Nickel-Catalyzed Suzuki–Miyaura Reactions of Unactivated Halides with Alkyl Boranes
and
Planar-Chiral Borabenzene Catalysts for Diels–Alder Reactions

by

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Submitted to the Department of Chemistry on August 16, 2010
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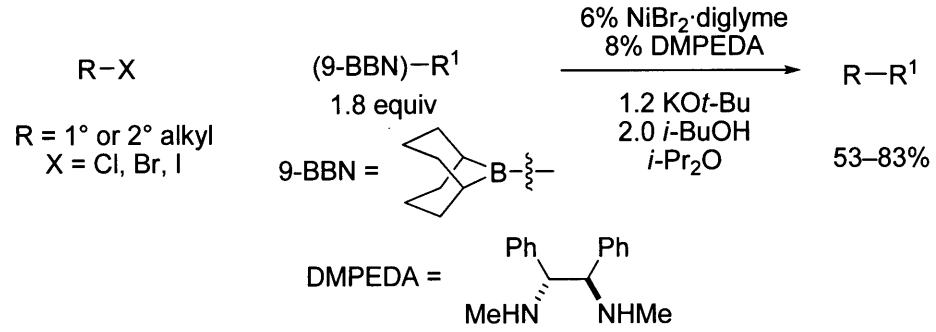
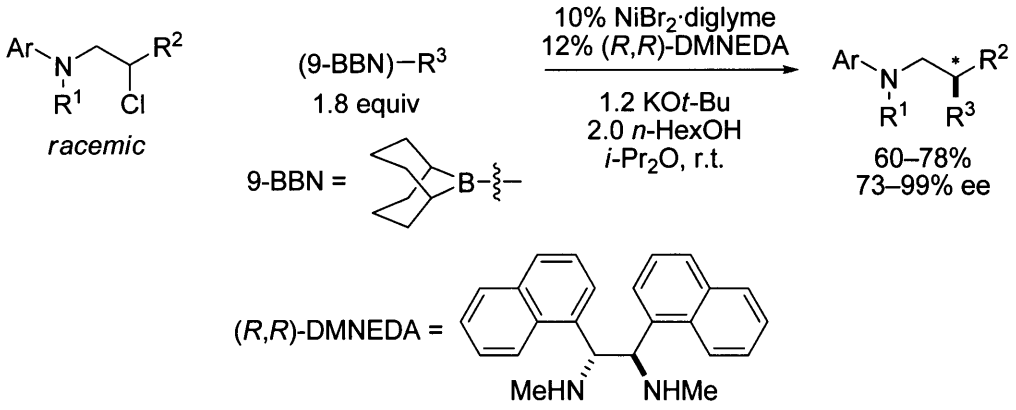
ABSTRACT

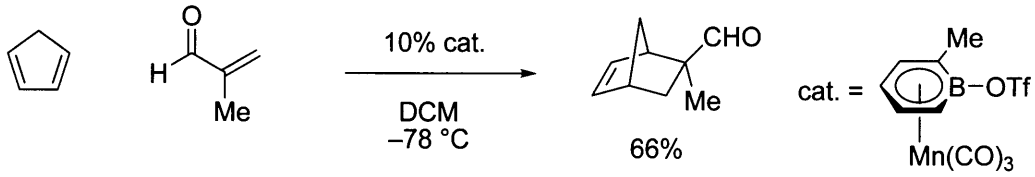
Part I describes the expansion in scope of a nickel-catalyzed coupling reaction of unactivated alkyl bromides and alkyl boranes to include unactivated alkyl chlorides. The new method is adapted for use outside of a glove box and is also found to be applicable not only to the coupling of primary chlorides, but also to the coupling of bromides and iodides, both primary and secondary.



This coupling reaction of chlorides is further adapted to the asymmetric coupling of β-chloro aryl alkyl amines. This work constitutes an extension of scope in terms of directing groups for the asymmetric Suzuki–Miyaura reactions of unactivated alkyl halides.



Part II details work towards an asymmetric Diels–Alder reaction between cyclopentadiene and methacrolein catalyzed by a planar-chiral boron Lewis acid. This system exhibits a level of turnover that is unprecedented in reactions mediated by planar chiral boron heterocycles. Computational studies shed light on the nature of the π-symmetry interaction between borabenzenes and complexed carbonyl groups. The selectivity of the borabenzene-catalyzed Diels–Alder reaction is also examined.



Thesis Supervisor: Gregory C. Fu
Title: Firmenich Professor of Chemistry

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ACKNOWLEDGMENTS

Forsan et haec olim meminisse juvabit

The Æneid. I, 203.

Χαλεπὰ τὰ καλά

The Republic. 4, 435c.

I think these two quotes accurately embody the spirit of the last five years: perhaps, someday it will help to remember these things; the good things are difficult things. And I have learned that difficult challenges are rarely undertaken successfully without help. I would not have made it without the aid and encouragement of the many people who supported and pushed me along the way.

I must thank my advisor and teacher, Prof. Gregory Fu, for the opportunity to work and grow in his lab. I appreciate the independence he has given me to pursue my interests and develop my own ideas. I thank him for being a great role model, for being a rigorous and demanding teacher, and for always expecting my best output.

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I thank Prof. Ken Houk for allowing me to study in his group at UCLA. I learned much about computational chemistry and about how to think about reactivity during my brief time there. My thanks also go to the members of the Houk lab, especially Paul and Claude, for welcoming me and helping me along the way.

The aikido clubs at Harvard and MIT have been there for me for nearly a decade. It is through their wisdom that I have learned to shoulder adversity and withstand conflict. I especially thank the instructors, Stroud-sensei and Hall-sensei. Under them, I have strived to be less of a worrier and more of a warrior.

I would very much like to thank my parents, without whom, I wouldn't have come even half as far. Their support and guidance, from the day I was born, cannot be measured. Their unyielding faith in me is a daily source of inspiration.

Finally, I thank Kara, my best friend, who has shared the ups and downs of life for me for the last two years. It is because of her that I found a life outside the lab. It is because of her that I have been able to pull through when the going was the toughest. This work would not have been possible without her.

TABLE OF CONTENTS

ABBREVIATIONS

9-BBN	9-borabicyclo[3.3.1]nonane
cod	1,5-cyclooctadiene
DCM	dichloromethane
DFT	density functional theory
diglyme	2-methoxyethyl ether
DMA	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylforamide
DMI	1,3-dimethyl-2-imidazolidinone
DMNEDA	*N,N'*-dimethyl-1,2-bis(1-naphthyl)ethylenediamine
DMPEDA	*N,N'*-dimethyl-1,2-diphenylethylenediamine
Eq	equation
equiv	equivalents
GC	gas chromatography
glyme	1,2-dimethoxyethane
HMDS	hexamethyldisilazide
HPLC	high pressure liquid chromatography
LDA	lithium diisopropylamide
RMSD	root mean square displacement
r.t.	room temperature
SFC	supercritical fluid chromatography
TBAF	tetrabutylammonium fluoride
TBAT	tetrabutylammonium difluorotriphenylsilicate
THF	tetrahydrofuran

Part I

Nickel-Catalyzed Suzuki–Miyaura Couplings of
Unactivated Halides with Alkyl Boranes

Chapter 1

Nickel-Catalyzed Suzuki–Miyaura Reactions of
Unactivated Alkyl Chlorides with Alkyl Boranes

A. Introduction

Metal-catalyzed cross-coupling reactions constitute an important set of tools for the synthetic organic chemist in the quest to create structures of ever-increasing diversity and complexity. Perhaps most prominent among the categories of cross-coupling reactions that form carbon–carbon bonds is the Suzuki–Miyaura reaction between an organic electrophile and an organoboron reagent. The Suzuki–Miyaura coupling's remarkable status is a result of various factors, including the ease of synthesis of the organoboron coupling reagents, the low toxicity of coupling partners and reaction by-products, and the high levels of functional group tolerance under the reaction conditions.[1]

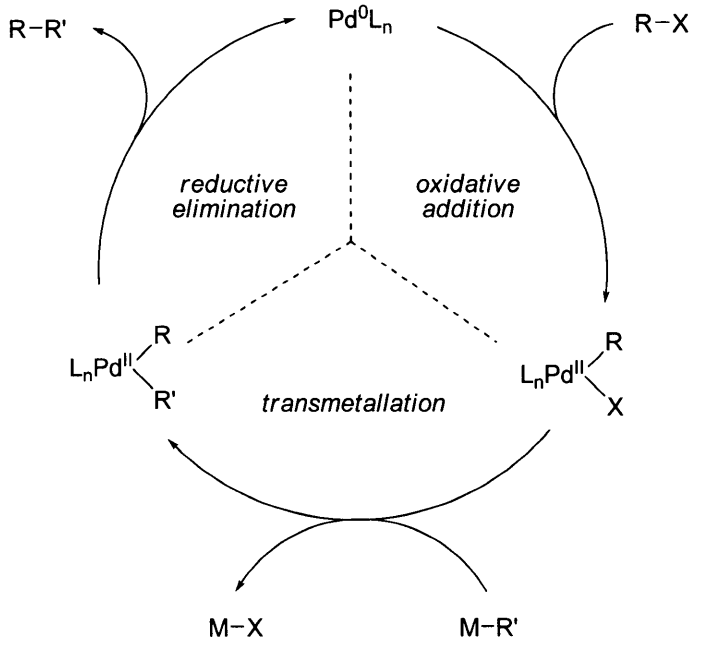
Depicted in Scheme 1 is the traditionally-accepted mechanism for palladium-catalyzed cross-coupling reactions. First, the catalytically active palladium(0) species undergoes oxidative addition of the electrophile to give an organopalladium(II) intermediate. Transmetallation with an appropriate organometallic reagent provides a diorganopalladium(II) compound that furnishes the product upon reductive elimination. The addition of base in the Suzuki–Miyaura reaction is important and its role in activating the organometallic reagent towards transmetallation has been studied.[2]

---

[1] For references on metal-catalyzed Suzuki–Miyaura reactions, see: (a) Miyaura, N. In *Metal-Catalyzed Cross-Coupling Reactions;* de Meijere, A., Diederich, F., Eds., Wiley-VCH: New York, 2004.; Chapter 2 (b) *Handbook of Organopalladium Chemistry for Organic Synthesis;* Negishi, E.-i., Ed.; Wiley Interscience: New York, 2002. (c) *Cross-Coupling Reactions: A Practical Guide;* Miyaura, N., Ed.; Topics in Current Chemistry Series 219; Springer-Verlag: New York, 2002. (d) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11–59.

[2] Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483 and references therein.

Scheme 1. Traditionally-accepted mechanism for palladium-catalyzed cross-coupling.



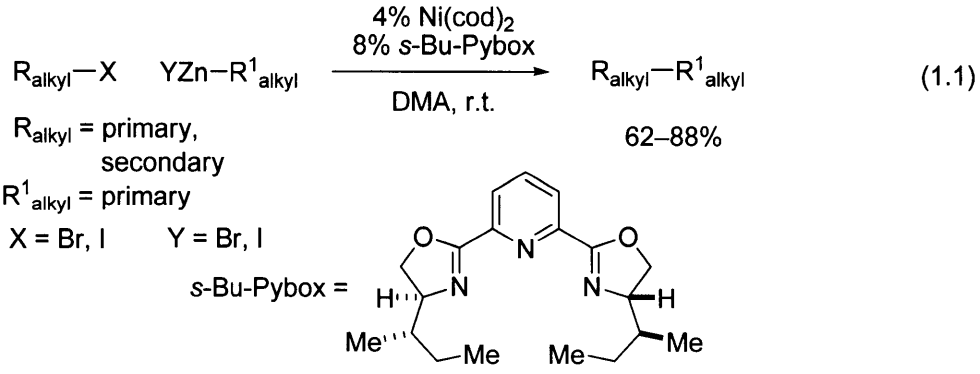
Most coupling methods using palladium are for the coupling of aryl, alkenyl, and activated alkyl (e.g., allylic) electrophiles. Comparatively few methods describe cross-coupling using unactivated alkyl electrophiles for two main reasons. First, alkylpalladium complexes readily undergo β-hydride eliminations in competition with the productive reaction pathway. Second, oxidative addition takes place more slowly with alkyl electrophiles. This decreased reactivity has been attributed to the lack of a proximal π-system that could complex the metal in a productive manner.[3,4]

The cross-coupling of unactivated *primary* alkyl halides and pseudohalides with

[3] Ref. 1b, p. 132.
[4] Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674–688.

palladium has been studied.[5,6] Much of this work centers around the use of palladium in conjunction with bulky, electron-rich trialkylphosphine ligands. The electronic properties of these ligands improve the rate of oxidative addition while their steric properties reduce undesired β-hydride elimination.

However, these methods were dramatically less effective when addressing the challenge of coupling of unactivated *secondary* alkyl electrophiles.[7] Such electrophiles display lower reactivity than their primary counterparts because it is believed that the oxidative addition is quite problematic. In the Fu group, this challenge prompted an examination of other catalyst systems, revealing that nickel-based catalysts suppressed the undesired β-hydride elimination in a manner that is still not well understood. The Fu group has developed methods for the coupling of unactivated halides using organozinc reagents (Eq. 1.1)[8] and *aryl*boron reagents (Eqs. 1.2–1.4).[9]



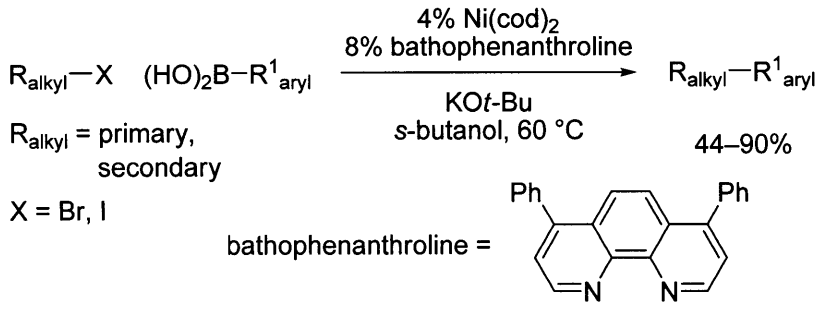
[5] For reviews of cross-couplings of alkyl electrophiles, see: (a) Ref. 4. (b) Netherton, M. R.; Fu, G. C. In *Topics in Organometallic Chemistry: Palladium in Organic Synthesis*; Tsuji, J., Ed.; Springer: New York, 2005. (c) Netherton, M. R.; Fu, G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525–1532.

[6] For specific references to work on the Suzuki–Miyaura reaction, see: (a) Ishiyama, T.; Abe, S.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1992**, 691–694. (b) Netherton, M. R.; Dai, C.; Neuschütz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099–10100. (c) Kirchhoff, J. H.; Dai, C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 1945–1947. d) Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3910–3912. (e) Kirchhoff, J. H.; Netherton, M. R.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662–13663.

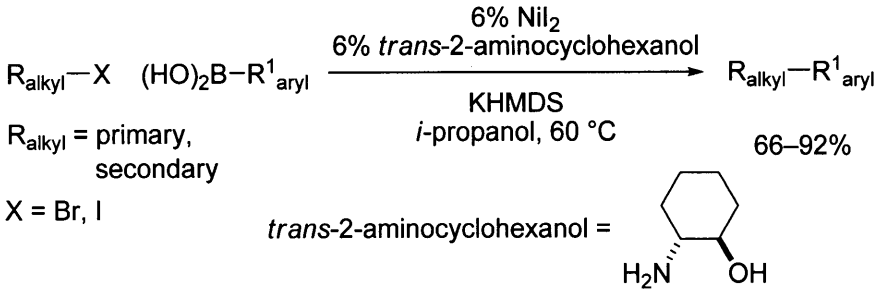
[7] For a review of cross-couplings with *secondary* alkyl halides, see: Rudolph, A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656–2670.

[8] Zhou, J.-R.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 14726–14727.

[9] (a) Zhou, J.-R.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 1340–1341. (b) González-Bobes, F.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 5360–5361.



(1.2)



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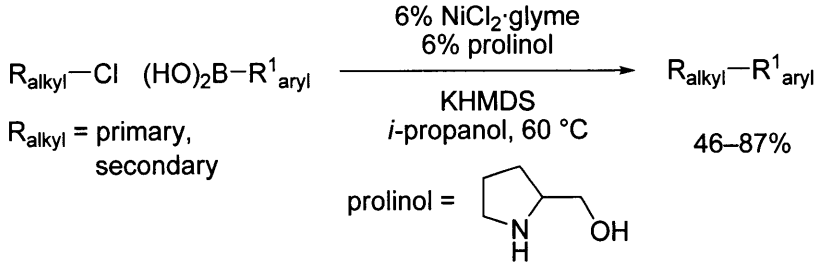
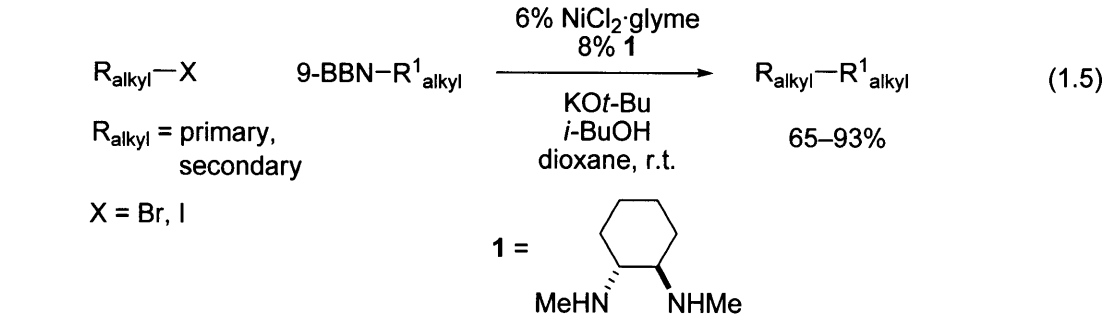
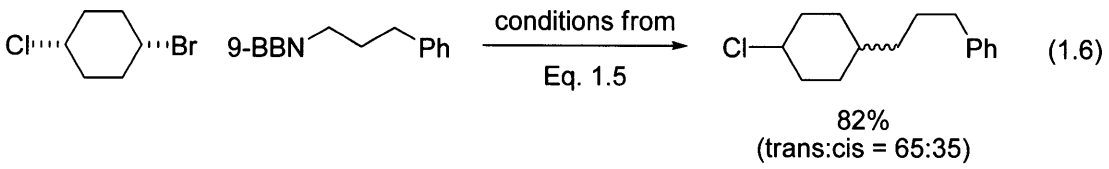


(1.4)

A significant breakthrough was achieved when Saito and Fu discovered that nickel, in combination with an appropriate diamine ligand, could effect the coupling of an unactivated secondary alkyl bromide with an *alkyl* 9-BBN reagent in good yields (Eq. 1.5).[10] In this methodology, alkyl chlorides showed greatly diminished reactivity relative to the corresponding bromide (Eq. 1.6). While the selectivity of bromides over chlorides was potentially very useful, the lack of reactivity with alkyl chlorides presented a challenge that might be addressed to increase the scope and synthetic utility of nickel-based cross-coupling chemistry.

[10] Saito, B.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 9602–9603.

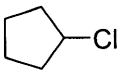
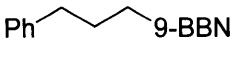
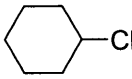
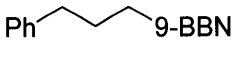

6% NiCl2·glyme
8% 1
KOt-Bu
i-BuOH
dioxane, r.t.
Ralkyl—X
9-BBN–R1alkyl
Ralkyl—R1alkyl
65–93%
Ralkyl = primary, secondary
X = Br, I
1 =
MeHN
NHMe
(1.5)


Cl
Br
9-BBN
Ph
conditions from
Eq. 1.5
Cl
Ph
82%
(trans:cis = 65:35)
(1.6)

B. Results and Discussion

The conditions for the cross-coupling of unactivated secondary alkyl bromides with alkylboron reagents provided a starting point for optimization.[10] While the coupling of cyclopentyl chloride could be achieved in moderate yield, coupling of cyclohexyl chloride provided only small amounts of the desired coupling product, and most of the mass balance was unreacted starting material (Table 1).

Table 1. Suzuki cross-coupling with nickel/diamine system (for reaction conditions, see Eq. 1.5 and Ref. 10).

entry	R_{alkyl}—Br	R^1_{alkyl}—9-BBN	yield (%)[a]
1			61
2			22

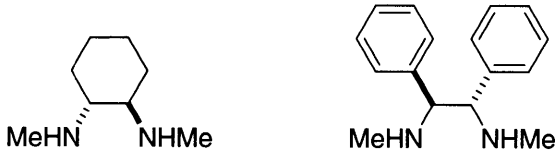
[a] GC yield versus an internal standard

A systematic examination of the reaction parameters showed that nickel(II) halide salts (NiX_2; X = F, Cl, Br, I) were not competent as nickel sources. On the other hand, more soluble nickel(II) halide complexes and $Ni(cod)_2$ were suitable. Of these, nickel(II) bromide 2-methoxyethyl ether complex ($NiBr_2$·diglyme) provided better yields. Optimization of the catalyst and ligand loadings showed that the addition of 6 mol% nickel and 8 mol% ligand provided the best yields.

Ligand optimization revealed that diols, phosphines, and amino alcohols did not afford any conversion under the conditions examined. Bis(oxazoline)-based,[11] 2,6-

[11] For a representative example of the use of a box ligand in nickel-catalyzed cross-couplings, see: Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 5010–5011.

bis(oxazolinyl)pyridine-based,[12] and 2,2′-bipyridine-based[13] ligands, which bear sp^2-hybridized nitrogen atoms and had previously been used as ligands in nickel-catalyzed cross-couplings, did not provide good yields with unactivated secondary alkyl electrophiles. Improvements to the yield of the coupling reaction were finally achieved when an acyclic 1,2-diamine, specifically, (±)-DMPEDA (**2**), was used. Bis(monomethylation) was important as the unsubstituted parent diamine, the bis(benzylated) diamine, and the tetra(methylated) variant provided significantly lower yields.



1 **2**

DMPEDA

Dioxane served as a starting point for an examination of the effects of solvent. Since the boron reagent was prepared as a solution in dioxane, initial optimization used a 1:1 mixture of dioxane and a variable co-solvent. Diisopropyl ether yielded the best results, and the use of co-solvents with diisopropyl ether failed to provide further improvements in yield. Strongly coordinating co-solvents, like *N,N*-dimethylformamide, gave essentially none of the desired product, and most of the starting material was found to be consumed at the end of the reaction. The use of alcohols, alkanes, or aromatic hydrocarbons as solvents resulted in poorer conversions.

Suzuki–Miyaura reactions typically require a stoichiometric amount of base to

[12] For a representative example of the use of a pybox ligand in nickel-catalyzed cross-couplings, see: Lundin, P. M.; Esquivias, J.; Fu, G. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 154–156.

[13] For a representative example of the use of a bipyridine as a ligand in nickel-catalyzed cross-couplings, see: Powell, D. A.; Maki, T.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 510–511.

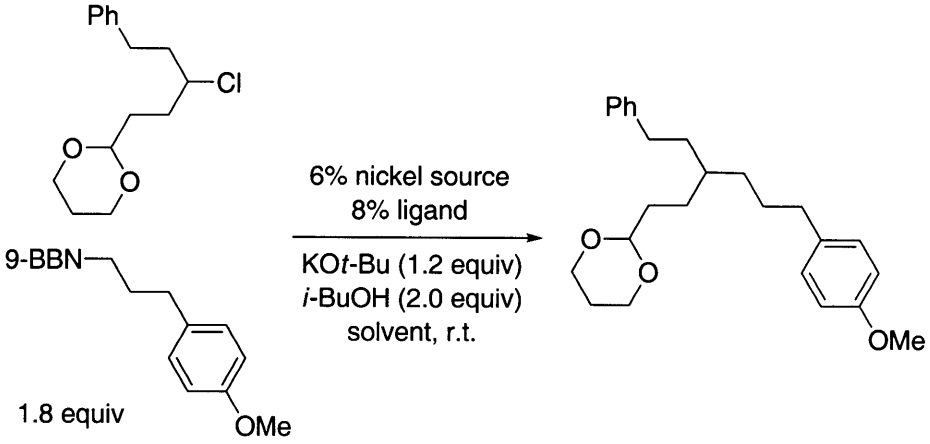
activate the boron reagent to transmetallation in the catalytic cycle,[1a,2] and the present work is no exception. An alkoxide base, generated in situ by the reaction of potassium *tert*-butoxide and isobutanol, is used. Inorganic bases, including fluorides, carbonates, and phosphates, were ineffective at promoting the reaction. Potassium hexamethyldisilazide was suitable as a base but provided inferior yields relative to *tert*-butoxide. Interestingly, when lithium was employed as the counter ion in the base (e.g., LiHMDS or LiO*t*-Bu), the reaction failed to provide any desired product. Potassium *tert*-butoxide alone was also unsuitable as a base. The increased steric bulk may reduce the reactivity of the boronate species to transmetallation. The use of potassium hydride offered results comparable to those obtained with potassium *tert*-butoxide, but in terms of practicality and safety, the use of the *tert*-butoxide as a base was better.

The amount of nucleophile was systematically optimized. It was found that using 1.8 equivalents of nucleophile provided the best yields, and further increases in the amount of nucleophile did not further increase the yield.

The reaction was run at a relatively high concentration (0.5 M in electrophile), and slight dilution (0.25 M) did not seem to affect the yield of the reaction. More dramatic changes in concentration led to poor conversion. The major changes from the starting point of the optimization (Eq. 1.5) are summarized in Table 2.

Since the optimization of solvent for the reaction had been carried out with co-solvent mixtures, a final screen of single-component ethereal solvents was conducted. These results are summarized in Table 3, and the result with dioxane is also listed for comparison. Diethyl ether and methyl *t*-butyl ether as solvents give somewhat lower yields but can be employed as an alternative to diisopropyl ether if desired.

Table 2. Optimization of reaction parameters for an alkyl–alkyl Suzuki cross-coupling reaction of an unactivated secondary alkyl chloride.



entry	nickel source	ligand	solvent	yield (%)[a]
1	$NiCl_2$·glyme	**1**	dioxane	9
2	$NiBr_2$·diglyme	**1**	dioxane	14
3	$NiBr_2$·diglyme	**2**	dioxane	43
4	$NiBr_2$·diglyme	**2**	*i*-Pr_2O	86

[a] Determined by GC versus a calibrated internal standard (average of two experiments).

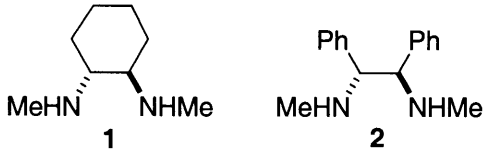
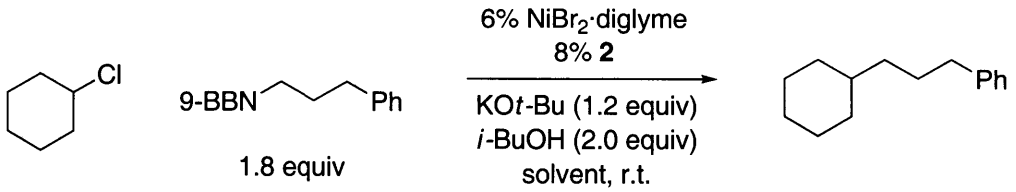


Table 3. Effect of different ethers as solvents on an alkyl–alkyl Suzuki cross-coupling.



ether	yield (%)[a]	starting material (%)[a]
tetrahydrofuran	10	48
1,4-dioxane	44	22
methyl *t*-butyl ether	69	0
diethyl ether	72	0
diisopropyl ether	79	2

[a] Determined by GC versus a calibrated internal standard

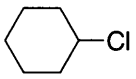
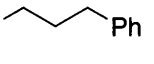
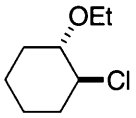
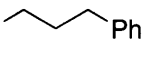
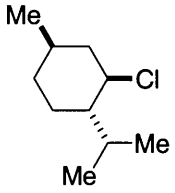
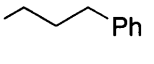
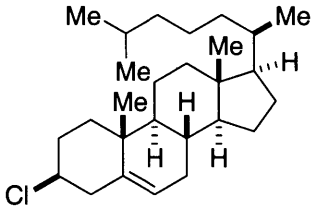
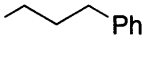
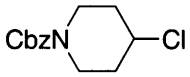
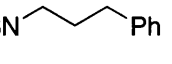
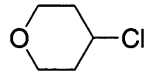
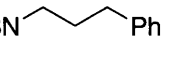
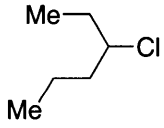
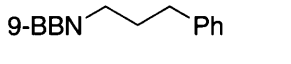
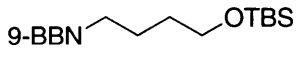
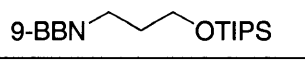
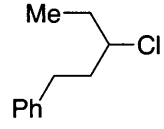
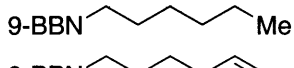
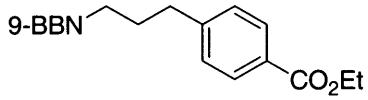
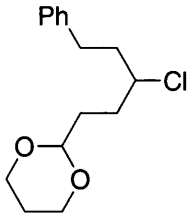
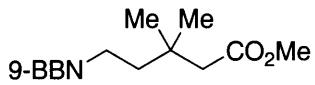
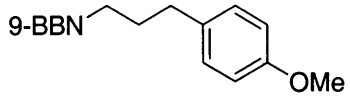
Previous work in alkyl–alkyl Suzuki cross-coupling reactions showed that the reaction was quite sensitive, such that reactions carried out without the aid of a glove box proceeded in lower yield even with longer reaction times. Since both the nickel source and the base can be somewhat hygroscopic,[14] adventitious water was thought to be a possible problem. The addition of powdered 4 Å molecular sieves was found to be helpful in increasing the yield of the desired coupling products, although the reaction time had to be increased from 1 to 2 days. Nevertheless, this represented an important procedural advance by eliminating the necessity of using an inert-atmosphere glove box.

The scope for this reaction is fairly broad (Table 4). The reaction tolerates both cyclic (entries 1–6) and acyclic (entries 7–13) electrophiles, including heterocyclic compounds (entries 5–6). Various functional groups, such as alkenes (entry 4), acetals (entries 12–13), alkyl (entries 2, 6, and 13) and silyl ethers (entries 8–9), and esters (entries 11–12), are tolerated. On an increased 6.5-mmol scale, one gram of coupling product could be obtained using the optimized conditions with any loss in reactivity (Table 4, entry 1).

Additionally, it was found that the conditions optimized for the coupling of secondary chlorides could be applied without modification to the coupling of secondary bromides and iodides (Table 5, entries 1–8). Primary chlorides, bromides, and iodides also served as suitable electrophiles in this reaction (entries 9–11).

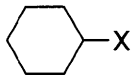
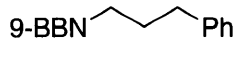
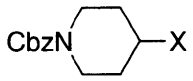
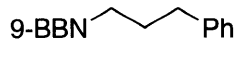
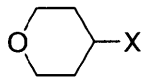
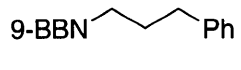
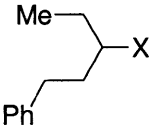
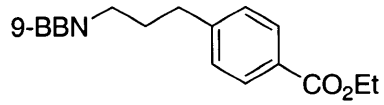
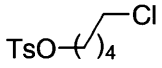
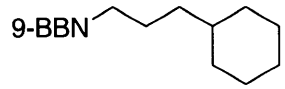
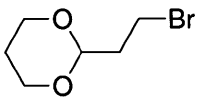
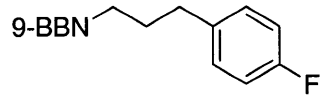
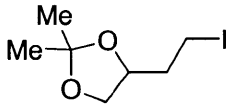
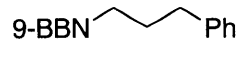
[14] The hydroscopic nature of the nickel bromide 2-methoxyethyl ether complex was examined. At a relative humidity of 60%, after 5 minutes, some discoloration of the bright orange salt to a green color, presumably from the formation of a hydrate, was observed. After 120 minutes, not only had the entire sample (about 50 mg) turned green, but the sample had also collected a noticeable amount of moisture.

Table 4. Alkyl–alkyl cross-coupling of unactivated secondary alkyl chlorides. (For conditions, see Table 2, entry 4.)

entry	R–Cl	9-BBN–R[1] [a]	yield (%)[b]
1			80
2			69[c]
3			53[c]
4			67[d]
5			70
6			71
7			72
8			64
9			64
10			74
11			72
12			81
13			83

[a] 1.8 equiv of nucleophile is used. [b] Isolated yield (average of two experiments).
[c] Diastereoselectivity: >20:1 trans:cis (relative to the proximal substituent).
[d] Diastereoselectivity: 2:1 β:α.

Table 5. Alkyl–alkyl cross-coupling of unactivated alkyl halides. (For conditions, see Table 2, entry 4.)

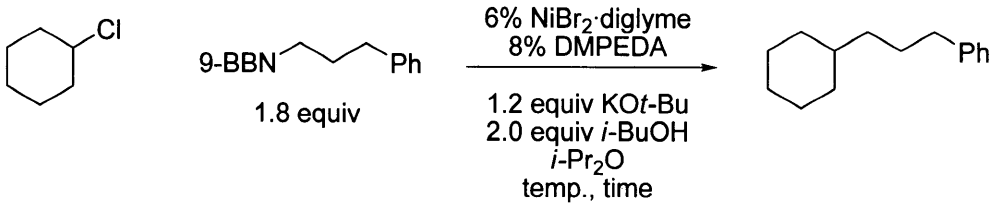
entry	R–X	9-BBN–R^1 [a]	yield (%)[b]
1 2			X = Br: 75 X = I: 75
3 4			X = Br: 65 X = I: 64
5 6			X = Br: 74 X = I: 76
7 8			X = Br: 75 X = I: 76
9			63
10			70
11			78

[a] 1.8 equivalents of nucleophile used.

[b] Isolated yield (average of two experiments).

Optimization studies indicated that conventional heating or cooling negatively impacted the overall efficiency of the reaction. In this light, microwave conditions were explored in an attempt to lower reaction times. The results are summarized in Table 6. After 3.5 hours in a microwave reactor at 60 °C, full conversion could be achieved, and the desired coupling product was isolated in 74% yield (Table 6, entry 4).

Table 6. Effect of using microwave reactor on reaction times and yields.



temperature (° C)	time (h)	yield (%)
r.t.	48	80[a]
40 (μwave heating)	12	8[b]
60 (μwave heating)	2.5	57[b]
60 (μwave heating)	3.5	74[a]
80 (μwave heating)	1.3	35[b]

[a] 1.0 mmol scale. Average of two experiments. [b] 0.2 mmol scale.

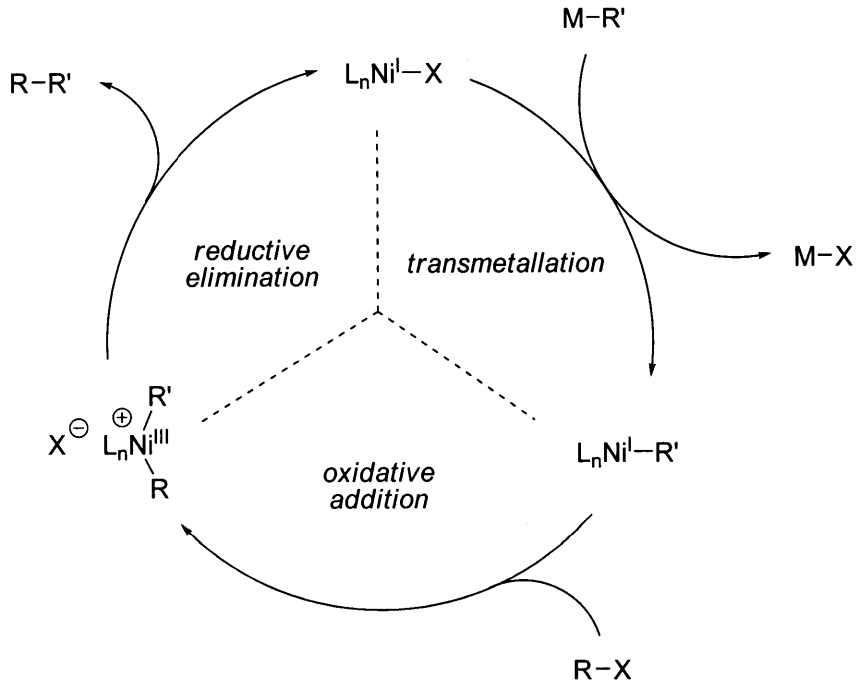
Limitations do exist in the scope of this reaction. Tertiary halides do not provide any coupling product, and no starting material is observed at the end of the reaction. With benzylic chlorides, none of the desired product was formed. While some steric bulk adjacent to the coupling center is tolerated (Table 4, entry 3), lower yields were observed. In acyclic systems, vicinal substitution led to low conversions. Together, these results hint at an upper bound for the steric accessibility of the catalytic nickel center.

Vicic and co-workers have studied the related coupling of an alkyl electrophile with an alkyl*zinc* reagent.[15] Based on work using stoichiometric amounts of plausible intermediates, the authors suggest that the catalytically active nickel species is engaged in a Ni(I)/Ni(III) couple and that the transmetallation of the organometallic reagent occurs before oxidative addition of the nucleophile (Scheme 2), in contrast to the traditionally

[15] Jones, G. D.; Martin, J. L.; MacFarland, C.; Allen, O. R.; Hall, R. E.; Haley, A. D.; Brandon, R. J.; Konovalova, T.; Desrochers, P. J.; Pulay, P.; Vicic, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 13175–13183. For an earlier mechanistic proposal for nickel-catalyzed alkyl–alkyl Negishi reactions, see: Anderson, T. J.; Jones, G. D.; Vicic, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 8100–8101.

accepted mechanism for palladium-catalyzed cross-coupling reactions (Scheme 1). In addition, the oxidative addition is proposed to take place first via a single electron transfer that cleaves the carbon–halide bond, followed by a bond formation between the carbon-centered radical and the nickel. Phillips and co-workers have studied this mechanism computationally.[16] While the authors could not locate a transition state for the transmetallation process, they located transition states for both the oxidative addition and reductive elimination steps, with reasonably valued activation energies in the gas phase.

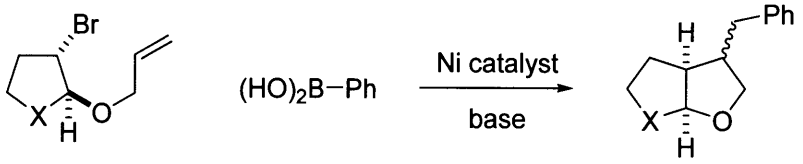
Scheme 2. Vicic's proposed catalytic cycle for nickel-catalyzed alkyl-alkyl cross-coupling reactions.



Several observations in the Fu lab are also consistent with the proposed mechanism. First, sulfonates, which are frequently competent electrophiles in palladium

[16] Lin, X.; Phillips, D. L. *J. Org. Chem.* **2008**, *73*, 3680–3688.

cross-coupling chemistry, are unreactive under the conditions for nickel-catalyzed cross-coupling reported in the Fu lab.[17] This is in line with the fact that, compared to tosylates, alkyl halides have lower reduction potentials.[18] In addition, in an example where the substrate bears a pendant olefin, cyclization can take place during the cross-coupling reaction, and the observed endo:exo selectivity is almost identical to that observed with a simple tributyltin hydride mediated free-radical process (Eq. 1.7).[19] This result supports the idea that both reactions proceed through a common radical intermediate.



(1.7)

X = CH_2
X = O

X = CH_2: (2:1 endo:exo)
X = O: (>20:1 endo:exo)

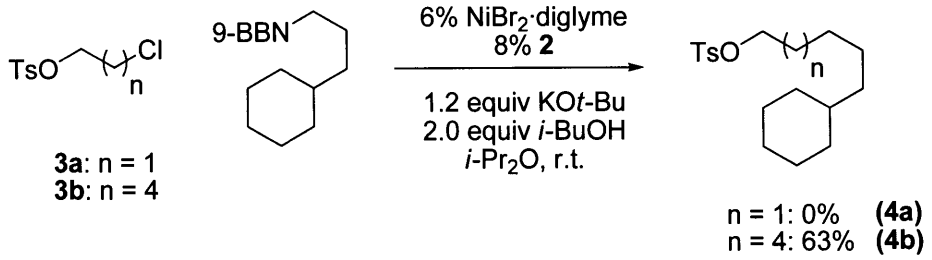
Several pieces of data in the present work also support the Vicic proposal. For example, an electron-withdrawing group proximal to—but not conjugated with—the alkyl radical intermediate would be expected to destabilize the radical. As seen in Eq. 1.8, the placement of a tosylate vicinal to a primary chloride (**3a**) prevents formation of any product. On the other hand, when the tosylate is more spatially removed (**3b**) such that the inductive effect might be reasonably small, the reaction proceeds without complications. This contrast is probably not steric in nature since reasonably hindered substrates (Table 4, entries 2–3) still couple to give some product, albeit in reduced yield. The selective coupling of a chloride over a tosylate in Eq. 1.8 also reinforces the fact that

[17] For an example of a nickel-catalyzed Kumada reaction using a tosylate electrophile, see: Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222–4223. This chemistry uses diene ligands, allowing the chemistry to proceed, presumably, through a different catalytic pathway.

[18] Lipshutz, B. H.; Wilhelm, R. S.; Nugent, S. T.; Little, R. D.; Baizen, M. M. *J. Org. Chem.* **1983**, *48*, 3306–3308.

[19] González-Bobes, F.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *128*, 5360–5361 and references therein.

tosylates are poor electrophiles in this reaction, due to the radical nature of the oxidative addition.



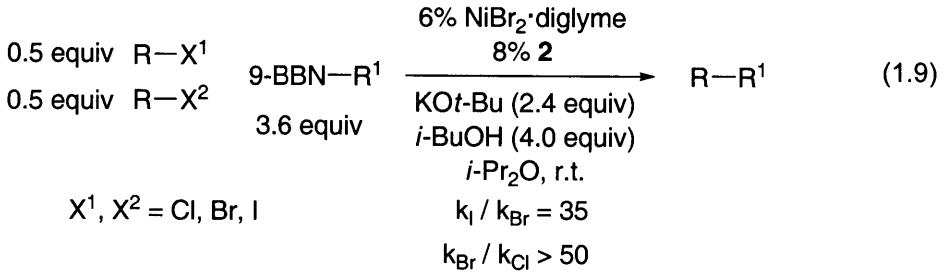
3a: n = 1
3b: n = 4

n = 1: 0% **(4a)**
n = 4: 63% **(4b)**

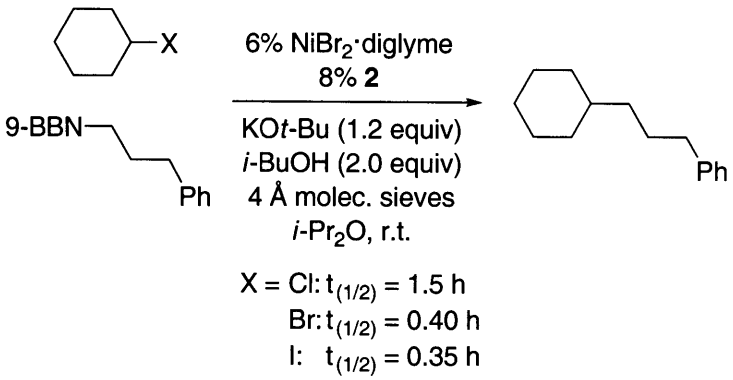
(1.8)

The mechanistic proposal by Vicic does not fully address the nature of the turnover-limiting step. According to Phillips' gas-phase calculations, the recombination of the alkyl radical with nickel could likely present the highest barrier. The transition state for the transmetallation step could not be found, but it is assumed that the barrier for this step is not the highest.

Rate data for reactions with chloride, bromide, and iodide electrophiles in competition experiments suggests that iodides react in preference to bromides, which react in preference to chlorides. However, separately, the bromides and iodides react with comparable rates, while the chlorides react more slowly. The experimental set up is shown in Eqs. 1.9 and 1.10. This suggests, in contradiction to the data presented by Phillips, that oxidative addition is not the turnover-determining step. That the oxidative addition is not the turnover-determining step is also supported by the rate law for the reaction of bromides, where it was found that the reaction was first-order in both catalyst and nucleophile, but zeroth-order with respect to the electrophile.



(1.9)



(1.10)

In the case of chlorides, the kinetic data are not as well-behaved and more difficult to interpret. Nevertheless, examination of the data reveals that the order of the reaction in electrophile is probably not zero order. Therefore, with chlorides, the oxidative addition may be, at least partially, turnover limiting.

C. Conclusions

This chapter has detailed the development of a catalytic system, based on the combination of a nickel salt and a diamine ligand, that is effective for the coupling of unactivated secondary alkyl chlorides with primary alkylboron reagents. In the context of previous work, this new system helps to expand the substrate scope for alkyl–alkyl Suzuki–Miyaura reactions from alkyl bromides and iodides to include alkyl chlorides, both primary and secondary. The procedure is robust enough for use outside of a glove box and has been shown to be effective on a gram-scale. Kinetic studies indicate that oxidative addition for alkyl bromides and iodides under these conditions is not turnover-limiting, although the oxidative addition step with alkyl chlorides may be at least partially turnover-limiting.

D. Experimental

I. General

The following reagents were purchased and used as received: 9-BBN dimer (Aldrich), $NiBr_2$·diglyme (Aldrich; somewhat hygroscopic), KO*t*-Bu (Acros), *i*-BuOH (anhydrous, Aldrich), and *i*-Pr_2O (anhydrous, Aldrich). Molecular sieves (4 Å, powdered, <5 μm; Aldrich) were flame-dried. Ligand **2** (DMPEDA) was synthesized according to a procedure by Alper[20] and purified by flash chromatography (it is also available from Acros).

II. Preparation of Materials

Synthesis of starting materials. These procedures have not been optimized.

Synthesis of chlorides.

Representative procedure A: In a 500-mL round-bottom flask, equipped with stir bar and reflux condenser, a secondary alcohol (68 mmol, prepared according to a typical literature procedure[21]) was dissolved in dichloromethane (150 mL) and successively treated with tosyl chloride (14 g, 71 mmol), 4-dimethylaminopyridine (0.82 g, 6.8 mmol), and triethylamine (14 mL). This mixture was stirred at reflux overnight. After cooling to room temperature, the reaction mixture was washed with 1 N aqueous hydrochloric acid (2 × 100 mL), saturated sodium bicarbonate solution (100 mL), and brine (100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo.

The crude tosylate was dissolved in toluene (50 mL) in a 100-mL round-bottom flask. To this solution were added tetrabutylammonium chloride (33 g, 120 mmol) and potassium carbonate (25 g, 180 mmol). The mixture was stirred overnight at 50 °C under

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[20] Kuznetsov, V. F.; Jefferson, G. R.; Yap, G. P. A.; Alper, H. *Organometallics* **2002**, *21*, 4241–4248.
[21] Masutani, K.; Minowa, T.; Hagiwara, Y.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1106.

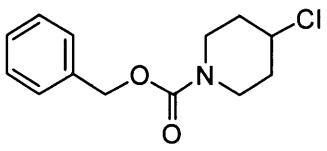
nitrogen. The reaction was quenched with ice water (100 mL) and extracted with 25% ethyl acetate/hexanes (100 mL, 50 mL). The combined organic extracts were washed with water (2 × 100 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo.

Representative procedure B: In a 300-mL round-bottom flask, triphenylphosphine dichloride (5.0 g, 15 mmol) and imidazole (1.1 g, 15 mmol) were dissolved in dichloromethane (100 mL) at 0 °C. After stirring for 5 minutes, the secondary alcohol (14 mmol) was added drop-wise at 0 °C. The reaction was allowed to warm to room temperature while stirring, and stirring was continued for an additional 2 hours at room temperature. The solvents were then removed in vacuo, and pentane (100 mL) was added. The solid cake was broken up with a spatula, and the resulting suspension in pentane was stirred vigorously for 30 minutes and then filtered. The filtrate was concentrated in vacuo to give the crude product.

Synthesis of bromides. In a 300-mL round-bottom flask, triphenylphosphine dibromide (6.5 g, 15 mmol) and imidazole (1.1 g, 15 mmol) were dissolved in dichloromethane (100 mL) at 0 °C. After stirring for 5 minutes, the secondary alcohol (14 mmol) was added drop-wise at 0 °C. The reaction was allowed to warm to room temperature, and stirring was continued for an additional 2 hours at room temperature. The solvents were then removed in vacuo, and pentane (100 mL) was added. The mixture was stirred vigorously for 30 minutes and then filtered. The filtrate was concentrated in vacuo to give the crude product.

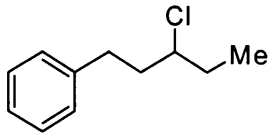
Synthesis of iodides. In a 300-mL round-bottom flask, triphenylphosphine (9.8 g, 38 mmol) and imidazole (2.6 g, 38 mmol) were dissolved in dichloromethane (100 mL) and

cooled to 0 °C. Iodine (9.6 g, 38 mmol) was added portion-wise at 0 °C over 2 minutes. After the addition, the mixture was stirred for 15 minutes, and 3-hexanol (3.0 g, 25 mmol) was added drop-wise at 0 °C. The reaction was allowed to warm to room temperature while stirring, and stirring was continued for an additional 2 hours at room temperature. The solvents were then removed in vacuo, and pentane (100 mL) was added. The mixture was stirred vigorously for 30 minutes and then filtered. The filtrate was concentrated in vacuo to give the crude product.



Benzyl 4-chloro-1-piperidinecarboxylate [885274-98-6]. Prepared by procedure A from benzyl 4-hydroxy-1-piperidinecarboxylate (2.35 g, 10.0 mmol). The crude material was purified by silica gel chromatography (gradient 5% ethyl acetate/hexanes to 20% ethyl acetate/hexanes). Pale-yellow oil. 1.27 g (50% over 2 steps). R_f = 0.25 (25% ethyl acetate/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.25 (m, 5H), 5.13 (s, 2H), 4.23 (septet, 1H, J = 3.7 Hz), 3.76 (ddd, 2H, J = 13.4, 7.5, 3.6 Hz), 3.43 (ddd, 2H, J = 13.5, 7.4, 3.7 Hz), 2.03 (br s, 2H), 1.83 (br s, 2H).



(3-Chloropentyl)benzene [4830-96-0]. Prepared by procedure A from 1-phenyl-3-pentanol (11.0g, 67.5 mmol). The crude material was vacuum distilled through a Vigreux

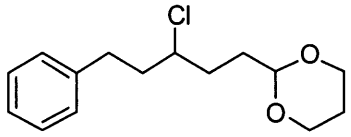
column (bp 46 °C, 250 mtorr). Colorless oil. 3.95 g (32% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.25 (m, 2H), 7.23–7.18 (m, 3H), 3.81 (m, 1H), 2.95–2.85 (m, 1H), 2.80–2.69 (m, 1H), 2.10–1.95 (m, 2H), 1.90–1.65 (m, 2H), 1.03 (t, 3H, J = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 128.7, 128.6, 126.2, 64.9, 39.9, 32.9, 31.7, 11.0.

