New Approaches for the Synthesis of Alkenes

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Abstract

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Alkenes are an important class of compounds common among biologically active molecules and often used as intermediates in organic synthesis. Many alkenes can exist in two stereoisomeric forms (E and Z), which have different structures and properties. The selective formation of the two isomers is an important synthetic goal that has driven the development of new transformations. Here, we describe the development of three new methods of alkene synthesis. The first is a diastereodivergent approach to styrene synthesis through hydroarylation of terminal alkynes. The reaction conditions for this method can be tuned to give either the Z- or E-styrene in high yields and excellent selectivities. This method relies on the tandem catalysis of a Sonogashira cross coupling followed by alkyne semireduction. The second transformation has enabled the synthesis of isomerically pure Z-alkenes from simple starting materials. Using a new mechanistic approach to hydroalkylation, we developed the silver-catalyzed Z-selective alkene synthesis via reductive cross coupling of alkynes with alkyl boranes. Preliminary mechanistic studies have shown that a 1,2-metallate rearrangement of the silver boronate intermediate is the key to the stereochemical

outcome of this reaction. The third method has not yet been fully developed, and builds upon the previous Z-selective hydrolkylation. In this new transformation, the focus is to efficiently couple secondary alkyl boranes with alkynes to generate highly complex, enantioenriched Z-alkenes. Preliminary work for this project is discussed herein, and demonstrates the viability of this reaction.

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LIST OF ABBREVIATIONS

(*R*)-DTBM-SEGPHOS:	(*R*)-(−)-5,5′-Bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole
9-BBN	9-Borabicyclo[3.3.1]nonane
Ac:	Acetyl
Ad:	Adamantyl
Ag:	Silver
Ar:	Aryl
Au:	Gold
BINAP:	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
Bn:	Benzyl
Boc:	tert-Butyloxycarbonyl
Bz:	Benzoyl
C:	Celsius
Cu:	Copper
Cy:	Cyclohexyl
dba:	dibenzylideneacetone
DACH Trost:	(1*S*,2*S*)-(–)-1,2-Diaminocyclohexane-*N*,*N*′-bis(2-diphenylphosphinobenzoyl)
DavePhos:	2-Dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl
dppf:	diphenyl phosphine ferrocene
dppp:	diphenyl phosphine propane
DCM:	Dichloromethane

Equiv:	Equivalent
EtOAc:	Ethyl acetate
Et_2O:	Diethyl ether
Et:	Ethyl
FTIR:	Fourier transform infrared spectroscopy

Abbreviations for FTIR peaks

s:	strong
m:	medium
w:	weak
b:	broad

h:	Hour
HPLC:	High performance liquid chromatography
HRMS:	High resolution mass spectrometry
Hz:	Hertz
IAd:	1,3-diadamantyl imidazolium
IBox:	(2-(4'-dimethylaminophenyl)-6-iodobenzoxazole)
ICy:	1,3-dicyclohexyl imidazolium
IMes:	1,3-Bis-(2,4,6-trimethylphenyl)imidazolium
i-Pr:	isopropyl
IPr:	1,3-Bis-(2,6-diisopropylphenyl)imidazolium
IPr*:	1,3-bis[2,6-bis(diphenylmethyl)-4-methylphenyl]imidazolium
I*t*-Bu:	1,3-Bis-(tert-butyl)imidazolium
Me:	Methyl
MeOD:	deuterated methanol
Mes:	Mesityl

MHz:	Megahertz
mol:	Mole
n-Bu:	*n*-butyl
NHC:	N-heterocyclic carbene
NMR:	Nuclear Magnetic Resonance

Abbreviations for NMR splitting patterns

s:	singlet
d:	doublet
t:	triplet
q:	quartet
p:	pentet
m:	multiplet
br:	broad
dd:	doublet of doublets
dt:	doublet of triplets
ddt:	doublet of doublet of triplets

OTf:	Trifluoromethanesulfonate
OTs:	p-Toluenesulfonate
Ph:	Phenyl
PMHS:	polymethylhydrosiloxane
ppm:	parts per million
QPhos:	1,2,3,4,5-Pentaphenyl-1′-(di-*tert*-butylphosphino)ferrocene
RuPhos**:**	2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
rt:	room temperature
SPhos:	2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl

SIMes:	1,3-Bis-(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium
SIPr:	,3-Bis-(2,6-diisopropylphenyl))-4,5-dihydroimidazolinium
t-Bu:	tert-butyl
TBS:	Tert-butyldimethylsilyl
TFA:	Trifluoroacetic acid
THF:	Tetrahydrofuran
THP:	Tetrahydropyran
TIPS:	Triisopropylsilyl
TLC:	Thin layer chromatography
TMB:	1,3,5-Trimethoxybenzene
TMDSO:	Tetramethyldisiloxane
tol:	Tolyl
Tri:	1,4-bis[2,6-bis(propan-2-yl)phenyl]-3-phenyl-4,5-dihydro-1H-1,2,4-triazolium
Xantphos:	4,5-bis(dipheylphosphino)-9,9-dimethylxanthene
XPhos:	2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl
Xyl-MeOBIPHEP:	(*R*)-2,2′-Bis[bis(3,5-dimethyl)phosphino]-6,6′-dimethoxy-1,1′-biphenyl

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To David, you have been patient, supportive, and kind. Thank you for letting me lean on you in times of frustration and for celebrating with me in times of success. I could not have gotten through the final few years of this experience without you.

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DEDICATION

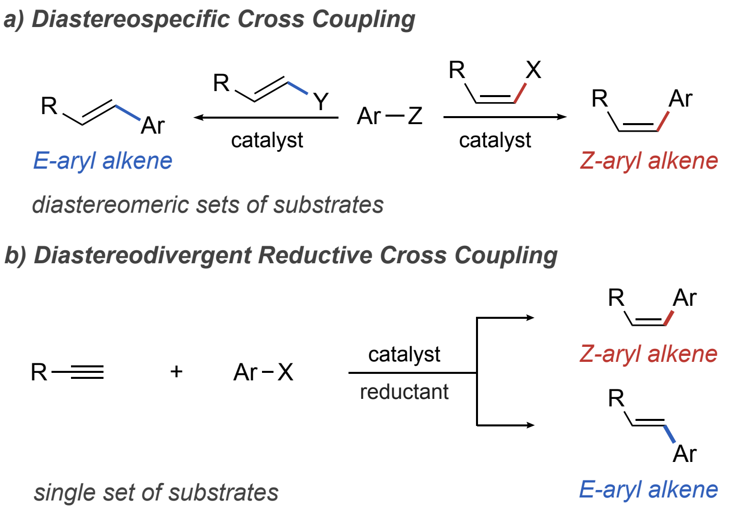
To my Dad and Melissa.

Chapter 1. DIASTEREODIVERGENT REDUCTIVE CROSS COUPLING OF ALKYNES THROUGH TANDEM CATALYSIS: *Z*- AND *E*-SELECTIVE HYDROARYLATION OF TERMINAL ALKYNES

1.1 INTRODUCTION

Alkenes play an important role in organic chemistry, both as common structural elements of organic molecules and as intermediates in organic synthesis. The preparation of the E and Z isomers of an alkene generally requires the synthesis of two different sets of precursors,[1,2] often using different synthetic routes. For example, in extensively used cross-coupling reactions, the stereochemistry of the alkene product is determined by the stereochemistry of the starting material.[2] As a result, the synthesis of *E*- and *Z*-aryl alkenes involves separate cross-coupling reactions of two diastereomeric alkene fragments with a functionalized arene (Scheme 1.1a).

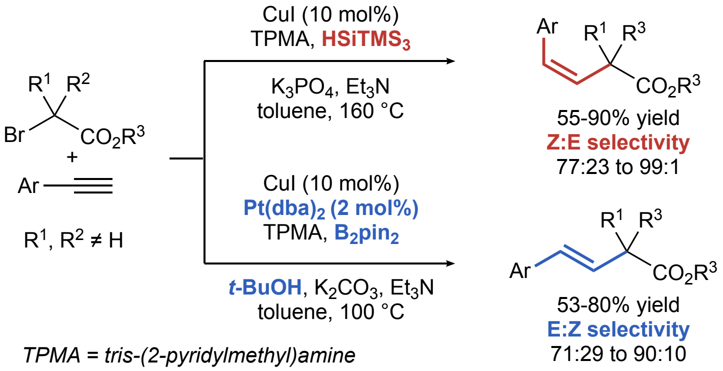
Although rare, stereodivergent methods that allow the synthesis of both alkene isomers from the same starting materials are known. For example, both isomers can be formed by the semireduction of an alkyne.[3–7] Whereas this approach allows control over the double bond geometry and stereodivergence, no new carbon-carbon bond is formed. A more efficient approach is offered by alkene cross metathesis,[8–10] which leads to fragment coupling through the formation of a new double bond and allows the control of the double bond geometry. The stereochemistry of the product is primarily determined by the catalyst used in the reaction.[11–15] The downside of this approach is that the selective formation of the desired cross metathesis product often necessitates the use of specific combinations of substrates and/or a large excess of one of the substrates.



Scheme 1.1. Stereoselectivity in Cross Coupling

Reductive cross-coupling reactions of alkynes also provide an excellent opportunity for stereodivergent alkene synthesis. Like the alkene cross metathesis reaction, these transformations are responsible both for the formation of a new C-C bond and for setting the stereochemistry of the alkene product. Therefore, in principle, a single hydroarylation reaction could provide access to both diastereoisomers of an aryl alkene from a single alkyne substrate (Scheme 1.1b). Despite the development of numerous reactions for the hydroarylation of alkynes, diastereodivergent methods remain rare.[16]

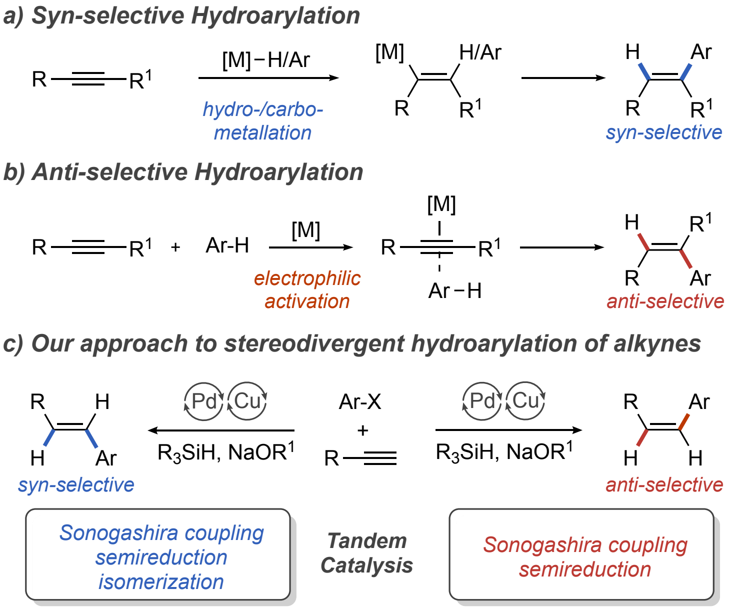
Recently, a diastereodivergent hydroalkylation of aryl alkynes (Scheme 1.2) was reported by Nishikata et al.[17] demonstrating the feasibility of diastereodivergent reductive cross-coupling. Although no detailed mechanistic analysis was reported, the diastereodivergence seems to result from fundamentally different mechanisms for the two reactions. The *Z*-products are proposed to be formed through radical bromoalkylation, followed by the reduction of alkenyl bromide. The formation of *E*-alkenes, on the other hand, likely involves hydroboration followed by Suzuki cross-coupling.



Scheme 1.2. Diastereodivergent Reductive Alkylation

Mechanistic analysis of known hydroarylation reactions suggests why stereodivergence has been difficult to achieve. Most current methods are based on syn-stereospecific carbo-[18–22] or hydrometalation[23–25] of alkynes, which forces the syn-selective hydroarylation and prevents the formation of the other isomer (Scheme 1.3a).

To our knowledge, the only approach to catalytic anti-selective hydroarylation was developed by Fujiwara in 2000 (Scheme 1.3b).[26–28] Using a palladium or platinum catalyst, anti-selective hydroarylation is accomplished through electrophilic activation of alkynes.[28–30] Unfortunately, the Friedel-Crafts mechanism[31] of this reaction limits the scope to highly electron-rich arenes and electrophilic alkynes, such as propiolates. Furthermore, products of dialkenylation and diarylation are often formed. Finally, it is important to note that all three mechanistic approaches to hydroarylation shown in Scheme 1.3 (a and b) have been difficult to apply to reactions of terminal alkynes, making hydroarylation of this important class of substrates particularly challenging.[32,33]



Scheme 1.3. Methods for the Hydroarylation of Alkynes

Seeking to exploit the full potential of hydroarylation chemistry, we were interested in developing a diastereodivergent hydroarylation of terminal alkynes that would provide access to both *Z*- and *E*-aryl alkenes. Considering the diastereospecific nature of current hydroarylation methods we decided to explore a fundamentally different approach based on tandem catalysis.

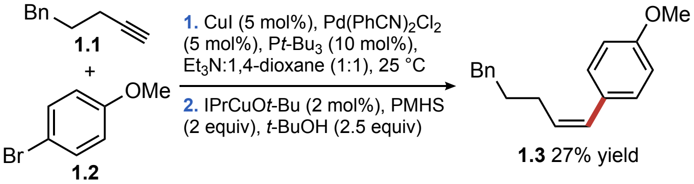
Tandem catalysis has recently received a lot of attention as an efficient strategy for the development of new catalytic transformations.[34,35] Performing two or more catalytic reactions in the same flask enables a more economical use of energy and time, and minimizes the use of reaction workup and product purification.[34] At the same time, tandem catalysis allows the development of transformations that are difficult to accomplish relying on a single catalytic cycle.[36–42]

We reasoned that the *Z*-selective hydroarylation could be achieved using tandem Sonogashira coupling[43,44] and *Z*-selective semireduction.[5] Based on the seminal work by Sadighi et al.[45] and the subsequent work by Tsuji[46] and our group,[47] we planned to use the same NHC copper catalyst to promote Sonogashira coupling and to achieve semireduction in the presence of a silane and an alcohol (Scheme 1.3c). *E*-aryl alkenes could be accessed using the same catalyst system through Sonogashira coupling and semireduction, followed by isomerization of the Z product. *E*-styrenes are known to be significantly more stable than Z isomers, and several distinct mechanisms for palladium-catalyzed isomerization have been established.[48]

1.2 REACTION DEVELOPMENT: *Z*-SELECTIVE HYDROARYLATION OF TERMINAL ALKYNES

Based on our general strategy outlined in Scheme 1.3c, we initially explored *Z*-selective hydroarylation and found that Sonogashira coupling under a variety of known conditions followed by in situ copper-catalyzed semireduction was an ineffective method for hydroarylation. The best result (27% yield) was obtained using modified Fu-Buchwald Sonogashira conditions[49] with conditions for the semireduction previously reported by our group[47] (

Scheme 1.4, See Experimental for details).



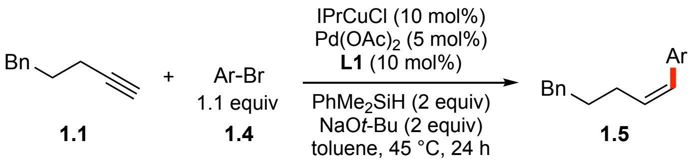
Scheme 1.4. 2 step-1 pot Sonogashira followed by *Z*-selective semireduction

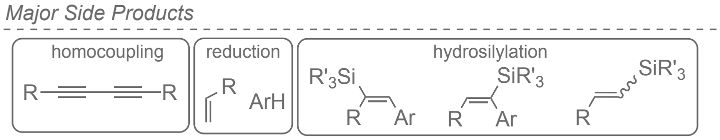
These results demonstrate the major challenge in tandem catalysis of ensuring that the catalytic reactions involved in the process are mutually compatible. Cross-talk between components of different catalytic cycles often leads to side reactions and catalyst deactivation or decomposition.[34,35] In our case, the major concern was the ability of palladium catalysts to react with silanes and unsaturated compounds in a variety of ways. For example, previously, when the product of a Sonogashira reaction was treated with a silane *in situ*, exclusive formation of the alkane product was observed,[50] consistent with the general propensity of palladium complexes to promote over-reduction of aryl alkynes.[5,51] Palladium catalysts have also been shown to promote isomerization of *Z*-alkenes[52] in the presence of hydride donors, such as tin hydrides and silanes.[53] Furthermore, palladium-catalyzed hydrosilylation of alkenes[54,55] and alkynes[56–58] is also known. Overall, even though both Sonogashira and semireduction reactions are well-established, merging them into a single process presents significant challenges, and requires a catalyst system that will selectively promote the desired combination of reactions and suppress other well-established reaction pathways.

Based on this analysis, we focused on finding a combination of a palladium catalyst and a silane that would minimize the possible side reactions. Considering our previous work on the *Z*-selective semireduction of alkynes, we focused on exploring various combinations of IPrCuO*t*-Bu and palladium catalysts in the presence of a silane and an alkoxide (Table 1.1). We observed a wide range of reactions promoted by various Cu/Pd catalyst combinations, including alkyne homocoupling, reduction of the aryl bromide,[50] and hydrosilylation of the terminal and internal alkynes (see Experimental for details).[54]

The performance of various phosphine ligands in the hydroarylation reaction revealed some general trends that guided further reaction development. Homocoupling of the alkyne was a major product with common bidentate ligands, such as BINAP (Table 1.1, entry 1). Monodentate trialkyl phosphine ligands, such as PCy_3, fully suppressed the homocoupling, but greatly decreased conversion (entry 2).

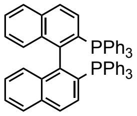
Table 1.1. Reaction Development



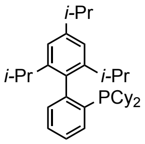


entry	*deviation from above*	*yield*[a]	*conversion*
1.	BINAP	14%	71%
2.	PCy$_3$	2%	44%
3.	Xphos	8%	100%
4.	Sphos	26%	100%
5.	none	47%	100%
6.	Me$_2$*i*-PrSiH	5% (91%)[b]	100%
7.	Me$_2$*i*-PrSiH, MeOH[c]	94%	100%

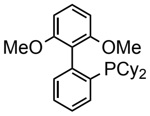
Ar = 4-butylbenzene [a]GC yields reported. [b]Yield after 72 h reported in parenthesis. [c]MeOH added after the consumption of **1.1** (2 h). Total reaction time 4 h.



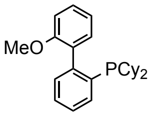
BINAP



Xphos



Sphos



L1

With dialkylbiaryl phosphine ligands,[59,60] such as XPhos and SPhos, full consumption of the starting material was achieved, although hydrosilylation and reduction of the starting materials dominated (entries 3 and 4). Interestingly, ligand **L1**[61] showed significantly higher selectivity for the desired alkene product than the closely related SPhos (entries 4 vs 5). The use of **L1** eliminated the aryl bromide reduction and suppressed hydrosilylation of the alkynes, resulting in increased yield of the hydroarylation product (entry 5). Hydrosilylation was further suppressed by switching to dimethylisopropylsilane (Me$_2$*i*-PrSiH), resulting in clean formation of the Sonogashira product and a slow semireduction (entry 6). Full conversion of the Sonogashira product was achieved only after 72 h, and the product was obtained in 87% yield and 28:1 *Z:E* selectivity. The semireduction was dramatically faster when 1.5 equivalents of MeOH was added after the Sonogashira coupling was completed (entry 7). Within two hours of the MeOH addition we observed the formation of the desired Z alkene in 94% yield and 19:1 *Z:E* selectivity. Once the terminal alkyne (**1.1**) has been consumed, the timing of the MeOH addition is not critical. The same results were obtained with MeOH added two or twenty-four hours after the start of the reaction.

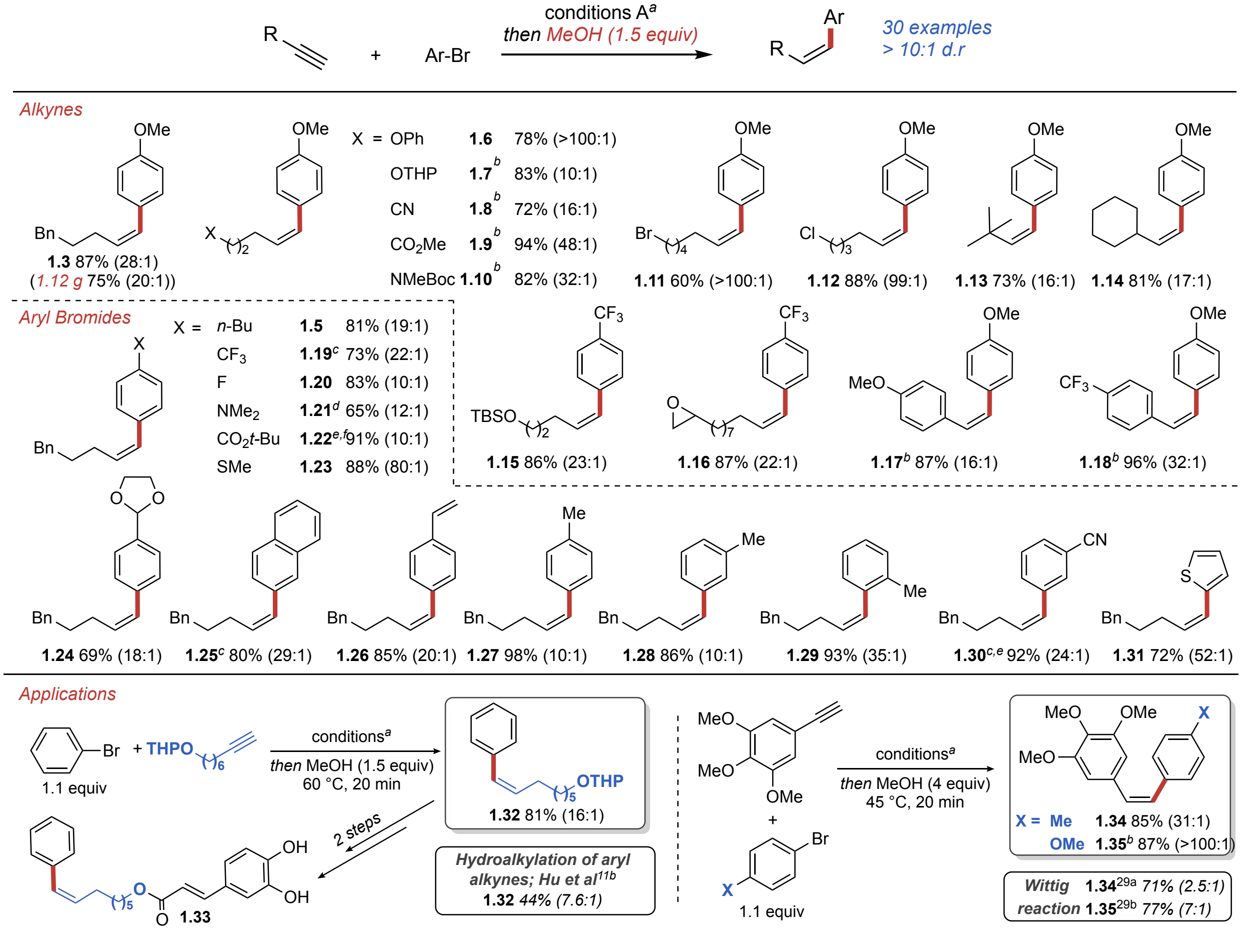
In a control experiment, we discovered that adding the silane at the beginning of the reaction was beneficial. Under standard conditions described in entry 7 (Table 1.1), 99% of the Sonogashira product was formed after 2 h, while in the absence of the silane, only 24% of the coupling product was formed at the same time point.[62] Another interesting aspect of our Sonogashira reaction is the tolerance of a copper co-catalyst. Previously, Buchwald et al. have documented deleterious effect of copper co-catalysts in a Sonogashira reaction promoted by a closely related palladium catalyst stabilized by XPhos ligand.[63]

1.3 SUBSTRATE SCOPE: *Z*-SELECTIVE HYDROARYLATION

Having established the reactions conditions for the *Z*-selective hydroarylation of terminal alkynes (Table 1.1, entry 7), we explored the scope of the reaction (Table 1.2). Alkynes containing reductively labile functional groups such as an alkyl chloride (**1.12**), alkyl bromide (**1.11**), ester (**1.9**), and nitrile (**1.8**) were compatible with this reaction. In addition, the reaction could be successfully performed in the presence of epoxides (**1.16**), silyl ethers (**1.15**), and protected amines (**1.10**). Notably, both electron-rich and electron-deficient aryl alkynes were competent coupling partners in this reaction (**1.17** and **1.18**).

A wide range of aryl bromides could also be used as substrates (Table 1.2). Both electron-rich (**1.3** and **1.21**) and electron-poor (**1.19**, **1.22** and **1.30**) aryl bromides were viable substrates, as were heteroaryl bromides. A variety of functional groups were tolerated on the arene substrate, including thioethers (**1.23**), acetals (**1.24**), and alkenes (**1.26**). Finally, products derived from ortho-, meta-, and para-substituted aryl bromides were isolated in high yields and good to excellent diastereoselectivities (**1.27-1.29**).

Table 1.2. Scope of *Z*-Selective Hydroarylation

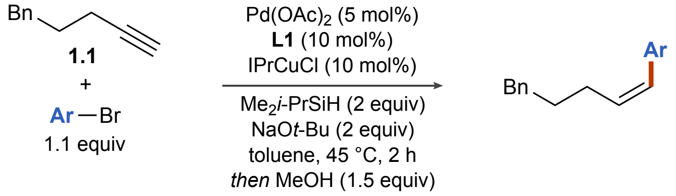


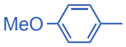
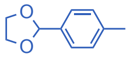
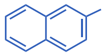
Reactions performed on 0.5-mmol scale. Reported are isolated yields of purified mixtures of product diastereoisomers. *Z*:*E* ratios of products determined by GC analysis of crude reaction mixtures are reported in paranthesis. [a]Conditions: IPrCuCl (10 mol%), $Pd(OAc)_2$ (5 mol%), **L1** (10 mol%), Me_2*i*-PrSiH (2 equiv), NaO*t*-Bu (2 equiv), toluene, 45 °C, 2 h. [b]Reaction conditions: IPrCuCl (10 mol%), $Pd(OAc)_2$ (5 mol%), **L1** (10 mol%), Me_2*i*-PrSiH (2 equiv), LiO*t*-Bu (2 equiv), toluene, 45 °C, 3 h, then MeOH (4 equiv) and NaO*t*-Bu (2 equiv), 60 °C. [c]*i*-BuOH was used instead of MeOH. [d]Reaction performed at 0 °C. [e]*t*-BuOH was used instead of MeOH and the semireduction was performed at 60 °C after addition of alcohol. [f]Reaction was monitored by GC.

To demonstrate the utility of the new method, we prepared **1.3** on a gram scale. We also used the hydroarylation reaction in the synthesis of biologically relevant compounds shown in Table 1.2. These applications allow us to make a direct comparison to other methods previously used to accomplish the synthesis of aryl alkenes. Compound **1.32** was used in the synthesis of caffeic acid derivative **1.33**, which showed selective antiproliferative activity in certain highly metastatic carcinoma cell lines.[64] The compound was originally prepared using a Wittig reaction (25% yield and 3.3:1 *Z:E* selectivity).[64] More recently, Hu et al. prepared **1.32** by *Z*-selective hydroalkylation of aryl acetylenes using 3 equiv of the alkyl iodide (44% yield and 7.6:1 *Z*:*E* selectivity).[32] The hydroarylation of terminal alkynes shown in Table 1.2 provided **1.32** in 81% yield and 16:1 *Z:E* selectivity. Compounds **1.34** and **1.35** are among the most active analogues of natural product Combretastatin A4, which is a potent inhibitor of tubulin polymerization.[65] Like many other analogues, these have been prepared with relatively low *Z*-selectivity using Wittig reaction.[66,67] Using our hydroarylation reaction both compounds were prepared in high yield (>80%) and with excellent *Z*-selectivity (>30:1).

To ensure high *Z*-selectivity in synthesis of compounds shown in Table 1.2, we monitored the reaction progress by TLC, and stopped the reactions when the products of the Sonogashira coupling were consumed. Careful monitoring of the reaction progress by gas chromatography (GC) established that in several representative cases, high Z-selectivity (10:1) can be achieved in a twenty-minute window within the first hour after the addition of MeOH (Table 1.3). In the absence of MeOH, isomerization is significantly slower and good *Z*-selectivity is observed even 24 h after the complete consumption of the Sonogashira product (Table 1.1, entry 6: after 96 h, we obtained the *Z*-alkene in 87% yield and *Z:E* = 11:1).

Table 1.3. Change in *Z*-Selectivity Over Time



Ar	20 min	25 min	30 min	35 min	40 min	Yield[d]
	20:1	18:1	13:1	10:1	10:1	92 - 95
	>100:1[c]	18:1	18:1	17:1	13:1	70 - 79
[b] 	28:1	28:1	27:1	26:1	25:1	84 - 89

[a]Reported selectivities of crude reaction mixture. [b]*i*-BuOH used instead of MeOH [c]Reaction mixture contains <10% of alkyne. [d]Combined yields of *Z* and *E* isomers.

We found it convenient that the rate of the semireduction can be adjusted by varying the temperature and the alcohol additive. The semireduction of internal alkynes containing an electron-deficient arene was slow in the presence of MeOH and significantly faster in the presence of isobutanol (*i*-BuOH). For example, with MeOH as an additive, the syntheses of compounds **1.19** and **1.25** required more than 24 h, while with *i*-BuOH the reductions were completed in less than 2 h. Conversely, under the standard reaction conditions, the reduction of the Sonogashira products with electron-rich aryl bromides (**1.21**) was completed in several minutes, which made monitoring the reaction progress difficult and resulting in low *Z*-selectivity. At a lower temperature, the reduction was completed in 6 h. Finally, in syntheses of several products shown in Table 1.2, we used LiO*t*-Bu instead of NaO*t*-Bu. We noticed that this was required with more acidic alkynes that contain electron-withdrawing groups. In these reactions, NaO*t*-Bu was completely ineffective in promoting Sonogashira coupling and we could recover the starting materials. Monitoring reactions between different alkynes and the two bases by in situ ^{1}H NMR did not reveal any clear differences in these reactions.

1.4 REACTION DEVELOPMENT: *E*-SELECTIVE HYDROARYLATION OF TERMINAL ALKYNES

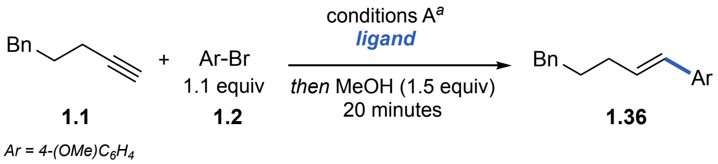
Next, we explored the development of *E*-selective hydroarylation of alkynes. The formation of the *E* isomer would involve the execution of the following three catalytic processes in tandem: Sonogashira coupling, semireduction, and alkene isomerization (Scheme 1.3c). The feasibility of this approach was supported by the strong thermodynamic preference for the *E* isomer of aryl alkenes. For example, the equilibrium constant for isomerization of *Z*-1-phenyl-1-propene to the E isomer is 32.2.[48] Furthermore, several mechanisms for palladium-catalyzed alkene isomerization have been established through detailed mechanistic studies.[48]

Despite numerous documented mechanisms for palladium-catalyzed isomerization of aryl alkenes, previous efforts to develop preparatively useful method for this transformation encountered significant problems. Spencer et al. have shown that $(MeCN)_2PdCl_2$ promotes alkene isomerization through a cationic intermediate.[52] Good yields and selectivities are obtained under mild reaction conditions. However, the reaction is limited to electron-rich aryl alkenes that can support the formation of the carbenium intermediate. A more general method based on reversible hydropalladation of alkenes was later developed by Jung et al.[53] However, they found that if silane is used as a hydride source, a significant amount of alkane product is formed well before the thermodynamic *E:Z* ratio of alkenes can be reached. To avoid the reduction of alkenes, Jung et al. used *n*-Bu_3SnH (2.2 equivalents) as a hydride source.

Based on Jung's report and our observation that isomerization of the *Z*-alkene occurs after the Sonogashira product is completely consumed, we explored the formation of *E*-alkenes using the standard reaction conditions and a range of phosphine ligands (Table 1.4). QPhos and DavePhos provided promising initial results and showed fast isomerization to the *E*-isomer. Unfortunately, after 24 h, the reaction with the QPhos ligand afforded the alkene mixture with *E:Z* ratio of only 5.2:1.

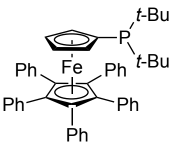
In the reaction with DavePhos, we observed a significant amount of hydrosilylation products before *E*-alkene was the dominant component in the mixture. **L1**, which was initially optimized

Table 1.4. Isomerization of the Aryl Alkene Product

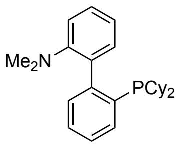


entry	*ligand*	*yield*[b]	*E:Z ratio*
1.	QPhos	100%	1.9:1
2.	DavePhos	81%	1:2.5
3.	SPhos	69%	1:2.8
4.	RuPhos	81%	1:1.2
5.	**L1**	90%	1:29
6.	**L1** (*6 days*)	95%	2:1
7.	**L1** (*5 equiv of MeOH, 24 h*)	94%	>100:1

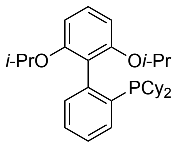
[a] See Table 2. [b] Combined yields of *E*- and *Z*-alkenes determined by GC.



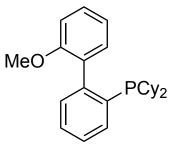
QPhos



DavePhos



RuPhos



L1

for the formation of Z isomer, led to the slowest isomerization of the *Z*-alkene, but with no side reactions. Even after 6 days, 95% of the alkene was present as a mixture of the two isomers (*E:Z* = 2:1) (entry 6).

Prompted by the excellent combined yield of the alkene obtained with **L1**, we explored the effect of other reaction parameters on isomerization hoping to identify a perturbation of the standard reaction conditions that would allow us to achieve full isomerization of *Z*-alkenes. Surprisingly, we found that *E*-alkenes could be obtained using the standard conditions for *Z*-selective hydroarylation with one simple change in reaction stoichiometry. With a larger excess of MeOH additive (5 equiv), isomerization proceeds within 24 h to provide *E*-alkenes in excellent yield and high selectivity (*E:Z* >100:1)(entry 7). In contrast to the *Z*-selective hydroarylation, strict monitoring of the reaction progress was not necessary, as we generally observed <5% yield of the alkane over-reduction product after 24 h.

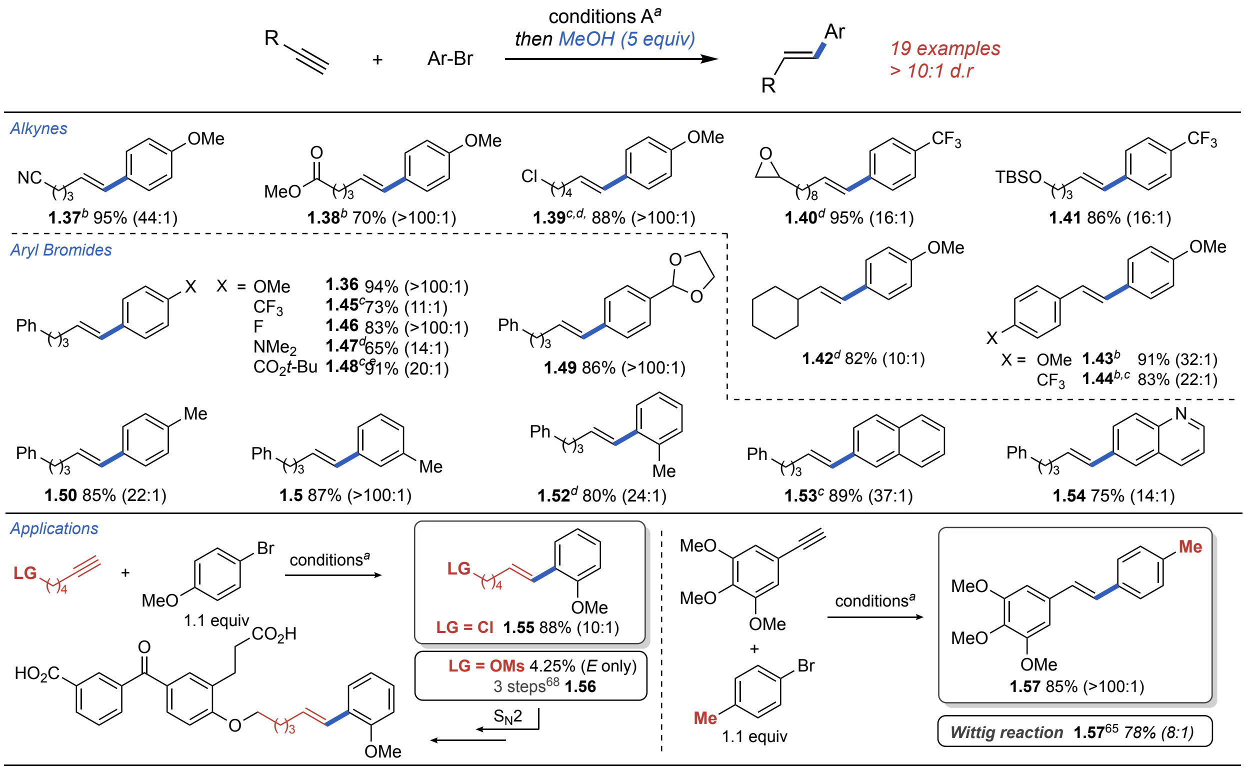
1.5 SUBSTRATE SCOPE: *E*-SELECTIVE HYDROARYLATION

The addition of excess MeOH allowed the synthesis of a wide range of *E*-aryl alkenes in yields and diastereoselectivities that were comparable to those observed in the synthesis of *Z*-alkenes (Table 1.5) We observed a similar functional group compatibility and general scope of the reaction. Nitriles, esters, epoxides, alkyl halides, tertiary amines, acetals, and silyl ethers were all compatible with the reaction conditions. Both aryl and alkyl alkynes were, again, viable substrates.

We have also used the *E*-selective hydroarylation in the synthesis of biologically active compounds or their precursors. Electrophile **1.56** was previously used in the synthesis of **LY223982**, a Leukotriene B_4 antagonist developed by Ely Lilly & Co.[68] **1.56** was originally prepared in 3 steps and 5% yield and was used in alkylation of a phenol en route to the target molecule.[68] We have prepared an alternative electrophile **1.55** in one step from commercially available materials, in 88% yield and in excellent selectivity (>100:1). We have also prepared **1.57** in 85% yield and >100:1 selectivity. In the context of an SAR study of Combretastatin A4,[65] **1.57** was previously prepared using Wittig reaction in 71% yield as a mixture of E and Z isomers (E:Z = 1:2.5).

Overall, the two hydroarylation reactions shown in Table 1.2 and Table 1.5 allow us to access both *Z*- and *E*-aryl alkenes, using one set of starting materials and reagents, and one catalyst system.

Table 1.5. Scope and Applications of the *E*-Selective Hydroarylation

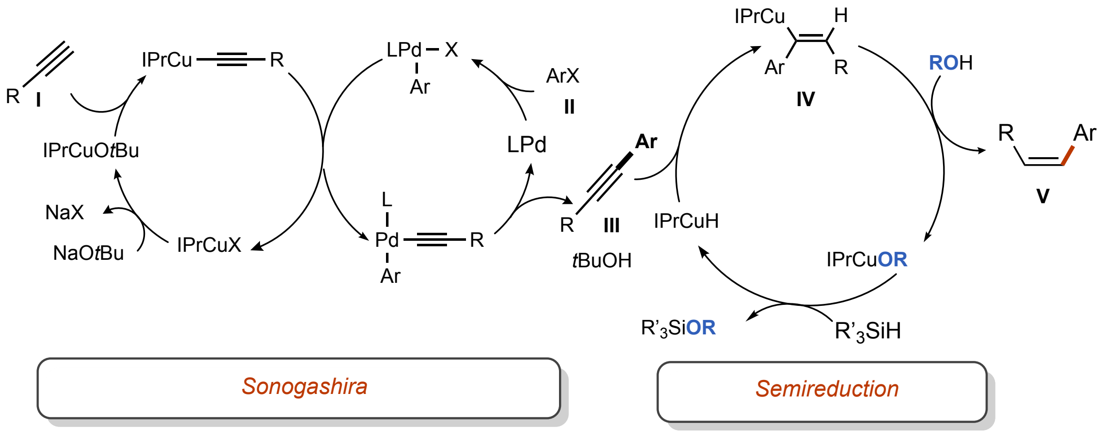


Reactions performed on 0.5-mmol scale. Reported are isolated yields of purified mixtures of product diastereoisomers. *E*:*Z* ratios of products determined by GC analysis of crude reaction mixtures are reported in paranthesis. [a]Conditions: IPrCuCl (10 mol%), Pd(OAc)$_2$ (5 mol%), **L1** (10 mol%), Me$_2$*i*-PrSiH (2 equiv), NaO*t*-Bu (2 equiv), toluene, 45 °C. [b]Reaction conditions: Pd(OAc)$_2$ (5 mol%), **L1** (10 mol%), IPrCuCl (10 mol%), Me$_2$*i*-PrSiH (2 equiv), LiO*t*-Bu (2 equiv) toluene, 45 °C, 2 h, then NaO*t*-Bu (2 equiv) and MeOH (4 equiv) 60 °C. [c]*i*-BuOH used instead of MeOH, [d]Reaction placed at 60 °C after addition of alcohol. [d]0.5 equiv Me$_2$*i*-PrSiH added after 2 h in addition to 5.0 equiv MeOH, [e]*t*-BuOH used instead of MeOH. [f]Pd(OAc)$_2$ (10 mol%), **L1** (20 mol%).

1.6 MECHANISTIC STUDIES

1.6.1 *Proposed Mechanism: Z-Selective Hydroarylation*

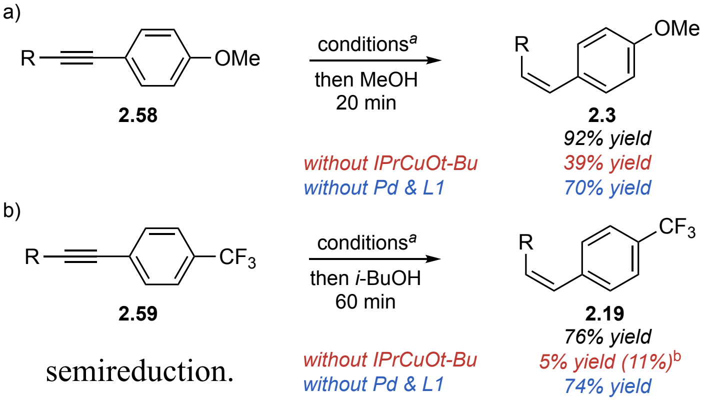
Considering the established mechanisms of the Sonogashira coupling[44] and the copper-catalyzed semireduction,[46,47] a plausible mechanism for the *Z*-selective hydroarylation is presented in Scheme 1.5. Monitoring the reaction progress confirmed that the starting materials (**I** and **II**) are fully converted to the Sonogashira product **III** before the semireduction.



Scheme 1.5. Plausible Mechanism of *Z*-Selective Hydroarylation

1.6.2 *Role of Pd and Cu Catalysts in the Z-Selective Semireduction*

In the context of this general mechanism, we were interested in understanding the relative contributions of the two catalysts to the individual steps of the reaction. First, we explored the role of the palladium catalyst in the semireduction and found evidence that under certain reaction conditions the semireduction of the Sonogashira product is more complicated than Scheme 1.5 suggests. Experiments presented in Scheme 1.6a show that both palladium and copper catalysts independently promote selective semireduction. These results suggest that in the catalytic hydroarylation both catalysts likely contribute to the semireduction of intermediate **III**.[69] However, in the absence of the copper catalyst, palladium-catalyzed semireduction does not result in complete conversion and the maximum yield of the semireduction product was 41% after 24 h (see Experimental). Furthermore, the relative contributions of the palladium and copper catalysts to the semireduction depend on the alcohol additive used in the reaction.



