Boron-mediated Transition-metal Catalyzed Selective Synthesis of Diverse Alkenes

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Abstract

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The stereoselective synthesis of alkenes has been one of the central objectives in organic chemistry. Significant advances in synthetic methodology have made mono- and disubstituted alkenes widely accessible from a variety of readily available precursors. However, increased steric hindrance in more highly substituted alkenes limits the effectiveness of these methods, and as a result, the efficient and selective synthesis of highly substituted alkenes remains a formidable challenge. Boron exhibits unique reactivity that enables highly chemo- and stereoselective transformations and facile access to diverse functional groups, making organoboron compounds versatile intermediates in organic synthesis. Herein, we reported three new boron-mediated transition-metal catalyzed reactions that highly regio- and stereoselectively afford diverse alkenes with valuable functionality.

The first reaction, described in Chapter 1, is a method for the synthesis of allylic alcohols via a copper-catalyzed reductive coupling of terminal alkynes with α-chloro boronic esters, followed by in situ oxidation of the boronic ester to an alcohol. The

reaction is highly *E*-selective and exhibits broad functional group tolerance. Mechanistic studies suggest that cross-coupling of the alkenyl copper intermediate with the α-chloro boronic ester proceeds via a stereospecific 1,2-metalate shift. With support from mechanistic insights, we established a robust synthesis of chiral allylic alcohols from terminal alkynes and readily accessible enantioenriched organoboron precursors.

Following this development, Chapter 2 describes a highly regio- and diastereoselective synthesis of trisubstituted alkenes via nickel-catalyzed hydroalkylation of alkynyl boronamides. In this transformation, boryl groups serve as versatile directing groups that can control the regioselectivity of the hydroalkylation and enables productively replacement via cross-coupling. Preliminary studies support the hydrometalation mechanism and the formation of alkyl radical intermediates.

Finally, Chapter 3 described a regiodivergent and stereoselective synthesis of tetrasubstituted alkenes via palladium catalyzed direct trifunctionalization of terminal alkynes using organoboranes and allylic carbonates as coupling partners. Incorporation of the allylic electrophile can be accomplished with either branched and linear selectivity and with excellent diastereo- and enantioselectivity, allowing access to a range of highly complex 1,4-dienes. Experimental evidence supports that enantioselective allylic substitution proceeds through a dynamic kinetic resolution and inner-sphere reductive elimination pathway. Proposed mechanism involves alkynyl boron-ate formation followed by a palladium-promoted 1,2-metalate shift that controls the regio- and diastereoselectivity of the alkene formation.

Notably, these three strategies exploit distinct properties of boron to achieve desired regio- and stereocontrol: the first and third employ stereoselective 1,2-metallate shift of tetracoordinated boron-ate complexes, whereas the second relies on intrinsic electronic bias between carbon and boron.

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List of Abbreviations

9-BBN	9-borabicyclo[3.3.1]nonane
aam	anthranilamidato
Ac	acetyl
Ar	aryl
B	base
Bn	benzyl
Boc	tert-butyloxycarbonyl
C	Celsius
Cat	catalyst
COD	1,5-cyclooctadiene
COSY	correlation spectroscopy
CPME	cyclopentyl methyl ether
Cy	cyclohexyl
dan	1,8-diaminonaphthalene
dba	dibenzylideneacetone
DCE	1,2-dichloroethane
DCM	dichloromethane
DEMS	diethoxymethylsilane
DMAc	N,N-dimethylacetamide
DME	dimethoxyethane
DMF	dimethylformamide
DMMS	dimethoxydimethylsilane
dppbz	1,2-bis(diphenylphosphino)benzene
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dpph	1,6-bis(diphenylphosphino)hexane
dppp	1,3-bis(diphenylphosphino)propane
E^+	electrophile
EI	electron ioization
equiv	equivalents
ESI	electrospray ionization
Et	ethyl
FID	flame ionization detector
FTIR	Fourier transform infrared

FTIR band abbreviations

s	strong
m	medium
w	weak

br	broad

GC	gas chromatography
h	hour
Hex	hexanes
HMTSO	hexamethyldisiloxane
HPLC	high pressure liquid chromatography
Hz	hertz
IMes	1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene
IPr	1,3-bis-(2,6-diisopropylphenyl)imidazolium
i-Pr	isopropyl
IR	infrared
KIE	kinetic isotope effect
L	ligand
M	metal
Me	methyl
MIDA	N-methyliminodiacetoxy
min	minutes
mol	mole
MS	mass spectrometry
MTBE	methyl tert-butyl ether
MTPA	α-methoxy-α-trifluoromethylphenylacetic acid
nbd	norbornadiene
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

NOESY	nuclear overhauser effect spectroscopy
OTf	trifluoromethanesulfonate
PC	photo catalyst
Ph	phenyl
Phth	phthalimide

pin	pinacol
PMHS	polymethylhydrosiloxane
ppb	parts per billion
ppm	parts per million
R.E.	reductive elimination
rac	racemic
Rf	retention factor
SET	single electron transfer
SIPr	1,3-bis-(2,6-diisopropylphenyl)imidazolinium
SN2	substitution nucleophilic bimolecular
TBAF	tetrabutylammoium fluoride
TBS	tert-butyldimethylsilyl
tbtpy	4,4′,4″-tri-tert-butyl-2,2′:6′,2″-terpyridine
t-Bu	tert-butyl
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxy
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TM	transition metal
TMB	1,3,5-trimethoxybenzene
TMCTS	2,4,6,8-tetramethylcyclotetrasiloxane
TMDSO	tetramethyldisiloxane
TMPDA	N,N,N’,N’-Tetramethyl-p-phenylenediamine
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

Acknowledgement

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DEDICATION

To my parents and grandparents

Chapter 1 Stereospecific and Regioselective Synthesis of *E*-Allylic Alcohols through Reductive Cross Coupling of Terminal Alkynes

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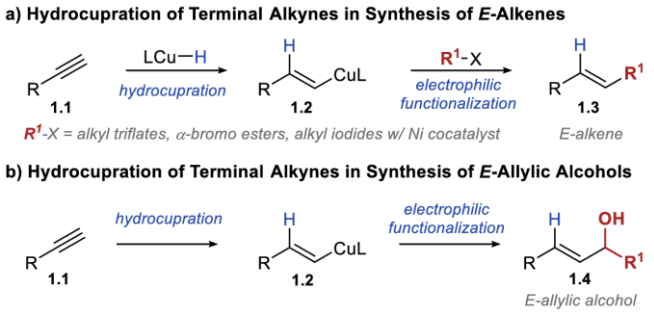
1.1 Introduction

Hydroalkylation of terminal alkynes is a powerful method for making disubstituted alkenes with different substitution patterns and high selectivity.[1-9] Our group has developed several catalytic hydroalkylation reactions that produce *E*-alkenes using an approach with two key steps (Scheme 1.1a): first, hydrocupration of an alkyne[10,11] (**1**) forms an alkenyl copper intermediate (**2**) with precise control over the regio- and diastereoselectivity;[12-18] second, the alkenyl copper intermediate stereospecifically reacts with various alkyl electrophiles, such as alkyl triflates,[6] α-halo carbonyls,[8] or alkyl halides in the presence of a metal cocatalyst to yield *E*-alkene products (**3**).[7] The successful implementation of this strategy requires identifying alkyl electrophiles that are sufficiently reactive to overcome the relatively low reactivity of alkenyl copper complexes, but do not react with copper hydride complexes.

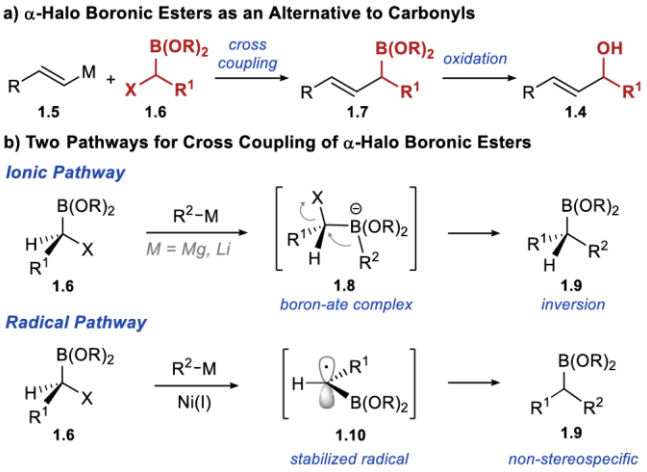
Scheme 1.1 Hydrocupration in Transformations of Terminal Alkynes



We have been interested in expanding the hydroalkylation approach to enable synthesis of *E*-alkenes with simultaneous introduction of a functional group in the allylic position. Allylic alcohols are particularly attractive targets for such a transformation as they are often featured in bioactive molecules and synthetic intermediates.[19] We reasoned that terminal alkynes can be transformed into allylic alcohols with anti-Markovnikov selectivity through hydrocupration and reaction of the alkenyl copper intermediate (**1.2**) with an appropriate electrophile (Scheme 1.1b).

The most intuitive way to access allylic alcohols from the alkenyl copper intermediate is reaction with aldehydes or ketones. Unfortunately, integrating carbonyls into the hydroalkylation approach outlined in Scheme 1a presents several challenges. NHC supported copper hydride complexes involved in formation of the alkenyl copper intermediate efficiently add to carbonyls and promote their reduction.[20-23] Another challenge stems from relatively low reactivity of alkenyl copper intermediates. Despite numerous examples of reactions of allylic[24-31] and propargylic[32,33] copper complexes with carbonyls, we found that under a variety of reaction conditions, stoichiometric reactions between NHC-supported alkenyl copper complexes and aldehydes do not occur.

Scheme 1.2 α-Halo Boronic Esters as Electrophiles



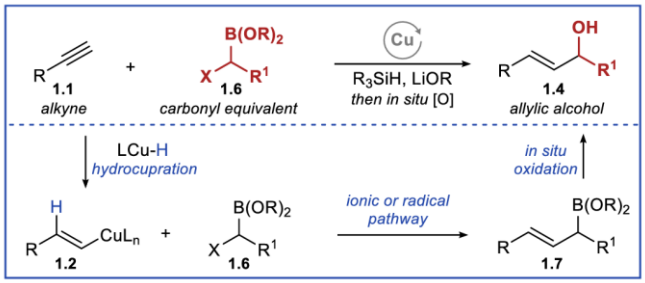
α-Halo boronic esters (**1.6**) can act as a functional equivalent of carbonyl electrophiles. They can be made directly from aldehydes and ketones[34] and provide allylic alcohols (**1.4**) after cross-coupling with alkenyl organometallic reagents (**1.5**) and in situ oxidation (Scheme 1.2a).[35] Furthermore, the key cross-coupling with organometallic compounds can proceed via two distinct mechanisms (Scheme 1.2b). As Matteson's pioneering work has shown, with nucleophilic organolithium and Grignard reagents, the cross-coupling involves the formation of boron-ate complexes (**1.8**) and a subsequent 1,2-metallate shift.[36-39] Alternatively, transition metal catalyzed cross-coupling reactions involve stabilized α-boryl radical intermediates[40-43] (**1.10**) formed through single electron transfer (SET) reduction of α-halo boronic esters.[44-48] Even though the same cross coupling product (**1.9**) is formed in both pathways, mechanistic differences produce two different stereochemical outcomes: the ionic pathway is stereospecific (inversion at the α stereocenter), while the radical pathway leads to the loss of stereochemical information.

Alkenyl copper complexes are both nucleophilic and capable of SET reduction of activated organohalides.[8] As a result, both ionic and radical mechanisms offer plausible pathways for coupling with α-halo boronic esters. This creates an opportunity to combine the unique reactivity of α-halo boronic esters with established hydrocupration of alkynes and develop a new method for the synthesis of allylic alcohols. As shown in Scheme 3, allylic alcohols (**1.4**) would be generated

through a convergent reductive cross coupling of terminal alkynes (**1.1**) and α-halo boronic esters (**1.6**), followed by in situ oxidation.

The importance of allylic alcohols in organic synthesis has prompted the development of numerous approaches for their synthesis.[19] For example, asymmetric synthesis of allylic alcohols can be accomplished through kinetic resolution,[49] dynamic kinetic resolution,[50,51] reduction of enones,[52,53] allylic substitution,[54,55] or through organocatalytic reactions.[56] Among methods that result in the formation of a new C-C bond, the most general is the addition of organozinc reagents derived from alkynes through hydrometallation and transmetalation. This approach was pioneered by Oppolzer[57] and further developed by Walsh,[58-60] Seto,[61,62] Wipf,[63] and others.[64-66] Other organometallic reagents have also been used, but with less success.[67-70]

Scheme 1.3 Proposed Synthesis of Allylic Alcohols

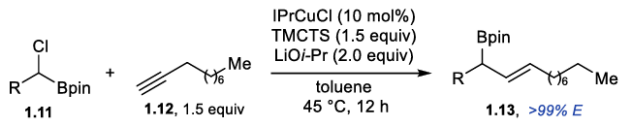


The key feature of the transformation shown in Scheme 1.3 is that it avoids stoichiometric formation of alkenyl metal reagents from alkynes. The benefits of using alkynes directly have been amply demonstrated[71,72] through the pioneering work of Jamison,[73,74] Montgomery,[75-81] Krische,[82,83] and others[84-86] on reductive cross coupling of alkynes with carbonyls. Their approach has provided excellent results in asymmetric synthesis of allylic alcohols starting with internal alkynes.[73,81,83,86] Although terminal alkynes have also been used in these reactions,[77-80] unlike internal alkynes, they have not been amenable to applications in asymmetric synthesis of allylic alcohols.[76,81] We set out to address this challenge by pursuing the development of the asymmetric anti-Markovnikov reductive cross coupling of terminal alkynes and α-halo boronic esters.[87] In the process, we aimed to resolve the underlying mechanistic ambiguity (ionic vs radical) of the reaction and exploit the stereochemical consequences of the actual mechanism.

1.2 Results and Discussion

Following the approach outlined in Scheme 1.3, we developed a copper-catalyzed reductive coupling of alkynes and α-halo boronic esters (Table 1.1). The best results were obtained using IPrCuCl as the precatalyst, tetramethylcyclotetrasiloxane (TMCTS) as the hydride source, and LiO*i*-Pr as the turnover reagent (entry 1). A modest excess of alkyne (1.5 equiv) relative to the α-chloro Bpin was used in the reaction.

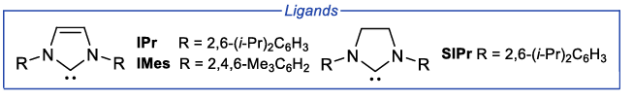
Table 1.1 Reaction Development



entry	change from standard conditions	yield
1	none	88%
2	SIPrCuCl *instead of* IPrCuCl	78%
3	IMesCuCl *instead of* IPrCuCl	19%
4	PMHS *instead of* TMCTS	79%
5	DMMS *instead of* TMCTS	24%
6	NaO*i*-Pr *instead of* LiO*i*-Pr	43%
7	LiO*t*-Bu *instead of* LiO*i*-Pr	76%
8	LiOMe *instead of* LiO*i*-Pr	0%
9	THF *instead of* toluene	31%
10	benzene *instead of* toluene	87%
11	isooctane *instead of* toluene	77%
12	25 °C *instead of* 45 °C	47%
14[b]	$Cl(CH_2)Bpin$ *instead of* **1.11**	94%
15[b]	$Br(CH_2)Bpin$ *instead of* **1.11**	58%
16[b]	$I(CH_2)Bpin$ *instead of* **1.11**	0%

[a]Yield determined by GC using internal standard. R = n-Butyl, [b]Product was **1.13-H** with R=H.

Ligands

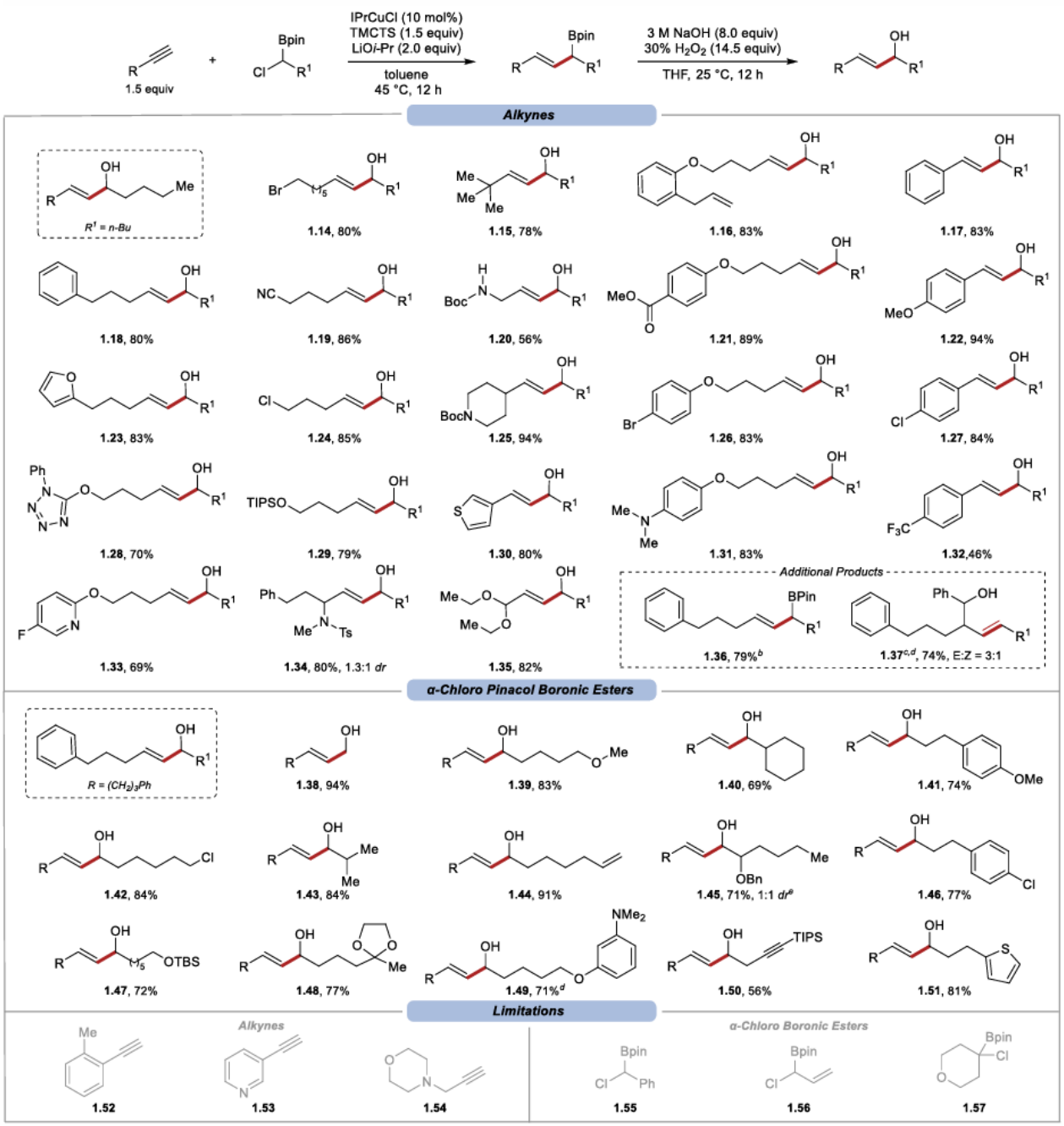


The results in Table 1 show how different reaction parameters affect the yield of the desired product. The highest yields were obtained with copper catalysts supported by IPr and SIPr ligands. IMes, which is closely related to IPr and SIPr, only afforded 19% of **1.13** (entries 2 and 3). The identity of the silane was critical to the success of the reaction.

While cyclic tetramer TMCTS and closely related PMHS showed good reactivity, structurally similar monomeric silanes like DMMS gave diminished yields (entries 4 and 5). Other silanes gave little or no desired product. Lithium isopropoxide and lithium *tert*-butoxide both worked well as turnover reagents (entries 1 and 7) but changing the counter ion to sodium produced inferior results (entry 6). Lithium methoxide also performed poorly, possibly due to low solubility (entry 8). At lower temperature (25 °C), only 47% yield of the product was formed after 12 h (entry 12), and the reaction required 3 days to complete. Less sterically demanding $Cl(CH_2)Bpin$ performed better than **1.11** (entry 14). Interestingly, more reactive α-bromo and α-iodo boronic esters performed worse as substrates in the reaction (entries 15 and 16).

Using our optimized conditions, we explored the scope of the reaction. After in situ oxidation of the allylic boronic esters, various allylic alcohols were obtained in good yields (Table 1.2). In general, we observed only the *E* isomer of the allylic alcohols in ^{1}H NMR of the crude reaction mixtures. Careful GC analysis of the crude reaction mixture containing product **1.18** using authentic samples of *E* and *Z* isomers confirmed an *E*/*Z* ratio greater than 200:1. Alkynes containing alkyl bromides (**1.14**), alkyl chlorides (**1.24**), nitriles (**1.19**), esters (**1.21**), protected

Table 1.2 Substrate Scope



[a]Yields of isolated products are reported. Reactions performed on 0.5 mmol scale. [b]Allylic boronic ester isolated without oxidation (see SI). [c]Reaction of **36** with benzaldehyde. [d]Reactions performed on 0.25 mmol scale. [e]Starting α-chloro boronic ester was a 1:1 mixture of diastereoisomers.

amines (**1.25**), protected alcohols (**1.29**), aryl chlorides (**1.27**), aryl bromides (**1.26**), sulfonamides (**1.34**), and acetals (**1.35**) were well tolerated. The presence of mildly acidic Boc-protected primary amine (**1.20**) was not detrimental for the reaction, although the yield of the desired product was diminished. Aryl acetylenes with electron-donating (**1.22**) and mildly electron-withdrawing (**1.27**) functional groups performed well, while the presence of a strongly electron-withdrawing group

(**1.32**) resulted in a diminished yield. The reaction also tolerated alkynes with sterically demanding alkyl substituents (**1.15**). Several heterocycles could successfully be incorporated into the alkyne substrates, including furans (**1.23**), tetrazoles (**1.28**), thiophenes (**1.30**), and fluoro pyridines (**1.33**).

Allylic boronic ester **1.36** can be isolated after careful column chromatography in 79% yield. This allows a range of other products to be accessed using established transformations of allylic boronic esters.[88-90] In some instances, crude allylic boronic ester can be used directly in subsequent transformations. For example, when benzaldehyde is added to the crude reaction mixture containing **1.36**, transposed homoallylic alcohol **1.37** is obtained in 74% overall yield.

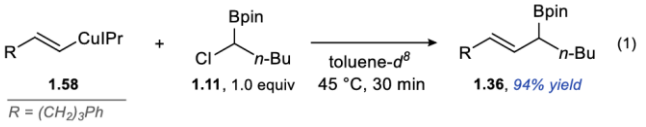
We also investigated the reactivity of various α-chloro Bpins and found that their functional group compatibility is similar to the selectivity observed in reactions of functionalized alkynes. The unsubstituted α-chloro boronic ester (**1.38**) gave an excellent yield, while additional substitution at the β position of boronic esters (**1.43** and **1.45**) resulted in lower yields.

We noted several limitations of the new reaction. Ortho-substituted aryl alkynes (**1.52**) and alkynes containing strongly coordinating groups (**1.53**, **1.54**) gave low yields of allylic alcohol products. α-Chloro boronic esters containing aryl (**1.55**) or alkenyl (**1.56**) substituents at the α-carbon provided no allylic alcohol product. Similarly, α, α-dialkyl-α-halo boronic esters (**1.57**) did not afford the expected tertiary allylic alcohols, indicating the negative effect of steric hindrance on the reaction.

The catalytic alkenylation reaction of α-chloro boronic esters is a complement and not a replacement for the stoichiometric reactions performed using alkenyl lithium or Grignard reagents. An excellent recent study by Kazmaier et al.[91] has shown that consistently high yields in stoichiometric alkenylation reactions are observed when at least one of the reactants is sterically hindered. Trisubstituted, *Z*-disubstituted, and 2-alkenyl organometallic reagents generally perform well. With less hindered organometallic reagents, only sterically hindered α-chloro boronic esters perform well. The trends we observed in the catalytic reaction are complementary: less hindered α-chloro boronic esters perform the best and *E*-alkenyl fragments are delivered.

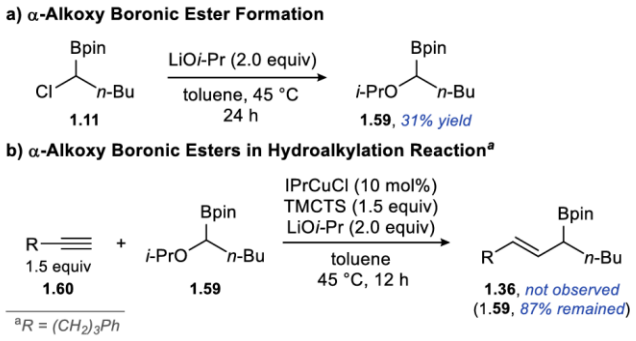
We had two main goals in mind when exploring the reaction mechanism. First, we wanted to establish if the alkenyl copper complex is a catalytic intermediate in the reaction. Second, we wanted to determine if the cross coupling of the alkenyl copper and α-chloro boronic esters proceeds through a radical or ionic mechanism. Establishing the exact mechanism was important because of the differences in the stereochemical outcomes of the two pathways and implications that would have on the synthesis of chiral allylic alcohols.

Scheme 1.4 Stoichiometric Addition of Alkenyl Copper to α-Chloro Bpin



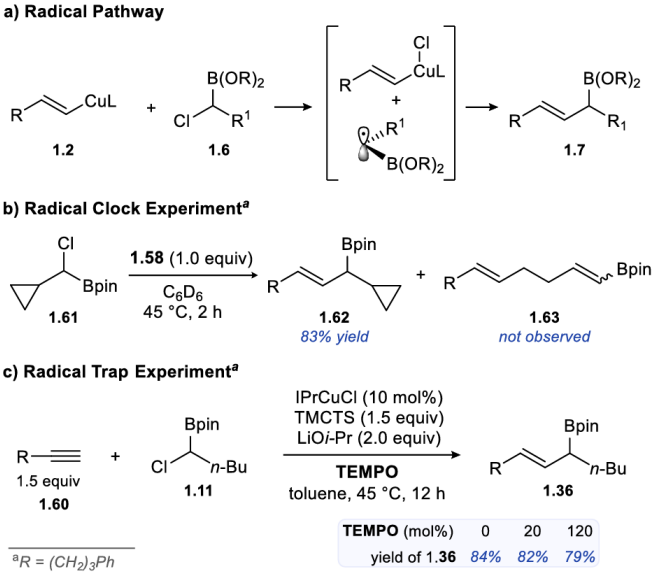
Initial mechanistic experiments focused on presumed intermediates in the catalytic reaction. In a stoichiometric experiment, we found that reacting alkenyl copper complex **1.58** with α-chloro boronic ester **1.11** quickly produces allylic boronic ester **1.36** (Scheme 1.4). This result supports the proposed involvement of an alkenyl copper intermediate and its reaction with α-chloro boronic esters.

Scheme 1.5 α-Alkoxy Boronic Esters as Intermediates



We also examined α-alkoxy boronic esters as possible intermediates in the reaction. As expected, LiO*i*-Pr reacts with α-chloro boronic ester **1.11** at 45 °C to produce α-alkoxy boronic ester **1.59** (Scheme 1.5a).[92] However, the reaction is slower than the catalytic hydroalkylation reaction performed at the same temperature and affords only 17% of **1.59** after 12 h, and 31% after 24 h. Furthermore, when used as a substrate in a catalytic reaction, α-isopropoxy boronic ester **1.59** did not afford the desired product (Scheme 1.5b) with 87% of **1.59** remaining after 12 h. Together, these results make α-isopropoxy boronic esters unlikely intermediates in the reaction.

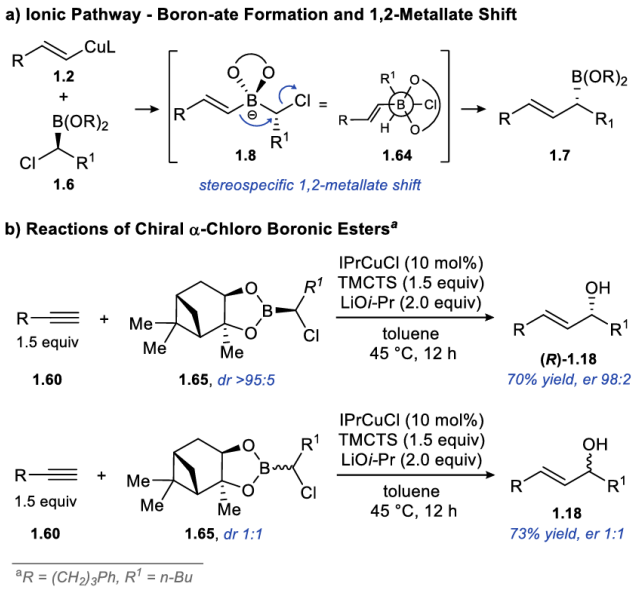
Scheme 1.6 Radical Mechanism



Next, we focused on exploring the mechanism of the key reaction between the alkenyl copper intermediate and the electrophile. A plausible radical mechanism involving SET reduction of α-chloro boronic esters by the alkenyl copper intermediate is presented in Scheme 1.6a. α-Chloro boronic esters have been shown to undergo SET reduction[44-48] to form the stabilized alkyl radical. At the same time, alkenyl copper complex (**1.2**) is known to reduce α-bromo carboxylic esters through SET.[8]

To evaluate the relevance of the proposed radical mechanism, we performed radical clock and radical trap experiments. Alkenyl copper **1.58** reacts with cyclopropyl α-chloro Bpin (**1.61**) to produce only the unrearranged product **1.62** in 83% yield (Scheme 1.6b). We also found that up to 120 mol% of TEMPO can be added to the catalytic reaction without a significant decrease in the yield of the allylic boronic ester (Scheme 5c). The results of the two experiments are inconsistent with the SET mechanism and the formation of free radical intermediates.[93,94]

Scheme 1.7 Ionic Mechanism

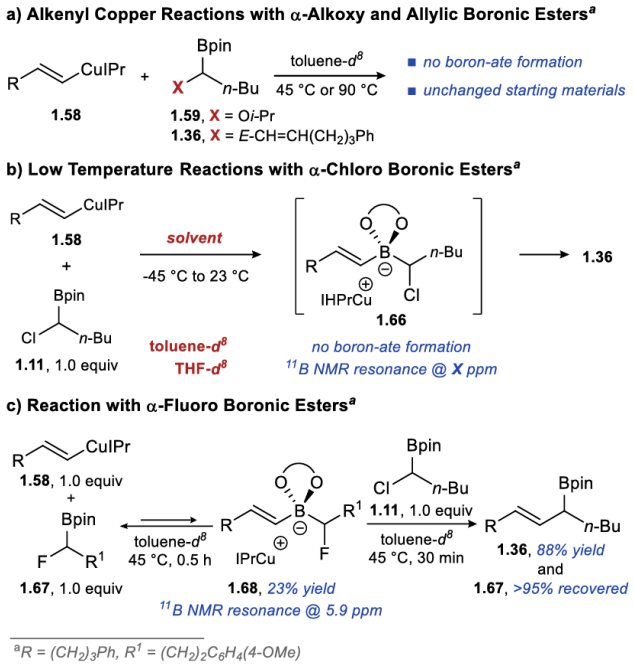


An alternative mechanistic hypothesis for the cross coupling is presented in Scheme 1.7a. The addition of alkenyl copper (**1.2**) to the α-chloro boronic ester (**1.6**) forms a boron-ate complex (**1.8**). This complex undergoes a 1,2-metallate shift exclusively through a conformation with antiperiplanar arrangement of the migrating alkenyl group and the leaving group at the α carbon (see **1.64**).[38] As a result, the cross coupling is stereospecific and proceeds with the inversion of configuration at the α-carbon.

To probe this alternative mechanistic hypothesis, we investigated the reaction with a single enantiomer of α-chloro boronic ester **1.65** (>99% ee, >95:5 dr), prepared using α-pinane diol as a chiral auxiliary (Scheme 1.7). The *R* configuration of the obtained allylic alcohol **(*R*)-1.18** indicates inversion of configuration at the α-carbon of the boronic ester. There is also strong

support for the stereospecificity of the reaction. The enantiomeric ratio of the allylic alcohol **(*R*)-1.18** (98:2) reflected the diastereomeric ratio of the starting α-chloro boronic ester (>95:5). Furthermore, the chiral auxiliary alone had no effect on reaction selectivity: a 1:1 mixture of diastereoisomeric α-chloro boronic esters produced racemic allylic alcohol **1.18** (Scheme 1.7b). Overall, the stereochemical outcomes of these experiments are fully consistent with an ionic mechanism involving boron-ate formation and stereospecific 1,2-metallate shift.[95]

Scheme 1.8 Boron-ate Complex Formation



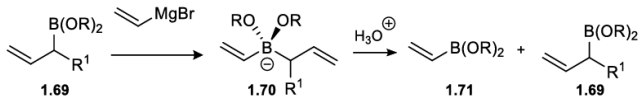
With evidence pointing to the ionic mechanism, we searched for evidence supporting the formation of the boron-ate complex in stoichiometric reactions of alkenyl copper intermediate with various boronic esters. Monitoring stoichiometric reactions of alkenyl copper intermediate (**1.58**) with α-isopropoxy boronic ester **1.59** or allylic boronic ester **1.36** by in situ ^{1}H and ^{11}B NMR showed no change of the starting materials even at 90 °C (Scheme 1.8a). Similarly, monitoring a stoichiometric reaction of **1.58** and α-chloro boronic ester **1.11** in toluene-d^8 at temperatures between -50 °C and 25 °C (Scheme 1.8b) did not provide definitive evidence for the formation of the boron-ate intermediate.

However, the same experiment performed in THF-d^8 provided evidence consistent with the presence of a low concentration of boron-ate intermediate **1.66** within the temperature range (broad resonance in ^{11}B NMR at 4.8 ppm). These results support reversible, though unfavorable, boron-ate formation in a reaction of α-chloro boronic esters. Presumably, the higher dielectric constant of THF (ε=7.6 for THF vs ε=2.4 for toluene) increases the concentration of **1.66**. Furthermore, in a reaction with α-fluoro boronic ester **1.67**, we saw evidence of the boron-ate formation in 23%

yield within 30 min (Scheme 1.8c). The balance of the starting materials remained unchanged after an additional 2 h.

Upon addition of α-chloro boronic ester **1.11** to the reaction mixture containing boron-ate complex **1.68**, we observed full recovery of the α-fluoro boronic ester (**1.67**) and the formation of cross-coupling product **1.36**. These results argue for a reversible and thermodynamically unfavorable formation of the boron-ate complex **1.68**.

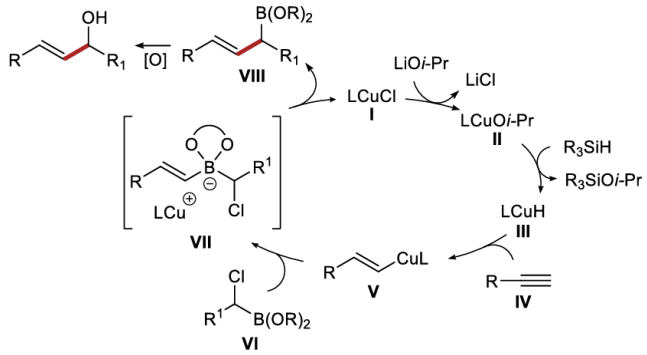
Scheme 1.9 Addition of Alkenyl Grignard to Allylic Boronic Ester



The reactions of the alkenyl copper intermediate with various boronic esters provide a mechanistic basis for understanding the differences in the scopes of this catalytic reaction and the stoichiometric alkenylation with organolithium and Grignard reagents (see above). Kazmaier has recently shown that the main side reaction in stoichiometric alkenylation is the addition of the organometallic reagent to the allylic boronic ester product (Scheme 1.9).[91] Protonolysis of the resulting boron-ate complex (**1.70**) at the end of the reaction provides a mixture of the desired allylic boronic ester (**1.69**) and the undesired vinyl boronic ester (**1.71**). As a result, good yields in stoichiometric reactions are realized only with substrates that can sterically impede the formation of boron-ate complex **1.70**.

We found that the alkenyl copper intermediate does not react with allylic boronic esters, or if it does, the reaction is reversible and thermodynamically unfavorable (see Scheme 1.8a). As a result, the main side reaction described by Kazmaier does not occur in the copper-catalyzed transformation,[96] extending the scope to less sterically demanding substrates.

Scheme 1.10 Proposed Mechanism



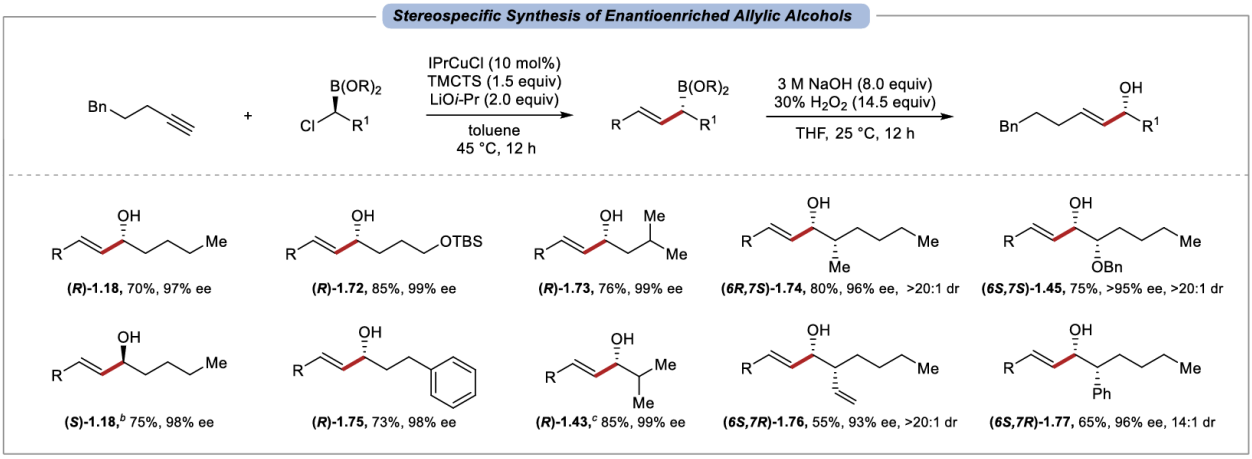
Based on our mechanistic investigation and the established chemistry of copper hydride complexes, we suggest the formation of allylic alcohols proceeds through the mechanism shown in Scheme 1.10. The process starts with the formation of copper hydride (**III**) through transmetalation of copper alkoxide with a silane,[10] followed by the formation of alkenyl copper complex (**V**) through

hydrocupration of the terminal alkyne.[10] Addition to α-chloro boronic ester forms boron-ate complex (**VII**). Finally, 1,2-metallate shift, and subsequent oxidation, produce the desired allylic alcohol.

Our mechanistic studies suggest that the new reaction can be applied in the robust and highly selective synthesis of chiral allylic alcohols from terminal alkynes. We demonstrated that the stereochemistry of the starting materials fully controls the absolute configuration and enantiomeric excess of the allylic alcohols. The required enantioenriched α-chloro boronic ester can be accessed in several ways using different starting materials.[97] A highly selective asymmetric synthesis from alkyl boronic esters was originally discovered by Matteson[98] and developed by others[99] and relies on chiral auxiliaries. Jacobsen[100] recently reported an approach based on enantioselective catalytic 1,2-metallate shift, while the method reported by XU[34] uses carbonyls as starting materials. Finally, enantioselective hydrogenation also provides access to highly enantioenriched α-chloro boronic esters.[101]

In practice, we found Matteson's synthesis of chiral α-chloro boronic esters using readily available and affordable α-pinanediol to be highly selective and easy to execute. A range of chiral α-chloro Bpinane esters (pinane = pinane diol) were prepared by this method and used in the hydroalkylation reaction to provide chiral allylic alcohols (Table 1.3). Boronic esters with branching in the β and γ positions gave excellent selectivity (**1.43** and **1.73**). Even boronic esters with linear alkyl substituents reacted with excellent selectivity. This is particularly attractive given that enantioenriched di-alkyl allylic alcohols are difficult to access by direct alkenylation of linear unbranched aldehydes.[102] Products **1.18**, **1.72**, and **1.75** were all obtained in high stereoselectivity and yield, showcasing the utility of our method. Furthermore, access to both (+)-and (-) isomers of pinane diol auxiliary allowed us to prepare *R* and *S* enantiomers of alcohol **1.18**. Enantioenriched α-chloro Bpin esters performed as well as Bpinane esters, providing **1.43** in excellent enantiopurity. Finally, Matteson's homologation method allowed the synthesis of highly enantioenriched allylic alcohols containing two stereocenters with high diastereoselectivity (**1.45**, **1.74**, **1.76**, and **1.77**).

Table 1.3 Synthesis of Enantioenriched Allylic Alcohols



[a]Yields of isolated products are reported. Reactions performed on 0.5 mmol scale. Enantiomeric excess of allylic alcohols determined by chiral HPLC. Boronic ester of (+)-pinanediol was used. R = $(CH_2)_3Ph$. [b]Boronic ester of (-)-pinanediol was used with the opposite absolute configuration at the α carbon. [c]Bpin ester was used.

1.3 Conclusion

In conclusion, we have developed a method for the convergent synthesis of allylic alcohols directly from terminal alkynes. This transformation involves reductive cross coupling of an alkyne with an α-chloro boronic ester followed by in situ oxidation of the boronic ester to an alcohol. The process is highly selective for the *E*-alkene and tolerates a broad range of functional groups. Experimental studies support a mechanism that involves hydrocupration of the alkyne and formation of the alkenyl copper intermediate. Cross coupling of the intermediate with an α-chloro boronic ester involves boronic formation and 1,2-metallate shift. The overall process is stereospecific and proceeds with inversion at the stereocenter of the α-chloro boronic ester, allowing for the convenient synthesis of enantioenriched allylic boronic ester products. This reaction integrates hydrometallation and boron-ate chemistry eschewing the need for stoichiometric organometallic reagents to form the boron-ate complex.

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 Agilent 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, C_6D_6: δ 7.16 ppm, or CD_2Cl_2: δ 5.32 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, C_6D_6: δ 128.0 ppm or CD_2Cl_2: δ 54.0 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). 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 an Agilent 5973 GC-MS and a Bruker Esquire LC ion trap mass spectrometer. Specific rotations ($[\alpha]_D^t$) were measured using Jasco P-2000 Polarimeter at the indicated temperature with a sodium lamp (λ = 589 nm) with a 100 mm cell and concentrations (g/(100mL)) reported in the corresponding solvent. 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 and 5.5 min @ 250 °C.

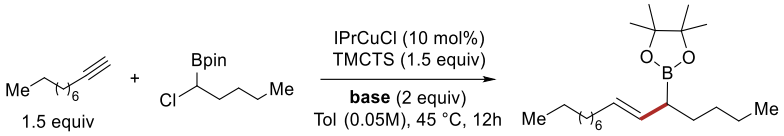
Materials: THF, CH_2Cl_2, ether, benzene, and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous isooctane was purchased from Millipore Sigma and was subsequently degassed and stored over 4Å molecular sieves. Pinacolborane was purchase from TCI America and distilled 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. Commercial reagents were purchased from Millipore Sigma, TCI America, GFS-Chemicals, Ark-Pharm, Combi-Blocks, Oakwood Chemicals, Strem Chemicals and Alfa Aesar.

1.4.2. Reaction Development

All the reactions shown in table S1 to table S6 were performed on a 0.05 mmol scale. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, base, copper catalyst, solvent, internal standard, silane, and alkyne, respectively. The reaction mixture was stirred at room temp for 5

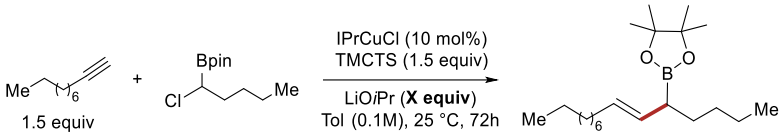
minutes, until the yellow color disappeared. Then α-chloro boronic ester was added with the internal standard trimethoxybenzene (TMB). The reaction mixture was vigorously stirred at the indicated temperature for the specified time. An aliquot (100 µL) was taken and then analyzed by ^{1}H NMR or gas chromatography.

Table 1.4 Base Screen



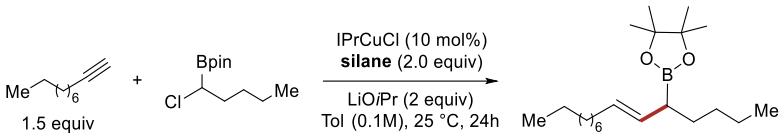
Entry	Base	Yield (%)
1	LiO*i*Pr	93
2	NaO*i*Pr	65
3	KOEt	74
4	LiO*t*Bu	68
5	NaOMe	22
6	LiOMe	0

Table 1.5 Base Equivalence



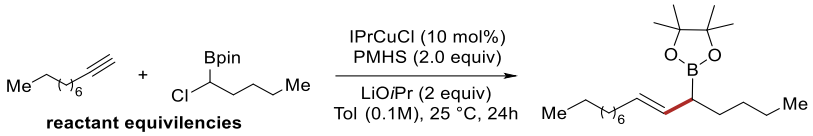
Entry	Equivalents	Yield (%)
1	1	45
2	1.5	59
3	2	76
4	3	32

Table 1.6 Silane Screen



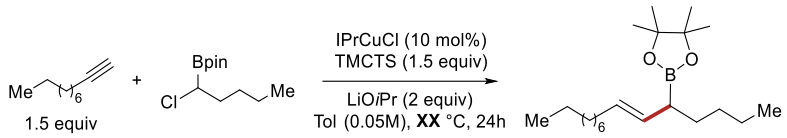
Entry	Silane	Yield (%)
1	TMCTS	70
2	PMHS	60
3	$Me(MeO)_2SiH$	54
4	$PhSiH_3$	12
5	Ph_3SiH	5
6	Et_3SiH	0
7	TMDSO	7
8	$(EtO)_3SiH$	16
9	$Me(EtO)_2SiH$	6

Table 1.7 Stoichiometry Screen



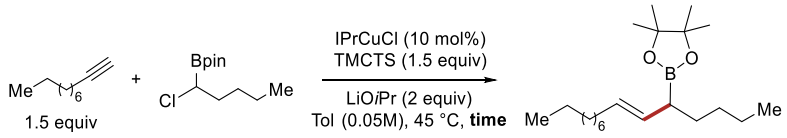
Entry	Ratio of Alkyne : α-Cl Bpin	Yield (%)
1	2 : 1	64
2	1.5 : 1	75
3	1 : 1	44
4	1 : 1.5	47
5	1 : 2	43

Table 1.8 Temperature Screen



Entry	Temperature	Yield (%)
1	25	61
2	45	84
3	60	82
4	90	75

Table 1.9 Reaction Time Screen



Entry	Time (hours)	Yield (%)
1	3.5	82
2	8	93
3	30	94
4	96	91

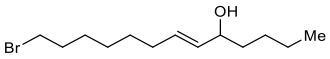
1.4.3 General Procedure A

In a nitrogen-filled glovebox, a 20 ml scintillation vial was charged with IPrCuCl (0.05 mmol, 0.1 equiv), LiO*i*-Pr (1 mmol, 2 equiv) and a stir bar. To the vial was added TMCTS (0.75 mmol, 1.5 equiv), alkyne (0.75 mmol, 1.5 equiv) and toluene (0.05 M) and the resulting mixture was stirred at 25 °C. A bright yellow color was immediately observed, and the reaction mixture was stirred for 5 minutes with the bright yellow color dissipating to a pale yellow. α-Chloro boronic ester (0.5

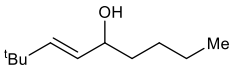
mmol, 1.0 equiv) was then added to the reaction vial and the reaction mixture was stirred at 45 °C overnight. The vial was opened to air and THF was added (4 mL), at which point the reaction mixture was cooled to 0 °C. A solution of NaOH (1.0 mL, 3 mmol, 6 equiv) and H_2O_2 (30 % *w/w* in H_2O, 850 µL, 7.5 mmol, 15 equiv) was added dropwise to the cooled reaction mixture and resulting mixture was stirred for 5 minutes before removal from the ice bath. After 12 h at room temperature, the reaction mixture was passed through a plug of silica gel, concentrated, and loaded onto an alumina flash chromatography column (neutral, Brockman II, doped with 5% diethylmethylamine). The column was flushed with ten column volumes of hexanes before the product was eluted with a mixture of hexanes/EtOAc.

1.4.4 Characterization of Products

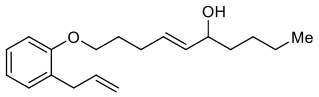
Racemic Allylic Alcohol Products



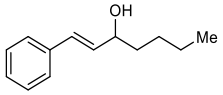
(6*E*)-13-bromotridec-6-en-5-ol (1.14) was prepared according to general procedure A and was purified by alumina chromatography, 0-30% EtOAc in hexanes and was isolated as a colorless liquid (110 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.66 – 5.58 (m, 1H), 5.46 (dd, *J* = 15.3, 7.1 Hz, 1H), 4.04 (q, *J* = 6.5 Hz, 1H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.03 (q, *J* = 7.1 Hz, 2H), 1.85 (p, *J* = 7.5 Hz 2H), 1.61 – 1.52 (m, 3H), 1.45 – 1.29 (m, 10H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.4, 131.6, 73.1, 37.1, 33.9, 32.8, 32.0, 29.0, 28.2, 28.0, 27.7, 22.7, 14.1. MS-ESI (m/z): $[M]^+$ calculated for $C_{13}H_{25}BrO$, 276.1; found 276.0. FTIR (neat, cm^{-1}): 3349 (br), 2931 (s), 1669 (w), 1465 (s), 1378 (m), 1259 (m), 1127 (m), 969 (s), 897 (w).



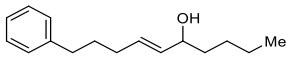
(3*E*)-2,2-dimethylnon-3-en-5-ol (1.15) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a light yellow oil (66 mg, 78% yield). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 5.65 (d, *J* = 15.7 Hz, 1H), 5.36 (dd, *J* = 15.6, 7.1 Hz, 1H), 4.03 (q, *J* = 6.6 Hz, 1H), 1.57-1.47 (m, 2H), 1.39 – 1.21 (m, 5H), 1.01 (s, 9H), 0.90 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 128.0, 73.5, 37.2, 32.8, 29.6, 27.8, 22.7, 14.1. GCMS (EI) calculated for $[M]^+$ 170.2, found 170.2. FTIR (neat, cm^{-1}): 3341 (br), 2956 (s), 2861 (s), 1662 (w), 1463 (m), 1364 (m), 1131 (w), 1023 (m), 972 (m).



(6*E*)-10-[2-(prop-2-en-1-yl)phenoxy]dec-6-en-5-ol (1.16) was prepared according to general procedure A and was purified by alumina chromatography, 0-40% EtOAc in hexanes and was isolated as a yellow oil (121 mg, 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 – 7.09 (m, 2H), 6.95 – 6.75 (m, 2H), 5.99 (ddt, *J* = 16.8, 9.9, 6.6 Hz, 1H), 5.69 (dt, *J* = 13.9, 6.6 Hz, 1H), 5.51 (dd, *J* = 15.4, 6.9 Hz, 1H), 5.16 – 4.95 (m, 2H), 4.13 – 3.91 (m, 3H), 3.40 (d, *J* = 6.7 Hz, 2H), 2.25 (q, *J* = 7.1 Hz, 2H), 1.89 (p, *J* = 6.6 Hz, 2H), 1.55 – 1.26 (m, 7H), 0.97 – 0.82 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 137.1, 134.1, 130.6, 129.8, 128.7, 127.3, 120.4, 115.3, 111.2, 73.0, 67.0, 37.1, 34.5, 29.0, 28.8, 27.7, 22.7, 14.1. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{19}H_{27}O$, 271.2; found 271.1. FTIR (neat, cm^{-1}): 3357 (br), 3075 (w), 2930 (s), 2859 (s), 1637 (w), 1600 (m), 1493 (s), 1454 (s), 1243 (s), 1047 (s), 970 (s), 911 (m), 750 (s).

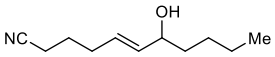


(1*E*)-1-phenylhept-1-en-3-ol (1.17) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a yellow oil (79 mg, 83% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 7.29 – 7.23 (m, 2H), 7.15 – 7.02 (m, 3H), 6.45 (d, *J* = 14.7 Hz, 1H), 6.09 (dd, *J* = 15.9, 6.4 Hz, 1H), 4.00 (q, *J* = 5.6 Hz, 1H), 1.55 – 1.22 (m, 6H), 1.00 (s, 1H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 137.5, 133.6, 130.0, 128.9, 127.7, 126.9, 73.0, 37.6, 28.1, 23.1, 14.3. GCMS (EI) calculated for $[M]^+$ 190.1, found 190.1. FTIR (neat, cm^{-1}): 3350 (br), 3026 (m), 2929 (s), 2858 (s), 1599 (w), 1494 (m), 1448 (m), 1131 (m), 966 (s), 749 (s), 693 (s).

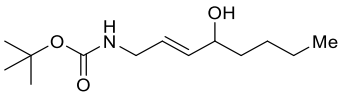


(6*E*)-10-phenyldec-6-en-5-ol (1.18) was prepared according to general procedure A and was purified by alumina chromatography, 0-25% EtOAc in hexanes and was isolated as a clear light yellow liquid (93 mg, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.24 – 7.13 (m, 3H), 5.71 – 5.59 (m, 1H), 5.47 (ddt, *J* = 15.3, 6.9, 1.3 Hz, 1H), 4.04 (q, *J* = 6.6 Hz, 1H), 2.62 (t, *J* = 7.3 Hz, 2H), 2.08 (q, *J* = 6.8 Hz, 2H), 1.72 (p, *J* = 7.7 Hz, 2H), 1.55 – 1.46 (m, 3H), 1.38 – 1.24 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 133.7, 131.4, 128.5, 128.4, 125.8, 73.2, 37.1, 35.4, 31.8, 31.0, 27.8, 22.7, 14.1. GCMS (EI) calculated for $[M]^+$ 232.2,

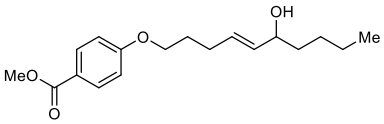
found 232.0. FTIR (neat, cm^{-1}): 3359 (br), 3025 (m), 2929 (s), 2857 (s), 1603 (w), 1496 (m), 1453 (m), 968 (m), 746 (m), 699 (s).



(5*E*)-7-hydroxyundec-5-enenitrile (1.19) was prepared according to general procedure A and was purified by alumina chromatography, 0-70% EtOAc in hexanes and was isolated as a clear colorless oil (78 mg, 86% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66 – 5.50 (m, 2H), 4.07 (q, *J* = 5.9 Hz, 1H), 2.25 (q, *J* = 7.1 Hz, 2H), 2.26 – 2.15 (m, 2H), 1.76 (p, *J* = 7.4 Hz, 2H), 1.57 – 1.46 (m, 3H), 1.38 – 1.24 (m, 4H) 0.91 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.5, 128.5, 119.6, 72.6, 37.1, 30.9, 27.6, 24.8, 22.6, 16.4, 14.1. GCMS (EI) calculated for $[M]^+$ 181.1, found 181.3. FTIR (neat, cm^{-1}): 3434 (br), 2931 (s), 2859 (s), 2247 (m), 1669 (w), 1456 (m), 1379 (m), 1133 (m), 970 (s), 897 (w), 731 (w).

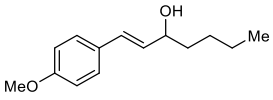


***tert*-butyl (*E*)-(4-hydroxyoct-2-en-1-yl)carbamate (1.20)** was prepared according to general procedure A and was obtained as a colorless liquid (69 mg, 56% yield) after purification by alumina chromatography (0-60% EtOAc in hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 – 5.52 (m, 2H), 4.57 (s, 1H), 4.16 – 4.04 (m, 1H), 3.80 – 3.62 (m, 2H), 1.57 – 1.48 (m, 2H), 1.45 (s, 9H), 1.41 – 1.18 (m, 5H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 135.0, 127.3, 79.5, 77.4, 76.9, 72.3, 42.0, 37.0, 28.5, 27.6, 22.7, 14.1. MS-ESI (m/z): $[M+Na]^+$ $C_{13}H_{25}NNaO_3$, 266.2, found 266.0. FTIR (neat, cm-1): 3355 (br), 2930 (s), 2860 (s), 1708 (s), 1695 (s), 1527 (s), 1251 (m), 1172 (s), 970 (m), 864 (w), 733 (m).

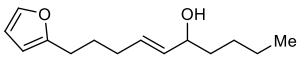


methyl 4-{[(4*E*)-6-hydroxydec-4-en-1-yl]oxy}benzoate (1.21) was prepared according to general procedure A and was purified by alumina chromatography, 0-45% EtOAc in hexanes and was isolated as a clear yellow oil (137 mg, 89% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 – 7.94 (m, 2H), 6.93 – 6.85 (m, 2H), 5.74 – 5.61 (m, 1H), 5.52 (dd, *J* = 15.5, 6.8 Hz, 1H), 4.10 – 3.97 (m, 3H), 3.88 (s, 3H), 2.24 (q, *J* = 7.1 Hz, 2H), 1.90 (p, *J* = 6.7 Hz, 2H), 1.58-1.42 (m, 3H), 1.36 – 1.23 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 162.9, 134.3, 131.6, 130.2, 122.4, 114.1, 72.9, 67.3, 51.9, 37.1, 28.6, 28.5, 27.7, 22.6, 14.1. MS-ESI (m/z): $[M+Na]^+$

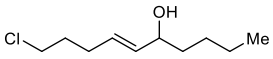
calculated for $C_{18}H_{26}NaO_4$, 329.2; found, 329.2. FTIR (neat, cm^{-1}): 3421 (br), 2952 (s), 2870 (s), 1719 (s), 1606 (s), 1511 (s), 1435 (s), 1254 (s), 1105 (s), 670 (s), 771 (s), 679 (s).



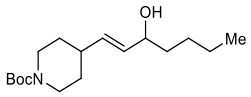
(1*E*)-1-(4-methoxyphenyl)hept-1-en-3-ol (1.22) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a yellow oil (103 mg, 94% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 6.89 – 6.82 (m, 2H), 6.51 (d, *J* = 15.8 Hz, 1H), 6.08 (dd, *J* = 15.9, 7.0 Hz, 1H), 4.25 (q, *J* = 6.3 Hz, 1H), 3.81 (s, 3H), 1.66 – 1.50 (m, 3H), 1.44 – 1.28 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 130.6, 129.7, 129.6, 127.7, 114.0, 73.2, 55.3, 37.2, 27.7, 22.7, 14.1. GCMS (EI) calculated for $[M]^+$ 220.1, found 220.1. FTIR (neat, cm^{-1}): 3366 (br), 2930 (s), 2858 (m), 1608 (m), 1511 (s), 1464 (w), 1249 (s), 1174 (m), 1036 (m), 967 (w), 817 (w).



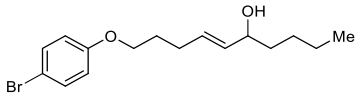
(6*E*)-10-(furan-2-yl)dec-6-en-5-ol (1.23) was prepared according to general procedure A and was purified by alumina chromatography, 0-45% EtOAc in hexanes and was isolated as a yellow oil (92 mg, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.28 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.98 (dd, *J* = 3.1, 1.0 Hz, 1H), 5.63 (dt, *J* = 15.2, 6.7 Hz, 1H), 5.48 (dd, *J* = 15.4, 7.0 Hz, 1H), 4.04 (q, *J* = 6.7 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.09 (q, *J* = 7.2 Hz, 2H), 1.73 (p, *J* = 7.9 Hz, 2H), 1.58 – 1.47 (m, 3H), 1.39 – 1.29 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1, 140.8, 134.0, 131.0, 110.1, 104.9, 73.1, 37.1, 31.6, 27.7, 27.6, 27.4, 22.7, 14.1. GCMS (EI) calculated for $[M]^+$ 222.2, found 222.2. FTIR (neat, cm^{-1}): 3355 (br), 2944 (s), 2859 (s), 1669 (w), 1597 (m), 1506 (s), 1147 (s), 1007 (s), 969 (s), 923 (w), 796 (m), 727 (s).



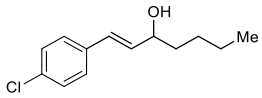
(6*E*)-10-chlorodec-6-en-5-ol (1.24) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a light yellow oil (81 mg, 85% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 5.41 – 5.21 (m, 2H), 3.88-3.76 (m, 1H), 3.10 (t, *J* = 6.6 Hz, 2H), 1.89 (q, *J* = 6.5 Hz, 2H), 1.51 – 1.22 (m, 8H), 0.95 – 0.77 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.7, 129.6, 72.9, 44.3, 37.1, 32.0, 29.3, 27.7, 22.7, 14.1. GCMS (EI) calculated for $[M]^+$ 190.1, found 190.1. FTIR (neat, cm^{-1}): 3358 (br), 2929 (s), 2859 (s), 1669 (w), 1467 (m), 1271 (m), 1130 (m), 970 (s), 730 (w), 655 (m).



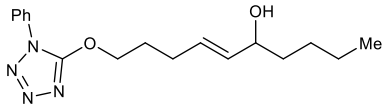
tert-butyl 4-[(1*E*)-3-hydroxyhept-1-en-1-yl]piperidine-1-carboxylate (1.25) was prepared according to general procedure A and was purified by alumina chromatography, 0-65% EtOAc in hexanes and was isolated as a yellow oil (140 mg, 94% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.58 (dd, *J* = 15.6, 6.2 Hz, 1H), 5.45 (dd, *J* = 16.3, 6.8 Hz, 1H), 4.17-3.96 (m,z 3H), 2.72 (t, *J* = 12.7 Hz, 2H), 2.18 – 2.02 (m, 1H), 1.70 – 1.62 (m, 2H), 1.57-1.47 (m, 2H), 1.45 (s, 9H), 1.40 – 1.17 (m, 7H), 0.89 (t, *J* = 6.9, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 135.0, 132.0, 79.3, 72.8, 38.4, 37.1, 31.7, 28.4, 27.6, 22.6, 14.0. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{17}H_{31}NNaO_3$, 320.2; found 320.3. FTIR (neat, cm^{-1}): 3437 (br), 2931 (s), 2858 (s), 1700 (s), 1419 (s), 1366 (s), 1171 (s), 970 (s), 867 (m), 769 (m), 679 (m).



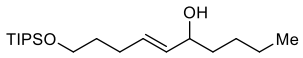
(6*E*)-10-(4-bromophenoxy)dec-6-en-5-ol (1.26) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a yellow oil (135 mg, 83% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 2H), 6.81 – 6.72 (m, 2H), 5.67 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.51 (dd, *J* = 15.4, 6.8 Hz, 1H), 4.05 (q, *J* = 6.5 Hz, 1H), 3.93 (t, *J* = 6.4 Hz, 2H), 2.22 (q, *J* = 7.1 Hz, 2H), 1.86 (p, *J* = 6.7 Hz, 2H), 1.58 – 1.46 (m, 2H), 1.40 – 1.21 (m, 5H) 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 134.2, 132.2, 130.3, 116.3, 112.7, 72.9, 67.4, 37.1, 28.6, 28.6, 27.7, 22.7, 14.1. MS-ESI (m/z): $[M-OH]^+$ calculated for $C_{16}H_{22}BrO$, 309.1; found 309.1. FTIR (neat, cm^{-1}): 3358 (br), 2929 (s), 2858 (s), 1591 (m), 1487 (s), 1285 (s), 1243 (s), 1071 (s), 970 (s), 821 (s), 640 (m).



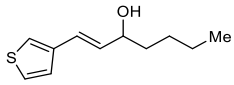
(1*E*)-1-(4-chlorophenyl)hept-1-en-3-ol (1.27) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a yellow solid (89 mg, 80% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 7.09 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.27 (d, *J* = 15.8 Hz, 1H), 5.94 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.95 (q, *J* = 6.1 Hz, 1H), 1.50 – 1.23 (m, 6H), 1.04 (s, 1H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 135.9, 134.2, 133.4, 129.0, 128.6, 128.0, 72.7, 37.6, 28.0, 23.1, 14.3. GCMS (EI) calculated for $[M]^+$ 224.1, found 224.1. FTIR (neat, cm^{-1}): 3348 (br), 2955 (s), 2929 (s), 2858 (s), 1491 (s), 1465 (w), 1090 (m), 1012 (m), 966 (m), 857 (w), 809 (m).



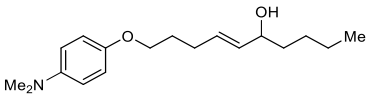
(6*E*)-10-[(1-phenyl-1H-1,2,3,4-tetrazol-5-yl)oxy]dec-6-en-5-ol (1.28) was prepared according to general procedure A and was purified by alumina chromatography, 0-60% EtOAc in hexanes and was isolated as a yellow liquid (110.1 mg, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 2H), 7.56 - 7.49 (m, 2H), 7.48 – 7.40 (m, 1H), 5.71 – 5.57 (m, 1H), 5.55 - 5.46 (m, 1H), 4.64 (t, *J* = 6.5 Hz, 2H), 4.03 (q, *J* = 6.4 Hz, 1H), 2.28 – 2.13 (m, 2H), 2.00 (dt, *J* = 8.1, 6.3 Hz, 2H), 1.74 (br, 1H), 1.61 – 1.39 (m, 2H), 1.38 – 1.19 (m, 4H), 0.94 – 0.84 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 134.9, 133.5, 129.6, 129.2, 129.0, 121.6, 73.5, 72.7, 37.1, 28.2 (2C), 27.7, 22.6, 14.1. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{17}H_{23}N_4O$, 299.2; found, 299.0. FTIR (neat, cm^{-1}): 3412 (br), 2955 (m), 2929 (m), 2858 (m), 1596 (s), 1563 (s), 1505 (s), 1460 (m), 1381 (w), 1021 (w), 759 (m).



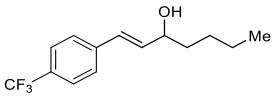
(6*E*)-10-{[tris(propan-2-yl)silyl]oxy}dec-6-en-5-ol (1.29) was prepared according to general procedure A and was purified by alumina chromatography, 0-55% EtOAc in hexanes and was isolated as a light yellow oil (129 mg, 79% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66 (dt, *J* = 15.2, 6.5 Hz, 1H), 5.48 (dd, *J* = 15.4, 7.0 Hz, 1H), 4.04 (q, *J* = 6.6 Hz, 1H), 3.69 (t, *J* = 6.4 Hz, 2H), 2.12 (q, *J* = 6.9 Hz, 2H), 1.68 – 1.44 (m, 5H), 1.37-1.26 (m, 4H), 1.12-1.01 (m, 21H), 0.90 (t, *J* = 6.8, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.6, 131.6, 73.2, 62.8, 37.2, 32.6, 28.6, 27.8, 22.7, 18.1, 14.1, 12.3, 12.1. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{19}H_{40}NaO_2Si$, 351.3; found, 351.3. FTIR (neat, cm^{-1}): 3347 (br), 2940 (s), 2865 (s), 1463 (m), 1382 (w), 1107 (s), 968 (m), 882 (m), 789 (w), 680 (m).



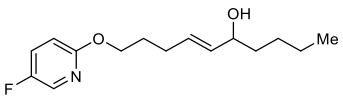
(1*E*)-1-(thiophen-3-yl)hept-1-en-3-ol (1.30) was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a yellow solid (79 mg, 80% yield). ^{1}H NMR (300 MHz, C_6D_6) δ 6.99 (dd, *J* = 5.1, 1.3 Hz, 1H), 6.84 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.77 (d, *J* = 1.8 Hz, 1H), 6.38 (d, *J* = 15.9 Hz, 1H), 5.92 (dd, *J* = 15.9, 6.5 Hz, 1H), 3.97 (q, *J* = 6.7 Hz, 1H), 1.55 – 1.23 (m, 6H), 1.04 (s, 1H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 140.1, 133.4, 126.1, 125.4, 124.3, 122.2, 72.9, 37.6, 28.1, 23.1, 14.3. GCMS (EI) calculated for $[M]^+$ 196.1, found 196.1. FTIR (neat, cm^{-1}): 3366 (br), 2955 (s), 2929 (s), 2857 (s), 1465 (w), 1129 (w), 963 (s), 864 (w), 830 (w), 769 (s).



(6*E*)-10-[4-(dimethylamino)phenoxy]dec-6-en-5-ol (1.31) was prepared according to general procedure A and was purified by alumina chromatography, 0-60% EtOAc in hexanes and was isolated as a light red solid (120 mg, 83% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 – 6.69 (m, 4H), 5.73 – 5.62 (m,1H), 5.51 (dd, *J* = 15.4, 6.9 Hz, 1H), 4.05 (q, *J* = 6.5 Hz, 1H), 3.91 (t, *J* = 6.4 Hz, 2H), 2.87 (s, 6H), 2.22 (q, *J* = 6.8 Hz, 2H), 1.84 (p, *J* = 6.6 Hz, 2H), 1.59 – 1.47 (m, 2H), 1.40 – 1.25 (m, 5H) 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.5, 145.8, 134.0, 130.7, 115.6, 115.1, 73.0, 67.9, 41.9, 37.1, 29.0, 28.7, 27.7, 22.7, 14.1. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{18}H_{28}NO$, 274.2, found 274.3. FTIR (neat, cm^{-1}): 3368 (br), 2933 (s), 2869 (s), 1517 (s), 1476 (w), 1253 (m), 1045 (w), 963 (w), 824 (w).

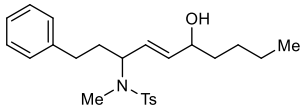


(1*E*)-1-[4-(trifluoromethyl)phenyl]hept-1-en-3-ol (1.32) was prepared according to general procedure A and was purified by alumina chromatography, 0-50% EtOAc in hexanes and was isolated as a yellow solid (59 mg, 46% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 6.61 (d, *J* = 15.9 Hz, 1H), 6.33 (dd, *J* = 15.9, 6.4 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 1H), 1.71 – 1.55 (m, 4H), 1.40 – 1.33 (m, 3H), 0.92 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.44, 135.47, 129.45 (q, *J* = 32.8 Hz), 128.65, 126.67, 125.60 (q, *J* = 4.0 Hz), 124.3 (q, *J* = 272.0 Hz), 77.42, 76.91, 72.81, 37.16, 27.69, 22.74, 14.10. ^{19}F NMR (470 MHz, $CDCl_3$) δ -65.5. GCMS (EI) calculated for $[M]^+$ 258.1, found 258.1. FTIR (neat, cm^{-1}): 3363 (br), 2933 (m), 2859 (w), 1616 (w), 1326 (s), 1166 (m), 1124 (s), 1068 (s), 1016 (w), 969 (w), 820 (w).

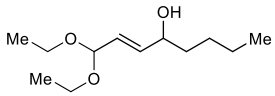


(6*E*)-10-[(5-fluoropyridin-2-yl)oxy]dec-6-en-5-ol (1.33) was prepared according to general procedure A and was purified by alumina chromatography, 0-60% EtOAc in hexanes and was isolated as a yellow liquid (92.3 mg, 69% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 – 7.90 (m, 1H), 7.32 (ddd, *J* = 9.1, 7.6, 3.1 Hz, 1H), 6.76 – 6.65 (m, 1H), 5.68 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.56 – 5.39 (m, 1H), 4.25 (t, *J* = 6.5 Hz, 2H), 4.04 (q, *J* = 6.6 Hz, 1H), 2.20 (q, *J* = 7.3 Hz, 2H), 1.96 – 1.70 (m, 2H), 1.62 – 1.45 (m, 3H),1.34 – 1.20 (m, 4H), 0.99 – 0.77 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 155.4 (d, *J* = 245.6 Hz), 134.1, 133.1 (d, *J* = 25.0 Hz), 130.6, 126.6 (d, *J* = 21.1 Hz), 111.7, 73.0, 65.8, 37.1, 28.7, 28.6, 27.7, 22.7, 14.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ -142.6.

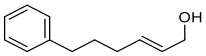
MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{15}H_{22}FNO_2Na$, 290.2; found, 290.0. FTIR (neat, cm^{-1}): 3390 (br), 2955 (m), 2930 (m), 2858 (m), 1487 (s), 1372 (m), 1227 (m), 1013 (w), 826 (w), 739 (w).



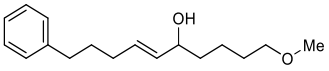
N-[(4*E*)-6-hydroxy-1-phenyldec-4-en-3-yl]-N,4-dimethylbenzene-1-sulfonamide (1.34) was prepared according to general procedure A and was purified by alumina chromatography, 0-60% EtOAc in hexanes and was isolated as a yellow liquid (167.0 mg, 80% yield) with 1.3:1 dr. ^{1}H NMR (300 MHz, $CDCl_3$) major δ 7.68 (d, J = 8.3, 2H), 7.32 - 7.26 (m, 4H), 7.23 – 7.18 (m, 1H), 7.18 – 7.11 (m, 2H), 5.53 – 5.31 (m, 2H), 4.48 (q, J = 7.3 Hz, 1H), 3.97 – 3.85 (m, 1H), 2.73 (s, 3H), 2.61 (t, J = 8.2 Hz, 2H), 2.41 (s, 3H), 1.85 – 1.71 (m, 2H), 1.40 – 1.18 (m, 7H), 0.89 (t, J = 6.9 Hz, 3H) minor δ 7.67 (d, J = 8.3, 2H), 7.32 - 7.26 (m, 4H), 7.23 – 7.18 (m, 1H), 7.18 – 7.11 (m, 2H), 5.53 – 5.31 (m, 2H), 4.48 (q, J = 7.3 Hz, 1H), 3.97 – 3.85 (m, 1H), 2.72 (s, 3H), 2.61 (t, J = 8.2 Hz, 2H), 2.41 (s, 3H), 1.85 – 1.71 (m, 2H), 1.40 – 1.18 (m, 7H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) major δ 143.2, 141.5, 137.0, 136.8, 129.6, 128.5, 128.5, 127.5, 127.0, 126.1, 72.3, 58.1, 37.0, 33.9, 32.7, 28.8, 27.7, 22.7, 21.6, 14.1. minor δ 143.2, 141.5, 137.0, 136.8, 129.6, 128.5, 128.5, 127.4, 126.9, 126.1, 72.2, 58.1, 36.9, 33.9, 32.7, 28.8, 27.6, 22.7, 21.6, 14.1. (Assignment of ^{13}C NMR signals of each diastereomers based on the assumption that the relaxation time of each corresponding carbons in those two compounds are identical.) MS-ESI (m/z): $[M+NH_4]^+$ calculated for $C_{24}H_{37}N_2O_3S$, 433.2; found, 433.1. FTIR (neat, cm^{-1}): 3525 (br), 3026 (m), 2955 (s), 2929 (s), 2860 (s), 1598 (m), 1495 (s), 1465 (s), 1333 (s), 1266 (s), 1158 (s), 1088 (m), 975 (m), 925 (m), 815 (s), 737 (s), 660 (m).



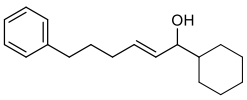
(2*E*)-1,1-diethoxyoct-2-en-4-ol (1.35) was prepared according to general procedure A and was purified by alumina chromatography, 0-50% EtOAc in hexanes and was isolated as a light yellow oil (88 mg, 82% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, J = 15.7, 6.0 Hz, 1H), 5.69 (dd, J = 15.1, 4.5 Hz, 1H), 4.90 (d, J = 5.1 Hz, 1H), 4.21 – 4.06 (m, 1H), 3.65 (p, J = 7.6 Hz, 2H), 3.56 – 3.44 (m, 2H), 1.59 – 1.45 (m, 3H), 1.39 – 1.28 (m, 4H), 1.22 (t, J = 7.0 Hz, 6H), 0.94 – 0.85 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.2, 127.4, 101.1, 71.9, 61.0, 36.8, 27.6, 22.6, 15.2, 14.0. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{12}H_{24}NaO_3$, 239.2; found 239.0. FTIR (neat, cm^{-1}): 3408 (br), 2974 (s), 2930 (s), 2872 (s), 1675 (w), 1467 (m), 1337 (m), 1134 (s), 1052 (s), 980 (s).



