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I am submitting herewith a dissertation written by Yuhong Ju entitled "Organoboron Halides in Organic Synthesis." I have examined the final paper copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

George W. Kabalka, Major Professor

We have read this dissertation
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Accepted for the Council:

Vice Provost and Dean of
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ORGANOBORON HALIDES IN ORGANIC SYNTHESIS

A Dissertation
Presented for the
Doctor of Philosophy
Degree

The University of Tennessee, Knoxville

Yuhong Ju
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DEDICATION

This dissertation is dedicated

to my parents Youli Ju and Shulan Wang

Who have raised me with love and inspired me to be always strong in my life.

My husband Qifeng Tao for his support,

And my beloved daughter Yuchen (Nina) Tao for her

patience and being always with me during this work.

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ABSTRACT

This dissertation summarizes our recent researches in organoboron halides chemistry. The coordination of the very effective Lewis acids, boron halides or organoboron halides, with weak Lewis bases, carbonyl compounds mediated a series of new reactions. These newly-discovered reactions include reductive bromination of aromatic aldehydes to give rise to benzyl bromides; alkylation and chloroalkylation of aromatic aldehydes by alkylboron dichloride and dialkylboron chloride; dialkenylation of aldehydes to 1,3,5-triaryl-1,5-dihalo-1,4-dienes with alkynes mediated by boron trihalides; addition of aldehydes with styrenes to form 1,3-diaryl-1,3-dihalo-propanes in the presence of boron halides, and reactions of aromatic aldehydes with styrenes and (*E*)-β-methylstyrene to afford 1,3-diaryl-3-chloro-1-propanaols stereo- and regioselectively.

The new synthetic methodologies involving organoboron halides developed in this dissertation are important transformations in modern organic synthesis. Mild reaction conditions and tolerance of various organic functional groups are advantages of utilizing boron reagents in synthesis.

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LISTS OF SYMBOLS AND ABBREVIATIONS

AcOH	Acetic acid
Ar	Aryl
Alpine-Borane	*B*-Iso-2-pinocampheyl-9-borabicyclo[3.3.1]nonane
Eapine-Borane	*B*-Iso-2-ethylapopinocampheyl-9-borabicyclo[3.3.1]nonane
9-BBN	9-Borabicyclo[3.3.1]nonane
B-X-9-BBN	*B*-halo-9-borabicyclo[3.3.1]nonane, (X = Br, I)
Bu	Butyl
BuLi	Butyl lithium
t-BuOK	Potassium *tert*-butoxide
°C	Degree Celsius
C_6D_6	Bezene-d_6
$CDCl_3$	Chloroform-*d*
CH_2Cl_2	Methylene chloride
Chx	Cyclohexyl
Δ	Heat
d	Doublet
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DME	Ethylene glycol dimethyl ether
ee	Enantiomeric excess
Et	Ethyl
Et_3N	Triethylamine

Et_2O	Diethyl ether
GC	Gas Chromatography
H_2O_2	Hydrogenperoxide
$HSiEt_3$	Triethylsilane
Hz	Hertz
Ipc_2BH	Diisopinocampheylborane
$IpcBH_2$	Isopinocampheylborane
Ipc_2BCl	*B*-chlorodiisopinocampheylborane (DIP-Chloride)
J	Proton-proton coupling constant
K_2CO_3	Potassium carbonate
m	Multiplet
Me	Methyl
MeOH	Methanol
mins	Minutes
NaOH	Sodium hydroxide
NMR	Nuclear magnetic resonance spectroscopy
[O]	Oxidation
Ph	Phenyl
Pr	Propyl
R	Alkyl
r.t.	Room temperature
s	Singlet

t	Triplet
Sia_2BH	Disiamylborane
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Tetramethylsilane

Chapter 1. Boron halides in organic synthesis

1.1 Scope of this dissertation

This dissertation is focused on newly discovered reactions involving boron halides and their derivatives. These reactions include (a) reductive bromination of aromatic aldehydes, (b) alkylation and chloroalkylation of aryl aldehydes, (c) dialkenylation of aryl aldehydes by phenylacetylene in the presence of boron trihalides, (d) boron trihalides and phenylboron dichloride promoted addition of aryl aldehydes to alkenes. A brief description of reactions using organoboron halides, alkylations of carbonyl compounds, the coordination of boron halides to carbonyl compounds, and haloboration of alkynes and alkenes by boron trihalides will be presented in this chapter because they are fundamental to understanding the new chemistry discussed in this dissertation.

1.1.1 Historical aspects of organoboron halides in organic chemistry

Boron halide chemistry was initiated almost two hundred years ago when the boron trifluoride-ammonia complex ($BF_3 \cdot NH_3$) was isolated.[1] The empty *p*-orbital on electron deficient boron (III) causes most boron compounds to be Lewis acids. The Lewis acidities of boron trihalides have been measured and found to be in the order of $BF_3 < BCl_3 < BBr_3 < BI_3$,[2] exactly the reverse of the order expected on the basis of the relative σ-donor strengths of the halide anions. The main reason for this anomaly is that the B-X bonds contain a π-component, which is formed by the overlap of a filled *p*-orbital on the halogen with the empty *p*-orbital on the boron. Because the latter orbital is used to form a

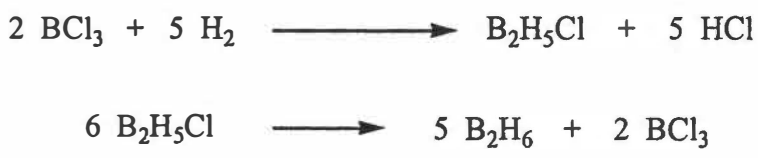
σ-bond when BX_3 coordinates with a Lewis base, the π-component is completely destroyed by complex formation. The strengths of the π-component increase in the order of I < Br < Cl < F, and the amount of π-bond energy that is lost on complex formation increases as the atomic weight of the halogen decreases. Evidently, as far as the extent of complex formation is concerned, this is a more important factor than the corresponding decrease in the σ-donor strength of halogen.[3] The synthetic applications of BX_3 Lewis acids in organic synthesis include the cleavage of ethers, acetals and esters,[4, 5] stereoselective glycosidation of glycols under mild conditions,[6] Aldol condensation reactions,[7] Friedel-Crafts reactions[8] and other acid-related reactions.

Organoboranes were first synthesized in 1859 by Frankland (**Scheme 1-1**).[9] Since then, an enormous amount of research work has been reported and reactions of organoboron halides in organic synthesis have been well documented.[10] Monochlorodiborane was observed by Schlesinger and Burg in 1931, although it was found to be highly unstable (**Scheme 1-2**).[11]

Practical methods for the preparation and application of organoboron halides have been developed during the search for new hydroborationg agents. Hydroboration of alkenes and alkynes provides a variety of organoboranes.[12-16] The development of halogen-substituted borane derivatives has attracted much attention in the last fifty years,

$$3\,(C_2H_5)_2Zn + 2\,(C_2H_5O)_3B \longrightarrow 2\,(C_2H_5)_3B + 3\,Zn(OC_2H_5)_2$$

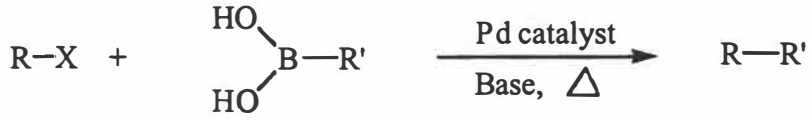
Scheme 1-1 Synthesis of organoboranes



Scheme 1-2 Formation of monochlorodiborane and its disproportionation

the halogen atoms on boron in organoboron halides serve as blocking groups and allow the formation of mono- or dialkylboron halides selectively. The presence of one or two halogen atoms influences the Lewis acidities of organoboranes so that the reagents differ considerably in their reactivities. In general, they are used stoichiometrically in organic transformations under anhydrous reaction conditions because moisture in the air will cause their rapid decomposition.

Lewis acid-promoted carbon-carbon bond formation is one of the most important process in modern organic synthesis. Classically, Friedel-Crafts reactions, the Diels-Alder reaction, and the Mukaiyama Aldol synthesis are catalyzed by ordinary Lewis acids such as $AlCl_3$, $TiCl_4$, BF_3 or $SnCl_4$. Organoboron halides have also been widely used to enolize carbonyl compounds regioselectively[17] and to reduce prochiral carbonyl compounds to optically active alcohols enantioselectively.[18] Boron halides derivatives have also been utilized to promote a number of organic reactions including condensations, alkylations, as well as halogenations of alcohols, aldehydes and benzylic alcohols to the corresponding bromides.[19] One of the most successful and widely used example is Suzuki cross coupling reaction (**Scheme 1-3**).[20]



Scheme 1-3 Suzuki cross coupling reaction

1.2 Reductions of functional groups via boron reagents

There are five categories of boron-based reducing reagents: hydroborates ($NaBH_4$, Bu_4NBH_4, $NaBH_3CN$, and KR_3BH etc.); boranes; borane complexes with amines, phosphines etc.; trialkylboranes; and mixtures composed of a hydroborate and a salt of a transition metal or f-block metal.[21] These five categories can be further divided into two main types in terms of their electronic nature: nucleophilic reducing agents such as the hydroborates ("basic"), and electrophilic reducing agents such as the boranes ("acidic"). Although aldehydes and ketones can be easily reduced by both hydroborates and boranes, in many other cases compounds which are readily reduced by one type are not reduced by the other. The reduction of functional groups by hydroborates will be discussed very briefly while the reduction by boranes and their derivatives will be covered in more detail.

1.2.1 Reductions involving hydroborates

The hydroborates generally behave as nucleophilic reagents, and the reactivities of different functional groups towards hydroborates are consistent with their Electrophilicities: acid chloride > aldehyde > ketone > ester > amide > alkyl halide. Carboxylic acids and alkenes are generally not reduced by hydroborates.

The decreasing reducing power of tetrahydroborates is in the order of $Al(BH_4)_3$ > $Mg(BH_4)_2$ > $LiBH_4$ > $NaBH_4$ > $Cd(BH_4)_2$,[14] It should be noted that lithium borohydride is usually used in an ethereal solvent, whereas sodium borohydride is generally used in aqueous or alcohol media and, of course, the solvents influence reactivity.[22] $Zn(BH_4)_2$ is about as reactive as $NaBH_4$, but is less basic and can be used to reduce base-sensitive compounds.[23]

Reaction solvents significantly affect the rate of the hydroborate reductions. The reduction of a carbonyl group by nucleophilic attack at carbon by borohydride is greatly facilitated by electrophilic attack at the carbonyl oxygen.[24] Protic solvents, or an added electrophile, enhance the reduction whereas solvents which strongly solvate the counter-ion decrease the reduction rate. Crown ethers,[25] polar aprotic solvents,[26] or cations with poor complexing ability[27] will diminish the rate of reduction. On the other hand, the reduction of alkyl halides by $NaBH_4$ is not dependent on the complexation and is faster than ester and nitro group reduction in dimethyl sulphoxide.[28] $NaBH_3CN$ in hexamethylphosphoramide also reduces alkyl halide in preference to aldehydes and ketones.[29]

The kinetic nucleophilicities of substituted hydroborates ($M^+R_3BH_4^-$) decrease in the order of trialkylhydroborate > trialkoxyhydroborate > tetrahydroborate and the same is true for reduction.

Regio- and chemoselectivities of hydroborates are usually very diverse compared to borane derivatives, an area reviewed by Brown.[30] They will not be discussed here.

1.2.2 Reduction using boranes and their derivatives

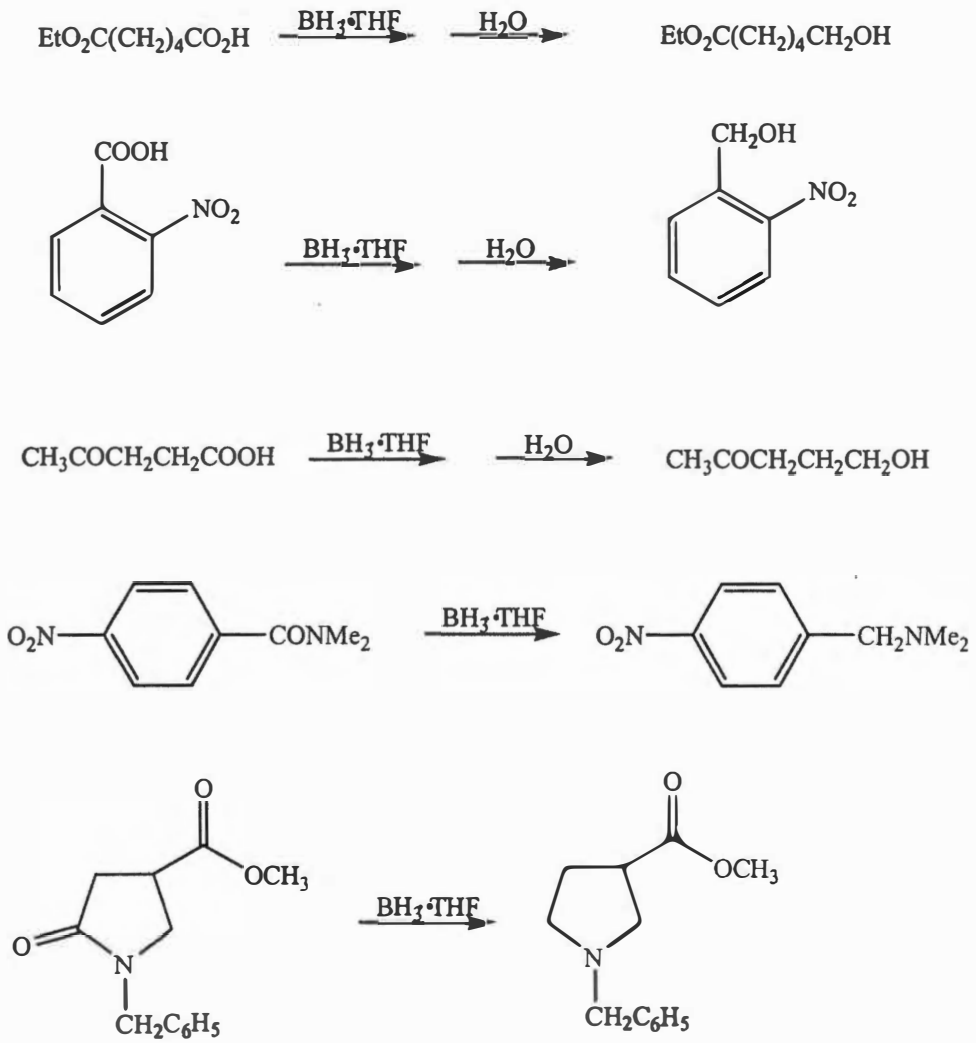
In contrast to hydroborates, boranes and their derivatives may be considered as electrophilic reducing agents, they will attack electron rich species and reduce them. Boranes and derivatives readily reduce carboxylic acids, alkenes and alkynes. For instance, BH_3·THF was used to selectively reduce acid and amide[31] functions in the presence of an ester. Boranes complex with all species bearing lone pairs of electrons, these include oxygen, sulfur and nitrogen of the group V or group VI elements. Examples include BH_3·THF, BH_3·SMe_2, BH_3·NH_3, BH_3· *tert*-$BuNH_2$ and BH_3·pyridine.

Commonly used borane derivatives include monoakylboranes (thexylborane, isopinocampheylborane), dialkylboranes (disiamylborane, dicyclohexylborane, 9-BBN, diisopinocampheylborane), trialkylboranes [*B*-siamyl-9-BBN, Alpine-borane$^{(R)}$], catecholborane, monochloroborane, dichloroborane, thexylchloroborane, and *B*-chlorodiisopinocampheylborane (DIP-Chloride), etc. These reagents are more selective than borane because of electronic and steric effects that are caused by the alkyl substituents, and they play an important role in the field of asymmetric reduction.

1.2.2.1 Reduction of carbonyl functions via boranes

Although the most well known reaction involving borane is the hydroboration of carbon-carbon multiple bonds,[15] it is not the focus of this dissertation. Only the reductions of functional groups will be discussed in this section.

Most aldehydes and ketones are readily reduced to the corresponding alcohols by BH_3·THF at 0 °C.[32] The borane-THF complex was reported to reduce carboxylic acids and amide even in the presence of other functional groups (**Scheme 1-4**).[31-35]



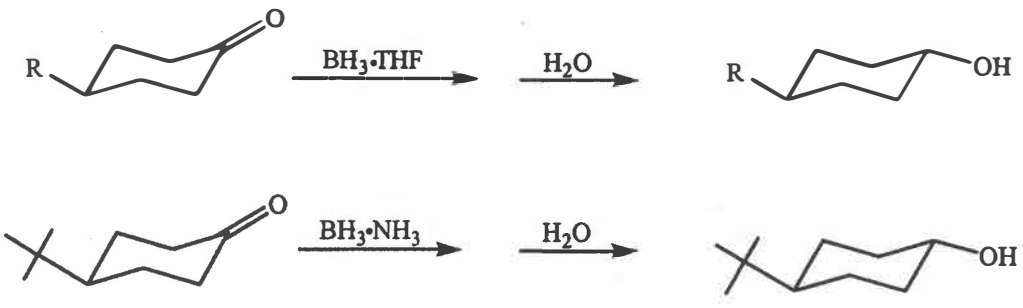
Scheme 1-4 Selective reduction by BH_3·THF

The diastereoselectivity of borane reducing agents towards cyclic ketones generally favors the formation of the more stable equatorial alcohol, with the hydride attacking from the more hindered axial direction (**Scheme 1-5**).[36, 37]

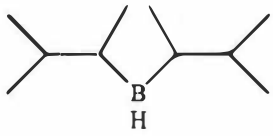
1.2.2.2 Reduction via alkylboranes

The reducing power of alkylated boranes is not as strong as borane because they are weaker Lewis acids than borane, but they are more selective and react under milder conditions. The structures of some commonly used alkylboranes are listed in **Figure 1-1**. Examples of reductions utilizing alkylboranes are enormous; only representative examples will be described in this section.

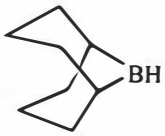
Disiamylborane reduces γ-lactones to the corresponding γ-hydroxyaldehydes. This transformation is quite general and applicable to a variety of γ-lactones (**Scheme 1-6**).[38] Disiamylborane also reacts with tertiary amides to give aldehydes as products (**Scheme 1-7**).[38]



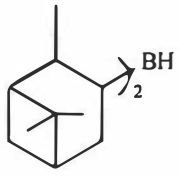
Scheme 1-5 Reduction of cycloalkanones by BH_3·THF and BH_3·NH_3



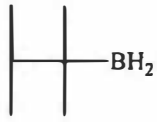
disiamyborane
(Sia_2BH)



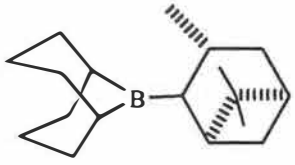
9-borabicyclo[3.3.1]nonane
(9-BBN)



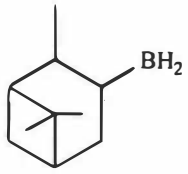
diisopinocampheylborane
Ipc_2BH



thexylborane

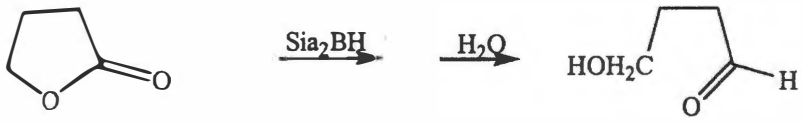


B-isopincampheyl-9-
borabicyclo[3.3.1]nonane
Aldrich: Alpine-Borane

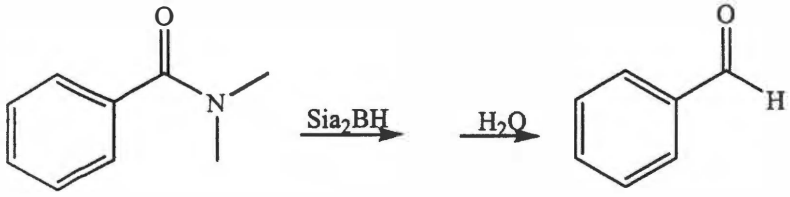


isopinocampheylborane
$IpcBH_2$

Figure 1-1 Structures and names of alkylborane reducing agents



Scheme 1-6 Reduction of γ-lactones

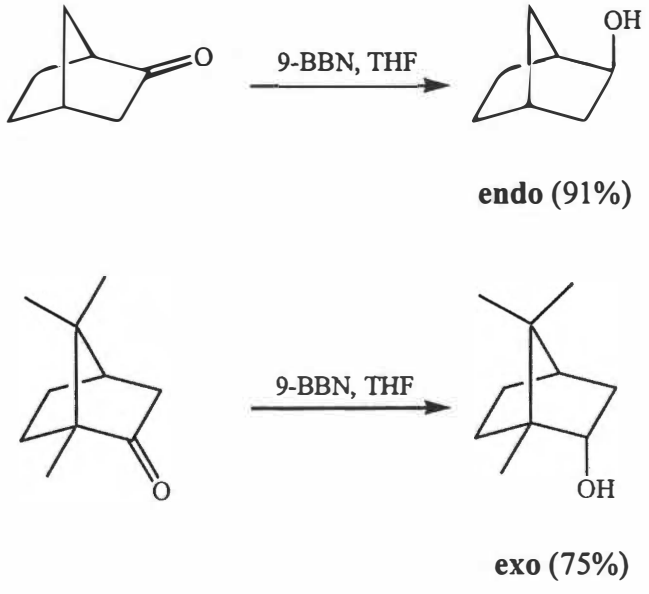


Scheme 1-7 Reduction of tertiary amide

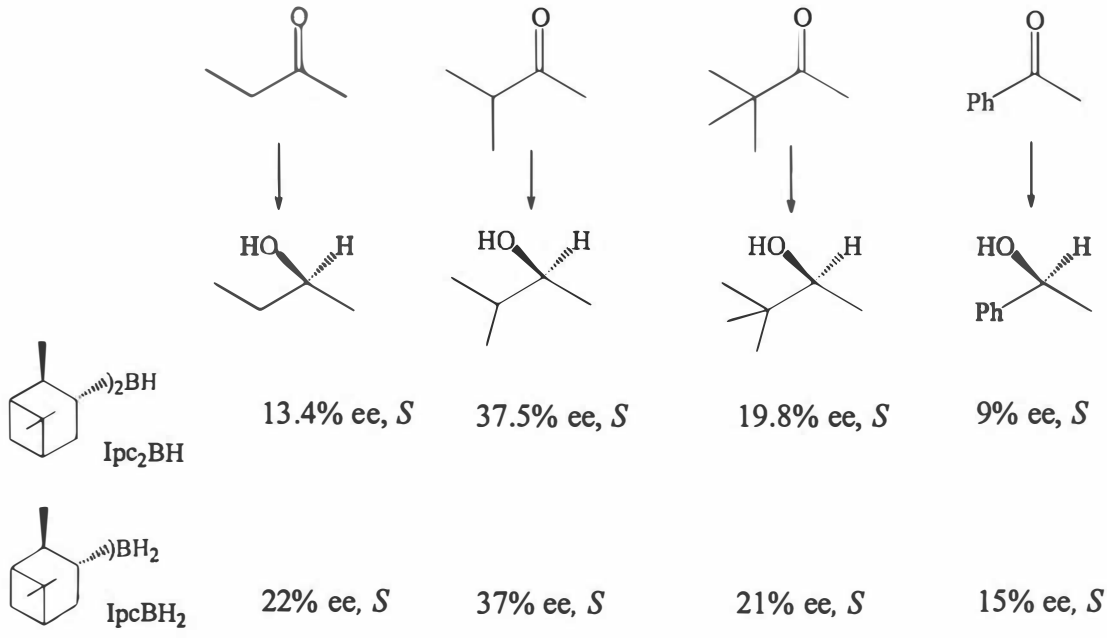
The reduction of cyclic and bicyclic ketones with 9-BBN yields predominantly the less stable epimers as the result of attack from less hindered side.[39] **(Scheme 1-8)**

Diisopinocampheylborane (Ipc_2BH) and isopinocampheylborane ($IpcBH_2$) are very good chiral hydroboration agents, but proved unsatisfactory as chiral reducing agents **(Scheme 1-9)**.[40]

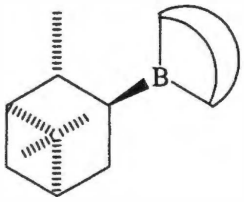
Trialkylboranes are ineffective reductants, but hindered trialkylboranes will reduce aldehydes and ketones under extremely mild conditions, with the elimination of highly substituted alkenes by β-hydrogen transfer to the carbonyl carbon.[41] Examples include Midland's Alpine-Borane[42] (*B*-iso-2-pinocampheyl-9-borabicyclo[3.3.1]nonane) and Eapine-Borane (*B*-iso-2-ethylapopinocampheyl-9- borabicyclo[3.3.1]nonane) synthesized by Brown and co-workers **(Figure 1-2)**.[43] During the last twenty years,



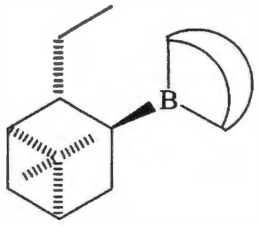
Scheme 1-8 Stereochemistry of 9-BBN reduction



Scheme 1-9 Asymmetric reduction via Ipc_2BH and $IpcBH_2$



Alpine-Borane



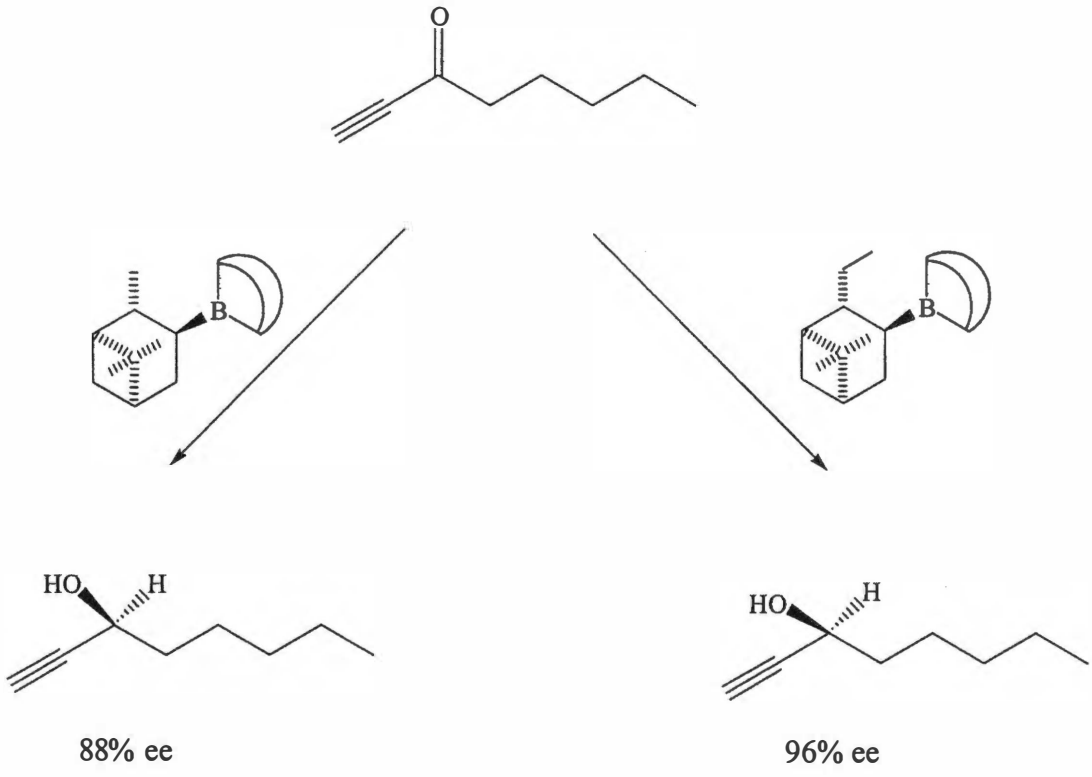
Eapine-Borane

Figure 1-2 Alpine-Borane and Eapine-Borane

asymmetric reduction via trialkylboranes has been well developed. The prerequisite boranes are readily prepared by hydroboration and tolerate many functional groups because there is no hydride present on the boron. The critical factor in asymmetric synthesis is to achieve high degree of asymmetry: high enantiomeric purity (high ee). The representative reductions of prochiral acetylenic ketones to optically active propargylic alcohols are representative and are depicted in **Scheme 1-10**.[43]

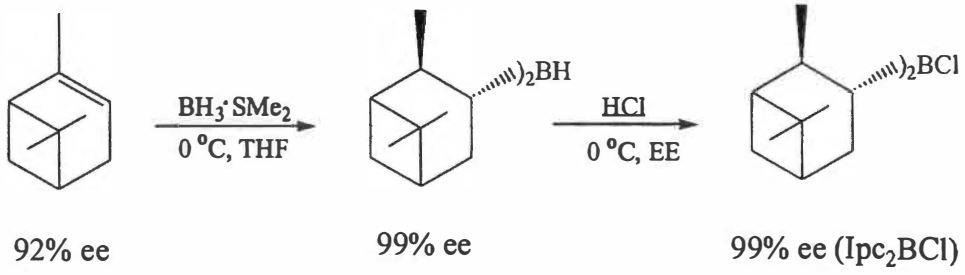
1.2.2.3 Asymmetric reduction via dialkylboron halide: Ipc_2BCl

One advantange of using organoborane reducing agents is that electronic and steric demands can be tuned by varying the groups attached to boron; even halogen atoms can be introduced to change the Lewis acidity of boron. Brown has investigated the reactivity of dialkylboron chloride with the assumption that the halogen might increase the Lewis acidity and thus increase the rate of reduction.[44] *B*-Chlorodiisopinocamphenylborane (DIP-Chloride, Aldrich Chemical Company) is indeed an efficient reductant in asymmetric reduction relative to trialkylboranes.[45]

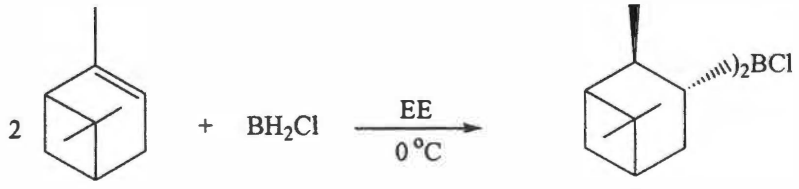


Scheme 1-10 Asymmetric reduction via Alpine-Borane and Eapine-Borane

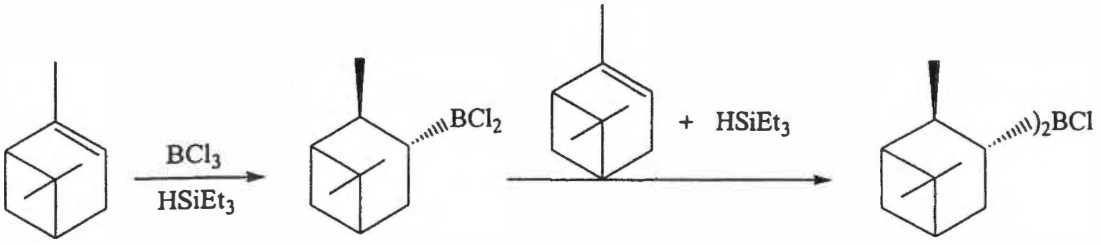
B-Chlorodiisopinocamphenylborane can be prepared from commercially available α-pinene in high chemical and optical purities by hydroboration with borane followed by treatment with gaseous HCl (**Scheme 1-11**).[46] Alternatively, direct hydroboration of α-pinene with monochloroborane affords the desired *B*-chlorodiisopinocamphenylborane (**Scheme 1-12**).[47] Matteson[48] developed a convenient method for preparing alkylboron dihalides or dialkylboron halide by haloboration of alkenes using a haloborane/trialkysilane mixture(**Scheme 1-13**).



Scheme 1-11 Preparation of Ipc_2BCl via hydroboration using borane

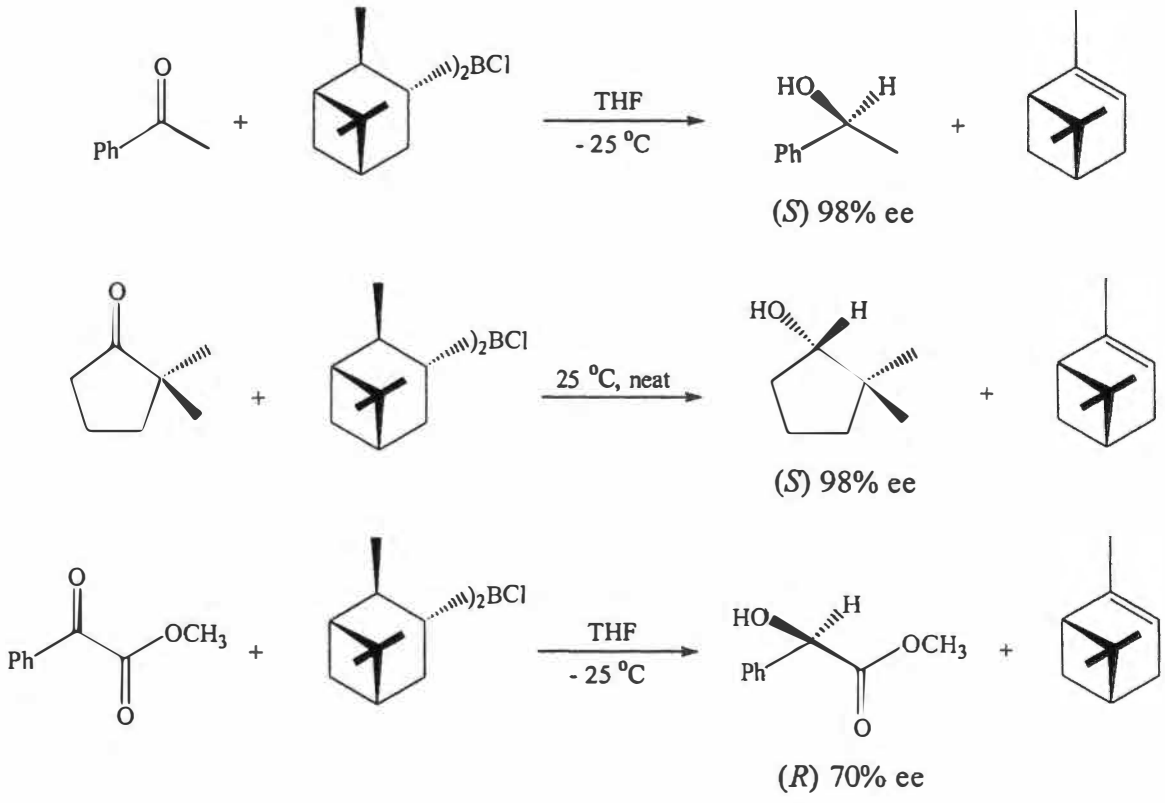


Scheme 1-12 Preparation of Ipc_2BCl via hydroboration using monochloroborane

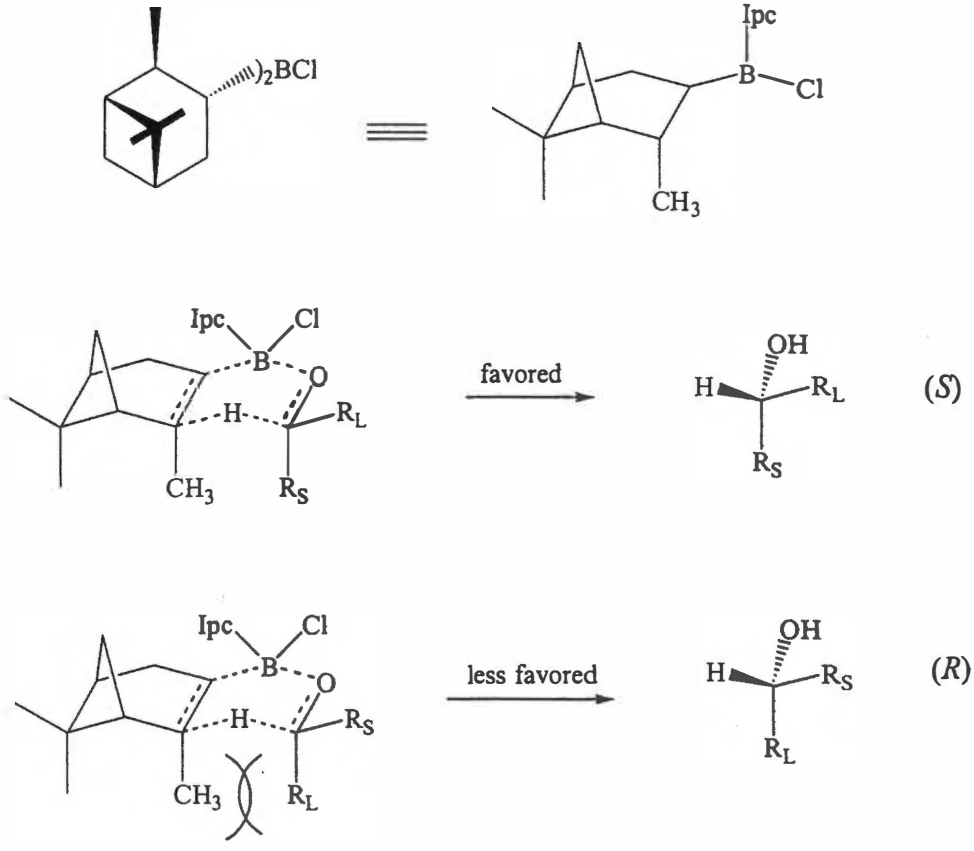


Scheme 1-13 Preparation of Ipc_2BCl via hydroboration using haloborane/trialkysilane mixture

B-Chlorodiisopincamphenylborane (Ipc_2BCl) is capable of reducing aryl alkyl ketones with enantiomeric excesses ranging from 79.3%-100%.[45] **Scheme 1-14** contains some examples using (-)-Ipc_2BCl, an exceptionally efficient chiral reducing agent. Many functional groups are compatible with this reagent. Both (+)-Ipc_2BCl and (-)-Ipc_2BCl enantiomers are commercially available, either enantiomer of the alcohol can be synthesized. The synthetic application of this reagent in pharmaceutical research is very promising.[49] As background to the reductive bromination of aromatic aldehydes via isopinocamphenylboron dibromide which will be presented in chapter 2 of this dissertation, a proposed reduction reaction pathway is shown in **Scheme 1-15**,[45] similar to that proposed by Midland for Alpine-Borane reduction.[50] A six-membered, cyclic, "boat-like" transition state is the key intermediate. *Syn* elimination of the boron moiety and the β-hydrogen results in the optically pure (+)-α-piene. In the preferred transition state, only the smaller alkyl group (R_S) encounters a *syn* axial methyl interaction while the bulky alkyl group (R_L) assumes an equatorial-like orientation. This explains the predorminant formation of the *S* isomer of the alcohols.



