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**BORON AND METAL HALIDES
IN ORGANIC SYNTHESIS**

A Dissertation

Presented for the

Doctor of Philosophy

Degree

University of Tennessee, Knoxville USA

Scott T. Borella

August 2007

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DEDICATION

To all who have served as my teachers, advisors, coaches, and everyone who has inspired
me to learn and continue to learn,

Thank You

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There are many people who deserve to be acknowledged for their effort and influence in helping me to pursue an advanced degree in chemistry.

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ABSTRACT

This dissertation summarizes the recent use of organoboron and metal halides to form new carbon-carbon bonds. Several novel reactions have been discovered. These include the halovinyl alkenylation of alkoxides with alkenylboron dihalides; alkynylation of alkoxides with alkynylboron dihalides; boron trichloride and ferric chloride-mediated allylation of alkoxides. The results of these studies strongly imply a cationic mechanism, and prompted a reinvestigation of the boron trihalide mediated alkyne-aldehyde coupling reaction. The olefin stereochemistry of the resultant 1,5-dihalo-1,4-pentadienes can be influenced by controlling the reaction temperature and the sequence of reagent addition. The reaction methodology of the research described herein can be characterized as atom-efficient, environmentally friendly, and capable of generating the desired products in good to high yields.

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LIST OF SYMBOLS AND ABBREVIATIONS

SYMBOLS (units of measure)

°	degrees
g	grams
Hz	Hertz
h	hour(s)
kg	kilograms
L	liters
M	molar
MHz	Mega Hertz
min	minutes
mL	milliliters
mM	millimolar
mm	millimoles
mg	milligrams
T	Temperature

ABBREVIATIONS

AAA	Asymmetric Allylic Alkylation
ACN	Acetonitrile
AcOH	Acetic Acid
AIBN	2,2'-azobisisobutyronitrile
aq	Aqueous

Ar	Aryl
Ba(OH) ₂	Barium Hydroxide
BP	Boiling Point
Bn	Benzyl
Br	Bromide
°C	Degrees Celsius
Calcd	Calculated
cat.	Catalytic
CDCl ₃	Deuteriochloroform
Cl	Chloride
CN	Nitrile
CNMR	¹³ Carbon Nuclear Magnetic Resonance
CS ₂	Carbon Disulfide
CsF	Cesium Fluoride
Cy	Cyclohexyl
DCM	Dichloromethane
DMF	<i>N,N</i> -dimethylformamide
d	doublet
dd	doublet of doublets
dq	doublet of quartets
EA	Elemental Analysis
Et ₂ O	Diethyl Ether
EtOAc	Ethyl Acetate

H ₂ O	Water
HNMR	¹ Hydrogen Nuclear Magnetic Resonance
HRMS	High Resolution Mass Spectrometry
I ₂	Iodine
IR	Infra-Red Spectroscopy
<i>J</i>	Proton-proton coupling constant
K ₃ PO ₄	Potassium Phosphate
Li	Lithium
Me	Methyl
MeI	Methyl Iodide
MP	Melting Point
m	multiplet
N ₃	Azide
Na ₂ CO ₃	Sodium Bicarbonate
NaH	Sodium Hydride
NBS	<i>N</i> -Bromosuccinimide
<i>n</i> -Bu	normal butyl
(<i>n</i> -Bu) ₃ SnH	tris- <i>n</i> -butyltin hydride
<i>n</i> -BuLi	normal butyllithium
NMR	Nuclear Magnetic Resonance
PdCl ₂	Palladium(II) Chloride
Ph	Phenyl
PMA	Phosphomolybdic Acid in Ethanol

PPh ₃	Triphenylphosphine
OH	Hydroxyl
ORTEP	Oak Ridge Thermal Ellipsoid Plot
q	quartet
R	Substituent other than Hydrogen or Halide
r.t.	Room Temperature
SiO ₂	Silica Gel
S _N 2	Substitution Nucleophilic Bimolecular
t	triplet
<i>t</i> -BuLi	tertiary butyllithium
TBAF	tetra- <i>n</i> -butylammonium fluoride
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Tetramethylsilane / Trimethylsilyl
Tf	Trifluoromethanesulfonyl
UV	Ultra Violet
X	Halide

Chapter 1: Boron and Metal Halides in Organic Synthesis

1.1 Scope of this Dissertation

This dissertation is centered on the reactions of aliphatic alcohols and aldehydes primarily with boron Lewis acids and, in some cases, transition and other main group metal halides. Several novel reactions have been developed. These include: (1) alkenylation of allylic and benzylic alcohols with alkenylboron dihalides; (2) alkynylation of alcohols with alkynylboron dihalides; (3) allylation of aliphatic alcohols with boron trichloride and (4) iron(III) chloride. In addition, a reinvestigation of the alkyne-aldehyde coupling reaction with boron trichloride and boron tribromide was conducted. Each chapter will illustrate the synthetic utility of the newly discovered reactions, describe relationships with the published literature, and discuss relevant mechanistic interpretations. This chapter will underscore the pertinent background information that is crucial to understanding the chemistry discussed in this dissertation.

1.1.1 Historical Aspects of Boron and Metal Halides in Organic Chemistry

The first published account of a boron trihalide complex was reported by J.L. Gay-Lussac describing boron trifluoride-ammonia ($\text{BF}_3 \cdot \text{NH}_3$).¹ Boron and metal halides are Lewis acids. The concept of Lewis acidity, named after American physical chemist Gilbert Norton Lewis, is based upon a molecule's ability to accept a pair of electrons.² Electron pair donors are Lewis bases and electron pair acceptors are Lewis acids. In the valence bond formalism, boron complexes function as Lewis acids due to an electron deficient valence shell. The electron pair donor contains filled π -orbitals while the boron complex can accept the π -electrons due to an incomplete octet. The result is a newly

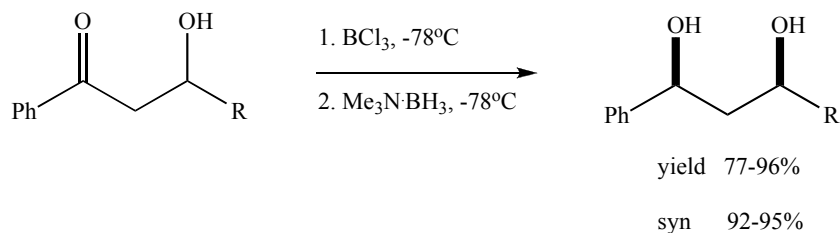
formed σ -bond. Interestingly, the halogen's electronegativity does not influence the relative acidity of the boron trihalide molecule; the observed Lewis acidity of boron trihalide complexes are $\text{BI}_3 > \text{BBr}_3 > \text{BCl}_3 > \text{BF}_3$;³ more favorable lone-pair orbital overlap from the halide to the metal center decreases the observed Lewis acidity. Similar arguments can be made to other main group metal halide Lewis acids.

With regard to transition metals, those containing small d^n configurations are more Lewis acidic than those with higher d^n configurations. For example, titanium(IV) chloride, TiCl_4 , is a d^0 complex while copper(II) chloride, CuCl_2 , is a d^9 complex. The titanium(IV) chloride is significantly more electron deficient, therefore it is a stronger Lewis acid.

1.1.2 Reactions of Boron Halides in Organic Chemistry

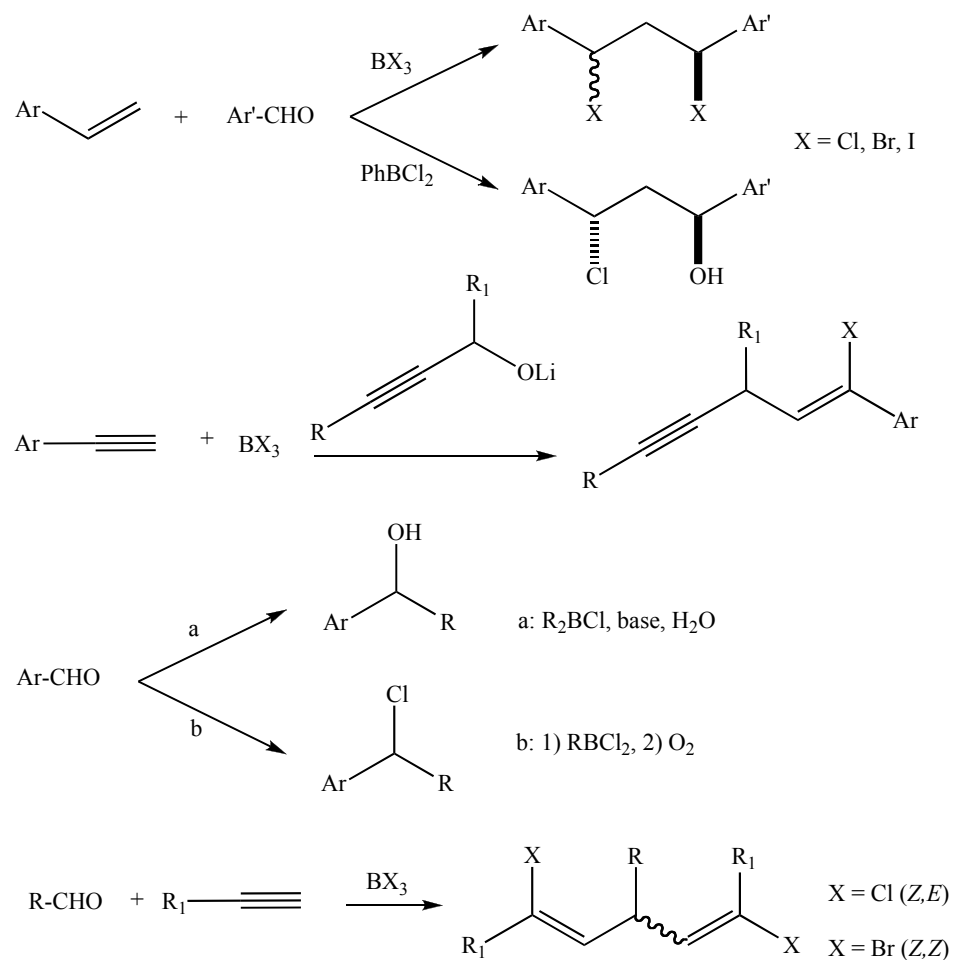
The reaction diversity of boron halides, especially boron trichloride, have been known for nearly fifty years.⁴ Traditionally, boron trihalides have realized synthetic utility in the cleavage of ethers, acetals, and esters,^{5,6} stereoselective glycosidation of glycols,⁷ Aldol condensations,⁸ and Freidel-Crafts reactions.⁹ Achiral boron trichloride has been shown to reduce β -hydroxyketones to *syn*-1,3-diols in high diastereoselectivity (Scheme 1-1).¹⁰

Scheme 1-1 Asymmetric reduction of β -hydroxyketones with boron trichloride

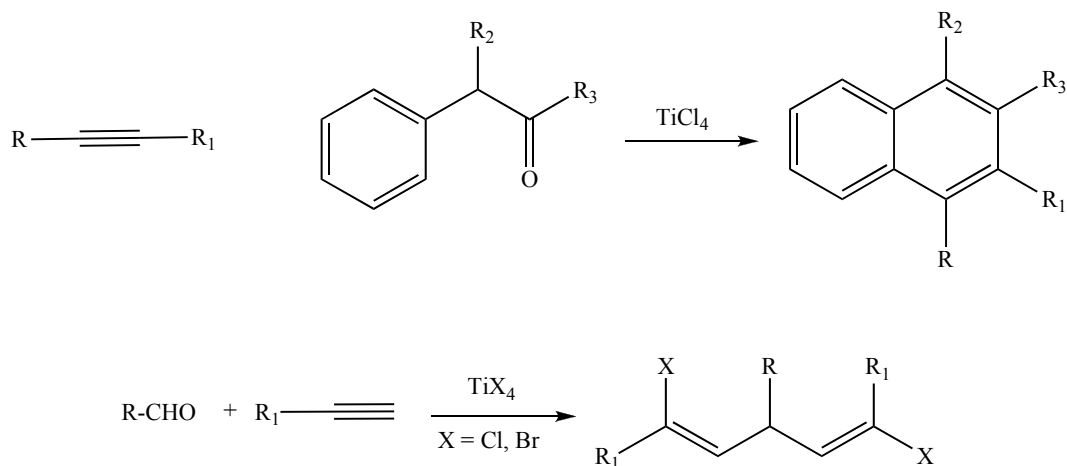


The Kabalka group has developed several reactions using boron¹¹ and metal halide¹² Lewis acids (**Schemes 1-2** and **1-3**). This chemistry serves as the basis for the research in this dissertation.

Scheme 1-2 Kabalka group boron trihalide reactions



Scheme 1-3 Kabalka group metal halide reactions



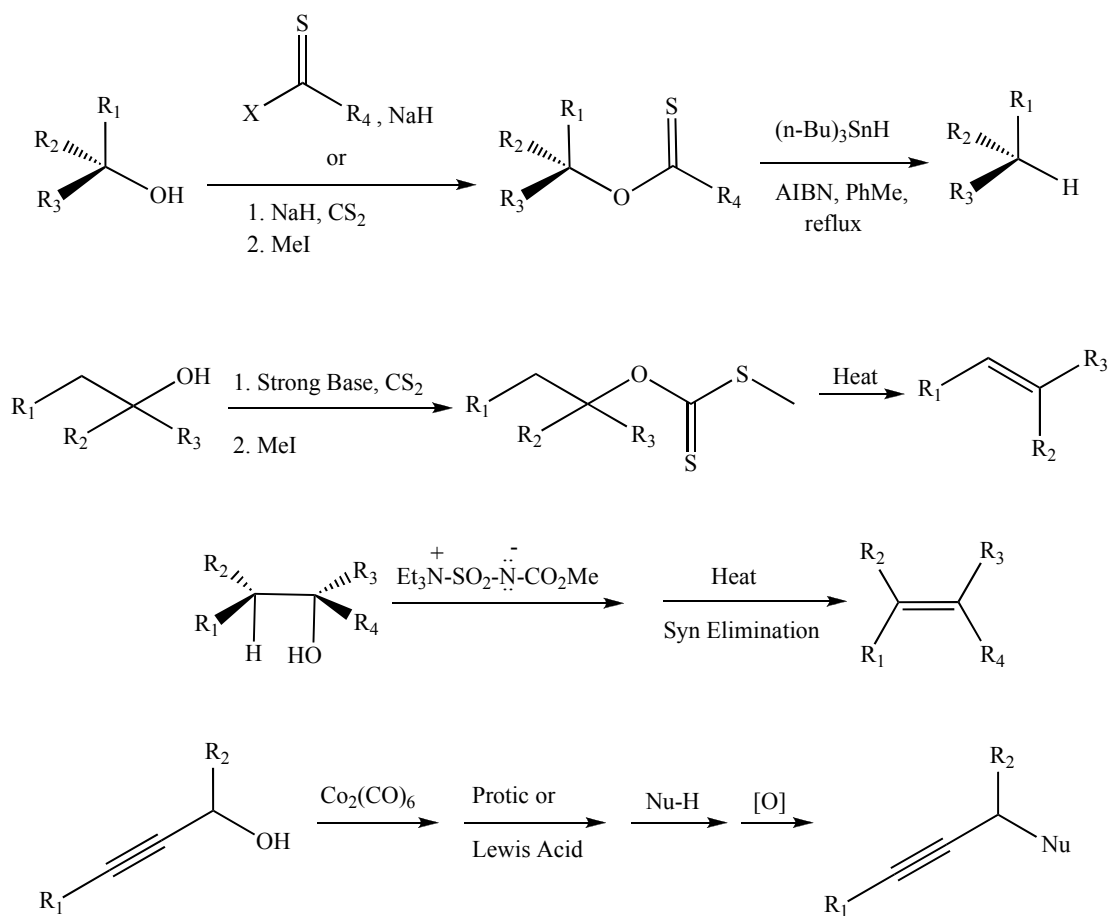
1.2 Aliphatic Alcohol Functional Group Conversion

Aliphatic alcohols are among the most readily available starting materials for modern synthetic chemistry. Consequently, numerous reactions have been developed to transform an alcohol into a new functional group, followed by a coupling or replacement reaction. Some of the more popular and versatile reactions used in target-oriented synthesis include the Barton-McCombie radical deoxygenation,¹³ Chugaev elimination,¹⁴ Burgess dehydration,¹⁵ and the Nicholas reaction¹⁶ (**Scheme 1-4**).

In addition to the functional group conversions of aliphatic alcohols shown in Scheme 1-4, several cross-coupling reactions of aliphatic alcohols have been developed. The majority of these reactions are based upon the use of transition metal catalysts. For example, in 2001 Buchwald reported the cross coupling of simple aliphatic alcohols and aryl iodides with a Cu(I) catalyst using 1,10-phenanthroline as a ligand.¹⁷ Notably, when chiral secondary benzylic alcohols are used, the coupling proceeds with retention of

configuration. Although the coupling reaction is capable of proceeding without the need of an inert atmosphere or exclusion of water, it requires a temperature of 110 °C for a period of 18-24 hours.

Scheme 1-4 Functional group transformation of aliphatic alcohols



Examples have been reported with iron,¹⁸ rhenium,¹⁹ and gold²⁰ complexes, all of which are focused on propargylic alcohols. In 2003, the Kabalka group reported the rhodium catalyzed coupling of allylic alcohols with vinylboronic acids in the presence of

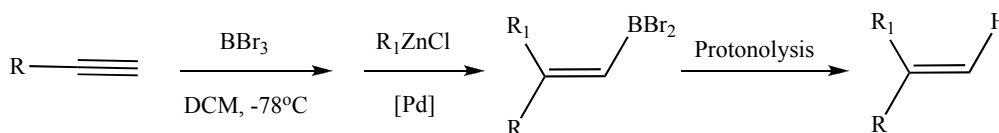
ionic liquids.²¹ The largest percentage of catalytic transition metal coupling reactions of aliphatic alcohols use ruthenium²² and palladium²³ complexes.

Efforts have been made to circumvent the use of transition metal catalysts by using main group Lewis acids. Recent reports employ bismuth trichloride²⁴ to mediate substitution of propargylic alcohols with a variety of carbon and heteroatom nucleophiles, and indium trichloride²⁵ for reactions of silyl nucleophiles with benzyl alcohols. Lastly, Sanz has reported that propargylic alcohols can be substituted *metal-free* using *p*-toluene sulfonic acid monohydrate as a catalyst.²⁶

1.3 Boron Trihalide Haloboration of Alkynes

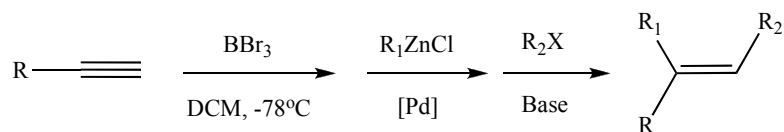
The reaction of trihaloboranes with unsaturated hydrocarbons was first reported by Lappert,²⁷ while the direct haloboration of alkynes in a *syn* fashion was reported by Blackborow.²⁸ It is believed that the haloboration and hydroboration mechanism are analogous. Initial applications of haloboration to terminal alkynes were directed toward catalytic cross coupling with organozinc compounds in the presence of a palladium catalyst. It was observed that the *syn*-haloboration adduct selectively coupled with the organozinc compound at the vinyl bromide. Protonolysis afforded the *gem*-disubstituted alkene (**Scheme 1-5**).

Scheme 1-5 Synthesis of *gem*-substituted alkenes



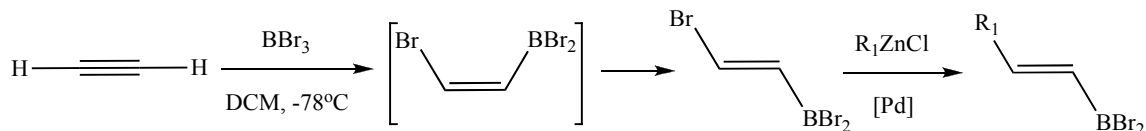
Trisubstituted alkenes were obtained by reacting the *gem*-disubstituted alkenylboron dibromide with an alkyl halide in the presence of base (**Scheme 1-6**).²⁹

Scheme 1-6 Synthesis of tri-substituted alkenes



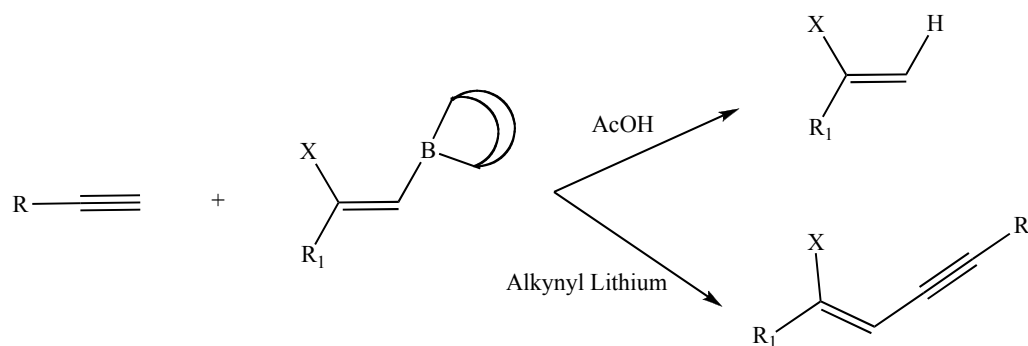
Interestingly, the haloboration of acetylene with boron tribromide followed by coupling with the organozinc compound and palladium catalyst afforded the (*E*)-1-alkenyldibromoborane. It is presumed that the bromoboration of acetylene proceeds with *syn*-addition and spontaneous isomerization to the (*E*)-isomer (**Scheme 1-7**).³⁰

Scheme 1-7 Bromoboration of acetylene

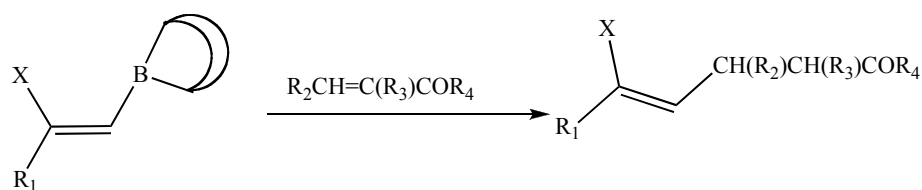


Haloboration with *B*-halo-borabicyclo[3.3.1]nonane (9-BBN) has also been shown to be synthetically useful. Suzuki has developed efficient routes to vinylhalo alkenes and 1,3-enynes (**Scheme 1-8**),³¹ stereospecific (*Z*)- δ -halo- γ,δ -unsaturated ketones (**Scheme 1-9**),²² and (*Z,Z*)-1-bromo-1,3-dienes and (*Z,E*)-1,3-dienes (**Scheme 1-10**).³³

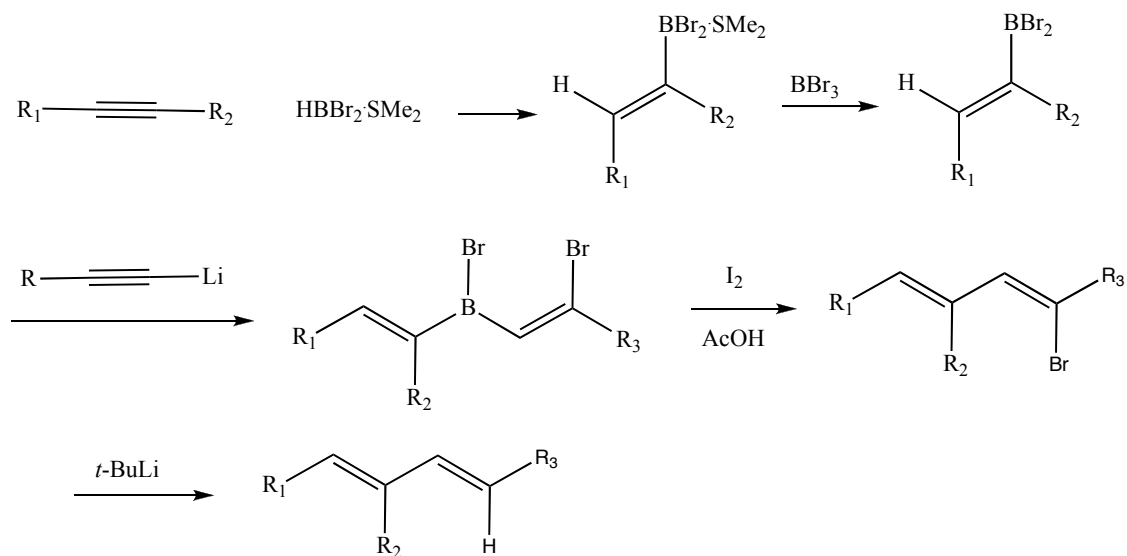
Scheme 1-8 Synthesis of 1,3-enynes



Scheme 1-9 Synthesis of (Z)- δ -halo- γ,δ -unsaturated ketones



Scheme 1-10 Synthesis of (Z,E)-1,3-dienes



1.4 Addition of Organoboron Halides to Carbonyl Compounds

Carbonyl compounds, especially aldehydes and ketones, constitute ideal starting materials in synthesis due to the polarized carbon-oxygen double bond. This feature allows regioselective chemical reactions to take place at either the carbon or oxygen center. Consequently, numerous reactions have been developed to control the chemo-, regio-, and stereoselectivity of the resultant products.

One of the most common reactions of carbonyl compounds is the Grignard reaction of aldehydes and ketones to generate alcohols.³⁴ The organic component of the Grignard reagent can act as a nucleophile with attack occurring at the carbon center resulting in a new carbon-carbon bond. There is evidence to support both a single electron transfer pathway (radical) and a concerted pathway.³⁵

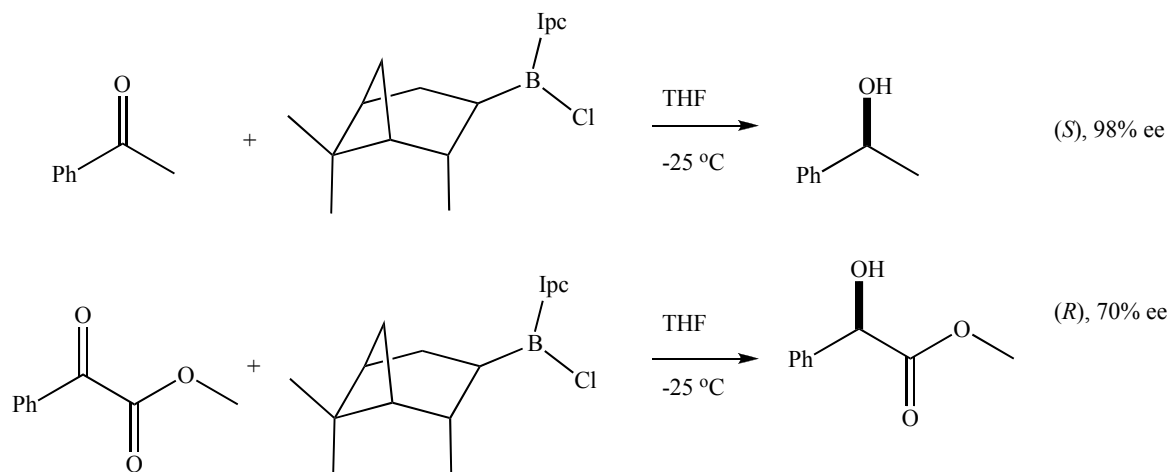
Several other organometallic compounds are capable of alkylating carbonyl compounds. Reactions involving organolithium³⁶ and organozinc³⁷ compounds behave very similar to Grignard reagents. Additionally, chromium(III) (Nozaki-Hiyama-Kishi) and samarium(II) (Kagan-Molander) have been shown to exhibit similar reactivity when used with alkyl halides.