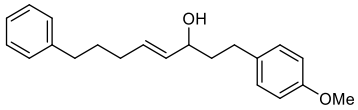
(2*E*)-6-phenylhex-2-en-1-ol (1.38), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35%, EtOAc in hexanes and was isolated as a light green oil (83 mg, 94% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.31 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H) 5.80 – 5.53 (m, 2H), 4.05 (d, *J* = 4.8 Hz, 1H), 2.62 (t, *J* = 7.9 Hz, 2H), 2.09 (q, *J* = 6.2 Hz, 2H), 1.71 (p, *J* = 7.6 Hz, 2H), 1.32 (m, 1H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 143.0, 132.6, 130.1, 128.8, 128.6, 126.1, 63.8, 35.7, 32.2, 31.4. GCMS (EI) calculated for $[M]^+$ 176.1, found 176.1. FTIR (neat, cm^{-1}): 3333 (br), 3025 (s), 2929 (s), 2856 (s), 1669 (w), 1603 (w), 1495 (m), 1458 (m), 1086 (m), 970 (s), 747 (s), 698 (s).



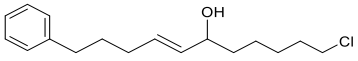
(6*E*)-1-methoxy-10-phenyldec-6-en-5-ol (1.39), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-45%, EtOAc in hexanes and was isolated as a colorless oil (108 mg, 82% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.31 – 7.23 (m, 2H), 7.21 – 7.12 (m, 3H) 5.70 – 5.59 (m, 1H), 5.46 (dd, *J* = 15.4, 6.9 Hz, 1H), 4.08 – 3.96 (m, 1H), 3.34 (t, *J* = 6.5 Hz, 2H), 3.28 (s, 3H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.07 (q, *J* = 7.0 Hz, 2H), 1.70 (p, *J* = 7.6 Hz, 2H), 1.58 – 1.46 (m, 5H), 1.45 – 1.32 (m, 2 H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 142.6, 133.9, 131.0, 128.4, 128.3, 125.7, 72.7, 72.7, 58.2, 37.2, 35.3, 31.8, 31.1, 29.9, 22.2. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{17}H_{26}O$, 245.2; found 245.0. FTIR (neat, cm^{-1}): 3400 (br), 3025 (m), 2929 (s), 2857 (s), 1670 (w), 1603 (w), 1496 (m), 1453 (s), 1118 (s), 968 (s), 748 (m), 699 (s).



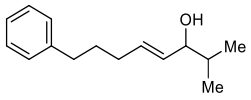
(2*E*)-1-cyclohexyl-6-phenylhex-2-en-1-ol (1.40), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-30%, EtOAc in hexanes and was isolated as a colorless oil (89 mg, 69% yield). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.27 (t, *J* = 7.5 Hz, 2H), 7.21 – 7.14 (m, 3H) 5.62 (dt, *J* = 14.1, 6.7 Hz, 1H), 5.46 (dd, *J* = 15.4, 7.4 Hz, 1H), 3.74 (t, *J* = 6.9 Hz, 1H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.08 (q, *J* = 7.2 Hz, 2H), 1.84 (d, *J* = 13.0 Hz, 1H), 1.76 – 1.62 (m, 6H), 1.44 – 1.29 (m, 2H), 1.27 – 1.12 (m, 3H), 0.96 (qd, *J* = 12.4, 3.6 Hz, 2H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 143.0, 132.7, 132.4, 128.8, 128.6, 126.0, 77.9, 44.2, 35.8, 32.3, 31.6, 29.3, 29.1, 27.1, 26.7, 26.6. GCMS (EI) calculated for $[M]^+$ 258.2, found 258.3. FTIR (neat, cm^{-1}): 3367 (br), 3025 (m), 2922 (s), 2851 (s), 1603 (w), 1496 (m), 1450 (s), 1080 (w), 1003 (m), 969 (m), 891 (w), 747 (m), 698 (s).



(*E*)-1-(4-methoxyphenyl)-8-phenyloct-4-en-3-ol (1.41), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a clear yellow liquid (115 mg, 74% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.22 – 7.07 (m, 5H), 6.86 – 6.78 (m, 2H), 5.67 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.50 (dd, *J* = 15.4, 6.8 Hz, 1H), 4.13 – 3.99 (m, 1H), 3.79 (s, 3H), 2.64 (h, *J* = 6.8 Hz, 4H), 2.09 (q, *J* = 7.1 Hz, 2H), 1.92 – 1.64 (m, 4H), 1.41 (d, *J* = 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 142.4, 134.1, 133.4, 131.9, 129.4, 128.5, 128.4, 125.8, 113.9, 72.4, 55.3, 39.2, 35.5, 31.8, 31.0. MS-ESI (m/z): $[M+NH4]^+$ calculated for $C_{21}H_{30}NO_2$, 328.2, found 328.1. FTIR (neat, cm^{-1}): 3389 (br), 3061 (m), 2931 (s), 2855 (s), 1879 (w), 1668 (m), 1611 (s), 1519 (s), 1245 (s), 970 (m), 821 (m), 699 (m).

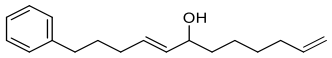


(4*E*)-11-chloro-1-phenylundec-4-en-6-ol (1.42) was prepared according to general procedure A and was purified by alumina chromatography, 0-30% EtOAc in hexanes and was isolated as a yellow liquid (118 mg, 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 3H), 7.23 – 7.13 (m, 3H), 5.66 (dt, *J* = 13.1, 7.4 Hz, 1H), 5.47 (ddt, *J* = 15.4, 7.0, 1.3 Hz, 1H), 4.05 (q, *J* = 6.5 Hz, 1H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.69 – 2.57 (m, 2H), 2.08 (q, *J* = 6.9 Hz, 2H), 1.83 – 1.67 (m, 4H), 1.56 – 1.34 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 133.5, 131.6, 128.5, 128.3, 125.8, 72.9, 45.0, 37.1, 35.4, 32.6, 31.8, 30.9, 26.8, 24.8. MS-ESI (m/z): $[M-OH]^+$ calculated for $C_{17}H_{24}Cl$, 263.2; found, 263.0. FTIR (neat, cm^{-1}): 3366 (br), 3025 (m), 2932 (s), 2857 (s), 1602 (w), 1495 (s), 1453 (s), 1309 (m), 969 (s), 768 (m), 699 (s).

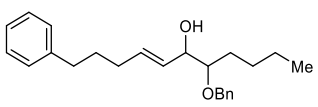


(4*E*)-2-methyl-8-phenyloct-4-en-3-ol (1.43), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-30%, EtOAc in hexanes and was isolated as a colorless oil (91 mg, 84% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.31 – 7.24 (m, 2H), 7.22 – 7.10 (m, 3H) 5.65 (dt, *J* = 15.4, 6.6 Hz, 1H), 5.47 (dd, *J* = 15.4, 6.6 Hz, 1H), 3.76 (t, *J* = 6.6 Hz, 1H), 4.92 (ddt, *J* = 10.2, 2.4, 1.3 Hz, 1H), 4.01 (q, *J* = 6.6 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.62 (t, *J* = 7.4 Hz, 2H), 2.09 (q, *J* = 7.1 Hz, 2H), 1.78 – 1.59 (m, 3H) 1.48 – 1.36 (m, 1H), 0.89 (dd, *J* = 12.6, 6.8 Hz, 6H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 143.0, 132.5, 132.4, 128.9, 128.7, 126.1, 78.4, 35.8, 34.3, 32.3, 31.6, 18.5, 18.4. GCMS (EI) calculated for $[M]^+$ 218.2, found 218.1.

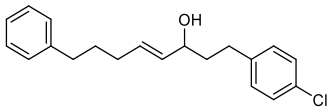
FTIR (neat, cm^{-1}): 3376 (br), 3026 (m), 2930 (s), 2870 (s), 1603 (w), 1496 (m), 1457 (s), 1382 (w), 1014 (s), 969 (s), 746 (m), 699 (s).



(4*E*)-1-phenyldodeca-4,11-dien-6-ol (1.44), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35%, EtOAc in hexanes and was isolated as a colorless oil (121 mg, 93% yield). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.29 – 7.23 (m, 2H), 7.20 – 7.13 (m, 3H) 5.82 (ddt, *J* = 17.0, 10.2, 6.6 Hz, 1H), 5.67 – 5.60 (m, 1H), 5.46 (ddt, *J* = 15.3, 7.0, 1.4 Hz, 1H), 4.99 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.92 (ddt, *J* = 10.2, 2.4, 1.3 Hz, 1H), 4.01 (q, *J* = 6.6 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.06 (p, *J* = 7.3 Hz, 4H), 1.70 (p, *J* = 7.7 Hz, 2H), 1.53 – 1.30 (m, 7H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 143.0, 139.5, 134.3, 131.6, 128.9, 128.7, 126.1, 114.5, 73.3, 37.7, 35.7, 34.2, 31.5, 29.9, 25.5. GCMS (EI) calculated for $[M]^+$ 258.2, found 258.3. FTIR (neat, cm^{-1}): 3347 (br), 3062 (m), 3025 (m), 2928 (s), 2856 (s), 1640 (m), 1496 (s), 1453 (s), 968 (s), 909 (m), 747 (m), 699 (s).

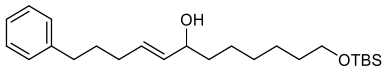


(*E*)-7-(benzyloxy)-1-phenylundec-4-en-6-ol (1.45), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35%, EtOAc in hexanes and was isolated as a clear colorless liquid (125 mg, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (S,S- / R,R-) 7.28 – 6.82 (m, 10H), 5.78 – 5.58 (m, 1H), 5.51 – 5.34 (m, 1H), 4.62 – 4.40 (m, 2H), 4.15 (dd, *J* = 7.0, 3.3 Hz, 0.5H), 3.95 (t, *J* = 6.9 Hz, 0.5H), 3.35 (dt, *J* = 8.0, 3.7 Hz, 0.5H), 3.24 (q, *J* = 6.1 Hz, 0.5H), 2.54 (t, *J* = 7.7 Hz, 2H), 2.03 (q, *J* = 7.1 Hz, 2H), 1.65 (m, 2H), 1.57 – 1.47 (m, 1H), 1.50 – 1.25 (m, 3H), 1.21 (m, 3H), 0.81 (td, *J* = 7.2, 3.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) (S, S- / R, R-) δ 142.5, 138.7, 133.9, 129.0, 128.7, 128.6, 128.6, 128.0, 127.8, 125.9, 82.9, 73.8, 72.6, 35.5, 32.1, 30.9, 29.4, 28.1, 23.1, 14.2. (S, R- / R, S-) δ142.5, 138.5, 133.5, 129.8, 128.6,128.6, 128.4, 128.0,127.9, 125.8, 82.6, 74.4, 72.4, 35.5, 32.1, 30.9, 30.2, 27.3, 22.9, 14.2. MS-ESI (m/z): $[M+NH4]^+$ calculated for $C_{24}H_{36}NO_2$, 370.3, found 370.2. FTIR (neat, cm^{-1}): 3448 (br), 3084 (w), 2929 (s), 1696 (w), 1603 (w), 1497 (m), 1453 (m), 1376 (m), 1222 (m), 1065 (m), 969 (m), 690 (m).

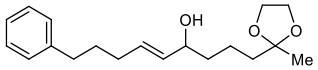


(4*E*)-1-(4-chlorophenyl)-8-phenyloct-4-en-3-ol (1.46), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-40%, EtOAc in hexanes and was isolated as a colorless oil (119 mg, 77% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.38 – 7.07

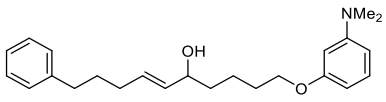
(m, 9H), 5.67 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.50 (dd, *J* = 15.3, 6.8 Hz, 1H), 4.03 (q, *J* = 6.7 Hz, 1H), 2.78 – 2.53 (m, 4H), 2.08 (q, *J* = 6.8 Hz, 2H), 1.88 – 1.63 (m, 4H), 1.48 (s, 1H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 142.9, 141.3, 133.8, 132.1, 131.7, 130.3, 128.8, 128.7, 126.1, 72.5, 39.2, 35.7, 32.2, 31.5, 31.4. GCMS (EI) calculated for $[M]^+$ 314.1, found 314.2. FTIR (neat, cm^{-1}): 3348 (br), 3025 (m), 2929 (s), 2856 (s), 1603 (w), 1491 (s), 153 (s), 1092 (s), 1015 (s), 969 (s), 835 (m), 748 (m), 699 (s).



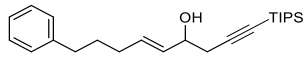
(*E*)-12-((tert-butyldimethylsilyl)oxy)-1-phenyldodec-4-en-6-ol (1.47), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35%, EtOAc in hexanes and was isolated as a clear colorless liquid (141 mg, 72% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.21 (m, 3H), 7.20 (m, 2H), 5.67 (dt, *J* = 15.4, 6.5 Hz, 1H), 5.50 (dd, *J* = 15.4, 6.9 Hz, 1H), 4.06 (q, *J* = 6.5 Hz, 1H), 3.63 (t, *J* = 6.5 Hz, 2H), 2.65 (t, *J* = 7.7 Hz, 2H), 2.11 (q, *J* = 7.1 Hz, 2H), 1.75 m, 2H), 1.53 (m, 3H), 1.35 (s, 5H), 1.33 – 1.24 (m, 2H), 0.93 (s, 9H), 0.09-0.05 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 133.7, 131.5, 128.6, 128.4, 125.8, 73.2, 63.4, 37.4, 35.5, 32.9, 31.8, 31.0, 29.5, 26.1, 25.9, 25.6, 18.5, -5.1. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{24}H_{41}OSi$, 373.3, found 373.3. FTIR (neat, cm^{-1}): 3355 (br), 3062 (m), 2929 (s), 2856 (s), 1496 (m), 1462 (m), 1361 (w), 1255 (m), 1099 (s), 968 (m), 836 (s), 775 (m).



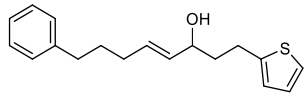
(*E*)-1-(2-methyl-1,3-dioxolan-2-yl)-9-phenylnon-5-en-4-ol (1.48), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35%, EtOAc in hexanes and was isolated as a clear colorless liquid (117 mg, 77% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.23 (m, 2H), 7.17 (m, 3H), 5.65 (dt, *J* = 15.4, 6.5 Hz, 1H), 5.47 (ddt, *J* = 15.3, 6.9, 1.3 Hz, 1H), 4.05 (q, *J* = 6.2 Hz, 1H), 3.99 – 3.83 (m, 4H), 2.67 – 2.56 (t, *J* = 7.7 Hz, 2H), 2.08 (q, *J* = 7.4 Hz, 2H), 1.70 (m, 4H), 1.56 – 1.39 (m, 4H), 1.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 133.6, 131.5, 128.5, 128.4, 125.8, 110.2, 73.0, 64.7, 39.1, 37.6, 35.4, 31.8, 30.9, 23.8, 20.2. MS-ESI (m/z): $[M+NH4]^+$ calculated for $C_{19}H_{32}NO_3$, 322.2; found 322.0. FTIR (neat, cm^{-1}): 3448 (br), 3026 (m), 2929 (s), 1696 (m), 1603 (m), 1497 (m), 1376 (m), 1222 (m), 1065 (m), 969 (m), 690 (m).



(6*E*)-1-[3-(dimethylamino)phenoxy]-10-phenyldec-6-en-5-ol (1.49), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35%, EtOAc in hexanes and was isolated as a yellow oil (65 mg, 71% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.30 – 7.22 (m, 2H), 7.21 – 7.03 (m, 4H), 6.32 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.72 – 6.19 (m, 2H), 5.73 – 5.60 (m, 1H), 5.48 (dd, *J* = 15.4, 6.9 Hz, 1H), 4.10 – 4.00 (m, 1H), 3.93 (t, *J* = 6.5 Hz, 2H), 2.90 (s, 6H), 2.62 (t, *J* = 7.8, 2H), 2.08 (q, *J* = 7.1 Hz, 2H), 1.82 – 1.64 (m, 4H), 1.61 – 1.43 (m, 5H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 160.6, 152.6, 143.0, 134.1, 131.7, 130.0, 128.8, 128.6, 126.0, 105.9, 102.5, 99.9, 73.2, 68.0, 40.8, 37.5, 35.7, 32.1, 31.4, 29.8, 22.5. MS-ESI (m/z): $[M+H]^+$ calculated for $C_{24}H_{34}NO_2$, 368.3; found 368.3. FTIR (neat, cm^{-1}): 3388 (br), 3025 (m), 2930 (s), 2857 (s), 1614 (s), 1502 (s), 1452 (s), 1353 (m), 1239 (s), 1151 (s), 969 (m), 827 (w), 749 (m), 686 (m).



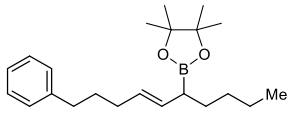
(*E*)-9-phenyl-1-(triisopropylsilyl)non-5-en-1-yn-4-ol (1.50), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a clear yellow liquid (104 mg, 56% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 8.3, 6.4 Hz, 2H), 7.19 – 7.09 (m, 3H), 5.80 – 5.65 (m, 1H), 5.52 (ddt, *J* = 15.4, 6.3, 1.4 Hz, 1H), 4.19 (q, *J* = 6.1 Hz, 1H), 2.64 – 2.56 (t, *J* = 7.7 Hz, 2H), 2.55 – 2.40 (m, 2H), 2.05 (q, *J* = 7.1 Hz, 2H), 1.70 (q, *J* = 7.8 Hz, 2H), 1.05-0.98 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 132.5, 131.4, 128.6, 128.4, 125.8, 104.5, 83.8, 70.9, 35.5, 31.8, 30.8, 29.5, 18.8, 11.4. MS-ESI (m/z): $[M+NH4]^+$ calculated for $C_{24}H_{42}NOSi$, 388.3; found 388.2. FTIR (neat, cm^{-1}): 3338 (br), 3063 (m), 2940 (s), 2864 (s), 2173 (s), 1495 (m), 1464 (m), 1382 (m), 1243 (w), 966 (m), 883 (m), 746 (w).



(*E*)-8-phenyl-1-(thiophen-2-yl)oct-4-en-3-ol (1.51), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-35% EtOAc in hexanes and was isolated as a clear yellow liquid (116 mg, 81% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.4 Hz, 2H), 7.18 – 7.10 (m, 3H), 7.07 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.87 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.76 (d, *J* = 2.3 Hz, 1H), 5.64 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.46 (ddt, *J* = 15.4, 7.0, 1.3 Hz, 1H), 4.07 (q, *J* = 6.7 Hz, 1H), 2.87 (td, *J* = 7.9, 2.2 Hz, 2H), 2.64 – 2.53 (m, 2H), 2.05 (q, *J* = 7.1 Hz, 2H), 1.98 – 1.77 (m, 2H), 1.69 (q, *J* = 7.8 Hz, 2H), 1.43 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 142.4, 133.1, 132.2, 128.5, 128.4, 126.8, 125.8, 124.3, 123.1, 77.6, 76.7, 72.1, 39.1, 35.5, 31.8, 30.9, 26.0. MS-ESI (m/z): $[M-OH]^+$ calculated for $C_{18}H_{22}S$, 269.1, found 268.9. FTIR (neat, cm^{-}

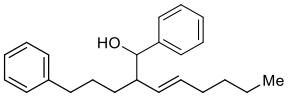
[1]): 3369 (br), 3062 (m), 2922 (s), 2854 (s), 1653 (w), 1603 (m), 1497 (m), 1453 (m), 1030 (m), 969 (m), 850 (w), 698 (s).

Allylic Boronic Ester Product



(*E*)-4,4,5,5-tetramethyl-2-(10-phenyldec-6-en-5-yl)-1,3,2-dioxaborolane (1.36), the reaction was run according to general procedure A, but instead of oxidizing after 12 hours the crude reaction mixture was filtered through a silica gel plug. The filtrate was washed with brine (3 × 25 mL). The organic phase was dried over Na_2SO_4, and then concentrated under vacuum. It was then purified by silica gel chromatography, 0-5% diethyl ether in hexanes and was isolated as a colorless liquid (116 mg, 68% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.20 – 7.16 (m, 3H), 5.46 – 5.31 (m, 2H), 2.64 – 2.57 (m, 2H), 2.04 (ddd, *J* = 7.5, 6.1, 3.7 Hz, 2H), 1.76 (d, *J* = 7.5 Hz, 1H), 1.73 – 1.63 (m, 2H), 1.56 – 1.28 (m, 6H), 1.24 (s, 12H), 0.95 – 0.84 (t, *J* = 6.8, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 131.7, 129.2, 128.6, 128.3, 125.7, 83.1, 35.3, 32.4, 31.6, 31.5, 30.8, 24.9, 24.8, 22.8, 14.2. ^{11}B NMR (96 MHz, $CDCl_3$) δ 32.15. MS-ESI (m/z): $[M+H]^+$ calculated for $C_{22}H_{36}BO_2$, 343.3; found 343.2. FTIR (neat, cm^{-1}): 2927 (s), 2857 (m), 1718 (w), 1617 (w), 1457 (w), 1371 (m), 1319 (m), 1269 (w), 1143 (s).

Homoallylic Alcohol Product



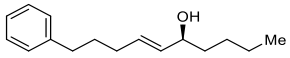
(*E*)-2-butyl-1,7-diphenylhept-3-en-1-ol (1.37), the reaction was performed according to general procedure A (at a 0.25 mmol scale), but instead of oxidizing the product *in situ*, the crude reaction mixture was filtered through a silica gel plug with EtOAc (25 mL). The filtrate was washed with brine (3 × 25 mL). The organic phase was dried over Na_2SO_4, and then concentrated under vacuum to afford the crude allylic boronic ester (**1.36**). The purity of crude allylic boronic ester was determined by ^{1}H NMR. This crude allylic boronic ester (0.2 mmol, 1.0 equiv) was added to a vial, followed by benzyl aldehyde (0.8 mmol, 4.0 equiv) and anhydrous toluene (1 mL, 0.2 M). The reaction mixture was allowed to stir at 60 °C overnight under N_2 atmosphere. Upon completion, the solvent was removed under vacuum and the residue was purified by silica gel chromatography (0-15% EtOAc in hexanes) and isolated as a colorless liquid (60 mg, 74% yield overall) as a mixture of isomers (3:1, *E*:*Z*) as measured by ^{1}H NMR. The dr could not be established by ^{1}H NMR but is expected to be 1:1.[1] ^{1}H NMR (300 MHz, $CDCl_3$) *major isomer:* δ 7.28 – 7.04 (m, 8H), 7.02 – 6.97 (m, 2H), 5.64 (dt, *J* = 11.0, 7.3 Hz, 1H), 4.30 – 4.21 (m, 1H), 2.67 – 2.11 (m, 4H), 2.06 – 1.92 (m, 2H), 1.57 – 1.12 (m, 8H), 0.87 – 0.78 (m, 3H) *minor isomer peak:* δ 5.54 (dt, *J* = 15.4,

6.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) *major isomer:* δ 142.8, 142.6, 135.2, 129.9, 128.4, 128.3, 128.3, 127.6, 127.1, 125.7, 77.6, 77.5, 76.7, 46.0, 35.9, 32.0, 31.1, 29.2, 27.8, 22.5, 14.1. *minor isomer* δ 142.8, 142.6, 135.2, 129.9, 128.4, 128.3, 128.3, 127.6, 127.1, 125.7, 77.0, 46.0, 35.9, 32.5, 31.8, 30.6, 27.8, 22.3, 14.1. MS-ESI (m/z): $[M+NH4]^+$ calculated for $C_{23}H_{34}NO$, 340.3, found 340.1. FTIR (neat, cm^{-1}): 3368 (br), 3026 (m), 2956 (s), 2929 (s), 1603 (w), 1496 (m), 1464 (m), 1457 (m), 1363 (w), 1013 (m), 969 (m), 746 (m), 698(s).

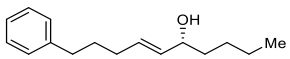
Single Stereocenter Enantioenriched Products

Enantioenriched allylic alcohols (*R*)-**1.18**, (*S*)-**1.18**, (*R*)-**1.72**, (*R*)-**1.73**, and (*R*)-**1.75** were prepared according to general procedure A using enantioenriched α-chloro pinanediol boronic esters and 5-phenylpentyne (**1.60**). Allylic alcohol (*R*)-**1.43** was prepared according to general procedure A using enantioenriched α-chloro pinacol boronic ester and 5-phenylpentyne (**1.60**). Enantiomeric excess (ee) was determined by chiral HPLC either of the product alcohol or the benzoyl derivative of the product alcohol.

Note: Because mobile phases with low polarity (often < 0.1% iPrOH in hexanes) were used in HPLC analyses of benzoyl derivatives, retention times of some isomers may not be identical in the results of chiral and enantioenriched samples due to minor solvent variations.

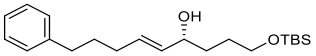


(5*S*,6*E*)-10-phenyldec-6-en-5-ol ((*S*)-1.18), compound was prepared according to general procedure A and was purified by alumina chromatography, 0-25% EtOAc in hexanes and was isolated as a colorless oil (104 mg, 75% yield, 98% ee). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.30 – 7.23 (m, 2H), 7.21 – 7.14 (m, 3H), 5.64 (dt, *J* = 14.1, 6.7 Hz, 1H), 5.47 (dd, *J* = 15.9, 7.0 Hz, 1H), 4.01 (q, *J* = 6.7 Hz, 1H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.07 (q, *J* = 7.2 Hz, 2H), 1.70 (p, *J* = 7.5 Hz, 2H), 1.55 – 1.39 (m, 3H), 1.36 – 1.26 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 143.0, 134.4, 131.5, 128.7, 128.4, 126.1, 73.3, 37.6, 35.7, 32.2, 31.5, 28.2, 23.1, 14.3. GCMS (EI) calculated for $[M]^+$ 232.2, found 232.0. FTIR (neat, cm^{-1}): 3342 (br), 3026 (m), 2928 (s), 2857 (s), 1604 (w), 1496 (m), 1453 (m), 968 (m), 746 (m), 699 (s). Enantiomeric excess was determined by chiral HPLC of the alcohol. CHIRALPAK AD-H column (0.2% 2-PrOH in hexane, 0.6 mL/min) with t_r = 62.7 min (minor), 67.5 min (major). $[\alpha]_D^{23}$ = -5.2 (c 0.81, CHCl3).

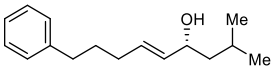


(5*R*,6*E*)-10-phenyldec-6-en-5-ol ((*R*)-1.18) was prepared according to general procedure A and was purified by alumina chromatography, 0-25% EtOAc in hexanes and was isolated as a colorless oil (97 mg, 70% yield, 97% ee). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.32 – 7.22 (m, 2H), 7.21 – 7.12

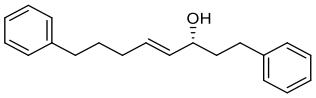
(m, 3H), 5.68 – 5.59 (m, 1H), 5.46 (dd, *J* = 15.4, 7.0 Hz, 1H), 4.01 (q, *J* = 6.5 Hz, 1H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.07 (q, *J* = 7.0 Hz, 2H), 1.70 (p, *J* = 7.2 Hz, 2H), 1.56 – 1.38 (m, 3H), 1.35 – 1.25 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 143.0, 134.4, 131.5, 128.9, 128.7, 126.1, 73.3, 37.6, 35.7, 32.2, 31.5, 28.2, 23.1, 14.3. GCMS (EI) calculated for $[M]^+$ 232.2, found 232.0. FTIR (neat, cm^{-1}): 3345 (br), 3026 (m), 2929 (s), 2856 (s), 1604 (w), 1496 (m), 1453 (m), 968 (m), 746 (m), 699 (s). Enantiomeric excess was determined by chiral HPLC of the alcohol. CHIRALPAK AD-H column (0.2% 2-PrOH in hexane, 0.6 mL/min) with t_r = 61.6 min (major), 70.9 min (minor). $[\alpha]_D^{23}$ = +4.9 (c 0.51, CHCl3).



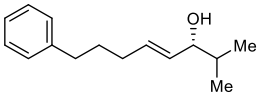
(4*R*,5*E*)-1-[(tert-butyldimethylsilyl)oxy]-9-phenylnon-5-en-4-ol ((*R*)-1.72) was prepared according to general procedure A and was purified by alumina chromatography, 0-30% EtOAc in hexanes and was isolated as a yellow liquid (148.0 mg, 85% yield) with 99% ee. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 2H), 7.22 – 7.14 (m, 3H), 5.76 – 5.58 (m, 1H), 5.49 (ddt, *J* = 15.4, 6.7, 1.3 Hz, 1H), 4.16 – 3.97 (m, 1H), 3.74 – 3.54 (m, 2H), 2.77 – 2.54 (m, 3H), 2.38 (s, 1H), 2.17 – 1.99 (m, 2H), 1.80 – 1.53 (m, 6H), 0.90 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 133.6, 131.1, 128.5, 128.3, 125.8, 72.6, 63.4, 35.4, 34.7, 31.8, 30.9, 29.0, 26.0, 18.4, -5.3. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{21}H_{35}OSi$, 331.2; found, 331.0. FTIR (neat, cm^{-1}): 3364 (br), 3026 (m), 2926 (s), 2855 (s), 1604 (w), 1463 (m), 1255 (m), 1096 (s), 1005 (m), 968 (m), 835 (s), 775 (m), 698 (m). Enantiomeric excess was determined by chiral HPLC results of its benzoyl derivative. CHIRALPAK AD-H column (0.05% 2-PrOH in hexane, 0.6 mL/min) with t_r = 14.7 min (major), 16.1 min (minor). $[\alpha]_D^{22}$ = +5.8 (c 1.15, CHCl3).



(4*R*,5*E*)-2-methyl-9-phenylnon-5-en-4-ol ((*R*)-1.73) was prepared according to general procedure A and was purified by alumina chromatography, 0-20% EtOAc in hexanes and was isolated as a yellow liquid (88.1 mg, 76% yield) with 99% ee. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 - 2.26 (m, 2H), 7.20 - 7.17 (m, 3H), 5.66 (dt, *J* = 15.0, 6.9 Hz, 1H), 5.47 (dd, *J* = 15.4, 7.6 Hz, 1H), 4.12 (q, *J* = 7.5 Hz, 1H), 2.62 (t, *J* = 8.2 Hz, 2H), 2.08 (q, *J* = 7.4 Hz, 2H), 1.73 - 1.69 (m, 3H), 1.52 – 1.37 (m, 2H), 1.36 – 1.23 (m, 2H), 0.98 – 0.88 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 134.0, 131.3, 128.5, 128.4, 125.8, 71.4, 46.6, 35.5, 31.8, 31.0, 24.7, 23.0, 22.6. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{16}H_{24}ONa$, 255.2; found, 255.0. FTIR (neat, cm^{-1}): 3356 (br), 3025 (w), 2953 (s), 2928 (s), 2866 (m), 1495 (m), 1453 (m), 968 (m), 747 (w), 698 (s). Enantiomeric excess was determined by chiral HPLC of its benzoyl derivative. CHIRALPAK AD-H column (0.1% 2-PrOH in hexane, 0.6 mL/min) with t_r = 14.5 min (major), 16.0 min (minor). $[\alpha]_D^{22}$ = +8.2 (c 1.03, CHCl3).

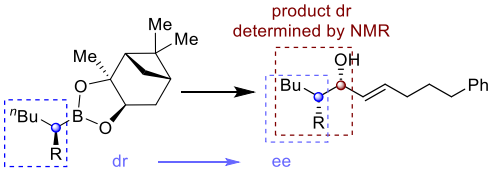


(3*R*,4*E*)-1,8-diphenyloct-4-en-3-ol ((*R*)-1.74) was prepared according to general procedure A and was purified by alumina chromatography, 0-20% EtOAc in hexanes and was isolated as a yellow liquid (102.1 mg, 73% yield) with 98% ee. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 - 7.28 (m, 4H), 7.24 – 7.15 (m, 6H), 5.69 (dt, *J* = 15.5, 6.6 Hz, 1H), 5.59 – 5.46 (m, 1H), 4.10 (q, *J* = 6.6 Hz, 1H), 2.79 – 2.55 (m, 3H), 2.23 – 2.01 (m, 2H), 1.96 – 1.65 (m, 4H), 1.54 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 142.1, 133.4, 131.9, 128.5, 128.4, 128.4, 125.9, 125.8, 72.4, 38.9, 35.5, 31.9, 31.8, 30.9. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{20}H_{24}ONa$, 303.2; found, 303.0. FTIR (neat, cm^{-1}): 3354 (br), 3025 (m), 2928 s), 2856 (s), 1602 (m), 1495 (s), 1456 (s), 1030 (m), 969 (m), 769 (s), 698 (s). Enantiomeric excess was determined by chiral HPLC of the alcohol. CHIRALPAK AD-H column (0.4% 2-PrOH in hexane, 0.6 mL/min) with t_r = 61.5 min (major), 67.3 min (minor). $[\alpha]_D^{22}$ = +4.9 (c 0.98, CHCl3).

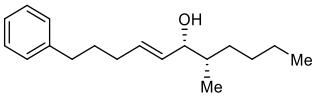


(3*R*,4*E*)-2-methyl-8-phenyloct-4-en-3-ol ((*R*)-1.43) was prepared according to general procedure A starting from enantioenriched α-chloro pinacol boronic ester and was purified by alumina chromatography, 0-20% EtOAc in hexanes and was isolated as a yellow liquid (92.9 mg, 85% yield) with 99% ee. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 2H), 7.22 – 7.14 (m, 3H), 5.66 (dtd, *J* = 15.4, 6.5, 0.9 Hz, 1H), 5.48 (ddt, *J* = 15.4, 7.2, 1.3 Hz, 1H), 3.96 – 3.47 (m, 1H), 2.76 – 2.42 (m, 2H), 2.28 – 1.97 (m, 2H), 1.90 – 1.66 (m, 3H), 1.44 (s, 1H), 0.93 (dd, *J* = 14.3, 6.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 132.6, 131.8, 128.5, 128.4, 125.8, 78.3, 35.5, 33.9, 31.9, 31.1, 18.3, 18.3. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{15}H_{22}ONa$, 241.2; found, 241.0. FTIR (neat, cm^{-1}): 3385 (br), 3026 (m), 2956 (s), 2929 (s), 2870 (m), 1603 (w), 1496 (s), 1453 (s), 1381 (w), 1013 (m), 969 (m), 746 (m), 699 (s). Enantiomeric excess was determined by chiral HPLC results of its benzoyl derivative. CHIRALPAK AD-1 column (0.2% 2-PrOH in hexane, 0.6 mL/min) with t_r = 19.5 min (major), 23.6 min (minor). $[\alpha]_D^{22}$ = -5.9 (c 1.08, CHCl3).

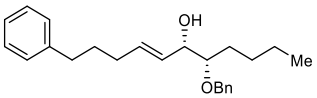
Characterization of Consecutive Enantioenriched Stereocenter Products



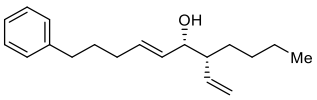
The diastereomeric ratio (dr) of compounds **(6*R*,7*S*)-1.74**, **(6*S*,7*S*)-1.45**, **(6*S*,7*R*)-1.76**, and **(6*S*,7*R*)-1.77** was determined by ^{1}H NMR. Enantiomeric excess (ee) of compounds **(6*R*,7*S*)-1.74**, **(6*S*,7*S*)-1.45**, **(6*S*,7*R*)-1.76**, and **(6*S*,7*R*)-1.77** was determined by analysis of the corresponding alkyl boronate precursors.



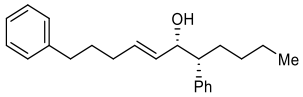
(4*E*,6*R*,7*S*)-7-methyl-1-phenylundec-4-en-6-ol ((6*R*,7*S*)-1.74) was prepared according to general procedure A and was purified by alumina chromatography, 0-20% EtOAc in hexanes and was isolated as a yellow liquid (104.2 mg, 80% yield) with 96% ee and >20:1 dr. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.19 (td, *J* = 5.5, 4.9, 2.9 Hz, 3H), 5.76 – 5.57 (m, 1H), 5.49 (m, 1H), 3.92 (dd, *J* = 6.9, 4.9 Hz, 1H), 2.63 (dd, *J* = 8.7, 6.7 Hz, 2H), 2.10 (q, *J* = 6.6 Hz, 2H), 1.80 – 1.66 (m, 2H), 1.59 – 1.03 (m, 9H), 0.94 – 0.85 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 132.1, 128.5, 128.4, 125.8, 77.6, 77.0, 76.7, 39.0, 35.5, 32.4, 31.9, 31.0, 29.6, 23.1, 14.8, 14.2. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{18}H_{28}ONa$, 283.2; found, 283.1. FTIR (neat, cm^{-1}): 3380 (br), 3025 (m), 2955 (s), 2928 (s), 2856 (s), 1496 (m), 1453 (s), 1377 (w), 968 (m), 744 (m), 698 (s). The ee was determined based on its precursor S45. $[\alpha]_D^{23}$ = -14.3 (c 1.16, CHCl3).



(4*E*,6*S*,7*S*)-7-(benzyloxy)-1-phenylundec-4-en-6-ol ((6*S*,7*S*-1.45) was prepared according to general procedure A and was purified by alumina chromatography, 0-40% EtOAc in hexanes and was isolated as a yellow liquid (132.1 mg, 75% yield) with >20:1 er and >20:1 dr. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 – 7.17 (m, 7H), 7.13 – 7.05 (m, 3H), 5.79 – 5.60 (m, 1H), 5.39 (ddt, *J* = 15.4, 7.2, 1.5 Hz, 1H), 4.62 – 4.38 (m, 2H), 3.95 (t, *J* = 6.9 Hz, 1H), 3.24 (td, *J* = 6.2, 4.8 Hz, 1H), 2.63 – 2.48 (m, 2H), 2.10 – 1.95 (m, 2H), 1.70 – 1.60 (m, 2H), 1.59 – 1.10 (m, 7H), 0.81 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 138.4, 133.5, 129.8, 128.5, 128.4, 128.3, 127.9, 127.8, 125.7, 82.7, 74.3, 72.5, 35.4, 31.9, 30.8, 30.1, 27.2, 23.0, 14.1. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{24}H_{32}O_2Na$, 375.2; found, 375.1. FTIR (neat, cm^{-1}): 3436 (br), 3026 (m), 2929 (s), 2857 (s), 1603 (w), 1495 (m), 1453 (s), 1207 (w), 1093 (s), 1028 (m), 970 (m), 744 (m), 698 (s). The er was determined based on its precursor S42. $[\alpha]_D^{23}$ = +19.7 (c 1.28, CHCl3).

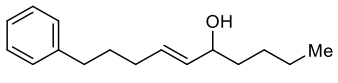


(4*E*,6*S*,7*R*)-7-ethenyl-1-phenylundec-4-en-6-ol ((6*S*,7*R*)-1.76) was prepared according to general procedure A and was purified by alumina chromatography, 0-30% EtOAc in hexanes and was isolated as a yellow liquid (75.0 mg, 55% yield) with 93% ee and >20:1 dr. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.21 – 7.12 (m, 3H), 5.79 – 5.52 (m, 2H), 5.52 – 5.38 (m, 1H), 5.23 – 5.07 (m, 2H), 3.83 (t, *J* = 7.1 Hz, 1H), 2.63 (dd, *J* = 8.6, 6.8 Hz, 2H), 2.18 – 1.95 (m, 3H), 1.81 – 1.66 (m, 3H), 1.47 (m, 1H), 1.36 – 1.15 (m, 5H), 0.93 – 0.81 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 139.4, 133.2, 131.4, 128.5, 128.3, 125.7, 118.0, 75.2, 51.1, 35.4, 31.8, 30.9, 30.1, 29.5, 22.7, 14.0. MS-ESI (m/z): $[M+Na]^+$ calculated for $C_{19}H_{28}ONa$, 295.2; found, 295.1. FTIR (neat, cm^{-1}): 3420 (br), 3026 (m), 2929 (s), 2858 (s), 1635 (w), 1496 (m), 1452 (m), 969 (m), 912 (m), 735 (m), 698 (m). The ee was determined based on its precursor S46. $[\alpha]_D^{23}$ = +7.3 (c 1.13, CHCl3).

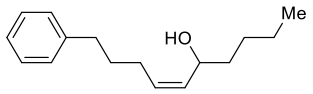


(4*E*,6*S*,7*R*)-1,7-diphenylundec-4-en-6-ol ((6*S*,7*R*)-1.77) was prepared according to general procedure A and was purified by alumina chromatography, 0-30% EtOAc in hexanes and was isolated as a yellow liquid (111.6 mg, 65% yield) with 96% ee and 14:1 dr. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 – 6.78 (m, 10H), 5.70 (dt, *J* = 15.5, 6.6 Hz, 1H), 5.62 – 5.34 (m, 1H), 4.14 (t, *J* = 7.6 Hz, 1H), 2.99 – 2.48 (m, 3H), 2.11 (q, *J* = 7.1 Hz, 2H), 1.84 – 1.67 (m, 3H), 1.67 – 1.51 (m, 1H), 1.43 – 1.37 (m, 1H), 1.32 – 1.03 (m, 4H), 0.81 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 141.7, 133.5, 131.8, 128.9, 128.6, 128.6, 128.4, 126.8, 125.8, 52.8, 35.5, 31.9, 31.8, 30.9, 29.7, 22.8, 14.1, 11.1. MS-ESI (m/z): $[M+NH_4]^+$ calculated for $C_{23}H_{34}ON$, 340.3; found, 340.2. FTIR (neat, cm^{-1}): 3435 (br), 3062 (w), 3026 (m), 2928 (s), 2857 (s), 1602 (m), 1497 (s), 1457 (m), 1378 (w), 1081 (w), 1030 (m), 969 (m), 747 (m), 699 (s). The ee was determined by its precursor S47. $[\alpha]_D^{23}$ = -12.9 (c 1.14, CHCl3).

1.4.5 Determination of Stereochemistry



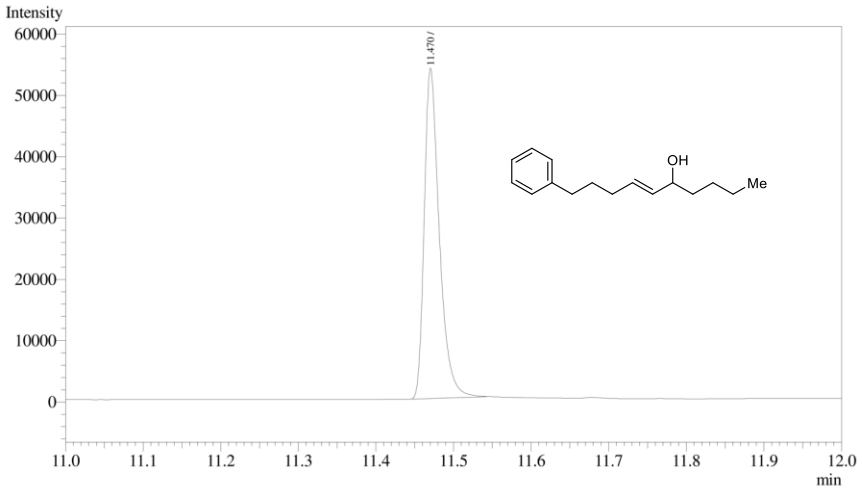
1.18



***Z*-1.18**

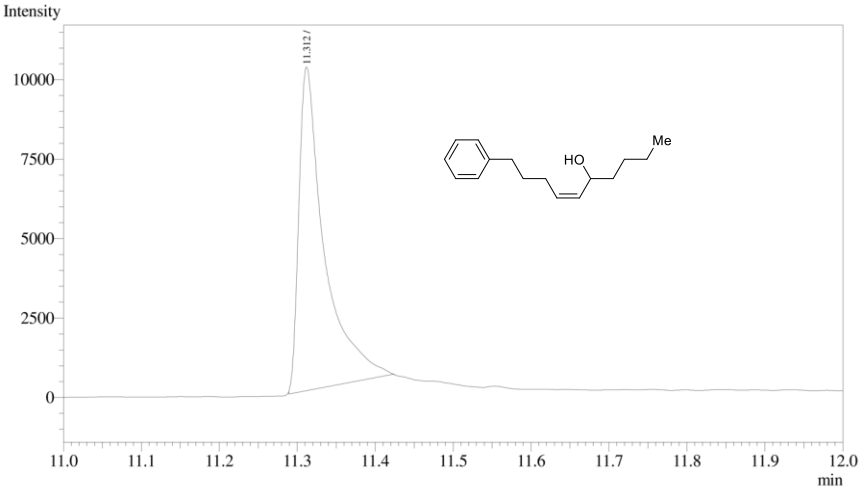
1.18 and ***Z*-1.18** have been previously synthesized and characterized.[103] Provided are GC traces of pure **1.18**, ***Z*-1.18**, a mixture of both pure isomers, and a GC trace of the crude reaction mixture of the synthesis of **1.18** at the end of the oxidation as described in general procedure A.

Figure 1.1 GC Trace of Isolated 1.18



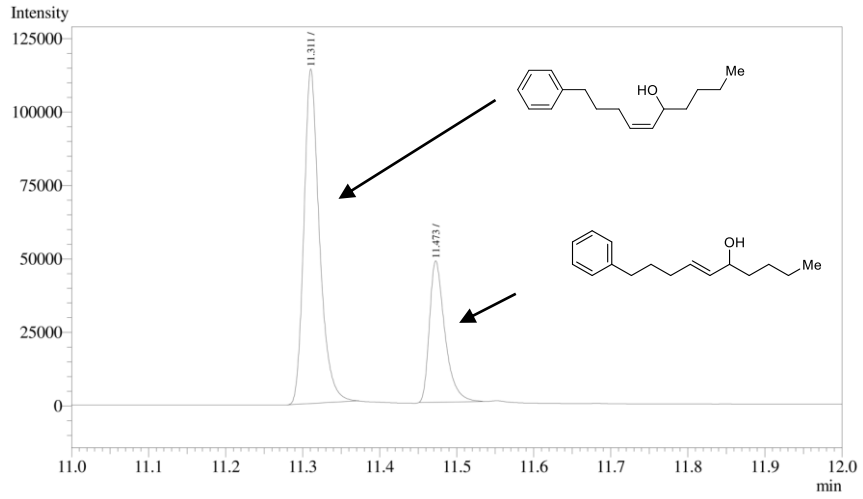
Peak#	Ret.Time	Area	Height	Conc.
1	11.470	72761	52203	100.000
Total		72761	52203	

Figure 1.2 GC Trace of Isolated *Z*-1.18



Peak#	Ret.Time	Area	Height	Conc.
1	11.312	23196	10012	100.000
Total		23196	10012	

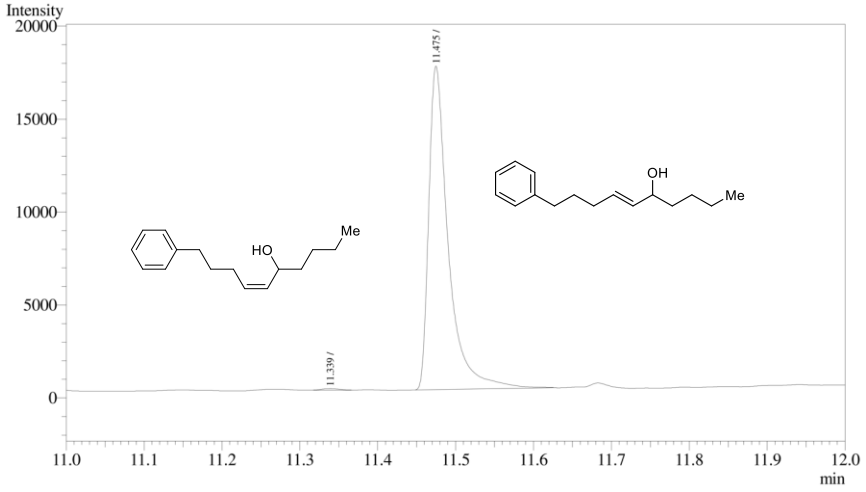
Figure 1.3 GC Trace of a Mixture of 1.18 and *Z*-1.18



Peak#	Ret.Time	Area	Height	Conc.
1	11.311	160028	112310	70.424
2	11.473	67207	47372	29.576
Total		227235	159682	

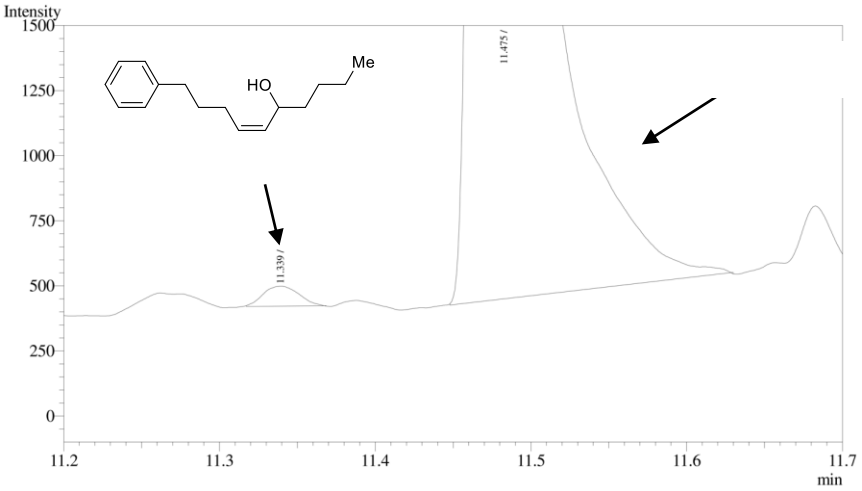
E/Z selectivity was determined by GC analysis of an aliquot taken from a crude reaction mixture at the end of the oxidation as described in general procedure A.

Figure 1.4 GC Trace of Crude Reaction Mixture



Peak#	Ret.Time	Area	Height	Conc.
1	11.339	119	75	0.390
2	11.475	30424	17161	99.610
Total		30543	17236	

Figure 1.5 Magnified GC Trace of Crude Reaction Mixture



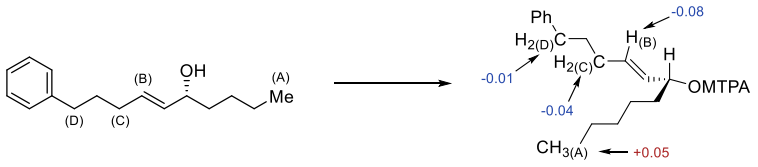
Peak#	Ret.Time	Area	Height	Conc.
1	11.339	119	75	0.390
2	11.475	30424	17161	99.610
Total		30543	17236	

The relative concentration of the two isomers is 255:1 *E* to *Z*.

1.4.6 Mosher Ester Analysis

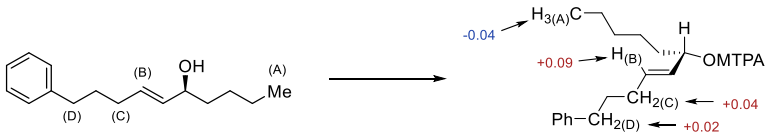
The absolute configuration of compounds **(*R*)-1.18**, **(*S*)-1.18**, and **(*R*)-1.43** was determined by Mosher ester analysis. Preparation of the mosher esters was performed according to a previously reported procedure.[104]

Table 1.10 Mosher Ester Analysis of (*R*)-1.18



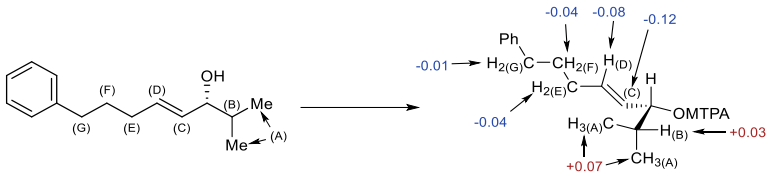
	δ *S*-ester	δ *R*-ester	$\Delta\delta^{SR} = (\delta_S - \delta_R)$	
	(*R*)-1.18-(*S*) (ppm)	**(*R*)-1.18**-(*R*) (ppm)	ppm	Hz (500 MHz)
CH_3-(A)	0.87	0.82	+0.05	+25
CH-(B)	5.76	5.84	-0.08	-40
CH_2-(C)	2.03	2.07	-0.04	-20
CH_2-(D)	2.57	2.58	-0.01	-5

Table 1.11 Mosher Ester Analysis of (*S*)-1.18



	δ *S*-ester	δ *R*-ester	$\Delta\delta^{SR} = (\delta_S - \delta_R)$	
	(*S*)-1.18-(*S*) (ppm)	**(*S*)-1.18**-(*R*) (ppm)	ppm	Hz (500 MHz)
CH_3-(A)	0.83	0.87	-0.04	-20
CH-(B)	5.85	5.76	+0.09	+45
CH_2-(C)	2.08	2.04	+0.04	+20
CH_2-(D)	2.59	2.57	+0.02	+10

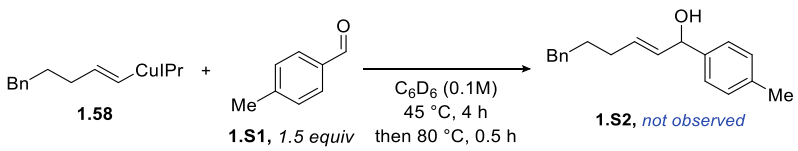
Table 1.12 Mosher Ester Analysis of (*R*)-1.43



	δ *S*-ester	δ *R*-ester	$\Delta\delta^{SR} = (\delta_S - \delta_R)$	
	(*R*)-1.43-(*S*) (ppm)	**(*R*)-1.43**-(*R*) (ppm)	ppm	Hz (500 MHz)
2x CH_3-(A)	0.90	0.83	+0.07	+35
CH-(B)	1.90	1.87	+0.03	+15
CH-(C)	5.32	5.44	-0.12	-60
CH-(D)	5.76	5.84	-0.08	-40
CH_2-(E)	2.05	2.09	-0.04	-20
CH_2-(F)	1.66	1.70	-0.04	-20
CH_2-(G)	2.57	2.58	-0.01	-5

1.4.7 Addition of Alkenyl Copper to Aldehydes

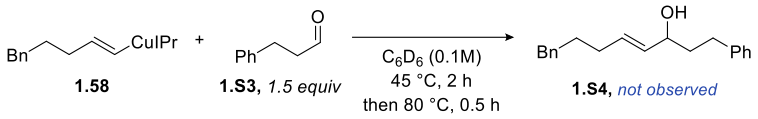
Scheme 1.11 Addition to Aryl Aldehydes



In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (14.6 mg, 0.025 mmol, 1.0 equiv). To this vial was added *p*-tolualdehyde (**1.S1**) (4.5 mg, 0.038 mmol, 1.5 equiv), internal standard TMB (2.1 mg, 0.013 mmol) and C_6D_6 (0.1 M). The

reaction was stirred for 4 hours at 45 °C and then an aliquot (100 µL) was analyzed by NMR. No product was observed, and the reaction temperature was increased to 80 °C for 30 minutes at which point the reaction mixture was analyzed by NMR and GC-MS and no product formation was observed.

Scheme 1.12 Addition to Alkyl Aldehydes



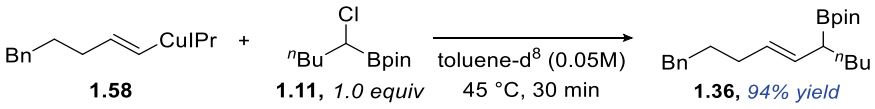
1.58 **1.S3,** *1.5 equiv* **1.S4,** *not observed*

In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (14.6 mg, 0.025 mmol, 1.0 equiv). To this vial was added 3-phenylpropinal (**1.S3**) (4.5 mg, 0.038 mmol, 1.5 equiv), internal standard TMB (2.1 mg, 0.013 mmol) and C_6D_6 (0.1 M). The reaction was stirred for 4 hours at 45 °C and then an aliquot (100 µL) was analyzed by NMR. No product was observed, and the reaction temperature was increased to 80 °C for 30 minutes at which point the reaction mixture was analyzed by NMR and GC-MS and no product formation was observed.

1.4.8 Mechanistic Studies

1.4.8.1 Stoichiometric Reaction with Alkenyl Copper and α-Chloro Boronic Ester

Scheme 1.13 Stoichiometric Reaction with Alkenyl Copper and α-Chloro Boronic Ester



1.58 **1.11,** *1.0 equiv* **1.36,** *94% yield*

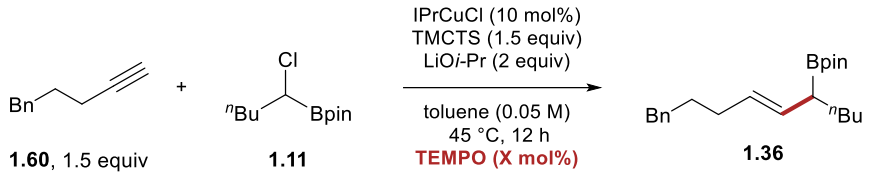
In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (17.9 mg, 0.03 mmol, 1.0 equiv). To this vial was added α-chloro boronic ester (**1.11**) (7.0 mg, 0.03 mmol, 1.0 equiv), internal standard TMB (2.5 mg, 0.02 mmol) and toluene-d^8 (0.05 M). The reaction yield was monitored by NMR.

Table 1.13 Stoichiometric Reaction of Alkenyl Copper and α-Chloro Boronic Ester

Time	Yield of 1.36 (%)
10 minutes	87
30 minutes	94
1.5 hours	95

1.4.8.2 Radical Trap Probe

Scheme 1.14 Radical Trap Probe



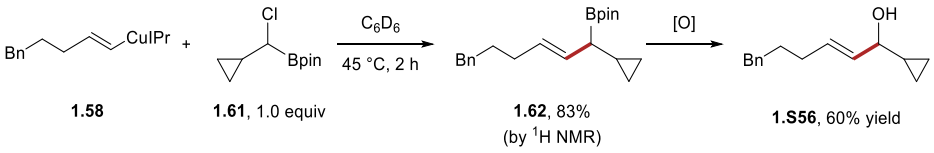
In a nitrogen-filled glovebox, a scintillation vial was charged with a stir bar, LiO*i*-Pr (20.2mg, 0.40 mmol, 2.0 equiv) and IPrCuCl (9.8 mg, 0.02 mmol, 0.1 equiv). To this vial was added 5-phenylpentyne (**1.60**) (48.0 mg, 0.30 mmol, 1.5 equiv), TMCTS (72.2 mg, 0.3 mmol, 1.5 equiv) and toluene (0.05 M). The resulting mixture was then stirred at 25 °C until the yellow color faded. α-Chloro boronic ester (**1.11**) (46.6 mg, 0.20 mmol), internal standard TMB (36.1 mg, 0.20 mmol) and required amount of TEMPO was transferred to the reaction flask. The reaction mixture was stirred at 45 °C overnight. Then, an aliquot (100 µL) from the reaction mixture was passed through a plug of silica with ethyl acetate, concentrated and analyzed by NMR. Table 1.14 shows the product yield with different amounts of TEMPO.

Table 1.14 Radical Trap Probe

Entry	mol % of TEMPO	Yield of 1.36 (%)
1	0	83
2	20	82
3	150	73

1.4.8.3 Radical Clock Experiment

Scheme 1.15 Radical Clock Experiment

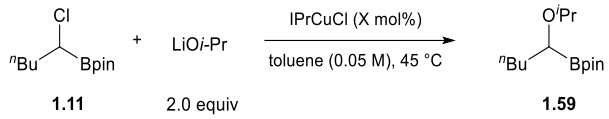


In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (119.5 mg, 0.20 mmol). To this vial was added α-chloro boronic ester (**1.61**) (53.2 mg, 0.20 mmol, 1 equiv) internal standard TMB (33.4 mg, 0.20 mmol) and C_6D_6 (0.05 M). The reaction mixture was stirred at 45 °C for 2 h and analyzed by NMR (NMR yield of the allylic boronic ester = 84%). Then the reaction mixture was then oxidized with H_2O_2/NaOH following general procedure A. The resulting mixture was passed through a plug of silica, concentrated, and then purified by silica chromatography (0-20% EtOAc and hexanes) to afford **1.S56** as a yellow liquid (26.0 mg, 60% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.22 – 7.14 (m, 3H), 5.79 – 5.64 (m, 1H), 5.61 - 5.53 (m, 1H), 3.45 (dd, J = 8.0, 6.0 Hz, 1H), 2.63 (dd, J = 8.6, 6.7 Hz, 2H), 2.21 – 2.02 (m, 2H), 1.83 – 1.67 (m, 2H), 1.61 (s, 1H), 1.05 - 0.94 (m, 1H), 0.63 – 0.45 (m,

2H), 0.39 – 0.30 (m, 1H), 0.29 – 0.17 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 132.0, 131.5, 128.6, 128.4, 125.8, 35.5, 31.9, 31.0, 17.7, 3.2, 2.1. MS-ESI (m/z): $[M\text{-}OH]^+$ calculated for $C_{15}H_{19}$, 199.1; found, 198.8. FTIR (neat, cm^{-1}): 3358 (br), 3025 (s), 2958 (s), 2923 (s), 1668 (m), 1467 (m), 1032 (m), 978 (s), 730 (w).

1.4.8.4 Evaluating α-Isopropoxy Boronic Ester as a Potential Intermediate

Scheme 1.16 α-Isopropoxy Boronic Ester Formation

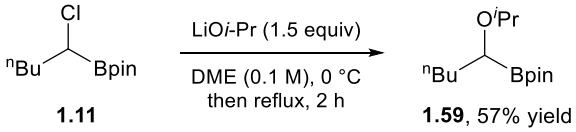


In a nitrogen-filled glovebox, a scintillation vial was charged with a stir bar and LiO*i*-Pr (13.2 mg, 0.20 mmol, 2.0 equiv) and required amount of IPrCuCl catalyst (no catalyst or 4.9 mg, 0.01 mol, 0.1 equiv). To this vial was added α-chloro boronic ester (**1.11**) (23.3 mg, 0.10 mmol), internal standard TMB (8.4 mg, 0.05 mmol) and toluene (0.05 M). The reaction mixture was stirred at 45 °C. An aliquot (100 µL) of the crude reaction mixture, at the reported times, was passed through a plug of silica with ethyl acetate, concentrated, and analyzed by NMR.

Table 1.15 Formation of α-Isopropoxy Boronic Ester

Time (hours)	Yield of 1.59 (%)	
	No IPrCuCl	10 mol% IPrCuCl
2	6	8
4	9	10
8	12	14
12	17	20
27	31	43

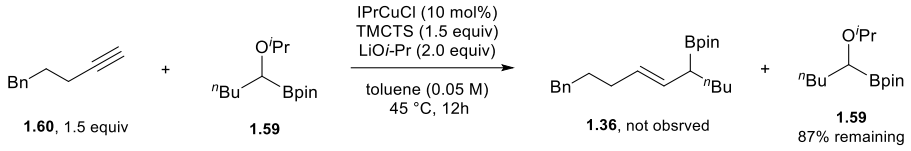
Scheme 1.17 Synthesis of α-Isopropoxy Boronic Ester



4,4,5,5-tetramethyl-2-[1-(propan-2-yloxy)pentyl]-1,3,2-dioxaborolane (**1.59**), A flask was charged with LiO*i*-Pr (200 mg, 3.0 mmol, 1.5 equiv) and anhydrous DME (20 mL). The solution was cooled to 0 °C and **1.11** (465 mg, 2.0 mmol, 1.0 equiv) was added. The reaction was warmed to room temperature and then refluxed for 2 hours. The reaction mixture was filtered through a plug of silica and concentrated under vacuum. The crude product was then purified by silica gel chromatography (15% Et_2O in hexanes) to give **1.59** as a colorless liquid (293 mg, 57% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.52 (hept, J = 6.0 Hz, 1H), 3.19 (t, J = 6.9 Hz, 1H), 1.61 – 1.55 (m,

2H), 1.40-1.28 (m, 4H), 1.26 (s, 6H), 1.25 (s, 6H), 1.13 (d, J = 6.1 Hz, 6H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 83.5, 71.2, 31.7, 28.8, 24.9, 24.5, 22.8, 22.2, 14.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.59. GCMS (EI) calculated for $[M]^+$ 256.2, found 256.2. FTIR (neat, cm^{-1}): 2974 (s), 2927 (s), 2861 (s), 1457 (m), 1388 (s), 1146 (s), 1049 (m), 967 (w), 847 (w).

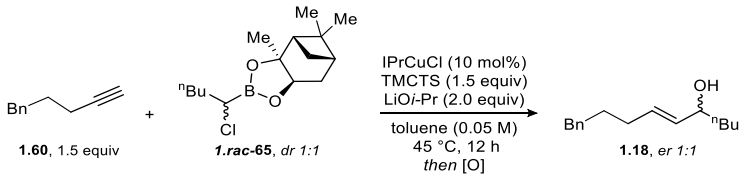
Scheme 1.18 α-Isopropoxy Boronic Ester in Hydroalkylation Reaction



According to general procedure A, in a nitrogen-filled glovebox, a scintillation vial was charged with a stir bar, LiO*i*-Pr (13.2mg, 0.20 mmol, 2.0 equiv) and IPrCuCl (4.9 mg, 0.01 mmol, 0.1 equiv). To this vial was added 5-phenylpentyne (**1.60**) (21.6 mg, 0.15 mmol, 1.5 equiv), TMCTS (36.0 mg, 0.15 mmol, 1.5 equiv) and toluene (0.05 M). The resulting mixture was then stirred at 25 °C until the yellow color disappeared. α-Isopropoxy pentyl boronic ester (**1.59**) (25.6 mg, 0.10 mmol) and internal standard TMB (9.4 mg, 0.56 mmol) were transferred to the reaction mixture. The reaction mixture was stirred at 45 °C overnight. The reaction was then concentrated and analyzed by NMR. The allylic boronic ester product (**1.36**) was not observed and 87% of the starting α-isopropoxy boronic ester (**1.59**) was present in the final reaction mixture.

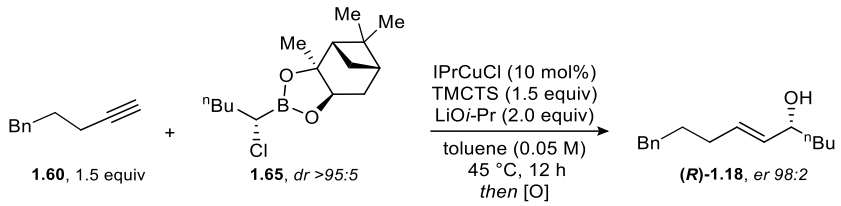
1.4.8.5 Investigating the Ionic Mechanism and Origin of Enantioselectivity

Scheme 1.19 Stereochemistry with Diastereomeric Mixture of α-Chloro Bpinane



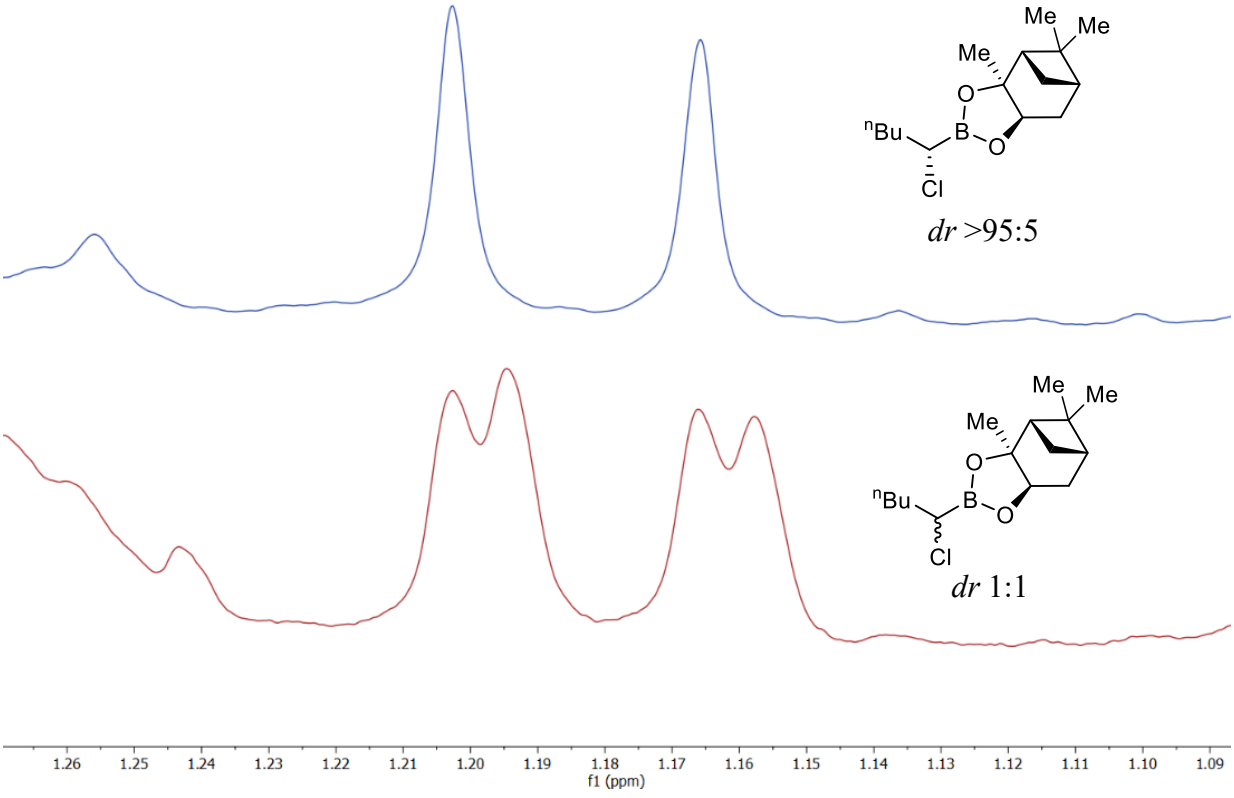
The α-chloro pinanediol boronic ester with a diastereomeric mixture of (**1.65**) was prepared according to according to a reported procedure from compound **1.11**.[107] The diastereomeric ratio was assessed using the characteristic pinanyl proton that appears as a doublet between δ 1.1-1.2 in $CDCl_3$ (J = 11.1 Hz) and was found to be 1:1.[105] The reaction was performed according to general procedure A (16 mg, 73% yield) with characterization matching compound **1.18**. The resulting alcohol (**1.18**) was a 1:1 mixture of the *R* and *S* enantiomer. Enantiomeric ratio of the alcohol product was determined by chiral HPLC. CHIRALPAK AD-H column (0.02% 2-PrOH in hexanes, 0.6 mL/min, detected at 220 nm wavelength) with t_r = 68.9 min (major), 79.7 min (minor).

Scheme 1.20 Stereochemistry with Diastereomerically Pure α-Chloro Bpinane



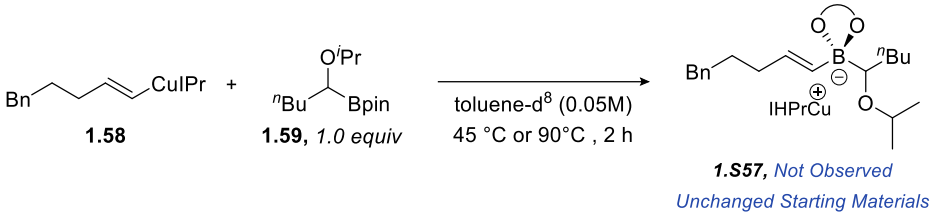
The enantioenriched α-chloro pinanediol boronic ester was prepared as referenced above (**1.65**). The diastereomeric ratio was assessed using the characteristic pinanyl proton that appears as a doublet between δ 1.1-1.2 in $CDCl_3$ (J = 11.1 Hz) compared to the racemic sample and was found to be >20:1. The resulting alcohol is listed as product (**(*R*)-1.18**) and was found to have an enantiomeric ratio of 98:2.

Figure 1.6 ^{1}H NMR Determination of 1.65's Diastereomeric Ratio



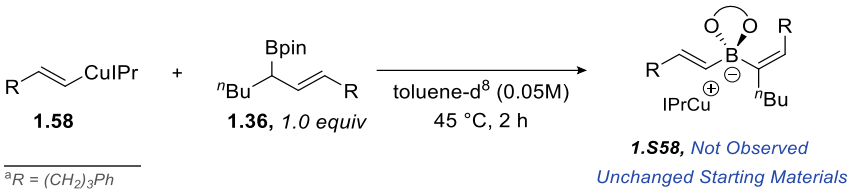
1.4.8.6 Investigation of Boron-ate Complex Formation

Scheme 1.21 Reaction of Alkenyl Copper and α-Isopropoxy Boronic Ester



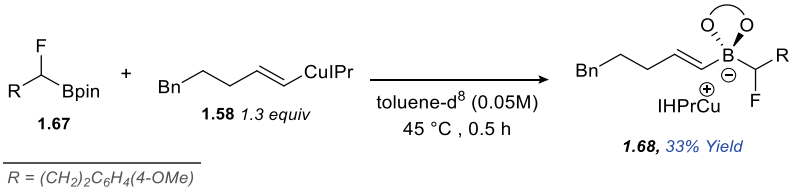
In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (1.**58**) (14.6 mg, 0.025 mmol, 1.0 equiv). To this vial was added α-isopropoxy boronic ester (**1.59**) (6.4 mg, 0.025 mmol, 1.0 equiv), internal standard TMB (2.1 mg, 0.013 mmol) and toluene-d^8 (0.05 M). The reaction was stirred at 45 °C and monitored by ^{1}H and ^{11}B NMR. This procedure was repeated with the reaction stirred at 90 °C instead of 45 °C. In both cases there was no change observed in the starting materials or evidence for boron-ate formation (**1.S57**) by ^{1}H and ^{11}B NMR.

Scheme 1.22 Reaction of Alkenyl Copper and Allylic Boronic Ester



In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (14.6 mg, 0.025 mmol, 1.0 equiv). To this vial was added the allylic boronic ester (**1.36**) (8.6 mg, 0.025 mmol, 1.0 equiv), internal standard TMB (2.1 mg, 0.013 mmol) and toluene-d^8 (0.05 M). The reaction was stirred at 45 °C monitored by ^{1}H and ^{11}B NMR. There was no change observed in the starting materials or evidence for boron-ate formation (**1.S58**) by ^{1}H and ^{11}B NMR.

Scheme 1.23 Reaction of Alkenyl Copper and α-Fluoro Boronic Ester



α-Fluoro boronic ester (**1.67**) was prepared according to a previously reported procedure.[108]

In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (29.9 mg, 0.05 mmol, 1.3 equiv). To this vial was added the α-fluoro boronic ester (**1.67**) (11.3 mg, 0.04 mmol, 1.0 equiv), internal standard TMB (4.2 mg, 0.03 mmol) and toluene-d^8 (0.05 M). The reaction was stirred at 45 °C and monitored by ^{1}H and ^{11}B NMR.