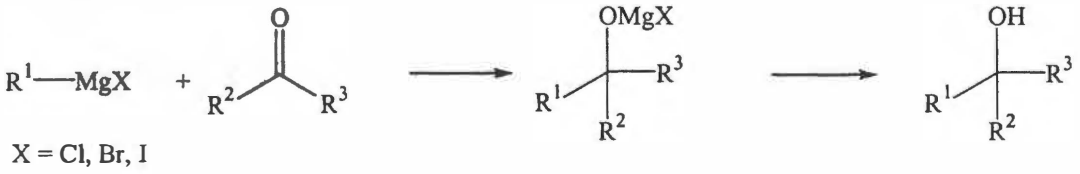
Scheme 1-14 Reduction of prochiral arylalkyl, α-tertiary ketones and keto esters via (-)-Ipc_2BCl



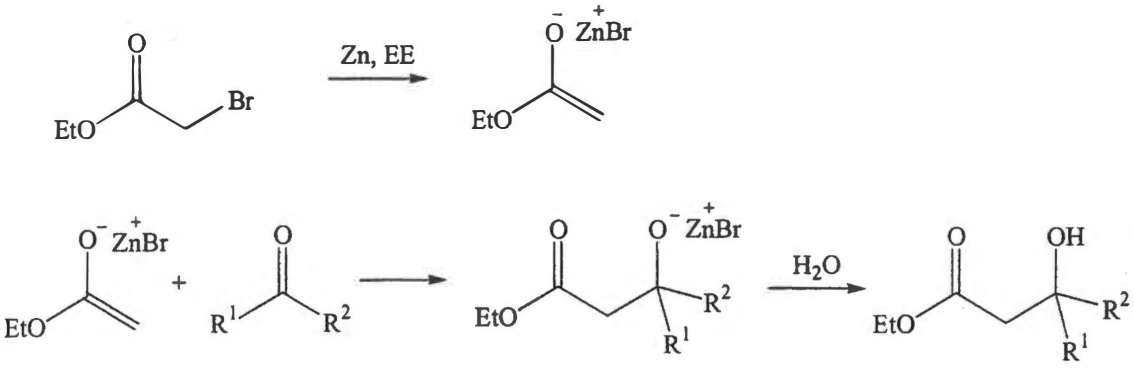
Scheme 1-15 Mechanism for Ipc_2BCl asymmetric reduction

1.3 Alkylation of carbonyl with organoboron compounds

Alkylation of carbonyl compounds by organometallic reagents is one of the most useful reactions in synthetic organic chemistry. Only reactive alkylmetals such as the organomagnesium (Grignard reagent),[51] organolithium,[52] organozinc[53] and certain organotransition metal reagents[54] can generally be utilized to alkylate carbonyl compounds. Organomagnesium reagents react with formaldehyde to give primary alcohols, (**Scheme 1-16**) other aldehydes give secondary alcohols, and ketones give tertiary alcohols. It is advisable to decompose the magnesium salt of alcohol with aqueous ammonium chloride when the alcohol is sensitive to acid. Organolithium reagents are more reactive than Grignard reagents. In reactions with α,β-unsaturated ketones, lithium compounds predominantly give 1,2-addition products, whereas Grignard reagents react predominantly by 1,4-addition. Organozinc compounds are one of the first classes of main-group organometallic compounds prepared. These popular organometallic reagents were replaced by the more reactive organomagnesium compounds and organolithium compounds. The Reformatsky reaction (addition of zinc ester enolates to aldehydes) has remained in use by organic chemists (**Scheme 1-17**).[55]



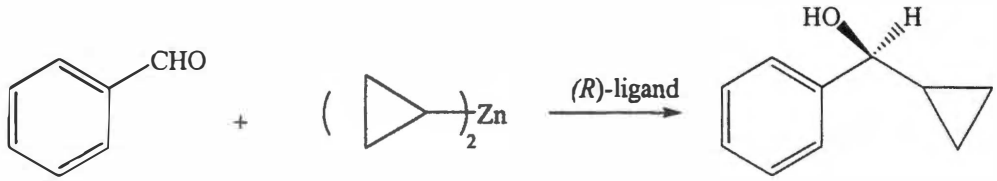
Scheme 1-16 Grignard reaction of carbonyl compounds



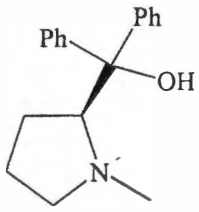
Scheme 1-17 Reformatsky reaction

In the past twenty years, asymmetric organozinc addition to carbony compounds has been a fruitful research area. One example is given in **Scheme 1-18** in which an *in situ* generated chiral zinc complex is used to generate a chiral product.[56]

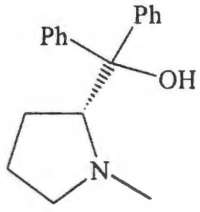
Organoboranes do not normally react with carbonyl compounds in a Grignard-like fashion with the exception of allylborane, alkenylborane and alkynylborane reagents.[57-61] The stereoselective crotylboration of α-oxycarboxylic acids (and related research by our group[62]) is one of the many examples of allylboration of carbonyl groups (**Scheme 1-19**). Asymmetric allyl- and crotylboration of carbonyl compounds using chiral *B*-allylbis(2-isocaranyl)borane are valuable methods in natural products synthesis.[59] A Grignard-like addtion of *B*-alkenyl-9-borabicyclo[3.3.1]nonanes to aldehydes was reported by Jacob and Brown in 1970s (**Scheme 1-20**).[60] The addition of *B*-alkenyl-9-BBN to aldehydes affords the corresponding allylic alcohol with the retention of the double bond stereochemistry. The *B*-allyl-9-BBN addition to carbonyl compounds is relatively more facile than reactions of alkenylboranes.[60]



(*S*) 86%, ee

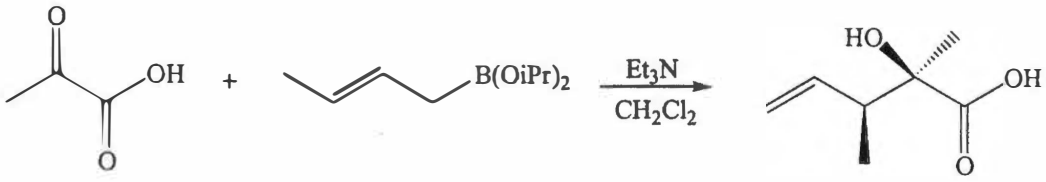


(*S*)-ligand



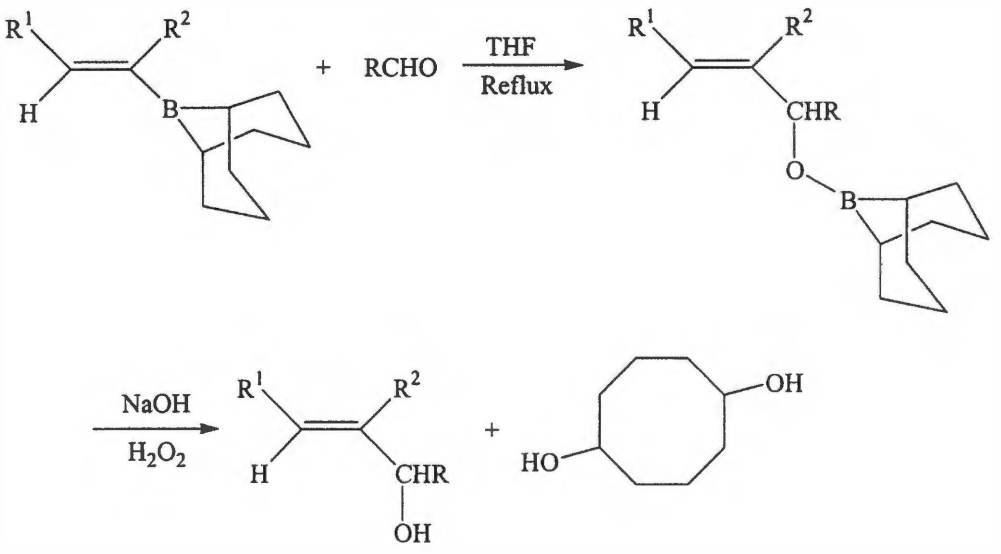
(*R*)-ligand

Scheme 1-18 Asymmetric dicyclopropylzinc addition to benzaldehyde



Syn/Anti = 99/1

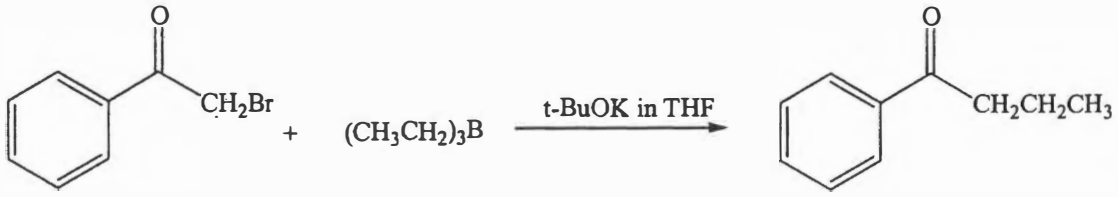
Scheme 1-19 Stereoselective crotylboration of α-oxycarboxylic acid



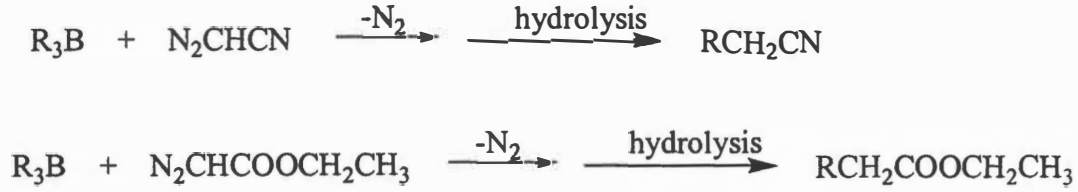
Scheme 1-20 Grignard-like addition of *B*-alkenyl-9-BBN to aldehydes

Although α-alkylation of α-halo carbonyl compounds[63] (**Scheme 1-21**), diazoacetonitrile and ethyl diazoacetate[64] (**Scheme 1-22**) via organoboron compounds have been achieved, none involve direct alkylation of the carbonyl function. 1,4-Conjugated addtion of organoborane to α,β-unsaturated carbonyl derivatives have been investigated by Brown and coworkers[65, 66] (**Scheme 1-23**) and involve free radical chain mechanism (**Scheme 1-24**). However, the alkylation of carbonyl compounds by organoboranes under nonradical conditions has not been reported except for a few unique cases.

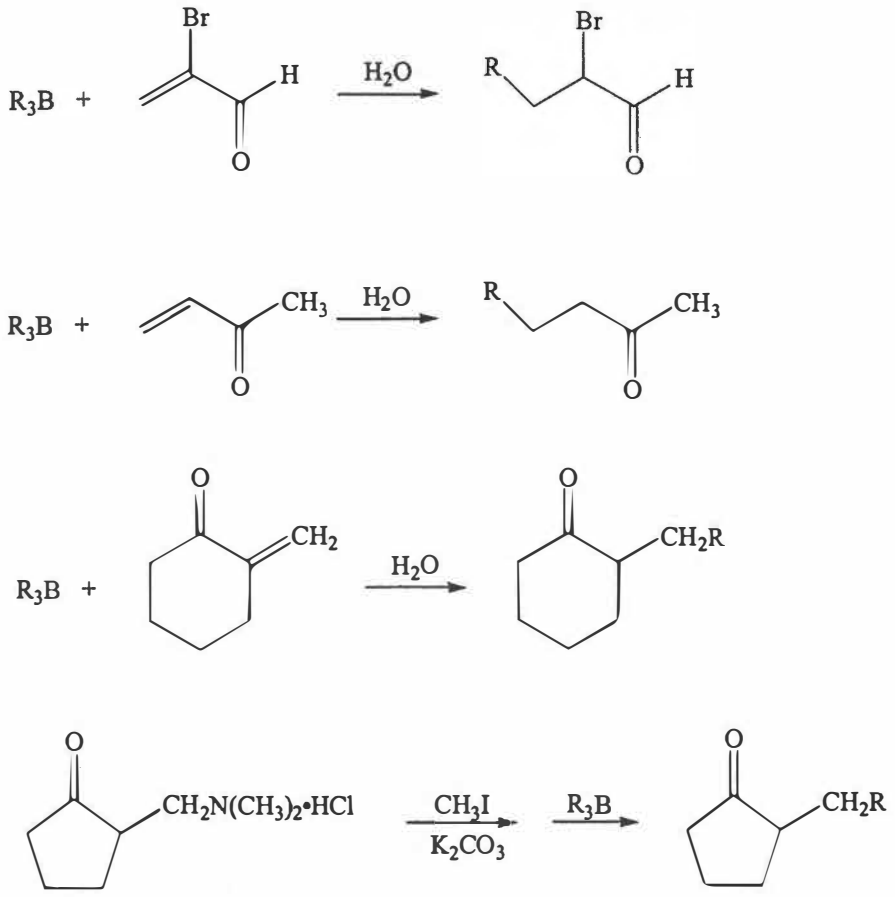
The few known alkylborane carbonyl alkylation reactions require unusually reactive organoboranes. For example, 1-boraadamantane reacts with carbonyl compounds to give rise to an air stable heterocyclic cage intermediate which is too stable to have any



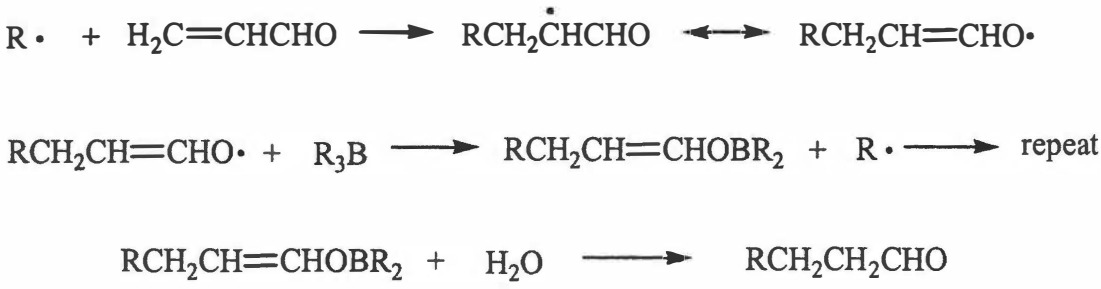
Scheme 1-21 α-Alkylation of ketones by trialkylboranes



Scheme 1-22 Alkylation of diazoacetonitrile and ethyl diazoacetate via tralkylboranes



Scheme 1-23 β-Alkylation of carbonyl compounds (1,4-addtion) using trialkylboranes

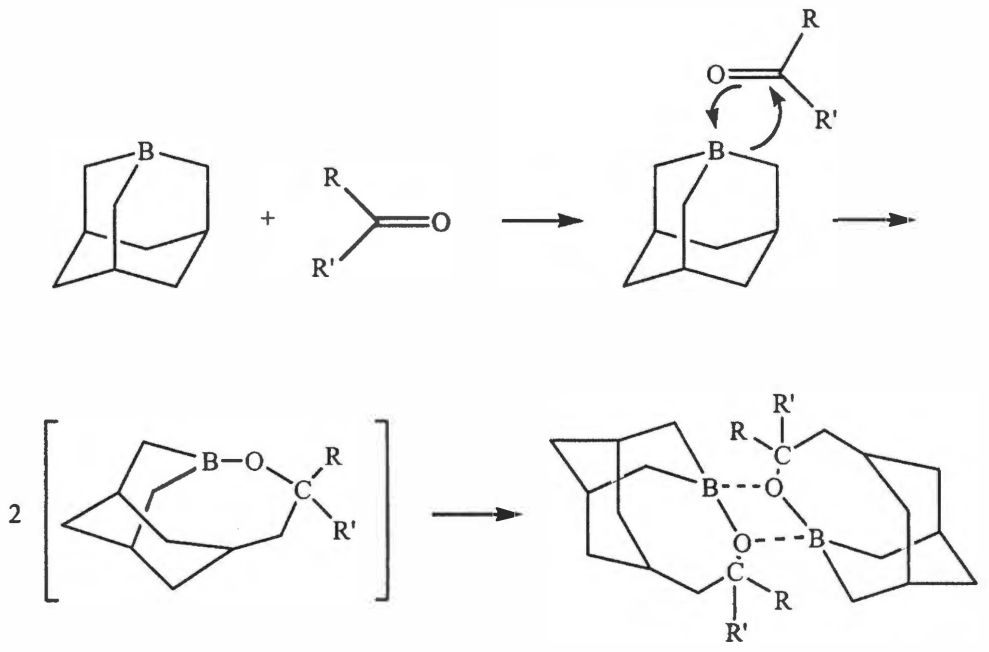


Scheme 1-24 Free radical chain mechanism of organoborane 1,4-addition to α,β-unsaturated carbony compounds

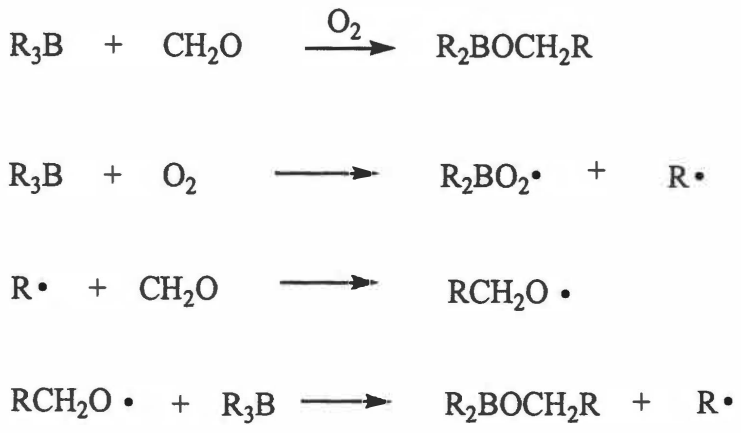
synthetic utility (**Scheme 1-25**).[67] One free radical reaction (**Scheme 1-26**) was reported by Brown.[68, 69] Finally, modification[70] of the carbonyl group has been used to achieve alkylation (**Scheme 1-27**) along with activation of the carbonyl group by neighboring groups (**Scheme 1-28**).[71]

1.4 Haloboration of alkynes and alkenes with boron halides

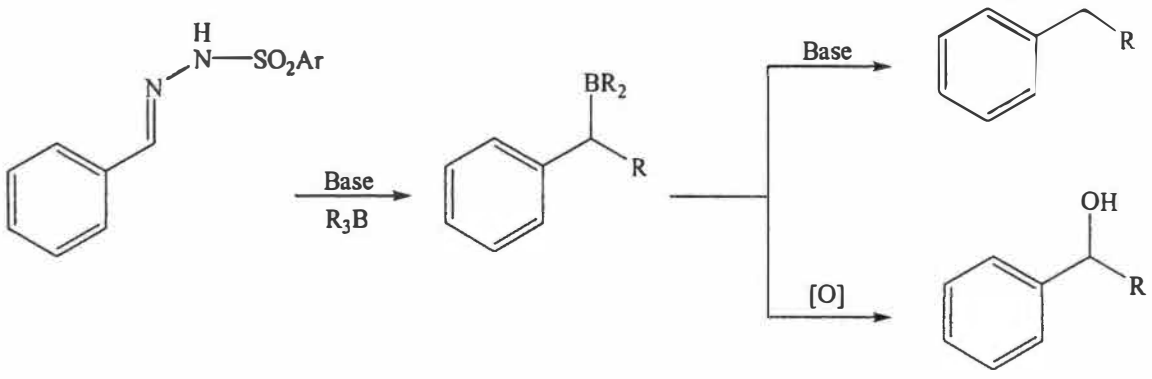
Boron trihalides and phenylboron dichloride react with acetylenes to afford 2-halo- or 2-phenylalkenyl boranes. These haloboration reactions and their applications in organic chemistry have been extensively reviewed.[72] The reactions usually occur in a stereo-, regio-, and chemoselective fashion via the *syn* addition of the B-X moiety to the substituted acetylenes except that *anti* addition occurs for acetylene, generating the corresponding (*Z*)- and (*E*)-2-halo-1-alkenylboranes (**Scheme 1-29**).[73] The stereoselectivity of the haloboration of phenylacetylene by BX_3 (X = Cl, Br, I) was studied by Blackborow in detail.[74]



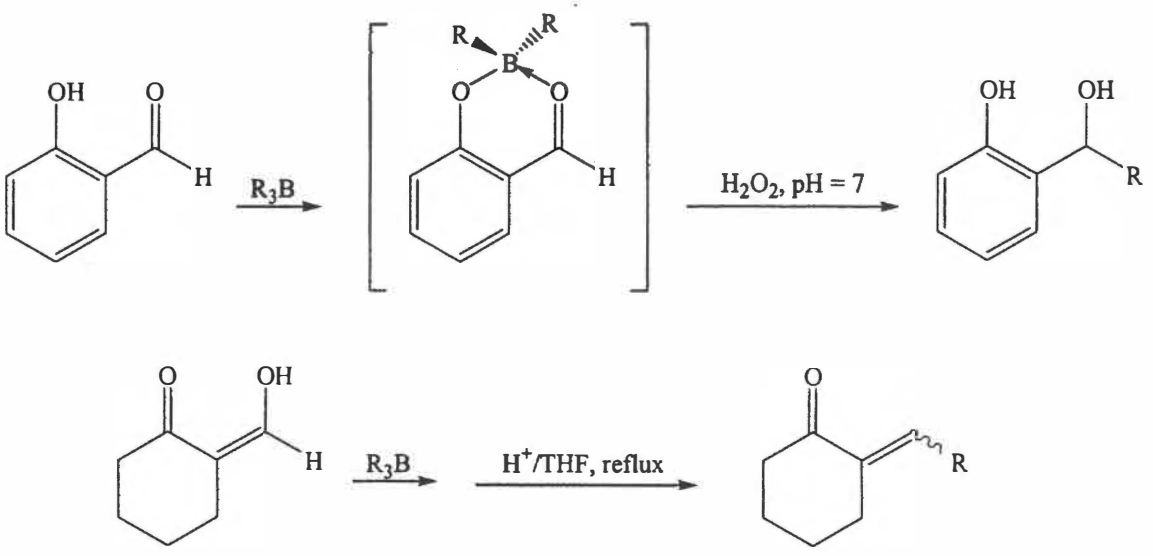
Scheme 1-25 Reaction of 1-boraadamantane with carbonyl compounds



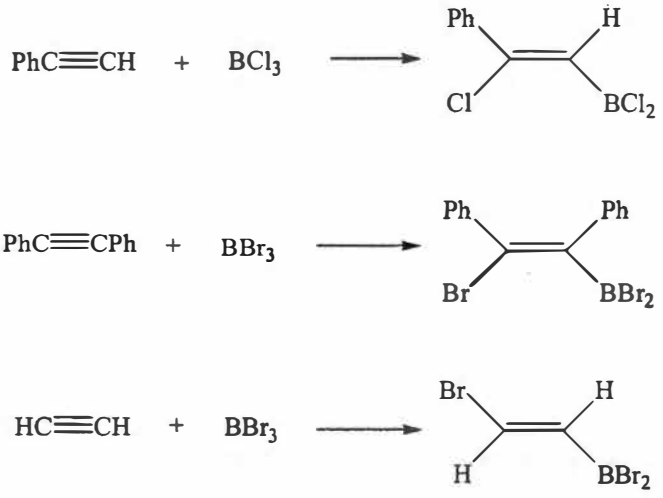
Scheme 1-26 Organoboranes addition to formaldehyde induced by oxygen



Scheme 1-27 Alkylation of aldehydes (arenesulfonyl)hydrazone with trialkylboranes



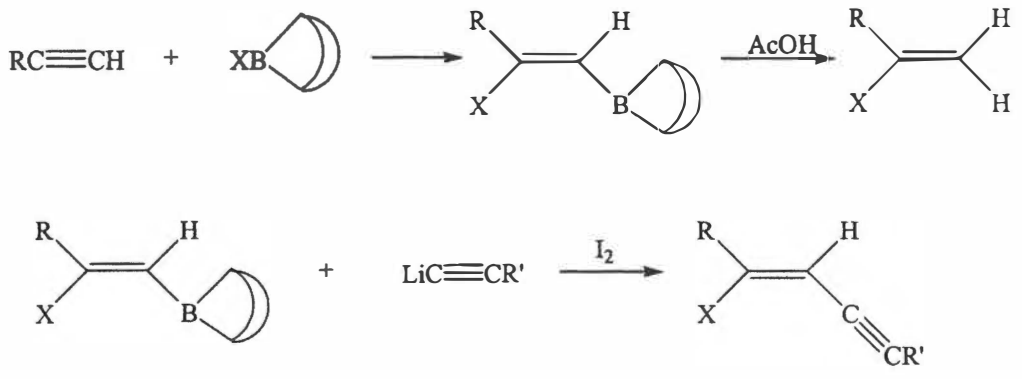
Scheme 1-28 Alkylation of *o*-hydroxyarylaldehyde and α-formylketones via trialkylboranes



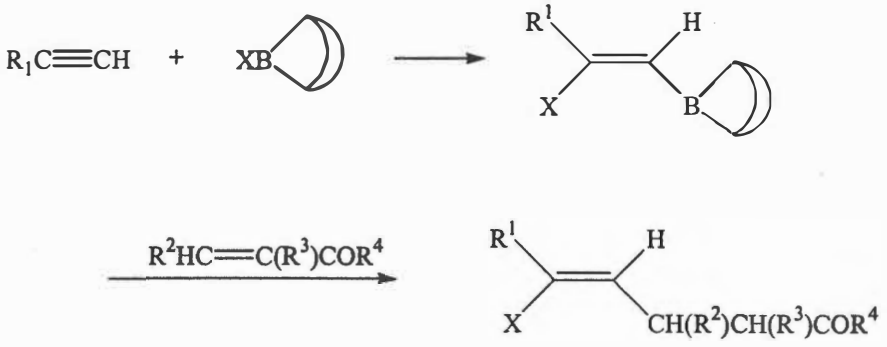
Scheme 1-29 Haloboration of alkynes by boron halides

The reactivity of boron halides addition to carbon-carbon triple bonds is consistent with the Lewis acidity discussed at the beginning of this chapter in the order of $BF_3 < BCl_3 < BBr_3 < BI_3$. This trend was confirmed by Lappert and Prokai who noted that bromoboration of diphenylacetylene occurs readily around 25 °C whereas chloroboration doesn't take place under the same reaction condition.[73]

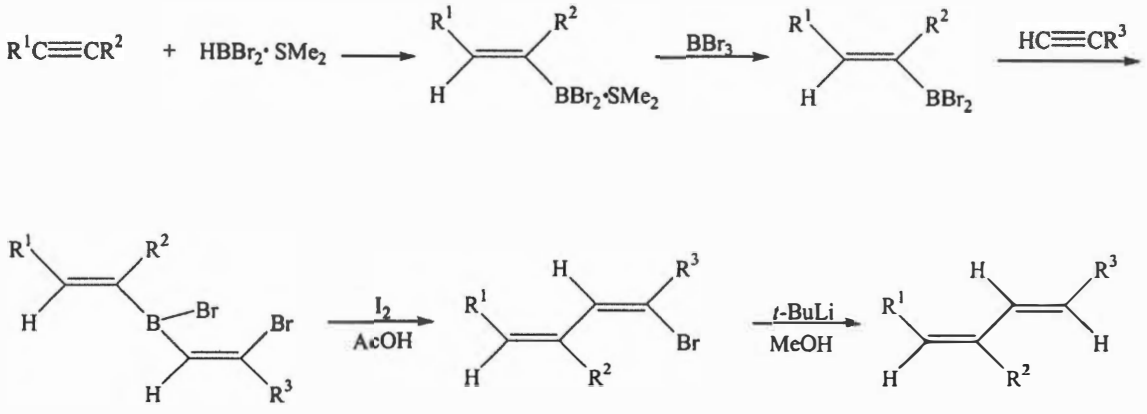
The haloboration of alkynes with boron trihalides and *B*-halo-9-borabicyclo[3.3.1]nonanes (*B*-X-9-BBN, X = Br, I) generate valuable intermediates.[75] Suzuki and coworkers have demonstrated various applications of haloboration reaction in organic synthesis, such as selective synthesis of alkenes and 1,3-enynes via *B*-X-9-BBN[76] (**Scheme 1-30**), stereospecific synthesis of (*Z*)-δ-halo-γ,δ-unsaturated ketones[77] (**Scheme 1-31**), direct and selective synthesis of (*Z,Z*)-1-bromo-1,3-dienes and (*E, Z*)-1,3-dienes[78] (**Scheme 1-32**). Conversion of the haloboration adduct 2-halo-1-alkenylboron halide to 2-halo-1-alkenylboronic esters provides a variety of precursors for Suzuki type cross coupling reactions. One example is shown in **Scheme 1-33**.[79]



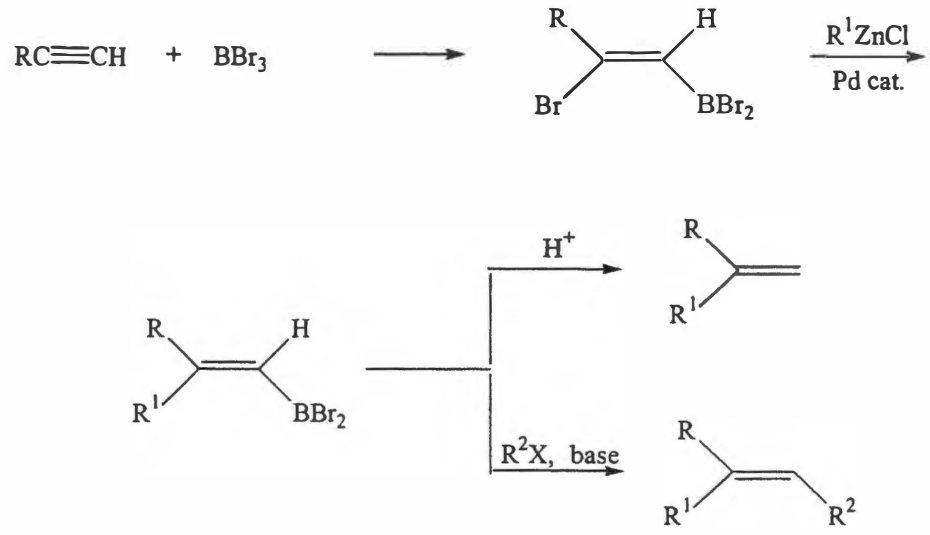
Scheme 1-30 Synthesis of alkenes and 1,3-enynes via *B*-X-9-BBN



Scheme 1-31 Stereospecific synthesis of (*Z*)-δ-halo-γ,δ-unsaturated ketones via the haloboration of terminal alkynes



Scheme 1-32 Synthesis of (*Z, Z*)-1-bromo-1,3-dienes and (*E, Z*)-1,3-dienes

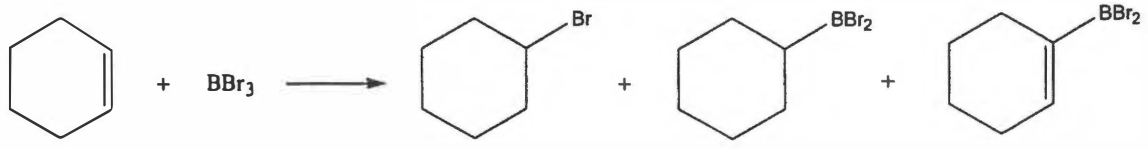


Scheme 1-33 Synthesis of di- and trisubstituted alkenes

Haloboration of olefins has been reported in only a few cases by Lappert,[80] chloroboration and Lewis acid (BCl_3) catalyzed cationic polymerization appeares to compete; Bromoboration of cyclohexene gave mixtures containing substitution products **(Scheme 1-34)**.

1.5 Statement of problem

Reduction of carbonyl compounds using organoboron compounds has been extensively studied during the past fifty years. And diisopinocamphenyl-boron chloride and isopinocamphenylboron dichloride have been widely used for asymmetric reduction of carbonyl compounds. This dissertation is focus on the reactions of boron halide derivatives with carbonyl compounds. Reductive bromination using isopinocamphenylboron dibromide was investigated (Chapter 2).



Scheme 1-34 Bromoboration of cyclohexene

Alkylation and chloroalkylation of aromatic aldehydes by alkylboron dichloride and dialkylboron chloride were also investigated (Chapter 3). Attempts to alkylate aryl aldehyde tosylhydrazones via alkyboron halides gave an unexpected homocoupling reaction resulting in stilbene formation (Chapter 4).

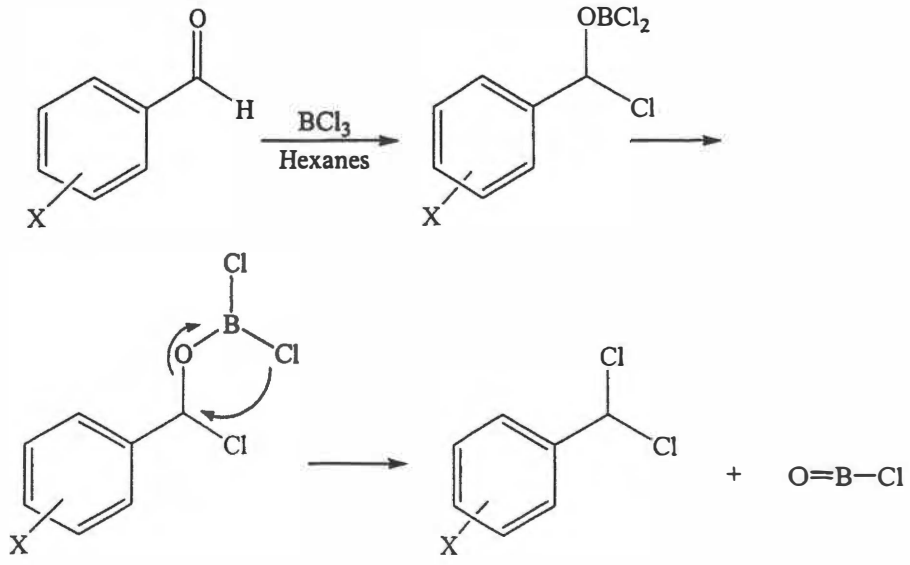
Dialkenylation of aldehydes to generate 1,3,5-triaryl-1,5-dihalo-1,4-dienes brings two haloalkenyl groups to the carbonyl carbon (Chapter 5). Addition of aromatic aldehydes to styrenes to form 1,3-diaryl-1,3-dihalo-propanes and reactions of aromatic aldehydes with styrenes and (*E*)-β-methylstyrene to afford 1,3-diaryl-3-chloro-1-propanaols stereo- and regioselectively were also examined in the course of this study (Chapter 6).

Chapter 2. Reductive bromination of aromatic aldehydes using alkylboron dibromides

2.1 Introduction

The chlorination of aryl aldehydes to the corresponding *gem*-dichlorides is a very useful transformation in organic synthesis since the product dichloroarylmethanes are of value in the pharmaceutical and agricultural industries. Generally, PCl_5 is used to generate geminal dichlorides. Other methods include the use of $PhCCl_3/FeCl_3$, SeO_2/Me_3SiCl, $SOCl_2$/DMF and $SOCl_2/(Me_2N)_3PO$ as chlorination reagents. Recently, the oxophilic *d*-block metal chlorides were used to chlorinate aromatic aldehydes. However, all these methods require either high temperature or toxic reagents. Boron trichloride has been extensively used as a reagent for the cleavage of a wide variety of ethers. To our knowledge, boron trichloride has not been utilized to convert aldehydes to the corresponding geminal dichlorides. During a recent study of an Aldol-Grob reaction sequence catalyzed by boron trihalides, researchers in our group found that BCl_3 failed as a catalyst. On closer examination, they discovered that BCl_3 reacts with aromatic aldehydes to generate the corresponding geminal dichlorides in excellent yields (**Scheme 2-1**).[81] The reaction provides an efficient method for generating these useful products.

The reactions of aromatic aldehydes with boron tribromide and boron triiodide were reported to produce dibromomethylbenzene and diiodomethylbenzene.[82] The



Scheme 2-1 Reaction of BCl_3 with aromatic aldehydes

reactivities of aromatic aldehydes with BCl_3, BBr_3 and BI_3 are consistent with the reactivities discussed earlier in Chapter 1.

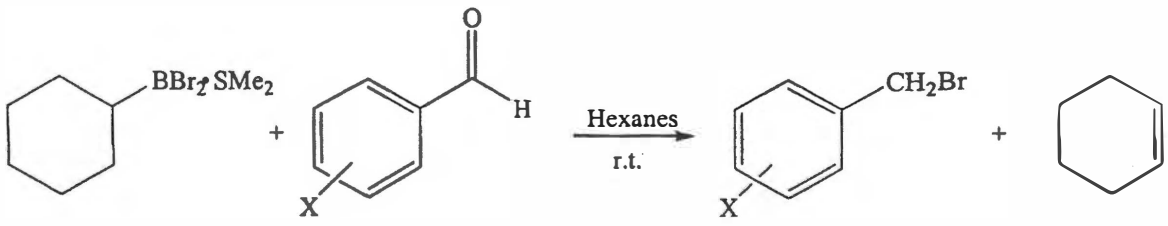
We examined the reaction of dicyclohexylboron bromide with aryl aldehydes and found that no reaction occurred at room temperature although reduction of aldehydes occurred upon heating.[83] (Dialkylboron halildes are known to be effective reducing agents.[40, 84, 85]) Boron tribromide has been used to convert benzyl alcohols to the corresponding benzyl bromides.[86] We then investigated the reaction of cyclohexylboron dibromide with aryl aldehydes and found no alkylation reaction, instead, the corresponding benzyl bromides slowly formed. The formation of benzyl bromides in this reaction was unexpected, the direct conversion of aromatic aldehydes to benzyl bromides

derivatives had been achieved in only two prior instances; these involved the use of a mixture of trimethylaminoboron hydride and bromine[87] or the use of a mixture of lithium bromide, chlorotrimethylsilane, and tetramethyldisiloxane.[88]

2.2 Results and discussion

2.2.1 Reductive bromination of aromatic aldehydes with cyclohexylboron dibromide (ChxBBr$_2$)

The reaction of cyclohexylboron dibromide-dimethyl sulfide complex with aryl aldehydes at room temperature in hexanes slowly formed benzyl bromide (**Scheme 2-2**). If the reaction mixture was refluxed, benzyl bromide is formed rapidly, but dibromomethylbenzene occured as a side product via a double migration of halogen as has been observed in the reaction of aromatic aldehydes with boron trihalides.[81, 82] The detection of cyclohexene by GC/MS analysis of reaction mixture indicated that the reduction involved the β-hydrogen in the cycohexyl group.



Scheme 2-2 Reductive bromination of aromatic aldehydes with cyclohexylboron dibromide-dimethyl sulfide complex

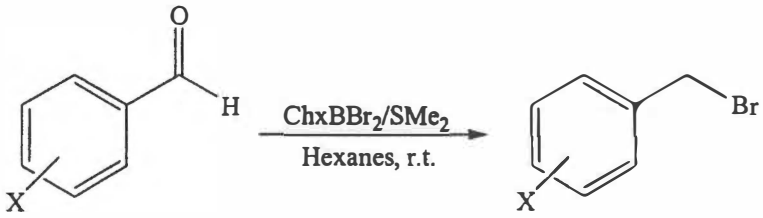
A variety of aryl aldehydes were subjected to this new reaction, the results are tabulated in **Table 2-1**. The reaction of cyclohexylboron dibromide with aryl aldehydes resulted in the formation of the corresponding benzyl bromides in moderate yields along with a small amount of dibromomethylbenzenes. As can be seen from the data in **Table 2-1**, all of the aldehydes investigated were successfully converted to the corresponding benzyl bromides. However, aromatic aldehydes containing strong electron withdrawing substituents were reduced at a slower rate and generated lower yields. Since isopinocampheylboron dibromide is a more efficient reducing agent than cyclohexylboron dibromide, only a few aromatic aldehydes were evaluated using cyclohexylboron dibromide-dimethyl sulfide complex in **Table 2-1**.

2.2.2 Reductive bromination of aromatic aldehydes with isopinocampheylboron dibromide ($IpcBBr_2$)

Isopinocampheylboron dibromide is one of the most efficient reagents for reducing carbonyl compounds via β-hydrogen transfer reactions.[89] The β-hydrogen in the isopinocampheyl moiety is a tertiary hydrogen while the β-hydrogen in cyclohexyl is secondary, the *B*-alkyl group is transformed into an olefin as the elimination takes place to form a highly substituted olefin. 2,6,6-Trimethylbicyclo[3.1.1]hept-2-ene, is more readily formed than cyclohexene under the same reaction condition.(**Figure 2-1**)

The reactions of isopinocampheylboron dibromide-dimethyl sulfide complex with aryl aldehydes bearing a variety of substituents yielded the corresponding benzyl bromide in excellent yields. It is noteworthy that the carbon-carbon double bond presented in *trans*-cinnamaldehyde was not affected in this reaction. The experimental results are

Table 2-1 The reactions of aryl aldehydes with cyclohexylboron dibromide-dimethyl sulfide complexat room temperature



Entry	Substrate	Product [a]	Time (hr)	Yields (%) [b]
1	C_6H_5CHO	$C_6H_5CH_2Br$ (**201**)	18	65
2	4-ClC_6H_4CHO	4-$ClC_6H_4CH_2Br$ (**202**)	24	57
3	2-FC_6H_4CHO	2-$FC_6H_4CH_2Br$ (**203**)	28	56
4	4-$CH_3C_6H_4CHO$	4-$CH_3C_6H_4CH_2Br$ (**204**)	14	62
5	4-(NC)C_6H_4CHO	4-(NC)$C_6H_4CH_2Br$ (**205**)	30	59
6	C_6H_5CH=$CHCHO$	C_6H_5CH=$CHCH_2Br$ (**206**)	16	51

[a] All reaction products exhibited physical and spectral characteristics in accord with literature values.

[b] Isolated yields based on aldehydes.

Figure 2-1 Trisubstituted olefin vs disubstituted cyclohexene

summarized in **Table 2-2**.[90]

2.2.3 Mechanistic study

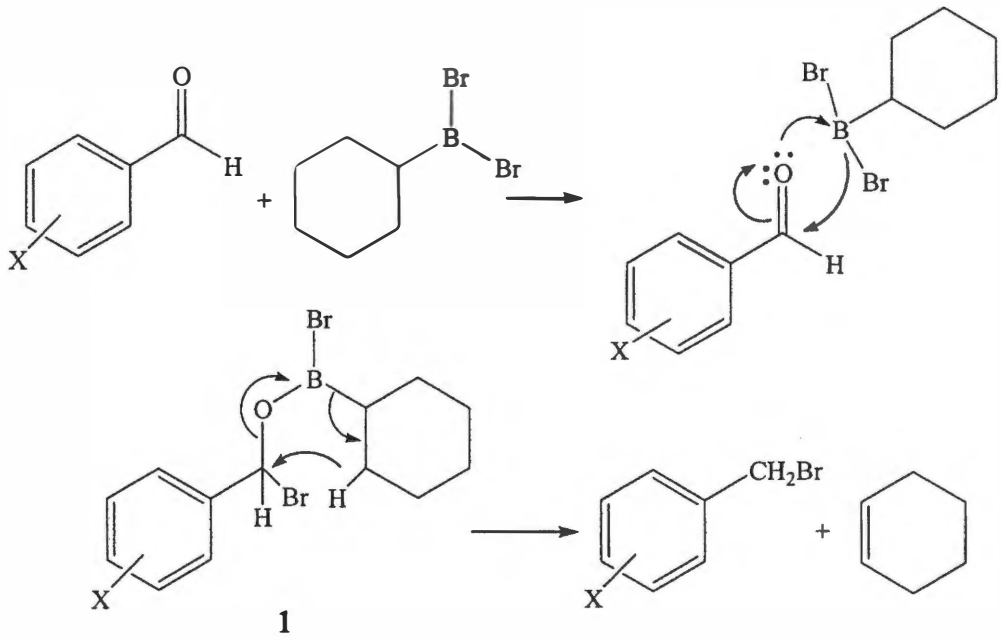
A study of the possible reaction mechanism was conducted by monitoring the reaction of *p*-bromobenzaldehyde and cyclohexylboron dibromide-dimethyl sulfide in a NMR tube (C_6D_6). Benzyl bromide could form via a bromoalkoxylborane **1** (**Scheme 2-3**), or via a dibromoalkoxylborane **2**, (**Scheme 2-4**). The result of a preliminary carbon-13 NMR experiment would appear to favor the formation of **1** for reactions involving cyclohexylboron dibromide. Thus, when *p*-bromobenzaldehyde and cyclohexylboron dibromide-dimethyl sulfide complex were mixed, the characteristic C-13 resonance of the carbonyl carbon (~190 ppm) disappeared immediately, a broad resonance appeared at 77 ppm as an indication of a complex between the carbonyl group and the electron deficient boron. (**Figure 2-2**) A new C-13 resonance appeared at 86 ppm over a period of hours, (**Figure 2-3**) Hydrolysis at this point led to regeneration of the starting material along with small quantities of benzylbromide. The resonance at 77 ppm disappeared after 30 hours, benzyl bromide gradually formed as indicated by the appearance of a new C-13 resonance at 40 ppm (**Figure 2-4**).

Table 2-2 The reactions of aryl aldehydes with isopinocampheylboron dibromide-dimethyl sulfide at room temperature

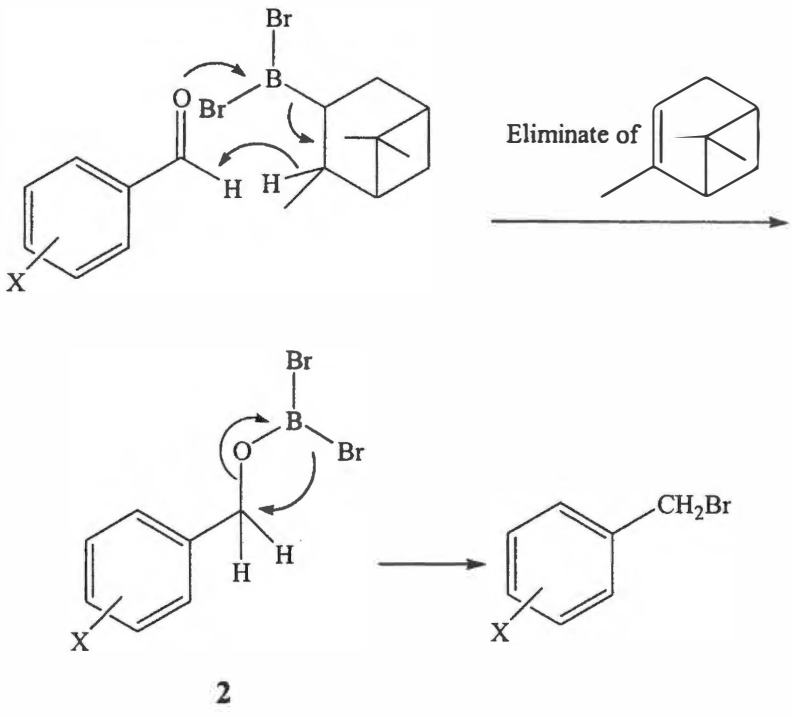
Entry	Substrate	Product [a]	Time(hr)	Yield(%)[b]
1	C_6H_5CHO	$C_6H_5CH_2Br$ (**201**)	3	85
2	4-ClC_6H_4CHO	4-$ClC_6H_4CH_2Br$ (**202**)	3	80
3	2-FC_6H_4CHO	2-$FC_6H_4CH_2Br$ (**203**)	5	78
4	4-$CH_3C_6H_4CHO$	4-$CH_3C_6H_4CH_2Br$ (**204**)	1	80
5	4-$(NC)C_6H_4CHO$	4-$(NC)C_6H_4CH_2Br$ (**205**)	5	82
6	$C_6H_5CH=CHCHO$	$C_6H_5CH=CHCH_2Br$ (**206**)	3	70
7	4-BrC_6H_4CHO	4-$BrC_6H_4CH_2Br$ (**207**)	3	87
8	4-FC_6H_4CHO	4-$FC_6H_4CH_2Br$ (**208**)	5	85
9	2-$CH_3C_6H_4CHO$	2-$CH_3C_6H_4CH_2Br$ (**209**)	1	83
10	4-$NO_2C_6H_4CHO$	4- $NO_2C_6H_4CH_2Br$ (**210**)	10	65
11	1-$C_{10}H_7CHO$	$C_{10}H_7CH_2Br$ (**211**)	3	75
12	1,4-$(OHC)_2C_6H_4$	1,4-$(BrCH_2)_2C_6H_4$ (**212**)	5	81
13	2-alloxylC_6H_4CHO	2-alloxy$C_6H_4CH_2Br$ (**213**)	3	65

[a] All reaction products exhibited physical and spectral characteristics in accord with literature values.