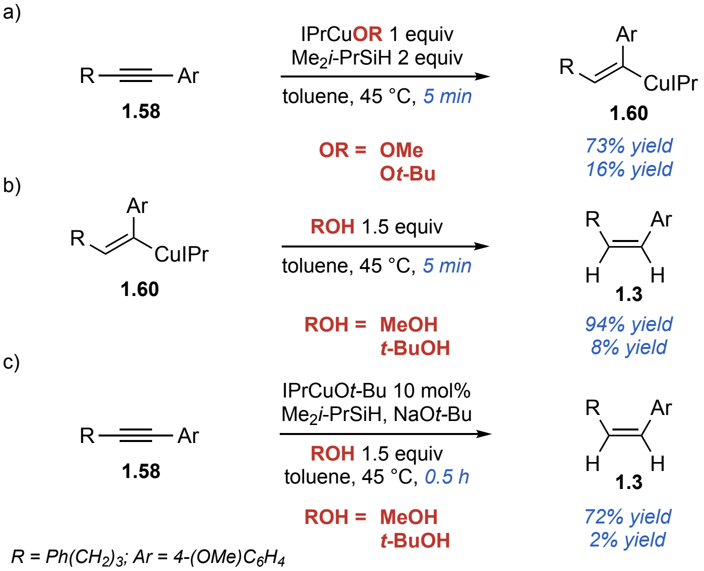
[a]Pd(OAc)$_2$ (5 mol%), **L1** (10 mol%), IPrCuO*t*-Bu (10 mol%), Me$_2$*i*-PrSiH (2 equiv), NaO*t*-Bu (1 equiv), *t*-BuOH (1 equiv), toluene, 45 °C. [b]Yield after 24 h. R = Ph(CH$_2$)$_3$.

Scheme 1.6. Role of Pd and Cu Catalysts in the *Z*-Selective Semireduction

When *i*-BuOH is used instead of MeOH, the contribution of the palladium catalyst is significantly reduced, and the semireduction is mostly effected by the copper catalyst (Scheme 1.6b). Control experiments presented in the Experimental confirm that palladium contribution depends on the alcohol additive and not the substrate of the reaction.

1.6.3 *Effect of MeOH on Z-Selective Semireduction*

We were also interested in understanding the role of the alcohol additive and the reasons for the changes to the standard conditions that were necessary with certain substrates. Initially, we explored the mechanism behind the significant acceleration of the semireduction in the presence of MeOH additive, which we observed in both *E*- and *Z*-selective hydroarylation reaction. We found that the rate of the stoichiometric hydrocupration is significantly higher using IPrCuOMe vs IPrCuO*t*-Bu (Scheme 1.7a) (See Experimental for complete kinetics data), although IPrCuOMe is only partially soluble in toluene. Considering that the alkoxide group plays no role in the hydrocupration of the alkyne, this observation implies significant difference in the rate of IPrCuH formation from IPrCuOR and a silane. These results are consistent with a computational study, which attributed a high activation barrier for the reaction between NHCCuOR and trialkylsilanes to significant steric repulsion in the transition state.[70] Surprisingly, this effect has not been experimentally observed in reactions mediated by (NHC)CuH.



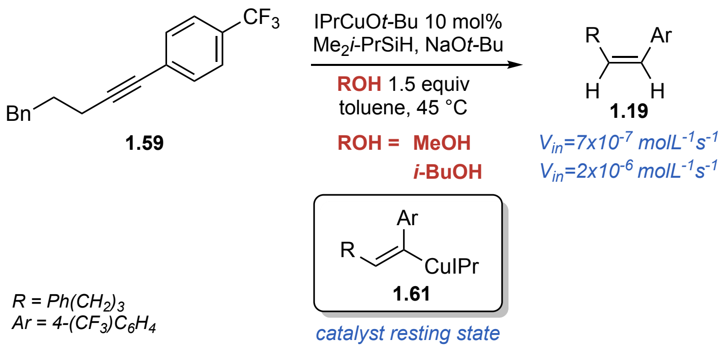
Scheme 1.7. Effect of MeOH on Semireduction

The rate of protonation of the alkenyl copper intermediate **1.60** was also significantly higher with MeOH than with *t*-BuOH, as demonstrated by the stoichiometric experiment shown in Scheme 1.7b. Consistent with stoichiometric experiments, we found that the catalytic semireduction of **1.58** was significantly faster in the presence of MeOH than in the presence of *t*-

BuOH (Scheme 1.7c). Significant concentration of the alkenyl copper intermediate **1.60** was observed during copper-catalyzed semireduction in the presence of either alcohol. This result indicates that the protonation of the intermediate is at least partially rate limiting. Overall, it is likely that MeOH accelerates the semireduction by facilitating both the formation of the IPrCuH and the protonation of the alkenyl copper intermediate.

1.6.4 *i-BuOH in Semireduction*

To understand the effect of *i*-BuOH additive in reactions with electron-deficient aryl bromides, we did initial rate measurements for the semireduction performed in the presence of MeOH and *i*-BuOH (Scheme 1.8). The experiment confirmed that the reaction is faster in the presence of *i*-BuOH. In both reactions, we observed a significant amount of the alkenyl copper intermediate (**1.61**) throughout the course of the reaction (18-20% of alkenyl copper in the reaction with 20 mol% loading of IPrCuO*t*-Bu, see Experimental for details). These results suggest that the resting state of the catalyst in the reaction of electron-deficient alkynes is the alkenyl copper intermediate and that the turnover limiting step is the protonation of this intermediate. Somewhat surprisingly, these results indicate that the protonation of the alkenyl copper intermediate is significantly faster with *i*-BuOH than with MeOH.

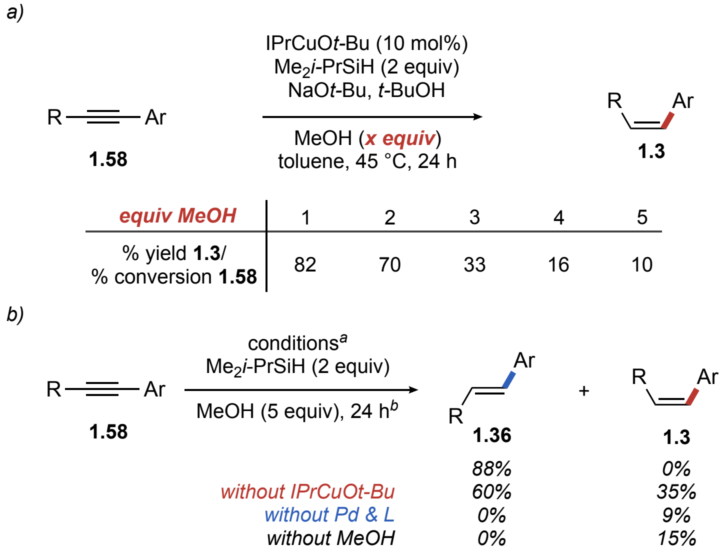


Scheme 1.8. *i*-BuOH in Semireduction

1.6.5 *Role of Pd and Cu Catalysts in the E-Selective Hydroarylation*

Finally, we also explored aspects of the reaction mechanism specific to the conditions employed in the synthesis of *E*-aryl alkenes. In this case, the relative contributions of palladium and copper catalysts to the semireduction was dramatically different from their contributions in the *Z*-selective reaction. With 5 equivalents of MeOH, copper-catalyzed semireduction of the Sonogashira product provides only 10% of the desired product and 10% conversion. The data in Scheme 1.9a shows the impact the increasing amounts of methanol have on the copper-catalyzed semireduction. These results are consistent with competitive protonation of IPrCuH by methanol we previously observed in the semireduction reaction.[47]

The major implication of these results is that under conditions used in *E*-selective hydroarylation, the semireduction is predominantly mediated by the palladium catalyst and is promoted by excess MeOH. Experiments shown in Scheme 1.9b confirm the more prominent role of the palladium catalyst and the key role of MeOH in *E*-selective hydroarylation.



equiv MeOH	1	2	3	4	5
% yield **1.3**/ % conversion **1.58**	82	70	33	16	10

	1.36	**1.3**
	88%	*0%*
without IPrCuOt-Bu	*60%*	*35%*
without Pd & L	*0%*	*9%*
without MeOH	*0%*	*15%*

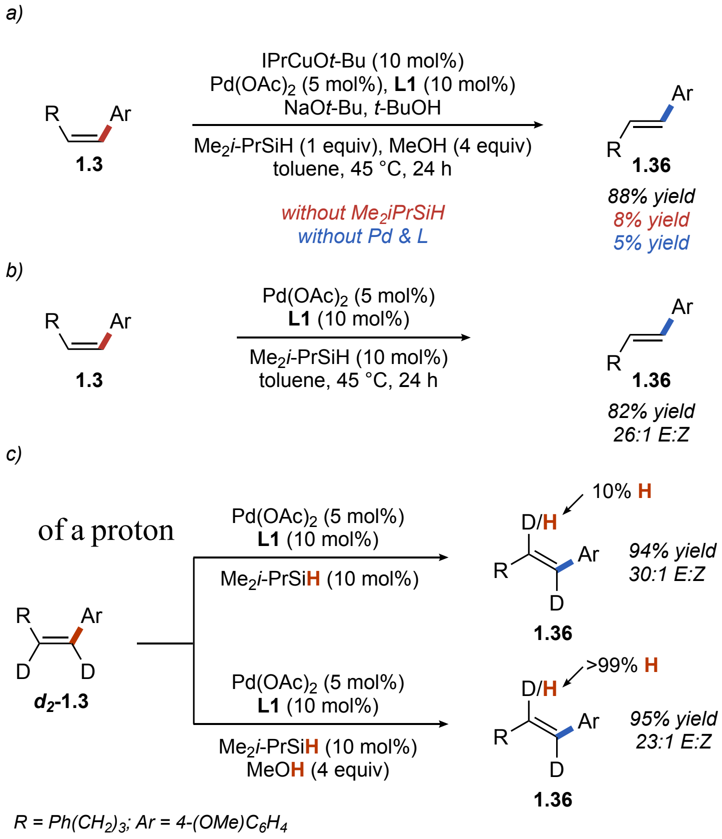
R = Ph(CH$_2$)$_3$, Ar = 4-(MeO)C$_6$H$_4$. ^{a}Conditions: IPrCuO*t*-Bu (10 mmol%), Pd(OAc)$_2$ (5 mol%), **L1** (10 mol%), NaO*t*-Bu (1 equiv), *t*-BuOH (1 equiv), toluene 45 °C. ^{b}No further progress observed after 24 h.

Scheme 1.9. Role of Pd Catalyst ad MeOH in *E*-Selective Hydroarylation

1.6.6 *Palladium-Catalyzed Alkene Isomerization*

We were also interested in understanding the mechanism of alkene isomerization in the *E*-selective hydroarylation. Based on available precedents, isomerization through reversible hydrocupration of aryl alkenes seems unlikely under the conditions employed in our reaction.[4,71] Control experiments shown in Scheme 1.9b and Scheme 1.10a demonstrate that isomerization requires both the palladium catalyst and the silane. Furthermore, we found that isomerization can be effectively accomplished using only the palladium catalyst and a substoichiometric amount of a silane (Scheme 1.10b). Interestingly, in contrast to the results reported by Jung,[53] we did not observe the formation of the alkane products. Based on observations we made during the development of the reaction, we believe that both the ligand and the silane used in the reaction are responsible for this difference.

Considering the conditions necessary for isomerization, it seems likely that the formation of *E*-aryl alkene proceeds though a reversible hydropalladation of the alkene, one of the established mechanisms for alkene isomerization. Further evidence for this mechanism was provided by isotope incorporation experiments (Scheme 1.10c). With 10 mol% of silane, we observed selective and full incorporation of a proton into ***d*₂-1.3**. The position of the proton incorporation is consistent with the established regioselectivity of styrene hydropalladation.[72] In the presence of MeOH, we observed the complete exchange of the same deuterium label, suggesting that the mechanism remains the same in the presence of methanol. The extent of deuterium exchange in the presence of MeOH suggests fast exchange between Pd-H and MeOH.[73]



Scheme 1.10. Palladium Catalyzed Aryl Alkene Isomerization

In summary, our exploration of the reaction mechanism provided insight into the roles of the two catalysts and the effects that alcohol additives and various changes from the standard reaction conditions have on the reaction. The most interesting finding is that the alcohol additive changes the role of each of the two catalysts in the hydroarylation. *i*-BuOH inhibits palladium catalyzed semireduction, while excess MeOH, suppresses copper-catalyzed semireduction and promotes both the palladium-catalyzed semireduction and alkene isomerization. This complementary reactivity of the two metal catalysts is essential for the success of the hydroarylation.

1.7 CONCLUSION

In conclusion, we have developed a diastereodivergent method for hydroarylation of terminal alkynes. The new method involves a sequence of catalytic reactions promoted by a combination of palladium and copper catalysts operating in tandem. The *Z*-selective hydroarylation is achieved through Sonogashira coupling of alkynes and aryl bromides, followed by semireduction. The *E*-selective hydroarylation involves an additional isomerization of the Z-aryl alkene. The new hydroarylation reactions allow access to both isomers of aryl alkenes using the same set of starting materials, and the same combination of catalysts. The hydroarylation reactions have excellent substrate scopes and functional group compatibility and provide the desired products in high yields and with high diastereoselectivity. Mechanistic experiments indicate different roles of palladium and copper catalysts in *Z*- and *E*-selective hydroarylation reactions. While both are involved in the Sonogashira coupling, the semireduction is predominantly promoted by a copper catalyst in the *Z*-selective reaction, while the palladium catalyst is necessary for both the semireduction and isomerization in the *E*-selective reaction.

1.8 EXPERIMENTAL

1.8.1 *General Information*

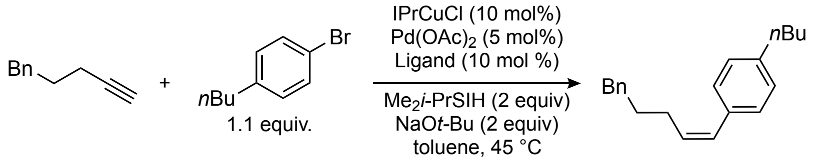
All reactions were performed under a nitrogen atmosphere with flame-dried or oven-dried (120 °C) glassware, using standard Schlenk techniques, or in a glovebox (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 µm, 230-400 mesh. 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 ($CDCl_3$ (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. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), coupling constants in Hertz (Hz), integration. Mass spectra were collected on a JEOL HX-110 mass spectrometer. GC analysis was performed on a Shimadzu GC-2010 instrument with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 μm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5 min @ 250 °C.

Materials: THF, CH_2Cl_2, Ether, benzene, and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous methanol was purchased from Millipore Sigma, and was subsequently degassed and stored over 4Å molecular sieves. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and were stored over 4Å molecular sieves prior to use. Commercial reagents were purchased from Millipore Sigma, TCI America, GFS-Chemicals, Ark-Pharm, Combi-Blocks, Oakwood Chemicals, Strem Chemicals and Alfa Aesar. Dimethylisopropylsilane (Me_2*i*-PrSiH) was purchased from Gelest Inc and was degassed and stored over 4Å molecular sieves.

1.8.2 *Reaction Development (Table 1.1)*

All reactions were performed on a 0.05 mmol scale with the stoichiometry shown in Tables S1-S3. In a nitrogen-filled glovebox a dram vial was charged with a stir bar, NaO*t*-Bu, 5-phenyl-1-pentyne, 1,3,5-trimethoxy benzene (TMB, used as an internal standard for GC), Pd(OAc)$_2$, IPrCuCl, ligand (Table 1.6), 1-bromo-4-butylbenzene, silane (Table 1.7) and toluene. The reaction mixture was stirred at 45 ºC and monitored by Gas Chromatography for reaction completion. Aliquots were taken at 4 h, 8 h, and 24 h time points.

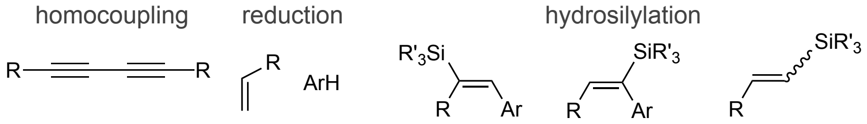
Table 1.6. Ligand Screen



1.1 **1.4** **1.5**

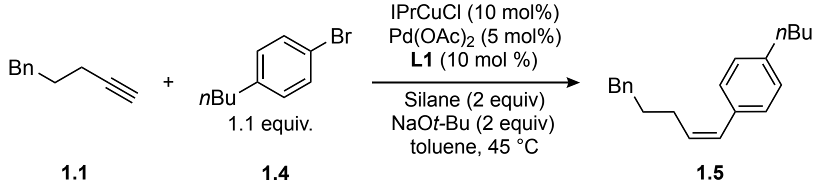
Entry	**Ligand**	**Temperature** (ºC)	**Time (h)**	**Yield (%)**
1	XPhos	45	24	8
2	**L1**	45	24	47
3	**L1**	25	24	0
4	RuPhos	45	24	1
5	PCy$_3$	45	24	0
6	dppf	45	24	0
7	dppp	45	24	0
8	DTBM-SEGPhos	45	24	0
9	DavePhos	45	24	21
10	BINAP	45	24	0
11	Xyl-MeOBIPHEP	45	24	0
12	DACH Trost	45	24	0
13	SPhos	45	24	26
14	QPhos	45	24	13

Major Side Products^a



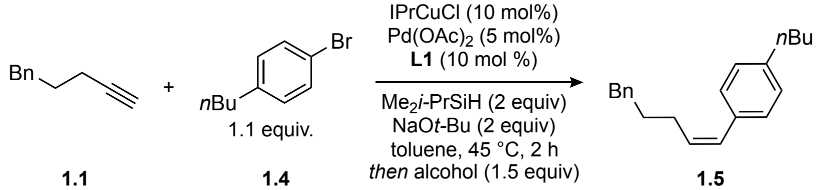
^{a}Side products determined by GC-MS analysis of the aliquots and known palladium chemistry.

Table 1.7. Silane Screen



Entry	Silane	Time (h)	Sonogashira Yield (%)	Z-alkene Yield (%)
1	$\mathrm{Me_2PhSiH}$	24	5	27
2	$\mathrm{MePh_2SiH}$	24	5	18
3	$\mathrm{Ph_3SiH}$	24	9	10
4	$\mathrm{Ph_2SiH_2}$	24	0	0
5	$\mathrm{PhSiH_3}$	24	0	0
6	$\mathrm{Et_3SiH}$	24	3	0
7	*t*-$\mathrm{Bu_2SiH_2}$	24	0	6
8	$\mathrm{Me_2}$*i*-PrSiH	24	91	0
9	*t*-$\mathrm{Bu_2MeSiH}$	24	86	0
10	(O*t*-Bu)$_2$MeSiH	24	0	25
11	$\mathrm{(OEt)_3SiH}$	24	2	0
12	$\mathrm{(OMe)_2MeSiH}$	24	0	0
13	$\mathrm{(OEt)_2MeSiH}$	24	0	0
14	TMDSO	24	10	12
15	PMHS	24	1	6

Table 1.8. Alcohol Additive Screen

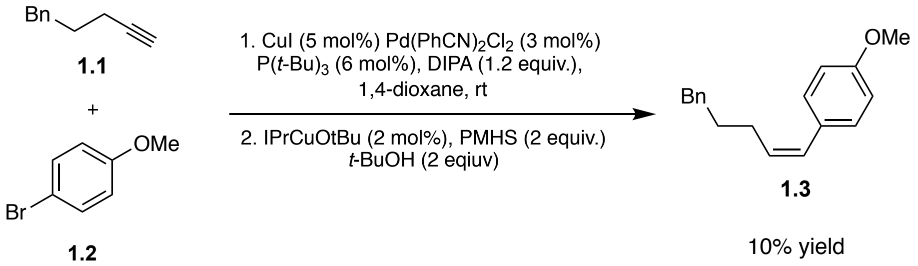


Entry	Alcohol	Time (h)*	Sonogashira Yield (%)	Z-alkene Yield (%)	Z:E Ratio
1	MeOH	4	0	100	33/1
2	*i*-BuOH	4	0	100	25/1
3	Neopentanol	4	0	100	21/1
4	*t*-BuOH	4	73	27	--
5	*i*-PrOH	4	17	58	--

1.8.3 *Standard Sonogashira Coupling Followed by Semireduction*

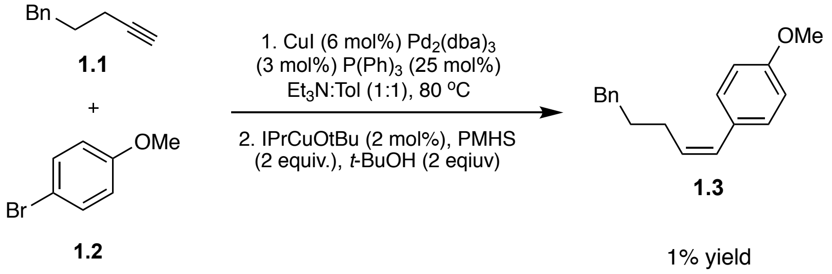
General Procedure (Scheme 1.4)

All manipulations were performed in a nitrogen-filled glovebox. Each Sonogashira coupling was performed according to the procedure reported in the literature. Reactions were performed on a 0.05 mmol scale and monitored by GC. Sonogashira coupling was determined to be complete upon full consumption of the aryl bromide. Standard semireduction conditions[47] were then applied, and reactions were allowed to stir at 25 °C for 1 h, at which point a 30 μL aliquot was taken, pushed through a plug of silica with EtOAc, and analyzed by GC. Every reaction was heated to 45 °C, 60 °C and 90 °C to encourage semireduction. At each temperature, reactions were monitored by GC, and if no change was seen after 1 h, reactions were moved to the next temperature. Reactions were monitored at 90 °C until no further change occurred.



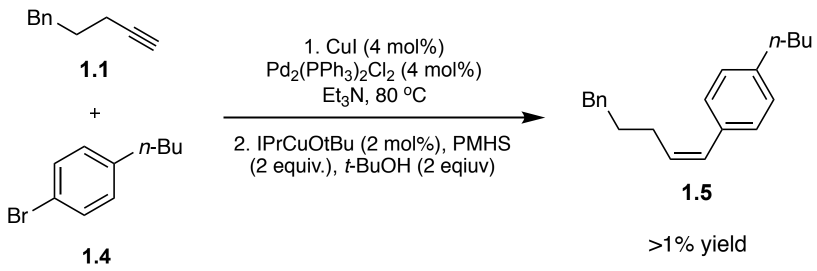
Scheme 1.11. Literature Sonogashira Followed by Semireduction

Sonogashira coupling[49] determined complete at 16 h. Semireduction was stopped at 20 h. Yield determined by GC.



Scheme 1.12. Literature Sonogashira Followed by Semireduction

Sonogashira coupling[74] determine complete at 24 h. Semireduction was stopped at 24 h. Yield determined by GC.



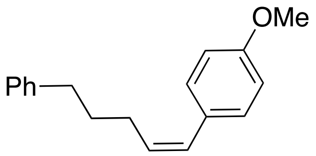
Scheme 1.13. Literature Sonogashira Followed by Semireduction

Sonogashira coupling[75] determined complete at 16 h. Semireduction was stopped at 24 h. Yield determined by GC.

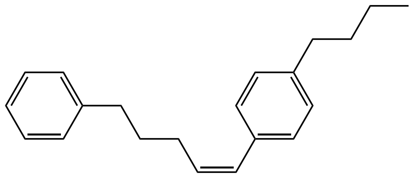
1.8.4 *General Procedure for the Hydroarylation of Terminal Alkynes: Synthesis of Z-Styrenes (Table 1.2)*

In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and NaO*t*-Bu (96.1 mg, 1.00 mmol, 2.0 equiv). To this was added alkyne (0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.8 mg, 0.025 mmol, 0.100 equiv) IPrCuCl (24.4 mg, 0.050 mmol, 0.10 equiv), **L1** (19 mg, 0.050 mmol, 0.10 equiv), aryl bromide (0.550 mmol, 1.10 equiv), Me_2*i*-PrSiH (102.3 mg, 1.00 mmol, 2.00 equiv), and toluene (5 mL). The reaction mixture was stirred at 45 °C, and the reaction progress was monitored by TLC. When the starting alkyne was fully consumed, methanol (24.0 mg, 0.750 mmol, 1.5 equiv) was added and stirring was continued at 45 °C. Upon consumption of the internal alkyne (as monitored by TLC), the reaction mixture was diluted with diethyl ether and filtered through a pad of silica gel. An aliquot was analyzed by GC to obtain the dieastereoselectivity of the reactions. The crude reaction mixture was concentrated under reduced pressure and the product was purified by silica gel chromatography. The ratio of stereoisomers for each product was again determined by GC analysis of the isolated product.

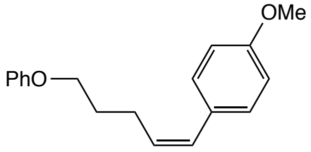
1.8.5 *Characterization of Hydroarylation Products: Z-Styrenes (Table 1.2)*



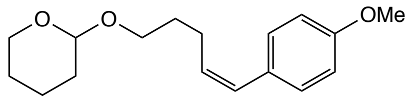
1-methoxy-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.3), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 20:1). The compound was purified by silica gel chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (110.0 mg, 87% yield, Z:E = 28:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.44 – 7.17 (m, 7H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.47 (d, *J* = 11.7 Hz, 1H), 5.69 (dt, *J* = 11.7, 7.2 Hz, 1H), 3.88 (s, 3H), 2.73 (t, *J* = 7.7 Hz, 2H), 2.55 – 2.27 (dt, *J* = 7.6, 7.2 Hz, 2H), 1.87 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 158.6, 142.7, 131.3, 130.7, 130.3, 129.0, 128.8, 128.6, 126.1, 113.9, 55.6, 35.9, 32.1, 28.5. GCMS (EI) calculated for [M]+ 252.15, found 252.3. FTIR (neat, cm^{-1}): 3028(m), 3006(m), 2924(m), 2857(m), 1605(s), 1508(s), 1247(s), 673(s).



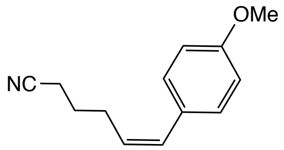
1-butyl-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.5), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv of MeOH, monitoring the reaction progress by TLC (100% Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 19:1).The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 5%) and isolated as a colorless oil (113 mg, 81% yield, Z:E = 19:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.43 – 6.99 (m, 11H), 6.41 (d, *J* = 11.6 Hz, 1H), 5.65 (dt, *J* = 11.6, 7.3 Hz, 1H), 2.81 – 2.49 (m, 5H), 2.49 – 2.30 (m, 3H), 1.93-1.69 (m, 2H), 1.69 – 1.52 (m, 2H), 1.47 – 1.28 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 141.3, 135.3, 131.9, 129.4, 128.8, 128.6, 128.4, 128.3, 125.8, 35.7, 35.5, 33.7, 31.8, 28.3, 22.5, 14.1. GCMS (EI) calculated for [M]+ 278.20, found 278.3. FTIR (neat, cm^{-1}): 3062(m), 2955(m), 2929(m), 2857(m), 1604(s), 1454(s), 844(s), 752(s) 699(s).



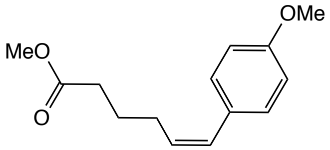
1-methoxy-4-[(1*Z*)-5-phenoxypent-1-en-1-yl]benzene (1.6), compound was prepared according to the general procedure, TLC in 10% EtOAc/Hex showed that the starting alkyne was consumed after 3 h. After the addition of 1.5 equiv of MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 80:1).The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (105 mg, 78% yield, Z:E > 100:1). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 2H), 7.27 – 7.20 (m, 2H), 6.98 – 6.90 (m, 1H), 6.92 – 6.82 (m, 4H), 6.41 (d, *J* = 11.5 Hz, 1H), 5.68 – 5.55 (m, 1H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.82 (s, 3H), 2.53 (q, *J* = 7.3 Hz, 2H), 1.95 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 158.4, 130.3, 130.1, 129.5, 129.3, 120.7, 120.1, 114.7, 113.7, 67.3, 55.4, 29.7, 25.3. GCMS (EI) calculated for [M]+ 268.15, found 268.1. FTIR (neat, cm^{-1}): 3005 (m), 2937(m), 2863(m), 2172(m), 1601(s), 1510(s), 837(s), 753(s) 691(s).



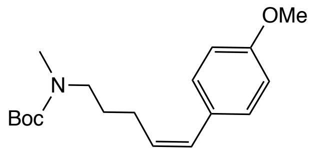
2-{[(4*Z*)-5-(4-methoxyphenyl)pent-4-en-1-yl]oxy}oxane (1.7), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 9:1).The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (104 mg, 75% yield, Z:E = 10:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.37 (d, *J* = 11.4 Hz, 1H), 5.58 (dt, *J* = 11.4, 7.3 Hz, 1H), 4.55 (s, 1H), 3.87 – 3.73 (m, 5H), 3.52 – 3.37 (m, 2H), 2.53 – 2.23 (m, 2H), 1.89 – 1.41 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 130.8, 130.5, 130.1, 128.8, 113.7, 98.95, 67.0, 62.4, 55.4, 30.9, 30.2, 25.6, 25.4, 19.7. GCMS (EI) calculated for [M]+ 276.17, found 276.3. FTIR (neat, cm^{-1}): 3006(m), 2942(m), 2869(m), 2246(s), 1608(s), 1511(s), 839(s), 734(m).



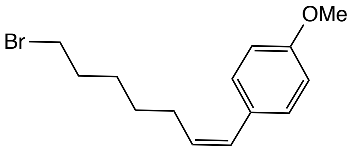
(5*Z*)-6-(4-methoxyphenyl)hex-5-enenitrile (1.8), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 3 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 16:1).The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (72 mg, 72% yield, Z:E = 16:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.45 (d, *J* = 11.6 Hz, 1H), 5.49 (dt, *J* = 11.6, 7.1 Hz, 1H), 3.82 (s, 3H), 2.55 – 2.40 (m, 2H), 2.42 – 2.27 (m, 2H), 1.91 – 1.72 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 130.5, 130.0, 129.8, 128.3, 119.7, 113.9, 55.4, 27.6, 25.9, 16.8. GCMS (EI) calculated for [M]+ 201.12, found 201.2. FTIR (neat, cm^{-1}): 3054(m), 2985(m), 2924(m), 2838(m), 2305(s), 2248(s), 1608(s), 1266(m) 895(s) 839(9).



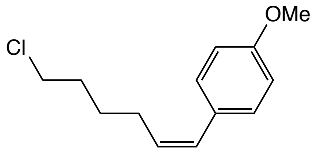
methyl (5*Z*)-6-(4-methoxyphenyl)hex-5-enoate (1.9), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 45:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (111 mg, 94% yield, Z:E = 48:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.39 (d, *J* = 11.6 Hz, 1H), 5.70 - 5.38 (m, 1H), 3.81 (s, 3H), 3.65 (s, 3H), 2.45 - 2.27 (m, 4H), 1.88 - 1.68 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0, 158.4, 130.2, 130.1, 130.0, 129.3, 113.7, 55.3, 51.5, 33.6, 28.0, 25.2. GCMS (EI) calculated for [M]+ 234.13, found 234.2. FTIR (neat, cm^{-1}): 3005(m), 2949(m), 2836(m), 2255(m), 1736(s), 1608(s), 836(s), 734(s).



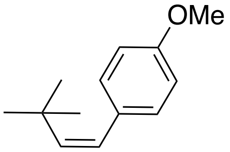
tert-butyl N-[(4*Z*)-5-(4-methoxyphenyl)pent-4-en-1-yl]-N-methylcarbamate (1.10), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 3 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 30:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a pale yellow oil (119 mg, 82% yield, Z:E = 32:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.36 (d, *J* = 11.6 Hz, 1H), 5.56 (dt, *J* = 11.6, 7.1 Hz, 1H), 3.81 (s, 3H), 3.22 (t, *J* = 7.3 Hz, 2H), 2.82 (s, 3H), 2.46 – 2.21 (m, 2H), 1.75 – 1.56 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3, 155.9, 130.5, 130.0, 128.9, 127.1, 113.7, 79.3, 55.3, 48.7, 34.3, 28.6, 26.0. GCMS (EI) calculated for [M]+ 305.20, found 305.1. FTIR (neat, cm^{-1}): 3005(m), 2974(m), 2932(m), 2836(m), 1694(s), 1608(s), 1511(s), 883(s).



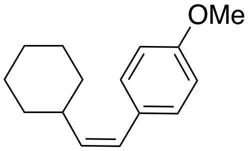
1-[(1*Z*)-7-bromohept-1-en-1-yl]-4-methoxybenzene (1.11), compound was prepared according to the general procedure, TLC in 10% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv of MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 1 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 90:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (85 mg, 60% yield, Z:E > 100:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.36 (d, *J* = 11.6 Hz, 1H), 5.55 (dt, *J* = 11.6, 7.2 Hz, 1H), 3.82 (s, 3H), 3.40 (t, *J* = 6.8 Hz, 2H), 2.50 – 2.18 (m, 2H), 2.00 – 1.72 (m, 2H), 1.53 – 1.33 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 131.1, 130.4, 130.0, 128.6, 113.6, 55.4, 34.1, 32.8, 29.3, 28.5, 28.0. GCMS (EI) calculated for [M]+ 282.06, found 282.1. FTIR (neat, cm^{-1}): 3003(m), 2926(m), 2852(m), 2172(m), 1609(s), 1511(s), 835(s), 734(s) 678(s).



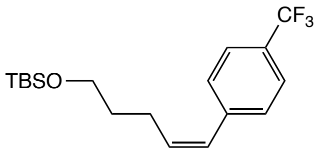
1-[(1*Z*)-6-chlorohex-1-en-1-yl]-4-methoxybenzene (1.12), compound was prepared according to the general procedure, TLC in 10% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv of MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 2 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 90:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (99.3 mg, 88% yield, Z:E = 99:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.38 (d, *J* = 11.5 Hz, 1H), 5.72 – 5.41 (m, 1H), 3.82 (s, 3H), 3.52 (t, *J* = 6.6 Hz, 2H), 2.48 – 2.26 (m, 2H), 1.89 –-1.74 (m, 2H), 1.68 – 1.55 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.4, 130.7, 130.4, 130.0, 129.0, 113.7, 55.4, 45.0, 32.3, 27.9, 27.3. GCMS (EI) calculated for [M]+ 224.10, found 224.2. FTIR (neat, cm^{-1}): 3054(m), 2958(m), 2864(m), 2305(m), 1608(s), 1511(s), 896(s), 741(s).



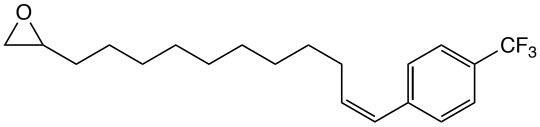
1-[(1Z)-3,3-dimethylbut-1-en-1-yl]-4-methoxybenzene (1.13) compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 15:1). The compound was purified by silica gel chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (69.0 mg, 73% yield, Z:E = 16:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.10 (d, *J* = 8.1 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.35 (d, *J* = 12.5 Hz, 1H), 5.56 (d, *J* = 12.5 Hz, 1H), 3.80 (s, 3H), 0.99 (s, 9H). ^{13}C NMR (126 MHz, Chloroform-d) δ 158.2, 142.7, 131.8, 130.2, 126.9, 113.1, 55.3, 34.2, 31.4. GCMS (EI) calculated for [M]+ 190.29, found 190.5. FTIR (neat, cm-1): 2927 (s), 2852 (s), 1605(s), 1509(s), 1245(s), 6774(m).



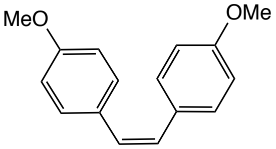
1-[(Z)-2-cyclohexylethenyl]-4-methoxybenzene (1.14) compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 15:1). The compound was purified by silica gel chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (88.0 mg, 81% yield, Z:E = 17:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.26 (d, *J* =8.8 Hz, 2H), 6.92 (d, 8.8 Hz, 2H), 6.30 (d, *J* = 11.7 Hz, 1H), 5.50 – 5.40 (t, *J* = 11.7, 1H), 3.86 (s, 3H), 2.72 – 2.54 (m, 1H), 1.88 – 1.68 (m, 5H), 1.45 – 1.16 (m, 5H). ^{13}C NMR (126 MHz, Chloroform-d) δ 158.3, 137.7, 130.7, 129.9, 126.4, 113.7, 55.4, 37.0. 33.5, 26.2, 25.9. GCMS (EI) calculated for [M]+ 216.32, found 216.5. FTIR (neat, cm-1): 2925 (s), 2850 (s), 1608(s), 1511(s), 1245(s), 677(m).



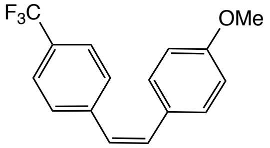
tert-butyldimethyl{[(5*Z*)-6-[4-(trifluoromethyl)phenyl]hex-5-en-1-yl]oxy}silane (1.15), compound was prepared according to the general procedure, TLC in 10% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv of MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 23:1).The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (148 mg, 86% yield, Z:E = 23:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 6.44 (d, *J* = 11.8 Hz, 1H), 5.95 – 5.63 (m, 1H), 3.63 (t, *J* = 6.2 Hz, 2H), 2.58 – 2.21 (m, 2H), 1.83 – 1.58 (m, 2H), 0.02 (s, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.4, 134.9, 129.1, 128.6 (q, *J* = 31.9 Hz), 128.1, 125.2 (q, *J* = 4.1 Hz), 124.4 (q, *J* = 271.7 Hz), 62.5, 33.0, 26.0, 25.2, 18.4, -5.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.5. GCMS (EI) calculated for [M]+ 358.19, found 358.3. FTIR (neat, cm^{-1}): 3013(m), 2930(m), 2865(m), 2175(m), 1919(s), 1616(m), 1473(s), 836(s) 775(s).



2-[(9*Z*)-10-[4-(trifluoromethyl)phenyl]dec-9-en-1-yl]oxirane (1.16), compound was prepared according to the general procedure, TLC in 10% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv of MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 22:1).The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (143 mg, 87% yield, Z:E = 22:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 6.42 (d, *J* = 11.7 Hz, 1H), 5.77 (dt, *J* = 11.7, 7.3 Hz, 1H), 3.03 – 2.82 (m, 1H), 2.74 (t, *J* = 4.5 Hz, 1H), 2.56 – 2.39 (m, 1H), 2.39 – 2.20 (m, 2H), 1.72 – 1.03 (m, 21H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.5, 135.5, 131.9, 129.0, 128.5 (q, *J* = 32.3 Hz), 125.1 (q, *J* = 3.7 Hz), 124.4 (q, *J* = 271.0 Hz), 52.5, 47.2, 32.6, 29.9, 29.5, 29.4, 29.2, 29.0, 28.7, 26.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.4. GCMS (EI) calculated for [M]+ 326.19, found 326.3. FTIR (neat, cm^{-1}): 3055(m), 2929(m), 2855(m), 2305(m), 1613(s), 1422(s), 896(s), 740(s).

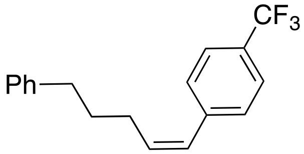


1-methoxy-4-[(*Z*)-2-(4-methoxyphenyl)ethenyl]benzene (1.17), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 16:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 45%) and isolated as a white solid (105 mg, 87% yield, Z:E = 16:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 8.7 Hz, 4H), 6.77 (d, *J* = 8.7 Hz, 4H), 6.44 (s, 2H), 3.79 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 130.2, 130.1, 128.5, 113.7, 55.3. GCMS (EI) calculated for [M]+ 240.12, found 240.2. FTIR (neat, cm^{-1}): 3054(m), 2958(m), 2937(m), 2838(m), 1607(s), 1511(s), 836(s), 740(s).

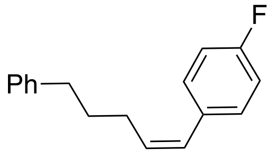


1-[(*Z*)-2-(4-methoxyphenyl)ethenyl]-4-(trifluoromethyl)benzene (1.18), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 31:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a pale yellow oil (133 mg, 96% yield, Z:E = 32:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 12.2 Hz, 1H), 6.50 (d, *J* = 12.2 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 159.2, 141.5, 132.0, 130.3, 129.2, 128.9 (q, *J* = 32.1 Hz), 128.5, 127.3, 125.3 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 271.6 Hz), 113.9, 55.3.

^{19}F NMR (471 MHz, CDCl$_3$) δ -62.5. GCMS (EI) calculated for [M]+ 278.09, found 278.1. FTIR (neat, cm^{-1}): 3010(m), 2956(m), 2837(m), 1607(s), 1508(s), 882(s), 830(s) 730(s).

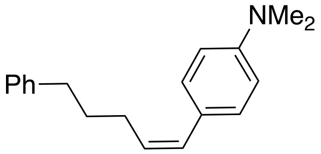


1-[(1*Z*)-5-phenylpent-1-en-1-yl]-4-(trifluoromethyl)benzene (1.19), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2h. After the addition of 1.5 equiv *i*-BuOH, monitoring the reaction progress by TLC (100% Hex) revealed that the internal alkyne intermediate was consumed after 2 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 20:1). The compound was purified by silica gel column chromatography (100% Hex) and a filtration through a short plug of alumina (100% Hex). The compound was isolated as a clear colorless oil (107 mg, 73% yield, Z:E = 22:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.41 – 7.05 (m, 8H), 6.46 (d, *J* = 11.6 Hz, 1H), 5.81 (dt, *J* = 11.7, 7.4 Hz, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.35 (dt, *J* = 7.6, 7.3 Hz, 2H), 1.81 (p, *J* = 7.6Hz, 2H). GCMS (EI) calculated for [M]+ 290.13, found 290.5. ^{19}F NMR (471 MHz, Chloroform-d) δ -65.2. ^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.1, 141.1, 134.8, 129.0, 128.6 (q, *J* = 35.2 Hz), 128.5, 128.2, 127.7, 126.0, 125.5 (q, *J* = 3.0 Hz), 124.4 (q, *J* = 276.5 Hz), 35.6, 31.6, 28.1. FTIR (neat, cm^{-1}): 3088(w), 3065(w), 3028(m), 2931(m). 2849(w), 1612(w), 1478(w), 1322(s), 1165(s), 1120(s), 1068(s), 673(s).



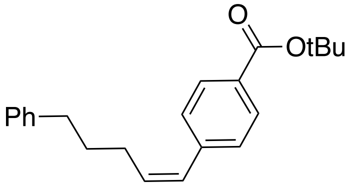
1-fluoro-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.20), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2h.

After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (100% Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 9:1). The compound was purified by silica gel column chromatography (100% Hex) and a filtration through a short plug of alumina. The compound was isolated as a clear colorless oil (105 mg, 83% yield, Z:E = 10:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.35 – 7.23 (m, 3H), 7.23 – 7.13 (m, 4H), 7.04 – 6.95 (m, 2H), 6.39 (d, *J* = 11.7 Hz, 1H), 5.68 (dt, *J* = 11.6, 7.3 Hz, 1H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.33 (dt, *J* = 7.6, 7.3 Hz, 2H), 1.79 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 161.5 (d, *J* = 246.1 Hz), 142.3, 133.8 (d, *J* = 3.1 Hz), 132.5, 130.4 (d, *J* = 7.9 Hz), 128.6, 128.4, 128.3, 125.9, 115.1 (d, *J* = 21.3 Hz), 35.6, 31.7, 28.1. ^{19}F NMR (471 MHz, Chloroform-d) δ -123.5. GCMS (EI) calculated for [M]+ 240.13, found 240.2. FTIR (neat, cm^{-1}): 3058(w), 3028(w), 2931(m), 1597(m), 1500(m), 1456(m), 1225(s), 1158(s), 857(m).

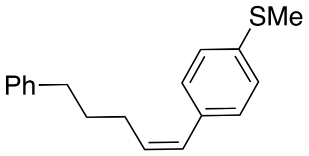


N,N-dimethyl-4-[(1*Z*)-5-phenylpent-1-en-1-yl]aniline (1.21), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, the reaction mixture was then moved to 0 ºC to slow the rate of isomerization, and the reaction progress was monitored progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 6 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 12:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (10% Et_2O/Hex). Compound was isolated as a clear colorless liquid (85 mg, 65% yield, Z:E = 12:1). ^{1}H

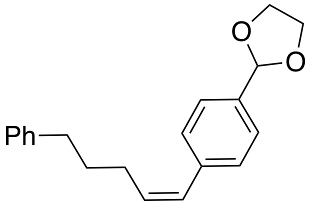
NMR (500 MHz, Chloroform-d) δ 7.16 (t, *J* = 7.5 Hz, 2H), 7.11 – 7.05 (m, 5H), 6.59 (d, *J* = 8.7 Hz, 2H), 6.25 (d, *J* = 11.6 Hz, 1H), 5.42 (dt, *J* = 11.5, 7.2 Hz, 1H), 2.84 (s, 6H), 2.56 (t, *J* = 7.8 Hz, 2H), 2.31 (dt, *J* = 7.6, 7.2Hz, 2H), 1.69 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 149.3, 142.6, 129.8, 129.1, 128.6, 128.4, 126.5, 125.8, 112.3, 40.6, 35.7, 32.0, 28.5. GCMS (EI) calculated for [M]+ 265.18, found 265.3. FTIR (neat, cm^{-1}): 3088(w), 3036(m), 2924(m), 2849(m), 2797(w), 1605(s), 1515(s), 1351(m), 1158(m), 679(s).



tert-butyl 4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzoate (1.22), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv *t*-BuOH to prevent transesterification, monitoring the reaction progress by GC revealed that the internal alkyne intermediate was consumed after 75 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 9:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→15%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil. (128 mg, 79% yield, Z:E = 10:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.10 (m, 5H), 7.12 – 7.00 (m, 2H), 6.36 (d, *J* = 11.7 Hz, 1H), 5.68 (dt, *J* = 11.7, 7.3 Hz, 1H), 2.53 (t, *J* = 7.5, 2H), 2.27 (dt, *J* = 7.5, 7.3 Hz, 2H), 1.68 (p, *J* = 7.5 Hz, 2H), 1.50 (s, 9H). ^{13}C NMR (126 MHz, Chloroform-d) δ 165.7, 142.2, 141.9, 134.5, 130.1, 129.4, 128.7, 128.6, 128.5, 128.4, 125.9, 80.9, 35.5, 31.6, 28.3, 28.3. GCMS (EI) calculated for [M]+ 322.19, found 322.4. FTIR (neat, cm^{-1}): 3058(w), 3028(m), 2976(s), 2931(s), 2849(m), 1709(s), 1597(s), 1456(s), 1292(s), 1165(s), 1105(s), 852(m), 740(m), 695(s), 681(m).