Figure 1.7 ^{11}B NMR of the Reaction of 1.58 with 1.67

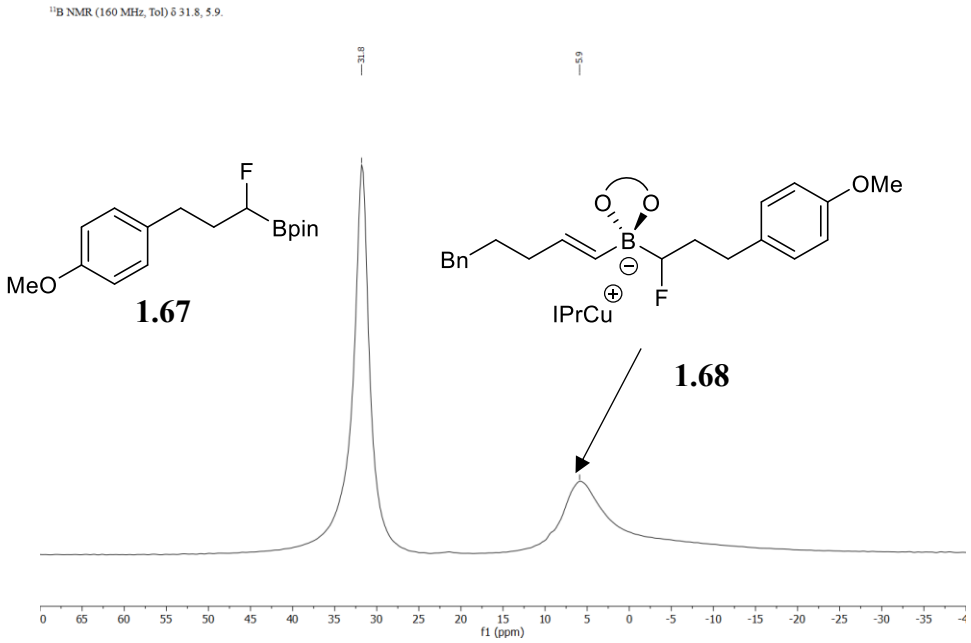
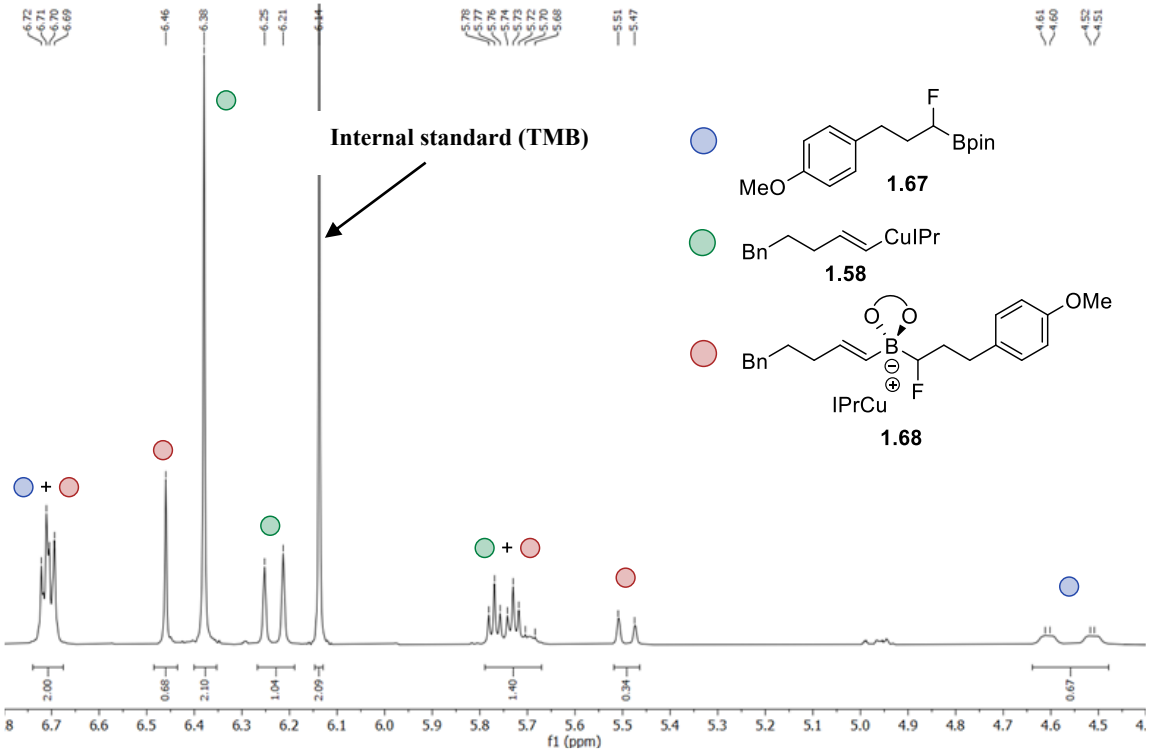
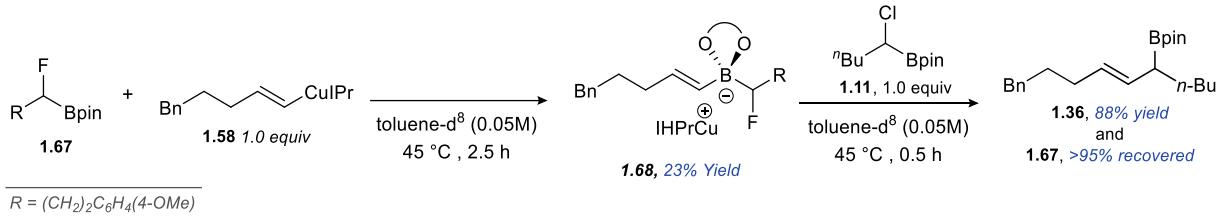


Figure 1.8 Magnified ^{1}H NMR of the Reaction of 1.58 with 1.67



Scheme 1.24 Reversible Formation of Boron-ate Complex 1.68



In a nitrogen-filled glovebox, a 4 mL scintillation vial was charged with a stir bar and alkenyl copper (**1.58**) (14.6 mg, 0.025 mmol, 1.0 equiv). To this vial was added the α-fluoro boronic ester (**1.67**) (8.6 mg, 0.025 mmol, 1.0 equiv), internal standard TMB (2.1 mg, 0.013 mmol) and toluene-d^8 (0.05 M). The reaction was stirred at 45 °C and was monitored by ^{1}H and ^{11}B NMR for 2.5 hours. Between 30 minutes and 2.5 hours there was no observed change by ^{1}H or ^{11}B NMR. After 2.5 hours α-chloro boronic ester (**1.11**) (5.8 mg, 0.025 mmol, 1.0 equiv) was added and the reaction was stirred for 30 minutes at 45 °C and monitored by ^{1}H and ^{11}B NMR.

Figure 1.9 Magnified ^{1}H NMR of the Reaction of 1.58 with 1.67 after 2.5 h

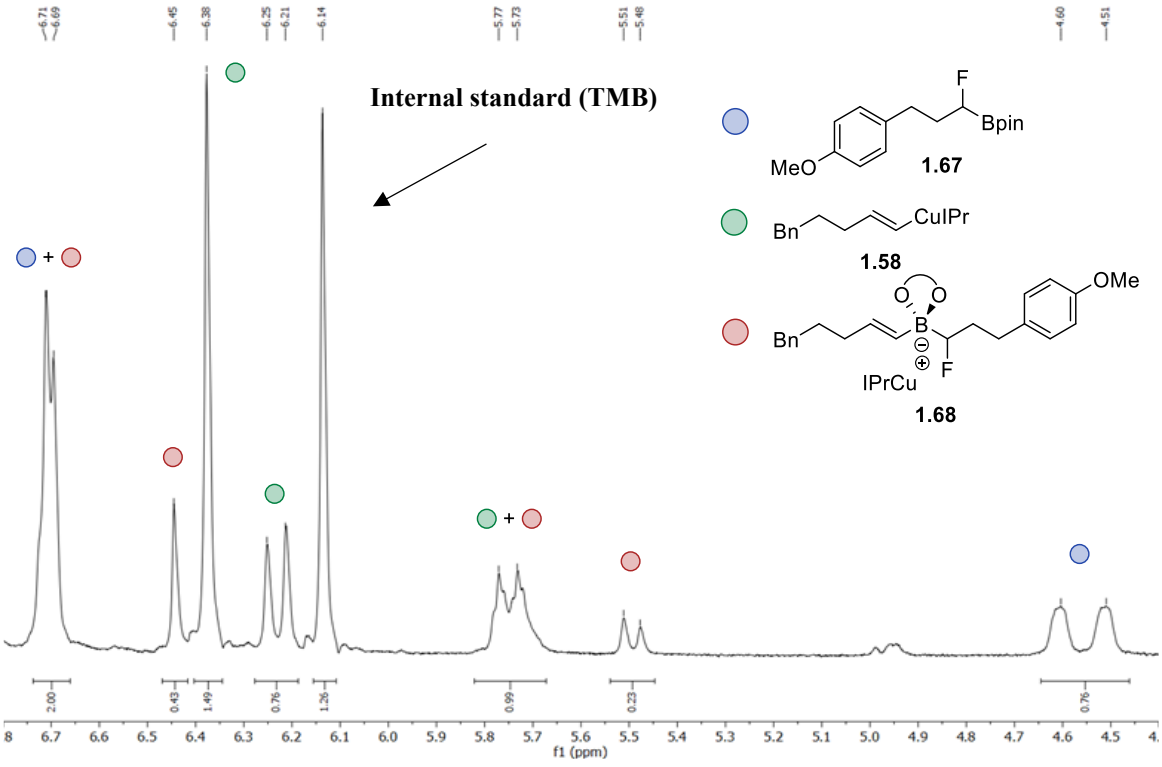
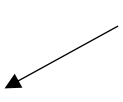
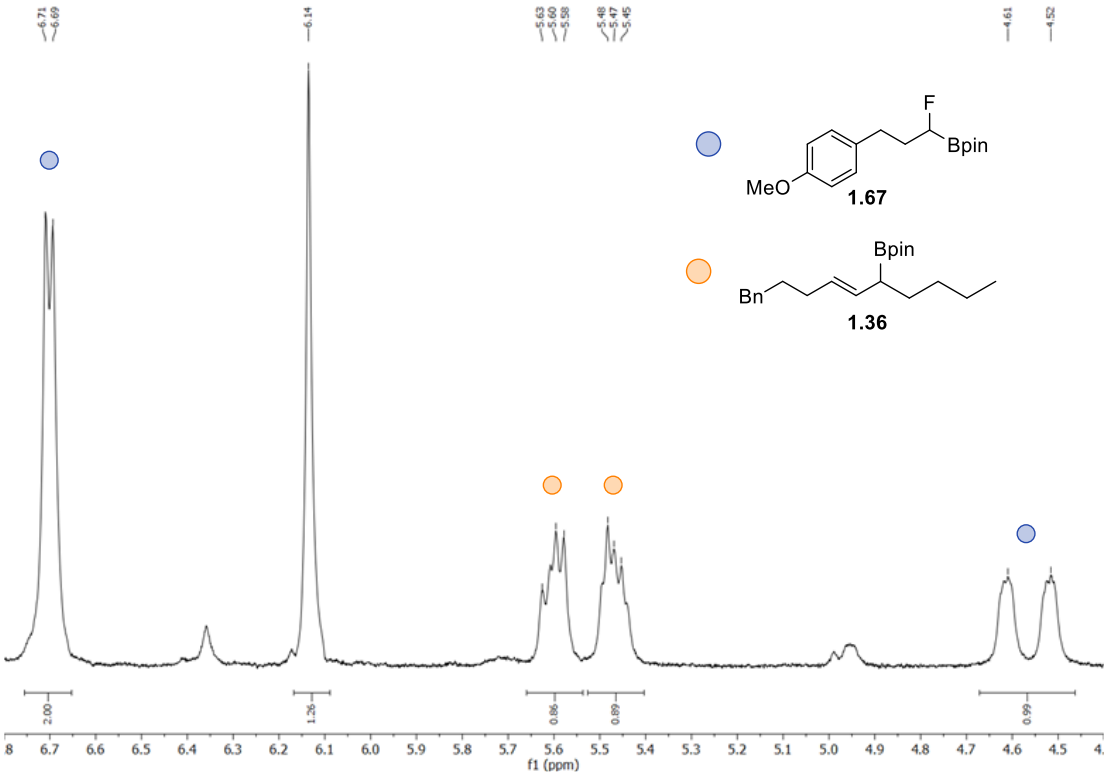
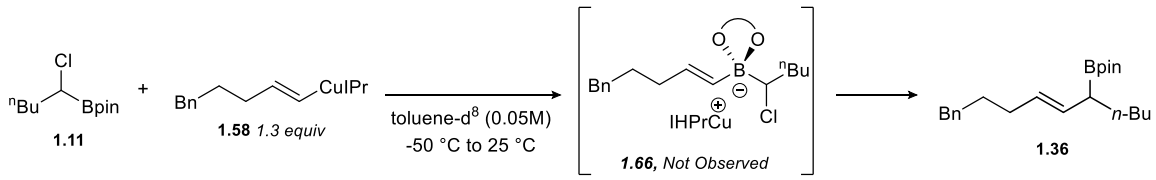


Figure 1.10 Magnified 1H NMR of the Reaction of 1.58 with 1.67, then Addition of 1.11



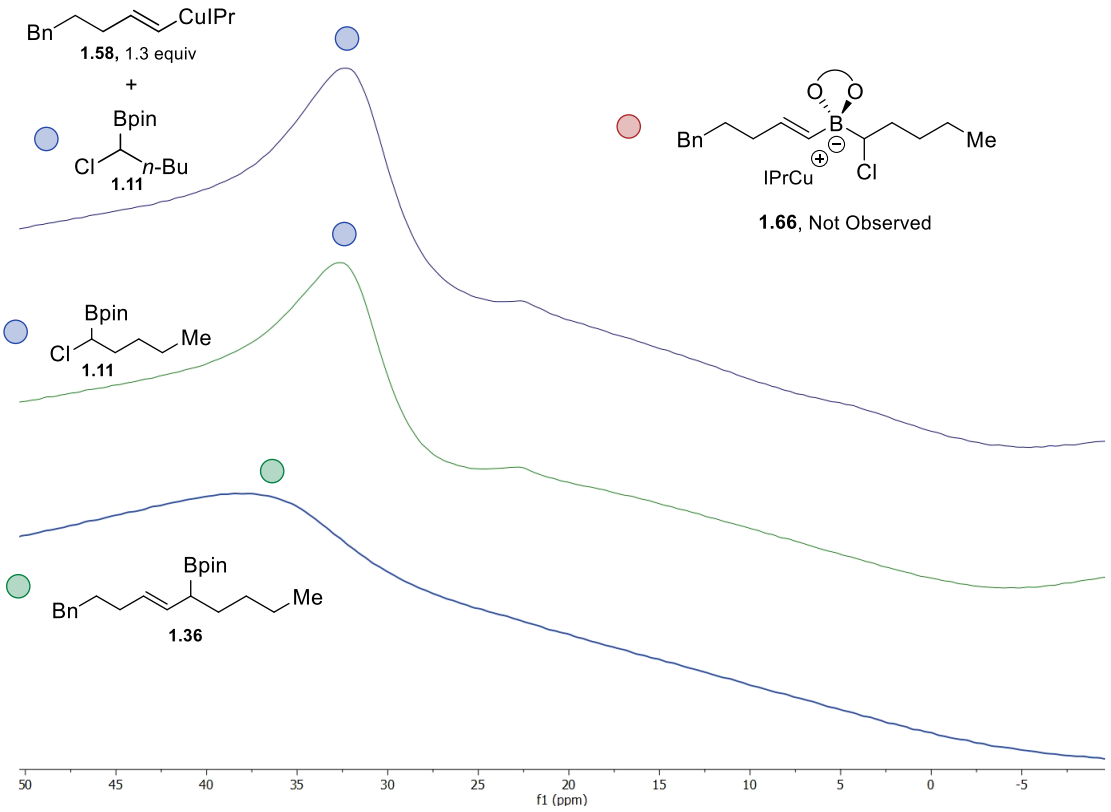


Scheme 1.25 Reaction of Alkenyl Copper and α-Chloro Boronic Ester at Low Temperature



In a nitrogen-filled glovebox, a quartz J-Young NMR tube was charged with alkenyl copper (**1.58**) (23.3 mg, 0.04 mmol, 1.3 equiv) and internal standard TMB (2.5 mg, 0.02 mmol) along with 300 µL of toluene-d^8. The NMR tube was sealed removed from the glovebox. It was then frozen in liquid nitrogen and the α-chloro boronic ester (**1.11**) (7.0 mg, 0.03 mmol, 1.0 equiv) was added under nitrogen in solution of toluene-d^8 (0.1 M). The NMR tube was kept in a liquid nitrogen bath until just before it was to be analyzed, at which time it was warmed to -78 °C, gently shaken, and inserted into the pre-cooled NMR probe. The reaction was monitored by ^{1}H and ^{11}B NMR beginning at -50 °C and warming up to 25 °C in regular temperature increments, taking ^{1}H and ^{11}B at each increment. After reaching 25 °C the reaction was removed from the NMR, briefly shaken in order to mix the insoluble IPrCuCl crashing out of solution and then returned to the NMR.

Figure 1.11 ^{11}B NMR at -50 °C in toluene-d^8



^{11}B NMR at -50 °C in toluene-d^8 of **1.11** (middle spectrum), **1.36** (lower spectrum) and the reaction of 1.3 equiv of **1.58** with **1.11** (top spectrum).

Figure 1.12 ^{11}B NMR of the Reaction in Toluene-d^8 at Increasing Temperatures

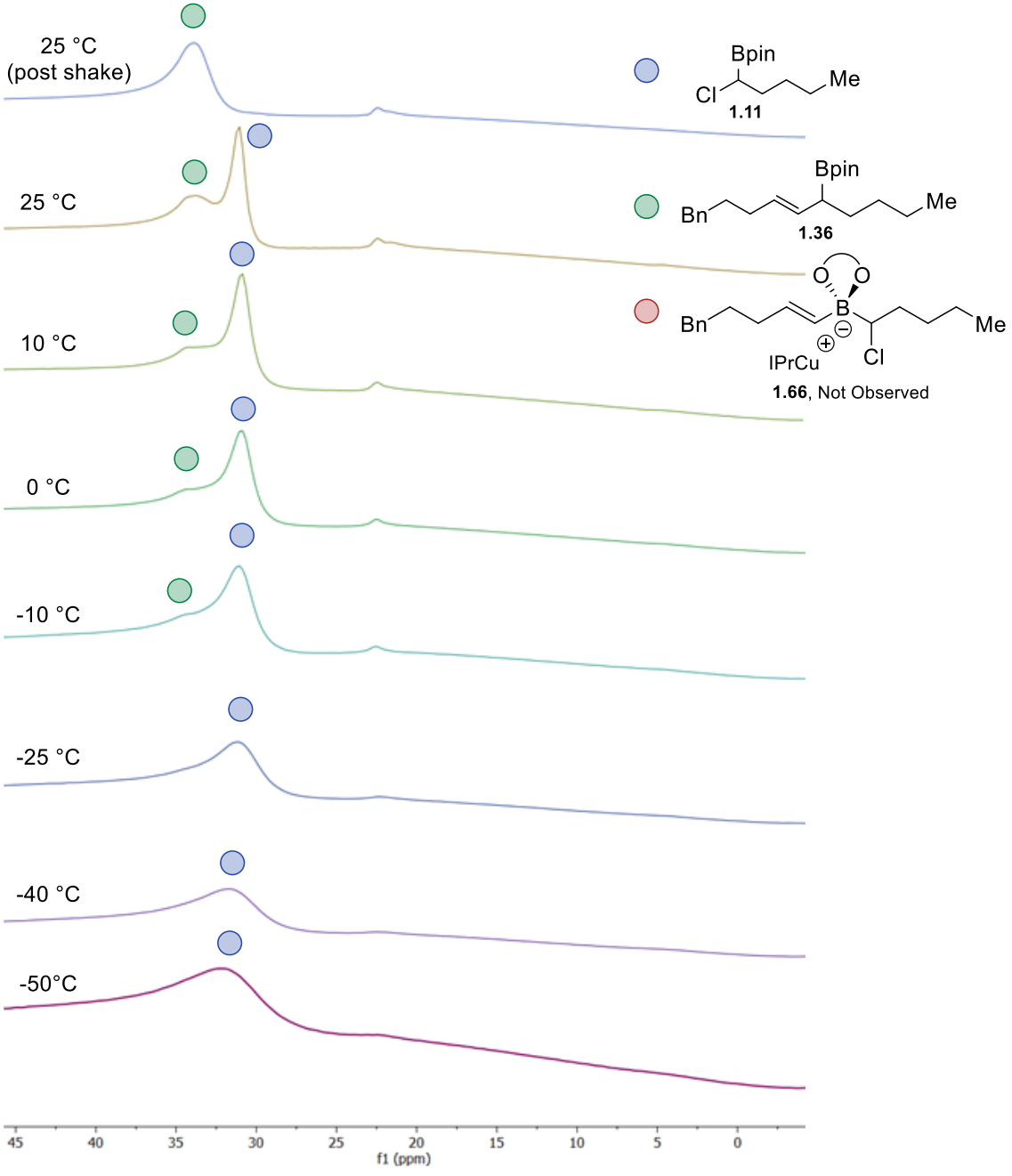
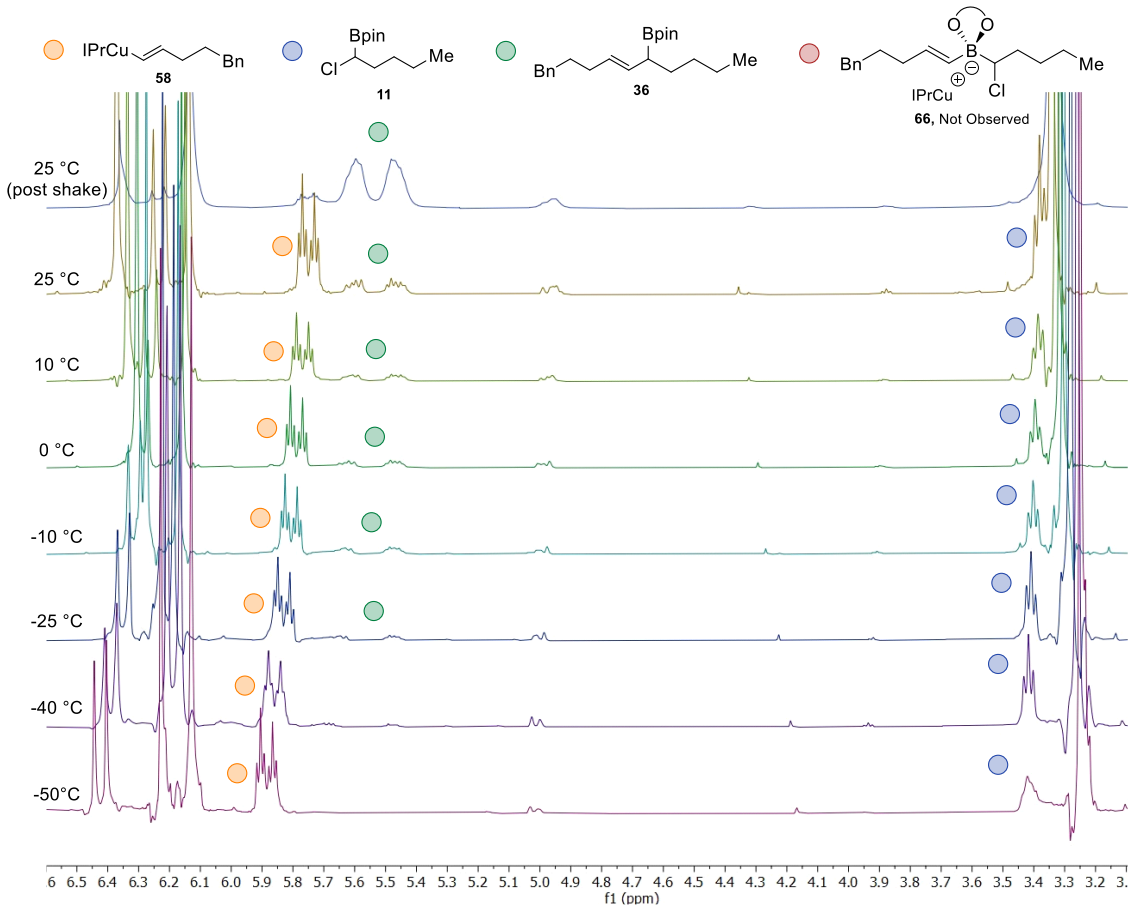
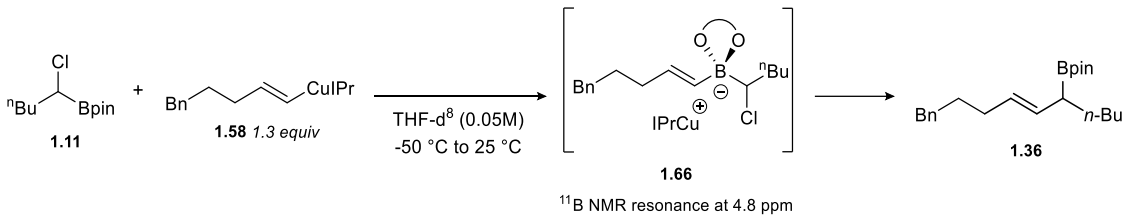


Figure 1.13 ^{1}H NMR of the Reaction in Toluene-d^{8} at Increasing Temperatures



Scheme 1.26 Reaction of Alkenyl Copper and α-Chloro Boronic Ester in THF-*d*^{8}



^{11}B NMR resonance at 4.8 ppm

In a nitrogen-filled glovebox, a quartz J-Young NMR tube was charged with alkenyl copper (**1.58**) (23.3 mg, 0.04 mmol, 1.3 equiv) and internal standard TMB (2.5 mg, 0.02 mmol) along with 300 µL of THF-*d*^{8}. The NMR tube was sealed removed from the glovebox. It was then frozen in liquid nitrogen and the α-chloro boronic ester (**1.11**) (7.0 mg, 0.03 mmol, 1.0 equiv) was added under nitrogen in solution of THF-d^{8} (0.1 M). The NMR tube was kept in a liquid nitrogen bath until just before it was to be analyzed, at which time it was warmed to -78 °C, gently shaken, and inserted into the pre-cooled NMR probe. The reaction was monitored by ^{11}B NMR beginning at -50 °C and warming up to 25 °C in regular temperature increments, taking ^{11}B at each increment.

Figure 1.14 ^{11}B NMR at -50 °C in THF-d^8

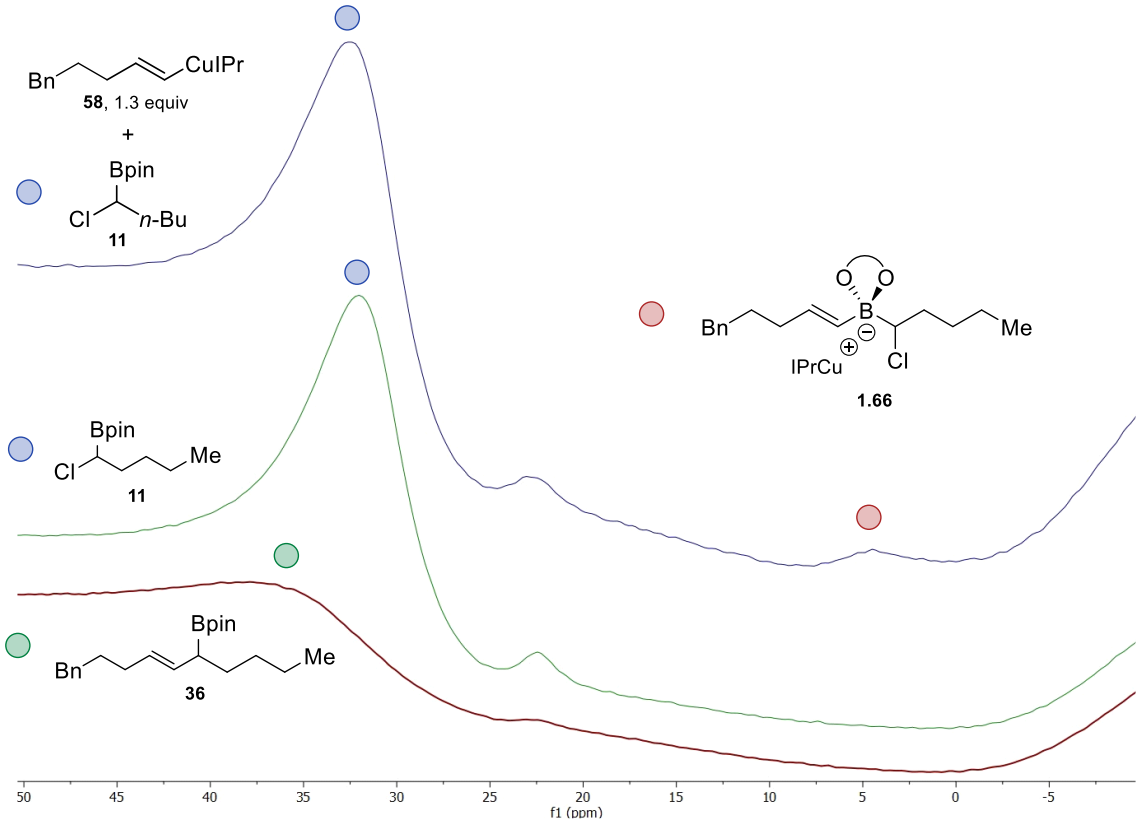
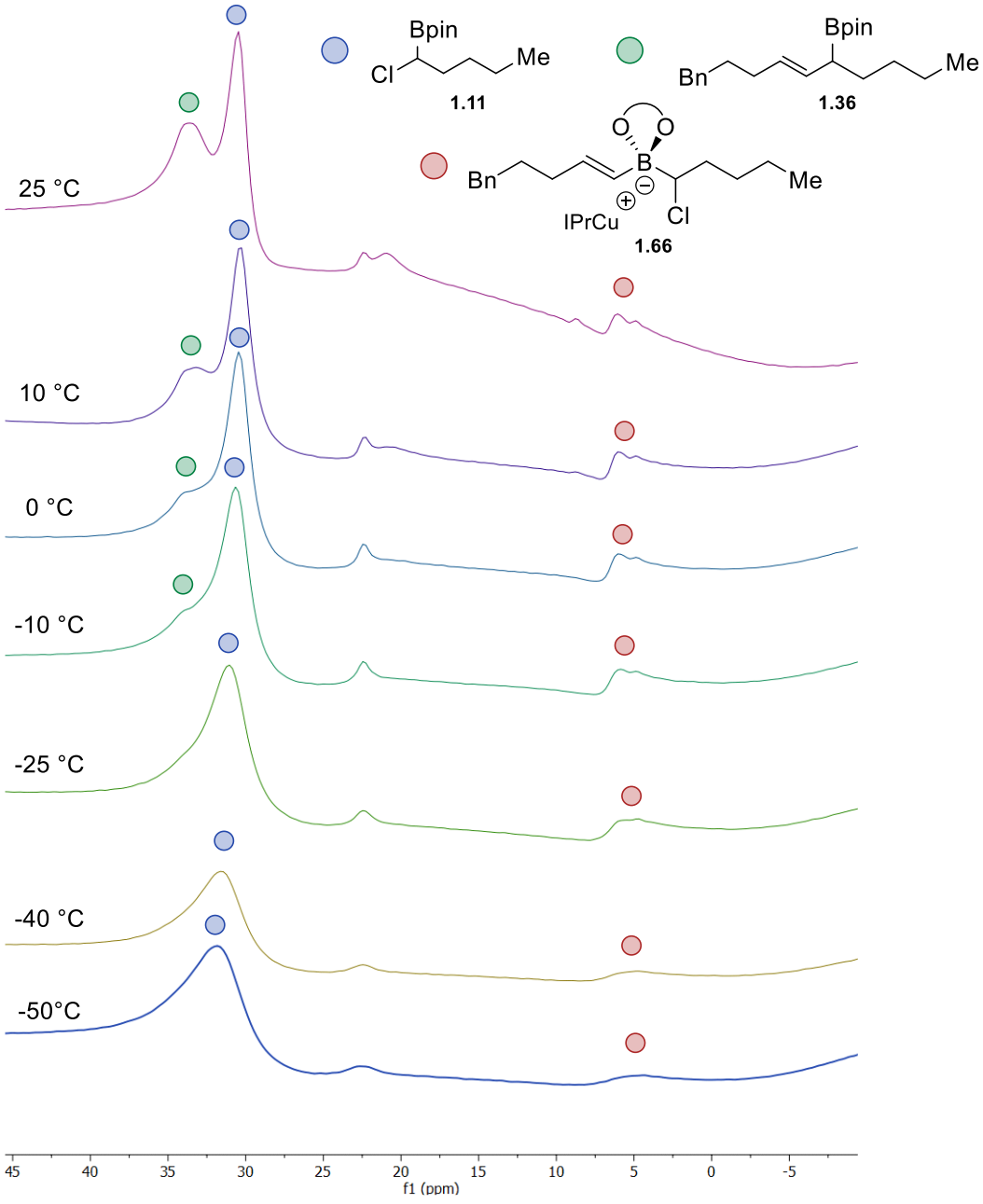


Figure 1.15 ^{11}B NMR of the Reaction in THF-d^8 at Increasing Temperatures



1.5 References for Chapter 1

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Chapter 2 Regio- and Diastereoselective Synthesis of Trisubstituted Alkenes Through Hydroalkylation of Alkynyl Boronamides

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2.1 Introduction

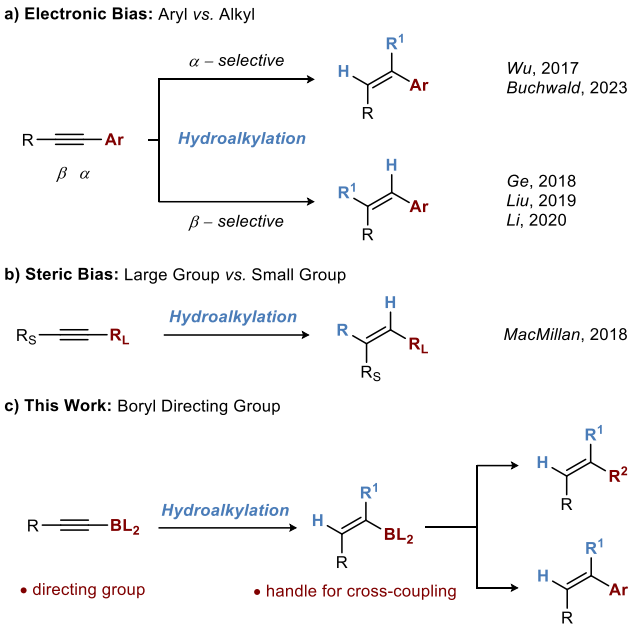
Substituted alkenes are versatile synthetic intermediates[1] and common structural elements found in biologically active molecules and natural products.[2] As a result, improving access to this important class of compounds remains an important goal of synthetic organic chemistry. In recent years, hydroalkylation of alkynes has emerged as a powerful new approach to alkene synthesis. The most significant impact of hydroalkylation has been in the synthesis of disubstituted alkenes. Various hydroalkylation reactions now allow transformation of terminal alkynes into all three isomers of disubstituted alkenes with excellent regio- and diastereoselectivity.[3]

Hydroalkylation has had more limited applications in the synthesis of tri-substituted alkenes. The main challenge that prevents broader application of this approach has been the control of regioselectivity in the hydroalkylation of nonsymmetrical internal alkynes. So far, two main strategies have been used to address this challenge. Good regioselectivity has been achieved with activated aryl alkynes, where electronic bias introduced by an aryl group controls the regioselectivity (Scheme 2.1a).[4] Alternatively, sterically demanding alkyl substituents that introduce steric bias have also been used to impart good selectivity (Scheme 2.1b).[3b] While successful, these strategies provide access to an inherently limited scope of trisubstituted alkenes.

To develop a more general hydroalkylation method for the synthesis of trisubstituted alkenes, we envisioned the use of functionalized alkynes containing a directing group. Ideally, the directing group would control the regioselectivity of the reaction and then, after the reaction, could be removed from the molecule in a productive way. With these considerations in mind, we chose to focus on boryl directing groups (Scheme 2.1c), which have been used to control transition metal-catalyzed[5] and radical[6] addition reactions to unsaturated compounds. Derivatives of boronic acids such as boronic esters, *N*-coordinated boronic esters, and boronamides can be easily incorporated through borylation[7] of terminal alkynes and would allow us to explore directing groups with a wide range of steric and electronic properties. At the same time, these groups[8] could all be removed in a subsequent cross-coupling reaction that would provide access to a range of trisubstituted alkenes.

In this article, we report nickel-catalyzed hydroalkylation of alkynyl boronamides using alkyl halides as coupling partners. Introducing the boryl directing group into terminal alkynes allows the control of regioselectivity in the hydroalkylation and provides access to trisubstituted *E*-alkenyl boronamides[9] with high selectivity. We also show that the resulting alkenyl boronamides can be used to access trisubstituted alkenes, including those with all alkyl substituents.

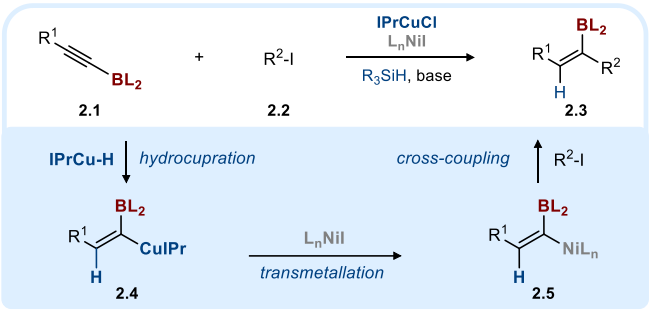
Scheme 2.1 Regiocontrol in hydroalkylation of disubstituted alkynes.



2.2 Results and Discussion

Our initial approach to the synthesis of trisubstituted alkenes is based on the method for hydroalkylation of terminal alkynes our group reported in 2019 (Scheme 2.2).[3e] We envisioned that the hydroalkylation of boryl alkyne **2.1** would proceed through copper hydride formation, followed by hydrocupration, and the nickel-catalyzed cross coupling of the alkenyl copper intermediate (**2.4**) with an alkyl halide. The main question we tried to answer is if boryl groups are compatible with alkenyl copper formation and if they could control the regioselectivity of the process.

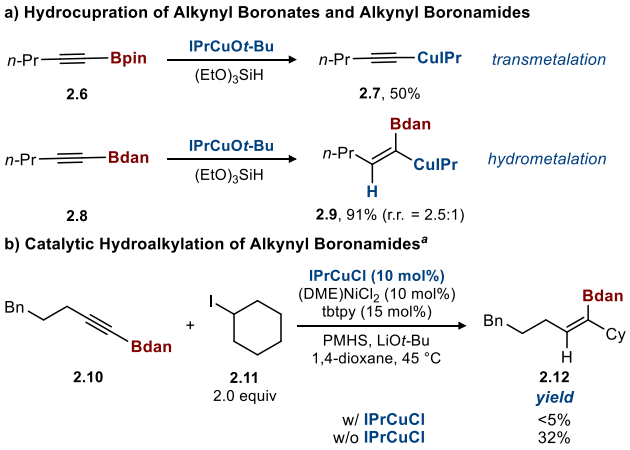
Scheme 2.2 Reaction Design



A stoichiometric reaction between alkynyl Bpin **2.6** and IPrCuH formed by premixing IPrCuO*t*-Bu[10] and $(EtO)_3SiH$[11] resulted in exclusive formation of copper acetylide **2.7** and no formation of the alkenyl copper complex (Scheme 2.3a). The formation of the copper hydride intermediate was indicated by the formation of $(EtO)_3SiO$*t*-Bu byproduct, suggesting that hydrocupration of the alkynyl Bpin had failed.

To prevent the copper acetylide formation, we turned to bromamides specifically designed by Suginome[12] to suppress transmetalation by lowering Lewis acidity of the boron.[13] With alkynyl Bdan **2.8** in place of alkynyl Bpin, the desired alkenyl copper complex **2.9** is formed in 91% yield and 2.5:1 regioselectivity, with no apparent formation of the copper acetylide (Scheme 2.3a). Encouraged by this result, we explored the catalytic hydroalkylation of alkynyl Bdan with cyclohexyl iodide as a coupling partner and a silane as a hydride source (Scheme 2.3b). In a reaction promoted by the nickel-copper catalyst system previously used in hydroalkylation of terminal alkynes, we did not observe the formation of the desired trisubstituted alkene **2.12**. However, a control experiment performed without the copper co-catalyst produced 32% of the desired alkene product.

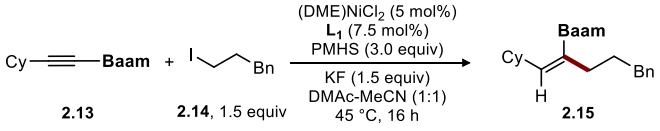
Scheme 2.3 Preliminary Results



With the results described in Scheme 2.3b as the starting point, we were able to develop an efficient nickel-catalyzed reductive coupling of alkynyl boronamides and alkyl iodides (Table 2.1). The best results were obtained using catalyst prepared in situ from (DME)$NiCl_2$ and di-(2-picolyl)amine ligand (**L_1**), with anhydrous KF as the turnover reagent. The results in Table 2.1 show how the changes of different reaction parameters affect the yield of the desired product. The highest yields were obtained with derivatives of boronic acids that have relatively low Lewis acidity, such as Baam[12c] and Bdan.[12a, 12b] Both BMIDA[14] and Bpin, which are widely used in synthetic chemistry, gave lower yields of the desired product (entries 3 and 4). The identity of the ligand was critical to the success of the reaction, with ligand **L_1** providing the best results. Surprisingly, no previous uses of this ligand in nickel catalysis have been reported. Ligands **L_2** and **L_3** have been used in nickel catalyzed transformations,[15] together with other derivatives of **L_1**. However, both **L_2** and **L_3** were less effective in this reaction. The result obtained with **L_2** suggests that deprotonation of the central nitrogen is not essential for catalysis. Among several classes of ligands commonly used in nickel hydride chemistry, only bipyridine ligands afforded the desired product in significant yields, with dtbbpy providing 56% yield (entry 7).

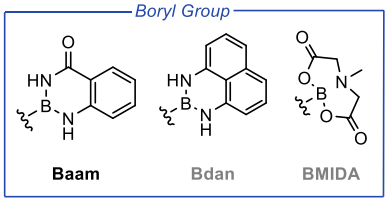
The catalyst prepared in situ using terpyridine (tpy) ligand provided virtually no product (entry 8) and that is representative of the performances of catalysts supported by other classes of ligands. The highest yield of the desired product was obtained using a DMAc-MeCN solvent mixture. DMAc alone performed well in the initial test reaction (entry 9), but worse with other alkynyl boronamide substrates. MeCN alone provided a lower yield of the desired product (entry 10). While polymeric PMHS showed good reactivity, structurally related silanes like monomeric DEMS and dimeric TMDSO gave diminished yields (entries 11 and 12). Finally, control experiments indicated that the reaction did not proceed in the absence of the ligand, the nickel precatalyst, or the silane.

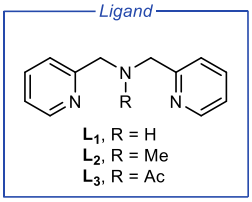
Table 2.1 Reaction Parameters



2.13 **2.14**, 1.5 equiv **2.15**

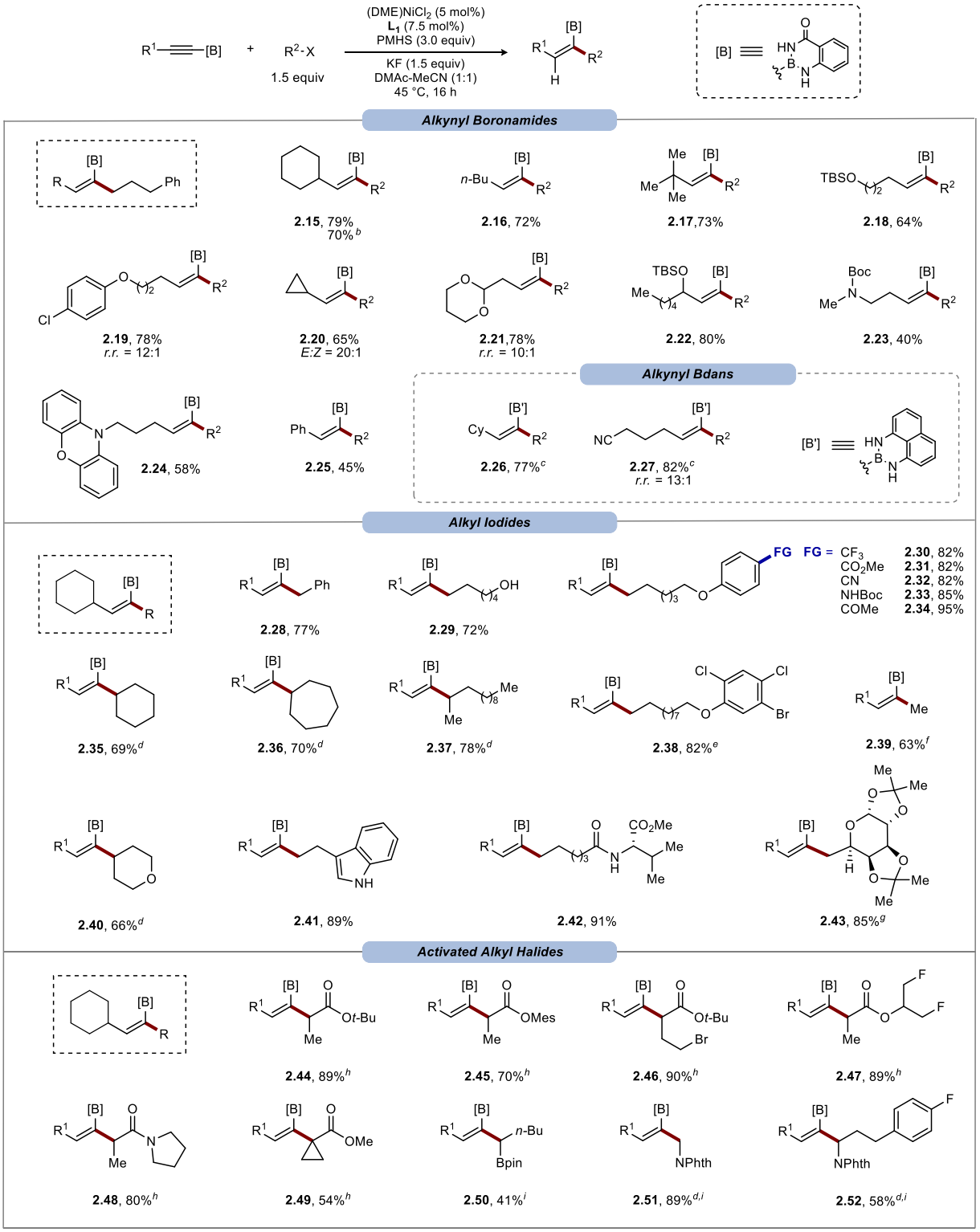
Entry	*Change from Standard Conditions*	*Yield*
1	none	85% (79%)
2	**Bdan** instead of **Baam**	82%
3	**BMIDA** instead of **Baam**	52%
4	**Bpin** instead of **Baam**	<5%
5	L_2 instead of L_1	72%
6	L_3 instead of L_1	35%
7	**dtbbpy** instead of L_1	56%
8	**tpy** instead of L_1	<5%
9	DMAc as solvent	82%
10	MeCN as solvent	48%
11	DMES instead of PMHS	64%
12	TMDSO instead of PMHS	46%





We explored the scope of the reaction using standard reaction conditions described in Table 2.1 (entry 1). A wide range of trisubstituted alkenyl boronamides were isolated with excellent *E*-selectivity and in most cases good regioselectivity (Table 2.2). Alkynyl boronamides containing protected alcohols (**2.18**), acetals (**2.21**), aryl chlorides (**2.19**), propargylic leaving groups (**2.22**), protected amines (**2.23**), and nitrogen-containing heteroarenes (**2.24**) are well tolerated. Sterically demanding alkynyl boronamides, such as **2.15**, **2.17**, and **2.20** performed well under the reaction conditions, while aryl alkynyl boronamides gave a diminished yield (**2.25**). Related alkynyl Bdans

Table 2.2 Substrate Table



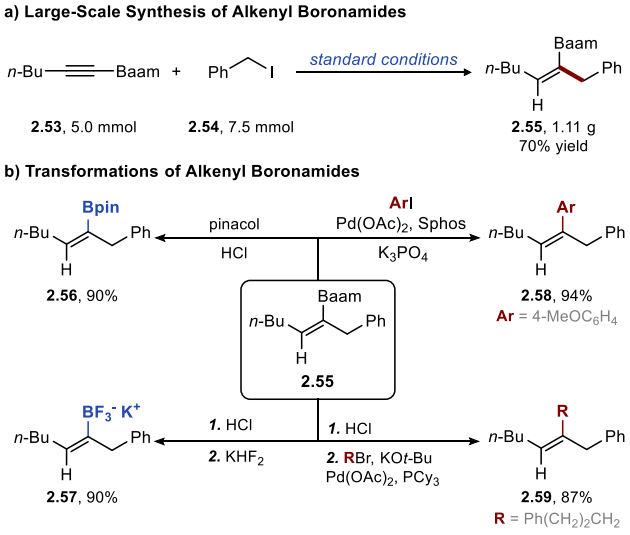
[a] Yields of isolated products are reported. Reactions performed on 0.50 mmol scale. Regioselectivities and diastereoselectivities of isolated products > 20:1 unless specifically noted. [b] 1.5 equiv alkyl bromide with 50 mol% KI was used instead of alkyl iodide. [c] Alkynyl Bdan was used instead of Baam. [d] DMAc:MeCN = 7:3. [e] Reactions performed on 0.25 mmol scale. [f] 1.5 equiv MeOTs with 50 mol% Bu_4NI was used instead of alkyl iodide. [g] Reaction time = 72 h. [h] Alkyl bromide was used instead of alkyl iodide. [i] Alkyl chloride was used instead of alkyl iodide at 60 °C.

can also be used in the reaction without significant drop in yield of the desired alkene products (**2.26** and **2.27**). The resulting alkenyl Bdan products are more resistant to hydrolysis and less prone to decomposition during silica gel purification than the Baam analogues.[12c]

We also investigated the reactivity of various alkyl iodides and found that both structural and functional group diversity are well tolerated. The reaction can be accomplished in the presence of free alcohols (**2.29**), ketones (**2.34**), esters (**2.31**), nitriles (**2.32**), aryl halides (**2.38**), and protected amines (**2.33**). Alkyl iodides derived from tryptophol (**2.41**), valine (**2.42**), and galactose (**2.43**) were also successfully used in the reaction. Secondary alkyl iodides (**2.35**, **2.36**, **2.37**, and **2.40**) generally performed well under slightly modified conditions. Hydromethylation can be achieved using MeOTs as the electrophile with a catalytic amount of TBAI (**2.39**). Alkyl bromides can also be used as coupling partners in the presence of catalytic amount of KI as an additive (**2.15**).

To further expand access to trisubstituted alkenes, we explored the reactivity of several classes of activated alkyl halides. A variety of secondary α-bromo carbonyl compounds,[3f] including esters (**2.44**-**47**) and amides (**2.48**) provided the desired trisubstituted alkenes. Examination of several tertiary α-bromo esters revealed that cyclic tertiary esters yielded moderate results (**2.49**), while acyclic counterparts proved unreactive. When α,γ-dibromo ester was used as the substrate, the cross-coupling reaction occurred selectively α to the carbonyl, while the γ bromide was preserved (**2.46**). α-chloro boronic esters[16,17] and α-chloro phthalimides,[18] which can serve as functional equivalents of carbonyl and imino electrophiles, also participate in the reaction. Allylic boronic esters (**2.50**) and allylic amines (**2.51** and **2.52**) were prepared in moderate to good yields.

Scheme 2.4 Applications



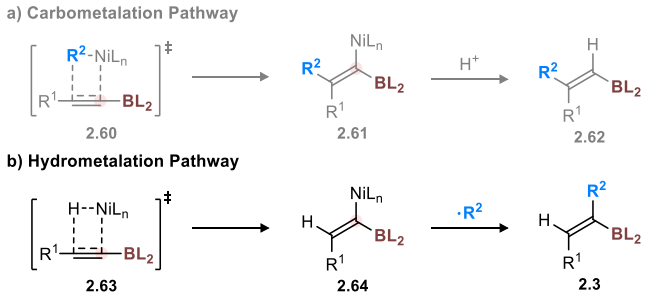
To illustrate the practical utility of the hydroalkylation reaction, trisubstituted alkenyl boronamide **2.55** was synthesized on gram scale in 70% yield and used in further transformations. Alkenyl boronamide **2.55** could be used to prepare trisubstituted pinacol boronic ester **2.56** and trifluoroborate salt **2.57**. Direct arylation of **2.55** can be performed with retention of the double

bond geometry to afford trisubstituted alkene **2.58** in 94% yield.[19] Finally, trisubstituted alkene **2.59** was synthesized in 87% yield by deprotection and subsequent Pd-catalyzed alkylation without alkene isomerization.[20]

Closely related nickel-catalyzed reactions for hydroalkylation of alkynes have been proposed to involve either hydrometalation or carbometalation as the key step of the reaction mechanism.[4c-e] Initially, we evaluated these two categories of reaction mechanisms in the context of the regioselectivity observed in hydroalkylation of alkynyl boronamides.

The boryl directing groups direct the insertion of boryl-substituted alkynes into transition metal complexes with the boryl group proximal to the metal center. The same selectivity has been observed across different metal catalysts and different types of insertion reactions.[5] The proximal selectivity has been attributed to electronic effects of boryl groups[5d, 5f] or to their direct interactions with the metal center.[5c] In our case, if the carbometalation step were a part of the reaction mechanism (Scheme 2.5a), it would be regio-determining and would be expected to provide the other regioisomer of the alkene product (**2.62**). On the other hand, the mechanism involving hydrometalation (Scheme 2.5b) is consistent with the observed regioselectivity. If the hydrometalation were product determining, the expected proximal regioselectivity in this step would lead to the observed selectivity of the hydroalkylation. The reversible hydrometalation, while not product determining, is also compatible with the observed selectivity.[21] The performance of Baam, Bdan, and BMIDA groups suggests electronic effects as a significant contributor to the observed regioselectivity. However, we cannot exclude additional contribution from a direct interaction between the metal and Baam directing group.

Scheme 2.5 Regioselectivity in Carbometalation and Hydroalkylation Pathways

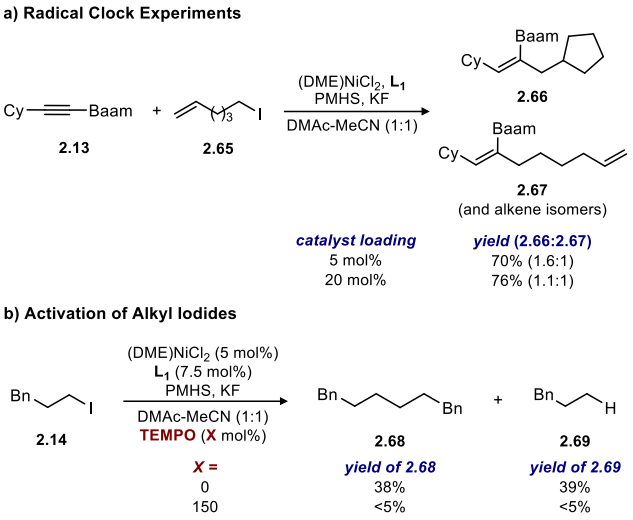


The hydrometalation mechanism has not been extensively explored in nickel-catalyzed hydroalkylation of alkynes. As a result, we based our further mechanistic analysis on more detailed investigations of closely related hydroalkylations of alkenes.[22] Four related, but distinct, mechanisms that involve nickel (I/III) catalytic cycle have been proposed in these reactions.[23] The main difference between the four alternatives is in the timing of the alkyl halide activation relative to the nickel hydride formation and the hydrometalation steps.

To further test hydrometalation as the key step of the reaction and probe which variant of hydrometalation mechanism is most likely in our case, we did a set of preliminary experiments.

Alkynyl boronamide **2.13** and 6-iodo-1-hexene (**2.65**) were subjected to standard conditions and delivered the cyclized product **2.66** in 43% yield and a mixture of uncyclized alkene isomers **2.67** in 27% yield (Scheme 2.6a). The ratio of the cyclized and the linear product (**2.66**:**2.67**) depends on the catalyst concentration, indicating that the alkyl radical lifetime changes with nickel catalyst concentration. This is a strong indication for the formation of a free alkyl radical intermediate that is being trapped by a nickel catalyst,[24] one of the hallmarks of hydroalkylation mechanisms that involve a hydrometalation step.

Scheme 2.6 Studies of the Reaction Mechanism



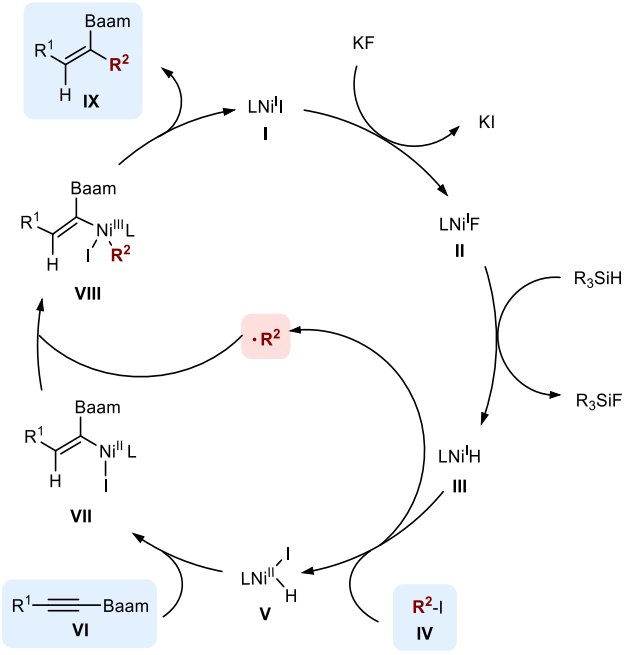
We also explored conditions for the formation of the alkyl radical. We found that under the reaction conditions in the absence of the alkyne (Scheme 2.6b), homodimerization of the alkyl halide was observed (**2.68**) together with the formation of the dehalogenation product **2.69**. Furthermore, the formation of the two products was fully suppressed in the presence of 1.5 equiv of TEMPO, with 80% of the alkyl halide retained, and TEMPOH adduct as the major new product. The results of these experiments are consistent with the formation of the alkyl radical intermediate in a reaction of an alkyl halide with a nickel hydride complex formed in the presence of a silane. When present, TEMPO reacts with the nickel hydride and prevents the reaction with the alkyl halide.[25] Similar experiments performed in the absence of the silane with high loading of nickel(I) complexes indicated an inefficient formation of alkyl radicals.

Considering the results of our experiments and the available information about related hydroalkylation of alkenes,[23] we propose a mechanism presented in Scheme 2.7. The hydroalkylation reaction is initiated by ligated Ni^{I} precursor **I**, which then generates nickel hydride species **III** in the presence of potassium fluoride and the silane. Subsequently, **III** reacts with alkyl iodide to form an alkyl radical and $Ni^{II}H$ species **V**, followed by regioselective hydrometalation of the alkynyl boronamide to give alkenyl nickel (II) species **VII**.[26] The capture of the alkyl radical to form Ni^{III} intermediate **VIII** is followed by a reductive elimination to release the desired trisubstituted product and regenerate **I**. Based on the available data, the product determining step

can be either the hydrometalation or the reductive elimination. Further studies are required to differentiate between the available mechanistic hypothesis and determine the step(s) responsible for the observed regioselectivity.

There are indications that an alternative mechanism is operational with activated alkyl bromides. In their investigation of the mechanism for reductive coupling of α-bromo carbonyls, Fu et al have proposed bromine atom transfer by nickel (I) catalyst prior to the formation of the nickel hydride complex.[22e, 27] We suspect that a similar alternative mechanism may be operational in our case with activated alkyl halides.

Scheme 2.7 Proposed Reaction Mechanism



2.3 Conclusion

We have developed a nickel-catalyzed hydroalkylation of alkynyl boronamides. The reaction allows reductive cross coupling of alkynyl boronamides with several classes of coupling partners, including primary and secondary alkyl iodides, α-bromo esters, α-chloro phthalimides, and α-chloro boronic esters. The reaction can be successfully performed in the presence of alcohols, Boc-protected primary and secondary amines, ketones, esters, aryl halides, and nitriles. After purification, the alkenyl boronamide products are obtained with generally high regio- and diastereoselectivity. We have demonstrated that boryl functional group that controlled the regiochemistry of the hydroalkylation reaction can be efficiently removed in a subsequent cross-coupling reaction. Palladium catalyzed alkylation and arylation reactions of alkenyl boronamides provide access to a variety of trisubstituted alkenes. Preliminary exploration of the reaction mechanism indicates hydrometalation of the alkynyl boronamide as the key step in activation of

the alkyne. The nickel hydride intermediate is implicated in the activation of the alkyl halide and results in the formation of the free alkyl radical intermediate that is trapped by a nickel complex.

2.4 Experimental

2.4.1. General Information

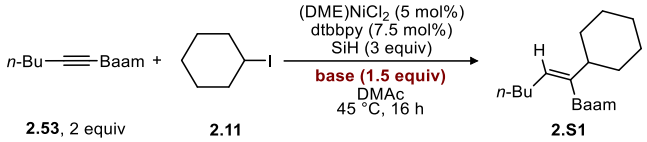
All reactions were performed under a nitrogen atmosphere with flame-dried or oven-dried (120 °C) glassware, using standard Schlenk techniques, or in a glovebox (Genisis). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agilent Technologies Inc. (60Å, 40-60 μm, 230-400 mesh). Infrared (IR) spectra were recorded on a FTIR Perkin Elmer Frontier 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 acetone-d_6: δ 2.05 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 acetone-d_6: δ 29.8 and 206.3 ppm). In most of ^{13}C NMR spectra of boron-containing compounds, the carbon directly attached to the boron atom was not detected due to quadrupolar relaxation. ^{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). 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 an Agilent 5973 GC-MS and a Bruker Esquire LC 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 two temperature programs were used: **#1**. 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C and 5.5 min @ 250 °C; **#2**. 2 min @ 40 °C, 15 °C/min to 320 °C and 5.5 min @ 320 °C.

Materials: THF, CH_2Cl_2, Et_2O, benzene and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous DMAc, MeCN and *t*-AmylOH were purchased from Millipore Sigma and were subsequently degassed and stored over 4Å molecular sieves. 1,4-dioxane was distilled over CaH_2, degassed, and stored over 4Å molecular sieves. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and used as received. Commercial reagents were purchased from Millipore Sigma, TCI America, Ark-Pharm, Combi-Blocks, Oakwood Chemicals, Aaron Chemicals, Enamine, Ambeed and Alfa Aesar.

2.4.2. Reaction Development

All the reactions shown in Table 2.3 to Table 2.12 were performed on a 0.05 mmol scale. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, base, nickel salt, ligand, solvent, respectively. The reaction mixture was stirred at 45 °C for 15 minutes, and then alkyl iodide, a mixture of alkyne and an internal standard (TMB), and silane were added. The reaction mixture was vigorously stirred at 45 °C for 16 h. An aliquot (100 μL) was taken and then analyzed by ^{1}H NMR or gas chromatography.

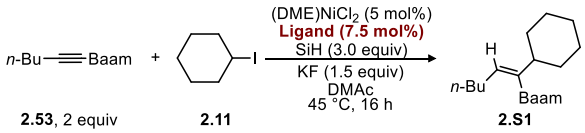
Table 2.3 Base Screen



SiH = 1,1,3,3,5,5,7,7-Octamethyltetrasiloxane

Entry	*Base*	*Yield (%)*
1	Na_2CO_3	34
2	K_2CO_3	28
3	NaF	trace
4	**KF**	**60**
5	CsF	30
6	K_3PO_4	34
7	KO*t*-Bu	trace

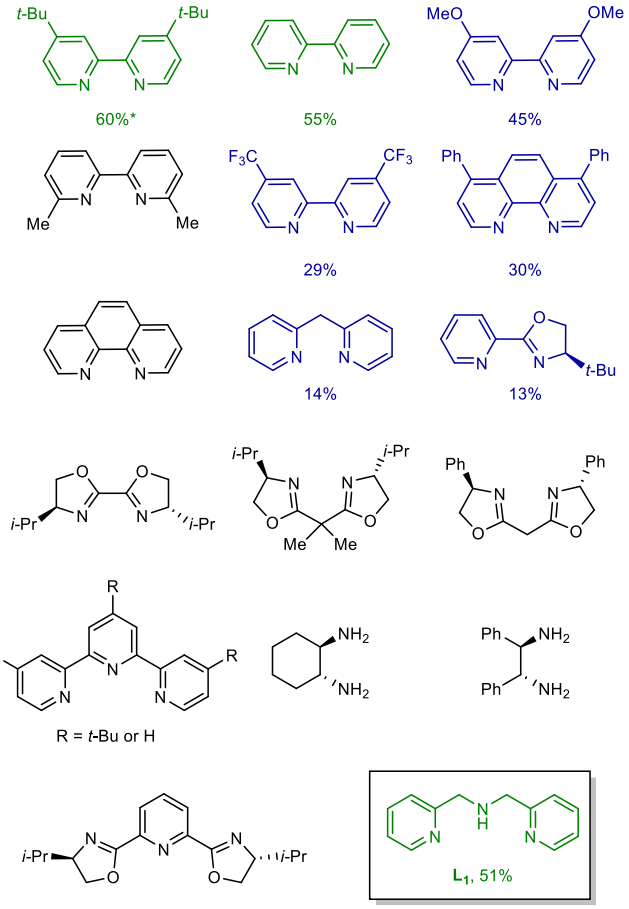
Table 2.4 Ligand Screen



2.53, 2 equiv **2.11** **2.S1**

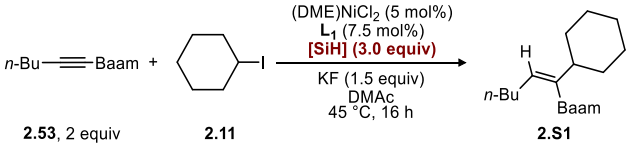
SiH = 1,1,3,3,5,5,7,7-Octamethyltetrasiloxane

Green: > 50% Blue: 5 ~ 50% Black: < 5%



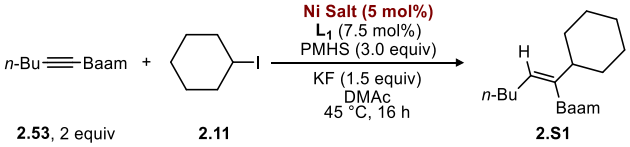
* Attempt to further improve the yield using **dtbbpy** was unsuccessful.

Table 2.5 Silane Screen



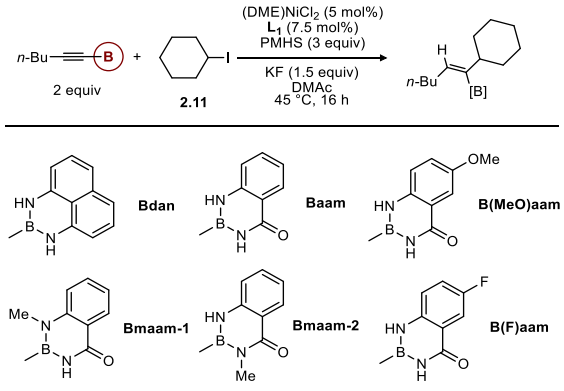
Entry	*Silane*	*Yield (%)*
1	**PMHS**	**62**
2	$(EtO)_3SiH$	32
3	DEMS	31
4	DMMS	20
5	TMDSO	27
6	HMTSO	25

Table 2.6 Ni Source Screen



Entry	*Ni salt*	*Yield (%)*
1	**$(DME)NiCl_2$**	**62**
2	$NiCl_2$	54
3	$NiBr_2$	42
4	$(diglyme)NiBr_2$	33
5	NiI_2	18
6	$Ni(COD)_2$	trace
7	$Ni(OAc)_2{\cdot}4H_2O$	trace

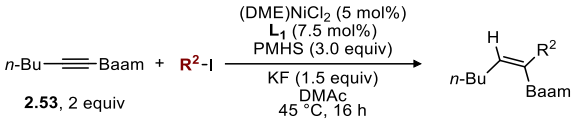
Table 2.7 Boryl Directing Group Screen



Entry	*[B]*	*Yield (%)*

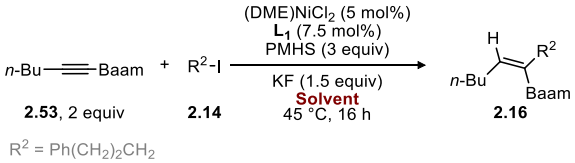
1	Bdan	53
2	**Baam**	**62**
3	B(MeO)aam	60
4	Bmaam-1	53
5	Bmaam-2	59
6	B(F)aam	48

Table 2.8 Alkyl Iodide Screen



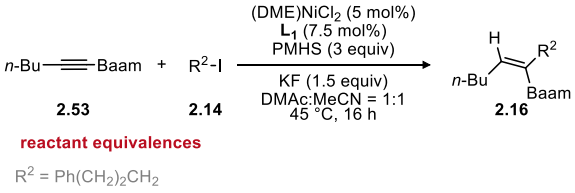
Entry	*R^2*	*Yield (%)*
1	3-phenyl propyl (1 °)	70
2	cyclohexyl (2 °)	63
3	*t*-butyl (3 °)	<5%

Table 2.9 Solvent Screen



Entry	*Solvent*	*Yield (%)*
1	DMAc	70
2	MeCN	49
3	THF	trace
4	20% *i*-PrOH in DMA	72
5	40% *i*-PrOH in DMA	60
6	10% MeCN in DMA	74
7	**50% MeCN in DMA**	**77**

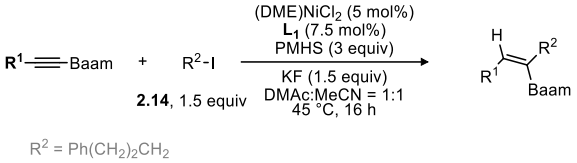
Table 2.10 Stoichiometry Screen



Entry	*Ratio of Alkyne and R^2I*	*Yield (%)*
1	2:1	77
2	1.5:1	70
3	1.2:1	60
4	**1:1.5**	**72***
5	1:2	72

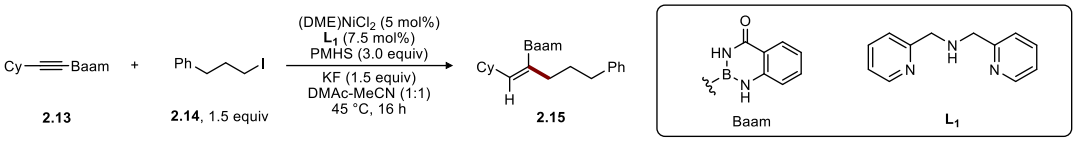
*Alkyne was chosen as the limiting reagent in further development, due to its higher value than alkyl iodide.

Table 2.11 Alkyne Screen



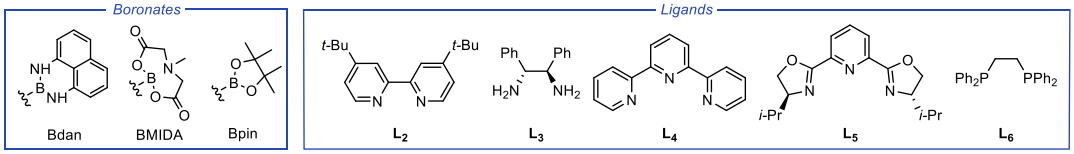
Entry	*R^1*	*Yield (%)*
1	*n*-Butyl (1 °)	72
2	**Cyclohexyl (2 °)**	**85**
3	*t*-Butyl (3 °)	74

Table 2.12 Reaction Parameters (Detailed)



entry	*change from standard conditions*	*yield*
1	none	85% (79%)
2	Bdan instead of Baam	82%
3	BMIDA instead of Baam	52%
4	Bpin instead of Baam	n.d.
5	L_2 instead of L_1	56%
6	L_3 instead of L_1	n.d.
7	L_4 instead of L_1	n.d.
8	L_5 instead of L_1	30%
9	L_6 instead of L_1	8%
10	NaF instead of KF	n.d.
11	CsF instead of KF	33%
12	KO*t*-Bu instead of KF	n.d.
13	DMAc as solvent	82%
14	MeCN as solvent	48%
15	THF as solvent	6%
16	NiI_2 instead of (DME)$NiCl_2$	79%
17	$Ni(COD)_2$ instead of (DME)$NiCl_2$	44%
18	DMES instead of PMHS	64%
19	TMDSO instead of PMHS	46%
20	no L_1, (DME)$NiCl_2$ or PMHS	n.d.

[a]Yields determined by ^{1}H NMR using standard. Isolated yield reported in parenthesis.



2.4.3. General Procedures

2.4.3.1 General Procedure A – Standard

In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with (DME)$NiCl_2$ (5.5 mg, 0.025 mmol, 0.05 equiv), di-(2-picolyl)amine (**L_1**, 7.5 mg, 0.033 mmol, 0.075 equiv), anhydrous KF (43.5 mg, 0.75 mmol, 1.5 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of alkyl halide (0.75 mmol, 1.5 equiv), alkyne (0.50 mmol, 1.0 equiv) and PMHS (90 µL, 1.5 mmol, 3.0 equiv). The reaction

mixture was vigorously stirred at 45 °C for 16 h. The vial was then removed from the glovebox, and the reaction mixture was diluted with 20% aqueous lithium chloride solution (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography. The column was flushed with ten column volumes of hexanes to remove PMHS-related residue before the product was eluted with a EtOAc/hexanes or acetone/hexanes mixture.

2.4.3.2 General Procedure B – with Iodide Salt Additives

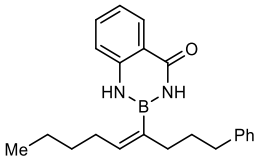
In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with (DME)$NiCl_2$ (5.5 mg, 0.025 mmol, 0.05 equiv), di-(2-picolyl)amine (**L_1**, 7.5 mg, 0.033 mmol, 0.075 equiv), anhydrous KF (43.5 mg, 0.75 mmol, 1.5 equiv), KI or TBAI (0.25 mmol, 0.5 equiv), and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled to room temperature followed by addition of alkyl bromide or methyl tosylate (0.75 mmol, 1.5 equiv), alkyne (0.50 mmol, 1.0 equiv) and PMHS (90 μL, 1.5 mmol, 3.0 equiv). The reaction mixture was vigorously stirred at 45 °C for 16 h. The vial was then removed from the glovebox, and the reaction mixture was diluted with 20% aqueous lithium chloride solution (10 mL) and then extracted with EtOAc (2 × 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography. The column was flushed with ten column volumes of hexanes to remove PMHS-related residue before the product was eluted with a EtOAc/hexanes mixture.

2.4.3.2 General Procedure C – Preparation of Alkyne Starting Materials

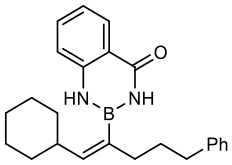
According to the reference[28], a flame-dried Schlenk flask was charged with alkyne (1.2 equiv) and THF (0.5 M) under nitrogen atmosphere. The resulting solution was cooled to −78 °C and a solution of *n*-butyllithium (1.1 equiv, 1.6 M in hexane) was added dropwise. After stirring at −78 °C for 1 h, triisopropyl borate (1.0 equiv) was added in one portion. After stirring at −78 °C for 2 h, a solution of HCl in 1,4-dioxane (1.2 equiv, 4.0 M) was added dropwise. The dry ice bath was removed the reaction mixture was allowed to slowly warm to room temperature in 30 min. The resulting mixture was concentrated *in vacuo* and the residue was suspended in *t*-butyl methyl ether. The suspension was filtrated through a plug of Celite, and the filtrate was concentrated *in vacuo* to yield the crude diisopropyl alkynyl boronate.

The crude diisopropyl boronate was dissolved in toluene (0.20 M), and anthranilamide (1.0 equiv) was added. The mixture was stirred at 110 °C in an open round bottom flask for 3 h. The reaction mixture was cooled down to room temperature and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexanes/acetone as the eluent).

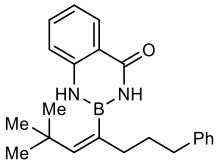
2.4.4. Characterization of Products



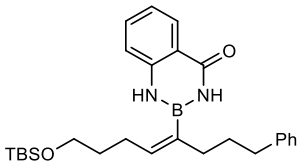
2-[(4*E*)-1-phenylnon-4-en-4-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.16**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (134 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.0 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.29 – 7.25 (d, *J* = 3.8 Hz, 2H), 7.17 (dd, *J* = 18.7, 7.2 Hz, 4H), 7.09 (d, *J* = 7.7 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.33 (s, 1H), 5.90 (t, *J* = 7.5 Hz, 1H), 2.62 (t, *J* = 7.5 Hz, 2H), 2.22 (t, *J* = 7.7 Hz, 2H), 2.14 – 2.10 (m,, 2H), 1.73 – 1.68 (m, 2H), 1.41 – 1.28 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 144.5, 142.2, 140.9, 133.7, 129.0, 128.5, 128.3, 125.8, 121.6, 118.8, 117.6, 37.1, 35.6, 32.3, 31.8, 22.3, 14.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.3. MS-ESI (m/z): $[MH]^+$ calculated for $C_{22}H_{28}BN_2O$, 347.2; found 347.1. FTIR (neat, cm^{-1}): 3295 (br), 2924 (w), 2857 (w), 1652 (s), 1613 (s), 1483 (s), 1147 (m), 760 (m), 698 (m).



