Copper-Catalyzed Reactions of Organoboron Compounds

Richard P. Rucker

A dissertation

submitted in partial fulfillment of the

requirements for the degree of:

Doctor of Philosophy

University of Washington

2013

Reading Committee:

Prof. Gojko Lalic, Chair

Prof. Forrest Michael

Prof. D. Michael Heinekey

Program Authorized to Offer Degree:

Department of Chemistry

University of Washington

Abstract

Copper-Catalyzed Reactions of Organoboron Compounds

Richard P. Rucker

Chairperson of the Supervisory Committee:
Professor Gojko Lalic
Department of Chemistry

The discovery, development, scope, and mechanistic studies of three new copper-catalyzed transformations of organoboron compounds are described herein. Specifically, Chapter 1 details the development and scope of the first general method for S_N2'-selective substitution of primary allylic chlorides using aryl boronic esters as nucleophiles. The formal anti-Markovnikov hydroamination of 9-alkyl-9-BBN derivatives, which are conveniently prepared from the hydroboration of terminal alkenes, to give tertiary alkyl amines is discussed in Chapter 2. Chapter 3 describes the development, scope, and mechanistic studies of the copper-catalyzed electrophilic amination of aryl boronic esters and its application to the synthesis of hindered *N*,*N*-dialkyl anilines.

Table of Contents

List of Schemes

List of Figures

List of Tables

List of Abbreviations

Ac:	Acetyl
Ad:	Adamantyl
Ar:	Aryl
BBN:	Borabicyclo[3.3.1]nonane
Bn:	Benzyl
Boc:	*tert*-Butyloxycarbonyl
Bz:	Benzyl
C:	Celsius
Cy:	Cyclohexyl
DNB:	1,3-dinitrobenzene
E^+:	Electrophile
eg:	ethylene glycol
eq:	Equation
equiv:	Equivalent
ESI-MS:	Electrospray ionization mass spectrometry
Et:	Ethyl
FTIR:	Fourier transform infrared spectroscopy
h:	Hour
HRMS:	High resolution mass spectrometry
Hz:	Hertz
ICy:	1,3-Bis-dicyclohexyl imidazolium
IMes:	1,3-Bis-(2,4,6-trimethylphenyl)imidazolium
*i*Pr:	isopropyl
IPr:	1,3-Bis-(2,6-diisopropylphenyl)imidazolium
L:	Ligand
Me:	Methyl
Mes:	2,4,6-trimethylphenyl
MHz:	Megahertz
mol:	Mole
mp:	Melting point
ND:	Not determined
neop:	neopentylglycol
NHC:	*N*-heterocyclic carbene
NMR:	Nuclear magnetic resonance

Abbreviations for NMR splitting patterns

s:	singlet
d:	doublet
t:	triplet
q:	quartet
p:	pentet
m:	multiplet
br:	broad

Nu:	Nucleophile
OTs:	*p*-Toluenesulfonate
Ph:	Phenyl
pin:	pinacol
ppm:	parts per million
rt:	room temperature
*t*Bu:	*tert*-butyl
*t*Pent:	*tert*-pentyl
TBS:	*tert*-butyldimethylsilyl
THF:	Tetrahydrofuran
TIPS:	Triisopropylsilyl
TLC:	Thin layer chromatography
TMB:	1,3,5-trimethoxybenzene
TMS:	Trimethylsilyl
tol:	Tolyl
Ts:	*p*-Toluenesulfonyl
Xantphos:	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene

Acknowledgements

I am deeply indebted to many people whom without their support this work would not have been possible. First, I would like to thank my brother, Victor C. Rucker, Ph.D., who first introduced me to chemistry while I was in high school and whose counsel throughout the years has proven invaluable. Victor, you have always been there for me; for that, my gratitude cannot be expressed. Without the support and love of my father, Perry C. Rucker, I would never have realized my full potential. Dad, I cannot thank you enough for all of your sacrifices and encouragement you gave me, even during our family's most tumultuous days. My oldest brother, Perry C. Rucker, Jr., through his hard work and efforts, showed me that any goal is obtainable.

Second, I would like to thank Prof. Gojko Lalic, my advisor at the University of Washington, for his patience, persistence, and exceptional technical capability and work ethic. Gojko, you are not only my advisor, but also a role model and an inspiration. In addition, I must thank my coworkers at the University of Washington, all of whom are not only excellent researchers, but also good friends. I will continue to value your friendship throughout the years ahead.

I would also like to give thanks to Prof. Debra D. Dolliver, who enabled my understanding of organic chemistry through her clarity of instruction and gave me the opportunity to perform research in her laboratory.

Lastly, I cannot thank Alicia F. McGhee enough for her love, support, encouragement, and friendship during my entire graduate school career. Alicia, you are the most important person in my life, and I love you.

Dedication

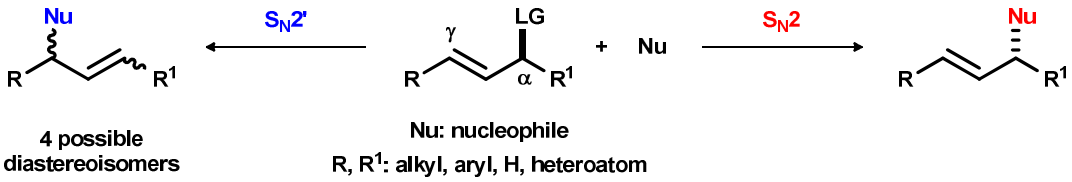
This work is dedicated to the memory of my loving mother,
Debra I. McGregor Rucker

Chapter 1 – Copper-catalyzed Regioselective Substitution of Allylic Chlorides by Organoboron Compounds[1]

Section 1. Introduction

The substitution of allylic electrophiles by carbon and heteroatom-based nucleophiles has been a subject of intense interest for almost a century. In this transformation, bond formation between the electrophile and nucleophile can occur at the α carbon—S_N2—or at the γ carbon—S_N2' (See **Scheme 1**). The uncatalyzed reactions of allylic electrophiles with most nucleophiles yield products with little regioselectivity.[2] In particular, the regiocontrol of allylic substitution with anionic, carbon-based (hard) nucleophiles to generate primarily the S_N2'-selective product is difficult.[3]

Scheme 1.1.



It has been known for over 40 years that the addition of stoichiometric or catalytic amounts of transition-metal salts can influence the regioselectivity of nucleophilic substitution of allylic electrophiles to such an extent that the S_N2 or S_N2'-substituted product can be accessed selectively.[4] Today, allylic substitution reactions have been developed which are catalyzed by a number of transition metals.[5] For soft (heteroatom-based) nucleophiles, the palladium-catalyzed allylic substitution reactions are historically the most well-developed and include the robust, S_N2'-selective Tsuji-Trost reaction.[6] Unfortunately, efforts to extend palladium-based systems to include harder nucleophiles

(i.e., carbon-based nucleophiles) have typically afforded the linear S_N2-product.[7] As a result, researchers in the field have investigated other transition metals for possible solutions to address this unmet challenge.

To this end, the pioneering discovery by Crabbe and coworkers that stoichiometric amounts of dimethyl lithium cuprate—an anionic copper(I) salt—could promote the S_N2'-selective alkylation of allylic acetates introduced a new approach for carbon-carbon bond formation and regiocontrolled elaboration of allylic substrates.[8] As the interest in developing these types of reactions continued to increase, improvements in efficiency were realized by Goering,[9] who employed catalytic copper salts in conjunction with Grignard reagents, and Bäckvall and van Koten, who in 1995 introduced a system using a chiral thiolate as a ligand for the promotion of an asymmetric, S_N2'-selective alkylation of allylic acetates.[10] Since these seminal contributions, the copper-catalyzed allylic alkylation reaction has matured into a widely-used synthetic method for the regioselective substitution of allylic electrophiles by sp^3-based carbon nucleophiles, such as Grignard, organolithium, and organozinc reagents.[11]

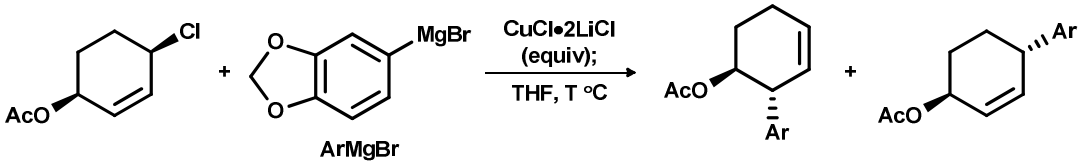
In contrast, the analogous substitution reactions of allylic electrophiles by sp^2-based carbon nucleophiles (allylic *arylation* and allylic *alkenylation*) are comparatively underdeveloped; specifically, most reactions are not regioselective and give mixtures of linear (S_N2) and branched (S_N2') products. Before our research in this arena began, there existed only Hoveyda's 2008 report of a general, copper-catalyzed S_N2'-selective alkenylation of allylic phosphates using alkenylalane nucleophiles.[12] The inability to exert regiocontrol in the substitution of allylic substrates by sp^2-based organometallic

reagents has been noted in the literature as a limitation of this methodology for over 20 years.[13] The lack of regiocontrol in allylic substitution has been attributed in part to two factors: First, the reactivity of sp^2-based nucleophiles is lower than their sp^3-based counterparts (support for this can be found by comparing the *p*Ka's of the carbanions under consideration); and second, the reactivity of the organocopper intermediates obtained upon treatment of a copper salt with a nucleophile are inherently different.

The difference in reactivity of sp^2- and sp^3-based nucleophiles in copper-catalyzed allylic substitution reactions was studied by Bäckvall, who proposed on the basis of systematic changes in solvent, temperature, catalyst loading, and addition time of the nucleophile that two discrete organocopper intermediates can exist and each is responsible for formation of a different regioisomer.[14] An S_N2'-selective reaction can be achieved by using reaction conditions that promote the formation of a monoaryl copper(I) nucleophilic intermediate, whereas reaction conditions which promote the formation of an anionic diaryl cuprate are unselective for either regioisomer. Specifically, Bäckvall demonstrated that stoichiometric reactions of pre-formed monoaryl cuprates with allylic chlorides are S_N2'-selective, whereas the pre-formed diaryl cuprates are not regioselective (Entries 1 and 2, Table 1). Furthermore, an increase in S_N2'-selectivity was observed when the aryl Grignard reagent was added slowly to the solution (Entries 3—5, Table 1). The authors demonstrated that, by using a high catalyst loading, long addition time of the aryl Grignard reagent, and performing the reaction at room temperature, all of which encourage the formation of monoaryl copper(I) complexes, "a

certain degree of regiocontrol" can be achieved, with S_N2': S_N2 selectivity averaging at about 10:1.[14b]

Table 1.1.



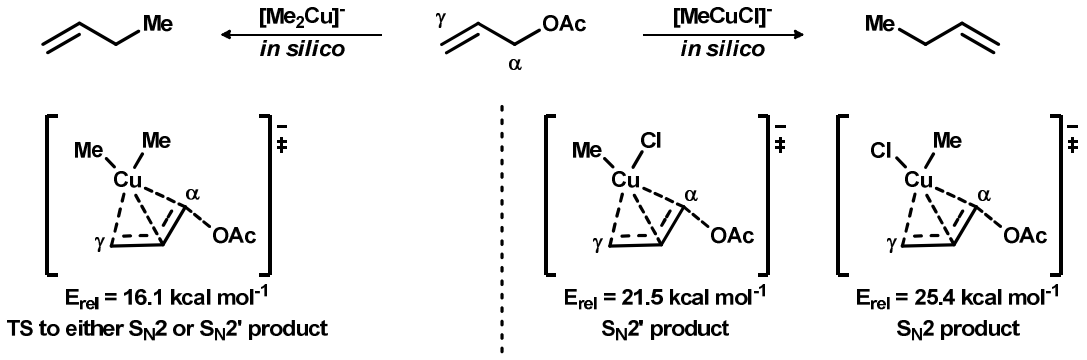
Entry	Addition time, ArMgBr	Stoichiometry of ArMgBr	CuCl•2LiCl (equiv)	T °C	$S_N2':S_N2$
1[a]	NA	1.0	1.0	20	91:9
2[a]	NA	2.0	1.0	20	46:54
3	1 min	1.0	0.5	20	40:60
4	1 h	1.0	0.5	20	65:35
5	1 h	1.0	1.0	20	74:26
6	1 h	1.0	0.5	-23	49:51

[a] CuCl•2LiCl and ArMgBr were premixed for 1.5 h at 0 °C.

An alternate explanation for the difference in the regioselectivity of homocuprate and heterocuprate complexes was proposed by Nakamura,[15] who examined the reaction coordinates of homo- and heterocuprates with allyl acetate using computational analysis. On the basis of these studies, Nakamura proposed that reaction of dimethyl lithium cuprate, a homocuprate, with allyl acetate, will result in a nonregioselective reaction, thus providing a theoretically-derived verification of experimental observations. In contrast, reaction of the heterocuprate MeCu(Cl)Li with allyl acetate was calculated to favor formation of the γ-substituted product due to the differences in transition-state energies of the diastereomeric organocopper (III) complexes formed upon oxidative addition of the heterocuprate into the allylic substrate. This effect is a consequence of the in-phase mixing of C=C π^* and C-LG σ^* (LG = acetate for this study) orbitals to create a new,

mixed LUMO, which is more extended on the carbon γ to the leaving group and is lower in energy than the C=C π^* and C-LG σ^* orbitals themselves.[16] Computational studies also indicated that, as a result of the electronic differences of the two ligands bound to a heterocuprate, the Cu $3d_{xz}$ orbital—the HOMO—is desymmetrized, with the quadrant *trans* to the less σ-donating ligand having a larger coefficient and capable of in-phase mixing with the more extended portion of the LUMO of the allylic electrophile. As a result of these two effects, heterocuprates prefer to undergo oxidative addition with the allylic substrate such that the in-phase mixing of the Cu $3d_{xz}$ orbital component *trans* to the weaker σ-donating ligand occurs with the mixed and more pronounced LUMO component of the allylic electrophile on the γ carbon. Consequently, the regioselectivity of allylic substitution using a heterocuprate can, at least qualitatively, be predicted by considering the relative *trans* effect (σ-donor ability) of the heterocuprate's two different ligands.[15,17] In this specific case, the stronger σ-donating group, in this case a methyl substituent, prefers to be *trans* to the α carbon of the allylic electrophile; whereas the weaker σ-donating chloride ligand prefers to be *trans* to the γ carbon. Due to these stereoelectronic effects, the S_N2' product is released upon reductive elimination.

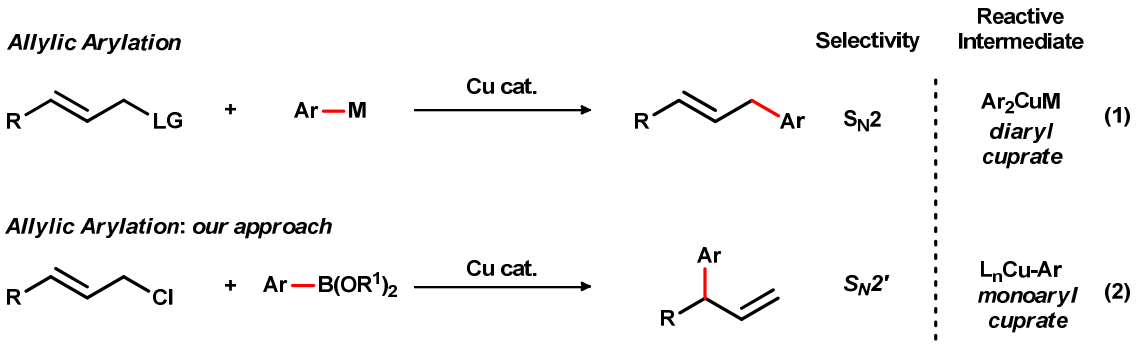
Scheme 1.2.



Even with this experimental and theoretical insight, by 2010 there still existed no general method for the regioselective substitution of primary allylic electrophiles by aryl nucleophiles, although a few examples employing special substrates or reaction conditions were known. For instance, Hoveyda found that vinylsilane electrophiles bearing a longer γ(carbon)-silicon bond could participate in allylic arylation by diarylzinc nucleophiles to give the S_N2' product selectively.[5a] In addition, Tomioka noted that cinnamyl bromides, together with some aliphatic allylic bromides, could undergo a highly S_N2'-selective substitution by electron-rich aryl Grignard reagents if they were added slowly to the reaction mixture at low temperatures.[5b,5c] Although these are highly selective transformations, they rely on special substrates and reaction conditions; as such, their utility is limited.

Another common feature of copper-catalyzed allylic arylation reactions is the use of highly reactive organometallic reagents as nucleophilic carbon sources. Such reagents are known to promote the formation of diaryl cuprates, which are directly responsible for a nonregioselective substitution reaction (Scheme 3, eq. 1).[14b] We reasoned that the formation of diaryl cuprates could be prevented if less reactive arylboronic esters were used as nucleophiles (Scheme 3, eq 2). This approach is particularly appealing considering the availability, stability, and excellent functional group compatibility of arylboronic esters.[18] Furthermore, when we started the project there were no examples of organoboron compounds being used in copper-catalyzed allylic alkylation or arylation reactions.

Scheme 1.3.



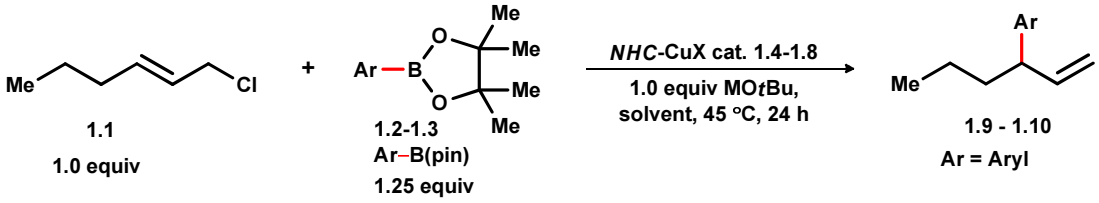
Section 2. Results

In preliminary screening experiments, we discovered that the S_N2'-selective addition of **1.2** to 1-chloro-2-hexene (**1.1**) can be achieved using copper(I) complexes **1.4**—**1.7** as catalysts in the presence of a stoichiometric amount of potassium *tert*-butoxide (KO*t*Bu). The best S_N2' selectivity, as determined by GC analysis of the crude reaction mixture, was obtained with **1.4**, while catalysts **1.5**—**1.7** provided a higher rate and lower selectivity. Both the alkoxide and the copper catalyst were necessary for an efficient reaction. Interestingly, allylic arylation of **1.1** with phenyl Grignard and **1.4** as a catalyst resulted in exclusive formation of the product of S_N2 reaction, in agreement with previously published results.[19]

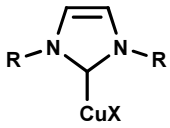
In the process of reaction optimization, we discovered that the highest selectivity is obtained with readily available **1.8** as a catalyst in 1,4-dioxane (Table 2, entry 5). Among the alkali *tert*-butoxides, potassium alkoxide provided the highest yield. With electron-poor boronic esters, such as **1.3**, both sodium and potassium alkoxides could be successfully used, with slightly better selectivity obtained with sodium alkoxide (Table 1, entries 9 and 10). Overall, the best results were obtained using reaction conditions

described in entry 8 for electron-rich boronic esters and in entry 10 for electron-poor boronic esters.

Table 1.2

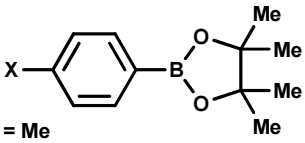


entry	Ar	NHC-CuX	mol%	MO*t*Bu	solvent	$S_N2':S_N2$[a]	yield (%)[a]
1	1.2	1.4	10	KO*t*Bu	THF	20:1	99
2	1.2	1.5	10	KO*t*Bu	THF	8:1	99
3	1.2	1.6	10	KO*t*Bu	THF	8:1	99
4	1.2	1.7	10	KO*t*Bu	THF	3:1	94
5	1.2	1.8	10	KO*t*Bu	1,4-dioxane	42:1	92
6	1.2	1.8	10	NaO*t*Bu	1,4-dioxane	50:1	30
7	1.2	1.8	10	LiO*t*Bu	1,4-dioxane	35:1	6
8	1.2	1.8	5	KO*t*Bu	1,4-dioxane	48:1	98
9	1.3	1.8	5	KO*t*Bu	1,4-dioxane	18:1	91
10	1.3	1.8	5	NaO*t*Bu	1,4-dioxane	20:1	95



NHC-CuX

1.4: R = 2,4,6-$Me_3C_6H_2$, X = Cl
1.5: R = Me, X = Cl
1.6: R = cyclohexyl, X = Cl
1.7: R = adamantyl, X = Cl
1.8: R = 2,4,6-$Me_3C_6H_2$, X = O^{t}Bu



1.2: X = Me
1.3: X = formyl

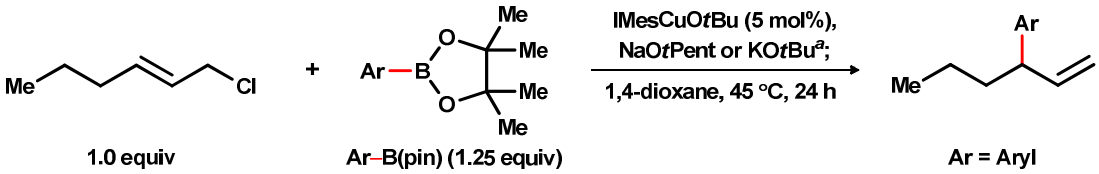
[a] Determined by GC analysis.

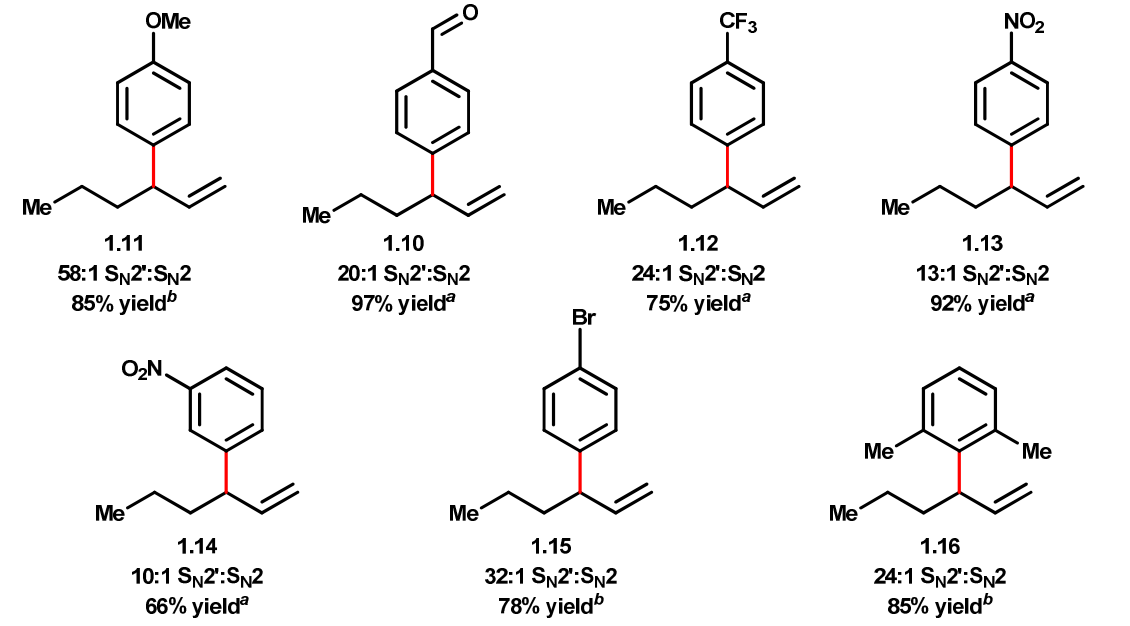
1.2.a. Scope of Aryl Boronic Esters

With the optimized reaction conditions in hand, we explored the reactivity of various aryl boronic esters. The reaction can be successfully performed in the presence of a variety of functional groups, including formyl and nitro groups, which are not compatible with previously described copper-catalyzed allylic substitution reactions (1.10

and 1.13—1.14, Table 2). Furthermore, we observed a direct correlation between the electron-donating ability of the aryl substituents and the regioselectivity of substitution. Steric properties of the boronic ester, on the other hand, had little effect on the reaction outcome, as demonstrated by the reaction of the *ortho*,*ortho*-disubstituted arylboronic ester with allylic chloride **1.1** to give product **1.16**.

Table 1.3





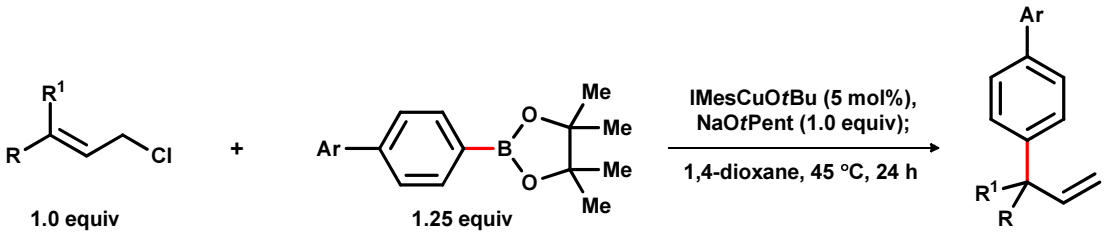
Reactions were performed on a 0.5 mmol scale. Yields are of isolated product. [a] 1.0 equiv of sodium *tert*-pentoxide was used. [b] 1.0 equiv of potassium *tert*-butoxide was used.

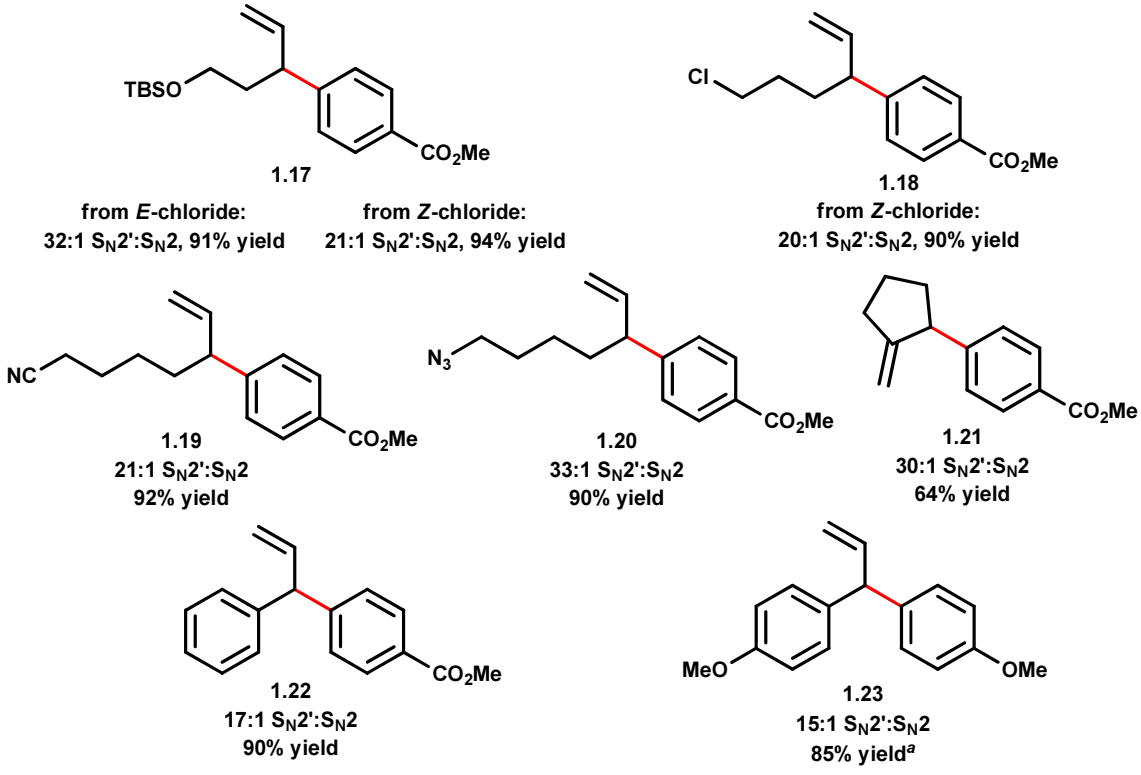
1.2.b. Scope of Allylic Chlorides

The scope of the allylic arylation was further explored in reactions with a variety of allylic chlorides. It was discovered that both *E*- and *Z*-substituted electrophiles can be

used in the reaction with similar success (Table 4, **1.17**). Azides (Table 4, **1.20)**, nitriles (**1.19**), chlorides (**1.18**), and TBS-protected alcohols are all compatible with the reaction conditions, further demonstrating the exceptional functional group tolerance of the reaction. Finally, cyclic and aryl-substituted allylic chlorides are also suitable substrates for allylic arylation (Table 4, **1.21**—**1.23**).

Table 1.4





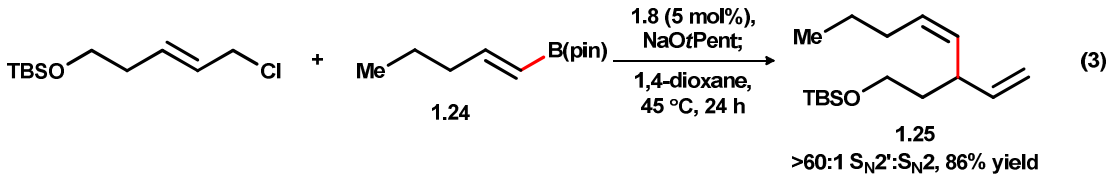
Reactions were performed on a 0.5 mmol scale. Yields are of isolated product. [a] 1.0 equiv of potassium *tert*-butoxide was used.

1.2.c. Allylic Alkylation and Allylic Alkenylation

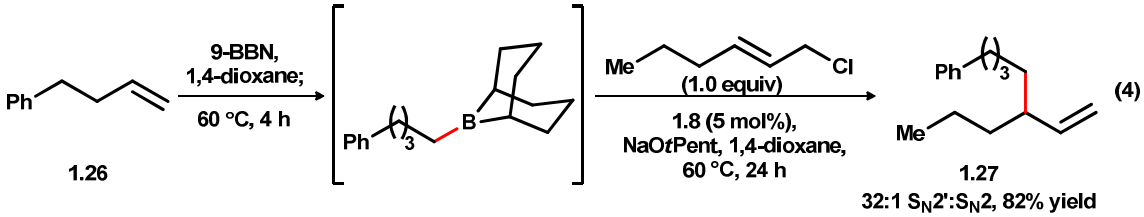
In addition to allylic arylation, we discovered that organoboron reagents can also be used as nucleophiles in copper-catalyzed alkenylation and alkylation of primary allylic electrophiles. With pentenyl boronic ester (**1.24**), the alkenylation product (**1.25**) is obtained in good yield and excellent selectivity (Scheme 4, eq. 3). Allylic alkylation, on the other hand, can be accomplished using trialkylboranes formed in situ from an alkene such as **1.26** and 9-BBN (Scheme 4, eq 4). The hydroboration-allylic alkylation sequence allows highly efficient and selective one-pot coupling of terminal alkenes and allylic chlorides to give products such as **1.27**.

Scheme 1.4

Allylic Alkenylation



Allylic Alkylation

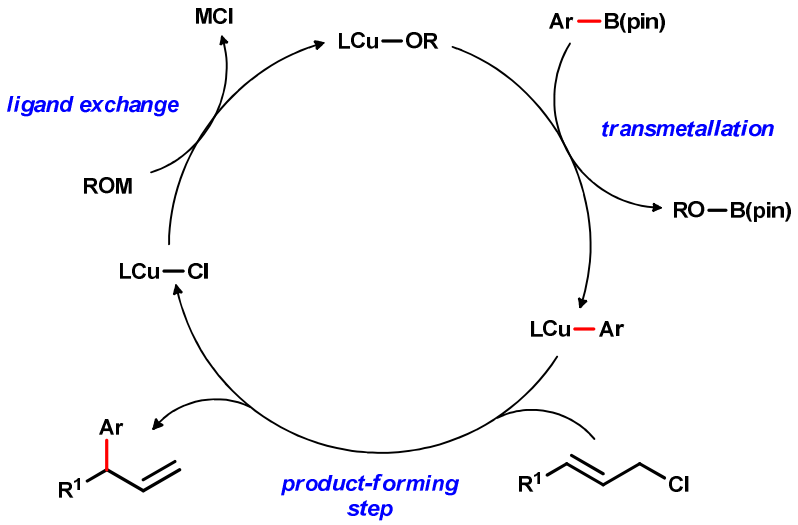


Section 3. Mechanism

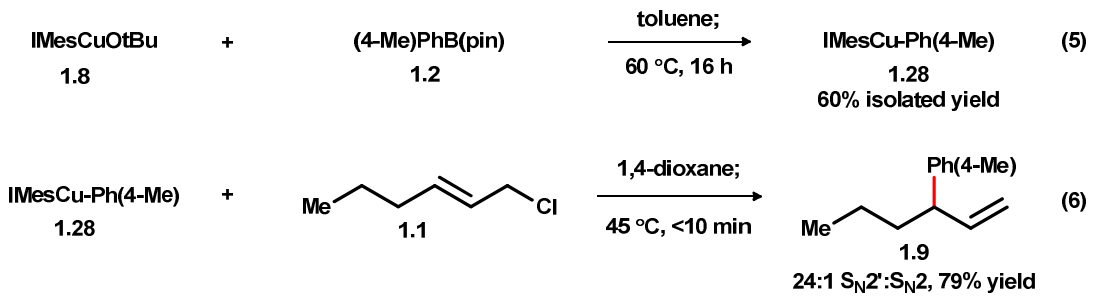
In an attempt to provide a better understanding of the source of the observed S_N2' selectivity, we studied the mechanism of the reaction, with the catalytic cycle presented in Scheme 5 as a working hypothesis. We were able to isolate the product of

transmetallation (**1.28**) from a stoichiometric reaction of **1.8** and **1.2** (Scheme 5, eq 5) and provide direct evidence for transmetallation from boron to copper(I) alkoxide.[20] The isolation of **1.28** also allowed us to investigate the potential role of this complex in the second step of the proposed catalytic cycle.

Scheme 1.5



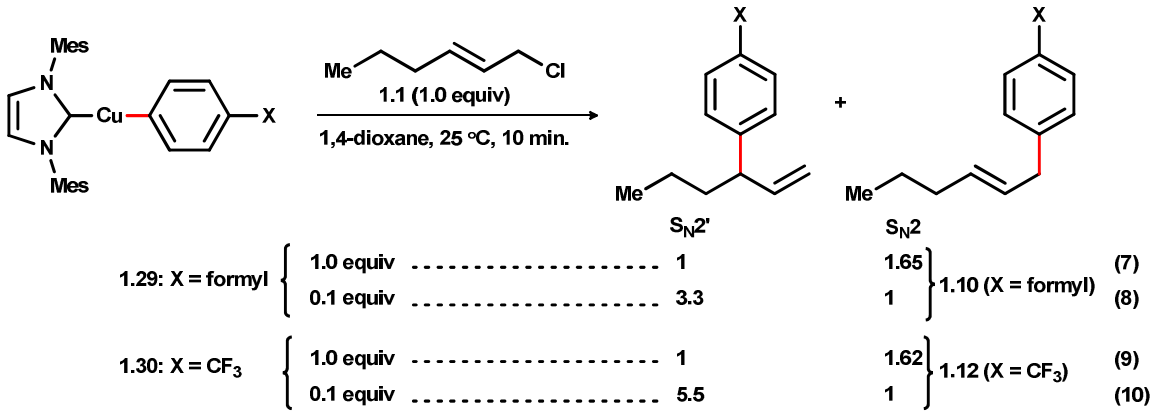
Evidence for transmetallation and subsequent allylic substitution:



A stoichiometric reaction of **1.28** and **1.1** resulted in the formation of the expected product within seconds, in good yield and with selectivity comparable to that obtained in a catalytic reaction (Scheme 1.5, eq 6). Furthermore, **1.28** is a competent catalyst and can be used instead of **1.8**. Together, these results support the idea that the aryl copper intermediate is the reactive nucleophile responsible for the selectivity observed in

catalytic reactions. Finally, in the last step of the catalytic cycle, copper(I) alkoxide is regenerated from copper(I) chloride and potassium *tert*-butoxide in a well-precedented transformation.[21]

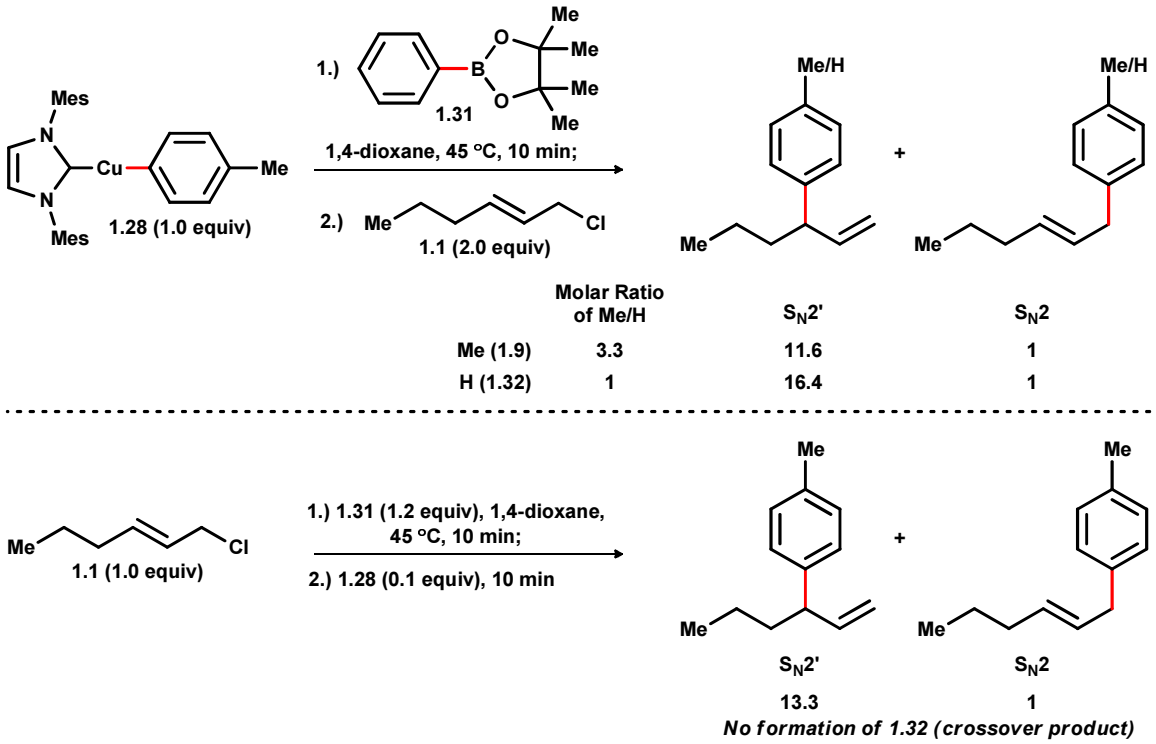
Scheme 1.6



Two other electron-deficient monoaryl copper(I) complexes, **1.29** and **1.30**, were also prepared in a manner analogous to **1.28** in order to study the influence of electronics on the regioselectivity of the second step of our proposed catalytic cycle. Interestingly, the stoichiometric reactions of these complexes with (*E*)-2-hexenyl chloride **1.1** indicated that the intrinsic S_N2'-selectivity of these systems is diminished, when compared to the more electron-rich copper complex **1.28**, to such an extent that a non-regioselective reaction results (compare Scheme 6, equations 7 and 9 with Scheme 5, equation 6). However, when a catalytic amount of either copper-aryl complex **1.29** or **1.30** is employed, a moderately S_N2'-selective arylation of allylic chloride **1.1** is observed (compare equations 8 and 10 with equations 7 and 9, Scheme 6). The cause of this interesting dichotomy is unknown and warrants further investigation.

In light of the observed high S_N2'-selectivity of arylation of a variety of primary allylic electrophiles, the formation of a diaryl cuprate and its participation as a nucleophile using the catalytic conditions described in Tables **1.3** and Table **1.4** does not seem likely. However, we were interested in the possibility that formation of either a

Scheme 1.7



diaryl homocuprate or a diaryl(pinacolato)borate could occur through reaction of an *NHC*-ligated copper(I) aryl complex with an aryl boronic ester. To test this possibility, we performed the crossover experiment shown at the top of Scheme **1.7**, in which an equimolar amount of IMesCu-(4-Me)Ph complex **1.28** was premixed with phenyl boronic(pinacolato)ester **1.31** before addition of allylic chloride **1.1**. The crossover products **1.9** and **1.32**, corresponding to transfer of the tolyl and phenyl groups, respectively, were obtained in a 3.3:1 molar ratio with S_N2'-selectivity that was

attenuated to that observed in a catalytic reaction using either aryl boronic ester alone. However, in a subsequent experiment, we established that product formation through oxidative addition of a catalytic amount of IMesCu-(4-Me)Ph **1.28** into electrophile **1.1** and reductive elimination occurs much faster than the process(es) leading to crossover product formation (bottom of Scheme **1.7**); therefore, the formation of either a diaryl cuprate or diarylborate should not be of significant concern when using the catalytic conditions described in Tables **1.3** and **1.4**.

Section 4. Conclusion

In conclusion, we have developed the first general S_N2'-selective allylic arylation reaction using a copper(I) catalyst and aryl boronic esters as nucleophiles. The reaction has a broad substrate scope and can be performed in the presence of a variety of functional groups including formyl, carbomethoxy, nitrilo, azido, chloro, bromo, and nitro groups. Each step of our proposed catalytic cycle has been supported with experimental evidence, including the preparation and isolation of neutral monoaryl copper(I) complexes formed by transmetallation with aryl boronic esters, as well as the demonstration of these complexes' inherent preference for substitution to give either the S_N2' or S_N2 product in stoichiometric reactions with allylic chlorides. Finally, the development of this reaction was essential to providing the groundwork for a future asymmetric variant.[22]

Section 5. Experimental

General:

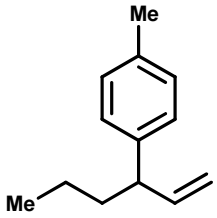
All reactions were performed under a nitrogen atmosphere, using flame-dried glassware unless otherwise indicated. Column chromatography was performed on a Biotage Iso-1SV flash purification system using silica gel (Agela Technologies Inc., 60Å, 40-60 μm, 230-400 mesh). Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum RX I spectrometer. IR peak absorbencies are represented as follows: s = strong, m = medium, w = weak, br = broad. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-300 or AV-500 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual $CHCl_3$ (7.26 ppm) or C_6D_6 (7.16 ppm). ^{13}C chemical shifts are reported in parts per million downfield of TMS and are referenced to the carbon resonance of the solvent ($CDCl_3$: δ 77.2 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constants in Hertz (Hz). Mass spectra were collected on a JEOL HX-110 Mass spectrometer, a Bruker Esquire 1100 Liquid Chromatograph – Ion Trap Mass Spectrometer or a Hewlett Packard 5971A Gas Chromatograph – Mass Spectrometer. Regioselectivity was determined by GC analysis using a Shimadzu GC-2010 with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 μm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5 min @ 250 °C. Materials THF, CH_2Cl_2, Et_2O and toluene were degassed and dried on columns of neutral alumina. 1,4-dioxane was distilled from purple Na/benzophenone ketyl, and stored over 4Å molecular sieves. Deuterated solvents were purchased from

Cambridge Isotope Laboratories, Inc. 1,4-Dioxane-d^8 and THF-d^8 were distilled from purple Na/benzophenone ketyl. All other deuterated solvents were degassed and dried over 4Å molecular sieves. Commercial reagents were purchased from Sigma-Aldrich Co., VWR international, LLC., or STREM Chemicals, Inc., and were used as received.