Organoboranes are also capable of alkylating carbonyl compounds, although they normally do not react in the same manner as Grignard and other organometallic reagents; the most common exceptions include allyl-,³⁸ alkenyl-,^{22, 39} and alkynylboranes.⁴⁰ Scheme 1-2 highlights the ability of organoboron halides to alkylate and halogenate carbonyl compounds.^{11, 41}

Finally, the reducing ability of organoboranes have been well documented.⁴² The predominate organoboron halide reducing agent is diisopinocampheylboron chloride

(Ipc_2BCl). This compound can reduce aldehydes and ketones in nearly quantitative yield with very high levels of enantiomeric excess. Furthermore, Ipc_2BCl has virtually no side reactions, is commercially available in both enantiomeric forms, and has found utility in the pharmaceutical synthesis of prozac.⁴³ Reductions of carbonyl compounds with Ipc_2BCl are shown in Scheme 1-11.

Scheme 1-11 Reduction of carbonyl compounds with Ipc_2BCl



1.5 Statement of Problem

Organoboron halides can react with carbonyl compounds to form new carbon-carbon and carbon-halogen bonds, and have found utility in the coupling of propargylic alkoxides with aryl acetylenes to form stereodefined 1,4-enynes (**Scheme 1-2**). Similar coupling reactions involving allyloxides (Chapter 2) and benzyloxides (Chapter 3) with aryl acetylenes and boron trihalide were not known. Alkynylboron dihalides are also not known to participate in coupling reactions with alkoxides (Chapter 4). Additionally, the mechanism associated with the boron trihalide mediated coupling reaction of alkoxides is

not known. Finally, it is also not known why boron tribromide only produces the (*Z,Z*)-isomer while boron trichloride produces the (*Z,E*)-isomer in the alkyne-aldehyde coupling reaction (**Scheme 1-2**, Chapter 6).

Chapter 2: Alkenylation of Allylic Alcohols with Alkenylboron Dihalides

2.1 Introduction

Asymmetric allylic alkylation (AAA) of allylic halides, carbonates, carboxylates, and phosphates is one of the more useful methods of forming carbon-carbon bonds in synthesis.⁴⁴ The reactions are typically mediated by transition metal catalysts specifically designed to induce enantioselectivity.^{45,46} Unfortunately, AAA reactions suffer a noteworthy drawback since the formation of π -allyl metal intermediates complicate regioselective bond formation.⁴⁷ Although AAA reactions involving soft nucleophiles have been well studied, the same reactions with hard nucleophiles (Grignard or zinc) often require transmetallation to the more reactive copper intermediate.^{48,49} When organoboron nucleophiles are used, the corresponding boronic acids generally are converted to lithium⁵⁰ or zinc borates.⁵¹

In 2004, the Kabalka group reported the regio- and stereoselective synthesis of 1,4-enynes via propargylic alcohols and vinylboron dihalides (**Scheme 1-2**).^{11d} This reaction is a noteworthy improvement on propargylation reactions since transition metal complexes are not needed to stabilize propargylic cationic intermediates.⁵² The synthesis of 1,4-enynes using organoboron dihalides is an extremely atom economical process, tolerant of a wide variety of functional groups, and generates moderate to high yields of the desired products with nearly quantitative olefin stereoselectivity.

The successful halovinyl alkenylation of propargylic alcohols to form 1,4-enynes in moderate to high yields lends to the postulate that a similar reaction may take place with allylic alcohols to form stereodefined 1,4-pentadienes. To our knowledge, the

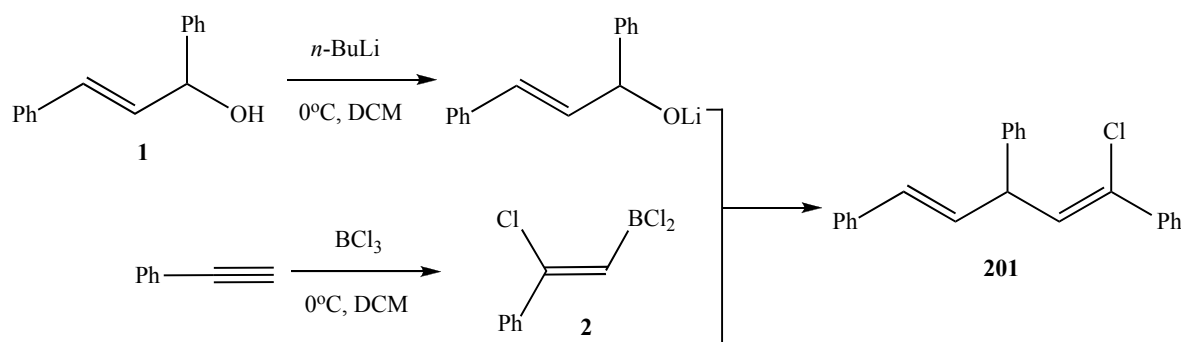
coupling of an allylic alcohol with a halovinyl moiety in the absence of a transition metal or Lewis acid has not been reported.

2.2 Results and Discussion

2.2.1 Alkenylation of Allylic Alcohols with Boron Trichloride and Tribromide

The successful alkenylation of propargylic alcohols with alkenylboron dihalides prompted an examination of allylic alcohols with alkenylboron dihalides. To examine the viability of this reaction, (*E*)-1,3-diphenyl-prop-2-en-1-ol, **1**, was allowed to react with vinylboron dihalide **2** as shown in Scheme 2-1.⁵³

Scheme 2-1 Boron trichloride mediated alkenylation of allylic alcohols



The resultant product, (1*Z*,4*E*)-1-chloro-1,3,5-triphenyl-1,4-pentadiene (**201**), was isolated in 83% yield. HNMR produced a single dd resonance for the methine hydrogen at 4.94 ppm. This would indicate splitting by two different vinyl hydrogens. The coupling constants of 9 Hz are associated with *cis*-vicinal coupling in alkenes. CNMR provided further confirmation only one 1,4-pentadiene olefin configuration was present

due to the single methine sp^3 carbon at 48.5 ppm. The spectra are shown in Figures 2-1 and 2-2.

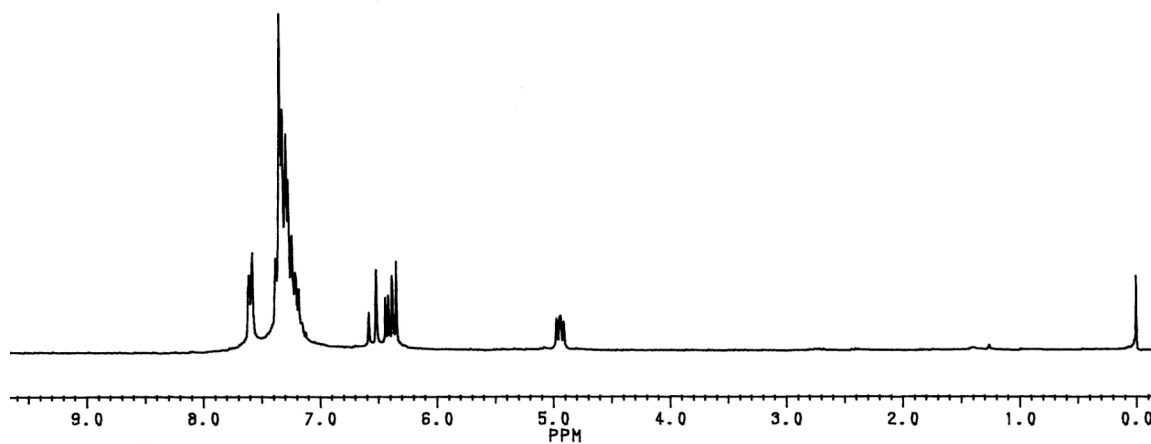


Figure 2-1 ^1H NMR of compound 201

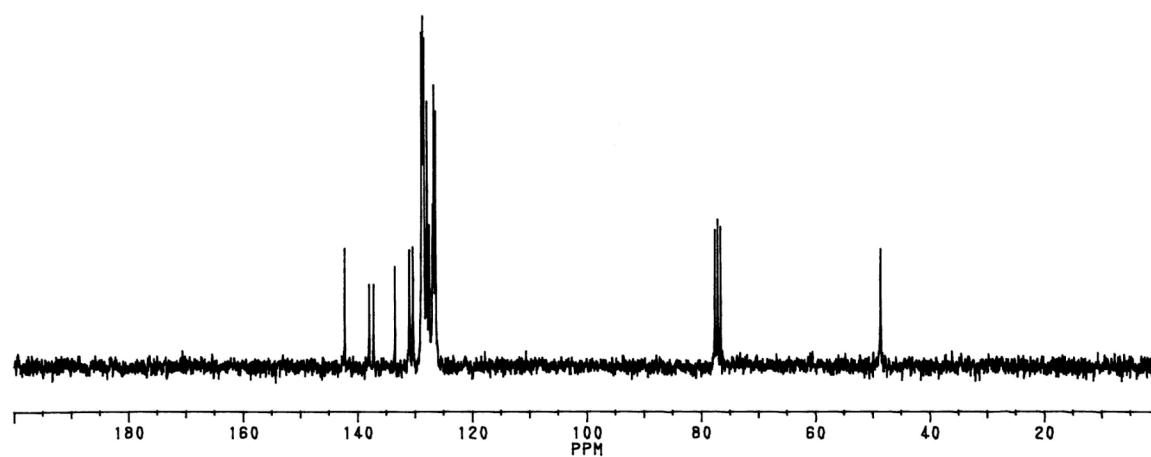
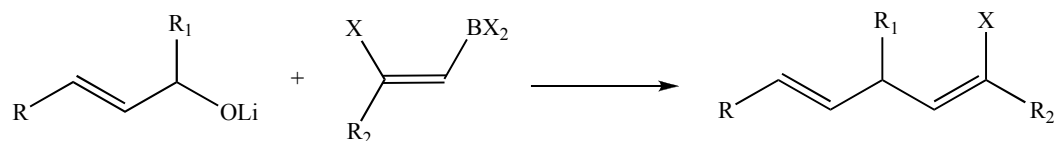


Figure 2-2 ^{13}C NMR of compound 201

To evaluate the scope of the reaction, a series of allylic alcohols and alkynes were subjected to the reaction outlined in Scheme 2-1. The results are presented in Table 2-1.

Table 2-1 Reaction of allylic alkoxides with alkenylboron dihalides



Entry	R	R ₁	R ₂	X	Yield (%)	Product
1	Ph	Ph	Ph	Cl	83	201
2	Ph	Ph	4-MePh	Cl	81	202
3	Ph	Ph	3-FPh	Cl	78	203
4	Ph	Ph	4-ClPh	Cl	79	204
5	Ph	Ph	4-BrPh	Cl	65	205
6	Ph	Ph	2-FPh	Cl	61	206
7	Ph	Ph	Ph	Br	71	207
8	Ph	Ph	4-MePh	Br	68	208
9	Ph	Ph	<i>n</i> -C ₄ H ₉	Br	62	209
10	Ph	Ph	<i>n</i> -C ₈ H ₁₇	Br	65	210
11	Ph	Me	3-FPh	Cl	77	211
12	Ph	Me	3-FPh	Br	58	212
13	Ph	Me	Ph	Br	53	213
14	(<i>E</i>)-PhCH=CH-	Ph	Ph	Cl	66	214

Table 2-1 continued

Entry	R	R ₁	R ₂	X	Yield (%)	Product
15	1-Naphthyl-	Ph	Ph	Cl	47	215

Although the reaction of boron trihalide with a terminal alkyne quantitatively produces vinylboron dihalide **2**,⁵⁴ the resultant yields from reactions using boron tribromide were slightly lower than those using boron trichloride; this is attributed to decomposition of the product during isolation using a silica gel column. In all cases the expected products were formed.

It is noteworthy that unsymmetrical allylic alcohols produce regiochemically pure products. This obviates the aforementioned limitation of transient π -allyl intermediates that are formed when using transition metal catalysts. Moreover, the reaction is not limited to allylic alcohols containing aromatic substitution at the allylic carbon. Aliphatic substitution (methyl) at the allylic position did not interfere with the reaction (**Table 2-1, 211-213**). It is especially interesting that the alcohol moiety can be directly used in this reaction; typically, alcohols are converted into more reactive leaving groups (Br, OTf, etc) before being used in coupling reactions. Primary allylic alcohols did afford the anticipated product.

2.2.2 Relationship to the Suzuki Reaction

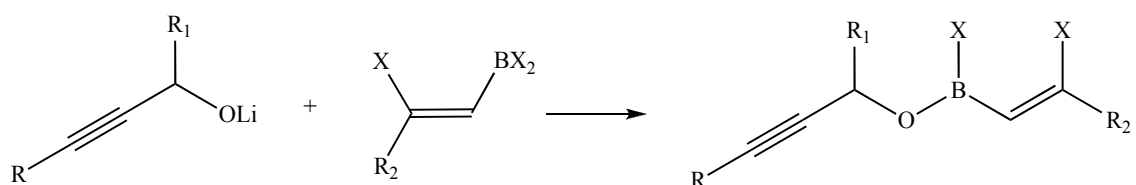
Since its discovery in 1979, the Suzuki reaction (**Scheme 2-2**) has proven to be one of the most widely utilized and practical transformations in modern synthetic

that the presence of base in the Suzuki reaction results in coordination to the boron atom – forming an intermediate borate – increasing the bond polarization of the boron-carbon bond. The increased polarization allows for the boron-carbon bond to break and form the cross-coupled product.

2.2.3 Mechanistic Study

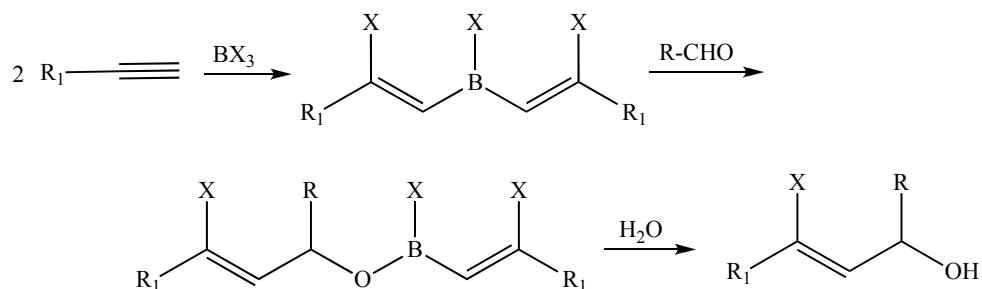
During the investigation of the alkenylation of propargylic alcohols (**Scheme 1-2**), a propargyloxyboron intermediate was proposed (**Scheme 2-3**).^{11d}

Scheme 2-3 A propargyloxyboron intermediate



This structure of this intermediate compound is based upon the following factors: (1) alkoxides are known to react with boron halides; (2) intramolecular rearrangements involving organoboranes are well documented; (3) quenching the reaction shown in Scheme 2-4 prior to completion afforded the corresponding (*Z*)-allylic alcohol.

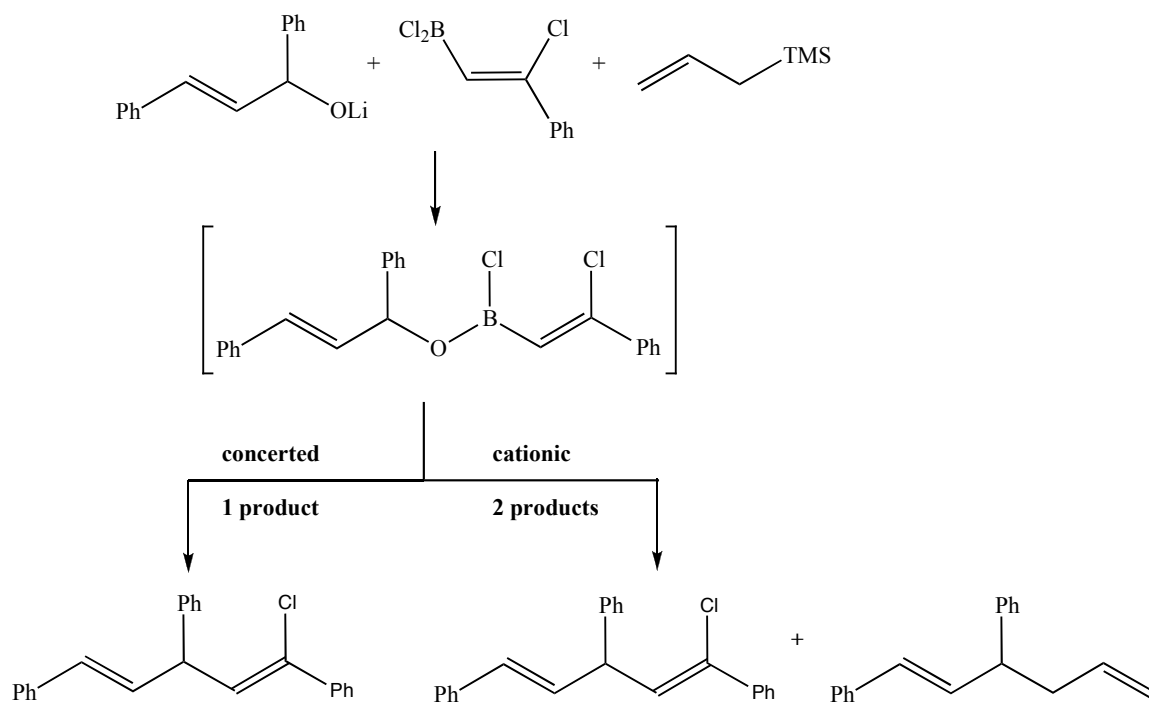
Scheme 2-4 Quenching divinylboron halide addition to aldehyde



It was also proposed, for both the alkenylation of propargylic alcohols and the alkyne-aldehyde coupling, that the resultant products are formed via an intramolecular migration. The formation of the resultant 1,4-pentadienes from allyloxides and vinylboron dihalides suggests that an intramolecular migration is a reasonable pathway. The experimental evidence, unfortunately, does not conclusively illustrate whether the migration proceeds with retention, inversion, or racemization of configuration at the C_{sp^3} -carbon.

In an effort to distinguish between a concerted or cationic mechanism, the competition reaction shown in Scheme 2-5 was designed.

Scheme 2-5 Reaction of allyloxide, vinylboron dihalide, and allyltrimethylsilane



The reaction in Scheme 2-5 afforded two products – the halovinyl alkenylation product and the allylation product in a ratio of 5:2. It is known that allylsilanes are capable of capturing cationic intermediates. If a carbocation is being formed, presumably due to the oxyboron halide species acting as a leaving group, the electron density of the allylsilane double bond should attack the carbocation. Since the allylation product was formed, an intramolecular migration appears unlikely.

2.3 Conclusion

The direct alkenylation of readily available allylic alcohols via alkenylboron dihalides represents a formal, transition metal-free Suzuki reaction. This reaction is highly regioselective for alkenylation at the allylic carbon, extremely stereoselective with respect to olefin configuration, and proceeds under mild reaction conditions in a highly atom economical fashion forming (*Z,E*)-1-halo-1,4-pentadienes in good yields.

2.4 Experimental Details

2.4.1 General Considerations

All reagents were used as received. Solvents were distilled from the appropriate drying agents under a nitrogen atmosphere. Column chromatography was performed using silica gel (60 Å, 230–400 mesh). Analytical thin-layer chromatography was performed using 250 µm silica (Analtech, Inc., Newark, DE). All glassware was oven-dried for at least 12 hours at 150 °C and cooled under argon or nitrogen. Reactions were magnetically stirred under argon or nitrogen and monitored on TLC plates using 254 nm UV light, staining with a 50% solution of PMA in EtOH, or development on in an iodine-

silica gel chamber.

2.4.2 Preparation of Alkenylboron Dihalide Complexes

Boron trihalide (1.5 mmol), alkyne (1.5 mmol) and dry dichloromethane (8 mL) were combined in a 50 mL round bottomed flask and stirred for 1 hour under a nitrogen atmosphere.

2.4.3 Representative Procedure for the Syntheses of (*Z,E*)-1-Halo-1,3,5-trisubstituted-1,4-pentadienes

Allylic alcohol (1.6 mmol) in dry dichloromethane (8 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 *M* solution in hexane) at 0°C and stirred at room temperature for 1 hour. The solution was then transferred to the alkenylboron dihalide and allowed to stir at room temperature overnight. Water (20 mL) was added and the reaction mixture and the product was extracted with ethyl acetate and dried over anhydrous MgSO₄. The solvents were removed under reduced pressure and the product purified by silica gel column chromatography using hexane as an eluent.

2.4.4 Characterization of Compounds 201-215

HNMR and CNMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for HNMR and CNMR spectra (CDCl₃) were referenced to TMS and CDCl₃ respectively. Microanalysis was performed by Atlantic Microlab, Inc. Norcross, Georgia.

(1*Z*,4*E*)-1-Chloro-1,3,5-triphenyl-1,4-pentadiene (201): ¹HNMR: δ 7.57–7.60 (m, 2H), 7.15–7.37 (m, 13H), 6.34–6.58 (m, 3H), 4.94 (dd, *J* = 8.98 and 8.88 Hz, 1H). ¹³CNMR: δ

142.1, 137.9, 137.1, 133.4, 130.9, 130.3, 128.7, 128.5, 128.3, 127.8, 127.4, 126.9, 126.6, 126.3, 48.5. Anal. Calcd for C₂₃H₁₉Cl: C, 83.50; H, 5.79. Found: C, 83.57; H, 5.65.

(1Z,4E)-1-Chloro-1-(4-methylphenyl)-3,5-diphenyl-1,4-pentadiene (202): ¹HNMR: δ 7.47–7.51 (m, 2H), 7.11–7.36 (m, 12H), 6.30–6.58 (m, 3H), 4.93 (dd, *J* = 9.03 and 8.98 Hz, 1H), 2.32 (s, 3H). ¹³CNMR: δ 142.3, 138.6, 137.2, 135.1, 133.5, 130.8, 130.4, 129.0, 128.7, 128.5, 127.8, 127.4, 127.4, 126.7, 126.5, 126.3, 48.4, 21.1. Anal. Calcd for C₂₄H₂₁Cl: C, 83.58; H, 6.14. Found: C, 83.92; H, 6.03.

(1Z,4E)-1-Chloro-1-(3-fluorophenyl)-3,5-diphenyl-1,4-pentadiene (203): ¹HNMR: δ 7.14–7.36 (m, 13H), 6.90–6.97 (m, 1H), 6.32–6.56 (m, 3H), 4.92 (dd, *J* = 8.98 and 8.96 Hz, 1H). ¹³CNMR: δ 164.6, 160.6, 141.8, 140.0, 136.9, 132.0, 131.1, 129.9, 129.5, 128.8, 128.5, 127.7, 127.5, 126.7, 126.31, 122.1, 115.6, 115.3, 113.9, 113.5, 48.5. Anal. Calcd for C₂₃H₁₈ClF: C, 79.19; H, 5.20. Found: C, 79.37; H, 5.55.

(1Z,4E)-1-Chloro-1-(4-chlorophenyl)-3,5-diphenyl-1,4-pentadiene (204): ¹HNMR: δ 7.16–7.41 (m, 14H), 6.34–6.61 (m, 2H), 6.09 (d, *J* = 9.28 Hz, 1H), 4.92 (dd, *J* = 9.73 and 9.59 Hz, 1H). ¹³CNMR: δ 141.8, 138.1, 137.2, 133.0, 131.1, 131.0, 130.0, 129.9, 129.8, 129.5, 128.7, 128.5, 127.8, 127.4, 126.8, 126.7, 126.3, 48.1. Anal. Calcd for C₂₃H₁₈Cl₂: C, 75.62; H, 4.97. Found: C, 75.47; H, 4.76.

(1Z,4E)-1-Chloro-1-(4-bromophenyl)-3,5-diphenyl-1,4-pentadiene (205): ¹HNMR: δ 7.16–7.46 (m, 14H), 6.33–6.57 (m, 3H), 4.91 (dd, *J* = 9.17 and 9.11 Hz, 1H). ¹³CNMR: δ 141.9, 137.0, 136.8, 132.3, 131.4, 131.0, 129.9, 129.0, 128.8, 128.5, 128.1, 127.7, 127.5, 126.9, 126.3, 122.7, 48.5. Anal. Calcd for C₂₃H₁₈BrCl: C, 67.40; H, 4.43. Found: C, 67.25; H, 4.36.

(1Z,4E)-1-Chloro-1-(2-fluorophenyl)-3,5-diphenyl-1,4-pentadiene (206): ^1H NMR: δ 7.02–7.52 (m, 14H), 6.37–6.63 (m, 3H), 4.95 (dd, J = 9.69 and 9.56 Hz, 1H). ^{13}C NMR: δ 162.5, 157.7, 141.9, 137.1, 133.4, 133.3, 131.0, 130.4, 130.1, 130.0, 128.7, 128.5, 128.1, 127.8, 127.4, 127.1, 126.8, 126.3, 124.0, 116.2, 115.8, 48.5. Anal. Calcd for $\text{C}_{23}\text{H}_{18}\text{ClF}$: C, 79.19; H, 5.20. Found: C, 79.33; H, 5.17.

(1Z,4E)-1-Bromo-1,3,5-triphenyl-1,4-pentadiene (207): ^1H NMR: δ 7.54–7.59 (m, 2H), 7.21–7.41 (m, 13H), 6.37–6.55 (m, 3H), 4.90 (dd, J = 8.94 and 8.88 Hz, 1H). ^{13}C NMR: δ 141.9, 139.7, 137.1, 132.1, 131.0, 130.0, 128.7, 128.5, 128.3, 127.8, 127.4, 126.8, 126.3, 126.1, 51.3. Anal. Calcd for $\text{C}_{23}\text{H}_{19}\text{Br}$: C, 73.61; H, 5.10. Found: C, 73.57; H, 5.22.

(1Z,4E)-1-Bromo-1-(4-methylphenyl)-3,5-diphenyl-1,4-pentadiene (208): ^1H NMR: δ 7.07–7.46 (m, 14H), 6.34–6.59 (m, 3H), 4.88 (dd, J = 8.79 and 8.70 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR: δ 142.0, 138.6, 137.1, 136.9, 131.2, 130.9, 130.1, 128.9, 128.7, 128.5, 127.8, 127.6, 127.4, 126.8, 126.3, 51.3. Anal. Calcd for $\text{C}_{24}\text{H}_{21}\text{Br}$: C, 74.04; H, 5.44. Found: C, 73.92; H, 5.09.

