Copper Boryl Heterobimetallic Complexes in the Copper-Catalyzed Hydrofunctionalization of Alkynes and Alkenyl Boronate Esters

James E. Baumann

A dissertation

submitted in partial fulfillment of the

requirements for the degree of

Doctor of Philosophy

University of Washington

2023

Reading Committee:

Gojko Lalic, Chair

Forrest E. Michael

Mathew R. Golder

Program Authorized to Offer Degree:

Chemistry

University of Washington

Abstract

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James E. Baumann

Chair of the Supervisory Committee:
Gojko Lalic
Department of Chemistry

Transition metal-catalyzed reactions are widely used in organic synthesis due in part to their ability to form carbon-carbon and carbon-heteroatom bonds selectively and efficiently from readily available starting materials. The key to the success of many of these complex transformations is the ability to access highly reactive and versatile organometallic intermediates that can facilitate the formation of these new bonds. Studying and understanding the role of said intermediates in elementary steps can further accelerate the development of important synthetic transformations. Presented herein are two reactions that explore the catalytic generation and further transformation of alkyl 1,1-boryl copper heterobimetallic complexes in the context of the hydrofunctionalization of unsaturated starting materials.

Chapter 1 describes the differential dihydrofunctionalization of terminal alkynes towards the synthesis of allylic boronate esters through the reductive three-component coupling of terminal alkynes, alkenyl bromides, and pinacolborane. This transformation is promoted by the cooperative action of a copper/palladium catalyst system and results in the hydrofunctionalization of both π-bonds of an alkyne. The synthesis of allylic boronate esters, using the present method, can be accomplished in the presence of a wide range of functional groups. Finally, the importance of subtle ligand effects on the performance of the palladium co-catalyst was explored by taking advantage of an isolated 1,1-copper boryl heterobimetallic complex.

Chapter 2 explores the use of transition metal catalysis to form ylide equivalents from readily available starting materials with the goal of using these intermediates to develop a catalytic Wittig-type olefination of carbonyls and imines. The key Wittig-type intermediate, a 1,1-copper boryl heterobimetallic complex, was obtained by hydrocupration of alkenyl boronate esters. Using imines as coupling partners, this methodology was applied to the synthesis of highly *E*-selective styrenes and sterically hindered aliphatic alkenes in the presence of a variety of functional groups. Mechanistic investigations revealed the source of the alkene diastereoselectivity as well as the role of the key heterobimetallic complex.

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Å	angstrom (10^{-10} m)
Ac	acetyl
acac	acetylacetonate
Ar	aryl
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
BrettPhos	2-(Dicyclohexylphosphino)3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl
Bz	benzoyl
C	Celsius
Cat	catalyst
Cp	cyclopentadienyl anion
CPME	cyclopentyl methyl ether
Cy	cyclohexyl
dan	1,8-diaminonaphthalene
dba	dibenzylideneacetone
dipp	di-*iso*-propyl phenyl
DMA	dimethyl formamide
DME	dimethoxyethane
dmdba	dimethoxydibenzylideneacetone
DMMS	dimethoxymethylsilane

dppbz	1,2-Bis(diphenylphosphino)benzene
dppe	1,2-Bis(diphenylphosphino)ethane
dppf	1,1'-Bis(diphenylphosphino)ferrocene
DTBM-SEGPHOS	(R)-(−)-5,5′-Bis[di(3,5-di-tert-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole
E^+	electrophile
EI	electron ionization
equiv	equivalents
ESI	electrospray ionization
Et	ethyl
EWG	electron withdrawing group
FID	flame ionization detector
FTIR	Fourier transform infrared
FTIR band abbreviations	
s	strong
m	medium
w	weak
br	broad
GC	gas chromatography
GPC	gel permeation chromatography
h	hour(s)
HMDS	bis(trimethylsilyl)amine
HMTSO	hexamethyldisiloxane

HWE	Horner-Wadsworth-Emmons
Hz	hertz
IPr	1,3-Bis-(2,6-diisopropylphenyl)imidazolium
i-Pr	isopropyl
IR	infrared
L	ligand
M	metal
Me	methyl
min	minute(s)
mol	mole
MS	mass spectrometry
MTBE	methyl *tert*-butyl ether
n-Bu	butyl
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance

NMR splitting pattern abbreviations

s	singlet
d	doublet
t	triplet
q	quartet
p	pentet
h	heptet
m	multiplet

br	broad
Opyr	pyridoate
ORTEP	Oak Ridge Thermal Ellipsoid Plot
OTf	trifluoromethanesulfonate
Ph	phenyl
pin	pinacol
PMHS	polymethylhydrosiloxane
ppm	parts per million
Rf	retention factor
RockPhos	2-di(tert-butyl)phosphino-2′,4′,6′-triisopropyl-3-methoxy-6-methylbiphenyl
SciOPP	1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene
SPhos	dicyclohexyl(2′,6′-dimethoxy[1,1′-biphenyl]-2-yl)phosphane
TBS	*tert*-butyldimethylsilyl
t-Bu	*tert*-butyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMB	1,3,5-trimethoxybenzne
TMDSO	tetramethyldisiloxane
TMS	tetramethylsilane

TMS	trimethylsilyl
Tri	2,4-bis[2,6-bis(1-methylethyl)phenyl]-2,4-dihydro-5-phenyl-3H-1, 2,4-Triazol-3-ylidene
Ts	*p*-toluenesulfonyl
XANTPHOS	(9,9-Dimethyl-9H-xanthene-4,5-diyl)bis(diphenyl phosphane)
XPhos	Dicyclohexyl[2′,4′,6′-tris(propan-2-yl)[1,1′-biphenyl]-2-yl]phosphane

ACKNOWLEDGEMENTS

I would like to start by thanking my graduate advisor, Gojko Lalic, for helping me to grow into the scientist and person that I have become. Our frequent discussions taught me not only how to think like an organic chemist, but also that obtaining a Ph.D. is about much more than what is contained within this document. The many lessons that I have learned and skills that I have acquired throughout my time at the University of Washington are in no small part thanks to the space that you curated for me and your faith in my success.

Additionally, I want to thank Forrest Michael for not only serving on my exam committees, but also acting as a mentor during my Ph.D. journey. I have appreciated your challenging and insightful questions as they were invaluable in aiding my understanding of both the chemistry that I worked on as well as the discipline of organic chemistry as a whole.

I would also like to thank all of the Lalic group lab members, past and present, that I had the chance to coexist with in BAG 192. Specifically, I want to thank Megan Armstrong for being a mentor, friend, and my rock early in my graduate career. Further, I want to thank Austin Shaff for being my "partner in crime" and for the constant conversation that made the bad days a bit better.

Finally, I could not imagine this experience without the support of my loving partner Daniel as well as our cat Cooper. Thank you for being my support network when I was down and for being my number one cheerleader when it was time for celebration.

DEDICATION

To my mom.

Chapter 1. DIFFERENTIAL DIHYDROFUNCTIONALIZATION: A DUAL CATALYTIC THREE COMPONENT COUPLING OF ALKYNES, ALKENYL BROMIDES, AND PINACOLBORANE

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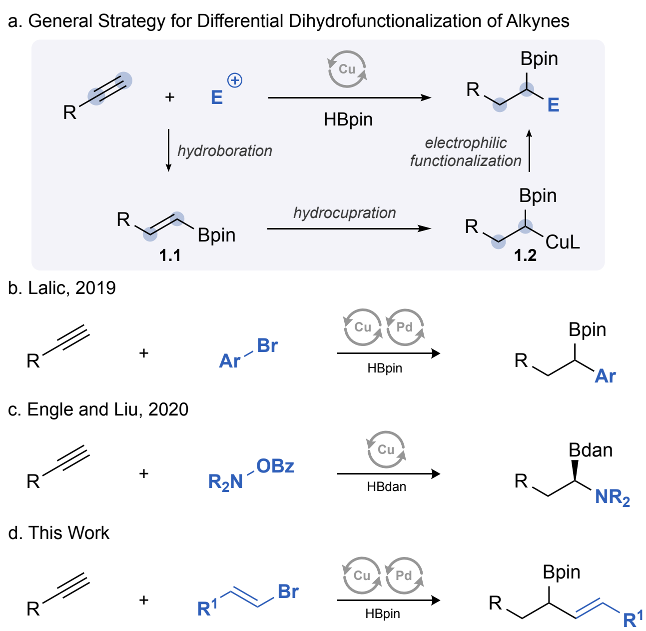
1.1 INTRODUCTION

Alkynes are extensively used in organic synthesis as readily available and versatile intermediates. They participate in a wide range of transformations, the most common of which are C-H functionalization of terminal alkynes, mono-addition to one of the π-bonds, and double addition to both π-bonds. Significantly less common are reactions that allow differential transformations of the two π-bonds present in alkynes.

Intrigued by the scarcity[1] and the synthetic potential of such transformations,[2–18] we became interested in the differential dihydrofunctionalization of alkynes. Our efforts towards this goal have focused on copper hydride chemistry,[19] which emerged as a powerful tool for the hydrofunctionalization of alkynes.[20–24] To this end, the Buchwald[25] and Mankad[26] groups have previously demonstrated that copper-catalyzed hydrofunctionalization of alkynes can be coupled with a subsequent reduction of the remaining π-bond.[27–34]

Our approach to the differential dihydrofunctionalization of alkynes is outlined in **Scheme 1.1a**. Inspired by a report from Sadighi,[35] we targeted the formation of the heterobimetallic intermediate **1.2** through the hydrocupration of alkenyl boronate ester **1.1**. Together with well-established copper-catalyzed hydroboration of alkynes,[36–40] this transformation provides access to the heterobimetallic intermediate **1.2** directly from terminal alkynes (**Scheme 1.1a**). Further electrophilic functionalization of this intermediate completes the differential dihydrofunctionalization reaction.



Scheme 1.1 Differential Dihydrofunctionalization of Alkynes.

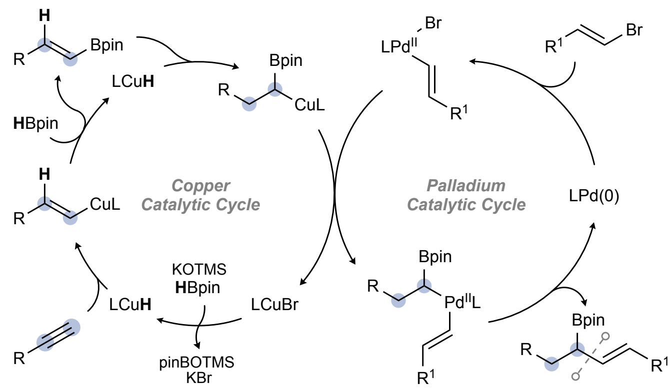
The key feature of the strategy outlined in **Scheme 1.1a** is that it allows systematic variation of the final functionalization step. In our initial report on differential dihydrofunctionalization of alkynes we described the synthesis of benzylic boronate esters through arylation of the heterobimetallic intermediate (**Scheme 1.1b**).[41] Soon after, Engle and Liu[42] used electrophilic amination of the heterobimetallic intermediate to develop an elegant and highly effective method for the synthesis of α-amino boronates (**Scheme 1.1c**).[43,44] Herein, we describe further exploration of the dihydrofunctionalization of alkynes and its application to the synthesis of other classes of boronate esters.

Pursuing the further development of differential dihydrofunctionalization, we decided to focus on the synthesis of allylic boronate esters (**Scheme 1.1d**). These compounds have been an attractive target for reaction development[45–48] as extremely versatile synthetic intermediates in which the interplay of the alkene and the boronate ester creates unique reactivity.[49] We recognized that differential dihydrofunctionalization offers a highly convergent approach to this important class of compounds through the coupling of readily available terminal alkynes, alkenyl bromides, and HBpin.

1.2 RESULTS AND DISCUSSION

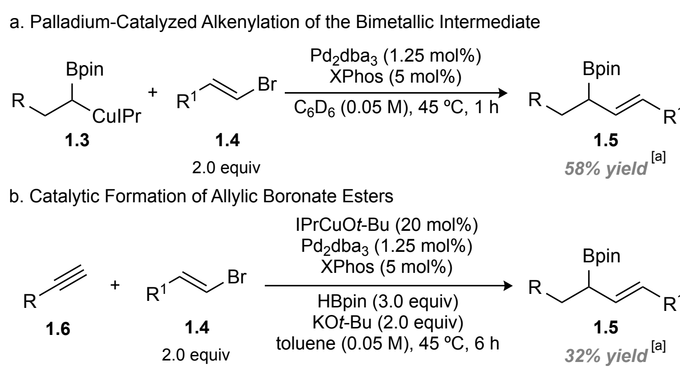
1.2.1 *Reaction Development*

The main challenge in developing this reaction was identifying a method for alkenylation of the heterobimetallic intermediate that can be effective in the context of the overall transformation. We were hoping to accomplish alkenylation of the heterobimetallic complex using a palladium co-catalyst according to the mechanism outlined in **Scheme 1.2**. To test the feasibility of the proposed palladium catalytic cycle, we explored catalytic alkenylation of a preformed heterobimetallic complex. An XPhos-supported[50,51] palladium catalyst proved effective, providing the product of the desired cross-coupling reaction in 58% yield (**Scheme 1.3a**). Even more encouraging were preliminary experiments exploring the catalytic differential hydroboration/hydroalkenylation reaction. Using an XPhos-supported palladium catalyst and the reaction conditions we had previously developed for the synthesis of benzylic boronate esters,[41] we obtained 32% yield of allylic boronate ester **1.5** (**Scheme 1.3b**).



Scheme 1.2 Proposed Mechanism for the Differential Dihydrofunctionalization of Alkynes.

In a subsequent screen, we evaluated the performance of various classes of phosphine ligands using commercially available representatives. With a range of monodentate triaryl and trialkyl phosphine ligands, as well as with a range of bidentate ligands, we observed very little (<5% yield) of the desired allylic boronate ester. The alkyne was generally consumed in all reactions and was mostly converted into oligomeric materials identified by GPC analysis. The alkenyl bromide was often reduced to an alkene or participated in Suzuki-type cross-coupling with

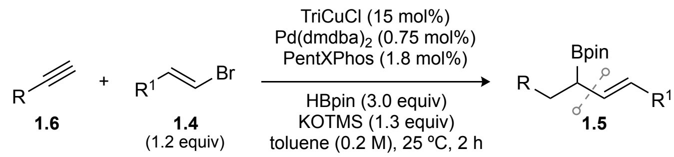


Scheme 1.3 Preliminary Results.

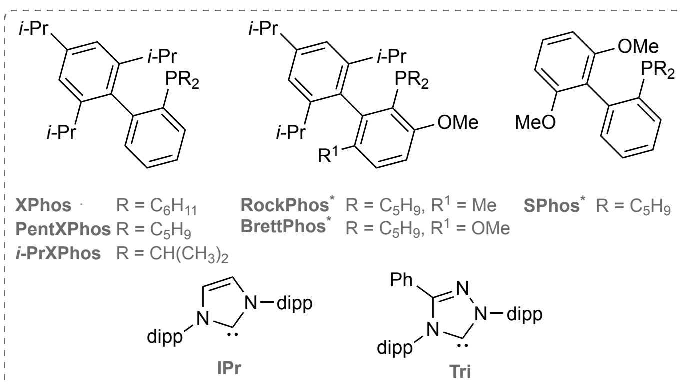
[a] Yield was determined by GC using 1,3,5-trimethoxybenzene as an internal standard. IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene. R = *p*-$(CH_3O)C_6H_4(CH_2)_3$ and R^1=$Ph(CH_2)_3$.

the intermediate alkenyl boronate ester. Although the same side reactions were observed with dialkylbiaryl phosphine ligands, the desired product was also formed in varying yields. We identified XPhos as the best performing dialkylbiaryl phosphine ligand under a wide range of conditions. Unfortunately, extensive optimization of the reaction parameters around the palladium-XPhos catalyst never yielded more than 40% of the desired product.

Table 1.1 Reaction Development



Entry	deviation from above	yield [%]
1	none	80 (80)[a]
2	XPhos instead of PentXPhos	24
3	*i*-PrXPhos instead of PentXPhos	25
4	SPhos* instead of PentXPhos	41
5	RockPhos* instead of PentXPhos	9
6	BrettPhos* instead of PentXPhos	12
7	$Pd(OAc)_2$ instead of $Pd(dmdba)_2$	52
8	$Pd(dba)_2$ instead of $Pd(dmdba)_2$	68
9	IPrCuCl instead of TriCuCl	71
10	*(R)*-DTBM-SEGPHOS instead of Tri	< 5
11	10 mol% TriCuCl	74
12	3.0 mol% $Pd(dmdba)_2$	43
13	KO*t*-Bu instead of KOTMS	48
14	NaOTMS instead of KOTMS	15



Unless otherwise noted, reactions were performed on 0.05 mmol scale. Yields determined by GC using *n*-octyl ether as an internal standard. [a] Isolated yield of the oxidized product allylic alcohol **1.5** from a reaction performed at 0.5 mmol shown in parenthesis. dmdba = 3,5,3',5'-dimethoxydibenzylidene-acetone. R = *p*-$(CH_3O)C_6H_4(CH_2)_3$, R^1 = $Ph(CH_2)_3$ and dipp = 2,6-diisopropylphenyl.

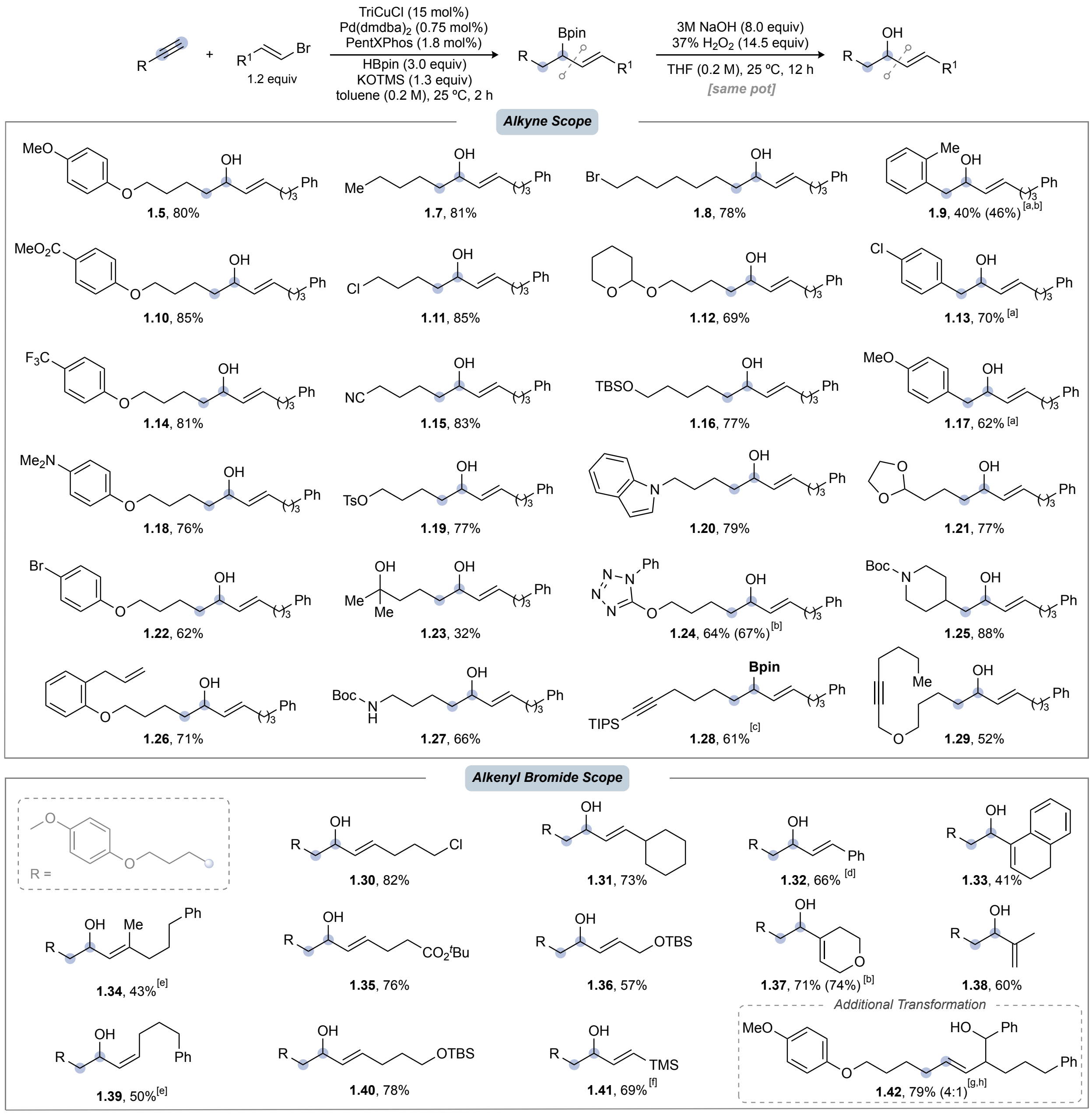
The key breakthrough that allowed the efficient synthesis of allylic boronate esters came from fine tuning of the XPhos ligand through the modification of the alkyl substituents on phosphorus. Using PentXPhos as the ligand, which features cyclopentyl substituents, we identified reaction conditions that afforded desired product **1.5** in 80% yield (**Table 1.1**). The remarkable effect of the PentXPhos ligand is demonstrated by results presented in **Table 1.1** (entries **1.1**–**1.6**). Closely related XPhos and *i*-PrXPhos provided only 24% and 25% yield of the desired product, respectively. Modifications of either aryl ring of the PentXPhos ligand backbone had a negative impact on the reaction. Dicyclopentyl SPhos,[52,53] RockPhos[54] and BrettPhos[55] ligands all gave significantly lower yields of the desired boronate ester (entries **4**, **5**, and **6**).

The contributions of other reaction variables are also summarized in **Table 1.1**. Commercially available $Pd(dmdba)_2$ was a superior palladium source, with $Pd(OAc)_2$ and Pd_2-$(dba)_3$ providing lower yields (entries **7** and **8**). The performance of the dmdba precursor could be attributed to the destabilization of the L_nPd^0-η^2 -dba complex, in favor of active L_nPd^0, commonly observed with more electron rich dba ligands.[56–58] Copper catalysts supported by NHC ligands gave the best results, although IPrCuCl (entry **9**) performed worse than TriCuCl. A catalyst prepared in situ from CuCl and (*R*)-DTBM-SEGPHOS (entry **10**) showed exclusive formation of the alkyl diboronate ester. Changes in copper catalyst loading had little effect on reaction outcome (entry **11**), while increasing palladium catalyst loading led to lower yields, isomerization of the product alkene, and the reduction of the alkenyl electrophile (entry **12**). A bulky base was necessary for efficient turnover, with KOTMS performing better than closely related *tert*-butyl alkoxides or sodium siloxides (entries **13** and **14**). The reaction was viable only in hydrocarbon solvents, with toluene and benzene giving the highest yields of the desired product (see **Table 1.6**).

1.2.2 *Substrate Scope*

Having developed a set of conditions for this differential dihydrofunctionalization, we next investigated the scope of the reaction. Allylic boronate esters initially formed in the reaction were

Table 1.2 Substrate Scope



Yields of isolated products are reported. Reactions performed on 0.5 mmol scale. [a] Reaction was run for 4 h followed by oxidation. [b] Shown in parenthesis is the H-NMR yield of the allylic boronate ester from a separate run using 1,3,5-trimethoxybenzene as an internal standard. [c] Following the initial 2 h reaction time the mixture was filtered through a plug of silica with Et_2O and purified by silica gel column chromatography. [d] *β*-bromostyrene was purchased as a (5:1) mixture of (*E*:*Z*) isomers, which was retained in the reaction. [e] Reaction was run for 24 h followed by oxidation, 1.5 equiv of alkenyl bromide was used. [f] Reaction was performed on a 1.0 mmol scale. [g] Following the initial 2 h reaction time 5 equiv of benzaldehyde was introduced and allowed to stir for 24 h at 60 °C before purification by silica gel column chromatography. [h] (*Z*:*E*) ratio.

oxidized in situ using NaOH/H_2O_2 to furnish allylic alcohols. We found that under the standard conditions, shown in **Table 1.2**, allylic alcohols could be synthesized from unactivated alkynes in the presence of a wide range of functional groups. Alkynes containing, esters (**1.10**), nitriles (**1.15**), acetals (**1.12**, **1.21**), tosylates (**1.19**), aryl and alkyl halides (**1.8**, **1.11**, **1.13**, and **1.22**), amines (**1.18**, **1.25** and **1.27**), protected and unprotected alcohols (**1.12**, **1.16**, and **1.23**), and nitrogen heterocycles (**1.20** and **24**) were well tolerated. Functionalization of aryl acetylenes (**1.9**, **1.13**, and **1.17**) also provided moderate yields. Selectivity for the functionalization of terminal alkynes was shown in the presence of a terminal alkene (**1.26**), an internal alkyne (**1.29**), and a silyl-protected alkyne (**1.28**).

We also explored variations of the alkenyl electrophile. Different substitution patterns were tolerated, including 1,1-disubstituted (**1.38**), cyclic trisubstituted (**1.37**), acyclic trisubstituted (**1.34**) and *Z*-alkenyl bromides (**1.39**). Alkene substitution at the position *cis* to the bromide resulted in lower yields despite longer reaction times and increased electrophile loadings. Additionally, conjugated alkenyl electrophiles (**1.32** and **1.33**) gave moderate to good yields. Esters, chlorides, and silyl ethers (**1.30**, **1.35**, and **1.36**) as well as heteroatoms in the propargylic and vinyl positions (**1.36** and **1.41**) were also tolerated.

The initially formed boronate esters can also be isolated or used in other transformations. After careful column chromatography, the allylic boronate ester (**1.28**) was obtained in 61% yield. A one-pot transformation of allylic boronate esters can be accomplished by the addition of benzaldehyde to the crude reaction mixture. The transposed homoallylic alcohol (**1.42**) was isolated in 79% overall yield based on the starting terminal alkyne and (4:1) *Z*:*E* diastereoselectivity.[59]

We also observed some limitations of the alkenyl electrophile scope. Little to no allylic boronate ester product was observed with tetrasubstituted alkenyl bromides, dienyl bromides, or alkenyl bromides with strongly electron withdrawing or donating substituents in the vinyl position.

Other halides and pseudo halides, such as alkenyl chlorides, iodides, and triflates, were not competent coupling partners in this differential dihydrofunctionalization.

1.2.3 *Mechanistic Investigation*

The key features of the mechanism shown in **Scheme 1.2** are the formation of the heterobimetallic complex and subsequent palladium catalyzed cross-coupling. Our previous work with an IPr-supported copper catalyst suggests that the formation of the heterobimetallic intermediate proceeds through two copper hydride additions, first to the alkyne and then to the alkenyl boronate intermediate.[41] We observed similar results with the triazole based NHC ligand (Tri). Heterobimetallic complex (**1.44**) is formed in the stoichiometric reaction of phenylacetylene, TriCuO*t*-Bu, and HBpin (**Scheme 1.4a**). Additionally, the reaction of alkenyl boronate **1.45** with an in situ generated copper hydride resulted in the formation of **1.44**, in good yield. After careful recrystallization, X-ray quality crystals of the heterobimetallic complex (**1.44**) were obtained (**Figure 1.1**).

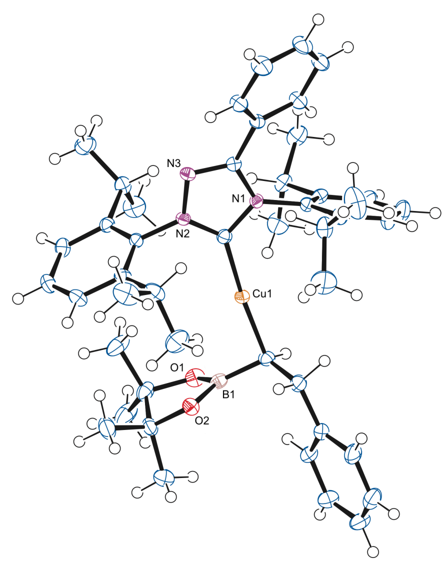
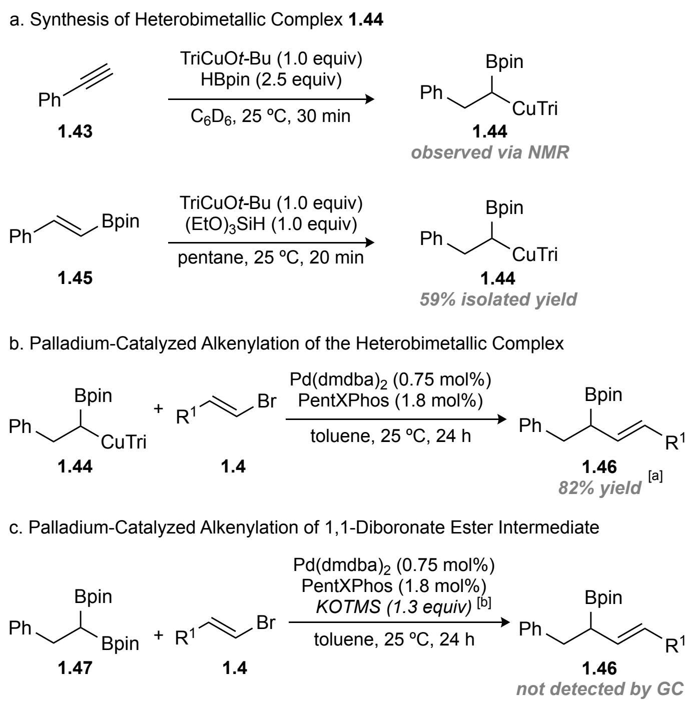


Figure 1.1 X-ray crystal structure of the heterobimetallic complex **1.44** with thermal ellipsoids at 50% probability. Disorder omitted for clarity.

Next, we turned our attention to the part of the reaction that involved alkenyl bromide. We demonstrated the feasibility of the palladium catalyzed cross-coupling of alkenyl bromide **1.4** and our isolated heterobimetallic complex (**1.44**) using the PentXPhos-supported palladium catalyst (**Scheme 1.4b**).



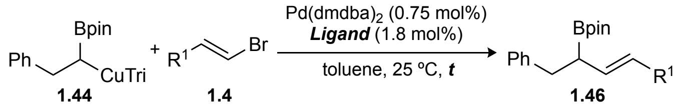
Scheme 1.4 Exploration of the Reaction Mechanism.

[a] Yield was determined by GC using 1,3,5-trimethoxybenzene as an internal standard. [b] Reaction was run both with and without KOTMS and gave the same result. R^1=Ph(CH_2)$_3$.

An alternative mechanism for the cross-coupling event, based on a report by Morken, would involve an alkyl diboronate ester as the active coupling partner.[47] To test this hypothesis, alkenyl bromide **1.4** and alkyl diboronate **1.47** were treated with Pd(dmdba)$_2$, PentXPhos and KOTMS. Under these conditions we did not observe the desired allylic boronate ester and instead only the homocoupled product of the electrophile was formed (**Scheme 1.4c**).

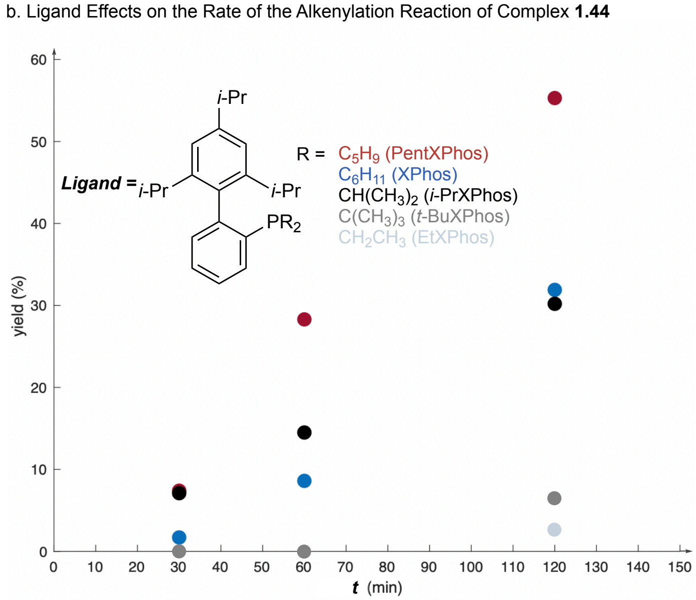
During reaction development, PentXPhos was found to be a uniquely effective ligand, with other XPhos variants providing significantly lower yield of the desired product. To better understand this effect, we explored the cross coupling of heterobimetallic complex **1.44** and alkenyl bromide **1.4** using palladium catalysts supported by different XPhos-type ligands.

a. Ligand Effects in the Alkenylation Reaction of Complex **1.44**



Ligand	none	PentXPhos	XPhos	*t*-BuXPhos	*i*-PrXPhos	EtXPhos
yield of 1.46 at 24 h	5%	82%	83%	47%	80%	6%

b. Ligand Effects on the Rate of the Alkenylation Reaction of Complex **1.44**



Scheme 1.5 Effects of Phosphine Ligands.

Reactions were performed on a 0.025 mmol scale with 1.2 equiv of alkenyl bromide **1.4**. To determine yields, aliquots taken from the reaction mixture and quenched with dibromotetrachloroethane before being analyzed by GC using 1,3,5- trimethoxybenzene as an internal standard. R^1=$Ph(CH_2)_3$.

While *t*-BuXPhos and EtXPhos gave inferior results, XPhos, PentXPhos, and *i*-PrXPhos all performed well and provided the allylic boronate ester in ~80% yield (**Scheme 1.5a**). A more detailed analysis of the reaction shown in **Scheme 1.5b** revealed that the reaction rate with PentXPhos is nearly double the rate of the reaction with XPhos or *i*-PrXPhos. The observed rate difference does not affect the overall outcome of the alkenylation of the preformed bimetallic intermediate (**Scheme 1.5a**). However, in the context of the dual catalytic cycle of differential dihydrofunctionalization, these rate differences become consequential. Increasing the concentration of palladium and XPhos or *i*-PrXPhos ligands to account for the lower rate of reaction observed with these catalysts does not improve their performance (see **Table 1.16**). These results are another example of the stringent requirements that dual catalytic cycles can impose on individual catalysts. Further investigation is necessary to fully elucidate the role of the phosphine ligands in the intricate interplay of the palladium and copper catalytic cycles of this reaction.

1.3 CONCLUSION

In summary, we have developed a new method for the synthesis of allylic boronate esters through differential dihydrofunctionalization of terminal alkynes enabled by cooperative action of copper and palladium catalysts. The new reaction has a broad substrate scope and is compatible with a variety of functional groups and substituted alkenyl bromides. Mechanistic experiments support the proposed catalytic cycle that involves hydrocupration of the initially formed alkenyl boronate ester, followed by palladium catalyzed alkenylation of the heterobimetallic intermediate. We also provide an insight into the unique performance of PentXPhos relative to other closely related ligands.

1.4 EXPERIMENTAL

1.4.1 *General Information*

All reactions were performed under a nitrogen atmosphere with flame-dried or oven-dried (120 °C) glassware, using standard Schlenk techniques, or in a glovebox (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). High Pressure Liquid Chromatography was performed using an Agilent LC column (Zorbax CN

PrepHT, 21.2 x 250mm, 7μm). 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 solvent peak ($CDCl_3$: *δ* 7.26 ppm or C_6D_6: *δ* 7.16 ppm). ^{13}C NMR 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 or C_6D_6: *δ* 128.0 ppm). ^{19}F NMR chemical shifts (*δ*) are reported in parts per million (ppm) and are referenced relative to the internal standard, hexafluorobenzene (C_6F_6: *δ* -164.9 ppm). ^{11}B NMR chemical shifts (*δ*) are reported in part per million (ppm). ^{31}P NMR chemical shifts (*δ*) are reported in parts per million (ppm) and are referenced relative to the external standard triphenylphosphine oxide ($OPPh_3$: *δ* 28.0 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), integration, and coupling constants in Hertz (Hz). Mass spectra were collected on a JEOL HX-110 mass spectrometer and Bruker EsquirelLC ion trap 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 @ 40 °C, 15 °C/min to 320 °C, 5.5 min @ 320 °C.

1.4.2 *Materials*

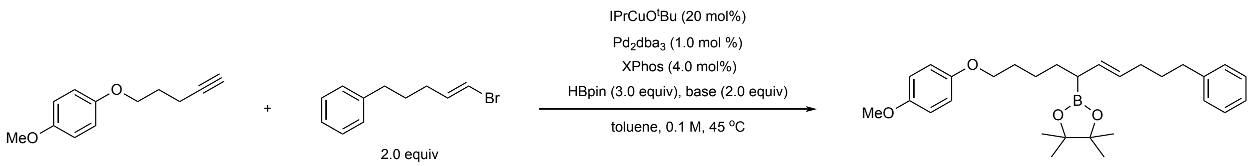
THF, CH_2Cl_2, ether, benzene, and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous isooctane was purchased from Millipore Sigma, and was subsequently degassed and stored over 4Å molecular sieves. Pinacolborane was purchase from TCI America and distilled over calcium hydride under reduced pressure prior to use. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and were stored over 4Å molecular sieves prior to use. Bis(3,5,3',5'-dimethoxydibenzylideneacetone) palladium(0) was purchased from Combi-Blocks and used as received. Other commercial reagents were purchased from Millipore Sigma, TCI America, GFS-Chemicals, Ark-Pharm, Combi-Blocks, Oakwood Chemicals, Strem Chemicals and Alfa Aesar.

1.4.3 *Reaction Development*

All reactions were performed on a 0.1 mmol scale. In a nitrogen-filled glovebox a dram vial was charged with a stir bar, alkoxide additive (**Table 1.3/1.4**), 1-methoxy-4-(pent-4-yn-1-yloxy)benzene, *n*-octyl ether (*n*-OE, used as an internal standard for GC), palladium (**Table 1.10/1.11**), copper (**Table 1.8/1.9**), palladium ligand **(Table 1.12/1.13/1.14)**, (4*E*)-5-bromo-4-penten-1-yl-benzene **(Table 1.7)**, HBpin **(Table 1.5)**, and solvent **(Table 1.6)**. The reaction mixture was stirred at 25 ºC. 20 µL aliquots were taken at 24 h, pushed through a plug of silica with 1.5 mL of a 30% solution of ether in hexanes and analyzed by Gas Chromatography.

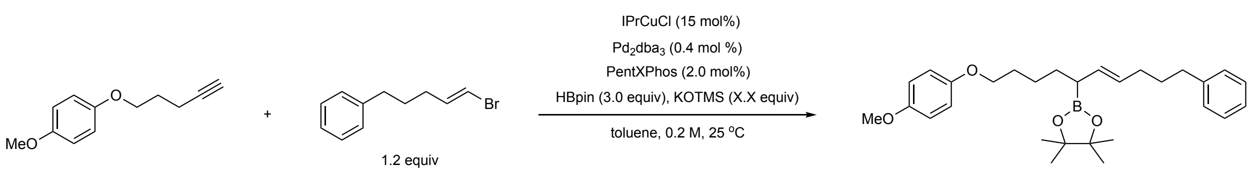
During preliminary reaction optimization, alkenyl chlorides, bromides, iodides and triflates were explored. Alkenyl bromides were found to be competent coupling partners, while alkenyl chlorides, iodides and triflates did not provide the desired product and were therefore not used in further reaction development.