1.5.a. Allylic arylation:

General arylation procedure:

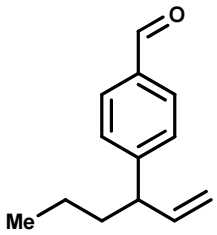
In a glove box, a scintillation vial was charged with a stir bar. To the vial was added boronic ester (1.25 equiv, 0.625 mmol), *tert*-butoxide (as specified in Tables X and X) (1.00 equiv, 0.500 mmol), and 1,4-dioxane (2.0 mL).After 10 minutes, IMesCuO-*tert*-butoxide (0.05 equiv, 0.025 mmol), dissolved in 0.5 mL of 1,4-dioxane, was added, and the mixture was stirred for another 10 min at ambient temperature. The allylic chloride was added (1.00 equiv, 0.500 mmol) in one portion and the scintillation vial was heated to 45 °C for 24 h. The vial was removed from the glove box, diluted with Et_2O, filtered through a plug of silica, concentrated *in vacuo*, and the crude reaction mixture was purified by silica gel chromatography.



1-(hex-1-en-3-yl)-4-methylbenzene (**1.9**)

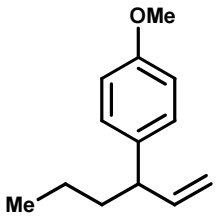
Compound was isolated as a colorless oil (73.8 mg, 85% yield, 60:1 mixture of isomers) after purification by silica gel column using hexanes as an eluent. ^{1}H NMR (300 MHz,

C_6D_6) δ 7.11 – 6.92 (m, 4H), 5.93 (ddd, *J* = 17.6, 10.3, 7.4 Hz, 1H), 5.15 – 4.84 (m, 2H), 3.17 (q, *J* = 7.4 Hz, 1H), 2.15 (s, 3H), 1.63 (m, 2H), 1.36 – 1.09 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 141.8, 135.6, 129.2, 127.6, 113.7, 49.3, 37.8, 21.1, 20.8, 14.1. HRMS calculated for $[M]^+$ 174.1409, found 174.1410. FTIR (neat, cm^{-1}): 3079 (w), 2927 (m), 1637 (m), 1513 (m), 1111 (w), 814 (m).



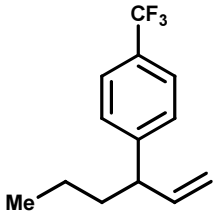
4-(hex-1-en-3-yl)benzaldehyde (**1.10**)

Compound was isolated as a light yellow oil (91.7 mg, 97% yield, 20:1 mixture of isomers) after purification by silica gel column chromatography (5 →15% EtOAc/hexanes). Major isomer; ^{1}H NMR (300 MHz, C_6D_6) δ 9.71 (s, 1H), 7.56 (d, *J* = 8.3 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 5.71 (ddd, *J* = 17.1, 10.3, 7.6 Hz, 1H), 5.02 – 4.73 (m, 2H), 3.03 (m, 1H), 1.51 – 1.39 (m, 2H), 1.18 – 0.99 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.4, 152.4, 141.6, 135, 130.4, 128.7, 115.3, 50.2, 37.8, 21.0, 14.3. HRMS calculated for $[M+H]^+$ 189.1279, found 189.1281. FTIR (neat, cm^{-1}): 3081 (w), 2930 (m), 2733 (m), 1703 (s), 1576 (m), 1108 (w), 828 (m).



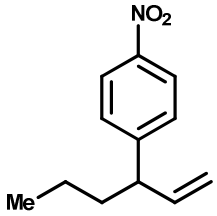
1-(hex-1-en-3-yl)-4-methoxybenzene (**1.11**)

Compound was isolated as a colorless oil (80.6 mg, 85% yield, 58:1 mixture of isomers) after purification by silica gel column chromatography (5 →20% EtOAc/hexanes). Major isomer; ^{1}H NMR (500 MHz, C_6D_6) δ 7.03 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 5.92 (ddd, *J* = 17.4, 10.3, 7.3 Hz, 1H), 5.01 (m, 2H), 3.34 (s, 3H), 3.15 (m, 1H), 1.65 – 1.58 (m, 2H), 1.39 – 1.12 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.1, 143.0, 136.8, 128.6, 113.9, 113.6, 55.3, 48.8, 37.8, 20.7, 14.1. HRMS calculated for $[M+H]^+$191.1434, found 191.1437. FTIR (thin film, cm-1): 3077 (w), 2872 (m), 1636 (m), 1512 (s), 1249 (s), 1038 (m), 829 (m).



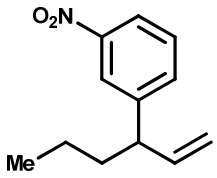
1-(hex-1-en-3-yl)-4-(trifluoromethyl)benzene (**1.12**)

Compound was isolated as a colorless oil (85.5 mg, 75% yield, 24:1 mixture of isomers) after purification by silica gel column chromatography (0 →15% EtOAc/hexanes). Major isomer; ^{1}H NMR (500 MHz, C_6D_6) δ 7.35 (d, *J* = 8.3 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 5.80 – 5.55 (m, 1H), 5.03 – 4.73 (m, 1H), 3.11 – 2.86 (m, 1H), 1.55 – 1.34 (m, 1H), 1.24 – 0.96 (m, 1H), 0.79 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9 (d, *J* = 1.0 Hz), 141.6, 128.6 (q, *J* = 32.3 Hz), 128.1, 125.5 (q, *J* = 3.7 Hz), 124.5 (q, *J* = 271.8 Hz), 114.8 (s), 49.6, 37.6, 20.7, 14.1. HRMS calculated for $[M]^+$228.1128, found 228.1130. FTIR (thin film, cm-1): 3082 (w), 2931 (m), 1327 (s), 1126 (m), 1609 (m), 917 (m), 839 (m).



1-(hex-1-en-3-yl)-4-nitrobenzene (**1.13**)

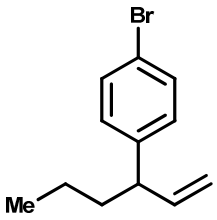
Compound was isolated as a light yellow oil (94.3 mg, 92% yield, 13:1 mixture of isomers) after purification by silica gel column chromatography (5 →20% EtOAc/hexanes). Major isomer; ^{1}H NMR (500 MHz, C_6D_6) δ 7.84 (d, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 8.7 Hz, 2H), 5.59 (ddd, *J* = 17.6, 10.2, 7.6 Hz, 1H), 4.87 (m, 2H), 2.92 (m, 1H), 1.43 – 1.27 (m, 2H), 1.13 – 0.93 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.5, 140.7, 128.4, 123.7, 115.4, 49.5, 37.4, 20.5, 13.9. HRMS calculated for $[M+H]^+$ 206.1179, found 206.1183. FTIR (thin film, cm-1): 3080 (w), 2932 (m), 1637 (m), 1519 (s), 1346 (s), 1110 (m), 919 (m), 853 (m).



1-(hex-1-en-3-yl)-3-nitrobenzene (**1.14**)

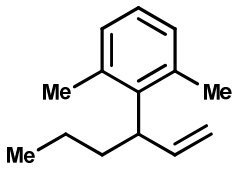
Compound was isolated as a light yellow oil (67.7 mg, 66% yield, 10:1 mixture of isomers) after purification by silica gel column chromatography (10 →20% EtOAc/hexanes). Major isomer; ^{1}H NMR (500 MHz, C_6D_6) δ 7.95 (s, 1H), 7.79 – 7.66 (d, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.78 (t, *J* = 7.9 Hz, 1H), 5.67 – 5.48 (m, 1H), 4.87 (m, 2H), 2.95 (m, 1H), 1.36 (m, 2H), 1.17 – 0.90 (m, 2H), 0.76 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 148.9, 146.7, 141.1, 133.6, 129.2, 122.6, 121.4, 115.1, 49.4, 37.5, 20.7,

14.0. HRMS calculated for $[M+H]^+$ 206.1179, found 206.1186. FTIR (thin film, cm-1): 3080 (w), 2931 (m), 1638 (m), 1530 (s), 1350 (s), 923 (m), 806 (m).



1-bromo-4-(hex-1-en-3-yl)benzene (**1.15**)

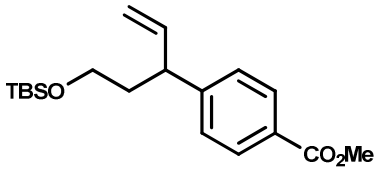
Compound was isolated as a colorless oil (92.4 mg, 78% yield, 32:1 mixture of isomers) after purification by silica gel column chromatography using hexanes as an eluent. Major isomer; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.3 Hz, 2H), 6.69 (d, J = 8.3 Hz, 2H), 5.81 – 5.59 (m, 1H), 4.97 – 4.82 (m, 2H), 2.95 (m, 1H), 1.55 – 1.32 (m, 2H), 1.21 – 0.91 (m, 2H), 0.78 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 142.1, 131.8, 129.7, 120.2, 114.2, 49.3, 37.7, 20.8, 14.1. HRMS calculated for $[M]^+$ 238.0357, found 238.0362. FTIR (thin film, cm-1): 3079 (w), 2929 (m), 1637 (m), 1488 (m), 1106 (w), 1011 (m), 824 (m).



2-(hex-1-en-3-yl)-1,3-dimethylbenzene (**1.16**)

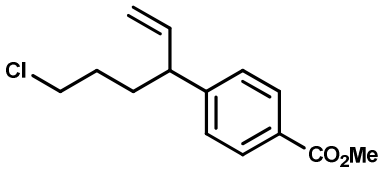
Compound was isolated as a colorless oil (79.9 mg, 85% yield, 24:1 mixture of isomers) after purification by silica gel column chromatography (0 →20% benzene/hexanes). ^{1}H NMR (500 MHz, C_6D_6) δ 7.02 - 6.92 (m, 3H), 6.01 (ddd, J = 17.3, 10.4, 5.0 Hz, 1H), 4.95 (m, 2H), 3.82 – 3.71 (m, 1H), 2.23 (s, 6H), 1.78 – 1.64 (m, 2H), 1.30 – 1.01 (m, 2H),

0.80 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 140.6, 136.8, 126.0, 113.8, 44.0, 35.3, 21.7, 21.5, 14.4. HRMS calculated for $[M]^+$ 188.1567, found 188.1566. FTIR (thin film, cm-1): 3075(w), 2931 (m), 1633 (m), 910 (m), 768 (m).



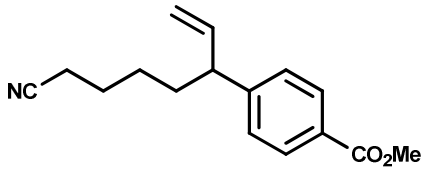
Methyl 4-(5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-3-yl)benzoate (1.17)

Compound was isolated as a colorless oil (157.5 mg, 94% yield, 32:1 mixture of isomers, from *Z* alkene) (152.1 mg, 91%, 21:1 mixture of isomers, from *E* alkene) after purification by silica gel column chromatography (0 →10% EtOAc in hexanes). Major isomer; ^{1}H NMR (500 MHz, C_6D_6) δ 8.13 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 5.77 (ddd, J = 17.5, 10.2, 7.5 Hz, 1H), 5.01 – 4.91 (m, 2H), 3.58 – 3.43 (m, 5H), 3.39 (dt, J = 10.0, 6.4 Hz, 1H), 1.80 (m, 2H), 0.96 (s, 9H), -0.01 (d, J = 5.4 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 149.6, 141.2, 129.9, 128.3, 127.9, 115.0, 60.5, 52.1, 45.8, 38.0, 26.0, 18.4, -5.3. HRMS calculated for $[M+H]^+$ 335.2041, found 335.2029. FTIR (neat, cm-1): 3081 (w), 3000 (w), 2953 (s),1725 (s), 1610 (m), 1278 (s), 1104 (s), 834 (s) 755 (m).



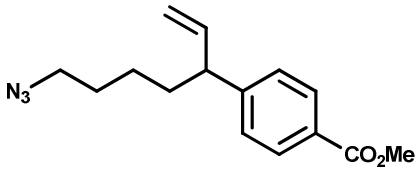
Methyl 4-(6-chlorohex-1-en-3-yl)benzoate (1.18)

Compound was isolated as a colorless oil (106.1 mg, 90% yield, 20:1 mixture of isomers) after purification by silica gel column chromatography (30 →80% benzene in hexanes). Major isomer; ^{1}H NMR (300 MHz, C_6D_6) δ 8.11 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 5.64 (ddd, *J* = 17.1, 10.3, 7.6 Hz, 1H), 5.00 – 4.74 (m, 2H), 3.53 (s, 3H) 3.03 (t, *J* = 6.4 Hz, 2H), 2.91 (q, *J* = 7.4 Hz, 1H), 1.62 – 1.17 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 149.3, 140.9, 130.0, 128.5, 127.7, 115.3, 52.1, 49.3, 44.9, 32.4, 30.6. HRMS calculated for $[M+H]^+$ 253.0996, found 253.1002. FTIR (neat, cm-1):3082 (w), 3000 (w), 2953 (m),1722 (s), 1609 (m), 1436 (m), 1280 (s), 912 (s), 733 (s).



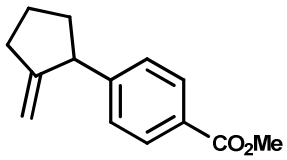
Methyl 4-(7-cyanohept-1-en-3-yl)benzoate (**1.19**)

Compound was isolated as a colorless oil (118.4 mg, 92% yield, 21:1 mixture of isomers) after purification by silica gel column chromatography (10 →40% EtOAc in hexanes). Major isomer; ^{1}H NMR (300 MHz, C_6D_6) δ 8.16 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 5.81 – 5.54 (m, 1H), 4.98 – 4.80 (m, 2H), 3.52 (s, 3H), 2.76 – 2.98 (m, 1H), 1.38 – 1.09 (m, 4H), 1.06 – 0.69 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 149.4, 140.9, 130.0, 128.4, 127.6, 119.6, 115.2, 52.1, 49.7, 34.4, 26.7, 25.3, 17.1. HRMS calculated for $[M+H]^+$ 244.1338, found 244.1333. FTIR (neat, cm-1):3075 (w), 3000 (w), 2947 (m), 2241 (m), 1721(s), 1609 (m), 1435 (m), 1281 (s), 919 (m).



Methyl 4-(7-azidohept-1-en-3-yl)benzoate (1.20)

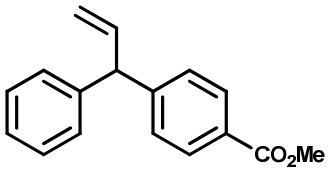
Compound was isolated as a light yellow oil (123.6 mg, 90% yield, 33:1 mixture of isomers) after purification by silica gel column chromatography (30 →80% benzene in hexanes). Major isomer; ^{1}H NMR (300 MHz, C_6D_6) δ 8.16 (d, *J* = 8.3 Hz, 2H), 6.97 (d, *J* = 8.2 Hz, 2H), 5.83 – 5.55 (m, 1H), 5.00 – 4.82 (m, 2H), 3.52 (s, 3H), 2.95 (m, 1H), 2.59 (t, *J* = 6.8 Hz, 2H), 1.34 (m, 2H), 1.23 – 0.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 149.6, 141.2, 130.0, 128.4, 127.7, 115.1, 52.1, 51.3, 49.9, 34.9, 28.8, 24.7. HRMS calculated for $[M+H]^+$274.1553, found 274.1557. FTIR (neat, cm-1):3079 (w), 2940 (m), 2095 (s), 1721 (s), 1609 (m), 1435 (m), 1279 (s).



Methyl 4-(2-methylenecyclopentyl)benzoate (1.21)

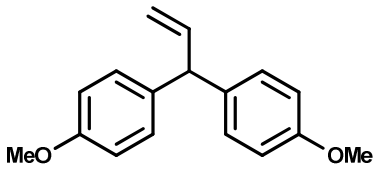
Compound was isolated as a white solid (69.1 mg, 64% yield, 30:1 mixture of isomers) after purification by silica gel column chromatography (0 →10% EtOAc in benzene). mp 38 °C. Major isomer; ^{1}H NMR (300 MHz, C_6D_6) δ 8.15 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 4.97 (d, *J* = 2.0 Hz, 1H), 4.60 (d, *J* = 2.0 Hz, 1H), 3.52 (s, 3H), 3.32 (t, *J* = 7.4 Hz, 1H), 2.47 – 2.15 (m, 2H), 1.95 – 1.77 (m, 1H), 1.65 – 1.26 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 156.0, 150.8, 129.8, 128.4, 128.1, 107.8, 52.1, 51.3, 36.6,

33.6, 24.9. HRMS calculated for $[M+H]^+$ 217.1227, found 217.1236. FTIR (thin film, cm-1): 3054 (w), 2987 (m), 1717 (s), 1610 (m), 1422 (m), 1265 (s), 896 (s).



Methyl 4-(1-phenylallyl)benzoate (1.22)

Compound was isolated as a clear liquid (114.2 mg, 90% yield, 17:1 mixture of isomers) after purification by silica gel column chromatography (0 →20% benzene in hexanes).Major isomer; ^{1}H NMR (300 MHz, C_6D_6) δ 8.18 (d, *J* = 8.3 Hz, 2H), 7.35 – 6.95 (m, 7H), 6.18 (ddd, *J* = 17.2, 10.2, 7.2 Hz, 1H), 5.17 (d, *J* = 10.2 Hz, 1H), 4.97 (d, *J* = 17.2 Hz, 1H), 4.61 (d, *J* = 7.2 Hz, 1H), 3.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.06, 148.71, 142.54, 139.89, 129.82, 128.72, 128.62, 128.39, 126.71, 117.06, 54.98, 52.07. HRMS calculated for $[M+H]^+$ 253.1229, found 253.1232. FTIR (thin film, cm-1): 3061 (w), 3028 (w), 2952 (m), 1723 (s), 1610 (m), 1436 (m), 1281 (s), 1112.8 (s), 701.7 (m).

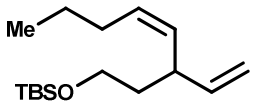


4,4`-(prop-2-ene-1,1-diyl)bis(methoxybenzene) (1.23)

Compound was isolated as a clear liquid (108.3 mg, 85% yield, 15:1mixture of isomers) after purification by silica gel column chromatography (0 →20% benzene in hexanes). Major isomer; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 – 6.99 (m, 4H), 6.85 – 6.71 (m, 4H),

6.24 (ddd, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.13 (d, *J* = 10.1 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.58 (d, *J* = 7.0 Hz, 1H), 3.39 – 3.21 (s, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 158.79, 141.93, 136.09, 129.97, 115.70, 114.20, 54.81, 53.83. HRMS calculated for $[M+H]^+$ 254.1306, found 254.1308. FTIR (thin film, cm-1): 3054 (m), 3005 (m), 2958 (m), 1636 (m), 1035 (s), 739 (s).

1.5.b. Allylic alkenylation:

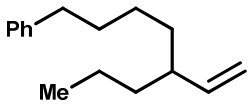


(*E*)-*tert*-butyldimethyl((4-vinylnon-5-en-1-yl)oxy)silane (1.25)

In a glove box, a scintillation vial was charged with a stir bar. To the vial was added (*E*)-4,4,5,5-tetramethyl-2-(pent-1-en-1-yl)-1,3,2-dioxaborolane (1.25 equiv, 139 μL 0.625 mmol), sodium-*tert*-pentoxide (1.00 equiv, 55.0 mg, 0.500 mmol), and 1,4-dioxane (2.0 mL). The resulting solution was allowed to stir at 45 °C for 10 minutes. After 10 minutes, IMesCuO-t-Bu (0.05 equiv, 11.0 mg, 0.025 mmol) in 0.5 mL 1,4-dioxane was added and the mixture stirred for another 10 min at ambient temperature. (*E*)-*tert*-butyl((5-chloropent-3-en-1-yl)oxy)dimethylsilane was added (1.00 equiv,118 mg, 0.500 mmol) in one portion and the scintillation vial was heated to45 °C for 24 h. The vial was removed from the glove box, and the reaction mixture was diluted with Et2O, filtered through a plug of silica, concentrated *in vacuo* and purified by silica gel chromatography. Compound was isolated as a colorless oil (116.2 mg, 86% yield) after purification by silica gel column chromatography (0 →10% benzene/hexanes). ^{1}H NMR (300 MHz, C_6D_6) δ 5.85 (ddd, *J* = 17.3, 10.2, 7.2 Hz, 1H), 5.68 – 5.33 (m, 2H), 5.27 – 4.93 (m, 2H),

3.72 (t, *J* = 6.4 Hz, 2H), 3.22 – 2.91 (m, 1H),2.10 – 1.97 (m, 2H), 1.90 – 1.62 (m, 2H), 1.51 – 1.35 (m, 2H), 1.09 (s, 9H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.17 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.2, 133.1, 130.9, 114.0, 61.1, 43.5, 38.2,35.2, 26.3, 23.1, 18.6, 13.9, -5.0. HRMS calculated for $[M+H]^+$ 269.2295, found 269.2298. FTIR (neat, cm-1): 3080 (w), 2859 (m), 1637 (m), 1102 (m), 969 (m).

1.5.c. Allylic alkylation:



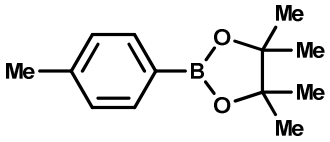
(5-vinyloctyl)benzene (**1.27**)

In a glove box, a scintillation vialwas charged with a stir bar. To the vial was added but-3-en-1-ylbenzene (1.25 equiv, 83.0 mg, 0.625 mmol), 9-Borabicyclo[3.3.1]nonane dimer (0.63 equiv, 152 mg, 0.313 mmol), and 1,4-dioxane (0.5 mL). The resulting solution was stirred at 60 °C for 4 h. After 4 h, the solution was transferred to a scintillation vial containing IMesCuOt-Bu (0.05 equiv, 11.0 mg, 0.025 mmol), sodium-*tert*-pentoxide (1.00 equiv, 56.0 mg, 0.50 mmol), and 1,4-dioxane (2.0 mL). The resulting solution was allowed to stir at25 °C for 10 minutes, and then (*E*)-2-hexenyl-1-chloride (1.00 equiv, 65.9 μL, 0.50 mmol) was added. The resulting solution was allowed to stir at 60 °C for 24 h. The vial was removed from the glove box, the reaction mixture was diluted with Et2O, filtered through a plug of silica, and concentrated *in vacuo*. Compound was isolated as a colorless oil (89.0 mg, 82% yield, 32:1 mixture of isomers) after purification by silica gel chromatography (0 →20% benzene/hexanes). Major isomer; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.01 (m, 5H), 5.57 (ddd, *J* = 16.9, 10.3, 8.9 Hz, 1H), 5.16 – 4.95

(m, 2H), 2.61 (t, *J* = 7.7 Hz, 2H), 2.13 – 1.91 (m, 1H), 1.80 – 1.55 (m, 2H), 1.52 – 1.14 (m, 8H), 0.99 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 142.9, 128.4, 128.2, 125.6, 113.9, 43.8, 37.3, 36.1, 34.9, 31.7, 27.0, 20.3, 14.2. HRMS calculated for $[M]^+$216.1879, found 216.1876. FTIR (neat, cm-1): 3064 (w), 2857 (m), 1639 (m), 956 (m), 745, (m), 698 (s).

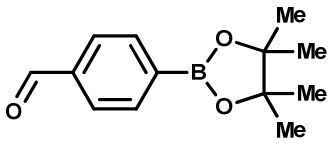
1.5.d. Synthesis of aryl boronic esters:

A flame-dried round bottom flask was charged with a stir bar and allowed to cool under N_2. Into the flask was added aryl boronic acid (1.0 equiv) and diol (1.0 equiv). Benzene was added (0.2 M solution of boronic acid) and the resulting solution was heated at the reflux for 1 h or until water layer separated. The solution was allowed to cool and MgSO4 (0.5 equiv) was added. The solution was filtered, and the solvent volume was reduced by half under reduced pressure. The resulting solution was transferred to a separatory funnel and anequal volume of pentane was added. The organic layer was washed three times with H2O, dried over MgSO4and filtered. Removal of the solvent under reduced pressure afforded the aryl boronic ester.



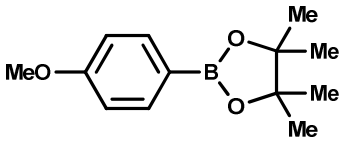
4,4,5,5-tetramethyl-2-p-tolyl-[1,3,2]dioxaborolane

Compound was isolated as a white solid (2.596 g, 85% yield). Spectral data matches the previously reported values.[23] ^{1}H NMR (300 MHz, C_6D_6) δ 8.13 (d, *J* = 7.9 Hz, 2H), 7.05 (dd, *J* = 8.1, 0.6 Hz, 2H), 2.06 (s, 3H), 1.13 (s, 12H).



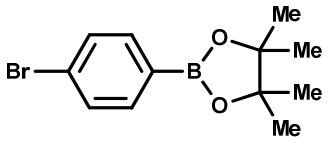
4-(4,4,5,5-tetramethyl-[1,3,2]-dioxaborolan-2-yl)benzaldehyde

Compound was isolated as a white solid (5.112 g, 86% yield). Spectral data matches the previously reported values.[24] ^{1}H NMR (300 MHz, C_6D_6) δ 9.64 (s, 1H), 8.05 (dd, *J* = 8.0, 3.0 Hz, 2H), 7.57 (dd, *J* = 8.2, 3.0 Hz, 2H), 1.08 (s, 12H).



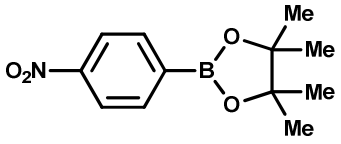
2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane

Compound was isolated as a colorless oil (1.912 g, 82% yield). Spectral data matches the previously reported values.[25] ^{1}H NMR (300 MHz, C_6D_6) δ 8.16 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 3.22 (s, 3H), 1.15 (s, 12H).



2-(4-bromophenyl)-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane

Compound was isolated as a white solid (2.733 g, 94% yield). Spectral data matches the previously reported values.[25] ^{1}H NMR (300 MHz, C_6D_6) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 1.07 (s, 12H).



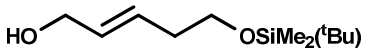
4,4,5,5-tetramethyl-2-(4-nitrophenyl)-[1,3,2]dioxaborolane

Compound was isolated as a yellow solid (538.8 mg, 72% yield). Spectral data matches the previously reported values.[26] ^{1}H NMR (300 MHz, C_6D_6) δ 7.82 (m, 4H), 1.05 (s, 12H).

1.5.e. Synthesis of allylic chlorides:

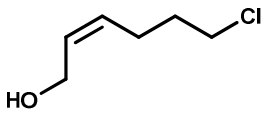
(*E*)-5-((*tert*-butyldimethylsilyl)oxy)pent-2-en-1-ol,[27] (*Z*)-6-chloro-hex-2-en-1-ol,[28] (*E*)-7-chlorohept-2-en-1-ol,[29] (*E*)-8-hydroxyoct-6-enenitrile,[30] (*E*)-1-chlorohex-2-ene,[31] (*Z*)-*tert*-butyl((5-chloropent-3-en-1-yl)oxy)dimethylsilane,[32] 1-(chloromethyl)cyclopent-1-ene,[31] and (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene[33] were all synthesized according to literature proce-dures, and ^{1}H NMR data match literature values.

Allylic Alcohols:



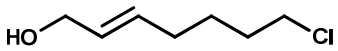
(*E*)-5-((*tert*-butyldimethylsilyl)oxy)pent-2-en-1-ol

Compound was isolated as a colorless oil (1.570g, 82% yield) together with minor impurities containing TBS group. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74 – 5.66 (m, 2H), 4.11 – 4.07 (m, 2H), 3.65 (t, *J* = 7.1 Hz, 2H), 2.31 – 2.24 (m, 2H), 1.34 (t, *J* = 5.8 Hz, 1H), 0.89 (s, 9H), 0.05 (s, 6H).



(*Z*)-6-chloro-hex-2-en-1-ol

Compound was isolated as a colorless oil (2.000 g, 93% yield). ^{1}H NMR ($CDCl_3$) δ 5.68 (dt,*J* = 6.6, 9.9 Hz, 1H),5.47 (dt, *J* = 6.6, 10.7 Hz, 1H), 4.23 (d,*J* = 6.4 Hz, 2H), 3.56 (t, *J* = 7.1 Hz, 2H), 2.88 (s, 1 H), 2.13 – 2.47 (m, 2 H), 1.67 – 2.06 (m,2 H).

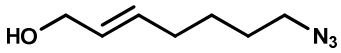


(*E*)-7-chlorohept-2-en-1-ol

Compound was isolated as a colorless oil (4.638 g, 53% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 – 5.53 (m, 2H), 4.24 – 3.88 (m, 2H), 3.54 (t, *J* = 6.6 Hz, 2H), 2.16 – 1.97 (m, 2H), 1.88 – 1.68 (m, 2H), 1.61 – 1.47 (m, 2H), 1.29 (s, 1H).

(*E*)-8-hydroxyoct-6-enenitrile

Compound was isolated as a colorless liquid (1.351 g, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85 – 5.47 (m, 2H), 4.03 – 4.17 (m, 2H), 2.35 (t, *J* = 6.9 Hz, 2H), 2.24 – 1.91 (m, 2H), 1.80 – 1.40 (m, 4H), 1.33 (s, 1H).



(*E*)-7-azidohept-2-en-1-ol

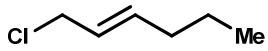
To a solution of 6-chloro-(2*E*)-heptene-1-ol (1.00 equiv, 1.00 mL, 6.817 mmol) in dry DMSO (14.0 mL) was added sodium iodide (0.10 equiv, 102.2 mg, 0.682 mmol) followed by sodium azide (2.00 equiv, 886.3 mg, 13.60 mmol). The reaction mixture was

vigorously stirred for 16 h at 45 °C then cooled to room temperature, diluted with Et_2O, and washed with H_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel column chromatography (20 →50% EtOAc/hexanes) and 6-azido-(2*E*)-hexen-1-ol was obtained as a light yellow oil (903.1 g, 85% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 5.56 – 5.24 (m, 2H), 3.77 – 3.89 (m, 2H), 2.65 (t, *J* = 6.4 Hz, 2H), 1.66 – 1.82 (m, 2H), 1.25 – 0.98 (m, 4H), 0.77 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.3, 129.7, 63.7, 51.4, 31.7, 28.4, 26.2. ESI-MS (MeOH, m/z):178.1 $[M+Na]^+$. FTIR (neat, cm-1): 3342 (m br), 2936 (m), 2097 (s), 1089 (m), 971 (m).

Allylic Chlorides:

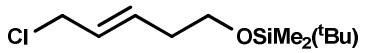
General:

The allylic chlorides were synthesized according to a modified literature procedure:[27] Dimethyl sulfide (2.00 equiv) was added over 10 min to a flame dried flask containing *N*-chlorosuccinimide (2.00 equiv) in dry CH_2Cl_2 at 0 °C. The milky white solution was stirred for 1 h then cooled to -20 °C, and the allylic alcohol (1.00 equiv) in dry CH_2Cl_2 was added dropwise over 30 min. The reaction mixture was allowed to warm to 0 °C and after 2 h was allowed to warm to 25 °C. After complete consumption of the alcohol, solvent was removed *in vacuo*, and the crude mixture was diluted with pentane and washed with H_2O. The aqueous layer was extracted with pentane and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The product was passed through a plug of silica using a mixture of pentane and ethyl acetate as an eluent to afford the pure allylic chloride.



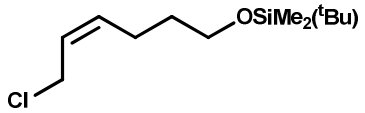
(*E*)-1-chlorohex-2-ene (**1.1**)

Compound was isolated as a colorless liquid (1.841 g, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (m, 1H), 5.69 – 5.53 (m, 1H), 4.03 (dd, *J* = 6.9, 0.8 Hz, 2H), 2.04 (m, 2H), 1.51 – 1.31 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).



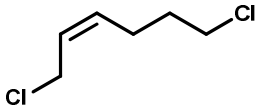
(*E*)-*tert*-butyl((5-chloropent-3-en-1-yl)oxy)dimethylsilane

Compound was isolated as a colorless liquid (1.327 g, 92% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 5.55 – 5.34 (m, 2H), 3.62 (d, *J* = 5.9 Hz, 2H), 3.42 (t, *J* = 6.5 Hz, 2H), 2.09 – 1.97 (m, 2H), 0.96 (s, 9H), 0.02 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.6, 127.9, 62.5, 45.4, 35.8, 26.1, 18.5, -5.1. ESI-MS (MeOH, m/z): 257.1 $[M+Na]^+$. FTIR (neat, cm-1): 3038 (w), 2956 (s), 1668 (w), 1472 (m) 1256 (m), 1104 (s), 837 (s).



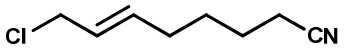
(*Z*)-*tert*-butyl((6-chlorohex-4-en-1-yl)oxy)dimethylsilane

Compound was isolated as a colorless liquid (1.458 g, 89% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 5.58 – 5.32 (m, 2H), 3.62 (d, *J* = 5.9 Hz, 2H), 3.42 (t, *J* = 6.5 Hz, 2H), 2.12 – 1.97 (m, 2H), 0.96 (s, 9H), 0.02 (s, 6H).



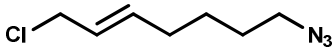
(*Z*)-1,6-dichlorohex-2-ene

Compound was isolated as a colorless liquid (1.635 g, 73% yield) after filtration through a plug of silica using pentane as an eluent. ^{1}H NMR (300 MHz, C_6D_6) δ 5.41 (dtt, *J* = 10.6, 7.8, 1.5 Hz, 1H), 5.05 (dt, *J* = 10.6, 7.7 Hz, 1H), 3.67 (d, *J* = 7.8 Hz, 2H), 2.96 (t, *J* = 6.5 Hz, 2H), 1.82 – 1.67 (m, 2H), 1.35 – 1.23 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.2, 127.0, 44.3, 39.3, 31.9, 24.3. (GC-MS, EI, m/z): 152 $[M]^+$. FTIR (neat, cm-1): 3027 (m), 2959 (s), 1653(m), 1251 (s), 756 (s), 650 (s).



(*E*)-8-chlorooct-6-enitrile

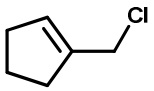
Compound was isolated as a colorless liquid (927.8 mg, 78% yield) after filtration through a plug of silica using 20% EtOAc in hexane as an eluent. ^{1}H NMR (300 MHz, C_6D_6) δ 5.47 – 4.95 (m, 2H), 3.61 (d, *J* = 6.5 Hz, 2H), 1.53 – 1.41 (m, 2H), 1.33 (t, *J* = 6.8 Hz, 2H), 1.00 – 0.73 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.6, 127.0, 119.6, 45.2, 31.1, 27.7, 24.7, 17.0. HRMS calculated for $[M+Na]^+$180.0550, found 180.0546. FTIR (neat, cm-1): 3036 (m), 2939 (s), 2247 (m), 1666 (m), 1251 (m), 969 (s), 674 (m).



(*E*)-7-azido-1-chlorohept-2-ene

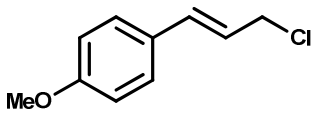
Compound was isolated as a light yellow liquid (639.7 mg, 93% yield) after filtration through a plug of silica using 10% EtOAc in hexane as an eluent. ^{1}H NMR (300 MHz, C_6D_6) δ 5.44 – 5.12 (m, 2H), 3.61 (d, *J* = 5.8 Hz, 2H), 2.60 (t, *J* = 6.6 Hz, 2H), 1.63 –

1.53 (m, 2H), 1.17 – 0.87 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.2, 126.7, 51.4, 45.4, 31.6, 28.4, 26.0. HRMS calculated for $[M]^+$ 172.0636, found 172.0673. FTIR (neat, cm-1): 3035 (w), 2939 (m), 2097 (s), 1666 (w), 1251 (m), 968 (m), 676 (m).



1-(chloromethyl)cyclopent-1-ene

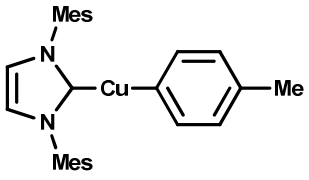
Compound was isolated as a colorless oil (816.2 mg, 86% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69 – 5.78 (m, 1H), 4.15 (d, *J* = 0.8 Hz, 2H), 2.49 – 2.29 (m, 4H), 2.04 – 1.85 (m, 2H).



(*E*)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene

Compound was isolated as a colorless oil (1.053g, 95% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 6.33 (d, *J* = 15.6 Hz, 1H), 6.11 – 5.86 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.38 (s, 3H).

1.5.f. Synthesis of (IMes)Cu(4-methylbenzene) complex (Equation 5):



Mes = 2,4,6-trimethylphenyl

(IMes)Cu(4-methylbenzene)

(4-methylbenzene)[1,3-dihydro-1,3-bis(2,4,6-trimethylphenyl)-2H-imidazol-2-ylidene]-Copper (**1.28**)

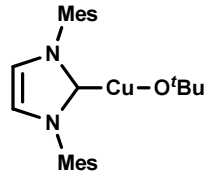
A 100 mL Schlenk flask was charged with a stir bar and flame-dried under vacuum. The flask was then transferred into a glove box and was charged with IMesCuO-*tert*-butoxide (1.1 equiv, 1.00 g, 2.27 mmol) and tolyl boronic(pinacolato) ester (1.0 equiv, 0.45 g, 2.06 mmol). Toluene was added (50 mL, 0.05 M). The resulting solution was heated to 60 °C for 16 h and then filtered over a pad of Celite. The solvent was then removed *in vacuo* until cloudy. An equal volume of pentane was added, and the flask was placed into the -20 °C freezer. After 24 h, the filtrate was removed by pipette and the crystals isolated by vacuum filtration. The crystals were then washed with pentane and transferred into a scintillation vial charged with a stir bar. Isooctane was added and the solution was vigorously stirred at room temperature for 0.5 h. The isooctane was then removed *in vacuo*. This process was repeated twice to yield the desired product as a white solid (575.5 mg, 61% yield). ^{1}H NMR (500 MHz, 1,4-dioxane-d^8) δ 7.22 (s, 2H), 7.07 (s, 4H), 6.80 (d, J = 7.4 Hz, 2H), 6.54 (d, J = 7.3 Hz, 2H), 2.35 (s, 6H), 2.17 (s, 12H), 2.04 (s, 3H); ^{13}C NMR (75 MHz, THF-d^8) δ 184.5, 162.5, 140.8, 139.7, 137.2, 135.8, 131.9, 130.1, 126.8, 123.2, 21.8, 21.4, 18.4. The same compound was independently prepared by addition of 4-MePhMgBr to IMesCuCl. Attempts to obtain HRMS were not successful.

1.5.g. Stoichiometric Reaction of (IMes)Cu(4-methylbenzene) with (E)-2-hexenyl-1-chloride (Equation 6)

In a glove box, a 1 dram vial was charged with a stir bar. To the vial was added (*E*)-2-hexenyl-1-chloride (1.00 equiv, 6.6 μL, 0.05 mmol) and internal standard 1,3,5-trimethoxybenzene (TMB) in 1,4-dioxane (0.25 mL). Separately, a solution of

(IMes)Cu(4-methylbenzene) (1.00 equiv, 23.0 mg, 0.05 mmol) in 1,4-dioxane (0.25 mL) was prepared. The solution of (IMes)Cu(4-methylbenzene)was added to a 1 dram vial containing (*E*)-2-hexenyl chloride and the resulting solution was stirred at 45 °C. After 5 minutes, an aliquot of the reaction analyzed by GC indicated complete conversion of (*E*)-2-hexenyl chloride. The arylation product was obtained in 79% yield (determined by GC analysis) as a mixture of isomers.

1.5.h. Catalyst synthesis:



Mes = 2,4,6-trimethylphenyl

IMesCuO-*tert*-butoxide (1.8)

(t-butoxy)[1,3-dihydro-1,3-bis(2,4,6-trimethylphenyl)-2H-imidazol-2-ylidene]-Copper

A 200 mL Schlenk flask was charged with a stir bar and flame-dried under vacuum. The flask was then transferred into a glove box and was charged with1,3-bis-(2,4,6-trimethylphenyl)-imidazolium chloride (IMes-chloride salt) (1.00 equiv, 3.41 g, 10.0 mmol), copper-*tert*-butoxide tetramer (CuO-*tert*-Bu)4(0.25 equiv, 1.37 g, 2.50 mmol), and sodium *tert*-butoxide (NaO- *tert* -Bu) (1.00 equiv, 0.96 g, 10.0 mmol). With vigorous stirring, THF was added in one portion (0.1 M, 100.0 mL). The resulting pale-orange solution was allowed to stir at room temperature for 4 h. The flask was taken out of the glovebox and the solvent was removed *in vacuo*. The flask was transferred to the glove

box and the solid scraped and suspended in toluene. The resulting solution was filtered over a pad of Celite, and the pad was washed with two portions of toluene. The solvent was removed *in vacuo* to yield the product as a pale yellow solid (4.08 g, 92% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 6.71 (s, 4H), 5.97 (s, 2H), 2.11 (s, 6H), 1.95 (s, 12H), 1.38 (s, 9H); ^{13}C NMR (125 MHz, THF-d^8) δ 182.3, 139.7, 137.3, 135.9, 130.0, 123.2, 36.8, 21.3, 18.2.