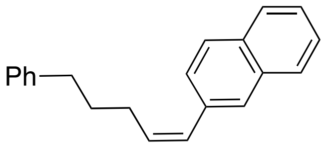


1-(methylsulfanyl)-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.23), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (5% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 1 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 80:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (118 mg, 88% yield, Z:E = 80:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.19 – 7.12 (m, 3H), 7.12 – 7.02 (m, 6H), 6.27 (d, *J* = 11.7 Hz, 1H), 5.56 (dt, *J* = 11.6, 7.3 Hz, 1H), 2.54 (t, *J* = 7.7 Hz, 2H), 2.38 (s, 3H), 2.26 (dt, *J* = 7.6, 7.3 Hz, 2H), 1.68 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.3, 136.6, 134.7, 132.5, 129.3, 128.7, 128.6, 128.4, 126.5, 125.8, 35.6, 31.8, 28.3 16.0. GCMS (EI) calculated for [M]+ 268.13, found 268.3. FTIR (neat, cm^{-1}): 3088(w), 3065(w), 3021(m), 2924(s), 2849(m), 1597(m), 1493(s), 1090(m), 830(m), 673(s)

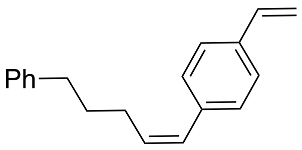


2-{4-[(1*Z*)-5-phenylpent-1-en-1-yl]phenyl}-1,3-dioxolane (1.24), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 45 min.

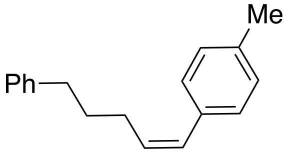
An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 18:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→15%). The compound was isolated as a clear colorless oil (102 mg, 69% yield, Z:E = 18:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.44 (d, J = 7.9 Hz, 2H), 7.26 (t, J = 7.5 Hz, 4H), 7.17 (dd, J = 14.7, 7.4 Hz, 3H), 6.45 (d, J = 11.7 Hz, 1H), 5.81 (s, 1H), 5.71 (dt, J = 11.6, 7.3 Hz, 1H), 4.18 – 4.06 (m, 2H), 4.06 – 3.97 (m, 2H), 2.63 (t, J = 7.8 Hz, 2H), 2.37 (dt, J = 7.6, 7.3 Hz, 2H), 1.78 (p, J = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.3, 138.7, 136.2, 133.1, 129.0, 128.8, 128.5, 128.4, 126.3, 125.8, 103.8, 65.4, 35.6, 31.7, 28.2. GCMS (EI) calculated for [M]+ 294.16, found 294.4. FTIR (neat, cm^{-1}): 3058(w), 3028(m), 2924(s), 2887(s), 2857(w), 1605(m), 1381(m), 1217(m), 1083(s), 941(m), 703(s), 681(s).



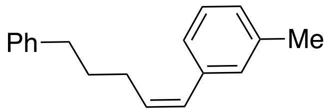
2-[(1*Z*)-5-phenylpent-1-en-1-yl]naphthalene (1.25), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv *i*-BuOH, monitoring the reaction progress by TLC (5% Et_2O in Hex) revealed that the internal alkyne intermediate was consumed after 20 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 29:1). The compound was purified by silica gel column chromatography (Et_2O/Hex 0→5%) and a filtration through a short plug of alumina (5% Et_2O/Hex). The compound was isolated as a clear colorless oil (109 mg, 80% yield, Z:E = 29:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.73 – 7.64 (m, 3H), 7.59 (s, 1H), 7.40 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 7.17 – 7.11 (m, 2H), 7.09 – 7.03 (m, 3H), 6.49 (d, J = 11.6 Hz, 1H), 5.67 (dt, J = 11.6, 7.3 Hz, 1H), 2.61 – 2.52 (m, 2H), 2.37 (dt J = 7.5, 7.3 Hz, 2H), 1.72 (p, J = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.4. 135.4, 133.5, 133.1, 132.4, 129.5, 128.6, 128.6, 128.4, 127.7, 127.7, 127.5, 127.4, 126.1, 125.9, 125.8, 35.6, 31.8, 28.4. GCMS (EI) calculated for [M]+ 272.16, found 272.3. FTIR (neat, cm^{-1}): 3051(m), 3021(m), 2924(s), 2849(m), 1597(m), 1493(m), 1448(m), 822(s), 748(s), 695(s).



1-ethenyl-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.26), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (5% Et_2O//Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 19:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→5%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (105 mg, 85% yield, Z:E = 20:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.34 (d, *J* = 7.7 Hz, 2H), 7.26 – 7.13 (m, 7H), 6.70 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.40 (d, *J* = 11.7 Hz, 1H), 5.82 – 5.58 (m, 2H), 5.22 (d, *J* = 10.9 Hz, 1H), 2.63 (t, *J* = 7.7 Hz, 2H), 2.37 (dt, *J* = 7.7, 7.2 Hz, 2H), 1.78 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.4, 137.5, 136.8, 136.0, 132.8, 129.1, 129.1, 128.6, 128.4, 126.2, 125.9, 113.6, 35.6, 31.8, 28.4. GCMS (EI) calculated for [M]+ 248.16, found 248.2. FTIR (neat, cm^{-1}): 3080(w), 3058(w), 3021(m), 3006(m), 2924(s), 2857(m), 1620(m), 1605(m), 1500(s), 1456(s), 986(m), 904(m), 845(s), 678(s).

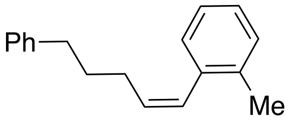


1-methyl-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.27), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (5% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 9:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (116 mg, 98% yield, Z:E = 10:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.35 – 7.05 (m,9H), 6.41 (d, *J* = 11.6 Hz, 1H), 5.65 (dt, *J* = 11.6, 7.3 Hz, 1H), 2.69 – 2.60 (m, 2H), 2.45 – 2.30 (m,5H), 1.79 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.4, 136.2, 134.9, 131.9, 129.2, 128.8, 128.6, 128.4, 128.4, 125.8, 35.6, 31.9, 28.3, 21.3. GCMS (EI) calculated for [M]+ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3058(w), 3021(m), 2924(s), 2857(m), 1597(w), 1508(w), 1448(m), 830(m), 695(s), 681(s).

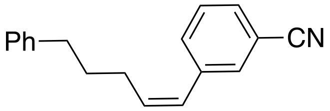


1-methyl-3-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.28), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (5% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 9:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (102 mg, 86% yield, Z:E = 10:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.19 – 7.02 (m, 6H), 6.99 –

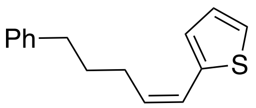
6.90 (m, 3H), 6.31 (d, *J* = 11.7 Hz, 1H), 5.57 (dt, *J* = 11.9, 7.3 Hz, 1H), 2.54 (t, *J* = 7.8 Hz, 2H), 2.32 – 2.21 (m, 5H), 1.68 (p, *J* = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.5, 137.8, 132.5, 129.6, 129.5, 128.6, 128.4, 128.2, 127.4, 125.9, 125.8, 123.3, 35.6, 31.8, 28.3, 21.6. GCMS (EI) calculated for [M]+ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3065(w), 3028(m), 2924(s), 2849(m), 1605(m), 1582(w), 1493(m), 1456(m), 792(m), 748(m), 675(s).



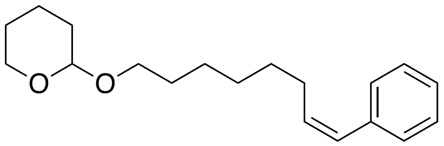
1-methyl-2-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.29), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (5% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 35:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (110 mg, 93% yield, Z:E = 35:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.20 – 6.96 (m, 9H), 6.36 (d, *J* = 11.4 Hz, 1H), 5.63 (dt, *J* = 11.5, 7.4 Hz, 1H), 2.48 (t, *J* = 7.6 Hz, 2H), 2.22 – 2.04 (m, 5H), 1.62 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.5, 136.9, 136.3, 132.4, 129.9, 129.1, 128.5, 128.4, 126.9, 125.8, 125.5, 120.1, 35.6, 31.8, 28.1, 20.0. GCMS (EI) calculated for [M]+ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3058(w), 3021(m), 2924(s), 2857(m), 1597(m), 1485(m), 1448(s), 1031(m), 740(s), 695(s).



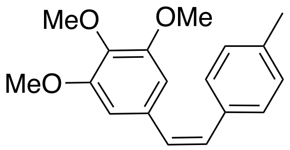
3-[(1*Z*)-5-phenylpent-1-en-1-yl]benzonitrile (1.30), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv *i*-BuOH, monitoring the reaction progress by GC revealed that the internal alkyne intermediate was consumed after 2 h. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 20:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→5%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (114 mg, 92% yield, Z:E = 24:1). ^1H NMR (300 MHz, Chloroform-d) δ 7.35 (m, 4H), 7.21 – 6.99 (m, 5H), 6.30 (d, *J* = 11.7 Hz, 1H), 5.71 (dt, *J* = 11.7, 7.4 Hz, 1H), 2.58 – 2.49 (t, *J* = 7.6Hz, 2H), 2.27 – 2.15 (m, 2H), 1.69 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 141.9, 139.8, 135.1, 133.1, 132.1, 130.0, 129.0, 128.8, 128.4, 127.2, 125.9, 119.0, 112.4, 35.4, 31.4, 28.0. GCMS (EI) calculated for [M]+ 247.14 found 247.3. FTIR (neat, cm^{-1}): 3058(m), 3021(m), 2924(s), 2857(m), 2223(s), 1597(m), 1448(m), 904(m), 800(s), 740(m), 695(s).



2-[(1*Z*)-5-phenylpent-1-en-1-yl]thiophene (1.31), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (10% Et_2O//Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 50:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→5%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (82 mg, 72% yield, Z:E = 52:1). ^1H NMR (500 MHz, Chloroform-d) δ 7.42 (s, 1H), 7.39 – 7.27 (m, 2H), 7.25 (d, J = 7.8 Hz, 3H), 7.09 – 6.96 (m, 2H), 6.62 (d, J = 11.1 Hz, 1H), 5.67 (dt, J = 11.5, 7.2 Hz, 1H), 2.76 (t, J = 7.8 Hz, 2H), 2.53 (dt, J = 7.5, 7.2 Hz, 2H), 1.90 (p, J = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.4, 140.9, 130.7, 128.6, 128.5, 127.2, 126.8, 125.9, 125.1, 122.3, 35.8, 31.4, 29.0. GCMS (EI) calculated for [M]+ 228.10, found 228.3. FTIR (neat, cm^{-1}): 3058(m), 3021(s), 2924(s), 2849(s), 1597(m), 1493(s), 1446(s), 1031(m), 845(m), 730(m), 740(s), 695(s).

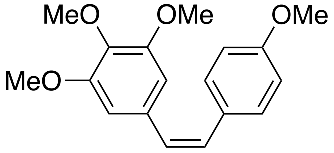


2-{[(7Z)-8-phenyloct-7-en-1-yl]oxy}oxane (1.32) compound was prepared according to the general procedure, TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, the reaction was moved to 60 °C and monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 30 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 16:1). The compound was purified by silica gel column chromatography (EtOAc/Hex 0→40%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (117 mg, 81% yield, Z:E = 16:1). This compound has been previously synthesized and spectra matches literature values.[32]



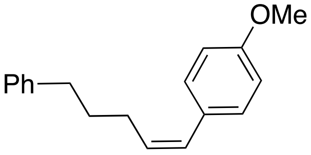
1,2,3-trimethoxy-5-[(Z)-2-(4-methylphenyl)ethenyl]benzene (1.34) compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2.5 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH, monitoring the reaction progress by

TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 20 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 31:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 25%) and isolated as a pale yellow oil (120 mg, 85% yield, Z:E = 31:1). This compound has been previously synthesized and spectra matches literature values.[66]



1,2,3-trimethoxy-5-[(Z)-2-(4-methoxyphenyl)ethenyl]benzene (1.35) compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH the reaction was moved to 60 °C and, monitoring the reaction progress by TLC (20% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 10 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = >100:1). The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 25%) and isolated as a pale yellow oil (131 mg, 87% yield, Z:E = >100:1). This compound has been previously synthesized and spectra matches literature values.[66]

1.8.6 *Gram Scale Reaction*

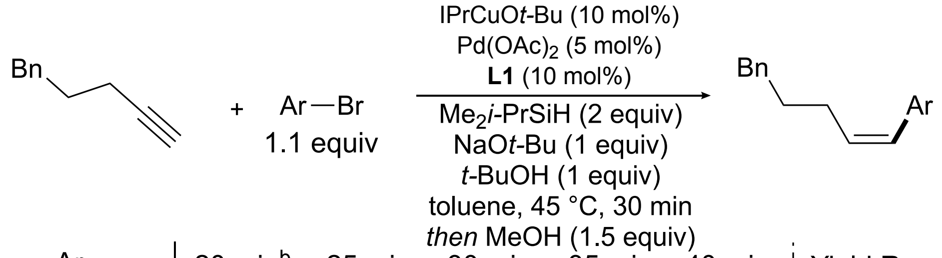


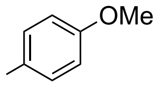
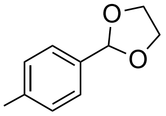
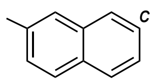
1-methoxy-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (1.3), compound was prepared according to the general procedure, TLC in 100% Hex showed that the starting alkyne was consumed after 2 h. After the addition of 1.5 equiv MeOH, monitoring the reaction progress by TLC (10% EtOAc/Hex) revealed that the internal alkyne intermediate was consumed after 15 min. An aliquot of the crude reaction mixture was analyzed by GC to obtain the isomeric ratio (Z:E = 18:1). The compound was purified by silica gel chromatography (EtOAc/Hex 0→10%) and a filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (1.1247 g, 75% yield, Z:E = 20:1).

1.8.7 *Selectivity Studies (Table 1.3)*

In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and NaO*t*-Bu (9.6 mg, 0.10 mmol, 2.0 equiv). To this was added 5-phenyl-1-pentyne (7.2 mg, 0.05 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.6 mg, 0.0025 mmol, 0.05 equiv) IPrCuCl (2.4 mg, 0.005 mmol, 0.10 equiv), **L1** (1.9 mg, 0.0050 mmol, 0.10 equiv), aryl bromide (0.055 mmol, 1.10 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.00 equiv), and toluene (0.5 mL). The reaction mixture was stirred at 45 °C, and the reaction progress was monitored by TLC. When the starting alkyne was fully consumed, methanol (2.4 mg, 0.0750 mmol, 1.5 equiv) was added and stirring was continued at 45 °C. 30 μL aliquots were taken at 20 min, 25 min, 30 min, 35 min and 40 min passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.9. Selectivity for Z-Styrene Over Time



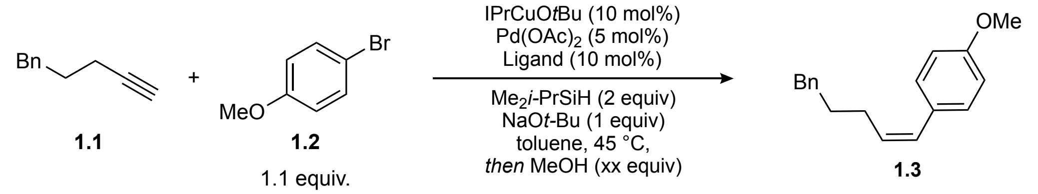
Ar =	20 min[b]	25 min	30 min	35 min	40 min	Yield Range
	20:1	18:1	13:1	10:1	10:1	92 - 95
	>100:1[d]	18:1	18:1	17:1	13:1	70 - 79
	28:1	28:1	27:1	26:1	25:1	84 - 89

[a] Selectivity determined by GC analysis of crude reaction mixture. [b] Time after the addition of alcohol. [c] *i*-BuOH used instead of MeOH. [d] Reaction mixture contains <10% internal alkyne.

1.8.8 *Optimization of E-Selective Hydroarylation (Table 1.4)*

In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and NaO*t*-Bu (9.6 mg, 0.100 mmol, 2 equiv). To this was added **1** (7.20 mg 0.050 mmol, 1.0 equiv), Pd(OAc)$_2$ (0.6 mg, 0.0025 mmol, 0.05 equiv) IPrCuCl (2.4 mg, 0.0050 mmol, 0.10 equiv), ligand (0.10 equiv), **1.2** (0.0550 mmol, 1.10 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.00 equiv), and toluene (0.5 mL). The reaction mixture was stirred at 45 °C, and the reaction progress was monitored by TLC. When the starting alkyne was fully consumed, methanol was added and stirring was continued at 45 °C. The reaction progress was monitored by GC for complete isomerization to the *E*-alkene. The reaction mixture was diluted with diethyl ether and filtered through a pad of silica gel. The crude reaction mixture was concentrated under reduced pressure and purified by silica gel chromatography. The ratio of stereoisomers for each product was determined by GC analysis of a crude reaction mixture.

Table 1.10. Reaction Development: *E*-Selective Hydroarylation



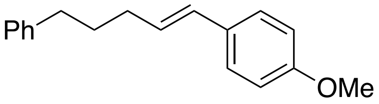
Entry	Ligand	Yield 20 min (E:Z)
1	QPhos	100% (1.9:1)
2	DavePhos	81% (1:2.5)
3	RuPhos	69% (1:2.8)
4	Sphos	81% (1:1.2)
5	L1	90% (1:29)
6	L1 (6 days)	95% (2:1)
7	L1 (5 equiv MeOH)	94% (>100:1)

[a]Combined yields and E:Z selectivity determined by GC

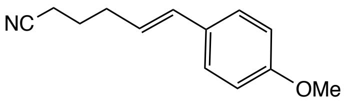
1.8.9 *General Procedure for the Hydroarylation of Terminal Alkynes: Synthesis of E-Styrenes (Table 1.5)*

In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and NaO*t*-Bu (96.1 mg, 1.00 mmol, 2 equiv). To this was added alkyne (0.50 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.8 mg, 0.025 mmol, 0.100 equiv) IPrCuCl (24.4 mg, 0.050 mmol, 0.10 equiv), **L1** (19 mg, 0.050 mmol, 0.10 equiv), aryl bromide (0.550 mmol, 1.10 equiv), Me$_2$*i*-PrSiH (102.3 mg, 1.00 mmol, 2.00 equiv), and toluene (5 mL). The reaction mixture was stirred at 45 °C, and the reaction progress was monitored by TLC. When the starting alkyne was fully consumed, methanol (80.1 mg, 2.50 mmol, 5.00 equiv) was added and stirring was continued at 45 °C. The reaction progress was monitored by GC for complete isomerization to the E-alkene (usually less than 24 h). The reaction mixture was diluted with diethyl ether and filtered through a pad of silica gel. The crude reaction mixture was concentrated under reduced pressure and purified by silica gel chromatography. The ratio of stereoisomers for each product was determined by GC analysis of a purified reaction mixture.

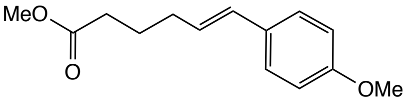
1.8.10 *Characterization of Hydroarylation Products: E-Styrenes (Table 1.5)*



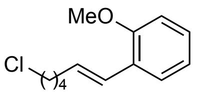
1-methoxy-4-[(1*E*)-5-phenylpent-1-en-1-yl]benzene (1.36), compound was prepared according to the general procedure. After 2 h TLC in 100% hexane showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 12 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the E-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →10%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (118 mg, 94% yield, 1 isomer). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.37 – 7.12 (m, 8H), 6.84 (d, *J* = 8.7 Hz,2H), 6.34 (d, *J* = 15.8 Hz, 1H), 6.09 (dt, *J* = 15.8, 6.8 Hz, 1H), 3.80 (s, 3H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.30 – 2.18 (m, 2H), 1.80 (p, *J* = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 158.8, 142.6, 130.8, 129.7, 128.6, 128.5, 128.4, 127.1, 125.8, 114.0, 55.4, 35.5, 32.7, 31.3. GCMs (EI) calculated for [M]+ 252.15, found 252.3. FTIR (neat, cm^{-1}): 3088(w), 3021(m), 2924(m), 1605(s), 1500(s), 1478(w), 1247(s), 1165(s), 1038(s), 964(m), 733(m), 673(s).



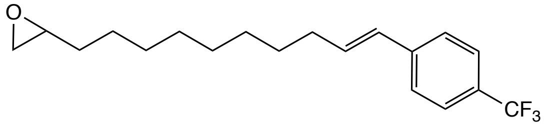
(5*E*)-6-(4-methoxyphenyl)hex-5-enenitrile (1.37), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH, the reaction mixture was stirred at 60 °C. After 12 hours a 30 μL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 45%) and isolated as a pale yellow oil (96 mg, 95% yield, E:Z = 44:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.29 (s, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.41 (d, *J* = 15.9 Hz, 1H), 5.98 (dt, *J* = 15.9, 7.1 Hz, 1H), 3.81 (s, 3H), 2.45 – 2.34 (m, 4H), 1.84 (p, *J* = 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 131.4, 130.0, 127.2, 125.4, 119.7, 114.0, 55.3, 31.7, 25.2, 16.4. GCMS (EI) calculated for [M]+ 201.12, found 201.2. FTIR (neat, cm^{-1}): 3004(m), 2935(m), 2836(m), 2245(m), 1607(s), 1512(s), 836(s), 736(s).



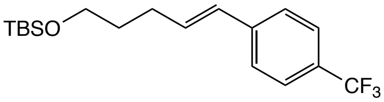
methyl (5*E*)-6-(4-methoxyphenyl)hex-5-enoate (1.38), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH, the reaction mixture was stirred at 60 °C. After 12 hours a 30 µL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a clear oil (81 mg, 70% yield, E:Z = >100:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.27 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.34 (d, J = 15.8 Hz, 1H), 6.11 – 5.95 (m, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 2.45 – 2.30 (m, 2H), 2.34 – 2.14 (m, 2H), 1.81 (p, J = 7.3 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 158.9, 130.5, 130.2, 127.4, 127.1, 114.0, 55.3, 51.5, 33.5, 32.4, 24.7. GCMS (EI) calculated for [M]+ 234.13, found 234.2. FTIR (neat, cm^{-1}): 3000(m), 2951(m), 2057(m), 1736(s), 1607(s), 1512(s), 839(s).



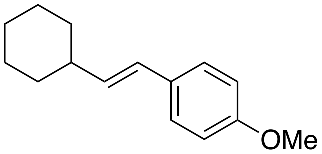
1-[(1*E*)-6-chlorohex-1-en-1-yl]-2-methoxybenzene (1.39), compound was prepared according to the general procedure. TLC in 10% EtOAc/Hex showed that the starting alkyne was fully consumed after 2 h. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 24 hours a 30 µL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (91 mg, 85% yield, E:Z = 10:1) ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.34 – 7.26 (m, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.34 (d, *J* = 15.8 Hz, 1H), 6.05 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.80 (s, 3H), 3.56 (t, *J* = 6.6 Hz, 2H), 2.30 – 2.16 (m, 2H), 1.92 – 1.76 (m, 2H), 1.70 – 1.55 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 130.6, 129.9, 127.2, 127.2, 114.1, 55.4, 45.1, 32.3, 32.2, 26.8. GCMS (EI) calculated for [M]+ 224.10, found 224.2. FTIR (neat, cm^{-1}): 3055(m), 2986(m), 2937(m), 2305(m), 1608(s), 1511(s), 896(s), 740(s).



2-[(9*E*)-10-[4-(trifluoromethyl)phenyl]dec-9-en-1-yl]oxirane (1.40), compound was prepared according to the general procedure. TLC in 10% EtOAc/Hex showed that the starting alkyne was fully consumed after 2 h. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 12 hours a 30 µL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (154 mg, 95% yield, E:Z = 16:1). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 2H), 6.48 – 6.26 (m, 2H), 2.96 – 2.84 (m, 1H), 2.79 – 2.70 (m, 1H), 2.50 – 2.42 (m, 1H), 2.23 (q, *J* = 7.2 Hz, 2H), 1.67 – 1.10 (m, 20H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.4. ^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.5, 134.2, 128.7, 128.7 (q, *J* = 32.1 Hz)), 125.6, 125.5 (q, *J* = 3.8 Hz) 124.4 (q, *J* = 271.6 Hz), 52.5, 47.2, 33.2, 32.6, 29.6, 29.5, 29.3, 29.2, 26.1. GCMS (EI) calculated for [M]+ 326.19, found 326.3. FTIR (neat, cm^{-1}): 3044(m), 2928(m), 2855(m), 1740(m), 1615(m), 1465(s), 834(s), 757(s),

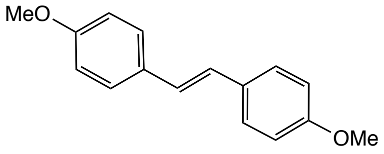


tert-butyldimethyl{[(4*E*)-5-[4-(trifluoromethyl)phenyl]pent-4-en-1-yl]oxy}silane (1.41), compound was prepared according to the general procedure. TLC in 10% EtOAc/Hex showed that the starting alkyne was fully consumed after 2 h. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 12 hours a 30 μL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (148 mg, 86% yield, E:Z = 16:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 2H), 6.59 – 6.16 (m, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.31 (q, *J* = 6.9 Hz, 2H), 1.79 – 1.58 (m, 2H), 0.91 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.5, 133.6, 129.2, 128.7 (q, *J* = 32.2 Hz), 126.2, 125.6 (q, *J* = 3.7 Hz), 124.5 (q, *J* = 271.7 Hz), 62.5, 32.4, 29.6, 26.1, 18.2, -5.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.4. GCMS (EI) calculated for [M]+ 358.19, found 358.3. FTIR (neat, cm^{-1}): 2930(m), 2895(m), 2858(m), 1915(m), 1615(s), 1473(s), 835(s), 735(s).

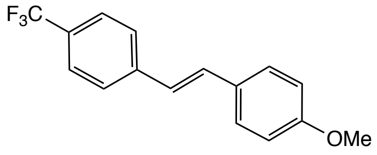


1-[(Z)-2-cyclohexylethenyl]-4-methoxybenzene (1.42) compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →10%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (118 mg, 94% yield, E:Z = 10:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.28 (d, *J* =

9.1 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.29 (d, *J* = 15.9 Hz, 1H), 6.03 (dd, *J* = 16.0, 6.9 Hz, 1H), 3.80 (s, 3H), 2.17 – 2.01 (m, 1H), 1.89 – 1.61 (m, 5H), 1.42 – 1.06 (m, 5H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 158.7, 134.8, 131.0, 127.1, 126.7, 114.0, 55.4, 41.2, 33.2, 26.3, 26.2. GCMS (EI) calculated for [M]+ 216.32, found 216.5. FTIR (neat, cm-1): 2923 (s), 2845 (s), 1605(s), 1511(s), 1246(s), 678(m).

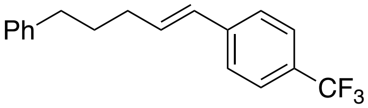


1-methoxy-4-[(*E*)-2-(4-methoxyphenyl)ethenyl]benzene (1.43), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2 h. After the addition of 2 equiv of NaO*t*-Bu and 4 equiv of MeOH, the reaction mixture was stirred at 60 °C. After 12 hours a 30 µL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by trituration with Hex and isolated as a white solid (109 mg, 91% yield, E:Z = 32:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.4 Hz, 4H), 7.06 – 6.71 (m, 6H), 3.83 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 130.2, 130.1, 128.5, 113.7, 55.3. GCMS (EI) calculated for [M]+ 240.12, found 240.2. FTIR (neat, cm^{-1}): 3055(m), 2987(m), 2305(m), 1609(s), 1514(s), 896(s), 740(s).



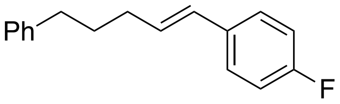
1-methoxy-4-[(*E*)-2-[4-(trifluoromethyl)phenyl]ethenyl]benzene (1.44), compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 2

h. After the addition of 2 equiv of NaO*t*-Bu and 6 equiv of *i*-BuOH, the reaction mixture was stirred at 60 °C. After 12 hours a 30 µL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a pale yellow solid (115 mg, 83% yield, E:Z = 22:1). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.58 (s, 4H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 16.4 Hz, 1H), 6.98 (d, *J* = 16.4 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 160.0, 141.3, 130.9, 129.6, 129.0 (q, *J* = 32.1 Hz), 126.4, 125.7 (q, *J* = 4.3 Hz), 125.1, 124.4 (q, *J* = 271.4 Hz), 114.4, 55.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.4. GCMS (EI) calculated for [M]+ 278.09, found 278.1. FTIR (neat, cm^{-1}): 3053(s), 2986(m), 2839(m), 2305(m), 1603(s), 1510(s), 835(s), 740(s).

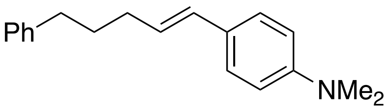


1-[(1*E*)-5-phenylpent-1-en-1-yl]-4-(trifluoromethyl)benzene (1.45), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 2.0 equiv of *i*-BuOH were added and the reaction mixture was stirred at 45 °C. After 1 h a 30 µL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Hex 100%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (120 mg, 83% yield, E:alkane = 11:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.7 Hz, 2H), 7.14 (s, 3H), 7.10 (d, *J* = 7.1 Hz, 3H), 6.32 (d, *J* = 15.9 Hz, 1H), 6.23 (dt, *J* = 15.3, 6.6 Hz, 1H), 2.58 (t, *J* = 7.7 Hz, 2H), 2.25 – 2.13 (m, 2H), 1.73 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.3, 141.4, 133.6, 129.3, 128.7 (q, *J* =19.5 Hz), 128.6, 128.5, 125.7, 125.6, 125.4 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 271.2

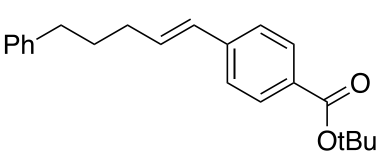
Hz), 35.5, 32.7, 30.9. GCMS (EI) calculated for [M]+ 290.12, found 290.5. FTIR (neat, cm^{-1}): 3028(m), 2934(m), 2858(w), 1615(m), 1454(w), 1326(s), 1164(s), 1122(s), 1068.2(s), 1016(w), 747(w), 699(m).



1-fluoro-4-[(1*E*)-5-phenylpent-1-en-1-yl]benzene (1.46), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 µL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Hex 100%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (103 mg, 86% yield, 1 isomer). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.29 – 7.17 (m, 5H), 7.14 (d, *J* = 6.7 Hz, 3H), 6.99 – 6.86 (m, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 6.09 (dt, *J* = 15.8, 6.8 Hz, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.19 (dt, *J* = 8.2, 7.6, 6.2 Hz, 2H), 1.85 – 1.66 (m, 2H). ^{19}F NMR (471 MHz, Chloroform-d) δ -123.85. ^{13}C NMR (126 MHz, Chloroform-d) δ 162.0 (d, *J* = 245.6 Hz), 142.4, 134.1 (d, *J* = 2.7 Hz), 130.4, 129.2, 128.6 (d, *J* = 17.5 Hz), 127.4 (d, *J* = 7.8 Hz), 125.9, 115.5, 115.4, 35.5, 32.6, 31.1. GCMS (EI) calculated for [M]+ 240.13, found 240.2. FTIR (neat, cm^{-1}): 3058(w), 3021(m), 2924(s), 2849(m), 1597(m), 1508(s), 1448(w), 1225(s), 1158(m), 956(m), 837(m), 748(m), 688(s).

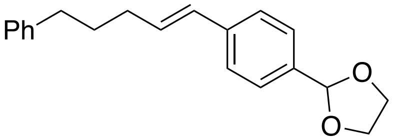


N,N-dimethyl-4-[(1*E*)-5-phenylpent-1-en-1-yl]aniline (1.47), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH and 0.50 equiv Me_2*i*-PrSiH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →15%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (124 mg, 93% yield, E:Z = 14:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.24 – 7.01 (m, 8H), 6.58 (d, *J* = 8.8 Hz, 2H), 6.21 (d, *J* = 15.8 Hz, 1H), 5.92 (dt, *J* = 15.7, 6.9 Hz, 1H), 2.84 (s, 6H), 2.56 (t, *J* = 7.6 Hz, 2H), 2.21 – 2.04 (m, 2H), 1.68 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 149.8, 142.7, 130.1, 128.6, 128.4, 126.9, 126.7, 126.4, 125.7, 112.7, 40.7, 35.5, 32.7, 31.5. GCMS (EI) calculated for [M]+ 265.18, found 265.3. FTIR (neat, cm^{-1}): 3085(w), 3028(m), 2934(m), 2854(m), 1615(s), 1512(s), 1351(m), 1146(m), 672(s).

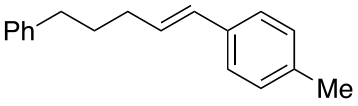


tert-butyl 4-[(1*E*)-5-phenylpent-1-en-1-yl]benzoate (1.48), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 2.0 equiv of *t*-BuOH (used to prevent transesterification) were added and the reaction mixture was stirred at 60 °C. After 30 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →10%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (125 mg, 78% yield, E:alkane = 10:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.93 (d, *J* = 7.8 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.34 – 7.24 (m, 2H), 7.21 (d, *J* = 7.3 Hz, 4H), 6.44 (d, *J* = 16.1 Hz, 1H), 6.36 (dt, *J* = 14.6, 6.5 Hz, 1H), 2.69 (t, *J* = 7.9 Hz, 2H), 2.33 – 2.25 (m, 2H), 1.84 (p, *J* = 7.1 Hz, 2H), 1.60 (s, 13H). ^{13}C

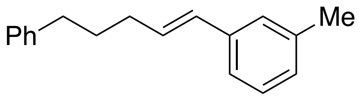
NMR (126 MHz, Chloroform-d) δ 142.3, 142.0, 133.3, 129.8, 129.7, 128.6, 128.5, 125.9, 125.7, 120.1, 80.9, 35.7, 32.7, 30.9, 28.4. GCMS (EI) calculated for [M]+ 322.19, found 322.4. FTIR (neat, cm^{-1}): 3027(w), 2977(m), 2932(m), 2857(m), 1710(s), 1606(s), 1455(m), 1367(m), 1293(s), 1165(s), 1118(s), 747(m), 699(m).



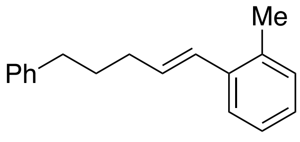
2-{4-[(1*E*)-5-phenylpent-1-en-1-yl]phenyl}-1,3-dioxolane (1.49), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 µL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →15%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (126 mg, 86% yield, 1 isomer). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.43 – 7.20 (m, 7H), 7.17 (d, *J* = 7.1 Hz, 3H), 6.37 (d, *J* = 15.9 Hz, 1H), 6.22 (dt, *J* = 15.8, 6.6 Hz, 1H), 5.77 (s, 1H), 4.21 – 3.89 (m, 4H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.31 – 2.13 (m, 2H), 1.79 (p, *J* = 7.6 Hz, 2H. ^{13}C NMR (126 MHz, Chloroform-d) δ 142.4, 138.8, 136.5, 131.3, 129.9, 128.5, 128.4, 126.7, 126.0, 125.8, 103.7, 65.3, 35.5, 32.6, 31.0. GCMS (EI) calculated for [M]+ 294.16, found 294.4. FTIR (neat, cm^{-1}): 3088(w), 3027(m), 2931(s), 2887(m), 2857(m), 1479(m), 1426(w), 1390(m), 1081(s), 969(s), 678(s).



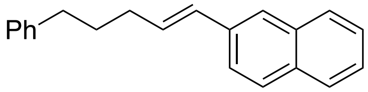
1-methyl-4-[(1*E*)-5-phenylpent-1-en-1-yl]benzene (1.50), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →5%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (101 mg, 85% yield, E:alkane = 22:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.40 – 7.20 (m, 7H), 7.15 (d, *J* = 7.9 Hz, 2H), 6.42 (d, *J* = 15.9 Hz, 1H), 6.23 (dt, *J* = 15.8, 6.8 Hz, 1H), 2.81 – 2.67 (t, *J* = 7.6 Hz, 2H), 2.38 (s, 3H), 2.36 – 2.23 (m, 2H), 1.86 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 1542.5 136.6, 135.2, 130.2, 129.6, 129.3, 128.6, 128.4, 126.0, 125.8, 35.5, 32.7, 31.2, 21.5. GCMS (EI) calculated for [M]+ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3080(w), 3021(m), 2924(s), 2849(m), 1605(w), 1508(m), 1453(m), 1032(w), 966(s), 735(m), 678(s).



1-methyl-3-[(1*E*)-5-phenylpent-1-en-1-yl]benzene (1.51), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →5%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (103 mg, 87% yield, 1 isomer). ^{1}H NMR (500 MHz, Chloroform-d) δ 7.35 – 7.24 (m, 2H), 7.24 – 7.12 (m, 6H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.38 (d, *J* = 15.8 Hz, 1H), 6.23 (dt, *J* = 15.2, 6.8 Hz, 1H), 2.68 (t, *J* = 7.8 Hz, 2H), 2.35 (s, 3H), 2.31 – 2.18 (m, 2H), 1.82 (p, *J* = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.3, 136.4, 134.9, 129.9, 129.3, 129.0, 128.3, 128.2, 125.7, 125.6, 35.3, 32.4, 31.0, 21.0. GCMS (EI) calculated for [M]+ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3059(w), 3022(m), 2931(s), 2849(m), 1603(w), 1502(m), 1454(m), 1031(w), 965(s), 738(m), 691(s).

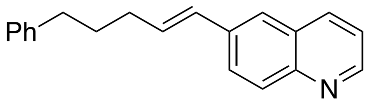


1-methyl-2-[(1*E*)-5-phenylpent-1-en-1-yl]benzene (1.52), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 5.0 equiv of MeOH and 0.50 equiv Me$_2$*i*-PrSiH were added and the reaction mixture was stirred at 45 °C. After 24 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et$_2$O/Hex 0 →5%) and filtration through a short plug of alumina (10% Et$_2$O/Hex). The compound was isolated as a clear colorless oil (95 mg, 80% yield, E:Z = 24:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.31 (d, J = 5.9 Hz, 1H), 7.18 (d, J = 7.2 Hz, 2H), 7.15 – 6.99 (m, 6H), 6.50 (dd, J = 15.6, 1.6 Hz, 1H), 6.00 (dt, J = 15.4, 6.9 Hz, 1H), 2.59 (t, J = 7.7 Hz, 2H), 2.29 – 2.11 (m, 5H), 1.73 (p, J = 7.7 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.5, 137.1, 135.0, 132.0, 130.3, 128.6, 127.0, 126.1, 125.9, 125.6, 35.5, 33.0, 31.5, 20.0. GCMS (EI) calculated for [M]+ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3062(w), 3026(m), 2931(s), 2856(m), 1602(w), 1495(m), 1454(m), 1031(w), 964(s), 743(s), 698(s).

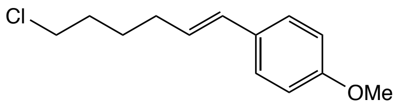


2-[(1*E*)-5-phenylpent-1-en-1-yl]naphthalene (1.53), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 2.0 equiv of *i*-BuOH were added and the reaction mixture was stirred at 45 °C. After

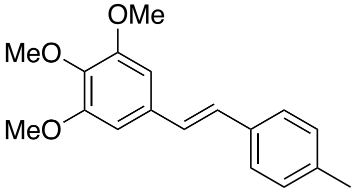
30 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →10%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (121 mg, 89% yield, E:alkane = 37:1). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.73 – 7.61 (m, 3H), 7.62 – 7.43 (m, 2H), 7.39 – 7.26 (m, 2H), 7.24 – 7.04 (m, 6H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.26 (dt, *J* = 15.7, 6.8 Hz, 1H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.21 (m, 2H), 1.77 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 142.5, 135.4, 133.9, 132.8, 131.2, 130.5, 128.6, 128.5, 128.2, 127.9, 127.8, 126.3, 125.9, 125.6, 125.5, 123.7, 35.6, 32.8, 31.2. GCMS (EI) calculated for [M]+ 272.16, found 272.3. FTIR (neat, cm^{-1}): 3058(m), 3028(m), 2931(m), 2855(m), 1598(m), 1496(m), 1478(m), 1453(m), 962(m), 745(s), 678(s).



6-[(1*E*)-5-phenylpent-1-en-1-yl]quinolone (1.54), compound was prepared according to the general procedure. After 2 h TLC in 100% Hex showed that the starting alkyne was fully consumed. 2.0 equiv of MeOH were added and the reaction mixture was stirred at 45 °C. After 1 h a 30 μL aliquot was taken and analysis by GC for confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography (Et_2O/Hex 0 →25%) and filtration through a short plug of alumina (10% Et_2O/Hex). The compound was isolated as a clear colorless oil (103 mg, 75% yield, E:alkane = 14:1). ^{1}H NMR (500 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.09 (dd, *J* = 16.2, 8.5 Hz, 2H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.65 (s, 1H), 7.44 – 7.30 (m, 4H), 7.25 (q, *J* = 10.7 Hz, 4H), 6.59 (d, *J* = 15.9 Hz, 1H), 6.43 (dt, *J* = 15.3, 6.8 Hz, 1H), 2.74 (t, *J* = 7.8 Hz, 2H), 2.41 – 2.31 (m, 2H), 1.89 (p, *J* = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-d) δ 149.8, 147.9, 142.3, 136.1, 135.8, 132.4, 129.7, 129.6, 128.6, 128.5, 128.4, 127.3, 125.9, 124.8, 121.4, 35.5, 32.7, 31.0. GCMS (EI) calculated for [M]+ 273.15, found 273.3. FTIR (neat, cm^{-1}): 3062(w), 3025(m), 2930(s), 1590(w), 1497(s), 1454(m), 1118(w), 962(m), 839(m), 747(m), 699(s).



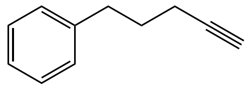
1-[(1*E*)-6-chlorohex-1-en-1-yl]-4-methoxybenzene (1.55), compound was prepared according to the general procedure. TLC in 10% EtOAc/Hex showed that the starting alkyne was fully consumed after 2 h. 5.0 equiv of *i*-BuOH were added and the reaction mixture was stirred at 45 °C. After 12 hours a 30 µL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 15%) and isolated as a colorless oil (99 mg, 88% yield, E:Z = >100:1) ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.34 – 7.26 (m, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.34 (d, *J* = 15.8 Hz, 1H), 6.05 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.80 (s, 3H), 3.56 (t, *J* = 6.6 Hz, 2H), 2.30 – 2.16 (m, 2H), 1.92 – 1.76 (m, 2H), 1.70 – 1.55 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 130.6, 129.9, 128.0, 127.2, 114.1, 55.4, 45.1 32.3, 32.2, 26.8. GCMS (EI) calculated for [M]+ 224.10, found 224.2. FTIR (neat, cm^{-1}): 3055(m), 2986(m), 2937(m), 2305(m), 1608(s), 1511(s), 896(s), 740(s).



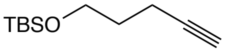
1,2,3-trimethoxy-5-[(E)-2-(4-methylphenyl)ethenyl]benzene (1.57) compound was prepared according to an altered general procedure. LiO*t*-Bu was used in place of NaO*t*-Bu as a turnover reagent. TLC in 20% EtOAc/Hex showed that the starting alkyne was consumed after 4 h. After the addition of 2 equiv of NaO*t*-Bu and 5 equiv of MeOH. The reaction mixture was stirred at 60

°C. After 24 hours a 30 μL was taken and analysis by GC confirmed complete isomerization to the *E*-alkene. The compound was purified by trituration with Hex and isolated as a white solid (115 mg, 85% yield, 1 isomer). This compound has been previously synthesized and spectra matches literature values.[66]

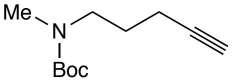
1.8.11 *Alkyne Starting Materials*



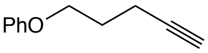
5-phenyl-1-pentyne (1.1) was purchased from GFS Chemical and distilled over calcium hydride under reduced pressure before use.