Table 1.3 Effect of Reaction Parameters: Base Identity



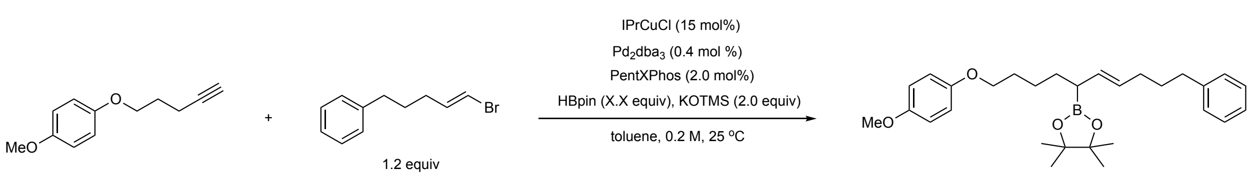
Entry	Base	Yield (%)
1	LiO*t*-Bu	13
2	NaO*t*-Bu	23
3	KO*t*-Bu	28
4	LiOMe	8
5	NaOMe	11
6	KOEt	21
7	LiO*i*-Pr	0
8	NaO*i*-Pr	17
9	NaOPent	22
10	NaOTMS	25
11	KOTMS	35

Table 1.4 Effect of Reaction Parameters: Base Equivalents



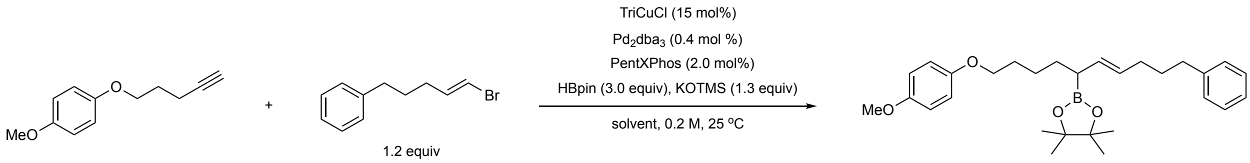
Entry	Base Equiv	Yield (%)
1	1.0	59
2	1.3	63
3	1.65	61
4	2.0	56

Table 1.5 Effect of Reaction Parameters: HBpin Equivalents



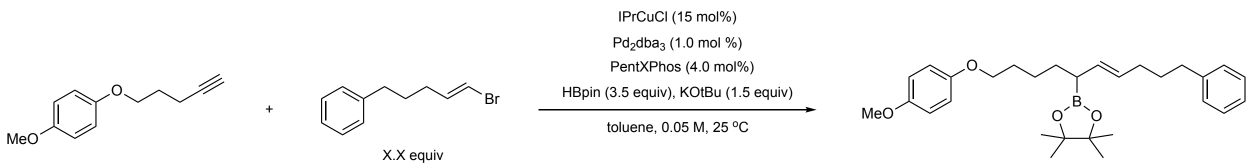
Entry	HBpin Equiv	Yield (%)
1	2.5	54
2	3.0	56
3	3.5	47

Table 1.6 Effect of Reaction Parameters: Solvent Identity



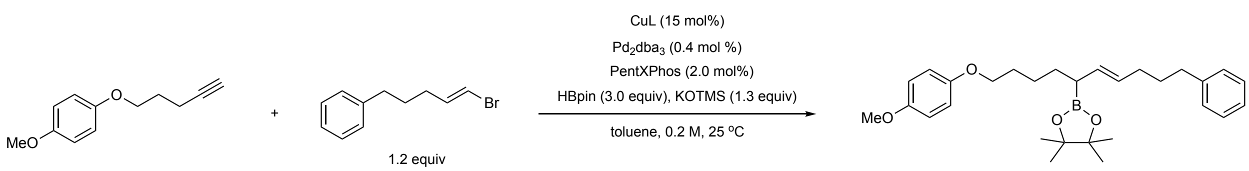
Entry	Solvent	Yield (%)
1	Toluene	73
2	Benzene	62
3	Isooctane	74
4	Xylenes	73
5	(Trifluoromethyl) benzene	61
6	Cyclohexane	69
7	THF	0
8	dioxane	12

Table 1.7 Effect of Reaction Parameters: Alkenyl Bromide Equivalents



Entry	Bromide Equiv	Yield (%)
1	1.0	59
2	1.2	65
3	1.5	63
4	2.0	60

Table 1.8 Effect of Reaction Parameters: Copper Source



Entry	Copper Precatalyst	Yield (%)
1	TriCuCl	71
2	Tri^{Me}CuCl	64
3	IPrCuCl	62
4	IPrCuBr	65
5	IPr^{MeO}CuCl	65
6	IPrCuO-*t*Bu	35

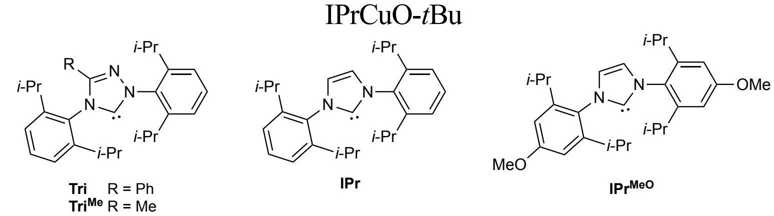
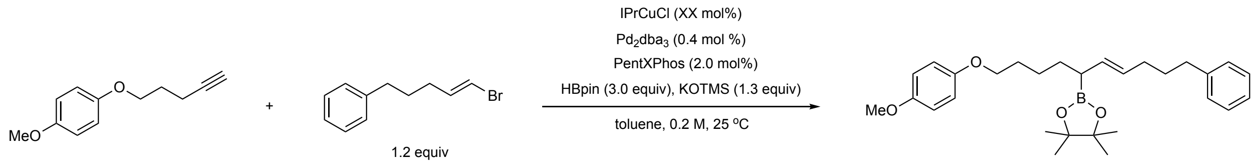
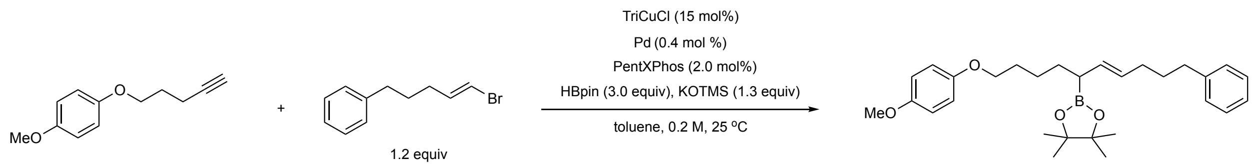


Table 1.9 Effect of Reaction Parameters: Copper Catalyst Loading



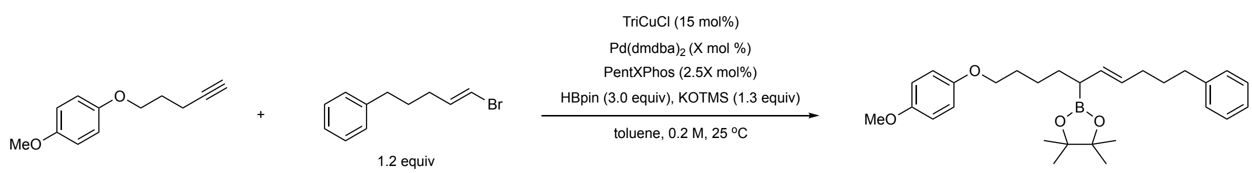
Entry	Copper Equiv	Yield (%)
1	0.10	47
2	0.15	60
3	0.20	51

Table 1.10 Effect of Reaction Parameters: Palladium Source



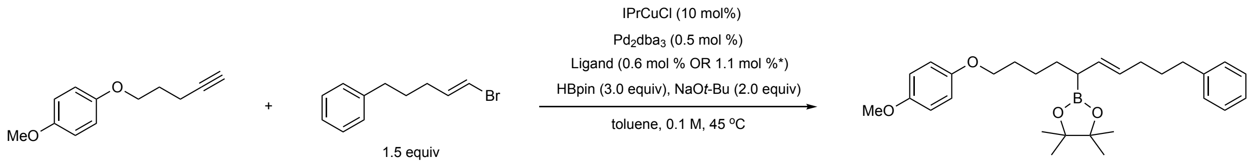
Entry	Palladium Precatalyst	Yield (%)
1	Pd(dmdba)2	77
2	Pd2dba3	70
3	[PdCl(allyl)]2	69
4	[PdCl(1-methylallyl)]2	67
5	[PdCl(1-phenylallyl)]2	68
6	Pd(acac)2	62
7	Pd(TFA)2	61
8	PdCl2(benzonitrile)	65
9	Pd(OAc)2	63
10	Pd[(*t*-BuP)3]2	13

Table 1.11 Effect of Reaction Parameters: Palladium Catalyst Loading



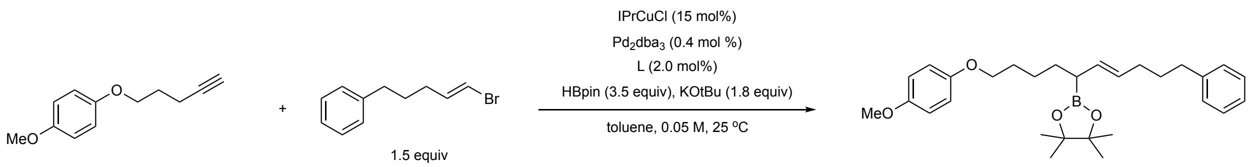
Entry	Palladium Equiv	Yield (%)
1	0.0050	78
2	0.0075	80
3	0.0100	72
4	0.0150	70

Table 1.12 Effect of Reaction Parameters: Palladium Ligand Identity 1



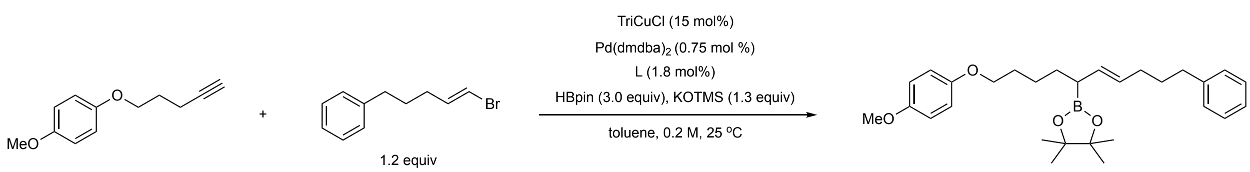
Entry	Alkyl Group - XPhos Backbone	Yield (%)
1	PCy_3*	0
2	Dppf	3
3	XPhos*	13
4	*t*-BuXANTPHOS	4

Table 1.13 Effect of Reaction Parameters: Palladium Ligand Identity 2

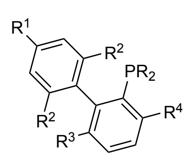


Entry	Alkyl Group - XPhos Backbone	Yield (%)
1	Cyclohexyl (XPhos)	35
2	Cyclopentyl (PentXPhos)	63
3	isopropyl (*i*-PrXPhos)	42
4	tertbutyl (*t*-BuXPhos)	5
5	Ethyl (EtXPhos)	0

Table 1.14 Effect of Reaction Parameters: Palladium Ligand Identity 3



Entry	Ligand	Yield (%)
1	PentXPhos	80
2	SPhos*	41
3	BrettPhos*	12
4	RockPhos*	9



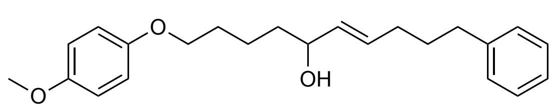
PentPhos R = C_5H_9, R^1 = *i*-Pr, R^2 = *i*-Pr, R^3 = H, R^4 = H
SPhos* R = C_5H_9, R^1 = H, R^2 = OMe, R^3 = H, R^4 = H
BrettPhos* R = C_5H_9, R^1 = *i*-Pr, R^2 = *i*-Pr, R^3 = OMe, R^4 = OMe
RockPhos* R = C_5H_9, R^1 = *i*-Pr, R^2 = *i*-Pr, R^3 = CH_3, R^4 = OMe

1.4.4 *General Procedure for Differential Dihydrofunctionalization*

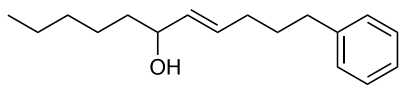
In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, KOTMS (83.4 mg, 0.650 mmol, 1.3 equiv), TriCuCl (42.4 mg, 0.075 mmol, 0.15 equiv), Pd(dmdba)$_2$ (3.1 mg, 0.004 mmol, 0.0075 equiv), PentXPhos (4.0 mg, 0.009 mmol, 0.018 equiv), alkyne (0.5 mmol, 1.0 equiv), alkenyl bromide (0.6 mmol, 1.2 equiv), HBpin (192.0 mg, 1.50 mmol, 3.0 equiv), toluene (2.5 mL, 0.2M) and the reaction was vigorously stirred at 25 °C. After 2 h a 20 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of a 30% solution of ether to hexanes and analyzed by GC. Upon consumption of the alkyne, the solution was transferred to a scintillation vial with 1.5 mL of THF. This solution was cooled to 0 °C using an ice-water bath. To this was added NaOH (1.0 mL, 3.0 mmol, 6.0 equiv, 3.0 M) and H_2O_2 (750 µL, 7.250 mmol, 14.5 equiv, 30% (w/w) in H_2O). The reaction mixture was allowed to warm to room temperature over the course of 10 min and further react for 20 h. At this point the reaction mixture was diluted with ether and H_2O, the aqueous layer was extracted 3x with ether, the combined organic layers were dried by Mg_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography.

1.4.5 *Characterization of Differential Dihydrofunctionalization Products*

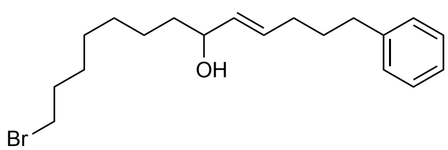
1.4.5.1 Allylic Alcohol Products



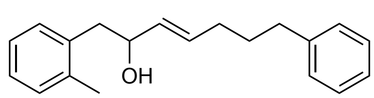
(6*E*)-1-(4-methoxyphenoxy)-10-phenyldec-6-en-5-ol (1.5), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (141 mg, 80% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.26 (d, 2H), 7.17 (t, *J* = 7.4 Hz, 3H), 6.82 (s, 4H), 5.66 (dt, *J* = 15.5, 6.3 Hz, 1H), 5.48 (dd, *J* = 15.5, 7.2 Hz, 1H), 4.08 (d, *J* = 6.3 Hz, 1H), 3.93 – 3.88 (t, 2H), 3.76 (s, 3H), 2.62 (t, *J* = 7.8 Hz, 2H), 2.08 (q, *J* = 7.2 Hz, 2H), 1.74 (m, 4H), 1.67 – 1.37 (m, 4H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 153.8, 153.3, 150.0, 142.4, 133.5, 131.8, 128.5, 125.8, 115.6, 114.7, 73.0, 68.6, 55.8, 37.1, 35.5, 31.8, 30.9, 29.4, 22.2. MS (ESI+) calculated for $[M+H-H2O]^+$ 337.2, found 337.2. FTIR (neat, cm^{-1}): 2405(br), 3024(w), 2933(s), 2857(m), 1507(s), 1453(m), 1288(w), 1231(s), 1039(s), 969(m), 824(m), 747(m), 699(m).



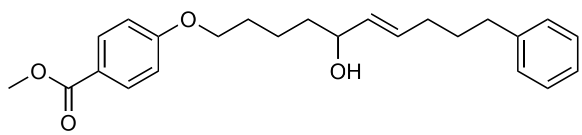
(4*E*)-1-phenylundec-4-en-6-ol (1.7), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (107 mg, 81% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.33 (m, 2H), 7.27 – 7.25 (m, 3H), 5.73 (dt, *J* = 14.3, 7.4 Hz, 1H), 5.55 (dd, *J* = 14.3, 7.1 Hz, 1H), 4.12 (dt, *J* = 7.1, 7.1 Hz, 1H), 2.69 (t, *J* = 7.1 Hz, 2H), 2.15 (dt, *J* = 7.4, 7.4 Hz, 2H), 1.80 (p, *J* = 7.1 Hz, 2H), 1.70 – 1.26 (m, 10H), 0.97 (t, *J* = 5.9 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.4, 133.7, 131.5, 128.5, 128.4, 125.8, 73.2, 37.4, 35.5, 31.9, 31.8, 31.0, 25.3, 22.7, 14.2. GCMS (EI) calculated for $[M]^+$ 246.2, found 246.2. FTIR (neat, cm^{-1}): 3349(br), 3025(m), 2928(s), 2855(s), 1603(w), 1498(m), 1453(s), 1129(m), 1029(m), 976(s), 745(m), 699(s).



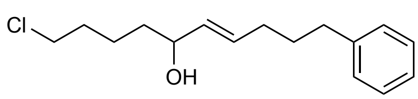
(4*E*)-13-bromo-1-phenyltridec-4-en-6-ol (1.8), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (138 mg, 78% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.16 (m, 2H), 7.12 – 7.05 (m, 3H), 5.50 (dt, J = 15.4, 6.5 Hz, 1H), 5.41 (dd, J = 15.4, 6.4, 1.3 Hz, 1H), 3.91 (q, J = 6.4 Hz, 1H), 2.95 (t, J = 6.8 Hz, 2H), 2.49 (t, J = 7.2 H, 2H), 1.94 (q, J = 6.5 Hz, 2H), 1.61 (p, J = 7.4 Hz, 2H), 1.54 – 1.22 (m, 6H), 1.17 – 1.11 (m, 4H), 1.09 – 1.01 (m, 2H), 0.97 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.6, 134.7, 130.7, 128.8, 128.7, 126.1, 72.9, 37.9, 35.7, 33.8, 32.1, 31.4, 29.8, 29.1, 28.4, 25.8. MS (ESI+) calculated for [M+H-H2O]$^+$ 335.1, found 335.1. FTIR (neat, cm^{-1}): 3350(br), 3024(m), 2928(s), 2854(s), 1669(w), 1603(m), 1495(m), 1452(s), 1246(m), 1065(m), 967(s), 747(m), 671(s).



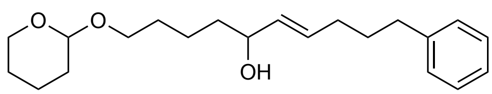
(3E)-1-(2-methylphenyl)-7-phenylhept-3-en-2-ol (1.9), compound was prepared according to a slightly modified procedure, the initial reaction was run for 4 h prior to oxidation. The compound was then purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (74 mg, 40% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.16 (m, 2H), 7.13 – 7.03 (m, 7H), 5.48 – 5.45 (m, 2H), 4.15 (q, J = 5.6 Hz, 1H), 2.79 (dd, J = 13.7, 7.7 Hz, 1H), 2.71 (dd, J = 13.6, 5.7 Hz, 1H), 2.42 (t, J = 7.7 Hz, 2H), 2.17 (s, 3H), 1.92 – 1.87 (m, 2H), 1.55 (h, J = 6.6 Hz, 2H), 1.26 (d, J = 6.4 Hz, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.6, 137.1, 136.8, 133.6, 130.8, 130.7, 130.6, 128.8, 128.6, 126.8, 126.2, 126.1, 73.0, 41.8, 35.6, 32.0, 31.2, 19.8. MS (ESI+) calculated for [M+H-H2O]$^+$ 263.2, found 263.2. FTIR (neat, cm^{-1}): 3379(br), 3061(w), 3025(m), 2932(s), 2857(m), 1495(s), 1458(s), 1028(m), 968(m), 744(s), 698(m).



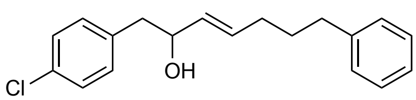
methyl 4-{[(6*E*)-5-hydroxy-10-phenyldec-6-en-1-yl]oxy}benzoate (1.10), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear yellow liquid (163 mg, 85% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.31 (m, 2H), 7.26 (t, J = 7.0 Hz, 3H), 5.73 (dt, J = 14.3, 7.4 Hz, 1H), 5.55 (dd, J = 15.5, 7.1 Hz, 1H), 4.12 (q, J = 6.8 Hz, 1H), 2.69 (t, J = 7.1 Hz, 2H), 2.15 (p, J = 7.1 Hz, 2H), 1.80 (p, J = 7.7, 7.1 Hz, 2H), 1.70 – 1.26 (m, 10H), 0.97 (t, J = 5.9 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.4, 133.7, 131.5, 128.5, 128.4, 125.8, 73.2, 37.4, 35.5, 31.9, 31.8, 31.0, 25.3 22.7, 14.2. MS (ESI+) calculated for $[M+H-H2O]^+$ 365.2, found 365.2. FTIR (neat, cm^{-1}): 3426(br), 3024(m), 2935(s), 2856(s), 1716(s), 1605(s), 1511(s), 1435(s), 1281(s), 1256(s), 1168(s), 1105(m), 1010(m), 969(m), 847(m), 771(s), 698(m).



(6*E*)-1-chloro-10-phenyldec-6-en-5-ol (1.11), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (113 mg, 85% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.17 (m, 2H), 7.11 – 7.06 (m, 3H), 5.44 (dt, J = 15.4, 7.2 Hz, 1H), 5.32 (dd, J = 15.4, 6.3 Hz, 1H), 3.78 (q, J = 6.3 Hz, 1H), 3.10 (t, J = 6.6 Hz, 2H), 2.48 (t, J = 7.7 Hz, 2H), 1.92 (q, J = 7.2 Hz, 2H), 1.59 (p, J = 7.5 Hz, 2H), 1.50 – 1.22 (m, 6H), 0.93 (s, 1H). ^{13}C NMR (75 MHz, Benzene-d_6) δ 142.5, 134.3, 130.9, 128.8, 128.7, 126.1, 72.6, 45.0, 36.9, 35.7, 32.8, 32.0, 31.3, 23.2. MS (ESI+) calculated for $[M+H-H2O]^+$ 249.1, found 249.1. FTIR (neat, cm^{-1}): 3364(br), 3026(m), 2933(s), 2857(s), 1669(w), 1603(m), 1495(m), 1455(s), 1309(m), 969(m), 745(m), 699(s), 649(w).

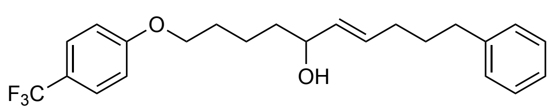


(6*E*)-1-(oxan-2-yloxy)-10-phenyldec-6-en-5-ol (1.12), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (111 mg, 69% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.16 (m, 2H), 7.10 – 7.07 (m, 3H), 5.48 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.39 (dd, *J* = 15.6, 6.3 Hz, 1H), 4.59 (s, 1H), 3.91 (q, *J* = 6.3 Hz, 1H), 3.88 – 3.78 (m, 2H), 3.42 – 3.38 (m, 1H), 3.36 – 3.32 (m, 1H), 2.47 (t, *J* = 7.7 Hz, 2H), 1.92 (q, *J* = 7.1 Hz, 2H), 1.80 – 1.72 (m, 1H), 1.67 – 1.40 (m, 10H), 1.37 – 1.30 (m, 1H), 1.26 – 1.23 (m, 2H), 1.06 (s, 1H). ^{13}C NMR (75 MHz, Benzene-d_6) δ 142.6, 134.7, 130.5, 128.8, 128.7, 126.1, 98.7, 72.8, 67.6, 61.7, 37.8, 35.7, 32.1, 31.4, 31.1, 30.2, 26.0, 22.8, 19.7. MS (ESI+) calculated for $[M+H-H2O]^+$ 315.1, found 315.1. FTIR (neat, cm^{-1}): 3445(br), 3025(m), 2938(s), 2858(s), 1603(w), 1453(m), 1352(m), 1246(m), 1145(s), 1030(m), 851(m), 755(s).

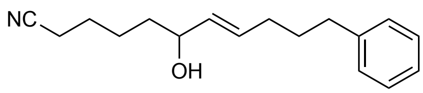


(3E)-1-(4-chlorophenyl)-7-phenylhept-3-en-2-ol (1.13), compound was prepared according to a slightly modified procedure, the initial reaction was run for 4 h prior to oxidation. The compound was then purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (150 mg, 70% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.19 (t, *J* = 7.6 Hz, 2H), 7.13 – 7.03 (m, 5H), 6.80 (d, *J* = 8.3 Hz, 2H), 5.39 (dt, *J* = 15.4, 6.5 Hz, 1H), 5.30 (dd, *J*

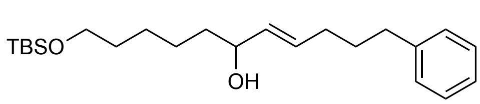
= 15.4, 6.2 Hz, 1H), 3.97 (q, J = 6.2 Hz, 1H), 2.57 – 2.48 (m, 2H), 2.41 (t, J = 7.7 Hz, 2H), 1.86 (q, J = 7.2 Hz, 2H), 1.54 (h, J = 7.4 Hz, 2H), 1.00 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.5, 137.3, 133.1, 132.4, 131.4, 128.8, 128.7, 128.6, 126.2, 73.4, 43.7, 35.6, 31.9, 31.2. MS (ESI+) calculated for [M+H-H2O]$^+$ 283.1, found 283.1. FTIR (neat, cm^{-1}): 3382(br), 3025(m), 2930(s), 2856(m), 1492(s), 1435(m), 1406(w), 1089(m), 1106(m), 968(m), 836(w), 804(m), 700(s).



(6*E*)-10-phenyl-1-[4-(trifluoromethyl)phenoxy]dec-6-en-5-ol (1.14), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (159 mg, 81% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.32 (d, J = 8.6 Hz, 2H), 7.16 (d, 2H), 7.11 – 7.06 (m, 3H), 6.56 (d, J = 8.6 Hz, 2H), 5.47 (dt, J = 15.3, 7.1 Hz, 1H), 5.37 (dd, J = 15.3, 6.2, Hz, 1H), 3.87 (q, J = 6.2 Hz, 1H), 3.45 (t, J = 6.6 Hz, 2H), 2.52 – 2.44 (t, 2H), 1.93 (q, J = 7.1 Hz, 2H), 1.65 – 1.30 (m, 8H), 0.92 (s, 1H). ^{13}C NMR (75 MHz, Benzene-d_6) δ 162.0, 142.5, 134.4, 131.0, 128.8, 127.1, 126.2, 122.8 (q, J = 32.4 Hz), 126.8 (q, J = 272.6 Hz), 114.8, 72.7, 68.1, 37.4, 35.7, 32.0, 31.3, 29.3, 22.4. ^{19}F NMR (470 MHz, Chloroform-d) δ -64.38. MS (ESI+) calculated for [M+H-H2O]$^+$ 375.2, found 375.2. FTIR (neat, cm^{-1}): 3365(br), 3026(w), 2932(s), 2858(m), 1615(s), 1519(m), 1330(s), 1258(s), 1160(s), 1111(s), 1067(m), 1009(m), 969(m), 835(m), 747(w), 699(m), 638(m).

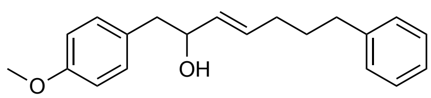


(7*E*)-6-hydroxy-11-phenylundec-7-enenitrile (1.15), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-40% EtOAc in hexanes and was isolated as a clear colorless liquid (106 mg, 83% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.21 – 7.18 (m, 2H), 7.10 – 7.08 (m, 3H), 5.44 (dt, J = 15.4, 7.6 Hz, 1H), 5.29 (dd, J = 15.4, 6.2 Hz, 1H), 3.72 (q, J = 6.2 Hz, 1H), 2.49 (t, J = 7.7 Hz, 2H), 1.92 (q, J = 7.2 Hz, 2H), 1.60 (p, J = 7.6 Hz, 2H), 1.38 (t, J = 7.1 Hz, 2H), 1.28 – 1.04 (m, 4H), 1.01 – 0.99 (m, 3H). ^{13}C NMR (75 MHz, Benzene-d_6) δ 142.5, 134.2, 130.9, 128.8, 128.7, 126.2, 119.5, 72.3, 36.7, 35.7, 32.0, 31.3, 25.5, 24.8, 16.7. MS (ESI+) calculated for $[M+H-H2O]^+$ 240.1, found 240.1. FTIR (neat, cm^{-1}): 3434(br), 3025(m), 2931(s), 2859(s), 2279(w), 2246(m), 1669(w), 1602(m), 1495(m), 1453(s), 1424(m), 1113(m), 1067(m), 1002(m), 969(s), 851(m), 755(s).

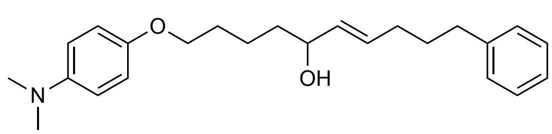


(4E)-11-[(tert-butyldimethylsilyl)oxy]-1-phenylundec-4-en-6-ol (1.16), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (144 mg, 77% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.17 (d, J = 14.3 Hz, 6H), 7.12 – 7.05 (m, 3H), 5.66 – 5.45 (m, 1H), 5.45 – 5.29 (m, 1H), 3.92 (q, J = 6.1 Hz, 1H), 3.55 (t, J = 6.4 Hz, 2H), 2.48 (t, J = 7.7 Hz, 2H), 1.93 (q, J = 7.2 Hz, 2H), 1.68 – 1.48 (m, 5H), 1.50 – 1.28 (m, 6H), 0.99 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.6, 134.7, 130.6, 128.8, 128.7, 126.1, 72.8, 63.3, 38.0, 35.7, 33.3, 32.1, 31.4, 26.3, 26.2, 25.8, 18.6, -5.1. MS (ESI+) calculated for $[M+H-H2O]^+$

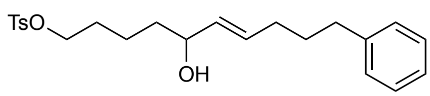
359.2, found 259.2. FTIR: 3350 (br, s), 3026 (m), 2929 (s), 2856 (s), 1603 (w), 1471 (s), 1255 (s), 1100 (s), 968 (m), 834 (s), 774 (m), 698 (m).



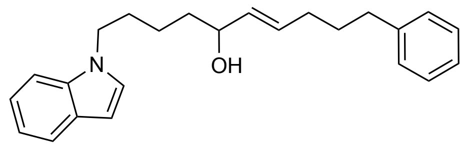
(3E)-1-(4-methoxyphenyl)-7-phenylhept-3-en-2-ol (1.17), compound was prepared according to a slightly modified procedure, the initial reaction was run for 4 h prior to oxidation. The compound was then purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear colorless liquid (92 mg, 62% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.16 (m, 2H), 7.10 – 7.03 (m, 5H), 6.78 (d, J = 8.1 Hz, 2H), 5.54 – 5.40 (m, 2H), 4.15 (q, J = 6.2 Hz, 1H), 3.31 (s, 3H), 2.77 – 2.65 (m, 2H), 2.42 (t, J = 7.7 Hz, 2H), 1.91 (q, J = 7.4 Hz, 2H), 1.55 (p, J = 7.4 Hz, 2H), 1.24 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 158.8, 142.7, 133.5, 131.0, 130.9, 130.6, 128.8, 128.6, 126.1, 114.1, 73.8, 54.8, 43.9, 35.6, 32.0, 31.3. MS (ESI+) calculated for $[M+H-H2O]^+$ 279.2, found 279.2. FTIR (neat, cm^{-1}): 3398(br), 3025(w), 2931(s), 2855(w), 2835(w), 1611(m), 1512(s), 1453(m), 1300(m), 1246(s), 1177(m), 1110(w), 1035(s), 969(m), 819(w), 748(m), 700(m).



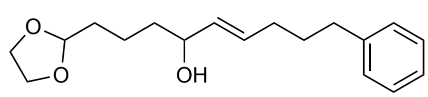
(6*E*)-1-[4-(dimethylamino)phenoxy]-10-phenyldec-6-en-5-ol (1.18), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear pink solid (139 mg, 76% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.16 (d, 2H), 7.13 – 7.05 (m, 3H), 6.94 (d, J = 8.8 Hz, 2H), 6.66 (d, J = 8.8 Hz, 2H), 5.52 – 5.44 (dt, J = 15.5, 7.4 Hz, 1H), 5.42 – 5.35 (dd, J = 15.5, 7.1 Hz, 1H), 3.90 (q, J = 7.4 Hz, 1H), 3.76 (t, J = 6.7 Hz, 2H), 2.56 (s, J = 1.1 Hz, 6H), 2.48 (t, J = 7.4 Hz, 2H), 1.93 (q, J = 7.1 Hz, 2H), 1.68 (q, J = 6.7 Hz, 2H), 1.64 – 1.39 (m, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 151.7, 145.7, 142.4, 133.5, 131.6, 128.5, 128.4, 125.8, 115.6, 115.2, 73.0, 68.6, 42.0, 37.1, 35.5, 31.8, 30.9, 29.4, 22.2. MS (ESI+) calculated for $[M+H]^+$ 368.2, found 368.2. FTIR (neat, cm^{-1}): 3399(br), 3025(m), 2934(s), 2856(s), 2793(m), 1513(s), 1475(m), 1452(m), 1294(m), 1243(s), 1294(m), 1243(s), 1056(m), 1029(m), 969(m), 947(w), 816(m), 747(m), 699(s).



(6*E*)-1-[(4-methylbenzenesulfonyl)oxy]-10-phenyldec-6-en-5-ol (1.19), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear colorless liquid (155 mg, 77% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.76 (d, J = 8.3 Hz, 2H), 7.16 (m, 2H), 7.10 (m, 3H), 6.71 (d, J = 8.3 Hz, 2H), 5.43 (dt, J = 15.4, 6.7 Hz, 1H), 5.28 (dd, J = 15.4, 6.6z, 1H), 3.83 (t, J = 6.4 Hz, 2H), 3.73 (q, J = 6.6 Hz, 1H), 2.48 (t, J = 6.7 Hz, 2H), 1.91 (q, J = 7.2 Hz, 2H), 1.84 (s, 3H), 1.59 (p, J = 6.6 Hz, 2H), 1.40 – 1.09 (m, 5H), 0.93 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 144.2, 142.6, 134.6, 134.3, 130.8, 129.9, 128.7, 128.6, 128.4, 128.2, 126.1, 72.4, 70.4, 37.0, 35.7, 31.3, 29.1, 21.7, 21.2. MS (ESI+) calculated for $[M+H-H2O]^+$ 385.2, found 385.2. FTIR (neat, cm^{-1}): 3552(br), 3417(br), 3025(m), 2930(s), 2854(m), 1598(m), 1495(m), 1452(m), 1359(s), 1176(s), 1097(m), 965(m), 929(m), 813(m), 664(m).

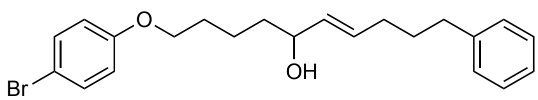


(6E)-1-(1H-indol-1-yl)-10-phenyldec-6-en-5-ol (1.20), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear yellow liquid (138 mg, 79% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.74 (d, J = 7.7 Hz, 1H), 7.26 – 7.18 (m, 5H), 7.09 (d, J = 7.6 Hz, 3H), 6.74 (d, J = 3.1 Hz, 1H), 6.54 (d, J = 3.1 Hz, 1H), 5.38 (dt, J = 15.4, 6.6 Hz, 1H), 5.27 (dd, J = 15.4, 6.4 Hz, 1H), 3.71 (q, J = 6.4 Hz, 1H), 3.55 (t, J = 7.0 Hz, 2H), 2.47 (t, J = 7.6 Hz, 2H), 1.89 (q, J = 7.2 Hz, 2H), 1.57 (p, J = 7.5 Hz, 2H), 1.47 – 1.40 (m, 2H), 1.35 – 1.31 (m, 1H), 1.26 – 1.07 (m, 3H), 0.84 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.5, 136.6, 134.2, 130.8, 129.4, 128.8, 128.7, 127.8, 126.2, 121.7, 121.5, 119.7, 109.8, 101.4, 72.6, 46.2, 37.1, 35.7, 32.0, 31.3, 30.3, 23.1. MS (ESI+) calculated for $[M+H-H2O]^+$ 330.3, found 330.3. FTIR (neat, cm^{-1}): 3395(br), 3056(w), 3025(m), 2931(s), 2856(m), 1495(m), 1463(s), 1315(m), 1232(w), 1076(w), 1011(w), 968(m), 740(s), 699(m).

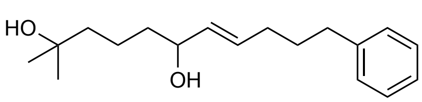


(5E)-1-(1,3-dioxolan-2-yl)-9-phenylnon-5-en-4-ol (1.21), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-60% EtOAc in hexanes and was isolated as a clear yellow liquid (112 mg, 77% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.16 (s, 6H), 7.08 (d, J = 7.5 Hz, 3H), 5.45 (dt, J = 15.5, 6.2 Hz, 1H), 5.36 (dd, J = 15.6, 6.1 Hz, 1H), 4.81 (t, J = 4.7 Hz, 1H), 3.89 (q, J = 6.3 Hz, 1H), 3.65 – 3.44 (m, 2H), 3.44 – 3.19 (m, 2H), 2.47 (t, J = 7.7 Hz, 2H), 1.90 (q, J = 7.2 Hz, 2H), 1.77 (tt, J = 7.5, 3.7 Hz, 2H), 1.72

– 1.37 (m, 6H), 1.03 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.7, 134.6, 130.6, 128.8, 128.6, 126.1, 104.9, 72.7, 64.8, 37.8, 35.7, 34.3, 32.0, 31.3, 20.6. MS (ESI+) calculated for [M+H-H2O]$^+$ 273.1, found 273.1. FTIR (neat, cm^{-1}): 3426(br), 3020(w), 2928(s), 2858(s), 1472(m), 1409(m), 1140(s), 1030(s), 966(s), 943(m), 906(w), 748(m), 700(s).

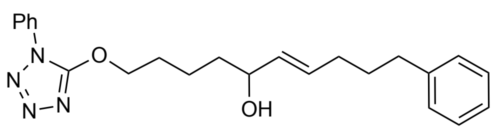


(6*E*)-1-(4-bromophenoxy)-10-phenyldec-6-en-5-ol (1.22), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (125 mg, 62% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.16 (m, 4H), 7.12 – 7.05 (m, 3H), 6.50 – 6.44 (d, 2H), 5.47 (dt, *J* = 15.3, 6.5 Hz, 1H), 5.37 (dd, *J* = 15.3, 6.6 Hz, 1H), 3.87 (q, *J* = 6.6 Hz, 1H), 3.44 (t, *J* = 6.4 Hz, 2H), 2.48 (t, *J* = 7.7 Hz, 2H), 1.93 (q, *J* = 6.5 Hz, 2H), 1.64 – 1.32 (m, 8H), 0.95 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 158.7, 142.5, 134.4, 132.6, 130.9, 128.8, 128.7, 128.4, 126.2, 116.6, 113.0, 72.7, 68.1, 37.5, 32.0, 31.3, 29.4, 22.4. MS (ESI+) calculated for [M+H-H2O]$^+$ 385.1, found 385.1. FTIR (neat, cm^{-1}): 3391(br), 3025(m), 2934(s), 2857(m), 1590(m), 1488(s), 1472(m), 1390(w), 1285(m), 1243(s), 1170(m), 1071(m), 1002(m), 969(m), 821(m), 742(w), 669(m).

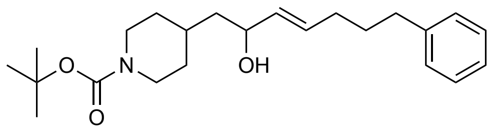


(7*E*)-2-methyl-11-phenylundec-7-ene-2,6-diol (1.23), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-40% EtOAc in hexanes and was isolated as a clear colorless liquid (44 mg, 32% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.16 (s, 2H), 7.10 – 7.07 (m, 3H), 5.58 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.49 (dd, *J* =

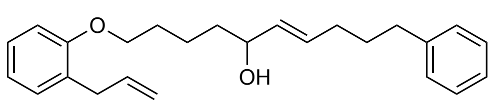
15.5, 6.7 Hz, 1H), 4.04 (q, J = 6.7, 1H), 2.50 (t, J = 7.7 Hz, 2H), 2.13 (s, 2H), 1.96 (q, J = 7.1 Hz, 2H), 1.69 – 1.26 (m, 8H), 1.12 (s, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.6, 134.7, 130.5, 128.8, 128.7, 72.6, 70.5, 43.9, 38.4, 35.7, 32.1, 31.4, 29.6, 29.5, 20.6. MS (ESI+) calculated for $[M+H-H2O]^+$ 259.1, found 259.1. FTIR (neat, cm^{-1}): 3367(br), 3025(m), 2929(s), 2855(m), 1452(m), 1375(m), 1153(m), 968(m), 637(w), 625(m).



(6E)-10-phenyl-1-[(1-phenyl-1H-1,2,3,4-tetrazol-5-yl)oxy]dec-6-en-5-ol (1.24), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-15% EtOAc in CH_2Cl_2 and was isolated as a clear yellow liquid (126 mg, 64% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.49 (d, J = 7.9 Hz, 2H), 7.21 – 7.18 (m, 2H), 7.11 – 7.06 (m, 3H), 6.99 (t, J = 7.6 Hz, 2H), 6.91 (d, J = 7.4 Hz, 1H), 5.45 (dt, J = 15.3, 6.5 Hz, 1H), 5.31 (dd, J = 15.3, 6.5 Hz, 1H), 4.22 (t, J = 6.6 Hz, 2H), 3.79 (d, J = 6.5z Hz, 1H), 2.48 (t, J = 7.6 Hz, 2H), 1.92 (q, J = 6.9 Hz, 2H), 1.67 – 1.53 (m, 2H), 1.52 – 1.14 (m, 6H), 0.92 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 160.5, 142.6, 134.4, 134.0, 130.8, 129.6, 128.8, 128.7, 128.6, 126.1, 121.6, 74.1, 72.4, 37.2, 35.7, 32.0, 31.3, 28.8, 21.9. MS (ESI+) calculated for $[M+H-H2O]^+$ 357.2, found 357.2. FTIR (neat, cm^{-1}): 3428(br), 3025(m), 2931.3(s), 2857(m), 1595(s), 1504(s), 1460(s), 1383(m), 1294(m), 1128(m), 1020(m), 969(m), 912(w), 760(s), 700(m).

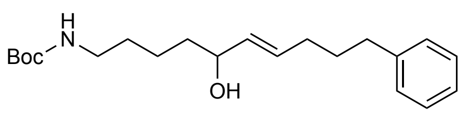


tert-butyl 4-[(3*E*)-2-hydroxy-7-phenylhept-3-en-1-yl]piperidine-1-carboxylate (1.25), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear colorless liquid (164 mg, 88% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.16 (m, 2H), 7.10 – 7.07 (m, 3H), 5.43 (dt, *J* = 15.4, 7.5 Hz, 1H), 5.32 (dd, *J* = 15.4, 6.7 Hz, 1H), 4.41 (s, 1H), 4.06 (s, 1H), 3.90 (q, *J* = 6.7 Hz, 1H), 2.51 – 2.46 (m, 4H), 1.92 (q, *J* = 7.2 Hz, 2H), 1.59 (p, *J* = 7.5 Hz, 2H), 1.48 (s, 9H), 1.42 – 1.26 (m, 3H), 1.14 – 1.08 (m, 1H), 1.04 – 0.91 (m, 3H). ^{13}C NMR (75 MHz, Benzene-d_6) δ 154.8, 142.5, 135.0, 130.2, 128.8, 128.7, 126.2, 78.9, 70.0, 44.7, 35.7, 33.1, 32.7, 32.1, 32.0, 31.4, 28.6. MS (ESI+) calculated for $[M+H-H2O]^+$ 356.2, found 356.2. FTIR (neat, cm^{-1}): 3437(br), 2975(s), 2925(s), 2854(s), 1694(s), 1426(s), 1365(m), 1278(m), 1169(s), 1087(m), 969(m), 870(m), 748(m), 669(m).