[b] Isolated yields based on aldehydes.



Scheme 2-3 Formation of benzyl bromide via bromoalkoxylborane 1



Scheme 2-4 Formation of benzyl bromide via dibromoalkoxylborane **2**

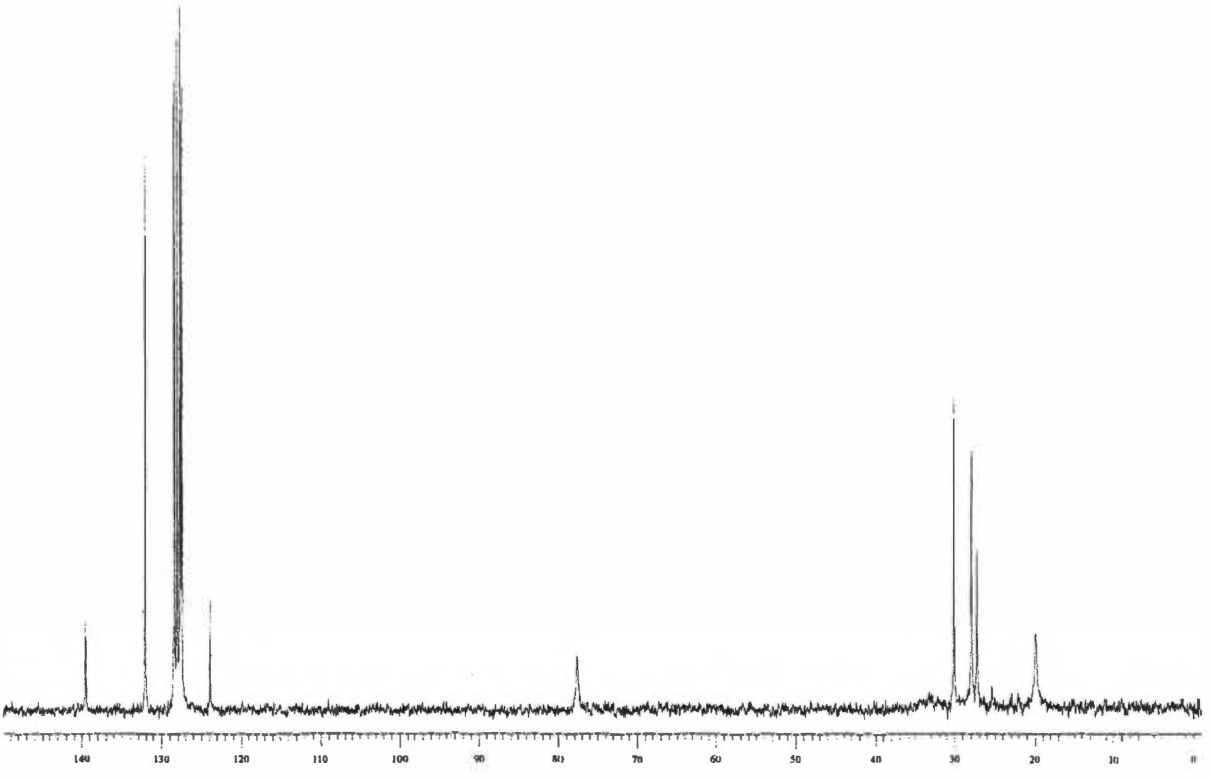


Figure 2-2 ^{13}C NMR spectrum of a mixture of 4-bromobenzaldehyde and cyclohexylboron dibromide-dimethyl sulfide complex (30 mins at room temperature)

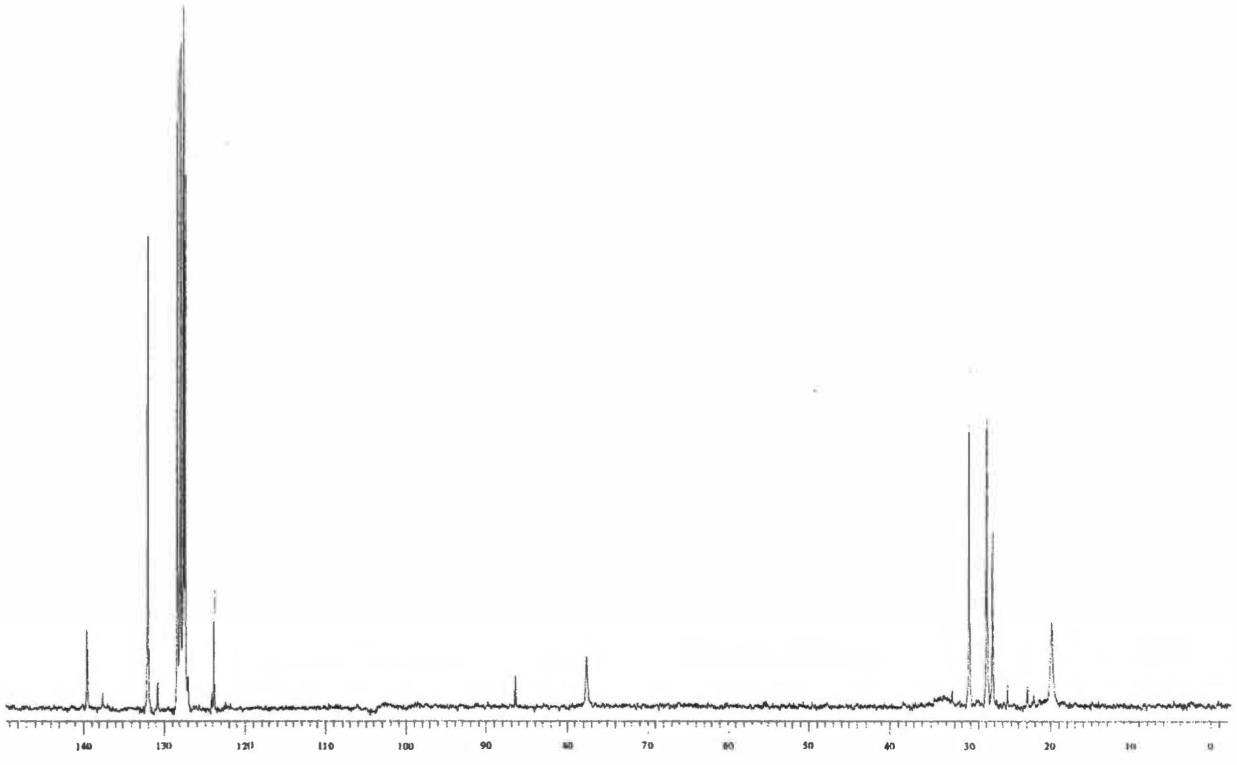


Figure 2-3 ^{13}C NMR spectrum of a mixture of 4-bromobenzaldehyde and cyclohexylboron dibromide-dimethyl sulfide complex (8 hrs at room temperature)

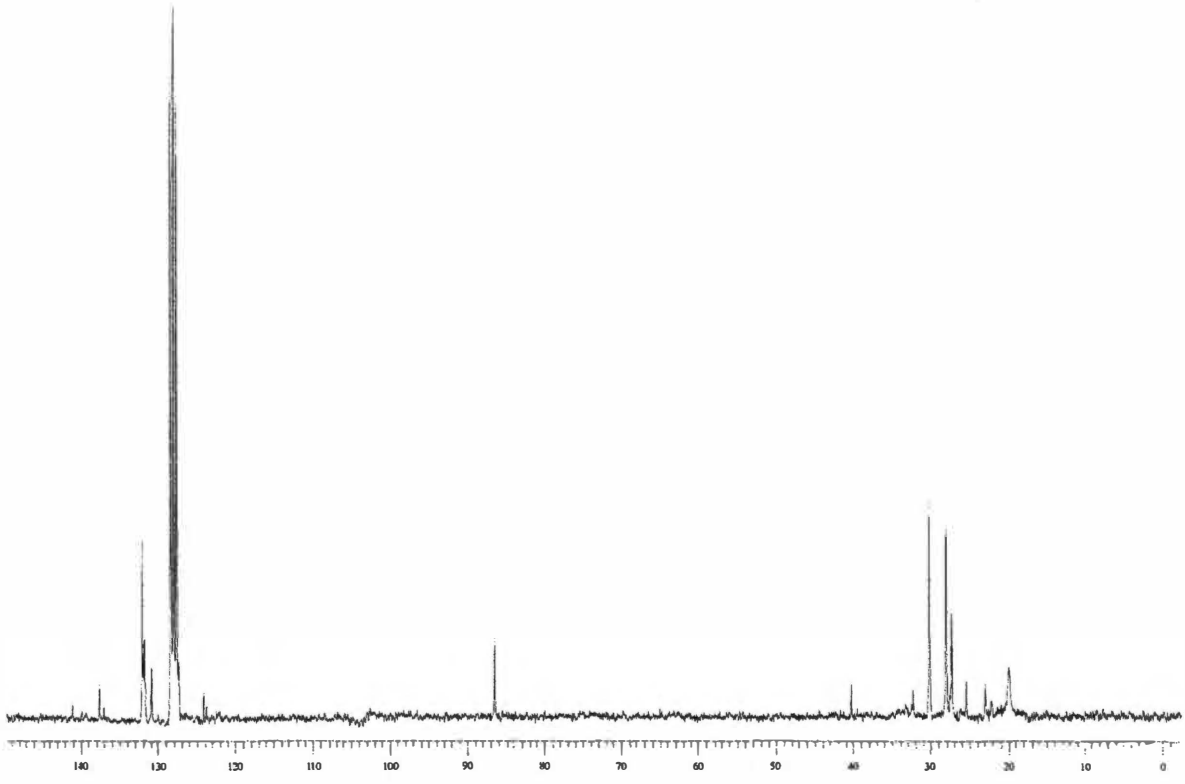


Figure 2-4 ^{13}C NMR spectrum of a mixture of 4-bromobenzaldehyde and cyclohexylboron dibromide-dimethyl sulfide complex (30 hrs at room temperature)

In a separate experiment, *p*-bromobenzaldehyde was allowed to react with dibromoborane–dimethylsulfide to generate **2** directly (as evidenced by the appearance of a C-13 resonance for the benzylic carbon at 65 ppm). Benzyl bromide formed in a matter of hours. When a solution of *p*-bromobenzaldehyde with isopinocampheylboron dibromide was monitored by carbon-13 NMR, benzyl bromide was formed immediately as evidenced by the appearance of a resonance at 65 ppm. A new resonance at 32 ppm then appeared over a period of hours indicative of the formation of benzyl bromide. Clearly, the chemistry shown in **Scheme 2-4** predominates when isopinocampheylboron dibromide is utilized.

2.3 Conclusion

Benzyl bromide derivatives are important intermediates in organic synthesis. The new synthetic method described herein provides a general, high yield synthesis of benzyl bromides from aromatic aldehydes and isopinocampheylboron dibromide in hexanes at room temperature. The reaction tolerates a variety of functional groups. The method is also useful for converting α,β-unsaturated aldehydes to the corresponding bromides. However, it is not suitable for the preparation of aryl alkyl bromides from carbonyl compounds containing enolizable hydrogens because boron dibromides can enolize compounds with α-hydrogen and catalyze Aldol condensation reactions.

2.4 Experimental

2.4.1 General considerations

All glassware, syringes and needles were dried in an oven heated to 150 °C for at least 12 hours and cooled under argon prior to use. All solvents were dried and distilled prior to use. All aldehydes were purchased from Aldrich Chemical Company and were used as received. Dibomoboron-dimethyl sulfide complex was obtained from Aldrich Chemical Company and used as received. Cyclohexene and α-pinene were obtained from Aldrich Chemical Company and were purified by distillation prior to use. All reactions were carried out in an argon atomosphere, magnetically stirred, and monitored by TLC analysis. Products were isolated by flash column chromatography.

All ^{1}H spectra were recorded in $CDCl_3$/TMS at 250 MHz; ^{13}C NMR spectra were recorded in $CDCl_3$/TMS at 62.9 MHz using a Brucker AC250 NMR spectrometer. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia.

2.4.2 Preparation of cyclohexylboron dibromide-dimethyl sulfide complex and isopincampheylboron dibromide-dimethyl sulfide complex

Cyclohexylboron dibromide-dimethyl sulfide complex and isopinocampheyl boron dibromide-dimethyl sulfide complex were prepared according to literature reports.[91]

A dry, 50 mL round-bottomed flask, equipped with a side arm capped with a silicone rubber septum, a magnetic stirring bar, a condenser, and a tube attached to a mineral oil bubbler, was flushed with argon. Dibromoboron-dimethylsulfide

($HBBr_2 \cdot SMe_2$) (10.0 mmol, 1.28 mL, neat) and cyclohexene (10.0 mmol, 1.10 mL) were added to the flask along with CH_2Cl_2 (8.0 mL) via syringes under vigorous stirring. The reaction mixture was refluxed at 40 °C. The progress of the reaction was monitored by gas chromatography analysis (GC) using *n*-decane as an internal standard. Isopinocampheyl boron dibromide-dimethyl sulfide complex was synthesized using a similar procedure by substituting α-pinene for cyclohexene.

2.4.3 Syntheses and characterizations of compounds 201-213

2.4.3.1 Representative procedure for the synthesis of a benzyl bromide

The reductive bromination of 4-chlorobenzaldehyde is representative: 4-chlorobenzaldehyde (2.0 mmol, 0.28 g) was dissolved in hexane (10 mL) at room temperature in a dry flask maintained under an argon atmosphere. Isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mmol, 2.0 mL of a 1.0 *M* solution in CH_2Cl_2) was added to the aldehyde at room temperature. The reaction mixture was allowed to stir at room temperature for 3 hrs, during which time a white precipitate formed. The mixture was then filtered and hydrolyzed with water, the organic layer separated, dried over anhydrous magnesium sulfate and the product isolated by flash column chromatography (hexane, silica gel) to yield 0.33g (80%) of the desired product.

2.4.3.2 Syntheses of compounds 201-213

Bromomethylbenzene (201):[92] The reaction of benzaldehyde (2.0 mmol, 0.21 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.29 g (85%) of

bromomethylbenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.14-7.06 (m, 5H), 4.96 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.0, 129.2, 128.8, 128.7, 38.4.

1-Bromomethyl-4-chlorobenzene (202): [93] The reaction of 4-chlorobenzaldehyde (2.0 mmol, 0.28 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.33 g (80%) of 1-bromomethyl-4-chlorobenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.31 (s, 4H), 4.45 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 136.3, 134.3, 130.3, 129.0, 32.3.

1-Bromomethyl-2-fluorobenzene (203): [94] The reaction of 2-fluorobenzaldehyde (2.0 mmol, 0.25 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.29 g (78%) of 1-bromomethyl-2-fluorobenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.37-7.32 (m, 1H), 7.26-7.22 (m, 1H), 7.12-6.99 (m, 2H), 4.47 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 162.6, 158.6, 131.2, 131.1, 130.5, 130.4, 125.2, 125.0, 124.4, 124.3, 115.7, 115.5, 25.7.

1-Bromomethyl-4-methylbenzene (204):[95] The reaction of 4-methylbenzaldehyde (2.0 mmol, 0.24 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.30 g (80%) of 1-bromomethyl-4-methylbenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.27 (d, 2H, J = 7.5 Hz), 7.13 (d, 2H, J = 7.6 Hz), 4.47 (s, 2H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 136.3, 134.6, 129.5, 128.9, 33.7, 21.2.

4-Bromomethyl-benzonitrile (205):[96] The reaction of 4-formylbenzonitrile (2.0 mmol, 0.26 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 M in CH_2Cl_2) was carried out as described in **2.4.3.1** and yielded 0.32 g (82%) of 4-bromomethyl-benzonitrile. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.39 (d, 2H, J = 7.9 Hz), 7.24 (d, 2H, J = 7.5 Hz), 4.52 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 142.3, 132.3, 130.1, 117.0, 112. 3, 38.3.

3-Bromo-propenylbenzene (206):[97] The reaction of 3-phenylpropenal (2.0 mmol, 0.26 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.28 g (70%) of 3-bromo-propenylbenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.39-7.14 (m, 5H), 6.52 (d, 1H, J = 16.8 Hz), 6.30 (m, 1H), 3.88 (d, 2H, J = 4.0); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 135.5, 131.5, 128.6, 127.8, 126.7, 123.8, 35.6.

1-Bromo-4-bromomethylbenzene (207):[98] The reaction of 4-bromobenzaldehyde (2.0 mmol, 0.37 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.44 g (87%) of 1-bromo-4-bromomethylbenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.47 (d, 2H, J = 8.4 Hz), 7.26 (d, 2H), 4.43 (s, 2H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 136.8, 133.0, 130.6, 122.5, 32.4.

1-Bromomethyl-4-fluorobenzene (208):[99] The reaction of 4-fluorobenzaldehyde (2.0 mmol, 0.25 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.32 g (85%) of 1-bromomethyl-4-fluorobenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.04-6.87

(m, 4H), 4.55 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 162.4, 162.3, 133.8, 130.8, 130.8, 115.9, 115.8, 38.6.

1-Bromomethyl-2-methylbenzene (209):[100] The reaction of 2-methylbenzaldehyde (2.0 mmol, 0.24 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.31 g (83%) of 1-bromomethyl-2-methylbenzene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.01- 6.99 (m, 4H), 4.58 (s, 2H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.7, 138.4, 129.5, 129.1, 128.6, 125.8, 32.0, 16.5.

1-Bromomethyl-4-nitrobenzene (210):[101] The reaction of 4-nitrobenzaldehyde (2.0 mmol, 0.30 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.28 g (65%) of 1-bromomethyl-4-nitrobenzene. ^1H NMR ($CDCl_3$/TMS) δ ppm 8.23-8.20 (d, 2H, J = 7.5 Hz), 7.58- 7.55 (d, 2H, J= 8.0 Hz,), 4.52 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 148.2, 144.8, 129.9, 124.1, 30.9.

1-Bromomethylnaphthalene (211):[102] The reaction of naphthalene-1-carbaldehyde (2.0 mmol, 0.30 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.33 g (75%) of 1-bromomethylnaphthalene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.68-7.10 (m, 7H), 4.95 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 133.8, 132.2, 130.2, 129.2, 128.5, 127.0, 126.2, 125.8, 125.0, 123.6, 36.0.

1,4-Bis(bromomethyl)benzene (212):[103] The reaction of benzene-1,4-dicarbaldehyde (2.0 mmol, 0.27 g) with isopinocampheylboron dibromide-dimethyl

sulfide complex (4.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.43 g (81%) of 1,4-bis(bromomethyl)benzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.37 (s, 4H), 4.48 (s, 4H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.0, 129.5, 32.8.

1-Allyloxy-2-bromomethylbenzene (213):[104] The reaction of 2-allyloxybenzaldehyde (2.0 mmol, 0.32 g) with isopinocampheylboron dibromide-dimethyl sulfide complex (2.0 mL, 1.0 *M* in CH_2Cl_2) was carried out as described previously in **2.4.3.1** and yielded 0.30 g (65%) of 1-allyloxy-2-bromomethylbenzene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 6.95-6.68 (m, 4H), 5.92 (dd, J = 15.6 Hz, J = 4.0 Hz, 1H), 5.24-5.23 (m, 2H), 4.63 (d, J = 4.2 Hz), 4.56 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 162.8, 138.2, 130.2, 129.7, 123.7, 121.3, 75.8, 29.5.

Chapter 3. Alkylation of aromatic aldehydes with alkylboron chloride derivatives

3.1 Introduction

The alkylation of aldehydes and ketones by organometallic reagents is one of the most important transformations for assembling a variety of useful carbon skeletons in synthetic organic chemistry. Generally, only reactive alkylmetals such as the organomagnesium,[51] organolithium,[52] organozinc[53] and certain organotransition metal reagents[54] can be utilized to alkylate carbonyl compounds. Organoboranes do not normally react with carbonyl compounds in a Grignard-like fashion with the exception of allylborane and vinylborane reagents.[58, 59, 60, 105] The few known alkylborane carbonyl alkylation reactions require reactive organoboranes,[67] free radical conditions,[68, 69] or activation of the carbonyl groups.[70, 71] However, a Grignard-like reaction involving organoborane reagents would possess a number of synthetic advantages including stereochemical control and the fact that a large number of functional substituents are unaffected in most organoborane transformations.

Our group recently reported the initial results of a study involving the alkylation of aryl aldehydes using dialkylboron chloride derivatives to produce the corresponding alcohols in good yields.[106] To our knowledge, saturated alkylboron halides reagents had not been previously used to alkylate carbonyl compounds. This portion of the study was designed to broaden the application of this new reaction.

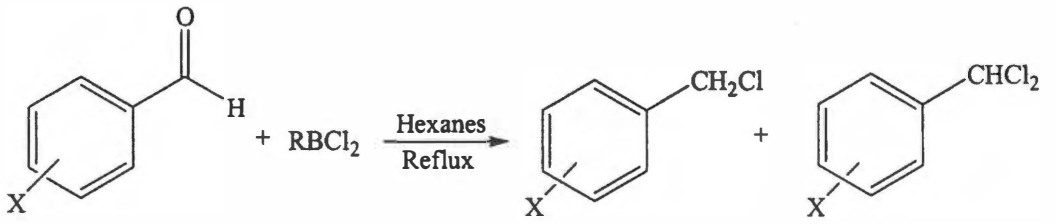
3.2 Results and discussion

The reactions of alkylboron dichlorides, dialkyboron chlorides with aromatic aldehydes under varying reaction conditions were investigated: in the absence of base, under reflux conditions, in the presence of base at room temperature, and in the presence of oxygen.

3.2.1 Alkylation of aromatic aldehydes with dialkylboron chlorides in the presence of base

3.2.1.1 Initial investigation

As noted earlier, a new method for converting aryl aldehydes into dichloroarylmethanes using boron trichloride was developed.[81, 82] The reaction appeared to proceed via an alkoxyboron chloride intermediate (see **Scheme 2-1**). It occurred to us that the use of an alkylboron derivative in place of boron trichloride could lead to a new alkylation reaction, which would provide a Grignard-like addition reaction. We thus examined the reaction of alkylboron dichloride reagents with aryl aldehydes but found that no reaction occurred in hexane solution at room temperature. However, a mixture of benzyl chloride and dichoromethylbenzene was formed when the reaction mixture was refluxed in hexane. This result indicates that, in addition to the formation of dichloroarylmethane, a reductive chlorination reaction occured (**Scheme 3-1**). The formation of dichloroarylmethane presumably occurs via a similar pathway to that reported for reactions of BCl_3 with aryl aldehydes.[81] However, the generation of benzyl chloride could occur via two reaction pathways, as has been observed in the reactions of

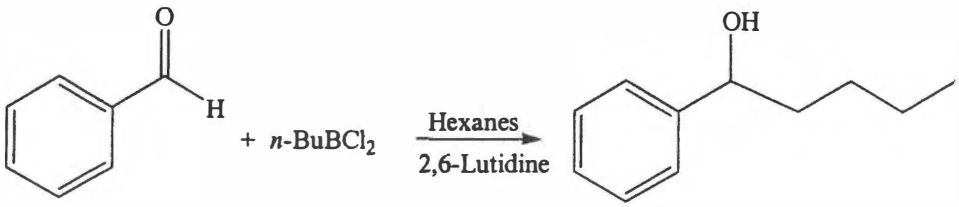


Scheme 3-1 Reaction of aryl aldehydes wit $RBCl_2$ under reflux condition

dialkylboron bromide-dimethyl sulfide complexes with aryl aldehydes.[90] The use of phenylboron dichloride (which has no transferable β-hydrogens) results in the exclusive formation of dichloromethylbenzene.

The reaction of *n*-butylboron dichloride with benzaldehyde led to the formation of a small amount of the desired alkylation product if the reaction was carried out in the presence of a base such as triethylamine, quinuclidine or 2,6-lutidine. In the case of 2,6-lutidine, 1-phenylpentanol (15% yield) was isolated from the reaction mixture (**Scheme 3-2**). Attempts to increase the yield of the alkylation product were unsuccessful.

Since the reactions of alkylboron dichloride reagents with aryl aldehydes did not lead to significant yields of alkylation products, we investigated reactions of dialkylboron chloride derivatives with aldehydes. We first examined the reaction of dicyclohexylboron chloride with benzaldehyde in hexane at room temperature and found that no reaction occurred. The reaction was then carried out in hexane at reflux. Surprisingly, the chloroalkylation product, chlorocyclohexylphenylmethane, was formed along with benzyl chloride. However, the yield of the chloroalkylation product was modest (25% isolated yield). The formation of benzyl chloride was not unexpected and had been



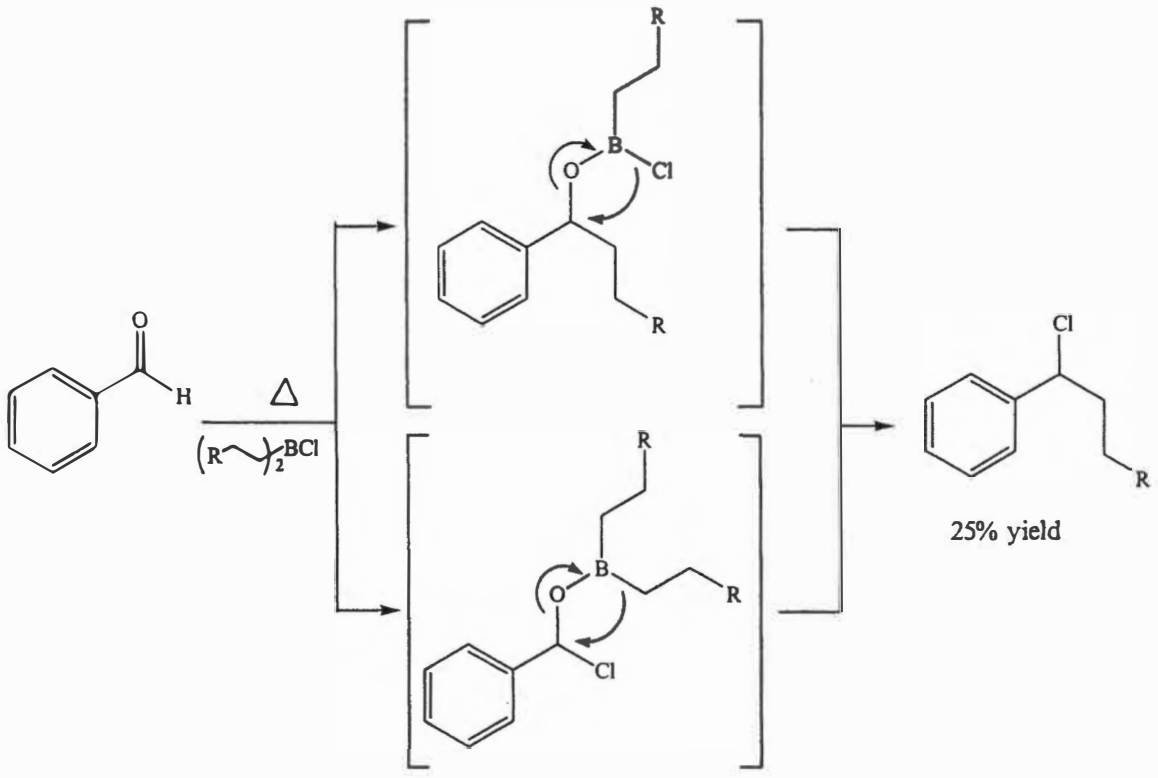
15% yield

Scheme 3-2 Reaction of benzaldehyde with *n*-butylboron dichloride in the presence of base

observed in the reaction of alkylboron dichloride with aryl aldehydes. The formation of the chloroalkylation product is unprecedented. Possible reaction pathways are presented in **Scheme 3-3**. Attempts to increase the yield of chloroalkylation products were unsuccessful.

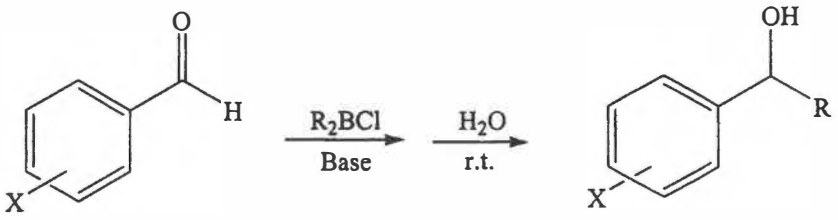
3.2.1.2 The reaction of dialkylboron chloride with aryl aldehydes in the presence of base

The reactions of dialkylboron chlorides with aryl aldehydes were then examined in the presence of various bases. Moderate to good yields of the desired alkylation products, arylalkylmethanols, were obtained. A series of aromatic aldehydes was subjected to the new alkylation reaction. Essentially all aldehydes examined were converted successfully to the corresponding arylalkylmethanols, **Table 3-1**.[107] In the case of anisaldehyde, cleavage of the ether group did not occur.[108] Also, the cyano group of 4-cyano-benzaldehyde was unaffected.[109] From the data in **Table 3-1**, it can be seen that boranes containing primary alkyl groups produce relatively low yields of the desired



Scheme 3-3 Reaction of aryl aldehydes with R_2BCl under reflux conditions

Table 3-1 Synthesis of 1-phenyl-1-alkanols via the reaction of aryl aldehydes with R_2BCl in the presence of 2,6-lutidine at room temperature



Entry	X =	R =	Product	Yield (%)[a]
1	H	Cyclohexyl	**301**	75
2	4-F	Cyclohexyl	**302**	90
3	4-Cl	Cyclohexyl	**303**	78
4	2-Cl	Cyclohexyl	**304**	49
5	4-Br	Cyclohexyl	**305**	76
6	2-CH_3	Cyclohexyl	**306**	65
7	4-CH_3	Cyclohexyl	**307**	78
8	4-CH_3O	Cyclohexyl	**308**	83
9	4-CN	Cyclohexyl	**309**	86
10	4-CHO	Cyclohexyl	**310**	66
11	H	Cyclopentyl	**311**	65
12	4-F	Cyclopentyl	**312**	78
13	4-Cl	Cyclopentyl	**313**	70
14	4-CH_3	Cyclopentyl	**314**	60

Table 3-1 (Continued)

Entry	X =	R =	Product	Yield (%)[a]
15	H	Norbornyl	**315**	25
16	4-Br	Norbornyl	**316**	28
17	4-CH_3	Norbornyl	**317**	25
18	H	*sec*-Butyl	**318**	60
19	4-F	*sec*-Butyl	**319**	75
20	4-Cl	*sec*-Butyl	**320**	70
21	4-Br	*sec*-Butyl	**321**	79
22	4-CH_3	*sec*-Butyl	**322**	67
23	2-CH_3	*sec*-Butyl	**323**	20
24	H	*n*-Hexyl	**324**	35
25	4-F	*n*-Hexyl	**325**	70
26	4-Cl	*n*-Hexyl	**326**	41
27	2-Cl	*n*-Hexyl	**327**	30
28	4-Br	*n*-Hexyl	**328**	40
29	4-CH_3	*n*-Hexyl	**329**	30
30	2-CH_3	*n*-Hexyl	**330**	25

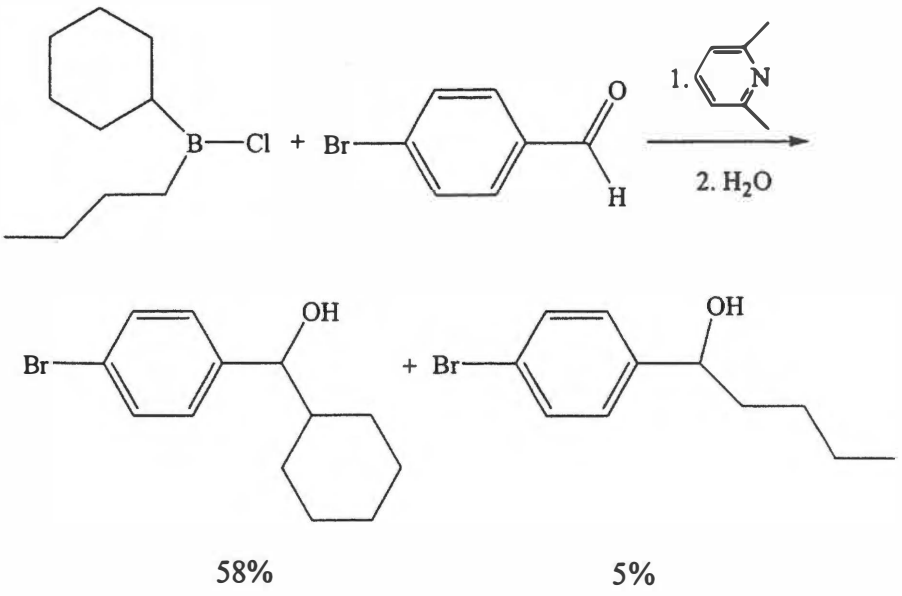
[a] Isolated yields based on starting aldehydes.

product compared to those containing secondary alkyl groups. Although it is not clear what leads to the low yields observed for boranes containing primary alkyl groups, it could be a consequence of steric effects.

We did find that the alkylation of aldehydes via boranes containing primary alkyl groups was much slower than reactions involving boranes containing secondary alkyl groups. In one reaction, 4-bromobenzaldehyde was allowed to react with cyclohexyl(*n*-butyl)boron chloride. As anticipated, the major product was cyclohexyl(4-bromophenyl)methanol (58% isolated yield) (**Scheme 3-4**) formed by preferential migration of the secondary alkyl group.

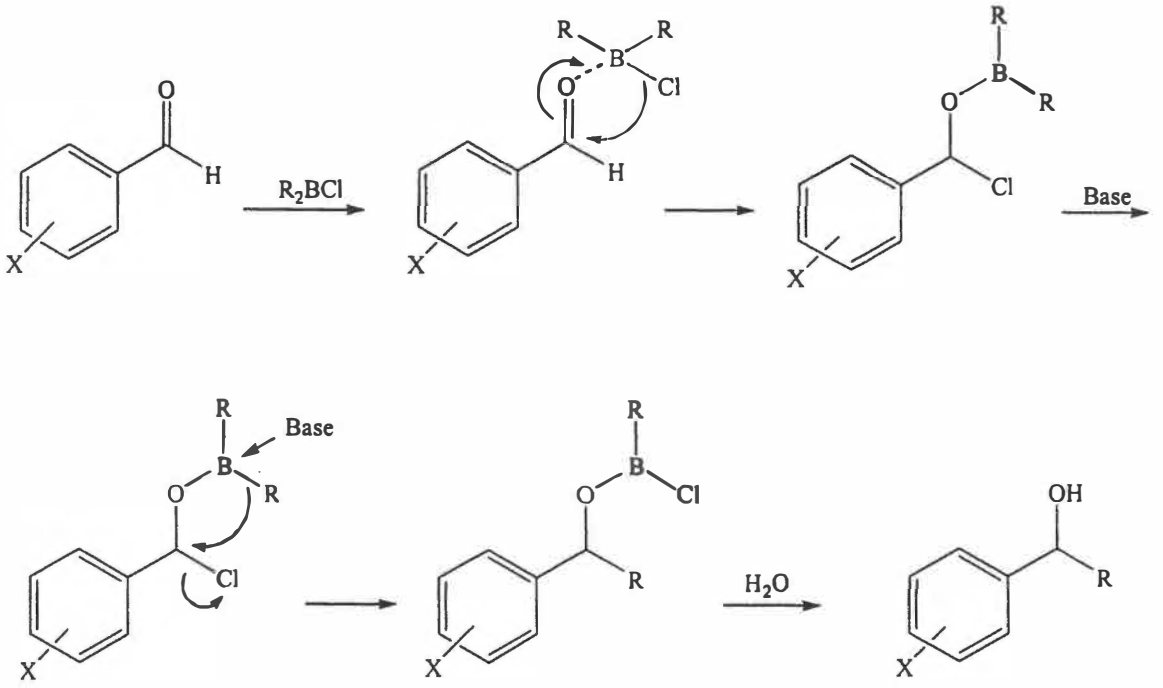
3.2.1.3 Possible reaction pathway

In order to investigate the reaction mechanism, a mixture of 4-bromobenzaldehyde and dicyclohexylboron chloride was monitored by NMR spectroscopy. Dicyclohexylboron chloride (1.0 *M* hexane solution) was added to 4-bromobenzaldehyde in hexane at –30 °C. The solvent was removed under reduced pressure to yield a yellow solid, which was then dissolved in benzene-d_6 for NMR analysis at room temperature. The characteristic ^{1}H and ^{13}C resonances for the aldehyde were absent in the resultant NMR spectra. Interestingly, no new resonances appeared in the ^{1}H and ^{13}C NMR spectra. Furthermore, upon addition of water (instead of a base), 4-bromobenzaldehyde was regenerated. These results suggest that 4-bromobenzaldehyde coordinates to dicyclohexylboron chloride. In a separate experiment, upon addition of Et_3N to the benzene-d_6 solution of the reaction mixture, a new doublet appeared at 5.11 ppm in the ^{1}H NMR and a new ^{13}C NMR resonance appeared at 83.4 ppm.



Scheme 3-4 Alkylation of 4-bromobenzaldehyde using cyclohexyl(*n*-butyl)boron chloride

Hydrolysis of this reaction mixture led to the formation of the alkylation product cyclohexyl(4-bromophenyl)methanol. In a third NMR experiment, a benzene-d_6 solution of the aldehyde and boron chloride was examined by ^{11}B NMR which revealed a resonance at 64.4 ppm (slightly upfield of the resonance at 78 ppm for dicyclohexylboron chloride) indicating a weak coordination of aldehyde with boron. Upon addition of Et_3N, the ^{11}B NMR signal shifted to 12.8 ppm, suggesting coordination of the amine to boron. However, the ^{11}B NMR data do not provide information about the reaction intermediate. On the basis of the NMR data, the alkylation of aldehydes presumably proceeds via coordination of the carbonyl to boron followed by migration of the alkyl group (**Scheme 3-5**).



Scheme 3-5 Mechanism of alkylation via R_2BCl in the presence of base

The reaction of tri(*n*-butyl)borane with aryl aldehydes was then investigated at reflux in the presence of base. It was discovered that no alkylation occurred. The results suggest that the chlorine atom plays a critical role in the alkylation reactions. Compared to trialkylboranes, chloroboranes are more electron-deficient and can coordinate more effectively to the carbonyl oxygen. It was noted that benzyl alcohols were also formed in small quantities along with the desired alkylated product in all the chloroborane reactions. Moreover, reduction of the aldehydes predominated if more hindered boron reagents such as di(3-methyl-2-butyl)boron chloride, di(*exo*-norbornyl)boron chloride and DIP-chloride were utilized; these organoboranes have been widely used as effective reducing reagents for carbonyl compounds.[40]

3.2.1.4 Choice of base

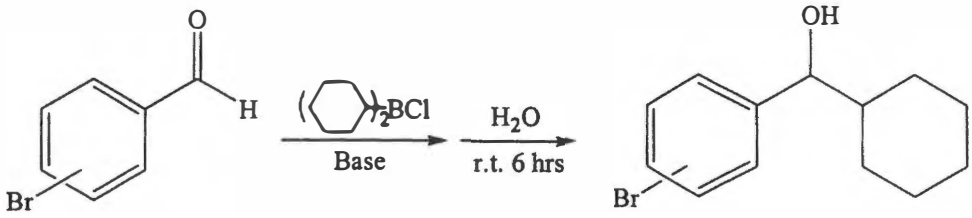
Although the role of base in the reaction is not clear, the base presumably coordinates to boron, increasing steric crowding, and thus induces the migration of an alkyl group. Alternatively, coordination of the base to the electron-deficient boron atom could increase the electron density on boron and facilitate the migration of the alkyl group. **Table 3-2** contains a summary of the reaction of 4-bromobenzaldehyde with dicyclohexylboron chloride in the presence of a variety of bases. It can be seen that all bases result in the formation of the desired product. Bulky bases tend to produce higher yield of products, which is consistent with results noted earlier. Strong nucleophiles, such as *n*-butyllithium also lead to higher yields of products.

3.2.2 Alkylation of aromatic aldehydes with dialkylboron chlorides in the presence of oxygen

Organoboranes are known to undergo autoxidation in the presence of oxygen and the reaction has been used to prepare alcohols and alkyl hydroperoxides as well as to initiate free radical reactions.[110] Trialkylboranes readily react with α,β-unsaturated carbonyl compounds through a free radical 1,4-addition reaction in the presence of air,[111] but they do not normally undergo 1,2-addition to saturated carbonyl compounds. Only formaldehyde was reported to react with trialkylboranes in the presence of air to produce alkylation products.[69] That reaction is believed to proceed via a free radical mechanism, since no alkylation occurs in the absence of oxygen.

We examined the reaction of dialkylboron chlorides with aryl aldehydes in the presence of oxygen and found that alkylation occurs more readily than the corresponding

Table 3-2 Reaction of 4-bromobenzaldehyde with dicyclohexylboron chloride in the presence of various bases



Entry	Base	Product	Yield (%)
1	Et_3N	**305**	60
2	Quinuclidine	**305**	74
3	Pyridine	**305**	40
4	2,6-Lutidine	**305**	76
5	DBU	**305**	76
6	*n*-BuLi	**305**	72
7	*t*-BuOK	**305**	76

alkylation carried out in the absence of oxygen but in the presence of base.

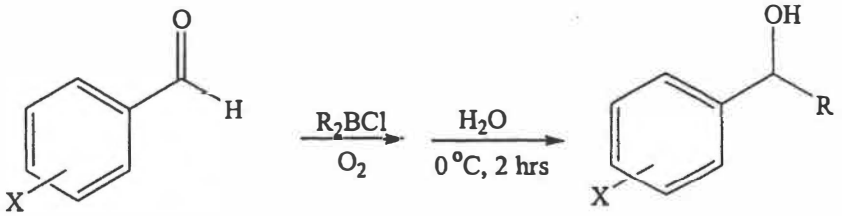
3.2.2.1 The reaction of dialkylboron chlorides with aryl aldehydes in the presence of oxygen

We first examined the reaction of dicyclohexylboron chloride with benzaldehyde in hexane at room temperature in the presence of oxygen. Surprisingly, the reaction occurs rapidly at room temperature and produces the desired alkylation product, cyclohexylphenylmethanol, in excellent yield. The reaction appears to be general for all aryl aldehydes studied (**Table 3-3**). The reaction proceeds most efficiently at 0 °C but partial reduction occurs when the reaction is carried out at room temperature. In contrast to alkylation reactions carried out in the absence of oxygen,[106, 107] organoboranes containing primary and hindered alkyl groups produce good yields of alkylation products.

