a (5%-phenyl)-methylpolysiloxane column (equivalent to USP phase G27) coupled to a flame ionization detector. GC/MS was performed on a (5%-phenyl)-methylpolysiloxane column (equivalent to USP phase G27) coupled to a quadrupole MSD. Dodecane (99+%, Alfa Aesar) was used as an internal standard for quantitation. Authentic samples of **20** and **21** (used for calibration curves and for comparison) were prepared by the previously published method.[4]

Grignard reagents were titrated with salicylaldehyde phenylhydrazone[5] and organolithium reagents were titrated with *N*-benzylbenzamide.[6]

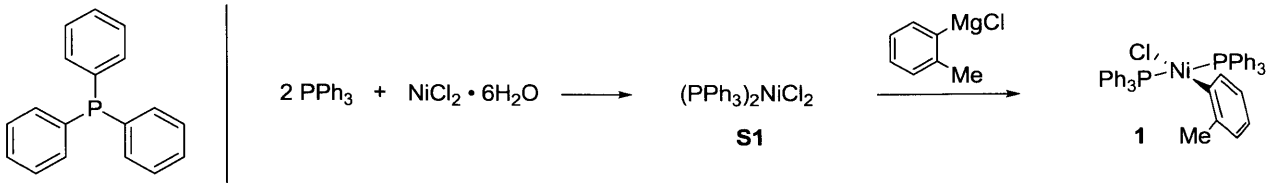
[4] Ng, S.-S., Ho, C.-Y., and Jamison, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 11513–11528.
[5] Love, B. E. and Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755–3756.
[6] Burchat, A. F.; Chong, J. M.; Nielsen, N. *J. Organomet. Chem.* **1997**, *542*, 281–283.

General Procedure for Synthesis of Complexes

L_nNiX_2: $NiCl_2 \cdot 6H_2O$ or $NiBr_2 \cdot 3H_2O$, EtOH, and a magnetic stir bar were placed in a round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then the phosphine was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration and washed twice with ethanol (and twice with ether in some instances). Drying under vacuum yielded the product.

$L_nNi(aryl)X$: L_nNiX_2 was placed in an oven-dried round-bottom flask containing a magnetic stir bar. Solvent (THF or CH_2Cl_2) was added, the solution was cooled to 0 °C with an ice bath, and Grignard reagent was added dropwise with vigorous stirring. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure with a rotary evaporator. MeOH was added, and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the precipitate was collected by vacuum filtration, washed with two portions of cold MeOH, and dried under high vacuum to yield the complex.

Synthesis and Characterization of Complexes



bis(triphenylphosphine)nickel(II) chloride (**S1**): $NiCl_2 \cdot 6H_2O$ (10 mmol, 2.377 g), EtOH (40 mL), and a magnetic stir bar were placed in a 100 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then PPh_3 (23 mmol, 6.033 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to reflux (~80 °C), causing a color change to dark blue/black. After 1 hour, the mixture was removed from heat and cooled to ca. 50 °C, at which time the solid was collected by vacuum filtration, washed twice with ethanol (15 mL) and twice with ether (15 mL). Drying under vacuum yielded **S1** (5.953 g, 91%) as a fine, deep blue powder.

***trans*-bis(triphenylphosphine)(2-methylphenyl)nickel(II) chloride** (**1**): **S1** (5 mmol, 3.271 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. CH_2Cl_2 (45 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (5 mmol, 0.945 M in THF, 5.29 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to turn brown-orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (20 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 3 min). After the suspension was cooled to 0 °C, the bright yellow precipitate was collected by vacuum filtration, washed with two 15 mL portions of Et_2O, and dried under high vacuum to yield **1** (3.153 g, 89%) as a fine, bright yellow powder.

mp 170–175 °C dec.

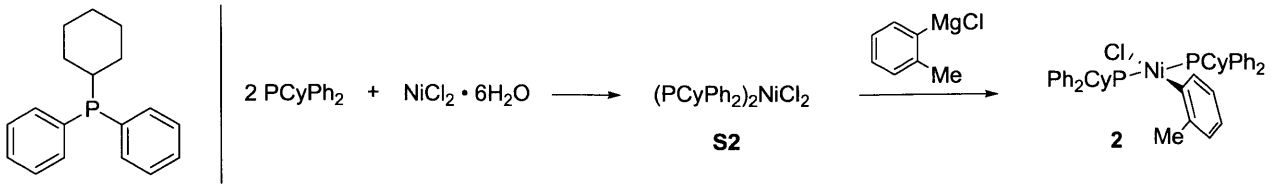
Anal. Calcd for $C_{43}H_{37}ClNiP_2$: C, 72.76; H, 5.25. Found: C, 72.81; H, 5.52.

^{1}H NMR (500 MHz, C_6D_6, δ): 7.84 – 7.71 (m, 12H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.06 – 6.94 (m, 18H), 6.46 (t, *J* = 7.2 Hz, 1H), 6.26 (t, *J* = 7.5 Hz, 1H), 6.19 (d, *J* = 7.4 Hz, 1H), 2.46 (s, 3H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 22.0.

^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 151.34 (t, J = 32.8 Hz), 144.10 (t, J = 3.3 Hz), 136.99 (t, J = 4.0 Hz), 135.16 (t, J = 5.5 Hz), 132.38 (t, J = 21.0 Hz), 129.71, 129.33 (t, J = 3.1 Hz), 127.97 (t, J = 4.7 Hz), 123.26 (t, J = 2.3 Hz), 122.32 (t, J = 2.3 Hz), 26.53.

FT-IR (ATR, cm^{-1}): 3055 (w), 1570 (w), 1561 (w), 1481 (w), 1451 (w), 1432 (s), 1359 (w), 1305 (w), 1275 (w), 1186 (w), 1154 w), 1095 (s), 1072 (w), 1027 (w), 999 (w), 852 (w), 749 (m), 738 (s), 701 (s), 688 (s).



bis(cyclohexyldiphenylphosphine)nickel(II) chloride (**S2**): $NiCl_2 \cdot 6H_2O$ (4 mmol, 0.951 g), EtOH (20 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then $PCyPh_2$ (8.5 mmol, 2.281 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 1 hour and then cooled to room temperature. Once cool, the solid was collected by vacuum filtration, washed twice with ethanol (10 mL) and twice with ether (10 mL). Drying under vacuum yielded **S2** (2.442 g, 92%) as a fine, deep green powder.[7]

***trans*-bis(cyclohexyldiphenylphosphine)(2-methylphenyl)nickel(II) chloride** (**2**): **S2** (2.42 mmol, 1.612 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (45 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (2.42 mmol, 0.986 M in THF, 2.45 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to lighten in color to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (15 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH, and dried under high vacuum to yield **2** (1.421 g, 81%) as a fine, yellow powder.

mp 172–173 °C dec.

Anal. Calcd for $C_{43}H_{49}ClNiP_2$: C, 71.54; H, 6.84. Found: C, 71.43; H, 6.74.

^{1}H NMR (500 MHz, C_6D_6, δ): 7.71 (s, 4H), 7.34 (s, 4H), 7.14 – 7.08 (m, 6H), 7.08 – 6.99 (m, 6H), 6.82 (d, J = 7.5 Hz, 1H), 6.66 (t, J = 6.9 Hz, 1H), 6.50 (t, J = 7.4 Hz, 2H), 2.95 (s, 3H), 2.64

[7] The complex may take on a variety of colors depending on the rate of crystallization, rate of cooling, and solvent used for synthesis due to varying proportions of tetrahedral and square planar isomers in the product.

(t, J = 10.7 Hz, 2H), 2.26 (d, J = 11.1 Hz, 2H), 2.00 (d, J = 10.8 Hz, 2H), 1.47 (dd, J = 22.5, 13.4 Hz, 4H), 1.38 (d, J = 12.3 Hz, 2H), 1.22 (q, J = 12.4 Hz, 2H), 1.10 (q, J = 12.4 Hz, 2H), 0.89 (q, J = 11.8 Hz, 2H), 0.71 (dq, J = 26.3, 13.1, 12.3 Hz, 4H).

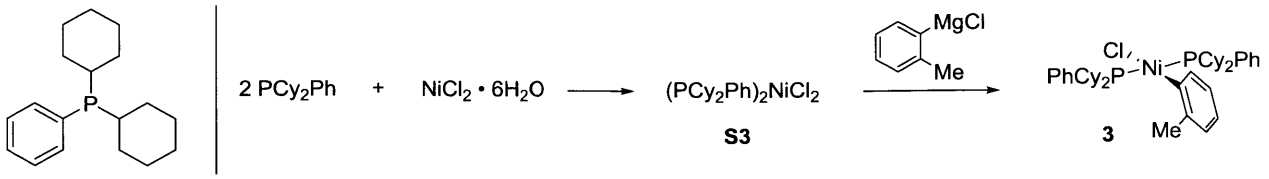
^{1}H NMR (500 MHz, CD_2Cl_2, δ): 7.49 – 7.14 (m, 20H), 6.56 (d, J = 6.6 Hz, 1H), 6.52 (t, J = 5.7 Hz, 1H), 6.39 (t, J = 6.5 Hz, 1H), 6.33 (d, J = 6.4 Hz, 1H), 2.59 (s, 3H), 2.17 (t, J = 10.6 Hz, 2H), 2.00 (d, J = 10.5 Hz, 2H), 1.65 (d, J = 10.4 Hz, 2H), 1.57 (d, J = 11.1 Hz, 2H), 1.47 (t, J = 11.5 Hz, 4H), 1.19 (q, J = 11.8, 11.4 Hz, 2H), 0.96 (q, J = 12.1, 10.3 Hz, 2H), 0.80 (q, J = 11.0, 10.2 Hz, 2H), 0.68 (q, J = 11.3, 10.4 Hz, 2H), 0.50 (q, J = 10.9 Hz, 2H).

^{31}P{^{1}H} NMR (202 MHz, C_6D_6, δ): 22.6 (s).

^{31}P{^{1}H} NMR (202 MHz, CD_2Cl_2, δ): 21.9 (s).

^{13}C{^{1}H} NMR (126 MHz, CD_2Cl_2, δ): 143.82 (t, J = 33.0 Hz), 143.73, 137.84, 134.63 (t, J = 5.2 Hz), 134.22 (t, J = 4.7 Hz), 129.71, 129.47, 129.30, 129.07 (t, J = 18.1 Hz), 127.82 (t, J = 4.2 Hz), 127.70 (t, J = 3.3 Hz), 127.53, 123.50, 122.53, 33.17 (t, J = 11.7 Hz), 28.57, 28.15, 27.37 (t, J = 5.4 Hz), 27.22 (t, J = 5.8 Hz), 26.53, 24.69.

FT-IR (ATR, cm^{-1}): 3047 (w), 2928 (m), 2852 (m), 1570 (w), 1561 (w), 1483 (m), 1449 (m), 1432 (m), 1372 (w), 1311 (w), 1292 (w), 1266 (m), 1205 (w), 1184 (w), 1173 (w), 1158 (w), 1117 (w), 1096 (m), 1076 (w), 1070 (w), 1027 (w), 999 (m), 915 (w), 889 (w), 850 (w), 733 (s), 692 (s).



bis(dicyclohexylphenylphosphine)nickel(II) chloride (S3): $NiCl_2 \cdot 6H_2O$ (5 mmol, 1.188 g), EtOH (25 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then PCy_2Ph (10.5 mmol, 2.881 g) was added in one portion, causing formation of deep purple solid. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration, washed twice with ethanol (15 mL) and twice with ether (15 mL). Drying under vacuum yielded **S3** (3.212 g, 95%) as a fine, purple powder.

***trans*-bis(dicyclohexylphenylphosphine)(2-methylphenyl)nickel(II) chloride (3)**: **S3** (14.37 mmol, 9.748 g) was placed in an oven-dried, 500 mL round-bottom flask containing a magnetic stir bar. Solvent (250 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (14.37 mmol, 0.865 M in THF, 16.61 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color from dark purple to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (100 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 10 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH, and dried under high vacuum to yield **3** (9.325 g, 88%) as a fine, yellow powder.

mp 149–150 °C dec.

Anal. Calcd for $C_{43}H_{61}ClNiP_2$: C, 70.36; H, 8.36. Found: C, 70.12; H, 8.38.

^{1}H NMR (500 MHz, C_6D_6, δ): 7.49 (s, 4H), 7.10 (app s, 7H), 6.76 – 6.58 (m, 3H), 3.51 (s, 3H), 2.52 (s, 4H), 2.42 – 2.21 (m, 4H), 1.95 – 0.83 (m, 36H).

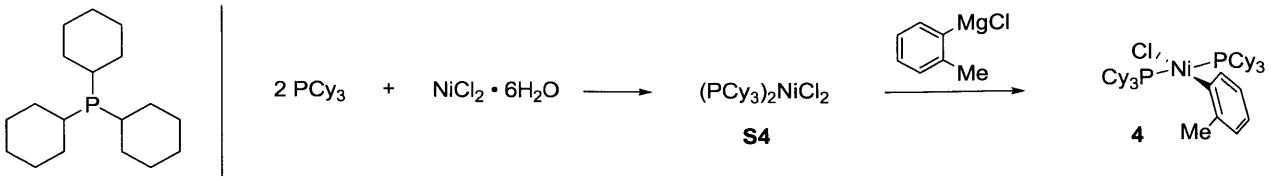
^{31}P{^{1}H} NMR (202 MHz, C_6D_6, δ): 16.09 (s).

$^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6, δ): 149.86 (t, J = 32.3 Hz), 142.76, 138.45, 132.91, 130.70 (t, J = 15.5 Hz), 127.09, 124.17, 122.27, 33.90 (t, J = 9.8 Hz), 33.32 (t, J = 9.7 Hz), 30.25 (d, J = 21.6 Hz), 29.47 (d, J = 7.5 Hz), 28.28 (t, J = 5.3 Hz), 28.09 (t, J = 6.2 Hz), 27.88 (t, J = 5.2 Hz), 27.66, 26.79 (d, J = 7.3 Hz).

FT-IR (ATR, cm^{-1}): 3049 (w), 2922 (m), 2852 (m), 1570 (w), 1561 (w), 1447 (m), 1432 (m), 1326 (w), 1296 (w), 1264 (m), 1203 (w), 1178 (w), 1115 (w), 1027 (w), 1003 (m), 917 (w), 889 (w), 848 (m), 731 (s), 695 (s).

The mp, ^1H, ^{31}P, ^{13}C, and IR spectra match those previously reported in the literature.[8]

[8] Standley, E. A. and Jamison, T. F.; *J. Am. Chem. Soc.* **2013**, *135*, 1585–1592.



bis(tricyclohexylphosphine)nickel(II) chloride (S4): $NiCl_2 \cdot 6H_2O$ (10 mmol, 2.377 g), EtOH (40 mL), and a magnetic stir bar were placed in a 100 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then PCy_3 (20.5 mmol, 5.749 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 1 hour and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration, washed twice with ethanol (20 mL) and twice with ether (20 mL). Drying under vacuum yielded **S4** (6.729 g, 97%) as a fine, purple powder.

***trans*-bis(tricyclohexylphosphine)(2-methylphenyl)nickel(II) chloride (4)**: **S4** (2.0 mmol, 1.381 g) was placed in an oven-dried, 250 mL round-bottom flask containing a magnetic stir bar. CH_2Cl_2 (180 mL[9]) was added, the mixture was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (2.0 mmol, 0.856 M in THF, 2.34 mL) was slowly added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to brown and ultimately dark yellow. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. THF (50 mL) was added to dissolve the product, which was then filtered through a short plug of Celite and washed with an additional 40 mL of THF, leaving any unreacted **S4** behind on the Celite. The (now pure) product was evaporated to dryness under reduced pressure, after which MeOH (20 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of MeOH (10 mL) and two portions of Et_2O (10 mL), and dried under high vacuum to yield **4** (6.873 g, 87%) as a fine, bright yellow powder.

[9] A large volume of solvent is necessary to dissolve $(PCy_3)_2NiCl_2$, which is poorly soluble in both THF and CH_2Cl_2. If the reaction is run with a slurry of **S4** in THF or CH_2Cl_2, the yield of **4** is reduced due to incomplete consumption of **S4**, though the product obtained is still of acceptable purity.

mp 163 °C.

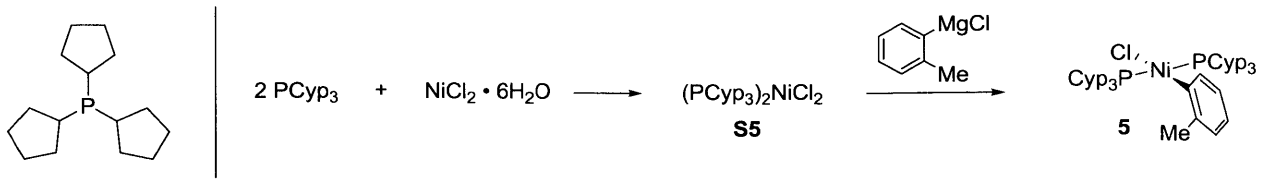
Anal. Calcd for $C_{43}H_{73}ClNiP_2$: C, 69.22; H, 9.86. Found: C, 69.15; H, 9.95.

^{1}H NMR (500 MHz, C_6D_6, δ): 7.54 (d, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.85 – 6.75 (m, 2H), 3.58 (s, 3H), 2.47 – 2.19 (m, 6H), 2.19 – 1.45 (m, 40H), 1.31 – 1.16 (m, 12H), 1.09 – 0.90 (m, 8H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 11.42.

^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 149.87 (t, J = 32.0 Hz), 143.64 (t, J = 2.4 Hz), 140.42 (t, J = 3.4 Hz), 126.84 (t, J = 3.0 Hz), 123.89 (t, J = 2.3 Hz), 122.21 (t, J = 2.3 Hz), 34.01 (t, J = 8.6 Hz), 30.91 (br s), 30.25, 29.79, 29.26, 28.39 (t, J = 5.3 Hz), 28.22 (t, J = 4.3 Hz), 27.0.

FT-IR (ATR, cm^{-1}): 2921 (s), 2850 (s), 1568 (w), 1561 (w), 1445 (s), 1421 (w), 1328 (w), 1300 (w), 1266 (m), 1229 (w), 1197 w), 1173 (m), 1126 (m), 1111 (m), 1074 (w), 1003 (m), 914 (m), 897 (m), 887 (m), 848 (s), 818 (w), 733 (s), 718 (m), 707 (w).



bis(tricyclopentylphosphine)nickel(II) chloride (S5): $NiCl_2 \cdot 6H_2O$ (6.66 mmol, 1.583 g), EtOH (30 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, and then $PCyp_3$ (13.32 mmol, 3.175 g, 3.22 mL) was added portionwise over 5 min, causing formation of deep purple solid. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration and washed twice with cold ethanol (15 mL). Drying under vacuum yielded **S5** (4.011 g, 99%) as a crystalline, maroon solid.

***trans*-bis(tricyclopentylphosphine)(2-methylphenyl)nickel(II) chloride (5)**: **S5** (3.81 mmol, 2.31 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. CH_2Cl_2 (60 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (3.81 mmol, 0.945 M in THF, 4.03 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (15 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 3 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with one portion of MeOH (10 mL) and one portion of Et_2O (10 mL), and dried under high vacuum to yield **5** (2.282 g, 90%) as a fine, bright yellow powder.

mp 139–140 °C dec.

Anal. Calcd for $C_{37}H_{61}ClNiP_2$: C, 67.19; H, 9.29. Found: C, 66.85; H, 9.30.

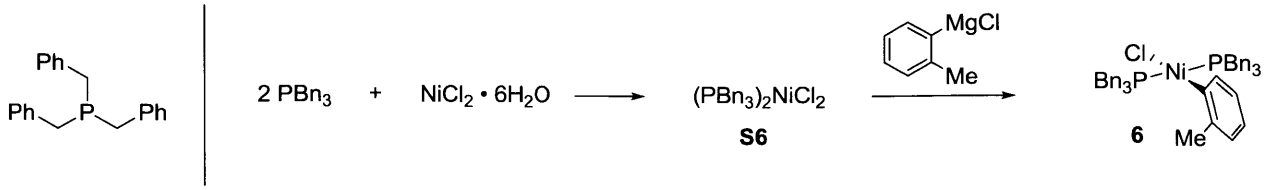
^{1}H NMR (300 MHz, C_6D_6, δ): 7.70 – 7.61 (m, 1H), 6.82 – 6.69 (m, 3H), 3.40 (s, 3H), 2.34 – 2.10 (m, 6H), 2.10 – 1.72 (m, 24H), 1.72 – 1.51 (m, 12H), 1.51 – 1.29 (m, 12H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 8.97.

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): 8.44.

$^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6, δ): 145.78 (t, J = 32.9 Hz), 144.36 (t, J = 2.9 Hz), 140.74 (t, J = 3.7 Hz), 126.56 (t, J = 3.1 Hz), 122.86 (t, J = 2.5 Hz), 121.68 (t, J = 2.3 Hz), 36.14 (t, J = 10.1 Hz), 30.39, 29.84, 28.42, 26.18 (t, J = 4.4 Hz), 25.87 (t, J = 4.5 Hz).

FT-IR (ATR, cm^{-1}): 3042 (w), 2945 (s), 2913 (s), 2867 (s), 1568 (w), 1561 (w), 1553 (w), 1473 (w), 1449 (m), 1423 (w), 1371 w), 1302 (w), 1264 (w), 1247 (w), 1236 (w), 1128 (m), 1065 (w), 1044 (w), 1029 (w), 1014 (w), 906 (m), 852 (w), 736 (s), 716 (w), 703 (w).



bis(tribenzylphosphine)nickel(II) chloride (**S6**): $NiCl_2 \cdot 6H_2O$ (8 mmol, 1.902 g), EtOH (30 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then PBn_3 (17 mmol, 5.174 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 30 min to fully crystallize the product. The solid was collected by vacuum filtration and washed twice with ethanol (5 mL). Drying under vacuum yielded **S6** (5.683 g, 96%) as a deep maroon, crystalline solid.

***trans*-bis(tribenzylphosphine)(2-methylphenyl)nickel(II) chloride** (**6**): **S6** (10.12 mmol, 7.472 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (200 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (10.12 mmol, 0.945 M in THF, 10.71 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color from deep maroon to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (40 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH, and dried under high vacuum to yield **6** (7.195 g, 90%) as a fine, bright yellow powder. Crystals suitable for single-crystal X-ray diffraction were grown by the slow diffusion of pentane into a toluene solution of **6** at 5 °C.

mp 178 °C dec.[10]

Anal. Calcd for $C_{49}H_{49}ClNiP_2$: C, 74.12; H, 6.22. Found: C, 74.40; H, 6.44.

[10] Begins to discolor at 172 °C.

^{1}H NMR (500 MHz, C_6D_6, δ): 7.32 (d, *J* = 7.5 Hz, 12H), 7.16 (t, *J* = 7.3 Hz, 12H), 7.09 (t, *J* = 7.3 Hz, 6H), 6.74 (td, *J* = 6.9, 2.0 Hz, 1H), 6.72 – 6.65 (m, 2H), 6.51 (d, *J* = 7.5 Hz, 1H), 3.13 (dt, *J* = 14.1, 2.2 Hz, 6H), 2.81 (dt, *J* = 14.3, 3.8 Hz, 6H), 2.11 (s, 3H).

^{31}P{^{1}H} NMR (203 MHz, C_6D_6, δ): 13.40.

^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 153.92 (t, J = 32.4 Hz), 143.08 (t, J = 2.6 Hz), 135.70 (t, J = 2.3 Hz), 134.84 (t, J = 3.4 Hz), 131.02 (t, J = 2.2 Hz), 128.78, 126.73, 124.34, 122.74, 28.71 (t, J = 8.6 Hz), 26.43.

FT-IR (ATR, cm^{-1}): 3085 (w), 3062 (w), 3029 (w), 2975 (w), 2919 (w), 2906 (w), 1600 (m), 1494 (m), 1453 (m), 1406 (m), 1264 (w), 1229 (w), 1068 (m), 1029 (w), 1016 (w), 912 (w), 856 (m), 837 (m), 822 (w), 813 (w), 781 (m), 774 (m), 736 (s), 695 (s).

bis(methyldiphenylphosphine)nickel(II) chloride (**S7**): $NiCl_2 \cdot 6H_2O$ (17.42 mmol, 4.141 g), EtOH (55 mL), and a magnetic stir bar were placed in a 100 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, and then PPh_2Me (38.32 mmol, 7.672 g, 7.13 mL) was added portionwise over 5 min. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration and washed twice with ethanol (5 mL). Drying under vacuum yielded **S7** (9.111 g, 99%) as a deep maroon, crystalline solid.

***trans*-bis(methyldiphenylphosphine)(2-methylphenyl)nickel(II) chloride** (**7**): **S7** (8.29 mmol, 4.394 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (55 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (8.29 mmol, 0.856 M in THF, 9.68 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (25 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min). After the suspension was cooled to 0 °C, the bright yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH (10 mL), and dried under high vacuum to yield **7** (3.940 g, 81%)[11] as a fine, bright yellow powder.

mp 139–140 °C dec.

Anal. Calcd for $C_{33}H_{33}ClNiP_2$: C, 67.67; H, 5.68. Found: C, 67.41; H, 5.78.

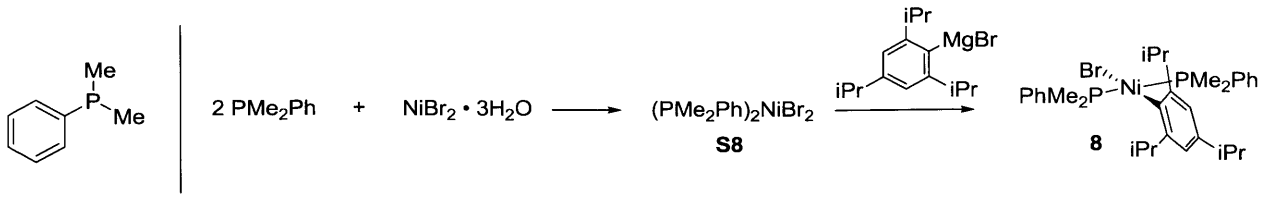
^{1}H NMR (500 MHz, C_6D_6, δ): 7.84 (br s, 4H), 7.62 (br s, 4H), 7.12 – 6.94 (m, 13H), 6.72 – 6.64 (m, 1H), 6.64 – 6.53 (m, 2H), 2.75 (s, 3H), 1.08 (s, 6H).

[11] Complex **7** is somewhat soluble in methanol, causing the lower yield in comparison to other complexes. The yield can be further raised by collecting a second crop of solid from the filtrate.

$^{31}P\{^{1}H\}$ NMR (121 MHz, C_6D_6, δ): 8.32.

$^{13}C\{^{1}H\}$ NMR (126 MHz, C_6D_6, δ): 153.09 (t, J = 33.7 Hz), 143.27, 136.02 (t, J = 3.8 Hz), 134.99 (t, J = 20.3 Hz), 133.84 (t, J = 5.2 Hz), 133.46 (t, J = 20.8 Hz), 133.26 (t, J = 5.4 Hz), 129.79, 129.56, 124.03, 122.55, 26.56, 12.94 (t, J = 15.7 Hz).

FT-IR (ATR, cm^{-1}): 3051 (w), 1570 (w), 1561 (w), 1484 (w), 1434 (m), 1372 (w), 1335 (w), 1309 (w), 1285 (w), 1186 (w), 1160 (w), 1098 (m), 1074 (w), 1027 (w), 1012 (w), 999 (w), 895 (m), 887 (s), 878 (s), 850 (w), 740 (s), 729 s), 692 (s).



bis(dimethylphenylphosphine)nickel(II) bromide (S8): $NiBr_2 \cdot 3H_2O$ (20 mmol, 5.451 g), EtOH (25 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, and then PMe_2Ph (42 mmol, 5.802 g, 5.98 mL) was added portionwise over 5 min, causing formation of a deep blue solution with maroon solid.[12] The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration and washed twice with ethanol (5 mL). Drying under vacuum yielded **S8** (9.423 g, 95%) as a dark red, crystalline solid.

***trans*-bis(dimethylphenylphosphine)(2,4,6-triisopropylphenyl)nickel(II) bromide (8)**: **S8** (6.00 mmol, 2.969 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (40 mL) was added, the solution was cooled to 0 °C with an ice bath, and 2,4,6-triisopropylmagnesium bromide (6.00 mmol, 0.447 M in THF, 13.42 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to dark yellow. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (30 mL) was added, the mixture was sonicated for 5 min, and then the flask was placed in a freezer at –30 °C for 16 hours to allow the product to crystallize.[13] The yellow, crystalline solid was collected by vacuum filtration, washed with two portions of cold MeOH (5 mL), and dried under high vacuum to yield **8** (3.085 g, 83%) as a yellow, crystalline solid.

mp 150 °C.

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[12] The solution appears blue in color due to the presence of the tetrahedral isomer in solution, whereas the square planar (deep red) isomer is favored in the solid state near room temperature.

[13] Complex **8** can be isolated without standing in a freezer, but the yield is considerably lower due to the high solubility of **8** in most solvents, including methanol.

Anal. Calcd for $C_{31}H_{45}BrNiP_2$: C, 60.23; H, 7.34. Found: C, 60.42; H, 7.33.

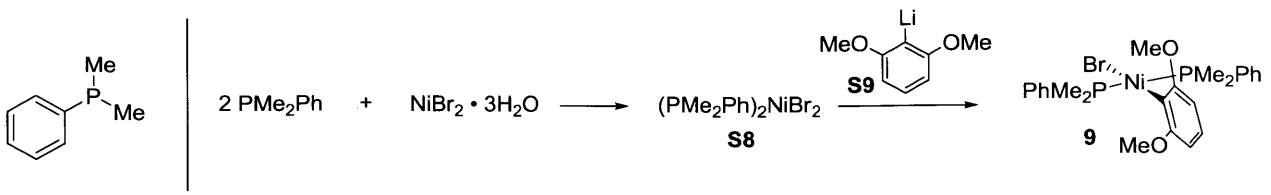
^{1}H NMR (500 MHz, C_6D_6, δ): 8.11 (tdd, J = 7.2, 5.0, 2.8 Hz, 4H), 7.13 (dt, J = 7.2, 1.3 Hz, 4H), 7.08 (t, J = 7.2 Hz, 2H), 6.81 (s, 2H), 4.86 (hept, J = 6.7 Hz, 2H), 2.81 (hept, J = 6.9 Hz, 1H), 1.27 – 1.21 (m, 30H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): –7.38.

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): –6.23.

^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 152.24 (t, J = 3.2 Hz), 148.42 (t, J = 32.9 Hz), 145.03 (t, J = 2.8 Hz), 136.02 (t, J = 19.6 Hz), 133.40 (t, J = 5.6 Hz), 129.91, 128.18 (t, J = 4.6 Hz), 120.46 (t, J = 3.3 Hz), 37.63, 34.20, 25.88, 24.88, 15.29 (t, J = 14.7 Hz).

FT-IR (ATR, cm^{-1}): 3051 (w), 2978 (w), 2960 (m), 2930 (m), 2867 (w), 1460 (w), 1434 (m), 1419 (m), 1380 (w), 1358 (w), 1292 (w), 1281 (w), 1238 (w), 1190 (w), 1158 (w), 1095 (m), 1050 (w), 1016 (w), 943 (m), 899 (s), 873 m), 839 (m), 748 (m), 742 (s), 731 (m), 723 (m), 707 (m), 694 (s), 677 (m).



1,3-dimethoxyphenyllithium (S9): 1,3-dimethoxybenzene (10 mmol, 1.382 g, 1.31 mL) and THF (25 mL) were placed in a 50 mL, oven-dried, round-bottom flask equipped with a magnetic stir bar. The flask was cooled to 0 °C with an ice bath and *n*-BuLi (8.20 mmol, 2.46 M in hexanes, 3.33 mL) was added dropwise. After stirring for 10 min, the flask was warmed to room temperature and stirred for 30 min. This reagent (**S9**) was used without purification.

***trans*-bis(dimethylphenylphosphine)(2,6-dimethoxyphenyl)nickel(II) bromide (9)**: **S8** (8.167 mmol, 4.041 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (25 mL) was added, the solution was cooled to 0 °C with an ice bath, and the previously prepared solution of **S9** was added dropwise via cannula with vigorous stirring. Near the end of the addition, the solution began to change in color to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (50 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min), and then the flask was placed in a freezer at –30 °C for 16 hours to allow the product to crystallize. The yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH, and dried under high vacuum to yield **9** (3.923 g, 87%) as a yellow solid. Crystals suitable for single-crystal X-ray diffraction were grown by the slow diffusion of pentane into a THF solution of **9** at 5 °C.

mp 190–192 °C dec.[14]

Anal. Calcd for $C_{24}H_{31}BrNiO_2P_2$: C, 52.22; H, 5.66. Found: C, 52.40; H, 5.53.

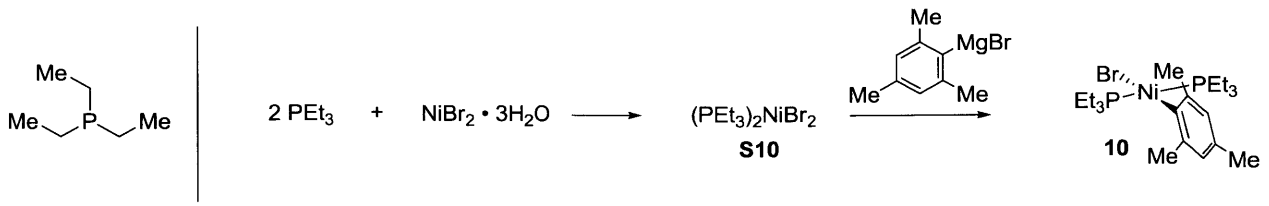
^{1}H NMR (500 MHz, CD_2Cl_2, δ): 7.63 – 7.57 (m, 4H), 7.34 – 7.30 (m, 6H), 6.80 (tt, J = 8.0, 1.8 Hz, 1H), 6.09 (d, J = 8.0 Hz, 2H), 3.62 (s, 6H), 1.23 (t, J = 3.8 Hz, 12H).

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): –5.09.

[14] Long, slow discoloration begins around 125 °C.

$^{13}C\{^{1}H\}$ NMR (126 MHz, CD_2Cl_2, δ): 162.82 (t, J = 4.0 Hz), 137.11 (d, J = 20.2 Hz), 131.29 (t, J = 5.4 Hz), 129.16 (t, J = 1.0 Hz), 127.95 (t, J = 4.6 Hz), 125.26 (t, J = 2.7 Hz), 122.33 (t, J = 36.8 Hz), 102.51 (t, J = 3.0 Hz), 54.85, 13.64 (t, J = 14.6 Hz).

FT-IR (ATR, cm^{-1}): 3077 (m), 2950 (m), 2909 (m), 2824 (w), 1619 (m), 1591 (m), 1572 (m), 1561 (m), 1475 (s), 1451 (m), 1434 (s), 1417 (s), 1261 (m), 1218 (s), 1152 (s), 1104 (s), 1091 (s), 1031 (m), 1022 (m), 1001 m), 938 (s), 908 (s), 901 (s), 871 (s), 846 (m), 839 (m), 783 (m), 751 (s), 736 (s), 710 (s), 703 (s), 688 (s), 675 (s).



bis(triethylphosphine)nickel(II) bromide (S10): $NiBr_2 \cdot 3H_2O$ (10 mmol, 2.726 g), EtOH (20 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, and then PEt_3 (21 mmol, 2.481 g, 3.09 mL) was added portionwise over 5 min. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration and washed twice with ethanol (5 mL) Drying under vacuum yielded **S10** (4.326 g, 95%) as a deep maroon, crystalline solid.

***trans*-bis(triethylphosphine)(2,4,6-trimethylphenyl)nickel(II) bromide (10)**: **S10** (9.51 mmol, 4.325 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (30 mL) was added, the solution was cooled to 0 °C with an ice bath, and 2,4,6-trimethylphenylmagnesium bromide (9.51 mmol, 0.877 M in THF, 10.84 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to dark yellow. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (25 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH, and dried under high vacuum to yield **10** (4.131 g, 88%) as a fine, yellow powder.

mp 158–159 °C.

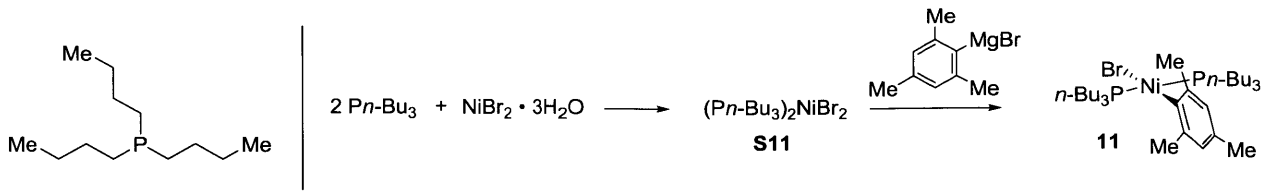
Anal. Calcd for $C_{21}H_{41}BrNiP_2$: C, 51.05; H, 8.36. Found: C, 51.15; H, 8.30.

^{1}H NMR (500 MHz, C_6D_6, δ): 6.63 (s, 2H), 2.96 (s, 6H), 2.23 (t, J = 1.6 Hz, 3H), 1.39 (dh, J = 11.0, 3.8 Hz, 12H), 0.93 (p, J = 7.6 Hz, 18H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 8.50.

$^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6, δ): 146.90 (t, J = 32.9 Hz), 141.44 (t, J = 3.3 Hz), 132.16 (t, J = 2.6 Hz), 126.47 (t, J = 3.1 Hz), 26.59, 20.85 (t, J = 0.9 Hz), 16.26 (t, J = 12.2 Hz), 8.63.

FT-IR (ATR, cm^{-1}): 2964 (m), 2932 (m), 2904 (m), 2878 (m), 1451 (m), 1406 (m), 1376 (w), 1363 (m), 1255 (w), 1033 (s), 1018 (m), 977 (w), 932 (w), 867 (w), 848 (m), 749 (s), 727 (s), 712 (s), 684 (s).



bis(tri-*n*-butylphosphine)nickel(II) bromide (S11): $NiBr_2 \cdot 3H_2O$ (30 mmol, 8.177 g), EtOH (100 mL), and a magnetic stir bar were placed in a 250 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, and then P(*n*-Bu)$_3$ (64 mmol, 12.948 g, 15.79 mL) was added portionwise over 5 min, causing formation of maroon solid. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was allowed to stand in a freezer at –30 °C for 3 hours,[15] after which the solid was collected by vacuum filtration and washed twice with ethanol (5 mL). Drying under vacuum yielded **S11** (16.61 g, 89%) as deep maroon, crystalline flakes.

bis(tri-*n*-butylphosphine)(2,4,6-trimethylphenyl)nickel(II) bromide (11): **S11** (4.67 mmol, 2.91 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (50 mL) was added, the solution was cooled to 0 °C with an ice bath, and 2,4,6-trimethylphenylmagnesium bromide (4.67 mmol, 0.877 M in THF, 5.32 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to brown. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (20 mL) was added and the mixture was sonicated for a few seconds, causing formation of a liquid layer of **11** at the bottom of the flask with a MeOH layer above it. The flask was placed in a freezer at –30 °C for 16 hours to induce the product to solidify. After standing in the freezer, the solid mass was isolated by filtration,[16] the solid was transferred to a vial and dried under high vacuum to yield **11** (2.771 g, 90%) as yellow-brown, waxy solid.

mp 42 °C.

Anal. Calcd for $C_{33}H_{65}BrNiP_2$: C, 59.83; H, 9.89. Found: C, 59.69; H, 9.89.

[15] Cooling the flask to 0 °C for 10 to 20 minutes is adequate, but the product is quite soluble in ethanol, so allowing the compound more time to crystallize will result in a higher yield.

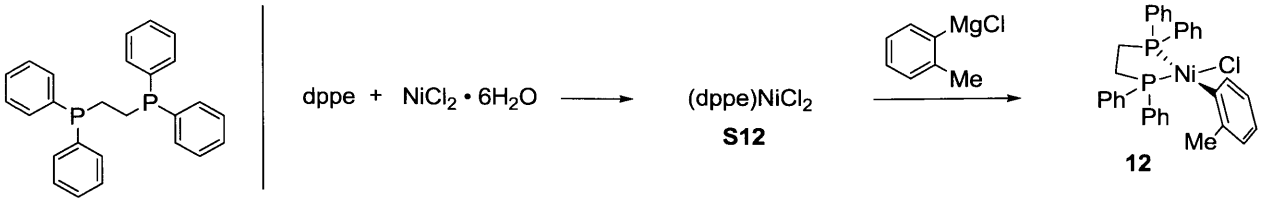
[16] Due to the high solubility of **11** in most solvents, the solid was not rinsed.

^{1}H NMR (300 MHz, C_6D_6, δ): 6.61 (s, 2H), 3.08 (s, 6H), 2.25 (t, J = 1.5 Hz, 3H), 1.65 – 1.54 (m, 12H), 1.54 – 1.40 (m, 12H), 1.24 (h, J = 7.2 Hz, 12H), 0.87 (t, J = 7.3 Hz, 18H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 2.75.

^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 146.74 (t, J = 33.0 Hz), 141.90 (t, J = 3.4 Hz), 132.24 (t, J = 2.6 Hz), 126.33 (t, J = 3.3 Hz), 26.85, 26.65, 25.19 (t, J = 6.1 Hz), 24.49 (t, J = 11.8 Hz), 20.66, 13.93.

FT-IR (ATR, cm^{-1}): 2956 (s), 2928 (s), 2872 (s), 2861 (s), 1464 (m), 1458 (s), 1449 (m), 1417 (m), 1406 (m), 1376 (m), 1365 m), 1341 (w), 1302 (w), 1281 (w), 1259 (w), 1229 (w), 1206 (w), 1192 (w), 1165 (w), 1089 (m), 1052 (w), 1018 (m), 971 (w), 910 (m), 901 (s), 843 (s), 794 (m), 774 (m), 763 (m), 723 (s), 712 (s).



[1,2-bis(diphenylphosphino)ethane]nickel(II) chloride (S12): $NiCl_2 \cdot 6H_2O$ (9.6 mmol, 2.282 g), EtOH (30 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then dppe (9.66 mmol, 3.849 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration and washed twice with ethanol (5 mL). Drying under vacuum yielded **S12** (4.956 g, 98%) as a fine, orange powder.

***cis*-[1,2-bis(diphenylphosphino)ethane](2-methylphenyl)nickel(II) chloride (12)**: **S12** (3.92 mmol, 2.07 g) was placed in an oven-dried, 250 mL round-bottom flask containing a magnetic stir bar. THF (200 mL) was added, the mixture was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (3.92 mmol, 0.986 M in THF, 3.98 mL) was added dropwise with vigorous stirring. Partway through the addition, the solution became completely homogeneous and began to change color to yellow. After complete addition of the Grignard reagent, the solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (20 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH (5 mL), and dried under high vacuum to yield **12** (1.92 g, 84%) as a fine, bright yellow powder.

mp 190–192 °C dec.

Anal. Calcd for $C_{33}H_{31}ClNiP_2$: C, 67.90; H, 5.35. Found: C, 68.28; H, 5.66.

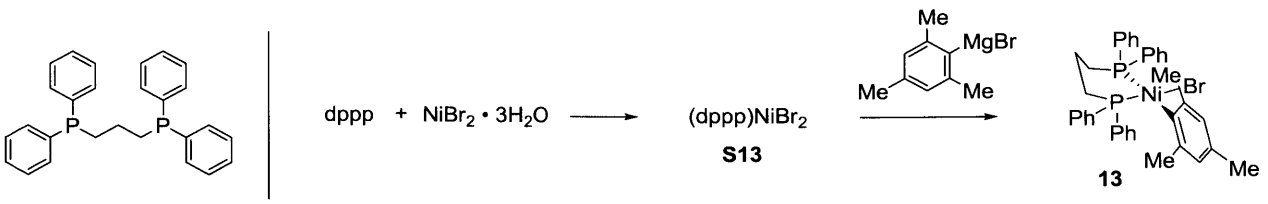
^{1}H NMR (500 MHz, CD_2Cl_2, δ): 8.16 (dd, J = 10.9, 7.3 Hz, 4H), 7.77 (ddd, J = 9.2, 7.1, 1.8 Hz, 2H), 7.62 – 7.41 (m, 9H), 7.31 (t, J = 7.1 Hz, 1H), 7.20 (dt, J = 8.4, 4.7 Hz, 1H), 7.07 (td, J =

7.7, 2.6 Hz, 2H), 6.71 (dd, *J* = 10.8, 7.6 Hz, 2H), 6.59 (dd, *J* = 6.0, 2.9 Hz, 2H), 6.45 – 6.39 (m, 1H), 2.58 – 2.34 (m, 2H), 2.34 – 2.09 (m, 4H), 1.60 (tdd, *J* = 14.4, 11.7, 6.7 Hz, 1H).

$^{31}P\{^{1}H\}$ NMR (121 MHz, CD_2Cl_2, δ): 53.09 (d, *J* = 17.9 Hz), 35.78 (d, *J* = 17.8 Hz).

$^{13}C\{^{1}H\}$ NMR (126 MHz, CD_2Cl_2, δ): 158.03 (dd, J = 86.1, 38.5 Hz), 143.71 (t, J = 2.0 Hz), 136.17 (dd, J = 3.1, 1.7 Hz), 134.97 (d, J = 11.2 Hz), 134.08 (d, J = 11.2 Hz), 133.14 (d, J = 10.3 Hz), 132.20 (d, J = 8.4 Hz), 131.92 (d, J = 2.6 Hz), 131.66 (d, J = 1.5 Hz), 131.28 (d, J = 2.1 Hz), 130.87 (dd, J = 47.8, 0.6 Hz), 130.73 (d, J = 2.3 Hz), 130.39 (dd, J = 31.9, 0.8 Hz), 130.35 (d, J = 2.7 Hz), 129.72 (dd, J = 56.0, 5.0 Hz), 129.38 (d, J = 9.2 Hz), 129.28 (d, J = 10.5 Hz), 129.02 (dd, J = 6.3, 2.4 Hz), 128.94 (d, J = 9.4 Hz), 127.94 (d, J = 10.1 Hz), 123.49 (dd, J = 6.3, 1.7 Hz), 122.71 (t, J = 1.2 Hz), 29.34 (dd, J = 27.7, 21.7 Hz), 25.50 (q, J = 1.7 Hz), 22.22 (dd, J = 26.0, 11.4 Hz).

FT-IR (ATR, cm^{-1}): 3051 (w), 1561 (w), 1434 (m), 1421 (w), 1098 (m), 1026 (m), 1012 (w), 999 (w), 873 (w), 817 (m), 749 m), 742 (s), 708 (m), 692 (s), 679 (m), 652 (m).



[1,3-bis(diphenylphosphino)propane]nickel(II) bromide (S13): $NiBr_2 \cdot 3H_2O$ (10 mmol, 2.726 g), EtOH (25 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then dppp (10 mmol, 4.124 g) was added in one portion, causing formation of red solid. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration, washed twice with ethanol (5 mL) and twice with ether (5 mL). Drying under vacuum yielded **S13** (5.59 g, 89%) as a fine, red powder.

***cis*-[1,3-bis(diphenylphosphino)propane](2,4,6-trimethylphenyl)nickel(II) bromide (13)**: **S13** (3.95 mmol, 2.492 g) was placed in an oven-dried, 250 mL round-bottom flask containing a magnetic stir bar. THF (110 mL) and CH_2Cl_2 (35 mL) were added, the mixture was cooled to 0 °C with an ice bath, and 2,4,6-trimethylphenylmagnesium bromide (3.95 mmol, 0.877 M in THF, 4.50 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to red. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (25 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min). After the suspension was cooled to 0 °C, the orange precipitate was collected by vacuum filtration, washed with two portions of MeOH (10 mL), and dried under high vacuum to yield **13** (2.251 g, 85%) as a fine, bright orange powder.

mp 176–178 °C dec.

mp 215–218 °C dec (sealed tube).

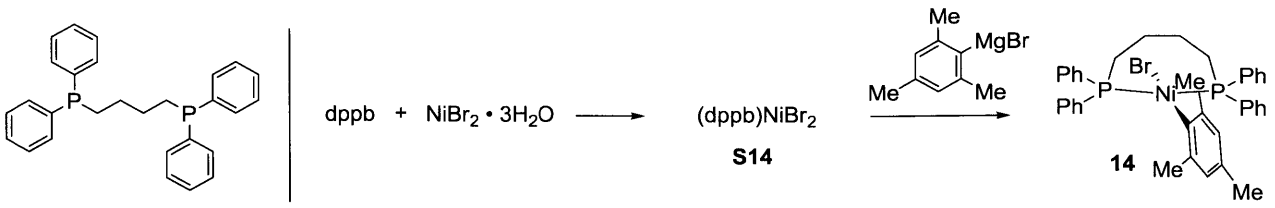
Anal. Calcd for $C_{36}H_{37}BrNiP_2$: C, 64.51; H, 5.56. Found: C, 64.68; H, 5.57.

^{1}H NMR (500 MHz, CD_2Cl_2, δ): 7.85 (t, *J* = 8.5 Hz, 4H), 7.53 – 7.42 (m, 6H), 7.30 (t, *J* = 9.2 Hz, 4H), 7.22 (t, *J* = 8.2 Hz, 2H), 6.99 (t, *J* = 7.5 Hz, 4H), 6.04 (s, 2H), 2.66 (s, 6H), 2.49 (t, *J* = 8.8 Hz, 2H), 2.17 (t, *J* = 8.4 Hz, 2H), 1.93 (s, 3H), 1.86 – 1.71 (m, 2H).

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): 21.05 (d, *J* = 42.1 Hz), –5.59 (d, *J* = 42.0 Hz).

^{13}C{^{1}H} NMR (126 MHz, CD_2Cl_2, δ): 151.44 (dd, J = 79.8, 32.4 Hz), 140.30 (dd, J = 3.5, 1.8 Hz), 133.69 (d, J = 36.5 Hz), 133.54 (d, J = 9.8 Hz), 133.40 (d, J = 9.8 Hz), 133.01 (dd, J = 49.4, 3.2 Hz), 131.98 (dd, J = 1.9, 0.8 Hz), 130.22 (d, J = 2.2 Hz), 129.90 (d, J = 2.4 Hz), 128.74 (d, J = 9.1 Hz), 127.60 (d, J = 9.8 Hz), 127.14 (dd, J = 6.3, 2.4 Hz), 29.16 (dd, J = 21.7, 5.0 Hz), 27.13 (dd, J = 19.5, 3.5 Hz), 26.23 (dd, J = 2.1, 1.5 Hz), 20.02, 19.23 (d, J = 3.7 Hz).

FT-IR (ATR, cm^{-1}): 3057 (w), 3044 (w), 2975 (w), 2911 (w), 2893 (w), 2868 (w), 1483 (w), 1432 (m), 1419 (w), 1371 (w), 1363 (w), 1309 (w), 1262 (w), 1190 (w), 1154 (w), 1095 (m), 1072 (w), 1027 (w), 1009 (w), 999 w), 970 (m), 936 (w), 852 (w), 835 (m), 794 (w), 733 (s), 690 (s), 654 (s).



[1,4-bis(diphenylphosphino)butane]nickel(II) bromide (S14): $NiBr_2 \cdot 3H_2O$ (5 mmol, 1.363 g), EtOH (60 mL), and a magnetic stir bar were placed in a 100 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then dppb (5 mmol, 2.132 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min, during which time a green solid formed. The flask was cooled to room temperature, after which the solid was collected by vacuum filtration, washed twice with ethanol (5 mL) and twice with ether (5 mL). Drying under vacuum yielded **S14** (3.284 g, 96%) as a fine, pale green powder.

***trans*-[1,4-bis(diphenylphosphino)butane](2,4,6-trimethylphenyl)nickel(II) bromide (14)**: **S14** (2 mmol, 1.290 g) was placed in an oven-dried, 250 mL round-bottom flask containing a magnetic stir bar. THF (150 mL) was added, which formed a slurry of **S14**.[17] 2,4,6-trimethylphenylmagnesium bromide (2.10 mmol, 0.755 M in THF, 2.78 mL) was added dropwise over 40 min with vigorous stirring. Over the course of the addition, the reaction mixture changed in color from green to brown, and finally orange at the end of the addition, as well as becoming fully homogeneous. The solution was stirred for an additional 15 min, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (20 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH (5 mL), two portions of ether (20 mL), and dried under high vacuum to yield **14** (1.177 g, 86%) as a fine, yellow powder.

mp 159–163 °C dec.

[17] **S14** is very poorly soluble in many solvents. The product **14** is very soluble in THF, however, so slow addition of the Grignard is essential to prevent addition of two equivalents to each nickel. As the reaction progresses, more and more **S14** dissolves into solution, which eventually becomes completely homogeneous.

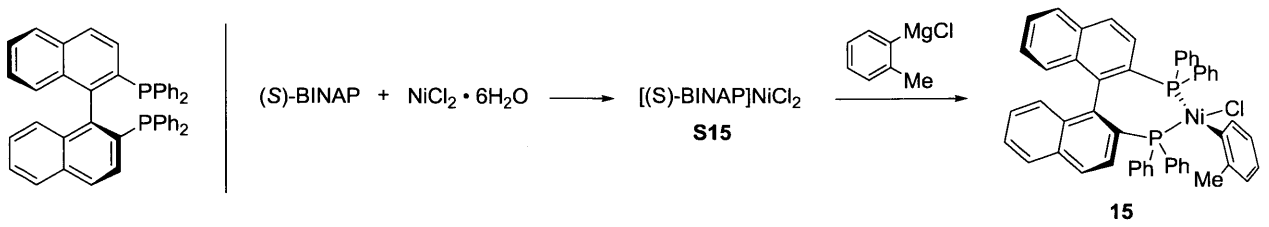
Anal. Calcd for $C_{37}H_{39}BrNiP_2$: C, 64.95; H, 5.74. Found: C, 65.01; H, 5.79.

^{1}H NMR (500 MHz, CD_2Cl_2, δ): 7.53 – 7.41 (m, 8H), 7.33 (t, J = 7.3 Hz, 4H), 7.23 (t, J = 7.5 Hz, 8H), 6.12 (s, 2H), 2.45 (s, 6H), 1.87 (s, 3H), 1.36 (s, 4H), 0.86 – 0.74 (m, 4H).

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): 13.24.

^{13}C{^{1}H} NMR (126 MHz, CD_2Cl_2, δ): 143.56 (t, J = 33.2 Hz), 141.92, 133.94 (t, J = 5.1 Hz), 133.01 (t, J = 19.3 Hz), 132.71, 129.59, 127.83 (t, J = 4.4 Hz), 126.90, 26.11, 20.32.

FT-IR (ATR, cm^{-1}): 3053 (m), 2909 (m), 2867 (m), 1483 (m), 1434 (s), 1180 (m), 1158 (m), 1121 (m), 1095 (m), 1072 (m), 1026 (m), 1016 (m), 999 (m), 843 (m), 738 (s), 692 (s).



[(*S*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene]nickel(II) chloride (S15):[18] $NiCl_2 \cdot 6H_2O$ (4.10 mmol, 0.975 g) and a magnetic stir bar were placed into a dry, 100 mL round-bottom flask. The flask was put under vacuum and the contents gently heated with a heat gun until most of the nickel chloride appeared light orange.[19,20] The flask was cooled, refilled with nitrogen and then (*S*)-(−)-BINAP (4.00 mmol, 2.491 g) was added followed by dry acetonitrile (50 mL). A reflux condenser was fitted to the flask and the mixture was heated to reflux for 24 hours. Once cool, the now black solution was passed through a short plug of Celite to remove unreacted $NiCl_2$. The filtrate was evaporated to dryness under reduced pressure and then dried under high vacuum to yield **S15** (2.828 g, 94%) as a fine, black powder.

***cis*-[(*S*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene](2-methylphenyl)nickel(II) chloride (15)**: **S15** (17.66 mmol, 13.287 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. CH_2Cl_2 (300 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (17.66 mmol, 0.986 M in THF, 17.91 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color from dark purple to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (55 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the bright yellow precipitate was collected by vacuum filtration, washed with two portions of MeOH (15 mL) and two portions of ether (20 mL), and dried under high vacuum to yield **15** (13.867 g, 97%, 56:44 dr) as

[18] This procedure is a modification of that reported for the synthesis of (Tol-BINAP)$NiCl_2$. See Thomson, R. J. and Evans, D. A. *J. Am. Chem. Soc.* **2005**, *127*, 10506–10507.

[19] It is not ideal to completely dehydrate the $NiCl_2 \cdot 6H_2O$ to anhydrous $NiCl_2$—ca. 1 equivalent of water is useful to accelerate the rate of reaction.

[20] The dehydrated $NiCl_2$ forms an extremely fine powder and can easily travel up into the vacuum manifold. A piece of cotton, laboratory tissue, or glass wool placed into the vacuum line is recommended.

a fine, yellow powder. Crystals suitable for single-crystal X-ray diffraction were grown by the slow diffusion of pentane into a $CHCl_3$ solution of **15** at 5 °C.

mp 159–160 °C dec.

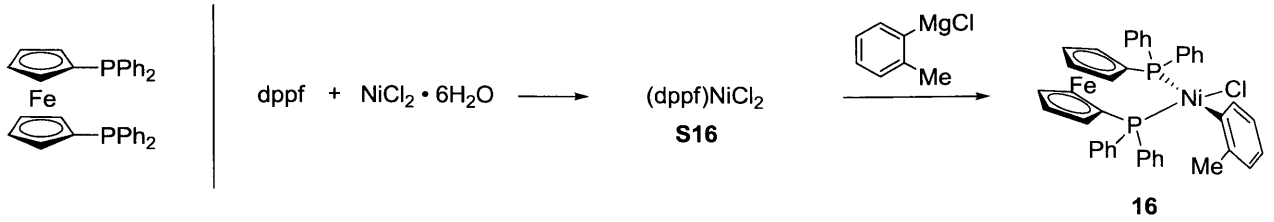
Anal. Calcd for $C_{51}H_{39}ClNiP_2$: C, 75.81; H, 4.87. Found: C, 75.86; H, 5.09.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.43 (dd, J = 10.1, 8.7 Hz, 1H), 8.30 (t, J = 9.3 Hz, 1H), 8.16 – 8.08 (m, 2H), 8.05 – 7.97 (m, 2H), 7.95 (ddd, J = 7.0, 5.5, 1.2 Hz, 1H), 7.91 (dd, J = 8.9, 1.7 Hz, 1H), 7.82 (ddd, J = 8.8, 1.9, 0.8 Hz, 1H), 7.79 – 7.70 (m, 3H), 7.66 – 7.60 (m, 2H), 7.60 – 7.56 (m, 1H), 7.56 – 7.46 (m, 9H), 7.45 – 7.23 (m, 9H), 7.22 – 7.08 (m, 6H), 7.07 – 7.02 (m, 2H), 6.98 (dddd, J = 13.6, 8.3, 6.7, 1.3 Hz, 2H), 6.89 (tdd, J = 8.3, 7.3, 3.4, 2.1 Hz, 4H), 6.86 – 6.72 (m, 9H), 6.69 (ddd, J = 12.4, 7.2, 1.6 Hz, 2H), 6.64 (tq, J = 6.3, 1.8 Hz, 6H), 6.60 – 6.51 (m, 6H), 6.50 – 6.30 (m, 2H), 3.24 (s, 3H), 2.80 (s, 3H).

^{31}P{^{1}H} NMR (203 MHz, $CDCl_3$, δ): 33.47 (d, J = 22.2 Hz, major isomer), 29.13 (d, J = 21.7 Hz, minor isomer), 15.58 (d, J = 22.2 Hz, major isomer), 15.08 (d, J = 21.8 Hz, minor isomer).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 34.25 (d, J = 21.8 Hz, major isomer), 29.72 (d, J = 21.2 Hz, minor isomer), 16.58 (d, J = 21.7 Hz, major isomer), 15.11 (d, J = 21.1 Hz, minor isomer).

FT-IR (ATR, cm^{-1}): 3053 (w), 1559 (w), 1499 (w), 1477 (w), 1434 (m), 1371 (w), 1307 (w), 1208 (w), 1180 (w), 1158 (w), 1115 (w), 1091 (w), 1027 (m), 998 (w), 871 (w), 846 (w), 818 (m), 776 (w), 746 (m), 733 (m), 727 (m), 692 (s), 673 (m).



[1,1'-bis(diphenylphosphino)ferrocene]nickel(II) chloride (S16): $NiCl_2 \cdot 6H_2O$ (8.5 mmol, 2.02 g), EtOH (25 mL), and a magnetic stir bar were placed in a 50 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then dppf (8.5 mmol,[21] 4.712 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration, washed twice with ethanol (20 mL) and twice with ether (20 mL). Drying under vacuum yielded **S16** (5.667 g, 97%) as a deep green, microcrystalline solid.

***cis*-[1,1'-bis(diphenylphosphino)ferrocene](2-methylphenyl)nickel(II) chloride (16)**: **S16** (6.81 mmol, 4.658 g) was placed in an oven-dried, 250 mL round-bottom flask containing a magnetic stir bar. Dichloromethane (180 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (6.81 mmol, 0.945 M in THF, 7.21 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color from green to orange. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (25 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 5 min). After the suspension was cooled to 0 °C, the yellow precipitate was collected by vacuum filtration, washed with two portions of cold MeOH (10 mL), and dried under high vacuum to yield **16** (4.795 g, 95%) as a fine, bright yellow powder.

mp 179–180 °C m dec.[22]

Anal. Calcd for $C_{41}H_{35}ClFeNiP_2$: C, 66.58; H, 4.77. Found: C, 66.61; H, 4.82.

[21] Due to the low solubility of dppf in EtOH, it is not suggested to use an excess of ligand, as it may contaminate the product.

[22] Begins to discolor at 161 °C.

^{1}H NMR (500 MHz, C_6D_6, δ): 8.67 (t, J = 8.4 Hz, 2H), 8.35 – 8.23 (m, 4H), 7.73 (t, J = 6.4 Hz, 1H), 7.44 (t, J = 7.1 Hz, 1H), 7.25 – 7.18 (m, 4H), 7.03 (t, J = 4.9 Hz, 1H), 6.99 (d, J = 5.6 Hz, 1H), 6.95 (t, J = 7.0 Hz, 2H), 6.91 – 6.78 (m, 3H), 6.74 (t, J = 7.4 Hz, 1H), 6.69 (t, J = 6.3 Hz, 2H), 6.65 (t, J = 7.2 Hz, 1H), 6.50 (d, J = 7.3 Hz, 1H), 5.28 (s, 1H), 4.14 (s, 1H), 4.04 (s, 1H), 3.85 (s, 1H), 3.71 (s, 1H), 3.66 (s, 1H), 3.61 (s, 1H), 3.41 (s, 1H), 2.94 (s, 3H).

^{1}H NMR (500 MHz, CD_2Cl_2, δ): 8.25 (dt, J = 7.9, 5.5 Hz, 4H), 8.06 (ddd, J = 9.8, 6.5, 3.0 Hz, 2H), 7.58 – 7.48 (m, 7H), 7.35 (t, J = 7.3 Hz, 2H), 7.26 (d, J = 6.6 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.84 (td, J = 7.8, 2.6 Hz, 2H), 6.68 (t, J = 9.5 Hz, 2H), 6.51 (t, J = 7.4 Hz, 1H), 6.38 (t, J = 7.2 Hz, 1H), 6.18 (d, J = 7.4 Hz, 1H), 5.23 (s, 1H), 4.63 (s, 1H), 4.33 (s, 1H), 4.27 (s, 1H), 4.12 (s, 1H), 4.10 (s, 1H), 3.60 (dd, J = 2.2, 1.1 Hz, 1H), 3.40 (q, J = 1.3 Hz, 1H), 2.52 (s, 3H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 30.42 (d, J = 24.6 Hz), 12.33 (d, J = 24.7 Hz).

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): 30.08 (d, J = 26.0 Hz), 12.68 (d, J = 26.1 Hz).

FT-IR (ATR, cm^{-1}): 3051 (w), 1475 (w), 1430 (m), 1386 (w), 1363 (w), 1303 (w), 1192 (w), 1182 (w), 1162 (w), 1095 (w), 1067 (w), 1026 (m), 999 (w), 824 (w), 742 (s), 729 (m), 695 (s).

bis[1,1'-bis(dicyclohexylphosphino)ferrocene]nickel(II) chloride (S17): $NiCl_2 \cdot 6H_2O$ (1.15 mmol, 0.273 g), EtOH (10 mL), and a magnetic stir bar were placed in a 25 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then dcpf (1.15 mmol, 0.665 g) was added in one portion, causing formation of green solid. The flask was fitted with a reflux condenser, and the mixture was heated to 80 °C for 30 min and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration, washed twice with ethanol (5 mL) and twice with ether (5 mL). Drying under vacuum yielded **S17** (0.795 g, 98%) as a fine, light green powder.

***trans*-bis[1,1'-bis(dicyclohexylphosphino)ferrocene](2-methylphenyl)nickel(II) chloride (17)**: **S17** (1 mmol, 0.708 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. CH_2Cl_2 (65 mL) was added, the partially heterogeneous mixture was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (1 mmol, 0.945 M in THF, 1.06 mL) was very slowly added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color from green to brown-red. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. CH_2Cl_2 (15 mL) was added to dissolve the product, which was then filtered through a small plug of Celite and washed with an additional 10 mL of CH_2Cl_2, leaving any unreacted **S17** behind on the Celite. The filtrate was evaporated to dryness under reduced pressure, after which MeOH (10 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min). After the suspension was cooled to 0 °C, the bright red precipitate was collected by vacuum filtration, washed with two portions of MeOH, and dried under high vacuum to yield **17** (676 mg, 83%) as a fine, red powder. Crystals suitable for single-crystal X-ray diffraction were grown by the slow diffusion of pentane into a THF solution of **17** at 5 °C.

mp 198 °C dec.[23] **mp** 238–240 °C dec (sealed tube).

Anal. Calcd for $C_{41}H_{59}ClFeNiP_2$: C, 64.47; H, 7.79. Found: C, 64.74; H, 7.60.

^{1}H NMR (500 MHz, CD_2Cl_2, δ): 7.32 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.81 (td, *J* = 7.1, 1.8 Hz, 1H), 6.69 (td, *J* = 7.3, 1.0 Hz, 1H), 6.66 (dd, *J* = 6.8, 1.1 Hz, 1H), 4.65 (q, *J* = 2.1 Hz, 2H), 4.57 (q, *J* = 2.0 Hz, 2H), 4.37 (dt, *J* = 2.6, 1.3 Hz, 2H), 4.34 (dt, *J* = 2.6, 1.3 Hz, 2H), 3.49 (s, 3H), 2.76 – 2.66 (m, 2H), 2.54 – 2.45 (m, 2H), 1.78 (d, *J* = 11.8 Hz, 2H), 1.73 – 1.57 (m, 8H), 1.53 (d, *J* = 12.7 Hz, 2H), 1.49 – 1.25 (m, 10H), 1.25 – 1.07 (m, 8H), 1.04 – 0.80 (m, 6H), 0.77 – 0.67 (m, 2H), 0.19 (qt, *J* = 13.0, 3.8 Hz, 2H).

^{1}H NMR (300 MHz, C_6D_6, δ): 7.42 (dd, *J* = 7.1, 1.3 Hz, 1H), 6.98 (td, *J* = 7.1, 1.6 Hz, 1H), 6.91 (td, *J* = 7.1, 1.3 Hz, 1H), 6.84 (dd, *J* = 7.1, 1.6 Hz, 1H), 4.61 (dt, *J* = 2.6, 1.2 Hz, 2H), 4.31 (td, *J* = 2.4, 1.0 Hz, 2H), 4.18 (dt, *J* = 2.5, 1.2 Hz, 2H), 4.14 (td, *J* = 2.4, 1.1 Hz, 2H), 3.75 (s, 3H), 3.22 – 3.06 (m, 2H), 3.03 – 2.90 (m, 2H), 1.92 – 1.71 (m, 6H), 1.70 – 1.31 (m, 18H), 1.30 – 1.07 (m, 6H), 1.07 – 0.82 (m, 8H), 0.58 – 0.39 (m, 2H).

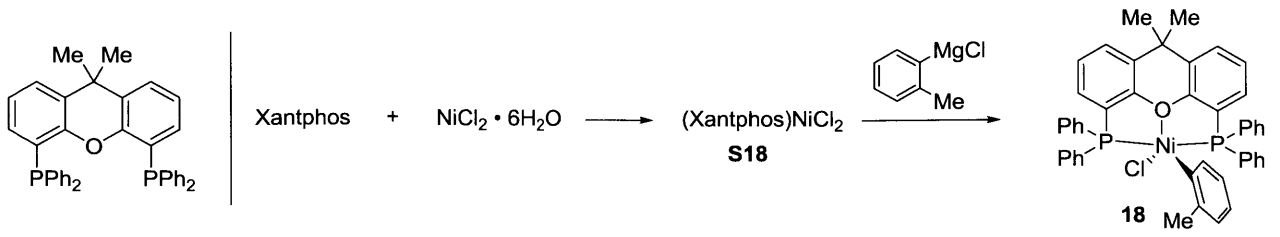
^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): –5.56.

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): –4.99.

^{13}C{^{1}H} NMR (126 MHz, CD_2Cl_2, δ): 150.61 (t, J = 31.3 Hz), 146.18 (t, J = 2.2 Hz), 136.69 (t, J = 3.3 Hz), 125.44 (t, J = 2.9 Hz), 124.15 (t, J = 2.3 Hz), 122.08 (t, J = 2.1 Hz), 72.68 (t, J = 3.1 Hz), 71.97 (t, J = 3.0 Hz), 70.91 (t, J = 2.1 Hz), 70.78 (t, J = 15.4 Hz), 69.81 (t, J = 2.0 Hz), 35.82 (t, J = 10.2 Hz), 34.85 (t, J = 8.0 Hz), 31.64 (t, J = 4.3 Hz), 30.65 (t, J = 2.6 Hz), 29.85 (t, J = 3.1 Hz), 29.43 (t, J = 2.7 Hz), 28.61 (t, J = 8.0 Hz), 28.57 (t, J = 3.6 Hz), 28.18 (t, J = 7.0 Hz), 27.16, 27.12.

FT-IR (ATR, cm^{-1}): 3092 (w), 3040 (w), 2924 (s), 2850 (s), 1568 (w), 1561 (w), 1445 (m), 1387 (w), 1371 (w), 1346 (w), 1328 w), 1294 (w), 1264 (m), 1231 (w), 1199 (w), 1175 (w), 1162 (m), 1132 (w), 1031 (m), 1005 (m), 915 (w), 893 (w), 846 (m), 822 (m), 736 (s), 720 (w), 703 (w), 679 (w).

[23] Discolors at 181 °C.



[4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene]nickel(II) chloride (S18): $NiCl_2 \cdot 6H_2O$ (8.9 mmol, 2.115 g), *n*-BuOH (50 mL), and a magnetic stir bar were placed in a 100 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then Xantphos (8.9 mmol, 5.15 g) was added in one portion. The flask was fitted with a reflux condenser, and the mixture was heated to reflux (120 °C) for 2 hours. The solution initially takes on a green color, which darkened to a deep purple/black during heating. Once cool, the flask was chilled to 0 °C for 10 min, after which the solid was collected by vacuum filtration, washed twice with ethanol (5 mL) and twice with ether (5 mL). Drying under vacuum yielded **S18** (5.398 g, 86%) as a fine, purple-gray powder.

***trans*-[4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene](2-methylphenyl)nickel(II) chloride (18)**: **S18** (8.13 mmol, 5.758 g) was placed in an oven-dried, 250 mL round-bottom flask containing a magnetic stir bar. THF (200 mL) was added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (8.13 mmol, 0.945 M in THF, 8.60 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to bright red. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (50 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 3 min). After the suspension was cooled to 0 °C, the orange precipitate was collected by vacuum filtration, washed with two portions of Et_2O (15 mL), and dried under high vacuum to yield **18** (5.704 g, 92%) as a fine, orange powder. Crystals suitable for single-crystal X-ray diffraction were grown by the slow diffusion of pentane into a toluene solution of **18** at 5 °C.

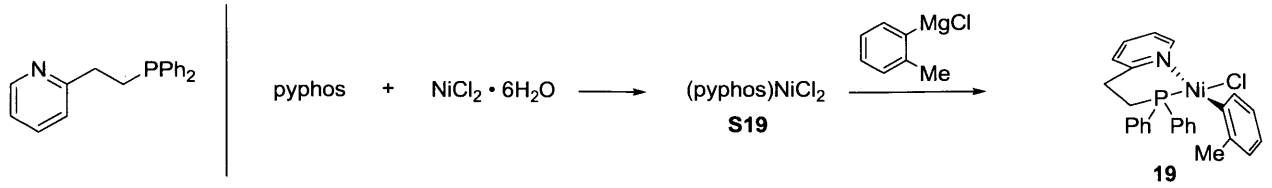
mp 194–196 °C dec.

Anal. Calcd for $C_{46}H_{39}ClNiOP_2$: C, 72.33; H, 5.15. Found: C, 72.53; H, 5.30.

^{1}H NMR (300 MHz, C_6D_6, δ): 8.73 – 8.63 (m, 4H), 7.45 – 7.37 (m, 1H), 7.31 (dt, J = 8.2, 4.6 Hz, 2H), 7.13 – 6.99 (m, 9H), 6.92 – 6.74 (m, 4H), 6.72 – 6.53 (m, 7H), 6.37 (t, J = 7.2 Hz, 1H), 5.72 (t, J = 7.2 Hz, 1H), 5.67 (t, J = 7.0 Hz, 1H), 3.77 (s, 3H), 1.54 (s, 3H), 1.43 (s, 3H).

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 8.13 (major), 2.80 (minor).

FT-IR (ATR, cm^{-1}): 3053 (w), 2969 (w), 1561 (w), 1477 (w), 1458 (w), 1434 (m), 1400 (s), 1363 (w), 1264 (m), 1238 (m), 1214 m), 1197 (m), 1147 (w), 1119 (w), 1093 (m), 1068 (w), 1027 (w), 999 (w), 876 (w), 843 (w), 789 (w), 733 s), 692 (s).



[2-(2-(diphenylphosphino)ethyl)pyridine]nickel(II) chloride (S19): $NiCl_2 \cdot 6H_2O$ (12 mmol, 2.852 g), EtOH (15 mL), and a magnetic stir bar were placed in a 25 mL round-bottom flask. The flask was sealed with a rubber septum, the solution was sparged with nitrogen for 15 min, the septum was removed, and then pyphos (12.36 mmol, 3.601 g) was added in one portion, causing the solution to become deep red. The flask was fitted with a reflux condenser, and the mixture was heated to reflux (80 °C) for 2 hours and then cooled to room temperature. Once cool, the flask was chilled to 0 °C for 20 min, after which the solid was collected by vacuum filtration and washed twice with ethanol (5 mL). Drying under vacuum yielded **S19** (4.551 g, 90%) as an intensely colored, crystalline purple solid.

***cis*-[2-(2-(diphenylphosphino)ethyl)pyridine](2-methylphenyl)nickel(II) chloride (19)**:[24] **S19** (3.23 mmol, 1.358 g) was placed in an oven-dried, 100 mL round-bottom flask containing a magnetic stir bar. THF (50 mL) and CH_2Cl_2 (20 mL) were added, the solution was cooled to 0 °C with an ice bath, and *o*-tolylmagnesium chloride (3.23 mmol, 0.945 M in THF, 3.41 mL) was added dropwise with vigorous stirring. Near the end of the addition, the solution began to change in color to yellow. The solution was stirred for 15 min at 0 °C, after which the stir bar was removed and the solution was evaporated to dryness under reduced pressure. MeOH (25 mL) was added and the mixture was sonicated until a uniform suspension was obtained (approximately 2 min). After the suspension was cooled to 0 °C, the precipitate was collected by vacuum filtration, washed with two portions of Et_2O (10 mL), and dried under high vacuum to yield **19** (1.253 g, 82%) as a fine, bright yellow powder. Crystals suitable for single-crystal X-ray diffraction were grown by the slow diffusion of pentane into a toluene solution of **19** at 5 °C.

mp 166–167 °C dec.

[24] The arrangement of the two donor atoms of the ligand is *cis*, but to completely specify the structure of complex **19**, it should also be noted that the nitrogen of the pyridine is *trans* to the chloride ligand.

Anal. Calcd for $C_{26}H_{25}ClNNiP$: C, 65.52; H, 5.29; N, 2.94. Found: C, 65.29; H, 5.33; N, 2.96.

^{1}H NMR (500 MHz, CD_2Cl_2, δ): 9.47 (ddd, J = 5.7, 1.1, 0.6 Hz, 1H), 8.08 (ddt, J = 11.0, 6.7, 1.4 Hz, 2H), 7.64 (td, J = 7.6, 1.7 Hz, 1H), 7.47 – 7.38 (m, 3H), 7.26 – 7.20 (m, 2H), 7.17 (dd, J = 7.5, 1.4 Hz, 1H), 7.12 (ddd, J = 7.7, 1.5, 0.8 Hz, 1H), 7.07 – 7.02 (m, 2H), 6.84 (dddd, J = 10.5, 6.7, 1.8, 1.2 Hz, 2H), 6.46 (tdd, J = 7.5, 1.6, 0.5 Hz, 1H), 6.40 (tt, J = 7.0, 1.0 Hz, 1H), 6.26 (ddd, J = 7.3, 1.4, 0.7 Hz, 1H), 3.88 (ddd, J = 14.2, 11.3, 3.2 Hz, 1H), 3.52 (dddd, J = 30.8, 13.9, 7.3, 3.1 Hz, 1H), 2.66 (s, 3H), 2.64 (dddd, J = 14.8, 9.6, 7.3, 3.2 Hz, 1H), 1.91 (dddd, J = 14.6, 11.3, 10.3, 3.1 Hz, 1H).

^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2, δ): 26.51.

FT-IR (ATR, cm^{-1}): 3053 (w), 2980 (w), 2965 (w), 1607 (w), 1570 (w), 1561 (w), 1483 (m), 1456 (w), 1449 (m), 1432 (m), 1412 (w), 1369 (w), 1339 (w), 1315 (w), 1164 (w), 1098 (m), 1065 (w), 1029 (w), 1020 (w), 999 (w), 962 w), 927 (w), 915 (w), 889 (w), 861 (w), 774 (m), 763 (s), 744 (s), 729 (s), 694 (s), 667 (m).

Procedure for Carbonyl Ene reaction

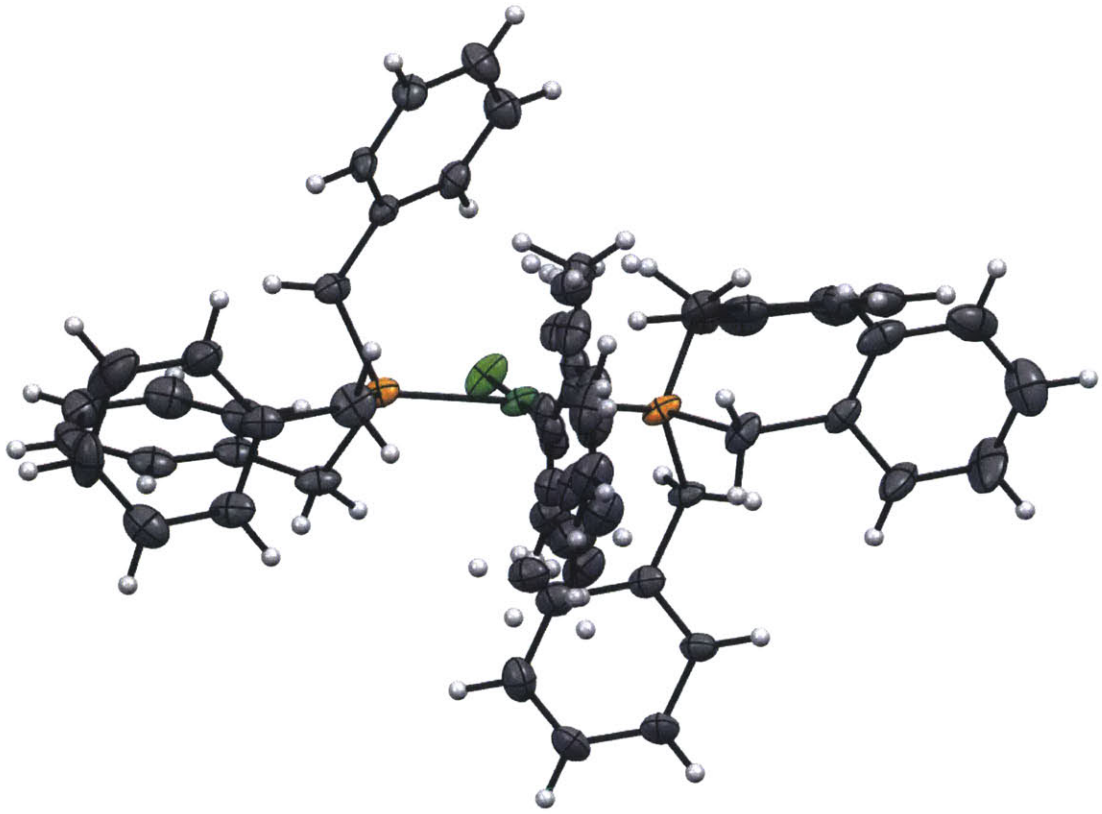
A 1 dram vial was charged with a magnetic stir bar, the desired precatalyst (0.10 mmol), 1-octene (2.5 mmol, 427 μL), triethylamine (3 mmol, 418.1 μL), benzaldehyde (0.50 mmol, 50.8 μL), toluene (2 mL), and dodecane (50.0 μL). This mixture was stirred for ca. 30 seconds, after which TESOTf (0.875 mmol) was added. The vial was sealed with a PTFE-lined screw cap and stirred at room temperature. After the desired length of time (48 hours for all screening reactions), the reaction mixture was quenched by addition of 500 μL of methanol. Approximately 100 μL of the crude reaction mixture was then diluted into 1 mL of EtOAc and the solution analyzed by GC.

X-Ray Diffraction Characterization of Complexes

Low-temperature diffraction data (φ-and ω-scans) were collected on a Bruker-AXS X8 Kappa Duo diffractometer coupled to a Smart Apex2 CCD detector with Mo Kα radiation (λ = 0.71073 Å) from an IμS micro-source for the structures of compounds **6**, **9**, **15**, **17**, and **18** and on a Siemens Platform three-circle diffractometer coupled to a Bruker-AXS Smart Apex CCD detector with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) for the structure of compound **19**. The structures were solved by direct methods using SHELXS[25] and refined against F^2 on all data by full-matrix least squares with SHELXL-97,[26] following established refinement strategies.[27] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms bound to carbon were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups). Details of the data quality and a summary of the residual values of the refinements are listed in tables S1 to S6.

[25] Sheldrick, G. M. *Acta Cryst.* **1990**, A46, 467-473.
[26] Sheldrick, G. M. *Acta Cryst.* **2008**, A64, 112-122.
[27] Müller, P. *Crystallogr. Rev.* **2009**, *15*, 57-83.

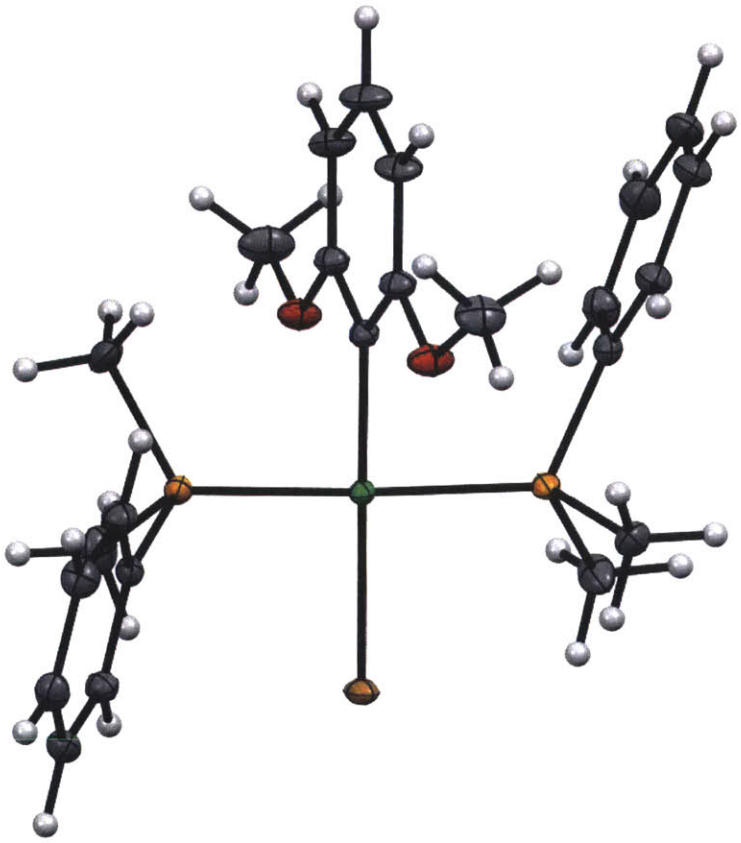
Figure S1. Thermal Ellipsoid Depiction of Compound 6, (PBn_3)



Compound **6** crystallizes in the non-centrosymmetric orthorhombic space group *Pnn*2 with one molecule of **6** and two half molecules of toluene in the asymmetric unit. The *o*-tolyl ligand on the nickel atom is disordered over three positions. In addition, the two half toluene molecules are located near crystallographic twofold axes (which reduces their occupancy to 50%) and both are disordered over four positions (corresponding to two independent position in each case, the other two positions are generated by said twofold axes). Those disorders were refined with the help of similarity restraints on 1-2 and 1-3 distances as well as planarity restraints for the aromatic rings. In addition, similar ADP as well as rigid bond restraints for anisotropic displacement parameters were applied to all atoms. The structure of compound **6** is a racemic twin (twin law -1 0 0 0 -1 0 0 0 -1); the twin ratio refined to 0.46(2).

The complete data for this structure are on file with the CCDC under entry BOHTUP.

Figure S2. Thermal Ellipsoid Depiction of Compound 9



Compound **9** crystallizes in centrosymmetric triclinic space group *P*-1 with one molecule of **9** in the asymmetric unit. The structure determination was straightforward and in all respects routine.

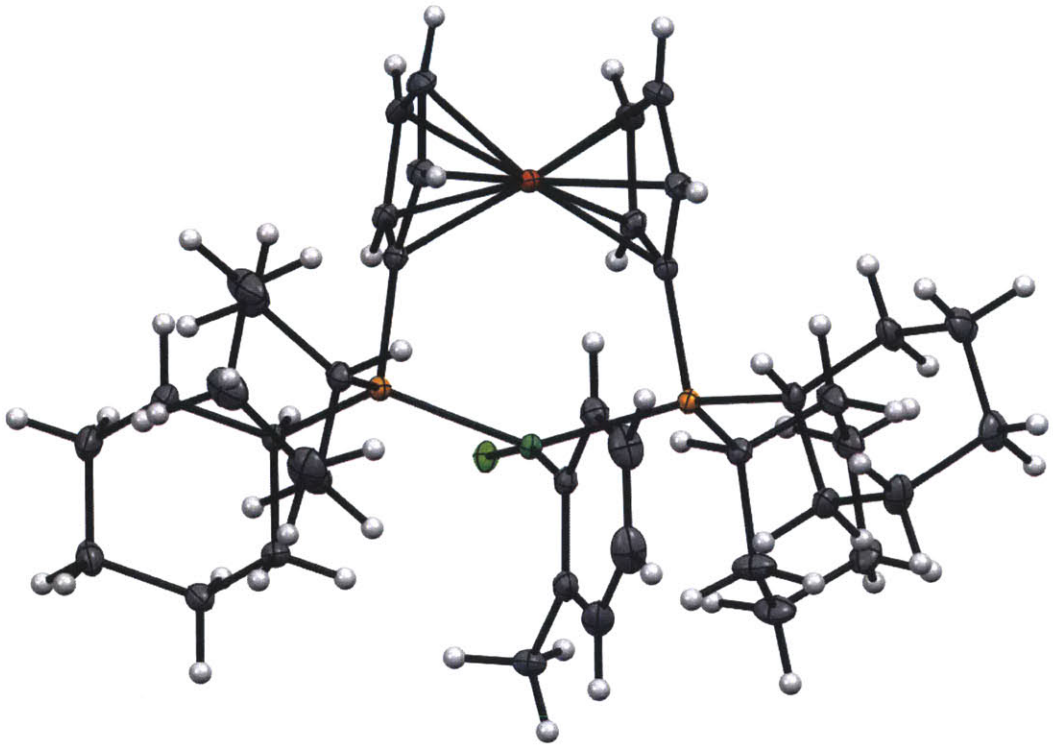
The complete data for this structure are on file with the CCDC under entry BOHVAX.

Figure S3. Thermal Ellipsoid Depiction of Compound 15

Compound **15** crystallizes in the chiral orthorhombic space group $P2_12_12_1$ with one molecule of **15** and three molecules of highly disordered chloroform in the asymmetric unit. The *o*-tolyl ligand on the nickel atom is disordered over two positions, two of the chloroform molecules are disordered over two-, and the third one over three positions. All disorders were refined with the help of similarity restraints on 1-2 and 1-3 distances and displacement parameters as well as rigid bond restraints for anisotropic displacement parameters.

The complete data for this structure are on file with the CCDC under entry BOHVEB.

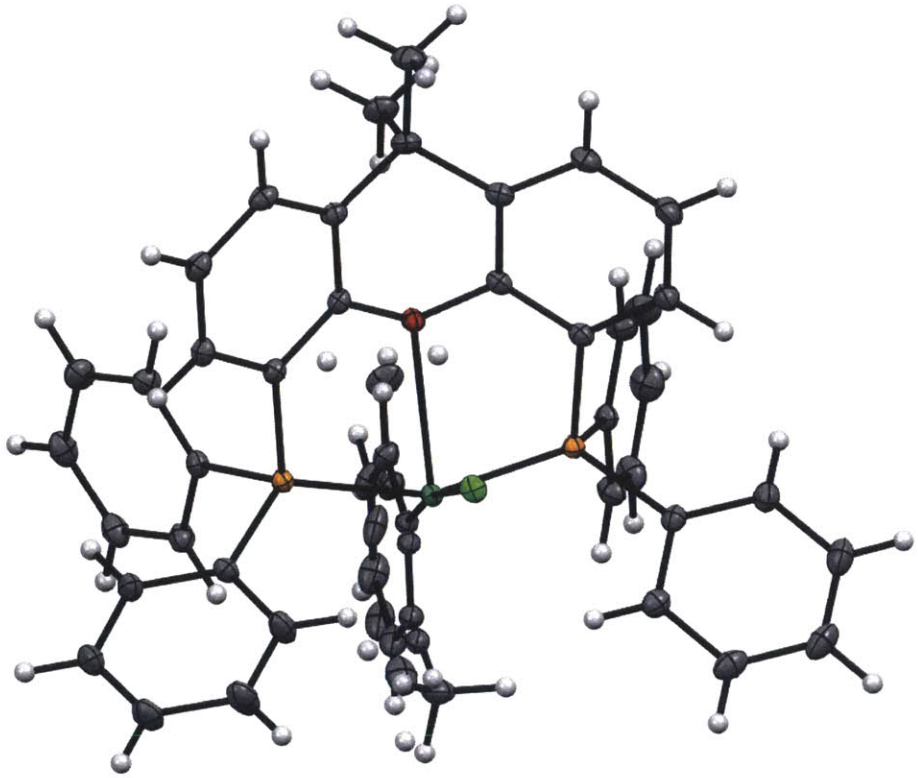
Figure S4. Thermal Ellipsoid Depiction of Compound 17



Compound **17** crystallizes in the centrosymmetric monoclinic space group $P2_1/n$ with one molecule of **17** and half a molecule of pentane in the asymmetric unit. The pentane is located on a crystallographic inversion center and disordered accordingly. The presence of only one half pentane molecule ($C_{2.5}H_6$) leads to a non-integer number of carbon atoms in the empirical formula.

The complete data for this structure are on file with the CCDC under entry BOHVIF.

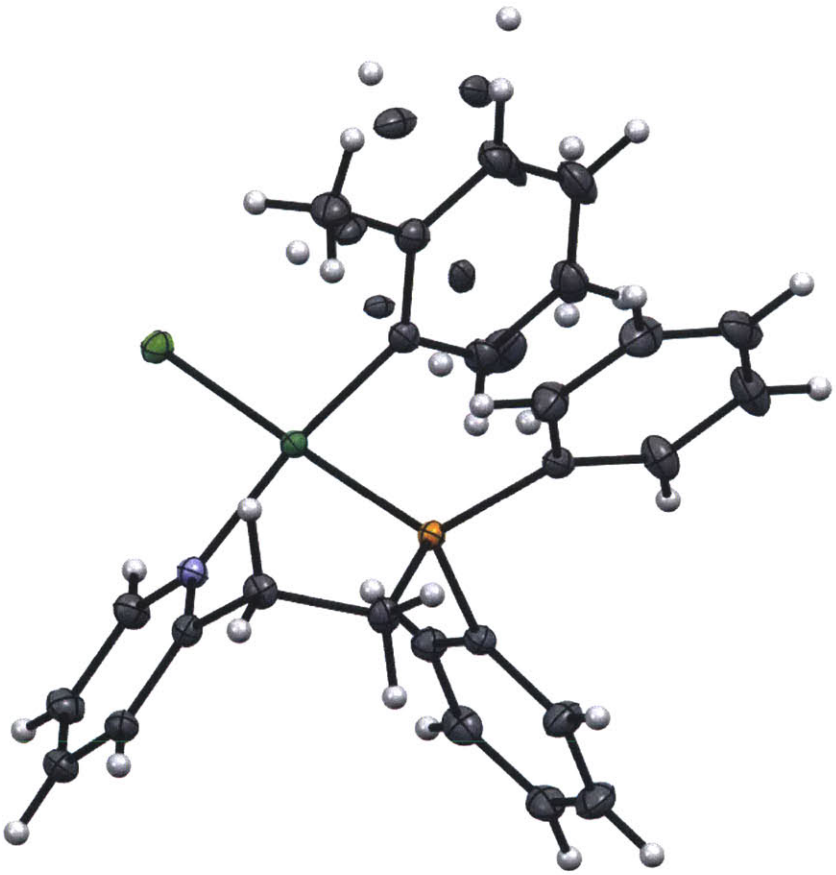
Figure S5. Thermal Ellipsoid Depiction of Compound 18



Compound **18** crystallizes in centrosymmetric triclinic space group *P*-1 with one molecule of **18** and one toluene molecule in the asymmetric unit. The *o*-tolyl ligand on the nickel atom is disordered over two positions. This disorder was refined with the help of similarity restraints on 1-2 and 1-3 distances and displacement parameters as well as rigid bond restraints for anisotropic displacement parameters. In addition similarity restraints on 1-2 and 1-3 distances were applied to the solvent toluene molecule.

The complete data for this structure are on file with the CCDC under entry BOHVOL.

Figure S6. Thermal Ellipsoid Depiction of Compound 19



Compound **19** crystallizes in centrosymmetric triclinic space group *P*-1 with one molecule of **19** in the asymmetric unit. The *o*-tolyl ligand on the nickel atom is disordered over two positions. This disorder was refined with the help of similarity restraints on 1-2 and 1-3 distances and displacement parameters as well as rigid bond restraints for anisotropic displacement parameters.

The complete data for this structure are on file with the CCDC under entry BOHVUR.

Table S1. Crystal data and structure refinement for compound 6

Identification code	x13037_c	
Empirical formula	C_{56} H_{57} Cl Ni P_2	
Formula weight	886.12	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	*Pnn*2	
Unit cell dimensions	a = 19.513(2) Å	α= 90°
	b = 13.4026(16) Å	β= 90°
	c = 17.861(2) Å	γ= 90°
Volume	4671.2(10) $Å^3$	
Z	4	
Density (calculated)	1.260 Mg/m^3	
Absorption coefficient	0.578 mm^{-1}	
F(000)	1872	
Crystal size	0.32 x 0.27 x 0.22 mm^3	
Theta range for data collection	1.55 to 31.62°	
Index ranges	-28<=h<=28, -19<=k<=19, -26<=l<=26	
Reflections collected	388284	
Independent reflections	15646 [R_{int} = 0.0606]	
Completeness to theta = 31.62°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8834 and 0.8367	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	15646 / 1691 / 827	
Goodness-of-fit on F^2	1.081	
Final R indices [I>2σ(I)]	R1 = 0.0543, wR2 = 0.1478	
R indices (all data)	R1 = 0.0585, wR2 = 0.1500	
Absolute structure parameter	0.47(2)	
Largest diff. peak and hole	0.601 and -0.638 e.$Å^{-3}$	

Table S2. Crystal data and structure refinement for compound 9

Identification code	x13082	
Empirical formula	C_{24} H_{31} Br Ni O_2 P_2	
Formula weight	552.05	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	*a* = 10.0063(11) Å	α= 112.352(2)°
	b = 10.9419(12) Å	β= 91.166(2)°
	c = 12.6991(13) Å	γ= 105.448(2)°
Volume	1227.9(2) $Å^3$	
Z	2	
Density (calculated)	1.493 Mg/m^3	
Absorption coefficient	2.565 mm^{-1}	
F(000)	568	
Crystal size	0.349 x 0.166 x 0.097 mm^3	
Theta range for data collection	1.750 to 31.507°	
Index ranges	-14<=*h*<=14, -16<=*k*<=16, -18<=*l*<=18	
Reflections collected	94777	
Independent reflections	8191 [R_{int} = 0.0274]	
Completeness to theta = 25.242°	100.0%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7462 and 0.6057	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8191 / 0 / 277	
Goodness-of-fit on F^2	1.031	
Final *R* indices [$I>2\sigma(I)$]	*R*1 = 0.0177, *wR*2 = 0.0452	
R indices (all data)	*R*1 = 0.0198, *wR*2 = 0.0459	
Largest diff. peak and hole	0.471 and -0.203 $e.Å^{-3}$	

Table S3. Crystal data and structure refinement for compound 15

Identification code	x13036	
Empirical formula	$C_{54}\ H_{42}\ Cl_{10}\ Ni\ P_2$	
Formula weight	1166.03	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 12.7779(10) Å	α= 90°
	b = 19.4532(15) Å	β= 90°
	c = 20.8196(16) Å	γ= 90°
Volume	5175.1(7) Å^3	
Z	4	
Density (calculated)	1.497 Mg/m^3	
Absorption coefficient	0.991 mm^{-1}	
F(000)	2376	
Crystal size	0.32 x 0.18 x 0.16 mm^3	
Theta range for data collection	1.43 to 31.51°	
Index ranges	-18<=h<=18, -28<=k<=28, -30<=l<=30	
Reflections collected	340839	
Independent reflections	17188 [R_{int} = 0.0801]	
Completeness to theta = 31.51°	99.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8576 and 0.7422	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	17188 / 854 / 819	
Goodness-of-fit on F^2	1.059	
Final R indices [I>2σ(I)]	R1 = 0.0328, wR2 = 0.0927	
R indices (all data)	R1 = 0.0351, wR2 = 0.0938	
Absolute structure parameter	0.009(7)	
Largest diff. peak and hole	0.469 and -0.297 e.Å^{-3}	

Table S4. Crystal data and structure refinement for compound 17

Identification code	x13044	
Empirical formula	$C_{43.50}$ H_{65} Cl Fe Ni P_2	
Formula weight	799.91	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 18.6663(8) Å	α= 90°
	b = 10.5178(5) Å	β= 99.8910(10)°
	c = 20.6999(9) Å	γ= 90°
Volume	4003.6(3) Å^3	
Z	4	
Density (calculated)	1.327 Mg/m^3	
Absorption coefficient	1.009 mm^{-1}	
F(000)	1708	
Crystal size	0.30 x 0.05 x 0.04 mm^3	
Theta range for data collection	1.36 to 31.54°	
Index ranges	-27<=h<=27, -15<=k<=15, -30<=l<=30	
Reflections collected	148218	
Independent reflections	13352 [R_{int} = 0.0569]	
Completeness to theta = 31.54°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9655 and 0.7517	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	13352 / 3 / 464	
Goodness-of-fit on F^2	1.063	
Final R indices [I>2σ(I)]	$R1$ = 0.0308, $wR2$ = 0.0693	
R indices (all data)	$R1$ = 0.0410, $wR2$ = 0.0727	
Largest diff. peak and hole	0.437 and -0.316 e.Å^{-3}	

Table S5. Crystal data and structure refinement for compound 18

Identification code	x13042	
Empirical formula	C_{53} H_{47} Cl Ni O P_2	
Formula weight	856.01	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	a = 11.7668(9) Å	α= 82.914(2)°
	b = 11.9557(9) Å	β= 69.1860(10)°
	c = 16.0572(12) Å	γ= 83.528(2)°
Volume	2089.6(3) $Å^3$	
Z	2	
Density (calculated)	1.360 Mg/m^3	
Absorption coefficient	0.645 mm^{-1}	
F(000)	896	
Crystal size	0.33 x 0.29 x 0.28 mm^3	
Theta range for data collection	1.36 to 31.51°	
Index ranges	-17<=h<=17, -17<=k<=17, -23<=l<=23	
Reflections collected	158740	
Independent reflections	13906 [R_{int} = 0.0248]	
Completeness to theta = 31.51°	99.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8410 and 0.8148	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	13906 / 264 / 574	
Goodness-of-fit on F^2	1.024	
Final R indices [I>2σ(I)]	R1 = 0.0258, wR2 = 0.0692	
R indices (all data)	R1 = 0.0275, wR2 = 0.0704	
Largest diff. peak and hole	0.520 and -0.259 e.$Å^{-3}$	

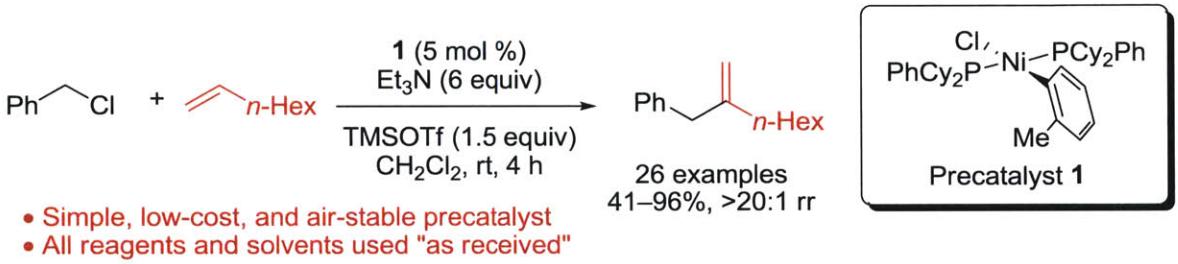
Table S6. Crystal data and structure refinement for compound 19

Identification code	13011	
Empirical formula	C_{26} H_{25} Cl N Ni P	
Formula weight	476.60	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	a = 8.1455(16) Å	α= 88.412(3)°
	b = 11.363(2) Å	β= 76.658(3)°
	c = 12.665(2) Å	γ= 74.636(3)°
Volume	1099.1(4) Å^3	
Z	2	
Density (calculated)	1.440 Mg/m^3	
Absorption coefficient	1.090 mm^{-1}	
F(000)	496	
Crystal size	0.35 x 0.07 x 0.07 mm^3	
Theta range for data collection	1.86 to 31.01°	
Index ranges	-11<=h<=11, -16<=k<=16, -18<=l<=18	
Reflections collected	32480	
Independent reflections	6961 [R_{int} = 0.0297]	
Completeness to theta = 31.01°	99.2%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9276 and 0.7015	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6961 / 259 / 337	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2σ(I)]	R1 = 0.0284, wR2 = 0.0691	
R indices (all data)	R1 = 0.0346, wR2 = 0.0723	
Largest diff. peak and hole	0.418 and -0.299 e.Å^{-3}	

Chapter 2

Alkenes as Vinylmetal Equivalents: The Nickel-Catalyzed Mizoroki–Heck Reaction of Benzyl Chlorides and Terminal Alkenes

Abstract



The air-stable nickel(II) complex *trans*-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$ (**1**) was employed as a precatalyst for the Mizoroki−Heck-type, room temperature, internally selective coupling of substituted benzyl chlorides with terminal alkenes. This reaction, which employs a terminal alkene as an alkenylmetal equivalent, provides rapid, convergent access to substituted allylbenzene derivatives in high yield and with regioselectivity greater than 95:5 in nearly all cases. The reaction is operationally simple, can be carried out on the benchtop with no purification or degassing of solvents or reagents, and requires no exclusion of air or water during setup. Synthesis of the precatalyst is accomplished through a straightforward procedure that employs inexpensive, commercially available reagents, requires no purification steps, and proceeds in high yield.