FT-IR (neat) 2944, 1496, 1454, 747, 699 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{11}H_{15}Cl$: 182.1, found: 182.2 (M^+).



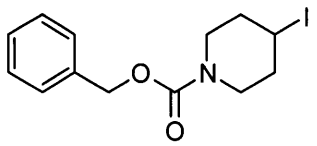
2-(3-Chloro-5-phenylpentyl)-1,3-dioxane. Prepared by procedure A from 1-(1,3-dioxan-2-yl)-5-phenylpentan-3-ol (3.00 g, 12.0 mmol). The crude material was purified by silica gel chromatography (10% ethyl acetate/hexanes). Colorless oil. 1.65 g (42% over 2 steps). R_f = 0.2 (10% ethyl acetate/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.25 (m, 2H), 7.25–7.15 (m, 3H), 4.53 (m, 1H), 4.07 (m, 2H), 3.87 (m, 1H), 3.73 (tt, 2H, J = 2.3 Hz, 12.1 Hz), 2.91–2.80 (m, 1H), 2.80–2.69 (m, 1H), 2.11–1.98 (m, 3H), 1.95–1.78 (m, 3H), 1.70 (m, 1H), 1.32 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 128.7, 128.6, 126.2, 101.7, 67.0, 62.9, 40.2, 32.8, 32.8, 32.2, 25.9.

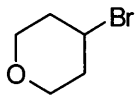
FT-IR (neat) 2961, 2853, 1496, 1454, 1377, 1147, 886, 700 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{15}H_{21}ClO_2$: 268.1, found: 267.1 ($M^+ - H$).



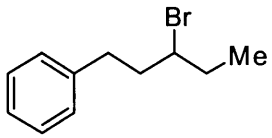
Benzyl 4-iodo-1-piperidinecarboxylate [885275-00-3]. The crude material, prepared from benzyl 4-hydroxy-1-piperidinecarboxylate (5.88 g, 25.0 mmol), was purified by column chromatography (gradient 5% ethyl acetate/hexanes to 15% ethyl acetate/hexanes). Pale-yellow oil. 4.75 g (55%). R_f = 0.25 (25% ethyl acetate/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.28 (m, 5H), 5.13 (s, 2H), 4.46 (p, 1H, J = 6.2 Hz), 3.70–3.60 (m, 2H), 3.45–3.37 (m, 2H), 2.03 (br s, 4H).



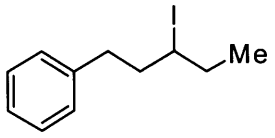
4-Bromotetrahydropyran [25637-16-5]. The crude material, prepared from tetrahydropyran-4-ol, was purified by column chromatography (gradient 5% ethyl acetate/hexanes to 10% ethyl acetate/hexanes). Colorless oil. R_f = 0.3 (10% ethyl acetate/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (m, 1H), 4.00–3.90 (m, 2H), 3.60–3.48 (m, 2H), 2.23–2.12 (m, 2H), 2.10–1.97 (m, 2H).



(3-Bromopentyl)benzene [65266-94-6]. The crude material, prepared from 1-phenyl-3-pentanol (2.30 g, 14.0 mmol), was purified by column chromatography (hexanes). TLC R_f = 0.3 (hexanes). Colorless oil. 1.69 g (63 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.15 (m, 5H), 3.94 (m, 1H), 2.95–2.85 (m, 1H), 2.80–2.70 (m, 1H), 2.20–2.05 (m, 2H), 1.92–1.83 (m, 2H), 1.04 (t, 3H, 7.3 Hz).



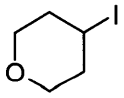
(3-Iodopentyl)benzene [65266-94-6]. The crude material, prepared from 1-phenyl-3-pentanol (4.10 g, 25.0 mmol), was purified by column chromatography (hexanes). Colorless oil. 3.63 g (53%). TLC R_f = 0.3 (hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.15 (m, 5H), 4.03 (septet, 1H, J = 4.4 Hz), 2.95–2.85 (m, 1H), 2.80–2.65 (m, 1H), 2.25–2.12 (m, 1H), 2.03–1.74 (m, 3H), 1.03 (t, 3H, 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 128.7, 128.6, 126.2, 42.0, 41.6, 35.8, 34.0, 14.2.

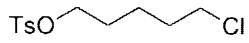
FT-IR (neat) 2965, 1603, 1496, 1453, 746, 698 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{11}H_{15}I$: 274.0, found: 147.0 (M^+ – I).



4-Iodotetrahydropyran [25637-18-7]. The crude material, prepared from tetrahydropyran-4-ol (1.07 g, 10.5 mmol), was purified by column chromatography (gradient 5% ethyl acetate/hexanes to 10% ethyl acetate/hexanes). Colorless oil. 1.89 g (85%). R_f = 0.3 (10% ethyl acetate/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (p, 1H, J = 4.4 Hz), 3.87–3.77 (m, 2H), 3.58–3.48 (m, 2H), 2.20–2.10 (m, 4H).



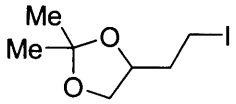
5-chloropentyl *p*-toluenesulfonate [92948-25-9]. Prepared by tosylation (procedure A, step 1) from 5-chloropentan-1-ol (2.45 g, 20.0 mmol). The crude material was purified by column chromatography (50% Et_2O/hexanes). Colorless oil. 4.82 g (87%). TLC $R_f = 0.3$.

^1H NMR (400 MHz, $CDCl_3$) δ 7.82–7.76 (m, 2H), 7.37–7.33 (m, 2H), 4.03 (t, 2H, $J = 6.3$ Hz), 3.48 (t, 2H, $J = 6.6$ Hz), 2.46 (s, 3H), 1.76–1.63 (m, 4H), 1.51–1.41 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 133.2, 130.0, 128.0, 70.3, 44.7, 32.0, 28.3, 23.0, 21.8.

FT-IR (neat) 2957, 2870, 1598, 1457, 1359, 1189, 1177, 1098, 947, 816, 664 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{12}H_{17}ClO_3S$: 276.1, found: 276.0 (M^+).



4-(2-iodoethyl)-2,2-dimethyl-1,3-dioxolane. [98095-37-5]. Prepared from 4-(2-hydroxyethyl)-2,2-dimethyl-1,3-dioxolane (2.39 g, 16.4 mmol). The crude material was purified by column chromatography (5% Et_2O/hexanes). Colorless oil. 2.60 g (61%). TLC $R_f = 0.1$.

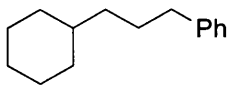
^1H NMR (400 MHz, $CDCl_3$) δ 4.22–4.14 (m, 1H), 4.09 (dd, 1H, $J = 6.1$, 8.0 Hz), 3.58 (dd, 1H, $J = 6.5$, 8.0 Hz), 3.31–3.19 (m, 2H), 2.16–1.98 (m, 2H), 1.41 (s, 3H), 1.35 (s, 3H).

III. Suzuki Cross-Coupling Reactions

General procedure for the preparation of the boron reagent. 9-BBN dimer (220 mg,

0.90 mmol) was added to a flask (with side arm and stir bar), which was then sealed with a septum and successively evacuated and back-filled with argon three times. *i*-Pr_2O (0.75 mL) and the alkene (1.8 mmol) were added, and the reaction mixture was stirred at 60 °C for 1 h. The mixture was allowed to cool to r.t., and then KO*t*-Bu (150 mg, 1.2 mmol) and *i*-BuOH (180 μL, 2.0 mmol) were added in single portions under a positive pressure of argon. The resulting solution was stirred under argon for 30 min.

General procedure for the Suzuki reaction. $NiBr_2$·diglyme (21 mg, 0.060 mmol) and 4 Å molecular sieves (200 mg) were added to a 5-mL oven-dried round-bottom flask (stir bar), which was then sealed with a septum and successively evacuated and back-filled with argon three times. *i*-Pr_2O (0.8 mL) was added, followed by *N,N'*-dimethyl-(±)-1,2-diphenyl-ethanediamine (18 μL, 0.080 mmol). The mixture was stirred for 30 min, resulting in the formation of a pale-blue slurry. Next, the alkyl halide (1.0 mmol) and then the solution of the boron reagent (1.5 M; 1.8 mmol) were added by syringe. The reaction mixture was stirred vigorously at room temperature for 2 days. Then, it was passed through a short plug of silica gel, eluting with 1:1 Et_2O/hexanes. The solvent was removed, and the product was purified by flash chromatography.



(3-Cyclohexylpropyl)benzene (Table 4, entry 1) [170661-44-6]. Cyclohexyl chloride (119 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used.

The product was purified by flash chromatography (cyclohexane). Colorless oil. First run: 160 mg (79%). Second run: 162 mg (80%).

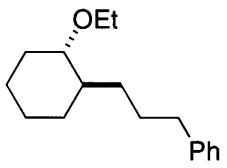
TLC: R_f = 0.7 (cyclohexane; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 2H), 7.21–7.14 (m, 3H), 2.56 (t, 2H, J = 7.8 Hz), 1.75–1.59 (m, 7H), 1.30–1.07 (m, 6H), 0.97–0.80 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 128.4, 128.2, 125.6, 37.6, 37.2, 36.3, 33.4, 28.8, 26.7, 26.4.

FT-IR (neat) 2958, 2930, 2859, 1496, 1454, 745, 697 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{15}H_{22}$: 202.2, found: 202.2 (M^+).



***trans*-(3-(2-Ethoxycyclohexyl)propyl)benzene (Table 4, entry 2).** *trans*-1-Chloro-2-ethoxycyclohexane (163 mg, 1.0 mmol; prepared according to a literature procedure[22]) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (2%→5% EtOAc/hexanes). Clear oil. First run: 166 mg (67%). Second run: 176 mg (71%). The product was assigned the *trans* stereochemistry by examining the coupling constant of the methine at 2.81 ppm.

TLC: R_f = 0.55 (10% EtOAc/hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 2H), 7.20–7.14 (m, 3H), 3.68–3.60 (m, 1H),

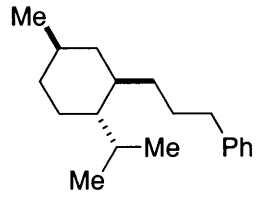
[22] Mendonca, G. F.; Sanseverino, A. M.; De Mattos, M. C. S. *Synthesis* **2003**, 45–48.

3.37–3.29 (m, 1H), 2.81 (ddd, 1H, J = 4.2, 9.6, 9.6 Hz), 2.68–2.51 (m, 2H), 2.07–2.01 (m, 1H), 1.87–1.50 (m, 7H), 1.37–1.07 (m, 5H), 1.17 (t, 3H, J = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 128.5, 128.3, 125.6, 82.2, 64.1, 43.2, 36.6, 32.2, 31.6, 30.6, 28.9, 25.6, 24.9, 15.8.

FT-IR (neat) 2928, 2858, 1496, 1449, 1104, 747, 698 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{17}H_{26}O$: 246.2, found: 246.2 (M^+).



(3-((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)propyl)benzene (Table 4, entry 3). (–)-Menthyl chloride (187 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (cyclohexane). Clear oil. First run: 135 mg (52%). Second run: 140 mg (54%). The product was assigned the stereochemistry where the isopropyl group and the newly formed C–C bond are *trans* by a combination of COSY, HSQC, and HMBC experiments.

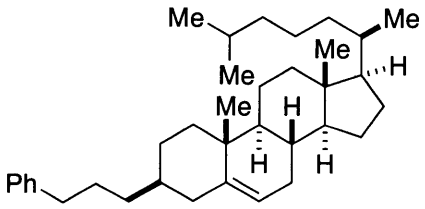
TLC: R_f = 0.7 (cyclohexane; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 2H), 7.21–7.15 (m, 3H), 2.66–2.49 (m, 2H), 2.00–1.90 (m, 1H), 1.75–1.40 (m, 6H), 1.35–1.05 (m, 3H), 1.11–0.72 (m, 9H), 0.70 (d, 3H, J = 6.9 Hz), 0.70–0.59 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 128.5, 128.3, 125.7, 46.7, 41.4, 38.8, 36.7, 35.5, 33.0, 32.6, 28.0, 26.5, 24.5, 23.0, 21.8, 15.4.

FT-IR (neat) 2954, 2928, 2866, 1453, 1368, 745, 698 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{19}H_{30}$: 258.2, found: 258.3 (M^+).



3-(3-Phenylpropyl)cholest-5-ene (Table 4, entry 4). Cholesteryl chloride (405 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (hexanes). Waxy solid. mp 65–70 °C. First run: 326 mg (67%). Second run: 328 mg (67%). The product was isolated as an inseparable 2:1 (α:β) mixture of two diastereomers.[23]

TLC: R_f = 0.5 (hexanes; PMA).

^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 2H), 7.20–7.14 (m, 3H), 5.29–5.25 (m, 1H, major diastereomer), 5.23–5.20 (m, 1H, minor diastereomer), 2.58 (t, 2H, *J* = 8.4 Hz), 2.10–1.85 (m, 45H), 0.67 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (both diastereomers) 143.7, 143.0, 128.50, 128.47, 128.4, 128.3, 125.7, 119.3, 57.0, 56.3, 50.6, 42.4, 40.0, 39.8, 39.6, 39.4, 37.5, 37.4, 37.0, 36.4, 36.3, 35.9, 34.2, 32.0, 29.3, 28.9, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.0, 19.6, 18.8, 12.0.

FT-IR (neat) 2933, 2867, 1461, 1376, 746, 648 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{36}H_{56}$: 488.4, found: 488.5 (M^+).

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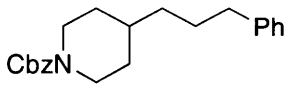
[23] The stereochemistry was assigned by analogy to: Okamura, W. H.; Mitra, M. N.; Pirio, M. R.; Mourino, A.; Carey, S. C.; Norman, A. W. *J. Org. Chem.* **1978**, *43*, 574–580.



Benzyl 4-(3-phenylpropyl)piperidine-1-carboxylate (Table 4, entry 5). Benzyl 4-chloropiperidine-1-carboxylate (254 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (5%→15% EtOAc/hexanes). White solid. mp 150 °C (dec). First run: 240 mg (71%). Second run: 229 mg (68%).

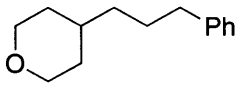
TLC: R_f = 0.15 (10% EtOAc/hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.20 (m, 7H), 7.20–7.10 (m, 3H), 5.11 (s, 2H), 4.15 (br s, 2H), 2.74 (br s, 2H), 2.59 (t, 2H, 7.6 Hz), 1.80–1.55 (m, 4H), 1.50–1.34 (m, 1H), 1.32–1.24 (m, 2H), 1.16–1.04 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 142.6, 137.1, 128.6, 128.45, 128.39, 128.0, 127.9, 125.8, 67.0, 45.0, 44.4, 36.2, 35.9, 28.6, 24.5.

FT-IR (neat) 2931, 2856, 1700, 1430, 1235, 749, 698 cm^{-1}.

MS (ESI) *m/z* (M^+) calcd for $C_{22}H_{27}NO_2$: 337.2, found: 338.2 ($M + H^+$), 360.2 ($M + Na^+$).



4-(3-Phenylproply)tetrahydro-2*H*-pyran (Table 4, entry 6). 4-Chlorotetrahydro-pyran (108 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used.

The product was purified by flash chromatography (5%→15% EtOAc/hexanes). Colorless oil. First run: 149 mg (73%). Second run: 141 mg (69%).

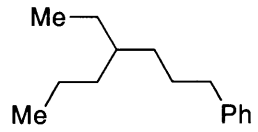
TLC: R_f = 0.25 (10% EtOAc/hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 2H), 7.20–7.14 (m, 3H), 3.93 (ddd, 2H, J = 11.5, 4.7, 1.2 Hz), 3.35 (td, 2H, 12.0, 1.8 Hz), 2.59 (t, 2H, 7.7 Hz), 1.70–1.42 (m, 5H), 1.35–1.20 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 128.5, 128.4, 125.8, 68.3, 36.7, 36.2, 35.1, 33.3, 28.4.

FT-IR (neat) 2928, 2842, 1096, 748, 699 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{14}H_{20}O$: 204.2, found: 204.2 (M^+).



(4-Ethylheptyl)benzene (Table 4, entry 7). 3-Chlorohexane (139 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (cyclohexane). Colorless oil. First run: 145 mg (71%). Second run: 149 mg (73%).

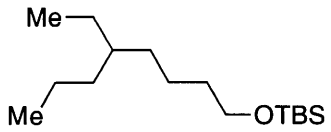
TLC: R_f = 0.65 (cyclohexane; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 2H), 7.21–7.15 (m, 3H), 2.58 (t, 2H, J = 7.7 Hz), 1.64–1.52 (m, 2H), 1.34–1.17 (m, 9H), 0.92–0.78 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 128.5, 128.3, 125.7, 38.7, 36.6, 35.7, 33.0, 28.8, 26.0, 20.0, 14.6, 11.0.

FT-IR (neat) 2958, 2930, 1495, 1454, 746, 697 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{15}H_{24}$: 204.2, found: 204.3 (M^+).



***tert*-Butyl(5-ethyloctyloxy)dimethylsilane (Table 4, entry 8).** 3-Chlorohexane (139 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of (but-3-enyloxy)(*tert*-butyl)dimethylsilane (prepared according to a literature procedure[24]) with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (hexanes). Colorless oil. First run: 180 mg (66%). Second run: 172 mg (63%).

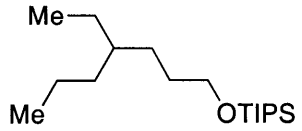
TLC: R_f = 0.3 (hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (t, 2H, *J* = 6.6 Hz), 1.55–1.45 (m, 2H), 1.38–1.15 (m, 11H), 0.88 (s, 9H), 0.87 (t, 3H, *J* = 7.2 Hz), 0.82 (t, 3H, *J* = 7.3 Hz), 0.05 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 63.4, 38.8, 35.7, 33.5, 33.1, 26.1, 26.0, 23.0, 20.0, 18.5, 14.5, 11.0, –5.1.

FT-IR (neat) 2958, 2930, 2860, 1463, 1255, 1102, 836, 774 cm^{-1}.

MS (EI) *m/z* (M^+) calcd $C_{16}H_{36}OSi$: 272.2, found: 215.2 (M^+ – *t*-Bu).



[24] Ferrie, L.; Reymond, S.; Capdevielle, P.; Cossy, J. *Org. Lett.* **2007**, *9*, 2461–2464.

(4-Ethylheptyloxy)triisopropylsilane (Table 4, entry 9). 3-Chlorohexane (139 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allyloxytriisopropylsilane (prepared according to a literature procedure[25]) with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (hexanes). Colorless oil. First run: 189 mg (63%). Second run: 198 mg (66%).

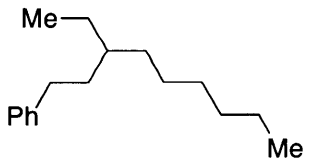
TLC: R_f = 0.3 (hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, 2H, *J* = 6.9 Hz), 1.56–1.46 (m, 2H), 1.34–1.16 (m, 9H), 1.14–1.00 (m, 21H), 0.87 (t, 3H, *J* = 6.8 Hz), 0.83 (t, 3H, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 64.1, 38.6, 35.7, 30.3, 29.1, 26.0, 20.0, 18.2, 14.6, 12.2, 11.0.

FT-IR (neat) 2959, 2942, 2867, 1464, 1105, 883 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{18}H_{40}OSi$: 300.3, found: 257.3 (M^+ – *i*-Pr).



(3-Ethylnonyl)benzene (Table 4, entry 10). (3-Chloropentyl)benzene (183 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of 1-hexene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (hexanes). Colorless oil. First run: 170 mg (73%). Second run: 172 mg (74%).

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[25] Frye, S. V.; Eliel, E. L. *J. Am Chem. Soc.* **1988**, *110*, 484–489.

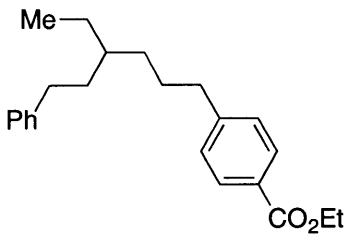
TLC: R_f = 0.7 (hexanes; UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 2H), 7.21–7.15 (m, 3H), 2.58 (t, 2H, J = 7.8 Hz), 1.67–1.51 (m, 2H), 1.40–1.20 (m, 13H), 0.92–0.80 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 128.5, 128.4, 125.6, 38.8, 35.4, 33.3, 33.2, 32.1, 29.9, 26.7, 25.9, 22.8, 14.3, 10.9.

FT-IR (neat) 2959, 2925, 2857, 1454, 743, 697 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{17}H_{28}$: 232.2, found: 232.3 (M^+).



Ethyl 4-(4-ethyl-6-phenylhexyl)benzoate (Table 4, entry 11). (3-Chloropentyl)benzene (183 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of ethyl 4-allylbenzoate (prepared according to a literature procedure[26]) with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (5%→10% EtOAc/hexanes). Colorless oil. First run: 230 mg (71%). Second run: 234 mg (72%).

TLC: R_f = 0.3 (10% EtOAc/hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.89 (m, 2H), 7.30–7.20 (m, 4H), 7.20–7.10 (m, 3H), 4.33 (q, 2H, J = 7.1 Hz), 2.61 (t, 2H, J = 7.6 Hz), 2.52 (dd, 2H, J = 12.4, 5.5 Hz), 1.65–1.48 (m, 4H), 1.34 (t, 3H, J = 7.2 Hz), 1.40–1.23 (m, 5H), 0.82 (t, 3H, J = 7.0 Hz).

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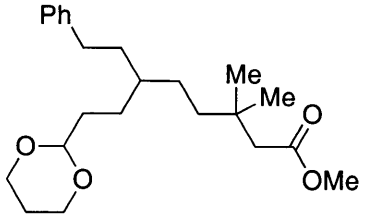
[26] Piazza, C.; Knochel, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 3263–3265.

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 148.4, 143.2, 129.7, 128.6, 128.5, 128.45, 128.42, 125.7, 60.9, 38.5, 36.5, 35.2, 33.3, 32.7, 28.3, 25.8, 14.5, 10.9.

FT-IR (neat) 2933, 2859, 1718, 1275, 1106, 761, 699 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{23}H_{30}O_2$: 338.2, found: 338.3 (M^+).



Methyl 6-(2-(1,3-dioxan-2-yl)ethyl)-3,3-dimethyl-8-phenyloctanoate (Table 4, entry 12). 2-(3-Chloro-5-phenylpentyl)-1,3-dioxane (139 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of 3,3-dimethyl-pent-4-enoic acid methyl ester with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (CH_2Cl_2→7.5% EtOAc/CH_2Cl_2). Colorless oil. First run: 309 mg (82%). Second run: 301 mg (80%).

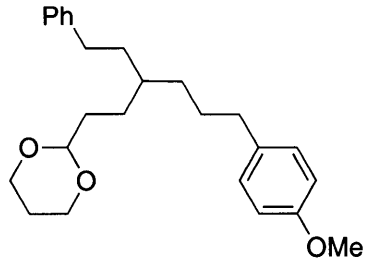
TLC: R_f = 0.5 (20% EtOAc/hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.23 (m, 2H), 7.19–7.13 (m, 3H), 4.83 (t, 1H, *J* = 5.2 Hz), 4.13–4.07 (m, 2H), 3.76 (td, 2H, *J* = 11.8, 1.9 Hz), 3.63 (s, 3H), 2.61–2.54 (m, 2H), 2.14–2.01 (m, 1H), 1.62–1.50 (m, 5H), 1.42–1.24 (m, 9H), 0.98 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 143.1, 128.5, 128.4, 125.7, 102.8, 67.0, 51.2, 45.8, 38.9, 37.6, 35.5, 33.3, 33.1, 32.6, 27.6, 27.5, 27.4, 26.0.

FT-IR (neat) 2954, 2856, 1736, 1145, 746, 700 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{23}H_{36}O_4$: 376.3, found: 375.3 ($M^+ - H$).



2-(6-(4-Methoxyphenyl)-3-phenethylhexyl)-1,3-dioxane (Table 4, entry 13). 2-(3-Chloro-5-phenylpentyl)-1,3-dioxane (139 μL, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (5%→10% EtOAc/hexanes). Colorless oil. First run: 314 mg (82%). Second run: 321 mg (84%).

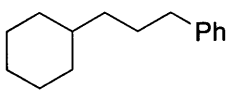
TLC: R_f = 0.5 (10% EtOAc/hexanes; PMA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.22 (m, 2H), 7.18–7.12 (m, 3H), 7.09–7.05 (m, 2H), 6.84–6.79 (m, 2H), 4.46 (t, 1H, *J* = 5.2 Hz), 4.12–4.06 (m, 2H), 3.78 (s, 3H), 3.77–3.69 (m, 2H), 2.60–2.47 (m, 4H), 2.14–2.00 (m, 1H), 1.62–1.51 (m, 6H), 1.45–1.29 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 143.1, 135.0, 129.4, 128.5, 128.4, 125.7, 113.8, 102.8, 83.8, 67.0, 55.4, 36.9, 35.5, 33.1, 33.0, 32.4, 28.8, 27.5, 26.0.

FT-IR (neat) 2928, 2856, 1512, 1245, 748, 700 cm^{-1}.

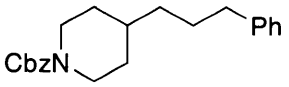
MS (EI) *m/z* (M^+) calcd for $C_{25}H_{34}O_3$: 382.2, found: 382.2 (M^+).



(3-Cyclohexylpropyl)benzene (Table 5, entry 1) [170661-44-6]. Cyclohexyl bromide (163 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of

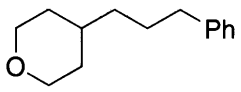
allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 152 mg (75%). Second run: 151 mg (75%).

Table 5, entry 2. Cyclohexyl iodide (210 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 148 mg (73%). Second run: 158 mg (78%).



Benzyl 4-(3-phenylpropyl)piperidine-1-carboxylate (Table 5, entry 3). Benzyl 4-bromopiperidine-1-carboxylate (298 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 217 mg (64%). Second run: 221 mg (66%).

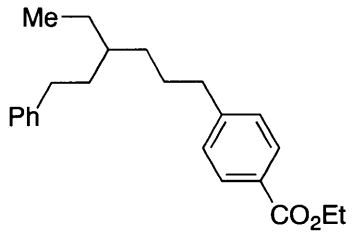
Table 5, entry 4. Benzyl 4-iodopiperidine-1-carboxylate (345 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 216 mg (64%). Second run: 220 mg (65%).



4-(3-Phenylproply)tetrahydro-2*H*-pyran (Table 5, entry 5). 4-Bromotetrahydropyran (165 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used.

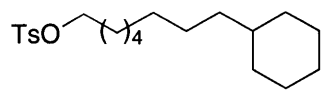
First run: 144 mg (71%). 156 mg (76%).

Table 5, entry 6. 4-Iodotetrahydropyran (212 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 159 mg (78%). 155 mg (75%).



Ethyl 4-(4-ethyl-6-phenylhexyl)benzoate (Table 5, entry 7). (3-Bromopentyl)benzene (227 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of ethyl 4-allylbenzoate (prepared according to a literature procedure[26]) with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 260 mg (77%). Second run: 251 mg (74%).

Table 5, entry 8. (3-Iodopentyl)benzene (274 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of ethyl 4-allylbenzoate (prepared according to a literature procedure[26]) with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. First run: 254 mg (75%). Second run: 265 mg (78%).



8-Cyclohexyloctyl 4-methylbenzenesulfonate (Table 5, entry 9). 5-Chloropentyl 4-methylbenzenesulfonate (277 mg, 1.0 mmol) and a solution of the boron reagent prepared

by hydroboration of allylcyclohexane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (5% Et_2O/hexanes). Colorless oil. First run: 236 mg (64%). Second run: 230 mg (62%).

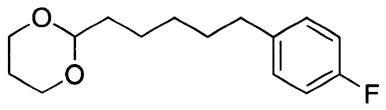
TLC: R_f = 0.5 (25% Et_2O/hexanes; $KMnO_4$).

^1H NMR ($CDCl_3$) δ 7.78 (d, 2H, *J* = 8.3 Hz), 7.34 (d, 2H, *J* = 8.3 Hz), 4.01 (t, 2H, *J* = 6.5 Hz), 2.44 (s, 3H), 1.71–1.55 (m, 7H), 1.32–1.07 (m, 16H), 0.90–0.78 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 144.7, 133.6, 129.9, 128.0, 70.8, 37.8, 37.6, 33.6, 29.9, 29.5, 29.0, 28.9, 26.90, 26.87, 26.6, 25.4, 21.7.

FT-IR (neat) 3063, 3027, 2986, 2933, 2858, 1604, 1496, 1454, 1378, 1369, 1248, 1215, 1156, 1055, 859, 747, 699 cm^{-1}.

MS (DART) *m/z* (M^++ NH_4) calcd for $C_{21}H_{38}NO_3S$: 384.3, found: 384.3 (M^+).



2-(5-(4-Fluorophenyl)pentyl)-1,3-dioxane (Table 5, entry 10). 2-(2-Bromoethyl)-1,3-dioxane (195 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of 1-allyl-4-fluorobenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (5% Et_2O/hexanes). Pale-yellow oil. First run: 172 mg (68%). Second run: 181 mg (72%).

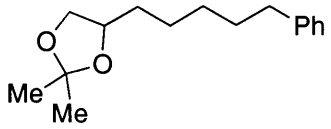
TLC: R_f = 0.3 (25% Et_2O/hexanes; UV).

^1H NMR ($CDCl_3$) δ 7.13–7.07 (m, 2H), 6.98–6.91 (m, 2H), 4.49 (t, 1H, *J* = 5.1 Hz), 4.12–4.06 (m, 2H), 3.79–3.70 (m, 2H), 2.56 (t, 2H, *J* = 7.6 Hz), 2.15–2.00 (m, 1H), 1.64–1.54 (m, 4H), 1.46–1.28 (m, 5H).

^{13}C NMR ($CDCl_3$) δ 129.8, 129.7, 115.2, 114.9, 102.4, 67.0, 35.3, 35.1, 31.6, 29.1, 26.0, 23.9.

FT-IR (neat) 2929, 2855, 1601, 1510, 1221, 1146, 998, 824 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{15}H_{21}FO_2$: 252.2, found: 251.1 (M^+ – H).



2,2-Dimethyl-4-(5-phenylpentyl)-1,3-dioxolane (Table 5, entry 11). 4-(2-Iodoethyl)-2,2-dimethyl-1,3-dioxolane (256 mg, 1.0 mmol) and a solution of the boron reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography (5% Et_2O/hexanes). Colorless oil. First run: 198 mg (79%). Second run: 194 mg (78%).

TLC: R_f = 0.5 (25% Et_2O/hexanes; $KMnO_4$).

^{1}H NMR ($CDCl_3$) δ 7.31–7.25 (m, 2H), 7.20–7.15 (m, 3H), 4.10–4.00 (m, 2H), 3.49 (t, 1H, *J* = 7.1 Hz), 2.61 (t, 2H, *J* = 7.6 Hz), 1.72–1.54 (m, 3H), 1.54–1.18 (m, 11H).

^{13}C NMR ($CDCl_3$) δ 142.8, 128.5, 128.4, 125.8, 108.7, 76.2, 69.7, 36.0, 33.7, 31.5, 29.4, 27.1, 25.9, 25.8.

FT-IR (neat) 3063, 3027, 2986, 2933, 2858, 1604, 1496, 1454, 1378, 1369, 1248, 1215, 1156, 1055, 859, 747, 699 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{16}H_{24}O_2$: 248.2, found: 248.2 (M^+).

IV. Kinetic Data

General procedure for the preparation of the boron reagent. In the glovebox,

9-BBN dimer (1.1 g, 4.5 mmol) was added to a 20-mL vial equipped with stir bar. To this was sequentially added diisopropyl ether (3.75 mL) and allylbenzene (1.2 mL, 9.0 mmol). The capped and sealed vial is heated at 60 °C for 1 hour with vigorous stirring. After cooling to room temperature, the solution was diluted to 6 mL with diisopropyl ether. KO*t*-Bu (0.73 g, 6.0 mmol) and *i*-BuOH (0.90 mL, 10.0 mmol) were added sequentially, and the mixture is stirred for 30 minutes.

General procedure for kinetic studies. A 4-mL vial equipped with stir bar is charged with $NiBr_2$·diglyme (4.2 mg, 0.012 mmol), *N,N'*-dimethyl-(±)-1,2-diphenyl-ethanediamine (3.6 μL, 0.018 mmol), and diisopropyl ether (0.10 mL). The mixture was stirred for 30 minutes, resulting in the formation of a pale-blue slurry. A solution of cyclohexyl bromide and tetradecane (standard) in diisopropyl ether was added, followed by the solution of the activated boron reagent. An aliquot (100 mL) was removed at 5, 10, 15, and 20 minutes. The amount of product was determined by GC analysis calibrated against tetradecane as the internal standard. The initial rates are determined by best fit of the first 20 minutes of reaction.

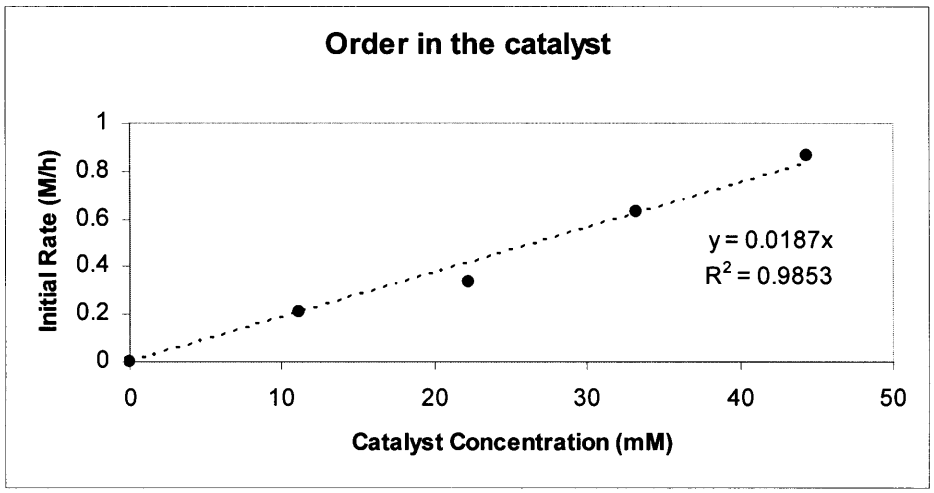
Order in the catalyst:

Table S1. Observed initial rates as a function of catalyst concentration.

$[\text{Ni cat.}]_0$ (mM) [a]	rate_{obs} (M / h)
0	0
11.1	0.207
22.2	0.339
33.3	0.629
44.4	0.862

[a] Reactions were run with $[\text{electrophile}]_0 = 0.370$ M and $[\text{nucleophile}]_0 = 0.667$ M.

Figure S1.

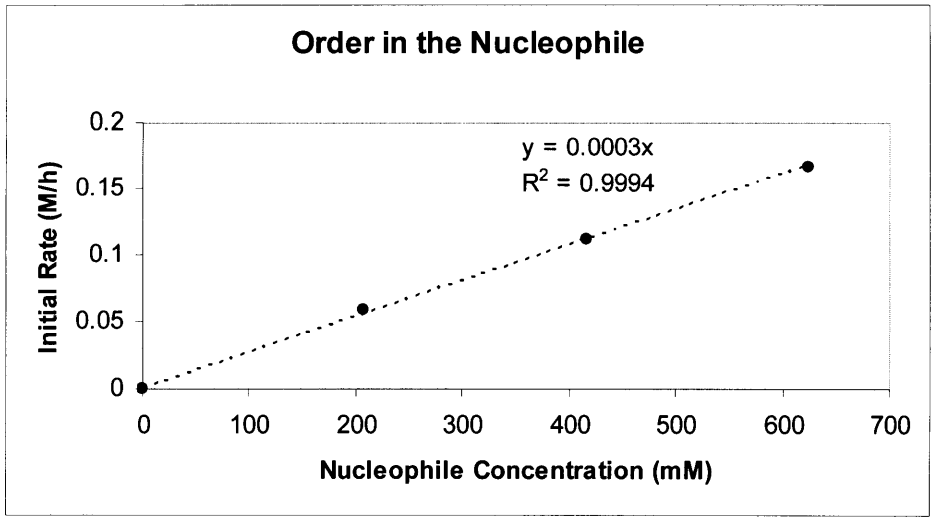


Order in the nucleophile:

[nucleophile]$_0$ (mM) [a]	rate$_{obs}$ (M / h)
0	0
208	0.0584
417	0.112
625	0.166

[a] Reactions were run with [catalyst]$_0$ = 0.0222 M and [electrophile]$_0$ = 1.48 M.
[b] Kinetics were not well-behaved at this concentration of nucleophile.

Figure S2.



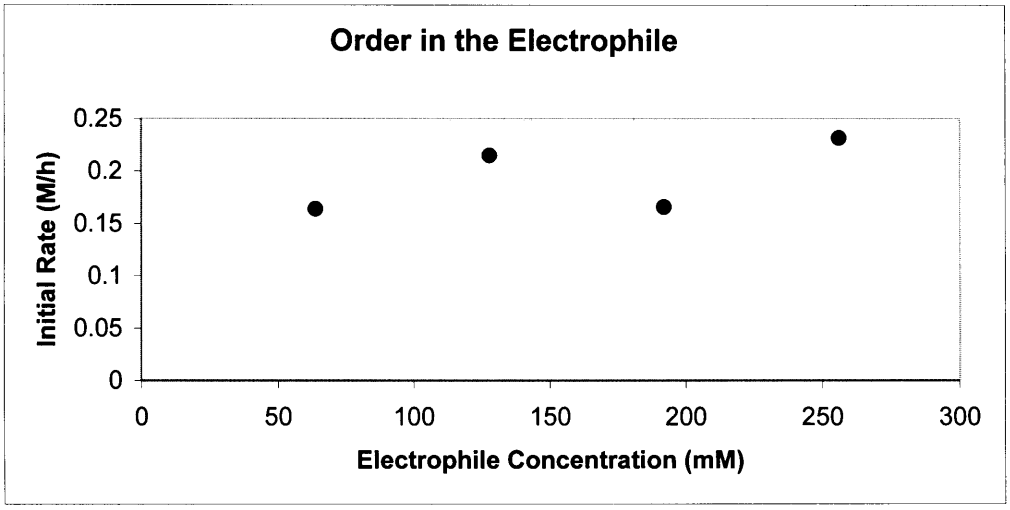
Order in the electrophile:

Table S3. Observed initial rates as a function of electrophile concentration.

$[electrophile]_0$ (mM) [a]	$rate_{obs}$ (M / h)
0	0
64	0.164
128	0.215
192	0.166
256	0.232

[a] Reactions were run with $[catalyst]_0 = 0.0154$ M and $[nucleophile]_0 = 0.923$ M.

Figure S3.



V. ^{1}H NMR Spectra

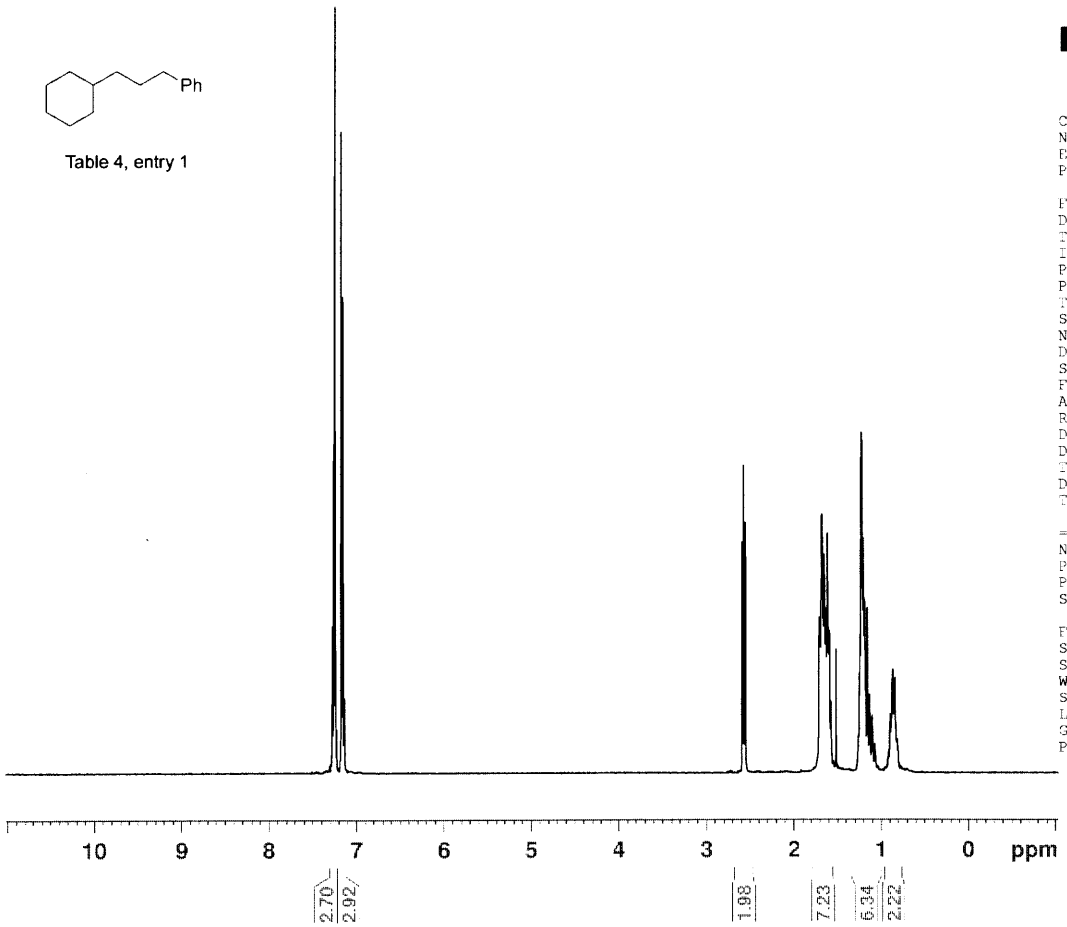


Table 4, entry 1

BRUKER

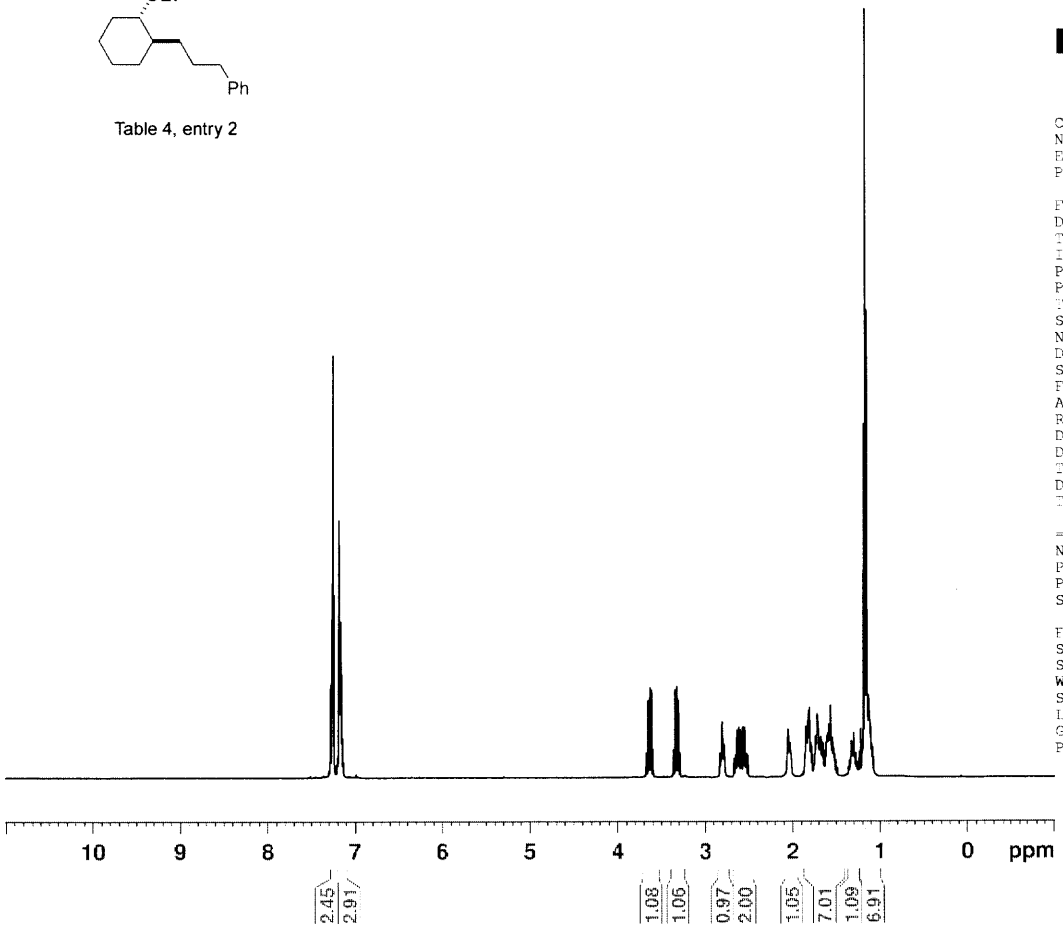
```
Current Data Parameters
NAME          ZL-III-299A
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_          20081004
Time              17.27
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   181
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.07 usec
PL1                0.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300142 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Table 4, entry 2



BRUKER

```
Current Data Parameters
NAME          ZL-IV-033A
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20091011
Time               15.20
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   114
DW                60.400 usec
DE                 6.00 usec
TE                293.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 15.07 usec
PL1                 0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300106 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

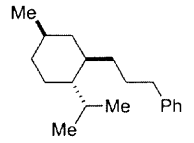


Table 4, entry 3

BRUKER

```
Current Data Parameters
NAME                 ZL-IV-036B
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_               20091012
Time                    17.03
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                3.9584243 sec
RG                        128
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      15.07 usec
PL1                      0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                         65536
SF               400.1300227 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

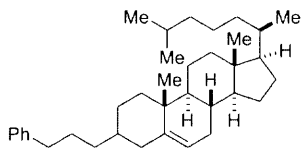


Table 4, entry 4

BRUKER

```
Current Data Parameters
NAME          ZL-IV-027A
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20091011
Time              15.30
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    0
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                  128
DW               60.400 usec
DE                6.00 usec
TE              293.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                15.07 usec
PL1                0.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                65536
SF          400.1300117 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

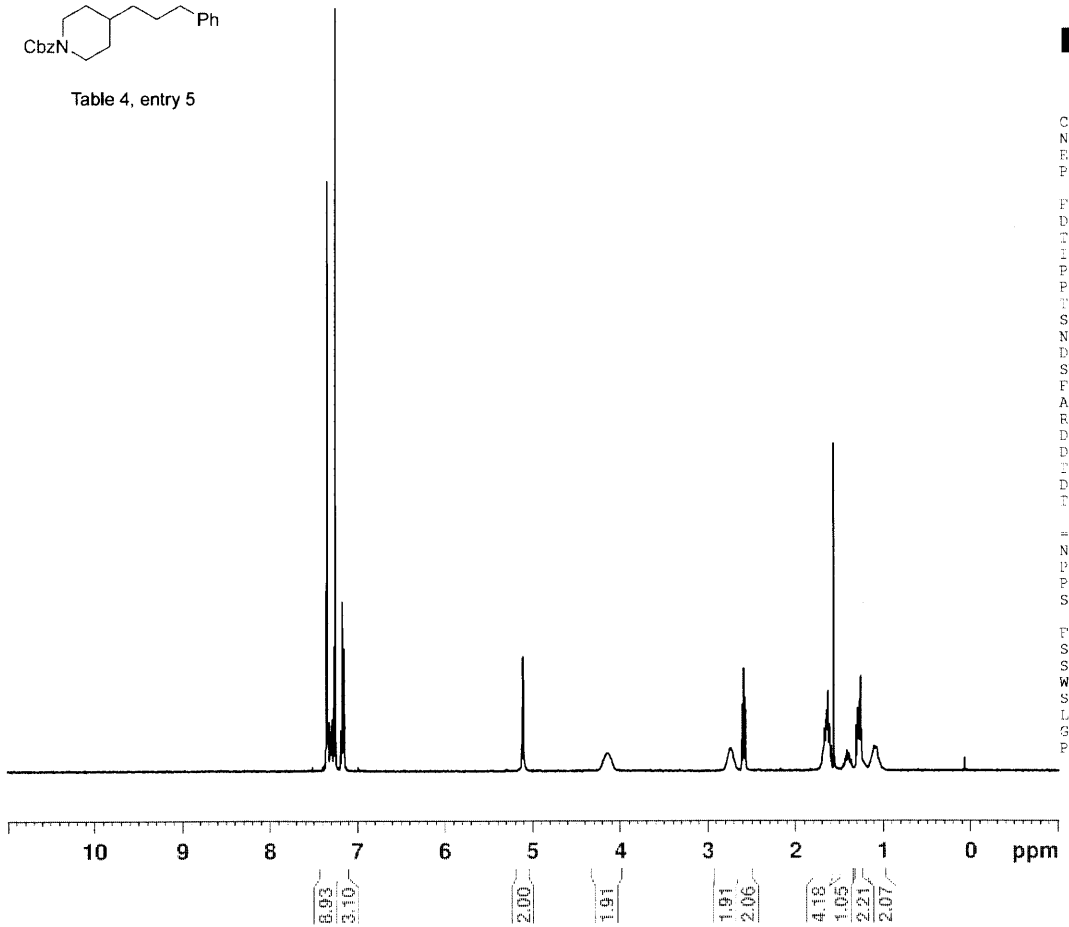


Table 4, entry 5

```
Current Data Parameters
NAME                 ZL-IV-020B
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_               20091012
Time                    11.06
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         0
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                      287.4
DW                     60.400 usec
DE                      6.00 usec
TE                     293.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                     65536
SF               400.1300104 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

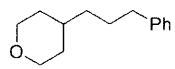
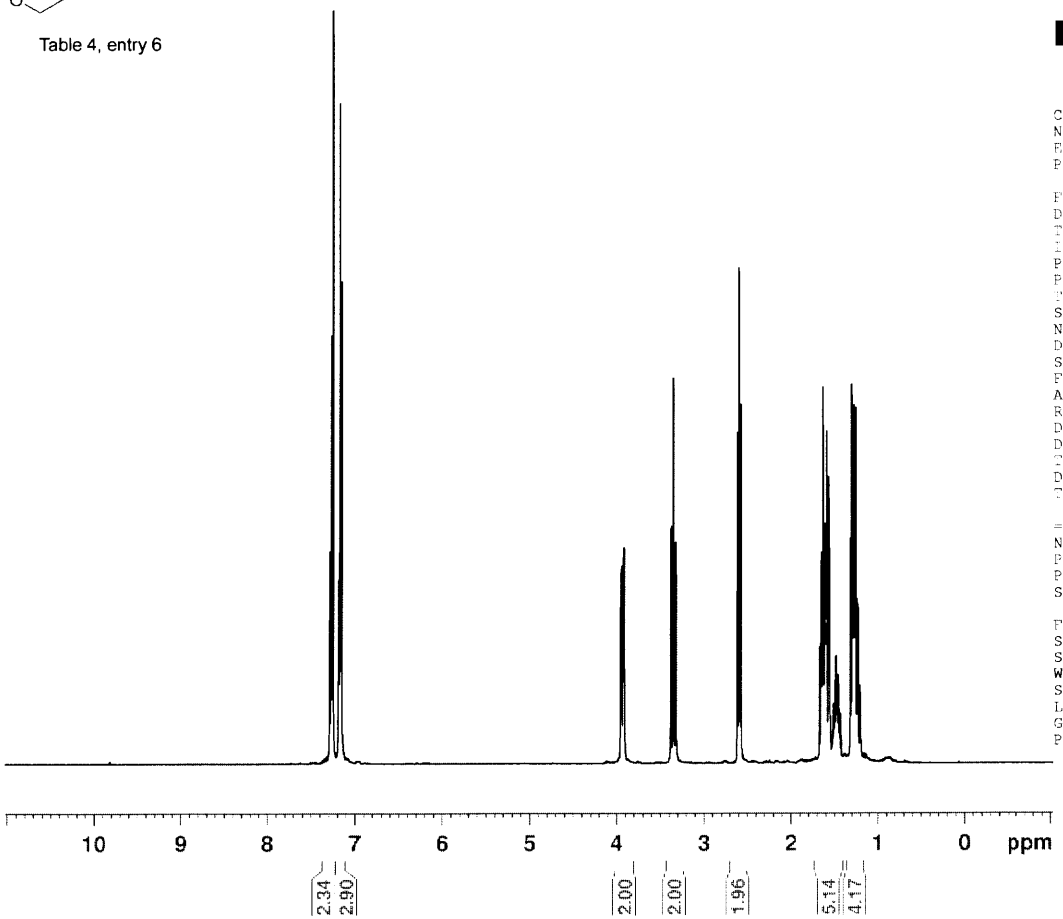


Table 4, entry 6



BRUKER