3.2.2.2 Possible reaction pathway

In an effort to probe the mechanism of the reaction, dicyclohexylboron chloride (1.0 *M* in hexane) was added to 4-bromobenzaldehyde in hexane at –30 °C. The solvent was removed under reduced pressure to yield a yellow solid which was then re-dissolved in benzene-d_6 for NMR analysis. Interestingly, the characteristic ^{1}H and ^{13}C resonances of the aldehyde group were absent in the NMR spectra and no new resonances were observed. Furthermore, upon addition of water, 4-bromobenzaldehyde was regenerated. This suggests that 4-bromobenzaldehyde reversibly coordinates to dicyclohexylboron chloride. In a separate experiment, after oxygen was introduced to a benzene solution of the yellow solid, a new doublet appeared at 5.11 ppm in the ^{1}H NMR and a corresponding resonance appeared at 83.4 ppm in the ^{13}C NMR. Hydrolysis of the

Table 3-3 Synthesis of arylalkylmethanols via the reaction of aryl aldehydes with R_2BCl in the presence of oxygen at 0 °C



Entry	X =	R =	Product	Yield (%)[a,b]
1	H	Cyclohexyl	**301**	90
2	4-F	Cyclohexyl	**302**	95
3	4-Cl	Cyclohexyl	**303**	98
4	2-Cl	Cyclohexyl	**304**	63
5	4-Br	Cyclohexyl	**305**	95
6	2-CH_3	Cyclohexyl	**306**	88
7	4-CH_3	Cyclohexyl	**307**	96
8	4-CH_3O	Cyclohexyl	**308**	98
9	4-CHO	Cyclohexyl	**310**	84[c]
10	4-CN	Cyclohexyl	**309**	92
11	H	Cyclopentyl	**311**	92
12	4-F	Cyclopentyl	**312**	99
13	4-Br	Cyclopentyl	**331**	92
14	4-CH_3	Cyclopentyl	**314**	91
15	H	Norbornyl	**315**	76

Table 3-3 (Continued)

Entry	X =	R =	Product	Yield (%)[a,b]
16	4-Br	Norbornyl	**316**	73
17	4-CH_3	Norbornyl	**317**	75
18	H	*sec*-Butyl	**318**	65
19	4-F	*sec*-Butyl	**319**	74
20	4-Cl	*sec*-Butyl	**320**	67
21	4-Br	*sec*-Butyl	**321**	70
22	4-CH_3	*sec*-Butyl	**322**	71
23	2-CH_3	*sec*-Butyl	**323**	55
24	H	*n*-Hexyl	**324**	84[d]
25	4-Cl	*n*-Hexyl	**325**	75[d]
26	4-Br	*n*-Hexyl	**328**	65[d]
27	4-CH_3	*n*-Hexyl	**329**	72[d]
28	2-CH_3	*n*-Hexyl	**330**	81[d]

[a] Isolated yields based on starting aldehydes.

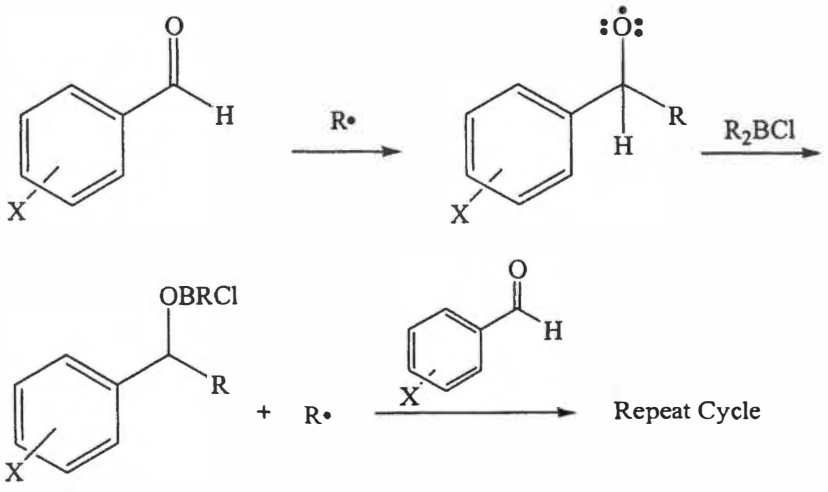
[b] Physical and spectroscopic data are consistent with literature values.

[c] Two equivalents of borane were used.

[d] Significant quantities of the product contaning the secondary alkyl group are formed.

reaction mixture led to the formation of the desired alkylation product, (4-bromophenyl)cyclohexyl-methanol.

The alkylation reaction is rapid but no alkylation occurs in the presence of a radical scavenger such as galvinoxyl. In addition, when both primary and secondary alkyl groups are present, as is generally the case when alkyl boron halides are formed via hydroboration, the secondary group reacts preferentially. These observations support the postulation that the reaction is occurring via a radical pathway, such as the one outlined in **Scheme 3-6**. A similar pathway was reported for the reaction of trimethylboron with formaldehyde.[69]



Scheme 3-6 Radical pathway for the alkylation via R_2BCl in the presence of oxygen

3.2.3 Alkylation of aromatic aldehydes using alkylboron dichlorides

3.2.3.1 Alkylation of aromatic aldehydes with alkylboron dichlorides in the presence of oxygen at room temperature

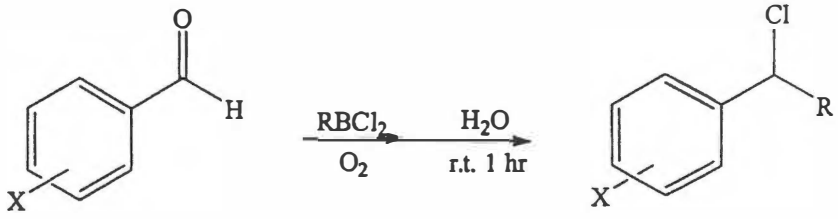
Since only one alkyl group in dialkylboron chloride is transferred to the carbonyl carbon, the reaction would be more efficient if monoalkylboron dichlorides could be utilized. Thus, we examined the reaction of alkylboron dichlorides with aryl aldehydes in the presence of oxygen. Interestingly, instead of alkylarylmethanols, the reaction produces the chloroalkylation products exclusively at room temperature.[112] We also noted that a small quantity of benzyl chloride formed along with the desired alkylation products, an observation made earlier.[106, 107] α,α-Dichlorotoluenes are also formed in small quantities if reactions are carried out at higher temperatures.[81, 82]

A series of aryl aldehydes was subjected to the reaction sequence. Essentially all aldehydes were successfully converted to the corresponding chlorides (**Table 3-4**).

3.2.3.2 Possible reaction pathway

In contrast to the reaction of di(*n*-hexyl)boron chloride with aromatic aldehydes in the presence of oxygen as shown in **Table 3-3**, isomeric products **324, 325, 328, 329** and **330** arising from migration of a secondary alkyl group are not observed in the reaction of *n*-butylboron dichloride with aryl aldehydes. This suggests that the reaction of monoalkylboron dichlorides proceeds via a different pathway. NMR spectroscopy was used to monitor a representative reaction. Benzaldehyde was mixed with one equivalent of *n*-butylboron dichloride in benzene-d_6 and the ^{1}H and ^{13}C resonances of carbonyl group were no longer observable. In addition, no new resonances related to carbonyl

Table 3-4 Synthesis of arylalkyl chlorides via reaction of aryl aldehydes with $RBCl_2$ in the presence of oxygen at room temperature



Entry	X =	R =	Product	Yields (%)[a]
1	H	*n*-Butyl	**332**	62
2	4-F	*n*-Butyl	**333**	85
3	4-Cl	*n*-Butyl	**334**	75
4	2-Cl	*n*-Butyl	**335**	50
5	3-Cl	*n*-Butyl	**336**	51
6	4-Br	*n*-Butyl	**337**	63
7	3-Br	*n*-Butyl	**338**	45
8	4-CH_3	*n*-Butyl	**339**	55[b]
9	4-CHO	*n*-Butyl	**340**	73
10	H	Cyclohexyl	**341**	81
11	4-Cl	Cyclohexyl	**342**	79
12	2-Cl	Cyclohexyl	**343**	20
13	4-Br	Cyclohexyl	**344**	86
14	3-Br	Cyclohexyl	**345**	16

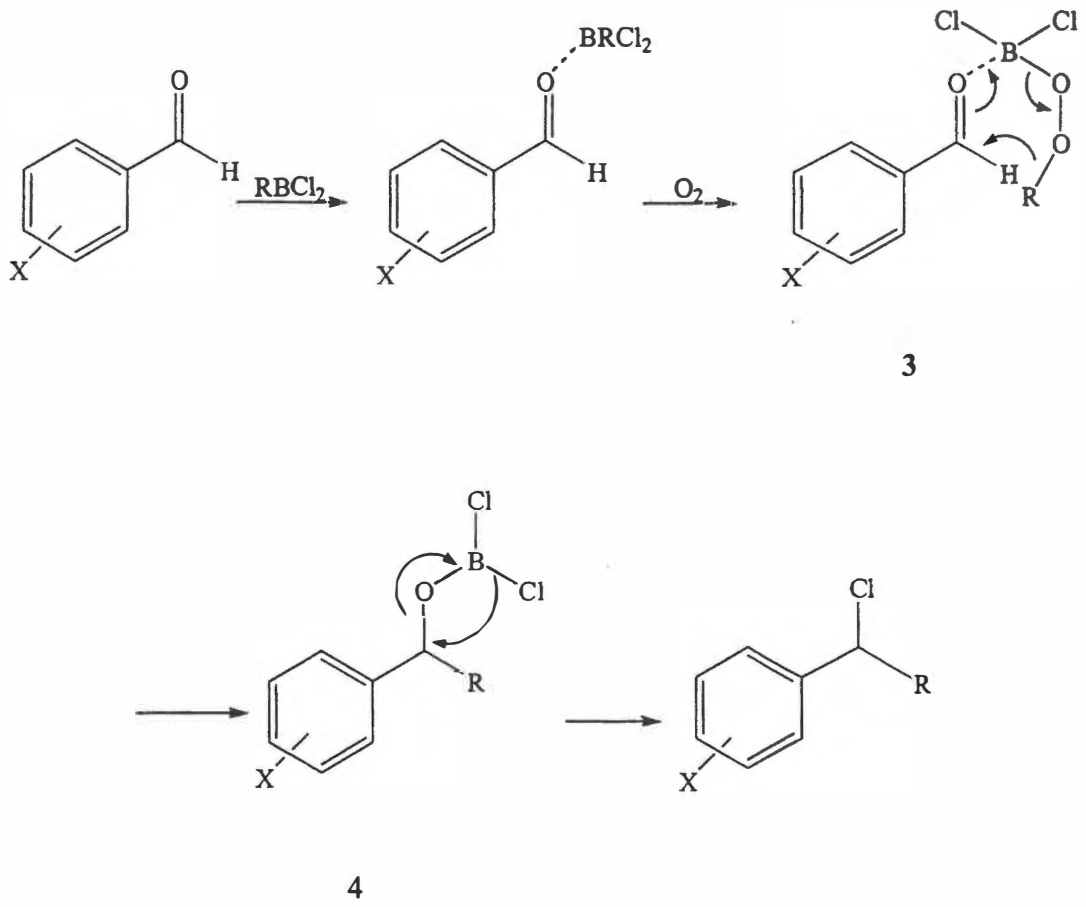
Table 3-4 (Continued)

Entry	X =	R =	Product	Yields (%)[a]
15	4-F	Cyclohexyl	**346**	92
16	4-CHO	Cyclohexyl	**347**	67
17	H	*sec*-Butyl	**348**	65
18	4-Cl	*sec*-Butyl	**349**	67
19	4-F	*sec*-Butyl	**350**	74
20	2-CH_3	*sec*-Butyl	**351**	25[b]

[a] Isolated yields based on starting aldehydes.

[b] Isolated by vacuum distillation.

group were observed. (Only reductive chlorination occurred, leading to the formation of benzyl chloride if reaction times were prolonged). In a separate experiment, oxygen was introduced to the reaction mixture and the NMR spectra revealed that the chloroalkylation product, 1-chloro-pentylbenzene, gradually formed. Furthermore, the addition of a radical scavenger, galvinoxyl did not inhibit the alkylation reaction. It is likely that this reaction proceeds via oxidation of the organoborane to form a peroxide intermediate which then undergoes alkyl transfer through an intramolecular six-membered ring transition state **3**, to give the borinate ester **4**. The product would then form after migration of the chlorine (**Scheme 3-7**). In a separate experiment, a reaction was carried out at –20 °C and no alkylation occurred, but *n*-butyl peroxide was isolated upon hydrolysis of the reaction mixture. This experiment supports the presence of a peroxide intermediate in the reaction.



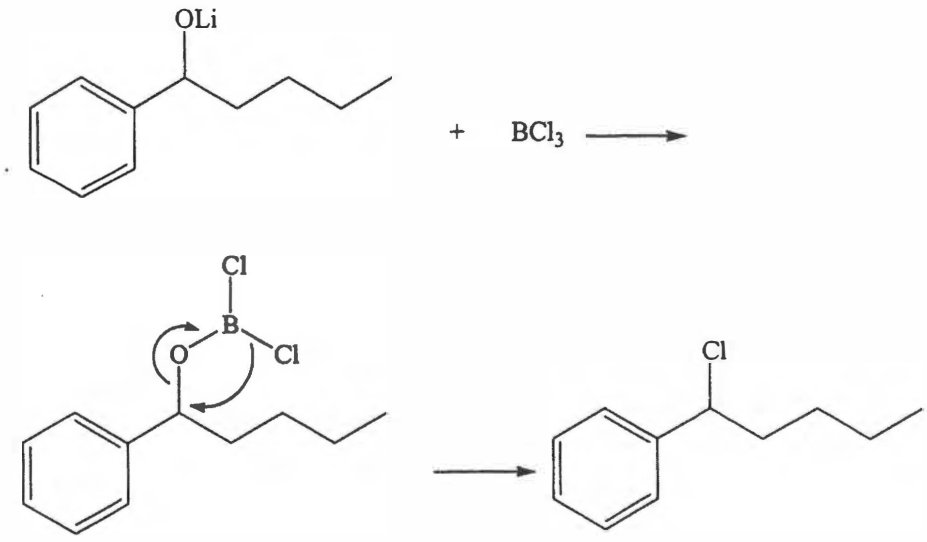
Scheme 3-7 Possible reaction mechanism of aryl aldehydes with $RBCl_2$ in the presence of oxygen

In order to confirm that a boronate ester could be chlorinated, 1-phenylpentyloxyboron dichloride was prepared by the reaction of lithium 1-phenylpentyloxide with BCl_3 which gradually led to the formation of benzyl chloride at room temperature (**Scheme 3-8**).

3.3 Conclusion

A new alkylation reaction has been developed which provides a potentially useful alternative to traditional Grignard and organolithium reactions. The reaction occurs under mild reaction conditions and tolerates a variety of functional groups. It is limited to aldehydes that do not possess α-hydrogens due to the well-known enolization reactions that occur in the presence of boron halides.

The reaction of aryl aldehydes with dialkylboron chlorides in the presence of base affords the desired alkylation products, arylalkylmethanol derivatives, in good yields,



Scheme 3-8 Formation of (1-chloropentyl)-benzene

benzyl chlorides are also formed in amall quantities. The reaction of aryl aldehydes with dialkylboron chlorides in the presence of oxygen generates the alkylation products in excellent yields. Monoakylboron dichlorides react with aryl aldehydes in the presence of oxygen to produce the corresponding chloroalkylation products arylalkylchlorides in good yields, this reaction is the most atom efficient alkylation reaction.

3.4 Experimental

3.4.1 General considerations

All glassware, syringes and needles were dried in an oven heated to 150 °C for at least 12 hours and cooled under argon prior to use. All solvents were dried and distilled prior to use. All aldehydes were purchased from Aldrich Chemical Company, and were used as received. Dicyclohexylboron chloride (1.0 *M* solution in hexane) was obtained from Aldrich Chemical Company and used as received; all other dialkylboron chlorides (dicyclopentylboron chloride, di(*sec*-butyl)boron chloride, di(*exo*-norbomyl)boron chloride and di(*n*-hexyl)boron chloride were prepared according to literature procedures.[113] Cyclohexyl(*n*-butyl)boron chloride was synthesized via the reaction of *n*-butylboron dichloride with cyclohexene and triethylsilane.[48(b)] *n*-Butylboron dichloride (1.0 *M* solution in hexane) was obtained from Aldrich Chemical Company and used as received. Cyclohexylboron dichloride and *sec*-butylboron dichloride were prepared by hydroboration of the corresponding alkenes with $HBCl_2{\cdot}SMe_2$ followed by addition of BCl_3.[91] Cyclohexene, cyclopentene, 1-hexene and norbomene were purchased from Aldrich Chemical Company and were purified by distillation prior to use. *cis*-2-Butene

was obtained from Aldrich Chemical Company and used as received. All reactions were run in an argon atomosphere, magnetically stirred and monitored by TLC analysis. Products were isolated by flash column chromatography using silica gel (60 Å 230-400 mesh) with hexanes as eluent for aryalkyl chlorides and methylene chloride for aryalkylmethanols.

All ^{1}H spectra were recorded in $CDCl_3$ or C_6D_6/TMS at 250 MHz, ^{13}C NMR spectra were recorded in $CDCl_3$ or C_6D_6/TMS at 62.9 MHz using a Brucker AC250 NMR spectrometer. In cases where more than one isomer formed, the NMR shifts of all isomers are reported. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia. Melting points are uncorrected. HR-ER-MS was obtained using a ZAB-EQ instrument.

3.4.2 General experimental procedures

3.4.2.1 Syntheses of arylalkylmethanols in the presence of base

Benzaldehyde (3.0 mmol, 0.32 g) was dissolved in hexane (10 mL) contained in a dry, argon-flushed, 50 mL round-bottomed flask. Dicyclohexylboron chloride (3.0 mmol, 3.0 mL of a 1.0 *M* hexane solution) was added via syringe and the solution allowed to stir for 30 mins at room temperature. 2,6-Lutidine (3.0 mmol, 0.32 g) was then added and the mixture stirred for 5 hrs at room temperature. A precipitate formed, which contained boron (as determined by NMR analysis). Isolation of the product was accomplished by adding hydrogen peroxide (0.5 mL of a 30% aqueous solution) and sodium hydroxide (3.0 mmol, 1.0 mL of a 3.0 *M* aqueous solution) to the reaction mixture (This method oxidized the remaining alkylboron bond). Alternatively, water could be added to the

mixture and the product isolated from the organic phase. After separation of the organic layer, 0.43 g of the desired product (75% yield) was isolated by column chromatography

3.4.2.2 Syntheses of arylalkylmethanols in the presence of oxygen

4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) was dissolved in hexane (10 mL) contained in a dry, argon-flushed, septum sealed, 50 mL round-bottomed flask and the mixture cooled to 0 °C in an ice bath. Dicyclohexylboron chloride (3.0 mmol, 3.0 mL of 1.0 *M* hexane solution) was added via a syringe to yield a yellow solution. Oxygen gas was introduced over the reaction solution by means of an oxygen filled balloon attached to an 18 gauge needle. The reaction solution gradually turned colorless. After being stirred at room temperature for 1 h, the reaction solution was hydrolized. The organic layer was separated, dried over anhydrous $MgSO_4$, the solvent removed and the product isolated by column chromatography to yield 0.66 g (98% yield) of the desired product, (4-chlorophenyl)cyclohexylmethanol.

3.4.2.3 Syntheses of arylalkyl chlorides in the presence of oxygen

Benzaldehyde (4.2 mmol, 0.44 g) was dissolved in hexane (10 mL) contained in a dry, argon-flushed, septum sealed, 50 mL round-bottomed flask. *n*-Butylboron dichloride (4.2 mmol, 4.2 mL of a 1.0 *M* hexane solution) was added via a syringe and the solution allowed to stir at room temperature. Oxygen gas was introduced to the reaction solution via a syringe needle attached to an oxygen filled balloon. The reaction solution gradually turned cloudy. After 1 hr, the reaction mixture was filtered. The filtrate was then hydrolyzed with water. The organic layer was separated, dried over anhydrous $MgSO_4$, and the product isolated by column chromatography to afford 0.49 g (62%) of the desired

product, 1-(1-chloropentyl)benzene. Compounds 1-(1-chloropentyl)-4-methylbenzene (**339**) and 1-(1-chloro-2-methylbutyl)-2-methylbenzene (**351**) (**Table 3-4**) decompose on silica-gel column. Therefore, they were purified by vacuum distillation.

3.4.3 Syntheses and NMR characterizations of compounds 301-351

Cyclohexylphenylmethanol (301):[114] Benzaldehyde (3.0 mmol, 0.32 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.43 g (75%) of cyclohexylphenylmethanol, a colorless oil. ^{1}H NMR: δ ppm 7.36–7.23 (m, 5H), 4.35 (d, 1H, J = 7.2 Hz), 1.90 (s, 1H), 2.01–0.94 (m, 11H). ^{13}C NMR: δ ppm 143.6, 128.2, 127.4, 126.6, 79.4, 44.9, 29.3, 28.8, 26.4, 26.1, 26.0.

Cyclohexyl-(4-fluorophenyl)methanol (302): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) and allowed to react as described in **3.4.2.1** to yield 0.56 g (90%) of cyclohexyl-(4-fluorophenyl)methanol, a colorless oil. ^{1}H NMR: δ ppm 7.21–6.93 (m, 4H), 4.25 (d, 0.5H, J = 4.4 Hz), 4.23 (d, 0.5H, J = 4.4 Hz), 2.65 (s, 1H), 1.93–0.81 (m, 11H). ^{13}C NMR: δ ppm 163.9, 160.0, 139.3, 139.2, 128.1, 128.0, 114.56, 114.6, 78.5, 44.9, 29.0, 28.8, 26.3, 25.9. Anal. Calcd for $C_{13}H_{17}FO$: C, 74.97; H, 8.23. Found: C, 74.85; H, 8.24.

(4-Chlorophenyl)-cyclohexylmethanol (303):[115] 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.53 g (78%) of (4-chlorophenyl)-cyclohexylmethanol, a white solid, m.p. 73.0–74.0 °C (lit. 74.0–75.0 °C). ^{1}H NMR: δ ppm 7.27 (d, 2H, J = 7.5 Hz), 7.17 (d, 2H, J = 8.2 Hz), 4.28 (d, 1H, J = 6.8 Hz), 2.31(s,

1H), 1.91–0.85 (m, 11H). ^{13}C NMR: δ ppm 142.0, 132.9, 128.2, 127.9, 78.5, 44.9, 29.1, 28.6, 26.3, 25.9.

(2-Chlorophenyl)-cyclohexylmethanol (304): 2-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.33 g (49%) of (2-chlorophenyl)cyclohexylmethanol, a white solid, m.p. 85.0–86.0 °C. ^{1}H NMR: δ ppm 7.48–7.13 (m, 4H), 4.90 (d, 0.5H, J = 3.7 Hz), 4.87 (d, 0.5H, J = 3.7 Hz), 2.10 (d, 1H, J = 3.7 Hz), 1.87–1.08 (m, 11H). ^{13}C NMR δ ppm 141.1, 132.4, 129.3, 128.2, 128.1, 126.7, 74.9, 43.9, 29.4, 27.8, 26.3, 26.2, 26.0. Anal. Calcd for $C_{13}H_{17}ClO$: C, 69.48; H, 7.62. Found: C, 69.27; H, 7.67.

(4-Bromophenyl)cyclohexylmethanol (305):[115] 4-Bromobenzaldehyde (3.0 mmol, 0.56 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.61 g (76%) of (4-bromophenyl)-cyclohexylmethanol, a white solid, m.p. 70.0-71.0 °C (lit. 71.5-72.5 °C). ^{1}H NMR: δ ppm 7.26 (d, 2H, J = 6.9 Hz), 7.16 (d, 2H, J = 7.0 Hz), 4.34 (d, 1H, J = 6.9 Hz), 1.90 (s, 1H), 1.73–0.93 (m, 11H). ^{13}C NMR: δ ppm 142.6, 131.2, 128.3, 121.1, 78.6, 45.0, 29.2, 28.6, 26.4, 26.2, 26.0.

Cyclohexyl-*o*-tolylmethanol (306):[116] 2-Methyl-benzaldehyde (3.0 mmol, 0.36 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.40 g (65%) of cyclohexyl-*o*-tolylmethanol, a colorless oil. ^{1}H NMR: δ ppm 7.38–7.08 (m, 4H), 4.60 (d, 1H, J = 7.1 Hz), 2.29 (s, 3H), 1.99–1.03 (m, 12H). ^{13}C NMR: δ ppm 142.0, 135.0, 130.2, 127.0, 126.2, 126.00, 75.0, 44.5, 29.5, 28.5, 26.3, 26.0, 19.4.

Cyclohexyl-*p*-tolylmethanol (307):[117] 4-Methylbenzaldehyde (3.0 mmol, 0.36 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.48 g (78%) of cyclohexyl-*p*-tolylmethanol, a white solid, m.p. 41.0-42.0 °C (lit. 41.0-42.0 °C). ^{1}H NMR: δ ppm 7.16 (d, 2H, J = 8.3 Hz), 7.11 (d, 2H, J = 8.3 Hz), 4.27 (d, 1H, J = 7.0 Hz), 2.32 (s, 3H), 1.99 (s, 1H), 1.95–0.90 (m, 11H). ^{13}C NMR: δ ppm 140.7, 136.9, 128.8, 126.5, 79.1, 44.8, 29.2, 28.9, 26.4, 26.0, 21.0.

Cyclohexyl(4-methoxyphenyl)methanol (308):[118] 4-Methoxylbenzaldehyde (3.0 mmol, 0.41 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.55 g (83%) of cyclohexyl(4-methoxyphenyl)methanol, a white solid, m.p. 81.0–82.0 °C (lit. 82.0–83.0 °C). ^{1}H NMR: δ ppm 7.21 (d, 2H, J = 8.4 Hz), 6.86 (d, 2H, J = 8.8 Hz), 4.29 (d, 1H, J = 7.6 Hz), 3.80 (s, 1H), 2.02–1.03 (m, 12H). ^{13}C NMR: δ ppm 158.9, 135.8, 127.7, 113.5, 79.0, 55.2, 44.9, 29.2, 29.1, 26.4, 26.1, 26.0.

(4-Cyclohexyl-hydroxymethyl)benzonitrile (309): 4-Formylbenzonitrile (3.0 mmol, 0.39 g) and dicyclohexylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.56 g (86%) of, (4-cyclohexyl-hydroxymethyl)benzonitrile, a white solid, m.p. 82.0–83.0 °C. ^{1}H NMR: δ ppm 7.61 (d, 2H, J = 8.3 Hz), 7.41 (d, 2H, J = 8.3 Hz), 4.48 (d, 0.5H, J = 2.5 Hz), 4.45 (d, 0.5H, J = 2.5 Hz), 2.17 (d, 1H, J = 3.0 Hz), 1.85–0.94 (m, 11H). ^{13}C NMR: δ ppm 148.9, 131.9, 127.3, 118.9, 110.9, 78.3, 45.0, 29.2, 28.1, 26.2, 26.0, 25.9. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.86; H, 7.97; N, 6.54.

Cyclohexyl-[4-(cyclohexyl-hydroxymethyl)phenyl]methanol (310): Benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g) and dicyclohexylboron chloride (6.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.60 g (66%) of cyclohexyl-[4-(cyclohexyl-hydroxymethyl)phenyl]methanol, a white solid, m.p. 153.0–154.0 °C. ^{1}H NMR: δ ppm 7.25(s, 4H), 4.35 (d, 2H, J = 7.2 Hz), 2.00–0.88 (m, 24H). ^{13}C NMR: δ ppm 142.8, 126.5, 79.2, 44.9, 29.3, 28.8, 26.4, 26.0. HR-EI-MS: Calcd for $C_{20}H_{26}$ $[M-2H_2O]^+$, 266.2035. Found: *m/z* 266.2046.

Cyclopentylphenylmethanol (311):[119] Benzaldehyde (3.0 mmol, 0.32 g) and dicyclopentylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield d 0.34 g (65%) of cyclopentylphenylmethanol, a colorless liquid. ^{1}H NMR δ ppm 7.34–7.25 (m, 5H), 4.38 (d, 1H, J = 8.4 Hz), 2.56–1.15 (m, 10H); ^{13}C NMR δ ppm 144.4, 128.3, 127.5, 126.4, 79.1, 47.6, 29.4, 25.5, 25.4.

Cyclopentyl(4-fluorophenyl)methanol (312): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and dicyclopentylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.45 g (78%) of cyclopentyl(4-fluorophenyl)methanol, a colorless liquid. ^{1}H NMR δ ppm 7.31–7.25 (m 2H), 7.03–6.96 (m, 2H), 4.35 (d, 1H, J = 8.4 Hz), 2.20–1.02 (m, 10H); ^{13}C NMR δ ppm 164.0, 160.1, 140.2, 128.1, 127.9, 115.2, 114.8, 78.4, 47.7, 29.4, 25.4, 25.3. HRMS: Calcd for $C_{12}H_{15}FO$ $[M]^+$, 194.110. Found: *m/z* 194.111. Anal. Calcd for $C_{12}H_{15}FO$: C, 74.20; H, 7.78. Found: C, 74.21; H, 7.89.

(4-Chlorophenyl)cyclopentylmethanol (313):[120] 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and dicyclopentylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.44 g (70%) of (4-

chlorophenyl)cyclopentylmethanol, a colorless liquid. ^{1}H NMR δ ppm 7.26 (dd, 4H, J = 8.7 Hz), 4.34 (d, 1H, J = 8.3 Hz), 2.25 (s, 1H), 2.21–1.06 (m, 9H); ^{13}C NMR δ ppm 142.8, 133.0, 128.3, 127.8, 79.2, 47.6, 29.3, 25.4 25.3.

Cyclopentyl-*p*-tolylmethanol (314): 4-Methylbenzaldehyde (3.0 mmol, 0.36 g) and dicyclopentylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.34 g (60%) of cyclopentyl-*p*-tolylmethanol, a colorless liquid. ^{1}H NMR δ ppm 7.17 (dd, 4H, J = 8.1 Hz), 4.34 (d, 1H, J = 8.5 Hz), 2.33 (s, 3H), 2.25–1.12 (m, 10H); ^{13}C NMR δ ppm 141.5, 137.1, 128.9, 126.4, 78.9, 47.5, 29.4, 25.5, 25.4, 21.1. HRMS: Calcd for $C_{13}H_{18}O$ $[M]^+$, 190.136. Found: *m/z* 190.137. Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.92; H, 9.65.

Bicyclo[2.2.1]hept-2-ylphenylmethanol (315):[121] Benzaldehyde (3.0 mmol, 0.32 g) and di(*exo*-norbornyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.15 g (25%) of bicyclo[2,2,1]hept-2-ylphenylmethanol, a colorless oil. ^{1}H NMR δ ppm 7.35–7.21 (m, 5H), 4.16 (d, 0.5H, J = 9.6 Hz), 4.10 (d, 0.5H, J = 10.0 Hz), 1.50–0.80 (m, 12H); ^{13}C NMR δ ppm 144.5, 143.1, 128.2, 127.5, 127.4, 127.2, 126.8, 78.8, 49.9, 49.4, 38.7, 38.3, 35.8, 34.9, 34.2, 30.1, 29.9, 28.7.

Bicyclo[2.2.1]hept-2-yl(4-bromophenyl)methanol (316): 4-Bromobenzaldehyde (3.0 mmol, 0.55 g) and di(*exo*-norbornyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.24 g (28%) of bicyclo[2,2,1]hept-2-yl(4-bromophenyl)methanol, a colorless oil. ^{1}H NMR δ ppm 7.47–7.42 (m, 2H), 7.20–7.16 (m, 2H), 4.18 (d, 0.6H, J = 9.4 Hz), 4.10 (d, 0.4H, J = 9.9 Hz), 2.48–0.84 (m, 12H); ^{13}C NMR δ ppm 143.44, 142.1, 131.4, 128.9, 128.4, 121.4, 121.3, 78.2, 77.3, 50.2, 49.5,

38.8, 38.3, 36.9, 35.9, 35.4, 34.3, 30.1, 29.9, 28.6. HRMS: Calcd for $C_{14}H_{17}BrO$ $[M]^+$, 280.046. Found: *m/z* 280.045. Anal. Calcd for $C_{14}H_{17}BrO$: C, 59.80; H, 6.09. Found: C, 59.99; H, 6.15.

Bicyclo[2.2.1]hept-2-yl(*p*-tolyl)methanol (317): 4-Methylbenzaldehyde (3.0 mmol, 0.36 g) and di(*exo*-norbornyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.16 g (25%) of bicyclo[2,2,1]hept-2-yl(*p*-tolyl)methanol, a colorless oil. ^{1}H NMR δ ppm 7.244–7.10 (m, 4H), 4.16 (d, 0.4H, *J* = 9.8 Hz), 4.10 (d, 0.6H, *J* = 10.1 Hz), 2.33 (s, 3H), 2.51–0.85 (m, 12H); ^{13}C NMR δ ppm 141.6, 140.1, 137.3, 137.1, 128.9, 127.2, 126.6, 78.7, 77.8, 50.0, 49.3, 38.8, 38.4, 37.0, 36.5, 35.4, 34.4, 30.0, 28.7, 21.1. HRMS: Calcd for $C_{15}H_{20}O$ $[M]^+$, 216.151. Found: *m/z* 216.150. Anal. Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.00; H, 9.43.

2-Methyl-1-phenylbutan-1-ol (318):[122] Benzaldehyde (3.0 mmol, 0.32 g) and di(*sec*-butyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.30 g (60%) of 2-methyl-1-phenylbutan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.35–7.24 (m, 5H), 4.49 (d, 0.45H, *J* = 6.0 Hz), 4.40 (d, 0.55H, *J* = 7.3 Hz), 1.99 (s, 1H), 1.78–0.84 (m, 6H), 0.73(d, 3H, *J* = 6.9 Hz). ^{13}C NMR: δ ppm 143.9, 143.6, 128.1, 127.8, 127.3, 127.2, 126.7, 126.4, 78.7, 78.0, 41.9, 41.6, 25.8, 24.8, 15.0, 14.0, 11.6, 11.3.

1-(4-Fluorophenyl)-2-methylbutan-1-ol (319): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and di(*sec*-butyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.41 g (75%) of 1-(4-fluorophenyl)-2-methylbutan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.22–6.90 (m, 4H), 4.42, (d, 0.40H, *J* = 5.9 Hz),

4.34 (d, 0.60H, J = 6.9 Hz), 2.07 (s, 1H), 1.64–0.67 (m, 6H), 0.65 (d, 3H, J = 6.8 Hz). ^{13}C NMR: δ ppm 164.0, 163.9, 160.1, 160.0, 139.5, 139.3, 139.2, 128.3, 128.1, 127.9, 127.8, 115.0, 114.7, 78.0, 77.5, 42.0, 41.7, 25.7, 24.8, 14.9, 13.9, 11.6, 11.2. HR-EI-MS: Calcd for $C_{11}H_{13}F$ $[M\text{-}H_2O]^+$, 164.1001. Found: *m/z* 164.0996.

1-(4-Chlorophenyl)-2-methylbutan-1-ol (320):[123] 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and di(*sec*-butyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.42 g (70%) of 1-(4-chlorophenyl)-2-methylbutan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.29 (d, 2H, J = 8.6 Hz), 7.21 (d, 2H, J = 8.4 Hz), 4.49 (d, 0.45 H, J = 5.9 Hz), 4.39 (d, 0.55 H, J = 6.7 Hz), 2.07 (s, 1H), 1.74–0.85 (m, 6H), 0.72 (d, 3H, J = 6.8 Hz). ^{13}C NMR: δ ppm 142.3, 141.9, 132.9, 132.7, 128.2, 128.0, 127.7, 78.0, 77.2, 41.9, 41.6, 25.7, 24.7, 14.9, 13.8, 11.6, 11.3.

1-(4-Bromophenyl)-2-methylbutan-1-ol (321): 4-Bromobenzaldehyde (3.0 mmol, 0.55 g) and di(*sec*-butyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.58 g (79%) of 1-(4-bromophenyl)-2-methylbutan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.42 (d, 2H, J = 8.3 Hz), 7.12 (d, 2H, J = 8.1 Hz), 4.43 (d, 0.45 H, J = 5.2 Hz), 4.34 (d, 0.55 H, J = 6.1 Hz), 2.39 (d, 1H, J = 2.5 Hz), 1.68–0.84 (m, 6H), 0.70 (d, 3H, J = 6.7 Hz). ^{13}C NMR: δ ppm 142.78, 142.7, 131.1, 128.3, 128.0, 121.0, 120.8, 77.9, 77.1, 41.8, 41.5, 25.7, 24.7, 14.8, 13.7, 11.6, 11.22. Anal. Calcd for $C_{11}H_{15}BrO$: C, 54.34; H, 6.22. Found: C, 54.28; H, 6.24.

2-Methyl-1-(*p*-tolyl)-butan-1-ol (322):[124] 4-Methylbenzaldehyde (3.0 mmol, 0.36 g) and di(*sec*-butyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.36 g (67%) of 2-methyl-1-(*p*-tolyl)-butan-1-ol, a

colorless oil. ^{1}H NMR: δ ppm 7.20 (d, 2H, J = 9.2 Hz), 7.11 (d, 2H, J = 8.2 Hz), 4.42 (d, 0.40 H, J = 6.1 Hz), 2.32 (s, 3H), 2.03 (s, 1H), 1.74–0.83 (m, 6H), 0.71 (d, 3H, J = 6.7 Hz). ^{13}C NMR: δ ppm 140.9, 140.6, 136.9, 136.7, 128.7, 126.6, 126.3, 78.5, 78.0, 41.8, 41.5, 25.7, 24.9, 21.0, 15.9, 14.1, 11.6, 11.2.

2-Methyl-1-(*o*-tolyl)-butan-1-ol (323):[122] 2-Methylbenzaldehyde (3.0 mmol, 0.36 g) and di(*sec*-butyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.11g (20%) of 2-methyl-1-(*o*-tolyl)-butan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.44–7.10 (m, 4H), 4.79 (d, 0.55 H, J = 5.5 Hz), 4.67 (d, 0.45 H, J = 7.2 Hz), 2.33 (s, 1.5 H), 2.31 (s, 1.5H), 1.80–0.87 (m, 7H), 0.77 (d, 3H, J = 6.8 Hz). ^{13}C NMR: δ ppm 142.2, 135.1, 134.6, 130.2, 127.0, 126.9, 126.2, 126.1, 125.9, 74.8, 73.7, 41.1, 40.6, 26.4, 24.4, 19.4, 19.2, 15.4, 13.6, 11.9, 11.2.

1-Phenylheptan-1-ol (324): [125] Benzaldehyde (3.0 mmol, 0.32 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.20g (35%) of 1-phenylheptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.34–7.21 (m, 5H), 4.57 (t, 1H, J = 5.7 Hz), 2.40 (s, 1H), 1.77–0.84 (m, 13H). ^{13}C NMR: δ ppm 144.9, 128.3, 127.3, 125.9, 74.5, 39.0, 31.7, 29.1, 25.7, 22.5, 14.0.

1-(4-Fluorophenyl)heptan-1-ol (325): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.44g (70%) of 1-(4-fluorophenyl)heptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.30–6.96 (m, 4H), 4.58 (t, 1H, J = 6.4 Hz), 2.38 (s, 1H), 1.72–0.84 (m, 13H). ^{13}C NMR: δ ppm 164.0, 160.1, 140.6, 140.6, 127.5, 127.4, 115.2, 114.9, 73.9,

39.1, 31.7, 29.1, 25.7, 22.5, 14.0. Anal. Calcd for $C_{13}H_{19}FO$: C, 74.25; H, 9.11. Found: C, 74.31; H. 9.21.

1-(4-Chlorophenyl)heptan-1-ol (326):[126] 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.28g (41%) of 1-(4-chlorophenyl)heptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.31 (d, 2H, J = 8.0 Hz), 7.24 (d, 2H, J = 8.4 Hz), 4.60 (t, 1H, J = 6.4 Hz), 2.20 (s, 1H), 1.72–0.84 (m, 13H). ^{13}C NMR: δ ppm 143.4, 133.0, 128.5, 127.2, 73.9, 39.1, 31.7, 29.1, 25.6, 22.5, 14.0.

1-(2-Chlorophenyl)heptan-1-ol (327): 2-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.20g (30%) of 1-(2-chlorophenyl)heptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.53–7.13 (m, 4H), 5.08 (t, 1H, J = 4.9 Hz), 2.41 (s, 1H), 1.73–0.84 (m, 13H). ^{13}C NMR: δ ppm 142.4, 131.8, 129.3, 128.2, 127.0, 70.6, 37.6, 31.8, 29.1, 25.7, 22.6, 14.1. Anal. Calcd for $C_{13}H_{19}ClO$: C, 68.86; H, 8.44. Found: C, 68.61; H, 8.45.

1-(4-Bromophenyl)heptan-1-ol (328):[127] 4-Bromobenzaldehyde (3.0 mmol, 0.56 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.33g (40%) of 1-(4-bromophenyl)heptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.43 (d, 2H, J = 8.4 Hz), 7.16 (d, 2H, J = 8.4 Hz), 4.56 (t, 1H, J = 6.5 Hz), 2.35 (s, 1H), 1.70–0.84 (m, 13H). ^{13}C NMR: δ ppm 143.8, 131.4, 127.6, 121.0, 73.9, 39.0, 31.7, 29.1, 25.6, 22.5, 14.0.

1-(*p*-Tolyl)heptan-1-ol (329):[128] 4-Methylbenzaldehyde (3.0 mmol, 0.36 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described

in **3.4.2.1** to yield 0.19 g (30%) of 1-(*p*-tolyl)heptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.22 (d, 2H, J = 8.0 Hz), 7.14 (d, 2H, J = 8.0 Hz), 4.60 (t, 1H, J = 6.5 Hz), 2.34 (s, 3H), 1.88 (s, 1H), 1.82–0.84 (m, 13H). ^{13}C NMR: δ ppm 142.0, 137.1, 129.0, 125.8, 74.5, 39.0, 31.7, 29.2, 25.8, 22.6, 21.1, 14.0.

1-(*o*-Tolyl)heptan-1-ol (330):[129] 2-Methylbenzaldehyde (3.0 mmol, 0.36 g) and di(*n*-hexyl)boron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.1** to yield 0.15 g (25%) of 1-(*o*-tolyl)heptan-1-ol, a colorless oil. ^{1}H NMR: δ ppm 7.47–7.10 (m, 4H), 4.91 (t, 1H, J = 5.6 Hz), 2.33 (s, 3H), 1.81 (s, 1H), 1.75–0.84 (m, 13H). ^{13}C NMR: δ ppm 143.1, 134.4, 130.1, 127.0, 126.2, 125.1, 70.7, 38.1, 31.8, 29.2, 26.0, 22.6, 19.0, 14.0.