Introduction

Among the multitude of methods for the synthesis of alkenes, the Mizoroki–Heck reaction (MHR) continues to find frequent use in organic synthesis.[1,2] The MHR has become a valuable means to access alkenes of all types, including in enantioselective fashion, and has been widely employed in academic settings for the synthesis of chemical intermediates and natural products[3] and industrially[4] for the production of pharmaceuticals,[5] agrochemicals,[6] and monomers for materials applications.[7]

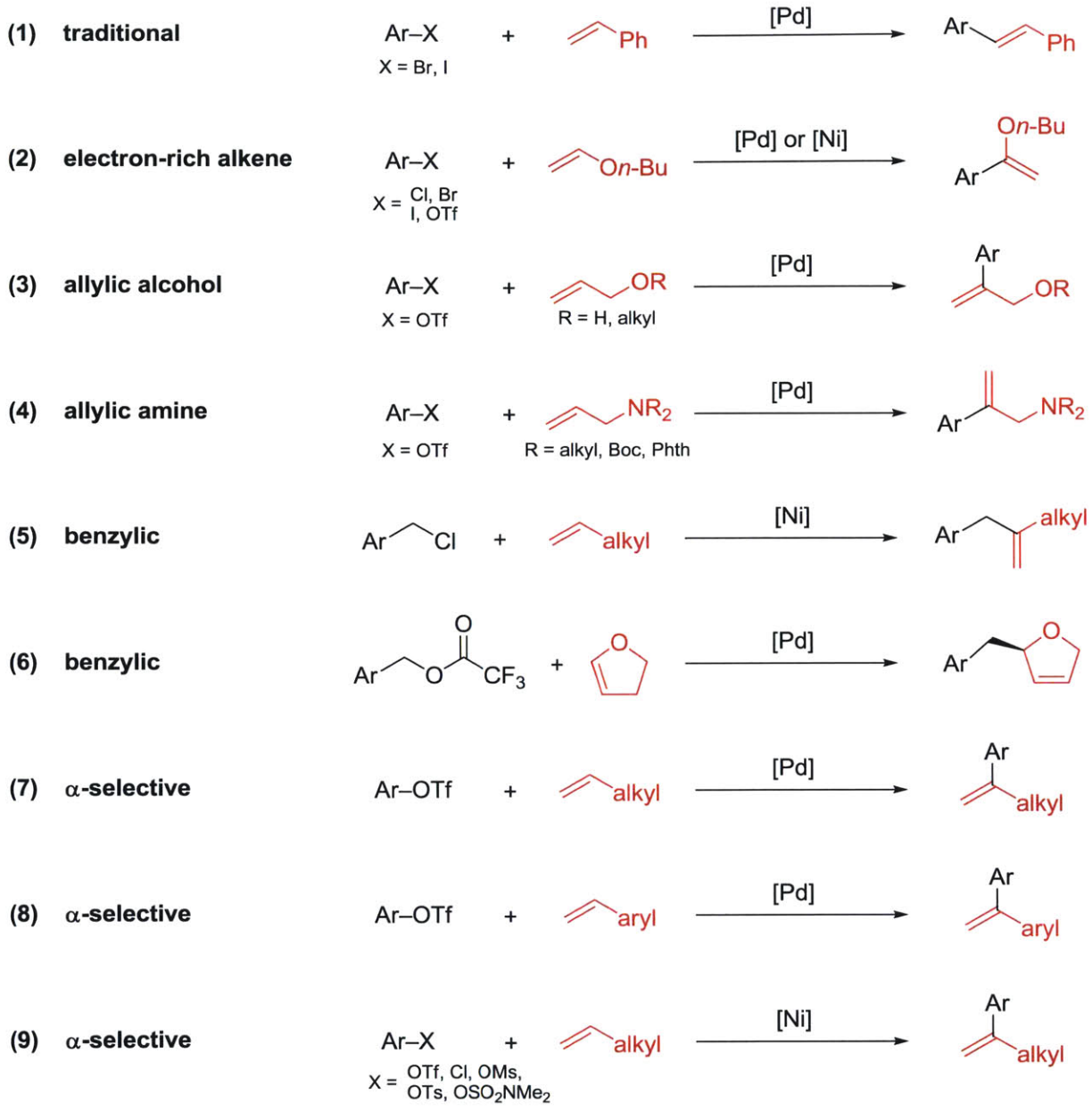
The first reported couplings of this type employed electron deficient alkenes, such as styrenes and acrylates,[8] which have gone on to define the prototypical Mizoroki–Heck reaction (Scheme 1, eq 1). Since its inception, a principal interest in the Mizoroki–Heck reaction has been regiocontrol with terminal (monosubstituted) alkenes.[9] Alkenes bearing an electron-withdrawing group (styrenes, acrylates, enones, etc.) have a strong, inherent bias for reaction at the position distal from the substituent, which is defined as the β position; this bias is strong enough to override catalyst, solvent, or other factors in almost all circumstances. Conversely, electron rich alkenes are generally primed for reaction at the proximal, or α position, again due to the electronic differentiation of the two positions of the alkene. (Scheme 1, eq 2).[10,11,12]

In contrast to either of those two alkene classes, however, simple aliphatic alkenes (such as α-olefins) have seen considerably less attention in the context of the MHR. One contributing factor is the difficulty of controlling the regiochemical outcome of such reactions, given that the α and β positions of the alkene are not electronically differentiated and the steric differentiation of the two positions does not necessarily provide high selectivity by itself. It is not the intention to exhaustively summarize the enormous body of work that has been carried out on the MHR and related reactions; this work has been extensively chronicled in reviews and books. However, selected examples (as shown in Scheme 1) are presented to illustrate the advances made in the α-selective MHR, and therefore the framework into which this work fits.

Certain privileged alkenes, such as allylic alcohols[13] (Scheme 1, eq 3) and amines[14] (Scheme 1, eq 4), are biased through chelation effects to allow for high terminal or internal selectivity, depending on the appropriate choice of metal, ligand, and solvent.

A significant development came in 2011, when Jamison and coworkers reported conditions that allowed the highly selective (better than 95:5 α:β selectivity) MHR with simple, electronically unbiased alkenes, including α-olefins (Scheme 1, eq 5).[15] This reaction protocol

Scheme 1. Regiochemistry of the Mizoroki–Heck Reaction



used widely available and readily-prepared benzyl chlorides as the coupling partner, which allowed the synthesis of substituted allylbenzenes in excellent yield and with excellent selectivity in all cases.

Subsequently, the Zhou group published three significant contributions to this area of research, the first being the palladium-catalyzed, enantioselective MHR of benzyl trifluoroacetates with 2,3-dihydrofuran (Scheme 1, eq 6).[16] The MHR of 2,3-dihydrofuran was

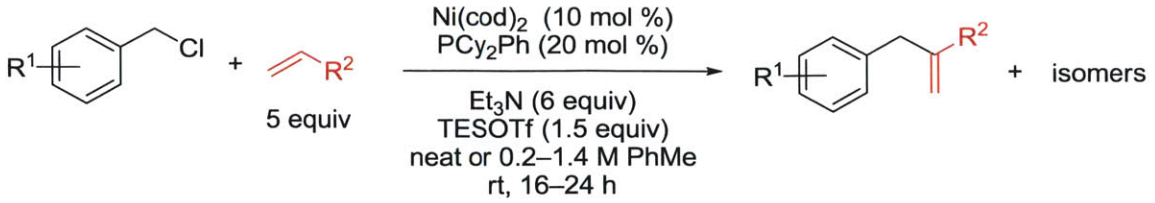
previously known, however it was previously not possible to achieve good enantioselectivity, regioselectivity, and also avoid isomerization of the products.[17] The method reported by Zhou was exceptionally selective in all three of these areas. Second, Zhou and coworkers reported the α-selective MHR of aryl triflates with unbiased monosubstituted alkenes (Scheme 1, eq 7).[18] The selectivity was generally greater than 10:1 α:β with simple substrates, and often considerably higher when additional biasing factors, such as *ortho*-substitution on the aryl triflate, were present. This protocol was also applicable to other types of alkenes, such as allylic alcohols and allylic amines. Unfortunately, the moderate selectivity observed in many cases combined with the inability to separate the α and β products by silica gel chromatography complicates the use of this method in some situations. Third, a related method for the α-selective MHR of vinylarenes was disclosed by Zhou and coworkers (Scheme 1, eq 8).[19] The same catalyst system presented in their previous work was found to provide the desired 1,1-diaryl alkenes in excellent yield and with outstanding selectivity in almost all cases.

Following these reports, Jamison and coworkers disclosed a nickel-catalyzed method for the α-selective MHR of aryl triflates with unbiased monosubstituted alkenes (Scheme 1, eq 9).[20] This method provided selectivity of better than 19:1 α:β in all instances, regardless of the substitution pattern of the aryl triflate or alkene. Additionally, alternative electrophiles, such as aryl tosylates, mesylates, chlorides, and sulfonamides were demonstrated to work when a halide-scavenging additive (TESOTf) was added to the reaction. This report is, arguably, the capstone of decades of development of the α-selective MHR; although shortcomings still remain, the most significant challenges have been thoroughly addressed through this and other work.

Generally speaking, the behavior of benzyl electrophiles in the MHR remains much less well-studied than aryl and vinyl electrophiles, despite the inclusion of benzyl halides in Heck's seminal 1972 report.[8c] This is at least in part due to the propensity for alkene isomerization observed with these types of electrophiles—that is, the isomerization of the product allylbenzene to the corresponding styrene readily takes place. Regardless, a number of methods have indeed been developed employing benzyl (pseudo-)halides as coupling partners.[21]

As a part of our laboratory's ongoing work in the area of stereo- and regiocontrolled synthesis of alkenes via coupling reactions, we were interested in further developing our previously reported method (Scheme 2)[15] for the coupling of benzyl chlorides to terminal alkenes catalyzed by $Ni(cod)_2$ and PCy_2Ph.

Scheme 2. Existing Methodology for the MHR of Alkenes with Benzyl Chlorides



We sought to make the reaction operationally simpler by removing the need for the use of inert-atmosphere techniques (glovebox or glovebag) to set up each reaction. Furthermore, the cost of $Ni(cod)_2$ is considerably higher than many Ni(II) sources,[22] its quality from commercial suppliers varies significantly (even within batches from the same supplier), and it has a limited shelf life if not stored cold and under an inert atmosphere. Of course, the laboratory synthesis of $Ni(cod)_2$ is well established,[23] but it requires Schlenk or glovebox techniques and does not obviate the need for storage and use under an inert atmosphere. Thus, we sought to reduce the cost and operational complexity of this method by devising an air-stable precatalyst, which would enable this chemistry to be carried out on the benchtop with no use of a glovebox or even any air-free techniques required.

In this report, we describe the preparation and use of the first air-stable nickel precatalyst for internally-selective Heck reactions of terminal, electronically unbiased alkenes and benzyl chlorides. The reaction proceeds at room temperature to provide 1,1-disubstituted alkenes; no exclusion of air or moisture is required during the setup of each reaction, and no drying, degassing, or purification of any reagents is required, in stark contrast to what is typically required for nickel(0)-catalyzed reactions.

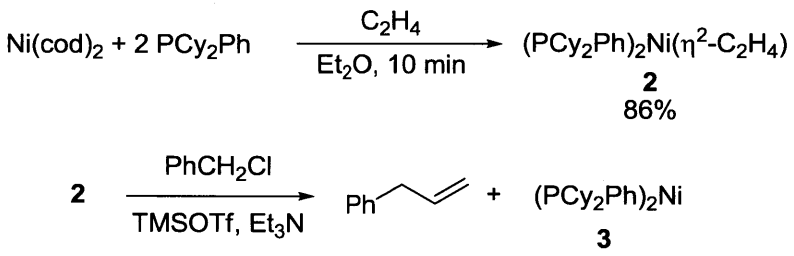
Preliminary Investigations of cod-Free Precatalysts

During early investigations of trying to extend the scope of this reaction to include disubstituted alkenes, we observed that catalysts comprising the combination of $Ni(cod)_2$ and PCy_2Ph effected benzylation of the cod ligands themselves in preference to the intended alkene substrate in some instances. This observation led us to hypothesize that cod was coordinating to nickel with greater affinity than the intended alkene, effectively acting as a competitive inhibitor and thereby causing a significant rate reduction of the desired transformation. Thus, removing cod from the reaction could allow for a greater turnover frequency and/or a reduced catalyst

loading, and potentially allow for the use of more sterically hindered alkenes or even disubstituted alkenes as viable substrates.

A search of the literature brought the stable and isolable, though air-sensitive, complex $(PPh_3)_2Ni(\eta^2\text{-}C_2H_4)$ to our attention.[24] This complex is readily synthesized by combining $Ni(cod)_2$, PPh_3, and ethylene in diethyl ether; analogously, $(PCy_2Ph)_2Ni(\eta^2\text{-}C_2H_4)$ (**2**) was produced by the combination of $Ni(cod)_2$, PCy_2Ph, and ethylene in ether to form a yellow solid in excellent yield, as illustrated in Scheme 3. We had hoped the additional steric hindrance of PCy_2Ph (compared to PPh_3) would endow the complex with greater stability toward oxygen; however, although more tolerant of exposure to oxygen than $(PPh_3)_2Ni(\eta^2\text{-}C_2H_4)$, **2** still decomposes in air within a few minutes of exposure, so its use still requires inert atmosphere techniques.

Scheme 3. Synthesis of $(PCy_2Ph)_2Ni(\eta^2\text{-}C_2H_4)$ and Evaluation as a Precatalyst[a]



[a]Complex **3** was not isolated; its yield was determined indirectly to be >98% based on the amount of allylbenzene formed (measured by GC).

Treatment of complex **2** with benzyl chloride, Et_3N, and TESOTf facilitates the benzylation of ethylene to yield allylbenzene and $(PCy_2Ph)_2Ni(0)$ (**3**), which is believed to be the catalytically active species.[25] Even at half the catalyst loading (5 mol % instead of 10 mol % employed in our previously published method), the coupling of benzyl chloride with 1-octene proceeds faster than when $Ni(cod)_2$ and PCy_2Ph are used as the catalyst, which we construe as evidence that cod is reducing the rate of reaction. Furthermore, addition of cod to a reaction catalyzed by **2** retards the rate relative to a control experiment in which no cod was added. Thus, we had clearly established the detrimental effect the presence of cod has on this coupling reaction.

These results provide the first definitive evidence showing the cod ligands in $Ni(cod)_2$ are not innocent in a reaction such as this coupling. Given the widespread use of $Ni(cod)_2$ as a

precursor to homogeneous Ni(0) species in organic synthesis, this result has significant implications for a variety of aspects of nickel catalysis. As researchers continue to seek more highly active catalysts to allow more challenging couplings or lower catalyst loadings, this finding is likely to shape the development of new catalysts and reactions.

Synthesis and Characterization of Air-Stable Precatalyst

Although precatalyst **2** had proven interesting and had provided valuable information regarding the role of cod in the reaction, it still required inert-atmosphere techniques for its synthesis, storage, and usage. As such, we began to examine other possible precatalysts that would possess the same properties, but also tolerate storage under air. A number of complexes of the form *trans*-$(PR_3)_2Ni(aryl)X$ (where R = Ph, Cy, Et; and X = Cl, Br) have been demonstrated to be air stable with prudent choice of the substituents on the aryl ring, for example, when the aryl group is an *o*-tolyl or 2-napthyl moiety. Though first reported in 1960 by Chatt and Shaw,[26] there have been relatively few reported uses for these complexes.[27] With this inspiration, we attempted the synthesis of the complex *trans*-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$ (**1**) and determined that it can be conveniently synthesized in a two-step procedure beginning from $NiCl_2 \cdot 6H_2O$ and PCy_2Ph, followed by addition of 1 equiv of *o*-tolylmagnesium chloride to yield **1** as a yellow, diamagnetic, air-stable solid (Scheme 4).[28] Alternatively, the ligand PCy_2Ph can be easily synthesized from dichlorophenylphosphine and cyclohexylmagnesium chloride, which can either be made from chlorocyclohexane or purchased commercially. No purification steps (aside from the isolation) are required in this sequence, making the synthesis of precatalyst **1** remarkably convenient.

Scheme 4. Synthesis of *trans*-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$

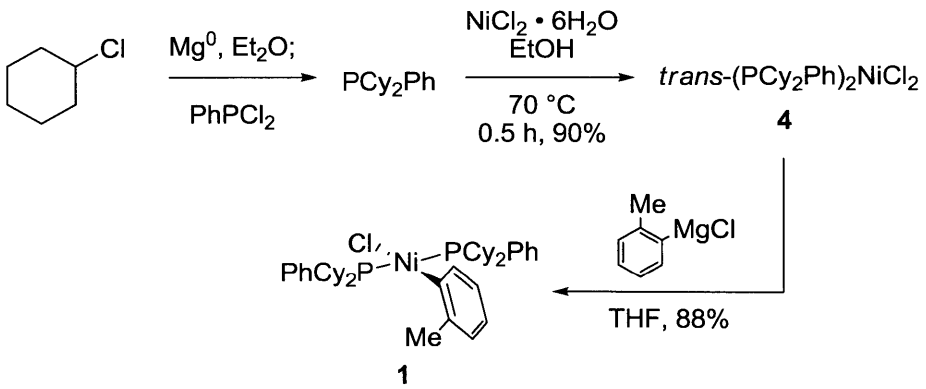
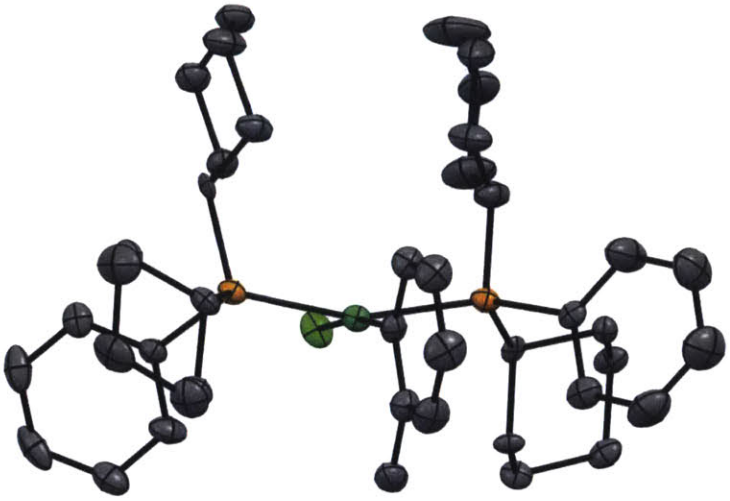
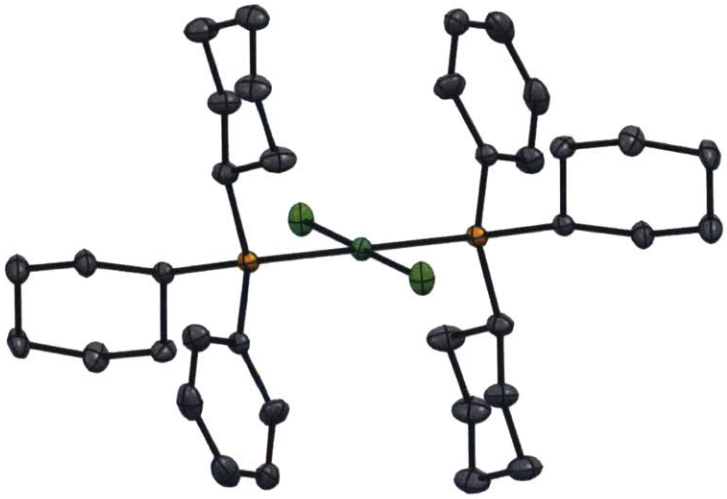


Figure 1. Single-Crystal X-Ray Diffraction Characterization of Complexes 1 and 4[a]



trans-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$ (**1**)



trans-$(PCy_2Ph)_2NiCl_2$ (**4**)

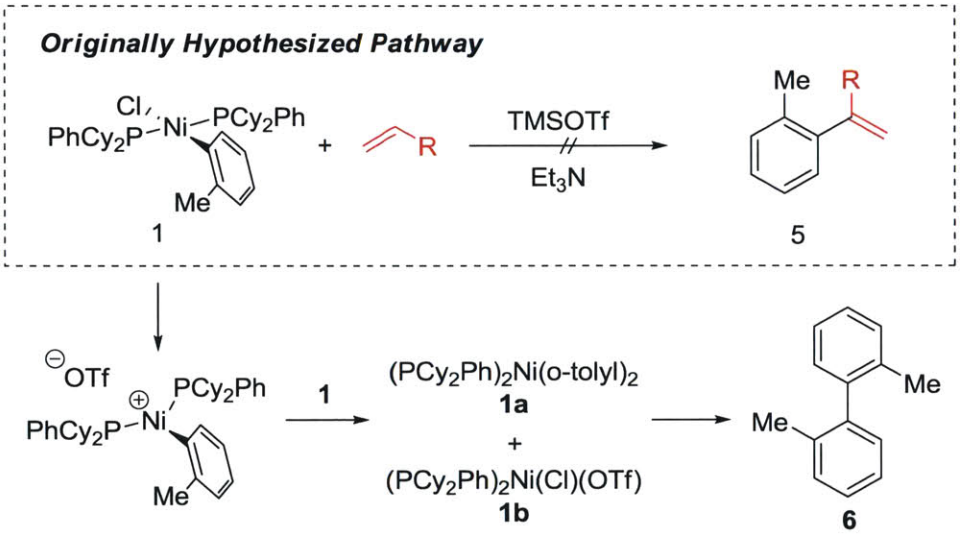
[a]Thermal ellipsoid representations of single-crystal X-Ray structures of complexes 1 and 4. Ellipsoids are shown at 50% probability; hydrogen atoms, solvent of crystallization, and disorder are omitted for clarity. The complete represenations are available in the Experimental Section.

Precatalyst **1** as well as the intermediate complex *trans*-$(PCy_2Ph)_2NiCl_2$ (**4**)[29] have both been characterized by single-crystal X-ray diffraction (see thermal ellipsoid representations in Figure 1); **4** adopts a nearly ideal square planar geometry with *trans* stereochemistry. This complex is diamagnetic, air-stable, and can be stored exposed to air at room temperature indefinitely. Likewise, complex **1** assumes square planar geometry with *trans* stereochemistry and is stable toward air. The geometry of **4** is slightly distorted toward a tetrahedral arrangement,

as indicated by the observed P–Ni–P bond angle of 161.74(2)° and Cl–Ni–C bond angle of 170.4(4)°, both noticeably shy of the ideal 180°.[30]

Upon treatment of complex **1** with an alkene, silyl triflate, and base, reduction from the Ni(II) precatalyst to the catalytically active Ni(0) species occurs within minutes at room temperature. Initially, we hypothesized this to occur by arylation of the alkene as illustrated in Scheme 5; however, 2,2′-dimethylbiphenyl (**6**, 97% yield by gas chromatography) is formed rather than styrene **5**. Indeed, treatment of the precatalyst with TMSOTf effects reduction to a nickel(0) species and **6** even in the complete absence of any alkene. This suggests that, following chloride abstraction from **1**, transmetallation with another molecule of **1** to produce **1a** and **1b** occurs. Subsequently, reductive elimination of **6** from complex **1a** is evidently the means by which production of nickel(0) takes place. This, in turn, suggests that only half of the precatalyst is ultimately reduced; presumably, the other half is converted to the catalytically inactive $(PCy_2Ph)_2Ni(Cl)(OTf)$ (**1b**), unless reduction of **1b** through another mechanism is concurrently active.[31]

Scheme 5. Mechanism of Activation of Precatalyst 1



Entry into a nickel(0) manifold from nickel(II) promoted by an additive such as a silyl triflate is unprecedented. In the vast majority of cases, reduction of a nickel(II) species to the catalytically active form is effected in one of four ways:[32] (1) by consumption of an organometallic reactant present in the reaction, such as a boronic acid;[33] (2) by an exogenous

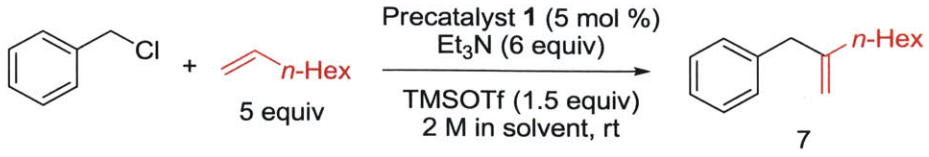
reductant such as zinc, manganese, or sodium–mercury amalgam, which is added to carry out the reduction by electron transfer; (3) by addition of an organometallic reagent such as $AlMe_3$, Et_2Zn, or MeMgBr, which can effect reduction through two successive transmetallations to yield a dialkylnickel(II) complex, which undergoes reductive elimination to yield an alkane and a nickel(0) species;[34] or (4) by addition of a hydride donor such as DIBAL, methanol, or isopropanol.[35,36] The ability to enter into a nickel(0) catalytic cycle at room temperature and without the use of pyrophoric or strongly basic reagents represents a new and potentially valuable means of entry into nickel(0) species that could be employed for a wide variety of nickel(0)-catalyzed reactions.

Reaction Optimization

Having established the competence of precatalyst **1** for this coupling reaction, we began optimizing the reaction, ultimately arriving at the conditions described in Table 1, with the conditions in entry 4 being chosen as our fully optimized conditions. With our previously published conditions[15] (10 mol % $Ni(cod)_2$, 20 mol % PCy_2Ph, 6 equiv of Et_3N, 1.75 equiv of TESOTf) as a starting point, we began by investigating the reaction under solvent-free (neat) conditions and we observed that these conditions performed quite poorly. We attribute this to the low solubility of precatalyst **1** in triethylamine, which causes very slow activation. However, even in toluene, activation of the precatalyst is not facile, as entry 2 highlights: even after 1 h, only 2% of product has been produced, and although the reaction ultimately does reach completion, it requires nearly 24 h to do so. At this time, we also confirmed once more that the addition of cod to the reaction mixture does indeed reduce the rate of reaction (entry 3).

Intriguingly, changing the reaction solvent to dichloromethane facilitated rapid activation of the catalyst and a greatly accelerated coupling, requiring only 4 h for the reaction to reach complete conversion (cf. entries 2 and 4), which corresponds approximately to a 5-fold rate enhancement. At present, we are unaware of any nickel(0)-catalyzed cross couplings carried out in a solvent of dichloromethane, making this reaction unique in that regard.[37,38] The change from toluene to CH_2Cl_2 also allows for a reduction of the excess of alkene required (cf. entries 4–9). In toluene, changing from 5 to 2 equiv of alkene caused a marked decrease in the yield, even after 24 h of reaction time (92% vs 54%). However, in CH_2Cl_2, changing from 5 to 2 equiv of alkene ultimately affords the product in only a slightly diminished yield (96% vs 84%), though

Table 1. Optimization of Reaction Parameters[a]



Entry	Change from above conditions	% Yield at time (h)		
		1	3	24
1	Neat	1	3	11
2	PhMe	2	40	92
3	PhMe, 10 mol % 1,5-cod added	2	16	76
4	CH_2Cl_2	51	68	96
5	CH_2Cl_2, 2 equiv 1-octene	35	52	84
6	CH_2Cl_2, 1.3 equiv 1-octene	21	40	79
7	CH_2Cl_2, 1 equiv 1-octene	19	38	68
8	PhMe, 3.5 equiv 1-octene	1	11	73
9	PhMe, 2 equiv 1-octene	1	8	54
10	CH_2Cl_2, TESOTf inst. TMSOTf	48	65	95
11	CH_2Cl_2, Et^{i}Pr$_2$N instead of Et_3N	2	6	12
12	Purified and degassed reagents[b]	59	76	95

[a]All yields were determined by gas chromatography against a calibrated internal standard. All reagents were used "as received" except where explicitly stated. Many reactions were complete prior to 24 hours, but were run for the full 24 hours for comparison purposes. [b]Liquid reagents and solvents were dried over a suitable drying agent and distilled, followed by three cycles of freeze-pump-thaw degassing.

the reaction rate is decreased. As the excess further decreases, however, the yield begins to drop considerably, ultimately to 68% when a 1:1 stoichiometry of benzyl chloride and alkene is used.

Also interesting is the marked reduction in yield observed when Hünig's base (Et*i*-Pr$_2$N) is used instead of triethylamine (cf. entries 4 and 11). Though of similar thermodynamic basicity, this likely suggests that the sterically less hindered Et_3N is capable of deprotonating the nickel hydride (formed after β-hydride elimination, Scheme 8, vide infra) much more efficiently.

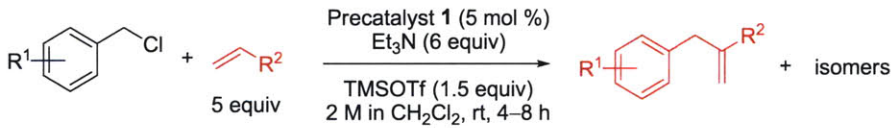
Prior to beginning this optimization process, one of the changes we investigated was whether the use of dried and degassed solvents and reagents is necessary to obtain satisfactory results. Preliminary trials showed that using reagents and solvents "as received" had no negative

effects on the yield of the reaction; however, a direct comparison was carried out to rigorously verify this observation. As the comparison between entries 4 and 12 indicates, the reaction does appear to proceed more rapidly when purified and degassed reagents are employed, but ultimately, the same is achieved in both cases. We attribute this difference in rate to the oxygen-mediated decomposition of some portion of the catalyst when unpurified reagents are employed, causing the effective catalyst loading to be slightly less than the nominal loading.[39] Having verified the absence of negative effects, we opted to carry out the remainder of the optimization without purification or degassing of any reagents, taking the conditions described in entry 4 as our optimized conditions.

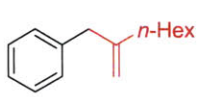
Substrate Scope

Having satisfactorily optimized the conditions for the coupling reaction, we next examined the scope of the reaction, the results of which are shown in Scheme 6. Several aspects are noteworthy: first, the reaction is highly selective for the branched product over the linear product across a wide variety of electronically and sterically differentiated benzyl chlorides and alkenes. The selectivity, described by the ratio between the branched product and the sum of all other isomers observed, is greater than 95:5 in nearly all instances, which not only indicates an intrinsically high selectivity for the branched product over the linear product but also shows that isomerization of the product after its formation is extremely minimal.[40]

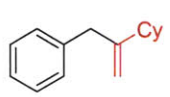
Scheme 6. Substrate Scope for the Developed Mizoroki–Heck Reaction[a]



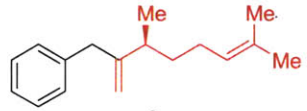
unsubstituted



7
92% yield, 98:2

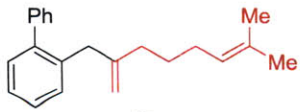


8
70% yield, 93:7

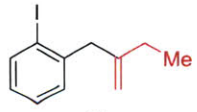


9
47% yield, 93:7

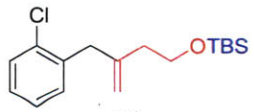
ortho-substituted



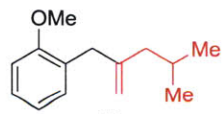
10
87% yield, 96:4



11
84% yield, 95:5

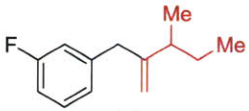


12[b]
90% yield, 96:4

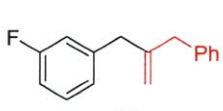


13
69% yield, 95:5

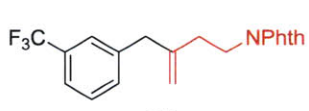
meta-substituted



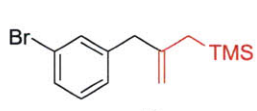
14
75% yield, 96:4



15
92% yield, 97:3

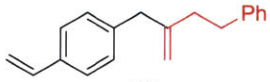


16[c]
83% yield, 99:1

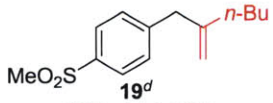


17
50% yield, 97:3

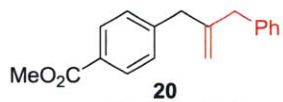
para-substituted



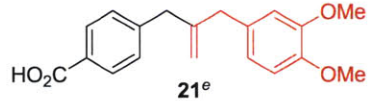
18
85% yield, 97:3



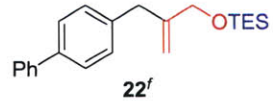
19[d]
80% yield, 98:2



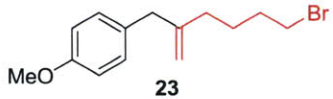
20
83% yield, 98:2



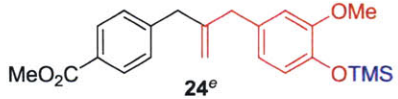
21[e]
82% yield, >95:5



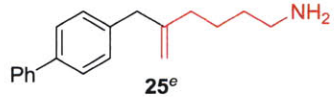
22[f]
88% yield, >99:1



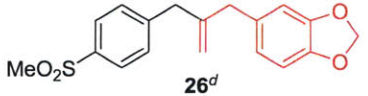
23
77% yield, 96:4



24[e]
96% yield, >99:1

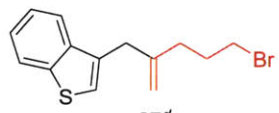


25[e]
69% yield, >95:5

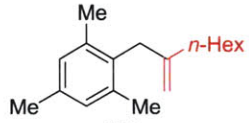


26[d]
67% yield, 99:1

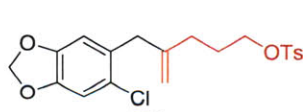
multiply-substituted and heteroaromatic



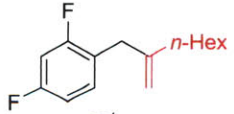
27[d]
78% yield, 94:6



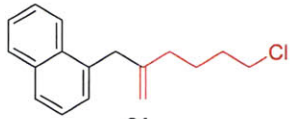
28[g]
41% yield, 96:4



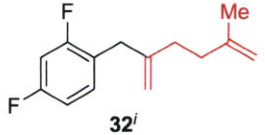
29[d]
52% yield, >95:5



30[h]
89% yield, 97:3



31
90% yield, 83:17



32[i]
61% yield, 97:3

[a]Yields listed are isolated yields. Ratios reported represent the ratio of the major (branched) product to the sum of all other isomers as determined by GC. Ratios reported as >95:5 were determined by NMR. [b]TBSOTf and 3 equiv of 3-buten-1-ol used in place of TMSOTf. [c]3 equiv of alkene used. [d]TESOTf used in place of TMSOTf. [e]Excess TMSOTf used to effect in situ protection. [f]TESOTf and 3 equiv of allyl alcohol used in place of TMSOTf. [g]Ratio was 78:22 prior to purification. The linear and branched products were separable by column chromatography. [h]Reaction carried out on a 10 mmol scale. [i]Product contained an inseparable byproduct (ca. 10% by mass) formed by the oligomerization of 2-methyl-1,5-hexadiene.

Substitution in the *ortho*, *meta*, and *para* positions of the benzyl chloride is well tolerated, including fluorine, chlorine, bromine, and iodine substituents (e.g., **11**, **12**, **14**, **15**, **17**). Some addition of nickel into the C–I bond was observed, but the yield of the corresponding desired product (**11**) was not significantly diminished. The tolerance of aryl halides is a significant feature of this method, since this enables the construction of halogen-substituted allylbenzene derivatives, which can then be directly used in further cross-coupling reactions, if desired. Oxidative addition of Ni(0) phosphine complexes into aryl fluorides,[41] chlorides,[42] bromides, and iodides[43] is well established, so the excellent chemoselectivity of the oxidative addition into the benzyl sp^3 C–Cl bond in preference to the sp^2 C–X bonds suggests the former occurs significantly faster than the latter.

As examples **23**, **27**, **29**, and **31** demonstrate, primary alkyl chlorides, bromides, and tosylates are all tolerated; again, this speaks to the excellent chemoselectivity of the oxidative addition into the benzyl sp^3 C–Cl bond in preference to primary sp^3 C–Cl, sp^3 C–Br, and sp^3 C–OTs bonds. As with their aryl counterparts, oxidative addition by nickel(0) into these types of bonds is well documented.[44] Construction of these 1° alkyl electrophiles could prove useful, whether it be for nucleophilic substitution reactions, for cross couplings, or in the preparation of nucleophilic organometallic reagents such as Grignard, organolithium, or organozinc reagents.

Additionally, as a part of our efforts to increase the convenience and flexibility of this method, we also explored the use of alternative silyl triflate additives. In the majority of cases, TMSOTf can be used in place of the more expensive TESOTf with no detrimental effects, though there are some instances in which the greater Lewis acidity of TMSOTf compared to that of TESOTf causes partial decomposition of substrates. Likewise, TBSOTf is also a competent silyl triflate additive for this reaction. Given the interchangeability of these additives, researchers may find it convenient to be able to use any of these silyl triflates, depending on what is readily available.

Using these three different silyl triflate additives, we demonstrated that in situ protection of free alcohols, carboxylic acids, and amines is possible on both the alkene and benzyl chloride

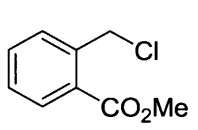
coupling partners, directly yielding protected alcohols (**12**, **22**), phenols (**24**), and following aqueous workup, free carboxylic acids (**21**) and amines (**25**). As illustrated by example **17**, allyltrimethylsilane is a competent alkene coupling partner, though some protiodesilylation does occur (ca. 15%). In this particular example, the protiodesilylated material was separable by column chromatography, allowing clean isolation of **17**, though in modest yield.

Also of considerable interest is the marked unreactivity of styrenes compared to α-olefins, as evidenced by the formation of **18** in high yield from 4-vinylbenzyl chloride and 3-butenylbenzene with no observable reaction at the styrene. Gratifyingly, sulfur-containing functional groups, such as sulfones (**19**, **26**) and benzothiophene (**27**) are tolerated with no apparent poisoning of the catalyst. Lastly, methylene acetals (**26**, **29**) are compatible with the reaction conditions.

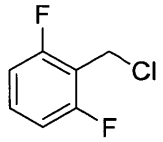
While most reactions proceed in good to excellent yield, a reduction in yield typically results from substitution on the *ortho* positions of the benzyl chloride or substitution adjacent to the olefin. Examples **8**, **9**, **14**, and **28** demonstrate this trend, since all four are obtained in a lower yield than substrates containing similar functional groups but connected in different positions. Additionally, there are several other specific conditions that greatly reduce the yield of the reaction or in some cases completely prevent product formation. Such examples are outlined in Chart 1.

Chart 1. Substrates that Did Not Provide the Desired Benzylation Products

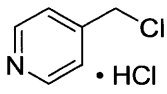
Benzyl chlorides



33



34



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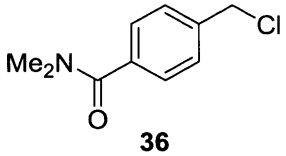
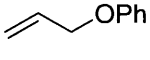
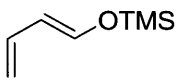


36

Alkenes



37



38

39

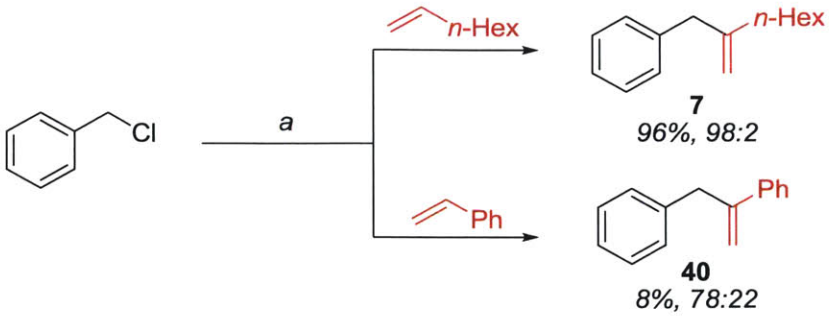
An ester moiety at the *ortho* position appears to completely prevent catalytic turnover; intriguingly, this functional group is well tolerated in the 4-position of the aromatic ring, suggesting it may be interfering with the catalytic cycle through chelation to the nickel center

after oxidative addition. Substitution of both the 2- and 6-positions of the benzyl chloride with fluorine (**34**) prevents product formation, leading to exclusive formation of the homocoupled product 1,2-bis(2,6-difluorophenyl)ethane. However, 2,4-difluorobenzyl chloride (**30**, **32**) is a competent substrate, indicating that the combination of the steric hindrance and the electron poor nature of 2,6-difluorobenzyl chloride is problematic, especially given that 2,4,6-trimethylbenzyl chloride is a competent substrate (**28**). Additionally, 4-(chloromethyl)pyridine (**34**, as the HCl salt) does not provide any product; it is unclear if this is due to reaction with the silyl triflate or because the nitrogen is able to coordinate to nickel, disrupting the catalytic cycle. Finally, 4-(chloromethyl)-*N*,*N*-dimethylbenzamide (**36**) did not provide any of the desired product, likely due to reaction of the amide with the silyl triflate.

A number of alkenes also provided very little or no product; allyl phenyl ether (**37**) underwent coupling but also reacts with TESOTf, as does the coupling product, both of which decomposed to a significant extent. Diene **38** decomposed under the reaction conditions, and the rate of reaction of cyclohexene (**39**) was extremely low, with only traces of product formed, even after 48 h of reaction time.

The profound selectivity for reaction with terminal, electronically unbiased alkenes in preference to styrenes (as evidenced by example **18**) is a surprising and interesting outcome, which we felt warranted further investigation. As shown in Scheme 7, the reaction between benzyl chloride and 1-octene proceeded in high yield as expected; however, the analogous reaction with styrene provided **40** in only 8% yield. Of further interest is the regiochemical outcome of the reaction with styrene: though not as selective as with aliphatic alkenes, substitution at the internal position is still favored in a 78:22 ratio. To date, the highest regioselectivity reported for styrene is 40:60 in favor of the linear product, making this a significant improvement from a theoretical standpoint, despite the low yield.[45]

Scheme 7. Comparison of Styrene and α-Olefins[a]



[a]Reaction conditions: precatalyst **1** (5 mol %), 5 equiv of alkene (1-octene or styrene), Et_3N (6 equiv), TMSOTf (1.5 equiv), 2 M in CH_2Cl_2. Yields and ratios were determined by GC. **40** was independently synthesized to provide an authentic sample.

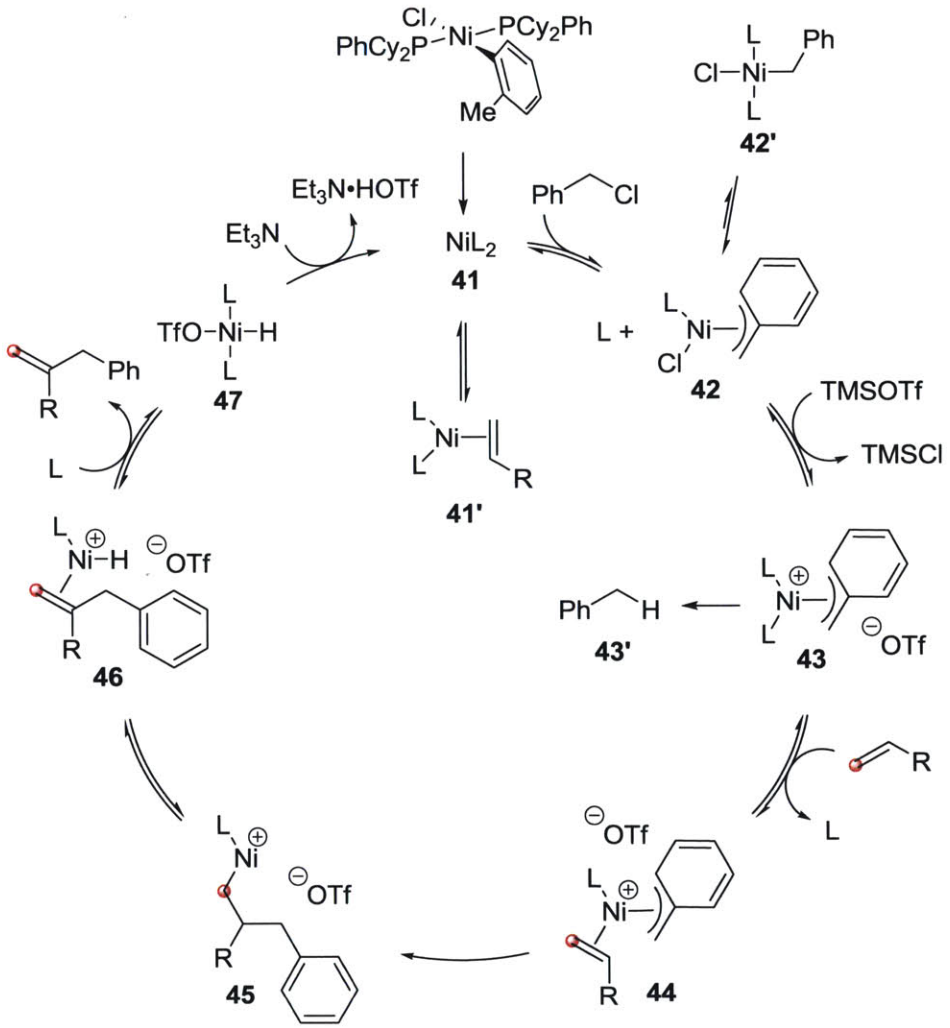
Proposed Mechanism

During NMR spectroscopic characterization of complex **1**, we observed that dissolution in CD_2Cl_2 caused the solution to take on a markedly red color compared to the pure yellow color observed in benzene-d_6. This difference is also reflected in the NMR spectra of the complex in C_6D_6 compared to CD_2Cl_2; the ^{31}P NMR spectrum in C_6D_6 shows only a single peak at 16.1 ppm, whereas the spectrum in CD_2Cl_2 shows three signals: one at 15.0 ppm, corresponding to **1**, as well as a signal at 3.1 ppm for free PCy_2Ph and one downfield signal at 44.9 ppm, presumably $(PCy_2Ph)Ni(o\text{-tolyl})Cl$ or a CD_2Cl_2 adduct thereof. On this basis, it is reasonable to suggest that dichloromethane promotes or stabilizes dissociation of one PCy_2Ph ligand, which we hypothesize is necessary during the course of the reaction to allow coupling to occur, as outlined in the proposed mechanism (Scheme 8).

The proposed mechanism begins with reduction of the precatalyst **1** to the NiL_2 species **41** (via the mechanism presented in Scheme 5), followed by rapid oxidative addition to yield **42**, which is in equilibrium with **42′**. Abstraction of chloride by the silyl triflate yields cationic nickel species **43**, which facilitates alkene coordination to yield **44**.[46] This species undergoes β-migratory insertion with the indicated regiochemistry to produce **45**, with nickel bonded to the less substituted of the two carbons comprising the alkene. The migratory insertion step is likely irreversible, and it also determines the regiochemical outcome of the reaction: insertion as shown (**44** to **45**) will ultimately provide the branched (desired) product, whereas insertion with the opposite regiochemistry will lead to formation of the linear product.

Following migratory insertion, β-hydride elimination to form nickel hydride **46** takes place. Product release, ligand association, and deprotonation by Et_3N complete the catalytic cycle. One commonly observed side product (**43′**), formed by the formal protonation of benzyl nickel species **43**, is often produced in small quantities during the course of the reaction. As the concentration of alkene decreases, the equilibrium between **43** and **44** shifts more toward **43**, which results in a higher concentration of **43** at any given time, causing reduction product **43′** to be formed in greater amounts. We suspect this is the root cause for the decrease in yield observed as the amount of alkene used in the reaction is reduced or when more sterically hindered alkenes are used.

Scheme 8. Hypothesized Mechanism[a]



[a]Migratory insertion (**44** to **45**) occurs to form the new nickel–carbon bond to the less substituted carbon of the alkene, which is marked with a red circle for emphasis.

We hypothesize that the principal factor responsible for formation of the branched product in preference to the linear product is the steric differentiation of the two ends of the alkene, which manifests itself as a difference in energy between the incipient 1° C–Ni and 2° C–Ni bonds formed during migratory insertion (**44** to **45**). The less hindered 1° C–Ni bond is lower in energy, and as such, the transition state leading to its formation is also lower in energy. The uniformly high selectivity observed across a range of electronically diverse substrates supports this hypothesis, suggesting that electronic factors are of secondary importance in determining the regiochemical outcome of the migratory insertion and thus of the reaction. The comparison between styrene and an aliphatic olefin (Scheme 7) further supports this hypothesis: while the branched product is still the major product, the selectivity is indeed reduced compared to electronically unbiased alkenes.

Conclusion

In summary, we have developed a convenient protocol for the internally selective benzylation of terminal alkenes using the air-stable precatalyst *trans*-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$ (**1**). This precatalyst is easily prepared from commercially available $NiCl_2{\cdot}6H_2O$, PCy_2Ph, and *o*-tolylmagnesium chloride in a high yielding, two-step procedure and can be stored open to air at room temperature with no measurable loss of purity or activity. Furthermore, all reagents used in the reaction can be used "as received" with no purification or even any degassing necessary. The reaction is tolerant of substitution on both the benzyl chloride and alkene coupling partners, allowing rapid access to a wide variety of substituted allylbenzene derivatives. Additionally, this study has provided useful information regarding the commonly employed nickel(0) source $Ni(cod)_2$, demonstrating that the cod ligands are not innocent under all circumstances. This finding has wider implications for the field of nickel(0) catalysis, where $Ni(cod)_2$ is frequently used as a precursor to a variety of Ni(0) complexes.

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(28) During the course of these studies, a sample of **4** was allowed to stand open to the atmosphere at room temperature for 4 months. No change in the ^{1}H, ^{13}C, or ^{31}P NMR spectra was observed, nor was the sample observed to be hygroscopic, and reactions run using precatalyst that had been allowed to stand for several months showed no difference from reactions run using freshly-prepared precatalyst.

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(31) A control experiment using 5 mol % of *trans*-$(PCy_2Ph)_2NiCl_2$ as the precatalyst produced a trace of product (<1%), whereas a control experiment with no catalyst added produced

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(46) Based on the observation that the rate of the reaction is dependent on the concentration of alkene and the observation that the amount of side product **43′** formed increases at lower alkene concentrations, we hypothesize that **43** is the resting state of the catalyst.

Chapter 2

Alkenes as Vinylmetal Equivalents: The Nickel-Catalyzed Mizoroki–Heck Reaction of Benzyl Chlorides and Terminal Alkenes

Experimental Section

Materials, Methods, and General Considerations

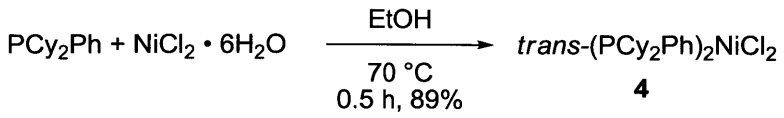
For couplings catalyzed by *trans*-$(PCy_2Ph)_2Ni(o\text{-tolyl})Cl$ (**1**), no precaution to exclude air or water was taken, non-dried glassware was employed, and all reagents and solvents were used as received. For reactions requiring dry and/or oxygen-free conditions, tetrahydrofuran, toluene, dichloromethane, triethylamine, diethyl ether, benzene, and acetonitrile were degassed by sparging with nitrogen and dried by passage through a column of activated alumna on an SG Water solvent purification system. Manipulation of all air-sensitive reagents was carried out in a glovebox (MBraun Unilab) filled with dry nitrogen. Couplings using $(PCy_2Ph)_2Ni(\eta^2\text{-}C_2H_4)$ (**2**) required the exclusion of oxygen, so all liquid reagents were degassed by three freeze-pump-thaw cycles. Liquid alkenes were distilled from sodium metal, CaH_2 or 4Å molecular sieves as appropriate. Thin-layer chromatography was carried out on EMD Millipore 60 F_{254} glass-backed plates (silica gel, 250 μm coating thickness) and spots were visualized using UV light, basic potassium permanganate, ethanolic phosphomolybdic acid (PMA), or ceric ammonium nitrate (CAN) stains. Column chromatography was carried out on a Biotage Isolera chromatography system using SNAP KP-Sil columns (silica gel, 50 μm average particle size). Bis(1,5-cyclooctadiene)nickel(0)[1] was purchased from Strem Chemicals (Newburyport, MA) and stored at –30 °C in a glovebox. Ethylene and 1-butene were purchased from Sigma-Aldrich (Milwaukee, WI). Benzene-d_6 (99.6% atom D, Sigma-Aldrich) for NMR spectroscopy of oxygen-sensitive species was degassed by three freeze-pump-thaw cycles prior to usage and stored over activated 4Å molecular sieves. All other chemicals were purchased from Sigma-Aldrich (Milwaukee, WI), Alfa Aesar (Ward Hill, MA), TCI America (Portland, OR), Oakwood Products, Inc. (West Columbia, SC), or GFS Chemicals (Columbus, OH).

^1H NMR Spectra were obtained on either a Varian Mercury 300 (at 300 MHz) or Varian Inova 500 (at 500 MHz); ^{13}C spectra were recorded on a Varian Mercury 300 (at 75 MHz) or a Varian Inova 500 (at 126 MHz) with ^1H decoupling; ^{31}P spectra were recorded on either a Varian Mercury 300 (at 121 MHz) or a Varian Inova 500 (at 202 MHz) with ^1H decoupling. Chemical shifts (^1H and ^{13}C) are reported in parts per million relative to TMS (δ = 0.00 ppm) and were referenced to the residual solvent peak; ^{31}P NMR spectra were referenced to an external standard

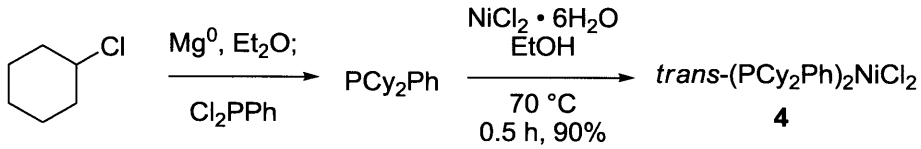
[1] The physical appearance of the bis(1,5-cyclooctadiene)nickel(0) used for all experiments was bright yellow-orange and crystalline, with block-shaped crystals ca. 0.4–0.8 mm on each side. Samples appearing as dull yellow powder, yellow-gray powder, or any sample with visible black spots (nickel) may give poor results, as these conditions all indicate at least some level of decomposition.

of 85% phosphoric acid (δ = 0.00 ppm). The following designations are used to describe multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), br (broad), v (very), app (apparent). IR spectra were obtained on an Agilent Cary 630 FT-IR spectrometer equipped with an ATR accessory. Intensities are reported relative to the most intense peak of the spectrum and are defined as follows: w (weak, intensity between 0 and 33.3%), m (medium, between 33.3% and 66.6%), and s (strong, between 66.6% and 100%). Gas chromatography (GC) was performed on an Agilent 5870 GC (HP-5 column) with a flame ionization detector. GC/MS was performed on an Agilent 5870 GC (HP-5ms column) with an Agilent 5975C MSD. Dodecane (99+%, Alfa Aesar) was used as an internal standard for quantitation. Exact masses (high resolution mass spectra) were obtained on a Bruker Daltonics APEX IV 4.7T FT-ICR spectrometer operating with electrospray ionization (ESI) in positive ion mode. Samples not suitable for ESI were ionized using an IonSense DART ion source operating in positive ion mode.

Synthesis and Characterization of Complexes



***trans*-bis(dicyclohexylphenylphosphine)nickel(II) chloride (4, Method A).** To a 25 mL round-bottom flask equipped with a magnetic stir bar was added $NiCl_2 \cdot 6H_2O$ (0.50 mmol, 119 mg) and PCy_2Ph (1.05 mmol, 288 mg). Ethanol (10 mL) was added, the flask fitted with a reflux condenser, placed under an atmosphere of argon, and the mixture was heated to 70 °C. After 30 minutes, the mixture was cooled to 0 °C with a water-ice bath and the solid collected by vacuum filtration. The solid was washed twice with cold ethanol (5 mL) and twice with cold ether (5 mL). Drying under vacuum[2] yielded **4** (302 mg, 89%) as a fine, purple powder.



***trans*-bis(dicyclohexylphenylphosphine)nickel(II) chloride (4, Method B).** An oven dried, 500 mL, two-neck, round-bottom flask was charged with a magnetic stir bar and magnesium turnings (251 mmol, 6.10 g), fitted with a reflux condenser and rubber septum, and the apparatus thoroughly flushed with argon. Diethyl ether (50 mL) was transferred to the flask along with a single crystal of iodine. The septum was removed and replaced with a dropping funnel containing chlorocyclohexane (254 mmol, 30.10 mL) in 250 mL of anhydrous diethyl ether. Approximately 15 mL of this chlorocyclohexane solution was added to the flask, which was then gently warmed with a heating mantle to initiate the reaction, as indicated by disappearance of the iodine color and mild bubbling of the ether. Following initiation, the chlorocyclohexane solution was added at such a rate so as to keep the solution at a moderate reflux without external heating (ca. 1–2 drops per second). After complete addition of the chlorocyclohexane solution, the mixture was heated to reflux for 1 hour, after which the flask was cooled to –30 °C and a solution of phenyldichlorophosphine (100 mmol, 13.57 mL) in 100 mL of diethyl ether was added dropwise with vigorous stirring. After addition of the phenyldichlorophosphine, the

[2] It is suggested to place a piece of cotton or glass wool inside the inlet adapter connected to the flask to prevent fine particles of **4** from traveling into the vacuum manifold.

solution was allowed to warm to room temperature and stirred for 1 hour. The reaction was quenched with saturated aqueous ammonium chloride and the ether layer washed twice with water. The ether was evaporated under reduced pressure and 200 mL of ethanol were added, followed by $NiCl_2 \cdot 6H_2O$ (45 mmol, 10.70 g), after which the solution was heated to 70 °C for 30 minutes. The mixture was cooled to 0 °C with a water-ice bath and the solid collected by vacuum filtration. The solid was washed with two 15 mL portions of cold ethanol and two 15 mL portions of diethyl ether. The solid was collected and dried under vacuum for several hours to yield **4** (27.46 g, 90%) as a fine, purple powder.

mp 225–226 °C dec (lit.[3] 226–228 °C dec).

^{1}H NMR (500 MHz, C_6D_6, δ): 7.80 (d, J = 7.6 Hz, 4H), 7.27 (t, J = 7.5 Hz, 4H), 7.00 (t, J = 7.5 Hz, 2H), 3.59 (br s, 4H), 2.52 (d, J = 10.7 Hz, 4H), 2.05 (q, J = 11.5, 11.0 Hz, 4H), 1.96 – 1.72 (m, 16H), 1.61 (d, J = 10.0 Hz, 4H), 1.32 (q, J = 12.5 Hz, 4H), 1.25 – 1.10 (m, 8H).

^{1}H NMR (500 MHz, CD_2Cl_2, δ): 7.82 (app s, 4H), 7.43 (app s, 4H), 7.09 (app s, 2H), 2.57 – 2.12 (m, 8H), 1.89 (d, J = 12.6 Hz, 4H), 1.80 – 1.61 (m, 12H), 1.56 (q, J = 11.8, 4H), 1.42 – 1.28 (m, 12H), 1.22 (q, J = 12.8 Hz, 4H).

^{13}C{^{1}H} NMR (126 MHz, CD_2Cl_2, δ): 131.80 (br s), 127.46, 31.70 (br s), 30.09 (br s), 28.00, 27.12.

^{31}P{^{1}H} (121 MHz, CD_2Cl_2, δ) ca. 25 (v br s). See discussion below for details.

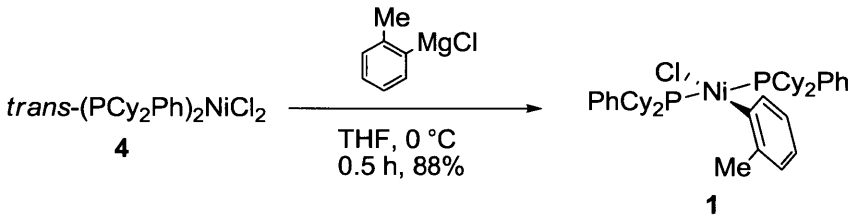
FT-IR (ATR, cm^{-1}): 3075 (w), 3051 (w), 2928 (s), 2850 (m), 1445 (m), 1434 (s), 1294 (w), 1266 (w), 1199 (w), 1186 (w), 1171 (m), 1111 (m), 1098 (w), 999 (m), 914 (w), 895 (w), 887 (w), 846 (m), 818 (w), 740 (s), 697 (s), 688 (s).

Crystals suitable for single-crystal X-ray diffraction analysis were obtained by slow evaporation (at room temperature) of a THF/ethanol solution of the complex. Slow evaporation of THF/isopropanol, benzene/ethanol, and benzene/isopropanol solutions also yielded satisfactory crystals.

Initial attempts to characterize **4** by ^{31}P NMR spectroscopy showed no signals, even after several hundred transients on a CD_2Cl_2 solution nearly saturated with **4**. Further attempts to obtain a

[3] Stone, P. J. and Zvi, D. *Inorg. Chim. Acta* **1970**, *5*, 434–438. Samples prepared by Methods A and B, neither of which had been recrystallized, both melted at 225–226 °C dec.

spectrum, including collecting an even larger number of transients, yielded a spectrum with an extremely broad signal centered at approximately 25 ppm spanning from ca. 120 to –70 ppm and two small singlets, one at 3.13 ppm (PCy_2Ph) and one at 45.59 ($OPCy_2Ph$). The presence of these two signals suggests some decomposition of the complex (caused by oxygen—a J-Young tube was not used) in the time required to obtain the spectrum, which was several hours. The location of the peak's maximum is very sensitive to the phasing of the spectrum, so determination of a precise chemical shift is not possible. Given the appearance of the ^{1}H and ^{13}C spectra, which have multiple broadened signals, it is apparent that the proximity to the nickel atom is allowing very rapid relaxation for some atoms of the complex, causing severe broadening. Since the phosphorus atoms are directly bonded to nickel, it is not surprising that they experience this effect to a greater extent. These results were verified on several different spectrometers to rule out hardware or acquisition problems.



***trans*-bis(dicyclohexylphenylphosphine) nickel(*o*-tolyl) chloride (1)**: *trans*-$(PCy_2Ph)_2NiCl_2$ (**4**, 15.46 mmol, 10.49 g) was added to an oven-dried, round-bottom flask with a magnetic stir bar. Tetrahydrofuran (250 mL) was added and the mixture stirred for 10 minutes. This homogeneous solution was cooled to 0 °C with an ice bath and *o*-tolylmagnesium chloride (15.46 mmol, 0.865 M in THF, 17.87 mL) was added dropwise at a rate of ca. 2 drops per second with vigorous stirring. Near the end of the addition, the solution began to lighten in color from dark purple to red-orange. The solution was allowed to stir for 30 minutes at 0 °C, after which anhydrous methanol (15 mL) was added to quench any unreacted Grignard reagent. The stir bar was removed and the solution was evaporated to dryness under reduced pressure. Anhydrous methanol (100 mL) was added and the mixture was sonicated until a uniform, yellow suspension with no large aggregates was obtained (approx. 15 minutes). After cooling to 0 °C, the yellow

precipitate was collected by vacuum filtration, washed with two portions of cold methanol, and dried under high vacuum[4] to yield **1** (9.97 g, 88%) as a fine, yellow powder.

mp 149–150 °C dec.

^{1}H NMR (500 MHz, C_6D_6, δ): 7.49 (s, 4H), 7.10 (app s, 7H), 6.76 – 6.58 (m, 3H), 3.51 (s, 3H), 2.52 (s, 4H), 2.42 – 2.21 (m, 4H), 1.95 – 0.83 (m, 36H).

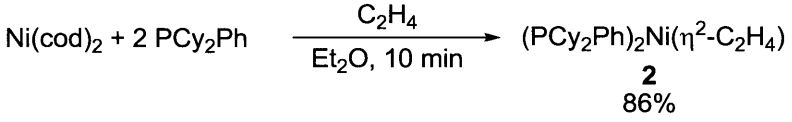
^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 149.86 (t, J = 32.3 Hz), 142.76, 138.45, 132.91, 130.70 (t, J = 15.5 Hz), 127.09, 124.17, 122.27, 33.90 (t, J = 9.8 Hz), 33.32 (t, J = 9.7 Hz), 30.25 (d, J = 21.6 Hz), 29.47 (d, J = 7.5 Hz), 28.28 (t, J = 5.3 Hz), 28.09 (t, J = 6.2 Hz), 27.88 (t, J = 5.2 Hz), 27.66, 26.79 (d, J = 7.3 Hz).

^{31}P{^{1}H} (202 MHz, C_6D_6, δ): 16.09 (s).

^{31}P{^{1}H} (202 MHz, CD_2Cl_2, δ): 15.00 (s), 44.89 (s), 3.13 (s). 3049 (w), 2922 (m), 2852 (m), 1570 (w), 1561 (w), 1447 (m), 1432 (m), 1326 (w), 1296 (w), 1264 (m), 1203 (w), 1178 (w), 1115 (w), 1027 (w), 1003 (m), 917 (w), 889 (w), 848 (m), 731 (s), 695 (s).

HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{43}H_{61}ClNiP_2$, 733.3363; found, 733.3354. $[M - Cl]^+$ calcd for $C_{43}H_{61}ClNiP_2$, 697.3596; found, 697.3592.

Crystals suitable for single-crystal X-ray diffraction analysis were obtained by the slow evaporation (at room temperature) of a THF solution of the complex. An ether solution also yielded high-quality crystals.



ethylenebis(dicyclohexylphenylphosphine)nickel(0) (**2**): In a glovebox, $Ni(cod)_2$ (2.00 mmol, 0.550 g) and PCy_2Ph (4.00 mmol, 1.098 g) were combined in a 20 mL vial with a magnetic stir bar and diethyl ether (12 mL) was added, yielding an intensely colored, dark red solution. After stirring for 10 minutes, ethylene was bubbled through the solution, causing a rapid change in the color to orange and subsequently to bright yellow. Ethylene was bubbled through the solution for an additional 10 minutes, after which the vial was sealed and allowed to stand at –20 °C to complete the precipitation. The precipitate was collected by vacuum filtration and washed with

[4] As with complex **4**, complex **1** forms a very fine powder. It is therefore suggested to place a piece of cotton or glass wool inside the inlet adapter connected to the flask to prevent fine particles of **1** from traveling into the vacuum manifold.

two small portions of cold diethyl ether. Drying under vacuum yielded the complex as a fine, yellow powder (1.048 g, 86%).

^{1}H NMR (300 MHz, C_6D_6, δ): 7.65 – 7.56 (m, 4H), 7.09 – 7.00 (m, 6H), 2.43 (s, 4H), 2.33 – 2.19 (m, 4H), 2.19 – 2.06 (m, 4H), 2.00 – 1.84 (m, 4H), 1.77 – 1.61 (m, 8H), 1.61 – 1.50 (m, 4H), 1.50 – 1.37 (m, 4H), 1.37 – 1.10 (m, 12H), 1.09 – 0.91 (m, 4H).

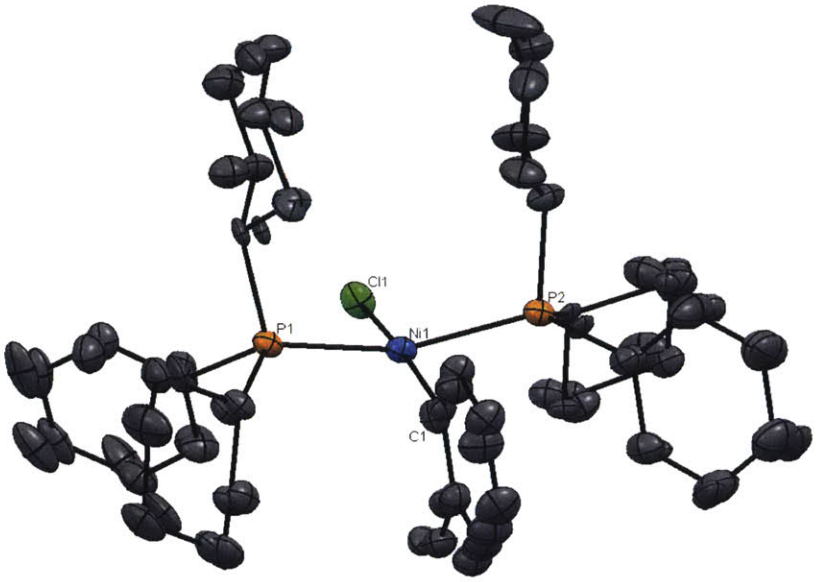
^{13}C{^{1}H} NMR (126 MHz, C_6D_6, δ): 134.85 (dd, J = 10.9, 8.2 Hz), 133.99 (t, J = 6.0 Hz), 127.18 (t, J = 3.9 Hz), 39.69 (t, J = 6.3 Hz), 35.18 (dd, J = 10.8, 9.7 Hz), 30.20 (t, J = 3.2 Hz), 29.54, 27.92 (t, J = 6.0 Hz), 27.62 (t, J = 4.3 Hz), 26.87.

^{31}P{^{1}H} NMR (121 MHz, C_6D_6, δ): 37.6 ppm.

FT-IR (ATR, cm^{-1}): 3074 (w), 3047 (w), 2922 (s), 2848 (m), 1481 (w), 1445 (m), 1434 (m), 1335 (w), 1270 (w), 1203 (w), 1180 (m), 1111 (w), 1001 (m), 882 (s), 848 (m), 742 (s), 697 (s).

X-Ray Diffraction Characterization

Figure S1. Thermal ellipsoid depiction of complex 1



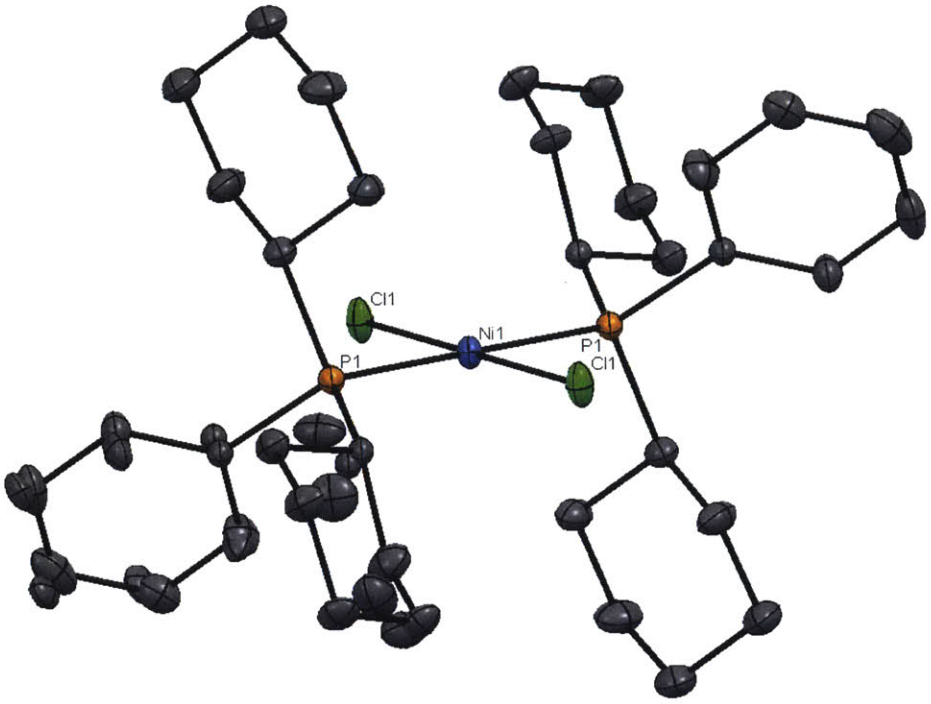
Ellipsoid probability set at 50%.

Table S1. Selected Bond Angles and Distances from the X-Ray Structure of Complex 1

Atoms	*Distance (Å)*	*Atoms*	*Angle (Deg.)*
Ni(1)–P(1)	2.2318(5)	P(1)–Ni(1)–P(2)	160.740(17)
Ni(1)–P(2)	2.2402(5)	C(1A)–Ni(1)–Cl(1)	166.5(4)
Cl(1)–Ni(1)	2.2203(4)	C(1)–Ni(1)–Cl(1)	170.4(4)
C(1A)–Ni(1)	1.877(13)	C(1A)–Ni(1)–P(1)	89.5(6)
C(1)–Ni(1)	1.911(11)	C(1)–Ni(1)–P(1)	91.8(5)
		Cl(1)–Ni(1)–P(1)	91.464(16)
		C(1A)–Ni(1)–P(2)	92.9(6)
		C(1)–Ni(1)–P(2)	89.2(5)
		Cl(1)–Ni(1)–P(2)	90.628(16)

The complete data for this structure are on file with the CCDC under entry SEVDOO.

Figure S2. Thermal ellipsoid depiction of complex 4



Ellipsoid probability set at 50%.

Table S2. Selected Bond Angles and Distances from the X-Ray Structure of Complex 4

Atoms	*Distance (Å)*	*Atoms*	*Angle (Deg.)*
Cl(1)–Ni(1)	2.1628(4)	Cl(1)#1–Ni(1)–Cl(1)	179.999(12)
Ni(1)–Cl(1)#1	2.1628(4)	P(1)#1–Ni(1)–P(1)	180
Ni(1)–P(1)#1	2.2511(4)	Cl(1)#1–Ni(1)–P(1)#1	90.762(14)
Ni(1)–P(1)	2.2511(4)	Cl(1)–Ni(1)–P(1)#1	89.238(14)
		Cl(1)#1–Ni(1)–P(1)	89.238(14)
		Cl(1)–Ni(1)–P(1)	90.762(14)

The complete data for this structure are on file with the CCDC under entry SEVDUU.

Table S3. Crystal Data and Structure Refinement for Complex 1

Identification code	x12154	
Empirical formula	C43 H61 Cl Ni P2	
Formula weight	734.02	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P-1*	
Unit cell dimensions	a = 10.5776(7) Å	α= 103.8850(10)°
	b = 12.2542(8) Å	β= 94.5290(10)°
	c = 17.3312(11) Å	γ = 113.7470(10)°
Volume	1956.8(2) $Å^3$	
Z	2	
Density (calculated)	1.246 Mg/m^3	
Absorption coefficient	0.675 mm^{-1}	
F(000)	788	
Crystal size	0.27 x 0.19 x 0.15 mm^3	
Theta range for data collection	1.23 to 31.00°	
Index ranges	-14<=h<=15, -17<=k<=17, -25<=l<=25	
Reflections collected	96996	
Independent reflections	12389 [R(int) = 0.0299]	
Completeness to theta = 31.00°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9056 and 0.8367	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12389 / 2152 / 717	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0372, wR2 = 0.0958	
R indices (all data)	R1 = 0.0436, wR2 = 0.1000	
Largest diff. peak and hole	0.705 and -0.831 $e.Å^{-3}$	

Crystallographer's Comments: The position of the Ph ring is disordered over two positions. EADP was required.

Table S4. Crystal Data and Structure Refinement for Complex 4

Identification code	x12157	
Empirical formula	C36 H54 Cl2 Ni P2	
Formula weight	678.34	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P-1*	
Unit cell dimensions	a = 9.4047(5) Å	α= 112.7030(10)°
	b = 10.1216(6) Å	β= 107.6740(10)°
	c = 10.5171(6) Å	γ = 91.3780(10)°
Volume	868.53(9) $Å^3$	
Z	1	
Density (calculated)	1.297 Mg/m^3	
Absorption coefficient	0.828 mm^{-1}	
F(000)	362	
Crystal size	0.58 x 0.47 x 0.19 mm^3	
Theta range for data collection	2.21 to 31.00°	
Index ranges	-13<=h<=13, -14<=k<=14, -15<=l<=15	
Reflections collected	31072	
Independent reflections	5529 [R(int) = 0.0274]	
Completeness to theta = 31.00°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8598 and 0.6456	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5529 / 595 / 248	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0281, wR2 = 0.0726	
R indices (all data)	R1 = 0.0302, wR2 = 0.0738	
Largest diff. peak and hole	0.600 and -0.811 $e.Å^{-3}$	

Crystallographer's Comments: The position of the Ph ring on both $PPhCy_2$ ligands is disordered; on P1 over three and on P2 over two positions. EADP was required. One SUMP used for the three-fold disorder.

Procedures for Nickel-catalyzed Benzylation Reactions

General Procedure A: To an 8 mL screw-top vial containing a magnetic stir-bar was added precatalyst **1** (0.050 mmol, 36.7 mg), alkene (5.00 mmol), triethylamine (6.00 mmol, 836 μL), the benzyl chloride (1.00 mmol), and CH_2Cl_2 (500 μL). After stirring the mixture for a few seconds, silyl triflate (1.5 mmol) was added, the vial capped, and left to stir for 4 to 8 hours as indicated. After the necessary time had elapsed, the reaction mixture was allowed to stir open to the air for 5 minutes, after which it was passed through a 4 cm plug of silica gel (pre-wetted with dichloromethane). The silica gel plug was washed with 25 mL of dichloromethane followed by 25 mL of a 1:1 mixture of hexanes/ethyl acetate. After concentration under reduced pressure, the crude material was purified by column chromatography on silica gel with the indicated eluent.

General Procedure B (modification for substrates with free –OH, $-NH_2$, $-CO_2H$ groups): To an 8 mL screw-top vial containing a magnetic stir-bar was added alkene (3.00–5.00 mmol), triethylamine (6.00–12.00 mmol), the benzyl chloride (1.00 mmol), and CH_2Cl_2 (500 μL). The mixture was cooled to 0 °C, after which the appropriate silyl triflate (4.50–10.00 mmol) was added dropwise. After the addition was complete, the mixture was warmed to room temperature, precatalyst **1** (0.050 mmol, 36.7 mg) was added, the vial was closed with a screw-cap, and the mixture was stirred at room temperature for 4 to 8 hours as indicated. Work-up and purification were carried out as indicated for each substrate.

General Procedure C (modification for reactions run with precatalyst 2): In a glovebox, precatalyst **2** (0.05 mmol, 31.8 mg) was added to an 8 mL screw-top vial containing a magnetic stir-bar. To the catalyst was added alkene (5.00 mmol), triethylamine (6.00 mmol, 836 μL), the benzyl chloride (1.00 mmol), and toluene (500 μL). After briefly stirring the mixture, silyl triflate (1.5 mmol) was added, the vial capped, and left to stir for the indicated length of time (12–24 hours). After this length of time, the reaction was worked up and purified as in General Procedure A.

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(2-methyleneoctyl)benzene (7): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), benzyl chloride (1.00 mmol, 115 µL), 1-octene (5 mmol, 785 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.46) yielded **7** (186 mg, 92%, 98:2 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.31 – 7.27 (m, 2H), 7.22 – 7.17 (m, 3H), 4.82 (dtt, J = 2.0, 1.2, 0.6 Hz, 1H), 4.72 (dtt, J = 2.0, 1.3, 0.7 Hz, 1H), 3.33 (s, 2H), 1.99 – 1.94 (m, 2H), 1.47 – 1.39 (m, 2H), 1.33 – 1.22 (m, 5H), 0.88 (t, J = 6.9 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 149.39, 140.05, 129.14, 128.36, 126.11, 111.05, 43.18, 35.58, 31.91, 29.16, 27.75, 22.79, 14.25.

The ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[5]

8

(2-cyclohexylallyl)benzene (8): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), benzyl chloride (1.00 mmol, 115 µL), vinylcyclohexane (5 mmol, 684 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.53) yielded **8** (140 mg, 70%, 93:7 ratio) as a clear, colorless liquid.

[5] Matsubara, R.; Gutierrez, A. C.; Jamison, T. F. *J. Am. Chem. Soc.* **2011**, *133*, 19020–19023.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.31 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 4.84 (dq, J = 1.7, 0.8 Hz, 1H), 4.64 – 4.62 (m, 1H), 3.37 (s, 2H), 1.89 – 1.59 (m, 4H), 1.33 – 1.03 (m, 4H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 154.66, 140.37, 129.27, 128.33, 126.01, 109.63, 43.55, 41.98, 32.64, 26.88, 26.55.

The ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[5]

9

(S)-(3,7-dimethyl-2-methyleneoct-6-enyl)benzene (9): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), benzyl chloride (1.00 mmol, 115 µL), (*S*)-(+)-β-citronellene (5 mmol, 910 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.58) yielded **9** (108 mg, 47%, 93:7 ratio) as a clear, colorless liquid.

$[\alpha]_D^{20}$ = + 0.13 (c 24.90, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.34 (tq, J = 7.8, 1.1 Hz, 2H), 7.28 – 7.22 (m, 3H), 5.13 (tdd, J = 5.9, 2.2, 0.8 Hz, 1H), 4.91 (dq, J = 1.7, 0.8 Hz, 1H), 4.68 (q, J = 1.5 Hz, 1H), 3.43 – 3.34 (m, 2H), 2.19 (h, J = 6.9 Hz, 1H), 2.04 – 1.93 (m, 2H), 1.74 (q, J = 1.3 Hz, 3H), 1.68 – 1.63 (m, 3H), 1.57 (ddt, J = 13.4, 8.7, 7.0 Hz, 1H), 1.40 (ddt, J = 13.6, 8.6, 6.8 Hz, 1H), 1.09 (dd, J = 6.9, 0.7 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 154.03, 140.14, 131.38, 129.47, 128.31, 126.04, 124.81, 110.39, 41.16, 38.86, 35.86, 25.97, 25.86, 20.18, 17.81.

FT-IR (ATR, cm^{-1}): 3083 (w), 3066 (w), 3029 (w), 2964 (w), 2917 (m), 2857 (w), 1641 (w), 1604 (w), 1496 (w), 1453 (m), 1376 (w), 1108 (w), 1074 (w), 1031 (w), 893 (m), 832 (w), 729 (m), 697 (s).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{17}H_{24}$, 229.1951; found, 229.1975.

10

2-(7-methyl-2-methyleneoct-6-enyl)biphenyl (10): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 2-(chloromethyl)biphenyl **S1** (1.00 mmol, 203 mg), 7-methyl-1,6-octadiene (5 mmol, 825 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for 10 seconds, after which TMSOTf (1.50 mmol, 271 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 7 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.40) yielded **10** (253 mg, 87%, 96:4 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.54 – 7.34 (m, 9H), 5.26 – 5.17 (m, 1H), 5.00 – 4.95 (m, 1H), 4.70 – 4.65 (m, 1H), 3.46 – 3.42 (m, 2H), 2.11 – 2.00 (m, 4H), 1.84 (d, J = 4.6 Hz, 3H), 1.72 (d, J = 4.4 Hz, 3H), 1.54 – 1.44 (m, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 149.79, 142.46, 141.88, 137.06, 131.44, 130.50, 130.12, 129.26, 128.03, 127.29, 126.92, 126.17, 124.67, 111.43, 39.88, 36.05, 27.99, 27.78, 25.85, 17.82.

FT-IR (ATR, cm^{-1}): 3061 (w), 3023 (w), 2967 (w), 2926 (w), 2857 (w), 1645 (w), 1598 (w), 1479 (m), 1438 (m), 1376 (w), 1106 (w), 1072 (w), 1052 (w), 1011 (w), 891 (m), 830 (w), 772 (m), 746 (s), 723 (w), 701 (s).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{22}H_{26}$, 291.2107; found, 291.2103.

11

1-iodo-2-(2-methylenebutyl)benzene (11): A magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 2-iodobenzyl chloride (1.00 mmol, 252 mg), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial, which was fitted with a rubber septum. A stream of 1-butene gas was bubbled through the solution for 10 minutes to saturate the solution, after which the reaction was kept under a static atmosphere of 1-butene with a balloon. Trimethylsilyl triflate (1.50 mmol, 271 μL) was added via syringe and the reaction mixture was

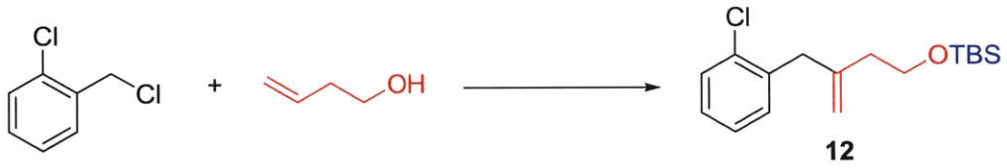
allowed to stir for 6 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.64) yielded **10** (229 mg, 84%, 95:5 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.86 (dd, J = 7.9, 1.3 Hz, 1H), 7.31 (td, J = 7.5, 1.3 Hz, 1H), 7.24 (ddd, J = 7.6, 1.7, 0.4 Hz, 1H), 6.93 (td, J = 7.8, 1.8 Hz, 1H), 4.93 (qd, J = 1.5, 0.7 Hz, 1H), 4.57 (qt, J = 1.5, 0.9 Hz, 1H), 3.50 (s, 1H), 2.12 (qdd, J = 7.4, 1.6, 0.8 Hz, 2H), 1.13 (t, J = 7.4 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 149.23, 142.73, 139.55, 130.23, 128.24, 127.96, 110.58, 101.75, 47.49, 29.12, 12.47.

FT-IR (ATR, cm^{-1}): 3061 (w), 2965 (w), 2934 (w), 2878 (w), 1647 (w), 1585 (w), 1561 (w), 1464 (m), 1434 (m), 1374 (w), 1046 (w), 1011 (s), 891 (s), 742 (s), 714 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{11}H_{13}I$, 273.0135; found, 273.0132.



12

***tert*-butyl(3-(2-chlorobenzyl)but-3-enyloxy)dimethylsilane (12):** Following General Procedure B, a magnetic stir bar, 2-chlorobenzyl chloride (1.00 mmol, 126 µL), 3-buten-1-ol (3 mmol, 258 µL), Et_3N (9.00 mmol, 1254 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was cooled to 0 °C, after which TBSOTf (4.5 mmol, 1033 µL) was added dropwise. After the addition was complete, the mixture was warmed to room temperature, precatalyst **1** (0.050 mmol, 36.7 mg) was added, the vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. After this time, the reaction mixture was allowed to stir open to the air for 5 minutes, then passed through a 4 cm plug of silica gel (pre-wetted with dichloromethane). The silica gel plug was washed with 25 mL of dichloromethane followed by 25 mL of a 1:1 mixture of hexanes:ethyl acetate. After concentration under reduced pressure, the crude material was purified by column chromatography on silica gel (5% EtOAc/Hex, R_f = 0.45) to yield **12** (280 mg, 90%, 96:4 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.36 (dd, J = 7.8, 1.4 Hz, 1H), 7.25 – 7.14 (m, 3H), 4.91 – 4.89 (m, 1H), 4.67 – 4.65 (m, 1H), 3.76 (t, J = 7.0 Hz, 2H), 3.50 (s, 2H), 2.29 (dd, J = 7.0, 0.7 Hz, 2H), 0.91 (s, 9H), 0.07 (s, 6H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 144.64, 137.44, 134.60, 131.20, 129.59, 127.72, 126.78, 113.21, 62.40, 40.33, 39.45, 26.10, 18.47, -5.15.

FT-IR (ATR, cm^{-1}): 3075 (w), 2954 (w), 2930 (m), 2896 (w), 2859 (w), 1647 (w), 1473 (m), 1443 (w), 1387 (w), 1361 (w), 1253 (m), 1095 (s), 1052 (m), 1039 (m), 1005 (w), 938 (w), 895 (m), 832 (s), 811 (m), 774 (s), 746 (s), 682 (m), 662 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{17}H_{29}OClSi$, 311.1592; found, 311.1594.

13

1-methoxy-2-(4-methyl-2-methylenepentyl)benzene (13): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 2-methoxybenzyl chloride (1.00 mmol, 157 mg), 4-methyl-1-pentene (5 mmol, 633 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 5 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.27) yielded **13** (141 mg, 69%, 95:5 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.24 – 7.19 (m, 1H), 7.17 – 7.13 (m, 1H), 6.92 (td, J = 7.4, 1.1 Hz, 1H), 6.88 (dd, J = 8.2, 1.1 Hz, 1H), 4.77 (dt, J = 2.1, 1.0 Hz, 1H), 4.62 (dt, J = 2.5, 1.5 Hz, 1H), 3.82 (s, 2H), 3.33 (s, 2H), 1.96 – 1.83 (m, 4H), 0.91 (dd, J = 6.4, 0.7 Hz, 6H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 157.67, 147.91, 130.68, 128.54, 127.35, 120.47, 111.77, 110.52, 55.46, 46.09, 35.92, 26.22, 22.63.

FT-IR (ATR, cm^{-1}): 3072 (w), 2954 (m), 2924 (w), 2911 (w), 2870 (w), 2837 (w), 1645 (w), 1600 (w), 1589 (w), 1492 (m), 1464 (m), 1384 (w), 1367 (w), 1322 (w), 1289 (w), 1242 (s), 1182 (w), 1162 (w), 1109 (m), 1052 (m), 1033 (m), 889 (m), 749 (s), 725 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{14}H_{20}O$, 205.1587; found, 205.1589.

14

1-fluoro-3-(3-methyl-2-methylenepentyl)benzene (14): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 3-fluorobenzyl chloride (1.00 mmol, 145 mg), 3-methyl-1-pentene (5 mmol, 628 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.63) yielded **14** (144 mg, 75%, 96:4 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.30 – 7.24 (m, 1H), 7.02 – 6.99 (m, 1H), 6.97 – 6.91 (m, 2H), 4.92 (dq, J = 1.6, 0.8 Hz, 1H), 4.70 (q, J = 1.5 Hz, 1H), 3.47 – 3.26 (m, 2H), 2.11 – 2.02 (m, 1H), 1.58 – 1.34 (m, 2H), 1.07 (d, J = 6.9 Hz, 2H), 0.89 (t, J = 7.4 Hz, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 163.05 (d, J = 245.2 Hz), 153.15, 142.88 (d, J = 7.1 Hz), 129.65 (d, J = 8.3 Hz), 125.08 (d, J = 2.8 Hz), 116.20 (d, J = 20.9 Hz), 112.96 (d, J = 21.1 Hz), 110.90, 40.95 (d, J = 1.7 Hz), 40.83, 28.30, 19.66, 11.82.

FT-IR (ATR, cm^{-1}): 3079 (w), 2964 (m), 2928 (w), 2878 (w), 1643 (w), 1615 (m), 1589 (s), 1488 (s), 1447 (s), 1378 (w), 1249 (s), 1136 (m), 1074 (w), 1005 (w), 960 (m), 895 (s), 878 (m), 858 (w), 785 (s), 761 (s), 740 (w), 688 (s).

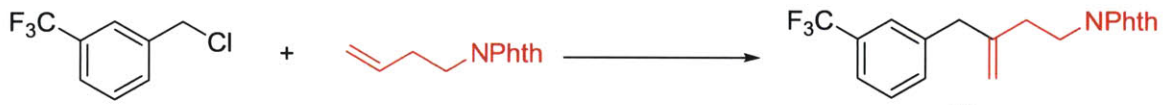
HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{13}H_{17}F$, 193.1387; found, 193.1378.

15

1-(2-benzylallyl)-3-fluorobenzene (15): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 3-fluorobenzyl chloride (1.00 mmol, 145 mg), allylbenzene (5 mmol, 662 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 μL) was added in one portion. The vial was closed with a screw-cap and the mixture

was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, *Rf* = 0.36) yielded **15** (208 mg, 92%, 97:3 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.33 – 7.28 (m, 2H), 7.28 – 7.21 (m, 2H), 7.18 – 7.14 (m, 2H), 6.95 – 6.85 (m, 3H), 4.90 – 4.88 (m, 1H), 4.87 – 4.85 (m, 1H), 3.28 (s, 2H), 3.27 (s, 2H).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 163.05 (d, *J* = 245.3 Hz), 147.73, 142.21 (d, *J* = 7.2 Hz), 139.34, 129.79 (d, *J* = 8.3 Hz), 129.18, 128.50, 126.36, 124.90 (d, *J* = 2.7 Hz), 115.98 (d, *J* = 21.0 Hz), 114.02, 113.18 (d, *J* = 21.0 Hz), 42.29, 41.92 (d, *J* = 1.7 Hz).
FT-IR (ATR, cm^{-1}): 3083 (w), 3068 (w), 3031 (w), 2906 (w), 2831 (w), 1647 (w), 1615 (m), 1589 (m), 1486 (s), 1449 (m), 1438 (m), 1249 (m), 1134 (m), 1074 (w), 1029 (w), 964 (w), 897 (m), 874 (m), 785 (s), 761 (m), 757 (m), 738 (s), 697 (s), 688 (s).
HRMS (DART, *m/z*): M^+ calcd for $C_{16}H_{15}F$, 226.1152; found, 226.1144.



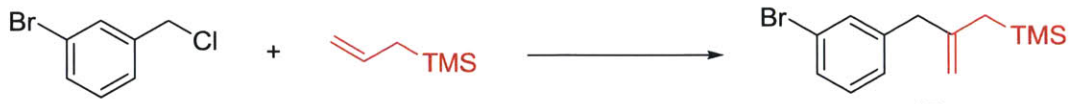
16

2-(3-(3-(trifluoromethyl)benzyl)but-3-enyl)isoindoline-1,3-dione (16): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 3-(trifluoromethyl)benzyl chloride (1.00 mmol, 155 µL), *N*-(3-buten-1-yl)phthalimide (3 mmol, 604 mg), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. Following work-up according to the general procedure, silica gel chromatography (70% CH_2Cl_2/Hex, R_f = 0.54) yielded **16** (298 mg, 83%, 99:1 ratio) as a clear, colorless liquid that solidified on standing at 5 °C.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.86 – 7.81 (m, 2H), 7.73 – 7.69 (m, 2H), 7.48 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 4.87 – 4.85 (m, 1H), 4.72 – 4.70 (m, 1H), 3.84 (t, *J* = 7.1 Hz, 2H), 3.49 (s, 2H), 2.37 (t, *J* = 7.1 Hz, 2H).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, δ): 168.15, 144.57, 140.10, 133.87, 132.60 (q, J = 1.4 Hz), 132.00, 130.62 (q, J = 31.9 Hz), 128.78, 125.80 (q, J = 3.8 Hz), 124.22 (q, J = 272.6 Hz), 123.13, 123.12 (q, J = 3.0 Hz), 114.70, 41.84, 36.19, 34.18.

The ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[5]



17

(2-(3-bromobenzyl)allyl)trimethylsilane (17): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 3-bromobenzyl chloride (1.00 mmol, 128 μL), allyltrimethylsilane (5 mmol, 795 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, Rf = 0.60) yielded **17** (142 mg, 50%, 97:3 ratio) as a clear, colorless liquid.

^1H NMR (500 MHz, $CDCl_3$, δ): 7.37 – 7.34 (m, 2H), 7.17 (dd, J = 8.3, 7.7 Hz, 1H), 7.15 – 7.11 (m, 1H), 4.67 (dt, J = 1.8, 0.9 Hz, 1H), 4.61 – 4.59 (m, 1H), 3.28 – 3.22 (m, 2H), 1.49 (d, J = 1.0 Hz, 2H), 0.07 (s, 9H).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, δ): 146.05, 142.37, 132.18, 129.90, 129.32, 127.91, 122.50, 110.26, 44.77, 26.25, –1.10.

FT-IR (ATR, cm^{-1}): 3074 (w), 2956 (w), 2900 (w), 1634 (w), 1594 (w), 1568 (w), 1473 (w), 1423 (w), 1247 (m), 1154 (w), 1070 (w), 998 (w), 835 (s), 770 (s), 694 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{13}H_{19}BrSi$, 283.0512; found, 283.0521.

18

1-(2-methylene-4-phenylbutyl)-4-vinylbenzene (18): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 4-vinylbenzyl chloride (1.00 mmol, 141 μL), 4-phenyl-1-butene (5 mmol, 751 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500

μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.34) yielded **18** (211 mg, 85%, 97:3 ratio) as a clear, colorless liquid.[6]

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.39 – 7.31 (m, 2H), 7.31 – 7.22 (m, 2H), 7.21 – 7.08 (m, 5H), 6.71 (dd, J = 17.6, 10.9 Hz, 1H), 5.72 (dt, J = 17.6, 0.8 Hz, 1H), 5.21 (dt, J = 10.9, 0.8 Hz, 1H), 4.95 – 4.85 (m, 1H), 4.85 – 4.77 (m, 1H), 3.36 (s, 2H), 2.84 – 2.70 (m, 2H), 2.37 – 2.21 (m, 2H).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 148.42, 142.11, 139.46, 136.78, 135.67, 129.29, 128.44, 128.40, 126.33, 125.91, 113.23, 111.71, 43.17, 37.23, 34.38.
FT-IR (ATR, cm^{-1}): 3085 (w), 3066 (w), 3027 (w), 2924 (w), 2859 (w), 1645 (w), 1630 (w), 1604 (w), 1509 (m), 1496 (w), 1455 (w), 1438 (w), 1406 (w), 1287 (w), 1111 (w), 1076 (w), 1031 (w), 1018 (w), 988 (m), 895 (s), 850 (m), 826 (m), 744 (m), 731 (m), 697 (s).
HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{19}H_{20}$, 249.1638; found, 249.1652.

19

1-(2-methylenehexyl)-4-(methylsulfonyl)benzene (19): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 4-(methylsulfonyl)benzyl chloride (1.00 mmol, 205 mg), 1-hexene (5 mmol, 621 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (20% EtOAc/Hex, R_f = 0.27) yielded **19** (202 mg, 80%, 98:2 ratio) as a clear, colorless liquid.

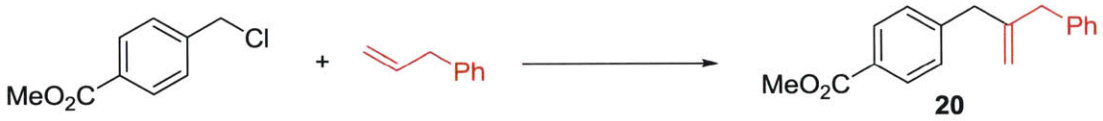
[6] In the absence of an inhibitor (such as 4-*t*-butylcatechol) compound **18** undergoes slow polymerization if stored neat at room temperature. However, compound **18** was stored for several weeks in the absence of inhibitor frozen in benzene at –30 °C with no polymerization observed.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.82 – 7.78 (m, 2H), 7.35 – 7.31 (m, 2H), 4.84 – 4.81 (m, 1H), 4.69 – 4.66 (m, *J* = 0.6 Hz, 1H), 3.36 (s, 2H), 3.00 (s, 3H), 1.93 – 1.87 (m, 2H), 1.41 – 1.32 (m, 2H), 1.27 – 1.18 (m, 2H), 0.82 (t, *J* = 7.3 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 147.70, 146.49, 129.84, 127.29, 112.06, 44.46, 42.71, 35.07, 29.61, 22.24, 13.89.

FT-IR (ATR, cm^{-1}): 3075 (w), 2958 (w), 2930 (w), 2861 (w), 1647 (w), 1596 (w), 1458 (w), 1438 (w), 1408 (w), 1303 (s), 1147 (s), 1089 (m), 1018 (w), 957 (m), 908 (m), 895 (m), 770 (m), 759 (s), 729 (s).

HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{14}H_{20}O_2S$, 253.1257; found, 253.1250.



20

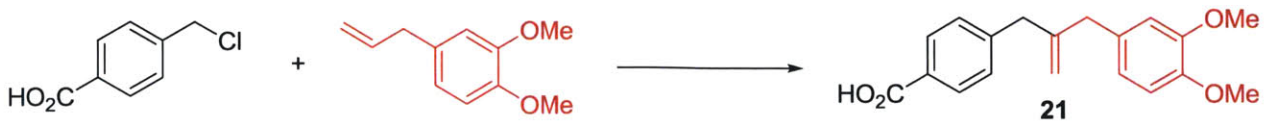
methyl 4-(2-benzylallyl)benzoate (20): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), methyl 4-(chloromethyl)benzoate (1.00 mmol, 185 mg), allylbenzene (5 mmol, 662 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (5% EtOAc/Hex, R_f = 0.33) yielded **20** (221 mg, 83%, 98:2 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.98 – 7.95 (m, 2H), 7.32 – 7.28 (m, 2H), 7.24 – 7.20 (m, 2H), 7.16 – 7.12 (m, 2H), 4.90 – 4.88 (m, 1H), 4.85 – 4.83 (m, 1H), 3.91 (s, 3H), 3.32 (s, 2H), 3.27 (s, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 167.19, 147.56, 145.11, 139.21, 129.76, 129.24, 129.14, 128.47, 128.25, 126.35, 114.12, 52.11, 42.37, 42.15.

FT-IR (ATR, cm^{-1}): 3064 (w), 3029 (w), 2952 (w), 2904 (w), 2842 (w), 1719 (s), 1647 (w), 1609 (m), 1576 (w), 1496 (w), 1453 (w), 1434 (m), 1415 (w), 1311 (w), 1274 (s), 1192 (m), 1177 (m), 1106 (s), 1076 (w), 1027 (w), 968 (w), 899 (m), 867 (w), 757 (s), 731 (s), 697 (s).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{18}H_{18}O_2$, 267.1380; found, 267.1366.