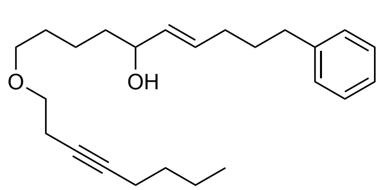


(6*E*)-10-phenyl-1-[2-(prop-2-en-1-yl)phenoxy]dec-6-en-5-ol (1.26), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (130 mg, 71% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.12 (m, 3H), 7.12 – 7.05 (m, 4H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 6.07 (ddt, *J* = 16.8, 10.0, 6.7 Hz, 1H), 5.48 (dt, *J* = 15.4, 6.6 Hz, 1H), 5.38 (dd, *J* = 15.4, 6.2 Hz, 1H), 5.11 (d, *J* = 16.8, 1H), 5.04 (d, *J* = 10.0, 1H), 3.89 (q, *J* = 6.2 Hz, 1H), 3.63 (t, *J* = 6.3 Hz, 2H), 3.51 (d, *J* = 6.7 Hz, 2H), 2.49 (t, *J* = 7.6 Hz, 2H), 1.94 (q, *J* = 7.1 Hz, 2H), 1.65

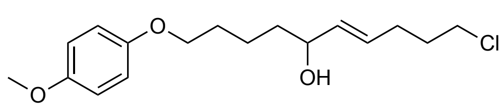
– 1.56 (m, 4H), 1.55 – 1.37 (m, 4H), 0.94 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 157.2, 142.5, 137.6, 134.5, 130.8, 130.2, 129.0, 128.8, 128.7, 127.6, 126.1, 120.8, 115.4, 111.5, 72.8, 67.9, 37.5, 35.7, 34.9, 32.0, 31.3, 29.7, 22.6. MS (ESI+) calculated for [M+H-H2O]$^+$ 347.2, found 347.2. FTIR (neat, cm^{-1}): 3366(br), 3061(m), 3025(m), 2934(s), 2857(s), 1600(m), 1494(s), 1453(s), 1388(m), 1243(s), 1126(m), 1047(m), 969(m), 912(m), 750(s), 669(m).



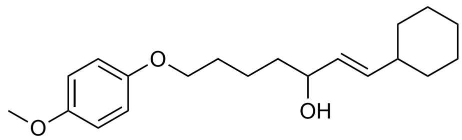
tert-butyl N-[(6E)-5-hydroxy-10-phenyldec-6-en-1-yl]carbamate (1.27), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-50% EtOAc in hexanes and was isolated as a clear colorless liquid (114 mg, 66% yield). ^{1}H NMR (300 MHz, Benzene-d_6) δ 7.22 – 7.16 (m, 2H), 7.11 – 7.08 (m, 3H), 5.49 (dt, *J* = 15.5, 6.4 Hz, 1H), 5.36 (dd, *J* = 15.5, 6.6 Hz 1H), 4.04 (s, 1H), 3.84 (s, 1H), 2.96 (s, 2H), 2.49 (t, *J* = 7.6 Hz, 2H), 1.93 (q, *J* = 6.4 Hz, 2H), 1.68 – 1.53 (m, 2H), 1.47 (s, 9H), 1.39 – 1.19 (m, 6H), 1.12 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 156.1, 142.6, 134.7, 130.4, 128.8, 128.7, 126.1, 78.5, 72.5, 40.7, 37.5, 35.7, 32.0, 31.4, 30.4, 28.6, 22.9. MS (ESI+) calculated for [M+H-H2O]$^+$ 330.1, found 330.1. FTIR (neat, cm^{-1}): 3419(br), 3358(br), 2947(s), 2931(s), 2858(m), 1690(s), 1512(s), 1453(m), 1365(s), 1250(s), 1172(s), 1007(w), 968(m), 748(m), 700(m).



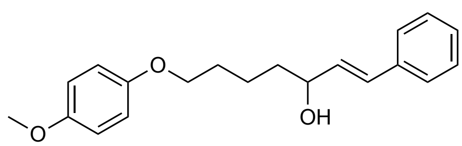
(6*E*)-1-(oct-3-yn-1-yloxy)-10-phenyldec-6-en-5-ol (1.29), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear yellow liquid (93 mg, 52% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.20 – 7.17 (m, 2H), 7.10 – 7.07 (m, 3H), 5.48 (dt, J = 15.4, 7.1 Hz, 1H), 5.38 (dd, J = 15.4, 6.2 Hz, 1H), 3.89 (q, J = 6.2 Hz, 1H), 3.44 (t, J = 7.2 Hz, 2H), 3.24 (t, J = 6.2 Hz, 2H), 2.52 – 2.38 (m, 4H), 2.10 – 2.06 (m, 2H), 1.92 (q, J = 7.1 Hz, 2H), 1.67 – 1.23 (m, 12H), 1.02 (s, 1H), 0.81 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, Benzene-d_6) δ 142.6, 134.7, 130.5, 128.8, 128.7, 126.1, 81.4, 77.5, 72.8, 71.0, 70.0, 37.7, 35.7, 32.0, 31.5, 31.4, 30.1, 22.7, 22.2, 20.7, 18.9, 13.8. MS (ESI+) calculated for [M+H-H2O]$^+$ 339.2, found 339.2. FTIR (neat, cm^{-1}): 3408(br), 3061(w), 3025(m), 2931(s), 2859(s), 1669(w), 1603(w), 1496(m), 1453(s), 1433(m), 1363(m), 1114(s), 968(m), 747(m), 669(m).



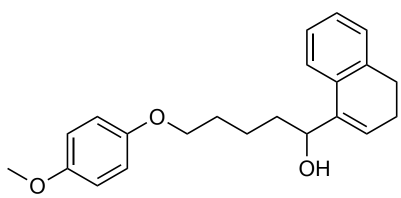
(6E)-10-chloro-1-(4-methoxyphenoxy)dec-6-en-5-ol (1.30), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (129 mg, 82% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 6.86 – 6.76 (m, 4H), 5.38 – 5.24 (m, 2H), 3.82 (q, J = 5.6 Hz, 1H), 3.67 (t, J = 5.9 Hz, 2H), 3.35 (s, 3H), 3.10 (t, J = 6.6 Hz, 2H), 1.90 (q, J = 7.1 Hz, 2H), 1.65 – 1.62 (m, 2H), 1.53 – 1.33 (m, 6H), 0.93 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.3, 153.8, 135.3, 129.0, 115.7, 115.0, 72.5, 68.5, 55.3, 44.3, 37.5, 32.2, 29.7, 29.5, 22.5. MS (ESI+) calculated for [M+H-H2O]$^+$ 295.1, found 295.1. FTIR (neat, cm^{-1}): 3418(br), 2995(m), 2911(s), 2865(s), 1673(w), 1591(w), 1513(s), 1435(s), 1397(m), 1289(s), 1231(s), 1180(s), 1107(m), 1037(m), 969(m), 823(m).



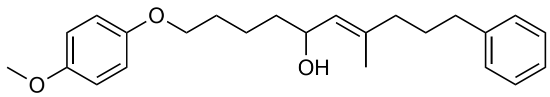
(1E)-1-cyclohexyl-7-(4-methoxyphenoxy)hept-1-en-3-ol (1.31), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (116 mg, 73% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 6.88 – 6.73 (m, 4H), 5.51 (dd, J = 15.5, 6.5 Hz, 1H), 5.39 (dd, J = 15.5, 6.5 Hz, 1H), 3.91 (q, J = 6.5 Hz, 1H), 3.67 (t, J = 6.1 Hz, 2H), 3.35 (s, 3H), 1.87 (q, J = 6.5 Hz, 1H), 1.72 – 1.60 (m, 6H), 1.57 – 1.44 (m, 4H), 1.24 – 1.01 (m, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.3, 153.9, 137.0, 131.7, 115.7, 115.0, 72.9, 68.5, 55.3, 40.7, 37.7, 33.4, 33.3, 29.8, 26.5, 26.4, 22.6. MS (ESI+) calculated for $[M+H-H2O]^{+}$ 301.2, found 301.2. FTIR (neat, cm^{-1}): 3416(br), 2927(s), 2853(s), 1508(s), 1470(m), 1446(m), 1393(w), 1289(w), 1230(s), 1180(w), 1106(w), 1039(m), 970(m), 823(m), 748(w).



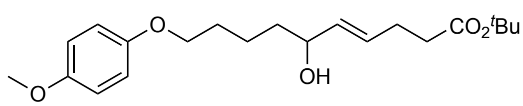
(1*E*)-7-(4-methoxyphenoxy)-1-phenylhept-1-en-3-ol (1.32), compound was prepared according to the reported procedure from a mixture of alkenyl bromide isomers (5:1, *E:Z*) and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (103 mg, 66% yield) as a mixture of isomers (5:1, *E:Z*). ^{1}H NMR (500 MHz, Benzene-d_6) *major isomer:* δ 7.31 – 7.24 (m, 2H), 7.19 – 7.13 (m, 3H), 7.08 – 7.05 (m, 1H), 6.86 – 6.74 (m, 4H), 6.44 (d, J = 15.9, 1H), 6.08 (dd, J = 15.9, 6.2 Hz, 1H), 3.99 (q, J = 6.2 Hz, 1H), 3.66 (t, J = 6.4 Hz, 2H), 3.35 (s, 3H), 1.66 – 1.44 (m, 6H), 1.00 (s, 1H). *minor isomer:* δ 6.40 (d, J = 11.7, 1H), 5.54 (dd, J = 11.7, 9.1 Hz, 1H), 4.51 – 4.47 (m, 1H), 3.60 (t, J = 6.4 Hz, 2H), 0.45 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ *major isomer: δ* 154.4, 153.9, 137.5, 133.4, 130.1, 128.9, 126.9, 115.8, 115.1, 72.8, 68.5, 55.3, 29.8, 22.5. *minor isomer: δ* 137.3, 135.7, 130.7, 129.2, 128.6, 127.5, 67.8, 37.8, 29.7, 22.4. MS (ESI+) calculated for $[M+H-H2O]^+$ 295.2, found 295.2. FTIR (neat, cm^{-1}): 3407(br), 3023(w), 2938(s), 2864(m), 2057(w), 1843(w), 1591(w), 1507(s), 1465(m), 1394(w), 1231(s), 1179(m), 1038(s), 986(m), 824(s), 748(m), 694(s).



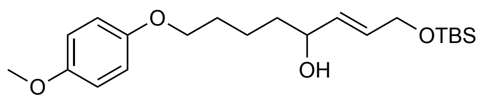
1-(3,4-dihydronaphthalen-1-yl)-5-(4-methoxyphenoxy)pentan-1-ol (1.33), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless solid (69 mg, 41% yield). ^{1}H NMR (500 MHz, Benzene-d_6) *δ* 7.47 (d, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.78 (q, *J* = 9.1 Hz, 4H), 6.00 (t, *J* = 5.4 Hz, 1H), 4.50 (t, *J* = 6.2 Hz, 1H), 3.63 (t, *J* = 5.9 Hz, 2H), 3.35 (s, 3H), 2.54 (t, *J* = 8.6 Hz, 2H), 2.07 – 1.99 (m, 2H), 1.76 – 1.72 (m, 1H), 1.67 – 1.61 (m, 4H), 1.54 – 1.48 (m, 1H), 1.36 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) *δ* 154.4, 153.9 140.2, 137.1, 134.0, 128.4, 127.1, 126.7, 124.4, 123.6, 115.8, 115.0, 72.1, 68.5, 55.3, 36.4, 29.7, 28.8, 23.2, 23.1. MS (ESI+) calculated for $[M+H-H2O]^+$ 321.2, found 321.2. FTIR (neat, cm^{-1}): 3417(br), 3057(w), 2837(s), 2865(m), 2831(m), 1510(s), 1474(m), 1289(w), 1231(s), 1107(w), 1037(m), 826(m), 741(m).



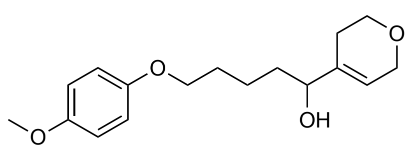
(6E)-1-(4-methoxyphenoxy)-7-methyl-10-phenyldec-6-en-5-ol (1.34), compound was prepared according to a slightly modified procedure, the initial reaction used 1.5 equiv of the respective alkenyl bromide and was run for 24 h prior to oxidation. The compound was then purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (78 mg, 43% yield). ^{1}H NMR (500 MHz, Benzene-*d$_6$*) *δ* 7.20 – 7.17 (m, 2H), 7.10 – 7.09 (m, 3H), 6.82 – 6.76 (m, 4H), 5.18 (d, *J* = 6.4 Hz, 1H), 4.26 (q, *J* = 6.4 Hz, 1H), 3.67 (t, *J* = 6.4 Hz, 2H), 3.35 (s, 3H), 2.47 (t, *J* = 7.7 Hz, 2H), 1.90 (t, *J* = 7.6 Hz, 2H), 1.72 – 1.50 (m, 6H), 1.48 (d, *J* = 1.3 Hz, 3H), 1.49 – 1.40 (m, 2H), 0.91 (s, 1H). ^{13}C NMR (126 MHz, Benzene-*d$_6$*) *δ* 154.4, 154.0, 142.7, 137.3, 129.5, 128.8, 128.7, 126.1, 115.8, 115.1, 68.5, 68.4, 55.3, 39.4, 38.0, 35.8, 29.9, 22.6, 16.5. MS (ESI+) calculated for [M+H-H2O]$^{+}$ 351.2, found 351.2. FTIR (neat, cm^{-1}): 3399(br), 3024(w), 2936(s), 2861(m), 1510(s), 1474(m), 1453(m), 1392(w), 1289(w), 1231(s), 1180(w), 1107(w), 1039(s), 824(s), 748(m), 700(m), 523(w).



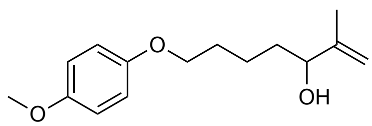
tert-butyl (4E)-6-hydroxy-10-(4-methoxyphenoxy)dec-4-enoate (1.35), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-40% EtOAc in hexanes and was isolated as a clear colorless liquid (138 mg, 76% yield). ^{1}H NMR (500 MHz, Benzene-*d$_6$*) *δ* 6.84 – 6.77 (m, 4H), 5.48 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.39 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.83 (q, *J* = 6.1 Hz, 1H), 3.66 (t, *J* = 6.4 Hz, 2H), 3.35 (s, 3H), 2.24 (t, *J* = 6.5 Hz, 2H), 2.19 – 2.15 (m, 2H), 1.70 – 1.59 (m, 2H), 1.52 – 1.39 (m, 4H), 1.39 (s, 7H), 1.05 (s,1H). ^{13}C NMR (126 MHz, Benzene-*d$_6$*) *δ* 172.2, 154.3, 153.9, 135.1, 129.1, 115.7, 115.0, 79.9, 72.5, 68.5, 55.3, 37.5, 35.3, 29.8, 28.2, 28.0, 22.5. MS (ESI+) calculated for [M+H-H2O]$^{+}$ 347.2, found 347.2. FTIR (neat, cm^{-1}): 3441(br), 2976(s), 2936(s), 2866(m), 1727(s), 1507(s), 1466(m), 1442(w), 1367(s), 1235(s), 1149(s), 969(m), 825(s), 748(w).



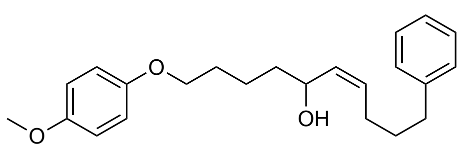
(2E)-1-[(tert-butyldimethylsilyl)oxy]-8-(4-methoxyphenoxy)oct-2-en-4-ol (1.36), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear colorless liquid (108 mg, 57% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 6.83 – 6.77 (m, 4H), 5.72 (dd, J = 15.4, 5.7 Hz, 1H), 5.66 (dt, J = 15.4, 4.3 Hz, 1H), 4.07 (d, J = 4.3 Hz, 2H), 3.93 – 3.91 (m, 1H), 3.64 (t, J = 6.4 Hz, 2H), 3.35 (s, 3H), 1.63 – 1.56 (m, 2H), 1.53 – 1.39 (m, 4H), 0.99 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.3, 153.9, 133.7, 129.8, 115.7, 115.0, 72.1, 68.5, 63.5, 55.3, 37.5, 29.7, 26.2, 22.5, 18.6, -5.0. MS (ESI+) calculated for [M+H-H2O]$^{+}$ 363.2, found 363.2. FTIR (neat, cm^{-1}): 3423(br), 2928(s), 2956(s), 1507(s), 1471(s), 1441(w), 1389(w), 1232(s), 1180(m), 1109(s), 1042(s), 970(m), 744(w), 667(w).



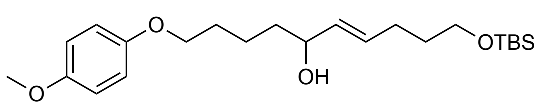
1-(3,6-dihydro-2H-pyran-4-yl)-5-(4-methoxyphenoxy)pentan-1-ol (1.37), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-10% EtOAc in CH_2Cl_2 and was isolated as a clear colorless liquid (109 mg, 71% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 6.84 – 6.77 (m, 4H), 5.32 (s, 1H), 4.03 – 4.01 (m, 2H), 3.70 – 3.65 (m, 4H), 3.61 – 3.57 (m, 1H), 3.35 (s, 3H), 1.95 (d, J = 16.9 Hz, 1H), 1.80 (d, J = 16.7 Hz, 1H), 1.66 – 1.61 (m, 2H), 1.51 – 1.48 (m, 1H), 1.44 – 1.37 (m, 3H), 0.93 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.4, 153.8, 138.7, 121.1, 115.8, 115.0, 75.0, 68.4, 65.4, 64.4, 55.3, 34.9, 29.7, 24.5, 22.7. MS (ESI+) calculated for $[M+H-H2O]^+$ 275.2, found 275.2. FTIR (neat, cm^{-1}): 3434(br), 2931(s), 2864(s), 2833(s), 1504(s), 1463(s), 1385(m), 1288(m), 1229(s), 1128(m), 1034(s), 971(w), 939(w), 826(s), 745(m).



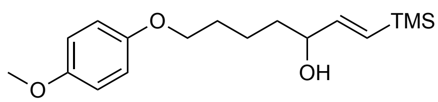
7-(4-methoxyphenoxy)-2-methylhept-1-en-3-ol (1.38), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (75.0 mg, 60% yield). ^{1}H NMR (500 MHz, Chloroform-d) δ 6.83 (s, 4H), 4.95 (s, 1H), 4.84 (s, 1H), 4.09 (t, J = 6.4 Hz, 1H), 3.91 (t, J = 6.6, 2H), 3.77 (s, 3H), 1.79 (q, 6.6 Hz, 2H), 1.73 (s, 3H), 1.67 – 1.42 (m, 4H). ^{13}C NMR (126 MHz, Chloroform-d) δ 153.8, 153.3, 147.6, 115.6, 114.8, 111.2, 75.9, 68.6, 55.9, 34.8, 29.4, 22.3, 17.6. GCMS (EI) calculated for $[M]^+$ 250.2, found 250.2. FTIR (neat, cm^{-1}): 3449(br), 3052(m), 2940(s), 2872(m), 1509(s), 1465(m), 1265(s), 1232(s), 1039(m), 901(w), 826(m), 738(s), 704(m).



(6Z)-1-(4-methoxyphenoxy)-10-phenyldec-6-en-5-ol (1.39), compound was prepared according to a slightly modified procedure, the initial reaction used 1.5 equiv of the respective alkenyl bromide and was run for 24 h prior to oxidation. The compound was then purified by silica gel column chromatography, 0-20% EtOAc in hexanes and was isolated as a clear colorless liquid (89 mg, 50% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.19 – 7.17 (m, 2H), 7.10 – 7.06 (m, 3H), 6.83 – 6.77 (m, 4H), 5.42 – 5.31 (m, 2H), 4.27 (q, J = 6.5 Hz, 1H), 3.66 (t, J = 6.4 Hz, 2H), 3.36 (s, 3H), 2.47 (td, J = 7.4, 2.6 Hz, 2H), 2.03 – 1.90 (m, 2H), 1.69 – 1.61 (m, 2H), 1.56 (p, J = 7.6 Hz, 4H), 1.48 – 1.37 (m, 4H), 0.92 (s, 1H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.4, 153.9, 142.4, 134.2, 131.0, 128.8, 128.7, 115.8, 115.0, 68.5, 67.5, 55.3, 37.8, 35.7, 31.7, 29.8, 27.4, 22.4. MS (ESI+) calculated for [M+H-H2O]$^+$ 337.2, found 337.2. FTIR (neat, cm^{-1}): 3416(br), 3001(w), 2935(s), 2859(m), 1508(s), 1463(m), 1289(w), 1232(s), 1107(w), 1039(s), 824(s), 746(m), 700(m).

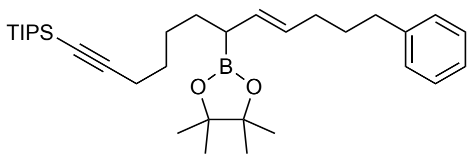


(6E)-10-[(tert-butyldimethylsilyl)oxy]-1-(4-methoxyphenoxy)dec-6-en-5-ol (1.40), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear colorless liquid (159 mg, 78% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 6.85 – 6.75 (m, 4H), 5.52 (dt, J = 15.3, 6.3 Hz, 1H), 5.44 (dd, J = 15.3, 5.9 Hz, 1H), 3.89 (q, J = 5.9 Hz, 1H), 3.66 (t, J = 6.1 Hz, 2H), 3.53 (t, J = 6.0 Hz, 2H), 3.35 (s, 3H), 2.08 (q, J = 7.0 Hz, 2H), 1.67 – 1.62 (m, 2H), 1.62 – 1.38 (m, 6H), 0.99 (s, 9H), 0.92 (s, 1H), 0.07 (s, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.4, 153.9, 134.6, 130.7, 115.8, 115.0, 72.7, 68.6, 62.6, 55.3, 37.7, 32.8, 29.8, 28.9, 26.2, 22.5, 18.5, -5.1. MS (ESI+) calculated for [M+H-H2O]$^+$ 391.2, found 391.2. FTIR (neat, cm^{-1}): 3418(br), 2934(s), 2857(s), 1510(s), 1470(m), 1388(m), 1288(w), 1232(s), 1180(m), 1104(s), 1040(s), 969(m), 836(s), 755(s), 662(w).



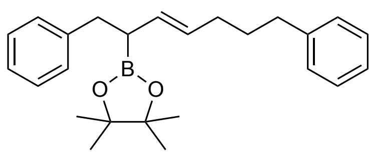
(1E)-7-(4-methoxyphenoxy)-1-(trimethylsilyl)hept-1-en-3-ol (1.41), compound was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-15% EtOAc in hexanes and was isolated as a clear colorless liquid (109 mg, 71% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 6.80 (q, J = 9.2 Hz, 4H), 6.06 (dd, J = 18.8, 5.7 Hz, 1H), 5.85 (d, J = 18.8 Hz, 1H), 3.90 (q, J = 5.7 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 3.35 (s, 3H), 1.69 – 1.61 (m, 2H), 1.57 – 1.49 (m, 1H), 1.47 – 1.39 (m, 3H), 1.07 (s, 1H), 0.11 (s, 9H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 154.4, 153.9, 150.0, 115.8, 115.1, 74.3, 68.5, 55.3, 37.1, 29.7, 22.5, -1.1. MS (ESI+) calculated for $[M+H-H2O]^{+}$ 291.2, found 291.2. FTIR (neat, cm^{-1}): 3422(br), 2949(s), 2908(m), 2865(w), 1508(s), 1466(m), 1441(w), 1231(s), 1180(w), 1107(w), 1039(s), 990(m), 865(s), 837(s), 742(m), 692(w).

1.4.5.2 Allylic Boronate Ester Products



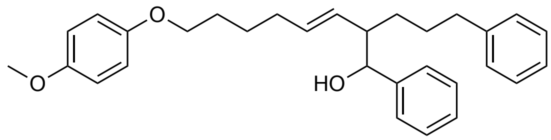
[(8E)-12-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)dodec-8-en-1-yn-1yl]tris(propan-2-yl) (1.28), compound was prepared according to a slightly modified procedure. In the place of oxidation by H_2O_2/NaOH the crude product mixture was filtered through a plug of silica and washed with ether. Volatiles were removed under pressure and the desired compound was obtained by silica gel column chromatography, 0-15% EtOAc in hexanes, as a clear colorless liquid (154 mg, 61% yield). ^{1}H NMR (300 MHz, Benzene-d_6) δ 7.18 – 7.16 (m, 2H), 7.10 (m, 3H), 5.63 (dd, J = 15.4, 8.4 Hz, 1H), 5.49 (dt, J = 15.4, 6.5 Hz, 1H), 2.54 (t, J = 6.3, 2H), 2.19 – 1.93 (m, 5H), 1.58 (m, 8H), 1.20 (d, J = 6.1 Hz, 18H), 1.16 – 1.09 (m, 3H), 1.06 (s, 12H). ^{13}C NMR (75

MHz, Benzene-d_6) δ 142.9, 132.2, 129.4, 128.8, 128.6, 126.0, 110.0, 83.0, 80.1, 35.6, 32.7, 31.9, 30.9, 29.5, 28.8, 24.9, 20.2, 19.0, 12.3, 11.8. ^{11}B NMR (96 MHz, Benzene-d_6) δ 32.41. MS (ESI+) calculated for $[M+H]^+$ 523.4, found 523.4. FTIR (neat, cm^{-1}): 3026(w), 2938(s), 2864(s), 2169(m), 1454(m), 1370(s), 1319(s), 1267(w), 1214(w), 1143(s), 968(m), 883(m), 744(w), 698(m), 622(w).



(3E)-1,7-diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-3-ene (1.46), compound was prepared according to a slightly modified procedure, the initial reaction was run for 4 h prior to oxidation. Additionally, in the place of oxidation by H_2O_2/NaOH the crude product mixture was filtered through a plug of silica and washed with hexanes. Volatiles were removed under pressure and the desired compound was obtained by silica gel column chromatography, 0-10% EtOAc in hexanes, as a clear colorless liquid with minor impurities present (82% yield determined by GC). Further attempts at purification were unsuccessful and led to additional decomposition.^{1}H NMR (500 MHz, Benzene-d_6) δ 7.25 (d, J = 7.5 Hz, 2H), 7.24 – 7.15 (m, 4H), 7.07 (t, J = 7.4 Hz, 4H), 5.66 (dd, J = 14.7, 8.3 Hz, 1H), 5.48 (dt, J = 14.7, 6.7 Hz, 1H), 3.08 (dd, J = 13.7, 6.7 Hz, 1H), 2.90 (dd, J = 13.4, 6.7 Hz, 1H), 2.46 (t, J = 7.5 Hz , 2H), 2.40 (q, J = 8.1 Hz , 1H) 1.97 (q, J = 7.2 Hz, 2H), 1.58 (p, J = 7.3 Hz, 2H), 1.00 (d, J = 7.2 Hz, 12H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 142.9, 142.4, 131.5, 130.0, 129.4, 128.8, 128.6, 128.4, 126.0, 125.9, 83.1, 37.8, 35.4, 32.6, 31.7, 24.9, 24.8. ^{11}B NMR (96 MHz, Benzene-d_6) δ 33.81. MS (ESI+) calculated for $[M+H]^+$ 377.3, found 377.3. FTIR (neat, cm^{-1}): 3060(w), 3025(m), 2997(s), 2929(s), 2855(w), 1623(w), 1495(m), 1379(s), 1325(s), 1211(m), 1143(s), 969(m), 862(m), 698(m).

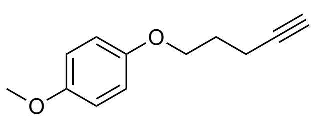
1.4.5.3 Homoallylic Alcohol Product



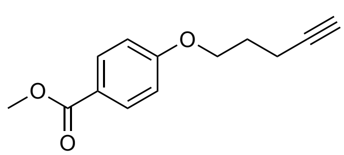
(3E)-8-(4-methoxyphenoxy)-1-phenyl-2-(3-phenylpropyl)oct-3-en-1-ol (1.42), in a nitrogen-filled glovebox, a dram vial was charged with a stir bar, KOTMS (83.4 mg, 0.650 mmol, 1.3 equiv), TriCuCl (42.4 mg, 0.075 mmol, 0.15 equiv), $Pd(dmdba)_2$ (3.1 mg, 0.004 mmol, 0.0075 equiv), PentXPhos (4.0 mg, 0.009 mmol, 0.018 equiv), 1-methoxy-4-(pent-4-yn-1-yloxy)benzene (95.1 mg, 0.5 mmol, 1.0 equiv), (4*E*)-5-bromo-4-penten-1-yl-benzene (135.1 mg, 0.6 mmol, 1.2 equiv), HBpin (192.0 mg, 1.50 mmol, 3.0 equiv), toluene (2.5 mL, 0.2M) and the reaction was vigorously stirred at 25 °C. After 2 h a 20 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of a 30% solution of ether to hexanes and analyzed by GC. Upon consumption of the alkyne, benzaldehyde (255.1 µL, 2.5 mmol, 5.0 equiv) was added to the crude reaction mixture and the temperature was elevated to 60 °C for 20 h. The reaction mixture was cooled to room temperature and filtered through a plug of silica with ether. Volatiles were removed under vacuum and the title compound was purified by silica gel column chromatography, 0-30% EtOAc in hexanes and was isolated as a clear colorless liquid (176 mg, 79% yield) as a mixture of isomers (4:1, *Z:E*). ^1H NMR (500 MHz, Benzene-d_6) *major isomer:* δ 7.29 (d, J = 7.1 Hz, 2H), 7.25 – 7.11 (m, 5H), 7.04 (t, J = 9.4 Hz, 3H), 6.85 – 6.77 (m, 4H), 5.51 (dt, J = 11.1, 7.3 Hz, 1H), 5.21 (t, J = 11.1 Hz, 1H), 4.27 (d, J = 5.9 Hz, 1H), 3.63 (q, J = 6.7 Hz, 2H), 3.36 (s, 3H), 2.68 – 2.59 (m, 1H), 2.44 – 2.33 (m, 2H), 1.94 – 1.89 (m, 2H), 1.64 – 1.51 (m, 4H), 1.50 – 1.20 (m, 5H), 1.12 (s, 1H). *minor isomer:* δ 7.29 (d, J = 7.1 Hz, 2H), 7.25 – 7.11 (m, 5H), 7.04 (t, J = 9.4 Hz, 3H), 6.85 – 6.77 (m, 4H), 5.34 (dt, J = 15.5, 6.6 Hz, 1H), 5.21 (t, J = 11.1 Hz, 1H), 4.27 (d, J = 5.9 Hz, 1H), 3.63 (q, J = 6.7 Hz, 2H), 3.36 (s, 3H), 2.68 – 2.59 (m, 1H), 2.44 – 2.33 (m, 2H), 2.24 (s, 1H),1.94 –

1.89 (m, 2H), 1.64 – 1.51 (m, 4H), 1.50 – 1.20 (m, 5H), 1.12 (s, 1H).. ^{13}C NMR (126 MHz, Benzene-d_6) *major isomer:* δ 154.4, 153.9, 144.0, 142.8, 133.6, 130.6, 128.7, 128.6, 127.5, 127.2, 126.0, 115.8, 115.1, 77.4, 68.4, 55.3, 46.2, 36.3, 31.7, 29.7, 29.3, 27.8, 26.5. *minor isomer:* δ 154.4, 153.9, 144.0, 142.8, 134.4, 131.1, 128.7, 128.6, 127.5, 127.3, 126.0, 115.8, 115.1, 77.1, 68.4, 55.3 51.9, 36.1, 32.6, 29.7, 29.2, 27.8, 26.2. MS (ESI+) calculated for [M+H-H2O]$^+$ 427.2, found 427.2. FTIR (neat, cm^{-1}): 3486(br), 3085(m), 3061(m), 3026(s), 2937(s), 2859(s), 1814(w), 1602(m), 1507(s), 1452(s), 1390(m), 1288(m), 1230(s), 1106(m), 1039(s), 913(w), 824(m), 748(s).

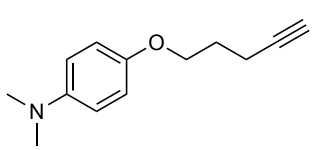
1.4.6 *Synthesis and Characterization of Alkyne Starting Materials*



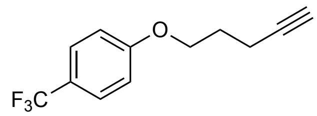
1-methoxy-4-(pent-4-yn-1-yloxy)benzene (1.6) was synthesized according to a known literature procedure and has been previously characterized.[60]



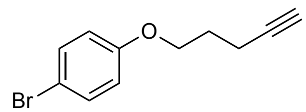
methyl 4-(pent-4-yn-1-yloxy)benzoate was synthesized according to a known literature procedure and has been previously characterized.[61]



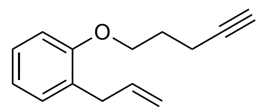
N,N-dimethyl-4-(pent-4-yn-1-yloxy)aniline was synthesized according to a known literature procedure and has been previously characterized.[24]



1-(pent-4-yn-1-yloxy)-4-(trifluoromethyl)benzene was synthesized according to a known literature procedure and has been previously characterized.[24]

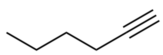


1-bromo-4-(pent-4-yn-1-yloxy)benzene was synthesized according to a modified procedure and has been previously characterized.[24]

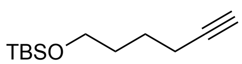


1-(pent-4-yn-1-yloxy)-2-(prop-2-en-1-yl)benzene (1.48) was synthesized according to a modified procedure. To a flame dried 200 mL RBF was added Cs_2CO_3 (4887 mg, 15.0 mmol, 1.50 equiv) and KI (166 mg, 1.0 mmol, 0.10 equiv) and the flask was flushed with N_2 and outfitted with a reflux condenser. Under N_2, dry acetonitrile (33 mL, 0.3M) was added via syringe. 2-(prop-2-en-1-yl)phenol (1430 µL, 11.0 mmol, 1.10 equiv) was added via syringe followed by drop-wise addition of 5-chloro-1-pentyne (1060 µL, 10 mmol, 1.00 equiv). This was allowed to stir overnight at 85 ºC. The crude mixture was diluted with ether and aqueous HCl (1.0M).The water layer was extracted 3x with ether. The combined organic layers were dried with magnesium sulfate and concentrated under vac. The crude oil was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, to afford (**1.48**) as a clear colorless liquid (1162 mg, 83% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.09 – 7.04 (m, 2H), 6.84 (t, J = 7.2 Hz, 1H), 6.57 (d, J = 8.0 Hz, 1H), 6.01

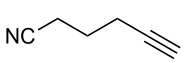
– 5.93 (m, 1H), 5.05 – 4.99 (m, 2H), 3.62 (d, J = 5.1 Hz, 2H), 3.38 (d, J = 6.3 Hz, 1H), 2.13 (t, J = 6.8 Hz, 2H), 1.75 (s, 1H), 1.66 (t, J = 6.5 Hz, 2H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 156.9, 137.4, 130.3, 128.9, 127.6, 120.9, 115.4, 111.5, 83.5, 69.4, 66.1, 34.8, 28.6, 15.5. GCMS (EI) calculated for $[M]^+$ 200.1, found 200.1. FTIR (neat, cm^{-1}): 3299(s), 3075(m), 3025(w), 3003(w), 2939(m), 2873(w), 1637(w), 1600(m), 1493(s), 1453(s), 1389(w), 1289(w), 1243(s), 1126(m), 1051(s), 995(w), 914(m), 751(s).



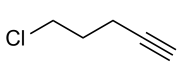
1-hexyne was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



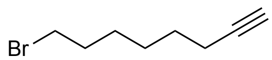
tert-butyldimethyl(hex-5-yn-1-yloxy)silane was synthesized according to a modified procedure and has been previously characterized.[62]



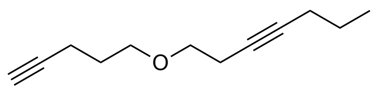
hex-5-ynenitrile was purchased from Oakwood Chemical and distilled over calcium hydride under reduced pressure before use.



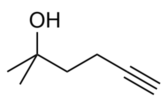
5-chloropent-1-yne was purchased from TCI America and distilled over calcium hydride under reduced pressure before use.



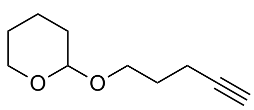
8-bromooct-1-yne was synthesized according to a modified procedure and has been previously characterized.[20]



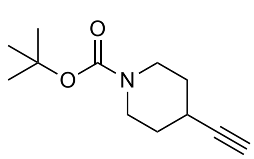
1-(pent-4-yn-1-yloxy)oct-3-yne was synthesized according to a known literature procedure and has been previously characterized.[63]



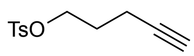
2-methylhex-5-yn-2-ol was synthesized according to a modified procedure and has been previously characterized.[64]



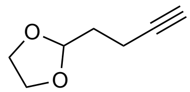
2-(pent-4-yn-1-yloxy)tetrahydra-2H-pyran was synthesized according to a known literature procedure and has been previously characterized.[65]



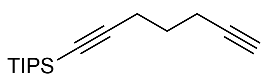
N-Boc-4-ethynylpiperidine was purchased from Combi-Blocks and used without further purification.



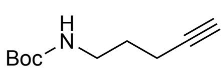
pent-4-yn-1-yl 4-methylbenzene-1-sulfonate was synthesized according to a known literature procedure and has been previously characterized.[66]



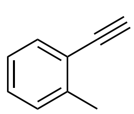
2-(but-3-yn-1-yl)-1,3-dioxolane was synthesized according to a known literature procedure and has been previously characterized.[67]



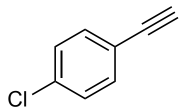
(hepta-1,6-diyn-1-yl)tris(propan-2-yl)silane was synthesized according to a known literature procedure and has been previously characterized.[68]



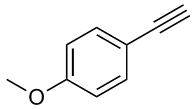
tert-butyl N-(pent-4-yn-1-yl)carbamate was synthesized according to a known literature procedure and has been previously characterized.[69]



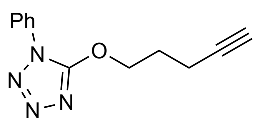
1-ethynyl-2-methylbenzene was purchased from TCI America and distilled over calcium hydride before use.



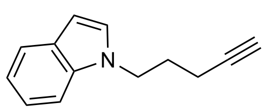
1-chloro-4-ethynylbenzene was purchased from TCI America and used without further purification.



1-ethynyl-4-methoxybenzene was purchased from Alfa Aesar and was used without further purification.

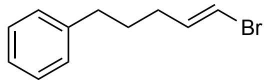


5-(pent-4-yn-1-yloxy)-1-phenyl-1H-1,2,3,4-tetrazole was synthesized according to a known literature procedure and has been previously characterized.[70]

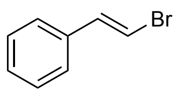


1-(pent-4-yn-1-yl)-1H-indole was synthesized according to a known literature procedure and has been previously characterized.[24]

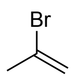
1.4.7 *Synthesis and Characterization of Alkenyl Bromide Starting Materials*



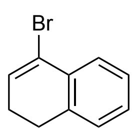
(4*E*)-5-bromo-4-penten-1-yl-benzene (1.4) was synthesized according to a modified procedure and has been previously characterized.[70]



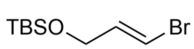
[(1E)-2-bromoethenyl]benzene was purchased from Combi-Blocks as a mixture of isomers (5:1 *E:Z)* and distilled over calcium hydride under reduced pressure prior to use.



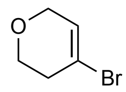
2-bromoprop-1-ene was purchased from Millipore Sigma and vacuum transferred over calcium hydride prior to use.



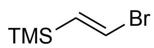
4-bromo-1,2-dihydronaphthalene was synthesized according to a known literature procedure and has been previously characterized.[71]



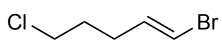
{[(2E)-3-bromoprop-2-en-1-yl]oxy}(tert-butyl)dimethylsilane was synthesized according to a known literature procedure and has been previously characterized.[72]



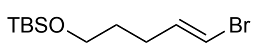
4-bromo-3,6-dihydro-2H-pyran was purchased from Combi-Blocks and vacuum transferred over calcium hydride prior to use.



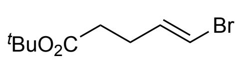
[(1E)-2-bromoethenyl]trimethylsilane was purchased from Millipore Sigma and vacuum transferred over calcium hydride prior to use.