```
Current Data Parameters
NAME          ZL-IV-019B
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20091007
Time               19.36
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   128
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 15.07 usec
PL1                 0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300139 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Table 4, entry 7

BRUKER

```
Current Data Parameters
NAME                  ZL-IV-023
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_              20091004
Time                   15.40
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT
NS                        16
DS                         0
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    298.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                     65536
SF             400.1300098 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

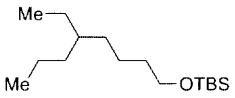


Table 4, entry 8

BRUKER

```
Current Data Parameters
NAME                  ZL-IV-034
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_              20091004
Time                   15.19
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         0
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    298.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                     65536
SF               400.1300113 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

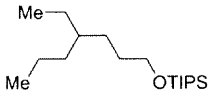


Table 4, entry 9


```
Current Data Parameters
NAME                  ZL-EV-028
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_              20091005
Time                    15.51
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         0
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    298.2 K
D1                1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                       15.07 usec
PL1                       0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF               400.1300120 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00
```

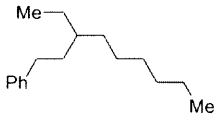


Table 4, entry 10


```
Current Data Parameters
NAME                  ZL-IV-015
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_              20091004
Time                    15.01
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         0
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    298.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                     65536
SF             400.1300119 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

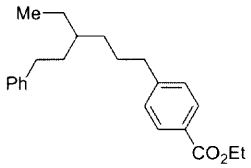


Table 4, entry 11


```
Current Data Parameters
NAME                ZL-IV-037A
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20081007
Time                 10.42
INSTRUM              spect
PROBHD   5 mm QNP 1H/13
PULPROG              zg30
TD                  65536
SOLVENT              CDCl3
NS                      16
DS                       0
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                   456.1
DW                  60.400 usec
DE                   6.00 usec
TE                  292.2 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   14.00 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   65536
SF            400.1300220 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

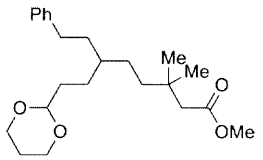


Table 4, entry 12

BRUKER

```
Current Data Parameters
NAME          ZL-IV-041A
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081007
Time              10.57
INSTRUM           spect
PROBHD   5 mm QNP 1H/13
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   12
DS                    0
SWH            8279.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                  362
DW               60.400 usec
DE                6.00 usec
TE              292.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                1H
P1                14.00 usec
PL1                0.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                65536
SF          400.1300097 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

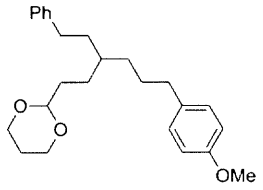


Table 4, entry 13

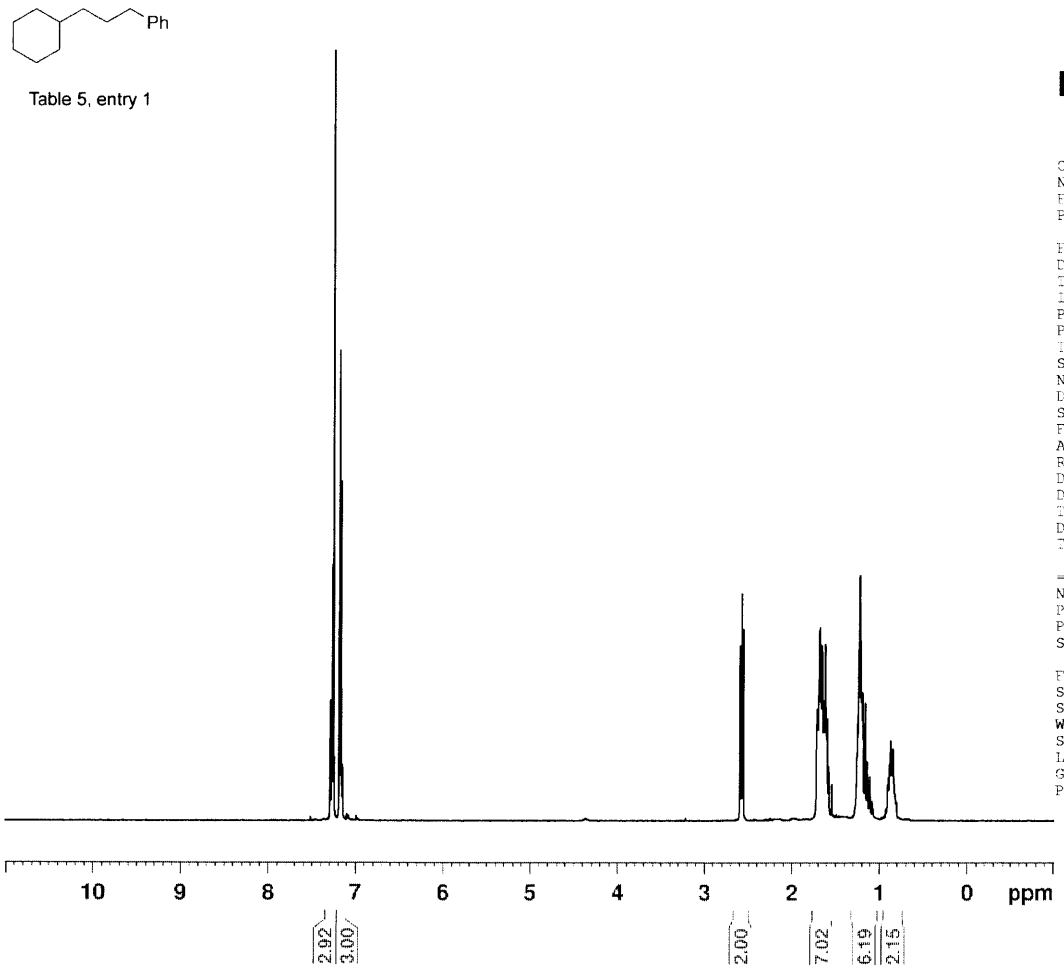
BRUKER

```
Current Data Parameters
NAME          ZL-IV-040B
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081008
Time               13.14
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   128
DW                60.400 usec
DE                 6.00 usec
TE                294.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.07 usec
PL1                0.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300137 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



BRUKER

```
Current Data Parameters
NAME                  ZL-IV-064A
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20081218
Time                       12.05
INSTRUM                    spect
PROBHD    5 mm BBO BB-1H
PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                            16
DS                             0
SWH                     8278.146 Hz
FIDRES                  0.126314 Hz
AQ                      3.9584243 sec
RG                           181
DW                       60.400 usec
DE                        6.00 usec
TE                       293.2 K
D1                    1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                          1H
P1                        15.07 usec
PL1                        0.00 dB
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                         65536
SF                  400.1300096 MHz
WDW                           EM
SSB                            0
LB                         0.30 Hz
GB                             0
PC                         1.00
```

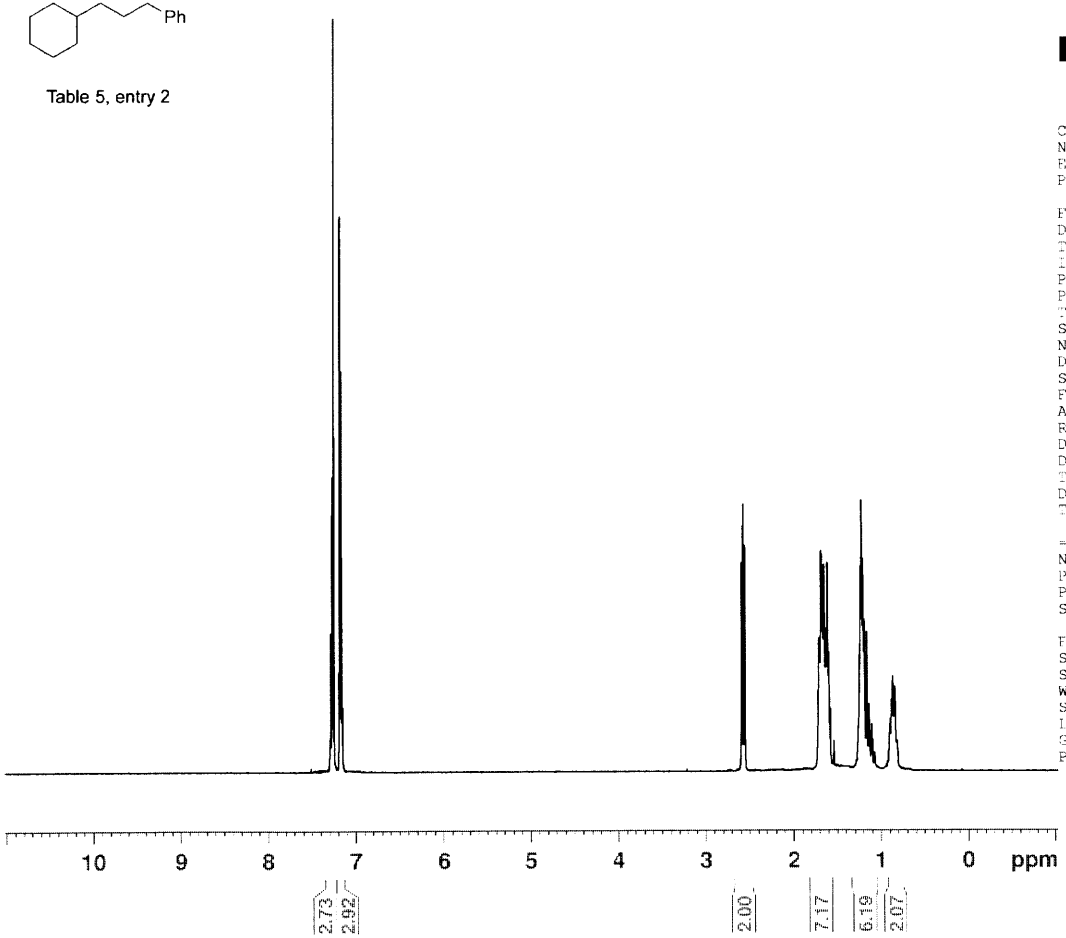


Table 5, entry 2

BRUKER

```
Current Data Parameters
NAME                  ZL-IV-064C
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20081218
Time                       12.50
INSTRUM                    spect
PROBHD    5 mm BBO BB-1H
PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                            16
DS                             2
SWH                     8278.146 Hz
FIDRES                  0.126314 Hz
AQ                      3.9584243 sec
RG                           128
DW                        60.400 usec
DE                         6.00 usec
TE                        293.2 K
D1                    1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                          1H
P1                         15.07 usec
PL1                         0.00 dB
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                         65536
SF                  400.1300099 MHz
WDW                           EM
SSB                            0
LB                          0.30 Hz
GB                             0
PC                          1.00
```

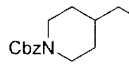
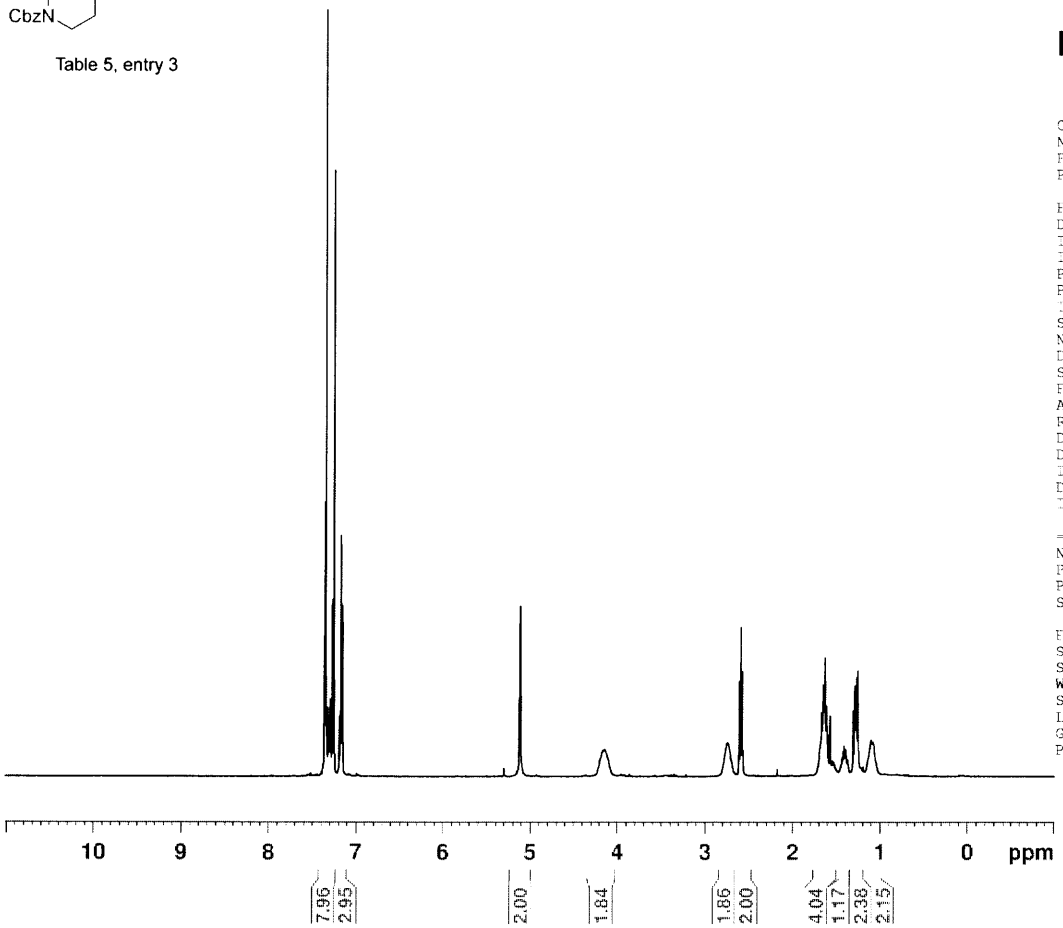


Table 5, entry 3



BRUKER

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PROCNO                 1

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INSTRUM           spect
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PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    0
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                  128
DW               60.400 usec
DE                6.00 usec
TE               293.2 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                1H
P1                15.07 usec
PL1                0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                65536
SF          400.1300099 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
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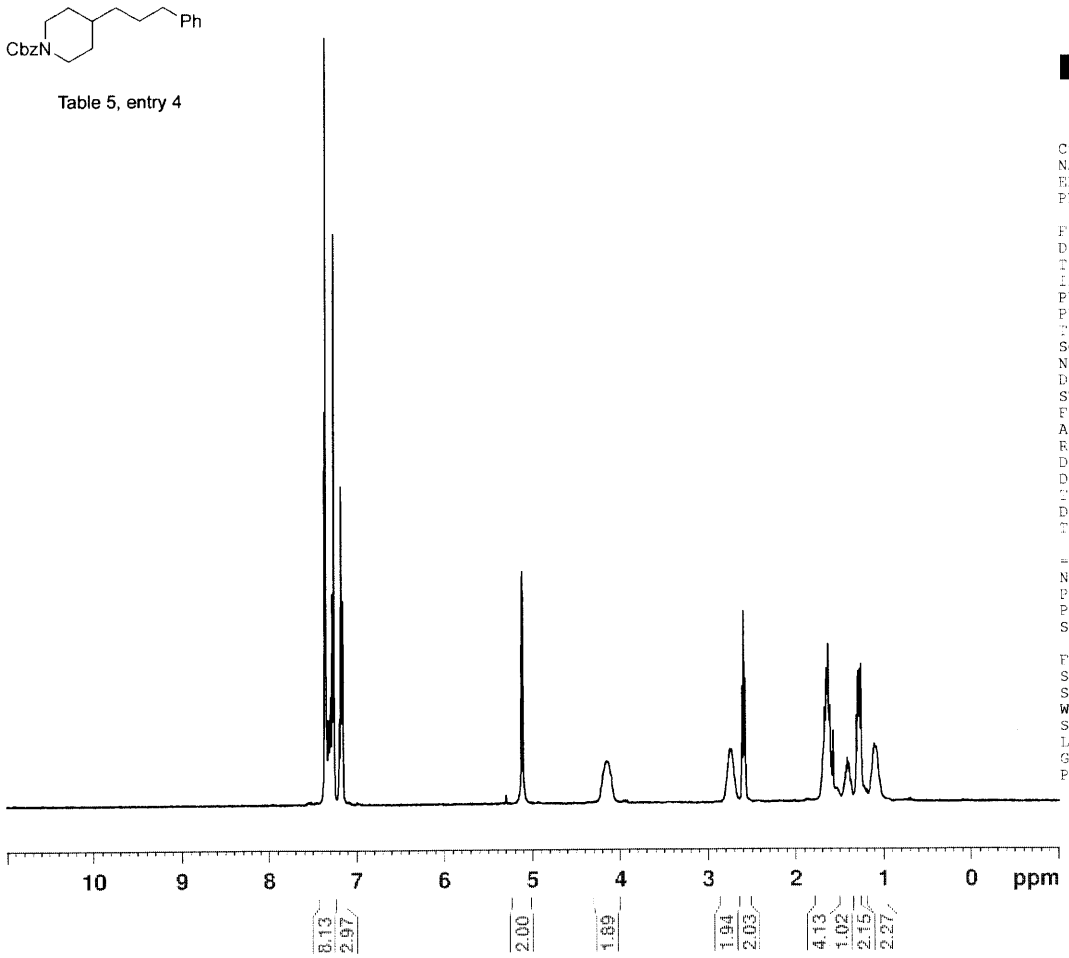

Table 5, entry 4

BRUKER

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PROCNO                         1

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Time                       15.13
INSTRUM                    spect
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PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                            16
DS                             0
SWH                     8278.146 Hz
FIDRES                  0.126314 Hz
AQ                    3.9584243 sec
RG                         456.1
DW                        60.400 usec
DE                         6.00 usec
TE                        291.2 K
D1                   1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                          1H
P1                        14.00 usec
PL1                        0.00 dB
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                         65536
SF                  400.1300094 MHz
WDW                           EM
SSB                            0
LB                         0.30 Hz
GB                             0
PC                         1.00
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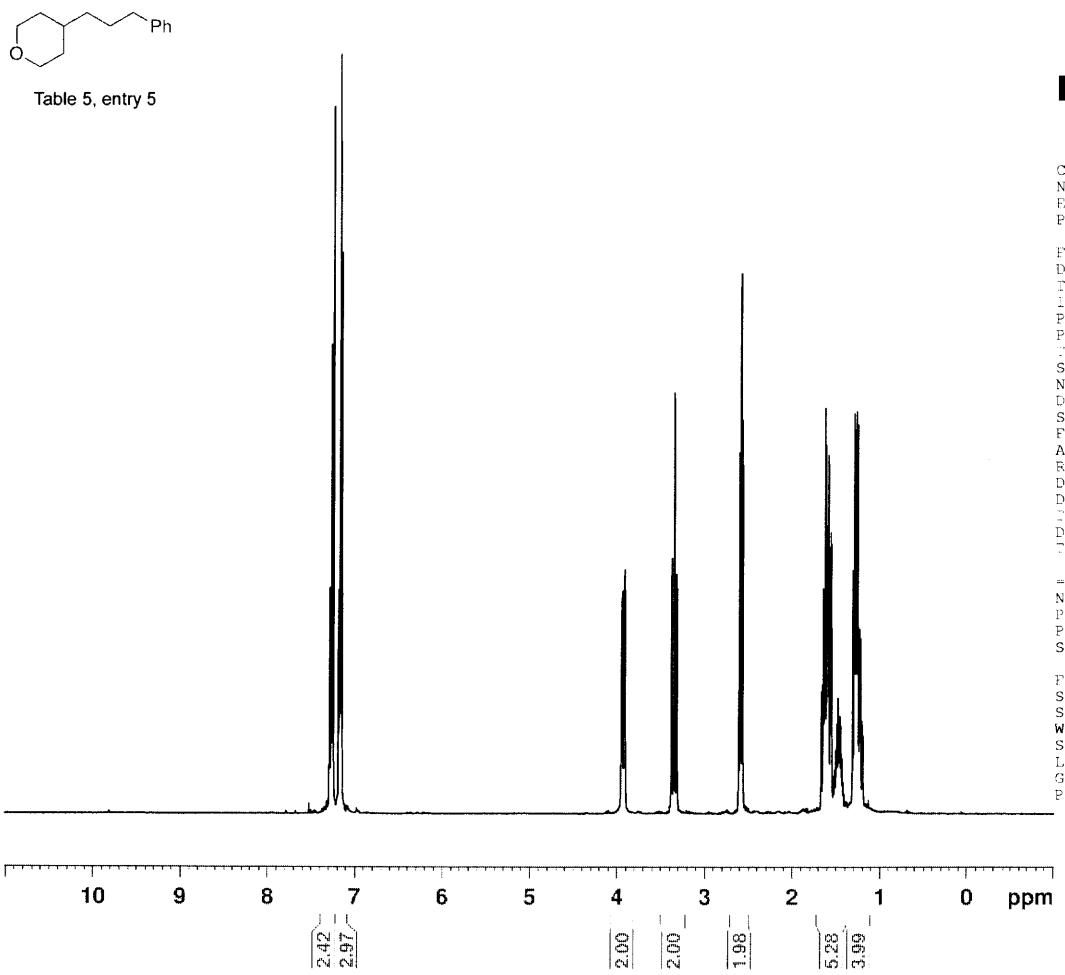

BRUKER

```
Current Data Parameters
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EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081218
Time               17.50
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   128
DW                60.400 usec
DE                 6.00 usec
TE                293.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.07 usec
PL1                0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300145 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
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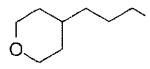

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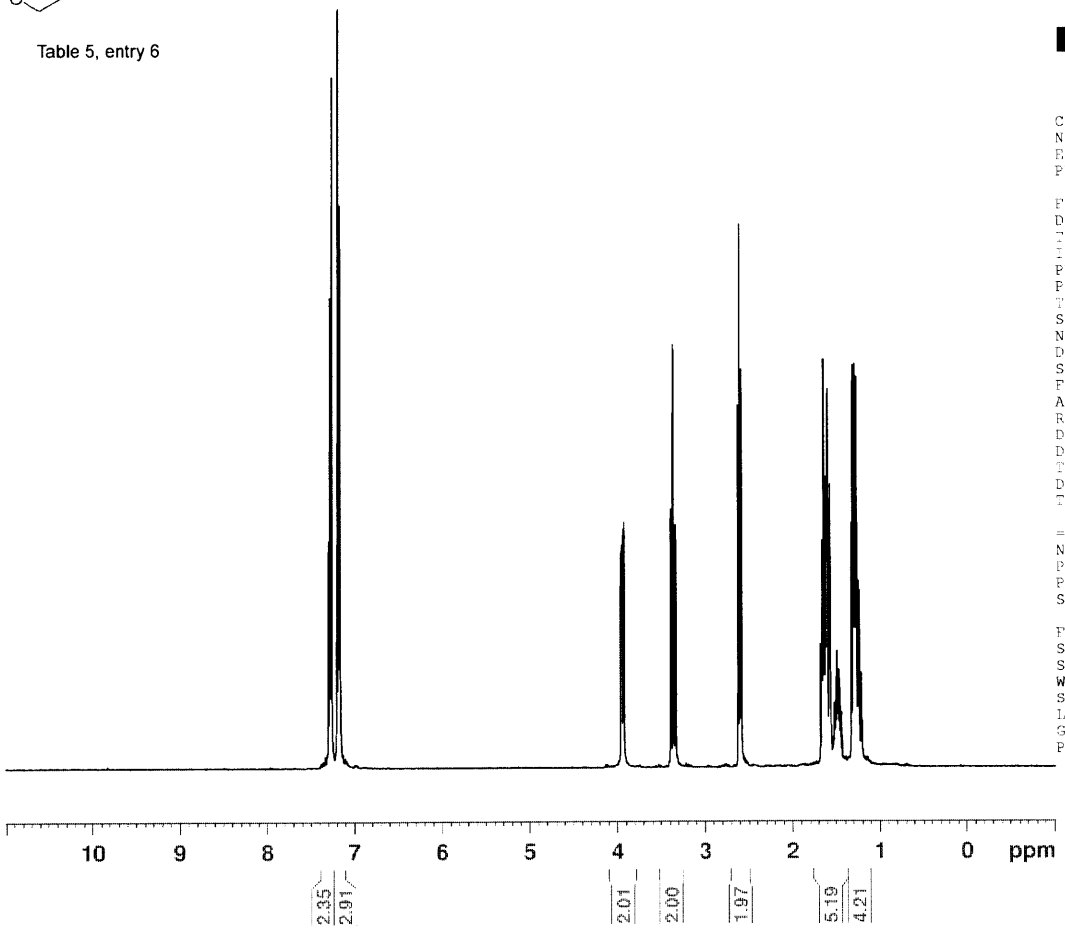

BRUKER

```
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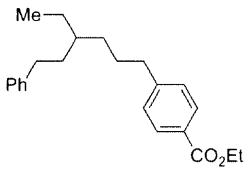
NAME                  ZL-IV-067B
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20081218
Time                       17.42
INSTRUM                    spect
PROBHD    5 mm BBO BB-1H
PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                            16
DS                             0
SWH                     8278.146 Hz
FIDRES                  0.126314 Hz
AQ                      3.9584243 sec
RG                           128
DW                        60.400 usec
DE                         6.00 usec
TE                        293.2 K
D1                    1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                          1H
P1                        15.07 usec
PL1                        0.00 dB
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                         65536
SF                  400.1300098 MHz
WDW                           EM
SSB                            0
LB                         0.30 Hz
GB                             0
PC                         1.00
```



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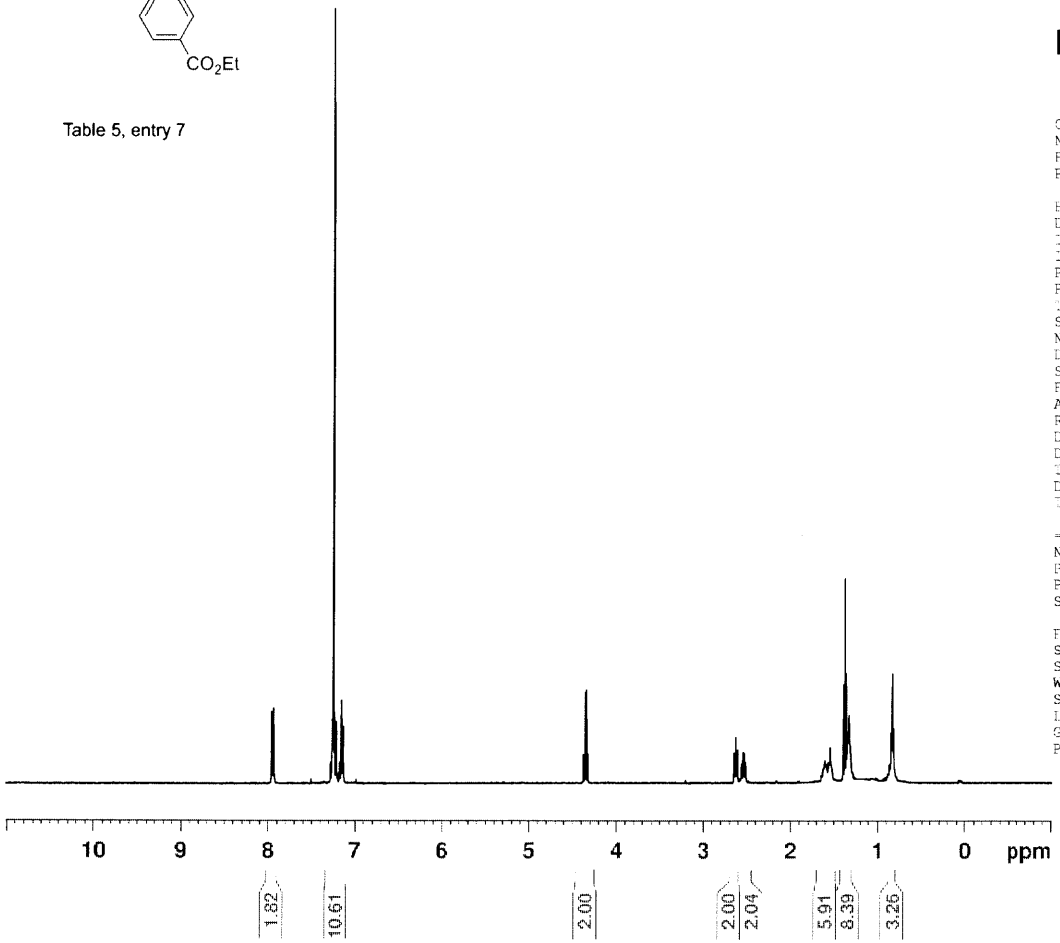



```
Current Data Parameters
NAME          ZL-IV-071A
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081219
Time               16.28
INSTRUM            spect
PROBHD   5 mm QNP 1H/13
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    0
SWH            8278.146 Hz
FIDRES        0.126314 Hz
AQ            3.9584243 sec
RG                456.1
DW               60.400 usec
DE                6.00 usec
TE               291.2 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                14.00 usec
PL1                0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                65536
SF         400.1300128 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

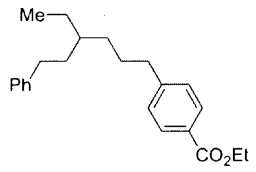
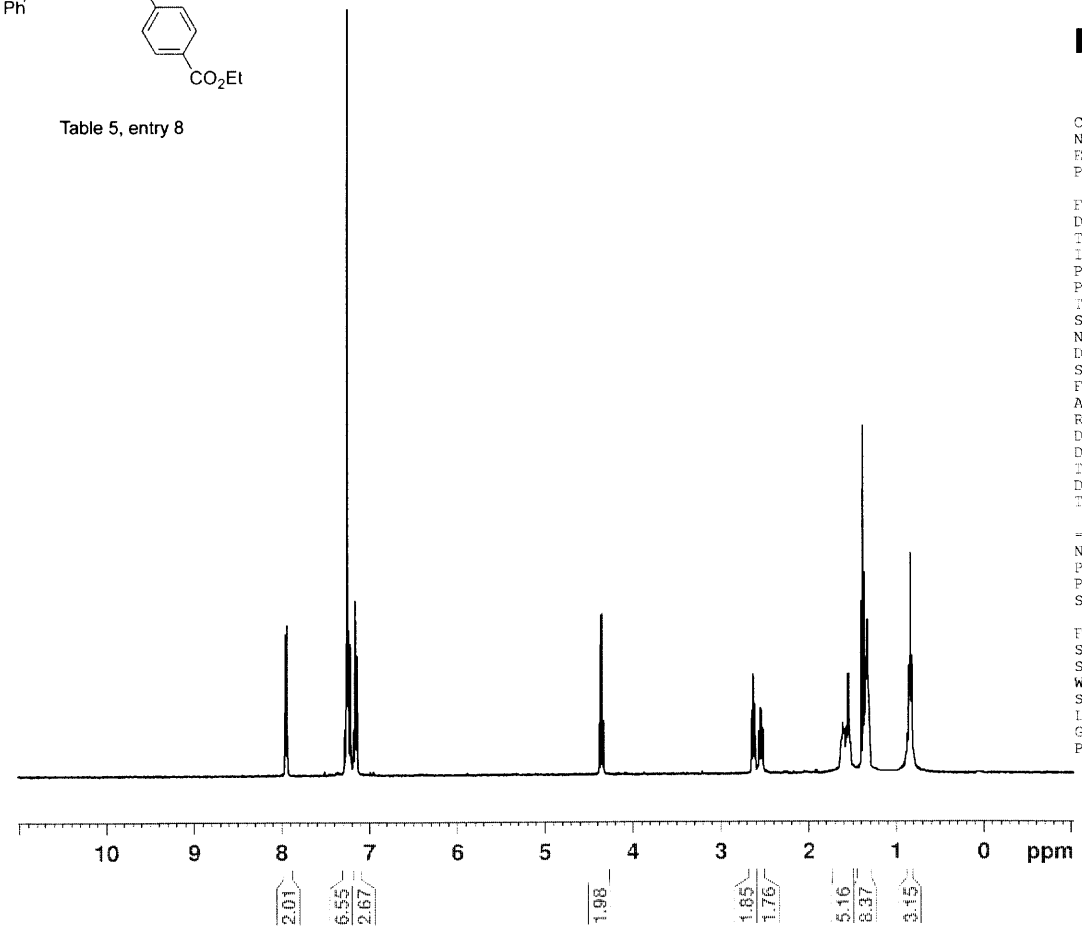


Table 5, entry 8

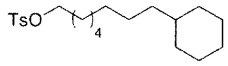



```
Current Data Parameters
NAME          ZL-IV-071C
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081219
Time               17.11
INSTRUM            spect
PROBHD   5 mm QNP 1H/13
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9584243 sec
RG                   512
DW                60.400 usec
DE                 6.00 usec
TE                291.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.00 usec
PL1                0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300112 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



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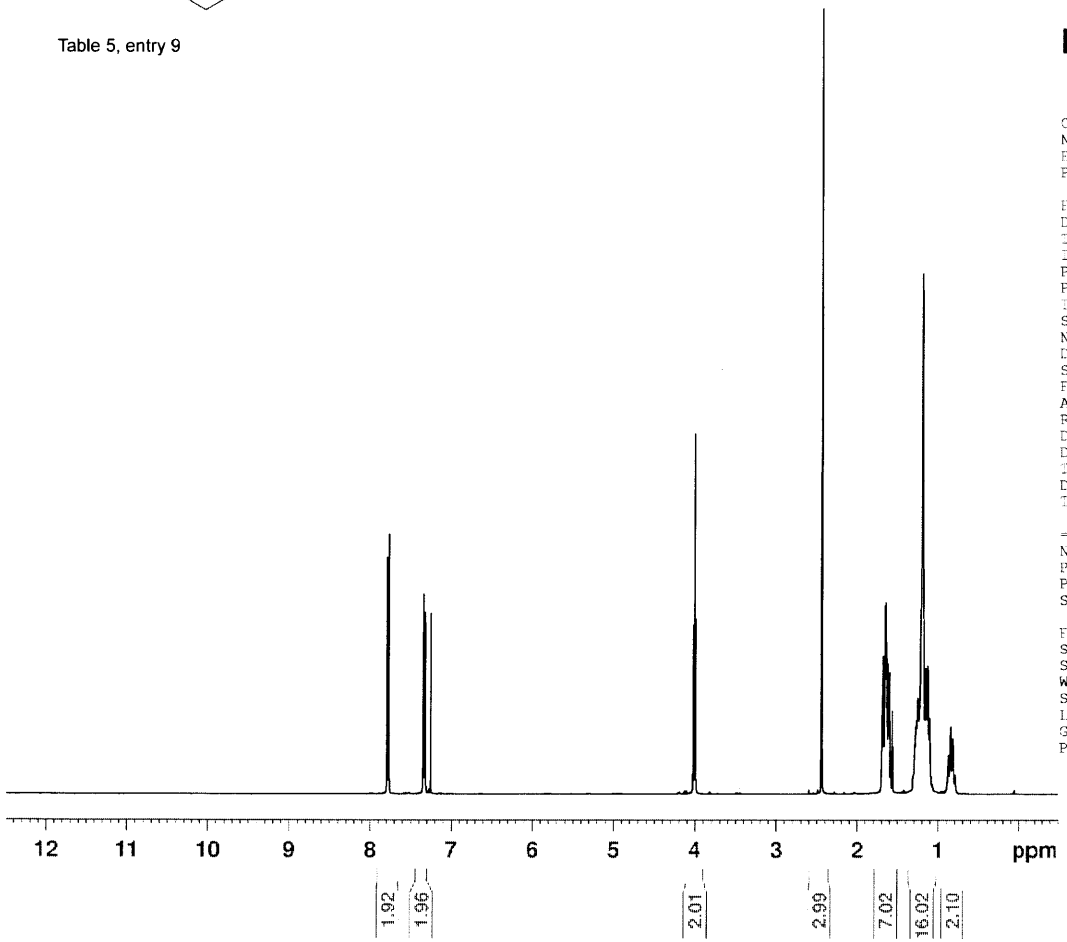


BRUKER

```
Current Data Parameters
NAME      ZL-V-200_1_col
EXPNO                  1
PROCNO                 1

P2 - Acquisition Parameters
Date_           20100417
Time              13.32
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    0
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                  128
DW               60.400 usec
DE                6.00 usec
TE               296.2 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                1H
P1               15.07 usec
PL1               0.00 dB
SFO1        400.1324710 MHz

P2 - Processing parameters
SI                65536
SF          400.1300109 MHz
WDW                  EM
SSB                   0
LB                0.30 Hz
GB                    0
PC                1.00
```

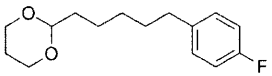
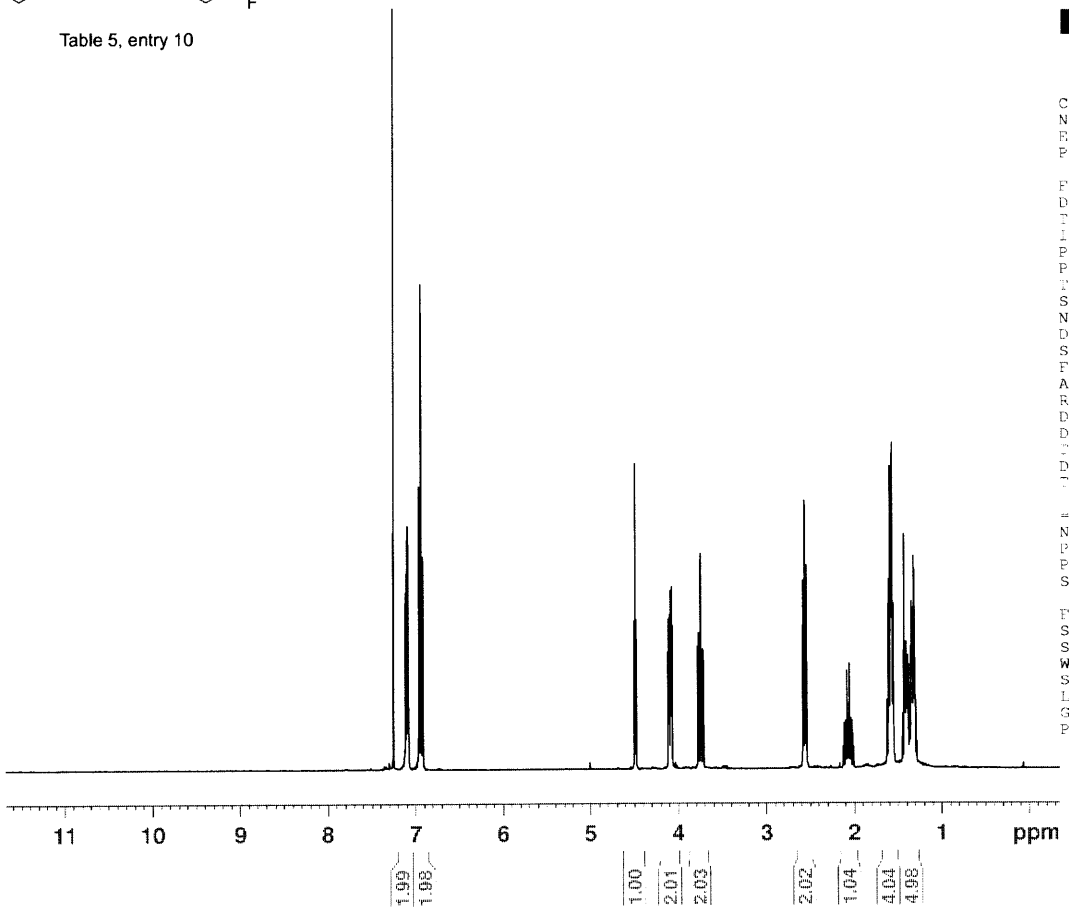


Table 5, entry 10



BRUKER

```
Current Data Parameters
NAME      ZI-V-190_Br_col1
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20130416
Time              13.04
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   256
DW                60.400 usec
DE                 6.00 usec
TE                296.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.07 usec
PL1                0.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300103 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