4-(2-(3,4-dimethoxybenzyl)allyl)benzoic acid (21): Following General Procedure B, a magnetic stir bar, 4-(chloromethyl)benzoic acid (1.00 mmol, 171 mg), methyl eugenol (5.00 mmol, 860 µL), Et_3N (8.00 mmol, 1115 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was cooled to 0 °C, after which TMSOTf (3.00 mmol, 543 µL) was added dropwise. After the addition was complete, the mixture was warmed to room temperature, precatalyst **1** (0.050 mmol, 36.7 mg) was added, the vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. After this time, water (1.5 mL) was added to the reaction mixture, which was then allowed to stir open to the air for 10 minutes. To this mixture was added 20 mL CH_2Cl_2 and 10 mL of 1 M HCl, the phases were separated, and the organic phase was collected. The aqueous layer was extracted twice more with CH_2Cl_2 and the combined organic extracts dried over Na_2SO_4. After concentration under reduced pressure, the crude material was purified by column chromatography on silica gel (EtOAc/CH_2Cl_2 gradient 0% to 20%, R_f = 0.48 in 100% EtOAc). The material obtained from the column was further purified by mixed solvent recrystallization from $CHCl_3$/hexanes to yield **21** (256 mg, 82%, >95:5 ratio) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 12.35 (br s, 1H), 8.08 – 8.02 (m, 2H), 7.28 – 7.24 (m, 3H), 6.81 (d, J = 8.1 Hz, 1H), 6.71 – 6.66 (m, 1H), 6.66 – 6.64 (m, 1H), 4.94 – 4.91 (m, 1H), 4.86 – 4.84 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.34 (s, 2H), 3.23 (s, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 172.06, 149.05, 147.73, 146.32, 131.76, 130.45, 129.44, 127.44, 121.23, 114.11, 112.35, 111.33, 56.08, 55.99, 42.21, 42.11.

FT-IR (ATR, cm^{-1}): 3066 (w), 3005 (w), 2971 (m), 2936 (m), 2906 (m), 2840 m br, 2673 (w), 2549 (w), 1684 (s), 1639 (m), 1607 (m), 1589 (m), 1576 (m), 1514 (s), 1462 (m), 1417 (s), 1343 (m), 1318 (s), 1283 (s), 1257 (s), 1231 (s), 1182 (s), 1149 (s), 1137 (s), 1126 (s), 1029 (s), 1020 (s), 934 (s), 895 (s), 858 (s), 804 (s), 749 (s), 703 (s).

HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{19}H_{20}O_4$, 313.1434; found, 313.1430.

22

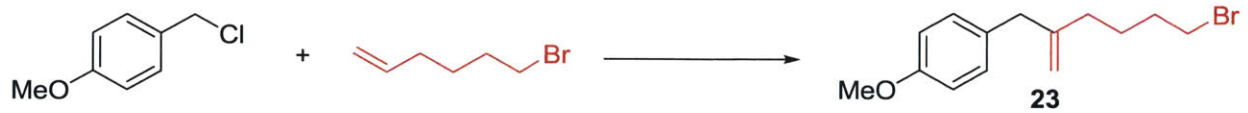
(2-(biphenyl-4-ylmethyl)allyloxy)triethylsilane (22): Following General Procedure B, a magnetic stir bar, 4-(chloromethyl)biphenyl (1.00 mmol, 203 mg), allyl alcohol (3 mmol, 204 μL), Et_3N (9.00 mmol, 1254 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was cooled to 0 °C, after which TESOTf (4.5 mmol, 1018 μL) was added dropwise. After the addition was complete, the mixture was warmed to room temperature, precatalyst **1** (0.050 mmol, 36.7 mg) was added, the vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. After this time, the reaction mixture was allowed to stir open to the air for 5 minutes, then passed through a 4 cm plug of silica gel (pre-wetted with dichloromethane). The silica gel plug was washed with 25 mL of dichloromethane followed by 25 mL of a 1:1 mixture of hexanes:ethyl acetate. After concentration under reduced pressure, the crude material was purified by column chromatography on silica gel (20% CH_2Cl_2/Hex, R_f = 0.26) to yield **22** (298 mg, 88%, >99:1 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.62 – 7.58 (m, 2H), 7.55 – 7.52 (m, 2H), 7.47 – 7.42 (m, 2H), 7.36 – 7.32 (m, 1H), 7.30 – 7.26 (m, 2H), 5.19 (t, J = 1.6 Hz, 1H), 4.89 (dq, J = 2.9, 1.3 Hz, 1H), 4.09 (s, 2H), 3.43 (s, 2H), 0.97 (td, J = 8.0, 1.1 Hz, 8H), 0.62 (qd, J = 8.0, 1.1 Hz, 6H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 147.94, 141.19, 139.17, 138.60, 129.50, 128.85, 127.18, 127.16, 127.13, 111.08, 65.20, 39.36, 6.94, 4.60.

FT-IR (ATR, cm^{-1}): 3061 (w), 3031 (w), 2954 (m), 2911 (w), 2878 (m), 1654 (w), 1600 (w), 1488 (m), 1458 (w), 1412 (w), 1238 (w), 1102 (m), 1076 (m), 1007 (m), 973 (w), 901 (m), 807 (m), 759 (s), 738 (s), 725 (s), 695 (s).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{22}H_{30}OSi$, 339.2139; found, 339.2140.



23

1-(6-bromo-2-methylenehexyl)-4-methoxybenzene (23): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 4-methoxybenzyl chloride (1.00 mmol, 136 μL), 6-bromo-1-hexene (5 mmol, 668 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane

(500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 6 hours. Following work-up according to the general procedure, silica gel chromatography (5% EtOAc/Hex, R_f = 0.42) yielded **23** (218 mg, 77%, 96:4 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, , δ): 7.12 – 7.08 (m, 2H), 6.86 – 6.82 (m, 2H), 4.83 – 4.80 (m, 1H), 4.78 – 4.75 (m, 1H), 3.80 (s, 2H), 3.39 (t, J = 6.8 Hz, 2H), 3.28 (s, 2H), 2.01 – 1.96 (m, 2H), 1.87 – 1.79 (m, 2H), 1.62 – 1.54 (m, 2H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ): 158.10, 148.72, 131.75, 129.98, 113.82, 111.41, 55.37, 42.15, 34.38, 33.96, 32.40, 26.10.

FT-IR (ATR, cm^{-1}): 3074 (w), 3005 (w), 2937 (w), 2909 (w), 2837 (w), 1645 (w), 1611 (w), 1583 (w), 1509 (s), 1464 (w), 1438 (m), 1300 (m), 1244 (s), 1175 (m), 1106 (w), 1037 (m), 895 (m), 846 (m), 807 (m), 755 (s), 733 (s), 679 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{14}H_{19}OBr$, 283.0692; found, 283.0702.

methyl 4-(2-(3-methoxy-4-(trimethylsilyloxy)benzyl)allyl)benzoate (24): Following General Procedure B, a magnetic stir bar, methyl (4-chloromethyl)benzoate (1.00 mmol, 185 mg), eugenol (3 mmol, 462 μL), Et_3N (9.00 mmol, 1254 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was cooled to 0 °C, after which TMSOTf (4.5 mmol, 814 μL) was added dropwise. After the addition was complete, the mixture was warmed to room temperature, precatalyst **1** (0.050 mmol, 36.7 mg) was added, the vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. After this time, the reaction mixture was allowed to stir open to the air for 5 minutes, then passed through a 4 cm plug of silica gel (pre-wetted with dichloromethane). The silica gel plug was washed with 25 mL of dichloromethane followed by 25 mL of a 1:1 mixture of hexanes:ethyl acetate. After concentration under reduced pressure, the crude material was purified by column

chromatography on silica gel (10% EtOAc/Hex, R_f = 0.37) to yield **24** (369 mg, 96%, >99:1 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.98 – 7.95 (m, 2H), 7.22 – 7.20 (m, 2H), 6.79 – 6.76 (m, 1H), 6.62 – 6.57 (m, 2H), 4.92 – 4.89 (m, 1H), 4.84 – 4.82 (m, 1H), 3.90 (s, 3H), 3.78 (s, 3H), 3.32 (s, 2H), 3.20 (s, 2H), 0.25 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 167.14, 150.71, 147.78, 145.21, 142.92, 132.71, 129.68, 129.21, 128.18, 121.29, 120.67, 113.85, 112.86, 55.51, 52.06, 42.12, 42.05, 0.39.

FT-IR (ATR, cm^{-1}): 2954 (w), 2906 (w), 2840 (w), 1721 (s), 1609 (w), 1510 (s), 1464 (w), 1449 (w), 1436 (m), 1415 (m), 1274 (s), 1249 (s), 1231 (s), 1190 (m), 1178 (m), 1154 (m), 1102 (s), 1039 (m), 1020 (m), 897 (s), 839 (s), 811 (s), 753 (s), 733 (m), 705 (m).

HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{22}H_{28}O_4$, 385.1830; found, 385.1835.

25

5-(biphenyl-4-ylmethyl)hex-5-en-1-amine (25): To an 8 mL screw-cap vial equipped with a magnetic stir bar was added 1-amino-5-hexene (3.00 mmol, 379 µL), Et_3N (12.00 mmol, 1673 µL), and CH_2Cl_2 (500 µL). The mixture was cooled to 0 °C, after which TMSOTf (6.00 mmol, 1086 µL) was added dropwise. After the addition was complete, the mixture was warmed to room temperature and a syringe and needle were used to withdraw the bottom layer of $Et_3N{\cdot}HOTf$. Next, 4-(chloromethyl)-biphenyl (1.00 mmol, 203 mg) and precatalyst **1** (0.050 mmol, 36.7 mg) were added to the mixture. A second portion of TMSOTf (2.00 mmol, 362 µL) was added, the vial was closed with a screw-cap, and the mixture was stirred at room temperature for 8 hours. After this time, water (1.5 mL) was added to the reaction mixture, which was then allowed to stir open to the air for 10 minutes. To this mixture was added 20 mL CH_2Cl_2 and 10 mL water, and the aqueous phase was basified with 3 M NaOH to adjust the pH >12. The phases were separated and the organic phase was collected. The aqueous layer was extracted twice more with CH_2Cl_2 and the combined organic extracts dried over Na_2SO_4. After concentration under reduced pressure, the crude material was purified by column chromatography on silica gel that had been pretreated with several column volumes of 1% Et_3N

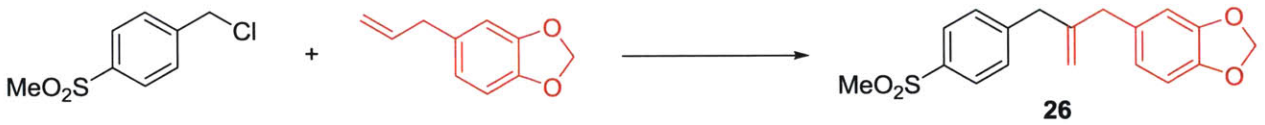
in CH_2Cl_2 ($MeOH/CH_2Cl_2$, 0% to 10% $MeOH/CH_2Cl_2$, R_f = 0.13 in 2% $MeOH/CH_2Cl_2$) to yield **25** (183 mg, 69%, >95:5 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.60 (dq, J = 7.1, 1.0 Hz, 2H), 7.56 – 7.52 (m, 2H), 7.46 – 7.42 (m, 2H), 7.34 (ddt, J = 8.5, 6.7, 1.2 Hz, 1H), 7.29 – 7.25 (m, 2H), 4.89 – 4.87 (m, 1H), 4.82 – 4.80 (m, 1H), 3.39 (s, 2H), 2.69 (td, J = 6.9, 0.7 Hz, 2H), 2.06 – 2.00 (m, 2H), 1.56 – 1.40 (m, 4H), 1.24 (s, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 148.81, 141.08, 139.04, 138.99, 129.46, 128.78, 127.12, 127.07, 127.05, 111.40, 42.71, 42.18, 35.28, 33.50, 24.94.

FT-IR (ATR, cm^{-1}): 3379 w br, 3079 (w), 3029 (w), 2928 (m), 2857 (w), 1645 (w), 1600 (w), 1561 (w), 1518 (w), 1486 (m), 1438 (w), 1408 (w), 1109 (w), 1076 (w), 1009 (m), 891 (m), 846 (m), 809 (m), 759 (s), 729 (s), 695 (s).

HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{19}H_{23}N$, 266.1903; found, 266.1898.



26

5-(2-(4-(methylsulfonyl)benzyl)allyl)benzo[*d*][1,3]dioxole (26): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 4-(methylsulfonyl)benzyl chloride (1.00 mmol, 205 mg), safrole (5 mmol, 741 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (30% EtOAc/Hex, R_f = 0.33) yielded **26** (221 mg, 67%, 99:1 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.84 – 7.79 (m, 2H), 7.31 – 7.27 (m, 2H), 6.67 (d, J = 7.9 Hz, 1H), 6.58 (d, J = 1.7 Hz, 1H), 6.53 (dt, J = 7.9, 1.1 Hz, 1H), 5.87 (s, 2H), 4.91 – 4.87 (m, 1H), 4.81 – 4.77 (m, 1H), 3.30 (s, 2H), 3.14 (s, 2H), 3.02 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ): 147.54, 146.95, 145.96, 145.91, 138.29, 132.45, 129.87, 127.24, 121.78, 114.32, 109.11, 107.96, 100.76, 44.35, 41.93, 41.59.

FT-IR (ATR, cm^{-1}): 3075 (w), 2902 (w), 1647 (w), 1596 (w), 1503 (m), 1488 (s), 1441 (m), 1408 (w), 1361 (w), 1303 (s), 1244 (s), 1186 (m), 1147 (s), 1089 (m), 1037 (s), 957 (m), 906 (s), 858 (m), 809 (m), 770 (m), 759 (s), 725 (s).

HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{18}H_{18}O_4$, 331.0999; found, 331.1000.

27

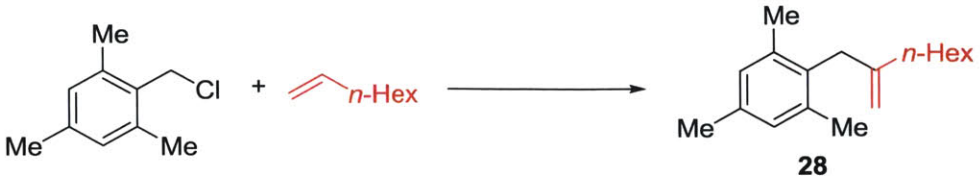
3-(5-bromo-2-methylenepentyl)benzo[*b*]thiophene (27): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 3-(chloromethyl)benzo[*b*]thiophene (1.00 mmol, 183 mg), 5-bromo-1-pentene (5 mmol, 592 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (20% CH_2Cl_2/Hex, R_f = 0.48) yielded **27** (231 mg, 78%, 94:6 ratio) as a yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.90 – 7.87 (m, 1H), 7.77 – 7.75 (m, 1H), 7.43 – 7.34 (m, 2H), 7.16 (td, J = 1.0, 0.4 Hz, 1H), 4.96 (tt, J = 1.3, 0.6 Hz, 1H), 4.91 (tq, J = 1.4, 0.7 Hz, 1H), 3.62 – 3.59 (m, 2H), 3.42 (t, J = 6.7 Hz, 2H), 2.26 – 2.21 (m, 2H), 2.08 – 2.01 (m, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 145.38, 140.62, 139.03, 133.77, 124.29, 123.96, 123.15, 122.94, 122.12, 112.67, 35.93, 34.04, 33.33, 30.85.

FT-IR (ATR, cm^{-1}): 3072 (w), 2932 (w), 2904 (w), 2844 (w), 1647 (w), 1458 (w), 1427 (m), 1359 (w), 1249 (m), 1205 (w), 1156 (w), 1076 (w), 1020 (w), 968 (w), 897 (m), 835 (m), 755 (s), 727 (s).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{14}H_{15}BrS$, 295.0151; found, 295.0164.



28

1,3,5-trimethyl-2-(2-methyleneoctyl)benzene (28): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 2,4,6-trimethylbenzyl chloride (1.00 mmol, 169 mg), 1-octene (5 mmol, 785 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 8 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.65) yielded **28** (100 mg, 41%, 96:4 ratio[7]) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 6.88 (s, 2H), 4.72 – 4.69 (m, 1H), 4.21 – 4.19 (m, 1H), 3.28 – 3.26 (m, 2H), 2.30 (s, 3H), 2.23 (s, 6H), 2.21 – 2.13 (m, 2H), 1.63 – 1.52 (m, 2H), 1.44 – 1.30 (m, 6H), 0.98 – 0.91 (m, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 147.21, 137.01, 135.30, 133.69, 128.69, 108.65, 37.64, 35.64, 31.98, 29.30, 28.16, 22.83, 21.02, 19.83, 14.28.

FT-IR (ATR, cm^{-1}): 2958 (m), 2926 (s), 2857 (m), 1645 (w), 1615 (w), 1484 (w), 1458 (m), 1445 (m), 1376 (w), 1031 (w), 1012 (w), 908 (m), 897 (m), 850 (m), 733 (s), 714 (w).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{18}H_{28}$, 245.2264; found, 245.2278.

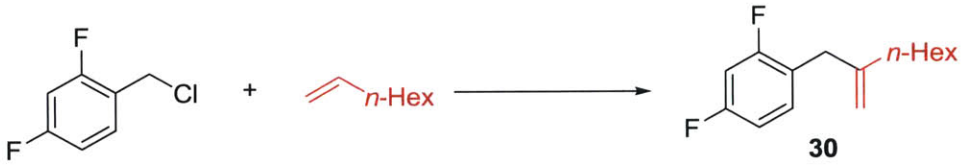
29

4-((6-chlorobenzo[*d*][1,3]dioxol-5-yl)methyl)pent-4-enyl 4-methylbenzenesulfonate (29): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 6-chloropiperonyl chloride (1.00 mmol, 205 mg), 4-pentenyl tosylate (3 mmol, 721 mg), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TESOTf (1.50 mmol, 339 µL) was added in

[7] The ratio of isomers was 78:22 prior to column chromatography. In this particular instance, the linear and branched products were separable by column chromatography.

one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (20% EtOAc/Hex, R_f = 0.37) yielded **29** (213 mg, 52%, >95:5 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.79 – 7.75 (m, 2H), 7.35 – 7.31 (m, 2H), 6.79 (s, 1H), 6.60 (s, 1H), 5.94 (s, 2H), 4.74 – 4.72 (m, 1H), 4.60 – 4.57 (m, 1H), 4.02 (t, J = 6.4 Hz, 2H), 3.26 (s, 2H), 2.43 (s, 3H), 2.06 – 1.98 (m, 2H), 1.86 – 1.75 (m, 2H).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 146.80, 146.74, 145.63, 144.80, 133.10, 129.90, 129.87, 127.93, 125.70, 112.26, 110.22, 109.72, 101.70, 70.05, 39.56, 31.39, 26.86, 21.69.
FT-IR (ATR, cm^{-1}): 2958 (w), 2902 (w), 1598 (w), 1505 (m), 1477 (s), 1358 (m), 1231 (m), 1190 (m), 1175 (s), 1117 (m), 1098 (m), 1037 (m), 973 (m), 929 (s), 910 (s), 835 (m), 813 (m), 751 (s), 731 (s), 690 (m), 662 (s).
HRMS (ESI, *m/z*): $[M + NH_4]^+$ calcd for $C_{20}H_{21}O_5ClS$, 426.1136; found, 426.1123.



30

2,4-difluoro-1-(2-methyleneoctyl)benzene (30): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.50 mmol, 367 mg), 2,4-difluorobenzyl chloride (10.0 mmol, 1.63 g), 1-octene (50 mmol, 7.85 mL), Et_3N (60 mmol, 8.36 mL), and dichloromethane (5 mL) were added to a 25 mL round-bottom flask. The flask was fitted with a rubber septum and an argon inlet and the mixture was stirred for 5 minutes, after which TMSOTf (15.0 mmol, 2.71 mL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 4 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.67) yielded **30** (2.12 g, 89%, 97:3 ratio) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.17 – 7.11 (m, 1H), 6.84 – 6.76 (m, 2H), 4.85 – 4.82 (m, 1H), 4.67 – 4.64 (m, 1H), 3.32 (s, 2H), 2.03 – 1.98 (m, 2H), 1.50 – 1.42 (m, 2H), 1.35 – 1.25 (m, 6H), 0.92 – 0.87 (m, 3H).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, δ): 161.74 (dd, J = 246.5, 11.8 Hz), 161.17 (dd, J = 247.8, 11.7 Hz), 147.85, 131.79 (dd, J = 9.4, 6.3 Hz), 122.74 (dd, J = 16.2, 3.8 Hz), 111.16, 111.03 (dd, J = 20.9, 3.8 Hz), 103.68 (dd, J = 26.4, 25.1 Hz), 35.88, 34.91 (d, J = 2.4 Hz), 31.94, 29.19, 27.79, 22.82, 14.21.

FT-IR (ATR, cm^{-1}): 2958 (w), 2930 (m), 2859 (w), 1647 (w), 1619 (m), 1604 (m), 1505 (s), 1460 (w), 1438 (w), 1428 (m), 1277 (m), 1262 (m), 1137 (s), 1089 (m), 970 (s), 895 (m), 848 (s), 826 (w), 791 (m), 733 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{15}H_{20}F_2$, 239.1606; found, 239.1606.

31

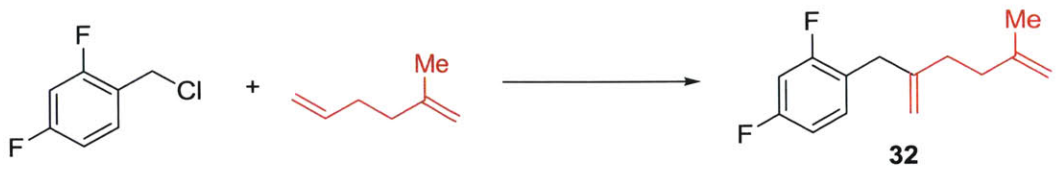
1-(6-chloro-2-methylenehexyl)naphthalene (31): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 1-(chloromethyl)naphthalene (1.00 mmol, 177 mg), 6-chloro-1-hexene (5 mmol, 662 μL), Et_3N (6.00 mmol, 836 μL), and dichloromethane (500 μL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 μL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 6 hours. Following work-up according to the general procedure, silica gel chromatography (CH_2Cl_2/hexanes gradient 0% to 20%, R_f = 0.59 in 20% CH_2Cl_2/hex) yielded **31** (233 mg, 90%, 83:17 ratio) as a clear, colorless liquid.

^1H NMR (500 MHz, $CDCl_3$, δ): 8.06 – 8.01 (m, 1H), 7.91 – 7.86 (m, 1H), 7.81 – 7.76 (m, 1H), 7.56 – 7.48 (m, 2H), 7.45 (dd, J = 8.2, 7.0 Hz, 1H), 7.37 (ddt, J = 7.0, 1.3, 0.7 Hz, 1H), 4.93 – 4.90 (m, 1H), 4.68 – 4.66 (m, 1H), 3.83 (s, 2H), 3.57 (t, J = 6.6 Hz, 2H), 2.17 – 2.10 (m, 2H), 1.86 – 1.78 (m, 2H), 1.75 – 1.67 (m, 2H).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, δ): 147.84, 135.66, 133.95, 132.51, 128.73, 127.43, 127.15, 125.85, 125.59, 125.59, 124.41, 112.02, 45.11, 40.04, 35.49, 32.29, 25.03.

FT-IR (ATR, cm^{-1}): 3068 (w), 3046 (w), 2939 (w), 2865 (w), 1647 (w), 1596 (w), 1509 (w), 1443 (w), 1397 (w), 1300 (w), 1262 (w), 1218 (w), 1165 (w), 1078 (w), 1016 (w), 893 (m), 791 (s), 776 (s), 731 (m).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{17}H_{19}Cl$, 259.1248; found, 259.1254.



32

2,4-difluoro-1-(5-methyl-2-methylenehex-5-enyl)benzene (32): Following General Procedure A, a magnetic stir bar, precatalyst **1** (0.050 mmol, 36.7 mg), 2,4-difluorobenzyl chloride (1.00 mmol, 163 mg), 2-methyl-1,5-hexadiene (5 mmol, 675 µL), Et_3N (6.00 mmol, 836 µL), and dichloromethane (500 µL) were added to an 8 mL screw-cap vial. The mixture was stirred for ca. 10 seconds, after which TMSOTf (1.50 mmol, 271 µL) was added in one portion. The vial was closed with a screw-cap and the mixture was stirred at room temperature for 6 hours. Following work-up according to the general procedure, silica gel chromatography (pentane, R_f = 0.51) yielded **32** (136 mg, 61%, 96:4 ratio) as a clear, colorless liquid. This product contained an impurity of oligomerized 2-methyl-1,5-hexadiene (ca. 10% by mass) that could not be separated by column chromatography.

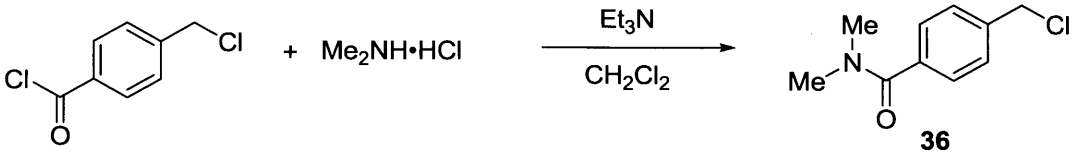
^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.17 – 7.09 (m, 1H), 6.85 – 6.72 (m, 2H), 4.87 – 4.84 (m, 1H), 4.74 – 4.71 (m, 1H), 4.70 – 4.67 (m, 2H), 3.34 (s, 2H), 2.16 (qd, J = 7.4, 3.9 Hz, 4H), 1.72 (dd, J = 1.5, 0.8 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 161.71 (dd, J = 246.5, 11.8 Hz), 161.10 (dd, J = 247.8, 11.7 Hz), 147.34 (app t, J = 0.9 Hz), 145.52, 131.80 (dd, J = 9.4, 6.2 Hz), 122.53 (dd, J = 16.2, 3.8 Hz), 111.43, 111.10 (dd, J = 21.0, 3.8 Hz), 110.24, 103.74 (dd, J = 26.4, 25.1 Hz), 36.07, 34.97 (d, J = 2.4 Hz), 33.94, 22.55.

FT-IR (ATR, cm^{-1}): 3079 (w), 2934 (w), 2859 (w), 1649 (w), 1619 (m), 1604 (m), 1503 (s), 1440 (m), 1427 (m), 1374 (w), 1277 (m), 1262 (m), 1136 (s), 1091 (m), 966 (s), 889 (s), 848 (s), 792 (m), 731 (w).

HRMS (DART, *m/z*): $[M + H]^+$ calcd for $C_{14}H_{16}F_2$, 223.1293; found, 223.1311.

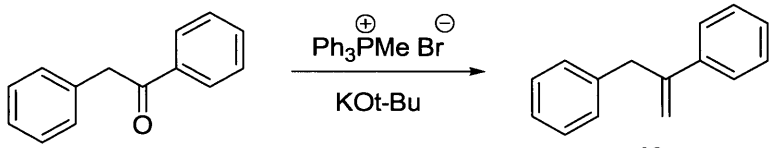
Synthesis of Substrates and Authentic Samples



36

4-(chloromethyl)-*N*,*N*-dimethylbenzamide (36):[8] To an oven-dried, 100 mL round-bottom flask equipped with a magnetic stir bar was added 4-(chloromethyl)benzoyl chloride (20 mmol, 3.78 g) and $Me_2NH \cdot HCl$ (25 mmol, 2.04 g). Dichloromethane (50 mL) was added, the flask was fitted with a rubber septum and attached to an argon line. The mixture was cooled to 0 °C with an ice bath and Et_3N (60 mmol, 8.36 mL) was added dropwise over the course of 20 minutes. The reaction mixture was allowed to warm to room temperature and stirred for another 1 hour, after which the organic phase was washed twice with water and once with brine. The organic phase was dried over Na_2SO_4, concentrated in vacuo, and purified by column chromatography on silica gel (80:15:5 EtOAc:Hex:MeOH, R_f in 80% EtOAc/Hex = 0.36) to yield **36** (3.57g, 90%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.42 (app s, 4H), 4.60 (s, 2H), 3.11 (br s, 3H), 2.98 (br s, 3H).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 171.01, 138.80, 136.42, 128.59, 127.54, 45.68, 39.60, 35.38.
HRMS (ESI, *m/z*): $[M + H]^+$ calcd for $C_{10}H_{13}ClNO$, 198.0680; found, 198.0672.



40

prop-2-ene-1,2-diyldibenzene (40): In an oven-dried, 100 mL, 2-necked round-bottom flask equipped with a magnetic stir bar was added KO*t*-Bu (10 mmol, 1.12 g). A reflux condenser was fitted to one neck of the flask and a rubber septum to the other. The apparatus was purged with dry argon for several minutes, after which 25 mL of THF were added. The septum was removed

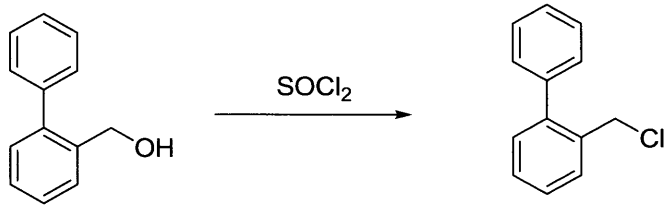
[8] **36** was prepared according to a modified procedure based on that reported in Ray, N. C.; Bull, R. J.; Finch, H.; Van den Heuvel, M.; Bravo, J. A. Oxazole and Thiazole Derivatives and their Uses. Int. Pat. Appl. WO 2008/096093, 2008.

and methyltriphenylphosphonium bromide (12 mmol, 4.29 g) was added portion-wise through the second neck of the flask (against a flow of argon) causing immediate formation of an intensely colored, yellow slurry. After complete addition of the methyltriphenylphosphonium bromide, the rubber septum was replaced and the reaction heated to 60 °C. A solution of 2-phenylacetophenone (11 mmol, 2.16 g) in 10 mL of THF was added dropwise via syringe. The reaction mixture was held at 60 °C until the yellow color faded, indicating complete consumption of the phosphorane. The reaction mixture was cooled to room temperature and the solvent removed under reduced pressure, after which the reaction mixture was triturated with pentane (25 mL) for 10 minutes. The slurry was filtered through a pad of diatomaceous earth and the residue washed with a few milliliters of pentane. Concentration of the filtrate followed by column chromatography on silica gel (pentane, R_f = 0.30) yielded the product **40** as a clear, colorless liquid (1.73 g, 89%).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.53 (dq, J = 7.3, 1.2 Hz, 2H), 7.41 – 7.29 (m, 7H), 7.29 – 7.24 (m, 1H), 5.59 (ddd, J = 2.0, 1.2, 0.6 Hz, 1H), 5.11 (dt, J = 2.4, 1.2 Hz, 1H), 3.92 (t, J = 1.4 Hz, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 146.93, 140.79, 139.54, 129.00, 128.42, 128.32, 127.52, 126.17, 114.62, 41.66.

The ^{1}H and ^{13}C NMR spectra are in agreement with those previously reported in the literature.[9]



S1

2-(chloromethyl)biphenyl (S1): To an oven-dried, 50 mL round-bottom flask equipped with a magnetic stir bar was added 2-biphenylmethanol (5.23 mmol, 1.00 g). The flask was fitted with a rubber septum, an argon inlet, and 20 mL of CH_2Cl_2 were added, which yielded a slightly heterogeneous mixture. After cooling this mixture to 0 °C, the argon inlet was replaced with a connection to a mineral oil bubbler, and $SOCl_2$ (10 mmol, 0.73 mL) was added dropwise over

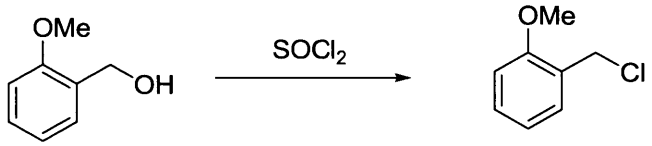
[9] Alacid, E. and Nájera, C. *Org. Lett.* **2008**, *10*, 5011–5014.

the course of 20 minutes, causing the solution to become homogeneous. The solution was allowed to warm to room temperature and stirred for an additional 3 hours, after which the mixture was quenched by the cautious addition of 1 M aqueous $NaHCO_3$, washed once with saturated aqueous $NaHCO_3$, once with water, and once with brine. After drying the organic phase over Na_2SO_4 and evaporation under reduced pressure, the crude product mixture was purified by column chromatography on silica gel (5% EtOAc/Hex, R_f = 0.30) to yield the product **S1** (0.871g, 82%) as a clear, colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.66 – 7.62 (m, 1H), 7.56 – 7.50 (m, 4H), 7.50 – 7.43 (m, 3H), 7.40 – 7.36 (m, 1H), 4.62 (s, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 142.13, 140.23, 134.98, 130.61, 130.41, 129.22, 128.61, 128.39, 128.02, 127.54, 44.56.

The ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[10]



S2

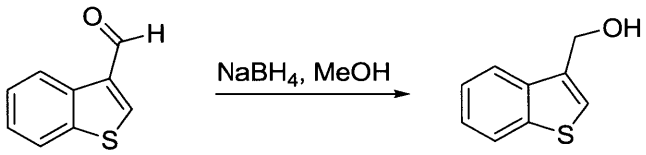
1-(chloromethyl)-2-methoxybenzene (S2): Following the same procedure used for **S1**, 2-methoxybenzyl alcohol (7.24 mmol, 0.962 mL) was added to an oven-dried, 50 mL round-bottom flask equipped with a magnetic stir bar and rubber septum. Dichloromethane (25 mL) was added, the mixture was cooled to 0 °C, the argon inlet replaced with a connection to a mineral oil bubbler, and $SOCl_2$ (15 mmol, 1.09 mL) was added dropwise over the course of 20 minutes. The mixture was allowed to warm to room temperature and stirred for an additional 3 hours, after which the mixture was quenched by the cautious addition of 1 M aqueous $NaHCO_3$, washed once with saturated aqueous $NaHCO_3$, once with water, and once with brine. After drying the organic phase over Na_2SO_4 and evaporation under reduced pressure, the crude product mixture was purified by column chromatography on silica gel (5% EtOAc/Hex, R_f = 0.19) to yield the product **S3** (0.779g, 69%) as a clear, colorless liquid.

[10] Savarin, C. and Liebeskind, L. S. *Org. Lett.* **2001**, *3*, 2149–2152.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.36 (ddt, J = 7.5, 1.7, 0.4 Hz, 1H), 7.34 – 7.30 (m, 1H), 6.95 (td, J = 7.5, 1.1 Hz, 1H), 6.92 – 6.89 (m, 1H), 4.67 (s, 2H), 3.89 (s, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 157.38, 130.59, 130.13, 125.78, 120.65, 110.81, 55.55, 41.70.

The ^{1}H and ^{13}C NMR spectra are consistent with those previously reported in the literature.[11]



S3

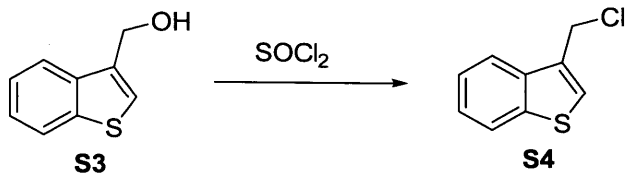
benzo[b]thiophen-3-ylmethanol (S3): Thiophene-3-carboxaldehdye (6.17 mmol, 1.00 g) was added to a 50 mL round-bottom flask equipped with a magnetic stir bar. Methanol (15 mL) was added, the mixture stirred for several minutes to dissolve the aldehyde, and then $NaBH_4$ (6.17 mmol, 0.228 g) was added in several portions over the course of 20 minutes. Stirring was continued until the reaction was determined to be complete by TLC (CH_2Cl_2, R_f of starting aldehyde = 0.72, R_f of **S3** = 0.29), which was ca. 30 minutes after beginning the addition of $NaBH_4$. The reaction mixture was quenched by careful addition of water (10 mL), after which the mixture was extracted 3x with CH_2Cl_2, and the combined organic extracts dried over Na_2SO_4. After concentration in vacuo, the crude product was purified by column chromatography on silica gel (100% CH_2Cl_2) to afford **S4** (0.86 g, 85%) as a pale yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.89 – 7.84 (m, 2H), 7.43 – 7.35 (m, 3H), 4.93 – 4.91 (m, 2H), 1.91 (br s, 1H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 140.89, 137.77, 136.07, 124.70, 124.33, 123.94, 123.00, 122.05, 59.90.

The ^{1}H and ^{13}C NMR spectra are in agreement with those previously reported in the literature.[12]

[11] Amin, S.; Hecht, S. S.; Hoffman, D. *J. Org. Chem.* **1981**, *46*, 2394–2398.
[12] Paul, N. M.; Taylor, M.; Kumar, R.; Deschamps, J. R.; Luedtke, R. R.; Newman, A. H. *J. Med. Chem.* **2008**, *51*, 6095–6109.



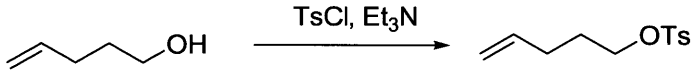
S3 S4

3-(chloromethyl)benzo[*b*]thiophene (S4): Following the same procedure as **S2**, benzo[*b*]thiophen-3-ylmethanol **(S3)** (5.23 mmol, 0.86 g) was dissolved into 15 mL of CH_2Cl_2 in 50 a mL, oven-dried, round-bottom flask. The flask was fitted with a rubber septum, a connection to a mineral oil bubbler, and cooled to 0 °C, after which $SOCl_2$ (8.4 mmol, 0.613 mL) was added dropwise over 20 minutes. The mixture was allowed to warm to room temperature and stirred for an additional 3 hours, after which the mixture was quenched by the cautious addition of 1 M aqueous $NaHCO_3$, washed once with saturated aqueous $NaHCO_3$, once with water, and once with brine. After drying of the organic phase over Na_2SO_4 and evaporation under reduced pressure, the crude product mixture was purified by column chromatography on silica gel (50% Hex/CH_2Cl_2, R_f = 0.70) to yield the product **S4** (0.634g, 66%) as a pale yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.94 – 7.89 (m, 2H), 7.51 – 7.40 (m, 3H), 4.87 (d, J = 0.7 Hz, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 140.62, 137.32, 131.97, 126.39, 124.91, 124.53, 123.05, 122.01, 39.68.

The ^{1}H and ^{13}C NMR spectra are in agreement with those previously reported in the literature.[12]



S5

pent-4-enyl 4-methylbenzenesulfonate (S5): To a dry, 100 mL round-bottom flask equipped with a magnetic stir bar was added TsCl (15 mmol, 2.85 g) and 4-DMAP (1 mmol, 0.122 g). The flask was sealed with a rubber septum and connected to an argon inlet. Dichloromethane (35 mL) and triethylamine (20 mmol, 2.79 mL) were added via syringe and the flask was cooled to 0 °C with an ice bath, after which 4-penten-1-ol (12.48 mmol, 1.29 mL) was added dropwise via syringe. The mixture was allowed to warm to room temperature and stirring was continued for an additional 1 hour. The reaction mixture was quenched by the slow addition of water (25 mL), the

phases were separated and the organic phase was washed once with saturated aqueous ammonium chloride, once with water, and once with brine. After drying of the organic phase over Na_2SO_4 and concentration under reduced pressure, the crude reaction product was purified by column chromatography on silica gel (80% CH_2Cl_2/Hex, R_f in CH_2Cl_2 = 0.81) to yield **S5** as a clear, colorless liquid (2.85 g, 95%).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.76 – 7.70 (m, 2H), 7.30 (ddt, J = 8.0, 1.3, 0.9 Hz, 2H), 5.69 – 5.59 (m, 1H), 4.93 – 4.86 (m, 2H), 3.98 (t, J = 6.4 Hz, 2H), 2.39 (s, 3H), 2.03 (dtt, J = 7.8, 6.6, 1.4 Hz, 2H), 1.68 (dtd, J = 8.4, 6.7, 5.4 Hz, 2H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 144.71, 136.54, 132.96, 129.79, 127.75, 115.72, 69.78, 29.27, 27.86, 21.51.

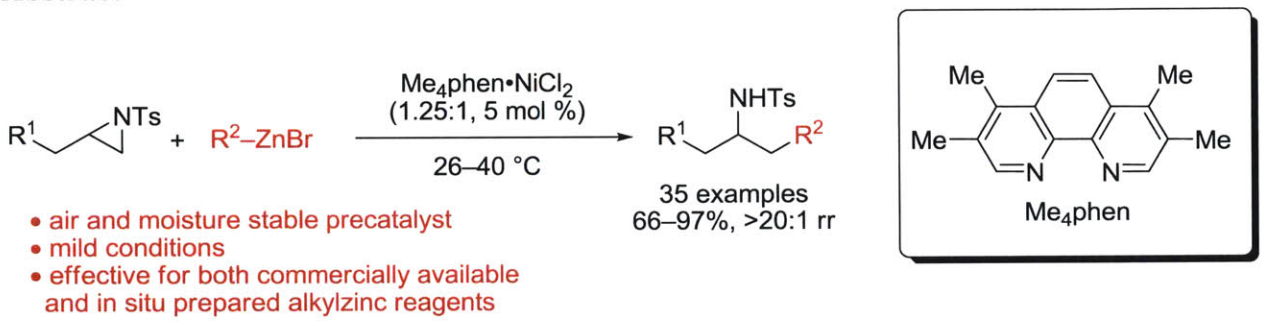
The ^{1}H and ^{13}C NMR spectra are in agreement with those previously reported in the literature.[13]

[13] Stokes, B. J.; Opra, S. M.; Sigman, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 11408–11411.

Chapter 3

Ring-Opening, Negishi-type Cross-Coupling of 2-Substituted *N*-Tosylaziridines with Alkylzinc Halides

Abstract



The nickel-catalyzed cross-coupling of aliphatic *N*-tosylaziridines with aliphatic organozinc reagents is described. The reaction protocol displays complete regioselectivity for reaction at the less hindered C–N bond, and the products are furnished in good to excellent yield for a broad selection of substrates. An air-stable nickel(II) chloride/ligand precatalyst was also developed and employed for the reaction. In addition to increasing the activity of this catalyst system, this also greatly improves the practicality of this reaction, as the use of the very air-sensitive $Ni(cod)_2$ is avoided. Finally, mechanistic investigations, including deuterium-labeling studies, show that the reaction proceeds with overall inversion of configuration at the terminal position of the aziridine by way of aziridine ring opening by Ni (inversion), transmetallation (retention), and reductive elimination (retention).

Introduction

The transition-metal-catalyzed activation of alkyl halides has attracted enormous attention over the past decade, wherein palladium, nickel, and copper in particular have proven to be exceptionally effective catalysts for many diverse transformations,[1] particularly for $C(sp^3)$–$C(sp^3)$ bond-forming reactions.[2] Nevertheless, the vast majority of cross-coupling reactions utilize carbon–halogen or carbon–OSO_2R electrophiles; those involving oxidative addition into a C–N bond of the electrophile have received much less attention.[3] The C–N bond, while generally weaker than the corresponding C–O bond, is less polarized and therefore generally less prone to undergo oxidative insertion by a metal.

The aziridine functionality represents a versatile building block in contemporary synthetic chemistry. Like other three-membered heterocycles such as epoxides, aziridines possess significant ring strain that renders them susceptible to nucleophilic ring opening. In many cases, these ring-opening reactions proceed with high regioselectivity, and various carbon- and heteroatom-based nucleophiles have been investigated over the past several years. In particular, the addition of organocuprates has proven to be an efficient strategy for C–C bond-forming reactions with aziridines.[4]

The oxidative addition of transition metals into aziridines to form azametallacycle intermediates can also be effected under mild conditions.[5] For instance, 2-arylaziridines have been shown to undergo facile ring-expanding carbonylation reactions to form β-lactams under rhodium catalysis.[6] This transformation proceeds with high selectivity for insertion into the benzylic C–N bond. Notably, however, simple alkylaziridines proved unreactive under these conditions.[7]

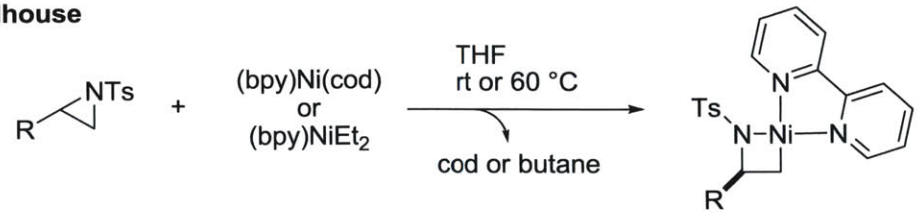
In 2002, Hillhouse demonstrated that aliphatic *N*-sulfonylaziridines could undergo oxidative insertion of nickel to form stable, isolable azanickelacyclobutane complexes (Scheme 1a).[8,9] Interestingly, the oxidative insertion occurred with complete regioselectivity for insertion into the less substituted aziridine C–N bond. Investigations using a deuterium-labeled aziridine provided clear evidence for an S_N2-type mechanism. A few years later, the Wolfe group reported the stoichiometric insertion of palladium into the terminal position of aliphatic aziridines containing a tethered olefin.[10] Based on the relationship between tether length and reactivity, it was postulated that the alkene was functioning as a directing group, the presence of which was critical for successful insertion. Only after changing the electronic nature of the aziridine, by

employing the more strongly activating nosyl group, did it in one instance prove possible to promote the oxidative insertion without the use of the alkene directing group.

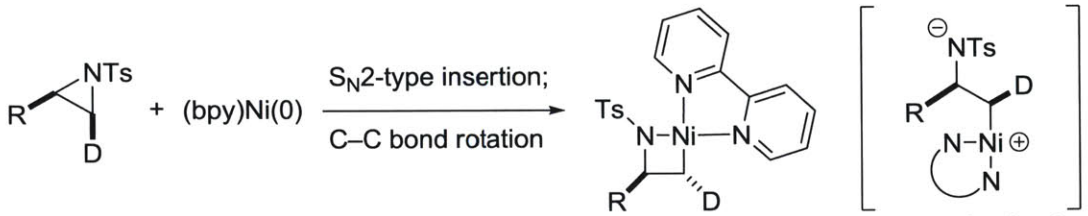
Although these pioneering contributions showed great promise for the development of catalytic activation of aziridines in direct cross-coupling reactions, the first catalytic coupling reaction remained elusive for another decade. In 2012, the first direct cross-coupling reaction was reported by Doyle and coworkers. In this report, it was shown that nickel can catalyze the addition of alkylzinc halides to styrene-derived *N*-tosylaziridines (Scheme 1b).[11] The reaction proceeds with complete regioselectivity in which the weaker, benzylic C–N bond is broken.[12] Notably, it was found necessary to use the electron-deficient alkene dimethyl fumarate as a π-accepting ligand to induce reductive elimination and prevent β-hydride elimination.[13] Shortly thereafter, the Doyle group demonstrated that the reaction sequence could be extended to include aliphatic aziridines (Scheme 1c), which were unreactive under the previously-developed conditions.[14] The activation of these challenging substrates was elegantly achieved by changing the *N*-sulfonyl group from tosyl to cinsyl (Cn), which contains an electron deficient alkene in the *ortho* position of the arylsulfonyl group. By using this protecting group, the cross-coupling products were obtained in moderate to good yields with C–C bond formation on the least substituted side being favored, though in only moderate regioselectivity (up to 80:20). The majority of the scope focused on arylzinc reagents; however, a few aliphatic examples were also given. The newly designed cinsyl group is likely to serve a dual purpose in this transformation by acting as a directing group for the oxidative insertion into the aziridine and by inducing reductive elimination in analogy to dimethyl fumarate employed in the protocol for 2-arylaziridines. Interestingly, in contrast to the stoichiometric studies by Hillhouse[8] and Wolfe,[10a] when a deuterium-labeled aziridine was subjected to the reaction conditions, a mixture of diastereomers, arising from epimerization at the terminal position, was obtained. This is indicative of a single-electron transfer (SET) mechanism or an S_N2-type activation followed by Ni–C bond homolysis.

Scheme 1. Existing Methods of Activating and Cross-Coupling Aziridines

(1) Hillhouse



R = H, Me, *n*-Bu, *i*-Pr
50–70%



hypothesized intermediate

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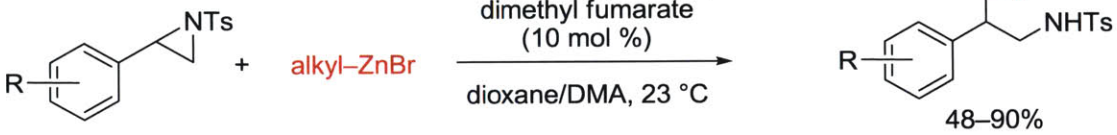
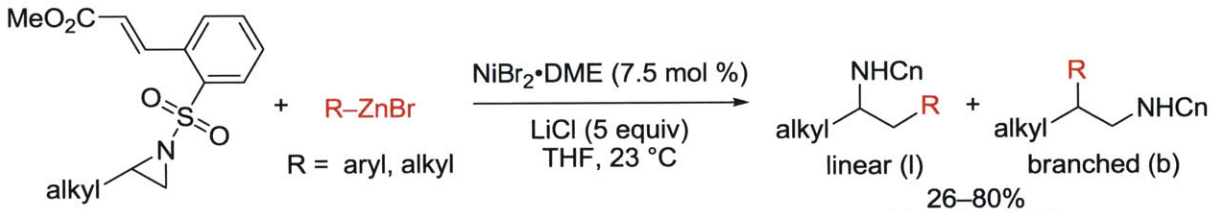
(2) Doyle 2012:



48–90%

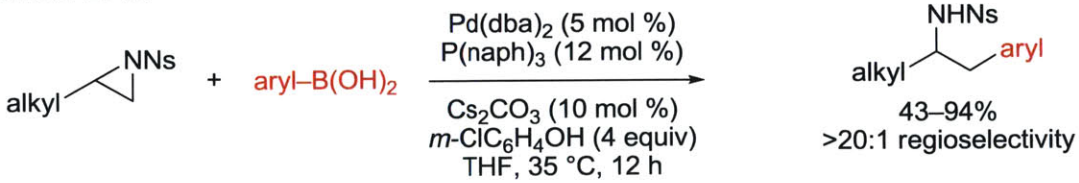
(3) Doyle 2013:



linear (l) branched (b)

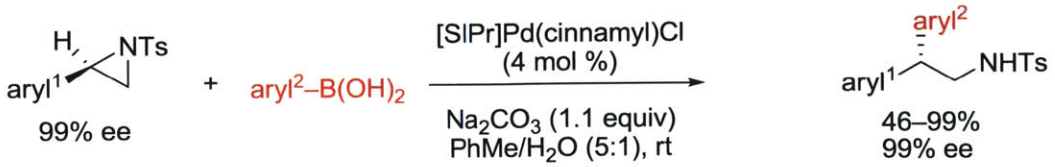
26–80%
l:b = 2.5–4.9:1

(4) Michael 2013:



43–94%
>20:1 regioselectivity

(5) Minakata 2014:



99% ee

46–99%
99% ee

Soon thereafter, Michael and coworkers reported a highly efficient, palladium-catalyzed cross-coupling of aliphatic *N*-nosylaziridines with arylboronic acids (Scheme 1d).[15] The transformation proceeds with complete regioselectivity for the terminal position, and the products are obtained in good yields. The addition of *m*-chlorophenol was found to be critical in order to promote transmetallation and to prevent a detrimental β-hydride elimination pathway. Through a deuterium-labeling study, the reaction was shown to proceed with complete inversion of configuration, which is consistent with the observations previously made on the stoichiometric systems. More recently, Minakata and co-workers demonstrated a stereo- and regiospecific palladium-catalyzed coupling of 2-arylaziridines and arylboronic acids.[16] Through the use of a Pd/NHC catalyst system, the C–N bond activation occurs at the more substituted position with excellent specificity for stereochemical inversion. Interestingly, the enantiopurity is maintained through the reaction, enabling the synthesis of tertiary stereogenic centers with high enantiopurity (Scheme 1e).

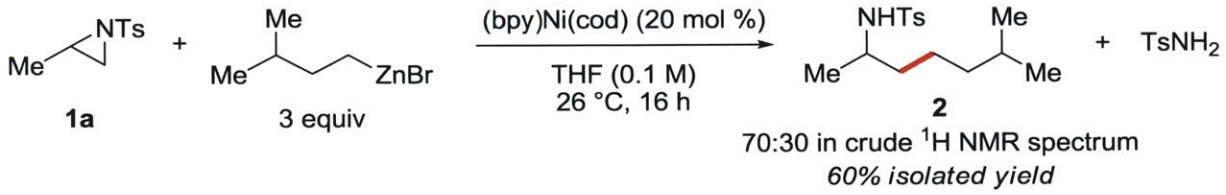
While all of the above-mentioned protocols provide access to a wide variety of sulfonamide products arising from different combinations of aziridines and coupling partners (aziridine/nucleophile: aryl/alkyl, alkyl/aryl, alkyl/alkyl, aryl/aryl), no C–C bond-forming reaction of unactivated aliphatic aziridines and aliphatic coupling partners that provides complete regioselectivity has been reported to date. Therefore, we decided to study the nickel-catalyzed cross-coupling of aliphatic *N*-tosylaziridines with aliphatic organozinc reagents (Scheme 1f).[17] The reaction protocol developed through these studies displays complete regioselectivity for addition to the terminal position of the aziridine, and the sulfonamide products are furnished in good to excellent yield for a broad selection of substrates. Moreover, we have developed an air-stable nickel(II) chloride/ligand precatalyst that can be handled and stored outside a glovebox. This greatly improves the practicality of this reaction, as the use of the very air-sensitive $Ni(cod)_2$ can be avoided. Finally, mechanistic studies, including deuterium-labeling studies to determine the stereochemical course of the reaction, were performed.

Preliminary Investigation

We initiated our studies by examining the reaction of methyl-substituted aziridine **1a** using the bipyridine Ni(0) complex employed in the stoichiometric studies by Hillhouse.[8,18] In terms of the organometallic coupling partner, organozinc reagents were chosen as they generally

display high stability and improved functional group compatibility.[19] Furthermore, a number of organozinc reagents are commercially available as THF solutions (nominally 0.5 M), and we therefore began our studies using these reagents. Employing 20 mol % of (bpy)Ni(cod)$_2$ provided the cross-coupled product **2** as a single regioisomer in 60% isolated yield (Scheme 2). Analysis of the crude reaction mixture after workup showed that the product was formed in a 70:30 ratio to $TsNH_2$, and essentially no other organic products were observed by NMR and GC/MS.

Scheme 2. Initial Successful Conditions



This byproduct plausibly arises from β-hydride abstraction and later hydrolysis of the resulting imine.[20] Reducing the catalyst loading to 10 mol % resulted in similar product distribution and yield; however, the time required for full consumption of the aziridine was significantly increased to 44 h.

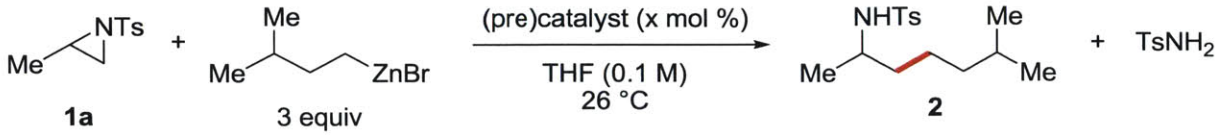
Investigation of Alternative Nickel Sources and Reaction Optimization

In order to improve the practicality of the procedure and avoid the use of Ni(cod)$_2$, we decided to develop a precatalyst system that could tolerate air and atmospheric moisture.[21,22] Furthermore, studies by Hillhouse on the synthesis of azanickelacyclobutanes had demonstrated that a cod-free Ni(0) system underwent insertion into the aziridine at a faster rate than when cod was present. This improved reactivity has also been demonstrated in a number of other instances. Consequently, we desired to identify a cod-free nickel precatalyst system for this transformation. Attempts to use $NiCl_2$•DME as the nickel source led to only low conversion, even after prolonged reaction times, and therefore, a different nickel source was required.

It is well-established that the combination of bpy- or phen-derived ligands with nickel(II) salts in aqueous or ethanolic solutions can yield nickel–ligand adducts.[23] Initial investigations with adducts of bpy and phen, nominally (bpy)$NiCl_2$ and (phen)$NiCl_2$, respectively, showed them to be competent precatalysts (Table 1). A brief optimization showed the best outcome was

obtained when 5 mol % of (phen)$NiCl_2$ was employed, conditions which cleanly yielded the desired product in a 72:28 ratio of product to $TsNH_2$ with a 63% isolated yield.

Table 1. Preliminary Examination of Alterative Nickel Sources[a]

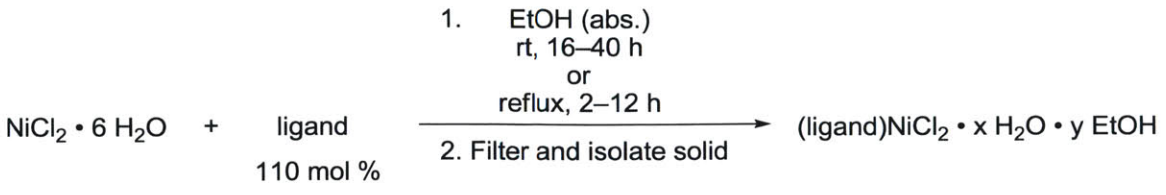


	(pre)catalyst	mol %	conversion	time (h)	2 : $TsNH_2$	yield (%)
1	(bpy)Ni(cod)	20	full	16	70:30	60
2	L + $NiCl_2$•DME	10	24	16	–[b]	–[c]
3	(bpy)$NiCl_2$	10	~65%[b]	16	–[b]	–[c]
4	(bpy)$NiCl_2$	10	full	40	70:30	–[c]
5	(phen)$NiCl_2$	10	full	15	72:28	62
6	(phen)$NiCl_2$	5	full	17	72:28	63

[a]Reactions were carried out on 0.25 mmol scale. Conversion and P:$TsNH_2$ ratio were determined by ^{1}H NMR analysis of the crude reaction mixture. [b]Conversion and ratio could not be accurately determined due to signals from the starting material overlapping with the product in the ^{1}H NMR. [c] isolated yield not determined.

Encouraged by these results, we set out to test substituted bpy and phen derivatives in an effort to obtain a further improvement to the outcome of the reaction. We synthesized a library of roughly 15 different diimine-nickel complexes (by the method shown in Scheme 3) suitable for use as precatalysts.

Scheme 3. Synthesis of Diimine/Nickel Precatalysts[a]



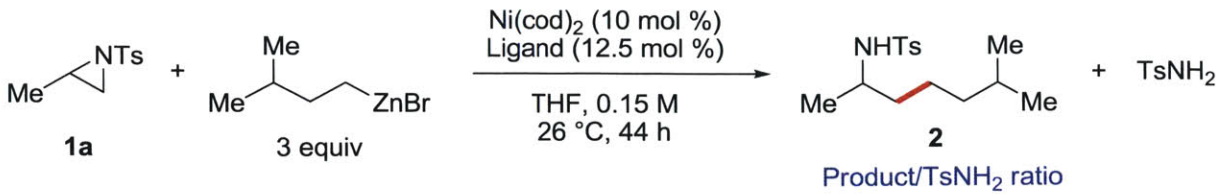
[a]Complexes synthesized by this method (as adopted from various literature protocols) contained indeterminate amounts of both water and ethanol. Elemental analyses were carried out to attempt to ascertain the exact values of x and y. See Experimental Section for full details.

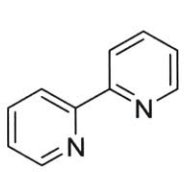
This investigation showed that ligands with substitution *ortho* to the donor nitrogen atoms performed significantly worse than all other substitution patterns; 3,4,7,8-tetramethyl-1,10-phenanthroline (Me_4phen) provided the best results, however, no further meaningful relationships between the substitution pattern on the ligand and the outcome of the reaction could be discerned. Troublingly, however, inconsistent results were obtained when using precatalysts prepared at different times or with only slight variation in the method of preparation, which therefore cast doubt on the veracity of the results obtained from this screen.

Consequently, the ligand screen was carried out with $Ni(cod)_2$ as the nickel source, despite our desire to avoid its use (Scheme 4). Changing the 2,2′-bipyridine (bpy) ligand to the more electron-rich 4,4′-dimethoxy-2,2′-bipyridine provided an increase in product ratio (75:25), but the reaction was less clean and a trace of halide-opened aziridine was observed.[24] Employing 1,10-phenanthroline (phen) as the ligand did not increase the yield, but the reaction was faster and considerably cleaner. Further screening of phenanthroline derivatives identified 3,4,7,8-tetramethyl-1,10-phenanthroline (Me_4phen) as the best ligand, improving the ratio to 82:18 and an isolated yield of 70%.

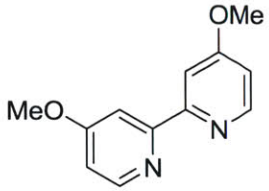
At this point, we returned to the nickel(II) precatalysts derived from Me_4phen (and other ligands) to try to make sense of the results we had previously obtained and hopefully to be able to devise a suitable air-stable precatalyst. A search of the literature initially yielded no illuminating information relating to these inconsistencies: the procedures reported for the synthesis of (bpy)$NiCl_2$ were straightforward and seemingly robust—the minor variations in synthetic approaches reported appeared to all yield roughly equivalent results. Ultimately, after an extensive investigation of all of the precatalysts by elemental analysis, the reasons for the erratic outcomes became clear: the compositions of the complexes were, in most cases, nowhere near the expected (ideal) 1:1 ratio of ligand to nickel. In many cases there was considerably more ligand present that expected—in some cases as much as 2:1 ligand to nickel (the complete details of these analyses are provided in the Experimental Section). Our caution with regard to the veracity of the screening results with these precatalysts had therefore been warranted, since the stoichiometry was not equivalent for all of the ligands tested.

Scheme 4. Ligand Screen using $Ni(cod)_2$ as the Nickel Source[a]

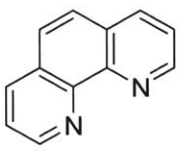




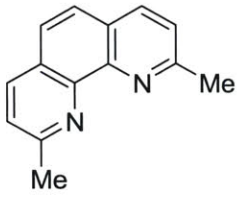
>95% conv.
67:33[b]



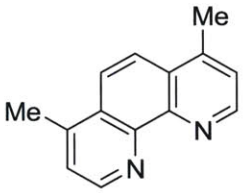
>95% conv.
75:25[b]



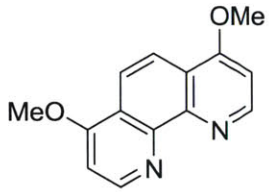
>95% conv.
69:31



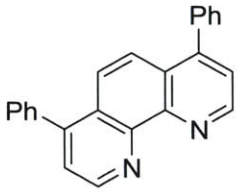
<30% conv.
not determined



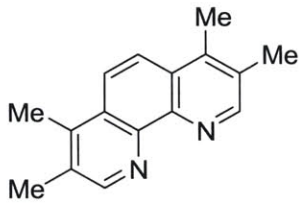
>95% conv.
71:29



>95% conv.
71:29



>95% conv.
78:22



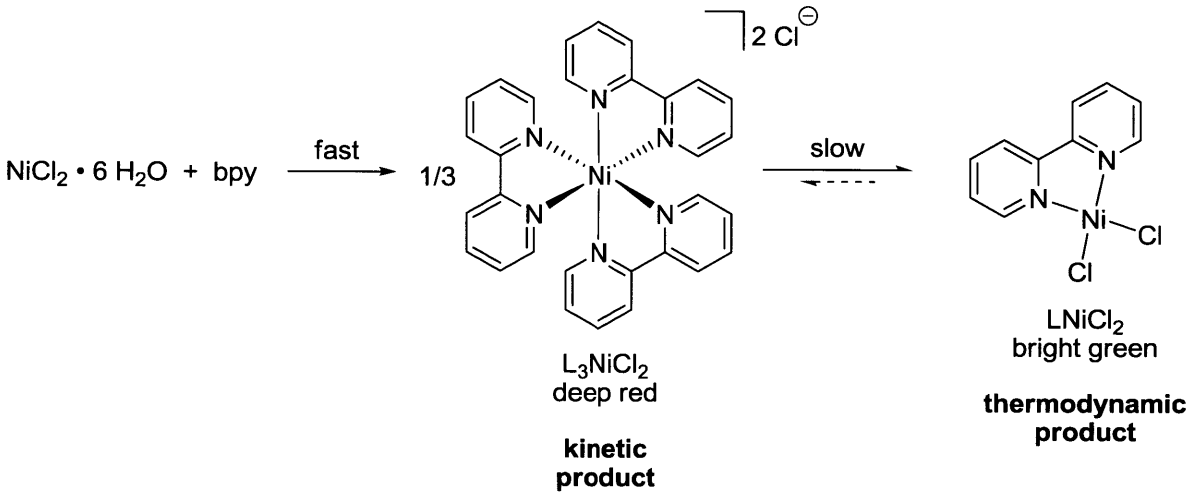
>95% conv.
82:18
(70% isolated yield)

[a]Reactions were carried out on 0.25 mmol scale. Conversion and P:$TsNH_2$ ratio were determined by ^1H NMR analysis of the crude reaction mixture. Isolated yields were not determined except in the case of Me_4phen, which provided the most promising result of the screen. [b]Side-products (halide-opening of the aziridine) were produced which overlap with the diagnostic signals in the ^1H NMR. The presence of these species precludes exact determination of conversion and ratio.

Identification of the nature of the discrepancies regarding these complexes, unfortunately, did not in and of itself provide a solution to this issue, however. A more thorough investigation of the early literature on the preparation of bpy and phen complexes of divalent transition metals revealed the underlying cause for variation between ligands: nickel(II) readily combines with diimine ligands to provide adducts which vary in stoichiometry from between 1–3 ligands per nickel, which also vary in their hydration states. Additionally, the most thermodynamically stable ratio can vary with the identity of the ligand. For instance, the combination of bpy and $NiCl_2 \cdot 6H_2O$ in ethanol initially yields a metastable complex of the structure $(bpy)_3NiCl_2 \cdot xH_2O$ (in which x can be up to 10), even when the ligand and nickel sources are mixed in a 1:1

ratio.[23a,b] If the reaction is stopped at this point, the 3:1 complex is isolated and the remainder of the Ni is removed during the isolation. Upon extended reaction time at ambient temperature or upon heating, a complex of the nominal composition (bpy)$NiCl_2$•xH_2O is subsequently formed, where x is normally equal to one (Scheme 5). The temperature and time required for the conversion to the 1:1 complex varies *and* this is an equilibrium process, meaning it may not be possible to get exclusively a 1:1 complex.

Scheme 5. Simplified Reaction Scheme for Interaction of $NiCl_2$•$6H_2O$ with bpy[a]



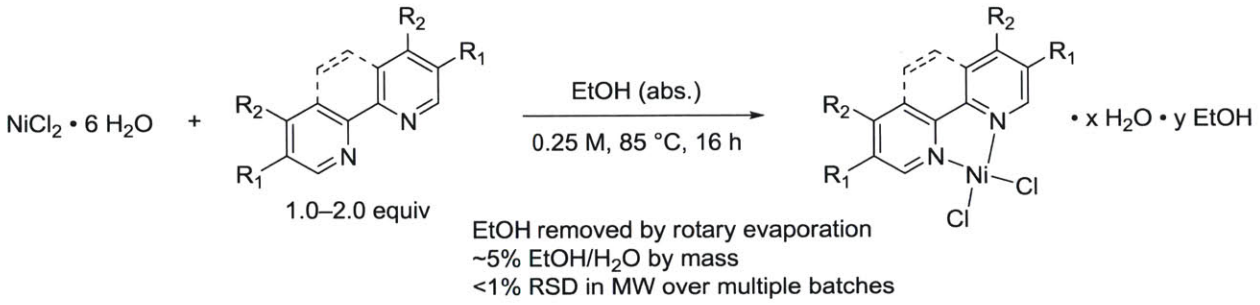
[a]$NiCl_2$•$6H_2O$ exists as $(H_2O)_4NiCl_2$•$2H_2O$, where the geometry at nickel is octahedral, the two chloride ligands are *trans* to each other, and the remaining two water molecules bridge between the aqua ligands. Because of this, this scheme neglects a considerable number of putative intermediates that exist between $NiCl_2$•$6H_2O$ and $(bpy)_3NiCl_2$ and that exist between $(bpy)_3NiCl_2$ and $(bpy)NiCl_2$.

Precatalysts prepared at ambient and at elevated temperatures gave vastly different outcomes for the catalytic coupling reaction. As established through elemental analyses, an excess of ligand caused a beneficial outcome, whereas an excess of nickel was significantly detrimental to the reaction, regardless of the identity of the ligand.

Despite significant efforts, a clean 1:1 complex of Ni(II) and Me_4phen could never be obtained: samples synthesized at room temperature contained a 2:1 L:Ni ratio, but samples prepared at elevated temperatures contained a 2:3 ratio, wherein there was excess of nickel. When the latter complex was used as the precatalyst in the reaction, the reaction did not proceed past even 50% conversion. To neutralize these differences, a different approach for the precatalyst synthesis was devised. Rather than isolating the precatalyst as a solid by filtration

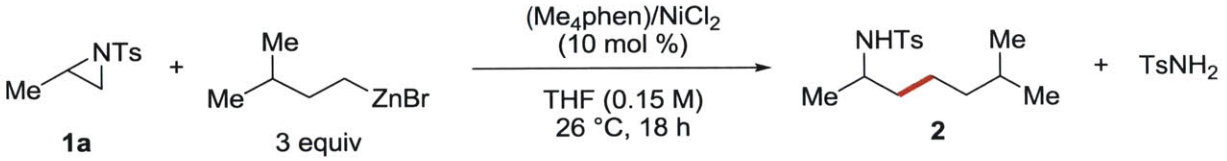
from the ethanol solution in which it is heated, the solvent was simply removed with a rotary evaporator, yielding a solid with a precisely known ratio of ligand to nickel, although the exact connectivity was unknown (Scheme 6). A series of precatalysts with varying ratios of ligand (Me_4phen) to nickel were synthesized and evaluated in the coupling reaction.

Scheme 6. Revised Synthetic Approach for Generation of $LNiCl_2$ Precatalysts



In general, all of the precatalysts functioned well, furnishing the coupled product **2** in good yield (Table 2). The ratio of product to $TsNH_2$ generally improved with increasing amounts of ligand. However, the best result in terms of isolated yield versus amount of ligand employed was provided by the precatalyst containing 1.25 equiv of ligand to nickel, furnishing the product in 79% yield.

Table 2. Evaluation of Excess Ligand on Coupling Reaction[a]

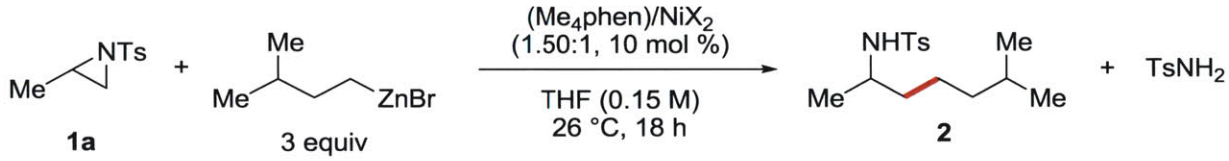


	L : Ni	2 : $TsNH_2$	yield (%)
1	1.00 : 1	80:20	77
2	1.25 : 1	82:18	79
3	1.50 : 1	84:16	80
4	1.75 : 1	86:14	–[b]
5	2.00 : 1	86:14	–[b]

[a]Precatalysts were synthesized according to the procedure outlined in Scheme 6. Reactions were carried out on 0.25 mmol scale. Ratio of P:$TsNH_2$ was determined by ^1H NMR analysis of the crude reaction mixture. All reactions achieved complete conversion in the allotted time. [b]isolated yield was not determined.

The effect of the counterion was also investigated. A series of six precatalysts were synthesized (according to the method described above in Scheme 6) incorporating six different counterions at a ratio of 1.50:1 ligand/nickel. These precatalysts were tested in the coupling reaction, the results of which are described in Table 3. Generally, no significant differences were observed, although the BF_4^- ion appeared to promote the halide-opening of the aziridine, leading to a poor reaction outcome. Given the wide availability of $NiCl_2 \cdot 6H_2O$, coupled with its slightly higher yield than other nickel sources, we selected it for further trials.

Table 3. Effect of Counterion Identity on Coupling Reaction[a]



	nickel source	2 : $TsNH_2$
1	$NiCl_2 \cdot 6H_2O$	84:16
2	$NiBr_2 \cdot 3H_2O$	82:18
3	$Ni(OAc)_2 \cdot 4H_2O$	82:18
4	$Ni(NO_3)_2 \cdot 6H_2O$	80:20
5	$NiSO_4 \cdot 6H_2O$	82:18
6	$Ni(BF_4)_2 \cdot 6H_2O$	–[b]

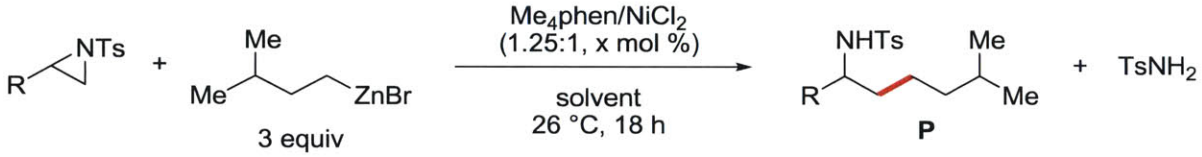
[a]Precatalysts were synthesized according to the procedure outlined in Scheme 6. Reactions were carried out on 0.50 mmol scale. Ratio of P:$TsNH_2$ was determined by ^1H NMR analysis of the crude reaction mixture. All reactions achieved complete conversion in the allotted time. [b]due to the presence of halide-opened products, ratio could not be accurately determined.

Having finally completed the ligand optimization and having also devised a reliable synthesis of a precatalyst incorporating this ligand, we began the evaluation of substituted aziridines. However, the reactions of aziridines with longer and more complex substituents turned out to work less well, often providing incomplete conversion and significant amounts of $TsNH_2$. For instance, when 2-(chlorobutyl)-*N*-tosylaziridine was tested, the product was obtained

in a yield of 67% along with significant amounts of $TsNH_2$. Consequently, we decided to study the effect of solvent additives, concentration, and changes to the catalyst loading (Table 4) in an effort to improve the outcome across variously substituted aziridines.

Adding CH_2Cl_2 to the reaction had a beneficial effect on the outcome, providing the product in 84% yield. Unfortunately, however, a byproduct derived from the organozinc reagent (3-methyl-1-butanol), which proved challenging to separate from the product, was also formed. The formation of this byproduct was prevented by employing 1,2-dichloroethane (DCE) as an additive, resulting in a yield of 77%.[25] The last improvement was achieved by lowering the catalyst loading to 5 mol %, which provided the product in 88% yield. Gratifyingly, these new conditions were also applicable to the initially tested 2-methylaziridine, affording **2** in 85% yield.

Table 4. Evaluation of Solvent, Concentration, and Catalyst Loading[a]



	R	catalyst mol %	solvent	conc. (M)	yield[b] (%)
1	$Cl(CH_2)_4$	10	THF	0.150	67
2	$Cl(CH_2)_4$	10	THF/CH_2Cl_2 (3:1)	0.125	84
3	$Cl(CH_2)_4$	10	THF/DCE (3:2)	0.125	66
4	$Cl(CH_2)_4$	10	THF/DCE (3:2)	0.100	77
5	$Cl(CH_2)_4$	5	THF/DCE (3:2)	0.100	88
6	Me	5	THF/DCE (3:2)	0.100	85

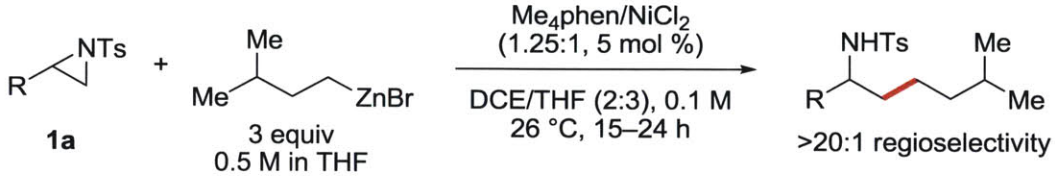
[a]Precatalysts were synthesized according to the procedure outlined in Scheme 6. Reactions were carried out on 0.25 mmol scale. Ratio of P:$TsNH_2$ was determined by ^1H NMR analysis of the crude reaction mixture. All reactions achieved complete conversion in the allotted time. [b]isolated yield of pure material obtained after purification by column chromatography.

Reaction Scope

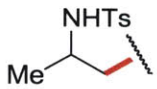
The optimized conditions were first evaluated by varying the aziridine component. As demonstrated in Scheme 7, the reaction worked well for a wide variety of aziridines.[26] Linear

and branched aliphatic substituents all provided the products **3**–**6** in good to excellent yields (66–96%). The α-branched cyclohexyl substrate required a slightly elevated temperature to allow the reaction to reach completion. Substituents containing additional functional groups were also well-tolerated, including an alkyl chloride (**7**), ester (**8**), and a phthalimide-protected amine (**9**).

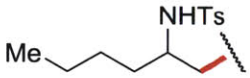
Scheme 7. Reaction Scope of Aziridines[a]



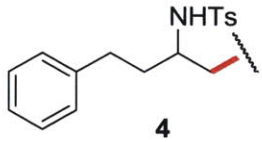
alkyl-substituted



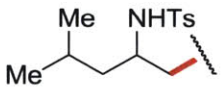
2
86% yield



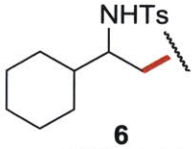
3
96% yield



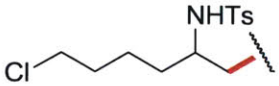
4
94% yield



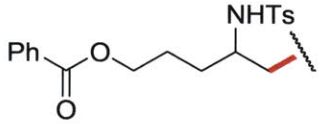
5
89% yield



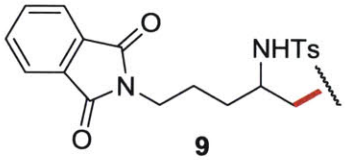
6
66% yield
(35 °C)



7
90% yield

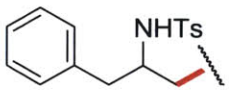


8
85% yield

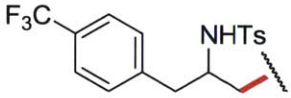


9
69% yield
(40 °C)

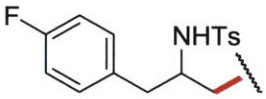
benzyl-substituted



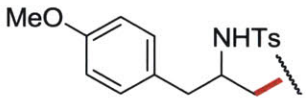
10
97% yield



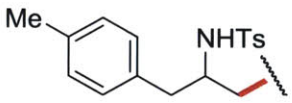
11
84% yield



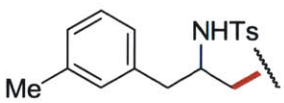
12
96% yield



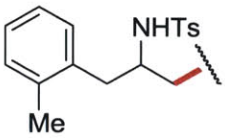
13
97% yield



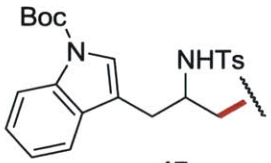
14
97% yield



15
95% yield



16
96% yield



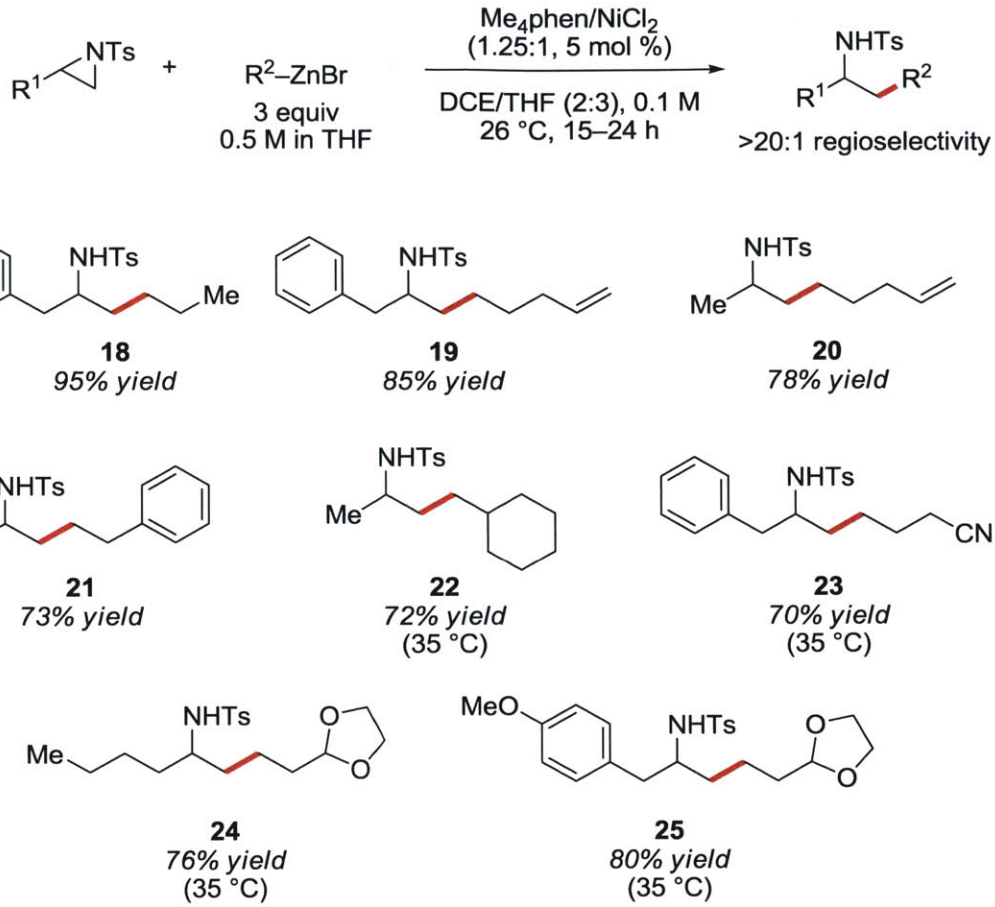
17
93% yield

[a]All reactions were carried out on 0.5 mmol scale. Yield reported is of isolated material that has been purified by column chromatography and that is completely free of residual solvent.

Investigation of 2-benzyl aziridines was of high priority, as the resulting products complement the motif obtained by the previously published methods that use arylzinc reagents or arylboronic acids as coupling partners.[14,15] Fortuitously, the benzyl-substituted aziridines turned out to work especially well, furnishing the products in excellent yields (84–97%). In general, the outcome seemed to be unaffected by both the electronic properties and the substitution pattern of the aromatic ring. Both electron-withdrawing (**11** and **12**) and electron-donating (**13**–**16**) substituents were tolerated, and the substitution pattern did not affect the outcome. An indole-containing substrate also worked well, affording the product **17** in 93% yield. This particular substrate was also evaluated without the *N*-Boc protecting group; however, this did not lead to the formation of any of the desired coupling product.

Next, a number of organozinc reagents were evaluated (Scheme 8).[27] The reaction worked well for both alkene- and arene-containing organozinc reagents, furnishing the products **19**–**21** in good yields (73–85%). Interestingly, the use of 2-phenethylzinc bromide led to the formation of a significant amount of styrene when the Me_4phen ligand system was employed. By replacing Me_4phen with phen, the formation of styrene was largely suppressed and a considerably cleaner reaction outcome was obtained. The more sterically hindered cyclohexylmethylzinc bromide also underwent cross-coupling to furnish the product **22** in 72% yield. As with the cyclohexylaziridine, a slightly higher temperature was required. Importantly, the reaction proved tolerant of a nitrile-containing organozinc reagent, furnishing the product **23** in 70% yield. This was particularly pleasing, since the nitrile group is quite versatile and can serve as entry to ketones and amines. Notably, the reaction did not proceed when cyanoethylzinc bromide was used. Instead, polymerization of the reaction mixture was observed, presumably due to the rapid formation of acrylonitrile through β-hydride elimination. Finally, an acetal-containing organozinc reagent was evaluated. The products were obtained with high yields (76 and 80%) for both an aliphatic and benzylic aziridine (**24** and **25**).

Scheme 8. Reaction Scope of Commercially Available Organozinc Reagents[a]

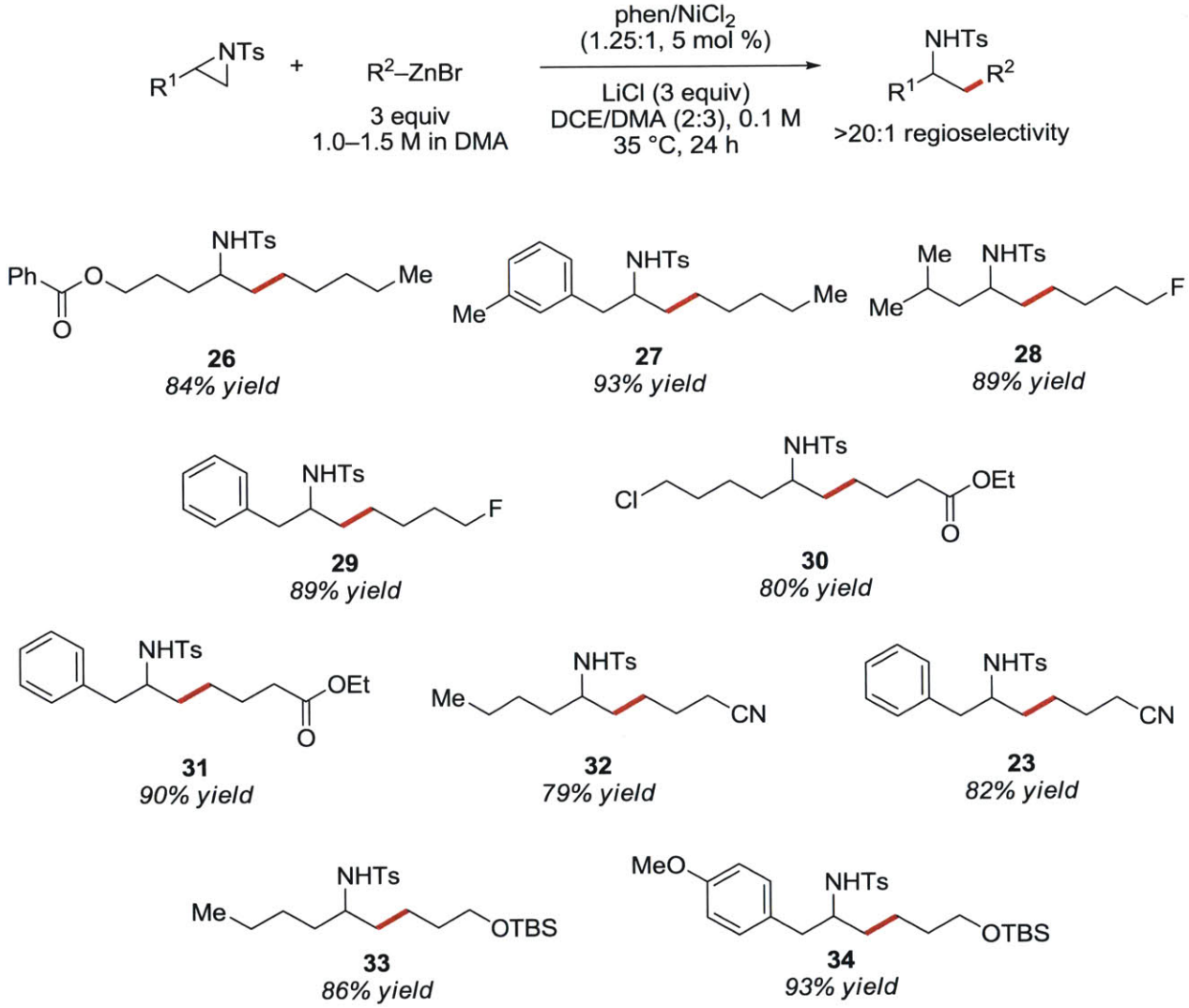


[a]All reactions were carried out on 0.5 mmol scale. Yield reported is of isolated material that has been purified by column chromatography and is completely free of residual solvent.

As a final improvement of the developed cross-coupling reaction, we decided to expand the reaction protocol to include the use of more easily accessible organozinc reagents made in DMA,[28] without the use of highly activated (Rieke-type) zinc.[29] Initial attempts to use these reagents showed an almost complete lack of reactivity, suggesting that DMA could be an unsuitable solvent for this transformation. However, when the reaction of a commercially purchased organozinc reagent in THF was spiked with DMA, the outcome was not significantly altered. It is well known that lithium halides can combine with organozinc reagents to form lithium organozincate adducts of the structure $RZnX_2^- Li^+$.[30] These zincates generally display improved nucleophilicity over standard organozinc reagents of the type RZnX. This fact led us to suspect that the commercially available alkylzinc halide reagents, made from Rieke zinc, may

contain trace amounts of lithium halide salts. Indeed, after a short evaluation of reaction parameters, we found that the addition of LiCl was critical to the reactivity of the organozinc reagents in DMA. In the absence of added LiCl, the transmetallation did not occur at an adequate rate to allow the coupling reaction to proceed.

Scheme 9. Reaction Scope of Non-Commercially Available Organozinc Reagents[a]



[a]All reactions were carried out on 0.5 mmol scale. Yield reported is of isolated material that has been purified by column chromatography and is completely free of residual solvent.

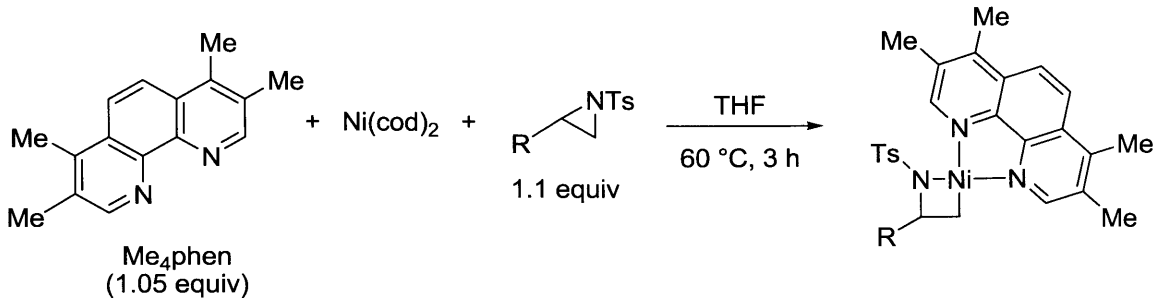
As before, a number of alkylzinc reagents worked well in combination with a variety of aziridines (Scheme 9). Both a linear aliphatic and a fluoride-containing reagent furnished the

products (**26**–**29**) in good to excellent yields (84–93%). An ester was also tolerated, and the products were formed in high yields (80–90%) for both an aliphatic and a benzylic aziridine (**30** and **31**). Cyanopropylzinc bromide turned out to work better in DMA than in THF, providing the products (**23** and **32**) in high yields (79–82%). Lastly, a TBS-protected alcohol was evaluated, which furnished the products (**33** and **34**) in high yields (86–93%). It should be noted that the reactivity in DMA is generally diminished compared to the THF system—in some instances, reactions employing Me_4phen did not reach completion, even upon extended reaction or under modified conditions. Consequently, the precatalyst derived from 1,10-phenanthroline was employed for the majority of the reactions.

Mechanistic Investigations

After having demonstrated that the protocol worked well with a broad selection of substrates, we decided to study the reaction in more detail to attempt to elucidate the mechanism. Doyle and co-workers have recently described that the azametallacycle formed from styrene-derived aziridines and (bpy)Ni(cod) did not work well in their coupling reaction.[11] Only with the addition of dimethyl fumarate were they able to obtain the coupling product, which was formed in a low yield (18%). Consequently, we were interested in determining whether the azanickelacyclobutane complexes first described by Hillhouse are involved in the present reaction and, if so, whether the oxidative insertion of nickel occurs with stereochemical inversion as was the case in Hillhouse's work. Moreover, we wanted to determine the overall stereochemical course at the terminal carbon in the cross-coupling reaction sequence through deuterium-labeling studies. We commenced our studies by synthesizing the necessary azanickelacyclobutane complexes. Following a protocol similar to that described by Hillhouse,[8] two complexes **35** and **36** were synthesized in excellent yields (86–96%) starting from Me_4phen and $Ni(cod)_2$ (Scheme 10). The complexes are poorly soluble in THF, allowing their isolation by precipitation from the reaction mixture. Complex **35** was characterized by single-crystal X-ray diffraction, which confirmed its composition and connectivity to be directly analogous to the corresponding complex containing bpy instead of Me_4phen. Unfortunately, the quality of the crystal analyzed was not superb, and so the structure was not of suitable quality to allow reliable analysis of bond distances and angles.

Scheme 10. Synthesis of Azanickelacyclobutanes



R = Me **35** *96% yield*

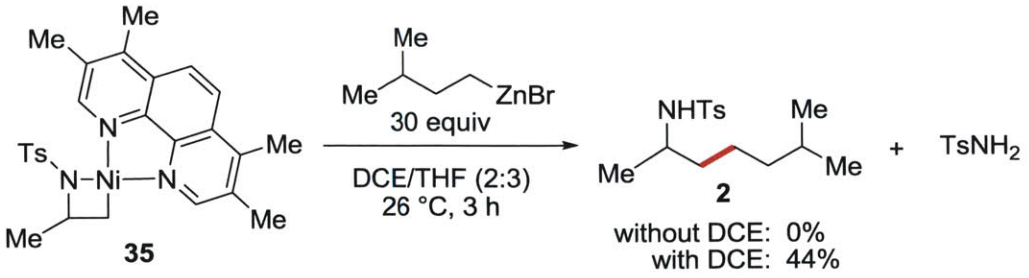
R = PMB **36** *86% yield*

In both cases, only the regioisomer derived from oxidative insertion of nickel into the terminal C–N bond was formed. During the synthesis of these complexes, we observed a significant difference in the rate of oxidative insertion depending on the aziridine substituent. For instance, both the PMB- and methylaziridines reacted much faster than the corresponding hexyl-substituted aziridine (not shown). Whereas the insertion occurred at ambient temperature for the two former, an elevated temperature (60 °C) was found to be necessary for the latter case.

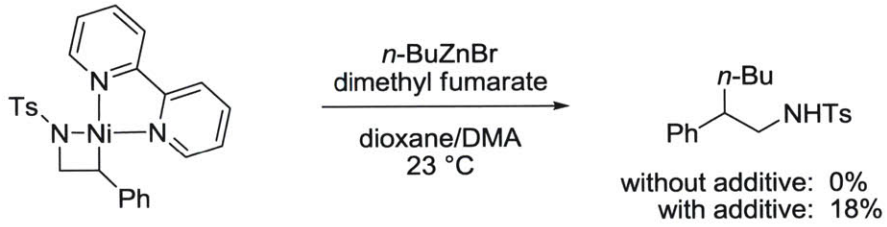
With these complexes in hand, we then studied their ability to undergo transmetallation with the organozinc reagent (Scheme 11a). We initially subjected **35** to the reaction conditions, mimicking the first catalytic turnover (based on 10 mol % of catalyst) using 30 equiv of the organozinc reagent. Interestingly, no coupling product was observed under these conditions; all of the metallacycle had been consumed with concomitant formation of *p*-toluenesulfonamide. The reaction was heterogeneous, and we therefore hypothesized that the insolubility of the complex could be the cause of this result. Interestingly, when DCE was added to the mixture, the solution became much less heterogeneous, and in this case, the cross-coupling product **2** was formed in a 55:45 ratio to $TsNH_2$ (80% combined NMR yield). This experiment demonstrates that the azametallacycle is indeed a competent reaction intermediate,[31] and moreover, the results suggest that the improved reaction outcome when using DCE as a co-solvent is due to an increased solubility of the catalytic intermediates. The azametallacycle **35** also worked well as a precatalyst (5 mol %) in the coupling reaction between **1a** and 4-fluorobutylzinc bromide, furnishing the product **37** in 88% yield (Scheme 11b).

Scheme 11. Investigation of the Role of DCE as an Additive/Solvent

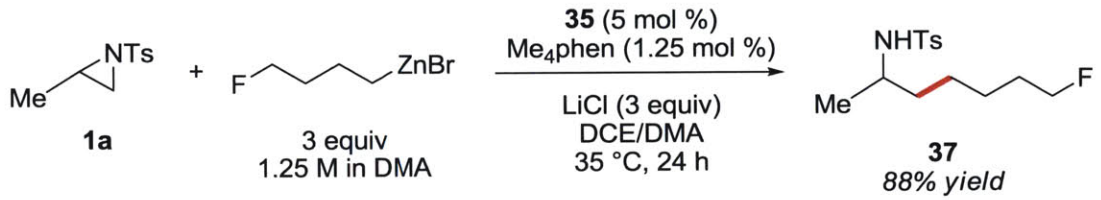
(a)



Compare to Doyle, 2012:

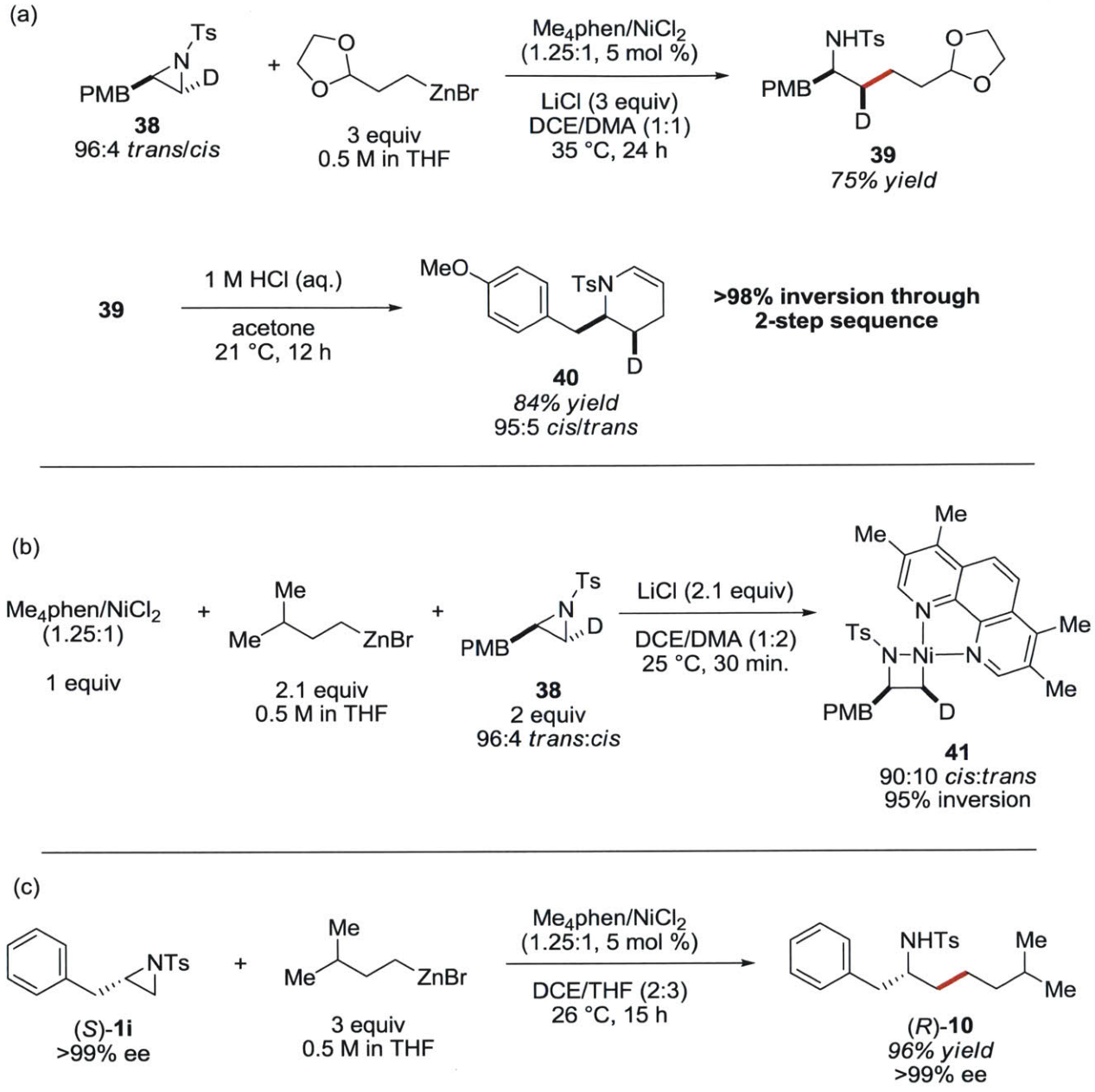


(b)



After having obtained results that support the intermediacy of the azametallacycle in the reaction mechanism, we decided to examine the stereochemical course of reaction. In order to do so, a deuterium-labeled version of the PMB-substituted aziridine **38** was synthesized and subjected to the coupling conditions (Scheme 12a). The acetal-containing organozinc reagent was chosen for this study since the resulting coupling product easily could be transformed in one step to an enamine (tetrahydropyridine) **40**,[32] which would allow for the determination of stereochemical configuration by NMR analysis. The cross-coupling product **39** was formed in 75% yield, and upon treatment with aqueous HCl in acetone, cyclized to **40** in 84% yield.

Scheme 12. Stereochemical Analysis of Coupling Reaction



Analysis by NMR spectroscopy[33] showed that the product was formed with essentially complete (>98%) inversion at the deuterium-labeled carbon atom.[34] This result is in accordance with the stoichiometric studies by Hillhouse and in contrast to the studies by Doyle, where epimerization is observed in the coupling reaction.[14]

To further ascertain in which step of the mechanism the inversion occurs, the corresponding azametallacycle of the deuterium-labeled aziridine **38** was investigated (Scheme

12b). Under conditions similar to the cross-coupling reaction, azanickelacyclobutane **41** was successfully formed with 95% inversion at the labeled (C3) position, thereby confirming that the stereochemical inversion occurs in the oxidative insertion step.