(1Z,4E)-1-Bromo-1-(*n*-butyl)-3,5-diphenyl-1,4-pentadiene (209): ^1H NMR: δ 7.17–7.39 (m, 10H), 6.29–6.53 (m, 2H), 5.88 (d, J = 9.18 Hz, 1H), 4.70 (dd, J = 8.77 and 8.75 Hz, 1H), 2.47–2.52 (m, 2H), 1.47–1.64 (m, 2H), 1.26–1.38 (m, 2H), 0.92 (t, J = 7.24 Hz, 3H). ^{13}C NMR: δ 142.3, 137.2, 130.5, 129.4, 128.6, 128.5, 127.7, 127.3, 126.6, 126.3, 50.4, 41.2, 30.3, 21.6, 13.8. Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{Br}$: C, 70.99; H, 6.52. Found: C, 71.31; H, 6.87.

(1Z,4E)-1-Bromo-1-(*n*-octyl)-3,5-diphenyl-1,4-pentadiene (210): ^1H NMR: δ 7.18–7.39 (m, 10H), 6.30–6.52 (m, 2H), 5.88 (d, J = 9.30 Hz, 1H), 4.71 (dd, J = 8.68 and 8.70 Hz,

1H), 2.46–2.51 (m, 2H), 1.56–1.61 (m, 2H), 1.16–1.37 (m, 2H), 0.87 (t, $J = 7.21$ Hz, 3H). ^{13}C NMR: δ 147.4, 142.3, 137.2, 130.5, 129.5, 129.2, 128.6, 128.5, 127.7, 127.3, 126.6, 126.2, 50.3, 41.7, 31.8, 29.3, 28.4, 28.1, 22.7, 14.1. Anal. Calcd for $\text{C}_{25}\text{H}_{31}\text{Br}$: C, 72.98; H, 7.59. Found: C, 72.68; H, 7.87.

(1Z,4E)-1-Chloro-1-(3-fluorophenyl)-3-methyl-5-phenyl-1,4-pentadiene (211):

^1H NMR: δ 6.97–7.33 (m, 9H), 6.05–6.23 (m, 3H), 3.68–3.72 (m, 1H), 1.28 (d, $J = 6.73$ Hz, 3H). ^{13}C NMR: δ 164.6, 160.7, 137.3, 132.1, 131.9, 131.1, 130.9, 129.7, 129.6, 129.2, 128.6, 128.5, 127.6, 127.2, 126.6, 126.1, 122.0, 115.4, 115.0, 113.7, 113.4, 37.4, 19.7. Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{ClF}$: C, 75.39; H, 5.62. Found: C, 75.28; H, 5.87.

(1Z,4E)-1-Bromo-1-(3-fluorophenyl)-3-methyl-5-phenyl-1,4-pentadiene (212):

^1H NMR: δ 6.97–7.38 (m, 9H), 6.13–6.25 (m, 3H), 3.63–3.67 (m, 1H), 1.29 (d, $J = 6.84$ Hz, 3H). ^{13}C NMR: δ 164.4, 160.7, 137.3, 135.6, 131.9, 1129.7, 129.6, 129.3, 128.5, 127.6, 127.3, 126.1, 126.2, 115.4, 115.1, 115.0, 114.6, 40.3, 19.6. Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{BrF}$: C, 65.27; H, 4.87. Found: C, 65.38; H, 4.97.

(1Z,4E)-1-Bromo-1,5-diphenyl-3-methyl-1,4-pentadiene (213): ^1H NMR: δ 7.15–7.55 (m, 10H), 6.08–6.50 (m, 3H), 3.63–3.70 (m, 1H), 1.28 (d, $J = 6.85$ Hz, 3H). ^{13}C NMR: δ 139.8, 137.4, 134.5, 132.9, 132.2, 129.4, 18.5, 128.2, 127.6, 127.2, 26.6, 126.2, 124.7, 40.3, 19.7. HRMS for $\text{C}_{18}\text{H}_{17}\text{Br}$: 312.0514. Found: 312.0518.

(1Z,4E,6E)-1-Chloro-1,3,7-triphenyl-1,4,6-heptatriene (214): ^1H NMR: δ 7.20–7.61 (m, 15H), 6.01–6.74 (m, 5H), 4.67 (dd, $J = 8.97$ and 8.79 Hz, 1H). ^{13}C NMR: δ 142.1, 137.9, 137.3, 137.1, 134.5, 133.3, 132.0, 131.4, 130.7, 129.5, 128.6, 128.3, 127.7, 127.4, 126.5, 126.3, 48.4. Anal. Calcd for $\text{C}_{25}\text{H}_{21}\text{Cl}$: C, 84.14; H, 5.93. Found: C, 83.92; H,

6.28.

(1Z,4E)-1-Chloro-5-naphthyl-3,5-diphenyl-1,4-pentadiene (215): ^1H NMR: δ 7.23–8.22 (m, 17H), 6.36–6.58 (m, 3H), 5.06 (dd, $J = 8.79$ and 8.71 Hz, 1H). ^{13}C NMR: δ 144.3, 139.8, 136.7, 133.6, 133.4, 130.4, 128.8, 128.7, 128.5, 128.5, 128.3, 127.8, 127.4, 126.8, 126.6, 126.3, 126.0, 125.7, 125.6, 123.6, 48.9. HRMS for $\text{C}_{27}\text{H}_{21}\text{Cl}$: 380.1332. Found: 380.1337.

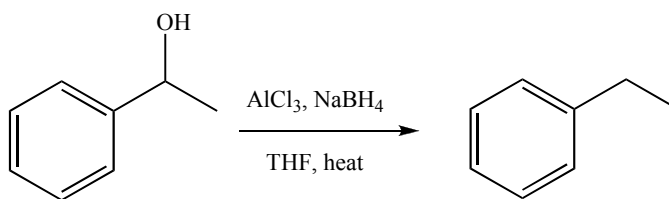
Chapter 3: Alkenylation of Benzylic Alcohols with Alkenylboron Dihalides

3.1 Introduction

Benzylic alcohols have found utility in synthetic chemistry as attractive starting materials in complex syntheses. Direct transformations of the hydroxyl group in benzylic alcohols have appeared in the literature, however these reactions typically involve converting the hydroxyl species into a more effective leaving group such as a halide or ester. Fortunately, several direct transformations have appeared, the most promising of which is the allylation using allyltrimethylsilane.^{25, 57}

One general transformation is based upon dehydroxylation⁵⁸ (recall that the Barton-McCombie radical deoxygenation is a popular approach to replace a hydroxyl group with hydrogen). Lewis acids have also been employed to replace hydroxyl moieties for hydrogen. For example, in 1987 Ono and coworkers reported the successful dehydroxylation of secondary benzylic alcohols in the presence of aluminum chloride and sodium borohydride as shown in Scheme 3-1.^{58b}

Scheme 3-1 Dehydroxylation of secondary benzylic alcohols

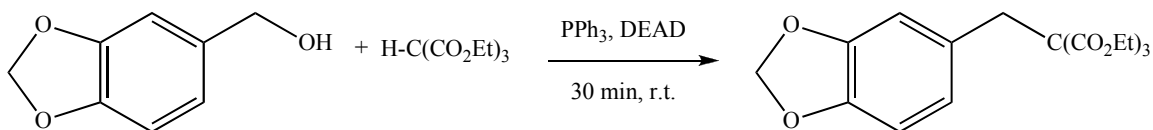


In the context of forming new carbon-carbon bonds, several attractive transformations have been reported.⁵⁹ Among these, Gravotto and coworkers have shown

benzylic alcohols can undergo dehydrative alkylation under Mitsunobu conditions

(Scheme 3-2).^{59a}

Scheme 3-2 Mitsunobu alkylation of benzylic alcohols

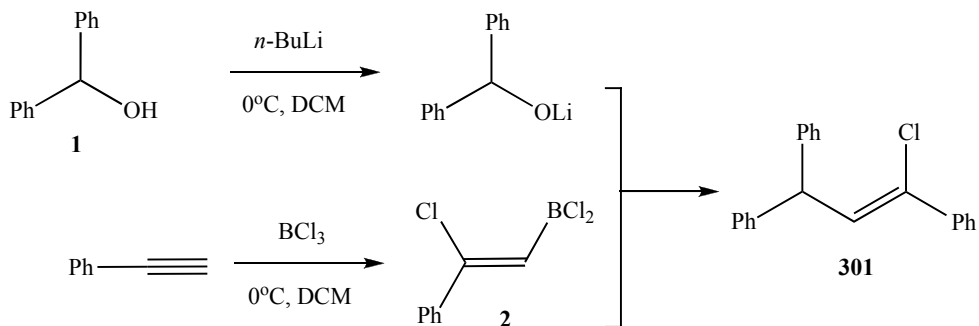


The aforementioned examples illustrate the potential uses of benzylic alcohols in synthesis, and the results outlined in Chapter 2 exemplify the capability of alkenylboron dihalides to be coupled with allylic alcohols (via their alkoxides). We postulated that alkenylboron dihalides could couple with benzylic alcohols. To our knowledge, the direct substitution of a benzylic hydroxyl group with a halovinyl species has not been achieved with either a Lewis acid or transition metal complex.

3.2 Results and Discussion

To examine the feasibility of substituting a hydroxyl group with a halovinyl species via organoboron dihalides, diphenylmethanol **1** and alkenylboron dihalide **2** were subjected to the reaction shown in Scheme 3-3.⁶⁰

Scheme 3-3 Reaction of diphenylmethanol with alkenylboron dichloride



Compound **301** was isolated in 79% yield. The HNMR of compound **301** produced two doublets at 6.59 and 5.42 ppm. These resonances correspond to the vinyl and methine hydrogens, respectively, and both had coupling constants of 9 Hz. This value is associated with *cis*-vicinal coupling. CNMR indicated only one methine resonance at 50.8 ppm. The spectra are shown in Figures 3-1 and 3-2. Furthermore, a single crystal of compound **302** (**Figure 3-3**) was subjected to x-ray diffraction indicating that the (*Z*)-isomer is formed.

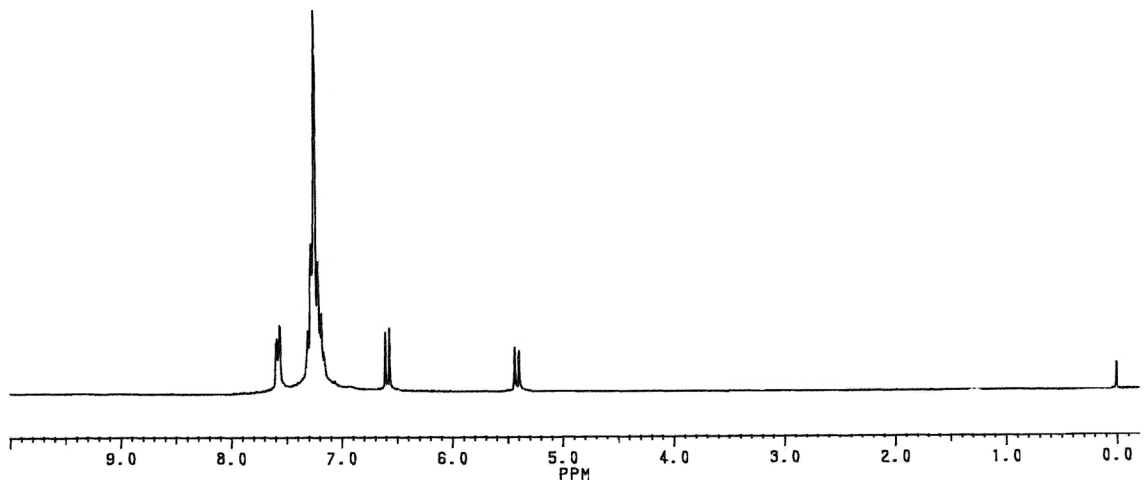


Figure 3-1 HNMR of compound **301**

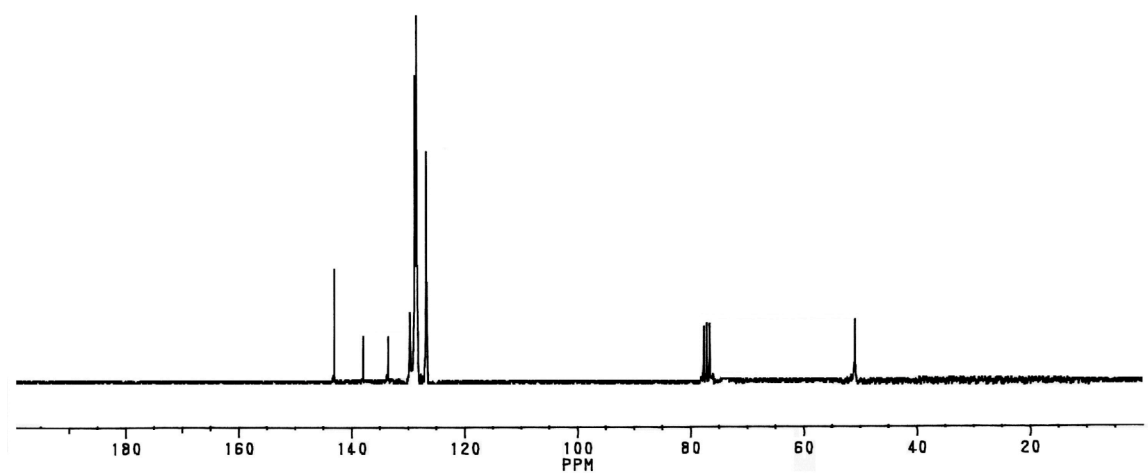


Figure 3-2 CNMR of compound **301**

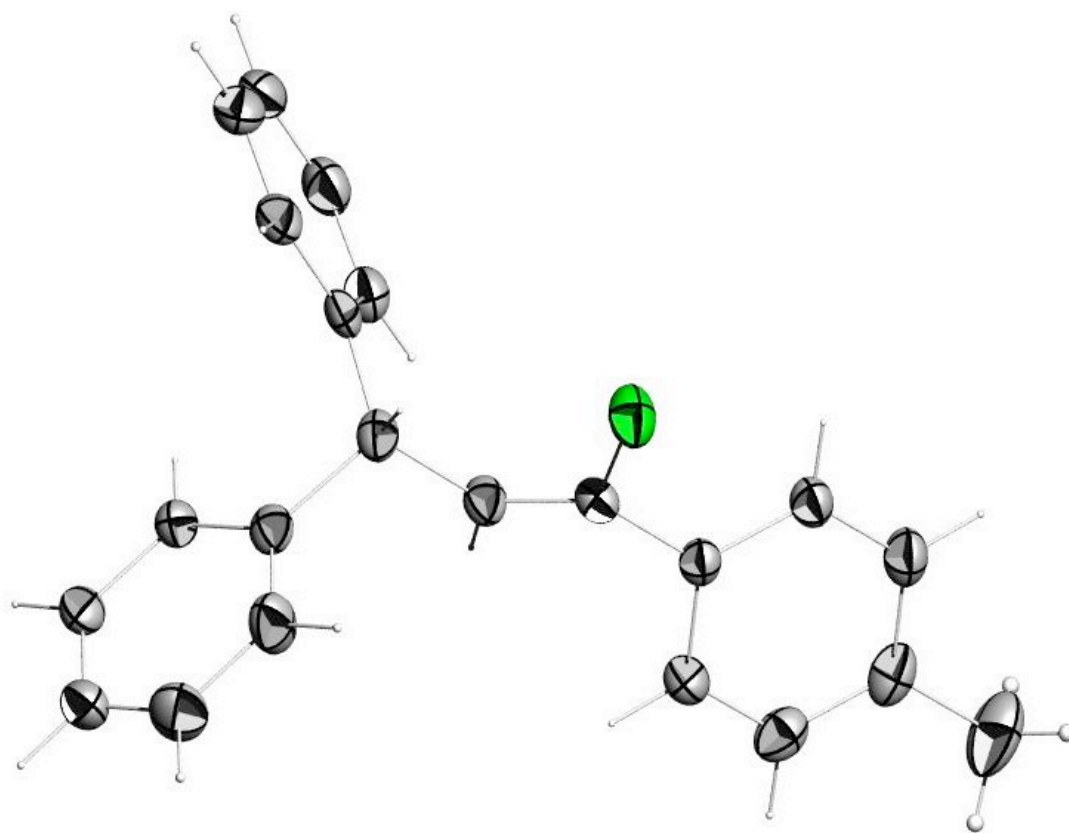
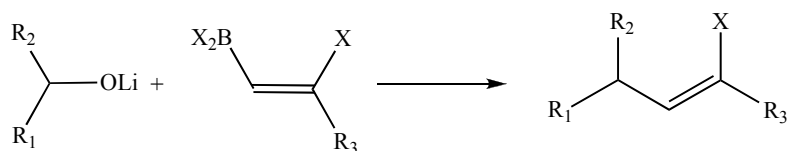


Figure 3-3 ORTEP of compound **302**

The scope of the reaction was then explored with a variety of benzylic alcohols and alkenylboron dihalides as shown in Scheme 3-3. The results are presented in Table 3-1.

Table 3-1 Reaction of benzylic alkoxides with alkenylboron dihalides



Entry	R ₁	R ₂	R ₃	X	Yield (%)	Product
1	Ph	Ph	Ph	Cl	79	301
2	Ph	Ph	4-MePh	Cl	58	302
3	Ph	Ph	Ph	Br	74	303
4	Ph	Ph	4-MePh	Br	53	304
5	4-MeOPh	4-MeOPh	Ph	Cl	73	305
6	4-MeOPh	4-MeOPh	3-FPh	Cl	75	306
7	4-MeOPh	4-MeOPh	4-MePh	Br	59	307
8	4-FPh	4-FPh	4-MePh	Cl	76	308
9	4-ClPh	Ph	Ph	Cl	69	309
10	2-MePh	Ph	4-MePh	Cl	77	310
11	4-NO ₂	Ph	4-MePh	Br	44	311
12	Ph	Me	Ph	Br	64	312
13	4-MeSPh	Me	Ph	Cl	65	313
14	2-MeOPh	Me	Ph	Cl	32	314

Table 3-1 continued

Entry	R ₁	R ₂	R ₃	X	Yield (%)	Product
15	2-Phenanthryl	Me	Ph	Cl	70	315
16	2-Phenanthryl	Me	4-MePh	Cl	62	316

3.2.1 Alkenylation of Benzylic Alcohols with Boron Trichloride and Tribromide

The data compiled in Table 3-1 indicates that the desired products derived from aryl alkynes were produced in good yields when using boron trichloride and boron tribromide. Similar to the transformation outlined in Chapter 2, reactions carried out with boron tribromide produced slightly lower yields than boron trichloride; this is attributed to decomposition during isolation of the product on silica gel. Fortunately, all reactions were stereoselective with respect to retention of halovinyl configuration; the (*Z*)-stereoisomer was formed in all cases. Moreover, it is interesting that aryl methoxy substituents were tolerated in the reaction; as stated earlier, a classic reaction of boron trihalides is the cleavage of ethers. Additionally, the reaction is tolerant of both electron donating and withdrawing functional groups and does not appear to be sensitive to steric factors around the benzylic carbon.

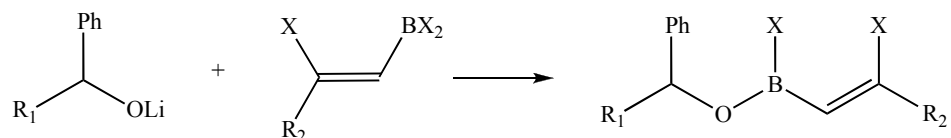
Secondary benzylic alcohols are most suitable for the reaction; diarylbenzylic alcohols and aryl-aliphatic (methyl substituents) benzylic alcohols afforded the expected products. Surprisingly, a reaction conducted with phenylethylmethanol and boron

trichloride did not undergo the halovinyl alkenylation. Primary benzylic alcohols also did not undergo halovinyl alkenylation.

3.3 Mechanistic Study

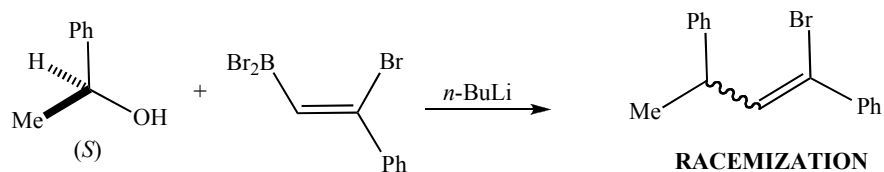
Two specific reactions were designed to probe the mechanism of the reaction to determine whether the process is concerted (with inversion or retention), or proceeds via a cationic process. It is reasonable to assume that the benzylic alkoxide should attack the boron of the halovinyl boron dihalide to form a benzyloxyboron halide intermediate (**Scheme 3-4**).

Scheme 3-4 Formation of the benzyloxyboron halide intermediate



The first test reaction involved a chiral benzylic alcohol (**Table 3-1**, entry 12) as shown in Scheme 3-5.

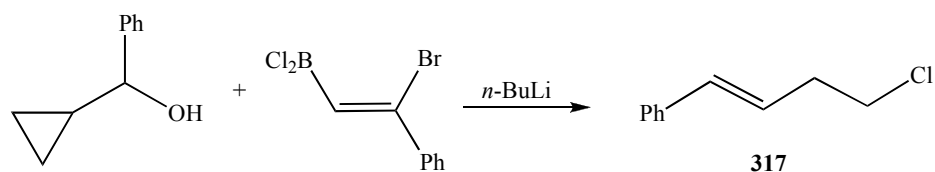
Scheme 3-5 Reaction of chiral benzylic alcohol with alkenylboron dibromide



The reaction led to a racemic product, which supports a cationic mechanism.

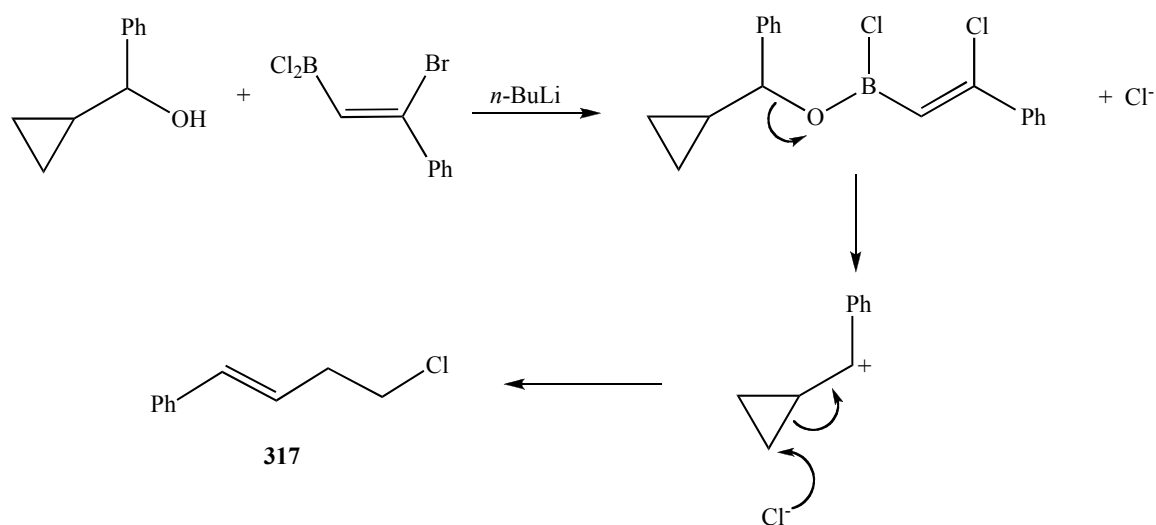
The second reaction designed to gain mechanistic insight involved the reaction of phenylcyclopropylmethanol with an alkenylboron dichloride. The result is shown in Scheme 3-6.

Scheme 3-6 Reaction of phenylcyclopropylmethanol and alkenylboron dichloride



The formation of the ring-opening product supports a mechanism involving a carbocation since it is known that the highly strained geometry of the cyclopropyl group gives the carbons the ability to behave as “sp²-hybridized” carbons. A possible mechanism is shown in Scheme 3-7.

Scheme 3-7 Ring opening of cyclopropyl substituent



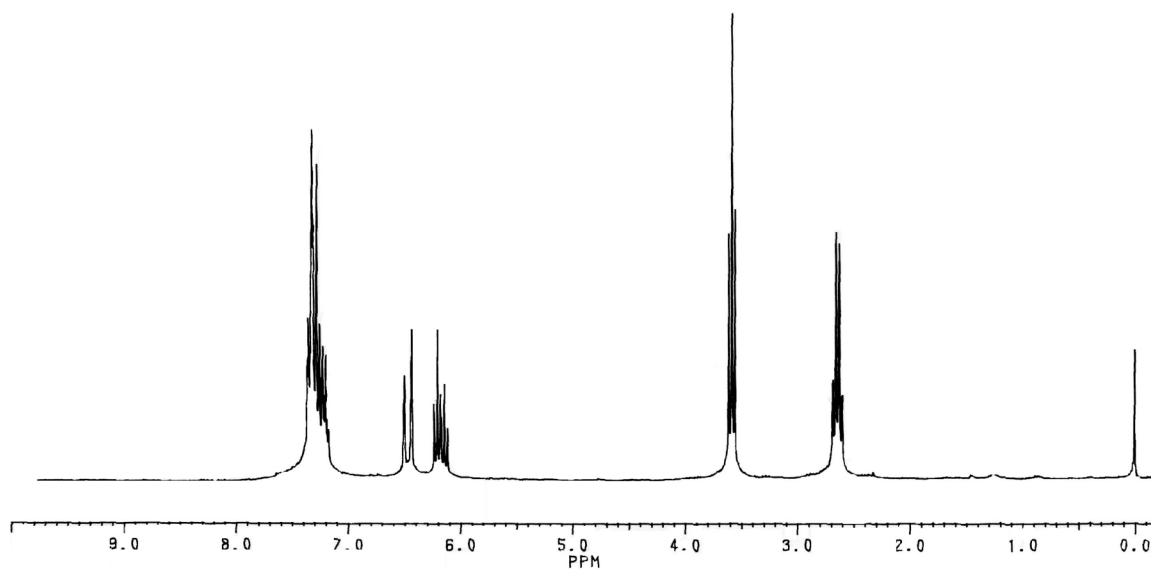


Figure 3-4 1H NMR of compound **317**

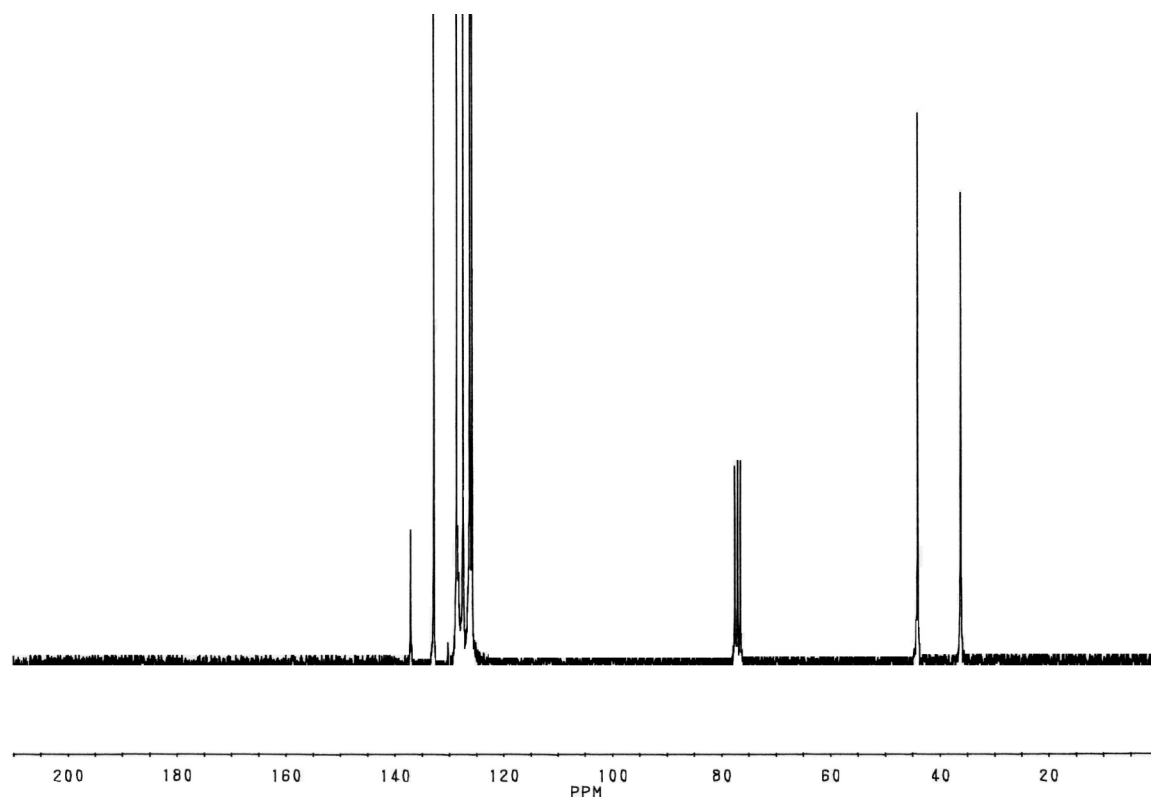


Figure 3-5 13C NMR of compound **318**

It is possible to postulate that a radical pathway could lead to the observation that chiral alcohols racemize and cyclopropyl rings open, however it does not seem likely that a radical pathway is involved. First, none of the reactants typically act as radical initiators in chemical synthesis. Second, radical reactions typically involve a distribution of several products, especially products derived from homocoupling. These were not observed. In all cases, only one product was formed.