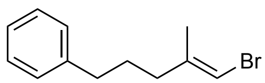
(1E)-1-bromo-5-chloropent-1-ene was synthesized according to a known literature procedure and has been previously characterized.[73]



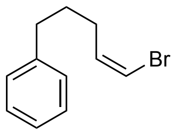
{[(4E)-5-bromopent-4-en-1-yl]oxy}(tert-butyl)dimethylsilane was synthesized according to a known literature procedure and has been previously characterized.[73]



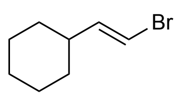
tert-butyl (4E)-5-bromopent-4-enoate was synthesized according to a known literature procedure and has been previously characterized.[73]



[(4E)-5-bromo-4-methylpent-4-en-1-yl]benzene was synthesized according to a modified literature procedure and has been previously characterized.[47]



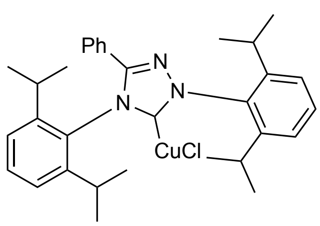
[(4Z)-5-bromopent-4-en-1-yl]benzene was synthesized according to a modified literature procedure and has been previously characterized.[74]



[(1E)-2-bromoethenyl]cyclohexane was synthesized according to a known literature procedure and has been previously characterized.[73]

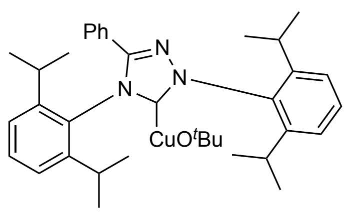
1.4.8 *Synthesis and Characterization of Catalysts and Ligands*

1.4.8.1 Copper Catalysts



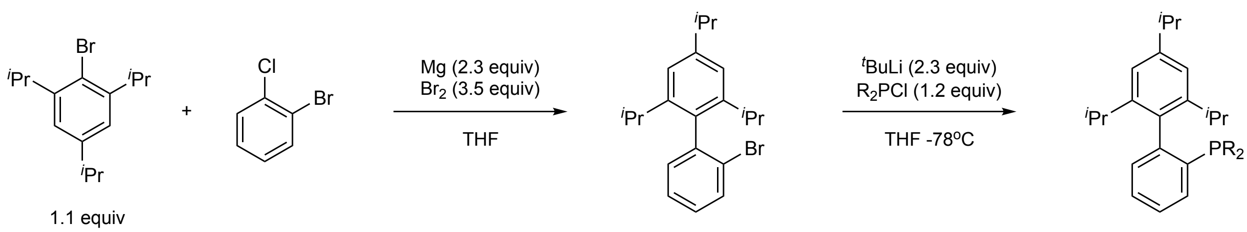
TriCuCl, chloro{1,4-bis[2,6-bis(propan-2-yl)phenyl]-3-phenyl-1,2,4-triazol-5-ylidene}copper(I) (1.49), was synthesized according to a modified procedure from TriHCl.[75] In a nitrogen glovebox, a 100 mL flame dried round bottom flask was charged with a stir bar, TriHCl (2,000.0 mg, 4.0 mmol, 1.0 equiv), KO^{t}Bu (493.7 mg, 4.4 mmol, 1.1 equiv), and anhydrous THF

(40.0 mL, 0.10 M). This mixture was stirred for 1 h at 25 °C. Next, CuCl (475.2 mg, 4.8 mmol, 1.2 equiv) was added and the suspension was allowed to stir for 20 h. The flask was then removed from the glovebox and the mixture was filtered through a plug of silica and washed with anhydrous CH_2Cl_2. Solvent was removed by rotary evaporation and the pure copper complex was obtained by recrystallization in CH_2Cl_2/wet pentane as a white crystalline solid (1936 mg, 86% yield). ^1H NMR (500 MHz, Benzene-d_6) δ 7.47 (d, J = 7.9 Hz, 2H), 7.25 (t, J = 7.7 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.10 (d, J = 7.7 Hz, 2H), 7.03 (d, J = 7.5 Hz, 2H), 6.82 (t, J = 7.4 Hz, 1H), 6.74 (t, J = 7.4 Hz, 2H), 2.86 (hept, J = 6.8 Hz, 2H), 2.66 (hept, J = 6.5 Hz, 2H), 1.41 – 1.34 (m, 12H), 1.16 (d, J = 6.8 Hz, 6H), 0.83 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 153.3, 146.1, 145.6, 135.3, 132.1, 131.8, 131.5, 131.2, 129.0, 125.2, 125.2, 124.5, 29.4, 25.0, 24.6, 23.8, 22.7.



TriCuO^{t}Bu, {1,4-bis[2,6-bis(propan-2-yl)phenyl]-3-phenyl-1,2,4-triazol-5-ylidene}(tert-butoxy)copper(I) (1.50), was synthesized according to a modified procedure. In a nitrogen glovebox, a 20 mL screw cap vial was charged with a stir bar, TriCuCl (1500 mg, 2.65 mmol, 1.0 equiv), and anhydrous THF (8.0 mL). To this was added NaO^{t}Bu (254.7 mg, 2.65 mmol, 1.0 equiv) using the remaining THF (8.0 mL, 0.15M total). This was allowed to stir at 25 °C for 20 h. The solvent was then removed via vacuum in the glovebox and evaporated with anhydrous pentane. The resulting white solid was dissolved in anhydrous toluene and filtered through a plug of celite with excess toluene. The toluene was removed via vacuum in the glovebox, using pentane to co-evaporate, to give TriCuO^{t}Bu as a white solid (1270 mg, 79% yield). ^1H NMR (500 MHz, Benzene-d_6) δ 7.50 (d, J = 7.9 Hz, 2H), 7.29 (t, J = 7.6 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.14 (d, J = 8.2 Hz, 2H), 7.04 (d, J = 7.7 Hz, 2H), 6.83 (t, J = 7.4 Hz, 1H), 6.76 (t, J = 7.5 Hz, 2H), 2.93 (hept, J = 6.9 Hz, 2H), 2.70 (hept, J = 6.7 Hz, 2H), 1.45 (d, 6.7 Hz, 6H), 1.43 (d, 6.7 Hz, 6H), 1.38 (s, 9H), 1.19 (d, J = 6.7 Hz, 6H), 0.85 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 152.8, 146.1, 145.6, 136.0, 132.7, 131.4, 131.2 131.0, 129.0, 125.5, 125.1, 124.3, 66.4, 37.0, 29.4, 25.0, 24.4, 24.0, 22.8.

1.4.8.2 General Synthesis of Phosphine Ligands

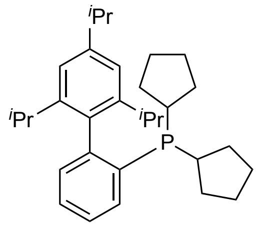


Step 1: A 100 mL Schlenk flask was charged with magnesium turnings (1020 mg, 41.8 mmol, 2.3 equiv) and flame dried under vacuum. This was then put under an atmosphere of N_2 and outfitted with a reflux condenser and stir bar. To this was added anhydrous THF (18.0 mL, 1.0 M) and with vigorous stirring was added dibromoethane (~50 µL). 1-Bromo-2,4,6-triisopropylbenzene (5.0 mL, 20.0 mmol, 1.1 equiv) was added in three portions. After all aryl bromide was added the reaction was heated to 80 °C overnight. Next, the reaction mixture was cooled to room temperature and 1- bromo-2-chlorobenzene (2.1 mL, 18.2 mmol, 1.0 equiv) was added slowly. This was heated at 60 °C for 3 h. It was then cooled to room temperature and further to 0 °C. To this bromine (3.3mL, 72.8 mmol, 3.5 equiv) was added dropwise via syringe. The reaction was then allowed to stir overnight at 25 °C. At this point sodium sulfite (20.0 mL, 10% aqueous solution) was added to the reaction mixture and the solution was stirred for 10 minutes.

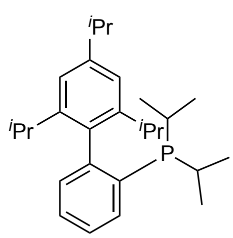
The mixture was transferred to a separatory funnel and the aqueous layer was removed. The organic layer was washed again with sodium sulfite solution and subsequently washed with brine. The individual aqueous layers were then back-extracted with ether and the combined organic layers were dried over MgSO4, filtered, and the solvent was removed with the aid of a rotary evaporator. The resulting solid was recrystallized from hot ethyl acetate and obtained as a white crystalline powder (4140 mg, 63%). 2'-bromo-2,4,6-tris(propan-2-yl)-1,1'-biphenyl has been previously characterized.

Step 2: To a flame dried 100 mL Schlenk flask, outfitted with a stir bar, under N_2, was added 2'-bromo-2,4,6-tris(propan-2-yl)-1,1'-biphenyl (2.8 g, 8.0 mmol, 1.0 equiv). To this was added 40.0 mL of anhydrous ether and the reaction was cooled to -78 °C. *t*-butyl lithium (1.7M in pentane) (10.8 mL, 18.4 mmol, 2.3 equiv) was added in a dropwise fashion over 10 min. This was allowed to stir for 45 min. Still at -78C chlorodi*alkyl*phosphine (9.6 mmol, 1.2 equiv) was added over the course of 5 min. This was allowed to react at -78C for 1 h and then brought to room temperature and stirred overnight. The solution was quenched with sat. aqueous NH_4Cl and the aqueous layer was extracted with ether three times. The combined organic layers were washed with water and brine sequentially and dried of $MgSO_4$.

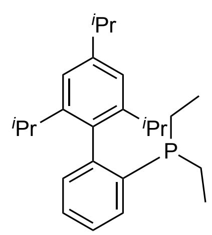
1.4.8.3 Characterization of Phosphine Ligands



PentXPhos, dicyclopentyl[2',4',6'-tris(propan-2-yl)-[1,1'-biphenyl]-2-yl]phosphane (1.51), was prepared according to reported procedure and was purified by silica gel column chromatography, 0-10% CH_2Cl_2 in hexanes and the resulting white powder was recrystallized with hot MeOH to afford a white crystalline solid (1940 mg, 54% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.51 (d, J = 7.1 Hz, 1H), 7.23 (s, 3H), 7.19 – 7.16 (m, 3H), 2.86 (hept, J = 6.8 Hz, 1H), 2.76 (hept, J = 6.7 Hz, 2H), 2.03 (p, J = 9.1 Hz, 2H), 1.75 – 1.62 (m, 4H), 1.62 – 1.41 (m, 10H), 1.40 (d, J = 6.8 Hz, 6H), 1.31 (d, J = 11.4 Hz, 2H), 1.25 (d, J = 6.9 Hz, 6H), 1.13 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 148.5, 147.2, 147.1, 146.8, 140.1, 140.0, 137.0, 132.8, 131.1, 126.8, 120.8, 37.1, 37.0, 34.8, 31.8, 31.7, 31.2, 30.72, 30.6, 26.9, 26.8, 26.4, 26.2, 26.2, 24.4, 23.2. ^{31}P NMR (121 MHz, Benzene-d_6) δ -13.56. MS (ESI+) calculated for $[M+H]^+$ 449.4, found 449.4. FTIR (neat, cm^{-1}): 2956(s), 2865(m), 1606(w), 1449(m), 1380(m), 1359(m), 1315(w), 1121(w), 1059(w), 875(w), 766(m), 650(w), 517(w).

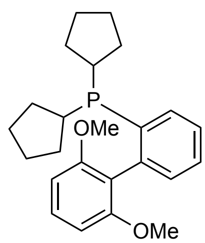


***i*-PrXphos, bis(propan-2-yl)[2',4',6'-tris(propan-2-yl)-[1,1'-biphenyl]-2-yl]phosphane (1.52)**, was prepared according to reported procedure and was purified by silica gel column chromatography, 0-10% CH_2Cl_2 in hexanes and the resulting white powder was recrystallized with hot MeOH to afford a white solid (1647 mg, 56% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.41 (d, J = 4.5 Hz, 1H), 7.22 (s, 3H), 7.16 – 7.14 (m, 3H), 2.88 (hept, J = 6.8 Hz, 1H), 2.69 (hept, J = 6.7 Hz, 2H), 1.92 – 1.86 (m, 2H), 1.38 (d, J = 6.8 Hz, 6H), 1.27 (d, J = 6.9 Hz, 6H), 1.11 (d, J = 6.7 Hz, 6H), 1.05 – 0.99 (m, 12H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 148.6, 148.0, 147.4, 146.7, 138.6, 138.5, 136.9, 132.0, 131.7, 126.8, 120.7, 34.8, 31.2, 26.3, 24.4, 23.9, 23.8, 23.0, 21.6, 21.4, 19.0, 18.9. ^{31}P NMR (121 MHz, Benzene-d_6) δ -0.46. MS (ESI+) calculated for $[M+H]^+$ 397.4, found 397.4. FTIR (neat, cm^{-1}): 3050(w), 2959(s), 2901(w), 2865(m), 1606(w), 1460(m), 1382(m), 1361(m), 1152(w), 1002(w), 875(m), 765(m), 658(w).

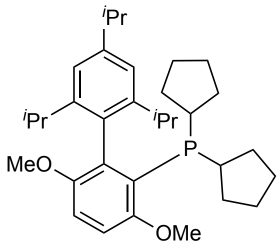


EtXPhos, diethyl[2',4',6'-tris(propan-2-yl)-[1,1'-biphenyl]-2-yl]phosphane (1.53), was prepared according to the reported procedure and was purified by silica gel column chromatography, 0-10% CH_2Cl_2 in hexanes and the resulting white powder was recrystallized with hot MeOH to afford a white solid (932 mg, 32% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.39 (d, J = 7.0 Hz, 1H), 7.23 (s, 2H), 7.21 – 7.16 (m, 2H), 7.16 – 7.13 (m, 1H), 2.87 (hept, J = 6.9 Hz, 1H), 2.69 (hept, J = 6.8 Hz, 2H), 1.52 – 1.40 (m, J = 7.7 Hz, 5H), 1.37 (d, J = 6.9 Hz, 6H), 1.26 (d, J = 6.9 Hz, 6H), 1.12 (d, J = 6.8 Hz, 6H), 0.92 (dt, J = 15.1, 7.6 Hz, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 148.6, 147.4, 147.2, 146.8, 138.9, 138.8, 137.1, 131.3, 130.7, 127.2, 120.8, 34.8, 31.1, 26.0, 23.1, 20.0, 19.9, 10.2, 10.1. ^{31}P NMR (121 MHz, Benzene-d_6) δ -26.22. MS (ESI+)

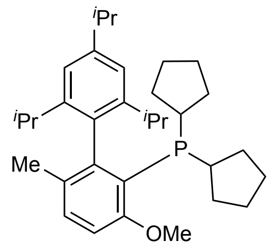
calculated for $[M+H]^+$ 369.4, found 369.4. FTIR (neat, cm^{-1}): 2958(s), 2929(w), 2870(w), 1460(m), 1359(w), 1125(w), 874(w), 749(w).



SPhos*, dicyclopentyl({2',6'-dimethoxy-[1,1'-biphenyl]-2-yl})phosphane (1.54), was prepared according to a modified version of the reported procedure (*Step 2)* starting from 2'-bromo-2,6-dimethoxy-1,1'-biphenyl, which has been previously characterized.[76] The title compound was purified by silica gel column chromatography, 0-15% CH_2Cl_2 in hexanes and the resulting white powder was recrystallized with hot MeOH to afford a white solid (1852 mg, 61% yield). ^1H NMR (500 MHz, Benzene-d_6) δ 7.59 (d, J = 6.5 Hz, 1H), 7.37 (d, J = 6.4 Hz, 1H), 7.28 – 7.17 (m, 3H), 6.42 (d, J = 8.3 Hz, 2H), 3.32 (s, 6H), 2.08 (h, J = 8.0 Hz, 2H), 1.82 (h, J = 6.8 Hz, 2H), 1.74 – 1.59 (m, 4H), 1.58 – 1.35 (m, 10H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 158.1, 142.8, 142.5, 140.6, 140.5, 131.9, 131.6, 131.5, 128.9, 128.3, 127.0, 120.9, 103.7, 54.9, 39.3, 39.2, 31.9, 31.7, 31.3, 31.1, 27.2, 27.1, 26.3, 26.2. ^{31}P NMR (121 MHz, Benzene-d_6) δ -6.93. MS (ESI+) calculated for $[M+H]^+$ 383.2, found 383.2. FTIR (neat, cm^{-1}): 2996(w), 2949(s), 2862(m), 1588(s), 1470(s), 1430(m), 1282(w), 1245(s), 1112(s), 1002(w), 780(w), 725(w).



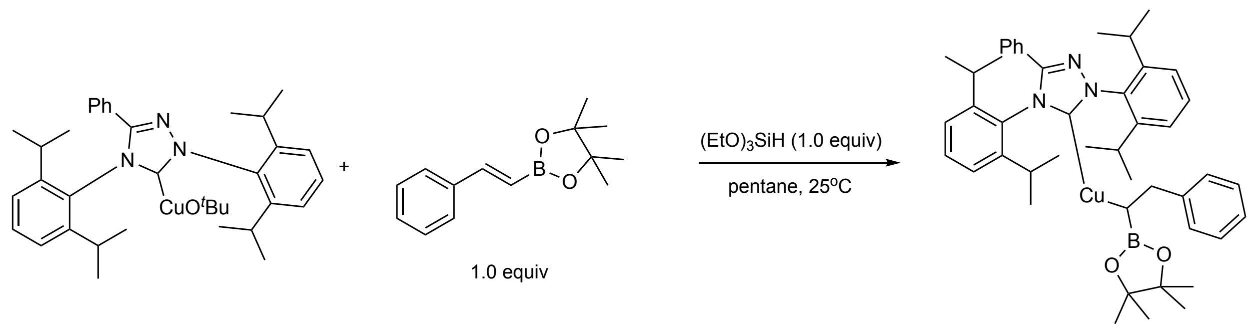
BrettPhos*, dicyclopentyl[3,6-dimethoxy-2',4',6'-tris(propan-2-yl)-[1,1'-biphenyl]-2-yl]phosphane (1.55), was prepared according to a modified version of the reported procedure (*Step 2)* starting from 2-bromo-3,6-dimethoxy-2',4',6'-tris(propan-2-yl)-1,1'-bipheny, which has been previously characterized.[55] The title compound was purified by silica gel column chromatography, 0-20% CH_2Cl_2 in hexanes and the resulting white powder was recrystallized with hot MeOH to afford a white solid (591 mg, 46% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.26 (s, 2H), 6.56 (d, J = 8.9 Hz, 1H), 6.48 (d, J = 8.9 Hz, 1H), 3.36 (s, 3H), 3.11 (s, 3H), 2.89 – 2.83 (m, 3H), 2.82 – 2.76 (m, 2H), 1.88 – 1.84 (m, 2H), 1.78 – 1.74 (m,2H), 1.68 – 1.60 (m, 4H), 1.5 – 1.39 (m, 8H), 1.46 (d, J = 6.8 Hz, 2H), 1.24 (d, J = 6.7 Hz, 6H), 1.20 (d, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 157.2, 157.2, 152.5, 152.5, 148.0, 146.8, 139.0, 138.8, 133.8, 133.8, 129.0, 120.6, 111.0, 109.1, 100.4, 54.9, 54.1, 37.6, 37.5, 34.6, 32.9, 32.7, 31.9, 31.8, 31.4, 27.2, 27.1, 26.4, 26.4, 25.7, 24.3, 23.9. ^{31}P NMR (121 MHz, Benzene-d_6) δ -6.93. MS (ESI+) calculated for $[M+H]^+$ 509.3, found 509.3. FTIR (neat, cm^{-1}): 2946(s), 2864(m), 2834(w), 1456(m), 1426(m), 1389(w), 1254(m), 1165(w), 1150(w), 1090(w), 1023(w), 874(w).



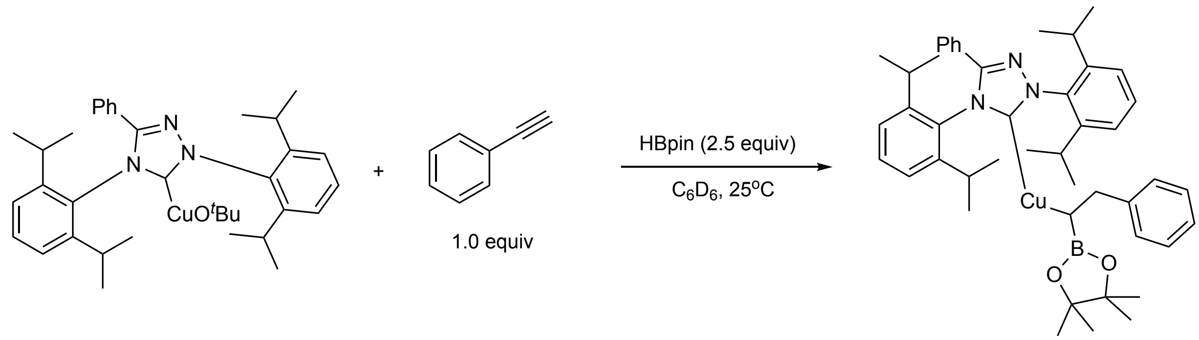
RockPhos*, **dicyclopentyl[3-methoxy-6-methyl-2',4',6'-tris(propan-2-yl)-[1,1'-biphenyl]-2-yl]phosphane (1.56),** was prepared according to a modified version of the reported procedure (*Step 2)* starting from 2-bromo-3-methoxy-6-methyl-2',4',6'-tris(propan-2-yl)-1,1'-biphenyl, which has been previously characterized.[54] The title compound was purified by silica gel column chromatography, 0-20% CH_2Cl_2 in hexanes and the resulting white powder was recrystallized with hot MeOH to afford a white solid (763 mg, 62% yield). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.23 (s, 2H), 7.12 (d, J = 8.4 Hz, 1H), 6.47 (d, J = 8.4 Hz, 1H), 3.32 (s, 3H), 2.87 (p, J = 6.9 Hz, 1H), 2.82 – 2728 (m, 4H), 1.92 (s, 3H), 1.90 – 1.85 (m, 2H), 1.78 – 1.74 (m, 2H), 1.70 – 1.46 (m, 12H), 1.41 (d, J = 6.8 Hz, 6H), 1.25 (d, J = 6.9 Hz, 6H), 1.14 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, Benzene-d_6) δ 161.4, 149.5, 149.2, 148.1, 146.0, 137.1, 137.1, 132.2, 130.1, 130.1, 121.2, 109.2, 54.6, 37.6, 37.5, 34.6, 32.9, 32.7, 31.8, 31.7, 31.1, 27.2, 27.2, 26.4, 26.3, 25.2, 25.0, 24.4, 21.4. ^{31}P NMR (121 MHz, Benzene-d_6) δ -8.17. MS (ESI+) calculated for $[M+H]^+$ 493.3, found 493.3. FTIR (neat, cm^{-1}): 2954(s), 2916(m), 2857(w), 1694(w), 1567(m), 1432(w), 1260(m), 1125(m), 1004(w), 780(w).

1.4.9 *Mechanistic Studies*

1.4.9.1 Synthesis and Characterization of the Heterobimetallic Intermediate

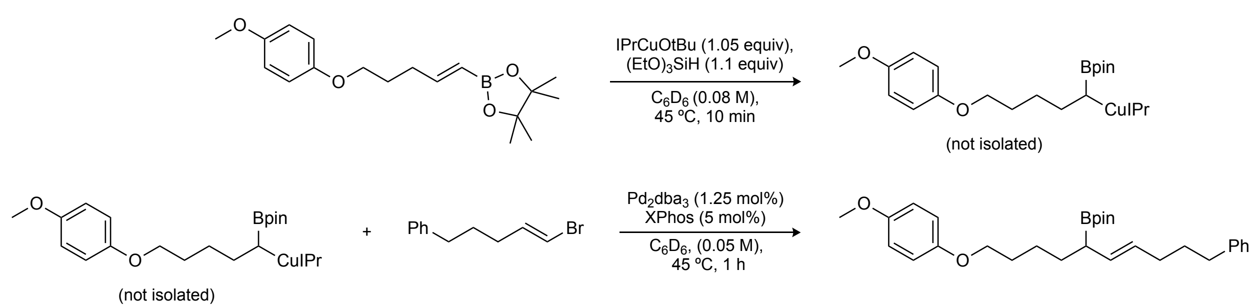


In a nitrogen glovebox, a 20 mL screw cap vial was charged with a stir bar, TriCuO*t*-Bu (120 mg, 0.2 mmol, 1.0 equiv) and anhydrous pentane (3.0 mL, 0.075 M). Triethoxysilane (37.0 μL, 0.2 mmol, 1.0 equiv) was added and the mixture was stirred for 5 min. The solution turned a deep red color. A solution of trans-2-phenylvinyl(pinacol)boronate (46.0 mg, 0.2 mmol, 1.0 equiv) in 1 mL of anhydrous pentane was then added and the mixture was stirred for 1 h. The resulting off white precipitate was collected by filtration and washed with minimal cold pentane to afford the complex as an off-white solid (91.0 mg, 59% yield). Crystallographic information is represented in Section 9.5. ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.48 (d, J = 7.8 Hz, 2H), 7.44 (d, J = 7.4 Hz, 2H), 7.28 (t, J = 7.8 Hz, 1H), 7.21 (t, J = 6.9 Hz, 3H), 7.05 (t, J = 6.7 Hz, 3H), 6.83 (t, J = 7.3 Hz, 1H), 6.76 (t, J = 7.5 Hz, 1H), 3.44 (dd, J = 14.6, 11.0 Hz, 1H), 2.96 – 2.89 (m, 3H), 2.69 (s, 6.9 Hz, 2H), 1.47 (t, J = 5.6 Hz, 6H), 1.43 (t, J = 6.6 Hz, 6H), 1.20 (t, J = 5.6 Hz, 6H), 1.05 (s, 6H), 1.00 (s, 6H), 0.87 (d, J = 6.7 Hz, 6H).



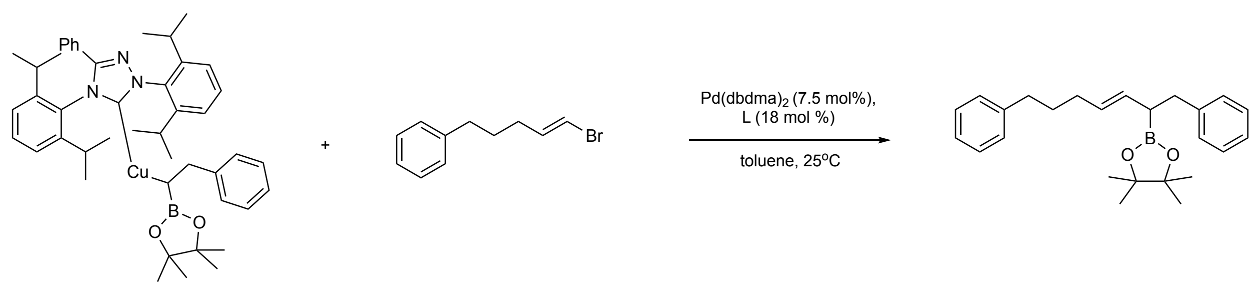
In a nitrogen filled glovebox, a 1-dram vial was charged with a stir bar, TriCuO^{t}Bu (12 mg, 0.02 mmol, 1.0 equiv), and benzene-d_6 (100 µL, 0.2 M). Pinacolborane (7.2 µL, 0.05 mmol, 2.5 equiv) was added and the mixture was stirred for 1 minute followed by the addition of phenyl acetylene (2.2 µL, 0.02 mmol, 1.0 equiv). This mixture was allowed to stir for 20 min at 25 °C before being diluted into 350 µL benzene-d_6 and analyzed by ^{1}H NMR. Product was confirmed to have been made, as the spectrum matched the isolated sample (1.44).

1.4.9.2 Initial Exploration of Alkenyl Bromides as Electrophilic Coupling Partners



In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, IPrCuO-*t*Bu (55.2 mg, 0.105 mmol, 1.05 equiv) and 1 mL of C_6D_6. To this solution, triethoxysilane (22.0 µL, 0.110 mmol, 1.10 equiv) was added. Upon addition a bright orange color was observed, and the solution was allowed to stir at 45 °C for 5 minutes. After the five minutes a solution of alkenyl boronate ester (31.6 mg, 0.100 mmol, 1.00 equiv) in 200 µL of C_6D_6 was added. The color of the solution slowly faded to a brown color and after 5 minutes of stirring at 45 °C, an aliquot was taken and the heterobimetallic intermediate was confirmed via ^{1}H-NMR. To a separate dram vial was added $Pd_2(dba)_3$ (1.1 mg, 0.00125 mmol, 0.0125 equiv) and XPhos (2.4 mg, 0.0050 mmol, 0.050 equiv). After addition of 800 µL C_6D_6 this mixture was allowed to stir at 45 °C for 5 minutes before being transferred into the premixed heterobimetallic complex mixture, followed by the addition of alkenyl bromide (45 mg, 0.200 mmol, 2.00 equiv). The vial was outfitted with a Teflon screw cap and allowed to stir at 45 °C. After 1 h a 100 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of a 30% solution of ether to hexanes and analyzed by GC with *n*-octyl ether as an internal standard.

1.4.9.3 Palladium-Catalyzed Cross Coupling of the Heterobimetallic Intermediate and Alkenyl Bromides

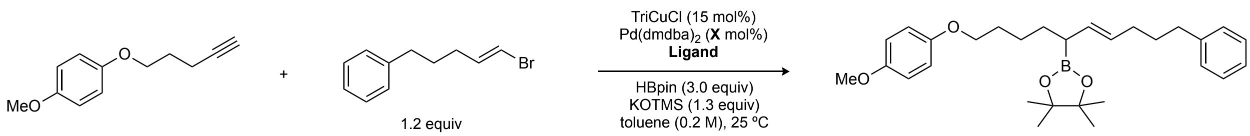


In a nitrogen filled glovebox, to a 1.5-mL vial was added a stir bar, heterobimetallic intermediate (44) (19.0 mg, 0.025 mmol, 1.0 equiv), ligand (0.00045 mmol, 0.018 equiv) (see Table S12), $Pd(dmdba)_2$ (0.15 mg, 0.00019 mmol, 0.008 equiv), (4*E*)-5-bromo-4-penten-1-yl-benzene (6.8 mg, 0.030 mmol, 1.2 equiv), trimethoxybenzene (1.4 mg, 0.008 mmol, 0.33 equiv), and toluene (125 µL, 0.2 M). 20 µL aliquots were taken at 0.5, 1, 2, and 24 h and quenched into a solution of dibromotetrachloroethane (24.4 mg, 0.075 mmol, 3 equiv) in toluene (100 µL). The resulting 120 µL solutions were pushed through a plug of silica with 1.3 mL of a 30% solution of ether to hexanes and analyzed by Gas Chromatography.

Table 1.15 Stoichiometric Alkyl Group Phosphine Study Results

Entry	Ligand	Yield of Allyl Bpin (%)			
		0.5 h	***1 h***	***2 h***	***24 h***
1	no ligand	0	0	2	5
2	PentXPhos	7	28	55	82
3	XPhos	2	9	32	83
4	*t*-BuXPhos	0	2	3	47
5	*i*-PrXPhos	7	15	30	80
6	EtXPhos	0	0	3	6

1.4.9.4 Palladium/Ligand Concentration Experiment

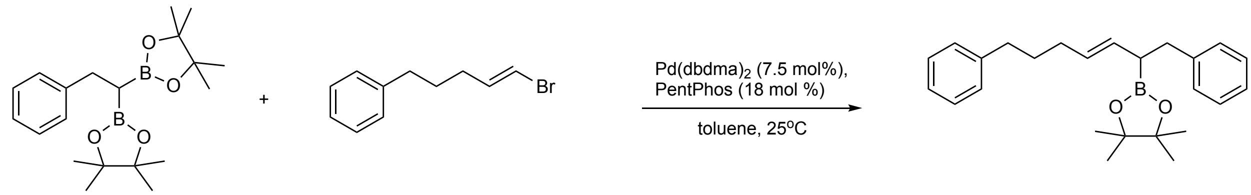


Following the General Procedure (Section 1.4.4), various concentrations of Pd/L were used to perform 0.05 mmol scale reactions. Yields were determined by GC using *n*-octyl ether as an internal standard.

Table 1.16 Increased Concentration of Pd/XPhos and Pd/i-PrXPhos Results

Entry	X	Ligand	2 h yield (%)	24 h yield (%)
1	1.5 mol%	XPhos (3.6 mol%)	8	25
2	1.5 mol%	*i*-PrXPhos (3.6 mol%)	10	17
3	2.25 mol%	XPhos (5.4 mol%)	14	26
4	2.25 mol%	*i*-PrXPhos (5.4 mol%)	18	20

1.4.9.5 Palladium Catalyzed Cross Coupling of an Alkyl 1,1-diboronate Ester

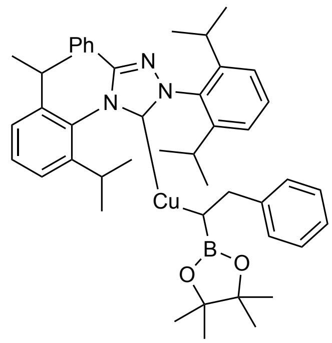


In a nitrogen filled glovebox, to a 1-dram vial was added a stir bar, PentXPhos (0.4 mg, 0.0009 mmol, 0.018 equiv), $Pd(dmdba)_2$ (0.3 mg, 0.00038 mmol, 0.008 equiv), (4*E*)-5-bromo-4-penten-1-yl-benzene (13.5 mg, 0.060 mmol, 1.2 equiv), 4,4,5,5-tetramethyl-2-[2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,3,2-dioxaborolane (17.9 mg, 0.050 mmol, 1.0 equiv) followed by the addition of KOTMS (8.3mg, 0.065 mmol, 1.3 equiv). Toluene (0.25 mL, 0.2 M) was added to both vials, and they were allowed to stir at 25 °C. 20 µL aliquots were taken at 2 h and 24 h, pushed through a plug of silica with 1.5 mL of a 30% solution of ether to hexanes and analyzed by Gas Chromatography. Trimethoxybenzene was used as an internal standard for analysis.

Table 1.17 Results of the 1,1-diboronate Ester Study

Entry	Conditions	2 h yield (%)	24 h yield (%)
1	without KOTMS	0	0
2	with KOTMS	0	0

1.4.9.6 Crystallization of the Heterobimetallic Intermediate (**1.44**)



In a nitrogen filled glovebox, a 1-dram vial was charged with (1.44) copper complex (15 mg, 0.025 mmol) the solid was dissolved in a minimum amount of anhydrous THF. Anhydrous *n*-pentane was layered on top. The dram vial was placed in a -25 °C freezer for 6 days to afford colorless square crystals.

A colorless prism, measuring 0.20 x 0.20 x 0.05 mm^3 was mounted on a loop with oil. Data was collected at -173 °C on a Bruker APEX II single crystal X-ray diffractometer, Mo-radiation, equipped with a Miracol X-ray optical collimator.

Crystal-to-detector distance was 40 mm and exposure time was 20 seconds per frame for all sets. The scan width was 0.5°. Data collection was 100% complete to 25° in ϑ. A total of 41280 reflections were collected covering the indices, -13<=h<=12, -31<=k<=31, -25<=l<=25. 10611 reflections were symmetry independent and the R_{int} = 0.0647 indicated that the data was of better than average quality (0.07). Indexing and unit cell refinement indicated a primitive monoclinic lattice. The space group was found to be P 2_1/n (No. 14).

The data was integrated and scaled using SAINT, SADABS within the APEX2 software package by Bruker.[77]

Solution by direct methods (SHELXT[78] or SIR97[79,80]) produced a complete heavy atom phasing model consistent with the proposed structure. The structure was completed by difference

Fourier synthesis with SHELXL.[81–83] Scattering factors are from Waasmair and Kirfel.[84] Hydrogen atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms with C---H distances in the range 0.95-1.00 Angstrom. Isotropic thermal parameters U_{eq} were fixed such that they were 1.2U_{eq} of their parent atom Ueq for CH's and 1.5U_{eq} of their parent atom U_{eq} in case of methyl groups. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares.

Table 1.18 summarizes the data collection details. **Figure 1.2** shows an ORTEP[85] of the asymmetric unit.

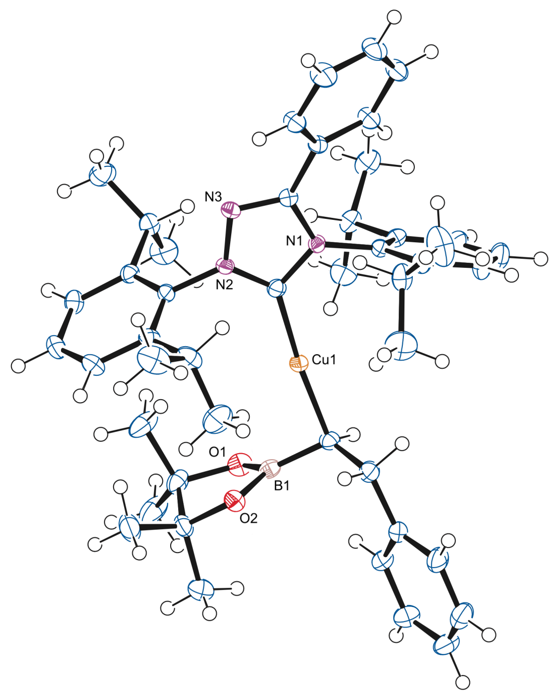


Figure 1.2 ORTEP[85] of the **1.44** with thermal ellipsoids at the 50% probability level. Disorder omitted for clarity. The aryl-alkenyl Bpin bonded with the Cu appears to be disordered.

Table 1.18 Crystallographic Data: Heterobimetallic Complex **1.44**

Empirical formula	C46 H59 B Cu N3 O2
Formula weight	760.31

Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2_1/n	
Unit cell dimensions	a = 9.7448(6) Å	α= 90°.
	b = 23.8897(15) Å	β= 103.483(3)°.
	c = 18.8275(13) Å	γ = 90°.
Volume	4262.2(5) $Å^3$	
Z	4	
Density (calculated)	1.185 Mg/m^3	
Absorption coefficient	0.551 mm^{-1}	
F(000)	1624	
Crystal size	0.200 x 0.200 x 0.050 mm^3	
Theta range for data collection	1.401 to 28.337°.	
Index ranges	-13<=h<=12, -31<=k<=31, -25<=l<=25	
Reflections collected	41280	
Independent reflections	10611 [R(int) = 0.0647]	
Completeness to theta = 25.000°	100.0 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10611 / 48 / 509	
Goodness-of-fit on F^2	1.086	
Final R indices [I>2sigma(I)]	R1 = 0.0522, wR2 = 0.1035	
R indices (all data)	R1 = 0.0792, wR2 = 0.1128	

Largest diff. peak and hole 0.392 and -0.488 e.Å^{-3}

1.5 References for Chapter 1

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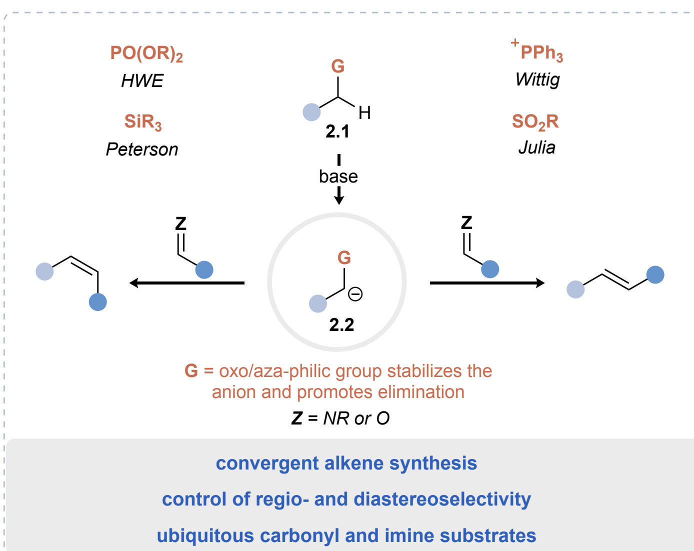
Chapter 2. STEREOSELECTIVE COPPER-CATALYZED OLEFINATION OF IMINES

2.1 INTRODUCTION

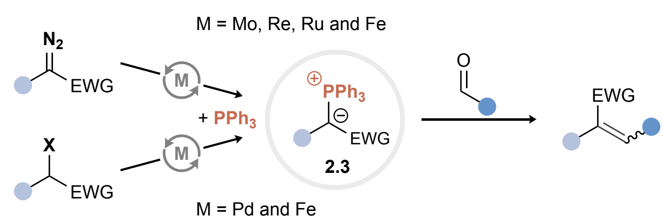
Wittig-type olefination is a powerful synthetic tool that enables the construction of a new carbon-carbon σ-bond with precise control over the geometry of the newly formed π-bond.[1–10] These features are shared by two state-of-the-art catalytic methods for alkene synthesis: olefin cross-metathesis[11–26] and the hydroalkylation of alkynes.[27–40] What makes Wittig-type olefination reactions particularly valuable is that they operate on carbonyls and imines, which are ubiquitous in organic chemistry. Examples of such reactions include Wittig,[1,3,4,41–43] HWE,[44–46] Peterson,[47–51] and Julia[52–58] olefinations, which all follow the general form shown in **Scheme 2.1**.



Scheme 2.1 Stoichiometric Wittig-Type Reactions.

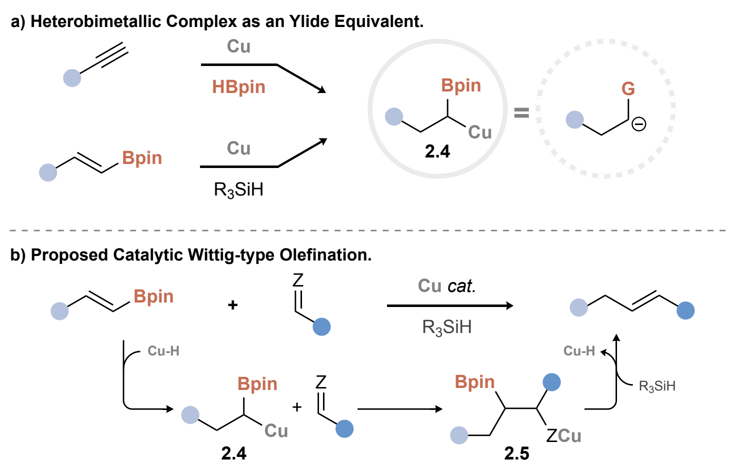
The key intermediate in Wittig-type olefination reactions are carbanions stabilized by an oxo/aza-philic moiety. While exact mechanisms of individual reactions vary, the nucleophilicity of these intermediates generally drives the formation of a new σ-bond in a reaction with a π-electrophile. The oxo/aza-philic group then facilitates the elimination to form the new π-bond.[3,5] For example, with phosphonium ylides the phosphonium group stabilizes the adjacent negative charge and facilitates alkene formation through elimination of the phosphine oxide.

In contrast to the state-of-the-art methods for alkene synthesis, Wittig-type reactions have been conceived as stoichiometric processes. Over time, significant effort has been devoted to the development of catalytic Wittig-type reactions, with a major focus on recovering the anion stabilizing group G (see **2.2**). For example, P(III)/P(V) oxidation state cycling has been leveraged in turning over phosphine reagents and accomplishing Wittig/HWE reactions catalytic in a phosphine reagent.[59–67] However, this approach does not address the key issue related to ylide synthesis: to access ylides, the anion precursors (**2.1**) are prepared from more readily available starting materials and then treated with a full equivalent of a base. As a result, the catalytic Wittig reactions centered on phosphine recycling work with a very narrow range of specialized substrates that facilitate the ylide formation. Efforts to transform other Wittig-type reactions into similar catalytic processes have not been as fruitful.[68–72] Therefore, stoichiometric forms of Wittig-type reactions remain by far the most common.



Scheme 2.2 Metal-Catalyzed Wittig-Type Reactions.