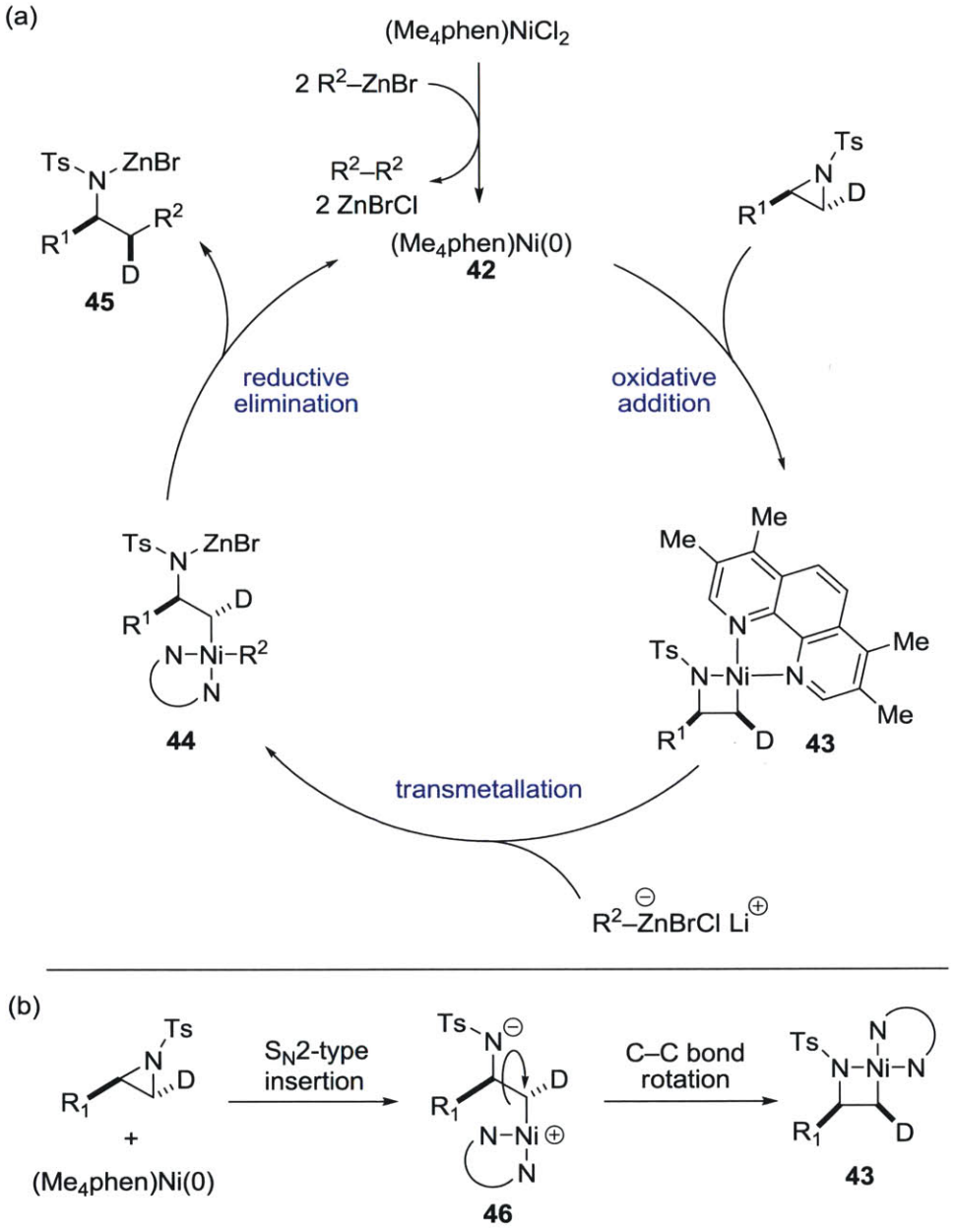
As a final mechanistic experiment, we investigated whether enantioenriched aziridines could undergo cross-coupling reaction without loss or erosion of enantiopurity at the internal (2-position) of the aziridine. On the basis of the hypothesized mechanism (vide infra), we anticipated that no erosion should take place, and indeed, when enantiopure aziridine (*S*)-1i was subjected to the coupling conditions, the sulfonamide product (*R*)-10 was formed in excellent yield (96%) and with preserved stereochemistry (>99% ee) (Scheme 12c).

Proposed Mechanism

On the basis of these mechanistic studies, we propose a catalytic cycle for the regioselective cross-coupling reaction as outlined in Scheme 13. The nickel(II) precatalyst is activated by two successive transmetallations of the organozinc reagent followed by reductive elimination.[35] This releases the active nickel(0) catalyst **42**, which can then undergo oxidative insertion into the less hindered C–N bond of the aziridine. This step proceeds via an S_N2-type mechanism (inversion) involving attack of nickel at C3 followed by C–C bond rotation (**46**) and ring closure to form azanickelacyclobutane **43**.[36] Subsequent transmetallation (by way of retention) with the organozinc reagent forms intermediate **44**, which undergoes reductive elimination (with retention) to release the product **45** (ZnBr adduct) and a nickel(0) species which re-enters the catalytic cycle.

On the basis of our findings, we hypothesize that the active transmetallating agent is a lithium organozincate, which are known to be more nucleophilic and generally undergo faster transmetallation than unmodified organozinc reagents. For the reactions performed with DMA as a co-solvent, addition of LiCl was found to be necessary for product formation. As previously discussed, the outcome of the reaction is improved when an excess of ligand-to-nickel is used. Since the oxidative addition proceeds smoothly in the absence of excess ligand, we hypothesize that the additional ligand may be involved in the reductive elimination step.

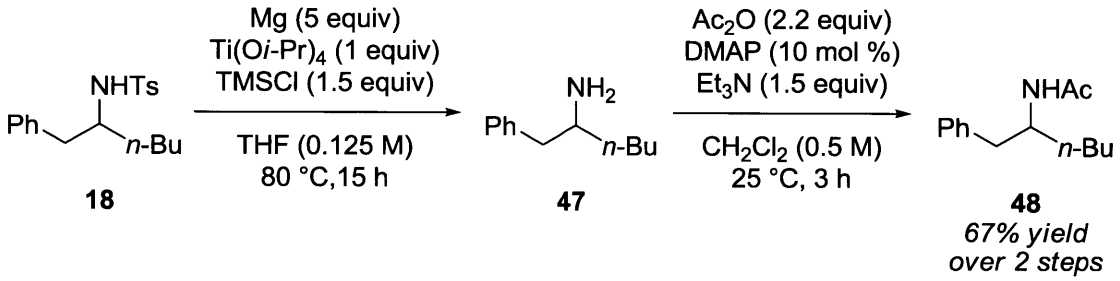
Scheme 13. Hypothesized Mechanism of Nickel-Catalyzed Coupling Reaction



The sulfonamide moiety can be found in a great number of biologically active molecules, including the APIs of numerous drugs, such as sildenafil (erectile dysfunction), sultiame (epilepsy), and brinzolamide (glaucoma).[37] It is also considered a carboxylic acid isostere and has been shown to increase metabolic stability when introduced into certain peptide-like molecules.[38] However, this stability is also the reason why this moiety is sometimes avoided, as it can be challenging to cleave. For that reason, we decided to demonstrate that the tosyl protecting group can be reductively cleaved to the free amine, if desired. Following an adapted

literature procedure, the sulfonamide **18** was successfully cleaved using magnesium as a reductant in the presence of titanium tetraisopropoxide.[39] The resulting amine was isolated (after acetylation to form **48**) in 67% yield over two steps (Scheme 14).

Scheme 14.



Conclusion

In summary, we have developed the first ligand-controlled, nickel-catalyzed cross-coupling of unactivated aliphatic *N*-tosylaziridines with aliphatic organozinc reagents. The reaction protocol displays complete regioselectivity for reaction at the less hindered C–N bond, and the products are furnished in good to excellent yield for a broad selection of substrates. Moreover, the use of the very air-sensitive $Ni(cod)_2$ was avoided by the development of an air-stable nickel(II) chloride/ligand precatalyst that can be handled and stored outside a glovebox. Besides improving the practicality of the protocol, the exclusion of 1,5-cyclooctadiene from the system also improved the reactivity of the catalyst. Finally, mechanistic investigations, including deuterium-labeling studies, showed that the reaction proceeds with overall inversion of configuration at the terminal position of the aziridine through nucleophilic aziridine ring opening (S_N2-type) by Ni (inversion), transmetallation (retention), and reductive elimination (retention). These results are in contrast to the previously reported nickel-catalyzed reactions, in which scrambling of the stereoconfiguration at the terminal carbon atom is observed.

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(25) It should be noted that the DCE is able to act as an oxidant by reaction with the nickel(0) catalyst. However, the rate with which this reaction proceeds is lower than the rate of the aziridine activation. When full conversion of the aziridine is obtained, the reaction will eventually discolor due to this reaction. For a reference on this type of reaction, see: (a) Takahashi, S.; Suzuki, Y.; Hagihara, N. *Chem. Lett.* **1974**, 1363–1366. For a related reaction with DCM, see: (b) Csok, Z.; Vechorkin, O.; Harkins, S. B.; Scopelliti, R.; Hu, X. *J. Am. Chem. Soc.* **2008**, *130*, 8156–8157.

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(31) Although the stoichiometric experiments in Scheme 11a indicate that transmetallation with azanickelacyclobutane **43** does proceed, the outcome (product ratios) of those experiments is significantly different from the results obtained in the coupling reaction. Since the relative rates of azametallacycle formation (ring closure) from **46** and transmetallation is unknown, the possibility of transmetallation occurring from the open structure **46** in the catalytic reaction cannot be excluded.

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Chapter 3

Ring-Opening, Negishi-type Cross-Coupling of 2-Substituted *N*-Tosylaziridines with Alkylzinc Halides

Experimental Section

Materials, Methods, and General Considerations

All solvents were degassed by sparging with nitrogen gas and dried by passage through a column of activated alumna on an SG Water solvent purification system. Manipulation of all air-sensitive reagents was carried out in a glovebox (MBraun Unilab) filled with dry nitrogen. Thin-layer chromatography was carried out on EMD Millipore 60 F254 glass-backed plates (silica gel, 250 μm coating thickness) and visualized using UV light (254 nm), basic potassium permanganate or ceric ammonium molybdate stains. Column chromatography was carried out on a Biotage Isolera chromatography system using pre-packed SNAP HP-Sil columns (silica gel, 25 μm average particle size). NMR spectra were acquired on a Bruker Avance (operating at 400 MHz for ^{1}H, 101 MHz for ^{13}C, and 376 MHz for ^{19}F) or Varian Inova 500 spectrometer (operating at 500 MHz for ^{1}H and 126 MHz for ^{13}C). Chemical shifts (^{1}H and ^{13}C) are reported in parts per million relative to TMS (δ = 0.00 ppm) and were referenced to the residual solvent peak ($CDCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.16 ppm for ^{13}C NMR; CD_2Cl_2, 5.32 ppm for ^{1}H NMR, CD_2Cl_2, 53.84 ppm for ^{13}C).[1] The following designations are used to describe multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), hept (heptet), br (broad), app (apparent). GC/MS was performed on an Agilent 5870 GC (HP-5ms column) with an Agilent 5975C MSD. IR spectra were obtained on an Agilent Cary 630 FT-IR spectrometer equipped with an ATR (attenuated total reflectance) accessory. Exact masses (high resolution mass spectra) were obtained on a Bruker Daltonics APEX IV 4.7 T FT-ICR spectrometer operating with electrospray ionization (ESI) in positive ion mode or with direct analysis in real time (DART) ionization in positive ion mode.

Chloramine-T trihydrate (98%), Titanium(IV) isopropoxide (99.999% trace metal basis), *N*,*N*-dimethylacetamide (DMA) (anhydrous, 98.8%) were purchased from Sigma-Aldrich and used without further purification (unless otherwise stated). Bis(1,5-cyclooctadiene)nickel(0) was purchased from Strem Chemicals (Newburyport, MA). Nickel(II) chloride hexahydrate (ReagentPlus) was purchased from Sigma-Aldrich. Zinc dust (99.9%, ~325 mesh, lot# B1592115) was purchased from Strem Chemicals (Newburyport, MA). Mg powder (100–200 mesh, 99.6% (metals basis excluding Ca)) was purchased from Alfa Aesar. Schwartz's reagent (Cp_2ZrHCl) (95%) was purchased from Strem Chemicals (Newburyport, MA). 3,4,7,8-

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tetramethyl-1,10-phenanthroline (Me_4phen) was purchased from Accela (San Diego, CA) and 1,10-phenanthroline (phen) was purchased from Sigma-Aldrich. All isotope-labeled compounds and solvents were purchased from Cambridge Isotopes Laboratories.

The following commercially available solutions of organozinc reagents in tetrahydrofuran (THF) were purchased from Sigma-Aldrich (lot #): 3-methylbutylzinc(II) bromide (SHBD1447), propylzinc(II) bromide (SHBC2061), cyclohexylzinc(II) bromide (SHBB5989), 4-pentenylzinc(II) bromide (SHBB5327), phenethylzinc(II) bromide (SHBC9654), 2-(1,3-dioxan-2-yl)ethylzinc(II) bromide (SHBD1335V), 3-cyanopropylzinc(II) bromide (SHBB1012).

Synthesis of Ni(II)-Precatalysts

To a tared round bottom flask was added $NiCl_2$•$6H_2O$ (1.00 equiv) and the desired ligand (x equiv). *It is important to note the exact masses of $NiCl_2$•$6H_2O$ and ligand added to accurately determine the effective molecular weight of the resulting precatalyst.* Absolute EtOH and a magnetic stir bar were added to the flask and a reflux condenser was attached. The mixture was heated to 85 °C for the length of time indicated, after which the flask was cooled to ambient temperature, the magnetic stir bar was removed, and the solvent was removed with a rotary evaporator. The solid so obtained was then dried under vacuum to remove entrained ethanol and water. The mass of the product was then compared to the theoretical yield to determine the effective molecular weight ($MW_{effective}$) of the precatalyst. The effective molecular weight is defined as:

$$MW_{effective} = \frac{mass_{measured}}{mass_{theoretical}} \cdot \left(MW_{NiCl_2} + MW_{ligand} \cdot \frac{mmol_{ligand}}{mmol_{NiCl_2 \cdot 6H_2O}} \right)$$

$$mass_{theoretical} = MW_{NiCl_2} \cdot mmol_{NiCl_2 \cdot 6H_2O} + MW_{ligand} \cdot mmol_{ligand}$$

$$MW_{effective} = \frac{mass_{measured}}{MW_{NiCl_2} \cdot mmol_{NiCl_2 \cdot 6H_2O} + MW_{ligand} \cdot mmol_{ligand}} \cdot \left(MW_{NiCl_2} + MW_{ligand} \cdot \frac{mmol_{ligand}}{mmol_{NiCl_2 \cdot 6H_2O}} \right)$$

For example, the $MW_{effective}$ of a batch of precatalyst with a 1:1.25 nickel:ligand ratio on a 0.500 mmol scale, which was found to have a mass of 228.9 mg, can be calculated as follows:

$$mass_{theoretical} = 212.5\ mg = 129.60\frac{g}{mol} \cdot 0.500\ mmol\ NiCl_2 \cdot 6H_2O + 236.31\frac{g}{mol} \cdot 0.625\ mmol\ ligand$$

$$MW_{effective} = 457.8\frac{g}{mol} = \frac{228.9\ mg}{212.5\ mg} \cdot \left(129.60\frac{g}{mol} + 236.31\frac{g}{mol} \cdot \frac{0.625\ mmol}{0.50\ mmol}\right)$$

Substance	**Molecular Weight (MW, $^{g}/_{mol}$)**
$NiCl_2$•$6H_2O$	237.69
$NiCl_2$	129.60
3,4,7,8-tetramethyl-1,10-phenanthroline (Me_4phen)	236.31
1,10-phenanthroline (phen)	180.21

Phen/$NiCl_2$ (1.25:1) precatalyst

Following the general procedure, $NiCl_2$•$6H_2O$ (20.00 mmol, 4.754 g) and 1,10-phenanthroline (25.00 mmol, 4.505 g) were reacted in absolute EtOH (50 mL) at 85 °C for 16 h. After cooling to ambient temperature and removal of the magnetic stir bar, the solvent was removed with a rotary evaporator, after which the solid was dried under vacuum (50 mTorr at 50 °C for 3 h). The effective molecular weight of the resulting light green solid was found to be 379.28 g/mol (theoretical 354.85 g/mol), corresponding to a purity of approximately 94% by mass.

Me_4phen/$NiCl_2$ (1.25:1) precatalyst

Following the general procedure, $NiCl_2$•$6H_2O$ (6.00 mmol, 1.426 g) and 3,4,7,8-tetramethyl-1,10-phenanthroline (7.50 mmol, 1.772 g) were reacted in absolute EtOH (50 mL) at 85 °C for 16 h. After removal of the magnetic stir bar, the solvent was removed with a rotary evaporator, after which the green solid was dried under vacuum (50 mTorr at 50 °C for 3 h). The effective molecular weight of the resulting greenish solid was found to be 458.53 g/mol (theoretical 425.99 g/mol), corresponding to a purity of approximately 93% by mass.

Three separate batches (ranging from 0.50 to 6.00 mmol) were made using this procedure and that the purity ranged from 93 to 94%.

Table SI 1. Elemental Analysis of Diimine/Nickel(II) Chloride Complexes

	ligand	ratio[a]	synthesis[b]		theoretical % ($LNiCl_2$)				found[c]				found (duplicate)			
			time (h)	temp. (°C)	C	H	N	Cl	C	H	N	Cl	C	H	N	
1	bpy	1 : 1	16	22 / 22	42.03	2.82	9.80	24.81	39.61	3.34	9.18		39.73	3.43	9.24	1
2	4,4'-dimethoxy-bpy	1 : 1	16	22 / 22	41.68	3.50	8.10	20.50	41.59	3.99	7.81		41.62	3.97	7.75	2
3	4,4'-di-*t*-butyl-bpy	1 : 1	16	22 / 22	54.32	6.08	7.04	17.82	53.31	6.09	6.92		53.15	6.00	6.81	3
4	2,2'-biquinoline	1 : 1	16	22 / 22	56.02	3.13	7.26	18.37	55.78	3.24	7.35					4
5	5,5'-dimethyl-bpy	1 : 1	40	22 / 22	45.92	3.85	8.93	22.59	45.50	3.99	8.83		45.37	3.93	8.84	5
6	phen	1 : 1	48	22 / 22	46.52	2.60	9.04	22.89	52.86	4.26	9.78		52.76	4.17	9.77	6
7	phen	1 : 1	16	85 / 22	46.52	2.60	9.04	22.89	43.98	3.11	8.52	21.74	44.08	3.03	8.48	7
8	phen	3 : 1	3	22 / 22	64.51	3.61	12.54	10.58	62.57	4.90	10.90	9.14	62.66	4.77	11.01	8
9	phen	3 : 1	3	22 / 100	63.02	4.76	11.02	9.30	62.68	4.55	11.39	9.56	62.63	4.49	11.29	9
10	2,9-dimethyl-phen	1 : 1	16	22 / 22	49.77	3.58	8.29	20.99	49.89	3.57	8.37					10
11	4,7-dimethoxy-phen	1 : 1	16	22 / 80	45.46	3.27	7.57	19.17	44.30	3.69	7.45		44.19	3.79	7.38	11
12	4,7-diphenyl-phen	1 : 1	40	22 / 22	62.39	3.49	6.06	15.35	65.60	4.11	6.38		65.62	4.08	6.34	12
13	3,4,7,8-tetramethyl-phen	1 : 1	16	22 / 22	52.52	4.41	7.66	19.38	56.30	5.23	8.22		56.44	5.34	8.33	13
14	3,4,7,8-tetramethyl-phen	1 : 1	4	85 / 22	52.52	4.41	7.66	19.38	45.37	5.26	5.42	21.12	45.25	5.08	5.40	14
15	3,4,7,8-tetramethyl-phen	1 : 1	16	85 / 22	52.52	4.41	7.66	19.38	44.72	5.42	5.37	20.24	44.82	5.30	5.47	15
16	3,4,7,8-tetramethyl-phen	1 : 1	16	85 / 75	52.52	4.41	7.66	19.38	43.07	4.15	6.23	23.01	43.22	4.20	6.18	16
17	4,7-dimethyl-phen	1 : 1	16	22 / 22	49.77	3.58	8.29	20.99	54.22	4.57	8.88		54.33	4.58	9.02	17
18	pyphos	1 : 1	2	85 / rt	54.21	4.31	3.33	16.85	54.39	4.49	3.36					18
19	2,2-dipyridylmethane	1 : 1	1	130 / rt	44.07	3.36	9.34	23.65	53.19	4.52	11.16		53.00	4.40	11.06	19
20	4,5-diazafluoren-9-one	1 : 1	24	rt / rt	42.38	1.92	8.89	22.74	52.97	3.41	10.44		52.88	3.32	10.49	20

[a]Ratio refers to the stoichiometry of the ligand and nickel added to the reaction vessel and is a nominal value only. [b]Complexes were synthesized according to the method described in Scheme 3 of the main text. Temperature of synthesis / temperature of drying, which was done for 3 h in all instances. [c]Chloride was not determined in all instances, and duplicate results were only determined for CHN analyses.

Table SI 1. Elemental Analysis of Diimine/Nickel(II) Chloride Complexes, continued

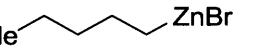
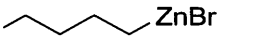
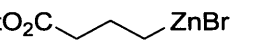
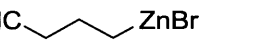
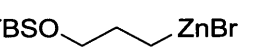
difference from $LNiCl_2$[d]				difference from $LNiCl_2$ (duplicate)			plausible formula[e]	theoretical %				difference				difference (duplicate)		
C	H	N	Cl	C	H	N		C	H	N	Cl	C	H	N	Cl	C	H	N
-2.42	0.52	-0.62		-2.30	0.61	-0.56	$LNiCl_2•H_2O$	39.54	3.32	9.22		0.07	0.02	-0.04		0.19	0.11	0.02
-0.09	0.49	-0.29		-0.06	0.47	-0.35	$LNiCl_2$	41.68	3.50	8.10	20.50	-0.09	0.49	-0.29		-0.06	0.47	-0.35
-1.01	0.01	-0.12		-1.17	-0.08	-0.23	$LNiCl_2$	54.32	6.08	7.04	17.82	-1.01	0.01	-0.12		-1.17	-0.08	-0.23
-0.24	0.11	0.09					$LNiCl_2$	56.02	3.13	7.26	18.37	-0.24	0.11	0.09				
-0.42	0.14	-0.10		-0.55	0.08	-0.09	$LNiCl_2$	45.92	3.85	8.93	22.59	-0.42	0.14	-0.10		-0.55	0.08	-0.09
6.34	1.66	0.74		6.24	1.57	0.73	$L_2NiCl_2•3H_2O$	52.98	4.08	10.30	13.03	-0.12	0.18	-0.52		-0.22	0.09	-0.53
-2.54	0.51	-0.52	-1.15	-2.44	0.43	-0.56	$LNiCl_2•H_2O$	43.97	3.07	8.55	21.63	0.01	0.04	-0.03	0.11	0.11	-0.04	-0.07
-1.94	1.29	-1.64	-1.44	-1.85	1.16	-1.53	$L_3NiCl_2•2EtOH$	63.02	4.76	11.02	9.30	-0.45	0.14	-0.12	-0.16	-0.36	0.01	-0.01
-0.34	-0.21	0.37	0.26	-0.39	-0.27	0.27	L_3NiCl_2	62.83	3.81	12.21	10.30	-0.15	0.74	-0.82	-0.74	-0.20	0.68	-0.92
0.12	-0.01	0.08					$LNiCl_2$	49.77	3.58	8.29	20.99	0.12	-0.01	0.08				
-1.16	0.42	-0.12		-1.27	0.52	-0.19	$LNiCl_2$	44.43	3.20	7.40	19.98	-0.13	0.49	0.05		-0.24	0.59	-0.02
3.21	0.62	0.32		3.23	0.59	0.28	$L_3Ni_2Cl_4•3H_2O$	65.99	4.15	6.41	10.82	-0.39	-0.04	-0.03		-0.37	-0.07	-0.07
3.78	0.32	0.56		3.92	0.93	0.67	$L_3Ni_2Cl_4•3H_2O$	56.40	5.32	8.22	13.87	-0.10	-0.09	0.00		0.04	0.02	0.11
-7.15	0.85	-2.24	1.74	-7.27	0.67	-2.26	$L_2Ni_3Cl_6•3EtOH$	45.66	5.04	5.60	21.28	-0.29	0.22	-0.18	-0.16	-0.41	0.04	-0.20
-7.80	1.01	-2.29	0.86	-7.70	0.89	-2.19	$L_2Ni_3Cl_6•4EtOH•2H_2O$	44.41	5.59	5.18	19.66	0.31	-0.17	0.19	0.58	0.41	-0.29	0.29
-9.45	-0.26	-1.43	3.63	-9.30	-0.21	-1.48	$L_2Ni_3Cl_6•2H_2O$	42.83	4.04	6.24	23.70	0.24	0.11	-0.01	-0.69	0.39	0.16	-0.06
4.45	0.99	0.59		4.56	1.00	0.73	$L_3Ni_2Cl_4•3H_2O$	53.78	4.51	8.96	15.12	0.44	0.06	-0.08		0.55	0.07	0.06
0.18	0.18	0.03					$LNiCl_2$	54.21	4.31	3.33	16.85	0.18	0.18	0.03				
9.32	1.36	1.82		8.93	1.04	1.72	unknown											
10.59	1.49	1.55		10.50	1.40	1.60	$L_2NiCl_2•EtOH$	53.38	3.36	10.37	13.13	-0.41	0.05	0.07		-0.50	-0.04	0.12

[d]The length of the horizontal bars is proportional to the absolute difference from theoretical. They are intended as a visual aid to assist in quick assessment of in what way the analysis differs from theoretical. [e]This is a suggested formula that most closely fits with the data from the analyses, but is not proof of composition.

Synthesis of Organozinc Reagents[2]

A flame dried Schlenk flask was charged with zinc dust[3] (1.37 g, 21.0 mmol, 1.4 equiv) and dry *N*,*N*-dimethylacetamide (DMA) (10.0 mL). I_2 (190 mg, 0.75 mmol, 5 mol %) was added to this suspension and the mixture was stirred until the yellow color had disappeared (typically 1 minute). Alkyl bromide (15.0 mmol) was then added and the reaction was heated to 70 °C for 12 h (GC analysis was used to check for full conversion). After cooling to ambient temperature, the Schlenk flask was transferred to glovebox and the remaining zinc dust was allowed to settle. The solution was filtered through a PTFE syringe filter (VWR, 25 mm disk size, 0.2 μm pore size) and the resulting organozinc solution was stored in a 20 mL scintillation vial in the glovebox. Alternatively, if desired, the solution can be transferred by cannula to a Schlenk flask under argon.

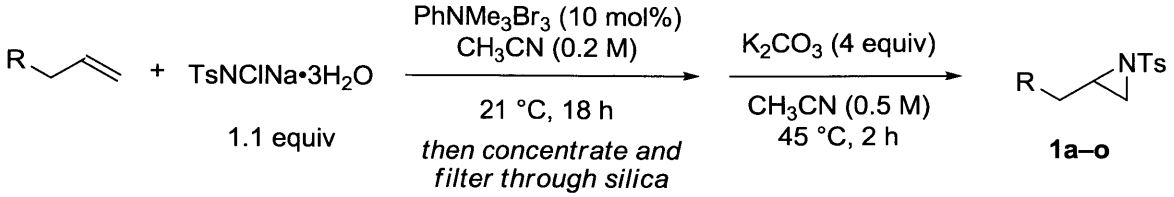
The concentration of the organozinc reagent was determined by titration following the procedure of Knochel:[4] A flame-dried 4 mL vial was charged with I_2 (127.0 mg, 0.50 mmol) and flushed with argon. The iodine was dissolved in 2.0 mL of a 0.5 M solution of LiCl in anhydrous THF. The solution was cooled to 0 °C using an ice bath and the organozinc reagent was added dropwise until the brown color disappeared.

Alkyl bromide (15.0 mmol)	**Organozinc Reagent**	**Concentration**
1-bromopentane (1.86 mL)		1.0 M
1-bromo-4-fluorobutane (1.64 mL)		1.25 M
ethyl 4-bromobutanoate (2.15 mL)		1.05 M
4-bromobutanenitrile (1.49 mL)		1.0 M
(3-bromopropoxy)(*tert*-butyl)dimethylsilane (2.40 mL, 10.0 mmol scale)		1.0 M

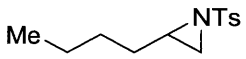
[2] This procedure was developed and reported in Huo, S. *Org. Lett.* **2003**, *5*, 423–425.
[3] Armarego, W. L. F. and Chai, C. L. L., Eds. Purification of Laboratory Chemicals, 6th Ed; Elsevier: Oxford, U.K., 2009.
[4] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890–891.

Synthesis and Characterization of Aziridines

General Procedure[5]



To a mixture of Chloramine-T trihydrate (1.55 g, 5.5 mmol) and alkene (5.0 mmol) in CH_3CN (25 mL) at ambient temperature was added $PhNMe_3Br_3$ (188.0 mg, 0.50 mmol). The reaction was stirred vigorously for 15 h and then concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (5–10 mL) and filtered through a short column (silica gel, 3 cm diameter x 4 cm height), eluting with 150 mL of a 10% EtOAc/hexanes mixture. After evaporation of the solvent, the residue was dissolved in CH_3CN (10 mL). K_2CO_3 (2.77 g, 20.0 mmol) was added and the mixture was stirred vigorously at 45 °C for 2 h. After cooling to ambient temperature, the mixture was diluted with Et_2O (20 mL) and filtered through Celite. The filter cake was washed with Et_2O, after which the filtrate was concentrated and then subjected to column chromatography on silica gel using pre-packed Biotage SNAP HP-Sil columns (50 g, 25 μm).



2-butyl-1-tosylaziridine (1b): Following the general procedure, starting from 1-hexene (620 μL, 5.0 mmol), **1b** was isolated by column chromatography on silica gel (EtOAc/hexanes gradient 0 to 15%) in 66% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.85–7.80 (m, 2H), 7.36–7.31 (m, 2H), 2.72 (tt, J = 7.3, 4.8 Hz, 1H), 2.63 (d, J = 7.0 Hz, 1H), 2.44 (s, 3H), 2.05 (d, J = 4.6 Hz, 1H), 1.60–1.49 (m, 1H), 1.39–1.29 (m, 1H), 1.28–1.17 (m, 4H), 0.81 (t, J = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.5, 135.4, 129.7, 128.1, 40.6, 34.0, 31.1, 29.0, 22.3, 21.8, 14.0.

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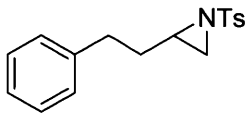
[5] This procedure is an adaptation of that reported in Jeong, J. U.; Tao, B.; Sagasser, I.; Henniges, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1998**, *120*, 6844–6845.

FT-IR (ATR, cm^{-1}): 2958, 2931, 2862, 1597, 1456, 1321, 1157, 1090, 712.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{13}H_{19}NO_2S$, 254.1209; found, 254.1214.



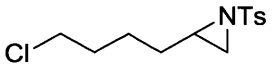
2-phenethyl-1-tosylaziridine (1c): Following the general procedure, starting from homoallylbenzene (750 μL, 5.0 mmol), **1c** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 59% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.87–7.79 (m, 2H), 7.37–7.31 (m, 2H), 7.29–7.24 (m, 2H), 7.21–7.15 (m, 1H), 7.15–7.09 (m, 2H), 2.78 (tt, J = 7.5, 4.8 Hz, 1H), 2.67–2.53 (m, 2H), 2.61 (d, J = 6.9 Hz, 1H), 2.45 (s, 3H), 2.05 (d, J = 4.5 Hz, 1H), 1.88 (dddd, J = 13.9, 8.8, 7.4, 5.0 Hz, 1H), 1.67 (dtd, J = 14.1, 8.1, 6.4 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.6, 140.8, 135.1, 129.8, 128.6, 128.4, 128.1, 126.2, 39.8, 34.0, 33.2, 33.1, 21.7.

FT-IR (ATR, cm^{-1}): 3028, 2926, 2856, 1597, 1454, 1320, 1157, 1090, 692.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{19}NO_2S$, 302.1209; found, 302.1219.



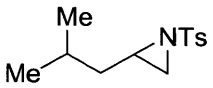
2-(4-chlorobutyl)-1-tosylaziridine (1d): Following the general procedure, starting from 6-chlorohex-1-ene (660 μL, 5.0 mmol), **1d** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 59% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.85–7.79 (m, 2H), 7.38–7.31 (m, 2H), 3.42 (td, J = 6.6, 1.0 Hz, 2H), 2.72 (tt, J = 7.1, 4.5 Hz, 1H), 2.64 (d, J = 7.0 Hz, 1H), 2.45 (s, 3H), 2.07 (d, J = 4.5 Hz, 1H), 1.75–1.58 (m, 3H), 1.44–1.27 (m, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.7, 135.1, 129.8, 128.1, 44.7, 40.0, 33.8, 31.9, 30.6, 24.3, 21.8.

FT-IR (ATR, cm^{-1}): 2939, 2865, 1597, 1456, 1319, 1157, 1091, 712.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{13}H_{18}ClNO_2S$, 288.0820; found, 288.0832.



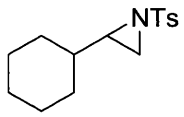
2-isobutyl-1-tosylaziridine (1e): Following the general procedure, starting from 4-methylpent-1-ene (635 μL, 5.0 mmol), **1e** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 67% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.85–7.80 (m, 2H), 7.36–7.31 (m, 2H), 2.79 (tdd, J = 7.0, 6.0, 4.6 Hz, 1H), 2.63 (d, J = 7.0 Hz, 1H), 2.44 (s, 3H), 2.02 (d, J = 4.6 Hz, 1H), 1.67–1.56 (m, 1H), 1.40–1.26 (m, 2H), 0.89 (d, J = 1.9 Hz, 3H), 0.87 (d, J = 2.0 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.5, 135.4, 129.8, 128.1, 40.6, 39.2, 34.2, 26.9, 22.9, 22.1, 21.8.

FT-IR (ATR, cm^{-1}): 2957, 2930, 2872, 1597, 1466, 1320, 1156, 1090, 712.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{13}H_{19}NO_2S$, 254.1209; found, 254.1219.



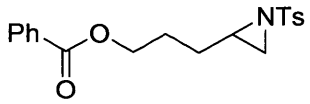
2-cyclohexyl-1-tosylaziridine (1f): Following the general procedure, starting from vinylcyclohexane (694 μL, 5.0 mmol), **1f** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 10%) in 75% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.85–7.80 (m, 2H), 7.36–7.31 (m, 2H), 2.60 (d, J = 7.0 Hz, 1H), 2.53 (td, J = 7.2, 4.6 Hz, 1H), 2.45 (s, 3H), 2.10 (d, J = 4.6 Hz, 1H), 1.74–1.56 (m, 4H), 1.50 (m, 1H), 1.22–0.86 (m, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.5, 135.2, 129.7, 128.2, 45.3, 39.5, 32.8, 30.3, 29.7, 26.1, 25.7, 25.5, 21.8.

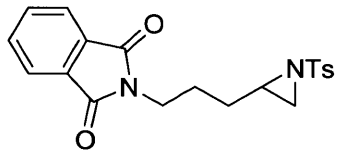
FT-IR (ATR, cm^{-1}): 2925, 2852, 1598, 1449, 1321, 1158, 1093, 886, 719.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{15}H_{21}NO_2S$, 280.1366; found, 280.1369.



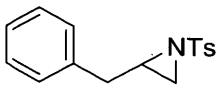
3-(1-tosylaziridin-2-yl)propyl benzoate (1g): Following the general procedure, starting from pent-4-en-1-yl benzoate (694 μL, 5.0 mmol), **1g** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 30%) in 47% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.03–7.98 (m, 2H), 7.86–7.81 (m, 2H), 7.59–7.53 (m, 1H), 7.47–7.41 (m, 2H), 7.36–7.31 (m, 2H), 4.26 (td, J = 6.4, 2.3 Hz, 2H), 2.84–2.77 (m, 1H), 2.66 (d, J = 6.9 Hz, 1H), 2.41 (s, 3H), 2.11 (d, J = 4.5 Hz, 1H), 1.84–1.70 (m, 3H), 1.52–1.41 (m, 1H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 166.5, 144.7, 135.1, 133.1, 130.3, 129.8, 129.6, 128.5, 128.1, 64.0, 39.7, 34.0, 28.1, 26.2, 21.7.
FT-IR (ATR, cm^{-1}): 2926, 1714, 1598, 1451, 1318, 1271, 1157, 1095, 709.
HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{19}H_{21}NO_4S$, 360.1264; found, 360.1269.



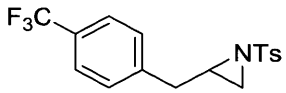
2-(3-(1-tosylaziridin-2-yl)propyl)isoindoline-1,3-dione (1h): Following the general procedure, starting from 2-(pent-4-en-1-yl)isoindoline-1,3-dione (1.08 g, 5.0 mmol), **1h** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 40%) in 59% yield as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.86–7.79 (m, 4H), 7.74–7.69 (m, 2H), 7.35–7.29 (m, 2H), 3.69–3.57 (m, 2H), 2.80–2.73 (m, 1H), 2.63 (d, J = 6.9 Hz, 1H), 2.40 (s, 3H), 2.09 (d, J = 4.5 Hz, 1H), 1.68–1.58 (m, 3H), 1.42–1.31 (m, 1H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 168.2, 144.5, 134.9, 134.0, 132.0, 129.7, 128.0, 123.2, 39.4, 37.1, 33.8, 28.6, 25.9, 21.6.
FT-IR (ATR, cm^{-1}): 2935, 1771, 1706, 1596, 1396, 1320, 1157, 712.
HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{20}H_{20}N_2O_4S$, 385.1217; found, 385.1200.



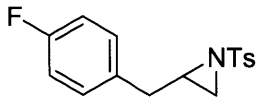
2-benzyl-1-tosylaziridine (1i): Following the general procedure, starting from allylbenzene (665 μL, 5.0 mmol), **1i** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 50% yield as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.71–7.66 (m, 2H), 7.24–7.19 (m, 2H), 7.18–7.12 (m, 3H), 7.07–7.02 (m, 2H), 2.95 (tdd, J = 7.0, 5.2, 4.6 Hz, 1H), 2.81 (dd, J = 14.5, 5.2 Hz, 1H), 2.71 (d, J = 6.9 Hz, 1H), 2.69 (dd, J = 14.6, 7.2 Hz, 1H), 2.42 (s, 3H), 2.16 (d, J = 4.5 Hz, 1H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.4, 137.1, 135.0, 129.7, 128.8, 128.5, 128.0, 126.6, 41.3, 37.6, 32.9, 21.7.
FT-IR (ATR, cm^{-1}): 3029, 2920, 1597, 1454, 1319, 1157, 691.
HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{16}H_{17}NO_2S$, 288.1053; found, 288.1063.



1-tosyl-2-(4-(trifluoromethyl)benzyl)aziridine (1j): Following the general procedure, starting from allylbenzene (881 μL, 5.0 mmol), **1j** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 21% yield as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.63–7.58 (m, 2H), 7.34 (app d, J = 8.0 Hz, 2H), 7.16 (app d, J = 8.0 Hz, 2H), 7.11 (app d, J = 8.0 Hz, 2H), 2.99 (dd, J = 14.2, 4.0 Hz, 1H), 2.91 (ddt, J = 8.4, 7.1, 4.2 Hz, 1H), 2.79 (d, J = 6.8 Hz, 1H), 2.54 (dd, J = 14.2, 8.3 Hz, 1H), 2.40 (s, 3H), 2.20 (d, J = 4.4 Hz, 1H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.7, 141.4 (q, J = 1.5 Hz), 134.7, 129.6, 129.1, 128.9 (q, J = 32.4 Hz), 128.0, 125.3 (q, J = 3.8 Hz, 2C), 124.3 (q, J = 271.8 Hz), 41.3, 37.4, 32.6, 21.5.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -62.4 (s).
FT-IR (ATR, cm^{-1}): 2934, 1597, 1319, 1158, 1123, 1066, 907, 715.
HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{16}F_3NO_2S$, 356.0927; found, 356.0932.



2-(4-fluorobenzyl)-1-tosylaziridine (1k): Following the general procedure, starting from 1-allyl-4-fluorobenzene (675 μL, 5.0 mmol), **1k** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 49% yield as a white solid.

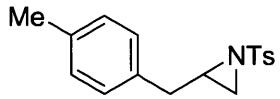
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.67–7.61 (m, 2H), 7.20 (app d, J = 8.2 Hz, 2H), 7.00–6.93 (m, 2H), 6.82–6.76 (m, 2H), 2.92–2.82 (m, 2H), 2.74 (d, J = 6.6 Hz, 1H), 2.56–2.48 (m, 1H), 2.43 (s, 3H), 2.16 (d, J = 4.3 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 161.8 (d, J = 244.5 Hz), 144.6, 134.8, 132.9 (d, J = 3.2 Hz), 130.3 (d, J = 8.0 Hz, 2C), 129.7, 128.0, 115.3 (d, J = 21.3 Hz, 2C), 41.5 (d, J = 1.5 Hz), 36.8, 32.8, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -116.4 (tt, J = 8.8, 5.4 Hz).

FT-IR (ATR, cm^{-1}): 3003, 2926, 1599, 1509, 1320, 1219, 1157, 1090, 710, 690.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{16}H_{16}FNO_2S$, 306.0959; found, 306.0971.



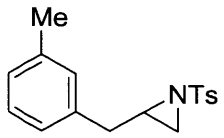
2-(4-methylbenzyl)-1-tosylaziridine (1m): Following the general procedure, starting from 1-allyl-4-methylbenzene (765 μL, 5.0 mmol), **1m** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 47% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.71–7.65 (m, 2H), 7.25–7.20 (m, 2H), 6.99–6.91 (m, 4H), 2.93 (tdd, J = 7.0, 5.3, 4.6 Hz, 1H), 2.76 (dd, J = 14.5, 5.3 Hz, 1H), 2.71–2.61 (m, 2H), 2.43 (s, 3H), 2.30 (s, 3H), 2.15 (d, J = 4.5 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.3, 136.2, 135.1, 134.0, 129.6, 129.2, 128.7, 128.0, 41.5, 37.2, 33.0, 21.8, 21.2.

FT-IR (ATR, cm^{-1}): 2922, 1597, 1515, 1320, 1158, 1090, 710, 690.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{19}NO_2S$, 302.1209; found, 302.1214.



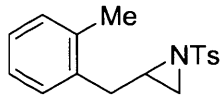
2-(3-methylbenzyl)-1-tosylaziridine (1n): Following the general procedure, starting from 1-allyl-3-methylbenzene (760 μL, 5.0 mmol), **1n** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 55% yield as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.71–7.65 (m, 2H), 7.21 (app d, J = 8.0 Hz, 2H), 7.09–7.03 (m, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.88–6.83 (m, 2H), 2.98–2.91 (m, 1H), 2.76 (dd, J = 14.4, 5.4 Hz, 1H), 2.72 (d, J = 6.9 Hz, 1H), 2.65 (dd, J = 14.4, 7.1 Hz, 1H), 2.42 (s, 3H), 2.24 (s, 3H), 2.17 (d, J = 4.5 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.3, 138.1, 137.1, 135.0, 129.6, 129.6, 128.5, 127.9, 127.4, 125.8, 41.5, 37.6, 33.0, 21.7, 21.4.

FT-IR (ATR, cm^{-1}): 2920, 1597, 1451, 1320, 1157, 1090, 711, 691.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{19}NO_2S$, 302.1209; found, 302.1206.



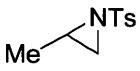
2-(2-methylbenzyl)-1-tosylaziridine (1o): Following the general procedure, starting from 1-allyl-2-methylbenzene (740 μL, 5.0 mmol), **1o** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 42% yield as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.69–7.63 (m, 2H), 7.19 (app d, J = 7.9 Hz, 2H), 7.11–6.96 (m, 4H), 2.95 (tt, J = 6.9, 4.9 Hz, 1H), 2.83 (dd, J = 14.7, 5.1 Hz, 1H), 2.71 (dd, J = 14.7, 6.9 Hz, 1H), 2.71 (d, J = 6.9 Hz, 1H), 2.42 (s, 3H), 2.20 (s, 3H), 2.15 (d, J = 4.5 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.4, 136.2, 135.4, 134.9, 130.3, 129.6, 129.5, 127.9, 126.8, 126.1, 40.6, 34.6, 33.0, 21.7, 19.6.

FT-IR (ATR, cm^{-1}): 2922, 1597, 1451, 1320, 1157, 1090, 710, 690.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{19}NO_2S$, 302.1209; found, 302.1223.



Synthesis of 2-methyl-1-tosylaziridine (1a): The product was synthesized following a procedure analogous to the one described by Kristensen[6]: 2-Methylaziridine (790 μL, 10.0 mmol, 90% purity) was added to a biphasic mixture of EtOAc (15 mL) and 1M K_2CO_3 (15 mL) at 0°C. Under vigorous stirring, a solution of 4-methylbenzenesulfonyl chloride (1.91 g, 10.0 mmol) in EtOAc (15 mL) was added dropwise. After 1 h, the reaction was allowed to reach ambient temperature and stirred for another 12 h. The phases were separated and the organic phase was washed with H_2O (2 x 15 mL), dried over Na_2SO_4 and concentrated. The crude product was subjected to column chromatography on silica gel (EtOAc/hexanes, 25:75) affording the product **1a** in 95% yield as white solid.

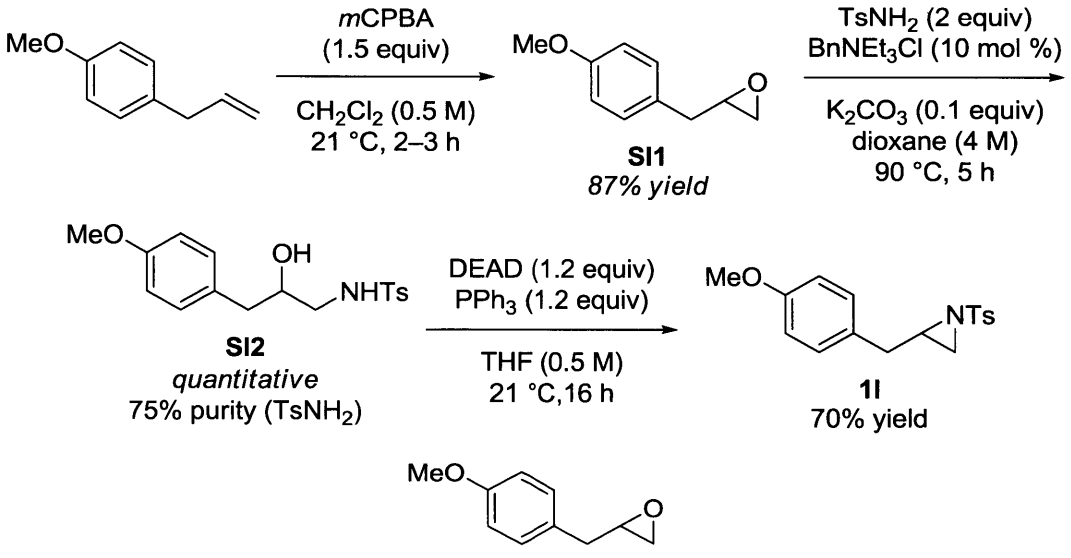
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.85-7.80 (m, 2H), 7.36-7.31 (m, 2H), 2.83 (dqd, J = 6.9, 5.6, 4.6 Hz, 1H), 2.61 (d, J = 7.0 Hz, 1H), 2.44 (s, 3H), 2.02 (d, J = 4.6 Hz, 1H), 1.25 (d, J = 5.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 144.5, 135.5, 129.8, 127.9, 35.9, 34.8, 21.7, 16.9.

FT-IR (ATR, cm^{-1}): 2977, 2931, 1597, 1452, 1399, 1318, 1155, 980, 851, 711, 688.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{10}H_{13}NO_2S$, 212.0740; found, 212.0733.

Synthesis of PMB aziridine (1l)



[6] Bornholdt, J.; Felding, J.; Clausen, R. P.; Kristensen, J. L. *Chem.—Eur. J.* **2010**, *16*, 12474–12480.

2-(4-methoxybenzyl)oxirane (SI1): A solution of 1-allyl-4-methoxybenzene (50.0 mmol, 7.410 g) in CH_2Cl_2 (75 mL) in a 250 mL round bottom flask was cooled to 0°C with an ice bath. *m*-chloroperbenzoic acid (12.1 g of <77% purity; ca. 50 mmol) was added portion wise over 10 minutes. The mixture was allowed to warm to ambient temperature and then stirred until TLC indicated complete consumption of the starting material (approximately 2 h). If complete conversion is not obtained within 2 h, an additional portion of *m*CPBA (ca. 3 g) may be added and the mixture stirred an additional 1 h. After completion, sat. aq. $NaHCO_3$ (75 mL) was slowly added and the mixture was stirred vigorously until gas evolution had ceased, after which the mixture was poured into a separatory funnel. The organic layer was separated and washed with 1 M aq. sodium sulfite, once with brine, and then dried over Na_2SO_4. After removal of the solvent with a rotary evaporator, the crude product was purified by chromatography on silica gel (EtOAc/hexanes, gradient 5:95 to 20:80) to afford the desired product **SI1** in 87% yield as a colorless liquid.

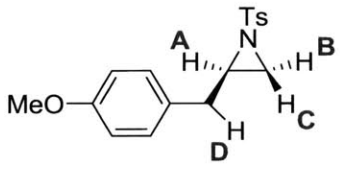
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.20–7.14 (m, 2H), 6.89–6.83 (m, 2H), 3.80 (s, 3H), 3.12 (tdd, J = 5.5, 3.9, 2.7 Hz, 1H), 2.87 (dd, J = 14.6, 5.5 Hz, 1H), 2.81–2.73 (m, 2H), 2.53 (dd, J = 5.0, 2.7 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.4, 129.9, 129.1, 113.9, 55.1, 52.5, 46.6, 37.7.

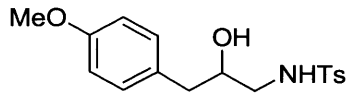
FT-IR (ATR, cm^{-1}): 2995, 2911, 2836, 1612, 1511, 1243, 1177, 1032, 830, 815.

NOEDIFF Analysis of Aziridine (1l)

		Percent enhancement			
	δ (ppm)	2.91	2.70	2.61	2.14
		A	**B**	**D**	**C**
Irradiated proton	**A**		4.6	1.0	
	B	7.2			26.1
	C		27.3	2.8	



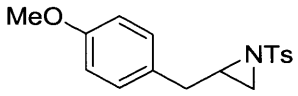
Only the signals relevant to the stereochemical assignment of the ring protons are included. **A** is the methine proton, and **B** (2.70 ppm) and **C** (2.14 ppm) are the geminal protons, where **B** is *cis* to **A**.



***N*-(2-hydroxy-3-(4-methoxyphenyl)propyl)-4-methylbenzenesulfonamide (SI2):** An oven-dried round bottom flask equipped with a magnetic stir bar was charged with epoxide **SI1** (42.2 mmol, 6.93 g), 4-methylbenzenesulfonamide (84.4 mmol, 14.45 g), K_2CO_3 (4.2 mmol, 0.581 g), $BnNEt_3Cl$ (4.2 mmol, 0.957 g), and anhydrous dioxane (10.0 mL). The flask was fitted with a reflux condenser and the mixture was heated to 90°C. When complete consumption of the starting material was indicated by TLC after approximately 5 hours, the mixture was cooled to ambient temperature, diluted with CH_2Cl_2 (50 mL) and then filtered through a 2 cm pad of Celite, which was thoroughly washed with CH_2Cl_2 (150 mL). Purification by flash chromatography on silica gel (EtOAc/hexanes, gradient 35:65 to 80:20) yielded the product **SI2** as a white solid (18.4 g). Based on ^{1}H NMR spectroscopic analysis, the product contained about 40 mol % of $TsNH_2$ as an impurity, which corresponds to ca. 75% purity by mass. Accounting for this, the yield of the desired product is >98%. The mixture was carried on to the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.76–7.69 (m, 2H), 7.35–7.27 (m, 2H), 7.08–7.02 (m, 2H), 6.87–6.80 (m, 2H), 4.91 (br t, J = 6.2 Hz, 1H), 3.86 (dddd, J = 8.3, 7.6, 5.0, 3.3 Hz, 1H), 3.79 (s, 3H), 3.12 (ddd, J = 12.8, 7.0, 3.2 Hz, 1H), 2.86 (ddd, J = 12.5, 7.5, 4.5 Hz, 1H), 2.72 (dd, J = 13.8, 5.0 Hz, 1H), 2.61 (dd, J = 13.8, 8.3 Hz, 1H), 2.43 (s, 3H), 1.99 (br s, 1H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.5, 143.6, 143.6*, 139.3*, 136.7, 130.4, 129.9, 129.8*, 129.1, 127.2, 126.5*, 114.2, 71.4, 55.4, 48.0, 40.2, 21.6, 21.6* (*denotes signals from $TsNH_2$).
HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{21}NO_4S$, 336.1264, found 336.1271.

4-methylbenzenesulfonamide ($TsNH_2$):
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.84–7.79 (m, 2H), 7.33–7.30 (m, 2H), 4.82 (br s, 2H), 2.43 (s, 3H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.8, 139.2, 129.9, 126.6, 21.7.
FT-IR (ATR, cm^{-1}): 3493, 3267, 2922, 1512, 1322, 1245, 1154, 1091, 1032, 811, 728, 662.



2-(4-methoxybenzyl)-1-tosylaziridine (1l): To a dry 250 mL round bottom flask containing a magnetic stir bar was added **SI2** (25 mmol, 11.0 g, 75% purity) and PPh_3 (29.5 mmol, 7.74 g). The flask was fitted with a rubber septum, purged with argon and then THF (50.0 mL) was added. The flask was cooled to 0°C with an ice bath and diethyl azodicarboxylate (DEAD) (29.5 mmol, 5.137 g, 4.65 mL) was added drop-wise over a period of 10 minutes, after which the ice bath was removed and the mixture was allowed to stir at ambient temperature for 16 h. The reaction mixture was evaporated under reduced pressure. Et_2O (200 mL) was added and the reaction was stirred for 20 minutes. The solids were removed by filtration through a 3 cm pad of Celite, washing with Et_2O, and the filtrate was concentrated with a rotary evaporator. This crude oil so obtained was chromatographed on silica gel (EtOAc/hexanes, gradient 20:80 to 45:55), which yielded the desired aziridine **1l** as a white solid (70%). If necessary, recrystallization from hexanes/ethanol can also be carried out.

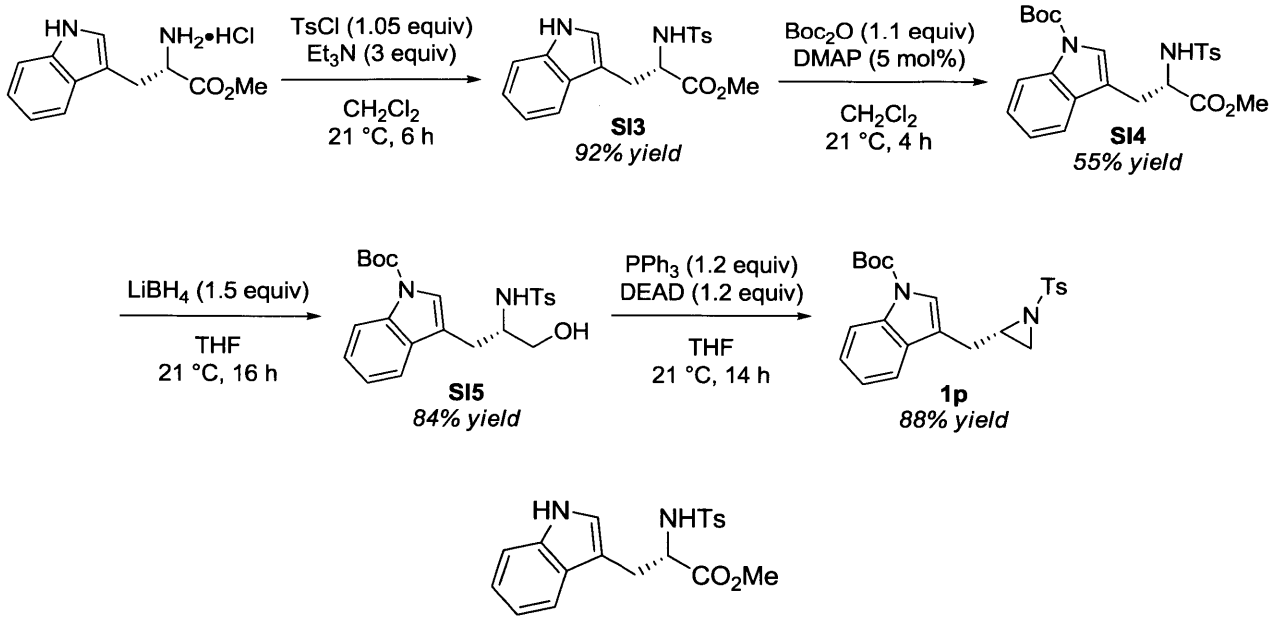
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.70–7.66 (m, 2H), 7.25–7.19 (m, 2H), 6.98–6.92 (m, 2H), 6.71–6.65 (m, 2H), 3.77 (s, 3H), 2.91 (tt, J = 7.1, 4.8 Hz, 1H, **A**), 2.77 (dd, J = 14.5, 5.1 Hz, 1H), 2.70 (d, J = 6.9 Hz, 1H, **B**), 2.61 (dd, J = 14.5, 7.2 Hz, 1H), 2.43 (s, 3H), 2.14 (d, J = 4.6 Hz, 1H, **C**).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.5, 144.4, 135.0, 129.8, 129.6, 129.1, 128.0, 113.9, 55.3, 41.6, 36.7, 32.9, 21.7.

FT-IR (ATR, cm^{-1}): 3001, 2918, 2837, 1512, 1320, 1246, 1158, 711, 693.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{19}NO_3S$, 318.1158, found 318.1158.

Synthesis of Indole Aziridine (1p)



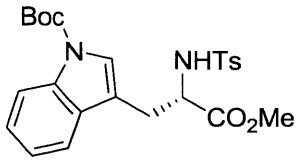
methyl tosyl-L-tryptophanate (SI3): To a suspension of L-tryptophan methyl ester hydrochloride (5.09 g, 20.0 mmol) and 4-methylbenzenesulfonyl chloride (4.00 g, 21.0 mmol) in CH_2Cl_2 (40 mL) at 0°C was added Et_3N (8.40 mL, 60.0 mmol). After 15 min., the mixture was allowed to warm to ambient temperature and stirred for 6 h. The reaction was diluted with H_2O (60 mL) and extracted with Et_2O (2 x 100 mL). The organic phase was washed with sat. aq. NH_4Cl (2 x 60 mL) and brine (60 mL). After drying over Na_2SO_4, the solution was concentrated to afford an off-white solid. The solid was dissolved in a minimum of EtOAc with stirring and hexane was added slowly. The resulting precipitate was filtered off and dried *in vacuo* to afford the product **SI3** in 92% yield as an off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.04 (br s, 1H), 7.64–7.58 (m, 2H), 7.44 (d, J = 7.9 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.21–7.14 (m, 3H), 7.07 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 7.04 (br d, J = 2.3 Hz, 1H), 5.08 (d, J = 8.9 Hz, 1H), 4.25 (dt, J = 8.7, 5.6 Hz, 1H), 3.43 (s, 3H), 3.24 (app d, J = 5.6 Hz, 2H), 2.38 (s, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 171.8, 143.6, 136.7, 136.2, 129.6, 127.3, 127.2, 123.5, 122.3, 119.8, 118.6, 111.4, 109.1, 56.1, 52.5, 29.4, 21.6.

FT-IR (ATR, cm^{-1}): 3402, 3053, 2953, 2921, 1735, 1597, 1427, 1331, 1156, 1089, 908, 729.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{19}H_{20}N_2O_4S$, 373.1217; found, 373.1216.



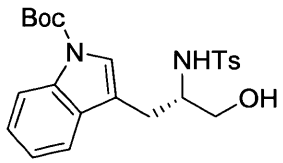
***tert*-butyl 3-(3-methoxy-2-((4-methylphenyl)sulfonamido)-3-oxopropyl)-1*H*-indole-1-carboxylate (SI4):** To a mixture of **SI3** (3.72 g, 10.0 mmol) and di-*tert*-butyl dicarbonate (2.40 g, 11.0 mmol) in dry CH_2Cl_2 (15 mL) at ambient temperature was added 4-dimethylaminepyridine (61 mg, 0.50 mmol). The reaction was stirred for 4 h, after which it was diluted with CH_2Cl_2 (10 mL). The organic phase was washed with H_2O (15 mL), dried (Na_2SO_4) and concentrated. The crude product was subjected to column chromatography on silica gel (EtOAc/hexanes, gradient 5:95 to 25:75) affording the product **SI4** in 55% yield as white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.07 (d, J = 8.3 Hz, 1H), 7.56 (app d, J = 8.3 Hz, 2H), 7.39 (dt, J = 7.8, 1.0 Hz, 1H), 7.36 (s, 1H), 7.29 (ddd, J = 8.7, 7.4, 1.5 Hz, 1H), 7.19 (ddd, J = 8.1, 7.3, 1.1 Hz, 1H), 7.12 (app d, J = 8.1 Hz, 2H), 5.12 (d, J = 9.0 Hz, 1H), 4.25 (ddd, J = 9.1, 6.5, 5.4 Hz, 1H), 3.50 (s, 3H), 3.16 (ddd, J = 14.6, 5.4, 1.0 Hz, 1H), 3.09 (dd, J = 14.6, 6.6 Hz, 1H), 2.36 (s, 3H), 1.68 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 171.6, 149.5, 143.6, 136.5, 135.5, 130.0, 129.5, 127.1, 124.7, 124.6, 122.7, 118.8, 115.4, 114.1, 83.9, 55.8, 52.7, 29.2, 28.3 (3C), 21.7.

FT-IR (ATR, cm^{-1}): 3289, 2981, 1729, 1452, 1369, 1255, 1152, 1085, 729.

HRMS (DART, *m/z*): $[M+NH_4]^+$ calcd for $C_{24}H_{28}N_2O_6S$, 490.2006; found, 490.2000.



***tert*-butyl 3-(3-hydroxy-2-((4-methylphenyl)sulfonamido)propyl)-1*H*-indole-1-carboxylate (SI5):** To a solution of **SI4** (803 mg, 1.70 mmol) in dry THF (5.1 mL) at 0°C was added $LiBH_4$ (56 mg, 2.55 mmol). After 15 min., the mixture was allowed to warm to ambient temperature and stirred for 18 h. The reaction was diluted with EtOAc (20 ml), cooled to 0°C and then quenched by dropwise addition of sat. aq. NH_4Cl until gas evolution ceased. After addition of H_2O (15 mL), the phases were separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (15 ml), dried over Na_2SO_4 and

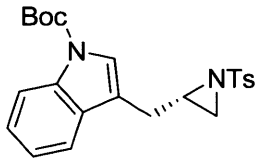
concentrated. The crude product was subjected to column chromatography on silica gel (EtOAc/hexanes, 40:60) affording the product **SI5** in 84% yield as white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.04 (d, J = 8.3 Hz, 1H), 7.43 (app d, J = 8.3 Hz, 2H), 7.30–7.25 (m, 2H), 7.23 (dt, J = 7.8, 1.0 Hz, 1H), 7.12 (ddd, J = 8.0, 7.1, 1.0 Hz, 1H), 6.96 (app d, J = 7.9 Hz, 2H), 4.71 (d, J = 6.7 Hz, 1H), 3.79–3.69 (m, 1H), 3.69–3.61 (m, 1H), 3.52 (dtt, J = 8.6, 6.3, 4.4 Hz, 1H), 2.90 (ddd, J = 14.6, 6.1, 1.0 Hz, 1H), 2.75 (dd, J = 14.6, 8.3 Hz, 1H), 2.32 (s, 3H), 2.11 (br s, 1H), 1.68 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 149.6, 143.4, 136.4, 135.6, 129.9, 129.3, 126.7, 124.5, 124.2, 122.6, 118.7, 115.8, 115.4, 83.8, 65.0, 55.2, 28.3 (3C), 27.5, 21.7.

FT-IR (ATR, cm^{-1}): 2978, 2936, 1727, 1452, 1368, 1256, 1150, 1089, 907, 727.

HRMS (DART, *m/z*): $[M+NH_4]^+$ calcd for $C_{23}H_{28}N_2O_5S$, 462.2057; found, 462.2059.



***tert*-butyl 3-((1-tosylaziridin-2-yl)methyl)-1*H*-indole-1-carboxylate (1p):** Diethyl azodicarboxylate (0.23 mL, 1.48 mmol) was added dropwise to a mixture of **SI5** (600 mg, 1.35 mmol) and PPh_3 (388 mg, 1.48 mmol) in dry THF (2.7 mL) at 0°C. After 10 minutes, reaction was allowed to warm ambient temperature and stirred for 20 h. The reaction was then concentrated and dissolved in a minimum of CH_2Cl_2. Hexane was added, and the resulting precipitate was filtered off. The filtrate was concentrated and the crude product was subjected to column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) affording the product **1p** in 88% yield as white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.06 (br d, J = 8.2 Hz, 1H), 7.52 (app d, J = 8.3 Hz, 2H), 7.37 (d, J = 7.6 Hz, 1H), 7.29 (td, J = 7.8, 7.1, 1.2 Hz, 2H), 7.20–7.15 (m, 1H), 6.96 (d, J = 8.1 Hz, 2H), 3.03–2.94 (m, 2H), 2.82 (d, J = 6.5 Hz, 1H), 2.60 (dd, J = 16.2, 9.1 Hz, 1H), 2.34 (s, 3H), 2.24 (d, J = 4.1 Hz, 1H), 1.67 (s, 9H).

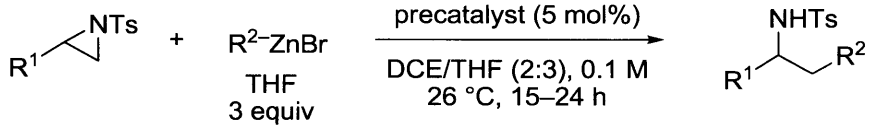
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 149.6, 144.3, 135.4, 134.4, 130.0, 129.1, 127.7, 124.4, 123.6, 122.5, 118.9, 116.1, 115.2, 83.6, 40.1, 33.3, 28.3 (3C), 27.2, 21.9.

FT-IR (ATR, cm^{-1}): 2980, 2927, 1727, 1597, 1452, 1366, 1155, 1090, 908, 727, 710.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{23}H_{26}N_2O_4S$, 427.1686; found, 427.1690.

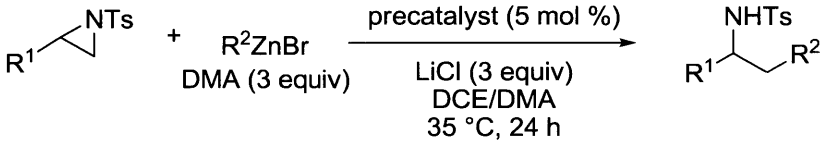
Procedures for Nickel-Catalyzed Cross-Coupling Reactions

Method A (employing commercially available organozinc reagents solutions in THF):[7]



To a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was added aziridine (0.50 mmol) and precatalyst (0.025 mmol, 5 mol %; 11.4 mg for **Me$_4$phen** catalyst or 9.4 mg for **phen** catalyst, respectively). The vial was capped (PTFE-lined screw cap) and purged with nitrogen followed by addition of dichloroethane (DCE) (2.0 mL). The organozinc solution (1.5 mmol, 0.5 M in THF, 3.0 mL) was added.[8] The reaction mixture was stirred at 26°C for 15-24 h in an aluminum block. The reaction was quenched with aq. 3M HCl (2 mL) and extracted with Et_2O (3 x 1 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The crude products were purified by column chromatography on silica gel using pre-packed Biotage SNAP HP-Sil columns (25 g, 25 μm).

Method B (employing synthesized organozinc reagents solutions in DMA):

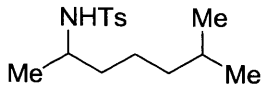


[7] For the screening reactions using $Ni(cod)_2$, a similar protocol was employed with the following modifications: In a glovebox, $Ni(cod)_2$ (10 mol %) and ligand (12.5 mol %) were added to a 4 ml vial. Aziridine (0.4 mmol) and THF (0.2 mL) were then added, but DCE was omitted. The vial was capped with a PTFE-lined screw cap, removed from the glovebox, the 3-methylbutylzinc bromide (0.5 M, 2.4 mL) was added, and the mixture was stirred at ambient temperature for 44 h. After this time, the reactions were worked up according to the general procedure.

[8] Generally, all reactions turned deep blue upon addition of the alkylzinc reagent, after which the reaction slowly turned red/brownish.

To a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was added aziridine (0.50 mmol) and precatalyst (0.025 mmol, 5 mol %; 11.4 mg for **Me_4phen** catalyst or 9.4 mg for **phen** catalyst, respectively). The vial was capped (PTFE-lined screw cap) and purged with nitrogen after which it was transferred to a glovebox. Anhydrous LiCl (64.0 mg, 1.50 mmol) and DCE (2.0 mL) was added. A solution of organozinc bromide in DMA (1.20 mL, 1.25M, 1.50 mmol) was added[8] and the reaction mixture was stirred vigorously at 35°C for 24 h using an aluminum heating block. After cooling to ambient temperature, the reaction was quenched with sat. aq. NH_4Cl (1.5 mL) and diluted with diethylether (1 mL). Phases were separated and the aqueous phase was extracted with Et_2O (2 x 1 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The crude products were purified by column chromatography on silica gel using pre-packed Biotage SNAP HP-Sil columns (25 g, 25 μm).

Characterization of Cross-Coupling Products



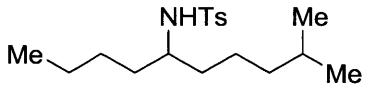
4-methyl-*N*-(6-methylheptan-2-yl)benzenesulfonamide(2): Following the general method **A** (using precatalyst **Me$_4$phen**), **2** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 86% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.79–7.73 (m, 2H), 7.29 (app d, J = 8.0 Hz, 2H), 4.33 (br s, 1H), 3.29 (hept, J = 6.6 Hz, 1H), 2.42 (s, 3H), 1.45–0.97 (m, 7H), 1.04 (d, J = 6.5 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H), 0.78 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.4, 129.7, 127.2, 50.2, 38.6, 37.8, 27.9, 23.4, 22.6, 22.6, 21.9, 21.6.

FT-IR (ATR, cm^{-1}): 3277, 2953, 2933, 2869, 1599, 1423, 1321, 1159, 1094, 813, 661.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{15}H_{25}NO_2S$, 284.1679; found, 284.1693.



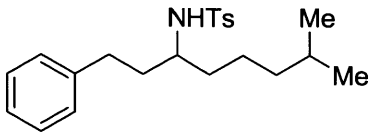
4-methyl-*N*-(9-methyldecan-5-yl)benzenesulfonamide (3): Following the general method **A** (using precatalyst **Me$_4$phen**), **3** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 96% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.78–7.72 (m, 2H), 7.28 (app d, J = 8.0 Hz, 2H), 4.20 (br s, 1H), 3.25–3.14 (m, 1H), 2.42 (s, 3H), 1.46–0.93 (m, 13H), 0.82–0.75 (m, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.6, 129.6, 127.2, 54.3, 38.8, 35.4, 35.0, 27.9, 27.5, 23.2, 22.6 (3C), 21.6, 14.0.

FT-IR (ATR, cm^{-1}): 3282, 2932, 2865, 1599, 1458, 1423, 1321, 1158, 1094, 909, 813, 732, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{18}H_{31}NO_2S$, 326.2148; found, 326.2146.



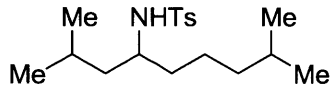
4-methyl-*N*-(7-methyl-1-phenyloctan-3-yl)benzenesulfonamide (4): Following the general method **A** (using precatalyst **Me$_4$phen**), **4** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 94% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.74 (app d, J = 8.2 Hz, 2H), 7.30–7.27 (m, 2H), 7.27–7.22 (m, 2H), 7.20–7.15 (m, 1H), 7.07–7.03 (m, 2H), 4.33 (br s, 1H), 3.26 (h, J = 6.7 Hz, 1H), 2.58 (ddd, J = 14.3, 10.3, 6.4 Hz, 1H), 2.50 (ddd, J = 13.8, 10.3, 6.2 Hz, 1H), 2.42 (s, 3H), 1.73 (ddt, J = 13.9, 10.1, 5.8 Hz, 1H), 1.63 (ddt, J = 13.8, 10.2, 6.4 Hz, 1H), 1.45–1.23 (m, 3H), 1.21–0.93 (m, 4H), 0.78 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 141.7, 138.5, 129.7, 128.5, 128.4, 127.2, 126.0, 54.0, 38.7, 37.1, 35.3, 31.8, 27.9, 23.1, 22.6, 21.6.

FT-IR (ATR, cm^{-1}): 3277, 2951, 2934, 2866, 1599, 1454, 1422, 1321, 1156, 1092, 908, 813, 731, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{31}NO_2S$, 374.2148; found, 374.2154.



***N*-(2,8-dimethylnonan-4-yl)-4-methylbenzenesulfonamide (5):** Following the general method **A** (using precatalyst **Me$_4$phen**), **5** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 89% yield as a colorless oil.

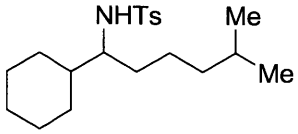
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.79–7.72 (m, 2H), 7.31–7.27 (m, 2H), 4.11 (d, J = 8.5 Hz, 1H), 3.31–3.20 (m, 1H), 2.42 (s, 3H), 1.62–1.49 (m, 1H), 1.44–1.29 (m, 2H), 1.29–0.94 (m, 7H), 0.80 (t, J = 6.5 Hz, 6H), 0.78 (d, J = 6.6 Hz, 3H), 0.74 (d, J = 6.5 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 138.7, 129.6, 127.2, 52.5, 44.9, 38.8, 35.8, 27.9, 24.6, 22.9, 22.9, 22.6, 22.6, 22.4, 21.6.

FT-IR (ATR, cm^{-1}): 3279, 2954, 2937, 2869, 1599, 1459, 1423, 1321, 1158, 1094, 911, 813,

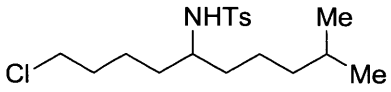
662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{18}H_{31}NO_2S$, 326.2148; found, 326.2166.



***N*-(1-cyclohexyl-5-methylhexyl)-4-methylbenzenesulfonamide (6):** Following the general method **A** (using precatalyst **Me$_4$phen**) at 35°C, **6** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 15%) in 66% yield as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.77–7.72 (m, 2H), 7.30–7.26 (m, 2H), 4.23 (s, 1H), 3.05 (tt, J = 9.0, 4.9 Hz, 1H), 2.41 (s, 3H), 1.75–1.66 (m, 2H), 1.66–1.57 (m, 2H), 1.56–1.47 (m, 1H), 1.41–1.25 (m, 3H), 1.21–0.82 (m, 10H), 0.75 (d, J = 6.6 Hz, 3H), 0.75 (d, J = 6.6 Hz, 3H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 138.8, 129.6, 127.2, 59.2, 41.7, 38.8, 32.1, 28.9, 28.5, 27.9, 26.5, 26.4, 26.4, 23.6, 22.6, 22.5, 21.6.
FT-IR (ATR, cm^{-1}): 3281, 2925, 2853, 1599, 1448, 1323, 1158, 1093, 813, 664.
HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{20}H_{33}NO_2S$, 374.2124; found, 374.2134.

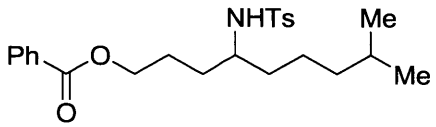


***N*-(1-chloro-9-methyldecan-5-yl)-4-methylbenzenesulfonamide (7):** Following the general method **A** (using precatalyst Me$_4$phen), **7** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 90% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.78–7.74 (m, 2H), 7.31–7.27 (m, 2H), 4.58 (d, J = 8.4 Hz, 1H), 3.41 (t, J = 6.7 Hz, 2H), 3.23–3.13 (m, 1H), 2.41 (s, 3H), 1.63 (p, J = 6.7 Hz, 2H), 1.49–1.20 (m, 7H), 1.17–0.91 (m, 4H), 0.77 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 138.5, 129.7, 127.2, 54.1, 44.8, 38.7, 35.4, 34.6, 32.4, 27.9, 23.2, 22.7, 22.6, 21.6.

FT-IR (ATR, cm^{-1}): 3278, 2950, 2867, 1599, 1448, 1423, 1321, 1154, 1093, 910, 814, 732, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{18}H_{30}ClNO_2S$, 360.1759; found, 360.1747.



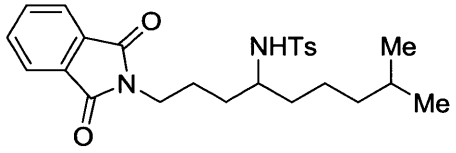
8-methyl-4-((4-methylphenyl)sulfonamido)nonyl benzoate (8): Following the general method **A** (using precatalyst **Me_4phen**), **8** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 85% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.04–7.99 (m, 2H), 7.78–7.73 (m, 2H), 7.59–7.53 (m, 1H), 7.48–7.40 (m, 2H), 7.29–7.24 (m, 2H), 4.28 (br s, 1H), 4.22 (t, J = 6.5 Hz, 2H), 3.33–3.22 (m, 1H), 2.37 (s, 3H), 1.83–1.54 (m, 3H), 1.52–1.21 (m, 4H), 1.18–0.93 (m, 4H), 0.77 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 166.6, 143.4, 138.4, 133.0, 130.4, 129.7, 129.7, 128.5, 127.1, 64.7, 54.0, 38.7, 35.6, 31.9, 27.9, 24.9, 23.3, 22.5, 21.6.

FT-IR (ATR, cm^{-1}): 3281, 2953, 2868, 1717, 1600, 1452, 1316, 1272, 1157, 1094, 908, 730, 710, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{24}H_{33}NO_4S$, 454.2023; found, 454.2012.



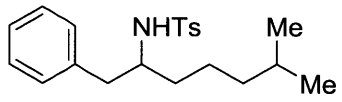
***N*-(1-(1,3-dioxoisoindolin-2-yl)-8-methylnonan-4-yl)-4-methylbenzenesulfonamide (9):** Following the general method **A** (using precatalyst **Me_4phen**) at 40 °C, **9** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 35%) in 69% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.87–7.80 (m, 2H), 7.77–7.68 (m, 4H), 7.26–7.22 (m, 2H), 4.32 (br d, J = 7.7 Hz, 1H), 3.59 (t, J = 7.1 Hz, 2H), 3.30–3.19 (m, 1H), 2.34 (s, 3H), 1.72–1.16 (m, 7H), 1.15–0.88 (m, 4H), 0.75 (d, J = 6.6 Hz, 3H), 0.74 (d, J = 6.6 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 168.4, 143.2, 138.5, 134.0, 132.2, 129.7, 127.1, 123.3, 53.9, 38.6, 37.7, 35.6, 32.5, 27.9, 24.7, 23.2, 22.5, 22.5, 21.5.

FT-IR (ATR, cm^{-1}): 3281, 2951, 2932, 2867, 1771, 1705, 1598, 1396, 1324, 1157, 1092, 909, 719, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_4S$, 479.1975; found, 479.1964.



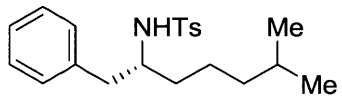
4-methyl-*N*-(6-methyl-1-phenylheptan-2-yl)benzenesulfonamide (10): Following the general method **A** (using precatalyst **Me_4phen**), **10** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 97% yield as waxy solid.

^1H NMR (400 MHz, $CDCl_3$, δ): 7.69–7.64 (m, 2H), 7.26–7.16 (m, 5H), 7.06–7.00 (m, 2H), 4.23 (br s, 1H), 3.47–3.36 (m, 1H), 2.70 (app d, J = 6.2 Hz, 2H), 2.41 (s, 3H), 1.47–1.13 (m, 4H), 1.12–0.93 (m, 3H), 0.77 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.0, 137.4, 129.7, 129.7, 128.6, 127.2, 126.6, 55.2, 41.7, 38.6, 34.7, 28.0, 23.3, 22.6, 22.5, 21.6.

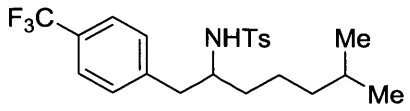
FT-IR (ATR, cm^{-1}): 3280, 2952, 2930, 2867, 1599, 1454, 1420, 1322, 1156, 1092, 908, 813, 731, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{21}H_{29}NO_2S$, 382.1811; found, 382.1821.



(*R*)-4-methyl-*N*-(6-methyl-1-phenylheptan-2-yl)benzenesulfonamide (*R*-10): Following the general method **A** (using precatalyst **Me_4phen**), (*R*)-**10** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 96% yield as white solid. The enantiomeric excess was determined by HPLC using a Chiralpak AD-H column [hexane/*i*-PrOH (90:10)]; flow rate 1.0 ml/min; τ_{major} = 9.7 min, τ_{minor} = 8.8 min (>99% ee).

$[\alpha]_D^{20}$ = + 1.2° (c = 2.5, CH_2Cl_2).



4-methyl-*N*-(6-methyl-1-(4-(trifluoromethyl)phenyl)heptan-2-yl)benzenesulfonamide (11): Following the general method **A** (using precatalyst **Me$_4$phen**), **11** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 84% yield as white solid.

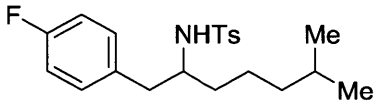
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.63–7.58 (m, 2H), 7.44 (app d, J = 8.0 Hz, 2H), 7.24–7.18 (m, 2H), 7.15 (app d, J = 8.0 Hz, 2H), 4.27 (d, J = 8.2 Hz, 1H), 3.49–3.38 (m, 1H), 2.82 (dd, J = 13.6, 6.4 Hz, 1H), 2.73 (dd, J = 13.6, 6.3 Hz, 1H), 2.40 (s, 3H), 1.47–1.14 (m, 4H), 1.13–0.95 (m, 3H), 0.78 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 141.9 (q, J = 1.5 Hz), 137.8, 129.9, 129.6, 128.8 (q, J = 32.3 Hz), 127.0, 125.3 (q, J = 3.8 Hz, 2C), 124.3 (q, J = 271.9 Hz), 55.3, 41.6, 38.6, 35.3, 27.9, 23.3, 22.5, 22.5, 21.5.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -62.4 (s).

FT-IR (ATR, cm^{-1}): 3277, 2958, 2933, 2870, 1619, 1598, 1464, 1443, 1312, 1151, 1131, 1112, 1068, 1021, 811, 663.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{28}F_3NO_2S$, 428.1866; found, 428.1845.



***N*-(1-(4-fluorophenyl)-6-methylheptan-2-yl)-4-methylbenzenesulfonamide (12):** Following the general method **A** (using precatalyst **Me$_4$phen**), **12** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 96% yield as white solid.

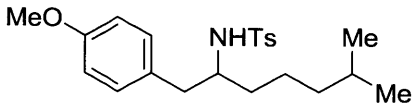
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.69–7.64 (m, 2H), 7.26 (app d, J = 8.1 Hz, 2H), 7.04–6.98 (m, 2H), 6.94–6.87 (m, 2H), 4.26 (br s, 1H), 3.48–3.32 (m, 1H), 2.74 (dd, J = 13.8, 6.5 Hz, 1H), 2.67 (dd, J = 13.8, 6.0 Hz, 1H), 2.44 (s, 3H), 1.48–1.15 (m, 4H), 1.14–0.95 (m, 3H), 0.80 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 161.8 (d, J = 244.6 Hz), 143.3, 138.0, 133.2 (d, J = 3.3 Hz), 131.0 (d, J = 7.9 Hz, 2C), 129.7, 127.1, 115.3 (d, J = 21.2 Hz, 2C), 55.4 (d, J = 0.7 Hz) , 40.9, 38.6, 34.9, 28.0, 23.3, 22.6, 22.5, 21.6.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -116.5 (tt, J = 8.8, 5.4 Hz).

FT-IR (ATR, cm^{-1}): 3280, 2951, 2929, 2868, 1600, 1510, 1322, 1221, 1155, 1093, 812, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{21}H_{28}FNO_2S$, 400.1717; found, 400.1712.



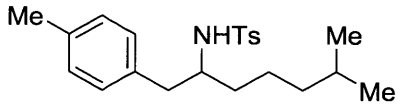
***N*-(1-(4-methoxyphenyl)-6-methylheptan-2-yl)-4-methylbenzenesulfonamide (13):** Following the general method **A** (using precatalyst **Me$_4$phen**), **13** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 15:85 to 25:75) in 97% yield as colorless, viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.63 (m, 2H), 7.25–7.21 (m, 2H), 6.96–6.91 (m, 2H), 6.77–6.72 (m, 2H), 4.18 (d, J = 8.1 Hz, 1H), 3.78 (s, 3H), 3.37 (ddt, J = 13.8, 7.8, 5.8 Hz, 1H), 2.70–2.58 (m, 2H), 2.41 (s, 3H), 1.46–0.91 (m, 7H), 0.78 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.4, 143.1, 143.1, 138.1, 138.1, 130.5, 129.6, 129.4, 129.3, 127.1, 113.9, 55.4, 55.4, 55.3, 40.6, 40.6, 38.6, 34.7, 27.9, 23.3, 22.6, 22.5, 21.6.

FT-IR (ATR, cm^{-1}): 3283, 2950, 2867, 1612, 1512, 1246, 1156, 812, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{31}NO_3S$, 390.2097, found 390.2105.



4-methyl-*N*-(6-methyl-1-(*p*-tolyl)heptan-2-yl)benzenesulfonamide (14): Following the general method **A** (using precatalyst **Me$_4$phen**), **14** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 97% yield as colorless oil.

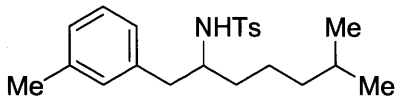
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.62 (m, 2H), 7.25–7.20 (m, 2H), 7.02 (app d, J = 7.7 Hz, 2H), 6.93–6.88 (m, 2H), 4.19 (br s, 1H), 3.46–3.32 (m, 1H), 2.70–2.59 (m, 2H), 2.41 (s, 3H), 2.31 (s, 3H), 1.46–1.14 (m, 4H), 1.13–0.93 (m, 3H), 0.78 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 138.1, 136.2, 134.2, 129.6, 129.5, 129.2, 127.2,

55.2, 41.1, 38.6, 34.8, 28.0, 23.3, 22.6, 22.6, 21.6, 21.2.

FT-IR (ATR, cm^{-1}): 3283, 2951, 2927, 2867, 1599, 1448, 1420, 1156, 1093, 909, 812, 731, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{31}NO_2S$, 374.2148; found, 374.2153.



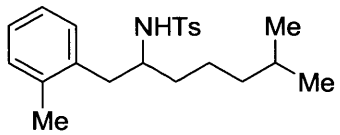
4-methyl-*N*-(6-methyl-1-(*m*-tolyl)heptan-2-yl)benzenesulfonamide (15): Following the general method **A** (using precatalyst **Me_4phen**), **15** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 95% yield as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.66–7.61 (m, 2H), 7.25–7.20 (m, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.02–6.98 (m, 1H), 6.84–6.78 (m, 2H), 4.19 (d, *J* = 7.9 Hz, 1H), 3.40 (ddt, *J* = 13.7, 7.7, 6.1 Hz, 1H), 2.70–2.60 (m, 2H), 2.41 (s, 3H), 2.27 (s, 3H), 1.48–0.95 (m, 7H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.0, 138.0, 138.0, 137.4, 130.3, 129.6, 128.4, 127.3, 127.1, 126.6, 55.3, 41.5, 38.6, 34.8, 27.9, 23.3, 22.6, 22.5, 21.6, 21.4.

FT-IR (ATR, cm^{-1}): 3281, 3024, 2952, 2926, 2867, 1599, 1322, 1156, 1092, 813, 732, 701, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{31}NO_2S$, 374.2148, found 374.2158.



4-methyl-*N*-(6-methyl-1-(*o*-tolyl)heptan-2-yl)benzenesulfonamide (16): Following the general method **A** (using precatalyst **Me_4phen**), **16** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 96% yield as waxy solid

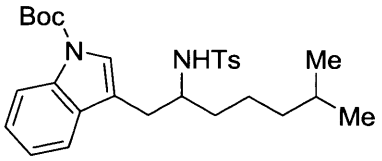
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.59 (app d, *J* = 8.3 Hz, 2H), 7.19 (app d, *J* = 8.0 Hz, 2H), 7.12–7.02 (m, 3H), 6.98–6.93 (m, 1H), 4.32 (br s, 1H), 3.42–3.31 (m, 1H), 2.77 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.69 (dd, *J* = 13.8, 7.7 Hz, 1H), 2.39 (s, 3H), 2.18 (s, 3H), 1.50–1.30 (m, 3H), 1.27–1.15 (m, 1H), 1.09–0.94 (m, 3H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 137.8, 136.5, 136.1, 130.6, 130.5, 129.6, 127.1,

126.8, 126.0, 54.4, 39.7, 38.7, 35.1, 28.0, 23.3, 22.6, 22.5, 21.6, 19.6.

FT-IR (ATR, cm^{-1}): 3280, 2952, 2868, 1599, 1458, 1420, 1322, 1156, 1093, 908, 813, 730, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{22}H_{31}NO_2S$, 396.1968; found, 396.1955.



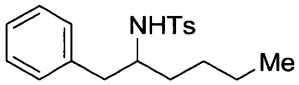
***tert*-butyl 3-(6-methyl-2-((4-methylphenyl)sulfonamido)heptyl)-1*H*-indole-1-carboxylate (17):** Following the general method **A** (using precatalyst **Me$_4$phen**), **17** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 93% yield as white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.05 (br d, *J* = 7.7 Hz, 1H), 7.52 (app d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.31–7.26 (m, 2H), 7.18 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H), 7.04 (app d, *J* = 8.1 Hz, 2H), 4.32 (br s, 1H), 3.48 (h, *J* = 6.7 Hz, 1H), 2.82 (dd, *J* = 14.6, 6.1 Hz, 1H), 2.75 (dd, *J* = 14.4, 6.7 Hz, 1H), 2.33 (s, 3H), 1.68 (s, 9H), 1.59–1.35 (m, 3H), 1.32–1.00 (m, 4H), 0.80 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 149.6, 143.0, 137.5, 135.6, 130.4, 129.3, 126.8, 124.4, 124.1, 122.6, 119.1, 116.4, 115.3, 83.7, 54.0, 38.7, 35.8, 31.3, 28.3 (3C), 28.0, 23.4, 22.6, 22.6, 21.6.

FT-IR (ATR, cm^{-1}): 3279, 2930, 2868, 1729, 1599, 1452, 1368, 1255, 1152, 1086, 731, 663.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{28}H_{38}N_2O_4S$, 521.2444; found, 521.2450.



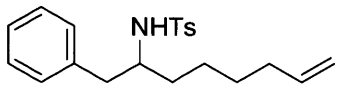
4-methyl-*N*-(1-phenylhexan-2-yl)benzenesulfonamide (18): Following the general method **A** (using precatalyst **Me$_4$phen**), **18** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 95% yield as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.63 (m, 2H), 7.26–7.16 (m, 5H), 7.03–6.99 (m, 2H), 4.23 (br s, 1H), 3.42 (tq, *J* = 7.8, 6.1 Hz, 1H), 2.68 (app d, *J* = 6.2 Hz, 2H), 2.41 (s, 3H), 1.50–1.38 (m, 1H), 1.36–1.07 (m, 5H), 0.77 (t, *J* = 7.0 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.0, 137.4, 129.7, 129.6, 128.6, 127.1, 126.6, 55.1, 41.4, 34.1, 27.6, 22.4, 21.6, 14.0.

FT-IR (ATR, cm^{-1}): 3282, 3028, 2932, 2862, 1599, 1454, 1420, 1321, 1155, 1092, 909, 813, 730, 699, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{19}H_{25}NO_2S$, 354.1498; found, 354.1508.



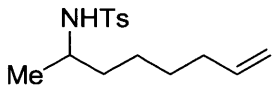
4-methyl-*N*-(1-phenyloct-7-en-2-yl)benzenesulfonamide (19): Following the general method **A** (using precatalyst **Me_4phen**), **19** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 85% yield as a colorless oil.

^1H NMR (400 MHz, $CDCl_3$, δ): 7.69–7.62 (m, 2H), 7.26–7.16 (m, 5H), 7.06–6.97 (m, 2H), 5.70 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 4.97–4.87 (m, 2H), 4.20 (d, J = 8.1 Hz, 1H), 3.42 (ddt, J = 11.9, 7.7, 6.2 Hz, 1H), 2.68 (d, J = 6.2 Hz, 2H), 2.41 (s, 3H), 1.95–1.87 (m, 2H), 1.51–1.37 (m, 1H), 1.37–1.07 (m, 5H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.7, 138.0, 137.3, 129.7, 129.6, 128.6, 127.1, 126.6, 114.5, 55.1, 41.5, 34.2, 33.6, 28.5, 24.9, 21.6.

FT-IR (ATR, cm^{-1}): 3278, 2927, 2859, 1640, 1599, 1496, 1454, 1419, 1322, 1154, 1090, 908, 813, 750, 700, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{21}H_{27}NO_2S$, 358.1835, found 358.1847.



4-methyl-*N*-(oct-7-en-2-yl)benzenesulfonamide (20): Following the general method **A** (using precatalyst **Me_4phen**), **20** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 78% yield as colorless oil.

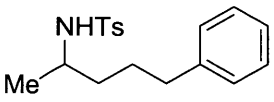
^1H NMR (400 MHz, $CDCl_3$, δ): 7.78–7.73 (m, 2H), 7.29 (app d, J = 7.9 Hz, 2H), 5.72 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H), 4.99–4.88 (m, 2H), 4.24 (br d, J = 8.1 Hz, 1H), 3.29 (dh, J = 8.1, 6.5 Hz, 1H), 2.42 (s, 3H), 1.94 (tdd, J = 6.6, 5.3, 1.4 Hz, 2H), 1.40–1.30 (m, 2H), 1.29–1.08 (m, 4H),

1.03 (d, J = 6.6 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.8, 138.4, 129.7, 127.2, 114.5, 50.0, 37.4, 33.6, 28.6, 25.1, 21.8, 21.6.

FT-IR (ATR, cm^{-1}): 3275, 2975, 2931, 2859, 1640, 1599, 1424, 1320, 1157, 1092, 907, 814, 661.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{15}H_{23}NO_2S$, 282.1522; found, 282.1511.



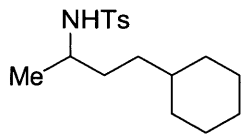
4-methyl-*N*-(5-phenylpentan-2-yl)benzenesulfonamide (21): Following the general method **A** (using precatalyst **phen**), **21** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 73% yield as colorless oil.

^1H NMR (400 MHz, $CDCl_3$, δ): 7.78–7.71 (m, 2H), 7.30–7.22 (m, 4H), 7.20–7.14 (m, 1H), 7.10–7.05 (m, 2H), 4.25 (d, J = 8.2 Hz, 1H), 3.34 (dh, J = 8.2, 6.5 Hz, 1H), 2.49 (t, J = 7.6 Hz, 2H), 2.41 (s, 3H), 1.64–1.34 (m, 4H), 1.01 (d, J = 6.5 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.3, 142.1, 138.4, 129.7, 128.4, 128.4, 127.1, 125.9, 50.0, 37.1, 35.5, 27.3, 21.9, 21.6.

FT-IR (ATR, cm^{-1}): 3273, 3026, 2968, 2930, 2861, 1599, 1495, 1453, 1424, 1318, 1155, 1090, 813, 698, 661.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{18}H_{23}NO_2S$, 318.1522; found, 318.1510.



***N*-(4-cyclohexylbutan-2-yl)-4-methylbenzenesulfonamide (22):** Following the general method **A** (using precatalyst **Me_4phen**) at 35°C, **22** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 72% yield as colorless oil.

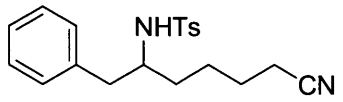
^1H NMR (400 MHz, $CDCl_3$, δ): 7.78–7.73 (m, 2H), 7.32–7.27 (m, 2H), 4.16 (br d, J = 8.3 Hz, 1H), 3.26 (dh, J = 8.2, 6.6 Hz, 1H), 2.42 (s, 3H), 1.71–1.45 (m, 5H), 1.39–1.28 (m, 2H), 1.21–

0.92 (m, 6H), 1.03 (d, J = 6.5 Hz, 3H), 0.84–0.68 (m, 2H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.2, 138.4, 129.7, 127.2, 50.3, 37.3, 34.8, 33.3, 33.2, 33.1, 26.7, 26.4, 21.9, 21.6.

FT-IR (ATR, cm^{-1}): 3273, 2922, 2851, 1599, 1448, 1425, 1319, 1159, 1093, 907, 813, 729, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{17}H_{27}NO_2S$, 332.1655; found, 332.1661.



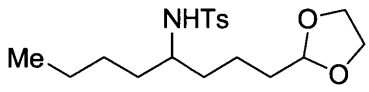
***N*-(6-cyano-1-phenylhexan-2-yl)-4-methylbenzenesulfonamide (23):** Following the general method **A** (using precatalyst **Me_4phen**) at 35 °C, **23** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 35%) in 70% yield as a pale yellow oil. The product was dried under vacuum (50 mTorr at 80°C) for 8 h to remove traces of 1,6-dicyanohexane, which partially co-elutes with the product.

^1H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.60 (m, 2H), 7.28–7.17 (m, 5H), 7.00–6.94 (m, 2H), 4.22 (d, J = 8.2 Hz, 1H), 3.43 (ddt, J = 12.8, 8.1, 6.4 Hz, 1H), 2.70–2.58 (m, 2H), 2.43 (s, 3H), 2.22 (t, J = 7.0 Hz, 2H), 1.60–1.30 (m, 6H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 143.3, 137.7, 137.1, 129.7, 129.3, 128.6, 127.0, 126.6, 119.6, 54.8, 41.4, 33.4, 25.0, 24.5, 21.5, 16.9.

FT-IR (ATR, cm^{-1}): 3280, 2943, 2864, 2255, 1599, 1323, 1154, 1089, 907, 726, 701, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{20}H_{24}N_2O_2S$, 357.1631, found 357.1627.



***N*-(1-(1,3-dioxolan-2-yl)octan-4-yl)-4-methylbenzenesulfonamide (24):** To a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was added aziridine (0.50 mmol) and precatalyst **phen** (9.4 mg, 0.025 mmol, 5 mol %). The vial was capped (PTFE-lined screw cap) and purged with nitrogen after which it was transferred to a glovebox. Anhydrous LiCl (64.0 mg, 1.50 mmol), DCE (1.0 mL) and DMA (1.0 mL) was added followed by the organozinc solution (1.5 mmol, 0.5M in THF, 3.0 mL). The reaction was stirred at 35°C for 24 h in an aluminum

heating block. After cooling to ambient temperature, the reaction was quenched with sat. aq. NH_4Cl (1.5 mL) and diluted with Et_2O (1 mL). Phases were separated and the aqueous phase was extracted with diethylether (2 x 1 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The crude products were purified by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 35%) to afford the product **24** in 76% yield as colorless oil.

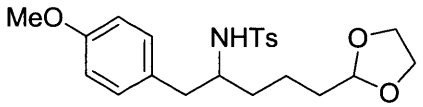
Product is unstable to acid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.77–7.72 (m, 2H), 7.31–7.27 (m, 2H), 4.73 (t, J = 4.7 Hz, 1H), 4.18 (d, J = 8.4 Hz, 1H), 3.98–3.88 (m, 2H), 3.88–3.76 (m, 2H), 3.26–3.15 (m, 1H), 2.42 (s, 3H), 1.55–1.21 (m, 8H), 1.21–1.01 (m, 4H), 0.78 (t, J = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 138.5, 129.6, 127.1, 104.4, 64.9, 54.1, 35.0, 34.6, 33.6, 27.5, 22.5, 21.6, 19.8, 14.0.

FT-IR (ATR, cm^{-1}): 3280, 2930, 2864, 1598, 1425, 1322, 1156, 1092, 1026, 942, 814, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{18}H_{29}NO_4S$, 378.1710; found, 378.1703.



***N*-(5-(1,3-dioxolan-2-yl)-1-(4-methoxyphenyl)pentan-2-yl)-4-methylbenzene sulfonamide (25):** To a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was added aziridine (0.50 mmol) and precatalyst **Me$_4$phen** (11.4 mg, 0.025 mmol, 5 mol %). The vial was capped (PTFE-lined screw cap) and purged with nitrogen after which it was transferred to a glovebox. Anhydrous LiCl (64.0 mg, 1.50 mmol), DCE (1.0 mL) and DMA (1.0 mL) was added followed by the organozinc solution (1.5 mmol, 0.5M in THF, 3.0 mL). The reaction was stirred at 35°C for 24 h in an aluminum heating block. After cooling to ambient temperature, the reaction was quenched with sat. aq. NH_4Cl (1.5 mL) and diluted with Et_2O (1 mL). Phases were separated and the aqueous phase was extracted with Et_2O (2 x 1 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The crude products were purified by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 35%) to afford the product **25** in 80% yield as colorless oil.

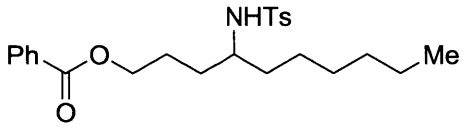
Product is unstable to acid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.65–7.61 (m, 2H), 7.25–7.20 (m, 2H), 6.92–6.87 (m, 2H), 6.76–6.70 (m, 2H), 4.73 (t, *J* = 4.6 Hz, 1H), 4.25 (d, *J* = 8.2 Hz, 1H), 3.97–3.87 (m, 2H), 3.86–3.79 (m, 2H), 3.78 (s, 3H), 3.42–3.32 (m, 1H), 2.64 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.57 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.41 (s, 3H), 1.56–1.24 (m, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.4, 143.1, 137.9, 130.5, 129.6, 129.1, 127.1, 114.0, 104.3, 64.9, 55.3, 55.2, 40.2, 34.3, 33.4, 21.6, 19.9.

FT-IR (ATR, cm^{-1}): 3289, 2948, 2880, 1612, 1512, 1322, 1302, 1247, 1156, 1092, 1033, 907, 725, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{22}H_{29}NO_5S$, 442.1659; found, 442.1660.



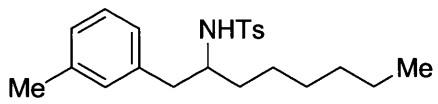
4-((4-methylphenyl)sulfonamido)decyl benzoate (26): Following the general method **B** (using precatalyst **phen**), **26** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 84% yield as white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.04–7.98 (m, 2H), 7.77–7.73 (m, 2H), 7.60–7.53 (m, 1H), 7.48–7.41 (m, 2H), 7.29–7.24 (m, 2H), 4.24 (br s, 1H), 4.22 (t, *J* = 6.6 Hz, 2H), 3.34–3.22 (m, 1H), 2.38 (s, 3H), 1.84–1.57 (m, 3H), 1.51–0.99 (m, 11H), 0.84 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 166.6, 143.3, 138.4, 133.0, 130.4, 129.7, 129.6, 128.5, 127.1, 64.7, 53.9, 35.2, 31.8, 31.7, 29.1, 25.4, 24.8, 22.6, 21.6, 14.2.