3.4 Conclusion

Benzylic alcohols are capable of undergoing halovinyl alkenylation via alkenylboron dichlorides and bromides in good yields. The reaction is stereospecific with respect to retention of the halovinyl olefin configuration and appears to proceed through a cationic mechanism, a postulation supported by racemization of a chiral benzylic alcohol (**Scheme 3-5**) and ring opening of a cyclopropyl substituent (**Scheme 3-6**). In all cases, the (*Z*)-stereoisomers were found to be the major product as confirmed by NMR and X-ray crystallography.

3.5 Experimental Details

3.5.1 General Considerations

All reagents were used as received. Solvents were distilled from the appropriate drying agents under a nitrogen atmosphere. Column chromatography was performed using silica gel (60 Å, 230–400 mesh). Analytical thin-layer chromatography was performed using 250 µm silica (Analtech, Inc., Newark, DE). All glassware was oven-dried for at least 12 hours at 150 °C and cooled under argon or nitrogen. Reactions were

magnetically stirred under argon or nitrogen and monitored on TLC plates using 254 nm UV light, staining with a 50% solution of PMA in EtOH, or development on in an iodine-silica gel chamber.

3.5.2 Representative Procedure for the Synthesis of (*Z*)-1-Halo-trisubstituted olefins

Boron trihalide (1.5 mmol), alkyne (1.5 mmol), and dry dichloromethane (8 mL) were combined in a 50 mL flask and stirred for 1 h at room temperature. In a separate flask, the benzylic alcohol (1.6 mmol) in dry dichloromethane (8 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 *M* solution in hexanes) at 0 °C and warmed to room temperature. After stirring at room temperature for 30 min, the solution was transferred to the first flask and the mixture was allowed to stir overnight. Water (20 mL) was added to quench the reaction. The reaction mixture was extracted with ethyl acetate which was separated and dried over anhydrous MgSO₄. The solvent was removed *in vacuo* and the product purified by silica gel column chromatography using hexane as an eluent.

3.5.3 Characterization of Compounds 301-316

¹HNMR and ¹³CNMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for ¹HNMR and ¹³CNMR spectra (CDCl₃) were referenced to TMS and CDCl₃ respectively. Microanalysis was performed by Atlantic Microlab, Inc. Norcross, Georgia.

(*Z*)-1-Chloro-1,3,3-triphenyl-1-propene (301): ¹HNMR: δ 7.56–7.59 (m, 2H), 7.17–7.30 (m, 13H), 6.59 (d, *J* = 9.47 Hz, 1H), 5.42 (d, *J* = 9.47 Hz, 1H). ¹³CNMR: δ 142.9, 137.8, 133.4, 129.5, 128.6, 128.3, 126.6, 50.8. Anal. Calcd for C₂₁H₁₇Cl: C, 82.75; H,

5.62. Found: C, 82.57; H, 5.65.

(Z)-1-Chloro-1-(4-methylphenyl)-3,3-diphenyl-1-propene (302): ^1H NMR: δ 7.48–7.51 (m, 2H), 7.12–7.34 (m, 12H), 6.55 (d, J = 9.47 Hz, 1H), 5.40 (d, J = 9.47 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR: δ 143.1, 138.7, 135.2, 133.5, 129.0, 128.6, 128.3, 126.5, 50.8, 21.1.

Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{Cl}$: C, 82.87; H, 6.01. Found: C, 82.92; H, 6.03.

(Z)-1-Bromo-1,3,3-triphenyl-1-propene (303): ^1H NMR: δ 7.53–7.54 (m, 2H), 7.13–7.52 (m, 13H), 6.65 (d, J = 9.41 Hz, 1H), 5.36 (d, J = 9.41 Hz, 1H). ^{13}C NMR: δ 142.7, 139.6, 133.3, 128.6, 128.3, 128.2, 127.7, 126.6, 126.2, 53.6. Anal. Calcd for $\text{C}_{21}\text{H}_{17}\text{Br}$: C, 72.22; H, 4.91. Found: C, 72.59; H, 4.61.

(Z)-1-Bromo-1-(4-methylphenyl)-3,3-diphenyl-1-propene (304): ^1H NMR: δ 7.44–7.47 (m, 2H), 7.10–7.34 (m, 12H), 6.62 (d, J = 9.37 Hz, 1H), 5.35 (d, J = 9.37 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR: δ 142.8, 138.7, 136.9, 132.4, 128.9, 128.6, 128.3, 127.6, 126.6, 126.3, 53.6, 21.1. Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{Br}$: C, 72.73; H, 5.27. Found: C, 72.69; H, 6.11.

(Z)-1-Chloro-1-phenyl-3,3-di-(4-methoxy)phenyl-1-propene (305): ^1H NMR: δ 7.59–7.62 (m, 2H), 7.31–7.35 (m, 3H), 7.17 (d, J = 8.61 Hz, 4H), 6.85 (d, J = 8.61 Hz, 4H), 6.54 (d, J = 9.58 Hz, 1H), 5.31 (d, J = 9.58 Hz, 1H), 3.78 (s, 6H). ^{13}C NMR: δ 158.2, 137.9, 135.4, 130.1, 129.2, 128.6, 128.3, 126.6, 113.4, 55.2, 49.1. Anal. Calcd for $\text{C}_{23}\text{H}_{21}\text{ClO}_2$: C, 75.71; H, 5.80. Found: C, 75.47; H, 5.96.

(Z)-1-Chloro-1-(3-fluoro)phenyl-3,3-di-(4-methoxy)phenyl-1-propene (306): ^1H NMR: δ 7.19–7.37 (m, 3H), 7.17 (d, J = 8.63 Hz, 4H), 6.94–6.97 (m, 1H), 6.85 (d, J = 8.63 Hz, 4H), 6.58 (d, J = 9.49 Hz, 1H), 5.30 (d, J = 9.49 Hz, 1H), 3.74 (s, 6H). ^{13}C NMR: δ 164.5, 160.6, 158.3, 140.1, 140.0, 135.0, 131.3, 131.1, 129.8, 129.1, 122.1,

115.5, 115.2, 114.0, 113.5, 55.1, 49.1. Anal. Calcd for $C_{23}H_{20}ClFO_2$: C, 72.15; H, 5.27.

Found: C, 72.22; H, 5.36.

(Z)-1-Bromo-1-(4-methyl)phenyl-3,3-di-(4-methoxy)phenyl-1-propene (307):

^1H NMR: δ 7.44 (d, J = 8.21 Hz, 2H), 7.08–7.17 (m, 6H), 6.83 (d, J = 8.67 Hz, 4H), 6.55

(d, J = 9.37 Hz, 1H), 5.24 (d, J = 9.37 Hz, 1H), 3.77 (s, 6H), 2.33 (s, 3H). ^{13}C NMR:

δ 142.9, 137.8, 133.4, 129.5, 128.6, 128.3, 126.6, 50.8. Anal. Calcd for $C_{24}H_{23}BrO_2$: C,

68.09; H, 5.48. Found: C, 67.93; H, 5.45.

(Z)-1-Chloro-1-(4-methyl)phenyl-3,3-di-(4-fluoro)phenyl-1-propene (308): ^1H NMR:

δ 7.48 (d, J = 8.05, 2H), 7.11–7.19 (m, 6H), 6.93–7.00 (m, 4H), 6.45 (d, J = 9.37 Hz,

1H), 5.34 (d, J = 9.37 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR: δ 163.6, 159.7, 138.9, 138.6,

134.9, 133.9, 129.7, 129.6, 129.0, 128.2, 126.5, 115.6, 115.3, 49.3, 21.1. Anal. Calcd for

$C_{22}H_{17}ClF_2$: C, 74.47; H, 4.83. Found: C, 74.88; H, 4.99.

(Z)-1-Chloro-1,3-diphenyl-3-(4-chloro)phenyl-1-propene (309): ^1H NMR: δ 7.56–7.60

(m, 2H), 7.13–7.35 (m, 12H), 6.53 (d, J = 9.40 Hz, 1H), 5.36 (d, J = 9.40 Hz, 1H).

^{13}C NMR: δ 142.5, 141.4, 137.7, 133.9, 132.4, 129.6, 128.9, 129.8, 128.7, 128.3, 128.2,

126.8, 126.6, 50.2. Anal. Calcd for $C_{21}H_{16}Cl_2$: C, 74.35; H, 4.75. Found: C, 74.39; H,

4.87.

(Z)-1-Chloro-1-(4-methyl)phenyl-3-(2-methyl)phenyl-3-phenyl-1-propene (310):

^1H NMR: δ 7.49 (d, J = 8.22 Hz, 2H), 7.11–7.30 (m, 11H), 6.51 (d, J = 9.23 Hz, 1H), 5.55

(d, J = 9.23 Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H). ^{13}C NMR: δ 143.0, 141.3, 138.7, 136.7,

135.1, 133.3, 130.7, 129.0, 128.8, 128.5, 128.1, 126.6, 126.5, 126.4, 126.2, 47.5, 21.1,

19.9. Anal. Calcd for $C_{23}H_{21}Cl$: C, 82.99; H, 6.36. Found: C, 83.28; H, 6.49.

(Z)-1-Bromo-1-(4-methyl)phenyl-3-(4-nitro)phenyl-3-phenyl-1-propene (311):

^1H NMR: δ 8.14–8.17 (m, 2H), 7.93–7.97 (m, 1H), 7.29–7.62 (m, 11H), 6.26 (d, J = 9.57 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR: δ 147.9, 147.2, 139.5, 133.0, 129.3, 128.8, 128.6, 128.5, 128.2, 123.7, 52.9, 26.0. Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_2\text{S}$: C, 69.82; H, 8.27. Found: C, 69.83; H, 8.28.

(Z)-1-Bromo-1,3-diphenyl-1-butene (312): ^1H NMR: δ 7.46–7.51 (m, 2H), 7.16–7.40 (m, 8H), 6.28 (d, J = 9.02 Hz, 1H), 4.10 (dq, J = 9.02; 7.06 Hz, 1H), 1.45 (d, J = 7.06 Hz, 3H). ^{13}C NMR: δ 144.4, 139.7, 136.0, 128.5, 128.4, 128.1, 127.6, 127.0, 126.4, 124.2, 42.5, 20.6. Anal. Calcd for $\text{C}_{16}\text{H}_{15}\text{Br}$: C, 66.91; H, 5.26. Found: C, 66.79; H, 5.35.

(Z)-1-Chloro-1-phenyl-3-thiomethyl-1-butene (313) ^1H NMR: δ 7.08–7.45 (m, 8H), 6.14 (d, J = 9.02 Hz, 1H), 4.11 (dq, J = 9.02; 6.97 Hz, 1H), 2.42 (s, 3H), 2.30 (s, 3H), 1.42 (d, J = 6.97 Hz, 3H). ^{13}C NMR: δ 141.9, 138.3, 136.0, 135.1, 131.9, 131.2, 128.9, 127.5, 127.1, 126.3, 39.1, 21.0, 20.8, 16.1. Anal. Calcd for $\text{C}_{18}\text{H}_{19}\text{ClS}$: C, 71.38; H, 6.32. Found: C, 71.81; H, 6.18.

(Z)-1-Chloro-1-phenyl-3-(2-methoxyphenyl)-1-butene (314): ^1H NMR: δ 6.85–7.58 (m, 9H), 6.38 (d, J = 8.99 Hz, 1H), 4.41 (dq, J = 8.99; 7.01 Hz, 1H), 3.83 (s, 3H), 1.46 (d, J = 7.01 Hz, 3H). ^{13}C NMR: δ 157.2, 138.4, 133.2, 132.1, 131.5, 128.2, 127.6, 127.3, 126.5, 120.6, 110.9, 55.4, 35.0, 20.2. Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{ClO}$: C, 74.86; H, 6.28. Found: C, 75.14; H, 6.21.

(Z)-1-Chloro-1-phenyl-3-(2-phenanthryl)-1-butene (315): ^1H NMR: δ 8.61–8.72 (m, 2H), 7.22–7.87 (m, 12H), 6.38 (d, J = 9.17 Hz, 1H), 4.44 (dq, J = 9.17; 6.94 Hz, 1H), 1.63 (d, J = 6.94 Hz, 3H). ^{13}C NMR: δ 143.1, 138.1, 132.4, 132.2, 132.1, 130.7, 130.4, 130.2,

128.9, 128.6, 128.5, 128.3, 126.6, 126.1, 122.6, 120.6, 40.3, 21.1. Anal. Calcd for $C_{24}H_{19}Cl$: C, 84.07; H, 5.59. Found: C, 84.13; H, 5.32.

(Z)-1-Chloro-1-(4-methylphenyl)-3-(2-phenanthryl)-1-butene (316): ^1H NMR: δ 8.60-8.70 (m, 2H), 7.08-7.85 (m, 11H), 6.32 (d, $J = 8.98$ Hz, 1H), 4.42 (dq, $J = 8.98$; 6.95 Hz, 1H), 2.30 (s, 3H), 1.60 (d, $J = 6.95$ Hz, 3H). ^{13}C NMR: δ 143.2, 138.4, 132.2, 132.1, 130.7, 130.4, 130.2, 128.9, 128.8, 128.6, 126.6, 126.4, 126.1, 122.6, 120.5, 40.3, 21.1. Anal. Calcd for $C_{25}H_{21}Cl$: C, 84.14; H, 5.93. Found: C, 84.28; H, 6.16.

(E)-1-Phenyl-4-chloro-1-butene (317): ^1H NMR: δ 7.20-7.36 (m, 5H), 6.43-6.50 (m, 1H), 6.14-6.23 (m, 1H), 3.56-3.61 (m, 2H), 2.60-2.69 (m, 2H). ^{13}C NMR: δ 137.0, 132.7, 128.5, 127.3, 126.1, 125.7, 43.9, 36.1.

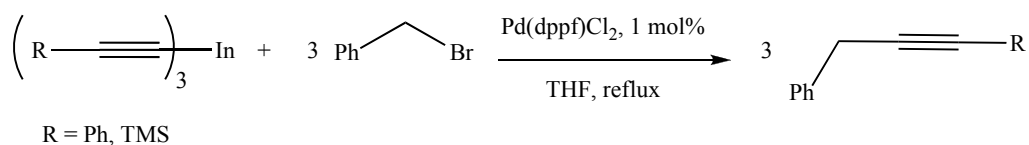
Chapter 4: Alkynylation of Alcohols with Alkynylboron Dihalides

4.1 Introduction

Alkynes are proving to be synthetically viable starting materials in modern synthesis⁶¹ finding utility in materials science⁶² and as a common structural feature in natural products.⁶³ Alkynes have very similar reactivity when compared to alkenes. Terminal alkynes are the most acidic of the hydrocarbons. The facile removal of the terminal hydrogen with base permits an alkyne to act as a viable nucleophile in S_N2 reactions.

The Sonagashira reaction⁶⁴ is traditionally used to couple copper acetylides with aryl or vinyl electrophiles, but the reaction suffers limitations such as loss of product yield due to homocoupling and the tendency of propargylic acetylides to undergo allene isomerization at high temperatures. Synthetic routes focused on transition metal-catalyzed alkynylation have not been thoroughly developed with respect to electrophilic propargylic, allylic, and benzylic species.⁶⁵ For example, Sarandeses has reported that trialkynyl indium can couple with benzylic electrophiles in the presence of a palladium catalyst as shown in Scheme 4-1.^{65c}

Scheme 4-1 Indium promoted palladium-catalyzed alkynylation



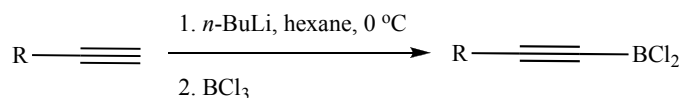
Chapters 2 and 3 contain descriptions of the synthetic utility of alkenylboron dihalides as halovinyl synthons of use in the direct substitution of propargylic, allylic,

and benzylic alcohols through their alkoxides. In a continuation of this study, alkynylboron dihalides were investigated as reactive intermediates. A direct, transition metal-free substitution of aliphatic hydroxyl groups with an alkynyl species would be of considerable value to modern organic synthesis.

4.2 Results and Discussion

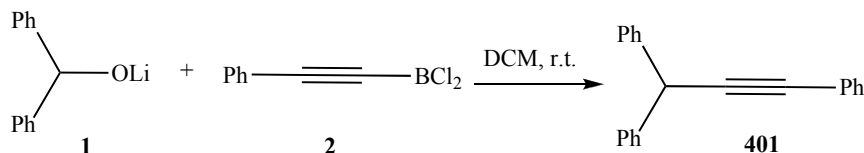
The current method of preparing alkynylboron dihalides involves a low temperature boron-tin exchange reaction with alkynylstannanes.⁶⁶ Given the known toxicity of organostannanes, we postulated that it might be possible to prepare alkynylboron dihalides by simply treating a terminal alkyne with base and then adding boron trihalide to the solution to allow for an S_N2-like reaction to place as shown in Scheme 4-2.

Scheme 4-2 Preparation of alkynylboron dihalides



To examine the feasibility of using alkynylboron dihalides as synthons for alkynyl species in synthesis, Diphenylmethanol **1** was subjected to alkynylboron dihalide **2** as shown in Scheme 4-3.⁶⁷

Scheme 4-3 Preparation of compound **401**



1,3,3-Triphenyl-1-propyne **401** was isolated in 68% yield. The HNMR displays a singlet resonance at 5.19 ppm indicating a methine hydrogen, and CNMR shows two resonances at 89.4 and 80.0 ppm corresponding to an alkyne. Figures 4-1 and 4-2 do not indicate the presence of an allene isomer.

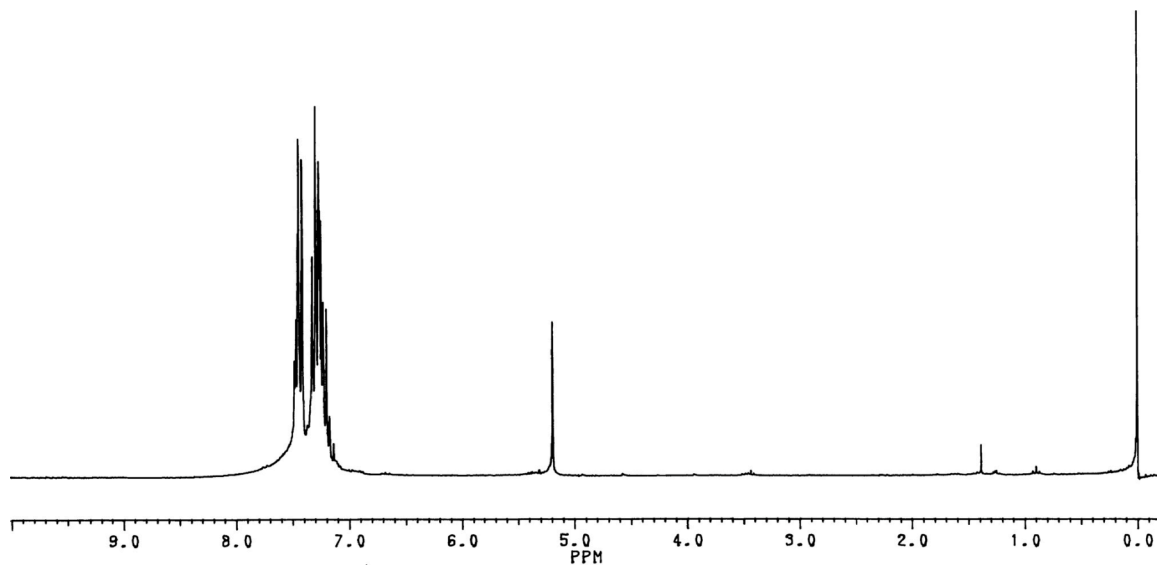


Figure 4-1 HNMR of compound **401**

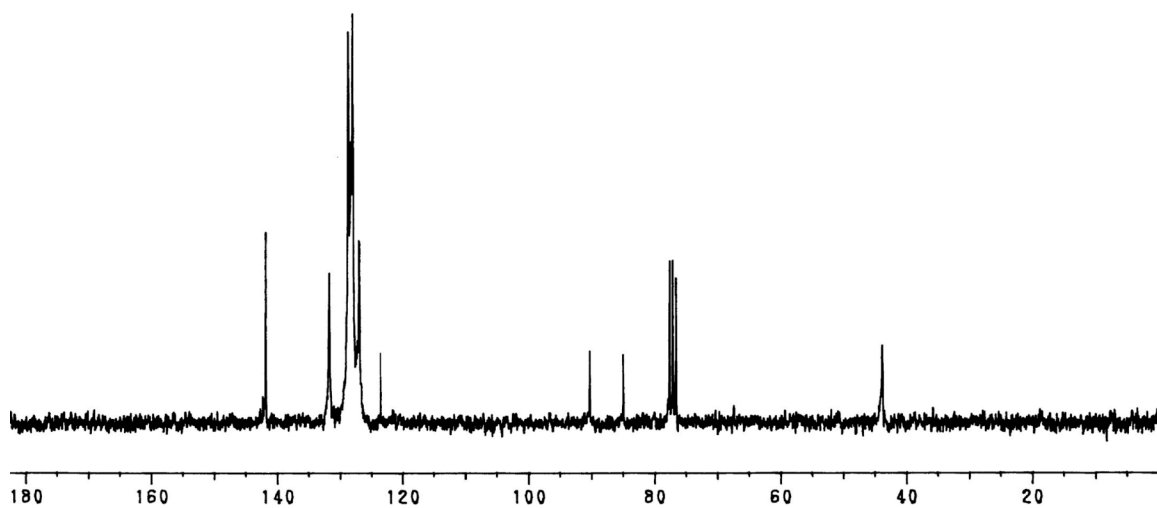
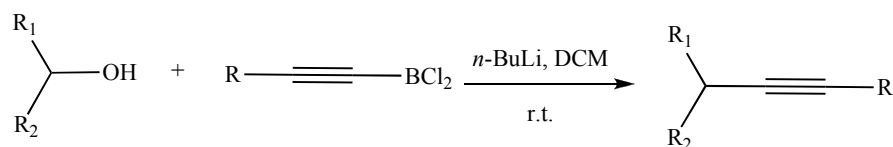


Figure 4-2 CNMR of compound **402**

Since alkynylboron dihalides can apparently serve as practical synthons, the scope of the reaction was then evaluated with a variety of benzylic, allylic, and propargylic alcohols.

The results are shown in Table 4-1.

Table 4-1 Reaction of benzylic, allylic, and propargylic alkoxides with alkynylboron dihalides



Entry	R	R ₁	R ₂	Yield (%)	Product
1	Ph	Ph	Ph	68	401
2	4-MePh	Ph	Ph	64	402
3	2-FPh	Ph	Ph	76	403
4	Ph	4-MeOPh	4-MeOPh	81	404
5	4-MePh	4-MeOPh	4-MeOPh	77	405
6	Ph	4-FPh	4-FPh	74	406
7	4-MeO	4-FPh	4-FPh	57	407
8	Ph	Ph	4-ClPh	84	408
9	2-FPh	Ph	4-ClPh	71	409
10	Ph	Ph	2-MePh	57	410
11	2-FPh	Ph	Me	26	411
12	Ph	Ph	(<i>E</i>)-PhCH=CH	93	412

Table 4-1 continued

Entry	R	R ₁	R ₂	Yield (%)	Product
13	2-FPh	Ph	(<i>E</i>)-PhCH=CH	86	413
14	Ph	Ph	(<i>E,E</i>)-PhCH=CH- CH=CH	71	414
15	Ph	4-ClPh	PhC $\equiv$ C	69	415
16	Ph	4-MePh	PhC $\equiv$ C	77	416
17	4-MePh	4-MePh	PhC $\equiv$ C	83	417
18	<i>n</i> -Octyl	4-MePh	PhC $\equiv$ C	37	418

4.2.1 Alkynylation of Benzylic, Allylic, and Propargylic Alcohols with Alkynylboron Dihalides

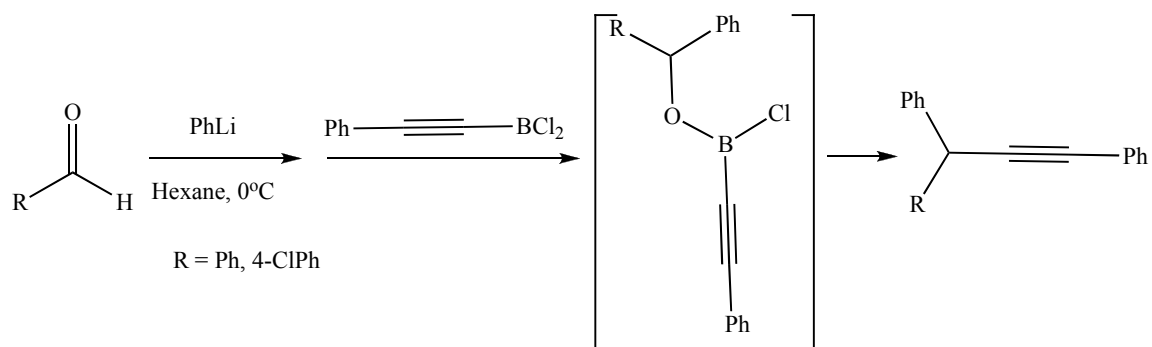
The data compiled in Table 4-1 indicates the desired products are formed in good to high yields from alkynylboron dichlorides and benzylic, allylic, or propargylic alcohols through their alkoxides. Diaryl secondary benzylic alcohols (entries 1-10) formed the desired products in good yields and were tolerant of a variety of electronic substituents. The reaction also proceeded with aryl-aliphatic substitution. Aryl-alkenyl alcohols (entries 12-14) formed the resultant 1,4-enynes in good to high yields, while aryl-alkynyl alcohols (entries 15-18) generated 1,4-diynes in good yield. Notably, 1,4-enynes and 1,4-diynes are intermediates often found in routes to natural products. This facile route through alkynylboron dihalides and alkoxides under mild conditions may

help simplify complex natural product syntheses. Most importantly, the reaction allows for secondary internal alkynes to be synthesized cleanly under mild conditions; the aforementioned limitation of allene isomerization is avoided. It should also be noted that transition metal-catalyzed coupling and alkyne metathesis do not provide clean routes to secondary internal alkynes.