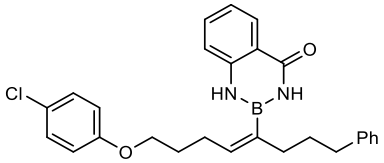
2-[(1*E*)-1-cyclohexyl-5-phenylpent-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.15**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (147 mg, 79% yield). Compound **2.15** could also be prepared according to General Procedure B using KI (41.5 mg, 0.25 mmol, 0.5 equiv) and (3-bromopropyl)benzene (149.2 mg, 0.75 mmol, 1.5 equiv), and was isolated as a white solid (130 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.51 (ddd, *J* = 8.5, 7.4, 1.7 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.22 – 7.12 (m, 4H), 7.04 (s, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.29 (s, 1H), 5.71 (d, *J* = 9.9 Hz, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.19 (td, *J* = 7.7, 1.3 Hz, 2H), 2.11 – 2.01 (m, 1H), 1.72 – 1.58 (m, 7H), 1.28 – 1.08 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 146.6, 144.5, 142.2, 133.7, 129.0, 128.5, 128.3, 125.7, 121.6, 118.8, 117.6, 41.0, 37.0, 35.6, 33.9, 31.7, 25.8, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.0. MS-ESI (m/z): $[MH]^+$ calculated for $C_{24}H_{30}BN_2O$, 373.2; found 373.2. FTIR (neat, cm^{-1}): 3269 (br), 2921 (w), 2854 (w), 1639 (m), 1614 (s), 1486 (s), 1285 (m), 899 (m), 751 (s).



2-[(3*E*)-2,2-dimethyl-7-phenylhept-3-en-4-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.17**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (127 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.29 – 7.25 (m, 2H), 7.20 – 7.12 (m, 4H), 7.02 – 6.93 (m, 2H), 6.27 – 6.20 (m, 1H), 5.83 (t, *J* = 1.4 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.20 – 2.16 (m, 2H), 1.73 – 1.65 (m, 2H), 1.01 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 149.8, 144.4, 142.2, 133.7, 129.1, 128.5, 128.3, 125.8, 121.6, 118.7, 117.6, 39.1, 35.7, 34.3, 31.6, 31.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.3. MS-ESI (m/z): $[MH]^+$ calculated for $C_{22}H_{28}BN_2O$, 347.2; found 347.2. FTIR (neat, cm^{-1}): 3306 (br), 2926 (w), 2855 (w), 1657 (s), 1614 (s), 1517 (s), 1486 (s), 1096 (m), 834 (m), 702 (s).

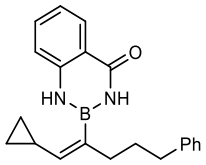


2-[(4*E*)-8-[(tert-butyldimethylsilyl)oxy]-1-phenyloct-4-en-4-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.18**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (148 mg, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.56 – 7.47 (m, 1H), 7.28 – 7.25 (m, 2H), 7.22 – 7.07 (m, 5H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.46 (s, 1H), 5.91 (t, *J* = 7.6 Hz, 1H), 3.64 (t, *J* = 6.1 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.25 – 2.20 (m, 4H), 1.74 – 1.60 (m, 4H), 0.85 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 144.5, 142.2, 140.4, 133.6, 129.1, 128.5, 128.3, 125.8, 121.6, 118.9, 117.6, 62.5, 37.1, 35.7, 33.1, 31.8, 28.4, 26.0, 18.4, -5.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.9. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{40}BN_2O_2Si$, 463.3; found 463.2. FTIR (neat, cm^{-1}): 3285 (br), 2930 (w), 2860 (w), 1655 (s), 1613 (s), 1512 (s), 1486 (s), 1147 (m), 762 (m), 732 (s), 697 (m).

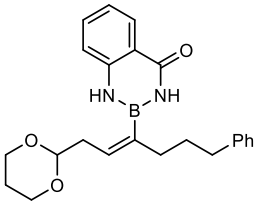


2-[(4*E*)-8-(4-chlorophenoxy)-1-phenyloct-4-en-4-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.19**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-25% EtOAc in hexanes, and isolated as a white solid (180 mg, 78% yield), 12:1 r.r. ^{1}H NMR (500 MHz, $CDCl_3$) major δ 8.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.48 (ddd, *J* = 8.6, 7.4, 1.7 Hz, 1H), 7.28 (s, 3H), 7.22 – 7.09 (m, 6H), 6.92 – 6.78 (m, 3H), 6.42 (s, 1H),

5.91 (t, *J* = 7.7 Hz, 1H), 3.96 (t, *J* = 5.9 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.38 – 2.34 (m, 2H), 2.25 (t, *J* = 7.7 Hz, 2H), 1.90 – 1.83 (m, 2H), 1.73 – 1.67 (m, 2H). minor δ 8.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.48 (ddd, *J* = 8.6, 7.4, 1.7 Hz, 1H), 7.28 (s, 3H), 7.22 – 7.09 (m, 6H), 6.92 – 6.78 (m, 3H), 6.42 (s, 1H), 5.46 (s, 1H), 3.96 (t, *J* = 5.9 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.52 – 2.48 (m, 2H), 2.25 (t, *J* = 7.7 Hz, 2H), 1.90 – 1.83 (m, 2H), 1.73 – 1.67 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 157.3, 144.3, 142.1, 139.2, 133.7, 129.4, 129.1, 128.5, 128.4, 125.9, 125.8, 121.8, 118.9, 117.6, 116.1, 67.0, 37.2, 35.7, 31.8, 28.9, 28.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.7. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{29}ClBN_2O_2$, 459.2; found 459.1. FTIR (neat, cm^{-1}): 3297 (br), 2921 (w), 2860 (w), 1652 (s), 1613 (s), 1510 (s), 1480 (s), 1242 (m), 730 (m).

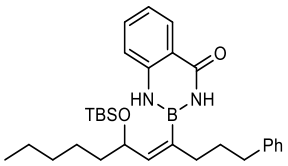


2-[(1*E*)-1-cyclopropyl-5-phenylpent-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.20**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (107 mg, 65% yield), 12:1 *E:Z* ratio. ^{1}H NMR (500 MHz, $CDCl_3$) major δ 8.22 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.24 (m, 3H), 7.20 – 7.12 (m, 4H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.53 – 6.41 (m, 1H), 5.30 (d, *J* = 9.9 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.20 (t, *J* = 7.8 Hz, 2H), 1.72 – 1.67 (m, 2H), 1.58 – 1.51 (m, 1H), 0.85 – 0.72 (m, 2H), 0.47 – 0.36 (m, 2H).minor δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.24 (m, 3H), 7.20 – 7.12 (m, 4H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.53 – 6.41 (m, 1H), 5.43 (d, *J* = 9.9 Hz, 1H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.37 (t, *J* = 7.8 Hz, 2H), 1.81 – 1.77 (m, 2H), 1.58 – 1.51 (m, 1H), 0.90 – 0.88 (m, 2H), 0.52 – 0.49 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 145.6, 144.5, 142.2, 133.7, 129.1, 128.5, 128.3, 125.8, 121.6, 118.9, 117.6, 36.7, 35.6, 31.9, 13.3, 7.7. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.0. MS-ESI (m/z): $[MH]^+$ calculated for $C_{21}H_{24}BN_2O$, 331.2; found 331.1. FTIR (neat, cm^{-1}): 3294 (br), 2924 (w), 2854 (w), 1652 (m), 1612 (s), 1485 (s), 1149 (m), 907 (m), 721 (s).

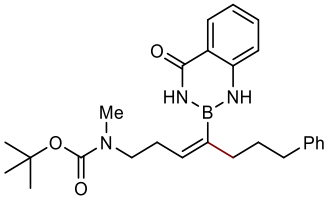


2-[(2*E*)-1-(1,3-dioxan-2-yl)-6-phenylhex-2-en-3-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.21**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (151 mg, 78% yield), 10:1 r.r. ^{1}H NMR (500 MHz, $CDCl_3$) major δ 8.20 (t, *J* = 8.2 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.32 – 7.23 (m, 3H), 7.22 – 7.13 (m, 4H), 6.99 (d, *J* = 8.0 Hz, 1H), 5.93 (t, *J* = 7.9 Hz, 1H), 4.97 (t, *J* = 5.2 Hz, 1H), 4.12 – 3.93 (m, 4H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.40 – 2.35 (m, 2H),

2.28 – 2.21 (m, 2H), 1.85 – 1.81 (m, 2H), 1.71 – 1.67 (m, 2H). minor δ 8.20 (t, *J* = 8.2 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.32 – 7.23 (m, 3H), 7.22 – 7.13 (m, 4H), 7.02 (d, *J* = 8.0 Hz, 1H), 5.39 (s, 1H), 4.97 (t, *J* = 5.2 Hz, 1H), 4.12 – 3.93 (m, 4H), 2.65 (t, *J* = 7.7 Hz, 2H), 2.45 – 2.44 (m, 2H), 2.28 – 2.21 (m, 2H), 1.95 – 1.91 (m, 2H), 1.71 – 1.67 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) major δ 166.9, 144.7, 142.2, 139.5, 133.5, 128.9, 128.4, 128.3, 128.3, 125.7, 121.4, 118.9, 117.5, 103.6, 64.8, 37.1, 35.6, 32.9, 31.9, 26.7. minor δ 160.5, 145.1, 142.0, 139.5, 133.4, 128.8, 128.4, 128.3, 125.8, 121.1, 118.7, 117.4, 103.4, 65.0, 38.5, 35.5, 32.2, 29.6, 28.9. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.0. MS-ESI (m/z): $[MH]^+$ calculated for $C_{23}H_{28}BN_2O_3$, 391.2; found 391.1. FTIR (neat, cm^{-1}): 3323 (br), 2925 (w), 2854 (w), 1653 (s), 1613 (s), 1515 (s), 1485 (s), 1146 (m), 1054 (w), 908 (m), 762 (s), 728 (s).

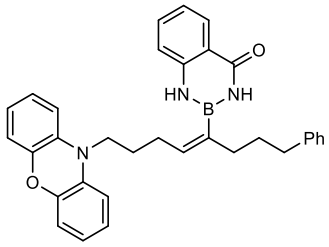


2-[(4*E*)-6-[(tert-butyldimethylsilyl)oxy]-1-phenylundec-4-en-4-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.22**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (200 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.28 (d, *J* = 7.4 Hz, 2H), 7.24 – 7.12 (m, 5H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 5.96 (d, *J* = 8.3 Hz, 1H), 4.25 – 4.21 (m, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.31 – 2.15 (m, 2H), 1.75 – 1.71 (m, 2H), 1.65 – 1.41 (m, 2H), 1.33 – 1.20 (m, 6H), 0.88 – 0.84 (m, 12H), 0.03 – 0.02 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 144.3, 144.0, 142.0, 133.7, 129.1, 128.4, 128.4, 125.8, 121.7, 118.9, 117.5, 77.4, 77.2, 76.9, 72.6, 38.6, 36.9, 35.6, 31.8, 31.5, 25.9, 25.3, 22.6, 18.2, 14.0, -3.6, -4.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.2. MS-ESI (m/z): $[MH]^+$ calculated for $C_{30}H_{46}BN_2O_2Si$, 505.3; found 505.2. FTIR (neat, cm^{-1}): 3324 (br), 2928 (m), 2856 (w), 1658 (m), 1615 (s), 1517 (m), 1486 (s), 1258 (m), 1143 9m), 834 (m), 761 (s).

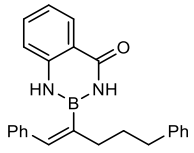


***tert*-butyl N-methyl-N-[(3*E*)-4-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)-7-phenylhept-3-en-1-yl]carbamate** (**2.23**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (90 mg, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 7.55 – 7.47 (m, 1H), 7.30 – 7.23 (m, 3H), 7.18 – 7.10 (m, 5H), 5.93 (t, *J* = 7.7 Hz, 1H), 3.89 (d, *J* = 7.7 Hz, 2H), 2.95 (s, 3H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.25 (t, *J* = 7.5 Hz, 2H), 1.80 – 1.58 (m, 4H), 1.51 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 156.2, 145.3, 142.1, 138.7, 133.6, 128.7, 128.5, 128.3,

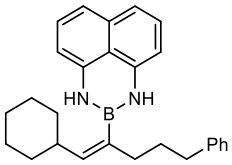
125.7, 121.2, 118.8, 118.1, 80.1, 50.1, 36.9, 35.4, 35.2, 31.1, 29.7, 28.5. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.5. MS-ESI (m/z): $[MH\text{-}CH_2]^+$ calculated for $C_{25}H_{33}BN_3O_3$, 434.2; found 434.2. FTIR (neat, cm^{-1}): 3262 (br), 2981 (m), 2929 (m), 1652 (s), 1614 (s), 1486 (s), 1365 (m), 1147 (s), 905 (m), 730 (s).



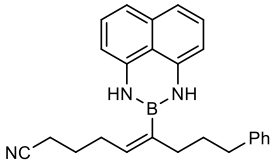
2-[(4*E*)-8-(10H-phenoxazin-10-yl)-1-phenyloct-4-en-4-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.24**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (148 mg, 58% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.9 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.26 (m, 2H), 7.22 – 7.12 (m, 5H), 6.95 (d, *J* = 8.2 Hz, 1H), 6.74 (t, *J* = 8.5 Hz, 2H), 6.65 – 6.60 (m , 4H), 6.42 (d, *J* = 8.0 Hz, 2H), 6.31 – 6.28 (m, 1H), 5.94 (t, *J* = 7.2 Hz, 1H), 3.59 – 3.35 (m, 2H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.27 – 2.22 (m, 4H), 1.80 – 1.69 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 145.0, 144.3, 142.1, 138.6, 137.0, 133.8, 133.2, 129.0, 128.5, 128.4, 125.8, 123.6, 121.8, 120.8, 118.8, 117.7, 115.4, 111.4, 43.1, 37.1, 35.7, 31.6, 29.3, 25.3. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.3. MS-ESI (m/z): $[MH]^+$ calculated for $C_{33}H_{33}BN_3O_2$, 514.3; found 514.2. FTIR (neat, cm^{-1}): 3297 (br), 2926 (w), 2851 (w), 1653 (m), 1613 (m), 1483 (s), 1267 (m), 908 (m), 729 (m).



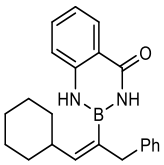
2-[(1*E*)-1,5-diphenylpent-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.25**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (83 mg, 45% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.35 – 7.23 (m, 10H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.08 – 7.02 (m, 2H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.34 – 6.16 (m, 1H), 2.74 (t, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.8 Hz, 2H), 1.92 – 1.84 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 144.4, 142.0, 139.8, 138.2, 133.7, 129.1, 128.5, 128.5, 128.4, 128.1, 127.4, 125.9, 121.7, 118.8, 117.6, 38.0, 35.6, 31.4. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.3. MS-ESI (m/z): $[MH]^+$ calculated for $C_{24}H_{24}BN_2O$, 367.2; found 367.1. FTIR (neat, cm^{-1}): 3271 (br), 3033 (w), 2931 (w), 2857 (w), 1652 (s), 1613 (s), 1510 (s), 1485 (s), 1147 (m), 907 (m), 732 (s), 696 (s).



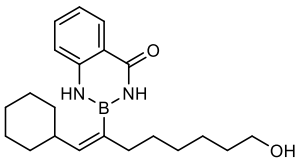
3-[(1*E*)-1-cyclohexyl-5-phenylpent-1-en-2-yl]-2,4-diaza-3-boratricyclo[7.3.1.0^{5,13}]trideca-1(13),5,7,9,11-pentaene (**2.26**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-10% EtOAc in hexanes, and isolated as a yellow liquid (153 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.22 – 7.15 (m, 3H), 7.15 – 7.10 (m, 2H), 7.06 – 7.01 (m, 2H), 6.30 (dd, *J* = 7.3, 1.8 Hz, 2H), 5.69 – 5.46 (m, 3H), 2.64 (t, *J* = 5.6, 2H), 2.23 – 2.11 (m, 3H), 1.79 – 1.60 (m, 7H), 1.29 – 1.08 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 142.5, 141.2, 136.4, 128.6, 128.4, 127.6, 125.8, 119.8, 117.6, 105.8, 41.0, 37.3, 35.7, 34.1, 31.8, 26.0, 25.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.7. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{32}BN_2$, 395.3; found 395.2. FTIR (neat, cm^{-1}): 3407 (br), 2920 (w), 2848 (w), 1597 (s), 1501 (m), 1413 (m), 1315 (w), 818 (m), 761 (m).



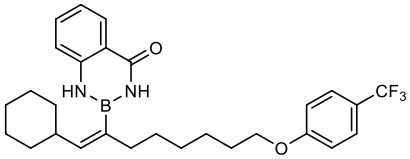
(5*E*)-6-{2,4-diaza-3-boratricyclo[7.3.1.0^{5,13}]trideca-1(13),5,7,9,11-pentaen-3-yl}-9-phenylnon-5-enenitrile (**2.27**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a yellow liquid (155 mg, 82% yield), 13:1 r.r. ^{1}H NMR (500 MHz, $CDCl_3$) major δ 7.33 – 7.27 (m, 2H), 7.23 – 7.16 (m, 3H), 7.15 – 7.09 (m, 2H), 7.061 – 7.01 (m, 2H), 6.34 – 6.31 (m, 2H), 5.71 – 5.68 (m, 1H), 5.68 – 5.57 (m, 2H), 2.69 – 2.63 (m, 2H), 2.36 – 2.31 (m, 4H), 2.23 – 2.14 (m, 2H), 1.81 – 1.73 (m, 4H). minor δ 7.33 – 7.27 (m, 2H), 7.23 – 7.16 (m, 3H), 7.15 – 7.09 (m, 2H), 7.06 – 7.01 (m, 2H), 6.36 – 6.34 (m, 2H), 5.68 – 5.57 (m, 2H), 5.40 (s, 1H), 2.69 – 2.63 (m, 2H), 2.36 – 2.31 (m, 4H), 2.23 – 2.14 (m, 2H), 1.81 – 1.73 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 140.9, 136.2, 135.2, 128.5, 128.3, 127.6, 125.7, 120.0, 119.7, 117.6, 105.9, 37.3, 35.7, 31.5, 30.5, 25.4, 16.3. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.7. MS-ESI (m/z): $[MH]^+$ calculated for $C_{25}H_{27}BN_3$, 380.2; found 380.1. FTIR (neat, cm^{-1}): 3396 (br), 3264 (w), 2924 (w), 2849 (w), 2248 (w), 1598 (s), 1584 (m), 1312 (m), 1143 (m), 820 (s), 764 (s).



2-[(1*E*)-1-cyclohexyl-3-phenylprop-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.28**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-10% EtOAc in hexanes, and isolated as a white solid (132 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.31 – 7.27 (m, 2H), 7.24 – 7.16 (m, 3H), 7.10 (t, *J* = 7.4, 1H), 6.98 – 6.86 (m, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 5.99 (s, 1H), 5.88 (d, *J* = 10.0 Hz, 1H), 3.48 (s, 2H), 2.24 – 2.09 (m, 1H), 1.75 – 1.61 (m, 5H), 1.29 – 1.12 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 148.6, 144.3, 140.7, 133.6, 129.0, 128.6, 128.6, 126.4, 121.6, 118.8, 117.6, 44.1, 41.0, 33.8, 25.8, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.9. MS-ESI (m/z): $[MH]^+$ calculated for $C_{22}H_{26}BN_2O$, 345.2; found 345.1. FTIR (neat, cm^{-1}): 3323 (br), 2917 (m), 2851 (w), 1649 (s), 1616 (m), 1520 (m), 1484 (m), 1143 (w), 767 (m), 731 (s).

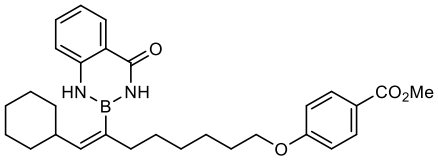


2-[(1*E*)-1-cyclohexyl-8-hydroxyoct-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.29**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-40% EtOAc in hexanes, and isolated as a white solid (128 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 – 8.06 (m, 1H), 7.52 (td, *J* = 8.2, 1.8 Hz, 1H), 7.17 – 6.92 (m, 3H), 6.45 – 6.39 (m, 1H), 5.69 (d, *J* = 9.8 Hz, 1H), 3.62 (t, *J* = 6.6 Hz, 2H), 2.14 (t, *J* = 7.2 Hz, 2H), 2.09 – 2.02 (m, 1H), 1.71 – 1.51 (m, 8H), 1.36 – 1.10 (m, 11H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 146.4, 144.5, 133.9, 129.1, 121.8, 118.9, 117.7, 62.9, 41.1, 37.5, 34.0, 32.7, 30.1, 29.1, 25.9, 25.7, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.1. MS-ESI (m/z): $[MH]^+$ calculated for $C_{21}H_{32}BN_2O_2$, 355.2; found 355.2. FTIR (neat, cm^{-1}): 3386 (br), 3294 (br), 2919 (m), 2850 (w), 1615 (s), 1516 (m), 1486 (m), 1056 (m), 754 (m).

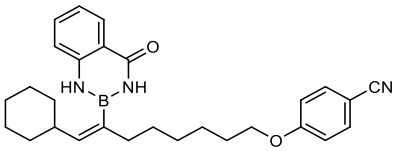


2-[(1*E*)-1-cyclohexyl-8-[4-(trifluoromethyl)phenoxy]oct-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.30**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (205 mg, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.51 (m, 3H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.08 – 7.01 (m, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.37 (s, 1H), 5.70 (d, *J* = 10.0 Hz, 1H), 3.96 (t, *J* = 6.5 Hz, 2H), 2.16 (t, *J* = 7.4 Hz, 2H), 2.07 – 2.03 (m, 1H), 1.80 – 1.73 (m, 2H), 1.71 – 1.26 (m, 11H), 1.27 – 1.09 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 161.6, 146.3, 144.6, 133.8, 129.0, 126.8 (q, $J_{C\text{-}F}$= 3.7 Hz), 124.6 (q, $J_{C\text{-}F}$ = 270.7 Hz), 122.5 (q, $J_{C\text{-}F}$= 32.6

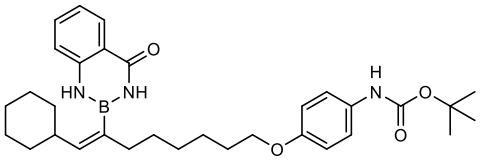
Hz),118.8, 117.7, 114.4, 68.1, 41.0, 37.5, 33.9, 30.1, 29.0, 25.8, 25.8, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.6. ^{19}F NMR (470 MHz, $CDCl_3$) δ -64.4. MS-ESI (m/z): $[MH]^+$ calculated for $C_{28}H_{35}BF_3N_2O_2$, 499.3; found 499.2. FTIR (neat, cm^{-1}): 3306 (br), 2922 (m), 2862 (w), 1654 (m), 1613 (s), 1518 (m0, 1486 (m), 1324 (s), 1256 (m), 1108 (s), 1067 (m), 761 (m).



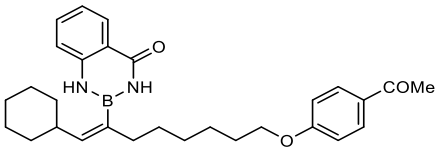
Methyl 4-{[(7*E*)-8-cyclohexyl-7-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)oct-7-en-1-yl]oxy}benzoate (**2.31**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (200 mg, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.98 – 7.93 (m, 2H), 7.57 – 7.46 (m, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (s, 1H), 7.02 (d, *J* = 8.2 Hz, 1H), 6.87 (dd, *J* = 9.2, 2.6 Hz, 2H), 6.53 – 6.30 (m, 1H), 5.69 (d, *J* = 9.9 Hz, 1H), 3.97 (t, *J* = 6.5 Hz, 2H), 3.87 (s, 3H), 2.15 (t, *J* = 7.3 Hz, 2H), 2.08 – 2.04 (m, 1H), 1.78 – 1.57 (m, 7H), 1.46 – 1.32 (m, 6H), 1.24 – 1.08 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 166.6, 162.9, 146.0, 144.6, 133.7, 131.5, 128.9, 122.2, 121.5, 118.8, 117.6, 114.0, 68.0, 51.8, 40.9, 37.5, 33.8, 29.9, 29.0, 25.8, 25.7, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.8. MS-ESI (m/z): $[MH]^+$ calculated for $C_{29}H_{38}BN_2O_4$, 489.3; found 489.2. FTIR (neat, cm^{-1}): 3196 (br), 2921 (w), 2860 (w), 1706 (m), 1656 (m), 1602 (m), 1509 (m), 1251 (s), 1168 (s), 1099 (m), 748 (s).



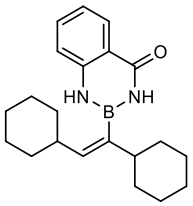
4-{[(7*E*)-8-cyclohexyl-7-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)oct-7-en-1-yl]oxy}benzonitrile (**2.32**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (188 mg, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.60 – 7.45 (m, 3H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.07 – 7.02 (m, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 6.47 – 6.34 (m, 1H), 5.69 (d, *J* = 9.9 Hz, 1H), 3.96 (t, *J* = 6.5 Hz, 2H), 2.16 (t, *J* = 7.1 Hz, 2H), 2.10 – 2.02 (m, 1H), 1.79 – 1.73(m, 2H), 1.71 – 1.58 (m, 5H), 1.48 – 1.31 (m, 6H), 1.25 – 1.07 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 162.3, 146.0, 144.6, 133.8, 133.6, 128.8, 121.4, 119.2, 118.6, 117.6, 115.1, 103.3, 68.2, 40.8, 37.4, 33.7, 29.8, 28.8, 28.8, 25.7, 25.6, 25.5. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.9. MS-ESI (m/z): $[MH]^+$ calculated for $C_{28}H_{35}BN_3O_2$, 456.3; found 456.2. FTIR (neat, cm^{-1}): 3338 (m), 2921 (w), 2851 (w), 2224 (w), 1657 (m), 1604 (s), 1508 (s), 1486 (m), 1258 (m), 1170 (m), 729 (s).



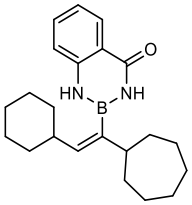
***tert*-butyl N-(4-{[(7*E*)-8-cyclohexyl-7-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)oct-7-en-1-yl]oxy}phenyl)carbamate** (**2.33**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-40% EtOAc in hexanes, and isolated as a white solid (233 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.53 – 7.49(m, 1H), 7.26 – 7.21 (m, 2H), 7.17 – 7.05 (m, 2H), 7.03 – 7.01 (m, 1H), 6.83 – 6.74 (m, 2H), 6.50 – 7.42 (m, 2H), 5.69 (d, *J* = 9.9 Hz, 1H), 3.93 – 3.84 (m, 2H), 2.15 (t, *J* = 6.9 Hz, 2H), 2.10 – 2.01 (m, 1H), 1.74 – 1.57 (m, 7H), 1.50 (s, 9H), 1.45 – 1.30 (m, 6H), 1.24 – 1.06 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 154.9, 153.3, 145.9, 144.6, 133.6, 131.5, 128.9, 121.4, 120.4, 118.6, 117.7, 114.7, 79.8, 68.0, 40.9, 37.4, 33.7, 29.9, 29.1, 29.0, 28.3, 25.7, 25.7, 25.5. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.0. MS-ESI (m/z): $[MH]^+$ calculated for $C_{32}H_{45}BN_3O_4$, 546.3; found 546.2. FTIR (neat, cm^{-1}): 3327 (w), 3280 (br), 2924 (w), 2849 (w), 1696 (m), 1657 (s), 1615 (s), 1513 (s), 1227 (m), 1155 9(m), 827 (m), 765 (s).



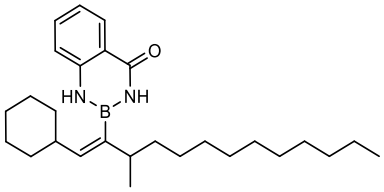
2-[(1*E*)-8-(4-acetylphenoxy)-1-cyclohexyloct-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.34**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (224 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.95 – 7.87 (m, 2H), 7.56 – 7.48 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 4.7 Hz, 1H), 7.03 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.94 – 6.86 (m, 2H), 6.53 – 6.36 (m, 1H), 5.69 (d, *J* = 9.9 Hz, 1H), 3.98 (t, *J* = 6.5 Hz, 2H), 2.54 (s, 3H), 2.16 (t, *J* = 7.3 Hz, 2H), 2.09 – 2.03 (dt, *J* = 10.6, 3.8 Hz, 1H), 1.78 – 1.58 (m, 7H), 1.47 – 1.33 (m, 6H), 1.24 – 1.07 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 166.6, 163.1, 146.3, 146.2, 144.5, 133.7, 130.6, 130.1, 129.0, 121.6, 121.6, 118.8, 117.6, 114.1, 68.1, 41.0, 37.5, 33.9, 30.0, 29.0, 26.3, 25.8, 25.8, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.5. MS-ESI (m/z): $[MH]^+$ calculated for $C_{29}H_{38}BN_2O_3$, 473.3; found 473.2. FTIR (neat, cm^{-1}): 3299 (br), 2921 (m), 2850 (w), 1656 (s), 1598 (s), 1509 (m), 1489 (s), 1254 (s), 1170 (m), 727 (s).



2-[(1*E*)-1,2-dicyclohexylethenyl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.35**) was prepared according to General Procedure A but a 7:3 mixture of DMAc and MeCN was used as the solvent. It was purified by silica gel column chromatography, 0-15% acetone in hexanes, and isolated as a white solid (116 mg, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.53 (td, *J* = 7.5, 1.7 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.04 – 6.98 (m, 2H), 6.34 (s, 1H), 5.61 (d, *J* = 9.7 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.94 – 1.88 (m, 1H), 1.73 – 1.55 (m, 10H), 1.29 – 1.05 (m, 10H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 144.4, 143.0, 133.8, 129.3, 121.8, 118.9, 117.6, 45.6, 41.4, 34.1, 34.0, 26.8, 26.2, 26.0, 25.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.5. MS-ESI (m/z): $[MH]^+$ calculated for $C_{21}H_{30}BN_2O$, 337.2; found 337.2. FTIR (neat, cm^{-1}): 3318 (br), 2919 (m), 2849 (w), 1633 (s), 1614 (s), 1518 (s), 1484 (s), 1149 (w), 701 (s).

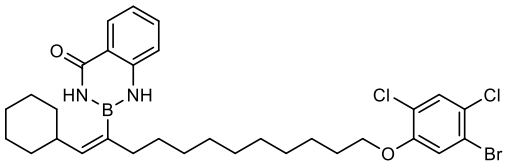


2-[(1*E*)-1-cycloheptyl-2-cyclohexylethenyl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.36**) was prepared according to General Procedure A but a 7:3 mixture of DMAc and MeCN was used as the solvent. It was purified by silica gel column chromatography, 0-15% acetone in hexanes, and isolated as a white solid (122 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.53 (td, *J* = 8.1, 1.8 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.07 – 6.94 (m, 2H), 6.33 (s, 1H), 5.61 (d, *J* = 9.9 Hz, 1H), 2.19 – 2.13 (m, 1H), 1.93 – 1.87 (m, 1H), 1.75 – 1.34 (m, 17H), 1.20 – 1.04 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 144.4, 142.6, 133.8, 129.3, 121.8, 119.0, 117.6, 48.6, 41.2, 36.2, 34.1, 27.8, 27.1, 26.0, 25.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.5. MS-ESI (m/z): $[MH]^+$ calculated for $C_{22}H_{32}BN_2O$, 351.2; found 351.2. FTIR (neat, cm^{-1}): 3292 (br), 2918 (m), 2850 (w), 1633 (m), 1613 (s), 1517 (m), 1485 (m), 1345 (m), 1149 (m), 761 (s).

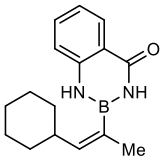


2-[(1*E*)-1-cyclohexyl-3-methyltridec-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.37**) was prepared according to General Procedure A but a 7:3 mixture of DMAc and MeCN was used as the solvent. It was purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (165 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.56 – 7.49 (m, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.05 – 6.95 (m, 2H), 6.32 – 6.30 (m, 1H), 5.61 (d, *J* = 9.9 Hz, 1H), 2.20 –2.13 (m, 1H), 1.97 – 1.91 (m, 1H), 1.66 – 1.56 (m, 5H), 1.34 – 1.22 (m, 18H), 1.19 – 1.08 (m, 5H), 1.02 (d, *J* = 6.8

Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 144.5, 143.7, 133.7, 129.1, 121.6, 118.8, 117.6, 41.3, 41.2, 37.1, 34.0, 33.9, 31.9, 29.7, 29.7, 29.6, 29.4, 27.8, 25.8, 25.6, 22.7, 21.4, 14.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.5. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{44}BN_2O$, 423.4; found 423.3. FTIR (neat, cm^{-1}): 3305 (br), 2921 (s), 2851 (m), 1656 (s), 1616 (s), 1516 (s), 1480 (s), 1147 (m), 900 (m), 760 (s).

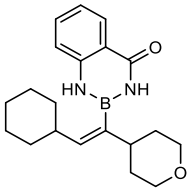


2-[(1*E*)-12-(5-bromo-2,4-dichlorophenoxy)-1-cyclohexyldodec-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.38**) was prepared according to General Procedure A but in a 0.25 mmol scale. It was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (130 mg, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, J = 7.9, 1.4 Hz, 1H), 7.56 (s, 1H), 7.54 – 7.49 (m, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.09 – 7.02 (m, 2H), 6.98 (s, 1H), 6.43 – 6.38 (m, 1H), 5.69 (d, J = 9.8 Hz, 1H), 3.97 (t, J = 6.5 Hz, 2H), 2.13 (t, J = 7.6 Hz, 2H), 2.09 – 2.02 (m, 1H), 1.84 – 1.73 (m, 2H), 1.69 – 1.60 (m, 4H), 1.48 – 1.42 (m, 2H), 1.34 – 1.09 (m, 18H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 154.4, 146.2, 144.5, 133.7, 133.7, 133.1, 129.1, 122.2, 121.6, 118.9, 117.6, 114.6, 112.3, 69.7, 41.0, 37.6, 33.9, 30.2, 29.5, 29.5, 29.4, 29.4, 29.2, 28.9, 25.9, 25.8, 25.7. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.0. MS-ESI (m/z): $[MH]^+$ calculated for $C_{31}H_{41}BBrCl_2N_2O_2$, 633.2; found 633.2. FTIR (neat, cm^{-1}): 3294 (br), 2918 (m), 2849 (w), 1650 (m), 1612 (s), 1517 (m), 1486 (s), 1346 (m), 1282 (m), 1149 (w), 760 (s), 732 (s).

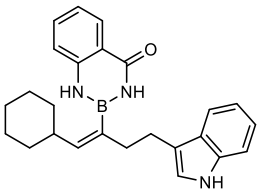


2-[(1*E*)-1-cyclohexylprop-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.39**) was prepared according to General Procedure B using TBAI (92.2 mg, 0.25 mmol, 0.5 equiv) and methyl *p*-toluenesulfonate (139.5 mg, 0.75 mmol, 1.5 equiv). It was purified by silica gel column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (84 mg, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, J = 7.9, 1.7 Hz, 1H), 7.58 – 7.47 (m, 1H), 7.19 – 7.05 (m, 2H), 7.03 (d, J = 8.2 Hz, 1H), 6.46 (s, 1H), 5.77 (d, J = 9.8 Hz, 1H), 2.15 – 2.07 (m, 1H), 1.85 (d, J = 1.8 Hz, 3H), 1.72 – 1.59 (m, 5H), 1.26 – 1.09 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 147.8, 144.5, 133.8, 129.2, 121.8, 118.9, 117.6, 41.0, 33.9, 25.9, 25.7, 23.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.3. MS-ESI (m/z): $[MH]^+$ calculated for $C_{16}H_{22}BN_2O$, 269.2; found 269.0.

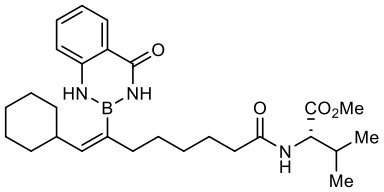
FTIR (neat, cm^{-1}): 3207 (br), 2918 (m), 2851 (w), 1639 (m), 1612 (s), 1517 (m), 1487 (m), 1348 (m), 1150 (m), 757 (s).



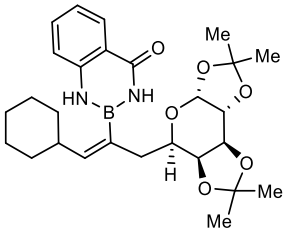
2-[(1*E*)-2-cyclohexyl-1-(oxan-4-yl)ethenyl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.40**) was prepared according to General Procedure A but a 7:3 mixture of DMAc and MeCN was used as the solvent. It was purified by silica gel column chromatography, 0-30% acetone in hexanes, and isolated as a white solid (110 mg, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.54 (ddd, *J* = 8.5, 7.5, 1.8 Hz, 1H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.07 – 6.99 (m, 2H), 6.35 (s, 1H), 5.65 (dd, *J* = 9.8, 1.0 Hz, 1H), 4.01 – 3.92 (m, 2H), 3.39 (td, *J* = 11.7, 2.4 Hz, 2H), 2.34 – 2.21 (m, 1H), 2.04 – 1.90 (m, 1H), 1.67 – 1.48 (m, 9H), 1.21 – 1.06 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 144.2, 143.8, 134.0, 129.3, 122.1, 119.0, 117.6, 68.3, 42.1, 41.4, 34.0, 33.4, 25.9, 25.7. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.9. MS-ESI (m/z): $[MH]^+$ calculated for $C_{20}H_{28}BN_2O_2$, 339.2; found 339.2. FTIR (neat, cm^{-1}): 3306 (br), 2925 (m), 2849 (w), 1610 (s), 1520 (s), 1486 (s), 1127 (m), 765 (s).



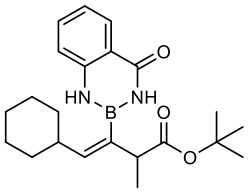
2-[(1*E*)-1-cyclohexyl-4-(1H-indol-3-yl)but-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.41**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a yellow solid (177 mg, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.96 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.18 – 7.14 (m, 1H), 7.12 – 7.07 (dt, *J* = 12.2, 7.4 Hz, 2H), 6.94 – 6.89 (m, 2H), 6.57 (d, *J* = 7.9 Hz, 1H), 5.86 (s, 1H), 5.81 (d, *J* = 9.9 Hz, 1H), 2.88 (t, *J* = 7.2 Hz, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 2.10 – 2.01 (m, 1H), 1.70 – 1.57 (m, 5H), 1.22 – 1.08 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 147.5, 144.4, 136.3, 133.6, 128.7, 127.4, 122.0, 121.9, 121.4, 119.2, 118.9, 118.4, 117.6, 115.5, 111.4, 40.9, 37.5, 33.8, 26.6, 25.8, 25.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.2. MS-ESI (m/z): $[MH]^+$ calculated for $C_{25}H_{29}BN_3O$, 398.2; found 398.2. FTIR (neat, cm^{-1}): 3346 (br), 2920 (w), 2849 (w), 1617 (s), 1518 (m), 1487 (m), 1148 (w), 753 (s).



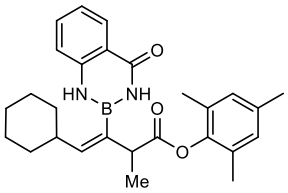
Methyl (2*S*)-2-[(7*E*)-8-cyclohexyl-7-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl) oct-7-enamido]-3-methylbutanoate (**2.42**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-30% EtOAc in hexanes, and isolated as a white solid (220 mg, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.17 – 7.05 (m, 3H), 6.85 (d, *J* = 9.3 Hz, 1H), 6.10 – 5.99 (m, 1H), 5.65 (d, *J* = 9.8 Hz, 1H), 4.57 (dd, *J* = 8.8, 5.0 Hz, 1H), 3.73 (s, 3H), 2.22 (t, *J* = 7.3 Hz, 2H), 2.17 – 2.10 (m, 3H), 2.04 – 2.00 (m, 1H), 1.68 – 1.57 (m, 7H), 1.36 – 1.31 (m, 4H), 1.20 – 1.07 (m, 5H), 0.93 – 0.88 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 172.8, 166.8, 145.6, 144.9, 133.5, 128.7, 121.2, 118.6, 117.8, 56.9, 51.9, 40.9, 37.2, 36.0, 33.6, 31.0, 29.2, 28.4, 25.7, 25.5, 25.4, 18.9, 17.8. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.1. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{41}BN_3O_4$, 482.3; found 482.2. FTIR (neat, cm^{-1}): 3284 (br), 2925 (m), 2851 (w), 1739 (m), 1644 (s), 1617 (s), 1486 (s), 1148 (m), 762 (m).



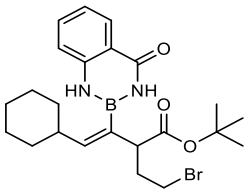
2-[(1*E*)-1-cyclohexyl-3-[(1*S*,2*R*,6*R*,8*R*,9*S*)-4,4,11,11-tetramethyl-3,5,7,10,12-pentaoxatricyclo[7.3.0.0^{2,6}]dodecan-8-yl]prop-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.43**) was prepared according to General Procedure A but the reaction mixture was stirred at 45 °C for 72 h. It was purified by silica gel column chromatography, 0-40% EtOAc in hexanes, and isolated as a white solid (210 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.49 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.27 (s, 1H), 7.15 – 7.05 (m, 2H), 6.99 (dd, *J* = 8.2, 1.2 Hz, 1H), 5.83 (d, *J* = 10.0 Hz, 1H), 5.56 (d, *J* = 5.1 Hz, 1H), 4.59 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.30 (dd, *J* = 5.1, 2.4 Hz, 1H), 4.16 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.77 (ddd, *J* = 9.4, 4.3, 1.9 Hz, 1H), 2.51 (dd, *J* = 14.1, 9.4 Hz, 1H), 2.30 (dd, *J* = 14.1, 4.4 Hz, 1H), 2.17 – 2.10 (m, 1H), 1.67 – 1.56 (m, 5H), 1.47 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H), 1.25 – 1.08 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 149.6, 144.8, 133.5, 129.0, 121.3, 118.9, 117.7, 109.2, 108.6, 96.7 72.8, 71.0, 70.5, ,69.9, 40.9, 37.3, 33.8, 33.7, 26.1, 25.9, 25.8, 25.6, 25.5, 25.0, 24.4. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.6. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{38}BN_2O_6$, 497.3; found 497.2. FTIR (neat, cm^{-1}): 3314 (br), 2921 (m), 2854 (w), 1739 (m), 1614 (m), 1519 (m), 1483 (s), 1219 (m), 1148 (s), 845 (m), 763 (m).



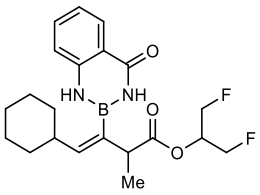
***tert*-butyl (3*E*)-4-cyclohexyl-2-methyl-3-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin- 2-yl)but-3-enoate** (**2.44**) was prepared according to General Procedure A, purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (170 mg, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.52 (ddd, *J* = 8.4, 7.2, 1.7 Hz, 1H), 7.23 (s, 1H), 7.18 – 7.07 (m, 2H), 7.04 (dd, *J* = 8.2, 1.1 Hz, 1H), 5.84 (d, *J* = 10.1 Hz, 1H), 3.19 – 3.07 (m, 1H), 2.18 – 2.05 (m, 1H), 1.71 – 1.57 (m, 5H), 1.44 (s, 9H), 1.24 (d, *J* = 7.3 Hz, 3H), 1.22 – 1.06 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 166.5, 148.0, 144.5, 133.6, 128.9, 121.4, 118.8, 117.7, 80.6, 47.3, 40.8, 33.4, 33.4, 27.9, 25.7, 25.4, 25.4, 17.2. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.2. MS-ESI (m/z): $[MH]^+$ calculated for $C_{22}H_{32}BN_2O_3$, 383.2; found 383.1. FTIR (neat, cm^{-1}): 3332 (br), 2975 (w), 2924 (m), 2849 (w), 1708 (m), 1654 (s), 1614 (s), 1514 (s), 1486 (s), 1148 (s), 728 (s).



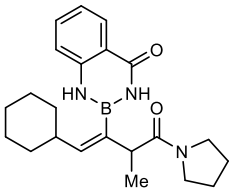
2,4,6-trimethylphenyl (3*E*)-4-cyclohexyl-2-methyl-3-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzo diazaborinin-2-yl)but-3-enoate (**2.45**) was prepared according to General Procedure A with alkyl bromide and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (155 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.50 (ddd, *J* = 8.5, 7.2, 1.7 Hz, 1H), 7.41 (s, 1H), 7.23 (s, 1H), 7.14 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H), 7.01 (d, *J* = 8.1 Hz, 1H), 6.89 (s, 2H), 6.04 (d, *J* = 10.1 Hz, 1H), 3.58 (q, *J* = 7.2 Hz, 1H), 2.28 (s, 3H), 2.21 – 2.14 (m, 1H), 2.09 (s, 6H), 1.72 – 1.56 (m, 5H), 1.46 (d, *J* = 7.3 Hz, 3H), 1.30 – 1.10 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 166.5, 149.5, 145.6, 144.4, 135.5, 133.7, 129.6, 129.3, 128.9, 121.6, 118.9, 117.9, 46.7, 40.8, 33.4, 25.7, 25.4, 25.4, 20.7, 17.8, 16.2. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.6. MS-ESI (m/z): $[MH]^+$ calculated for $C_{27}H_{34}BN_2O_3$, 445.3; found 445.2. FTIR (neat, cm^{-1}): 3318 (br), 3256 9 (w), 2923 (w), 2854 (w), 1748 (m), 1646 (m), 1616 (m), 1521 (m), 1486 (s), 1132 (s), 805 (m), 754 (m).



***tert*-butyl (3*E*)-2-(2-bromoethyl)-4-cyclohexyl-3-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)but-3-enoate** (**2.46**) was prepared according to General Procedure A with alkyl bromide and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (213 mg, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, J = 7.9, 1.8 Hz, 1H), 7.52 (ddd, J = 8.4, 7.2, 1.6 Hz, 1H), 7.36 – 7.27 (m, 1H), 7.19 – 7.11 (m, 2H), 7.05 (d, J = 8.2 Hz, 1H), 5.94 (dd, J = 10.2, 2.4 Hz, 1H), 3.53 – 3.22 (m, 3H), 2.36 – 1.95 (m, 3H), 1.72 – 1.57 (m, 5H), 1.46 (s, 9H), 1.29 – 1.10 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 150.4, 144.4, 133.7, 129.0, 121.7, 118.9, 117.8, 51.3, 40.9, 34.1, 33.4, 33.3, 31.3, 28.0, 25.7, 25.4, 25.3. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.9. MS-ESI (m/z): $[MH]^+$ calculated for $C_{23}H_{33}BBrN_2O_3$, 475.2; found 475.1. FTIR (neat, cm^{-1}): 3308 (br), 2924 (w), 2850 (w), 1710 (w), 1652 (m), 1614 (s), 1512 (m), 1486 (s), 1146 (s), 731 (s).

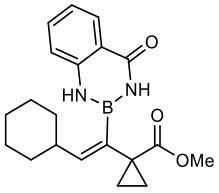


1,3-difluoropropan-2-yl (3*E*)-4-cyclohexyl-2-methyl-3-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzo diazaborinin-2-yl)but-3-enoate (**2.47**) was prepared according to General Procedure A with alkyl bromide and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (180 mg, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, J = 7.9, 1.7 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.22 – 7.11 (m, 2H), 7.03 (d, J = 8.1 Hz, 1H), 6.96 (s, 1H), 5.87 (d, J = 10.1 Hz, 1H), 5.25 (tp, $J_{H\text{-}F}$ = 20.0 Hz, J = 4.5 Hz, 1H), 4.65 – 4.55 (m, 4H)., 3.31 (q, J = 7.2 Hz, 1H), 2.09 – 2.01 (m, 1H), 1.71 – 1.55 (m, 5H), 1.32 (d, J = 7.2 Hz, 3H), 1.23 – 1.07 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 166.5, 148.4, 144.4, 133.7, 128.8, 121.6, 118.8, 117.7, 81.3, 80.5 (dd, $J_{C\text{-}F}$ = 172.4, 6.9 Hz), 80.4 (dd, $J_{C\text{-}F}$ = 172.4, 6.9 Hz), 70.5 (t, $J_{C\text{-}F}$ = 20.2 Hz), 46.2, 41.0, 33.2 (d, $J_{C\text{-}F}$ = 3.2 Hz), 25.6, 25.4 (d, $J_{C\text{-}F}$ = 4.1 Hz), 17.2. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ -235.7, -236.2. MS-ESI (m/z): $[MH]^+$ calculated for $C_{21}H_{28}BF_2N_2O_3$, 405.2; found 405.2. FTIR (neat, cm^{-1}): 3394 (br), 2925 (w), 2852 (w), 1735 (m), 1655 (s), 1613 (s), 1512 (s), 1487 (s), 1164 (m), 729 (s).

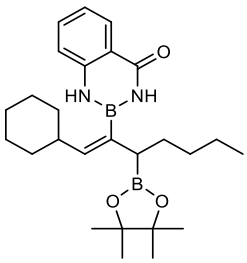


2-[(1*E*)-1-cyclohexyl-3-methyl-4-oxo-4-(pyrrolidin-1-yl)but-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.48**) was prepared according to General Procedure A with alkyl bromide and was purified by silica gel column chromatography, 0-70% EtOAc in hexanes, and isolated as a white solid (150 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$)

δ 8.31 (s, 1H), 8.20 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.49 (ddd, *J* = 8.5, 7.1, 1.7 Hz, 1H), 7.26 – 7.20 (m, 1H), 7.16 – 7.05 (m, 2H), 5.76 (d, *J* = 10.1 Hz, 1H), 3.61 – 3.44 (m, 4H), 3.38 – 3.32 (m, 1H), 2.21 – 2.13 (m, 1H), 2.02 – 1.95 (m, 2H), 1.91 – 1.85 (m, 2H), 1.72 – 1.54 (m, 5H), 1.28 – 1.01 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 166.9, 148.9, 144.9, 133.7, 128.9, 121.3, 118.8, 118.2, 47.2, 47.1, 46.3, 40.7, 33.8, 33.8, 26.4, 25.9, 25.6, 25.6, 24.4, 18.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.7. MS-ESI (m/z): $[MH]^+$ calculated for $C_{22}H_{31}BN_3O_2$, 380.2; found 380.2. FTIR (neat, cm^{-1}): 3250 (br), 3187 (w), 2926 (w), 2860 (w), 1658 (m), 1613 (s), 1519 (m), 1486 (m), 1152 (m), 915 (m), 762 (s).

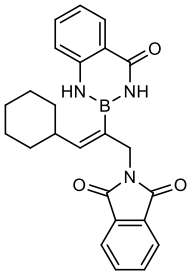


Methyl 1-[(1*E*)-2-cyclohexyl-1-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)ethe nyl]cyclopropane-1-carboxylate (**2.49**) was prepared according to General Procedure A with alkyl bromide and was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (95 mg, 54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.51 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 7.21 (s, 1H), 7.13 (td, *J* = 7.6, 7.2, 1.1 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 1H), 6.85 (s, 1H), 5.80 (d, *J* = 10.1 Hz, 1H), 3.60 (s, 3H), 2.18 – 2.10 (m, 1H), 1.69 – 1.57 (m, 5H), 1.44 – 1.37 (m, 2H), 1.23 – 1.06 (m, 5H), 1.02 – 0.95 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 166.6, 149.0, 144.5, 133.8, 129.2, 121.7, 119.0, 117.8, 52.3, 40.5, 33.5, 29.3, 25.8, 25.6, 16.3. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.6. MS-ESI (m/z): $[MH]^+$ calculated for $C_{20}H_{26}BN_2O_3$, 353.2; found 353.1. FTIR (neat, cm^{-1}): 3303 (br), 2924 (w), 2849 (w), 1711 (m), 1652 (s), 1612 (s), 1512 (s), 1486 (s), 1284 (m), 1145 (s), 726 (s).

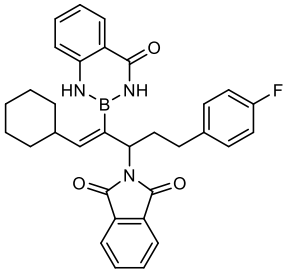


2-[(1*E*)-1-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-1-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-4-one (**2.50**) was prepared according to General Procedure A with alkyl chloride, but the reaction mixture was stirred at 60 °C for 16 h. It was purified by silica gel column chromatography, 0-20% EtOAc in hexanes, and isolated as a white solid (92 mg, 41% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.2 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.45 (s, 1H), 7.40 (s, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 5.70 (d, *J* = 10.0 Hz, 1H), 2.14 – 2.04 (m, 1H), 1.89 (t, *J* = 8.0 Hz, 1H), 1.67 – 1.07 (m, 28H), 0.83 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 145.9, 144.7, 133.6, 129.1, 121.4, 118.9, 117.6,

83.6, 41.0, 34.1, 34.0, 31.9, 30.0, 25.9, 25.7, 24.8, 24.7, 22.6, 14.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.4, 22.6. MS-ESI (m/z): $[MH]^+$ calculated for $C_{26}H_{41}B_2N_2O_3$, 451.3; found 451.3. FTIR (neat, cm^{-1}): 3256 (br), 2924 (m), 2849 (w), 1639 (m), 1615 (s), 1519 (m), 1487 (s), 1309 (m), 1143 (s), 822 (m), 763 (s).



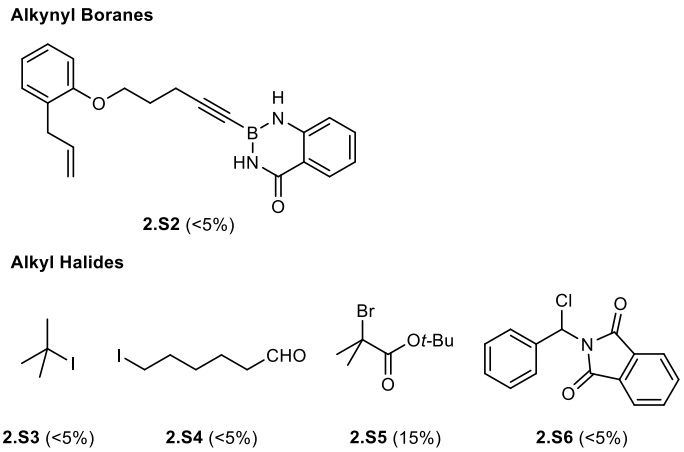
2-[(2*E*)-3-cyclohexyl-2-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)prop-2-en-1-yl]-2,3-dihydro-1H-isoindole-1,3-dione (**2.51**) was prepared according to General Procedure A with alkyl chloride, but a 7:3 mixture of DMAc and MeCN was used as the solvent, and the reaction mixture was stirred at 60 °C for 16 h. It was purified by silica gel column chromatography, 0-45% EtOAc in hexanes, and isolated as a white solid (184 mg, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.2 Hz, 1H), 7.84 – 7.81 (m, 2H), 7.73 – 7.69 (m, 2H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.45 (s, 1H), 7.13 (dd, *J* = 7.8, 3.4 Hz, 2H), 6.18 (d, *J* = 10.2 Hz, 1H), 4.36 (s, 2H), 2.24 – 2.18 (m, 1H), 1.71 – 1.57 (m, 5H), 1.26 – 1.10 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 166.5, 153.4, 144.5, 134.3, 133.8, 132.1, 129.1, 123.6, 121.9, 119.0, 118.0, 42.6, 40.8, 33.4, 25.8, 25.5. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.6. MS-ESI (m/z): $[MH]^+$ calculated for $C_{24}H_{25}BN_3O_3$, 414.2; found 414.1. FTIR (neat, cm^{-1}): 3267 (br), 2936 (w), 2851 (w), 1706 (s), 1639 (m), 1615 (s), 1512 (m), 1330 (m), 1149 (w), 713 (s).



2-[(1*E*)-1-cyclohexyl-5-(4-fluorophenyl)-2-(4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaborinin-2-yl)pent-1-en-3-yl]-2,3-dihydro-1H-isoindole-1,3-dione (**2.52**) was prepared according to General Procedure A with alkyl chloride, but a 7:3 mixture of DMAc and MeCN was used as the solvent, and the reaction mixture was stirred at 60 °C for 16 h. It was purified by silica gel column chromatography, 0-40% EtOAc in hexanes, and isolated as a white solid (156 mg, 58% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.81 – 7.77 (m, 2H), 7.73 – 7.69 (m, 2H), 7.55 – 7.52 (m, 1H), 7.40 – 7.27 (m, 2H), 7.17 – 7.13 (m, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.02 – 6.99 (m, 2H), 6.84 – 6.79 (m, 2H), 5.98 (dd, *J* = 10.2, 1.4 Hz, 1H),

4.97 – 4.91 (m, 1H), 2.63 – 2.47 (m, 3H), 2.14 – 2.00 (m, 2H), 1.75 – 1.54 (m, 5H), 1.18 – 0.96 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 166.6, 161.2 (d, J_{C-F} = 243.6 Hz), 149.6, 144.5, 136.3 (d, J_{C-F} = 3.2 Hz), 134.1, 133.7, 131.7, 129.7 (d, J_{C-F} = 7.8 Hz), 129.0, 123.3, 121.7, 118.9, 117.9, 115.0 (d, J_{C-F} = 21.1 Hz), 54.7, 41.0, 33.2, 32.6, 25.7, 25.3. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ -120.8. MS-ESI (m/z): $[MH]^+$ calculated for $C_{32}H_{32}BFN_3O_3$, 536.2; found 536.1. FTIR (neat, cm^{-1}): 3272 (br), 2963 (w), 2851 (w), 1704 (s), 1634 (s), 1616 (m), 1509 (s), 1485 (m), 1328 (m), 1144 (m), 710 (s).

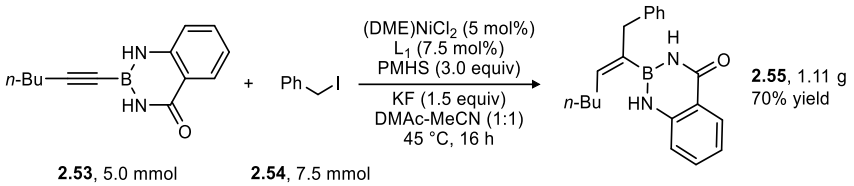
Table 2.13 Substrate Scope Limitation



2.4.5. Applications

2.4.5.1. Gram-scale Synthesis

Scheme 2.8 Gram-scale Synthesis



In a nitrogen-filled glovebox, a 100 mL round bottom flask was charged with (DME)$NiCl_2$ (55 mg, 0.25 mmol, 0.05 equiv), di-(2-picolyl)amine (**L1**, 75 mg, 0.33 mmol, 0.075 equiv), anhydrous KF (435 mg, 7.5 mmol, 1.5 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (50 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of **2.54** (1.63 g, 7.5 mmol, 1.5 equiv), **2.53** (1.13 g, 5.0 mmol, 1.0 equiv) and PMHS (900 µL, 15 mmol, 3.0 equiv). The flask was sealed with a rubber stopper and the reaction mixture was vigorously stirred at 45 °C for 16 h. The round bottom flask was removed from the glovebox, and the reaction mixture was diluted with 20% aqueous lithium chloride solution (50 mL) and then extracted with EtOAc (2 × 50 mL). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture

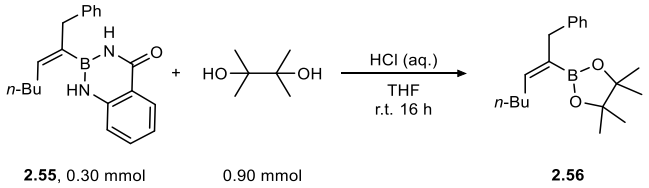
was further purified by silica gel column chromatography. The column was flushed with ten column volumes of hexanes before the product was eluted with 10~15% EtOAc in hexanes. **2.55** was isolated as a white solid (1.11 g, 70% yield).

2-[(2*E*)-1-phenylhept-2-en-2-yl]-1,2,3,4-tetrahydro-1,3,2-benzo-diazaborinin-4-one.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.23 – 7.18 (m, 3H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.00 (s, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.11 (s, 1H), 6.04 (t, *J* = 7.5 Hz, 1H), 3.52 (s, 2H), 2.22 – 2.18 (m, 2H), 1.45 – 1.28 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 144.2, 143.0, 140.7, 133.7, 129.1, 128.8, 128.7, 126.5, 121.8, 118.8, 117.6, 44.2, 32.4, 31.9, 22.4, 14.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.4. GC-MS EI (m/z): $[M]^+$ calculated for $C_{20}H_{23}BN_2O$, 318.2; found 318.2. FTIR (neat, cm^{-1}): 3316 (br), 2928 (w), 2865 (w), 1656 (m), 1614 (m), 1510 (m), 1486 (s), 1259 (w), 907 (s), 708 (s).

2.4.5.2. Synthesis of Alkenyl Bpin

Scheme 2.9 Synthesis of Alkenyl Bpin



2.55, 0.30 mmol 0.90 mmol **2.56**

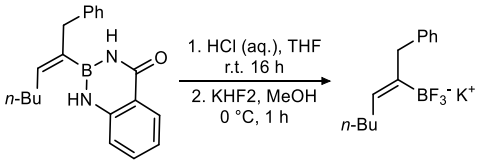
The reaction was performed according to the following modification of the literature procedure.[29] 25 mL round bottom flask was charged with **2.55** (95.5 mg, 0.30 mmol, 1.0 equiv), pinacol (106 mg, 0.90 mmol, 3.0 equiv), THF (3 mL, 0.1 M) and a stir bar. To the stirred solution was added 4 M aqueous HCl solution (4 mL) and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude was purified by silica gel column chromatography (5% EtOAc in hexanes) to afford the desired product as a colorless liquid (81.0 mg, 90% yield).

4,4,5,5-tetramethyl-2-[(2*E*)-1-phenylhept-2-en-2-yl]-1,3,2-dioxaborolane

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.12 (m, 5H), 6.05 (t, *J* = 7.4 Hz, 1H), 3.43 (s, 2H), 2.36 – 2.31 (m, 2H), 1.38 – 1.31 (m, 4H), 1.15 (s, 12H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3, 142.0, 129.1, 128.1, 125.6, 83.0, 43.0, 32.3, 31.0, 24.8, 22.4, 14.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.6. GC-MS EI (m/z): $[M]^+$ calculated for $C_{19}H_{20}BO_2$, 300.2; found 300.2. FTIR (neat, cm^{-1}): 2964 (w), 2924 (m), 2860 (w), 1615 (m), 1486 (m), 1403 (m), 1265 (m), 1143 (s), 695 (m).

2.4.5.3. Synthesis of Alkenyl Trifluoroborate

Scheme 2.10 Synthesis of Alkenyl Trifluoroborate



2.55, 0.30 mmol **2.57**

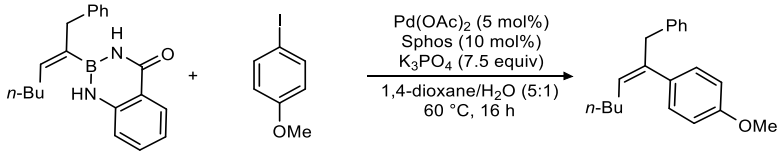
The reaction was performed according to the following modification of the literature procedure.[30,31] A 25 mL round bottom flask was charged with **2.55** (95.5 mg, 0.30 mmol, 1.0 equiv), THF (3 mL, 0.1 M) and a stir bar. To the stirred solution was added 4 M aqueous HCl solution (4 mL), and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (2 × 20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was dissolved in MeOH (3 mL, 0.1 M), and the resulting solution was cooled down to 0 °C. To the stirred solution was added 4.5 M aqueous KHF_2 solution (0.20 mL, 3.0 equiv), and the reaction mixture was stirred at 0 °C for 1 h and then concentrated *in vacuo.* The residue was extracted with hot acetone (3 × 5 mL), and the resulting acetone solution was concentrated *in vacuo.* The crude product was purified by recrystallization in acetone/hexanes to afford **2.57** as a white solid (75.7 mg, 90% yield).

Potassium Trifluoro[(2*E*)-1-phenylhept-2-en-2-yl]borate

^{1}H NMR (500 MHz, Acetone) δ 7.18 – 7.13 (m, 4H), 7.02 (tt, *J* = 6.7, 2.1 Hz, 1H), 5.21 – 5.16 (br, 1H), 3.27 (s, 2H), 2.23 – 2.18 (m, 2H), 1.32 – 1.18 (m, 4H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Acetone) δ 144.5, 133.3, 129.2, 127.3, 124.3, 43.5, 33.1, 30.0, 22.3, 13.6. ^{11}B NMR (160 MHz, Acetone) δ 3.0. ^{19}F NMR (470 MHz, Acetone) δ -138.9. MS-ESI (m/z): $[M-K]^-$ calculated for $C_{13}H_{17}BF_3$, 241.1; found 240.9. FTIR (neat, cm^{-1}): 2959 (w), 2930 (m), 2874 (w), 1491 (m), 1451 (m), 1107 (m), 988 (m), 936 (s), 910 (s), 706 (s)

2.4.5.4. Arylation of Alkenyl Boronamides

Scheme 2.11 Arylation of Alkenyl Boronamides



2.55,0.45 mmol **2.S41**, 0.30 mmol **2.58**

The reaction was performed according to the following modification of the literature procedure.[32] In a nitrogen-filled glovebox, a dram vial was charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv), Sphos (12.3 mg, 0.03 mmol, 0.10 equiv), K_3PO_4 (480 mg, 2.25 mmol, 7.5 equiv), **2.55** (143 mg, 0.45 mmol, 1.5 equiv), 4-iodoanisole (**2.S41**, 70.2 mg, 0.30 mmol, 1.0 equiv), and a stir

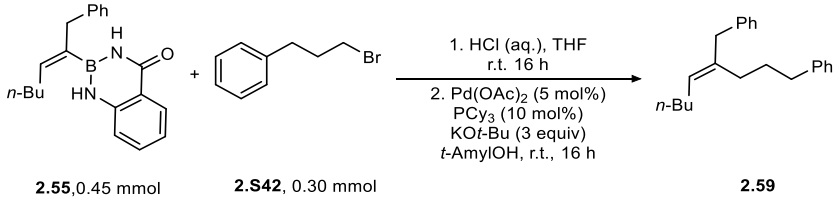
bar. To the vial was added a 5:1 mixture of 1,4-dioxane and water (3 mL, 0.1 M) and the resulting mixture was stirred at 60 °C for 16 h. The vial was then removed from the glovebox and the reaction mixture was diluted with water (10 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL), and the combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography (5% EtOAc in hexanes) to afford the desired product as a colorless liquid (79.0 mg, 94%).

1-methoxy-4-[(2*Z*)-1-phenylhept-2-en-2-yl]benzene.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 2H), 7.17 – 7.07 (m, 3H), 7.03 – 6.93 (m, 2H), 6.83 – 6.75 (m, 2H), 5.46 (t, *J* = 7.3 Hz, 1H), 3.78 (s, 3H), 3.61 (s, 2H), 2.00 – 1.96 (m, 2H), 1.35 – 1.23 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2, 140.3, 139.4, 133.5, 129.7, 129.6, 129.1, 128.2, 125.9, 113.4, 55.2, 45.9, 32.4, 28.9, 22.5, 14.1. GC-MS EI (m/z): $[M]^+$ calculated for $C_{20}H_{24}O$, 280.2; found 280.2. FTIR (neat, cm^{-1}): 3008 (w), 2955 (w), 2923 (w), 2835 (w), 1607 (w), 1510 (m), 1243 (m), 907 (s), 730 (s).

2.4.5.5. Alkylation of Alkenyl Boronamides

Scheme 2.12 Alkylation of Alkenyl Boronamides



2.55,0.45 mmol **2.S42**, 0.30 mmol **2.59**

The reaction was performed according to the following modification of the literature procedure. 3033[18, 21] A 25 mL round bottom flask was charged with **2.55** (143 mg, 0.45 mmol, 1.5 equiv), THF (4.5 mL, 0.1 M) and a stir bar. To the stirred solution was added 4 M aqueous HCl solution (6 mL) and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (2 × 20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude boronic acid was directly used for the next step without further purification.

In a nitrogen filled glovebox, a dram vial was charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv), PCy_3 (8.4 mg, 0.03 mmol, 0.10 equiv), KO*t*-Bu (100 mg, 0.9 mmol, 3.0 equiv), the crude boronic acid, 1-bromo-3-phenylpropane (**2.S42**, 59.7 mg, 0.30 mmol, 1.0 equiv), and a stir bar. To the vial was added *t*-Amyl alcohol (2 mL, 0.15 M) and the resulting mixture was stirred at room temperature for 16 h. The vial was removed from the glovebox and the reaction mixture was filtered through a short silica pad and then washed with Et_2O. The filtrate was concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography (pure hexanes) to afford the desired product as colorless liquid (76.0 mg, 87%).

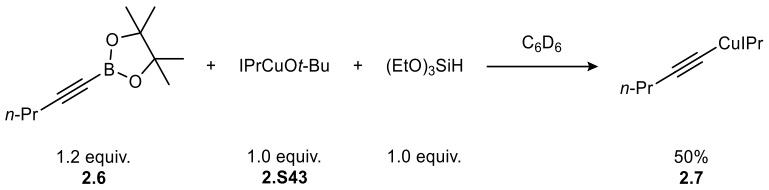
[(2*E*)-2-(3-phenylpropyl)hept-2-en-1-yl]benzene.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 4H), 7.31 – 7.23 (m, 6H), 5.36 (t, *J* = 7.2 Hz, 1H), 3.42 (s, 2H), 2.68 (t, *J* = 7.8 Hz, 2H), 2.14 – 2.09 (m, 4H), 1.85 – 1.73 (m, 2H), 1.48 – 1.41 (m, 4H), 1.05 – 1.00 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 140.7, 138.3, 129.1, 128.5, 128.4, 128.3, 128.0, 126.0, 125.8, 43.8, 36.0, 32.4, 30.2, 29.4, 27.7, 22.6, 14.2. GC-MS EI (m/z): $[M]^+$ calculated for $C_{22}H_{28}$, 292.2; found 292.2. FTIR (neat, cm^{-1}): 3056 (w), 2959 (w), 2928 (w), 2860 (w), 1495 (w),1453 (m), 905 (s), 728 (s).

2.4.6. Mechanistic Studies.

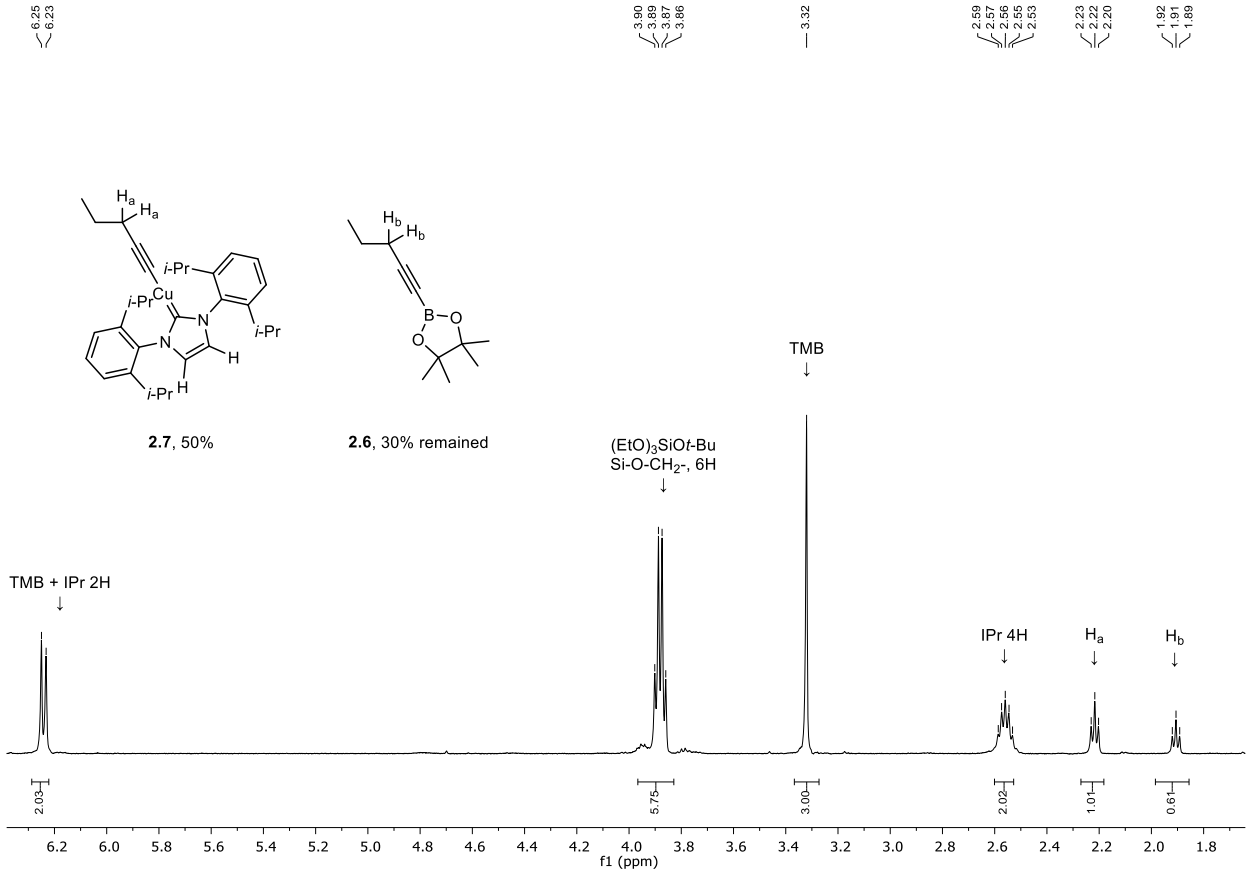
2.4.6.1. Stoichiometric Experiments.

Scheme 2.13 Stoichiometric Reaction of Alkynyl Bpin and CuH

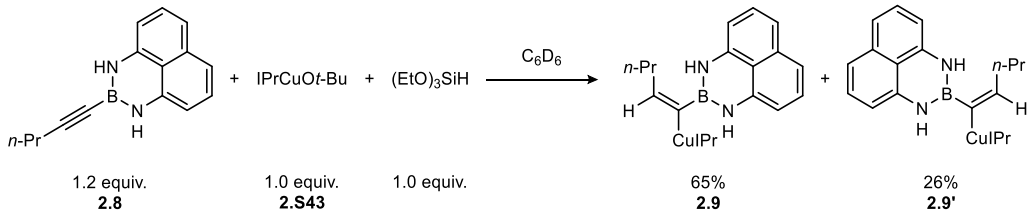


In a nitrogen-filled glovebox, a dram vial was charged with IPrCuO*t*-Bu (10.5 mg, 0.02 mmol, 1.0 equiv), TMB (1.1 mg, 0.067 mmol, 0.33 equiv), C_6D_6 (0.5 mL, 0.04 M) and a stir bar. To the solution was added $(EtO)_3SiH$ (3.3 mg, 0.02 mmol, 1.0 equiv) and the resulting mixture was stirred at room temperature for 2 min, followed by addition of the alkynyl Bpin **2.634**(4.7 mg, 0.024 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 5 minutes, and then transferred into a *J-Young* NMR tube. The tube was then sealed and removed from the glovebox. The reaction mixture was analyzed by ^{1}H NMR and the results are shown in Figure 2.1.

Figure 2.1 In-situ ^{1}H NMR Analysis of the Reaction of Alkynyl Bpin and CuH

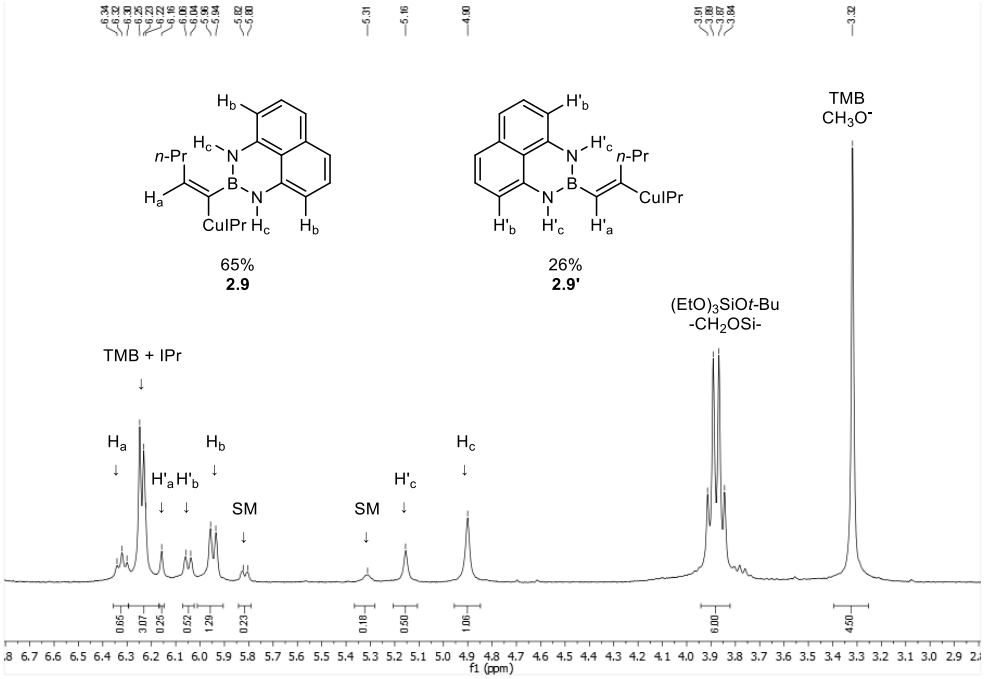


Scheme 2.14 Stoichiometric Reaction of Alkynyl Bdan and CuH



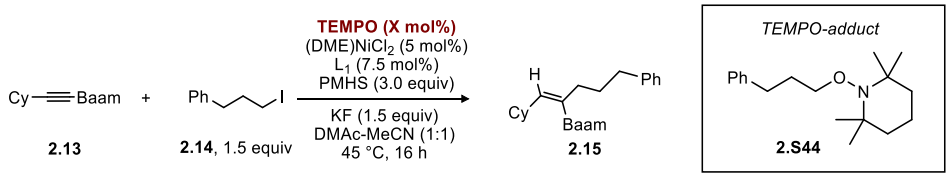
In a nitrogen-filled glovebox, a dram vial was charged with IPrCuO*t*-Bu (10.5 mg, 0.02 mmol, 1.0 equiv), TMB (1.7 mg, 0.01 mmol, 0.50 equiv), C_6D_6 (0.5 mL, 0.04 M) and a stir bar. To the solution was added $(EtO)_3SiH$ (3.3 mg, 0.02 mmol, 1.0 equiv) and the resulting mixture was stirred at room temperature for 2 min, followed by addition of the alkynyl Bdan **2.8** (5.6 mg, 0.024 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 5 minutes, and then transferred into a J-Young NMR tube. The tube was then sealed and removed from the glovebox. The reaction mixture was analyzed by ^{1}H NMR and the results are shown in Figure 2.2.