FT-IR (ATR, cm^{-1}): 3284, 2929, 2958, 1716, 1600, 1452, 1316, 1273, 1157, 1094, 907, 729, 710, 663.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{24}H_{33}NO_4S$, 454.2023; found, 454.2017.



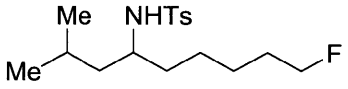
4-methyl-*N*-(1-(*m*-tolyl)octan-2-yl)benzenesulfonamide (27): Following the general method **B** (using precatalyst **phen**), **27** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 93% yield as pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.66–7.61 (m, 2H), 7.25–7.20 (m, 2H), 7.10 (t, J = 7.5 Hz, 1H), 6.99 (d, J = 7.6 Hz, 1H), 6.83–6.77 (m, 2H), 4.23 (br s, 1H), 3.40 (tq, J = 7.7, 6.1 Hz, 1H), 2.66 (dd, J = 13.6, 6.5 Hz, 1H), 2.61 (dd, J = 13.5, 5.9 Hz, 1H), 2.41 (s, 3H), 2.27 (s, 3H), 1.49–1.39 (m, 1H), 1.38–1.08 (m, 9H), 0.84 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 138.1, 138.0, 137.3, 130.3, 129.6, 128.5, 127.4, 127.1, 126.6, 55.2, 41.4, 34.6, 31.8, 29.0, 25.4, 22.6, 21.6, 21.5, 14.2.

FT-IR (ATR, cm^{-1}): 3282, 2926, 2857, 1599, 1449, 1421, 1322, 1155, 1092, 813, 732, 701, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{22}H_{31}NO_2S$, 396.1968; found, 396.1958.



***N*-(9-fluoro-2-methylnonan-4-yl)-4-methylbenzenesulfonamide (28):** Following the general method **B** (using precatalyst **phen**), **28** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 89% yield as a colorless oil.

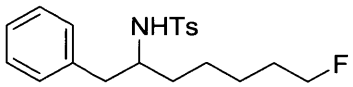
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.80–7.71 (m, 2H), 7.34–7.26 (m, 2H), 4.37 (dt, J = 47.3, 6.1 Hz, 2H), 4.22–4.12 (m, 1H), 3.26 (ddt, J = 14.3, 8.3, 6.4 Hz, 1H), 2.42 (s, 3H), 1.66–1.46 (m, 3H), 1.46–1.35 (m, 1H), 1.35–1.10 (m, 7H), 0.78 (d, J = 6.6 Hz, 3H), 0.71 (d, J = 6.5 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.1, 138.6, 129.5, 127.1, 83.9 (d, J = 164.1 Hz), 52.2, 44.6, 35.2, 30.2 (d, J = 19.5 Hz), 25.0 (d, J = 5.5 Hz), 24.6, 24.5, 22.7, 22.2, 21.5.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -218.29 (tt, J = 47.4, 25.1 Hz).

FT-IR (ATR, cm^{-1}): 3279, 2955, 2868, 1599, 1320, 1157, 1094, 910, 814, 731, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{28}FNO_2S$, 330.1898, found 330.1913.



***N*-(7-fluoro-1-phenylheptan-2-yl)-4-methylbenzenesulfonamide (29):** Following the general method **B** (using precatalyst **Me$_4$phen**), **29** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 89% yield as colorless oil.

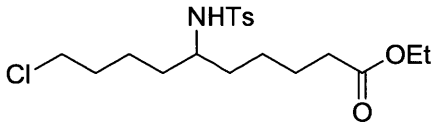
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.63 (m, 2H), 7.26–7.17 (m, 5H), 7.03–6.97 (m, 2H), 4.35 (dt, J = 47.3, 6.1 Hz, 2H), 4.25 (br s, 1H), 3.50–3.37 (m, 1H), 2.67 (app d, J = 6.3 Hz, 2H), 2.41 (s, 3H), 1.64–1.40 (m, 3H), 1.39–1.13 (m, 5H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 138.0, 137.3, 129.7, 129.5, 128.6, 127.1, 126.65, 84.0 (d, J = 164.3 Hz), 55.0, 41.5, 34.3, 30.3 (d, J = 19.5 Hz), 25.1, 24.9 (d, J = 5.5 Hz), 21.6.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -218.2 (tt, J = 47.7, 25.3 Hz).

FT-IR (ATR, cm^{-1}): 3281, 2936, 2861, 1599, 1454, 1424, 1322, 1154, 1092, 1032, 909, 814, 731, 700, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{20}H_{26}FNO_2S$, 364.1741; found, 346.1746.



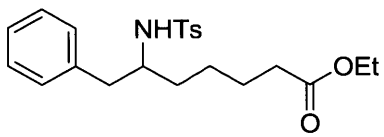
ethyl 10-chloro-6-((4-methylphenyl)sulfonamido)decanoate (30): Following the general method **B** (using precatalyst **phen**), **30** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 30%) in 80% yield as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.77–7.72 (m, 2H), 7.33–7.27 (m, 2H), 4.23 (d, J = 8.6 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.40 (t, J = 6.6 Hz, 2H), 3.27–3.15 (m, 1H), 2.43 (s, 3H), 2.17 (t, J = 7.5 Hz, 2H), 1.62 (p, J = 6.7 Hz, 2H), 1.48 (p, J = 7.6 Hz, 2H), 1.43–1.08 (m, 8H), 1.25 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 173.6, 143.4, 138.4, 129.7, 127.1, 60.3, 53.8, 44.7, 34.8, 34.3, 34.1, 32.3, 24.9, 24.7, 22.7, 21.6, 14.3.

FT-IR (ATR, cm^{-1}): 3281, 2942, 2864, 1730, 1598, 1447, 1424, 1322, 1153, 1091, 1023, 814, 662.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{19}H_{30}ClNO_4S$, 426.1476; found, 426.1460.



ethyl 6-((4-methylphenyl)sulfonamido)-7-phenylheptanoate (31): Following the general method **B** (using precatalyst **Me$_4$phen**), **31** was isolated by column chromatography on silica

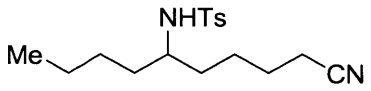
gel (EtOAc/hexanes, gradient 0% to 30%) in 90% yield as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.67–7.62 (m, 2H), 7.25–7.15 (m, 5H), 7.01–6.96 (m, 2H), 4.25 (d, J = 8.2 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.43 (tq, J = 7.9, 6.1 Hz, 1H), 2.65 (app d, J = 6.4 Hz, 2H), 2.41 (s, 3H), 2.16 (t, J = 7.5 Hz, 2H), 1.53–1.41 (m, 3H), 1.38–1.13 (m, 3H), 1.25 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 173.6, 143.3, 138.0, 137.1, 129.7, 129.6, 128.6, 127.1, 126.7, 60.4, 54.9, 41.4, 34.1, 34.1, 25.0, 24.6, 21.6, 14.4.

FT-IR (ATR, cm^{-1}): 3283, 2936, 2865, 1729, 1599, 1454, 1420, 1323, 1153, 1089, 1030, 911, 814, 730, 662.

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{29}NO_4S$, 404.1890; found, 404.1886.



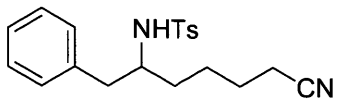
***N*-(1-cyanononan-5-yl)-4-methylbenzenesulfonamide (32):** Following the general method **B** (using precatalyst **phen** with DME in place of DCE), **32** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 35%) in 79% yield as a pale yellow oil. The product was dried under vacuum (50 mTorr at 80°C) for 8 h to remove traces of 1,6-dicyanohexane, which partially co-elutes with the product.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.79–7.71 (m, 2H), 7.35–7.28 (m, 2H), 4.20 (d, J = 8.5 Hz, 1H), 3.20 (ddt, J = 12.2, 8.4, 6.4 Hz, 1H), 2.43 (s, 3H), 2.25 (t, J = 7.1 Hz, 2H), 1.61–1.20 (m, 8H), 1.20–0.98 (m, 4H), 0.76 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 138.3, 129.6, 127.0, 119.7, 53.7, 34.7, 34.2, 27.4, 25.2, 24.4, 22.4, 21.5, 17.0, 13.9.

FT-IR (ATR, cm^{-1}): 3279, 2931, 2862, 2247, 1598, 1321, 1155, 1092, 1026, 815, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{17}H_{26}N_2O_2S$, 323.1788, found 323.1800.



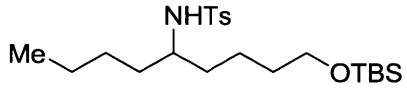
***N*-(6-cyano-1-phenylhexan-2-yl)-4-methylbenzenesulfonamide (23):** Following the general method **B** (using precatalyst **phen** with DME in place of DCE), **32** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 35%) in 82% yield as a pale yellow oil. The product was dried under vacuum (50 mTorr at 80°C) for 8 h to remove traces of 1,6-dicyanohexane, which partially co-elutes with the product.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.60 (m, 2H), 7.28–7.17 (m, 5H), 7.00–6.94 (m, 2H), 4.22 (d, J = 8.2 Hz, 1H), 3.43 (ddt, J = 12.8, 8.1, 6.4 Hz, 1H), 2.70–2.58 (m, 2H), 2.43 (s, 3H), 2.22 (t, J = 7.0 Hz, 2H), 1.60–1.30 (m, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 137.7, 137.1, 129.7, 129.3, 128.6, 127.0, 126.6, 119.6, 54.8, 41.4, 33.4, 25.0, 24.5, 21.5, 16.9.

FT-IR (ATR, cm^{-1}): 3280, 2943, 2864, 2255, 1599, 1323, 1154, 1089, 907, 726, 701, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{20}H_{24}N_2O_2S$, 357.1631, found 357.1627.



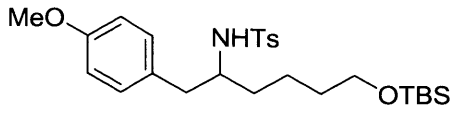
***N*-(1-((tert-butyldimethylsilyl)oxy)nonan-5-yl)-4-methylbenzenesulfonamide (33):** Following the general method **B** (using precatalyst **phen**), **33** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 20%) in 86% yield a colorless, viscous oil. This product was dried under vacuum (50 mTorr at 80 °C) for 4 h to remove traces of TBS–OH, which partially co-elutes with the product.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.79–7.70 (m, 2H), 7.30–7.26 (m, 2H), 4.14 (d, J = 8.5 Hz, 1H), 3.50 (td, J = 6.5, 2.7 Hz, 2H), 3.20 (dq, J = 8.4, 6.1 Hz, 1H), 2.42 (s, 3H), 1.45–1.01 (m, 12H), 0.88 (s, 9H), 0.78 (t, J = 7.0 Hz, 3H), 0.03 (s, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.0, 138.7, 129.5, 127.1, 62.9, 54.1, 34.8, 34.6, 32.6, 27.4, 26.0 (3C), 22.5, 21.5, 18.4, 13.9, -5.2.

FT-IR (ATR, cm^{-1}): 3281, 2930, 2858, 1599, 1324, 1252, 1159, 1093, 884, 813, 774, 662.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{22}H_{41}NO_3SSi$: 428.2649, found 428.2645.



***N*-(6-((tert-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)hexan-2-yl)-4-methylbenzene-sulfonamide (34):** Following the general method **B** (using precatalyst **phen**), **34** was isolated by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 25%) in 93% yield as a colorless, viscous oil. This product was dried under vacuum (50 mTorr at 80 °C) for 4 h to remove traces of TBS–OH, which partially co-elutes with the product.

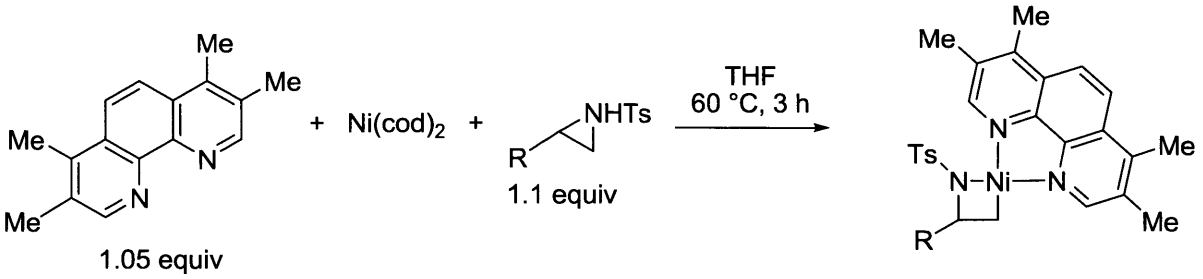
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68–7.61 (m, 2H), 7.26–7.20 (m, 2H), 6.94–6.88 (m, 2H), 6.78–6.71 (m, 2H), 4.18 (d, J = 8.1 Hz, 1H), 3.78 (s, 3H), 3.49 (td, J = 6.2, 2.7 Hz, 2H), 3.38 (h, J = 6.2 Hz, 1H), 2.61 (qd, J = 13.8, 6.1 Hz, 2H), 2.41 (s, 3H), 1.53–1.13 (m, 6H), 0.88 (s, 9H), 0.02 (s, 6H).

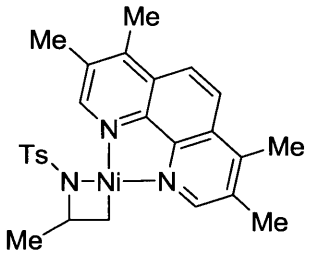
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.2, 142.9, 138.1, 130.3, 129.5, 129.4, 126.9, 113.8, 62.8, 55.3, 55.1, 40.3, 34.1, 32.4, 26.0 (3C), 21.6, 21.5, 18.3, -5.3.

FT-IR (ATR, cm^{-1}): 3282, 2929, 2857, 1612, 1512, 1247, 1156, 1092, 1035, 833, 811, 774, 661.

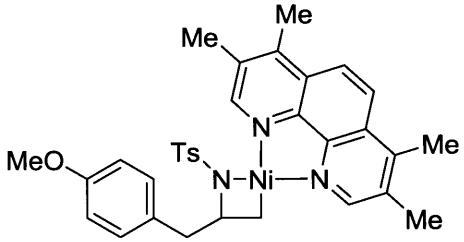
HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{26}H_{41}NO_4SSi$: 492.2598, found 492.2593.

Synthesis and Studies of Azanickelacyclobutanes

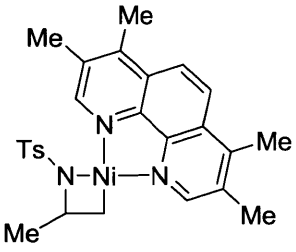




35
96% yield



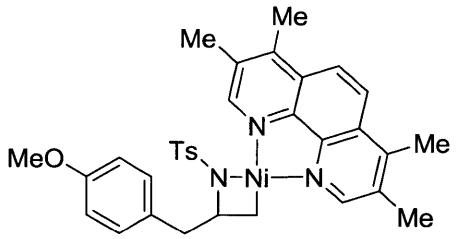
36
86% yield



(Me_4Phen)Ni{N(Ts)CH(CH_3)CH_2} (35): In a glovebox, an oven-dried scintillation vial (20 mL) was charged with a magnetic stir bar, 3,4,7,8-tetramethyl-1,10-phenanthroline (1.10 mmol, 259.9 mg), and $Ni(cod)_2$ (1.00 mmol, 275.1 mg). THF (6.0 mL) was added and the mixture was stirred for 10 minutes to yield a black suspension, after which 2-methyl-*N*-tosylaziridine **1a** (1.20 mmol, 253.6 mg) was added in one portion. This mixture was stirred at ambient temperature for 30 minutes, after which it was heated to 60°C for 3 h in an aluminum heating block. After cooling to ambient temperature, Et_2O (8 mL) was added and the mixture was stirred vigorously for 1 h. The bright red-orange precipitate was isolated by filtration through a sintered glass frit (medium porosity). The solid was washed with Et_2O (40 mL), transferred to a vial, and dried under high vacuum, which yielded the product **35** as a bright red-orange powder (96%).

^{1}H NMR (400 MHz, CD_2Cl_2, δ): 9.58 (s, 1H), 8.31–8.27 (m, 2H), 8.07 (d, J = 9.4 Hz, 1H), 8.00 (d, J = 9.4 Hz, 1H), 7.93 (s, 1H), 7.22–7.17 (m, 2H), 3.87 (dqd, J = 8.4, 6.3, 4.4 Hz, 1H), 2.67 (s, 3H), 2.60 (s, 3H), 2.54 (s, 3H), 2.42 (s, 3H), 2.35 (s, 3H), 1.22 (d, J = 6.3 Hz, 3H), 0.58 (dd, J = 8.4, 5.3 Hz, 1H), 0.06 (t, J = 4.9 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2, δ): 153.8, 150.0, 145.8, 143.9, 143.7, 143.6, 142.9, 140.4, 134.3, 133.3, 129.0, 127.6, 127.6, 127.0, 123.3, 122.3, 61.5, 26.9, 21.4, 18.0, 17.8, 15.0, 14.8, -4.1.



(Me_4Phen)Ni{N(Ts)CH(PMB)CH_2} (36): In a glovebox, an oven-dried scintillation vial (20 mL) was charged with a magnetic stir bar, 3,4,7,8-tetramethyl-1,10-phenanthroline (1.10 mmol, 259.9 mg), and $Ni(cod)_2$ (1.00 mmol, 275.1 mg). THF (10 mL) was added and the mixture was stirred for 10 minutes to yield a black suspension, after which 2-(4-methoxybenzyl)-*N*-tosylaziridine **1l** (1.20 mmol, 380.9 mg) was added in one portion. This mixture was stirred at ambient temperature for 30 minutes, after which it was heated to 60 °C for 3 h in an aluminum heating block. After cooling to ambient temperature, Et_2O (8 mL) was added and the mixture was vigorously stirred for 3 h. The bright red-orange precipitate was isolated by filtration through a sintered glass frit (medium porosity). The solid was washed with Et_2O (40 mL), transferred to a vial, and dried under high vacuum, which yielded the product **36** as a bright red-orange powder (86%).

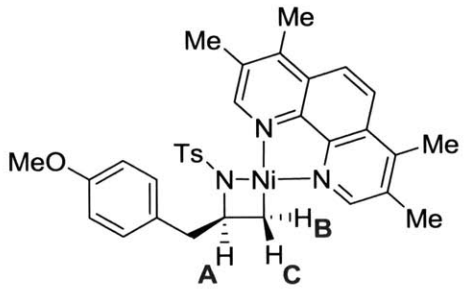
^{1}H NMR (400 MHz, CD_2Cl_2, δ): 9.61 (s, 1H), 8.33–8.28 (m, 2H), 8.07 (d, J = 9.3 Hz, 1H), 8.00 (d, J = 9.3 Hz, 1H), 7.90 (s, 1H), 7.20 (d, J = 7.9 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 6.80–6.74 (m, 2H), 3.91 (ddt, J = 11.9, 8.2, 3.9 Hz, 1H, **A**), 3.74 (s, 3H), 2.97 (dd, J = 13.1, 3.8 Hz, 1H), 2.77 (dd, J = 13.1, 10.5 Hz, 1H), 2.68 (s, 3H), 2.60 (s, 3H), 2.57 (s, 3H), 2.39 (s, 3H), 2.35 (s, 3H), 0.32 (dd, J = 8.3, 5.6 Hz, 1H, **B**), 0.20 (app t, J = 5.1 Hz, 1H, **C**).

^{13}C{^{1}H} NMR (126 MHz, CD_2Cl_2, δ): 158.1, 153.6, 149.9, 145.6, 143.9, 143.7, 143.4, 142.8,

140.6, 134.2, 133.2, 132.4, 130.6, 129.0, 127.6, 127.5, 126.9, 123.3, 122.3, 113.6, 67.1, 55.4, 45.7, 21.4, 18.0, 17.8, 15.0, 14.8, -7.0.

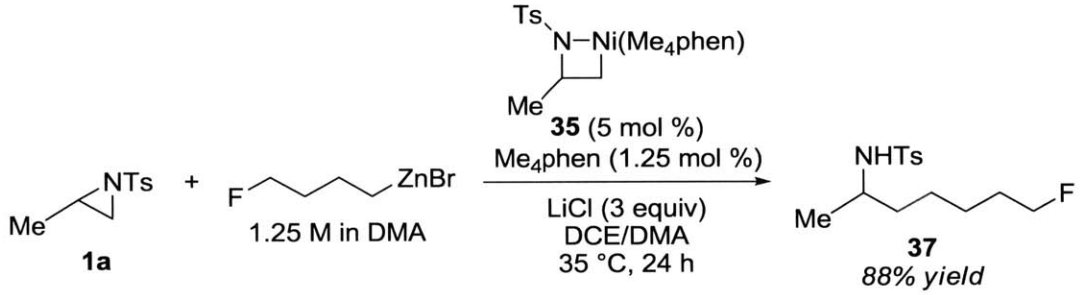
NOEDIFF analysis of azanickelacyclobutane 36

		Percent enhancement		
	δ (ppm)	3.91	0.32	0.20
		A	**B**	**C**
Irradiated proton	**A**		3.6	
	B	8.3		16.9
	C		17.0	



Only the signals relevant to the stereochemical assignment of the ring protons are included. **A** is the methine proton, and **B** (0.32 ppm) and **C** (0.20 ppm) are the geminal protons, where **B** is *cis* to **A**.

Azanickelacyclobutane applied as precatalyst:



***N*-(7-fluoroheptan-2-yl)-4-methylbenzenesulfonamide (37):** To a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was added 2-methyl-1-tosylaziridine **1a** (105.6 mg, 0.50 mmol) and 3,4,7,8-tetramethyl-1,10-phenanthroline (1.5 mg, 6.25 μmol). The vial was purged with nitrogen and then transferred to a glovebox where anhydrous LiCl (64.0 mg, 1.50 mmol) and (Me$_4$phen)Ni{N(Ts)CH(CH$_3$)CH$_2$} **35** (12.6 mg, 0.025 mmol) were added. DCE (2.0 mL) was added, resulting in a reddish suspension. A solution of (4-fluorobutyl)zinc(II) bromide in DMA (1.20 mL, 1.25M, 1.50 mmol) was added and the reaction mixture was stirred vigorously at 35°C for 24 h using an aluminum heating block. The reaction was quenched with sat. aq.

NH_4Cl (1.5 mL) and diluted with Et_2O (1 mL). Phases were separated and the aqueous phase was extracted with Et_2O (2 x 1 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The crude product was subjected to column chromatography on silica gel (25 g, EtOAc/hexanes, gradient 0% to 25%) affording the product **37** in 88% yield (based on 0.525 mmol) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.76 (app d, J = 8.3 Hz, 2H), 7.30 (app d, J = 8.0 Hz, 2H), 3.30 (hept, J = 6.5 Hz, 1H), 2.43 (s, 3H), 1.66–1.50 (m, 2H), 1.41–1.15 (m, 6H), 1.02 (d, J = 6.5 Hz, 3H).

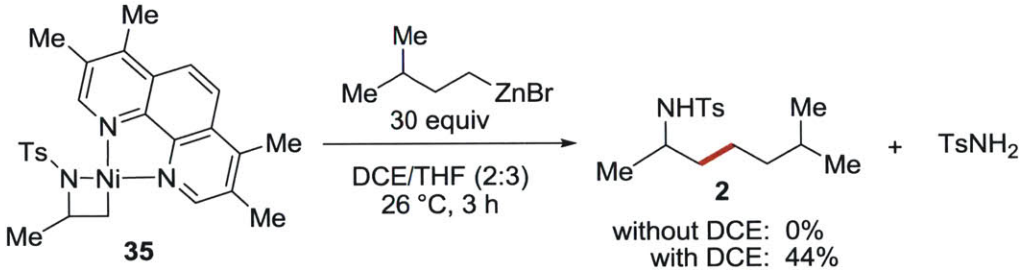
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.3, 138.4, 129.7, 127.1, 84.0 (d, J = 164.1 Hz), 50.0, 37.4, 30.3 (d, J = 19.5 Hz), 25.2, 24.9 (d, J = 5.4 Hz), 21.8, 21.6.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -218.3 (tt, J = 47.3, 25.3 Hz).

FT-IR (ATR, cm^{-1}): 3276, 2936, 2863, 1598, 1425, 1319, 1157, 1092, 1022, 986, 814, 661.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{14}H_{22}FNO_2S$, 288.1428; found, 288.1434.

Studies on the effect of DCE on $TsNH_2$ formation from azanickelacyclobutane:



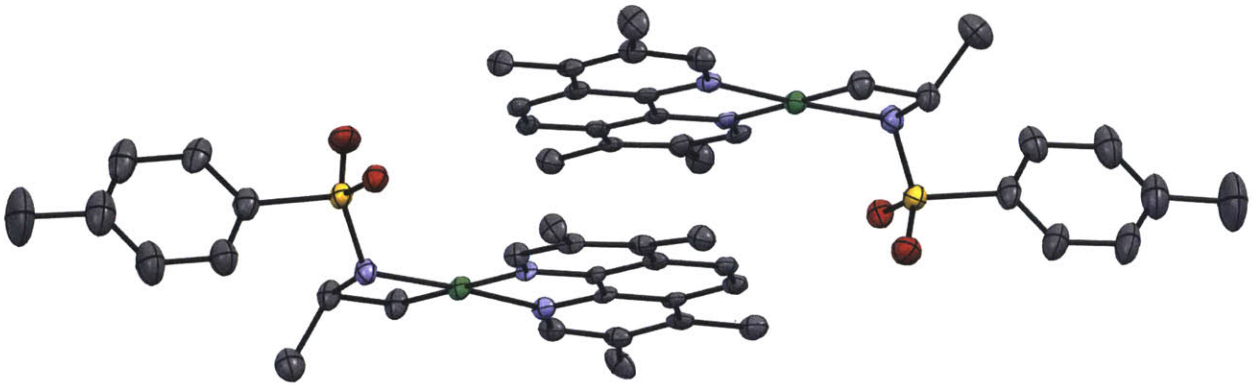
Inside a glovebox, a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was charged with (Me_4phen)Ni{N(Ts)CH(CH_3)CH_2} **35** (25.3 mg, 0.05 mmol). The complex was suspended in DCE (2.0 mL), resulting in a red suspension. A solution of 3-methylbutylzinc(II) bromide in THF (3.0 mL, 0.5M, 1.50 mmol) was added and the reaction mixture was stirred vigorously at 26 °C for 3 h using an aluminum heating block. The reaction was quenched with sat. aq. NH_4Cl (2.0 mL) and diluted with Et_2O (1 mL). Phases were separated and the aqueous phase was extracted with Et_2O (2 x 1.0 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The ratio of coupling product **2** to $TsNH_2$ was determined by ^{1}H NMR spectroscopic analysis of the crude mixture. Based on an internal standard (mesitylene) the combined yield of **2** and $TsNH_2$ was determined to be ~80%.

Table SI 2. Crystal data and structure refinement for compound 35

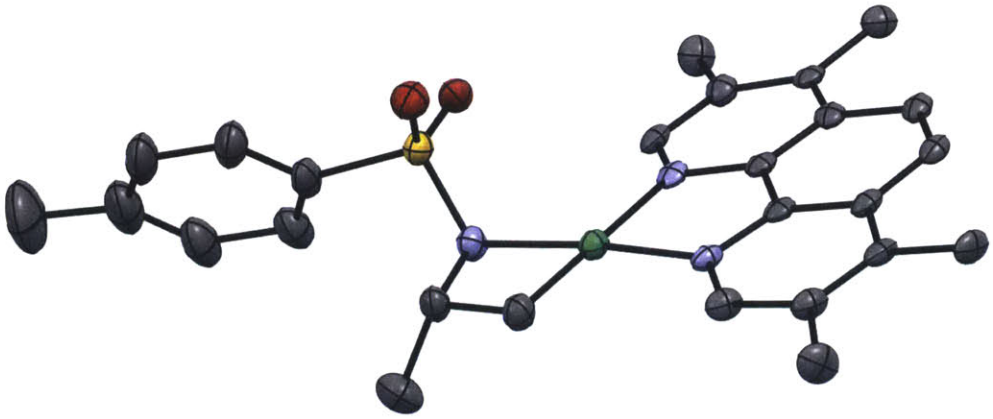
Identification code	x14022	
Empirical formula	$C_{26.25}H_{26.5}Cl_{0.5}N_3NiO_2S$	
Formula weight	524.504 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	*Pbca*	
Space group	orthorhombic	
Unit cell dimensions	a = 13.1842(18) Å	α= 90°
	b = 23.573(3) Å	β= 90°
	c = 33.224(5) Å	γ= 90°
Volume	10326(2) Å^3	
Z	16	
Density (calculated)	1.350 Mg/m^3	
Absorption coefficient	0.912 mm^{-1}	
F(000)	4376	
Crystal size	0.37 x 0.23 x 0.110 mm^3	
Theta range for data collection	1.23 to 29.58°	
Index ranges	-18<=h<=17, -32<=k<=30, -46<=l<=46	
Reflections collected	254508	
Independent reflections	14338 [R_{int} = 0.0720]	
Completeness to theta = 29.58°	98.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.906and 0.729	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	14338 / 1135 / 654	
Goodness-of-fit on F^2	1.128	
Final R indices [I>2σ(I)]	R1 = 0.1521 , wR2 = 0.3964	
R indices (all data)	R1 = 0.1718, wR2 = 0.4070	
Largest diff. peak and hole	4.139 and -4.795 e.Å^{-3}	

Thermal Ellipsoid Depictions of 35

Asymmetric Unit (racemic pair)

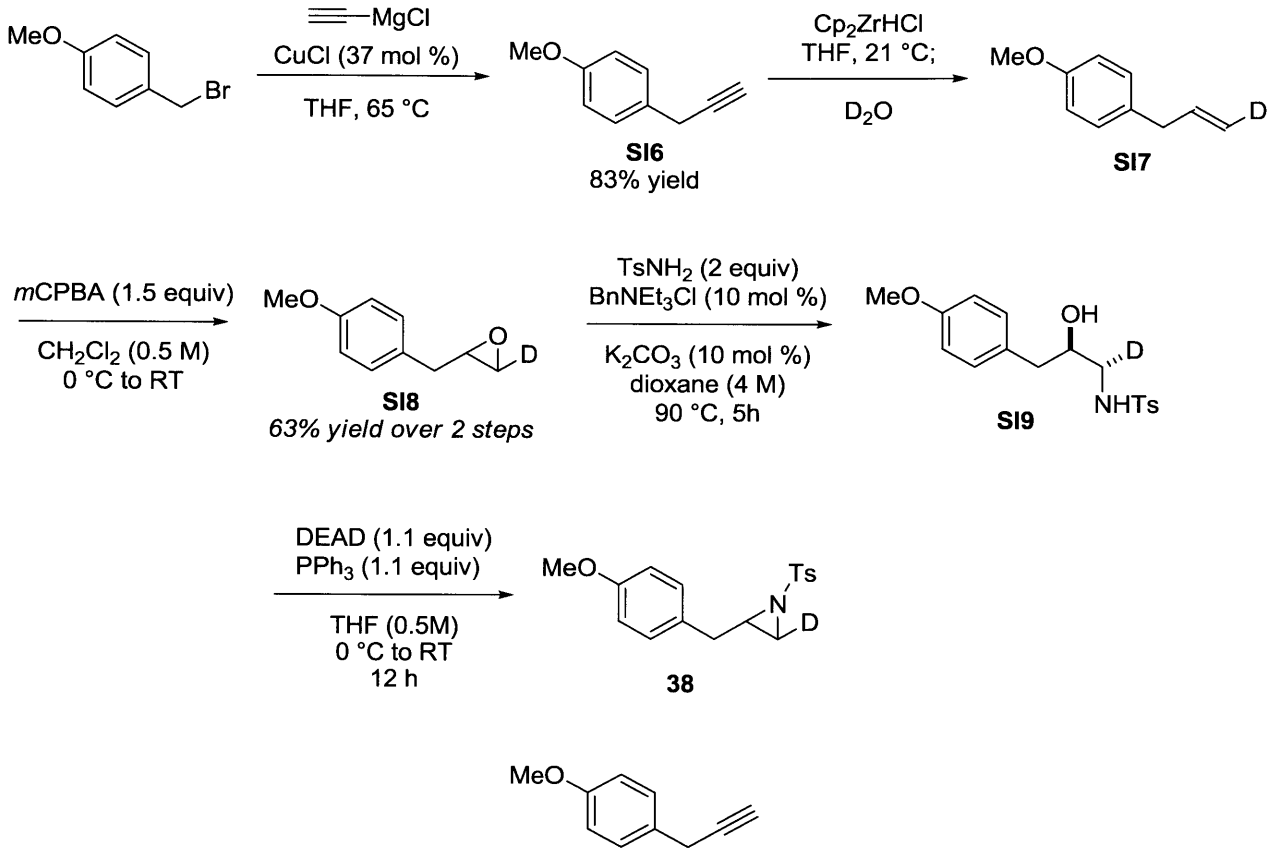


Single Molecule View



Data for this structure are not on file with the CCDC because the data are not of sufficient quality for publication.

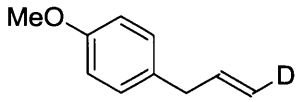
Synthesis of Deuterium-Labeled Aziridine



1-methoxy-4-(prop-2-yn-1-yl)benzene (SI6): To a suspension of CuCl (570 mg, 5.76 mmol) in dry THF (10.0 mL) at ambient temperature was added a solution of ethynylmagnesium chloride in THF (63 mL, 0.5M, 31.3 mmol) via a syringe. After 10 minutes of stirring, a solution of 1-(bromomethyl)-4-methoxybenzene (3.15 g, 15.7 mmol) in THF (5.0 mL) was added. The reaction was heated to reflux for 21 h. After cooling to ambient temperature, the reaction was quenched with sat. aq. NH_4Cl (75 mL) and diluted with Et_2O (100 mL). The biphasic suspension was filtered over Celite to remove solids. In a separatory funnel, the phases were separated and the organic phase was washed with H_20 (70 mL), dried over Na_2SO_4 and concentrated with a rotary evaporator. Purification by column chromatography (100 g HP-Sil, Et_2O/hexanes, gradient 0% to 5%) afforded the product **SI6** in 83% yield as a yellow liquid.

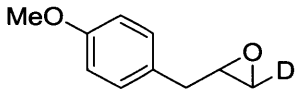
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.30–7.24 (m, 2H), 6.90–6.83 (m, 2H), 3.80 (s, 3H), 3.55 (d, J = 2.8 Hz, 2H), 2.17 (t, J = 2.7 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.6, 129.0, 128.3, 114.1, 82.6, 70.3, 55.5, 24.1.



***trans*-1-(allyl-3-*d*)-4-methoxybenzene (SI7):** In a glovebox, a dry, 500 mL round bottom flask was charged with a magnetic stir bar and $Cp_2Zr(H)Cl$ (Schwartz's reagent) (1.15 equiv, 32.3 mmol, 8.33 g). The flask was sealed with a rubber septum, removed from the glovebox, and attached to an argon line. Dry THF (350 mL) was transferred to this vessel by cannula to yield a slurry. Vigorous magnetic stirring was started and 1-methoxy-4-(prop-2-ynyl)benzene **SI6** (28 mmol, 4.09 g) was added as a solution in 50 mL THF over a period of 10 minutes. Over the course of the addition, the slurry became homogeneous and turned deep brown. After an additional 1 h of reaction time, D_2O (99.9% D) (25 mL) was added via syringe. The deep brown color faded within a few minutes to yield a homogeneous, light yellow solution, which was allowed to stir for an additional 12 h. The contents of the flask were transferred to a separatory funnel and water (200 mL) and Et_2O (200 mL) were added. The phases were separated and the organic layer was washed with H_2O (3 x 100 mL). The organic layer was dried over Na_2SO_4 and then concentrated with a rotary evaporator. Purification by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 10%) yielded 4.2 g of the desired deuterium-labelled alkene **SI7** as an impure, orange liquid that was carried on without additional purification. The chemical purity as determined by ^{1}H NMR spectroscopy was approximately 75%, the deuterium incorporation was measured to be >95%, and the *trans*:*cis* ratio was >20:1.

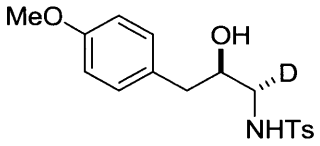
^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.14–7.08 (m, 2H), 6.87–6.81 (m, 2H), 5.95 (dtt, J = 16.7, 6.7, 1.5 Hz, 1H), 5.05 (dt, J = 17.0, 1.6 Hz, 1H), 3.79 (s, 3H), 3.36–3.31 (m, 2H).
HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{10}H_{11}DO$, 150.1024, found 150.1030.



***trans*-2-(4-methoxybenzyl)oxirane-3-*d* (SI8):** *trans*-1-(allyl-3-*d*)-4-methoxybenzene **SI7** (4.2 g, ca. 75% purity) was treated with *m*CPBA according to the procedure for the synthesis of **SI1** to yield *trans*-2-(4-methoxybenzyl)oxirane-3-*d* **SI8** as a clear, colorless liquid (2.93 g, 63% over two steps).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.20–7.15 (m, 2H), 6.89–6.84 (m, 2H), 3.80 (s, 3H), 3.12 (td, *J* = 5.4, 2.6 Hz, 1H), 2.87 (dd, *J* = 14.6, 5.6 Hz, 1H), 2.77 (dd, *J* = 14.6, 5.3 Hz, 1H), 2.52 (d, *J* = 2.7 Hz, 1H).

HRMS (DART, *m/z*): $[M+H]^+$ calcd for $C_{10}H_{11}DO_2$, 166.0973, found 166.0971.

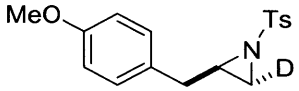


Amino-alcohol (SI9): Amino alcohol **SI9** was synthesized from *trans*-2-(4-methoxybenzyl)oxirane-3-*d* **SI8** according to the procedure used for the synthesis of **SI2**.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.77–7.69 (m, 2H), 7.34–7.28 (m, 2H), 7.08–7.03 (m, 2H), 6.86–6.81 (m, 2H), 4.87 (d, *J* = 7.3 Hz, 1H), 3.86 (ddd, *J* = 8.3, 5.0, 3.3 Hz, 1H), 3.79 (s, 3H), 3.11 (dd, *J* = 7.1, 3.1 Hz, 1H), 2.72 (dd, *J* = 13.8, 5.0 Hz, 1H), 2.61 (dd, *J* = 13.8, 8.3 Hz, 1H), 2.43 (s, 3H), 1.92 (br s, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.1, 143.3, 143.1*, 139.3*, 136.5, 130.2, 129.6, 129.5*, 129.3, 126.9, 126.2*, 113.8, 71.2, 67.8, 60.4, 55.1, 47.4 (t {1:1:1}, *J* = 18.0), 39.8, 25.4, 21.3, 21.3*, 20.9, 14.0 (*denotes signals from $TsNH_2$).

HRMS (ESI, *m/z*): $[M+NH_4]^+$ calcd for $C_{17}H_{20}DNO_4S$, 359.1146, found 359.1128.



***trans*-2-(4-methoxybenzyl)-1-tosylaziridine-3-*d* (38):** *trans*-2-(4-methoxybenzyl)-1-tosylaziridine-3-*d* **38** was synthesized from **SI9** according to the procedure used for the synthesis of **1l**. The *trans/cis* ratio was determined to be 96:4 by ^{1}H NMR spectroscopy (see assignment by NOE from **1l**).

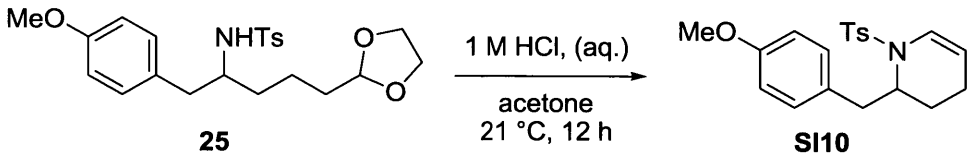
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.72–7.65 (m, 2H), 7.25–7.19 (m, 2H), 6.99–6.92 (m, 2H), 6.73–6.65 (m, 2H), 3.77 (s, 3H), 2.91 (dt, *J* = 7.2, 4.9 Hz, 1H), 2.77 (dd, *J* = 14.5, 5.1 Hz, 1H), 2.61 (dd, *J* = 14.5, 7.3 Hz, 1H), 2.43 (s, 3H), 2.14 (d, *J* = 4.5 Hz, 1H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 158.4, 144.4, 134.9, 129.8, 129.6, 129.1, 127.9, 113.9,

55.3, 41.5, 36.6, 32.7 (t {1:1:1}, J = 25.9 Hz), 21.7.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{17}H_{18}DNO_3S$, 341.1041, found 341.1042.

Stereochemical Analysis of Cross-Coupling Reaction



25 **SI10** *84% yield*

2-(4-methoxybenzyl)-1-tosyl-1,2,3,4-tetrahydropyridine (SI10): Following the procedure described by Harrity[9]: The acetal product **25** (59.0 mg, 0.142 mmol) was dissolved into 1.0 mL of acetone (HPLC grade) and transferred to a 4 mL dram vial containing a magnetic stir bar. To this solution was added 1.0 mL of aq. 1M HCl and the vial was capped. After stirring at ambient temperature for 16 h, the mixture was neutralized with aq. 1 M K_2CO_3 and extracted with EtOAc (3x). The combined organic phases were dried over Na_2SO_4, concentrated with a rotary evaporator, and then purified by chromatography on silica gel (EtOAc/hexane 0:100 to 15:85) to afford the product **SI10** in 84% yield as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.69–7.65 (m, 2H), 7.29–7.24 (m, 2H), 7.15–7.10 (m, 2H), 6.86–6.81 (m, 2H), 6.68 (dddd, J = 8.2, 2.2, 1.7, 1.0 Hz, 1H), 5.06 (dddd, J = 8.2, 5.2, 2.1, 1.2 Hz, 1H, **E**), 4.07 (ddddd, J = 10.4, 5.1, 4.3, 2.6, 1.0 Hz, 1H, **A**), 3.79 (s, 3H), 2.93 (ddd, J = 13.5, 5.1, 0.8 Hz, 1H), 2.67 (dd, J = 13.5, 10.4 Hz, 1H), 2.40 (s, 3H), 2.07 (dddd, J = 18.2, 12.7, 6.2, 2.2, 2.1 Hz, 1H, **C1**), 1.81 (ddddd, J = 18.2, 5.6, 5.4, 1.7, 1.2 Hz, 1H, **C2**), 1.44 (dddt, J = 13.7, 6.2, 2.6, 1.2 Hz, 1H, **B1**), 0.89 (ddddd, J = 13.7, 12.7, 5.6, 4.3, 0.8 Hz, 1H, **B2**).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ): 158.4, 143.5, 136.4, 130.4, 130.2, 129.8, 127.0, 123.6, 114.0, 108.4, 55.3, 54.5, 37.3, 21.6, 21.0, 17.2.

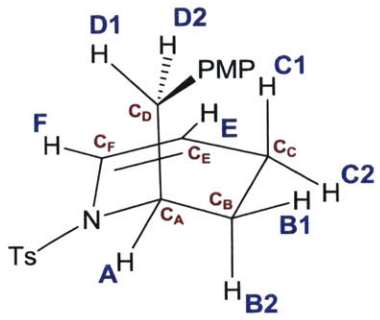
FT-IR (ATR, cm^{-1}): 2927, 2837, 1646, 1611, 1512, 1341, 1245, 1164, 1095, 1033, 950, 806, 683.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{20}H_{23}NO_3S$, 358.1471, found 358.1474.

[9] Pattenden, L. C.; Adams, H.; Smith, S. A.; Harrity, J. P. A. *Tetrahedron* **2008**, *64*, 2951–2961.

NMR analysis of SI10

Coupling constants were determined by direct measurement from the ^{1}H NMR spectrum where possible, and from the DQF COSY for all other cases by measurement from the appropriate slices.



Analysis of the 1D ^{1}H NMR allowed assignment of protons **F**, **E**, **D1**/**D2**, and **A** by chemical shift and basic *J*-coupling correlations. Subsequently, the HSQC was used to establish that the resonances at 2.07 and 1.81 ppm arise from a set of geminal protons and that the resonances at 1.44 and 0.89 ppm arise from a second set of geminal protons. Because **C1** and **C2** are allylic, it is likely that **C1**/**C2** should be downfield of **B1**/**B2**, and therefore the two most upfield resonances should correspond to **B1**/**B2**. This is supported by the gCOSY, which demonstrates that **A** is ^3J-coupled to **B1** and **B2**, but not to **C1** and/or **C2**, and that **E** is ^3J-coupled to **C1** and **C2**, though it is also weakly coupled to **B1** through a 4-bond W-type coupling. This arrangement of coupling constants demonstrates the connectivity to be $\mathbf{C_A}$–$\mathbf{C_B}$–$\mathbf{C_C}$–$\mathbf{C_E}$ rather than $\mathbf{C_A}$–$\mathbf{C_C}$–$\mathbf{C_B}$–$\mathbf{C_E}$. Further confirmation of this assignment was provided by the NOEDIFF experiments, which demonstrated that **A** is in spatial proximity to **B1** and **B2** and that **E** is in spatial proximity to **C1** and **C2**. Taken together, these data demonstrate the connectivity of the tetrahydropyridine ring to be [–$\mathbf{C_A}$–$\mathbf{C_B}$–$\mathbf{C_C}$–$\mathbf{C_E}$–$\mathbf{C_F}$–**N**–].

Having established the connectivity, the remaining assignments necessary are the stereochemical positioning of **B1**, **B2**, **C1**, and **C2**. The observed $^3J_{HH}$ coupling constant of 12.7 Hz between **C1** and **B2** strongly suggests a *pseudo*-antiperiplanar dihedral arrangement between these two hydrogens. Thus, both **B2** and **C2** must be *cis* to **A**, which completes the assignment of the tetrahydropyridine. As a final confirmation of the above assignments, presaturation of **D2** causes a 4.0% NOE enhancement of **C1**, confirming it is indeed *cis* to the PMB group, which must be in a pseudo-axial position.[9]

Coupling Constant Analysis of SI10

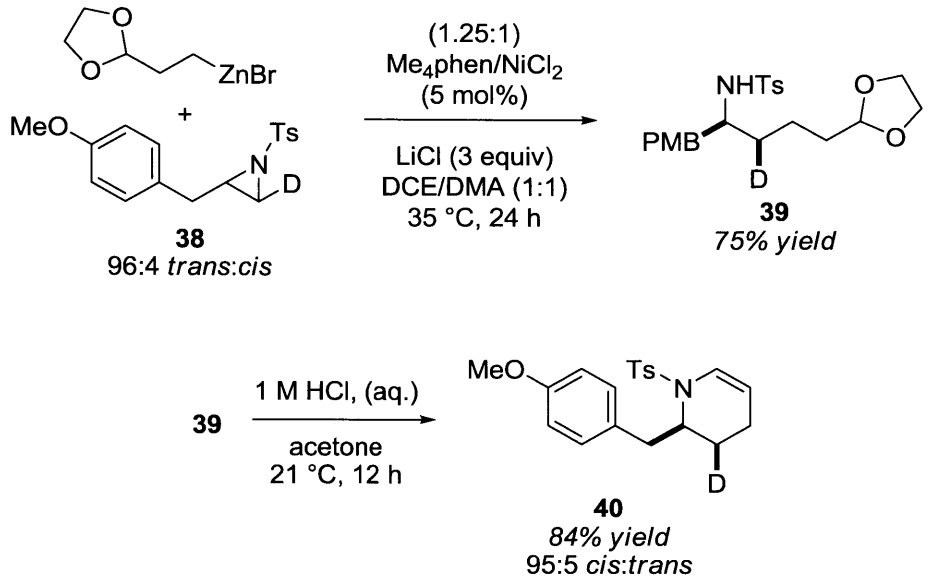
δ (ppm)		6.68	5.06	4.07	2.93	2.67	2.07	1.81	1.44	0.89
		F	**E**	**A**	**D1**	**D2**	**C1**	**C2**	**B1**	**B2**
6.68	**F**		8.2	1.0			2.2	1.7		
5.06	**E**	8.2					2.1	5.4	1.2	
4.07	**A**	1.0			5.1	10.4			2.6	4.3
2.93	**D1**			5.1		13.5				0.8
2.67	**D2**			10.4	13.5					
2.07	**C1**	2.2	2.1					18.2	6.2	12.7
1.81	**C2**	1.7	5.4				18.2		1.2	5.6
1.44	**B1**		1.2	2.6			6.2	1.2		13.7
0.89	**B2**			4.3	0.8		12.7	5.6	13.7	

The couplings highlighted in red are absent in **40**.

NOEDIFF Analysis of Enamine SI10

		Percent enhancement							
	δ (ppm)	5.06	4.07	2.93	2.67	2.07	1.81	1.44	0.89
		E	**A**	**D1**	**D2**	**C1**	**C2**	**B1**	**B2**
Irradiated proton	**A**			4.0				2.1	2.9
	D1		6.1		25.6				
	D2			26.7		4.1			
	C1	5.1			4.2		25.9	1.0	
	C2	7.2				25.6			3.2
	B1		4.5		1.5	3.3			26.2
	B2		6.6				4.8	29.7	

Cross-coupling reaction of deuterium-labeled aziridine:



To a flame-dried 8 mL screw-top vial containing a magnetic stir-bar was added *trans*-2-(4-methoxybenzyl)-1-tosylaziridine-3-*d* **38** (0.50 mmol) and precatalyst (**Me$_4$phen**, 11.4 mg, 0.025 mmol, 5 mol %). The vial was capped and purged with nitrogen after which it was transferred to a glovebox. Anhydrous LiCl (64.0 mg, 1.50 mmol), DCE (1.0 mL) and DMA (1.0 mL) was added followed by the organozinc solution (1.5 mmol, 0.5M in THF, 3.0 mL). The reaction was stirred at 35°C for 24 h in an aluminum heating block. After cooling to ambient temperature, the reaction was quenched with sat. aq. NH_4Cl (1.5 mL) and diluted with Et_2O (1 mL). Phases were separated and the aqueous phase was extracted with Et_2O (2 x 1 mL). The combined organic phases were dried over Na_2SO_4, plugged over a pad of silica gel (washing with Et_2O) and concentrated *in vacuo*. The crude products were purified by column chromatography on silica gel (EtOAc/hexanes, gradient 0% to 45%) to afford the product **39** in 75% yield as colorless oil. *Product is unstable to acid.*

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.65–7.60 (m, 2H), 7.25–7.20 (m, 2H), 6.92–6.87 (m, 2H), 6.76–6.70 (m, 2H), 4.73 (t, J = 4.7 Hz, 1H), 4.25 (d, J = 7.8 Hz, 1H), 3.95–3.87 (m, 2H), 3.86–3.79 (m, 2H), 3.78 (s, 3H), 3.36 (dq, J = 8.0, 6.1 Hz, 1H), 2.64 (dd, J = 13.8, 6.5 Hz, 1H), 2.57 (dd, J = 13.8, 6.0 Hz, 1H), 2.41 (s, 3H), 1.56–1.23 (m, 5H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 158.4, 143.1, 137.9, 130.4, 129.6, 129.2, 127.0, 113.9, 104.3, 64.9, 55.3, 55.1, 40.2, 33.9 (t {1:1:1}, J = 19.5 Hz), 33.4, 21.6, 19.8.

HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{22}H_{28}DNO_5S$, 443.1721, found 443.1704.

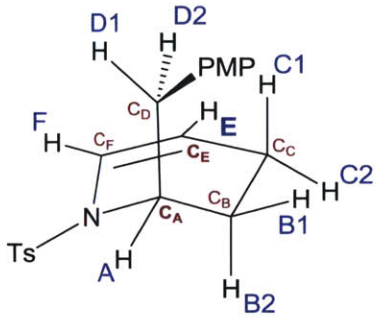
The deuterium-labeled acetal product **39** was cyclized to *cis*-2-(4-methoxybenzyl)-1-tosyl-1,2,3,4-tetrahydropyridine-3-*d* **40** by following the procedure described for the synthesis of **SI10**.

***cis*-2-(4-methoxybenzyl)-1-tosyl-1,2,3,4-tetrahydropyridine-3-*d* (40):**

^1H NMR (400 MHz, $CDCl_3$, δ): 7.70–7.65 (m, 2H), 7.29–7.25 (m, 2H), 7.15–7.10 (m, 2H), 6.86–6.81 (m, 2H), 6.68 (dddd, J = 8.2, 2.2, 1.7, 1.0 Hz, 1H), 5.06 (ddd, J = 8.2, 5.4, 2.1 Hz, 1H, **E**), 4.06 (dddd, J = 10.4, 5.1, 4.3, 1.0 Hz, 1H, **A**), 3.79 (s, 3H), 2.92 (ddd, J = 13.5, 5.1, 0.8 Hz, 1H), 2.67 (dd, J = 13.5, 10.4 Hz, 1H), 2.40 (s, 3H), 2.06 (dddd, J = 18.2, 12.7, 2.2, 2.1 Hz, 1H, **C1**), 1.81 (dddd, J = 18.2, 5.4, 1.7, 1.2 Hz, 1H, **C2**), 0.87 (dddd, J = 12.7, 5.6, 4.3, 0.8 Hz, 1H, **B2**).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$, δ): 158.4, 143.5, 136.5, 130.5, 130.2, 129.8, 127.0, 123.7, 114.0, 108.3, 55.4, 54.5, 37.3, 21.7, 20.7 (t, {1:1:1}, J = 20.2 Hz), 17.1.

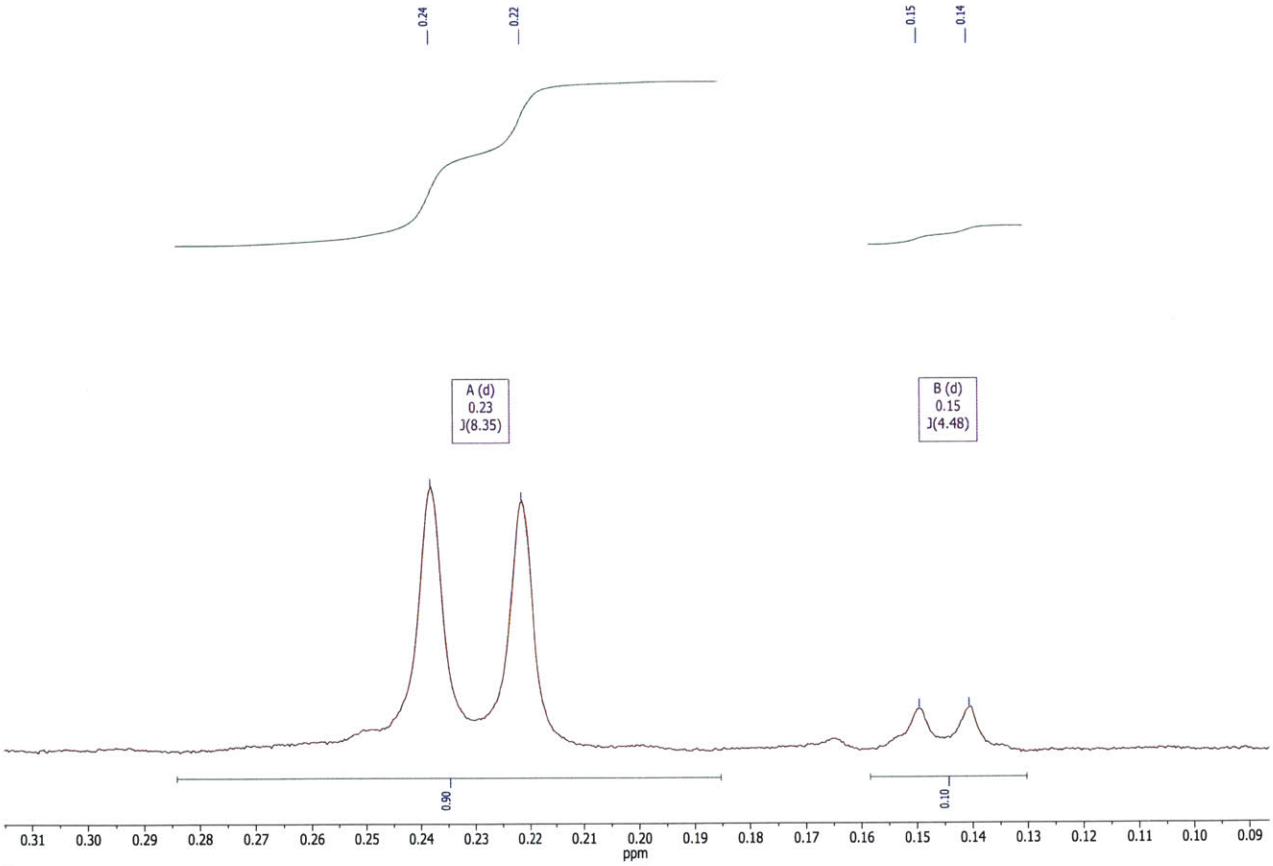
HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{20}H_{22}DNO_3S$, 359.1534, found 359.1543.



As evident from the NMR data above, the ^1H NMR spectrum lacks the signal for **B1** at 1.44 ppm. The coupling patterns of **E**, **A**, **B2**, **C1**, and **C2** all show simplification corresponding to the removal of one coupling partner. Critically, the 12.7 Hz coupling between **C1** and **B2** is still present, demonstrating that the proton *trans* to the PMB group is still present, which therefore shows that **B1** is the deuterated position.

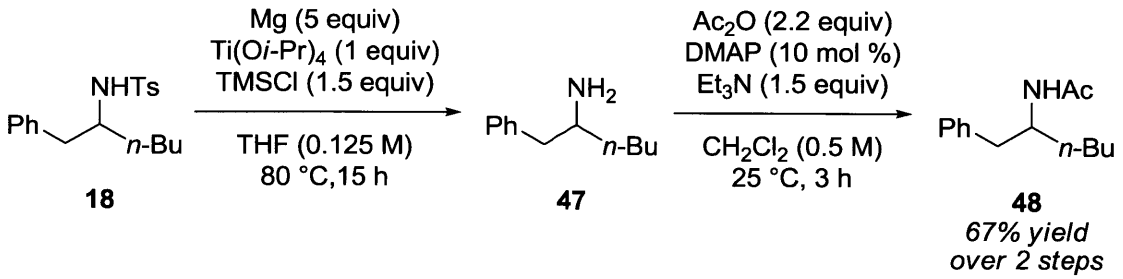
Synthesis of deuterium-labeled azanickelacyclobutane 41: To an oven-dried, 4 mL vial was added Me_4phen/$NiCl_2$ (1.25:1.00) (0.02 mmol, 9.2 mg), aziridine **38** (0.04 mmol, 12.7 mg), and a magnetic stir bar. The vial was taken into the glovebox and LiCl (0.01 mmol, ca. 0.5 mg), DMA (400 μL), and DCE (200 μL) were added. To this mixture was then added isopentylzinc bromide (0.5 M in THF, 0.04 mmol, 80 μL). The vial was capped with a PTFE-lined screw cap and allowed to stir at ambient temperature for 30 minutes, over which time the mixture first became deep blue and then subsequently turned red. After this length of time, the vial was fitted with a vacuum adapter and the solvent was removed in vacuo. CD_2Cl_2 was added to the residue, which afforded a heterogeneous, red mixture. This mixture was then filtered through a 2 cm plug of Celite in a glass pipette. The resulting clear, red solution was then analyzed by ^{1}H NMR spectroscopy. The *cis*/*trans* ratio was 90:10, which corresponds to 95% inversion.

Note: plastic syringes should be avoided during this sequence. On this scale, enough siloxanes are leached from the syringe bodies to cause a large contamination in the NMR spectrum, which in this instance can hamper analysis, since the peaks of interest overlap with the siloxanes.



^{1}H NMR spectrum of azanickelacyclobutane **41**.

Deprotection of Sulfonyl Group



The sulfonamide product was reductively cleaved following the procedure described by Okamoto[10]: To a flame-dried microwave reaction vial (Biotage, 2–5 mL) was added a magnetic stir-bar, 4-methyl-*N*-(1-phenylhexan-2-yl)benzenesulfonamide **18** (165.7 mg, 0.5 mmol) and magnesium powder (61.0 mg, 2.5 mmol). The vial was sealed using a cap with septum. The vial was purged with argon and THF (4.0 mL) was added followed by distilled Ti(O*i*Pr)4 (150 μL, 0.50 mmol) and TMSCl (100 μL, 0.75 mmol). The vial was heated to 80°C for 15 h using an oil bath. The reaction was cooled to ambient temperature and transferred (washing with 8 mL Et_2O) to a 20 mL scintillation vial containing Celite (0.5 g) and anhydrous NaF (0.5 g). Aqueous 3M NaOH (0.3 mL) was added and the mixture was stirred vigorously for 30 min. The mixture was filtered over Celite (washing with 5 mL Et_2O) and the filtrate was transferred to a separatory funnel. The phases were separated and organic phase was washed with aq. 3M NaOH (2 x 5 mL), H_2O (5 mL), dried over Na_2SO_4 and concentrated to afford a colorless oil. To the crude amine **47** in an 8 mL vial was added CH_2Cl_2 (1.0 mL) followed by triethylamine (105 μL, 0.75 mmol), acetic anhydride (105 μL, 1.1 mmol) and 4-dimethylaminopyridine (6.0 mg, 0.05 mmol). The reaction was stirred at ambient temperature for 3 h after which it was quenched with aq. 1M HCl (1.5 mL) and extracted with EtOAc (2 x 3 mL). The combined organic phases were dried over Na_2SO_4 and concentrated. The crude product was subjected to column chromatography on silica gel (25 g, EtOAc/hexanes, gradient 0:1 to 60:40) affording the product **48** in 67% yield as white solid.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.34–7.24 (m, 2H), 7.26–7.17 (m, 1H), 7.21–7.12 (m, 2H), 5.46 (br s, 1H), 4.24–4.09 (m, 1H), 2.81 (dd, J = 13.7, 6.4 Hz, 1H), 2.77 (dd, J = 13.6, 6.2 Hz, 1H),

[10] Shohji, N.; Kawaji, T.; Okamoto, S. *Org. Lett.* **2011**, *13*, 2626–2629.

1.95 (s, 3H), 1.57–1.44 (m, 1H), 1.39–1.20 (m, 5H), 0.87 (t, J = 6.9 Hz, 3H).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$, δ): 169.6, 138.2, 129.5, 128.4, 126.4, 50.2, 40.9, 33.7, 28.3, 23.5, 22.6, 14.1.

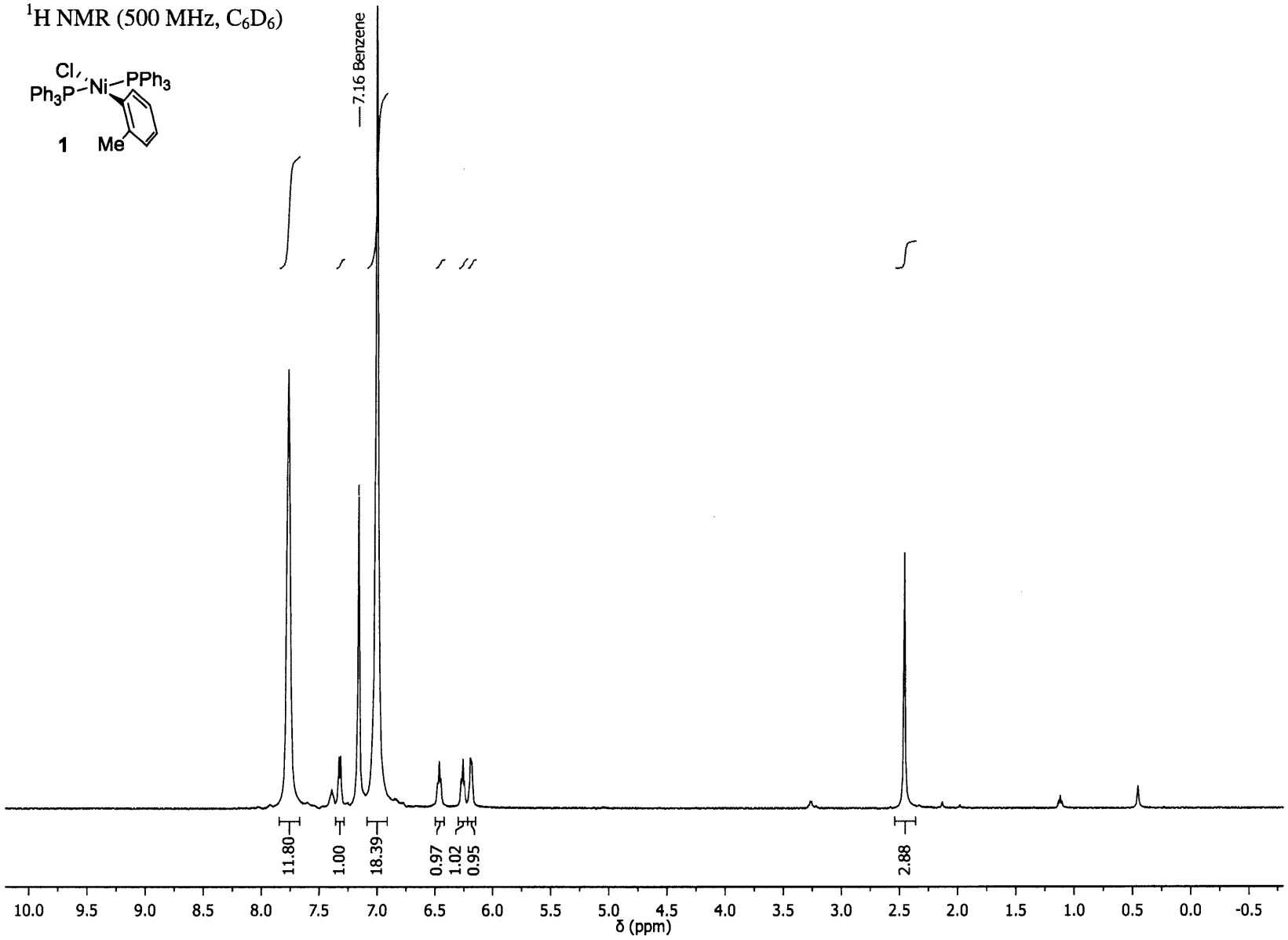
FT-IR (ATR, cm^{-1}): 3276, 3065, 3029, 2931, 2859, 1637, 1548, 1373, 1303, 908, 728, 698.

HRMS (ESI, *m/z*): $[M+H]^+$ calcd for $C_{14}H_{21}NO$, 220.1696; found, 220.1696.

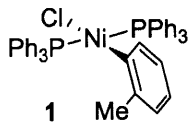
Appendix A

NMR Spectra for Chapter 1

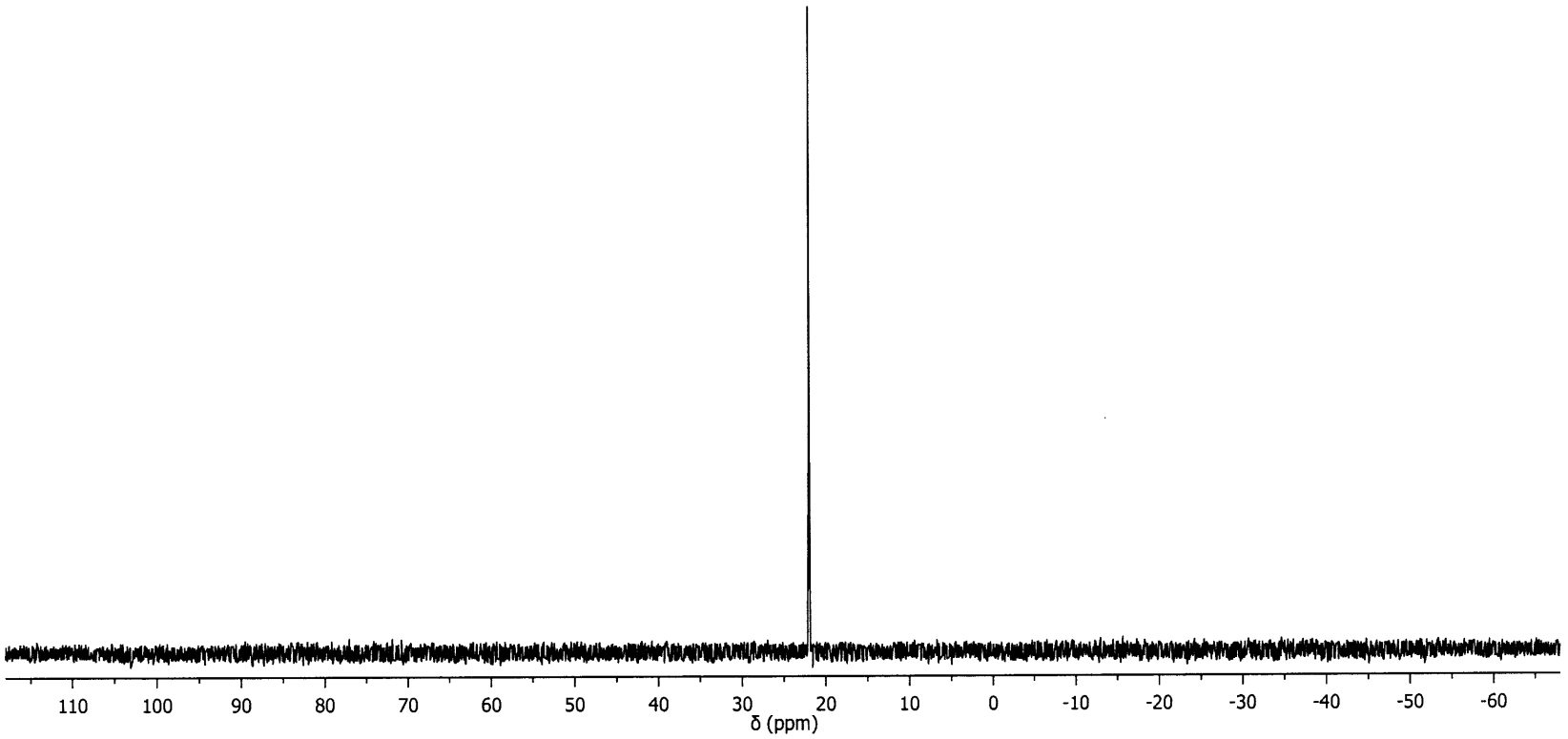
Air-Stable Nickel Precatalysts for Organic Synthesis

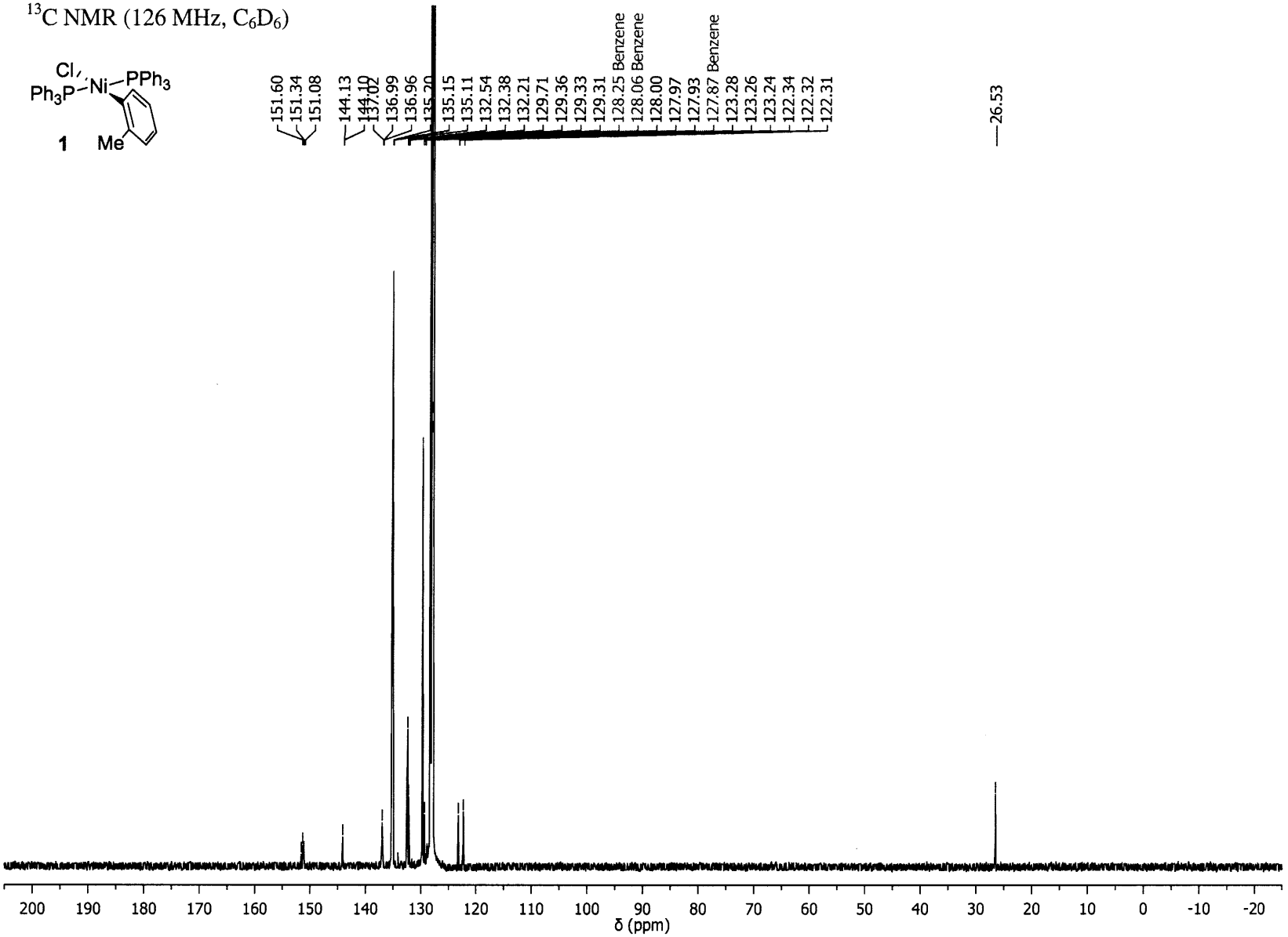

^{1}H NMR (500 MHz, C_6D_6)
Cl
Ph3P
Ni
PPh3
1
Me
7.16 Benzene
11.80
1.00
18.39
0.97
1.02
0.95
2.88
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

^{31}P NMR (121 MHz, C_6D_6)

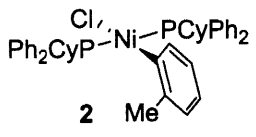


1



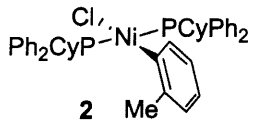

13C NMR (126 MHz, C6D6)
Cl
Ph3P
Ni
PPh3
1
Me
151.60
151.34
151.08
144.13
144.10
137.02
136.99
136.96
135.20
135.15
135.11
132.54
132.38
132.21
129.71
129.36
129.33
129.31
128.25 Benzene
128.06 Benzene
128.00
127.97
127.93
127.87 Benzene
123.28
123.26
123.24
122.34
122.32
122.31
26.53
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
δ (ppm)

^{1}H NMR (500 MHz, C_6D_6)



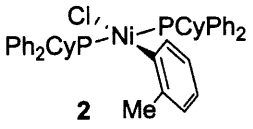
2

^{1}H NMR (500 MHz, CD_2Cl_2)



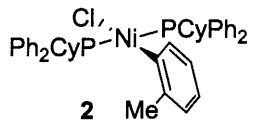
2

^{31}P NMR (203 MHz, C_6D_6)



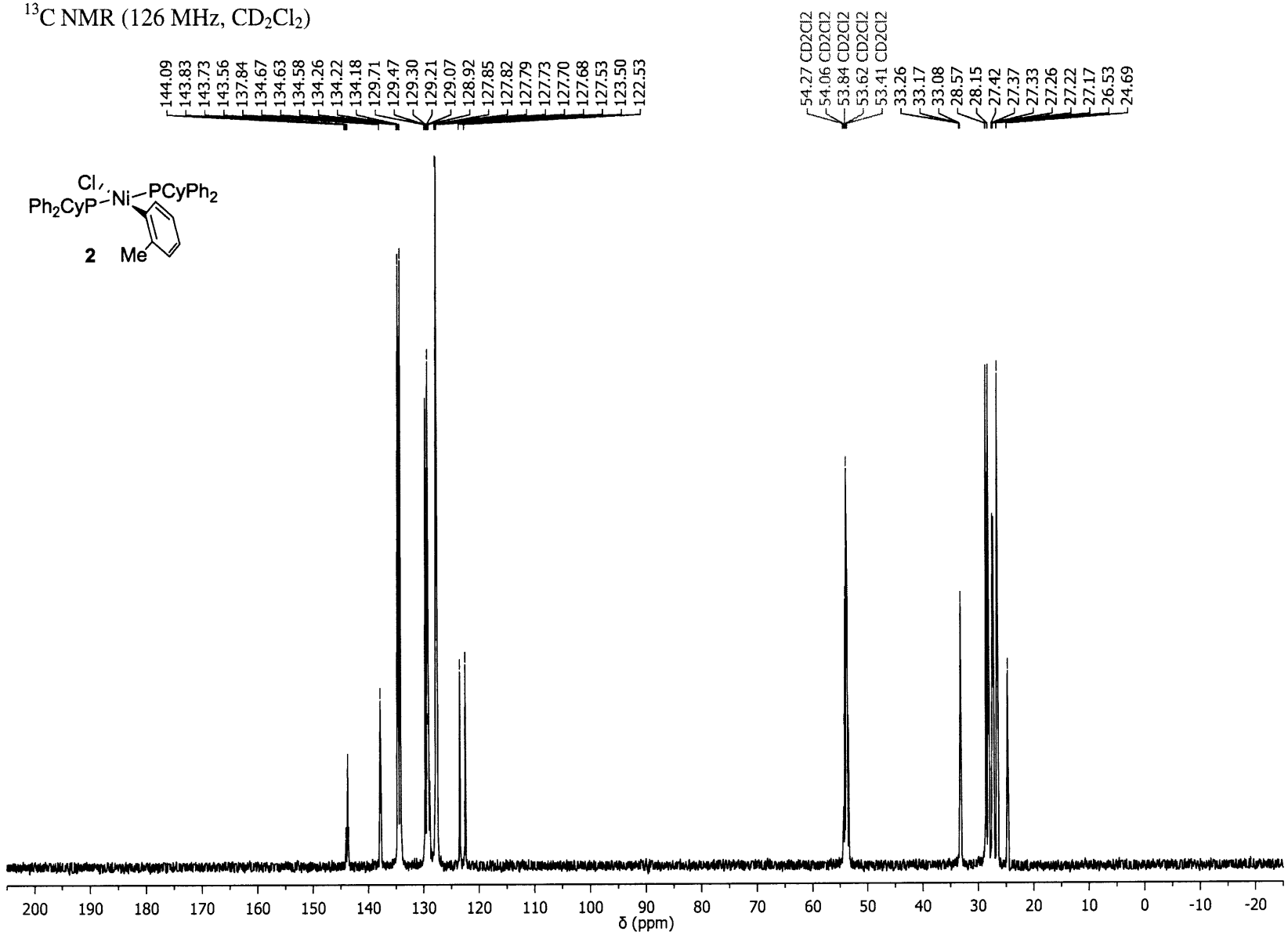
2

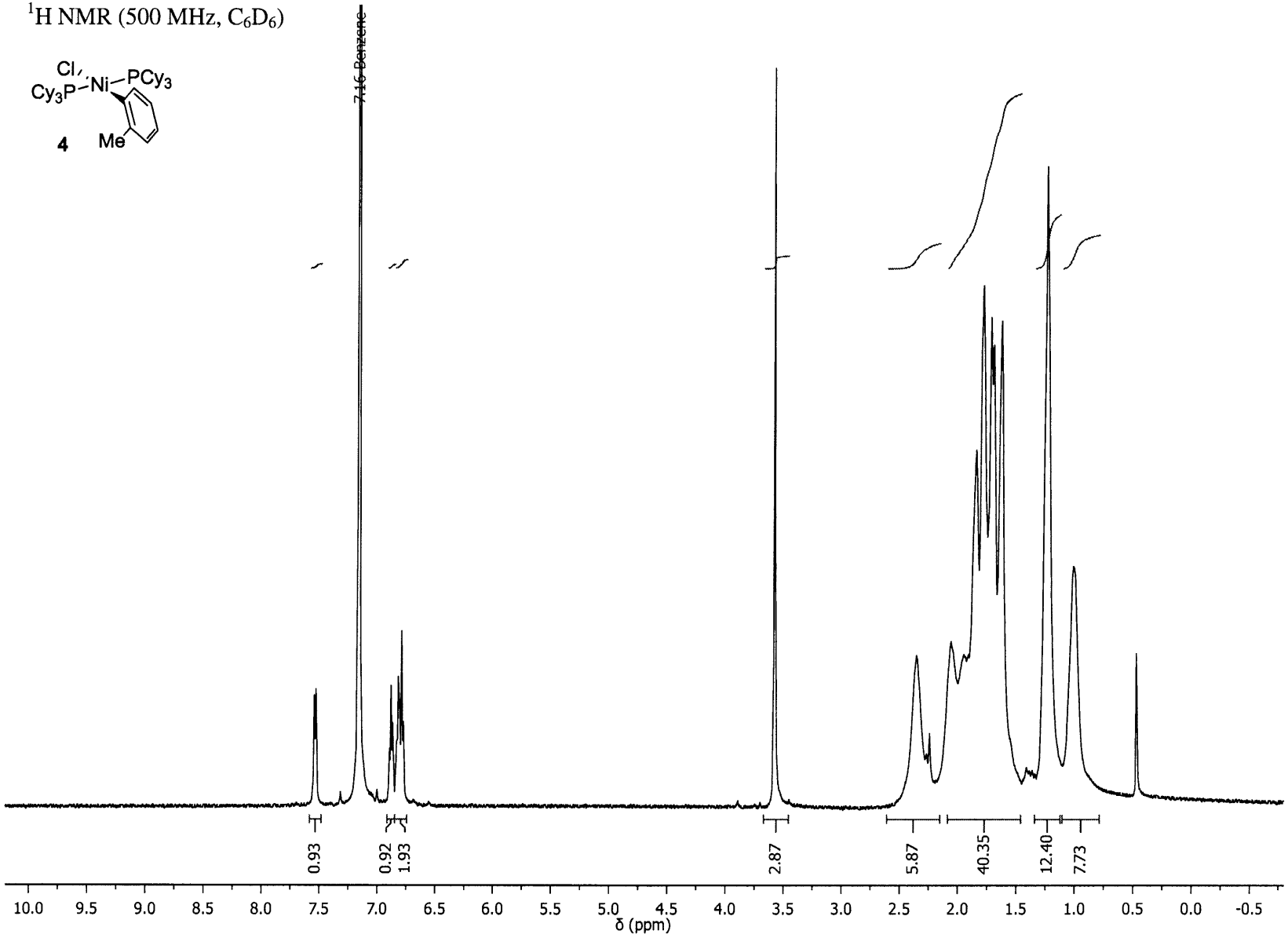
^{31}P NMR (121 MHz, CD_2Cl_2)



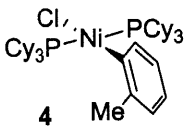
2

^{13}C NMR (126 MHz, CD_2Cl_2)



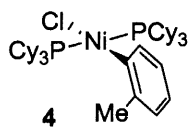

^{1}H NMR (500 MHz, C_6D_6)
Cl
Cy3P
Ni
PCy3
4
Me
7.16 Benzene
0.93
0.92
1.93
2.87
5.87
40.35
12.40
7.73
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

^{31}P NMR (121 MHz, C_6D_6)



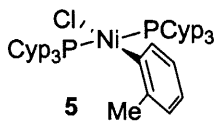
4

^{13}C NMR (126 MHz, C_6D_6)



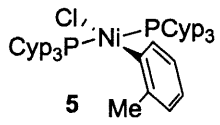
4

^{1}H NMR (300 MHz, C_6D_6)



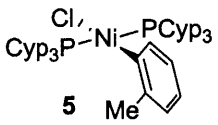
5

^{31}P NMR (121 MHz, C_6D_6)

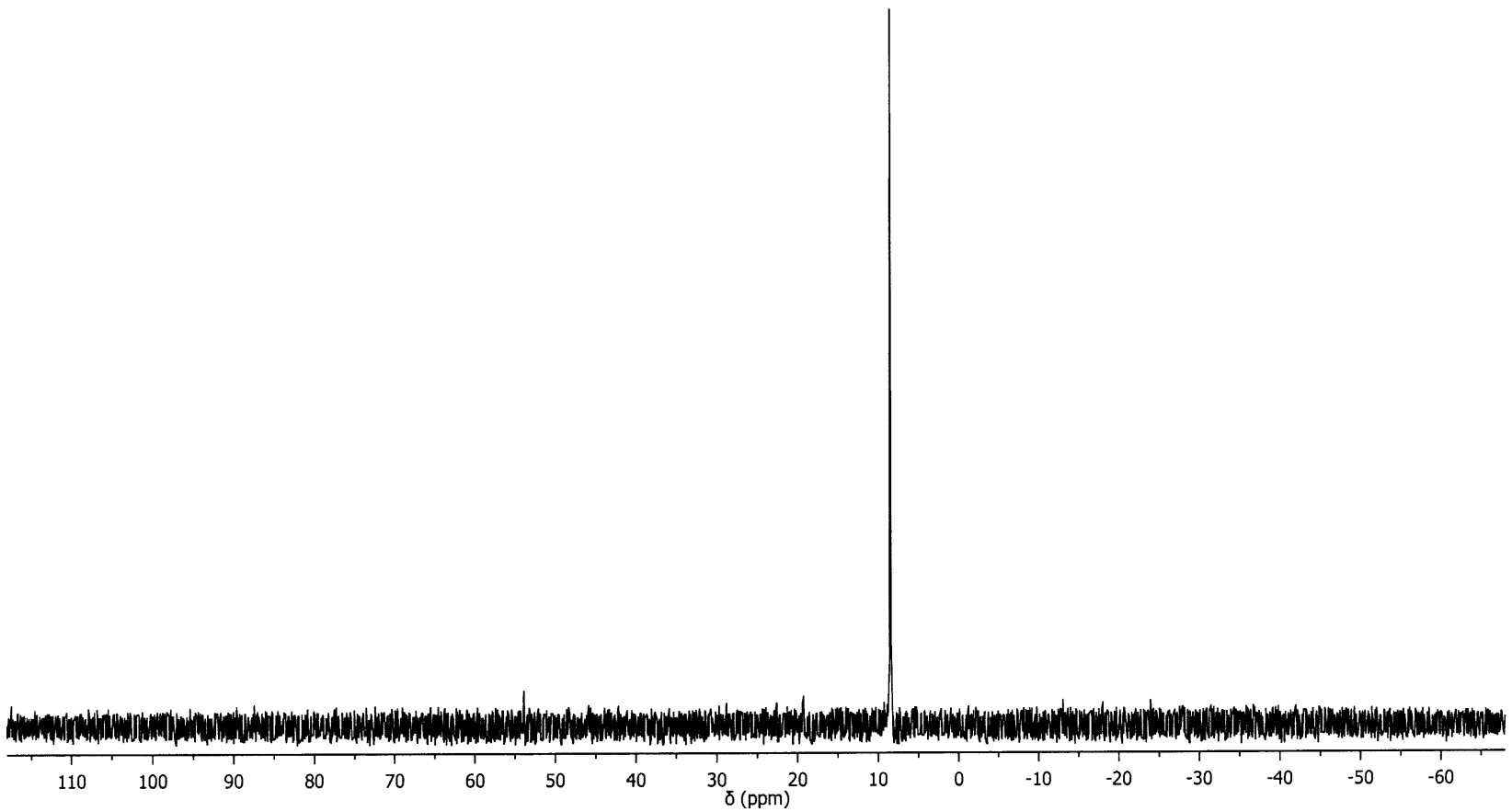


5

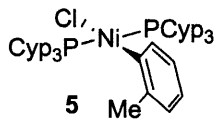
^{31}P NMR (121 MHz, CD_2Cl_2)

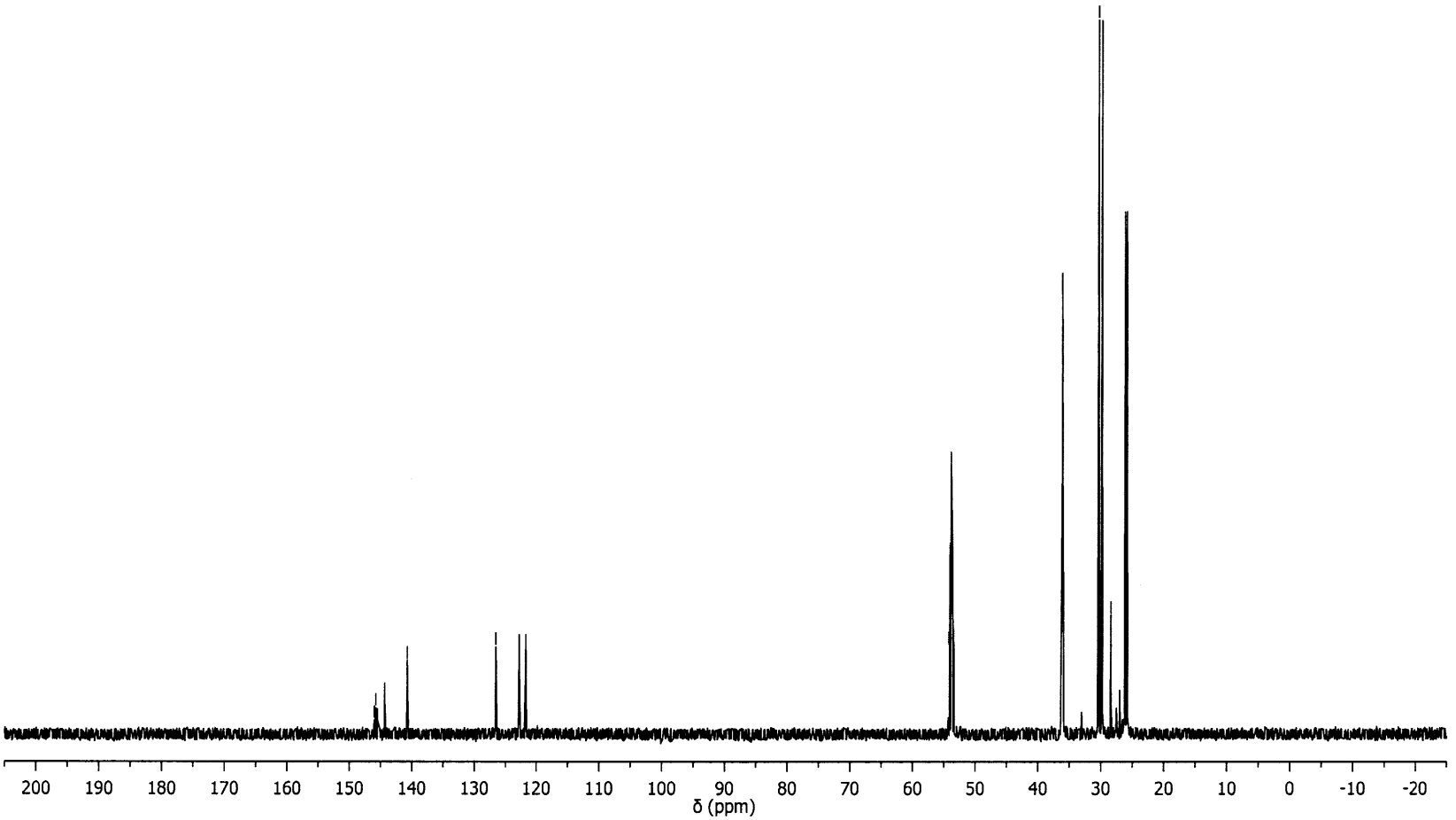


5

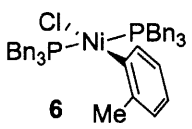


^{13}C NMR (126 MHz, CD_2Cl_2)



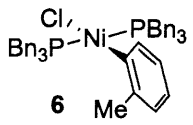


^{1}H NMR (500 MHz, C_6D_6)



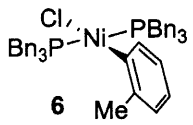
6

^{31}P NMR (203 MHz, C_6D_6)

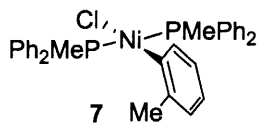


6

^{13}C NMR (126 MHz, C_6D_6)

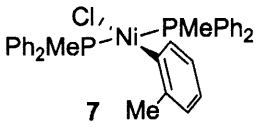


^{1}H NMR (500 MHz, C_6D_6)

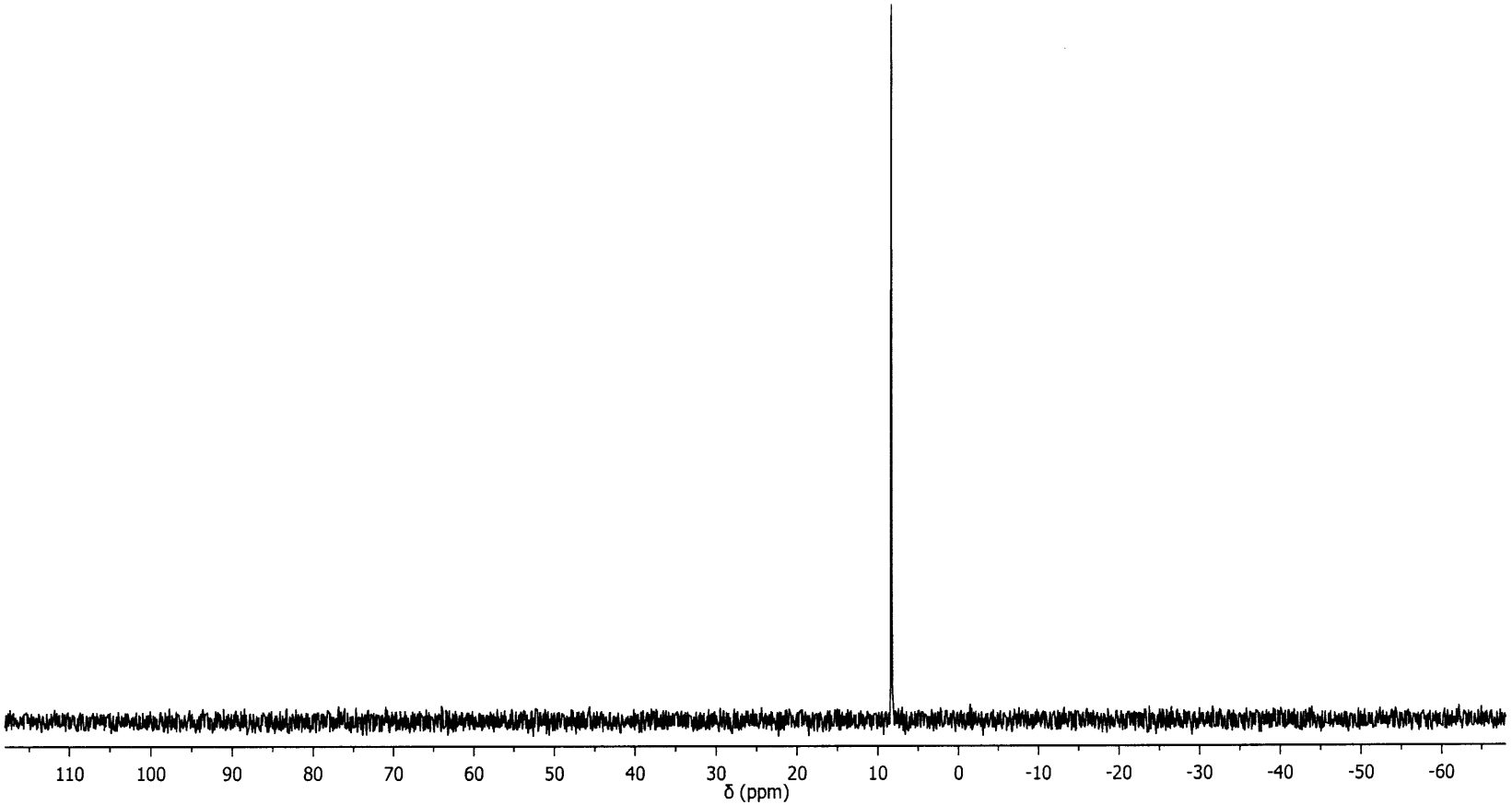


7

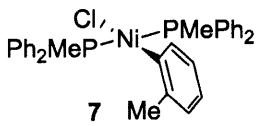
^{31}P NMR (121 MHz, C_6D_6)



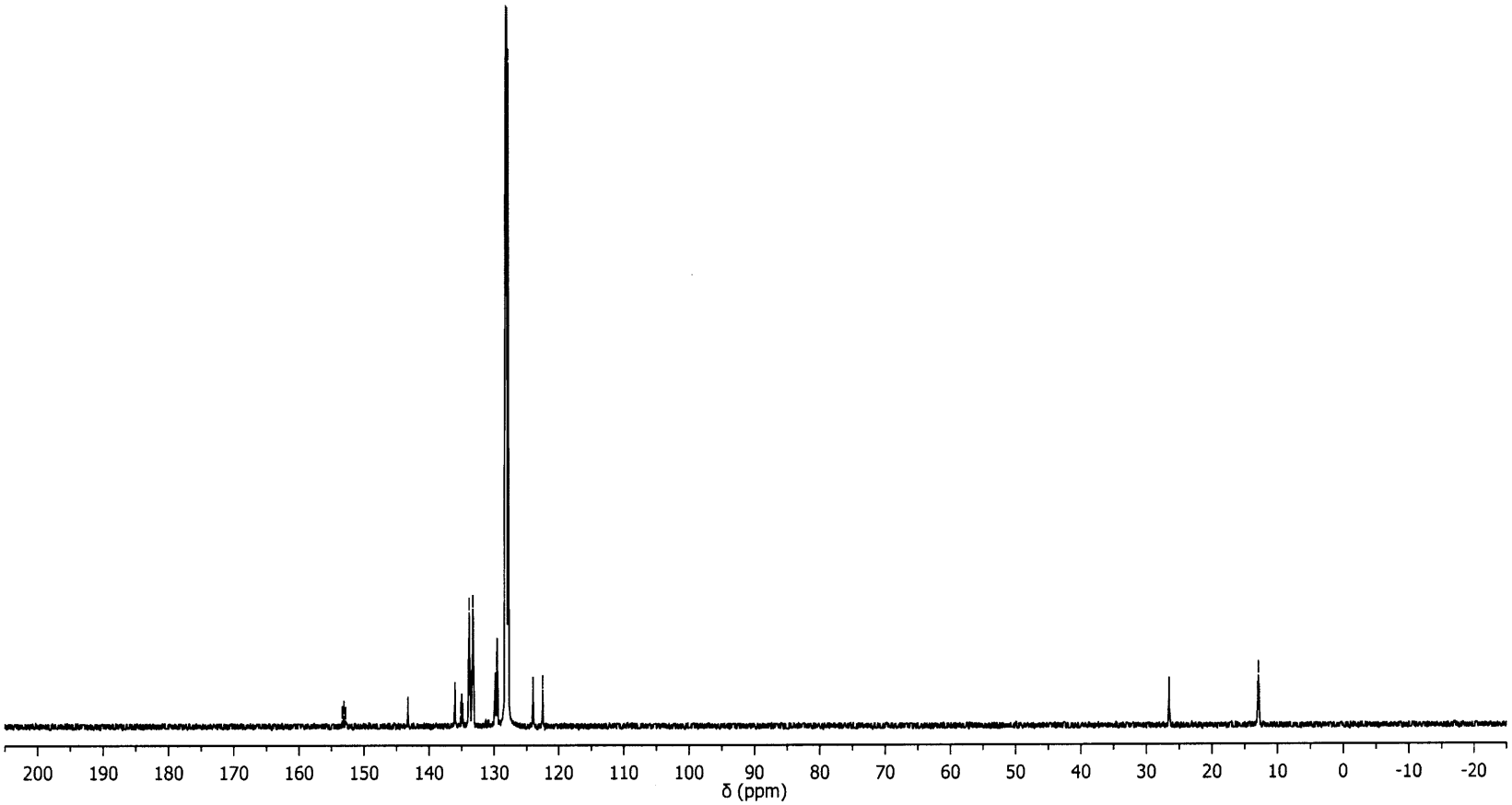
7



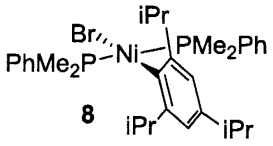
^{13}C NMR (126 MHz, C_6D_6)



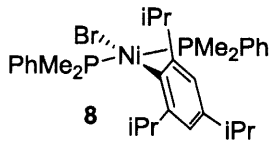
153.36
153.09
152.83
143.27
136.05
136.02
136.00
135.15
134.99
134.83
133.88
133.84
133.80
133.63
133.46
133.30
133.30
133.26
133.22
128.25 Benzene
128.06 Benzene
127.87 Benzene
124.03
122.55
26.56
13.06
12.94
12.81



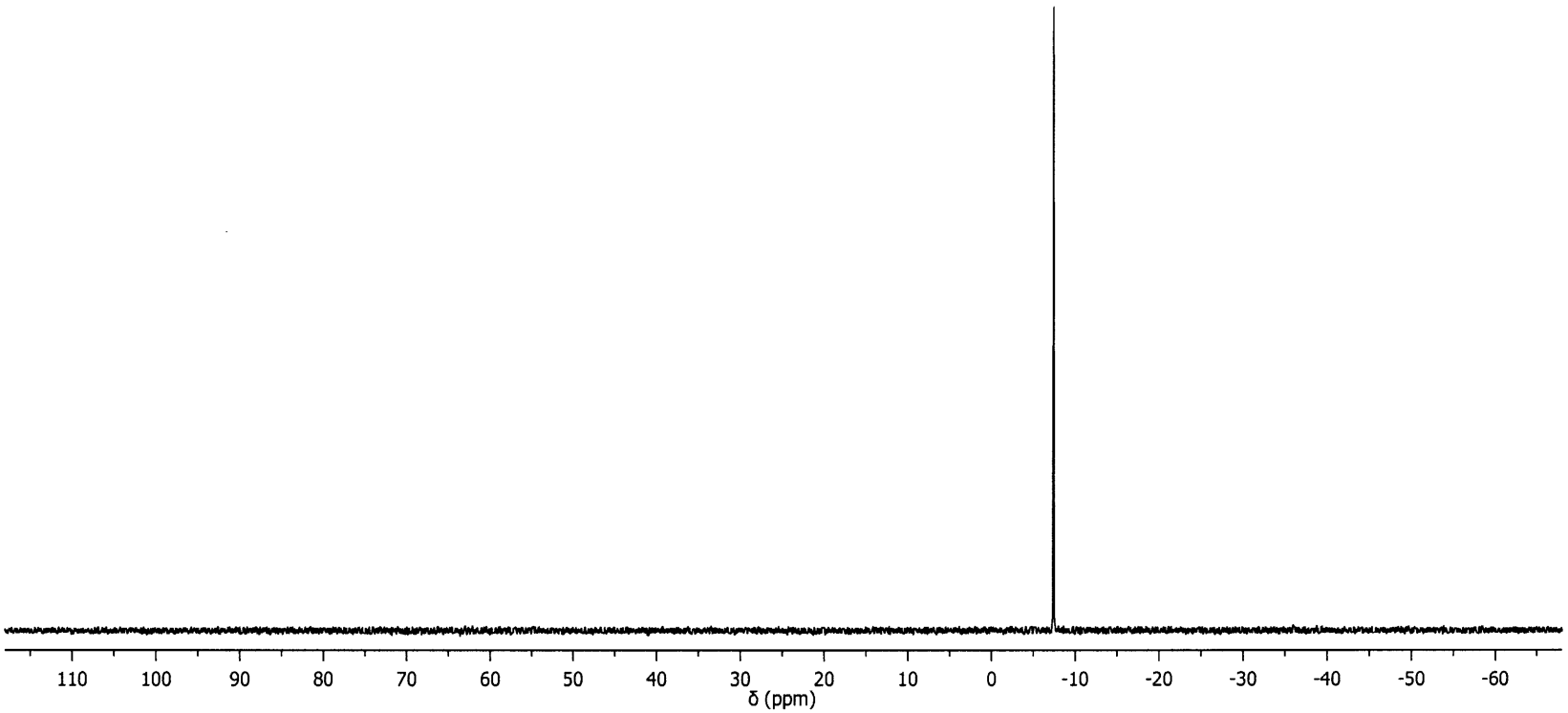
^{1}H NMR (500 MHz, C_6D_6)