4.2.2 Mechanistic Study

The identification of a cationic mechanism in Chapters 2 and 3 for alkenylation reactions via alkenylboron dihalides implies that a cationic mechanism should also be involved in alkoxide alkynylation with alkynylboron dichloride. It also seems reasonable that a similar oxyboron halide intermediate should also be formed. In accord with the results presented in Chapters 2 and 3, a tandem reaction was set up to explore the possibility of generating a secondary internal alkyne.

Scheme 4-4 A tandem reaction to internal alkynes



Fortunately, the tandem reaction afforded the anticipated products in good yield (R= Ph, 57% **401**; R= 4-ClPh, 64% **408**), although the yields are slightly lower when compared to

the original reaction conditions; it might be possible to increase the yield by using more than one equivalent of phenyllithium to ensure the Grignard-like reaction goes to completion.

4.3 Conclusion

Alkynylboron dichlorides can serve as viable synthons in the direct substitution of benzylic, allylic, and propargylic alkoxides to form internal acetylene derivatives. The reaction is tolerant to a variety of electronic substituents on the aromatic rings, and is capable of generating secondary internal alkynes, 1,4-enynes, and 1,4-diynes in good to high yields. Additionally, the reaction obviates the limitations associated with transition metal-catalyzed reactions and completely avoids undesirable allene isomerizations.

4.4 Experimental Details

4.4.1 General Considerations

All reagents were used as received. Solvents were distilled from the appropriate drying agents under a nitrogen atmosphere. Column chromatography was performed using silica gel (60 Å, 230–400 mesh). Analytical thin-layer chromatography was performed using 250 µm silica (Analtech, Inc., Newark, DE). All glassware was oven-dried for at least 12 hours at 150 °C and cooled under argon or nitrogen. Reactions were magnetically stirred under argon or nitrogen and monitored on TLC plates using 254 nm UV light, staining with a 50% solution of PMA in EtOH, or development on in an iodine-silica gel chamber.

4.4.2 Preparation of Alkynylboron Dihalides

A solution of alkyne (1.5 mmol) in dry hexane (8 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 M solution in hexane) at 0 °C. After stirring at room temperature for 30 min, boron trihalide (1.5 mmol) was added to the reaction mixture.

4.4.3 Representative Procedure for the Synthesis of Secondary Alkylacetylene Derivatives

Alcohol (1.6 mmol) in dry dichloromethane (8 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 M solution in hexane) at 0 °C and then warmed to room temperature. After stirring at room temperature for 30 min, this solution was transferred to the alkynylboron dihalide and the mixture was allowed to stir overnight. Water (20 mL) was added to quench the reaction. The mixture was extracted with ethyl acetate dried over anhydrous MgSO₄, the solvent removed *in vacuo*, and the product purified by silica gel column chromatography using hexane as an eluent. Products were detected on TLC plates using 254 nm UV light or staining with a 50% solution of PMA in EtOH.

4.4.4 Characterization of Compounds 401-418

Alcohols: (Table 4-1, entries 1 and 4) were purchased from Aldrich Chemical Company; 3, 11-14 were obtained by reduction of the corresponding ketones according to the literature procedure.⁶⁸ Compounds 8-10 were prepared from corresponding aryl aldehyde by reaction with phenylmagnesium bromide.⁶⁹ Compounds 15-18 were prepared according to the literature procedure.⁷⁰

¹HNMR and ¹³CNMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for ¹HNMR and ¹³CNMR spectra (CDCl₃) were referenced

to TMS and CDCl₃ respectively. Microanalysis was performed by Atlantic Microlab, Inc. Norcross, Georgia.

1,3,3-Triphenyl-1-propyne (401)⁷¹: ¹HNMR: δ 7.19–7.47 (m, 15H), 5.19 (s, 1H).

¹³CNMR: δ 141.7, 131.7, 128.6, 128.2, 127.9, 126.9, 123.5, 90.2, 84.9, 43.7.

1-(4-Methylphenyl)-3,3-diphenyl-1-propyne, (402): ¹HNMR: δ 7.07–7.45 (m, 14H), 5.19 (s, 1H), 2.32 (s, 3H). ¹³CNMR: δ 142.2, 141.9, 138.0, 131.5, 128.9, 128.6, 128.4, 128.0, 127.2, 126.8, 89.4, 80.0, 43.7, 21.3. Anal. Calcd for C₂₂H₁₈: C, 93.57; H, 6.43. Found: C, 93.34; H, 6.61.

1-(2-Fluorophenyl)-3,3-diphenyl-1-propyne (403): ¹HNMR: δ 7.14–7.42 (m, 13H), 6.96–6.99 (m, 1H), 5.19 (s, 1H). ¹³CNMR: δ 164.3, 160.4, 141.4, 129.7, 128.7, 127.9, 127.6, 127.0, 125.4, 118.6, 118.3, 115.5, 115.2, 91.3, 83.7, 43.7. Anal. Calcd for C₂₁H₁₅F: C, 88.09; H, 5.28. Found: C, 87.57; H, 5.09.

1-Phenyl-3,3-di(4-methoxyphenyl)-1-propyne, (404): ¹HNMR: δ 7.44–7.48 (m, 2H), 7.26–7.34 (m, 7H), 6.83–6.86 (m, 4H), 5.11 (s, 1H), 3.76 (s, 6H). ¹³CNMR: δ 156.4, 134.2, 131.6, 128.8, 128.2, 127.8, 123.6, 113.9, 90.8, 84.5, 55.2, 42.0. Anal. Calcd for C₂₃H₂₀O₂: C, 84.12; H, 6.14. Found: C, 83.97; H, 5.78.

1-(4-Methylphenyl)-3,3-di(4-methoxyphenyl)-1-propyne (405): ¹HNMR: δ 6.81–7.36 (m, 12H), 5.09 (s, 1H), 3.73 (s, 6H), 2.30 (s, 3H). ¹³CNMR: δ 158.3, 134.3, 131.4, 130.6, 129.1, 128.8, 126.4, 113.9, 90.0, 84.5, 55.3, 42.0, 21.3. HR-MS Calcd for C₂₄H₂₂O₂: 342.1620. Found: 342.1612.

1-Phenyl-3,3-di(4-fluorophenyl)-1-propyne (406): ¹HNMR: δ 6.95–7.48 (m, 13H), 5.14 (s, 1H). ¹³CNMR: δ 163.8, 159.9, 137.3, 131.6, 129.4, 129.3, 128.3, 128.2, 123.1,

115.6, 115.3, 89.6, 85.3, 42.2. HR-MS Calcd for C₂₁H₁₄F₂: 304.1064. Found: 304.1057.

1-(4-Methoxyphenyl)-3,3-di(4-fluorophenyl)-1-propyne (407): ¹HNMR: δ 6.61–7.41 (m, 12H), 5.14 (s, 1H), 3.80 (s, 3H). ¹³CNMR: δ 163.8, 159.8, 137.5, 133.0, 129.7, 129.6, 129.4, 129.2, 128.0, 115.6, 115.3, 113.9, 113.7, 88.1, 85.2, 55.3, 42.3. HR-MS Calcd for C₂₂H₁₆F₂: 334.1169. Found: 334.1161.

1,3-Diphenyl-3-(4-chlorophenyl)-1-propyne (408): ¹HNMR: δ 7.21–7.47 (m, 14H), 5.14 (s, 1H). ¹³CNMR: δ 141.2, 140.3, 132.7, 131.6, 129.2, 128.7, 128.2, 128.1, 127.8, 127.1, 123.2, 89.6, 85.2, 43.1. Anal. Calcd for C₂₁H₁₅Cl: C, 83.30; H, 4.99. Found: C, 83.77; H, 5.04.

1-(2-Fluorophenyl)-3-phenyl-3-(4-chlorophenyl)-1-propyne (409): ¹HNMR: δ 6.95–7.39 (m, 13H), 5.15 (s, 1H). ¹³CNMR: δ 164.3, 160.4, 140.7, 139.9, 132.9, 129.9, 129.7, 129.2, 128.8, 127.8, 127.5, 127.2, 118.7, 118.3, 115.6, 115.3, 90.7, 84.1, 43.1. Anal. Calcd for C₂₁H₁₄ClF: C, 78.63; H, 4.40. Found: C, 78.08; H, 4.32.

1,3-Diphenyl-3-(2-methylphenyl)-1-propyne (410): ¹HNMR: δ 7.15–7.52 (m, 14H), 5.37 (s, 1H), 2.31 (s, 3H). ¹³CNMR: δ 140.7, 139.4, 135.9, 131.6, 130.7, 128.8, 128.5, 128.2, 128.0, 127.9, 127.5, 127.3, 127.1, 126.7, 126.3, 123.6, 90.2, 84.5, 40.8, 19.7. Anal. Calcd for C₂₂H₁₈: C, 93.57; H, 6.43. Found: C, 93.13; H, 6.29.

1-(2-Fluorophenyl)-3-phenyl-1-butyne (411): ¹HNMR: δ 7.21–7.46 (m, 8H), 6.95–7.01 (m, 1H), 3.97 (q, *J* = 7.15 Hz, 1H), 1.57 (d, *J* = 7.15, 3H). ¹³CNMR: δ 164.3, 160.4, 143.0, 129.8, 129.6, 128.6, 128.6, 128.2, 127.5, 126.9, 126.8, 126.5, 118.6, 118.3, 115.2, 114.9, 93.7, 81.3, 32.4, 24.3. HR-MS Calcd for C₁₆H₁₃F: 224.1001. Found: 224.0995.

(*E*)-1,3,5-Triphenylpent-4-yne-1-ene (412): ¹HNMR: δ 7.16–7.48 (m, 15H), 6.75 (d, *J* =

15.6 Hz, 1H), 6.30 (dd, $J = 15.6$; 6.54 Hz, 1H), 4.71 (d, $J = 6.54$ Hz, 1H). $^{13}\text{CNMR}$: δ 140.2, 136.7, 131.6, 130.4, 129.5, 128.6, 128.5, 128.2, 127.7, 127.0, 126.5, 123.4, 88.8, 85.4, 41.2. Anal. Calcd for $\text{C}_{23}\text{H}_{18}$: C, 93.84; H, 6.16. Found: C, 93.52; H, 6.08.

(*E*)-5-(2-Fluorophenyl)-1,3-diphenylpent-4-yne-1-ene (413): $^1\text{HNMR}$: δ 7.19–7.47 (m, 13H), 6.89–6.97 (m, 1H), 6.71 (d, $J = 15.5$ Hz, 1H), 6.30 (dd, $J = 15.4$; 6.19 Hz, 1H), 4.71 (d, $J = 6.19$ Hz, 1H). $^{13}\text{CNMR}$: δ 164.3, 160.4, 141.8, 139.9, 136.7, 130.6, 129.8, 129.2, 128.5, 127.6, 126.5, 125.3, 125.2, 118.7, 118.3, 115.5, 115.0, 89.9, 84.2, 41.1. Anal. Calcd for $\text{C}_{23}\text{H}_{17}\text{F}$: C, 88.43; H, 5.49. Found: C, 88.65; H, 5.81.

(*E,E*)-1,5,7-Triphenylhepta-1,3-dien-6-yne (414): $^1\text{HNMR}$: δ 7.20–7.51 (m, 15H), 6.74–6.80 (m, 1H), 6.54–6.60 (m, 1H), 6.22–6.26 (m, 1H), 5.95 (dd, $J = 15.6$; 6.51 Hz, 1H), 4.68 (d, $J = 6.51$ Hz, 1H). $^{13}\text{CNMR}$: δ 140.3, 137.3, 133.6, 131.7, 130.8, 128.6, 127.7, 126.3, 88.8, 85.7, 41.9. Anal. Calcd for $\text{C}_{25}\text{H}_{20}$: C, 93.71; H, 6.29. Found: C, 93.44; H, 5.94.

1,5-Diphenyl-3-(4-chlorophenyl)-1,4-pentadiyne (415): $^1\text{HNMR}$: δ 7.26–7.61 (m, 14H), 5.16 (s, 1H). $^{13}\text{CNMR}$: δ 136.5, 133.4, 131.8, 128.8, 128.7, 128.4, 128.2, 122.7, 86.0, 83.1, 29.5. HR-MS Calcd for $\text{C}_{23}\text{H}_{15}\text{Cl}$: 326.0862. Found: 326.0854.

1,5-Diphenyl-3-(4-methylphenyl)-1,4-pentadiyne (416): $^1\text{HNMR}$: δ 7.16–7.56 (m, 14H), 5.15 (s, 1H), 2.33 (s, 3H). $^{13}\text{CNMR}$: δ 137.1, 135.0, 131.7, 129.4, 128.1, 127.2, 123.0, 86.8, 82.6, 29.7, 21.1. Anal. Calcd for $\text{C}_{24}\text{H}_{18}$: C, 94.08; H, 5.92. Found: C, 94.47; H, 5.84.

1-Phenyl-3,5-di(4-methylphenyl)-1,4-pentadiyne (417): $^1\text{HNMR}$: δ 7.07–7.56 (m, 13H), 5.15 (s, 1H), 2.35 (s, 3H), 2.31 (s, 3H). $^{13}\text{CNMR}$: δ 138.2, 137.1, 135.2, 131.7,

129.0, 128.2, 127.2, 123.1, 119.9, 86.9, 86.0, 82.7, 82.5, 29.7, 21.2. HR-MS Calcd for $C_{25}H_{20}$: 320.1565. Found: 320.1558.

1-Phenyl-3-(4-methylphenyl)trideca-1,4-diyne (418): ^1H NMR: δ 7.07–7.50 (m, 9H), 4.93 (s, 1H), 2.21–2.44 (m, 5H), 1.26–1.53 (m, 12H), 0.89 (t, J = 4.25 Hz, 3H).

^{13}C NMR: δ 136.9, 135.7, 131.8, 129.3, 128.6, 128.5, 128.1, 128.0, 127.1, 126.6, 126.1, 87.8, 83.2, 31.8, 31.6, 29.1, 28.9, 28.7, 22.7, 21.0, 18.9, 14.1. HR-MS Calcd for $C_{27}H_{32}$: 356.2504. Found: 356.2493.

Chapter 5: Allylation of Propargylic, Allylic, and Benzylic Alcohols

5.1 Introduction

The chemistry of carbocations has been thoroughly studied and has attracted considerable attention, most notably, the honor of the Nobel Prize in Chemistry for 1994 presented to George A. Olah. There have been extensive studies on carbocations generated from propargylic, allylic, and benzylic alcohols⁷² in addition to the cleavage reactions involving carbon-hydrogen,⁷³ carbon-carbon,⁷⁴ carbon-nitrogen,⁷⁵ and carbon-oxygen bonds.⁷⁶ Unfortunately, carbocations derived from these alcohols are not considered favorable intermediates in modern synthesis since they most often require strong Brønsted acid conditions to protonate the hydroxyl group. However, due to the synthetic viability of propargyl, allyl, and benzyl species in synthesis, it would be valuable to develop a straightforward method to substitute the hydroxyl moiety with an allyl species.

In 1972, K.M. Nicholas and R. Pettit reported that dicobalt hexacarbonyl-complexed propargylic alcohols were easily dehydrated upon treatment by acid to generate the corresponding 1,3-enynes; uncomplexed propargylic alcohols did not undergo the reaction.⁷⁷ The reaction of propargylic alcohols and nucleophiles with dicobalt complexes later became known as the Nicholas reaction (**Scheme 1-4**).¹⁶

Generally speaking, the Nicholas reaction allows for C-, O-, S-, and N-nucleophiles to readily replace propargylic alcohols with either a protic or Lewis acid. Decomplexation of the cobalt species is typically done using oxidative conditions involving reagents such as ceric ammonium nitrate. Reductive decomplexation is also

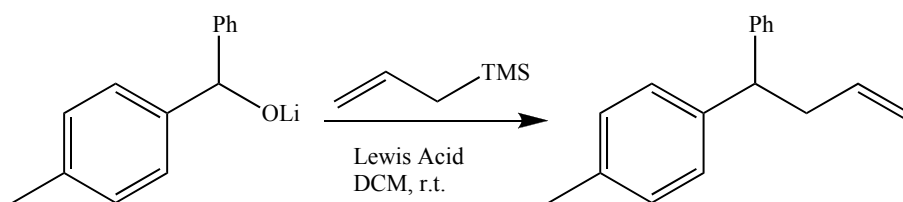
possible using Wilkinson's catalyst or lithium / liquid ammonia – the final product produces the corresponding alkene.

The results discussed in Chapters 2, 3, and 4 illustrate that the oxyboron halide species can act as a leaving group to generate an intermediate carbocation that is suitable for halovinyl alkenylation and alkynylation. It is known that allyltrimethylsilane can trap a cationic intermediate, therefore, if a cationic pathway is in place the direct allylation of propargylic, allylic, and benzylic alcohols with boron trichloride should be feasible.

5.2 Results and Discussion

Due to the apparent ability of the oxyboron halide species to act as a leaving group, it occurred to us that other Lewis acids might be able to function in a similar manner. To examine the feasibility of this presumption, several Lewis acids were allowed to react with lithium 4-methylbenzhydroxide and allyltrimethylsilane as shown in Table 5-1.

Table 5-1 Lewis acid promoted allylation of lithium 4-methylbenzhydroxide



Entry	Lewis Acid	Yield (%)
1	BCl ₃	96
2	FeCl ₃	95

Table 5-1 continued

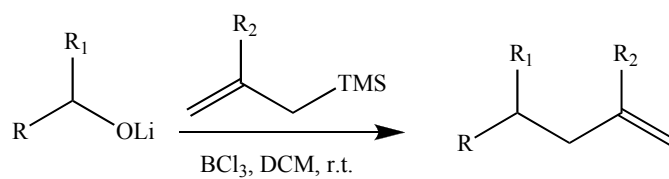
Entry	Lewis Acid	Yield (%)
3	AlCl ₃	77
4	SnCl ₄	77
5	SiCl ₄	27
6	CuCl ₂	0
7	NiCl ₂	0

5.2.1 Allylation Benzylic, Allylic and Propargylic Alcohols using Boron

Trichloride and Iron(III) Chloride

Due to the very high yields associated with boron trichloride and iron(III) chloride, in association with their relatively inexpensive commercial availability and low toxicity, the scope of the reaction was explored with a series of benzylic, allylic, and propargylic alcohols.⁷⁸

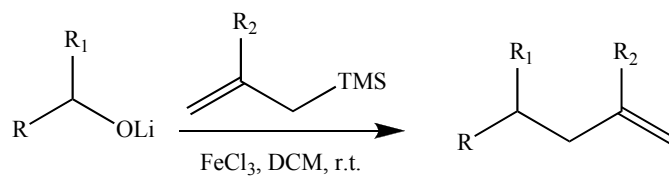
The reaction proceeded efficiently with boron trichloride and iron(III) chloride generating the anticipated products in good to high yields. It should be noted that five of the reactions attempted with iron(III) chloride produced the same products as boron trichloride; the boron trichloride results are not tabulated in Table 5-3 but are reported in the literature.^{78b} The reaction is tolerant to electron-donating and electron-withdrawing substituents. In addition, aryl-ether linkages are preserved when using boron trichloride. The results are shown in Tables 5-2 and 5-3.

Table 5-2 Boron trichloride allylation of benzylic, allylic and propargylic alkoxides

Entry	R	R_1	R_2	Yield (%)	Product
1	$PhC \equiv C$	Ph	H	76	501
2	$PhC \equiv C$	4-ClPh	H	73	502
3	4-MePhC $\equiv$ C	4-ClPh	H	67	503
4	$PhC \equiv C$	2-MePh	H	71	504
5	4-MePhC $\equiv$ C	2-MePh	H	57	505
6	4-MeOPhC $\equiv$ C	2-MePh	H	63	506
7	$PhC \equiv C$	3,4,5-(MeO) ₃ Ph	H	41	507
8	3-FPhC $\equiv$ C	3,4,5-(MeO) ₃ Ph	H	53	508
9	$PhC \equiv C$	4-FPh	H	64	509
10	<i>n</i> -butyl-C $\equiv$ C	4-ClPh	H	74	510
11	$PhC \equiv C$	4-ClPh	Me	65	511
12	4-MePhC $\equiv$ C	4-ClPh	Me	72	512
13	Ph	Ph	H	90	513
14	4-FPh	4-FPh	H	91	514
15	4-MeOPh	4-MeOPh	H	87	515

Table 5-2 continued

Entry	R	R ₁	R ₂	Yield (%)	Product
16	Ph	4-ClPh	H	96	516
17	Ph	(<i>E</i>)-PhCH=CH	H	78	517

Table 5-3 Iron(III) chloride allylation of benzylic, allylic and propargylic alkoxides

Entry	R	R ₁	R ₂	Yield (%)	Product
1	Ph	4-MePh	H	95	518
2	Ph	2-MePh	H	93	519
3	Ph	4-CNPh	H	40	520
4	Ph	6-(2,3-Dihydrobenzo[<i>b</i>][1,4]dioxine)Ph	H	75	521
5 ^a	Ph	Ph	H	96	522
6	Ph	2-Bicyclo[2.2.1]heptyl ^b	H	80	523
7	2-MeOPh	Me	H	83	524
8	Ph	<i>n</i> -Butyl-C $\equiv$ C	H	32	525

Table 5-3 continued

Entry	R	R ₁	R ₂	Yield (%)	Product
9 ^c	Ph	Ph-C $\equiv$ C	H	78	526

^a Reaction conducted triphenylmethanol

^b Mixture of endo and exo

^c Reaction conducted with 1,1,3-triphenylprop-2-yn-1-ol

HNMR of compound **515** clearly shows the presence of an allyl moiety. The resonance at approximately 5 ppm corresponds to the two terminal hydrogens in the allyl group. At approximately 5.7 ppm is the multiplet of the internal vinyl hydrogen. The triplet at approximately 3.9 is the methine hydrogen, the triplet at 2.7 is the aliphatic methylene hydrogens, and the singlet at 3.7 is the methoxy hydrogens. The spectra are shown in Figures 5-1 and 5-2.

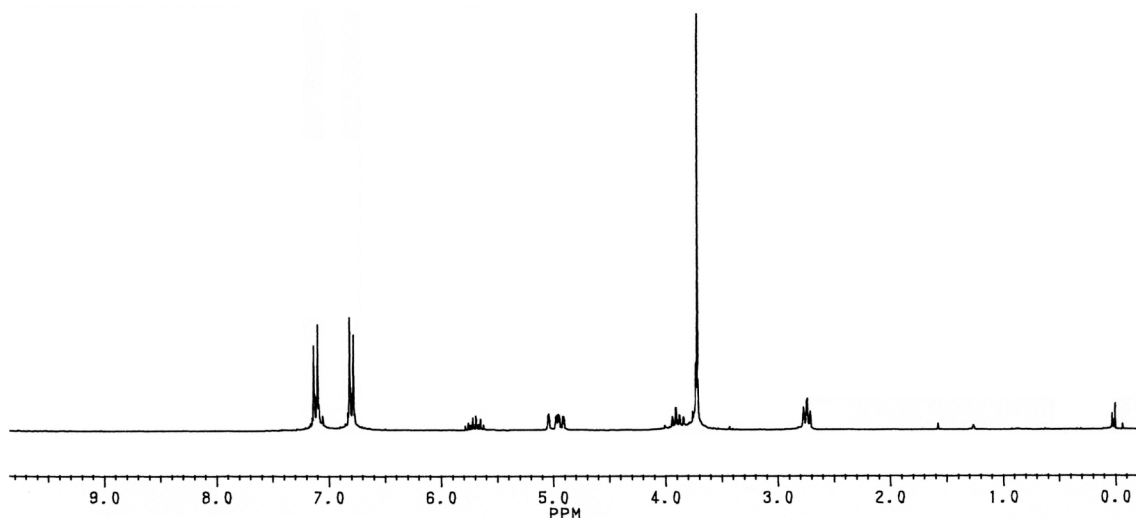


Figure 5-1 HNMR of compound **515**

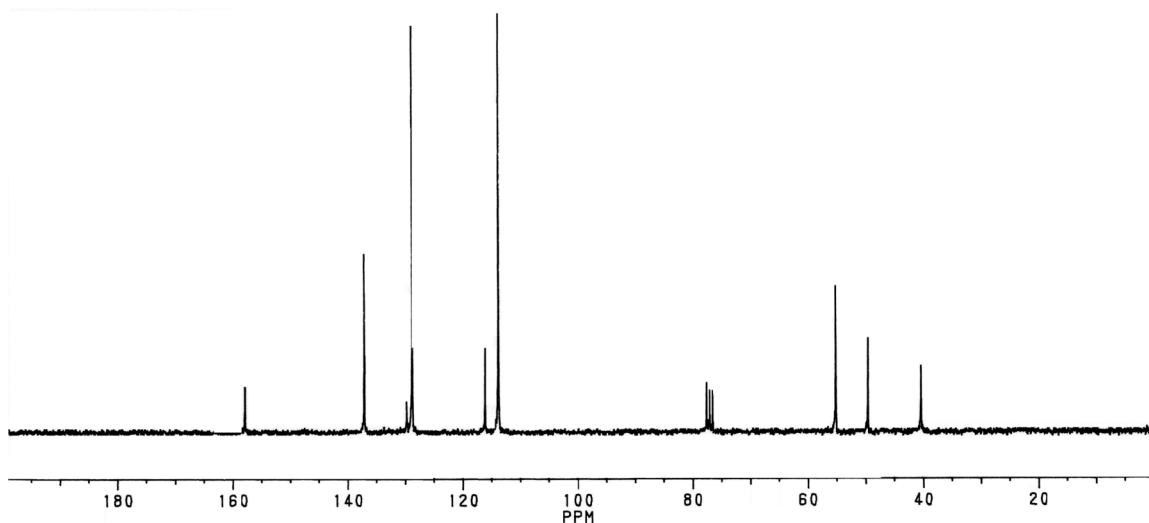


Figure 5-2 CNMR of compound **515**

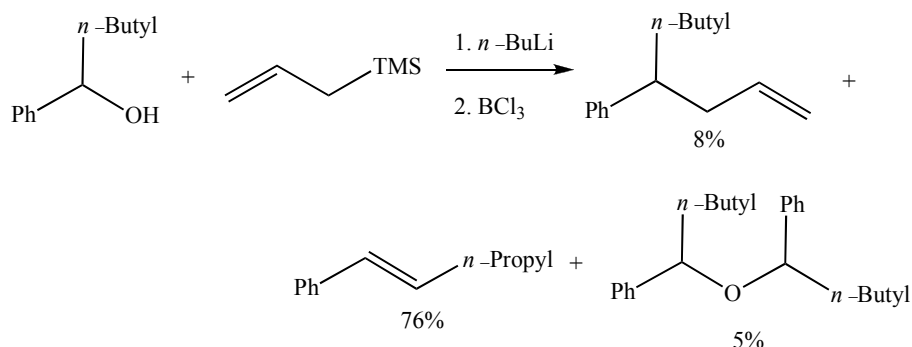
5.3. Mechanistic Study

In an effort to rule out the formation of an intermediate derived from the reaction of boron trichloride and allyltrimethylsilane, the two compounds were allowed to stir in a solution of dichloromethane. Only allyltrimethylsilane was detected by HNMR.