Section 6. References to Chapter 1

(1) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216.
(2) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.
(3) Streitwieser, A. *J. Org. Chem.* **2008**, *73*, 9426.
(4) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 1.
(5) (a) Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 4554; (b) Selim, K. B.; Yamada, K.-i.; Tomioka, K. *Chem. Commun.* **2008**, 5140; (c) Selim, K. B.; Matsumoto, Y.; Yamada, K.-i.; Tomioka, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 8733; (d) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 2895; (e) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *Org. Lett.* **2010**, *12*, 2438; (f) Piarulli, U.; Daubos, P.; Claverie, C.; Roux, M.; Gennari, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 234; (g) Demel, P.; Keller, M.; Breit, B. *Chem. Eur. J.* **2006**, *12*, 6669; (h) Yasui, H.; Mizutani, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 1410; (i) Consiglio, G.; Piccolo, O.; Roncetti, L.; Morandini, F. *Tetrahedron* **1986**, *42*, 2043; (j) Hiyama, T.; Wakasa, N. *Tetrahedron Lett.* **1985**, *26*, 3259; (k) Gomez-Bengoa, E.; Heron, N. M.; Didiuk, M. T.; Luchaco, C. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 7649; (l) Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 2756; (m) Mukaiyama, T.; Ishikawa, H. *Chem. Lett.* **1974**, 1077; (n) Ohmiya, H.; Makida, Y.; Li, D.; Tanabe, M.; Sawamura, M. *J. Am. Chem. Soc.* **2009**, *131*; (o) Lautens, M.; Dockendorff, M. C.; Fagnou, K.; Malicki, M. *Org. Lett.* **2002**, *4*, 1311.
(6) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395.
(7) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336.
(8) Rona, P.; Tokes, L.; Tremble, J.; Crabbe, P. *Chem. Commun.* **1969**, 43.
(9) Tseng, C. C.; Paisley, S. D.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2884.
(10) Klaveren, M. v.; Persson, E. S. M.; Villar, A. d.; Grove, D. M.; Bäckvall, J.-E.; Koten, G. v. *Tetrahedron Lett.* **1995**, *36*, 3059.
(11) (a) Alexakis, A.; Bäckvall, J. E.; Krause, N.; Pamies, O.; Dieguez, M. *Chem. Rev.* **2008**, *108*, 2796; (b) Falciola, C. A.; Alexakis, A. *Eur. J. Org. Chem.* **2008**, 3765; (c) Geurts, K.; Fletcher, S. P.; van Zijl, A. W.; Minnaard, A. J.; Feringa, B. L. *Pure Appl. Chem.* **2008**, *80*, 1025.
(12) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 446.
(13) (a) Arai, M.; Lipshutz, B. H.; Nakamura, E. *Tetrahedron* **1992**, *48*, 5709; (b) Lipshutz, B. H.; Elsworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 1351.
(14) (a) Bäckvall, J. E.; Sellen, M.; Grant, B. *J. Am. Chem. Soc.* **1990**, *112*, 6615; (b) Bäckvall, J.-E.; Persson, E. S. M.; Bombrun, A. *J. Org. Chem.* **1994**, *59*, 4126; (c) Bäckvall, J.-E.; Séllen, M. *J. Chem. Soc., Chem. Commun.* **1987**, 827.
(15) Yoshikai, N.; Zhang, S.-L.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 12862.
(16) Yoshikai, N. N., E. *Chem. Rev.* **2012**, *112*, 2339.
(17) Yamanaka, M.; Nakamura, a. E. *J. Am. Chem. Soc.* **2005**, *127*, 4697.
(18) Hall, D. G. *Boronic Acids*; Wiley-VCH: Weinheim, 2005.

(19) Tominaga, S.; Oi, Y.; Kato, T.; An, D. K.; Okamoto, S. *Tetrahedron Lett.* **2004**, *45*, 5585.
(20) Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 5792.
(21) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369.
(22) Shintani, R. T., K.; Takeda, M.; Hayashi, T. *Angew. Chem., Int. Ed. Engl.* **2011**, *50*, 8656.
(23) Cameron, K. S.; Pincock, A. L.; Thompson, J. A. *J. Org. Chem.* **2004**, *69*, 4954.
(24) Yu, L.; Lindsey, J. S. *Tetrahedron* **2001**, *57*, 9285.
(25) Zhu, W.; Ma, D. *Org. Lett.* **2006**, *8*, 261.
(26) Oehlke, A.; Auer, A. A.; Schreiter, K.; Hofmann, K.; Riedel, F.; Spange, S. *J. Org. Chem.* **2009**, *74*, 3316.
(27) Jensen, T.; Peders, H.; Bang-Andersen, B.; Madsen, R.; Joergensen, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 888.
(28) Holton, R. A.; Zoeller, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 2124.
(29) Zimmer, L. E.; Charette, A. B. *J. Am. Chem. Soc.* **2009**, *131*, 15624.
(30) Levine, S. G.; Bonner, M. P. *Tetrahedron Lett.* **1989**, *30*.
(31) Fox, R. J.; Lalic, G.; Bergman, R. G. *J. Am. Chem. Soc.* **2007**, *129*.
(32) Manning, P. T.; Misko, T. P. In *PCT Int. Appl.* 2005; Vol. WO 2005025620.
(33) Bouziane, A.; Helou, M.; Carboni, B.; Carreaux, F.; Demerseman, B.; Bruneau, C.; J., R. *Chem. Eur. J.* **2008**, *14*, 5630.

Chapter 2 – Copper-Catalyzed Electrophilic Amination of Alkyl Boranes: Formal anti-Markovnikov Hydroamination of Terminal Alkenes[1]

Section 1. Introduction and Context

The synthesis of alkyl amines is one of the most important and common tasks encountered in the preparation of biologically active molecules.[2] A recent analysis of reactions used in pharmaceutical industry suggests that this task is almost exclusively accomplished by either reductive amination of carbonyl compounds, or by substitution of alkyl halides or sulfonates.[3] The synthesis of alkyl amines from most other precursors usually requires functional group interconversion, followed by amination using one of the two standard methods. As a result, the development of new reactions for direct amination of other functional groups has attracted a lot of attention as a way to facilitate the synthesis of alkyl amines.[4]

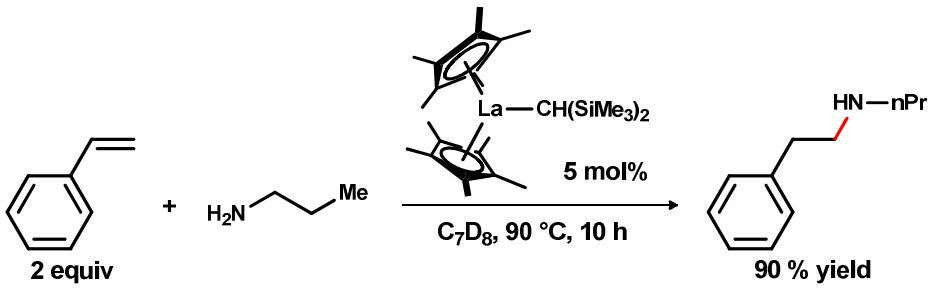
Alkenes are particularly attractive as synthetic precursors. They are readily available and have orthogonal reactivity to that of polar functional groups found in biologically active molecules. The most direct approach to obtain alkyl amines from alkenes is by addition of an amine across an alkene double bond.[5] This transformation has been the focus of numerous studies ever since initial reports of metal-catalyzed hydroamination under mild conditions appeared more than two decades ago.[6] Today, intramolecular hydroamination can be accomplished with a broad substrate scope and with a number of different catalysts.[7,8] Intermolecular hydroamination is significantly

less developed, with most successful examples being focused on the formation of the Markovnikov hydroamination product.[6a,9,10] The formation of the other regioisomer, the anti-Markovnikov product, still represents a major synthetic challenge.[11]

For many transition metal-catalyzed hydroamination reactions, the regiodetermining step is alkene insertion into a metal-amido bond.[5a] In a recent computational study of a rhodium-catalyzed propene hydroamination, Hartwig and coworkers found that alkene (1,2)-insertion to give the Markovnikov product was both kinetically and thermodynamically preferred over (2,1)-insertion.[12] This finding underlines the difficulties in developing metal-catalyzed anti-Markovnikov hydroamination of alkenes.

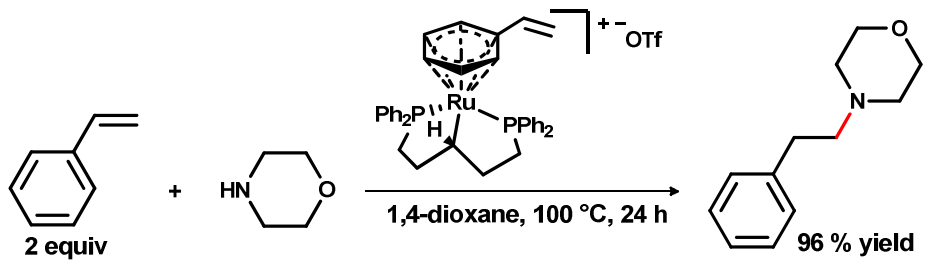
Despite these challenges, there are several examples of the anti-Markovnikov hydroamination of alkenes. In a seminal contribution, Tobin Marks described the lanthanide-catalyzed intermolecular hydroamination of vinylarenes and vinylsilanes with alkyl amines to give linear (anti-Markovnikov) products (Scheme 1).[13] The origin of regioselectivity is attributed to directing effects of the aryl group during alkene insertion into the metal-amido bond.[7c,14] For simple alkenes, however, Markovnikov selectivity (1,2-insertion) is observed.

Scheme 2.1



Following observations by Beller and coworkers,[15] Hartwig developed a rhodium-catalyzed anti-Markovnikov hydroamination of *para*-substituted vinylarenes with secondary amines.[16] Using a ruthenium catalyst, the same group was able to extend the scope to other vinylarenes and cyclic and acyclic secondary amines (Scheme 2).[17] Detailed mechanistic studies revealed that the ruthenium catalyst activates the arene towards nucleophilic attack through η^6-κ^1-coordination.[18] Therefore, the selective formation of linear (anti-Markovnikov) amine products in this case is mechanistically related to well-documented Michael-type additions of nucleophiles to activated alkenes.[19] An alternative approach to Michael-type additions involves activation of amine nucleophiles. For instance, Gunnoe and coworkers developed the copper-catalyzed addition of anilines to electron-deficient vinylarenes, in which the nucleophilicity of the amine is increased through formation of a metal-amide complex.[20]

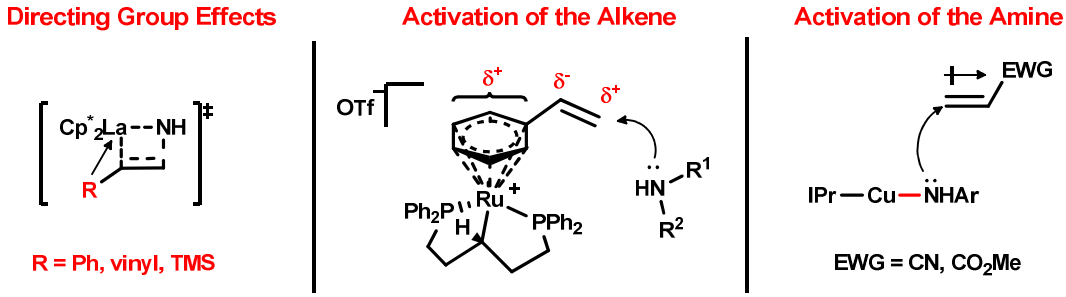
Scheme 2.2



Notwithstanding these contributions, it is apparent that transition-metal catalyzed alkene hydroamination to give anti-Markovnikov amines remains underdeveloped. In each of the above cases, anti-Markovnikov selectivity is observed only with activated alkenes, such as styrene or trimethylsilyl-substituted alkenes, or with uncommon instances of catalyst coordination and substrate or amine activation. These limitations, together with the requirement that an excess of alkene must be used in these

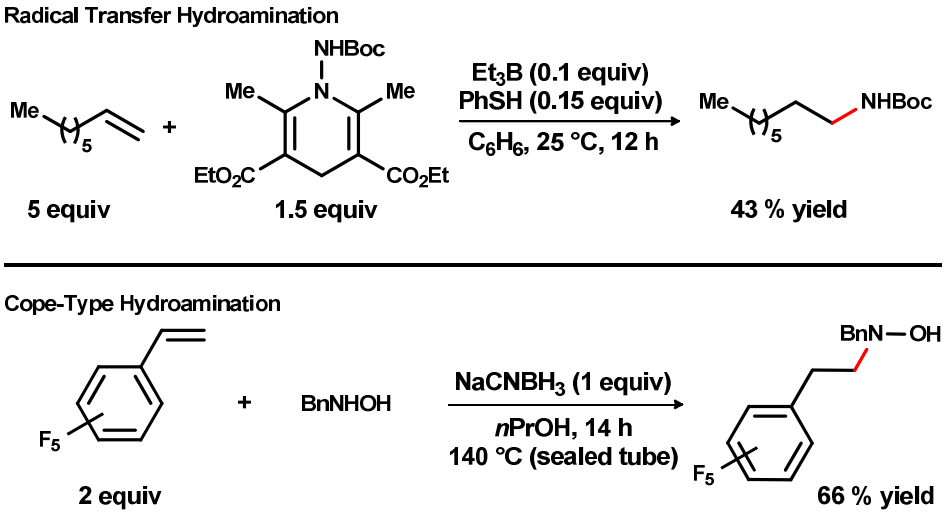
transformations, limits their utility. Furthermore, none of the existing procedures for transition metal-catalyzed, anti-Markovnikov hydroamination allows the preparation of acyclic, tertiary alkyl amines from alkenes.

Scheme 2.3



In view of the difficulties inherent to direct hydroamination of unactivated alkenes, other methods have been developed for the transformation of alkenes into amines. Stüder and coworkers developed a radical-transfer approach for the transformation of a variety of alkenes into primary and secondary Boc-protected amines (Scheme 2.4).[21] The regiochemistry of this process is determined by the relative stability of the isomeric alkyl radical intermediates formed in radical addition to the alkene. The group of Beauchemin has developed an intermolecular hydroamination of styrene derivatives and strained alkenes with unsubstituted and *N*-alkyl hydroxylamine (Scheme 3).[22] In this reaction, moderate to high anti-Markovnikov selectivity was observed with electron-poor alkenes.

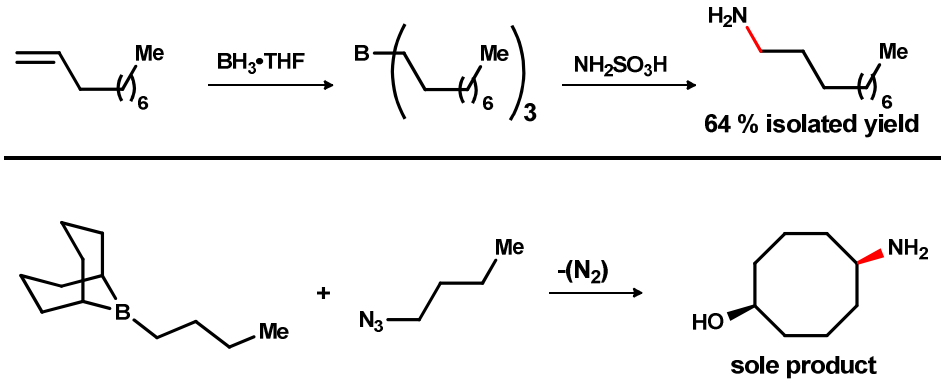
Scheme 2.4



Traditionally, the anti-Markovnikov hydrofunctionalization of alkenes is achieved by hydroboration and functionalization of the resulting alkyl borane. The classic example is the hydroboration/oxidation sequence, developed by H.C. Brown. This transformation is a robust, highly efficient, and practical method for the conversion of a variety of alkenes to alcohols with excellent regioselectivity.[23] Although less developed, the analogous hydroboration/amination sequence is still the most reliable and regioselective route to anti-Markovnikov hydroamination products. In this reaction, a variety of primary and secondary, but not tertiary, amines can be prepared. Specifically, primary amines can be generated by the use of chloramine, hydroxylamine-*O*-sulfonic acid, or ammonium hydroxide.[24] Unlike alkene hydration, alkene amination to give primary amines is inefficient. Most conditions allow amination of at most two alkyl groups of a trialkyl borane, limiting the yield based on the alkene to 67% (top of Scheme 4).[24b] Similar problems in organoboron chemistry are usually solved by using bulky, non-migrating groups on the borane, e.g., dicyclohexyl borane or 9-borabicyclo[3.3.1]nonane (9-BBN). In hydroboration/amination, however, this approach is ineffective as the

migration of secondary alkyl groups is faster than the migration of primary alkyl groups (bottom of Scheme 4).[24b,25] Methyl groups, on the other hand, have no significant migratory aptitude, and dimethylborane has been used to accomplish an efficient conversion of alkenes to primary amines.[24b] Unfortunately, the complex synthesis of this reagent has precluded its wider use in synthetic chemistry.[26]

Scheme 2.5



Secondary amines can be prepared by hydroboration followed by amination using primary organoazides; [27] this is usually accomplished in the presence of excess Lewis acid (BF_3 or $SiCl_4$).[28] Good yields of secondary amine products can be obtained using dichloroborane as the alkene hydroborating reagent.[25b,29] D.S. Matteson and coworkers have developed a related approach in which enantioenriched alkyl boronic esters are first converted into potassium trifluoroalkylborates en route to secondary amines by the action of potassium hydrogenfluoride and tetrachlorosilane.[30]

Overall, even though the hydroboration/amination sequence does provide excellent regioselectivity, it is rarely used in organic synthesis. Not only is the use of organoazides impractical, but many synthetic procedures are incompatible with strong Lewis acids used in the synthesis of secondary amines. Furthermore, the scope of

hydroboration/amination is limited to the synthesis of primary and secondary amines. However, the greatest obstacle to the development of a practical hydroboration/amination sequence that remained was the inefficient amination of alkyl boranes.

We were intrigued by the possibility that transition metal catalysis could be used to facilitate the amination of alkyl boranes and allow the development of an efficient hydroboration/amination sequence.[31] This approach was especially appealing to us because we had already demonstrated the utility of organoboron—copper transmetallation to affect the highly S_N2'-selective substitution of allylic chlorides by alkyl boranes,[32] in addition to other recent reports.[33] The key steps in these reactions are transmetallation from boron to copper followed by reaction of the organocopper intermediate with an electrophile.[34] By following the same strategy, our approach to amination of organoboron compounds would involve transmetallation from boron to copper, followed by well-precedented electrophilic amination of the organocopper intermediate.[35,36]

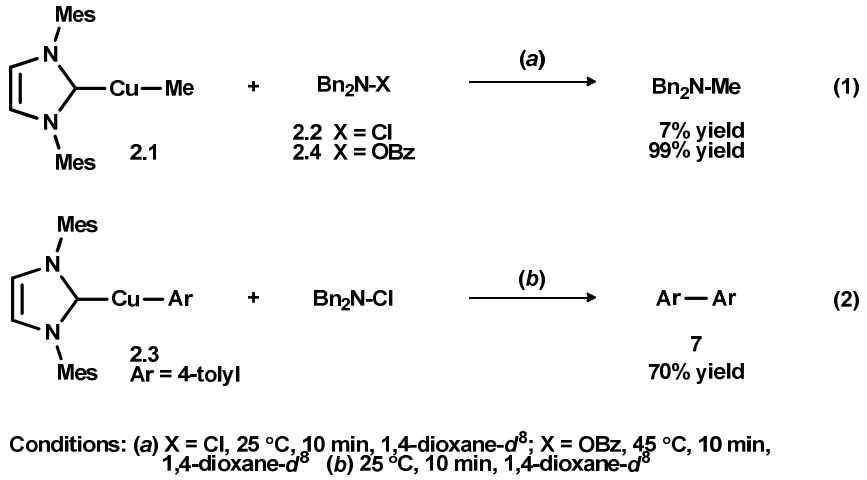
Section 2. Reaction Discovery and Optimization

2.2.a. Identification of electrophilic nitrogen source

Our first challenge was to identify an appropriate electrophile for functionalization of the proposed alkyl copper intermediate. Based on our experience with *NHC*-Cu complexes (*NHC* = *N*-heterocyclic carbene) as catalysts in reactions of organoboron compounds, we decided to explore the reactivity of **2.1**[37] in stoichiometric reactions with reagents used in electrophilic amination of organometallic nucleophiles. In reactions with more reactive electrophiles,[38,35b,35c,39] such as *N,N*-dibenzyl chloramine (**2.2**), we observed complete conversion of **2.1**, and the formation of a small amount (7%)

of the amination product that could not account for the disappearance of **2.1** (Scheme 2.6, equation 1).

Scheme 2.6



Conditions: (*a*) X = Cl, 25 °C, 10 min, 1,4-dioxane-d^8; X = OBz, 45 °C, 10 min, 1,4-dioxane-d^8 (*b*) 25 °C, 10 min, 1,4-dioxane-d^8

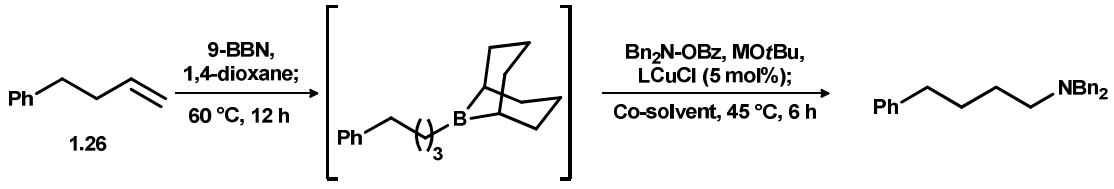
More insight into reactivity of chloramine **2.2** was obtained from its reaction with **2.3** (Scheme 2.6, equation 2), in which the oxidative homocoupling product 4,4'-dimethyl-1,1'-biphenyl was obtained in 70% yield. Gratifyingly, in a reaction with *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2.4**) the desired amination was obtained in 99% yield (Scheme 2.6, equation 1). *O*-benzoyl-*N*,*N*-dialkylhydroxylamines such as **2.4** are readily available[35c,40] and have previously been used in copper-catalyzed electrophilic amination of organozinc and Grignard reagents.[35b,35c]

2.2.b. Initial optimization with O-benzoyl-N,N-dibenzylhydroxylamine

Having identified suitable electrophiles for amination of *NHC*-Cu alkyl complexes, we turned our attention to the development of copper-catalyzed amination of alkyl boranes, and its application in the hydroamination of terminal alkenes. We first explored the electrophilic amination of the 9-alkyl-9-BBN derivative, prepared by hydroboration of 4-phenyl-1-butene (**2.5**), with 9-BBN. Hydroboration was performed in

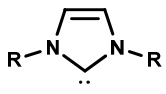
1,4-dioxane at 60 °C for 12 h, after which all of the components required for electrophilic amination were added to the reaction flask. In a catalytic reaction performed under conditions previously used by us in the alkylation of allylic chlorides by alkyl boranes,[32] the hydroamination product using **2.4** was obtained in less than 5% yield (Table 1, entry 1). However, a catalyst screen identified ICyCuCl as the best catalyst, providing the desired product in 16% yield (entry 2).

Table 2.1

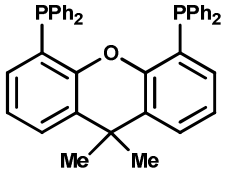


Entry[a]	M	L	Co-solvent	Yield[b]
1.	Na	IMes	1,4-dioxane	< 5%
2.	Na	ICy	1,4-dioxane	16%
3.	K	ICy	1,4-dioxane	11%
4.	Li	ICy	1,4-dioxane	56%
5.	Li	ICy	pentane	78%
6.	Li	IMe	pentane	39%
7.	Li	IAdm	pentane	43%
8.	Li	IPr	pentane	<5%
9.[c]	Li	xantphos	pentane	<5%
10.[d]	Li	ICy	pentane	97%

[a] All reactions conducted with 1.0 equiv each Bn_2N-OBz and MO*t*Bu at 0.2 M concentration. [b] Yield determined by GC analysis using *n*-dodecane as internal standard. [c] Catalyst formed in situ from xantphos and $(CuOtBu)_4$. [d] After 3 h, 0.3 equiv each Bn_2N-OBz and LiO*t*Bu was added to the reaction mixture.



IMes R = 2,4,6-trimethylphenyl
ICy R = cyclohexyl
IMe R = methyl
IAdm R = adamantyl
IPr R = 2,6-diisopropylphenyl



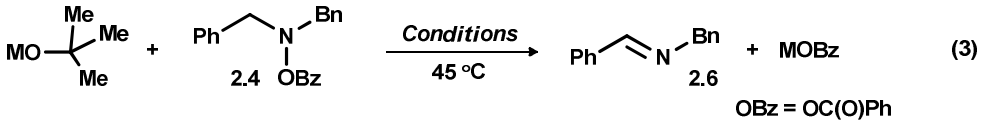
xantphos

Analysis of the crude reaction mixtures obtained in catalytic reactions indicated complete consumption of the electrophile and the formation of a single major product. After column chromatography, we isolated a significant amount of benzaldehyde, which

suggested that the major product of the reaction might be the imine formed by elimination of benzoate from *O*-benzoylhydroxylamine **2.4**.

Control experiments confirmed a fast formation of the imine **2.6** in a reaction of the electrophile **2.4** with sodium *tert*-pentoxide at room temperature (Scheme 2.7, equation 3 conditions *a*). While the elimination reaction was slower in the presence of alkyl borane ($t_{1/2}$ ~ 10 min, conditions *b*), it still effectively competed with the desired electrophilic amination. Further experiments revealed that the consumption of the electrophile was significantly slower with use of lithium *tert*-butoxide ($t_{1/2}$ ~ 120 min, conditions *c*). The deleterious consumption of **2.4** could be further attenuated if a noncoordinating solvent, such as benzene, was used (5% conversion after 2 h, conditions *d*), possibly due to the lower solubility of lithium *tert*-butoxide in this medium.

Scheme 2.7



Conditions	*Electrophile Conversion*
(*a*) 1,4-dioxane, NaO*t*Bu	>95% conversion within 10 minutes
(*b*) as above + alkyl borane	$t_{1/2}$ ~ 10 min
(*c*) 1,4-dioxane, LiO*t*Bu	$t_{1/2}$ ~ 120 min
(*d*) benzene, LiO*t*Bu	5% conversion at 120 min

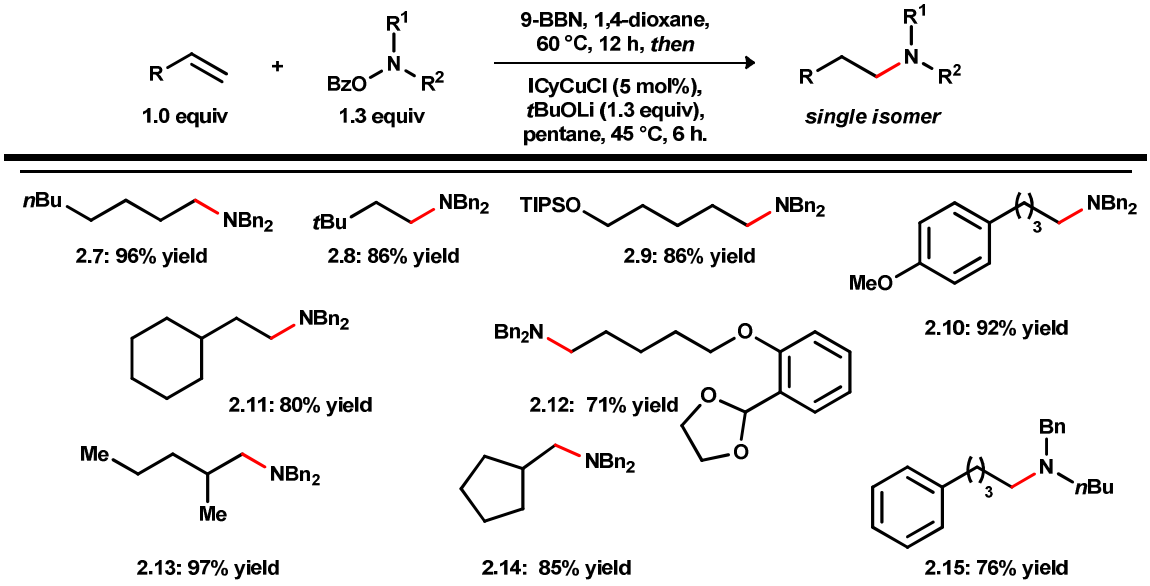
Guided by the results of control experiments, we were able to significantly improve the yield of the hydroamination product. In a catalytic reaction performed with lithium *tert*-butoxide instead of sodium *tert*-pentoxide, the desired product was obtained in 56% yield (Table 2.1, entry 4). Further improvement was achieved by addition of pentane to a hydroboration reaction performed in 1,4-dioxane (entry 5). Under these new conditions, ICyCuCl remained superior to other copper(I) catalysts and was chosen to be

used in further optimization of the reaction (Table 2.1, compare entry 5 with entries 6—9). After further modification, the highest yield was obtained when 1.3 equivalents of both the electrophile and alkoxide were used in the reaction (entry 10), providing the desired product as a single regioisomer in 97% yield.

Hydroamination of Alkenes by *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine

These conditions were found to catalyze the formal hydroamination of a number of monosubstituted terminal alkenes to give benzyl-protected primary amines (Table 2.2, **2.7**—**2.12**). Electrophile **2.4** could be used in conjunction with a sterically demanding *tert*-butyl substituent on the alkene partner to give **2.8**, as well as in reactions with 2,2-disubstituted alkenes to form products such as **2.11** and **2.13** without decrease in yield. Furthermore, benzyl-protected secondary amines such as **2.15** could also be prepared by this method.

Table 2.2

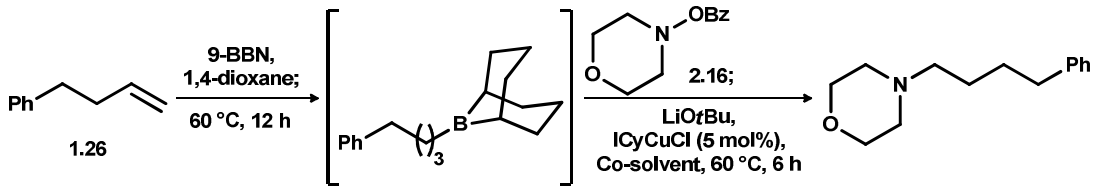


Hydroboration was performed in 1,4-dioxane, after which catalyst, lithium *tert*-butoxide (1.0 equiv), *O*-benzoyl-*N*,*N*-dialkylhydroxylamine (1.0 equiv) and pentane were added to the vial. After 3 h, 0.3 equiv each lithium *tert*-butoxide and *O*-benzoyl-*N*,*N*-dialkylhydroxylamine were added to the vial, and the reaction heated for 3 additional h. Reactions were conducted on a 0.5 mmol scale. Yields are of isolated products after column chromatography.

2.2.c: Optimization of Hydroamination Reaction for Other O-benzoylhydroxylamines

Unfortunately, with a variety of other electrophiles, such as 4-benzoyloxymorpholine **2.16**, we observed an alternative decomposition pathway under these reaction conditions. For example, the reaction with **2.6** provided no hydroamination product and instead resulted in almost quantitative formation of *tert*-butyl benzoate (Table 2.3, entry 1). To prevent the decomposition of **3** during the course of the reaction, we added the electrophile over a 6 h period and observed the formation of the hydroamination product in 52% yield (Table 1, entry 2). After further experimentation, it was determined that a co-solvent was unnecessary to the reaction efficiency (compare entries 2—5). A good yield of the product was achieved through use of toluene as solvent at 0.35 *M* (Table 2.3, entry 4). However, the formation of a small amount of toluene amination product[41] complicated the purification of the desired amine when the reaction was conducted at this concentration. After further dilution of the reaction mixture and adjustment of addition time, a 99% yield of the hydroamination product was obtained when 1.1 equiv of electrophile was added to a relatively dilute reaction mixture (0.05 M in alkyl borane) over 3 h at 60 °C (entry 8). In view of the difficulties often encountered in the purification of tertiary alkyl amines, it is important to note that these reaction conditions allowed pure hydroamination products to be isolated by an acid−base extraction.

Table 2.3



Entry[a]	Reaction Concentration (M)	2.16 Add'n Time (h)	Co-solvent	Yield[b]
1.[c,d]	0.20	N/A[d]	pentane	< 5%
2.[c,e]	0.20	6	pentane	52%
3.[c]	0.20	6	1,4-dioxane	78%
4.	0.35	6	toluene	74%
5.	0.20	6	toluene	85%
6.	0.10	6	toluene	86%
7.[f]	0.10	6	toluene	90%
8.[f]	0.05	3	toluene	99%

[a] Unless otherwise specified, all reactions conducted with 1.3 equiv each 2.16 and LiO*t*Bu. [b] Yield determined by GC analysis of crude reaction mixture obtained after initial workup described in the Experimental Text. [c] 1,4-Dioxane substituted for toluene as hydroboration solvent. [d] Reaction was conducted according to procedure outlined in Experimental Text. [e] Reaction temperature = 45 °C. [f] 1.1 equiv each 2.16 and LiO*t*Bu were used.

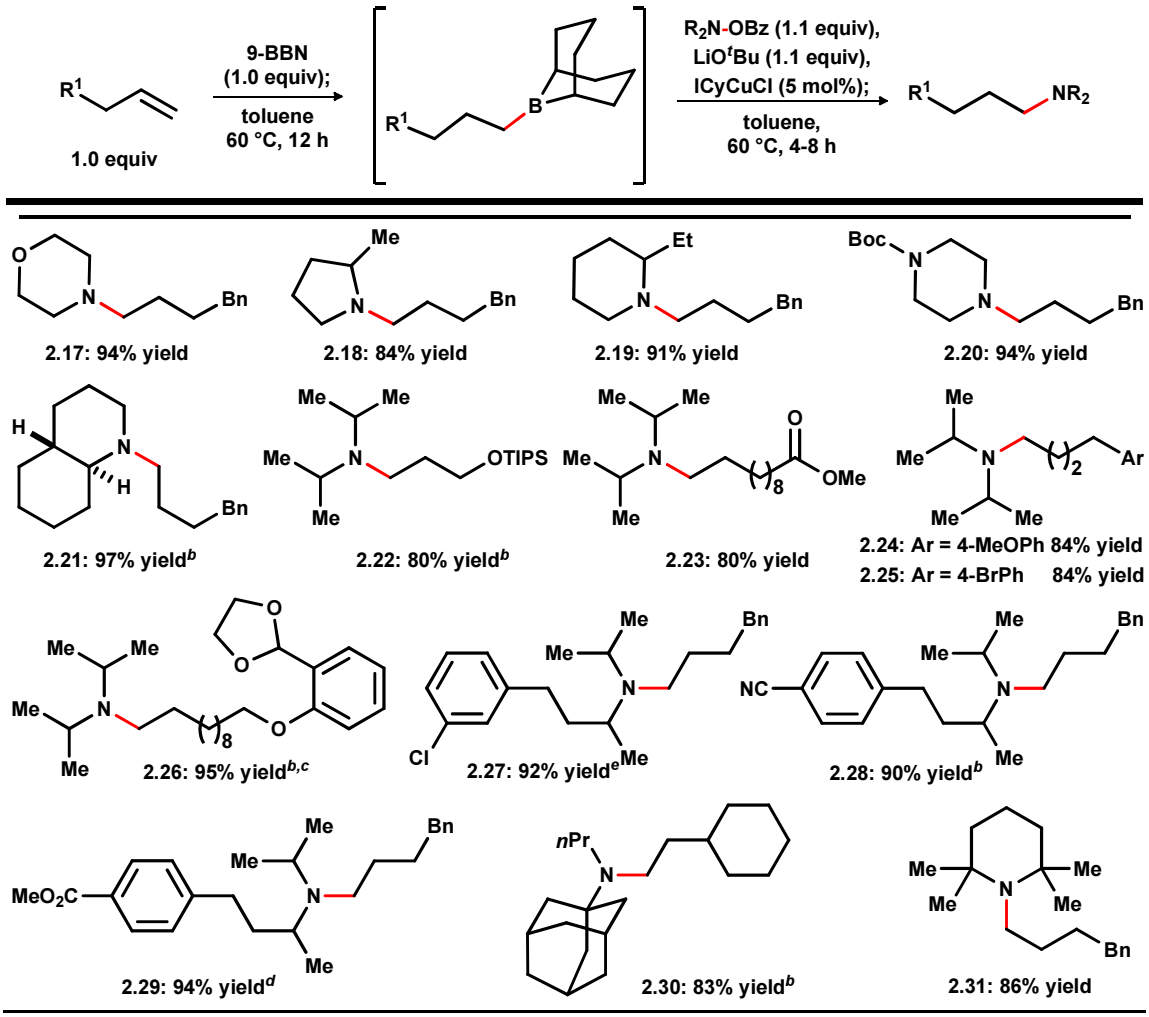
Section 3. Reaction scope.

The optimized reaction conditions and purification procedure proved to be quite general (Table 2.4). The highly selective anti-Markovnikov hydroamination of alkenes could be accomplished in the presence of esters, acetals, nitriles, aryl bromides, aryl chlorides, Boc-protected amines, and silyl and alkyl ethers.

The procedure could be used to prepare morpholine, piperidine, pyrrolidine, piperazine, and decahydroquinoline derivatives (compounds **2.17**−**2.21**). Equally good results were obtained in the preparation of acyclic amines, including sterically hindered *N*,*N*-diisopropyl-*N*-alkyl amines (**2.22**—**2.29**) and the adamantyl-substituted amine **2.30**. Even the highly hindered *N*-alkyl-2,2,6,6-tetramethylpiperidine **2.31** could be formed in

86% yield. The synthesis of such hindered trialkyl amines is not only impossible to achieve using the existing hydroamination methods but is also quite difficult to accomplish using standard reductive amination or alkylation techniques.[42] Finally, GC/MS analysis of the crude reaction mixture indicated that, for all of these examples, only the product of anti-Markovnikov hydroamination was formed.

Table 2.4

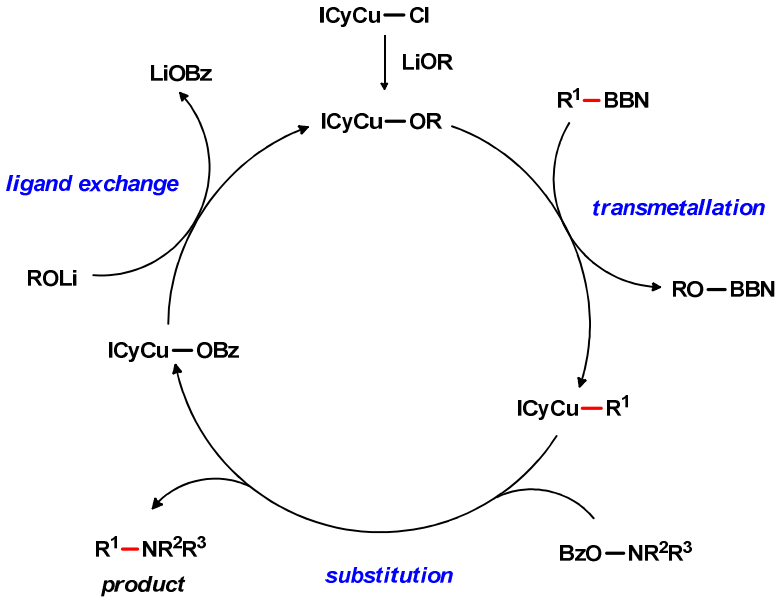


[a]Alkene (0.50 mmol), 9-BBN (0.5 mmol), R2N-OBz (0.55 mmol), and t-BuOLi (0.55 mmol) in 10 mL of toluene. R_2N–OBz was added over 4 h. Yields of isolated products are shown, unless otherwise noted. [b]Benzene was used as the solvent. [c]GC yield. After purification, the corresponding aldehyde was isolated in 92% yield. [d]2.5 mol % catalyst was used. [e]GC yield. The isolated yield was 72%.

Section 4. Mechanism

We propose that the amination of alkyl boron compounds proceeds according to the mechanism shown in Scheme 2.8. The reaction involves transmetallation from boron to copper[32,33h] followed by electrophilic amination of the alkylcopper intermediate.[35d] Finally, copper *tert*-butoxide is regenerated in a reaction with lithium *tert*-butoxide.[43] The most intriguing aspect of the proposed mechanism is the presence of a neutral alkyl copper(I) intermediate in a reaction performed at a relatively high temperature. Such complexes are known to decompose quickly above −35°C,[44] and to the best of our knowledge, there are no examples of fully characterized neutral alkyl copper(I) complexes containing β-hydrogen substituents. While similar intermediates have also previously been proposed in copper-catalyzed reactions of alkyl boranes,[33e,33h] there is little experimental evidence for their involvement.

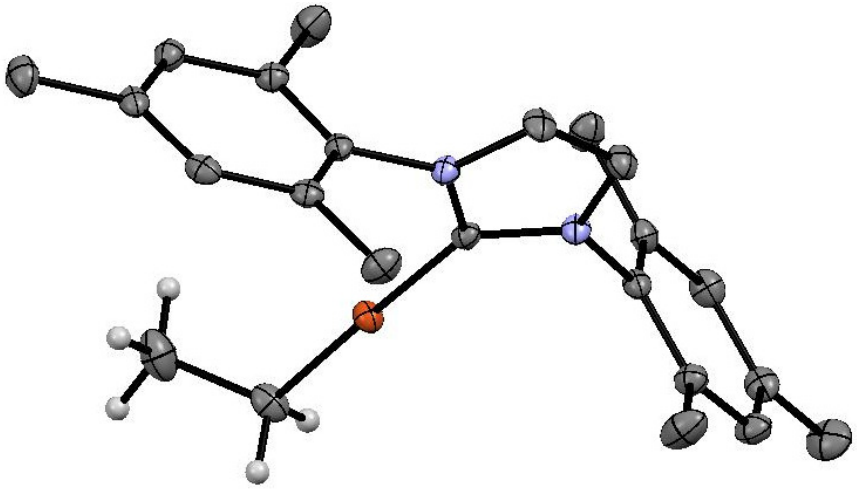
Scheme 2.8



In an effort to explore the role of alkyl copper(I) complexes in the amination reaction, we prepared IMesCuEt (**2.32**) by addition of ethyllithium to IMesCuCl at low

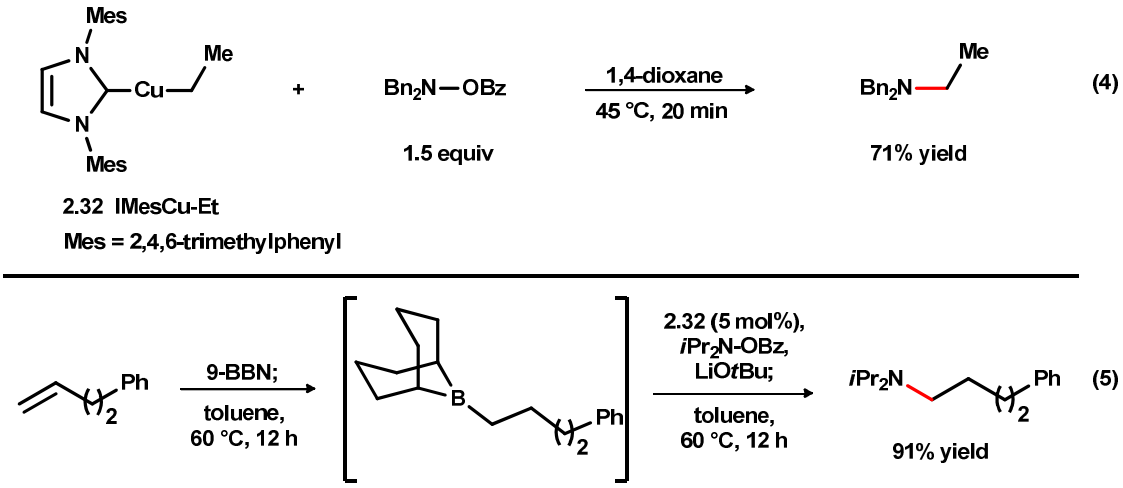
temperature. We were able not only to isolate the IMesCuEt complex, albeit in low yield (37%), but also to characterize it by X-ray diffraction (Figure 2.1). We discovered that the complex is stable in benzene for at least 4 h at 60°C if kept in the dark. However, it decomposes quite readily at room temperature upon exposure to light (~50% conversion after 4 h).