Figure 2.2 In-situ ^{1}H NMR Analysis of the Reaction of Alkynyl Bdan and CuH



2.4.6.2. Radical Trap Probe.

Scheme 2.15 Radical Trap Probe



In a nitrogen-filled glovebox, a dram vial was charged with (DME)NiCl2 (0.5 mg, 0.0025 mmol, 0.05 equiv), di-(2-picolyl)amine (L1, 0.8 mg, 0.0033 mmol, 0.075 equiv), anhydrous KF (4.4 mg, 0.075 mmol, 1.5 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (0.5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of alkyl iodide 14 (18.4 mg, 0.08 mmol, 1.5 equiv), alkyne **2.13** (11.3 mg, 0.05 mmol, 1.0 equiv) with TMB as the internal standard, PMHS (9 µL, 0.15 mmol, 3.0 equiv) and required amount of TEMPO. The reaction mixture was vigorously stirred at 45 °C for 16 h. Then, an aliquot (100 µL) from the reaction mixture was passed through a plug of silica with EtOAc, concentrated and analyzed by ^{1}H NMR. Table 2.14 shows the product yields with different amounts of TEMPO.

Table 2.14 Radical Trap Probe

Entry	*mol% of TEMPO*	*Yield of 2.15 (%)*
1	0	85
2	20	48

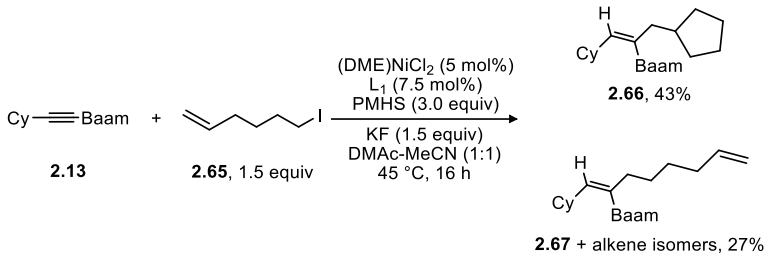
3	150	0

The TEMPO adduct **2.S44** was detected by HRMS from the crude of the reaction mixture with addition of 150 mol% TEMPO.

HRMS ESI (m/z): $[M+H]^+$ calculated for $C_{18}H_{30}ON$, 276.2322; found 276.2323.

2.4.6.3. Radical Clock Experiment.

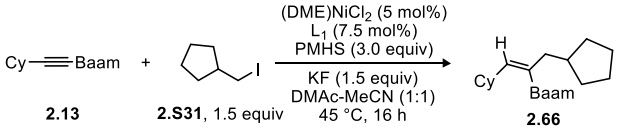
Scheme 2.16 Radical Clock Probe



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $(DME)NiCl_2$ (5.5 mg, 0.025 mmol, 0.05 equiv), di-(2-picolyl)amine (**L**$_1$, 7.5 mg, 0.033 mmol, 0.075 equiv), anhydrous KF (43.5 mg, 0.75 mmol, 1.5 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of 6-iodo-1-hexene (**2.65**) (157.5 mg, 0.75 mmol, 1.5 equiv), alkyne **2.13** (113 mg, 0.50 mmol, 1.0 equiv) and PMHS (90 µL, 1.5 mmol, 3.0 equiv). The reaction mixture was vigorously stirred at 45 °C for 16 h. The vial was then removed from the glovebox, and the reaction mixture was diluted with 20% aqueous lithium chloride solution (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography (0~15% EtOAc in hexanes) to afford a mixture of rearranged product and unrearranged products as a white solid (115 mg, 70% yield).

The ratio of rearranged product **2.66**: unrearranged product **2.67** and its olefin positional isomers = 61:39. The formation of rearranged product **2.66** was proved by GC and ^{1}H NMR analysis using authentic rearranged product as the reference. The ratio of rearranged: unrearranged product were determined by ^{1}H NMR analysis of the mixture. (Figure 2.5)

Scheme 2.17 Preparation of Unrearranged Product

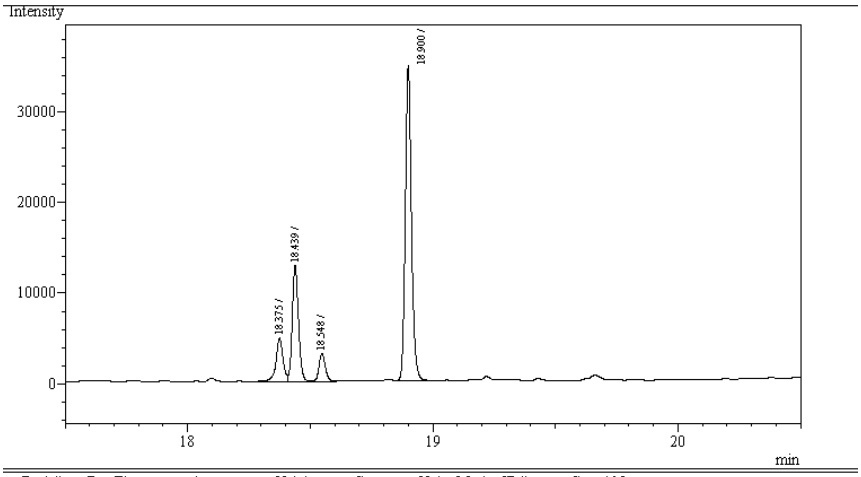


Authentic rearranged product (**2.66**) was prepared according to General Procedure A using (iodomethyl)cyclopentane (**2.S31**, 157.5 mg, 0.75 mmol, 1.5 equiv) and was purified by silica gel

column chromatography, 0-15% EtOAc in hexanes, and isolated as a white solid (137 mg, 82% yield).

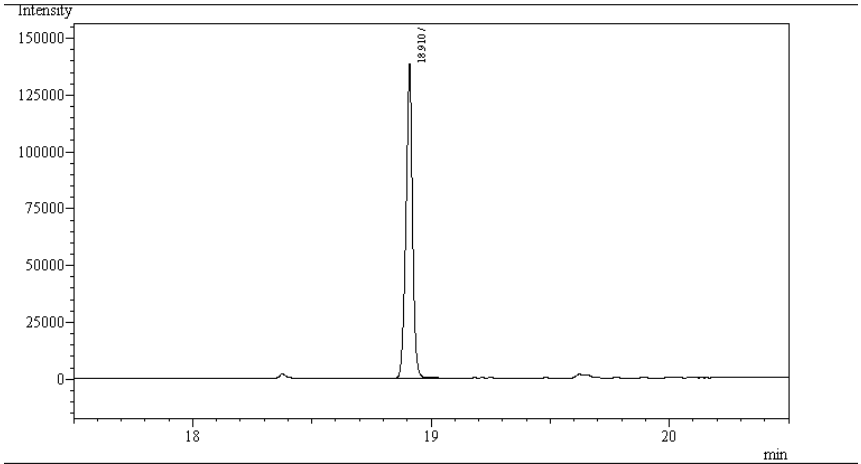
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.54 – 7.51 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 8.9 Hz, 2H), 6.41 (s, 1H), 5.68 (d, *J* = 9.9 Hz, 1H), 2.15 (d, *J* = 7.5 Hz, 2H), 2.09 – 2.05 (m, 1H), 1.83 – 1.77 (m, 1H), 1.73 – 1.54 (m, 9H), 1.49 – 1.44 (m, 2H), 1.25 – 1.06 (m, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 147.1, 144.4, 133.8, 129.3, 121.8, 119.0, 117.6, 44.4, 41.1, 40.1, 34.1, 32.6, 26.0, 25.7, 25.2. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.2. MS-ESI (m/z): $[MH]^+$ calculated for $C_{21}H_{30}BN_2O$, 337.2; found 337.1. FTIR (neat, cm^{-1}): 3314 (br), 2923 (m), 2850 (w), 1635 (s), 1613 (s), 1519 (s), 1485 (s), 1258 (m), 1148 (m), 764 (m).

Figure 2.3 GC Traces of the Mixture of Rearranged and Unrearranged Products



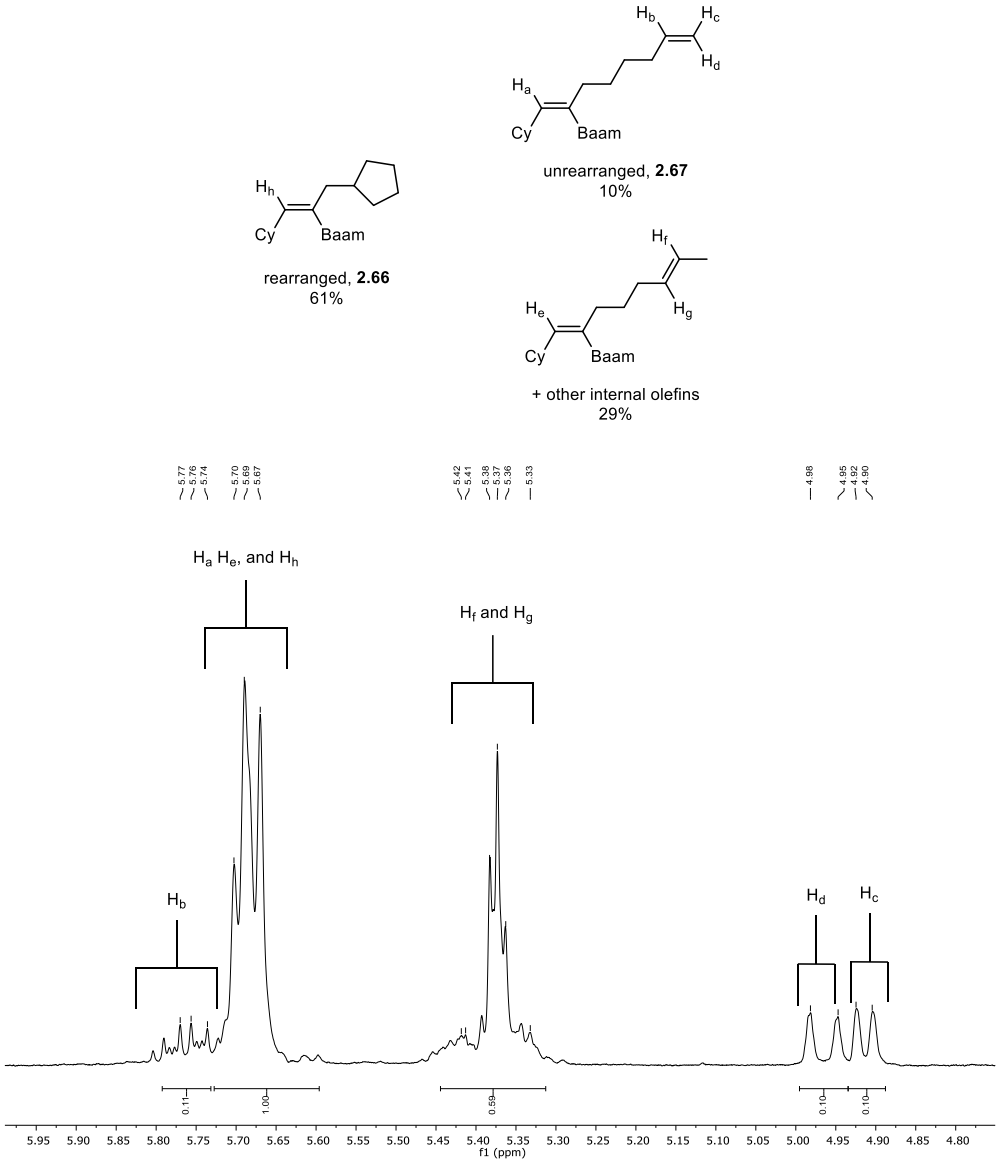
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	18.375	9810	4719	9.955				
2	18.439	22300	12373	22.628		V		
3	18.548	5436	3060	5.516		V		
4	18.900	61003	34054	61.901		V		
Total		98549	54206					

Figure 2.4 GC Traces of the Authentic Rearranged Product

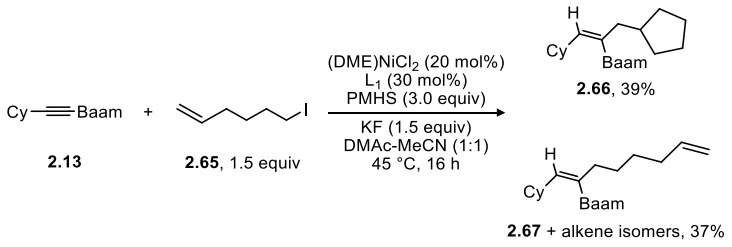


Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	18.910	266477	135813	100.000		V		
Total		266477	135813					

Figure 2.5 ^{1}H NMR analysis of the mixture of rearranged and unrearranged products



Scheme 2.18 Radical Clock Probe at High Catalyst Loading

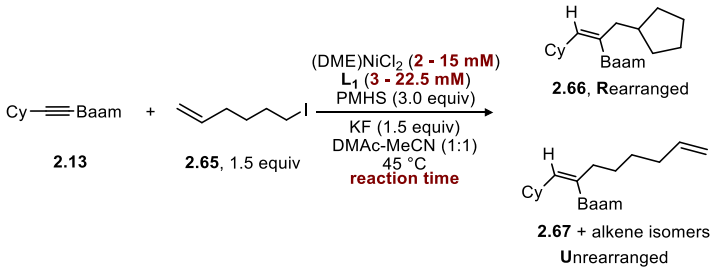


A radical clock experiment with higher catalyst loading was set according to above procedure but higher amount of (DME)$NiCl_2$ (22.4 mg, 0.1 mmol, 0.2 equiv), di-(2-picolyl)amine (**L**$_1$, 30.0 mg, 0.15 mmol, 0.3 equiv) was used instead of original catalyst loading. The mixture of rearranged

product **2.66** and unrearranged product **2.67** was isolated as a white solid (127 mg, 76%), and the ratio of **2.66** and **2.67** was determined by ^{1}H NMR using the same method above.

2.4.6.4. Effect of Catalyst Loading on the Ratio of Unrearranged to Rearranged Product.

Scheme 2.19 Radical Clock Probe at Different Catalyst Loading



In a nitrogen-filled glovebox, four dram vials were charged with anhydrous KF (8.7 mg, 0.15 mmol, 1.5 equiv) and a stir bar. To those vials were added required amount of (DME)$NiCl_2$ and di-(2-picolyl)amine (**L_1**), so that 2, 5,10, and 15 mol% of Ni and 3, 7.5, 15, 22.5 mol% of **L_1** were present in the four different reactions. To each reaction was added a 1:1 mixture of DMAc and MeCN (1.0 mL, 0.1 M) and the resulting mixtures were stirred at 45 °C for 15 min. The reaction mixtures were cooled down to room temperature followed by addition of alkyl iodide **2.65** (36.8 mg, 0.15 mmol, 1.5 equiv), alkyne **2.13** (22.6 mg, 0.10 mmol, 1.0 equiv) with TMB as the internal standard, PMHS (18 μL, 0.30 mmol, 3.0 equiv) to each reaction mixture. The reaction mixtures were vigorously stirred at 45 °C. Reaction progress was monitored by GC, and products were identified by GC-MS analysis. GC (temperature progress **#2**) trace of the mixture: t_R (**2.66**) = 18.900 min; t_R (**2.67** and olefin positional isomers) = 18.375 min, 18.439 min and 18.548 min.

We chose to examine reactions at 50~70% conversion to avoid complications due to induction period and the effects of low substrate concentration at the very end of the reaction. Yield of products and conversion were determined by GC using TMB as internal standard, and we assumed **2.66**, **2.67** and alkene positional isomers of **2.67** had the same response factors in GC. Reaction time and yield at each Ni concentration are listed below.

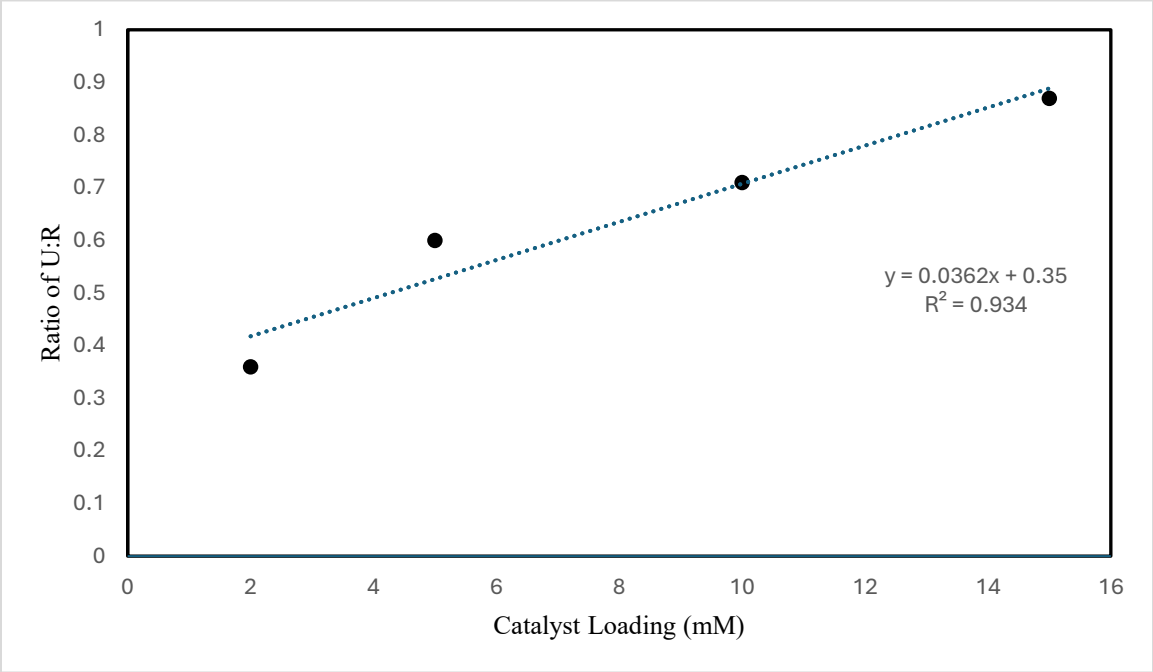
2 mM in catalyst. After 120 min, a 34% yield of a mixture of **2.66** (25%, rearranged) and **2.67** (9%, unrearranged, includes olefin positional isomers) was obtained, and the conversion at this point is 55%. U: R = 0.36.

5 mM in catalyst. After 90 min, a 48% yield of a mixture of **2.66** (30%, rearranged) and **2.67** (18%, unrearranged, includes olefin positional isomers) was obtained, and the conversion at this point is 66%. U: R = 0.60.

10 mM in catalyst. After 60 min, a 45% yield of a mixture of **2.66** (26%, rearranged) and **2.67** (19%, unrearranged, includes olefin positional isomers) was obtained, and the conversion at this point is 63%. U: R = 0.71.

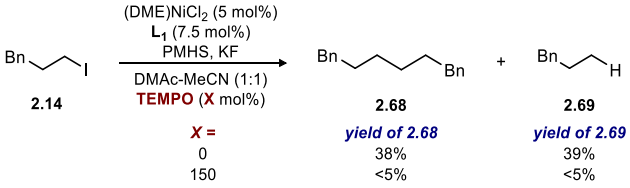
15 mM in catalyst. After 40 min, a 48% yield of a mixture of **2.66** (26%, rearranged) and **2.67** (22%, unrearranged, includes olefin positional isomers) was obtained, and the conversion at this point is 66%. U: R = 0.87.

Figure 2.6 Effect of Catalyst Loading on the U/R Ratio



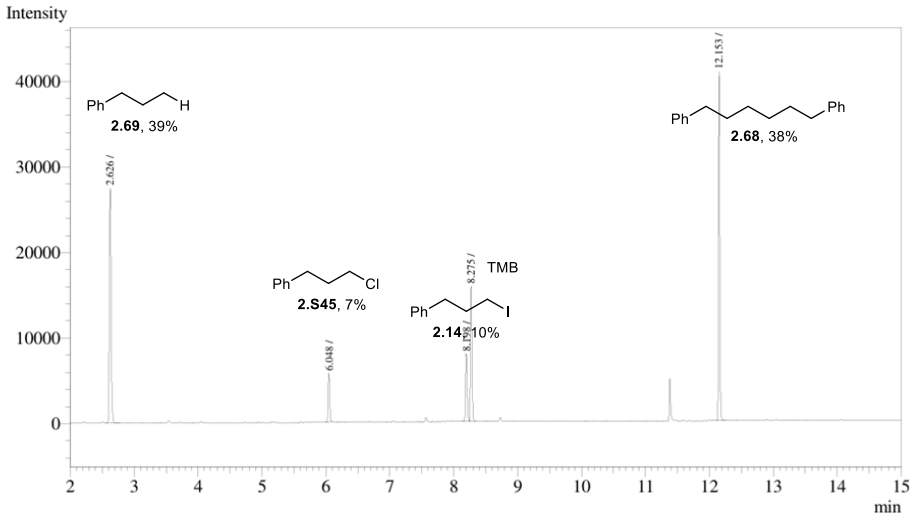
2.4.6.5. Activation of Alkyl Iodides.

Scheme 2.20 Activation of Alkyl Iodides



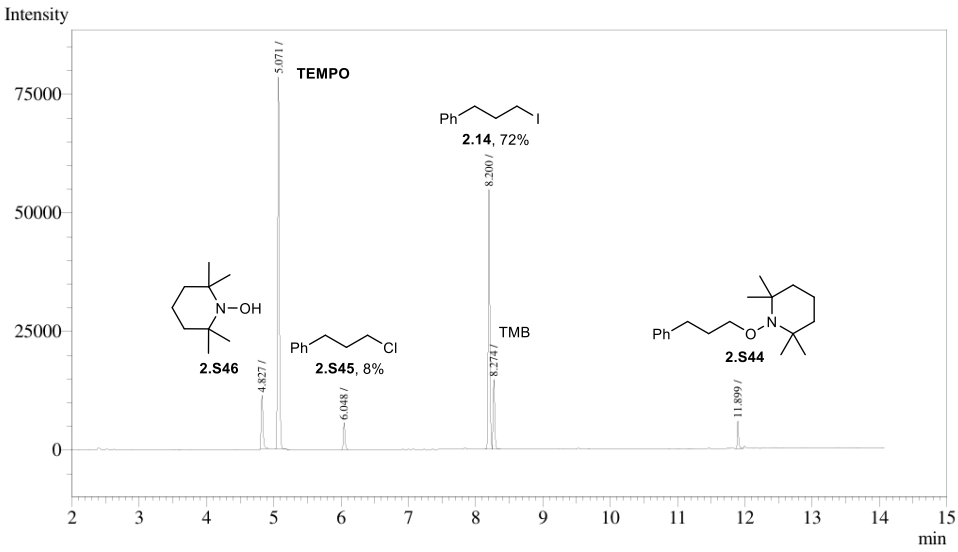
In a nitrogen-filled glovebox, a dram vial was charged with (DME)$NiCl_2$ (0.5 mg, 0.0025 mmol, 0.05 equiv), di-(2-picolyl)amine (**L1**, 0.8 mg, 0.0033 mmol, 0.075 equiv), anhydrous KF (4.4 mg, 0.075 mmol, 1.5 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (0.5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of alkyl iodide **2.14** (18.4 mg, 0.08 mmol, 1.5 equiv) with TMB as the internal standard, PMHS (9 µL, 0.15 mmol, 3.0 equiv) and required amount of TEMPO. The reaction mixture was vigorously stirred at 45 °C for 16 h. Then, an aliquot (50 µL) from the reaction mixture was passed through a plug of silica with EtOAc, concentrated and analyzed by GC (temperature progress **#1**) and GC-MS. The yield of **2.68**, **2.69** and **2.S45** was determined by GC using authentic sample commercially purchased or prepared according to literature.[35]

Figure 2.7 GC Traces of the Crude without TMEPO Addition



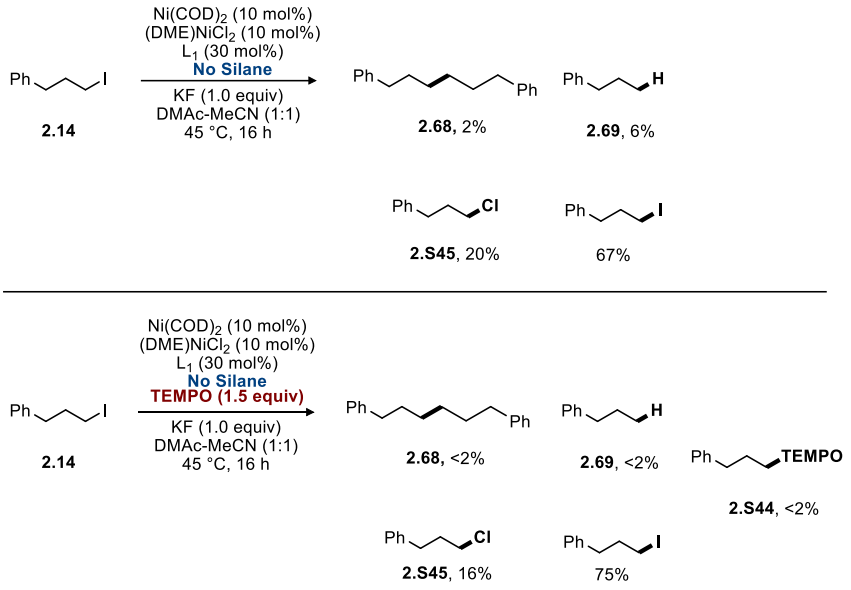
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	2.626	49461	27212	32.559				
2	6.048	9423	5603	6.203				
3	8.198	13617	7848	8.964				
4	8.275	26421	15572	17.392		V		
5	12.153	52988	39552	34.881				
Total		151910	95787					

Figure 2.8 GC Traces of the Crude with 150 mol% TMEPO Addition



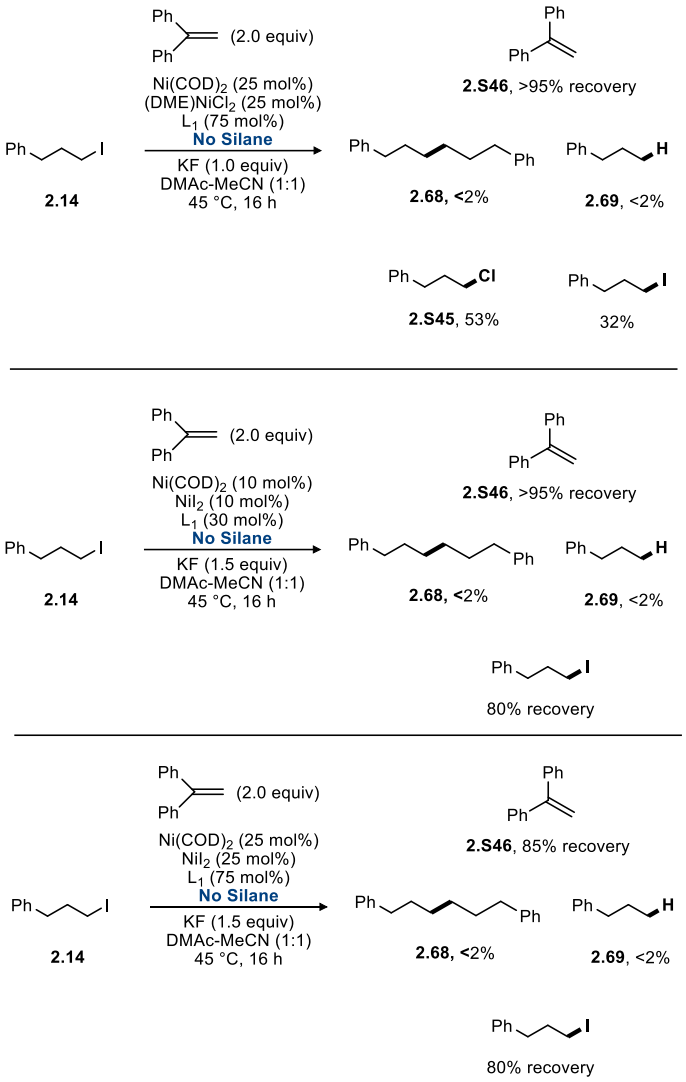
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4.827	21289	11064	7.258				
2	5.071	137064	77935	46.728				
3	6.048	9626	5555	3.282				
4	8.200	92771	53686	31.628				
5	8.274	24492	14517	8.350		V		
6	11.899	8078	5742	2.754				
Total		293320	168499					

Scheme 2.21 Activation of Alkyl Iodides without Silane Addition



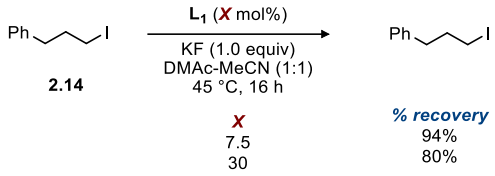
In a nitrogen-filled glovebox, a dram vial was charged with required amount of $(DME)NiCl_2$, $Ni(COD)_2$, di-(2-picolyl)amine (**L_1**), anhydrous KF (2.9 mg, 0.05 mmol, 1.0 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (0.5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of alkyl iodide **2.14** (12.3 mg, 0.05 mmol, 1.0 equiv) with TMB as the internal standard and required amount of TEMPO. The reaction mixture was vigorously stirred at 45 °C for 16 h. Then, an aliquot (50 µL) from the reaction mixture was passed through a plug of silica with EtOAc, concentrated and analyzed by GC (temperature progress **#1**). The yield of **2.68**, **2.69** and **2.S45** was determined by GC using authentic sample commercially purchased or prepared according to literature.[35]

Scheme 2.22 Radical Trap Probe without Silane Addition



In a nitrogen-filled glovebox, a dram vial was charged with required amount of (DME)$NiCl_2$, $Ni(COD)_2$, NiI_2, di-(2-picolyl)amine (**L_1**), anhydrous KF (2.9 mg, 0.05 mmol, 1.0 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (0.5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of alkyl iodide **2.14** (12.3 mg, 0.05 mmol, 1.0 equiv) with TMB as the internal standard and 1,1-diphenylethylene (**2.S46**, 18.0 mg, 0.1 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 45 °C for 16 h. Then, an aliquot (50 µL) from the reaction mixture was passed through a plug of silica with EtOAc, concentrated and analyzed by GC (temperature progress **#1**). The yield of **2.68**, **2.69**, **2.S45** and **2.S46** was determined by GC using authentic sample commercially purchased or prepared according to literature.[35]

Scheme 2.23 Activation of Alkyl Iodides without Ni Addition



In a nitrogen-filled glovebox, a dram vial was charged with required amount di-(2-picolyl)amine (**L1**), anhydrous KF (2.9 mg, 0.05 mmol, 1.0 equiv) and a stir bar. To the vial was added a 1:1 mixture of DMAc and MeCN (0.5 mL, 0.1 M) and the resulting mixture was stirred at 45 °C for 15 min. The reaction mixture was cooled down to room temperature followed by addition of alkyl iodide **2.14** (12.3 mg, 0.05 mmol, 1.0 equiv) with TMB as the internal standard. The reaction mixture was vigorously stirred at 45 °C for 16 h. Then, an aliquot (50 µL) from the reaction mixture was passed through a plug of silica with EtOAc, concentrated and analyzed by GC (temperature progress **#1**).

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Chapter 3 Enantioselective Trifunctionalization of Terminal Alkynes

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3.1 Introduction

Tri- and tetra-substituted alkenes are prevalent in bioactive molecules[1] and materials.[2] They also serve as versatile substrates in asymmetric transformations for stereospecific construction of vicinal chiral centers.[3] Relative to mono- and disubstituted alkenes, highly substituted alkenes exhibit increased steric congestion and severe eclipsing interactions. These features significantly limit the efficiency, scope, and stereoselectivity of traditional olefination methodologies,[4] such as carbonyl olefination[5] and alkene metathesis[6] in synthesis of highly substituted alkenes. Currently, the most versatile strategy for accessing tetrasubstituted alkenes is based on difunctionalization of internal alkynes, which has seen rapid development in the last decade.[7,8] However, the key carbometallation step in these reactions lacks inherent regioselectivity and the reactions require substrates with an electronically,[9] sterically,[9a,10] or coordinatively[11] biased alkyne limiting their scope. Overall, further development of methods for selective synthesis of highly substituted alkenes from readily available starting materials remains necessary.

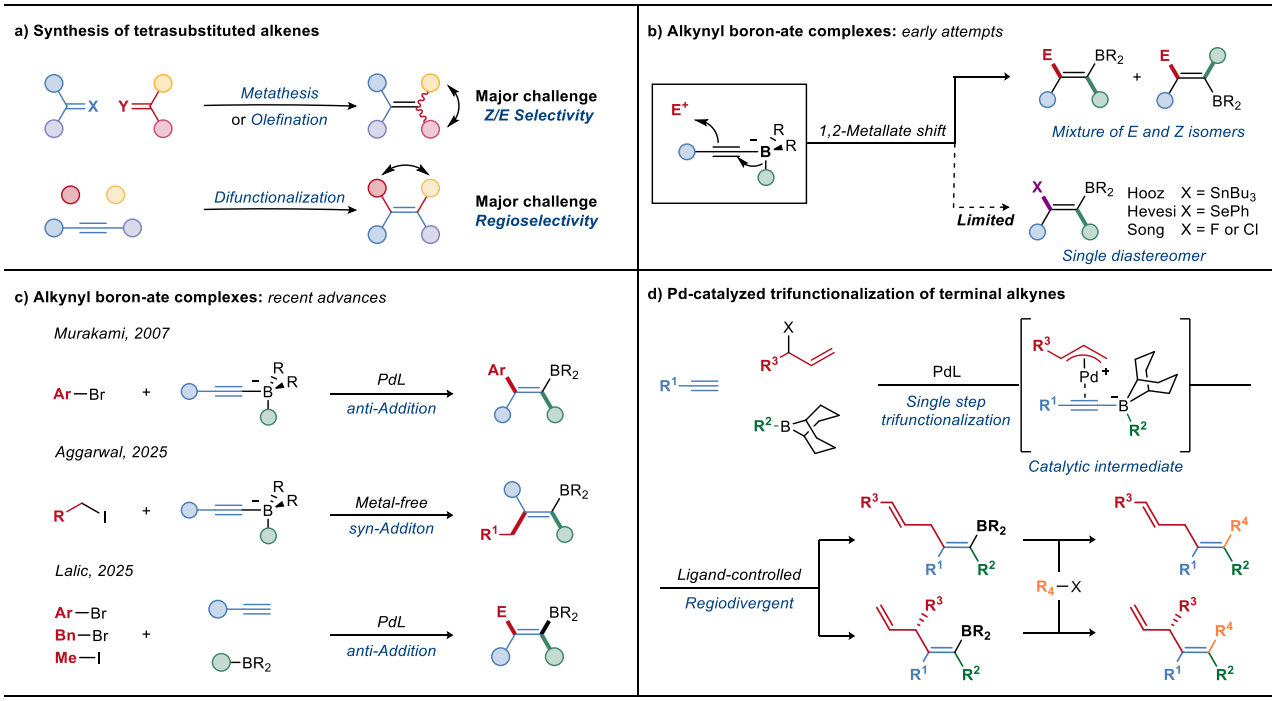
An intriguing approach to the synthesis of highly substituted alkenes involves electrophile-triggered 1,2-metalate shift of alkynyl boron-ate complexes, as first demonstrated by Brown[12] and Pelter[13] in 1970s. Although providing efficient access to tetrasubstituted alkenes, this approach initially afforded poor diastereocontrol.[13a,14] Good diastereoselectivity was limited to reactions forming cyclic products[15] or reactions with a narrow range of heteroatomic electrophiles.[16] In 2007, Murakami et al. addressed these limitations by introducing a Pd-catalyzed coupling of alkynyl boron-ate complexes with aryl halides.[17] More recently, Aggarwal reported an exceptionally versatile metal-free alkylation of alkynyl boron-ate complexes,[18] with the two approaches delivering excellent and complementary diastereoselectivity (Scheme 3.1c).

Building on the unique reactivity of alkynyl boron-ate complexes, we recently introduced direct metal-catalyzed trifunctionalization of terminal alkynes through electrophilic functionalization of alkynyl boron-ate intermediates formed in situ from alkynes and organoboranes (Scheme 3.1c).[19] This process provides a highly convergent strategy for the synthesis of tetrasubstituted alkenes and eliminates the need for stoichiometric organolithium reagents used in the formation of alkynyl boron-ate complexes. At the same time, the use of transition metal catalysts to initiate the 1,2-metallate allowed us to expand the scope of electrophiles in functionalization of alkynyl boron-ate complexes. We recognized that the same approach can be used to develop an enantioselective trifunctionalization of terminal alkynes by using prochiral electrophiles. Intriguingly, the same

transition metal catalyst that promotes 1,2-metalate shift could then also be used to control the enantioselectivity of the overall process that would afford highly complex chiral molecules featuring tri- and tetrasubstituted alkenes.

In this work, we present a palladium-catalyzed direct trifunctionalization of terminal alkynes using organoboranes and allylic carbonates as coupling partners (Scheme 3.1d). The new method enables efficient synthesis of tri- and tetrasubstituted alkenes with excellent regio- and diastereoselectivity. In addition to promoting 1,2-metallate rearrangement of the alkynyl boron-ate intermediate, the palladium catalyst plays a crucial role in controlling the substitution of allylic carbonates. Notably, the choice of ligand influences the regioselectivity of the allylation, enabling regiodivergent access to either linear products with excellent *E*-selectivity or branched products with high enantioselectivity. Finally, we also show that the alkenyl borane products can be further functionalized into a variety of tetrasubstituted alkenes without isolation or purification.

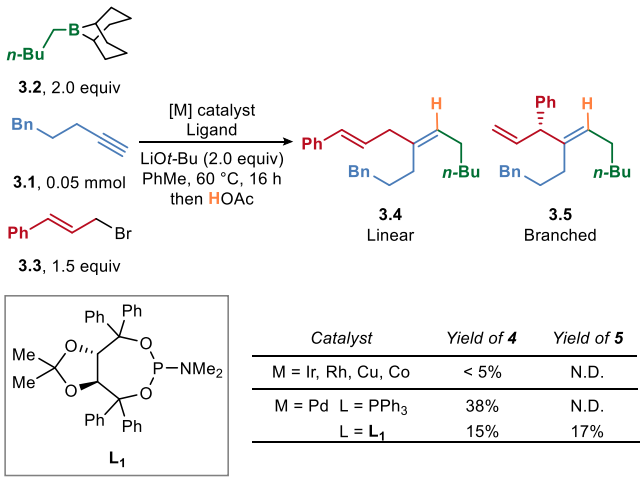
Scheme 3.1 Synthesis of Tetrasubstituted Alkenes and 1,2-Metallate Shift of Alkynyl Boron-ate Complexes



3.2 Results and Discussion

Seeking to incorporate complex prochiral electrophiles into direct trifunctionalization of alkynes, we were drawn to allylic electrophiles. While the enantioselective allylations of various boron-ate complexes are known,[20] reactions of preformed alkynyl boron-ate complexes with allylic electrophiles have been mired by low diastereoselectivity and only the products of the linear allylic substitution have be obtained.[21] Hoping to address these issues and control regio-, diastereo-, and enantioselectivity of the allylic substitution, we explored the reaction of terminal alkyne **3.1**, organoborane **3.2**, and cinnamyl bromide **3.3** in the presence of transition metal catalysts (Scheme 3.2). Various Ir, Rh, Co and Cu complexes proved ineffective, while Pd catalysts bearing diverse phosphine ligands furnished the desired product **3.4** in moderate yields and excellent diastereoselectivity. To our delight, phosphoramidite ligand $\mathbf{L_1}$ derived from TADDOL (α,α,α′,α′-tetraaryl-2,2-disubstituted-1,3-dioxolane-4,5-dimethanol) enabled branched-selective allylation, delivering branched product **3.5** in 17% yield, along with 15% of the linear isomer **3.4**. These findings prompted a systematic ligand evaluation to develop a ligand-controlled, regiodivergent allylation for accessing structurally diverse, highly substituted alkenes.

Scheme 3.2 Preliminary Results



Catalyst	*Yield of **4***	*Yield of **5***
M = Ir, Rh, Cu, Co	< 5%	N.D.
M = Pd L = PPh_3	38%	N.D.
L = $\mathbf{L_1}$	15%	17%

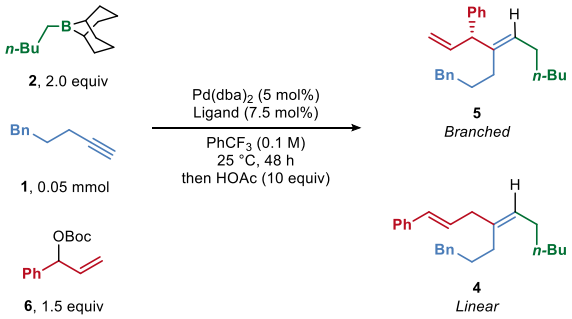
We evaluated a range of ligands in a reaction shown in Scheme 3.3, using allylic carbonate **3.6** as the electrophile. Ligand identity proved critical for both reaction efficiency and regioselectivity. Most phosphine ligands favored formation of the linear product as commonly observed in palladium catalyzed allylation reactions. The best results were obtained with phosphinooxazoline ligand $\mathbf{L_4}$, which furnished **3.4** in 85% yield with >99:1 l:b regioselectivity, while other phosphinooxazoline ligands provided significantly lower yields. Phosphoramidite ligands derived from scaffolds such as $\mathbf{L_2}$ (entry 2) and $\mathbf{L_3}$ (entry 3) also favored the formation of linear products, while TADDOL-derived phosphoramidite ligands promoted branched selectivity.

We improved branched selectivity of the TADDOL-derived ligands (entries 1 and 6) by replacing the dimethylamino moiety in the phosphoramidite backbone with piperidine (see SI, Tables S4 and

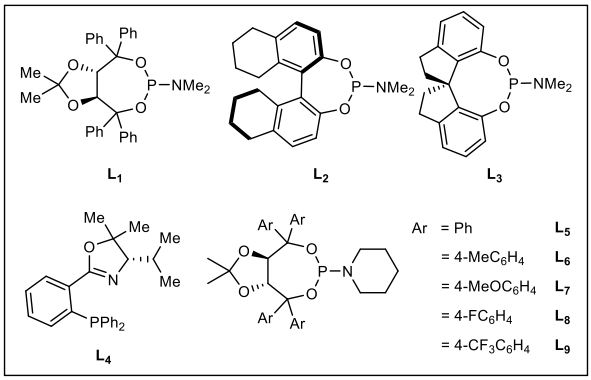
S5). Further investigation revealed that aryl substituents on the TADDOL backbone significantly influenced enantioselectivity. Electron-neutral (**L$_6$**, entry 7) and electron-donating (**L$_7$**, entry 8) substituents had minimal impact, whereas electron-withdrawing substituents (**L$_8$** and **L$_9$**, entries 9 and 10) led to a significant enhancement in enantioselectivity. The branched product **3.5** was obtained in 85% yield, 95:5 er, and 99:1 b:l regioselectivity using ligand **L$_9$** under the optimized conditions. To the best of our knowledge, this is the first TADDOL-derived phosphoramidite ligand that favors branched selectivity in Pd-catalyzed allylic substitution.

We also examined the structure of the tetrasubstituted alkenyl boranes formed in reactions shown in entries 5 and 10. In both reactions we observed a single regioisomer of the product. NMR analysis allowed us to establish the alkene configurations in both linear and branched allylation products, revealing a strong preference for anti-addition, which places allylic fragment and the group migrating in 1,2-metallate shift trans to each other. This selectivity complements the syn-selectivity observed in Aggarwal's recent work.[18]

Scheme 3.3 Ligand Effects

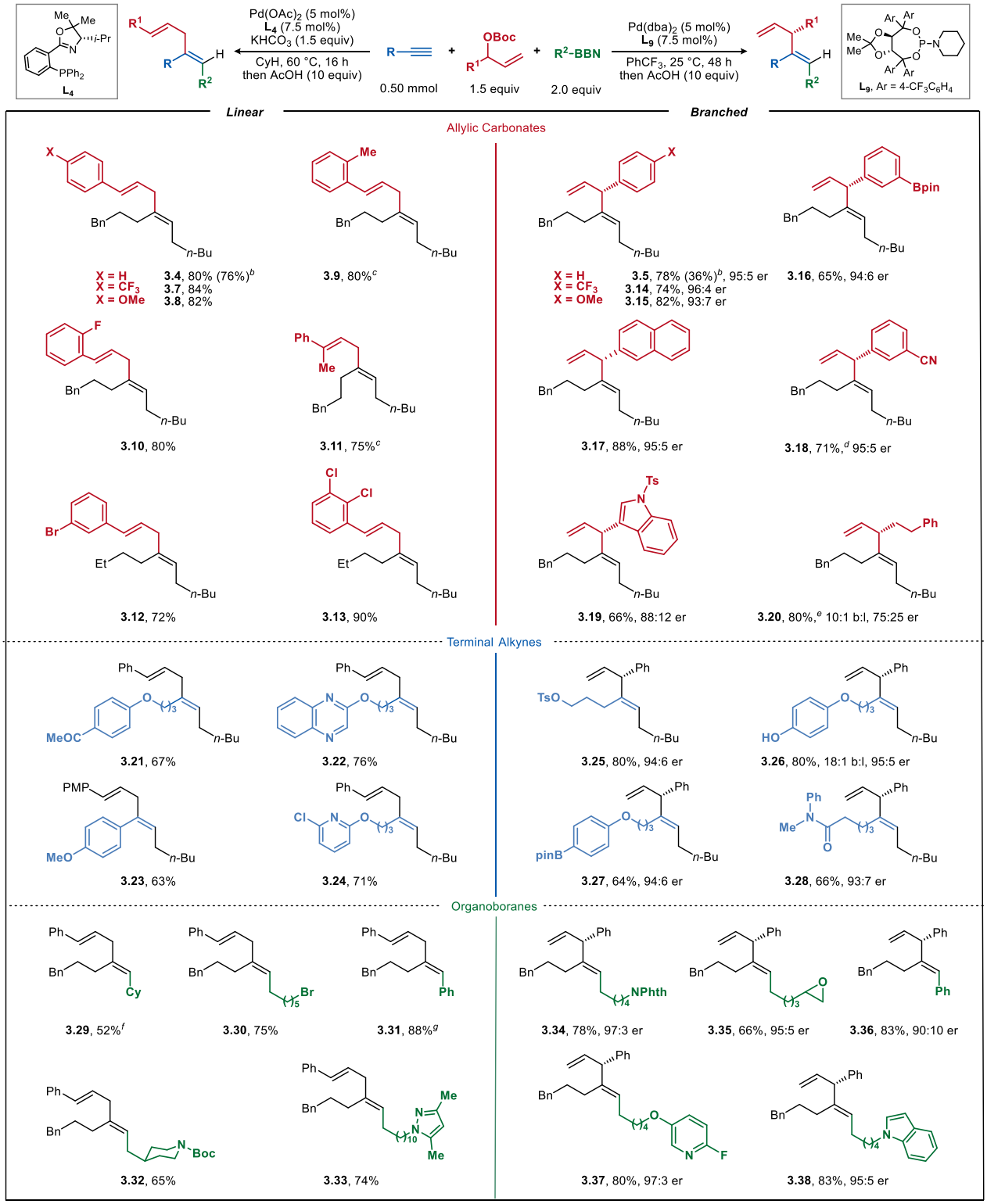


Entry	*Ligand*	*Yield*	*b:l ratio*	*er of 5*
1	**L$_1$**	57%	87:13	46:54
2	**L$_2$**	4%	3:97	NA
3	**L$_3$**	34%	4:96	NA
4	**L$_4$**	16%	1:>99	NA
5[b]	**L$_4$**	85%	1:>99	NA
6	**L$_5$**	58%	92:8	72:28
7	**L$_6$**	60%	95:5	76:24
8	**L$_7$**	46%	93:7	73:27
9	**L$_8$**	38%	92:8	91:9
10	**L$_9$**	85%	99:1	95:5



[b]Modified conditions: $Pd(OAc)_2$ (5 mol%), **L$_4$** (7.5 mol%), $KHCO_3$ (1.5 equiv), in cyclohexane (0.1 M), at 60 °C for 16 h.

Table 3.1 Substrate Scope



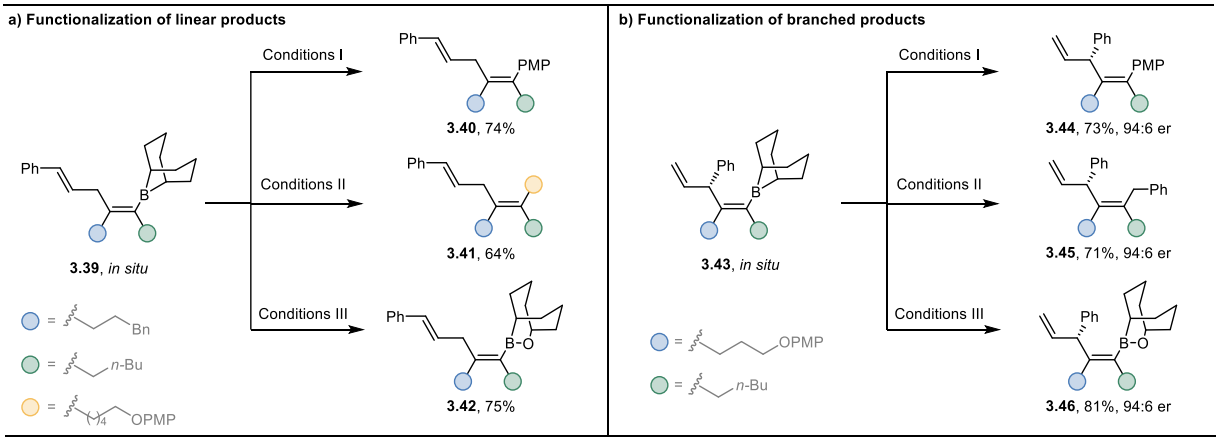
[a]Yields of isolated products are reported. Reactions performed on 0.50 mmol scale. Single isomer (> 20:1 d.r. and > 20:1 r.r.) was detected in ^{1}H NMR spectra of isolated products unless otherwise noted. Enantiomeric ratios determined by chiral HPLC analysis. [b]The linear isomer of allylic carbonate was used as a substrate; [c]80 °C; [d]$Pd(OAc)_2$ (5 mol%) and K_3PO_4 (2.0 equiv) were used instead of $Pd(dba)_2$; [e]**L$_7$** instead of **L$_9$**; [f]2.5 equiv organoborane, 45 °C; [g]40 h.

To assess the generality of the optimized conditions, we explored the reactivity of a broad array of substrates (Table 3.1). After in situ protodeboronation of the initially formed alkenyl boranes with acetic acid, the products were isolated and characterized as trisubstituted alkenes. Reactions proceed with excellent regio- and diastereoselectivity under both branched- and linear-selective conditions. For branched products, the high enantiomeric ratios initially observed with model substrates remained consistent across the expanded substrate scope. In the formation of linear products, the cinnamyl moiety was constructed with high *E*-selectivity.

Initial experiments conducted with a range of different allylic carbonates revealed broad and consistent reactivity. Various aryl- and heteroaryl-substituted allylic carbonates gave satisfactory yields, including those with electron-donating (**3.8**, **3.15**) or electron-withdrawing substituents (**3.7**, **3.10**, **3.14**, **3.18**). Cross-coupling handles, such as halides (**3.12**, **3.13**) and boronic esters (**3.16**), were well tolerated. The use of sterically demanding electrophiles (**3.9**, **3.11**) did not hinder construction of linear isomers. Alkyl-substituted allylic carbonates gave high yields when used in the synthesis of branched isomers, albeit with a decrease in enantioselectivity (**3.20**). Linear isomer of allylic carbonate **3.6** provided comparable results in the formation of linear product **3.4**, and a significantly lower yield in the formation of branched products **3.5**, albeit with high regio- and enantioselectivity.

We next evaluated the scope of alkyne and organoborane coupling partners. The reaction could be successfully performed in the presence of ketones (**3.21**), amides (**3.28**), phenols (**3.26**), quinoxalines (**3.22**), pyridines (**3.24**, **3.37**), pyrazoles (**3.33**), indoles (**3.38**), alkyl (pseudo)halides (**3.25**, **3.30**), *N*-Boc piperidines (**3.32**), phthalimides (**3.34**), and epoxides (**3.35**). Alkyl alkynes, arylboranes (**3.31**, **3.36**) and primary alkylboranes proved reliable in the synthesis of both branched and linear isomers. Additionally, aryl alkynes (**3.23**) and secondary alkylboranes (**3.29**) were competent in delivering linear products. We also noted that sterically hindered alkynes and alkylboranes provided low yields of desired products.

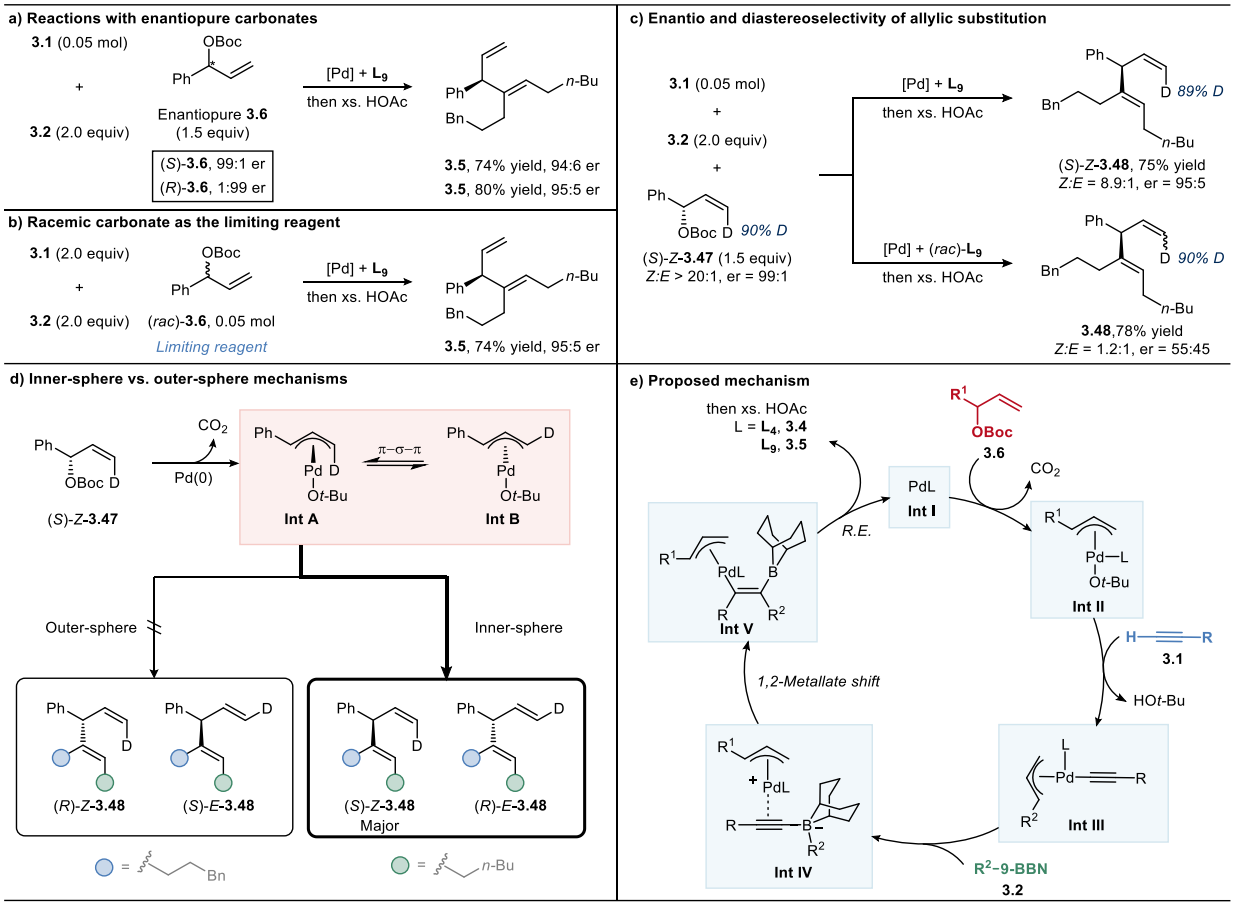
Scheme 3.4 Transformations of Alkenyl Boranes



Yields of isolated products are reported. Reaction performed on 0.50 mmol scale. Single isomer (> 20:1 d.r. and > 20:1 r.r.) was detected in ^{1}H NMR spectra of isolated products. The alkenylborane intermediates were prepared via slightly modified conditions and transformed in situ.
Conditions I: aryl iodide (2.5 equiv), NaO*t*-Bu (3.0 equiv), $Pd(OAc)_2$ (5 mol%), RuPhos (7.5 mol%), 60 °C. Conditions II: alkyl halide (3.0 equiv, bromide for **3.41**, iodide for **3.45**), LiO*i*-Pr (2.5 equiv), CuI (50 mol%), 45 °C (for **3.41**) or 80 °C (for **3.45**) in DMAc (0.1 M). Conditions III: trimethylamine *N*-oxide (3.0 equiv), 25 °C.

With access to a variety of tetrasubstituted alkenyl boranes, we explored their further functionalization to acyclic tetrasubstituted alkenes (Scheme 3.4). Oxidation of the alkenylboranes with trimethylamine *N*-oxide furnishes the corresponding tetrasubstituted alkenylborinic esters (**3.42**, **3.46**), which could be isolated and used in further transformations. Alternatively, the alkenylboranes can be directly cross coupled with aryl iodides without any workup or purification (**3.40**, **3.44**). Coupling with C(sp^3) electrophiles proceeds smoothly after a solvent swap followed by introduction of a Cu(I) catalyst and the corresponding alkyl halides (**3.41**, **3.45**). Notably, all transformations proceed without erosion of stereochemical fidelity. Together, these transformations underscore the capability of the reaction to streamline access to previously difficult-to-access chemical space.

Scheme 3.5 Mechanistic Studies



Following our investigation into the scope and synthesis of tetrasubstituted alkenes, we turned to mechanistic studies. Reactions employing enantioenriched allylic carbonates (*R*)- **3.6** and (*S*)- **3.6** under the standard branched-selective conditions proceeded with comparable efficiency, each furnishing the product **3.5** in > 70% yield and high er (Scheme 3.5a). Moreover, conducting the reaction with racemic allylic carbonate **3.6** as the limiting reagent gave the product **3.5** in 74% yield and high er (Scheme 3.5b). Taken together, these experiments indicate that, while minor

match/mismatch effects between the catalyst and substrates exist, a kinetic resolution is not a significant contributor to the overall selectivity of the reaction.[22] Instead, these results support a dynamic kinetic resolution process during the enantioselective allylic substitution.[23]

The formation of a new C–C bond between allylic carbonates and alkynes may proceed via either an inner-sphere reductive elimination[24] or an outer-sphere pathway[25] that would involve a reaction of π-allyl palladium complex with alkynyl boron-ate intermediate as a nucleophile. To distinguish between these mechanistic possibilities, a deuterium-labelled allylic carbonate, (*S*)-*Z*-**3.47**, was prepared and subjected to the branched-selective reaction conditions (Scheme 3.5c).[26] Based on the established stereochemistry of Pd-catalyzed allylic substitution (Scheme 3.5d), oxidative addition proceeds with inversion of configuration[27] to generate π-allyl complex **Int A**, which can equilibrate with complex **Int B** via *π–σ–π* isomerization.[28] In an outer-sphere pathway, C–C bond formation occurs with a second inversion, furnishing (*R*)-*Z*-**3.48** from **Int A** or (*S*)-*E*-**48** from **Int B**. By contrast, an inner-sphere pathway would proceed with retention of configuration, affording (*S*)-*Z*-**3.48** or (*R*)-*E*-**3.48** from the respective π-allyl complexes. Under the optimized reaction conditions for the branched-selective allylation we observed the formation of (*S*)-*Z*-**3.48**, consistent with an inner-sphere pathway. This result suggests that the 1,2-metallate shift is promoted by the palladium catalyst and precedes the allylation.

Based on our experimental findings and established mechanisms of 1,2-metallate shift[29] and palladium-catalyzed allylation,[23b] we propose the reaction mechanism presented in Scheme 3.5e. Initial oxidative addition of Pd(0) into the allylic carbonate provides Pd(II) complex **Int II** with concomitant CO_2 extrusion. Subsequent deprotonation of the terminal alkyne with **Int II** yields Pd acetylide **Int III**, which reacts with the Lewis acidic organoborane to provide complex **Int IV**. A diastereodetermining 1,2-metallate shift of the boron-ate complex is then triggered by the interaction with electrophilic *π*-allyl Pd complex, delivering the tetrasubstituted alkenyl Pd species **Int V**. Ligand-controlled, regiodivergent reductive elimination delivers tetrasubstituted alkene product and regenerates Pd(0).

3.3 Conclusion

We have developed palladium-catalyzed trifunctionalization of terminal alkynes using organoboranes and allylic carbonates as coupling partners. The new transformation provides access to highly substituted tri- and tetrasubstituted alkenes with excellent regio- and diastereoselectivity. In addition, the incorporation of the allylic electrophile can be accomplished with both branched and linear selectivity, and with excellent diastereo- and enantioselectivity, allowing access to a range of highly complex 1,4-dienes. We demonstrate the broad scope of the reaction and the ability to transform the initially formed tetrasubstituted alkenyl boranes into a range of tetrasubstituted alkenes. Finally, our mechanistic study supports the mechanism that involves alkynyl boron-ate formation followed by palladium-promoted 1,2-metalate shift that controls the regio- and diastereoselectivity of the alkene formation. The subsequent allylation of the alkenyl palladium intermediate is also controlled by the palladium catalyst, with a proper

choice of the ligand enabling high regio-, diastereo-, and enantioselectivity of the transformation. Overall, we demonstrate that metal-catalyzed transformations of the alkynyl boron-ate intermediates can be used with complex prochiral electrophiles to access highly complex chiral molecules from simple starting materials.

3.4 Experimental

3.4.1 General Information

3.4.1.1 Glassware, Chromatography, and Instrumentation

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).

Infrared (IR) spectra were recorded on a FTIR Perkin Elmer Frontier spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 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). ^{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). ^{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). 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 an Agilent 5973 GC-MS 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).

3.4.1.2 Solvents and Reagents

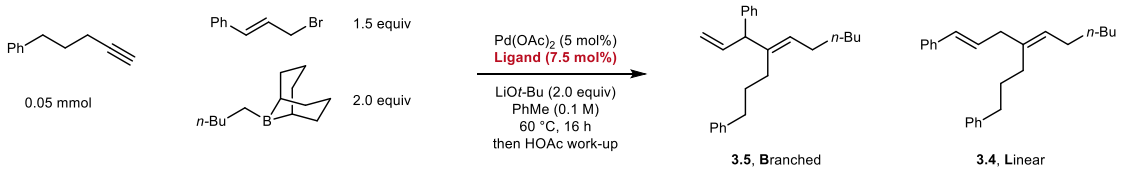
THF, CH_2Cl_2, Et_2O, and PhMe were degassed and dried by passing through columns of neutral alumina Anhydrous DMAc, $PhCF_3$, acetonitrile and cyclohexane were purchased from Millipore Sigma and were subsequently degassed and stored over 4Å molecular sieves. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and used as received.

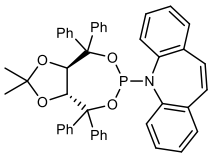
Commercial reagents and ligands were purchased from Millipore Sigma, TCI America, Combi-Blocks, Oakwood Chemicals, Strem Chemicals, Alfa Aesar, Aaron Chemicals, Enamine, Chemscene and Ambeed. 9-BBN dimer was purchased from Oakwood Chemicals and used as received.

3.4.2 Reaction Development

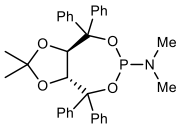
All reactions in Table 3.2~3.11 were performed on a 0.05 mmol scale. In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, base (if applicable), metal catalyst, ligand, and solvent stirred at 45 ºC for 10 minutes. Then, terminal alkyne with the internal standard 1,3,5-trimethoxybenzene (TMB), allylic electrophile, and alkylborane solution were added. The reaction mixture was vigorously stirred at the indicated temperature for 16 h. The vial was then removed from the glovebox and excess acetic acid (10 equivalence, 0.5 mmol) was added. The mixture was allowed to be stirred at room temperature for 1 h before an aliquot (50 μL) was taken and analyzed by gas chromatography. In all cases, the trisubstituted alkene product was >100:1 *E*:*Z*. Enantiomeric ratio was determined by HPLC analysis of isolated alkene product according to General Procedure D (see below).

Table 3.2 Ligand Screen

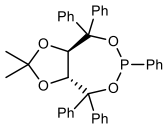




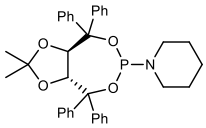
Yield trace
L:B ratio -



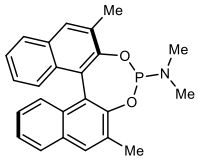
Yield 32%
L:B ratio 1:1



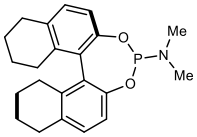
Yield 38%
L:B ratio 1:1



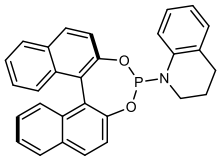
Yield L_5 29%
L:B ratio 1:6



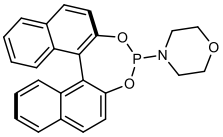
Yield 46%
L:B ratio 10:1



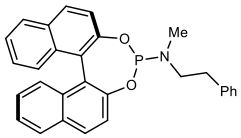
Yield 44%
L:B ratio 36:1



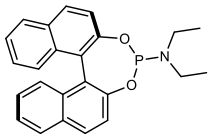
Yield 59%
L:B ratio > 50:1



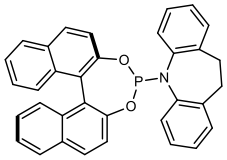
Yield 50%
L:B ratio 9:1



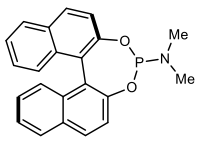
Yield 50%
L:B ratio 15:1



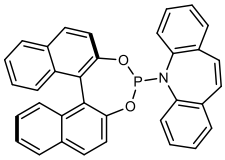
Yield 30%
L:B ratio 6.5:1



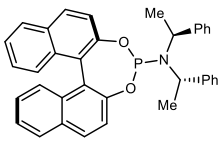
Yield 19%
L:B ratio 4:1



Yield 37%
L:B ratio 13:1



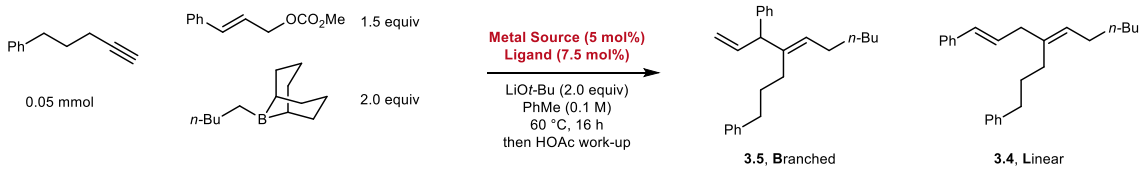
Yield 30%
L:B ratio 4:1



Yield 16%
L:B ratio 7:1

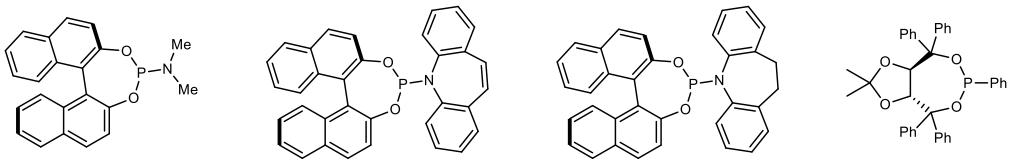
Ligand	Xphos	Sphos	PCy_3	PPh_3	$P(o\text{-tol})_3$	P^tBu_3	PMe^tBu_2
Yield (%)	trace	5	31	38	11	trace	26
L:B ratio	-	> 50:1	> 50:1	> 50:1	> 50:1	-	> 50:1
Ligand	**dppe**	**dppp**	**dppb**	**dppbz**	**Xantphos**	**BINAP**	**dppf**
Yield (%)	trace	trace	trace	trace	trace	trace	trace
L:B ratio	-	> 50:1	> 50:1	> 50:1	> 50:1	-	> 50:1

Table 3.3 Metal Catalyst Screen



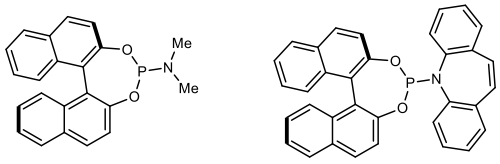
Metal Source = $[Ir(COD)Cl]_2$

Ligand =



Yield	Not Detected	5%	Not detected	8%
L:B ratio	-	> 50:1	-	> 50:1

Ligand =



				$P(o\text{-}tol)_3$	dppp

Metal Source = $[Rh(nbd)_2]BF_4$

Yield	5%	Not detected	Not detected	Not detected	6%
L:B ratio	> 50:1	-	-	-	> 50:1

Metal Source = $CoBr_2$

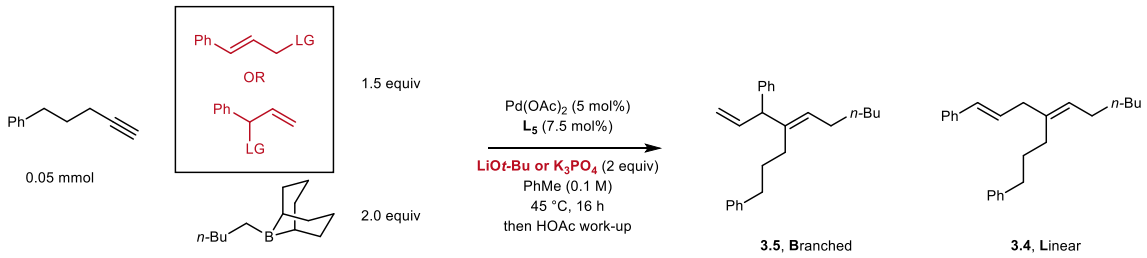
Yield	6%	Not detected	7%	Not detected	7%
L:B ratio	> 50:1	-	> 50:1	-	> 50:1

Metal Source: CuOAc or AgOAc

Ligand: **SPhos, DavePhos, BrettPhos, PCy_3, XantPhos** or **IPr NHC**

No desired product detected

Table 3.4 Electrophile Screen for Branched Conditions



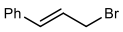
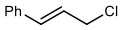
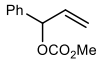
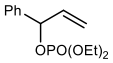
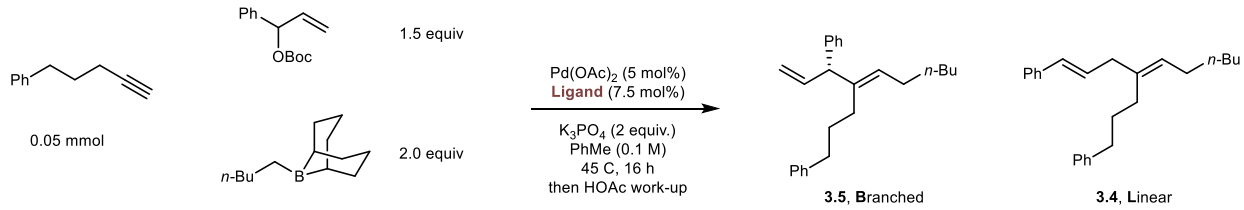
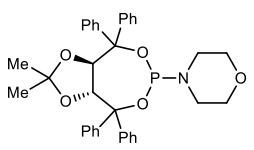
Electrophile	*Base*	*Yield*	*L:B ratio*
	LiO*t*-Bu	29%	1:6
	LiO*t*-Bu	24%	1:9
	LiO*t*-Bu	8%	1:9
	LiO*t*-Bu	24%	1:10
	K_3PO_4	42%	1:11
	K_3PO_4	38%	1:8
	K_3PO_4	32%	1:11

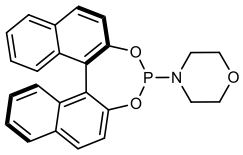
Table 3.5 Ligand Effects on Regioselectivity



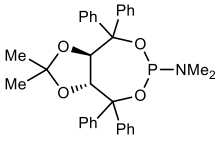
Selected Ligands



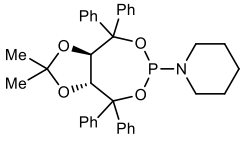
40% yield L:B = 1:9



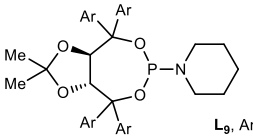
15% yield L:B = 2:1



32% yield L:B = 1:3.5



42% yield L:B = 1:11

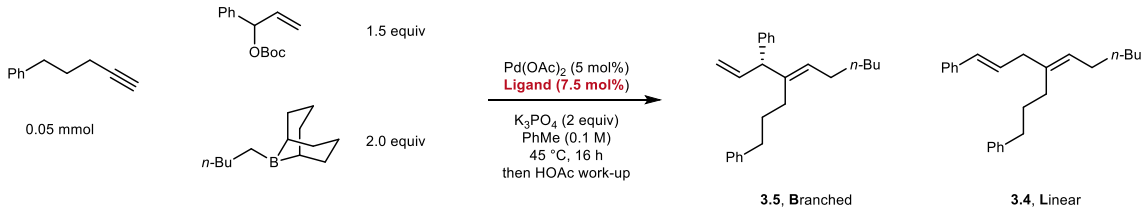


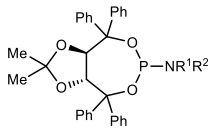
44% yield L:B = 1:15

L_9, Ar = 4-$CF_3C_6H_4$

Results for selected ligands are summarized in Table 3.5. The diol backbone of ligands shows a significant influence on the regioselectivity of the allylation: TADDOL-derived ligands favor formation of the branched product, whereas BINOL-derived ligands prefer to deliver the linear isomer. The amine moiety and side chain also influence the regioselectivity, though the effect is less pronounced (see Table 3.6, 3.7 for additional examples).