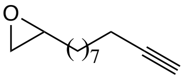
tert-butyldimethyl(pent-4-yn-1-yloxy)silane (1.62) was prepared according to a known procedure and has been previously characterized.[76]



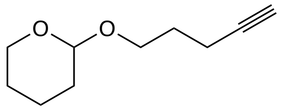
tert-butyl N-methyl-N-(pent-4-yn-1-yl)carbamate (1.63) was prepared according to a known procedure and has been previously characterized.[77]



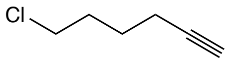
(pent-4-yn-1-yloxy)benzene (1.64) was prepared according to a known procedure and has been previously characterized.[78]



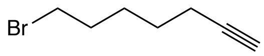
2-(dec-9-yn-1-yl)oxirane (1.65) was prepared according to a known procedure and has been previously characterized.[79]



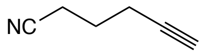
2-(pent-4-yn-1-yloxy)tetrahydra-2*H*-pyran (1.66) has been previously characterized and spectral data match literature values. [80]



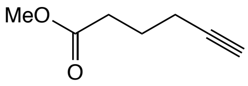
6-chlorohex-1-yne (1.67) was purchased from TCI America and distilled over calcium hydride under reduced pressure before use.



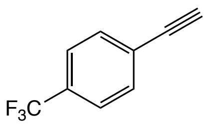
7-bromohept-1-yne (1.68) was prepared according to a known procedure and has been previously characterized.[81]



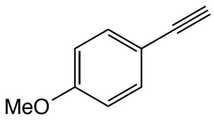
hex-5-ynenitrile (1.69) was purchased from Oakwood Chemical and distilled over calcium hydride under reduced pressure before use.



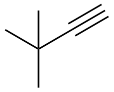
methyl hex-5-ynoate (1.70) was purchased from Fischer Scientific and distilled over calcium hydride under reduced pressure before use.



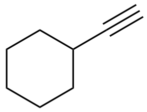
1-ethynyl-4-(trifluoromethyl)benzene (1.71) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



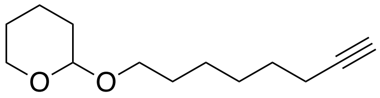
1-ethynyl-4-methoxybenzene (1.72) was purchase from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



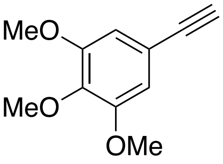
3,3-dimethylbut-1-yne (1.73) was purchased from Milipore Sigma and distilled over calcium hydride under reduced pressure before use.



ethynylcyclohexane (1.74) was purchased from Milipore Sigma and distilled over calcium hydride under reduced pressure before use.

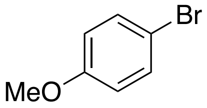


2-(oct-7-yn-1-yloxy)oxane (1.75) was prepared according to a known literature procedure and has been previously characterized.[82]

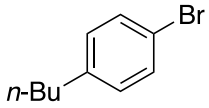


5-ethynyl-1,2,3-trimethoxybenzene (1.76) was prepared according to a known literature procedure and has been previously characterized.[83]

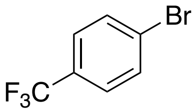
1.8.12 *Aryl Bromide Starting Materials*



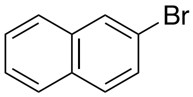
4-bromoanisole (1.2) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



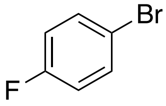
1-bromo-4-butylbenzene (1.4) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



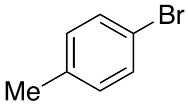
4-bromobenzotrifluoride (1.77) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



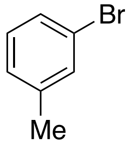
2-bromonaphthalene (1.78) was purchased from Ark-Pharm and used without purification.



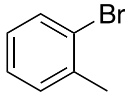
1-bromo-4-fluorobenzene (1.79) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



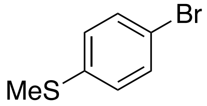
4-bromotoluene (1.80) was purchased form Alfa Aesar and using without purification.



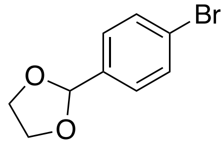
3-bromotoluene (1.81) was purchased form TCI America and distilled over calcium hydride under reduced pressure before use.



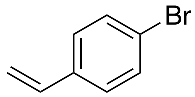
2-bromotoluene (1.82) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



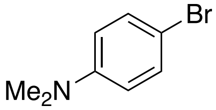
1-bromo-4-(methylsulfanyl)benzene (1.83) was purchased from Oakwood Chemicals and used without purification.



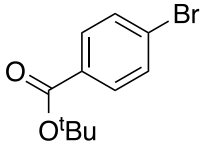
1-bromo-4-phenyl-1,3-dioxolane (1.84) was purchased from Ark-Pharm and distilled over calcium hydride under reduced pressure before use.



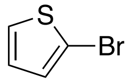
4-bromostyrene (1.85) was purchased from TCI America and degassed before use.



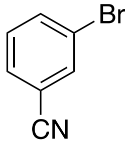
4-bromo-N,N-dimethylaniline (1.86) was purchased from Oakwood Chemicals and used without purification.



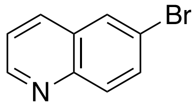
tert-butyl-4-bromobenzoate (1.87) was purchased from Ark-Pharm and distilled over calcium hydride under reduced pressure before use.



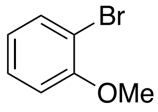
2-bromothiophene (1.88) was purchased from Combi-Blocks and distilled over calcium hydride under reduced pressure before use.



3-bromobenzonitrile (1.89) was purchased from Ark-Pharm and used without purification.

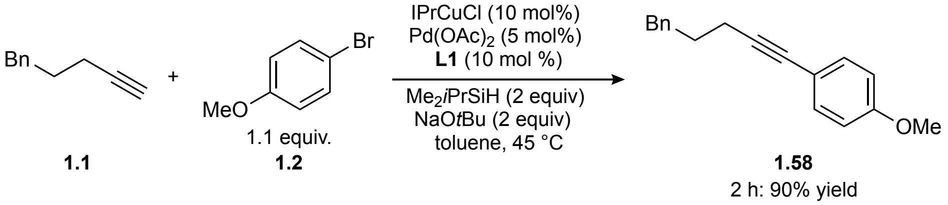


6-bromoquinoline (1.90) was purchased from Ark-Pharm and distilled over calcium hydride under reduced pressure before use.



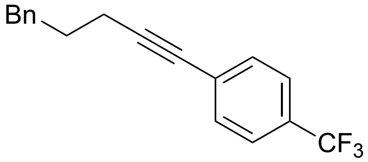
2-bromoanisole (1.91) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.

1.8.13 *Synthesis of Internal Alkyne Intermediate*



Scheme 1.14. Synthesis of Internal Alkyne

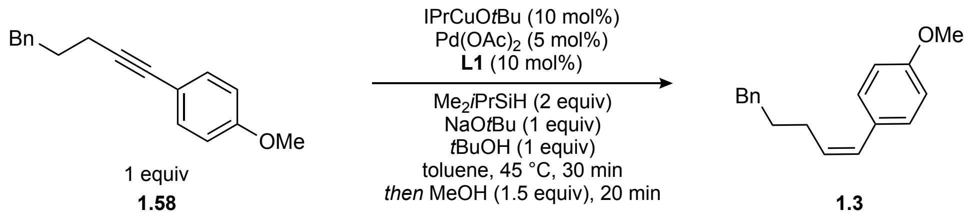
In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and NaO*t*-Bu (96.1 mg, 1.00 mmol, 2 equiv). To this was added alkyne (**1**) (0.50 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.8 mg, 0.025 mmol, 0.100 equiv) IPrCuCl (24.4 mg, 0.050 mmol, 0.10 equiv), **L1** (19 mg, 0.050 mmol, 0.10 equiv), aryl bromide (2.**2**) (102.9 mg, 0.550 mmol, 1.10 equiv), Me$_2$*i*-PrSiH (102.3 mg, 1.00 mmol, 2.00 equiv), and toluene (5 mL). The reaction mixture was stirred at 45 °C, and monitored by TLC until starting alkyne was fully consumed, 2 h. TLC 100% Hex. Compound was purified by silica gel column chromatography (Et$_2$O/Hex 0→10%) and passed through a short plug of alumina (10% Et$_2$O/Hex) **1.58** was isolated as a clear colorless liquid (113 mg, 90% yield). This compound has been previously synthesized and spectra matches literature values.[84]



1-(5-phenylpent-1-yn-1-yl)-4- (trifluoromethyl)benzene (1.59), was synthesized according to the above procedure, but has previously been synthesized and spectra matches literature values.[84]

1.8.14 *Mechanistic Studies: Semireduction*

Catalytic Semireduction: Contribution of Pd and Cu catalysts (Scheme 1.6)



Scheme 1.15. Conditions for Probing Mechanism of Catalytic Semireduction with MeOH

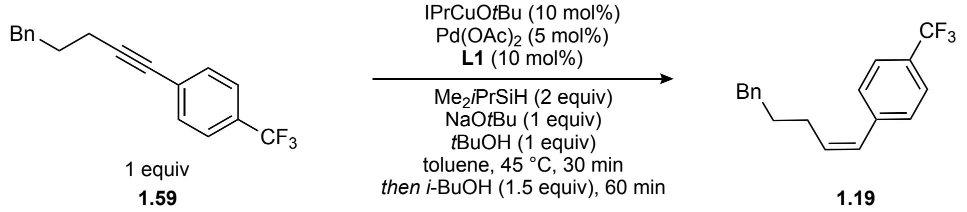
In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Pd(OAc)$_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), *t*-BuOH (3.7 mg, 0.050, 1.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then MeOH (2.4 mg, 0.075 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 45 °C and 30 µL aliquots were taken at 10 min, 20 min, 30 min and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.11. Relative Role of Pd/Cu Catalysts in Semireduction.

Reaction Conditions	yield (10 min)	yield (20 min)	yield (30 min)	yield (24 h)
Above Conditions	78%	86% (18:1) *	86% (18:1) *	80% (3:1) *
No Cu	38%	39%	40%	41%
No Pd/L	64%	70%	71%	99% (48:1) *

*Z:E diastereoselectivity determine by GC analysis. Yield of major isomer is reported

Catalytic Semireduction: EWG with *i*-BuOH (Scheme 1.6)



Scheme 1.16. Conditions Probing Mechanism of Catalytic Semireduction with *i*-BuOH with EWG

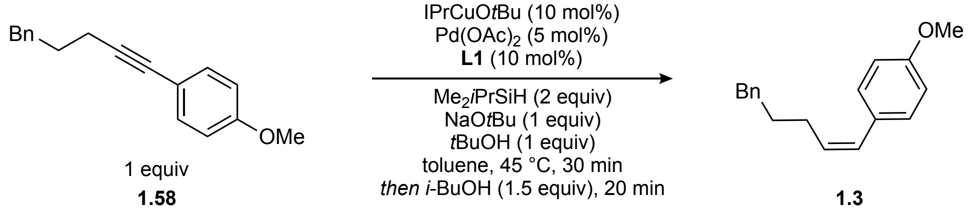
In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.59** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), $Pd(OAc)_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), *t*-BuOH (3.7 mg, 0.050, 1.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then *i*-BuOH (4.1 mg, 0.075 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 45 °C and 30 µL aliquots were taken at 30 min, 60 min and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.12. Catalytic Semireduction with EWG with *i*-BuOH.

Reaction Conditions	yield (30 min)	yield (60 min)	yield (24 h)
Above Conditions	58%	76% (38:1) *	36% (2:1) *
No Cu	1%	5%	11%
No Pd/L	40%	52%	74%

*Z:E diastereoselectivity determined by GC analysis. Yield of major isomer is reported

Catalytic Semireduction: *i*-BuOH with other Substrates (Scheme 1.6)



Scheme 1.17. Conditions Probing Mechanism of Catalytic Semireduction with *i*-BuOH for EDG

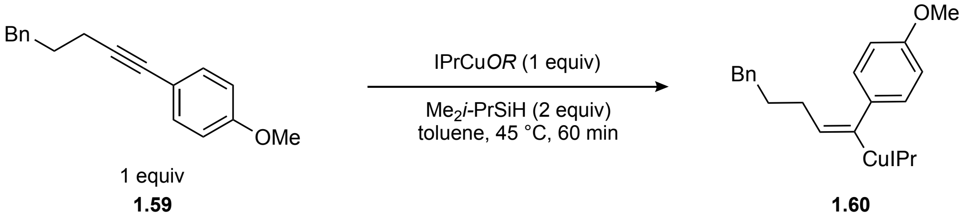
In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), $Pd(OAc)_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), *t*-BuOH (3.7 mg, 0.050, 1.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then *i*-BuOH (4.1 mg, 0.075 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 45 °C and 30 μL aliquots were taken at 10 min, 20 min, 30 min and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.13. Relative Contribution of Pd/Cu Catalysts with *i*-BuOH.

Reaction Conditions	yield (10 min)	yield (20 min)	yield (30 min)	yield (24 h)
Above Conditions	39%	57%	66%	74%
No Cu	1%	2%	6%	9%
No Pd/L	26%	39%	49%	56%

*Z:E diastereoselectivity determine by GC analysis. Yield of major isomer is reported

Stoichiometric Hydrocupration of Internal Alkyne: Effect of IPrCuOR (Scheme 1.)



Scheme 1.18. Stoichiometric Hydrocupration of Internal Alkyne with IPrCuOR.

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, IPrCuOR (0.050 mmol, 1.0 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C and 15 μL aliquots were taken every min for 10 min, and then every 5 min for 1 hour and passed through a short plug of silica in the glovebox with 1.5 mL of Ether and analyzed by Gas Chromatography. The reported yield of **1.60** is based on the yield of alkene obtained after quenching of the reaction mixture.

Table 1.14. Hydrocupration of Internal Alkyne with IPrCuO*t*-Bu

Time (min)	% **1.58**	% yield (**1.60**)
0	96	0
1	93	3
2	91	8
3	86	9

4	83	13
5	78	16
6	82	17
7	72	21
8	71	22
9	70	23
10	70	24
15	60	27
20	54	36
25	0	48
30	37	45
45	29	68
60	20	74

Table 1.15. Hydrocupration of Internal Alkyne with IPrCuOMe

Time (min)	% **1.58**	% yield (**1.60**)
0	100	0
1	47	51
2	28	65
3	26	73
4	23	74
5	20	73
6	18	78
7	19	78
8	17	80
9	15	85
10	15	86
15	13	88
20	13	88
25	13	87
30	10	90
45	10	93
60	8	93

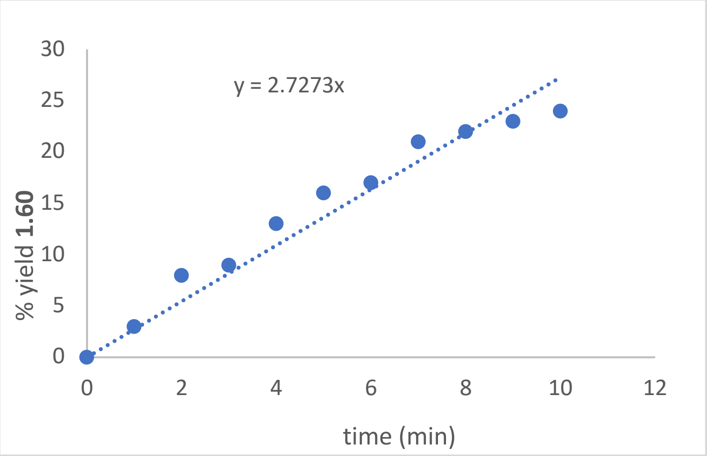


Figure 1.1. Hydrocupration of Internal Alkyne with IPrCuO*t*-Bu.

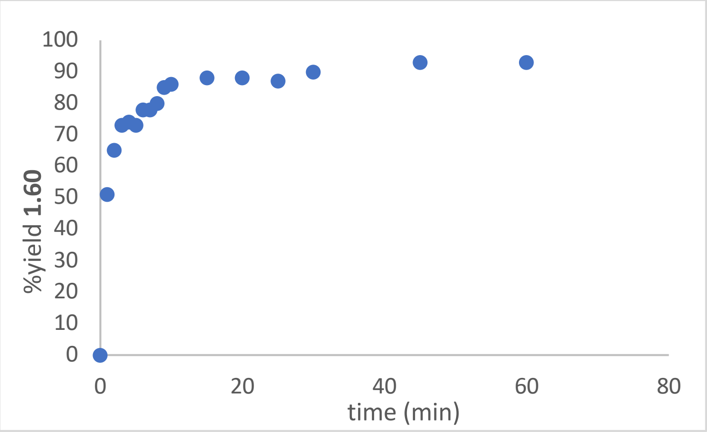


Figure 1.2. Hydrocupration of Internal Alkyne with IPrCuOMe.

Control Experiments for Quenching Alkenyl Copper with Dibromotetrachloroethane

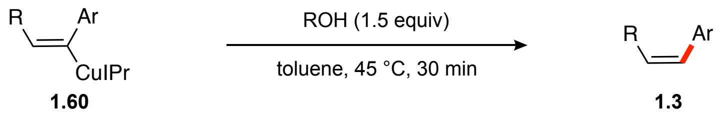
Quenching of IPrCuOt-Bu

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, IPrCuO*t*-Bu (2.6 mg, 0.0050 mmol, 0.1 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv), MeOH (2.4 mg, 0.075 mmol, 1.5 equiv), $Br_2Cl_4C_2$ (65.1 mg, 0.2 mmol, 4 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C and 15 µL aliquots were taken at 20 min 1 hour and 2 hours, passed through a short plug of silica with 1.5 mL of EtOAc and analyzed by Gas Chromatography. Over the course of the reaction there was no formation of alkenyl copper or vinyl bromide product and quantitative recovery of the internal alkyne. This indicated that in the presence of 4 equivalents of dibromotetrachloroehtane the catalyst could not turnover, thus confirming it as an effective quenching method.

Quenching of Alkenyl Copper

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv). To this was added **1.60** (3.5 mg, 0.0050 mmol, 0.1 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), NaO*t*-Bu (4.8 mg, 0.050 mmol, 1 equiv), MeOH (2.4 mg, 0.075 mmol, 1.50 equiv), $Br_2Cl_4C_2$ (65.1 mg, 0.2 mmol, 4 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C and 15 μL aliquots were taken at 20 min 1 hour and 2 hours, passed through a short plug of silica with 1.5 mL of EtOAc and analyzed by Gas Chromatography. Over the course of the reaction we observe only the formation of 1 equivalent of alkenyl bromide (relative to the amount of **2.60** used in the reaction) and the quantitative recovery of the internal alkyne. This indicated that in the presence of 4 equivalents of dibromotetrachloroehtane the alkenyl copper could not turnover and regenerate the active catalyst, thus confirming it as an effective quenching method.

Stoichiometric Protonation of Alkenyl Copper (1.60) (Scheme 1.7)



Scheme 1.19. Stoichiometric Protodemetalation with ROH

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, alkenyl copper **1.60** (17.6 mg, 0.050 mmol, 1.00 equiv). To this was added TMB (2.8 mg. 0.017 mmol, 0.33 equiv), alcohol (0.075 mmol, 1.5 equiv) and toluene (0.50 mL). The reaction was placed at 45 °C and 15 μL aliquots were taken every min for the first 5 min and then every 5 min for 20 min. Aliquots were quenched into $Br_2Cl_4C_2$ (1.6 mg, 0.005 mmol, 0.04 equiv) and passed through a short plug of silica with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.16. Stoichiometric Protonation of Alkenyl Copper with *t*-BuOH.

Time (min)	alkenyl copper (**1.60**)	% yield **1.3**	% yield **1.3** (corrected)
0	86	5	0
1	85	7	2
2	86	9	4
3	85	10	5
4	82	12	7
5	84	13	8
10	70	21	16
15	67	25	20
20	61	27	22

Table 1.17. Stoichiometric Protonation of Alkenyl Copper with MeOH.

Time (min)	alkenyl copper (**1.60**)	% yield **1.3**
0	100	0
1	34	68
2	22	79
3	0	90
4	0	94
5	0	94
10	0	104
15	0	105
20	0	106

Yields for *t*-BuOH are corrected to 0 based on initial formation of alkene before alcohol was added

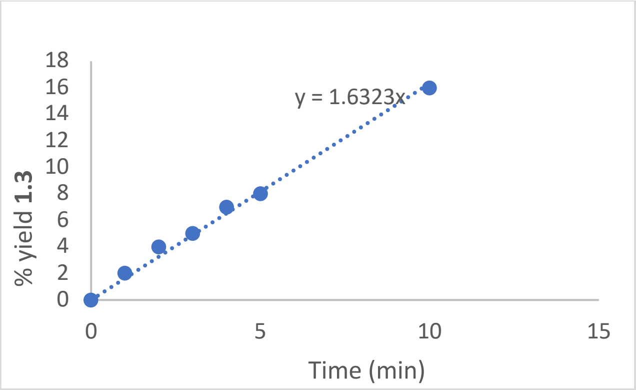


Figure 1.3. Stoichiometric Protonation of Alkenyl Copper with *t*-BuOH.

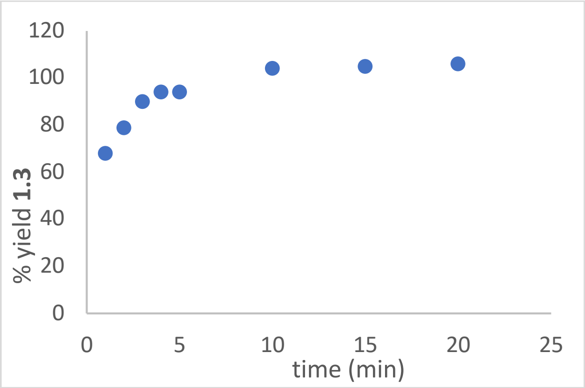
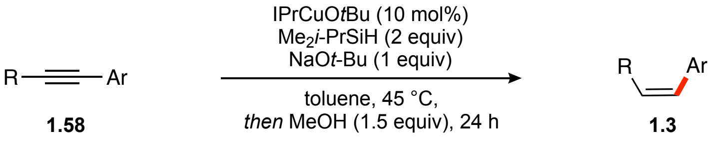


Figure 1.4. Stoichiometric Protonation of Alkenyl Copper with MeOH.

Copper-Catalyzed Semireduction of Sonogashira: Effect of ROH (Scheme 1.7)



Scheme 1.20. Catalytic Semireduction using ROH

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), alcohol (0.075 mmol, 1.5 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C 15 µL aliquots were taken, and quenched into $Br_2Cl_4C_2$ (3.4 mg, 0.004 mmol, 0.04 equiv) and diluted with 0.50 mL of Ether, passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.18. Copper-Catalyzed Semireduction of Sonogashira with MeOH.

Time (min)	% yield **1.3**
0	0
10	37
20	61
30	72
2 h	79
7 h	80
24 h	82

Table 1.19. Copper-Catalyzed Semireduction of Sonogashira with *t*-BuOH.

Time (min)	% **1.58**	% yield **1.3**
1	98	0
5	100	0
10	100	0
20	95	0
30	95	2
60	90	1
90	96	4
5 h	83	8
8 h	69	16
24 h	73	23

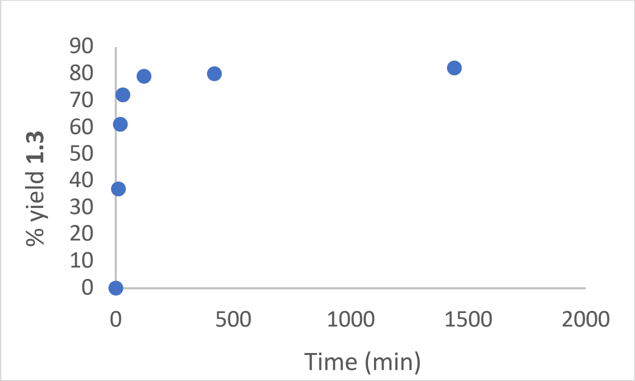


Figure 1.5. Copper-Catalyzed Semireduction of Sonogashira with MeOH.

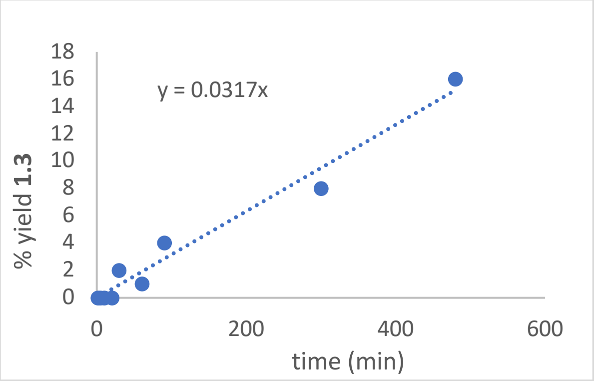
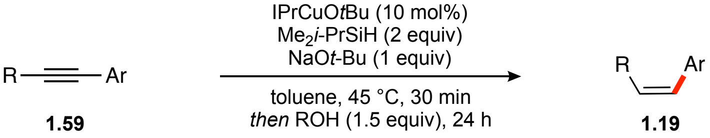


Figure 1.6. Copper-Catalyzed Semireduction of Sonogashira with *t*-BuOH.

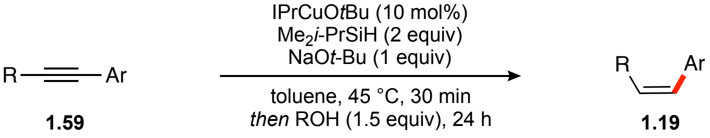
Copper Catalyzed Semireduction: Electron poor substrates and *i*-BuOH (Scheme 1.8)



Scheme 1.21. Catalytic Semireduction using *i*-BuOH

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.59** (14.4 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), alcohol (0.075 mmol, 1.5 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C 15 µL aliquots were taken, and quenched into $Br_2Cl_4C_2$ (3.4 mg, 0.004 mmol, 0.04 equiv) and diluted with 0.50 mL of Ether, passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Copper Catalyzed Semireduction: Electron poor substrates and *i*-BuOH (Scheme 1.8)



Scheme 1.22. Catalytic Semireduction using *i*-BuOH and EWG.

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.59** (14.4 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), alcohol (0.075 mmol, 1.5 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C 15 µL aliquots were taken, and quenched into $Br_2Cl_4C_2$ (3.4 mg, 0.004 mmol, 0.04 equiv) and diluted with 0.50 mL of Ether, passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.20. Copper-Catalyzed Semireduction of EWG Sonogashira with MeOH.

Time (min)	% **1.59**	% yield **1.19**	alkenyl copper
0	97	0	0
2	92	0	4
4	91	2	6
6	90	3	6
8	91	4	6
10	86	4	7
12	93	5	8
14	89	6	8
16	88	7	9
18	87	7	10
20	88	8	10

Table 1.21. Copper-Catalyzed Semireduction of EWG Sonogashira with *i*-BuOH.

Time (min)	% **1.59**	% yield **1.19**	alkenyl copper (**1.61**)
0	100	0	0
2	95	2	5
4	88	5	10
6	83	11	10
8	80	15	9
10	75	17	8
12	74	18	10
14	69	19	10
16	69	21	10

18	69	22	10
20	70	23	10

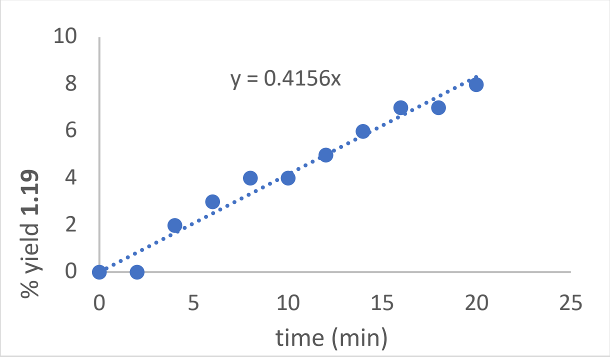


Figure 1.7. Copper-Catalyzed Semireduction of EWG Sonogashira with MeOH.

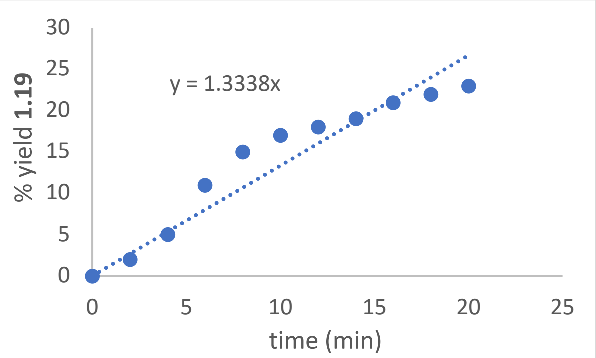
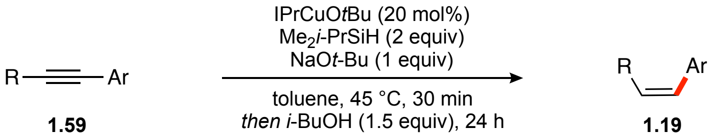


Figure 1.8. Copper-Catalyzed Semireduction of EWG Sonogashira with *i*-BuOH.

Copper-Catalyzed Semireduction: 20 mol% IPrCuO*t*-Bu with 1.59



Scheme 1.23. Catalytic Semireduction with 20 mol% IPrCuO*t*-Bu

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.59** (14.4 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), IPrCuO*t*-Bu (5.2 mg, 0.01 mmol, 0.20 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), *i*-BuOH (0.075 mmol, 1.5 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C 15 μL aliquots were taken, and quenched into $Br_2Cl_4C_2$ (3.4 mg, 0.004 mmol, 0.04 equiv) and diluted with 0.50 mL of Ether, passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.22. Copper-Catalyzed Semireduction: 20% IPrCuO*t*-Bu with **1.59**

Time (min)	% **1.59**	% yield **1.19**	alkenyl copper (**1.61**)
0	100	0	0
2	84	1	20
4	85	1	18
6	82	2	19
8	78	2	20
10	79	2	21
12	89	3	18
14	82	4	18
16	82	4	19
18	78	4	20
20	78	4	20
25	75	5	20
30	71	5	21
45	72	7	18
60	75	8	18
90	68	10	19
120	64	11	20

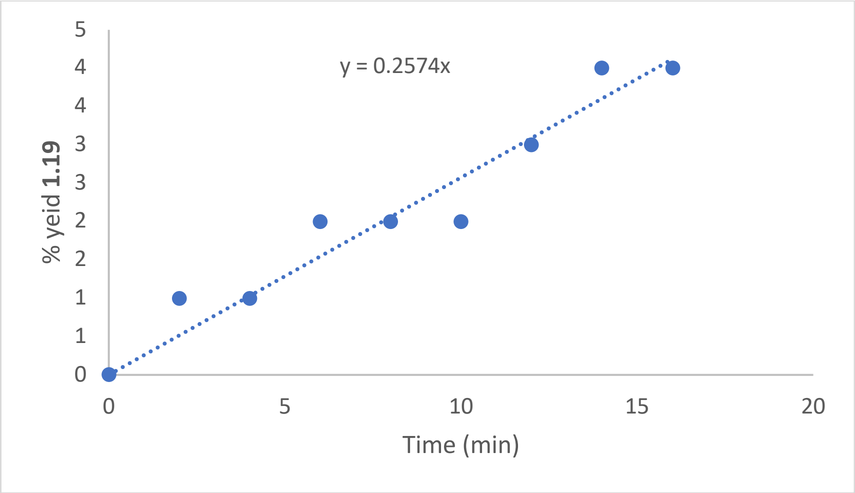
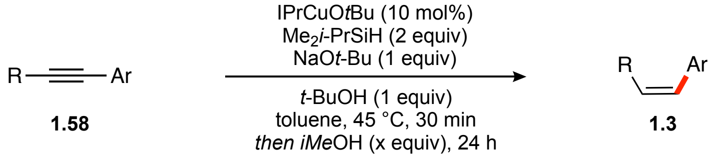


Figure 1.9. Copper-Catalyzed Semireduction of EWG Sonogashira with MeOH.

1.8.15 *Effect of MeOH Stoichiometry on Copper Catalyzed Semireduction*

Copper-catalyzed Semireduction of Sonogashira intermediate: Effect of MeOH

Table 2.23. Copper-Catalyzed Semireduction of Sonogashira intermediate: Effect of MeOH

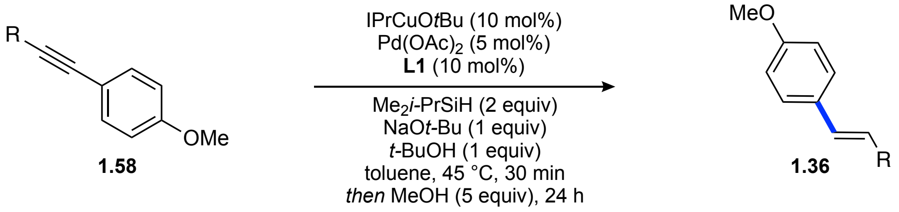


equiv of MeOH	Yield (30 min)	yield (4 h)	yield (7 h)	yield (24 h)
1	65%	70%	86%	89%
2	50%	66%	73%	75%
3	32%	33%	33%	35%
4	16%	16%	17%	17%
5	10%	10%	10%	10%

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me_2*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), *t*-BuOH (3.7 mg, 0.050, 1.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then MeOH (x equiv) was added. The reaction mixture was stirred at 45 °C and 30 μL aliquots were taken at 30 min, 4 h, 7 h and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

1.8.16 *Mechanistic Studies: Isomerization (Scheme 1.9)*

Catalytic Semireduction and Isomerization of the Sonogashira intermediate to the *E*-alkene



Scheme 1.24. Catalytic Semireduction and Isomerization of Internal Alkene

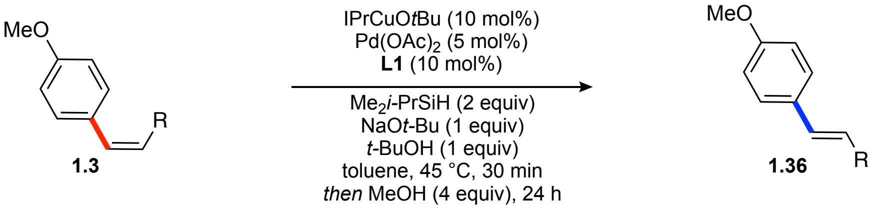
In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.58** (12.5 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Pd(OAc)$_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me$_2$*i*-PrSiH (10.2 mg, 0.10 mmol, 2.0 equiv), *t*-BuOH (3.7 mg, 0.050, 1.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then MeOH (8.0 mg, 0.25 mmol, 5 equiv) was added. The reaction mixture was stirred at 45 °C and 30 μL aliquots were taken at 20 min, 4 h, 7 h, and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.22. Relative Contribution of Pd/Cu Catalysts to Semireduction Isomerization

Reaction Conditions	yield (20 min)	yield (4 h)	yield (7 h)	yield (24 h)
Above Conditions	20%	50%	60%	88%
No Cu	0% (83%)[a]	0% (33%)[a]	40%	60%
No Pd/L	0% (97%)[a]	0% (95%)[a]	0% (95%)[a]	0% (90%)[a]
No MeOH	0% (100%)[a]	0% (97%)[a]	0% (92%)[a]	0% (87%)[a]

[a]Yield of Sonogashira starting material, mass balance is Z alkene.

Catalytic Semireduction and Isomerization of the *Z*-alkene to *E*-alkene (Scheme)



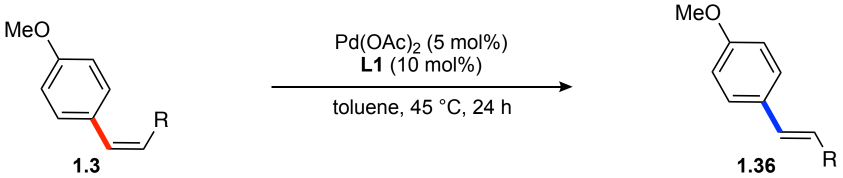
Scheme 1.25. Catalytic Isomerization of *Z*-Styrene to *E*-Styrene

In a nitrogen filled glovebox, a dram vial was charged with a stir bar, NaO*t*-Bu (4.8 mg, 0.050 mmol, 1.0 equiv). To this was added **1.3** (12.6 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Pd(OAc)$_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), IPrCuO*t*-Bu (2.6 mg, 0.005 mmol, 0.10 equiv), Me$_2$*i*-PrSiH (5.1 mg, 0.05 mmol, 1.0 equiv), *t*-BuOH (3.7 mg, 0.050, 1.0 equiv) and toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then MeOH (8.0 mg, 0.25 mmol, 4.0 equiv) was added. The reaction mixture was stirred at 45 °C and 30 µL aliquots were taken at 20 min, 4 h, 7 h, and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.23. Minimum System for Isomerization

Reaction Conditions	Yield (20 min)	Yield (4 h)	Yield (7 h)	Yield (12 h)	yield (24 h)
Above Conditions	80% (74:1)	85% (76:1)	88% (81:1)	88% (100:1)	88% (100:1)
No Me$_2$*i*-PrSiH	0%	0%	2%	3%	8%
No Pd/L	0%	0%	1%	1%	5%

Conditions for the Isomerization of *Z*-alkenes to *E*-alkenes (Scheme 1.10)



Scheme 1.26. Minimum System for Isomerization

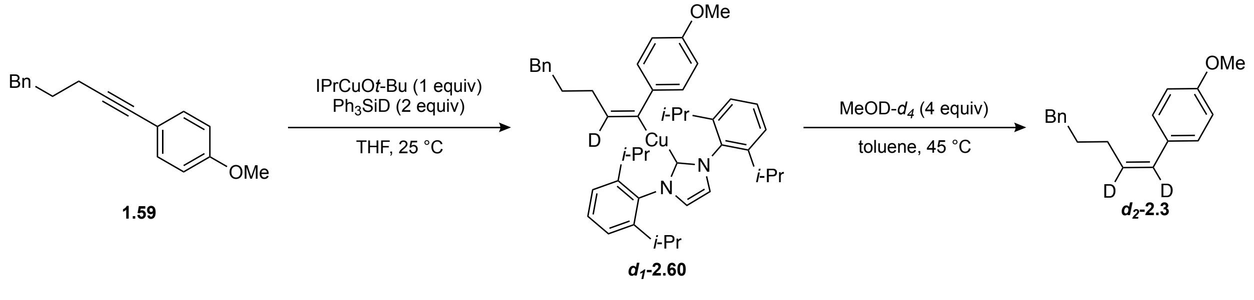
In a nitrogen filled glovebox, a dram vial was charged with a stir bar, **1.3** (12.6 mg, 0.050 mmol, 1.0 equiv), TMB (2.8 mg. 0.017 mmol, 0.33 equiv), Pd(OAc)$_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), Me$_2$*i*-PrSiH (0.50 mg, 0.005 mmol, 0.10 equiv) and toluene (0.50 mL) and the appropriate additive. The reaction mixture was stirred at 45 °C for 30 min, then MeOH (8.0 mg, 0.25 mmol, 4.0 equiv) was added. The reaction mixture was stirred at 45 °C and 30 μL aliquots were taken at 20 min, 4 h, 7 h, and 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography.

Table 1.24. Probing the System for Isomerization

Reaction Conditions	Yield (20 min)	yield (4 h)	yield (7 h)	yield (24 h)
10 mol% Me$_2$*i*-PrSiH	18%	47%	69%	88%[a]
10 mol% Me$_2$*i*-PrSiH w/ 4 equiv MeOH	9%	15%	46%	82%[a]
Pd$_2$dba$_3$ instead of Pd(OAc)$_2$	0%	0%	0%	2%
1 equiv Me$_2$*i*-PrSiH	34%	73%	80%	82%[a]
1 equiv Me$_2$*i*-PrSiH w/ 4 equiv MeOH	15%	23%	63%	85%[a]
2 equiv Me$_2$*i*-PrSiH	28%	95%[b]	82%	78%
2 equiv Me$_2$*i*-PrSiH w/ 4 equiv MeOH	11%	85%	93b[b]	81%
Pd$_2$dba$_3$ w/ 1 equiv Me$_2$*i*-PrSiH	8%	14%	18%	44%[c]
Pd$_2$dba$_3$ w/ 2 equiv Me$_2$*i*-PrSiH	8%	9%	20%	45%[c]

[a]Remaining material is overreduction to alkane. [b]Full isomerization complete, extended reaction times result in increased reduction to alkane. [c]Remaining material is *Z*-alkene.

1.8.17 *Mechanistic Studies: Deuterium Labeling (Scheme 2.10)*

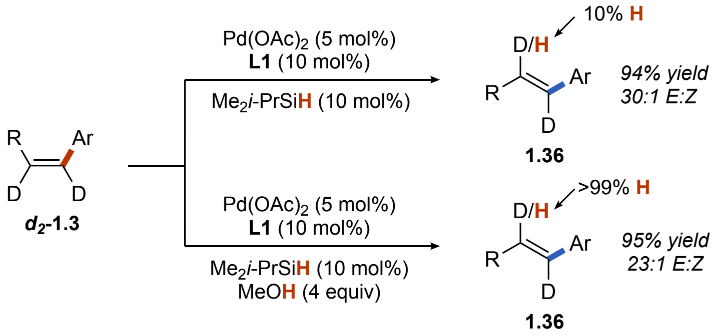


Scheme 1.27. Synthesis of d$_2$-*Z*-styrene (**d$_2$-1.3**)

In a nitrogen filled glovebox, IPrCuO*t*-Bu (394.7 mg, 0.750 mmol, 1.0 equiv) was weighed in a 20 mL scintillation vial, followed by 1000 μL THF. **1.58** (225.3 mg, 0.90 mmol, 1.2 equiv) was weighed out and transferred to the reaction with 3 aliquots of 500 μL of THF and reaction mixture was allowed to stir at 25 °C for 1 min resulting in an orange solution. Triphenylsilane-d_1[16] (391.7 mg, 1.5 mmol, 2.00 equiv) was weighed into a shell vial and transferred to the reaction with 3 aliquots of 500 μL THF at which point the reaction turned red. The reaction was vigorously stirred (1500 rpm) at 25 °C for 30 min after which the reaction turned back to a light orange. The reaction was concentrated in vaccuo, dissolved in minimal dichloromethane, layered with pentane and recrystallized at -35 °C. $\boldsymbol{d_1}$**-1.60** was then filtered and washed with cold pentane. $\boldsymbol{d_1}$**-1.60** was then dissolved in 2 ml of toluene and MeOD-d_4 (54.1 mg, 1.5 mmol, 2.0 equiv) was added. The reaction mixture was stirred until all the solids had dissolved, ~10 min. The reaction was then pushed through a plug of silica with excess EtOAc and purified by silica gel column chromatography. (0→5% EtOAc in hexanes).

Deuterirum Labeling

All glassware was washed with D_2O and then placed in an oven overnight. In a nitrogen filled glovebox, a dram vial was charged with a stir bar $\boldsymbol{d_2}$**-1.3** (12.5 mg, 0.050 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.60 mg, 0.0025 mmol, 0.05 equiv), **L1** (1.9 mg, 0.005 mmol, 0.10 equiv), Me_2*i*-PrSiH (0.50 mg, 0.010 mmol, 0.1 equiv), and d_8-toluene (0.50 mL). The reaction mixture was stirred at 45 °C for 30 min, then MeOH (x equiv) was added. The reaction mixture was stirred at 45 °C and 30 μL aliquots were taken at 24 h passed through a short plug of silica, washed with 1.5 mL of EtOAc and analyzed by Gas Chromatography to ensure completion. Then dimethyl isopterephthalate (2.6 mg, 0.017 mmol, 0.33 equiv) was added as internal standard and proton incorporation was determined by ^{1}H NMR in $CDCl_3$.