Figure 2.1. ORTEP of IMesCu(Et) (selected hydrogen atoms omitted for clarity) with thermal ellipsoids drawn at 50% probability level.



We also showed that IMesCuEt reacts at 45°C with electrophile **2.4** to produce the expected amination product in 71% yield (eq 4 in Scheme 2.9). Furthermore, when **2.32** was used as the catalyst in the hydroamination of **2.5**, the desired product was obtained in 91% yield (eq 5 in Scheme 2.9). The results of these experiments provide support for the proposed participation of neutral alkyl copper(I) complexes in the catalytic amination of alkyl boron compounds.

Scheme 2.9



Section 5. Conclusion

In conclusion, we have developed a one-pot hydroamination procedure that allows the direct formation of tertiary alkyl amines from terminal alkenes as a single regioisomer. The method is compatible with a wide variety of functional groups and can be used to prepare a range of both cyclic and acyclic amines. Furthermore, the procedure can be used to prepare highly sterically hindered amines that can be challenging to prepare even by well-established methods such as reductive amination and alkylation. The products of these reactions are isolated in analytical purity by use of a simple acid/base extraction. Finally, we have prepared and characterized a stable alkyl copper(I) complex capable of β-hydride elimination and also provided experimental evidence that supports their proposed role as intermediates in the formal anti-Markovnikov hydroamination reaction.

Section 6: Experimental

General

All reactions were performed under a nitrogen atmosphere with flame-dried glassware, using standard Schlenk techniques, or in a glove box (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 μm, 230-400 mesh). Ion Exchange Chromatography was performed using analytical grade cation exchange resin from sulfonic acid functionalized styrene (Bio-Rad Laboratories, 200-400 mesh, 5.2 meq/g). Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum RX I spectrometer. IR peak absorbencies are represented as follows: s = strong, m = medium, w = weak, br = broad. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AV-300 or AV-500 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual proteated solvent peak ($CDCl_3$ (7.26 ppm), C_6D_6 (7.16 ppm), or CD_2Cl_2 (5.32 ppm)). ^{13}C chemical shifts are reported in parts per million downfield of TMS and are referenced to the carbon resonance of the solvent ($CDCl_3$: δ 77.2 ppm, C_6D_6: δ 128.1 ppm, CD_2Cl_2: δ 54.0 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constants in Hertz (Hz). Mass spectra were collected on a JEOL HX-110 mass spectrometer. GC analysis was performed on a Shimadzu GC-2010 instrument with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 μm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5 min @ 250 °C.

Materials

Toluene and benzene were degassed and dried by passing through columns of neutral alumina. 1,4-dioxane was distilled from purple Na/benzophenone ketyl and stored over 4Å molecular sieves. All other solvents were used as received. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. Deuterated solvents were degassed and dried over 4Å molecular sieves before use. Commercial reagents were purchased from Sigma-Aldrich Co., VWR International, LLC., TCI Chemicals USA, or STREM Chemicals, Inc., and were used as received, except for 9-BBN (9-borabicyclo[3.3.1]nonane) dimer, which was recrystallized from dimethoxyethane (glyme).

O-benzoyl-*N*,*N*-dialkyl hydroxylamines were synthesized according to a literature procedure.[45] Terminal alkenes were all commercially available with the exception of triisopropyl(pent-4-en-1-yloxyl)silane,[46] 1-(but-3-en-1-yl)-4-methoxybenzene,[47] 1-bromo-4-(but-3-en-1-yl)benzene,[47a] and 2-(2-(pent-4-en-1-yloxy)phenyl)-1,3-dioxolane,[48] which were prepared according to literature procedures.

2.6.b. Reaction Optimization

Hydroboration of Terminal Alkenes

In a glove box, a 1 dram vial was charged with a stir bar. To the vial was added 9-BBN dimer (0.50 equiv), alkene (1.00 equiv), and solvent. The vial was capped and heated at 60℃ with stirring for 12 h.

Using *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine

In a glove box, 4-phenylbut-1-ene (1.00 equiv, 0.017 mL, 0.110 mmol) was subjected to the standard hydroboration conditions described above using 9-BBN dimer (0.50 equiv,

13.4 mg, 0.055 mmol), *n*-dodecane as internal standard, and 1,4-dioxane (0.20 mL, [alkene] = 0.55 M). After 12 h at 60℃, the reaction vial was allowed to reach room temperature, and MO*t*Bu (M = Na, K, Li; 1.00 equiv, 0.110 mmol), copper catalyst (0.05 equiv, 0.006 mmol), *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine (1.00 equiv, 36.2 mg, 0.110 mmol), 1,4-dioxane (0.075 ml) and the reaction co-solvent (0.275 ml) were added as indicated in **Table 2.1**. The vial was capped and stirred at 45 °C for 6 h. Yield of the desired product was determined by gas chromatography using *n*-dodecane as an internal standard.

Using 4-benzoyloxymorpholine

For all optimization reactions, 4-phenylbut-1-ene (1.00 equiv, 0.060 mL, 0.400 mmol) was subjected to the standard hydroboration conditions described above using 9-BBN dimer (0.50 equiv, 48.8 mg, 0.400 mmol) and solvent (1.00 mL, 0.40 M). After 12 h at 60℃, the dram vial was allowed to reach room temperature, and the contents were transferred to a 15 mL Schlenk tube. To the resulting solution was added lithium *tert*-butoxide (1.3 equiv, 41.6 mg, 0.520 mmol), ICyCuCl (0.05 equiv, 6.6 mg, 0.020 mmol), and solvent. Separately, a stock solution of the electrophile was prepared (0.400 mL of reaction co-solvent) and taken up in a gas-tight syringe (500 µL size). The Schenk tube assembly was put on the manifold using standard air-free techniques. The electrophile was added over the period indicated in **Table 2.3** to the stirred reaction mixture at 60 °C. After addition of the electrophile, the reaction was stopped and allowed to cool to room temperature. The crude product was isolated by diluting the reaction mixture with ether (5 mL) and then washing with aqueous saturated $NaHCO_3$ solution. The aqueous layer was then extracted with diethyl ether (2 x 10 mL), and the combined organic fractions

were dried over sodium sulfate. After filtering, 1,3-dinitrobenzene was added as an internal standard to the ether solution, and the yield of the product was determined by GC analysis of an aliquot of this solution.

2.6.c. Reactions of O-benzoyl-N,N-dibenzyl hydroxylamine with sodium tert-pentoxide and lithium tert-butoxide.

For the following reactions, conversion of *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine was determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as an internal standard. To obtain data for each time point in **Table 2.5**, aliquots (0.05 mL) were withdrawn from the reaction mixture and were diluted to 0.50 mL with benzene-d^6.

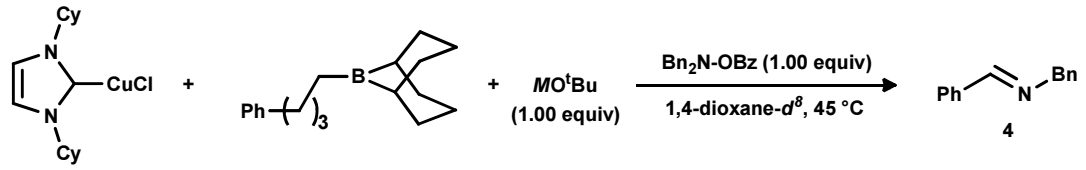
Entries 1, *4*, and *6*: In a glove box, a 1 dram vial was charged with a stir bar. To the vial was added either LiO^tBu or NaO^tBu (1.00 equiv, 0.110 mmol), 1,3,5-trimethoxybenzene as an internal standard, and 1,4-dioxane-d^8 (0.35 mL). To the resulting mixture was added *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine (1.00 equiv, 0.110 mmol) and 1,4-dioxane-d^8 (0.15 mL). The resulting mixture was capped and heated to 45℃ under stirring.

Entries 2 and *7*: The reactions were set up exactly as described for *Entries 1* and *4* except that ICyCuCl catalyst (0.05 equiv, 0.006 mmol) was added before addition of *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine.

Entries 3, *5*, and *8*: In a glove box, a 1 dram vial was charged with a stir bar. To the vial was added 9-BBN dimer (0.50 equiv, 13.4 mg, 0.055 mmol) , 4-phenyl-but-1-ene (1.00

equiv, 1.65×10^{-2} mL, 0.110 mmol), and 1,4-dioxane-d^8 (0.20 mL, 0.5 M). The vial was heated at 60 ℃ for 12 h and then cooled to room temperature. To the resulting solution was added either LiO^{t}Bu or NaO^{t}Bu (1.00 equiv, 0.110 mmol), 1,3,5-trimethoxybenzene, *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine (1.00 equiv, 0.110 mmol) and 1,4-dioxane-d^8 (0.30 mL). The resulting mixture was capped and heated to 45 ℃ with stirring

Table 2.5



Entry[a]	ICyCuCl (mol%)	9-(4-phenylbutyl)-9-borabicyclo[3.3.1]nonane (equiv)	*M*	% conversion of Bn$_2$N-OBz (min) 10	30	60	120	1020
1	0	0	Li	7	14	37	53	100
2	5	0	Li	35	50	61	71	100
3	0	1.00	Li	2	17	32	49	100
4[b]	0	0	Li	0	NA	NA	5	NA
5[b]	0	1.00	Li	0	NA	NA	2	NA
6	0	0	Na	93	100	100	100	100
7	5	0	Na	100	100	100	100	100
8	0	1.00	Na	50	67	74	81	100

[a] All reaction concentrations are 0.2 M. [b] Benzene-d^6 was used as reaction solvent.

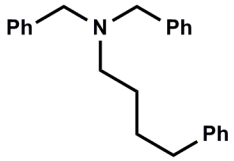
2.6.d. Hydroamination of Terminal Alkenes

Using *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine:

General procedure:

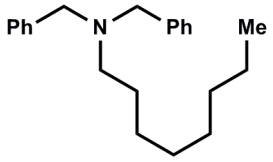
In a glove box, a scintillation vial was charged with a stir bar. To the vial was added 9-BBN dimer (0.50 equiv, 61.0 mg 0.250 mmol), 1,4-dioxane (1.00 mL), and the alkene (1.00 equiv, 0.500 mmol). After 12 h at 60 °C, the reaction mixture was cooled to room

temperature, and LiO^{t}Bu (1.00 equiv, 40.0 mg, 0.500 mmol), ICyCuCl (0.05 equiv, 8.3 mg, 0.003 mmol) and pentane (1.25 mL) were added with stirring. After 10 min, the *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine (1.05 equiv, 0.530 mmol) was added to the vial together with 1,4-dioxane (0.25 mL). The reaction mixture was stirred at 45 °C for 3 h, at which time another portion of LiO^{t}Bu (0.30 equiv, 12.0 mg, 0.150 mmol) and *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine (0.25 equiv, 0.130 mmol) were added. The reaction mixture were stirred for an additional 3 h at 45 °C, then diluted in diethyl ether, and filtered through a plug of silica using diethyl ether as the eluent. The solvent was removed under reduced pressure, and the crude product was purified by silica gel chromatography.



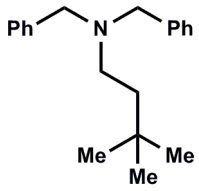
***N*,*N*-dibenzyl-4-phenylbutan-1-amine**

Compound was isolated as a colorless oil (147.5 mg, 90% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 15% Et_2O/hexanes over 7 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.37 (d, J = 7.4 Hz, 4H), 7.28 – 6.90 (m, 11H), 3.41 (s, 4H), 2.52 – 2.27 (m, 4H), 1.60 – 1.26 (m, 4H). ^{13}C NMR (125 MHz, C_6D_6) δ 142.8, 140.4, 129.1, 128.8, 128.6, 128.5, 127.2, 126.0, 58.8, 53.3, 35.9, 29.2, 26.9. HRMS calculated for $[M]^+$ 330.2212, found 330.2217. FTIR (neat, cm^{-1}): 3084(w), 2933(m), 1494(m), 1452(m), 1028(w).



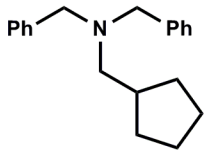
***N*,*N*-dibenzyloctan-1-amine (2.7)**

Compound was isolated as a colorless oil (147.8 mg, 96% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 10% Et_2O/hexanes over 6 CV). ^1H NMR (300 MHz, C_6D_6) δ 7.41 (d, J = 7.0 Hz, 4H), 7.31 – 7.04 (m, 6H), 3.48 (s, 4H), 2.40 (t, J = 7.1 Hz, 2H), 1.45 (m, 2H), 1.35 – 1.09 (m, 10H), 0.90 (t, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 128.9, 128.3, 126.8, 58.4, 53.6, 32.0, 29.6, 29.5, 27.4, 27.1, 22.8, 14.3. ESI-MS calculated for $[M+H]^+$ 310.2, found 310.3. FTIR (neat, cm^{-1}): 3062(w), 3026(w), 2926(s), 1494(w), 1452(m), 1367(w).



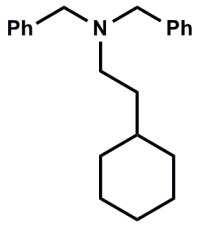
***N*,*N*-dibenzyl-3,3-dimethylbutan-1-amine (2.8)**

Compound was isolated as a colorless oil (121.7 mg, 86% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 15% Et_2O/hexanes over 6 CV). ^1H NMR (300 MHz, C_6D_6) δ 7.41 (d, J = 7.1 Hz, 4H), 7.28 – 7.04 (m, 6H), 3.49 (s, 4H), 2.49 – 2.41 (m, 2H), 1.48 – 1.41 (m, 2H), 0.77 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 128.9, 128.3, 126.9, 58.3, 49.4, 40.4, 30.0, 29.6. ESI-MS calculated for $[M+H]^+$ 282.2, found 282.3. FTIR (neat, cm^{-1}): 3062(w), 3027(w), 2954(s), 1493(w), 1452(m), 1364(m).



***N*,*N*-dibenzyl-1-cyclopentylmethanamine (2.14)**

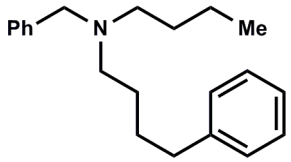
Compound was isolated as a colorless oil (118.9 mg, 85% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 10% Et_2O/hexanes over 6 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.40 (d, J = 7.3 Hz, 4H), 7.25 – 7.09 (m, 6H), 3.45 (s, 4H), 2.26 (d, J = 7.6 Hz, 2H), 2.09 – 1.94 (m, 1H), 1.74 – 1.61 (m, 2H), 1.46 – 1.37 (m, 4H), 1.22 – 1.02 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 128.9, 128.2, 126.8, 59.5, 58.7, 38.0, 31.1, 25.1. ESI-MS calculated for $[M+H]^+$ 268.2, found 268.2. FTIR (neat, cm^{-1}): 3061(w), 3026(m), 2948(s), 1494(m), 1451(m), 1369(w).



***N*,*N*-dibenzyl-2-cyclohexylethanamine (2.11)**

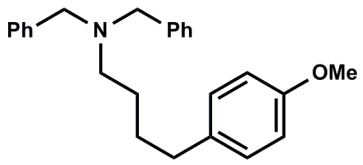
Compound was isolated as a colorless oil (124.8 mg, 81% yield) after purification by silica gel column chromatography (0 → 5% Et_2O/hexanes over 6 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.41 (d, J = 7.4 Hz, 4H), 7.26 – 7.07 (m, 6H), 3.48 (s, 4H), 2.42 (t, J = 7.4 Hz, 2H), 1.46 – 1.66 (m, 5H), 1.42 – 1.30 (m, 2H), 1.26 – 1.04 (m, 4H), 0.90 – 0.61 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 128.9, 128.2, 126.8, 58.4, 51.1, 35.8, 34.7,

33.6, 26.8, 26.5. ESI-MS calculated for $[M+H]^+$ 308.2, found 308.4. FTIR (neat, cm^{-1}): 3061(w), 3026(m), 2920(s), 2849(s), 1494(m), 1450(m), 1366(w).



***N*-benzyl-*N*-butyl-4-phenylbutan-1-amine (2.15)**

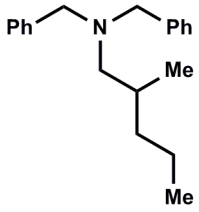
Compound was isolated as a colorless oil (111.9 mg, 76% yield) after purification by silica gel column chromatography (0 → 5% Et_2O/hexanes over 6 CV). ^1H NMR (300 MHz, C_6D_6) δ 7.38 (d, J = 7.3 Hz, 2H), 7.25 – 7.06 (m, 8H), 3.42 (s, 2H), 2.46 (t, J = 7.5 Hz, 2H), 2.40 – 2.26 (m, 4H), 1.65 – 1.49 (m, 2H), 1.49 – 1.32 (m, 4H), 1.34 – 1.18 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 140.4, 129.0, 128.6, 128.4, 128.2, 126.7, 125.7, 58.8, 53.7, 53.6, 35.9, 29.4, 29.3, 26.8, 20.7, 14.2. ESI-MS calculated for $[M+H]^+$ 296.2, found 296.2. FTIR (neat, cm^{-1}): 3025(w), 2930(s), 2795(w), 1494(m), 1453(m).



***N*,*N*-dibenzyl -4-(4-methoxyphenyl)butan-1-amine (2.10)**

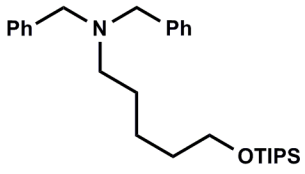
Compound was isolated as a colorless oil (168.8 mg, 94% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 5% Et_2O/hexanes over 6 CV). ^1H NMR (300 MHz, C_6D_6) δ 7.39 (d, J = 7.4 Hz, 4H), 7.28 – 7.05 (m, 6H), 6.96 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 3.43 (s, 4H), 3.34 (s,

3H), 2.43 – 2.29 (m, 4H), 1.58 – 1.39 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 140.2, 134.9, 129.4, 128.9, 128.3, 126.9, 113.8, 58.5, 55.4, 53.2, 34.8, 29.2, 26.6. ESI-MS calculated for $[M+H]^+$ 360.5, found 360.4. FTIR (neat, cm^{-1}): 3026(w), 2934(m), 2795(w), 1511(s), 1494(m), 1256(s), 1038(m).



***N*,*N*-dibenzyl -2-methylpentan-1-amine (2.13)**

Compound was isolated as a colorless oil (136.5 mg, 97% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 5% Et_2O/hexanes over 6 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.39 (d, J = 7.2 Hz, 4H), 7.21 (t, J = 7.4 Hz, 4H), 7.10 (t, J = 7.3 Hz, 2H), 3.52 (d, J = 13.6 Hz, 2H), 3.35 (d, J = 13.6 Hz, 2H), 2.17 (ddd, J = 20.3, 12.3, 7.3 Hz, 2H), 1.75 – 1.55 (m, 1H), 1.37 – 1.13 (m, 3H), 0.99 – 0.81 (m, 7H). ^{13}C NMR (125 MHz, CD_2Cl_2) δ 140.6, 129.3, 128.4, 127.0, 61.3, 59.2, 37.6, 31.1, 20.3, 18.4, 14.6. ESI-MS calculated for $[M+H]^+$ 282.2, found 282.3. FTIR (neat, cm^{-1}): 3062(w), 3027(w), 2955(s), 1494(m), 1452(m), 1372(m).



***N*,*N*-dibenzyl-5-((triisopropylsilyl)oxy)pentan-1-amine (2.9)**

Compound was isolated as a colorless oil (189.1 mg, 86% yield) after purification by silica gel column chromatography (0 → 30% benzene/hexanes over 3 CV, then 0 → 5% Et_2O/hexanes over 6 CV). ^1H NMR (300 MHz, C_6D_6) δ 7.40 (d, *J* = 7.3 Hz, 4H), 7.21 (t, *J* = 7.4 Hz, 4H), 7.10 (t, *J* = 7.3 Hz, 2H), 3.57 (t, *J* = 6.1 Hz, 2H), 3.44 (s, 4H), 2.37 (t, *J* = 6.9 Hz, 2H), 1.50 – 1.29 (m, 6H), 1.20 – 1.05 (m, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 128.9, 128.3, 126.8, 63.5, 58.4, 53.6, 33.1, 27.1, 23.8, 18.2, 12.2. ESI-MS calculated for $[M+H]^+$ 440.3, found 440.6. FTIR (neat, cm^{-1}): 3027(w), 2941(s), 2864(s), 1494(m), 1426(m), 1106(s), 909(m).

Using cyclic and acyclic *O*-benzoyl-*N*,*N*-dialkylhydroxylamines:

General procedure:

In a glove box, a one-dram vial was charged with a stir bar. To the vial was added 9-BBN dimer (0.50 equiv, 48.8 mg 0.200 mmol), toluene (1.00 mL, 0.40 M), and the alkene (1.00 equiv, 0.400 mmol). After 12 h at 60 °C, the reaction mixture was cooled to room temperature and transferred to a 15 mL Schlenk tube. To the resulting solution was added lithium *tert*-butoxide (1.10 equiv, 35.2 mg, 0.440 mmol), ICyCuCl (0.05 equiv, 6.6 mg, 0.020 mmol), and toluene (6.60 mL, 7.60 mL total volume, 0.05 M). Separately, a stock solution of the electrophile was prepared (0.400 mL of reaction co-solvent) and taken up in a gas-tight syringe (500 μL size). The Schenk tube assembly was put on the manifold using standard air-free techniques. The electrophile was added over 4 h to the stirred reaction mixture at 60 °C. After addition of the electrophile, the reaction was allowed to stir at 60 °C and the consumption of electrophile was monitored by tlc. Upon complete consumption of the electrophile, the reaction was cooled to room

temperature. The crude product was isolated by diluting the reaction mixture with ether (5 mL) and then washing with aqueous saturated $NaHCO_3$ solution. The aqueous layer was then extracted with diethyl ether (2 x 10 mL), and the combined organic fractions were dried over sodium sulfate. After filtration and removal of the solvent under reduced pressure, the crude product was obtained as an oil, which was further purified according to one of the following three procedures:

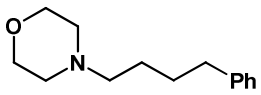
Purification Procedure **A**: Acid/Base Extraction

The crude product was transferred to a 60 mL separatory funnel using 2.5 mL portions of diethyl ether and hexane (5 mL total volume). The organic layer was extracted three times with 5 mL of a 3 M aqueous HCl solution. The organic layer was discarded. The *p*H of the aqueous layer was adjusted by dropwise addition of an aqueous 3 M NaOH solution until *p*H 10 was achieved. The resulting solution was then extracted three times with 10 mL portions of dichloromethane. The organic extracts were washed with 5 mL of saturated brine and then dried over sodium sulfate. Upon filtration and removal of solvent, the purified tertiary amine product was obtained as an oil.

Purification Procedure **B**: Acid-sensitive functional groups, such as the *tert*-butyl carbamate (BOC)-protected amine used in product **8**, and the tris(isopropyl)siloxy (TIPS)-protected alcohol used in product **9**, require the substitution of a weaker acid in place of aqueous HCl. This is readily accomplished by use of an aqueous 3 M sodium acetate and acetic acid solution buffered at *p*H 4. The purification procedure is identical to A except for this substitution.

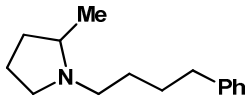
Purification Procedure **C**: Ion-Exchange Chromatography

The crude product was loaded on the cation exchange resin (200 mg resin/mmol product) using MeOH. The resin was subsequently washed with 4 CV of 2% dichloromethane in MeOH, then with 4 CV of 20% Et_3N in MeOH to elute the product.



4-(4-phenylbutyl)morpholine (2.17)

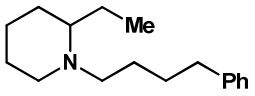
Compounds was isolated as a colorless oil (82.8 mg, 94% yield) after purification by ion exchange chromatography. Reaction time was 4 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.30 (m, 2H), 7.30 – 7.10 (m, 3H), 3.88 – 3.65 (m, 4H), 2.70 (t, J = 7.5 Hz, 2H), 2.59 – 2.32 (m, 6H), 1.84 – 1.45 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 128.5, 128.4, 125.8, 67.1, 59.1, 53.9, 35.9, 29.4, 26.3. HR-MS calculated for $[M+H]^+$ 220.1701, found 220.1693. FTIR (neat, cm^{-1}): 3083(w), 3024(w), 2935(s), 1603(w), 1453(s), 1118(s).



2-methyl-1-(4-phenylbutyl)pyrrolidine (2.18)

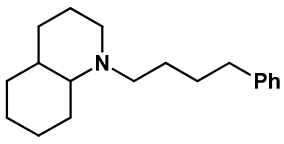
Compound was isolated as a colorless oil (73.1 mg, 84% yield) after purification by ion exchange chromatography. Reaction time was 3 h. ^{1}H NMR (300 MHz, MeOD) δ 7.39

– 7.05 (m, 5H), 3.24 – 3.00 (m, 1H), 2.94 – 2.73 (m, 1H), 2.64 (t, J = 6.8 Hz, 2H), 2.49 – 2.25 (m, 1H), 2.25 – 1.85 (m, 3H), 1.87 –3 1.34 (m, 7H), 1.11 (d, J = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 128.6, 128.4, 125.8, 60.5, 54.2, 54.1, 36.0, 32.8, 29.8, 28.5, 21.7, 19.0. HRMS calculated for $[M+H]^+$ 218.1908, found 218.1915. FTIR (neat, cm^{-1}): 3062(w), 3025(w), 2936(s), 1603(w), 1453(s), 1374(m), 746(s).



2-ethyl-1-(4-phenylbutyl)piperidine (2.19)

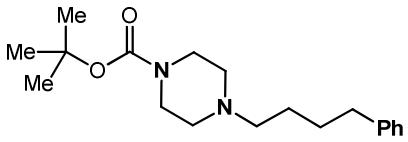
Compound was isolated as a colorless oil (89.6 mg, 91% yield) after acid base extraction **A**. Reaction time was 3 h. ^{1}H NMR (300 MHz, MeOD) δ 7.43 – 7.00 (m, 5H), 2.96 – 2.80 (m, 1H), 2.79 – 2.57 (m, 3H), 2.57 – 2.42 (m, 1H), 2.42 – 2.15 (m, 2H), 1.82 – 1.44 (m, 9H), 1.44 – 1.21 (m, 3H), 0.87 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, MeOD) δ 142.1, 128.1, 128.0, 125.4, 61.7, 52.8, 51.7, 35.3, 29.2, 28.7, 24.5, 23.8, 23.2, 23.0, 9.2. HRMS calculated for $[M+H]^+$ 246.2221, found 246.2215. FTIR (neat, cm^{-1}): 3054(w), 2933(s), 1734(m), 1437(s), 1265(s), 738(s).



1-(4-phenylbutyl)decahydroquinoline (2.21)

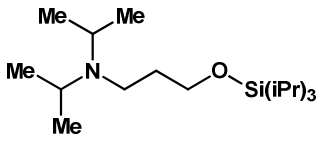
Compound was isolated as a colorless oil (105.8 mg, 97% yield) after purification by acid/base extraction **A**. Reaction time was 4 h. ^{1}H NMR (300 MHz, C_6D_6) δ 7.33 – 7.18 (m, 2H), 7.15 – 7.05 (m, 3H), 2.93 – 2.82 (m, 1H), 2.78 – 2.60 (m, 1H), 2.52 (t, J = 7.5

Hz, 2H), 2.35 – 2.12 (m, 1H), 2.12 – 1.94 (m, 2H), 1.83 – 1.31 (m, 11H), 1.30 – 1.05 (m, 4H), 1.06 – 0.76 (m, 2H). ^{13}C NMR (125 MHz, C_6D_6) δ 143.0, 128.8, 128.6, 126.0, 66.8, 54.2, 52.9, 42.6, 36.3, 33.6, 33.3, 30.9, 29.9, 26.6, 26.5, 26.2, 26.0. HR-MS calculated for $[M+H]^+$ 272.2378, found 272.2378. FTIR (neat, cm^{-1}): 3062(w), 3026(m), 2921(s), 1603(w), 1447(m), 1239(m), 698(s).



***tert*-butyl 4-(4-phenylbutyl)piperazine-1-carboxylate (2.20)**

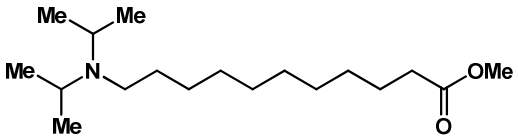
Compound was isolated as a pale yellow oil (119.7 mg, 94% yield) after purification by acid/base extraction **B**. Reaction time was 4 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.13 (m, 2H), 7.07 (t, J = 7.1 Hz, 3H), 3.38 – 3.25 (m, 4H), 2.52 (t, J = 7.6 Hz, 2H), 2.36 – 2.13 (m, 6H), 1.60 – 1.39 (m, 4H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, C_6D_6) δ 154.7, 142.8, 128.7, 128.7, 126.1, 79.0, 58.5, 53.3, 46.2, 44.6, 43.7, 36.1, 29.4, 28.5, 26.7. HR-MS calculated for $[M+H]^+$ 319.2385, found 319.2392. FTIR (neat, cm^{-1}): 3062(w), 3026(m), 2933(s), 1688(s), 1442(m), 1247(m), 1171(m), 1123(m), 1006(m).



***N*,*N*-diisopropyl-3-((triisopropylsilyl)oxy)propan-1-amine (2.22)**

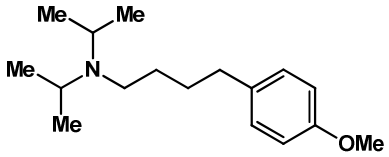
Compound was isolated as a pale yellow oil (101.0 mg, 80% yield) after purification by acid/base extraction **B**. Reaction time was 6 h. ^{1}H NMR (300 MHz, C_6D_6) δ 3.74 (t, J =

6.2 Hz, 2H), 3.07 – 2.85 (m, 2H), 2.68 – 2.47 (m, 2H), 1.80 – 1.65 (m, 2H), 1.21 – 1.10 (m, 21H), 1.00 (d, J = 6.6 Hz, 12H). ^{13}C NMR (125 MHz, C_6D_6) δ 70.7, 62.0, 48.5, 41.6, 34.8, 32.4, 26.7, 22.5, 21.0, 18.4, 12.4. HR-MS calculated for $[M+H]^+$ 316.3035, found 316.3045. FTIR (neat, cm^{-1}): 2962(s), 2865(s), 1464(m), 1106(s).



methyl 11-(diisopropylamino)undecanoate (2.23)

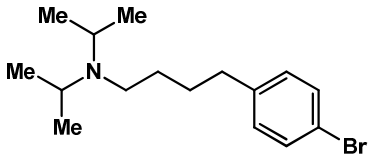
Compound was isolated as a colorless oil (96.8 mg, 81% yield) after purification by acid/base extraction **A**. Reaction time was 6 h. ^{1}H NMR (300 MHz, C_6D_6) δ 3.46 (s, 3H), 3.15 – 2.97 (m, 2H), 2.60 – 2.41 (m, 2H), 2.30 – 2.15 (m, 2H), 1.79 – 1.54 (m, 4H), 1.47 – 1.18 (m, 12H), 1.10 (d, J = 6.6 Hz, 12H). ^{13}C NMR (125 MHz, C_6D_6) δ 173.3, 50.9, 48.3, 45.1, 34.2, 31.7, 30.2, 30.1, 29.9, 29.7, 29.5, 28.2, 27.8, 25.3, 21.1. HR-MS calculated for $[M+H]^+$ 300.2902, found 300.2913. FTIR (neat, cm^{-1}): 2928(s), 2855(m), 1743(s), 1465(m), 1204(m), 1172(m).



***N*,*N*-diisopropyl-4-(4-methoxylphenyl)butan-1-amine (2.24)**

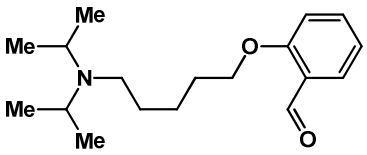
Compound was isolated as a pale yellow oil (88.7 mg, 84% yield) after purification by acid/base extraction **A**. Reaction time was 4 h. ^{1}H NMR (300 MHz, C_6D_6) δ 7.06 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.34 (s, 3H), 2.92 (hept, J = 6.6 Hz, 2H), 2.55 (t, J

= 7.6 Hz, 2H), 2.38 (t, *J* = 7.1 Hz, 2H), 1.73 – 1.55 (m, 2H), 1.54 – 1.35 (m, 2H), 0.97 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (125 MHz, C_6D_6) δ 158.5, 135.1, 129.6, 114.2, 54.8, 48.1, 44.7, 35.5, 30.9, 29.8, 21.0. HR-MS calculated for $[M+H]^+$ 264.2327, found 264.2339. FTIR (neat, cm^{-1}): 3033(w), 2962(s), 1751(w), 1465(m), 1245(s), 1039(m).



4-(4-bromophenyl)-*N*,*N*-diisopropylbutan-1-amine (2.25)

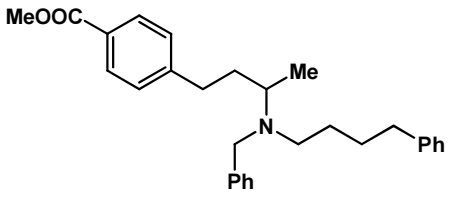
Compound was isolated as a pale yellow oil (104.7 mg, 84% yield) after purification by acid/base extraction **A**. Reaction time was 4 h. ^{1}H NMR (300 MHz, C_6D_6) δ 7.27 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 2H), 2.99 – 2.76 (m, 2H), 2.39 – 2.21 (m, 4H), 1.53 – 1.26 (m, 4H), 0.95 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (125 MHz, C_6D_6) δ 142.0, 131.6, 130.5, 119.8, 48.1, 44.6, 35.6, 30.7, 29.2, 21.0. HR-MS calculated for $[M+H]^+$ 312.1326, found 312.1320. FTIR (neat, cm^{-1}): 3035(w), 2963(s), 1892(w), 1751(w), 1488(m), 1072(m), 1011(m), 829(m), 677(m).



2-((5-(diisopropylamino)pentyl)oxy)benzaldehyde (2.26)

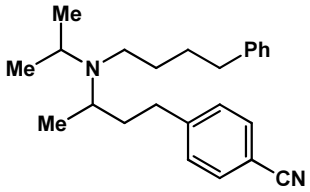
Compound was isolated as a colorless oil (123.9 mg, 92% yield) after purification by acid/base extraction **A**. Reaction time was 5 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.52 (d, *J* = 0.8 Hz, 1H), 7.83 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.53 (ddd, *J* = 8.4, 7.3, 1.9 Hz, 1H), 7.10

– 6.89 (m, 2H), 4.08 (t, *J* = 6.4 Hz, 2H), 3.10 – 2.90 (m, 2H), 2.40 (s, 2H), 2.11 – 1.77 (m, 2H), 1.48 (d, *J* = 7.1 Hz, 4H), 1.00 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 161.7, 136.0, 128.3, 125.0, 120.6, 112.6, 68.6, 48.5, 45.2, 31.3, 29.2, 24.0, 20.8. HR-MS calculated for $[M+H]^+$ 292.2276, found 292.2281. FTIR (neat, cm^{-1}): 3076(w), 2952(s), 2811(w), 2758(w), 1694(s), 1458(m), 1243(m), 1042(m).



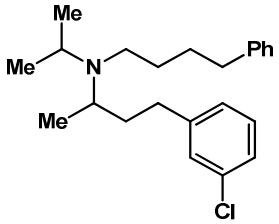
methyl 4-(3-(benzyl(4-phenylbutyl)amino)butyl)benzoate (2.29)

Compound was isolated as a colorless oil (161.0 mg, 94% yield) after purification by column chromatography (0-30% ethyl acetate in hexanes over 8 CV). Reaction time was 4 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 7.1 Hz, 2H), 7.27 – 7.19 (m, 4H), 7.16 – 7.07 (m, 4H), 6.95 (d, *J* = 8.3 Hz, 2H), 3.60 – 3.52 (m, 4H), 3.21 (d, *J* = 13.9 Hz, 1H), 2.75 – 2.54 (m, 2H), 2.43 – 2.35 (m, 4H), 2.28 – 2.14 (m, 1H), 1.70 – 1.25 (m, 6H), 0.80 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 148.7, 142.7, 141.3, 129.7, 128.7, 128.5, 128.4, 128.3, 128.1, 127.6, 126.6, 125.6, 54.1, 53.4, 52.0, 49.1, 35.9, 35.8, 33.4, 29.2, 28.3, 13.5. HRMS calculated for $[M+H]^+$ 430.2746, found 430.2735. FTIR (neat, cm^{-1}): 3061(w), 3026(w), 2929(s), 1721(s), 1609(m), 1453(m), 1279(s), 738(m).



4-(3-(isopropyl(4-phenylbutyl)amino)butyl)benzonitrile (2.28)

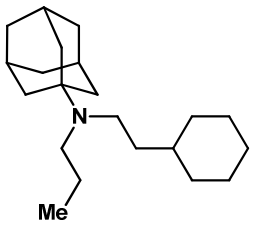
Compound was isolated as a colorless oil (124.8 mg, 90% yield) after acid/base extraction **A**. Reaction time was 8 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.1 Hz, 2H), 7.27 – 7.16 (m, 7H), 3.15 – 2.90 (m, 1H), 2.82 – 2.75 (m, 2H), 2.67 – 2.32 (m, 5H), 1.78 – 1.32 (m, 6H), 1.12 – 0.90 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 142.9, 132.2, 129.3, 128.5, 128.4, 125.8, 119.4, 109.4, 51.9, 48.0, 44.4, 37.6, 36.1, 34.0, 30.1, 29.5, 22.7, 19.6, 17.5. HRMS calculated for $[M+H]^+$ 349.2643, found 349.2646. FTIR (neat, cm^{-1}): 3086(w), 2961(s), 2226(m), 1606(s), 1453(s), 1152(m), 737(m).



***N*-(4-(3-chlorophenyl)butan-2-yl)-*N*-isopropyl-4-phenylbutan-1-amine (2.27)**

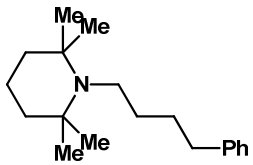
Compound was isolated as a colorless oil (108.6 mg, 76% yield) after purification by column chromatography (0-20% MeOH in CH_2Cl_2 over 8 CV with 0.1% acetic acid as an additive) followed by acid/base extraction **A**. Reaction time was 6 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.21 – 7.10 (m, 5H), 6.96 – 6.90 (m, 2H), 2.92 – 2.86 (m, 1H), 2.78 – 2.54 (m, 4H), 2.48 – 2.24 (m, 3H), 1.86 – 1.24 (m, 6H), 1.01 (d, J = 6.7 Hz, 3H), 0.95 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz,

MeOD) δ 146.6, 143.9, 135.0, 130.8, 129.5, 129.4, 129.3, 127.8, 126.7, 126.6, 53.3, 49.5, 45.8, 38.3, 36.9, 31.0, 30.5, 22.5, 20.1, 17.4. HRMS calculated for $[M+H]^+$ 358.2301, found 358.2296. FTIR (neat, cm^{-1}): 3062(w), 2961(s), 1597(m), 1453(m), 1079(w), 908(s), 733(s).



***N*-(2-cyclohexylethyl)-*N*-propyladamantan-1-amine (2.30)**

Compound was isolated as a colorless oil which solidified upon standing (101.2 mg, 83% yield) after acid/base extraction **A**. Reaction time was 4 h. ^1H NMR (300 MHz, C_6D_6) δ 2.66 – 2.54 (m, 2H), 2.54 – 2.39 (m, 2H), 2.02 (s, 3H), 1.85 – 1.39 (m, 20H), 1.39 – 1.10 (m, 3H), 1.04 – 0.84 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 50.5, 46.2, 40.0, 37.0, 36.8, 36.5, 33.7, 29.8, 29.7, 26.8, 26.5, 12.1, 12.0. ESI-MS calculated for $[M+H]^+$ 304.3, found 304.3. FTIR (neat, cm^{-1}): 2917(s), 2849(s), 1447(m), 1084(s) 1154(m).



2,2,6,6-tetramethyl-1-(4-phenylbutyl)piperidine (2.31)

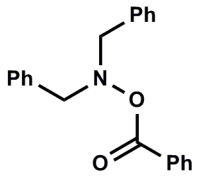
Compound was isolated as a colorless oil (93.7 mg, 86% yield) after purification by acid/base extraction **A**. Reaction time was 4 h. ^1H NMR (300 MHz, C_6D_6) δ 7.25 – 7.13 (m, 2H), 7.13 – 7.04 (m, 3H), 2.53 (t, J = 7.4 Hz, 2H), 2.45 – 2.25 (m, 2H), 1.69 – 1.28

(m, 10H), 1.01 (s, 12H). ^{13}C NMR (125 MHz, C_6D_6) δ 143.1, 128.7, 128.6, 126.0, 54.5, 45.3, 41.6, 36.4, 36.1, 29.7, 27.7, 18.2. HRMS calculated for $[M]^+$ 274.2535, found 274.2527. FTIR (neat, cm^{-1}): 3082(w), 2928(s), 1377(m), 1262(m), 1129(m).

2.6.e. Synthesis of O-benzoyl-N,N-hydroxylamines

General:

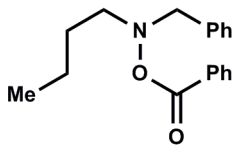
The *O*-benzoyl-*N*,*N*-dialkyl hydroxylamines were synthesized according to a modified literature procedure.[35c] To an oven-dried reaction flask under nitrogen was added potassium hydrogen phosphate (1.50 equiv) and benzoyl peroxide (1.00 equiv) followed by DMF (1.0 M). With vigorous stirring, the secondary amine (2.00 equiv) was added, and the resulting mixture stirred for 24 h at 25 °C. Distilled water was added, and the mixture was stirred until all solids were dissolved. Ethyl acetate was added, and the organic layer was extracted with sodium hydroxide (0.1 M). The organic layer was separated, and the aqueous layer was extracted twice more with ethyl acetate. The organic layers were then combined, washed with water and brine, dried over $MgSO_4$, and concentrated. The crude product was purified as indicated below.



***O*-benzoyl-*N*,*N*-dibenzylhydroxylamine**

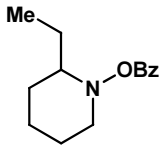
Compound was isolated as a white solid (1740.1 mg, 73% yield) after recrystallization from hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J = 8.1, 2H), 7.52 – 7.21 (m, 13H),

4.21 (s, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 136.1, 133.0, 129.5, 129.4, 128.5, 128.4, 127.8, 62.2.