Table 3.6 Branched Conditions – Amine Moiety Effects





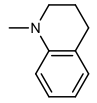
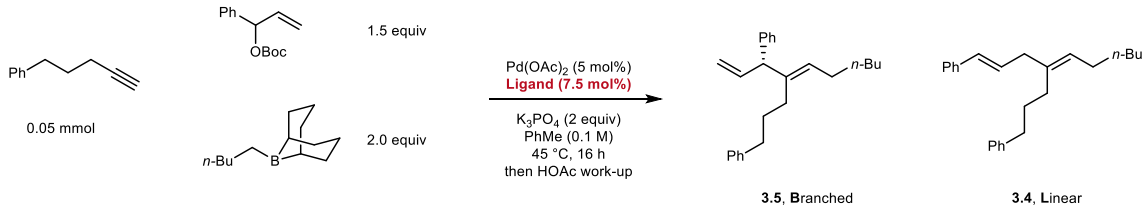
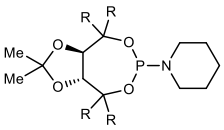
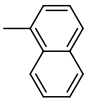
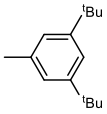
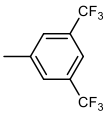
-NR^1R^2 =		Yield	L:B ratio
		17%	1:1.5
		40%	1:4
		9%	1:6
		trace	-
		trace	-
		25%	1:5
		42%	1:11
		40%	1:8
		trace	-

Table 3.7 Branched Conditions – Side Chain Effects





R =	Yield	L:B ratio	e.r. of 3.5
—*n*-Hex	20%	1:1	-
	7%	1:7	-
	8%	1:20	-
	trace	-	-

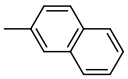
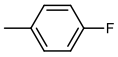
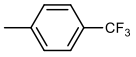
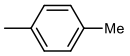
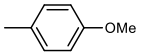
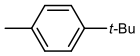
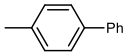
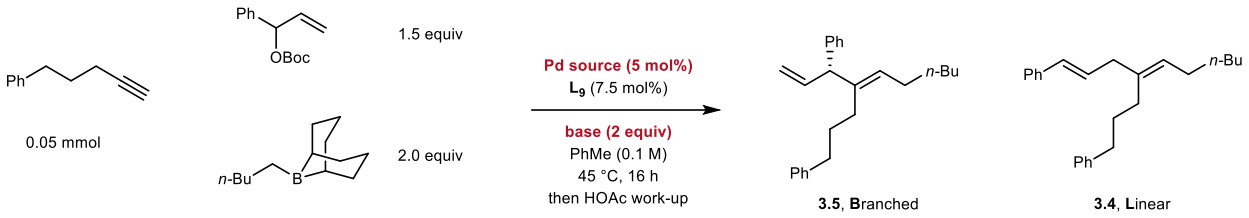
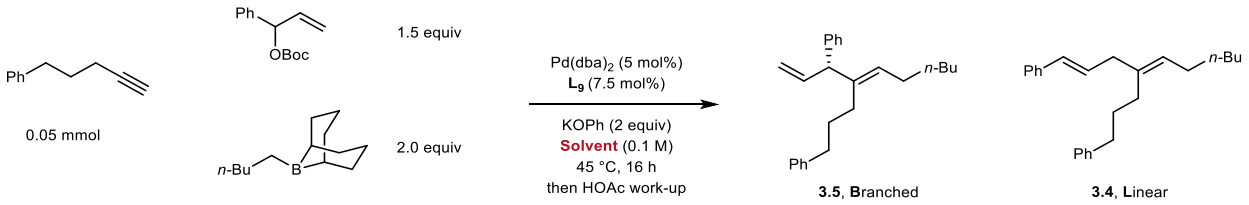
	R =	Yield	L:B ratio	e.r. of 3.5
L_5	—Ph	42%	1:11	72:28
		52%	1:16	73:27
L_8		35%	1:13	90:10
L_9		44%	1:15	**95:5**
L_6		35%	1:15	69:31
L_7		30%	1:12	64:36
		15%	1:10	50:50
		52%	1:15	82:18

Table 3.8 Base Screen for Branched Conditions, Part I



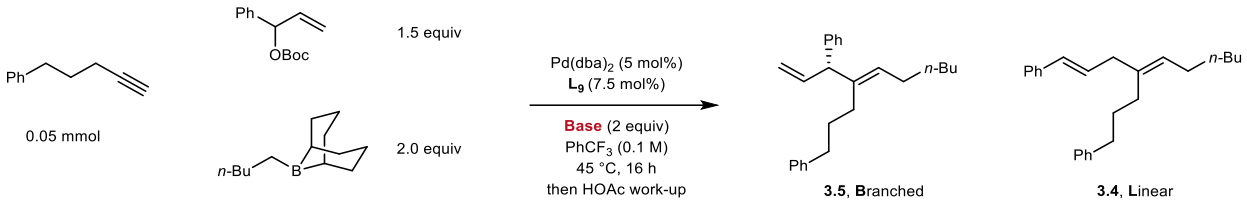
Entry	*Pd source*	*Base*	*Yield (%)*	*L:B ratio*
1	$Pd(OAc)_2$	K_3PO_4	44	1:15
2	$Pd(dba)_2$	K_3PO_4	50	1:20
3	$Pd(dba)_2$	Li_2CO_3	50	1:23
4	$Pd(dba)_2$	LiOTMS	23	1:29
5	$Pd(dba)_2$	LiOMe	36	1:20
6	**$Pd(dba)_2$**	**KOPh**	**51**	**1:40**
7	$Pd(dba)_2$	NaOPh	50	1:18
8	$Pd(dba)_2$	2-*t*-BuC_6H_4OK	trace	-
9	$Pd(dba)_2$	CsOPiv	trace	-
10	$Pd(dba)_2$	Cs_2CO_3	11%	1:6

Table 3.9 Solvent Screen for Branched Conditions



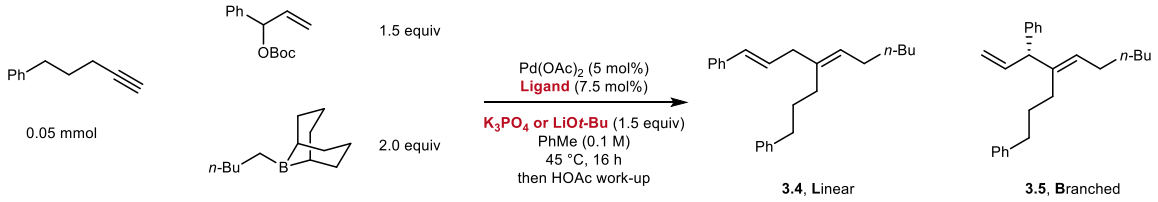
Entry	*Solvent*	*Yield (%)*	*L:B ratio*
1	PhMe	51	1:40
2	benzene	33	1:32
3	C_6D_6	27	1:6
4	DCM	36	1:7
5	THF	13	1:25
6	DMAc	trace	-
7	1,4-dioxane	21	1:3
8	xylenes	10	1:32
9	PhCl	56	1:22
10	cyclohexane	57	1:29
11	isooctane	51	1:19
12	pentane	57	1:23
13	mesitylene	55	1:36
14	CCl_4	trace	-
15	acetonitrile	trace	-
16	**$PhCF_3$**	**54**	**1:40**

Table 3.10 Base Screen for Branched Conditions, Part II



Entry	*Base*	*Yield (%)*	*L:B ratio*
1	KOPh	54	1:40
2	K_3PO_4	68	1:44
3	K_2CO_3	71	1:44
4	Na_2CO_3	20	1:40
6	Cs_2CO_3	60	1:45
7	NaOAc	70	1:35
8	LiF	38	1:31
9	KF	trace	-
10	No Base	68	1:40
11	**No Base (at 25 °C for 40 h)**	**81**	**1:> 50 (e.r. = 95:5)**

Table 3.11 Ligand Screen for Linear Conditions



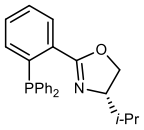
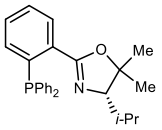
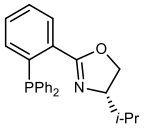
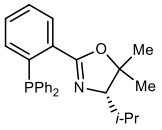
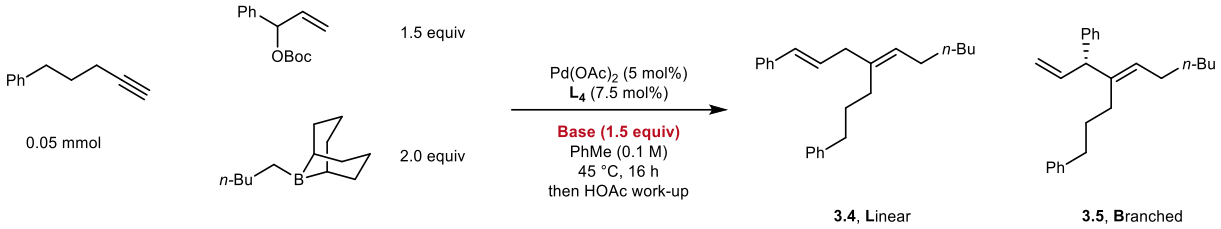
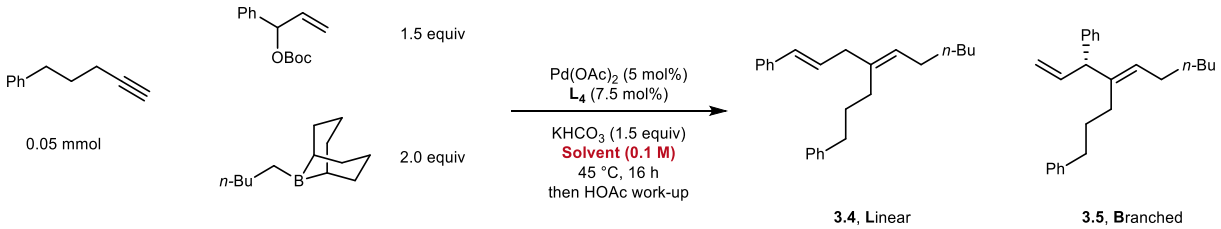
Base = K_3PO_4 ***Yield*** ***L:B ratio***	PPh_3 12% > 50:1	 36% > 50:1	 **L_4** 67% > 50:1
Base = LiO*t*-Bu ***Yield*** ***L:B ratio***	PPh_3 trace -	 35% > 50:1	 57% > 50:1

Table 3.12 Base Screen for Linear Conditions



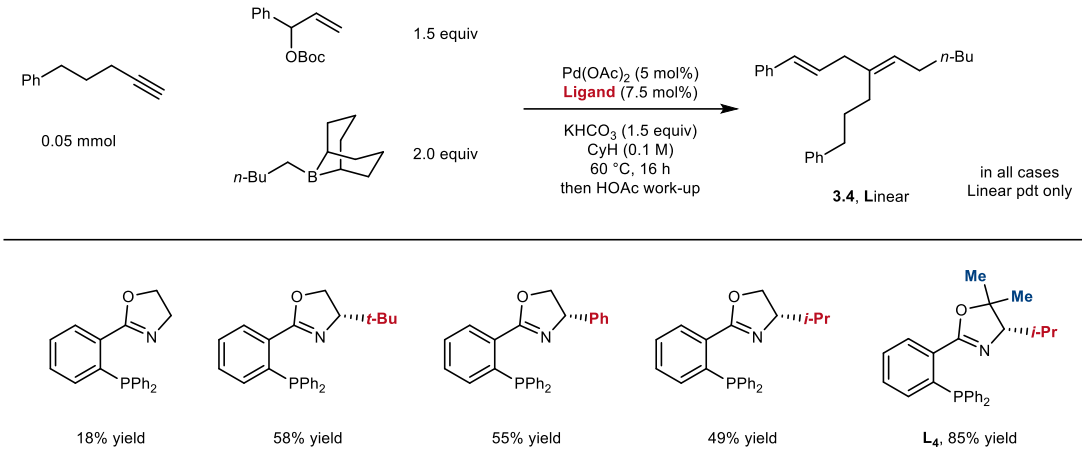
Entry	*Base*	*Yield (%)*	*L:B ratio*
1	K_3PO_4	67	> 50:1
2	Cs_2CO_3	60	> 50:1
3	Na_2CO_3	51	> 50:1
4	**$KHCO_3$**	**73**	**> 50:1**
6	KF	26	> 50:1
7	CsF	trace	-
8	NaOH	59	> 50:1
9	NaOAc	52	> 50:1
10	KOPh	41	> 50:1
11	LiOTMS	trace	-

Table 3.13 Solvent Screen for Linear Conditons



Entry	*Base*	*Yield (%)*	*L:B ratio*
1	THF	45%	> 50:1
2	1,4-dioxane	68%	> 50:1
3	CPME	63%	> 50:1
4	MTBE	78%	> 50:1
6	PhMe	73%	> 50:1
7	PhF	72%	> 50:1
8	DCM	37%	> 50:1
9	isooctane	81%	> 50:1
10	CyH	82%	> 50:1
11	*i*-PrOH	21%	> 50:1
12	DCM	37%	> 50:1
13	**CyH at 60 °C**	**85%**	**> 50:1**

Table 3.14. Linear Conditions – Ligand Effect



3.4.3 General Procedures

3.4.3.1 General Procedure A: Preparation of Alkylboranes

In a nitrogen-filled glovebox, a dram vial was charged with a stir bar, 9-BBN dimer (0.75 mmol, 1.0 equiv, calculated as 1.5 mmol 9-BBN monomer) and the corresponding solvent (CyH for linear conditions, or $PhCF_3$ for branched conditions, 1.0 M). Alkene (1.8 mmol, 1.2 equiv) was then added carefully. The reaction mixture was stirring at 60 °C for at least 2 hours then used in the coupling reactions without purification or removal of solvent.

3.4.3.2 General Procedure B: Linear Conditions

In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(OAc)_2$ (5.5 mg, 0.025 mmol, 0.05 equiv), **L4** (14.0 mg, 0.038 mmol, 0.075 equiv), $KHCO_3$ (75.0 mg, 0.75 mmol, 1.5 equiv) and a stir bar. To the vial was added CyH (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was cooled down to room temperature followed by the addition of terminal alkyne (0.50 mmol, 1.0 equiv), allylic carbonate (0.75 mmol, 1.5 equiv) and 1.0 M organoborane solution in CyH (1.0 mL, 1.0 mmol, 2.0 equiv) prepared according to general procedure A. The reaction mixture was vigorously stirred at 60 °C for 16 h.

The vial was removed from the glovebox and allowed to cool to room temperature. Acetic acid (285 µL) was then added, and the mixture was allowed to stir at room temperature for 25 min. The reaction mixture was then neutralized by the addition of saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with ethyl acetate (20 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was further purified by silica gel column chromatography, eluted with an ethyl acetate/hexanes or diethyl ether/hexanes mixture.

3.4.3.3 General Procedure C: Branched Conditions

In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L9** (31.9 mg, 0.038 mmol, 0.075 equiv) and a stir bar. To the vial was added $PhCF_3$ (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added allylic carbonate (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne (0.50 mmol, 1.0 equiv), and 1.0 M organoborane solution in $PhCF_3$ (1.0 mL, 1.0 mmol, 2.0 equiv) prepared according to general procedure A. The reaction mixture was vigorously stirred at 25 °C for 40 h.

The vial was removed from the glovebox. Acetic acid (285 µL) was then added, and the mixture was allowed to stir at room temperature for 25 min. The reaction mixture was then neutralized by the addition of saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with ethyl acetate (20 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography, eluted with an ethyl acetate/hexanes or diethyl ether/hexanes mixture.

3.4.3.4 General Procedure D: Determination of Enantiomeric Ratio of Product

The enantiomeric ratio of the majority of our substrates was determined by the HPLC analysis of the corresponding alcohol after hydroboration-oxidation of the product.

For small scale reactions, the reaction mixture after the addition of acetic acid was concentrated *in vacuo*, and the residue was purified by prep-TLC (2% diethyl ether in hexanes) to afford the pure alkene **3.5**.

In a nitrogen-filled glovebox, a 4 mL dram vial was charged with the alkene (0.02 mmol, 1.0 equiv), 9-BBN dimer (0.012 mmol, 1.2 equiv) and a stir bar. The mixture was diluted with THF (400 µL, 0.05 M) and stirred at room temperature for 2 h. The vial was removed from the glovebox, and $NaBO_3 \cdot 4H_2O$ (15.4 mg, 0.10 mmol, 5 equiv) was added. The resulting mixture was further diluted with H_2O (400 µL) and allowed to be stirred at room temperature for 16 h before quenched by the addition of saturated $NaHCO_3$ solution. The reaction mixture was extracted by ethyl acetate (2 mL), and the extract was concentrated *in vacuo.* The residue was purified by prep-TLC (typically 20% ethyl acetate in hexanes) and the pure alcohol was analyzed by HPLC. Racemic samples were prepared according to General Procedure C using (±)-**L9**.

3.4.3.5 General Procedure E: Synthesis of Allylic Carbonate Starting Materials

n-Butyllithium solution (1.1 equiv) was slowly added to a solution of allylic alcohol (5 mmol, 1.0 equiv) in THF (0.5 M) at 0 °C under N_2 atmosphere, and the resulting solution was stirred at 0 °C for 1 h. Boc_2O (1.0 equiv) was then slowly added, and the reaction mixture was stirred at room temperature for 16 h. The reaction was quenched by slow addition of saturated NH_4Cl solution (10

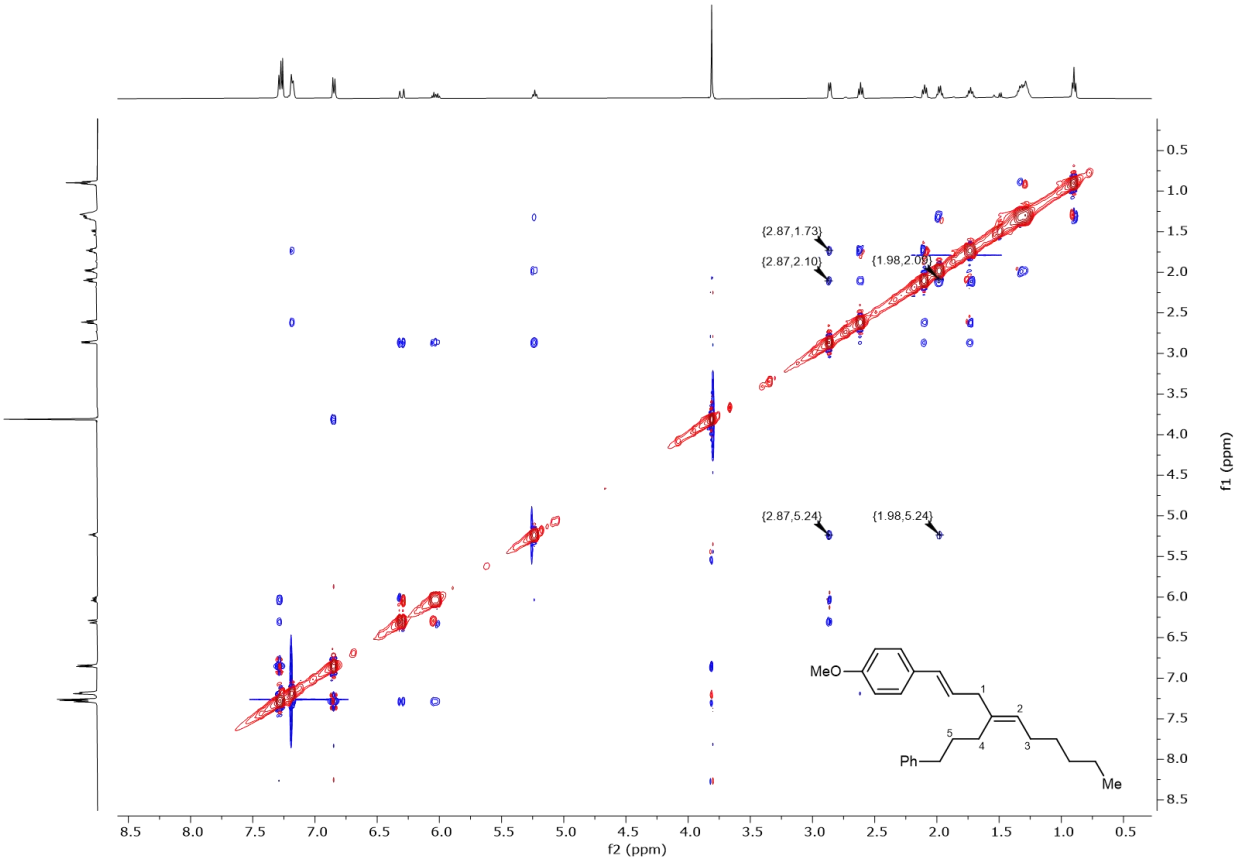
mL) and extracted by ethyl acetate (20 mL). The organic layer was washed by 1 M HCl solution (10 mL) and then brine (10 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (typically eluted with diethyl ether in hexanes) to afford allylic carbonate starting materials.

3.4.4 Determination of Product Stereochemistry

3.4.4.1 NOESY Analysis of Trisubstituted Alkene 3.8

The stereochemistry of **3.8** was determined by NOESY analysis and the configurations of trisubstituted carbon-carbon double bonds in the remaining linear trisubstituted alkenes and tetrasubstituted alkenyl borinic ester **3.42** were assigned by an analogy.

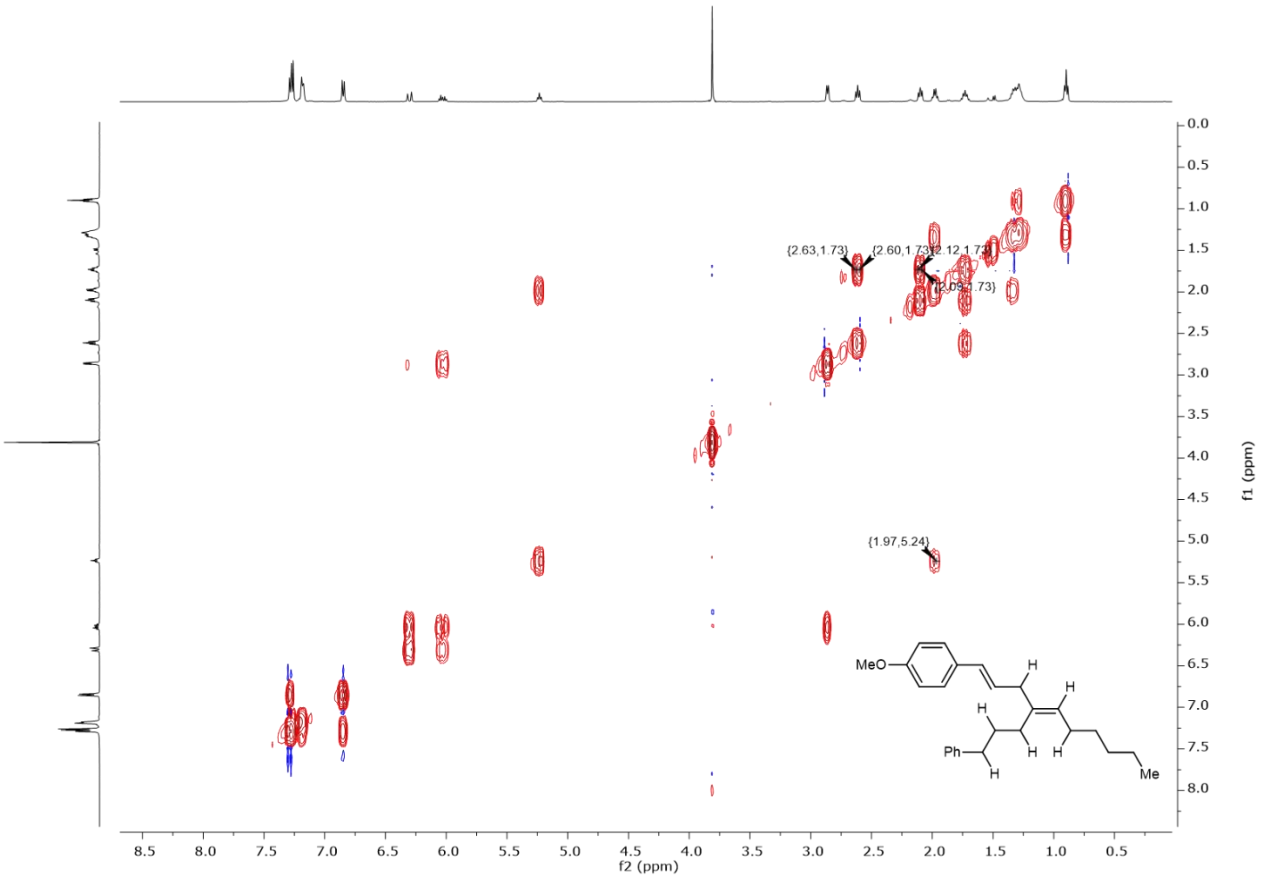
Figure 3.1 NOESY Analysis of 3.8



In the NMR spectrum shown above, the NOE between **H1-H2**, **H1-H4**, **H2-H3**, **H3-H4** were clearly observed. Meanwhile, no NOE between **H1-H3**, **H2-H4** or **H2-H5** were observed. These results indicate that (*E*)- **3.8** was obtained from our methodology.

3.4.4.2 COSY Spectrum of Trisubstituted Alkene 3.8

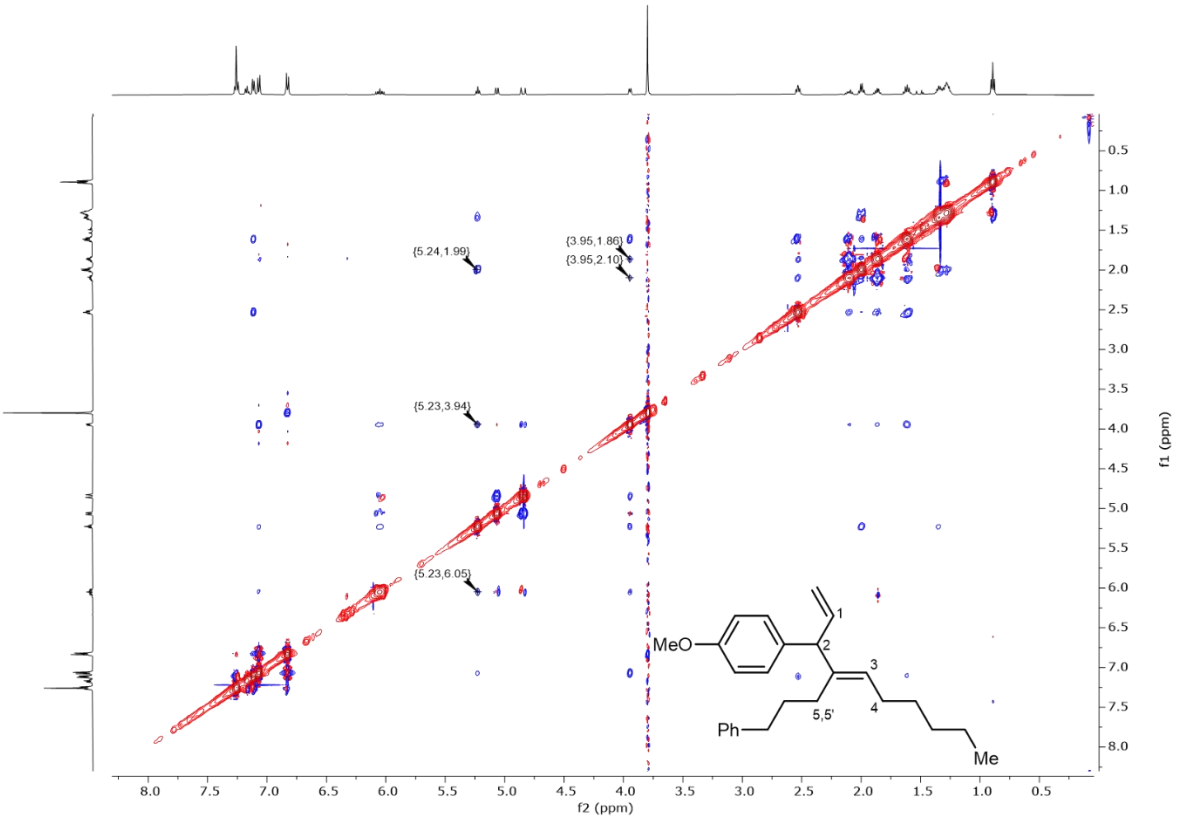
Figure 3.2 COSY Spectrum of 3.8



3.4.4.3 NOESY Analysis of Trisubstituted Alkene 3.15

The stereochemistry of **3.15** was determined by NOESY analysis and the configurations of trisubstituted carbon-carbon double bonds in the remaining branched trisubstituted alkenes and tetrasubstituted alkenyl borinic ester **3.46** were assigned by an analogy.

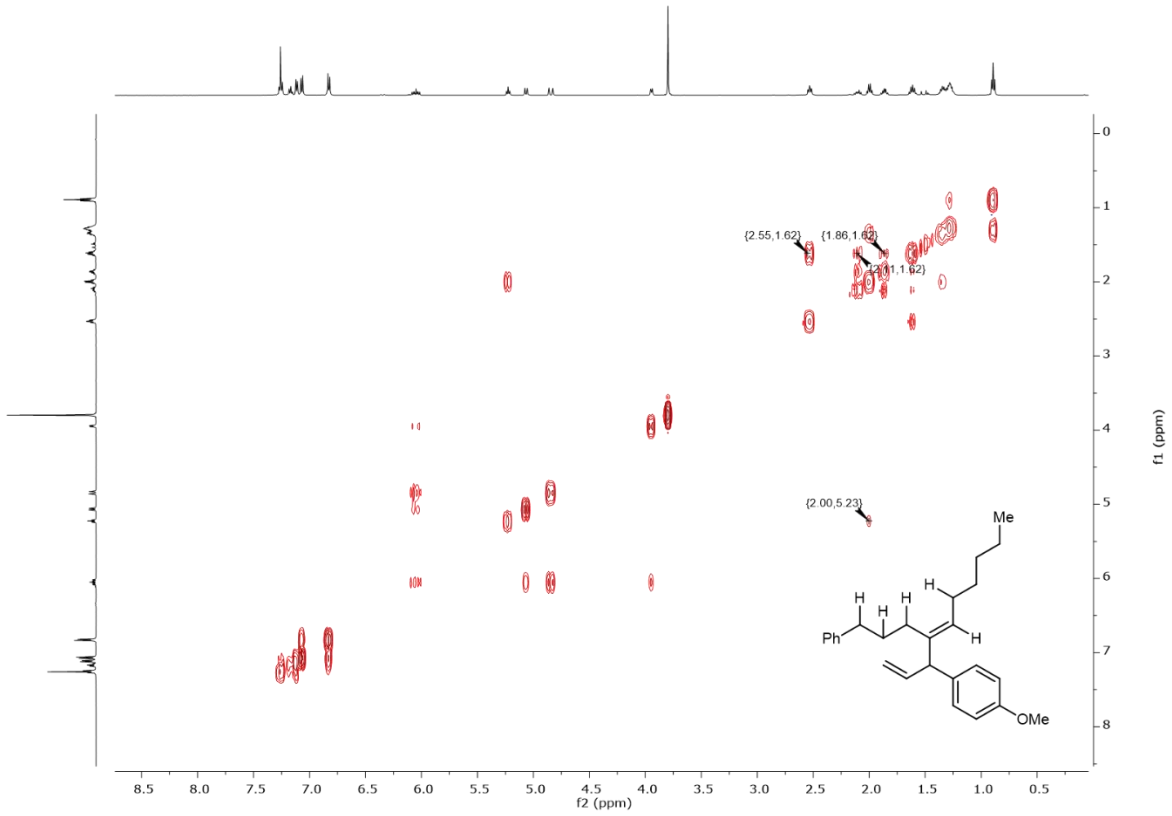
Figure 3.3 NOESY Analysis of 3.15



In the NMR spectrum shown above, the NOE between **H1-H3**, **H2-H3**, **H2-H5**, **H3-H4** was clearly observed. Meanwhile, no NOE between either **H2-H4** or **H3-H5** was observed. These results indicate that (*E*)-**3.15** was obtained from our methodology.

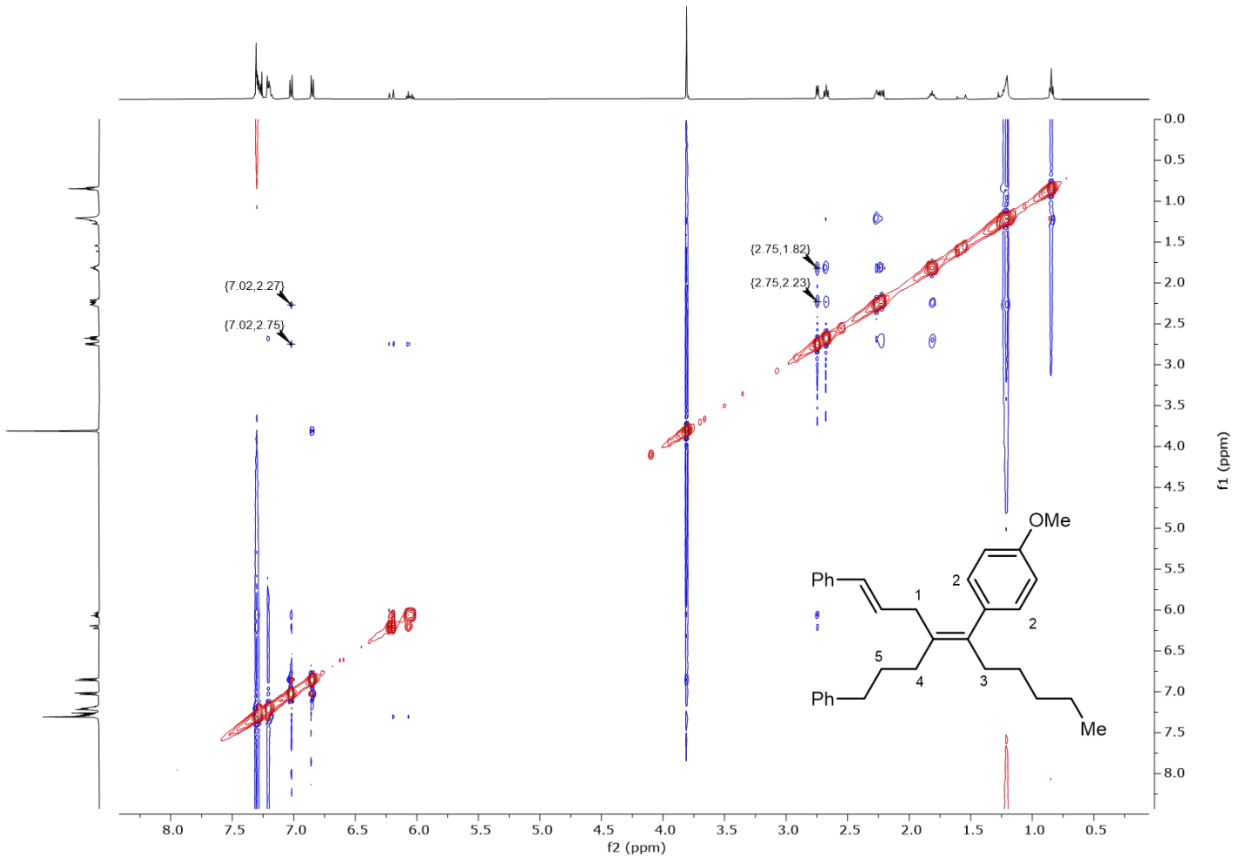
3.4.4.4 COSY Spectrum of Trisubstituted Alkene 3.15

Figure 3.4 COSY Analysis of 3.15



3.4.4.5 NOESY Analysis of Tetrasubstituted Alkene 3.40

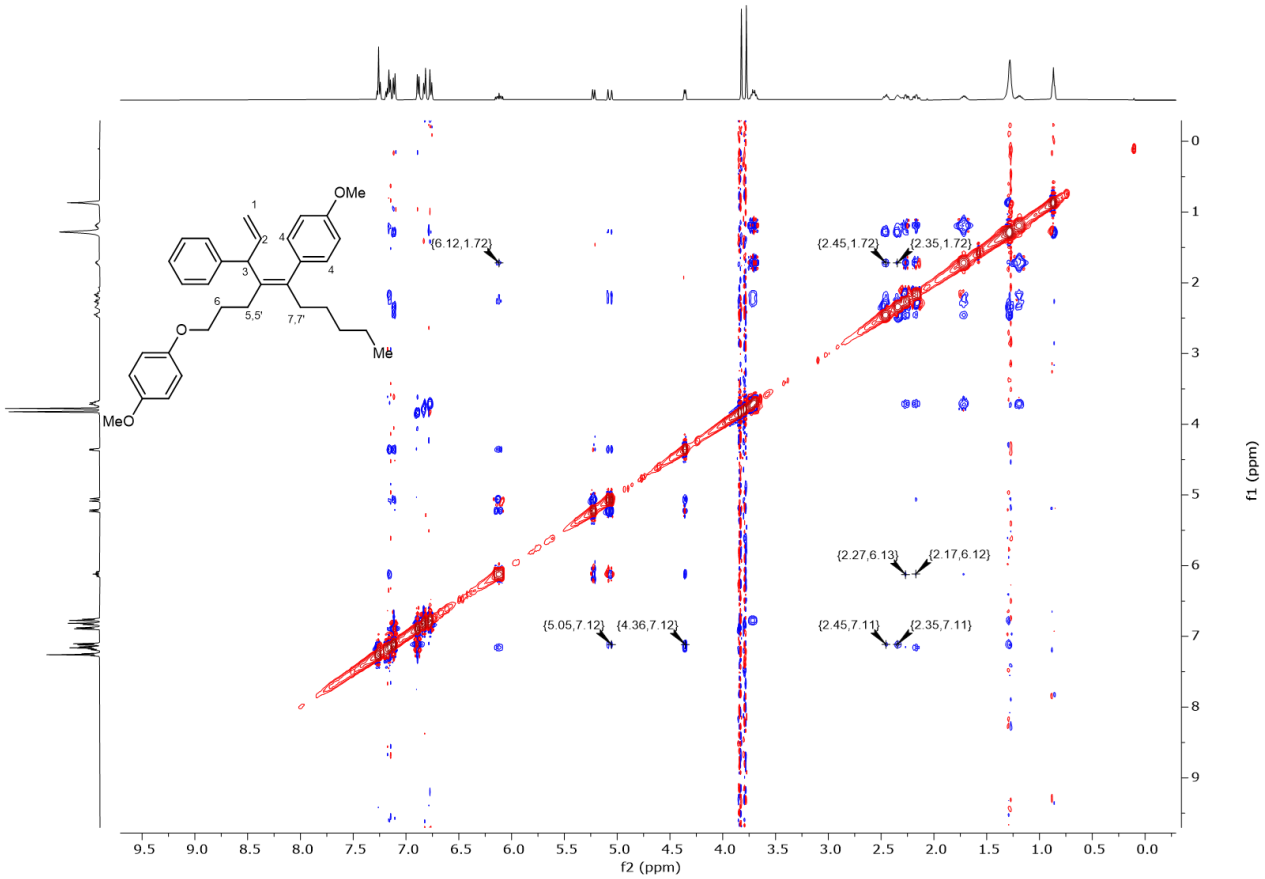
Figure 3.5 NOESY Analysis of 3.40



In the NMR spectrum shown above, the NOE between **H1-H2**, **H2-H3**, **H1-H4**, **H1-H5** was clearly observed. Meanwhile, no NOE between either **H2-H4** or **H2-H5** was observed. These results indicate that (*Z*)-**3.40** was obtained from our methodology.

3.4.4.6 NOESY Analysis of Tetrasubstituted Alkene 3.44

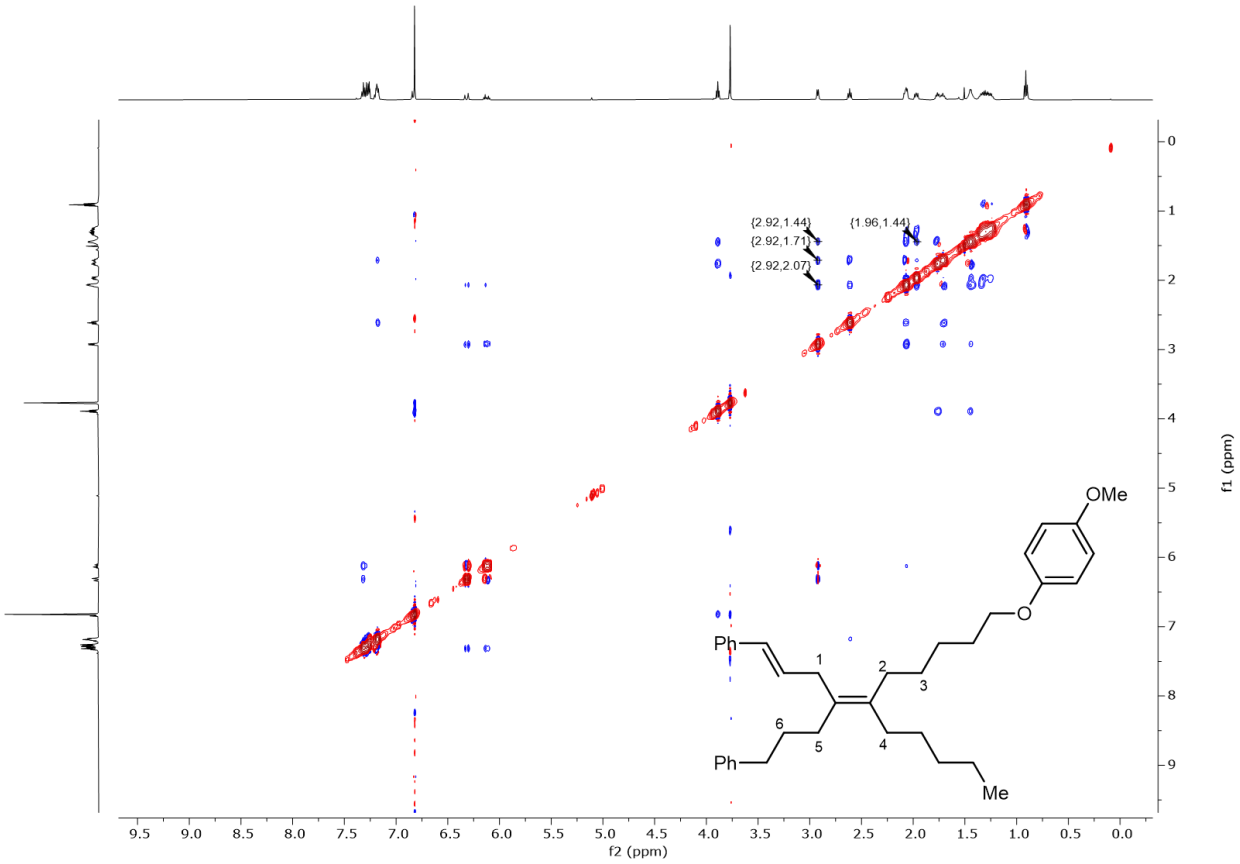
Figure 3.6 NOESY Analysis of 3.44



In the NMR spectrum shown above, the NOE between **H1-H4**, **H3-H4**, **H2-H5, H2-H5'**, **H2-H6**, **H4-H7**, **H4-H7'**, **H6-H7** and **H6-H7'** were clearly observed. Meanwhile, no NOE between **H1-H7**, **H2-H7**, **H3-H7**, **H4-H5** or **H4-H6** were observed. These results indicate that (*Z*)-**3.44** was obtained from our methodology.

3.4.4.7 NOESY Analysis of Tetrasubstituted Alkene 3.41

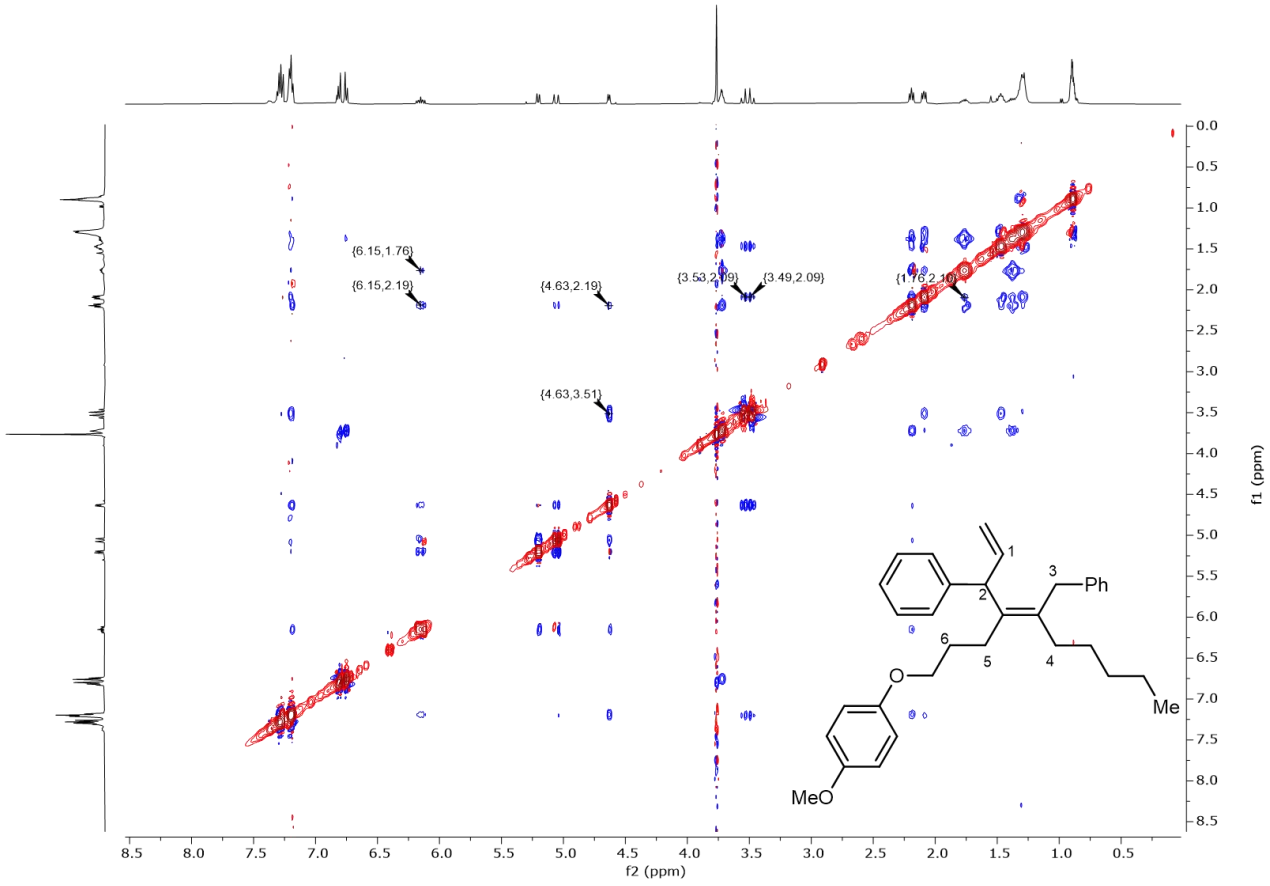
Figure 3.7 NOESY Analysis of 3.41



In the NMR spectrum shown above, the NOE between **H1-H3**, **H1-H6** and **H3-H4** were clearly observed. Meanwhile, no NOE between either **H1-H6** or **H3-H6** was observed. **H2** and **H5** can't be distinguished by ^{1}H NMR. These results indicate that (*Z*)-**3.41** was obtained from our methodology.

3.4.4.8 NOESY Analysis of Tetrasubstituted Alkene 3.45

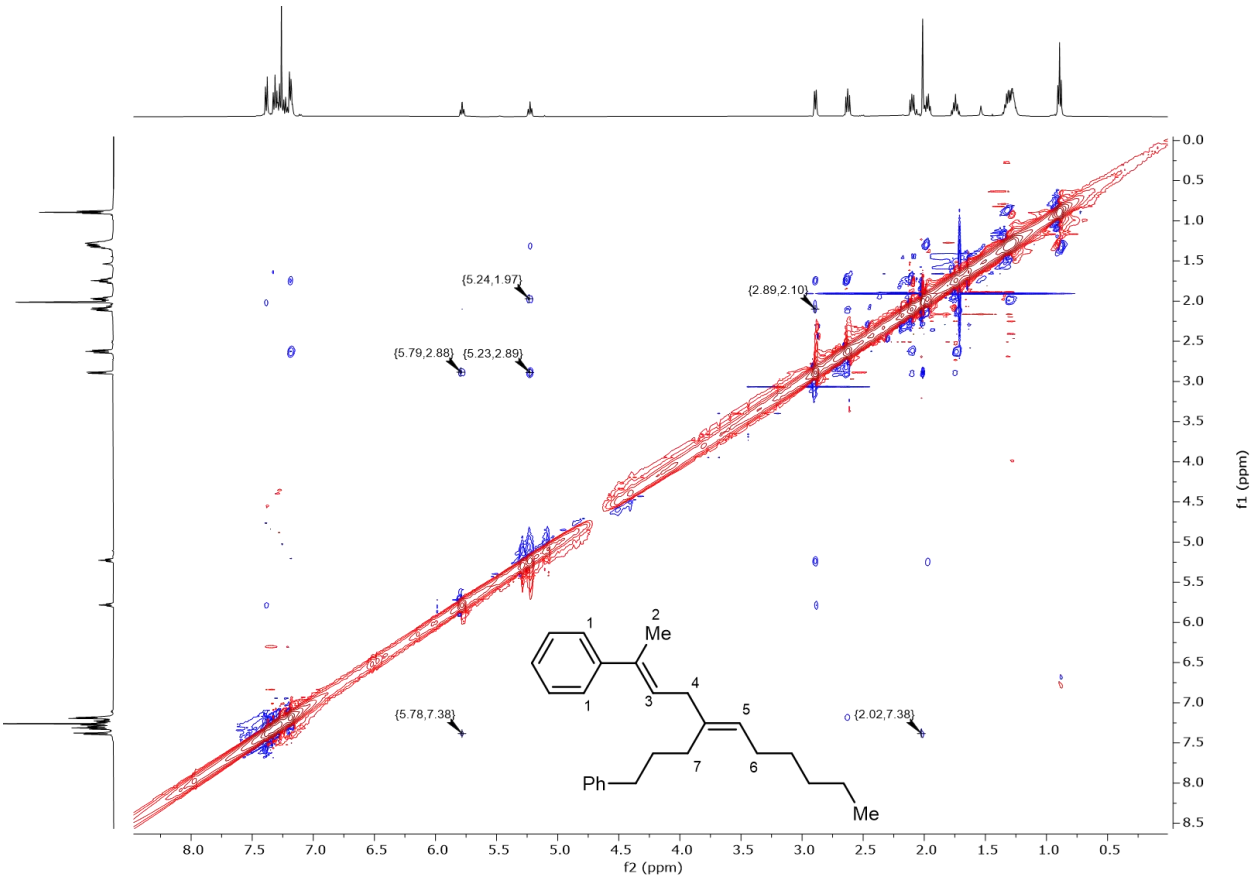
Figure 3.8 NOESY Analysis of 3.45



In the NMR spectrum shown above, the NOE between **H1-H5**, **H1-H6**, **H2-H3**, **H3-H4** and **H4-H6** were clearly observed. Meanwhile, no NOE between **H1-H4**, **H2-H4**, **H3-H5** or **H3-H6** were observed. These results indicate that (*Z*)-**3.45** was obtained from our methodology.

3.4.4.9 NOESY Analysis of Bis-trisubstituted Alkene 3.11

Figure 3.9 NOESY Analysis of 3.11



In the NMR spectrum shown above, the NOE between **H1-H2**, **H1-H3**, **H4-H5**, **H4-H7** and **H5-H6** were clearly observed. Meanwhile, no NOE between **H2-H3**, **H4-H6** or **H5-H7** were observed. These results indicate that (*E,E*)-**3.11** was obtained from our methodology.

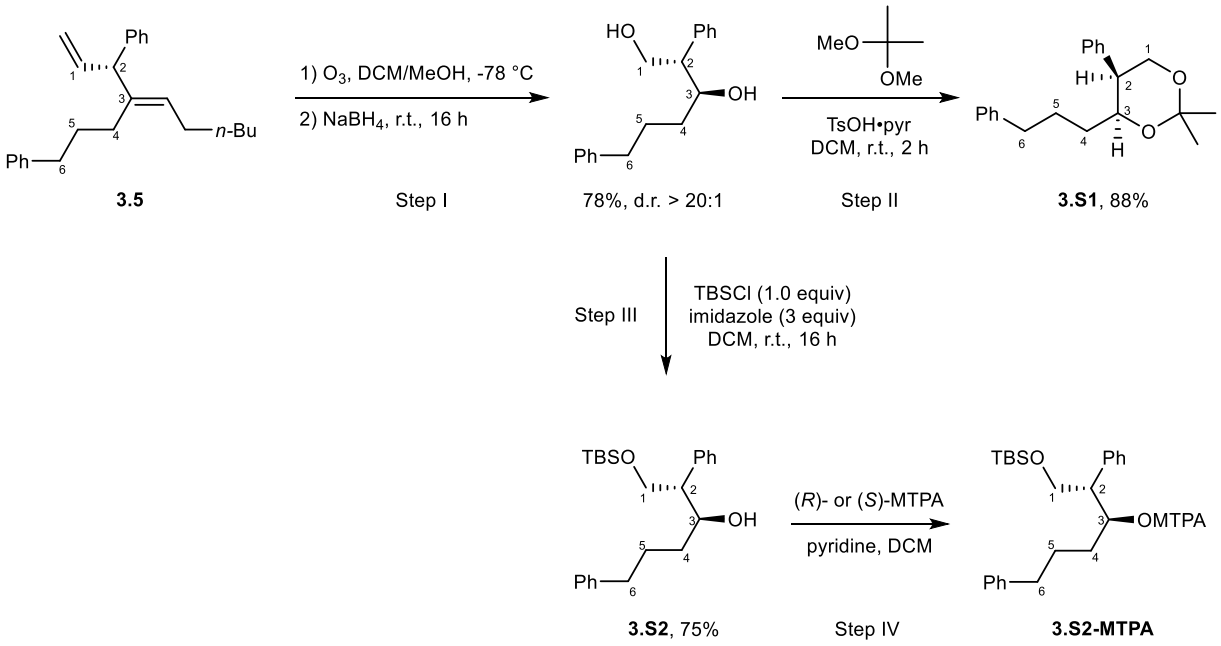
3.4.4.10 Determination of Absolute Configuration of Branched Products

The absolute configuration of branched products was determined using Mosher ester analysis and comparison with known compounds.

3.4.4.10.1 Determination of Absolute Configuration using Mosher Ester Analysis

The absolute configuration of C_2 in trisubstituted alkene **3.5** was determined according to literature.[26, 30] The absolute configurations of other trisubstituted alkenes and tetrasubstituted alkenes afforded under branched-selective conditions were assigned by analogy.

Scheme 3.6 Determination of the Absolute Configuration of C_2



Step I. Ozonolysis and Reduction of 3.5

A Dreschel bottle was charged with **3.5** (150 mg, 0.40 mmol), 20 mL DCM, 4 mL MeOH and a stir bar. The resulting solution was cooled down to -78 °C and ozone was bubbled through at -78 °C until the solution turns blue (~30 minutes). Then air was bubbled to get rid of excess ozone, and $NaBH_4$ (76 mg, 2.0 mmol, 5.0 equiv) was added to the solution in portions. The resulting mixture was allowed to be warmed up slowly to room temperature and stirred overnight. The reaction mixture was quenched by addition of saturated NH_4Cl solution (20 mL) and extracted by ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4 and

concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluted with 0-30% ethyl acetate/hexanes) to afford (2S,3S)-2,6-diphenylhexane-1,3-diol as a yellow gel (84.4 mg, 0.31 mmol, 78% yield).

(2*S*,3*S*)-2,6-diphenylhexane-1,3-diol

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.31 – 7.25 (m, 5H), 7.21 – 7.14 (m, 3H), 4.03 (td, *J* = 6.9, 2.5 Hz, 2H), 3.94 (dd, *J* = 10.8, 6.6 Hz, 1H), 2.89 (td, *J* = 6.9, 4.3 Hz, 1H), 2.60 (t, *J* = 7.3 Hz, 2H), 1.95 – 1.77 (m, 3H), 1.75 – 1.63 (m, 1H), 1.56 – 1.44 (m, 1H), 1.44 – 1.32 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 138.7, 129.5, 128.9, 128.6, 128.5, 127.4, 126.0, 72.6, 64.7, 53.3, 35.9, 34.7, 27.9.

MS (ESI) calculated for $[M+Na]^+$ 293.2, found 293.1.

FTIR (neat, cm^{-1}): 3298, 3023, 2935, 2845, 1496, 1452, 1105, 1040, 698.

$\boldsymbol{\alpha_D^{25}}$ = +17.6 ° (c 0.80, $CHCl_3$).

Step II. Determination of Relative Configuration of C_2 and C_3

A flame-dried 25 mL round-bottom flask was charged with a stir bar and pyridinium *p*-toluene sulfonate (7.6 mg, 0.03 mmol, 0.20 equiv). To this flask was added a solution of (2*S*,3*S*)-2,6-diphenylhexane-1,3-diol (40.6 mg, 0.15 mmol, 1.0 equiv) in DCM (4 mL), and then 2,2-dimethoxypropane (47.0 mg, 0.45 mmol, 3.0 equiv) was added dropwise to the mixture. The reaction mixture was allowed to stir at room temperature for 2 hours, and quenched with saturated $NaHCO_3$ solution (10 mL). The resulting mixture was extracted by DCM (20 mL) and the organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluted with 0-5% ethyl acetate in hexanes) to afford **3.S1** as a colorless liquid (41.0 mg, 0.13 mmol, 88% yield). The relative configuration of C_2 and C_3 was determined by careful NMR coupling constant analysis and NOESY analysis.

(4*S*,5*S*)-2,2-dimethyl-5-phenyl-4-(3-phenylpropyl)-1,3-dioxane (3.S1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 6.9 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.25 (t, *J* = 7.5 Hz, 3H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.13 – 7.08 (m, 2H), 4.35 (dd, *J* = 11.7, 4.0 Hz, 1H), 4.20 (ddd, *J* = 7.2, 6.6, 3.4 Hz, 1H), 3.89 (dd, *J* = 11.7, 2.0 Hz, 1H), 2.56 – 2.45 (m, 3H), 1.74 – 1.67 (m, 1H), 1.59 – 1.52 (m, 7H), 1.28 – 1.23 (m, 2H).

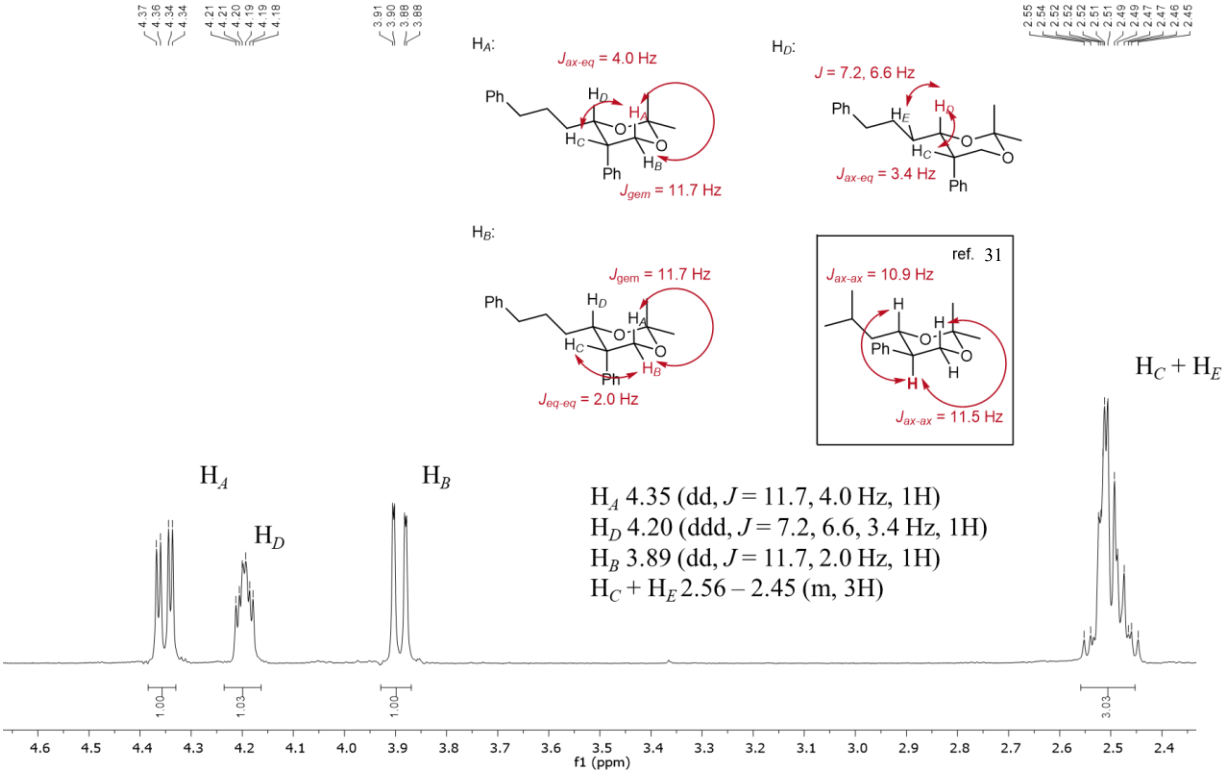
^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 140.8, 129.8, 128.4, 128.4, 128.2, 126.7, 125.8, 99.0, 71.2, 65.6, 43.9, 35.9, 33.4, 29.5, 27.5, 19.2.

GCMS (EI) calculated for $[M-CH_3]^+$ 305.2, found 305.3.

FTIR (neat, cm^{-1}): 3470, 3026, 2928, 2863, 1495, 1453, 1253, 1084, 834, 746, 699.

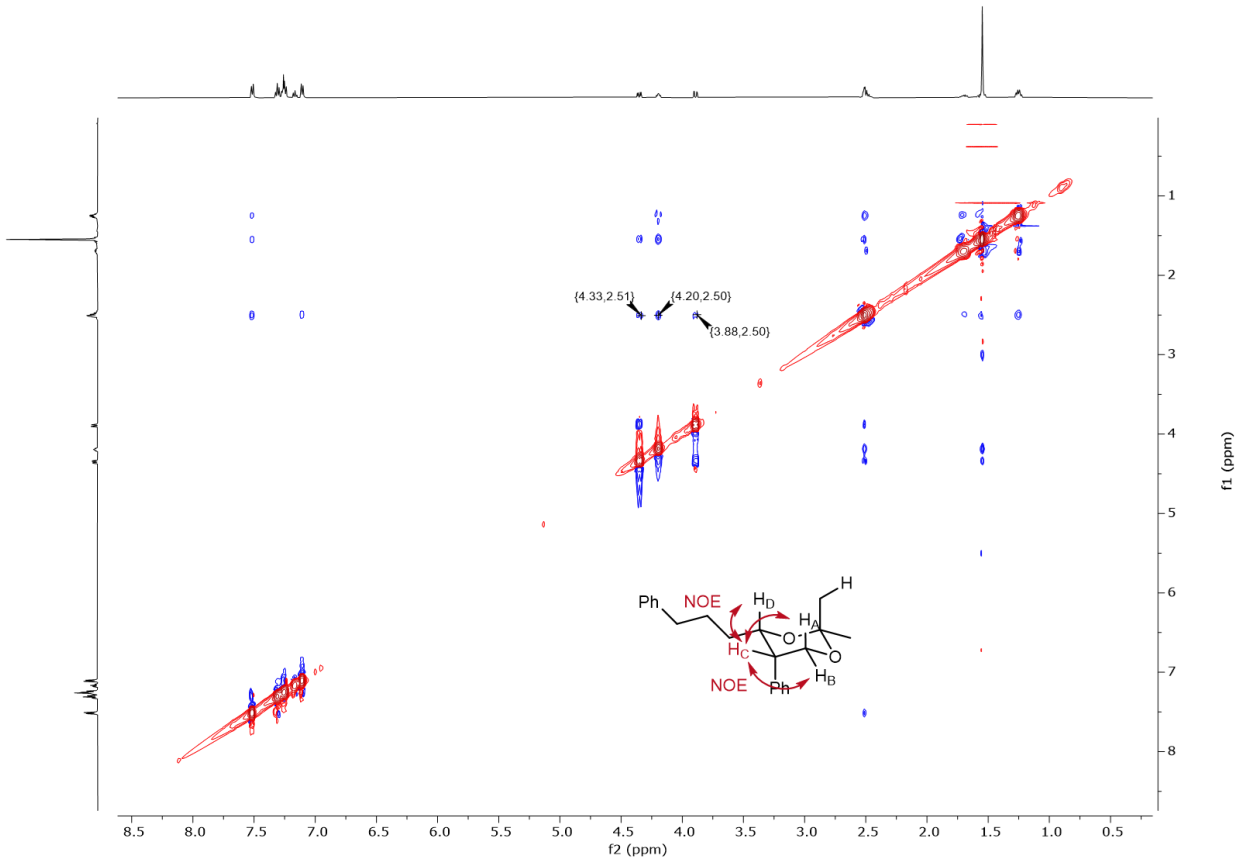
$\boldsymbol{\alpha_D^{25}}$ = +24.4 ° (c 1.11, $CHCl_3$).

Figure 3.10 Coupling Constant Analysis of 3.S1



According to the ^{1}H NMR spectrum of **3.S1** above, the coupling constants between the benzylic proton $\mathbf{H_C}$ and its adjacent protons are relatively small ($\mathbf{H_A}$-$\mathbf{H_C}$ is 4.0 Hz, $\mathbf{H_B}$-$\mathbf{H_C}$ is 2.0 Hz, and $\mathbf{H_D}$-$\mathbf{H_C}$ is 3.4 Hz), consistent with an equatorial orientation of $\mathbf{H_C}$ in the preferred chair conformation. In contrast, in a literature reported structural similar compound but with *trans*- relative configuration, the axial benzylic proton has two significant larger coupling constants (J ~ 11 Hz) with its adjacent axial protons. These data confirm that the alkyl group and phenyl group are *cis*- in **3.S1**.

Figure 3.11 NOESY Analysis of 3.S1



In the NMR spectrum shown above, the NOE between **H_C-H_A**, **H_C-H_B**, and **H_C-H_D** were clearly observed. These results indicate that **H_C** and **H_D** are *cis*-, which is consistent with the coupling constant analysis results.

According to the analysis above, the relative configuration of C_2 and C_3 was assigned as (*S*,*S*) or (*R*,*R*).

Step III. Protection of Primary Alcohol.

To a flame dried 25 mL round bottom flask was added TBSCl (22.6 mg, 0.15 mmol, 1.0 equiv), (2*S*,3*S*)-2,6-diphenylhexane-1,3-diol (40.6 mg, 0.15 mmol) prepared above, imidazole (30.6 mg, 0.45 mmol, 3.0 equiv), and a stir bar. To the mixture was added 10 mL DCM and the resulting solution was stirred at room temperature overnight. To the reaction mixture was added 1M aqueous HCl solution (10 mL) and the organic layer was separated. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (eluted with 0-15% ethyl acetate in hexanes) to afford **3.S2** as light-yellow oil (43.3 mg, 0.11 mol, 75% yield, 95:5 e.r.).

(2*S*,3*S*)-1-((*tert*-butyldimethylsilyl)oxy)-2,6-diphenylhexan-3-ol (**3.S2**)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, 7H), 7.20 – 7.14 (m, 3H), 4.11 (dt, *J* = 8.5, 4.2 Hz, 1H), 4.05 (dd, *J* = 10.0, 7.2 Hz, 1H), 3.92 (dd, *J* = 9.9, 4.9 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.34 (s, 1H), 1.95 – 1.77 (m, 1H), 1.75 – 1.64 (m, 1H), 1.55 – 1.35 (m, 2H), 0.90 (s, 9H), 0.02 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 139.6, 129.5, 128.5, 128.4, 126.9, 125.8, 72.8, 65.6, 52.5, 35.9, 34.4, 28.0, 26.0, 18.3, -5.4, -5.5.

GCMS (EI) calculated for $[M\text{-}CH_3]^+$ 369.2, found 369.3.

FTIR (neat, cm^{-1}): 3070, 2993, 2938, 2864, 1496, 1380, 1198, 751, 699.

$\boldsymbol{\alpha_D^{25}}$ = +25.8 ° (c 0.80, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC. CHIRALPAK AD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 7.6 min (minor), 8.3 min (major).

Step IV. Determine the absolute configuration of *C*$_3$ by Mosher ester analysis.

The Mosher ester analysis was carried out according to a modified literature procedure.[32] In a nitrogen-filled glove box, a 4 mL dram vial was charged with **3.S2** (7.7 mg, 0.02 mmol), *R*-(−)-MTPA-Cl (15.2 mg, 0.06 mmol, 3.0 equiv) and a stir bar. The mixture was diluted with anhydrous DCM (500 µL, 0.04 M) and then pyridine (7.9 mg. 0.10 mmol, 5.0 equiv) was added. The same procedure was repeated but using *S*-(+)-MTPA-Cl. These vials were removed from the glovebox, and diluted with 1 M HCl (1 mL). The organic phase was dried over anhydrous Na_2SO_4, and then concentrated *in vacuo*. The crude was purified by silica gel column chromatography (eluted with 0-10% ethyl acetate in hexanes) to afford desired Mosher ester as a colorless liquid (quant. yield).

NOTE: *R*-(−)-MTPA-Cl will afford (*S*)-Mosher ester **3.S2**-(*S*)-**MTPA**. *S*-(+)-MTPA-Cl will afford (*R*)-Mosher ester **3.S2**-(*R*)-**MTPA**.

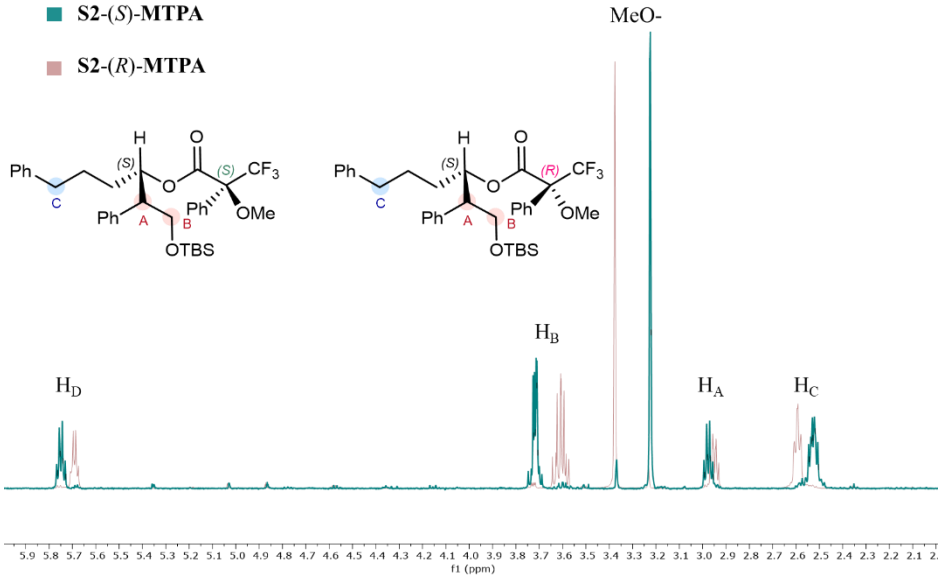
3.S2-(*S*)-MTPA

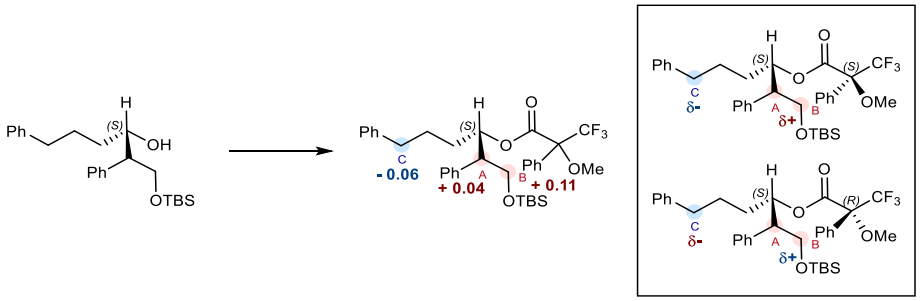
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 5H), 7.26 – 7.22 (m, 5H), 7.21 – 7.15 (m, 3H), 7.10 – 7.06 (m, 2H), 5.75 (q, *J* = 6.0 Hz, 1H), 3.72 (dd, *J* = 6.0, 2.7 Hz, 2H), 3.23 (s, 3H), 2.98 (q, *J* = 6.3 Hz, 1H), 2.57 – 2.47 (m, 2H), 1.68 – 1.58 (m, 4H), 0.85 (s, 9H), -0.07 (d, *J* = 8.4 Hz, 6H).

3.S2-(*R*)-MTPA

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.39 – 7.30 (m, 3H), 7.29 – 7.24 (m, 2H), 7.22 – 7.16 (m, 4H), 7.14 – 7.08 (m, 4H), 5.69 (q, *J* = 5.8 Hz, 1H), 3.66 – 3.56 (m, 2H), 3.38 (s, 3H), 2.95 (dt, *J* = 7.4, 5.5 Hz, 1H), 2.59 (td, *J* = 7.1, 1.5 Hz, 2H), 1.69 – 1.59 (m, 4H), 0.85 (s, 9H), -0.08 (d, *J* = 14.1 Hz, 6H).

Figure 3.12 Mosher Ester Analysis





	δ *R*-ester	δ *S*-ester	Δδ*SR* = (δ*S* - δ*R*)	
	S2-(*R*)-**MTPA** (ppm)	**S2**-(*S*)-**MTPA** (ppm)	ppm	Hz (500 MHz)
CH-(A)	2.95	2.98	+0.03	+15
CH_2-(B)	3.61	3.72	+0.11	+55
CH_2-(C)	2.59	2.53	-0.06	-30

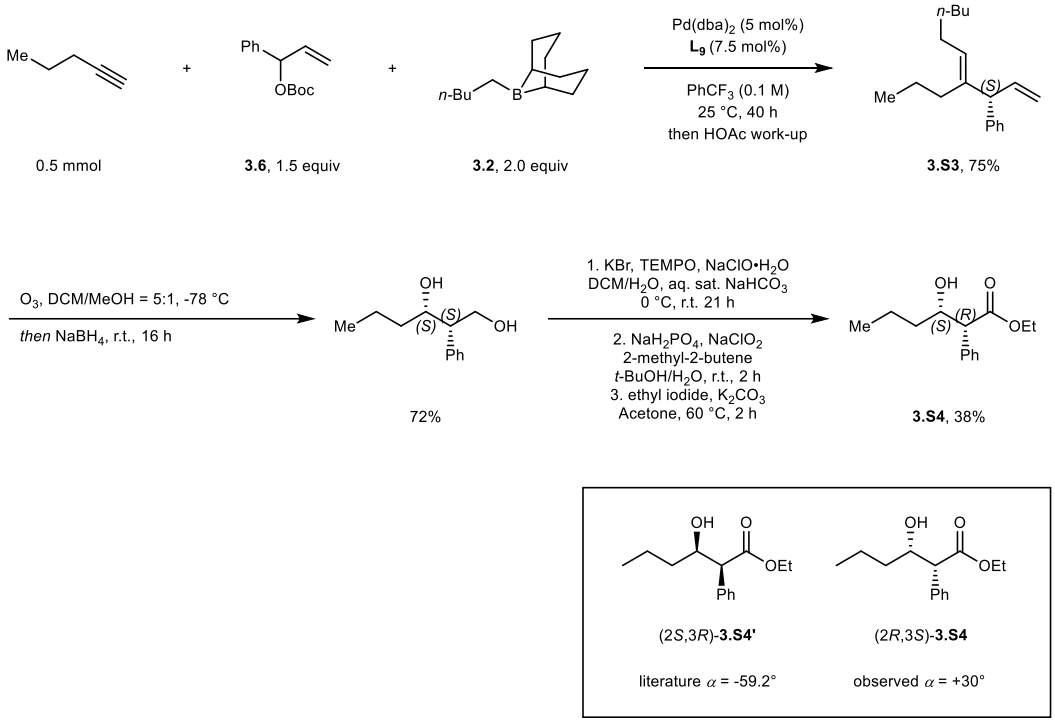
Comparison of relative chemical shifts of protons A, B, and C in the ^{1}H NMR spectra of the two Mosher esters **3.S2**, allowed us to assign the absolute configuration of C_3 as (*S*) according to the reported procedure.32 Given the relative configuration of C_2 and C_3 determined in Step II, the configuration at C_2 was assigned as (*S*). Accordingly, the absolute configuration of the branched product **3.5** was determined to be (*S*).

3.4.4.10.2 Determination of Absolute Configuration Using Comparison with Known Compounds

The absolute configuration of C_2 in branched products can also be determined by comparing the optical rotation of the *β*-hydroxy ester **3.S4** derived from alkenes with that reported in literature.[33]

(2*S*,3*S*)-2-phenylhexane-1,3-diol was prepared from branched product **3.S3** according to the ozonolysis-reduction procedure described above.