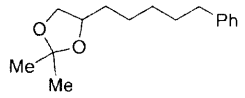


Table 5, entry 11

BRUKER

```
Current Data Parameters
NAME      ZL-V-201_1_col
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130417
Time              13.01
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    0
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                101.6
DW               60.400 usec
DE                6.00 usec
TE              296.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                15.07 usec
PL1                0.00 dB
SFO1        400.1324710 MHz

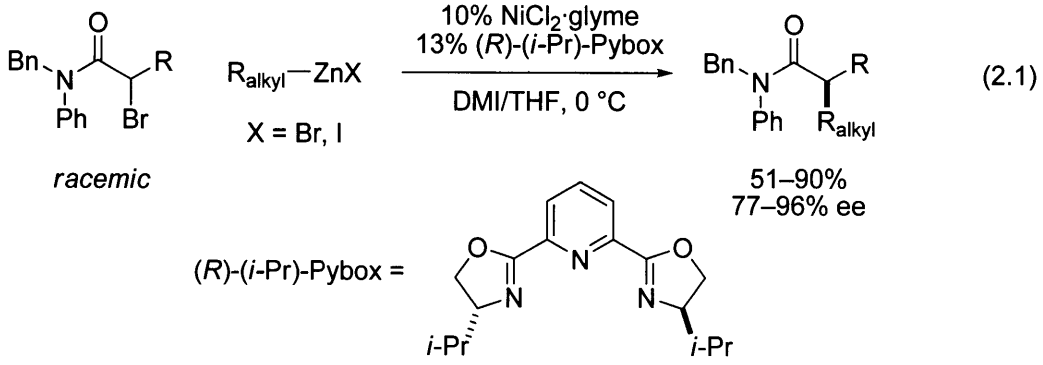
F2 - Processing parameters
SI                65536
SF          400.1300091 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

Chapter 2

Asymmetric Nickel-Catalyzed Suzuki-Miyaura Reactions of
β-Chloro Alkyl Aryl Amines

A. Introduction

While the chemistry described in Chapter 1 is synthetically useful, such cross-couplings could garner increased utility if they could be rendered stereoselective.[27] In terms of nickel-catalyzed cross-coupling reactions of secondary electrophiles, the number of stereoselective methods has been rather limited. In many of these cases, the chemistry involves the coupling of activated electrophiles, for example, α-halo carbonyl compounds (Eqs. 2.1–2.5),[28] benzylic halides (Eqs. 2.6–2.7),[29] allylic halides (Eq. 2.8),[30] and propargylic halides (Eq. 2.9).[31]



(2.1)

---

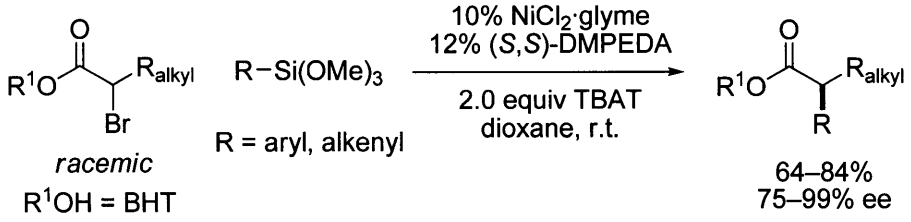
[27] For leading references on stereoselective synthesis, see: (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994. (b) Gawley, R. E.; Aubé, J. *Principles of Asymmetric Synthesis*; Tetrahderon Organic Chemistry, 14; Pergamon: Tarrytown, NY, 1996.

[28] (a) For asymmetric Negishi reactions of α-bromo amides, see: Fischer, C.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 4594–4595. (b) For asymmetric Hiyama reactions of α-bromo esters, see: Dai, X.; Strotman, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 3302–3303. (c) For asymmetric Negishi reactions of α-bromo ketones with organozinc reagents, see: Lundin, P. M.; Esquivias, J.; Fu, G. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 154–156. (d) For asymmetric Kumada reactions of α-bromo ketones, see: Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264–1266. (e) For asymmetric Negishi reactions of α-bromo ketones with organozirconium reagents, see: Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 5010–5011.

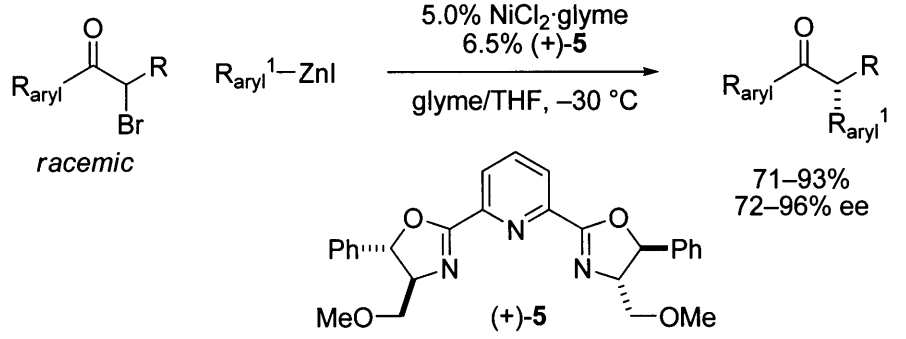
[29] (a) For asymmetric Negishi reactions of benzylic bromides and chlorides, see: Arp, F. O.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 10482–10483. (b) For asymmetric Sonogashira reactions of benzylic bromides, see: Caeiro, J.; Peréz Sestelo, J.; Sarandeses, L. A. *Chem. Eur. J.* **2008**, *14*, 741–746.

[30] For asymmetric Negishi reactions of allylic chlorides, see: Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 2756–2757.

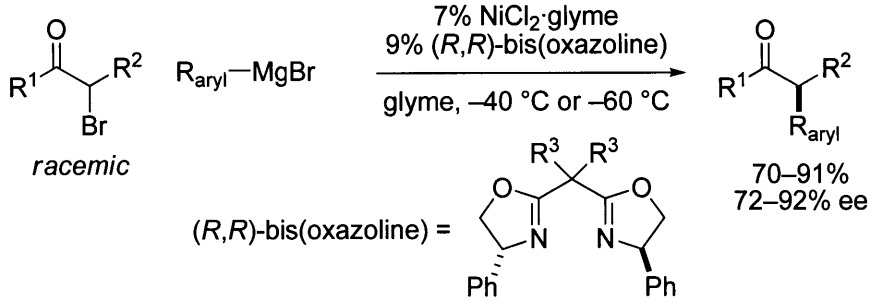
[31] For asymmetric Negishi reactions of propargylic bromides, see: Smith, S. W.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 12645–12647.


10% NiCl2·glyme
12% (S,S)-DMPEDA
2.0 equiv TBAT
dioxane, r.t.
R–Si(OMe)3
R = aryl, alkenyl
racemic
R1OH = BHT
64–84%
75–99% ee

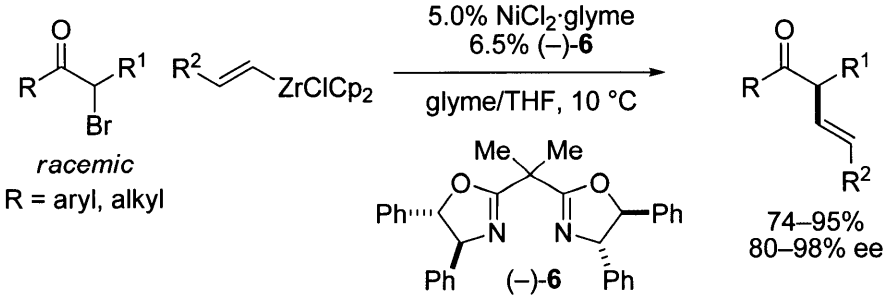
(2.2)


5.0% NiCl2·glyme
6.5% (+)-5
glyme/THF, –30 °C
racemic
71–93%
72–96% ee
(+)-5

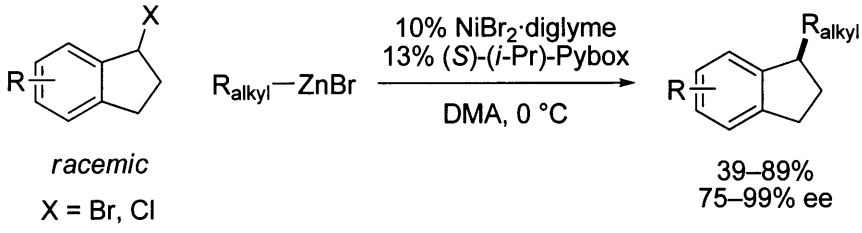
(2.3)


7% NiCl2·glyme
9% (R,R)-bis(oxazoline)
glyme, –40 °C or –60 °C
racemic
70–91%
72–92% ee
(R,R)-bis(oxazoline) =

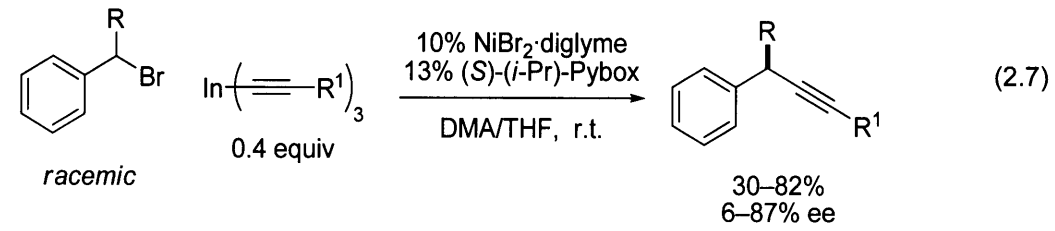
(2.4)


5.0% NiCl2·glyme
6.5% (–)-6
glyme/THF, 10 °C
racemic
R = aryl, alkyl
74–95%
80–98% ee
(–)-6

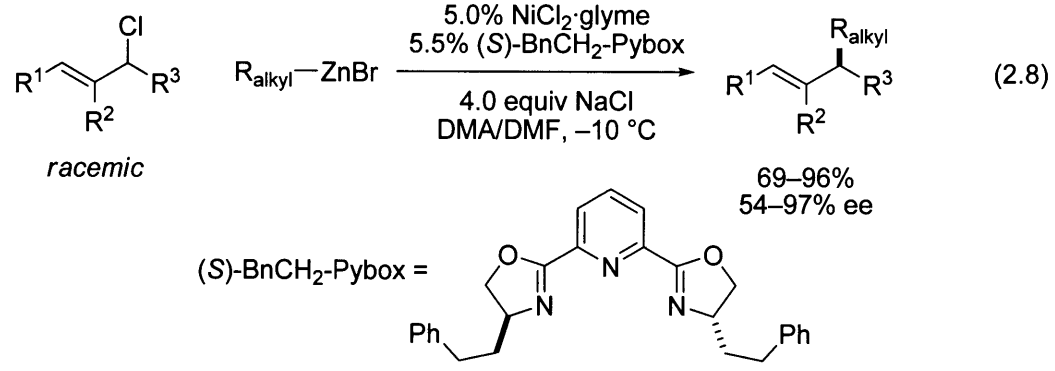
(2.5)


10% NiBr2·diglyme
13% (S)-(i-Pr)-Pybox
DMA, 0 °C
racemic
X = Br, Cl
39–89%
75–99% ee

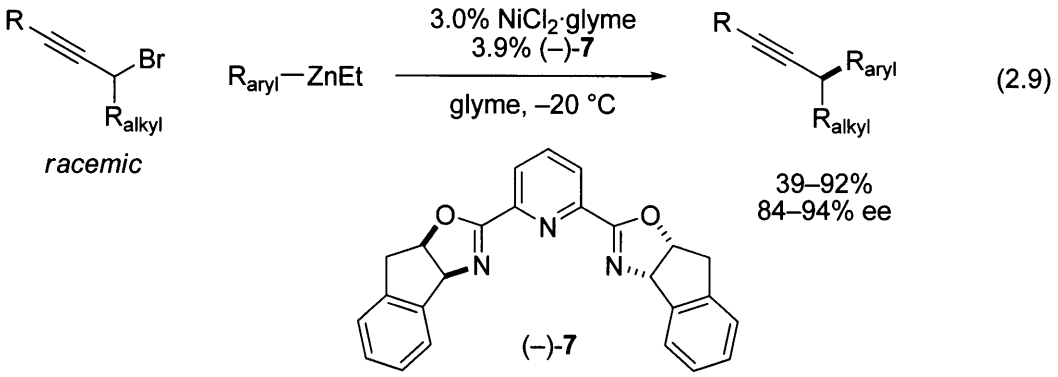
(2.6)



(2.7)



(2.8)



(2.9)

One important aspect of all of these reactions is that they are stereoconvergent, meaning that both enantiomers of the electrophile preferentially lead to the same enantiomer of product. Thus, the reaction is not a simple kinetic resolution. The radical nature of the proposed oxidative addition provides for a mechanism wherein the scission of the carbon–halogen bond potentially allows both enantiomers of the starting material to be converted to one preferred diastereomer in the oxidative addition. In addition, other mechanistic proposals involving a reversible oxidative addition or a racemization

pathway through homolysis of the carbon–nickel bond also can account for the observed stereoconvergence.

In 2008, the Fu group reported a stereoconvergent, nickel-catalyzed asymmetric Suzuki–Miyaura reaction of unactivated alkyl electrophiles, specifically, homobenzylic bromides (Eq. 2.9),[32] allowing the asymmetric coupling *unactivated* alkyl electrophiles. In this chemistry, the aryl ring in the substrate has a profound effect on the selectivity of the reaction. Homologation of the homobenzylic halide by a single methylene unit away from the aryl ring (**8c**) causes a precipitous drop in selectivity compared with similarly functionalized homobenzylic electrophiles (**8a**, **8b**). A cyclic substrate (**8d**), where the interaction of the catalyst with the aryl ring is potentially disrupted, also couples with low selectivity. Thus, it is highly likely that an interaction between the catalyst and the aryl ring is critical for these high levels of stereoselectivity.

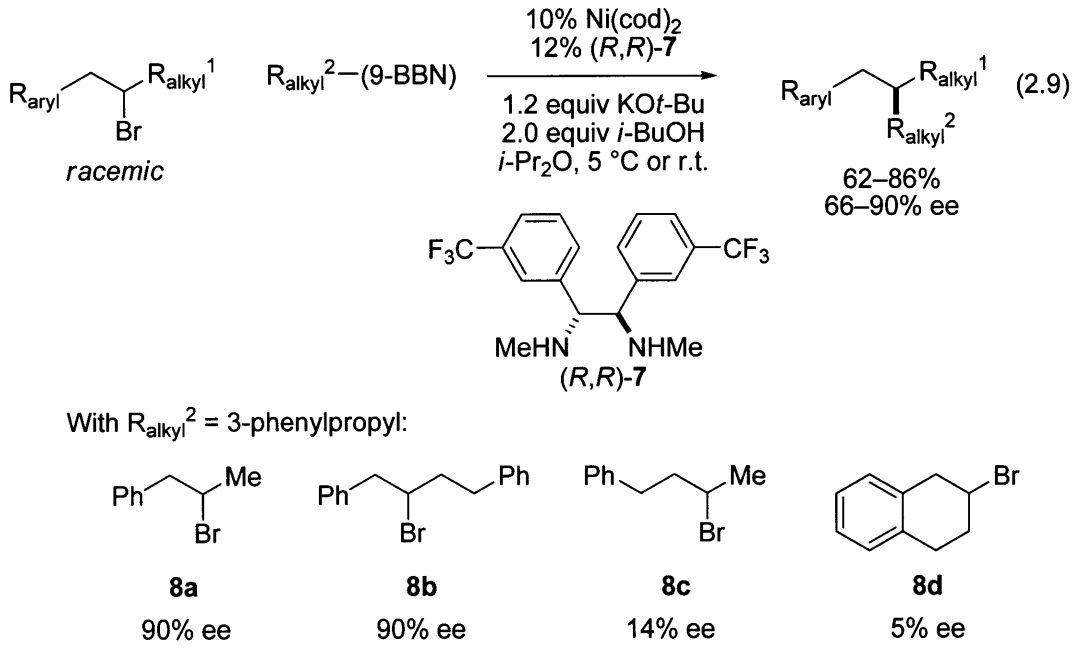


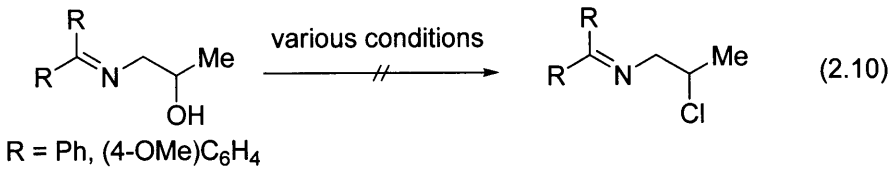
Figure 1. Spatial relationship of the "directing group" and selectivity in an asymmetric alkyl–alkyl cross-coupling of unactivated secondary alkyl bromides.

[32] Saito, B.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 6694–6695.

This hypothesis was tested by attempting to use other types of "directing groups" instead of a simple aryl ring. Specifically, the current project aims to examine the efficacy of amines as "directing groups." In order to isolate the effect of the directing nitrogen from other potentially stronger directing groups, amides and carbamates were intentionally avoided in this particular study.

B. Results and Discussion

The first substrates examined in this project were imines. Benzophenone imines have found great success as protecting groups for glycine in synthetic methods.[33] The original proposed route to these compounds started with Schiff base formation between commercially available amino alcohols and benzophenone. Halogenation of the imine alcohol intermediate might then provide the desired starting material. Unfortunately, the desired halide could not be isolated cleanly due to decomposition during purification (Eq. 2.10). Substituted benzophenone imines also failed to provide the desired halide.



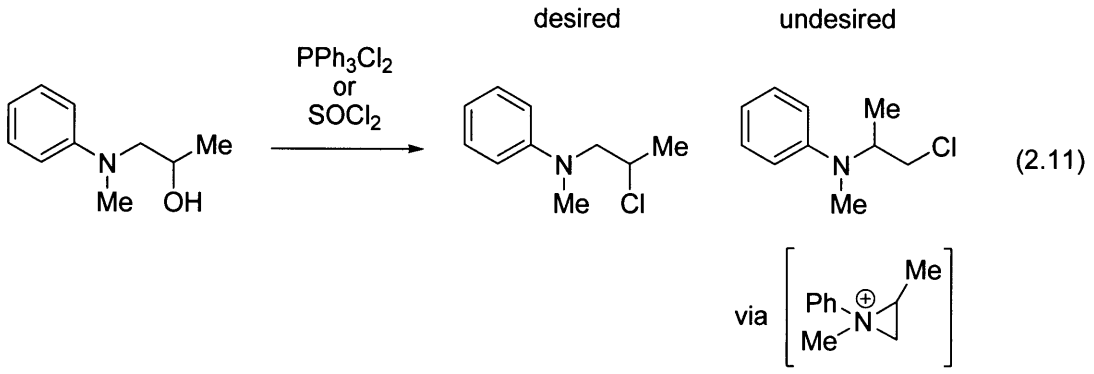
(2.10)

At this point, a new class of substrates was examined: simple amines. Given the nucleophilicity of amines and the proximity of the amine and electrophilic center in the starting material, there were some concerns about the stability of such compounds, especially towards the formation of aziridine or aziridinium species. Tertiary anilines turned out to be fairly stable and could be stored at 0 °C without significant degradation after four weeks. On the other hand, secondary amines, including anilines, and trialkylamines were noticeably more reactive, and pronounced discoloration of the starting material was observed after one week even when stored at 0 °C.

The nucleophilicity of the amine also created another problem for substrate synthesis. Typical procedures attempted included the halogenation of amino alcohols

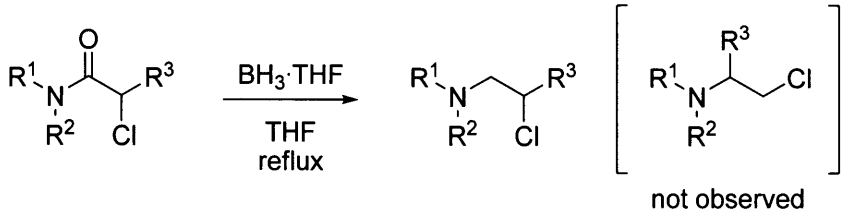
[33] For representative examples of the use of benzophenone imines as protecting groups in asymmetric chemistry, see: (a) López, A.; Pleixats, R. *Tetrahedron: Asymmetry* **1998**, *9*, 1967–1977. (b) O'Donnell, M. J.; Esikova, I. A.; Shullenberger, D. F.; Wu, S. In *Phase-Transfer Catalysis*; Halpern, M. E., Ed.; ACS Symposium Series 659; ACS: Washington, D. C., 1997. Chapter 10. (c) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1997**, *38*, 8595–8598. (d) Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414–12415. (e) Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **1999**, *121*, 6519–6520.

using dichlorotriphenylphosphorane or thionyl chloride. However, these halogenation procedures resulted in some rearrangement to the primary amine (Eq. 2.11). Presumably, the highly electrophilic chlorosulfite or phosphonium intermediate is easily attacked by the adjacent nucleophilic nitrogen to form an aziridinium ion, which is subsequently trapped by chloride. Selectivities varied from 4:1 (secondary:primary) to 1:2 (secondary:primary), depending on the functional groups on the substrate.



(2.11)

An alternative approach to substrate synthesis involving the reduction of α-chloro amides was explored. The α-chloro amides could be synthesized from an amine and an α-chloroacyl chloride.[34] A literature procedure for the reduction of a similar compound using borane was to be quite effective.[35] No isomerization to the primary amine was observed with this procedure (Eq. 2.12).



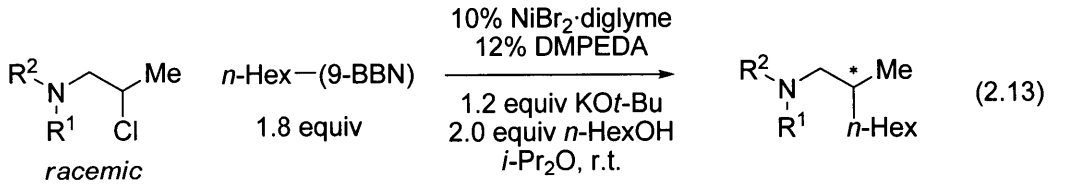
(2.12)

The first cross-coupling reactions attempted used benzylmethylamine **9a** and dibenzylamine **9b**. The initial conditions were based on precedented conditions (see

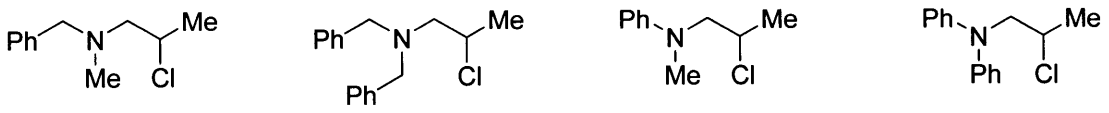
[34] The α-chloroacyl chloride is readily made according to literature procedure: Harpp, D. N.; Bao, L. Q.; Black, C. J.; Gleason, J. G.; Smith, R. A. *J. Org. Chem.* **1975**, *40*, 3420–3427.
[35] Zhdankin, V. V.; Nemykin, V. N.; Karimov, R. R.; Kazhkenov, Z.-G. *Chem. Comm.* **2008**, 6131–6133.

Chapter 1) and are depicted in Eq. 2.13. The dibenzylamine (**9b**) showed no reactivity and no consumption of starting material (see below). The benzylmethylamine (**9a**) gave a yield of 75%. An assay that fully resolved the two enantiomers of product could not be found on HPLC, but best method for assay showed significant enantioenrichment (70±10% ee).

Given the success of 1-benzylmethylamino-2-chloropropane as substrate, the substitution pattern of the amine was explored with hopes for better selectivity and a better assay for enantioselectivity. Like dibenzylamine **9b**, diphenylamine **9d** was essentially unreactive. These results may suggest a steric limitation in terms of substitution on the nitrogen. The phenylmethylamine **9c** provided a clean HPLC assay and good selectivity (75% ee) which was further improved by decreasing the concentration of the reaction (0.1 M, 83% ee). Given the increased stability and safety[36] of the aniline (**9c**) relative to the benzyl methyl amine (**9a**), the anilines were chosen as the substrate class for further optimization.



(2.13)



9a 75% 70±10% ee

9b 0%

9c >75% 75% ee

9d 0%

A survey of various bis(methylated) diamines was undertaken to examine the

[36] Aromatic nitrogen mustards are reported to be less toxic and less carcinogenic than their aliphatic counterparts. This is consistent with the trend in observed relative reactivity. See: Woo, Y.-T.; Acros, J. C.; Lai, D. Y. In *Handbook of Carcinogen Testing,* 2nd ed. Milman, H. A., Weisurger, E. K., Eds. Noyes Publishing: Park Ridge, NJ, 1994; Chapter 1.

effect of these ligands. The ligands were synthesized by a two-step sequence: a diaza-Cope rearrangement according to a procedure by Chin and co-workers[37] and subsequent methylation according to a procedure by Alper (Scheme 3).[20]

Scheme 3. Synthesis of bis(methylated) diamine ligands.

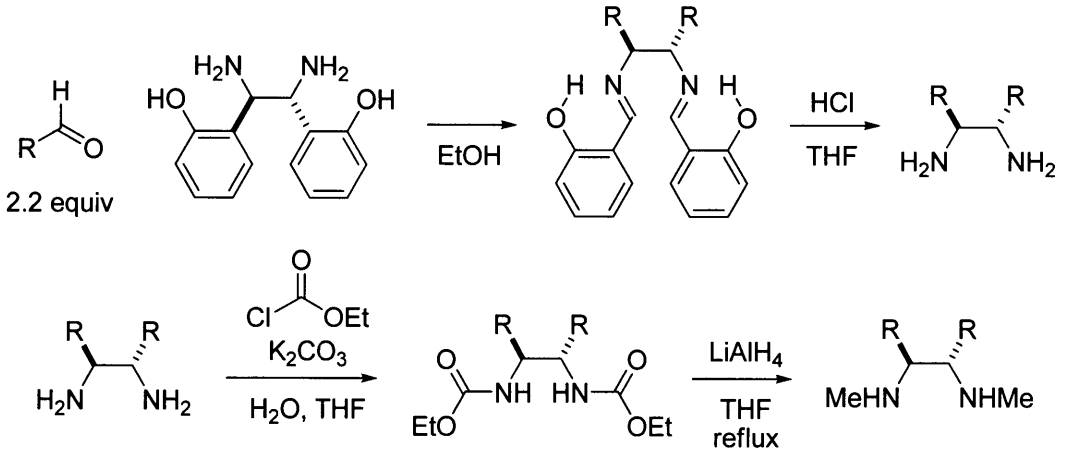


Table 7 illustrates the results using the newly synthesized ligands. For comparison, the best result obtained at this stage (with DMPEDA) is listed in entry 1. The ligand bearing *meta*-trifluoromethyl groups on the aryl rings (entry 2), which had been the best for the homobenzylic electrophiles,[32] provided disappointingly low selectivity as did the 3-furyl substituted ligand (entry 4). Replacing the phenyl rings with 2-naphthyl (entry 5) or 4-dimethylaminophenyl (entry 3) was unfruitful, but the 1-naphthyl-substituted diamine (DMNEDA, entry 6) improved the enantioselectivity of the reaction (89% ee). Optimization of other reaction parameters, including solvent, failed to improve the selectivity of the reaction, and alkyl bromides underwent cross-coupling with slightly lower selectivities (87% ee). The optimized conditions are shown in Eq. 2.14.

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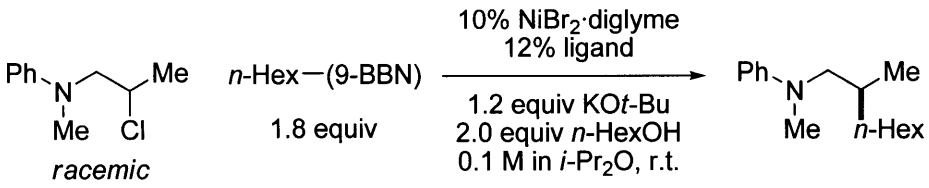
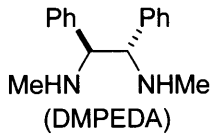
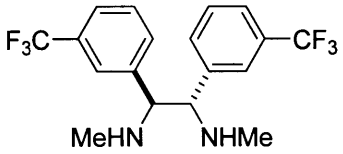
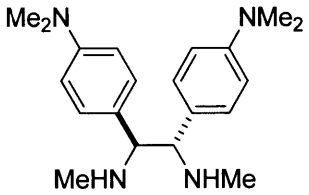
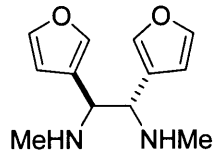
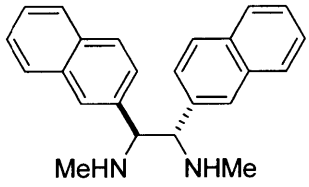
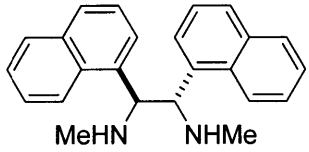
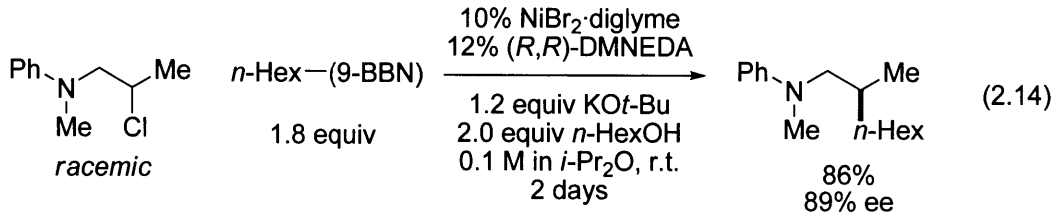
[37] Kim, H.; Nguyen, Y.; Yen, C. P.-H.; Chagal, L.; Lough, A. J.; Kim, B. M.; Chin, J. *J. Am. Chem. Soc.* **2008**, *130*, 12184–12191.

Table 7. Effect of varying ligands on an asymmetric Suzuki reaction.



entry	ligand	yield (%)[a]	ee (%)[b]
1	 (DMPEDA)	86	83
2		73	77
3		78	80
4		88	73
5		85	79
6	 (DMNEDA)	86	89

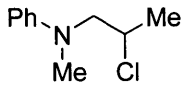
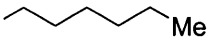
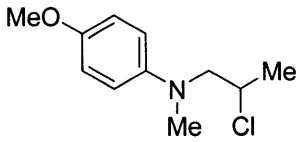
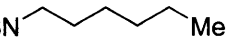
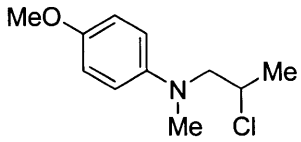
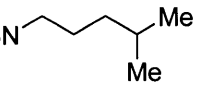
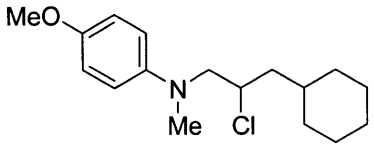
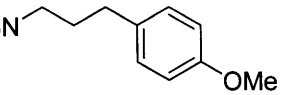
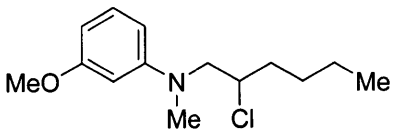
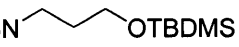
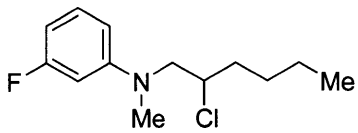
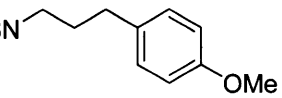
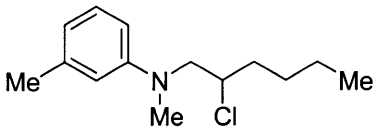
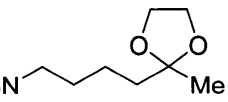
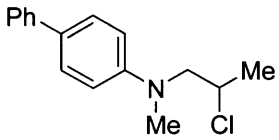
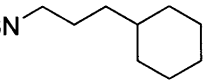
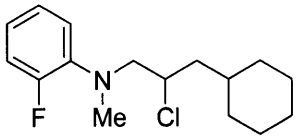
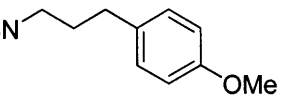
[a] GC versus a calibrated internal standard. [b] ee determined by HPLC analysis.



(2.14)

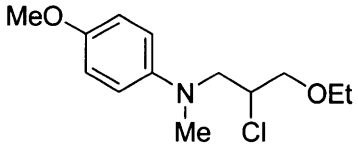
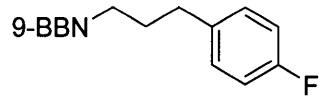
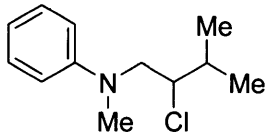
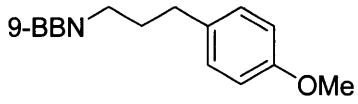
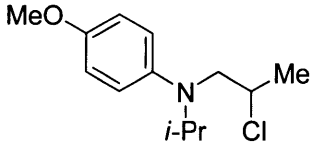
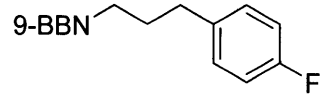
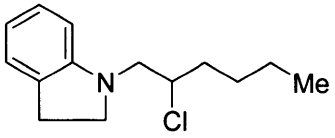
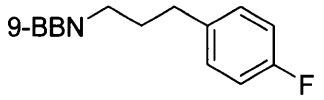
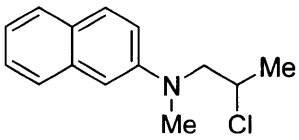
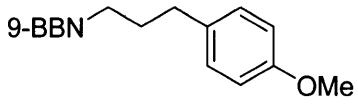
The scope for this method is shown in Table 8 and Table 9. Substitution in the *meta*- and *para*-positions of the aryl ring is well-tolerated (Table 8, entries 2–8). *Ortho*-substitution was detrimental to conversion, and in the one case that did work (Table 8, entry 9), a diminished ee (73%) was obtained. Electron-donating groups (e.g., *p*- and *m*-methoxy) are tolerated, whereas electron-withdrawing groups (e.g., *p*-CF_3) are not. Branching β to the electrophilic center on the alkyl chain is acceptable (Table 8, entries 2, 9), but even weakly coordinating groups like ethers can be detrimental to the selectivity (Table 9, entry 1). More proximal substitution α to the electrophilic center results in lower yield of the coupling product (Table 9, entry 2). The electrophile coupling partner is not limited to only those possessing *N*-methyl groups since *N*-isopropyl substitution is also tolerated (Table 9, entry 3). In addition, an indoline can serve as the *N*-aryl-*N*-alkyl directing group, providing the coupling product with high selectivity (Table 9, entry 4) Silyl ethers (Table 8, entry 5) and acetals (Table 8, entry 7) are both tolerated on the nucleophilic coupling partner.

Table 8. Asymmetric alkyl–alkyl cross-couplings of unactivated secondary alkyl chlorides directed by anilines. (For conditions, see Eq. 2.14.)

entry	electrophile	nucleophile[a]	% yield[b]	% ee[c]
1			67	88
2			76	99
3			78	86
4			66	95
5			60	93[d]
6			70	91
7			64	92
8			68	85
9			68	73

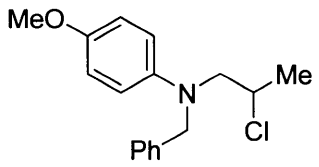
[a] 1.8 equivalents of nucleophiled used. [b] Average of two experiments.
[c] Average of two experiments. Determined by chiral HPLC.
[d] The ee was measured on the desilylated compound.

Table 9. Asymmetric alkyl–alkyl cross-couplings of unactivated secondary alkyl chlorides directed by anilines: more functionalized substrates. (For conditions, see Eq. 2.14.)

entry	electrophile	nucleophile[a]	% yield[b]	% ee[c]
1			74	4
2			43[d]	96
3			64	86
4			76	99
5			70	83

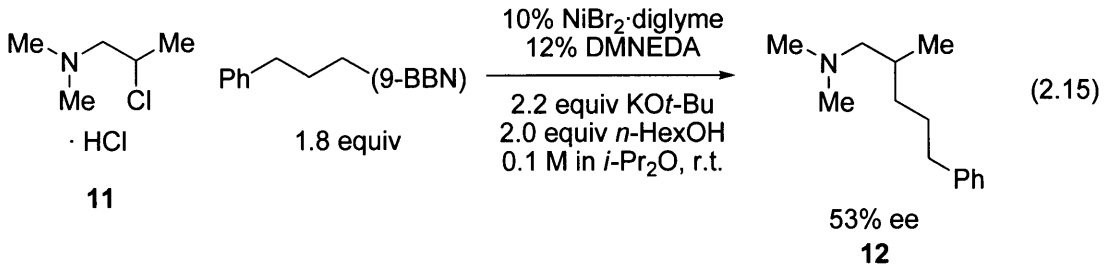
a 1.8 equivalents of nucleophile used. *b* Average of two experiments.
c Average of two experiments. Determined by chiral HPLC.
d 20 mol% $NiBr_2$·diglyme and 24 mol% DMNEDA were used.

The lack of reactivity observed with dibenzyl- (**9b**) and diphenyl- (**9d**) amines was also observed with benzylarylamines (e.g., **10**). In these cases, no conversion of the starting material is observed. Again, it is hypothesized that the increased steric bulk or coordinating ability of the second aryl ring is responsible for the lack of reactivity. Given the apparent increased stability of these types of electrophiles towards decomposition over time, a steric argument seems more likely given the available data.



10

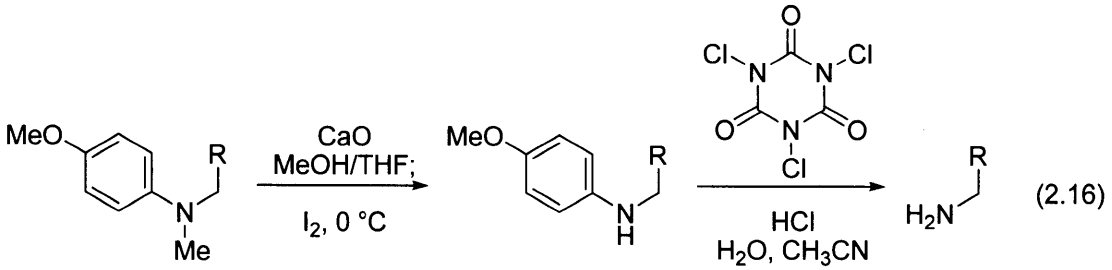
In an effort to identify whether the amine or the aryl ring is the directing group, a trialkylamine hydrochloride salt (**11**) was employed as the starting material (Eq. 2.15). With the addition of another equivalent of potassium *tert*-butoxide to unmask the free amine in situ, coupling was achieved, albeit in lower yield (26%). The ee of the product trialkylamine (**12**) could not be assayed via HPLC or SFC. However, one of the methyl groups could be replaced with an ethoxyacyl group by treatment with excess ethyl chloroformate in refluxing benzene.[38] This carbamate was used to determine the selectivity of the coupling reaction of the amine, and significant enantioenrichment (57% ee) is observed. This result indicates that the nitrogen atom and its lone pair cannot be ruled out as the "directing group." While the aryl ring could be important in achieving high enantioselectivity, its effect could be predominantly steric in nature. However, the ability of a relatively weakly coordinating ether (Table 9, entry 1) to be highly detrimental to the selectivity of the reaction, presumably through competitive binding to the catalyst complex, suggests that the "directing group" may be the extended π-system of the aniline.



(2.15)

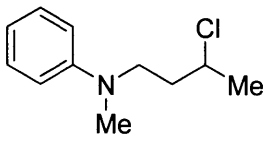
[38] Kraiss, G.; Nádor, K. *Tetrahedron Lett.* **1971**, *12*, 57–58.

Demethylation of the para-methoxyphenylmethyl amine could be accomplished by treatment with a combination of calcium oxide and iodine.[39] Subsequent oxidation of the secondary aniline with trichloroisocyanuric acid afforded the primary amine (Eq. 2.16).[40] These deprotections allowed the determination of absolute stereochemistry by correlation to reported amines.[41] It was found that the (*R*,*R*) ligand provides the (*S*) product. Interestingly, the corresponding configuration of ligand also gives the same sense of stereoinduction in the asymmetric coupling of homobenzylic bromides[32] but the opposite stereochemistry when a carbamate is the directing group.[42]



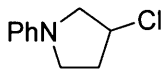
(2.16)

The spatial relationship between the directing group and the electrophilic center is crucial in this reaction. Homologation by a single methylene unit (**13a**) causes the selectivity to drop drastically, and the cyclic electrophile **13b** also couples with low selectivity. This is analogous to the result observed with homobenzylic amines (Figure 1, **8c** and **8d**).



13a

0% ee



13b

41% ee

[39] Acosta, K.; Cessac, J. W.; Rao, P. N.; Kim, H. K. *J. Chem. Soc., Chem. Comm.* **1994**, 1985–1986.
[40] Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2004**, *47*, 7075–7078.
[41] Enders, D.; Schubert, H. *Angew. Chem.* **1984**, *96*, 368–369.
[42] Owston, N. A.; Fu, G. C. *Manuscript in preparation.*

C. Conclusions

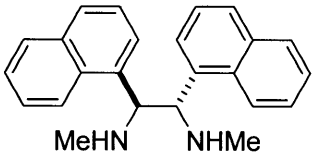
The coupling of unactivated secondary alkyl halides was successfully extended to the enantioselective coupling of unactivated secondary alkyl chlorides bearing anilines. The present work builds upon previous work using directing groups in the coupling of unactivated secondary electrophiles and demonstrates that *N*-alkyl anilines can also serve as "directing groups." While these classes of anilines give the best results, the ability to couple a simple trialkylamine with some selectivity is also demonstrated. Further mechanistic work is ongoing.

D. Experimental

I. General

The following reagents were purchased and used as received: 9-BBN dimer (Aldrich), $NiBr_2$·diglyme (Aldrich; somewhat hygroscopic), KO*t*-Bu (Acros), *n*-HexOH (anhydrous, Aldrich), and *i*-Pr_2O (anhydrous, Aldrich). 2,2′-((1*R*,2*R*)-1,2-Diaminoethane-1,2-diyl)diphenol [(*R*,*R*)-dpen] and 2,2′-((1*S*,2*S*)-1,2-diaminoethane-1,2-diyl)diphenol [(*S*,*S*)-dpen] were purchased from Diaminopharm.

II. Preparation of Materials



Synthesis of the ligand. Enantiopure (*S*,*S*)-N^1,N^2-dimethyl-1,2-di(naphthalene-1-yl)ethane-1,2-diamine was synthesized from (*R*,*R*)-dpen and 1-naphthaldehyde according to a procedure by Chin,[37] methylated according to a procedure by Alper,[20] and purified by flash chromatography (0.1:2.9:97 conc. $NH_4OH_{(aq)}$:MeOH:DCM) to give the ligand. The (*R*,*R*) enantiomer is synthesized by the same method, except starting with (*S*,*S*)-dpen.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27–8.14 (m, 2H), 7.72–7.54 (m, 6H), 7.41–7.30 (m, 6H), 4.69 (s, 2H), 2.23 (s, 6H), 2.08 (br s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 133.9, 132.3, 128.8, 127.6, 125.5, 125.3, 125.2, 125.1, 123.3, 35.1. (a single peak is likely obscured by the triplet at 77 ppm from $CDCl_3$)

FT-IR (KBr) 2945, 2790, 1943, 1596, 1507, 1394, 1162, 1136, 1104 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{24}H_{24}N_2$: 340.2, found: 340.1 (M^+).

$[\alpha]^{23}_D = +77.1°$ (c = 0.0113, $CHCl_3$).

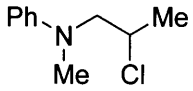
Synthesis of starting materials. These procedures have not been optimized.

Representative procedure for the synthesis of tertiary amide from secondary amines: In a 500-mL round-bottom flask, equipped with stir bar, a secondary amine (20 mmol) was dissolved in dichloromethane (150 mL) and cooled to 0 °C. To this mixture is added triethylamine (4.2 mL, 30 mmol), followed by an α-chloro acyl chloride (20 mmol) dropwise at 0 °C. The cooling bath is removed, and the reaction is allowed to warm to room temperature. After 2 hours, the reaction is quenched by pouring into 1 M HCl (50 mL). The organics are washed with water (50 mL) and brine (50 mL), then dried over sodium sulfate. After filtration, the solution is concentrated to yield the crude amide.

Representative procedure for the synthesis of tertiary amide from primary amines: The primary amide is synthesized according to the procedure using secondary amines. The crude amide is dissolved in dry THF (100 mL) in an oven-dried 250-mL round-bottom flask equipped with stir bar under nitrogen. To this solution at 0 °C is added sodium hydride (0.48 g, 20 mmol). After stirring for 30 min at 0 °C, methyl iodide (1.2 mL, 20 mmol) is added dropwise over 1 minute. The reaction is stirred for 2 hours at 0 °C, and then quenched with methanol. After concentration, the residual oil is partitioned between diethyl ether (100 mL) and water (100 mL). The organics are washed with water (50 mL) and brine (50 mL) and dried over sodium sulfate. After filtration, concentration provides the crude secondary amide.