***O*-benzoyl-*N*-benzyl-*N*-butylhydroxylamine**

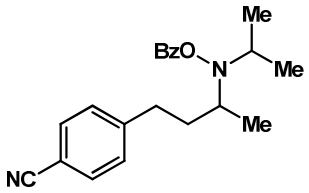
Compound was isolated as a colorless oil (1031.0 mg, 74% yield) after purification by silica gel chromatography (0 → 20% Et2O/hexanes). ^{1}H NMR (500 MHz, C_6D_6) δ 8.03 (d, *J* = 7.1 Hz, 2H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 2H), 7.06 – 6.96 (m, 4H), 3.98 (s, 2H), 2.83 (t, *J* = 7.1 Hz, 2H), 1.58 – 1.45 (m, 2H), 1.36 – 1.26 (m, 2H), 0.77 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 135.9, 133.0, 129.7, 129.5, 128.5, 128.4, 127.9, 127.7, 63.6, 58.4, 29.1, 20.5, 14.0. ESI-MS calculated for $[M+H]^+$ 284.2, found 284.4. FTIR (neat, cm^{-1}): 3063(w), 2958(m), 2871(w), 1743(s), 1451(m), 1246(s), 1062 (m).



2-ethylpiperidin-1-yl benzoate

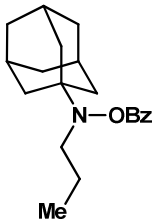
Compound was isolated as a colorless oil (880.0 mg, 78% yield) after purification by column chromatography (0-20% ethyl acetate in hexanes over 8 CV). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.1 Hz, 2H), 7.15 – 6.95 (m, 3H), 3.60 – 3.49 (m, 1H), 2.46 – 2.62 (m, 2H), 1.73 – 1.28 (m, 8H), 1.03 – 0.77 (d, *J* = 36.1 Hz, 3H). ^{13}C NMR (126 MHz,

$CDCl_3$) δ 165.0, 132.9, 129.6, 129.4, 128.4, 68.1, 58.1, 30.0, 25.9, 25.5, 23.7, 9.6. HRMS calculated for $[M+H]^+$ 234.1494, found 234.1493. FTIR (neat, cm^{-1}): 3062(w), 2938(s), 1740(s), 1451(m), 1244(s), 708(s).



***O*-benzoyl-*N*-(4-(4-cyanophenyl)butan-2-yl)-*N*-isopropylhydroxylamine**

Compound was isolated as a colorless oil (1443.3 mg, 53% yield) after removal of the amine through ion exchange chromatography followed by purification by column chromatography (0-20% diethyl ether in hexanes). ^1H NMR (300 MHz, C_6D_6) δ 8.11 (d, J = 8.2, 2H), 7.15 – 6.95 (m, 5H), 6.83 (d, J = 8.0 Hz, 2H), 3.16 – 3.02 (m, 2H), 2.92 – 2.60 (m, 1H), 2.74 – 2.54 (m, 1H), 1.75 – 1.43 (m, 1H), 1.44 – 1.28 (m, 1H), 1.08 (d, J = 6.2 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 148.3, 133.1, 132.1, 129.5, 129.4, 128.5, 128.3, 119.1, 109.5, 57.0, 53.7, 53.5, 36.4, 32.7, 20.6, 12.5. HRMS calculated for $[M+H]^+$ 337.1916, found 337.1899. FTIR (neat, cm^{-1}): 3062(w), 2977(s), 2226(m), 1743(s), 1606(w), 1245(s), 709(s).



***O*-benzoyl-*N*-(adamantan-1-yl)-*N*-propylhydroxylamine**

Compound was isolated as a colorless oil (683.8 mg, 37% yield), which solidified upon standing, after purification by column chromatography (0 – 10% Et_2O in hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 – 7.99 (m, 2H), 7.60 – 7.53 (m, 1H), 7.44 (t, J = 7.5 Hz, 2H), 2.99 – 2.86 (m, 2H), 2.10 (s, 3H), 1.90 – 1.80 (m, 6H), 1.71 – 1.59 (m, 6H), 1.57 – 1.45 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6) δ 165.6, 132.8, 130.6, 129.8, 128.7, 60.2, 51.7, 38.6, 36.9, 29.7, 21.6, 12.1. ESI-MS calculated for $[M+Na]^+$ 336.2, found 336.2. FTIR (neat, cm^{-1}): 3045(m), 2911(s), 1739(s), 1265(s), 740(s).

2.6.f. Synthesis of IMesCu(Et) ***2.32***

IMesCu(Et) (2.32)

(ethyl)[1,2-dihydro-1,3-bis(2,4,6-trimethylphenyl)-2H-imidazol-2-ylidene]-Copper

The title compound was synthesized according to a modified literature procedure.[37] A 15 mL Schlenk bomb was charged with a stir bar and flame-dried under vacuum. The flask was then transferred into a glove box and IMesCuCl (1.0 equiv, 400 mg, 1.0 mmol) followed by THF (8.0 mL, 0.1 M) were added. Out of the glove box, the flask was cooled to -78 °C at which point ethyl lithium (1.0 equiv, 2.0 mL, 1.0 mmol) was added dropwise over 30 min. The reaction was allowed to stir for 1 h before warming to 0 °C. The reaction was transferred into the glove box and stirred at 20 °C for 10 min, and then the mixture was filtered through a pad of celite. The solvent was then removed *in vacuo* followed by addition of toluene (10 mL) to the dark brown solid; the resulting slurry was stirred for 10 min before 20 mL of pentane was added. This mixture was filtered through a pad of celite and concentrated *in vacuo* to dryness. The resulting brown solid was taken up in THF (ca. 5 mL) and pentane was added until the solution became cloudy (ca. 20

mL). The mixture was filtered through a pad of celite to give a transparent solution and a white powder upon concentration (144 mg, 37% yield). ^{1}H NMR (500 MHz, C_6D_6) δ 6.86 (s, 4H), 6.16 (s, 2H), 2.21 (s, 6H), 2.17 (s, 12H), 1.80 (t, J = 8.0 Hz, 3H), 0.70 (q, J = 8.0 Hz, 2H). ^{13}C NMR (126 MHz, THF-d^8) δ 183.9, 138.3, 136.2, 134.7, 128.8, 121.5, 20.2, 17.2, 13.4, 0.6. Crystals suitable for x-ray analysis were obtained by vapor diffusion of pentane into a saturated solution of THF. Upon exposure of a solution of IMesCu(Et) in C_6D_6 to ambient light at 25 °C in a sealed NMR tube, 50% decomposition was observed after 4 h. The decomposition was monitored by ^{1}HNMR signatures indicative of the disappearance of the ethyl signals of **2.32** and the appearance of signals corresponding to ethane. At 60 °C in a sealed NMR tube protected from light, no decomposition of IMesCuEt was observed after 4 h. However, complete decomposition occurred after 24 h.

Stoichiometric Reaction of IMesCu(Et):

In a glove box, a 1 dram vial was charged with a stir bar. To the vial was added *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine (1.50 equiv, 11.7 mg, 0.037 mmol) and 1,4-dioxane-d^8 (0.25 mL). Separately, to a shell vial was added IMesCu-Et (1.0 equiv, 9.8 mg, 0.025 mmol) and 1,4-dioxane-d^8 (0.25 mL). The resulting solution was then added dropwise over 10 min to the reaction vial containing *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine with stirring at 45℃. After 1 h 1,3,5-trimethoxybenzene as internal standard was added and the reaction yield was determined by NMR comparison against 1,3,5-trimethoxybenzene.

Hydroamination of 4-phenylbut-1-ene using IMesCu(Et) as a catalyst:

In a glove box, a one-dram vial was charged with a stir bar. To the vial was added 9-BBN dimer (0.50 equiv, 12.2 mg 0.050 mmol), toluene (0.20 mL, 0.40 M), and phenyl butene (1.00 equiv, 13.2 mg, 0.100 mmol). After 12 h at 60 °C, the reaction mixture was cooled to room temperature and lithium *tert*-butoxide (1.10 equiv, 8.8 mg, 0.110 mmol), *O*-benzoyl-*N*,*N*-dibenzyl hydroxylamine (1.10 equiv, 24.3 mg, 0.110 mmol), and toluene (1.3 mL) were added. Finally IMesCuEt (0.050 equiv, 2.0 mg, 0.005 mmol) in toluene (0.5 mL, 2.0 mL total) was added dropwise over 1 min at 60 °C. The reaction vial was capped and allowed to stir at 60 °C for 4 h before 1,3,5-trimethoxybenzene as internal standard was added and the reaction yield was determined by GC analysis.

Section 7. References to Chapter 2

(1) (a) Rucker, R. P. Whittaker., A. M.; Dang, H.; Lalic, G. *J. Am. Chem. Soc.* **2012**, *134*, 6571; (b) Lalic, G.; Rucker, R. P. *Synlett* **2013**, *24*, 269.
(2) Henkel, T.; Brunne, R. M.; Muller, H.; Reichel, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 643.
(3) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337.
(4) Constable, D. J. C.; Dunn, P. J.; Hayler, J. D.; Humphrey, G. R.; Leazer, J. J. L.; Linderman, R. J.; Lorenz, K.; Manley, J.; Pearlman, B. A.; Wells, A.; Zaks, A.; Zhang, T. Y. *Green Chem.* **2007**, *9*, 411.
(5) (a) Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795; (b) Hultzsch, K. C. *Adv. Synth. Catal.* **2005**, *347*, 367; (c) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 3368.
(6) (a) Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738; (b) Seligson, A. L.; Trogler, W. C. *Organometallics* **1993**, *12*, 744.
(7) (a) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748; (b) Hong, S.; Kawaoka, A. M.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 15878; (c) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673; (d) Kim, J. Y.; Livinghouse, T. *Org. Lett.* **2005**, *7*, 1737; (e) Leitch, D. C.; Payne, P. R.; Dunbar, C. R.; Schafer, L. L. *J. Am. Chem. Soc.* **2009**, *131*, 18246; (f) Manna, K.; Xu, S.; Sadow, A. D. *Angew. Chem., Int. Ed.* **2011**, *50*, 1865; (g) Watson, D. A.; Chiu, M.; Bergman, R. G. *Organometallics* **2006**, *25*, 4731; (h) Wood, M. C.; Leitch, D. C.; Yeung, C. S.; Kozak, J. A.; Schafer, L. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 354.
(8) (a) Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 1070; (b) Cochran, B. M.; Michael, F. E. *J. Am. Chem. Soc.* **2008**, *130*, 2786; (c) Han, X.; Widenhoefer, R. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1747; (d) Hesp, K. D.; Tobisch, S.; Stradiotto, M. *J. Am. Chem. Soc.* **2009**, *132*, 413; (e) Julian, L. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 13813; (f) Liu, Z.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 1570; (g) Michael, F. E.; Cochran, B. M. *J. Am. Chem. Soc.* **2006**, *128*, 4246; (h) Ohmiya, H.; Moriya, T.; Sawamura, M. *Org. Lett.* **2009**, *11*, 2145.
(9) (a) Brunet, J.-J.; Chu, N.-C.; Rodriguez-Zubiri, M. *Eur. J. Inorg. Chem.* **2007**, *2007*, 4711; (b) Dorta, R.; Egli, P.; Zürcher, F.; Togni, A. *J. Am. Chem. Soc.* **1997**, *119*, 10857; (c) McBee, J. L.; Bell, A. T.; Tilley, T. D. *J. Am. Chem. Soc.* **2008**, *130*, 16562; (d) Zhang, J.; Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2006**, *128*, 1798; (e) Zhou, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 12220; (f) Zhang, X. E., T. J.; Hultzsch, K. C. *Angew. Chem., Int. Ed. Engl.* **2012**, *51*, 394; (g) Brinkmann, C. B., A. G. M.; Hill, M. S.; Procopiou, P. A. *J. Am. Chem. Soc.* **2012**, *134*, 2193.
(10) Sevov, C. S. Z., J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 11960.
(11) (a) Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795; (b) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675.
(12) Tye, J. W.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 14703.
(13) Li, Y.; Marks, T. J. *Organometallics* **1996**, *15*, 3770.
(14) Ryu, J.-S.; Li, G. Y.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 12584.

(15) Beller, M.; Trauthwein, H.; Eichberger, M.; Breindl, C.; Herwig, J.; Müller, T. E.; Thiel, O. R. *Chem. Eur. J.* **1999**, *5*, 1306.
(16) Utsunomiya, M.; Kuwano, R.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 5608.
(17) Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 2702.
(18) Takaya, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5756.
(19) Gasc, M. B. L., A.;Perie, J. J. *Tetrahedron* **1983**, *39*.
(20) (a) Munro-Leighton, C.; Blue, E. D.; Gunnoe, T. B. *J. Am. Chem. Soc.* **2006**, *128*, 1446; (b) Munro-Leighton, C.; Delp, S. A.; Alsop, N. M.; Blue, E. D.; Gunnoe, T. B. *Chem. Commun.* **2008**, 111.
(21) (a) Guin, J.; Fröhlich, R.; Studer, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 779; (b) Guin, J.; Mück-Lichtenfeld, C.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2007**, *129*, 4498.
(22) Moran, J.; Gorelsky, S. I.; Dimitrijevic, E.; Lebrun, M.-E.; Bédard, A.-C.; Séguin, C.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2008**, *130*, 17893.
(23) Brown, H. C.; Rao, B. C. S. *J. Am. Chem. Soc.* **1956**, *78*, 5694.
(24) (a) Brown, H. C.; Heydkamp, W. R.; Breuer, E.; Murphy, W. S. *J. Am. Chem. Soc.* **1964**, *86*, 3565; (b) Brown, H. C.; Kim, K.-W.; Srebnik, M.; Bakthan, S. *Tetrahedron* **1987**, *43*, 4071; (c) Kabalka, G. W.; Sastry, K. A. R.; McCollum, G. W.; Yoshioka, H. *J. Org. Chem.* **1981**, *46*, 4296.
(25) (a) Brown, H. C.; Midland, M. M.; Levy, A. B.; Brown, H. C.; Wetherill, R. B.; Suzuki, A.; Sono, S.; Itoh, M. *Tetrahedron* **1987**, *43*, 4079; (b) Brown, H. C.; Salunkhe, A. M.; Singaram, B. *J. Org. Chem.* **1991**, *56*, 1170.
(26) (a) Brown, H. C.; Cole, T. E.; Srebnik, M.; Kim, K. W. *J. Org. Chem.* **1986**, *51*, 4925; (b) Brown, H. C.; Srebnik, M.; Cole, T. E. *Organometallics* **1986**, *5*, 2300.
(27) Brown, H. C.; Suzui, A.; Sonao, S.; Itoh, M.; Midland, M. M. *J. Am. Chem. Soc.* **1971**, *93*, 4329.
(28) Hupe, E.; Marek, I.; Knochel, P. *Org. Lett.* **2002**, *4*, 2861.
(29) Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1976**, *98*, 1798.
(30) Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153.
(31) (a) Molander, G. A.; Vargas, F. *Org. Lett.* **2007**, *9*, 203; (b) Molander, G. A.; Sandrock, D. L. *Org. Lett.* **2007**, *9*, 1597; (c) Molander, G. A.; Shin, I. *Org. Lett.* **2012**, *14*, 3138.
(32) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216.
(33) (a) Tomita, D.; Kanai, M.; Shibasaki, M. *Chem. Asian. J.* **2006**, *1*, 161; (b) Takaya, J. T., S.; Ukai, K.; Iwasawa, N. *Org. Lett.* **2008**, *2008*, 2697; (c) Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 5792; (d) Yamamoto, Y. K., N.; Harada, Y. *Chem. Commun.* **2008**, 2010; (e) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 2895; (f) Ohmiya, H.; Yokokawa, N.; Sawamura, M. *Org. Lett.* **2010**, *12*, 2438; (g) Shintani, R. T., K.; Takeda, M.; Hayashi, T. *Angew. Chem., Int. Ed. Engl.* **2011**, *50*, 8656; (h) Uehling, M. R.; Marionni, S. T.; Lalic, G. *Org. Lett.* **2012**, *14*, 362.
(34) Partyka, D. V. *Chem. Rev.* **2011**, *111*, 1529.

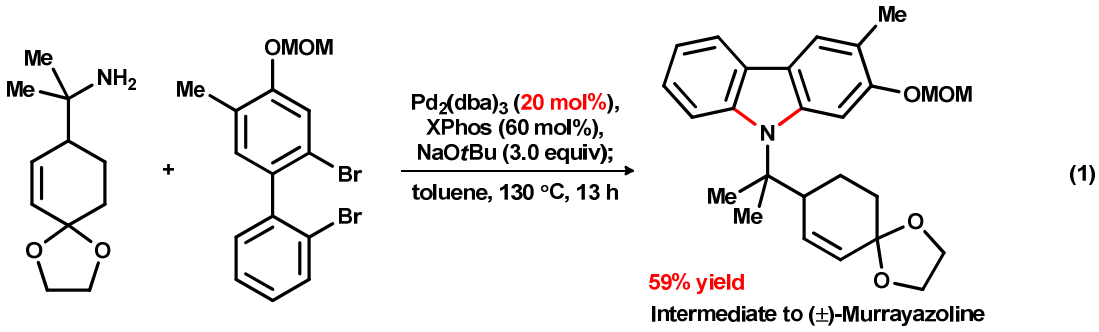
(35) (a) Berman, A. M.; Johnson, J. S. *J. Org. Chem.* **2004**, *70*, 364; (b) Berman, A. M.; Johnson, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 5680; (c) Berman, A. M.; Johnson, J. S. *J. Org. Chem.* **2006**, *71*, 219; (d) Campbell, M. J.; Johnson, J. S. *Org. Lett.* **2007**, *9*, 1521.
(36) (a) Erdik, E. A., M. *Chem. Rev.* **1989**, *89*, 1947; (b) Ciganek, E. *Organic Reactions* **2009**, 1.
(37) Goj, L. A.; Blue, E. D.; Delp, S. A.; Gunnoe, T. B.; Cundari, T. R.; Pierpont, A. W.; Petersen, J. L.; Boyle, P. D. *Inorg. Chem.* **2006**, *45*, 9032.
(38) Ciganek, E. *Org. React.* **2008**, *72*, 1.
(39) (a) Barker, T. J.; Jarvo, E. R. *J. Am. Chem. Soc.* **2009**, *131*, 15598; (b) Casarini, A.; Dembech, P.; Lazzari, D.; Marini, E.; Reginato, G.; Ricci, A.; Seconi, G. *J. Org. Chem.* **1993**, *58*, 5620; (c) Hatakeyama, T.; Yoshimoto, Y.; Ghorai, S. K.; Nakamura, M. *Org. Lett.* **2010**, *12*, 1516; (d) He, C.; Chen, C.; Cheng, J.; Liu, C.; Liu, W.; Li, Q.; Lei, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 6414; (e) Zhang, Z.; Yu, Y.; Liebeskind, L. S. *Org. Lett.* **2008**, *10*, 3005; (f) Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 1912.
(40) (a) Phanstiel, O.; Wang, Q. X.; Powell, D. H.; Ospina, M. P.; Leeson, B. A. *J. Org. Chem.* **1999**, *64*, 803; (b) Marsura, A.; Cuong, L.-D.; Gellon, G. *Synthesis* **1985**, 537.
(41) Ni, Z.; Zhang, Q.; Xiong, T.; Zheng, Y.; Li, Y.; Zhang, H.; Zhang, J.; Liu, Q. *Angew. Chem., Int. Ed.* **2012**, *51*, 1244.
(42) (a) Abdel-Magid, A. F.; Mehrman, S. J. *Org. Proc. Res. Dev.* **2006**, *10*, 971; (b) Baxter, E. W.; Reitz, A. B. *Org. React.* **2002**, *59*, 1.
(43) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369.
(44) (a) Goj, L. A.; Blue, E. D.; Delp, S. A.; Gunnoe, T. B.; Cundari, T. R.; Pierpont, A. W.; Petersen, J. L.; Boyle, P. D. *Inorganic Chemistry* **2006**, *45*, 9032; (b) Whitesides, G. M.; Stedronsky, E. R.; Casey, C. P.; San Filippo, J. *J. Am. Chem. Soc.* **1970**, *92*, 1426.
(45) Rucker, R. P. W., A. M.; Dang, H.; Lalic, G. *Angew. Chem., Int. Ed. Engl.* **2012**, *124*, 4019.
(46) (a) Huang, J.; Wu, C.; Wulff, W. D. *J. Am. Chem. Soc.* **2007**, *129*, 13366; (b) Phukan, P.; Bauer, M.; Maier, M. E. *Synthesis* **2003**, *9*, 1324.
(47) (a) Molander, G. A.; Sandrock, D. L. *J. Am. Chem. Soc.* **2008**, *130*, 15792; (b) Datta, S.; Chang, C.-L.; Yeh, K.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2003**, *125*, 9294.
(48) Coulter, M. M.; Dornan, P. K.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 6932.

Chapter 3 – Copper-Catalyzed Electrophilic Amination of Aryl Boronic Esters: Synthesis of Hindered Anilines[1]

Section 1. Introduction

The synthesis of aromatic and heteroaromatic amines has attracted considerable attention in the last two decades, chiefly as a result of the numerous applications of these compounds in the pharmaceutical industry and medicinal chemistry.[2] The development of several transition metal-catalyzed couplings of aryl halides with amines[3] has provided a practical method for synthesis of a wide range of anilines.[4] In particular, the palladium-catalyzed Buchwald-Hartwig coupling is a powerful and commonly-used reaction in synthetic chemistry. However, some important challenges remain. For example, bromo- and iodo-substituted anilines cannot be prepared directly using these methods. More importantly, the preparation of hindered anilines is still a major challenge.[5] This is illustrated by the low yield obtained in a palladium-catalyzed double N-arylation of a *tert*-butyl amine derivative *en route* to (±)-Murrayazoline (equation 1),[6] as well as in the total synthesis of (+)-Psychotetramine described by Baran and coworkers.[7]

Scheme 3.1



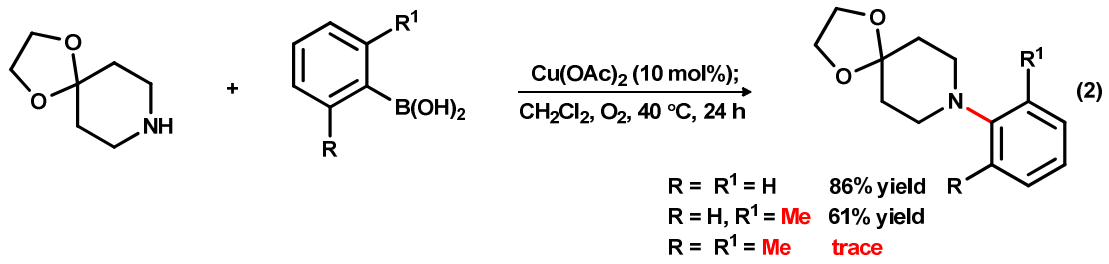
(1)

The methods currently available for preparing hindered anilines require the formation of highly reactive intermediates, such as benzynes[8] or organometallic

reagents.[9-10] The most general of these reactions, by Knochel and coworkers, involves oxidative coupling of organometallic reagents with hindered lithium amides in the presence of stoichiometric amounts of copper.[9b] In a rare instance of catalytic synthesis of hindered anilines, Berman and Johnson reported three examples of the electrophilic amination of aryl zinc reagents by hindered electrophiles.[9a,11] A common feature of the procedures reported by the groups of Johnson and Knochel is that a significant excess (≥2 equivalents) of one of the coupling components is necessary. Furthermore, both methods require a stoichiometric amount of a Grignard, aryl lithium, or aryl zinc reagent.

Aryl boronic acids and their derivatives offer significant advantages over the organometallic reagents currently used in synthesis of hindered anilines. They are stable, readily available, and compatible with a wide range of functional groups. However, previous attempts by Berman and Johnson[9a] and others[12] to develop electrophilic amination of these compounds have been unsuccessful. A related oxidative amination of organoboron reagents developed by Lam,[13] Chan,[14] and Evans[15] is highly sensitive to steric properties of amine substrates and cannot be used for the synthesis of hindered anilines. This limitation is apparent when examining the yields of aniline products obtained in the series of copper-catalyzed reactions utilizing the cyclic amine 1,4-dioxa-8-azaspiro[4.5]decane with increasingly sterically-hindered aryl boronic acids (Scheme 3.2).[16]

Scheme 3.2



Herein, we describe a catalytic method for the synthesis of hindered anilines from aryl and heteroaryl boronic esters compatible with a wide range of functional groups, including aryl iodides and bromides.

Section 2. Discovery and Optimization

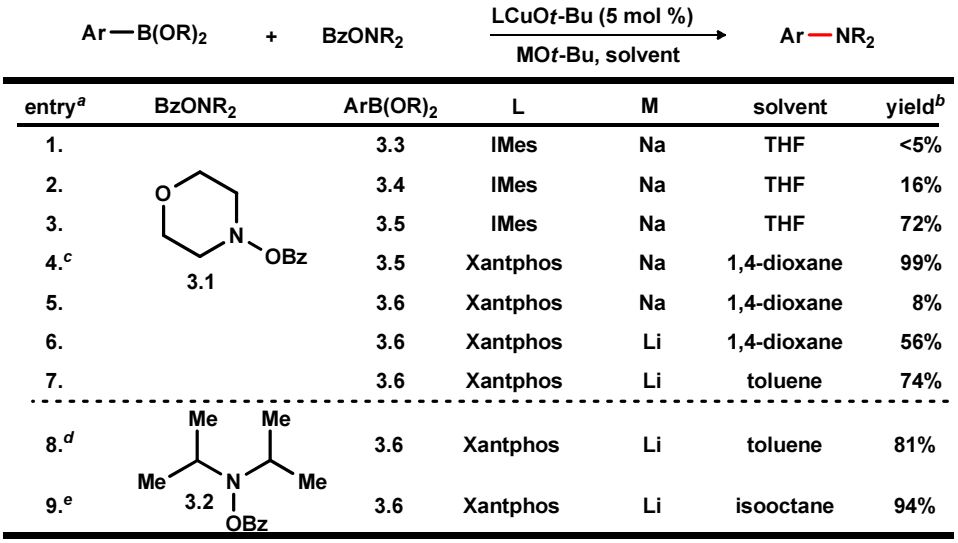
In an initial experiment, we explored the reactivity of aryl boronic ester **3.3** and 4-benzoyloxymorpholine **3.1** in the presence of sodium *tert*-butoxide and IMesCuO*t*Bu as a catalyst.[17] Upon full conversion of the electrophile, the desired aniline was obtained in less than 5% yield (Table 3.1, entry 1).

We speculated that the low yield of the aniline was a consequence of slow transmetallation of the aryl boronic ester. Indeed, reactions with ethylene glycol **(3.4**) and neopentyl glycol (**3.5**) esters, which are known to undergo transmetallation faster than the corresponding pinacol esters,[18] provided the aniline product in 16 and 72% yield, respectively (Table 3.1, entry 2 and 3).

In a catalyst screen performed with boronic ester **3.5** and electrophile **3.1**, we identified XantphosCuO-*t*Bu, a complex prepared from Xantphos ligand and $(CuO\text{-}tBu)_4$,[19] as the best catalyst. In a reaction using this catalyst in 1,4-dioxane as solvent, the desired aniline was obtained in 99% yield (Table 3.1, entry 4). Unfortunately, a reaction with the more hindered boronic ester **3.6** resulted in the

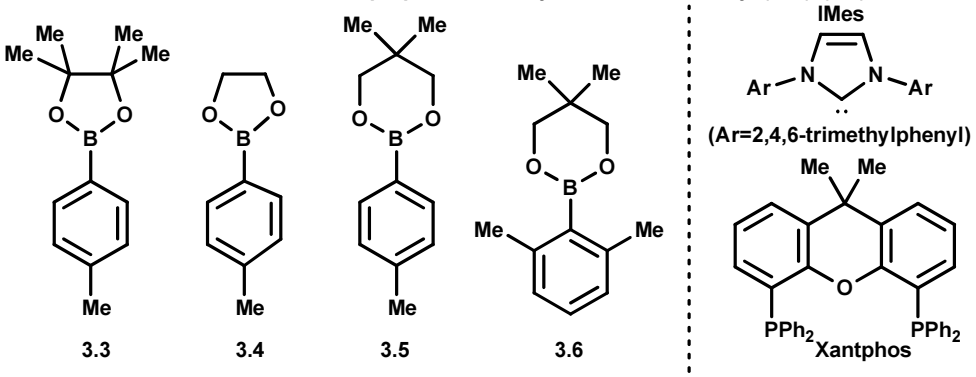
formation of the desired aniline in only 8% yield, together with 83% yield of *tert*-butyl benzoate (Table 3.1, entry 5).

Table 3.1



entry[a]	$BzONR_2$	$ArB(OR)_2$	L	M	solvent	yield[b]
1.		3.3	IMes	Na	THF	<5%
2.		3.4	IMes	Na	THF	16%
3.		3.5	IMes	Na	THF	72%
4.[c]	3.1	3.5	Xantphos	Na	1,4-dioxane	99%
5.		3.6	Xantphos	Na	1,4-dioxane	8%
6.		3.6	Xantphos	Li	1,4-dioxane	56%
7.		3.6	Xantphos	Li	toluene	74%
8.[d]	3.2	3.6	Xantphos	Li	toluene	81%
9.[e]		3.6	Xantphos	Li	isooctane	94%

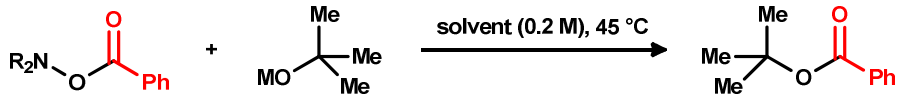
[a] $ArB(OR)_2$ (1.2 equiv), $BzONR_2$ (1.0 equiv), MO*t*-Bu (1.0 equiv), 25 °C, 12 h. [b] determined by GC. [c] Catalyst was formed in situ from Xatphos and $(CuOt\text{-}Bu)_4$. [d] Reaction performed at 45 °C. [e] 60 °C, 1.0 M. Toluene used to prepare the catalyst. OBz = *O*-benzoyl (OC(O)Ph)

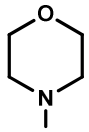


In fact, a control experiment revealed that *tert*-butylbenzoate forms in nearly quantitative yield in a reaction of 4-benzoyloxymorpholine (**3.1**) with sodium *tert*-butoxide after only 10 minutes at room temperature (Table 3.2, entry 1). However, we found that the background reaction of the electrophile with an alkoxide can be suppressed if less reactive lithium *tert*-butoxide is used (Table 3.2, entry 2). When this change was implemented along with the use of a non-coordinating solvent, a further decrease in the

rate of decomposition of **3.1** was observed (Table 3.2, entry 3). Interestingly, the formation of *tert*-butyl benzoate could be completely suppressed when using these conditions with the sterically-hindered electrophile *O*-benzoyl-*N*,*N*-diisopropylhydroxylamine **3.2** (Table 3.2, entry 4); however, when more sodium *tert*-butoxide was used, the rate of consumption of **3.2** was more pronounced (result not shown).

Table 3.2



Entry	R_2N–OBz	M	Solvent	Timepoint (min) % Yield *t*-butyl benzoate (% electrophile conversion) 10 min	120 min
1[a]		Na	1,4-dioxane-d^8	92 (94)	97 (100)
2		Li	1,4-dioxane-d^8	34 (57)	85 (86)
3		Li	benzene-d^6	22 (21)	33 (66)
4	$(iPr)_2N-OBz$	Li	benzene-d^6	0 (0)	0 (0)

[a] Reaction conducted at 25 °C.

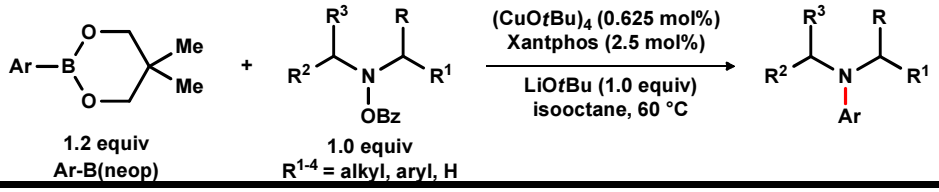
Consistent with the above findings, a reaction with boronic ester **3.6** and electrophile **3.1** performed in toluene and using lithium *tert*-butoxide afforded the desired aniline in 74% yield (Table 3.1, entry 7). The same conditions could also be used to prepare highly hindered *N*,*N*-diisopropyl-2,6-dimethylaniline from boronic ester **3.6** and electrophile **3.2** (Table 3.1, entry 8). Finally, the best result (94% yield) was obtained when this reaction was performed in a concentrated isooctane solution using catalyst prepared from Xantphos and $(CuOtBu)_4$ in toluene (Table 3.1, entry 9).

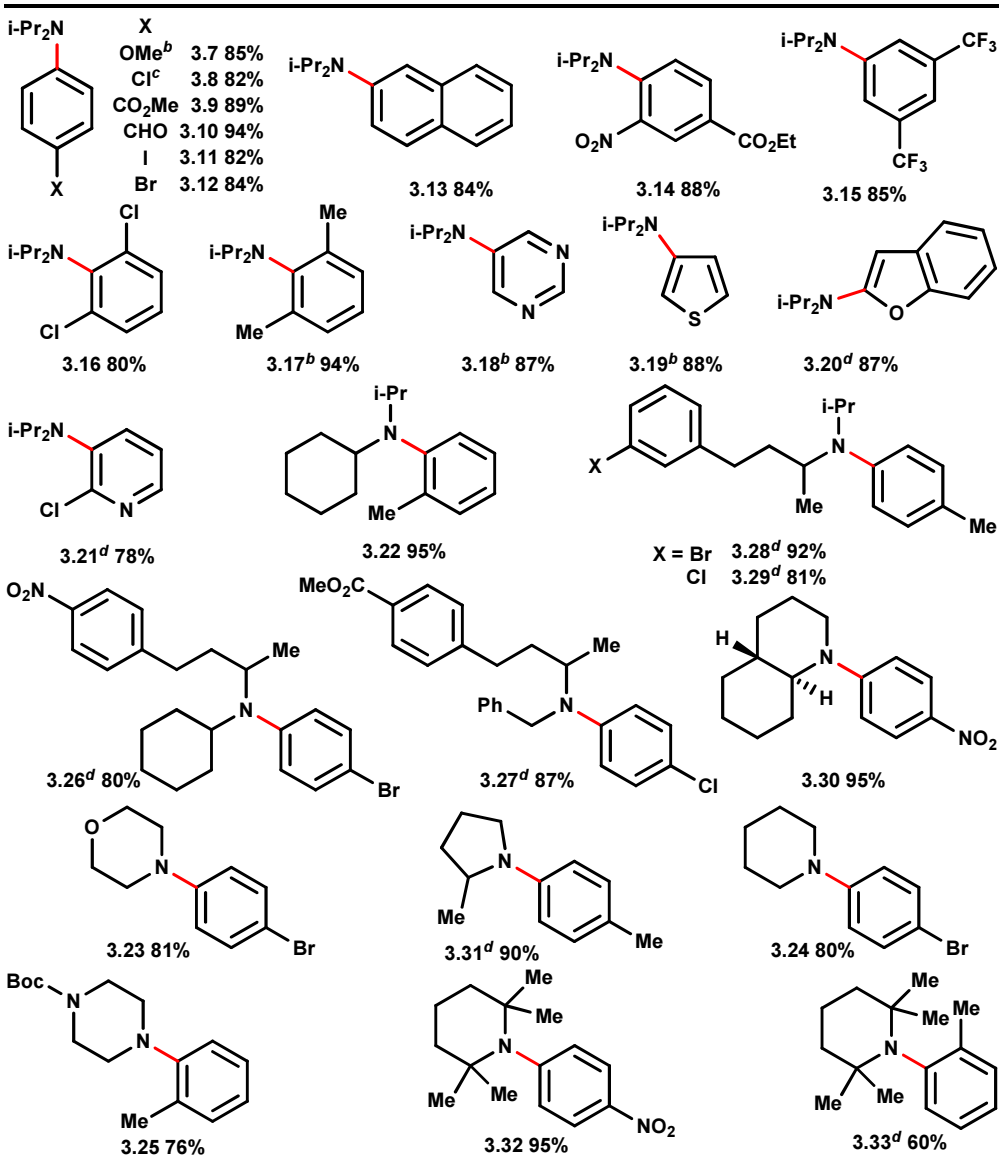
Section 3. Scope

The optimized reaction conditions proved to be remarkably general. We found that reactions with diisopropylamine-derived electrophile **3.2** could be performed in the presence of a number of functional groups, including formyl, carbomethoxy, nitro, methoxy, trifluoromethyl, iodo, and bromo groups (Table 3.3, **3.7** and **3.9**—**3.12**). As the synthesis of anilines **3.16** and **3.17** suggest, hindered boronic esters are well-tolerated in the reaction. In addition, a variety of heteroaromatic boronic esters, including 2-chloropyridine-3-boronic ester, can also be used as nucleophiles (Table 2, compounds **3.18—3.21**). In most reactions, 2.5 mol % of the catalyst was sufficient to accomplish the full conversion in less than 12 h, while the sterically hindered boronic esters required a higher catalyst loading. Finally, as the synthesis of **3.8** demonstrates, the reaction can be successfully performed on a 5 mmol scale.

To establish the full scope of the amination reaction, we explored the reactivity of various electrophiles. *O*-benzoyl hydroxylamines derived from common cyclic amines, such as pyrrole, piperidine, morpholine, piperazine, and decahydroisoquinoline can be used in the reaction (**3.23**—**3.25** and **3.30**—**3.31**). Electrophiles bearing functional groups, such as nitro, carbomethoxy, bromo and chloro groups, are also viable substrates and provide the aniline products in excellent yields (**3.26**—**3.29**). The steric properties of an electrophile have no significant effect on the outcome of the reaction. Even a highly hindered electrophile derived from 2,2,6,6-tetramethylpiperidine could be coupled with nitrophenyl boronic ester in 87% yield, and the 2-methylphenyl boronic ester provided **3.33** in 60% yield. The preparation of **3.33** is especially notable, as it is the most hindered aniline prepared to date through either catalytic or stoichiometric techniques.

Table 3.3



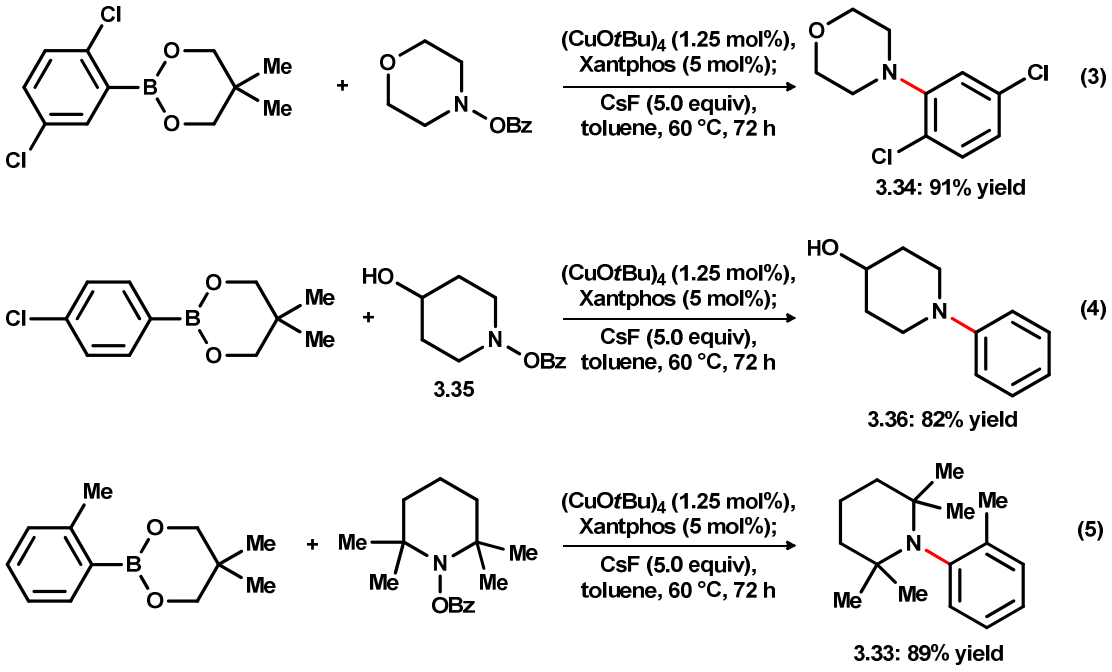


[a] Reactions performed on 0.5 mmol scale. Yields of isolated products are reported. neop = neopentyl glycol. [b] 5 mol% of the catalyst were used. [c] The reaction was performed on a 5 mmol scale. [d] 2.5 mol% of the catalyst were used at 45 °C. OBz = *O*-benzoyl.

An extension of the substrate scope could be achieved if lithium *tert*-butoxide is replaced with CsF. This change was particularly beneficial in coupling hindered boronic

esters with less-hindered electrophiles (Scheme 3.3, equation 3). Furthermore, CsF allowed the reaction to be performed in the presence of acidic functional groups, as demonstrated by the reaction of 4-hydroxypiperidine-derived electrophile **3.35** to give **3.36** shown in equation 4 (Scheme 3.3). Under the conditions using alkoxide, both of these products were obtained in less than 20% isolated yield. Finally, the extremely hindered aniline **3.33** could be prepared in 89% yield using this procedure (Scheme 3.3, equation 5).

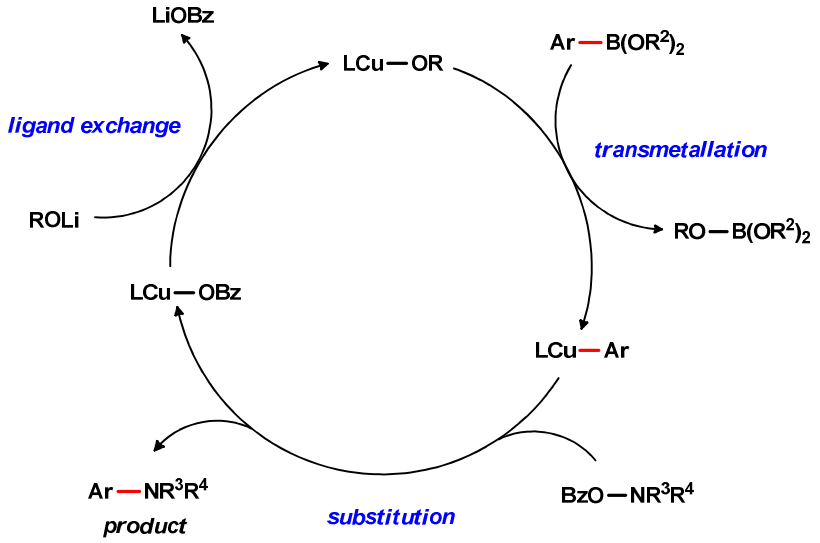
Scheme 3.3



Section 4. Mechanism

We propose that the amination reaction proceeds according to the mechanism shown in Scheme 2. The reaction involves transmetallation from boron to copper, with subsequent electrophilic amination of the aryl copper intermediate. Finally, the reactive copper alkoxide is regenerated with lithium alkoxide.