In addition to the evidence supporting a cationic intermediate put forth in Chapters 2 and 3, additional evidence was obtained in the reactions of alkoxides, allyltrimethylsilane, boron trichloride and iron(III) chloride. First, the reaction of phenyl-*n*-butylmethanol and allyltrimethylsilane with boron trichloride yielded the products shown in Scheme 5-1. The allylation product was formed in only 8% yield, while the major product in this reaction was due to elimination in the starting material. Upon removal of the proton, the alkoxide should attack boron trichloride to form the oxyboron dichloride intermediate. This species should act as the leaving group to generate an

intermediate carbocation. Loss of the adjacent proton would then generate the major product

Scheme 5-1 Boron trichloride mediated reaction of phenyl-*n*-butylmethanol and allyltrimethylsilane

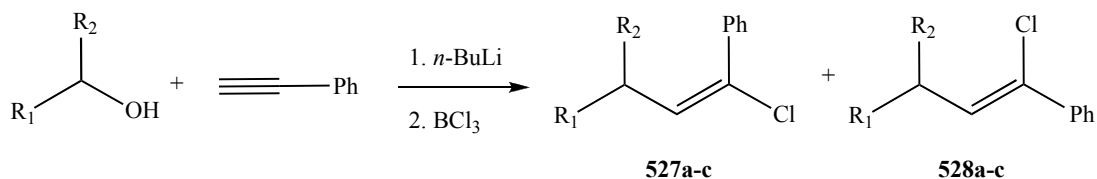


It is unlikely that an E2 mechanism occurs. First, if the *n*-butyllithium is presumed to remove the proton in the elimination, then it would be reasonable that an equivalent of HCl would be formed in the reaction pathway since a lone pair on oxygen would be required to attack the boron followed by loss of HCl to make the oxyboron dihalide species. The equivalent of hydrochloric acid would certainly add across the allylation product; this was not observed.

Alkoxides can react with phenylacetylene in the presence of boron trichloride. In all cases, the (*E*)-stereoisomer was the major product. Since the alcohol is most certainly more acidic than phenylacetylene, the oxyboron dihalide species would be generated first to produce the carbocation intermediate. The alkyne would then attack the carbocation to form the more thermodynamically stable (*E*)-stereoisomer. This procedure to generate the (*E*)-product is especially interesting since it does not involve a Brønsted acid. Recall

that the (*Z*)-isomer was the major product when using alkenylboron dihalides and benzylic alcohols (Chapter 3). The results are shown in Table 5-4.

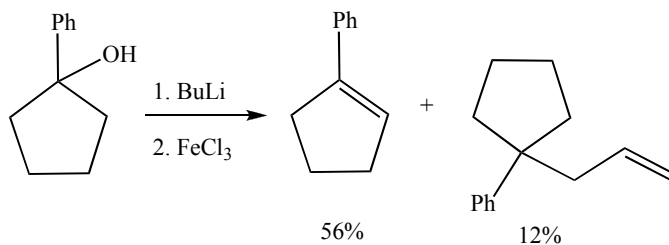
Table 5-4 BCl₃-mediated coupling of lithium alkoxides and phenylacetylene



Entry	R ₁	R ₂	Yield (%)	<i>E</i> : <i>Z</i>	Products
1	Ph	Ph	84	90 : 10	527a, 528a
2	Ph	6-(2,3Dihydro-benzo[<i>b</i>][1,4]dioxine)	87	95 : 05	527b, 528b
3	Ph	4-FPh	80	60 : 40	527c, 528c

Finally, in the reaction conducted with ferric chloride, a similar allylation – elimination product distribution to Scheme 5-2 was found (**Scheme 5-2**).

Scheme 5-2 Reaction of phenylcyclopentanol and allyltrimethylsilane with ferric chloride



In both reactions, the elimination product was the major product formed. It would be reasonable to postulate an oxyiron dichloride species acting as the leaving group to generate an intermediate carbocation.

5.4 Conclusion

The successful allylation of aliphatic alkoxides mediated by boron trichloride and ferric chloride provides further confirmation that these reactions are proceeding through carbocation intermediates. In addition, it is now possible to produce (*E*)-halovinylalkenyl species by making a small variation in the reaction sequence of aliphatic alcohols, phenylacetylene, and boron trichloride.

5.5 Experimental Details

5.5.1 General Considerations

All reagents were used as received. Solvents were distilled from the appropriate drying agents under a nitrogen atmosphere. Column chromatography was performed using silica gel (60 Å, 230–400 mesh). Analytical thin-layer chromatography was performed using 250 µm silica (Analtech, Inc., Newark, DE). All glassware was oven-dried for at least 12 hours at 150 °C and cooled under argon or nitrogen. Reactions were magnetically stirred under argon or nitrogen and monitored on TLC plates using 254 nm UV light, staining with a 50% solution of PMA in EtOH, or development on in an iodine-silica gel chamber.

5.5.2 Representative Procedure for Boron Trichloride Allylation

A solution of alcohol (1.5 mmol) in dry dichloromethane (10 mL) was treated

with *n*-butyllithium (1.0 mL of a 1.6 *M* solution in hexanes) at 0 °C and the mixture warmed to room temperature. After stirring at room temperature for 30 min, allyltrimethylsilane (1.8 mmol) and boron trichloride (1.5 mL of a 1.0 *M* solution in dichloromethane) were added. The reaction mixture was allowed to stir 10 hours at room temperature. Water (20 mL) was added to quench the reaction. The reaction mixture was extracted with ethyl acetate, the water removed and the organic layer dried over anhydrous MgSO₄. The solvent was removed *in vacuo* and the product purified by silica gel column chromatography.

5.5.3 Representative Procedure for Iron(III) Chloride Allylation

A solution of alcohol (1.5 mmol) in dry dichloromethane (10 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 *M* solution in hexanes) at 0 °C and the solution warmed to room temperature. After stirring at room temperature for 30 min, allyltrimethylsilane (1.8 mmol) and iron trichloride (1.6 mmol) were added. The mixture was allowed to stir for 6 hours. Water (20 mL) was added to quench the reaction, the mixture extracted with ethyl acetate, the water separated and the organic layer dried over anhydrous MgSO₄. The solvent was removed *in vacuo* and the product purified by silica gel column chromatography using hexane as an eluent. Products were detected on TLC plates using 254 nm UV light or staining with a 50% solution of PMA in EtOH.

5.5.4 Characterization of Compounds 501-528

¹HNMR and ¹³CNMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for ¹HNMR and ¹³CNMR spectra (CDCl₃) were referenced

to TMS and CDCl_3 respectively. Microanalysis was performed by Atlantic Microlab, Inc. Norcross, Georgia.

3,5-Diphenyl-1-hexen-4-yne (501): Known compound.¹⁹

3-(4-Chlorophenyl)-5-phenyl-1-hexen-4-yne (502): ^1H NMR: δ 7.13–7.29 (m, 10H), 5.80–5.91 (m, 1H), 5.03–5.10 (m, 2H), 3.86 (t, $J = 7.01$ Hz, 1H), 2.50–2.56 (m, 2H). ^{13}C NMR: δ 139.8, 134.9, 132.5, 131.6, 128.9, 128.5, 128.2, 127.9, 123.4, 117.4, 90.3, 84.1, 42.6, 37.9. Anal. Calcd for $\text{C}_{18}\text{H}_{15}\text{Cl}$: C, 81.04; H, 5.67. Found: C, 80.52; H, 5.53.

3-(4-Chlorophenyl)-5-(4-methylphenyl)-1-hexen-4-yne (503): ^1H NMR: δ 7.07–7.44 (m, 8H), 5.79–5.95 (m, 1H), 5.04–5.10 (m, 2H), 3.87 (t, $J = 6.97$ Hz, 1H), 2.52–2.57 (m, 2H), 2.36 (s, 3H). ^{13}C NMR: δ 139.9, 137.9, 135.0, 132.5, 131.5, 128.9, 128.7, 128.5, 120.3, 117.3, 89.5, 84.1, 42.6, 37.9, 21.4. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{Cl}$: C, 81.27; H, 6.10. Found: C, 80.83; H, 5.82.

3-(2-Methylphenyl)-5-phenyl-1-hexen-4-yne (504): ^1H NMR: δ 7.05–7.53 (m, 9H), 5.81–5.98 (m, 1H), 5.02–5.12 (m, 2H), 4.04 (t, $J = 7.07$ Hz, 2H), 2.46–2.52 (m, 2H), 2.36 (s, 3H). ^{13}C NMR: δ 139.5, 135.6, 134.8, 131.6, 130.4, 128.3, 127.7, 126.9, 126.3, 125.6, 124.9, 116.9, 91.3, 83.1, 41.2, 5.0, 19.3. HRMS Calcd for $\text{C}_{19}\text{H}_{18}$: 246.1409. Found: 246.1404.

3-(2-Methylphenyl)-5-(4-methylphenyl)-1-hexen-4-yne (505): ^1H NMR: δ 7.07–7.58 (m, 8H), 5.88–6.02 (m, 1H), 5.05–5.16 (m, 2H), 4.08 (t, $J = 7.03$ Hz, 2H), 2.50–2.56 (m, 2H), 2.37 (s, 3H), 2.32 (s, 3H). ^{13}C NMR: δ 139.7, 137.7, 135.7, 134.7, 131.5, 130.4, 128.9, 127.7, 126.7, 126.3, 116.9, 90.5, 83.1, 41.3, 35.0, 21.4, 19.3. Anal. Calcd for $\text{C}_{20}\text{H}_{20}$: C, 92.26; H, 7.74. Found: C, 92.01; H, 7.62.

3-(2-Methylphenyl)-5-(4-methoxyphenyl)-1-hexen-4-yne (506): ^1H NMR: δ 6.81–7.58 (m, 8H), 5.89–6.03 (m, 1H), 5.07–5.17 (m, 2H), 4.09 (t, J = 7.07 Hz, 2H), 3.80 (s, 3H), 2.46–2.60 (m, 2H), 2.37 (s, 3H). ^{13}C NMR: δ 159.5, 135.6, 130.5, 129.2, 127.6, 126.8, 126.3, 124.8, 124.2, 117.0, 116.6, 114.3, 91.2, 83.0, 55.2, 41.2, 35.0, 19.3. Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{O}$: C, 86.92; H, 7.29. Found: C, 86.39; H, 7.25.

3-(3,4,5-Trimethoxyphenyl)-5-phenyl-1-hexen-4-yne (507): ^1H NMR: δ 7.24–7.66 (m, 5H), 6.68 (s, 2H), 5.87–5.97 (m, 1H), 5.08–5.18 (m, 2H), 3.82–4.02 (m, 7H), 3.68 (s, 3H), 2.56–2.61 (m, 2H). ^{13}C NMR: δ 153.1, 137.1, 135.4, 131.6, 128.5, 128.2, 127.8, 123.5, 117.1, 104.6, 90.8, 83.9, 60.8, 56.1, 42.7, 38.8. Anal. Calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3$: C, 78.23; H, 6.88. Found: C, 78.14; H, 6.71.

3-(3,4,5-Trimethoxyphenyl)-5-(3-fluorophenyl)-1-hexen-4-yne (508): ^1H NMR: δ 6.99–7.37 (m, 4H), 6.64 (s, 2H), 5.84–5.97 (m, 1H), 5.09–5.18 (m, 2H), 3.63–3.91 (m, 7H), 3.61 (s, 3H), 2.56–2.61 (m, 2H). ^{13}C NMR: δ 164.3, 160.4, 153.2, 136.9, 135.5, 131.5, 129.8, 129.7, 127.4, 118.2, 117.2, 116.8, 115.4, 115.0, 105.7, 91.9, 82.8, 60.8, 56.1, 42.5, 38.8. HR-MS Calcd for $\text{C}_{21}\text{H}_{21}\text{FO}_3$: 340.1475. Found: 340.1469.

3-(4-Fluorophenyl)-5-phenyl-1-hexen-4-yne (509): ^1H NMR: δ 6.98–7.45 (m, 9H), 5.83–5.94 (m, 1H), 5.05–5.13 (m, 2H), 3.89 (t, J = 7.00 Hz, 2H), 2.53–2.85 (m, 2H). ^{13}C NMR: δ 163.7, 159.8, 135.2, 131.6, 129.1, 129.0, 128.6, 128.5, 128.2, 127.9, 127.1, 123.5, 117.3, 115.4, 115.1, 90.7, 84.0, 42.8, 37.8. HR-MS Calcd for $\text{C}_{18}\text{H}_{15}\text{F}$: 250.1158. Found: 250.1150.

3-(4-Chlorophenyl)-1-nonen-4-yne (510): ^1H NMR: δ 7.11–7.34 (m, 4H), 5.73–5.84 (m, 1H), 4.91–5.06 (m, 2H), 3.52–3.64 (m, 1H), 2.23–2.45 (m, 2H), 2.15–2.21 (m, 2H), 1.37–

1.55 (m, 4H), 0.91 (t, $J = 6.53$ Hz, 3H). ^{13}C NMR: δ 140.6, 135.3, 132.3, 128.9, 128.4, 116.9, 84.1, 80.6, 42.9, 37.4, 31.1, 21.9, 18.4, 13.6. Anal. Calcd for $\text{C}_{16}\text{H}_{19}\text{Cl}$: C, 77.87; H, 7.76. Found: C, 77.35; H, 7.64.

2-Methyl-3-(4-chlorophenyl)-5-phenyl-1-hexen-4-yne (511): ^1H NMR: δ 7.24–7.43 (m, 9H), 4.77–4.84 (m, 2H), 3.93–3.99 (m, 2H), 2.46–2.54 (m, 2H), 1.78 (s, 3H). ^{13}C NMR: δ 142.1, 140.3, 132.5, 131.6, 128.8, 128.5, 128.2, 127.8, 123.5, 113.4, 90.6, 83.9, 46.8, 36.7, 22.4. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{Cl}$: C, 81.27; H, 6.10. Found: C, 81.03; H, 5.99.

2-Methyl-3-(4-chlorophenyl)-5-(4-methylphenyl)-1-hexen-4-yne (512): ^1H NMR: δ 7.07–7.37 (m, 8H), 4.75–4.83 (m, 2H), 3.93–3.99 (m, 2H), 2.39–2.59 (m, 2H), 2.32 (s, 3H), 1.78 (s, 3H). ^{13}C NMR: δ 142.2, 140.5, 137.9, 132.4, 131.5, 128.9, 128.8, 128.5, 113.3, 89.9, 83.9, 46.9, 36.8, 22.5, 21.4. Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{Cl}$: C, 81.48; H, 6.50. Found: C, 81.31; H, 6.36.

4,4-Diphenyl-1-butene (513): Known compound.²⁵

4,4-Di-(4-fluorophenyl)-1-butene (514): Known compound.⁷⁹

4,4-Di-(4-methoxyphenyl)-1-butene (515): Known compound.⁸⁰

4-(4-Chlorophenyl)-4-phenyl-1-butene (516): Known compound.²⁵

(*E*)-1,3-Diphenyl-1,5-hexadiene (517): Known compound.⁸¹

4-(4-Methylphenyl)-4-phenyl-1-butene (518): Known compound.⁸²

4-(2-Methylphenyl)-4-phenyl-1-butene (519): Known compound.⁸²

4-(4-Cyanophenyl)-4-phenyl-1-butene (520): Known compound.⁸³

4-(6-(2,3-Dihydrobenzo[*b*][1,4]dioxine))-4-phenyl-1-butene (521): ^1H NMR (250 MHz, CDCl_3): δ 7.11–7.29 (m, 5H), 6.68–6.78 (m, 3H), 5.65–5.76 (m, 1H), 4.92–5.06 (m,

2H), 4.18 (s, 2H), 3.89 (t, $J=7.88$ Hz), 2.72-2.78 (m, 2H). ^{13}C NMR (CDCl_3): δ 144.6, 143.2, 141.8, 137.9, 136.8, 128.3, 127.7, 126.1, 120.7, 117.0, 116.5, 116.2, 64.3, 64.2, 50.5, 39.9. Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$: C, 81.17; H, 6.81. Found: C, 81.57; H, 6.49.

4,4,4-Triphenyl-1-butene (522): Known compound.⁸⁴

4-(2-Bicyclo[2.2.1]heptyl)-4-phenyl-1-butene (523): ^1H NMR (250 MHz, CDCl_3): δ 7.06–7.30 (m, 5H), 5.46-5.60 (m, 1H), 4.79-4.90 (m, 1H), 2.16-2.39 (m, 4H), 0.99-1.63 (m, 10H). ^{13}C NMR (CDCl_3): δ 145.1, 144.0, 137.2, 137.1, 128.7, 128.2, 128.1, 127.9, 127.6, 125.8, 115.4, 52.2, 51.2, 48.0, 47.3, 40.6, 39.4, 39.2, 38.3, 37.7, 37.0, 36.6, 35.6, 35.2, 30.4, 28.7. HRMS Calcd for $\text{C}_{17}\text{H}_{22}$: 226.1722. Found: 226.1716.

4-(2-Methoxyphenyl)-4-methyl-1-butene (524): Known compound.⁸⁵

4-Phenyl-1-nonen-4-yne (525): Known compound.¹⁹

1,3,3-Triphenyl-5-hexen-1-yne (526): ^1H NMR (250 MHz, CDCl_3): δ 7.17–7.51 (m, 15H), 5.97-6.08 (m, 1H), 5.09-5.26 (m, 2H), 3.39 (d, $J = 6.42$ Hz). ^{13}C NMR (CDCl_3): δ 136.8, 135.8, 135.5, 129.6, 128.6, 128.4, 127.3, 127.1, 126.1, 116.7, 113.1, 107.4, 35.0. Anal. Calcd for $\text{C}_{24}\text{H}_{20}$: C, 93.46; H, 6.54. Found: C, 93.52; H, 6.29.

(E)-1-Chloro-1,3,3-triphenyl-1-propene (527a): Known compound.⁸⁶

(E)-1-Chloro-3-(6-(2,3-dihydrobenzo[*b*][1,4]dioxine))-3-phenyl-1-propene (527b): ^1H NMR: δ 7.11–7.36 (m, 9H), 6.73–6.81 (m, 2H), 6.57–6.65 (m, 2H), 6.38 (d, $J = 10.8$ Hz, 1H), 4.67 (d, $J = 11.4$ Hz, 1H), 4.20–4.23 (m, 4H). ^{13}C NMR: δ 138.1, 137.9, 137.7, 136.7, 131.4, 128.8, 128.6, 128.3, 128.0, 126.9, 121.0, 117.3, 116.9, 64.4, 64.3, 49.9. HR-MS Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$: 266.1307. Found: 266.1295.

(E)-3-(4-Fluorophenyl)-3-phenyl-1-propene (527c): ^1H NMR: δ 7.00–7.61 (m, 13H),

6.50 (d, $J = 10.5$ Hz, 1H), 4.73 (d, $J = 10.8$ Hz, 1H).

(Z)-1-Chloro-1,3,3-triphenyl-1-propene (528a): Known compound.⁶⁰

(Z)-3-(4-Fluorophenyl)-3-phenyl-1-propene (528c): Known compound.⁶⁰

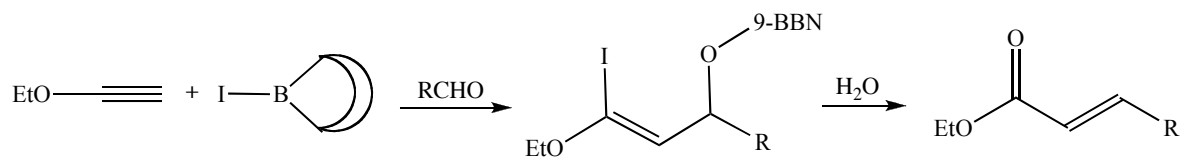
Chapter 6: Boron Trihalide Alkyne-Aldehyde Coupling Reaction

6.1 Introduction

The alkyne-aldehyde coupling reaction has found applications in modern synthetic chemistry due to its ability to generate viable starting materials for complex molecules. Some of the more attractive products from this reaction include propargylic⁸⁷ and allylic alcohols,⁸⁸ α,β -unsaturated ketones,⁸⁹ enynols,⁹⁰ and naphthalene compounds.^{12b, 91} Moreover, the alkyne-aldehyde coupling reaction has been modified to proceed intramolecularly to generate α -alkylidenecycloalkanones⁹² and cycloalkenones.⁹³

The first example of an alkenylborane carbonyl addition reaction was reported by Suzuki as shown in Scheme 6-1.⁹⁴

Scheme 6-1 Synthesis of (*E*)- α,β -unsaturated esters via *B*-I-9-BBN adducts



The reaction proceeded smoothly and produced the products in good yields. This reaction is tolerant of aromatic and aliphatic aldehydes, and most importantly, the olefin stereochemistry from the haloboration reaction was retained during carbonyl addition. However, alkenylboron dihalides have not been used as nucleophiles in carbonyl addition reactions.

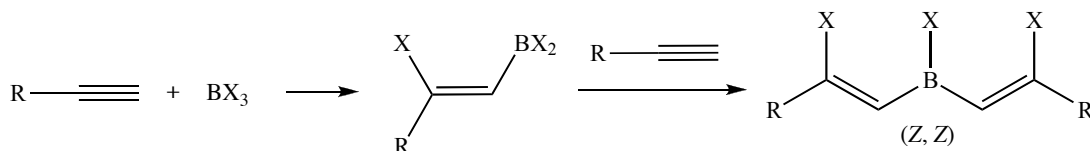
The synthetic utility of alkenylboron dihalides has been discussed in the previous chapters with respect to the direct substitution of hydroxyl groups through their

corresponding alkoxides. Given the similarity of alkenylboron dihalides to reagents that can function as Grignard-type reactants, it is reasonable to postulate that preformed alkenylboron halides derived from the haloboration of alkynes and boron trihalide might act as nucleophiles in carbonyl reactions.

6.1.1 Initial Investigation

The haloboration reaction and its applications have been previously discussed. It is also possible for the alkenylboron dihalide to haloborate a second equivalent of alkyne as shown in Scheme 6-2.

Scheme 6-2 Boron trihalide dialkenylation



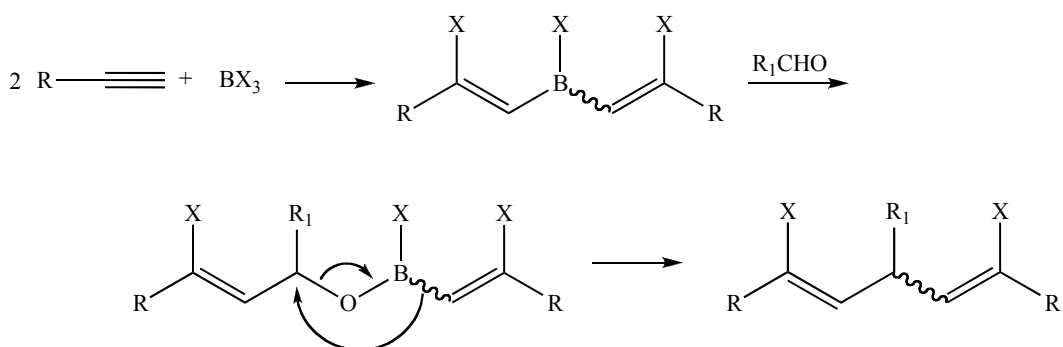
It should be noted that the reaction in Scheme 6-2 only proceeds when the halogen is chloride, bromide, or iodide. As with monohaloboration, second and third haloborations proceed with *syn*-addition, although it becomes increasingly difficult to obtain the dialkenylation and trialkenylation products when the halogen is chloride. Studies by Blackborow have shown the corresponding (*Z,E*) and (*Z,Z,E*) isomers do form but the product ratio was solvent dependent.⁹⁵ For example, the reaction of 1-hexyne and boron tribromide at -80 °C in DCM formed the (*Z,Z*) isomer exclusively while a 4:1 ratio of (*Z,Z*) and (*Z,E*) isomers were formed in petroleum spirit.

More recently, the Kabalka group has expanded upon the work of Suzuki and developed a new alkyne-aldehyde coupling reaction (**Scheme 1-2**).^{11a} This reaction constitutes the first example of a halovinyl species participating in carbonyl addition reaction. It is interesting that the resultant products have different stereochemistry based upon the halogen that is used. In all cases the reactions produced the desired products in good to high yields with nearly exclusive olefin stereoselectivity.

6.1.2 Initial Mechanistic Studies

A detailed mechanistic investigation of the new alkyne-aldehyde coupling reaction was not completed in the initial communication.^{11a} The sequence shown in Scheme 6-3 reasonably presumes that a dihalovinylboron halide species attacks the aldehyde in a Grignard-like fashion. Intramolecular rearrangement then affords the desired product.

Scheme 6-3 Initial mechanism for dialkenylation of aldehydes



This mechanism was based upon the observation that quenching the reaction prior to completion afforded the corresponding (*Z*)-allylic alcohol; no conclusions were made as to whether the coupling is concerted or otherwise. With respect to olefin

stereochemistry, (*Z,E*)-products derived from boron trichloride were attributed to thermodynamics while the (*Z,Z*)-products from boron tribromide were attributed to kinetics. This coincides with the fact that chloroborations of the second alkyne are much slower than the corresponding bromoborations. In addition, it is known that bromoboration of alkynes form kinetically controlled (*Z,Z*)-dihalovinylboron bromides.⁹⁵

6.2 Results and Discussion

The structure of the intermediate oxyboron halide compound in Scheme 6-3 is nearly identical to the intermediate formed from allyloxides and halovinylboron dihalides in Scheme 2-5 [With respect to chronology, the order of study was: dialkenylation of aldehydes, halovinyl alkenylation of propargyl alcohols, halovinyl alkenylation of allylic alcohols, halovinyl alkenylation of benzylic alcohols, alkynylation of alcohols, and allylation of alcohols]. However, further experimentation with allyltrimethylsilane (**Scheme 2-5**), and the results outlined in Chapters 3, 4, and 5 strongly indicate a cationic mechanism is taking place. Therefore, it is possible the dihalovinylboron halide dialkenylation of aldehydes is also proceeding via a cationic mechanism.