Representative procedure for the reduction of amides to amines: The amide is dissolved in dry THF (100 mL) in an oven-dried 3-neck 300-mL round bottom flask, equipped with stir bar and reflux condenser. To this solution is added borane·THF (20 mL) dropwise. After the addition is complete, the solution is heated to reflux for 18 hours.

After cooling to room temperature, the reaction is quenched with 1 M sodium hydroxide solution (10 mL). This mixture is concentrated, diluted with diethyl ether (100 mL), and washed with water (100 mL) and brine (100 mL) and dried over sodium sulfate. After filtration, concentration provided the crude amine chloride.



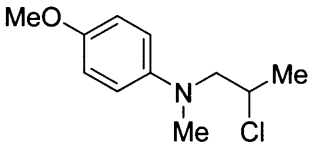
***N*-(2-Chloropropyl)-*N*-methylaniline.** Synthesized from *N*-methylaniline (1.97 mL, 20.0 mmol) and 2-chloropropanoyl chloride (2.16 mL, 20.0 mmol). Purified by chromatography (0%→5% Et_2O/hexanes). Yellow oil. 1.14 g (31% over 2 steps).

^1H NMR (400 MHz, $CDCl_3$) δ 7.28–7.23 (m, 2H), 6.76–6.67 (m, 2H), 4.28 (sextet, 1H, J = 7.2 Hz), 3.68–3.61 (dd, 1H, J = 6.5, 15.2 Hz), 3.52–3.45 (dd, 1H, J = 7.3, 15.2 Hz), 3.04 (s, 3H), 1.53 (d, 3H, J = 1.53).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 129.5, 116.9, 112.0, 61.2, 55.3, 40.0, 23.2.

FT-IR (neat) 2976, 1601, 1509, 1353, 748, 692 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{10}H_{14}ClN$: 183.1, found: 183.1 (M^+).



***N*-(2-Chloropropyl)-4-methoxy-*N*-methylaniline.** Synthesized from 4-methoxy-*N*-methylaniline (1.37 g, 10.0 mmol) and 2-chloropropanoyl chloride (0.99 mL, 10 mmol). Yellow oil. 1.20 g (53% over 2 steps).

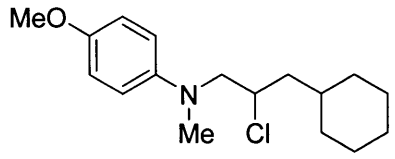
^1H NMR (400 MHz, $CDCl_3$) δ 6.87–6.82 (m, 2H), 6.71–6.65 (m, 2H), 4.24 (sextet, 1H, J

= 6.6 Hz), 3.77 (s, 3H), 3.60–3.53 (dd, 1H, J = 6.4, 15.0 Hz), 3.43–3.36 (dd, 1H, J = 7.3 Hz, 15.0 Hz), 2.97 (s, 3H), 1.52 (d, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 143.7, 115.1, 114.0, 62.3, 56.0, 40.35, 23.2.

FT-IR (neat) 2928, 1513, 1246, 1040, 814 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{11}H_{16}ClNO$: 213.1, found: 213.1 (M^+).



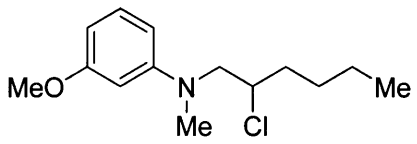
***N*-(2-Chloro-3-cyclohexylpropyl)-4-methoxy-*N*-methylaniline.** Synthesized from 4-methoxy-*N*-methylaniline (1.37 g, 10.0 mmol) and 2-chloro-3-cyclohexylpropionyl chloride (1.74 mL, 10.0 mmol). Yellow oil. 1.12 g (37% over 2 steps)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87–6.82 (m, 2H), 6.70–6.64 (m, 2H), 4.27–4.15 (m, 1H), 3.76 (s, 3H), 3.55–3.40 (m, 2H), 2.96 (s, 3H), 1.80–1.55 (m, 7H), 1.36–1.06 (m, 3H), 1.01–0.71 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 143.9, 115.1, 114.1, 61.2, 58.7, 56.0, 43.9, 40.4, 34.7, 34.4, 32.0, 26.7, 26.5, 26.2.

FT-IR (neat) 2923, 2850, 1513, 1448, 1247, 1041, 813 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{17}H_{26}ClNO$: 295.2, found: 295.2 (M^+).



***N*-(2-Chlorohexyl)-3-methoxy-*N*-methylaniline.** Synthesized from 3-methoxyaniline (1.37 g, 10.0 mmol) and 2-chlorohexanoyl chloride (1.69 g, 10.0 mmol). Yellow oil.

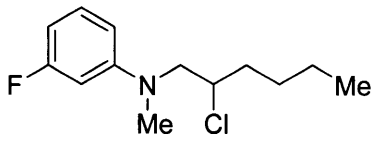
1.63 g (62% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, 1H, J = 8.2, 8.2 Hz), 6.33–6.28 (m, 2H), 6.24–6.21 (m, 1H), 4.21–4.12 (m, 1H), 3.80 (s, 3H), 3.85 (m, 2H), 3.03 (s, 3H), 1.91–1.78 (m, 1H), 1.70–1.50 (m, 2H), 1.44–1.22 (m, 3H), 0.91 (t, 3H, J = 7.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 150.2, 130.2, 105.2, 101.5, 98.8, 60.9, 60.2, 55.3, 40.2, 35.9, 28.8, 22.5, 14.2.

FT-IR (neat) 2956, 2931, 2872, 1612, 1577, 1500, 1456, 1247, 1169, 1056, 824, 750, 687 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{14}H_{22}ClNO$: 255.1, found: 255.1 (M^+).



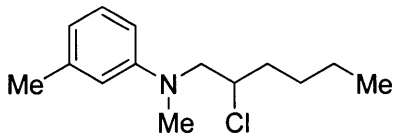
***N*-(2-Chlorohexyl)-3-fluoro-*N*-methylaniline.** Synthesized from 3-fluoro-*N*-methylaniline (1.13 mL, 10.0 mmol) and 2-chlorohexanoyl chloride (1.69 g, 10.0 mmol). Yellow oil. 1.78 g (74% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.10 (m, 1H), 6.45–6.38 (m, 2H), 6.38–6.31 (m, 1H), 4.18–4.10 (m, 1H), 3.57 (d, 2H, J = 6.8 Hz), 3.03 (s, 3H), 1.85–1.77 (m, 1H), 1.70–1.61 (m, 1H), 1.64–1.21 (m, 4H), 0.91 (t, 3H, J = 7.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4 (d, J = 242.8 Hz), 150.4, 130.4 (d, J = 10.4 Hz), 107.6 (d, J = 21.6 Hz), 99.1 (d, J = 26.2 Hz), 60.7, 60.0, 40.2, 35.8, 28.7, 22.5, 14.1.

FT-IR (neat) 2988, 2931, 2886, 1621, 1577, 1502, 1362, 1235, 1162, 1009, 822, 754, 682 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{13}H_{19}ClFN$: 243.1, found: 243.1 (M^+).



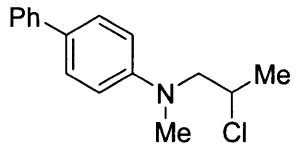
***N*-(2-Chlorohexyl)-*N*,3-dimethylaniline.** Synthesized from *N*-methyl-*m*-toluidine (2.00 g, 16.5 mmol) and 2-chlorohexanoyl chloride (2.47 mL, 16.5 mmol). Yellow oil. 2.31 g (58% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.10 (m, 1H), 6.65–6.46 (m, 3H), 4.20–4.11 (m, 1H), 3.63–3.51 (m, 2H), 3.02 (s, 3H), 2.32 (s, 3H), 1.89–1.78 (m, 1H), 1.72–1.55 (m, 2H), 1.47–1.25 (m, 3H), 0.91 (t, 3H, J = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 138.8, 129.1, 112.9, 110.4, 109.4, 59.2, 59.0, 39.7, 36.8, 28.9, 23.5, 22.2, 14.2.

FT-IR (neat) 2929, 2860, 1602, 1499, 1065, 764, 693, 668 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{14}H_{22}ClN$: 239.1, found: 239.1 (M^+).



***N*-(2-Chloropropyl)-*N*-methylbiphenyl-4-amine.** Synthesized from 4-biphenylamine (3.38 g, 20.0 mmol) and 2-chloropropanoyl chloride (1.97 mL, 20.0 mmol). White solid. 2.08 g (40% over 3 steps). mp 157 °C (dec.).

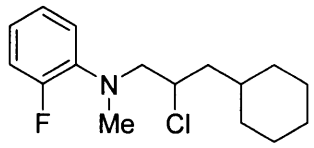
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.46 (m, 4H), 7.42–7.35 (m, 2H), 7.29–7.23 (m, 1H), 6.79–6.73 (m, 2H), 4.32 (sextet, 1H, J = 6.7 Hz), 3.68 (dd, 1H, J = 6.5, 15.2 Hz), 3.54 (dd, 1H, J = 7.3, 15.2 Hz), 3.09 (s, 3H), 1.57 (d, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 141.7, 129.2, 128.4, 127.8, 126.2, 126.0, 112.1,

60.0, 55.0, 39.8, 23.2.

FT-IR (neat) 2924, 2845, 1612, 1505, 1456, 1201, 816, 761, 697 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{16}H_{18}ClN$: 259.1, found: 259.1 (M^+).



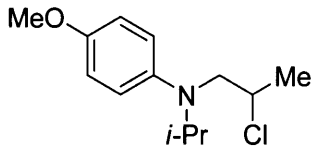
***N*-(2-Chloro-3-cyclohexylpropyl)-2-fluoro-*N*-methylaniline.** Synthesized from 2-fluoroaniline (1.44 mL, 15.0 mmol) and 2-chloro-3-cyclohexylpropionyl chloride (3.14 g, 15.0 mmol). Yellow oil. 1.80 g (42% over 3 steps).

^1H NMR (400 MHz, $CDCl_3$) δ 7.07–6.80 (m, 4H), 4.26–4.17 (m, 1H), 3.55–3.47 (m, 1H), 3.43–3.35 (m, 1H), 2.96 (s, 3H), 1.79–1.47 (m, 7H), 1.33–1.05 (m, 3H), 1.00–0.73 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8 (d, J = 304.8 Hz), 139.2 (d, J = 10.3 Hz), 124.6 (d, J = 4.2 Hz), 121.0 (d, J = 9.8 Hz), 119.2 (d, J = 4.5 Hz), 116.5 (d, J = 26.5 Hz), 62.4 (d, J = 7.3 Hz), 59.2 (d, J = 2.3 Hz), 43.8, 41.3, 34.9, 34.2, 32.1, 26.9, 26.5, 26.2.

FT-IR (neat) 2923, 2852, 1614, 1505, 1448, 1230, 746 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{16}H_{23}ClFN$: 283.2, found: 283.1 (M^+).



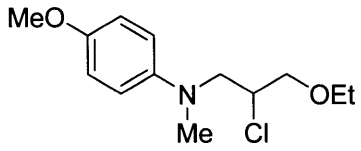
***N*-(2-Chloropropyl)-*N*-isopropyl-4-methoxyaniline.** Synthesized from 4-methoxy-*N*-isopropylaniline (2.70 g, 20.0 mmol) and 2-chloropropionyl chloride (1.97 mL, 20.0 mmol). Yellow oil. 1.74 g (34% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93–6.87 (m, 2H), 6.86–6.81 (m, 2H), 4.02–3.89 (m, 1H), 3.77 (s, 3H), 3.65 (septet, 1H, J = 6.7 Hz), 3.43–3.35 (dd, 1H, J = 5.2, 13.9 Hz), 3.12–3.03 (dd, 1H, J = 8.7, 14.0 Hz), 1.48 (d, 3H, J = 6.5 Hz), 1.13 (d, 3H, J = 6.6 Hz), 1.50 (d, 3H, J = 6.6 Hz). 61.2, 55.3, 40.0, 23.2

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 144.2, 121.2, 114.1, 62.0, 55.8, 55.4, 51.6, 22.4, 20.2, 19.8.

FT-IR (neat) 2963, 2935, 2866, 1509, 1219, 1042, 822, 612 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{13}H_{20}ClNO$: 241.1, found: 241.1 (M^+).



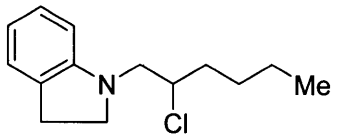
***N*-(2-Chloro-3-ethoxypropyl)-4-methoxy-*N*-methylaniline.** Synthesized from 4-methoxy-*N*-methylaniline (2.06 g, 15.0 mmol) and 2-chloro-3-ethoxypropionyl chloride (2.38 g, 15.0 mmol). Yellow oil. 2.02 g (52% over 2 steps)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86–6.80 (m, 2H), 6.72–6.67 (m, 2H), 4.23–4.16 (m, 1H), 3.77–3.70 (m, 1H), 3.75 (s, 3H), 3.63 (d, 2H, J = 4.8 Hz), 3.58–3.44 (m, 3H), 2.95 (s, 3H), 1.23 (t, 3H, J = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 145.1, 114.9, 113.9, 74.1, 66.8, 62.4, 56.1, 55.7, 39.8, 15.4.

FT-IR (neat) 2929, 2851, 1240, 1222, 1036, 750, 700 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{13}H_{20}ClNO_2$: 257.1, found: 257.1 (M^+).



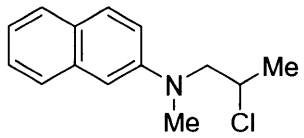
1-(2-Chlorohexyl)indoline. Synthesized from indoline (1.12 mL, 10.0 mmol) and 2-chlorohexanoyl chloride (1.69 g, 10.0 mmol). Yellow oil. 1.09 g (46% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.04 (m, 2H), 6.70–6.64 (m, 1H), 6.48–6.44 (m, 1H), 4.13–4.04 (m, 1H), 3.52–3.45 (m, 2H), 3.35 (dd, 2H, J = 6.6, 14.3 Hz), 3.29 (dd, 2H, J = 6.6, 14.3 Hz), 3.05–3.00 (m, 2H), 1.99–1.88 (m, 1H), 1.77–1.55 (m, 2H), 1.50–1.22 (m, 4H), 0.93 (t, 3H, J = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 129.5, 127.5, 124.7, 117.9, 106.5, 61.6, 57.6, 54.7, 35.9, 28.9, 28.8, 22.5, 14.2.

FT-IR (neat) 2956, 2930, 2859, 1607, 1489, 1267, 743 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{14}H_{20}ClN$: 237.1, found: 237.1 (M^+).



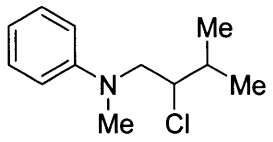
***N*-(2-Chloropropyl)-*N*-methylnaphthalen-2-amine.** Synthesized from 2-naphthylamine (2.00 g, 14.0 mmol) and 2-chloropropionyl chloride (1.38 mL, 14.0 mmol). White solid. 1.82 g (55% over 3 steps). mp 153 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.62 (m, 3H), 7.40–7.34 (m, 1H), 7.25–7.18 (m, 1H), 7.13–7.09 (m, 1H), 6.90–6.87 (m, 1H), 4.33 (sextet, 1H, J = 6.8 Hz), 3.76 (dd, 1H, J = 6.6, 15.2 Hz), 3.61 (dd, 1H, J = 7.3, 15.2 Hz), 3.15 (s, 3H), 1.55 (d, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 135.4, 128.8, 127.6, 126.5, 126.3, 126.2, 121.8, 116.1, 105.5, 59.9, 55.2, 39.8, 23.8.

FT-IR (neat) 2924, 2855, 1629, 1512, 824, 743 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{14}H_{16}ClN$: 233.1, found: 233.1 (M^+).



***N*-(2-chloro-3-methylbutyl)-*N*-methylaniline.** Synthesized from *N*-methylaniline (3.10 g, 20.0 mmol) and 2-chloro-3-methylbutanoyl chloride (2.16 mL, 20.0 mmol). Yellow oil. 1.36 g (32%).

^1H NMR (400 MHz, $CDCl_3$) δ 7.28–7.21 (m, 2H), 6.75–6.66 (m, 3H), 4.21–4.15 (m, 1H), 3.68 (dd, 1H, *J* = 6.0, 15.4 Hz), 3.55 (dd, 1H, *J* = 7.6, 15.4 Hz), 3.03 (s, 3H), 2.09–2.00 (m, 1H), 1.08–1.02 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 129.5, 116.8, 112.1, 67.1, 57.9, 40.1, 31.7, 20.8, 16.4.

FT-IR (neat) 2968, 2914, 1600, 1507, 1362, 1210, 747, 692 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{14}H_{22}ClNO$: 255.1, found: 255.1 (M^+).

III. Suzuki Cross-Coupling Reactions.

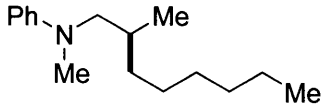
Alkyl borane is prepared inside of the glovebox by adding 9-BBN dimer (165 mg, 0.675 mmol) and alkene (1.35 mmol) sequentially into 0.7 mL diisopropyl ether in a sealed vial with stir bar (for a total concentration of ~1.5 M). The reaction is stirred at 60 °C for 1 hour on the benchtop and cooled to r.t.

In the glovebox, the activated borane solution is prepared by adding KO*t*-Bu (101mg, 0.9 mmol) and *n*-HexOH (188uL, 1.5 mmol) to a 4 mL vial with a stir bar. The nucleophile

solution, as prepared above, is added, and the reaction is stirred for 30 minutes.

Inside of a glovebox, to an oven-dried 10 mL vial is added $NiBr_2$-diglyme (26.7 mg, 0.075 mmol) and (*R*,*R*)-N^1,N^2-dimethyl-*trans*-1,2-di(naphthalen-1-yl)ethane-1,2-diamine (30.8mg, 0.090 mmol) in 6 mL of diisopropylether. After 30 minutes of stirring, Electrophile (0.75 mmol) is added, followed by the solution of activated borane dropwise over 2 min. The reaction is stirred 40 hours. The reaction mixture is filtered through silica gel eluting with 20 mL of ether. After concentration, the residual oil is diluted with 10 mL of hexanes and cooled to 0 °C for 30 minutes. The white precipitate is filtered off by syringe filter and the resultant solution is concentrated to give the crude product.

A second run is performed with the (*S*,*S*) enantiomer of the ligand.



(*S*)-*N*-Methyl-*N*-(2-methyloctyl)aniline (Table 8, entry 1). *N*-(2-Chloropropyl)-*N*-methylaniline (138 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-hexene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 117 mg (68%, 88% ee). Second run: 118 mg (68%, 88% ee).

The ee was determined by HPLC on an OJ-H column (hexanes, 1.0 mL / min) with t_r = 19.9 min (minor), 21.5 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 2H), 6.70–6.63 (m, 3H), 3.21 (dd, 1H, *J* = 6.6, 14.5 Hz), 3.02 (dd, 1H, *J* = 8.1, 14.5 Hz), 2.95 (s, 3H), 1.98–1.82 (m, 1H), 1.44–1.04

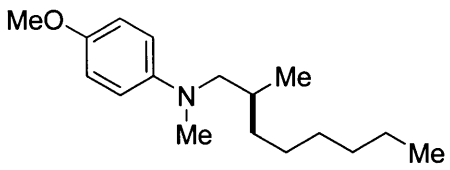
(m, 10H), 0.92–0.83 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 129.3, 115.7, 112.0, 60.1, 39.7, 35.0, 32.5, 32.1, 29.9, 27.3, 22.9, 18.0, 14.3.

FT-IR (neat) 2956, 2926, 2856, 1729, 1600, 1507, 1465, 992, 746, 691 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{16}H_{27}N$: 233.2, found: 233.2 (M^+).

$[\alpha]^{23}_D$ = +7.3° (c 0.0075, $CHCl_3$).



(*S*)-4-Methoxy-*N*-methyl-*N*-(2-methyloctyl)aniline (Table 8, entry 2). *N*-(2-Chloropropyl)-4-methoxy-*N*-methylaniline (160 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-hexene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 152 mg (77%, 99% ee). Second run: 148 mg (75%, 99% ee).

The ee was determined by HPLC on an OJ-H column (1% isopropanol/hexanes, 1.0 mL / min) with t_r = 8.6 min (minor), 9.5 min (major).

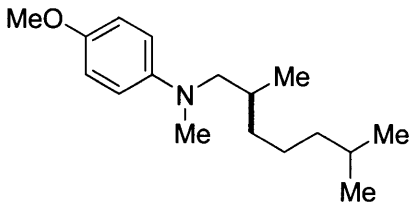
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86–6.80 (m, 2H), 6.69–6.62 (m, 2H), 3.76 (s, 3H), 3.11 (dd, 1H, *J* = 6.6, 14.3 Hz), 2.93 (dd, 1H, *J* = 8.1, 14.3 Hz), 2.87 (s, 3H), 1.91–1.78 (m, 1H), 1.44–1.00 (m, 10H), 0.91–0.84 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 145.3, 114.9, 113.9, 61.3, 56.1, 40.1, 35.0, 32.5, 32.1, 29.9, 27.3, 22.9, 18.1, 14.4.

FT-IR (neat) 2955, 2926, 2855, 1513, 1464, 1244, 1181, 1043, 811.3 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{17}H_{29}NO$: 263.2, found: 263.2 (M^+).

$[\alpha]^{23}_D$ = +4.4° (c 0.0051, $CHCl_3$).



(S)-*N*-(2,6-dimethylheptyl)-4-methoxy-N-methylaniline (Table 8, entry 3). *N*-(2-Chloropropyl)-4-methoxy-*N*-methylaniline (160 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-methylpent-1-ene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 150 mg (76%, 84% ee). Second run: 155 mg (79%, 85% ee).

The ee was determined by SFC on an OD-H column (2.5% MeOH/$CO_{2(l)}$, 3.0 mL / min, 100 bar) with t_r = 5.7 min (minor), 6.0 min (major).

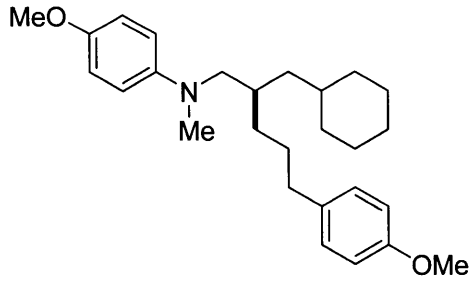
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86–6.80 (m, 2H), 6.69–6.63 (m, 2H), 3.76 (s, 3H), 3.10 (dd, 1H, *J* = 6.8, 14.4 Hz), 2.93 (dd, 1H, *J* = 8.0, 14.4 Hz), 2.87 (s, 3H), 1.90–1.80 (m, 1H), 1.58–1.46 (m, 1H), 1.42–1.31 (m, 2H), 1.31–1.19 (m, 1H), 1.18–1.01 (m, 3H), 0.91–0.84 (m, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 145.3, 115.0, 113.9, 61.3, 56.1, 40.1, 39.6, 35.2, 32.3, 28.2, 25.0, 23.0, 22.8, 18.1.

FT-IR (neat) 2954, 2928, 2868, 1514, 146, 1244, 1181, 1043, 811, 700 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{17}H_{29}NO$: 263.2, found: 263.1 (M^+).

$[\alpha]^{23}_D$ = +4.3° (c 0.0080, $CHCl_3$).



(*R*)-*N*-(2-(cyclohexylmethyl)-5-(4-methoxyphenyl)pentyl)-4-methoxy-*N*-methylaniline (Table 8, entry 4). *N*-(2-Chloro-3-cyclohexylpropyl)-4-methoxy-*N*-methylaniline (222 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 209 mg (68%, 93% ee). Second run: 200 mg (65%, 93% ee).

The ee was determined by SFC on an OD-H column (15% MeOH/CO_2(*l*), 3.0 mL / min, 100 bar) with t_r = 7.8 min (minor), 8.1 min (major).

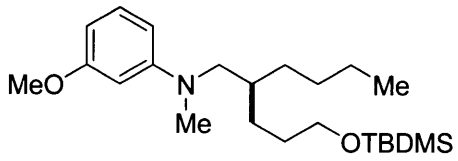
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09–7.04 (m, 2H), 6.85–6.79 (m, 4H), 6.68–6.63 (m, 2H), 3.79 (s, 3H), 3.76 (s, 3H), 3.07–2.96 (m, 2H), 2.81 (s, 3H), 2.53–2.47 (m, 2H), 1.92–1.81 (m, 1H), 1.72–1.50 (m, 7H), 1.43–1.07 (m, 8H), 0.92–0.73 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 151.4, 145.5, 135.0, 129.5, 114.9, 114.3, 113.9, 59.5, 56.1, 55.5, 40.5, 39.9, 35.7, 35.3, 34.4, 33.8, 33.6, 32.2, 28.8, 26.9, 26.7, 26.6.

FT-IR (neat) 2922, 2850, 1612, 1512, 1449, 1245, 1179, 1040, 811 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{27}H_{39}NO_2$: 409.3, found: 409.3 (M^+).

$[\alpha]^{23}_D$ = +8.4° (c 0.0066, $CHCl_3$).



(*S*)-*N*-(2-(3-(tert-butyldimethylsilyloxy)propyl)hexyl)-3-methoxy-*N*-methylaniline

(Table 8, entry 5). *N*-(2-chlorohexyl)-3-methoxy-*N*-methylaniline (192 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of allyloxy(*tert*-butyl)dimethylsilane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 177 mg (60%, 93% ee). Second run: 180 mg (61%, 93% ee).

The ee was determined by HPLC of the corresponding desilylated alcohol[43] on an AS-H column (1% isopropanol/hexanes, 1.0 mL / min) with t_r = 22.4 min (major), 23.9 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.07 (m, 1H), 6.30–6.27 (m, 1H), 6.27–6.19 (m, 2H), 3.79 (s, 3H), 3.57 (t, 2H, J = 6.6 Hz), 3.22–3.18 (m, 2H), 2.92 (s, 3H), 1.88–1.76 (m, 1H), 1.62–1.44 (m, 2H), 1.40–1.21 (m, 8H), 0.92–0.83 (m, 12H), 0.03 (s, 6H).

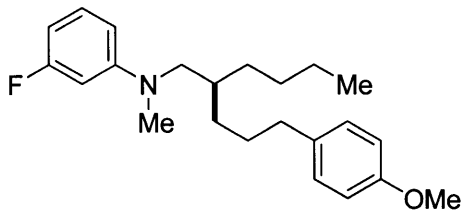
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 151.4, 129.9, 105.3, 100.7, 98.6, 63.8, 57.8, 55.3, 39.8, 36.7, 31.5, 30.0, 28.9, 27.8, 26.2, 23.4, 18.6, 14.3, –5.0.

FT-IR (neat) 2954, 2920, 2857, 1612, 1576, 1501, 1464, 1248, 1169, 1098, 835, 775 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{27}H_{43}NO_2Si$: 393.3, found: 393.3 (M^+).

$[\alpha]^{23}_D$ = +4.7° (c 0.0053, $CHCl_3$).

[43] The silyl ether was treated with 5 equivalents of 1 M TBAF in THF and stirred for 2 hours at room temperature.



(*S*)-3-Fluoro-*N*-(2-(3-(4-methoxyphenyl)propyl)hexyl)-*N*-methylaniline (Table 8, entry 6). *N*-(2-Chlorohexyl)-3-fluoro-*N*-methylaniline (183 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 246 mg (69%, 93% ee). Second run: 251 mg (70%, 90% ee).

The ee was determined by HPLC on an SFC column (gradient 5%→20% MeOH/$CO_{2(l)}$, 3.0 mL / min, 100 bar) with t_r = 6.5 min (minor), 6.7 min (major).

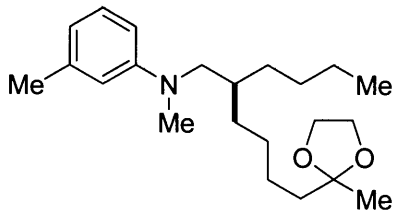
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.09 (m, 1H), 7.09–7.04 (m, 2H), 6.85–6.79 (m, 2H), 6.42–6.29 (m, 3H), 3.79 (s, 3H), 3.21–3.09 (m, 2H), 2.89 (s, 3H), 2.56–2.45 (m, 2H), 1.89–1.77 (m, 1H), 1.67–1.50 (m, 3H), 1.39–1.19 (m, 9H), 0.88 (t, 3H, J = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (d, J = 153.3 Hz), 157.9, 151.6 (d, J = 10.6 Hz), 134.8, 130.2 (d, J = 10.6 Hz), 129.5, 113.9, 107.6 (d, J = 2.1 Hz), 102.1 (d, J = 21.7 Hz), 98.9 (d, J = 30.0 Hz), 57.6, 55.5, 39.8, 36.5, 35.6, 31.44, 31.38, 28.92, 28.88, 23.4, 14.3.

FT-IR (neat) 2930, 2858, 1620, 1512, 1245, 821, 751, 683 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{23}H_{32}FNO$: 357.2, found: 357.2 (M^+).

$[\alpha]^{23}_D$ = +10.6° (c 0.0072, $CHCl_3$).



(*S*)-*N*-(2-Butyl-6-(2-methyl-1,3-dioxolan-2-yl)hexyl)-*N*,3-dimethylaniline (Table 8, entry 7). *N*-(2-Chlorohexyl)-*N*,3-dimethylaniline (180 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 2-(but-3-enyl)-2-methyl-1,3-dioxolane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 172 mg (66%, 92% ee). Second run: 165 mg (63%, 91% ee).

The ee was determined by SFC on an OD-H column (5% MeOH/$CO_{2(l)}$→20% MeOH/$CO_{2(l)}$, 3.0 mL / min, 100 bar) with t_r = 5.5 min (minor), 6.2 min (major).

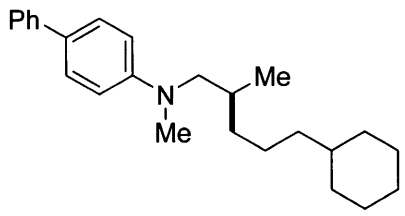
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13–7.07 (m, 1H), 7.09–7.04 (m, 2H), 6.52–6.47 (m, 3H), 3.97–3.87 (m, 4H), 3.14 (d, 2H, *J* = 7.3 Hz), 2.92 (s, 3H), 2.31 (s, 3H), 1.84–1.75 (m, 1H), 1.66–1.57 (m, 2H), 1.41–1.19 (m, 17H), 0.89 (t, 3H, *J* = 6.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 138.8, 129.1, 116.8, 112.9, 110.4, 109.4, 64.8, 57.9, 39.7, 39.4, 36.8, 31.9, 31.6, 28.9, 27.0, 24.8, 23.9, 23.4, 22.2, 14.3.

FT-IR (neat) 2929, 2860, 1602, 1499, 1065, 764, 693, 668 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{22}H_{37}NO_2$: 347.3, found: 347.2 (M^+).

$[\alpha]^{23}_D$ = +2.7° (c 0.0059, $CHCl_3$).



(*S*)-*N*-(5-Cyclohexyl-2-methylpentyl)-*N*-methylbiphenyl-4-amine (Table 8, entry 8). *N*-(2-Chloropropyl)-*N*-methylbiphenyl-4-amine (195 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of allylcyclohexane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 184 mg (70%, 85% ee). Second run: 172 mg (66%, 85% ee).

The ee was determined by HPLC on an OJ-H column (1% isopropanol/hexanes, 1.0 mL / min) with t_r = 19.3 min (minor), 23.8 min (major).

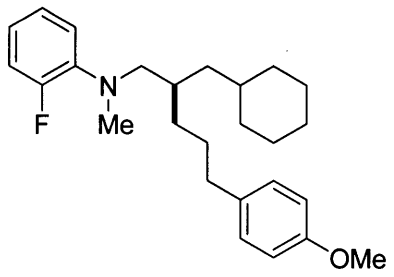
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.54 (m, 2H), 7.52–7.47 (m, 2H), 7.42–7.36 (m, 2H), 7.27–7.22 (m, 1H), 6.77–6.72 (m, 2H), 3.27 (dd, 1H, *J* = 6.6, 14.6 Hz), 3.07 (dd, 1H, *J* = 8.1, 14.6 Hz), 3.01 (s, 3H), 2.00–1.90 (m, 1H), 1.74–1.53 (m, 4H), 1.47–1.06 (m, 10H), 0.92 (d, 3H, *J* = 6.8 Hz), 0.94–0.80 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 141.5, 128.8, 128.4, 127.9, 126.4, 126.0, 112.1, 60.0, 39.8, 38.1, 37.9, 35.2, 33.8, 33.6, 32.5, 27.0, 26.7, 24.5, 18.0.

FT-IR (neat) 2922, 2850, 1612, 1525, 1490, 1200, 816, 761, 696 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{25}H_{35}N$: 349.3, found: 349.3 (M^+).

$[\alpha]^{23}_D$ = +7.6° (c 0.0060, $CHCl_3$).



(*R*)-*N*-(2-(cyclohexylmethyl)-5-(4-methoxyphenyl)pentyl)-2-fluoro-*N*-methylaniline (Table 8, entry 9). *N*-(2-Chloro-3-cyclohexylpropyl)-2-fluoro-*N*-methylaniline (213 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 210 mg (70%, 74% ee). Second run: 201 mg (67%, 72% ee).

The ee was determined by SFC on an OJ column (gradient 5%→20% MeOH/CO_2(*l*), 3.0 mL / min, 100 bar) with t_r = 9.7 min (minor), 10.9 min (major).

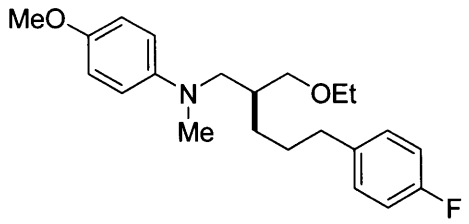
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09–7.04 (m, 2H), 7.03–6.94 (m, 2H), 6.91–6.85 (m, 1H), 6.84–6.78 (m, 3H), 3.78 (s, 3H), 3.01–2.89 (m, 2H), 2.78 (s, 3H), 2.48 (t, 2H, *J* = 7.7 Hz), 1.86–1.76 (m, 1H), 1.70–1.51 (m, 7H), 1.44–1.04 (m, 9H), 0.89–0.71 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 155.4 (d, *J* = 245.0 Hz), 137.8 (d, *J* = 23.2 Hz), 135.1, 129.4, 124.3 (d, *J* = 3.3 Hz), 120.7 (d, *J* = 7.7 Hz), 119.5 (d, *J* = 3.5 Hz), 116.3 (d, *J* = 21.1 Hz), 113.8, 59.8 (d, *J* = 3.9 Hz), 55.5, 40.7 (d, *J* = 2.4 Hz), 40.5, 35.7, 35.2, 34.3, 33.8, 32.9, 32.1, 31.1, 28.6, 26.9, 26.63, 26.57.

FT-IR (neat) 2923, 2851, 1612, 1512, 1449, 1246, 1040, 824, 748 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{26}H_{36}FNO$: 397.3, found: 397.3 (M^+).

$[\alpha]^{23}_D$ = +3.9° (c 0.0066, $CHCl_3$).



(*R*)-*N*-(2-(Ethoxymethyl)-5-(4-fluorophenyl)pentyl)-4-methoxy-*N*-methylaniline

(Table 9, entry 1). *N*-(2-Chloro-3-ethoxypropyl)-4-methoxy-*N*-methylaniline (194 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-allyl-4-fluorobenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 266 mg (72%, 4% ee). Second run: 280 mg (75%, 4% ee).

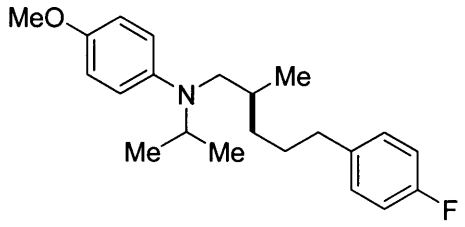