Transition metal catalysis has so far played a relatively minor role in the development of catalytic Wittig-type olefination reactions.[73,74] In the most common approach to metal catalyzed Wittig reactions, phosphonium ylides have been accessed through a catalytic reaction of phosphines with diazo alkanes[75–89] or alkyl halides[90–92] (**Scheme 2.2**). To be efficient, both reactions require the presence of an additional electron-withdrawing group (EWG) in the ylide precursor.[93] Despite these limitations, these examples have suggested a different approach to developing catalytic variants of Wittig-type reactions, in which metal catalysis enables efficient and convenient access to ylides and ylide-equivalents from readily available starting materials.



Scheme 2.3 Copper-Catalyzed Wittig-Type Olefination.

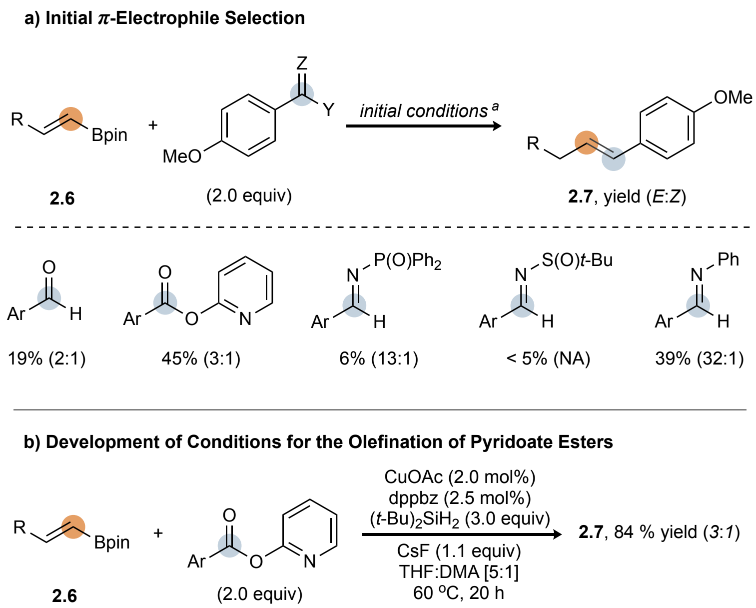
Exploring the idea of transition metal catalyzed formation of ylide equivalents, we focused on copper boryl heterobimetallic complex **2.4**. This complex can be accessed directly from alkynes or alkenyl boronate esters through copper hydride catalysis and has been identified as a key intermediate in copper-catalyzed reactions developed by our group and by others (**Scheme 2.3a**).[27,94–104] We recognized that the two reactive sites of this complex make it a functional equivalent of an ylide. As Meek, Cho and Yun groups have demonstrated, the copper boryl complex can react with π-electrophiles to form a new σ-bond.[99,105–109] Further, known bora-Wittig reactions rely on the ability of a boryl group to facilitate elimination of oxygen/nitrogen-based functional groups and promote the formation of a new π-bond.[110,111]

These unique properties of heterobimetallic complex **2.4** allowed us to envision the catalytic olefination of π-electrophiles shown in **Scheme 2.3b**. In the proposed transformation, the heterobimetallic intermediate is obtained by the reaction of alkenyl boronate ester with copper hydride. The addition of the intermediate to a carbonyl or an imine is followed by elimination to furnish the alkene product. Additionally, transmetalation of the addition product with a hydride donor allows catalyst turnover and the overall transformation without the use of a stoichiometric amount of a base.

2.2 RESULTS AND DISCUSSION

2.2.1 *Reaction Development*

We initiated the development of the proposed olefination reaction by examining a variety of π-electrophiles in a reaction with alkenyl boronic esters, performed in the presence of a copper catalyst and a silane (**Scheme 2.4a**). Aldehydes produced the desired alkene product in low yield, in part due to the reduction of the carbonyl outcompeting the desired reaction. We explored in situ formation of the aldehyde through the copper hydride mediated reduction of pyridoate esters. Keeping the aldehyde concentration low improved the yield, but the *E*:*Z* ratio of the alkene product remained low. Despite further development of reaction conditions, the diastereomeric ratio could not be improved beyond (3:1), although the yield was improved to >80% (**Scheme 2.4b**).



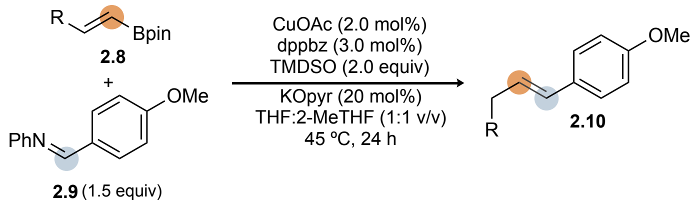
Scheme 2.4 π-Electrophiles.

Reactions were performed on 0.05 mmol scale. Yields determined by GC using trimethoxybenzene as an internal standard. [a]Reactions were conducted with CuOAc (2.0 mol%), dppbz (3.0 mol%), DMMS (2.0 equiv), KOPyr (1.0 equiv) at 45 ºC for 24 h in THF. R = $Ph(CH_2)_3$ and Ar = $MeOC_6H_4$.

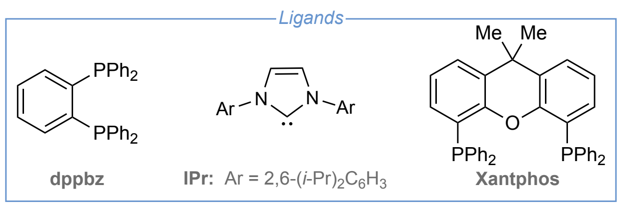
In an effort to improve the stereoselectivity of the reaction, we explored imine electrophiles and found that selectivity was heavily influenced by the substituent on the imine nitrogen.[112,113] Gratifyingly, simple aniline derived imines gave a >30:1 *E*:*Z* ratio of **2.7** under these conditions.

Using the preliminary results described in **Scheme 2.4** as a starting point, we developed the copper-catalyzed Wittig-type olefination of aryl imines, shown in **Table 2.1**. The best results were obtained with 2 mol% of a copper/dppbz catalyst, TMDSO as the hydride source, and a catalytic amount of potassium pyridoate (conjugate acid pKa = 17.0).[114]

Table 2.1 Reaction Development

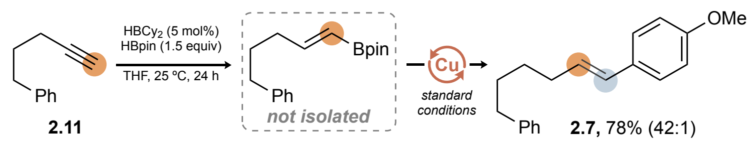


Entry	deviation from above	% yield [a]	E:Z [a]
1	none	87	43:1
2	IPr instead of dppbz	0	---
3	Xantphos instead of dppbz	40	33:1
4	PPh_3 instead of dppbz	0	---
5	NaOpyr instead of KOpyr	15	3:1
6	KOt-Bu instead of KOpyr	27	7:1
7	HMTSO instead of TMDSO	80	40:1
8	DMMS instead of TMDSO	18	13:1
9	DME instead of THF:2-MeTHF [1:1]	81	33:1
10	toluene instead of THF:2-MeTHF [1:1]	22	10:1
11	25°C instead of 45°C	40	210:1
12	60°C instead of 45°C	85	15:1
13	no KOpyr, CuOAc, dppbz, or TMDSO	0	---



[a] Reactions were performed on 0.05 mmol scale, and yields were determined by GC using trimethoxybenzene as an internal standard. TMDSO = 1,1,3,3-tetramethyldisiloxane, HMTSO = 1,1,3,3,5,5-hexamethyltrisiloxane, DMMS = dimethoxymethylsilane, THF = tetrahydrofuran, DME = dimethoxyethane, pin = pinacolato. R = p-$CH_3OC_6H_4O(CH_2)_3$.

While other bidentate phosphine ligands, such as Xantphos (**entry 3**), gave the desired alkene with good selectivity and yield, simple monodentate phosphine (**entry 4**) and NHC-supported (**entry 2**) copper complexes were not productive in the reaction. The identity of the base was very important for the success of the reaction. Replacing the potassium counter ion with sodium (**entry 5**) or switching to potassium *tert*-butoxide (**entry 6**) led to drastically lower selectivity and yield, with full consumption of the starting materials. Similarly, TMDSO and closely related HMTSO (**entry 7**) were the only silanes that gave good results, where other silanes, such as DMMS (**entry 8**), predominantly led to hydrosilylation of the alkenyl boronate ester. Most ethereal solvents gave good to excellent yields and selectivities (**entry 9** and **table S9**) while aromatic hydrocarbons such as toluene (**entry 10**), gave lower yields. Additionally, we found that a mixture of THF and 2-MeTHF gave the most consistent results throughout our exploration of the substrate scope. The reaction temperature also had a strong effect on the reaction outcome. At lower temperatures we observed diminished yield but increased selectivity, while at higher temperatures (**entries 11** and **12**) the yield was unchanged, and selectivity was lower. Finally, in the absence of the copper precatalyst, ligand, silane or base, we did not observe any of the desired alkene product (**entry 13**).



Scheme 2.5 One-Pot Transformation from Terminal Alkynes.

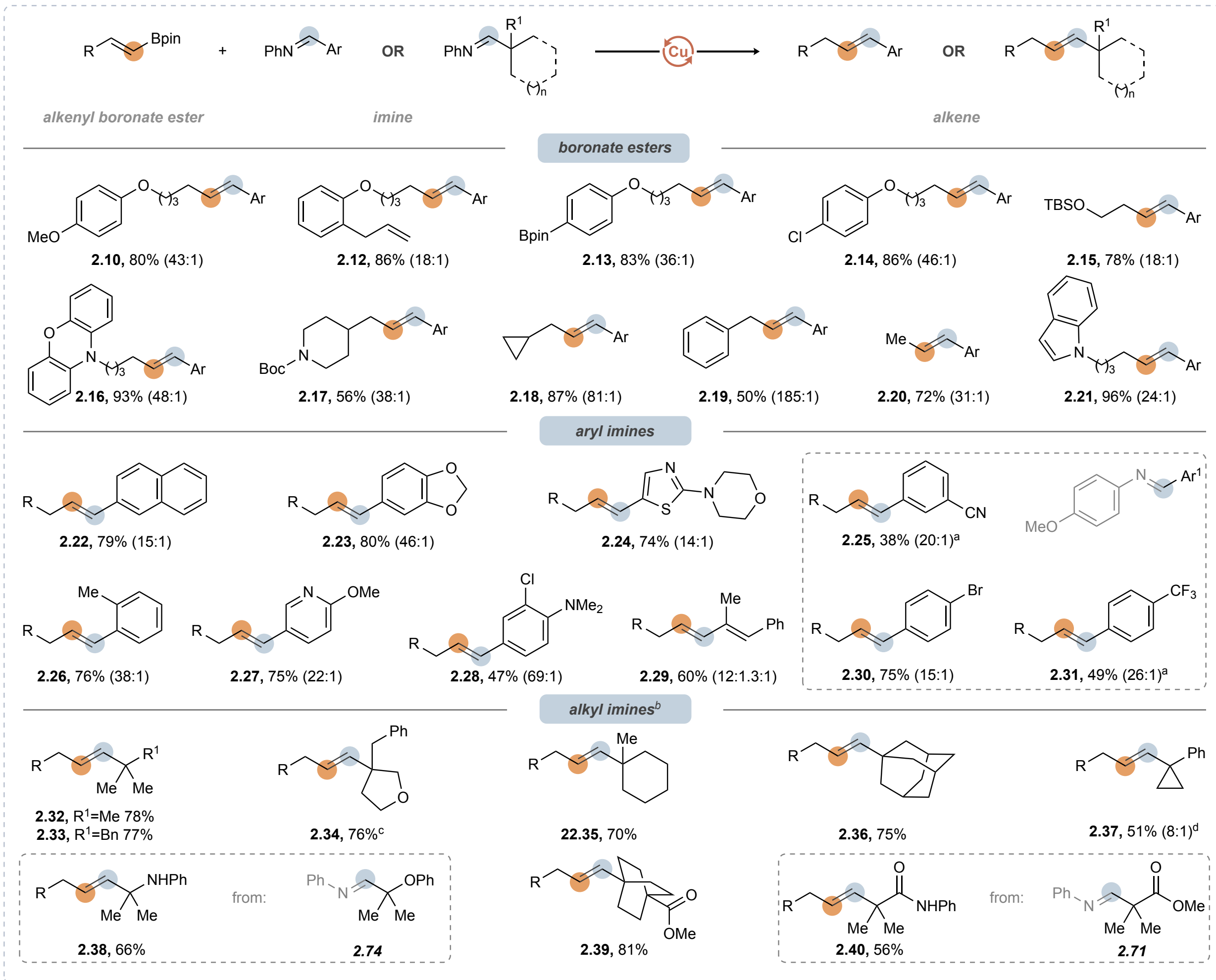
While alkenyl boronate esters are straightforward to synthesize and are generally stable, we wanted to explore if alkynes could be used as starting materials for the reaction in a one-pot procedure. As shown in **Scheme 2.5**, an alkyne can be transformed to an alkenyl boronate ester, which is then used in the olefination reaction without isolation.[115] The yield of the desired styrene and the diastereoselectivity are comparable to those obtained using an alkenyl boronate ester as the starting material.

2.2.2 *Substrate Scope*

After establishing reaction conditions that provided excellent yield and *E*-selectivity with our model substrate, we explored the scope of our olefination reaction (**Table 2.2**). We found that a variety of functional groups could be tolerated on the alkenyl boronate ester, including terminal alkenes (**2.12**), both aryl nucleophiles and electrophiles (**2.13** and **2.14**), a protected allylic alcohol

(**2.15**) and a Boc-protected secondary amine (**2.17**), as well as nitrogen-containing heterocycles (**2.16** and **2.21**). The reaction was also amenable to simple vinyl boronate esters (**2.20**) and *β*-styrenyl boronate esters (**2.19**), although with slightly diminished yield, likely due to the altered electronic properties of the starting π-bond.

Table 2.2 Substrate Scope



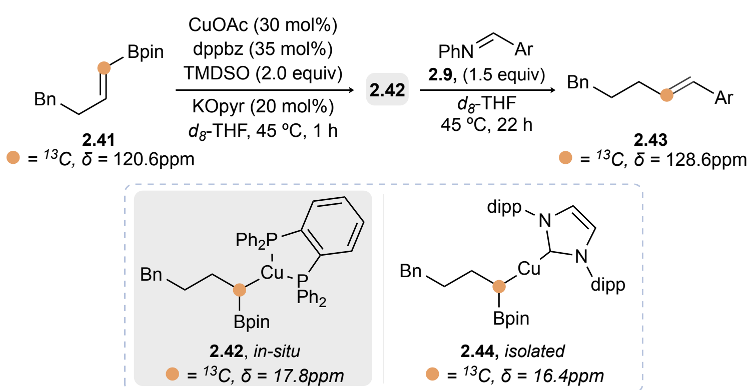
Yields of isolated products are reported. *E*:*Z* ratios were determined by GC. Reactions performed on 0.3 mmol scale with CuOAc (2.0 mol%), dppbz (3.0 mol%), TMDSO (2.0 equiv), KOPyr (0.2 equiv), and imine (1.5 equiv) at 45 °C for 24 h in a 1:1 mixture of THF and 2-MeTHF [0.1 M] with respect to alkenyl Bpin (1.0 equiv), unless otherwise stated. [a] Reaction was performed with CuOAc (2.0 mol%), (*p*-CF_3)dppbz (3.0 mol%), TMDSO (2.0 equiv), KOPyr (0.4 equiv), and imine (2.0 equiv) at 45 °C for 24 h in a 1:1 mixture of THF and 2-MeTHF [0.1 M] with respect to alkenyl Bpin (1.0 equiv). [b] Reactions performed on 0.5 mmol scale with CuOAc (2.0 mol%), dppbz (3.0 mol%), HMTSO (1.5 equiv), KOPyr (0.2 equiv), and imine (2.0 equiv) at 60 °C for 48 h in 2-MeTHF [0.2 M] with respect to alkenyl Bpin (1.0 equiv). [c] Reaction performed on 0.3 mmol scale. [d] SciOPP used instead of dppbz. R = *p*-$MeOC_6H_4O(CH_2)_3$. Ar = *p*-$MeOC_6H_4$.

We next turned our attention to the aryl imine scope and found that our reaction tolerates a variety of ortho, meta and para substituents (**2.26**, **2.22**, **2.23**, and **2.28**). In addition, several nitrogen-containing heterocycles are tolerated (**2.24** and **2.27**), further, conjugated imines provide 1,3-dienes in good yield (**2.29**). We found that under our standard reaction conditions, electron deficient aryl imines were readily reduced and did not produce the desired styrene products. However, using imines derived from more electron-rich anilines and a less electron-donating ligand, we were able to realize the transformation of *m*-cyano and *p*-trifluoromethyl aryl imines into the corresponding styrenes (**2.25** and **2.31**). We believe that the recovered yield and selectivity can be attributed to the decreased reduction of the starting imines and slower copper-catalyzed isomerization of the styrene π-bond.

Further, we found that our method could be applied to the synthesis of alkenes with quaternary carbons at the allylic position. These highly sterically encumbered alkenes are not only a challenge to synthesize using catalytic methods but are also formed in low yields using stoichiometric Wittig-type reactions.[116–118] By changing the hydride source and increasing the temperature to 60 °C we were able to produce alkenes showcasing a variety of substitution patterns and excellent selectivity (>200:1 selectivity). A simple *tert*-butyl group (**2.32**), as well as various cyclic and fused ring systems were tolerated (**2.35** and **2.36**). A cyclopropyl moiety (**2.37**), a simple methyl ester (**2.39**) and a tetrahydrofuran (**2.34**) were all tolerated under the reaction conditions. Curiously, when **2.74** and **2.71** were submitted to the reaction conditions, we did not observe the expected α-phenyl ether and α-methoxy ester alkenes, but instead we isolated the products arising from rearrangement prior to elimination. Finally, with alkyl imines containing α-hydrogen atoms we were unable to surpass 10% yield of the desired aliphatic alkene product under variety of reaction conditions.

2.2.3 *Mechanistic Investigation*

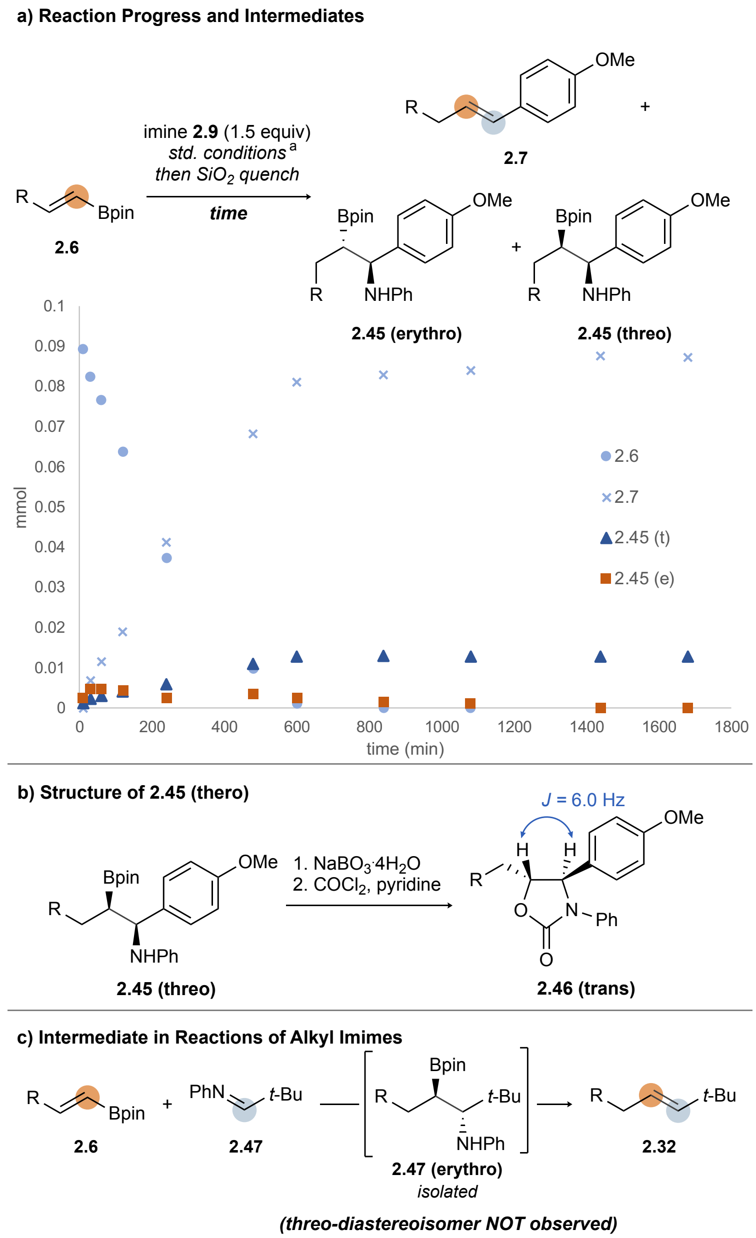
To better understand the mechanism of this reaction we performed several mechanistic experiments. Our first goal was to confirm the proposed role of a copper containing heterobimetallic complex as the intermediate in the reaction. Although phosphine ligated 1,1-boryl-copper heterobimetallic complexes have been proposed as catalytic intermediates before, they have only been characterized via ^{31}P-NMR analysis.[101] To gain a stronger and more specific confirmation for the involvement of the phosphine ligated heterobimetallic intermediate, we used a ^{13}C-enriched alkenyl boronate ester (**2.41**) as a substrate (**Scheme 2.6**). Submitting **2.41** to a premade solution of dppbzCuH gave rise to a new broad signal in the ^{13}C-NMR spectrum at δ = 17.8 ppm. The addition of imine **2.9** to this solution produced styrene **2.43**, along with disappearance of the broad signals corresponding to both the starting alkenyl boronate ester and the proposed intermediate (**2.42**).



Scheme 2.6 Heterobimetallic Intermediate.
Reactions were performed on 0.05 mmol scale. Ar = $MeOC_6H_4$.

While we were unable to isolate the dppbz ligated intermediate due to facile decomposition, a related known heterobimetallic species bearing an NHC ligand (**2.44**) was isolated and showed a broad signal in ^{13}C-NMR spectrum at δ = 16.4 ppm corresponding to the α-carbon, further validating our assignment of the phosphine ligated α-borylalkyl copper species.[94,100,101,103]

Next, we monitored the reaction of alkenyl Bpin **2.6** and aryl imine **2.9** by ^{1}H-NMR spectroscopy (**Scheme 2.7**). Within 30 minutes we observed consumption of starting material

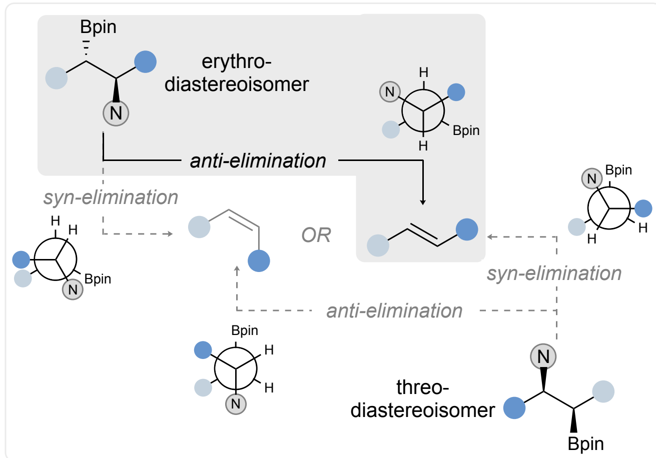


Scheme 2.7 Addition Products as Intermediates.
Reactions performed on 0.05 mmol scale. Yields determined by ^{1}H-NMR spectroscopy with trimethoxybenzene as an internal standard and *E*:*Z* ratios determined via GC analysis of crude reaction mixture. [a]See **Table 2.1**. R = Ph(CH$_2$)$_3$ and Ar = MeOC$_6$H$_4$.

accompanied by the formation of two diastereoisomers of 1,2-boryl amine addition product **2.45**. As the reaction progressed, one isomer appeared to gradually give rise to the product styrene and was fully consumed after 24 hours, while the other isomer accumulated to a constant concentration. Through careful isolation, conversion to the corresponding oxazolidinone (**2.46**), and NOESY and *J*-coupling analysis (**Scheme 2.7b**), we determined that the accumulated adduct was the threo-diastereoisomer. The threo-isomer of **2.45** appears not to eliminate under the reaction conditions, suggesting that the product is formed solely via the erythro-isomer. In the reaction with alkyl imines, we observed the formation of a single 1,2-boryl amine diastereoisomer that was fully consumed after 48 hours (**Scheme 2.7c**). Through similar ^{1}H-NMR analysis we identified this isomer as the erythro-diastereoisomer.

Together, these findings indicate that the erythro diastereoisomer of the addition intermediates gives rise to both the *E*-styrenes and *E*-aliphatic alkenes. Therefore, in both cases, the alkene formation involves anti-elimination, with no indication that the syn-elimination from the erythro-isomer occurs. Furthermore, the threo-isomer, when formed, does not undergo elimination under the reaction conditions (**Scheme 2.8**). We can speculate about explanations for the observations we made. First, it is likely that the increased bulk of the *tert*-butyl group prevents the formation of the syn-diastereoisomer in the initial addition to the alkyl imines. Second, the erythro-isomer of the addition product, in both reactions of alkyl and aryl imines, encounters the least steric hinderance undergoing anti-elimination, while the aryl threo-isomer must overcome increased steric hinderance in either syn- or anti-elimination.

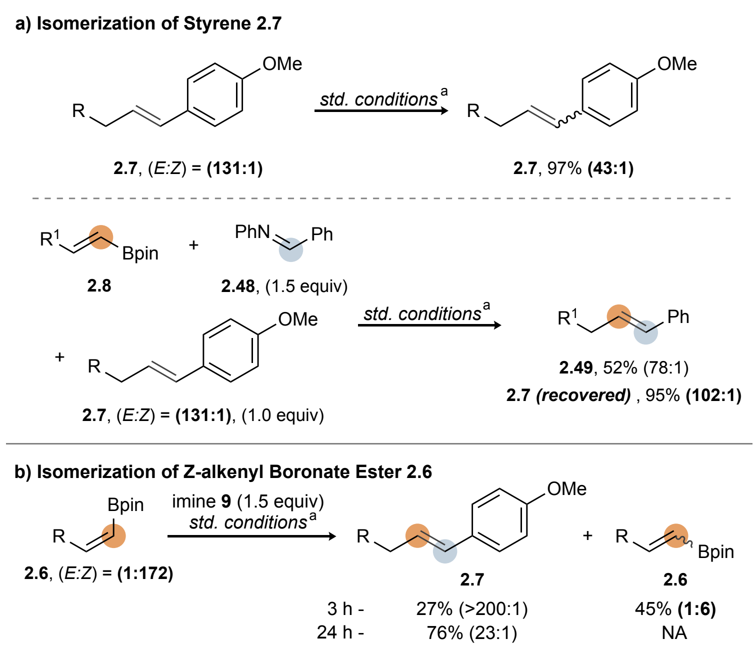
Interestingly, the understanding of the stereochemistry of the addition and the elimination processes provided unexpectedly little insight into the origin of the *Z*-alkene products and therefore the *E*:*Z* selectivity. The first clue about the origins of the *Z*-isomer in the reactions of aryl imines



Scheme 2.8 Stereochemistry of Alkene Formation.

came from the observation that the *E*:*Z* ratio diminishes during the reaction, suggesting isomerization of the styrene products.

Previously, copper hydride has been implicated in the isomerization of styrenes via hydrocupration and subsequent *β*-hydride elimination.[119,120] As expected, when we submitted an



Scheme 2.9 *E*/*Z* Isomerization.

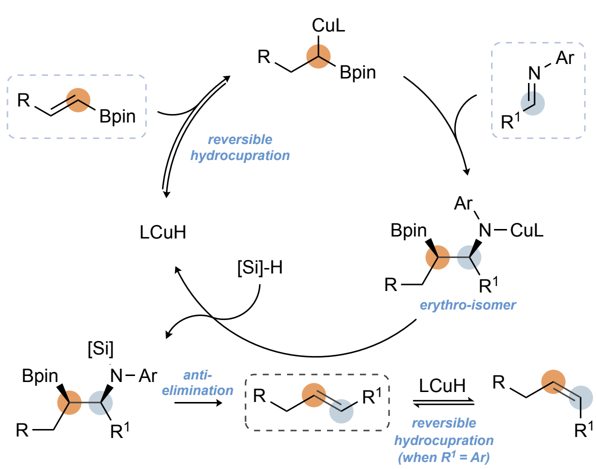
Reactions performed on 0.05 mmol scale. Yields determined by ^{1}H-NMR with trimethoxybenzene as an internal standard and *E*:*Z* ratios determined via GC analysis of crude reaction mixture. [a]See Table 2.1. R = $Ph(CH_2)_3$.

E-styrene **2.7** to the standard reaction conditions, we observed an erosion in the *E*:*Z* ratio from >100:1 to 43:1 (**Scheme 2.9a**). We also found that copper hydride mediated isomerization was not as facile in the presence of starting materials.

Overall, we conclude that *E*-styrene is formed with high selectivity in the elimination reaction and is then slowly isomerized in the process mediated by the copper catalyst. This conclusion is consistent with the observed dependence of *E*:*Z* selectivity on the electronics of the product styrene. We also noticed that for high selectivity, styrenes bearing electron-withdrawing groups required a more electron deficient copper catalyst, presumably to slow the reversible hydrometallation and isomerization.

In analogous experiments with alkene **2.32** we found no evidence for its isomerization under the reaction conditions. This observation suggests that aliphatic alkene products do not undergo hydrocupration under the reaction conditions and is consistent with high *E*-selectivity observed in reactions of aliphatic imines.

Finally, we found that the starting alkenyl boronate esters also undergo isomerization under the reaction conditions (**Scheme 2.9b**). When *Z*-enriched alkenyl boronate ester **2.6** was allowed to react under the standard conditions, we observed the erosion of the diastereomeric ratio from



Scheme 2.10 Proposed Mechanism.

(1:172) to (1:6) before full consumption and formation of the product alkene. This result shows that the initial hydrocupration event is likely reversible.

On the basis of these experiments, we propose that the reaction proceeds according to the mechanism outline in **Scheme 2.10**. The first step involves the reversible hydrocupration of an alkenyl boronate ester to form the key hetero-bimetallic intermediate.[94,121–124] Subsequently, this intermediate reacts with the carbonyl electrophile, followed by regeneration of copper hydride via an equivalent of silane.[125–127] The resulting anti-1,2-boryl *N*-silylamine eliminates to furnish the *E*-alkene product, which when R^1 is aryl can isomerize to give a mixture of *E*/*Z* styrenes.

2.3 Conclusion

In summary, we have developed a new method for the catalytic olefination of imines leveraging a catalytically generated copper-boryl heterobimetallic intermediate as an ylide equivalent. The new reaction is compatible with aryl and sterically hindered alkyl imines and can be performed in the presence of an array of functional groups. Mechanistic studies corroborate the proposed catalytic cycle, confirming the existence and function of the proposed heterobimetallic intermediate, and provide insights into the origins of selectivity of the newly formed π-bond.

2.4 Experimental

2.4.1 *General Information*

All reactions were performed under a nitrogen atmosphere with flame-dried or oven-dried (120 °C) glassware, using standard Schlenk techniques, or in a glovebox (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Isolera-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 μm, 230-400 mesh). High Pressure Liquid Chromatography was performed using an Agilent LC column (Zorbax CN

PrepHT, 21.2 x 250mm, 7µm). 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 solvent peak ($CDCl_3$: δ 7.26 ppm or C_6D_6: δ 7.16 ppm or d_8-THF: δ 3.58 ppm). ^{13}C NMR 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 or C_6D_6: δ 128.0 ppm or d_8-THF: δ 67.2 ppm). ^{19}F NMR chemical shifts (δ) are reported in parts per million (ppm) and are referenced relative to the internal standard, hexafluorobenzene (C_6F_6: δ -164.9 ppm). ^{11}B NMR chemical shifts (δ) are reported in parts per million (ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), integration, and coupling constants in Hertz (Hz). Mass spectra were collected on a JEOL HX-110 mass spectrometer and Bruker EsquireLC ion trap 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.

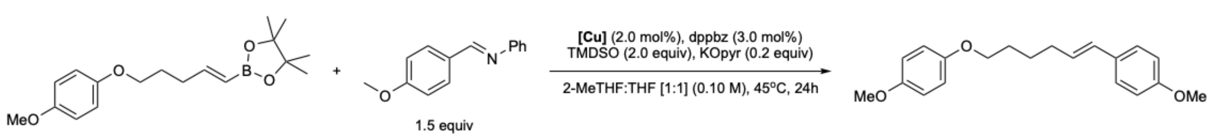
2.4.2 *Materials*

THF, CH_2Cl_2, ether, benzene, and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous isooctane was purchased from Millipore Sigma, and was subsequently degassed and stored over 4Å molecular sieves. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and were stored over 4Å molecular sieves prior to use. d_8-THF was dried using sodium/benzophenone ketal, distilled, then stored over 4Å molecular sieves. 1,1,3,3-Tetramethyldisiloxane and pinacol borane were vacuum transferred over calcium hydride followed by freeze pump thaw before use. Potassium pyridoate was synthesized according to a previously reported procedure.[128] Other commercial reagents were purchased from Millipore Sigma, TCI America, GFS-Chemicals, Ark-Pharm, Combi-Blocks, Oakwood Chemicals, Strem Chemicals and Alfa Aesar and used as received unless otherwise stated.

2.4.3 *Reaction Development*

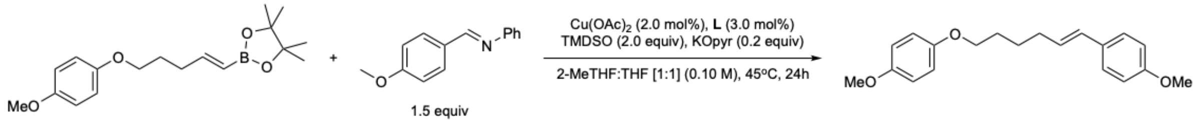
All reactions were performed on a 0.05 mmol scale. In a nitrogen-filled glovebox a dram vial was charged with a stir bar, copper **(Table 2.3)**, ligand **(Table 2.4)**, solvent **(Table 2.11)**, and mixed at 45 ºC for 5 minutes until the solution became homogenous. A separate dram vial was charged with a stir bar, the turnover reagent **(Table 2.8)**, premixed catalyst solution, followed by the hydride source **(Table 2.6)**, 2-[(*E*)-5-(4-methoxyphenoxy)pent-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, trimethoxybenzene (TMB, used as an internal standard for GC analysis), and (*E*)-1-(4-methoxyphenyl)-*N*-phenylmethanimine. The reaction mixture was stirred at the specified temperature. 20 µL aliquots were taken at 24 h, pushed through a plug of silica with 1.5 mL of ethyl acetate and analyzed by Gas Chromatography.

Table 2.3 Effect of Reaction Parameters: Copper Source



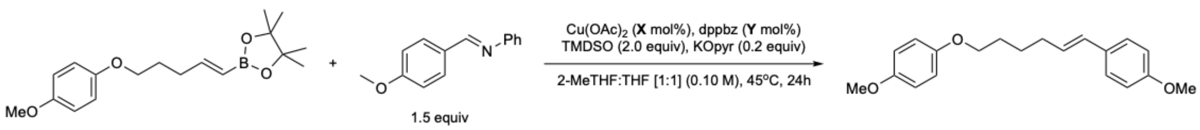
Entry	Copper Salt	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	CuOAc	0	88 (42:1)
2	$Cu(OAc)_2$	0	87 (35:1)
3	CuCl	0	82 (29:1)
4	CuI	0	87 (42:1)
5	CuOTf-benzene complex	0	72 (89:1)
6	CuF_2	91	0 (NA)
7	none	100	0 (NA)

Table 2.4 Effect of Reaction Parameters: Ligand Identity



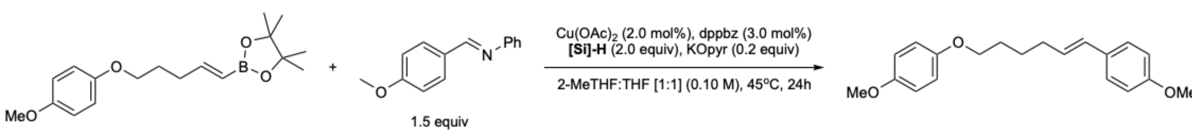
Entry	Ligand	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	dppbz	0	87 (43:1)
2	SciOPP	0	50 (25:1)
3	dppe	69	18 (14:1)
4	XantPhos	30	40 (33:1)
5	XPhos	87	0 (NA)
6	PPh_3	91	0 (NA)
7	IPr	88	0 (NA)
8	none	92	0 (NA)

Table 2.5 Effect of Reaction Parameters: Copper to Ligand Ratio and Catalyst Loading



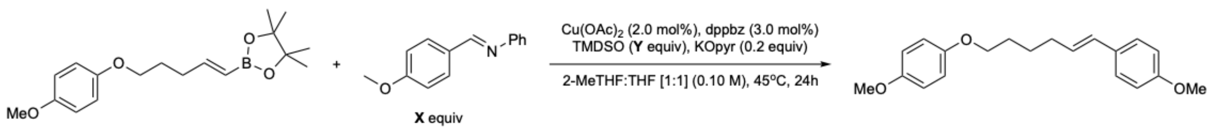
Entry	X:Y	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	2:3	0	89 (42:1)
2	1:1.5	0	85 (42:1)
3	5:7.5	0	86 (38:1)
4	2:1	41	55 (NA)
5	1:1	0	84 (42:1)
6	1:2	0	86 (42:1)

Table 2.6 Effect of Reaction Parameters: Hydride Source



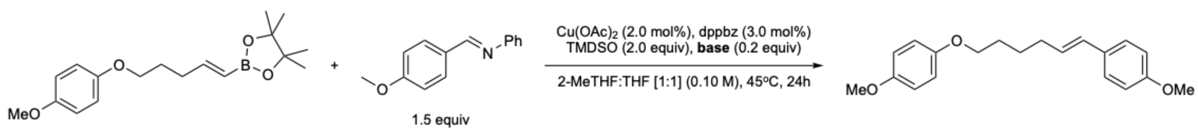
Entry	[Si]-H	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	TMDSO	0	87 (42:1)
2	HMTSO	0	80 (40:1)
3	PMHS	3	10 (4:1)
4	Ph_2SiH_2	12	30 (46:1)
5	Ph_2MeSiH	82	24 (10:1)
6	*t*-Bu_2SiH_2	92	6 (15:1)
7	$(EtO)_3SiH$	9	20 (10:1)
8	DMMS	0	18 (13:1)
9	none	99	0 (NA)

Table 2.7 Effect of Reaction Parameters: Imine to Hydride Ratio



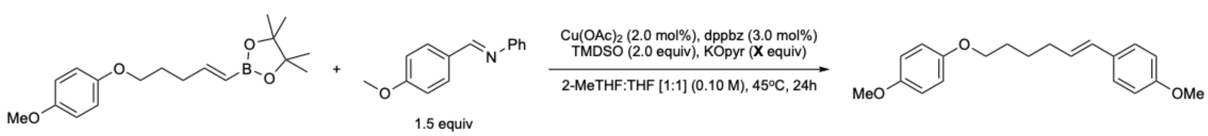
Entry	X:Y	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	1.5:2	0	87 (42:1)
2	1:2	0	73 (47:1)
3	2:2	0	87 (42:1)
4	1.5:1.5	0	76 (43:1)
5	1.5:1	0	74 (42:1)

Table 2.8 Effect of Reaction Parameters: Base Identity



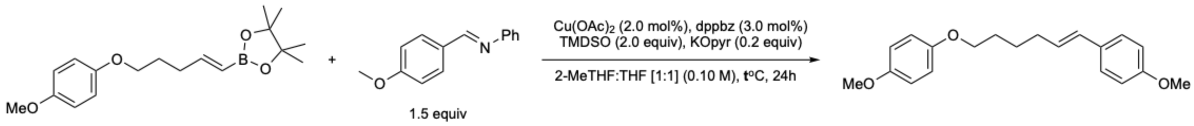
Entry	Base	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	2-KOPyr	0	87 (43:1)
2	3-KOPyr	61	30 (12:1)
3	4-KOPyr	80	13 (4:1)
4	KOPh	56	19 (10:1)
5	KO[o-*t*-BuC_4H_4]	0	67 (21:1)
6	KOMe	57	15 (10:1)
7	KO*t*-Bu	19	27 (7:1)
8	LiO*t*-Bu	98	0 (NA)
9	LiOPyr	88	0 (NA)
10	NaO*t*-Bu	66	29 (7:1)
11	NaOPyr	81	15 (3:1)
12	CsF	0	61 (14:1)
13	Cs_2CO_3	93	0 (NA)
14	none	99	0 (NA)

Table 2.9 Effect of Reaction Parameters: Base Loading



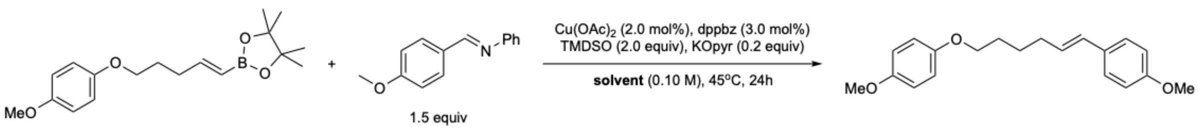
Entry	X	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	0.1	13	66 (18:1)
2	0.2	0	86 (42:1)
3	0.4	0	83 (46:1)
4	0.6	0	81 (46:1)
5	0.8	0	81 (46:1)

Table 2.10 Effect of Reaction Parameters: Temperature



Entry	X:Y	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	25	38	40 (210:1)
2	45	0	88 (42:1)
3	60	0	84 (15:1)

Table 2.11 Effect of Reaction Parameters: Solvent Identity



Entry	solvent	Unreacted Alkenyl Bpin [%]	Product Alkene Yield [% (*E*:*Z*)]
1	THF	0	82 (17:1)
2	2-MeTHF	0	86 (42:1)
3	Dioxane	0	76 (29:1)
4	DME	0	81 (33:1)
5	MTBE	46	46 (16:1)
6	CPME	46	45 (14:1)
7	toluene	70	22 (10:1)
8	isooctane	92	0 (NA)

2.4.4 *General Procedures*

2.4.4.1 Procedure A: Standard

In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.74 mg, 0.006 mmol, 0.02 equiv), dppbz (4.0 mg, 0.009 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (1.0 mL). The heterogenous mixture was stirred for 5 min at 45 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (8.0 mg, 0.060 mmol, 0.20 equiv), TMDSO (80.4 mg, 0.600 mmol, 2.0 equiv), alkenyl Bpin (0.300 mmol, 1.0 equiv), imine (0.450 mmol, 1.5 equiv), and a 1:1 mixture of THF:2-MeTHF (2.0 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 24 h a 20 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of ethyl acetate and analyzed by GC to determine the *E*:*Z* ratio. The crude reaction mixture was then purified by the appropriate workup procedure (Sections 2.4.4.5 – 2.4.4.7).