Scheme 3.4



While the transmetallation of aryl boronic esters with *NHC*-ligated copper complexes is known to result in monomeric, neutral arylcopper(I) intermediates which can be characterized,[17,20] to the best of our knowledge there are no examples of the corresponding phosphine-ligated arylcopper(I) complexes which have been prepared and isolated through any analogous transmetallation processes.[21] We were able to isolate and characterize by x-ray diffraction XantphosCu-(4-Me)Ph **3.37**, the product of transmetallation of XantphosCuOtBu with 4-tolyl (neopentyl)boronic ester **3.5** (Equation 6). The isolation of this bidentate phosphine-ligated arylcopper(I) complex provides evidence that organoboron—copper transmetallation can also be used to prepare monomeric, isolable phosphine-ligated aryl copper(I) complexes analogous to those supported by *NHC* ligands and stands as the only example of a monomeric arylcopper(I) complex supported by a bidentate phosphine ligand.[22]

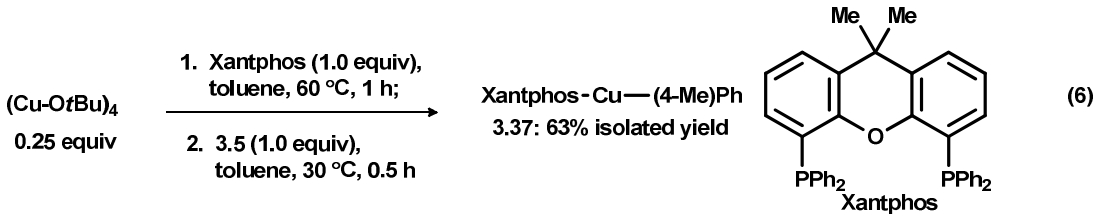
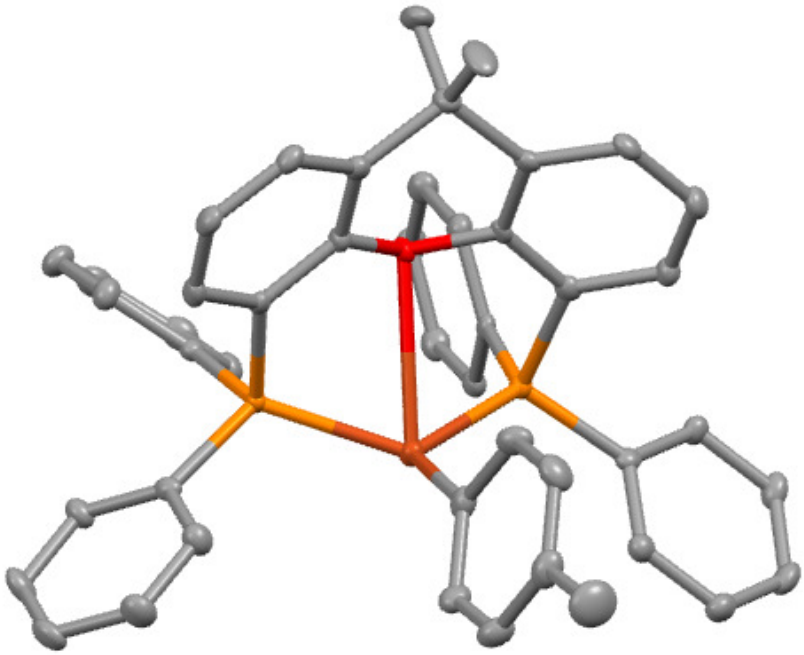


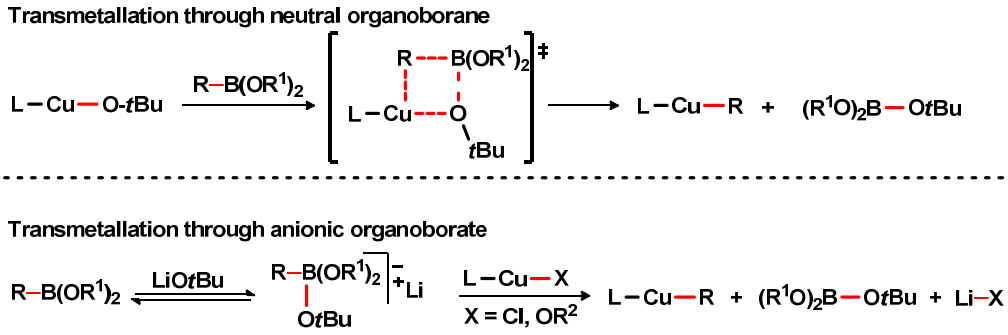
Figure 3.1 Ellipsoid Drawing of XantphosCu-(4-Me)Ph (3.37) (hydrogen atoms omitted for clarity).



Although the transmetallation of organoboron compounds with catalytic amounts of late transition metals such as palladium,[23] rhodium,[24] ruthenium,[25] gold,[26] and others[27] has been extensively described, the exact mechanism of organoboron—copper transmetallation remains a subject of debate.[28] Transmetallation of the organoboron compound with copper has been proposed to occur through either the neutral organoborane, in a process called σ-bond metathesis (top of Scheme 3.5).[20,29] Alternatively, organoboron—copper transmetallation has been proposed to occur through a reaction analogous to nucleophilic substitution by the anionic organoborate onto the copper center (bottom of Scheme 35).[30] To further complicate matters, it is now well-

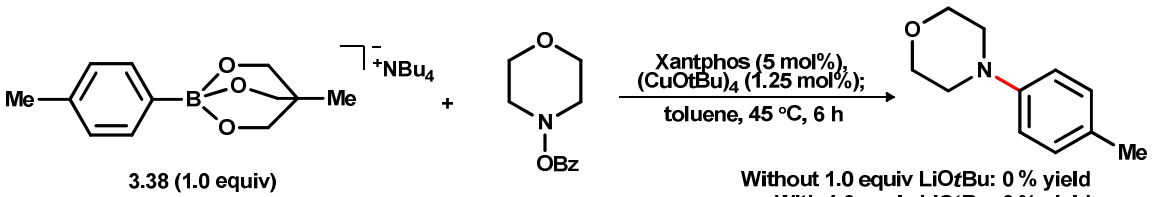
established that a significant amount of organoborate can exist in solution[31] due to rapid equilibrium with the neutral organoborane[27,32] in many conditions which utilize basic additives in conjunction with organoboron compounds.

Scheme 3.5



To test the possibility of transmetallation occurring through an anionic organoborate rather than the neutral organoborane, we subjected borate ester **3.38**, which cannot have a significant equilibrium with its neutral borane in solution, to amination using the 4-benzoyloxymorpholine electrophile **3.1** under standard catalytic conditions in the presence and absence of lithium *tert*-butoxide. In both cases, none of the desired product was detected by GC analysis of the crude reaction mixture, and in the reaction with added alkoxide, the electrophile was completely consumed within 6 h. These results are consistent with transmetallation occurring through the neutral organoborane..

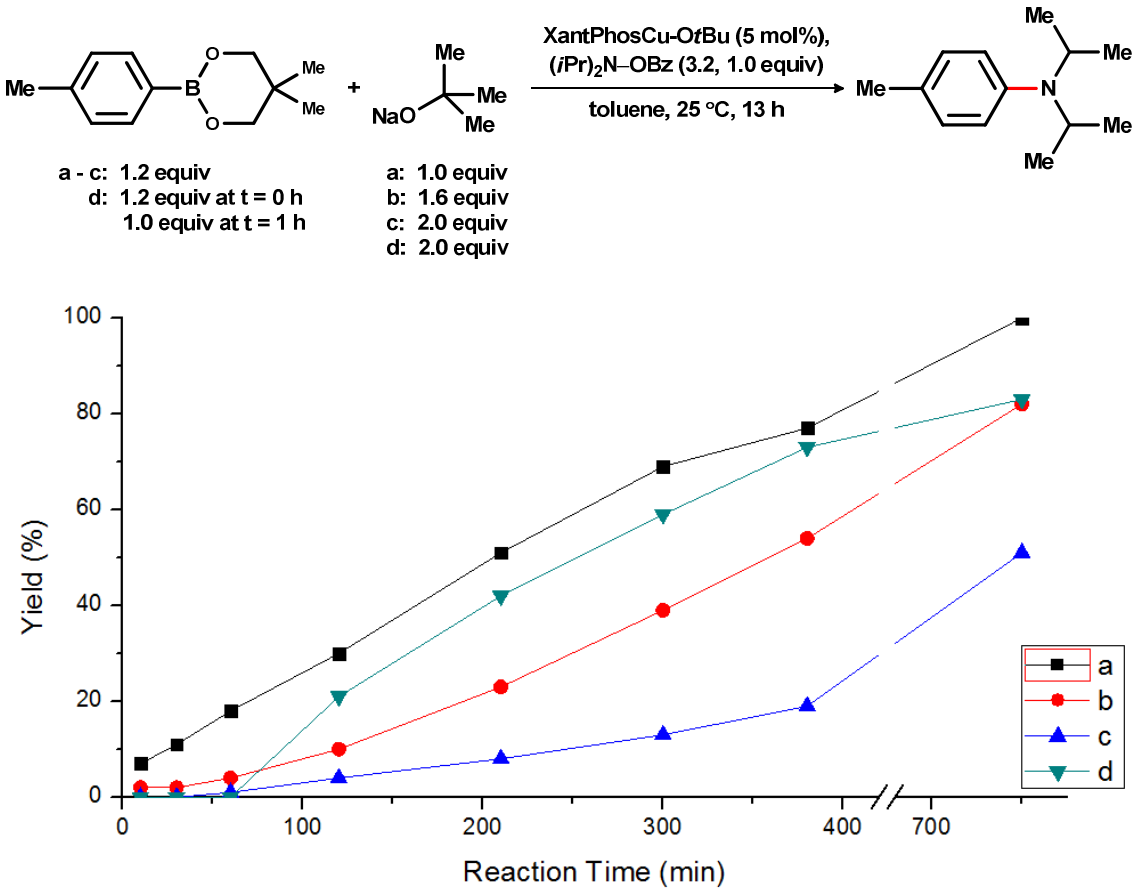
Scheme 3.6



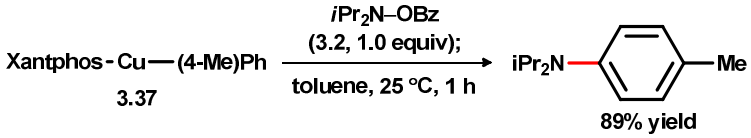
We also examined the efficiency of catalytic amination of electrophile **3.2** in reactions which utilized superstoichoimetric amounts of sodium *tert*-butoxide as the additive used to assist catalyst turnover. In these reactions, the formation of organoborate through reaction of the organoboron compound with alkoxide occurs quickly; this organoborate is in equilibrium with the neutral organoboron compound and is expected to further favor the formation of organoborate as more equivalents of sodium alkoxide are added.[18a,23] In a reaction using the optimal molar ratio of tolyl(neopentyl)boronic ester and sodium *tert*-butoxide (1.2 equiv of boronic ester to 1.0 equiv of alkoxide), the reaction proceeded efficiently to give the product in quantitative yield (conditions *a*, Figure 3.2). However, in a subsequent reaction using 1.6 equiv of alkoxide, only 82% of the desired product was obtained, with full conversion of the electrophile observed (conditions *b*, Figure 3.2). During the course of monitoring this experiment, the electrophile was shown to undergo steady decomposition during the first hour of the reaction with no significant amount of product formation observed. In fact, the consumption of electrophile was even more pronounced when 2.0 equiv of the alkoxide was used (approx. 50%, conditions *c*, Figure 3.2), and less than 5% of product formation was observed within the first hour of this reaction. Taken together, these experiments indicate that organoborate formation is significant when a reactive alkoxide, such as sodium *tert*-butoxide, is used in superstoichiometric amounts relative to the tolyl(neopentyl)boronic ester. As importantly, however, is the observation that product formation under conditions *b* and *c* is suppressed until a significant amount of the alkoxide has been consumed in side reactions with the electrophile (approx. 18% conversion of **3.2**, condition *b*; approx. 50% conversion of **3.2**, condition *c*).

Interestingly, we found that, by simply adding an extra equivalent of tolyl(neopentyl)boronic ester to the reaction described by conditions *c* after one hour, the desired reaction pathway became dominant again, due now to the presence of an excess molar amount of boronic ester to alkoxide (conditions *d*, Figure 3.2), which allows transmetallation of the copper(I) alkoxide with the neutral organoborane to occur. In the reactions using conditions *c* and conditions *d*, product formation is initially sluggish due to rapid reaction of the neutral tolyl(neopentyl)boronic ester with alkoxide to form an organoborate, which cannot undergo transmetallation with copper(I) alkoxide.

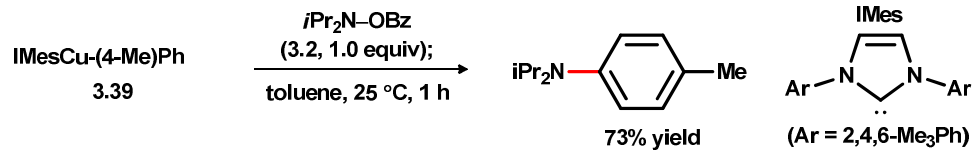
Figure 3.2 Effect of superstoichiometric amount of NaO*t*Bu on product yield.



We next focused our attention on the electrophilic amination of the putative aryl copper intermediate. In a stoichiometric reaction of electrophile **3.2** with Xantphos-supported copper aryl complex (**3.37**), the desired aniline was obtained in 89% yield (Equation 7). A similar result was obtained with IMes-supported arylcopper(I) complex (**3.39**),[14] which resulted in a 73% yield of aniline in less than 60 minutes at 25 °C (Equation 8). In addition, when used as a catalyst, both **3.37** and **3.39** provided results indistinguishable from those obtained using either XantphosCuO*t*Bu or IMesCuO*t*Bu catalyst in the amination of **3.2** with tolyl(neopentyl)boronic ester (IMesCuO*t*Bu is an effective catalyst for the amination of substrates with less-hindered aryl(neopentyl)boronic esters).



(7)



(8)

Section 5. Conclusion

In conclusion, we have developed a mild copper-catalyzed reaction for the synthesis of sterically hindered anilines from aryl and heteroaryl boronic esters. This method allowed us to prepare some of the most hindered anilines ever made. Furthermore, the new method is compatible with a wide range of functional groups, including chloro, bromo, iodo, carbomethoxy, nitro, hydroxyl, formyl, and methoxy, and can be used to prepare a wide variety of heteroaromatic amines. Furthermore, the isolation and characterization of **3.37** represents the first example of a monomeric

bidentate phosphine-ligated aryl copper(I) complex. We anticipate that the exceptionally broad substrate scope and reliability of this new procedure, together with the availability of a wide variety of aryl boronic esters, will make it a useful option for the synthesis of hindered anilines.

Section 6. Experimental

General

All reactions were performed under a nitrogen atmosphere with flame-dried glassware, using standard Schlenk techniques, or in a glove box (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 μm, 230-400 mesh). Ion Exchange Chromatography was performed using analytical grade cation exchange resin from sulfonic acid functionalized styrene (Bio-Rad Laboratories, 200-400 mesh, 5.2 meq/g). General method for purification by ion exchange chromatography is as follows: crude product was adsorbed on the cation exchange resin (200 mg resin/mmol product) using MeOH, and the resin was subsequently washed with 10% dichloromethane in MeOH over 4 CV, then 10% Et_3N in MeOH over 4 CV to elute the product. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum RX I spectrometer. IR peak absorbencies are represented as follows: s = strong, m = medium, w = weak, br = broad. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AV-300 or AV-500 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual proteated solvent peak ($CDCl_3$ (7.26 ppm), C_6D_6 (7.16 ppm), or CD_2Cl_2 (5.32 ppm)). ^{13}C chemical shifts are reported in parts per million downfield of TMS and are referenced to the carbon resonance of the solvent ($CDCl_3$: δ 77.2 ppm, C_6D_6: δ 128.1 ppm, CD_2Cl_2: δ 54.0 ppm, CD_3CN: δ 1.3 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet), integration, and coupling constants in Hertz (Hz). Mass spectra were collected on a JEOL HX-110 mass

spectrometer. GC analysis was performed on a Shimadzu GC-2010 instrument with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 μm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5 min @ 250 °C.

Materials

THF, CH_2Cl_2, diethyl ether, and toluene were degassed and dried by passing through columns of neutral alumina. 1,4-dioxane was distilled from purple Na/benzophenone ketyl and stored over 4Å molecular sieves. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. Deuterated solvents were degassed and dried over 4Å molecular sieves before use. Commercial reagents were purchased from Sigma-Aldrich Co., VWR International, LLC., or STREM Chemicals, Inc., and were used as received. Aryl boronic esters were prepared according to a literature procedure.[33]

3.6.a. Reaction Optimization

General:

All optimization reactions were performed in a glove box. A 1-dram vial was charged with a stir bar. To the vial was added alkoxide additive (1.00 equiv), aryl boronic ester (1.20 equiv), copper catalyst (0.05 equiv), *n*-dodecane (0.10 equiv), and solvent (0.1 M). To the resulting mixture was added *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine (1.00 equiv). The reaction vial was capped and stirred for 24 h with heating at the indicated temperature. Product yield was determined by GC comparison against *n*-dodecane as an internal standard.

Optimization of the aryl boronic ester backbone (Entries 1 – 3, Table 3.4):

Reactions were conducted according to the General Procedure using IMesCu-O*t*Bu (0.003 mmol, 1.1 mg), Na-O*t*Bu (0.050 mmol, 4.8 mg), and either 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane (0.060 mmol, 13.8 mg), 2-(*p*-tolyl)-1,3,2-dioxaborolane (0.060 mmol, 9.7 mg), or 5,5-dimethyl-2-(*p*-tolyl)-1,3,2-dioxaborinane (0.060 mmol, 12.2 mg) with THF as solvent (0.5 mL). To the resulting solution was added 4-benzoyloxymorpholine (0.050 mmol, 10.4 mg). Reactions were heated at 25 °C with stirring for 24 h.

Optimization of the catalyst (Entries 4 – 12, Table 3.4):

Reactions were conducted according to the General Procedure using the indicated copper catalysts (0.003 mmol), Na-O*t*Bu (0.050 mmol, 4.8 mg), and dimethyl-2-(*p*-tolyl)-1,3,2-dioxaborinane (0.060 mmol, 12.2 mg) with THF as solvent (0.5 mL). To the resulting solution was added 4-benzoyloxymorpholine (0.050 mmol, 10.4 mg). Reactions were heated at 25 °C with stirring for 24 h.

Note on Preparation of XantPhosCu-OtBu from XantPhos and $(Cu\text{-}OtBu)_4$:

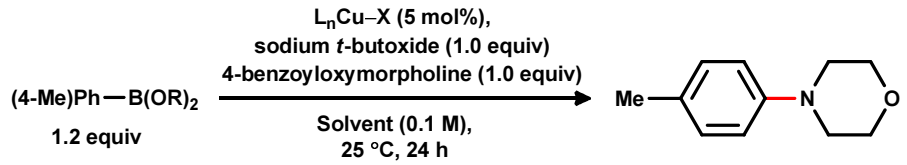
In a glove box, a 1-dram reaction vial was charged with a stir bar. To the vial was added Cu-O*t*Bu tetramer (0.25 equiv), XantPhos ligand (1.00 equiv) and solvent (0.1 M). The resulting mixture was allowed to stir at 45°C for 0.5 h. The mixture was used as a stock solution of the catalyst.

Optimization of the solvent (Entries 13 – 15, Table 3.4):

Reactions were conducted according to the General Procedure using XantPhosCu-O*t*Bu (0.003 mmol, 25 μL of a 0.1 M stock solution), Na-O*t*Bu (0.050 mmol, 4.8 mg), and 2-(*p*-tolyl)-5,5-dimethyl-1,3,2-dioxaborinane (0.060 mmol, 12.4 mg) with either diethyl

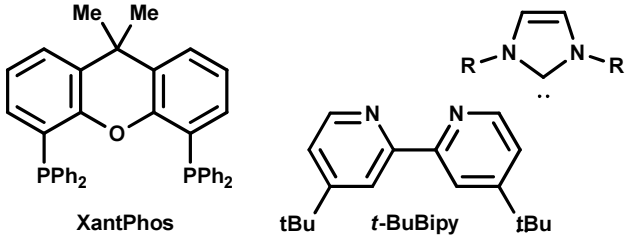
ether, dichloromethane, or 1,4-dioxane as solvent (0.475 mL). To the resulting mixture was added 4-benzoyloxymorpholine (0.050 mmol, 10.4 mg). Reactions were heated at 25 °C with stirring for 24 h.

Table 3.4



Entry	(4–Me)Ph–B(OR)$_2$	L$_n$Cu–X[a]	Solvent	Yield
1	3.1	IMesCu-OtBu	THF	< 5
2	3.2	IMesCu-OtBu	THF	16
3	3.3	IMesCu-OtBu	THF	72
4	3.3	CyIBoxCu-Cl	THF	< 1
5	3.3	IMeCu-Cl	THF	< 1
6	3.3	ICyCu-OtBu	THF	< 1
7	3.3	ItBuCu-Cl	THF	48
8	3.3	IAdCu-Cl	THF	60
9	3.3	IPrCu-OtBu	THF	0
10	3.3	tBuBipyCu-OtBu	THF	52
11	3.3	dppeCu-OtBu	THF	0
12	3.3	XantPhosCu-OtBu	THF	92
13	3.3	XantPhosCu-OtBu	diethyl ether	5
14	3.3	XantPhosCu-OtBu	DCM	0
15	3.3	XantPhosCu-OtBu	1,4-dioxane	99

[a] XantPhosCu-O*t*Bu is formed in situ from (Cu-O*t*Bu)$_4$ and XantPhos.



IMes R = 2,4,6-trimethylphenyl
IMe R = Methyl
ICy R = cyclohexyl
ItBu R = *t*-butyl
IAd R = adamantyl
IPr R = 2,6-diisopropylphenyl

Optimization of solvent, alkoxide additive, and concentration with 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (Table 3.5):

With 4-benzoyloxymorpholine:

Reactions were conducted according to the General Procedure using XantPhosCu-O*t*Bu (0.003 mmol, 25 μL of a 0.1 M stock solution prepared in either 1,4-dioxane or toluene), Na-O*t*Bu (0.050 mmol, 4.8 mg) or Li-O*t*Bu (0.050 mmol, 4.0 mg), and 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (0.06 mmol, 13.1 mg) with either 1,4-dioxane or toluene as solvent (0.475 mL). To the resulting mixture was added 4-benzoyloxymorpholine (0.050 mmol, 10.4 mg). The reaction vial was capped and stirred for 24 h at the indicated temperature.

With O-benzoyl-*N*,*N*-diisopropyl hydroxylamine:

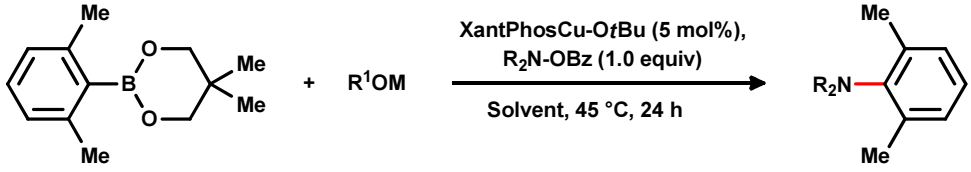
Reactions were conducted according to the General Procedure using XantPhosCu-O*t*Bu (0.003 mmol, 25 μL of a 0.1 M stock solution prepared in toluene), Li-O*t*Bu (0.050 mmol, 4.0 mg), and 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (0.06 mmol, 13.1 mg) with either toluene or isooctane as solvent (0.475 mL). To the resulting mixture was added *O*-benzoyl-*N*,*N*-diisopropyl hydroxylamine (0.050 mmol, 11.1 mg). The reaction vial was capped and stirred for 24 h at the indicated temperature.

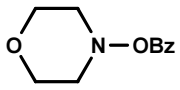
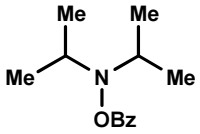
Optimization of Concentration with O-benzoyl-*N*,*N*-diisopropyl hydroxylamine *and* isooctane:

The 0.5 M scale reaction (Table 3.5, entry 5) was conducted according to the General Procedure using XantPhosCu-O*t*Bu (0.010 mmol, 100 μL of a 0.1 M stock solution prepared in toluene), Na-O*t*Bu (0.200 mmol, 16.0 mg), and 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (0.240 mmol, 52.3 mg) with isooctane as solvent (0.3 mL,

0.5 M) The 1.0 M scale reaction (Table 3.5, entry 6) was conducted according to the General Procedure using XantPhosCu-O*t*Bu (0.010 mmol, 40 μL of a 0.25 M stock solution prepared in toluene), Na-O*t*Bu (0.200 mmol, 16.0 mg), and 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (0.240 mmol, 52.3 mg) with isooctane as solvent (0.16 mL, 1.0 M). To the resulting mixture for both entries was added *O*-benzoyl-*N*,*N*-diisopropyl hydroxylamine (0.200 mmol, 44.3 mg). The reaction vial was capped and heated to 60 °C with stirring for 24 h.

Table 3.5



Entry[a]	R_2N-OBz	R^1OM	Solvent	Concentration (M)	Yield
1[b]		NaO-*t*Bu	1,4-dioxane	0.1	8
2		LiO-*t*Bu	1,4-dioxane	0.1	56
3		LiO-*t*Bu	toluene	0.1	74
4		LiO-*t*Bu	toluene	0.1	81
5[c]		LiO-*t*Bu	toluene/isooctane	0.5	87
6[c]		LiO-*t*Bu	toluene/isooctane (1:1)	1.0	94

[a] Reactions conducted with 1.2 equiv of boronic ester and 1.0 equiv of ROM. XantPhosCu-O*t*Bu is formed in situ from $(Cu\text{-}OtBu)_4$ and XantPhos. [b] Reaction is conducted at 25 °C and electrophile is completely consumed within 3 h. [c] Reaction conducted at 60 °C and toluene is used to prepare XantPhosCu-O*t*Bu catalyst.

Reactions of *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine with sodium *tert*-butoxide and lithium *tert*-butoxide (Table 3.2).

In a glove box, a 1 dram vial was charged with a stir bar. To the vial was added either Li-O*t*Bu or Na-O*t*Bu (1.00 equiv, 0.100 mmol), and 1,3,5-trimethoxybenzene as an internal standard. To the resulting mixture was added *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine (1.00 equiv, 0.100 mmol) and solvent (0.50 mL). The resulting mixture was capped and heated at 45 °C with stirring. Conversion of *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine was determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as an internal standard. To obtain data for each time point in Table S3, aliquots (0.05 mL) were withdrawn from the reaction mixture and were diluted to 0.50 mL with benzene-d^{6}.

3.6.b. Amination of Aryl Boronic Esters

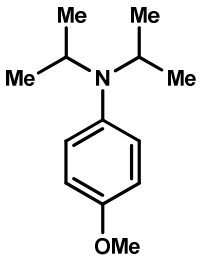
General procedure using alkoxides:

In a glove box, a dram vial was charged with a stir bar. To the vial was added Cu-O*t*Bu tetramer (0.025 equiv, 1.7 mg, 0.0125 mmol), xantphos (0.025 equiv, 7.2 mg, 0.0125 mmol), and toluene (100 μL). After stirring for 30 min at 25 °C, the mixture was transferred to a dram vial containing the boronic ester (1.20 equiv, 0.600 mmol), Li-O*t*Bu (1.00 equiv, 40.0 mg, 0.500 mmol), *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine (1.00 equiv, 0.500 mmol), and isooctane (300 μL). An additional 100 μL of isooctane was used to rinse the dram vial containing the catalyst into the reaction vial. The mixture was allowed to stir at the specified temperature until complete conversion of the hydroxylamine by TLC. The mixture was then diluted in dichloromethane (2 mL), and filtered through a silica plug using successively dichloromethane (5 mL) and then diethyl ether (5 mL) as

an eluent. The solvent was removed under reduced pressure, and the crude product was purified by silica gel chromatography or ion exchange chromatography.

General procedure using CsF:

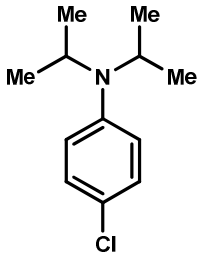
In a glove box, a dram vial was charged with a stir bar. To the vial was added Cu-O*t*Bu tetramer (0.025 equiv, 1.7 mg, 0.0125 mmol), xantphos (0.025 equiv, 7.2 mg, 0.0125 mmol), and toluene (100 μL). After stirring for 30 min at 25 °C, the mixture was transferred to a dram vial containing the boronic ester (1.20 equiv, 0.600 mmol), CsF (5.00 equiv, 379.7 mg, 2.500 mmol), *O*-benzoyl-*N*,*N*-dialkyl hydroxylamine (1.00 equiv, 0.500 mmol), and toluene (400 μL). The mixture was allowed to stir at 60 °C for 72 h. The mixture was then diluted in dichloromethane (2 mL), and filtered through a silica plug using successively dichloromethane (5 mL) and then diethyl ether (5 mL) as an eluent. The solvent was removed under reduced pressure, and the crude product was purified by silica gel chromatography.



_N_,_N_-diisopropyl-4-methoxyaniline (3.7)

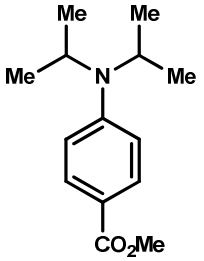
Compound was isolated as a yellow oil (105.6 mg, 85% yield) after purification by ion exchange chromatography. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 6.94 (d, J = 9.1 Hz, 1H), 6.77 (d, J = 9.0 Hz, 1H), 3.60 – 3.46 (m, 1H), 1.02 (d, J = 6.5 Hz, 6H ^{13}C NMR (126 MHz,

$CDCl_3$) δ 155.5, 140.6, 127.6, 113.4, 55.5, 48.6, 21.4.. ESI-MS calculated for $[M]^+$ 207.3, found 207.1. FTIR (neat, cm^{-1}): 3037(m), 2971(s), 1464(m), 1359(m), 1286(m), 1241(s).



4-chloro-*N*,*N*-diisopropylaniline (3.8)

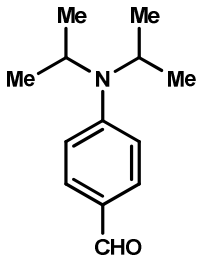
Compound was isolated as a colorless oil (870.4 mg, 82% yield) after purification by silica gel column chromatography (0 → 5% Et_2O/hexanes over 7 CV). ^1H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, J = 9.0 Hz, 2H), 6.81 (d, J = 9.0 Hz, 2H), 3.73 (sept, J = 6.7 Hz, 2H), 1.19 (d, J = 6.7 Hz, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 128.3, 123.1, 120.4, 47.7, 21.3. ESI-MS calculated for $[M+H]^+$ 212.1, found 212.1. FTIR (neat, cm^{-1}): 3051(m), 2972(s), 1595(m), 1499(s), 1265(s), 740(s).



methyl 4-(diisopropylamino)benzoate (3.9)

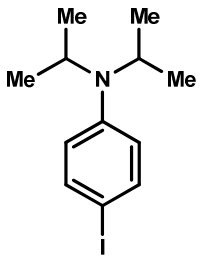
Compound was isolated as a white solid (104.8 mg, 89% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 7 CV). ^1H NMR (300

MHz, $CDCl_3$) δ 7.84 (d, *J* = 9.2 Hz, 1H), 6.77 (d, *J* = 9.2 Hz, 1H), 4.00 – 3.86 (m, 1H), 3.84 (s, 1H), 1.30 (d, *J* = 6.9 Hz, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3, 131.3, 120.6, 110.2, 47.8, 21.4. ESI-MS calculated for $[M]^+$ 235.3, found 235.1. FTIR (neat, cm^{-1}): 2971(s), 2875(m), 2251(m), 1705(s), 1605(s), 1434(s), 1278(s).



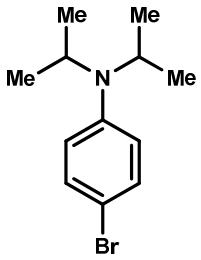
4-(diisopropylamino)benzaldehyde (3.10)

Compound was isolated as a yellow oil (106.0 mg, 94% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 6 CV). ^1H NMR (300 MHz, CD_2Cl_2) δ 9.67 (s, 1H), 7.64 (d, *J* = 9.1 Hz, 2H), 6.86 (d, *J* = 9.1 Hz, 2H), 4.00 (hept, *J* = 6.8 Hz, 2H), 1.33 (d, *J* = 6.9 Hz, 12H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 190.1, 153.6, 131.7, 125.5, 114.6, 48.3, 21.1. ESI-MS calculated for $[M]^+$ 205.3, found 205.1. FTIR (neat, cm^{-1}): 2972(s), 2930(s), 2872(m), 2853(m), 1867(w), 1681(s), 1423(s).



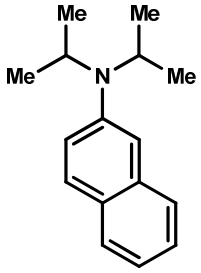
4-iodo-*N*,*N*-diisopropylaniline (3.11)

Compound was isolated as a white-pink solid (125.0 mg, 83% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 8 CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, *J* = 9.0 Hz, 2H), 6.63 (d, *J* = 9.0 Hz, 2H), 3.76 (hept, *J* = 6.8 Hz, 2H), 1.21 (d, *J* = 6.8 Hz, 12H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 148.5, 137.6, 120.4, 78.4, 48.1, 21.5. ESI-MS calculated for $[M]^+$ 303.2, found 303. FTIR (neat, cm^-): 3047(w), 2970(s), 2873(m), 2611(w), 1582(s), 1495(s), 1367(s), 1328(s), 1288(s), 591(w), 553(m).



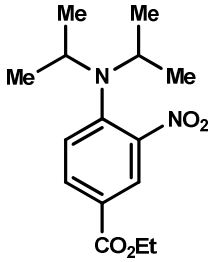
4-bromo-*N*,*N*-diisopropylaniline (3.12)

Compound was isolated as off white solid (107.6 mg, 84% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 6 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.27 (d, *J* = 9.1 Hz, 2H), 6.51 (d, *J* = 9.1 Hz, 2H), 3.32 (hept, *J* = 6.7 Hz, 2H), 0.91 (d, *J* = 6.7 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3, 131.3, 120.6, 110.2, 47.8, 21.4. ESI-MS calculated for $[M+H]^+$ 257.2, found 257. FTIR (neat, cm^{-1}): 3038(w), 2970(s), 2872(m), 2612(w), 1588(s), 1496(s), 1367(s), 1287(s), 732(m).



***N*,*N*-diisopropylnaphthalen-2-amine (3.13)**

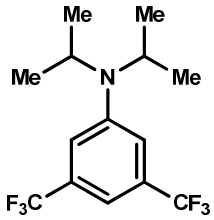
Compound was isolated as a yellow oil (94.9 mg, 84% yield) after purification by ion exchange chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.57 (m, 3H), 7.46 – 7.33 (m, 1H), 7.32 – 7.17 (m, 2H), 7.16 (d, J = 2.1 Hz, 1H), 3.90 (hept, J = 6.6 Hz, 2H), 1.30 (d, J = 6.7 Hz, 12H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 147.0, 135.4, 128.0, 127.9, 127.7, 126.7, 126.3, 122.7, 122.1, 112.8, 48.3, 21.8. ESI-MS calculated for $[M]^+$ 227.3, found 227.1. FTIR (neat, cm^{-1}): 3053(s), 2970(s), 1823(w), 1627(s), 1388(s), 1283(s), 1236(s), 1147(s), 1016(m).



ethyl 4-(diisopropylamino)-3-nitrobenzoate (3.14)

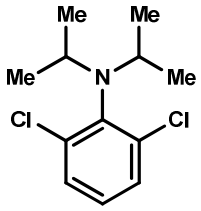
Compound was isolated as a orange oil (129.0 mg, 88% yield) after purification by silica gel column chromatography (0 → 15% ethyl acetate/hexanes over 9 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 8.18 (d, J = 2.1 Hz, 1H), 7.91 (dd, J = 8.5, 2.1 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H), 4.05 (q, J = 7.1 Hz, 2H), 3.22 (hept, J = 6.6 Hz, 2H), 0.96 (t, J = 7.1 Hz, 3H), 0.88 (d, J = 6.6 Hz, 12H). ^{13}C NMR (126 MHz, CD_3CN) δ 165.4, 150.4, 146.6, 132.4,

130.2, 126.8, 125.7, 62.2, 51.4, 21.7, 14.5. ESI-MS calculated for $[M]^+$ 294.4, found 294.1. FTIR (neat, cm^{-1}): 3690(w), 3053(s), 2985(s), 2684(w), 1719(m), 1610(m), 1367(w).



_N_,_N_-diisopropyl-3,5-bis(trifluoromethyl)aniline (3.15)

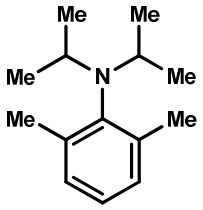
Compound was isolated as a yellow oil (133.6 mg, 85% yield) after purification by silica gel column chromatography (0 → 5% ethyl acetate/hexanes over 9 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.28 (s, 1H), 7.11 (s, 2H), 3.26 (hept, J = 6.8 Hz, 2H), 0.80 (d, J = 6.8 Hz, 12H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 149.5, 132.2 (q, J = 32.2 Hz), 124.7 (q, J = 272.4 Hz), 115.5, 109.3 (dt, J = 7.8, 3.8 Hz), 48.5, 21.3. ESI-MS calculated for $[M]^+$ 313.3, found 313.1. FTIR (neat, cm^{-1}): 3054(m), 2976(s), 1615(s), 1550(w), 1488(s), 1429(s), 1361(s), 1276(s), 1179(s), 1130(s).



2,6-dichloro-_N_,_N_-diisopropylaniline (3.16)

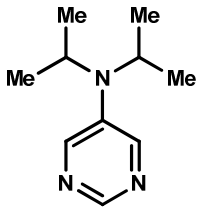
Compound was isolated as a white solid (98.8 mg, 80% yield) after purification by silica gel column chromatography (100% hexanes over 3 CV). ^{1}H NMR (300 MHz, CD_2Cl_2) δ

7.36 (d, J = 8.6 Hz, 1H), 7.29 (d, J = 2.5 Hz, 1H), 7.11 (dd, J = 2.5, 8.2 Hz, 1H), 3.50 (hept, J = 6.4 Hz, 2H), 1.02 (d, J = 6.5 Hz, 12H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 147.3, 132.0, 131.1, 126.8, 50.7, 21.3. ESI-MS calculated for $[M]^+$ 246.2, found 246. FTIR (neat, cm^{-1}): 3052(m), 2971(s), 1577(s), 1463(s), 1381(s), 1264(s), 1131(m), 1092(m), 742(s).



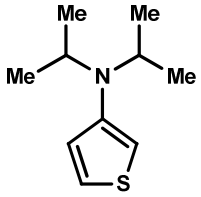
***N*,*N*-diisopropyl-2,6-dimethylaniline (3.17)**

Compound was isolated as a yellow oil (96.7 mg, 94% yield) after purification by ion exchange chromatography. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.02 – 6.96 (m, 2H), 6.96 – 6.90 (m, 1H), 3.55 (hept, J = 6.6 Hz, 2H), 2.26 (s, 6H), 1.02 (d, J = 6.4 Hz, 12H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 147.0, 141.4, 128.3, 125.4, 50.2, 23.7, 20.7. ESI-MS calculated for $[M+H]^+$ 206.3, found 206.1. FTIR (neat, cm^{-1}): 4197(w), 3054(s), 2987(s), 2855(m), 2855(w), 2305(m), 1422(m), 1266(s),



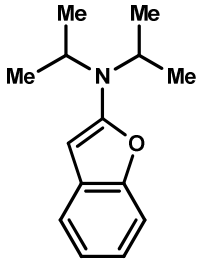
***N*,*N*-diisopropylpyrimidin-5-amine (3.18)**

Compound was isolated as a yellow solid (77.8 mg, 87% yield) after purification by silica gel column chromatography (0 → 30% ethyl acetate/hexanes over 12 CV). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.45 (s, 1H), 8.29 (s, 1H), 3.84 (hept, *J* = 6.8 Hz, 1H), 1.27 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, CD_3CN) δ 147.9, 144.6, 48.0, 21.0. $[M+H]^+$ 180.3, found 180.1. FTIR (neat, cm^{-1} 3052(s), 2985(s), 2886(m), 2688(w), 1367(w), 1264(s).



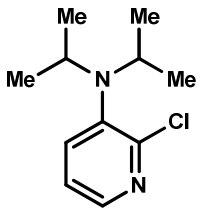
***N*,*N*-diisopropylthiophen-3-amine (3.19)**

Compound was isolated as a yellow brown oil (80.8 mg, 88% yield) after purification by silica gel column chromatography (0 → 10% diethyl ether/hexanes over 6 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 6.89 (dd, *J* = 5.2, 3.1 Hz, 1H), 6.72 (dd, *J* = 5.2, 1.5 Hz, 1H), 6.06 (dd, *J* = 3.1, 1.5 Hz, 1H), 3.34 (hept, *J* = 6.7 Hz, 2H), 0.99 (d, *J* = 6.7 Hz, 12H). ^{13}C NMR (126 MHz, CD_3CN) δ 148.9, 124.2, 124.0, 102.6, 49.2, 21.4. ESI-MS calculated for $[M+H]^+$ 183.3, found 183.1. FTIR (neat, cm^{-1}): 3052(s), 2971(s), 2871(m), 1537(s), 1264(s), 1126(m).



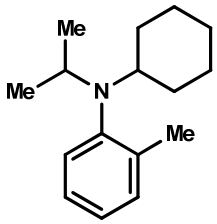
***N*,*N*-diisopropylbenzofuran-2-amine (3.20)**

Compound was isolated as a light orange solid (95.0 mg, 87% yield) after purification by silica gel column chromatography (0 → 5% ethyl acetate/hexanes over 6 CV). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.20 (d, *J* = 7.7 Hz, 2H), 7.03 (td, *J* = 7.5, 1.0 Hz, 1H), 6.95 – 6.82 (m, 1H), 5.34 (s, 1H), 3.76 (hept, *J* = 6.6 Hz, 2H), 1.30 (d, *J* = 6.8 Hz, 12H). ^{13}C NMR (126 MHz, CD_3CN) δ 161.5, 151.0, 132.3, 123.5, 119.9, 118.0, 109.9, 79.7, 49.1, 21.4. ESI-MS calculated for $[M]^+$ 217.3, found 217.1. FTIR (neat, cm^{-1}): 3853(s), 2984(s), 2305(m), 1581(s), 1368(m), 1264(s), 1130(m).



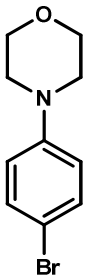
2-chloro-*N*,*N*-diisopropylpyridin-3-amine (3.21)

Compound was isolated as a yellow oil (82.4 mg, 78% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 8 CV). ^{1}H NMR (500 MHz, C_6D_6) δ 7.98 (dd, *J* = 4.5, 1.7 Hz, 1H), 7.04 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.51 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.28 (hept, *J* = 6.6 Hz, 2H), 0.89 (d, *J* = 6.5 Hz, 12H). ^{13}C NMR (126 MHz, CD_3CN) δ 155.2, 146.7, 142.9, 141.2, 123.5, 51.0, 21.5. ESI-MS calculated for $[M+H]^+$ 213.7, found 213. FTIR (neat, cm^{-1}): 3053(s), 2974(s), 1443(m), 1398(s), 1265(s).