The ee was determined by HPLC on an AD-H column (1% isopropanol/hexanes, 1.0 mL / min) with t_r = 6.5 min (minor), 7.3 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14–7.08 (m, 2H), 6.99–6.92 (m, 2H), 6.85–6.79 (m, 2H), 6.71–6.65 (m, 2H), 3.76 (s, 3H), 3.41 (q, 2H, *J* = 6.8 Hz), 3.35 (dd, 2H, *J* = 1.8, 4.5 Hz), 3.28 (dd, 1H, *J* = 8.4, 14.5 Hz), 3.07 (dd, 1H, *J* = 6.2, 14.5 Hz), 2.85 (s, 3H), 2.60–2.54 (m, 2H), 2.00–1.89 (m, 1H), 1.75–1.55 (m, 2H), 1.50–1.30 (m, 2H), 1.19 (t, 3H, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (d, *J* = 138.8 Hz), 151.4, 145.1, 138.3 (d, *J* = 3.1 Hz), 129.9 (d, *J* = 7.7 Hz), 115.1 (d, *J* = 21.0 Hz), 114.9, 113.9, 70.9, 66.6, 56.14, 56.08, 39.8, 37.9, 35.6, 29.5, 29.4, 15.4.

FT-IR (neat) 2927, 2856, 1511, 1245, 1220, 1041, 814, 750, 700 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{22}H_{30}FNO_2$: 359.2, found: 359.2 (M^+).



(*S*)-*N*-(5-(4-fluorophenyl)-2-methylpentyl)-*N*-isopropyl-4-methoxyaniline (Table 9, entry 3). *N*-(2-chloropropyl)-*N*-isopropyl-4-methoxyaniline (181 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-allyl-4-fluorobenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 160 mg (62%, 87% ee). Second run: 172 mg (67%, 85% ee).

The ee was determined by SFC on an OJ column (gradient 5%→10% MeOH/CO_2(*l*), 3.0 mL / min, 100 bar) with t_r = 5.4 min (major), 5.7 min (minor).

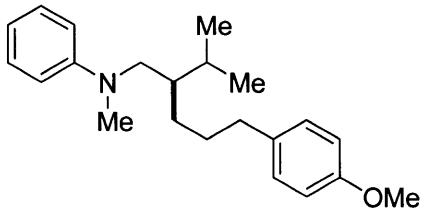
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12–7.05 (m, 2H), 6.98–6.91 (m, 2H), 6.87–6.78 (m, 4H), 3.77 (s, 3H), 3.66 (septet, 1H, *J* = 6.6), 2.83 (dd, 1H, *J* = 6.5, 13.5 Hz), 2.68 (dd, 1H, *J* = 7.5, 13.5 Hz), 2.60–2.44 (m, 2H), 1.70–1.40 (m, 4H), 1.07 (d, 3H, *J* = 6.6 Hz), 1.04 (d, 3H, *J* = 6.6 Hz), 0.85 (d, 3H, *J* = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3 (d, *J* = 242.6 Hz), 153.3, 144.0, 138.5 (d, *J* = 3.2 Hz), 129.9 (d, *J* = 7.6 Hz), 121.3, 115.1 (d, *J* = 21.0 Hz), 114.2, 55.7, 54.3, 51.6, 35.6, 34.6, 30.8, 29.2, 20.2, 19.8, 18.2.

FT-IR (neat) 2964, 2931, 2866, 1509, 1242, 1221, 1041, 822 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{22}H_{30}FNO$: 343.2, found: 343.1 (M^+).

$[\alpha]^{23}_D$ = +13.3° (c 0.0063, $CHCl_3$).



***N*-(2-isopropyl-5-(4-methoxyphenyl)pentyl)-*N*-methylaniline (Table 9, entry 3).** *N*-(2-Chloro-3-methylbutyl)-*N*-methylaniline (158 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used with $NiBr_2$-diglyme (53.4 mg, 0.150 mmol) and (*R*,*R*)-N^1,N^2-dimethyl-*trans*-1,2-di(naphthalen-1-yl)ethane-1,2-diamine (61.6mg, 0.180 mmol). The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 108 mg (44%, 95% ee). Second run: 103 mg (42%, 97% ee).

The ee was determined by HPLC on an AS-H column (1% isopropanol/hexanes, 1.0 mL / min) with t_r = 28.3 min (minor), 30.6 min (major).

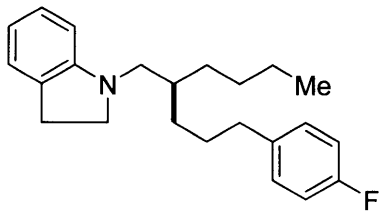
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 2H), 7.09–7.04 (m, 2H), 6.85–6.79 (m, 2H), 6.70–6.64 (m, 3H), 3.79 (s, 3H), 3.24 (dd, 1H, *J* = 7.0, 14.6 Hz), 3.15 (dd, 1H, *J* = 7.6, 14.6 Hz), 2.90 (s, 3H), 2.51 (t, 2H, *J* = 7.8 Hz), 1.86–1.76 (m, 1H), 1.76–1.55 (m, 3H), 1.41–1.18 (m, 2H), 0.92 (d, 3H, *J* = 6.9 Hz), 0.88 (d, 3H, *J* = 6.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 150.1, 134.9, 129.4, 129.3, 115.8, 113.9, 112.2, 55.5, 54.8, 42.1, 39.6, 35.7, 31.2, 28.3, 27.9, 19.6, 18.6.

FT-IR (neat) 2955, 2932, 2869, 1599, 1511, 1464, 1245, 1177, 1036, 829, 747, 692 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{22}H_{31}NO_2$: 325.2, found: 325.2 (M^+).

$[\alpha]^{23}_D$ = +5.4° (c 0.0056, $CHCl_3$).



(*S*)-1-(2-(3-(4-fluorophenyl)propyl)hexyl)indoline (Table 9, entry 4). 1-(2-Chlorohexyl)indoline (178 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-allyl-4-fluorobenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 199 mg (78%, 99% ee). Second run: 189 mg (74%, 99% ee).

The ee was determined by SFC on an OJ column (gradient 5%→20% MeOH/CO_2(*l*), 3.0 mL / min, 100 bar) with t_r = 7.4 min (major), 7.8 min (minor).

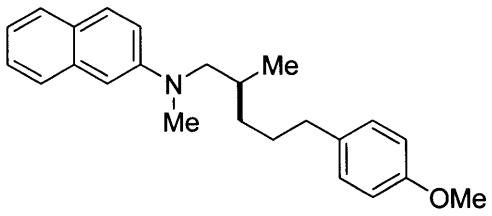
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.09 (m, 2H), 7.08–7.02 (m, 2H), 6.99–6.92 (m, 2H), 6.62 (t, 1H, *J* = 7.3 Hz), 6.41 (d, 1H, *J* = 7.7 Hz), 3.36–3.25 (m, 2H), 2.95 (t, 2H, *J* = 8.4 Hz), 2.88 (d, 2H, *J* = 7.2 Hz), 2.58 (t, 2H, *J* = 7.7 Hz), 1.76–1.57 (m, 3H), 1.49–1.23 (m, 8H), 0.90 (t, 3H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, *J* = 243.0 Hz), 153.6, 138.4 (d, *J* = 3.2 Hz), 129.86 (d, *J* = 7.6 Hz), 129.85, 127.5, 124.5, 117.2, 115.1 (d, *J* = 21.0 Hz), 106.5, 54.7, 54.4, 37.1, 35.7, 31.8, 31.7, 29.1, 28.9, 28.8, 23.4, 14.3.

FT-IR (neat) 2928, 2857, 1607, 1510, 1489, 1460, 1221, 1156, 832, 743, 714 cm^{-1}.

MS (APCI + ESI) *m/z* (M^+) calcd for $C_{23}H_{30}FN$: 339.2, found: 339.1 (M^+).

$[\alpha]^{23}_D$ = +0.97° (c 0.0071, $CHCl_3$).



(*S*)-*N*-(5-(4-Methoxyphenyl)-2-methylpentyl)-*N*-methylnaphthalen-2-amine (Table 9, entry 5). *N*-(2-Chloropropyl)-*N*-methylnaphthalen-2-amine (176 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used. The product was purified by flash chromatography on reverse phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 180 mg (69%, 83% ee). Second run: 185 mg (71%, 83% ee).

The ee was determined by HPLC on an OD-H column (1% isopropanol/hexanes, 1.0 mL / min) with t_r = 17.1 min (major), 18.6 min (minor).

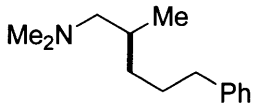
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.58 (m, 3H), 7.36–7.29 (m, 1H), 7.18–7.02 (m, 4H), 6.84–6.76 (m, 3H), 3.76 (s, 3H), 3.29 (dd, 1H, *J* = 6.8, 14.6 Hz), 3.14 (dd, 1H, *J* = 8.0, 14.6 Hz), 3.01 (s, 3H), 2.56–2.46 (m, 2H), 2.03–1.91 (m, 1H), 1.90–1.34 (m, 5H), 1.21–1.10 (m, 1H), 0.90 (d, 3H, *J* = 6.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 147.8, 135.4, 134.8, 129.4, 128.8, 127.6, 126.5, 126.3, 126.2, 121.8, 116.1, 113.9, 105.5, 59.9, 55.4, 39.8, 35.5, 34.4, 32.5, 31.1, 29.4, 17.9.

FT-IR (neat) 2929, 2857, 1628, 1600, 1512, 1245, 1177, 1036, 823, 744 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{24}H_{29}NO$: 347.2, found: 347.2 (M^+).

$[\alpha]^{23}_D$ = +11.9° (c 0.0072, $CHCl_3$).



(*S*)-*N*,*N*,2-trimethyl-5-phenylpentan-1-amine (Compound 12). 2-Chloro-*N*,*N*-dimethylpropylamine hydrochloride (119 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of allylbenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 1.2 mL, 1.8 mmol) were used in a slightly modified procedure where the electrophile is added to the suspension of nickel along with more KO*t*-Bu (84 mg, 0.75 mmol). The product was dissolved in DCM (20 mL), extracted with 2 M HCl (20 mL), washed with DCM (10 mL), basified with NaOH, and extracted with DCM (20 mL). After removing the solvent in vacuo, the crude material was purified by preparative thin layer chromatography (50% Et_2O/hexanes, R_f = 0.2). First run: 40 mg (26%, 59% ee). Second run: 44 mg (29%, 56% ee).

The product was derivatized in via a demethylation/acylation procedure to for the ethyl carbamate by treating the dimethylamine (**12**) in refluxing benzene (10 mL) with 3 equivalents of ethyl chloroformate for 3 hours, followed by an aqueous wash and concentration. The ee of the ethyl carbamate was determined by HPLC on an OD-H column (2% isopropanol/hexanes, 1.0 mL / min). t_r = 7.7 min (major), 9.0 min (minor).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.21–7.16 (m, 3H), 2.67–2.54 (m, 2H), 2.19 (s, 6H), 2.08 (dd, 1H, *J* = 6.8, 11.7 Hz), 2.02 (dd, 1H, 7.8, 11.8 Hz), 1.79–1.43 (m, 5H), 1.37–1.25 (m, 1H), 1.17–1.09 (m, 1H), 0.90 (d, 3H, *J* = 6.6 Hz).

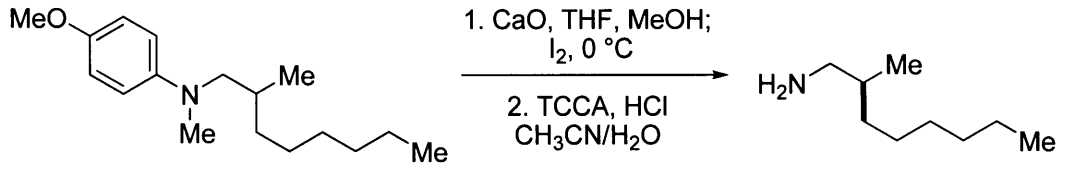
^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 128.6, 128.5, 125.8, 67.4, 46.2, 36.5, 35.2, 31.2, 29.3, 18.4.

FT-IR (neat) 2933, 2855, 2815, 2763, 1496, 1457, 747, 698 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{14}H_{23}N$: 205.2, found: 205.2 (M^+).

$[\alpha]^{23}_D = +1.0°$ (c 0.0231, $CHCl_3$).

III. Assignment of Absolute Stereochemistry.

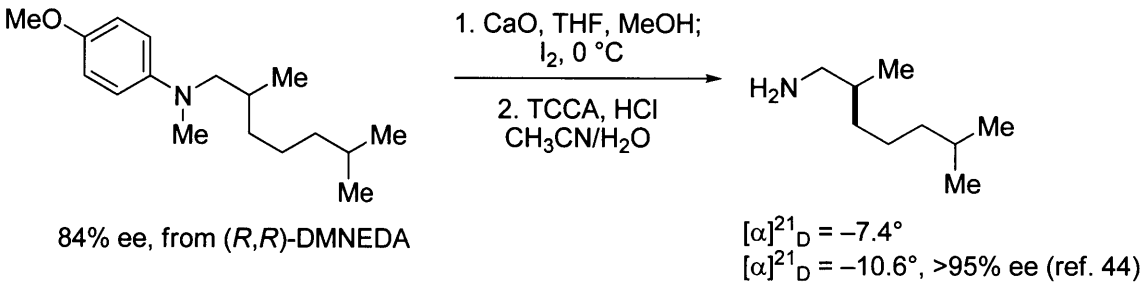


99% ee, from (*R*,*R*)-DMNEDA

$[\alpha]^{21}_D = -9.0°$
$[\alpha]^{21}_D = -8.4°$, >95% ee (ref. 44)

(*S*)-2-methyloctan-1-amine. In a 20-mL vial, 4-methoxy-*N*-methyl-*N*-(2-methyloctyl)aniline (150 mg, 0.57 mmol) was dissolved in a mixture of anhydrous THF (3.2 mL) and anhydrous MeOH (2.4 mL). Anhydrous calcium oxide (476 mg, 8.5 mmol) was added, and the mixture was cooled to 0 °C. Iodine (635 mg, 2.5 mmol) was added as a solution in 1 mL of THF. The reaction is stirred for 3.5 hours at 0 °C, diluted with 20 mL of DCM, and quenched with the addition of aqueous sodium thiosulfate (15%, 50 mL). The organics are washed with water (20 mL) and brine (10 mL), dried over sodium sulfate, and concentrated in vacuo to give a dark brown oil. The crude mixture is dissolved in a mixture of acetonitrile (0.8 mL) and water (0.8 mL). Trichloroisocyanuric acid (116 mg, 0.50 mmol) was added in a single portion followed by 2 M hydrochloric acid (1 mL). After stirring for 4 hours, the acetonitrile is removed in vacuo. The product is extracted into dichloromethane, and this solution is concentrated in vacuo. The crude material is purified by Kugelrohr distillation (oven 90 °C, 9 torr). 34 mg. 42%. The absolute stereochemistry of the cross-coupling product obtained with (*R*,*R*)-DMNEDA was determined to be (*S*) by comparison to the reported specific optical rotation.[44]

[44] Enders, D.; Schubert, H. *Angew. Chem.* **1984**, *96*, 368–369.



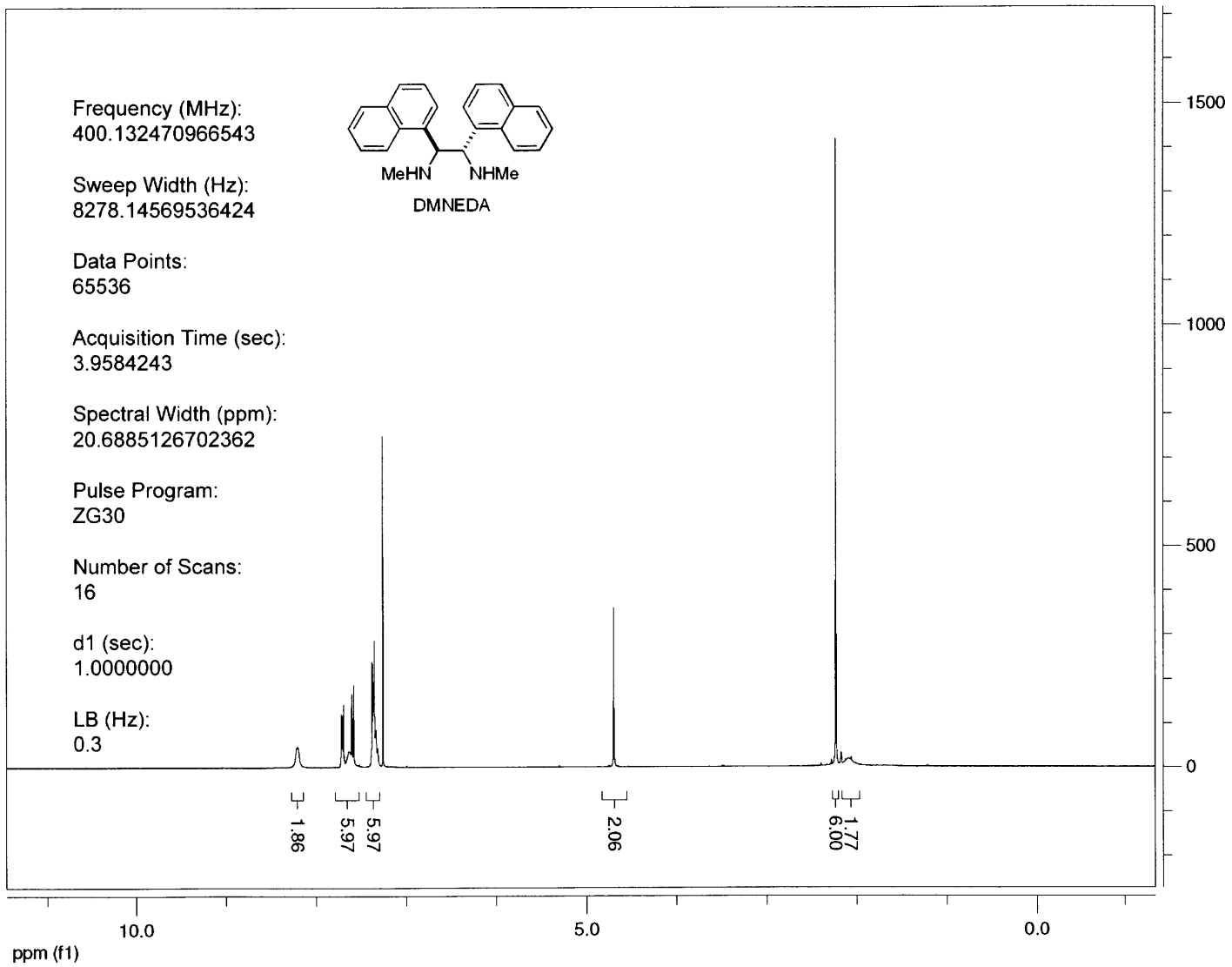
84% ee, from (*R*,*R*)-DMNEDA

$[\alpha]^{21}_D = -7.4°$

$[\alpha]^{21}_D = -10.6°$, >95% ee (ref. 44)

(*S*)-2,6-dimethylheptan-1-amine. The same conditions used for the synthesis of (*S*)-2-methyloctan-1-amine were used, except with *N*-(2,6-dimethylheptyl)-4-methoxy-*N*-methylaniline (150 mg, 0.57 mmol) as starting material. 31 mg. 38%. The absolute stereochemistry of the cross-coupling product obtained with ligand (*R*,*R*)-DMNEDA was determined to be (*S*) by comparison to the reported specific optical rotation.[44]

IV. ^{1}H NMR Spectra.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Data Points:
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Acquisition Time (sec):
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Spectral Width (ppm):
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Pulse Program:
ZG30
Number of Scans:
16
d1 (sec):
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LB (Hz):
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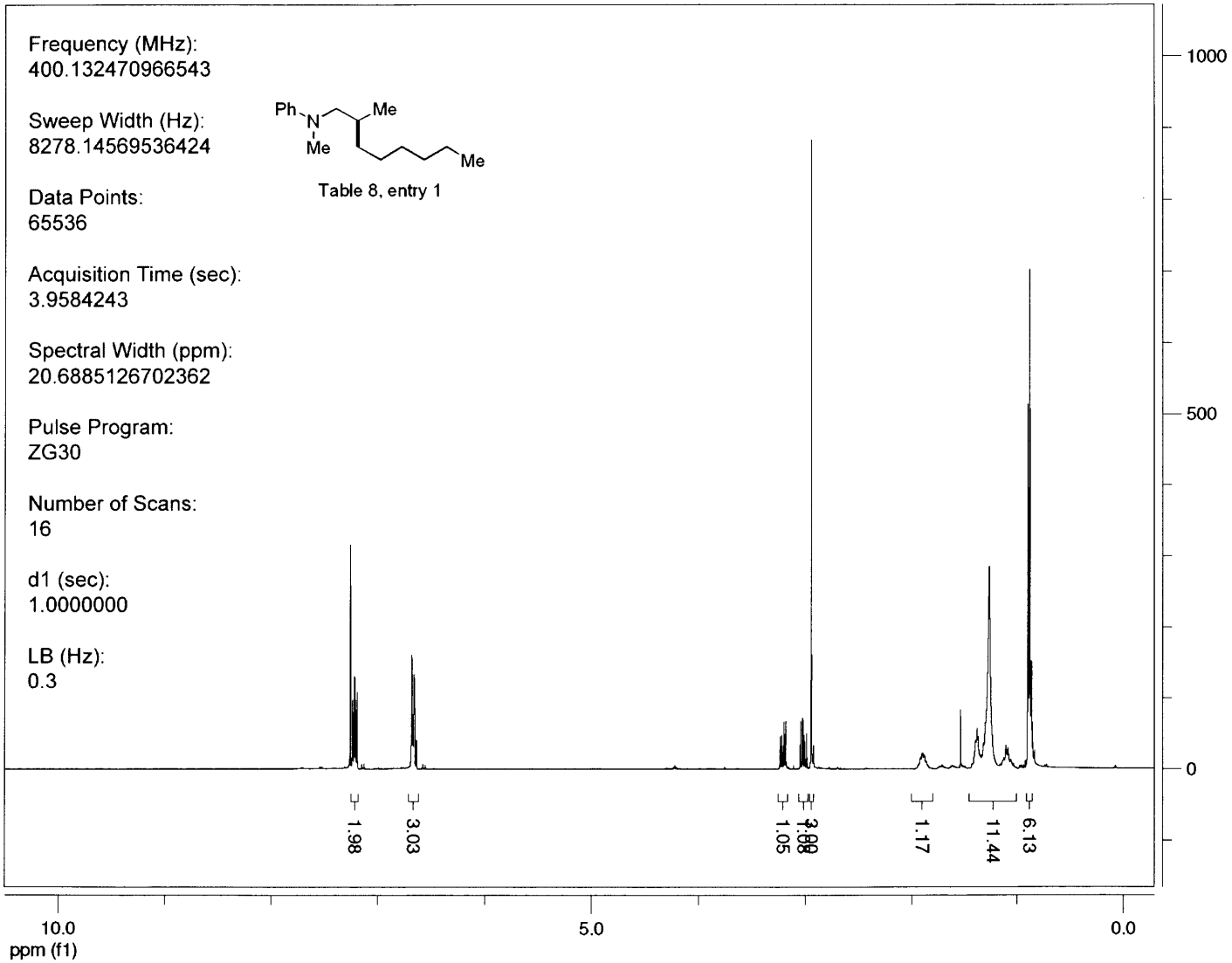
MeHN
NHMe
DMNEDA
1.86
5.97
5.97
2.06
1.77
6.00
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)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Sweep Width (Hz):
8278.14569536424
Data Points:
65536
Acquisition Time (sec):
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Spectral Width (ppm):
20.6885126702362
Pulse Program:
ZG30
Number of Scans:
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d1 (sec):
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LB (Hz):
0.3
Ph
N
Me
Me
Me
Table 8, entry 1
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3.03
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1.17
11.44
6.13
10.0
ppm (f1)
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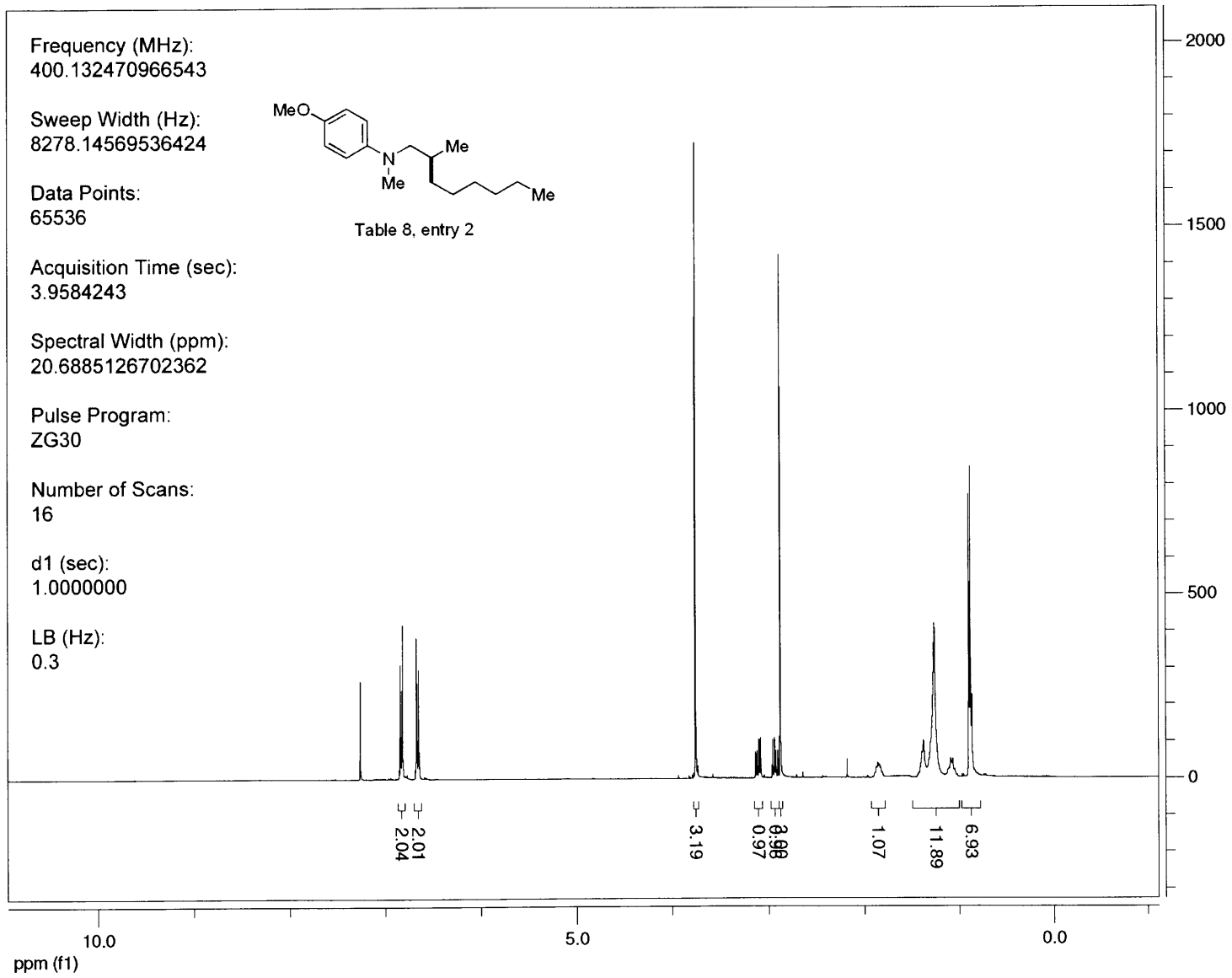
0.0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Spectral Width (ppm):
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LB (Hz):
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Me
Me
Me
Table 8, entry 2
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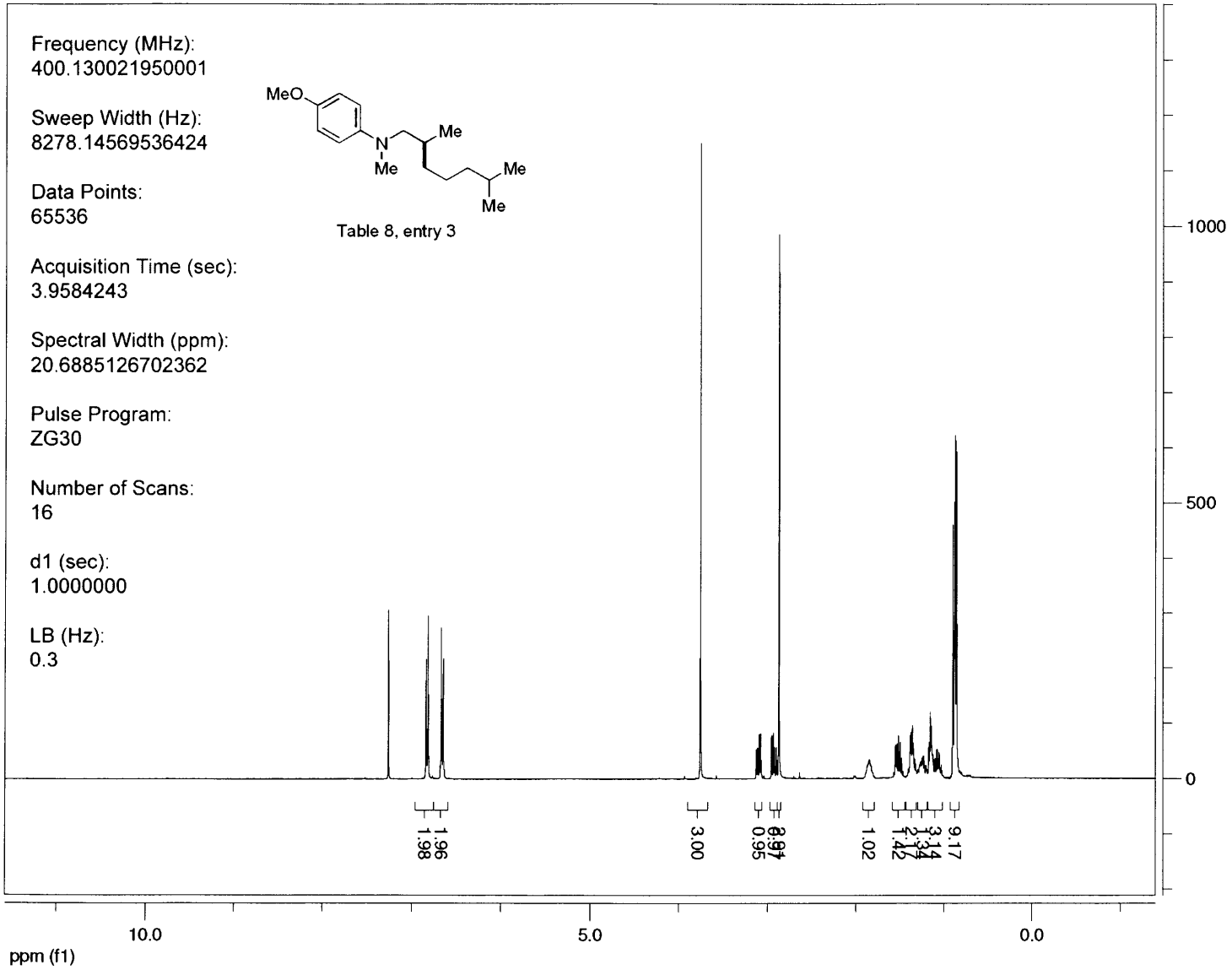
1.07
11.89
6.93
10.0
5.0
0.0
ppm (f1)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Spectral Width (ppm):
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Pulse Program:
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Number of Scans:
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LB (Hz):
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MeO
N
Me
Me
Me
Me
Table 8, entry 3
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500
0
1.98
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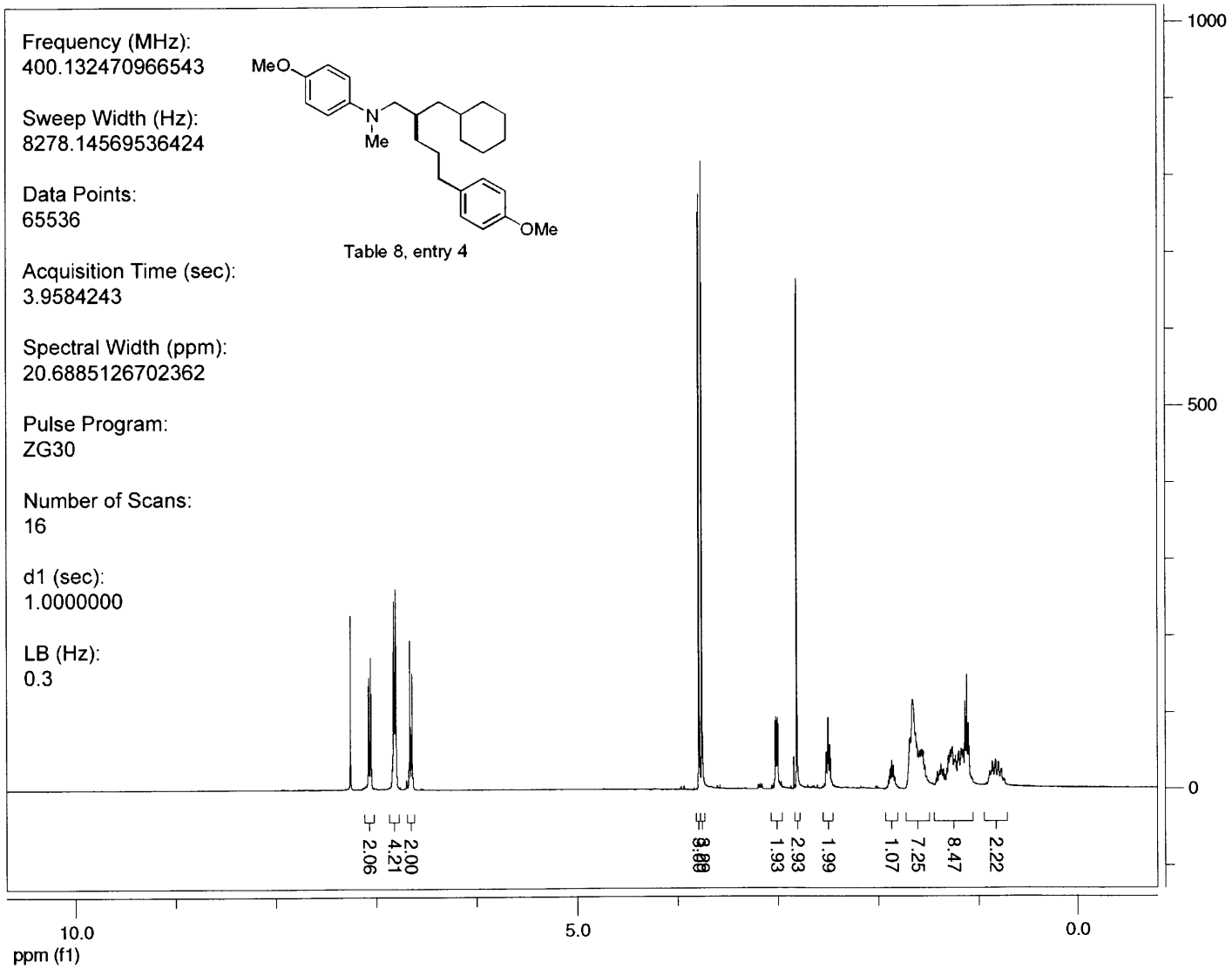
3.00
0.95
1.02
1.42
9.17
10.0
5.0
0.0
ppm (f1)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Me
OMe
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1.99
1.07
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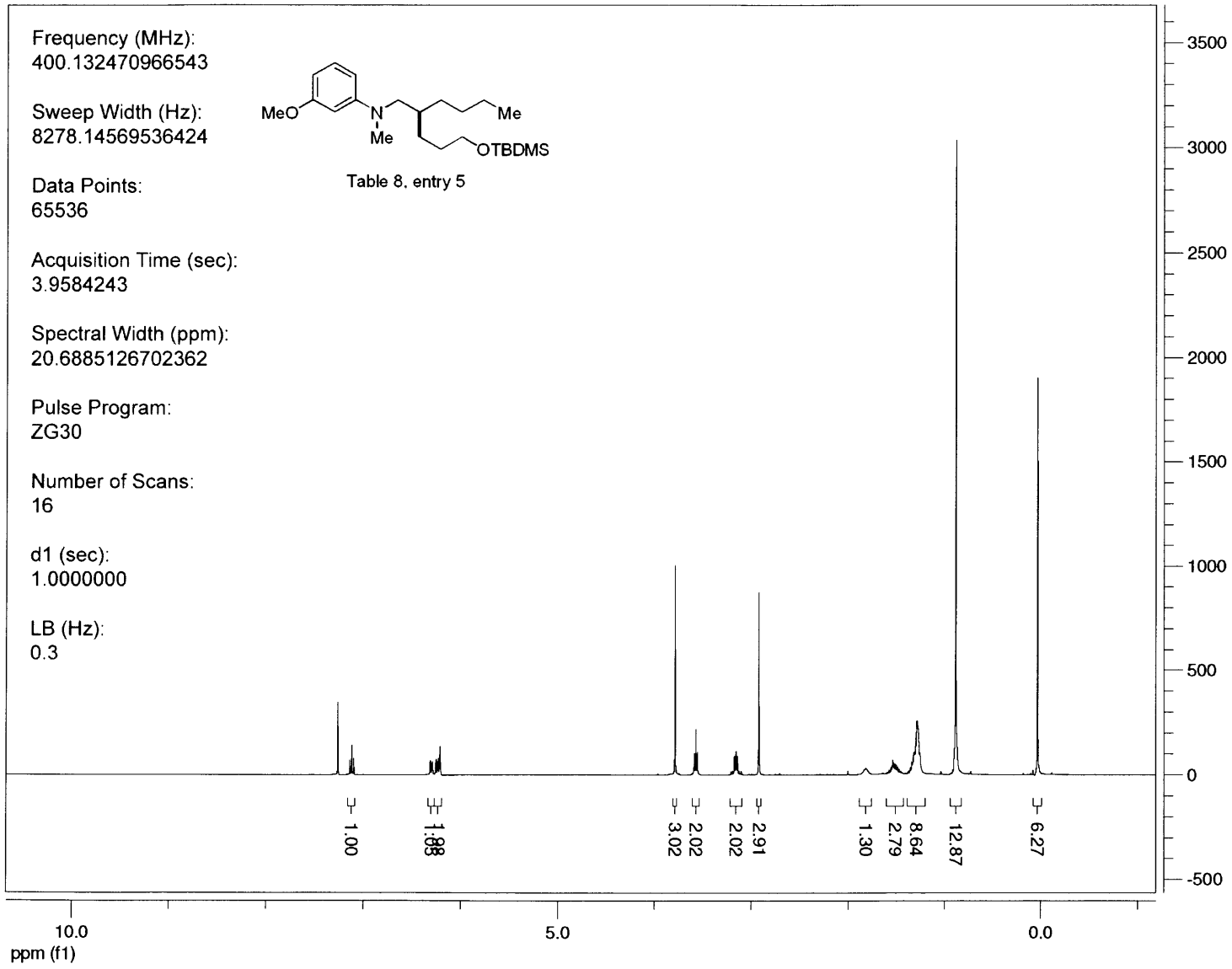
ppm (f1)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LB (Hz):
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1.88
1.88
3.02
2.02
2.02
2.91
1.30
2.79
8.64
12.87
6.27
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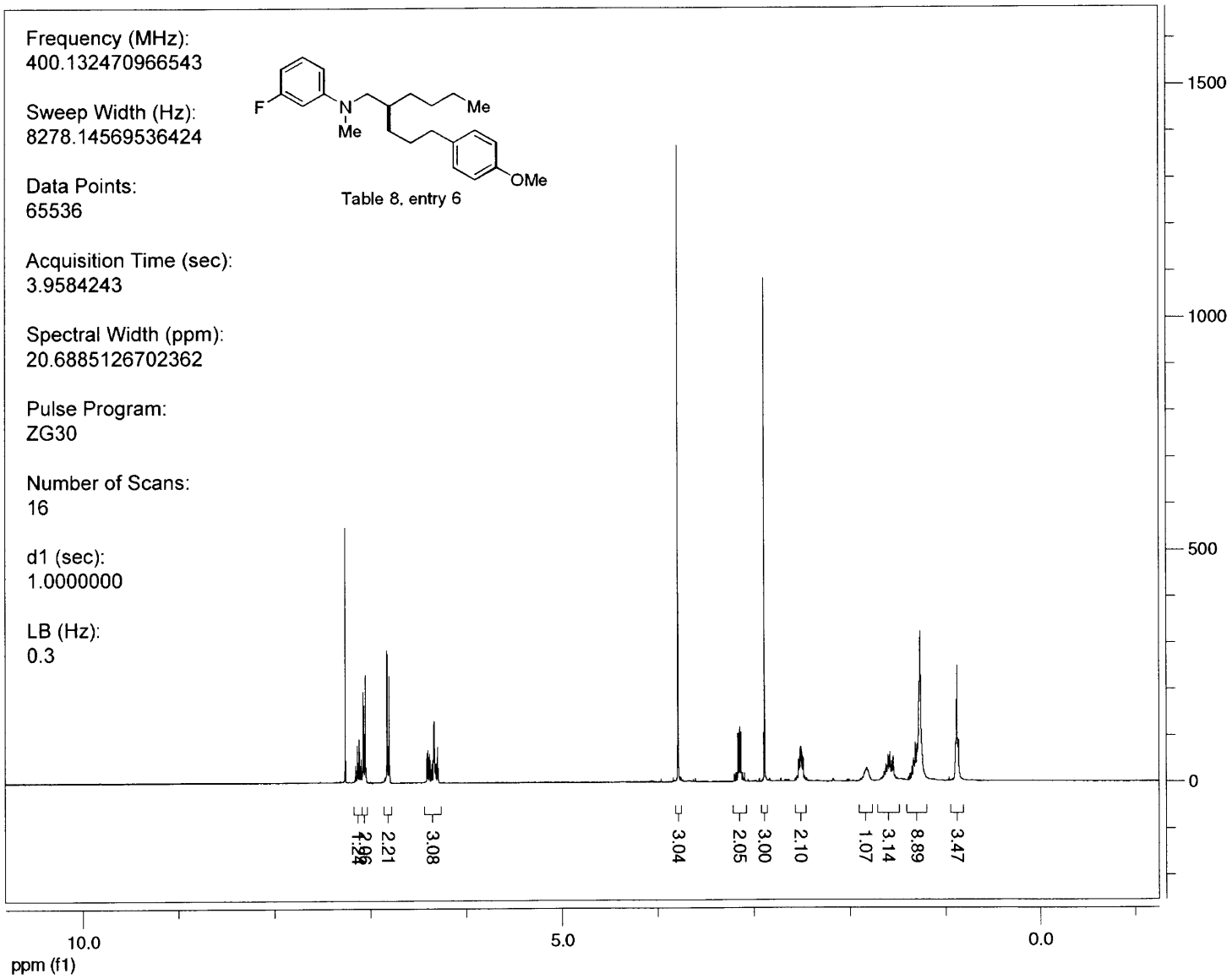
3000
2500
2000
1500
1000
500
0
-500
10.0
5.0
0.0
ppm (f1)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Spectral Width (ppm):
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N
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Me
Me
OMe
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1000
500
0
2.21
3.08
3.04
2.05
3.00
2.10
1.07
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8.89
3.47
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5.0
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ppm (f1)

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Data Points:
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Acquisition Time (sec):
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Spectral Width (ppm):
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Pulse Program:
ZG30

Number of Scans:
16

d1 (sec):
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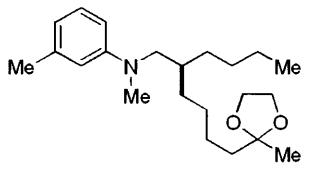
LB (Hz):
0.3



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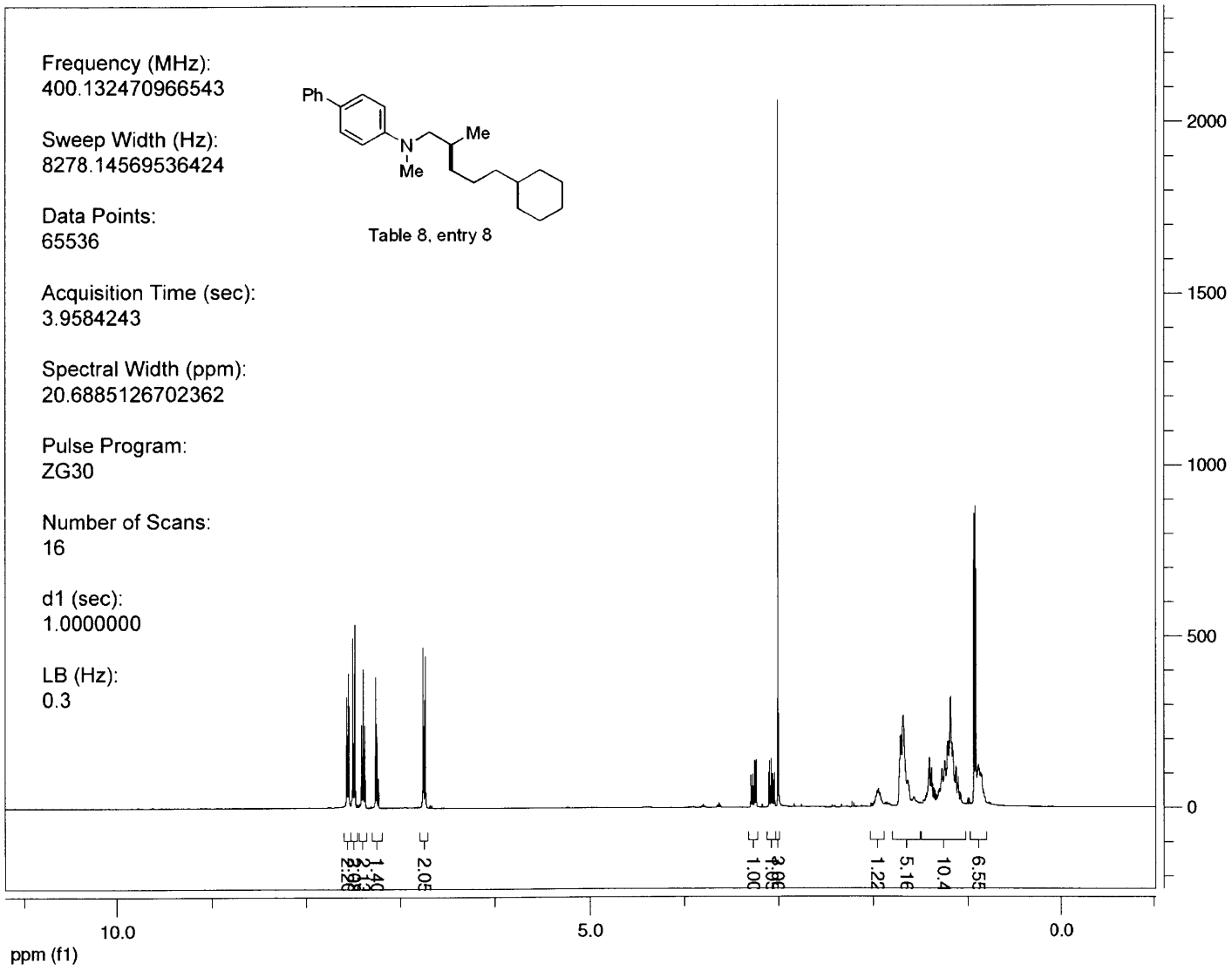
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Data Points:
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ZG30
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d1 (sec):
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LB (Hz):
0.3
Ph
N
Me
Me
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500
0
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5.16
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6.55
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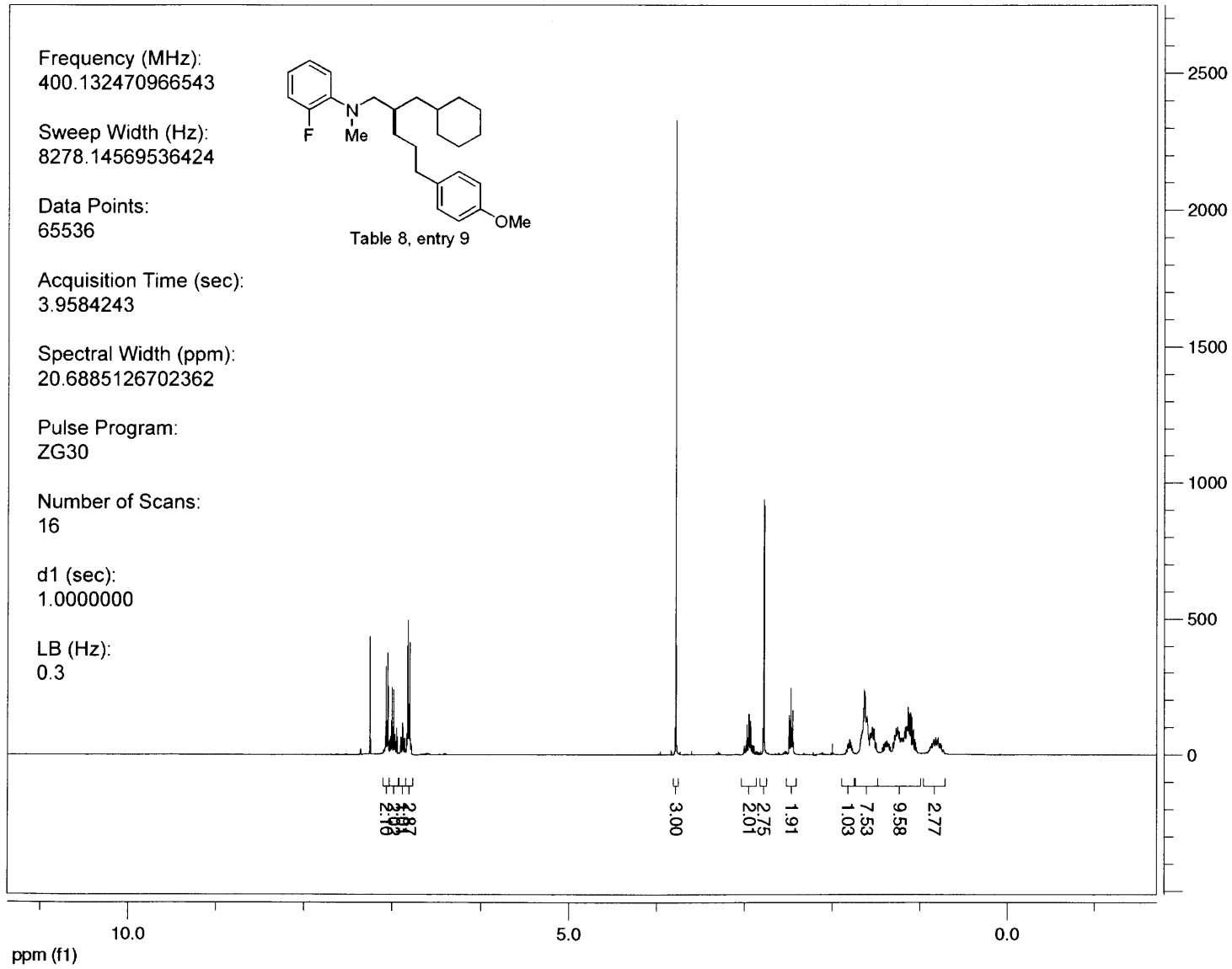
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Spectral Width (ppm):
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Pulse Program:
ZG30
Number of Scans:
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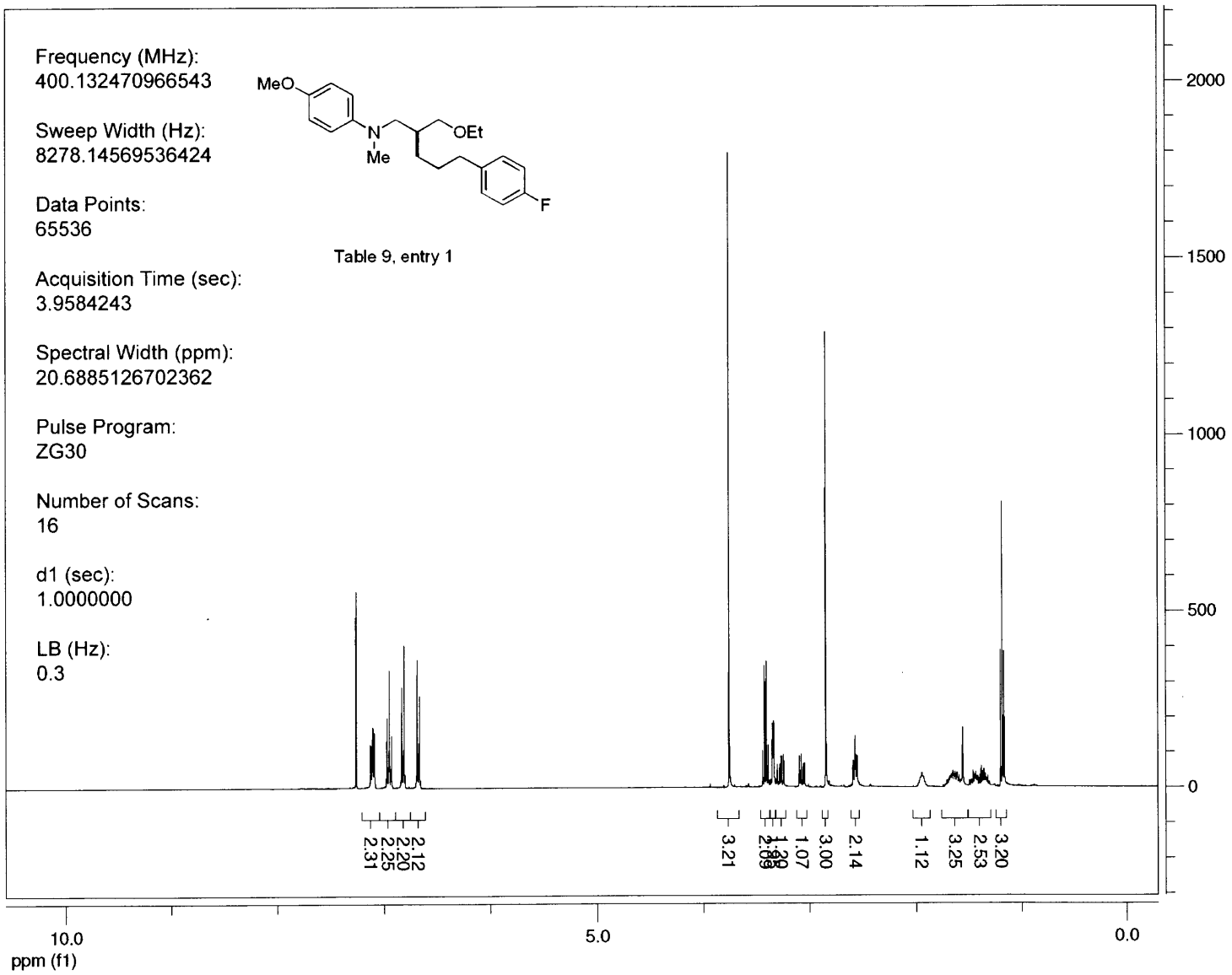
LB (Hz):
0.3
F
N
Me
OMe
Table 8, entry 9
2.16
2.01
3.00
2.75
2.01
1.91
1.03
7.53
9.58
2.77
2500
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)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Data Points:
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Spectral Width (ppm):
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Pulse Program:
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Number of Scans:
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d1 (sec):
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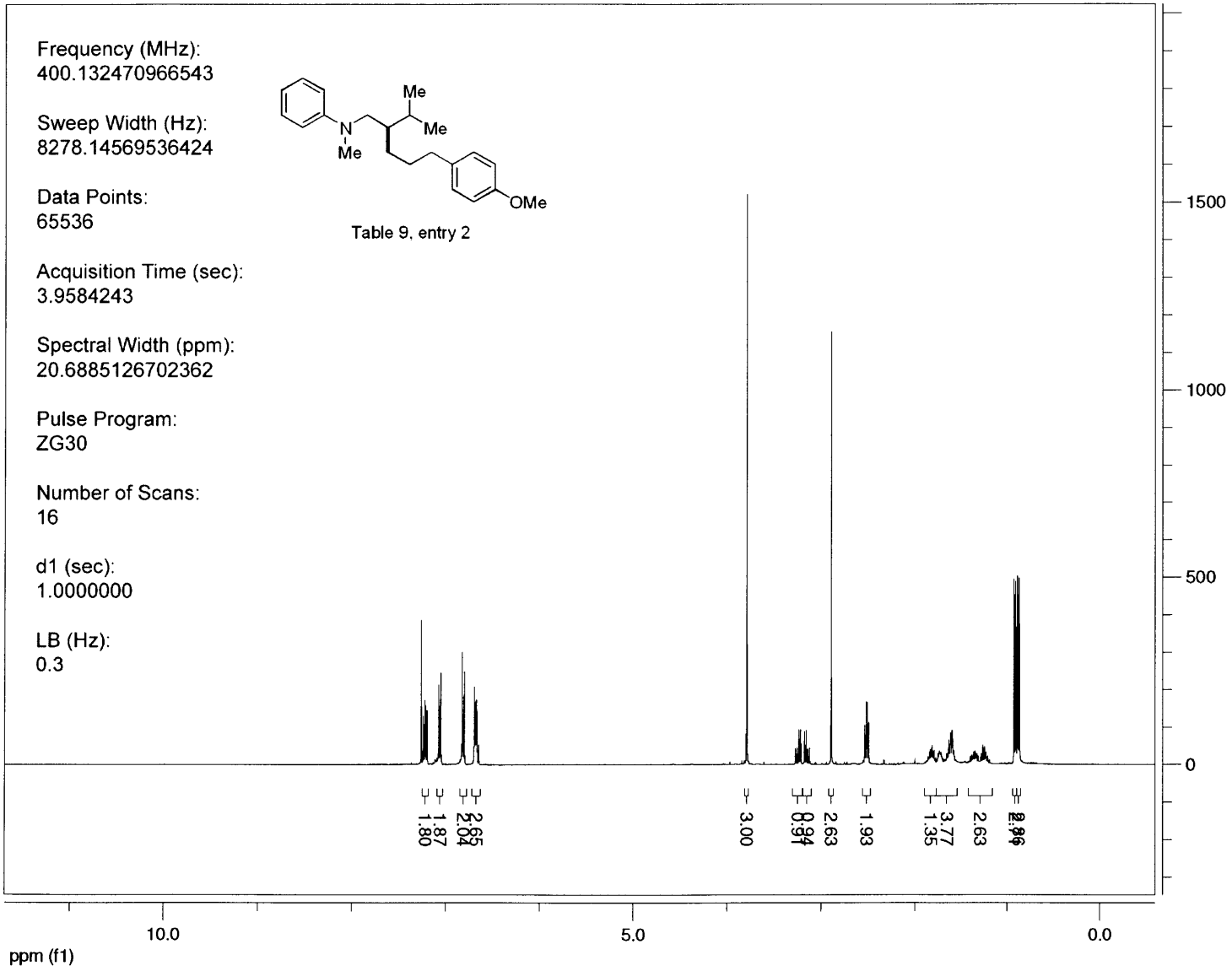
LB (Hz):
0.3
MeO
N
Me
OEt
F
Table 9, entry 1
2000
1500
1000
500
0
2.31
2.25
2.20
2.12
3.21
1.07
3.00
2.14
1.12
3.25
2.53
3.20
10.0
5.0
0.0
ppm (f1)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Data Points:
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Acquisition Time (sec):
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Spectral Width (ppm):
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Pulse Program:
ZG30
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d1 (sec):
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LB (Hz):
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Me
Me
N
Me
OMe
Table 9, entry 2
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1000
500
0
1.80
1.87
2.04
2.65
3.00
0.91
0.94
2.63
1.93
1.35
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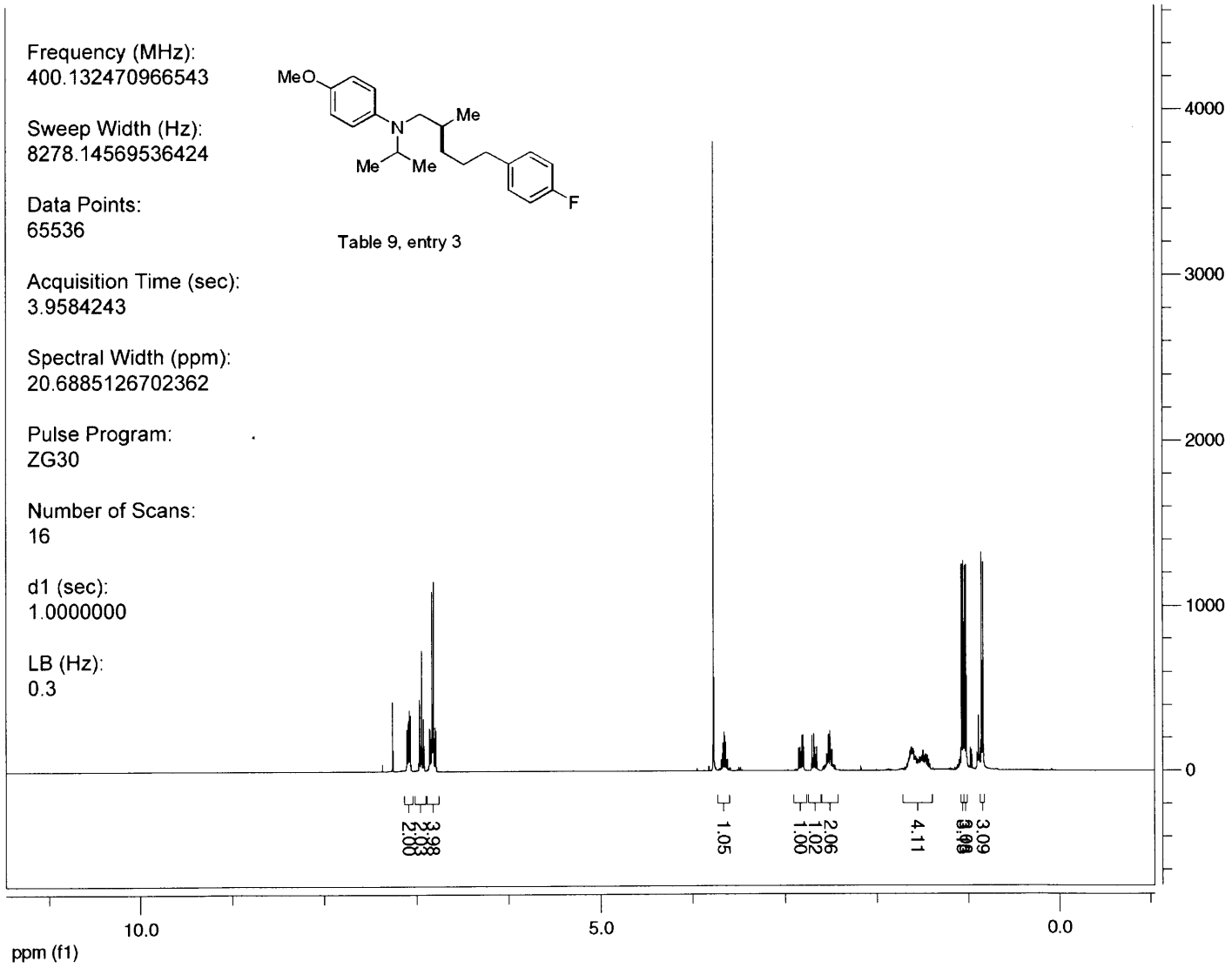
ppm (f1)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Spectral Width (ppm):
20.6885126702362
Pulse Program:
ZG30
Number of Scans:
16
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LB (Hz):
0.3
MeO
N
Me
Me
Me
F
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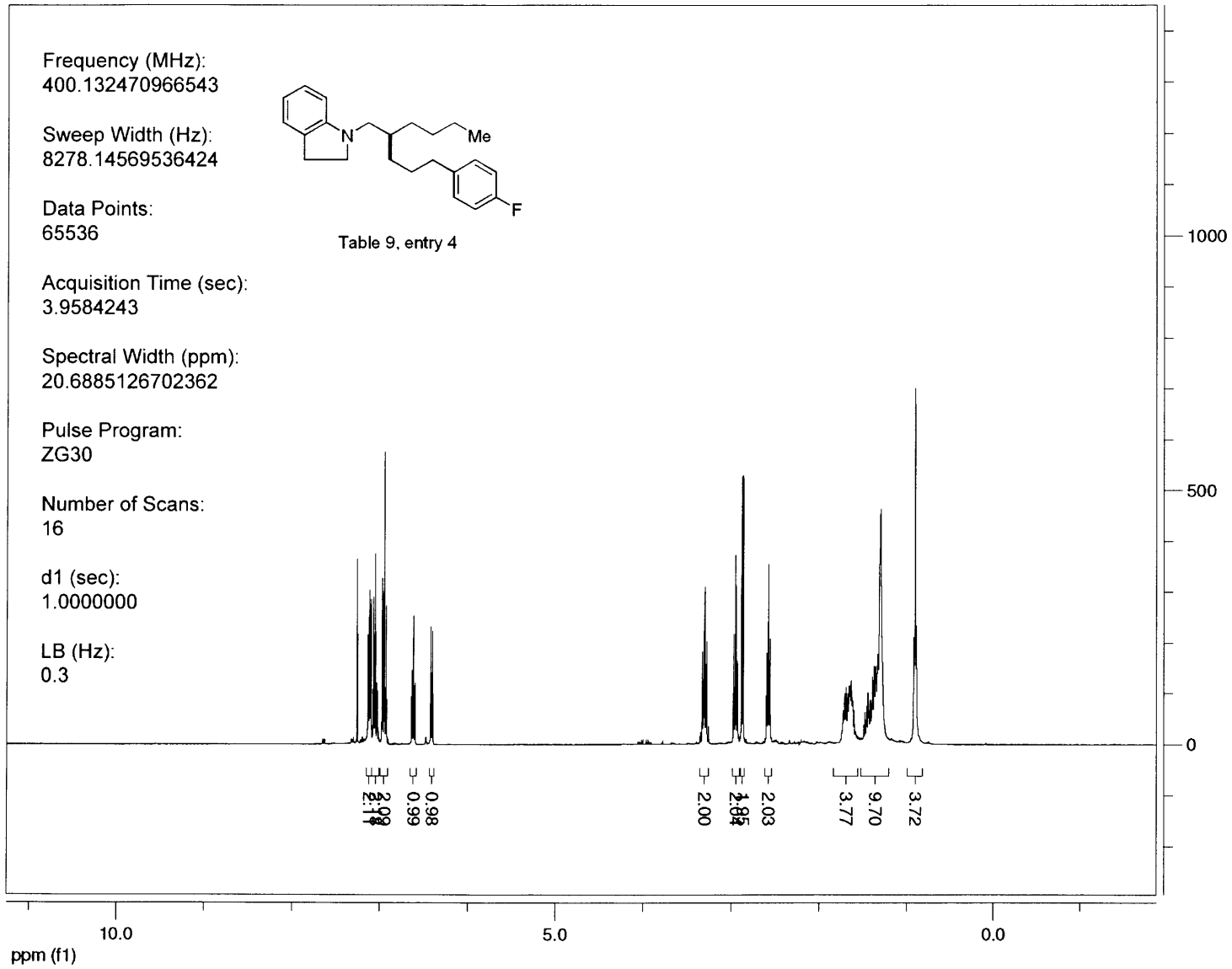
3000
2000
1000
0
1.05
4.11
10.0
5.0
0.0
ppm (f1)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Pulse Program:
ZG30
Number of Scans:
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d1 (sec):
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LB (Hz):
0.3
N
Me
F
Table 9, entry 4
1000
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2.03
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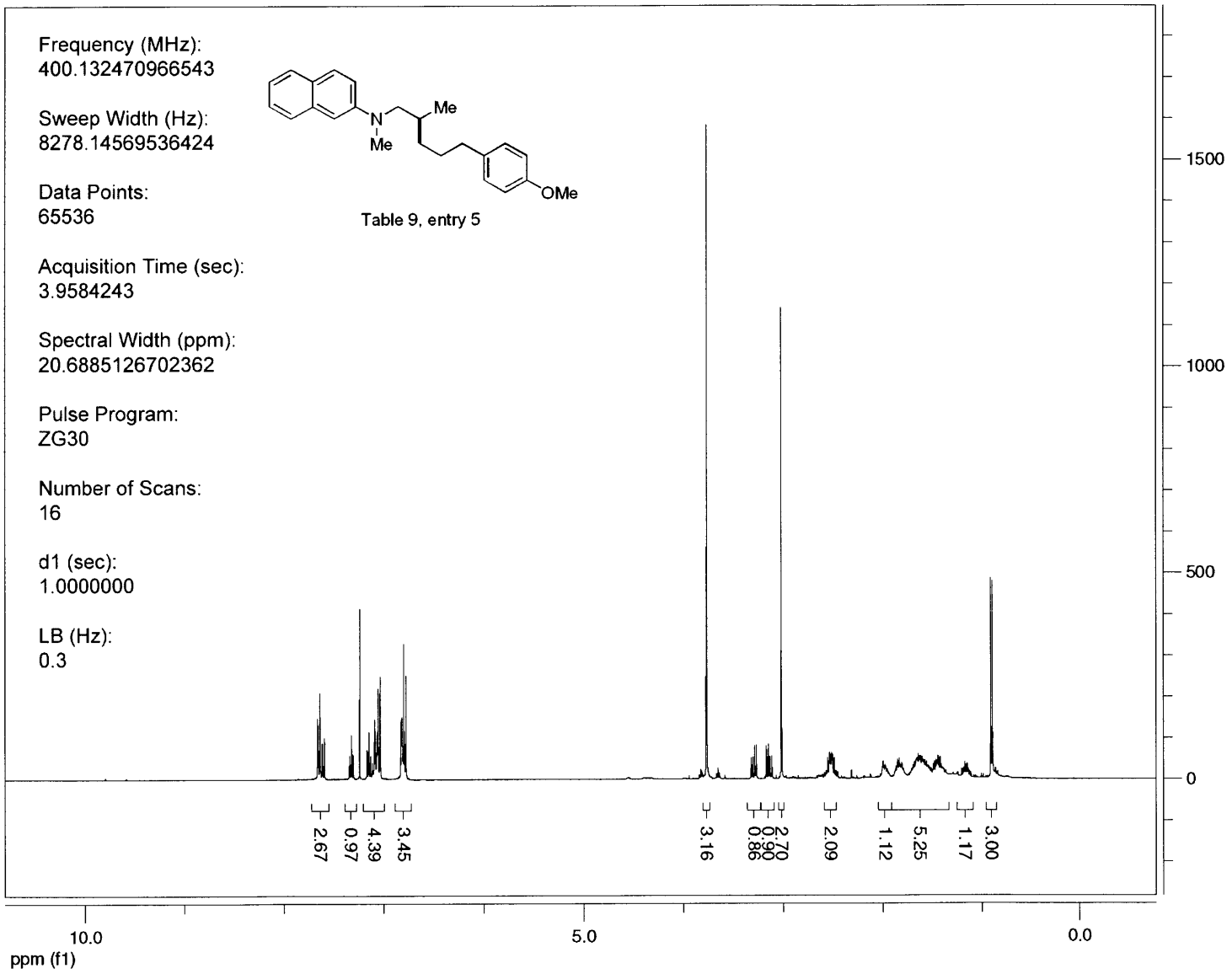
9.70
3.72
10.0
5.0
0.0
ppm (f1)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Data Points:
65536
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Spectral Width (ppm):
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Pulse Program:
ZG30
Number of Scans:
16
d1 (sec):
1.0000000
LB (Hz):
0.3
Me
N
Me
OMe
Table 9, entry 5
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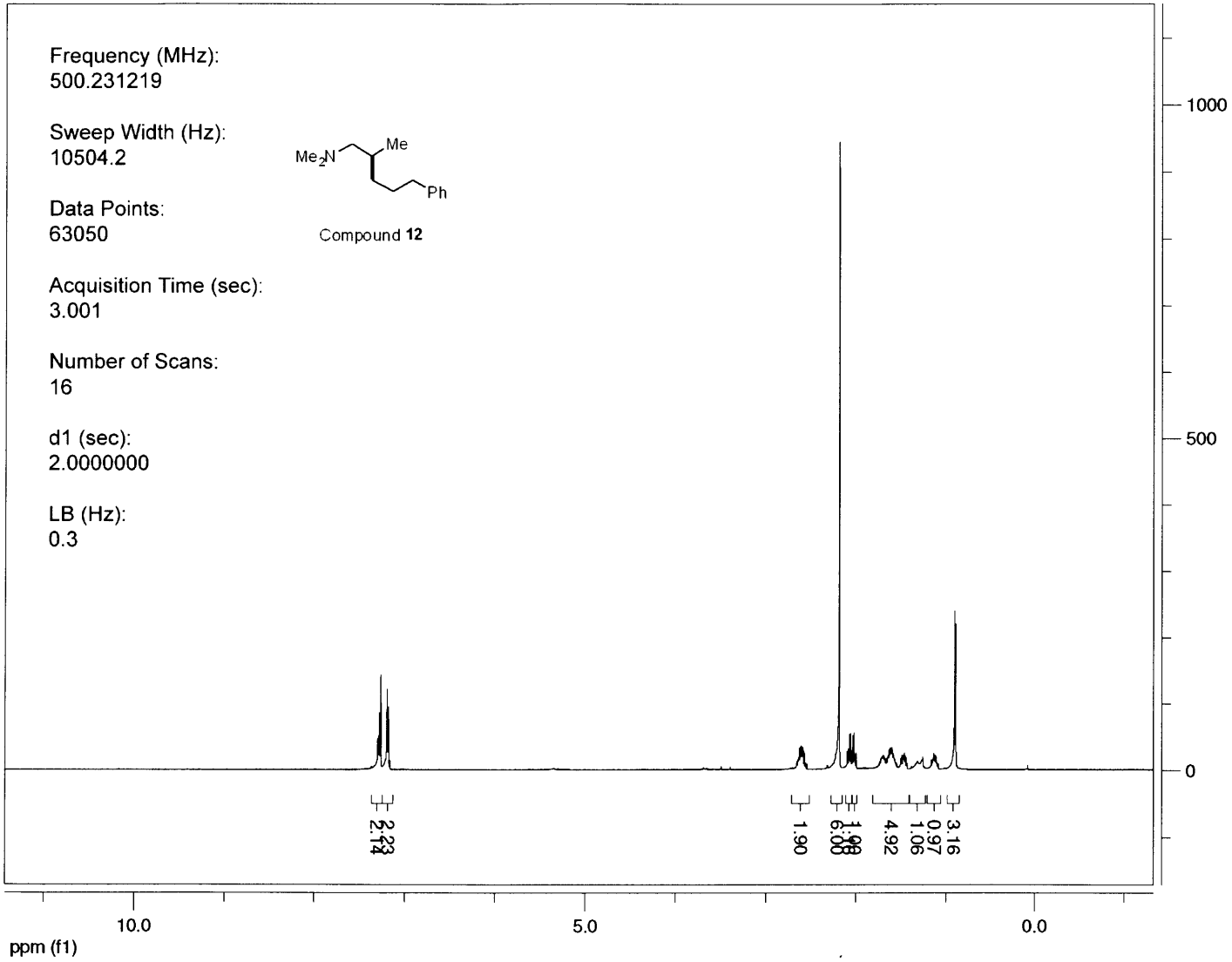
1000
500
0
2.67
0.97
4.39
3.45
3.16
0.90
0.86
2.70
2.09
1.12
5.25
1.17
3.00
10.0
5.0
0.0
ppm (f1)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10504.2
Data Points:
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Acquisition Time (sec):
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Number of Scans:
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d1 (sec):
2.0000000
LB (Hz):
0.3
Me
Me2N
Ph
Compound 12
1000
500
0
2.23
1.90
6.00
4.92
1.06
0.97
3.16
10.0
5.0
0.0
ppm (f1)

Part II

Planar-Chiral Borabenzene Catalysts for Diels–Alder Reactions

Chapter 3

Development of a Planar-Chiral Borabenzene Catalyst for Diels–Alder Cycloadditions

A. Introduction

Chiral Lewis acid catalysts have a prominent role in catalysis.[45] One of the most useful applications of chiral Lewis acids is for enantioselective additions to carbonyl compounds. The interaction between the carbonyl group and the Lewis acid is almost exclusively by means of a σ-symmetry interaction.[46] One of the ongoing projects in the Fu group has been to use a π-symmetry interaction, in addition to the σ-symmetry interaction, to activate the carbonyl group towards nucleophilic addition (Figure 2).[47] This design simultaneously allows electronic activation of the carbonyl group and greater organization of the catalyst–carbonyl adduct in the transition state, and it was thought that these two design elements together would improve prospects for the development of a versatile catalyst for the asymmetric addition of nucleophiles into carbonyl groups.

Borabenzenes[48,49] and azaborolides[50] can provide the desired simultaneous σ- and π-interactions with the carbonyl group. Appropriate substitution on the heterocyclic ring and complexation to a metal eliminates the planes of symmetry, resulting in a planar-chiral complex (Figure 3).

---

[45] For a review on Lewis-acid catalyzed reactions, see: (a) Yamamoto, H.; Cheon, C. H. Chiral Lewis Acids and Brønsted Acids in Asymmetric Synthesis. In *Catalytic Asymmetric Synhesis*, 3rd ed.; Ojima, I., Ed.; Wiley: Hoboken, N.J., 2010; Chapter 3. (b) *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH, New York, 2000; Vols. 1 and 2.

[46] For reviews on the aldol reaction, see: (a) *Modern Aldol Reactions*; Mahrwald, R., Ed.; Wiley-VCH: Weinheim, 2004. (b) Sawamura, M.; Ito, Y. Asymmetric Aldol Reactions–Discovery and Development. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 8B1. (c) Carreira, E. M. Recent Advances in Asymmetric Aldol Addition Reactions. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 8B2.

[47] Fu, G. C. *J. Org. Chem.* **2004**, *69*, 3245–3249.

[48] For pioneering studies of borabenzenes, see: (a) Herberich, G. E.; Greiss, G.; Heil, H. F. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 805–806. (b) Ashe, A. J., III; Shu, P. *J. Am. Chem. Soc.* **1971**, *93*, 1084–1085.

[49] For reviews on borabenzene chemistry, see: (a) Herberich, G. E.; Ohst, H. *Adv. Organomet. Chem.* **1986**, *25*, 199–236. (b) Fu, G. C. *Adv. Organomet. Chem.* **2001**, *47*, 101–119.

[50] For overviews of 1,2-azaborolyl chemistry, see: (a) Schmid, G. In *Comprehensive Heterocyclic Chemistry II*; Shinkai, I., Ed.; Elsevier: Oxford, U.K., 1996; Vol. 3, Chapter 3.17. (b) Schmid, G. *Comments Inorg. Chem.* **1985**, *4*, 17–32.

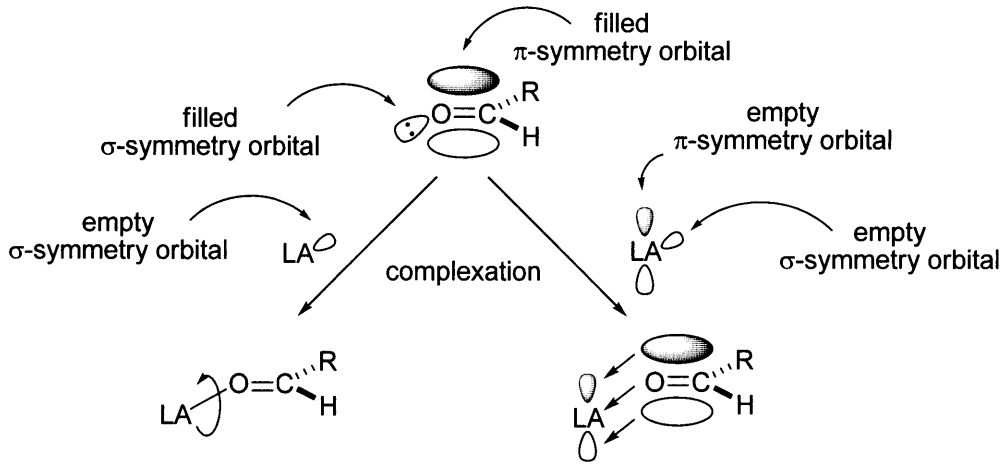


Figure 2. Lewis acid (LA) activation of a carbonyl group through σ-interactions only (left) and both σ- and π-interactions (right).

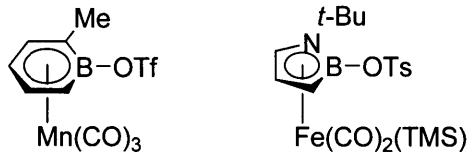
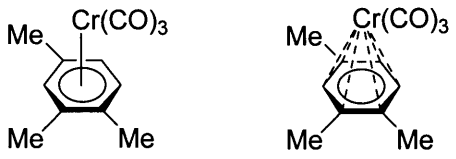


Figure 3. Examples of a metal-complexed borabenzene (left) and a metal-complexed azaborolide (right).

Along with central and axial chirality, planar chirality is one of the three classes of asymmetry described by the Cahn–Ingold–Prelog system.[51] Planar chirality is defined as chirality resulting from desymmetrization of an achiral plane by the presence of a ligand not in this plane. This definition is not always clearly well-defined. While η^6-complex **14** has no apparent stereogenic centers and can be considered to possess a chiral plane, it can be treated as having stereogenic centers if a different representation of the

[51] For discussions of planar chirality, see: (a) Paley, R. S. *Chem. Rev.* **2002**, *102*, 1493–1523. (b) Schlögl, K. *Top. Curr. Chem.* **1984**, *125*, 27–62. (a) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Experientia* **1956**, *12*, 81–124. (b) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415.

η^6-interaction (**15**) is used (Figure 4).[52] Nevertheless, because the borabenzene and the carbonyl group are co-planar to facilitate proper overlap of their π-systems,[53] planar chirality is still a useful concept in examining these complexes.



14 **15**

Figure 4. Complications in the definition of planar-chirality. In the same complex, one representation (left) has no stereogenic centers, while another representation of the same complex (right) does have stereogenic centers.

In the proposed model for stereoinduction, an aldehyde binds to the borabenzene in a co-planar fashion to maximize overlap of the π-systems. Steric repulsions between the ring substituent and the electrophile disfavor certain conformations (Figure 5, **16a** and **16b**). In the lowest energy conformation (Figure 5, **16c**), the approach of the nucleophile can take place via one of two possible Bürgi-Dunitz trajectories. Steric interactions with the metal and its ligands cause the nucleophile to approach from the other side of the borabenzene.

[52] Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 1121–1122.

[53] This is supported by a crystal structure of a vinylogous formamide coordinated to a borabenzene complex. The formamide is in plane with the borabenzene. See: Amendola, M. C.; Stockman, K. E.; Hoic, D. A.; Davis, W. M.; Fu, G. C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 267–269.

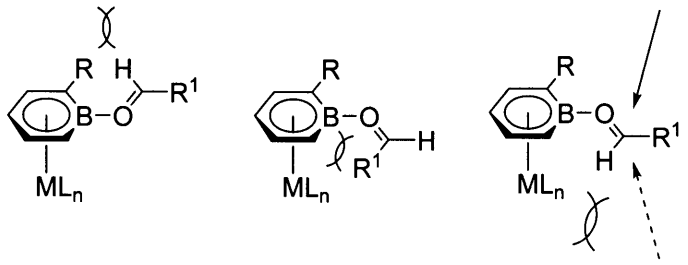
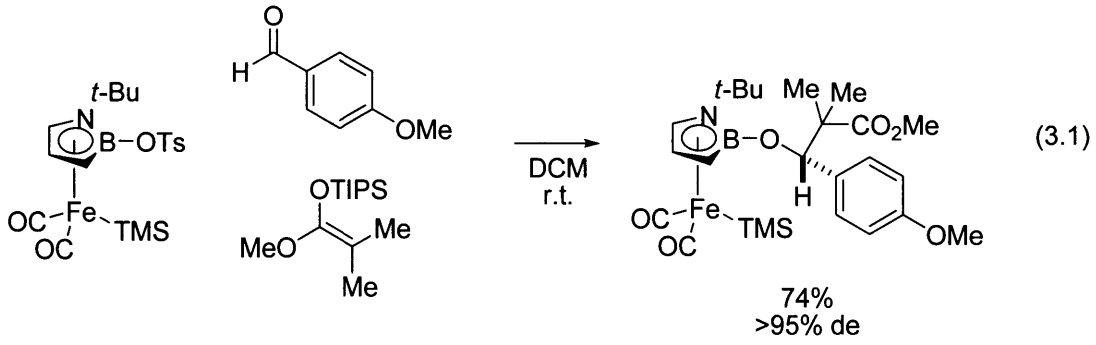


Figure 5. Model for stereoinduction in borabenzene-mediated nucleophilic additions to aldehydes.

While asymmetric induction and activation have been demonstrated with high levels of stereoselectivity (Eq. 3.1), challenges still remain in this chemistry.[54,55] The principal issue is that the relatively weak dative bond between the carbonyl oxygen and boron in the catalyst-reactant adduct becomes a much stronger boron–oxygen single bond with π-symmetry interactions in the product. The thermodynamic stability of this intermediate leads to a high barrier for the release of the product and effectively inhibits catalyst turnover.

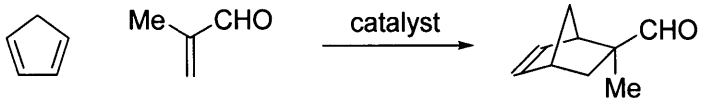


(3.1)