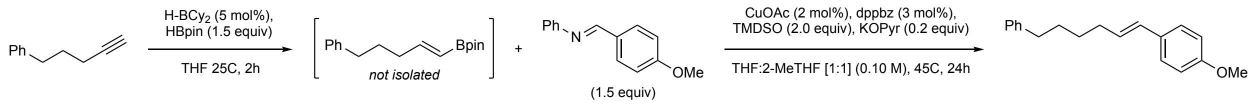
2.4.4.2 Procedure B: Electron Deficient Aryl Imines

In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.74 mg, 0.006 mmol, 0.02 equiv), (*p*-CF_3)dppbz (6.5 mg, 0.009 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (1.0 mL). The heterogenous mixture was stirred for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (16.0 mg, 0.120 mmol, 0.40 equiv), TMDSO (80.4 mg, 0.600 mmol, 2.0 equiv), alkenyl Bpin (0.300 mmol, 1.0 equiv), imine (0.600 mmol, 2.0 equiv), and a 1:1 mixture of THF:2-MeTHF (2.0 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 24 h a 20 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of ethyl acetate and analyzed by GC to determine the *E*:*Z* ratio. The crude reaction mixture was then purified by the appropriate workup procedure (Sections 2.4.4.5 – 2.4.4.7).

2.4.4.3 Procedure C: Tertiary Alkyl Imines

In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (1.20 mg, 0.010 mmol, 0.02 equiv), dppbz (6.7 mg, 0.015 mmol, 0.03 equiv), and 2-MeTHF (1.0 mL). The heterogenous mixture allowed to stir stirred for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (13.3 mg, 0.100 mmol, 0.20 equiv), HMTSO (156.4 mg, 0.750 mmol, 1.5 equiv), alkenyl Bpin (0.500 mmol, 1.0 equiv), imine (1.000 mmol, 2.0 equiv), and 2-MeTHF (1.5 mL, 0.20 M total). The reaction was vigorously stirred at 60 °C. After 48 h a 10 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of ethyl acetate and analyzed by GC to determine the *E*:*Z* ratio. The crude reaction mixture was then purified by the appropriate workup procedure (Sections 2.4.4.5 – 2.4.4.7).

2.4.4.4 Procedure D: One-Pot Procedure



In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, 5-phenyl-1-pentyne (19.0 mg, 0.100 mmol, 1.0 equiv), THF (0.2 mL), dicyclohexylborane (0.9 mg, 0.005 mmol, 0.05 equiv), and pinacolborane (19.2 mg, 0.150 mmol, 1.5 equiv) along with THF (0.1 mL). The vial was outfitted with a teflon lined cap and allowed to stir at 25 °C for 2 h. The volatiles were then removed under vacuum at 25 °C. A separate dram vial was charged with a stir bar, CuOAc (0.25 mg, 0.0025 mmol, 0.025 equiv), dppbz (1.34 mg, 0.003 mmol, 0.03 equiv), and THF (0.5 mL). The heterogenous mixture allowed to stir stirred for 5 min at 45 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (2.7 mg, 0.020 mmol, 0.20 equiv), TMDSO (26.8 mg, 0.200 mmol, 2.0 equiv), the alkenyl Bpin mixture, (*E*)-1-(4-methoxyphenyl)-*N*-phenylmethanimine (31.7 mg, 0.150 mmol, 1.5 equiv), and 2-MeTHF (0.5 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 24 h a 20 µL aliquot was taken and pushed through a plug of silica with 1.5 mL of ethyl acetate and analyzed by GC to determine the *E*:*Z* ratio. Upon consumption of the alkenyl Bpin, the crude reaction mixture was purified according to Workup Procedure 2.

2.4.4.5 Workup Procedure 1: Acid Sensitive Compounds

The crude reaction mixture was transferred to a 100 mL round bottom flask and the solvent was removed under vacuum using a roto-evaporator. Residual solvent was removed via co-evaporation using hexanes. The crude mixture was purified by silica gel column chromatography.

2.4.4.6 Workup Procedure 2: Acidic Workup

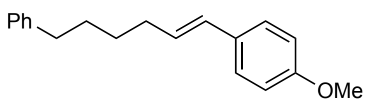
The crude reaction mixture was transferred to a 100 mL round bottom flask and the solvent was removed under vacuum using a roto-evaporator. Residual solvent was removed via co-evaporation using hexanes. The resulting crude oil was dissolved in hexanes (~50 mL) and a minimal amount of ether to afford a homogenous mixture. With vigorous stirring a 1.0 M solution of anhydrous HCl in ether (2.5 equiv) was added slowly (*to avoid clumping of the resulting precipitated amine salts*) to the mixture. After 15 minutes stirring at room temperature the mixture was filtered through a pad of celite and washed 3x with 20 mL of hexanes or a mixture of 10% ether in hexanes (*based upon the solubility of the desired alkene*). The solvent was removed under vacuum using a roto-evaporator and the crude mixture was purified by silica gel column chromatography.

2.4.4.7 Workup Procedure 3: Oxidative Workup

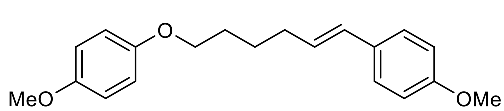
The crude reaction mixture was transferred to a 20 mL scintillation vial, charged with a stir bar, water (5.0 mL), THF (2.5 mL), and $NaBO_3 \cdot 4H_2O$ (1.5 equiv). The mixture was vigorously stirred for 2 h at 25 °C. At this point the reaction mixture was diluted with ether and H_2O, the aqueous layer was extracted 3x with ether, the combined organic layers were dried by Mg_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography.

2.4.5 *Characterization of Alkene Products*

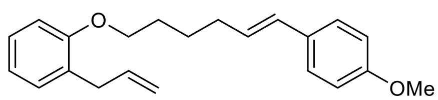
2.4.5.1 Styrene Products



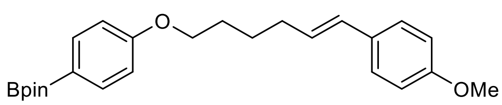
1-methoxy-4-[(1*E*)-6-phenylhex-1-en-1-yl]benzene (2.7), was prepared according to procedure A or D. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 34:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-60% CH_2Cl_2 in hexanes, and isolated as a clear colorless liquid (71 mg, 89% yield). *One-pot Procedure*: An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 42:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-60% CH_2Cl_2 in hexanes, and isolated as a clear colorless liquid (24.5 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 4H), 7.18 – 7.15 (m, 3H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 6.05 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.78 (s, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.22 – 2.18 (m, 2H), 1.67 (p, *J* = 7.6 Hz, 2H), 1.50 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 142.8, 130.8, 129.4, 128.8, 128.5, 128.4, 127.1, 125.8, 114.0, 55.4, 36.0, 33.0, 31.2, 29.3. GCMS (EI) calculated for $C_{19}H_{22}O$ $[M]^+$ 266.1, found 266.1. FTIR (neat, cm^{-1}): 2947 (m), 2877 (m), 2831 (w), 1608 (s), 1511 (s), 1423 (s), 1283 (m), 1139 (m), 1057 (m), 963 (m), 835 (m), 742 (m).



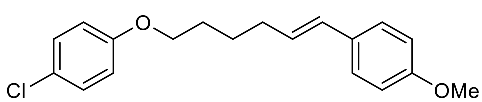
(*E*)-1-methoxy-4-(6-(4-methoxyphenoxy)hex-1-en-1-yl)benzene (2.10), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 43:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (75 mg, 80% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.8 Hz, 3H), 6.87 – 6.79 (m, 6H), 6.35 (d, *J* = 15.7 Hz, 1H), 6.09 (dt, *J* = 15.7, 6.9 Hz, 1H), 3.94 (t, *J* = 6.4 Hz, 2H), 2.28 – 2.24 (m, 2H), 1.85 – 1.81 (m, 2H), 1.79 – 1.61 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 153.8, 153.3, 130.7, 129.6, 128.4, 127.1, 115.5, 114.7, 114.0, 68.5, 55.8, 55.3, 32.8, 29.0, 26.0. GCMS (EI) calculated for $C_{20}H_{24}O_3$ $[M]^+$ 312.2, found 312.2. FTIR (neat, cm^{-1}): 3091(w), 2926(s), 2862(m), 2337(w), 1606(m), 1511(s), 1247(s) 1032(s), 971(s), 828(s), 738(s).



(*E*)-1-allyl-2-((6-(4-methoxyphenyl)hex-5-en-1-yl)oxy)benzene (2.12), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 18:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a clear, colorless liquid (84 mg, 86% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.7 Hz, 2H), 7.19 – 7.13 (m, 2H), 6.89 (td, *J* = 7.4, 1.2 Hz, 1H), 6.86 – 6.82 (m, 3H), 6.36 (d, *J* = 15.7 Hz, 1H), 6.10 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.00 (ddt, *J* = 17.0, 10.0, 6.7 Hz, 1H), 5.07 (dq, *J* = 17.0, 1.7 Hz, 1H), 5.03 (dq, *J* = 10.0, 1.7 Hz, 1H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.80 (s, 3H), 3.40 (d, *J* = 6.7 Hz, 2H), 2.30 – 2.25 (m, 2H), 1.90 – 1.81 (m, 2H), 1.72 – 1.62 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 156.8, 137.2, 130.7, 129.8, 129.6, 128.8, 128.4, 127.3, 127.1, 120.4, 115.4, 114.0, 111.2, 67.7, 55.3, 34.6, 32.8, 29.0, 26.1. GCMS (EI) calculated for $C_{22}H_{26}O_2$ $[M]^+$ 322.2, found 322.2. FTIR (neat, cm^{-1}): 3073(m), 2933(s), 2935(s), 1638(m), 1608(s), 1513(s), 1244(s), 966(s), 841(m), 751(s).

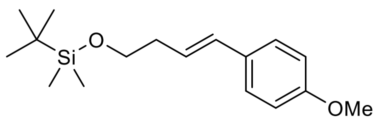


(*E*)-2-(4-((6-(4-methoxyphenyl)hex-5-en-1-yl)oxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.13), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 36:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (101 mg, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.25 (d, *J* = 15.8 Hz, 1H), 5.99 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.91 (t, *J* = 6.5 Hz, 2H), 3.70 (s, 3H), 2.19 – 2.15 (m, 2H), 1.78 – 1.71 (m, 2H), 1.58 – 1.52 (m, 2H), 1.24 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 158.8, 136.5, 130.7, 129.7, 128.3, 127.1, 114.0, 113.9, 110.0, 83.5, 67.6, 55.3, 32.7, 28.8, 26.0, 24.9. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.5. GCMS (EI) calculated for $C_{25}H_{33}BO_4$ $[M]^+$ 408.3, found 408.3. FTIR (neat, cm^{-1}): 3093(m), 3033(s), 2929(br), 1665(w), 1605(s), 1510(s), 1361(s), 1245(s), 1144(s), 973(s), 860(s).

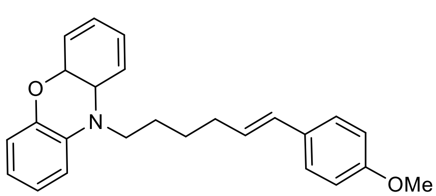


(*E*)-1-chloro-4-((6-(4-methoxyphenyl)hex-5-en-1-yl)oxy)benzene (2.14), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 46:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (81 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 10.2 Hz, 2H), 7.22 (d, *J* = 9.2 Hz, 2H), 6.87 – 6.79 (m, 4H), 6.35 (d, *J* = 15.8 Hz, 1H), 6.08 (dt, *J* = 15.8, 7.0 Hz, 1H), 3.95 (t, *J* = 6.5 Hz, 2H), 3.80 (s, 3H), 2.28 – 2.24 (m, 2H), 1.86 – 1.82 (m, 2H), 1.80 – 1.60 (m, 2H).^{13}C

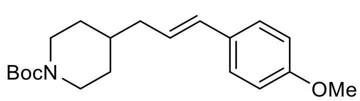
NMR (126 MHz, $CDCl_3$) δ 158.8, 157.8, 130.6, 129.7, 129.3, 128.2, 127.1, 125.4, 115.8, 114.0, 68.1, 55.3, 32.7, 28.8, 25.9. GCMS (EI) calculated for $C_{19}H_{21}ClO_2$ $[M]^+$ 316.1, found 316.1. FTIR (neat, cm^{-1}): 3090 (m), 2045 (s), 2916(s), 2541(m), 2059(m), 1877(m), 1677(w), 1615(s), 1246(s), 1173(s), 1037(s), 966(s), 823(s), 667(s).



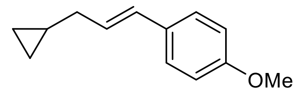
(*E*)-*tert*-butyl((4-(4-methoxyphenyl)but-3-en-1-yl)oxy)dimethylsilane (2.15), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 18:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a clear, colorless liquid (68 mg, 78% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.2 Hz, 3H), 6.84 (d, J = 8.2 Hz, 2H), 6.38 (d, J = 15.9 Hz, 1H), 6.08 (dt, J = 15.9, 7.0 Hz, 1H), 3.80 (s, 3H), 3.72 (t, J = 6.8 Hz, 2H), 2.44 – 2.38 (m, 2H), 0.91 (s, 9H), 0.07 (s, 6H). CNMR ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 131.0, 130.6, 127.1, 124.9, 113.9, 63.2, 55.3, 36.7, 26.0, 18.4, -5.2. GCMS (EI) calculated for $C_{17}H_{28}O_2Si$ $[M]^+$ 292.2, found 292.2. FTIR (neat, cm^{-1}): 3024(w), 2954(s), 2928(s), 2856(s), 1653(w), 1608(m), 1511(s), 1249(s), 1102(s), 965.4(m), 837(s).



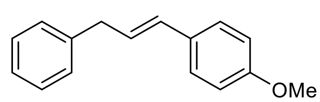
(*E*)-10-(6-(4-methoxyphenyl)hex-5-en-1-yl)-4a,10a-dihydro-10H-phenoxazine (2.16), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 48:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (103 mg, 93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 6.5 Hz, 2H), 6.90 (d, *J* = 6.5 Hz, 2H), 6.79 (dt, *J* = 8.0, 4.3 Hz, 2H), 6.67 (d, *J* = 4.3 Hz, 4H), 6.50 (d, *J* = 7.9 Hz, 2H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.12 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.84 (s, 3H), 3.53 (s, 2H), 2.32 (qd, *J* = 6.9, 1.5 Hz, 2H), 1.79 – 1.73 (m, 2H), 1.66 – 1.60 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 145.0, 133.4, 130.5, 130.0, 127.9, 127.2, 123.7, 120.8, 115.4, 114.0, 111.4, 55.3, 43.9, 32.7, 26.7, 24.3. GCMS (EI) calculated for $C_{25}H_{25}NO_2$ $[M]^+$ 371.2, found 371.2. FTIR (neat, cm^{-1}): 3061(m), 3005(m), 3030(m), 2931(s), 2835(m), 2618(w), 1622(m), 1514(s), 1373(s), 1271(s), 1175(s), 1123(s), 1036(s), 968(s), 838(m), 737(s).



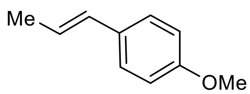
***tert*-butyl (*E*)-4-(3-(4-methoxyphenyl)allyl)piperidine-1-carboxylate (2.17**), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 38:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (55 mg, 56% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.32 (d, *J* = 15.7 Hz, 1H), 6.04 (dt, *J* = 15.7, 7.3 Hz, 1H), 4.08 (m, 2H), 3.80 (s, 3H), 2.68 (m, 2H), 2.15-2.12 (m, 2H), 1.71 – 1.69 (m, 2H), 1.57 – 1.51 (m, 1H), 1.45 (s, 9H), 1.18 – 1.13 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 155.0, 130.9, 130.5, 127.1, 126.3, 114.0, 79.3, 55.4, 40.1, 36.7, 32.1, 28.6. GCMS (EI) calculated for $C_{20}H_{29}NO_3$ $[M]^+$ 331.2, found 331.2. FTIR (neat, cm^{-1}): 3010(s), 2974(s), 2928(s), 2848(s), 2365(w), 2333(w), 1692(s), 1682(s), 1601(s), 1505(s), 1451(s), 1419(s), 1359(s), 1247(s), 1166(s), 962(s), 811(m), 763(m).



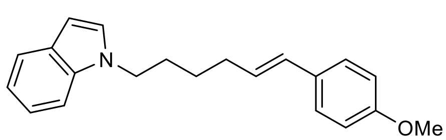
(*E*)-1-(3-cyclopropylprop-1-en-1-yl)-4-methoxybenzene (2.18), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 81:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a clear, colorless liquid (49 mg, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.8, 6.6 Hz, 1H), 3.81 (s, 3H), 2.11 (app. t, *J* = 6.6 Hz, 2H), 0.86 – 0.80 (m, 1H), 0.50 – 0.47 (m, 2H), 0.15 – 0.12 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 130.8, 129.2, 127.9, 127.1, 113.9, 55.3, 37.7, 10.5, 4.3. GCMS (EI) calculated for $C_{13}H_{16}O$ $[M]^+$ 188.1, found 188.1. FTIR (neat, cm^{-1}): 3075(s), 3000(s), 2909(s), 2834(s), 1668(w), 1511(s), 1246(s), 965(s), 838(s).



(*E*)-1-methoxy-4-(3-phenylprop-1-en-1-yl)benzene (2.19), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 185:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (34 mg, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 12.2, 8.6 Hz, 4H), 7.26 – 7.21 (m, 3H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.23 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.79 (s, 3H), 3.53 (d, *J* = 6.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 140.5, 130.5, 130.4, 128.7, 128.5, 127.3, 127.1, 126.2, 114.0, 55.3, 39.4. GCMS (EI) calculated for $C_{16}H_{16}O$ $[M]^+$ 224.1, found 224.1. FTIR (neat, cm^{-1}): 3085(m), 3059(m), 3026(s), 2999(s), 2951(s), 2923(s), 2903(s), 2833(s), 1666(w), 1650(w), 1607(s), 1575(m), 1505(s), 1450 (s), 1290(s), 1247(s), 1037(s), 962(s), 832(s).

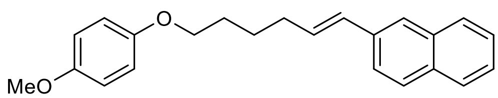


(*E*)-1-methoxy-4-(prop-1-en-1-yl)benzene (2.20), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 27:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a clear, colorless liquid (32 mg, 72% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.37 (d, J = 15.8 Hz, 1H), 6.17 – 6.06 (m, 1H), 3.82 (s, 3H), 1.88 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 130.8, 130.4, 126.9, 123.5, 113.9, 55.3, 18.5. GCMS (EI) calculated for $C_{10}H_{12}O$ $[M]^+$ 148.1, found 148.1. FTIR (neat, cm^{-1}): 3022(m), 2957(m), 2913(m), 2835(m), 2730(w), 1751(w), 1608(s), 1519(s), 1283(s), 1247(s), 1036(s), 839(s), 787(s).

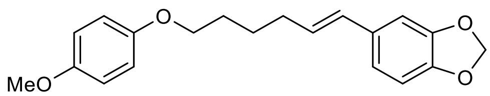


(*E*)-1-(6-(4-methoxyphenyl)hex-5-en-1-yl)-1H-indole (2.21), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 24:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a clear, colorless liquid (89 mg, 97% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.28 – 7.22 (m, 3H), 7.20 – 7.17 (m, 1H), 7.12 – 7.08 (m, 2H), 6.85 – 6.81 (m, 2H), 6.49 (dd,

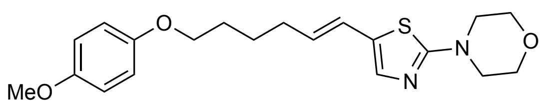
J = 3.1, 0.9 Hz, 1H), 6.30 (d, J = 15.8 Hz, 1H), 6.01 (dt, J = 15.8, 7.0 Hz, 1H), 4.15 (t, J = 7.1 Hz, 2H), 3.80 (s, 3H), 2.23 – 2.19 (m, 2H), 1.93 – 1.89 (m, 2H), 1.51 – 1.47 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 136.1, 130.6, 129.9, 128.7, 128.5, 128.0, 127.9, 127.2, 121.5, 121.1, 119.3, 114.1, 109.5, 101.1, 55.4, 46.4, 32.7, 29.9, 26.9. GCMS (EI) calculated for $C_{21}H_{23}NO$ $[M]^+$ 305.2, found 305.2. FTIR (neat, cm^{-1}): 3028(m), 2923(s), 2835(s), 1653(w), 1608(s), 1519(s), 1246(s), 967(s), 843(m).



(*E*)-2-(6-(4-methoxyphenoxy)hex-1-en-1-yl)naphthalene (2.22), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 15:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (78 mg, 79% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.75 (m, 3H), 7.67 (s, 1H), 7.58 (dd, J = 8.5, 1.8 Hz, 1H), 7.46 – 7.40 (m, 2H), 6.86 – 6.79 (m, 4H), 6.57 (d, J = 15.7 Hz, 1H), 6.37 (dt, J = 15.7, 6.9 Hz, 1H), 3.96 (t, J = 6.4 Hz, 2H), 3.77 (s, 3H), 2.40 – 2.29 (m, 2H), 1.89 – 1.83 (m, 2H), 1.73 – 1.67 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 135.3, 133.8, 132.7, 131.1, 130.4, 128.1, 127.9, 127.7, 126.2, 125.5, 125.4, 123.6, 115.5, 114.7, 68.4, 55.8, 32.9, 29.0, 25.9. GCMS (EI) calculated for $C_{23}H_{24}O_2$ $[M]^+$ 332.2, found 332.2. FTIR (neat, cm^{-1}): 3047(w), 2928(m), 1625(w), 1505(s), 1293(m), 1226(s), 946(s), 776(s).

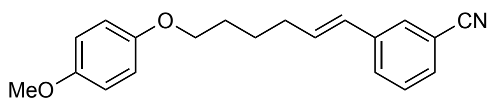


(*E*)-5-(6-(4-methoxyphenoxy)hex-1-en-1-yl)benzo[d][1,3]dioxole (2.23), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 46:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (79 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, *J* = 1.6 Hz, 1H), 6.83 (s, 4H), 6.77 – 6.72 (m, 2H), 6.31 (d, *J* = 15.7 Hz, 1H), 6.06 (dt, *J* = 15.7, 6.9 Hz, 1H), 5.93 (s, 2H), 3.93 (t, *J* = 6.4 Hz, 2H), 3.77 (s, 3H), 2.27 – 2.23 (m, 2H), 1.84 – 1.78 (m, 2H), 1.66 – 1.60 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 148.0, 146.7, 132.4, 129.8, 128.8, 120.3, 115.5, 114.7, 108.3, 105.4, 101.0, 68.4, 55.7, 32.7, 29.0, 25.9. GCMS (EI) calculated for $C_{20}H_{22}O_4$ $[M]^+$ 326.2, found 326.2. FTIR (neat, cm^{-1}): 3042(w), 2994(w), 2930(s), 2865(m), 1671(w), 1601(w), 1505(s), 1445(s), 1290(m), 1225(s), 1031(s), 967(s), 865(m), 822(s).

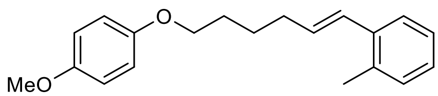


4-{5-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]-1,3-thiazol-2-yl}morpholine (2.24), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 14:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-50% EtOAc in a 60:40 mixture of benzene:hexanes, and isolated as a clear colorless liquid (83 mg, 74% yield, E:Z = 14:1). ^{1}H NMR (500 MHz, $CDCl_3$) *major isomer:* δ 6.96 (s, 1H), 6.82 (s, 4H), 6.37 (d, *J* = 15.5 Hz, 1H), 5.68 (dt, *J* = 15.5, 6.9 Hz, 1H), 3.91 (t, *J* = 6.4 Hz, 2H), 3.80 – 3.78 (m, 4H), 3.76 (s, 3H), 3.46 – 3.44 (m, 4H), 2.23 – 2.19 (m, 2H), 1.79 (p, *J* = 7.5 Hz, 2H), 1.60 (p, *J* = 7.5 Hz, 2H). *minor isomer:* δ 7.09

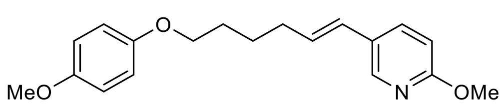
(s, 1H), 5.41 (dt, $J = 11.4$, 6.9 Hz, 1H), 2.39 – 2.35 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 153.8, 153.3, 137.0, 129.3, 127.5, 121.1, 115.5, 114.7, 68.5, 66.2, 55.8, 48.5, 32.7, 29.0, 25.9. GCMS (EI) calculated for $C_{20}H_{26}N_2O_3S$ $[M]^+$ 374.1, found 374.1. FTIR (neat, cm^{-1}): 2976 (w), 2935 (m), 2870 (m), 2857 (m), 2833 (w), 1506 (s), 1463 (m), 1442 (m), 1380 (w), 1275 (w), 1227 (s), 1110 (s), 1034 (s), 904 (m), 825 (m), 738 (w).



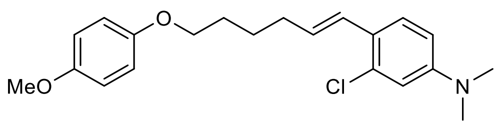
3-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]benzonitrile (2.25), was prepared according to procedure B. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 20:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-25% ether in hexanes, and isolated as an off white solid (36 mg, 38% yield). ^{1}H NMR (500 MHz, $CDCl_3$) *major isomer:* δ 7.60 (t, $J = 1.8$ Hz, 1H), 7.53 (dt, $J =$ 7.8, 1.6 Hz, 1H), 7.47 (dt, $J = 7.7$, 1.4 Hz, 1H), 7.38 (t, $J = 7.8$ Hz, 1H), 6.83 (s, 3H), 6.38 (d, $J =$ 15.9 Hz, 1H), 6.31 (dt, $J = 15.8$, 6.6 Hz, 1H), 3.95 (t, $J = 6.3$ Hz, 1H), 3.77 (s, 2H), 2.31 (dt, $J =$ 7.3, 6.6 Hz, 2H), 1.89 – 1.75 (m, 2H), 1.72 – 1.60 (m, 2H). *minor isomer:* δ 5.81 (dt, $J = 11.7$, 6.6 Hz, 1H), 3.90 (t, $J = 6.3$ Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 153.3, 139.1, 133.7, 130.3, 130.2, 129.5, 129.4, 128.3, 119.0, 115.5, 114.8, 112.8, 68.4, 55.9, 32.8, 29.0, 25.7. GCMS (EI) calculated for $C_{20}H_{21}NO_2$ $[M]^+$ 307.2, found 307.2. FTIR (neat, cm^{-1}): 3000 (w), 2939 (m), 2864 (m), 2832 (w), 2231 (m), 1592 (w), 1510 (s), 1472 (m), 1392 (w), 1249 (m), 1231 (s), 1108 (m), 1043 (m), 975 (m), 827 (m), 791 (m), 746 (m), 682 (w).



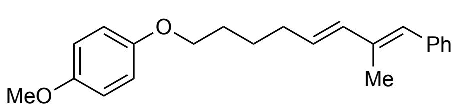
(*E*)-1-(6-(4-methoxyphenoxy)hex-1-en-1-yl)-2-methylbenzene (2.26), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 38:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (68 mg, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 6.9 Hz, 1H), 7.17 – 7.10 (m, 2H), 6.86 – 6.81 (m, 4H), 6.60 (d, *J* = 15.7, 1H), 6.10 (dt, *J* = 15.7, 6.9 Hz, 1H), 3.95 (t, *J* = 6.4 Hz, 2H), 3.77 (s, 3H), 2.33 (s, 3H), 2.32 – 2.29 (m, 2H), 1.87 – 1.81 (m, 2H), 1.67 (tt, *J* = 10.1, 6.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 137.0, 134.9, 131.9, 130.2, 128.1, 126.9, 126.0, 125.5, 115.5, 114.7, 68.5, 55.8, 33.0, 29.0, 26.0, 19.9. GCMS (EI) calculated for $C_{20}H_{24}O_2$ $[M]^+$ 296.2, found 296.2. FTIR (neat, cm^{-1}): 3018(m), 2933(s), 2861(s), 1666(w), 1505(s), 1240(s), 967(s), 823(s), 749(s).



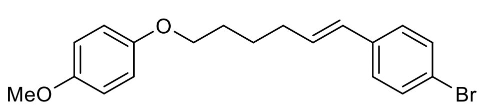
(*E*)-2-methoxy-5-(6-(4-methoxyphenoxy)hex-1-en-1-yl)pyridine (2.27), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 22:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40% CH_2Cl_2 and 5% ethyl acetate in hexanes, and isolated as a clear, colorless liquid (71 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 2.4 Hz, 1H), 7.61 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.85 – 6.80 (m, 4H), 6.68 (d, *J* = 8.6 Hz, 1H), 6.32 (d, *J* = 15.9 Hz, 1H), 6.11 (dt, *J* = 15.9, 6.8 Hz, 1H), 3.94 – 3.92 (app. m, 5H), 3.76 (s, 3H), 2.29 – 2.25 (m, 2H), 1.84 – 1.79 (m, 2H), 1.67 – 1.61 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.2, 153.7, 153.2, 144.9, 135.3, 129.9, 126.9, 126.3, 115.4, 114.6, 110.8, 68.3, 55.7, 53.4, 32.8, 28.9, 25.8. GCMS (EI) calculated for $C_{19}H_{23}NO_3$ $[M]^+$ 313.2, found 313.2. FTIR (neat, cm^{-1}): 3052(m), 2917(s), 1655(w), 1602(s), 1571(s), 1386(s), 1287(s), 1131(m), 951(m), 823(m), 747(m).



(*E*)-3-chloro-4-(6-(4-methoxyphenoxy)hex-1-en-1-yl)-*N*,*N*-dimethylaniline (2.28), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 69:1). The compound was purified according to workup procedure 1, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (51 mg, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.8 Hz, 1H), 6.88 – 6.80 (m, 4H), 6.70 (d, *J* = 15.7 Hz, 1H), 6.66 (d, *J* = 2.7 Hz, 1H), 6.59 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.03 (dt, *J* = 15.7, 7.0 Hz, 1H), 3.95 (t, *J* = 6.5 Hz, 2H), 3.77 (s, 3H), 2.94 (s, 7H), 2.32 – 2.28 (m, 2H), 1.86 – 1.81 (m, 2H), 1.69 – 1.62 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 150.2, 133.4, 129.1, 126.9, 126.2, 123.8, 115.5, 114.7, 112.6, 111.4, 68.5, 55.8, 40.4, 32.9, 28.9, 26.0. GCMS (EI) calculated for $C_{21}H_{26}ClNO_2$ $[M]^+$ 359.2, found 359.2. FTIR (neat, cm^{-1}): 3037(m), 2994(m), 2935(s), 1677(w), 1607(s), 1505(s), 1451(s), 1354(s), 1279(s), 1230(s), 1304(s), 962(s), 816(s), 746(m).

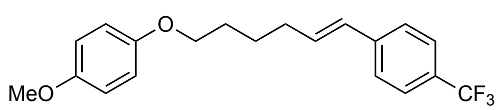


1-methoxy-4-{[(5*E*,7*E*)-7-methyl-8-phenylocta-5,7-dien-1-yl]oxy}benzene (2.29), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (5*E*,7*E*:5*Z*,7*E*:5*E*,7*Z* = 31:2:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-40% CH_2Cl_2 in hexanes, and isolated as a clear colorless liquid (58 mg, 60% yield). Significant isomerization was observed upon purification. The major isomer was assigned as (*E*,*E*) via NOSEY. ^{1}H NMR (500 MHz, $CDCl_3$) *major isomer:* δ 7.35 (t, *J* = 7.2 Hz, 2H), 7.30 (d, *J* = 7.2 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 6.85 (s, 4H), 6.45 (s, 1H), 6.28 (d, *J* = 15.6 Hz, 1H), 5.81 (dt, *J* = 15.6, 7.0 Hz, 1H), 3.95 (t, *J* = 7.6 Hz, 2H), 3.78 (s, 3H), 2.26 (dt, *J* = 7.6, 7.0 Hz, 2H), 2.00 (s, 3H), 1.83 (p, *J* = 7.6 Hz, 2H), 1.64 (p, *J* = 7.6 Hz, 2H). *minor isomer:* δ 6.83 (s, 4H), 6.44 (s, 1H), 6.02 (d, *J* = 11.6 Hz, 1H), 5.48 (dt, *J* = 11.6, 7.3 Hz, 1H), 3.92 (t, *J* = 7.6 Hz, 2H), 2.44 (dt, *J* = 7.6, 7.3 Hz, 1H), 2.04 (s, 2H). *minor isomer:* δ 6.84 (s, 4H), 6.63 (d, *J* = 15.6 Hz, 1H), 6.38 (s, 1H), 5.88 (dt, *J* = 15.6, 7.5 Hz, 1H), 2.21 (dt, *J* = 7.5, 7.0, 2H). ^{13}C NMR *major isomer:* δ 153.9, 153.4, 138.2, 135.9, 135.8, 129.9, 129.6, 129.3, 128.2, 126.4, 115.6, 114.8, 68.6, 55.9, 32.8, 29.1, 26.2, 14.1. *minor isomer*: δ 135.4, 134.8, 133.8, 132.5, 131.2, 129.7, 129.4, 129.2, 128.9, 128.6, 128.2, 128.2, 127.8, 127.0, 126.5, 126.1, 68.5, 33.00, 29.1, 29.0, 28.7, 26.8, 26.1, 21.4, 18.8. GCMS (EI) calculated for $C_{22}H_{26}O_2$ $[M]^+$ 322.2, found 322.2. FTIR (neat, cm^{-1}): 2981 (w), 2950 (w), 2926 (m), 2872 (w), 1509 (s), 1441 (m), 1389 (w), 1292 (m), 1236 (s), 1114 (w), 1033 (s), 957 (m), 825 (s), 746 (m).



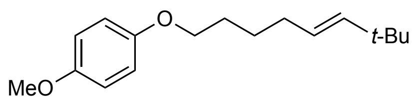
(*E*)-1-bromo-4-(6-(4-methoxyphenoxy)hex-1-en-1-yl)benzene (2.30), was prepared according to procedure A. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 15:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 40-60% CH_2Cl_2 in hexanes, and isolated as a white solid (81 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.85

– 6.80 (m, 4H), 6.34 (d, J = 15.8 Hz, 1H), 6.22 (dt, J = 15.8, 6.8 Hz, 1H), 3.94 (t, J = 6.4 Hz, 2H), 3.77 (s, 3H), 2.31 – 2.25 (m, 2H), 1.85 – 1.78 (m, 2H), 1.68 – 1.62 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.2, 136.7, 131.6, 131.5, 129.1, 127.5, 120.5, 115.4, 114.7, 68.3, 55.8, 32.7, 28.9, 25.7. GCMS (EI) calculated for $C_{19}H_{21}BrO_2$ $[M]^+$ 360.1, found 360.1. FTIR (neat, cm^{-1}): 3054(w), 2934(s), 2864(m), 1652(w), 1506(s), 1231(s), 1039(s), 973(s), 824(s), 703(m).

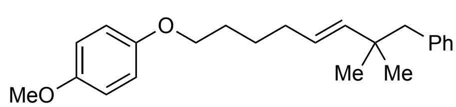


1-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]-4-(trifluoromethyl)benzene (2.31), was prepared according to procedure B. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 26:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-10% ether in hexanes, and isolated as a white solid (51 mg, 49% yield). ^{1}H NMR (500 MHz, $CDCl_3$) *major isomer:* δ 7.54 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 6.84 (s, 4H), 6.44 (d, J = 15.9 Hz, 1H), 6.34 (dt, J = 15.9, 7.1 Hz, 1H), 3.95 (t, J = 7.2 Hz, 2H), 3.77 (s, 3H), 2.32 (dt, J = 7.2, 7.1 Hz, 2H), 1.83 (p, J = 7.2 Hz, 2H), 1.68 (p, J = 7.2 Hz, 2H). *minor isomer:* δ 7.36 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 5.80 (dt, J = 11.7, 7.2 Hz, 1H), 3.90 (t, J = 7.1, 2H), 2.38 (dt, J = 7.2, 7.1 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 153.3, 141.4, 133.5, 129.2, 128.76 (q, J = 13.5 Hz), 126.3 (q, J = 216 Hz), 126.2, 125.6 (q, J = 3.8 Hz), 115.6, 114.8, 68.4, 55.9, 32.9, 29.1, 25.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ -65.4. GCMS (EI) calculated for $C_{20}H_{21}F_3O_2$ $[M]^+$ 350.1, found 350.1. FTIR (neat, cm^{-1}): 2941 (m), 2928 (w), 2867 (w), 2835 (w), 1613 (w), 1507 (s), 1414 (w), 1323 (s), 1231 (s), 1151 (m), 1113 (s), 1065 (m), 1015 (m), 973 (m), 828 (m), 746 (m).

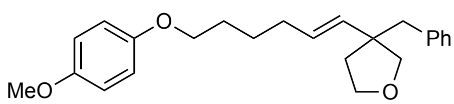
2.4.5.2 Tertiary Aliphatic Alkene Products



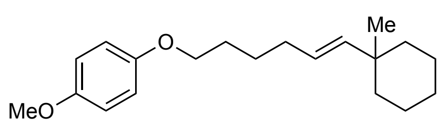
1-{[(5*E*)-7,7-dimethyloct-5-en-1-yl]oxy}-4-methoxybenzene (2.32), was prepared according to procedure C. The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-30% CH_2Cl_2 in hexanes, and isolated as a clear colorless liquid (102 mg, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 3H), 5.47 (d, *J* = 15.6 Hz, 1H), 5.31 (dt, *J* = 15.6, 6.5 Hz, 1H), 3.91 (t, *J* = 6.7 Hz, 2H), 3.77 (s, 2H), 2.08 – 2.01 (m, 2H), 1.75 (p, *J* = 6.6 Hz, 2H), 1.51 (p, *J* = 6.6 Hz, 2H), 0.99 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 153.5, 142.1, 124.4, 115.6, 114.8, 68.6, 55.8, 32.8, 32.5, 29.9, 29.0, 26.3. GCMS (EI) calculated for $C_{17}H_{26}O_2$ $[M]^+$ 262.2, found 262.2. FTIR (neat, cm^{-1}): 2952 (m), 2925 (m), 2864 (w), 2835 (w), 1507 (s), 1469(w), 1228 (s), 1107 (w), 1041 (s), 972 (m), 823 (m), 742 (w).



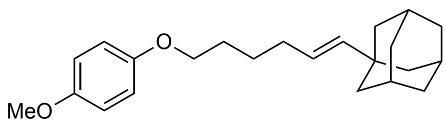
1-{[(5*E*)-7-benzyl-7-methyloct-5-en-1-yl]oxy}-4-methoxybenzene (2.33), was prepared according to procedure C. The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-5% ether in a 20:80 mixture of CH_2Cl_2:hexanes, and isolated as a clear colorless liquid (131 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.3 Hz, 2H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.10 (d, *J* = 7.3 Hz, 2H), 6.84 (s, 4H), 5.47 (d, *J* = 15.6, 1H), 5.22 (dt, *J* = 15.6, 6.7 Hz, 1H), 3.90 (t, *J* = 6.5 Hz, 2H), 3.77 (s, 3H), 2.56 (s, 2H), 2.09 – 2.04 (m, 2H), 1.73 (p, *J* = 6.7 Hz, 2H), 1.50 (p, *J* = 6.7 Hz, 2H), 0.98 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.86, 153.5, 140.4, 139.2, 127.6, 126.0, 125.9, 115.6, 114.8, 68.6, 55.8, 49.7, 36.9, 32.5, 29.0, 27.3, 26.2. GCMS (EI) calculated for $C_{23}H_{30}O_2$ $[M]^+$ 338.2, found 338.2. FTIR (neat, cm^{-1}): 2954 (m), 2938 (m), 2865 (m), 2834 (m), 1506 (s), 1468 (w), 1229 (s), 1180 (w), 1040 (s), 973 (m), 823 (m), 731 (m), 701 (m).