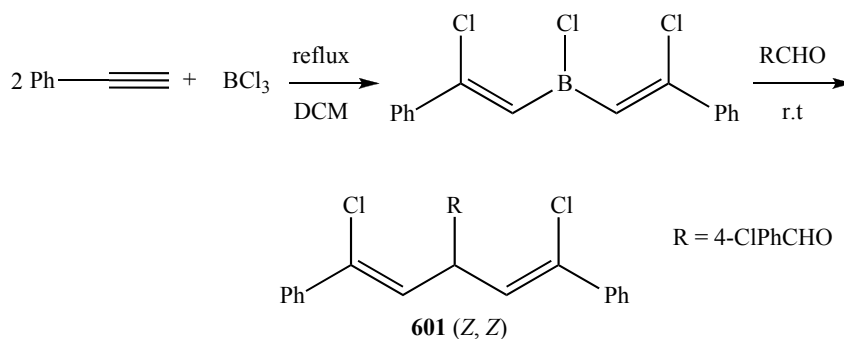
6.3 Mechanistic Study – Reactions with Boron Trichloride

The results discussed in Chapters 2 and 3 show the stereochemistry of the olefin is retained when coupled with alkoxides. This would imply the stereochemistry of the halovinyl species must already be formed prior to coupling; it also implies the stereochemistry must be determined prior to Grignard-like attack on the aldehyde. Unfortunately, this rationale does not coincide with the reported chloroboration of

alkynes, which indicates that the reaction of phenylacetylene with boron trichloride and aldehyde should give the (Z,Z)-product.

The original reaction of boron trichloride, phenylacetylene, and aldehyde was conducted at 0 °C. Since the chloroboration with the second equivalent of alkyne is slow, it is possible that it might not have proceeded to completion at that temperature. Moreover, it has been reported that (Z,Z)-di(2-chloro-2-phenylvinyl)boron chloride was originally purified by distillation and characterized prior to FT-NMR.^{4b} We postulated that the (Z,Z)-boron chloride species might have been formed during distillation. The reaction shown in Scheme 6-4 was designed to test this postulate.

Scheme 6-4 Boron trichloride dialkenylation of aldehydes under reflux conditions



Compound **601** was isolated in 78% yield with the (Z,Z)-product stereochemistry confirmed by NMR as shown in Figures 6-1 and 6-2. This is attributed to one vinyl hydrogen resonance at approximately 6.25 ppm, and one methine resonance at approximately 5.4 ppm indicating a symmetrical compound.

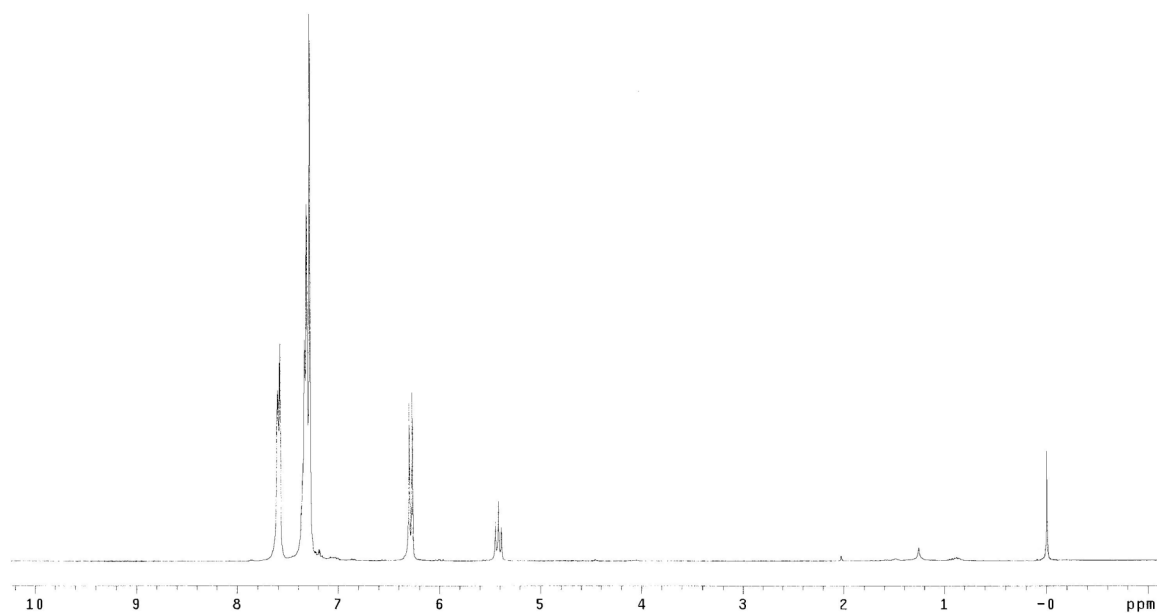


Figure 6-1 ¹H NMR of compound **601**

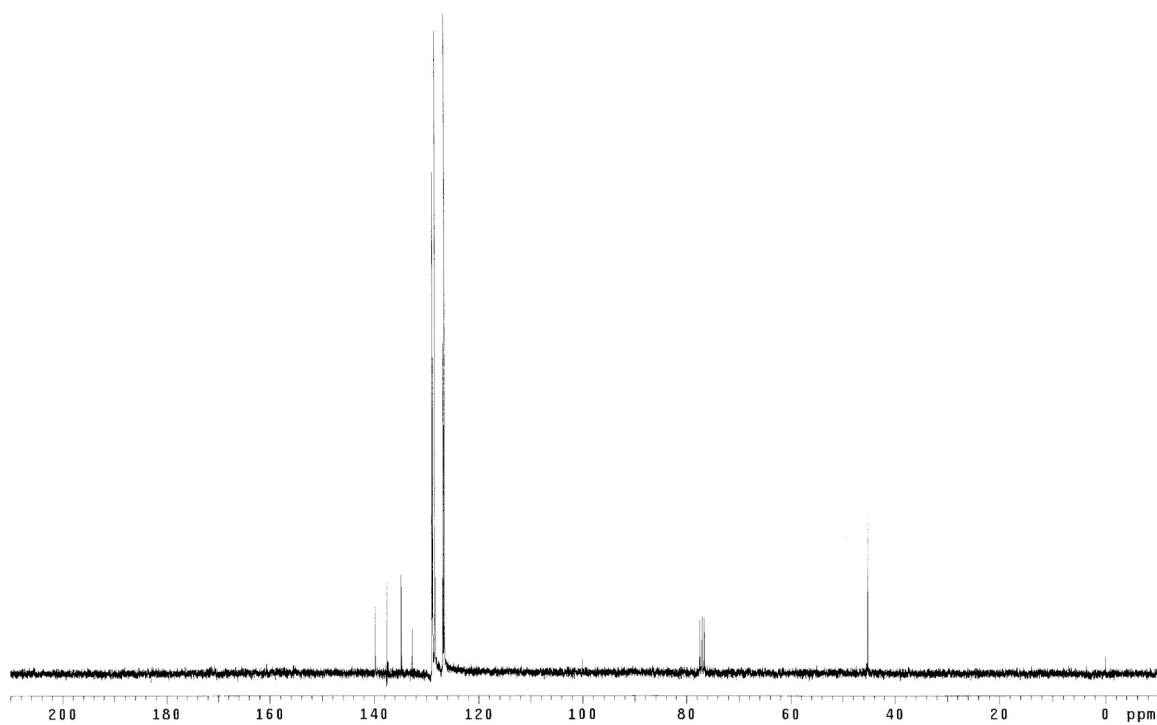
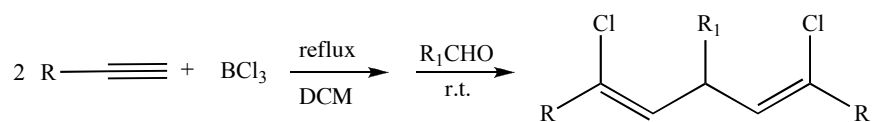


Figure 6-2 ¹³C NMR of compound **602**

The scope of the reaction was then examined with a series of alkynes and aldehydes as shown in Table 6-1.

Table 6-1 Reaction of dialkenylboron chlorides and aldehydes



Entry	R	R ₁	Yield (%)	Product
1	Ph	4-ClPh	78	601
2	Ph	4-BrPh	83	602
3	Ph	4-CNPh	82	603
4	Ph	2-MePh	76	604
5	Ph	Ph	60	605
6 ^a	Ph	(CH ₂ O) _n	35	606
7	Ph	<i>n</i> -Hexyl	50	607
8	4-MePh	4-ClPh	81	608
9	4-MePh	4-NO ₂ Ph	82	609
10	4-MePh	3,4-(MeO) ₂ Ph	34	610
11	4-BrPh	4-ClPh	75	611
12	3-MeOPh	4-CF ₃ Ph	48	612
13	3-FPh	4-ClPh	76	613

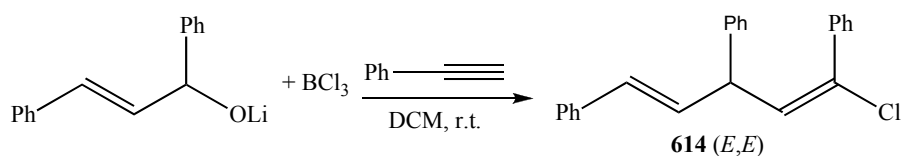
^a Reaction conducted with paraformaldehyde

The reaction afforded the desired (*Z,Z*)-product in good yields and tolerated electronically diverse substitution on the alkyne and aldehyde species. It is interesting that entry 7 generated the desired product. It is known that boron halides can participate in Aldol reactions with enolizable hydrogens. Subjecting the aliphatic alkyne to haloboration conditions appears to reduce the likelihood of the aliphatic aldehyde to enolize.

The successful formation of (*Z,Z*)-adducts in Table 6-1 would indicate that the formation of the corresponding (*Z,E*)-adducts formed from the reaction conducted at 0 °C with boron trichloride most likely occurred through a different mechanism. Consequently, it is also reasonable to state that at 0 °C the reaction of two equivalents of phenylacetylene and boron trichloride only produces the (*Z*)-(chlorovinyl)boron dichloride species.

In an effort to elucidate mechanistic insight, the reaction shown in Scheme 6-5 was performed.

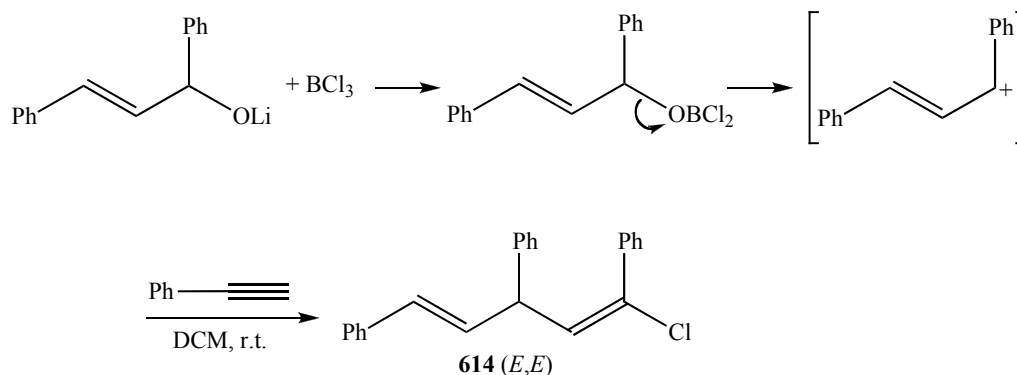
Scheme 6-5 Synthesis of (*E,E*)-1-Chloro-1,3,5-triphenyl-1,4-pentadiene



Compound **614** was isolated in 78% yield; the (*E,Z*)-isomer was obtained in 4% yield. The methine hydrogen coupling constants arising from the dd resonance are slightly larger than the (*E,Z*)-isomer **201** (11, 11; 9, 9). Moreover, when a competitive reaction in Scheme 6-5 was performed with allyltrimethylsilane in the mixture, the resultant

allylation product was formed (**Scheme 2-5**).⁹⁶ This strongly indicates a cationic mechanism is taking place. A possible mechanism is shown in Scheme 6-6.

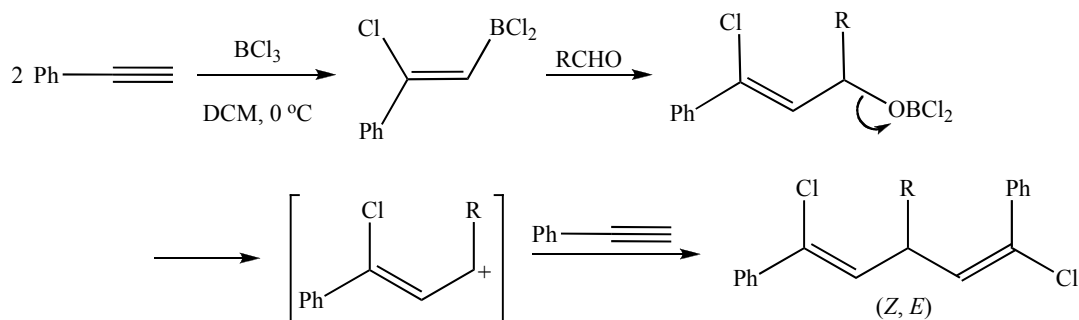
Scheme 6-6 Possible mechanism for the formation of compound **614**



The ability of the oxyboron dihalide species to serve as a viable leaving group to generate intermediate carbocations has been described in Chapter 5. Additionally, terminal alkynes are known to act as nucleophiles with carbocations. It should also be noted that the (*E,Z*)-isomer of compound **614** was generated using the reaction of allyloxides and alkenylboron dihalides in Chapter 2. Therefore, it is possible to create both stereoisomers by simply varying the reaction sequence.

Successful formation of product **614**, and the corresponding allylation product, provides sufficient information to postulate a modified mechanism for the reaction of two equivalents of phenylacetylene with boron trichloride and an aldehyde at 0 °C. At low temperature, the monovinylboron dihalide attacks the aldehyde, the resultant oxyboron dihalide species acts as a leaving group to generate an intermediate carbocation, the second molecule of alkyne attacks to carbocation to form the resultant (*Z,E*)-1,4-pentadiene (**Scheme 6-7**).

Scheme 6-7 Modified mechanism for the formation of (*Z,E*)-1,4-pentadienes with boron trichloride at 0 °C



6.4 Conclusion

Reaction temperature and the sequence of reagent addition appears to have a profound influence on the stereochemistry of the boron trihalide mediated alkyne-aldehyde coupling reaction. (*Z,E*)-1,4-pentadienes are formed with boron trichloride at low temperature, while (*Z,Z*)-1,4-pentadienes are formed using boron tribromide at low temperature or boron trichloride at reflux. Additionally, (*E,E*)-1-chloro-1,4-pentadienes can be formed by generating an intermediate oxyboron dichloride leaving group prior to addition of phenylacetylene; this method complements the formation of the corresponding (*E,Z*)-1-halo-1,4-pentadienes using alkenylboron dihalides and allyloxides as described in Chapter 2.

6.5 Experimental Details

6.5.1 General Considerations

All reagents were used as received. Solvents were distilled from the appropriate drying agents under a nitrogen atmosphere. Column chromatography was performed

using silica gel (60 Å, 230–400 mesh). Analytical thin-layer chromatography was performed using 250 µm silica (Analtech, Inc., Newark, DE). All glassware was oven-dried for at least 12 hours at 150 °C and cooled under argon or nitrogen. Reactions were magnetically stirred under argon or nitrogen and monitored on TLC plates using 254 nm UV light, staining with a 50% solution of PMA in EtOH, or development on in an iodine-silica gel chamber.

6.5.2 Representative Procedure for the Synthesis of (Z,Z)-1,3,5-Trisubstituted-1,5-Dichloro-1,4-pentadienes (601-613)

Alkyne (1.5 mmol) and boron trichloride (1.5 mmol, 1.5 mL of a 1.0 M DCM solution) were placed in a dry, argon-flushed, 50 mL round-bottomed flask equipped with a stirring bar and dissolved in 20 mL dry CH₂Cl₂. The solution was refluxed for 3 hrs and then cooled down to 0 °C using an ice-bath. Aldehyde (1.5 mmol) was dissolved in 5 mL of DCM and syringed into the original flask. The solution was allowed to stir for 2 hrs at 0 °C and then for 6 hrs at room temperature. The resulting mixture was hydrolyzed with water and extracted with hexanes. The organic layer was separated and dried over anhydrous MgSO₄. The product was isolated by flash column chromatography using hexane as an eluent.

6.5.3 Representative Procedure for the Synthesis of Compound 614

Alkoxide (1.5 mmol), phenylacetylene (1.5 mmol) and dry dichloromethane (8 mL) were combined in a 50 mL flask under a nitrogen atmosphere at 0 °C. Boron trihalide (1.5 mmol, 1.5 mL of 1.0 M solution in DCM) was added and stirred at room

temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with ethyl acetate and dried over anhydrous MgSO_4 . The product was isolated by column chromatography using hexane as an eluent.

6.5.4 Characterization of Compounds 601-614

(Z, Z)-1,5-Dichloro-1,5-diphenyl-3-(4-chlorophenyl)-1,4-pentadiene (601) Known compound.⁹⁷

(Z, Z)-1,5-Dichloro-1,5-diphenyl-3-(4-bromophenyl)-1,4-pentadiene (602) ^1H (250 MHz, CDCl_3): δ 7.61-7.20 (m, 14 H), 6.28 (d, 2 H), 5.39 (t, 1 H). ^{13}C (62.5 MHz, CDCl_3): δ 140.3, 137.6, 134.8, 131.8, 129.1, 126.7, 126.3, 126.7, 126.6, 120.7, 45.3.

(Z, Z)-1,5-Dichloro-1,5-diphenyl-3-(4-cyanophenyl)-1,4-pentadiene (603) Known compound.⁹⁷

(Z, Z)-1,5-Dichloro-1,5-diphenyl-3-(2-methylphenyl)-1,4-pentadiene (604) ^1H (300 MHz, CDCl_3): δ 7.59-7.18 (m, 14 H), 6.35 (d, 2 H), 5.50 (t, 1 H), 2.51 (s, 3 H). ^{13}C (75 MHz, CDCl_3): δ 140.5, 137.7, 136.4, 133.7, 130.8, 128.7, 128.3, 128.0, 127.8, 126.9, 126.8, 126.5, 126.4, 43.1, 19.9.

(Z, Z)-1,5-Dichloro-1,3,5-triphenyl-1,4-pentadiene (605) ^1H (300 MHz, CDCl_3): δ 7.63-7.24 (m, 15 H), 6.34 (d, 2 H), 5.47 (t, 1 H). ^{13}C (75 MHz, CDCl_3): δ 141.3, 137.7, 134.3, 128.8, 128.8, 128.3, 127.4, 127.3, 126.9, 126.6, 45.7. Calcd for $\text{C}_{17}\text{H}_{18}\text{Cl}_2$: C: 75.62; H: 4.97. Observed: C: 75.33; H: 4.80.

(Z, Z)-1,5-Dichloro-1,5-diphenyl-1,4-pentadiene (606) ^1H (300 MHz, CDCl_3): δ 7.61-7.35 (m, 10 H), 6.31 (t, 2 H), 4.39 (d, 2H). ^{13}C (75 MHz, CDCl_3): δ 137.2, 136.8, 129.4, 128.5, 128.4, 128.3, 126.6, 126.5, 126.3, 123.7, 122.4, 40.8, 29.7.

(Z, Z)-1,5-Dichloro-1,5-diphenyl-3-(*n*-hexyl)-1,4-pentadiene (607) ^1H (300 MHz, CDCl_3): δ 7.60-7.29 (m, 10 H), 6.01 (d, 2 H), 4.13 (m, 1 H), 1.63-1.58 (m, 2 H), 1.34-1.26 (m, 8 H), 0.90-0.86 (m, 3 H). ^{13}C (75 MHz, CDCl_3): δ 138.1, 133.3, 128.8, 128.5, 128.2, 126.5, 40.9, 34.9, 31.8, 29.3, 26.9, 22.6, 14.1.

(Z, Z)-1,5-Dichloro-1,5-di-(4-methylphenyl)-3-(4-chlorophenyl)-1,4-pentadiene (608) ^1H (300 MHz, CDCl_3): δ 7.50-7.12 (m, 12 H), 6.24 (d, 2 H), 5.39 (t, 1 H), 2.33 (s, 6 H). ^{13}C (75 MHz, CDCl_3): δ 140.0, 138.9, 134.7, 132.5, 129.0, 128.8, 128.8, 128.6, 126.5, 126.0, 45.1, 21.1.

(Z, Z)-1,5-Dichloro-1,5-di-(4-methylphenyl)-3-(4-nitrophenyl)-1,4-pentadiene (609) ^1H (300 MHz, CDCl_3): δ 8.10-7.06 (m, 12 H), 6.19 (d, 2 H), 5.47 (t, 1 H), 2.26 (s, 6 H). ^{13}C (75 MHz, CDCl_3): δ 149.1, 146.7, 139.2, 135.7, 134.4, 129.1, 128.3, 126.4, 124.9, 123.9, 53.4, 45.6, 21.1.

(Z, Z)-1,5-Dichloro-1,5-di-(4-methylphenyl)-3-(3,4-dimethoxyphenyl)-1,4-pentadiene (610) ^1H (300 MHz, CDCl_3): δ 7.55-6.82 (m, 11 H), 6.27 (d, 2 H), 5.37 (t, 1 H), 3.86 (s, 6 H), 2.35 (s, 6 H). ^{13}C (75 MHz, CDCl_3): δ 149.1, 147.9, 138.8, 138.2, 138.1, 138.0, 137.9, 137.7, 135.0, 134.1, 129.0, 126.7, 126.467, 119.1, 111.3, 110.8, 55.9, 45.3, 21.1. Calcd for $\text{C}_{25}\text{H}_{22}\text{Cl}_2$: C: 70.59; H: 5.21. Observed: C: 72.61; H: 5.80.

(Z, Z)-1,5-Dichloro-1,5-di-(4-bromophenyl)-3-(4-chlorophenyl)-1,4-pentadiene (611) ^1H (300 MHz, CDCl_3): δ 7.44-7.24 (m, 12 H), 6.28 (d, 2 H), 5.36 (t, 1 H). ^{13}C (75 MHz, CDCl_3): δ 139.2, 136.3, 133.8, 132.8, 131.4, 129.0, 128.7, 128.0, 127.0, 123.1, 45.2. Calcd for $\text{C}_{23}\text{H}_{12}\text{Cl}_3\text{Br}$: C: 49.55; H: 2.71. Observed: C: 48.23; H: 2.67.

(Z, Z)-1,5-Dichloro-1,5-di-(3-methoxyphenyl)-3-(4-trifluoromethylphenyl)-1,4-

pentadiene (612) ^1H (300 MHz, CDCl_3): δ 7.61-6.87 (m, 12 H), 6.33 (d, 2 H), 5.59 (t, 1 H), 3.82 (s, 6 H). ^{13}C (75 MHz, CDCl_3): δ 159.5, 145.3, 138.9, 135.0, 129.4, 127.8, 126.6, 125.8, 125.7, 119.0, 114.5, 112.7, 55.3, 45.6.

(Z, Z)-1,5-Dichloro-1,5-di-(3-fluorophenyl)-3-(4-chlorophenyl)-1,4-pentadiene (613)

^1H (300 MHz, CDCl_3): δ 7.39-6.97 (m, 12 H), 6.33 (d, 2 H), 5.40 (t, 1 H). ^{13}C (75 MHz, CDCl_3): δ 164.2, 139.60, 139.3, 133.6, 132.9, 129.9, 129.1, 128.9, 128.7, 127.5, 122.1, 116.0, 45.2.

(1E, 4Z)-1-Chloro-1,3,5-triphenyl-1,4-pentadiene (614) ^1H NMR (250 MHz, CDCl_3): δ

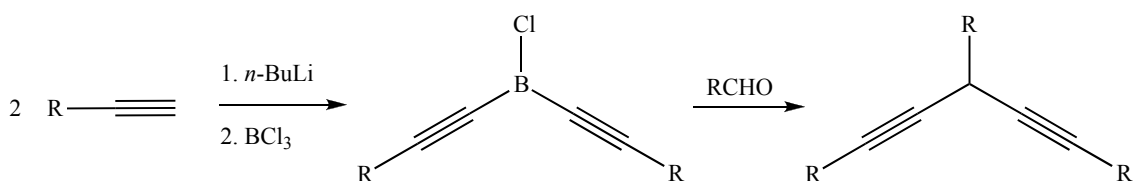
7.44-7.12 (m, 15H), 6.47-6.20 (m, 3H), 4.32 (dd, $J = 10.6$ and 10.5 Hz, 1H). ^{13}C NMR (CDCl_3): δ 142.2, 136.9, 131.6, 131.2, 130.7, 130.3, 128.8, 128.7, 128.5, 128.3, 127.6, 127.5, 126.8, 126.3, 48.4. Anal. Calcd for $\text{C}_{23}\text{H}_{19}\text{Cl}$: C: 83.50; H: 5.79. Found: C: 83.44; H: 5.82.

Chapter 7: Future Directions

7.1 Reaction of Aldehydes with Diorganoboron Halides

The results discussed in the previous chapters in addition to the chemistry highlighted in Schemes 1-2 and 1-3 are evident of the utility in applying boron Lewis acids to develop new carbon-carbon bonds. Given the success of utilizing alkenylboron dihalides and dialkenylboron halides in reactions with alcohols and aldehydes, the reaction of dialkynylboron halides and aldehydes might form the corresponding diynes as Shown in Scheme 7-1.

Scheme 7-1 Addition of dialkynylboron halides to aldehydes

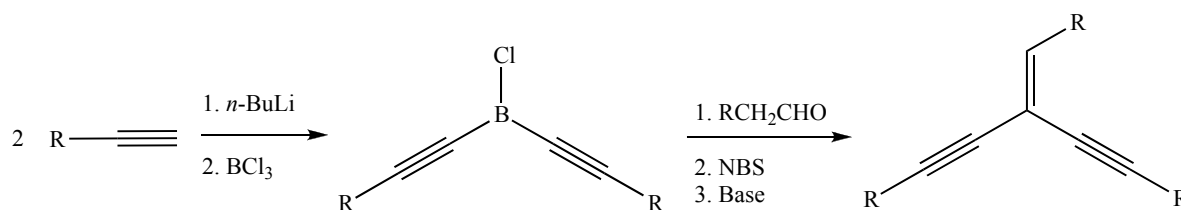


Traditional methods for synthesizing 1,4-diynes employ alkynyl metals such as Li ,⁹⁸ Mg ,⁹⁹ and Al .¹⁰⁰ Consequently, these intermediates are very basic and their applications in routes to complex molecules are often bypassed. As highlighted in Chapter 4, alkynylboron dichlorides are relatively mild reagents, easy to prepare, and tolerant to functional groups. This method would complement the Chapter 4 methodology using propargylic alcohols.