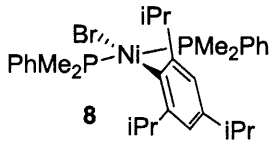
^{31}P NMR (121 MHz, C_6D_6)



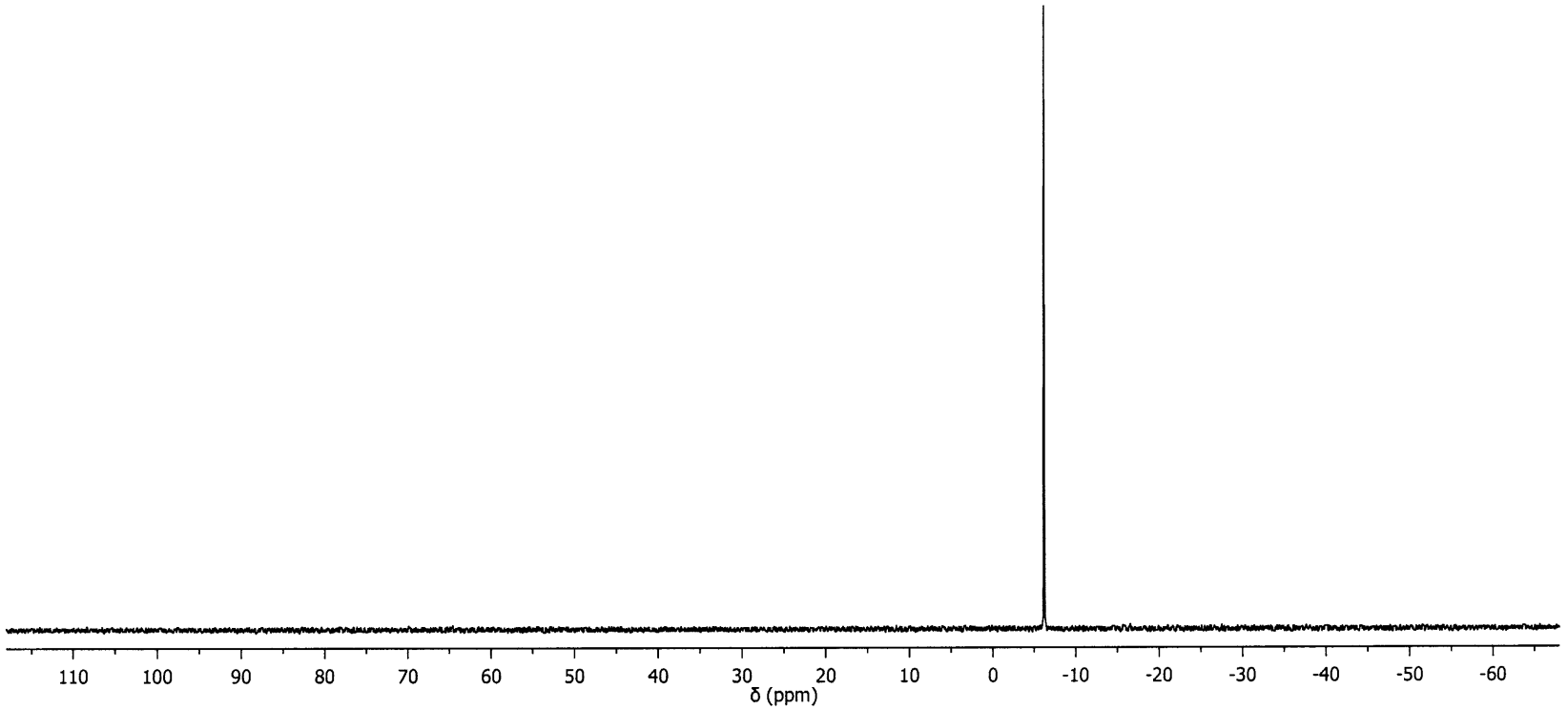
8



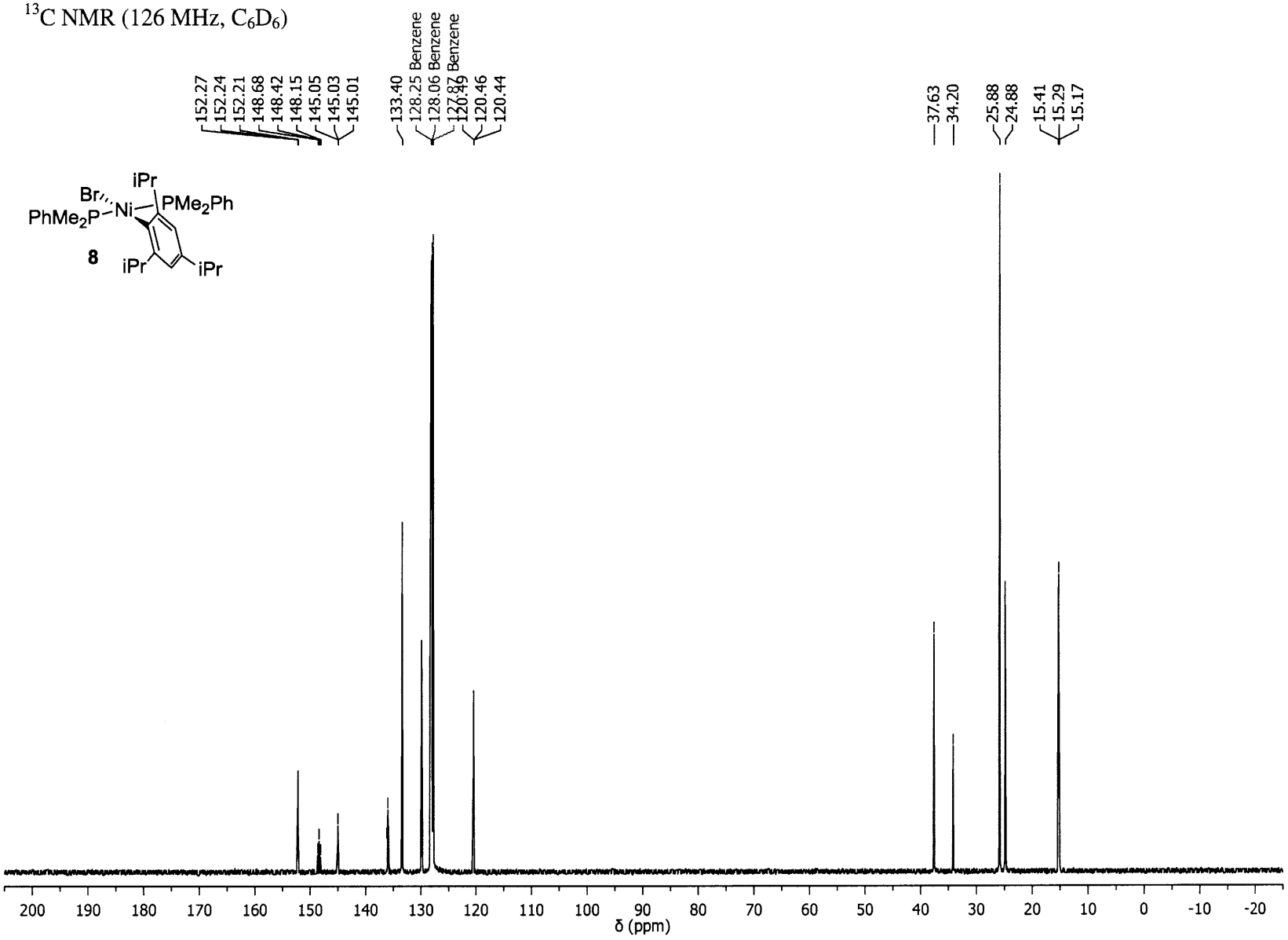
^{31}P NMR (121 MHz, CD_2Cl_2)



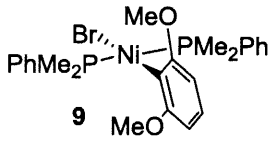
8



^{13}C NMR (126 MHz, C_6D_6)

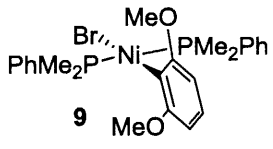


^{1}H NMR (500 MHz, CD_2Cl_2)



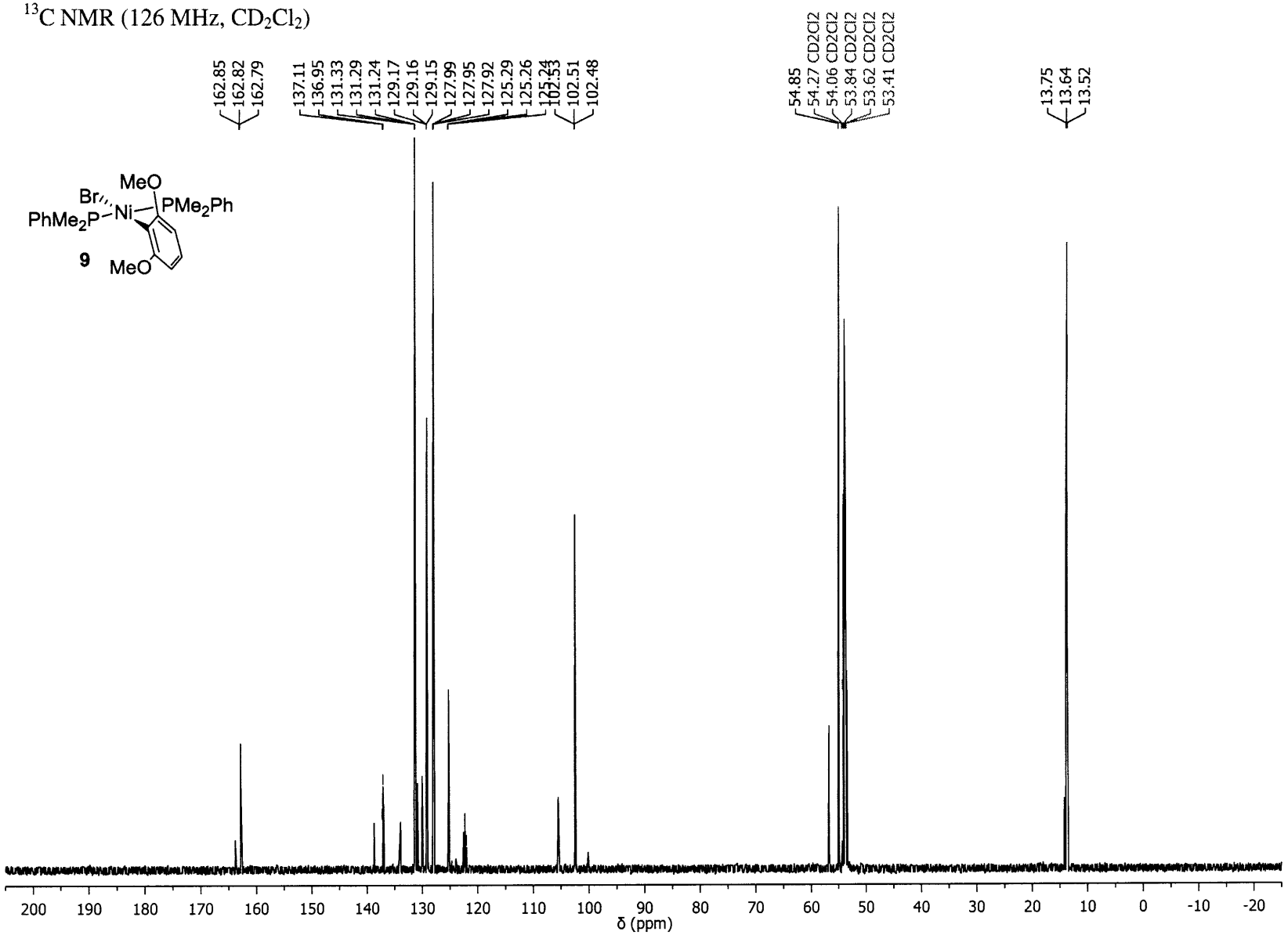
9

^{31}P NMR (121 MHz, CD_2Cl_2)

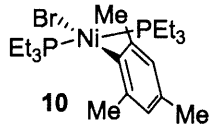


9

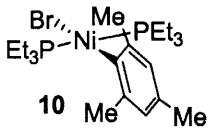
^{13}C NMR (126 MHz, CD_2Cl_2)



^{1}H NMR (500 MHz, C_6D_6)



^{31}P NMR (121 MHz, C_6D_6)



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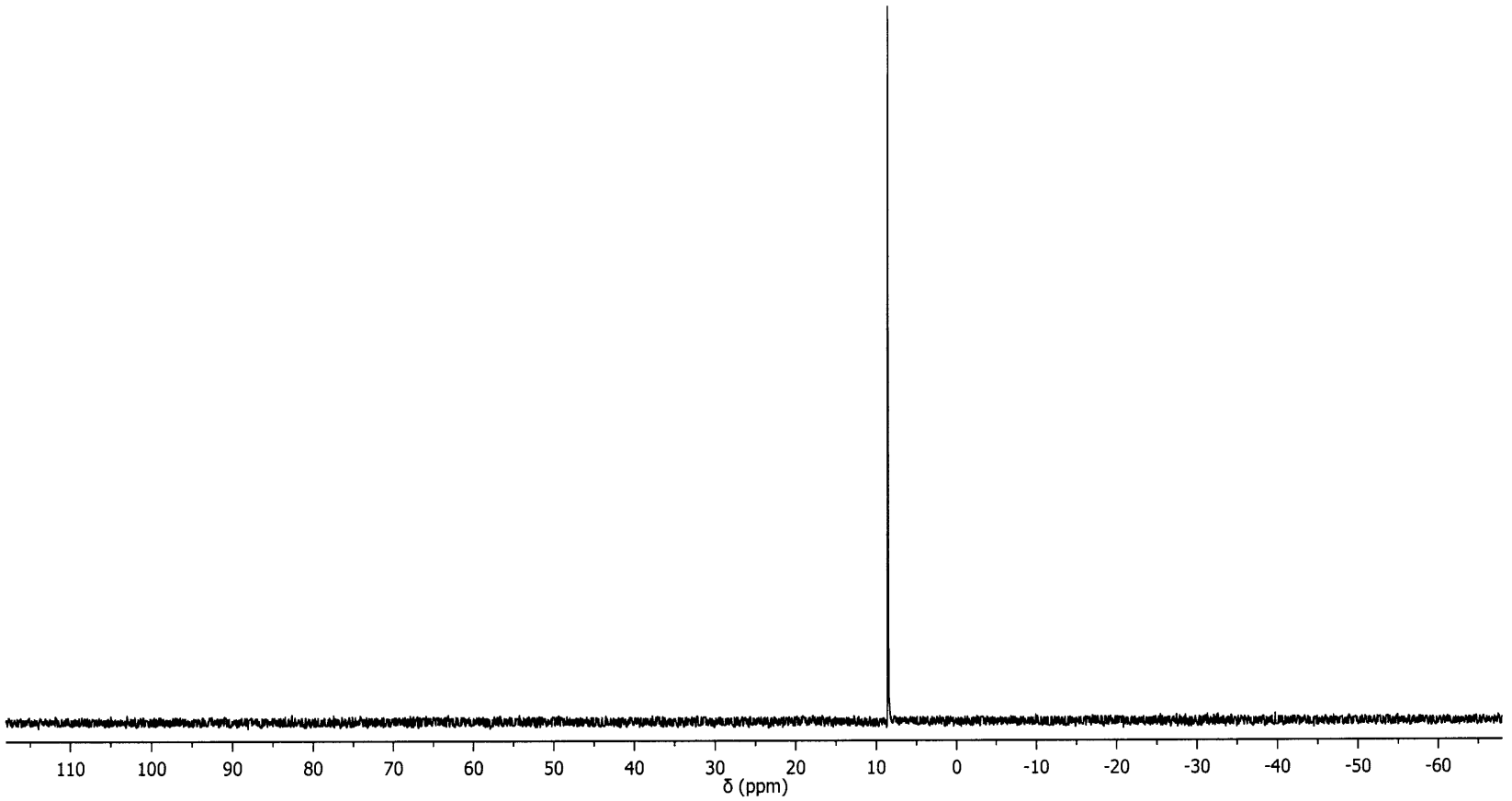
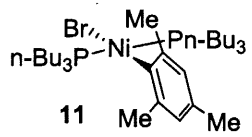
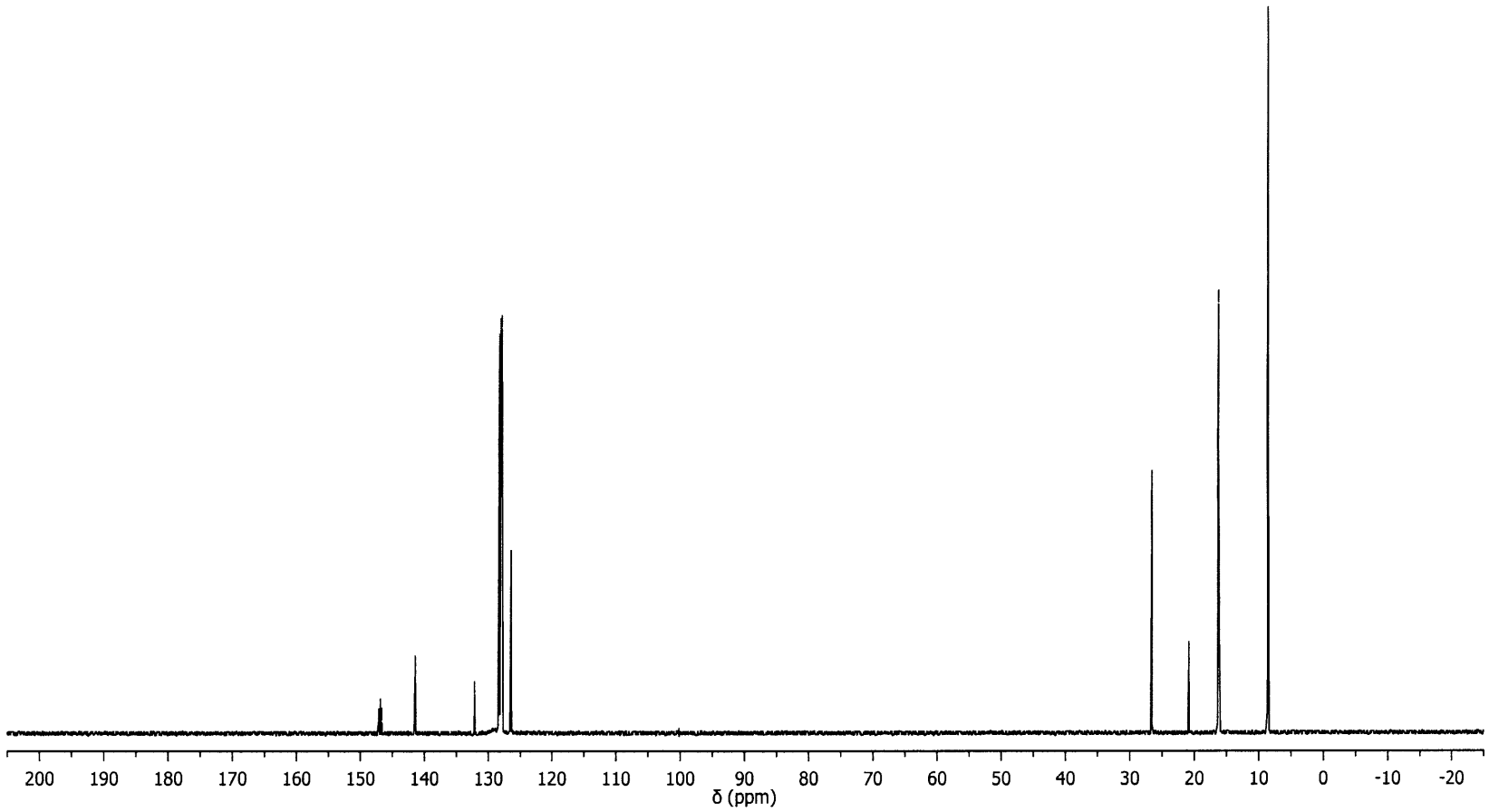


^{13}C NMR (126 MHz, C_6D_6)

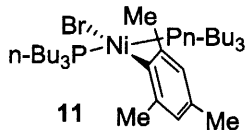


147.16
146.90
146.64
141.47
141.44
141.42
132.18
132.16
132.14
128.25 Benzene
128.06 Benzene
127.87 Benzene
126.50
126.47
126.45

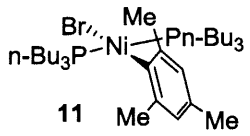
26.59
20.86
20.85
20.84
16.36
16.26
16.16
8.63



^{1}H NMR (300 MHz, C_6D_6)

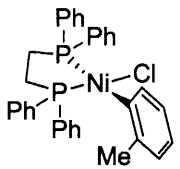


^{31}P NMR (121 MHz, C_6D_6)



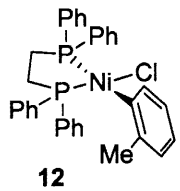
11

^{13}C NMR (126 MHz, C_6D_6)



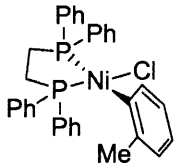
12

^{1}H NMR (500 MHz, CD_2Cl_2)



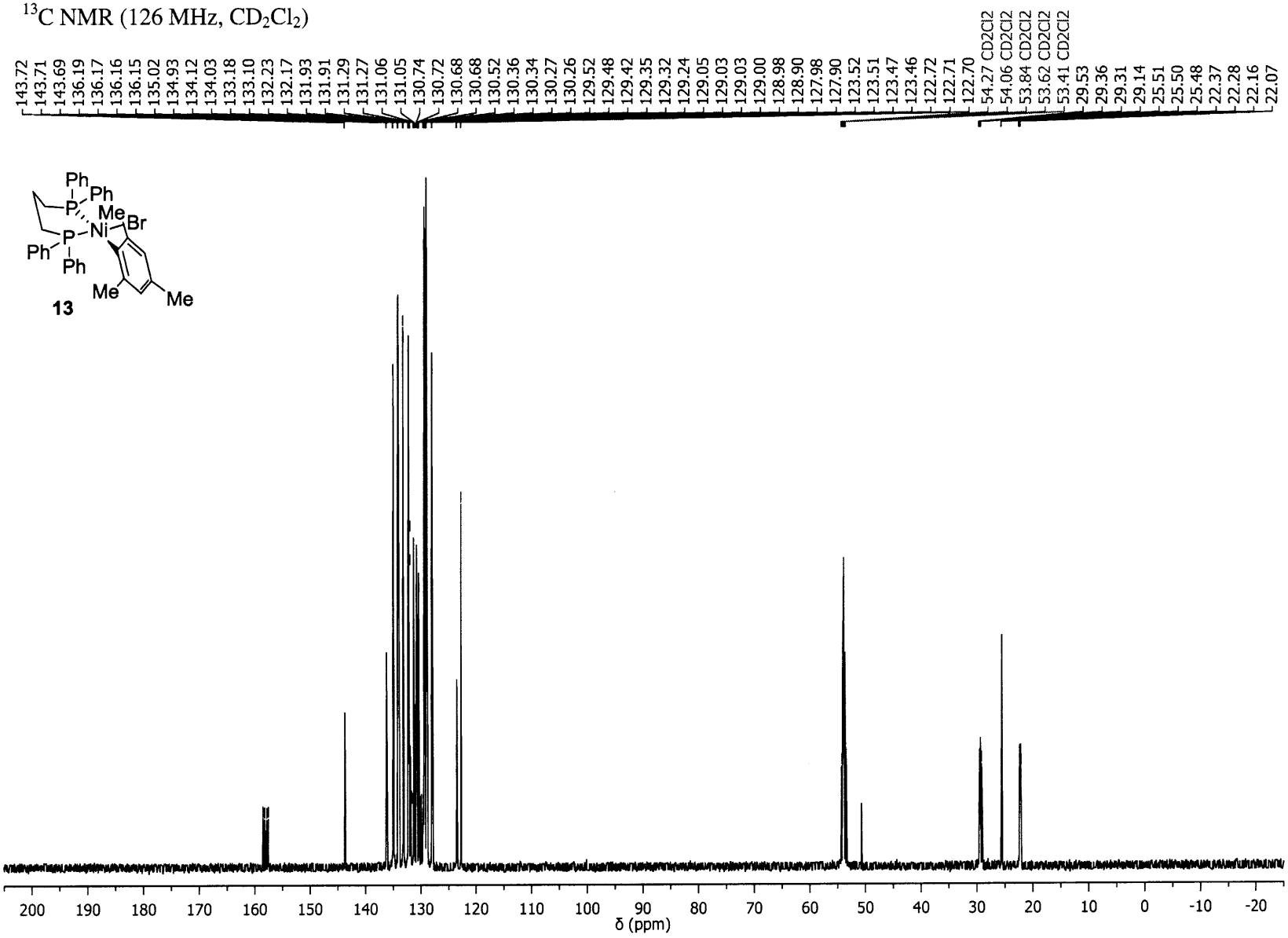
12

^{31}P NMR (121 MHz, CD_2Cl_2)

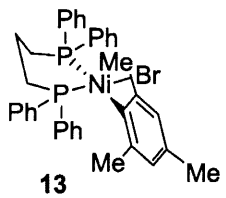


12

^{13}C NMR (126 MHz, CD_2Cl_2)

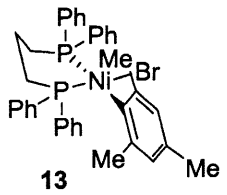


^{1}H NMR (500 MHz, CD_2Cl_2)



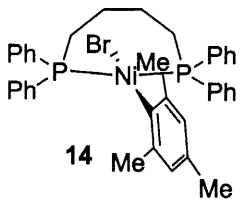
13

^{31}P NMR (121 MHz, CD_2Cl_2)

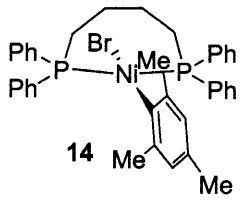


13

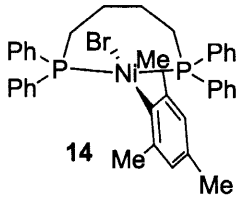
^{13}C NMR (126 MHz, CD_2Cl_2)



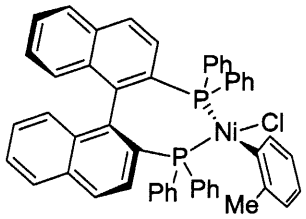
^{1}H NMR (500 MHz, CD_2Cl_2)



^{31}P NMR (121 MHz, CD_2Cl_2)

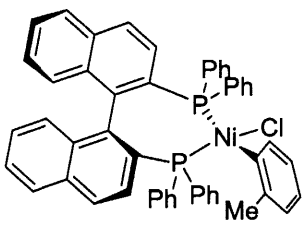


^{13}C NMR (126 MHz, CD_2Cl_2)



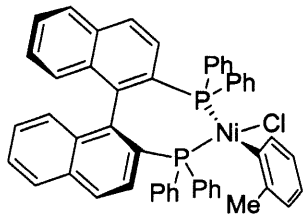
15

^{1}H NMR (500 MHz, $CDCl_3$)



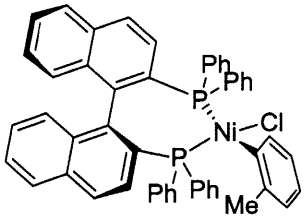
15

^{31}P NMR (203 MHz, $CDCl_3$)



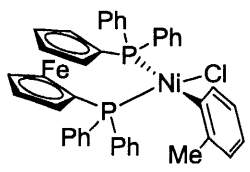
15

^{31}P NMR (121 MHz, C_6D_6)



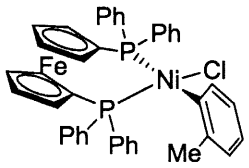
15

^{1}H NMR (500 MHz, C_6D_6)



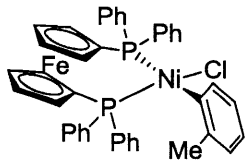
16

^{1}H NMR (500 MHz, CD_2Cl_2)



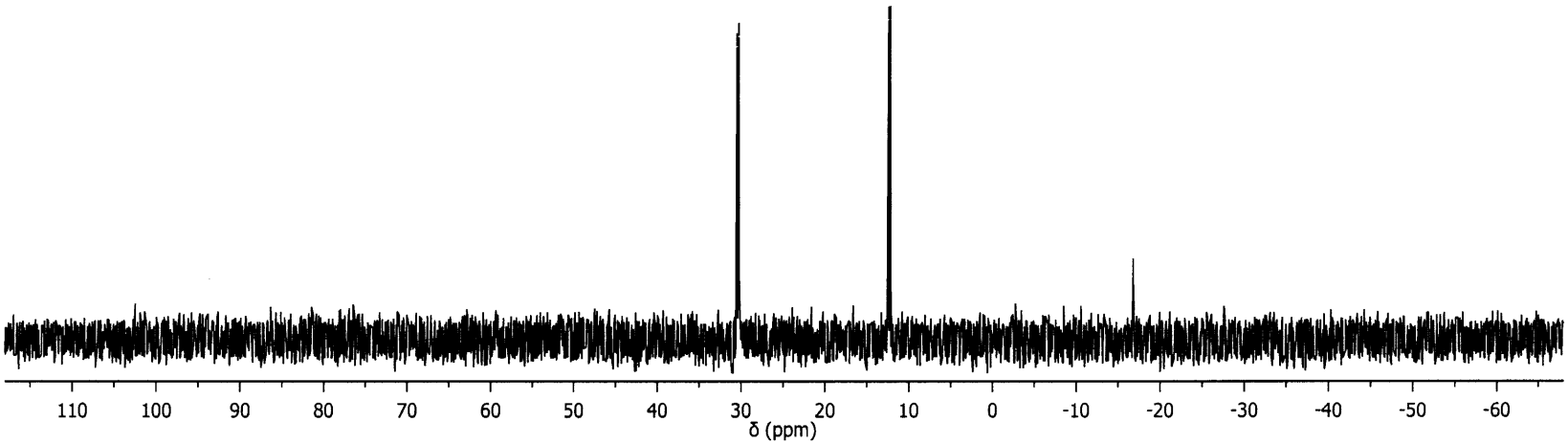
16

^{31}P NMR (121 MHz, C_6D_6)

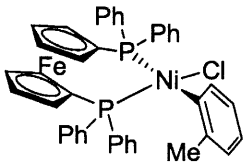


16

30.52
30.32
12.43
12.23

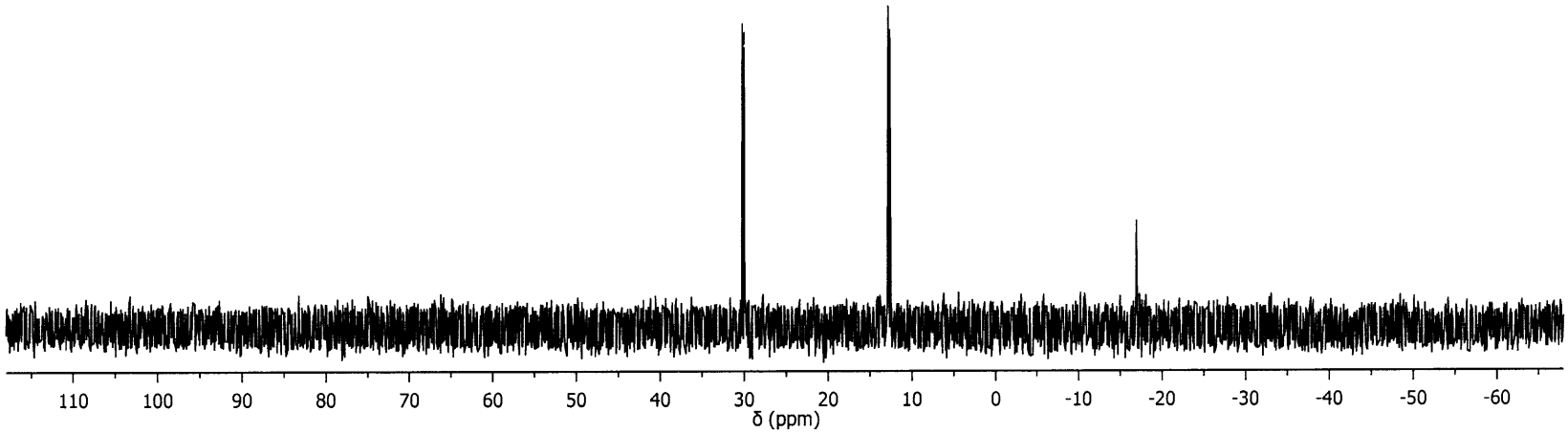


^{31}P NMR (121 MHz, CD_2Cl_2)

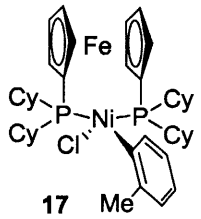


16

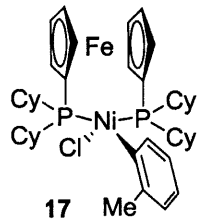
30.18
29.97
12.79
12.58



^{1}H NMR (300 MHz, C_6D_6)

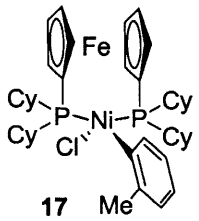


^{1}H NMR (500 MHz, CD_2Cl_2)

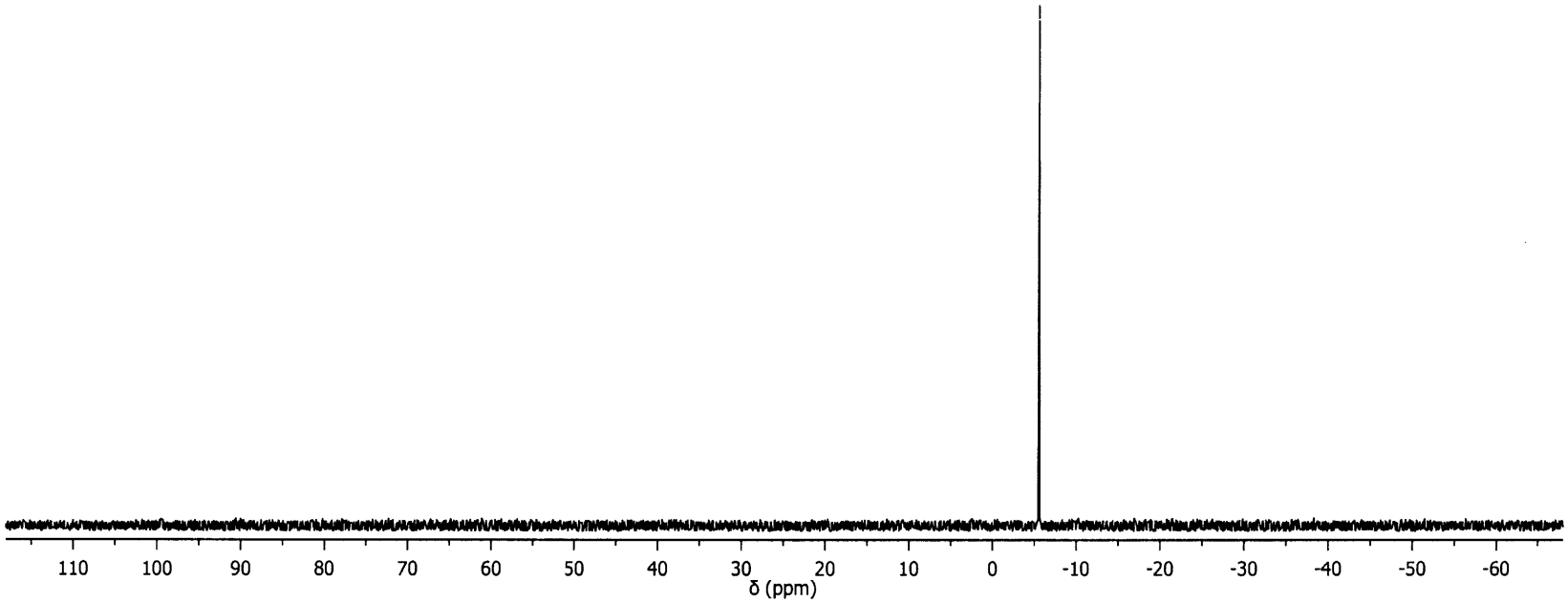


17

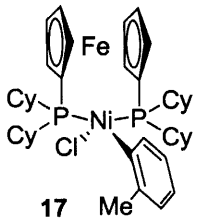
^{31}P NMR (121 MHz, CD_2Cl_2)



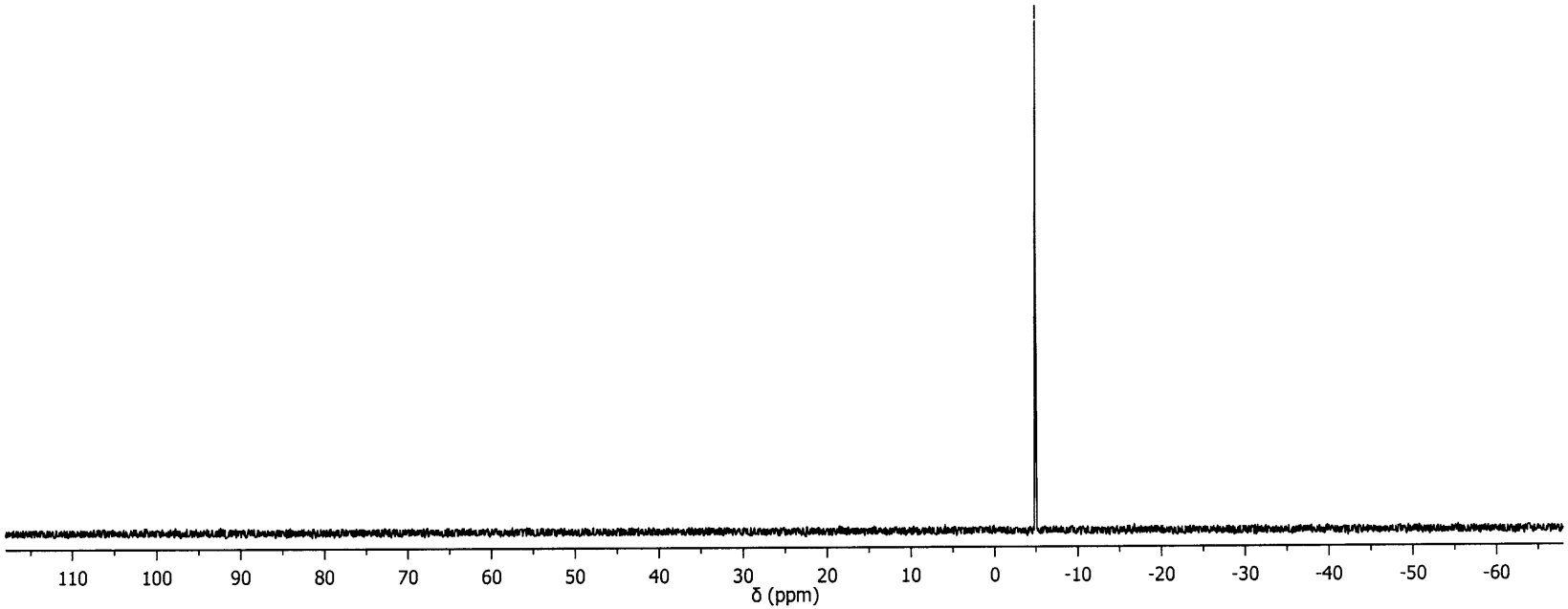
17



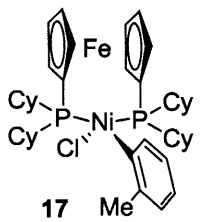
^{31}P NMR (121 MHz, C_6D_6)



17

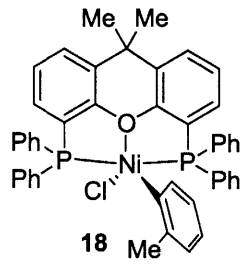


^{13}C NMR (126 MHz, CD_2Cl_2)



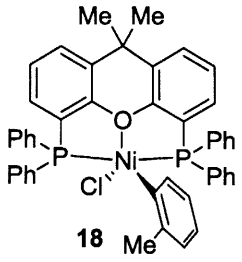
17

^{1}H NMR (300 MHz, C_6D_6)



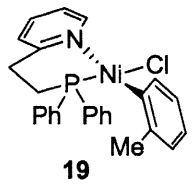
18

^{31}P NMR (121 MHz, C_6D_6)



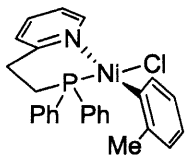
18

^{1}H NMR (500 MHz, CD_2Cl_2)

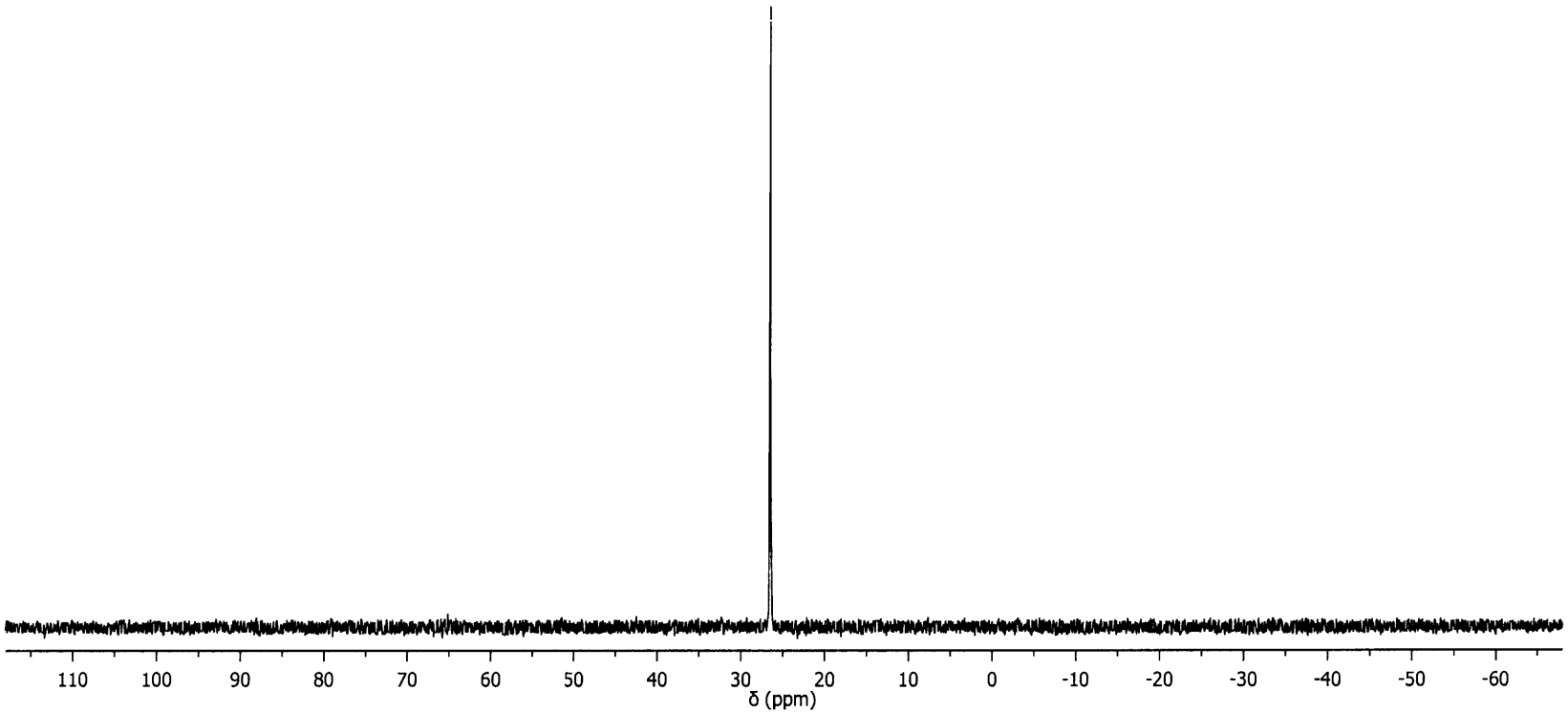


19

^{31}P NMR (121 MHz, CD_2Cl_2)



19

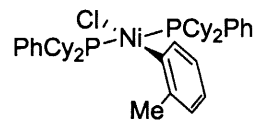


Appendix B

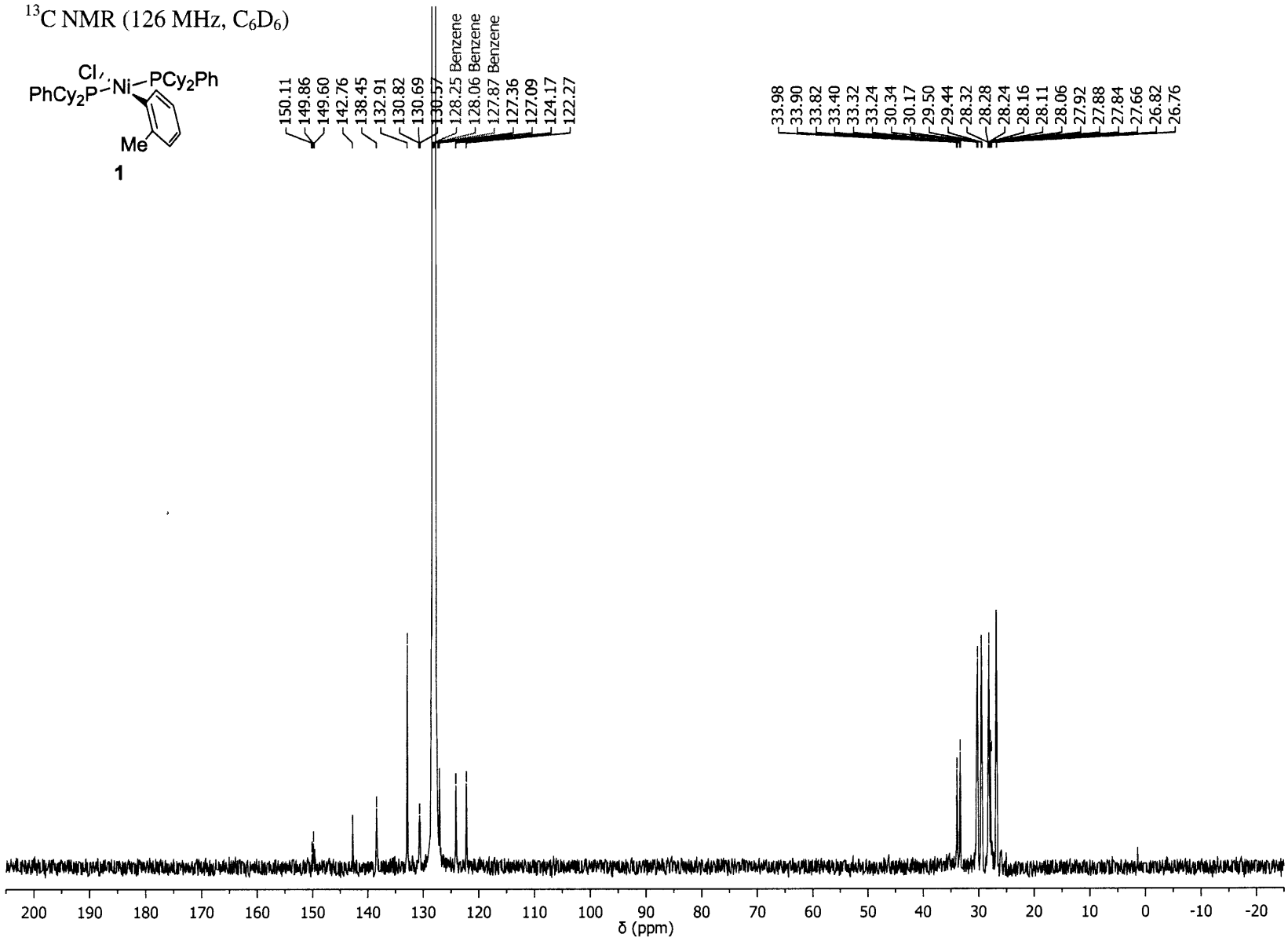
NMR Spectra for Chapter 2

Alkenes as Vinylmetal Equivalents: The Nickel-Catalyzed Mizoroki–Heck Reaction of Benzyl Chlorides and Terminal Alkenes

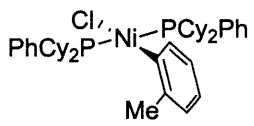
^{1}H NMR (500 MHz, C_6D_6)



1

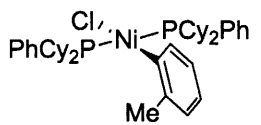

^{13}C NMR (126 MHz, C_6D_6)
Cl
PhCy2P
Ni
PCy2Ph
Me
1
150.11
149.86
149.60
142.76
138.45
132.91
130.82
130.69
128.57 Benzene
128.25 Benzene
128.06 Benzene
127.87 Benzene
127.36
127.09
124.17
122.27
33.98
33.90
33.82
33.40
33.32
33.24
30.34
30.17
29.50
29.44
28.32
28.28
28.24
28.16
28.11
28.06
27.92
27.88
27.84
27.66
26.82
26.76
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
δ (ppm)

^{31}P NMR (121 MHz, C_6D_6)



1

^{31}P NMR (202 MHz, CD_2Cl_2)

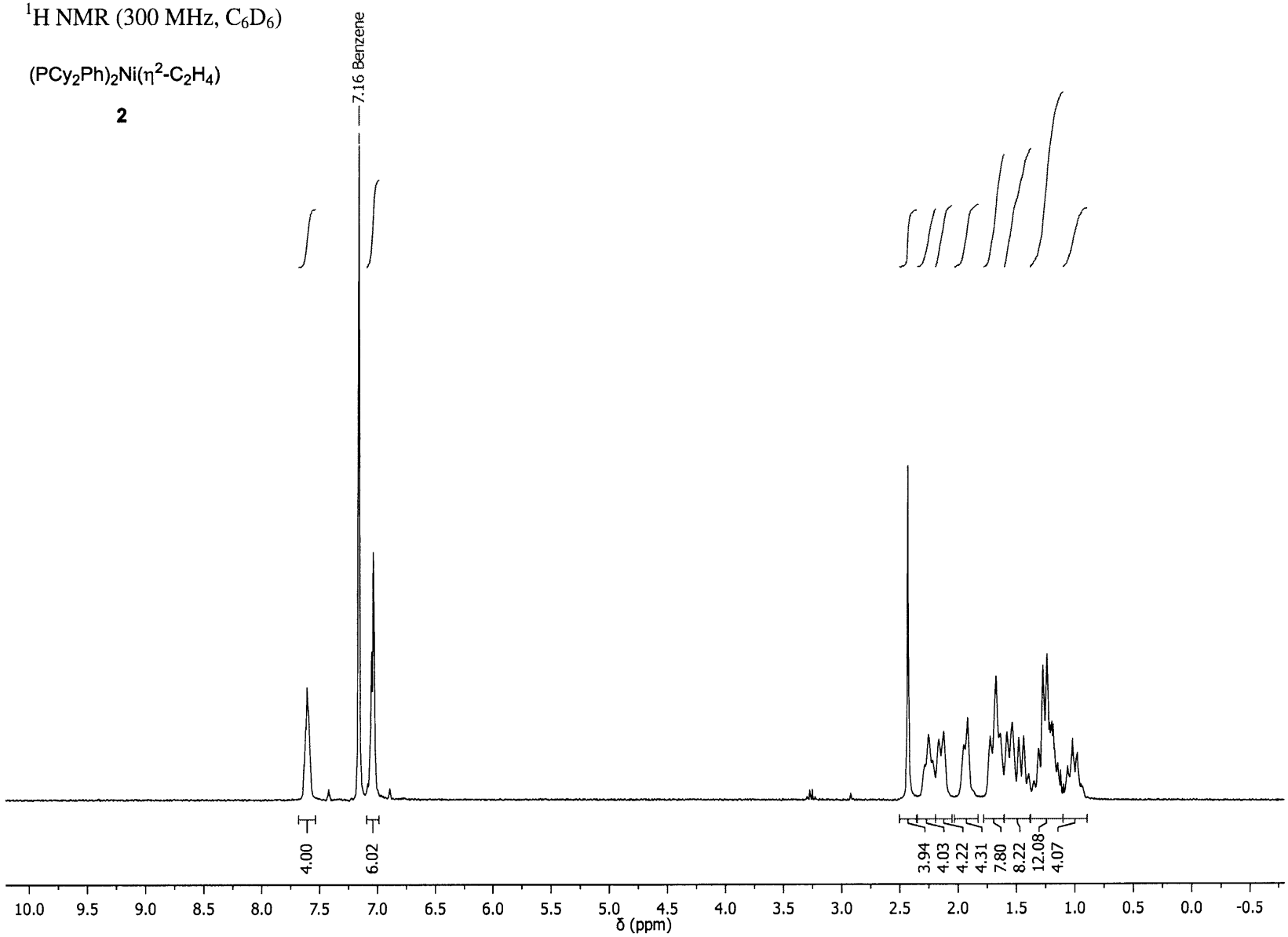


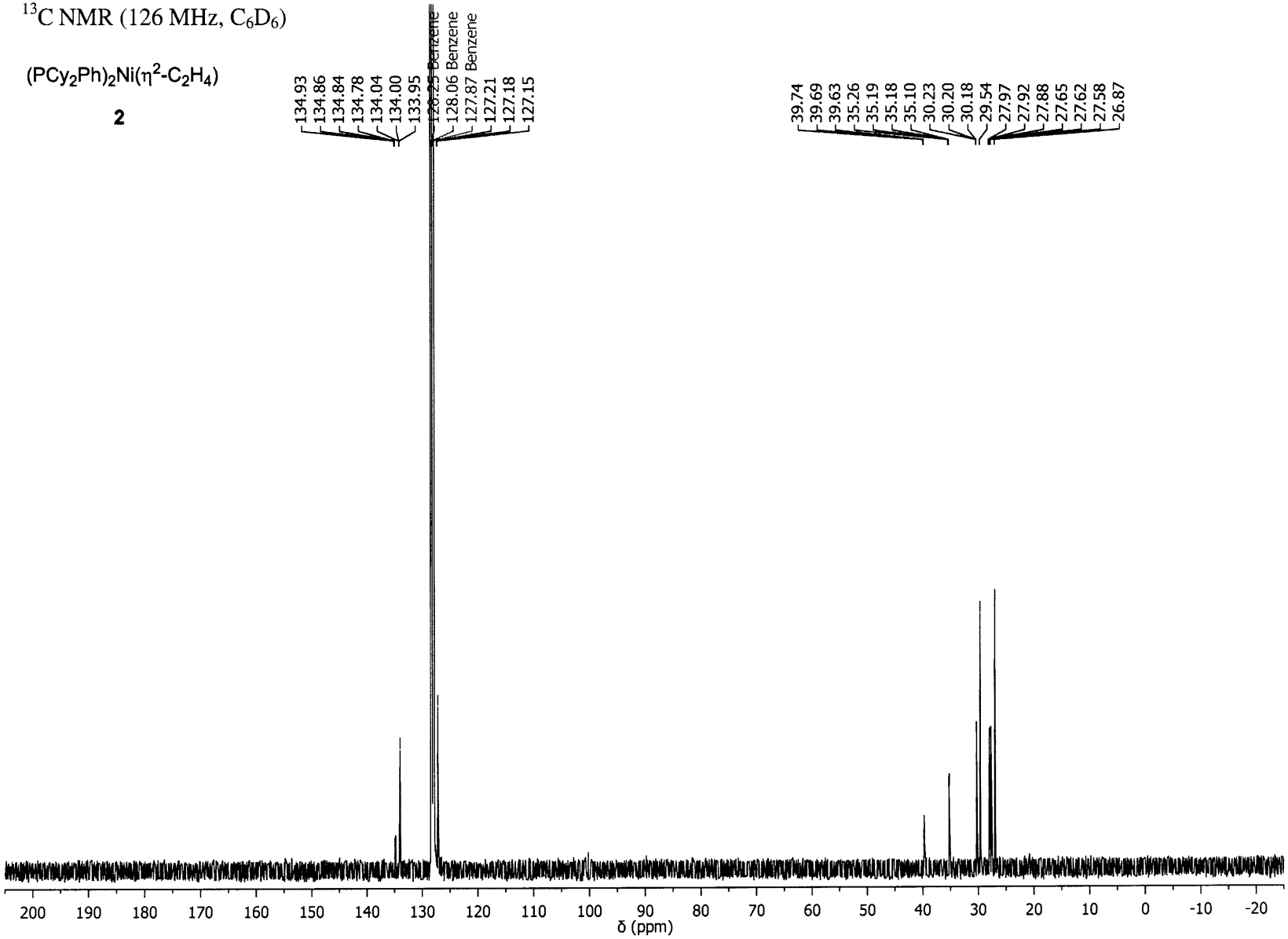
1

^{1}H NMR (300 MHz, C_6D_6)

$(PCy_2Ph)_2Ni(\eta^2\text{-}C_2H_4)$

2

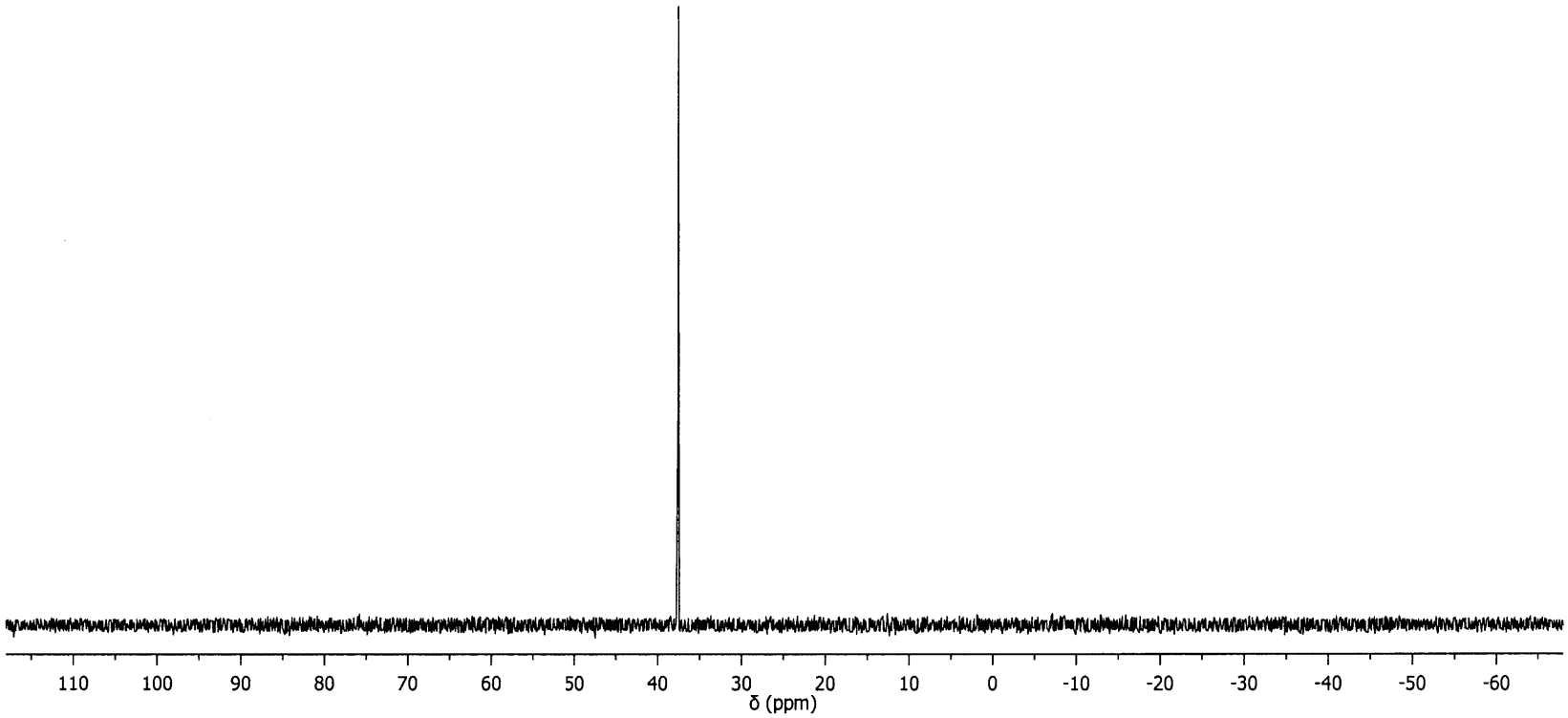



^{13}C NMR (126 MHz, C_6D_6)
$(PCy_2Ph)_2Ni(\eta^2\text{-}C_2H_4)$
2
134.93
134.86
134.84
134.78
134.04
134.00
133.95
128.25 Benzene
128.06 Benzene
127.87 Benzene
127.21
127.18
127.15
39.74
39.69
39.63
35.26
35.19
35.18
35.10
30.23
30.20
30.18
29.54
27.97
27.92
27.88
27.65
27.62
27.58
26.87
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
δ (ppm)

^{31}P NMR (121 MHz, C_6D_6)

$(PCy_2Ph)_2Ni(\eta^2\text{-}C_2H_4)$

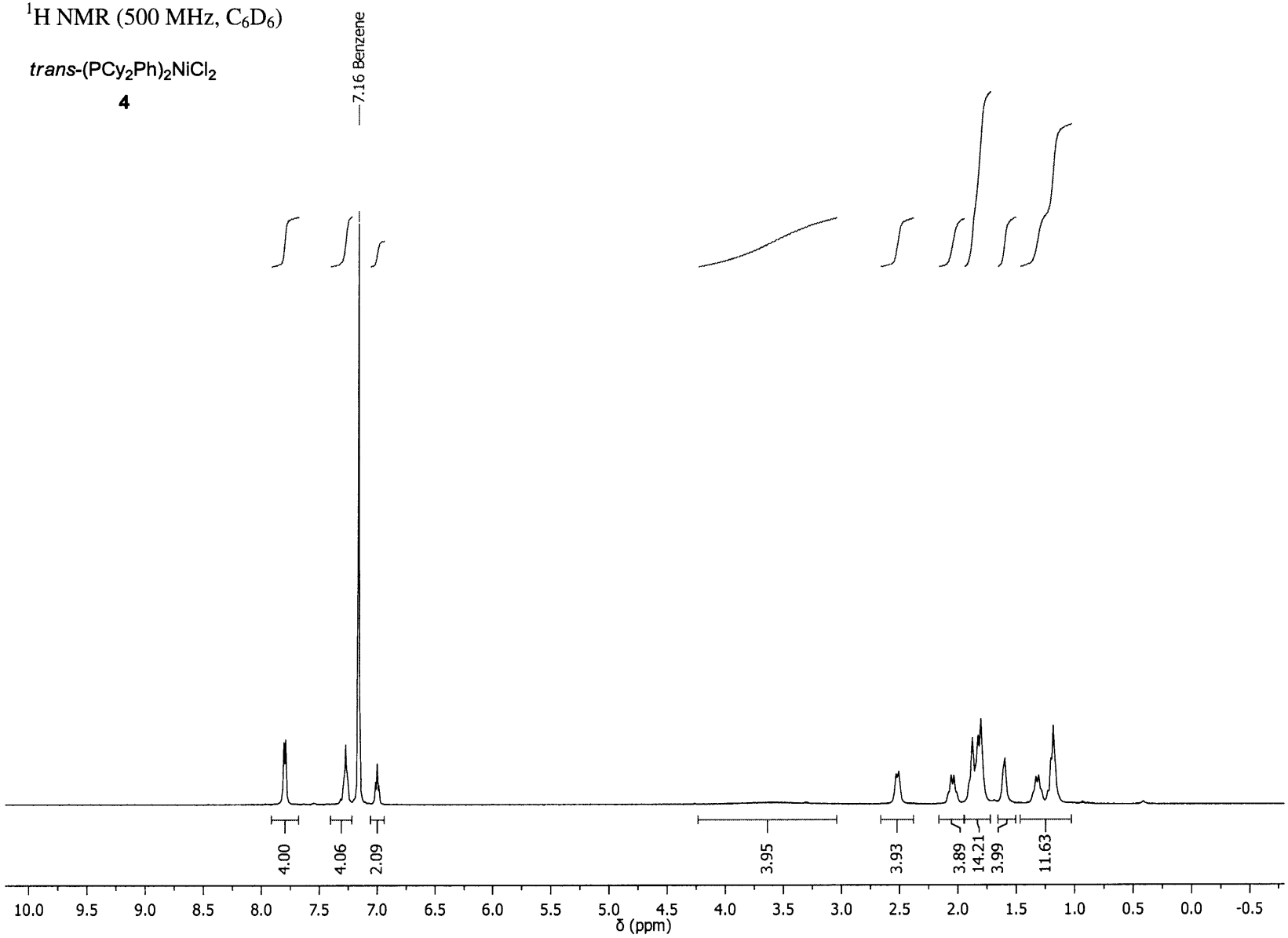
2



^{1}H NMR (500 MHz, C_6D_6)

trans-$(PCy_2Ph)_2NiCl_2$

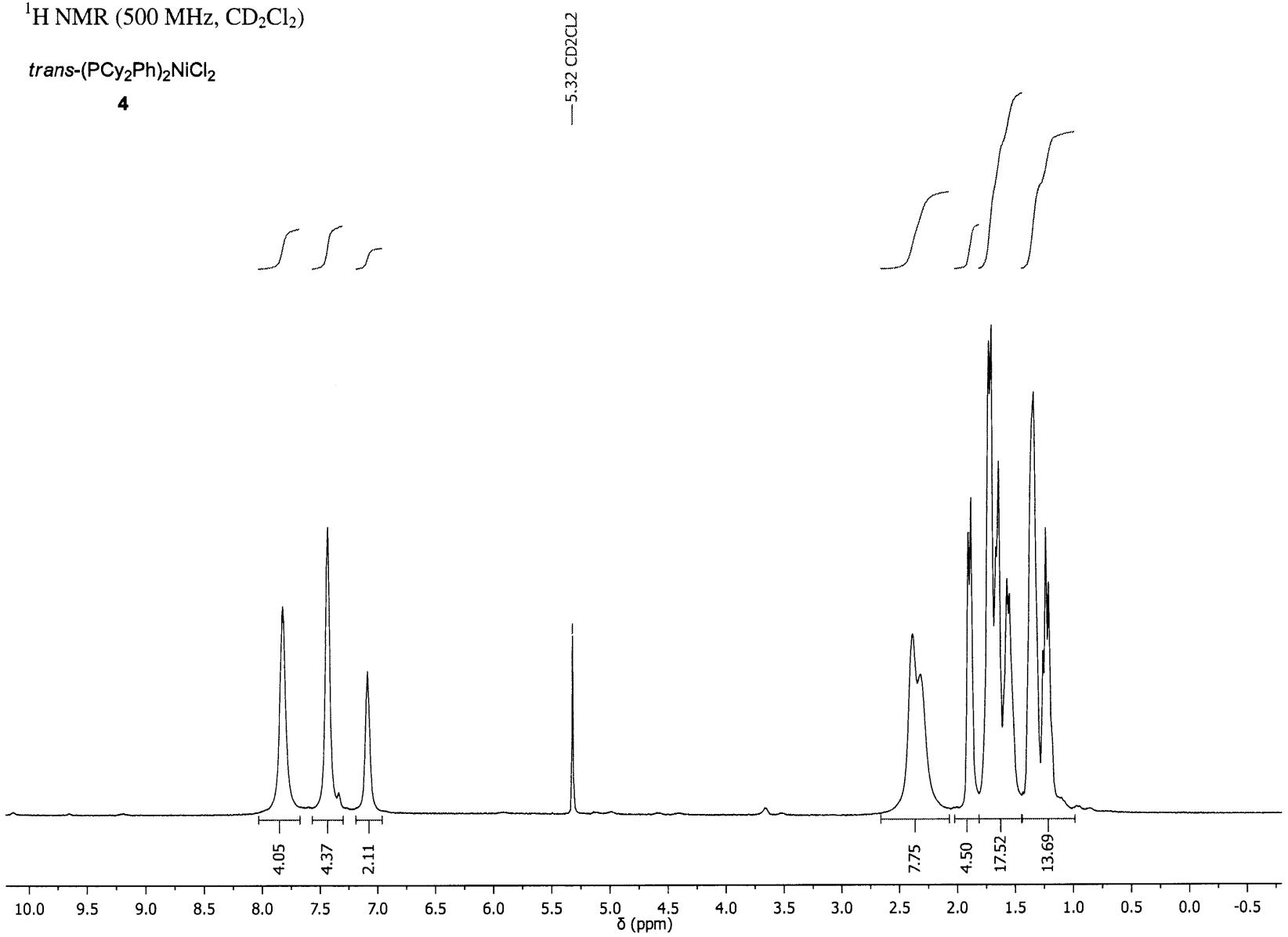
4



^{1}H NMR (500 MHz, CD_2Cl_2)

trans-$(PCy_2Ph)_2NiCl_2$

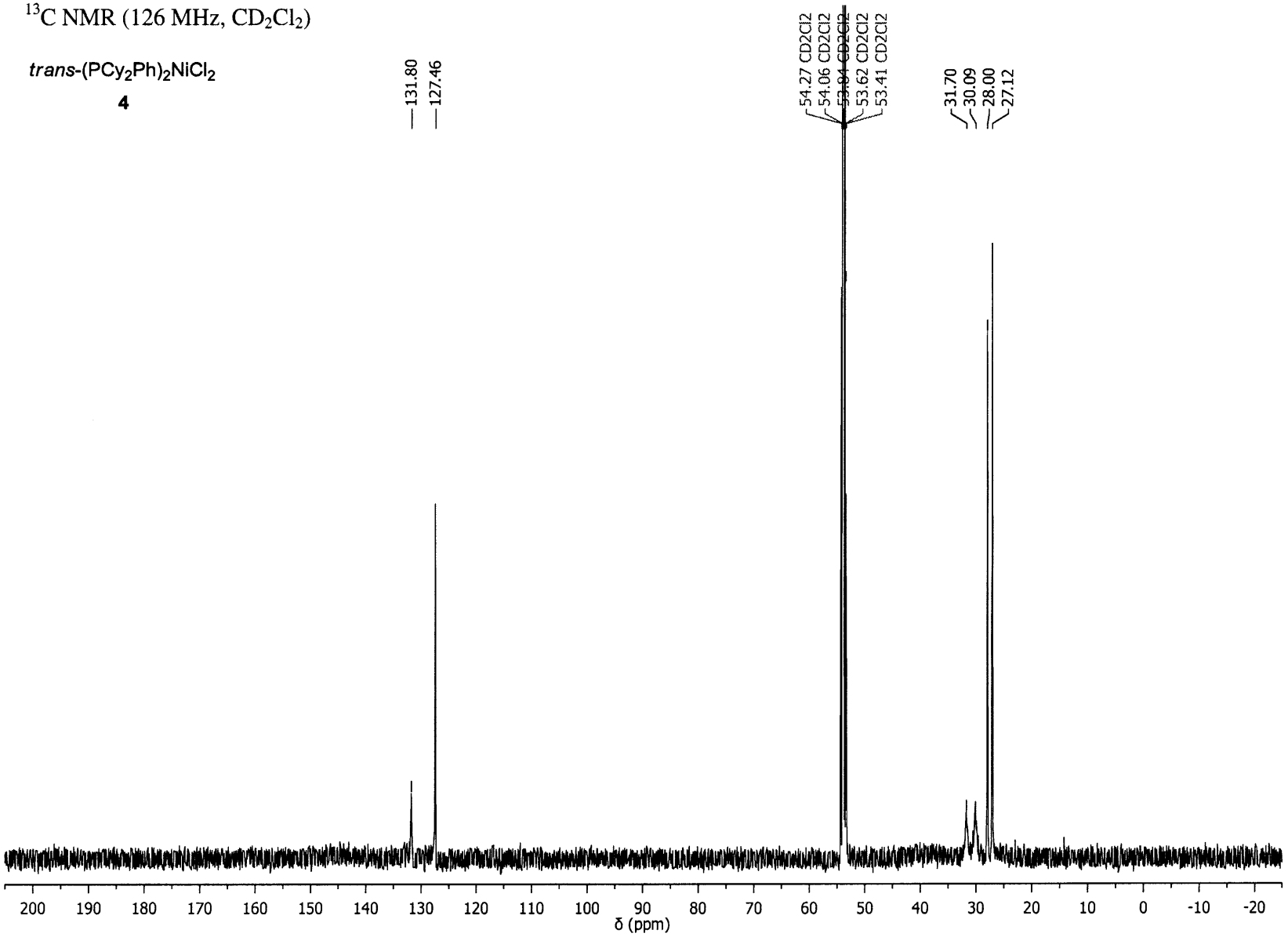
4



^{13}C NMR (126 MHz, CD_2Cl_2)

trans-$(PCy_2Ph)_2NiCl_2$

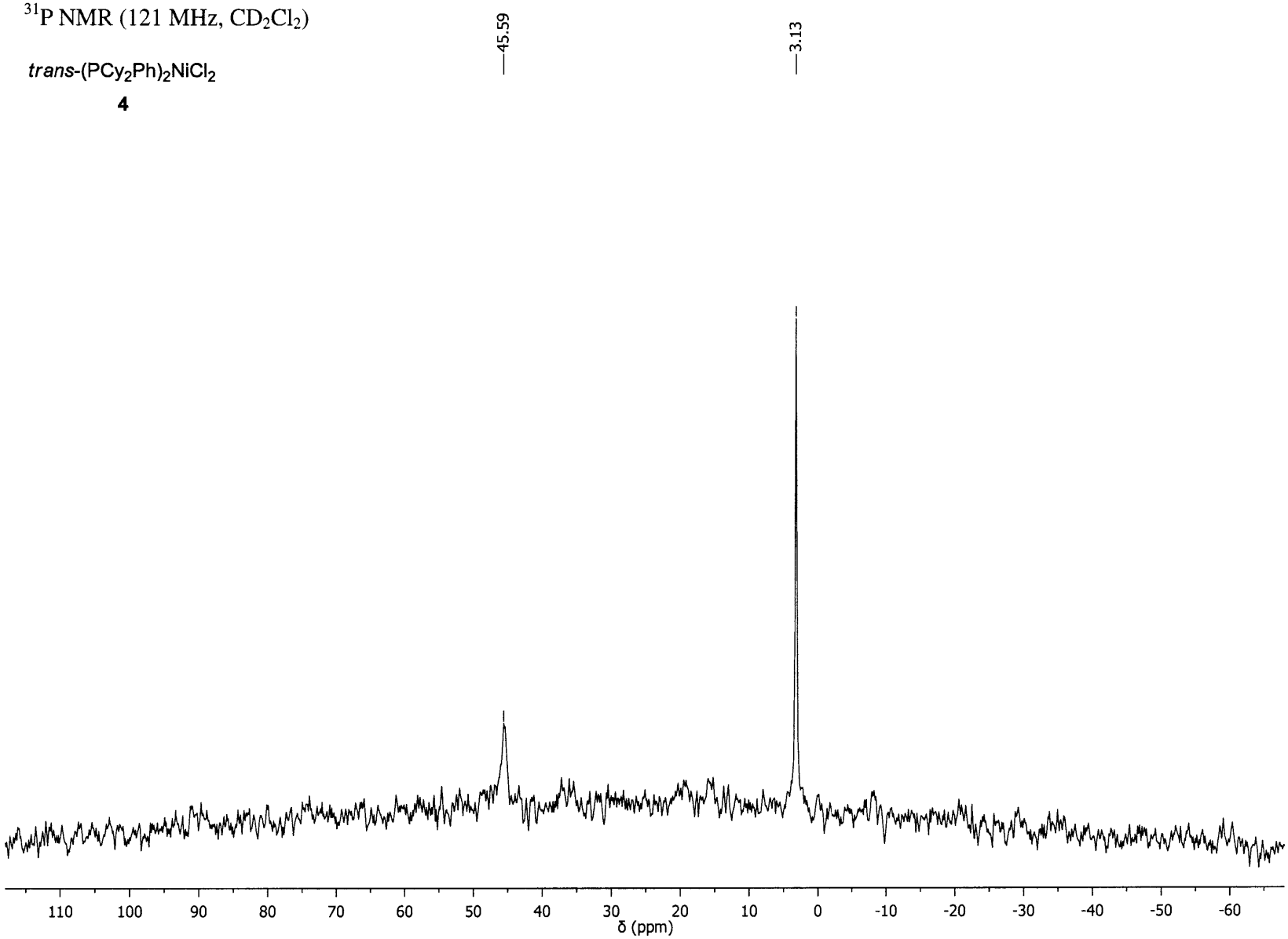
4



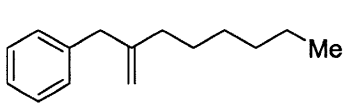
^{31}P NMR (121 MHz, CD_2Cl_2)

trans-$(PCy_2Ph)_2NiCl_2$

4

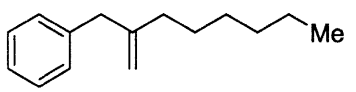


^{1}H NMR (500 MHz, $CDCl_3$)



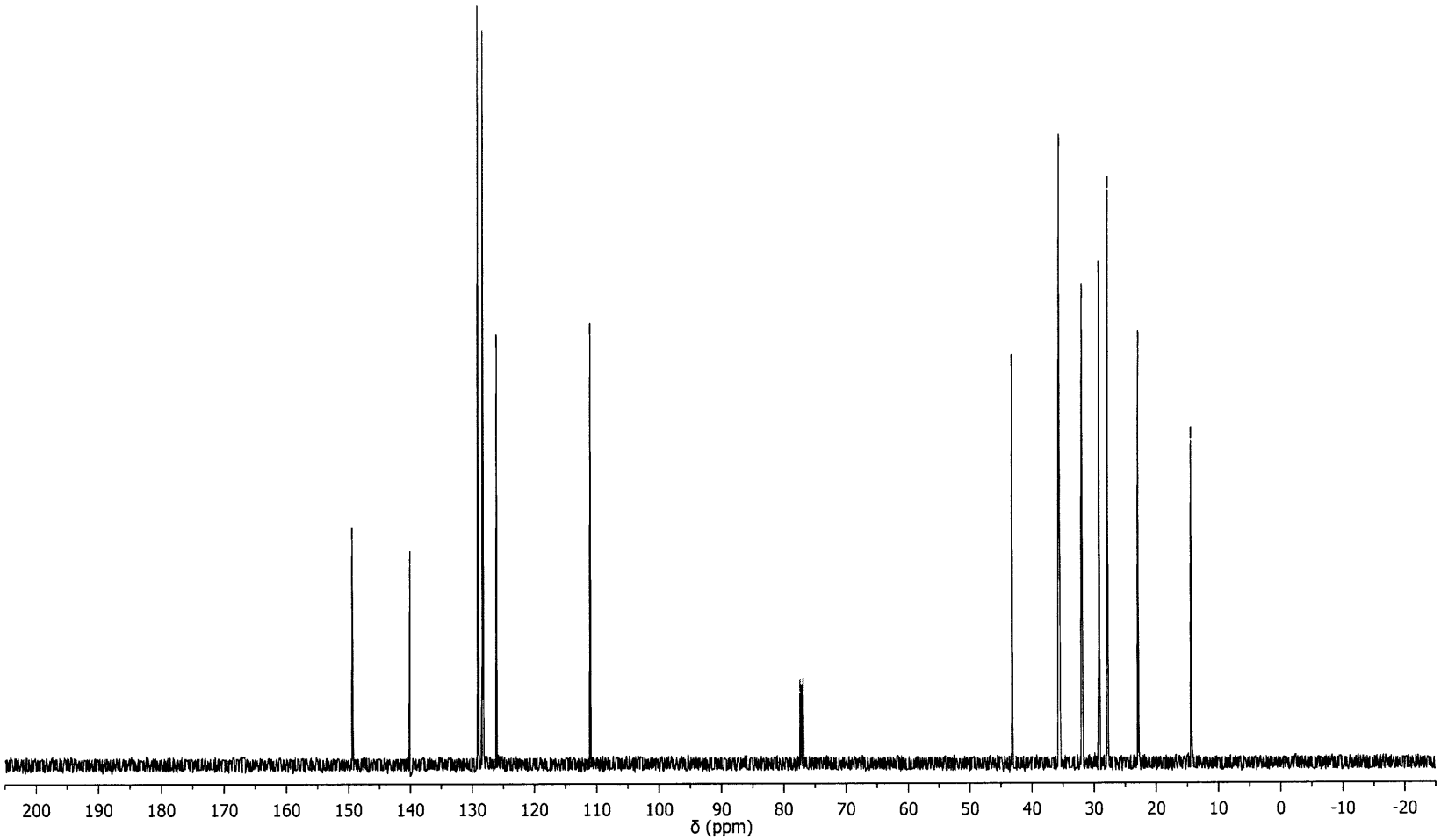
7

^{13}C NMR (126 MHz, $CDCl_3$)

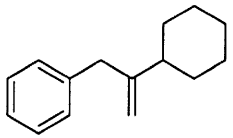


7

149.39
140.05
129.14
128.36
126.11
111.05
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
43.18
35.58
31.91
29.16
27.75
22.79
14.25

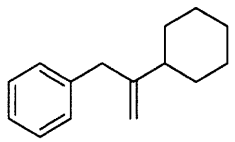


^{1}H NMR (500 MHz, $CDCl_3$)



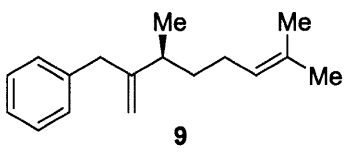
8

^{13}C NMR (126 MHz, $CDCl_3$)



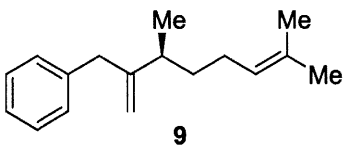
8

^{1}H NMR (500 MHz, $CDCl_3$)



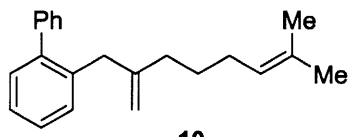
9

^{13}C NMR (126 MHz, $CDCl_3$)



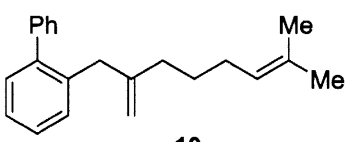
9

^{1}H NMR (500 MHz, $CDCl_3$)



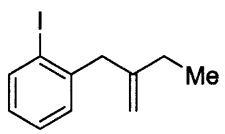
10

^{13}C NMR (126 MHz, $CDCl_3$)



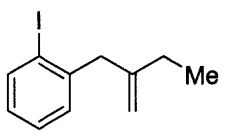
10

^{1}H NMR (500 MHz, $CDCl_3$)



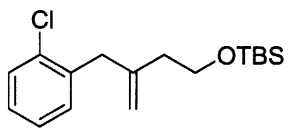
11

^{13}C NMR (126 MHz, $CDCl_3$)



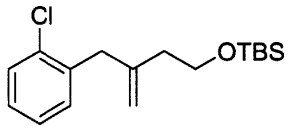
11

^{1}H NMR (500 MHz, $CDCl_3$)



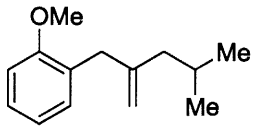
12

^{13}C NMR (126 MHz, $CDCl_3$)



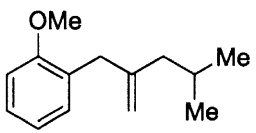
12

^{1}H NMR (500 MHz, $CDCl_3$)



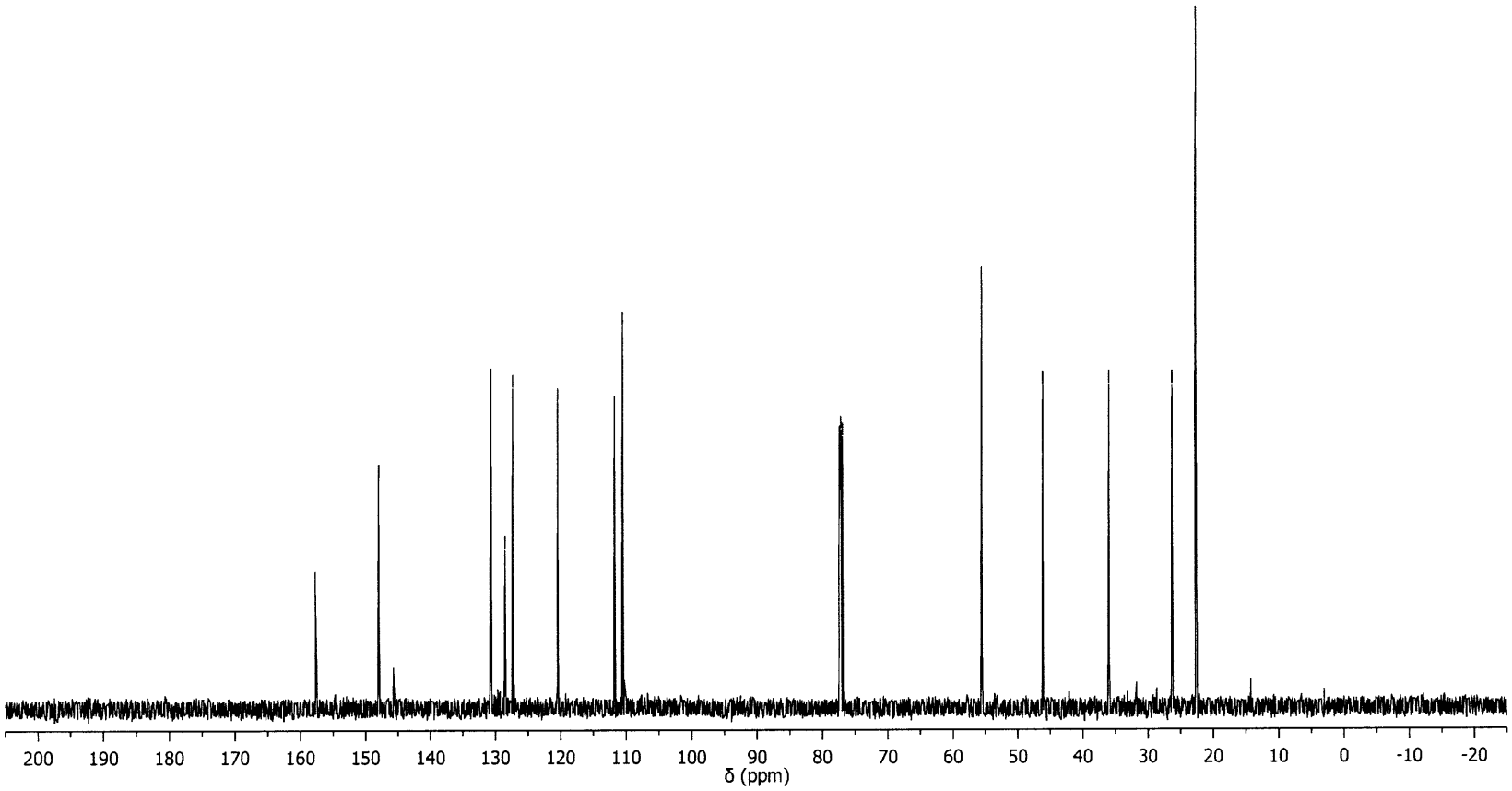
13

^{13}C NMR (126 MHz, $CDCl_3$)

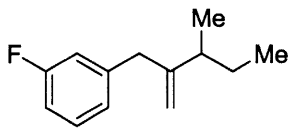


13

157.67
147.91
130.68
128.54
127.35
120.47
111.77
110.52
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
55.46
46.09
35.92
26.22
22.63

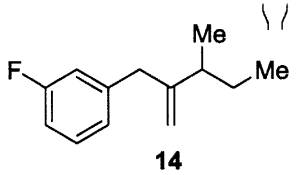


^{1}H NMR (500 MHz, $CDCl_3$)



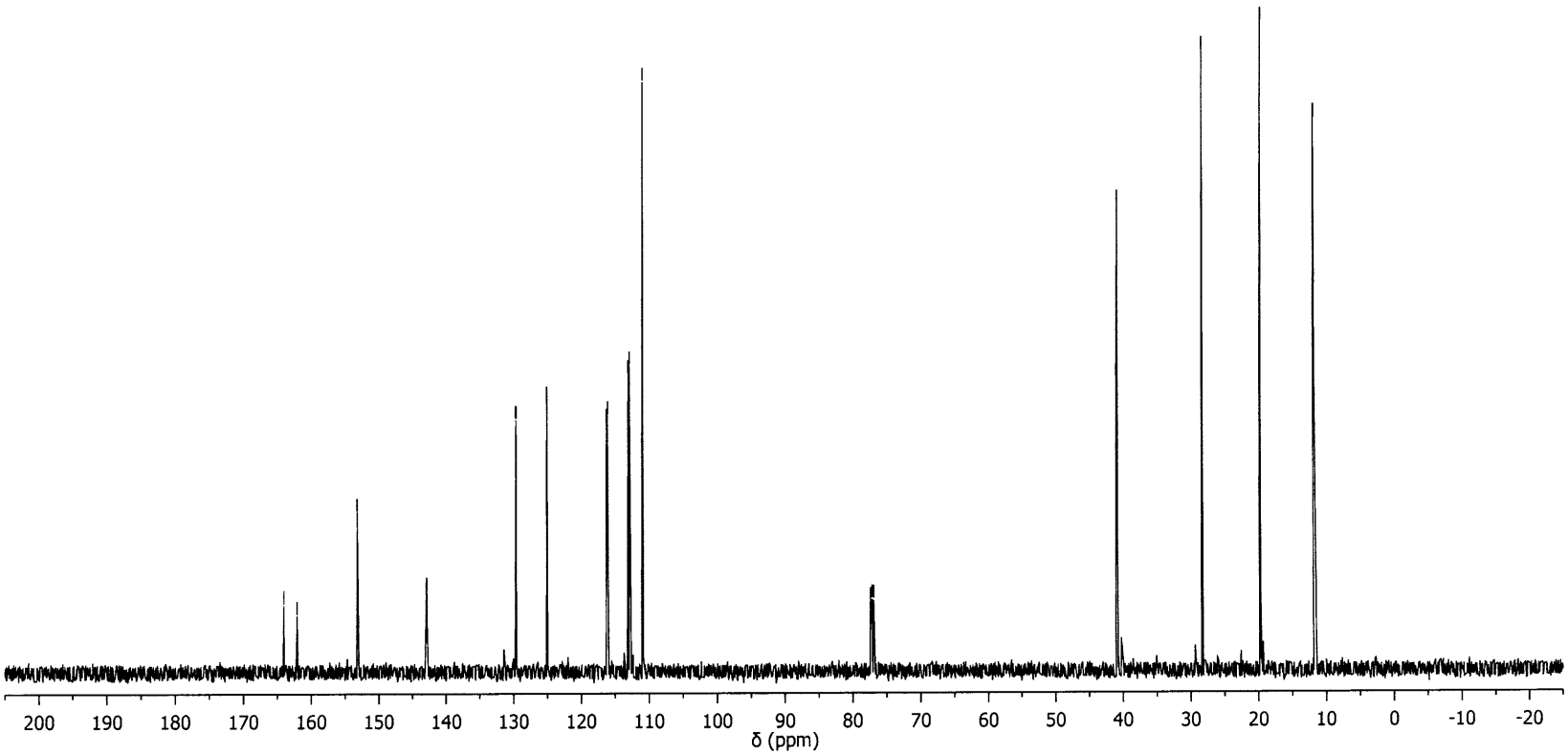
14

^{13}C NMR (126 MHz, $CDCl_3$)

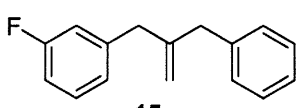


14

164.03
162.08
154.66
153.15
142.91
142.85
129.68
129.62
125.09
125.07
116.28
116.11
113.05
112.88
110.90
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
40.96
40.95
40.83
28.30
19.66
11.82

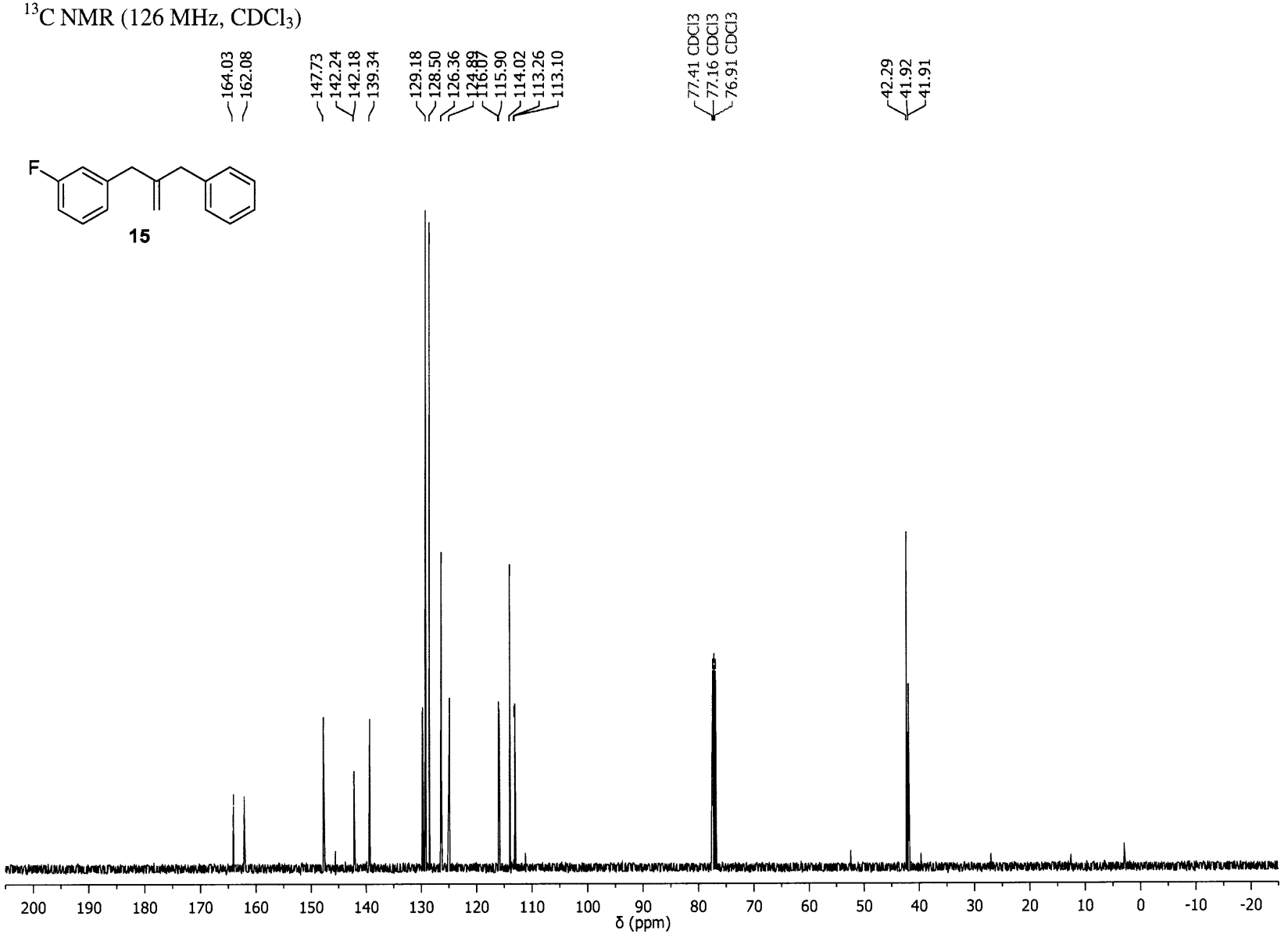


^{1}H NMR (500 MHz, $CDCl_3$)

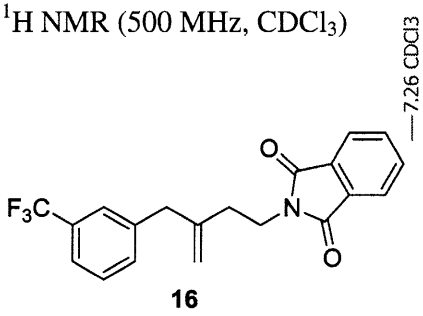


15

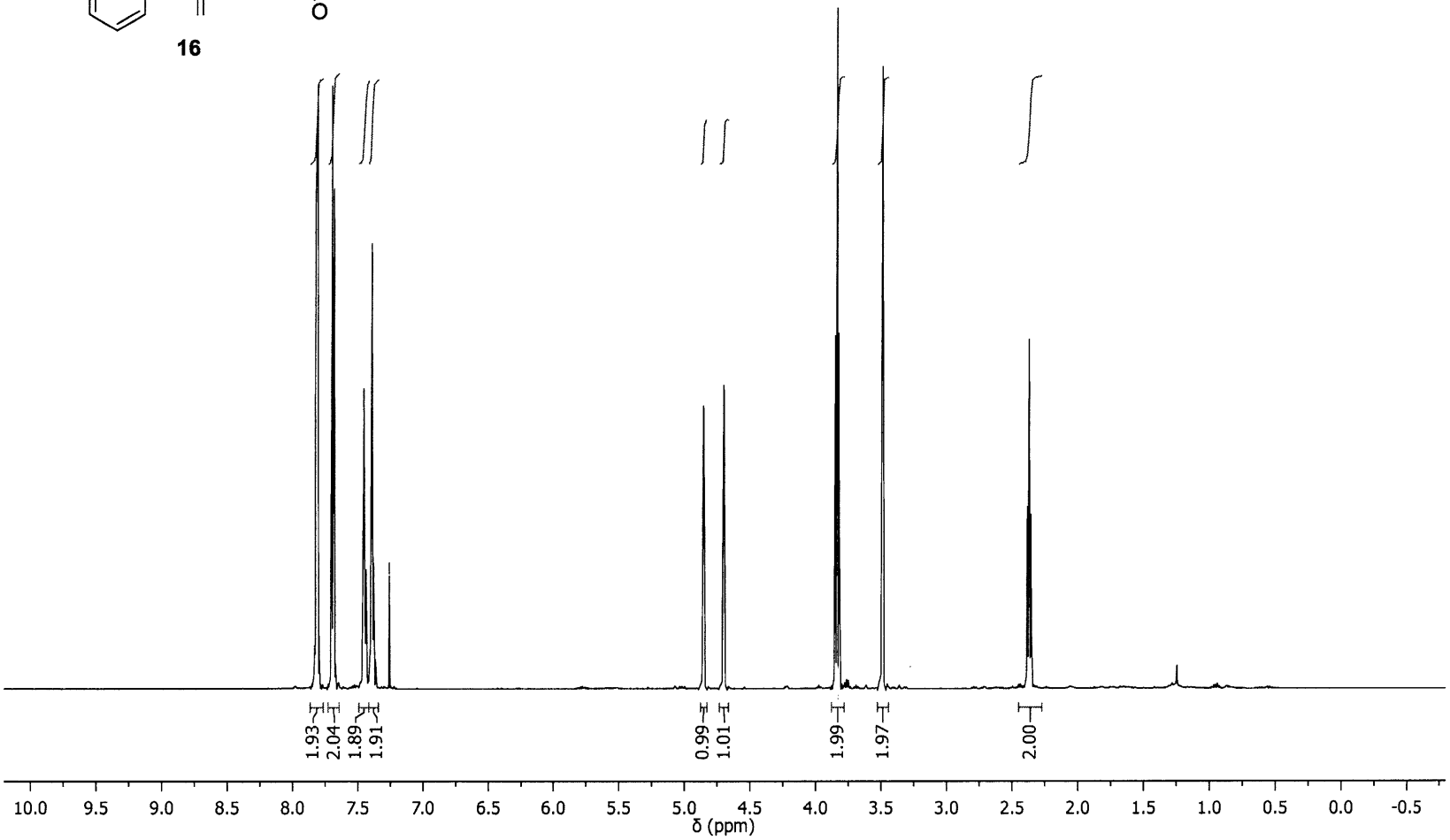
^{13}C NMR (126 MHz, $CDCl_3$)