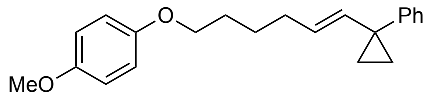
3-benzyl-3-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]oxolane (2.34), was prepared according to procedure C *(0.3 mmol scale)*. The compound was purified according to workup procedure 1, further by silica gel column chromatography, 0-30% CH_2Cl_2 in hexanes, and isolated as a clear colorless oil (84 mg, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.4 Hz, 2H), 6.83 (s, 4H), 5.48 (d, *J* = 15.7 Hz, 1H), 5.30 (dt, *J* = 15.7, 6.7 Hz, 1H), 3.97 – 3.92 (m, 1H), 3.90 – 3.83 (m, 3H), 3.77 (s, 3H), 3.68 (d, *J* = 8.2 Hz, 1H), 3.62 (d, *J* = 8.2 Hz, 1H), 2.78 (s, 2H), 2.08 (dt, *J* = 6.7, 7.2 Hz, 2H), 1.92 – 1.85 (m, 2H), 1.71 (p, *J* = 7.2 Hz, 2H), 1.50 (p, *J* = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 138.6, 134.0, 130.4, 129.3, 127.9, 126.2, 115.5, 114.7, 76.5, 68.5, 67.3, 55.8, 49.3, 44.1, 36.5, 32.5, 28.9, 25.9. GCMS (EI) calculated for $C_{24}H_{30}O_3$ $[M]^+$ 366.2, found 366.2. FTIR (neat, cm^{-1}): 2932 (m), 2859 (m), 2841 (w), 1508 (s), 1454 (w), 1229 (s), 1068 (w), 1040 (m), 972 (w), 906 (w), 824 (m), 731 (m), 702 (m), 522 (w).



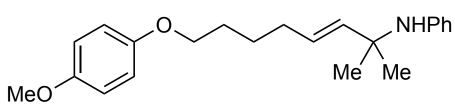
1-methoxy-4-{[(5*E*)-6-(1-methylcyclohexyl)hex-5-en-1-yl]oxy}benzene (2.35), was prepared according to procedure C. The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-30% CH_2Cl_2 in hexanes, and isolated as a clear colorless liquid (106 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 4H), 5.40 (d, *J* = 15.8 Hz, 1H), 5.33 (dt, J = 15.8, 6.3 Hz, 1H), 3.91 (t, J = 6.6 Hz, 2H), 3.77 (s, 3H), 2.09 – 2.05 (m, 2H), 1.77 (p, J = 6.6 Hz, 2H), 1.53 (p, J = 6.6 Hz, 2H), 1.47 – 1.42 (m, 6H), 1.41 – 1.33 (m, 2H), 1.28 – 1.21 (m, 2H), 0.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 153.5, 141.2, 125.9, 115.6, 114.8, 68.7, 55.8, 38.3, 35.7, 32.7, 29.0, 26.6, 26.3, 22.6. GCMS (EI) calculated for $C_{20}H_{30}O_2$ $[M]^+$ 302.1, found 302.1. FTIR (neat, cm^{-1}): 2925 (m), 2852 (w), 1508 (s), 1497 (w), 1445 (w), 1229 (s), 1180 (w), 1041 (m), 972 (w), 822 (m).



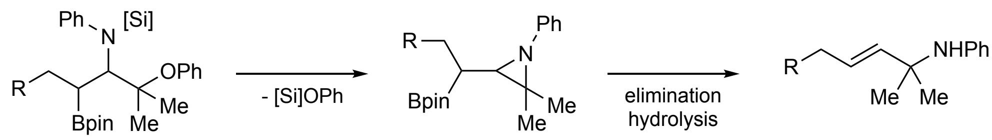
2-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]adamantane (2.36), was prepared according to procedure C. The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-30% CH_2Cl_2 in hexanes, and isolated as a clear colorless liquid (128 mg, 75% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 4H), 5.35 – 5.20 (m, 2H), 3.91 (t, J = 6.5 Hz, 2H), 3.77 (s, 3H), 2.08 – 1.96 (m, 5H), 1.78 – 1.49 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 153.4, 142.6, 124.4, 115.6, 114.7, 68.7, 55.8, 42.7, 37.1, 34.7, 32.6, 28.9, 28.7, 26.3. GCMS (EI) calculated for $C_{23}H_{32}O_2$ $[M]^+$ 340.2, found 340.2. FTIR (neat, cm^{-1}): 2930 (w), 2901 (m), 2846 (m), 1506 (s), 1452 (w), 1228 (s), 1106 (w), 1040 (m), 970 (m), 823 (m), 735 (w).



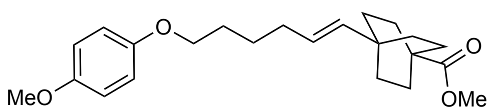
{1-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]cyclopropyl}benzene (2.37), was prepared according to procedure C. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (E:Z = 8:1). The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-20% CH_2Cl_2 in hexanes, 0-10% ether in hexanes (second column to remove residual aldehyde) and isolated as a waxy white solid (82 mg, 51% yield, E:Z = 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) *major isomer:* δ 7.30 – 7.26 (m, 4H), 7.24 – 7.14 (m, 1H), 6.82 (s, 4H), 5.42 (d, J = 15.3 Hz, 1H), 5.07 (dt, J = 15.3, 6.7 Hz, 1H), 3.88 (t, J = 6.5 Hz, 2H), 3.77 (s, 3H), 2.06 – 2.01 (m, 2H), 1.72 (p, J = 6.7 Hz, 2H), 1.47 (p, J = 6.7 Hz, 2H), 1.04 – 1.02 (m, 2H), 0.94 – 0.92 (m, 2H). *minor isomer:* δ 5.70 (d, J = 10.9 Hz, 1H), 5.52 (dt, J = 10.9, 6.7 Hz, 1H), 3.82 (t, J = 6.5 Hz, 2H), 2.11 – 2.08 (m, 2H), 1.12 – 1.10 (m, 2H), 1.01 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 137.3, 129.5, 128.4, 128.2, 126.2, 115.5, 114.7, 68.5, 55.8, 32.2, 29.0, 27.7, 26.0, 14.8. GCMS (EI) calculated for $C_{22}H_{26}O_2$ $[M]^+$ 322.2, found 322.2. FTIR (neat, cm^{-1}): 3074 (w), 2999 (w), 2935 (m), 2865 (m), 2832 (w), 1508 (s), 1464 (m), 1395 (w), 1229 (s), 1177 (m), 1022 (s), 979 (m), 943 (m), 825 (s), 745 (m).



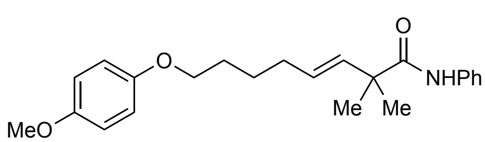
***N*-[(3*E*)-8-(4-methoxyphenoxy)-2-methyloct-3-en-2-yl]aniline (2.38)**, was prepared according to procedure C. The compound was purified according to workup procedure 1, further by silica gel column chromatography, 0-30% ether in hexanes, and isolated as a clear colorless oil (113 mg, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, J = 7.8 Hz, 2H), 6.86 (s, 4H), 6.73 – 6.69 (m, 3H), 5.67 – 5.58 (m, 2H), 3.93 (t, J = 7.1i Hz, 2H), 3.79 (s, 3H), 3.70 (s, br, 1H), 2.15 (dt, J = 7.5, 7.1 Hz, 2H), 1.79 (p, J = 7.1 Hz, 2H), 1.59 (p, J = 7.1 Hz, 2H), 1.40 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.4, 146.9, 138.3, 128.8, 128.3, 117.4, 115.9, 115.6, 114.8, 68.6, 55.9, 54.2, 32.2, 29.0, 26.0. GCMS (EI) calculated for $C_{22}H_{29}NO_2$ $[M]^+$ 339.2, found 339.2. FTIR (neat, cm^{-1}): 3441 (br), 2939 (m), 2868 (w), 2833 (w), 1600 (m), 1505 (s), 1317 (w), 1228 (s), 1038 (s), 974 (w), 823 (m), 746 (m).



*Proposed mechanistic rationale for the observed rearranged aliphatic alkene **2.38**.*

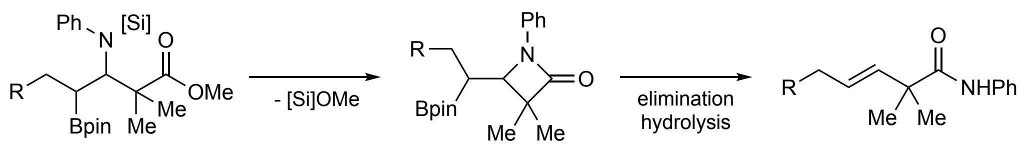


Methyl 4-[(1*E*)-6-(4-methoxyphenoxy)hex-1-en-1-yl]bicyclo[2.2.2]octane-1-carboxylate (2.39), was prepared according to procedure C. The compound was purified according to workup procedure 3, further by silica gel column chromatography, 0-20% ether in a 10:90 mixture of CH_2Cl_2:hexanes, and isolated as a white solid (150 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (s, 4H), 5.33 (d, *J* = 15.8 Hz, 1H), 5.25 (dt, *J* = 15.8, 6.5 Hz, 1H), 3.89 (t, *J* = 6.6 Hz, 2H), 3.76 (s, 3H), 3.64 (s, 3H), 2.05 – 2.01 (m, 2H), 1.80 – 1.77 (m, 6H), 1.73 (p, *J* = 6.5 Hz, 2H), 1.52 – 1.46 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.5, 153.7, 153.3, 139.5, 125.8, 115.5, 114.6, 68.5, 55.7, 51.6, 39.1, 32.7, 32.5, 31.0, 28.8, 28.5, 26.1. GCMS (EI) calculated for $C_{23}H_{32}O_4$ $[M]^+$ 372.2, found 372.2. FTIR (neat, cm^{-1}): 2944 (m), 2864 (m), 2837 (w), 1718 (s), 1505 (s), 1496 (m), 1289 (w), 1228 (s), 1040 (s), 982 (m), 821 (m), 735 (m).



(3*E*)-8-(4-methoxyphenoxy)-2,2-dimethyl-*N*-phenyloct-3-enamide (2.40), was prepared according to procedure C. The compound was purified according to workup procedure 1, further by silica gel column chromatography, 0-30% ether in hexanes, and isolated as a white solid (102 mg, 56% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (s, br, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.29 (t,

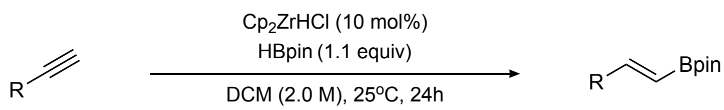
J = 7.9 Hz, 1H), 7.08 (t, J = 7.9 Hz, 2H), 6.84 (s, 4H), 5.81 – 5.72 (m, 2H), 3.95 (t, J = 6.3 Hz, 2H), 3.77 (s, 3H), 2.23 (dt, J = 7.5, 5.9 Hz, 2H), 1.82 (p, J = 7.5 Hz, 2H), 1.64 (p, J = 7.5 Hz, 2H), 1.37 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 153.9, 153.2, 138.2, 135.5, 131.4, 129.0, 124.2, 119.6, 115.5, 114.7, 68.4, 55.8, 45.7, 32.5, 29.0, 26.0, 25.4. GCMS (EI) calculated for $C_{23}H_{29}NO_3$ $[M]^+$ 367.2, found 367.2. FTIR (neat, cm^{-1}): 3349 (m), 2978 (w), 2939 (m), 2870 (m), 2840 (w), 1650 (m), 1599 (m), 1509 (s), 1437 (m), 1314 (m), 1231 (s), 1038 (m), 976 (m), 823 (m), 752 (m).



*Proposed mechanistic rationale for the observed rearranged aliphatic alkene **2.40**.*

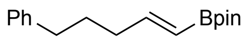
2.4.6 *Synthesis and Characterization of Alkenyl Boronate Ester Starting Materials*

2.4.6.1 Synthetic Procedure

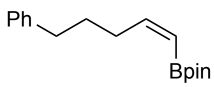


A flame dried 25 mL Schlenk flask under an atmosphere of nitrogen was charged with a stir bar, Schwartz's reagent (10 mol%), anhydrous CH_2Cl_2 (2.0 M) via syringe, and alkyne (1.0 equiv). The flask was outfitted with a septum, placed under a positive nitrogen atmosphere, and covered with aluminum foil to exclude light. To this mixture was added HBpin (1.1 equiv) slowly via syringe. The mixture was stirred at 25 °C. After 24 h the crude reaction mixture was filtered through a small plug of silica and washed 3x with 15 mL of CH_2Cl_2. The solvent was removed under vacuum via roto-evaporator and the corresponding alkenyl boronate esters were purified by silica gel column chromatography.

2.4.6.2 Characterization

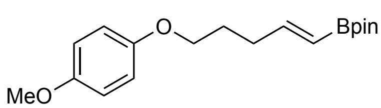


4,4,5,5-tetramethyl-2-[(1*E*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (2.6), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-10% ether in hexanes, and was isolated as a clear colorless liquid (1.1 g, 93% yield). This compound has been previously characterized and the resulting spectra matched those reported.[129]

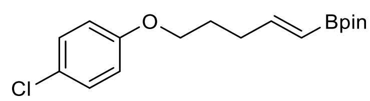


4,4,5,5-tetramethyl-2-[(1*Z*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (2.6), was prepared according to a modified procedure. A 25mL flame dried Schlenk flask under N_2 was outfitted with a stir bar and a septum. 5-phenyl-1-pentyne (796 µL, 5.25 mmol, 1.05 equiv) was added to the flask via syringe followed by anhydrous ether (10 mL, 0.5 M). The alkyne solution was cooled to -78 °C with a dry ice acetone bath and *n*-BuLi (3.1 mL, 5.25 mmol, 1.05 equiv, 1.7 M) was added dropwise at this temperature. The reaction mixture was allowed to stir at -78 °C for 1 hour after which a solution of 4,4,5,5-tetramethyl-2-(1-methylethoxy)-1,3,2-dioxaborolane (1.10 mL, 5.0 mmol, 1.0 equiv) in ether (5 mL) was added at -78 °C. The resulting mixture was stirred at -78 °C for 2 hours and then quenched with a solution of HCl in ether (7.5 mL, 7.5 mmol, 1.5 equiv, 1.0 M). The mixture was warmed to room temperature and filtered through a pad of celite, washed with ether (2x 25 mL), and the volatiles were removed under vacuum to afford a yellow oil (*will solidify if cooled to -40°C overnight*) which was used directly in the next step without further purification.

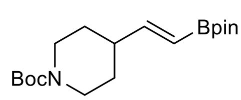
A 25mL flame dried Schlenk flask under N_2 was outfitted with a stir bar. Under a pillow of N_2 dicyclohexylborane (886 mg, 5.0 mmol, 1.0 equiv) was added to the flask followed by the addition of a septum. Anhydrous ether (10 mL, 0.5 M) was added via syringe followed by a solution of crude 4,4,5,5-tetramethyl-2-(5-phenylpent-1-ynyl)-1,3,2-dioxaborolane from the previous step in 5 mL of anhydrous ether. The heterogenous solution was allowed to stir at 25 °C for 1 hour before being cooled to 0 °C. To the now cooled heterogenous solution was added glacial acetic acid (315 μL, 5.5 mmol, 1.1 equiv) and the reaction was allowed to stir at this temperature for 15 minutes. Subsequently, ethanolamine (650 μL, 11.0 mmol, 2.2 equiv) was added via syringe and the solution was allowed to warm to room temperature with continued stirring. This solution was diluted with hexanes (30 mL) and the resulting suspension was filtered through a small plug of silica and washed with hexanes (3x 15 mL). The solvent was removed via roto-evaporation, the title compound was purified via silica gel column chromatography, 0-5 % EtOAc in hexanes, and obtained as a clear colorless oil (1.12 g, 82% yield). The title compound was analyzed by GC to obtain the isomeric ratio (*E*:*Z* = 1:172). This compound has been previously characterized and the resulting spectra matched those reported.[130]



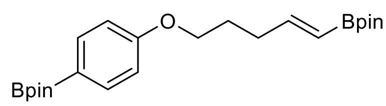
(*E*)-2-(5-(4-methoxyphenoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.8), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a white solid (3.02 g, 63% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (s, 4H), 6.66 (dt, *J* = 18.0, 6.4 Hz, 1H), 5.48 (dt, *J* = 18.0, 1.6 Hz, 1H), 3.91 (t, *J* = 6.4 Hz, 2H), 3.76 (s, 3H), 2.42 – 2.26 (m, 2H), 1.94 – 1.82 (m, 2H), 1.26 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.3, 153.2, 115.5, 114.6, 83.1, 67.9, 55.7, 32.1, 27.9, 24.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.6. GCMS (EI) calculated for $C_{18}H_{27}BO_4$ $[M]^+$ 318.2, found 318.2. FTIR (neat, cm^{-1}): 3074(w), 3040(w), 2976(s), 2931(s), 2874(m), 2839(m), 1639(s), 1590(s), 1509(m), 1370(s), 1225(s), 970(s), 828(s), 519(s).



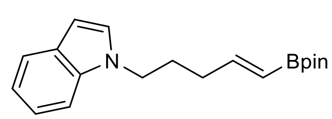
(*E*)-2-(5-(4-chlorophenoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.50), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a white solid (1.67 g, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.19 (m, 2H), 6.81 – 6.78 (m, 2H), 6.65 (dt, *J* = 18.0, 6.4 Hz, 1H), 5.48 (dt, *J* = 18.0, 1.7 Hz, 1H), 3.92 (t, *J* = 6.4 Hz, 2H), 2.35-2.30 (m, 2H), 1.94 – 1.86 (m, 2H), 1.26 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 153.0, 129.2, 125.4, 115.8, 83.1, 67.5, 32.0, 27.7, 24.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.5. GCMS (EI) calculated for $C_{17}H_{24}BClO_3$ $[M]^+$ 322.2, found 322.2. FTIR (neat, cm^{-1}): 3096(w), 3075(w), 2978(s), 2935(s), 2876(m), 1677(w), 1639(s), 1596(m), 1488(s), 1404(m), 1359(s), 1240(s), 1143(s), 904(s), 852(s), 815(s), 666(m).



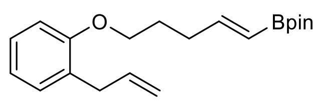
***tert*-butyl(*E*)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)piperidine-1-carboxylate (2.51)**, was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a white solid (1.77 g, 75% yield). This compound has been previously characterized and the resulting spectra matched those reported.[131]



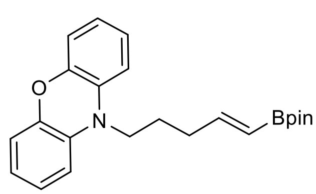
(*E*)-4,4,5,5-tetramethyl-2-(4-((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)oxy)phenyl)-1,3,2-dioxaborolane (2.52), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a white solid (1.48 g, 48% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.68 (dt, *J* = 17.9, 6.3 Hz, 1H), 5.60 – 5.42 (m, 1H), 4.03 – 3.98 (m, 2H), 2.39 – 2.32 (m, 2H), 1.99 – 1.89 (m, 2H), 1.35 (s, 12H), 1.29 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6, 153.1, 136.5, 136.5, 113.9, 83.5, 83.1, 67.0, 32.1, 27.8, 24.9, 24.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.8, 27.9. GCMS (EI) calculated for $C_{23}H_{36}B_2O_5$ $[M]^+$ 414.3, found 414.3. FTIR (neat, cm^{-1}): 3029(w), 2977(s), 2932(s), 2872(m), 1635(s), 1605(s), 1568(s), 1516(w), 1471(m), 1397(s), 1359(s), 1322(s), 1270(s), 1248(s), 1143(s), 1091(s), 957(m), 853(m), 733(w).



(*E*)-1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)-1H-indole (2.53), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a white solid (4.50 g, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.34 – 7.31 (m, 1H), 7.20 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.61 (dt, *J* = 18.0, 6.3 Hz, 1H), 6.48 (dd, *J* = 3.2, 0.9 Hz, 1H), 5.48 (dt, *J* = 17.9, 1.6 Hz, 1H), 4.13 (t, *J* = 7.0 Hz, 2H), 2.20 – 2.15 (m, 2H), 2.02 – 1.96 (m, 2H), 1.27 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.59, 135.96, 128.68, 127.85, 121.41, 121.00, 119.28, 109.42, 101.06, 83.19, 45.67, 32.80, 28.56, 24.84. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.2. GCMS (EI) calculated for $C_{19}H_{26}BNO_2$ $[M]^+$ 311.2, found 311.2. FTIR (neat, cm^{-1}): 3053(m), 2976(s), 2932(s), 2872(m), 1687(w), 1653(s), 1508(m), 1464(s), 1397(s), 1352(s), 1322(s), 1233(m), 1143(s), 972(m), 845(m), 741(s).

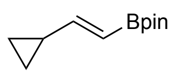


(*E*)-2-(5-(2-allylphenoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.54), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a clear, colorless liquid (0.40 g, 24% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 – 7.12 (m, 2H), 6.88 (app. t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.68 (dt, *J* = 18.0, 6.4 Hz, 1H), 5.98 (ddt, *J* = 16.7, 10.0, 6.7 Hz, 1H), 5.49 (d, *J* = 18.0 Hz, 1H), 5.11 – 4.96 (m, 2H), 3.97 (t, *J* = 6.2 Hz, 2H), 3.38 (d, *J* = 6.7 Hz, 2H), 2.39 – 2.35 (m, 2H), 1.96 – 1.90 (m, 2H), 1.27 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 153.3, 137.1, 129.8, 128.7, 127.3, 120.4, 115.4, 111.2, 83.0, 67.0, 34.6, 32.3, 28.1, 24.9. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.0. GCMS (EI) calculated for $C_{20}H_{29}BO_3$ $[M]^+$ 328.2, found 328.2. FTIR (neat, cm^{-1}): 3075(m), 2977(s), 2932(s), 2872(s), 1672(w), 1035(s), 1598(s), 1493(s), 1454(s), 1363(s), 1323(s), 1244(s), 1145(s), 996(s), 970(s), 912(m), 849(s), 751(s).

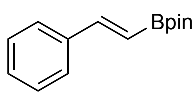


(*E*)-10-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)-10H-phenoxazine (2.55), was prepared according to the reported procedure, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a white solid (3.68 g, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (ddd, *J* = 8.0, 6.3, 2.8 Hz, 2H), 6.75 – 6.66 (m, 1H), 6.69 –

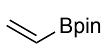
6.60 (m, 5H), 6.46 (dd, *J* = 7.7, 1.1 Hz, 2H), 5.55 (dt, *J* = 18.0, 1.6 Hz, 1H), 3.52 – 3.46 (m, 2H), 2.29 (qd, *J* = 7.3, 1.6 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.29 (s, 13H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 145.0, 133.3, 123.6, 120.8, 115.4, 111.4, 83.2, 43.5, 33.0, 24.8, 23.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.6. GCMS (EI) calculated for $C_{23}H_{28}BNO_3$ $[M]^+$ 377.2, found 377.2. FTIR (neat, cm^{-1}): 3065(m), 2976(s), 2932(s)1665(w), 1635(s), 1590(m), 1486(s), 1367(s), 1323(s), 1271(s), 1144(s), 997(m), 913(w), 849(s), 738(s).



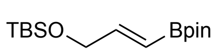
(E)-2-(2-cyclopropylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, was purchased from BLD Pharm and used without further purification.



(*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane, was purchased from TCI and used without further purification.



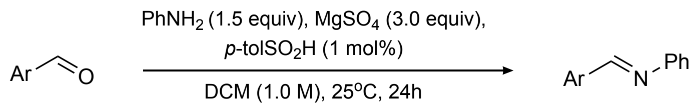
4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, was purchased from TCI and used without further purification.



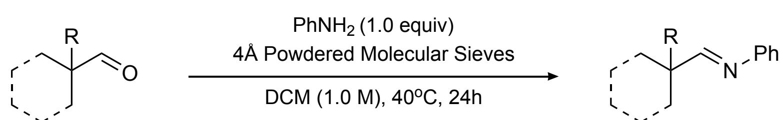
(*E*)-*tert*-butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)oxy)silane, was purchased from BLD Pharm and used without further purification.

2.4.7 *Synthesis and Characterization of Imine Starting Materials*

2.4.7.1 Synthetic Procedure

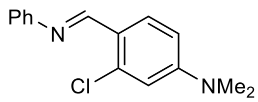


A flame dried 100 mL round bottomed flask was charged with a stir bar, $MgSO_4$ (3.0 equiv), and *p*-tolSO_3H (1 mol%), the flask was then outfitted with a septum and placed under positive nitrogen pressure. Anhydrous CH_2Cl_2 (1.0 M) was added to the flask via syringe. Freshly distilled aniline (1.5 equiv) was added via syringe followed by slow addition of the aldehyde (1.0 equiv) via syringe (for liquid aldehydes) or using a powder funnel (for solid aldehydes). The slurry was stirred overnight at 25 °C. The resulting mixture was filtered through a pad of celite and washed with CH_2Cl_2 (3x 10mL). The solvent was removed via roto-evaporation and the corresponding imines were purified by distillation or recrystallization.

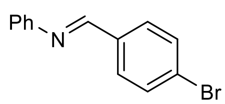


In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with a stir bar, powdered 4Å molecular sieves (1.0 g per 1.0 mmol of aldehyde), freshly distilled aniline (1.0 equiv), anhydrous CH_2Cl_2 (1.0 M), and aldehyde (1.0 equiv). The vial was outfitted with a Teflon lined screw cap. The mixture was vigorously stirred at 40 °C. After 24 h the heterogenous mixture was filtered through a pad of celite and washed 2x with 10 mL of anhydrous CH_2Cl_2. The solvent was removed via roto-evaporation and the corresponding imines were purified by distillation. The alkyl imines were stored in the freezer under an atmosphere of nitrogen.

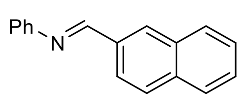
2.4.7.2 Characterization



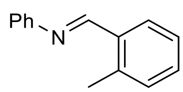
(*E*)-3-chloro-*N*,*N*-dimethyl-4-((phenylimino)methyl)aniline (2.56), was prepared according to the reported procedure, purified by recrystallization from a hot solution of 10% ethyl acetate in hexane, and was isolated as a yellow solid (0.52 g, 66% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.17 (d, J = 8.6 Hz, 1H), 7.44 – 7.32 (m, 2H), 7.26 – 7.17 (m, 3H), 6.72 – 6.61 (m, 2H), 3.05 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.1, 152.8, 152.8, 137.8, 129.4, 129.1, 125.4, 121.1, 121.0, 111.6, 110.8, 40.1. GCMS (EI) calculated for $C_{15}H_{15}ClN_2$ $[M]^+$ 258.1, found 258.1. FTIR (neat, cm^{-1}): 1672(w), 1635(m), 1575(s), 1512(m), 1448(w), 1367(m), 1277(m), 1029(m), 822(m), 756(s).



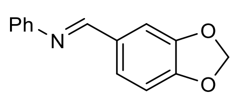
(*E*)-1-(4-bromophenyl)-*N*-phenylmethanimine (2.57), was prepared according to the reported procedure, purified by recrystallization from a hot solution of 10% ethyl acetate in hexane, and was isolated as a white solid (0.57 g, 73% yield), previously characterized and the resulting spectra matched those reported.[132]



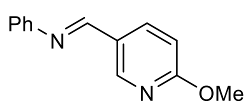
(*E*)-1-(naphthalen-2-yl)-*N*-phenylmethanimine (2.58), was prepared according to the reported procedure, purified by recrystallization from a hot solution of 10% ethyl acetate in hexane, and was isolated as a white solid (1.37 g, 82% yield), previously characterized and the resulting spectra matched those reported.[132]



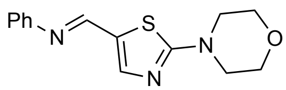
(*E*)-*N*-phenyl-1-(o-tolyl)methanimine (2.59), was prepared according to the reported procedure, purified by recrystallization from a hot solution of 10% ethyl acetate in hexane, and was isolated as a white solid (1.19 g, 84% yield), previously characterized and the resulting spectra matched those reported.[133]



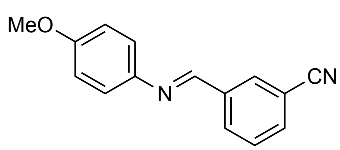
(*E*)-1-(benzo[d][1,3]dioxol-5-yl)-*N*-phenylmethanimine (2.60), was prepared according to the reported procedure, purified by recrystallization from a hot solution of 10% ethyl acetate in hexane, and was isolated as a white solid (0.49 g, 72% yield), previously characterized and the resulting spectra matched those reported.[133]



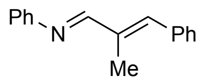
(*E*)-1-(6-methoxypyridin-3-yl)-*N*-phenylmethanimine (2.61), was prepared according to the reported procedure, purified by recrystallization from a hot solution of 10% ethyl acetate in hexane, and was isolated as a yellow solid (0.52 g, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, J = 2.3 Hz, 1H), 8.42 (s, 1H), 8.27 (dd, J = 8.7, 2.3 Hz, 1H), 7.41 – 7.38 (m, 2H), 7.25 – 7.19 (m, 3H), 6.84 (d, J = 8.7 Hz, 1H), 4.01 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.9, 152.0, 149.9, 137.1, 129.2, 126.2, 126.0, 120.9, 111.7, 53.9. GCMS (EI) calculated for $C_{13}H_{12}N_2O$ $[M]^+$ 212.1, found 212.1. FTIR (neat, cm^{-1}): 2976(m), 1653(w), 1621(s), 1501(s), 1443(s), 1390(s), 1356(s), 1322(s), 1291(s), 830(s), 751(s), 697(s).



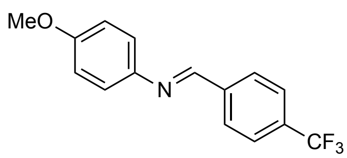
(*E*)-1-[2-(morpholin-4-yl)-1,3-thiazol-5-yl]-*N*-phenylmethanimine (2.62), was prepared according to the reported procedure, purified by recrystallization from hot EtOH, and was isolated as a yellow solid (0.96 g, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.58 (s, 1H), 7.35 (t, J = 7.8 Hz, 2H), 7.20 – 7.16 (m, 3H), 3.84 – 3.82 (m, 4H), 3.61 – 3.59 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 151.7, 151.1, 146.7, 129.2, 127.8, 125.7, 121,1, 66.1, 48.4. GCMS (EI) calculated for $C_{14}H_{15}N_3OS$ $[M]^+$ 273.1, found 273.1. FTIR (neat, cm^{-1}): 3078 (w), 2960 (m), 2865 (m), 1611 (m), 1585 (m), 1515, (s), 1441 (m), 1280 (s), 1194 (m), 1118 (s), 901 (m), 753 (m).



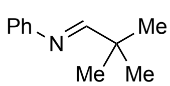
3-[(*E*)-[(4-methoxyphenyl)imino]methyl]benzonitrile (2.63), was prepared according to the reported procedure using *p*-anisidine instead of aniline, purified by recrystallization from a hot mixture of 10% EtOAc in hexanes, and was isolated as yellow needles (1.36 g, 91% yield). This compound has been previously characterized and the resulting spectra matched those reported.[134]



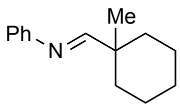
(1*E*,2*E*)-2-methyl-*N*,3-diphenylprop-2-en-1-imine (2.64), was prepared according to the reported procedure, purified by recrystallization from a hot mixture of 5% EtOAc in hexanes, and was isolated as a yellow solid (0.69 g, 78% yield). This compound has been previously characterized and the resulting spectra matched those reported.[135]



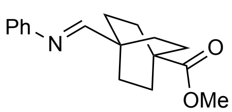
(*E*)-*N*-(4-methoxyphenyl)-1-[4-(trifluoromethyl)phenyl]methanimine (2.65), was prepared according to the reported procedure using *p*-anisidine instead of aniline, purified by recrystallization from a hot mixture of 5% EtOAc in hexanes, and was isolated as an off white solid (1.07 g, 96% yield). This compound has been previously characterized and the resulting spectra matched those reported.[134]



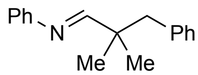
(1*E*)-2,2-dimethyl-*N*-phenylpropan-1-imine (2.66), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a clear colorless liquid (0.93 mg, 88% yield). This compound has been previously characterized and the obtained spectra matched those from the literature.[136]



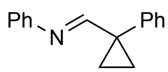
(*E*)-1-(1-methylcyclohexyl)-*N*-phenylmethanimine (2.67), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a clear colorless liquid (0.74 g, 67% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.00 (d, *J* = 7.7 Hz, 2H), 1.89 – 1.83 (m, 3H), 1.59 – 1.48 (m, 5H), 1.44 – 1.35 (m, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 153.0, 129.0, 125.2, 120.6, 40.1, 35.6, 35.5, 26.1, 22.6. GCMS (EI) calculated for $C_{14}H_{19}N$ $[M]^+$ 201.1, found 201.1. FTIR (neat, cm^{-1}): 3032 (w), 2926 (m), 2851 (m), 1698 (w), 1645 (m), 1594 (m), 1211 (w), 1073 (w), 764 (m), 740(w).



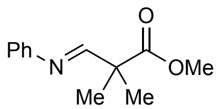
Methyl 4-[(*E*)-(phenylimino)methyl]bicyclo[2.2.2]octane-1-carboxylate (2.68), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a clear colorless liquid (0.68 g, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.16 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 2H), 3.67 (s, 3H), 1.88 (dd, *J* = 10.2, 5.5 Hz, 6H), 1.77 (dd, *J* = 10.2, 5.5 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.1, 171.3, 152.6, 129.1, 125.4, 120.6, 51.8, 39.6, 37.4, 28.3, 28.0. GCMS (EI) calculated for $C_{17}H_{21}NO_2$ $[M]^+$ 271.1, found 271.1. FTIR (neat, cm^{-1}): 2948 (m), 2917 (w), 2863 (m), 1718 (s), 1645 (m), 1593 (m), 1484 (w), 1427 (w), 1237 (m), 1062 (m), 1007 (w), 766 (m).



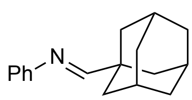
(1*E*)-2,2-dimethyl-*N*,3-diphenylpropan-1-imine (2.69), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a clear colorless liquid (0.78 g, 82% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.45 – 7.31 (m, 5H), 7.29 – 7.24 (m, 3H), 7.08 (d, *J* = 8.2 Hz, 2H), 2.94 (s, 2H), 1.28 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 152.7, 138.0, 130.6, 129.0, 128.0, 126.4, 125.3, 120.6, 46.6, 40.9, 24.7. GCMS (EI) calculated for $C_{17}H_{19}N$ $[M]^+$ 237.1, found 237.1. FTIR (neat, cm^{-1}): 3032 (w), 3028 (m), 2966 (m), 2924 (w), 2850 (w), 1646 (m), 1593 (m), 1487 (m), 1363 (w), 1219 (w), 1073 (w), 758 (m), 694 (m).



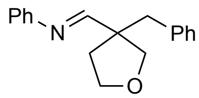
(*E*)-*N*-phenyl-1-(1-phenylcyclopropyl)methanimine (2.70), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a clear colorless liquid (0.30 g, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.44 (d, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.35 - 7.29 (m, 3H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.4 Hz, 2H), 1.61 (dd, *J* = 3.8, 2.9 Hz, 1H), 1.38 (dd, *J* = 3.8, 2.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 152.3, 141.4, 129.7, 129.0, 128.6, 127.1, 125.2, 120.8, 31.2, 17.2. GCMS (EI) calculated for $C_{16}H_{15}N$ $[M]^+$ 221.1, found 221.1. FTIR (neat, cm^{-1}): 3085 (w), 3061 (w), 1709 (w), 1635 (m), 1593 (m), 1487 (s), 1205 (w), 986 (m), 935 (w), 757 (m).



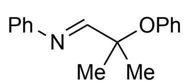
Methyl (3*E*)-2,2-dimethyl-3-(phenylimino)propanoate (2.71), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a HIGHLY hygroscopic colorless liquid (0.74 g, 79% yield). Care should be taken to avoid exposure to moisture, which causes hydrolysis within minutes at room temperature. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.26 – 7.07 (m, 5H), 3.40 (s, 3H), 1.53 (s, 6H). ^{13}C NMR (126 MHz, C_6D_6) δ 174.9, 166.1, 152.3, 129.3, 125.9, 121.1, 51.8, 48.4, 22.9. GCMS (EI) calculated for $C_{12}H_{15}NO_2$ $[M]^+$ 205.1, found 205.1. FTIR (neat, cm^{-1}): 2988 (m), 2975 (w), 2880 (w), 1736 (s), 1647 (m), 1595 (w), 1487 (w), 1268 (m), 1140 (s), 872 (w), 756 (m).



(*E*)-1-(adamantan-2-yl)-*N*-phenylmethanimine (2.72), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a waxy white solid (0.65 g, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 2H), 2.08 (app. s, 3H), 1.82 – 1.73 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 153.0, 129.0, 125.2, 120.7, 39.3, 39.0, 36.9, 28.1. GCMS (EI) calculated for $C_{17}H_{21}N$ $[M]^+$ 239.2, found 239.2. FTIR (neat, cm^{-1}): 2939 (w), 2902 (m), 2892 (m), 2843 (m), 1641 (m), 1592 (m), 1485 (m), 1447 (m), 1212 (w), 987 (w), 762 (m), 700 (m).



(*E*)-1-(3-benzyloxolan-3-yl)-*N*-phenylmethanimine (2.73), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a clear colorless liquid (0.23 g, 33% yield) along with 7 mg of the starting aldehyde. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.28 – 7.11 (m, 8H), 6.90 (d, *J* = 7.2 Hz, 2H), 4.02 (d, *J* = 8.7 Hz, 1H), 3.92 – 3.83 (m, 2H), 3.75 (d, *J* = 8.7 Hz, 1H), 3.03 (d, *J* = 2.6 Hz, 2H), 2.33 (ddd, *J* = 12.5, 7.3, 5.6 Hz, 1H), 1.96 (dt, *J* = 12.5, 7.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 152.0, 137.7, 130.1, 129.1, 128.4, 126.7, 125.7, 120.5, 75.1, 67.9, 53.5, 41.9, 35.1. GCMS (EI) calculated for $C_{18}H_{19}NO$ $[M]^+$ 265.1, found 265.1. FTIR (neat, cm^{-1}): 3029 (w), 2931 (w), 2858 (m), 1725 (w), 1646 (m), 1593 (m), 1486 (m), 1453 (w), 1210 (w), 1073 (m), 907 (m), 759 (m), 732 (m).



(1*E*)-2-methyl-2-phenoxy-*N*-phenylpropan-1-imine (2.74), was prepared according to the reported procedure, distilled under reduced pressure, and was isolated as a white solid (0.37 g, 38% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.35 – 7.27 (m, 3H), 7.13 (d, *J* = 7.6 Hz, 2H), 7.10 – 7.01 (m, 3H), 1.70 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 155.9, 151.4, 129.4, 129.3, 126.1, 122.4, 120.7, 120.4, 80.7, 25.0. GCMS (EI) calculated for $C_{16}H_{17}NO$ $[M]^+$ 239.1, found 239.1. FTIR (neat, cm^{-1}): 3063 (w), 2984 (m), 2935 (w), 2874 (w), 1651 (m), 1593 (s), 1486 (s), 1381 (w), 1227 (m), 1139 (s), 921 (w), 838 (w), 752 (m).

2.4.8 *Catalyst, Ligand, and Base Information*

1,2-bis(diphenylphosphino)benzene (dppbz), was purchased from Strem Chemicals and used as received.

1,2-bis[bis[3,5-di(t-butyl)phenyl]phosphino]benzene (SciOPP), was purchased from FUJIFILM and used as received.

[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]copper(I) chloride (IPrCuCl), was prepared according to a previously reported procedure and the spectra matched those from the literature.

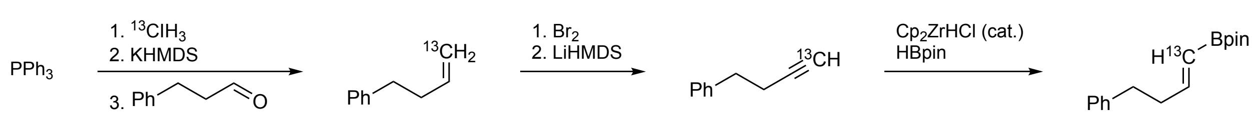
[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]copper(I) *tert*-butoxide (IPrCuO*t*-Bu), was prepared according to a previously reported procedure and the spectra matched those from the literature.

1,2-bis[4-(trifluoromethyl)phenyl]benzene (*p*-CF₃dppbz), was prepared according to a previously reported procedure and the spectra matched those from the literature.[137]

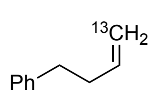
Potassium 2-pyridoate, was prepared according to a previously reported procedure and the spectra matched those from the literature.[128]

2.4.9 *Mechanistic Studies*

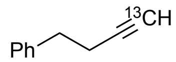
2.4.9.1 ^{13}C-NMR Study



Scheme 2.11 Outline for the Synthesis of ^{13}C-labeled Alkenyl Boronate Ester (**2.41**).