***N*-cyclohexyl-*N*-isopropyl-2-methylaniline (3.22)**

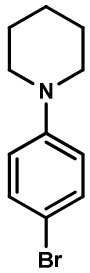
Compound was isolated as a yellow oil (110.0 mg, 95% yield) after purification by ion exchange chromatography. ^{1}H NMR (300 MHz, CD_3CN) δ 7.26 – 7.18 (m, 2H), 7.12 – 7.00 (m, 2H), 3.53 (hept, *J* = 6.8 Hz, 1H), 3.06 (tt, *J* = 10.7, 3.3 Hz, 1H), 2.14 (s, 3H), 1.90 – 1.80 (m, 2H), 1.74 – 1.59 (m, 2H), 1.59 – 1.48 (m, 1H), 1.37 – 1.10 (m, 2H), 1.04 (ddd, *J* = 15.4, 9.4, 3.3 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 147.5, 140.8, 130.7, 130.3, 125.8, 125.3, 59.4, 49.8, 32.1, 26.9, 26.5, 21.4, 19.4. ESI-MS calculated for $[M]^+$ 231.4, found 231.2. FTIR (neat, cm^{-1}): 3052(m), 2931(s), 1379(m), 1361(w), 1264(s), 1109(m), 1066(w).



4-(4-bromophenyl)morpholine (3.23)

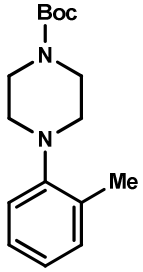
Compound was isolated as a white solid (98.1 mg, 81% yield) after purification by silica gel column chromatography (0 → 17% ethyl acetate/hexanes over 8 CV). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.35 (d, *J* = 9.1 Hz, 1H), 6.79 (d, *J* = 9.1 Hz, 1H), 3.91 – 3.66 (m, 2H), 3.21 – 2.94 (m, 2H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 151.1, 132.4, 117.7, 112.2, 67.3,

49.6. ESI-MS calculated for $[M+H]^+$ 242.1, found 242.9. FTIR (neat, cm^{-1}): 3684(w), 3053(s), 2986(s), 1494(m), 1265(s), 522(w).



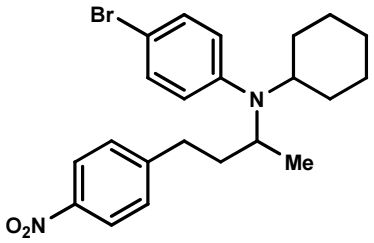
1-(4-bromophenyl)piperidine (3.24)

Compound was isolated as a white solid (96.2 mg, 80% yield) after purification by ion exchange chromatography. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.30 (d, J = 9.1 Hz, 2H), 6.79 (d, J = 9.1 Hz, 2H), 3.15 – 3.08 (m, 4H), 1.71 – 1.64 (dt, J = 11.2, 5.6 Hz, 4H), 1.62 – 1.54 (m, 2H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 151.86 (s), 132.18 (s), 118.33 (s), 111.01 (s), 54.22 (s), 54.12 – 54.05 (m), 53.89 (d, J = 27.2 Hz), 50.75 (s), 26.26 (s), 24.77 (s). ESI-MS calculated for $[M]^+$ 240.1, found 240. FTIR (neat, cm^{-1}): 3053(s), 2986(s), 2940(s), 1856(m), 2827(m), 2305(s), 1588(m), 1421(s), 1264(s), 1130(m), 895(s).



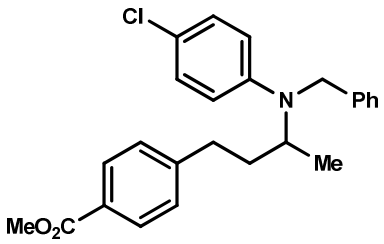
***tert*-butyl 4-(*o*-tolyl)piperazine-1-carboxylate (3.25)**

Compound was isolated as a yellow solid (105.2 mg, 76% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 6 CV). ^{1}H NMR (300 MHz, MeOD) δ 7.25 – 7.11 (m, 2H), 7.03 – 6.77 (m, 2H), 3.61 – 3.54 (m, 2H), 2.98 – 2.56 (m, 2H), 2.31 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (126 MHz, CD_3CN) δ 155.5, 152.5, 133.5, 131.9, 127.6, 124.3, 120.1, 80.0, 52.6, 28.5, 21.8, 17.9. ESI-MS calculated for $[M]^+$ 276.4, found 276. FTIR (neat, cm^{-1}): 3053(s), 2984(m), 2053(m), 1685(m), 1366(m), 1265(s), 1171(m).



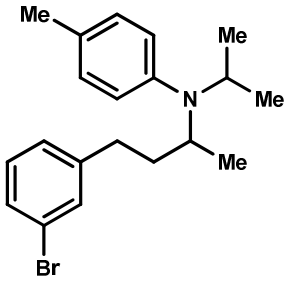
4-bromo-*N*-cyclohexyl-*N*-(4-(4-nitrophenyl)butan-2-yl)aniline (3.26)

Compound was isolated as a yellow oil (86.8 mg, 80% yield) after purification by silica gel column chromatography (0 → 15% ethyl acetate/hexanes over 9 CV). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.9 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 3.48 – 3.39 (m, 1H), 3.19 – 3.09 (m, 1H), 2.59 (t, *J* = 8.1 Hz, 2H), 1.92 – 1.82 (m, 1H), 1.79 – 1.63 (m, 5H), 1.59 – 1.52 (m, 1H), 1.42 – 1.35 (m, 2H), 1.25 – 1.14 (m, 5H), 1.05 – 0.95 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.2, 147.4, 146.4, 131.4, 129.1, 123.7, 121.0, 110.7, 58.7, 52.1, 37.2, 33.6, 32.8, 31.9, 26.3, 26.0, 25.9, 19.8. ESI-MS calculated for $[M+H]^+$ 431.1, found 431.3. FTIR (neat, cm^{-1}): 3053(m), 2988(w), 1420(w), 1267(s), 918(s).



methyl 4-(3-(benzyl(4-chlorophenyl)amino)butyl)benzoate (3.27)

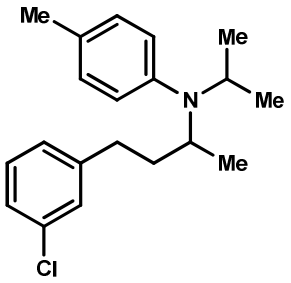
Compound was isolated as a colorless oil (178.2 mg, 87% yield) after purification by silica gel column chromatography (0 → 20% ethyl acetate/hexanes over 8 CV), then ion exchange chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 2H), 7.34 – 7.16 (m, 5H), 7.11 (d, J = 8.3 Hz, 2H), 7.05 (d, J = 9.2 Hz, 2H), 6.55 (d, J = 9.1 Hz, 2H), 4.38 (s, 2H), 3.98 (dq, J = 13.6, 6.7 Hz, 1H), 3.89 (s, 3H), 2.69 (t, J = 7.9 Hz, 2H), 1.99 – 1.91 (m, 1H), 1.83 – 1.74 (m, 1H), 1.21 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 147.9, 147.3, 139.6, 129.8, 128.9, 128.6, 128.4, 128.1, 126.8, 126.5, 121.7, 115.2, 53.6, 52.0, 48.4, 36.2, 33.4, 17.8. ESI-MS calculated for $[M+H]^+$ 408.2, found 408.3. FTIR (neat, cm^{-1}): 3053(m), 2986(w), 1718(s), 1496(m), 1265(s), 738(s).



***N*-(4-(3-bromophenyl)butan-2-yl)-*N*-isopropyl-4-methylaniline (3.28)**

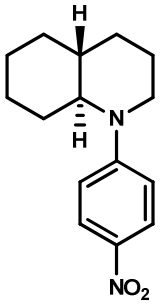
Compound was isolated as a colorless oil (166.3 mg, 92% yield) after purification by silica gel column chromatography (0 → 5% Et_2O/hexanes over 9 CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 2H), 7.02 (d, J = 8.2 Hz, 2H), 6.87 (d, J = 8.1 Hz, 2H),

6.79 – 6.70 (m, 2H), 3.50 – 3.36 (m, 1H), 3.28 – 3.17 (m, 1H), 2.49 – 2.29 (m, 2H), 2.21 (s, 3H), 1.78 – 1.65 (m 1H), 1.47 – 1.34 (m, 1H), 1.16 – 0.91 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.7, 145.0, 131.5, 129.9, 129.1, 128.9, 128.7, 127.1, 122.5, 121.0, 52.2, 48.4, 37.7, 33.2, 22.6, 21.4, 20.6, 19.2. ESI-MS calculated for $[M+H]^+$ 360.1, found 360.5. FTIR (neat, cm^{-1}): 3047(w), 2968(m), 1514(m), 1265(s), 739(s).



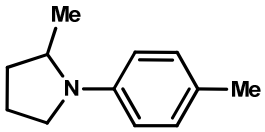
***N*-(4-(3-chlorophenyl)butan-2-yl)-*N*-isopropyl-4-methylaniline (3.29)**

Compound was isolated as a colorless oil (128.9 mg, 81% yield) after purification by silica gel column chromatography (0 → 15% ethyl acetate/hexanes over 7 CV, then 0 → 5% Et_2O/hexanes over 7 CV. ^{1}H NMR (300 MHz, C_6D_6) δ 7.19 (s, 1H), 7.17 – 7.09 (m, 3H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.91 (t, *J* = 7.7 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 3.52 (dq, *J* = 13.2, 6.6 Hz, 1H), 3.38 – 3.30 (m, 1H), 2.53 – 2.46 (m, 2H), 2.31 (s, 3H), 1.81 (tdd, *J* = 10.2, 8.8, 5.8 Hz, 1H), 1.59 – 1.45 (m, 1H), 1.25 – 1.00 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.7, 144.7, 134.1, 129.5, 129.1, 128.6, 128.0, 127.8, 127.6, 126.6, 125.9, 121.0, 52.2, 48.4, 37.6, 33.2, 22.5, 21.5, 20.5, 19.1. ESI-MS calculated for $[M+H]^+$ 315.2, found 315.3. FTIR (neat, cm^{-1}): 3054(m), 2987(w), 1419(w), 1265(s), 741(s).



(4aR,8aS)-1-(4-nitrophenyl)decahydroquinoline (3.30)

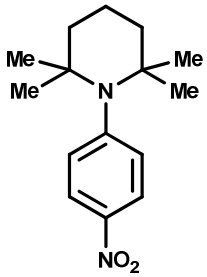
Compound was isolated as a yellow solid (123.7 mg, 95% yield) after purification by silica gel column chromatography (0 → 4% ethyl acetate/hexanes over 4 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 8.03 (d, *J* = 9.3 Hz, 2H), 6.32 (d, *J* = 9.3 Hz, 2H), 2.94 – 2.92 (m, 2H), 2.84 – 2.58 (m, 1H), 2.34 (td, *J* = 10.6, 3.0 Hz, 1H), 1.77 – 1.22 (m, 6H), 1.22 – 0.95 (m, 3H), 0.95 – 0.63 (m, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 155.51 (s), 138.25 (s), 126.18 (s), 114.54 (s), 64.96 (s), 54.22 (s), 54.00 (s), 53.78 (s), 44.08 (s), 40.12 (s), 33.72 (s), 30.55 (s), 27.70 (s), 26.75 (s), 25.77 (s), 23.54 (s). ESI-MS calculated for $[M+H]^+$ 260.3, found 260.1. FTIR (neat, cm^{-1}): 3053(m), 2986(m), 2934(m), 1594(m), 1421(m), 1312(m), 1264(s), 1113(w), 895(m), 705(s).



2-methyl-1-(*p*-tolyl)pyrrolidine (3.31)

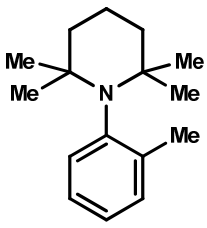
Compound was isolated as a colorless oil (79.1 mg, 90% yield) after purification by silica gel column chromatography (0 → 5% ethyl acetate/hexanes over 8 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.13 (d, *J* = 8.7 Hz, 2H), 6.56 (d, *J* = 8.5 Hz, 2H), 3.80 – 3.49 (m, 1H), 3.13 (dt, *J* = 12.4, 6.1 Hz, 1H), 2.88 (dt, *J* = 14.6, 6.9 Hz, 1H), 2.28 (s, 3H), 1.74 – 1.57

(m, 2H), 1.55 – 1.42 (m, 1H), 1.32 – 1.18 (m, 1H), 0.98 (d, J = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4, 129.7, 124.3, 112.0, 53.8, 48.5, 33.2, 23.4, 20.3, 19.6. ESI-MS calculated for $[M+H]^+$ 176.1, found 176.1. FTIR (neat, cm^{-1}): 3053(m), 2985(w), 1521(w), 1265(s).



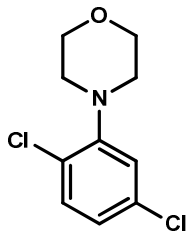
2,2,6,6-tetramethyl-1-(4-nitrophenyl)piperidine (3.32)

Compound was isolated as a yellow oil (114.3 mg, 87% yield) after purification by silica gel column chromatography (100% hexanes over 2CV). ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 9.0 Hz, 2H), 7.35 (d, J = 9.0 Hz, 2H), 1.74 (ddd, J = 11.3, 8.1, 3.2 Hz, 2H), 1.67 – 1.46 (m,4H), 1.32 – 1.14 (m, 2H), 1.03 (s,12H).^{13}C NMR (126 MHz, $CDCl_3$) δ 154.51, 145.69, 134.75, 123.21, 54.72, 42.14, 29.81, 18.27. ESI-MS calculated for $[M]^+$ 262.4, found 262.1. FTIR (neat, cm^{-1}): 3085(w), 2968(s), 2869(m), 1586(s), 1345(s), 1277(s), 1174(m), 1130(s), 1036(m),



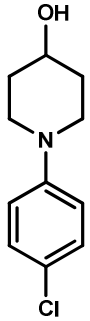
2,2,6,6-tetramethyl-1-(*o*-tolyl)piperidine (3.33)

Compound was isolated as a yellow oil (102.9 mg, 89% yield) after purification by silica gel column chromatography (100% hexanes over 2 CV). ^{1}H NMR (300 MHz, C_6D_6) δ 7.34 – 7.27 (m, 1H), 7.21 (dd, *J* = 5.5, 3.8 Hz, 1H), 7.10 – 7.01 (m, 2H), 2.37 (s, 3H), 1.93 – 1.71 (m, 1H), 1.70 – 1.42 (m, 5H), 1.25 (s, 6H), 0.79 (s, 6H). ^{13}C NMR (75 MHz, C_6D_6) δ 145.9, 141.5, 132.4, 130.9, 125.8, 125.5, 55.3, 42.4, 32.0, 25.7, 19.9, 19.0. ESI-MS calculated for $[M]^+$ 231.4, found 231.2. FTIR (neat, cm^{-1}): 3053(s), 2971(s), 1486(m), 1349(m), 1265(s), 895(m).



4-(2,5-dichlorophenyl)morpholine (3.34)

Compound was isolated as a colorless oil (105.8 mg, 91% yield) after purification by silica gel column chromatography (0 → 5% Et_2O/hexanes over 7 CV). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 2.2 Hz, 1H), 6.61 (dd, *J* = 8.4, 2.1 Hz, 1H), 3.64 – 3.43 (m, 4H), 2.60 – 2.36 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.0, 133.2, 131.5, 127.0, 123.7, 120.8, 67.0, 51.5. ESI-MS calculated for $[M+H]^+$ 232.0, found 232.1. FTIR (neat, cm^{-1}): 3054(s), 2986(m), 1421(w), 1265(s), 736(s).



4-hydroxy-1-(4-chlorophenyl)piperidine (3.36)

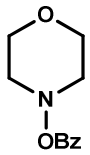
Compound was isolated as white needles (79.2 mg, 75% yield) after purification by silica gel column chromatography (40 → 70% Et_2O/hexanes over 7 CV). ^1H NMR (300 MHz, C_6D_6) δ 7.13 (d, *J* = 9.1 Hz, 2H), 6.43 (d, *J* = 9.0 Hz, 2H), 3.29 (dtt, *J* = 12.6, 8.4, 4.0 Hz, 1H), 3.15 – 2.97 (m, 2H), 2.39 (ddd, *J* = 12.6, 9.6, 3.2 Hz, 2H), 1.61 – 1.41 (m, 2H), 1.36 – 1.21 (m, 2H), 0.66 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 129.1, 124.4, 117.8, 67.8, 47.4, 34.1. ESI-MS calculated for $[M]^+$ 212.2, found 212.3. FTIR (neat, cm^{-1}): 3404(br), 2951(m), 1635(br), 1495(s), 1041(s), 733(s).

3.6.c. Synthesis of O-benzoyl-N,N-dialkyl hydroxylamines

General:

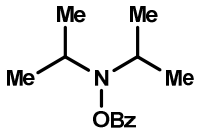
The *O*-benzoyl-*N*,*N*-dialkyl hydroxylamines were synthesized according to a modified literature procedure.[10a] To a reaction flask under nitrogen was added potassium hydrogen phosphate (5.00 equiv) and benzoyl peroxide (1.20 equiv), followed by DMF (1.0 M). With vigorous stirring, the secondary amine (1.00 equiv) was added, and the resulting mixture stirred for 25 °C until complete conversion of the amine as indicated by TLC. The solids were filtered off through a plug of silica using diethyl ether as the eluent. The

organics were concentrated and the crude product was purified by silica gel chromatography or ion exchange chromatography.



4-benzoyloxymorpholine (3.1)

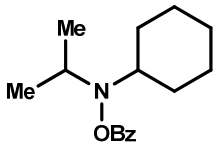
Compound was isolated as a white solid (2942.1 mg, 71% yield) after purification by silica gel column chromatography (0 → 50% diethyl ether/hexanes over 9 CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 – 7.80 (m, 2H), 7.57 (dd, *J* = 10.5, 4.4 Hz, 1H), 7.45 (t, *J* = 7.5 Hz,2H), 4.08 – 3.76 (m, 4H), 3.46 (d, *J* = 9.9 Hz, 2H), 3.05 (t, *J* = 10.7 Hz, 2H ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.59, 133.23, 129.47, 129.20, 128.49, 65.87, 57.02. ESI-MS calculated for $[M]^+$ 207.2, found 207. FTIR (neat, cm^{-1}): 3053(s), 2986(s), 2858(m) 1691(m), 1264(s), 1160(w), 895(m).



***O*-benzoyl-*N*,*N*-diisopropylhydroxylamine (3.2)**

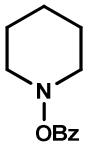
Compound was isolated as a light colored yellow oil which solidifies into a white crystalline product (1992.1 mg, 60% yield) after purification by silica gel column chromatography (0 → 20% ethyl acetate/hexanes over 9 CV). ^{1}H ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 – 7.92 (m, 2H), 7.57 (dd, *J* = 10.4, 4.4 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 3.85 – 2.97 (m, 2H), 1.17 (d, *J* = 6.4 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.33,

132.98, 129.61, 129.46, 128.48, 53.60, 19.97, 17.67. ESI-MS calculated for $[M]^+$ 221.3, found 221.1. FTIR (neat, cm^{-1}): 3053(s), 2984(s), 2939.8(m), 1737(s), 1601(w), 1584(w), 1421(s), 1384(m), 1264(s), 1025(s), 895(s), 746(s).



_O_-benzoyl-_N_-cyclohexyl-_N_-isopropylhydroxylamine (S1)

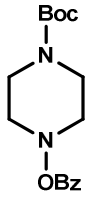
Compound was isolated as a white solid (991.7 mg, 40% yield) after purification by silica gel column chromatography (0 → 15% ethyl acetate/hexanes over 9CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 – 7.94 (m, 2H), 7.64 – 7.52 (m, 1H), 7.50 – 7.38 (m, 2H), 3.72 – 3.33 (m, 1H), 3.27 – 2.83 (m, 1H), 1.85 (dd, J = 33.2, 11.2 Hz, 4H), 1.63 (d, J = 11.6 Hz, 1H), 1.52 – 0.94 (m, 11H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.39, 133.02, 129.71, 129.55, 128.54, 61.88, 52.69, 30.10, 28.78, 26.01, 25.35. ESI-MS calculated for $[M]^+$ 261.4, found 261. FTIR (neat, cm^{-1}): 3053(s), 2986(s), 2684(m), 1710(m), 1601(w), 1266(s), 1158(w), 1082(w), 1063(w), 894(s), 743(s).



piperidin-1-yl benzoate (S2)

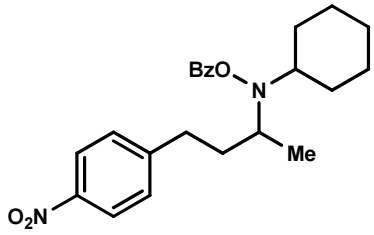
Compound was isolated as a white solid (2627.0 mg, 64% yield) after purification by silica gel column chromatography (0 → 20% diethyl ether/hexanes over 9CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 – 7.87 (m, 2H), 7.61 – 7.51 (m, 1H), 7.49 – 7.36 (m, 2H), 3.62

– 3.35 (m, 2H), 2.78 (m, J = 8.9, 8.3 Hz, 2H), 1.97 – 1.77 (m, 4H), 1.75 – 1.54 (m, 1H), 1.45 – 0.94 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.85, 133.01, 129.78, 129.52, 128.46, 77.16, 57.63, 25.09, 23.44. ESI-MS calculated for $[M]^+$ 205.3, found 205. FTIR (neat, cm^{-1}): 3943(w), 3053(s), 2985(s), 1732(s), 1421(m), 1264(s), 1177(w), 1068(m), 1016(m), 895(m),745(s).



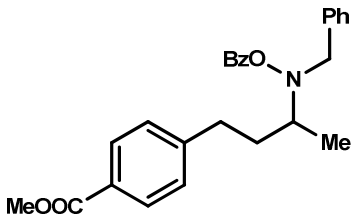
***tert*-butyl 4-(benzoyloxy)piperazine-1-carboxylate (S3)**

Compound was isolated as a white solid (1166.6 mg, 71% yield) after purification by silica gel column chromatography (0 → 20% ethyl acetate/hexanes over 9 CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 – 7.77 (m, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 4.05 (s, 2H), 3.53 – 3.26 (m, 4H), 2.92 (s, 2H), 1.48 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.99, 153.96, 132.81, 129.03, 128.78, 128.09, 79.65, 55.45, 41.56, 28.00. $[M+H]^+$ 307.4, found 307.8. FTIR (neat, cm^{-1}): 3053(s), 2986(s), 2938(m), 2857(w), 2830(w), 2684(m), 1739(m), 1601(w), 1421(s), 1265(s).



***O*-benzoyl-*N*-cyclohexyl-*N*-(4-(4-nitrophenyl)butan-2-yl)hydroxylamine (S4)**

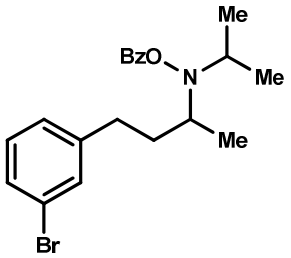
Compound was isolated as a colorless oil (235.0 mg, 29% yield) after purification by silica gel column chromatography (0 → 15% Et_2O/hexanes over 7 CV, then 0 → 30% ethyl acetate/hexanes over 7 CV), then ion exchange chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.7 Hz, 2H), 8.02 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (dd, *J* = 7.6, 8.4 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 3.42 – 3.21 (m, 1H), 3.16 – 2.95 (m, 2H), 2.95 – 2.70 (m, 1H), 1.94 – 1.69 (m, 4H), 1.69 – 1.49 (m, 3H), 1.44 – 1.14 (m, 8H). ^{13}C NMR (126 MHz, C_6D_6) δ 166.5, 151.1, 146.7, 133.5, 130.0, 129.8, 129.6, 128.9, 124.0, 62.0, 56.5, 31.0, 30.7, 26.2, 25.3, 25.1, 24.9. ESI-MS calculated for $[M+H]^+$ 397.2, found 397.2. FTIR (neat, cm^{-1}): 2984(m), 2940(w), 1738(s), 1448(m), 1374(s), 1245(s), 908(s).



methyl 4-(3-((benzoyloxy)(benzyl)amino)butyl)benzoate (S5)

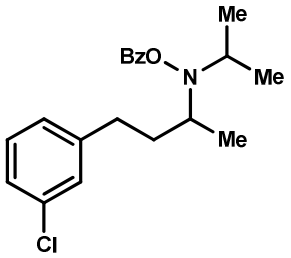
Compound was isolated as a colorless oil (1151.4 mg, 75% yield) after purification by silica gel column chromatography (0 → 15% Et_2O/hexanes over 9 CV). ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 – 7.85 (m, 4H), 7.59 – 7.50 (m, 1H), 7.48 – 7.37 (m, 4H), 7.33 – 7.23 (m, 3H), 7.19 (d, *J* = 8.2 Hz, 2H), 4.27 (d, *J* = 13.2 Hz, 1H), 4.09 (d, *J* = 13.2 Hz, 1H), 3.87 (s, 3H), 3.24 – 3.02 (m, 1H), 2.95 – 2.80 (m, 2H), 2.08 – 1.87 (m, 1H), 1.79 – 1.63 (m, 1H), 1.30 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 165.2, 148.0, 136.4, 132.9, 129.7, 129.5, 129.3, 128.6, 128.5, 128.4, 128.3, 127.7, 127.6, 59.3,

58.9, 51.9, 35.7, 32.6, 14.1. ESI-MS calculated for $[M]^+$ 440.2, found 440.3. FTIR (neat, cm^{-1}): 3030(w), 2949(m), 1742(s), 1720(s), 1279(s).



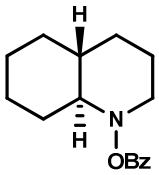
***O*-benzoyl-*N*-(4-(3-bromophenyl)butan-2-yl)-*N*-isopropylhydroxylamine (S6)**

Compound was isolated as a colorless oil (486.0 mg, 67% yield) after purification by silica gel column chromatography (0 → 10% Et_2O/hexanes over 7 CV), then ion exchange chromatography. ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.34 (s, 1H), 7.32 – 7.27 (m, 1H), 7.11 (d, J = 4.9 Hz, 2H), 3.43 – 3.38 (m, 1H), 3.23 (dt, J = 12.6, 6.3 Hz, 1H), 2.86 – 2.72 (m, 2H), 1.93 – 1.84 (m, 1H), 1.70 – 1.60 (m, 2H), 1.20 (d, J = 6.2 Hz, 3H), 1.13 (d, J = 6.2 Hz, 6H). ^{13}C NMR (126 MHz, C_6D_6) δ 166.6, 145.2, 133.4, 132.0, 130.3, 130.0, 129.7,129.3, 128.9, 127.6, 122.8, 57.4, 54.1, 32.6, 20.8. ESI-MS calculated for $[M+H]^+$ 390.1, found 390.2. FTIR (neat, cm^{-1}): 2979(m), 2876(w), 1739(s), 1451(m), 1257(s), 910(s).



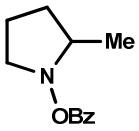
_O_-benzoyl-_N_-(4-(3-chlorophenyl)butan-2-yl)-_N_-isopropylhydroxylamine (S7)

Compound was isolated as a colorless oil (612.2 mg, 80% yield) after purification by silica gel column chromatography (0 → 10% Et_2O/hexanes over 7 CV). ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.27 – 7.01 (m, 4H), 3.53 – 3.30 (m, 1H), 3.23 (dt, J = 12.6, 6.3 Hz, 1H), 2.85 – 2.75 (m, 2H), 1.94 – 1.83 (m, 1H), 1.69 – 1.58 (m, 1H), 1.20 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.2 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 144.5, 134.0, 133.0, 129.6, 129.4, 128.7, 128.5, 126.8, 125.9, 57.1, 53.7, 32.2, 20.4. ESI-MS calculated for $[M+Na]^+$ 368.5, found 368.2. FTIR (neat, cm^{-1}): 2979(m), 2875(w), 1740(s), 1451(m), 1256(s), 908(s).



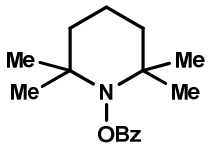
(4aR,8aS)-octahydroquinolin-1(2H)-yl benzoate (S8)

Compound was isolated as a white solid (1829.4 mg, 54% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes with 3% toluene as an additive over 9 CV). ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 3.58 (d, J = 9.5 Hz, 1H), 2.88 – 2.60 (m, 1H), 2.42 (t, J = 10.2 Hz, 1H), 1.97 (dt, J = 16.4, 11.6 Hz, 2H), 1.83 – 1.44 (m,6H), 1.46 – 0.90 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.26, 132.95, 129.66, 129.52, 128.45, 77.16, 71.71, 58.11, 41.36, 32.59, 31.39, 29.93, 25.78, 24.91, 24.68. ESI-MS calculated for $[M+H]^+$ 260.3, found 261. FTIR (neat, cm^{-1}): 3049(s), 2982(s), 1738(s), 1603(w), 1424(m), 1262(s), 1024(w), 704(s).



2-methylpyrrolidin-1-yl benzoate (S9)

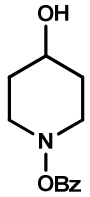
Compound was isolated as a colorless oil (529.4 mg, 56% yield) after purification by silica gel column chromatography (0 → 30% ethyl acetate/hexanes over 7 CV), then ion exchange chromatography. ^{1}H NMR (300 MHz, C_6D_6) δ 8.10 (d, *J* = 6.8 Hz, 2H), 7.12 – 6.98 (m, 3H), 3.65 – 3.40 (m, 1H), 3.22 – 2.92 (m, 1H), 2.74 (dt, *J* = 19.1, 8.7 Hz, 1H), 1.65 – 1.36 (m, 3H), 1.33 – 1.17 (m, 1H), 1.14 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 132.9, 129.6, 129.5, 128.4, 63.7, 56.3, 28.8, 20.5, 17.9. ESI-MS calculated for $[M+Na]^+$ 228.1, found 228.1. FTIR (neat, cm^{-1}): 3054(s), 2986(m), 1734(m), 1420(m), 1265(s).



2,2,6,6-tetramethylpiperidin-1-yl benzoate (S10)

Compound was isolated as a white solid (2522.0 mg, 64% yield) after purification by silica gel column chromatography (0 → 10% ethyl acetate/hexanes over 8 CV). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 – 7.95 (m, 2H), 7.62 – 7.54 (m, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 1.63 (ddd, *J* = 46.5, 29.7, 11.6 Hz, 6H), 1.28 (s, 6H), 1.12 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.57, 133.04, 129.95, 129.78, 128.65, 77.16, 60.62, 39.27, 32.18, 21.05, 17.21. ESI-MS calculated for $[M]^+$ 261.4, found 261.1. FTIR (neat, cm^{-1}): 3944(w),

3053(s), 2983(m), 2304(w), 1742(s), 1584(w), 1450(m), 1380(w), 1264(s), 1084(m), 1065(m), 1025(m).

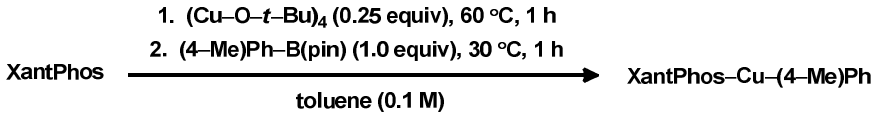


4-hydroxy piperidin-1-yl benzoate (3.35)

Compound was isolated as a white powder (759.0 mg, 79% yield) after purification by silica gel column chromatography (50 → 80% ethyl acetate/hexanes over 8 CV). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 3.92 (s, 1H), 3.63 - 3.52 (m, 1H), 3.39- 3.22 (m, 2H), 2.94 - 2.83 (m, 1H), 2.16 - 2.00 (m, 2H), 1.94 - 1.82 (m, 2H), 1.54 - 1.45 (m, 1H). ^{13}C NMR (126 MHz, C_6D_6) δ 164.9, 133.1, 129.4, 128.4, 67.1, 63.8, 54.3, 52.1, 33.0, 31.5. ESI-MS calculated for $[M+Na]^+$ 244.1, found 244.1. FTIR (neat, cm^{-1}): 3417(br), 3057(m), 2952(s), 1734(s), 1601(w), 1450(m), 1258(s), 1063(m).

3.6.d. Stoichiometric Reactions of Organocopper Complexes

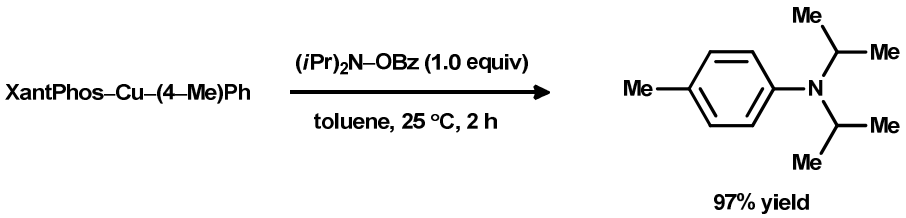
Preparation of XantPhosCu-(4-Me)Ph (**3.37**):



The reaction was performed according to a modified literature procedure.[17] A scintillation vial was charged with a stir bar. To the vial was added copper *tert*-butoxide tetramer (0.25 equiv, 0.125 mmol, 68.3 mg) and XantPhos (1.00 equiv, 0.500 mmol, 289.3 mg), and toluene (4.0 mL). The resulting solution was capped and stirred at 60 °C

for 1 h. After cooling to room temperature, 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane (1.00 equiv, 0.5 mmol, 109.1 mg) was added to the stirred heterogeneous mixture as a solution in toluene (1.0 mL, 0.1 M final concentration). The reaction vial was capped and allowed to stir at 30 °C for 1 h. Within 5 minutes of addition of tolyl boronic ester, the heterogenous mixture turned into a homogeneous solution. After 0.5 h of stirring, the homogeneous solution became a heterogeneous mixture with a large amount of precipitate. After 1 h of stirring, this precipitate was filtered and rinsed thoroughly with pentane (10 mL) and cold diethyl ether (3 x 2 mL portions) to afford XantPhosCu-(4-Me)Ph as a pale yellow solid (233.0 mg, 63.5% yield). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.54 (s, 2H), 7.48 – 7.18 (m, 26 H), 7.11 (s, 2 H), 3.92 (s, 1H), 6.74 (d, *J* = 6.9 Hz, 2 H), 6.60 (s, 2 H), 2.19 (s, 3 H), 1.67 (s, 6 H). ^{13}C NMR (125 MHz, CD_2Cl_2) δ 155.8, 143.2, 142.0, 138.0, 134.4, 133.4, 132.0, 130.0, 129.0, 128.5, 128.4, 128.2, 127.2, 125.0, 121.9, 28.4, 21.6. ^{31}P NMR (202 MHz, CD_2Cl_2) δ -16.49 (s).

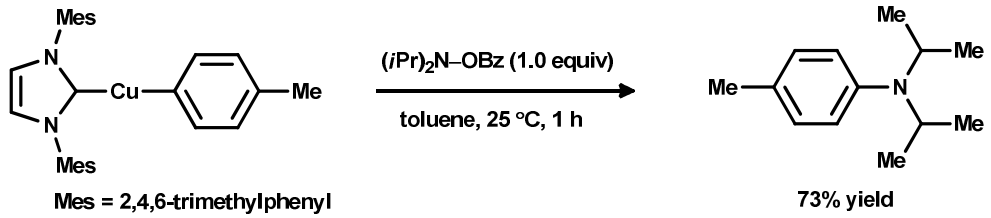
<u>With XantPhosCu-(4-Me)Ph:</u>



A 1-dram reaction vial was charged with a stir bar. To the vial was added XantPhosCu-(4-Me)Ph (1.00 equiv, 0.050 mmol, 36.7 mg) and toluene (0.25 mL). To a shell vial was added *O*-benzoyl-*N*,*N*-diisopropylhydroxylamine (1.00 equiv, 0.050 mmol, 11.1 mg), dodecane as an internal standard, and toluene (0.25 mL). The solution containing hydroxylamine was withdrawn and added to the stirred solution of XantPhosCu-(4-

Me)Ph over one minute. The vial was capped and stirred at 25 °C for 2 h. After 1 h, GC analysis using dodecane as an internal standard indicated the yield of *N*,*N*-diisopropyl-4-methylaniline was 89%. The yield of desired product had increased to 97% within 2 h. The reaction was finished within 2 h. This complex was also substituted for XantPhosCu-O-*t*-butoxide as a catalyst in a reaction using *O*-benzoyl-*N*,*N*-diisopropyl hydroxylamine and tolyl(neopentyl)boronic ester under the conditions described in **Table S1** (Entry 15). After 24 h reaction time, a 93% yield of product was obtained.

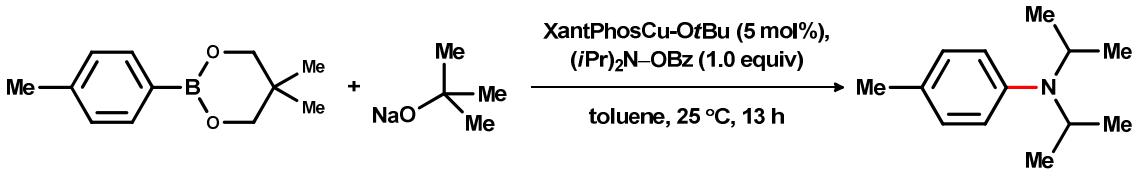
With IMesCu-(4-Me)Ph:[17]



A 1-dram vial was charged with a stir bar. To the vial was added *O*-benzoyl-*N*,*N*-diisopropylhydroxylamine (1.00 equiv, 0.100 mmol, 22.1 mg), 1,3,5-trimethoxybenzene, and toluene (0.2 mL). To a shell vial was added IMesCu-(4-Me)Ph (1.00 equiv, 0.100 mmol, 45.9 mg) and toluene (0.2 mL). This solution was then added over 1 min to the stirred solution of *O*-benzoyl-*N*,*N*-diisopropylhydroxylamine and the shell vial rinsed with toluene (0.1 mL). The reaction vial was capped and stirred at 25 °C. Yield of *N*,*N*-diisopropyl-4-methylaniline was determined by GC using 1,3,5-trimethoxybenzene as an internal standard. The reaction was completed within 1 h. This complex was also substituted for IMesCu-O-*t*-butoxide as a catalyst in a reaction using *O*-benzoyl-*N*,*N*-diisopropyl hydroxylamine and tolyl(neopentyl)boronic ester under the conditions

described in **Table S1** (Entry 15). After 24 h reaction time, an 82% yield of product was obtained in this catalytic reaction.

3.6.e. Reaction Rate as a Function of Added Equivalents of Sodium tert-Butoxide



Reactions a – c (Figure 3.2):

All reactions were performed in a glove box. A 1-dram reaction vial was charged with a stir bar. To the vial were added 2-(*p*-tolyl)-5,5-dimethyl-1,3,2-dioxaborinane (1.20 equiv, 0.120 mmol, 24.5 mg), XantPhosCu-O-*t*-butoxide (0.05 equiv, 0.005 mmol, 50 μL of a 0.1 M stock solution prepared in benzene-d^6), 1,3,5-trimethoxybenzene as an internal standard, varying amounts of sodium *tert*-butoxide (**a**: 1.00 equiv, **b**: 1.60, and **c**: 2.00 equiv) and 950 μL of benzene-d^6. To the resulting homogeneous solution was added *O*-benzoyl-*N*,*N*-diisopropyl hydroxylamine (1.00 equiv, 0.10 mmol, 22.1 mg), and the reaction vial was capped and heated to 25 °C with stirring. To obtain data for product yield and the conversion of *O*-benzoyl-*N*,*N*-diisopropyl hydroxylamine, 50 μL of the stirred solution was diluted to 500 μL with benzene-d^6 and the extent of conversion was determined by ^{1}H-NMR. To determine the yield of *N*,*N*-diisopropyl-4-methylaniline[34] (indicated as **a** – **b** in **Graph S1** below), 200 μL of this NMR solution was filtered through a pipette tip with 2 cm of silica and eluted directly into a GC vial with 2 mL of 1:1 (v:v) dichloromethane:ethyl acetate solution. 1,3,5-trimethoxybenzene was used as an internal standard for both GC and ^{1}H NMR analysis.

Reaction d (Figure 3.2):

To demonstrate that catalytic activity can be restored when excess base is present, the reaction with 2.00 equivalents of sodium *t*-butoxide was repeated. After 1 h, 2-(*p*-tolyl)-5,5-dimethyl-1,3,2-dioxaborinane (1.00 equiv, 0.100 mmol, 20.4 mg in addition to the amount already present initially) was added and the reaction was stirred at 25 °C. Yield of *N*,*N*-diisopropyl-4-methylaniline (indicated as **d** in the **Graph S1** below) was determined by filtering reaction aliquots through a pipette tip with 2 cm of silica, using 2 mL of a 1:1 (v:v) dichloromethane:ethyl acetate solution as an eluent, and then analyzing the reaction mixture by GC.

Section 7: References to Chapter 3

(1) Rucker, R. P. Whittaker., A. M.; Dang, H.; Lalic, G. *Angew. Chem., Int. Ed. Engl.* **2012**, *124*, 4019.
(2) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337.
(3) (a) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382; (b) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1348; (c) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609.
(4) (a) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400; (b) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954; (c) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534; (d) Maiti, D.; Fors, B. P.; Henderson, J. L.; Nakamura, Y.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 57; (e) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338; (f) Surry, D. S. B., S. L. *Chem. Sci.* **2011**, *2*, 27
(5) Iyer, S.; Kulkarni, G. M.; Ramesh, C.; Sattar, A. K. *Indian J. Chem., Sect. B* **2005**, *44B*, 1894.
(6) Ueno, A.; Kitawaki, T.; Chida, N. *Org. Lett.* **2008**, *10*, 1999.
(7) Foo, K.; Newhouse, T.; Mori, I.; Takayama, H.; Baran, P. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 2716.
(8) (a) Baston, E.; Maggi, R.; Friedrich, K.; Schlosser, M. *Eur. J. Org. Chem.* **2001**, *2001*, 3985; (b) Bolliger, J. L.; Frech, C. M. *Tetrahedron* **2009**, *65*, 1180; (c) Shi, L.; Wang, M.; Fan, C.-A.; Zhang, F.-M.; Tu, Y.-Q. *Org. Lett.* **2003**, *5*, 3515; (d) Tripathy, S.; LeBlanc, R.; Durst, T. *Org. Lett.* **1999**, *1*, 1973.
(9) (a) Berman, A. M.; Johnson, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 5680; (b) Del, A. V.; Dubbaka, S. R.; Krasovskiy, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 7838.
(10) (a) Berman, A. M.; Johnson, J. S. *J. Org. Chem.* **2006**, *71*, 219; (b) Campbell, M. J.; Johnson, J. S. *Org. Lett.* **2007**, *9*, 1521.
(11) (a) Barker, T. J.; Jarvo, E. R. *J. Am. Chem. Soc.* **2009**, *131*, 15598; (b) Barker, T. J.; Jarvo, E. R. *Synthesis* **2011**, 3954; (c) Barker, T. J.; Jarvo, E. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 8325; (d) Liu, S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2008**, *130*, 6918; (e) Yu, Y.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2004**, *6*, 2631; (f) Zhang, Z.; Yu, Y.; Liebeskind, L. S. *Org. Lett.* **2008**, *10*, 3005.
(12) He, C.; Chen, C.; Cheng, J.; Liu, C.; Liu, W.; Li, Q.; Lei, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 6414.
(13) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941.
(14) Chan, D. M. T.; Monaco, K. L.; Wang, R. P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933.
(15) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937.
(16) Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397.
(17) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216.
(18) (a) Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116; (b) Kakiuchi, F.; Matsuura, Y.; Kan, S.; Chatani, N. *J. Am. Chem. Soc.* **2005**, *127*, 5936; (c) Shintani, R.; Takatsu, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 3735.