(4-Bromophenyl)cyclopentylmethanol (331):[130] 4-Bromobenzaldehyde (3.0 mmol, 0.56 g) and dicyclopentylboron chloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.2** to yield 0.71 g (92%) of (4-bromophenyl)cyclopentylmethanol, a colorless liquid. ^{1}H NMR δ ppm 7.36 (d, 2H, J = 8.7 Hz), 7.08 (d, 2H, J = 8.9 Hz), 4.46 (d, 1H, J = 8.3 Hz), 2.20 (s, 1H), 2.01–1.51 (m, 9H); ^{13}C NMR δ ppm 139.2, 132.6, 130.9, 121.2, 78.6, 45.9, 25.9, 25.8.

(1-Chloropentyl)benzene (332):[131] Benzaldehyde (3.0 mmol, 0.32 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.34 g (62%) of (1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.38–7.21 (m, 5H), 4.83 (t, 1H, J = 7.4 Hz), 2.16–1.97 (m, 2H), 1.51–1.24 (m, 4H), 0.88 (t, 3H, J = 6.6 Hz). ^{13}C NMR: δ ppm 142.0, 128.6, 128.1, 126.9, 63.8, 39.7, 29.2, 22.1, 13.9.

1-(1-Chloropentyl)-4-fluorobenzene (333): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.51 g (85%) of 1-(1-chloropentyl)-4-fluorobenzene, a colorless liquid. ^{1}H NMR: δ ppm 7.36–7.30 (m, 2H), 7.04–6.97 (m, 2H), 4.81 (t, 1H, J = 7.45 Hz), 2.14–1.97 (m, 2H), 1.46–1.22 (m, 4H), 0.88 (t, 3H, J = 6.6 Hz). ^{13}C NMR: δ ppm 164.3, 160.4, 137.9, 137.9, 128.7, 128.6, 115.6, 115.2, 62.9, 39.8, 29.1, 22.1, 13.8. Anal. Calcd for $C_{11}H_{14}ClF$: C, 65.84; H, 7.03. Found: C, 65.90; H, 6.99.

1-Chloro-4-(1-chloropentyl)benzene (334): 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.49 g (75%) of 1-chloro-4-(1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.31 (dd, 4H, J = 3.3 Hz), 4.80 (t, 1H, J = 7.2 Hz), 2.12–1.97 (m, 2H), 1.44–1.22 (m, 4H), 0.89 (t, 3H, J = 6.7 Hz). ^{13}C NMR: δ ppm 140.5, 133.9, 128.7, 128.3, 62.8, 39.7, 29.1, 22.1, 13.9. HRMS: Calcd for $C_{11}H_{14}Cl_2$ $[M]^+$, 216.0473. Found: *m/z*, 216.0479. Anal. Calcd for $C_{11}H_{14}Cl_2$: C, 60.85; H, 6.50. Found: C, 60.96; H, 6.48.

1-Chloro-2-(1-chloropentyl)benzene (335): 2-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.33 g (50%) of 1-chloro-2-(1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.61–7.16 (m, 4H), 5.41 (t, 1H, J = 6.9 Hz), 2.09–1.99 (m, 2H), 1.54–1.30 (m, 4H), 0.90 (t, 3H, J = 6.8 Hz). ^{13}C NMR: δ ppm 139.3, 132.5, 129.4, 129.0, 128.4, 127.3, 59.1, 38.9, 28.9, 22.1, 13.9. HRMS: Calcd for $C_{11}H_{14}Cl_2$

$[M]^+$, 216.0473. Found: *m/z*, 216.0466. Anal. Calcd for $C_{11}H_{14}Cl_2$: C, 60.85; H, 6.50. Found: C, 60.86; H, 6.53.

1-Chloro-3-(1-chloropentyl)benzene (336): 3-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.33 g (51%) of 1-chloro-3-(1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.37 (s, 1H), 7.27–7.26 (m, 3H), 4.78 (t, 1H, J = 6.8 Hz), 2.12–1.98 (m, 2H), 1.48–1.26 (m, 4H), 0.89 (t, 3H, J = 6.9 Hz). ^{13}C NMR: δ ppm 144.0, 134.4, 129.9, 128.3, 127.2, 125.2, 62.8, 39.7, 29.1, 22.1, 13.9. HRMS: Calcd for $C_{11}H_{14}Cl_2$ $[M]^+$, 216.0473. Found: *m/z*, 216.0462. Anal. Calcd for $C_{11}H_{14}Cl_2$: C, 60.85; H, 6.50. Found: C, 60.72; H, 6.45.

1-Bromo-4-(1-chloropentyl)benzene (337): 4-Bromobenzaldehyde (3.0 mmol, 0.56 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.49 g (63%) of 1-bromo-4-(1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.47 (d, 2H, J = 8.4 Hz), 7.24 (d, 2H, J = 8.4 Hz), 4.78 (t, 1H, J = 7.5 Hz), 2.10–1.96 (m, 2H), 1.52–1.21 (m, 4H), 0.88 (t, 3H, J = 6.7 Hz). ^{13}C NMR: δ ppm 141.0, 131.7, 128.6, 122.0, 62.9, 39.6, 29.1, 22.1, 13.8. HRMS: Calcd for $C_{11}H_{14}BrCl$ $[M]^+$, 261.9945. Found: *m/z*, 261.9940.

1-Bromo-3-(1-chloropentyl)benzene (338): 3-Bromobenzaldehyde (3.0 mmol, 0.56 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.35 g (45%) of 1-bromo-3-(1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.53 (s, 1H), 7.44-7.17 (m, 3H), 4.77 (t, 1H, J = 7.1 Hz), 2.16–1.94 (m, 2H), 1.54–1.24 (m, 4H), 0.89 (t, 3H, J = 6.6 Hz). ^{13}C NMR: δ

ppm 144.2, 131.2, 130.1, 130.0, 125.6, 122.5, 62.7, 39.6, 29.1, 22.1, 13.8. HRMS: Calcd for $C_{11}H_{14}BrCl$ $[M]^+$, 261.9945. Found: *m/z*, 261.9952.

1-(1-Chloropentyl)-4-methylbenzene (339): 4-Methylbenzaldehyde (3.0 mmol, 0.36 g) and *n*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.32 g (55%) of 1-(1-chloropentyl)-4-methylbenzene, a colorless liquid. ^{1}H NMR: δ ppm 7.26 (d, 2H, J = 8.1 Hz), 7.14 (d, 2H, J = 8.0 Hz), 4.82 (t, 1H, J =7.1 Hz), 2.33 (s, 3H), 2.14–1.99 (m, 2H), 1.45–1.28 (m, 4H), 0.88 (t, 3H, J = 6.8 Hz). ^{13}C NMR: δ ppm 139.1, 138.0, 129.2, 126.8, 63.9, 39.7, 29.3, 22.1, 21.1, 13.9. HRMS: Calcd for $C_{12}H_{17}Cl$ $[M]^+$, 190.102. Found: *m/z*, 190.102.

1,4-Bis-(1-chloropentyl)benzene (340): Benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g) and *n*-butylboron dichloride (6.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.63 g (73%) of 1,4-bis-(1-chloropentyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.35 (s, 4H), 4.84 (t, 2H, J = 6.7 Hz), 2.33 (s, 3H), 2.14–1.99 (m, 4H), 1.50–1.26 (m, 8H), 0.89 (t, 6H, J = 6.7 Hz). ^{13}C NMR: δ ppm 142.0, 127.2, 63.4, 39.9, 29.2, 22.1, 13.9. HRMS: Calcd for $C_{16}H_{24}Cl_2$ $[M]^+$, 286.1255. Found: *m/z*, 286.1257.

(Chlorocyclohexylmethyl)benzene (341):[132] Benzaldehyde (3.0 mmol, 0.32 g) and cyclohexylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.51 g (81%) of (chlorocyclohexylmethyl)-benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.33–7.22 (m, 5H), 4.60 (d, 1H, J = 8.4 Hz), 2.21–0.86 (m, 11H). ^{13}C NMR: δ ppm 140.9, 128.3, 127.9, 127.5, 69.8, 45.7, 30.4, 30.3, 26.1, 25.9, 25.9.

1-Chloro-4-(chlorocyclohexylmethyl)benzene (342):[133] 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and cyclohexylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.58 g (79%) of 1-chloro-4-(chlorocyclohexylmethyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.30 (d, 2H, J = 8.7 Hz), 7.25 (d, 2H, J = 8.7 Hz), 4.57 (d, 1H, J = 8.3 Hz), 2.18–0.85 (m, 11H). ^{13}C NMR: δ ppm 139.4, 133.6, 128.9, 128.5, 68.8, 45.6, 30.3, 30.1, 26.0, 25.8.

1-Chloro-2-(chlorocyclohexylmethyl)benzene (343): 2-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and cyclohexylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.15 g (20%) of 1-chloro-2-(chlorocyclohexylmethyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.58–7.15 (m, 4H), 5.24 (d, 1H, J = 8.1 Hz), 2.16–0.84 (m, 11H). ^{13}C NMR: δ ppm 138.6, 132.7, 129.5, 129.3, 128.8, 127.0, 64.6, 45.0, 30.1, 29.5, 26.1, 26.0, 25.8. HRMS: Calcd for $C_{13}H_{16}Cl_2$ $[M]^+$, 242.0629. Found: *m/z*, 242.0641. Anal. Calcd for $C_{13}H_{16}Cl_2$: C, 64.21; H, 6.63. Found: C, 64.30; H, 6.70.

1-Bromo-4-(chlorocyclohexylmethyl)benzene (344): 4-Bromobenzaldehyde (3.0 mmol, 0.56 g) and cyclohexylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.74 g (86%) of 1-bromo-4-(chlorocyclohexylmethyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.43 (d, 2H, J = 8.4 Hz), 7.17 (d, 2H, J = 8.4 Hz), 5.54 (d, 1H, J = 8.2 Hz), 2.15–0.83 (m, 11H). ^{13}C NMR: δ ppm 139.8, 131.4, 129.1, 121.7, 68.7, 45.5, 30.2, 30.0, 26.0, 25.8, 25.7. HRMS: Calcd for $C_{13}H_{16}BrCl$ $[M]^+$, 288.0102. Found: *m/z*, 288.0114.

1-Bromo-3-(chlorocyclohexylmethyl)-benzene (345): 3-Bromobenzaldehyde (3.0 mmol, 0.56 g) and cyclohexylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.14 g (16%) of 1-bromo-3-(chlorocyclohexylmethyl)-benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.48 (s, 1H), 7.43–7.17 (m, 3H), 4.54 (d, 1H, J= 8.2 Hz), 2.17–0.88 (m, 11H). ^{13}C NMR: δ ppm 143.2, 131.0, 130.6, 129.9, 126.2, 122.3, 68.6, 45.6, 30.4, 30.0, 26.0, 25.8. HRMS: Calcd for $C_{13}H_{16}BrCl$ $[M]^{+}$, 288.0102. Found: *m/z*, 288.0096.

1-(Chlorocyclohexylmethyl)-4-fluorobenzene (346): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and cyclohexylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.63 g (92%) of 1-(chlorocyclohexylmethyl)-4-fluorobenzene, a colorless liquid. ^{1}H NMR: δ ppm 7.32–7.24 (m, 2H), 7.06–6.96 (m, 2H), 4.58 (d, 1H, J= 8.4 Hz), 2.20–0.84 (m, 11H). ^{13}C NMR: δ ppm 164.2, 160.3, 136.8, 129.3, 129.1, 115.4, 115.0, 68.9, 45.8, 30.2, 26.1, 25.9. Anal. Calcd for $C_{13}H_{16}ClF$: C, 68.87; H, 7.11. Found: C, 68.66; H, 7.14.

1,4-Bis-(chlorocyclohexylmethyl)benzene (347): Benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g) and cyclohexylboron dichloride (6.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.68 g (67%) of 1,4-bis-(chlorocyclohexylmethyl)benzene, a white solid, m.p. 94.5–96.0 °C. ^{1}H NMR: δ ppm 7.28 (s, 4H), 4.60 (d, 2H, J= 8.2 Hz), 2.19–0.83 (m, 22H). ^{13}C NMR: δ ppm 140.5, 127.4, 69.3, 45.6, 30.4, 30.1, 26.0, 25.9, 25.9. HRMS: Calcd for $C_{20}H_{28}Cl_2$ $[M]^{+}$, 338.1568. Found: *m/z*, 338.1561.

(1-Chloro-2-methylbutyl)benzene (348): Benzaldehyde (3.0 mmol, 0.32 g) and *sec*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.36 g (65%) of (1-chloro-2-methylbutyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.37–7.23 (m, 5H), 4.81 (d, 0.55H, J = 6.7 Hz), 4.70 (d, 0.45H, J = 8.0 Hz), 2.06–0.80 (m, 9H). ^{13}C NMR: δ ppm 141.1, 140.8, 128.3, 127.9, 127.7, 127.6, 127.4, 69.3, 69.1, 42.9, 42.6, 26.8, 26.0, 16.1, 15.3, 11.4, 10.8. Anal. Calcd for $C_{11}H_{15}Cl$: C, 72.32; H, 8.28. Found: C, 72.11; H, 8.15.

1-Chloro-4-(1-chloro-2-methylbutyl)benzene (349): 4-Chlorobenzaldehyde (3.0 mmol, 0.42 g) and *sec*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.44 g (67%) of 1-chloro-4-(1-chloro-2-methylbutyl)benzene, a colorless liquid. ^{1}H NMR: δ ppm 7.31 (d, 2H, J = 8.8 Hz), 7.26 (d, 2H, J = 8.7 Hz), 4.78 (d, 0.45H, J = 6.6 Hz), 4.66 (d, 0.55 H, J = 7.9 Hz), 2.01–0.79 (m, 9H). ^{13}C NMR: δ ppm 139.7, 139.4, 133.6, 133.5, 129.0, 128.8, 128.5, 68.3, 68.1, 42.9, 42.6, 26.8, 25.9, 16.0, 15.2, 11.4, 10.8. Anal. Calcd for $C_{11}H_{14}Cl_2$: C, 60.85; H, 6.50. Found: C, 60.90; H, 6.52.

1-(1-Chloro-2-methylbutyl)-4-fluorobenzene (350): 4-Fluorobenzaldehyde (3.0 mmol, 0.37 g) and *sec*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.45 g (74%) of 1-(1-chloro-2-methylbutyl)-4-fluorobenzene, a colorless liquid. ^{1}H NMR: δ ppm 7.35–7.28 (m, 2H), 7.05–6.99 (m, 2H), 4.79 (d, 0.40H, J = 6.8 Hz), 4.68 (d, 0.60 H, J = 8.0 Hz), 2.06–0.79 (m, 9H). ^{13}C NMR: δ ppm 164.2, 160.0, 136.7, 129.3, 129.2, 115.4, 115.0, 68.5, 68.2, 43.1, 42.7, 26.8, 26.0,

16.1, 15.3, 11.4, 10.8. Anal. Calcd for $C_{11}H_{14}ClF$: C, 65.84; H, 7.03. Found: C, 65.64; H, 67.11.

1-(1-Chloro-2-methylbutyl)-2-methylbenzene (351): 2-Methylbenzaldehyde (3.0 mmol, 0.36 g) and *sec*-butylboron dichloride (3.0 mL, 1.0 *M* in hexane) were allowed to react as described in **3.4.2.3** to yield 0.15 g (25%) of 1-(1-chloro-2-methylbutyl)-4-methylbenzene, a colorless liquid. ^{1}H NMR: δ ppm 7.51–7.10 (m, 4H), 5.07 (d, 0.40H, J = 7.0 Hz), 4.93 (d, 0.60 H, J = 8.9 Hz), 2.36 (s, 3H), 2.12–0.78 (m, 9H). ^{13}C NMR: δ ppm 139.5, 135.0, 130.4, 127.6, 127.6, 126.4, 126.2, 65.4, 65.1, 41.7, 41.5, 27.0, 26.0, 19.4, 19.3, 16.3, 15.5, 11.5, 10.7. HRMS: Calcd for $C_{12}H_{17}Cl$ $[M]^+$, 190.102. Found: *m/z*, 190.101.

Chapter 4. Alkylation of aryl aldehyde tosylhydrazones with alkylboron chloride and trialkyl borate: An unexpected homocoupling reaction

4.1 Introduction

During our investigation of alkylation reactions utilizing alkylboron chlorides derivatives[106, 107, 112] and alkylation of aryl aldehyde tosylhydrazones with trialkylboranes,[124] we discovered that alkylation of aryl aldehyde tosylhydrazones involving alkylboron chlorides produced stilbenes rather than alkylation products.

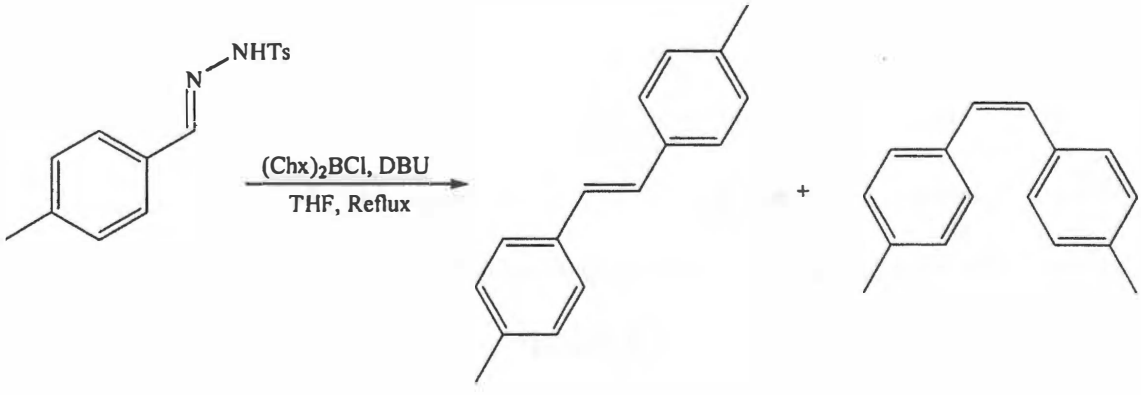
Stilbenes are important synthetic precursors to phenanthrene alkaloids as well as enantiomerically pure 1,2-diphenylethanes, 1,2-diamines, and diols. They also are used as optical brighteners and therapeutic agents for liver disorders. The conventional synthesis of stilbene products include Wittig reactions,[134] reductive coupling of carbonyls to olefins,[135] self-coupling of α-lithiated benzylic sulfones,[136] condensation of aldehyde tosylhydrazones with stabilized carbanions,[137] and reaction of aldehyde tosylhydrazones with benzotriazole-stabilized carbanions.[138] Since this new method provides a simple and inexpensive method for preparing stilbenes, we investigated the reaction in the presence of various boron compounds and bases. It was found that trimethyl borate and lithium *tert*-butoxide induced excellent yields of stilbene products.

4.2 Homocouping of aryl aldehyde tosylhydrazones in the presence of trimethyl borate and base

We first examined the alkylation of 4-methylbenzaldehyde tosylhydrazone with dicyclohexylboron chloride in the presence of DBU.[124] We found that the desired alkylation product, cyclohexyl(*p*-tolyl)methanol formed in only 10% yield. The major product was a mixture of *cis*- and *trans*-4,4′-dimethylstilbene (**Scheme 4-1**). Efforts to improve the alkylation yields using different base such as Bu_4NOH, *t*-BuLi, pyridine and 2,6-pyridine failed. But in all cases, we detected the formation of stilbenes as homocoupling products in moderate yields. Since this is a new, simple and inexpensive method of preparing stilbenes, we decided to investigate this new reaction.

4.2.1 Choice of different bases and boron compounds

The reactions of 4-methylbenzaldehyde tosylhydronzone with dicyclohexylboron chloride, *n*-butylboron dichloride, trimethylboron and trimethyl borate in the presence of



Scheme 4-1 Formation of 4,4′-dimethylstilbene from 4-methylbenzaldehyde tosylhydrazone

DBU were investigated. It was found that trimethyl borate induced excellent yields of stilbene products. Different bases were examined in an effort to optimize the reaction conditions. Strong nucleophilic bases such as Bu_4NOH, *n*-BuLi, *t*-BuOLi, lithium diisopropylamide (LDA) and the strongly hindered non-nucleophilic base DBU were employed in the reaction of 4-methylbenzaldehyde tosylhydrazone in the presence of trimethyl borate. The results were presented in **Table 4-1**. Lithium *tert*-butoxide was found be the base of choice since it is readily available, inexpensive and relatively easy to handle.

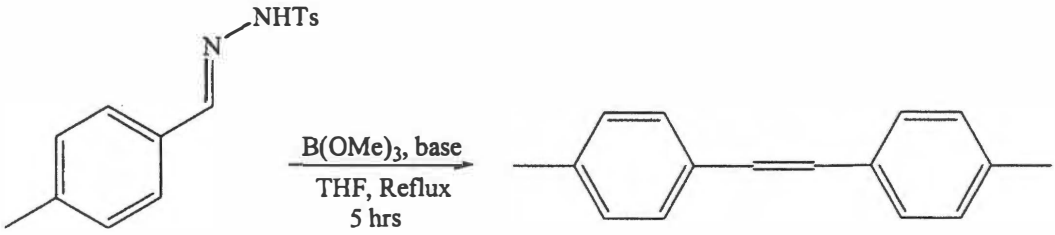
4.2.2 Results and discussion

A series of aryl aldehyde tosylhydrazones were subjected to the reaction sequence. Essentially, all gave excellent yields of stilbenes (**Table 4-2**). It should be noted that the successful reaction of the tosylhydrazone of 4-nitrobenzaldehyde (entry 11) required refluxing in DME, a higher reaction temperature than reactions carried out in THF. Interestingly, aryl aldehyde tosylhydrazones containing electron-withdrawing functionalities such as the cyano and nitro groups afforded *trans*-stilbenes as major products. These reactions proceeded relatively slowly.

4.2.3 Mechanistic study

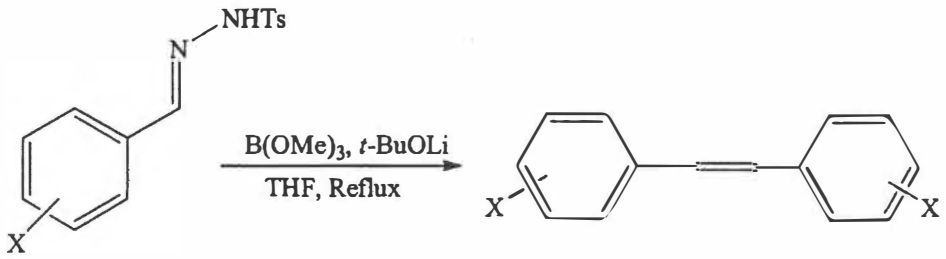
Although a detailed mechanistic study has not been carried out, the reaction presumably proceeds via the formation of an aryl carbene intermediate as shown in **Scheme 4-2**. Trimethyl borate reacts with the lithium tosylate to form a complex (which precipitates from the reaction mixture) and thus prevents the tosylate from reacting with

Table 4-1 Homocoupling of 4-methylbenzaldehyde tosylhydrazone with different bases under reflux condition



Entry	Base	*Trans/cis* isomer ratio	Yields (%)
1	DBU	55/45	42
2	Bu_4NOH	44/56	38
3	*n*-BuLi	51/49	65
4	*t*-BuOLi	50/50	80
5	LDA	47/53	40

Table 4-2 Synthesis of stilbenes via homocoupling of aryl aldehyde tosylhydrazones



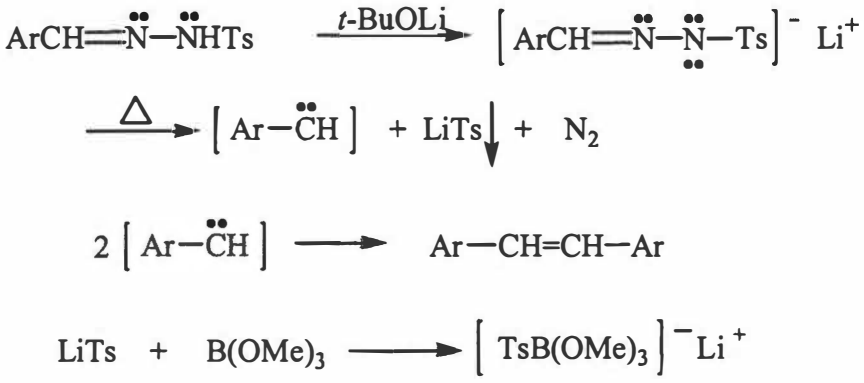
Entry	X =	Time (hr)	*Trans*/*cis* isomer ratio	Yields (%)[a,b]
1	H	6	48/52 (**401**)	82
2	4-F	10	49/51 (**402**)	87
3	4-Cl	8	58/42 (**403**)	87
4	4-Br	7	52/48 (**404**)	83
5	3-Br	7	46/54 (**405**)	80
6	2-Br	7	40/60 (**406**)	85
7	4-CH_3	5	57/43 (**407**)	81
8	4-CH_3O	5	48/52 (**408**)[c]	83
9	3-CH_3O	5	40/60 (**409**)[c]	88
10	2-CH_3O	5	50/50 (**410**)[c]	79
11	4-NO_2	12	91/9 (**411**)[c, d]	84
12	4-CN	10	99/1 (**412**)[c]	88

[a] Isolated yields of both trans and cis isomers.

[b] The physical properties and spectral characteristics of all prducts were consistent with literature values.

[c] *Trans* and *cis* isomer ratio were determined by NMR integration.

[d] DME as reaction solvent.



Scheme 4-2 Aryl carbene mediated coupling reaction of aryl aldehyde tosylhydrazones

the aryl carbene intermediate to form benzyl-4-methylphenylsulfone. In fact, benzyl-4-methylphenylsulfone has been observed in the reaction of all aryl aldehyde tosylhydrazones with lithium *tert*-butoxide in the absence of trimethyl borate, conditions which led to low yields of stilbenes. In order to confirm the existence of a carbene intermediate, 4-methylstyrene was added to a mixture of 4-methylbenzaldehyde tosylhydrazone, lithium *t*-butoxide and trimethyl borate in an effort to trap the carbene intermediate. As expected, a mixture of *trans* and *cis* 1,2-di-(4-methylphenyl)cyclopropane was isolated. Stoichiometric quantities of lithium *tert*-butoxide and trimethyl borate are required to produce high yields of stilbenes.

4.3 Conclusion

In conclusion, the homocoupling of aryl aldehyde tosylhydrazones in the presence of trimethyl borate and lithium tert-butoxide provides a simple, inexpensive, and efficient route to stilbenes, including stilbenes containing electron-withdrawing functional groups.

The method is particularly useful for preparing cyano- and nitro- substituted stilbenes in high stereoselectivity.

4.4 Experimental

4.4.1 General considerations

All glassware, syringes and needles were dried in an oven heated to 150 °C for at least 12 hours and cooled under argon prior to use. All solvents were dried and distilled prior to use. All aryl aldehyde tosylhydrazones were prepared by the reaction of aryl aldehydes with *p*-toluenesulfonhydrazide in ethanol.[139] Trimethyl borate was obtained from Aldrich Chemical Company and used as received. All reactions were run under an argon atomosphere, magnetically stirred and monitored by TLC analysis. Products were isolated by flash column chromatography.

All ^{1}H spectra were recorded in $CDCl_3$/TMS at 250 MHz, ^{13}C NMR spectra were recorded in $CDCl_3$/TMS at 62.9 MHz using a Brucker AC250 NMR spectrometer. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia.

4.4.2 General experimental procedure

The synthesis of stilbene is representative: benzaldehyde tosylhydrazone (3.0 mmol, 0.82 g) was dissolved in 20 mL of dry THF in a dry, argon-flushed, round-bottomed-flask equipped with a reflux condenser and magnetic stirring bar. Trimethyl borate (3.0 mmol, 0.31g, 0.30 mL) was then added via syringe followed by lithium *tert*-butoxide (3.0 mL, 1.0 *M* solution in hexanes) and the reaction mixture heated to gentle reflux for 6 h. The mixture was then cooled, hydrolyzed, the organic phase separated and

dried (anhydrous $MgSO_4$). Removal of solvent under reduced pressure followed by silica gel flash column chromatography with hexanes as eluent produces an 82% yield of stilbene.

4.4.3 Syntheses and characterizations of compounds 401-412

Stilbene (401):[140] A mixture of benzaldehyde tosylhydrazone (3.0 mmol, 0.82 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.21 g *trans*- and 0.23 g *cis*-stilbene (82%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.53-7.26 (m, 10H), 7.10 (s, 2H), *cis* isomer 7.26-7.15 (m, 10H), 6.59 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 137.32, 131.34, 128.65, 127.56, 126.49, *cis* isomer 137.22, 130.22, 128.84, 128.17, 127.06.

4,4′-Difluorostilbene (402):[141] A mixture of 4-fluorobenzaldehyde tosylhydrazone (3.0 mmol, 0.88 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.276 g *trans*- and 0.283 g *cis*-4,4′-difluorostilbene (87%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.48-7.42 (m, 4H), 7.10-6.96 (m, 6H), *cis* isomer 7.20-7.15 (m, 4H), 6.96-6.87 (m, 4H), 6.53 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 137.3, 128.7, 127.6, 126.5, *cis* isomer 163.8, 159.9, 132.9, 130.5, 130.4, 129.1, 115.4, 115.1.

4,4′-Dichlorostilbene (403):[142] A mixture of 4-chlorobenzaldehyde tosylhydrazone (3.0 mmol, 0.93 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.38 g *trans*- and 0.27 g *cis*-4,4′-dichlorostilbene (87%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans*

isomer 7.43-7.40 (dd, 4H, J = 7.5 Hz, J = 2.4 Hz), 7.34-7.30 (dd, 4H, J = 8.0 Hz, J = 2.7 Hz), 7.01 (s, 2H), *cis* isomer 7.25-7.11 (m, 8H), 6.55 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 135.5, 133.5, 128.9, 128.0, 127.7, *cis* isomer 135.3, 133.0, 130.1, 129.6, 128.5.

4,4′-Dibromostilbene (404):[136] A mixture of 4-bomobenzaldehyde tosylhydrazone (3.0 mmol, 1.06 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.44 g *trans*- and 0.40 g *cis*-4,4′-dibromostilbene (83%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.50-7.48 (m, 4H), 7.38-7.34 (m, 4H), 7.01 (s, 2H), *cis* isomer 7.36-7.32 (m, 4H), 7.10-7.06 (m, 4H), 6.53 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 135.9, 131.7, 128.2, 128.0, 121.7, *cis* isomer 135.6, 131.5, 130.4, 129.7, 121.2.

3,3′-Dibromostilbene (405):[143] A mixture of 3-bomobenzaldehyde tosylhydrazone (3.0 mmol, 1.06 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.37 g *trans*- and 0.44 g *cis*-3,3′-dibromostilbene (80%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.65-7.16 (m, 8H), 7.00 (s, 2H), *cis* isomer 7.3-7.05 (m, 8H), 6.55 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 137.0, 130.8, 130.2, 129.4, 128.5, 125.3, 122.9, *cis* isomer 138.7, 131.7, 130.4, 129.9, 129.8, 127.3, 122.4.

2,2′-Dibromostilbene (406):[144] A mixture of 2-bomobenzaldehyde tosylhydrazone (3.0 mmol, 1.06 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.34 g *trans*- and 0.51 g *cis*-2,2′-dibromostilbene (85%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans*

isomer 7.73-7.32 (m, 8H), 7.13 (s, 2H), *cis* isomer 7.60-7.15 (m, 8H), 6.77 (s, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 137.0, 130.9, 130.2, 129.2, 128.7, 126.7, 124.3, *cis* isomer 136.8, 133.1, 132.6, 129.9, 127.6, 127.1, 124.0.

4,4′-Dimethylstilbene (407):[145] A mixture of 4-methylbenzaldehyde tosylhydrazone (3.0 mmol, 0.86 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.29 g *trans*- and 0.26 g *cis*-4,4′-dimethylstilbene (81%). ^1H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.41-7.36 (d, 4H, $J = 7.7$ Hz), 7.17-7.14 (d, 4H, $J = 7.5$ Hz), 7.03 (s, 2H), 2.35 (s, 3H), *cis* isomer 7.17-7.14 (d, 4H, $J = 7.6$ Hz), 7.04-7.01 (d, 4H, $J = 7.7$ Hz), 6.51 (s, 2H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 137.3, 134.7, 129.3, 127.6, 126.3, 21.2, *cis* isomer 136.6, 134.5, 129.5, 128.7, 128.7, 21.2.

4,4′-Dimethoxylstilbene (408):[146] A mixture of 4-methoxylbenzaldehyde tosylhydrazone (3.0 mmol, 0.91 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 60 g mixture *trans*- and *cis*-4,4′-dimethoxylstilbene (81%). ^1H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.45-7.42 (d, 4H, $J = 7.5$ Hz), 7.22-7.19 (d, 4H, $J = 7.5$ Hz), 6.98 (s, 2H), 3.80 (s, 3H), *cis* isomer 6.91-6.88 (d, 4H, $J = 7.6$ Hz), 6.88-6.85 (d, 4H, $J = 7.5$ Hz), 6.44 (s, 2H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 159.8, 130.0, 128.4, 114.0, 55.7, *cis* isomer 159.6, 127.9, 126.6, 113.6, 55.3.

3,3′-Dimethoxylstilbene (409):[147] A mixture of 3-methoxylbenzaldehyde tosylhydrazone (3.0 mmol, 0.91 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.63

g mixture of *trans*- and *cis*-3,3′-dimethoxylstilbene (88%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.30-7.11 (m, 8H), 7.04 (s, 2H), 3.84 (s, 3H), *cis* isomer 7.02-6.71 (m, 8H), 6.57 (s, 2H), 3.65 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 160.0, 136.7, 129.5, 125.9, 121.9, 113.8, 113.1, 55.2, *cis* isomer 161.5, 136.2, 129.3, 124.1, 119.2, 113.4, 111.8, 55.0.

2,2′-Dimethoxylstilbene (410):[148] A mixture of 2-methoxylbenzaldehyde tosylhydrazone (3.0 mmol, 0.91 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.56 g mixture of *trans*- and *cis*-2,2′-dimethoxylstilbene (79%). ^{1}H NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 7.66-6.92 (m, 10H), 3.66 (s, 3H), *cis* isomer 7.31-6.79 (m, 1H), 3.62 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm: *trans* isomer 157.1, 129.9, 128.3, 126.4, 124.0, 120.7, 110.6, 55.5, *cis* isomer 156.6, 128.3, 127.1, 125.5, 123.5, 120.0, 110.5, 55.4.

4,4′-Dinitrostilbene (411):[149] A mixture of 4-nitro-benzaldehyde tosylhydrazone (3.0 mmol, 0.96 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield 0.67 g mixture of *trans*- and *cis*-4,4′-dinitro-stilbene (81%). ^{1}H NMR (DMSO) δ ppm: *trans* isomer 8.38 (d, 4H, J = 8.5 Hz), 7.91 (d, 4H, J = 8.2 Hz), 7.57 (s, 2H), *cis* isomer 8.13 (d, 4H, J = 7.9 Hz), 7.45 (d, 4H, J = 8.5 Hz), 6.97 (s, 2H); ^{13}C NMR (DMSO) δ ppm: *trans* isomer 147.7, 141.3, 128.4, 127.1, 124.1, *cis* isomer 146.5, 142.0, 131.4, 129.9, 123.8.

4,4′-Dicyanostilbene (412):[150] A mixture of 4-cyano-benzaldehyde tosylhydrazone (3.0 mmol, 0.91 g), trimethyl borate (0.31 g) and lithium *t*-butoxide (3.0 mL, 1.0 *M* solution in hexane) was allowed to react as described previously to yield

mainly 0.61 g *trans*-4,4'-dicyano-stilbene (81%). ^{1}H NMR (DMSO) δ ppm: *trans* isomer 7.65-7.52 (m, 4H), 7.30-7.21 (m, 4H), 6.75 (s, 2H); ^{13}C NMR (DMSO) δ ppm: *trans* isomer 140.9, 132.2, 129.4, 127.3, 116.5, 111.3.

Chapter 5. Dialkenylation of aryl aldehydes with alkynes in the presence of boron trihalides

5.1 Introduction

Our previous studies utilizing saturated dialkylboron chloride or alkylboron dichloride to alkylate aryl aldehydes led us to postulate that alkenylboranes and vinylboranes might react with carbonyl groups to generate allyl alcohols or 1,4-dienes as a result of alkenylation. Vinylboranes are very useful reagents in organic synthesis.[13, 21,] They are generally prepared by hydroboration of alkynes with boron hydrides,[151] by the reactions of boron trihalide with vinyltin, vinylzinc or vinylmercury compounds,[152] or by haloboration of 1-alkynes with boron halides.[73, 74, 153] Haloboration reactions and their applications in organic chemistry have been extensively reviewed.[72] The reactions usually occur in a stereo-, regio-, and chemoselective fashion via the *syn* addition of the B-X moiety to the carbon-carbon triple bond, generating the corresponding (*Z*)-2-halo-1-alkenylboranes.[72(b), (c), (d)] Simple vinylborane derivatives have been utilized in Grignard-like reactions to produce the allylic alcohols,[154] there is only one report in which a halovinylborane was used in a carbonyl addition reaction.[155]

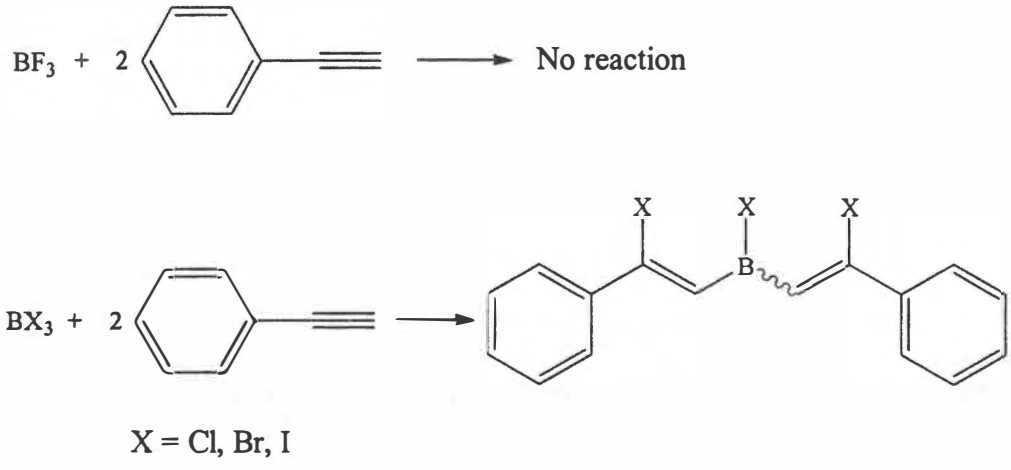
In this chapter, we report the results of a study involving carbonyl compounds with alkynes in the presence of boron trihalides: BF_3, BCl_3, BBr_3 and BI_3.

5.2 Results and discussion

We examined the alkenylation reaction of aromatic aldehydes with alkynes in the presence of BF_3, BCl_3, BBr_3 and BI_3. We found the expected dialkenylation product, 1,3,5-triaryl-1,5-dihalo-1,4-dienes, formed only with BCl_3, BBr_3 and BI_3, a result that is consistent with the reactivities of boron halides as discussed in chapter 1.