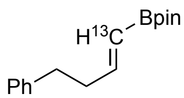
4-phenyl-1-butene-1-*^{13}C* (2.75), was prepared according to a modified procedure. A flame dried 100mL Schlenk flask under N_2 was charged with a stir bar followed by the addition of freshly recrystallized triphenylphosphine (3.8g, 14.7 mmol, 1.05 equiv) under a pillow of N_2 and then outfitted with a septum. The solid was dissolved in anhydrous ether (28 mL, 0.5 M). To this homogenous solution was added iodomethane-^{13}C (880 μL, 14.0 mmol, 1.0 equiv) at 25 °C. The solution was allowed to stir overnight at 25 °C. After 24 hours a solution of KHMDS in ether (26.6 mL, 0.5 M, 13.3 mmol 0.95 equiv) was added dropwise to the now heterogenous reaction mixture. The bright orange solution was allowed to stir for 3 hours at 25 °C. After 3 hours the mixture was cooled to -78 °C and a solution of 3-phenylpropionaldehyde (2.1 g, 15.4 mmol, 1.10 equiv) in 10 mL of anhydrous ether was added dropwise. After complete addition of the aldehyde the reaction was allowed warm up to 25 °C and stir overnight. After 20 hours the reaction mixture was quenched with sodium bicarbonate (10 ml) and water (10 ml). The aqueous layer was extracted with ether (3 × 20 ml) and the combined organic layers were dried with $MgSO_4$. After evaporation of the solvent (*WARNING: this compound can be lost on the roto-vap, care should be taken to ensure no loss of compound occurs during this step*) the title compound was purified by silica gel column chromatography, 10% ether in pentane, to afford a clear colorless oil (1.19 g, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.5 Hz, 2H), 7.23 - 7.20 (m, 3H), 5.89 (ddt, *J* = 17.0, 10.4, 6.6 Hz, 1H), 5.07 (dd, *J* = 153.4, 17.0 Hz, 1H), 5.01 (dd, *J* = 153.4, 10.4 Hz, 1H), 2.74 (t, *J* = 7.4 Hz, 2H), 2.41 (p, *J* = 7.0 Hz, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0, 138.2 (d, *J* = 69.3 Hz), 128.5 (d, *J* = 18.0 Hz), 125.9, 124.7 (d, *J* = 42.6 Hz), 115.0, 35.7, 12.9 (d, *J* = 42.7 Hz). GCMS (EI) calculated for $C_9{}^{13}CH_{12}$ $[M]^+$ 133.1, found 133.1. FTIR (neat, cm^{-1}): 3065 (w), 3029 (m), 2972 (w), 2925 (m), 2857 (w), 1619 (m), 1496 (s), 1454 (m), 996 (w), 902 (m), 745 (m), 697 (s).



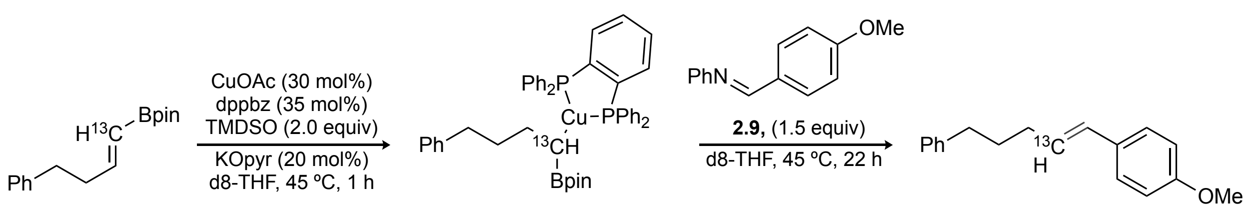
4-phenyl-1-butyne-1-^{13}*C* (2.76), was prepared according to a modified procedure. A flame dried 100 mL round bottom flask was charged with a stir bar, outfitted with a septum and was flushed with dry N_2 using a needle line. To the 100 mL flask was added **75** (1145 mg, 8.6 mmol, 1.0 equiv) via syringe followed by freshly distilled $CHCl_3$ (17 mL, 0.5 M). The homogenous mixture was cooled to 0 °C. To the cooled solution was added Br_2 (440 μL, 8.6 mmol, 1.0 equiv) dropwise via syringe and the reaction mixture was allowed to continue stirring at this temperature. After 1 hour the reaction mixture was quenched with a saturated aqueous solution of sodium thiosulfate (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml) and the combined organic layers were dried with $MgSO_4$. After evaporation of the solvent the dibromide was obtained as a yellow oil and was used in the next step without further purification.

A flame dried 50mL Schlenk flask under N_2 was charged with a stir bar followed by the addition of the crude dibromide and outfitted with a septum. The crude dibromide was dissolved in anhydrous THF (17 mL, 0.5M) and a solution of LiHMDS in THF (23.1 mL, 30.1 mmol, 3.5 equiv) was added slowly at 25 °C. The reaction mixture was subsequently heated to 60 °C in an oil bath and allowed to stir at that temperature overnight. After 16 hours the reaction mixture was cooled to room temperature and quenched by the addition of a saturated aqueous solution of NH_4Cl (15 mL). The aqueous layer was extracted with hexanes (3 × 20 ml) and the combined organic layers were dried with Na_2SO_4. After evaporation of the solvent (*WARNING: this compound can be lost on the roto-vap, care should be taken to ensure no loss of compound occurs during this step*) the title compound was purified by silica gel column chromatography, 20% ether in pentane, to afford a clear colorless oil (0.71 g, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, J = 7.6 Hz, 2H), 7.28 – 7.20 (m, 3H), 2.87 (t, J = 7.6 Hz, 2H), 2.53 – 2.48 (m, 2H), 1.99 (dt, J = 248.0, 2.4

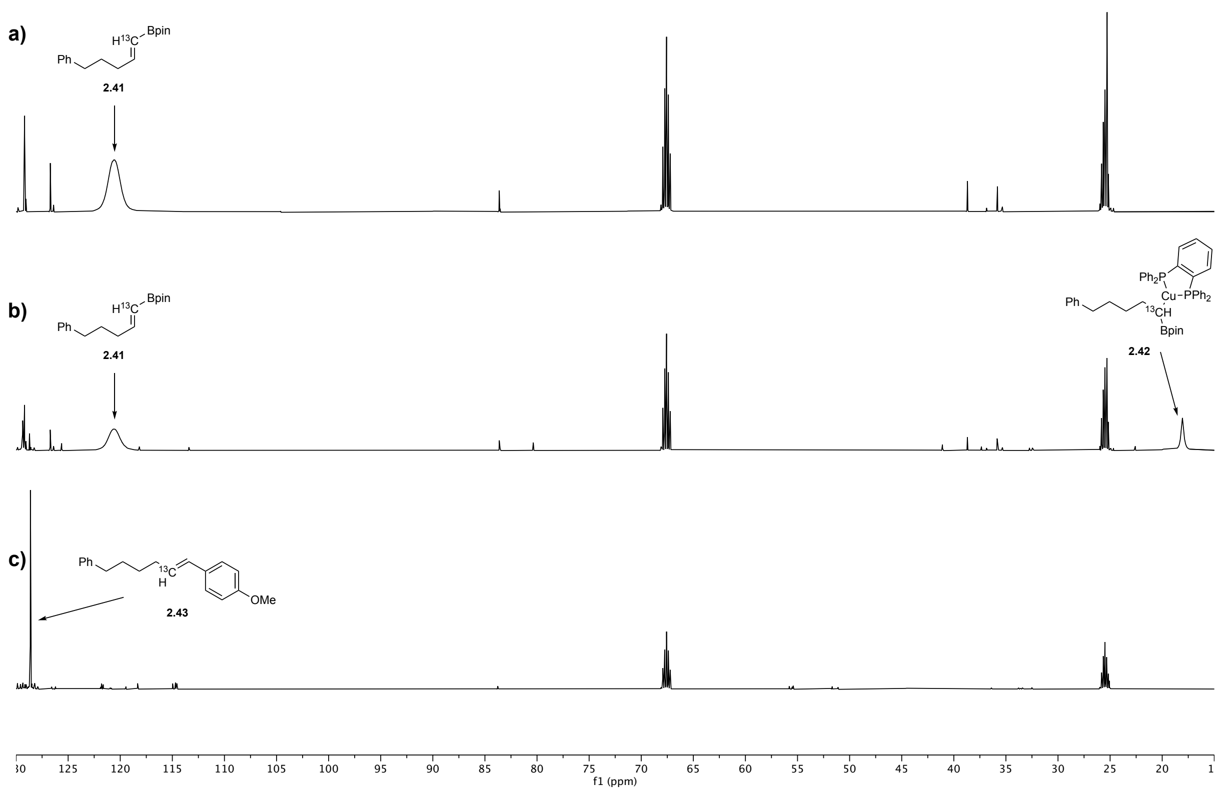
Hz, 1H).^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3 (d, J = 4.6 Hz), 140.6, 128.5, 126.5, 79.4, 69.0, 35.0 (d, J = 2.3 Hz), 20.7 (d, J = 10.5 Hz). GCMS (EI) calculated for $C_9{}^{13}CH_{10}$ $[M]^+$ 131.1, found 131.1. FTIR (neat, cm^{-1}): 3087 (w), 3064 (w), 3029 (m), 2930 (m), 2864 (w), 2094 (w), 1605 (w), 1496 (m), 1454 (m), 1078 (w), 1030 (w), 957 (w), 745 (m).



2-[(1*E*)-4-(phenyl)but-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane-1-*^{13}C* (2.41), was prepared according to the general procedure outlined in Section 2.4.6 using **2.76** as the starting alkyne, purified by silica gel column chromatography, 0-20% ether in hexanes, and was isolated as a clear colorless liquid (0.83 g, 80% yield). ^{1}H NMR (500 MHz, THF) δ 7.22 (t, J = 7.2 Hz, 1H), 7.16 (d, J = 6.7 Hz, 2H), 7.11 (t, J = 7.2 Hz, 1H), 6.63 (dtd, J = 18.0, 6.3, 3.0 Hz, 1H), 5.41 (ddt, J = 121.2, 18.0, 1.4 Hz, 1H), 2.70 (dd, J = 8.4, 7.6 Hz, 2H), 2.46 – 2.38 (m, 2H), 1.20 (s, 12H).^{13}C NMR (126 MHz, THF) δ 154.1, 153.6, 142.8, 129.22, 129.2, 126.7, 120.6(broad), 83.6, 83.6, 38.7, 35.8, 35.8, 25.3. ^{11}B NMR (160 MHz, THF) δ 27.40. GCMS (EI) calculated for $C_{15}{}^{13}CH_{23}BO_2$ $[M]^+$ 259.2, found 259.2. FTIR (neat, cm^{-1}): 3029 (w), 2979 (m), 2932 (m), 2857 (w), 1613 (s), 1497 (w), 1355 (s), 1318 (s), 1142 (s), 1004 (w), 972 (m), 849 (m), 698 (m).



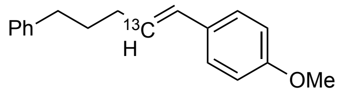
In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (1.84 mg, 0.015 mmol, 0.30 equiv), dppbz (10.0 mg, 0.023 mmol, 0.45 equiv), and a d_8-THF (0.5 mL). The heterogenous mixture was stirred for 5 min at 45 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the copper/ligand mixture was added KOPyr (1.3 mg, 0.010 mmol, 0.20 equiv) and TMDSO (17.6 mg, 0.100 mmol, 2.0 equiv). The bright yellow



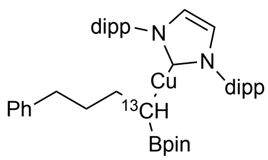
Scheme 2.12 Heterobimetallic Intermediate Formation and Reaction Monitoring by ^{13}C-NMR Spectroscopy.

solution was allowed to stir for 15 minutes at 45 °C. At this time alkenyl Bpin **(2.41)** (**Scheme 2.12a**) (13.0 mg, 0.050 mmol, 1.0 equiv) was added to the copper hydride mixture. The resulting mixture was allowed to stir for 1 hour at 45 °C before being cooled to room temperature and transferred to a J-Young tube and analyzed by^{13}C-NMR spectroscopy (**Scheme 2.12b**). In a nitrogen-filled glovebox, a new dram vial was charged with a stir bar, the solution containing the heterobimetallic intermediate, (*E*)-1-(4-methoxyphenyl)-*N*-phenylmethanimine (15.8 mg, 0.075

mmol, 1.5 equiv), and additional d_8-THF (0.5 mL). The reaction mixture was then vigorously stirred at 45 °C. After 24 hours the mixture was cooled to room temperature and transferred to a *J*-Young tube and analyzed by ^{13}C-NMR spectroscopy (**Scheme 2.12c**).



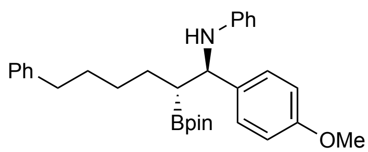
1-methoxy-4-[(1*E*)-5-phenylpent-1-en-1-yl]benzene (2.43), was isolated from the ^{13}C-NMR experiment detailed above. The compound was purified according to workup procedure 2, further by silica gel column chromatography, 0-60% CH_2Cl_2 in hexanes, and isolated as a clear colorless oil. ^{1}H NMR (500 MHz, C_6D_6) δ 7.26 – 7.21 (m, 2H), 7.21 – 7.17 (m, 2H), 7.13 – 7.06 (m, 3H), 6.83 – 6.76 (m, 2H), 6.33 (d, *J* = 15.9 Hz, 1H), 6.00 (ddt, *J* = 148.7, 15.9, 6.8 Hz, 1H), 3.32 (s, 3H), 2.52 (t, *J* = 7.3 Hz, 2H), 2.14 – 2.05 (m, 2H), 1.74 – 1.61 (m, 2H). ^{13}C NMR (126 MHz, C_6D_6) δ 159.5, 142.7, 131.1, 128.8, 128.7, 128.3, 126.1, 114.4, 62.3, 54.8, 35.7 (d, *J* = 3.6 Hz), 33.0, 32.7, 31.6 (d, *J* = 2.2 Hz). GCMS (EI) calculated for $C_{17}{}^{13}CH_{20}O$ $[M]^+$ 253.2, found 253.2. FTIR (neat, cm^{-1}): 3027 (w), 2934 (m), 2857 (w), 2835 (w), 1606 (s), 1509 (s), 1453 (m), 1243 (s), 1157 (m), 1034 (m), 963 (m), 836 (m), 745 (m).



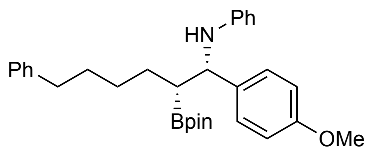
{1,3-bis[2,6-bis(propan-2-yl)phenyl]-2,3-dihydro-1H-imidazol-2-yl}[4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]copper-1-*^{13}*C (2.44), was prepared according to a previously reported procedure.[103] ^{1}H NMR δ 7.29 (t, *J* = 7.7 Hz, 2H), 7.23 – 7.18 (m, 6H), 7.13 – 7.10 (m, 1H), 7.05 – 7.00 (m, 2H), 7.00 (s, 2H), 2.58 (pd, *J* = 6.8, 4.0 Hz, 4H), 2.36 – 2.23 (m, 2H), 1.48 – 1.45 (m, 2H) 1.31 (dd, *J* = 9.2, 6.8 Hz, 12H), 1.20 (dd, *J* = 6.8, 3.2 Hz, 12H), 1.08 –

0.89 (m, 2H), 0.86 (s, 6H), 0.79 (s, 6H), 0.13 (dt, J = 116.7, 7.8 Hz, 1H).^{13}C NMR ^{13}C NMR (126 MHz, THF) δ 146.7, 145.5, 136.5, 130.9, 129.5, 128.6, 125.6, 124.8, 124.7, 124.0, 79.9, 39.9, 37.5, 37.5, 29.8, 29.7, 29.6, 29.3, 24.2, 24.2, 16.4(broad). ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.16.

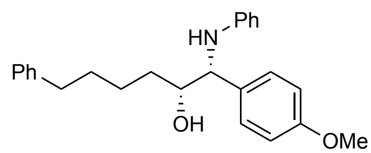
2.4.9.2 Analysis of the Addition Intermediates



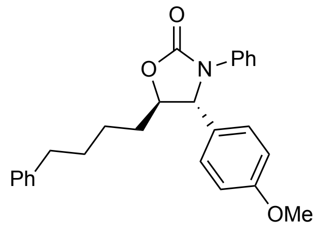
Anti-*N*-[1-(4-methoxyphenyl)-6-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]aniline (2.45 (erythro)), was prepared according to a modified version of procedure A. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.74 mg, 0.006 mmol, 0.02 equiv), dppbz (4.0 mg, 0.009 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (1.0 mL). The heterogenous mixture was stirred for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (8.0 mg, 0.060 mmol, 0.20 equiv), TMDSO (80.4 mg, 0.600 mmol, 2.0 equiv), 4,4,5,5-tetramethyl-2-[(1*E*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (81.7 mg, 0.300 mmol, 1.0 equiv), (*E*)-1-(4-methoxyphenyl)-N-phenylmethanimine (95.1 mg, 0.450 mmol, 1.5 equiv), and a 1:1 mixture of THF:2-MeTHF (2.0 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 4 h the reaction mixture was removed from the glovebox and passed through a small plug of silica with EtOAc, the solvent was then removed under vacuum. The two diastereoisomers of this compound were separated via HPLC purification of the crude reaction mixture. The anti-diastereoisomer was obtained as a mixture with the corresponding benzyl phenylamine. ^{1}H NMR (500 MHz, C_6D_6) δ .24 (d, J = 8.7 Hz, 1H), 7.12 – 7.03 (m, 7H), 6.74 (d, J = 8.7 Hz, 1H), 6.66 (tt, J = 7.3, 1.0 Hz, 1H), 6.60 (dd, J = 7.3, 1.0 Hz, 1H), 4.66 (app. t, J = 6.2 Hz, 1H), 4.40 (d, J = 5.9 Hz, 1H), 3.27 (s, 3H), 2.49 (t, J = 7.4 Hz, 2H), 1.61 – 1.46 (m, 4H), 1.33 – 1.22 (m, 2H), 0.96 (s, 6H), 0.91 (s, 6H), 0.89 – 0.83 (m, 1H). GCMS (EI) calculated for $C_{31}H_{40}BNO_3$ $[M]^+$ 485.3, found 485.3.



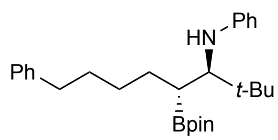
Syn-*N*-[1-(4-methoxyphenyl)-6-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]aniline (2.45 (threo)), was prepared according to a modified version of procedure A. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.74 mg, 0.006 mmol, 0.02 equiv), dppbz (4.0 mg, 0.009 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (1.0 mL). The heterogenous mixture was stirred for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (8.0 mg, 0.060 mmol, 0.20 equiv), TMDSO (80.4 mg, 0.600 mmol, 2.0 equiv), 4,4,5,5-tetramethyl-2-[(1*E*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (81.7 mg, 0.300 mmol, 1.0 equiv), (*E*)-1-(4-methoxyphenyl)-N-phenylmethanimine (95.1 mg, 0.450 mmol, 1.5 equiv), and a 1:1 mixture of THF:2-MeTHF (2.0 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 24 h the reaction mixture was removed from the glovebox and the solvent was removed under vacuum. The compound was purified via a short plug of silica (*WARNING: this compound decomposes upon prolonged exposure to silica*) eluting with 2CV 0% ether in hexanes, followed by 1CV 20% ether in hexanes, and finally 3CV 40% ether in hexanes (collected in this fraction). The solvent was removed under vacuum and the title compound was obtained as a mixture along with aldehyde and imine and used directly in the next step without further purification. ^1H NMR (500 MHz, C_6D_6) δ 7.21 (d, J = 7.8 Hz, 2H), 7.11 – 7.02 (m, 7H), 6.72 (d, J = 7.6 Hz, 2H), 6.66 (t, J = 7.6 Hz, 1H), 6.63 (d, J = 7.5 Hz, 1H), 4.68 (d, J = 6.6 Hz, 1H), 4.50 (app. t, J = 7.1 Hz, 1H), 3.26 (s, 3H), 2.49 – 2.45 (m, 2H), 1.60 – 1.52 (m, 2H), 1.30 – 1.24 (m, 4H), 1.01 (s, 12H), 0.99 – 0.95 (m, 1H). GCMS (EI) calculated for $C_{31}H_{40}BNO_3$ $[M]^+$ 485.3, found 485.3.



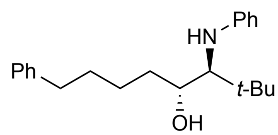
Syn-1-(4-methoxyphenyl)-6-phenyl-1-(phenylamino)hexan-2-ol (2.77), was prepared according to the following procedure: A 20 mL scintillation vial was charged with a stir bar, (**2.45(threo)**), a 1:2:2 mixture of benzene:THF:water (2.5 mL, 0.012 M total). This mixture was cooled to 0 °C with an ice bath. Sodium perborate tetrahydrate (45 mg, 0.029 mmol, 10.0 equiv) was added all at once. The heterogenous mixture was allowed to stir at 0 °C for 1 hour and then subsequently warmed up to 25 °C. After 4 hours the mixture was diluted with water and extracted 3x with EtOAc. The combined organic layers were dried with sodium sulfate, filtered, and the solvent was removed via roto-evaporation. The title compound was purified by silica gel chromatography, 5-45% ether in hexanes, and was isolated as a clear colorless oil (5.3 mg, 49% yield). ^1H NMR (500 MHz, C_6D_6) δ 7.20 – 7.18 (m, 2H), 7.10 – 7.03 (m, 7H), 6.73 (d, J = 8.6 Hz, 2H), 6.68 (tt, J = 7.3, 1.1 Hz, 1H), 6.53 (dd, J = 8.6, 1.1 Hz, 2H), 4.44 (s(br), 1H), 4.09 (d, J = 5.0 Hz, 1H), 3.48 (app dt, J = 8.1, 4.2 Hz, 1H), 3.28 (s, 3H), 2.46 (t, J = 7.2 Hz, 2H), 1.54 – 1.41 (m, 6H).^{13}C NMR (126 MHz, C_6D_6) δ 159.5, 148.1, 142.8, 133.8, 129.5, 128.8, 128.6, 128.6, 126.1, 118.1, 114.5, 114.4, 75.9, 62.6, 54.8, 36.2, 34.0, 31.7, 25.9. MS (ESI+) calculated for $C_{25}H_{30}NO_2^+$ $[M+H]^+$ 376.2, found 376.2.



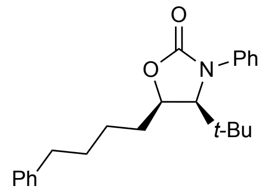
Trans-4-(4-methoxyphenyl)-3-phenyl-5-(4-phenylbutyl)-1,3-oxazolidin-2-one (2.46), was prepared according to the following procedure: To a flame dried 4 mL dram vial that had been outfitted with a N_2 needle and flushed with N_2 was added (**2.77**), anhydrous methylene chloride (0.5 mL, 0.03 M), freshly distilled pyridine (48 μL, 0.600 mmol, 40 equiv). The homogenous mixture was cooled to -78 °C and a solution of phosgene (32 μL, 0.060 mmol, 4.0 equiv, 20 wt% in toluene) was added dropwise. The reaction was allowed to stir at the same temperature for 2 hours followed by warming up to 0 °C. After an additional 1 hour at this temperature the reaction was diluted with EtOAc and water and the biphasic mixture was stirred for 1 hour to quench all excess phosgene. The aqueous layer was then extracted 3x with EtOAc. The combined organic layers were dried with sodium sulfate, filtered, sparged with nitrogen for 10 minutes (to remove any remaining phosgene), and finally the solvent was removed via roto-evaporation. The title compound was purified by silica gel chromatography, 10-60% ether in hexanes, and was isolated as a white solid (5.6 mg, 93% yield). ^{1}H NMR (500 MHz, C_6D_6) δ 7.60 (dd, *J* = 8.8, 1.1 Hz, 2H), 7.20 – 7.16 (m, 2H), 7.11 – 7.04 (m, 5H), 6.83 – 6.79 (m, 3H), 6.56 (d, *J* = 8.8 Hz, 1H), 4.42 (d, *J* = 6.0 Hz, 1H), 3.93 (ddd, *J* = 8.1, 6.0, 4.0 Hz, 1H), 3.16 (s, 3H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.44 – 1.30 (m, 6H).^{13}C NMR (126 MHz, C_6D_6) δ 160.1, 155.2, 142.5, 138.5, 130.6, 129.0, 128.7, 128.7, 128.4, 126.20, 124.2, 120.8, 114.9, 81.8, 65.7, 54.7, 36.0, 34.2, 31.4, 24.8. GCMS (EI) calculated for $C_{26}H_{27}NO_3$ $[M]^+$ 401.2, found 401.2. FTIR (neat, cm^{-1}): 2982 (w), 2929 (m), 2854 (w), 1742 (s), 1614 (m), 1513 (m), 1453 (w), 1357 (s), 1246 (m), 1177 (m), 1146 (s), 1031 (m), 838 (w).



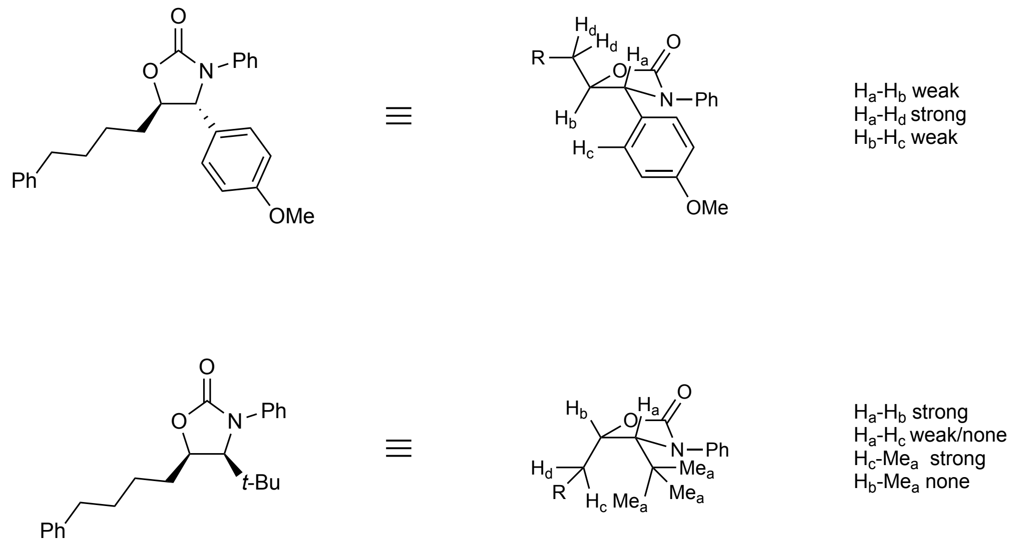
Anti-N-[1-(*tert*-butyl)-6-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]aniline (2.47 (erythro)), was prepared according to a modified version of procedure C. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (1.20 mg, 0.010 mmol, 0.02 equiv), dppbz (6.7 mg, 0.015 mmol, 0.03 equiv), and 2-MeTHF (1.0 mL). The heterogenous mixture allowed to stir stirred for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (13.3 mg, 0.100 mmol, 0.20 equiv), HMTSO (156.4 mg, 0.750 mmol, 1.5 equiv), 4,4,5,5-tetramethyl-2-[(1*E*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (136 mg, 0.500 mmol, 1.0 equiv), (1*E*)-2,2-dimethyl-N-phenylpropan-1-imine (161 mg,1.000 mmol, 2.0 equiv), and 2-MeTHF (1.5 mL, 0.20 M total). The reaction was vigorously stirred at 60 °C. After 24 h the reaction mixture was removed from the glovebox and the solvent was removed under vacuum. The compound was purified via quick silica gel column chromatography, 0-15% ether in hexanes (with 1% triethylamine as an additive). (*WARNING: this compound decomposes upon prolonged exposure to silica ~10 minutes*) The solvent was removed under vacuum and the title compound was obtained as a 1:1 mixture (starting alkenyl Bpin) and used directly in the next step without further purification. A cleaner sample was obtained via HPLC purification of an aliquot of the above mixture and used for spectroscopic analysis. ^{1}H NMR (500 MHz, C_6D_6) δ 7.08 – 7.05 (m, 2H), 6.68 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.3 Hz, 1H), 3.65 (app t, J = 8.8 Hz, 1H), 3.39 (d, J = 10.9 Hz, 1H), 2.50 (t, J = 7.2 Hz, 2H), 1.52 – 1.48 (m, 2H), 1.40 – 1.31 (m, 4H), 1.02 (s, 12H), 0.98 (s, 9H). GCMS (EI) calculated for $C_{28}H_{42}BNO_2$ $[M]^+$ 435.3, found 435.3.



Anti-1-(dimethyl)-7-phenyl-2-(phenylamino)septan-3-ol (2.78), was prepared according to the following procedure: A 20 mL scintillation vial was charged with a stir bar, (**2.47 (erythro)**), a 1:2:2 mixture of benzene:THF:water (5.0 mL, 0.012 M total). This mixture was cooled to 0 °C with an ice bath. Sodium perborate tetrahydrate (92.3 mg, 0.060 mmol, 10.0 equiv) was added all at once. The heterogenous mixture was allowed to stir at 0 °C for 1 hour and then subsequently warmed up to 25 °C. After 4 hours the mixture was diluted with water and extracted 3x with EtOAc. The combined organic layers were dried with sodium sulfate, filtered, and the solvent was removed via roto-evaporation. The title compound was purified by silica gel chromatography, 0-5% ether in CH_2Cl_2, and was isolated as a clear colorless oil (8.1 mg, 41% yield). ^{1}H NMR (500 MHz, C_6D_6) δ 7.21 – 7.15 (m, 4H), 7.10 – 7.07 (m, 3H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 7.2 Hz, 2H), 3.56 – 3.51 (m, 1H), 3.22 (dd, *J* = 10.0, 4.9 Hz, 1H), 3.16 (d, *J* = 10.0 Hz, 1H), 2.49 (t, *J* = 7.3 Hz, 2H), 1.56 – 1.39 (m, 3H), 1.28 – 1.21 (m, 1H), 1.17 – 1.08 (m, 2H), 0.86 (s, 9H). ^{13}C NMR (126 MHz, C_6D_6) δ 150.1, 142.9, 129.7, 128.8, 128.7, 128.6, 126.1, 117.6, 113.6, 73.1, 67.1, 36.4, 35.7, 34.4, 31.9, 30.5, 27.9, 26.2. MS (ESI+) calculated for $C_{22}H_{32}NO^+$ $[M+H]^+$ 326.2, found 326.2.

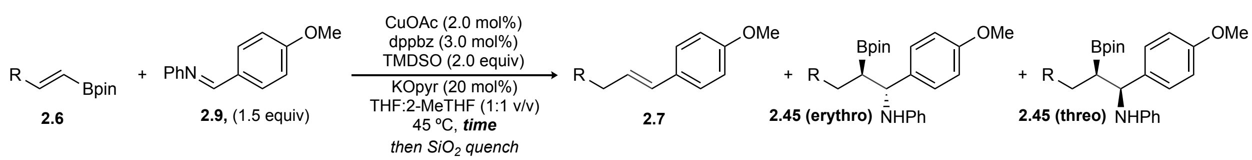


Cis-4-(*tert*-butyl)-3-phenyl-5-(4-phenylbutyl)-1,3-oxazolidin-2-one (2.79), was prepared according to the following procedure: To a flame dried 4 mL dram vial that had been outfitted with a N_2 needle and flushed with N_2 was added (**2.78**), anhydrous methylene chloride (1.0 mL, 0.03 M), freshly distilled pyridine (81 μL, 1.000 mmol, 40 equiv). The homogenous mixture was cooled to -78 °C and a solution of phosgene (53 μL, 0.100 mmol, 4.0 equiv, 20 wt% in toluene) was added dropwise. The reaction was allowed to stir at the same temperature for 2 hours followed by warming up to 0 °C. After an additional 1 hour at this temperature the reaction was diluted with EtOAc, and water and the biphasic mixture was stirred for 1 hour to quench all excess phosgene. The aqueous layer was then extracted 3x with EtOAc. The combined organic layers were dried with sodium sulfate, filtered, sparged with nitrogen for 10 minutes (to remove any remaining phosgene), and finally the solvent was removed via roto-evaporation. The title compound was purified by silica gel chromatography, 10-60% ether in hexanes, and was isolated as a white solid (6.2 mg, 76% yield). ^{1}H NMR δ 7.50 (d, *J* = 7.7 Hz, 2H), 7.23 – 7.20 (m, 2H), 7.14 – 7.10 (m, 5H), 6.92 (t, *J* = 7.4 Hz, 1H), 3.88 (ddd, *J* = 11.1, 6.3, 3.1 Hz, 2H), 3.43 (d, *J* = 6.3 Hz, 1H), 2.54 – 2.42 (m, 2H), 1.77 (dtd, *J* = 14.8, 11.0, 4.7 Hz, 1H), 1.55 – 1.44 (m, 3H), 1.38 – 1.26 (m, 1H), 1.20 – 1.14 (m, 1H), 0.70 (s, 9H).^{13}C NMR (126 MHz, C_6D_6) δ 155.7, 142.6, 140.9, 129.0, 128.8, 128.7, 128.4, 126.2, 124.7, 123.0, 80.2, 67.7, 37.1, 36.2, 31.5, 30.9, 30.5, 27.8, 27.2. GCMS (EI) calculated for $C_{23}H_{29}NO_2$ $[M]^+$ 351.2, found 351.2. FTIR (neat, cm^{-1}): 2960 (m), 2929 (m), 2860 (w), 1751 (s), 1600 (w), 1498 (m), 1456 (w), 1394 (m), 1216 (w), 1137 (m), 982 (w), 769 (m), 667 (m).



Scheme 2.13 NOESY Analysis of Oxazolidinones Derived from the Addition Intermediates **2.45 (threo)** and **2.47 (erythro)**.

In addition to the NOESY analysis we can further confirm our assignments of **2.45 (threo)** and **2.47 (erythro)** through the comparison of our experimentally determined coupling constants with those of similar oxazolidinones found in the literature.[138–140]



In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.25 mg, 0.002 mmol, 0.02 equiv), dppbz (1.3 mg, 0.003 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5 mL). The heterogenous mixture was stirred for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (2.7 mg, 0.020 mmol, 0.20 equiv), TMDSO (26.8 mg, 0.200 mmol, 2.0 equiv), 4,4,5,5-tetramethyl-2-[(1*E*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (27.2 mg, 0.100 mmol, 1.0 equiv), trimethoxybenzene (as an internal standard for ^{1}H-NMR analysis), (*E*)-1-(4-methoxyphenyl)-*N*-

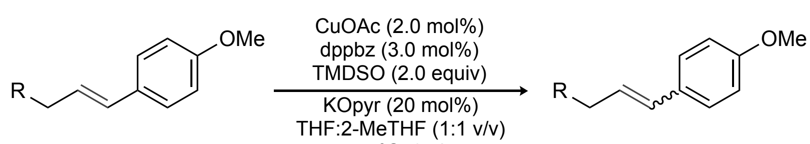
phenylmethanimine (31.7 mg, 0.150 mmol, 1.5 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After the specified time the vial was removed from the glovebox and a 50 μL aliquot of the crude reaction mixture was taken, passed through a plug of silica with 1.5 mL of EtOAc, and analyzed by GC to obtain the isomeric ratio. The reaction mixture was then diluted with EtOAc (2.0 mL), and passed through a plug of silica with EtOAc (3x 2.0 mL). The solvent and volatiles were removed via roto-evaporation and subsequent coevaporation with benzene. The crude reaction mixture was analyzed by ^{1}H-NMR spectroscopy and GC. The results are detailed in **Table 2.12**.

Table 2.12 Reaction Progress and Intermediate Monitoring by ^{1}H-NMR Spectroscopy

time (min)	**10**	**30**	**60**	**120**	**240**	**480**	**600**	**840**	**1080**	**1440**	**1680**
2.6	0.089	0.083	0.077	0.064	0.037	0.010	0.001	0.000	0.000	0.000	0.000
2.7	0.000	0.007	0.012	0.019	0.041	0.068	0.081	0.083	0.084	0.088	0.087
E:Z	NA	NA	NA	NA	200:1	114:1	85:1	65:1	46:1	42:1	42:1
2.45 (T)	0.001	0.002	0.003	0.004	0.006	0.011	0.013	0.013	0.013	0.013	0.013
2.45 (E)	0.003	0.005	0.005	0.004	0.003	0.004	0.003	0.001	0.001	0.000	0.000

All values in the table are given in mmols, calculated from peak areas relative to a known amount of trimethoxybenzene, from a single scan and baseline corrected ^{1}H-NMR spectra. E/Z ratios were determined by GC analysis of a 50 μL aliquot of the respective NMR sample.

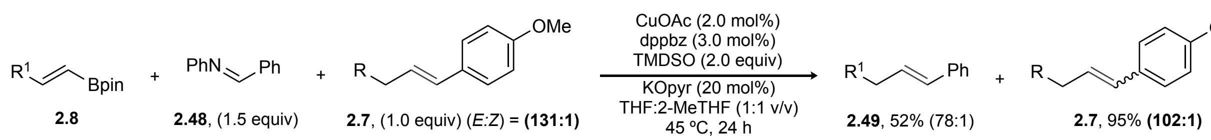
2.4.9.3 Isomerization Experiments



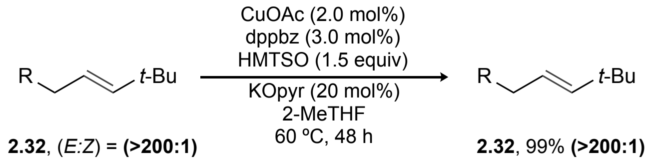
2.7, (*E*:*Z*) = **(131:1)** **2.7**, 97% **(43:1)**

E-enriched **2.7** was obtained via HPLC purification (0-1% IPA in hexanes) of an isolated sample of X and obtained as a clear colorless liquid (*E*:*Z*) = (131:1) as measured by GC. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.25 mg, 0.002 mmol, 0.02 equiv), dppbz (1.3 mg, 0.003 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5 mL). The heterogenous mixture was stirred for 5 min at 45 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (2.7 mg, 0.020

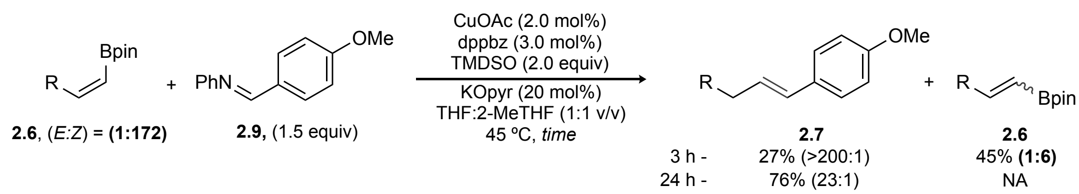
mmol, 0.20 equiv), TMDSO (26.8 mg, 0.200 mmol, 2.0 equiv), *E*-enriched **2.7** (26.6 mg, 0.100 mmol, 1.0 equiv), trimethoxybenzene (as an internal standard for GC analysis), and a 1:1 mixture of THF:2-MeTHF (0.5 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 24 h the vial was removed from the glovebox and a 50 µL aliquot of the crude reaction mixture was taken, passed through a plug of silica with 1.5 mL of EtOAc, and analyzed by GC to obtain the isomeric ratio and % recovery.



In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.25 mg, 0.002 mmol, 0.02 equiv), dppbz (1.3 mg, 0.003 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5 mL). The heterogenous mixture was stirred for 5 min at 45 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (2.7 mg, 0.020 mmol, 0.20 equiv), TMDSO (26.8 mg, 0.200 mmol, 2.0 equiv), *E*-enriched **2.7** (26.6 mg, 0.100 mmol, 1.0 equiv), (*E*)-2-(5-(4-methoxyphenoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (27.2 mg, 0.100 mmol, 1.0 equiv), trimethoxybenzene (as an internal standard for GC analysis), (*E*)-1-(4-methoxyphenyl)-*N*-phenylmethanimine (31.7 mg, 0.150 mmol, 1.5 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5 mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After 24 h the vial was removed from the glovebox and a 50 µL aliquot of the crude reaction mixture was taken, passed through a plug of silica with 1.5 mL of EtOAc, and analyzed by GC to obtain the isomeric ratio, % yield of **2.49**, and % recovery of **2.7**.



In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.25 mg, 0.002 mmol, 0.02 equiv), dppbz (1.3 mg, 0.003 mmol, 0.03 equiv), and 2-MeTHF (0.2 mL). The heterogenous mixture was allowed to stir for 5 min at 60 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (2.7 mg, 0.020 mmol, 0.20 equiv), HMTSO (31.3 mg, 0.150 mmol, 1.5 equiv), 1-{[(5*E*)-7,7-dimethyloct-5-en-1-yl]oxy}-4-methoxybenzene (26.2 mg, 0.100 mmol, 1.0 equiv), and 2-MeTHF (0.3 mL, 0.20 M total). The reaction was vigorously stirred at 60 °C. After 48 h a 50 μL aliquot was taken and pushed through a plug of silica with 1.5 mL of EtOAc and analyzed by GC to obtain the isomeric ratio and % recovery.



In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, CuOAc (0.25 mg, 0.002 mmol, 0.02 equiv), dppbz (1.3 mg, 0.003 mmol, 0.03 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5 mL). The heterogenous mixture was stirred for 5 min at 45 °C until pale yellow and homogenous. The mixture was cooled to room temperature. To the mixture was added KOPyr (2.7 mg, 0.020 mmol, 0.20 equiv), TMDSO (26.8 mg, 0.200 mmol, 2.0 equiv), 4,4,5,5-tetramethyl-2-[(1*Z*)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane (27.2 mg, 0.100 mmol, 1.0 equiv), trimethoxybenzene (as an internal standard for GC analysis), (*E*)-1-(4-methoxyphenyl)-*N*-phenylmethanimine (31.7 mg, 0.150 mmol, 1.5 equiv), and a 1:1 mixture of THF:2-MeTHF (0.5

mL, 0.10 M total). The reaction was vigorously stirred at 45 °C. After the specified time the vial was removed from the glovebox and a 50 μL aliquot of the crude reaction mixture was taken, passed through a plug of silica with 1.5 mL of EtOAc, and analyzed by GC to obtain the isomeric ratio and % yield.

2.5 References For Chapter 2

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VITA

James E. Baumann was born and raised in Denver, Colorado. In 2014, he moved to Golden, Colorado where he attended the Colorado School of Mines. After graduating with a Bachelor of Science in biochemistry in May of 2018, he moved to Seattle, Washington to pursue a doctoral degree in organic chemistry with Professor Gojko Lalic at the University of Washington. After earning his Ph.D. in December of 2023, he began a postdoctoral fellowship at Stanford working in the Medicinal Chemistry Knowledge Center as a member of Professor Kacper Rogala's lab.