An extension of using dialkynyl boron halides to synthesize 1,4-diynes would be cross-conjugated enediynes (Y-enynes). These compounds have found utility in several

areas due to their electronic and fluorescent properties.¹⁰¹ Since the reaction of aliphatic aldehydes and dialkenylboron dihalides can form 1,5-dihalo-1,4-pentadienes, we postulated that a similar reaction might occur with dialkynylboron halides as shown in Scheme 7-2.

Scheme 7-2 Synthesis of Y-enynes



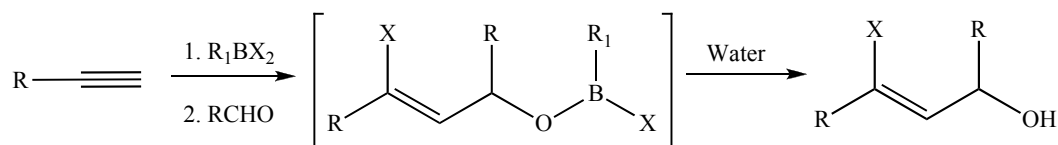
Since current routes to these compounds require the use of a palladium catalyst,^{101c, d} arylhalide substituents cannot be used as R-groups. The method shown in Scheme 7-2 would circumvent this limitation. Analogous chemistry could also be envisioned using diarylboron halides and diallylboron halides.

7.2 Preparation of Halogenated (Z)-Allylic Alcohols

Allylic alcohols have found utility in organic synthesis as viable starting materials in routes to complex molecules. Perhaps the most significant application of allylic alcohols is their ability to undergo asymmetric epoxidation. Discovered by Sharpless in 1980, prochiral allylic alcohols can be selectively epoxidized with a titanium(IV) diethyltartrate *tert*-butylhydroperoxide complex.¹⁰² The resultant chiral epoxide can then be subjected to a variety of reaction conditions to generate the desired chiral product.

Initial mechanistic studies in the boron trihalide alkyne-aldehyde coupling reaction were based upon quenching the reaction prior to completion to afford the resultant (Z)-halovinyl allylic alcohol. These compounds can be useful in synthesis since the vinyl halogen can be used in metal-catalyzed coupling reactions (Suzuki, Heck, Stille, etc.), the alcohol can be selectively oxidized to form α , β -unsaturated aldehydes, and the halovinyl olefin can undergo numerous reactions (cyclopropanation, epoxidation, dihydroxylation, etc) to afford novel substrates. It should be possible to obtain the monoalkenylation product by using controlling the stoichiometry and temperature of the coupling reaction. Additionally, the replacement of one halogen on boron with a phenyl group has been reported to successfully prohibit the allylchloride product (Scheme 7-3).¹⁰³

Scheme 7-3 Synthesis of (Z)-halovinyl allylic alcohols



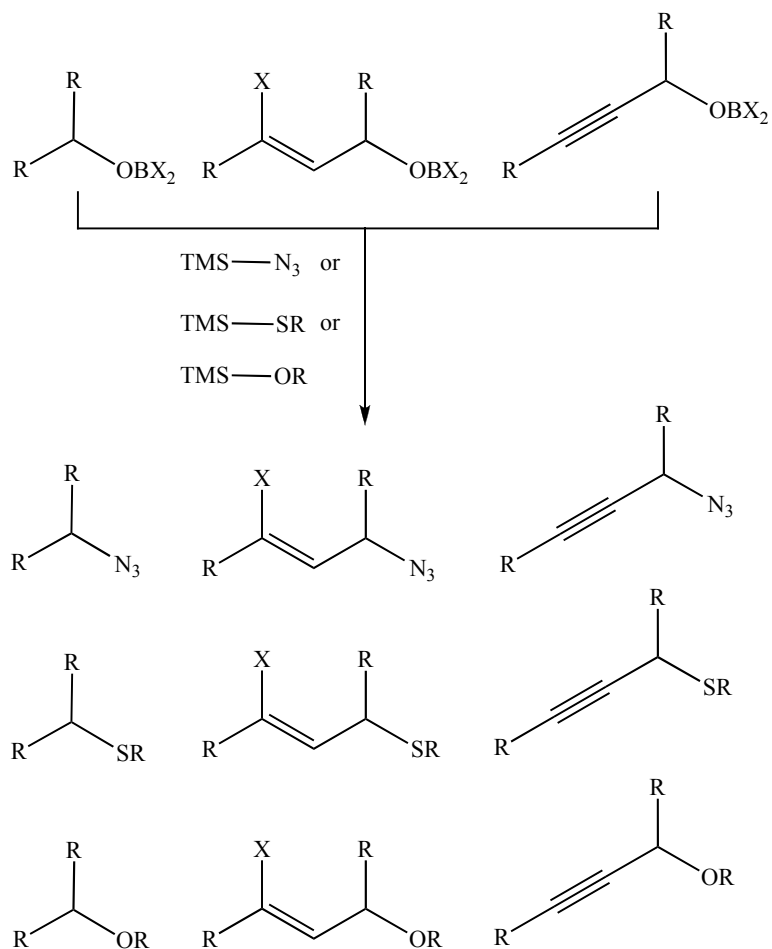
The sequence shown in Scheme 7-3 would circumvent the current limitations in synthesizing (Z)-halovinyl allylic alcohols. These methods do not allow for halovinyl products to form nor have they shown to efficiently form the appropriate organometallic intermediate species.¹⁰⁴

7.3 Heteroatom Nucleophilic Substitution of Alkoxides

The premise of this dissertation focused on forming new carbon-carbon bonds via intermediate organoboron halides. A method of forming carbon-nitrogen, carbon-

oxygen, and carbon-sulfur bonds would increase the synthetic utility of intermediate alkoxyboron halides (**Scheme 7-4**).

Scheme 7-4 Carbon-heteroatom bond formation via oxyboron halide intermediates



It might also be possible to use triethylsilane as a hydride source in a deoxygenation reaction, or silyl enol ethers to form ketones. The intermediate oxyboron halides can be easily generated from the corresponding alcohols or using a Grignard-like reaction with the appropriate carbonyl compounds.

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Appendix

A. X-ray Data for Compound 302

Table A-1 Crystal data and structure refinement for C₂₂H₁₉Cl

Parameter	Output	
Identification code	C ₂₂ H ₁₉ Cl	
Empirical formula	C ₂₂ H ₁₉ Cl	
Formula weight	318.82	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21	
Unit cell dimensions	a = 9.871(4) Å	$\alpha = 90^\circ$
	b = 10.243(4) Å	$\beta = 90.397(7)^\circ$
	c = 16.997(7) Å	$\gamma = 90^\circ$
Volume	1718.5(13) Å ³	
Z	4	
Density (calculated)	1.232 Mg/m ³	
Absorption coefficient	0.219 mm ⁻¹	
F(000)	672	
Crystal size	0.2 x 0.2 x 0.05 mm ³	
Theta range for data collection	1.20 to 26.31°.	
Index ranges	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -21 ≤ l ≤ 21	
Reflections collected	16168	
Independent reflections	6864 [R(int) = 0.0693]	
Completeness to theta = 26.31°	99.1 %	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6864 / 1 / 417	
Goodness-of-fit on F ²	1.029	
Final R indices [I > 2σ(I)]	R1 = 0.0501, wR2 = 0.1207	
R indices (all data)	R1 = 0.0613, wR2 = 0.1313	

Table A-1 continued

Parameter	Output
Absolute structure parameter	0.05(5)
Largest diff. peak and hole	0.334 and -0.340 e.Å ⁻³

Table A-2 Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å²x 10³) for C₂₂H₁₉Cl. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	X	y	z	U(eq)
C(1)	7491(3)	5114(3)	-934(2)	41(1)
C(2)	7655(3)	4851(3)	-1734(2)	46(1)
C(3)	8913(3)	4775(3)	-2049(2)	37(1)
C(4)	10026(3)	4958(3)	-1578(2)	34(1)
C(5)	9880(3)	5253(3)	-786(1)	29(1)
C(6)	8617(3)	5326(2)	-459(2)	28(1)
C(7)	8405(3)	5647(2)	414(2)	28(1)
C(8)	9677(3)	5365(3)	897(1)	32(1)
C(9)	9943(3)	4078(3)	1118(2)	36(1)
C(10)	11126(3)	3758(3)	1516(2)	46(1)
C(11)	12053(3)	4715(3)	1700(2)	45(1)
C(12)	11801(3)	5993(3)	1487(2)	42(1)
C(13)	10615(3)	6311(3)	1095(2)	38(1)
C(14)	7933(3)	7035(2)	504(2)	29(1)
C(15)	6896(2)	7458(2)	929(1)	25(1)
C(16)	6503(2)	8838(2)	1021(1)	25(1)
C(17)	6584(3)	9696(3)	387(2)	31(1)
C(18)	6295(3)	11003(3)	484(2)	36(1)
C(19)	5920(3)	11515(3)	1207(2)	37(1)
C(20)	5827(3)	10649(3)	1837(2)	34(1)

Table A-2 continued

Atom	x	y	z	U(eq)
C(21)	6109(3)	9335(3)	1745(2)	30(1)
C(22)	5596(4)	12934(3)	1310(2)	64(1)
C(23)	1300(3)	8720(3)	5955(2)	31(1)
C(24)	1288(3)	8436(3)	6754(2)	37(1)
C(25)	1459(3)	7170(3)	7011(2)	39(1)
C(26)	1627(3)	6176(3)	6462(2)	37(1)
C(27)	1623(3)	6469(3)	5666(2)	32(1)
C(28)	1461(2)	7741(2)	5404(1)	26(1)
C(29)	1465(2)	8000(2)	4513(1)	25(1)
C(30)	95(2)	7673(2)	4136(1)	25(1)
C(31)	-1098(3)	7856(3)	4531(2)	30(1)
C(32)	-2331(3)	7603(3)	4176(2)	37(1)
C(33)	-2369(3)	7174(3)	3400(2)	40(1)
C(34)	-1182(3)	6999(3)	2994(2)	40(1)
C(35)	50(3)	7239(3)	3358(2)	34(1)
C(36)	1845(2)	9383(2)	4325(1)	26(1)
C(37)	2995(2)	9795(2)	4013(1)	26(1)
C(38)	3339(2)	11175(2)	3859(1)	26(1)
C(39)	4647(3)	11638(3)	3986(2)	36(1)
C(40)	4939(3)	12948(3)	3900(2)	41(1)
C(41)	3939(3)	13839(3)	3688(2)	36(1)
C(42)	2645(3)	13371(3)	3554(2)	30(1)
C(43)	2348(3)	12059(2)	3631(1)	27(1)
C(44)	4261(4)	15271(3)	3604(2)	60(1)
Cl(1)	5923(1)	6349(1)	1468(1)	37(1)
Cl(2)	4254(1)	8676(1)	3772(1)	51(1)

Table A-3 Bond lengths (Å) for C₂₂H₁₉Cl

Atom-Atom Bond	Bond Length (Å)
C(1)-C(6)	1.386(4)
C(1)-C(2)	1.398(4)
C(1)-H(1)	0.9500
C(2)-C(3)	1.357(4)
C(2)-H(2)	0.9500
C(3)-C(4)	1.367(4)
C(3)-H(3)	0.9500
C(4)-C(5)	1.388(4)
C(4)-H(4)	0.9500
C(5)-C(6)	1.371(4)
C(5)-H(5)	0.9500
C(6)-C(7)	1.536(4)
C(7)-C(14)	1.505(3)
C(7)-C(8)	1.524(3)
C(7)-H(7)	1.0000
C(8)-C(13)	1.380(4)
C(8)-C(9)	1.395(4)
C(9)-C(10)	1.386(4)
C(9)-H(9)	0.9500
C(10)-C(11)	1.375(5)
C(10)-H(10)	0.9500
C(11)-C(12)	1.379(5)
C(11)-H(11)	0.9500
C(12)-C(13)	1.382(4)
C(12)-H(12)	0.9500
C(13)-H(13)	0.9500
C(14)-C(15)	1.329(4)
C(14)-H(14)	0.9500
C(15)-C(16)	1.474(4)
C(15)-Cl(1)	1.750(3)

Table A-3 continued

Atom-Atom Bond	Bond Length (Å)
C(16)-C(21)	1.390(4)
C(16)-C(17)	1.393(4)
C(17)-C(18)	1.378(4)
C(17)-H(17)	0.9500
C(18)-C(19)	1.389(4)
C(18)-H(18)	0.9500
C(19)-C(20)	1.394(4)
C(19)-C(22)	1.499(4)
C(20)-C(21)	1.384(4)
C(20)-H(20)	0.9500
C(21)-H(21)	0.9500
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-C(28)	1.383(4)
C(23)-C(24)	1.388(4)
C(23)-H(23)	0.9500
C(24)-C(25)	1.378(4)
C(24)-H(24)	0.9500
C(25)-C(26)	1.392(4)
C(25)-H(25)	0.9500
C(26)-C(27)	1.386(4)
C(26)-H(26)	0.9500
C(27)-C(28)	1.386(4)
C(27)-H(27)	0.9500
C(28)-C(29)	1.537(3)
C(29)-C(36)	1.500(3)
C(29)-C(30)	1.529(3)
C(29)-H(29)	1.0000
C(30)-C(31)	1.372(4)
C(30)-C(35)	1.395(4)

Table A-3 continued

Atom-Atom Bond	Bond Length (Å)
C(31)-C(32)	1.380(4)
C(31)-H(31)	0.9500
C(32)-C(33)	1.390(4)
C(32)-H(32)	0.9500
C(33)-C(34)	1.376(5)
C(33)-H(33)	0.9500
C(34)-C(35)	1.383(4)
C(34)-H(34)	0.9500
C(35)-H(35)	0.9500
C(36)-C(37)	1.325(3)
C(36)-H(36)	0.9500
C(37)-C(38)	1.477(4)
C(37)-Cl(2)	1.742(3)
C(38)-C(43)	1.387(3)
C(38)-C(39)	1.391(4)
C(39)-C(40)	1.380(4)
C(39)-H(39)	0.9500
C(40)-C(41)	1.390(4)
C(40)-H(40)	0.9500
C(41)-C(42)	1.382(4)
C(41)-C(44)	1.507(4)
C(42)-C(43)	1.382(4)
C(42)-H(42)	0.9500
C(43)-H(43)	0.9500
C(44)-H(44A)	0.9800
C(44)-H(44B)	0.9800
C(44)-H(44C)	0.9800

Table A-4 Bond angles (°) for C₂₂H₁₉Cl

Atom-Atom Bond	Bond Length (Å)
C(6)-C(1)-C(2)	119.9(3)
C(6)-C(1)-H(1)	120.0
C(2)-C(1)-H(1)	120.0
C(3)-C(2)-C(1)	120.5(3)
C(3)-C(2)-H(2)	119.8
C(1)-C(2)-H(2)	119.8
C(2)-C(3)-C(4)	119.7(3)
C(2)-C(3)-H(3)	120.2
C(4)-C(3)-H(3)	120.2
C(3)-C(4)-C(5)	120.6(3)
C(3)-C(4)-H(4)	119.7
C(5)-C(4)-H(4)	119.7
C(6)-C(5)-C(4)	120.4(2)
C(6)-C(5)-H(5)	119.8
C(4)-C(5)-H(5)	119.8
C(5)-C(6)-C(1)	118.9(2)
C(5)-C(6)-C(7)	122.3(2)
C(1)-C(6)-C(7)	118.8(2)
C(14)-C(7)-C(8)	112.3(2)
C(14)-C(7)-C(6)	110.2(2)
C(8)-C(7)-C(6)	111.3(2)
C(14)-C(7)-H(7)	107.6
C(8)-C(7)-H(7)	107.6
C(6)-C(7)-H(7)	107.6
C(13)-C(8)-C(9)	118.3(3)
C(13)-C(8)-C(7)	123.2(2)
C(9)-C(8)-C(7)	118.5(2)
C(10)-C(9)-C(8)	120.7(3)
C(10)-C(9)-H(9)	119.6
C(8)-C(9)-H(9)	119.6
C(11)-C(10)-C(9)	119.9(3)

Table A-4 continued

Atom-Atom Bond	Bond Length (Å)
C(11)-C(10)-H(10)	120.0
C(9)-C(10)-H(10)	120.0
C(10)-C(11)-C(12)	119.9(3)
C(10)-C(11)-H(11)	120.0
C(12)-C(11)-H(11)	120.0
C(11)-C(12)-C(13)	120.0(3)
C(11)-C(12)-H(12)	120.0
C(13)-C(12)-H(12)	120.0
C(8)-C(13)-C(12)	121.1(3)
C(8)-C(13)-H(13)	119.5
C(12)-C(13)-H(13)	119.5
C(15)-C(14)-C(7)	127.1(2)
C(15)-C(14)-H(14)	116.4
C(7)-C(14)-H(14)	116.4
C(14)-C(15)-C(16)	125.0(2)
C(14)-C(15)-Cl(1)	120.0(2)
C(16)-C(15)-Cl(1)	114.91(18)
C(21)-C(16)-C(17)	118.1(2)
C(21)-C(16)-C(15)	121.3(2)
C(17)-C(16)-C(15)	120.5(2)
C(18)-C(17)-C(16)	120.5(3)
C(18)-C(17)-H(17)	119.7
C(16)-C(17)-H(17)	119.7
C(17)-C(18)-C(19)	121.9(3)
C(17)-C(18)-H(18)	119.0
C(19)-C(18)-H(18)	119.0
C(18)-C(19)-C(20)	117.3(3)
C(18)-C(19)-C(22)	121.9(3)
C(20)-C(19)-C(22)	120.8(3)
C(21)-C(20)-C(19)	121.2(3)

Table A-4 continued

Atom-Atom Bond	Bond Length (Å)
C(21)-C(20)-H(20)	119.4
C(19)-C(20)-H(20)	119.4
C(20)-C(21)-C(16)	120.9(3)
C(20)-C(21)-H(21)	119.5
C(16)-C(21)-H(21)	119.5
C(19)-C(22)-H(22A)	109.5
C(19)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(19)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(28)-C(23)-C(24)	120.8(3)
C(28)-C(23)-H(23)	119.6
C(24)-C(23)-H(23)	119.6
C(25)-C(24)-C(23)	120.4(3)
C(25)-C(24)-H(24)	119.8
C(23)-C(24)-H(24)	119.8
C(24)-C(25)-C(26)	119.4(3)
C(24)-C(25)-H(25)	120.3
C(26)-C(25)-H(25)	120.3
C(27)-C(26)-C(25)	119.7(3)
C(27)-C(26)-H(26)	120.1
C(25)-C(26)-H(26)	120.1
C(26)-C(27)-C(28)	121.2(3)
C(26)-C(27)-H(27)	119.4
C(28)-C(27)-H(27)	119.4
C(23)-C(28)-C(27)	118.5(2)
C(23)-C(28)-C(29)	122.9(2)
C(27)-C(28)-C(29)	118.6(2)
C(36)-C(29)-C(30)	109.8(2)
C(36)-C(29)-C(28)	112.1(2)

Table A-4 continued

Atom-Atom Bond	Bond Length (Å)
C(30)-C(29)-C(28)	111.5(2)
C(36)-C(29)-H(29)	107.7
C(30)-C(29)-H(29)	107.7
C(28)-C(29)-H(29)	107.7
C(31)-C(30)-C(35)	119.0(2)
C(31)-C(30)-C(29)	121.6(2)
C(35)-C(30)-C(29)	119.3(2)
C(30)-C(31)-C(32)	121.2(2)
C(30)-C(31)-H(31)	119.4
C(32)-C(31)-H(31)	119.4
C(31)-C(32)-C(33)	119.5(3)
C(31)-C(32)-H(32)	120.3
C(33)-C(32)-H(32)	120.3
C(34)-C(33)-C(32)	120.0(2)
C(34)-C(33)-H(33)	120.0
C(32)-C(33)-H(33)	120.0
C(33)-C(34)-C(35)	120.1(3)
C(33)-C(34)-H(34)	120.0
C(35)-C(34)-H(34)	120.0
C(34)-C(35)-C(30)	120.2(3)
C(34)-C(35)-H(35)	119.9
C(30)-C(35)-H(35)	119.9
C(37)-C(36)-C(29)	127.1(2)
C(37)-C(36)-H(36)	116.5
C(29)-C(36)-H(36)	116.5
C(36)-C(37)-C(38)	125.1(2)
C(36)-C(37)-Cl(2)	119.9(2)
C(38)-C(37)-Cl(2)	115.01(19)
C(43)-C(38)-C(39)	118.2(2)
C(43)-C(38)-C(37)	120.8(2)
C(39)-C(38)-C(37)	120.9(2)

Table A-4 continued

Atom-Atom Bond	Bond Length (Å)
C(40)-C(39)-C(38)	120.6(3)
C(40)-C(39)-H(39)	119.7
C(38)-C(39)-H(39)	119.7
C(39)-C(40)-C(41)	121.2(3)
C(39)-C(40)-H(40)	119.4
C(41)-C(40)-H(40)	119.4
C(42)-C(41)-C(40)	117.9(3)
C(42)-C(41)-C(44)	121.1(3)
C(40)-C(41)-C(44)	120.9(3)
C(43)-C(42)-C(41)	121.2(3)
C(43)-C(42)-H(42)	119.4
C(41)-C(42)-H(42)	119.4
C(42)-C(43)-C(38)	120.8(2)
C(42)-C(43)-H(43)	119.6
C(38)-C(43)-H(43)	119.6
C(41)-C(44)-H(44A)	109.5
C(41)-C(44)-H(44B)	109.5
H(44A)-C(44)-H(44B)	109.5
C(41)-C(44)-H(44C)	109.5
H(44A)-C(44)-H(44C)	109.5
H(44B)-C(44)-H(44C)	109.5

Table A-5 Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for $\text{C}_{22}\text{H}_{19}\text{Cl}$.

The anisotropic displacement factor exponent takes the form:

$$-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	29(2)	57(2)	37(2)	-5(1)	5(1)	7(1)
C(2)	42(2)	56(2)	39(2)	-10(1)	-12(1)	2(2)
C(3)	46(2)	38(2)	26(1)	-2(1)	-2(1)	7(1)
C(4)	38(2)	38(2)	26(1)	6(1)	8(1)	7(1)
C(5)	28(1)	33(1)	25(1)	0(1)	2(1)	4(1)
C(6)	33(1)	21(1)	30(1)	0(1)	3(1)	1(1)
C(7)	31(1)	24(1)	30(1)	0(1)	7(1)	1(1)
C(8)	43(2)	34(1)	19(1)	-2(1)	8(1)	9(1)
C(9)	50(2)	33(2)	26(1)	4(1)	8(1)	6(1)
C(10)	61(2)	46(2)	30(2)	8(1)	6(1)	18(2)
C(11)	45(2)	66(2)	24(1)	1(1)	0(1)	20(2)
C(12)	45(2)	50(2)	30(2)	-9(1)	0(1)	5(1)
C(13)	47(2)	37(2)	31(1)	-4(1)	3(1)	7(1)
C(14)	34(1)	25(1)	27(1)	1(1)	6(1)	1(1)
C(15)	27(1)	27(1)	21(1)	-1(1)	0(1)	-2(1)
C(16)	22(1)	27(1)	26(1)	-4(1)	-1(1)	1(1)
C(17)	33(1)	33(1)	26(1)	0(1)	3(1)	2(1)
C(18)	31(2)	31(1)	45(2)	8(1)	2(1)	2(1)
C(19)	33(1)	29(2)	51(2)	-6(1)	1(1)	3(1)
C(20)	33(1)	34(2)	36(2)	-9(1)	1(1)	4(1)
C(21)	29(1)	33(1)	27(1)	-5(1)	0(1)	3(1)
C(22)	70(3)	31(2)	92(3)	-6(2)	12(2)	12(2)
C(23)	35(1)	29(1)	29(1)	2(1)	-1(1)	-1(1)
C(24)	42(2)	39(2)	29(1)	-2(1)	1(1)	-1(1)
C(25)	36(2)	50(2)	32(2)	8(1)	-3(1)	-5(1)
C(26)	35(2)	34(2)	42(2)	13(1)	-5(1)	0(1)
C(27)	30(1)	30(1)	35(1)	3(1)	-2(1)	-2(1)
C(28)	20(1)	30(1)	28(1)	5(1)	1(1)	-2(1)

Table A-5 continued

Atom	U¹¹	U²²	U³³	U²³	U¹³	U¹²
C(29)	26(1)	24(1)	26(1)	1(1)	5(1)	-1(1)
C(30)	30(1)	22(1)	23(1)	2(1)	2(1)	-1(1)
C(31)	31(1)	36(1)	22(1)	2(1)	1(1)	1(1)
C(32)	31(1)	49(2)	32(2)	10(1)	1(1)	1(1)
C(33)	43(2)	42(2)	34(2)	12(1)	-12(1)	-13(1)
C(34)	56(2)	40(2)	23(1)	1(1)	-2(1)	-11(1)
C(35)	41(2)	35(1)	26(1)	1(1)	6(1)	-5(1)
C(36)	24(1)	26(1)	26(1)	1(1)	3(1)	3(1)
C(37)	24(1)	30(1)	23(1)	4(1)	-1(1)	3(1)
C(38)	26(1)	32(1)	20(1)	2(1)	4(1)	-2(1)
C(39)	28(1)	42(2)	39(2)	7(1)	-1(1)	-3(1)
C(40)	29(2)	48(2)	45(2)	6(1)	0(1)	-12(1)
C(41)	44(2)	31(2)	34(2)	-2(1)	9(1)	-9(1)
C(42)	33(1)	28(1)	27(1)	2(1)	3(1)	1(1)
C(43)	25(1)	33(1)	22(1)	3(1)	2(1)	-4(1)
C(44)	67(2)	36(2)	77(3)	0(2)	15(2)	-17(2)
Cl(1)	44(1)	28(1)	39(1)	0(1)	15(1)	-3(1)
Cl(2)	36(1)	35(1)	83(1)	14(1)	25(1)	10(1)

Vita

Scott T. Borella, son of Thomas B. and Rosemary A. Borella, brother of Mark C. Borella, was born on 28 May 1980 at Magee Women's Hospital in Pittsburgh, PA USA. He attended grade school (K-5) at St. Sebastian's School and Carson Middle School (6-8) in the North Allegheny School district. Grades 9 and 10 were spent at North Allegheny Intermediate while grades 11 and 12 at North Allegheny Senior High. During his high school years he earned several first team All-America honors for swimming. Upon graduation in June 1998, he matriculated to Gannon University in Erie, PA USA where he studied chemistry with a minor in biology. After a one-year sojourn at the Pennsylvania College of Optometry in Elkins Park, he began graduate studies in chemistry at The University of Tennessee, Knoxville in January 2004. In March he joined the Kabalka research group and began investigating boron Lewis acids in synthesis during the summer. Upon recommendation from Professor Kabalka, he was selected in March 2006 to attend the 56th Meeting of Nobel Laureates and Students in Lindau, Germany through sponsorship of the Oak Ridge Associated Universities (ORAU). Upon successful defense of this dissertation, he accepted a position at Johns Hopkins University in Baltimore, MD USA to conduct postdoctoral research with Professor Gary H. Posner.