5.2.1 Dialkenylation of aryl aldehydes with aryl acetylenes in the presence of boron trifluoride

As noted earlier, haloboration of terminal aromatic alkynes with boron halides takes place readily for BBr_3 and BI_3, even at very low temperature; chloroboration occurs only at room temperature. Fluoroboration rarely occurs at even an elevated temperature (**Scheme 5-1**). As anticipated, the alkyenylation of aryl aldehydes with aryl acetylene in

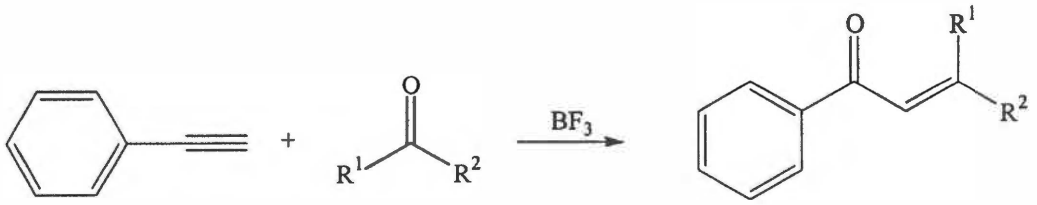


Scheme 5-1 Haloboration of phenylacetylene

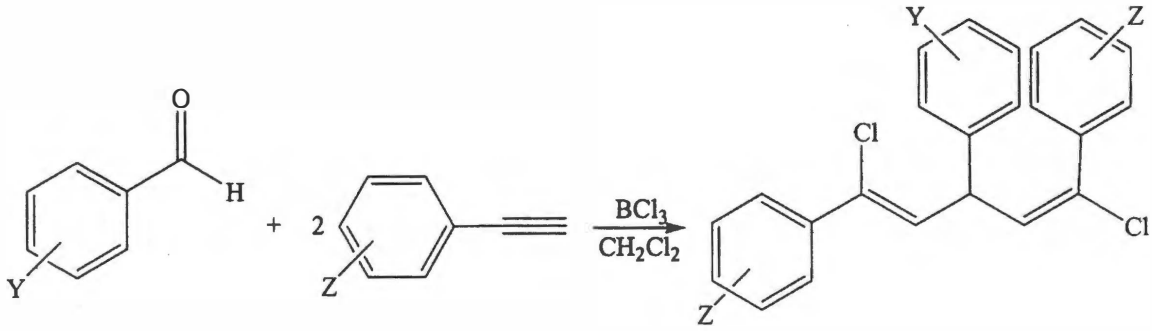
the presence of boron trifluoride did not give rise either to the monoalkenylation product (allylic alcohol) or the dialkenylation product (1,5-difluoro-1,4-diene). As a matter of fact, addition of carbonyl compounds to alkynes under the influence of BF_3 had been reported to afford α,β-unsaturated ketones as the main products (**Scheme 5-2**).[156]

5.2.2 Dialkenylation of aryl aldehydes with aryl acetylenes in the presence of boron trichloride

We examined the reaction of benzaldehyde with one equivalent of phenylacetylene in the presence of boron trichloride in CH_2Cl_2 at room temperature. The reaction generated the 1,4-pentadiene product along with the expected allylic alcohol. We then examined the reaction of benzaldehyde with two equivalents of phenylacetylene in the presence of boron trichloride and found that (*E,Z*)-1,5-dichloro-1,3,5-triphenyl-1,4-pentadiene was the major product (**Scheme 5-3**). Only a minor quantity of the *Z,Z* isomer formed along with a small quantity of dichloromethylbenzene (due to the direct halogenation of benzaldehyde by boron trichloride as noted in our earlier



Scheme 5-2 Addition of carbonyl compounds to alkynes under the influence of boron trifluoride



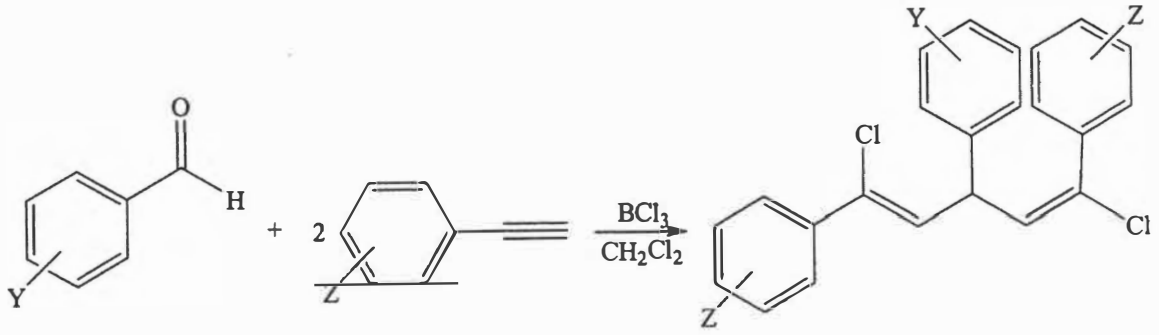
Scheme 5-3 Reaction of aryl aldehydes with aryl acetylene in the presence of BCl_3 at 0 °C: Synthesis of (*E,Z*)-1,3,5-triaryl-1,5-dichloro-1,4-pentadiene

studies).[106, 107, 112] To minimize the formation of undesired dichloromethylbenzene, the reaction was carried out in CH_2Cl_2 at 0 °C and 1,5-dichloro-1,3,5-triphenyl-1,4-pentadiene was isolated in good yield (65%).[157]

A series of aldehydes was subjected to the new reaction. All were converted to the corresponding 1,3,5-triaryl-1,5-dichloro-1,4-pentadiene derivatives in good to excellent yields (**Table 5-1**).[157] As can be seen from the data in **Table 5-1**, the reactions of arylacetylenes and aryl aldehydes bearing electron-withdrawing groups tend to proceed more slowly. The lower yields may be due to partial polymerization of the alkynes catalyzed by boron trichloride.[153]

Reactions involving aliphatic alkynes were also examined since aliphatic alkynes are stronger Lewis bases than aromatic alkynes and undergo chloroboration more readily. However, only traces of the desired products were observed, presumably due to the rapid polymerization of the diene products. Aliphatic aldehydes are not suitable substrates for

Table 5-1 Synthesis of (*E,Z*)-1,3,5-triaryl-1,5-dichloro-1,4-pentadienes at 0 °C



Entry	Y =	Z =	Time (hr)	Yields (%)[a,b]
1	H	H	6	65 (**501**)
2	4-F	H	8	73 (**502**)
3	4-Cl	H	8	70 (**503**)
4	4-Br	H	8	68 (**504**)
5	2-Br	H	8	65 (**505**)
6	4-CH_3	H	6	65 (**506**)
7	2-CH_3	H	6	61 (**507**)
8	4-CN	H	10	68 (**508**)[c]
9	4-NO_2	H	10	64 (**509**)
10	H	4-CH_3	6	67 (**510**)
11	4-F	4-CH_3	8	63 (**511**)
12	4- CH_3	4-CH_3	4	62 (**512**)
13	2- CH_3	4-CH_3	4	58 (**513**)
14	4-Br	4-CH_3	6	60 (**514**)
15	3-Br	4-CH_3	6	61 (**515**)

Table 5-1 (Continued)

Entry	Y =	Z =	Time (hr)	Yields (%)[a,b]
16	4-CN	4-CH_3	8	65 (**516**)
17	4-H	4-F	8	66 (**517**)
18	4-Cl	4-F	10	68 (**518**)
19	4-F	4-F	12	76 (**519**)
20	4-CH_3	4-F	6	62 (**520**)
21	2-CH_3	4-F	6	68 (**521**)
22	3-Br	4-F	10	65 (**522**)
23	4-Br	4-Br	8	64 (**523**)

a Isolated yields based on starting aldehydes.

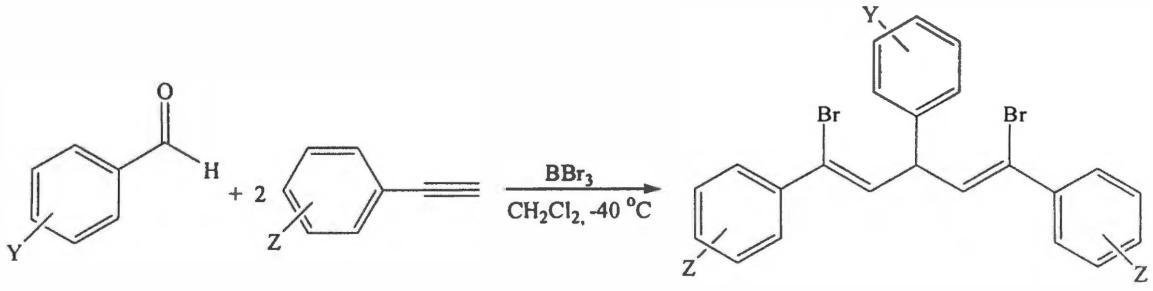
[b] All products were characterized by elemental analyses and NMR spectroscopy.

[c] Mixture of *E,Z* and *Z,Z* isomer, *E,Z*/*Z,Z* = 40/60.

the reactions due to known enolization reactions. Interestingly, reactions of aliphatic aldehydes without enolizable α-hydrogens, such as trimethylacetaldehyde and tribromoacetaldehyde, and aryl acetylenes produced only allylic alcohol products; no 1,4-diene products were observed.

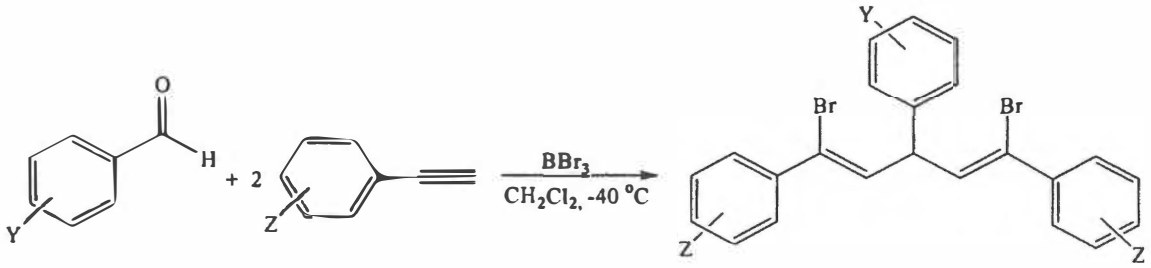
5.2.3 Dialkenylation of aryl aldehydes with aryl acetylenes in the presence of boron tribromide

Since haloboration of alkynes by boron tribromide is faster than haloborations utilizing boron trichloride[72,73] and the bromination of aryl aldehydes by boron tribromide had been reported to be quite facile,[82] dialkenylation reactions of aryl aldehydes using BBr_3 were carried out at –40 °C instead of 0 °C. Under these reaction conditions, (*Z,Z*)-1,3,5-triaryl-1,5-dibromo-1,4-pentadienes were generated in excellent yields along with minor quantities of the *E,Z* isomers (**Scheme 5-4**). A series of aldehydes allowed to react with aryl acetylene in the presence of BBr_3. The results are tabulated in **Table 5-2**.[157] As can be seen from the data in **Tables 5-1** and **5-2**, the yields of chlorinated diene



Scheme 5-4 Reaction of aryl aldehydes with aryl acetylene in the presence of BBr_3 at -40 °C: synthesis of (*Z,Z*)-1,3,5-triaryl-1,5-dibromo-1,4-pentadiene

Table 5-2 Synthesis of (*Z,Z*)-1,3,5-triaryl-1,5-dibromo-1,4-pentadienes at –40 °C



Entry	Y =	Z =	Time (hr)	Yields (%)[a,b]
1	4-F	H	4	91 (**524**)
2	2-F	H	4	88 (**525**)
3	4-Cl	H	4	95 (**526**)
4	4-Br	H	4	92 (**527**)
5	4-CH_3	H	3	80 (**528**)
6	2-CH_3	H	3	83 (**529**)
7	4-NO_2	H	10	80 (**530**)
8	4-F	4-CH_3	4	80 (**531**)
9	4-Cl	4-CH_3	4	77 (**532**)
10	4-Br	4-CH_3	4	70 (**533**)
11	4-F	4-Cl	10	83 (**534**)
12	4-Cl	4-Cl	8	86 (**535**)
13	4-Br	4-Cl	8	74 (**536**)
14	4-CH_3	4-Cl	6	89 (**537**)
15	2-CH_3	4-Cl	6	85 (**538**)

[a] Isolated yields based on the starting aldehydes.
[b] All products were characterized by elemental analyses and NMR spectroscopy.

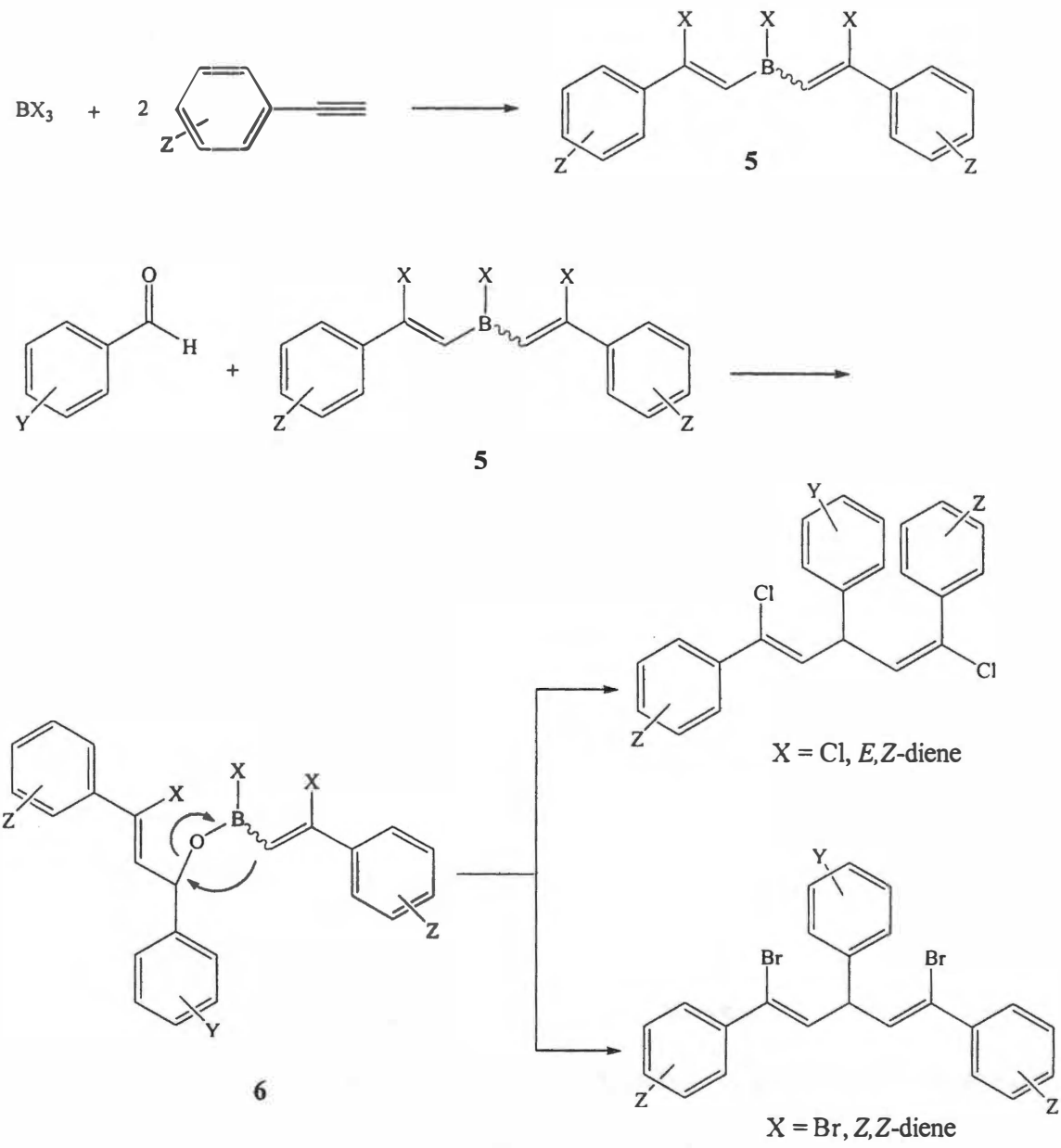
products are lower than brominated dienes (partial polymerization catalyzed by BCl_3), and reactions involving BBr_3 are also faster than those using BCl_3.

5.2.4 Dialkenylation of aryl aldehydes with aryl acetylenes in the presence of boron triiodide

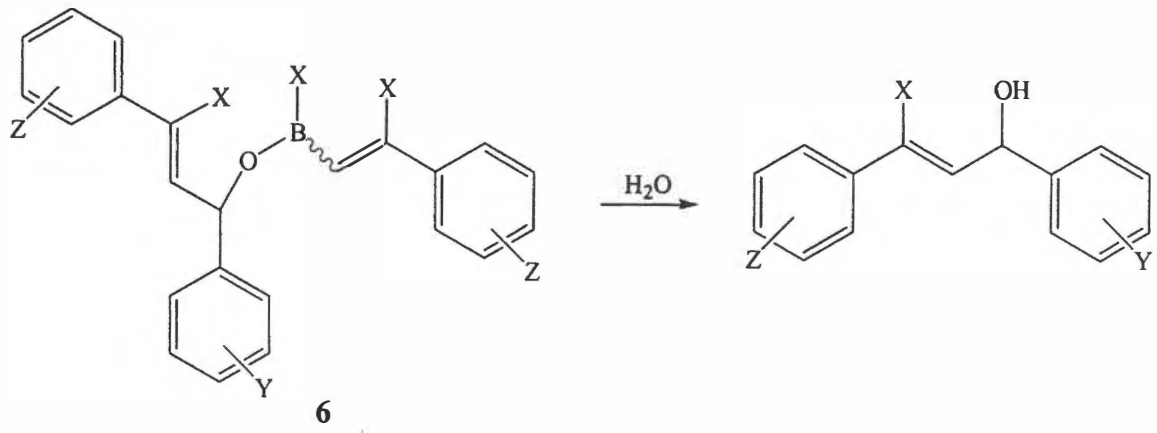
Although the haloboration of alkynes with boron triiodide is the fastest of all boron trihalides, the dialkenylation products generated by reaction of aryl aldehydes with phenylacetylene in the presence of boron triiodide are not photochemically stable.[158] We found the purification of the product 1,5-diiodo-1,4-pentadienes to be extremely difficult using flash column chromatography, the yields of the desired dienes were too low to be useful because of the loss of product on the column.

5.3 Possible reaction mechanism

Although a detailed mechanistic study has not yet been undertaken, the reaction most likely proceeds via a double-migration pathway as outlined in **Scheme 5-5**. Haloboration of the alkyne would generate di(halovinyl)boron halide intermediate **5** which would then add to the aldehyde in a Grignard-like fashion to form an allyloxylhalovinylboron halide intermediate, **6**, by migration of the first halovinyl group. Migration of the second halovinyl group would afford the final diene product. In control experiments in which BBr_3 and BCl_3 reactions were hydrolyzed prior to completion, the allylic alcohols expected from allyloxyhalovinylboron halide intermediate **6** were isolated from the product mixtures (**Scheme 5-6**). In a separate experiment, two equivalents of phenylacetylene were added to boron tribromide in CH_2Cl_2 to generate **5** (X = Br, Z = H)



Scheme 5-5 Proposed double migration pathway



Scheme 5-6 Hydrolytic formation of allylic alcohols from allyloxyhalovinylboron halide intermediate **6**

which was then treated with 4-chlorobenzaldehyde. The reaction generated the expected (*Z,Z*)-1,5-dibromo-1,4-diene. However, the reaction is faster if boron tribromide is simply introduced to a mixture of phenylacetylene and 4-chlorobenzaldehyde in CH_2Cl_2. At present, there is insufficient data to determine whether the conversion of **6** to either (*E,Z*)-diene or (*Z,Z*)-diene proceeds via a concerted rearrangement or a S_N1 mechanism.[159]

The formation of (*E,Z*)-1,5-dichloro-1,4-pentadienes is presumably due to the slow chloroboration of the second molecule aryl acetylene which leads to the more thermodynamically stable (*E, Z*)-chlorovinyl addition product (**Figure 5-1**). Presumably, migration of the vinyl groups proceeds with the retention of configuration. The bromoboration of alkynes by boron tribromide is reported to be very facile and the reactions tend to from the kinetically controlled (*Z,Z*)-di(halovinyl)boron bromide[73, 74] (**Figure 5-1**) which would then react with aryl aldehydes to generate (*Z,Z*)-1,5-dibormo-

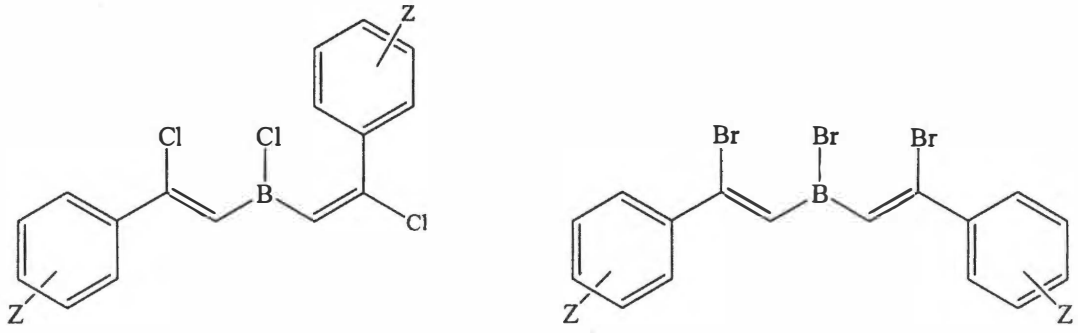


Figure 5-1 Thermodynamically stable (*E,Z*)-di(chlorovinyl)boron chloride and kinetically controlled (*Z,Z*)-di(bromovinyl)boron bromide

1,4-pentadienes with retention of the double bond configuration. Single crystals of (*E,Z*)-3-(4-bromophenyl)-1,5-dichloro-1,5-diphenyl-1,4-pentadiene (**Figure 5-2**) and (*Z,Z*)-1,5-dibromo-3-(4-fluorophenyl)-1,5-diphenyl-1,4-pentadiene (**Figure 5-3**) were analyzed by X-ray crystallography.

Other organoboron halides, including *n*-butylboron dichloride, cyclopentylboron dichloride, and phenylboron dichloride, were examined in place of boron trihalides, but none of the desired dienes were formed. These results indicate that the presence of a third halogen atom on the boron is essential for the reaction by polarizing the C=O bond to facilitate the migration of halovinyl moiety to the carbon.

5.4 Conclusion

In summary, we have discovered a novel dialkenylation reaction of aryl aldehydes with aryl acetylenes in the presence of boron trichloride and boron tribromide. The reaction is applicable to aryl aldehydes containing various functional groups but it is not

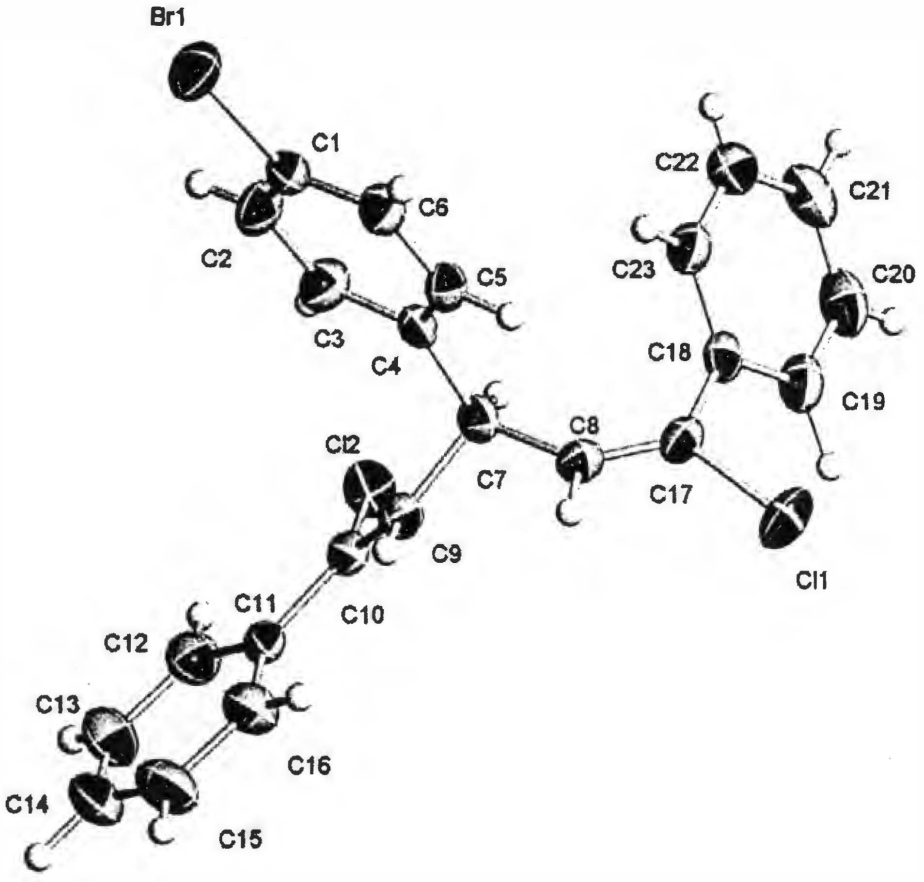


Figure 5-2 X-ray crystal structure of (*E,Z*)-3-(4-bromophenyl)-1,5-dichloro-1,5-diphenyl-1,4-pentadiene (**504**)

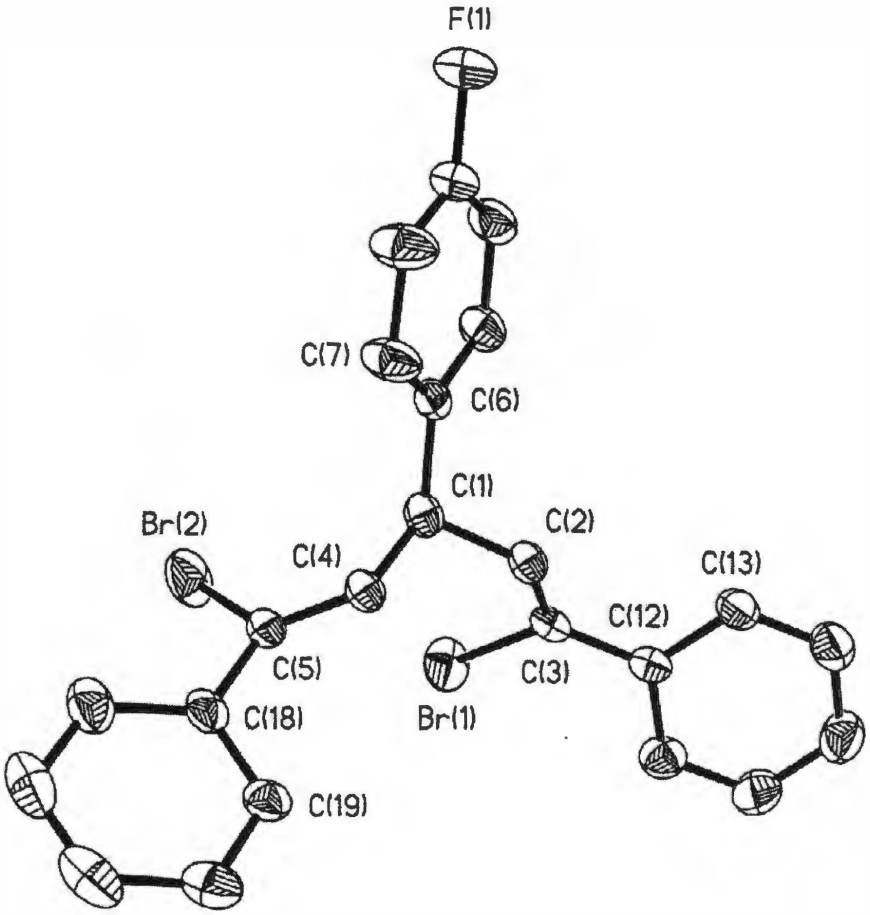


Figure 5-3 X-ray crystal structure of (*Z,Z*)-1,5-dibromo-3-(4-fluorophenyl)-1,5-diphenyl- 1,4-pentadiene (**524**)

potentially useful intermediates in organic synthesis due to the multifunctionality contained in the molecules which may be utilized in subsequent substitution and coupling reactions.

5.5 Experimental

5.5.1 General considerations

All glassware was dried in an oven at 150 °C and flushed with dry argon. All reactions were carried out under argon atmosphere. CH_2Cl_2 was distilled over CaH_2. All aldehydes and alkynes were purchased from Aldrich Chemical Company and used as received. Boron trichloride (1.0 *M* hexane solution) was purchased from Aldrich Chemical Company. Boron trfluoride etherate was purchased from Aldrich Chemical Company and used as received. Boron tribromide and triiodide (Aldrich Chemical Company) were diluted to 1 *M* CH_2Cl_2 solution. Prodcuts were purified by flash chromatography using silica gel (60 Å, 230-400 mesh) with hexanes as eluant except for compounds **508**, **509**, **516** and **530** (hexanes/EtOAc = 9/1 as eluent).

All ^1H spectra were recorded in $CDCl_3$/TMS at 250 MHz, ^{13}C NMR spectra were recorded in $CDCl_3$/TMS at 62.9 MHz using a Brucker AC250 NMR spectrometer. In cases where isomers were formed, the NMR shifts of all isomers are reported. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia.

5.5.2 General experimental procedures

5.5.2.1 Representative procedure for the synthesis of 1,3,5-triaryl-1,5-dichloro-1,4-pentadienes (501-523)

4-Fluorobenzaldehyde (0.92 g, 7.4 mmol) and phenylacetylene (1.51 g, 14.8 mmol) were placed in a dry argon-flushed, 50 mL round-bottomed flask equipped with a stirring bar and dissolved in dry CH_2Cl_2 (20 mL). Boron trichloride (8.0 mmol, 8.0 mL of a 1.0 *M* hexane solution) was added via a syringe. The solution was allowed to stir for 2 hrs at 0 °C in an ice bath and then for 6 hrs at room temperature. The reaction solution gradually turned dark purple. The resulting mixture was hydrolyzed with water and extracted into hexanes. The organic layer was separated and dried over anhydrous $MgSO_4$. The product was isolated by flash column chromatography.

5.5.2.2 Representative procedure for the synthesis of 1,3,5-triaryl-1,5-dibromo-1,4-pentadienes (524-538)

4-Chlorobenzaldehyde (0.42 g, 3.0 mmol) and phenylacetylene (0.61 g, 6.0 mmol) were placed in a dry argon-flushed, 50 mL round-bottomed flask equipped with a stirring bar and dissolved in dry CH_2Cl_2 (20 mL). Boron tribromide (3.0 mmol, 3.0 mL of a 1.0 *M* methylene chloride solution) was added via a syringe at -40 °C. The solution was allowed to stir for 4hrs at -40 °C in a dry ice-acetone bath. The reaction solution gradually turned purple. The resulting mixture was hydrolyzed with water and extracted into hexanes. The organic layer was separated and dried over anhydrous $MgSO_4$. The product was isolated by flash column chromatography.

5.5.3 Syntheses and characterizations of compounds 501-538

1,5-Dichloro-1,3,5-triphenyl-1,4-pentadiene (501). The reaction of benzaldehyde (3.0 mmol, 0.32 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.71 g (65%) of 1,5-dichloro-1,3,5-triphenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.57-7.21 (m, 15H), 6.26 (d, 1H, J = 9.2 Hz), 6.19 (d, 1H, J = 10.6 Hz), 4.88 (t, 1H, J = 10.1 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm 141.5, 137.6, 136.7, 133.7, 129.0, 128.9, 128.8, 128.3, 127.6, 127.2, 126.9, 126.5, 45.6. Anal. Calcd for $C_{23}H_{18}Cl_2$: C, 75.62; H, 4.97. Found: C, 75.48; H, 4.88.

1,5-Dichloro-3-(4-fluorophenyl)-1,5-diphenyl-1,4-pentadiene (502). The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.84 g (73%) of 1,5-dichloro-3-(4-fluorophenyl)-1,5-diphenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.58-6.99 (m, 14H), 6.22 (d, 1H, J = 9.1 Hz), 6.15 (d, 1H, J = 10.4 Hz), 4.85 (t, 1H, J = 9.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 163.7, 159.8, 137.4, 137.1, 136.6, 133.9, 133.3, 129.0, 128.9, 128.8, 128.7, 128.4, 127.3, 126.6, 115.8, 115.5, 44.9. Anal. Calcd for $C_{23}H_{17}Cl_2F$: C, 72.07; H, 4.47. Found: C, 72.32; H, 4.52.

1,5-Dichloro-3-(4-chlorophenyl)-1,5-diphenyl-1,4-pentadiene (503). The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.84 g (70%) of 1,5-dichloro-3-(4-chlorophenyl)-1,5-diphenyl-1,4-

pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.59-7.16 (m, 14H), 6.23 (d, 1H, J = 9.2 Hz), 6.14 (d, 1H, J = 10.6 Hz), 4.83 (t, 1H, J = 9.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 140.0, 137.4, 136.6, 134.3, 133.5, 132.8, 129.1, 128.9, 128.7, 128.6, 128.5, 128.4, 127.0, 126.6, 45.0. Anal. Calcd for $C_{23}H_{17}Cl_3$: C, 69.11; H, 4.29. Found: C, 69.80; H, 4.32.

3-(4-Bromophenyl)-1,5-dichloro-1,5-diphenyl-1,4-pentadiene (504). The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.91 g (68%) of 3-(4-bromophenyl)-1,5-dichloro-1,5-diphenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.56-7.09 (m, 14H), 6.21 (d, 1H, J = 9.1 Hz), 6.13 (d, 1H, J = 10.5 Hz), 4.81 (t, 1H, J = 9.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 140.4, 137.3, 136.5, 134.1, 133.5, 131.9, 129.1, 129.0, 128.7, 128.4, 126.9, 126.5, 120.8, 45.0. Anal. Calcd for $C_{23}H_{17}BrCl_2$: C, 62.19; H, 3.86. Found: C, 62.35; H, 3.84.

3-(2-Bromophenyl)-1,5-dichloro-1,5-diphenyl-1,4-pentadiene (505). The reaction of 2-bromobenzaldehyde (3.0 mmol, 0.56 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.88 g (65%) of 3-(2-bromophenyl)-1,5-dichloro-1,5-diphenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.65-7.07 (m, 14H), 6.33 (d, 1H, J = 8.5 Hz), 6.21 (d, 1H, J = 10.2 Hz), 5.11 (t, 1H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 141.6, 137.5, 136.7, 134.4, 133.6, 133.5, 129.1, 128.9, 128.8, 128.7, 128.4, 128.3, 128.2, 127.8, 127.0, 126.5, 123.9, 45.9. Anal. Calcd for $C_{23}H_{17}BrCl_2$: C, 62.19; H, 3.86. Found: C, 62.53; H, 3.59.

1,5-Dichloro-1,5-diphenyl-3-(*p*-tolyl)-1,4-pentadiene (506). The reaction of 4-methylbenzaldehyde (2.8 mmol, 0.36 g), ethynylbenzene (5.6 mmol, 0.57 g) and BCl_3 (2.8 mmol, 2.8 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.69 g (65%) of 1,5-dichloro-1,5-diphenyl-3-(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.58-7.15 (m, 14H), 6.26 (d, 1H, J = 9.2 Hz), 6.18 (d, 1H, J = 10.6 Hz), 4.84 (t, 1H, J = 10.0 Hz), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.5, 137.6, 136.7, 136.6, 133.5, 132.8, 129.5, 129.2, 128.9, 128.8, 128.3, 127.8, 127.1, 126.5, 45.2, 21.0. Anal. Calcd for $C_{24}H_{20}Cl_2$: C, 75.99; H, 5.31. Found: C, 76.10; H, 5.40.

1,5-Dichloro-1,5-diphenyl-3-(*o*-tolyl)-1,4-pentadiene (507). The reaction of 2-methylbenzaldehyde (2.8 mmol, 0.36 g), ethynylbenzene (5.6 mmol, 0.57 g) and BCl_3 (2.8 mmol, 2.8 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.65 g (61%) of 1,5-dichloro-1,5-diphenyl-3-(*o*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.54-7.10 (m, 14H), 6.29 (d, 1H, J = 9.0 Hz), 6.21 (d, 1H, J = 10.3 Hz), 4.91 (t, 1H, J = 9.9 Hz), 2.04 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 140.7, 137.5, 136.9, 136.0, 133.3, 132.4, 130.8, 129.4, 128.9, 128.8, 128.7, 128.3, 128.0, 126.7, 126.5, 43.0, 19.3. Anal. Calcd for $C_{24}H_{20}Cl_2$: C, 75.99; H, 5.31. Found: C, 76.15; H, 5.52.

1,5-Dichloro-3-(4-cyanophenyl)-1,5-diphenyl-1,4-pentadiene (508). The reaction of 4-cyanobenzaldehyde (3.0 mmol, 0.39 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.79 g (68%) of a mixture of *E,Z*- and *Z,Z*-1,5-dichloro-3-(4-cyanophenyl)-1,5-diphenyl-1,4-pentadiene. *E,Z*-isomer (40%): ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.62-7.23 (m, 14H), 6.23 (d, 1H, J = 9.0 Hz), 6.15 (d, 1H, J = 10.4 Hz), 4.91 (t, 1H,

J = 9.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 146.8, 137.0, 136.3, 134.9, 134.3, 132.6, 129.2, 128.5, 128.4, 128.0, 127.5, 126.5, 125.9, 118.6, 110.8, 45.6. *Z,Z*-isomer (60%): ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.64-7.22 (m, 14H), 6.31 (d, 2H, J = 8.9 Hz), 5.49 (t, 1H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 146.7, 137.2, 135.6, 132.6,129.1, 128.4, 128.2, 126.6, 125.8, 118.7, 110.7, 45.8. Anal. Calcd for $C_{24}H_{17}Cl_2N$: C, 73.85; H, 4.39; N, 3.59. Found: C, 73.63; H, 4.42; N, 3.72.

1,5-Dichloro-3-(4-nitrophenyl)-1,5-diphenyl-1,4-pentadiene (509). The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.46 g), ethynylbenzene (6.0 mmol, 0.61 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.79 g (64%) of a mixture of *E,Z*- and *Z,Z*- 1,5-dichloro-3-(4-nitrophenyl)-1,5-diphenyl-1,4-pentadiene. *E,Z*-isomer (42%): ^{1}H NMR ($CDCl_3$/TMS) δ ppm 8.18-7.47 (m, 14H), 6.24 (d, 1H, J = 9.2 Hz), 6.16 (d, 1H, J = 10.1 Hz), 4.94 (t, 1H, J = 9.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 148.6, 136.7, 136.2, 135.0, 134.4, 128.4, 128.1, 127.5,, 123.9, 45.4. *Z,Z*-isomer (58%): ^{1}H NMR ($CDCl_3$/TMS) δ ppm 8.20-7.26 (m, 14H), 6.33 (d, 2H, J = 8.6 Hz), 5.53 (t, 1H, J = 9.0 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 148.8, 148.6, 137.2, 135.7, 129.2, 128.4, 128.3, 126.6, 125.7, 124.0, 45.9. Anal. Calcd for $C_{23}H_{17}Cl_2NO_2$: C, 67.33; H, 4.18; N, 3.41. Found: C, 67.20; H, 4.22; N, 3.70.

1,5-Dichloro-3-phenyl-1,5-di(*p*-tolyl)-1,4-pentadiene (510). The reaction of benzaldehyde (3.0 mmol, 0.32 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.79 g (67%) of 1,5-dichloro-3-phenyl-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.48-7.12 (m, 13H), 6.22 (d, 1H, J = 9.2 Hz), 6.14 (d, 1H, J =

10.6 Hz), 4.87 (t, 1H, J = 10.0 Hz), 2.36(s, 3H), 2.34(s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 141.7, 138.8, 134.9, 133.7, 133.1, 129.0, 128.8, 128.7, 127.3, 126.8, 126.5, 45.6, 21.3, 21.1. Anal. Calcd for $C_{25}H_{22}Cl_2$: C, 76.34; H, 5.64. Found: C, 76.16; H, 5.71.

1,5-Dichloro-3-(4-fluorophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene (511). The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.78 g (63%) of 1,5-dichloro-3-(4-fluorophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.46 (d, 2H, J = 8.1 Hz), 7.31 (d, 2H, J = 8.1 Hz), 7.22-6.95 (m, 8H), 6.19 (d, 1H, J = 9.0 Hz), 6.10 (d, 1H, J = 10.5 Hz), 4.84 (t, 1H, J = 9.8 Hz), 2.35 (s, 3H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 163.7, 159.8, 139.0, 137.4, 134.7, 133.9, 133.7, 133.3, 129.0, 128.8, 128.6, 126.5, 126.4, 115.7, 44.9, 21.3, 21.1. Anal. Calcd for $C_{25}H_{21}Cl_2F$: C, 73.00; H, 5.15. Found: C, 72.83; H, 5.19.

1,5-Dichloro-1,3,5-tri(*p*-tolyl)-1,4-pentadiene (512). The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.76 g (62%) of 1,5-dichloro-1,3,5-tri(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.45(d, 2H, J = 8.2 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.18-7.11 (m, 8H), 6.21 (d, 1H, J = 9.1 Hz), 6.13 (d, 1H, J = 10.5 Hz), 4.84 (t, 1H, J = 9.9 Hz), 2.35-2.31(overlap, 9H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.8, 138.7, 136.4, 134.9, 133.9, 133.5, 132.8, 129.5, 128.9, 128.7, 127.1, 127.0, 126.4, 45.2, 21.3, 21.0. Anal. Calcd for $C_{26}H_{24}Cl_2$: C, 76.66; H, 5.94. Found: C, 76.62; H, 6.08.

1,5-Dichloro-3-(*o*-tolyl)-1,5-di(*p*-tolyl)-1,4-pentadiene (513). The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.71 g (58%) of 1,5-dichloro-3-(*o*-tolyl)-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.44-7.11 (m, 12H), 6.27 (d, 1H, *J*= 8.8 Hz), 6.16 (d, 1H, *J* = 10.3 Hz), 4.90 (t, 1H, *J* = 9.7 Hz), 2.35-2.33(overlap, 6H), 2.06 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.9, 138.8, 136.7, 134.5, 133.7, 133.5, 132.8, 132.4, 129.5, 128.9, 128.9, 127.4, 127.1, 125.9, 43.0, 21.3, 21.1, 19.3. Anal. Calcd for $C_{26}H_{24}Cl_2$: C, 76.66; H, 5.94. Found: C, 76.50; H, 5.84.

3-(4-Bromophenyl)-1,5-dichloro-1,5-di(*p*-tolyl)-1,4-pentadiene (514). The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.85 g (60%) of 3-(4-bromophenyl)-1,5-Dichloro-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.66-7.09 (m, 12H), 6.17 (d, 1H, *J* = 9.1 Hz), 6.09 (d, 1H, *J*= 10.5 Hz), 4.81 (t, 1H, *J* = 9.8 Hz), 2.36 (s, 3H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 140.7, 139.0, 134.6, 134.2, 133.7, 133.6, 131.8, 129.0, 128.6, 128.1, 126.4, 126.1, 120.7, 45.1, 21.3, 21.1. Anal. Calcd for $C_{25}H_{21}BrCl_2$: C, 63.58; H, 4.48. Found: C, 63.20; H, 4.48.

3-(3-Bromophenyl)-1,5-dichloro-1,5-di(*p*-tolyl)-1,4-pentadiene (515). The reaction of 3-bromobenzaldehyde (3.0 mmol, 0.56 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.86 g (61%) of 3-(3-bromophenyl)-1,5-dichloro-1,5-

di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.46-7.11 (m, 12H), 6.17 (d, 1H, J = 9.2 Hz), 6.09 (d, 1H, J = 10.4 Hz), 4.84 (t, 1H, J = 9.8 Hz), 2.34 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 143.9, 138.9, 134.4, 134.2, 133.6, 130.1, 129.8, 128.9, 128.4, 127.8, 126.3, 125.8, 122.7, 45.1, 21.2, 21.0. Anal. Calcd for $C_{25}H_{21}BrCl_2$: C, 63.58; H, 4.48. Found: C, 63.65; H, 4.58.

1,5-Dichloro-3-(4-cyanophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene (516). The reaction of 4-cyanobenzaldehyde (3.0 mmol, 0.39 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.81 g (65%) of 1,5-dichloro-3-(4-cyanophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.56-7.13 (m, 12H), 6.16 (d, 1H, J = 9.8 Hz), 6.09 (d, 1H, J = 10.2 Hz), 4.91 (t, 1H, J = 9.8 Hz), 2.34 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 149.0, 139.2, 134.7, 134.3, 134.2, 133.3, 132.5, 129.0, 128.4, 128.0, 127.2, 126.4, 125.1, 118.8, 110.6, 45.5, 21.2, 21.0. Anal. Calcd for $C_{26}H_{21}Cl_2N$: C, 74.64; H, 5.06; N, 3.35. Found: C, 74.55; H, 5.12; N, 3.30.

1,5-Dichloro-1,5-di(4-fluorophenyl)-3-phenyl-1,4-pentadiene (517). The reaction of benzaldehyde (3.0 mmol, 0.32 g), 1-ethynyl-4-fluorobenzene (6.0 mmol, 0.72 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.79 g (66%) of 1,5-dichloro-1,5-di(4-fluorophenyl)-3-phenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.56-7.02 (m, 14H), 6.19 (d, 1H, J = 10.1 Hz), 4.80 (t, 1H, J = 9.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 165.0, 164.8, 161.0, 160.8, 141.3, 133.7, 132.7, 132.0, 130.8, 130.7, 129.2, 128.9, 128.8, 128.5, 128.3, 127.5, 127.2,

127.1, 124.9, 115.9, 115.6, 115.5, 115.2, 111.1, 45.9. Anal. Calcd for $C_{23}H_{16}Cl_2F_2$: C, 68.84; H, 4.02. Found: C, 68.79; H, 4.09.

1,5-Dichloro-3-(4-chlorophenyl)-1,5-di(4-fluorophenyl)-1,4-pentadiene (518). The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), 1-ethynyl-4-fluorobenzene (6.0 mmol, 0.72 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.89 g (68%) of 1,5-dichloro-3-(4-chlorophenyl)-1,5-di(4-fluorophenyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.55-6.99 (m, 12H), 6.14 (d, 2H, J = 9.8 Hz), 4.77 (t, 1H, J = 9.7 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 165.1, 164.9, 161.1, 160.9, 139.7, 133.5, 133.1, 132.9, 132.6, 130.7, 130.6, 129.0, 128.6, 128.5, 128.3, 126.9, 115.7, 115.5, 115.3, 115.2, 45.1. Anal. Calcd for $C_{23}H_{15}Cl_3F_2$: C, 63.40; H, 3.47. Found: C, 63.59; H, 3.49.