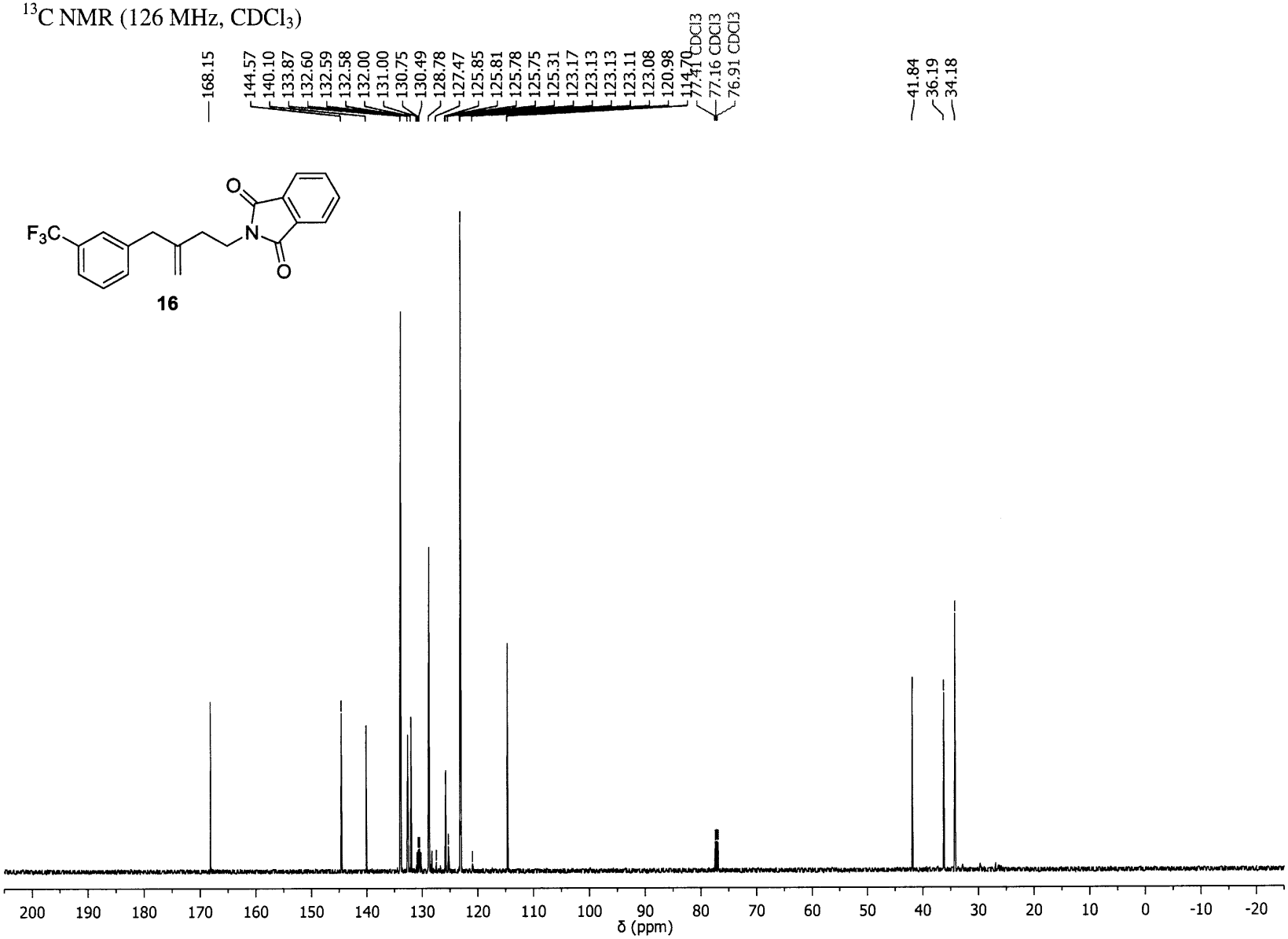
^{1}H NMR (500 MHz, $CDCl_3$)



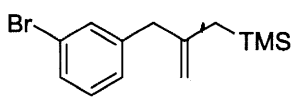
16



^{13}C NMR (126 MHz, $CDCl_3$)

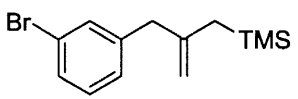


^{1}H NMR (500 MHz, $CDCl_3$)



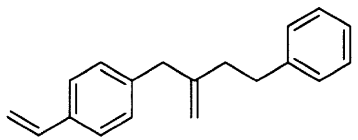
17

^{13}C NMR (126 MHz, $CDCl_3$)



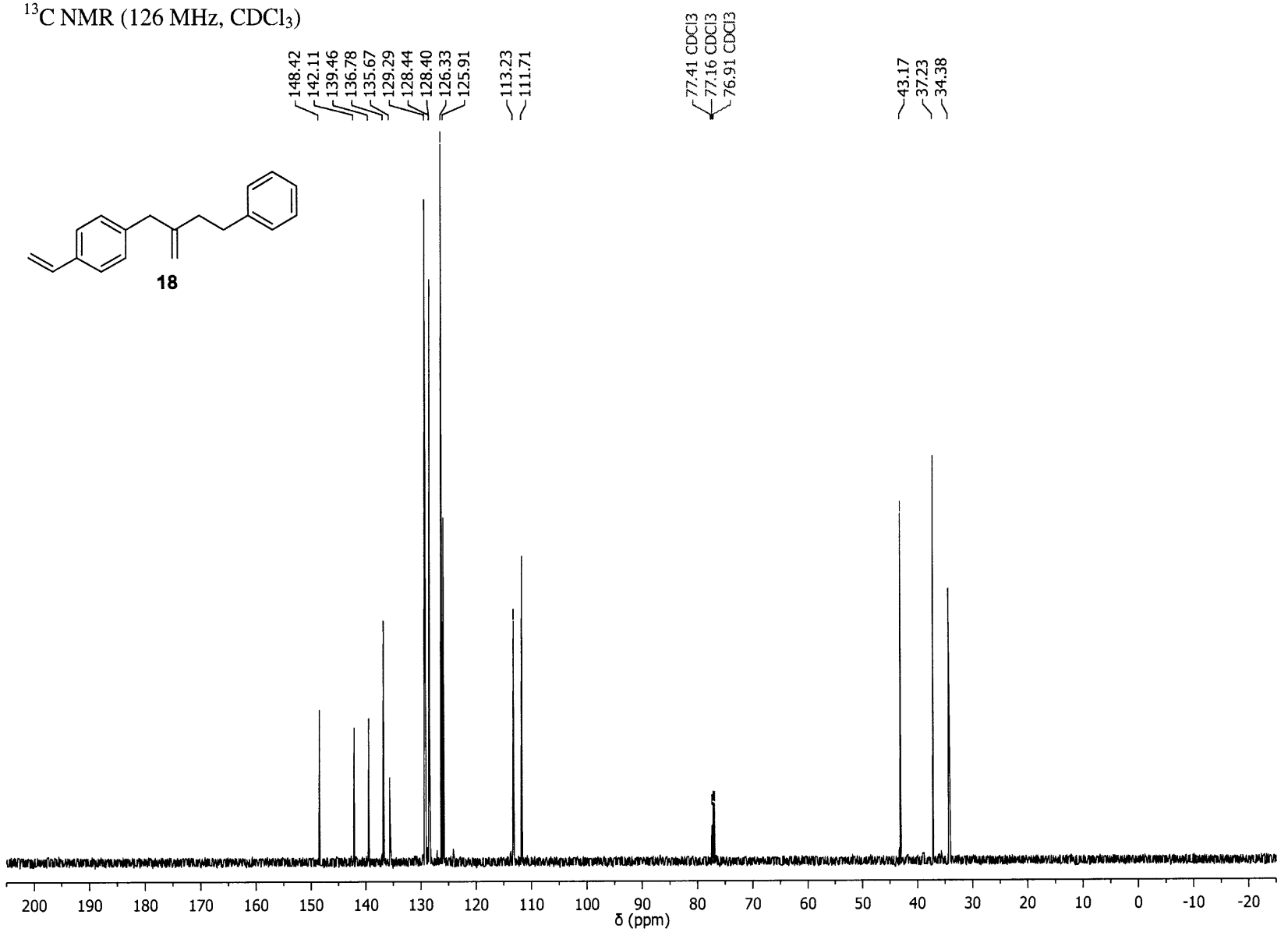
17

^{1}H NMR (500 MHz, $CDCl_3$)

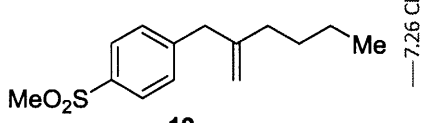


18

^{13}C NMR (126 MHz, $CDCl_3$)

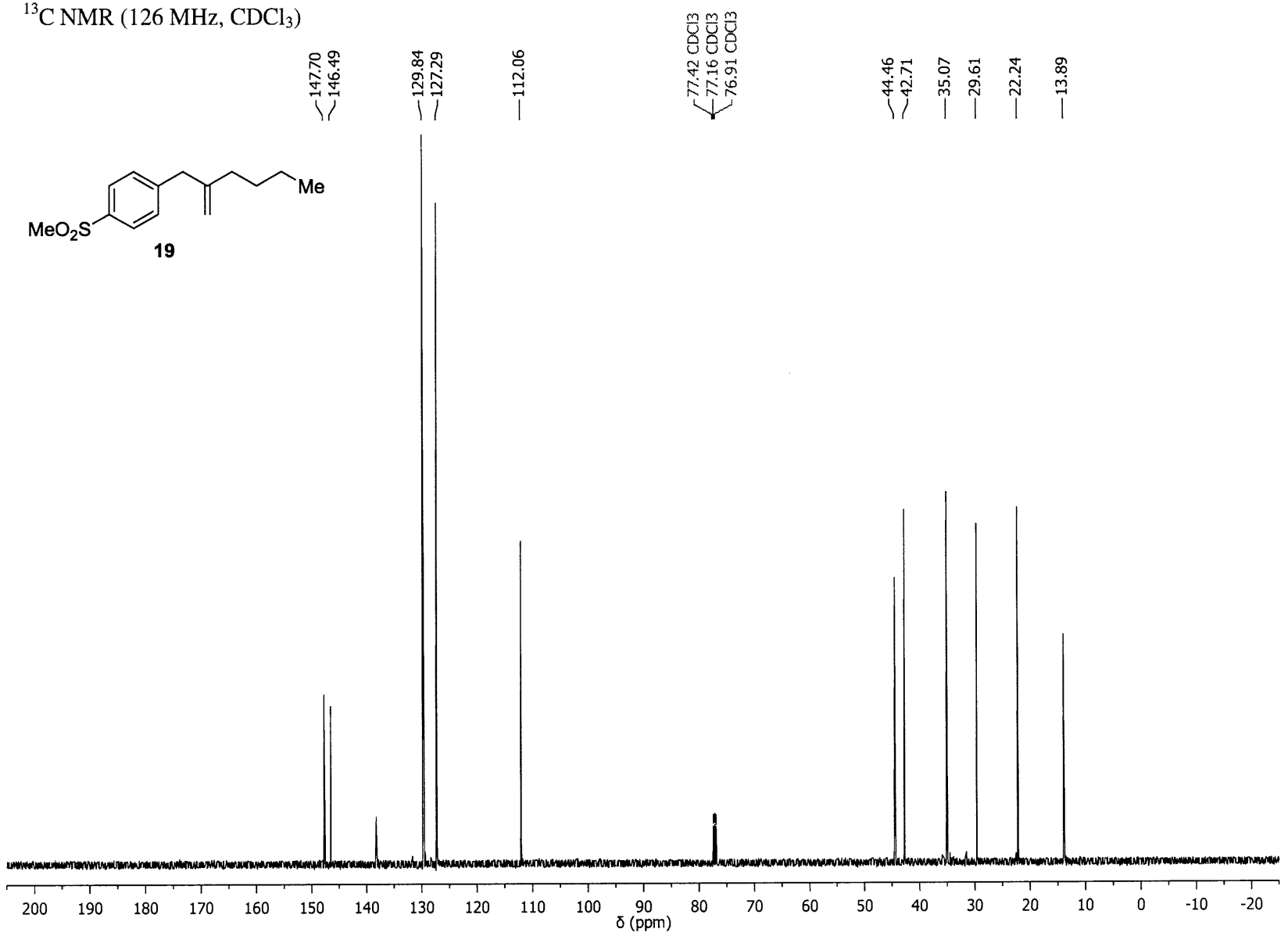


^{1}H NMR (500 MHz, $CDCl_3$)

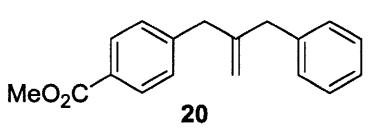


19

^{13}C NMR (126 MHz, $CDCl_3$)

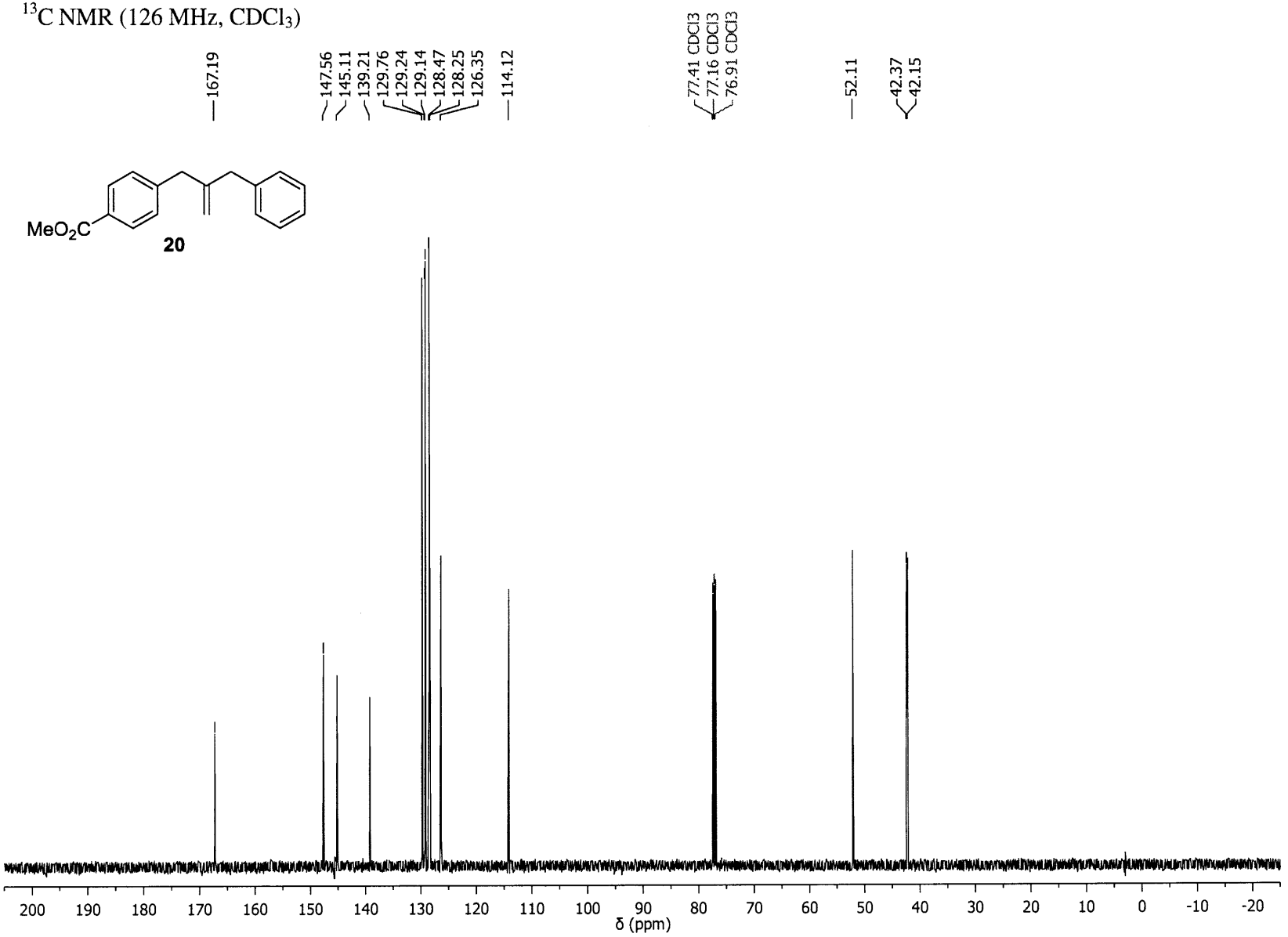


^{1}H NMR (500 MHz, $CDCl_3$)

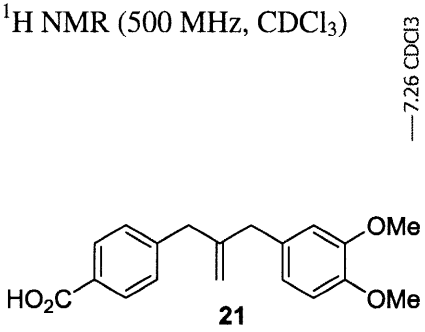


20

^{13}C NMR (126 MHz, $CDCl_3$)

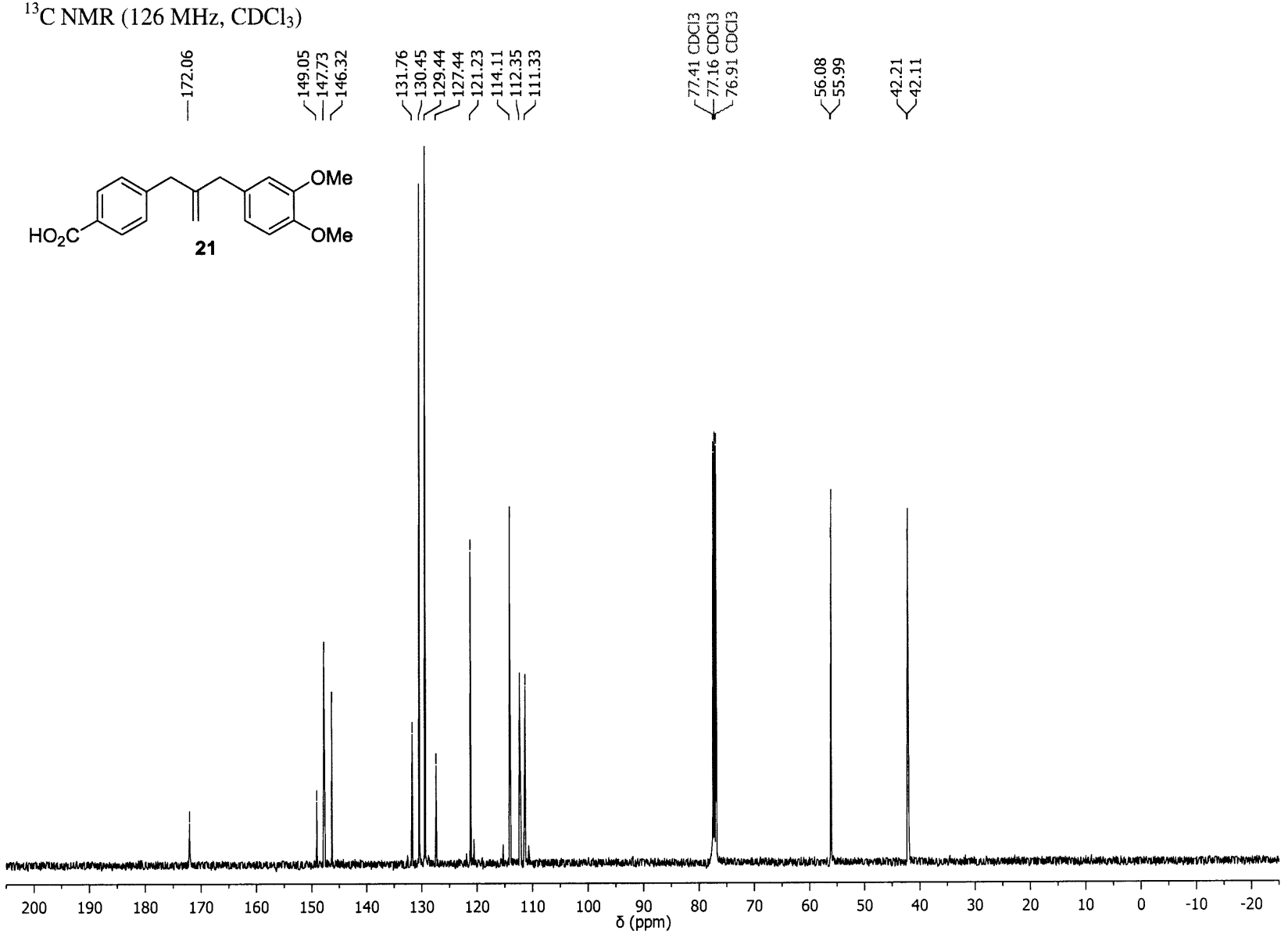


^{1}H NMR (500 MHz, $CDCl_3$)

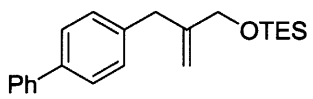


21

^{13}C NMR (126 MHz, $CDCl_3$)

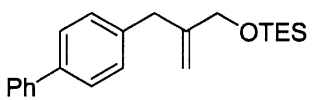


^{1}H NMR (500 MHz, $CDCl_3$)



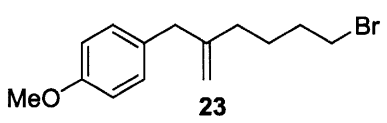
22

^{13}C NMR (126 MHz, $CDCl_3$)



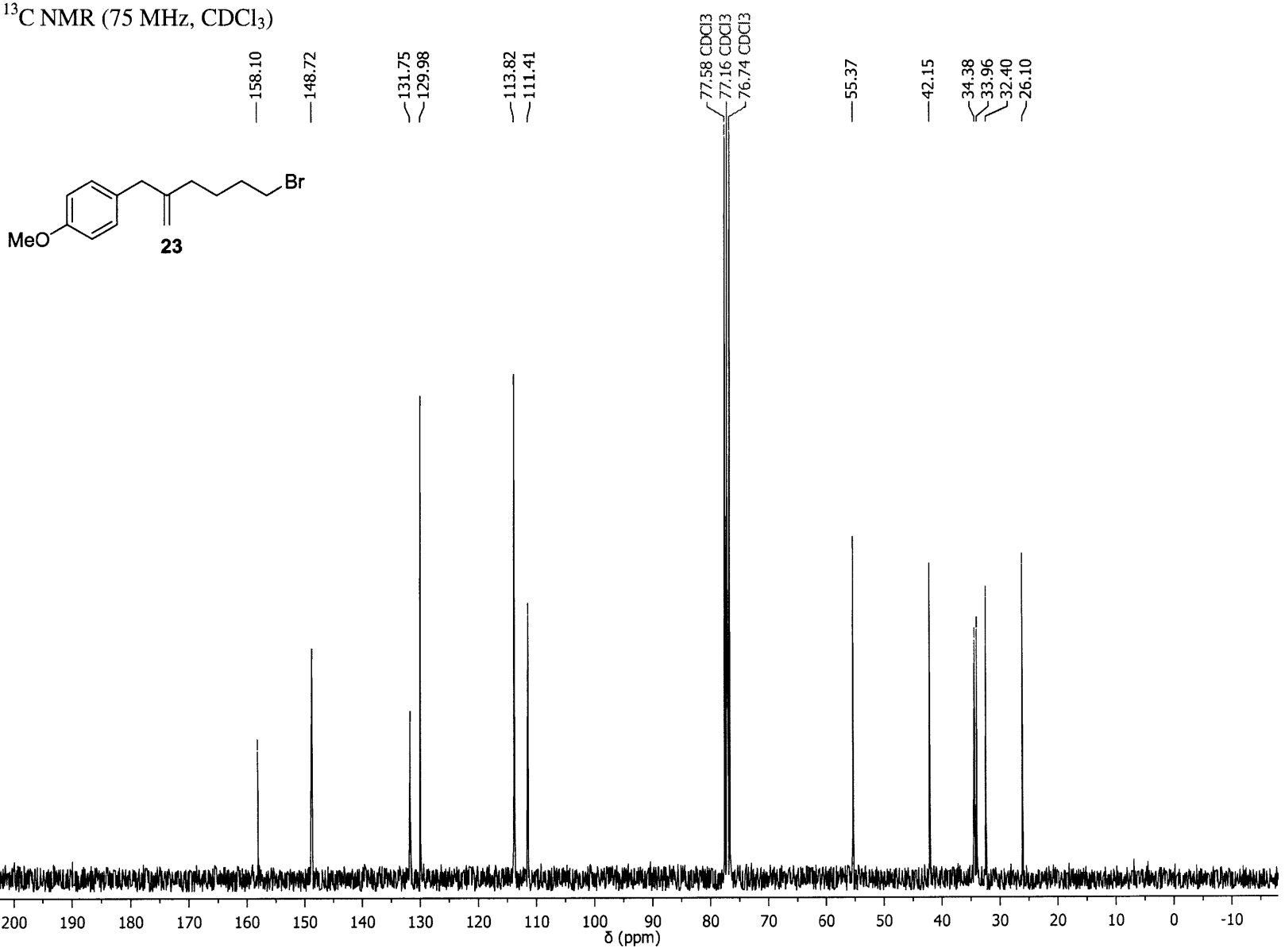
22

^{1}H NMR (500 MHz, $CDCl_3$)

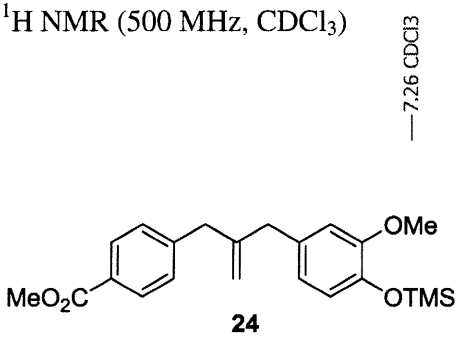


23

^{13}C NMR (75 MHz, $CDCl_3$)

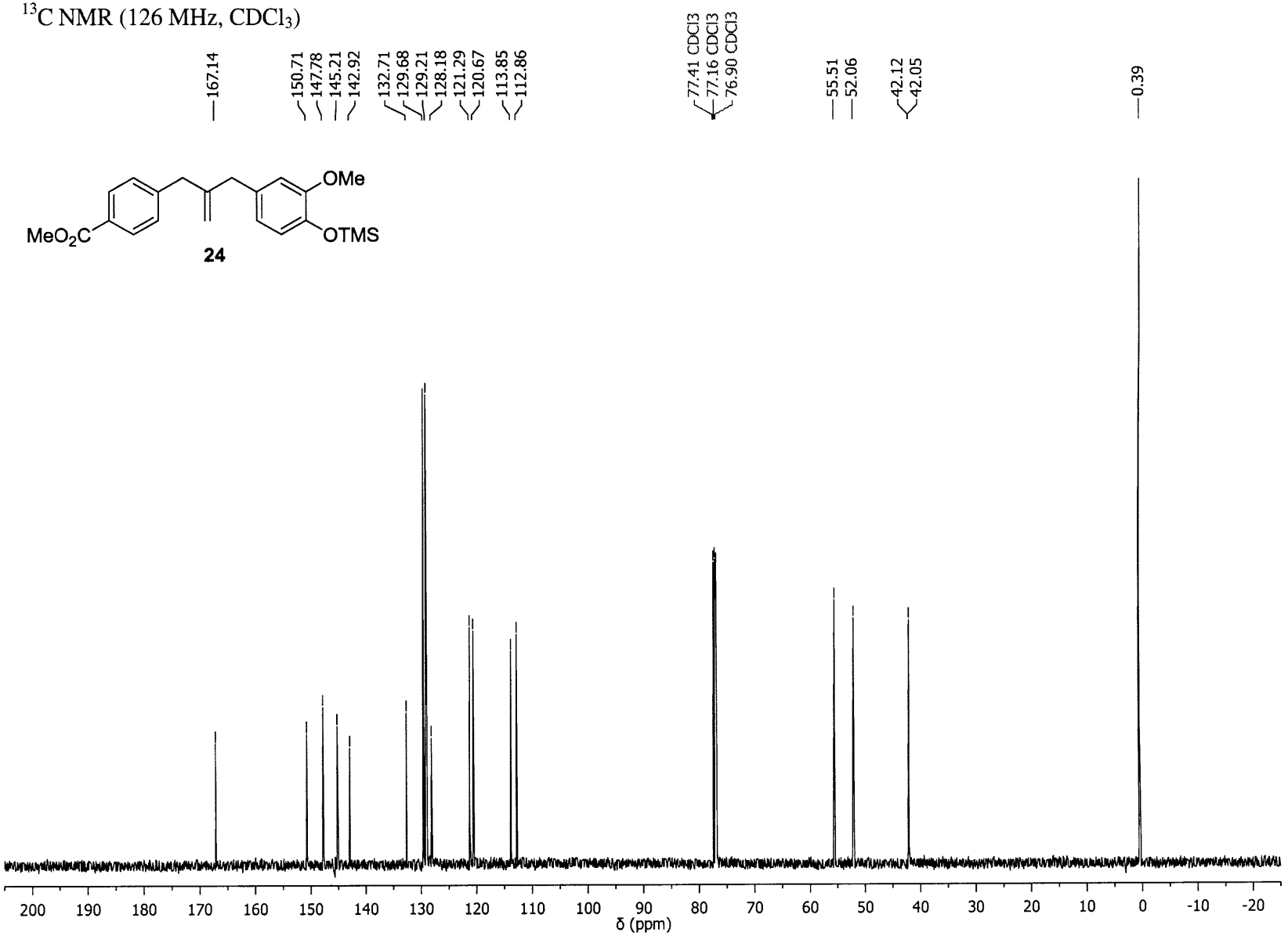


^{1}H NMR (500 MHz, $CDCl_3$)

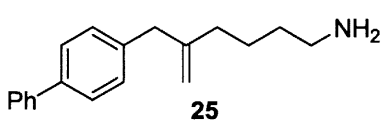


24

^{13}C NMR (126 MHz, $CDCl_3$)

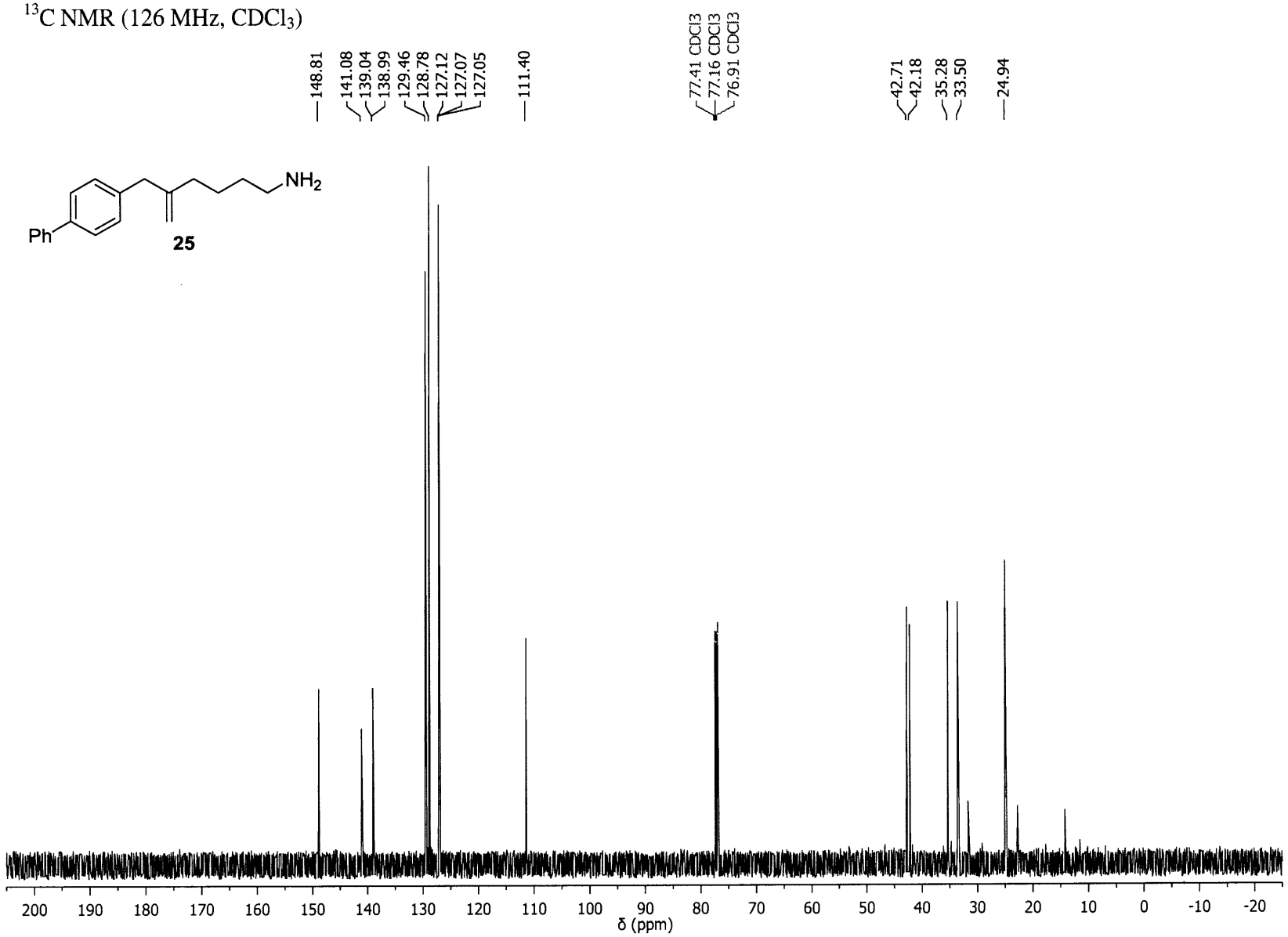


^{1}H NMR (500 MHz, $CDCl_3$)

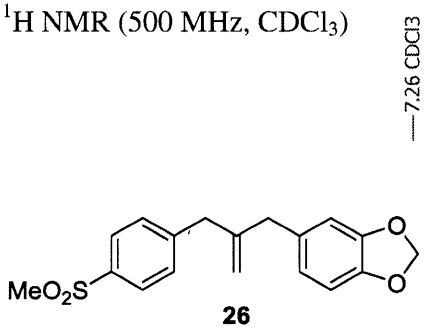


25

^{13}C NMR (126 MHz, $CDCl_3$)

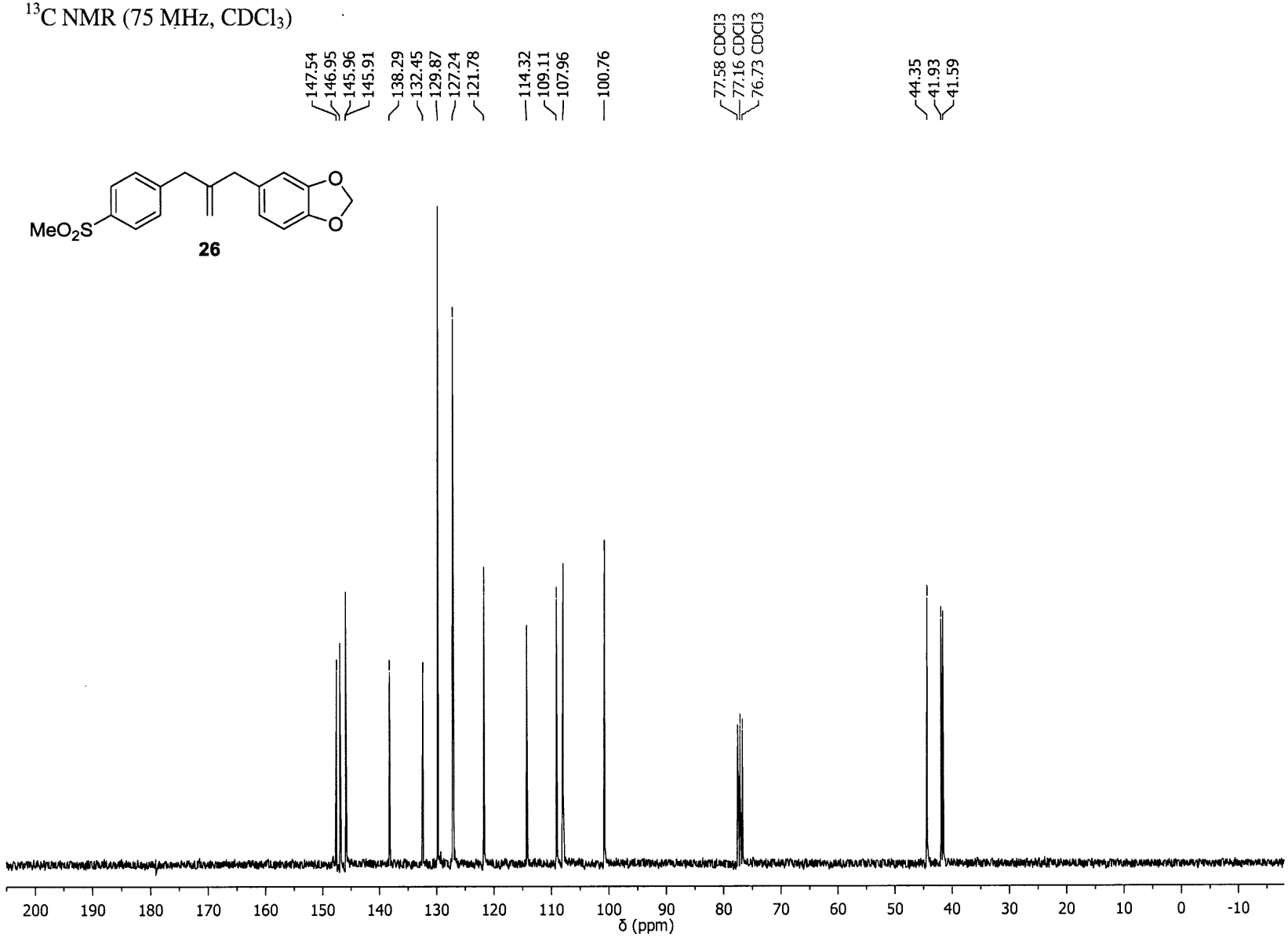


^{1}H NMR (500 MHz, $CDCl_3$)

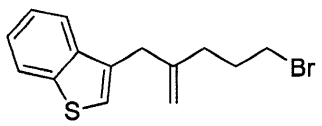


26

^{13}C NMR (75 MHz, $CDCl_3$)

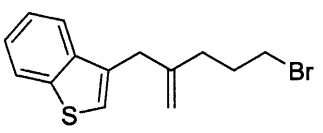


^{1}H NMR (500 MHz, $CDCl_3$)



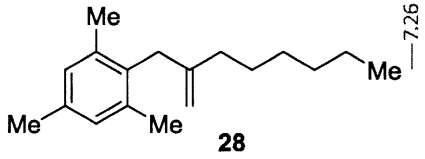
27

^{13}C NMR (126 MHz, $CDCl_3$)



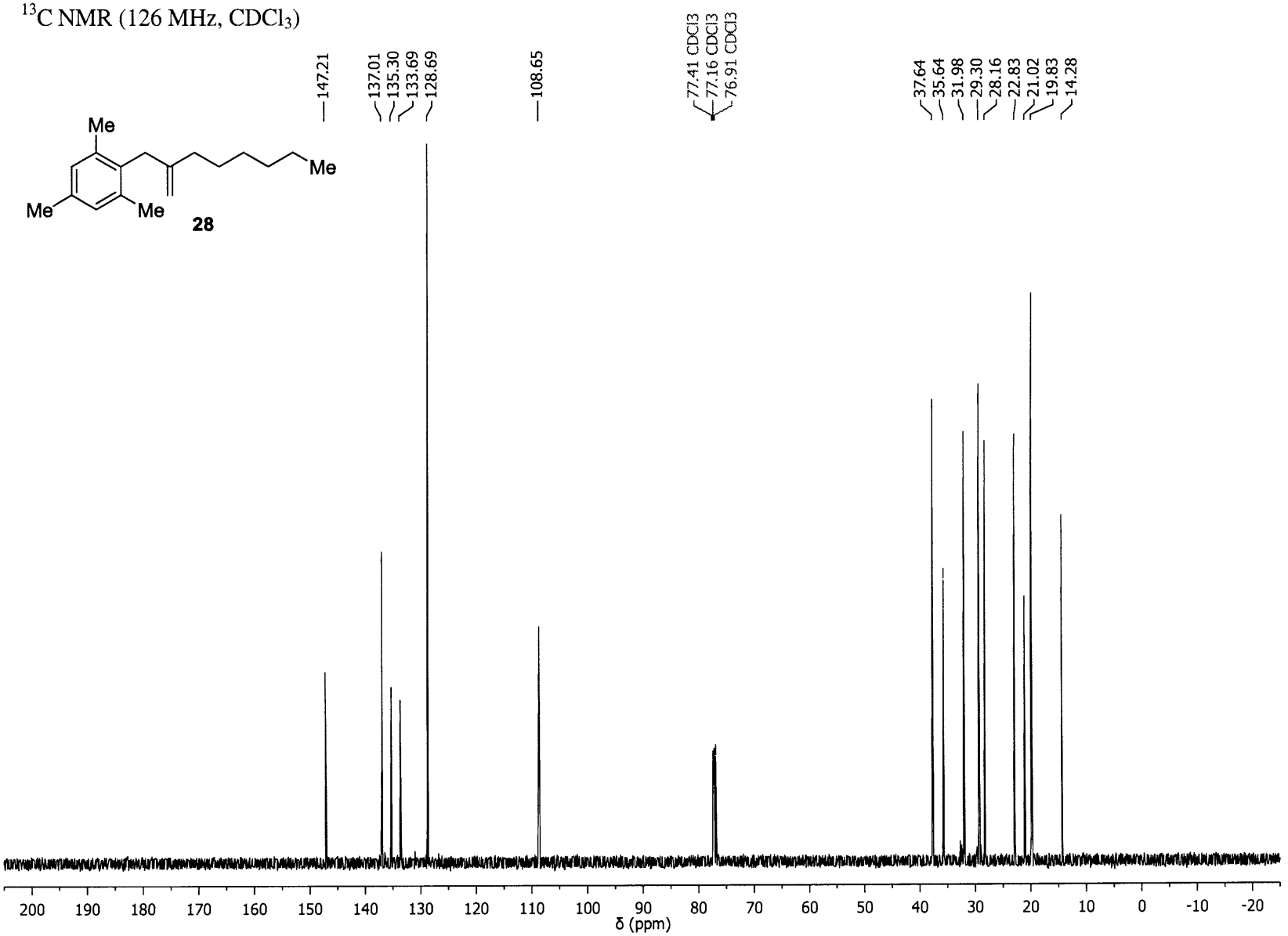
27

^{1}H NMR (500 MHz, $CDCl_3$)

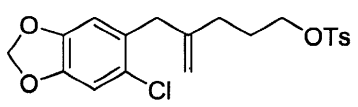


28

^{13}C NMR (126 MHz, $CDCl_3$)

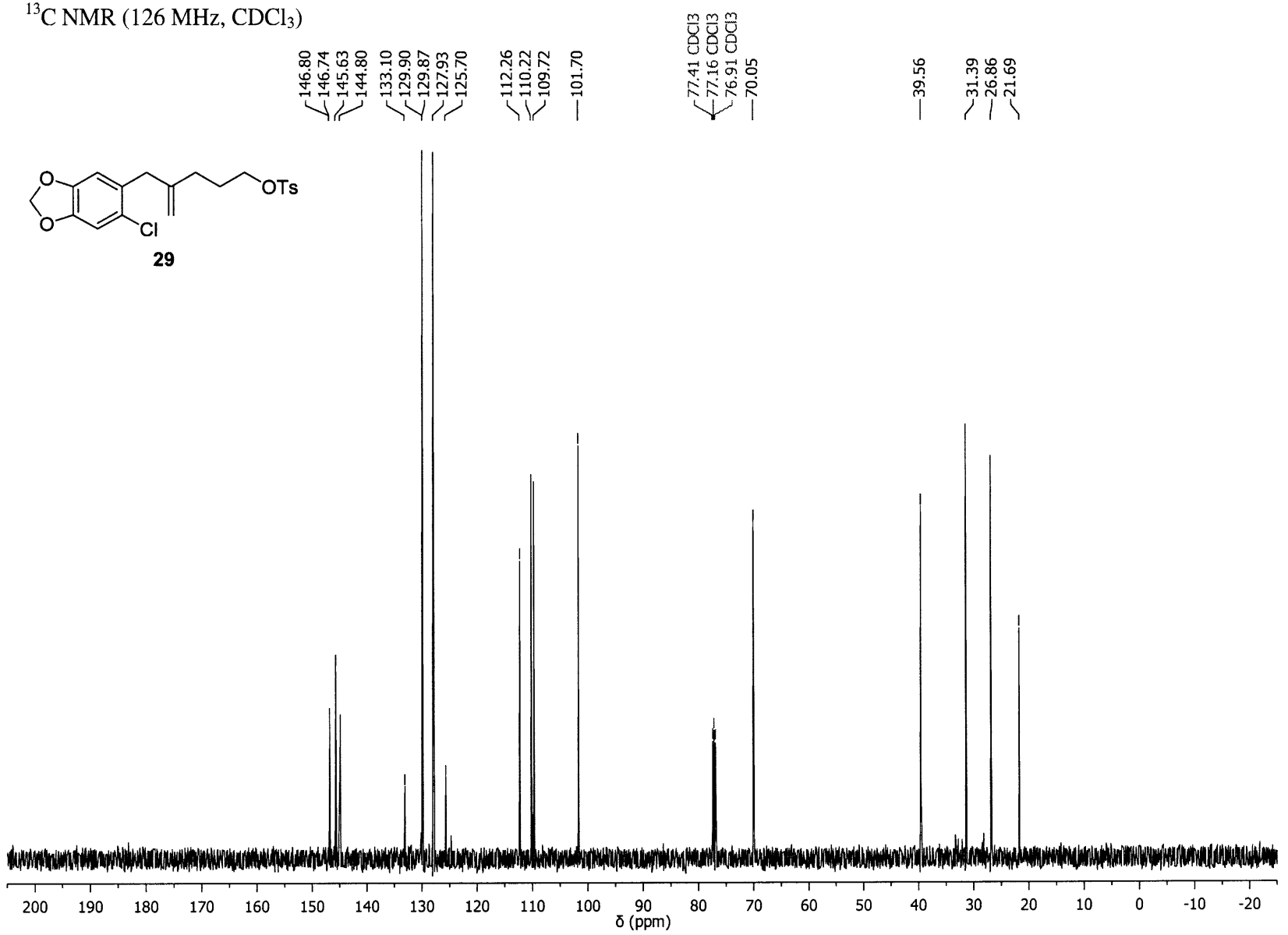


^{1}H NMR (500 MHz, $CDCl_3$)

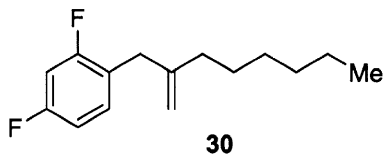


29

^{13}C NMR (126 MHz, $CDCl_3$)

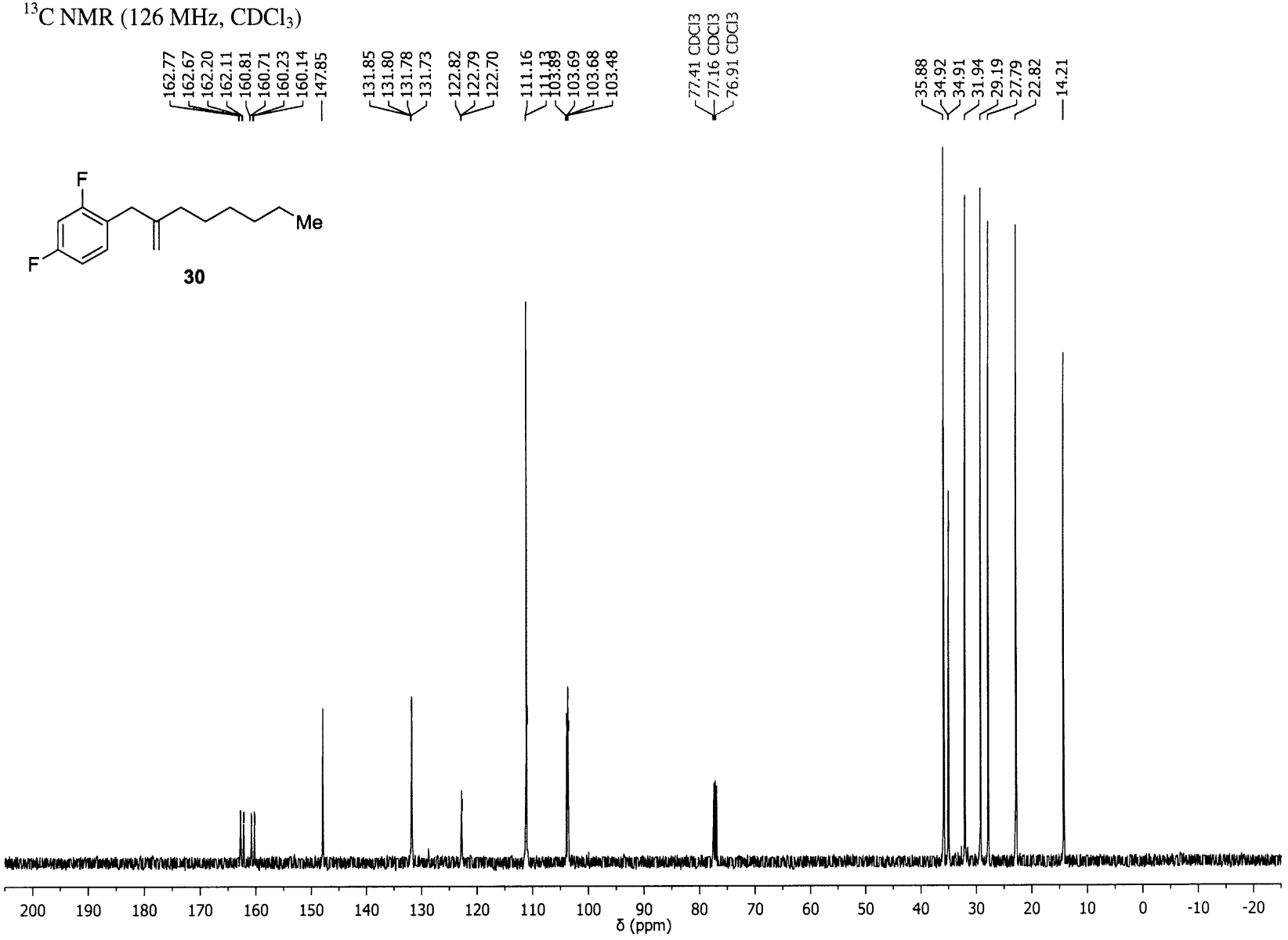


^{1}H NMR (500 MHz, $CDCl_3$)

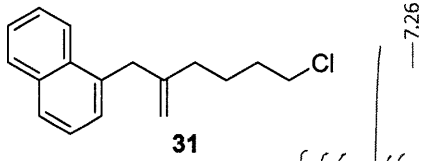


30

^{13}C NMR (126 MHz, $CDCl_3$)

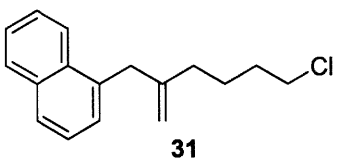


^{1}H NMR (500 MHz, $CDCl_3$)



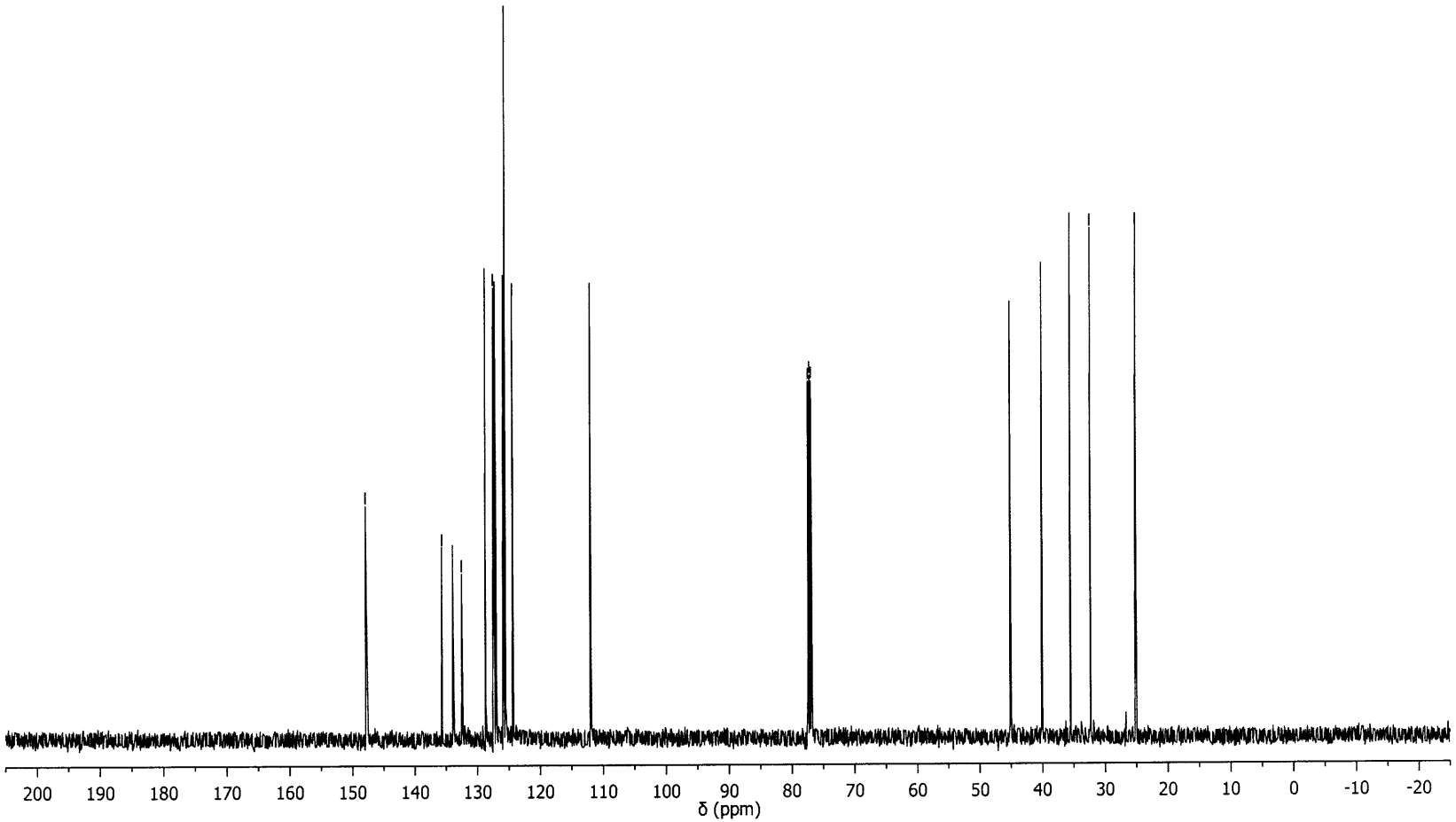
31

^{13}C NMR (126 MHz, $CDCl_3$)

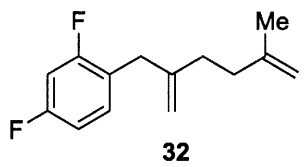


31

147.84
135.66
133.95
128.73
127.43
127.15
125.85
125.59
125.59
124.41
112.02
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
45.11
40.04
35.49
32.29
25.03

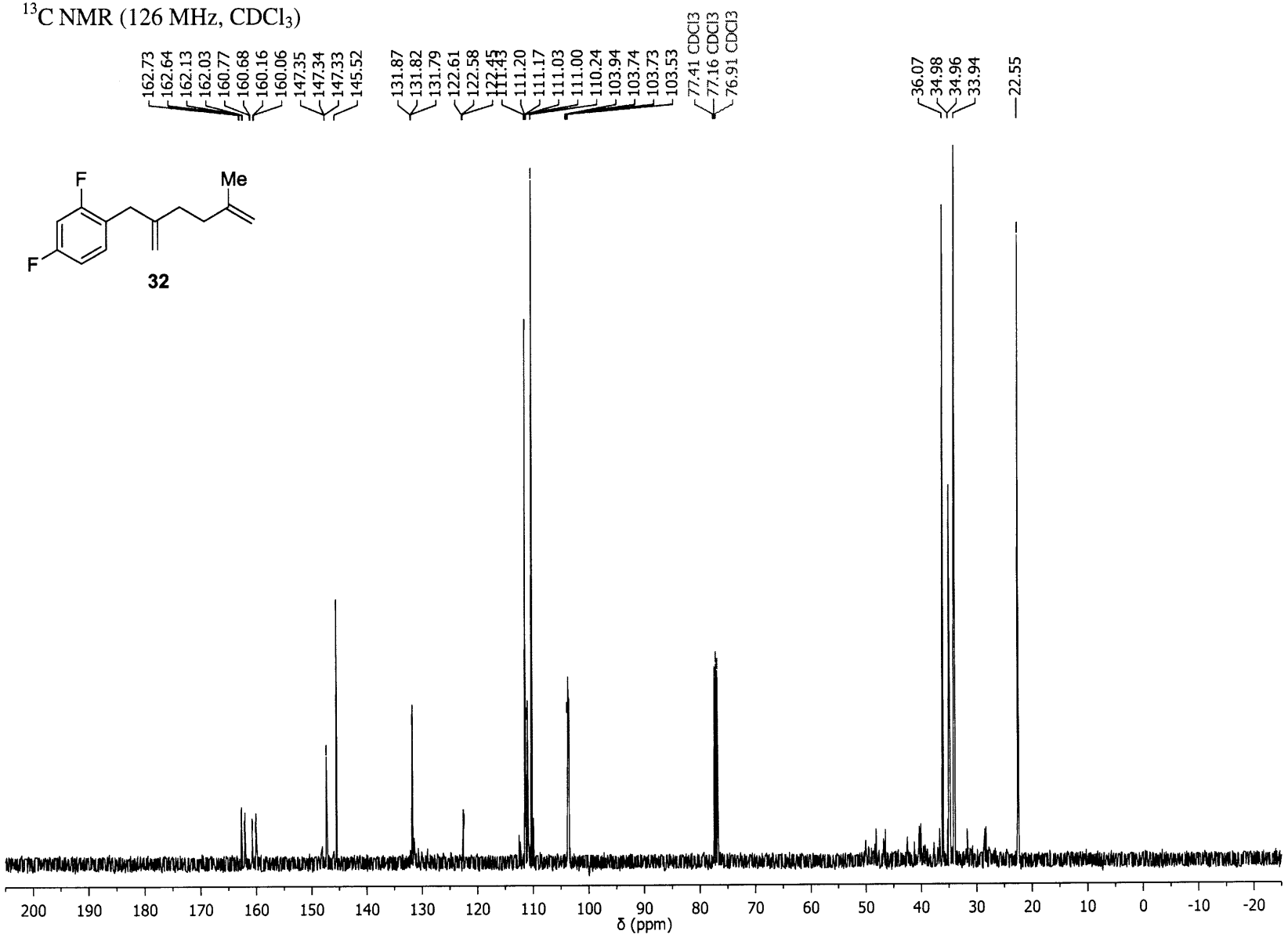


^{1}H NMR (500 MHz, $CDCl_3$)

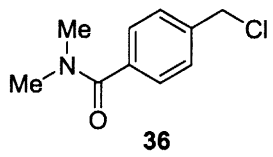


32

^{13}C NMR (126 MHz, $CDCl_3$)

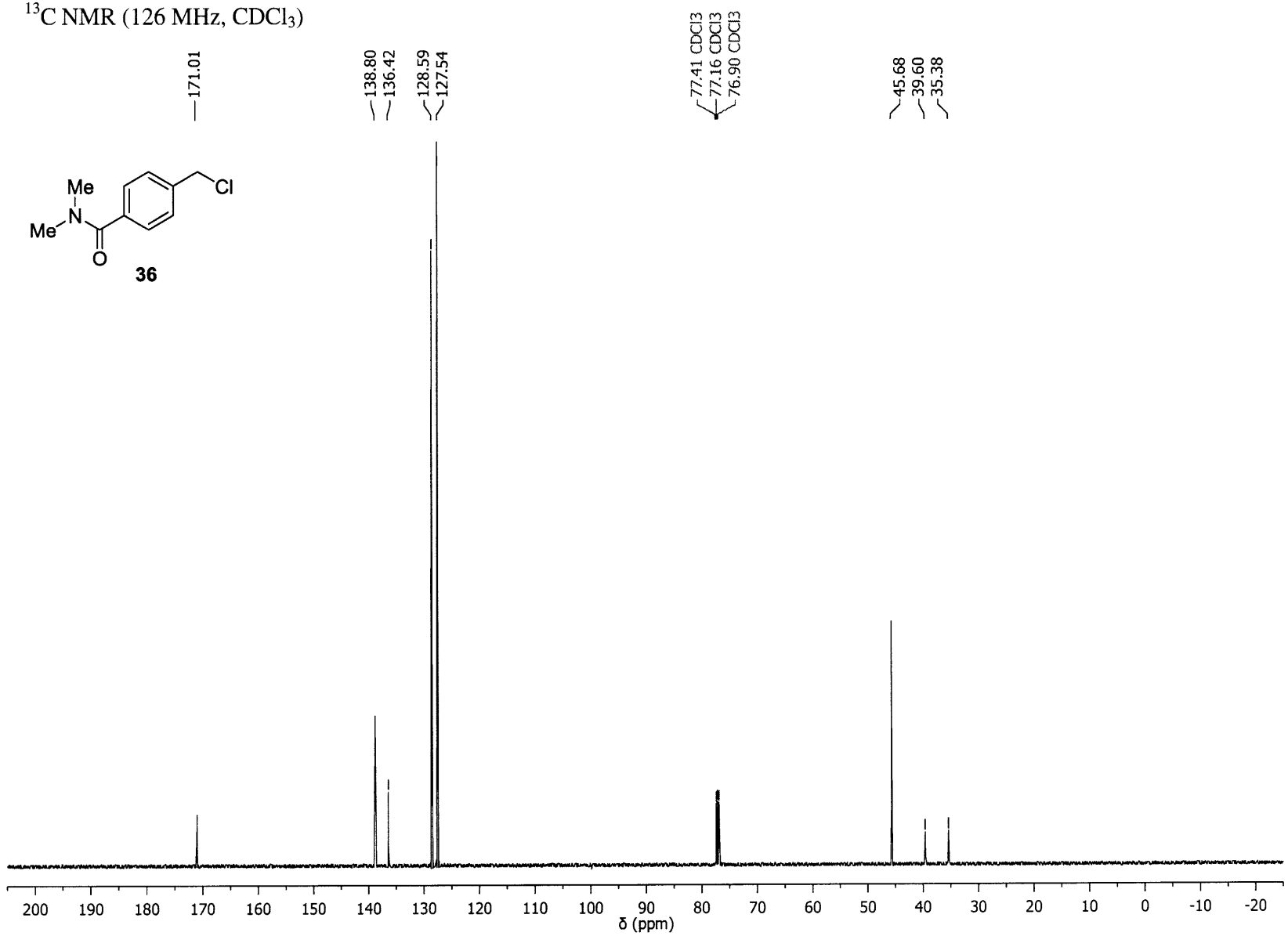


^{1}H NMR (500 MHz, $CDCl_3$)

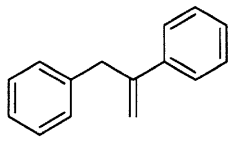


36

^{13}C NMR (126 MHz, $CDCl_3$)

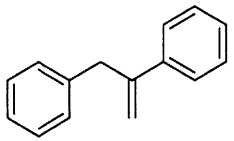


^{1}H NMR (500 MHz, $CDCl_3$)



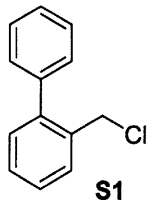
40

^{13}C NMR (126 MHz, $CDCl_3$)



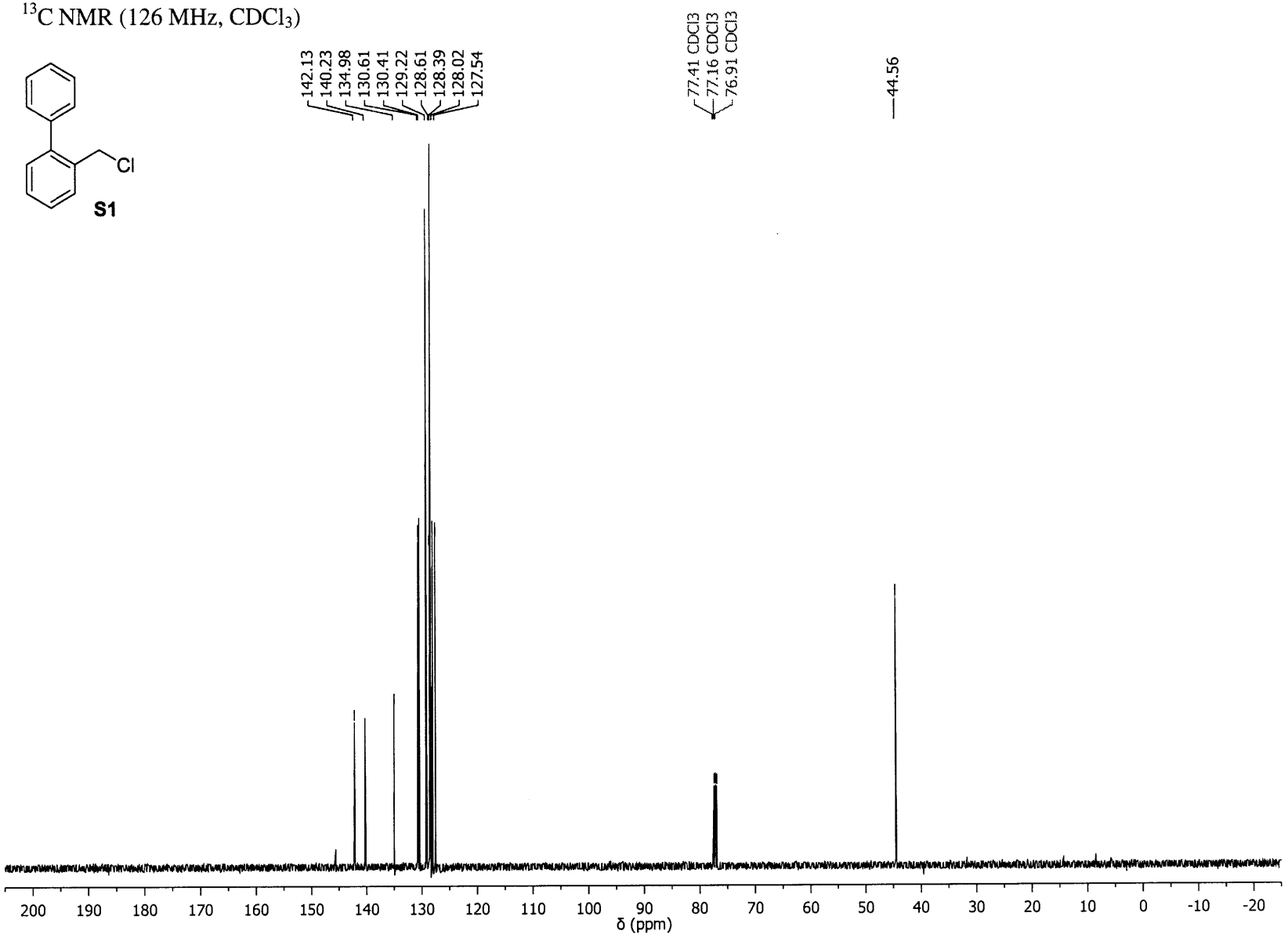
40

^{1}H NMR (500 MHz, $CDCl_3$)



S1

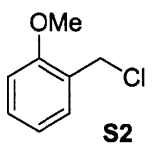
^{13}C NMR (126 MHz, $CDCl_3$)



^{1}H NMR (500 MHz, $CDCl_3$)

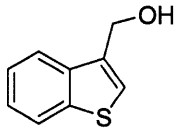
S2

^{13}C NMR (126 MHz, $CDCl_3$)



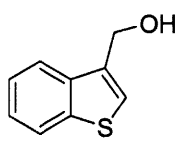
S2

^{1}H NMR (500 MHz, $CDCl_3$)



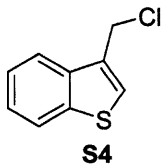
S3

^{13}C NMR (126 MHz, $CDCl_3$)



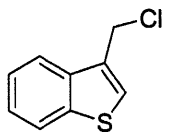
S3

^{1}H NMR (500 MHz, $CDCl_3$)



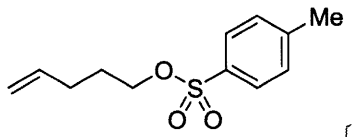
S4

^{13}C NMR (126 MHz, $CDCl_3$)



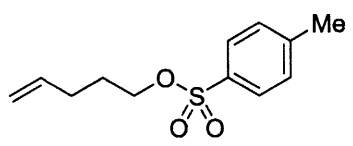
S4

^{1}H NMR (500 MHz, $CDCl_3$)



S5

^{13}C NMR (126 MHz, $CDCl_3$)



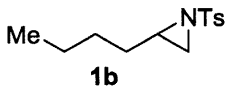
S5

Appendix C

NMR Spectra for Chapter 3

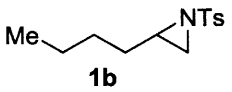
Ring-Opening, Negishi-type Cross-Coupling of 2-Substituted *N*-Tosylaziridines with Alkylzinc Halides

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



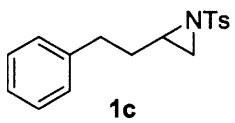
1b

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



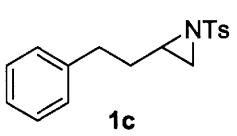
1b

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



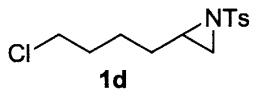
1c

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



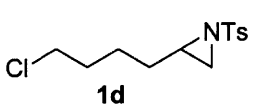
1c

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



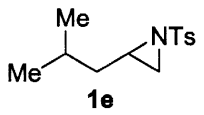
1d

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



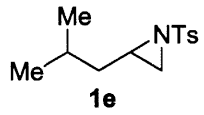
1d

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



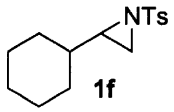
1e

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



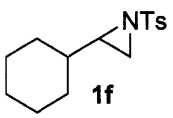
1e

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



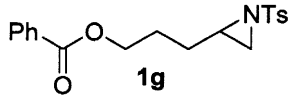
1f

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



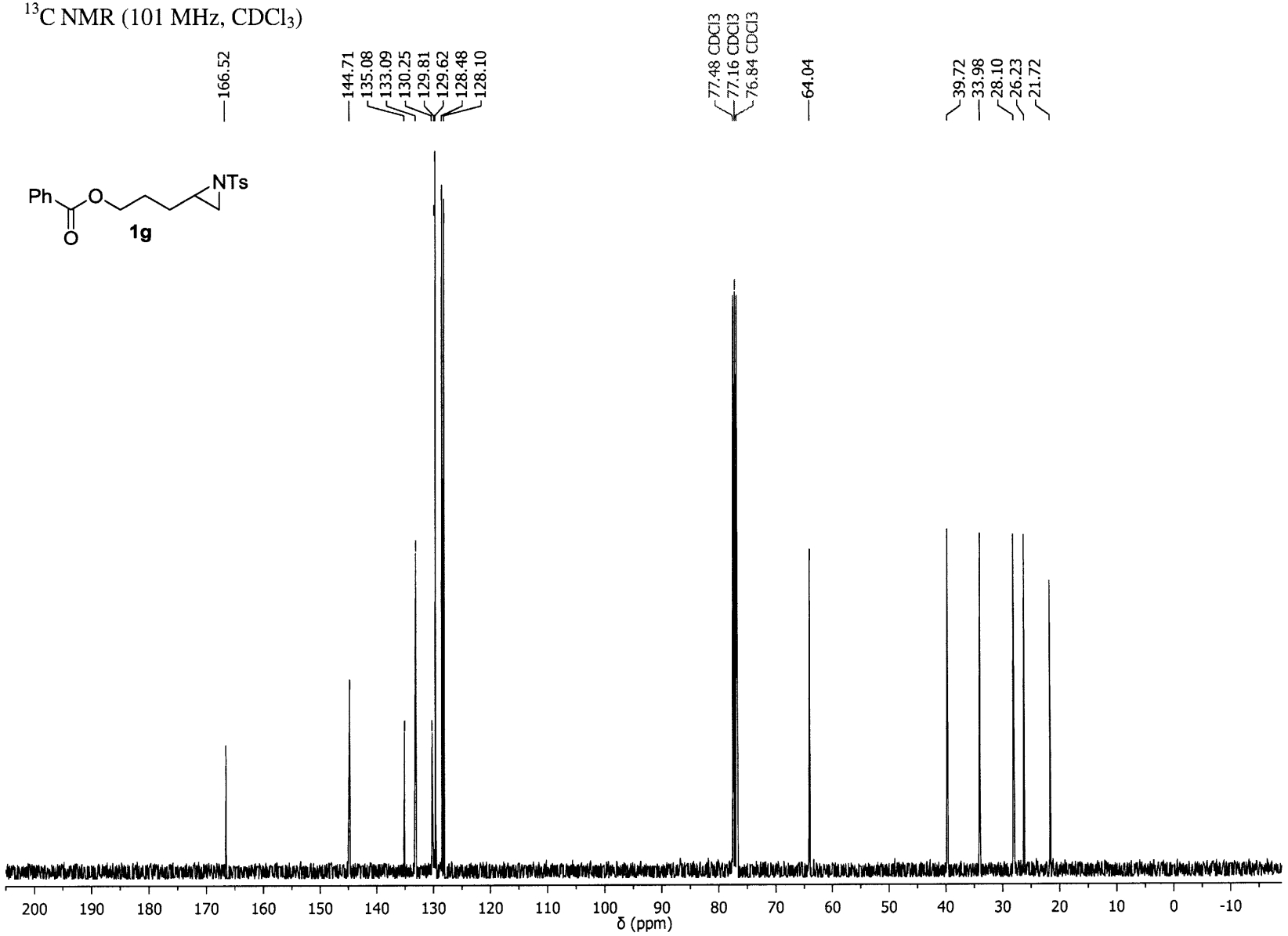
1f

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

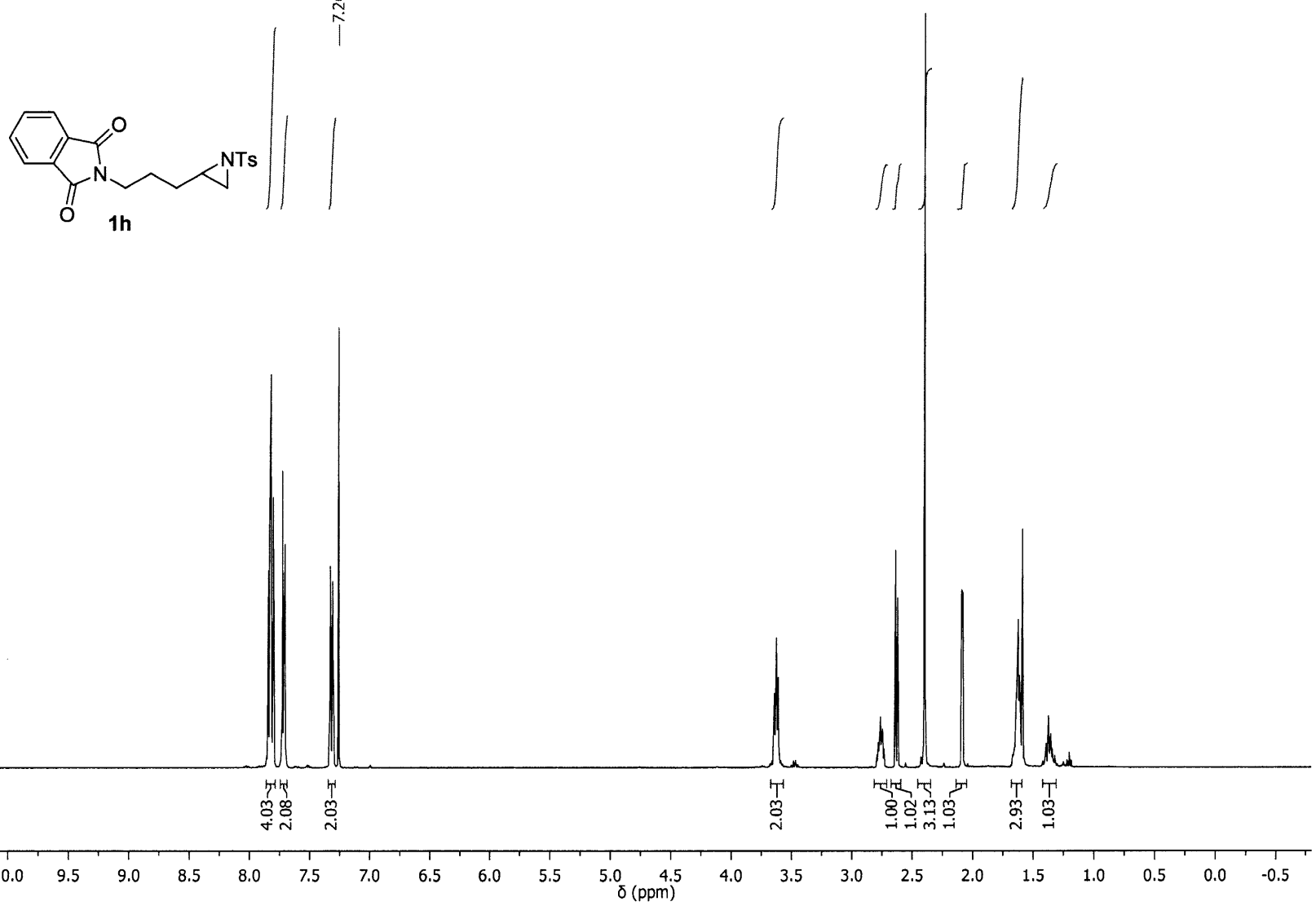


1g

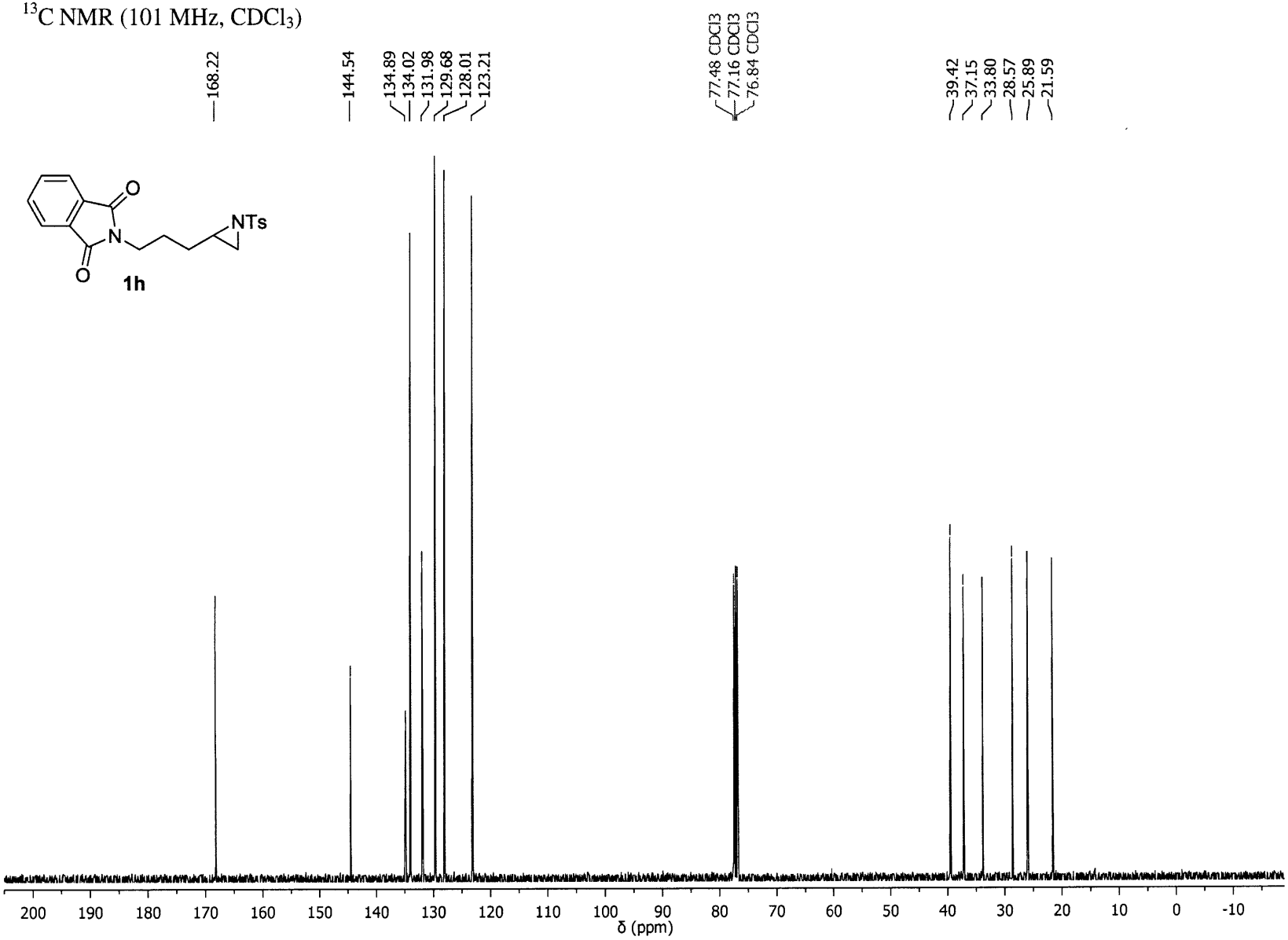
^{13}C NMR (101 MHz, $CDCl_3$)



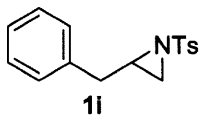
^{1}H NMR (400 MHz, $CDCl_3$)



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

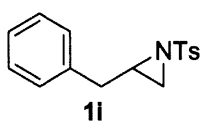


^{1}H NMR (400 MHz, $CDCl_3$)



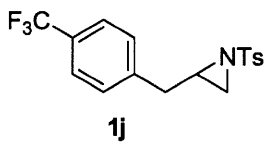
1i

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



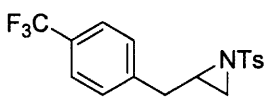
1i

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



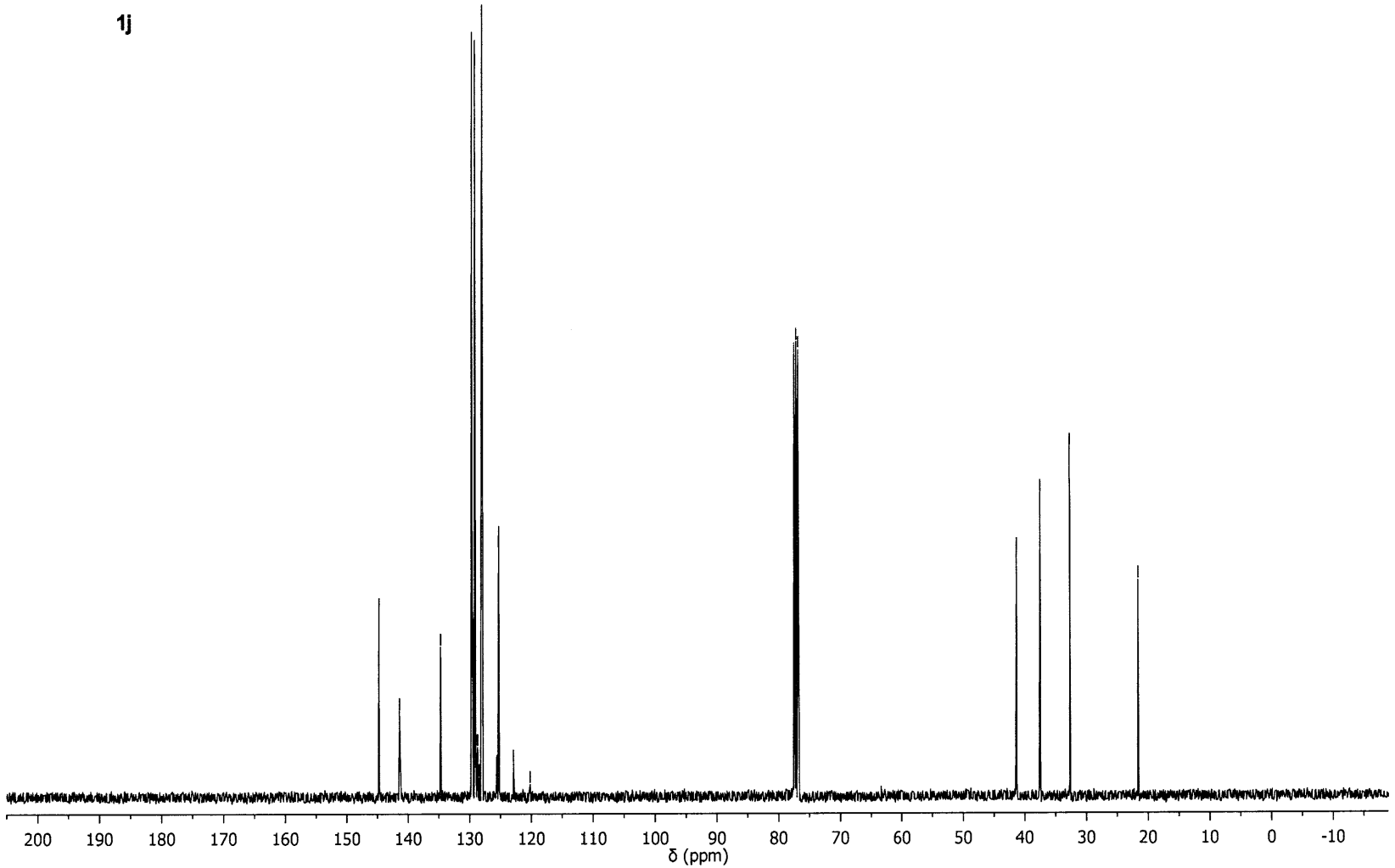
1j

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

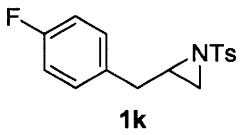


1j

144.72
141.43
141.42
141.40
141.39
134.72
129.62
129.36
129.12
129.03
128.71
128.39
128.32
127.95
125.36
125.33
125.29
125.25
122.91
120.21
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
41.28
37.44
32.62
21.53

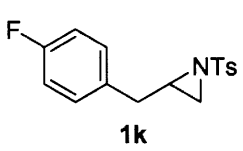


^{1}H NMR (400 MHz, $CDCl_3$)



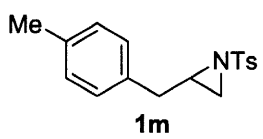
1k

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



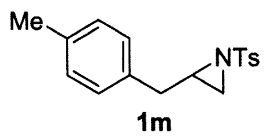
1k

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



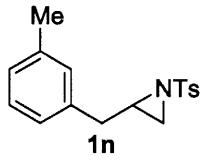
1m

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

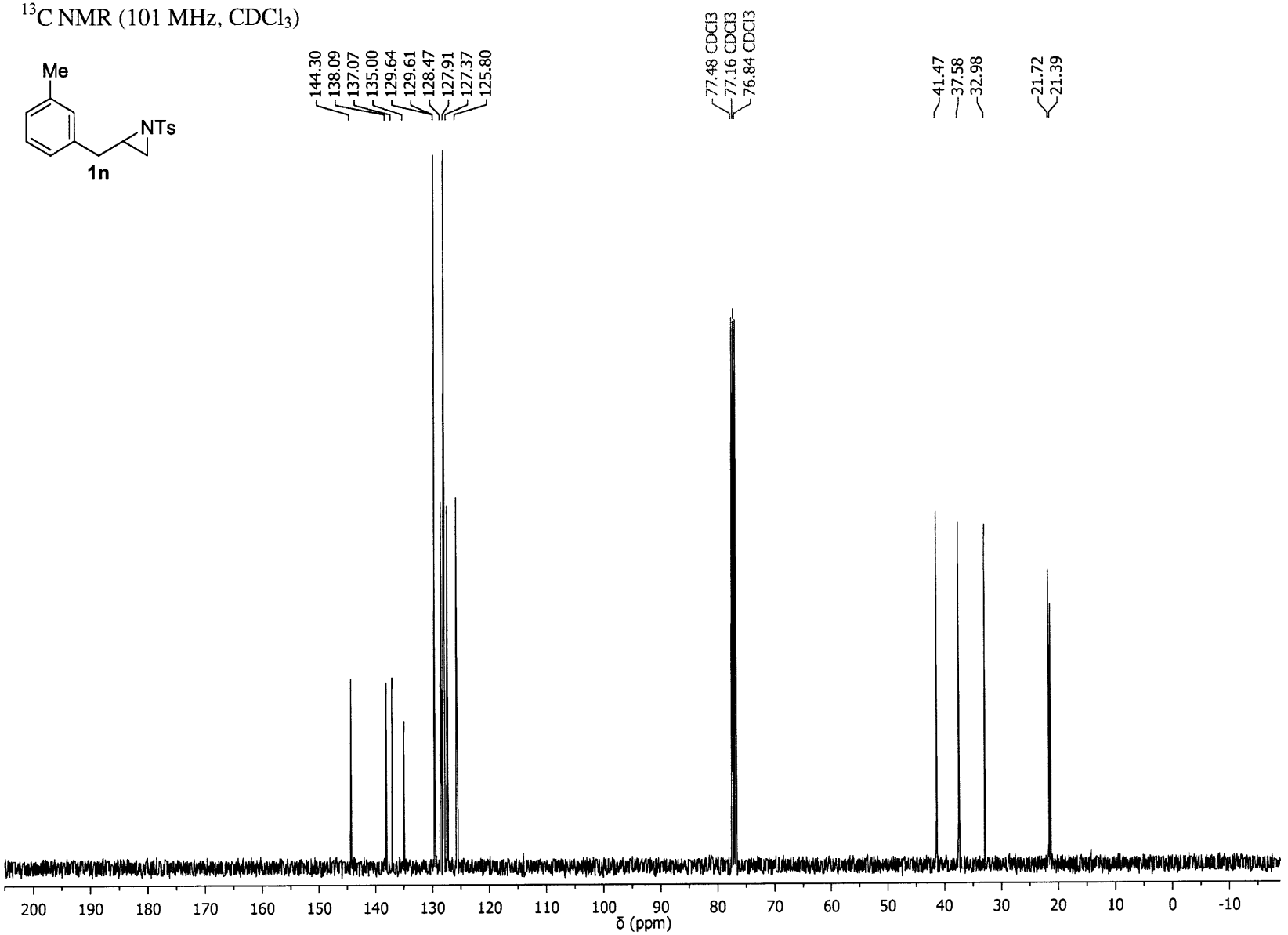


1m

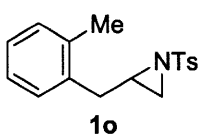
^{1}H NMR (400 MHz, $CDCl_3$)



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

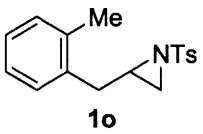


^{1}H NMR (400 MHz, $CDCl_3$)



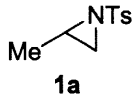
1o

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



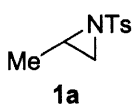
1o

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



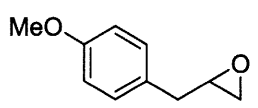
1a

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



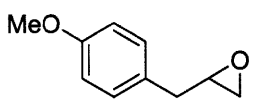
1a

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



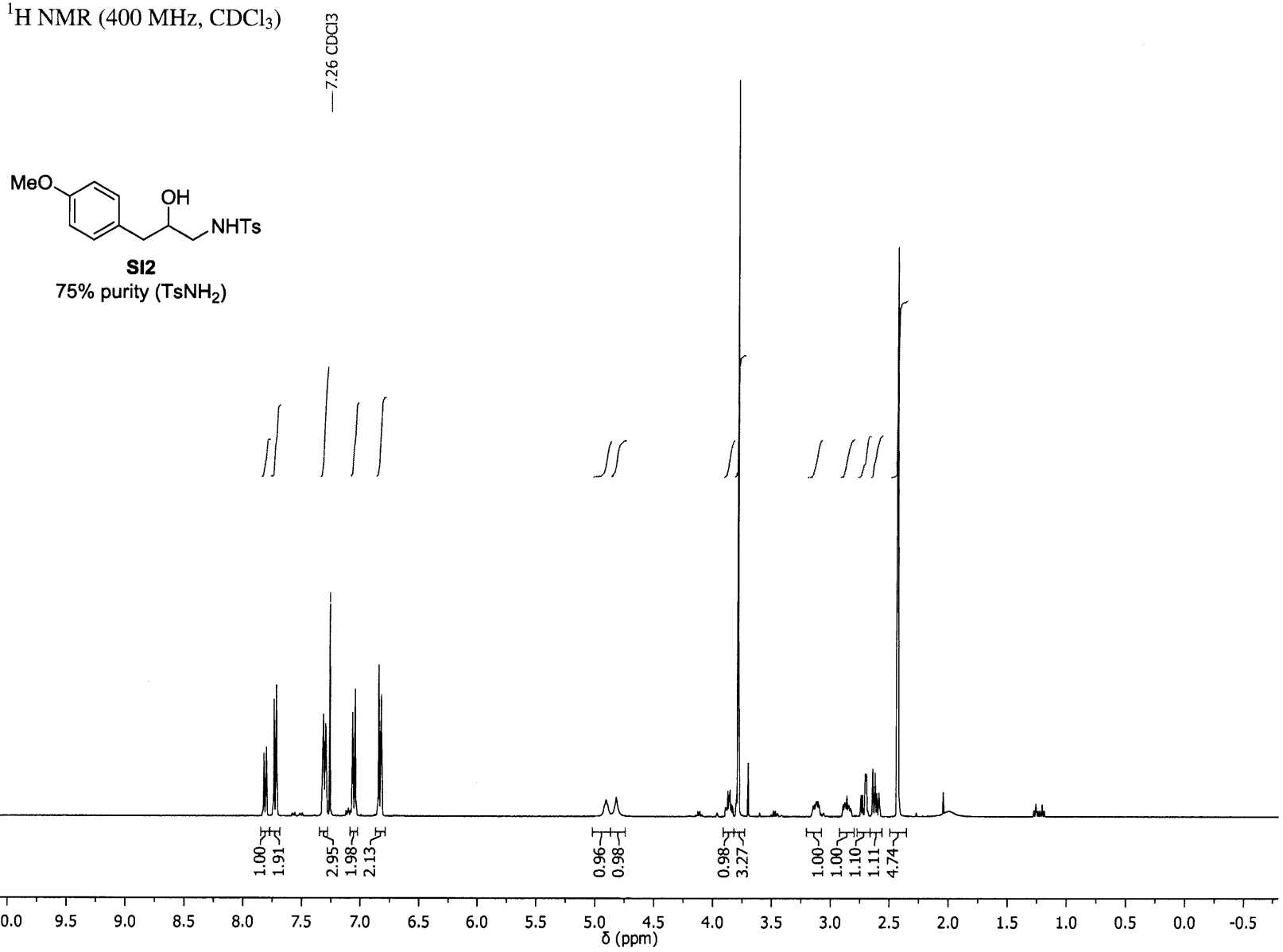
SI1

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

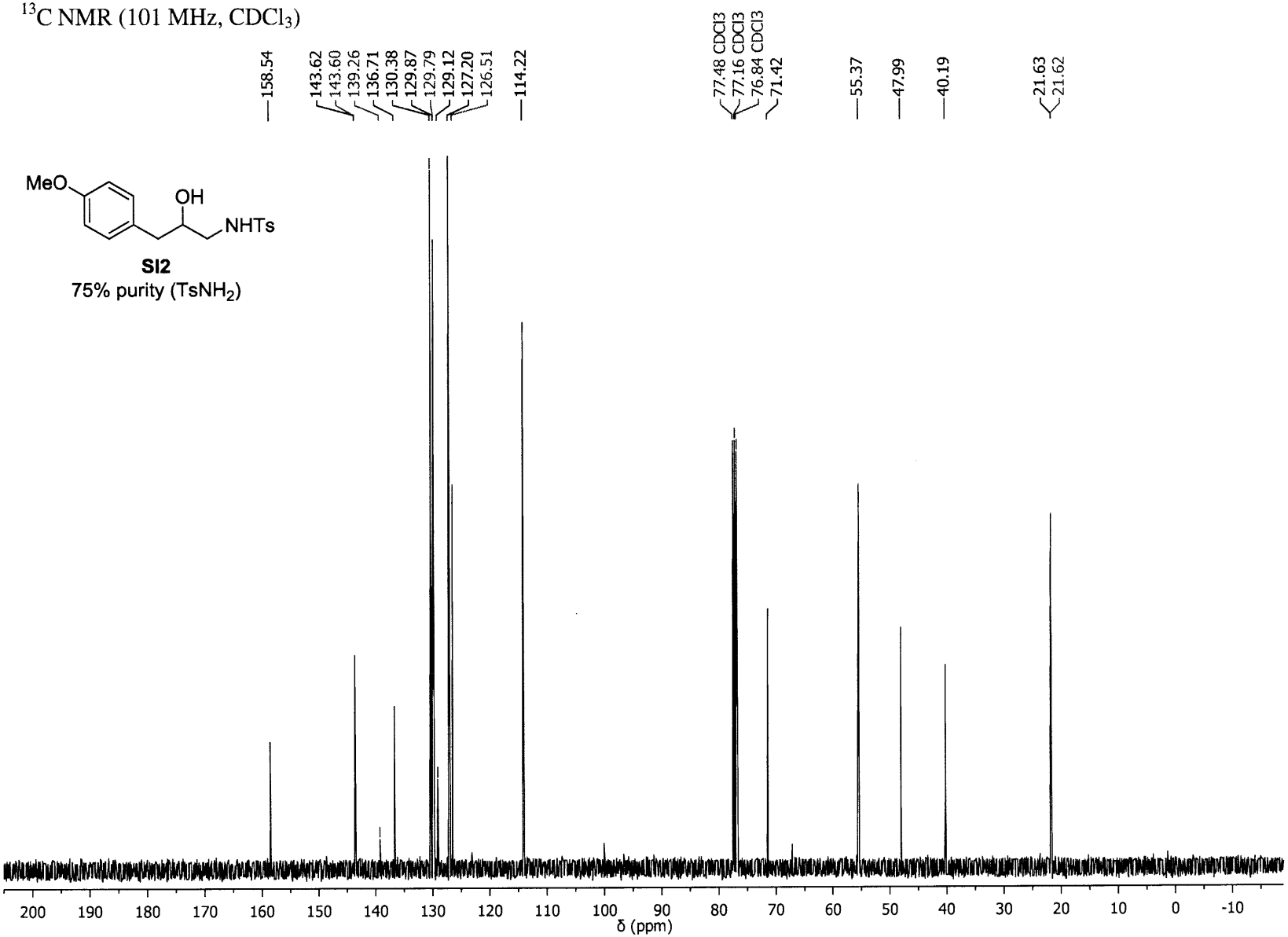


SI1

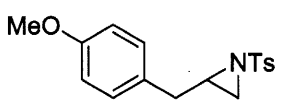
^{1}H NMR (400 MHz, $CDCl_3$)



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

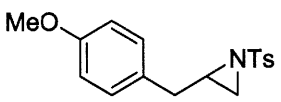


^{1}H NMR (400 MHz, $CDCl_3$)