Scheme 1.5. Hydride Incorporation During Isomerization of d$_2$-*Z*-Styrene using Me$_2$*i*-PrSiH and MeOH

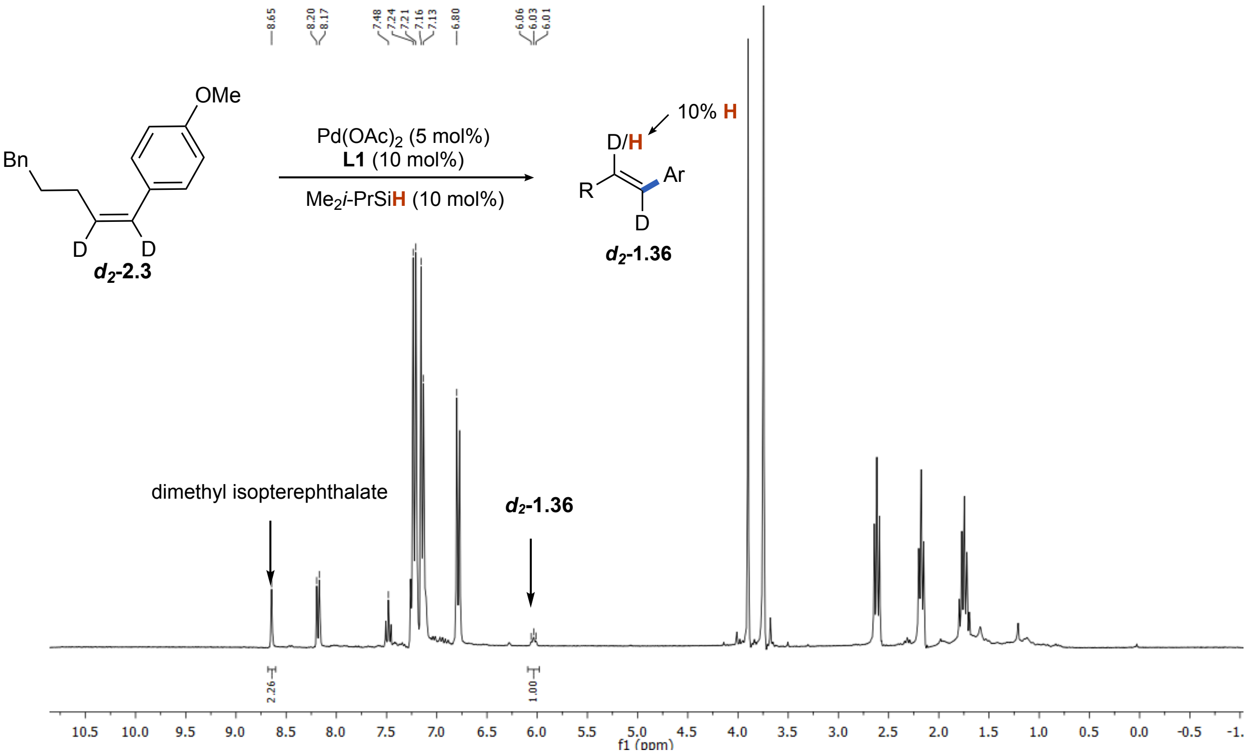


Figure 1.10. Hydride Incorporation during isomerization with 10 mol% silane.

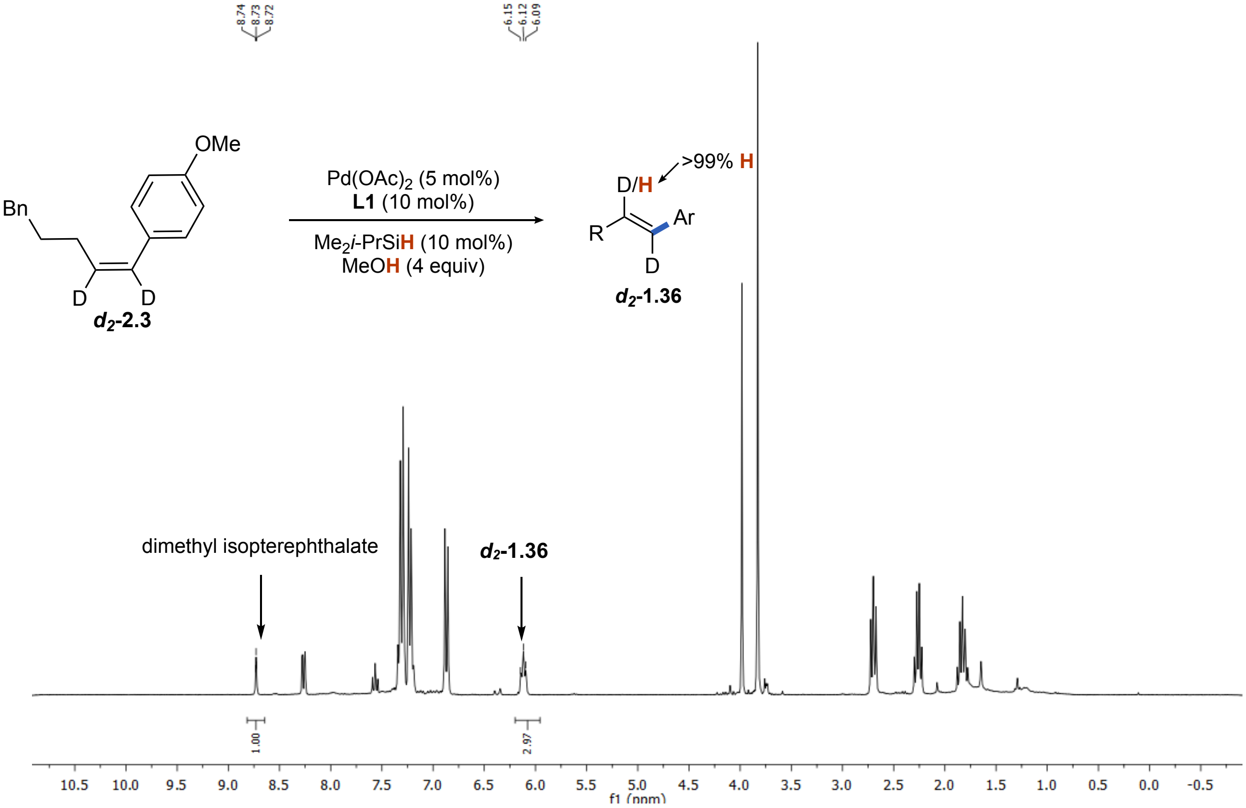


Figure 1.11. Hydride Incorporation during isomerization with 10 mol% silane and 4 equiv. MeOH.

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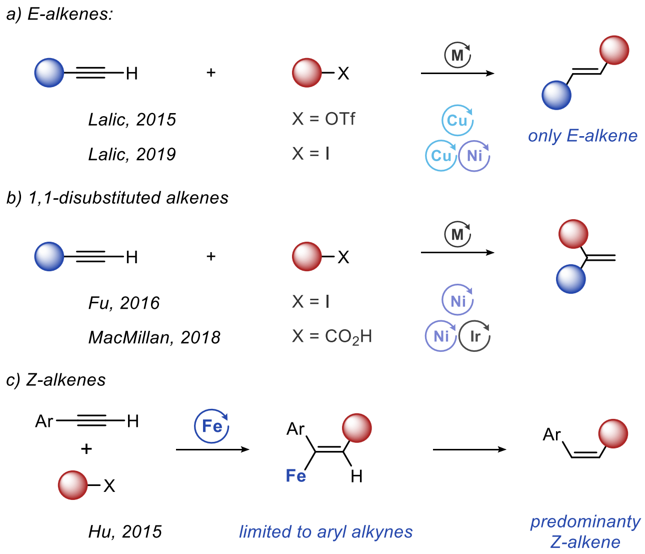
Chapter 2. SYNTHESIS OF ISOMERICALLY PURE (*Z*)-ALKENES FROM TERMINAL ALKYNES AND TERMINAL ALKENES: SILVER CATALYZED HYDROALKYLATION OF ALKYNES

2.1 INTRODUCTION

Alkenes serve as important intermediates in organic synthesis and are often found among pharmaceuticals and other biologically active compounds. The key feature of alkenes is the presence of a π bond, which hinders the rotation about the carbon-carbon σ-bond[1] and confers structural rigidity to alkenes. The hindered rotation also leads to two distinct stereoisomeric forms of disubstituted alkenes, denoted as E and Z.[2] An efficient synthesis of thermodynamically less stable *Z*-alkenes presents a complex set of challenges that continues to inspire the development of new synthetic methods.

The efficient synthesis of *Z*-alkenes must accomplish three important goals. The most basic goal is to form a double bond. The synthesis should also exert complete control over the double bond geometry, so that only the Z isomer of the alkene is formed. The synthesis of diastereopure products is particularly important considering the difficulties often encountered in the separation of alkene isomers. Finally, a *Z*-alkene should be constructed from two smaller fragments through the formation of a new C-C σ–bond.[3] Such a convergent approach to synthesis has long been recognized as key for the efficient build-up of molecular complexity.[4] Ideally, all three goals of *Z*-alkene synthesis (π bond formation, formation of only one isomer, and C-C σ bond formation) should be accomplished in *a single reaction*. Unfortunately, this is difficult to achieve using standard catalytic methods for the synthesis of *Z*-alkenes,[5] such as alkyne semireduction,[6] cross-coupling reactions,[7] alkene cross metathesis,[8] or alkene isomerization.[9]

We were intrigued by the idea that hydroalkylation of alkynes is one reaction that may allow us to accomplish all three goals of *Z*-alkenes synthesis. Hydroalkylation has already proven effective in the synthesis of *E*-alkenes through reductive coupling of terminal alkynes with alkyl iodides[10] or alkyl triflates (Scheme 2.1a).[11] The same approach is also effective when applied to the synthesis of 1,1-disubstituted alkenes (Scheme 2.1b).[12] Still, hydroalkylation reactions had limited success targeting *Z*-alkenes. Z-Selectivity has, so far, been achieved only in an iron-catalyzed radical hydroalkylation, reported by Hu et al. in 2015 (Scheme 2.1c). This method is limited to reactions of aryl acetylenes and yields mixtures of *E*- and *Z*-alkenes with varying selectivity.[13]



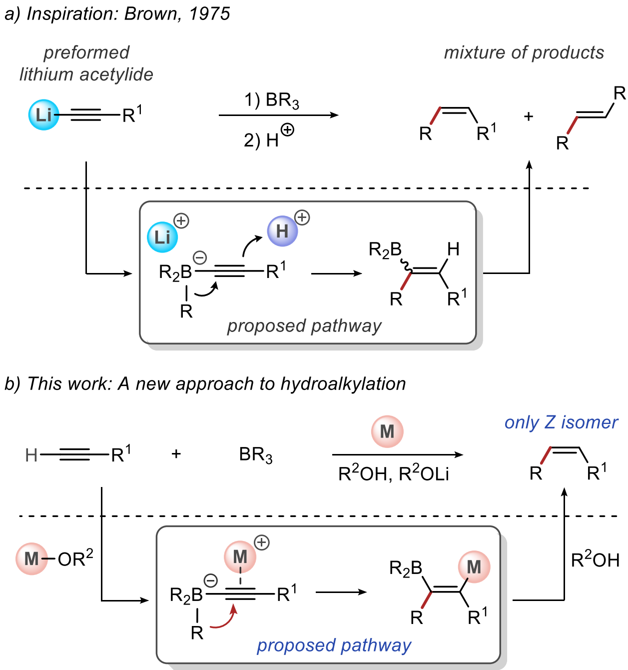
Scheme 2.1. Hydroalkylation of Alkynes

Unfortunately, other mechanistic paradigms used to accomplish hydroalkylation favor the formation of *E*-alkenes. As a result, to achieve the synthesis of pure *Z*-alkenes we need a fundamentally new approach to hydroalkylation of alkynes.

2.2 REACTION DEVELOPMENT

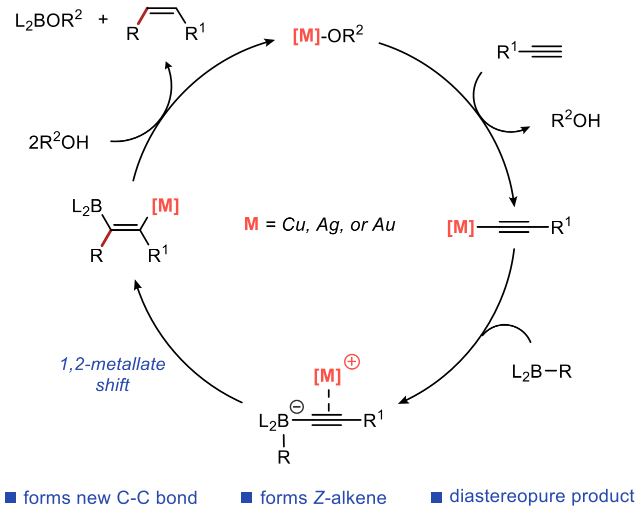
Here, we describe a catalytic method for the synthesis of diastereopure *Z*-alkenes through the coupling of terminal alkynes and alkylboranes. The development of this method was inspired by a 1975 report from H. C. Brown (Scheme 2.2a).[14] In the report, Brown showed that lithium acetylides readily add to alkylboranes to form borate complexes. Further reaction of the borate with a Brønsted acid leads to a 1,2-metallate shift[15,16] and the formation of both isomers of alkenyl borane, with Z being the major isomer. The stereochemical outcome has been attributed to the nature of the 1,2-metalate shift, which is proposed to proceed through a carbocation intermediate.[14c] Subsequent protodeboration provides a mixture of *Z*- and *E*-alkenes.[14c,17]

We reasoned that in the 1,2-metallate shift described by Brown, the Brønsted acid could be replaced by a cationic complex of a coinage metal (Scheme 2.2b). The 1,2-metallate shift promoted by π-acid coordination[18,19] to the alkyne has been shown to require antiperiplanar orientation of the π-acid and the migrating group[20] and would allow exclusive formation of the *Z*-alkene product. Furthermore, the coinage metal complex could be delivered in the form of a metal acetylide that would replace the lithium acetylide used in the reaction sequence described by Brown. Ultimately, these simple changes would allow us to develop a catalytic process that results in the exclusive formation of *Z*-alkenes.



Scheme 2.2. New Approach to Hydroalkylation

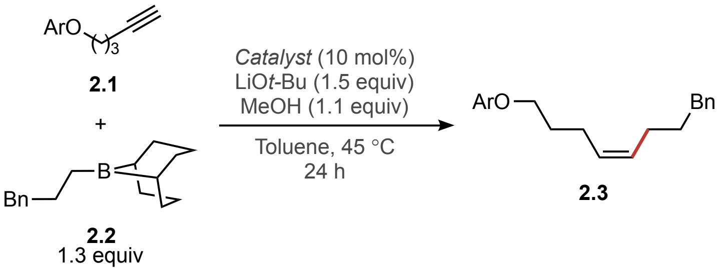
Scheme 2.3 shows the postulated mechanism of such a catalytic reaction. In the presence of an alkoxide base, a coinage metal catalyst promotes acetylide formation, which is followed by addition to the alkyl borane. Upon addition, the metal counterion coordinates to the alkyne and promotes the 1,2-metallate shift through π-activation of the alkyne. Finally, alkene formation is accomplished by protodeboration and protodemetallation of the intermediate in the presence of an alcohol additive.



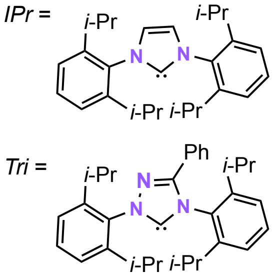
Scheme 2.3. Proposed Catalytic Cycle

With the broad strategy outlined in Scheme 2.3 in mind, we explored the reaction of alkyne **2.1** with alkylborane **2.2** in the presence of a copper, silver, or gold catalyst (Table 2.1). Surprisingly, the silver catalyst performed the best, even though silver complexes are expected to be the least π-acidic.[21] Crucially, only the Z isomer of alkene product **2.3** was formed in the reaction. Through further optimization of the reaction parameters, we found that a triazole carbene ligand and a nonpolar solvent provided the highest yield of the Z-alkene product. Under optimized conditions, complete conversion was achieved using a modest excess (1.3-1.5 equiv) of the alkylborane, which was prepared in situ from an alkene. Standard control experiments confirmed that the catalyst, base, and methanol were all necessary for the reaction (see ExperimentalI).

Table 2.1. Development of Hydroalkylation Reaction



Catalyst	*yield (%)*
IPrCuCl	*<5*
IPrAgCl	*52*
IPrAuCl	*0*
TriAgCl	*70*
TriAgCl[a]	***92***



The standard reaction conditions are bolded in red. [a]Isooctane was used instead of Toluene. Ar =methyl-4-benzoate,

2.3 SUBSTRATE SCOPE

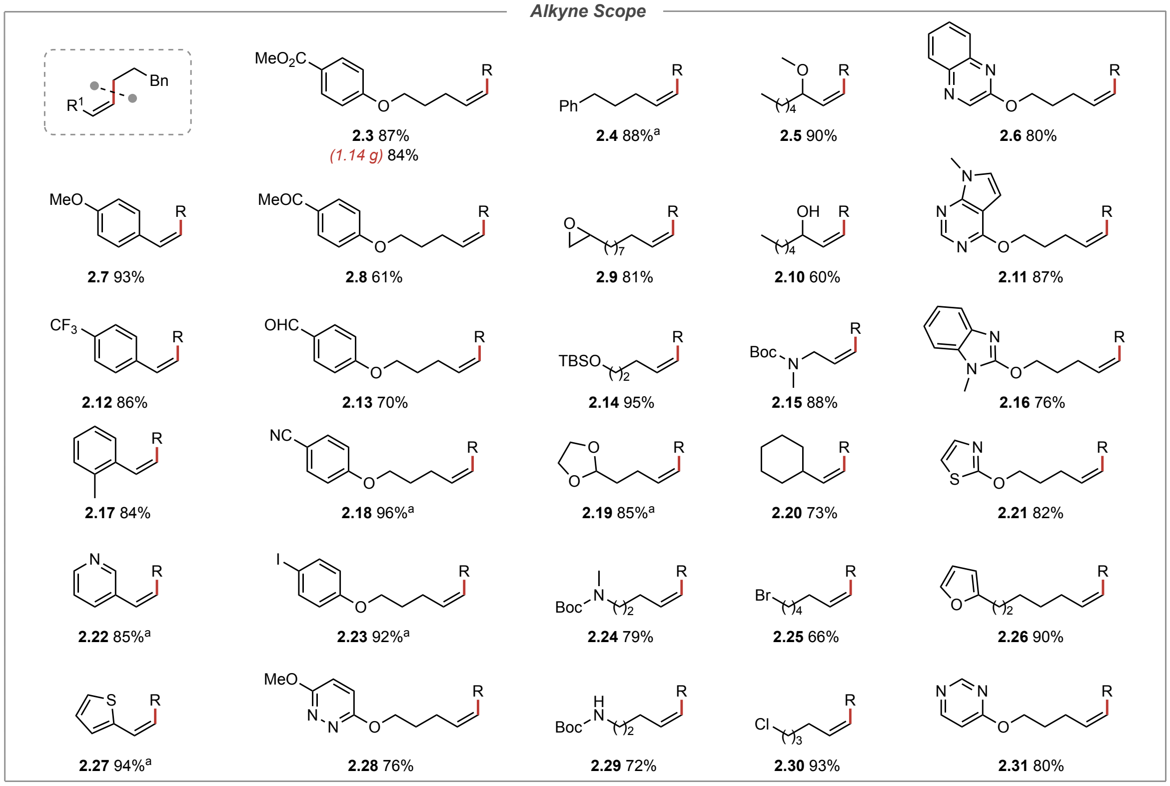
The new transformation proved to be remarkably general, providing *Z*-alkenes as exclusive products with a wide range of substrates (Table 2.2). Functionalized alkyl alkynes could be successfully used in the reaction together with both electron-rich and electron-poor aryl alkynes. Alkylboranes prepared in situ from a variety of terminal alkenes, including 1,1-disubstituted alkenes, could be used as substrates. Furthermore, a wide range of functional groups was tolerated. Alkene products were formed in the presence of alcohols, aldehydes, ketones, esters, nitriles, alkenes, Boc-protected primary and secondary amines, anilines, alkyl bromides, alkyl chlorides, aryl iodides, aryl bromides, aryl boronic esters, epoxides, acetals, and alkyl and silyl ethers. Heterocycles such as pyridine, thiazole, benzimidazole, benzopyrazine, pyrimidine, pyridazine, thiophene, and furan were also compatible with the reaction conditions. The reaction could be performed on preparative scale, yielding one gram of alkene **2.3**. Finally, in the synthesis of alkene **2.4**, careful analysis of the crude reaction mixture by GC and GC/MS using authentic samples of

Z and E isomers of the alkene revealed the presence of the very small amount of the E isomer (Z:E = 570:1). Similar GC/MS analysis of **2.3**, **2.17**, **2.35**, **2.39**, and **2.41**, in all cases, indicated the *Z*:*E* ratio was greater than 300:1.[22]

Several limitations in the scope of the hydroalkylation reaction were noted. While primary alkyl groups participate in the 1,2-metallate shift, secondary and tertiary alkyl, alkenyl, and aryl groups do not. Free amines, carboxylic acids, and carboxylates are not compatible with the reaction. We also noticed that the presence of an electron-withdrawing group two carbons away from the boron in alkyl boranes significantly lowers the yield of the reaction.

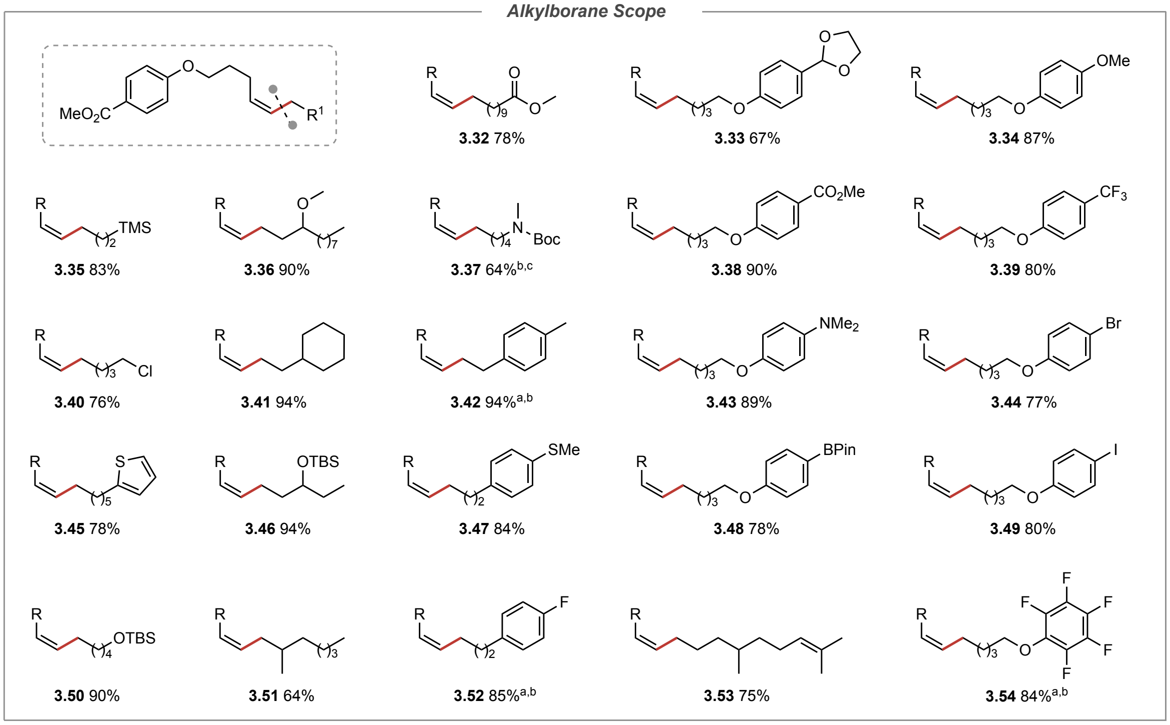
Table 2.2. Substrate scope of the *Z*-Selective Hydroalkylation of Alkynes

Alkyne Scope



2.3 87%
(1.14 g) 84%
2.4 88%[a]
2.5 90%
2.6 80%
2.7 93%
2.8 61%
2.9 81%
2.10 60%
2.11 87%
2.12 86%
2.13 70%
2.14 95%
2.15 88%
2.16 76%
2.17 84%
2.18 96%[a]
2.19 85%[a]
2.20 73%
2.21 82%
2.22 85%[a]
2.23 92%[a]
2.24 79%
2.25 66%
2.26 90%
2.27 94%[a]
2.28 76%
2.29 72%
2.30 93%
2.31 80%

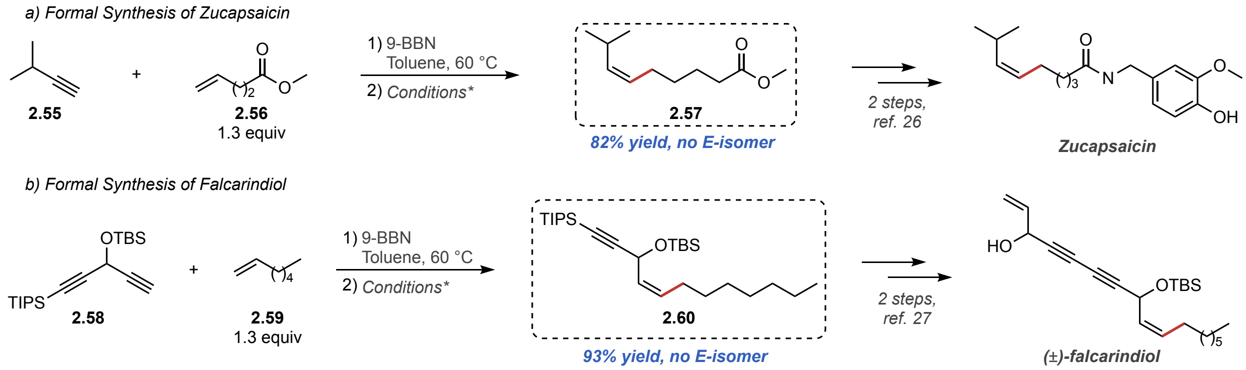
Alkylborane Scope



3.32 78%
3.33 67%
3.34 87%
3.35 83%
3.36 90%
3.37 64%[b,c]
3.38 90%
3.39 80%
3.40 76%
3.41 94%
3.42 94%[a,b]
3.43 89%
3.44 77%
3.45 78%
3.46 94%
3.47 84%
3.48 78%
3.49 80%
3.50 90%
3.51 64%
3.52 85%[a,b]
3.53 75%
3.54 84%[a,b]

Reactions performed on a 0.5 mmol scale. Alkylboranes were prepared in situ by stirring corresponding alkene (1 equiv) and 9-borabicyclo[3.3.1]nonane dimer (0.45 equiv) in toluene (2M) overnight at 60 °C. Reaction Conditions: TriAgCl (10 mol%), alkylborane (1.3 equiv) LiO*t*-Bu (1.5 equiv), MeOH (1.1 equiv), and Isooctane (5 mL), 45 °C, 16 h. [a]Reaction Conditions: IPrAgCl (10 mol%), alkyl borane (1.5 equiv), LiO*t*-Bu (2.0 equiv), MeOH (1.1 equiv), and toluene (5 mL), 60 °C, 16 h. [b]R = propylbenzene. [c]Yield determined by ^{1}H NMR.

We have explored the application of the new method in the synthesis of biologically active compounds. Zucapsaicin is used in the treatment of osteoarthritis and neuropathic pain (Scheme 2.4a).[23] The formal synthesis[24] of this synthetic analogue of capsaicin was accomplished by the synthesis of **2.57** in 82% yield as a single isomer. A formal racemic synthesis of the natural product falcarindiol[25] (Scheme 2.4b) was accomplished by preparing alkene **2.60** in 93% yield and 100% *Z*-selectivity. Falcarindiol has been shown to have a range of pharmacologically useful properties, including anticancer activity in breast cancer cells.[26]

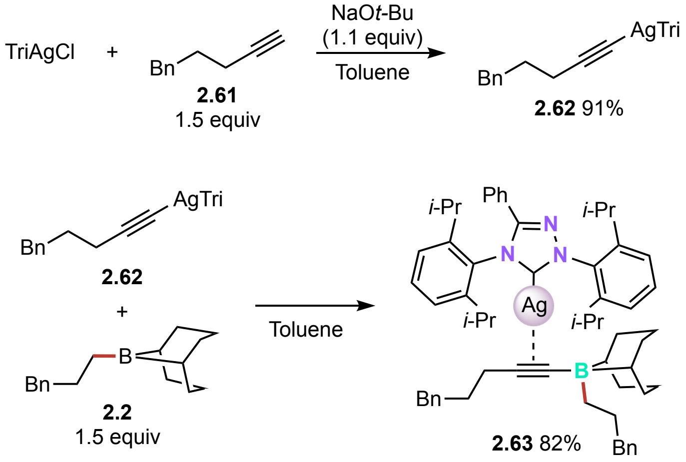


Reactions were performed on a 0.5 mmol scale.[a]Conditions: TriAgCl (10 mol%), Li-O*t*Bu (1.5 equiv), MeOH (1.1 equiv), and Isooctane (5 mL), 45 °C, 16 h.

Scheme 2.4. Applications of the *Z*-Selective Hydroalkylation

2.4 MECHANISTIC STUDIES

To probe the mechanism of the reaction, we explored the feasibility of the elementary steps in our postulated catalytic cycle (Scheme 2.5). In a stoichiometric reaction, we found that the silver catalyst, in the presence of an alkoxide, readily reacts with a terminal alkyne **2.61** to produce silver acetylide **2.62** (Scheme 2.5). The acetylide rapidly reacts with alkyl borane **2.2** to produce borate complex **2.63**. The X-ray structure of this complex (Figure 2.1) indicates that the silver cation associated with the borate is coordinated to the alkyne and is therefore poised to promote the 1,2-metallate shift. However, the unfavorable orientation of the migrating alkyl group is consistent with the observed stability of this intermediate. In a control experiment, we confirmed that the silver borate complex is a viable catalyst for the hydroalkylation reaction (see Experimental).



Scheme 2.5. Experiments Probing the Reaction Mechanism

These experimental observations provide direct support for some of the key aspects of the proposed reaction mechanism shown in Scheme 2.3 (M = Ag). Further studies are necessary to provide a more detailed understanding of the reaction mechanism, including the steps following the 1,2-metallate shift.

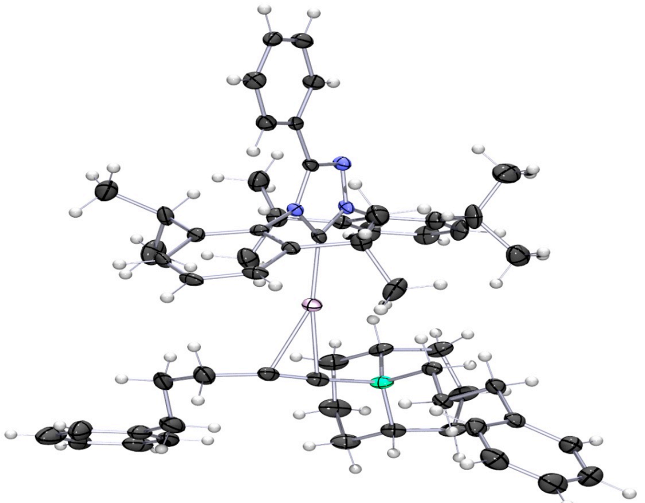


Figure 2.1 X-ray structure of borate complex **2.63** with thermal ellipsoids at 50% probability. Disorder in one phenyl group and one isopropyl group has been omitted for clarity

2.5 CONCLUSION

In conclusion, we have developed a *Z*-stereospecific method for the hydroalkylation of terminal alkynes. The new method involves the silver-catalyzed reductive cross coupling of primary alkylboranes with alkynes. This new method for forming *Z*-alkenes has excellent substrate scope and functional group compatibility and provides the desired products in high yields and with high diastereoselectivity. Mechanistic experiments indicate that our proposed reaction mechanism involving the 1,2-metallate shift of an alkyl boronate complex.

2.6 EXPERIMENTAL

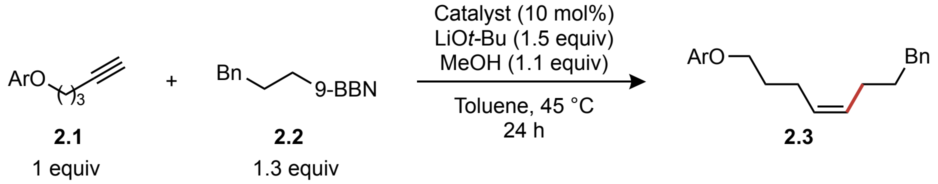
2.6.1 *General Information*

All reactions were performed under a nitrogen atmosphere with flame-dried or oven-dried (120 °C) glassware, using standard Schlenk techniques, or in a glovebox (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 µm, 230-400 mesh. 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 (CDCl3 (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 (CDCl3(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. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), coupling constants in Hertz (Hz), intergration. Mass spectra were collected on a JEOL HX-110 mass spectrometer. Gas Chromatography (GC) analysis was performed on a Shimadzu GC-2010 instrument with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 µm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5 min @ 250 °C. Materials: THF, CH2Cl2, ether, benzene, and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous methanol was purchased from Millipore Sigmaand was degassed and stored over 4Å molecular sieves. Isooctane was purchased from Fisher Scientific and was degassed and stored over 4Åmolecular sieves. 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, ArkPharm, Combi-Blocks, Oakwood Chemicals, Strem Chemicals and Alfa Aesar. 9-BBN Dimer was purchased from Millipore Sigma and recrystallized from THF.

2.6.2 *Reaction Development (Table 2.1)*

All reactions were performed on a 0.05 mmol scale with the stoichiometry shown in Table S1. In a nitrogen-filled glovebox a dram vial was charged with a stir bar, LiOt-Bu (1.5 equiv), catalyst, methyl 4-(pent-4-yn-1-yloxy)benzoate, 1,3,5-trimethoxy benzene (TMB, internal standard), 9-(3-phenylpropyl)-9-borabicyclo[3.3.1]nonane (1.3 equiv), methanol (1.1 equiv) and solvent. The reaction mixture was stirred at 45 °C and monitored by Gas Chromatography for reaction completion. An aliquot was taken every 24 hours.

Table 2.2. Reaction Development and Control Experiments

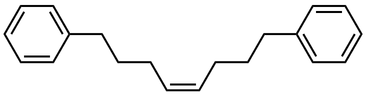


2.1 **2.2** **2.3**

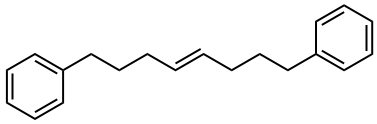
entry	*deviation from above*	*yield (%)*
1.	none	52
2.	IPrCuCl	<5
3.	IPrAuCl	0
4.	TriAgCl	70
5.	**TriAgCl, isooctane as solvent**	**92**
7.	MeOH as solvent	0
6.	No MeOH, in isooctane	<5
8.	No LiO-*t*Bu, in isooctane	0
9.	No TriAgCl, in isooctane	0

Ar = methyl 4-benzoate

2.6.3 *Verification of Product Stereochemistry and Determination of E/Z-Selectivity*



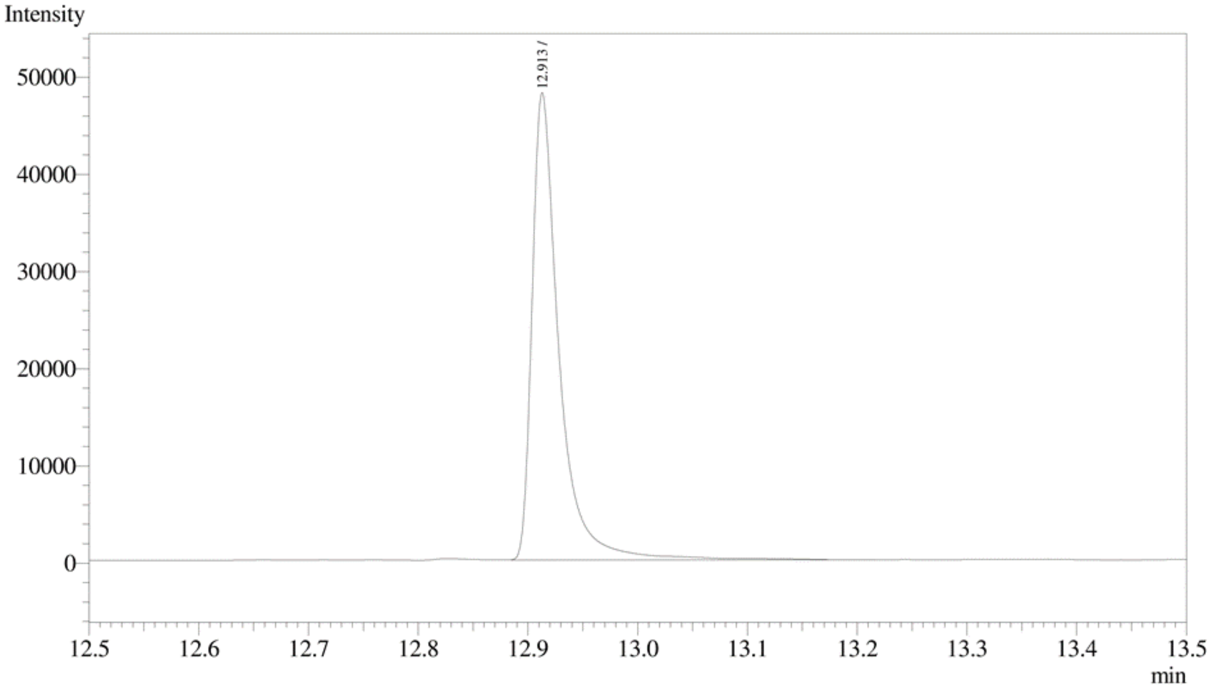
(*Z*)-1,8-diphenyloct-4-ene



(*E*)-1,8-diphenyloct-4-ene

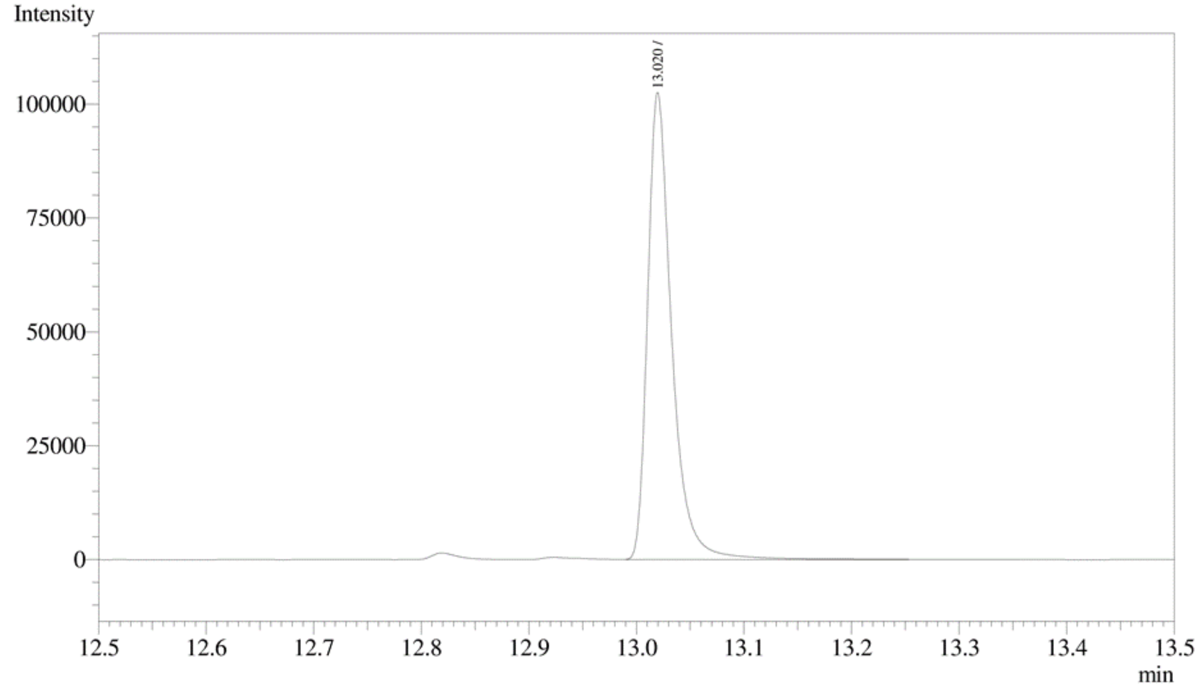
(*Z*)-1,8-diphenyloct-4-ene and (*E*)-1,8-diphenyloct-4-ene have been previously synthesized and characterized.[31] Provided are GC traces of pure (*Z*)-1,8-diphenyloct-4-ene, pure (*E*)-1,8-diphenyloct-4-ene, a mixture of both pure isomers, and a GC trace of the crude reaction mixture of the synthesis of (*Z*)-1,8-diphenyloct-4-ene using our method.

GC trace of pure (*Z*)-1,8-diphenyloct-4-ene.



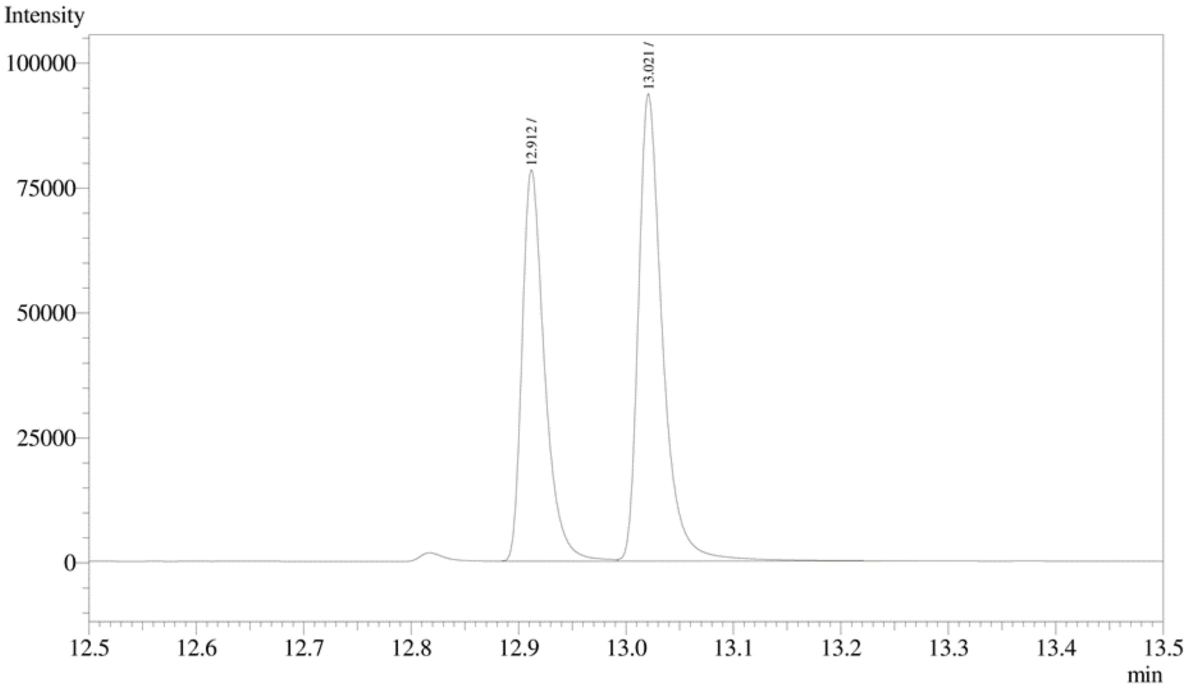
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	12.913	83088	46323	100.000		V		
Total		83088	46323					

GC trace of pure (*E*)-1,8-diphenyloct-4-ene.



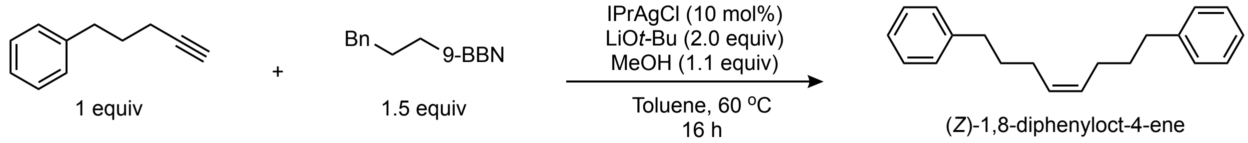
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	13.020	160590	100271	100.000				
Total		160590	100271					

GC trace of a mixture of (*Z*)-1,8-diphenyloct-4-ene and (*E*)-1,8-diphenyloct-4-ene.