(19) Lemmen, T. H.; Goeden, G. V.; Huffman, J. C.; Geerts, R. L.; Caulton, K. G. *Inorg. Chem.* **1990**, *29*, 3680.
(20) Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 5792.
(21) (a) Stollenz, M.; Meyer, F. *Organometallics* **2012**, *31*, 7708; (b) Yoshikai, N. N., E. *Chem. Rev.* **2012**, *112*, 2339; (c) Gschwind, R. M. *Chem. Rev.* **2008**, *108*, 3029.
(22) For an example of an isolated copper complex supported by PPh_3, see: Niemeyer, M. *Zeitschrift für anorganische und allgemeine Chemie* **2003**, *629*, 1535; for an example using triphos, see: Gambarotta, S.; Strologo, S.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *Organometallics* **1984**, *3*, 1444.
(23) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
(24) (a) Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229; (b) Takaya, Y.; Senda, T.; Kurushima, H.; Ogasawara, M.; Hayashi, T. *Tetrahedron: Asymmetry* **1999**, *10*, 4047.
(25) Tatamidani, H.; Yokota, K.; Kakiuchi, F.; Chatani, N. *J. Org. Chem.* **2004**, *69*, 5615.
(26) (a) Tsunoyama, H.; Sakurai, H.; Ichikuni, N.; Negishi, Y.; Tsukuda, T. *Langmuir* **2004**, *20*, 11293; (b) Carrettin, S.; Guzman, J.; Corma, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 2242.
(27) Partyka, D. V. *Chem. Rev.* **2011**, *111*, 1529.
(28) Dang, L.; Lin, Z.; Marder, T. B. *Organometallics* **2010**, *29*, 917.
(29) Kleeberg, C.; Dang, L.; Lin, Z.; Marder, T. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 5350.
(30) King, A. E.; Ryland, B. L.; Brunold, T. C.; Stahl, S. S. *Organometallics* **2012**, *31*, 7948.
(31) (a) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461; (b) Cammidge, A. N.; Goddard, V. H. M.; Gopee, H.; Harrison, N. L.; Hughes, D. L.; Schubert, C. J.; Sutton, B. M.; Watts, G. L.; Whitehead, A. J. *Org. Lett.* **2006**, *8*, 4071.
(32) Glaser, R.; Knotts, N. *The Journal of Physical Chemistry A* **2005**, *110*, 1295.
(33) Schnurch, M.; Holzweber, M.; Mihovilovic, M. D.; Stanetty, P. *Green Chem.* **2007**, *9*, 139.
(34) Wickham, P. P.; Hazen, K. H.; Guo, H.; Jones, G.; Reuter, K. H.; Scott, W. J. *J. Org. Chem.* **1991**, *56*, 2045.

Appendix A: Crystallographic Data for IMesCuEt (2.32, Chapter 2)

Table 1. Crystal data and structure refinement for aw06177_0m.

Identification code	aw06177_0m	
Empirical formula	C27 H37 Cu N2 O	
Formula weight	469.13	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P $\bar{1}$	
Unit cell dimensions	a = 8.4829(5) Å	α= 102.238(4)°.
	b = 11.4784(6) Å	β= 98.112(4)°.
	c = 14.0410(8) Å	γ = 107.368(4)°.
Volume	1244.20(12) $Å^3$	
Z	2	
Density (calculated)	1.252 Mg/m^3	
Absorption coefficient	0.898 mm^{-1}	
F(000)	500	
Crystal size	0.32 x 0.25 x 0.10 mm^3	
Theta range for data collection	1.93 to 33.25°.	
Index ranges	-12<=h<=13, -17<=k<=17, -20<=l<=21	
Reflections collected	25392	
Independent reflections	9527 [R(int) = 0.0514]	
Completeness to theta = 25.00°	100.0 %	
Max. and min. transmission	0.9156 and 0.7621	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9527 / 0 / 287	
Goodness-of-fit on F^2	1.009	
Final R indices [I>2sigma(I)]	R1 = 0.0487, wR2 = 0.0856	
R indices (all data)	R1 = 0.1012, wR2 = 0.1017	
Largest diff. peak and hole	0.529 and -0.577 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for aw06177_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	6083(2)	7074(2)	8044(1)	13(1)
C(2)	3623(2)	6191(2)	8497(1)	18(1)
C(3)	4235(2)	7424(2)	8999(2)	18(1)
C(4)	6744(2)	9267(2)	9070(1)	13(1)
C(5)	7718(2)	9735(2)	10040(1)	15(1)
C(6)	8688(2)	11018(2)	10358(1)	16(1)
C(7)	8681(2)	11813(2)	9744(1)	16(1)
C(8)	7660(2)	11313(2)	8782(1)	17(1)
C(9)	6678(2)	10036(2)	8430(1)	15(1)
C(10)	5565(3)	9501(2)	7395(2)	25(1)
C(11)	7731(3)	8904(2)	10737(2)	22(1)
C(12)	9728(2)	13200(2)	10109(2)	23(1)
C(13)	4548(2)	4792(2)	7261(1)	14(1)
C(14)	4985(2)	3890(2)	7653(1)	17(1)
C(15)	4699(2)	2715(2)	6999(2)	19(1)
C(16)	4000(2)	2442(2)	5987(1)	18(1)
C(17)	3568(2)	3368(2)	5626(1)	18(1)
C(18)	3824(2)	4555(2)	6251(1)	16(1)
C(19)	3330(2)	5538(2)	5847(2)	22(1)
C(20)	5731(3)	4152(2)	8745(2)	27(1)
C(21)	3724(3)	1169(2)	5298(2)	28(1)
C(22)	9859(2)	7446(2)	6782(2)	20(1)
C(23)	10576(3)	8652(2)	6454(2)	31(1)
C(24)	9294(3)	4222(2)	7041(2)	36(1)
C(25)	8825(3)	3236(2)	6050(2)	39(1)
C(26)	8996(3)	2076(2)	6330(2)	32(1)
C(27)	10323(2)	2644(2)	7286(2)	25(1)
N(1)	4762(2)	5993(1)	7925(1)	14(1)
N(2)	5728(2)	7945(1)	8716(1)	13(1)
Cu(1)	7945(1)	7271(1)	7407(1)	15(1)

O(1)	9986(2)	3728(1)	7784(1)	33(1)

Table 3. Bond lengths [Å] and angles [°] for aw06177_0m.

C(1)-N(2)	1.357(2)
C(1)-N(1)	1.360(2)
C(1)-Cu(1)	1.9022(18)
C(2)-C(3)	1.343(3)
C(2)-N(1)	1.380(2)
C(2)-H(2)	0.9500
C(3)-N(2)	1.382(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.391(2)
C(4)-C(9)	1.393(3)
C(4)-N(2)	1.440(2)
C(5)-C(6)	1.392(2)
C(5)-C(11)	1.506(3)
C(6)-C(7)	1.382(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.396(3)
C(7)-C(12)	1.506(2)
C(8)-C(9)	1.391(2)
C(8)-H(8)	0.9500
C(9)-C(10)	1.506(3)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-C(14)	1.388(3)
C(13)-C(18)	1.397(3)

C(13)-N(1)	1.436(2)
C(14)-C(15)	1.392(3)
C(14)-C(20)	1.503(3)
C(15)-C(16)	1.390(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.389(3)
C(16)-C(21)	1.503(3)
C(17)-C(18)	1.391(3)
C(17)-H(17)	0.9500
C(18)-C(19)	1.503(3)
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-C(23)	1.531(3)
C(22)-Cu(1)	1.9303(19)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-O(1)	1.426(3)
C(24)-C(25)	1.511(4)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-C(26)	1.507(3)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-C(27)	1.503(3)
C(26)-H(26A)	0.9900

C(26)-H(26B)	0.9900
C(27)-O(1)	1.421(3)
C(27)-H(27A)	0.9900
C(27)-H(27B)	0.9900

N(2)-C(1)-N(1)	102.89(15)
N(2)-C(1)-Cu(1)	129.69(12)
N(1)-C(1)-Cu(1)	127.42(13)
C(3)-C(2)-N(1)	106.33(16)
C(3)-C(2)-H(2)	126.8
N(1)-C(2)-H(2)	126.8
C(2)-C(3)-N(2)	106.55(16)
C(2)-C(3)-H(3)	126.7
N(2)-C(3)-H(3)	126.7
C(5)-C(4)-C(9)	122.55(16)
C(5)-C(4)-N(2)	119.08(16)
C(9)-C(4)-N(2)	118.35(15)
C(4)-C(5)-C(6)	117.57(17)
C(4)-C(5)-C(11)	122.06(16)
C(6)-C(5)-C(11)	120.37(16)
C(7)-C(6)-C(5)	121.90(17)
C(7)-C(6)-H(6)	119.0
C(5)-C(6)-H(6)	119.0
C(6)-C(7)-C(8)	118.80(16)
C(6)-C(7)-C(12)	120.88(17)
C(8)-C(7)-C(12)	120.31(17)
C(9)-C(8)-C(7)	121.36(18)
C(9)-C(8)-H(8)	119.3
C(7)-C(8)-H(8)	119.3
C(8)-C(9)-C(4)	117.79(16)
C(8)-C(9)-C(10)	121.27(17)
C(4)-C(9)-C(10)	120.94(16)
C(9)-C(10)-H(10A)	109.5
C(9)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5

C(9)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(5)-C(11)-H(11A)	109.5
C(5)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(5)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(7)-C(12)-H(12A)	109.5
C(7)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(7)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(14)-C(13)-C(18)	122.56(16)
C(14)-C(13)-N(1)	118.92(16)
C(18)-C(13)-N(1)	118.44(16)
C(13)-C(14)-C(15)	117.72(17)
C(13)-C(14)-C(20)	121.86(17)
C(15)-C(14)-C(20)	120.42(17)
C(16)-C(15)-C(14)	121.69(18)
C(16)-C(15)-H(15)	119.2
C(14)-C(15)-H(15)	119.2
C(17)-C(16)-C(15)	118.79(17)
C(17)-C(16)-C(21)	120.77(18)
C(15)-C(16)-C(21)	120.44(18)
C(16)-C(17)-C(18)	121.61(17)
C(16)-C(17)-H(17)	119.2
C(18)-C(17)-H(17)	119.2
C(17)-C(18)-C(13)	117.63(17)
C(17)-C(18)-C(19)	120.73(17)
C(13)-C(18)-C(19)	121.64(17)
C(18)-C(19)-H(19A)	109.5
C(18)-C(19)-H(19B)	109.5

H(19A)-C(19)-H(19B)	109.5
C(18)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(14)-C(20)-H(20A)	109.5
C(14)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(14)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(16)-C(21)-H(21A)	109.5
C(16)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(16)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(23)-C(22)-Cu(1)	118.71(15)
C(23)-C(22)-H(22A)	107.6
Cu(1)-C(22)-H(22A)	107.6
C(23)-C(22)-H(22B)	107.6
Cu(1)-C(22)-H(22B)	107.6
H(22A)-C(22)-H(22B)	107.1
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
O(1)-C(24)-C(25)	107.72(19)
O(1)-C(24)-H(24A)	110.2
C(25)-C(24)-H(24A)	110.2
O(1)-C(24)-H(24B)	110.2
C(25)-C(24)-H(24B)	110.2
H(24A)-C(24)-H(24B)	108.5
C(26)-C(25)-C(24)	103.87(19)

C(26)-C(25)-H(25A)	111.0
C(24)-C(25)-H(25A)	111.0
C(26)-C(25)-H(25B)	111.0
C(24)-C(25)-H(25B)	111.0
H(25A)-C(25)-H(25B)	109.0
C(27)-C(26)-C(25)	102.16(18)
C(27)-C(26)-H(26A)	111.3
C(25)-C(26)-H(26A)	111.3
C(27)-C(26)-H(26B)	111.3
C(25)-C(26)-H(26B)	111.3
H(26A)-C(26)-H(26B)	109.2
O(1)-C(27)-C(26)	105.13(17)
O(1)-C(27)-H(27A)	110.7
C(26)-C(27)-H(27A)	110.7
O(1)-C(27)-H(27B)	110.7
C(26)-C(27)-H(27B)	110.7
H(27A)-C(27)-H(27B)	108.8
C(1)-N(1)-C(2)	112.19(15)
C(1)-N(1)-C(13)	124.12(15)
C(2)-N(1)-C(13)	123.68(15)
C(1)-N(2)-C(3)	112.05(15)
C(1)-N(2)-C(4)	124.41(15)
C(3)-N(2)-C(4)	123.50(15)
C(1)-Cu(1)-C(22)	178.44(9)
C(27)-O(1)-C(24)	107.75(17)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for aw06177_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	14(1)	11(1)	13(1)	2(1)	2(1)	5(1)
C(2)	15(1)	18(1)	21(1)	4(1)	9(1)	5(1)
C(3)	17(1)	18(1)	21(1)	3(1)	11(1)	7(1)
C(4)	13(1)	11(1)	16(1)	2(1)	5(1)	5(1)
C(5)	16(1)	16(1)	14(1)	2(1)	6(1)	8(1)
C(6)	15(1)	19(1)	14(1)	-1(1)	3(1)	7(1)
C(7)	14(1)	13(1)	19(1)	0(1)	7(1)	5(1)
C(8)	18(1)	14(1)	19(1)	5(1)	7(1)	6(1)
C(9)	16(1)	15(1)	14(1)	2(1)	4(1)	7(1)
C(10)	33(1)	18(1)	19(1)	3(1)	-4(1)	6(1)
C(11)	28(1)	21(1)	17(1)	6(1)	4(1)	10(1)
C(12)	22(1)	16(1)	26(1)	1(1)	6(1)	3(1)
C(13)	13(1)	12(1)	16(1)	1(1)	5(1)	4(1)
C(14)	18(1)	16(1)	16(1)	3(1)	3(1)	6(1)
C(15)	21(1)	16(1)	20(1)	2(1)	3(1)	9(1)
C(16)	19(1)	16(1)	18(1)	-2(1)	6(1)	6(1)
C(17)	19(1)	21(1)	12(1)	1(1)	4(1)	5(1)
C(18)	14(1)	17(1)	16(1)	5(1)	6(1)	3(1)
C(19)	25(1)	21(1)	19(1)	7(1)	3(1)	6(1)
C(20)	39(1)	22(1)	19(1)	3(1)	-3(1)	13(1)
C(21)	34(1)	21(1)	25(1)	-4(1)	3(1)	12(1)
C(22)	18(1)	27(1)	14(1)	3(1)	6(1)	7(1)
C(23)	24(1)	36(1)	26(1)	7(1)	8(1)	1(1)
C(24)	26(1)	30(1)	58(2)	18(1)	13(1)	12(1)
C(25)	31(1)	51(2)	37(2)	27(1)	5(1)	9(1)
C(26)	34(1)	27(1)	25(1)	3(1)	9(1)	-2(1)
C(27)	20(1)	26(1)	32(1)	13(1)	8(1)	7(1)
N(1)	15(1)	12(1)	14(1)	2(1)	6(1)	5(1)
N(2)	15(1)	12(1)	14(1)	3(1)	6(1)	5(1)
Cu(1)	14(1)	15(1)	13(1)	2(1)	5(1)	4(1)

O(1)	51(1)	22(1)	23(1)	5(1)	10(1)	7(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for aw06177_0m.

	x	y	z	U(eq)
H(2)	2608	5577	8530	22
H(3)	3739	7853	9459	21
H(6)	9374	11356	11015	20
H(8)	7636	11856	8359	20
H(10A)	5590	10190	7082	38
H(10B)	4401	9069	7437	38
H(10C)	5979	8895	6994	38
H(11A)	6767	8838	11059	33
H(11B)	8787	9274	11248	33
H(11C)	7646	8057	10358	33
H(12A)	8982	13700	10219	35
H(12B)	10357	13446	9608	35
H(12C)	10525	13356	10737	35
H(15)	4989	2083	7252	23
H(17)	3085	3186	4936	22
H(19A)	2546	5810	6216	33
H(19B)	2777	5176	5138	33
H(19C)	4344	6269	5923	33
H(20A)	6685	4953	8963	41
H(20B)	6129	3462	8854	41
H(20C)	4867	4212	9129	41
H(21A)	2965	1056	4666	42
H(21B)	3216	501	5608	42
H(21C)	4813	1120	5171	42
H(22A)	10787	7372	7252	24
H(22B)	9533	6715	6186	24
H(23A)	9704	8719	5952	46

H(23B)	11554	8616	6167	46
H(23C)	10929	9393	7033	46
H(24A)	10137	5018	7013	43
H(24B)	8279	4407	7201	43
H(25A)	7650	3074	5701	46
H(25B)	9603	3508	5614	46
H(26A)	7915	1544	6437	38
H(26B)	9374	1561	5811	38
H(27A)	10237	2034	7696	30
H(27B)	11471	2889	7146	30

Appendix B: Crystallographic Data for XantphosCu-(4-Me)Ph (3.37, Chapter 3)

Table 1. Crystal data and structure refinement for xcutol_0m.

Identification code	xcutol_0m	
Empirical formula	C48 H43 Cl4 Cu O P2	
Formula weight	903.10	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P 1	
Unit cell dimensions	a = 9.5374(9) Å	α= 84.293(4)°.
	b = 10.6287(9) Å	β= 70.845(4)°.
	c = 11.2535(10) Å	γ = 75.681(5)°.
Volume	1043.92(16) $Å^3$	
Z	1	
Density (calculated)	1.437 Mg/m^3	
Absorption coefficient	0.893 mm^{-1}	
F(000)	466	
Crystal size	0.10 x 0.08 x 0.06 mm^3	
Theta range for data collection	1.92 to 28.33°.	
Index ranges	-12<=h<=12, -14<=k<=14, -15<=l<=14	
Reflections collected	44905	
Independent reflections	10359 [R(int) = 0.0457]	
Completeness to theta = 25.00°	99.9 %	
Max. and min. transmission	0.9484 and 0.9160	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10359 / 3 / 508	
Goodness-of-fit on F^2	1.021	
Final R indices [I>2sigma(I)]	R1 = 0.0347, wR2 = 0.0805	
R indices (all data)	R1 = 0.0416, wR2 = 0.0840	
Absolute structure parameter	0.004(7)	
Largest diff. peak and hole	0.602 and -0.464 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for xcutol_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	-193(3)	2977(3)	11603(2)	17(1)
C(2)	699(3)	2258(3)	12313(2)	19(1)
C(3)	86(3)	1693(3)	13503(2)	22(1)
C(4)	-1469(3)	1825(3)	14026(2)	23(1)
C(5)	-2382(3)	2509(3)	13338(3)	24(1)
C(6)	-1764(3)	3065(3)	12163(2)	20(1)
C(7)	-2144(4)	1251(4)	15295(3)	39(1)
C(8)	-1763(3)	3164(2)	8676(2)	13(1)
C(9)	-407(3)	2208(2)	8330(2)	12(1)
C(10)	-533(3)	945(2)	8217(2)	17(1)
C(11)	-1947(3)	682(2)	8432(2)	17(1)
C(12)	-3270(3)	1653(3)	8786(2)	17(1)
C(13)	-3196(3)	2926(2)	8916(2)	15(1)
C(14)	-4591(3)	4080(3)	9252(2)	17(1)
C(15)	-4251(3)	5035(2)	9992(2)	13(1)
C(16)	-5362(3)	5821(3)	10934(2)	16(1)
C(17)	-4970(3)	6704(3)	11536(2)	18(1)
C(18)	-3482(3)	6835(2)	11196(2)	15(1)
C(19)	-2335(3)	6057(2)	10254(2)	14(1)
C(20)	-2770(3)	5177(2)	9686(2)	11(1)
C(21)	-4736(3)	4751(3)	8007(3)	27(1)
C(22)	-6037(3)	3624(3)	9997(3)	29(1)
C(23)	151(3)	6934(2)	8394(2)	13(1)
C(24)	-689(3)	7070(2)	7560(2)	17(1)
C(25)	-217(3)	7669(3)	6396(2)	20(1)
C(26)	1109(3)	8113(3)	6038(2)	21(1)
C(27)	1969(3)	7967(2)	6852(2)	19(1)
C(28)	1473(3)	7393(2)	8029(2)	14(1)
C(29)	-162(3)	6994(2)	11020(2)	13(1)
C(30)	-539(3)	8352(2)	10967(2)	15(1)

C(31)	-373(3)	9058(3)	11873(2)	19(1)
C(32)	154(3)	8413(3)	12822(2)	20(1)
C(33)	510(3)	7076(3)	12895(2)	20(1)
C(35)	355(3)	6366(3)	11990(2)	17(1)
C(36)	2077(3)	3220(2)	6617(2)	14(1)
C(37)	2635(3)	4340(2)	6405(2)	18(1)
C(38)	3271(3)	4783(3)	5183(2)	23(1)
C(39)	3345(3)	4115(3)	4172(2)	22(1)
C(40)	2754(3)	3006(3)	4371(2)	23(1)
C(41)	2118(3)	2573(3)	5577(2)	19(1)
C(42)	2685(3)	1086(2)	8296(2)	14(1)
C(43)	4000(3)	605(2)	7337(2)	18(1)
C(44)	5000(3)	-542(3)	7501(3)	21(1)
C(45)	4698(3)	-1231(3)	8632(3)	23(1)
C(46)	3382(3)	-739(3)	9604(3)	24(1)
C(47)	2392(3)	408(3)	9442(2)	20(1)
C(48)	7542(4)	5201(3)	4639(3)	37(1)
C(49)	5600(4)	61(3)	3289(3)	36(1)
O(1)	-1611(2)	4413(2)	8772(2)	13(1)
P(1)	-301(1)	5983(1)	9860(1)	11(1)
P(2)	1360(1)	2650(1)	8235(1)	11(1)
Cl(1)	8937(1)	4814(1)	5374(1)	43(1)
Cl(2)	6474(1)	6824(1)	4913(1)	56(1)
Cl(3)	5779(1)	673(1)	1741(1)	44(1)
Cl(4)	3985(1)	-572(1)	3924(1)	42(1)
Cu(1)	597(1)	3828(1)	9978(1)	14(1)

Table 3. Bond lengths [Å] and angles [°] for xcutol_0m.

C(1)-C(2)	1.396(4)
C(1)-C(6)	1.405(4)
C(1)-Cu(1)	1.958(3)
C(2)-C(3)	1.413(4)
C(2)-H(2)	0.9500
C(3)-C(4)	1.381(4)
C(3)-H(3)	0.9500
C(4)-C(5)	1.379(4)
C(4)-C(7)	1.498(4)
C(5)-C(6)	1.396(4)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-C(13)	1.386(4)
C(8)-O(1)	1.389(3)
C(8)-C(9)	1.398(3)
C(9)-C(10)	1.398(3)
C(9)-P(2)	1.827(2)
C(10)-C(11)	1.383(4)
C(10)-H(10)	0.9500
C(11)-C(12)	1.387(4)
C(11)-H(11)	0.9500
C(12)-C(13)	1.396(3)
C(12)-H(12)	0.9500
C(13)-C(14)	1.540(3)
C(14)-C(22)	1.527(4)
C(14)-C(15)	1.528(3)
C(14)-C(21)	1.540(4)
C(15)-C(20)	1.383(3)
C(15)-C(16)	1.395(3)
C(16)-C(17)	1.395(4)

C(16)-H(16)	0.9500
C(17)-C(18)	1.382(4)
C(17)-H(17)	0.9500
C(18)-C(19)	1.403(3)
C(18)-H(18)	0.9500
C(19)-C(20)	1.394(3)
C(19)-P(1)	1.826(3)
C(20)-O(1)	1.383(3)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-C(28)	1.386(3)
C(23)-C(24)	1.397(4)
C(23)-P(1)	1.830(2)
C(24)-C(25)	1.383(4)
C(24)-H(24)	0.9500
C(25)-C(26)	1.382(4)
C(25)-H(25)	0.9500
C(26)-C(27)	1.392(4)
C(26)-H(26)	0.9500
C(27)-C(28)	1.387(4)
C(27)-H(27)	0.9500
C(28)-H(28)	0.9500
C(29)-C(35)	1.388(3)
C(29)-C(30)	1.399(3)
C(29)-P(1)	1.827(2)
C(30)-C(31)	1.394(3)
C(30)-H(30)	0.9500
C(31)-C(32)	1.379(4)
C(31)-H(31)	0.9500
C(32)-C(33)	1.377(4)
C(32)-H(32)	0.9500

C(33)-C(35)	1.392(3)
C(33)-H(33)	0.9500
C(35)-H(35)	0.9500
C(36)-C(37)	1.389(4)
C(36)-C(41)	1.401(3)
C(36)-P(2)	1.822(3)
C(37)-C(38)	1.395(4)
C(37)-H(37)	0.9500
C(38)-C(39)	1.373(4)
C(38)-H(38)	0.9500
C(39)-C(40)	1.396(4)
C(39)-H(39)	0.9500
C(40)-C(41)	1.377(4)
C(40)-H(40)	0.9500
C(41)-H(41)	0.9500
C(42)-C(43)	1.379(3)
C(42)-C(47)	1.393(4)
C(42)-P(2)	1.833(2)
C(43)-C(44)	1.387(4)
C(43)-H(43)	0.9500
C(44)-C(45)	1.385(4)
C(44)-H(44)	0.9500
C(45)-C(46)	1.391(4)
C(45)-H(45)	0.9500
C(46)-C(47)	1.382(4)
C(46)-H(46)	0.9500
C(47)-H(47)	0.9500
C(48)-Cl(1)	1.734(4)
C(48)-Cl(2)	1.772(4)
C(48)-H(48A)	0.9900
C(48)-H(48B)	0.9900
C(49)-Cl(4)	1.741(3)
C(49)-Cl(3)	1.767(3)
C(49)-H(49A)	0.9900
C(49)-H(49B)	0.9900

P(1)-Cu(1)	2.2455(7)
P(2)-Cu(1)	2.2461(6)

C(2)-C(1)-C(6)	114.0(2)
C(2)-C(1)-Cu(1)	124.9(2)
C(6)-C(1)-Cu(1)	121.1(2)
C(1)-C(2)-C(3)	123.4(2)
C(1)-C(2)-H(2)	118.3
C(3)-C(2)-H(2)	118.3
C(4)-C(3)-C(2)	120.5(3)
C(4)-C(3)-H(3)	119.7
C(2)-C(3)-H(3)	119.7
C(5)-C(4)-C(3)	117.6(2)
C(5)-C(4)-C(7)	121.1(3)
C(3)-C(4)-C(7)	121.3(3)
C(4)-C(5)-C(6)	121.5(3)
C(4)-C(5)-H(5)	119.3
C(6)-C(5)-H(5)	119.3
C(5)-C(6)-C(1)	123.0(3)
C(5)-C(6)-H(6)	118.5
C(1)-C(6)-H(6)	118.5
C(4)-C(7)-H(7A)	109.5
C(4)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(13)-C(8)-O(1)	120.1(2)
C(13)-C(8)-C(9)	123.9(2)
O(1)-C(8)-C(9)	116.0(2)
C(10)-C(9)-C(8)	116.9(2)
C(10)-C(9)-P(2)	124.60(19)
C(8)-C(9)-P(2)	118.06(18)
C(11)-C(10)-C(9)	120.4(2)
C(11)-C(10)-H(10)	119.8

C(9)-C(10)-H(10)	119.8
C(10)-C(11)-C(12)	121.1(2)
C(10)-C(11)-H(11)	119.4
C(12)-C(11)-H(11)	119.4
C(11)-C(12)-C(13)	120.3(2)
C(11)-C(12)-H(12)	119.9
C(13)-C(12)-H(12)	119.9
C(8)-C(13)-C(12)	117.4(2)
C(8)-C(13)-C(14)	118.4(2)
C(12)-C(13)-C(14)	124.2(2)
C(22)-C(14)-C(15)	111.9(2)
C(22)-C(14)-C(21)	110.7(2)
C(15)-C(14)-C(21)	108.2(2)
C(22)-C(14)-C(13)	111.1(2)
C(15)-C(14)-C(13)	107.6(2)
C(21)-C(14)-C(13)	107.2(2)
C(20)-C(15)-C(16)	117.3(2)
C(20)-C(15)-C(14)	118.8(2)
C(16)-C(15)-C(14)	123.9(2)
C(15)-C(16)-C(17)	120.5(2)
C(15)-C(16)-H(16)	119.7
C(17)-C(16)-H(16)	119.7
C(18)-C(17)-C(16)	120.7(2)
C(18)-C(17)-H(17)	119.6
C(16)-C(17)-H(17)	119.6
C(17)-C(18)-C(19)	120.3(2)
C(17)-C(18)-H(18)	119.9
C(19)-C(18)-H(18)	119.9
C(20)-C(19)-C(18)	117.2(2)
C(20)-C(19)-P(1)	117.87(17)
C(18)-C(19)-P(1)	124.47(19)
C(15)-C(20)-O(1)	120.2(2)
C(15)-C(20)-C(19)	123.9(2)
O(1)-C(20)-C(19)	115.8(2)
C(14)-C(21)-H(21A)	109.5

C(14)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(14)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(14)-C(22)-H(22A)	109.5
C(14)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(14)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(28)-C(23)-C(24)	119.0(2)
C(28)-C(23)-P(1)	118.68(19)
C(24)-C(23)-P(1)	121.84(19)
C(25)-C(24)-C(23)	120.4(2)
C(25)-C(24)-H(24)	119.8
C(23)-C(24)-H(24)	119.8
C(26)-C(25)-C(24)	120.1(3)
C(26)-C(25)-H(25)	119.9
C(24)-C(25)-H(25)	119.9
C(25)-C(26)-C(27)	120.1(2)
C(25)-C(26)-H(26)	120.0
C(27)-C(26)-H(26)	120.0
C(28)-C(27)-C(26)	119.6(2)
C(28)-C(27)-H(27)	120.2
C(26)-C(27)-H(27)	120.2
C(23)-C(28)-C(27)	120.8(2)
C(23)-C(28)-H(28)	119.6
C(27)-C(28)-H(28)	119.6
C(35)-C(29)-C(30)	119.2(2)
C(35)-C(29)-P(1)	117.46(19)
C(30)-C(29)-P(1)	123.31(19)
C(31)-C(30)-C(29)	120.0(2)
C(31)-C(30)-H(30)	120.0
C(29)-C(30)-H(30)	120.0

C(32)-C(31)-C(30)	119.8(2)
C(32)-C(31)-H(31)	120.1
C(30)-C(31)-H(31)	120.1
C(33)-C(32)-C(31)	120.9(2)
C(33)-C(32)-H(32)	119.6
C(31)-C(32)-H(32)	119.6
C(32)-C(33)-C(35)	119.6(2)
C(32)-C(33)-H(33)	120.2
C(35)-C(33)-H(33)	120.2
C(29)-C(35)-C(33)	120.5(2)
C(29)-C(35)-H(35)	119.7
C(33)-C(35)-H(35)	119.7
C(37)-C(36)-C(41)	118.4(2)
C(37)-C(36)-P(2)	118.29(18)
C(41)-C(36)-P(2)	123.26(19)
C(36)-C(37)-C(38)	120.8(2)
C(36)-C(37)-H(37)	119.6
C(38)-C(37)-H(37)	119.6
C(39)-C(38)-C(37)	120.1(2)
C(39)-C(38)-H(38)	120.0
C(37)-C(38)-H(38)	120.0
C(38)-C(39)-C(40)	119.8(2)
C(38)-C(39)-H(39)	120.1
C(40)-C(39)-H(39)	120.1
C(41)-C(40)-C(39)	120.1(2)
C(41)-C(40)-H(40)	120.0
C(39)-C(40)-H(40)	120.0
C(40)-C(41)-C(36)	120.8(2)
C(40)-C(41)-H(41)	119.6
C(36)-C(41)-H(41)	119.6
C(43)-C(42)-C(47)	118.6(2)
C(43)-C(42)-P(2)	124.77(19)
C(47)-C(42)-P(2)	116.34(19)
C(42)-C(43)-C(44)	120.9(2)
C(42)-C(43)-H(43)	119.6

C(44)-C(43)-H(43)	119.6
C(45)-C(44)-C(43)	120.7(2)
C(45)-C(44)-H(44)	119.7
C(43)-C(44)-H(44)	119.7
C(44)-C(45)-C(46)	118.5(2)
C(44)-C(45)-H(45)	120.7
C(46)-C(45)-H(45)	120.7
C(47)-C(46)-C(45)	120.7(3)
C(47)-C(46)-H(46)	119.6
C(45)-C(46)-H(46)	119.6
C(46)-C(47)-C(42)	120.6(2)
C(46)-C(47)-H(47)	119.7
C(42)-C(47)-H(47)	119.7
Cl(1)-C(48)-Cl(2)	111.98(17)
Cl(1)-C(48)-H(48A)	109.2
Cl(2)-C(48)-H(48A)	109.2
Cl(1)-C(48)-H(48B)	109.2
Cl(2)-C(48)-H(48B)	109.2
H(48A)-C(48)-H(48B)	107.9
Cl(4)-C(49)-Cl(3)	111.70(19)
Cl(4)-C(49)-H(49A)	109.3
Cl(3)-C(49)-H(49A)	109.3
Cl(4)-C(49)-H(49B)	109.3
Cl(3)-C(49)-H(49B)	109.3
H(49A)-C(49)-H(49B)	107.9
C(20)-O(1)-C(8)	116.20(18)
C(19)-P(1)-C(29)	104.95(11)
C(19)-P(1)-C(23)	104.19(11)
C(29)-P(1)-C(23)	103.75(11)
C(19)-P(1)-Cu(1)	100.19(8)
C(29)-P(1)-Cu(1)	118.14(8)
C(23)-P(1)-Cu(1)	123.24(8)
C(36)-P(2)-C(9)	104.61(11)
C(36)-P(2)-C(42)	103.75(11)
C(9)-P(2)-C(42)	103.99(11)

C(36)-P(2)-Cu(1)	126.63(8)
C(9)-P(2)-Cu(1)	100.93(7)
C(42)-P(2)-Cu(1)	114.35(8)
C(1)-Cu(1)-P(1)	116.44(8)
C(1)-Cu(1)-P(2)	117.96(8)
P(1)-Cu(1)-P(2)	119.25(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for xcutol_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	23(1)	13(1)	15(1)	-1(1)	-4(1)	-5(1)
C(2)	18(1)	24(1)	18(1)	-1(1)	-7(1)	-9(1)
C(3)	28(2)	24(1)	19(1)	6(1)	-12(1)	-11(1)
C(4)	32(2)	20(1)	17(1)	2(1)	-4(1)	-11(1)
C(5)	15(1)	24(2)	27(1)	1(1)	0(1)	-4(1)
C(6)	24(1)	17(1)	22(1)	7(1)	-12(1)	-9(1)
C(7)	40(2)	50(2)	24(2)	11(1)	-2(1)	-20(2)
C(8)	14(1)	10(1)	14(1)	-1(1)	-5(1)	-3(1)
C(9)	13(1)	14(1)	8(1)	-1(1)	-4(1)	-2(1)
C(10)	21(1)	11(1)	16(1)	-2(1)	-7(1)	1(1)
C(11)	24(1)	14(1)	16(1)	-2(1)	-8(1)	-6(1)
C(12)	20(1)	19(1)	14(1)	-1(1)	-6(1)	-9(1)
C(13)	16(1)	16(1)	12(1)	0(1)	-6(1)	-3(1)
C(14)	13(1)	18(1)	21(1)	-1(1)	-7(1)	-3(1)
C(15)	12(1)	13(1)	15(1)	3(1)	-6(1)	-2(1)
C(16)	10(1)	16(1)	18(1)	2(1)	-2(1)	-1(1)
C(17)	15(1)	19(1)	16(1)	-4(1)	0(1)	-1(1)
C(18)	17(1)	13(1)	15(1)	-2(1)	-4(1)	-3(1)
C(19)	14(1)	13(1)	12(1)	3(1)	-4(1)	-3(1)
C(20)	12(1)	7(1)	12(1)	1(1)	-4(1)	0(1)
C(21)	27(2)	27(2)	29(2)	-5(1)	-19(1)	5(1)
C(22)	10(1)	30(2)	47(2)	-11(1)	-6(1)	-6(1)

C(23)	16(1)	10(1)	11(1)	-3(1)	-3(1)	-1(1)
C(24)	17(1)	16(1)	17(1)	-2(1)	-5(1)	-3(1)
C(25)	24(1)	16(1)	19(1)	2(1)	-7(1)	-3(1)
C(26)	29(2)	17(1)	14(1)	5(1)	-5(1)	-7(1)
C(27)	18(1)	16(1)	21(1)	-1(1)	-2(1)	-8(1)
C(28)	15(1)	12(1)	15(1)	-1(1)	-4(1)	-1(1)
C(29)	9(1)	17(1)	13(1)	0(1)	-3(1)	-4(1)
C(30)	18(1)	16(1)	11(1)	0(1)	-3(1)	-5(1)
C(31)	22(1)	19(1)	18(1)	-4(1)	-1(1)	-10(1)
C(32)	23(1)	25(1)	16(1)	-5(1)	-6(1)	-10(1)
C(33)	20(1)	25(1)	15(1)	-1(1)	-6(1)	-5(1)
C(35)	15(1)	19(1)	14(1)	-1(1)	-3(1)	-2(1)
C(36)	11(1)	15(1)	14(1)	-2(1)	-5(1)	-2(1)
C(37)	14(1)	15(1)	21(1)	-2(1)	-3(1)	-1(1)
C(38)	20(1)	19(1)	26(1)	7(1)	-4(1)	-6(1)
C(39)	20(1)	28(2)	15(1)	8(1)	-4(1)	-4(1)
C(40)	26(2)	30(2)	14(1)	-2(1)	-7(1)	-7(1)
C(41)	20(1)	21(1)	17(1)	-3(1)	-4(1)	-7(1)
C(42)	15(1)	11(1)	17(1)	1(1)	-8(1)	-4(1)
C(43)	14(1)	15(1)	22(1)	0(1)	-4(1)	-1(1)
C(44)	12(1)	17(1)	26(1)	1(1)	1(1)	0(1)
C(45)	18(1)	15(1)	33(2)	2(1)	-10(1)	1(1)
C(46)	25(1)	20(1)	23(1)	6(1)	-9(1)	-2(1)
C(47)	19(1)	20(1)	19(1)	1(1)	-3(1)	-2(1)
C(48)	43(2)	37(2)	36(2)	-6(2)	-11(2)	-16(2)
C(49)	32(2)	41(2)	34(2)	4(1)	-10(1)	-10(2)
O(1)	10(1)	11(1)	15(1)	-2(1)	-2(1)	-1(1)
P(1)	12(1)	10(1)	12(1)	0(1)	-4(1)	-2(1)
P(2)	11(1)	11(1)	11(1)	-1(1)	-4(1)	-1(1)
Cl(1)	32(1)	38(1)	54(1)	5(1)	-12(1)	-2(1)
Cl(2)	37(1)	39(1)	85(1)	19(1)	-19(1)	-4(1)
Cl(3)	46(1)	48(1)	28(1)	10(1)	-6(1)	-3(1)
Cl(4)	34(1)	34(1)	47(1)	0(1)	1(1)	-10(1)
Cu(1)	16(1)	13(1)	13(1)	0(1)	-5(1)	-3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for xcutol_0m.

	x	y	z	U(eq)
H(2)	1775	2144	11978	23
H(3)	748	1219	13947	26
H(5)	-3455	2603	13671	29
H(6)	-2437	3525	11723	24
H(7A)	-2198	359	15202	59
H(7B)	-3171	1772	15693	59
H(7C)	-1502	1247	15822	59
H(10)	358	264	7990	20
H(11)	-2012	-177	8337	20
H(12)	-4232	1451	8941	20
H(16)	-6393	5755	11167	19
H(17)	-5735	7222	12188	22
H(18)	-3235	7454	11600	18
H(21A)	-5621	5488	8186	41
H(21B)	-4867	4130	7487	41
H(21C)	-3811	5061	7557	41
H(22A)	-6920	4363	10132	43
H(22B)	-5953	3258	10811	43
H(22C)	-6168	2958	9524	43
H(24)	-1589	6749	7794	20
H(25)	-806	7774	5841	23
H(26)	1435	8519	5236	25
H(27)	2890	8260	6603	22
H(28)	2046	7312	8593	17
H(30)	-907	8793	10314	18
H(31)	-623	9980	11836	23
H(32)	273	8897	13434	24
H(33)	859	6641	13560	23
H(35)	605	5444	12036	20

H(37)	2583	4809	7100	21
H(38)	3653	5548	5050	27
H(39)	3796	4407	3340	26
H(40)	2791	2550	3672	27
H(41)	1702	1827	5705	23
H(43)	4225	1065	6555	21
H(44)	5901	-858	6831	25
H(45)	5374	-2023	8742	27
H(46)	3160	-1196	10389	28
H(47)	1505	737	10119	24
H(48A)	6846	4603	4952	45
H(48B)	8030	5076	3722	45
H(49A)	6517	-627	3282	43
H(49B)	5541	768	3827	43

Vita

Richard P. Rucker was born and raised in southeastern Louisiana. After finishing high school, Richard obtained a B.S. in Chemistry from Louisiana State University in Baton Rouge, LA. During his undergraduate career, Richard first participated in organic chemistry research by exploring the synthesis and characterization of *N*-alkoxybenzimidazoyl azides for possible use in click-chemistry applications. Later, Richard studied materials chemistry, where he synthesized and characterized monodisperse, core-shell nanoparticles for multifunctional materials applications. For this work, Richard received the Department of Chemistry's Outstanding Undergraduate Research Award at Louisiana State University in 2008. During the last three years of his undergraduate career, Richard was a Quality Control Technician and later a Research and Development Intern for Waterbury Companies, Inc., where he studied the formulation of new aerosolized emulsions for applications in the professional pesticide industry, as well as developed GC methods for quantification of active ingredients per EPA regulations. After graduating from LSU, Richard moved to the University of Washington in Seattle and began his graduate career with Prof. Gojko Lalic. There, he contributed to the development of several new copper-catalyzed transformations useful for organic synthesis. After receiving his Ph.D. in November 2013, Richard will begin a post-doctoral fellowship with Prof. Michael Organ at York University in Toronto, Canada. There, Richard will prepare highly reactive organopalladium complexes and study their electronic properties through a combination of spectroscopic, computational, and experimental techniques.