1,5-Dichloro-1,3,5-tri(4-fluorophenyl)-1,4-pentadiene (519). The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 1-ethynyl-4-fluorobenzene (6.0 mmol, 0.72 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.96 g (76%) of 1,5-dichloro-1,3,5-tri(4-fluorophenyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.55-7.00 (m, 12H), 6.15 (m, 2H), 4.78 (t, 1H, J = 9.7 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 165.0, 164.9, 163.8, 161.1, 160.9, 159.9, 138.9, 133.5, 132.9, 132.7, 132.3, 130.7, 130.6, 128.9, 128.7, 128.5, 128.3,127.2, 115.9, 115.6, 115.5, 115.3, 115.2, 44.9. Anal. Calcd for $C_{23}H_{15}Cl_2F_3$: C, 65.89; H, 3.61. Found: C, 66.13; H, 3.74.

1,5-Dichloro-1,5-di(4-fluorophenyl)-3-(*p*-tolyl)-1,4-pentadiene (520). The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), 1-ethynyl-4-fluorobenzene (6.0

mmol, 0.72 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.77 g (62%) of 1,5-dichloro-1,5-di(4-fluorophenyl)-3-(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.55-6.99 (m, 12H), 6.17 (d, 2H, *J* = 9.9 Hz), 4.76 (t, 1H, *J* = 9.9 Hz), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 165.0,164.8, 161.0, 160.8, 138.2, 136.8, 133.8, 132.8, 132.4, 131.8, 130.8, 130.7, 129.6, 129.3, 128.5, 128.3, 127.7, 127.0, 115.5, 115.4, 115.2, 115.1, 45.3, 21.0. Anal. Calcd for $C_{24}H_{18}Cl_2F_2$: C, 69.41; H, 4.37. Found: C, 69.75; H, 4.45.

1,5-Dichloro-1,5-di(4-fluorophenyl)-3-(*o*-tolyl)-1,4-pentadiene (521). The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), 1-ethynyl-4-fluorobenzene (6.0 mmol, 0.72 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.84 g (68%) of 1,5-dichloro-1,5-di(4-fluorophenyl)-3-(*o*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.53-6.97 (m, 12H), 6.21 (d, 2H, *J* = 9.6 Hz), 4.83 (t, 1H, *J* = 9.6 Hz), 2.06 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 164.9, 164.8, 161.0, 160.8, 140.4, 138.9, 133.6, 132.9, 132.4, 131.4, 130.9, 130.7, 130.6, 129.5, 128.4, 128.3, 127.8, 126.9, 126.7, 115.5, 115.4, 115.0, 43.0, 19.3. Anal. Calcd for $C_{24}H_{18}Cl_2F_2$: C, 69.41; H, 4.37. Found: C, 69.64; H, 4.49.

1,5-Dichloro-3-(3-bromophenyl)-1,5-di(4-fluorophenyl)-1,4-pentadiene (522). The reaction of 3-bromobenzaldehyde (3.0 mmol, 0.56 g), 1-ethynyl-4-fluorobenzene (6.0 mmol, 0.72 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 0.94 g (65%) of 1,5-dichloro-3-(3-bromophenyl)-1,5-di(4-fluorophenyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.56-7.00 (m, 12H), 6.14 (d, 2H, *J* = 9.6 Hz), 4.77 (t, 1H, *J* = 9.8 Hz). ^{13}C NMR

($CDCl_3$/TMS) δ ppm 165.0,164.8, 161.1, 160.9, 143.5, 133.3, 132.7, 132.5, 130.7, 130.6, 130.4, 130.2, 128.5, 128.3, 126.5, 123.0, 115.7, 115.5, 115.3, 115.2, 45.3. Anal. Calcd for $C_{23}H_{15}BrCl_2F_2$: C, 57.53; H, 3.15. Found: C, 57.45; H, 3.28.

1,3,5-Tri(4-bromophenyl)-1,5-dichloro-1,4-pentadiene (523). The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 1-bromo-4-ethynylbenzene (6.0 mmol, 1.09 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in hexane) was carried out as described in **5.4.2.1** and produced 1.16 g (64%) of 1,3,5-tri(4-bromophenyl)-1,5-dichloro-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.52-7.07 (m, 12H), 6.18-6.14 (d, overlap, 2H, J = 9.5, J = 10.8 Hz), 4.74 (t, 1H, J = 10.0 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.9, 136.1, 135.3, 133.2, 132.5, 132.0, 131.6, 131.5, 130.2, 128.8, 128.6, 128.0, 127.2, 123.4, 123.2, 121.1, 45.1. Anal. Calcd for $C_{23}H_{15}Br_3Cl_2$: C, 45.89; H, 2.51. Found: C, 45.94; H, 2.60.

1,5-Dibromo-3-(4-fluorophenyl)-1,5-diphenyl-1,4-pentadiene (524). The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), ethynylbenzene (6.0 mmol, 0.61 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.29 g (91%) of (*Z,Z*)-1,5-dibromo-3-(4-fluorophenyl)-1,5-diphenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.58-7.00 (m, 14H), 6.40 (d, 2H, J = 8.9 Hz), 5.31 (t, 1H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 163.8, 159.8, 139.4, 136.5, 130.7, 129.0, 128.9, 128.3, 127.7, 127.3, 115.8, 115.5, 50.7. Anal. Calcd for $C_{23}H_{17}Br_2F$: C, 58.50; H, 3.63. Found: C, 58.41; H, 3.72.

1,5-Dibromo-3-(2-fluorophenyl)-1,5-diphenyl-1,4-pentadiene (525). The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.37 g), ethynylbenzene (6.0 mmol, 0.61 g)

and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.25 g (88%) of (*Z,Z*)-1,5-dibromo-3-(2-fluorophenyl)-1,5-diphenyl-1,4-pentadiene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.56-7.10 (m, 14H), 6.60 (d, 2H, *J*= 8.7 Hz), 5.33 (t, 1H, *J* = 8.7 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 162.8, 158.9, 139.5, 130.4, 130.3, 130.1, 128.8, 128.7, 128.3, 128.0, 127.7, 127.1, 124.4, 116.2, 115.9, 48.4. Anal. Calcd for $C_{23}H_{17}Br_2F$: C, 58.50; H, 3.63. Found: C, 58.61; H, 3.57.

1,5-Dibromo-3-(4-chlorophenyl)-1,5-diphenyl-1,4-pentadiene (526). The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), ethynylbenzene (6.0 mmol, 0.61 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.35 g (93%) of (*Z,Z*)-1,5-dibromo-3-(4-chlorophenyl)-1,5-diphenyl-1,4-pentadiene. *Z,Z*-isomer (Major): ^1H NMR ($CDCl_3$/TMS) δ ppm 7.55-7.23 (m, 14H), 6.37 (d, 2H, J = 8.8 Hz), 5.30 (t, 1H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.4, 132.9, 130.5, 129.0, 128.9, 128.4, 127.7, 50.9. *E,Z*-isomer (2% isolated): ^1H NMR ($CDCl_3$/TMS) δ ppm 7.53-7.16 (m, 14H), 6.39 (d, 1H, *J* = 10.3 Hz), 6.30 (d, 1H, *J* = 9.0 Hz), 4.73 (t, 1H, *J* = 9.6 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.5, 139.2, 138.1, 132.8, 132.3, 130.4, 129.0, 128.6, 128.3, 127.9, 126.8, 123.5, 48.8. Anal. Calcd for $C_{23}H_{17}Br_2Cl$: C, 56.53; H, 3.51. Found: C, 56.04; H, 3.50.

1,5-Dibromo-3-(4-bromophenyl)-1,5-diphenyl-1,4-pentadiene (527). The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), ethynylbenzene (6.0 mmol, 0.61 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.47 g (92%) of (*Z,Z*)-1,5-dibromo-3-(4-bromophenyl)-1,5-diphenyl-1,4-pentadiene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.56-7.21 (m, 14H), 6.37 (d, 2H,

J = 8.8 Hz), 5.28 (t, 1H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.8, 139.3, 131.9, 130.3, 129.2, 128.9, 128.3, 127.7, 120.8, 50.8. Anal. Calcd for $C_{23}H_{17}Br_2Cl$: C, 51.82; H, 3.21. Found: C, 51.99; H, 3.26.

1,5-Dibromo-1,5-diphenyl-3-(*p*-tolyl)-1,4-pentadiene (528). The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), ethynylbenzene (6.0 mmol, 0.61 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.12 g (80%) of (*Z,Z*)-1,5-dibromo-1,5-diphenyl-3-(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.58-7.14 (m, 14H), 6.43 (d, 2H, J = 8.9 Hz), 5.30 (t, 1H, J = 8.9 Hz), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.6, 137.8, 136.5, 131.2, 129.5, 128.7, 128.2, 127.7, 127.3, 126.8, 51.0, 21.0. Anal. Calcd for $C_{24}H_{20}Br_2$: C, 61.56; H, 4.31. Found: C, 61.83; H, 4.35.

1,5-Dibromo-1,5-diphenyl-3-(*o*-tolyl)-1,4-pentadiene (529). The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), ethynylbenzene (6.0 mmol, 0.61 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.17 g (83%) of (*Z,Z*)-1,5-dibromo-1,5-diphenyl-3-(*o*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.54-7.14 (m, 14H), 6.44 (d, 2H, J = 8.7 Hz), 5.34 (t, 1H, J = 8.7 Hz), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 140.2, 139.4, 136.5, 131.5, 130.8, 128.7, 128.2, 127.7, 127.0, 126.8, 126.5, 126.4, 48.8, 20.1. Anal. Calcd for $C_{24}H_{20}Br_2$: C, 61.56; H, 4.31. Found: C, 61.27; H, 4.42.

1,5-Dibromo-3-(4-nitrophenyl)-1,5-diphenyl-1,4-pentadiene (530). The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.46 g), ethynylbenzene (6.0 mmol, 0.61 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in

5.4.2.2 and produced 1.20 g (80%) of (*Z,Z*)-1,5-dibromo-3-(4-nitrophenyl)-1,5-diphenyl-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 8.18-7.31 (m, 14H), 6.44 (d, 2H, J = 8.8 Hz), 5.42 (t, 1H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 148.2, 146.8, 138.9, 129.3, 129.1, 128.6, 128.4, 127.7, 124.0, 51.3. Anal. Calcd for $C_{23}H_{17}Br_2NO_2$: C, 55.34; H, 3.43; N, 2.81. Found: C, 55.60; H, 3.53; N, 2.87.

1,5-Dibromo-3-(4-fluorophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene (531). The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.20 g (80%) of (*Z,Z*)-1,5-dibromo-3-(4-fluorophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.46-6.96 (m, 12H), 6.35 (d, 2H, J = 8.9 Hz), 5.30 (t, 1H, J = 8.9 Hz), 2.31 (s, 6H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 163.6, 159.7, 138.8, 136.5, 129.8, 128.9, 128.8, 127.5, 127.3, 115.8, 115.3, 50.6, 21.1. Anal. Calcd for $C_{25}H_{21}Br_2F$: C, 60.02; H, 4.23. Found: C, 60.33; H, 4.52.

1,5-Dibromo-3-(4-chlorophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene (532). The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.20 g (77%) of (*Z,Z*)-1,5-dibromo-3-(4-chlorophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.44 (d, 4H, J = 8.2 Hz), 7.29 (s, 4H), 7.11 (d, 4H, J = 8.2 Hz), 6.34 (d, 2H, J = 8.9 Hz), 5.28 (t, 1H, J = 8.9 Hz), 2.33 (s, 6H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.5, 138.9, 136.5, 132.6, 129.6, 128.9, 128.8, 127.6, 50.7, 21.1. Anal. Calcd for $C_{25}H_{21}Br_2Cl$: C, 58.11; H, 4.10. Found: C, 58.29; H, 4.33.

1,5-Dibromo-3-(4-bromophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene (533). The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 1-ethynyl-4-methylbenzene (6.0 mmol, 0.70 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.18 g (70%) of (*Z,Z*)-1,5-dibromo-3-(4-bromophenyl)-1,5-di(*p*-tolyl)-1,4-pentadiene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.46-7.06 (m, 12H), 6.33 (d, 2H, J = 8.9 Hz), 5.26 (t, 1H, J = 8.9 Hz), 2.32 (s, 6H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.9, 138.9, 136.5, 131.8, 129.5, 128.9, 127.5, 120.7, 50.8, 21.1. Anal. Calcd for $C_{25}H_{21}Br_3$: C, 53.51; H, 3.77. Found: C, 53.21; H, 3.99.

1,5-Dibromo-1,5-di(4-chlorophenyl)-3-(4-fluorophenyl)-1,4-pentadiene (534). The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 1-chloro-4-ethynylbenzene (6.0 mmol, 0.82 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.35 g (83%) of (*Z,Z*)-1,5-dibromo-1,5-di(4-chlorophenyl)-3-(4-fluorophenyl)-1,4-pentadiene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.51-7.00 (m, 12H), 6.39 (d, 2H, J = 8.9 Hz), 5.26 (t, 1H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 163.8, 159.9, 137.7, 136.1, 134.8, 131.0, 128.9, 128.8, 128.4, 126.1, 115.9, 115.6, 50.7. Anal. Calcd for $C_{23}H_{15}Br_2Cl_2F$: C, 51.05; H, 2.79. Found: C, 51.37; H, 2.65.

1,5-Dibromo-1,3,5-tri(4-chlorophenyl)-1,4-pentadiene (535). The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), 1-chloro-4-ethynylbenzene (6.0 mmol, 0.82 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.44 g (86%) of (*Z,Z*)-1,5-dibromo-1,3,5-tri(4-chlorophenyl)-1,4-pentadiene. ^1H NMR ($CDCl_3$/TMS) δ ppm 7.51-7.26 (m, 12H), 6.38 (d, 2H, J = 8.9 Hz), 5.25 (t, 1H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 138.8, 137.6, 134.8, 132.9,

130.8, 129.0, 128.9, 128.7, 128.4, 126.3, 50.8. Anal. Calcd for $C_{23}H_{15}Br_2Cl_3$: C, 49.55; H, 2.71. Found: C, 49.82; H, 2.69.

1,5-Dibromo-3-(4-bromophenyl)-1,5-di(4-chlorophenyl)-1,4-pentadiene (536). The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 1-chloro-4-ethynylbenzene (6.0 mmol, 0.82 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.34 g (74%) of (*Z,Z*)-1,5-dibromo-3-(4-bromophenyl)-1,5-di(4-chlorophenyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.49-7.20 (m, 12H), 6.37 (d, 2H, J = 8.9 Hz), 5.23 (t, 1H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.4, 137.6, 134.8, 131.9, 130.5, 129.1, 128.9, 128.4, 126.4, 121.0, 50.9. Anal. Calcd for $C_{23}H_{15}Br_3Cl_2$: C, 45.89; H, 2.51. Found: C, 46.11; H, 2.66.

1,5-Dibromo-1,5-di(4-chlorophenyl)-3-(*p*-tolyl)-1,4-pentadiene (537). The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), 1-chloro-4-ethynylbenzene (6.0 mmol, 0.82 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.43 g (89%) of (*Z,Z*)-1,5-dibromo-1,5-di(4-chlorophenyl)-3-(*p*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.46-7.16 (m, 12H), 6.43 (d, 2H, J = 8.7 Hz), 5.31 (t, 1H, J = 8.7 Hz), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.7, 137.8, 136.4, 134.6, 131.8, 128.9, 128.3, 126.9, 126.5, 125.3, 48.8, 20.2. Anal. Calcd for $C_{24}H_{18}Br_2Cl_2$: C, 53.67; H, 3.38. Found: C, 53.92; H, 3.45.

1,5-Dibromo-1,5-di(4-chlorophenyl)-3-(*o*-tolyl)-1,4-pentadiene (538). The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), 1-chloro-4-ethynylbenzene (6.0 mmol, 0.82 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **5.4.2.2** and produced 1.37 g (85%) of (*Z,Z*)-1,5-dibromo-1,5-di(4-

chlorophenyl)-3-(*o*-tolyl)-1,4-pentadiene. ^{1}H NMR ($CDCl_3$/TMS) δ ppm 7.49-7.08 (m, 12H), 6.44 (d, 2H, J = 8.7 Hz), 5.50 (t, 1H, J = 8.7 Hz), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm 139.7, 137.8, 136.4, 134.6, 131.8, 130.9, 128.9, 128.3, 127.2, 126.9, 126.5, 125.3, 49.6, 21.2. Anal. Calcd for $C_{24}H_{18}Br_2Cl_2$: C, 53.67; H, 3.38. Found: C, 53.72; H, 3.39.

Chapter 6. Boron halide promoted addition reaction of aromatic aldehydes with alkenes

6.1 Introduction

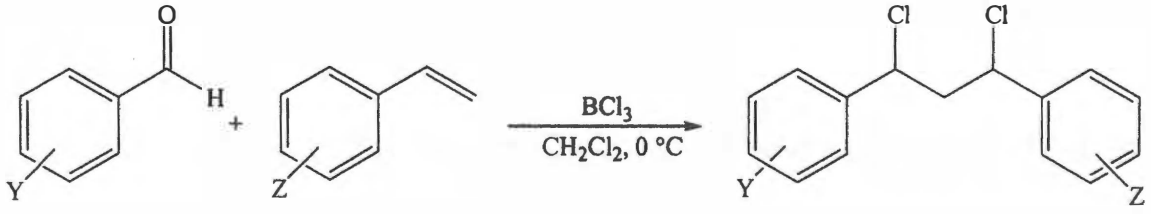
The addition reaction of aldehydes with alkenes is a very important method for the formation of new carbon-carbon bonds in synthetic organic chemistry.[160] This reaction has been widely used in natural product synthesis because the products have an array of functional groups which can be subjected to further transformations. The reactions of carbonyl compounds with alkenes are generally catalyzed by Lewis acids such as BF_3,[161, 162] $AlCl_3$,[163] $FeCl_3$,[164] $SnCl_4$,[163(b), 165] $TiCl_4$,[166] $BiCl_3$,[167] and alkylaluminum chlorides.[168] Boron trihalides have also been extensively used for C-O bond cleavage, halogenation of aldehydes, haloboration of alkynes[72(b)] and enolization of carbonyl compounds.[169] However, boron trichloride and triboromide promoted addition reactions of aldehydes with alkenes have not been explored. In fact, BCl_3 has been reported to be an ineffective promoter for ene reactions of aldehydes with alkenes since low yields of the desired products (homoallylic alcohols) are obtained.[163 (b)] In our continuing efforts to explore haloboration of alkenes via boron halide, we discovered that BCl_3 and BBr_3 are very effective in promoting the addition of aryl aldehydes to styrenes. The reactions produce diastereomeric mixtures of 1,3-dihalo-1,3-diarylpropanes,[170] which are very useful intermediates in organic synthesis,[171] they have been used to prepare arylcyclopropanes,[172] centrohexaindane[173] and pyrazolidine.[174] The reaction of aryl aldehydes with alkenes in the presence of phenylboron dichloride regio- and

stereoselectively generates *anti*-β-chloroalcohols.[175] These β-chloroalcohols are useful intermediates because they can be subjected to a number of transformations such as halogenation, substitution, cyclization and oxidation reactions to generate mixed 1,3-dihalogenated diarylpropanes, cyclic ethers and ketones.

6.2 Results and disscusion

6.2.1 Boron trichloride promoted addition of aryl aldehydes to styrenes

Initially, we examined the reaction of benzaldehyde with freshly distilled styrene. When a mixture of benzaldehyde and styrene (1:1 ratio in CH_2Cl_2) was treated with one equivalent of boron trichlorde at 0 °C, only polymerization was observed. We then utilized commercially available styrene, which contained 4-*tert*-butylcatechol as a stabilizer to prevent polymerization. The reaction produced racemic diastereomeric (*R,R/S,S* and *R,S/S,R*) mixtures of 1,3-dichloro-1,3-diphenylpropane in excellent yields (**Scheme 6-1**). When reactions were carried out at room temperature, chlorination of benzaldehyde occurred as noted in Chapter 2.[81]



Scheme 6-1 Boron trichloride promoted addition of aryl aldehydes to styrenes: formation of 1,3-dichloro-1,3-diphenylpropanes at 0 °C

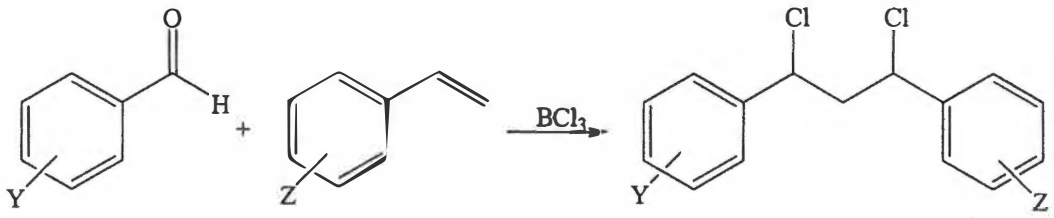
A series of aryl aldehydes was then subjected to the new reaction. Essentially, all aldehydes generated 1,3-dichloro-1,3-diarylpropanes in excellent yields. The results are summarized in **Table 6-1**. Aldehydes containing electron-withdrawing substituents such as Cl, F, CN and NO_2 reacted at a slower rate. NMR analyses of the products revealed an equal mixture of *syn* and *anti* isomers. In addition, it was observed that products with electron-donating substituents tended to decompose during chromatography on silica gel, resulting in relatively low isolated yields.

6.2.2 Boron tribromide promoted addition of aryl aldehydes to styrenes

Since 1,3-dibromopropanes are synthetically more valuable than the corresponding 1,3-dichloropropanes, we examined the reaction of aryl aldehydes with styrenes in the presence of boron tribromide. The bromination of aryl aldehydes by boron tribromide is extremely fast due to the rapid dibromo-de-oxo-bisubstitution of aryl aldehydes by BBr_3.[82] Consequently we carried out the reactions by slowly adding BBr_3 to mixtures of aryl aldehydes and styrene (1:1 ratio) at -40 °C. Similar to the addition reactions promoted by BCl_3, diastereomeric mixtures of 1,3-dibromo-1,3-diarylpropanes were formed rapidly and in good to excellent yields (**Scheme 6-2**).

A series of aryl aldehydes was then subjected to the new reaction. Essentially, all aldehydes generated 1,3-dibromo-1,3-diarylpropanes in good yields (**Table 6-2**). Aldehydes and styrenes containing electron-withdrawing substituents reacted at a slower rate. NMR analyses of the product 1,3-dibromo-1,3-diarylpropanes formed revealed (similar to the reaction of BCl_3) an equal mixture of the racemic *anti* and *syn* isomers. The *anti*-isomer (*R,R*) of 1,3-dibromo-1,3-di(4-fluorophenyl)propane (**637**) was

Table 6-1 Synthesis of 1,3-dichloro-1,3-diphenylpropanes



Entry	Y =	Z =	Time (hr)	*anti/syn*	Yields (%)[a,b]
1	H	H	10	53/47	90 (**601**)
2	4-F	H	18	55/45	98 (**602**)
3	2-F	H	18	52/48	97 (**603**)
4	4-Cl	H	12	50/50	97 (**604**)
5	2-Cl	H	12	49/51	95 (**605**)
6	4-Br	H	10	60/40	96 (**606**)
7	3-Br	H	10	58/42	96 (**607**)
8	2-Br	H	10	42/58	95 (**608**)
9	4-CH_3	H	5	40/60	70 (**609**)[c]
10	2-CH_3	H	5	55/45	68 (**610**)[c]
11	4-CN	H	24	60/40	80 (**611**)
12	4-NO_2	H	48	52/48	99 (**612**)
13	4-CHO	H	12	55/45	92 (**613**)
14	4-F	4-F	48	52/48	98 (**614**)
15	2-F	4-F	48	60/40	99 (**615**)
16	4-Cl	4-F	48	50/50	98 (**616**)

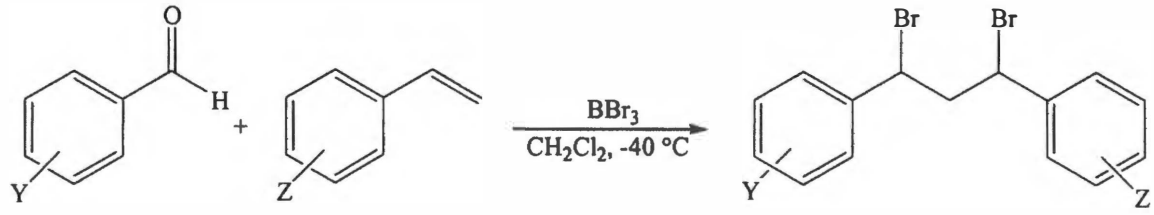
Table 6-1 (Continued)

Entry	Y =	Z =	Time (hr)	*Anti/syn*	Yields (%)[a,b]
17	2-Cl	4-F	48	48/52	93 (**617**)
18	4-Br	4-F	48	46/54	95 (**618**)
19	2-Br	4-F	48	41/59	90 (**619**)
20	4-CHO	4-F	48	60/40	90 (**620**)
21	4-CH_3	4-F	36	47/53	74 (**621**)
22	2-CH_3	4-F	36	42/58	70 (**622**)
23	4-NO_2	4-F	48	51/49	98 (**623**)
24	2-F	4-CH_3	10	56/44	85 (**624**)[c]
25	4-Cl	4-CH_3	6	52/48	83 (**625**)[c]
26	2-Cl	4-CH_3	6	50/50	83 (**626**)[c]
27	4-Br	4-CH_3	6	51/49	82 (**627**)[c]
28	2-Br	4-CH_3	6	45/55	80 (**628**)[c]
29	4-CH_3	4-CH_3	3	47/53	68 (**629**)[c]
30	2-CH_3	4-CH_3	3	46/54	70 (**630**)[c]
31	4-CN	4-CH_3	12	60/40	45 (**631**)[c]
32	4-NO_2	4-CH_3	14	54/46	64 (**632**)[c]
33	4-CHO	4-CH_3	4	48/52	79 (**633**)[c]

[a] Isolated yields based on starting aldehydes.

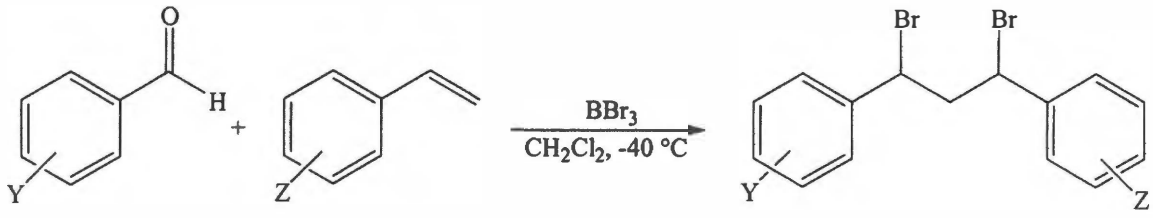
[b] All products were characterized by elemental analyses and NMR spectroscopy.

[c] Products partially decomposed during silica gel chromatography.



Scheme 6-2 Boron tribromide promoted addition of aryl aldehydes to styrenes: formation of 1,3-dibromo-1,3-diphenylpropanes at -40 °C

Table 6-2 Synthesis of 1,3-dibromo-1,3-diphenylpropanes via reaction of aryl aldehydes with styrenes at -40 °C



Entry	Y =	Z =	Time (hr)	*Anti/syn*	Yields (%)[a,b]
1	H	H	3	55/45	75 (**634**)[c]
2	4-F	H	6	52/48	98 (**635**)
3	4-CH_3	H	2	50/50	60 (**636**)[c]
4	4-F	4-F	10	51/49	96 (**637**)
5	2-F	4-F	10	50/50	95 (**638**)
6	4-Br	4-F	10	47/53	76 (**639**)
7	3-Br	4-F	10	49/51	90 (**640**)
8	4-F	4-CH_3	6	46/54	76 (**641**)[c]
9	4-Cl	4-CH_3	4	45/55	76 (**642**)[c]
10	4-Br	4-CH_3	4	49/51	74 (**643**)[c]
11	4-CH_3	4-CH_3	1	48/52	85 (**644**)[c]

[a] Isolated yields based on starting aldehydes.

[b] All products were characterized by elemental analyses and NMR spectroscopy.

[c] Products partially decomposed during silica gel chromatography.

isolated and characterized by X-ray crystallography (**Figure 6-1**) and NMR. In addition, the products with electron-donating substituents tended to decompose during chromatography on silica gel, resulting in relatively low isolated yields. 1,3-Dibromo-1,3-diarylpropanes were found to be especially susceptible to decomposition, and therefore the yields were lower than the corresponding 1,3-dichloro-1,3-diphenylpropanes.

6.2.3 Boron triiodide promoted addition of aryl aldehydes to styrenes

We then examined the addition of benzaldehydes to styrene in the presence of boron triiodide at –70 °C in a dry ice-acetone bath, and isolated the corresponding racemic 1,3-diiodo-1,3-diphenylpropane diastereomers (**Scheme 6-3**) in less than 40% yield due to the facile iodination of the carbonyl group and its subsequent decomposition on silica gel.[129] 1,3-Diiodo-1,3-diphenylpropane is not stable at room temperature; it decomposes and forms elemental iodine readily at room temperature. This result is consistent with the known instability of C-I bond.[176] The homolytic cleavage of the C-I bond produces benzylic radical and iodine atom.

Only benzaldehyde and 4-fluorobenzaldehyde were observeded to react with styrene in the presence of BI_3; a 38% yield of 1,3-diiodo-1,3-diphenylpropane and a 30% yield of 1,3-diiodo-1-(4-fluorophenyl)-3-phenylpropane were isolated as yellowish oils. Further efforts to obtain a higher yield of the desired 1,3-diiodo-1,3-diphenylpropanes failed.

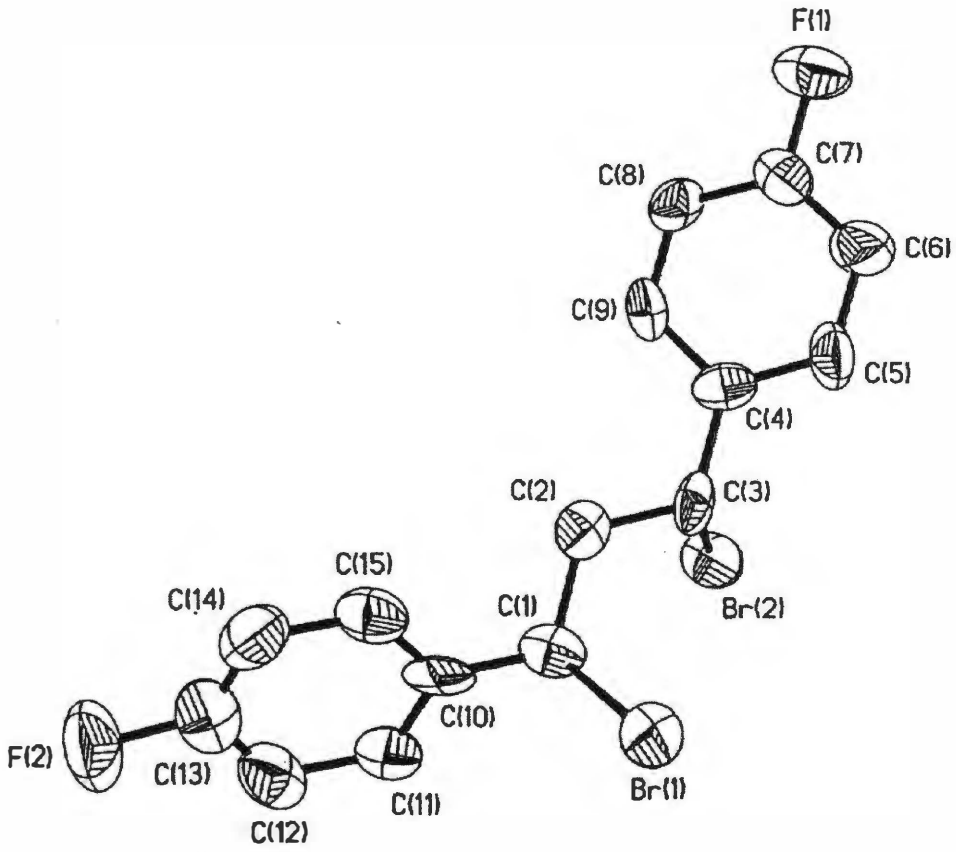
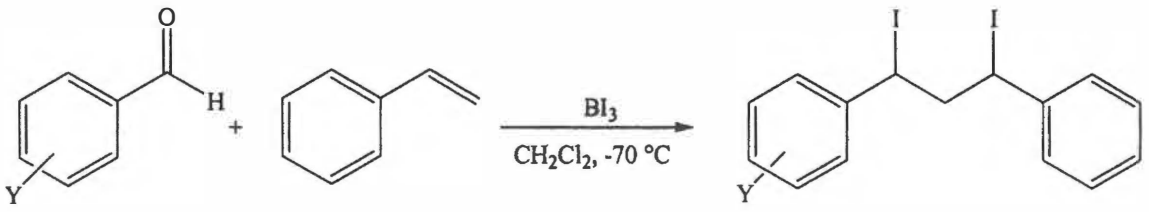


Figure 6-1 X-ray crystal structure of (*R,R*) *anti*-1,3-dibromo-1,3-di(4-fluorophenyl)-propane **(637)**

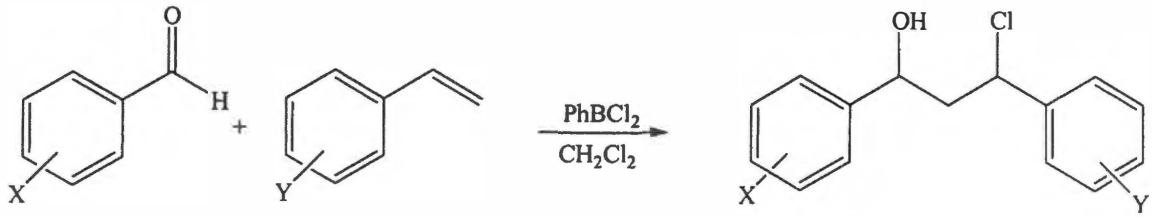


Scheme 6-3 Boron triiodide promoted addition of aryl aldehydes to styrenes: formation of 1,3-diiodo-1,3-diphenylpropanes at -70 °C

6.2.4 Addition of aryl aldehydes to styrenes in the presence of phenylboron dichloride

When aryl aldehydes were allowed to react with styrenes in the presence of boron trihalides (to produce 1,3-dihalo-1,3-diarylpropanes[170]), β-chloroalcohols were detected, but the yields were low. In a continuation of this study, we investigated the reaction of aryl aldehydes with alkenes in the presence of phenylboron dichloride and discovered that it produced β-chloroalcohols in good to excellent yields (**Scheme 6-4**).

Initially, styrene was allowed to react with one equivalent of phenylboron dichloride in CH_2Cl_2 at room temperature to form the haloboration intermediate.[80(c)] Then, one equivalent of 4-chlorobenzaldehdye was introduced at −10 °C. The reaction solution turned yellow. After 1 hr, the reaction was hydrolyzed and 3-chloro-1-(4-chlorophenyl)-3-phenylpropanol was isolated in good yield. Alternatively, the reaction could be carried out by introducing phenylboron dichloride to a mixture of styrene and 4-chlorobenzaldehye in CH_2Cl_2 at −10 °C. We noted that freshly distilled styrene produced



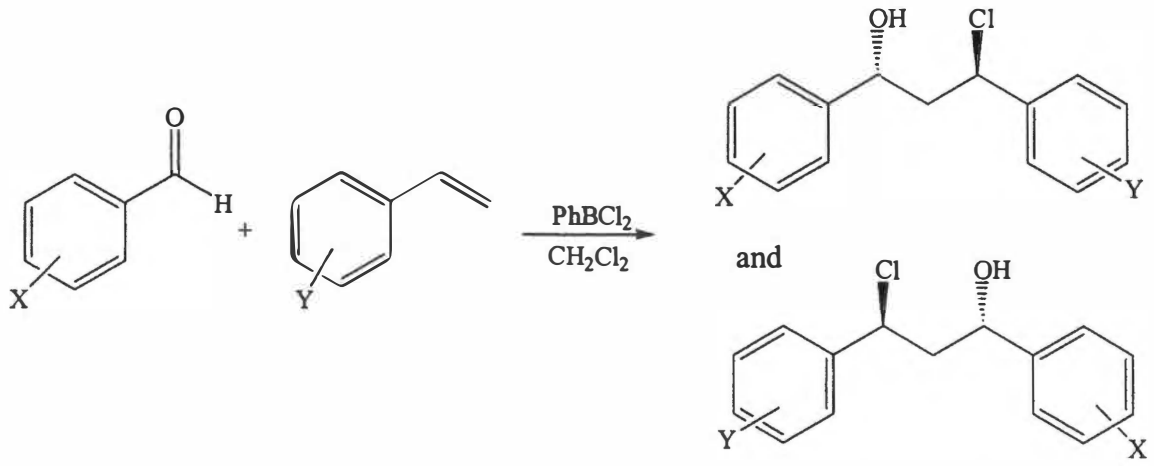
Scheme 6-4 Synthesis of 1,3-diaryl-3-chloropropanols

only polymerization products whereas commercially available styrene containing 4-*tert*-butylcatechol produced good yields of the desired product. NMR characterizations of the β-chloroalcohols revealed that the products were generated regio- and diastereoselectively, the predominant products are the *anti*-diastereoisomers (*R,R/S,S* enantiomer pair) and with the aryl groups only at the 1,3-positions (**Table 6-3**).

Heteroaromatic aldehydes such as 3-pyridinecarbaldehyde also reacted with styrene to generate 3-chloro-1-(3-pyridinyl)-3-phenylpropanols in excellent yields (**Table 6-4**). However, the reactions were slow compared to the reactions of aromatic aldehydes.

From the data in **Table 6-3** and **Table 6-4**, it can be seen that the reactions of aldehydes and styrenes containing electron-withdrawing groups required a higher eaction temperature, but gave higher yields of products. The reactions of aldehydes and styrenes containing electron-donating groups were faster but produced lower yields of the desired products due to the facile chlorination of the product alcohols to form 1,3-dichloro compounds.[170]

Table 6-3 Synthesis of *anti*-1,3-diaryl-3-chloropropanols

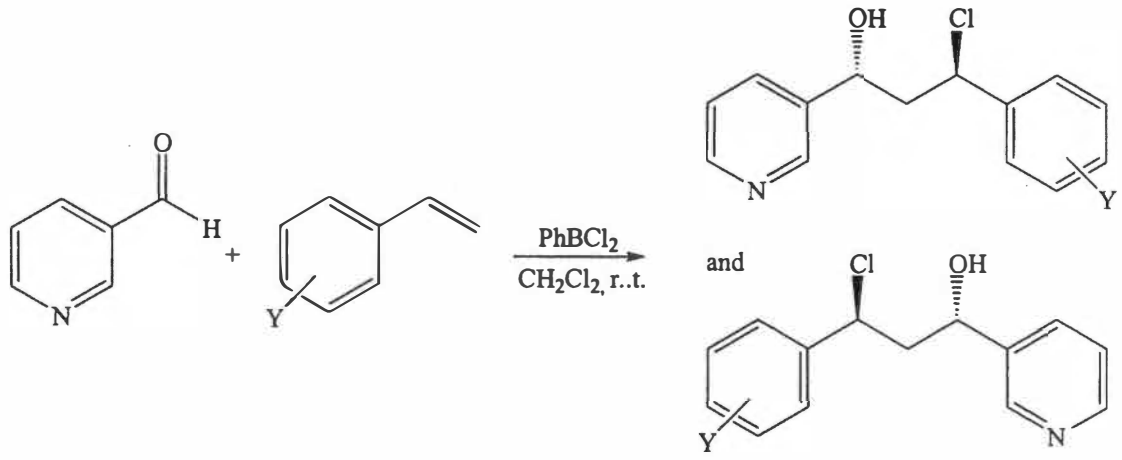


Entry	X =	Y =	T (°C)	Time (hr)	*anti* (%)	Yields (%)[a,b]
1	H	H	-10	1	83	76 (**645**)
2	4-F	H	0	2	93	87 (**646**)
3	2-F	H	0	2	80	79 (**647**)
4	4-Cl	H	-10	1	84	79 (**648**)
5	4-Br	H	-10	1	86	82 (**649**)
6	2-CH_3	H	-20	0.5	92	56 (**650**)
7	4-CH_3	H	-20	0.5	89	45 (**651**)
8	4-CN	H	25	6	84	96 (**652**)
9	4-NO_2	H	25	4	86	90 (**653**)
10	4-CHO	H	-10	1.5	86	86 (**654**)

[a] Isolated yields based on the starting aldehydes.

[b] All compounds were characterized by elemental analyses and NMR spectroscopy.

Table 6-4 Synthesis of *anti*-3-aryl-3-chloro-1-(3-pyridinyl)propanols



Entry	Y =	Time (hr)	*anti* (%)	Yields (%)[a,b]
1	H	20	88	90 (**655**)
2	4-F	30	92	84 (**656**)
3	4-Cl	24	91	85 (**657**)
4	2-Cl	24	95	91 (**658**)
5	4-CH_3	10	88	64 (**659**)

[a] Isolated yields based on the starting aldehydes.

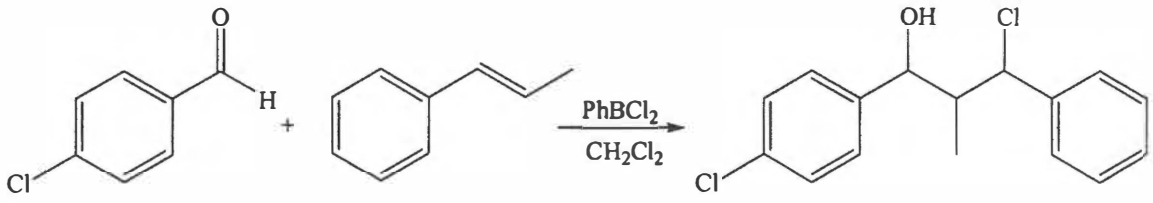
[b] All compounds were characterized by elemental analyses and NMR spectroscopy.