Scheme 3.7 Derivation of Branched Products and Comparing Optical Rotation



β-hydroxy ester **S4** was synthesized according to a modified literature procedure.[34]

In a 50 mL round bottom flask, (2*S*,3*S*)-2-phenylhexane-1,3-diol (35.0 mg, 0.18 mmol, 1.0 equiv) was dissolved in DCM (12 mL). To the pale-yellow solution KBr (6.4 mg, 0.054 mmol, 30 mol%) and saturated $NaHCO_3$ solution (6.0 mL) were added. The reaction mixture was cooled to 0 °C. TEMPO (8.4 mg, 0.054 mmol, 30 mol%) and $NaOCl{\cdot}5H_2O$ (32.6 mg, 0.20 mmol, 1.1 equiv) dissolved in water (18 mL) were added. The resulting emulsion was stirred vigorously at room temperature for 16 h, and then additional KBr (6.4 mg, 0.054 mmol, 30 mol%) and TEMPO (8.4 mg, 0.054 mmol, 30 mol%), followed by $NaOCl{\cdot}5H_2O$ (14.8 mg, 0.09 mmol, 0.5 equiv) dissolved in water (3 mL) were added to the mixture. The reaction mixture was allowed to stir at room temperature for an additional 2 h, and then quenched by the addition of saturated $Na_2S_2O_3$ solution (20 mL) and saturated $NaHCO_3$ solution (30 mL). Additional DCM (40 mL) was added, and the organic layer was separated and washed with brine (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude *β*-hydroxy aldehyde as an orange oil. The crude mixture was used directly in the next step.

In a 25 mL round bottom flask, NaH_2PO_4 (75.5 mg, 0.63 mmol, 3.5 equiv) and $NaClO_2$ (97.7 mg, 1.08 mmol, 6.0 equiv) were suspended in *t*-BuOH (6.0 mL). 2-Methyl-2-butene (2.2 mL, 20.7 mmol, 115 equiv), followed by water (2 mL) was added and the resulting solution was stirred at room temperature for 10 min. The solution was then transferred to another 25 mL flask containing crude *β*-hydroxy aldehyde. The resulting yellow solution was stirred at room temperature for 2 h, before ethyl acetate (40 mL) and water (40 mL) were added. The organic layer was separated,

washed with brine (20 mL), dried over Na_2SO_4 and concentrated *in vacuo* to obtain the crude *β*-hydroxy carboxylic acid as an orange oil. The crude mixture was used directly in the next step.

A flame-dried 25 mL round-bottom flask was charged with a stir bar and anhydrous K_2CO_3 (50.0 mg, 0.36 mmol, 2.0 equiv). To this flask was added a solution of crude *β*-hydroxy carboxylic acid in anhydrous acetone (10 mL), and then ethyl iodide (59 μL, 0.72 mmol, 4.0 equiv) was added in one portion to the mixture. The reaction mixture was stirred at 60 °C for 3 hours, and then cooled down to room temperature. The resulting mixture was diluted with ethyl acetate (30 mL) and saturated NH_4Cl solution (20 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluted with 0-20% ethyl acetate in hexanes) to afford **3.S4** as a yellow liquid (16.0 mg, 0.068 mmol, 38% yield). The ^1H and ^{13}C NMR data matched the literature values of its enantiomer.[33]

ethyl (2*R*,3*S*)-3-hydroxy-2-phenylhexanoate (3.S4)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 4.28 – 4.04 (m, 3H), 3.56 (d, *J* = 6.3 Hz, 1H), 2.37 (s, 1H), 1.56 – 1.38 (m, 4H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 135.3, 129.4, 128.8, 127.9, 72.1, 61.1, 57.5, 36.7, 19.1, 14.2, 14.1.

$\boldsymbol{\alpha_D^{20}}$ = +32 ° (c 1.6, $CHCl_3$).

Reported optical rotation of ethyl (2*S*,3*R*)-3-hydroxy-2-phenylhexanoate is of the opposite sign from what we obtained for compound **3.S4** ($\boldsymbol{\alpha_D^{25}}$ = -59 ° (c 1.9, $CHCl_3$))[33] and we assigned the absolute configuration of **3.S4** as (2*R*, 3*S*). Consequently, the absolute configuration of C_2 in branched product **3.S3** was assigned to be (*S)*, consistent with the results obtained from Mosher ester analysis.

Overall, Mosher ester analysis and correlation with a compound of known absolute stereochemistry allowed us to assign the absolute configuration of chiral products shown in Table 3.1.

3.4.5 Determination of Regioselectivity and Diastereoselectivity

3.4.5.1 General Information for Determining Regioselectivity and Diastereoselectivity

The regioselectivity and diastereoselectivity of following reactions were determined by GC and GC-MS analysis of reaction crudes.

For linear-selective reaction. In a nitrogen-filled glovebox, a 4 mL dram vial was charged with $Pd(OAc)_2$ (0.6 mg, 0.0025 mmol, 0.05 equiv), **L4** (1.4 mg, 0.0038 mmol, 0.075 equiv), $KHCO_3$ (7.5 mg, 0.075 mmol, 1.5 equiv) and a stir bar. To the vial was added CyH (400 μL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was cooled down to room temperature followed by the addition of terminal alkyne **3.1** (7.2 mg, 0.050 mmol, 1.0 equiv), the corresponding allylic carbonate (0.075 mmol, 1.5 equiv) and 1.0 M alkylborane **3.2** solution in CyH (100 μL, 0.1 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 60 °C for 16 h. The vial was removed from the glovebox. Acetic acid (20 μL) was then added. The mixture was allowed to stir at room temperature for 25 min before aliquots (50 μL) were taken and analyzed by GC-MS and GC.

For branched-selective reaction. In a nitrogen-filled glovebox, a 4 mL dram vial was charged with $Pd(dba)_2$ (1.4 mg, 0.0025 mmol, 0.05 equiv), **L9** (3.2 mg, 0.0038 mmol, 0.075 equiv) a stir bar. To the vial was added $PhCF_3$ (400 μL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added the corresponding carbonate (0.075 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (7.2 mg, 0.05 mmol, 1.0 equiv), and 1.0 M alkylborane **3.2** solution in $PhCF_3$ (100 μL, 0.10 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h. The vial was removed from the glovebox. Acetic acid (20 μL) was then added. The mixture was allowed to stir at room temperature for 25 min before aliquots (50 μL) were taken and analyzed by GC-MS and GC.

Note: Regioselectivity was determined by gas GC analysis using authentic samples of the linear- or branched-selective products as reference standards. Minor diastereomers were identified by GC–MS, and their ratios relative to the major diastereomer were quantified by GC. In all cases, we assumed that isomers have identical reflection factors in GC analysis.

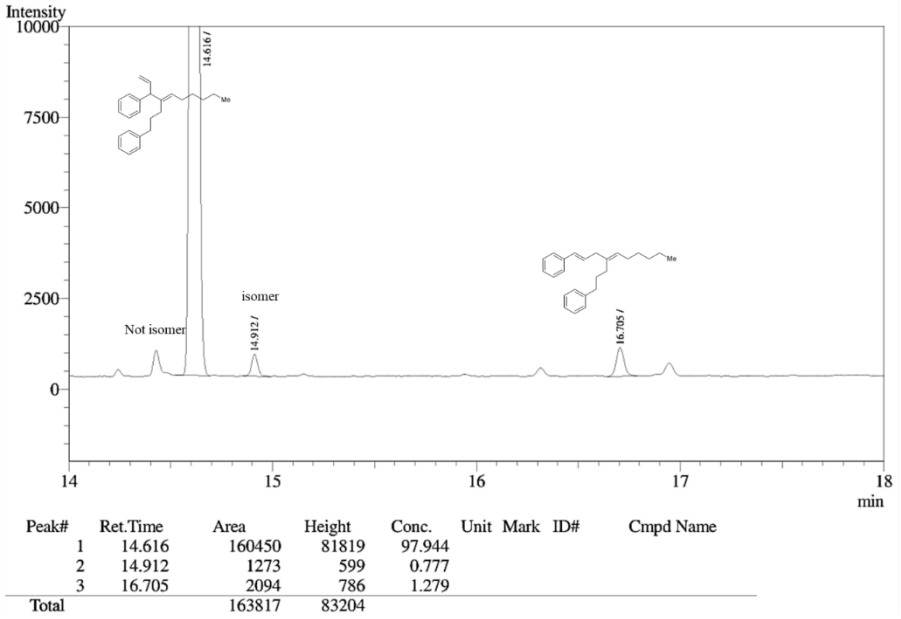
To evaluate the generality of the reaction, we selected a series of allylic carbonates bearing electron-donating (–OMe), electron-withdrawing ($–CF_3$), and electronically neutral (–H) substituents on the aryl ring as representative electrophiles. Under both linear- and branched-selective conditions, the corresponding trisubstituted alkenes were obtained with excellent regioselectivity (>200:1 l:b under linear-selective conditions and >50:1 b:l under branched-selective conditions) and outstanding diastereoselectivity (>100:1).

3.4.5.2 Regioselectivity and Diastereoselectivity of 3.5

The GC and GC-MS analysis results of reaction crude of **3.5** under branched-selective conditions were shown in Figure 3.13 and 3.14.

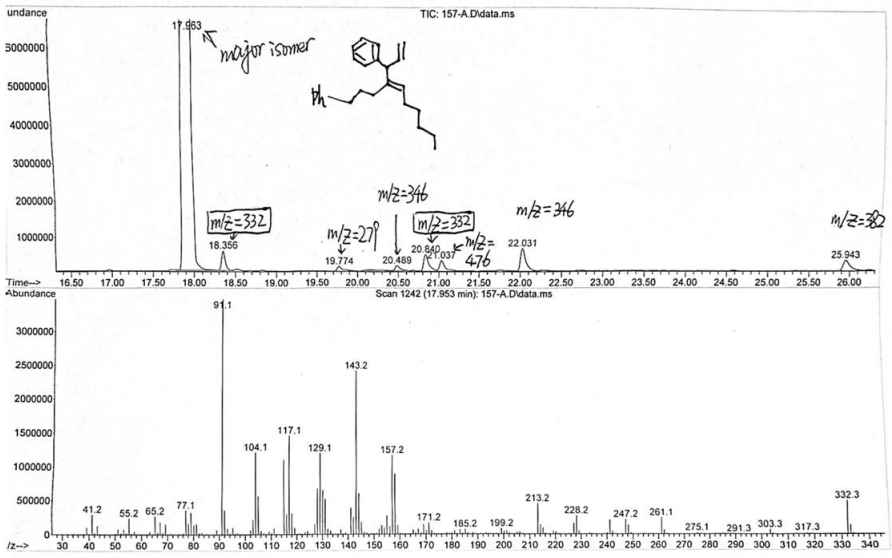
The regioisomeric ratio is equal to 77:1 (branched:linear), and the diastereomeric ratio is equal to 126:1.

Figure 3.13 GC Traces of the Reaction Crude of 3.5



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	14.616	160450	81819	97.944				
2	14.912	1273	599	0.777				
3	16.705	2094	786	1.279				
Total		163817	83204					

Figure 3.14 GC-MS Traces of the Reaction Crude of 3.5

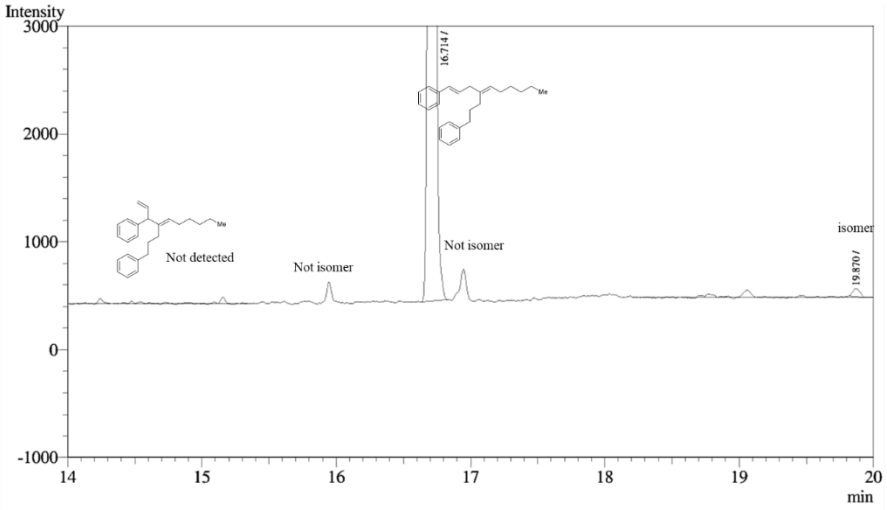


3.4.5.3 Regioselectivity and Diastereoselectivity of 3.4

The GC analysis results of the reaction crude of **3.4** under linear-selective conditions were shown in Figure 3.15.

The regioisomeric ratio is greater than 300:1(linear:branched), and the diastereomeric ratio is equal to 262:1.

Figure 3.15 GC Traces of the Reaction Crude of 3.4



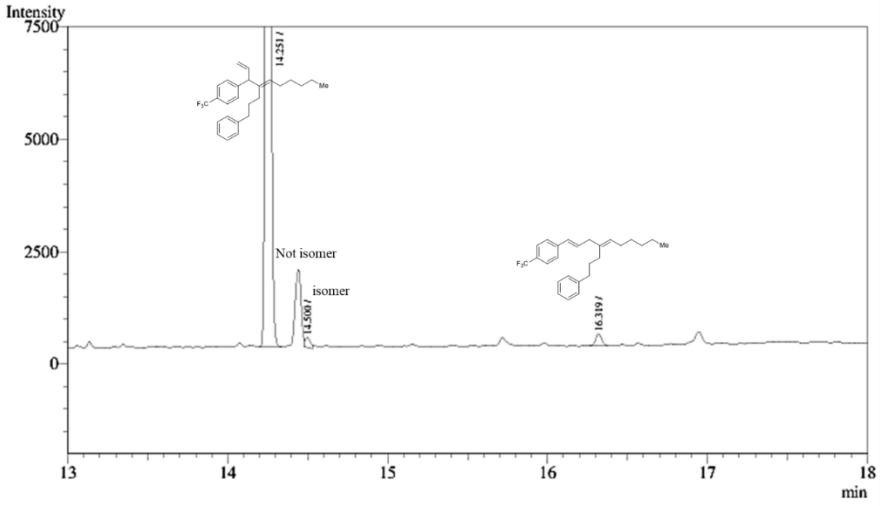
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	16.714	69304	25785	99.621				
2	19.870	264	74	0.379				
Total		69568	25859					

3.4.5.4 Regioselectivity and Diastereoselectivity of 3.14

The GC analysis results of the reaction crude of **3.14** under branched-selective conditions were shown in Figure 3.16.

The regioisomeric ratio is equal to 96:1 (brached:linear), and the diastereomeric ratio is equal to 122:1.

Figure 3.16 GC Traces of the Reaction Crude of 3.14



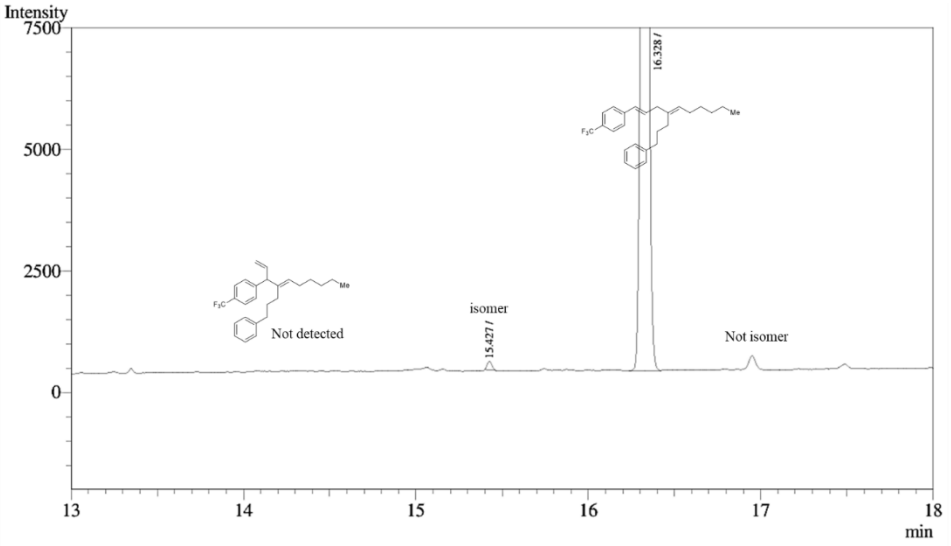
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	14.251	60741	32865	98.172				
2	14.500	497	222	0.803				
3	16.319	634	257	1.025				
Total		61872	33344					

3.4.5.5 Regioselectivity and Diastereoselectivity of 3.7

The GC analysis results of the reaction crude of **3.7** under linear-selective conditions were shown in Figure 3.17.

The regioisomeric ratio is greater than 300:1(linear:branched), and the diastereomeric ratio is equal to 208:1.

Figure 3.17 GC Traces of the Reaction Crude of 3.7



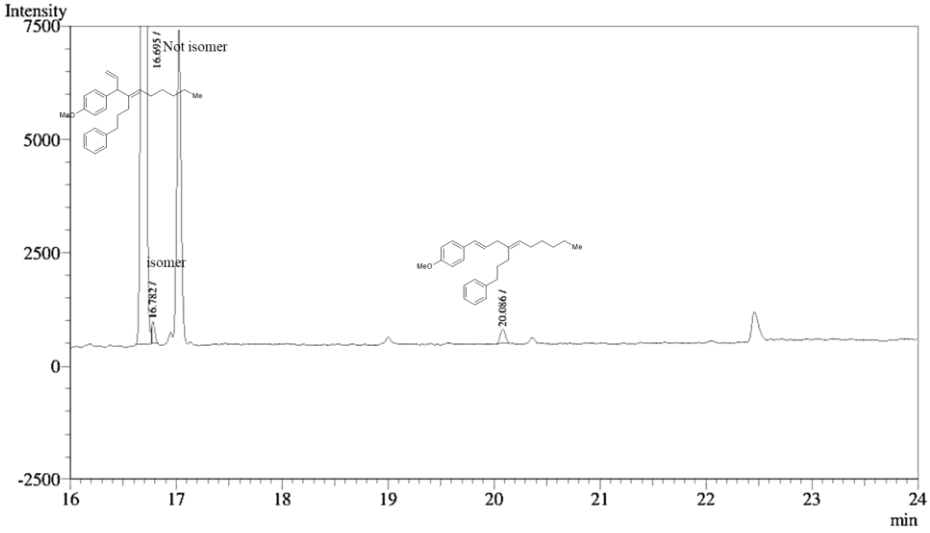
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	15.427	335	173	0.477				
2	16.328	69847	27431	99.523				
Total		70182	27604					

3.4.5.6 Regioselectivity and Diastereoselectivity of 3.15

The GC analysis results of the reaction crude of **3.15** under branched-selective conditions were shown in Figure 3.18.

The regioisomeric ratio is equal to 96:1 (branched:linear), and the diastereomeric ratio is equal to 101:1.

Figure 3.18 GC Traces of the Reaction Crude of 3.15



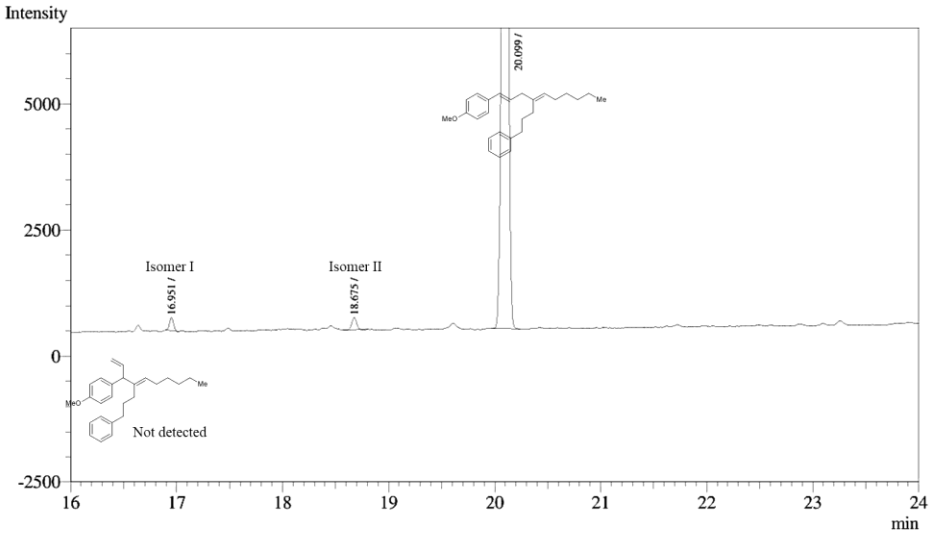
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	16.695	97572	37115	98.015				
2	16.782	962	485	0.966		V		
3	20.086	1014	301	1.019				
Total		99548	37901					

3.4.5.7 Regioselectivity and Diastereoselectivity of 3.8

The GC analysis results of the reaction crude of **3.8** under linear-selective conditions were shown in Figure 3.19.

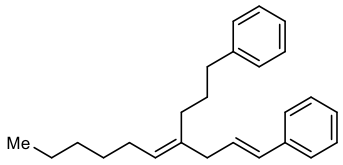
The regioisomeric ratio is greater than 300:1(linear:branched), and the diastereomeric ratio is equal to 100:1:1 (two possible diastereomers were noticed).

Figure 3.19 GC Traces of the Reaction Crude of 3.8



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	16.951	663	255	0.933				
2	18.675	695	237	0.978				
3	20.099	69706	19049	98.089				
Total		71064	19541					

3.4.6 Characterization of Linear Products



((1*E*,4*E*)-4-hexylidenehept-1-ene-1,7-diyl)dibenzene (3.4) was prepared according to general procedure B, purified by silica gel column chromatography (0-2% diethyl ether in hexanes), and isolated as a colorless oil (132.6 mg, 80% yield).

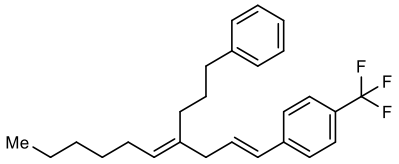
Using *tert*-butyl cinnamyl carbonate instead of **6** also furnished **3.4** in 76% isolated yield with similar high diastereoselectivity (> 20:1 d.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.32 – 7.26 (m, 4H), 7.25 – 7.14 (m, 4H), 6.36 (d, *J* = 15.7 Hz, 1H), 6.18 (ddd, *J* = 15.7, 7.9, 6.2 Hz, 1H), 5.24 (t, *J* = 7.2 Hz, 1H), 2.89 (d, *J* = 7.0 Hz, 2H), 2.62 (t, *J* = 7.8 Hz, 2H), 2.16 – 2.05 (m, 2H), 1.98 (q, *J* = 7.2 Hz, 2H), 1.79 – 1.65 (m, 2H), 1.38 – 1.25 (m, 6H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 137.9, 137.4, 131.0, 129.5, 128.6, 128.5, 128.4, 127.1, 127.0, 126.2, 125.8, 40.8, 36.0, 31.8, 30.2, 30.0, 29.9, 28.0, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 332.3, found 332.3.

FTIR (neat, cm^{-1}): 3026, 2954, 2926, 2856, 1605, 1495, 1453, 964, 745, 692.



1-((1*E*,4*E*)-4-(3-phenylpropyl)deca-1,4-dien-1-yl)-4-(trifluoromethyl)benzene (3.7) was prepared according to general procedure B, purified by silica gel column chromatography (0-3% diethyl ether in hexanes), and isolated as a colorless oil (168.2 mg, 84% yield).

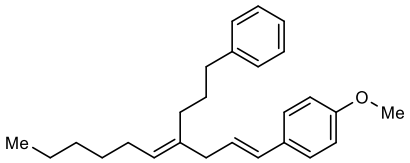
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.21 – 7.15 (m, 3H), 6.37 (d, *J* = 15.9 Hz, 1H), 6.27 (dt, *J* = 15.9, 6.9 Hz, 1H), 5.24 (t, *J* = 7.1 Hz, 1H), 2.90 (d, *J* = 7.0 Hz, 2H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.09 (t, *J* = 7.9 Hz, 2H), 1.98 (q, *J* = 7.2 Hz, 2H), 1.76 – 1.68 (m, 2H), 1.39 – 1.22 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 141.4, 137.0, 132.4, 129.8, 128.9 (q, $J_{C\text{-}F}$ = 32.2 Hz), 128.5, 128.4, 127.6, 126.3, 125.9, 125.54 (q, $J_{C\text{-}F}$ = 3.4 Hz), 124.0 (q, $J_{C\text{-}F}$ = 271.6 Hz), 40.8, 36.0, 31.8, 30.2, 30.0, 29.9, 28.1, 22.8, 14.2.

^{19}F NMR (470 MHz, $CDCl_3$) δ -65.3.

GCMS (EI) calculated for $[M]^+$ 400.2, found 400.3.

FTIR (neat, cm^{-1}): 2929, 2856, 1616, 1323, 1163, 1109, 1066, 1016, 951, 698.



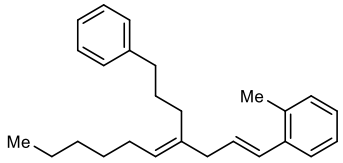
1-methoxy-4-((1*E*,4*E*)-4-(3-phenylpropyl)deca-1,4-dien-1-yl)benzene (3.8) was prepared according to general procedure B, purified by silica gel column chromatography (0-5% diethyl ether in hexanes), and isolated as a colorless oil (149.0 mg, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 4H), 7.21 – 7.16 (m, 3H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.30 (d, *J* = 15.7 Hz, 1H), 6.03 (ddd, *J* = 15.6, 7.8, 6.4 Hz, 1H), 5.23 (t, *J* = 7.3 Hz, 1H), 3.81 (s, 3H), 2.86 (d, *J* = 7.0 Hz, 2H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.10 (t, *J* = 7.9 Hz, 2H), 1.98 (q, *J* = 7.2 Hz, 2H), 1.77 – 1.68 (m, 2H), 1.35 – 1.24 (m, 6H), 0.93 – 0.87 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 142.7, 137.7, 130.8, 130.3, 128.5, 128.4, 127.3, 127.2, 126.9, 125.8, 114.0, 55.4, 40.8, 36.0, 31.8, 30.2, 30.0, 29.9, 28.0, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 362.3, found 362.3.

FTIR (neat, cm^{-1}): 2953, 2927, 2855, 1607, 1510, 1454, 1245, 1174, 1036, 966, 698.



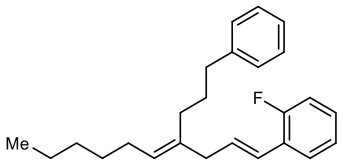
1-methyl-2-((1*E*,4*E*)-4-(3-phenylpropyl)deca-1,4-dien-1-yl)benzene (3.9) was prepared according to general procedure B but at 80 °C instead of 60 °C, purified by silica gel column chromatography (0-2% diethyl ether in hexanes), and isolated as a colorless oil (138.2 mg, 80% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 6.6 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.20 – 7.11 (m, 6H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.04 (ddd, *J* = 15.7, 8.5, 5.6 Hz, 1H), 5.25 (t, *J* = 7.3 Hz, 1H), 2.62 (t, *J* = 7.9 Hz, 2H), 2.33 (s, 3H), 2.16 – 2.07 (m, 2H), 1.99 (q, *J* = 7.2 Hz, 2H), 1.80 – 1.70 (m, 2H), 1.36 – 1.25 (m, 6H), 0.92 – 0.85 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 137.5, 137.0, 135.0, 130.8, 130.2, 128.9, 128.5, 128.4, 127.1, 127.0, 126.1, 125.8, 125.7, 41.1, 36.1, 31.8, 30.2, 30.0, 29.9, 28.0, 22.7, 20.0, 14.2.

GCMS (EI) calculated for $[M]^+$ 346.3, found 346.3.

FTIR (neat, cm^{-1}): 3023, 2927, 2857, 1603, 1495, 1453, 1315, 966, 741, 696.



1-fluoro-2-((1*E*,4*E*)-4-(3-phenylpropyl)deca-1,4-dien-1-yl)benzene (3.10) was prepared according to general procedure B, purified by silica gel column chromatography (0-3% diethyl ether in hexanes), and isolated as a colorless oil (140.2 mg, 80% yield).

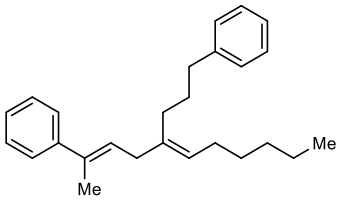
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (td, J = 7.7, 1.8 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.19 – 7.14 (m, 4H), 7.07 (t, J = 7.6 Hz, 1H), 7.02 (dd, J = 10.8, 8.1 Hz, 1H), 6.52 (d, J = 16.0 Hz, 1H), 6.25 (dt, J = 16.0, 7.2 Hz, 1H), 5.24 (t, J = 7.2 Hz, 1H), 2.91 (d, J = 7.2 Hz, 2H), 2.61 (t, J = 7.8 Hz, 2H), 2.14 – 2.06 (m, 2H), 1.98 (q, J = 7.2 Hz, 2H), 1.78 – 1.68 (m, 2H), 1.35 – 1.25 (m, 6H), 0.89 (t, J = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1 (d, $J_{C\text{-}F}$ = 248.4 Hz), 142.5, 137.2, 132.1 (d, $J_{C\text{-}F}$ = 4.5 Hz), 128.5, 128.4, 128.2 (d, $J_{C\text{-}F}$ = 8.2 Hz), 127.3, 127.2 (d, $J_{C\text{-}F}$ = 4.1 Hz), 125.8, 125.6 (d, $J_{C\text{-}F}$ = 12.3 Hz), 124.1 (d, J = 3.6 Hz), 123.3 (d, $J_{C\text{-}F}$ = 3.6 Hz), 115.7 (d, $J_{C\text{-}F}$ = 22.3 Hz), 41.2, 36.0, 31.8, 30.2, 30.0, 29.8, 28.0, 22.7, 14.2.

^{19}F NMR (470 MHz, $CDCl_3$) δ -121.7.

GCMS (EI) calculated for $[M]^+$ 350.2, found 350.3.

FTIR (neat, cm^{-1}): 3026, 2926, 2856, 1609, 1486, 1455, 1229, 1031, 967, 751, 698.



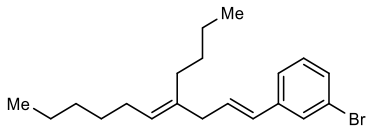
((4*E*,6*E*)-4-hexylideneoct-6-ene-1,7-diyl)dibenzene (3.11) was prepared according to general procedure B but at 80 °C instead of 60 °C, purified by silica gel column chromatography (0-2% diethyl ether in hexanes), and isolated as a colorless oil (130.0 mg, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.37 (m, 2H), 7.34 – 7.27 (m, 4H), 7.24 – 7.17 (m, 4H), 5.78 (ddt, J = 7.5, 6.0, 1.4 Hz, 1H), 5.23 (t, J = 7.1 Hz, 1H), 2.89 (d, J = 7.3 Hz, 2H), 2.65 – 2.60 (m, 2H), 2.13 – 2.08 (m, 2H), 2.01 (d, J = 1.2 Hz, 3H), 1.97 (q, J = 7.2 Hz, 2H), 1.80 – 1.72 (m, 2H), 1.33 – 1.25 (m, 6H), 0.89 (t, J = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.1, 142.7, 137.6, 135.6, 128.5, 128.4, 128.4, 128.3, 126.9, 126.7, 126.4, 125.8, 36.5, 36.2, 31.8, 30.4, 30.4, 29.9, 28.0, 22.7, 15.8, 14.3.

GCMS (EI) calculated for $[M]^+$ 346.2, found 346.3.

FTIR (neat, cm^{-1}): 3032, 2928, 2857, 1603, 1495, 1453, 1247, 1072, 909, 732, 697.



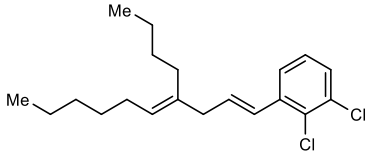
1-bromo-3-((1*E*,4*E*)-4-butyldeca-1,4-dien-1-yl)benzene (3.12) was prepared according to general procedure B, purified by silica gel column chromatography (100% hexanes), and isolated as a colorless oil (125.7 mg, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 6.30 (d, *J* = 15.7 Hz, 1H), 6.24 – 6.14 (m, 1H), 5.19 (t, *J* = 7.2 Hz, 1H), 2.87 (d, *J* = 7.0 Hz, 2H), 2.06 – 1.98 (m, 4H), 1.37 – 1.27 (m, 10H), 0.93 – 0.87 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.2, 137.6, 131.4, 130.1, 129.8, 129.5, 129.0, 127.0, 124.8, 122.9, 40.7, 31.8, 30.7, 30.1, 29.9, 28.0, 22.9, 22.8, 14.2, 14.2.

GCMS (EI) calculated for $[M]^+$ 348.1, found 348.1.

FTIR (neat, cm^{-1}): 2956, 2925, 2856, 1591, 1560, 1471, 1072, 961, 769, 682.



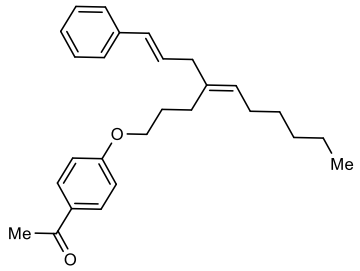
1,2-dichloro-3-((1*E*,4*E*)-4butyldeca-1,4-dien-1-yl)benzene (3.13) was prepared according to general procedure B, purified by silica gel column chromatography (0-5% DCM in hexanes), and isolated as a colorless oil (153.0 mg, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.31 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.13 (t, *J* = 7.9 Hz, 1H), 6.77 (dd, *J* = 15.6, 1.8 Hz, 1H), 6.17 (dt, *J* = 15.7, 7.1 Hz, 1H), 5.22 (t, *J* = 7.2 Hz, 1H), 2.93 (d, *J* = 7.1 Hz, 2H), 2.11 – 1.99 (m, 4H), 1.41 – 1.26 (m, 10H), 0.97 – 0.84 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.6, 137.5, 134.1, 133.5, 131.0, 128.7, 127.5, 127.3, 127.2, 125.1, 41.0, 31.9, 30.8, 30.2, 30.0, 28.1, 23.0, 22.9, 14.3, 14.3.

GCMS (EI) calculated for $[M]^+$ 338.2, found 338.2.

FTIR (neat, cm^{-1}): 2955, 2926, 2857, 1581, 1508, 1451, 1410, 1230, 1044, 969, 770.



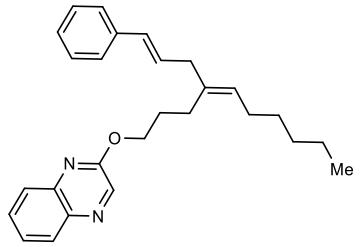
1-(4-{[(4*E*)-4-[(2*E*)-3-phenylprop-2-en-1-yl]dec-4-en-1-yl]oxy}phenyl)ethan-1-one (3.21) was prepared according to general procedure B, purified by silica gel column chromatography (2-15% ethyl acetate in hexanes), and isolated as a white solid (130.0 mg, 67% yield).

1H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.9 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.81 (d, J = 8.9 Hz, 2H), 6.31 (d, *J* = 15.7 Hz, 1H), 6.14 – 6.05 (m, 1H), 5.21 (t, *J* = 7.2 Hz, 1H), 3.90 (t, *J* = 6.3 Hz, 2H), 2.82 (d, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 2.17 (t, *J* = 7.6 Hz, 2H), 1.92 (q, *J* = 7.4 Hz, 2H), 1.86 – 1.78 (m, 2H), 1.26 – 1.20 (m, 2H), 1.19 – 1.12 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H).

13C NMR (126 MHz, CDCl3) δ 196.8, 163.1, 137.7, 136.2, 131.2, 130.7, 130.3, 129.1, 128.6, 128.1, 127.1, 126.1, 114.2, 67.6, 40.7, 31.7, 29.8, 28.0, 27.6, 26.4, 26.3, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 390.3, found 390.3.

FTIR (neat, cm^{-1}): 2954, 2919, 2871, 1674, 1597, 1268, 1177, 825, 693.



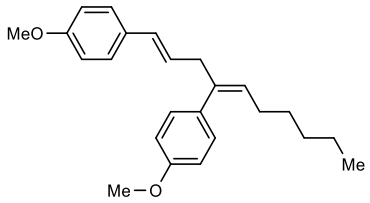
2-{[(4*E*)-4-[(2*E*)-3-phenylprop-2-en-1-yl]dec-4-en-1-yl]oxy}quinoxaline (3.22) was prepared according to general procedure B, purified by silica gel column chromatography (0-5% ethyl acetate in hexanes), and isolated as a colorless oil (153.0 mg, 76% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.68 - 7.64 (m, 1H), 7.59 – 7.52 (m, 1H), 7.35 (d, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.24 – 6.17 (m, 1H), 5.30 (t, *J* = 7.1 Hz, 1H), 4.47 (t, *J* = 6.4 Hz, 2H), 2.94 (d, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 8.2 Hz, 2H), 2.03 (q, *J* = 7.4 Hz, 2H), 1.99 – 1.93 (m, 2H), 1.36 – 1.29 (m, 2H), 1.28 – 1.20 (m, 4H), 0.83 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 140.6, 139.8, 138.8, 137.8, 136.4, 131.2, 130.2, 129.2, 129.0, 128.6, 128.0, 127.3, 127.1, 126.6, 126.2, 66.3, 40.7, 31.8, 29.8, 28.1, 27.4, 26.6, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 400.3, found 400.3.

FTIR (neat, cm^{-1}): 2959, 2928, 2853, 1577, 1415, 1295, 1217, 1107, 969, 760, 643.



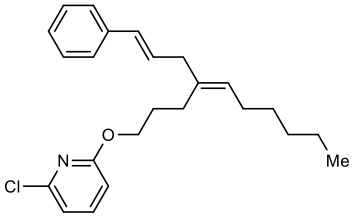
1-methoxy-4-[(1*E*,4*Z*)-4-(4-methoxyphenyl)deca-1,4-dien-1-yl]benzene (3.23) was prepared according to general procedure B, purified by silica gel column chromatography (2% ethyl acetate in hexanes), and isolated as a colorless oil (110.0 mg, 63% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 6.06 (dt, *J* = 15.9, 7.0 Hz, 1H), 5.47 (d, *J* = 1.4 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.17 (d, *J* = 6.9 Hz, 2H), 1.97 (q, *J* = 7.4 Hz, 2H), 1.35 – 1.31 (m, 3H), 1.28 – 1.20 (m, 5H), 0.84 (t, *J* = 7.1 Hz 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 158.2, 138.7, 133.8, 130.8, 130.4, 129.6, 128.5, 127.3, 126.8, 114.0, 113.5, 55.4, 55.3, 42.8, 31.7, 30.0, 29.2, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 350.2, found 350.2.

FTIR (neat, cm^{-1}): 2923, 2855, 1597, 1358, 1177, 921, 701, 662, 550.



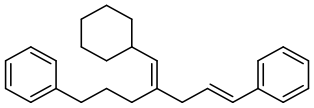
2-chloro-6-{[(4*E*)-4-[(2*E*)-3-phenylprop-2-en-1-yl]dec-4-en-1-yl]oxy}pyridine (3.24) was prepared according to general procedure B, purified by silica gel column chromatography (0-5% acetone in hexanes), and isolated as a colorless oil (136.0 mg, 71% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (t, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 6.42 (d, *J* = 15.7 Hz, 1H), 6.23 - 6.16 (m, 1H), 5.29 (t, *J* = 7.3 Hz, 1H), 4.30 (t, *J* = 6.4 Hz, 2H), 2.93 (d, *J* = 7.0 Hz, 2H), 2.24 (t, *J* = 7.6 Hz, 2H), 2.03 (q, *J* = 7.3 Hz, 2H), 1.90 (q, *J* = 7.1 Hz, 2H), 1.39 – 1.22 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 148.5, 140.6, 137.9, 136.5, 131.1, 129.3, 128.6, 127.8, 127.1, 126.2, 116.2, 109.3, 66.4, 40.7, 31.8, 29.8, 28.0, 27.5, 26.6, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 383.2, found 383.2.

FTIR (neat, cm^{-1}): 2923, 2867, 1591, 1441, 1298, 1159, 966, 785, 691.



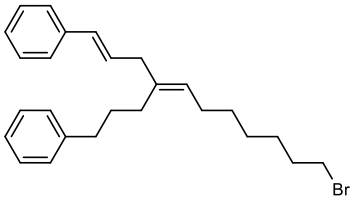
((1*E*,4*E*)-4-(cyclohexylmethylene)hept-1-ene-1,7-diyl)dibenzene (3.29) was prepared according to general procedure B but at 45 °C instead of 60 °C, and 2.5 equiv of cyclohexyl 9-BBN was used. The crude was purified by silica gel column chromatography (0-2% diethyl ether in hexanes), and compound **29** was isolated as a colorless oil (90.0 mg, 52% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 6H), 7.25 – 7.17 (m, 4H), 6.37 (d, *J* = 15.7 Hz, 1H), 6.18 (dt, *J* = 15.7, 7.0 Hz, 1H), 5.08 (d, *J* = 9.3 Hz, 1H), 2.88 (d, *J* = 7.2 Hz, 2H), 2.63 (t, *J* = 7.7 Hz, 2H), 2.18 – 2.06 (m, 3H), 1.79 – 1.57 (m, 7H), 1.33 – 0.97 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 137.9, 135.6, 133.3, 130.9, 129.6, 128.6, 128.5, 128.4, 127.0, 126.2, 125.8, 40.7, 37.1, 36.0, 33.8, 30.5, 30.1, 26.2, 26.2.

GCMS (EI) calculated for $[M]^+$ 344.3, found 344.3.

FTIR (neat, cm^{-1}): 3029, 2921, 2850, 1603, 1495, 1448, 1030, 964, 765, 693.



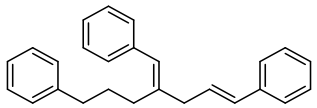
((1*E*,4*E*)-4-(7-bromoheptylidene)hept-1-ene-1,7-diyl)dibenzene (3.30) was prepared according to general procedure B, purified by silica gel column chromatography (10-35% DCM in hexanes), and isolated as a colorless oil (159.0 mg, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 2H), 7.22 – 7.15 (m, 4H), 7.14 – 7.07 (m, 4H), 6.27 (d, *J* = 15.8 Hz, 1H), 6.08 (dt, *J* = 15.7, 7.0 Hz, 1H), 5.13 (t, *J* = 7.2 Hz, 1H), 3.31 (t, *J* = 6.9 Hz, 2H), 2.80 (d, *J* = 7.1 Hz, 2H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.01 (t, *J* = 6.4 Hz, 2H), 1.90 (q, *J* = 7.0 Hz, 2H), 1.77 (p, *J* = 7.0 Hz, 2H), 1.68 – 1.60 (m, 2H), 1.37 – 1.30 (m, 2H), 1.29 – 1.19 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 137.8, 137.8, 131.0, 129.3, 128.6, 128.5, 128.4, 127.0, 126.7, 126.2, 125.8, 40.8, 36.0, 34.1, 32.9, 30.2, 30.0, 29.9, 28.6, 28.2, 27.9.

GCMS (EI) calculated for $[M]^+$ 424.4, found 424.4.

FTIR (neat, cm^{-1}): 3024, 2931, 2859, 1495, 1449, 964, 746, 696.



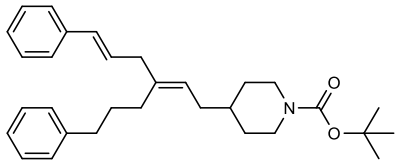
[(1*E*,4*E*)-5-phenyl-2-(3-phenylpropyl)penta-1,4-dien-1-yl]benzene (3.31) was prepared according to general procedure B but running the reaction for 40 h instead of 16 h, purified by silica gel column chromatography (0-4% diethyl ether in hexanes), and isolated as a colorless oil (149.0 mg, 88% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.40 – 7.24 (m, 8H), 7.27 – 7.18 (m, 5H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.43 (s, 1H), 6.32 (dt, *J* = 15.7, 7.1 Hz, 1H), 3.13 (d, *J* = 7.0 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.44 – 2.32 (m, 2H), 1.97 – 1.87 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 141.6, 138.3, 137.7, 131.8, 128.7, 128.6, 128.6, 128.5, 128.4, 128.2, 127.2, 126.7, 126.2, 126.2, 125.9, 41.1, 36.0, 30.6, 30.0.

GCMS (EI) calculated for $[M]^+$ 338.2, found 338.2.

FTIR (neat, cm^{-1}): 2927, 2858, 1739, 1597, 1368, 1274, 1159, 966, 744, 696.



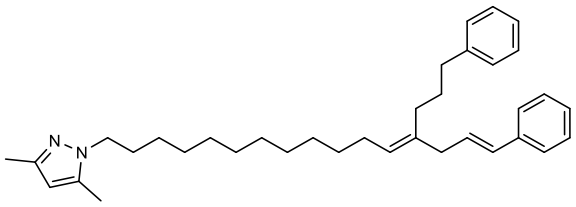
***tert*-butyl 4-((2*E*,5*E*)-6-phenyl-3-(3-phenylpropyl)hexa-2,5-dien-1-yl)piperidine-1-carboxylate (3.32)** was prepared according to general procedure B, purified by silica gel column chromatography (0-15% diethyl ether in hexanes), and isolated as a colorless oil (150.0 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 6H), 7.22 – 7.14 (m, 4H), 6.35 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.8, 7.0 Hz, 1H), 5.22 (t, *J* = 7.4 Hz, 1H), 4.05 (d, *J* = 13.3 Hz, 2H), 2.89 (d, *J* = 7.0 Hz, 2H), 2.70 – 2.63 (m, 2H), 2.63 – 2.58 (t, *J* = 7.9 Hz, 2H), 2.07 (t, *J* = 8.6 Hz, 2H), 1.91 (t, *J* = 7.1 Hz, 2H), 1.71 (m, 2H), 1.65–1.60 (m, 2H), 1.46 (s, 9H), 1.41 – 1.36 (m, 1H), 1.10 – 1.01 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 142.5, 139.1, 137.8, 131.2, 129.2, 128.6, 128.5, 128.4, 127.1, 126.2, 125.9, 124.4, 79.3, 60.5, 40.8, 36.9, 36.0, 34.8, 32.2, 30.1, 30.0, 28.6.

MS (ESI) calculated for $[M+Na]^+$ 482.3, found 482.3.

FTIR (neat, cm^{-1}): 2978, 2931, 2853, 1688, 1421, 1364, 1164, 964, 749, 693.



3,5-dimethyl-1-[(12*E*,15*E*)-16-phenyl-13-(3-phenylpropyl)hexadeca-12,15-dien-1-yl]-1H-pyrazole (3.33) was prepared according to general procedure B, purified by silica gel column chromatography (0-10% ethyl acetate in hexanes), and isolated as a colorless oil (189.0 mg, 74% yield).

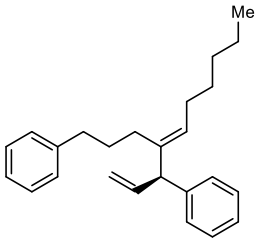
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.32 – 7.25 (m, 4H), 7.23 – 7.14 (m, 4H), 6.36 (d, *J* = 15.7 Hz, 1H), 6.17 (dt, *J* = 15.7, 7.0 Hz, 1H), 5.77 (s, 1H), 5.24 (t, *J* = 7.2 Hz, 1H), 3.93 (dd, *J* = 8.2, 6.7 Hz, 2H), 2.88 (d, *J* = 7.0 Hz, 2H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.22 (s, 6H), 2.21 (s, 6H), 2.14 – 2.07 (m, 2H), 1.98 (q, *J* = 7.2 Hz, 2H), 1.81 – 1.70 (m, 4H), 1.43 – 1.22 (m, 16H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 142.6, 138.5, 137.9, 137.4, 131.0, 129.5, 128.6, 128.5, 128.4, 127.1, 127.0, 126.2, 125.8, 104.8, 48.9, 40.8, 36.0, 30.6, 30.2, 30.2, 30.0, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 28.0, 26.9, 13.6, 11.2.

MS (ESI) calculated for $[M+H]^+$ 511.4, found 511.5.

FTIR (neat, cm^{-1}): 2923, 2854, 1600, 1509, 1451, 1230, 956, 825, 748, 699.

3.4.7 Characterization of Branched Product



(*S,E*)-(4-hexylidenehept-6-ene-1,5-diyl)dibenzene (3.5) was prepared according to general procedure C, purified by silica gel column chromatography (0-2% diethyl ether in hexanes), and isolated as a colorless oil (129.0 mg, 78% yield, 95:5 e.r.). The absolute configuration of the chiral center was determined in Chapter 4.9.

Using *tert*-butyl cinnamyl carbonate instead of **6** furnished **5** in 35% isolated yield with similar high diastereo and enantioselectivity (> 20:1 d.r., 95:5 e.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 4H), 7.22 – 7.14 (m, 4H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.12 – 6.04 (m, 1H), 5.25 (t, *J* = 7.2 Hz, 1H), 5.09 (d, *J* = 11.0 Hz, 1H), 4.87 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.00 (d, *J* = 7.2 Hz, 1H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.15 – 2.09 (m, 1H), 2.01 (q, *J* = 7.2 Hz, 2H), 1.91 – 1.85 (m, 1H), 1.65 – 1.59 (m, 2H), 1.39 – 1.27 (m, 6H), 0.90 (t, *J* = 6.1 Hz, 3H).

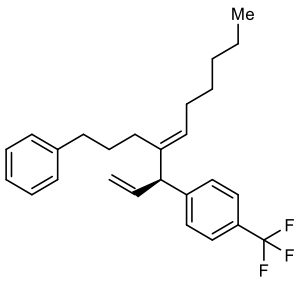
^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 142.5, 140.8, 140.6, 128.8, 128.5, 128.3, 128.3, 128.1, 126.3, 125.8, 115.4, 55.8, 36.1, 31.8, 30.7, 30.1, 29.8, 28.1, 22.7, 14.3.

GCMS (EI) calculated for $[M]^+$ 332.3, found 332.3.

FTIR (neat, cm^{-1}): 2955, 2926, 2857, 1600, 1495, 1452, 912, 735, 698.

$\boldsymbol{\alpha_D^{25}}$ = - 63.8 ° (c 1.15, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 10.0 min (major), 13.5 min (minor).



(*S,E*)-1-(4-(3-phenylpropyl)deca-1,4-dien-3-yl)-4-(trifluoromethyl)benzene (3.14) was prepared according to general procedure C, purified by silica gel column chromatography (0-3% diethyl ether in hexanes), and isolated as a colorless oil (148.0 mg, 74% yield, 96:4 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 14.8 Hz, 4H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 6.7 Hz, 2H), 6.05 (ddd, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.26 (t, *J* = 7.1 Hz, 1H), 5.13 (dt, *J* = 10.2, 1.4 Hz, 1H), 4.86 (dt, *J* = 17.1, 1.5 Hz, 1H), 4.05 (d, *J* = 7.2 Hz, 1H), 2.54 (h, *J* = 6.0 Hz, 2H), 2.15 – 2.08 (m, 1H), 2.02 (q, *J* = 7.2 Hz, 2H), 1.88 – 1.80 (m, 1H), 1.60 (p, *J* = 7.7 Hz, 2H), 1.38 – 1.25 (m, 6H), 0.90 (t, *J* = 7.0 Hz, 3H).

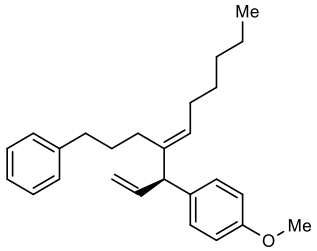
^{13}C NMR (126 MHz, $CDCl_3$) δ 146.9, 142.4, 140.0, 139.9, 129.1, 129.0, 128.7 (q, J_{C-F} = 32.2 Hz), 128.5, 128.4, 125.9, 125.3 (q, J_{C-F} = 3.8 Hz), 122.4 (q, J_{C-F} = 271.9 Hz), 116.2, 55.6, 36.1, 31.8, 30.7, 30.1, 29.7, 28.1, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 400.2, found 400.3.

FTIR (neat, cm^{-1}): 2958, 2930, 2856, 1616, 1498, 1453, 1323, 1164, 1123, 1068, 698.

$\boldsymbol{\alpha_D^{25}}$ = - 59.6 ° (c 1.13, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (1.0% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 14.5 min (minor), 19.1 min (major).



(*S,E*)-1-methoxy-4-(4-(3-phenylpropyl)deca-1,4-dien-3-yl)benzene (3.15) was prepared according to general procedure C, purified by silica gel column chromatography (0-5% diethyl ether in hexanes), and isolated as a light-yellow oil (148.5 mg, 82% yield, 93:7 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.23 (m, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 6.9 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.05 (ddd, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.23 (t, *J* = 7.2 Hz, 1H), 5.07 (dt, *J* = 10.2, 1.5 Hz, 1H), 4.84 (dt, *J* = 17.1, 1.7 Hz, 1H), 3.95 (d, *J* = 7.0 Hz, 1H), 3.80 (s, 3H), 2.53 (td, *J* = 7.6, 2.1 Hz, 2H), 2.13 – 2.06 (m, 1H), 2.03 – 1.97 (m, 2H), 1.89 – 1.84 (m, 1H), 1.65 – 1.57 (m, 2H), 1.37 – 1.24 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H).

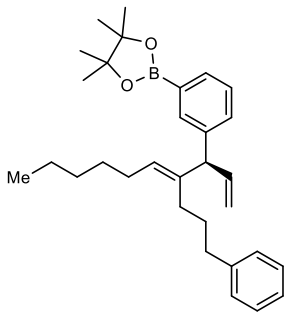
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2, 142.5, 141.1, 140.8, 134.6, 129.6, 128.5, 128.3, 127.8, 125.7, 115.1, 113.7, 55.2, 54.9, 36.1, 31.8, 30.7, 30.1, 29.8, 28.0, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 362.3, found 362.3.

FTIR (neat, cm^{-1}): 2926, 2856, 1608, 1508, 1454, 1245, 1175, 1037, 913, 698.

$\boldsymbol{\alpha_D^{25}}$ = - 61.2 ° (c 1.29, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK AD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 30.4 min (minor), 35.9 min (major).



(*S,E*)-4,4,5,5-tetramethyl-2-(4-((4-(1-phenylallyl)dec-4-en-1-yl)oxy)phenyl)-1,3,2-dioxaborolane (3.16) was prepared according to general procedure C, purified by silica gel chromatography (0-8% ethyl acetate in hexanes), and isolated as a colorless liquid (153.0 mg, 64%, 94:6 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.9 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 2H), 7.23 – 7.16 (m, 3H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.09 (ddd, *J* = 17.2, 10.2, 7.2 Hz, 1H), 5.29 (t, *J* = 7.2 Hz, 1H), 5.10 (dt, *J* = 10.1, 1.1 Hz, 1H), 4.88 (dt, *J* = 17.2, 1.7 Hz, 1H), 4.02 (d, *J* = 7.6 Hz, 1H), 3.88 (t, *J* = 6.4 Hz, 2H), 2.30 – 2.22 (m, 1H), 2.08 – 2.02 (m, 2H), 2.01 – 1.96 (m, 1H), 1.80 – 1.73 (m, 2H), 1.33 (s, 12H), 1.31 – 1.19 (m, 6H), 0.87 (t, *J* = 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 161.7, 142.4, 140.7, 139.6, 136.6, 136.6, 128.8, 128.7, 128.3, 126.4, 115.5, 113.9, 83.6, 67.2, 55.7, 31.8, 29.8, 28.3, 28.0, 27.9, 26.6, 24.9, 22.7, 14.2.

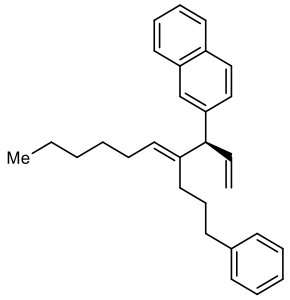
^{11}B NMR (160 MHz, $CDCl_3$) δ 31.7.

MS (ESI) calculated for $[M+K]^+$, 497.3, found 497.4.

FTIR (neat, cm^{-1}): 2928, 2859, 1356, 1320, 1142, 966, 855, 710, 696.

α_D^{25} = -54.5 ° (c 0.64, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after oxidation of boronic ester moiety to phenol with sodium perborate monohydrate. CHIRALPAK OD-H column (0.5% 2-PrOH in hexanes, 1.0 mL/min, detected at 220 nm wavelength) with t_r = 52.3 min (major), 57.6 min (minor).



(*S,E*)-2-(4-(3-phenylpropyl)deca-1,4-dien-3-yl)naphthalene (3.17) was prepared according to general procedure C, purified by silica gel chromatography (0-5% ethyl acetate in hexanes), and isolated as a colorless liquid (169.0 mg, 88%, 95:5 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.73 (m, 3H), 7.59 (s, 1H), 7.44 (m, 2H), 7.30 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.22 (t, *J* = 8.2 Hz, 2H), 7.15 (dd, *J* = 8.5, 6.2 Hz, 1H), 7.07 (d, *J* = 7.0 Hz, 2H), 6.15 (ddd, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.30 (t, *J* = 7.2 Hz, 1H), 5.13 (dt, *J* = 10.2, 1.5 Hz, 1H), 4.90 (dt, *J* = 17.1, 1.7 Hz, 1H), 4.16 (d, *J* = 7.1 Hz, 1H), 2.52 (td, *J* = 7.5, 3.6 Hz, 2H), 2.14 (dt, *J* = 13.5, 7.9 Hz, 1H), 2.03 (q, *J* = 7.3 Hz, 2H), 1.90 (dt, *J* = 13.5, 7.8 Hz, 1H), 1.65 (p, *J* = 7.8 Hz, 2H), 1.37 (m, 2H), 1.29 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H).

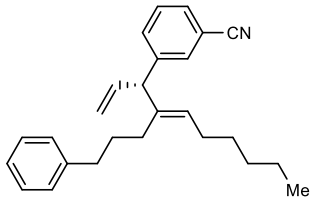
^{13}C NMR (126 MHz, CDCl3) δ 142.4, 140.7, 140.5, 140.1, 133.7, 132.5, 128.5, 128.4, 128.3, 127.8, 127.8, 127.7, 127.5, 127.1, 125.9, 125.8, 125.4, 115.8, 55.8, 36.1, 31.8, 30.7, 30.1, 29.8, 28.1, 22.7, 14.3.

GCMS (EI) calculated for $[M]^+$ 382.3, found 382.3.

FTIR (neat, cm^{-1}): 3026, 2925, 2856, 1630, 1600, 1496, 1454, 914, 744, 698.

α_D^{25} = -60.6 ° (c 0.98, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to general procedure D and then tosylation with TsCl. CHIRALPAK OD-H column (1.0% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 26.5 min (minor), 42.9 min (major).



(*S*,*E*)-3-(4-(3-phenylpropyl)deca-1,4-dien-3-yl)benzonitrile (3.18) was prepared according to general procedure C using K_3PO_4 (1.5 equiv) and $Pd(OAc)_2$ (5 mol%) instead of $Pd(dba)_2$, purified by silica gel chromatography (0-5% ethyl acetate in hexanes), and isolated as a colorless liquid (127.0 mg, 71%, 95:5 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.45 (m, 1H), 7.41 (s, 1H), 7.37 – 7.32 (m, 2H), 7.25 – 7.22 (m, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 6.9 Hz, 2H), 5.98 (ddd, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.20 (t, *J* = 7.2 Hz, 1H), 5.12 (d, *J* = 10.2 Hz, 1H), 4.80 (d, *J* = 17.1 Hz, 1H), 3.98 (d, *J* = 7.0 Hz, 1H), 2.57 – 2.47 (q, *J* = 7.8 Hz, 2H), 2.11 – 2.04 (m, 1H), 1.98 (q, *J* = 7.3 Hz, 2H), 1.81 – 1.74 (m, 1H), 1.62 – 1.55 (m, 2H), 1.36 – 1.22 (m, 6H), 0.87 (t, *J* = 7.1 Hz, 3H).

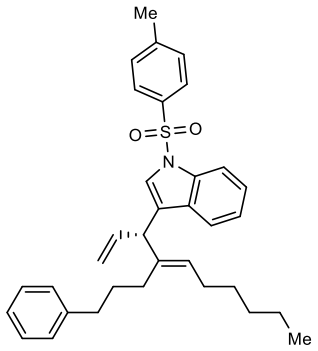
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2, 142.2, 139.5, 133.4, 132.4, 130.2, 129.4, 129.1, 128.5, 128.4, 126.0, 119.2, 116.6, 112.4, 55.1, 36.0, 31.8, 30.7, 30.0, 29.7, 28.0, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 357.3, found 357.3.

FTIR (neat, cm^{-1}): 2954, 2927, 2856, 2229, 1454, 917, 797, 697.

α_D^{25} = -64.2° (c 0.82, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to general procedure D and then acylation with 4-nitrobenzoyl chloride. CHIRALPAK AD-H column (5.0% 2-PrOH in hexanes, 1.5 mL/min, detected at 254 nm wavelength) with t_r = 12.1 min (minor), 14.3 min (major).



(*S,E*)-3-(4-(3-phenylpropyl)deca-1,4-dien-3-yl)-1-tosyl-1H-indole (3.19) was prepared according to general procedure B, purified by silica gel chromatography (0-15% ethyl acetate in hexanes), and isolated as a colorless liquid (174.0 mg, 66%, 88:12 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.20 – 7.13 (m, 4H), 7.09 – 7.02 (m, 4H), 6.97 (d, *J* = 6.9 Hz, 2H), 5.96 (ddd, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.07 (t, *J* = 7.2 Hz, 1H), 5.03 (d, *J* = 10.1 Hz, 1H), 4.86 (d, *J* = 17.1 Hz, 1H), 4.04 (d, *J* = 7.0 Hz, 1H), 2.42 (t, *J* = 7.5 Hz, 2H), 2.18 (s, 3H), 2.06 – 1.98 (m, 1H), 1.95 – 1.83 (m, 3H), 1.58 – 1.46 (m. 2H), 1.20 – 1.14 (m, 4H), 1.12 – 1.06 (m, 2H), 0.77 (t, *J* = 7.2 Hz, 3H).

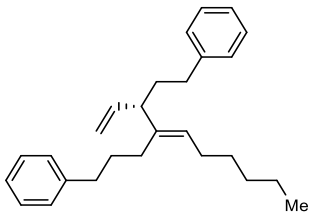
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 142.3, 138.6, 138.3, 135.8, 135.3, 130.8, 129.8, 128.8, 128.4, 128.4, 126.8, 125.8, 124.6, 124.6, 124.4, 123.1, 120.6, 116.0, 113.9, 47.0, 36.2, 31.7, 30.9, 30.1, 29.6, 28.0, 22.6, 21.6, 14.2.

MS(ESI**):** calculated for $[M+Na]^+$ 548.3, found 548.3.

FTIR (neat, cm^{-1}): 2956, 2920, 2854, 1598, 1448, 1368, 1170, 740, 574.

α_D^{25} = +16.4 º (c 0.73, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC directly. CHIRALPAK OD-H column (1.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 5.2 min (minor), 7.1 min (major).



(*S,E*)-(4-hexylidene-3-vinylheptane-1,7-diyl)dibenzene (3.20) was prepared according to general procedure C but using **L$_7$** instead of **L$_9$** as the ligand, purified by silica gel column chromatography (0-2% diethyl ether in hexanes), and isolated as a colorless oil (144.0 mg, 80%

yield, 10:1 b:l, 75:25 e.r.). The absolute configuration of the chiral center was assigned by analogy. The branched: linear ratio was determined by NMR analysis.

^{1}H NMR (500 MHz, $CDCl_3$) major δ 7.31 – 7.26 (m, 4H), 7.21 – 7.14 (m, 7H), 5.71 (ddd, *J* = 16.9, 10.4, 8.0 Hz, 1H), 5.21 (t, *J* = 7.2 Hz, 1H), 5.03 – 4.95 (m, 2H), 2.63 – 2.53 (m, 5H), 2.11 – 1.95 (m, 4H), 1.84 – 1.64 (m, 4H), 1.37 – 1.24 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H).

minor δ 7.31 – 7.26 (m, 4H), 7.21 – 7.14 (m, 7H),5.50 – 5.34 (m, 2H), 5.13 (t, *J* = 7.2 Hz, 1H), 2.78 – 2.65 (m, 6H), 2.11 – 1.95 (m, 4H), 1.84 – 1.64 (m, 4H), 1.37 – 1.24 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H).

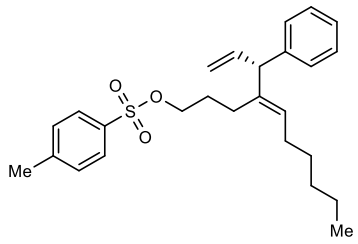
^{13}C NMR (126 MHz, $CDCl_3$) major δ 142.8, 142.5, 142.3, 140.6, 128.5, 128.5, 128.4, 128.4, 126.2, 125.8, 125.7, 114.1, 50.4, 36.3, 35.1, 34.0, 31.8, 31.0, 29.9, 29.7, 28.0, 22.7, 14.3.

GCMS (EI) calculated for $[M]^+$ 360.3, found 360.3.

FTIR (neat, cm^{-1}): 3027, 2925, 2856, 1604, 1496, 1454, 1075, 909, 733, 697.

$\boldsymbol{\alpha_D^{25}}$ = -19.4 ° (c 1.30, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (1.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 20.1 min (major), 31.2 min (minor).



(*S,E*)-4-(1-phenylallyl)dec-4-en-1-yl 4-methylbenzenesulfonate (3.25) was prepared according to general procedure C, purified by silica gel column chromatography (2-8% ethyl acetate in hexanes), and isolated as a colorless oil (170.0 mg, 80% yield, 94:6 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 7.0 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 6.7 Hz, 2H), 6.02 (ddd, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.26 (t, *J* = 7.2 Hz, 1H), 5.08 (dt, *J* = 10.2, 1.5 Hz, 1H), 4.84 (dt, *J* = 17.2, 1.7 Hz, 1H), 3.94 - 3.89 (m, 3H), 2.44 (s, 3H), 2.10 – 2.04 (m, 1H), 1.98 (q, *J* = 7.7 Hz, 2H), 1.86 – 1.80 (m, 1H), 1.63 – 1.56 (m, 2H), 1.35 – 1.24 (m, 6H), 0.89 (t, *J* = 7.1 Hz, 3H).

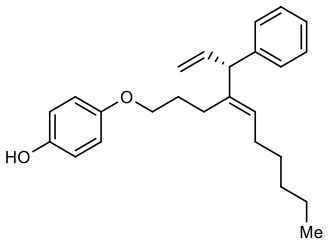
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 142.2, 140.4, 138.8, 133.4, 129.9, 129.2, 128.7, 128.4, 128.0, 126.5, 115.7, 70.5, 55.7, 31.7, 29.7, 28.2, 28.0, 26.2, 22.7, 21.8, 14.2.

GCMS (EI) calculated for $[M]^+$ 426.2, found 426.2.

FTIR (neat, cm^{-1}): 2954, 2932, 2839, 1605, 1512, 1245, 1174, 1028, 962, 741, 833.

α_D^{25} = -51.7 º (0.80, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 45.1 min (major), 56.5 min (minor).



(*S*,*E*)-4-((4-(1-phenylallyl)dec-4-en-1-yl)oxy)phenol (3.26) was prepared according to general procedure C, purified by silica gel chromatography (0-10% ethyl acetate in hexanes), and isolated as a colorless liquid (145.4 mg, 80%, 20:1 b:l, 95:5 e.r.). The absolute configuration of the chiral center was assigned by analogy. The branched: linear ratio was determined by NMR analysis.

^{1}H NMR (500 MHz, $CDCl_3$) major δ 7.31 - 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 6.74 (s, 4H), 6.09 (ddd, *J* = 17.2, 10.2, 7.2 Hz, 1H), 5.29 (t, *J* = 7.2 Hz, 1H), 5.10 (d, *J* = 11.6 Hz, 1H), 4.88 (d, *J* = 17.1 Hz, 1H), 4.02 (d, *J* = 7.3 Hz, 1H), 3.80 (t, *J* = 6.4 Hz, 2H), 2.29 - 2.21 (m, 1H), 2.09 – 2.04 (m, 2H), 2.01 – 1.94 (m, 1H), 1.77 – 1.71 (m, 2H), 1.38 – 1.32 (m, 2H), 1.31 – 1.24 (m, 5H), 0.89 (t, *J* = 6.9 Hz, 3H).

minor δ 7.36 – 7.33 (m, 2H), 7.22 – 7.16 (m, 3H), 6.78 (s, 4H), 6.38 (d, *J* = 15.9 Hz, 1H), 6.22 – 6.15 (m, 1H), 5.39 (t, *J* = 6.3 Hz, 1H), 3.91 – 3.89 (m, 2H), 2.88 (d, *J* = 7.5 Hz, 2H), 2.29 – 2.21 (m, 1H), 2.09 – 2.04 (m, 2H), 2.01 – 1.94 (m, 1H), 1.77 – 1.71 (m, 2H), 1.38 – 1.32 (m, 2H), 1.31 – 1.24 (m, 5H), 0.89 (t, *J* = 6.9 Hz, 3H).

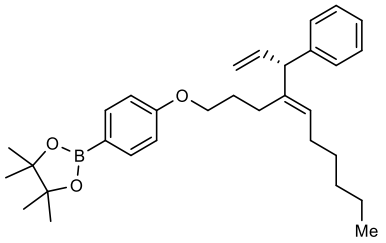
^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 149.5, 142.5, 140.8, 139.8, 128.8, 128.7, 128.4, 126.2, 116.1, 115.7, 115.6, 68.2, 55.7, 31.8, 29.8, 28.5, 28.1, 26.7, 22.7, 14.2.

GCMS (EI): calculated for $[M]^+$ 364.2, found 364.3.

FTIR (neat, cm^{-1}): 3399, 2924, 2861, 1639, 1508, 1414, 1231, 1030, 825, 700.

α_D^{25} = -45.0 º (0.90, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC directly. CHIRALPAK AD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 12.7 min (minor), 13.9 min (major).



(*S,E*)-4,4,5,5-tetramethyl-2-(4-((4-(1-phenylallyl)dec-4-en-1-yl)oxy)phenyl)-1,3,2-dioxaborolane (3.27) was prepared according to general procedure C, purified by silica gel column chromatography (2-8% ethyl acetate in hexanes), and isolated as a colorless oil (153.0 mg, 64% yield, 94:6 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.9 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 2H), 7.23 – 7.16 (m, 3H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.09 (ddd, *J* = 17.2, 10.2, 7.2 Hz, 1H), 5.29 (t, *J* = 7.2 Hz, 1H), 5.10 (dt, *J* = 10.1, 1.1 Hz, 1H), 4.88 (dt, *J* = 17.2, 1.7 Hz, 1H), 4.02 (d, *J* = 7.6 Hz, 1H), 3.88 (t, *J* = 6.4 Hz, 2H), 2.30 – 2.22 (m, 1H), 2.08 – 2.02 (m, 2H), 2.01 – 1.96 (m, 1H), 1.80 – 1.73 (m, 2H), 1.33 (s, 12H), 1.31 – 1.19 (m, 6H), 0.87 (t, *J* = 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 161.7, 142.4, 140.7, 139.6, 136.6, 136.6, 128.8, 128.7, 128.3, 126.4, 115.5, 113.9, 83.6, 67.2, 55.7, 31.8, 29.8, 28.3, 28.0, 27.9, 26.6, 24.9, 22.7, 14.2.

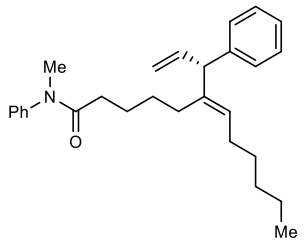
^{11}B NMR (160 MHz, $CDCl_3$) δ 31.7.

MS (ESI): calculated for $[M+Na]^+$ 497.3, found 497.4.

FTIR (neat, cm^{-1}): 2978, 2956, 2872, 1605, 1357, 1245, 1143, 1092, 861, 702, 654.

α_D^{25} = -43.3 º (0.80, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after oxidation of boronic ester moiety to phenol with sodium perborate monohydrate. CHIRALPAK AD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 12.6 min (minor), 13.6 min (major).



(*S*,*E*)-N-methyl-N-phenyl-6-(1-phenylallyl)dodec-6-enamide (3.28) was prepared according to general procedure C, purified by silica gel chromatography (2-8% ethyl acetate in hexanes), and isolated as a colorless liquid (133.3 mg, 66%, 93:7 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.19 – 7.15 (m, 1H), 7.15 – 7.10 (m, 4H), 6.02 (ddd, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.18 (t, *J* = 7.2 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.82 (d, *J* = 17.2 Hz, 1H), 3.93 (d, *J* = 7.0 Hz, 1H), 3.24 (s, 3H), 2.02 – 1.92 (m, 5H), 1.74 – 1.66 (m, 1H), 1.55 – 1.44 (m, 2H), 1.33 – 1.25 (m, 6H), 1.21 – 1.13 (m, 2H), 0.88 (t, *J* = 7.0 Hz, 3H).

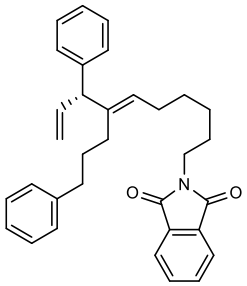
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 144.4, 142.6, 140.9, 140.5, 129.8, 128.8, 128.3, 128.0, 127.8, 127.5, 126.3, 115.4, 55.5, 37.4, 34.1, 31.8, 30.1, 29.8, 28.6, 28.0, 25.7, 22.7, 14.2.

GCMS (EI): calculated for $[M]^+$ 403.3, found 403.3.

FTIR (neat, cm^{-1}):2923, 2864, 1653, 1596, 1412, 1299, 912, 730, 699.

α_D^{25} = -43.6° (0.90, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK AD-H column (5.0% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 23.0 min (major), 25.0 min (minor).



2-[(6*E*,8*S*)-8-phenyl-7-(3-phenylpropyl)deca-6,9-dien-1-yl]-2,3-dihydro-1*H*-isoindole-1,3-dione (3.34) was prepared according to general procedure C, purified by silica gel column chromatography (15% diethyl ether in hexanes), and isolated as a colorless oil (186.0 mg, 78% yield, 97:3 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.84 (m, 2H), 7.72 – 7.68 (m, 2H), 7.32 – 7.26 (m, 3H), 7.25 (s, 1H), 7.22 (d, *J* = 6.3 Hz, 1H), 7.17 (q, *J* = 8.2 Hz, 3H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.12 – 6.04 (m, 1H), 5.25 (t, *J* = 7.2 Hz, 1H), 5.09 (d, *J* = 9.2 Hz, 1H), 4.88 (d, *J* = 18.9 Hz, 1H), 4.01 (d, *J* = 7.2 Hz, 1H), 3.71 (t, *J* = 7.2 Hz, 2H), 2.54 (t, *J* = 7.3 Hz, 2H), 2.15 – 2.09 (m, 1H), 2.03 (q, *J* = 7.2 Hz, 2H), 1.92 – 1.85 (m, 1H), 1.71 (p, *J* = 7.4 Hz, 2H), 1.62 (p, *J* = 7.6 Hz, 2H), 1.46 – 1.33 (m, 4H).

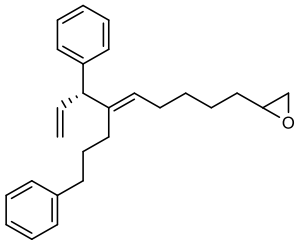
^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 142.5, 142.4, 140.9, 140.7, 133.9, 132.2, 128.7, 128.4, 128.3, 127.5, 126.3, 125.7, 123.2, 115.4, 55.7, 38.0, 36.0, 30.6, 30.0, 29.5, 28.6, 27.9, 26.7.

MS(ESI): calculated for $[M+NH_4]^+$ 495.3, found 495.3.

FTIR (neat, cm^{-1}): 2938, 2853, 1776, 1699, 1397, 1042, 913, 704.

α_D^{25} = -70.1 ° (c 0.67, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (10% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 21.2 min (major), 28.2 min (minor).