[54] Liu, S.-Y.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 15352–15353. The observed stereochemistry of the product is consistent with the proposed model for stereoinduction. See text and Figure 5.

[55] For a related study on the use of planar-chiral boron complexes in asymmetric addition reactions to imines, see: Liu, S.-Y.; Lo, M. M.-C.; Fu, G. C. *Tetrahedron* **2006**, *62*, 11343–11349.

One possible way to overcome this lack of catalytic turnover is to employ the boron Lewis acid in a reaction that does not result in a B–O single bond. The chosen reaction to test this new approach was the cycloaddition of cyclopentadiene with methacrolein (Eq. 3.2).[56,57,58]



(3.2)

[56] For a reviews of catalytic asymmetric Diels–Alder reactions, see: (a) Evans, D. A.; Johnson, J. S. Diels–Alder Reactions. In *Comprehensive Asymmetric Catalysis*. Jacobsen, E. N., Paltz, A., Yamamoto, H., Eds. Springer: Berlin, 2004; Vol. 3, pp 1177–1236. (b) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007–1019.

[57] For early examples of catalyzed cycloadditions between cyclopentadiene and methacrolein, see: (a) Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1483–1484. (b)Northcott, C. J.; Valenta, Z. *Can. J. Chem.* **1987**, *65*, 1917–1922. (c) Takemura, H.; Komeshima, N.; Takahashi, I.; Hashimoto, S.-i.; Ikota, N.; Tomioka, K.; Koga, K.. *Tetrahedron Lett.* **1987**, *28*, 5687–5690.

[58] For interesting examples of boron-catalyzed asymmetric Diels–Alder reactions, see: (a) Hawkins, J. M.; Loren, S.; Nambu, M. *J. Am. Chem. Soc.* **1994**, *116*, 1657–1660. (b) Hawkins, J. M.; Loren, S. *J. Am. Chem. Soc.* **1991**, *113*, 7794–7795. (c) Corey, E. J.; Loh, T.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8966–8967.

B. Results and Discussion

The synthesis of borabenzene complexes was well-established in the Fu group.[59] The cyclization to form stannane **17** and the transmetallation to form boracycle **18** were modified to improve the yields of these reactions. After unsuccessful attempts to synthesize the negatively charged chromium complex **23b**, the synthesis of the isoelectronic, neutral manganese borabenzene complex **22** was successfully undertaken (Scheme 4). It was believed that the anionic nature of the chromium complex might be in part responsible for difficulties in the synthesis.

Treatment of the methoxide adduct **22** with triflic anhydride led to the formation of the triflate adduct (**23a**). Methyl triflate was formed as a by-product and removed in vacuo. By ^{19}F NMR, the triflate **23a** was observed to be free of both methyl triflate and triflic anhydride, which might also serve as Lewis acid catalysts. Trimethylsilyl triflate and methyl triflate did not cleanly convert complex **22** to desired triflate **23a**.

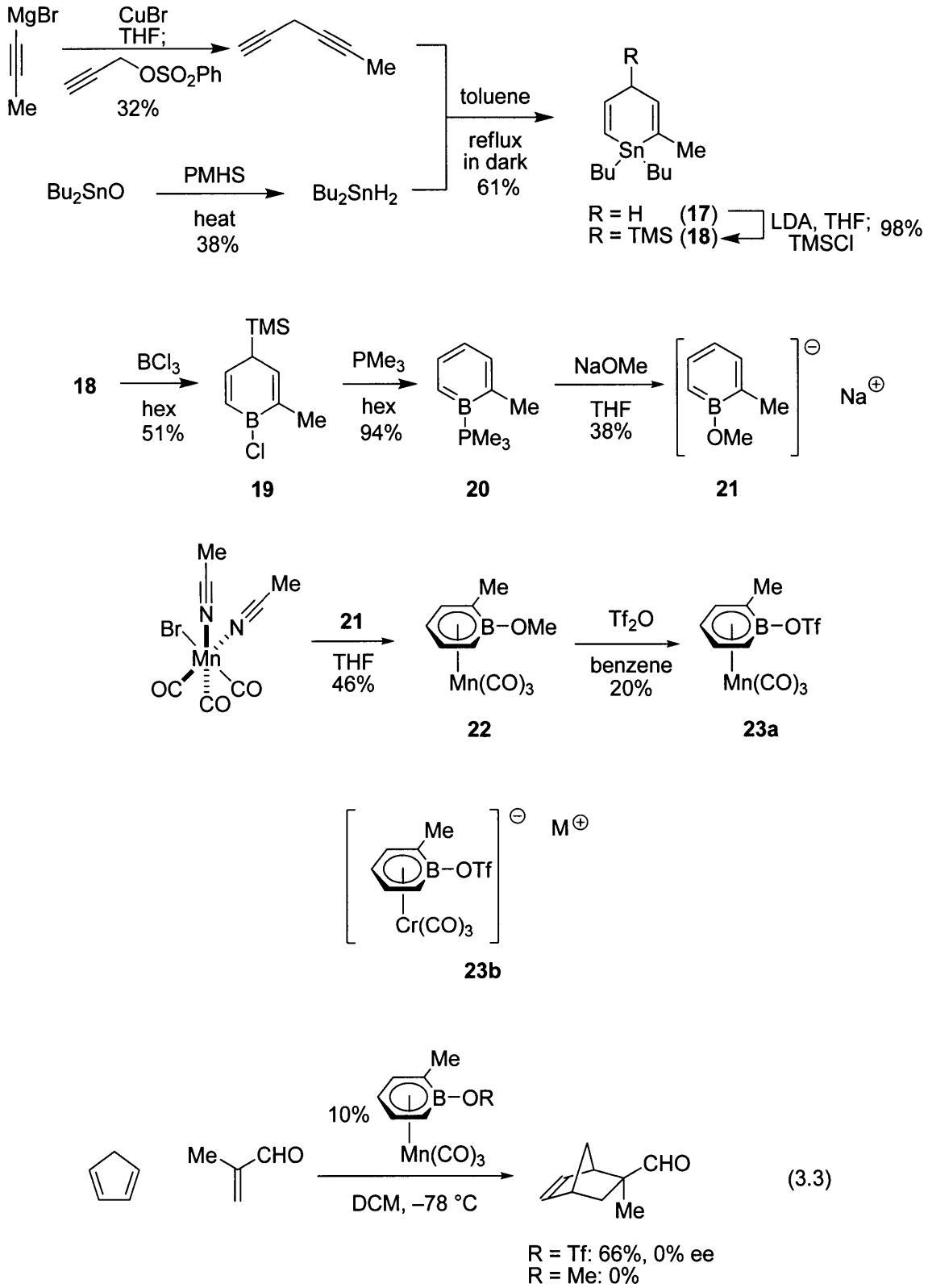
At –78 °C, after 2 hours, a 66% yield of the cycloadduct between cyclopentadiene and methacrolein could be obtained when 10 mol% of the newly synthesized Lewis acid (**23a**) was used (Eq. 3.3, R = Tf). No Diels–Alder cycloaddition was observed when methoxide adduct **22** was used (Eq. 3.3, R = Me) instead of the triflate adduct **23a**. This suggests that the catalytic center is indeed at boron and not at the transition metal.

Manganese complex **22** could be successfully resolved by the means of semi-preparative HPLC. The separated enantiomers appeared to be configurationally stable and were converted to the corresponding triflates (**23a**). However, application of the enantioenriched triflate in Diels–Alder reactions provided only racemic product (Eq. 3.3).

---

[59] (a) Smith, M. J. Room-Temperature Stille Couplings of Aryl Iodides and Studies on Borabenzene Chromium Complexes. M. S. Thesis, Massachusetts Institute of Technology, Cambridge, MA. September 2001. (b) Lee, E. C. unpublished results.

Scheme 4. Synthesis of activated manganese borabenzene **23**.



C. Conclusions

This chapter describes the first example of a catalytically active planar-chiral borabenzene complex with catalyst turnover, and control experiments suggest that the site of reactivity is indeed at boron. Nevertheless, when the resolved catalyst was employed in a Diels–Alder reaction, the product was observed to be racemic. While the selectivity and reactivity issues have now been independently tackled, future work should focus on developing systems that integrate ideas from both precedents into a single catalytic asymmetric method.

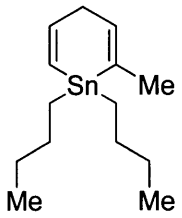
D. Experimental

I. General

All reagents were obtained from commercial sources (e.g., Sigma-Aldrich, Alfa Aesar). Hexa-1,4-diyne is synthesized according to a literature procedure,[60] distilled under nitrogen (105 °C, 760 torr), and used immediately. Dibutylstannane was synthesized according to a literature procedure.[61] Tricarbonyl-bis(acetonitrile) manganese(I) bromide was synthesized according to a literature procedure.[62]

II. Synthetic Procedures

1-Trimethylphosphine-2-methylborabenzene was synthesized from a procedure adapted from the procedure reported for the synthesis of 1-trimethylphosphine-2-*t*-butylborabenzene.[59a]



1,1-dibutyl-2-methyl-1,4-dihydrostannine (17). Freshly distilled hexa-1,4-diyne (5.0 g, 64 mmol) and dibutylstannane (16g, 67 mmol) were add to anhydrous toluene (100 mL) in a 250-mL oven-dried round-bottom flask equipped with stir bar and reflux condenser under nitrogen. The system is wrapped in aluminum foil to exclude light and stirred at reflux under nitrogen for 24 hours. After cooling, the reaction mixture is filtered through Celite and concentrated on high vacuum. The resulting gel is thoroughly washed with

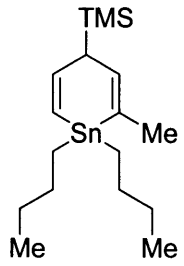
[60] Verkruijsse, H. D.; Hasselaar, M. *Synthesis* **1979**, 292–293.
[61] Hayashi, K.; Iyoda, J.; Shiihara, J. *J. Organomet. Chem.* **1967**, *10*, 81–94.
[62] Farona, M. F.; Kraus, K. F. *Inorg. Chem.* **1970**, *9*, 1700–1704.

hexanes (200 mL). The filtrate is concentrated in vacuo, and the residual oil is distilled on high vacuum. 12 g. 61%. b.p. 78 °C (550 mtorr). Clear oil.

^{1}H NMR (C_6D_6) δ 6.68–6.60 (m, 1H), 6.32–6.25 (m, 1H), 6.13–6.09 (m, 1H), 3.04–2.92 (m, 2H), 2.11–1.99 (m, 3H), 1.65–1.29 (m, 8H), 1.03–0.86 (m, 10H).

^{13}C NMR ($CDCl_3$) δ 145.4, 137.0, 125.2, 36.5, 29.6, 27.4, 27.3, 13.9, 10.0.

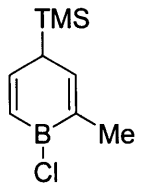
MS (ESI) *m/z* (M^+) calcd for $C_{14}H_{26}Sn$: 314.1, found: 313.1 ($M^+ - H$).



(1,1-dibutyl-2-methyl-1,4-dihydrostannin-4-yl)trimethylsilane (18). 1,1-Dibutyl-2-methyl-1,4-dihydrostannine (12 g, 39 mmol) in 20 mL THF was added with a solution of LDA (2 M in THF, 20 mL, 40 mmol) dropwise over 2 minutes at –78 °C. The reaction is stirred 2 hours at –78 °C, and chlorotrimethylsilane (4.7 g, 43 mmol) is added dropwise over 1 minute. The reaction is stirred for 2 hours at –78 °C, allowed to warm to room temperature, and then stirred for another 20 hours. The reaction mixture is diluted with 50 mL hexanes, washed with water (2 × 100 mL), saturated aqueous sodium bicarbonate solution (150 mL), and brine (50 mL). The organic layer is dried over sodium sulfate, filtered, and concentrated in vacuo to yield the crude material which was estimated to be approximately 90% pure by ^{1}H NMR and carried onto the next step without purification. 15 g. 98%. Yellow oil.

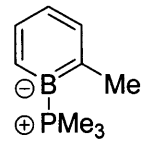
^{1}H NMR ($CDCl_3$) δ 6.67–6.60 (m, 1H), 6.12–6.09 (m, 1H), 5.99–5.92 (m, 1H), 2.91–2.83

(m, 1H), 1.96 (s, 3H), 1.65–1.29 (m, 8H), 1.03–0.86 (m, 10H), 0.02 (s, 9H).



(1-chloro-2-methyl-1,4-dihydroborinin-4-yl)trimethylsilane (19). An oven-dried 3-neck 100-mL round-bottom flask equipped with stir bar and distillation setup with a Schlenk tube receiver is charged with (1,1-dibutyl-2-methyl-1,4-dihydrostannin-4-yl)trimethylsilane (15 g, 38 mmol). The system is successively evacuated and backfilled with argon 3 times. Anhydrous hexanes (25 mL) are added, and the solution is cooled to –78 °C. Boron trichloride (1 M in hexanes, 38 mL, 38 mmol) is added dropwise over 2 minutes at –78 °C. The reaction is allowed to warm to room temperature and stirred another 2 hours. The mixture is heated to 120 °C to remove most of the hexanes, then cooled to –78 °C. Vacuum is applied and the mixture is allowed to warm slowly to prevent bumping. The product is vacuum distilled. 3.7 g. 51%. b.p. 37 °C (400 mtorr). Orange oil.

^{1}H NMR ($CDCl_3$) δ 7.27–7.22 (m, 1H), 6.70–6.64 (m, 1H), 6.46–6.40 (m, 1H), 3.57 (d, 1H, J = 5.2 Hz), 2.04 (s, 3H), 0.07 (s, 9H).



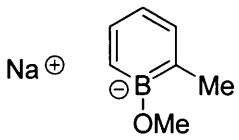
2-methyl-1-(trimethylphosphonio)borinin-1-uide (20). (1-Chloro-2-methyl-1,4-dihydroborinin-4-yl)trimethylsilane (3.9 g, 19 mmol) was dissolved in anhydrous

hexanes (20 mL) in the glovebox in 50-mL oven-dried round-bottom flask. The flask is equipped with stir bar and sealed with a septum, brought outside the glovebox, and cooled to –78 °C. Trimethylphosphine (2.0 mL, 19 mmol) is added as a solution in anhydrous hexanes (10 mL) dropwise over 2 minutes. The reaction is warmed to room temperature and stirred another 2 hours, after which the solids are collected by vacuum filtration and washed with hexanes. 3.0 g. 94%.

^{1}H NMR (C_6D_6) δ 7.85–7.76 (m, 1H), 7.69–7.61 (m, 1H), 7.28–7.22 (m, 1H), 7.05–6.98 (m, 1H), 2.50 (s, 3H), 0.72 (d, 9H, J = 11.2 Hz).

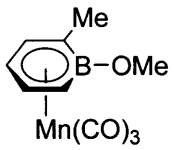
^{11}B NMR (C_6D_6) δ 18.9 (d, J = 105.8 Hz).

^{13}C NMR (C_6D_6) δ 136.1 (d, J = 15.2 Hz), 131.7 (d, J = 17.7 Hz), 120.7, 24.8 (d, J = 2.7 Hz), 10.8 (d, J = 41 Hz).



sodium 1-methoxy-2-methylborinin-1-uide (21). In a glove box, 2-methyl-1-(trimethylphosphonio)borinin-1-uide (3.0 mg, 20 mmol) and sodium methoxide (0.99 g, 18 mmol) are mixed in anhydrous THF (20 mL) in a sealed 40-mL vial and heated to 60 °C for 20 hours. The mixture is filtered and concentrated in vacuo. The residual solids are triturated over pentane/ether (1:1, 30 mL) for 1.5 hours, then filtered. The solids are dried on vacuum. The material appeared to be about 80% pure. 0.99 g. 38%.

^{1}H NMR (THF-d_8) δ 6.05–5.92 (m, 1H), 5.92–5.75 (m, 1H), 5.75–5.62 (m, 1H), 5.47–5.39 (m, 1H), 3.00 (s, 3H), 1.60 (s, 3H).

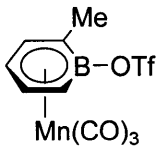


1-methoxy-2-methylborinin-1-uide manganese tricarbonyl (22). Sodium 1-methoxy-2-methylborinin-1-uide (100 mg, 0.70 mmol) and tricarbonyl-bis(acetonitrile) manganese(I) bromide (209 mg, 0.70 mmol) are mixed in THF (10 mL) in a 20-mL vial and heated to 60 °C for 18 hours. The solids are filtered off, and the filtrate is concentrated. The residual material is triturated in ether/pentane (1:1, 20 mL) for 1 hour. After filtering, the filtrate is concentrated to give a yellow oil. 83 mg. 46%.

The enantiomers could be separated by semi-preparative chiral HPLC on an OD–H column (1% isopropanol/hexanes, 1.5 mL / min). t_r = 18.3 min, 20.5 min.

^{1}H NMR ($CDCl_3$) δ 5.79 (dd, 1H, J = 6.1, 9.3 Hz), 5.73 (d, 1H, J = 5.8 Hz), 5.12 (t, 1H, J = 5.9 Hz), 3.76–3.74 (m, 1H), 3.73 (s, 3H), 1.77 (s, 3H).

^{11}B NMR ($CDCl_3$) δ 26.6.



1-trifluoromethanesulfonate-2-methylborinin-1-uide manganese tricarbonyl (23a). 1-Methoxy-2-methylborinin-1-uide manganese tricarbonyl (320 mg, 1.2 mmol) is dissolved in benzene (4 mL) in a 20-mL vial equipped with a stir bar. Triflic anhydride (1.0 mL, 6.0 mmol) was added dropwise over 1 minute. The solution is stirred at 60 °C for 18 hours, then concentrated in vacuo. 92 mg. 20%.

^{1}H NMR ($CDCl_3$) δ 5.84–5.76 (m, 2H), 5.23 (t, 1H, J = 12.0 Hz), 4.41 (d, 1H, J = 24.5

Hz), 1.79 (s, 3H).

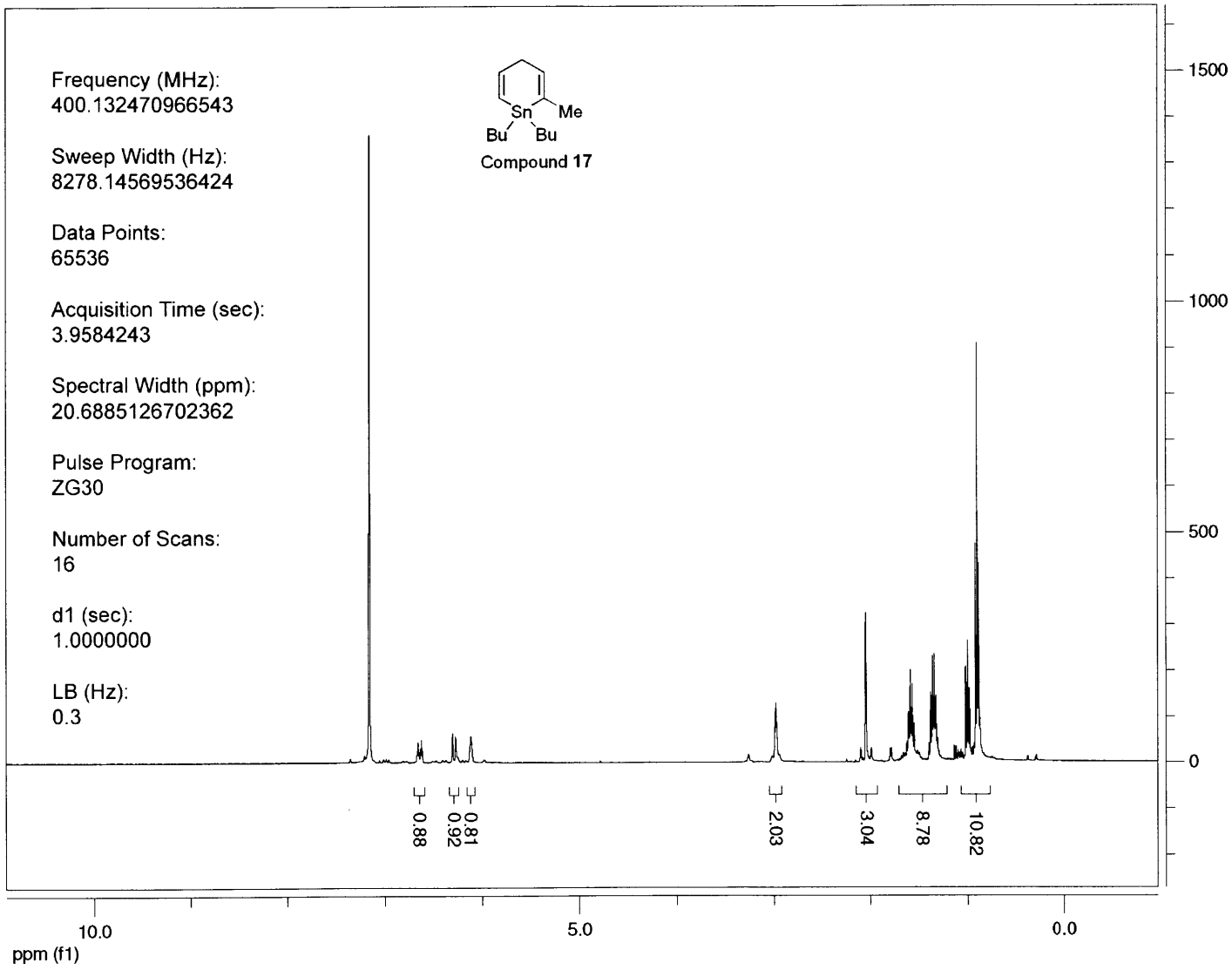
^{11}B NMR ($CDCl_3$) δ 25.5.

^{19}F NMR ($CDCl_3$) δ –76.7.

III. Diels–Alder Reactions

In a 4-mL vial, methacrolein (42 μL, 0.50 mmol) and 1-trifluoromethanesulfonate-2-methylborinin-1-uide manganese tricarbonyl (19 mg, 0.050 mmol) are mixed in DCM (0.5 mL) and cooled to –78 °C. Cyclopentadiene (122 μL, 1.5 mmol), freshly cracked from dicyclopentadiene and distilled, is added by syringe at –78 °C dropwise over 1 minute. The reaction is stirred 1 hour at –78 °C, and then 1 mL of water is added. The aqueous layer is extracted with ether (2 × 1 mL). The combined organic extracts are dried over $MgSO_4$, filtered, and concentrated. The enantiomeric excess was measured to be <5% ee by ^1H NMR observation of the aldehyde C–H peak in the presence of 100 mol% $Eu(hfc)_3$ (δ 12.40, 12.36).

IV. ^1H NMR Spectra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Pulse Program:
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Bu
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3.04
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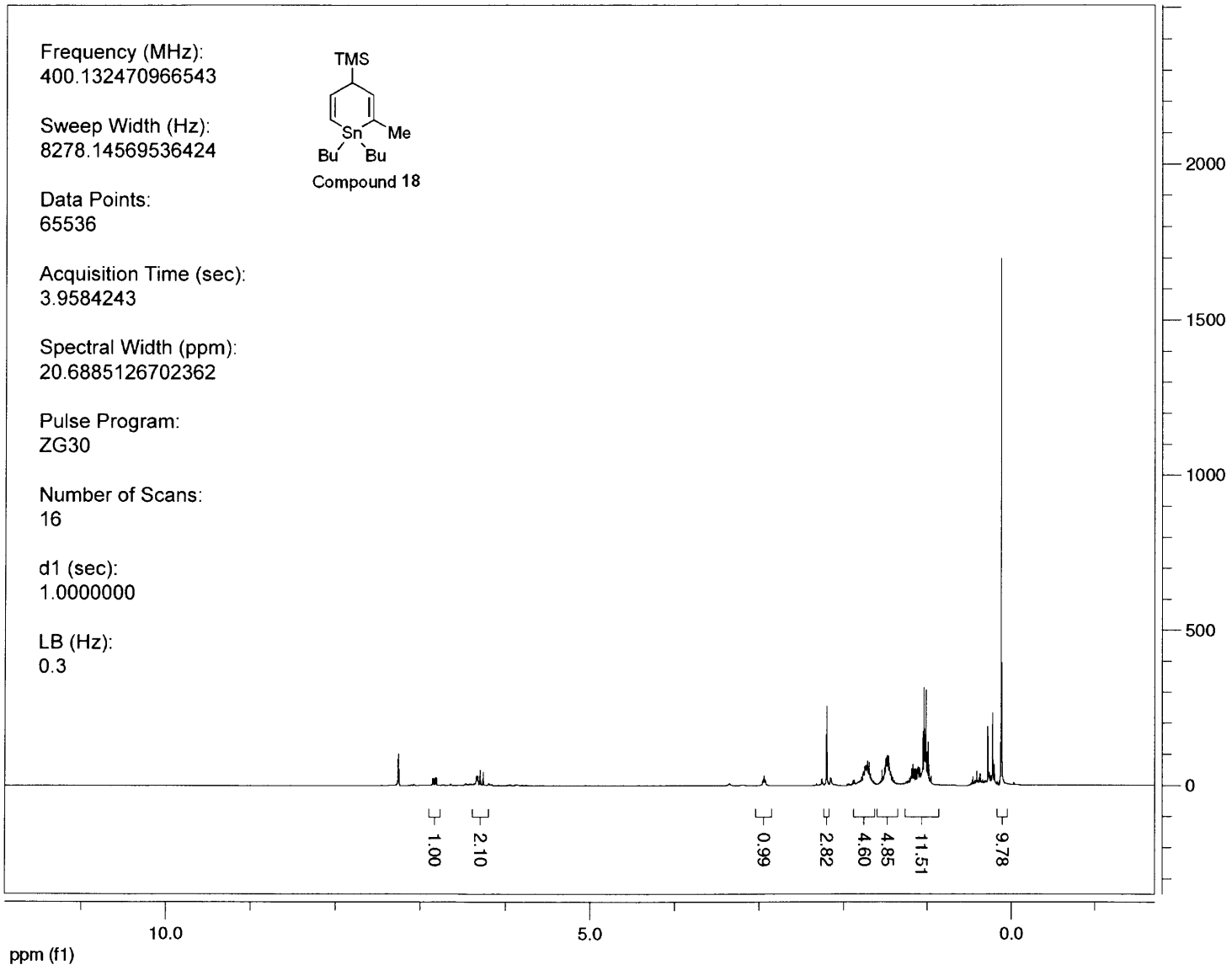
ppm (f1)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Bu
Bu
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1000
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10.0
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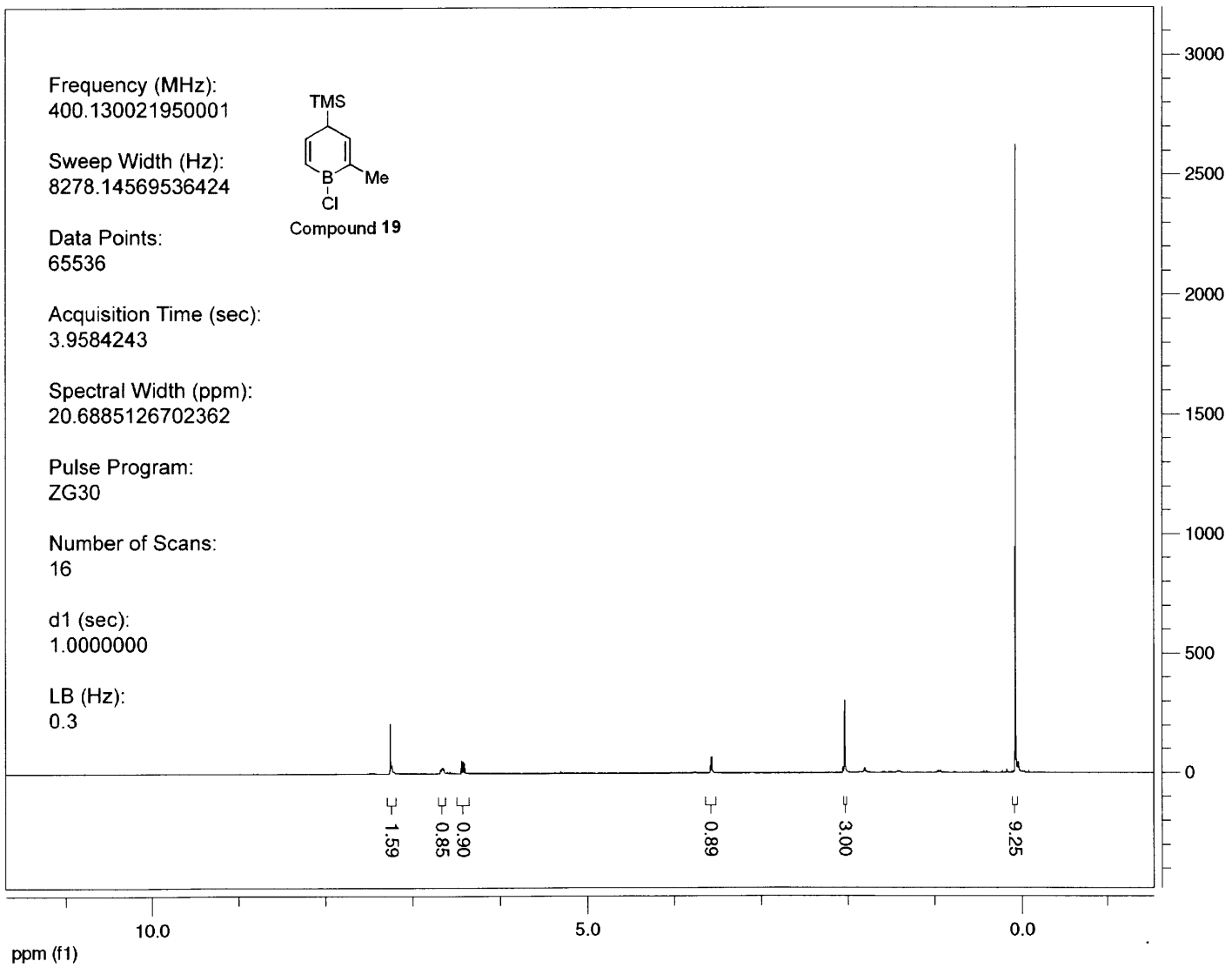
ppm (f1)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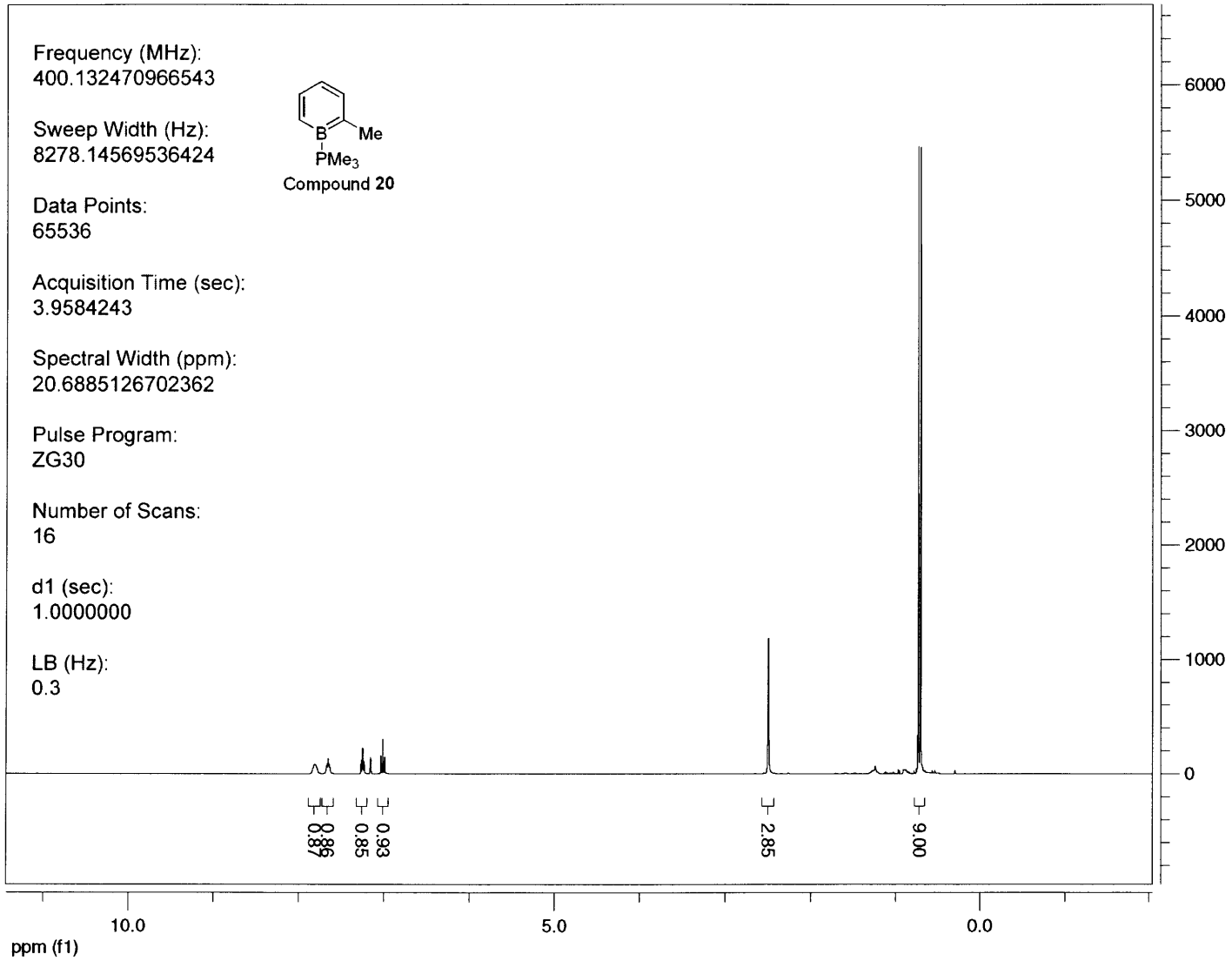
ppm (f1)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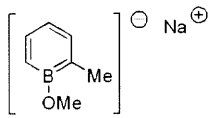
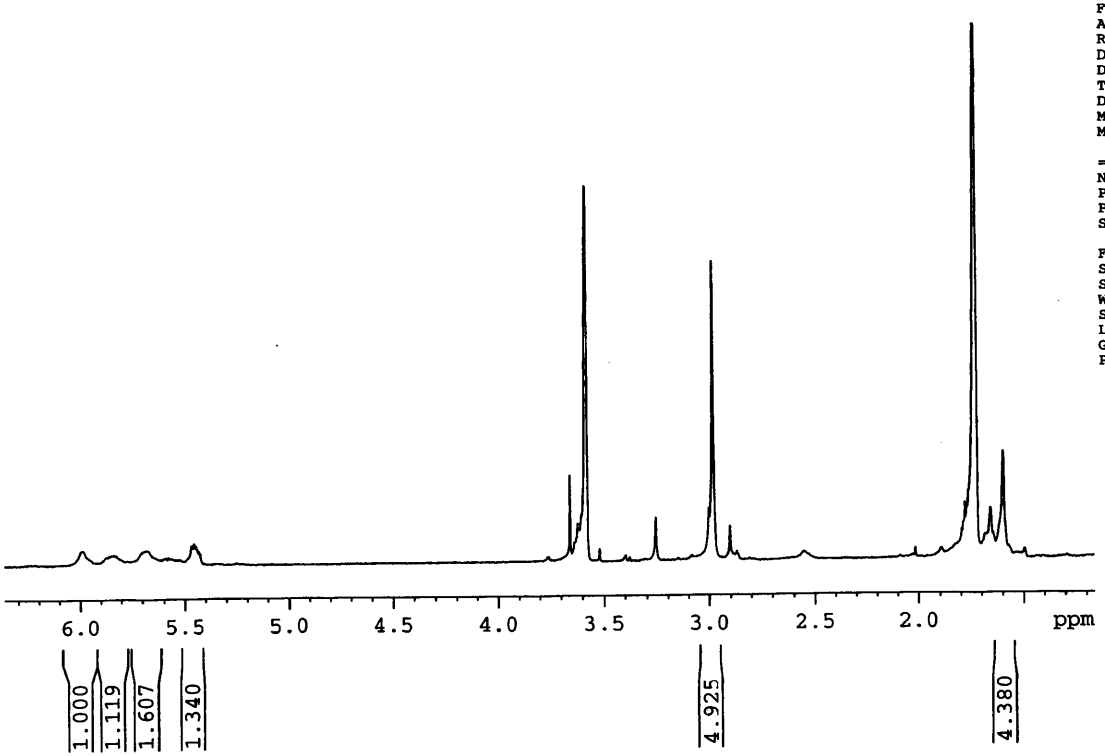


Compound **21**

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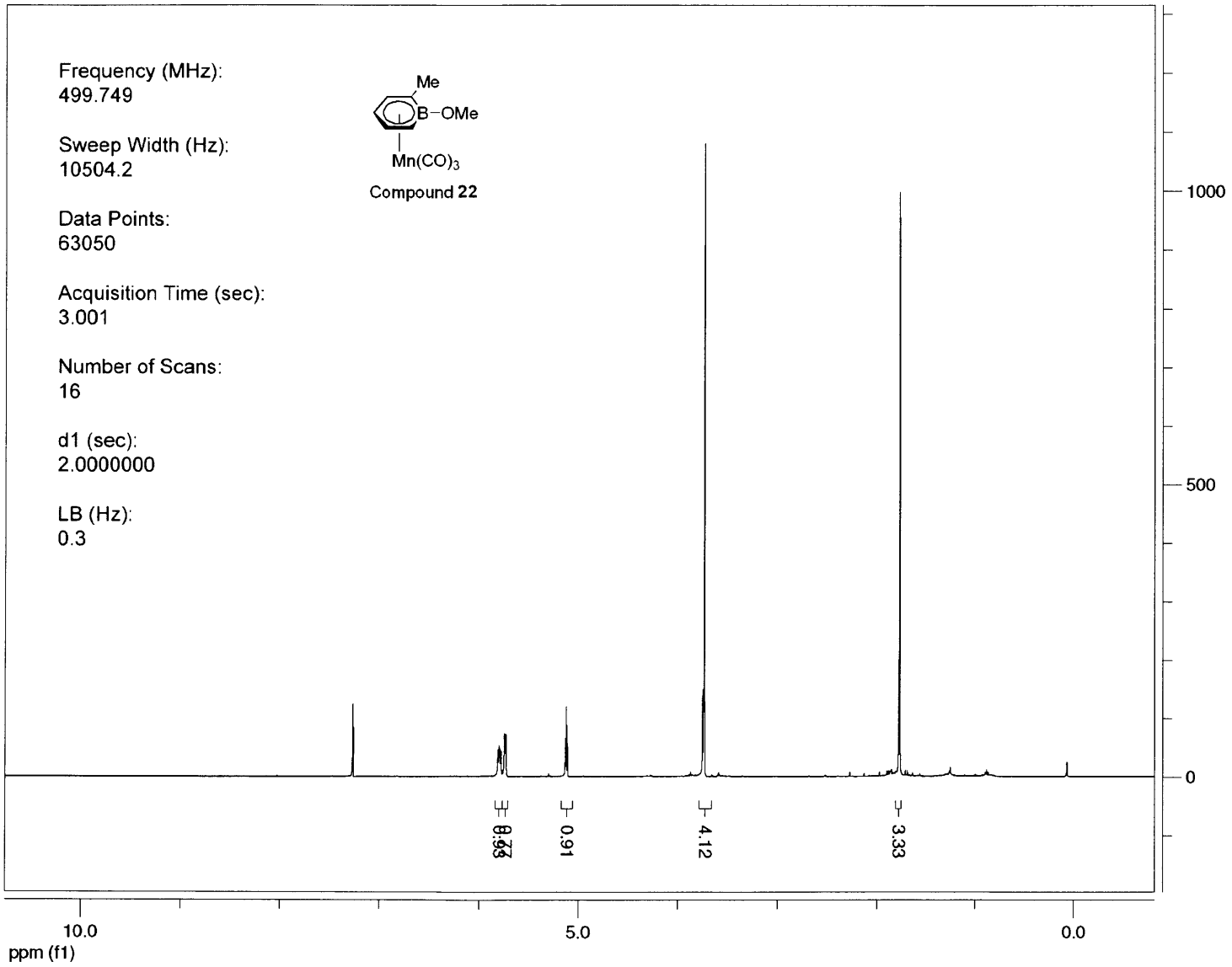
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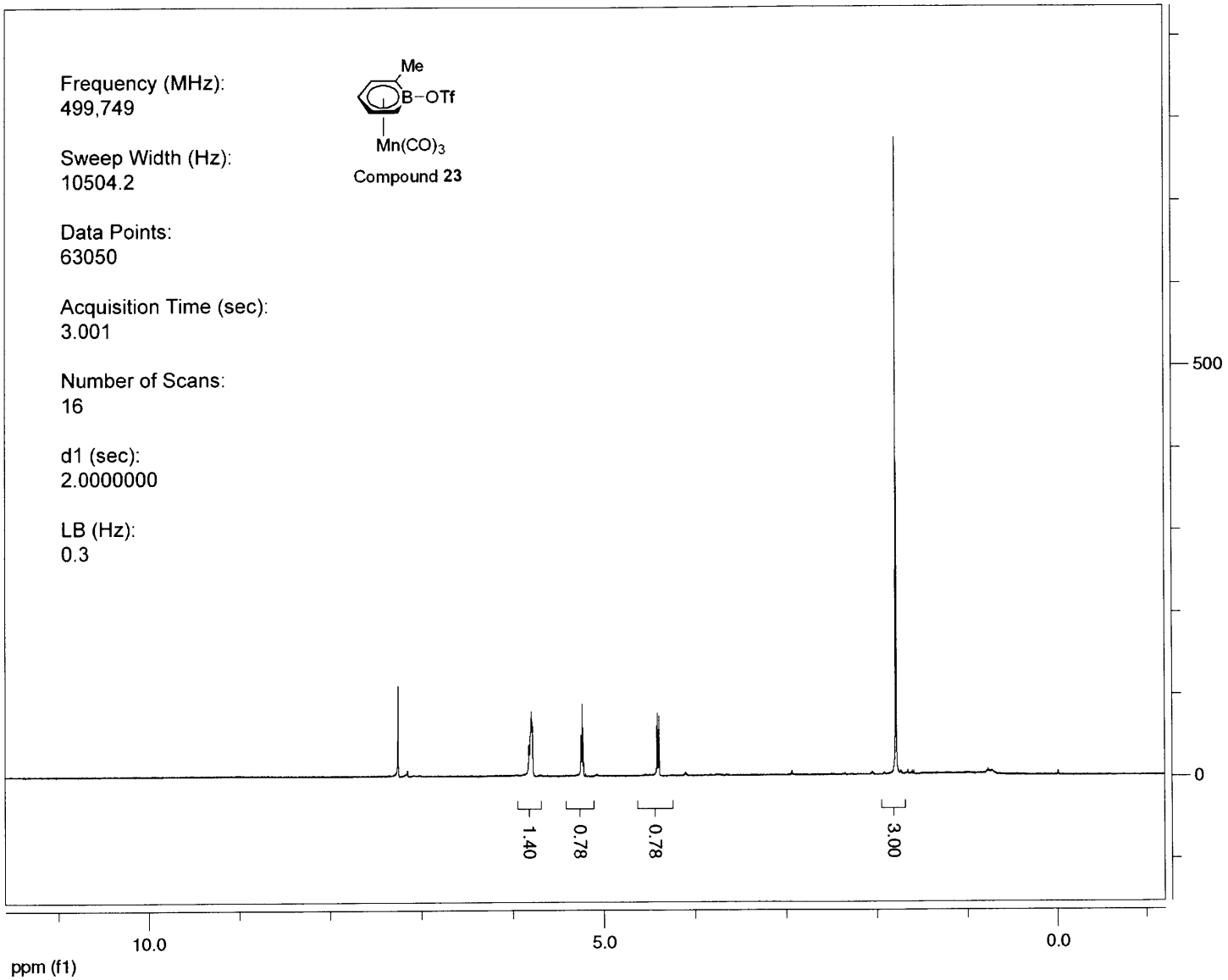
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Chapter 4

Theoretical Study of Properties and Reactions of Borabenzenes and Borabenzene Complexes

A. Introduction

With the rapid increase in computing power over the recent years, computational chemistry has experienced a correlated increase in complexity and accuracy.[63] Very popular among the methods for computational chemistry is density functional theory (DFT). DFT reduces the collection of n electrons in a standard Hartree–Fock analysis ($3n$ degrees of freedom) to an electron density (3 degrees of freedom), greatly reducing the computational time required for a given electronic system (Figure 6). Although Kohn and Hohenberg proved that the density functional for the total energy is well-defined and represents the correct ground state energy, neither this functional nor the exchange-correlation functional is available. In practice, implementation of DFT relies on the use of functionals that are empirically parameterized against experimental data.[64]

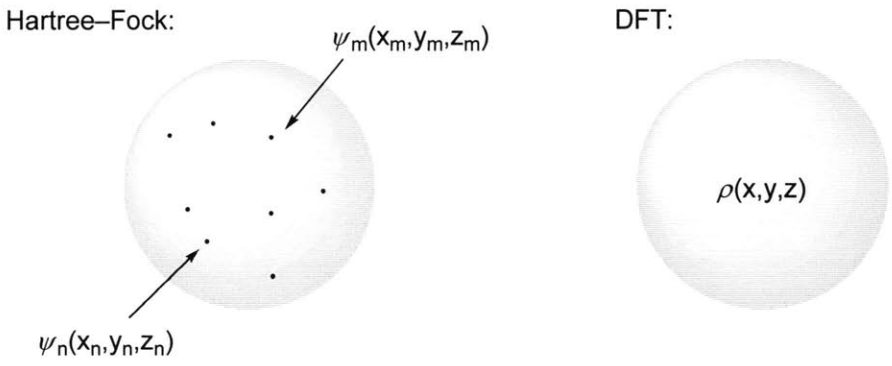


Figure 6. Simplified comparison of Hartree–Fock methods requiring the quantum mechanical treatment of all electrons to density functional theory requiring only the electron density.

[63] Fantacci, S.; Amat, A.; Sgamellotti, A. *Acc. Chem. Res.* **2010**, *43*, 802–813.
[64] Young, D. C. Density Functional Theory. *Computational Chemistry: A Practical Guide for Applying Techniques to Real-World Problems*; Wiley: New York, 2001; pp 42–48.

The most popularly used functional is the hybrid B3LYP,[65] which takes an admixture of the Hartree-Fock exchange energy with an energy derived from the Becke three-parameter exchange functional and the Lee-Yang-Parr correlation functional, the latter two being experimentally parameterized. Using this functional, various aspects of chemistry, including physical properties and reaction kinetics, have been studied.[66]

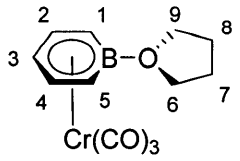
With some of the experimental work on borabenzenes in hand, the power of DFT was applied towards understanding some of the more subtle electronic and steric effects that govern the chemistry of borabenzenes.

[65] Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652.
[66] Bachrach, S. M. *Computational Organic Chemistry*; Wiley-Interscience: Hoboken, N.J., 2007.

B. Results and Discussion

Since the accuracy of the empirically parameterized aspect of B3LYP cannot be determined a priori, benchmarking studies were carried out in order to ascertain the reliability of this method for use with metal-complexed borabenzenes. Specifically, the accuracy of geometry and energy calculations need to be evaluated.

For this purpose, the structure of THF adduct **24** was optimized in silico and compared to the crystal structure of the same compound.[67] The main difference is that the three carbonyl groups of one complex are rotated approximately 30° about the borabenzene–chromium axis relative to the carbonyl groups of the other.[68] The root mean square displacement (RMSD) was 0.34 Å, and the corresponding RMSD without the three carbonyl groups was only 0.14 Å. This provided relatively high confidence concerning the accuracy of geometry optimizations. Table 10 lists several comparisons between selected structural parameters of the computed structure and the structure obtained from X-ray crystallography.



24

[67] Amendola, M. C.; Stockman, K. E.; Hoic, D. A.; Davis, W. M.; Fu, G. C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 267–269. CCSD database entry RIHGAQ.

[68] The rotation of the chromium tricarbonyl moiety relative to η^6-coordinated benzene has been estimated to be less than 0.4 kcal mol^{-1}. See: Kukolich, S. G.; Sickafoose, S. M.; Flores, L. D.; Breckenridge, S. M. *J. Chem. Phys.* **1975**, *101*, 331–346.

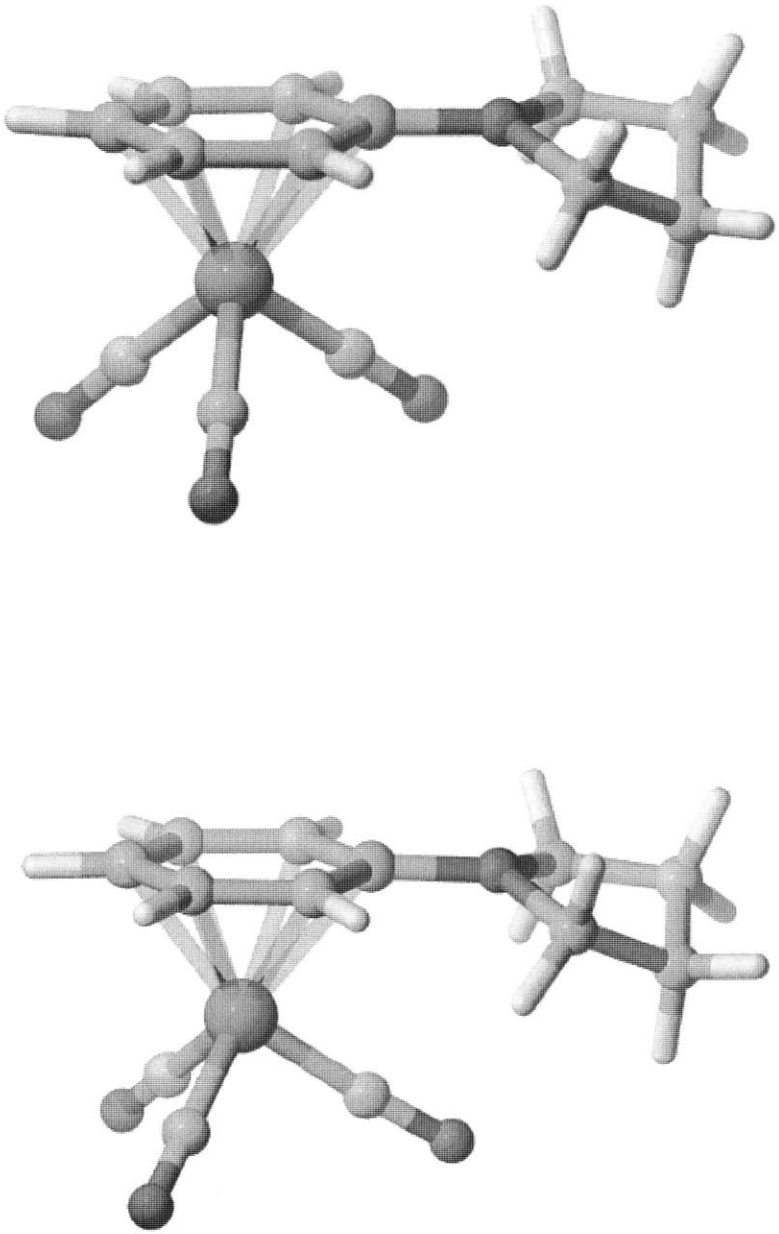


Figure 7. Crystal structure (top) and computed structure (bottom) of **24**.

Table 10. Selected structural parameters for crystal and computed structures of **24**.

Structural Parameter	Crystal Structure	Computed Structure
d_{B-O}	1.47 Å	1.51 Å
d_{B-Cr}	2.33 Å	2.34 Å
d_{C2-Cr}	2.23 Å	2.28 Å
d_{C4-Cr}	2.23 Å	2.28 Å
θ (C1–B–O)	120.4°	120.2°
$\theta_{dihedral}$ (C1–B–O–C6)	–157.8	–160.3°

Since experimentally derived energies for borabenzenes and metal–complexed borabenzenes were not readily available, energies were benchmarked according to the rotational barrier about the phenyl–oxygen bond in anisole. The obtained value of 4.7 kcal mol^{-1} is about 1 kcal mol^{-1} higher than the highest experimentally determined value.[69] This potential for systematic overestimation of activation energy must be kept in mind. For *B*-methoxyboratabenzene, the barrier to rotation was calculated to be 4.5 kcal mol^{-1}. This result suggests that the factors that favor the planar form of both anisole and *B*-methoxyboratabenzene are operating comparably in both species.

anisole *B*-methoxyboratabenzene

Surprisingly, the rotational barriers for aldehydes complexed to the borabenzene were higher by approximately a factor of two. These data shed light onto the nature of the interaction between the carbonyl and borabenzene. An analysis of the charges on a complexed methacrolein in the planar (**25b**) and perpendicular (**25b**‡) conformations indicates that the sum of the charges in the planar conformation is 0.18 elementary units

[69] A value of 3.6 kcal mol^{-1} was deduced from torsional frequencies. See: Schaefer, T.; Penner, G. H. *Can. J. Chem.* **1988**, *66*, 1635–1640 and references therein.

lower. This means that there is greater electron density on methacrolein when the borabenzene and the carbonyl are in plane and conjugation is possible, and therefore, the predominant π-symmetry interaction is actually donation from the borabenzene into the carbonyl group.

To further probe this interesting result, calculations were performed using various substituted borabenzenes. The rotational barriers about the B–O bond were calculated and plotted against both Hammett σ and σ^+ parameters (Figure 8, Table 11).[70,71] The correlation was higher when using σ^+ (R^2 = 0.94) than when using σ (R^2 = 0.57), suggesting a significant contribution from resonance effects. A negative slope was obtained (ρ = –2.9), suggesting that the substituents are stabilizing a positive charge by resonance. These results are consistent with π-donation from the borabenzene into the carbonyl group.

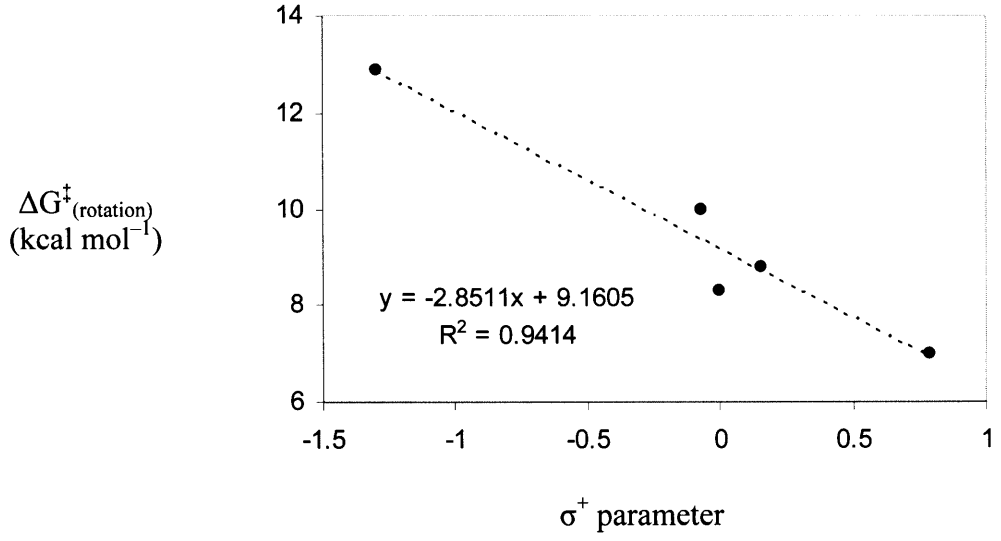
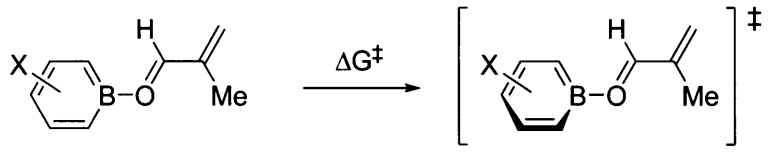


Figure 8. Plot of the calculated barrier of rotation (kcal mol^{-1}) about the boron–carbonyl bond vs. Hammett σ^+ parameter.

[70] Ansyln, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry*; University Science Books: Sausaliot, CA, 2006; pp 451–453.
[71] σ^+ and σ values were obtained from: Gokel, G. W. *Dean's Handbook of Organic Chemistry*, 2nd Ed.; McGraw-Hill: New York, 2004; pp 7.4–7.11.

Table 11. Substituent effects on calculated rotational barriers about the boron–carbonyl bond in substituted borabenzenes.



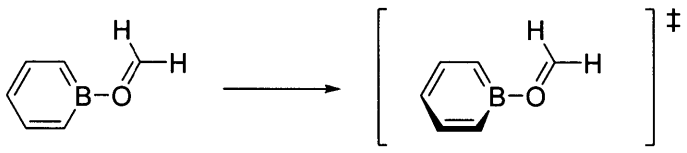
25a: R = *p*-NO_2
25b: R = H
25c: R = *m*-NH_2
25d: R = *p*-F
25e: R = *p*-NH_2

25a‡: R = *p*-NO_2
25b‡: R = H
25c‡: R = *m*-NH_2
25d‡: R = *p*-F
25e‡: R = *p*-NH_2

Substituent (X–)	Rotational Barrier (kcal mol^{-1})	σ Parameter	σ^+ Parameter
p-NO_2– (**25a**)	7.0	0.78	0.79
H– (**25b**)	8.3	0.00	0.00
m-NH_2– (**25c**)[72]	8.8	–0.16	0.16
p-F– (**25d**)	10.0	0.34	–0.07
p-NH_2– (**25e**)	12.9	–0.66	–1.3

When borabenzene-formaldehyde adduct (**26**) is examined, it is found that the rotational barrier (9.7 kcal mol^{-1}) is similar to that of the methacrolein adduct (**25b**). In addition, the total charge on formaldehyde is higher when it is perpendicular to the plane of the borabenzene by 0.18 elementary units relative to the co-planar conformation. Therefore, it is likely that the back-donation is a common feature among all aldehydes, not just those bearing α,β-unsaturation.

[72] The conformation where the aldehyde is rotated away from the 3-amino group is lower in energy, and thereforefore, this is considered to be the ground state for this analysis.



26 **26‡**

This result concerning the nature of the π-symmetry interaction is at first unsettling because it seems as if the borabenzene might not effectively activate a complexed carbonyl to nucleophilic attack. However, the σ activation of the carbonyl group is still significant and in the case where the borabenzene is also coordinated in an η^6 fashion to a magnesium tricarbonyl, the polarization of the carbonyl group of the bound methacrolein (3.0 D) is larger than that of the free methacrolein (2.7 D).

Coordination of a metal to the borabenzene in the gas phase produced some interesting effects. In some cases, the complexed methacrolein was found to twist out of the plane of the borabenzene about the boron–carbonyl bond. The magnitude of the twist was strongly correlated to the identity of the η^6-coordinated metal. For the chromium complex (**27**), almost no out-of-planar twist is observed. With the manganese complex (**28**), the methacrolein was rotated out of plane by 38° away from the metal. The differences in ground state conformations are probably due to the difference in charges: the chromium complex is overall neutral while the manganese complex is +1 charged. These results are summarized in Figure 9.

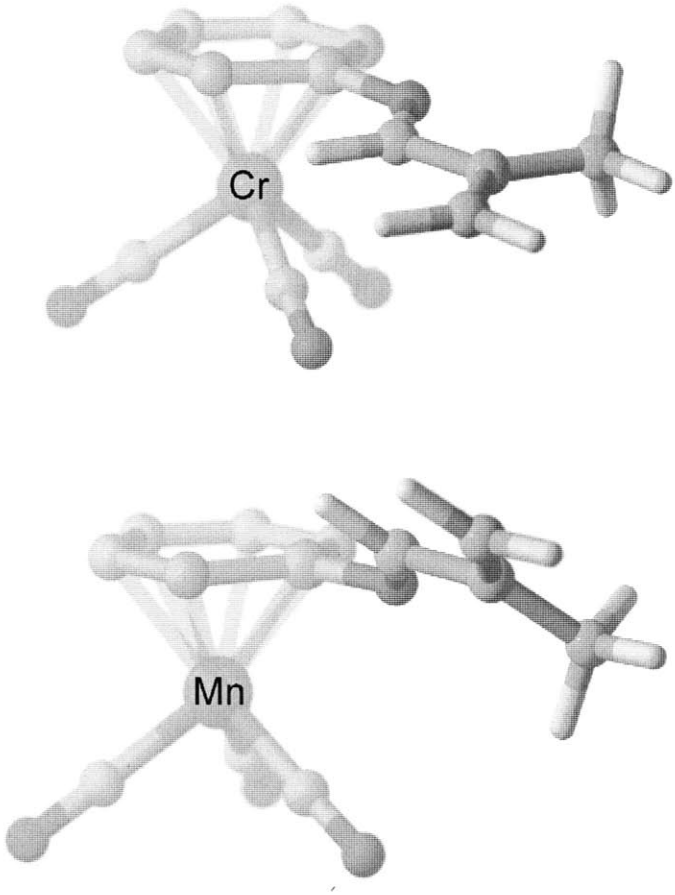


Figure 9. Methacrolein adducts with a chromium borabenzene complex (top) and a manganese borabenzene complex (bottom). Some hydrogen atoms have been omitted for clarity.

Finally, the power of DFT was turned towards examining the nature of catalytic activity of the borabenzene complexes in Diels–Alder cycloadditions. The results are depicted in Figure 10 and Figure 11. Of the different possible orientations for the transition states, the exo transition states were favored[73] with the methacrolein in the s-

[73] It is well established that in cycloadditions between cyclopentadiene and methacrolein, the exo product is the major product. For example, see: Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238–1256 and references therein.