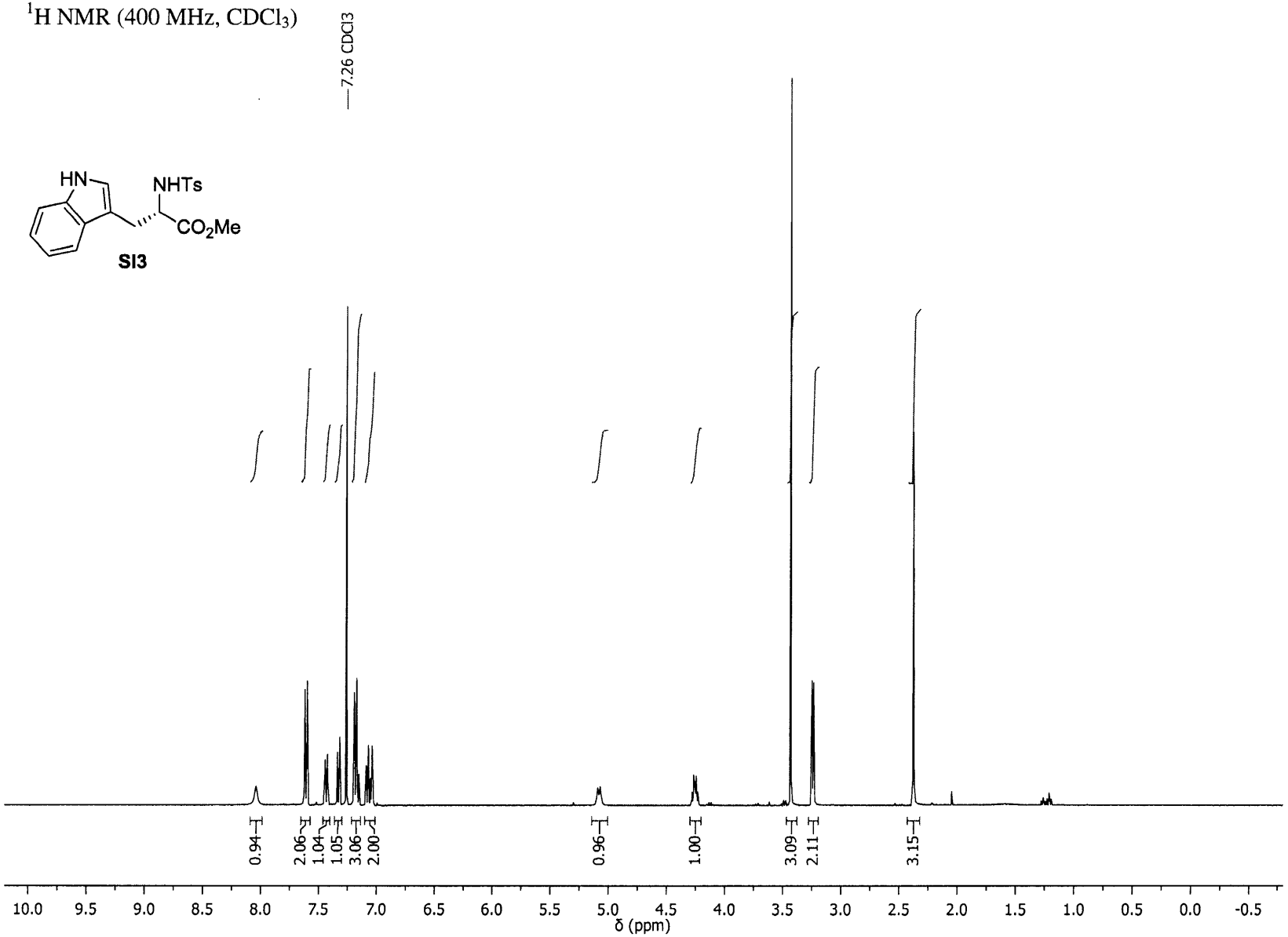
1l

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

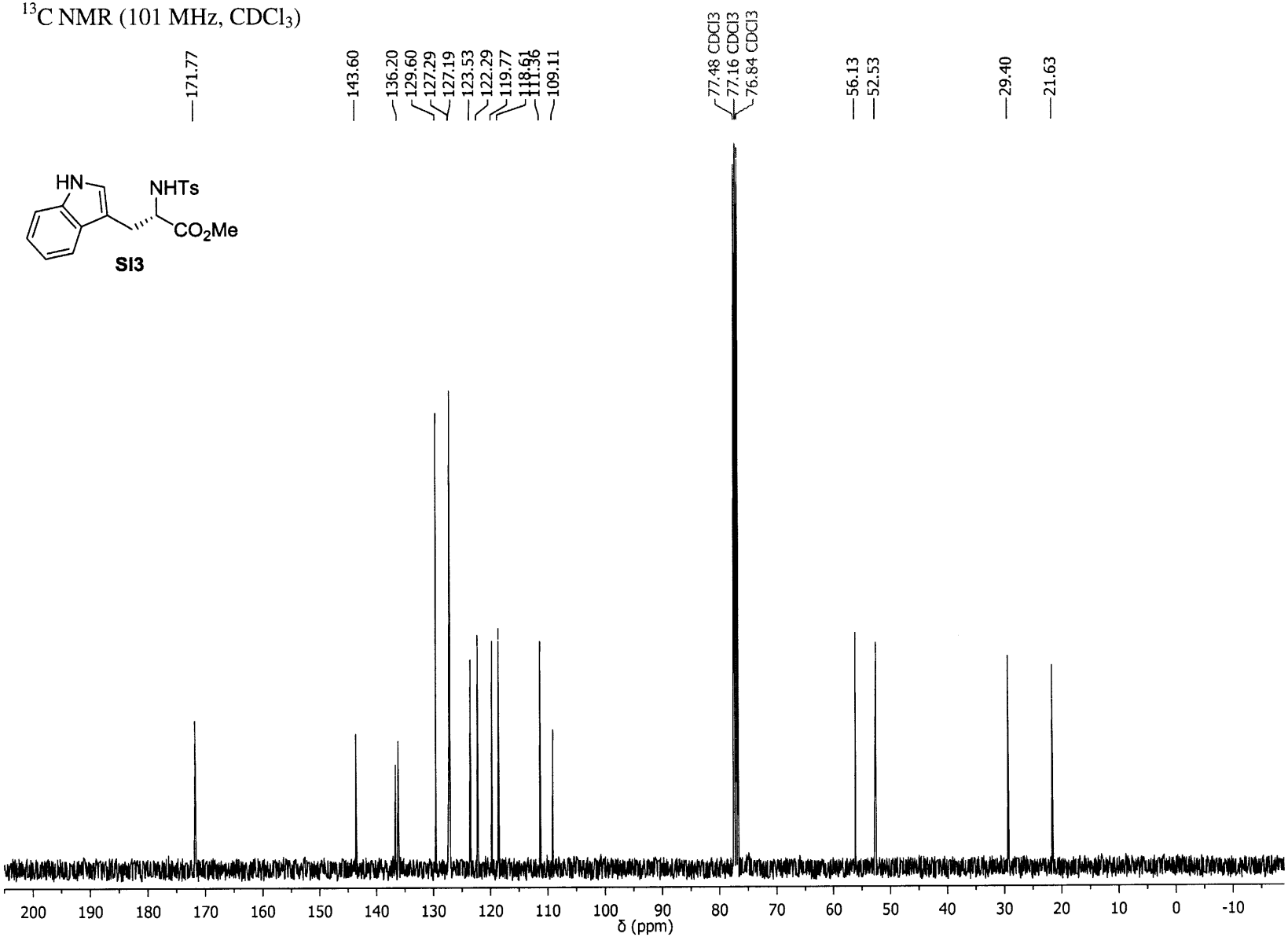


1l

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



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



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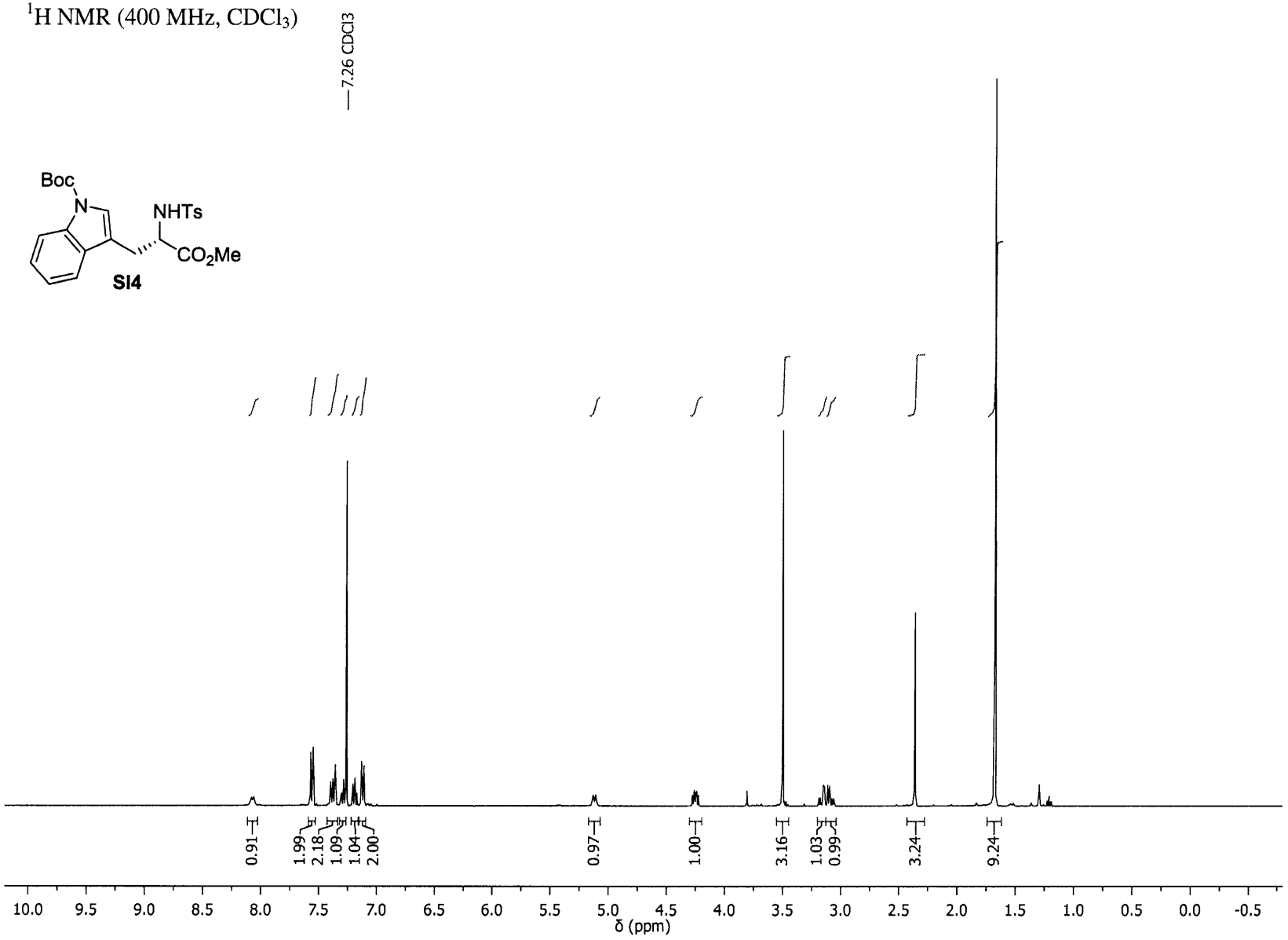
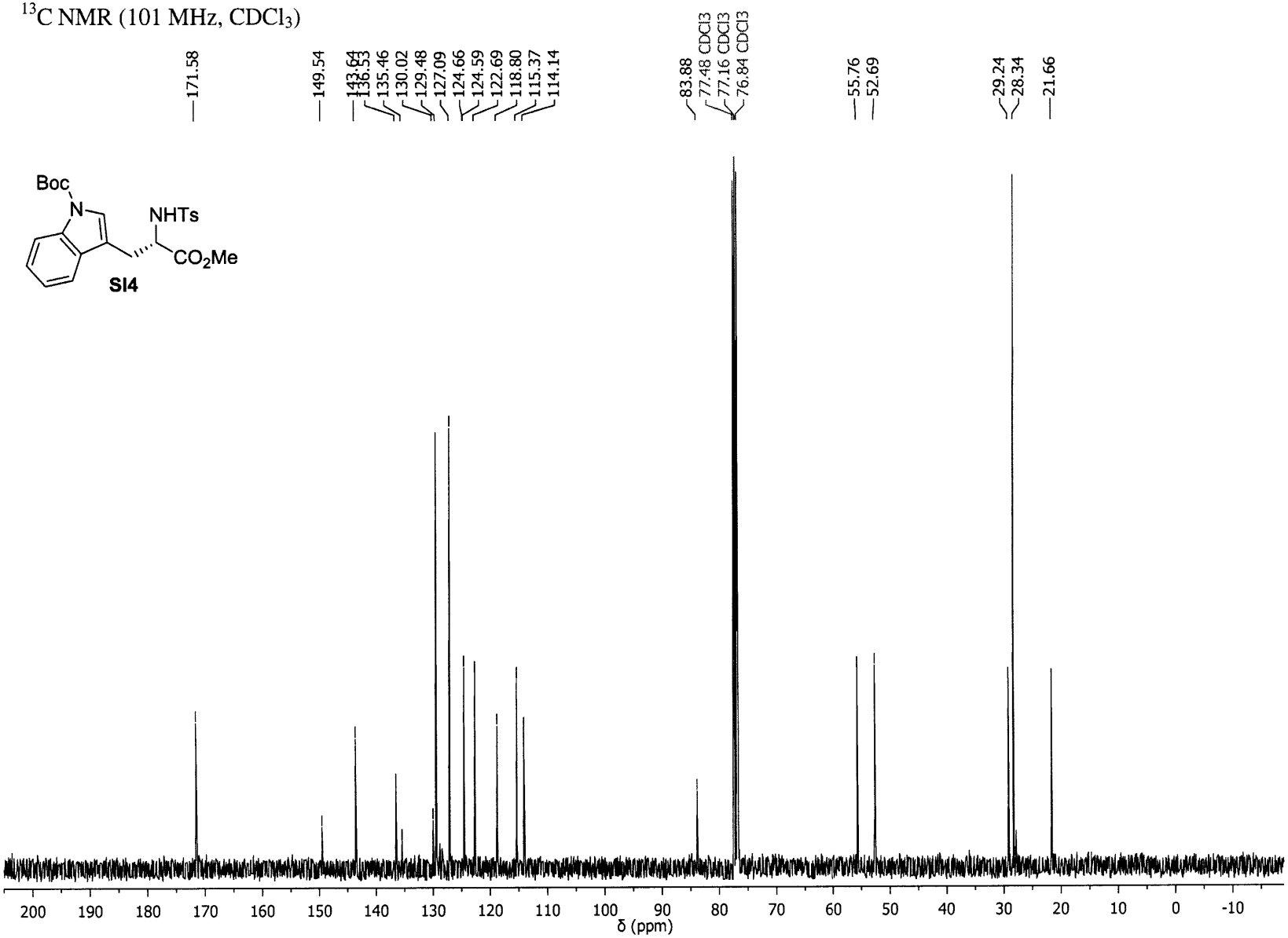
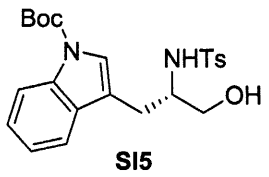


^{13}C NMR (101 MHz, $CDCl_3$)

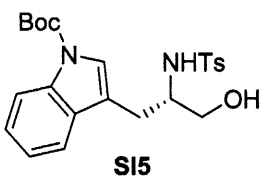


^{1}H NMR (400 MHz, $CDCl_3$)



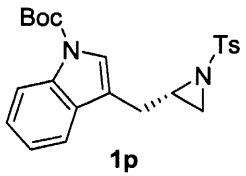
SI5

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



SI5

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



1p

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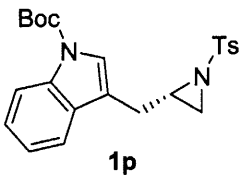
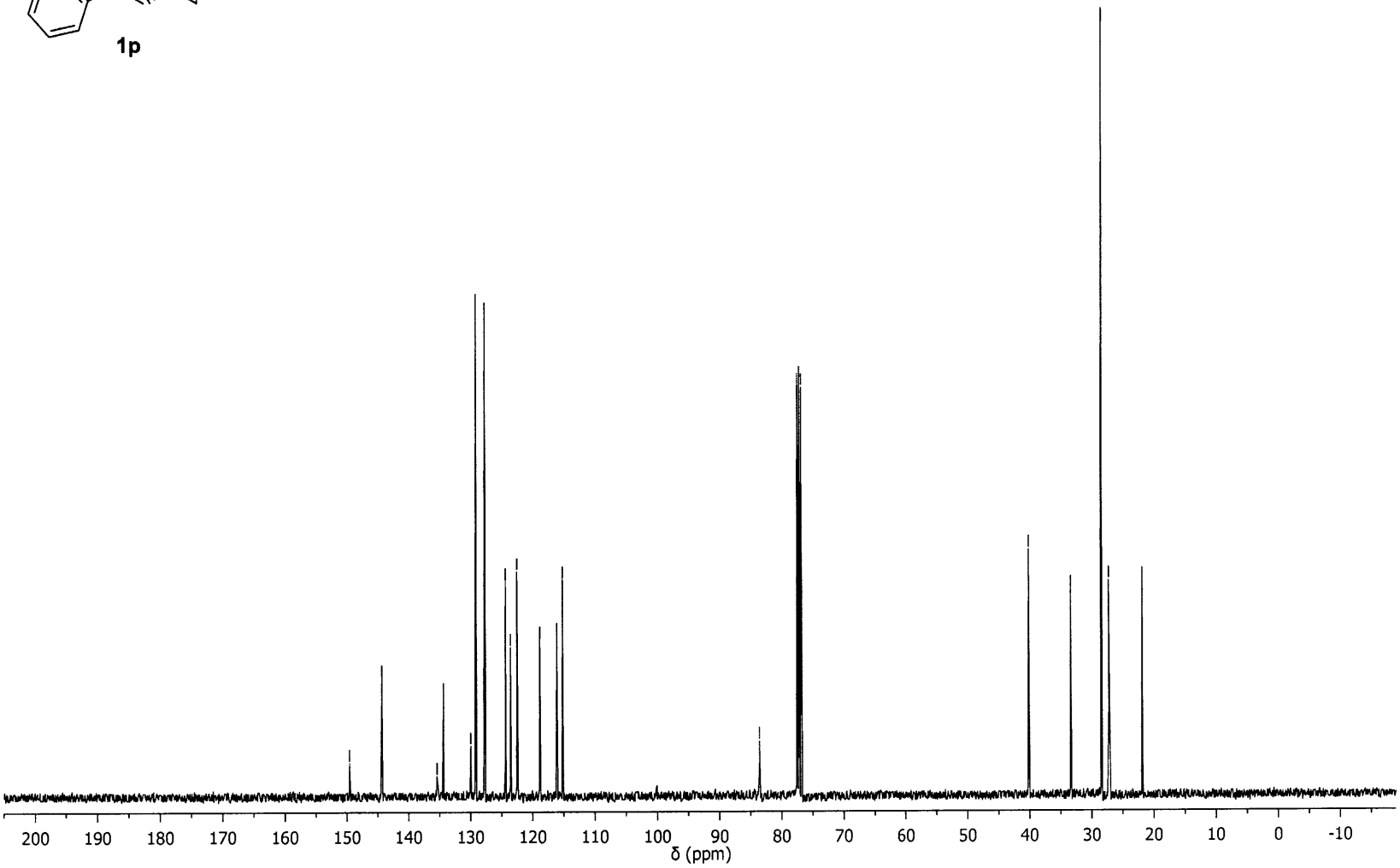
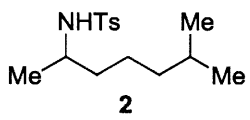


1p

149.56
144.30
135.43
134.36
129.99
129.08
127.67
124.38
123.56
122.53
118.86
116.11
115.19
83.58
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
40.09
33.33
28.34
27.19
21.76

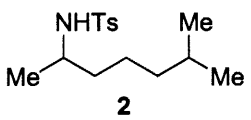


^{1}H NMR (400 MHz, $CDCl_3$)



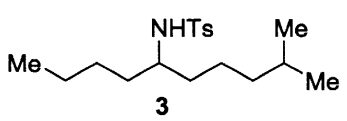
2

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



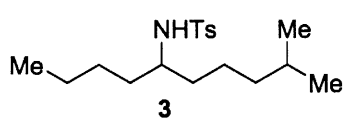
2

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



3

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



3

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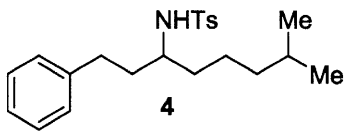

4

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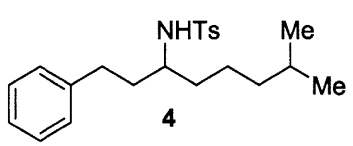
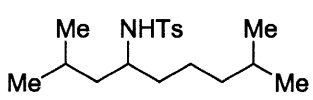


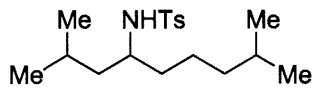
4

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



5

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



5

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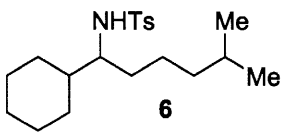
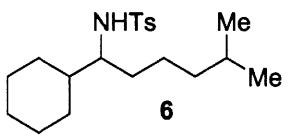


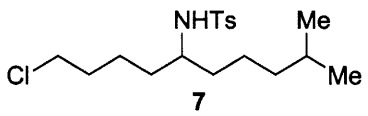
6

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



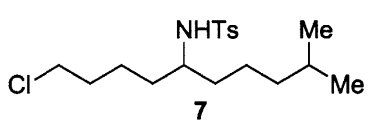
6

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



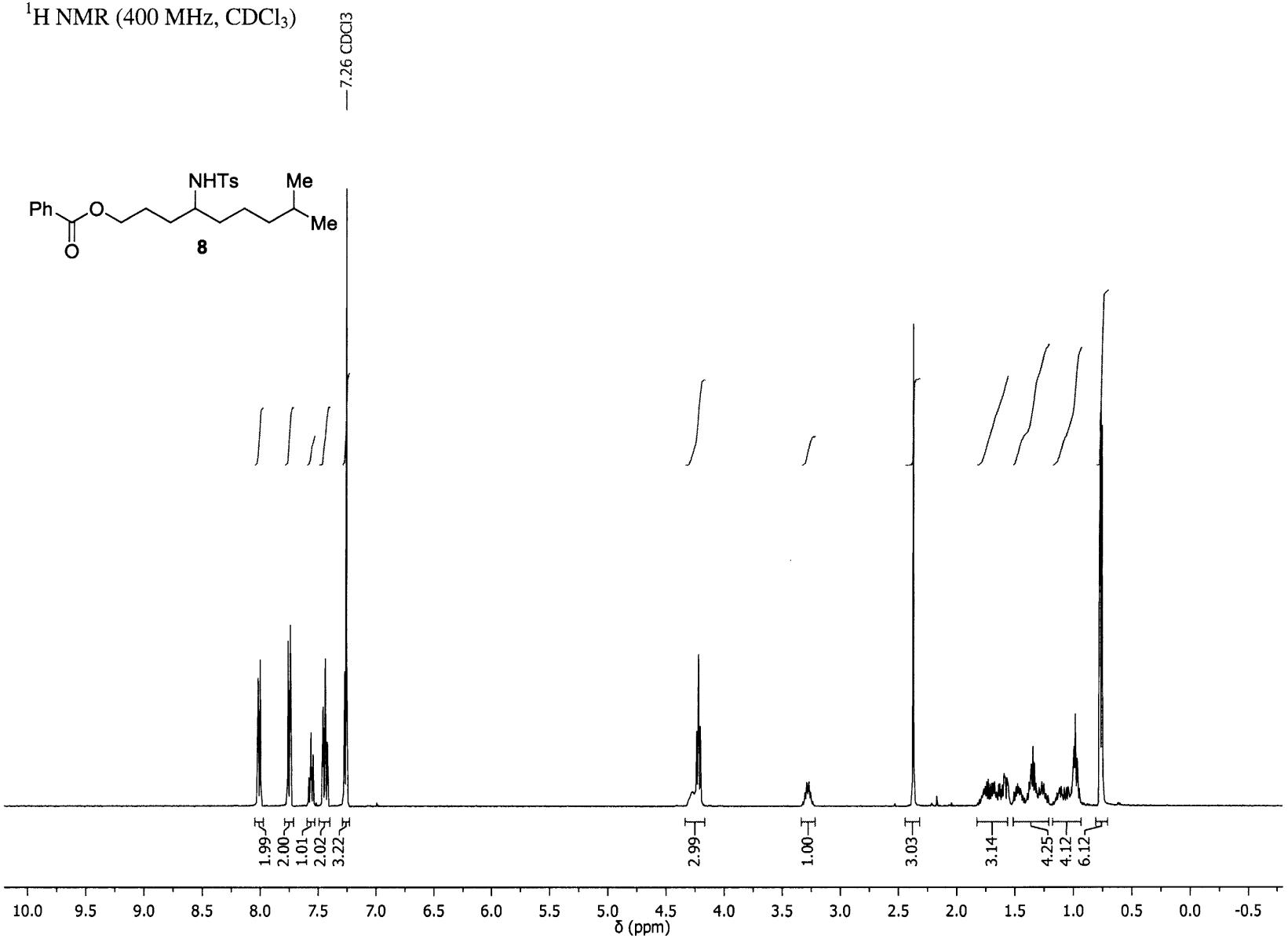
7

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

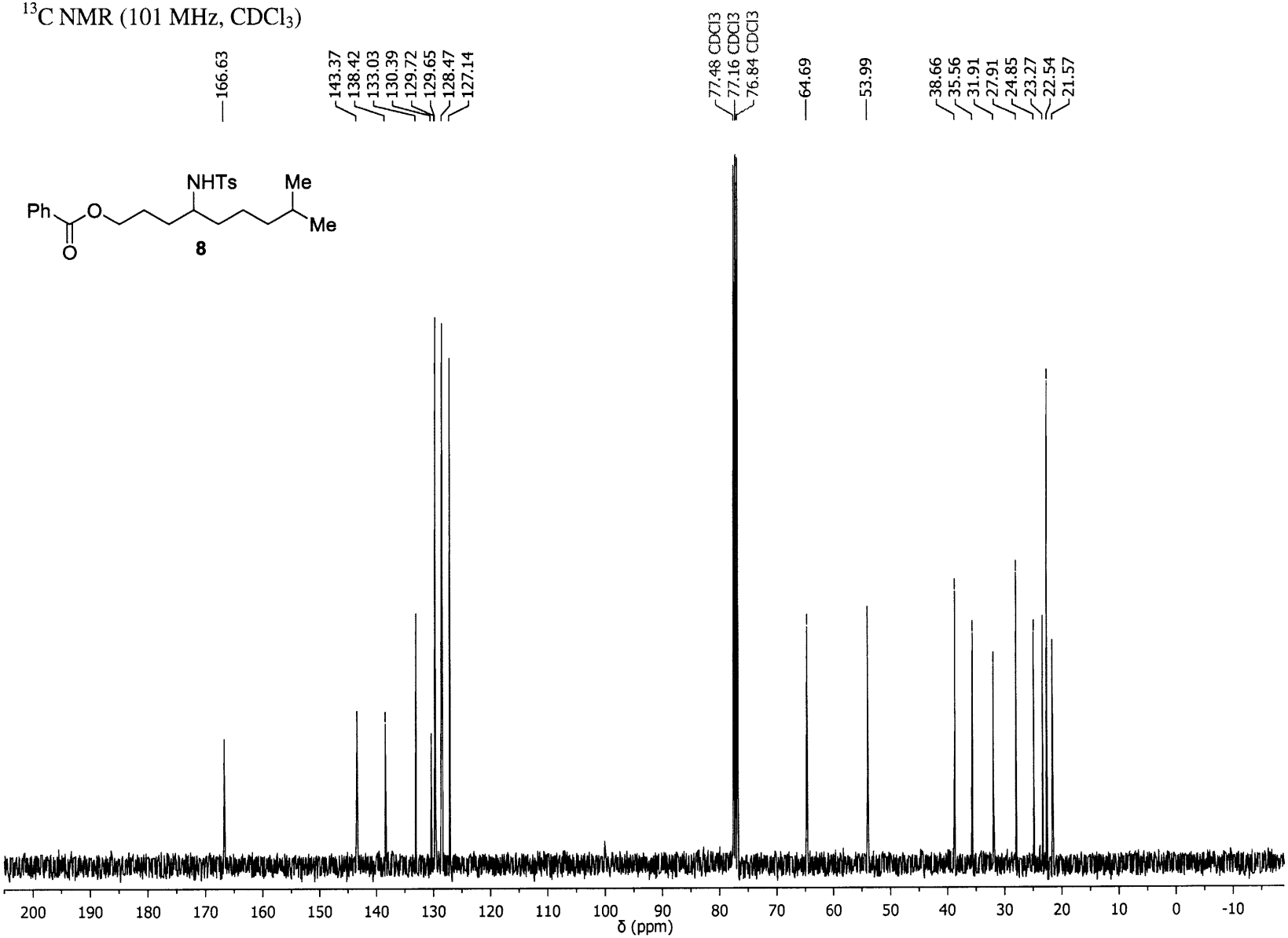


7

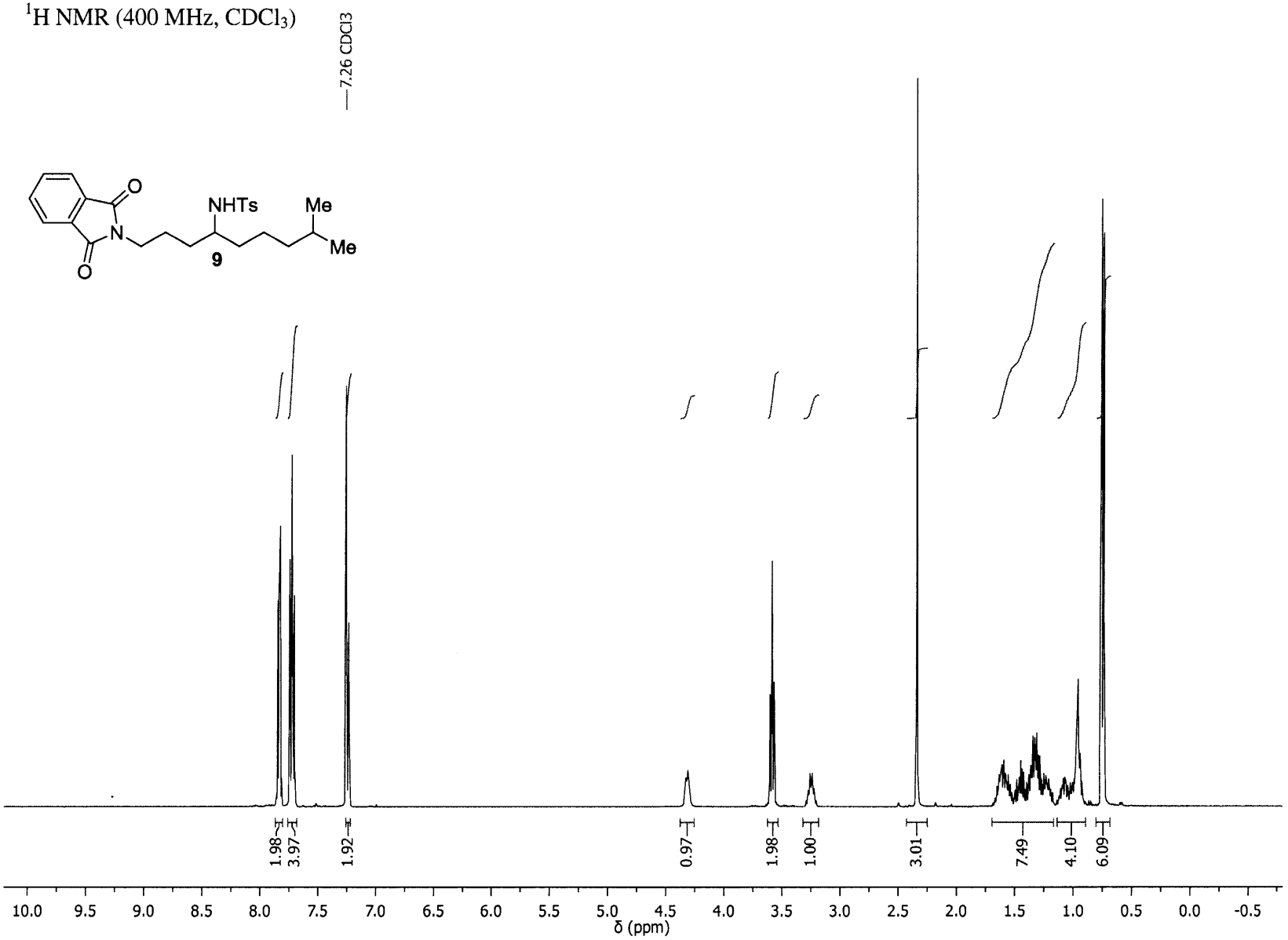
^{1}H NMR (400 MHz, $CDCl_3$)



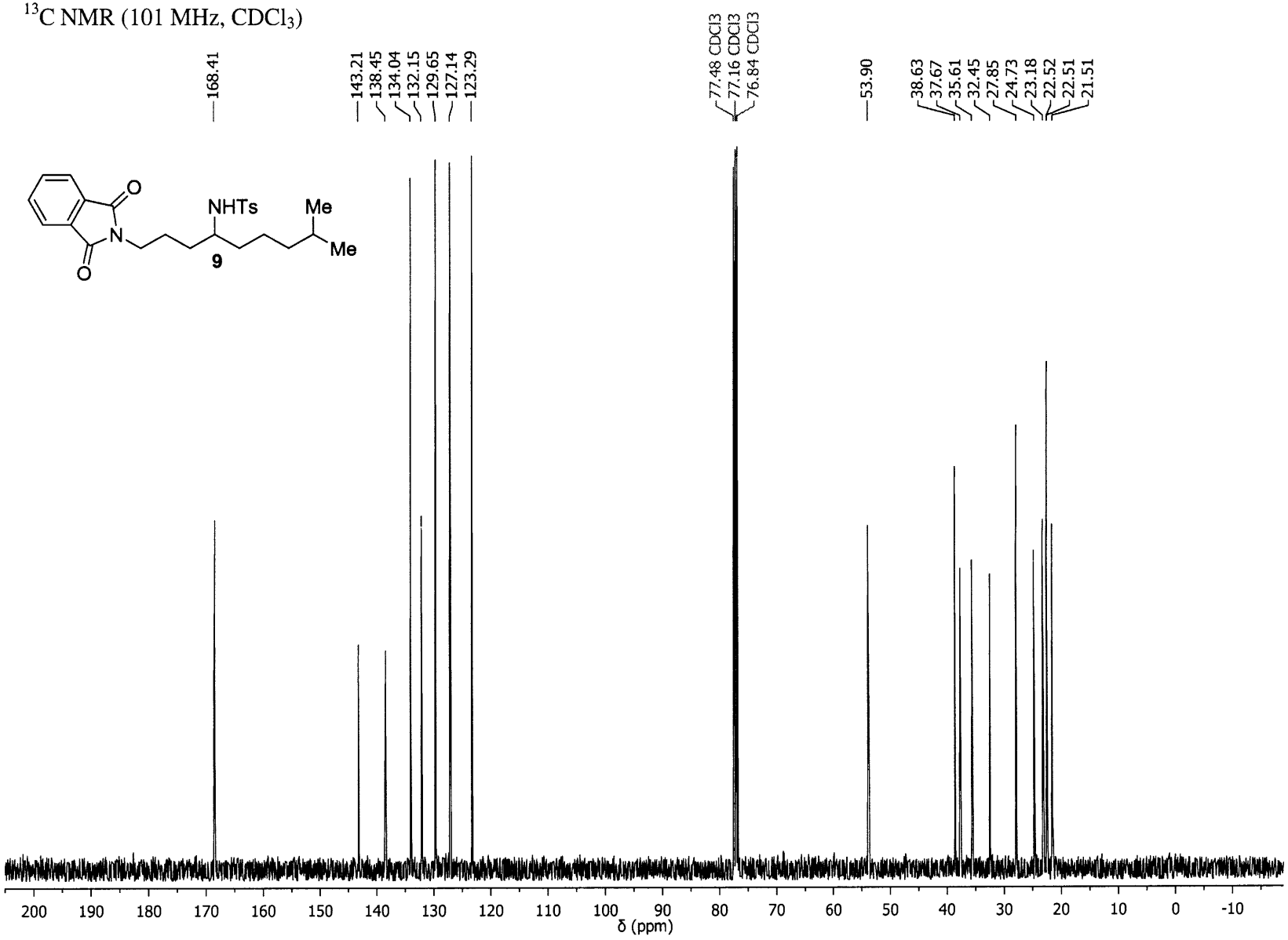
^{13}C NMR (101 MHz, $CDCl_3$)



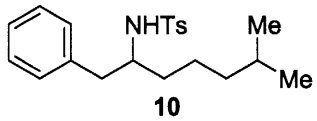
^{1}H NMR (400 MHz, $CDCl_3$)



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

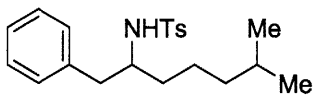


^{1}H NMR (400 MHz, $CDCl_3$)



10

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



10

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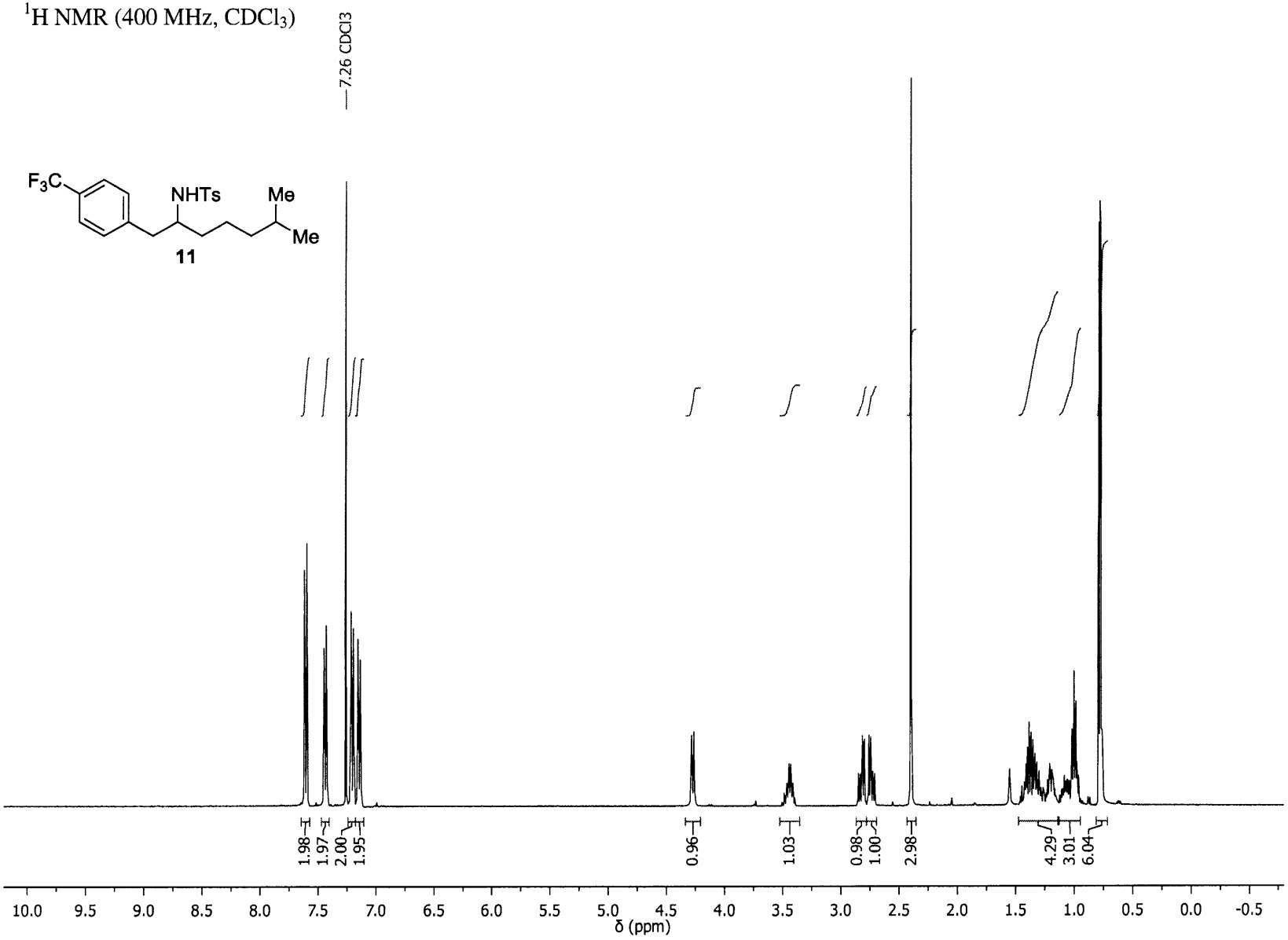
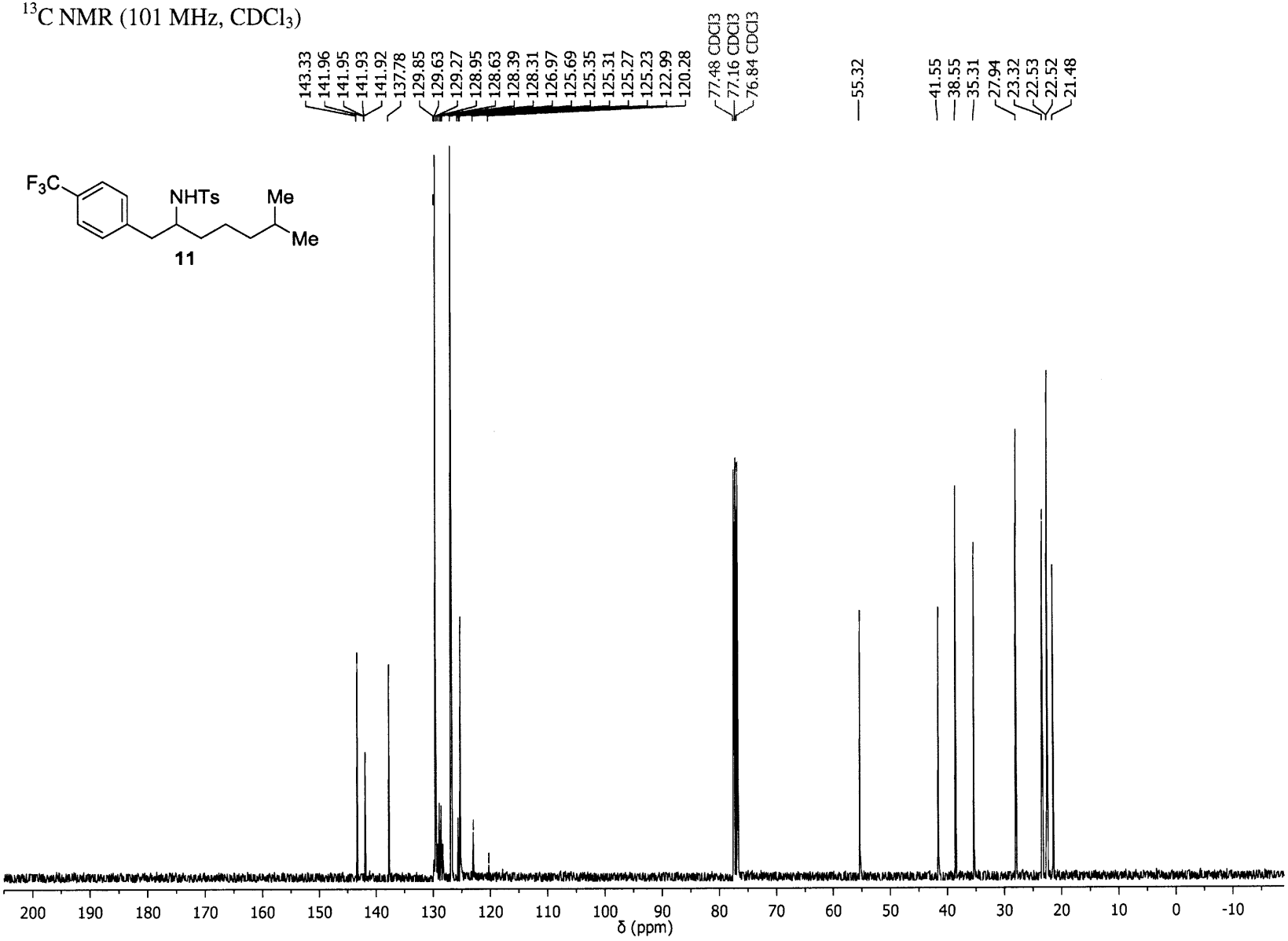
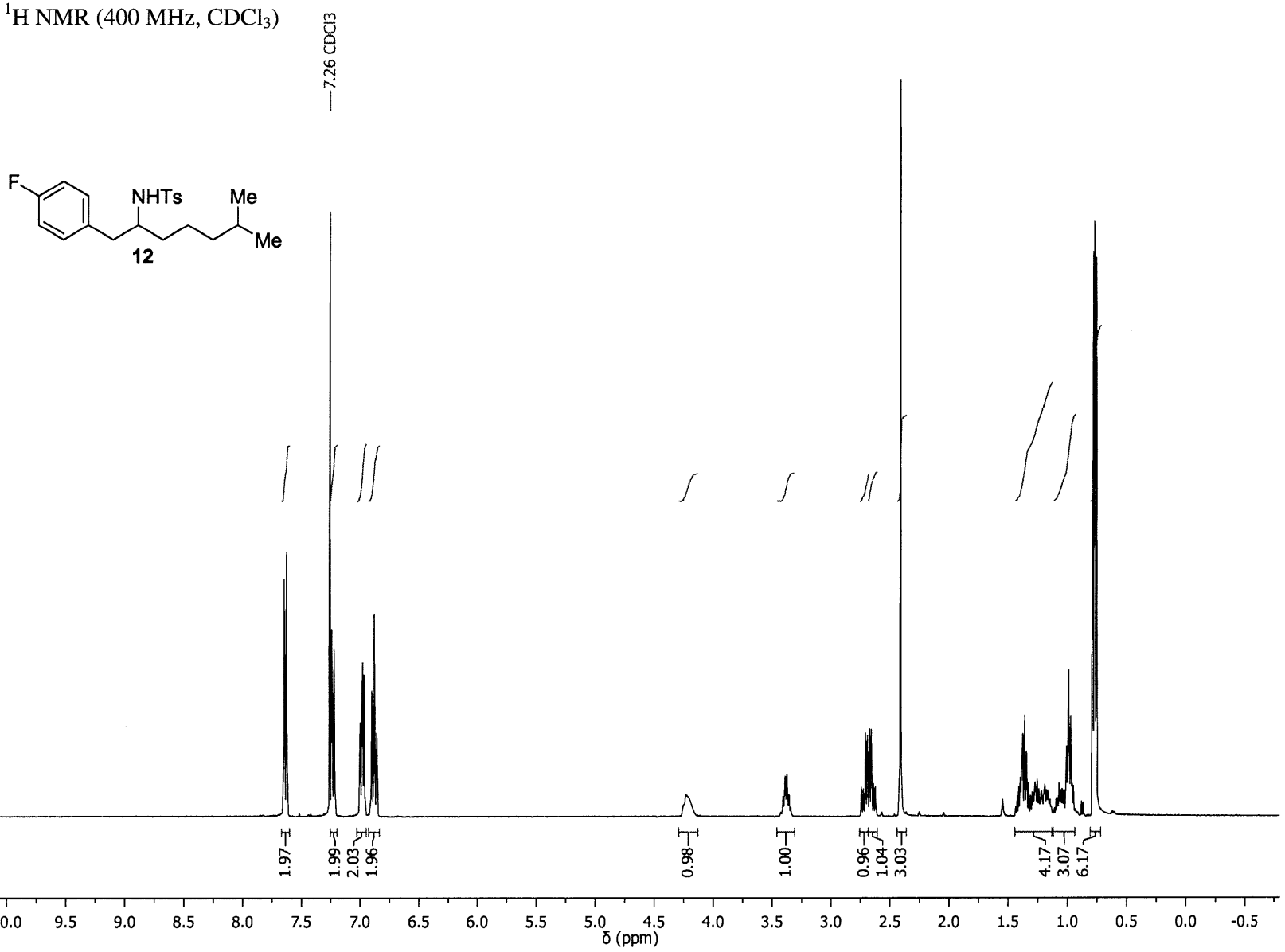


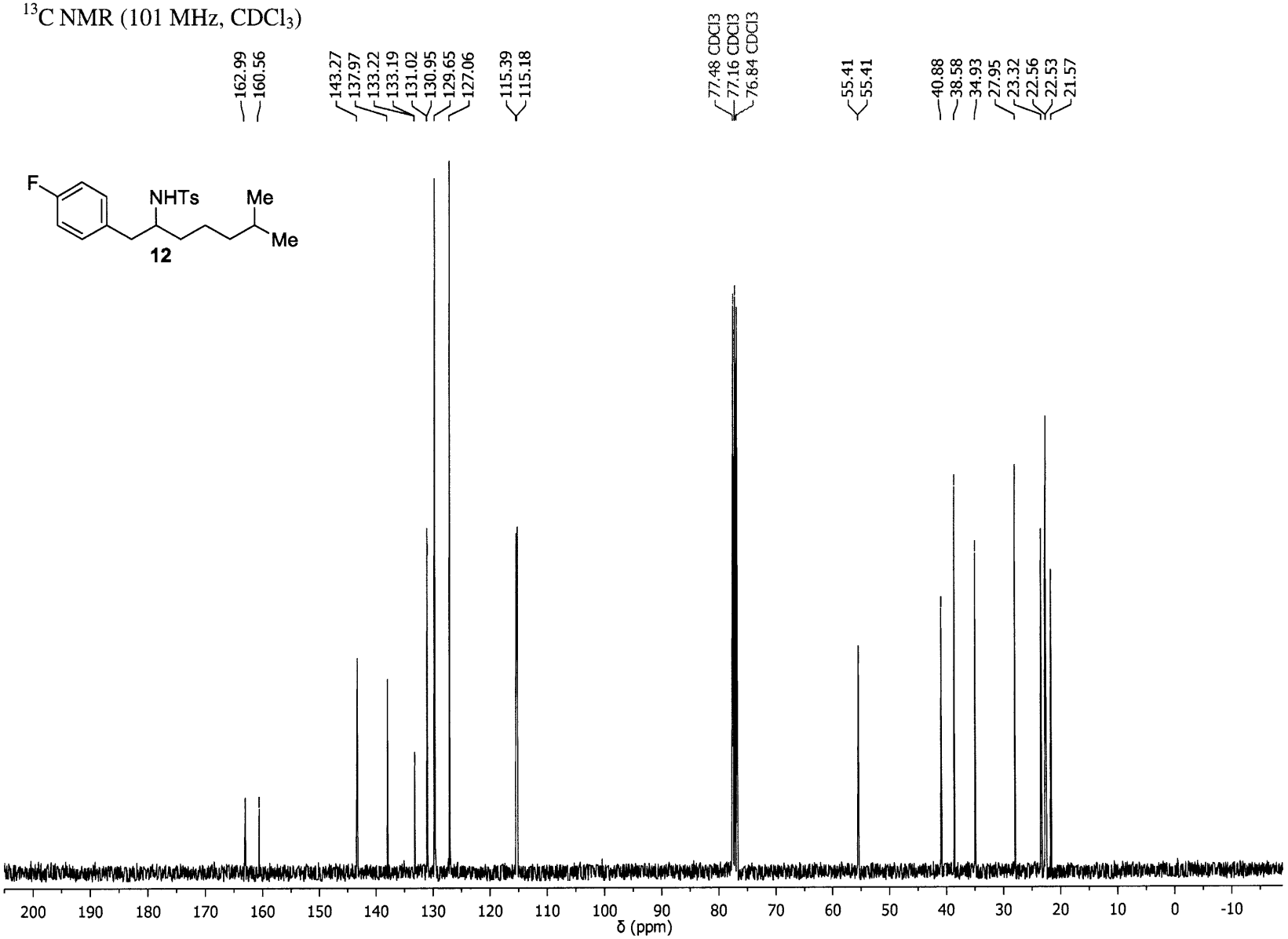
^{13}C NMR (101 MHz, $CDCl_3$)



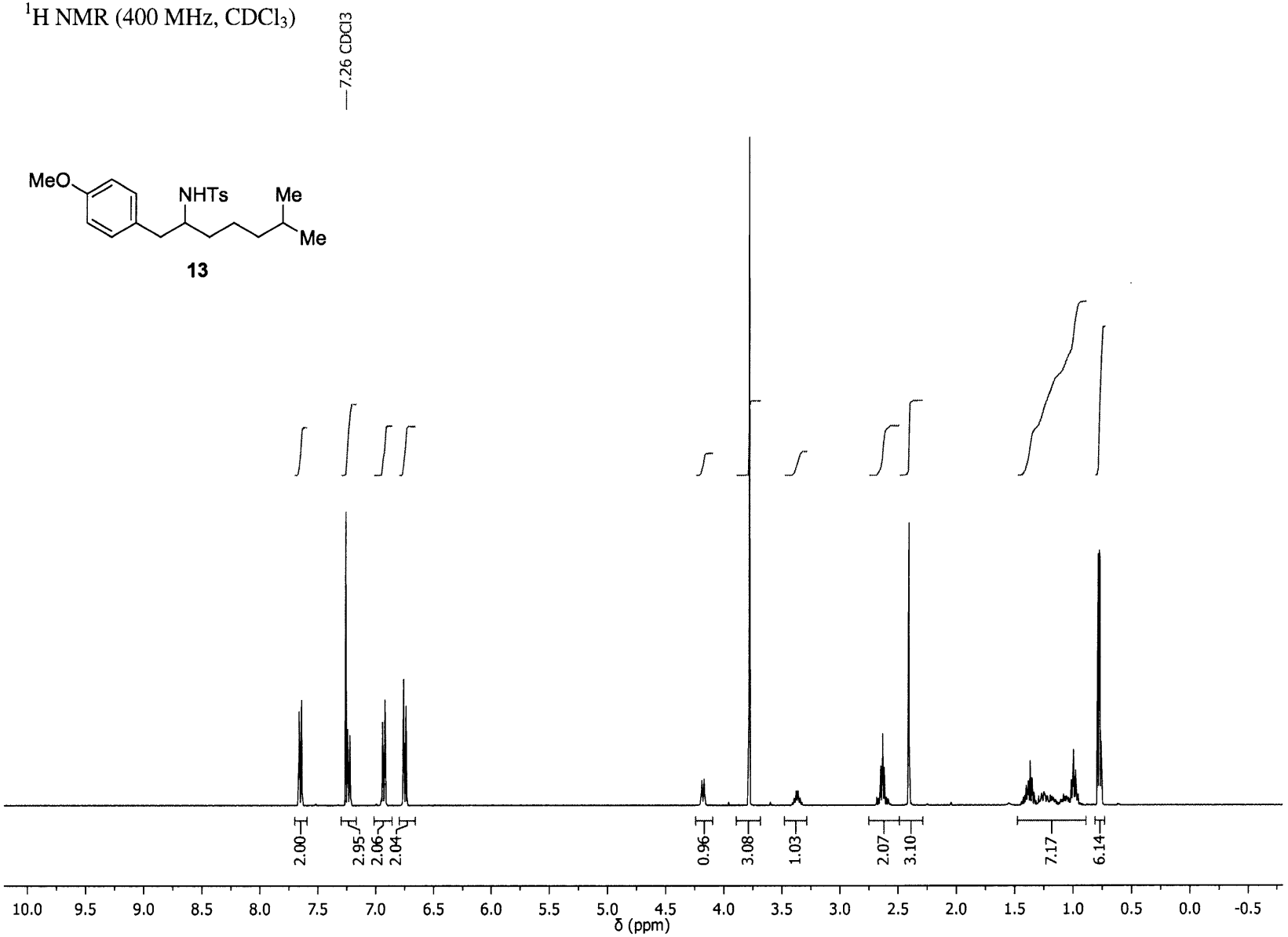
^{1}H NMR (400 MHz, $CDCl_3$)



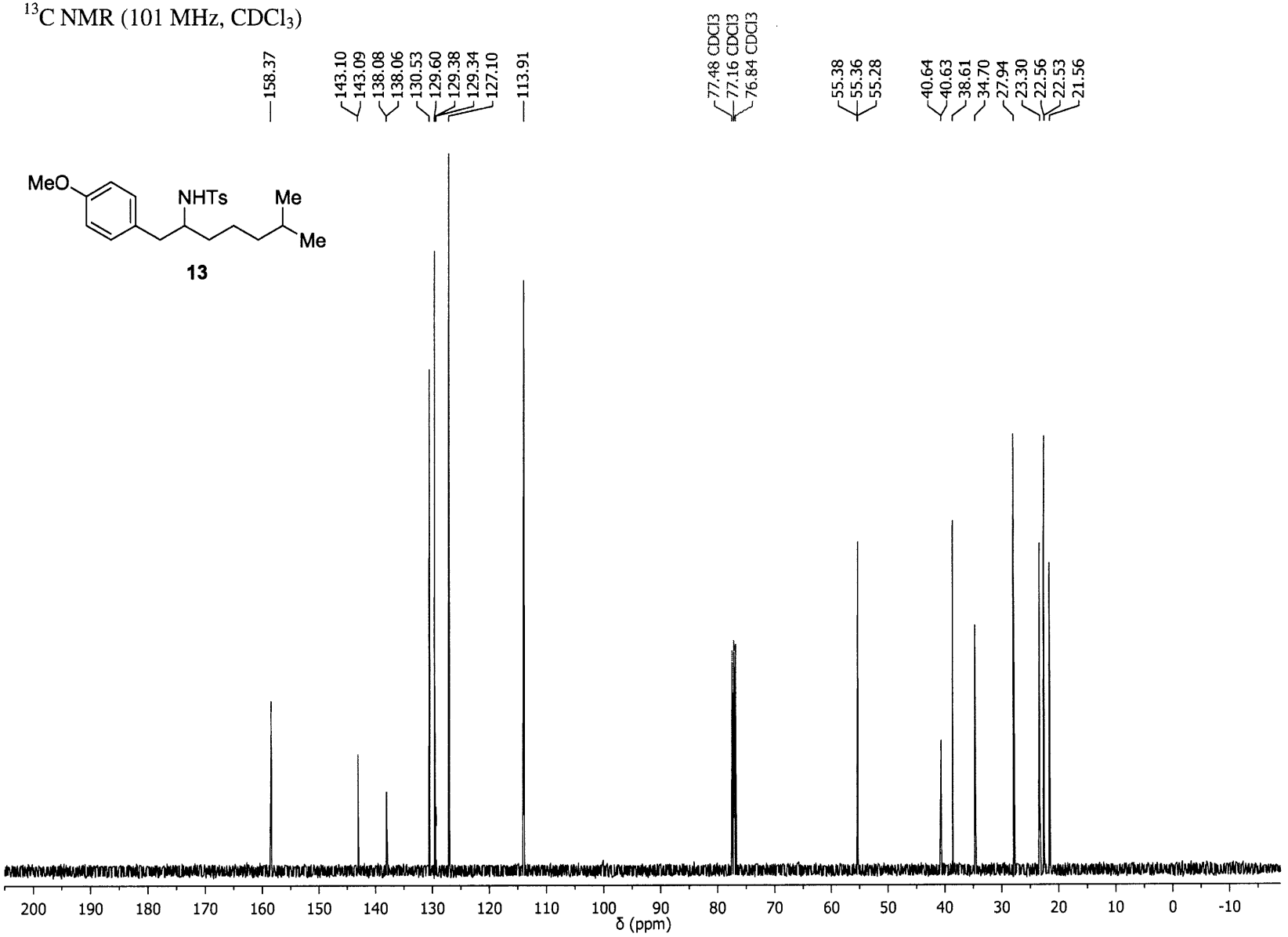
^{13}C NMR (101 MHz, $CDCl_3$)



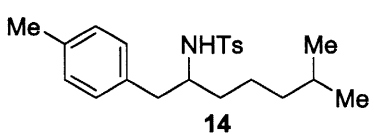
^{1}H NMR (400 MHz, $CDCl_3$)



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

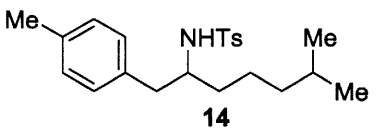


^{1}H NMR (400 MHz, $CDCl_3$)



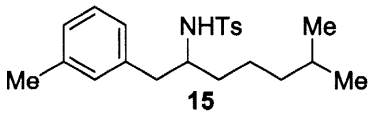
14

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



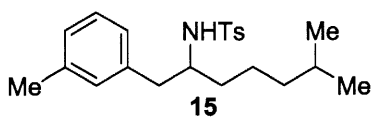
14

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



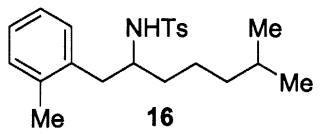
15

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



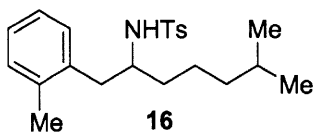
15

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



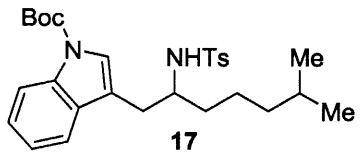
16

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



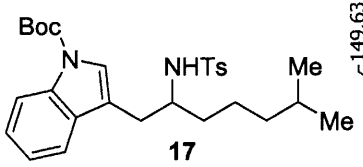
16

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



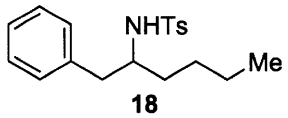
17

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



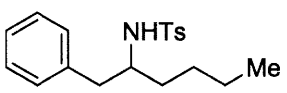
17

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



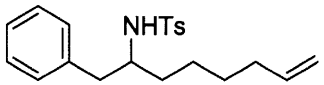
18

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



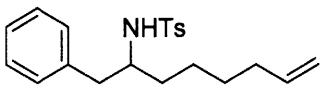
18

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

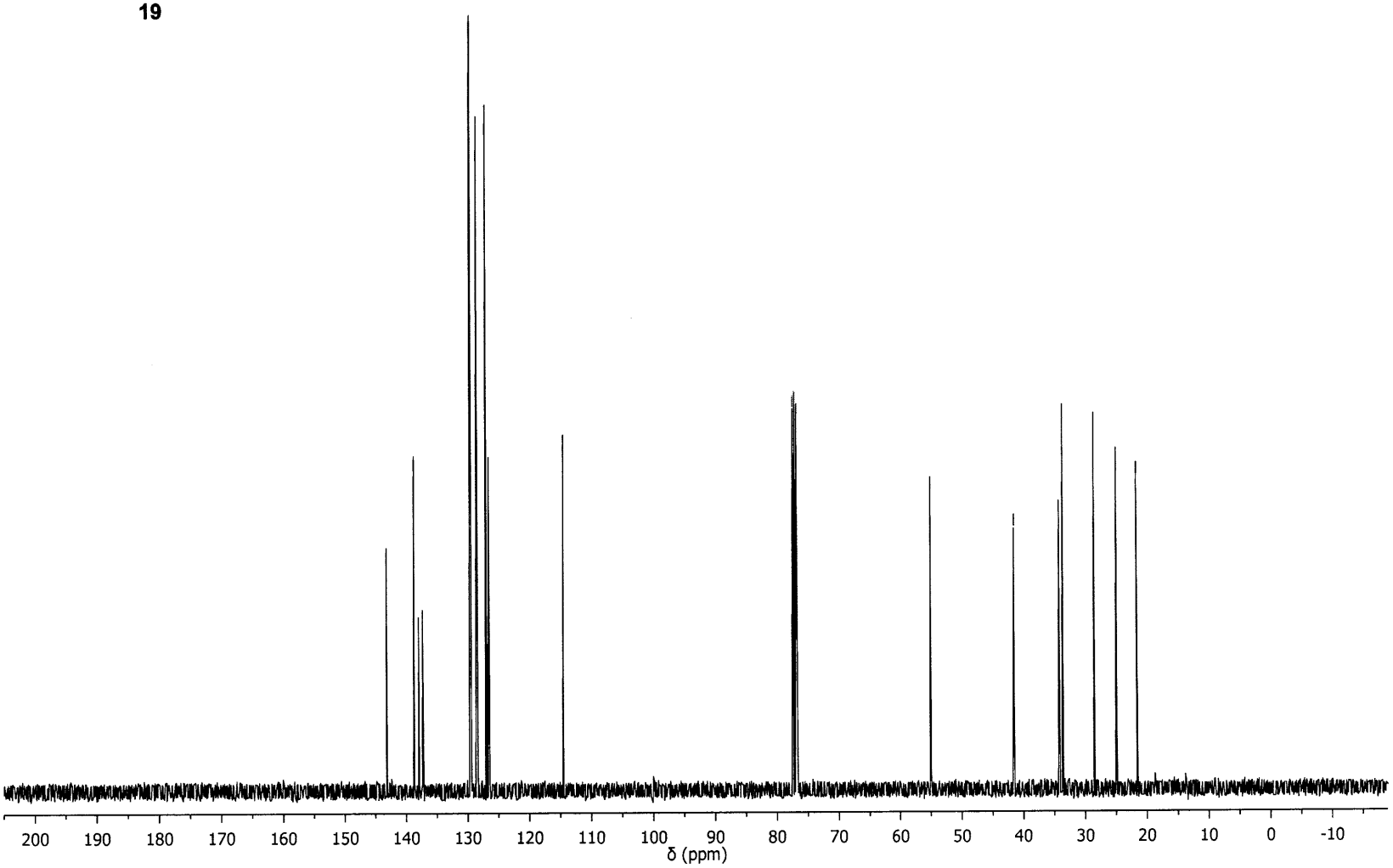


19

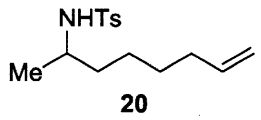
^{13}C NMR (101 MHz, $CDCl_3$)



19

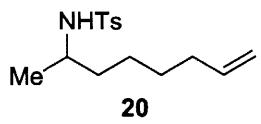


^{1}H NMR (400 MHz, $CDCl_3$)



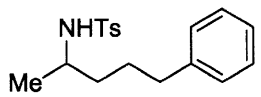
20

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



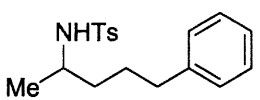
20

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



21

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



21

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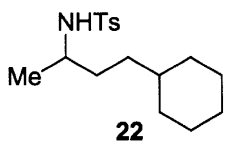
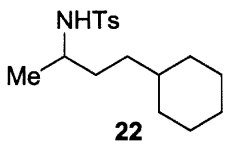


22

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



22

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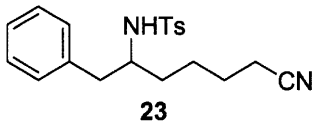
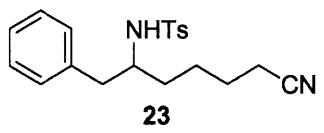


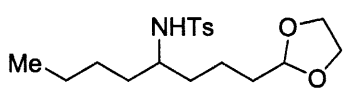
23

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



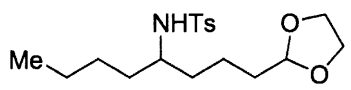
23

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



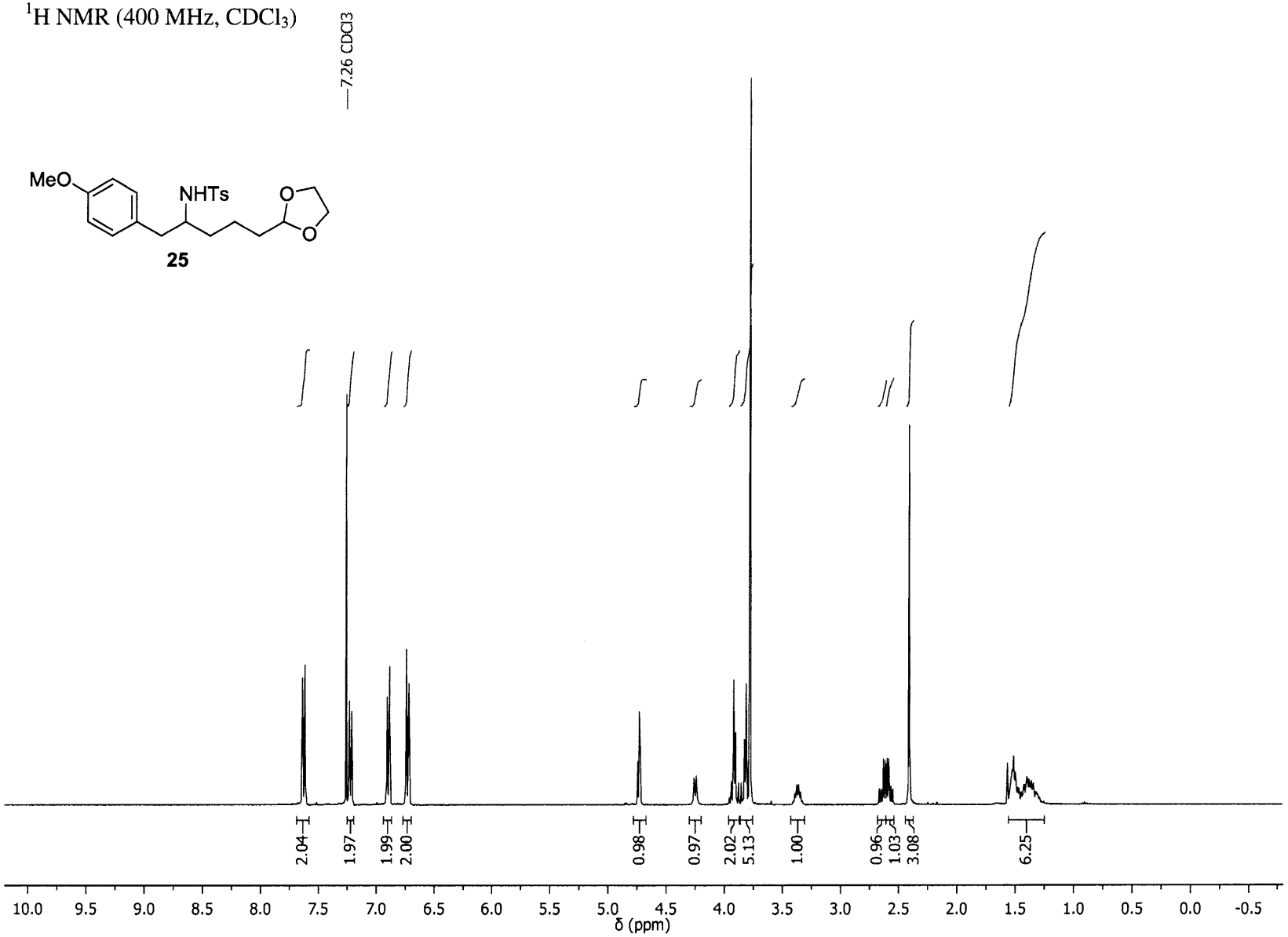
24

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

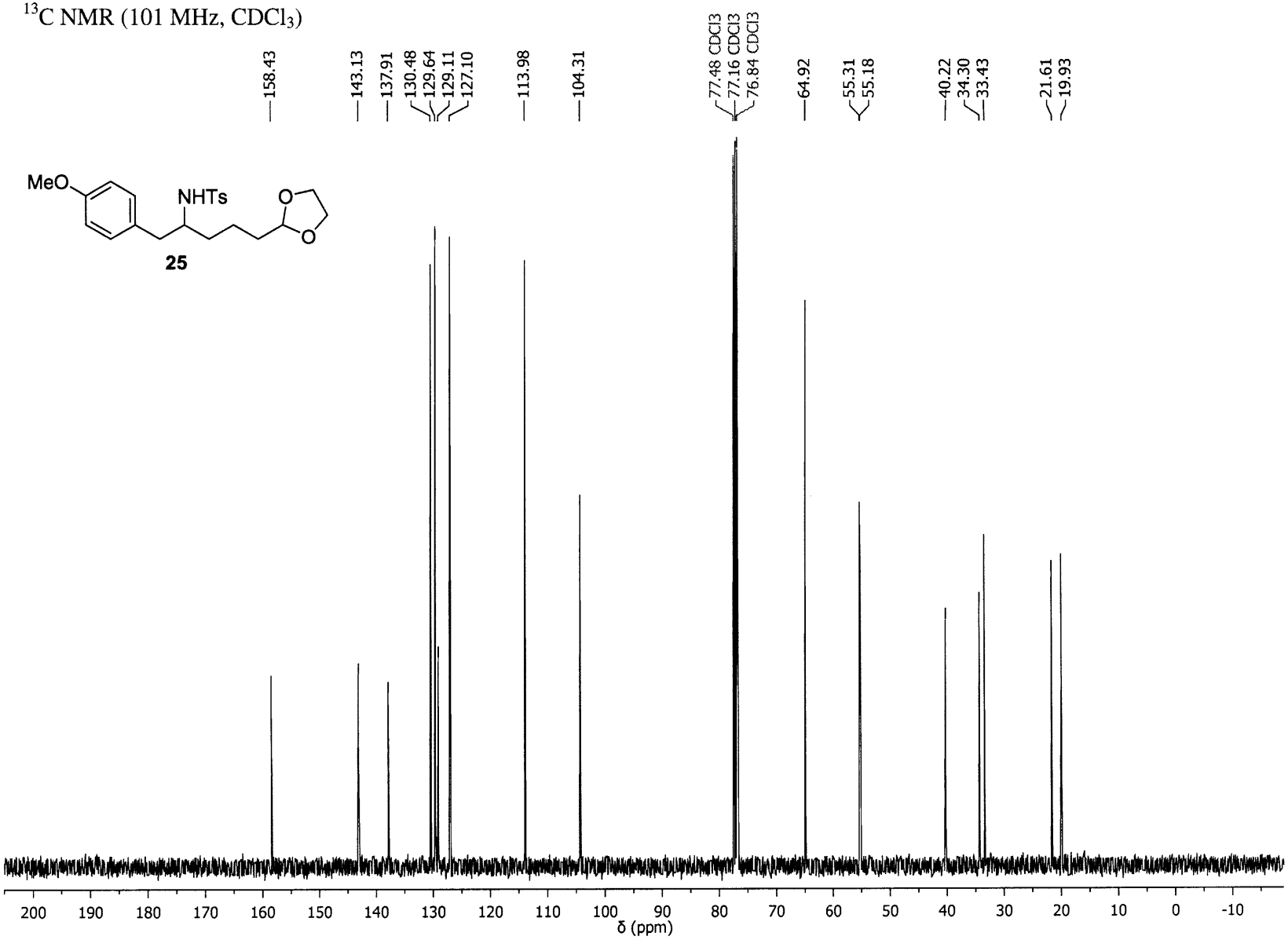


24

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



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



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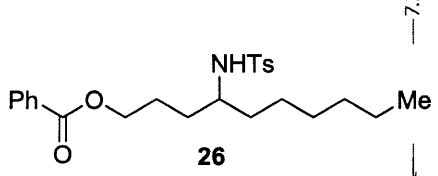
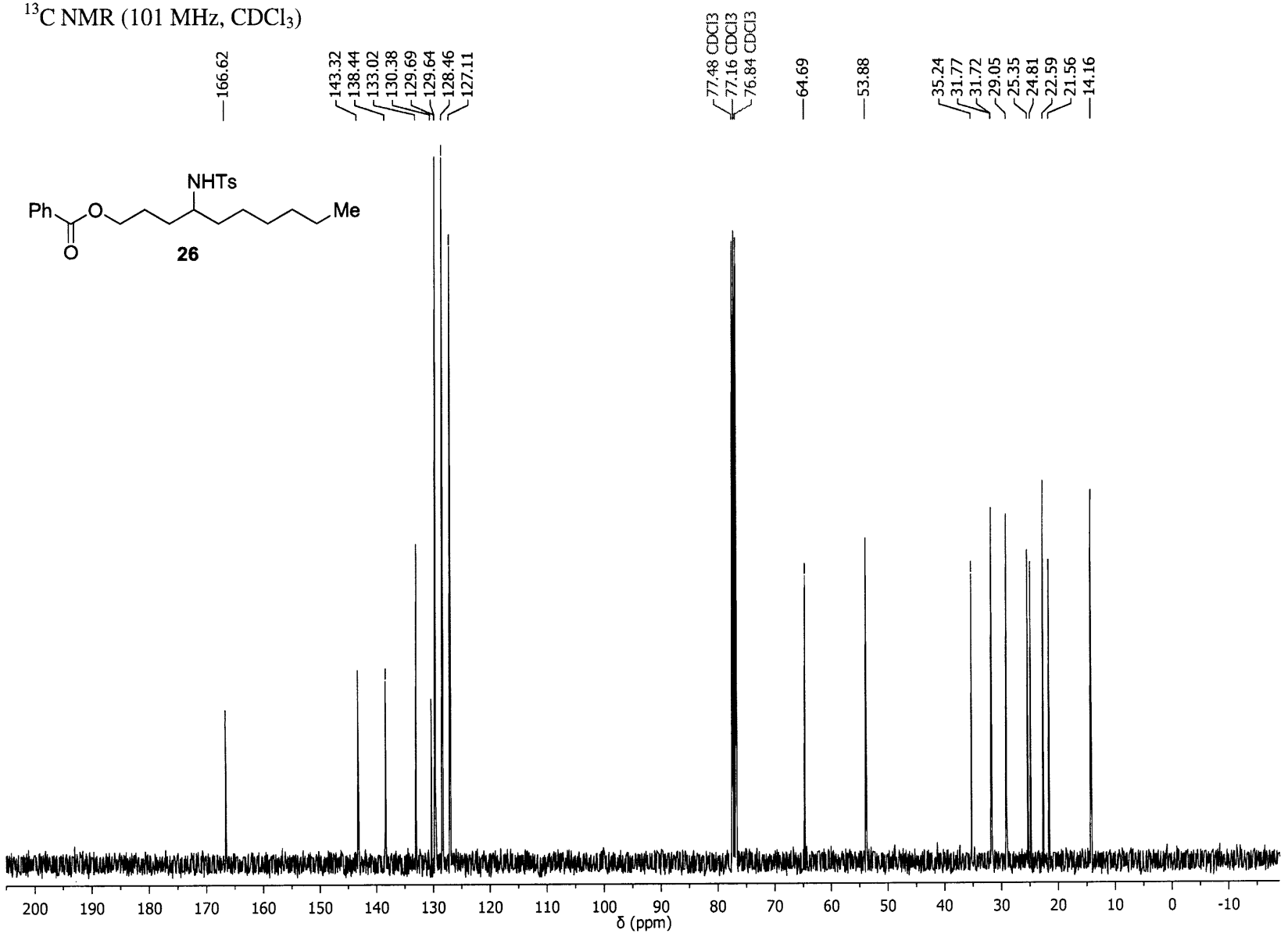


26

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



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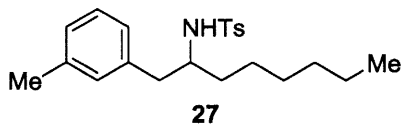
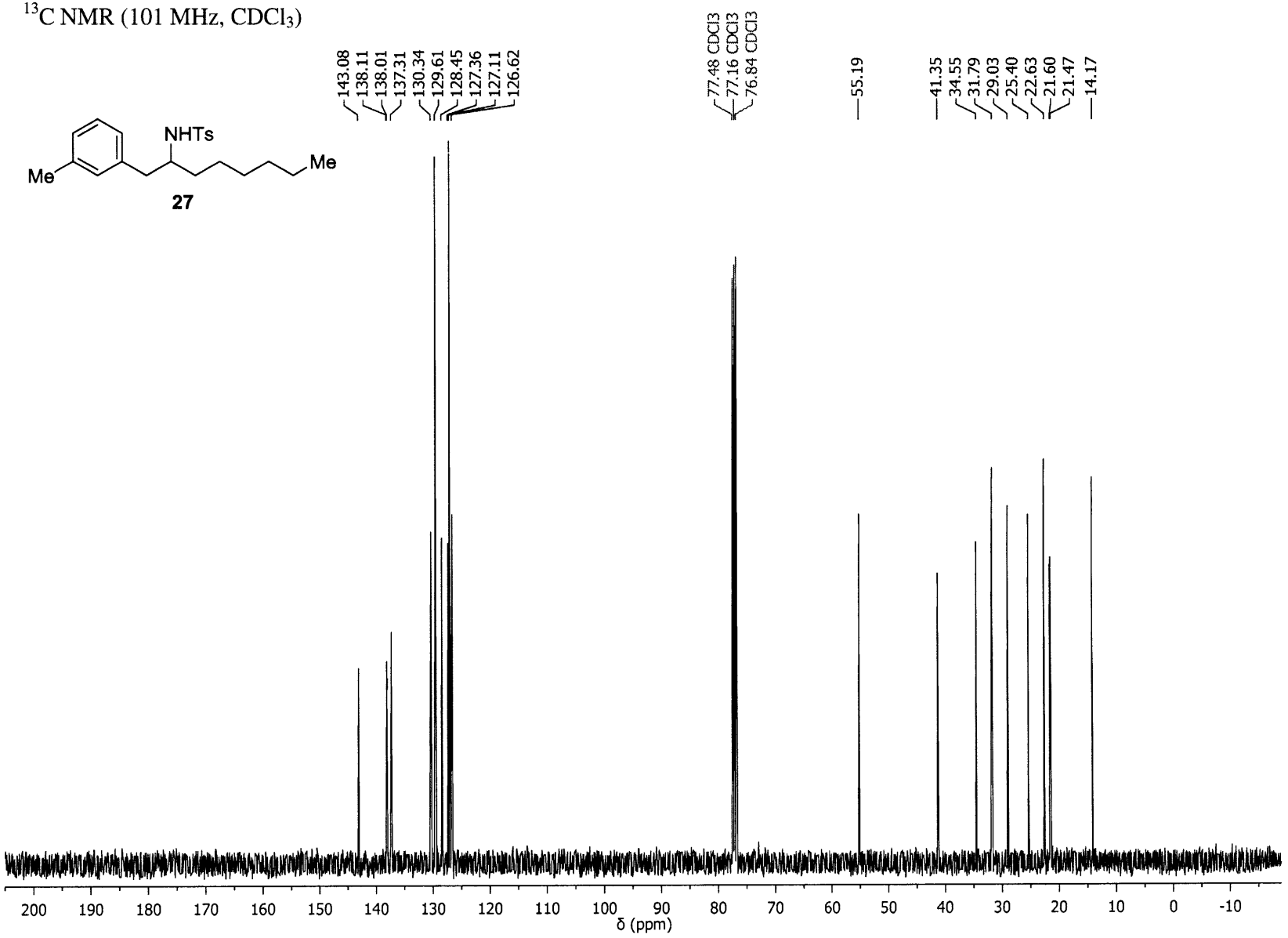
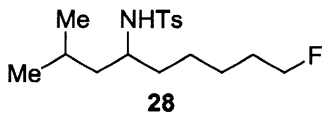


27

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

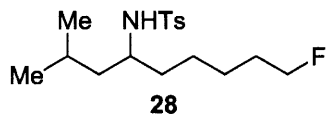


^{1}H NMR (400 MHz, $CDCl_3$)



28

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



28

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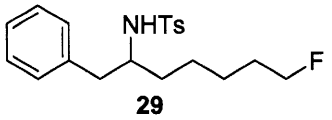

29

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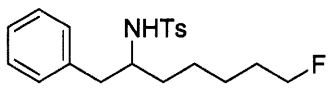

29

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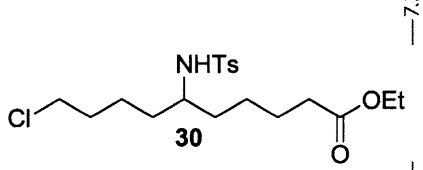

30

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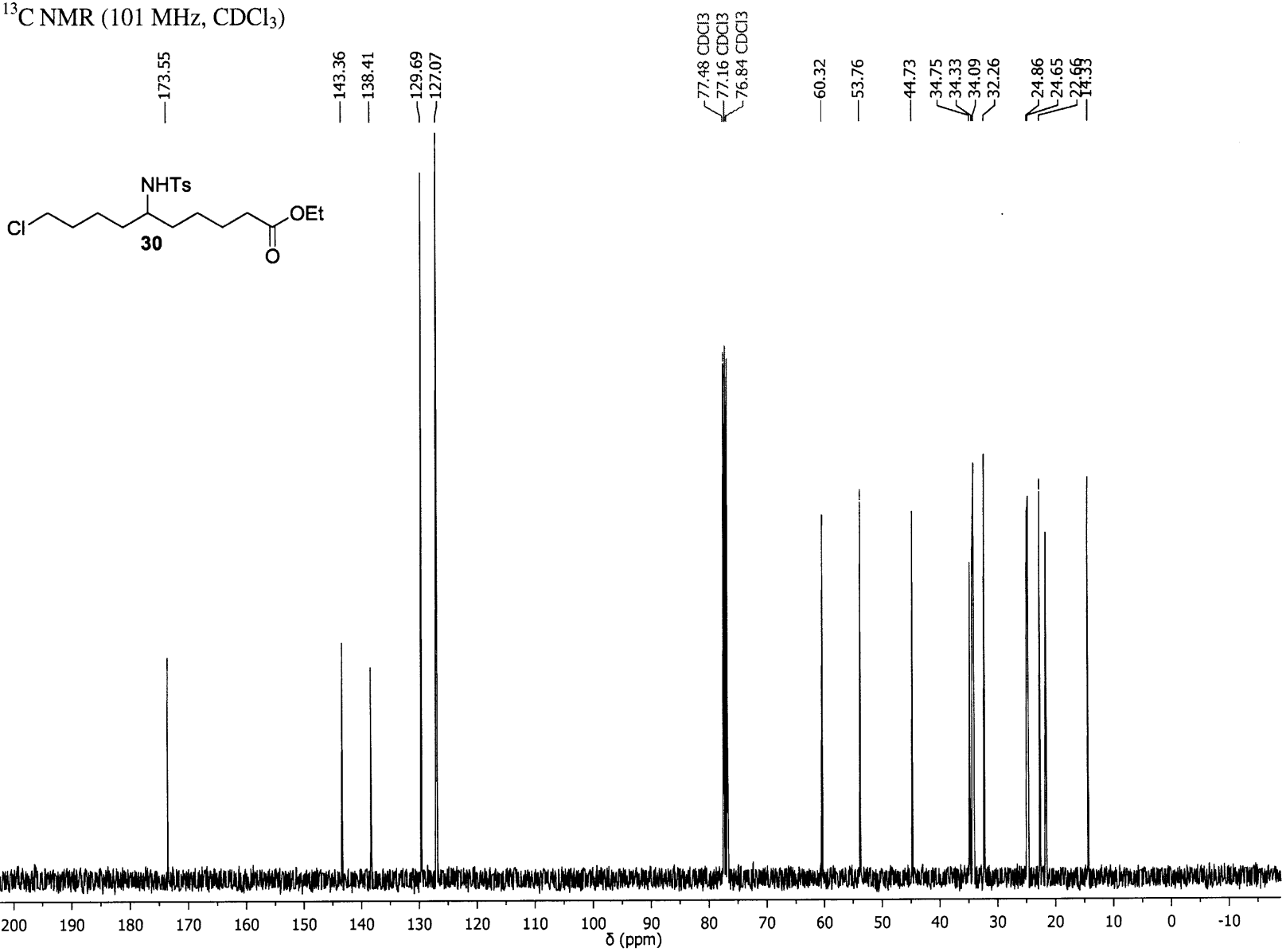
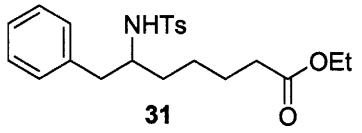


^{1}H NMR (400 MHz, $CDCl_3$)



31

500

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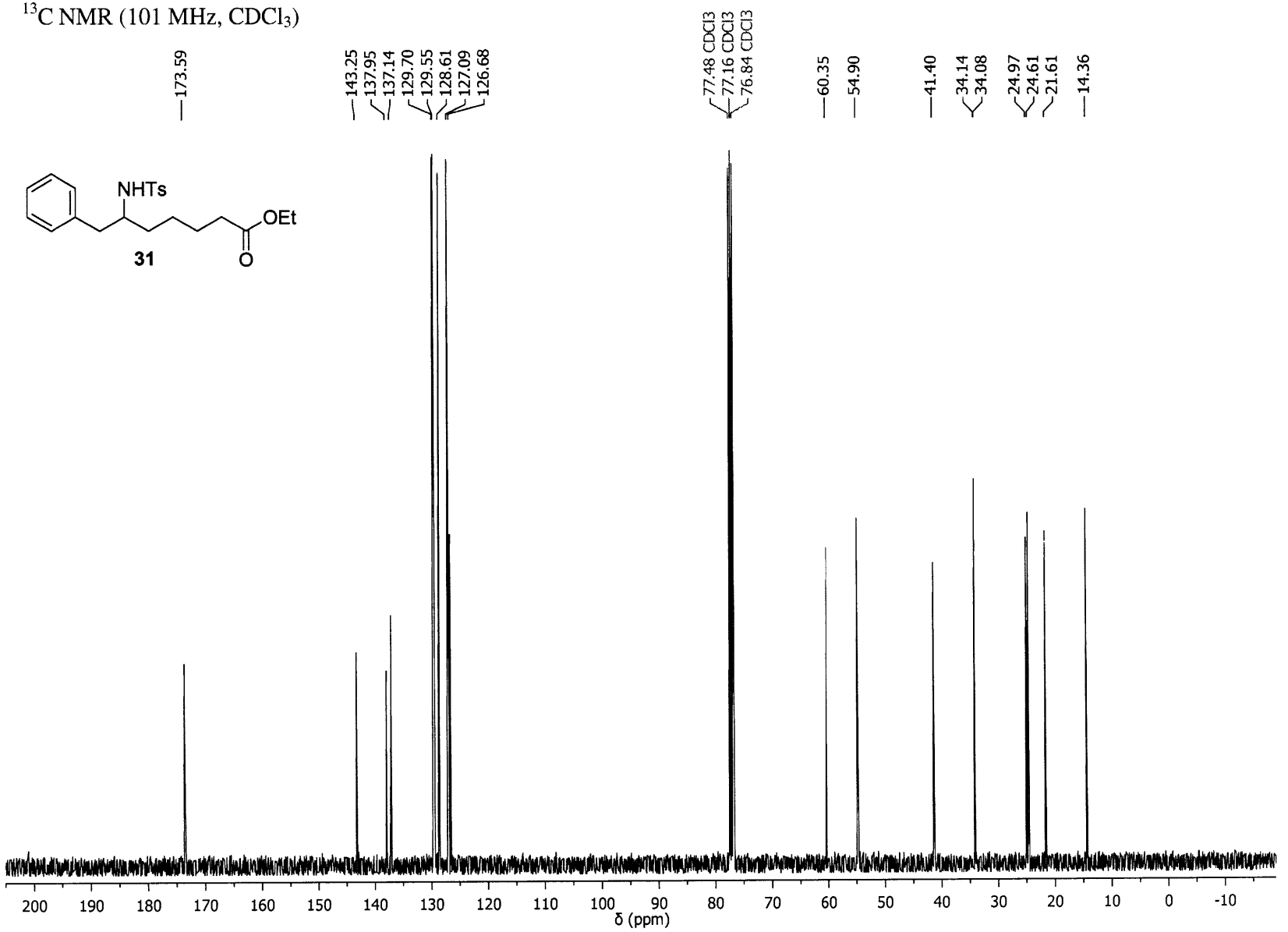

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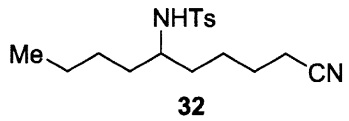

32

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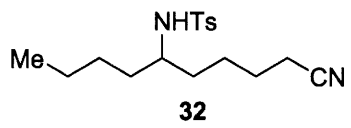

32

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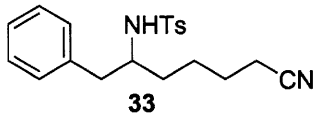

33

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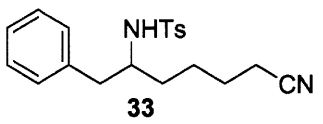

33

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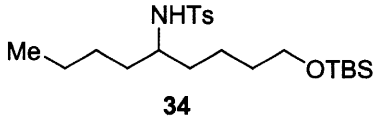
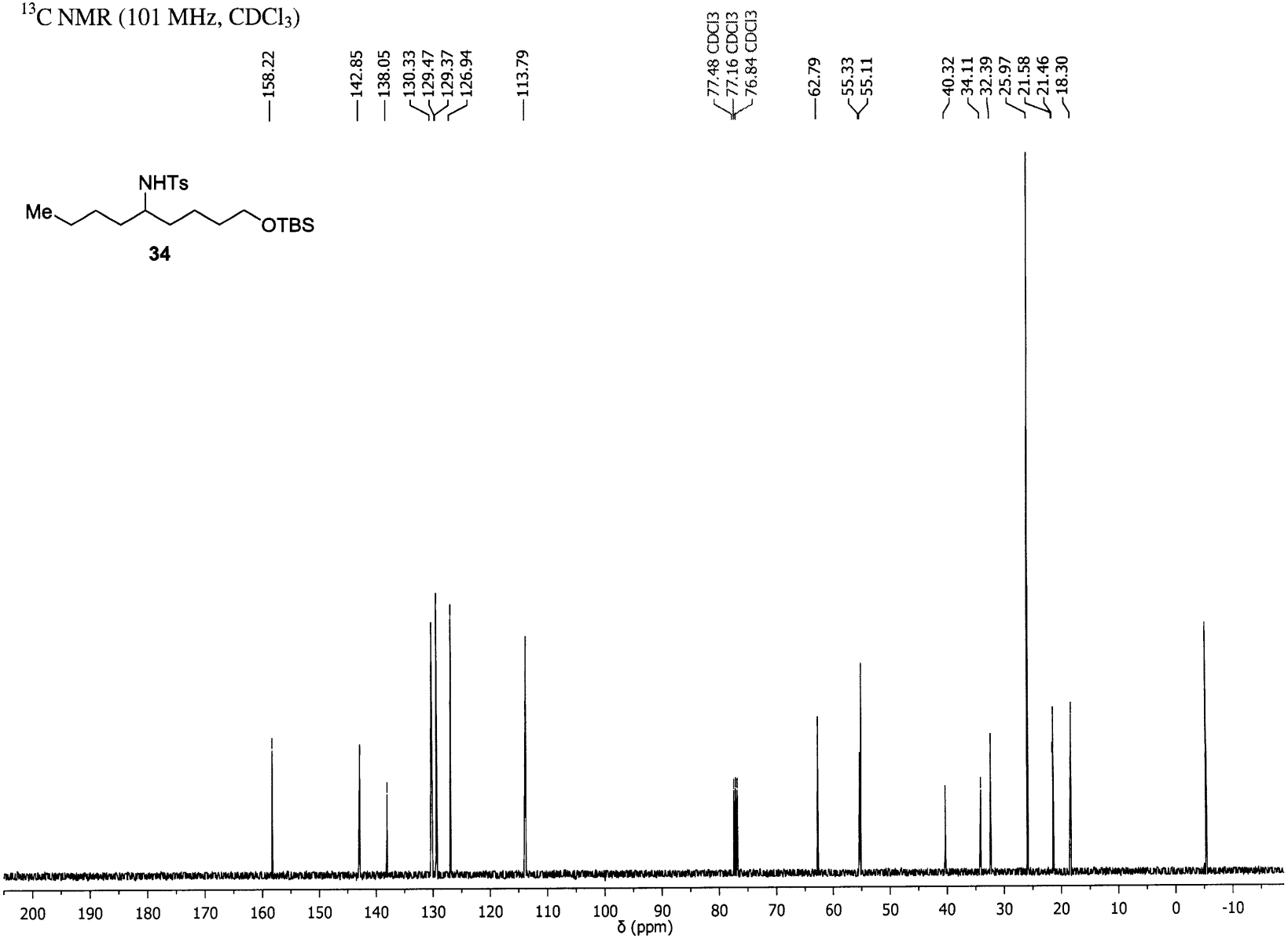
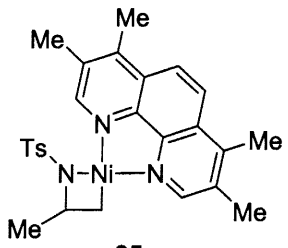


34

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

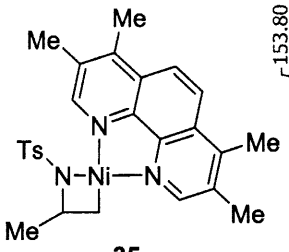


^{1}H NMR (400 MHz, $CDCl_3$)



35

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



35

153.80
150.04
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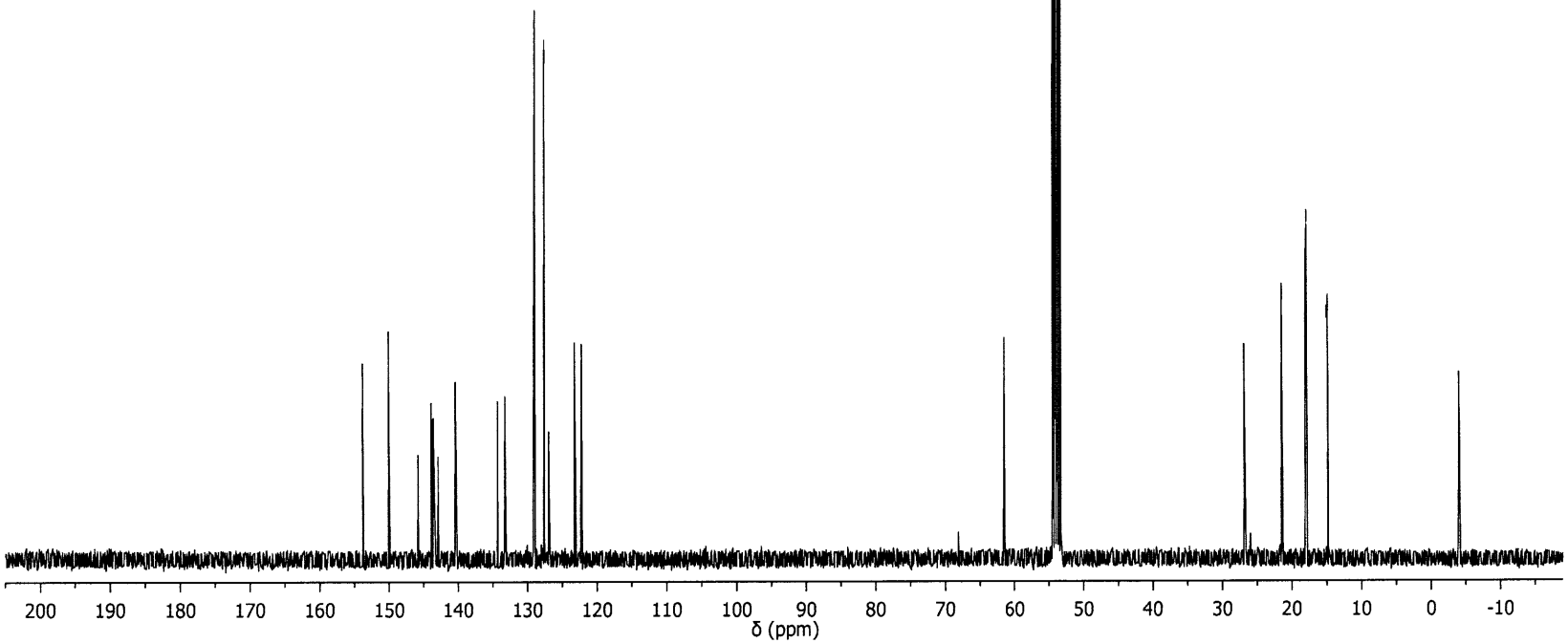
143.92
143.71
143.61
142.92
140.43
134.34
133.28
128.97
127.61
127.59
127.00
123.27
122.25

61.53
54.38 CD_2Cl_2
54.11 CD_2Cl_2
53.84 CD_2Cl_2
53.57 CD_2Cl_2
53.30 CD_2Cl_2

26.87
21.45
18.01
17.84
15.01
14.81

-4.09



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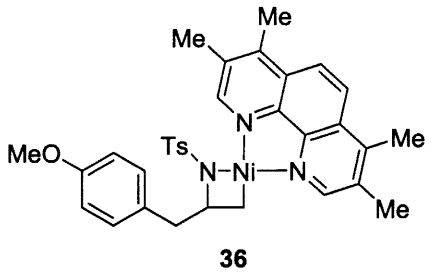

36

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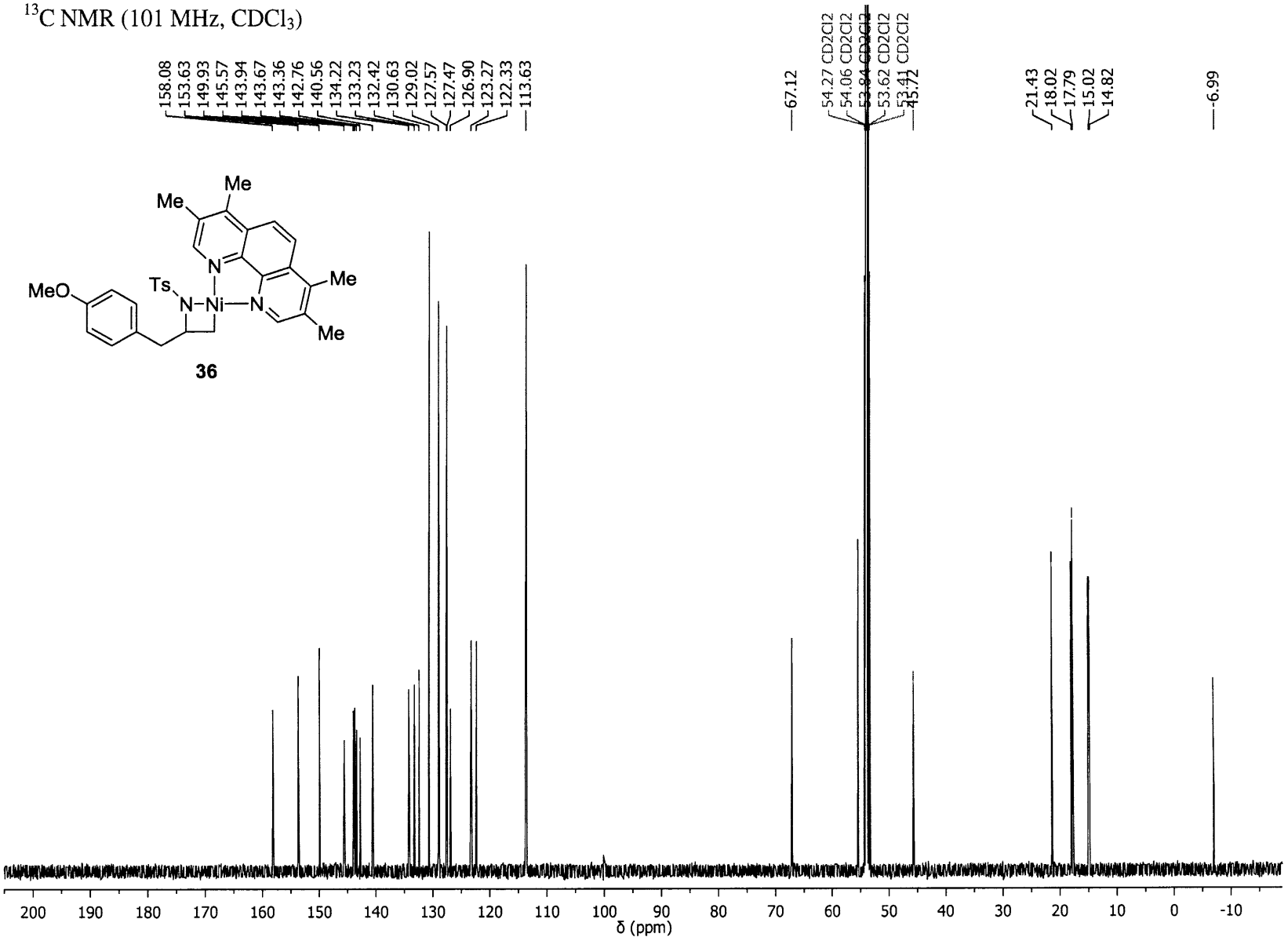
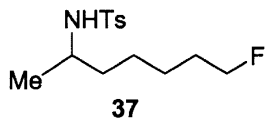


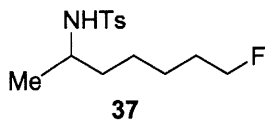
36

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



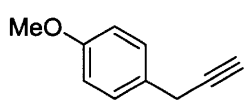
37

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



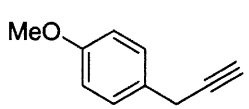
37

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



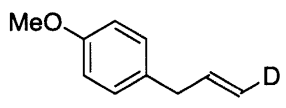
SI6

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



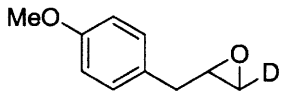
SI6

^{1}H NMR (500 MHz, $CDCl_3$)



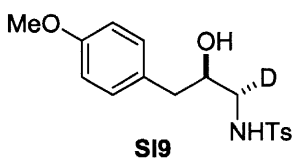
SI7

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



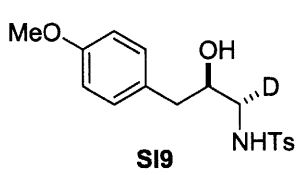
SI8

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



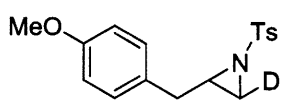
SI9

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



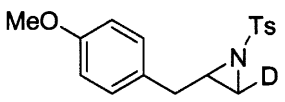
SI9

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



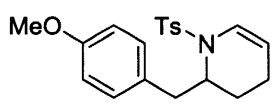
38
96:4 *trans*:*cis*

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



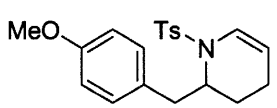
38
96:4 *trans*:*cis*

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



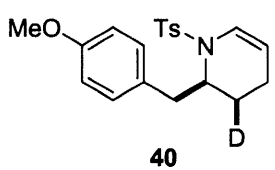
SI10

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



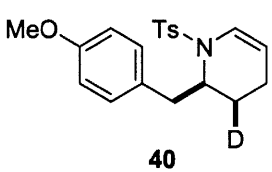
SI10

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



40
95:5 *cis*:*trans*

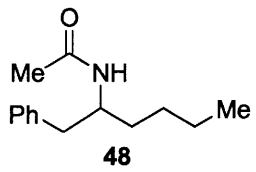
^{13}C NMR (101 MHz, $CDCl_3$)



40

95:5 *cis*:*trans*

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



48

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