2-((*S*,*E*)-5-phenyl-4-(3-phenylpropyl)deca-6,9-dien-1-yl)oxirane (3.35) was prepared according to general procedure C, purified by silica gel column chromatography (1-7% ethyl acetate in hexanes), and isolated as a colorless oil (119.0 mg, 66% yield, 95:5 e.r.). The absolute configuration of the chiral center was assigned by analogy. No diastereomeric peaks were noticed in ^{1}H NMR.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.0 Hz, 2H), 7.26 – 7.23 (m, 2H), 7.22 – 7.15 (m, 4H), 7.11 (d, *J* = 6.9 Hz, 2H), 6.07 (ddd, *J* = 17.2, 10.2, 7.2 Hz, 1H), 5.23 (t, *J* = 7.2 Hz, 1H), 5.09 (dt, *J* = 10.2, 1.5 Hz, 1H), 4.87 (dt, *J* = 17.1, 1.7 Hz, 1H), 4.00 (d, *J* = 7.2 Hz, 1H), 2.92 – 2.88 (m, 1H), 2.75 (t, *J* = 4.5 Hz, 1H), 2.53 (t, *J* = 7.9 Hz, 2H), 2.47 – 2.44

(m, 1H), 2.11 (dt, *J* = 13.6, 8.3 Hz, 1H), 2.03 (q, *J* = 7.1 Hz, 2H), 1.91 – 1.84 (m, 1H), 1.62 (q, *J* = 7.9 Hz, 2H), 1.56 – 1.49 (m, 3H), 1.44 – 1.38 (m, 3H).

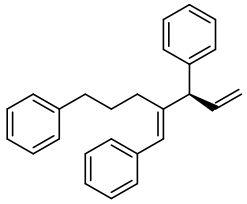
^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 142.4, 141.0, 140.7, 128.7, 128.4, 128.3, 128.3, 127.5, 126.3, 125.8, 115.5, 55.7, 52.4, 47.2, 36.0, 32.4, 30.7, 30.1, 29.8, 27.9, 25.8.

GCMS (EI) calculated for $[M]^+$ 360.2, found 360.2.

FTIR (neat, cm^{-1}): 3025, 2934, 2859, 1490, 1454, 919, 752, 698.

α_D^{25} = -54.5 ° (c 0.69, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after ozonolysis-reduction and TBS protection derivation according to Chapter 4.9. CHIRALPAK AD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 8.4 min (major), 9.4 min (minor).



(*S*,*E*)-(2-(1-phenylallyl)pent-1-ene-1,5-diyl)dibenzene (3.36) was prepared according to general procedure C, purified by silica gel column chromatography (0-3% diethyl ether in hexanes), and isolated as a colorless oil (140.0 mg, 83% yield, 90:10 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 9H), 7.24 – 7.15 (m, 4H), 7.12 – 7.04 (m, 2H), 6.38 (s, 1H), 6.19 (ddd, *J* = 17.1, 10.2, 7.1 Hz, 1H), 5.19 (dt, *J* = 10.2, 1.4 Hz, 1H), 4.97 (dt, *J* = 17.1, 1.6 Hz, 1H), 4.21 (d, *J* = 7.1 Hz, 1H), 2.54 (t, *J* = 7.6 Hz, 2H), 2.43 – 2.33 (m, 1H), 2.16 – 2.03 (m, 1H), 1.85 – 1.69 (m, 2H).

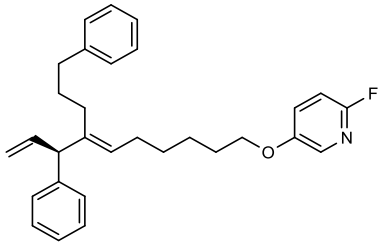
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.6, 142.2, 142.0, 140.4, 138.3, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 127.8, 126.6, 126.3, 125.9, 116.2, 55.8, 36.0, 30.6, 30.3.

GCMS (EI) calculated for $[M]^+$ 338.2, found 338.2.

FTIR (neat, cm^{-1}): 3026, 2935, 2856, 1739, 1600, 1493, 1274, 1253, 1161, 745, 697.

$\boldsymbol{\alpha_D^{25}}$ = -41.2 ° (c 1.06, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (5.0% 2-PrOH in hexanes, 1.0 mL/min, detected at 254 nm wavelength) with t_r = 23.0 min (major), 37.7 min (minor).



(*S,E*)-2-fluoro-5-((8-phenyl-7-(3-phenylpropyl)deca-6,9-dien-1-yl)oxy)pyridine (3.37) was prepared according to general procedure C, purified by silica gel column chromatography (0-10% diethyl ether in hexanes), and isolated as a colorless oil (177.5 mg, 80% yield, 97:3 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 3.2 Hz, 1H), 7.33 – 7.24 (m, 5H), 7.23 – 7.13 (m, 4H), 7.10 (d, *J* = 7.5 Hz, 2H), 6.68 (dd, *J* = 9.0, 3.5 Hz, 1H), 6.07 (ddd, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.24 (t, *J* = 7.2 Hz, 1H), 5.09 (dt, *J* = 10.2, 1.6 Hz, 1H), 4.87 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.24 (t, *J* = 6.7 Hz, 2H), 4.00 (d, *J* = 7.1 Hz, 1H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.16 – 2.06 (m, 1H), 2.04 (q, *J* = 7.0 Hz, 2H), 1.92 – 1.82 (m, 1H), 1.79 – 1.71 (m, 2H), 1.65 – 1.58 (m, 2H), 1.47 – 1.37 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 155.4 (d, $J_{C\text{-}F}$ = 245.2 Hz), 142.5 (d, $J_{C\text{-}F}$ = 7.7 Hz), 140.9, 140.8, 133.2 (d, $J_{C\text{-}F}$ = 25.9 Hz), 128.8, 128.5, 128.4, 128.3, 127.7, 126.7, 126.5, 126.4, 125.8, 115.5, 111.7 (d, $J_{C\text{-}F}$ = 4.5 Hz), 66.6, 55.8, 36.1, 30.7, 30.1, 29.8, 29.0, 28.0, 25.9.

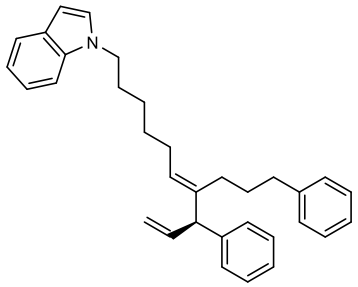
^{19}F NMR (470 MHz, $CDCl_3$) δ -142.7.

MS (ESI) calculated for $[M+H]^+$ 444.3, found 444.3.

FTIR (neat, cm^{-1}): 3026, 2930, 2864, 1740, 1606, 1487, 1447, 1225, 825, 735, 699.

$\boldsymbol{\alpha_D^{25}}$ = -43.2 ° (c 1.14, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (5.0% 2-PrOH in hexanes, 1.0 mL/min, detected at 220 nm wavelength) with t_r = 15.0 min (major), 19.9 min (minor).



(*S,E*)-1-(8-phenyl-7-(3-phenylpropyl)deca-6,9-dien-1-yl)-1H-indole (3.38) was prepared according to general procedure C, purified by silica gel column chromatography (0-10% diethyl ether in hexanes), and isolated as a colorless oil (185.2 mg, 83% yield, 95:5 e.r.). The absolute configuration of the chiral center was assigned by analogy.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.25 (m, 8H), 7.22 – 7.13 (m, 6H), 6.55 (d, *J* = 3.2 Hz, 1H), 6.10 (ddd, *J* = 17.2, 10.2, 7.2 Hz, 1H), 5.25 (t, *J* = 7.1 Hz, 1H), 5.14 (d, *J* = 10.2 Hz, 1H), 4.92 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.16 (t, *J* = 7.1 Hz, 2H), 4.04 (d, *J* = 7.2 Hz, 1H), 2.57 (t, *J* = 7.7 Hz, 2H), 2.16 – 2.10 (m, 1H), 2.04 (q, *J* = 7.2 Hz, 2H), 1.94 – 1.83 (m, 3H), 1.69 – 1.60 (m, 2H), 1.45 – 1.33 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 142.5, 141.1, 140.7, 136.1, 128.7, 128.7, 128.5, 128.4 (2 C), 127.9, 127.5, 126.4, 125.8, 121.4, 121.1, 119.3, 115.5, 109.5, 101.0, 55.7, 46.5, 36.1, 30.7, 30.3, 30.1, 29.6, 27.9, 26.9.

GCMS (EI) calculated for $[M]^+$ 447.3, found 447.4.

FTIR (neat, cm^{-1}): 3028, 2931, 2856, 1600, 1463, 1452, 1316, 1166, 1012, 909, 736, 699.

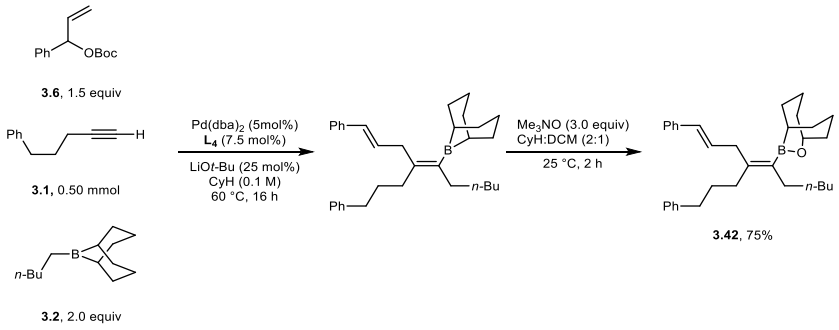
$\boldsymbol{\alpha_D^{25}}$ = -40.8 ° (c 1.14, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC after ozonolysis-reduction and TBS protection derivation according to Chapter 4.9. CHIRALPAK AD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 8.4 min (major), 9.4 min (minor).

3.4.8. Synthesis of Tetrasubstituted Alkenes

3.4.8.1 Oxidative Work-up of the Linear Intermediate 3.39

Scheme 3.8 Oxidative Work-up of the Linear Intermediate



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L4** (14.0 mg, 0.038 mmol, 0.075 equiv), LiO*t*-Bu (10.3 mg, 0.125 mmol, 0.25 equiv) and a stir bar. To the vial was added CyH (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was added to allylic carbonate **3.6** (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.50 mmol, 1.0 equiv), and 1.0 M alkylborane solution in CyH (1.0 mL, 1.0 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 60 °C for 16 h. The reaction mixture was then cooled down to room temperature, followed by addition of solution of Me_3NO (112.5 mg, 3.0 equiv) in DCM (2.5 mL). The mixture was allowed to stir at room temperature for 2 h before being concentrated *in vacuo* and purified by silica gel chromatography (0-5% diethyl ether in hexanes as eluent).

10-((1*E*,4*E*)-1-phenyl-4-(3-phenylpropyl)deca-1,4-dien-5-yl)-9-oxa-10-borabicyclo[3.3.2] decane (3.42) was isolated as a light-yellow oil (175.5 mg, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 5H), 7.26 – 7.20 (m, 3H), 7.21 – 7.12 (m, 4H), 6.31 (d, *J* = 15.9 Hz, 1H), 6.14 (dt, *J* = 15.9, 6.7 Hz, 1H), 4.71 – 4.58 (m, 1H), 3.03 (d, *J* = 6.7 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.11 – 2.02 (m, 4H), 1.92 – 1.83 (m, 4H), 1.79 – 1.64 (m, 7H), 1.54 – 1.43 (m, 5H), 1.30 – 1.24 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 141.5, 138.1, 130.6, 130.6, 128.6 (2C), 128.3, 126.9, 126.2, 125.7, 73.7, 39.9, 36.4, 32.5, 31.8, 30.8, 30.8, 30.7, 30.7, 26.5, 26.4, 22.7, 22.5, 14.3.

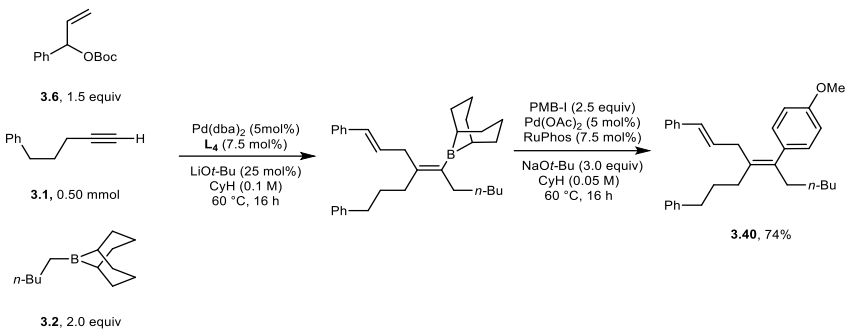
^{11}B NMR (160 MHz, $CDCl_3$) δ 52.3.

MS (ESI) calculated for $[M+NH_4]^+$ 486.4, found 486.4.

FTIR (neat, cm^{-1}): 2926, 2856, 1707, 1606, 1452, 1411, 1298, 969, 735, 698.

3.4.8.2 Arylation of the Linear Intermediate 3.39

Scheme 3.9 Arylation of the Linear Intermediate



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L4** (14.0 mg, 0.038 mmol, 0.075 equiv), LiO*t*-Bu (10.3 mg, 0.125 mmol, 0.25 equiv) and a stir bar. To the vial was added CyH (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was added to allylic carbonate **3.6** (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.50 mmol, 1.0 equiv), and 1.0 M alkylborane solution in CyH (1.0 mL, 1.0 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 60 °C for 16 h.

A separate 20 mL scintillation vial was charged with $Pd(OAc)_2$ (5.5 mg, 0.025 mmol, 0.05 equiv), RuPhos (17.5 mg, 0.038 mmol, 0.075 equiv), NaO*t*-Bu (147.0 mg, 1.5 mmol, 3.0 equiv), and a stir bar. To the vial was added CyH (5 mL) and the resulting mixture was stirred at 60 °C for 5 min. To the catalyst mixture 4-iodoanisole (292.5 mg, 1.25 mmol, 2.5 equiv) was added, and then the previously prepared alkenylborane reaction mixture was directly transferred into the vial. The resulting mixture was vigorously stirred at 60 °C for 16 h. The vial was removed from the glovebox, and the reaction mixture was concentrated *in vacuo* and purified by silica gel chromatography (0-10% diethyl ether in hexanes as eluent).

((1*E*,4*Z*)-4-(1-(4-methoxyphenyl)hexylidene)hept-1-ene-1,7-diyl)dibenzene (**3.40**) was isolated as a light-yellow oil (162.0 mg, 74% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 6H), 7.23 – 7.18 (m, 4H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.21 (dt, *J* = 15.7, 1.6 Hz, 1H), 6.05 (dt, *J* = 15.7, 6.7 Hz, 1H), 3.81 (s, 3H), 2.75 (dd, *J* = 6.7, 1.7 Hz, 2H), 2.67 (t, *J* = 7.7 Hz, 2H), 2.30 – 2.18 (m, 4H), 1.88 – 1.77 (m, 2H), 1.26 – 1.17 (m, 6H), 0.87 – 0.82 (m, 3H).

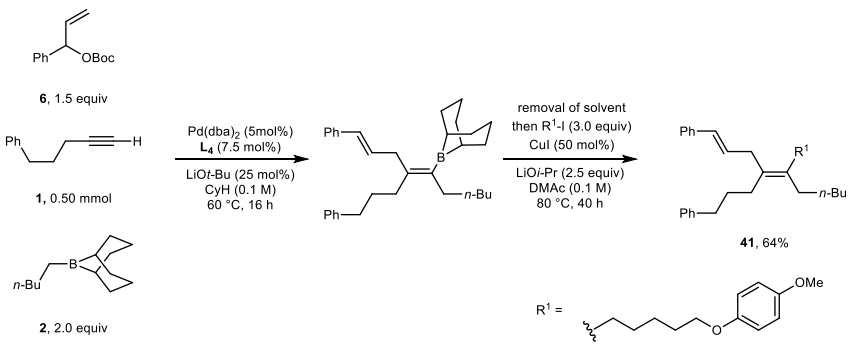
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 142.6, 138.0, 138.0, 136.0, 133.1, 130.5, 129.8, 129.4, 128.6 (2C), 128.4, 126.9, 126.1, 125.8, 113.4, 55.2, 37.0, 36.2, 34.4, 31.9, 30.8, 30.8, 28.2, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 438.3, found 438.4.

FTIR (neat, cm^{-1}): 3031, 2929, 2861, 1607, 1508, 1453, 1242, 1035, 908, 732, 697.

3.4.8.3 Alkylation of the Linear Intermediate 3.39

Scheme 3.10 Alkylation of the Linear Intermediate



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L4** (14.0 mg, 0.038 mmol, 0.075 equiv), LiO*t*-Bu (10.3 mg, 0.125 mmol, 0.25 equiv) and a stir bar. To the vial was added CyH (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was added to allylic carbonate **3.6** (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.50 mmol, 1.0 equiv), and 1.0 M alkylborane solution in CyH (1.0 mL, 1.0 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 60 °C for 16 h. The solvent was removed *in vacuo* in the glovebox, and the residue was dissolved in 5 mL DMAc.

A separate 20 mL scintillation vial was charged with CuI (47.5 mg, 0.25 mmol, 0. 50 equiv), LiO*i*-Pr (82.5 mg, 1.25 mmol, 2.5 equiv), and a stir bar. The previously prepared alkenylborane reaction mixture in DMAc was transferred into the vial, followed by the addition of 1-[(5-iodopentyl)oxy]-4-methoxybenzene[33] (480.3 mg, 1.50 mmol, 3.0 equiv). The resulting mixture was vigorously stirred at 80 °C for 40 h. The vial was removed from the glovebox, and the reaction mixture was diluted with 20 mL brine and extracted with 20 mL ethyl acetate. The organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo.* The crude product was purified by silica gel chromatography (0-10% diethyl ether in hexanes as eluent).

((1*E*,4*Z*)-4-(1-(4-methoxyphenoxy)undecan-6-ylidene)hept-1-ene-1,7-diyl)dibenzene (**3.41**) was isolated as a colorless oil (168.0 mg, 64% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, 6H), 7.21 – 7.15 (m, 4H), 6.81 (s, 4H), 6.31 (d, *J* = 15.7 Hz, 1H), 6.11 (dt, *J* = 15.8, 6.5 Hz, 1H), 3.88 (t, *J* = 6.5 Hz, 2H), 3.76 (s, 3H), 2.91 (d, *J* = 6.5 Hz, 2H), 2.61 (t, *J* = 7.7 Hz, 2H), 2.11 – 2.02 (m, 4H), 2.01 – 1.92 (m, 2H), 1.81 – 1.66 (m, 4H), 1.51 – 1.37 (m, 4H), 1.37 – 1.22 (m, 6H), 0.90 (t, *J* = 7.1 Hz, 3H).

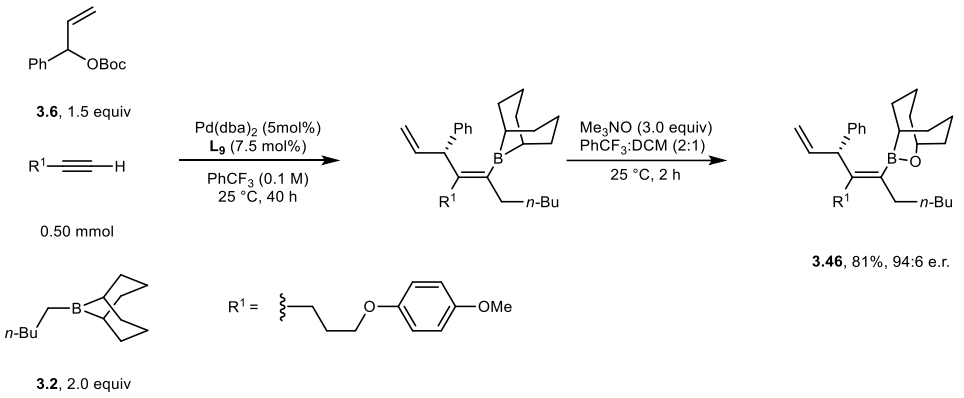
^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 153.4, 142.7, 138.0, 136.0, 130.4, 130.1, 129.6, 128.6, 128.5, 128.4, 126.9, 126.1, 125.7, 115.5, 114.7, 68.7, 55.8, 36.2, 35.4, 32.3, 31.9, 31.5, 30.9, 29.5, 29.1, 27.9, 26.5, 22.8, 14.3.

MS (ESI) calculated for $[M+NH_4]^+$ 542.4, found 542.3.

FTIR (neat, cm^{-1}): 2929, 2858, 1603, 1507, 1453, 1229, 1040, 909, 823, 733, 697.

3.4.8.4 Oxidative Work-up of the Branched Intermediate 3.43

Scheme 3.11 Oxidative Work-up of the Branched Intermediate



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L9** (31.9 mg, 0.038 mmol, 0.075 equiv), and a stir bar. To the vial was added $PhCF_3$ (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was added to allylic carbonate **3.6** (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne 1-methoxy-4-(pent-4-yn-1-yloxy)benzene (0.50 mmol, 1.0 equiv), and 1.0 M alkylborane solution in $PhCF_3$ (1.0 mL, 1.0 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h. To this vial was added the solution of Me_3NO (112.5 mg, 3.0 equiv) in DCM (2.5 mL). The mixture was allowed to stir at room temperature for 2 h before being concentrated *in vacuo* and purified by silica gel chromatography (0-5% diethyl ether in hexanes as eluent).

(*R*,*E*)-11-[1-(4-methoxyphenyl)-5-(1-phenylprop-2-en-1-yl)undec-5-en-6-yl]-10-oxa-11-borabicyclo[4.3.2]undecane (**3.46**) was isolated as a colorless oil (208.2 mg, 81% yield, 94:6 e.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 4H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.83 (d, *J* = 9.2 Hz, 2H), 6.76 (d, *J* = 9.2 Hz, 2H), 6.27 (ddd, *J* = 17.1, 10.3, 6.7 Hz, 1H), 5.28 (d, *J* = 10.2 Hz, 1H), 5.22 (d, *J* = 17.2 Hz, 1H), 4.73 (d, *J* = 3.2 Hz, 1H), 4.61 (d, *J* = 6.9 Hz, 1H), 3.78 (s, 3H), 3.73 – 3.64 (m, 2H), 2.25 (t, *J* = 8.4 Hz, 2H), 2.19 – 2.06 (m, 2H), 1.98 – 1.87 (m, 5H), 1.76 – 1.36 (m, 15H), 1.24 – 1.15 (m, 1H), 0.96 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.6, 153.3, 143.3, 142.1, 139.4, 128.4, 128.2, 126.1, 116.5, 115.4, 114.6, 73.8, 68.7, 55.8, 55.8, 32.6, 31.8, 31.7, 30.9, 30.5, 30.3, 26.5, 26.4, 26.2, 22.7, 22.5, 22.4, 14.2.

^{11}B NMR (160 MHz, $CDCl_3$) δ 50.7.

MS (ESI) calculated for $[M+NH_4]^+$ 532.4, found 532.3.

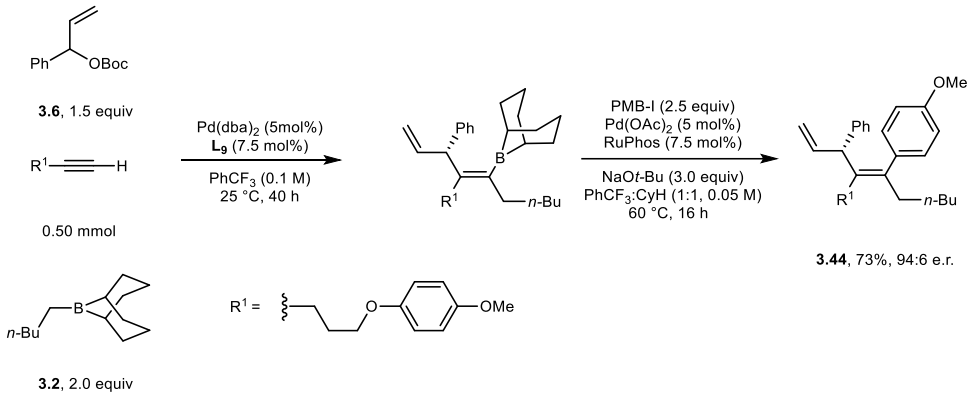
FTIR (neat, cm^{-1}): 2923, 2856, 1507, 1450, 1228, 1040, 910, 823, 731, 700.

$\boldsymbol{\alpha_D^{25}}$ = +63.3 ° (c 1.01, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC analysis directly using the product. CHIRALPAK OD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 6.5 min (minor), 8.3 min (major).

3.4.8.5 Arylation of the Branched Intermediate 3.43

Scheme 3.12 Arylation of the Branched Intermediate



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L$_9$** (31.9 mg, 0.038 mmol, 0.075 equiv), and a stir bar. To the vial was added $PhCF_3$ (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was added to allylic carbonate **3.6** (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne (0.50 mmol, 1.0 equiv), and 1.0 M alkylborane solution in CyH (1.0 mL, 1.0 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 60 °C for 16 h.

A separate 20 mL scintillation vial was charged with $Pd(OAc)_2$ (5.5 mg, 0.025 mmol, 0.05 equiv), RuPhos (17.5 mg, 0.038 mmol, 0.075 equiv), NaO*t*-Bu (147.0 mg, 1.5 mmol, 3.0 equiv), and a stir bar. To the vial was added CyH (5 mL) and the resulting mixture was stirred at 60 °C for 5 min. To the catalyst mixture 4-iodoanisole (292.5 mg, 1.25 mmol, 2.5 equiv) was added, and then the previously prepared alkenylborane reaction mixture was transferred into the vial. The resulting mixture was vigorously stirred at 60 °C for 16 h. The vial was removed from the glovebox, and the reaction mixture was concentrated *in vacuo* and purified by silica gel chromatography (0-10% diethyl ether in hexanes as eluent).

(*R*,*Z*)-1-methoxy-4-(4-(3-(4-methoxyphenoxy)propyl)-3-phenyldeca-1,4-dien-5-yl)benzene (**3.44**) was isolated as a yellow oil (171.0 mg, 73% yield, 94:6 e.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 3H), 7.20 – 7.13 (m, 3H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H), 6.12 (ddd, *J* = 16.9, 10.3, 6.4 Hz, 1H), 5.22 (d, *J* = 10.2 Hz, 1H), 5.07 (dd, *J* = 17.2, 1.7 Hz, 1H), 4.36 (d, *J* = 6.4 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.75 – 3.66 (m, 2H), 2.48 – 2.42 (m, 1H), 2.38 – 2.22 (m, 2H), 2.20 – 2.14 (m, 1H), 1.76 – 1.66 (m, 1H), 1.32 – 1.24 (m, 6H), 1.23 – 1.14 (m, 1H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 153.7, 153.2, 143.1, 139.4, 139.4, 135.4, 135.1, 129.6, 128.3, 128.2, 126.1, 116.3, 115.3, 114.6, 113.5, 68.5, 55.7, 55.2, 52.3, 34.5, 32.0, 30.3, 28.0, 26.1, 22.7, 14.2.

GCMS (EI) calculated for $[M]^+$ 484.3, found 484.4.

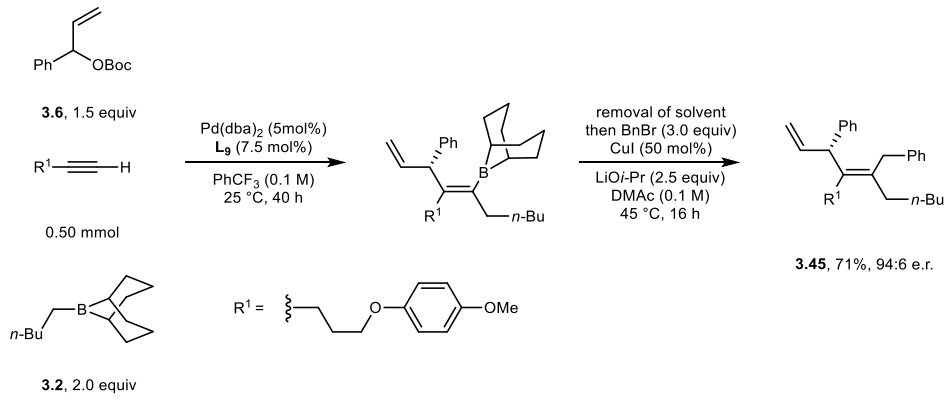
FTIR (neat, cm^{-1}): 2957, 2933, 2859, 1507, 1229, 1158, 1037, 910, 731, 702.

$\boldsymbol{\alpha_D^{25}}$ = +67.2 ° (c 0.87, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC analysis after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK OD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 16.7 min (minor), 19.7 min (major).

3.4.8.6 Alkylation of the Branched Intermediate 3.43

Scheme 3.13 Alkylation of the Branched Intermediate



In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.05 equiv), **L$_9$** (31.9 mg, 0.038 mmol, 0.075 equiv), and a stir bar. To the vial was added $PhCF_3$ (4 mL) and the resulting mixture was stirred at 60 °C for 5 min. The reaction mixture was added to allylic carbonate **3.6** (0.75 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne (0.50 mmol, 1.0 equiv), and 1.0 M alkylborane solution in $PhCF_3$ (1.0

mL, 1.0 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h. The solvent was removed *in vacuo* in the glovebox, and the residue was dissolved in 5 mL DMAc.

A separate 20 mL scintillation vial was charged with CuI (47.5 mg, 0.25 mmol, 0. 50 equiv), LiO*i*-Pr (82.5 mg, 1.25 mmol, 2.5 equiv), and a stir bar. The previously prepared alkenylborane reaction mixture in DMAc was transferred into the vial, followed by the addition of benzyl bromide (256.5 mg, 1.50 mmol, 3.0 equiv). The resulting mixture was vigorously stirred at 45 °C for 16 h. The vial was removed from the glovebox, and the reaction mixture was diluted with 20 mL brine and extracted with 20 mL ethyl acetate. The organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo.* The crude product was purified by silica gel chromatography (0-5% diethyl ether in hexanes as eluent).

(*R*,*Z*)-1-[6-benzyl-5-(1-phenylprop-2-en-1-yl)undec-5-en-1-yl]-4-methoxybenzene (**3.45**) was isolated as a colorless oil (166.0 mg, 71% yield, 94:6 e.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 4H), 7.23 – 7.17(m, 6H), 6.81 (d, *J* = 9.2 Hz, 2H), 6.75 (d, *J* = 9.2 Hz, 2H), 6.15 (ddd, *J* = 16.9, 10.1, 6.9 Hz, 1H), 5.20 (dd, *J* = 10.1, 1.6 Hz, 1H), 5.06 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.63 (d, *J* = 7.0 Hz, 1H), 3.76 (s, 3H), 3.76 – 3.69 (m, 2H), 3.58 – 3.45 (m, 2H), 2.19 (t, *J* = 8.3 Hz, 2H), 2.11 – 3.06 (m, 2H), 1.80 – 1.72 (m, 1H), 1.34 – 1.25 (m, 7H), 0.91 – 0.88 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.7, 153.3, 142.8, 140.9, 139.1, 135.6, 134.8, 128.6, 128.4, 128.4, 128.3, 126.3, 125.9, 116.5, 115.4, 114.7, 68.6, 55.9, 51.5, 36.8, 32.4, 31.7, 30.2, 28.6, 26.8, 22.7, 14.3.

GCMS (EI) calculated for $[M]^+$ 468.3, found 468.4.

FTIR (neat, cm^{-1}): 2957, 2933, 2859, 1507, 1229, 1158, 1037, 910, 731, 702.

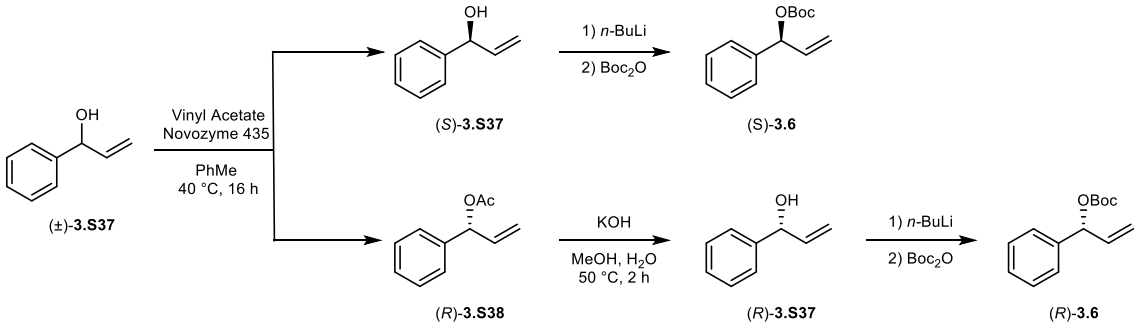
$\boldsymbol{\alpha_D^{25}}$ = +88.4 ° (c 0.40, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC analysis after hydroboration-oxidation derivation according to General Procedure D. CHIRALPAK AD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 20.0 min (major), 28.1 min (minor).

3.4.9 Mechanistic Study

3.4.9.1 Preparation of Enantioenriched Allylic Carbonates

Scheme 3.14 Preparation of Enantioenriched Allylic Carbonates



(*R*)-**3.6** and (*S*)-**3.6** were synthesized using a modified literature procedure and have been characterized previously. [35]

To a 50 mL round bottom flask was added (±)-**3.S37** (1.34 g, 10 mmol), vinyl acetate (4.30 g, 50 mmol), Novozyme 435 (200 mg) and a stir bar. Anhydrous PhMe (10 mL, 1.0 M) was added, and the resulting mixture was stirred at 40 °C for 16 h. The resulting mixture was filtered with Celite, and the filtrate was concentrated *in vacuo.* The residue was purified by silica gel chromatography (0-20% ethyl acetate in hexanes) to afford (*R*)- **3.S38** (845 mg, 4.80 mmol, 48% yield) and (*S*)- **3.S37** (616 mg, 4.60 mmol, 46% yield).

The resulting acetate (*R*)- **3.S38** and a stir bar were placed in a 25 mL round bottom flask, and a solution of KOH (403 mg, 7.2 mmol, 1.5 equiv) in H_2O and MeOH (1:1, 10 mL) was slowly added. The resulting mixture was stirred at 50 °C for 2 h and then extracted with ethyl acetate (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford (*R*)- **3.S37** with 95% yield (611 mg).

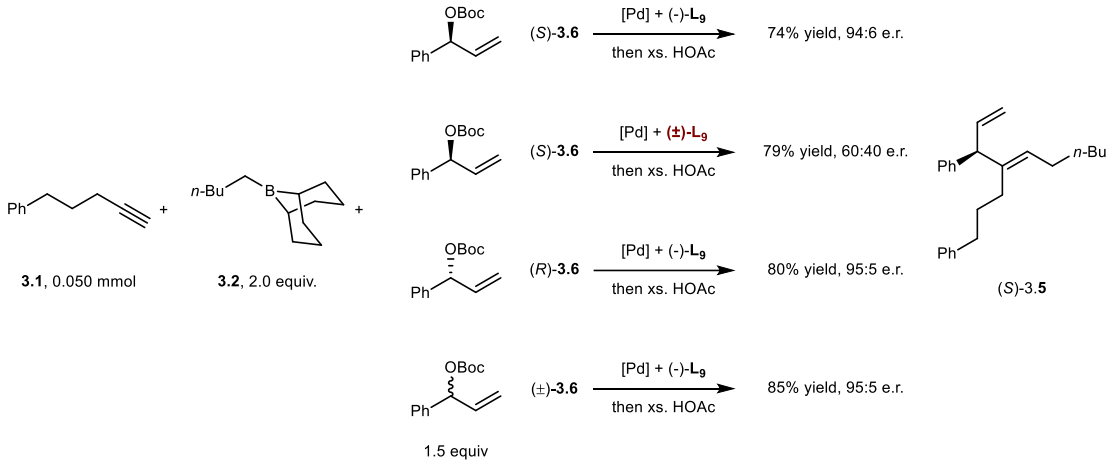
(*S*)- **3.6** was prepared according to General Procedure E using (*S*)- **3.S37**, and isolated as a light-yellow liquid (818 mg, 3.5 mmol, 76% yield, 99:1 e.r.). Spectral data matches that of (±)-**3.6**.

(*R*)- **3.6** was prepared according to General Procedure E using (*R*)- **3.S37**, and isolated as a light-yellow liquid (886 mg, 3.8 mmol, 83%, 1:99 e.r.). Spectral data matches that of (±)-**3.6**.

Enantiomeric ratio was determined by chiral HPLC analysis. CHIRALPAK AD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 3.2 min (*R*), 3.6 min (*S*).

3.4.9.2 Mechanistic Studies of Kinetic Resolution

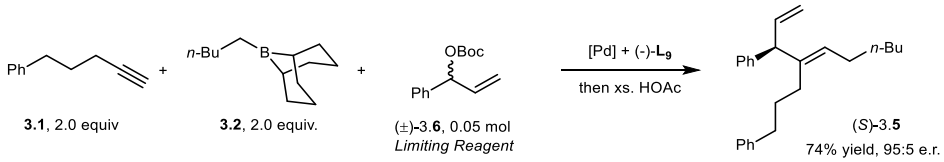
Scheme 3.15 Kinetic Resolution



In a nitrogen-filled glovebox, a 4 mL dram vial was charged with $Pd(dba)_2$ (1.4 mg, 0.0025 mmol, 0.05 equiv), **L9** or (±)**-L9** (3.2 mg, 0.0038 mmol, 0.075 equiv), internal standard 1,3,5-trimethoxylbenzene (4.2 mg, 0.025 mmol, 0.5 equiv) and a stir bar. To the vial was added $PhCF_3$ (400 μL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added the corresponding allylic carbonate **3.6** (0.075 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.050 mmol, 1.0 equiv), and 1.0 M alkylborane **3.2** solution in $PhCF_3$ (100 μL, 0.10 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h.

The vial was removed from the glovebox. Acetic acid (20 μL) was then added. The mixture was allowed to stir at room temperature for 25 min before an aliquot (50 μL) was taken and analyzed by gas chromatography. The enantiomeric ratios were determined by HPLC analysis according to General Procedure D.

Scheme 3.16 Allylic Carbonate as the Limiting Reagent



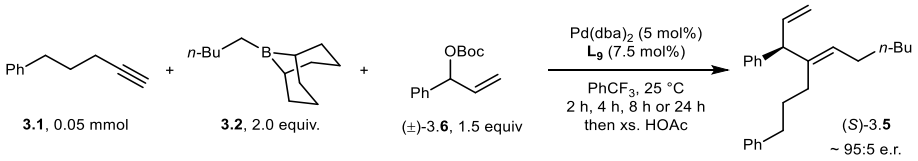
In a nitrogen-filled glovebox, a 4 mL dram vial was charged with $Pd(dba)_2$ (1.4 mg, 0.0025 mmol, 0.05 equiv), **L9** (3.2 mg, 0.0038 mmol, 0.075 equiv), internal standard 1,3,5-trimethoxylbenzene (4.2 mg, 0.025 mmol, 0.5 equiv) and a stir bar. To the vial was added $PhCF_3$ (400 μL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added racemic allylic carbonate **3.6** (0.05 mmol, 1.0 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The

resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.10 mmol, 2.0 equiv), and 1.0 M alkylborane **3.2** solution in $PhCF_3$ (100 µL, 0.10 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h.

The vial was removed from the glovebox. Acetic acid (20 µL) was then added. The mixture was allowed to stir at room temperature for 25 min before an aliquot (50 µL) was taken and analyzed by gas chromatography. The enantiomeric ratio of alkene **3.5** was determined by HPLC analysis according to General Procedure D.

3.4.9.3 Reaction Monitoring

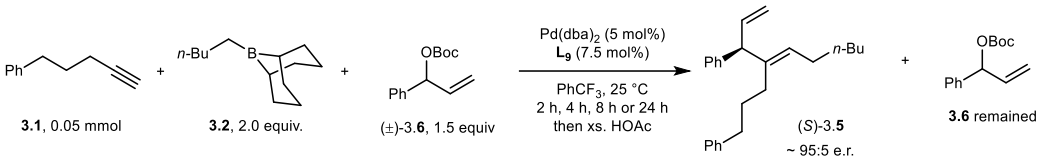
Scheme 3.17 Reaction Monitoring (I)



In a nitrogen-filled glovebox, a 4 mL dram vial was charged with $Pd(dba)_2$ (1.4 mg, 0.0025 mmol, 0.05 equiv), **L9** (3.2 mg, 0.0038 mmol, 0.075 equiv), internal standard 1,3,5-trimethoxylbenzene (4.2 mg, 0.025 mmol, 0.5 equiv) and a stir bar. To the vial was added $PhCF_3$ (400 µL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added allylic carbonate **3.6** (0.075 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.05 mmol, 1.0 equiv), and 1.0 M alkylborane **3.2** solution in $PhCF_3$ (100 µL, 0.10 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 2 h. Three additional reactions were set according to the same procedure but were allowed to be stirred at 25 °C for 4 h, 8 h and 24 h before addition of acetic acid.

Those vials were removed from the glovebox. Acetic acid (20 µL) was then added. The mixtures were allowed to stir at room temperature for 25 min before aliquots (50 µL) were taken and analyzed by gas chromatography. The enantiomeric ratios of alkene **3.5** were determined by HPLC analysis according to General Procedure D. Table 3.15 entry 1-4 shows the conversions of terminal alkyne **3.1** and the enantiomeric excess of alkene **3.5** in each reaction.

Scheme 3.18 Reaction Monitoring (II)

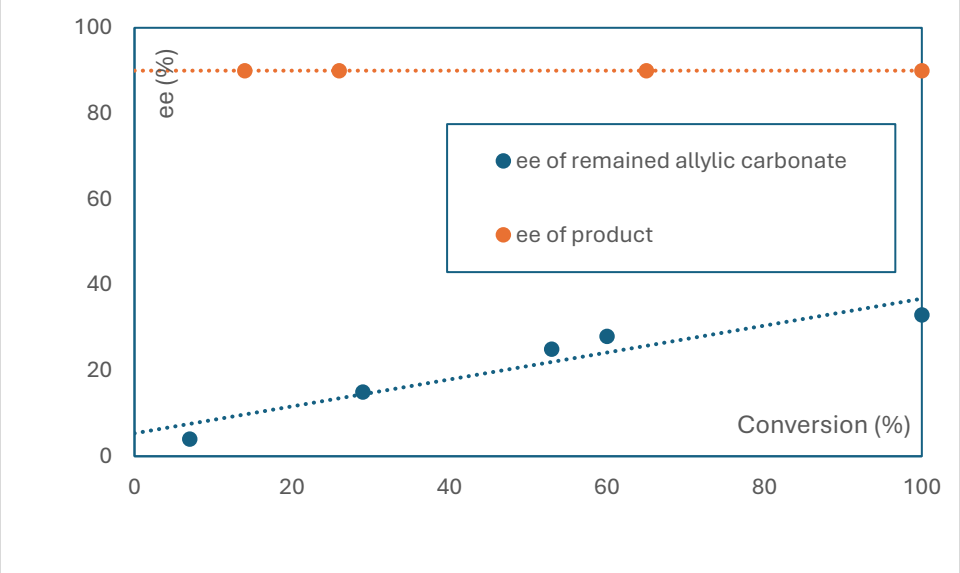


In a nitrogen-filled glovebox, five reactions were conducted according to the same procedure above, and they were allowed to be stirred at 25 °C for 2 h, 4 h, 6 h, 8 h and 24 h before addition of acetic acid. Those vials were removed from the glovebox. Acetic acid (20 μL) was then added. The mixtures were allowed to stir at room temperature for 25 min before aliquots (50 μL) were taken and analyzed by gas chromatography. The remaining reaction mixtures were passed through a short silica plug with ethyl acetate separately. The allylic carbonate **3.6** remaining in each reaction mixture was isolated by prep-TLC (5% ethyl acetate in hexanes) and analyzed by HPLC. Table 3.15 entry 5~9 shows the conversions of terminal alkyne **3.1** and the enantiomeric excess of allylic carbonate **3.6** remaining in each reaction. Figure 3.20 shows the results of reaction monitoring.

Table 3.15 Reaction Monitoring

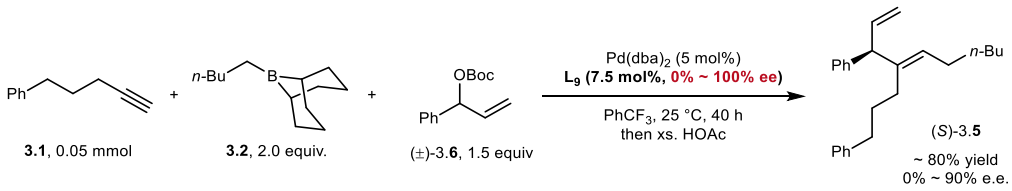
Entry	*Time (h)*	*Conversion of 3.1 (%)*	*e.e. of 3.5 (%)*	*e.e. of 3.6 (%)*
1	2	14	90	
2	4	26	90	
3	8	65	90	
4	24	100	90	
5	2	7		4
6	4	29		15
7	6	53		25
8	8	60		28
9	24	100		33

Figure 3.20 Reaction Monitoring



3.4.9.4 Non-linear Effect Testing

Scheme 3.19 Non-linear Effect Testing



In a nitrogen-filled glovebox, a series of ligand mixtures with different enantiomeric excesses were prepared by mixing enantiomeric pure **L9** and racemic **L9** in the corresponding ratio. A 4 mL dram vial was charged with $Pd(dba)_2$ (1.4 mg, 0.0025 mmol, 0.05 equiv), the ligand (100% e.e., 3.2 mg, 0.0038 mmol, 0.075 equiv), internal standard 1,3,5-trimethoxylbenzene (4.2 mg, 0.025 mmol, 0.5 equiv) and a stir bar. To the vial was added $PhCF_3$ (400 μL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added allylic carbonate **3.6** (0.075 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of terminal alkyne **3.1** (0.05 mmol, 1.0 equiv), and 1.0 M alkylborane **3.2** solution in $PhCF_3$ (100 μL, 0.10 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h. Six additional reactions were set according to the same procedure but using ligand with 0%, 20%, 40%, 50%, 60% and 80% enantiomeric excesses.

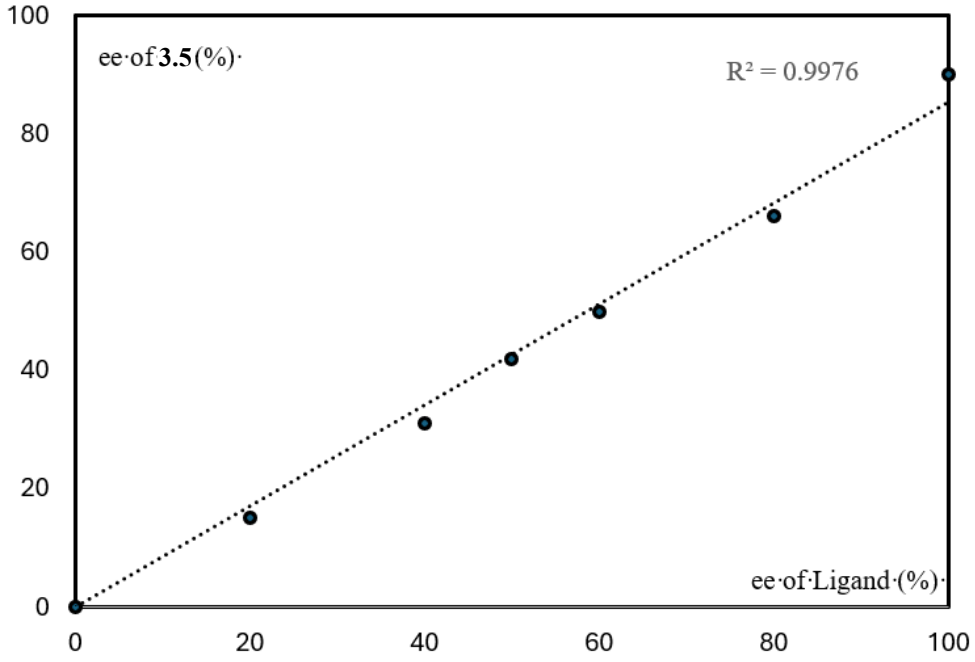
Those vials were removed from the glovebox. Acetic acid (20 μL) was then added. The mixtures were allowed to stir at room temperature for 25 min before aliquots (50 μL) were taken and analyzed by gas chromatography. The enantiomeric ratios of alkene **3.5** were determined by HPLC

analysis according to General Procedure D. Table 3.16 shows the enantiomeric excess of the ligand and alkene **3.5** in each reaction. Figure 3.21 shows that there is no NLE in this catalytic reaction.

Table 3.16 Non-linear Effect Study

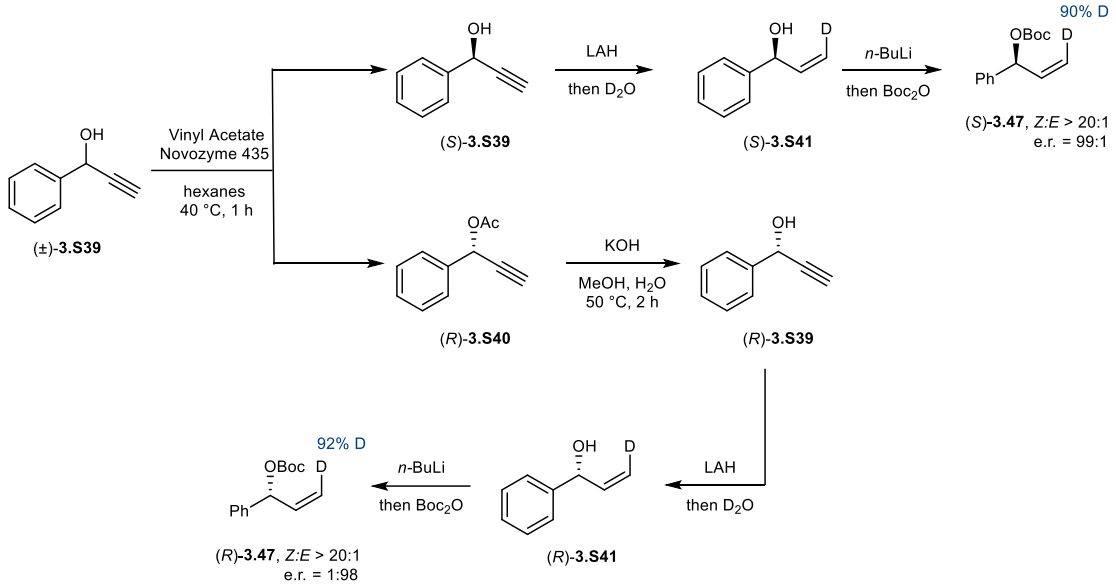
Entry	*e.e. of ligand (%)*	*e.e. of 3.5 (%)*
1	0	0
2	20	15
3	40	31
4	50	42
5	60	50
6	80	66
7	100	90

Figure 3.21 Non-linear Effect Study



3.4.9.5 Preparation of Deuterium-labeled Allylic Carbonates

Scheme 3.20 Preparation of Deuterium-labeled Allylic Carbonates



(*R*)-**3.47** and (*S*)-**3.47** were synthesized using a modified literature procedure and have been characterized before. [26, 36]

To a 50 mL round bottom flask was added (±)-**3.S39** (1.34 g, 10 mmol), vinyl acetate (4.30 g, 50 mmol), Novozyme 435 (750 mg) and a stir bar. Hexanes (20 mL, 0.5 M) was added, and the resulting mixture was stirred at 40 °C for 1 h. The resulting mixture was filtered with Celite®, and the filtrate was concentrated *in vacuo.* The residue was purified by silica gel chromatography (0-20% ethyl acetate in hexanes) to afford (*R*)-**3.S40** (810 mg, 4.6 mmol, 46% yield) and (*S*)-**3.S39** (620 mg, 4.6 mmol, 46% yield).

The resulting acetate (*R*)-**3.S40** and a stir bar were placed in a 25 mL round bottom flask, and a solution of KOH (403 mg, 7.2 mmol, 1.5 equiv) in H_2O and MeOH (1:1, 10 mL) was slowly added. The resulting mixture was stirred at 50 °C for 2 h and then extracted with ethyl acetate (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford (*R*)-**3.S39** with 90% yield (550 mg, 4.1 mmol).

Spectral data of (*S*)-**3.S39** and (*R*)-**3.S39** match that of (±)-**3.S39**.

(*R*)-**3.S41** and (*S*)-**3.S41** were synthesized using a modified literature procedure. [26]

A flame-dried, 50 mL round-bottomed flask was charged with $LiAlH_4$ powder (157 mg, 4.1 mmol, 0.90 equiv), anhydrous THF (10 mL), and cooled to 0 °C. (*S*)-**3.S39** (620 mg, 4.6 mmole) was added dropwise over 5 minutes. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The reaction was quenched slowly with D_2O (1.0 mL, Aldrich 99.9%) at

0°C. The resulting mixture was treated with 1.0 M aqueous solution of NaOH (5 mL) and stirred at room temperature for 2 h. The resulting mixture was filtered, and the filtrate was extracted with ethyl acetate (10 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product (610 g, 4.5 mmol, 98% yield) was used in the next reaction without further purification.

(*R*)-**3.S41** was synthesized from (*R*)-**3.S39** using the same procedure.

(*S*)-**3.47** was prepared according to General Procedure E using (*S*)-**3.S41**, and isolated as a light-yellow liquid (740 mg, 3.2 mmol, 70%). Deuterium incorporation ratio was determined by NMR analysis. Enantiomeric ratio was determined by HPLC analysis using racemic **3.6** as the racemic sample.

(*R*)-**3.47** was prepared according to General Procedure E using (*R*)-**3.S41**, and isolated as a light-yellow liquid (705 mg, 3.0 mmol, 75%). Deuterium incorporation ratio was determined by NMR analysis. Enantiomeric ratio was determined by HPLC analysis using racemic **3.6** as the racemic sample. CHIRALPAK AD-H column (0.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 3.2 min (*R*), 3.6 min (*S*).

Figure 3.22 NMR Analysis of (*S*)-3.47

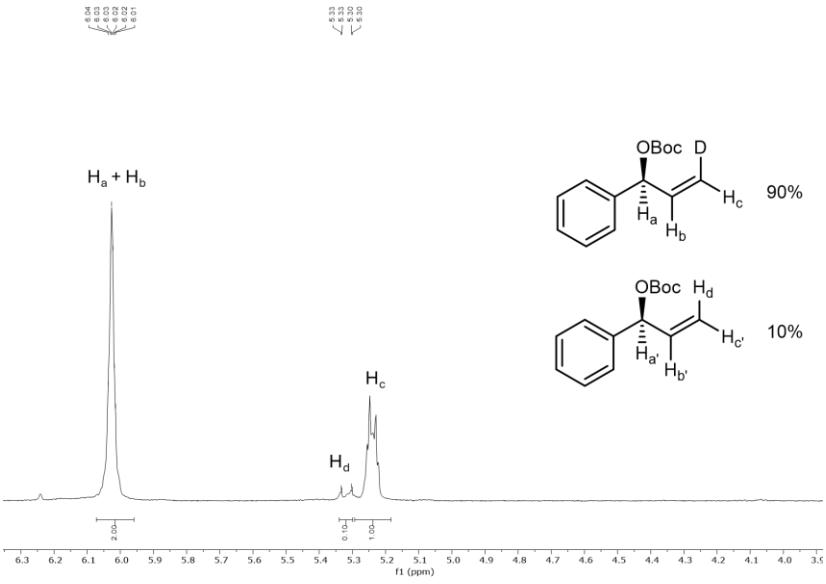
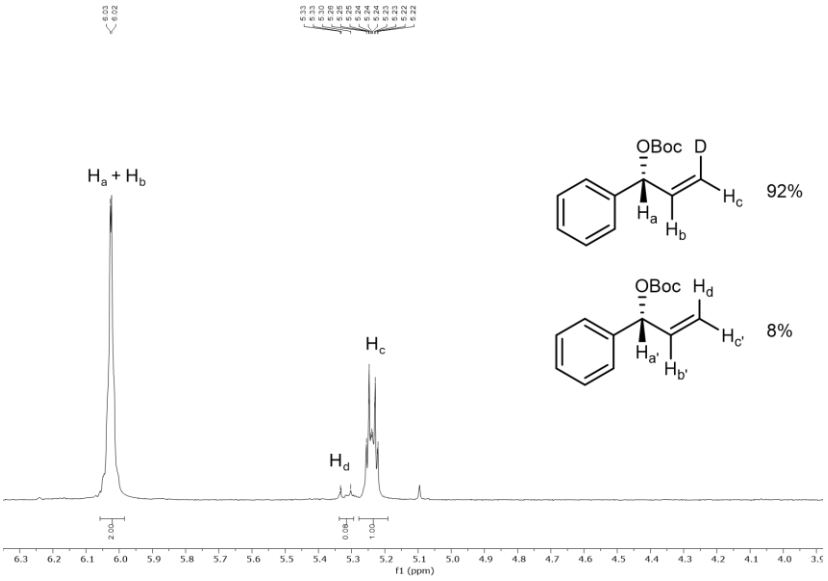
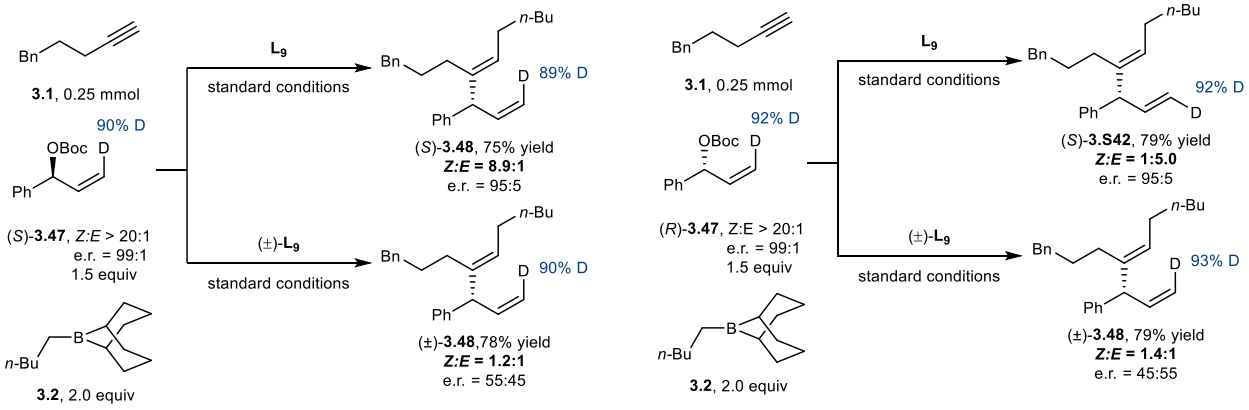


Figure 3.23 NMR Analysis of (*R*)-3.47



3.4.9.6 D-labeling Experiments

Scheme 3.21 D-labeling Experiments

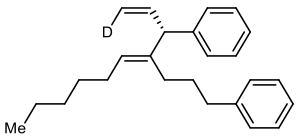


In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $Pd(dba)_2$ (7.2 mg, 0.0125 mmol, 0.05 equiv), **L9** or racemic **L9** (16.0 mg, 0.019 mmol, 0.075 equiv) and a stir bar. To the vial was added $PhCF_3$ (2 mL) and the resulting mixture was stirred at 60 °C for 5 min. To the reaction mixture was added (*S*)-**3.48** or (*R*)-**3.48** (88 mg, 0.375 mmol, 1.5 equiv) and the reaction mixture was stirred at 60 °C for 15 min. The resulting light-yellow solution was cooled down to room temperature followed by addition of **3.1** (36 mg, 0.25 mmol, 1.0 equiv), and 1.0 M alkylborane **3.2**

solution in $PhCF_3$ (0.5 mL, 0.50 mmol, 2.0 equiv). The reaction mixture was vigorously stirred at 25 °C for 40 h.

The vial was removed from the glovebox. Acetic acid (100 μL) was then added, and the mixture was allowed to stir at room temperature for 25 min. The reaction mixture was then neutralized by the addition of saturated aqueous $NaHCO_3$ solution (5 mL) and extracted with ethyl acetate (10 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was further purified by silica gel column chromatography, eluted with 2% diethyl ether in hexanes.

The deuterium incorporation ratios and *Z*/*E* ratios were determined by NMR analysis of purified products. The enantiomeric ratios were determined by HPLC analysis following General Procedure D using racemic **3.5** as the reference.



[(*S*,4*E*,6*Z*)-4-hexylidenehept-6-ene-1,5-diyl-7-*d*]dibenzene (*S*-**3.48**) was prepared according to the procedure above using (*S*)-**3.47** and **L9**, purified by silica gel column chromatography (2% diethyl ether in hexanes), and isolated as a colorless oil (62.5 mg, 75% yield, 95:5 e.r., 89% D-labeled, 8.9:1 *Z*/*E* ratio of the D-labeled C-C double bond). The absolute configuration of the chiral center was assigned by analogy. The deuterium incorporation ratios and *Z*/*E* ratios were determined by NMR analysis (see below).

^{1}H NMR (500 MHz, $CDCl_3$) major isomer δ 7.30 – 7.24 (m, 4H), 7.22 – 7.10 (m, 6H), 6.21 – 5.98 (m, 1H), 5.25 (t, *J* = 7.1 Hz, 1H), 5.08 (d, *J* = 10.2 Hz, 1H), 4.00 (d, *J* = 7.2 Hz, 1H), 2.59 – 2.45 (m, 2H), 2.15 – 2.08 (m, 1H), 2.01 (q, *J* = 7.3 Hz, 2H), 1.91 – 1.84 (m, 1H), 1.67 – 1.57 (m, 2H), 1.37 – 1.25 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) major isomer δ 142.6, 142.6, 140.8, 140.6, 128.8, 128.5, 128.4, 128.3, 128.1, 126.3, 125.8, 116.2 (t, $J_{C\text{-}D}$ = 23.7 Hz), 55.7, 36.1, 31.8, 30.7, 30.1, 29.8, 28.1, 22.7, 14.3.

GCMS (EI) calculated for $[M]^+$ 333.3, found 333.3.

FTIR (neat, cm^{-1}): 3029, 2927, 2862, 1600, 1492, 1452, 1216, 755, 698

$\boldsymbol{\alpha_D^{25}}$ = -62.0 ° (c 0.94, $CHCl_3$).

Enantiomeric ratio was determined by chiral HPLC analysis after hydroboration-oxidation derivation according to General Procedure D. (rac)-**3.5** was used as the racemic reference. CHIRALPAK AD-H column (2.5% 2-PrOH in hexanes, 1.5 mL/min, detected at 220 nm wavelength) with t_r = 10.0 min (major), 13.5 min (minor).

The deuterium incorporation ratios and *Z*/*E* ratios were determined by NMR analysis.

Figure 3.24 NMR Analysis of (*S*)-3.48

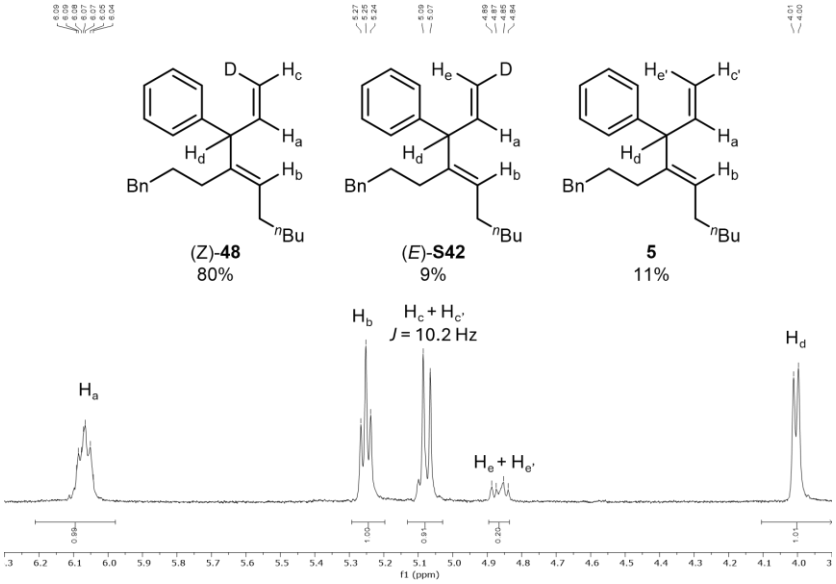


Figure 3.25 NMR Analysis of (±)-3.48

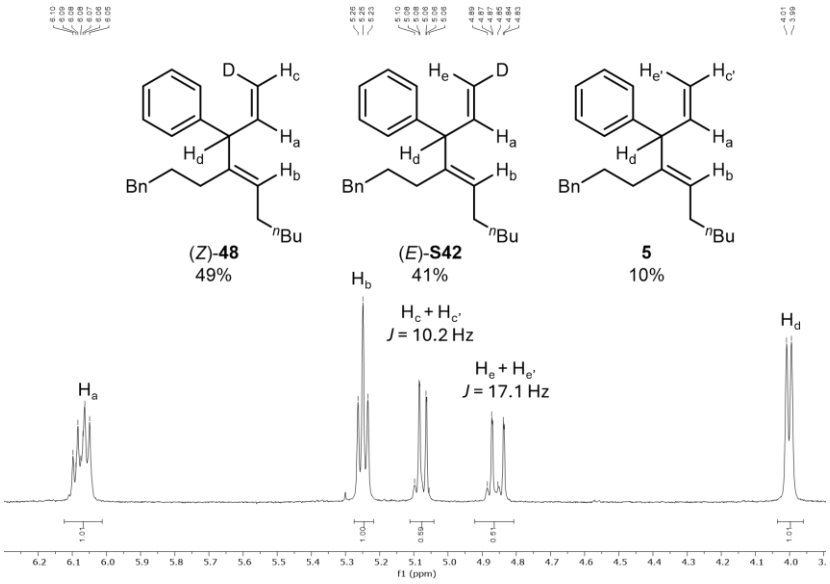


Figure 3.26 NMR Analysis of (*S*)-3.S42

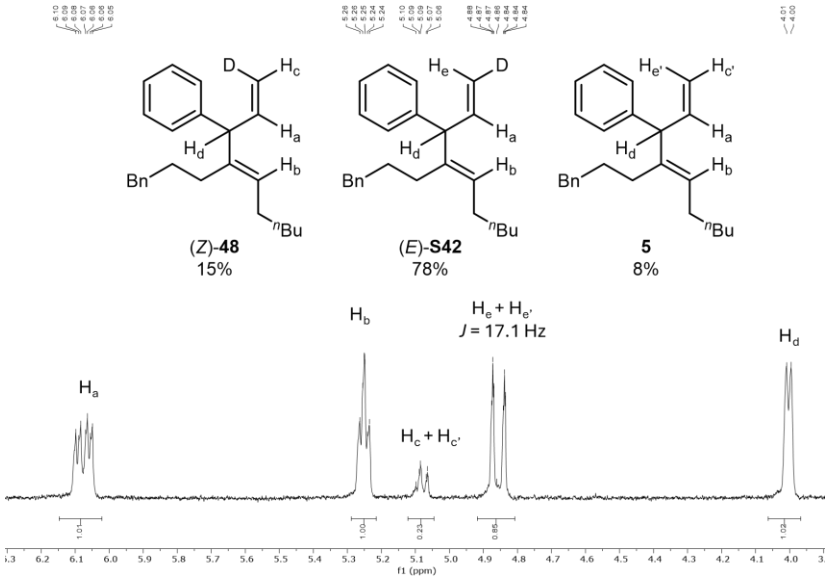
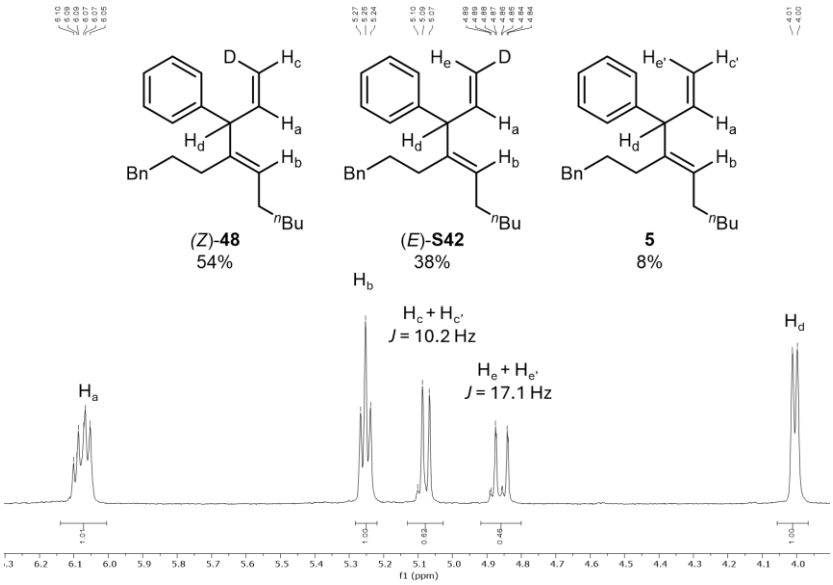
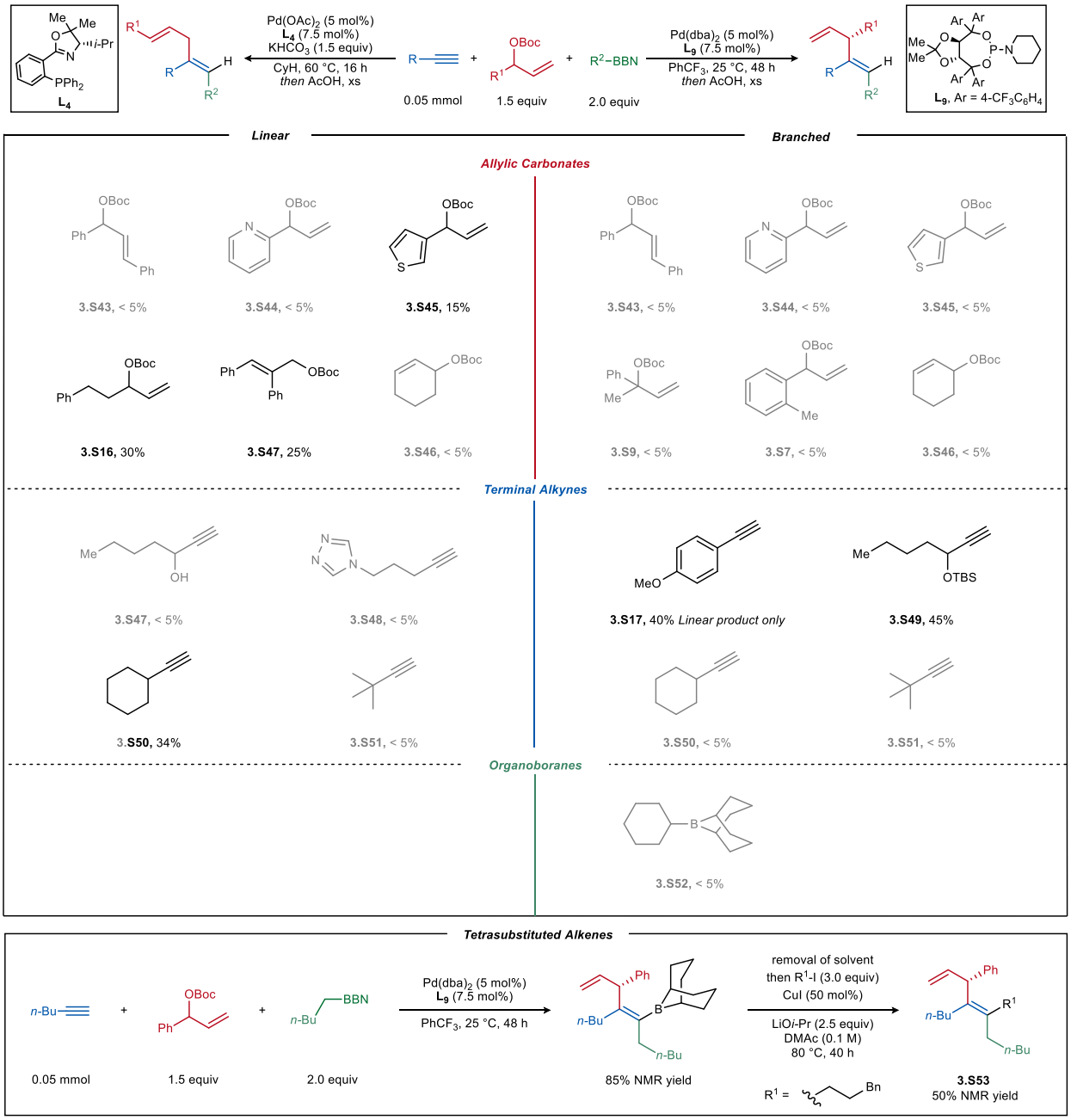


Figure 3.27 NMR Analysis of (±)-3.S42



3.4.10 Substrate Scope Limitations

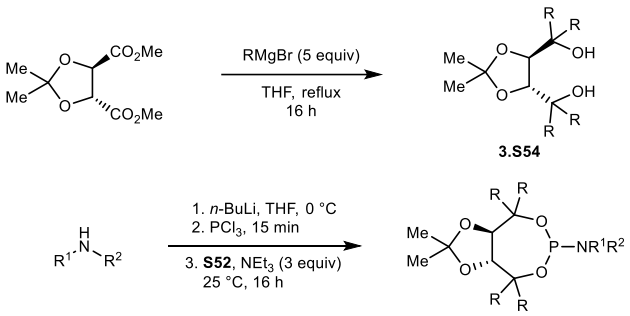
Table 3.17 Limited Substrates



3.4.11 Ligand Synthesis

Taddol-based phosphoramidite ligands used in this work were prepared according to modified literature procedure.[37,38] Other ligands were purchased from commercial sources.

Scheme 3.22 Synthesis of Ligands



Preparation of TADDOLs (3.S54). A flame-dried three-necked round-bottomed flask equipped with a reflux condenser was charged with Mg turnings (6.0 equiv) and an iodine crystal. The corresponding aryl bromide (5.0 equiv) dissolved in anhydrous THF (1.0 M). This solution was added dropwise to the Mg turnings via syringe, and gentle reflux was kept during the addition. After the addition, the reaction mixture was heated to reflux for additional 2 h and then cooled down to room temperature. A solution of dimethyl (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (1.0 equiv) was carefully added to the Grignard reagent. The resulting reaction mixture was heated to reflux for 16 h. The reaction was quenched by addition of saturated aqueous NH_4Cl solution, and the resulting mixture was extracted by ethyl acetate. The organic phases were washed with aqueous HCl solution (1 M) and then brine, dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography (typically eluent with 10~20% ethyl acetate in hexanes) to yield the desired TADDOL.

When R = phenyl, the TADDOL was purchased from Ambeed.

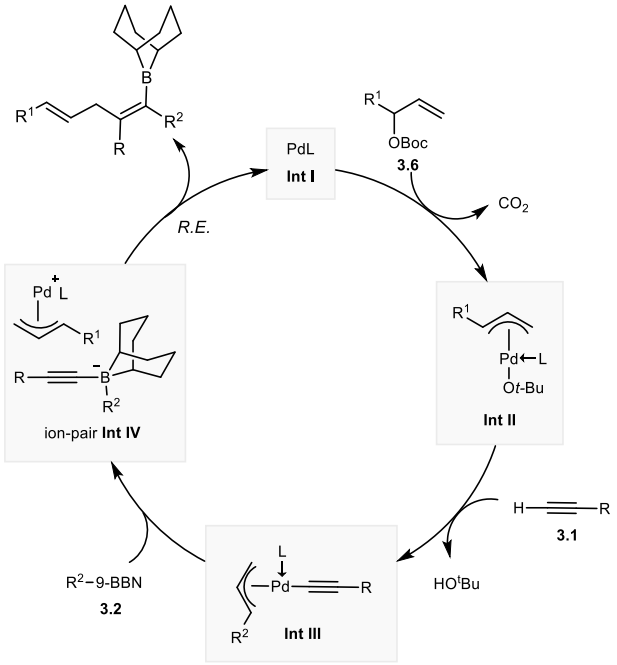
Preparation of phosphoramidite ligands. To a flame-dried round bottom flask equipped with a magnetic stir bar under an N_2 atmosphere was added the desired amine (1.0 equiv) and anhydrous THF (1.0 M). The reaction mixture was cooled to 0 °C and *n*-butyl lithium solution (2.5 M in hexanes, 1.1 equiv) was added dropwise. The reaction mixture is stirred at 0 °C for 1 h before phosphorous trichloride (1.0 equiv) is added in one portion. After stirring at 0 °C for 15 minutes, a solution of **S5** (1.0 equiv) and triethylamine (3.0 equiv) in THF (1.0 M) is added slowly. The reaction mixture is allowed to warm to room temperature and stirred for additional 16 h. The resulting slurry is filtered through a short neutral alumina pad and washed with THF. The filtrate was concentrated *in vacuo* to afford a light-yellow foam. The resulting ligands are typically pure enough in ^{1}H NMR and were directly used after drying under high vacuum. If necessary, the product can be further purified by silica gel column chromatography (10% ethyl acetate in hexanes, with 5% triethylamine).

L9 was prepared according to the procedure above using 4-bromobenzotrifluoride and piperidine. **L9** was characterized before. [39]

3.4.12 Alternative Mechanism

We cannot exclude the outer-sphere pathway for linear-selective allylation. We proposed the alternative mechanism below.

Scheme 3.23 Outer-sphere Mechanism for Linear-selective Allylation



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