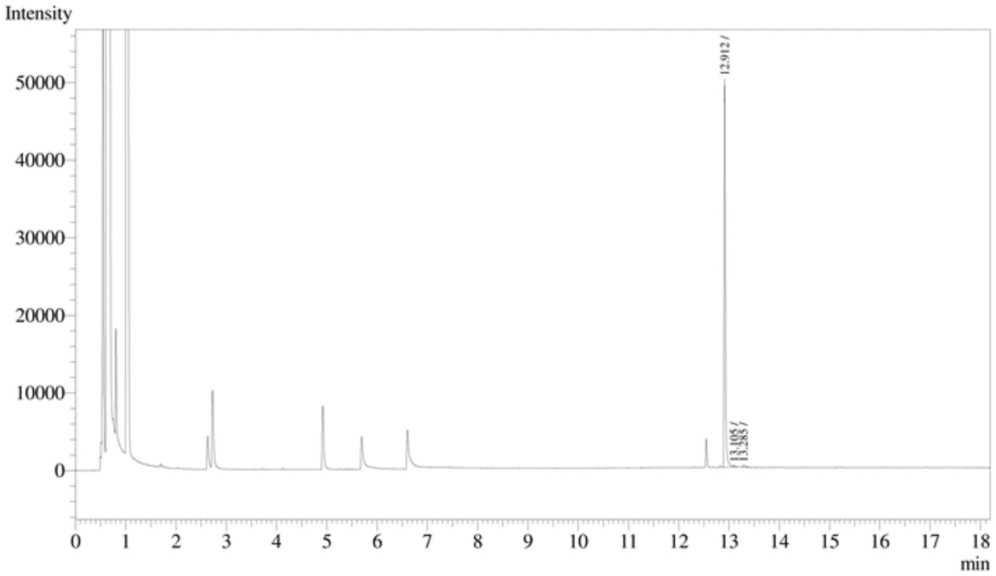


Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	12.912	113932	76951	43.816				
2	13.021	146089	90218	56.184		V		
Total		260021	167169					

E/Z selectivity of the following reaction was determined by GC/FID analysis of an aliquot taken from a crude reaction mixture at the end of the reaction:

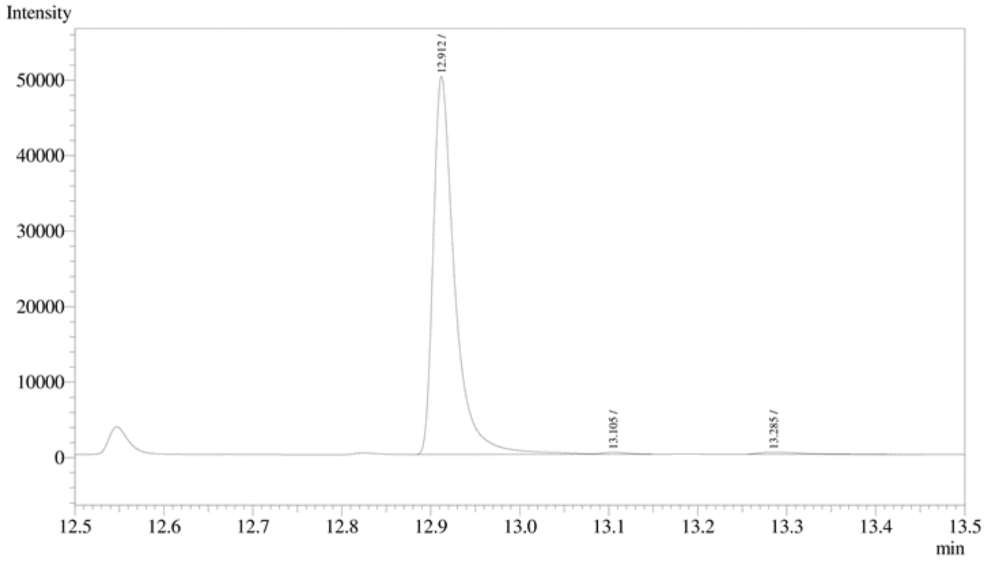


GC trace of crude reaction mixture from the above reaction



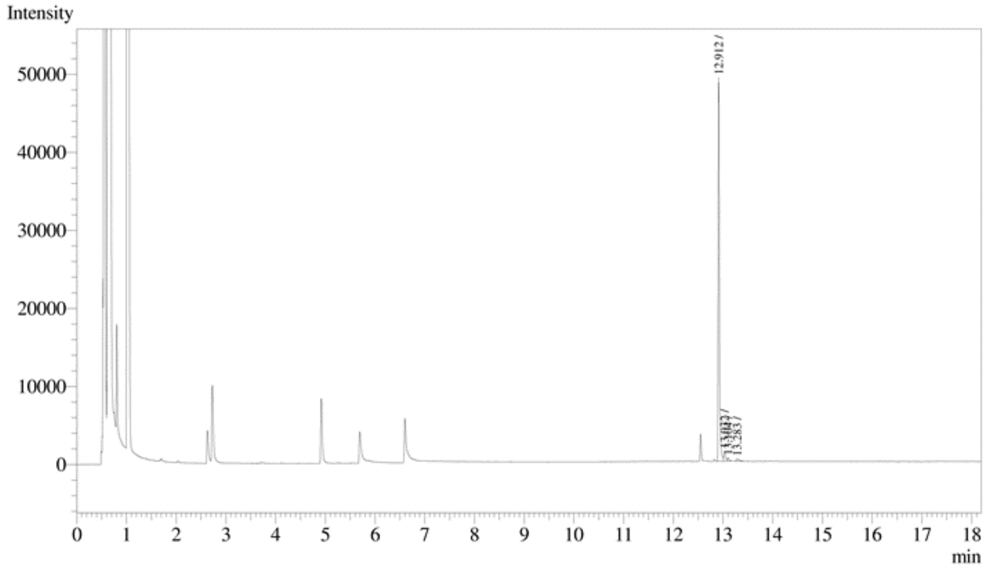
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	12.912	84234	49186	98.024				
2	13.105	569	274	0.662		V		
3	13.285	1129	296	1.314				
Total		85932	49756					

Expansion of the product peak from the reaction mixture for clarity.



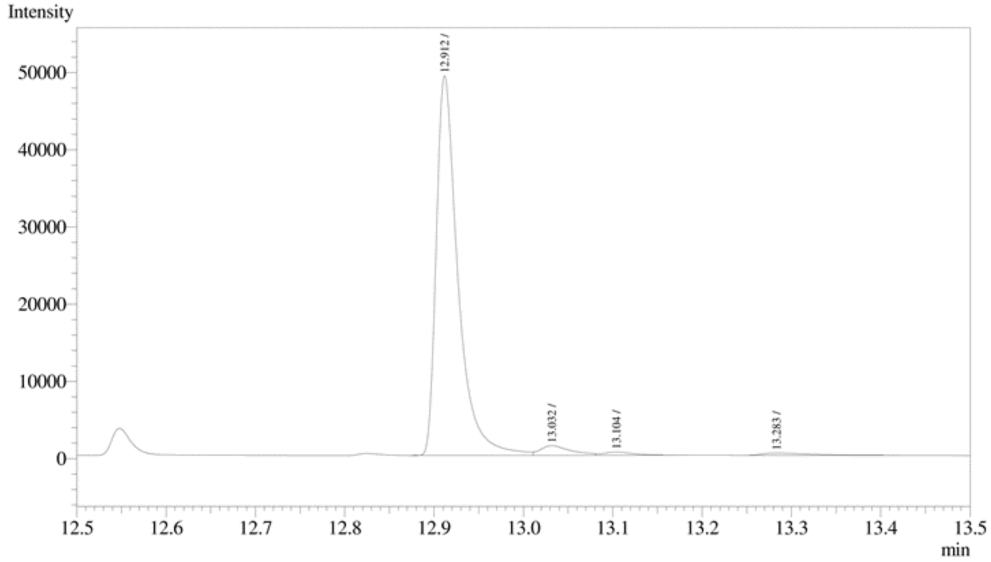
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	12.912	84234	49186	98.024				
2	13.105	569	274	0.662		V		
3	13.285	1129	296	1.314				
Total		85932	49756					

GC trace of the same sample from the crude reaction mixture with a spike of (*E*)-1,8-diphenyloct-4-ene



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	12.912	83069	48479	94.336				
2	13.032	2890	1251	3.282		V		
3	13.104	955	417	1.084		V		
4	13.283	1142	298	1.297				
Total		88056	50445					

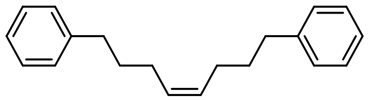
Expansion of the peaks for the product and (*E*)-1,8-diphenyloct-4-ene.



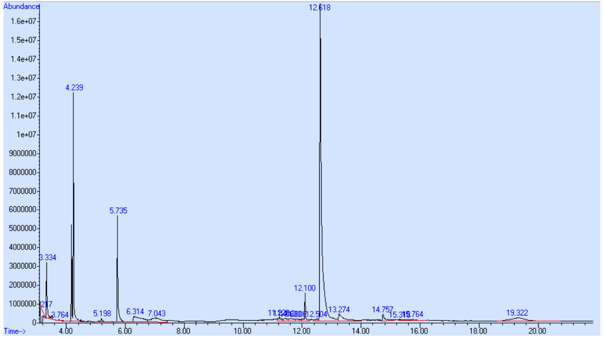
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	12.912	83069	48479	94.336				
2	13.032	2890	1251	3.282		V		
3	13.104	955	417	1.084		V		
4	13.283	1142	298	1.297				
Total		88056	50445					

Selected GC/MS Chromatograms

GC/MS (EI) for crude reaction of **2.4**

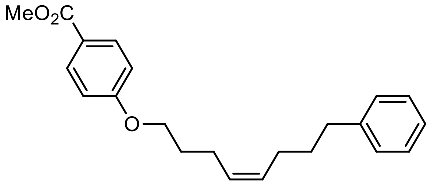


. Calculated $[M]^+$ 264.19

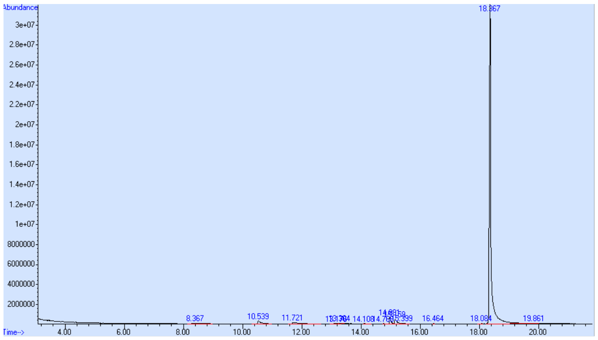


RT: 12.100 $[M]^+$ 238.2
RT: 12.504 $[M]^+$ 270.2
RT: 12.618 $[M]^+$ 264.1
RT: 13.274 $[M]^+$ 272.2
RT: 14.757 $[M]^+$ 404.3

GC/MS (EI) for **2.3**.

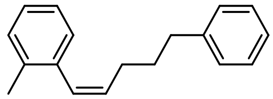


Calculated $[M]^+$ 338.19

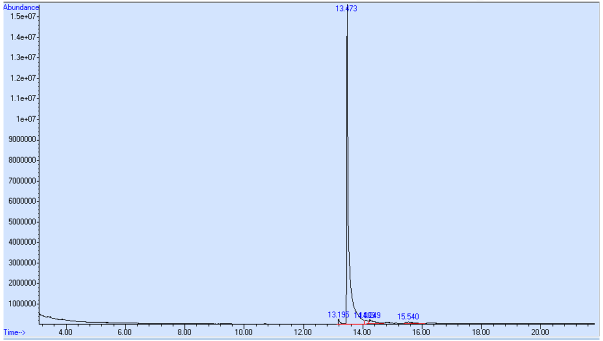


RT: 18.084 $[M]^+$ 346.1
RT: 18.367 $[M]^+$ 338.2
RT: 19.861 $[M]^+$ 438.2

GC/MS (EI) for **2.17**.



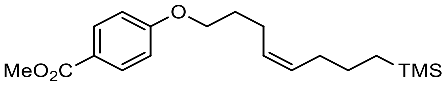
Calculated $[M]^+$ 236.16



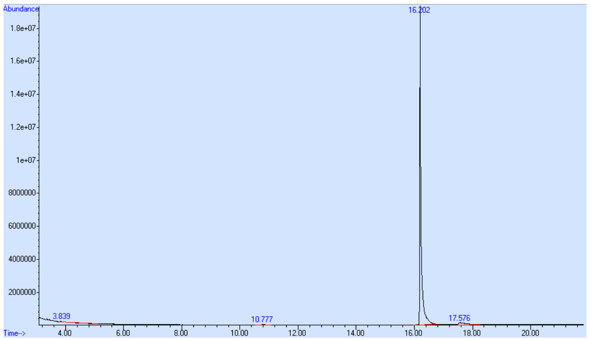
RT: 13.195 $[M]^+$ 228.2
RT: 13.473 $[M]^+$ 236.2
RT: 14.089 $[M]^+$ 246.3
RT: 14.249 $[M]^+$ 246.2
RT: 15.540 $[M]^+$ 264.1

GC/MS (EI) for **2.35**

.

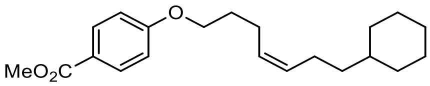


Calculated [M]$^+$ 330.20

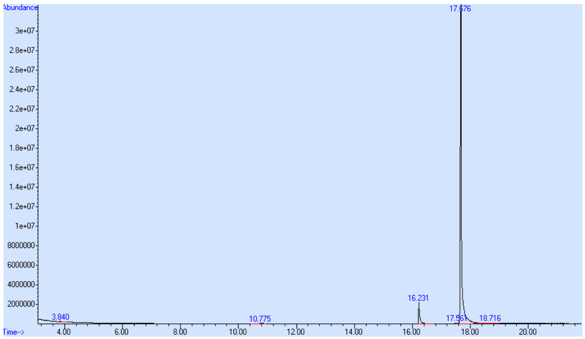


RT: 16.202 [M]$^+$ 334.2
RT: 17.576 [M]$^+$ 346.1

GC/MS (EI) for **2.41**.



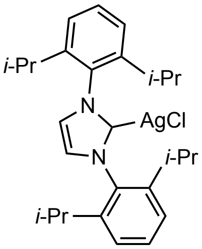
Calculated [M]$^+$ 330.22



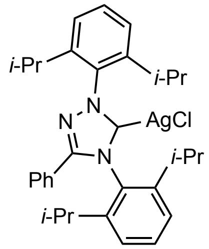
RT: 16.231 [M]$^+$ 334.2
RT: 17.561 [M]$^+$ 344.3
RT: 17.676 [M]$^+$ 330.2
RT: 18.716 [M]$^+$ 346.1

2.6.4 *Synthesis of TriAgCl and IPrAgCl*

The silver catalysts were synthesized using an adapted procedure from Sadighi et. al. that was used for the synthesis of SIPrAgCl.[32]



IPrAgCl, complex has been previously characterized.[33]



TriAgCl, complex was synthesized from TriHCl,[34] and isolated as a white solid (563.0 mg 77% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.64 – 7.50 (m, 2H), 7.48 – 7.39 (m, 3H), 7.39 – 7.28 (m, 6H), 2.71 – 2.55 (m, 2H), 2.55 – 2.40 (m, 2H), 1.41 – 1.17 (m, 18H), 1.00 (d, J = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 188.0 (dd, J(^{109}Ag^{13}C) = 265.2 Hz, J(^{107}Ag^{13}C) = 229.2 Hz), 153.6, 153.6, 145.7, 145.3, 134.9, 131.8, 131.7, 131.5, 131.5, 129.1, 128.0, 125.3, 124.4, 29.1, 25.1, 24.5, 23.9, 22.9.

2.6.5 *Hydroalkylation of Terminal Alkynes (Table 2.2)*

General Procedure:

In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and LiO*t*-Bu (1.5 or 2.0 equiv). To this was added silver catalyst (0.05 mmol, 0.10 equiv), alkyne (0.50 mmol, 1.0 equiv), alkylborane (1.3 or 1.5 equiv), methanol (17.6 mg, 0.55 mmol, 1.10 equiv), and solvent (5 mL). The reaction mixture was heated and stirred for 16 hours. After 16 hours, an aliquot of the crude reaction mixture was analyzed by GC, and the reaction was quenched with the addition of sodium perborate (150 mg, 0.75 mmol, 1.5 equiv) in 5 mL THF and 5 mL deionized water. The mixture was stirred at room temperature for 1 hour, and then extracted with ether (3 x 10 mL) and dried over MgSO$_4$. The crude mixture was concentrated under reduced pressure and purified by silica gel chromatography.

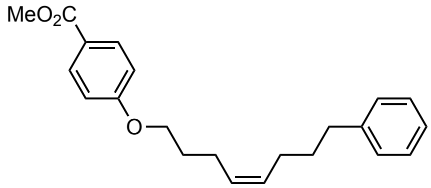
A: The general procedure was followed using TriAgCl (30.4 mg, 0.05 mmol, 0.10 equiv) as catalyst, 1.5 equivalents of LiO*t*-Bu (60 mg, 0.75 mmol) and 1.3 equivalents of alkylborane (0.65mmol) and the reaction was stirred in isooctane at 45 °C overnight.

B: The general procedure was followed using IPrAgCl (26.7 mg, 0.05 mmol, 0.10 equiv) as catalyst, 1.5 equivalents of LiO*t*-Bu (80 mg, 1.00mmol) and 1.5 equivalents of alkylborane (0.75mmol) and the reaction was stirred in toluene at 60 °C overnight.

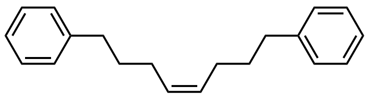
Most reactions were performed using general procedure A, however products **2.4**, **2.10**, **2.15**, **2.18**, **2.19, 2.23**, **2.42**, **2.52**, and **2.54**, were synthesized using general procedure B.

2.6.6 *Characterization of Z-Selective Hydroalkylation Products: Alkynes (Table 2.2)*

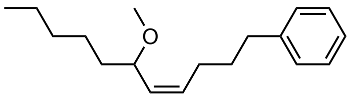
9-(3-phenylpropyl)-9-borabicyclo[3.3.1]nonane was used neat and was synthesized according to literature procedure.[35]



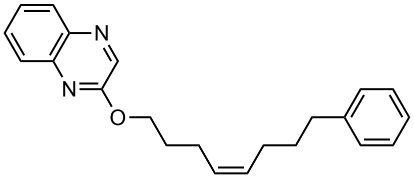
methyl 4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}benzoate (2.3), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (147.6 mg, 87% yield).^{1}H NMR (300 MHz, CDCl$_3$) δ 7.98 (d, *J* = 8.9 Hz, 2H), 7.36 – 7.27 (m, 1H), 7.25 – 7.21 (m, 1H), 7.20 – 7.09 (m, 3H), 6.89 (d, *J* = 8.9 Hz, 2H), 5.64 – 5.31 (m, 2H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.88 (s, 3H), 2.64 – 2.50 (m, 2H), 2.28 – 2.15 (m, 2H), 2.12 – 2.01 (m, 2H), 1.92 – 1.78 (m, 2H), 1.70 – 1.59 (m, 2H).^{13}C NMR (126 MHz, CDCl$_3$) δ 167.0, 163.0, 142.5, 131.7, 130.9, 128.8, 128.5, 128.4, 125.8, 122.5, 114.2, 67.3, 51.9, 35.6, 31.5, 29.1, 26.9, 23.6.GCMS (EI) calculated for $[M]^+$ 338.19, found 338.2. FTIR (neat, cm^{-1}): 2929(m), 2849(m), 2360(m), 1719(s), 1604(s), 1510(s), 1437(s), 1280(s), 1253(s), 1167(s), 1104(s).



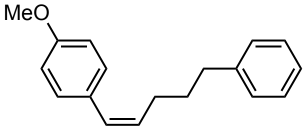
[(4*Z*)-8-phenyloct-4-en-1-yl]benzene (2.4), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (116.3 mg, 88% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 4H), 7.21 – 7.14 (m, 6H), 5.54 – 5.30 (m, 2H), 2.68 – 2.54 (m, 4H), 2.12 – 2.00 (m, 4H), 1.76 – 1.60 (m, 4H).^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 130.0, 128.6, 128.4, 125.8, 35.6, 31.6, 27.0. GCMS (EI) calculated for $[M]^+$ 264.19, found 264.2. FTIR (neat, cm^{-1}): 3061(m), 3005(m), 2931(m), 2856(m), 1602(m) 1495(s), 1452(s), 1217(s), 1030(s), 906(w).



[(4*Z*)-6-methoxyundec-4-en-1-yl]benzene (2.5), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (116.6 mg, 90% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 2H), 7.23 – 7.13 (m, 3H), 5.63 (dt, *J* = 10.9, 7.4 Hz, 1H), 5.23 (dd, *J* = 10.9, 9.2 Hz, 1H), 3.88 (dt, *J* = 9.2, 6.3 Hz, 1H), 3.23 (s, 3H), 2.73 – 2.54 (m, 2H), 2.24 – 2.01 (m, 2H), 1.80 – 1.64 (m, 2H), 1.41 – 1.19 (m, 8H), 0.88 (t, *J* = 6.6 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 142.3, 133.0, 131.4, 128.5, 128.5, 125.9, 76.6, 56.0, 35.7, 35.6, 32.0, 31.6, 27.5, 25.1, 22.8, 14.2. GCMS (EI) calculated for $[M]^+$ 260.21, found 260.3. FTIR (neat, cm^{-1}): 3025(m), 2929(m), 2857(m), 1603(s), 1496(s), 1452(s), 1332(m), 1124(s), 1097(s).

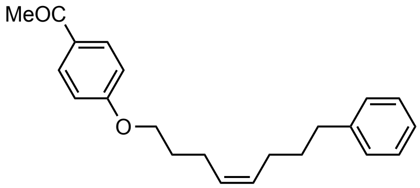


2-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}quinoxaline (2.6), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (133.5 mg, 80% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.46 (s, 1H), 8.01 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.81 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.66 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.55 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 7.26 – 7.19 (m, 2H), 7.19 – 7.08 (m, 3H), 5.57 – 5.34 (m, 2H), 4.47 (t, *J* = 6.5 Hz, 2H), 2.67 – 2.50 (m, 2H), 2.33 – 2.16 (m, 2H), 2.16 – 2.01 (m, 2H), 1.98 – 1.83 (m, 2H), 1.76 – 1.60 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 157.6, 142.5, 140.6, 139.9, 139.0, 130.7, 130.2, 129.1, 129.0, 128.5, 128.4, 127.3, 126.5, 125.8, 66.0, 35.6, 31.5, 28.8, 27.0, 23.8. GCMS (EI) calculated for [M]+ 332.19, found 332.2. FTIR (neat, cm^{-1}): 3004(m), 2928(m), 2855(m), 1944(w), 1571(s), 1497(s), 1414(s), 1305(s), 1221(s), 1136(s), 1019(m), 911(s).

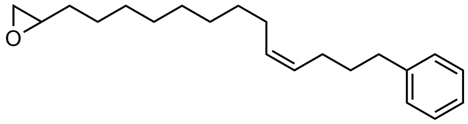


1-methoxy-4-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (2.7), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (117.9 mg, 93% yield).^{1}H NMR (300 MHz, CDCl$_3$) δ 7.34 – 7.27 (m, 1H), 7.24 – 7.12 (m, 6H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.37 (d, *J* = 11.6 Hz, 1H), 5.60 (dt, *J* = 11.6, 7.2 Hz, 1H), 3.82 (s, 3H), 2.70 – 2.60 (m, 2H), 2.45 – 2.30 (m, 2H), 1.85 – 1.70 (m, 2H).^{13}C NMR (126 MHz, CDCl$_3$) δ 158.3, 142.5, 131.1, 130.5, 130.1, 128.7, 128.6, 128.4, 125.8, 113.7, 55.4, 35.6, 31.9, 28.3. GCMS (EI) calculated for [M]$^+$ 252.15, found 252.2. FTIR (neat, cm$^-$

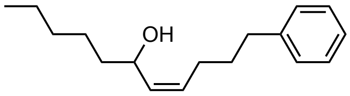
^{1}):3292(m), 3061(m), 3003(m), 2929(m), 2855(m), 1605(s), 1503(s), 1452(s), 1300(s), 1250(s), 1174(s), 1108(s), 1033(s), 837(s).



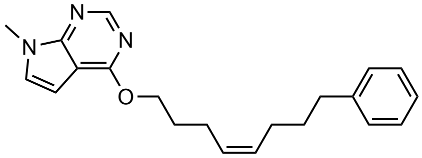
1-(4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}phenyl)ethan-1-one (2.8), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (97.8 mg, 61% yield).^{1}H NMR (300 MHz, CDCl$_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H), 7.28 (s, 1H), 7.23 (s, 1H), 7.20 – 7.08 (m, 3H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.56 – 5.30 (m, 2H), 4.01 (t, *J* = 6.3 Hz, 2H), 2.69 – 2.47 (m, 5H), 2.29 – 2.15 (m, 2H), 2.11 – 1.98 (m, 2H), 1.91 – 1.82 (m, 2H), 1.72 – 1.59 (m, 2H).^{13}C NMR (126 MHz, CDCl$_3$) δ 196.9, 163.2, 142.5, 130.9, 130.7, 130.3, 128.7, 128.5, 128.4, 125.8, 114.2, 67.4, 35.6, 31.5, 29.0, 26.9, 26.4, 23.6.GCMS (EI) calculated for [M]$^{+}$ 322.19, found 322.2. FTIR (neat, cm^{-1}): 3060(m), 3002(m), 2932(m), 2855(m), 1676(s), 1600(s), 1508(s), 1357(s), 1305(s), 1255(s), 1170(s), 1029(m), 955(s), 833(s).



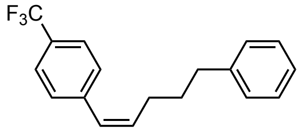
2-[(10*Z*)-14-phenyltetradec-10-en-1-yl]oxirane (2.9), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (122.0 mg, 81% yield).^{1}H NMR (300 MHz, CDCl$_3$) δ 7.31 – 7.26 (m, 2H), 7.21 – 7.14 (m, 3H), 5.51 – 5.26 (m, 2H), 2.95 – 2.85 (m, 1H), 2.78 – 2.72 (m, 1H), 2.66 – 2.57 (m, 2H), 2.46 (dd, *J* = 5.0, 2.7 Hz, 1H), 2.12 – 1.95 (m, 4H), 1.74 – 1.61 (m, 2H), 1.52 – 1.41 (m, 4H), 1.29 (s, 10H).^{13}C NMR (126 MHz, CDCl$_3$) δ 142.7, 130.6, 129.4, 128.5, 128.4, 125.7, 52.5, 47.2, 35.6, 32.6, 31.6, 29.8, 29.7, 29.6, 29.4, 27.4, 27.0, 26.1. GCMS (EI) calculated for $[M]^+$ 300.25, found 300.3. FTIR (neat, cm^{-1}): 3001(m), 2926(m), 2853(m), 1725(m), 1603(s), 1495(s), 1453(s), 1258(w), 1029(s).



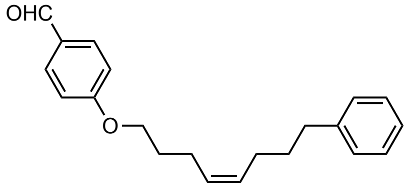
(4*Z*)-1-phenylundec-4-en-6-ol (2.10), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 60%) and isolated as a colorless oil (78.2 mg, 63% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.24 – 7.12 (m, 3H), 5.64 – 5.26 (m, 2H), 4.44 – 4.29 (m, 1H), 2.75 – 2.55 (m, 2H), 2.24 – 2.00 (m, 2H), 1.78 – 1.64 (m, 2H), 1.59 – 1.38 (m, 2H), 1.35 – 1.22 (m, 6H), 0.88 (t, J = 5.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 133.3, 131.6, 128.5, 128.4, 125.9, 67.8, 37.6, 35.5, 31.9, 31.4, 27.3, 25.1, 22.7, 14.1. GCMS (EI) calculated for $[M]^+$ 246.20, found 246.2. FTIR (neat, cm^{-1}): 3349(b), 3025(m), 3004(m), 2929(m), 2857(m), 1603(s), 1496(s), 1453(s), 1378(s), 1303(m), 1123(s), 1028(s), 910(s).



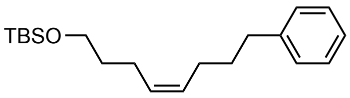
7-methyl-4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}-7H-pyrrolo[2,3-d]pyrimidine (2.11), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (146.7 mg, 87% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.25 – 7.19 (m, 2H), 7.20 – 7.06 (m, 3H), 6.99 (d, J = 3.4 Hz, 1H), 6.52 (d, J = 3.4 Hz, 1H), 5.58 – 5.33 (m, 2H), 4.51 (t, J = 6.6 Hz, 2H), 3.84 (s, 3H), 2.63 – 2.46 (m, 2H), 2.31 – 2.16 (m, 2H), 2.14 – 2.00 (m, 2H), 1.96 – 1.86 (m, 2H), 1.69 – 1.60 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9, 151.9, 150.9, 142.4, 130.5, 129.0, 128.4, 128.2, 126.6, 125.6, 105.5, 98.2, 65.7, 35.5, 31.4, 31.4, 28.9, 26.8, 23.7. GCMS (EI) calculated for $[M]^+$ 335.20, found 335.2. FTIR (neat, cm^{-1}): 3003(m), 2926(m), 2856(m), 1873(w), 1595(s), 1561(s), 1441(s), 1367(s), 1317(s), 1247(s), 1055(s), 1006(m), 888(m).



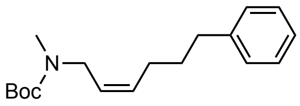
1-[(1*Z*)-5-phenylpent-1-en-1-yl]-4-(trifluoromethyl)benzene (2.12), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (124.3 mg, 86% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.27 (m, 3H), 7.24 – 7.09 (m, 4H), 6.46 (d, *J* = 11.6 Hz, 1H), 5.80 (dt, *J* = 11.6, 7.4 Hz, 1H), 2.72 – 2.57 (m, 2H), 2.43 – 2.26 (m, 2H), 1.87 – 1.71 (m, 2H)^{13}C NMR (126 MHz, $CDCl_3$) δ 142.1, 141.3, 134.8, 129.0, 128.6 (q, *J* = 27.6 Hz), 128.6, 128.5, 128.2, 126.0, 125.2 (q, *J* = 3.8 Hz), 124.5 (q, *J* = 271.9 Hz), 35.5, 31.6, 28.1.^{19}F NMR (470 MHz, $CDCl_3$) δ -65.4. GCMS (EI) calculated for $[M]^+$ 290.13, found 290.1. FTIR (neat, cm^{-1}): 3062(m), 3025(m), 2931(m), 2858(m), 1614(s), 1496(s), 1453(s), 1420(m), 1326(s), 1164(s), 1124(s), 1067(s), 1016(s), 837(s).



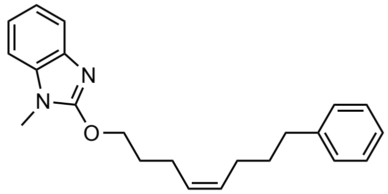
4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}benzaldehyde (2.13), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (108.2 mg, 70% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.82 (d, *J* = 8.7 Hz, 2H), 7.28 (s, 1H), 7.23 (s, 1H), 7.20 – 7.07 (m, 3H), 6.98 (d, *J* = 8.7 Hz, 2H), 5.57 – 5.30 (m, 2H), 4.03 (t, *J* = 6.3 Hz, 2H), 2.68 – 2.50 (m, 2H), 2.30 – 2.16 (m, 2H), 2.13 – 1.99 (m, 2H), 1.97 – 1.81 (m, 2H), 1.74 – 1.59 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 190.9, 164.3, 142.5, 132.1, 131.0, 129.9, 128.7, 128.5, 128.4, 125.8, 114.9, 67.6, 35.6, 31.5, 29.0, 27.0, 23.6. GCMS (EI) calculated for $[M]^+$ 308.18, found 308.2. FTIR (neat, cm^{-1}): 3016(m), 3003(m), 2924(m), 2854(m), 2735(m), 1694(s), 1590(s), 1574(s), 1497(s), 1393(s), 1310(m), 1257(m), 1158(s), 1029(s), 832(s), 750(s), 698(s).



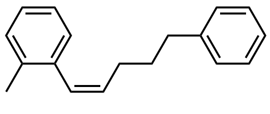
***tert*-butyldimethyl{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}silane (2.14),** compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (150.4 mg, 95% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 1H), 7.26 – 7.23 (m, 1H), 7.22 – 7.13 (m, 3H), 5.50 – 5.31 (m, 2H), 3.60 (t, J = 6.5 Hz, 2H), 2.68 – 2.51 (m, 2H), 2.15 – 2.00 (m, 4H), 1.75 – 1.62 (m, 2H), 1.61 – 1.50 (m, 2H), 0.90 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 129.9, 128.6, 128.4, 125.8, 62.8, 35.7, 33.0, 31.6, 27.0, 26.1, 23.7, 18.5, -5.1. GCMS (EI) calculated for $[M]^+$ 318.24, found 318.3. FTIR (neat, cm^{-1}): 3062(m), 3026(m), 3004(m), 2927(m), 2856(m), 1604(s), 1496(s), 1471(s), 1388(s), 1360(s), 1255(s), 1102(s), 836(s), 774(s), 698(s).



***tert*-butyl N-methyl-N-[(2*Z*)-6-phenylhex-2-en-1-yl]carbamate (2.15),** compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (127.7 mg, 88% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 7.23 – 7.11 (m, 3H), 5.66 – 5.48 (m, 1H), 5.48 – 5.31 (m, 1H), 3.83 (d, J = 5.0 Hz, 2H), 2.78 (s, 3H), 2.69 – 2.54 (m, 2H), 2.20 – 2.05 (m, 2H), 1.80 – 1.61 (m, 2H), 1.46 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8, 142.2, 132.4, 128.4, 128.4, 125.8, 79.4, 45.2, 35.5, 33.5, 31.4, 28.5, 26.9. GCMS (EI) calculated for $[M]^+$ 289.20, found 289.4. FTIR (neat, cm^{-1}): 3061(w), 3024(m), 2974(m), 2930(m), 2857(m), 1699(s), 1480(s), 1390(s) 1365(s), 1238(s), 1141(s), 1030(w), 879(s).

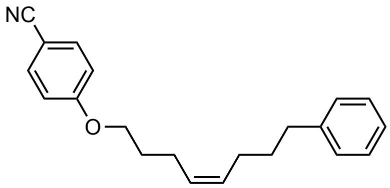


1-methyl-2-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}-1H-1,3-benzodiazole (2.16), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (127.6 mg, 76% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.50 (m, 1H), 7.30 – 7.27 (m, 2H), 7.25 – 7.22 (m, 1H), 7.22 – 7.09 (m, 6H), 5.55 – 5.37 (m, 2H), 4.55 (t, *J* = 6.5 Hz, 2H), 3.54 (s, 3H), 2.67 – 2.55 (m, 2H), 2.29 – 2.17 (m, 2H), 2.16 – 2.04 (m, 2H), 1.99 – 1.86 (m, 2H), 1.76 – 1.63 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 142.5, 140.2, 134.4, 130.8, 128.8, 128.5, 128.4, 125.8, 121.6, 120.9, 117.7, 108.0, 69.8, 35.6, 31.4, 29.1, 28.1, 26.9, 23.7 GCMS (EI) calculated for $[M]^+$ 334.20, found 334.2. FTIR (neat, cm^{-1}): 3003(m), 2923(m), 2855(m), 1603(w), 1514(s), 1452(m), 1021(m), 808(s).

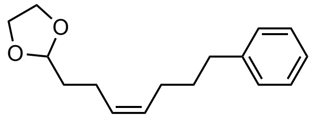


1-methyl-2-[(1*Z*)-5-phenylpent-1-en-1-yl]benzene (2.17), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (99.5 mg, 84% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.25 – 7.11 (m, 7H), 6.51 (d, *J* = 11.5 Hz, 1H), 5.78 (dt, *J* = 11.5, 7.4 Hz, 1H), 2.72 – 2.56 (m, 2H), 2.30 (s, 3H), 2.29 – 2.18 (m, 2H), 1.85 – 1.68 (m, 2H).^{13}C NMR (126 MHz,

$CDCl_3$) δ 142.5, 136.9, 136.3, 132.4, 129.9, 129.2, 128.5, 128.5, 128.4, 126.9, 125.8, 125.4, 35.6, 31.8, 28.1, 20.1. GCMS (EI) calculated for $[M]^+$ 236.16, found 236.2. FTIR (neat, cm^{-1}): 3024(m), 2920(m), 2855(m), 1602(s), 1485(s), 1453(s), 1435(m), 1104(s0, 1083(s), 1030(s).

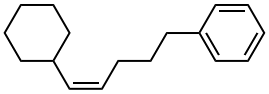


4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}benzonitrile (2.18), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (146.2 mg, 96% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.8 Hz, 2H), 7.34 – 7.26 (m, 1H), 7.26 – 7.23 (m, 1H), 7.21 – 7.10 (m, 3H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.58 – 5.31 (m, 2H), 3.98 (t, *J* = 6.3 Hz, 2H), 2.64 – 2.52 (m, 2H), 2.26 – 2.16 (m, 2H), 2.12 – 2.01 (m, 2H), 1.91 – 1.80 (m, 2H), 1.71 – 1.59 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4, 142.3, 134.0, 130.9, 128.5, 128.4, 128.3, 125.7, 119.3, 115.2, 103.7, 67.4, 35.5, 31.3, 28.8, 26.8, 23.4. GCMS (EI) calculated for $[M]^+$ 305.18, found 305.1. FTIR (neat, cm^{-1}): 3024(m), 3004(m), 2934(m), 2856(m), 2224(s), 1605(s), 1508(s), 1452(s), 1302(s), 1258(s), 1171(s), 1112(s), 1029(s).

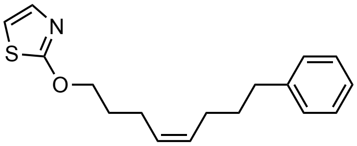


2-[(3*Z*)-7-phenylhept-3-en-1-yl]-1,3-dioxolane (2.19), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (104.4 mg, 85% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.21 – 7.13 (m, 3H), 5.50 – 5.32 (m, 2H), 4.86 (t, *J* = 4.8 Hz, 1H), 4.02 – 3.91 (m, 2H), 3.91 – 3.79 (m, 2H), 2.67 – 2.56 (m, 2H), 2.22 – 2.04 (m, 4H), 1.78 – 1.62 (m, 4H).^{13}C

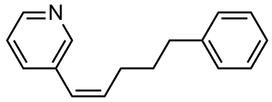
NMR (126 MHz, $CDCl_3$) δ 142.7, 130.2, 129.2, 128.5, 128.4, 125.8, 104.3, 65.0, 35.6, 34.0, 31.5, 26.9, 22.1. GCMS (EI) calculated for $[M]^+$ 246.16, found 246.2. FTIR (neat, cm^{-1}): 3061(m), 3024(m), 3003(m), 2928(m), 2857(m), 1602(s), 1495(s), 1452(s), 1359(s), 1138(s), 1055(s), 1030(s), 738(s), 699(s).



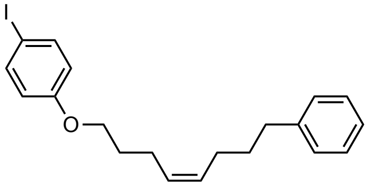
[(4*Z*)-5-cyclohexylpent-4-en-1-yl]benzene (2.20), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (83.7 mg, 73% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 2H), 7.24 – 7.10 (m, 3H), 5.37 – 5.12 (m, 2H), 2.72 – 2.52 (m, 2H), 2.30 – 2.00 (m, 3H), 1.75 – 1.51 (m, 6H), 1.35 – 0.96 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 136.7, 128.6, 128.4, 127.6, 125.8, 110.1, 36.5, 35.6, 33.5, 31.8, 27.2, 26.2, 26.1. GCMS (EI) calculated for $[M]^+$ 228.19, found 228.2. FTIR (neat, cm^{-1}): 3062(m), 3024(m), 2999(m), 2921(m), 2847(m), 1603(s), 1495(s), 1446(s), 1435(m), 1349(s), 1258(m), 1074(s), 1030(s).



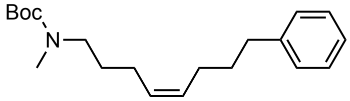
2-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}-1,3-thiazole (2.21), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (118.2 mg, 82% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.22 – 7.14 (m, 3H), 7.13 (d, *J* = 3.8 Hz, 1H), 6.67 (d, *J* = 3.8 Hz, 1H), 5.60 – 5.34 (m, 2H), 4.40 (t, *J* = 6.4 Hz, 2H), 2.68 – 2.55 (m, 2H), 2.26 – 2.14 (m, 2H), 2.14 – 2.02 (m, 2H), 1.94 – 1.81 (m, 2H), 1.75 – 1.62 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 142.5, 137.0, 130.8, 128.6, 128.5, 128.3, 125.7, 110.8, 71.1, 35.5, 31.4, 28.8, 26.9, 23.5. GCMS (EI) calculated for $[M]^+$ 287.13, found 287.1. FTIR (neat, cm^{-1}): 3003(m), 2931(m), 2855(m), 1523(s), 1461(m), 1380(s), 1308(s), 1236(s), 1162(s), 978(m), 907(m).



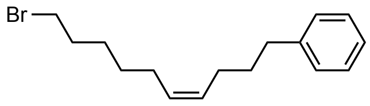
3-[(1*Z*)-5-phenylpent-1-en-1-yl]pyridine (2.22), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (94.6 mg, 85% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.45 (d, *J* = 3.7 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.25 – 7.09 (m, 5H), 6.39 (d, *J* = 11.7 Hz, 1H), 5.83 (dt, *J* = 11.7, 7.4 Hz, 1H), 2.70 – 2.56 (m, 2H), 2.41 – 2.28 (m, 2H), 1.87 – 1.71 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 149.8, 147.4, 142.1, 136.0, 135.2, 133.5, 128.6, 128.5, 126.0, 125.7, 123.3, 35.5, 31.6, 28.2. GCMS (EI) calculated for $[M]^+$ 223.14, found 223.1. FTIR (neat, cm^{-1}): 3048(m), 3026(m), 2931(m), 2857(m), 1602(s), 1566(s), 1474(s), 1420(s), 1399(s), 1265(s), 1176(s), 1024(s).



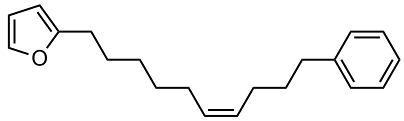
1-iodo-4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}benzene (2.23), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil 187.0 mg, 92% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.9 Hz, 2H), 7.32 – 7.27 (m, 2H), 7.23 – 7.11 (m, 3H), 6.67 (d, *J* = 8.9 Hz, 2H), 5.56 – 5.31 (m, 2H), 3.91 (t, *J* = 6.3 Hz, 2H), 2.66 – 2.52 (m, 2H), 2.26 – 2.16 (m, 2H), 2.13 – 2.03 (m, 2H), 1.89 – 1.78 (m, 2H), 1.73 – 1.59 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 142.5, 138.3, 130.8, 128.9, 128.5, 128.4, 125.8, 117.0, 82.6, 67.2, 35.6, 31.5, 29.1, 27.0, 23.7. GCMS (EI) calculated for $[M]^+$ 406.08, found 406.1. FTIR (neat, cm^{-1}): 3060(m), 3024(m), 3001(m), 2933(m), 2855(m), 1586(s), 1485(s), 1467(s), 1282(s), 1243(s), 1174(s), 819(s), 698(s).



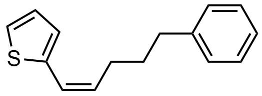
***tert*-butyl N-methyl-N-[(4*Z*)-8-phenyloct-4-en-1-yl]carbamate (2.24),** compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (123.2 mg, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.23 – 7.13 (m, 3H), 5.53 – 5.31 (m, 2H), 3.26 – 3.11 (m, 2H), 2.84 (s, 3H), 2.71 – 2.50 (m, 2H), 2.13 – 1.94 (m, 4H), 1.75 – 1.63 (m, 2H), 1.61 – 1.53 (m, 2H), 1.46 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 142.5, 130.1, 129.4, 128.5, 128.4, 125.8, 79.2, 48.8, 35.6, 34.2, 31.5, 28.6, 28.6, 26.9, 24.6. GCMS (EI) calculated for $[M]^+$ 317.24, found 317.2. FTIR (neat, cm^{-1}): 3062(m), 3005(m), 2974(m), 2929(m), 2858(m), 1695(s), 1479(s), 1391(s), 1365(s), 1303(s), 1166(s), 879(s), 754(s).



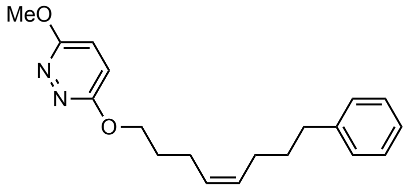
[(4*Z*)-10-bromodec-4-en-1-yl]benzene (2.25), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (96.9 mg, 66% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 2H), 7.22 – 7.12 (m, 3H), 5.49 – 5.29 (m, 2H), 3.40 (t, J = 6.8 Hz, 2H), 2.69 – 2.55 (m, 2H), 2.12 – 1.97 (m, 4H), 1.92 – 1.79 (m, 2H), 1.75 – 1.61 (m, 2H), 1.47 – 1.33 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 130.0, 129.9, 128.6, 128.4, 125.8, 35.6, 34.0, 32.9, 31.6, 29.0, 28.0, 27.2, 27.0. GCMS (EI) calculated for $[M]^+$ 294.10, found 294.1. FTIR (neat, cm^{-1}): 3060(m), 3002(m), 2930(m), 2855(m), 1602(s), 1495(s), 1452(s), 970(s).