trans conformation. [74] The transition states indicate a concerted, asynchronous cycloaddition, and a more complete bond to the β carbon of methacrolein is observed in the transition state.

With manganese, the difference in energy between the two diastereomeric transition states (Figure 10: **29a**‡ and **29b**‡) is only 0.2 kcal mol^{-1}, suggesting that asymmetric induction with the manganese complex would be a poor. This is consistent with the experimentally observed data (Chapter 3). The manganese tricarbonyl moiety may be too small to create a bias in terms of facial selectivity. Still, the calculated activation energies of 11.1 kcal mol^{-1} and 11.3 kcal mol^{-1} are significantly lower than the calculated barrier of 31.8 kcal mol^{-1} for the uncatalyzed reaction in the gas-phase.[75,76]

On the other hand, in the chromium complex, the two diastereomeric transition states (Figure 11: **30a**‡ and **30b**‡) are different in energy by 2.8 kcal mol^{-1}, with cyclopentadiene passing near the chromium tricarbonyl moiety in the favored transition state (**30b**‡).[77] Possibly, an electronic stabilization overrides steric factors that might exist between the chromium tricarbonyl moiety and the approaching diene. While the model for stereoinduction for nucleophilic addition to a planar-chiral borabenzene-activated aldehyde supposes that steric interactions with the metal and its other ligands govern the facial selectivity of the addition (Figure 5), it is plausible that in other reactions, electronic effects might dictate the stereochemical outcome. The activation energies (22.5

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[74] The higher reactivity of the s-*trans* conformation and the exo selectivity are consistent with other computed results. See: Pi, Z.; Li, S. *J. Phys. Chem. A* **2006**, *110*, 9225–9230.

[75] Barba, C.; Carmona, D.; García, J. I.; Lamata, M. P.; Mayoral, J. A.; Salvatella, L.; Viguri, F. *J. Org. Chem.* **2006**, *71*, 9831–9840.

[76] The activation enthalpy for cycloaddition between crotonaldehyde and cyclopentadiene is in good agreement with the calculated enthalphy. However, the calculation overestimates the activation entropy by about 20%. For the reaction in question, these data suggest a barrier of approximately 20 kcal mol^{-1}. See Ref. 75 for details.

[77] The shortest distance between a carbonyl group on the chromium and a hydrogen atom on cyclopentadiene in transition state **30b**‡ is about 2.5 Å.

kcal mol^{-1} and 25.2 kcal mol^{-1}) are higher than those for the manganese catalyst but still significantly lower than the uncatalyzed barrier (31.8 kcal mol^{-1}). The planar-chiral chromium catalyst could not be isolated to experimentally verify this result.

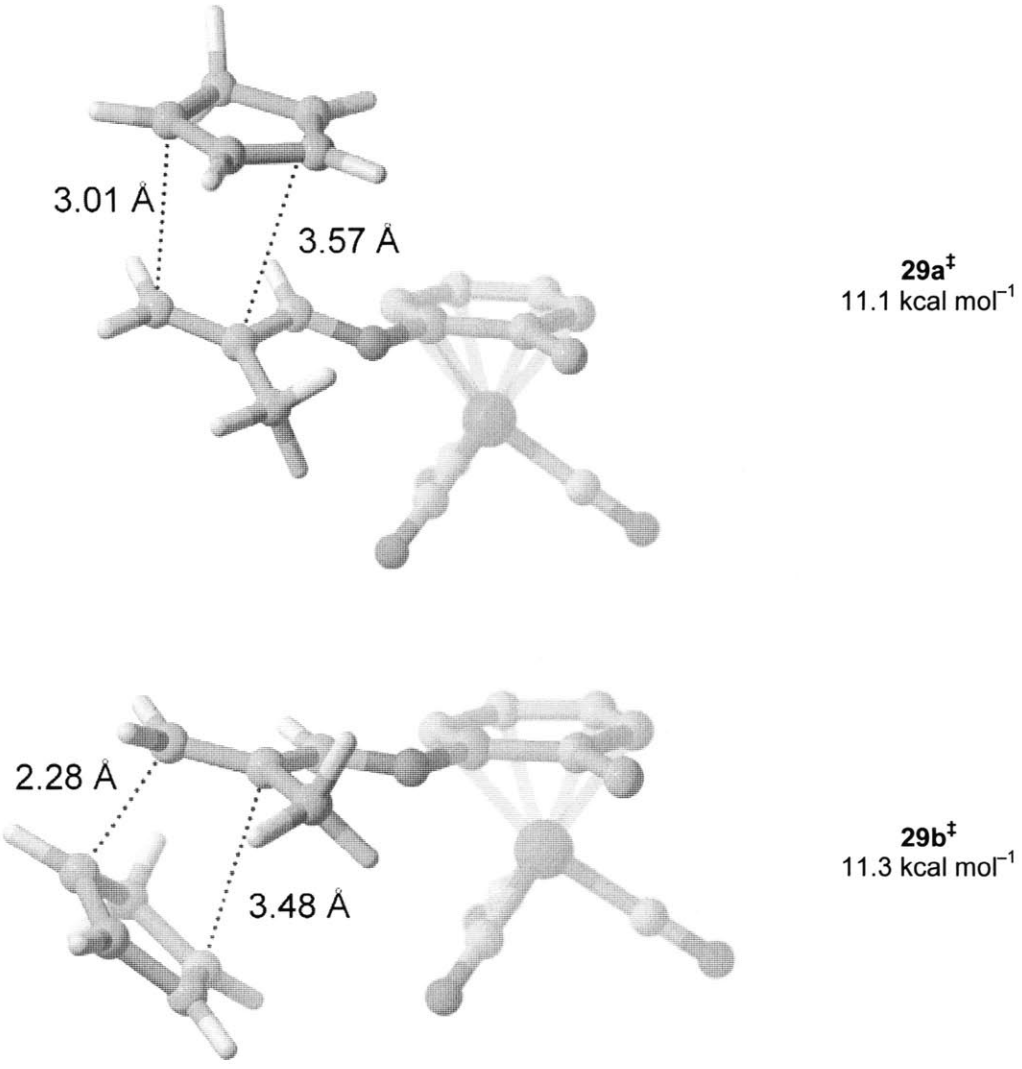

Figure 10. Transition states for the cycloaddition between cyclopentadiene and methacrolein, activated by a borabenzene-manganese complex. Some hydrogen atoms have been omitted for clarity.

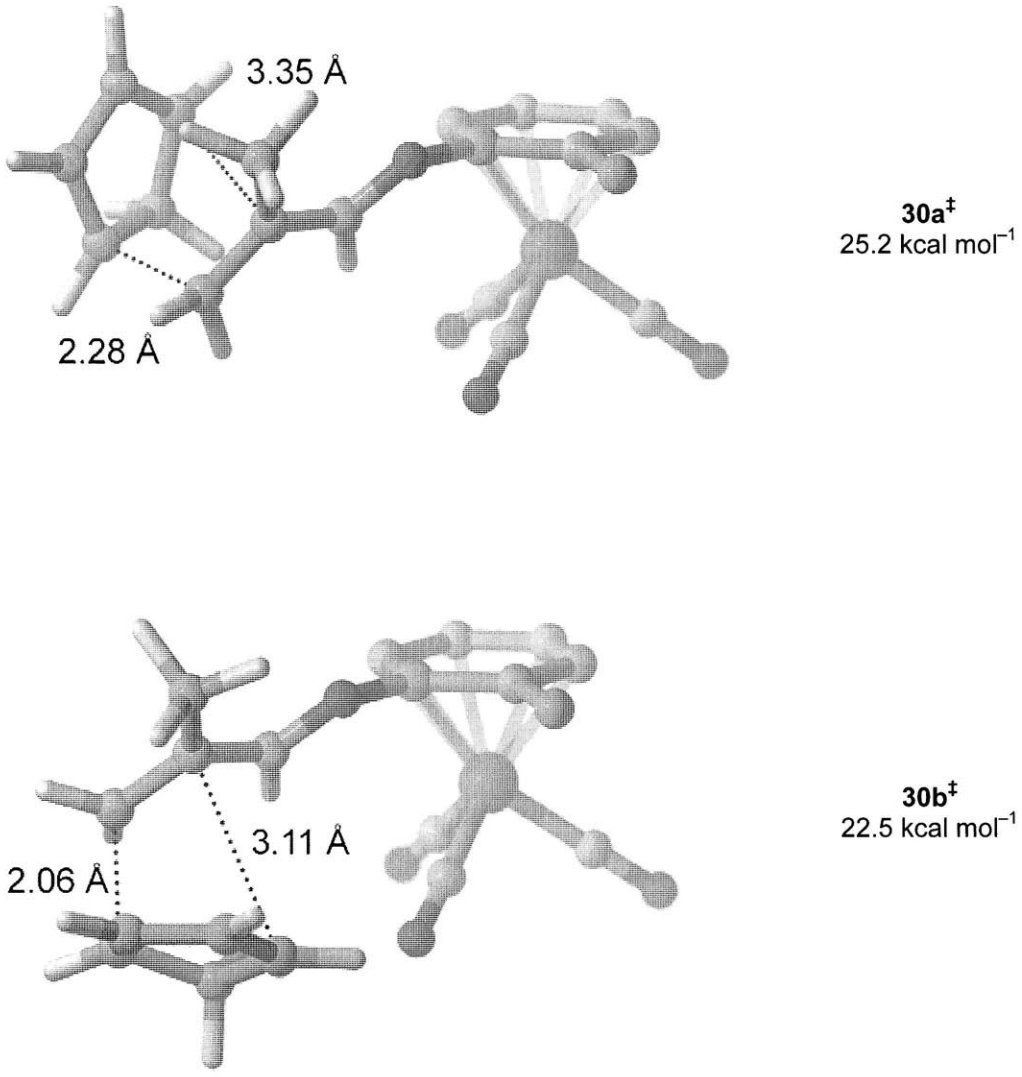

Figure 11. Transition states for the cycloaddition between cyclopentadiene and methacrolein, activated by a borabenzene-chromium complex. Some hydrogen atoms have been omitted for clarity.

C. Conclusions

In this chapter, density functional theory was used to examine the nature of borabenzenes and borabenzene complexes. Computational results suggest that the predominant π-symmetry interaction in a borabenzene-aldehyde adduct may be back-bonding from the borabenzene into the carbonyl. Computations also indicate that a manganese borabenzene complex (described in chapter 3), although catalytically active, would provide poor asymmetric induction in a Diels–Alder cycloaddition between methacrolein and cyclopentadiene. On the other hand, the corresponding chromium complex could provide selectivity if synthesized.

D. Experimental

Computational methods.

Geometry optimizations and frequency calculations were performed in the gas-phase with the B3LYP functional implemented in Gaussian 03.[78] The LANL2DZ basis set with effective core potential was used for transition metals, and the 6-31+G(d) basis set was employed for all other atoms except for fluorine, for which the modified 6-31+G(d′) basis set was used.[79,80] Charges were analyzed using the Natural Bond Orbitals model.[81]

Selected Atomic Coordinates. All Cartesian coordinates are in angstroms.

Compound **24**

C	–0.170708	–0.211643	0.010764
C	1.176044	–0.185190	0.437915
C	0.931406	2.391724	0.647890
C	–0.403916	2.233026	0.209912
C	–0.956722	0.964439	–0.094072
H	–0.621246	–1.153351	–0.294226
H	1.707538	–1.134021	0.416006
H	–1.027878	3.110196	0.054645
H	–1.977227	0.896550	–0.455630
B	1.768625	1.152505	0.782650
Cr	0.892828	1.243274	–1.387710
C	0.587967	0.044788	–2.747017
C	2.634212	1.382510	–1.868891
C	0.432376	2.621117	–2.514140
O	0.389678	–0.725256	–3.599673
O	3.785988	1.462233	–2.102524
O	0.135989	3.503839	–3.215829
H	1.271754	3.413743	0.799035
C	3.968524	2.537355	1.146031
C	4.130990	0.092764	1.149052
C	5.417214	2.103720	0.950168

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[78] Frisch, M. J. et al. *Gaussian 03*, Rev. C.02; Gaussian, Inc.; Wallingston, CT, **2004**.

[79] The Complete Basis Set (CBS) is described in: Petersson, G. A.; Bennett, A.; Tensfeldt, T. G.; Al-Laham, M. A.; Shirley, W. A. *J. Chem. Phys.* **1988**, *89*, 2193–2218.

[80] CBS has been shown to be more accurate for fluorine. For example, see: Jursic, B. S. *J. Mol. Struct.* **1999**, *465*, 193–196.

[81] Natural bond orbitals were used to calculate charges. This approach has largely replaced the use of Mulliken charges for ab initio calculations. See: Glendening, E., Landis, C. R., Weinhold, F., Eds. What are NBOs (and Other "Natural"-Type Orbitals)?, 2010. Natural Bond Orbital NBO 5* Homepage. http://www.chem.wisc.edu/~nbo5/ (accessed Jul 5, 2010) and references therein.

H	3.776808	3.038481	2.097244
H	3.555774	3.107621	0.315508
C	5.466976	0.690098	1.559444
H	4.118623	–0.272466	0.120137
H	3.723284	–0.652071	1.832344
H	5.652652	2.068229	–0.117448
H	6.108597	2.796123	1.439079
H	6.300971	0.097453	1.173008
H	5.551324	0.732912	2.651451
O	3.213023	1.255094	1.208565

Compound **25a**

C	–2.581124	1.233908	–0.028010
C	–1.199562	1.389441	–0.019269
C	–1.005688	–1.210785	–0.014326
C	–2.393107	–1.244485	–0.022994
C	–3.150077	–0.052795	–0.029777
H	–3.254553	2.084777	–0.033461
H	–0.803050	2.404213	–0.018205
H	–0.502461	–2.178459	–0.008108
H	–2.938270	–2.182784	–0.024392
B	–0.357287	0.148021	–0.012399
O	1.099002	0.358735	–0.004094
C	2.026023	–0.510060	–0.006035
H	1.754627	–1.568785	–0.017001
C	3.407430	–0.118794	0.005358
C	4.326795	–1.117297	0.002091
H	4.032038	–2.163810	–0.008680
H	5.392550	–0.909213	0.010294
C	3.754053	1.348301	0.020084
H	3.340116	1.856149	–0.858230
H	3.329770	1.840946	0.902111
H1	4.837892	1.490539	0.027676
N	–4.604723	–0.164884	–0.038920
O	–5.275364	0.876057	–0.044009
O	–5.108611	–1.296935	–0.041523

Transition state **25a**‡

C	–2.546864	0.997067	–0.767198
C	–1.162188	1.078189	–0.861578
C	–1.029167	–0.883969	0.850432
C	–2.416832	–0.871777	0.866235
C	–3.145867	0.043903	0.076719
H	–3.200175	1.655426	–1.330475
H	–0.742149	1.831255	–1.527508
H	–0.548473	–1.619676	1.496458

H	–2.983695	–1.560466	1.484312
B	–0.349331	0.119393	–0.042775
O	1.111470	0.236042	–0.176985
C	2.015875	–0.476629	0.359917
H	1.717379	–1.304142	1.008605
C	3.406732	–0.208522	0.125010
C	4.300048	–1.023109	0.742021
H	3.978518	–1.839908	1.383600
H	5.370715	–0.889965	0.618884
C	3.790874	0.938600	–0.774583
H	3.369987	0.806126	–1.777554
H	3.399648	1.886210	–0.387682
H	4.877878	1.017680	–0.859208
N	–4.602502	–0.001427	0.143687
O	–5.132354	–0.839504	0.886798
O	–5.248787	0.799467	–0.545150

1 imaginary frequency.

Compound **25b**

C	0.223143	0.154935	0.395279
C	1.598875	0.354008	0.263348
C	1.045178	2.655077	–0.830273
C	–0.296750	2.332579	–0.639596
C	–0.701672	1.117952	–0.044165
H	–0.163200	–0.759631	0.845854
H	2.270827	–0.426759	0.621676
H	1.256151	3.618215	–1.299135
H	–1.075800	3.027926	–0.953699
H	–1.765507	0.923761	0.077395
B	2.059132	1.638574	–0.367460
O	3.502972	1.810291	–0.488050
C	4.170644	2.782834	–0.974888
H	3.628540	3.642299	–1.376011
C	5.603929	2.755190	–0.998492
C	6.248952	3.825520	–1.532148
H	5.704119	4.678157	–1.929967
H	7.332671	3.869916	–1.581503
C	6.316518	1.550535	–0.434965
H	6.060283	1.402893	0.620279
H	6.019575	0.637792	–0.963852
H	7.400666	1.666285	–0.518732

Transition state **25b**‡

C	2.956080	1.034367	–0.566335
C	1.586523	1.245010	–0.350558
C	1.517900	–1.140148	0.694620

C	2.877756	–1.229533	0.381643
C	3.586717	–0.170148	–0.218780
H	3.560521	1.816544	–1.027932
H	1.163203	2.210659	–0.633463
H	1.035636	–2.006358	1.149478
H	3.422439	–2.150201	0.596482
H	4.648328	–0.292910	–0.423137
B	0.846812	0.145095	0.339181
O	–0.655703	0.280166	0.488077
C	–1.438652	0.140724	–0.487850
H	–1.010690	–0.106199	–1.465416
C	–2.865513	0.315171	–0.341271
C	–3.612779	0.150055	–1.457946
H	–3.158400	–0.089887	–2.416146
H	–4.694003	0.252720	–1.440758
C	–3.422104	0.651242	1.017566
H	–3.137958	–0.109131	1.753674
H	–3.021125	1.605622	1.377583
H	–4.512923	0.719154	0.985875

1 imaginary frequency.

Compound **25c**

C	–2.564610	1.206954	–0.029869
C	–1.178070	1.382062	–0.021808
C	–0.992097	–1.222320	0.057727
C	–2.387456	–1.263187	0.049246
C	–3.151677	–0.064169	0.002122
H	–3.232220	2.068343	–0.061166
H	–0.779903	2.396077	–0.049302
H	–0.476428	–2.185299	0.095610
B	–0.341864	0.132996	0.016286
O	1.102611	0.338560	0.010491
C	2.040059	–0.529012	–0.012443
H	1.773873	–1.587832	–0.039469
C	3.415807	–0.127477	–0.006296
C	4.363230	–1.101827	–0.032874
H	4.095572	–2.155332	–0.057903
H	5.422822	–0.864877	–0.030371
C	3.740440	1.345746	0.028373
H	3.306965	1.861772	–0.835781
H	3.318810	1.818023	0.922929
H	4.822277	1.505569	0.025025
H	–4.237747	–0.145561	–0.015852
N	–3.087322	–2.486809	0.027929
H	–2.570081	–3.274625	0.400659
H	–4.023515	–2.450429	0.415120

Transition state **25c**‡

C	–0.005863	–0.049993	–0.013273
C	–0.045422	–0.112973	1.388930
C	2.558904	0.010757	1.288731
C	2.448415	0.061638	–0.115792
C	1.185990	0.031453	–0.746060
H	–0.939332	–0.059232	–0.578786
H	–1.014612	–0.199011	1.879962
H	3.561351	0.023477	1.722571
B	1.287318	–0.079768	2.045711
O	1.363614	–0.132023	3.580440
C	1.429865	0.920256	4.254722
H	1.434660	1.880321	3.725589
C	1.497345	0.889782	5.703466
C	1.563819	2.089110	6.322094
H	1.566182	3.019813	5.759846
H	1.616989	2.171262	7.404119
C	1.487730	–0.443022	6.403486
H	1.539930	–0.314626	7.488010
H	0.578842	–1.003950	6.158130
H	2.335302	–1.057953	6.080178
H	1.139742	0.085386	–1.832957
N	3.603682	0.216472	–0.911450
H	4.444117	–0.185065	–0.511453
H	3.490047	–0.069031	–1.877757

1 imaginary frequency.

Compound **25d**

C	3.060460	1.174759	–0.000112
C	1.673390	1.326633	–0.000054
C	1.483999	–1.271390	0.000234
C	2.876393	–1.302366	0.000192
C	3.613981	–0.108360	0.000004
H	3.741981	2.023131	–0.000230
H	1.274060	2.340762	–0.000143
H	0.980894	–2.239391	0.000457
H	3.434344	–2.236840	0.000333
B	0.822092	0.085739	0.000075
O	–0.614687	0.296191	0.000088
C	–1.572964	–0.549867	–0.000164
H	–1.332034	–1.615263	–0.000551
C	–2.938608	–0.115648	0.000025
C	–3.907923	–1.069135	–0.000265
H	–3.664324	–2.128751	–0.000632
H	–4.961849	–0.808377	–0.000128

C	–3.230243	1.365152	0.000538
H	–2.792647	1.849878	0.880713
H	–2.792775	1.850459	–0.879381
H	–4.308325	1.548381	0.000675
F	4.971062	–0.214173	–0.000018

Transition state **25d**‡

C	3.037170	1.084454	–0.445437
C	1.661481	1.315235	–0.278386
C	1.470980	–1.154588	0.514223
C	2.856544	–1.257213	0.305998
C	3.586905	–0.163360	–0.155769
H	3.706337	1.864946	–0.804287
H	1.285266	2.313339	–0.504898
H	0.949842	–2.035374	0.890641
H	3.393922	–2.185174	0.495310
B	0.858257	0.165112	0.211970
O	–0.659413	0.341847	0.397827
C	–1.474422	0.110174	–0.519906
H	–1.088650	–0.230505	–1.488553
C	–2.902849	0.281777	–0.328715
C	–3.678765	–0.001709	–1.397948
H	–3.250601	–0.337092	–2.339612
H	–4.760364	0.093955	–1.359770
C	–3.408483	0.750495	1.009481
H	–3.109769	0.055822	1.802708
H	–2.981099	1.726444	1.266155
H	–4.498607	0.833643	1.006942
F	4.938245	–0.327321	–0.341879

1 imaginary frequency.

Compound **25e**

C	–2.554156	1.223996	–0.008966
C	–1.171874	1.353979	–0.004987
C	–1.026219	–1.235683	0.004534
C	–2.412546	–1.242318	–0.000463
C	–3.179044	–0.045599	–0.004985
H	–3.199291	2.104426	–0.018870
H	–0.759670	2.363560	–0.005491
H	–0.541290	–2.213290	0.012107
H	–2.961042	–2.186210	–0.004802
B	–0.323904	0.105821	0.000690
O	1.098549	0.291149	0.002024
C	2.061332	–0.566452	–0.003570
H	1.812425	–1.629118	–0.011877
C	3.422709	–0.137769	0.000585

C	4.407705	–1.079637	–0.004878
H	4.178788	–2.142460	–0.012561
H	5.457444	–0.803241	–0.001959
C	3.712645	1.344725	0.010821
H	3.276660	1.835823	–0.866750
H	3.273240	1.824450	0.892954
H	4.790720	1.529324	0.014069
N	–4.569741	–0.131696	–0.062770
H	–4.985101	–0.997138	0.258915
H	–5.086884	0.686000	0.235467

Transition state **25e**‡

C	–2.464370	–1.198667	0.288430
C	–1.068789	–1.217803	0.357018
C	–1.126862	1.317109	–0.155164
C	–2.509228	1.194124	–0.262983
C	–3.182388	–0.033031	–0.041758
H	–3.036876	–2.100502	0.514290
H	–0.593676	–2.153665	0.654854
H	–0.696846	2.307075	–0.313430
H	–3.120907	2.066990	–0.500966
B	–0.338839	0.062042	0.083314
O	1.126675	0.136764	0.346175
C	2.033603	–0.162242	–0.497251
H	1.726101	–0.528284	–1.481889
C	3.425876	–0.064093	–0.162715
C	4.328475	–0.431255	–1.110672
H	4.013325	–0.807937	–2.080599
H	5.397753	–0.363692	–0.934267
C	3.806972	0.453981	1.201433
H	3.372048	1.444080	1.378663
H	3.424974	–0.204235	1.990290
H	4.893710	0.524968	1.301369
N	–4.591934	–0.060693	–0.071405
H	–5.019657	0.656952	–0.645347
H	–4.995365	–0.969957	–0.267129

1 imaginary frequency.

Compound **26**

C	1.781867	1.100841	0.000000
C	0.409297	1.363993	0.000000
C	0.030933	–1.217923	0.000000
C	1.418344	–1.340487	0.000000
C	2.272454	–0.215188	0.000000
H	2.502781	1.918263	0.000000
H	0.080561	2.403358	0.000000

H	–0.545939	–2.144461	0.000000
H	1.880703	–2.327728	0.000000
H	3.348415	–0.377300	0.000000
B	–0.518265	0.184710	0.000000
C	–1.945702	0.501665	0.000000
O	–2.964104	–0.244312	0.000000
H	–3.937636	0.239742	0.000000
H	–2.864693	–1.330288	0.000000

Transition state **26**‡

C	1.604310	–0.064895	–1.233557
C	0.218574	0.141569	–1.279143
C	0.218575	0.141569	1.279142
C	1.604311	–0.064895	1.233557
C	2.282775	–0.165981	0.000000
H	2.155594	–0.147032	–2.146925
H	–0.287857	0.217023	–2.218682
H	–0.287856	0.217024	2.218682
H	2.155596	–0.147032	2.146925
H	3.341093	–0.323662	0.000000
B	–0.540367	0.254646	0.000000
O	–2.063553	0.481589	0.000000
C	–2.846484	–0.503597	0.000000
H	–3.904801	–0.345916	0.000001
H	–2.453881	–1.498967	0.000000

1 imaginary frequency

Compound **27**

C	0.000000	0.000000	0.000000
C	0.000000	0.000000	1.405968
C	2.591414	0.000000	1.285117
C	2.471743	–0.002711	–0.125964
C	1.208781	–0.014177	–0.757719
H	–0.939892	–0.055894	–0.544248
H	–0.976219	–0.074912	1.883282
H	3.358292	–0.060340	–0.753003
H	1.153456	–0.060979	–1.840456
B	1.340479	0.006673	2.117385
O	1.510726	–0.122319	3.568952
Cr	1.263316	–1.791015	0.656171
C	0.726932	–2.733471	2.126394
C	2.730839	–2.882310	0.427777
C	0.311406	–2.879185	–0.494648
O	0.361385	–3.219403	3.127623
O	3.671261	–3.554283	0.293070
O	–0.291430	–3.557497	–1.222084

C	0.604440	–0.340206	4.436109
H	–0.433532	–0.418862	4.108432
C	0.933851	–0.475562	5.827307
C	–0.098758	–0.685494	6.682281
H	–1.124996	–0.753289	6.330073
H	0.062042	–0.803544	7.749782
C	2.378592	–0.391265	6.249252
H	2.967139	–1.181481	5.769474
H	2.821015	0.565258	5.949149
H	2.472433	–0.495551	7.333521
H	3.591820	–0.075521	1.706501

Compound **28**

C	–0.178323	–0.032387	–0.137403
C	–0.299726	–0.117038	1.268737
C	2.284079	0.259300	1.422759
C	2.262853	0.317206	0.012869
C	1.076487	0.170263	–0.759269
H	–1.045710	–0.194131	–0.772844
H	–1.281067	–0.381309	1.659610
H	3.202528	0.418754	–0.527988
H	1.141401	0.193312	–1.841927
B	0.937659	0.088351	2.098494
O	0.914657	0.005260	3.576107
Mn	1.252640	–1.631844	0.534912
C	0.104694	–2.816554	–0.228139
C	1.432744	–2.664155	2.001063
C	2.659063	–2.441353	–0.283747
O	–0.635822	–3.548960	–0.712427
O	1.539372	–3.296142	2.959132
O	3.556791	–2.932381	–0.805275
C	–0.019659	0.421659	4.327387
H	–0.871143	0.930803	3.864627
C	0.032280	0.245025	5.748035
C	–1.033150	0.750864	6.425398
H	–1.852892	1.253475	5.917047
H	–1.107960	0.671905	7.506619
C	3.601729	0.389402	2.153890
H	3.767721	1.435989	2.443081
H	3.621144	–0.206211	3.071580
H	4.449099	0.083511	1.531355
C	1.202727	–0.461569	6.380378
H	1.309053	–1.476446	5.981478
H	2.137891	0.070463	6.172784
H	1.075622	–0.525653	7.463493

Transition state **29a**‡

C	1.887416	–0.527647	–2.227369
C	0.631026	–0.195579	–1.657274
C	1.767024	1.881851	–0.569384
C	2.955066	1.436901	–1.175253
C	3.028214	0.264410	–1.986956
H	2.003248	–1.433253	–2.818558
H	–0.190797	–0.887457	–1.841530
H	3.883955	1.972937	–0.984214
H	3.986963	–0.035380	–2.397592
B	0.522724	1.044488	–0.813883
O	–0.761295	1.442899	–0.214126
C	2.005240	–2.195407	0.150113
C	1.425003	–0.149697	1.639989
C	3.862458	–0.521821	0.816639
O	1.842043	–3.351760	0.212596
O	0.866709	0.039350	2.657092
O	4.914346	–0.614139	1.312038
C	–1.506671	0.619297	0.444560
H	–1.063523	–0.341352	0.710009
C	–2.799864	0.943075	0.872013
C	–3.479576	0.016236	1.690029
H	–2.904774	–0.779126	2.158328
H	–4.299129	0.386378	2.300392
C	1.794295	3.118713	0.303603
H	1.367862	3.979022	–0.232250
H	1.202937	2.985979	1.216342
H	2.815288	3.385331	0.602298
C	–3.436007	2.260999	0.524454
H	–3.475542	2.919549	1.402184
H	–2.886243	2.779849	–0.264255
H	–4.472367	2.109801	0.191126
H	–5.009607	–1.856316	1.383137
C	–4.601730	–1.283430	0.555045
C	–3.528232	–1.852667	–0.357400
C	–3.559790	–0.901436	–1.513787
H	–2.544289	–2.020359	0.086135
C	–4.722084	–0.169238	–1.466613
H	–2.823292	–0.881920	–2.309337
H	–5.058052	0.535715	–2.219217
C	–5.400727	–0.451338	–0.246775
H	–6.355954	–0.028300	0.047967
H	–3.880221	–2.838937	–0.707351
Cr	2.212300	–0.381648	0.021971

1 imaginary frequency.

Transition state **29b**‡

C	2.854338	1.239774	–1.618601
C	1.438365	1.282266	–1.589555
C	1.588193	1.693455	0.978742
C	2.983729	1.617604	0.818461
C	3.615993	1.399867	–0.442064
H	3.380029	1.034286	–2.548436
H	0.918846	1.110676	–2.532269
H	3.624919	1.678089	1.697134
H	4.697630	1.324993	–0.486402
B	0.749425	1.531852	–0.276732
O	–0.717696	1.624281	–0.191471
C	2.425704	–1.623108	–1.384630
C	0.783095	–1.223684	0.565120
C	3.322707	–1.268390	1.014906
O	2.550020	–2.432421	–2.218082
O	–0.173620	–1.765608	0.996129
O	4.038033	–1.857798	1.723846
C	–1.516412	0.819678	–0.811039
H	–1.068021	–0.065459	–1.268304
C	–2.885562	1.069855	–0.947428
C	–3.650890	0.167193	–1.715156
H	–3.130175	–0.561487	–2.331978
H	–4.581650	0.526322	–2.145792
C	1.010952	1.902311	2.363108
H	1.736466	1.662117	3.149802
H	0.704929	2.949590	2.501062
H	0.120938	1.285289	2.530153
C	–3.520336	2.303141	–0.360295
H	–2.870899	2.775682	0.380127
H	–3.735879	3.042856	–1.142993
H	–4.476811	2.054955	0.118795
H	–5.027020	–1.818669	–1.353962
C	–4.529854	–1.304113	–0.536391
C	–3.317190	–1.886054	0.165674
C	–3.246255	–1.074921	1.418538
H	–3.552132	–2.929879	0.438392
C	–4.419720	–0.381460	1.583284
H	–2.399590	–1.103337	2.093811
H	–4.679801	0.237008	2.435387
C	–5.237748	–0.575729	0.431021
H	–6.236004	–0.168602	0.300163
H	–2.378929	–1.929218	–0.390337
Cr	2.203161	–0.335974	–0.099961

1 imaginary frequency.

Transition state **30a**‡

C	1.119428	–0.404771	–2.165319
C	–0.138284	–0.602765	–1.554327
C	0.179664	1.692747	–0.352842
C	1.422324	1.759918	–1.017687
C	1.899294	0.745938	–1.893929
H	1.547180	–1.175458	–2.802239
H	–0.616205	–1.564766	–1.732881
H	2.085281	2.601452	–0.820539
H	2.877592	0.853176	–2.350228
B	–0.688323	0.486060	–0.663533
O	–1.981287	0.380401	0.015082
Mn	1.451871	–0.234208	0.044240
C	2.365127	–1.796115	–0.087247
C	0.539120	–0.816305	1.484291
C	2.767130	0.469314	1.078323
O	2.937899	–2.787103	–0.192919
O	–0.073283	–1.182542	2.390049
O	3.595404	0.935416	1.724741
C	–2.995375	–0.278803	–0.416570
H	–2.917856	–0.765639	–1.390808
C	–4.164668	–0.431835	0.375392
C	–5.158198	–1.198336	–0.163893
H	–5.041974	–1.696963	–1.121077
H	–6.075137	–1.400712	0.380594
C	–0.204065	2.808543	0.601690
H	0.181396	3.773154	0.252771
H	–1.289965	2.894559	0.700313
H	0.198665	2.642782	1.607752
C	–4.256727	0.239696	1.721067
H	–3.421501	–0.055551	2.365314
H	–4.216094	1.330172	1.616537
H	–5.190591	–0.024469	2.223155
H	–7.425372	–0.048468	–2.257038
C	–6.559509	0.593312	–2.137540
C	–5.382039	0.606749	–3.075984
C	–4.493724	1.673746	–2.492365
H	–4.894834	–0.370806	–3.203039
C	–5.128479	2.251438	–1.436059
H	–3.550285	1.984948	–2.928032
H	–4.764731	3.092671	–0.855020
C	–6.406099	1.585672	–1.217198
H	–7.121325	1.859365	–0.448584
H	–5.707419	0.895816	–4.089053

1 imaginary frequency.

Transition state **30b**‡

C	2.475386	0.265422	–2.010127
C	1.095690	0.300004	–1.709511
C	1.652848	1.926786	0.243883
C	2.999660	1.794688	–0.147364
C	3.420530	0.983759	–1.239036
H	2.846620	–0.381313	–2.801756
H	0.467189	–0.366410	–2.298035
H	3.775466	2.282703	0.441019
H	4.477121	0.906967	–1.472220
B	0.607476	1.217506	–0.608853
O	–0.781721	1.397265	–0.238679
Mn	2.288674	–0.323003	0.139554
C	2.762223	–1.988660	–0.390089
C	0.941027	–0.949131	1.142323
C	3.461835	–0.407818	1.520953
O	3.057226	–3.042225	–0.746521
O	0.050042	–1.342424	1.765791
O	4.208526	–0.445069	2.394462
C	–1.810802	1.031683	–0.949436
H	–1.616434	0.533471	–1.900880
C	–3.113683	1.333843	–0.560743
C	–4.143173	0.994787	–1.447255
H	–3.909764	0.646059	–2.449143
H	–5.120450	1.450572	–1.330542
C	1.313761	2.780151	1.446132
H	1.002540	3.780642	1.116580
H	0.482931	2.362442	2.022525
H	2.169272	2.904607	2.118743
C	–3.388664	2.059674	0.732860
H	–2.708929	1.741234	1.527349
H	–3.259023	3.141773	0.602793
H	–4.418204	1.889969	1.062851
H	–5.696187	–1.031265	–1.780745
C	–4.962922	–1.082642	–0.982967
C	–3.702250	–1.910915	–1.062342
C	–3.198511	–1.887396	0.350497
H	–3.984566	–2.943786	–1.329509
C	–4.146803	–1.334060	1.165276
H	–2.251945	–2.308816	0.669526
H	–4.086099	–1.240742	2.243607
C	–5.250213	–0.888398	0.360080
H	–6.163523	–0.448510	0.748888
H	–2.968465	–1.603088	–1.814883

1 imaginary frequency.

Curriculum Vitae

Zhe Lu

Education

Massachusetts Institute of Technology
Ph.D., Organic Chemistry, 2010
Thesis Title: "Nickel-Catalyzed Suzuki–Miyaura Reactions of Unactivated Halides with Alkyl Boranes and Towards the Development of Asymmetric Diels–Alder Reactions Catalyzed by Boron Heterocycles"
Advisor: Professor Gregory C. Fu

Harvard University
A.B., Chemistry and Physics, 2005
A.M., Chemistry, 2005
Advisor: Professor Eric N. Jacobsen

Awards

2010	Goodwin Medal
2009	Eli Lilly Graduate Fellowship in Organic Chemistry
2007	Martin Family Fellowship for Sustainability
2006	Department of Chemistry Outstanding Teaching Award

Publications

Lu, Z.; Fu, G. C. Alkyl–Alkyl Suzuki Cross-Couplings of Unactivated Secondary Alkyl Chlorides. *Angew. Chem., Int. Ed.* in press.

Vachal, P.; Hale, J. J.; Lu, Z.; Streckfuss, E. C.; Mills, S. G.; MacCoss, M.; Yin, D. H.; Algayer, K.; Manser, K.; Kesisoglou, F.; Ghosh, S.; Alani, L. L. Synthesis and Study of Alendronate Derivatives as Potential Prodrugs of Alendronate Sodium for the Treatment of Low Bone Density and Osteoporosis. *J. Med. Chem.* **2006**, *49*, 3060–3063.

Presentations

Lu, Z.; Fu, G. C. Suzuki–Miyaura Couplings of Secondary Unactivated Chlorides with Primary Alkyl Boron Reagents. 237th ACS National Meeting, Salt Lake City, UT. March 2009.

Lu, Z.; Fu, G. C. Putting the 'B' in Benzene: An Experimental and Theoretical Study of Borabenzenes. Metals in Synthesis Seminar. MIT, Cambridge, MA. March 2008.

Lu, Z.; White, D. E.; Jacobsen, E. N. Practical Synthesis of Oligomeric Salen Cobalt(III) Catalysts. Pfizer Summer Undergraduate Research Fellowship (SURF) Symposium. Pfizer, Ann Arbor, MI. October 2003.