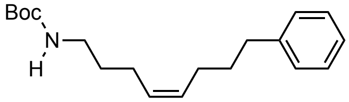
2-[(6*Z*)-10-phenyldec-6-en-1-yl]furan (2.26), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (127.3 mg, 90% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 3H), 7.23 – 7.14 (m, 3H), 6.28 (dd, *J* = 2.9, 2.0 Hz, 1H), 6.00 – 5.95 (m, 1H), 5.47 – 5.32 (m, 2H), 2.62 (t, *J* = 7.6 Hz, 4H), 2.13 – 1.97 (m, 4H), 1.73 – 1.60 (m, 4H), 1.41 – 1.32 (m, 4H).^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3, 142.4, 140.5, 130.1, 129.3, 128.3, 128.1, 125.5, 109.9, 104.4, 35.3, 31.3, 29.3, 28.7, 27.8, 27.0, 26.7. GCMS (EI) calculated for $[M]^+$ 282.20, found 282.1. FTIR (neat, cm^{-1}): 3025(m), 3002(m), 2928(m), 2855(m), 1655(m), 1597(s), 1507(s), 1460(s), 1350(w), 1147(s), 1079(s), 1007(s), 920(m), 796(s).



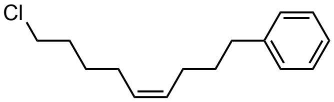
2-[(1*Z*)-5-phenylpent-1-en-1-yl]thiophene (2.27), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (107.4 mg, 94% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 3H), 7.24 – 7.14 (m, 3H), 7.10 (d, *J* = 2.3 Hz, 1H), 7.07 (d, *J* = 5.0 Hz, 1H), 6.40 (d, *J* = 11.6 Hz, 1H), 5.65 (dt, *J* = 11.6, 7.3 Hz, 1H), 2.79 – 2.57 (m, 2H), 2.41 (q, *J* = 7.3 Hz, 2H), 1.91 – 1.73 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 138.9, 131.7, 128.7, 128.6, 128.4, 125.9, 125.0, 123.5, 122.8, 35.7, 31.6, 28.7. GCMS (EI) calculated for $[M]^+$ 228.10, found 228.1. FTIR (neat, cm^{-1}): 3061(m), 3024(m), 2923(m), 2855(m), 1602(s), 1494(s), 1452(s), 1350(s), 1251(m), 1149(s), 1080(s), 1029(s).



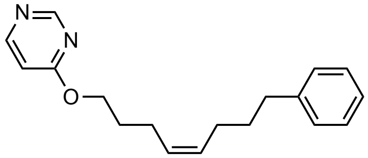
3-methoxy-6-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}pyridazine (2.28), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (118.6 mg, 76% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 1H), 7.26 – 7.22 (m, 1H), 7.21 – 7.11 (m, 3H), 6.98 – 6.79 (m, 2H), 5.57 – 5.26 (m, 2H), 4.40 (t, *J* = 6.5 Hz, 2H), 4.04 (s, 3H), 2.66 – 2.52 (m, 2H), 2.25 – 2.13 (m, 2H), 2.13 – 2.00 (m, 2H), 1.92 – 1.81 (m, 2H), 1.75 – 1.57 (m, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 161.9, 142.6, 130.5, 129.1, 128.5, 128.4, 125.8, 121.6, 121.4, 66.7, 54.6, 35.6, 31.5, 28.9, 26.9, 23.8. GCMS (EI) calculated for $[M]^+$ 312.18, found 312.2. FTIR (neat, cm^{-1}): 3005(m), 2936(m), 2856(m), 1696(s), 1602(s), 1463(m), 1421(s), 1383(s), 1267(s), 1015(s), 838(s), 750(s), 699(s).



***tert*-butyl N-[(4*Z*)-8-phenyloct-4-en-1-yl]carbamate (2.29),** compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 50%) and isolated as a colorless oil (109.7 mg, 72% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 7.24 – 7.10 (m, 3H), 5.53 – 5.24 (m, 2H), 4.49 (s, 1H), 3.22 – 2.95 (m, 2H), 2.69 – 2.53 (m, 2H), 2.15 – 1.96 (m, 4H), 1.74 – 1.61 (m, 2H), 1.56 – 1.50 (m, 2H), 1.45 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 142.6, 130.4, 129.2, 128.5, 128.4, 125.8, 79.2, 40.4, 35.6, 31.5, 30.1, 28.6, 26.9, 24.7. GCMS (EI) calculated for $[M]^+$ 303.22, found 303.1. FTIR (neat, cm^{-1}): 3438(b), 3355(b), 3005(m), 2927(m), 2857(m), 2247(s), 1694(s), 1524(s), 1455(s), 1363(s), 1250(m), 1168(m), 1030(m), 910(s), 852(m).



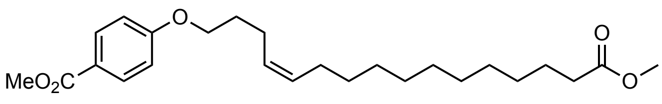
[(4*Z*)-9-chloronon-4-en-1-yl]benzene (2.30), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (109.6 mg, 93% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 2H), 7.24 – 7.13 (m, 3H), 5.54 – 5.25 (m, 2H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.72 – 2.51 (m, 2H), 2.17 – 1.95 (m, 4H), 1.83 – 1.63 (m, 4H), 1.53 – 1.41 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 130.2, 129.5, 128.5, 128.4, 125.8, 45.0, 35.5, 32.2, 31.5, 27.0, 26.9, 26.5. GCMS (EI) calculated for $[M]^+$ 236.13, found 236.1. FTIR (neat, cm^{-1}): 3061(m), 3002(m), 2925(m), 2855(m), 1602(s), 1494(s), 1452(s), 1433(s), 1309(s), 1275(m), 1029(s).



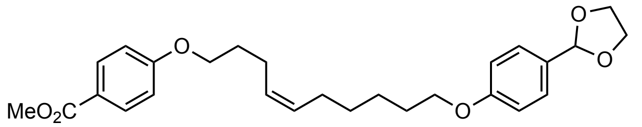
4-{[(4*Z*)-8-phenyloct-4-en-1-yl]oxy}pyrimidine (2.31), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (112.8 mg, 80% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.40 (d, *J* = 5.8 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.25 – 7.21 (m, 1H), 7.20 – 7.12 (m, 3H), 6.70 (dd, *J* = 5.8, 1.1 Hz, 1H), 5.57 – 5.27 (m, 2H), 4.35 (t, *J* = 6.6 Hz, 2H), 2.65 – 2.54 (m, 2H), 2.24 – 2.12 (m, 2H), 2.12 – 2.01 (m, 2H), 1.88 – 1.77 (m, 2H), 1.74 – 1.60 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 158.9, 157.3, 142.8, 131.0, 129.1, 128.8, 128.7, 126.1, 109.1, 66.3, 35.8, 31.7, 29.0, 27.2, 23.9. GCMS (EI) calculated for $[M]^+$ 282.17, found 282.1. FTIR (neat, cm^{-1}): 3005(m), 2933(m), 2856(m), 1582(s), 1560(s), 1470(s), 1462(s), 1396(s), 1374(s), 1305(s), 1163(m), 985(s), 834(s), 733(s).

2.6.7 *Characterization of Z-Selective Hydroalkylation Products: Alkylboranes*

Alkylboranes were used as a 2M solution in toluene and were synthesized according to literature procedure the day before use.[35]

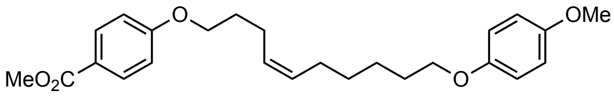


methyl 4-{[(4*Z*)-16-methoxy-16-oxohexadec-4-en-1-yl]oxy}benzoate (2.32), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (163.3 mg, 78% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 5.52 – 5.27 (m, 2H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.66 (s, 3H), 2.30 (t, *J* = 7.6 Hz, 2H), 2.25 – 2.15 (m, 2H), 2.06 – 1.95 (m, 2H), 1.89 – 1.81 (m, 2H), 1.64 – 1.57 (m, 2H), 1.36 – 1.14 (m, 16H).^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 166.9, 163.0, 131.6, 131.5, 128.1, 122.4, 114.1, 67.3, 51.9, 51.5, 42.0, 34.2, 29.8, 29.6, 29.5, 29.4, 29.2, 29.1, 27.3, 27.2, 25.0, 23.5. GCMS (EI) calculated for $[M]^+$ 418.27, found 418.3. FTIR (neat, cm^{-1}): 2998(m), 2925(m), 2853(m), 1726(s), 1720(s), 1605(s), 1511(s), 1434(s), 1279(s), 1253(s), 1167(s), 1104(s), 1024(m), 913(s).

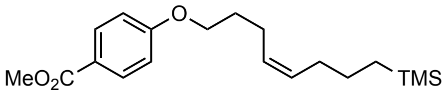


methyl 4-{[(4*Z*)-10-[4-(1,3-dioxolan-2-yl)phenoxy]dec-4-en-1-yl]oxy}benzoate (2.33), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (153.2 mg, 67% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 6.96 – 6.80 (m, 84), 5.75 (s, 1H), 5.50 – 5.30 (m, 2H), 4.17 – 4.05 (m, 2H), 4.03 – 3.98 (m, 2H), 3.92 (t, *J* = 6.5 Hz, 2H), 3.87 (s, 3H), 2.29 – 2.17 (m, 2H), 2.10 – 1.99 (m, 2H), 1.91 – 1.79 (m, 2H), 1.76 –

1.68 (m, 2H), 1.47 – 1.32 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 163.0, 160.0, 131.6, 131.1, 128.5, 127.9, 122.5, 114.4, 114.1, 103.8, 68.0, 67.3, 65.3, 51.9, 41.9, 29.5, 29.2, 29.0, 27.2, 25.7, 23.6. GCMS (ESI) calculated for $[M+H]^+$ 455.24, found 455.2. FTIR (neat, cm^{-1}): 3006(m), 2945(m), 2864(m), 1919(w), 1720(s), 1605(s), 1511(s), 1435(s), 1393(s), 1252(m), 1168(s), 912(m), 847(s).

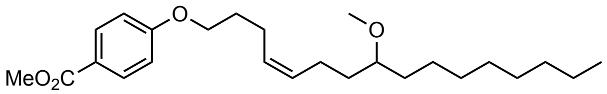


methyl 4-{[(4*Z*)-10-(4-methoxyphenoxy)dec-4-en-1-yl]oxy}benzoate (2.34), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (178.6 mg, 87% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 6.82 (s, 4H), 5.51 – 5.32 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.91 – 3.82 (m, 5H), 3.76 (s, 3H), 2.29 – 2.18 (m, 2H), 2.05 (q, *J* = 6.5 Hz, 2H), 1.92 – 1.80 (m, 2H), 1.78 – 1.65 (m, 2H), 1.48 – 1.32 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 163.0, 153.8, 153.4, 131.7, 131.2, 128.5, 122.5, 115.5, 114.7, 114.2, 68.6, 67.3, 55.8, 51.9, 29.5, 29.4, 29.1, 27.2, 25.8, 23.6. GCMS (EI) calculated for $[M]^+$ 412.22, found 412.2. FTIR (neat, cm^{-1}): 3053(m), 2986(m), 1711(s), 1606(s), 1502(s), 1421(s), 1262(s), 1169(s), 895(s), 738(s).

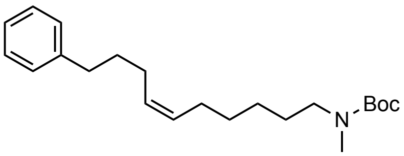


methyl 4-{[(4*Z*)-8-(trimethylsilyl)oct-4-en-1-yl]oxy}benzoate (2.35), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (139.0 mg, 83% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 5.49 – 5.32 (m, 1H), 4.01 (t, *J* = 6.4 Hz, 1H), 3.88 (s, 1H), 2.32 – 2.16 (m, 1H), 2.10 – 1.97 (m, 1H), 1.86 (p, *J* = 6.7 Hz, 1H), 1.37 –

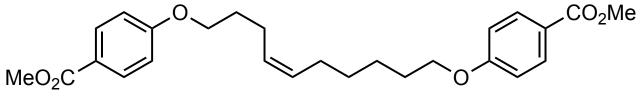
1.23 (m, 1H), 0.56 – 0.39 (m, 1H), -0.05 (s, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 130.2, 129.2, 128.5, 128.4, 125.8, 104.3, 65.0, 35.6, 34.0, 31.5, 26.9, 22.1. GCMS (EI) calculated for $[M]^+$ 334.20, found 334.2. FTIR (neat, cm^{-1}): 3003(m), 2950(m), 2873(m), 1914(w), 1721(s), 1606(s), 1511(s), 1434(s), 1279(m), 1254(m), 1167(s), 1104(s), 969(s), 844(s).



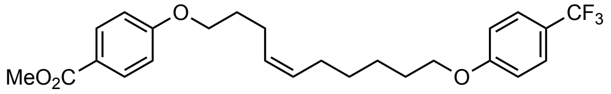
methyl 4-{[(4*Z*)-8-methoxyhexadec-4-en-1-yl]oxy}benzoate (2.36), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (182.8 mg, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.54 – 5.26 (m, 2H), 4.01 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.29 (s, 3H), 3.18 – 3.01 (m, 1H), 2.32 – 2.16 (m, 2H), 2.15 – 2.01 (m, 2H), 1.86 (p, *J* = 6.8 Hz, 2H), 1.54 – 1.35 (m, 4H), 1.27 (s, 12H), 0.88 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 163.0, 131.7, 131.0, 128.5, 122.5, 114.1, 80.4, 67.4, 56.4, 51.9, 33.5, 33.4, 32.0, 30.0, 29.7, 29.4, 29.1, 25.3, 23.6, 23.1, 22.8, 14.2. GCMS (EI) calculated for $[M]^+$ 404.29, found 404.3. FTIR (neat, cm^{-1}):3004(m), 2927(m), 2854(m), 1913(w), 1719(s), 1606(s), 1511(s), 1434(s), 1280(s), 1253(s), 1167(s), 1103(s), 1037(m), 970(s), 846(s), 757(s).



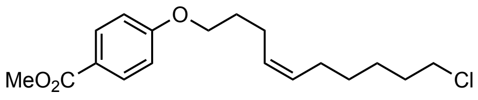
***tert*-butyl N-methyl-N-[(6*Z*)-10-phenyldec-6-en-1-yl]carbamate (2.37),** compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (As determined by NMR, 64% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 1H), 7.26 – 7.22 (m, 1H), 7.20 – 7.13 (m, 3H), 5.50 – 5.27 (m, 2H), 3.18 (t, *J* = 7.1 Hz, 2H), 2.82 (s, 3H), 2.68 – 2.56 (m, 2H), 2.15 – 1.91 (m, 4H), 1.74 – 1.61 (m, 2H), 1.50 – 1.43 (m, 11H), 1.36 – 1.24 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 142.7, 130.3, 129.6, 128.6, 128.4, 125.8, 79.2, 48.9, 35.6, 34.2, 32.2, 31.6, 29.6, 28.6, 27.4, 27.0, 26.5. GCMS (EI) calculated for $[M]^+$ 345.27, found 345.3. FTIR (neat, cm^{-1}): 3084(w), 3062(w), 3025(m), 3003(m), 2929(s) 2858(s), 1696(s), 1480(m), 1453(m), 1394(s), 1365(s), 1308(m), 1247(m), 1215(m), 1161(s).



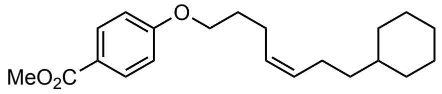
methyl 4-{[(4*Z*)-10-[4-(methoxycarbonyl)phenoxy]dec-4-en-1-yl]oxy}benzoate (2.38), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (198.4 mg, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.7 Hz, 4H), 6.95 – 6.80 (m, 4H), 5.51 – 5.31 (m, 2H), 4.04 – 3.92 (m, 4H), 3.88 (s, 3H), 3.87 (s, 3H), 2.31 – 2.16 (m, 2H), 2.05 (q, *J* = 6.4 Hz, 2H), 1.93 – 1.80 (m, 2H), 1.80 – 1.67 (m, 2H), 1.45 – 1.29 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 166.8, 162.9, 162.9, 131.6, 130.9, 128.5, 122.4, 122.3, 114.0, 68.0, 67.1, 51.8, 29.4, 29.0, 28.9, 27.1, 25.6, 23.5. GCMS (EI) calculated for $[M]^+$ 440.22, found 440.3. FTIR (neat, cm^{-1}): 3002(m), 2946(m), 2857(m), 1716(s), 1606(s), 1511(s), 1434(s), 1280(s), 1254(s), 1168(s), 1104(s), 1010(m), 970(m).



methyl 4-{[(4*Z*)-10-[4-(trifluoromethyl)phenoxy]dec-4-en-1-yl]oxy}benzoate (2.39), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (181.2 mg, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.6 Hz, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.05 – 6.70 (m, 4H), 5.50 – 5.31 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.94 (t, *J* = 6.5 Hz, 2H), 3.87 (s, 3H), 2.33 – 2.16 (m, 2H), 2.12 – 1.97 (m, 2H), 1.94 – 1.80 (m, 2H), 1.80 – 1.65 (m, 2H), 1.47 – 1.30 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 163.0, 161.7, 131.7, 131.0, 128.6, 126.9 (q, J = 3.7 Hz), 124.6 (q, J = 271.0 Hz), 122.7 (q, J =32.8 Hz), 122.5, 114.5, 114.1, 68.2, 67.3, 51.9, 29.5, 29.1, 29.0, 27.2, 25.7, 23.6. ^{19}F NMR (470 MHz, $CDCl_3$) δ -64.4. GCMS (EI) calculated for $[M]^+$ 450.20, found 450.3. FTIR (neat, cm^{-1}): 3005(m), 2942(m), 2858(m), 1716(s), 1606(s), 1511(s), 1435(s), 1329(s), 1255(s), 1168(s), 1112(m), 1067(s), 1009(s), 836(s).

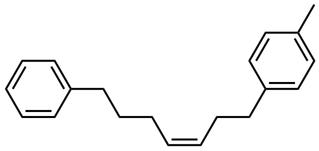


methyl 4-{[(4*Z*)-10-chlorodec-4-en-1-yl]oxy}benzoate (2.40), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (123.1 mg, 76% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 5.49 – 5.32 (m, 2H), 4.00 (t, J = 6.3 Hz, 2H), 3.88 (s, 3H), 3.49 (t, J = 6.7 Hz, 2H), 2.30 – 2.15 (m, 2H), 2.09 – 1.96 (m, 2H), 1.93 – 1.79 (m, 2H), 1.78 – 1.63 (m, 2H), 1.42 – 1.26 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 162.9, 131.6, 130.9, 128.6, 122.5, 114.1, 67.2, 51.8, 45.0, 32.5, 29.0, 27.1, 26.6, 23.5. GCMS (EI) calculated for $[M]^+$ 324.15, found 324.2. FTIR (neat, cm^{-1}): 3003(m), 2934(m), 2856(m), 1919(w), 1719(s), 1605(s), 1511(s), 1433(s), 1253(s), 1167(s), 1104(m), 846(s), 770(s).

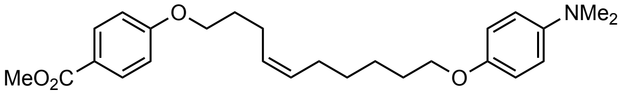


methyl 4-{[(4*Z*)-7-cyclohexylhept-4-en-1-yl]oxy}benzoate (2.41), compound was prepared according to general procedure A. The compound was purified by silica gel chromatographywith EtOAc/Hex (0 → 30%) and isolated as a colorless oil (155.2 mg, 94% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.50 – 5.26 (m, 2H), 4.00 (t, J = 6.3 Hz, 2H), 3.88 (s, 3H), 2.23 (q, J = 7.1 Hz, 2H), 2.09 – 1.94 (m, 2H), 1.85 (p, J = 6.8 Hz, 2H), 1.74

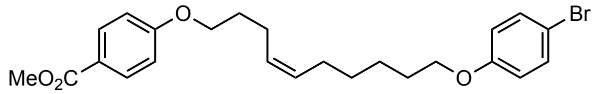
– 1.57 (m, 5H), 1.29 – 1.07 (m, 6H), 0.94 – 0.71 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 167.0, 163.0, 131.8, 131.7, 128.0, 122.5, 114.2, 67.4, 51.9, 37.6, 37.4, 33.4, 29.1, 26.8, 26.5, 24.7, 23.6. GCMS (EI) calculated for [M]$^+$ 330.22, found 330.2. FTIR (neat, cm^{-1}): 3003(m), 2919(m), 2848(m), 1914(w), 1720(s), 1605(s), 1511(s), 1435(m), 1252(s), 1167(s), 971(m) 845(s), 770(s).



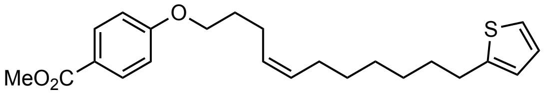
1-methyl-4-[(3*Z*)-7-phenylhept-3-en-1-yl]benzene (2.42), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (123.8 mg, 94% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.32 – 7.23 (m, 3H), 7.23 – 7.12 (m, 3H), 7.12 – 6.34 (m, 4H), 5.52 – 5.32 (m, 2H), 2.67 – 2.51 (m, 4H), 2.39 – 2.26 (m, 5H), 2.10 – 1.95 (m, 2H), 1.69 – 1.56 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 142.6, 139.1, 135.3, 130.1, 129.4, 129.1, 128.5, 128.5, 128.4, 125.8, 35.7, 35.6, 31.5, 29.5, 27.0, 21.1. GCMS (EI) calculated for [M]$^+$ 264.19, found 264.2. FTIR (neat, cm^{-1}): 3060(m), 3005(m), 2932(s), 2855(m), 1622(m), 1537(s), 1454(s), 1375(m) 1285(s), 1007(s), 909(m), 739(s).



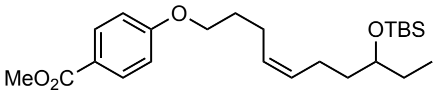
methyl 4-{[(4*Z*)-10-[4-(dimethylamino)phenoxy]dec-4-en-1-yl]oxy}benzoate (2.43), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (189.7 mg, 89% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 6.82 (d, *J* = 9.1 Hz, 2H), 6.73 (d, *J* = 9.1 Hz, 2H), 5.49 – 5.33 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.95 – 3.77 (m, 5H), 2.86 (s, 6H), 2.31 – 2.16 (m, 2H), 2.11 – 1.97 (m, 2H), 1.92 – 1.76 (m, 2H), 1.76 – 1.63 (m, 2H), 1.47 – 1.31 (m, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.9, 163.0, 151.5, 145.8, 131.6, 131.1, 128.4, 122.4, 115.5, 114.9, 114.1, 68.6, 67.3, 51.8, 41.9, 29.5, 29.4, 29.1, 27.2, 25.8, 23.6. GCMS (EI) calculated for $[M]^+$ 425.26, found 425.3. FTIR (neat, cm^{-1}): 3000(m), 2938(m), 2857(m), 2793(m), 1715(s), 1605(s), 1513(s), 1434(s), 1280(s), 1253(m), 1168(s), 1104(s), 1051(m), 856(s), 816(s).



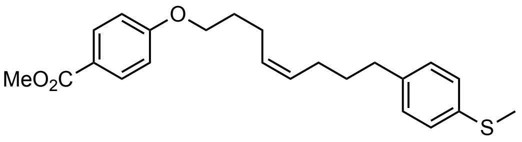
methyl 4-{[(4*Z*)-10-(4-bromophenoxy)dec-4-en-1-yl]oxy}benzoate (2.44), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (177.3 mg, 77% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 5.49 – 5.32 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.94 – 3.77 (m, 5H), 2.31 – 2.17 (m, 2H), 2.05 (q, *J* = 6.2 Hz, 2H), 1.86 (p, *J* = 6.6 Hz, 2H), 1.78 – 1.63 (m, 2H), 1.47 – 1.30 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 163.0, 158.3, 132.3, 131.7, 131.1, 128.6, 122.5, 116.4, 114.2, 112.7, 68.2, 67.3, 52.0, 29.5, 29.2, 29.1, 27.2, 25.8, 23.6. GCMS (EI) calculated for $[M]^+$ 460.12, found 460.1. FTIR (neat, cm^{-1}): 3003(m), 2940(m), 2857(m), 1716(s), 1605(s), 1510(s), 1488(s), 1282(m), 1253(m), 1168(s), 1104(s), 1002(s), 847(s), 738(s).



methyl 4-{[(4*Z*)-11-(thiophen-2-yl)undec-4-en-1-yl]oxy}benzoate (2.45), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (150.1 mg, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.9 Hz, 2H), 7.10 (dd, *J* = 5.1, 1.0 Hz, 1H), 6.99 – 6.83 (m, 3H), 6.80 – 6.71 (m, 1H), 5.53 – 5.28 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.88 (s, 3H), 2.79 (t, *J* = 7.6 Hz, 2H), 2.31 – 2.15 (m, 2H), 2.08 – 1.93 (m, 2H), 1.85 (p, *J* = 6.7 Hz, 2H), 1.72 – 1.58 (m, 2H), 1.37 – 1.22 (m, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.9, 162.9, 145.7, 131.6, 131.3, 128.2, 126.7, 123.9, 122.7, 122.4, 114.1, 67.2, 51.8, 31.8, 29.9, 29.6, 29.0, 29.0, 27.2, 23.5. GCMS (EI) calculated for $[M]^+$ 386.19, found 386.2. FTIR (neat, cm^{-1}): 3002(m), 2928(m), 2853(m), 1720(s), 1605(s), 1510(s), 1434(s), 1253(s), 1167(s), 1104(s), 969(m), 846(s), 770(s), 695(s).

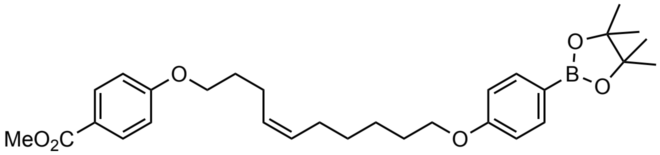


methyl 4-{[(4*Z*)-8-[(*tert*-butyldimethylsilyl)oxy]dec-4-en-1-yl]oxy}benzoate (2.46), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (190.4 mg, 91% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.97 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.51 – 5.30 (m, 2H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.56 (p, *J* = 5.6 Hz, 1H), 2.29 – 2.17 (m, 2H), 2.18 – 1.91 (m, 2H), 1.86 (p, *J* = 6.7 Hz, 2H), 1.50 – 1.37 (m, 4H), 0.91 – 0.80 (m, 12H), 0.03 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.9, 163.0, 131.6, 131.2, 128.3, 122.5, 114.1, 73.1, 67.3, 51.8, 36.6, 29.7, 29.1, 26.0, 23.6, 23.3, 18.2, 9.6, -4.3, -4.4. GCMS (EI) calculated for $[M]^+$ 420.27, found 420.2. FTIR (neat, cm^{-1}):3005(m), 2953(m), 2855(m), 1914(w), 1721(s), 1606(s), 1511(s), 1435(m), 1253(m), 1167(s), 1103(m), 1050(m), 835(m), 770(s).

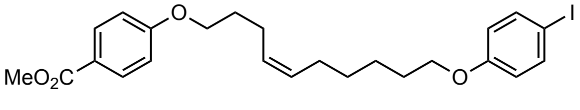


methyl 4-{[(4*Z*)-8-[4-(methylsulfanyl)phenyl]oct-4-en-1-yl]oxy}benzoate (2.47), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (161.0 mg, 84% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.98 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.51 – 5.33 (m, 2H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.88 (s, 3H), 2.58

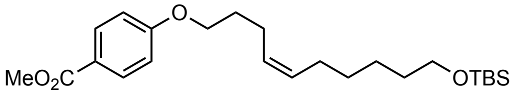
– 2.47 (m, 2H), 2.46 (s, 3H), 2.27 – 2.14 (m, 2H), 2.12 – 1.99 (m, 2H), 1.92 – 1.77 (m, 2H), 1.68 – 1.57 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 163.0, 139.6, 135.2, 131.7, 130.8, 129.0, 128.8, 127.2, 122.5, 114.1, 67.3, 51.9, 35.0, 31.4, 29.0, 26.8, 23.6, 16.4. GCMS (EI) calculated for $[M]^+$ 384.18, found 384.2. FTIR (neat, cm^{-1}): 3003(m), 2921(m), 2855(m), 1913(w), 1716(s), 1604(s), 1511(s), 1498(s), 1435(s), 1253(s), 1167(s), 1103(s), 1016(m), 835(s).



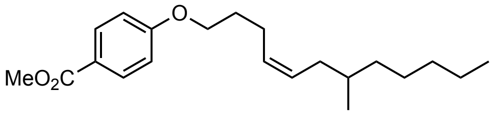
methyl 4-{[(4*Z*)-10-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]dec-4-en-1-yl]oxy}benzoate (2.48), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 50%) and isolated as a colorless oil (198.7 mg, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 6.93 – 6.82 (m, 4H), 5.50 – 5.31 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.94 (t, *J* = 6.5 Hz, 2H), 3.87 (s, 3H), 2.30 – 2.18 (m, 2H), 2.09 – 2.00 (m, 2H), 1.90 – 1.83 (m, 2H), 1.79 – 1.68 (m, 2H), 1.48 – 1.29 (m, 16H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 163.0, 161.8, 136.5, 131.6, 131.1, 128.5, 122.5, 114.1, 113.9, 83.6, 67.7, 67.3, 51.9, 42.0, 29.5, 29.12, 29.0, 27.2, 25.8, 24.9, 23.6. GCMS (ESI) calculated for $[M+H]^+$ 509.30, found 509.2. FTIR (neat, cm^{-1}): 3305(m), 2977(m), 2937(m), 2858(m), 1913(w), 1720(s), 1604(s), 1511(s), 1434(s), 1252(m), 1142(s), 962(s), 911(s), 846(s), 771(s), 734(s).



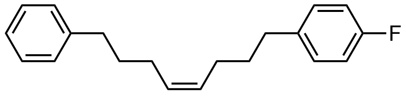
methyl 4-{[(4*Z*)-10-(4-iodophenoxy)dec-4-en-1-yl]oxy}benzoate (2.49), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (202.4 mg, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.7 Hz, 2H), 5.50 – 5.32 (m, 2H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.92 – 3.79 (m, 5H), 2.29 – 2.16 (m, 2H), 2.05 (q, *J* = 6.1 Hz, 2H), 1.86 (p, *J* = 6.8 Hz, 2H), 1.78 – 1.62 (m, 2H), 1.46 – 1.29 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 162.9, 159.0, 138.2, 131.6, 131.0, 128.5, 122.5, 117.0, 114.1, 82.5, 68.0, 67.2, 51.9, 29.5, 29.1, 29.0, 27.2, 25.7, 23.6. GCMS (ESI) calculated for $[M+H]^+$ 509.11, found 509.0. FTIR (neat, cm^{-1}): 3002(m), 2939(m), 2856(m), 1914(w), 1716(s), 1605(s), 1511(s), 1435(s), 1391(s), 1253(m), 1167(s), 1019(m), 909(s).



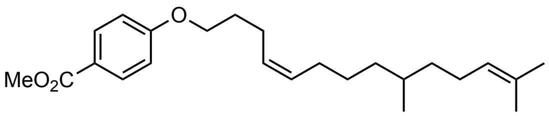
methyl 4-{[(4*Z*)-10-[(*tert*-butyldimethylsilyl)oxy]dec-4-en-1-yl]oxy}benzoate (2.50), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (189.9 mg, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.54 – 5.24 (m, 2H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.57 (t, *J* = 6.6 Hz, 2H), 2.29 – 2.15 (m, 2H), 2.02 (q, *J* = 6.4 Hz, 2H), 1.85 (p, *J* = 6.7 Hz, 2H), 1.52 – 1.42 (m, 2H), 1.35 – 1.25 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 162.9, 131.6, 131.2, 128.2, 122.4, 114.1, 67.3, 63.2, 51.8, 32.8, 29.5, 29.0, 27.2, 26.0, 25.5, 23.5, 18.4, -5.3. GCMS (EI) calculated for $[M]^+$ 420.27, found 420.4. FTIR (neat, cm^{-1}): 3004(w), 2930(m), 2856(m), 1721(s), 1606(s), 1511(s), 1434(s), 1279(2), 1254(s), 1167(s), 1103(s) 836(s).



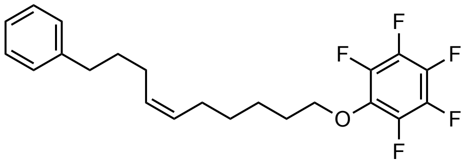
methyl 4-{[(4*Z*)-7-methyldodec-4-en-1-yl]oxy}benzoate (2.51), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (105.6 mg, 64% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 5.56 – 5.30 (m, 2H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 2.32 – 2.15 (m, 2H), 2.05 – 1.95 (m, 1H), 1.91 – 1.81 (m, 2H), 1.52 – 1.35 (m, 2H), 1.34 – 1.10 (m, 8H), 0.93 – 0.76 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 163.1, 131.7, 130.1, 129.0, 122.5, 114.2, 67.5, 51.9, 36.8, 34.7, 33.5, 32.3, 29.1, 27.0, 23.7, 22.8, 19.7, 14.2. GCMS (EI) calculated for $[M]^+$ 332.24, found 332.2. FTIR (neat, cm^{-1}): 2998(m), 2925(m), 2857(m), 1913(w), 1720(s), 1606(s), 1511(s), 1433(m), 1253(s), 1167(s), 1103(s), 970(s), 845(s).



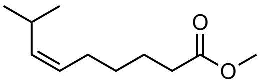
1-fluoro-4-[(4*Z*)-8-phenyloct-4-en-1-yl]benzene (2.52), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (118.6 mg, 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 7.17 – 7.08 (m, 2H), 7.03 – 6.91 (m, 2H), 5.58 – 5.29 (m, 2H), 2.68 – 2.54 (m, 4H), 2.06 (s, 4H), 1.78 – 1.58 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.34 (d, *J* = 243.0 Hz), 142.62, 138.20 (d, *J* = 3.1 Hz), 130.11, 129.83, 129.83 (d, *J* = 7.7 Hz), 128.56, 128.41, 125.82, 115.09 (d, *J* = 21.0 Hz), 35.61, 34.74, 31.65, 31.54, 26.99, 26.85. ^{19}F NMR (470 MHz, $CDCl_3$) δ -121.0. GCMS (EI) calculated for $[M]^+$ 282.18, found 282.2. FTIR (neat, cm^{-1}): 3053(m), 2986(m), 2857(m), 2304(m), 1509(s), 1421(m), 1265(s), 895(s), 746(s).



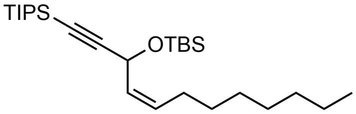
methyl 4-{[(4*Z*)-9,13-dimethyltetradeca-4,12-dien-1-yl]oxy}benzoate (2.53), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (138.7 mg, 75% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.50 – 5.30 (m, 2H), 5.09 (t, *J* = 7.1 Hz, 1H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 2.30 – 2.14 (m, 2H), 2.06 – 1.79 (m, 6H), 1.68 (s, 3H), 1.60 (s, 3H), 1.38 – 1.20 (m, 5H), 1.17 – 1.01 (m, 2H), 0.83 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 163.0, 131.6, 131.5, 131.0, 128.2, 125.1, 122.5, 114.1, 67.3, 51.8, 37.2, 36.7, 32.4, 29.1, 27.6, 27.2, 25.8, 25.6, 23.6, 19.6, 17.7. GCMS (EI) calculated for $[M]^+$ 372.27, found 372.3. FTIR (neat, cm^{-1}): 3006(m), 2925(m), 2854(m), 1720(s), 1606(s), 1510(s), 1434(s), 1279(s), 1253(s), 1167(s), 1104(s), 910(w), 846(s), 770(s).



1,2,3,4,5-pentafluoro-6-{[(6*Z*)-10-phenyldec-6-en-1-yl]oxy}benzene (2.54), compound was prepared according to general procedure B. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 20%) and isolated as a colorless oil (158.8 mg, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 7.24 – 7.15 (m, 3H), 5.57 – 5.27 (m, 2H), 4.16 (t, *J* = 6.5 Hz, 2H), 2.71 – 2.56 (m, 2H), 2.17 – 1.98 (m, 4H), 1.87 – 1.61 (m, 4H), 1.56 – 1.36 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 130.0, 129.9, 128.5, 128.4, 125.8, 75.9, 35.6, 31.6, 29.9, 29.4, 27.2, 27.0, 25.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ -159.9 (d, *J* = 20.5 Hz), -166.5 (t, *J* = 21.3 Hz), -166.9 (t, *J* = 21.7 Hz). GCMS (EI) calculated for $[M]^+$ 398.17, found 398.2. FTIR (neat, cm^{-1}): 3310 (m), 3004(m), 2935(m), 2858(m), 2658(w), 2467(w), 1512(s) 1453(m), 1387(s), 1312(s), 1159(s), 1028(m), 997(m), 746(s), 699(s).



methyl (6*Z*)-8-methylnon-6-enoate (2.57), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (75.1 mg, 82% yield). This compound has been previously synthesized and spectra match the literature values.[36]



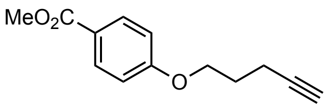
[(4*Z*)-3-[(*tert*-butyldimethylsilyl)oxy]dodec-4-en-1-yn-1-yl]tris(propan-2-yl)silane (2.60), compound was prepared according to general procedure A. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 30%) and isolated as a colorless oil (209.0 mg, 93% yield). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 5.67 – 5.28 (m, 2H), 5.14 (dd, *J* = 7.8, 1.0 Hz, 1H), 2.09 (q, *J* = 7.2 Hz, 2H), 1.40 – 1.18 (m, 10H), 1.06 (m, 21H), 0.99 – 0.79 (m, 12H), 0.14 (d, *J* = 3.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 131.1, 130.9, 108.7, 84.7, 59.8, 32.0, 29.6, 29.4, 29.4, 27.9, 25.9, 22.8, 18.7, 18.4, 14.2, 11.4, -4.3, -4.5. GCMS (EI) calculated for $[M]^+$ 345.27, found 345.3. FTIR (neat, cm^{-1}): 3020(w), 2928(s), 2893(s), 2864(s), 2168(w), 1463(m), 1387(w), 1361(w), 1314(w), 1252(m), 1075(s).

2.6.8 *Gram Scale Reaction*

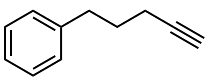
To a flame dried Schlenk flask filled with nitrogen and charged with a stir bar was added LiO*t*-Bu (480.3 mg, 6 mmol, 1.5 equiv). To this was added TriAgCl (243.6 mg, 0.4 mmol, 0.10 equiv), methyl-4-(pent-4-yn-1-yloxy)benzoate (873.0 mg, 4 mmol, 1.0 equiv), and isooctane (40 mL). Then, 9-(3-phenylpropyl)-9-borabicyclo[3.3.1]nonane (2M in toluene, 2.6 mL, 1.3 equiv) and methanol (2M in toluene, 2.2 mL, 1.1 equiv) were added and the reaction mixture was heated to

45 °C in an oil bath for 16 hours. After 16 hours, an aliquot of the crude reaction mixture was analyzed by GC, and the reaction was quenched with the addition of sodium perborate (1.20 g, 12 mmol, 3.0 equiv) in 40 mL THF and 40 mL deionized water. The mixture was stirred at room temperature for 1 hour and then extracted with ether (3 x 100 mL) and dried over $MgSO_4$. The crude mixture was concentrated under reduced pressure and purified by silica gel chromatography.

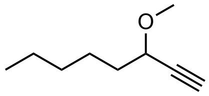
2.6.9 *Alkyne Starting Materials*



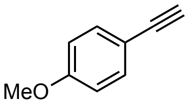
methyl 4-(pent-4-yn-1-yloxy)benzoate (2.1) was prepared according to a known procedure and has been previously characterized.[37]



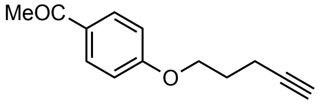
5-phenyl-1-pentyne (2.61) was purchased from GFS Chemical and distilled over calcium hydride under reduced pressure before use.



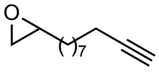
3-methoxyoct-1-yne (2.62) was prepared according to a known procedure and has been previously characterized.[38]



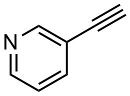
1-ethynyl-4-methoxybenzene (2.63) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



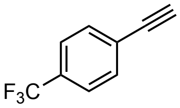
1-[4-(pent-4-yn-1-yloxy)phenyl]ethan-1-one (2.64) was prepared according to a known procedure and has been previously characterized.[39]



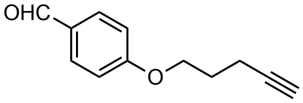
2-(dec-9-yn-1-yl)oxirane (2.65) was prepared according to a known procedure and has been previously characterized.[40]



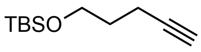
3-ethynylpyridine (2.66) was purchased from Ark Pharm and distilled over calcium hydride under reduced pressure before use.



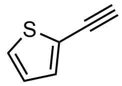
1-ethynyl-4-(trifluoromethyl)benzene (2.67) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



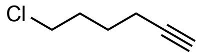
4-(pent-4-yn-1-yloxy)benzaldehyde (2.68) is commercially available from Aurora Building Blocks



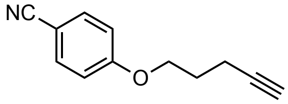
***tert*-butyldimethyl(pent-4-yn-1-yloxy)silane (2.69)** was prepared according to a known procedure and has been previously characterized.[41]



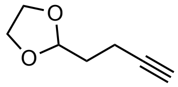
2-ethynylthiophene (2.70) was purchased from Combi-Blocks and distilled over calcium hydride under reduced pressure before use.



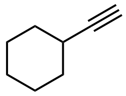
6-chlorohex-1-yne (2.71) was purchased from TCI America and distilled over calcium hydride under reduced pressure before use.



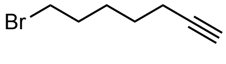
4-(pent-4-yn-1-yloxy)benzonitrile (2.72) was prepared according to a known procedure and has been previously characterized.[39]



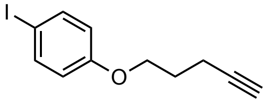
2-(but-3-yn-1-yl)-1,3-dioxolane (2.73) was prepared according to a known procedure and has been previously characterized.[42]



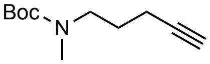
ethynylcyclohexane (2.74) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



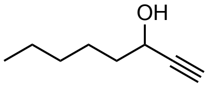
7-bromohept-1-yne (2.75) was prepared according to a known procedure and has been previously characterized.[39]



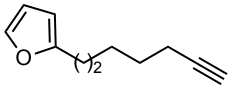
1-iodo-4-(pent-4-yn-1-yloxy)benzene (2.76) was prepared according to a known procedure and has been previously characterized.[39]



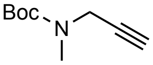
***tert*-butyl N-methyl-N-(pent-4-yn-1-yl)carbamate (2.77)** was prepared according to a known procedure and has been previously characterized.[43]



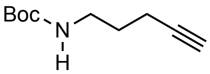
oct-1-yn-3-ol (2.78) was purchased from TCI America and distilled over calcium hydride under reduced pressure before use.



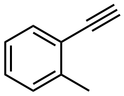
2-(hept-6-yn-1-yl)furan (2.79) was prepared according to a known procedure and has been previously characterized.[44]



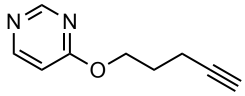
***tert*-butyl N-methyl-N-(prop-2-yn-1-yl)carbamate (2.80)** was prepared according to a known procedure and has been previously characterized.[45]



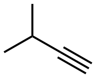
***tert*-butyl N-(pent-4-yn-1-yl)carbamate (2.81)** was prepared according to a known procedure and has been previously characterized.[46]



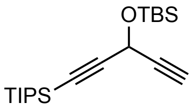
1-ethynyl-2-methylbenzene (2.82) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



4-(pent-4-yn-1-yloxy)pyrimidine (2.83). A reaction flask charged with a stir bar was flame-dried under vacuum and allowed to cool under nitrogen. The flask was then charged with triphenylphosphine (2.2 g, 24.0 mmol, 1.2 equiv), phenol (7.7 mmol, 1.1 equiv), THF (14.0 mL, 0.5 M) and 4-pentyn-1-ol (654.0 µL, 7.0 mmol, 1.0 equiv). The reaction mixture was cooled to 0 °C with an ice bath. To the cooled reaction mixture was added DIAD (1.6 mL, 8.4 mmol, 1.2 equiv) dropwise. The reaction mixture was allowed to warm to 23 °C and stirred overnight. THF was removed under reduced pressure and the mixture was suspended in hexanes and stirred vigorously for 30 min. The solid triphenylphosphine oxide was removed by passing the mixture through a plug of celite. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography. Compound was isolated as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.41 (d, *J* = 5.9 Hz, 1H), 6.72 (dd, *J* = 5.9, 1.0 Hz, 1H), 4.46 (t, *J* = 6.2 Hz, 2H), 2.36 (td, *J* = 7.0, 2.6 Hz, 2H), 2.12 – 1.88 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 158.4, 156.8, 108.8, 83.1, 69.2, 65.2, 27.8, 15.3. GCMS (EI) calculated for $[M]^+$ 162.08, found 162.20.

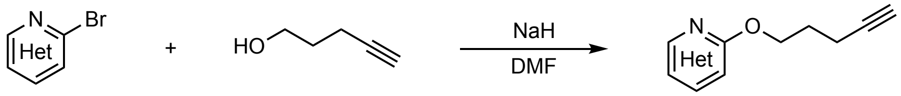


3-methylbut-1-yne (2.55) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.

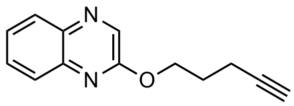


***tert*-butyldimethyl({1-[tris(propan-2-yl)silyl]penta-1,4-diyn-3-yl}oxy)silane (2.58).** The deprotected alcohol of **2.58** has been previously prepared.[47] TBS protection of the alcohol was performed according to a known literature procedure.[41] The compound was isolated as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.22 (d, J = 2.3 Hz, 1H), 2.47 (d, J = 2.3 Hz, 1H), 1.08 (s, 21H), 0.91 (s, 9H), 0.19 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 104.7, 85.5, 82.0, 71.7, 53.4, 25.8, 18.7, 18.4, 11.4, -4.4. GCMS (EI) calculated for $[M]^+$ 350.25, found 350.3. FTIR (neat, cm^{-1}): 3313(s), 2944(m), 2865(m), 2716(w), 2176(w), 1623(w), 1464(s), 1287(s), 1252(s), 1087(m), 996(m), 882(s), 836(s), 780(s) 633(m).

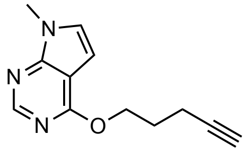
General Procedure for the Preparation of Heterocyclic Alkynes:



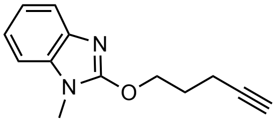
A reaction flask charged with stir bar was flame-dried under vacuum and allowed to cool under nitrogen. The flask was then charged with sodium hydride (1.5 equiv) and DMF (0.1 M). The reaction mixture was cooled to 0 °C with an ice bath. To the cooled reaction mixture was added 4-pentyn-1-ol (1.5 equiv) and the reaction mixture was allowed to stir for 30 minutes. After the indicated time, heterocyclic bromide (1.0 equiv) was added and the mixture was stirred for 2 hours. After 2 hours, the reaction mixture was quenched with water and extracted with diethyl ether. The extract was concentrated under reduced pressure and the crude product was purified by silica gel chromatography. The following alkynes were prepared using this procedure.



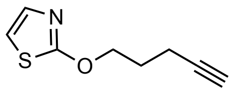
2-(pent-4-yn-1-yloxy)quinoxaline (2.84), compound was isolated as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.73 – 7.62 (m, 1H), 7.61 – 7.50 (m, 1H), 4.59 (t, *J* = 6.2 Hz, 2H), 2.44 (td, *J* = 7.0, 2.6 Hz, 2H), 2.09 (p, *J* = 6.6 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 140.6, 139.8, 139.2, 130.2, 129.2, 127.4, 126.7, 83.4, 69.1, 65.1, 27.9, 15.5. GCMS (EI) calculated for $[M]^+$ 212.09, found 212.1. FTIR (neat, cm^{-1}): 3245(s), 3058(w), 2960(m), 2852(m), 1849(w), 1573(s), 1466(s), 1416(s), 1314(s), 1223(s), 1141(s), 1029(s), 998(s), 959(s).



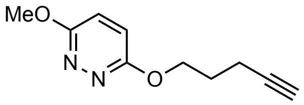
7-methyl-4-(pent-4-yn-1-yloxy)-7H-pyrrolo[2,3-d]pyrimidine (2.85), compound was isolated as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.00 (d, *J* = 3.4 Hz, 1H), 6.51 (d, *J* = 3.4 Hz, 1H), 4.62 (t, *J* = 6.2 Hz, 2H), 3.85 (s, 3H), 2.43 (td, *J* = 7.1, 2.6 Hz, 2H), 2.15 – 2.04 (m, 2H), 1.98 (t, *J* = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 152.3, 151.0, 126.8, 105.6, 98.3, 83.5, 69.0, 64.8, 31.4, 28.2, 15.5. GCMS (EI) calculated for $[M]^+$ 215.11, found 215.1. FTIR (neat, cm^{-1}): 3295(m), 3104(w), 2951(m), 1597(s), 1560(s), 1445(s), 1370(m), 1317(m), 1247(s), 1210(s), 1056(s), 884(m).



1-methyl-2-(pent-4-yn-1-yloxy)-1H-1,3-benzodiazole (2.86), compound was isolated as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 – 7.50 (m, 1H), 7.20 – 7.11 (m, 3H), 4.65 (t, *J* = 6.2 Hz, 2H), 3.56 (s, 3H), 2.42 (td, *J* = 7.0, 2.6 Hz, 2H), 2.10 (p, *J* = 6.6 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4, 140.1, 134.3, 121.5, 120.7, 117.6, 107.9, 83.0, 69.2, 68.7, 28.2, 27.9, 15.2. GCMS (EI) calculated for $[M]^+$ 214.11, found 214.1. FTIR (neat, cm^{-1}): 3190(m), 2955(m), 2931(m), 1622(s), 1540(s), 1456(s), 1375(s), 1288(s), 1211(s), 1042(s), 975(s), 892(w), 741(s).

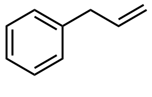


2-(pent-4-yn-1-yloxy)-1,3-thiazole (2.87), compound was isolated as colorless liquid. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 3.8 Hz, 1H), 6.67 (d, *J* = 3.8 Hz, 1H), 4.51 (t, *J* = 6.1 Hz, 2H), 2.44 – 2.30 (m, 2H), 2.12 – 1.93 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 136.7, 111.0, 82.7, 69.7, 69.2, 27.6, 14.9. GCMS (EI) calculated for $[M]^+$ 167.04, found 167.10.

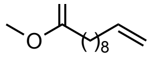


3-methoxy-6-(pent-4-yn-1-yloxy)pyridazine (2.88), compound was isolated as a white solid. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.92 – 6.90 (m, 2H), 4.52 (t, *J* = 6.2 Hz, 2H), 4.04 (s, 3H), 2.38 (td, *J* = 7.0, 2.6 Hz, 2H), 2.16 – 1.91 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 161.7, 121.4, 121.3, 83.3, 68.9, 65.6, 54.5, 27.8, 15.2. GCMS (EI) calculated for $[M]^+$192.09, found 192.10. FTIR (neat, cm-1) 3328(s), 2852(s), 2284(s), 1495(s), 1444(s), 1423(s), 1384(s), 1337(m), 1268(s), 1098(m), 1038(s), 1013(s), 949(s), 913(s), 949(s), 913(s), 839(s), 796(m). 729(s).

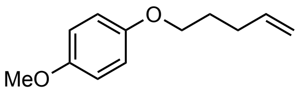
2.6.10 *Alkene Starting Materials for Alkylboranes*



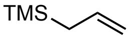
(prop-2-en-1-yl)benzene (2.89) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



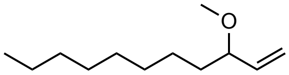
methyl undec-10-enoate (2.90) was prepared according to a known procedure and has been previously characterized.[48]



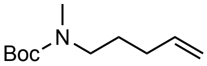
1-methoxy-4-(pent-4-en-1-yloxy)benzene (2.91) was prepared according to a known procedure and has been previously characterized.[49]



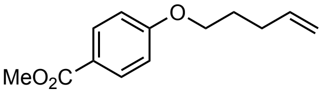
trimethyl(prop-2-en-1-yl)silane (2.92) was purchased from Oakwood Chemicals and distilled over calcium hydride under reduced pressure before use.



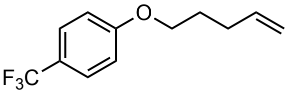
3-methoxyundec-1-ene (2.93) was prepared according to a known procedure and has been previously characterized.[50]



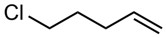
***tert*-butyl N-methyl-N-(pent-4-en-1-yl)carbamate (2.94)** is commercially available from Enamine Building Blocks.



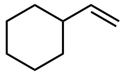
methyl 4-(pent-4-en-1-yloxy)benzoate (2.95) was prepared according to a known procedure and has been previously characterized.[51]



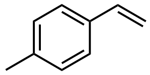
1-(pent-4-en-1-yloxy)-4-(trifluoromethyl)benzene (2.96) was prepared according to a known procedure and has been previously characterized.[52]



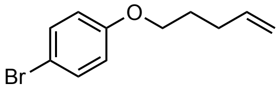
5-chloropent-1-ene (2.97) was purchased from Arctom Chemicals and distilled over calcium hydride under reduced pressure before use.



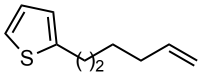
ethenylcyclohexane (2.98) was purchased from Alfa Aesar and distilled over calcium hydride under reduced pressure before use.



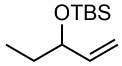
1-ethenyl-4-methylbenzene (2.99) was purchased from TCI America and distilled over calcium hydride under reduced pressure before use.



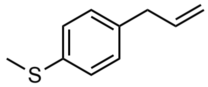
1-bromo-4-(pent-4-en-1-yloxy)benzene (2.100) was prepared according to a known procedure and has been previously characterized.[53]



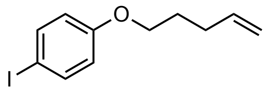
2-(hex-5-en-1-yl)thiophene (2.101) was prepared according to a known procedure and has been previously characterized.[54]



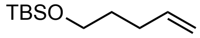
***tert*-butyldimethyl(pent-1-en-3-yloxy)silane (2.102)** was prepared according to a known procedure and has been previously characterized.[55]



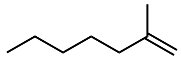
1-(methylsulfanyl)-4-(prop-2-en-1-yl)benzene (2.103) was prepared according to a known procedure and has been previously characterized.[56]



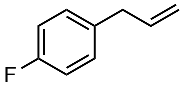
1-iodo-4-(pent-4-en-1-yloxy)benzene (2.104) was prepared according to a known procedure and has been previously characterized.[49]



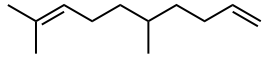
***tert*-butyldimethyl(pent-4-en-1-yloxy)silane (2.105)** was prepared according to a known procedure and has been previously characterized.[57]



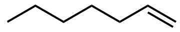
2-methylhept-1-ene (2.106) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.



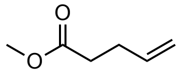
1-fluoro-4-(prop-2-en-1-yl)benzene (2.107) was prepared according to a known procedure and has been previously characterized.[58]



5,9-dimethyldeca-1,8-diene (2.108) was prepared according to a known procedure and has been previously characterized.[59]

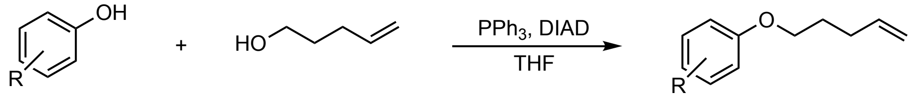


hept-1-ene (2.56) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.

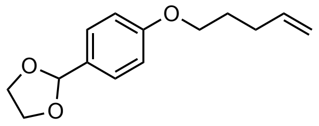


methyl pent-4-enoate (2.59) was prepared according to a known procedure and has been previously characterized.[60]

General Procedure for the Preparation of Different Alkenes:

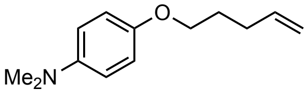


A reaction flask charged with stir bar was flame-dried under vacuum and allowed to cool under nitrogen. The flask was then charged with triphenylphosphine (2.2 g, 24.0 mmol, 1.2 equiv), phenol (7.7 mmol, 1.1 equiv), THF (14.0 mL, 0.5 M) and 4-penten-1-ol (654.0 µL, 7.0 mmol, 1.0 equiv). The reaction mixture was cooled to 0 °C with an ice bath. To the cooled reaction mixture was added DIAD (1.6 mL, 8.4 mmol, 1.2 equiv) dropwise. The reaction mixture was allowed to warm to 23 °C and stirred overnight. THF was removed under reduced pressure and the mixture was suspended in hexanes and stirred vigorously for 30 min. The solid triphenylphosphine oxide was removed by passing the mixture through a plug of celite. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography. The following alkenes were prepared using this procedure.

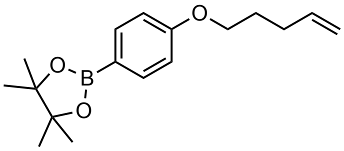


2-[4-(pent-4-en-1-yloxy)phenyl]-1,3-dioxolane (2.109), compound was isolated as a colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.41 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 5.86 (ddt, J = 16.9, 10.1, 6.6 Hz, 1H), 5.76 (s, 1H), 5.13 – 4.96 (m, 2H), 4.26 – 3.82 (m, 6H), 2.35 – 2.11 (m, 2H), 2.00 – 1.76 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 159.9, 137.8, 130.1, 127.9, 115.2, 114.5, 103.8, 67.3, 65.3, 30.1, 28.5. GCMS (EI) calculated for $[M]^+$ 234.13, found 234.1. FTIR (neat, cm$^-$

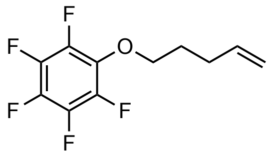
^{1}): 3075(s), 2944(m), 2881(m), 2759(m), 1640(s), 1615(s), 1515(s), 1435(s), 1393(s), 1304(m), 1246(m), 1078(m), 1011(m), 942(m), 829(s).



N,N-dimethyl-4-(pent-4-en-1-yloxy)aniline (2.110), compound was isolated as a light yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (d, *J* = 9.1 Hz, 2H), 6.76 (d, *J* = 9.1 Hz, 2H), 5.88 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.16 – 4.94 (m, 2H), 3.94 (t, *J* = 6.5 Hz, 2H), 2.88 (s, *J* = 10.3 Hz, 6H), 2.31 – 2.14 (m, 2H), 1.95 – 1.75 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6, 145.9, 138.1, 115.7, 115.1, 115.0, 68.1, 41.9, 30.3, 28.8. GCMS (EI) calculated for $[M]^+$ 205.15, found 205.2. FTIR (neat, cm^{-1}): 3074(m), 2939(m), 2791(m), 1635(m), 1516(s), 1456(s), 1339(w), 1243(s), 1057(m), 947(s), 816(s), 757(s).



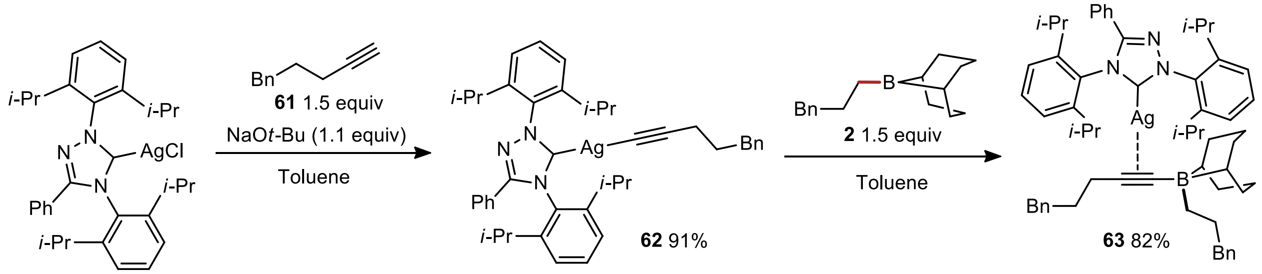
4,4,5,5-tetramethyl-2-[4-(pent-4-en-1-yloxy)phenyl]-1,3,2-dioxaborolane (2.111), compound was isolated as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.86 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.16 – 4.92 (m, 2H), 4.00 (t, *J* = 6.4 Hz, 2H), 2.34 – 2.16 (m, 2H), 1.97 – 1.79 (m, 2H), 1.35 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 137.9, 136.6, 115.3, 114.0, 83.6, 77.4, 67.1, 30.2, 28.5, 25.0. GCMS (EI) calculated for $[M]^+$ 288.19, found 288.1. FTIR (neat, cm^{-1}): 3076(m), 2977(m), 2944(m), 1605(s), 1558(s), 1516(s), 1397(s), 1361(s), 1246(s), 1143(s), 1090(s), 962(m), 860(s), 757(s).



1,2,3,4,5-pentafluoro-6-(pent-4-en-1-yloxy)benzene (2.112), compound was isolated as a colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.82 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.20 – 4.90 (m, 2H), 4.17 (t, *J* = 6.4 Hz, 2H), 2.37 – 2.15 (m, 2H), 1.97 – 1.77 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 137.4, 115.7, 75.1, 29.7, 29.2. GCMS (EI) calculated for [M]$^+$ 252.06, found 252.1. FTIR (neat, cm^{-1}): 3082(m), 2947(m), 2663(w), 1829(w), 1643(m), 1538(m), 1511(s), 1456(m), 1313(m), 1161(m), 1026(m), 995(m), 917(m).

2.6.11 *Mechanistic Studies*

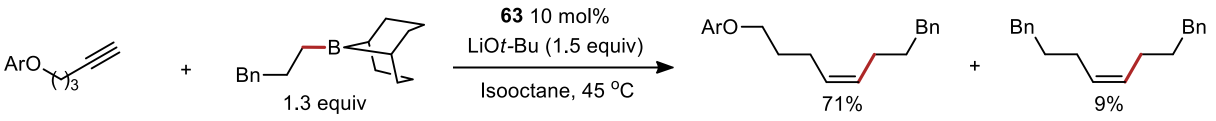
Synthesis of Silver Borate Complex 2.63



Synthesis of **2.62,** In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and TriAgCl (91.3 mg, 0.150 mmol, 1.0 equiv). To this was added NaO*t*-Bu (15.9 mg 0.165 mmol, 1.1 equiv), 5-phenyl-1-pentyne (32.4 mg 0.225 mmol, 1.5 equiv) and toluene (3 mL). The reaction mixture was stirred at 25 °C for 2 hours. After, 2 hours, the reaction mixture was filtered through a plug of celite and concentrated. The silver acetylide was then precipitated out with pentane, collected by vacuum filtration and washed several times with pentane. The product was isolated as a white powder (98.2 mg, 91% yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.62 – 7.47 (m, 2H), 7.44 – 7.27 (m, 9H), 7.24 – 7.17 (m, 2H), 7.17 – 7.06 (m, 3H), 2.70 – 2.56 (m, 4H), 2.56 – 2.41 (m, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 1.81 – 1.68 (m, 2H), 1.43 – 1.27 (m, 12H), 1.24 (d, *J* = 6.9 Hz, 6H), 0.97 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 153.3, 145.7, 145.3, 142.7, 135.2, 131.9, 131.5, 131.2, 128.9, 128.6, 128.1, 128.1, 125.5, 125.1, 124.3, 35.2, 32.0, 29.1, 29.0, 25.1, 24.5, 23.9, 22.8, 20.3

Synthesis of **2.63**, In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and Silver acetylide **2.62** (39.3 mg, 0.055 mmol, 1.0 equiv). To this was added alkylborane **2.2** (19.8 mg 0.083 mmol, 1.1 equiv) and toluene (3 mL). The reaction mixture was stirred at 25 °C for 1 hours. After 1 hour, the solvent was removed under vacuum and the borate complex was then precipitated out with pentane. It was then collected by vacuum filtration and washed several times with pentane. The complex was isolated as an off-white powder (43.6 mg, 82% yield). Crystallographic information is below. ^{1}H NMR (300 MHz, C_6D_6) δ 7.52 – 7.43 (m, 2H), 7.42 – 7.32 (m, 2H), 7.31 – 7.17 (m, 5H), 7.15 – 7.04 (m, 7H), 7.03 – 6.94 (m, 2H), 6.87 – 6.69 (m, 3H), 2.97 – 2.83 (m, 2H), 2.83 – 2.69 (m, 2H), 2.65 – 2.20 (m, 10H), 2.04 (s, 8H), 1.90 – 1.73 (m, 2H), 1.42 – 1.24 (m, 14H), 1.15 (d, *J* = 6.8 Hz, 6H), 0.87 – 0.63 (m, 10H).

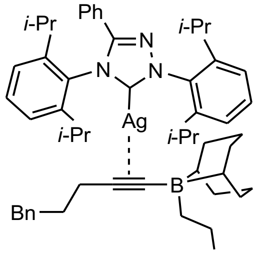
Catalytic Competency of the Borate Complex



Ar = methyl-4-benzoate

In a nitrogen filled glovebox, a dram vial was charged with a stir bar and LiO*t*-Bu (6.0 mg, 0.075 mmol, 1.5 equiv). To this was added Borate complex **2.63** (4.9 mg 0.005 mmol, 0.005 equiv), alkyne **1** (10.9 mg 0.05 mmol, 1.0 equiv), alkylborane **2.2** (15.6 mg, 0.065 mmol, 1.3 equiv), methanol (1.8 mg, 0.055 mmol, 1.10 equiv), isooctane (0.5 mL) and internal standard, TMB (4.2 mg, 0.05 mmol, 0.5 equiv). The reaction mixture was heated at 45°C and an aliquot of the crude reaction mixture was analyzed by GC after 16h.

Crystallization of 63 for X-ray Crystallography



63

In a nitrogen filled glove box, a dram vial was charged with borate complex **2.63** (14.6 or 13.4 mg, 0.015 mmol, 1 equiv). The solid was then crystallized from benzene and pentane.

Crystallography Data of 2.63

A colorless prism, measuring 0.09 x 0.07 x 0.04 mm^3 was mounted on a loop with oil. Data was collected at -173°C on a Bruker APEX II single crystal X-ray diffractometer, Mo-radiation. Crystal-to-detector distance was 40 mm and exposure time was 60 seconds per frame for all sets. The scan width was 0.5°. Data collection was 99.7% complete to 25° in ϑ. A total of 25311 merged reflections were collected covering the indices, -23<=h<=23, -17<=k<=17, -29<=l<=29. 12944 reflections were symmetry independent and the R_{int} = 0.1029 reflects the small sample size. Indexing and unit cell refinement indicated a primitive monoclinic lattice. The space group was found to be $P\ 2_1/n$ (No. 14).

The data was integrated and scaled using SAINT,[61] SADABS[62] within the APEX2[63] software package by Bruker.

Solution by direct methods (SHELXT[64] or SIR97[65,66]) produced a complete heavy atom phasing model consistent with the proposed structure. The structure was completed by difference Fourier synthesis with SHELXL97.[67-69] Scattering factors are from Waasmair and Kirfel.[70] Hydrogen atoms were placed in geometrically idealised positions and constrained to ride on their parent atoms with C---H distances in the range 0.95-1.00 Angstrom. Isotropic thermal parameters U_{eq} were fixed such that they were $1.2U_{eq}$ of their parent atom Ueq for CH's and $1.5U_{eq}$ of their parent atom U_{eq} in case of methyl groups. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares.

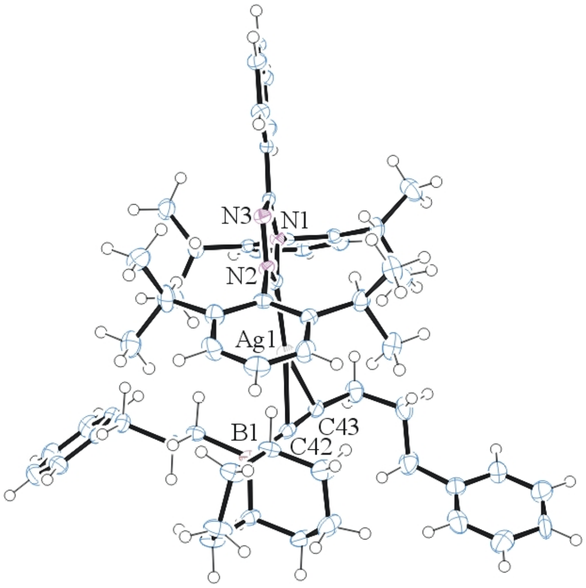


Figure 2.2. ORTEP[71] of the structure with thermal ellipsoids at the 50% probability level. Disorder omitted for clarity. One phenyl and one *i*-Pr unit are disordered.

Crystallographic data for the structures provided.

Empirical formula	C60 H75 Ag B N3
Formula weight	956.91
Temperature	99(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	$P\ 2_1/n$	
Unit cell dimensions	a = 17.5111(18) Å	α= 90°.
	b = 13.3239(14) Å	β= 94.480(4)°.
	c = 22.382(2) Å	γ = 90°.
Volume	5206.2(9) Å^3	
Z	4	
Density (calculated)	1.221 Mg/m^3	
Absorption coefficient	0.427 mm^{-1}	
F(000)	2032	
Crystal size	0.090 x 0.070 x 0.040 mm^3	
Theta range for data collection	1.424 to 28.373°.	
Index ranges	-23<=h<=23, -17<=k<=17, -29<=l<=29	
Reflections collected	25311	
Independent reflections	12944 [R(int) = 0.1029]	
Completeness to theta = 25.000°	99.7 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12944 / 33 / 596	
Goodness-of-fit on F^2	0.946	
Final R indices [I>2sigma(I)]	R1 = 0.0480, wR2 = 0.0793	
R indices (all data)	R1 = 0.1377, wR2 = 0.1037	
Largest diff. peak and hole	0.544 and -0.661 e.Å^{-3}	

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Chapter 3. SYNTHESIS OF ISOMERICALLY PURE *Z*-ALKENES FROM TERMINAL ALKYNES AND INTERNAL ALKENES

3.1 INTRODUCTION

Alkenes are an important class of organic molecules. They are common among pharmaceuticals and biologically active compounds and often serve as important synthetic intermediates in organic synthesis. The key structural feature of alkenes is the hindered rotation[1] about the π bond, which leads the two distinct E and Z stereoisomers.[2] The synthesis of thermodynamically less stable Z-alkenes presents a complex set of challenges that has long inspired the development of new synthetic methods.

The main challenge in the synthesis of complex Z-alkenes is the formation of a double bond and control of its geometry. Using a convergent approach that increases the efficiency of the synthesis is another important goal. [3-4] To meet this challenge, alkene synthesis must be accompanied by the formation of a new C-C σ bond that allows coupling of simple fragments into a more complex product. Ideally, a *single synthetic operation* would allow us to accomplish both goals of alkene synthesis: form a Z double bond and make a new C-C σ bond. Furthermore, this process should be stereospecific, with only the Z-isomer of the alkene being formed. Stereospecificity is particularly important considering the difficulties often encountered in the separation of alkene isomers.[5] Unfortunately, developing reactions that meet these requirements has proven to be quite challenging.

The most common methods for the synthesis of Z-alkenes, semireduction of alkynes[6-7] and cross coupling,[8] are stereospecific. However, these methods focus on only one aspect of the alkene synthesis. In cross-coupling reactions a new C-C σ bond is formed, but the double bond is formed in a separate step during the synthesis of coupling partners. Alkyne semireduction, on the other hand, forms a double bond but creates no new C-C bonds.

Alkene cross-metathesis[9-11] is unique among catalytic reactions in its ability to form a double bond through the coupling of two fragments. Remarkable progress in the design of new metathesis catalysts has also allowed control over the stereochemistry of the alkene. Nevertheless, this process is not stereospecific, and as a result, a mixture of Z and E isomers is often formed. Another challenge inherent to cross-metathesis reactions that stems from the fundamental similarity of the starting materials, is preventing the homo-metathesis of starting alkenes. This problem can be circumvented by selecting pairs of alkenes with differing reactivities and/or the use of a large excess of one of the coupling partners.

Hydroalkylation of alkynes has become a powerful new approach to alkene synthesis as it forms a new C-C σ bond while exhibiting control over the geometry of the new double bond (Figure 3.1a). This approach has proven to be useful in the synthesis of various classes of alkenes, including E-alkenes[12-14] and 1,1-disubstituted alkenes.[15-17]

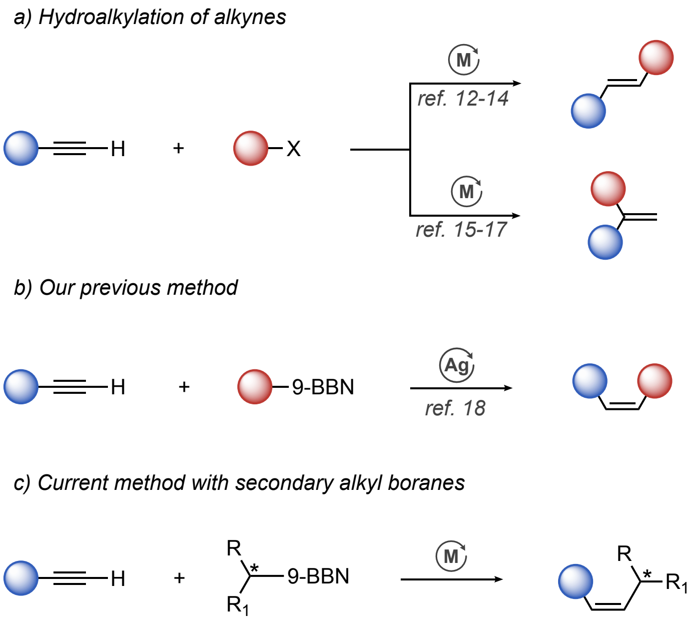


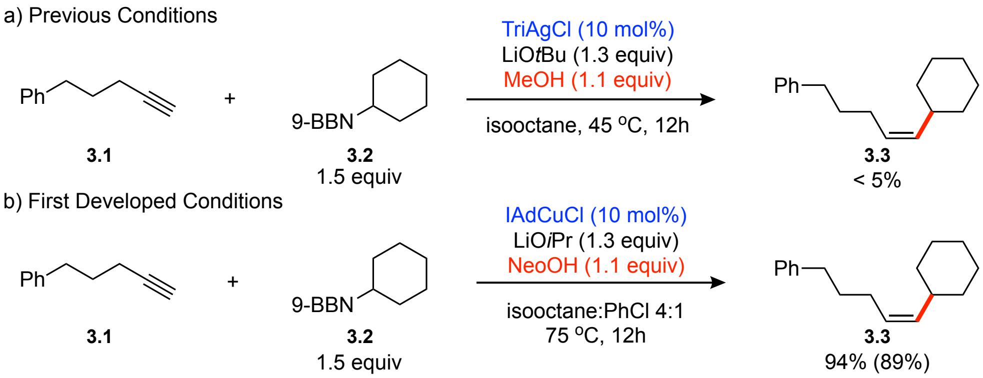
Figure 3.1 Methods for Hydroarylation of Alkynes

However, there are very few methods that effectively target the synthesis of Z-alkenes through hydroalkylation. Our group recently reported the silver catalyzed synthesis of *Z*-alkenes from terminal alkynes and alkyl boranes.[18] This method uses an entirely different mechanistic approach to the hydroalkylation of alkynes and exhibits remarkable stereoselectivity over the double bond (Figure 3.1). This reaction proved to be applicable to various terminal alkynes and primary alkylboranes. Nonetheless, the previously reported method was limited in the ability to carry out reductive cross coupling with secondary alkyl boranes. Enantiomerically enriched boranes would be viable substrates, allowing for the synthesis of highly complex *Z*-alkenes containing an α-stereocenter (Figure 3.1). This new method was inspired by the limitation of our prior work.

Herein, we report the current state of our work on the silver-catalyzed reductive cross coupling of terminal alkynes with secondary alkylboranes to give diastereopure *Z*-alkenes.

3.2 REACTION DEVELOPMENT

Preliminary investigation of the *Z*-selective reductive cross coupling of terminal alkynes with secondary alkyl boranes began with 5-phenyl-1-pentyne (**3.1**) and 9-cyclohexyl-9-borabicyclo[3.3.1]nonane (**3.2**) and the reaction conditions for our previous coupling with primary alkyl boranes, giving us trace product (**3.3**, Scheme 3.1a). We then tested a variety of silver and copper catalysts as well as alkoxide bases and found that a combination of IAdCuCl with LiO*i*Pr provided the desired product in the highest yield (Scheme 3.1b). Further explortation of reaction conditions lead us to use neopentyl alcohol instead of methanol as the best proton source.

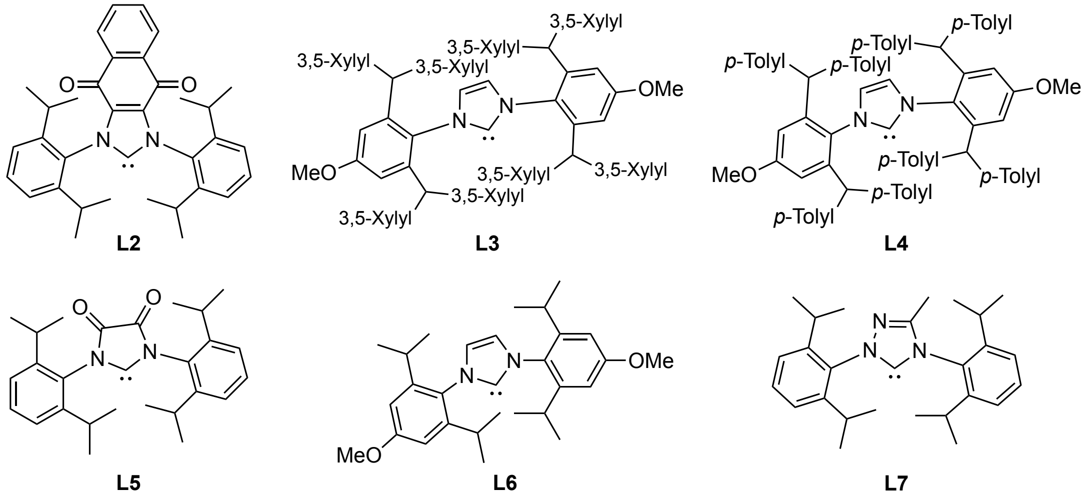


Scheme 3.1 First Iteration of Reaction Development

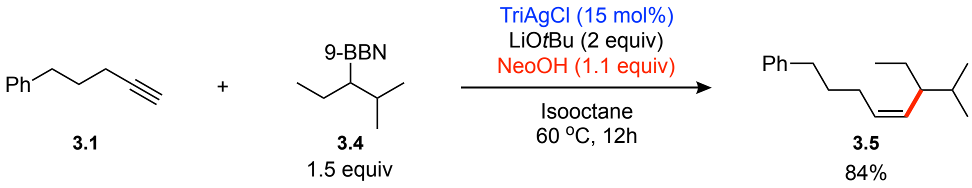
Unfortunately, upon further substrate probing, we found that more hindered alkyl boranes were not viable substrates using these conditions. We thus continued to probe the reaction conditions, this time using alkyl borane **3.4** and alkyne **3.1**. As shown in Table 3.1, a variety of NHC ligands were synthesized and used in the reaction, with the hopes of finding a new, more robust catalyst. NHCs with more steric bulk (**L3** and **L4)**[19] gave trace amount of the desired product. Silver catalysts made with **L6**[20] and **L7**[21] provided moderate yields, none greater than that of the original

TriAgCl. We hypothesized that an electron poor NHC may exhibit enhanced reactivity in our reaction due to the affinity for alkynyl π-electrons, however both **L2**[22] and **L5**[23] failed to improve product yield.

Table 3.1 Various NHC Ligands Synthesized and Tested in the Hydroalkylation Reaction.

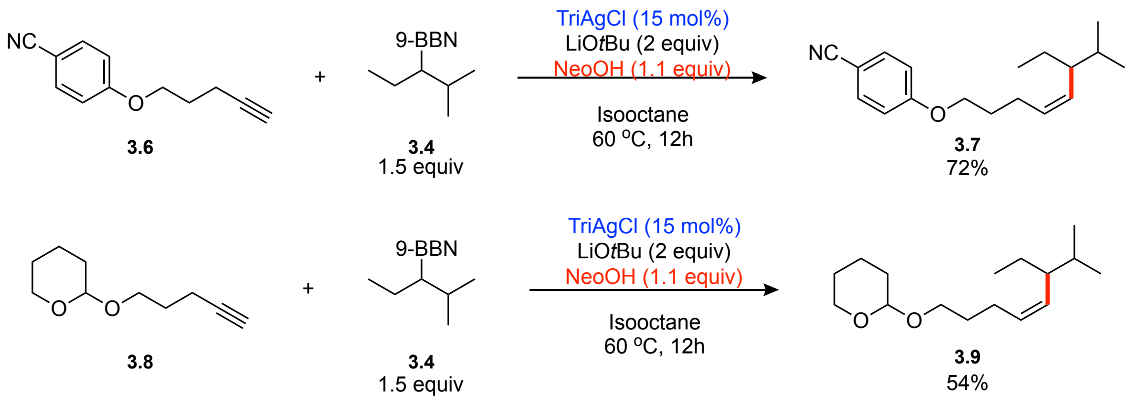


In the end, we found that a combination of our original catalyst, TriAgCl with LiO*t*Bu as the base and neopentyl alcohol as the proton source gave the desired product (**3.5**) in 84% yield (Scheme 3.2).



Scheme 3.2 Reaction Conditions for More Sterically Hindered Alkyl Boranes

Further screening of alkyl boranes proved that these conditions should be broadly applicable to boranes of more or less steric encumbrance. When tested with an enantiomerically enriched alkyl borane, the stereochemistry from the starting borane was retained in the product. Similarly, on first assessment, it appeared that a wide range of electronically differentiated terminal alkynes would be provided in high yields and excellent selectivity using these conditions. Unfortunately, we again ran into insufficient yields with many of the terminal alkynes tested (Scheme 3.3). The reductive cross coupling with both electron-rich and electron-poor terminal alkynes resulted in highly selective, yet low yielding reactions.



Scheme 3.3 Deteriorated Yields with Electronically Differentiated Alkynes

3.3 CURRENT STATE OF RESEARCH

The Lalic lab is currently still exploring the optimal reaction conditions for this silver catalyzed *Z*-selective coupling of terminal alkynes with secondary alkylboranes. Further reaction development is now being done using alkynes **3.6** and **3.9**, which contain electron withdrawing properties with alkyl borane **3.4**. Using these substrates that incorporate both electronic and steric effects should allow us to find conditions that are highly robust in scope.

3.4 CONCLUSION

Based on our previous work on the synthesis of isomerically pure (*Z*)-alkenes from terminal alkynes and alkenes, we set out to achieve a similarly diastereospecific reductive coupling of terminal alkynes with secondary alkylboranes. The steric hinderance of secondary alkyl boranes proved to be a challenging factor in the previous method. During reaction development we found two different sets of conditions that at first seemed promising, but were discovered to be less broadly applicable than we had hoped. At this point in time, two different sets of model substrates are being screened to find a set of reaction conditions that will give high yield and selectivity of various electronic and steric products.

3.5 EXPERIMENTAL

3.5.1 *General Information*

All reactions were performed under a nitrogen atmosphere with flame-dried or oven-dried (120 °C) glassware, using standard Schlenk techniques, or in a glovebox (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 µm, 230-400 mesh. 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 (CDCl3 (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 (CDCl3(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. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), coupling constants in Hertz (Hz), intergration. Mass spectra were collected on a JEOL HX-110 mass spectrometer. Gas Chromatography (GC) analysis was performed on a Shimadzu GC-2010 instrument with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 µm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5

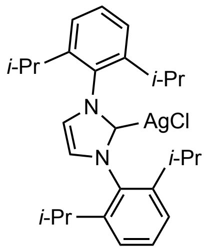
min @ 250 °C. Materials: THF, CH2Cl2, ether, benzene, and toluene were degassed and dried by passing through columns of neutral alumina. Anhydrous methanol was purchased from Millipore Sigmaand was degassed and stored over 4Å molecular sieves. Isooctane was purchased from Fisher Scientific and was degassed and stored over 4Åmolecular sieves. 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, ArkPharm, Combi-Blocks, Oakwood Chemicals, Strem Chemicals and Alfa Aesar. 9-BBN Dimer was purchased from Millipore Sigma and recrystallized from THF.

3.5.2 *Reaction Development*

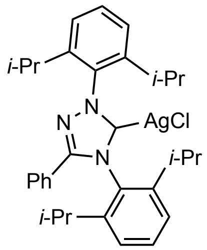
All reactions were performed on a 0.05 mmol scale with the stoichiometry shown in Table S1. In a nitrogen-filled glovebox a dram vial was charged with a stir bar, LiOt-Bu (1.5 equiv), catalyst, methyl 4-(pent-4-yn-1-yloxy)benzoate, 1,3,5-trimethoxy benzene (TMB, internal standard), 9-(2-methylpentan-3-yl)-9-borabicyclo[3.3.1]nonane (1.5 equiv), methanol (1.1 equiv) and solvent. The reaction mixture was stirred at 45 °C and monitored by Gas Chromatography for reaction completion. An aliquot was taken every 24 hours.

3.5.3 *Synthesis of TriAgCl and IPrAgCl*

The silver catalysts were synthesized using an adapted procedure from Sadighi et. al. that was used for the synthesis of SIPrAgCl.[24]



IPrAgCl, complex has been previously characterized.[25]



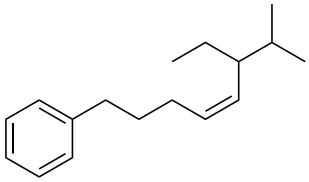
TriAgCl, complex has been previously characterized.[18]

3.5.4 *Hydroalkylation of Terminal Alkynes*

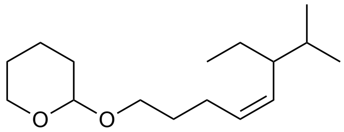
In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar and LiO*t*-Bu (80.0 mg, 1.0 mmol, 2.0 equiv). To this was added TriAgCl (45.7 mg, 0.075 mmol, 0.15 equiv), alkyne (0.50 mmol, 1.0 equiv), alkylborane (1.5 equiv), neopentyl alcohol (48.5 mg, 0.55 mmol, 1.10 equiv), and isooctane (5 mL). The reaction mixture was heated to 60 °C and stirred for 16 hours. After 16 hours, an aliquot of the crude reaction mixture was analyzed by GC, and the reaction was quenched with the addition of sodium perborate (150 mg, 0.75 mmol, 1.5 equiv) in 5 mL THF and 5 mL deionized water. The mixture was stirred at room temperature for 1 hour, and then extracted with ether (3 x 10 mL) and dried over $MgSO_4$. The crude mixture was concentrated under reduced pressure and purified by silica gel chromatography.

3.5.5 *Characterization of Z-Selective Hydroalkylation Products: Alkynes*

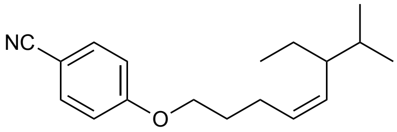
9-(2-methylpentan-3-yl)-9-borabicyclo[3.3.1]nonane was used neat and was synthesized according to literature procedure.[26]



[(4Z)-6-ethyl-7-methyloct-4-en-1-yl]benzene (3.5) compound was prepared according to the general procedure. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 10%) and isolated as a colorless oil (97.5 mg, 84% yield).

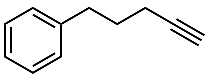


2-{[(4Z)-6-ethyl-7-methyloct-4-en-1-yl]oxy}oxane (3.7) compound was prepared according to the general procedure. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (69.1 mg, 54% yield).

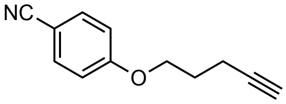


4-{[(4Z)-6-ethyl-7-methyloct-4-en-1-yl]oxy}benzonitrile (3.9) compound was prepared according to the general procedure. The compound was purified by silica gel chromatography with EtOAc/Hex (0 → 40%) and isolated as a colorless oil (98.4 mg, 72% yield).

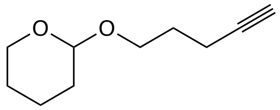
3.5.6 *Alkyne Starting Materials*



5-phenyl-1-pentyne (3.3) was purchased from GFS Chemical and distilled over calcium hydride under reduced pressure before use.

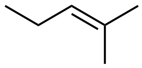


4-(pent-4-yn-1-yloxy)benzonitrile (3.6) was prepared according to a known procedure and has been previously characterized.[27]

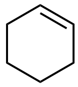


2-(pent-4-yn-1-yloxy)tetrahydra-2*H*-pyran (3.8) has been previously characterized and spectral data match literature values.[28]

3.5.7 *Alkene Starting Materials for Alkylboranes*



2-methyl-2-pentene (3.11) was purchased from Oakwood Chemicals and distilled over calcium hydride under reduced pressure before use.



Cyclohexene (3.12) was purchased from Millipore Sigma and distilled over calcium hydride under reduced pressure before use.

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