Aliphatic aldehydes and alkenes do not undergo the desired reaction. Aliphatic aldehydes simply enolize.[13, 14, 21] The reaction of aliphatic alkenes with aryl aldehydes produces mixtures of 1,3-dichloro compounds and ene–carbonyl adducts in low yield. Boron chlorides such as *n*-butylboron dichloride, *sec*-butylboron dichloride, *n*-hexylboron dichloride, cyclohexylboron dichloride and cyclopentylboron dichloride were found to be ineffective catalysts. Hexane, toluene, chloroform and methylene chloride were examined as reaction solvents, with CH_2Cl_2 being the most effective. Diethyl ether, THF and dioxane simply undergo cleavage.[108]

6.2.5 Addition of aryl aldehydes to (E)-β-methylstyrenes in the presence of phenylboron dichloride

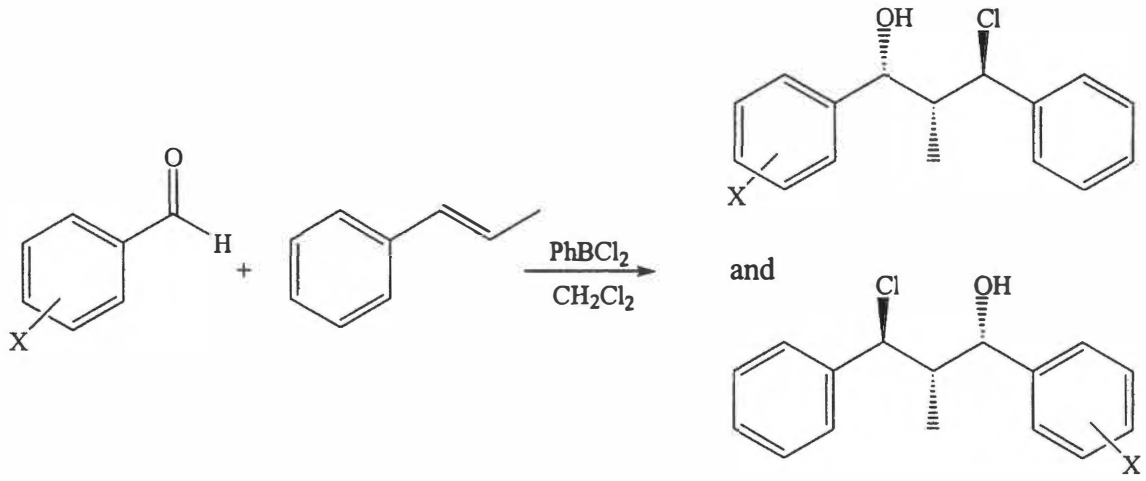
We then investigated the reaction of aryl aldehydes with (*E*)-β-methylstyrene in the presence of phenylboron dichloride; the reaction was initially carried out by introducing phenylboron dichloride to a mixture of (*E*)-β-methylstyrene and 4-chlorobenzaldehye in CH_2Cl_2 at –10 °C. We discovered that 3-chloro-1-(4-chlorophenyl)-2-methyl-3-phenylpropanol was formed as expected (**Scheme 6-5**).

A series of aryl aldehydes was allowed to react with (*E*)-β-methylstyrene in the presence of phenylboron dichloride. They all produced 1,3-diaryl-3-chloro-2-methylpropanols in good to excellent yields (**Table 6-5**). Interestingly, NMR data revealed that the reactions generated only a single regioisomer with the aryl groups at the 1,3- positions, similar to reactions using styrenes. In addition, the reaction predominantly produced the racemic *anti*-diastereoisomers, the *R*,*R*,*R* and *S*,*S*,*S*-isomers (enantiomer



Scheme 6-5 Synthesis of 3-chloro-1-(4-chlorophenyl)-2-methyl-3-phenylpropanol

Table 6-5 Synthesis of 1,3-diaryl-3-chloro-2-methyl-1-propanols



Entry	X =	T (°C)	Time (hr)	*anti* (%)[a]	Yields (%)[b,c]
1	4-F	0	2	94	94 (**660**)
2	2-F	0	2	92	95 (**661**)
3	4-Cl	-10	1.5	89	65 (**662**)
4	4-Br	-10	1	86	60 (**663**)
5	4-CH_3	-20	0.5	90	36 (**664**)
6	4-CN	25	48	98	97 (**665**)
7	4-NO_2	25	24	95	95 (**666**)

[a] *anti*-3-chloro-1-propanol isomer (in all cases, hydroxyl and methyl are *syn*).

[b] Isolated yields based on the starting aldehydes.

[c] All compounds were characterized by elemental analyses and NMR spectroscopy.

pair). The *anti*-isomers exhibit two sets of resonances (doublets of doublets) for the diastereotopic benzylic protons between 5.80–5.00 δ ppm. The corresponding resonances for the *syn*- isomers appear upfield at of 4.80–4.50 δ ppm. The X-ray structure analysis of 4-(3-chloro-1-hydroxy-2-methyl-3-phenylpropyl)benzenenitrile (**665**) confirmed the NMR assignment (**Figure 6-2**).

Aliphatic aldehydes and alkenes do not undergo the desired reaction. Boron chlorides such as *n*-butylboron dichloride, *sec*-butylboron dichloride, *n*-hexylboron dichloride, cyclohexylboron dichloride and cyclopentylboron dichloride were ineffective catalysts. Hexane, toluene, chloroform and CH_2Cl_2 were examined as reaction solvents, and CH_2Cl_2 was found to be the most effective.

The data in **Table 6-5** reveal that reactions of aldehydes containing electron-withdrawing groups require a higher reaction temperature, but give higher yields of products. The reactions of aldehydes containing electron-donating groups are faster but produce lower yields of the desired products due to the facile chlorination of the product alcohols to form 1,3-dichloro compounds.

6.2.6 Mechanistic postulation

6.2.6.1 Possible reaction pathway of boron-trihalide promoted additions of aryl aldehydes to styrenes

A detailed mechanistic study was not carried out. The reaction of aryl aldehydes with styrenes presumably proceeds through coordination of the carbonyl group to the boron trihalide followed by addition of the carbonyl carbon to the alkene to form carbocation **7**. Then a halide anion would add to the cation to form alkoxyboron

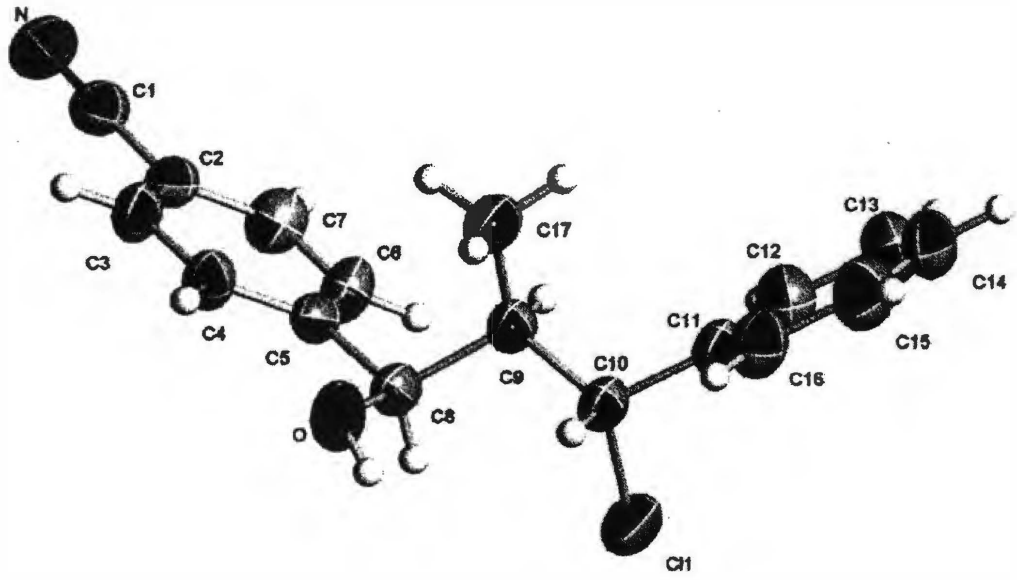


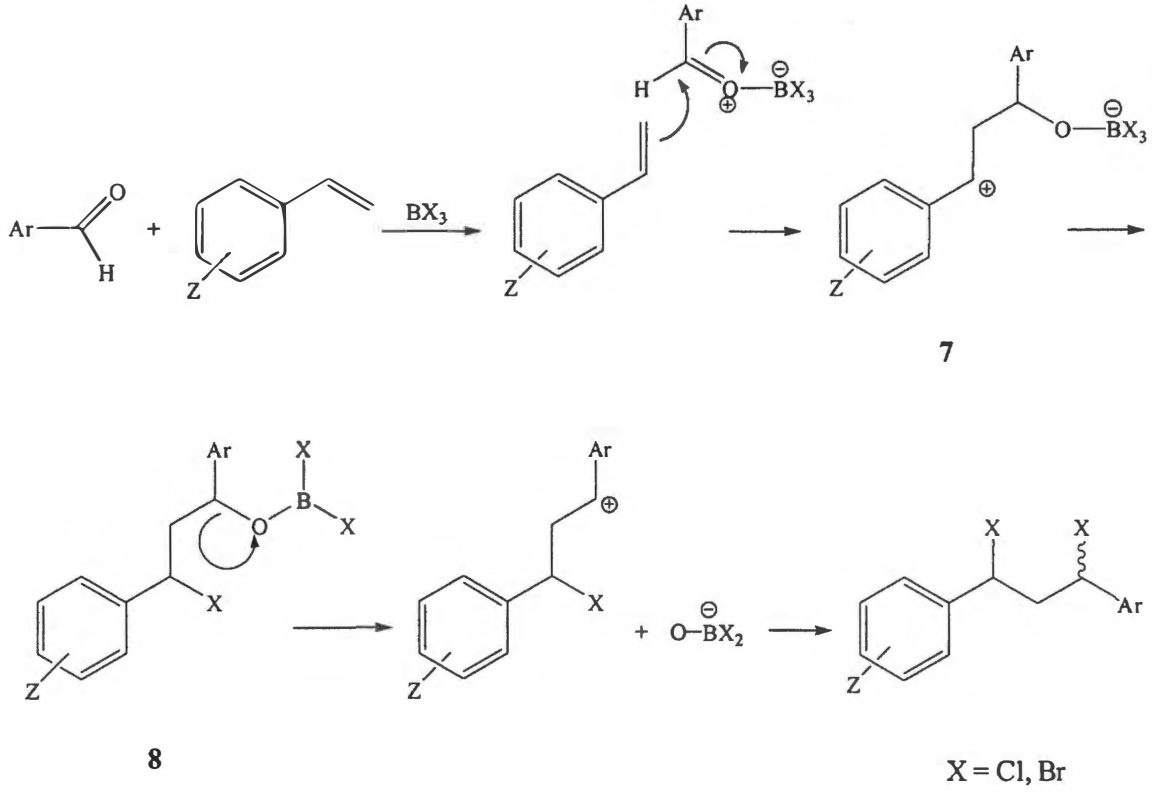
Figure 6-2 X-ray crystal structure of (*R,R,R*) *anti*-4-(3-chloro-1-hydroxy-2-methyl-3-phenylpropyl)benzenenitrile (**665**)

dihalide **8**. Loss of an oxyboron moiety from **8** would then generate another cation as a precursor to either 1,3-dichloro-1,3-diphenylpropanes or 1,3-dibromo-1,3-diphenylpropanes (**Scheme 6-6**). A similar intermediate has been observed in the $AlCl_3$-catalyzed ene reactions of aldehydes with aliphatic alkenes.[162(c), 163(a)]

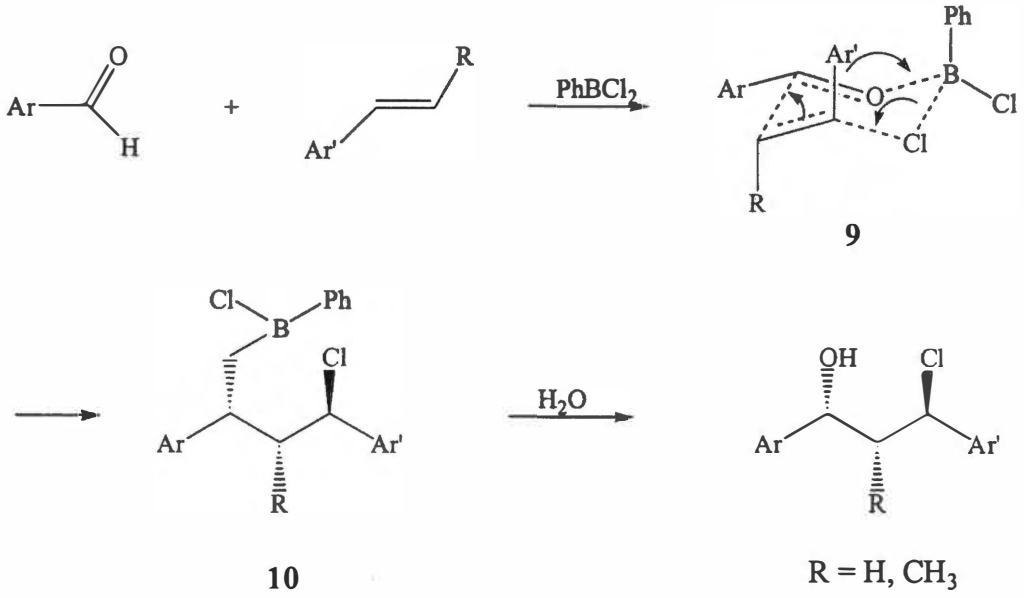
6.2.6.2 Possible reaction pathway of phenylboron dichloride mediated addition of aryl aldehydes to styrene and (*E*)-β-methylstyrene

In order to gain insight regarding the mechanism, the reaction of styrene and 4-chlorobenzaldehyde was monitored by NMR spectroscopy. Styrene and phenylboron dichloride were placed in a NMR tube containing $CDCl_3$. The NMR data indicated that no haloboration had occurred. 4-Chlorobenzaldehyde was then added to the reaction mixture; the NMR spectra revealed the rapid formation of a β-chloroalkoxyborane intermediate. Immediate hydrolysis of the mixture generated β-chloroalcohol. In a separate experiment, a boron complex was prepared by mixing 4-chlorobenzaldehyde with one equivalent of phenylboron dichloride in $CDCl_3$. Styrene was then added to the complex, and the reaction generated β-chloroalcohol after hydrolysis.

Based on these observations, the reaction presumably occurs via an electrophilic addition of the complexed aldehyde to styrene or (*E*)-β-methylstyrene in a concerted fashion to generate β-chloroalkoxyborane intermediate **10** from a six-membered chair transition state **9** (**Scheme 6-7**). The favored chair configuration **9** shown in **Scheme 6-7** is the key transition state to visualize and explain the formation of the *anti*-diastereoisomer as the major product.



Scheme 6-6 Proposed mechanism for the formation of 1,3-dihalo-1,3-diphenylpropanes via a cationic pathway



Scheme 6-7 Concerted mechanism for the synthesis of *anti*-β-chloroalcohols

6.3 Conclusion

In summary, boron trihalide promoted additions of styrenes to aryl aldehydes provide a new, highly efficient method for preparing diastereomeric mixtures of 1,3 dihalo-1,3-diarylpropanes, potentially useful building blocks in organic synthesis due to their bifunctionality. The advantage of using boron reagents in synthesis is fully realized in this new reaction: mild reaction conditions and a tolerance of functionalities such as cyano and nitro groups.

We have discovered a new reaction of styrenes and (*E*)-β-methylstyrene with aryl aldehydes promoted by phenylboron dichloride. The reaction stereo- and regioselectively generates a series of useful *anti*-1,3-diaryl-3-chloropropanols and *anti*-3-chloro-1,3-

diaryl-2-methylpropanols in excellent yields. The reaction is applicable to aromatic aldehydes with a various functional substituents such as cyano, nitro and even carbonyl groups. It is also applicable to heteroaromatic aldehydes like 3-pyridinecarbaldehyde.

6.4 Experimental

6.4.1 General considerations

All glassware, syringes and needles were dried in an oven heated to 150 °C for at least 12 hours and cooled under argon prior to use. All solvents were dried and distilled prior to use. All aryl aldehydes and styrenes were obtained from Aldrich Chemical Company and used as received. Boron trichloride (1 *M* solution in hexane), boron trfluoride etherate and phenylboron dichloride were purchased from Aldrich Chemical Company and used as received. Boron tribromide and triiodide (Aldrich Chemical Company) were diluted to 1 *M* CH_2Cl_2 solution. All reactions were conducted under an argon atomosphere, magnetically stirred and monitored by TLC analysis. Products were isolated by flash column chromatography.

All ^1H spectra were recorded in $CDCl_3$/TMS at 250 MHz, ^{13}C NMR spectra were recorded in $CDCl_3$/TMS at 62.9 MHz using a Brucker AC250 NMR spectrometer. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia. All melting points are uncorrected.

6.4.2 General experimental procedures

6.4.2.1 Representative procedure for the synthesis of 1,3-diaryl-1,3-dihalopropanes

Benzaldehyde (4.0 mmol, 0.41 g) and styrene (4.0 mmol, 0.42 g) were dissolved in methylene chloride (20 mL) at room temperature in a dry flask maintained under an argon atmosphere. The solution was cooled to 0 °C in an ice bath, and boron trichloride (4.3 mmol, 4.3 mL of a 1.0 *M* hexane solution) was then added via syringe. The reaction was stirred at 0 °C for 2 hrs and then at room temperature for 8 hrs, during which time the solution turned purple. The reaction mixture was then hydrolyzed, the organic layer separated, dried over anhydrous magnesium sulfate, and the product isolated by column chromatography (hexane, silica gel) to yield 0.95 g (90%) of 1,3-dichloro-1,3-diphenylpropane.

Compounds **611, 612, 613, 620, 623, 631, 632** and **633** were isolated by column chromatography using a mixture of hexane/ethyl acetate (95/5) as eluent.

6.4.2.2 Representative procedure for the synthesis of 1,3-diaryl-3-chloro-1-propanols

Benzaldehyde (4.0 mmol, 0.42 g) and styrene (4.0 mmol, 0.42 g) were dissolved in CH_2Cl_2 (10 mL) at room temperature in a dry round-bottomed flask under an argon atmosphere. The solution was cooled to –10 °C in a dry ice/acetone bath and phenylboron dichloride (4.0 mmol, 0.64 g) was added via syringe. The solution gradually turned yellow. After stirring at -10°C for 1 hr, the solution was hydrolyzed and extracted with hexanes. The organic layer was separated, dried over anhydrous

$MgSO_4$, concentrated under reduced pressure, and the product isolated by column chromatography (silica gel, CH_2Cl_2 as eluent) to afford 0.75 g (76%) of 3-chloro-1,4-diphenyl-1-propanol as a colorless liquid.

6.4.3 Syntheses and characterizations of compounds 601-666

1,3-Dichloro-1,3-diphenylpropane (601):[177] The reaction of benzaldehyde (3.0 mmol, 0.32 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.72 g (90%) 1,3-dichloro-1,3-diphenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.36-7.30 (m, 10H), 5.20 (dd, 1H, J = 6.5, 7.5 Hz), 4.79 (dd, 1H, J = 7.1, 7.8 Hz), 3.01-2.91 (m, 0.5H), 2.74-2.63 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.7, 140.1, 128.8, 128.6, 127.0, 60.7, 60.1, 49.6, 49.4.

1,3-Dichloro-1-(4-fluorophenyl)-3-phenylpropane (602): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.83 g (98%) 1,3-dichloro-1-(4-fluorophenyl)-3-phenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.36-7.28 (m, 7H), 7.05-6.97 (m, 2H), 5.20 (dd, 0.5H, J = 6.5 Hz), 5.17 (dd, 0.5H, J = 6.4 Hz), 4.80-4.71 (m, 1H), 2.96-2.87 (m, 0.5H), 2.68-2.56 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.5, 160.6, 140.6, 139.9, 136.8, 135.9, 128.8, 128.7, 128.6, 127.0, 126.9, 116.0, 115.9, 115.6, 115.5, 60.7, 60.6, 59.9, 59.3, 49.6, 49.5. Anal. Calcd for $C_{15}H_{13}Cl_2F$: C, 63.62; H, 4.63. Found: C, 63.77; H, 4.73.

1,3-Dichloro-1-(2-fluorophenyl)-3-phenylpropane (603): The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.37 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol,

3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.82 g (97%) 1,3-dichloro-1-(2-fluorophenyl)-3-phenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.47-6.99 (m, 9H), 5.57 (dd, 0.6H, *J* = 5.6, 5.4 Hz), 5.23 (dd, 0.6H, *J* = 5.4, 4.9 Hz), 5.03 (dd, 0.4H, *J* = 6.3 Hz), 4.91 (dd, 0.4H, *J* = 7.5Hz), 3.01-2.89 (m, 0.4H), 2.83-2.75 (m, 1.6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 161.7, 161.5, 157.7, 157.6, 140.7, 139.7, 130.4, 130.3, 130.2, 128.8, 128.6, 128.0, 127.8, 127.3, 126.9, 124.6, 124.5, 116.0, 115.7, 60.7, 60.6, 59.8, 53.8, 53.3, 53.2, 48.3, 48.1. Anal. Calcd for $C_{15}H_{13}Cl_2F$: C, 63.62; H, 4.63. Found: C, 63.65; H, 4.62.

1,3-Dichloro-1-(4-chlorophenyl)-3-phenylpropane (604): The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.87 g (97%) 1,3-dichloro-1-(4-chlorophenyl)-3-phenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.36-7.20 (m, 9H), 5.20-5.13 (m, 1H), 4.78-4.70 (m, 1H), 2.98-2.86 (m, 0.5H), 2.67-2.56 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.5, 139.9, 139.3, 138.6, 134.6, 134.4, 129.0, 128.8, 128.7, 128.5, 128.4, 127.0, 126.9, 60.6, 59.9, 59.8, 59.2, 49.5, 49.4. Anal. Calcd for $C_{15}H_{13}Cl_3$: C, 60.13; H, 4.37. Found: C, 60.36; H, 4.45.

1,3-Dichloro-1-(2-chlorophenyl)-3-phenylpropane (605): The reaction of 2-chlorobenzaldehyde (3.0 mmol, 0.42 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.85 g (95%) 1,3-dichloro-1-(2-chlorophenyl)-3-phenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.54-7.20 (m, 9H), 5.81 (dd, 0.6H, *J* = 10.3 Hz), 5.26 (dd, 0.6H, *J* = 10.4 Hz), 5.11 (dd, 0.4H, *J* = 9.2 Hz), 5.01 (dd, 0.4H, *J* = 8.5 Hz), 2.83-2.45 (m, 2H);

^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.7, 139.4, 138.0, 137.6, 132.4, 129.7, 129.5, 128.8, 128.7, 128.5, 127.4, 127.3, 127.2, 126.9, 60.6, 59.7, 56.8, 56.2, 48.5, 48.4. Anal. Calcd for $C_{15}H_{13}Cl_3$: C, 60.13; H, 4.37. Found: C, 60.55; H, 4.39.

1-(4-Bromophenyl)-1,3-dichloro-3-phenylpropane (606): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.55 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.99 g (96%) 1-(4-bromophenyl)-1,3-dichloro-3-phenylpropane, a colorless oil. ^1H NMR ($CDCl_3$/TMS) δ ppm, 7.47-7.20 (m, 9H), 5.20-5.11 (m, 1.5H), 4.76-4.70 (m, 0.5H), 2.97-2.85 (m, 0.25H), 2.66-2.54 (m, 1.75H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.5, 139.8, 139.7, 139.0, 131.9, 128.8, 128.7, 128.6, 126.9, 122.7, 122.5, 60.5, 59.8, 59.2, 49.4, 49.3. Anal. Calcd for $C_{15}H_{13}BrCl_2$: C, 52.36; H, 3.81. Found: C, 52.52; H, 3.88.

1-(3-Bromophenyl)-1,3-dichloro-3-phenylpropane (607): The reaction of 3-bromobenzaldehyde (3.0 mmol, 0.55 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.98 g (95%) 1-(3-bromophenyl)-1,3-dichloro-3-phenylpropane, a colorless oil. ^1H NMR ($CDCl_3$/TMS) δ ppm, 7.53-7.17 (m, 9H), 5.22-5.13 (m, 1H), 4.82-4.65 (m, 1H), 2.98-2.86 (m, 0.5H), 2.69-2.58 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 142.9, 142.3, 140.5, 139.8, 131.9, 131.7, 130.4, 130.1, 128.9, 128.8, 128.7, 127.0, 126.9, 125.7, 122.8 122.7, 60.6, 59.8, 59.7, 59.0, 49.6, 49.3. Anal. Calcd for $C_{15}H_{13}BrCl_2$: C, 52.36; H, 3.81. Found: C, 52.58; H, 3.89.

1-(2-Bromophenyl)-1,3-dichloro-3-phenylpropane (608): The reaction of 2-bromobenzaldehyde (3.0 mmol, 0.55 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol,

3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.98 g (95%) 1-(2-bromophenyl)-1,3-dichloro-3-phenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.56-7.09 (m, 9H), 5.79 (dd, 0.6H, J = 10.5Hz), 5.26 (dd, 0.6H, J = 10.6Hz), 5.09-5.00 (m, 0.8H), 2.80-2.41 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.7, 139.7, 139.3, 132.9, 129.8, 128.8, 128.6, 128.5, 128.1, 128.0, 127.3, 126.9, 122.7, 122.6, 60.6, 59.6, 59.4, 58.8, 48.6. Anal. Calcd for $C_{15}H_{13}BrCl_2$: C, 52.36; H, 3.81. Found: C, 52.39; H, 3.91.

1,3-Dichloro-1-phenyl-3-(*p*-tolyl)propane (609): The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.59 g (70%) 1,3-dichloro-1-phenyl-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.36-7.14 (m, 9H), 5.21-5.14 (m, 0.8H), 4.81-4.74 (m, 1.2H), 3.02-2.90 (m, 0.6H), 2.72-2.61 (m, 1.4H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.8, 140.2, 138.7, 138.6, 137.8, 137.1, 129.5, 129.4, 128.8, 128.7, 128.6, 127.0, 126.9, 60.7, 60.2, 60.1, 49.5, 49.4, 21.2. Anal. Calcd for $C_{16}H_{16}Cl_2$: C, 68.83; H, 5.78. Found: C, 69.23; H, 5.88.

1,3-Dichloro-1-phenyl-3-(*o*-tolyl)propane (610): The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.57 g (68%) 1,3-dichloro-1-phenyl-3-(*o*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.44-7.10 (m, 9H), 5.53-5.48 (m, 0.5H), 5.27-5.22 (m, 0.5H), 5.98 (dd, 0.5H, J = 8.4 Hz), 4.88 (dd, 0.5H, J = 7.4 Hz), 3.01-2.89 (m, 0.5H), 2.74-2.60 (m, 1.5H), 2.34 (s, 1.5H), 2.16 (s, 1.5H) ; ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.7, 140.2,

138.6, 138.0, 135.4, 135.1, 130.7, 130.6, 128.7, 128.5, 128.4, 128.3, 127.0, 126.9, 126.7, 126.6, 126.5, 126.4, 60.9, 60.0, 56.9, 56.1, 48.6, 48.5, 18.9, 18.8. Anal. Calcd for $C_{16}H_{16}Cl_2$: C, 68.83; H, 5.78. Found: C, 69.31; H, 5.79.

4-(1,3-Dichloro-3-phenylpropyl)benzonitrile (611): The reaction of 4-cyanobenzaldehyde (3.0 mmol, 0.39 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.70 g (80%) 4-(1,3-dichloro-3-phenylpropyl)benzonitrile, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.68-7.34 (m, 9H), 5.28-5.19 (m, 1.2H), 4.79-4.73 (m, 0.8H), 3.00-2.88 (m, 0.4H), 2.70-2.53 (m, 1.6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 145.8, 145.1, 140.3, 139.6, 132.7, 129.0, 128.9, 128.8, 127.9, 127.8, 127.0, 126.9, 118.2, 112.7, 112.5, 60.4, 59.6, 59.5, 58.7, 49.5, 49.3. Anal. Calcd for $C_{15}H_{13}Cl_2N$: C, 66.22; H, 4.52; N, 4.83. Found: C, 66.42; H, 4.52; N, 4.79.

1,3-Dichloro-1-(4-nitrophenyl)-3-phenylpropane (612): The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.45 g), styrene (3.0 mmol, 0.31 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.92 g (99%) 1,3-dichloro-1-(4-nitrophenyl)-3-phenylpropane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 8.21-7.23 (m, 9H), 5.33-5.21 (m, 1H), 4.85-4.74 (m, 1H), 3.01-2.89 (m, 0.5H), 2.72-2.60 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 147.8, 147.7, 147.4, 146.8, 140.2, 139.4, 128.9, 128.8, 128.7, 128.0, 127.9, 126.9, 126.8, 124.0, 60.3, 59.5, 59.1, 58.3, 49.3, 49.2. Anal. Calcd for $C_{15}H_{13}Cl_2NO_2$: C, 58.08; H, 4.22; N, 4.52. Found: C, 58.33; H, 4.33; N, 4.42.

1,4-Di(1′,3′-dichloro-3′-phenylpropyl)benzene (613): The reaction of benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g), styrene (6.0 mmol, 0.63 g) and BCl_3 (6.0 mmol, 6.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.24 g (92%) 1,4-di(1′,3′-dichloro-3′-phenylpropyl)benzene, a colorless crystal, m.p. 135.0–136.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomers: 7.70-7.34 (m, 14H), 5.24-5.18 (m, 4H), 2.65 (dd, 4H, J = 6.7, 7.2 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomers: 141.3, 140.7, 128.9, 128.7, 127.5, 127.0, 60.6, 60.1, 49.6. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, S; S, R*)-isomers: 7.38-7.22 (m, 14H), 4.84-4.72 (m, 4H), 3.01-2.89 (m, 2H). 2.72-2.61 (m, 2H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, S; S, R*)-isomers: 141.1, 140.5, 139.9, 128.9, 128.8, 127.6, 127.0, 59.9, 59.5, 49.3. Anal. Calcd for $C_{24}H_{22}Cl_4$: C, 63.74; H, 4.90. Found: C, 63.86; H, 4.95.

1,3-Dichloro-1,3-di(4-fluorophenyl)propane (614): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.89 g (98%) 1,3-dichloro-1,3-di(4-fluorophenyl)propane, a colorless crystal, m.p. 48.0-49.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.38-7.30 (m, 4H), 7.07-7.00 (m, 4H), 5.18 (t, 1H, J = 7.0 Hz), 4.7 (t, 1H, J = 7.4 Hz), 2.99-2.87 (m, 0.5H), 2.65-2.54 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.7, 164.6, 160.6, 136.6, 135.8, 128.9, 128.8, 128.7, 116.0, 115.9, 115.7, 115.6, 60.7, 59.9, 59.2, 49.8, 49.6. Anal. Calcd for $C_{15}H_{12}Cl_2F_2$: C, 59.82; H, 4.02. Found: C, 60.03; H, 4.08.

1,3-Dichloro-1-(2-fluorophenyl)-3-(4-fluorophenyl)propane (615): The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.37 g), 4-fluorostyrene (3.0 mmol, 0.37 g)

and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.90 g (99%) 1,3-dichloro-1-(2-fluorophenyl)-3-(4-fluorophenyl)-propane, a colorless oil. ^1H NMR ($CDCl_3$/TMS) δ ppm, 7.48-7.00 (m, 8H), 5.57-5.52 (m, 0.6H), 5.25-5.19 (m, 0.6H), 5.01-4.49 (m, 0.8H), 2.99-2.87 (m, 0.5H), 2.99-2.87 (m, 0.4H), 2.79-2.62 (m, 1.6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.7, 164.6, 161.5, 160.8, 160.6, 157.6, 136.7, 135.6, 130.5, 130.4, 130.3, 129.0, 128.8, 128.7, 128.6, 127.9, 127.6, 127.2, 124.6, 116.1, 115.9, 115.7, 115.6, 59.8, 59.0, 53.8, 53.2, 48.4, 48.2. Anal. Calcd for $C_{15}H_{12}Cl_2F_2$: C, 59.82; H, 4.02. Found: C, 59.99; H, 3.95.

1,3-Dichloro-1-(4-chlorophenyl)-3-(4-fluorophenyl)propane (616): The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.93 g (98%) 1,3-dichloro-1-(4-chlorophenyl)-3-(4-fluorophenyl)-propane, a colorless crystal, m.p. 43.0-44.0 °C. ^1H NMR ($CDCl_3$/TMS) δ ppm, 7.38-7.24 (m, 6H), 7.08-7.01 (m, 2H), 5.20-5.13 (m, 1.2H), 4.76-4.70 (m, 0.8H), 2.98-2.85 (m, 0.4H), 2.64-2.53 (m, 1.6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.7, 164.6, 160.6, 159.8, 139.1, 138.4, 136.5, 135.8, 134.6, 134.5, 129.1, 129.0, 128.9, 128.8, 128.7, 128.4, 116.0, 115.9, 115.7, 115.6, 59.8, 59.1, 49.6, 49.5. Anal. Calcd for $C_{15}H_{12}Cl_3F$: C, 56.72; H, 3.81. Found: C, 56.86; H, 3.81.

1,3-Dichloro-1-(2-chlorophenyl)-3-(4-fluorophenyl)propane (617): The reaction of 2-chlorobenzaldehyde (3.0 mmol, 0.42 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.95 g (99%) 1,3-dichloro-1-(2-chlorophenyl)-3-(4-fluorophenyl)-

propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.58-6.98 (m, 8H), 5.82-5.77 (m, 0.6H), 5.27-5.22 (m, 0.6H), 5.08-5.00 (m, 0.8H), 2.87-2.44 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.7, 164.5, 160.8, 160.6, 137.9, 136.7, 135.3, 132.5, 132.3, 129.7, 129.6, 129.2, 129.1, 128.8, 128.7, 128.5, 127.5, 127.4, 115.9, 115.8, 115.6, 115.5, 59.8, 58.8, 56.7, 56.1, 48.6. Anal. Calcd for $C_{15}H_{12}Cl_3F$: C, 56.72; H, 3.81. Found: C, 57.10; H, 3.98.

1-(4-Bromophenyl)-1,3-dichloro-3-(4-fluorophenyl)propane (618): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.03 g (95%) 1-(4-bromophenyl)-1,3-dichloro-3-(4-fluorophenyl) propane, colorless crystals, m.p. 49.0-50.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.50-7.00 (m, 8H), 5.20-5.12 (m, 1H), 4.76-4.69 (m, 1H), 2.97-2.85 (m, 0.5H), 2.64-2.53 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.6, 160.7, 160.6, 160.2, 139.6, 138.9, 136.5, 135.8, 132.0, 131.9, 128.9, 122.8, 122.6, 116.0, 115.9, 115.7, 115.6, 59.8, 59.1, 49.6, 49.4. Anal. Calcd for $C_{15}H_{12}BrCl_2F$: C, 49.76; H, 3.34. Found: C, 49.97; H, 3.36.

1-(2-Bromophenyl)-1,3-dichloro-3-(4-fluorophenyl)propane (619): The reaction of 2-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.98 g (90%) 1-(2-bromophenyl)-1,3-dichloro-3-(4-fluorophenyl) propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.59-6.98 (m, 8H), 5.79-5.74 (m, 0.5H), 5.28-5.22 (m, 0.5H), 5.09-4.98 (m, 1H), 2.82-2.40 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.7, 164.5, 160.7, 160.8, 160.5, 139.6, 139.3, 136.7, 136.6,

135.2, 133.0, 129.9, 129.3, 129.2, 128.8, 128.7, 128.1, 128.0, 122.7, 122.5, 115.9, 115.6, 115.5, 59.8, 59.3, 58.8, 58.7, 48.7. Anal. Calcd for $C_{15}H_{12}BrCl_2F$: C, 49.76; H, 3.34. Found: C, 49.60; H, 3.36.

1,4-Di[1′,3′-dichloro-3′-(4-fluorophenyl)propyl]benzene (620): The reaction of benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g), 4-fluorostyrene (6.0 mmol, 0.75 g) and BCl_3 (6.0 mmol, 6.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.32 g (90%) 1,4-di[1′,3′-dichloro-3′-(4-fluorophenyl)propyl]benzene, colorless crystal, m.p. 142.0–143.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomers: 7.40-7.34 (m, 8H), 7.09-7.02 (m, 4H), 5.21 (t, 4H, J = 6.7 Hz), 2.62 (t, 4H, J = 6.7 Hz). ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomers: 164.6, 160.7, 141.2, 136.6, 128.8, 128.7, 127.5, 127.5, 116.0, 115.6, 60.0, 59.8, 49.7. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, S; S, R*)-isomers: 7.38-7.34 (m, 8H), 7.06-7.00 (m, 4H), 4.83-4.69 (m, 4H), 2.99-2.87 (m, 2H). 2.67-2.57 (m, 2H). ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, S; S, R*)-isomers: 164.5, 160.6, 141.1, 140.6, 140.4, 135.7, 128.9, 127.5, 115.9, 115.5, 59.3, 59.1, 49.3. Anal. Calcd for $C_{24}H_{20}Cl_4F_2$: C, 59.04; H, 4.13. Found: C, 59.24; H, 4.28.

1,3-Dichloro-1-(4-fluorophenyl)-3-(*p*-tolyl)propane (621): The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.66 g (74%) 1,3-dichloro-1-(4-fluorophenyl)-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.38-6.88 (m, 8H), 5.19-5.12 (m, 1H), 4.79-4.71 (m, 1H), 2.99-2.86 (m, 0.5H), 2.67-2.55 (m, 1.5H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.5, 160.6, 138.7, 137.7, 136.9, 136.7, 136.1, 136.0, 129.5, 129.4, 128.9, 128.8,

126.9, 115.9, 115.8, 115.6, 115.5, 60.6, 59.9, 59.4, 49.6, 49.5, 21.1. Anal. Calcd for $C_{16}H_{15}Cl_2F$: C, 64.66; H, 5.09. Found: C, 64.69; H, 5.14.

1,3-Dichloro-1-(4-fluorophenyl)-3-(*o*-tolyl)propane (622): The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.62 g (70%) 1,3-dichloro-1-(4-fluorophenyl)-3-(*o*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.44-6.96 (m, 8H), 5.52-5.47 (m, 0.5H), 5.27-5.21 (m, 0.5H), 4.99-4.85 (m, 1H), 3.00-2.88 (m, 0.5H), 2.71-2.60 (m, 1.5H), 2.36 (s, 1.5H), 2.19 (s, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.6, 164.5, 160.7, 160.6, 138.5, 137.9, 136.8, 136.7, 136.0, 135.2, 130.8, 130.7, 128.9, 128.8, 128.7, 128.5, 128.4, 126.8, 126.5, 126.4, 115.9, 115.8, 115.6, 115.5, 60.2, 59.3, 56.9, 56.0, 48.8, 48.6, 19.0, 18.8. Anal. Calcd for $C_{16}H_{15}Cl_2F$: C, 64.66; H, 5.09. Found: C, 64.92; H, 5.04.

1,3-Dichloro-1-(4-fluorophenyl)-3-(4-nitrophenyl)propane (623): The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.45 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.96 g (98%) 1,3-dichloro-1-(4-fluorophenyl)-3-(4-nitrophenyl)propane, a yellow solid. m.p. 70.0-71.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 8.21 (d, 2H, J = 8.7 Hz), 7.58 (d, 2H, J = 8.7 Hz), 7.40-7.34 (m, 2H), 7.09-7.01 (m, 2H), 5.34-5.22 (m, 1.2H), 4.84-4.75 (m, 0.8H), 3.01-2.89 (m, 0.4H), 2.70-2.54 (m, 1.6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.7, 164.6, 160.7, 160.6, 147.9, 147.8, 147.4, 146.7, 136.2, 136.1, 135.4, 128.9, 128.8, 128.6, 128.1, 127.9, 124.0, 116.1, 115.9, 115.7, 115.6, 59.6, 59.1, 58.8, 58.2, 49.4,

49.2. Anal. Calcd for $C_{15}H_{12}Cl_2FNO_2$: C, 54.90; H, 3.69; N, 4.27. Found: C, 54.63; H, 3.68; N, 4.06.

1,3-Dichloro-1-(2-fluorophenyl)-3-(*p*-tolyl)propane (624): The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.37 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.76 g (85%) 1,3-dichloro-1-(2-fluorophenyl)-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.47-6.99 (m, 8H), 5.55 (t, 0.5H, J = 7.2 Hz), 5.20 (t, 0.5H, J = 6.7 Hz), 5.01 (dd, 0.5H, J = 8.7, 6.1 Hz), 4.91 (t, 0.5H, J = 7.2 Hz), 3.00-2.88 (m, 0.5H), 2.82-2.73 (m, 0.5H), 2.67 (t, 1H, J = 7.0 Hz), 2.35 (s, 1.5H), 2.33 (s, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 161.5, 157.6, 138.7, 138.5, 137.8, 136.7, 136.0, 130.4, 130.2, 130.1, 129.5, 129.4, 127.2, 127.0, 126.8, 124.6, 116.0, 115.7, 60.6, 59.8, 59.3, 59.2, 53.4, 48.2, 47.9, 21.1. Anal. Calcd for $C_{16}H_{15}Cl_2F$: C, 64.66; H, 5.09. Found: C, 64.69; H, 5.14.

1,3-Dichloro-1-(4-chlorophenyl)-3-(*p*-tolyl)propane (625): The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.78 g (83%) 1,3-dichloro-1-(4-chlorophenyl)-3-(*p*-tolyl)propane, a white solid, m.p. 46.0-47.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.30-7.11 (m, 8H), 5.14 (t, 1H, J = 7.0 Hz), 4.72 (t, 1H, J = 7.4 Hz), 2.96-2.84 (m, 0.5H), 2.64-2.53 (m, 1.5H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 139.2, 138.7, 138.6, 138.5, 137.6, 136.9, 134.4, 134.3, 129.5, 128.9, 128.4, 128.3, 126.9, 126.8, 60.5, 59.9, 59.8, 59.2, 49.4, 49.3, 21.1. Anal. Calcd for $C_{16}H_{15}Cl_3$: C, 61.27; H, 4.82. Found: C, 61.48; H, 4.90.

1,3-Dichloro-1-(2-chlorophenyl)-3-(*p*-tolyl)propane (626): The reaction of 2-chlorobenzaldehyde (3.0 mmol, 0.42 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.76 g (82%) 1,3-dichloro-1-(2-chlorophenyl)-3-(*p*-tolyl)propane, a colorless oil. ^1H NMR ($CDCl_3$/TMS) δ ppm, 7.58-7.14 (m, 8H), 5.81 (dd, 0.6H, J = 10.3, 7.0 Hz), 5.24 (dd, 0.6H, J= 10.4, 3.3 Hz), 5.12 (dd, 0.4H, J= 9.1, 5.5 Hz), 5.01 (dd, 0.4H, J= 8.5, 5.5 Hz), 2.84-2.47 (m, 2H), 2.36 (s, 1.2H), 2.24 (s, 1.8H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 138.8, 138.5, 138.2, 137.9, 136.5, 132.6, 129.8, 129.5, 129.4, 128.5, 127.5, 127.4, 127.2, 126.9, 60.6, 59.9, 59.7, 56.9, 56.3, 48.5, 48.3, 21.1. Anal. Calcd for $C_{16}H_{15}Cl_3$: C, 61.27; H, 4.82. Found: C, 61.47; H, 4.85.

1-(4-Bromophenyl)-1,3-dichloro-3-(*p*-tolyl)propane (627): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.88 g (82%) 1-(4-bromophenyl)-1,3-dichloro-3-(*p*-tolyl)propane, a white solid, m.p. 54.0-56.0 °C. ^1H NMR ($CDCl_3$/TMS) δ ppm, 7.45 (d, 2H, J= 8.3 Hz), 7.21 (dd, 4H, J = 7.2 Hz), 7.13 (d, 2H, J = 8.2 Hz), 5.16-5.10 (m, 1H), 4.75-4.69 (tm, 1H), 2.96-2.84 (m, 0.5H), 2.65-2.53 (m, 1.5H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 139.7, 139.1, 138.7, 138.6, 137.5, 136.9, 131.9, 131.8, 129.5, 129.4, 128.7, 128.6, 127.6, 126.9, 126.8, 123.9, 122.6, 122.5, 60.5, 59.9, 59.2, 49.4, 49.2, 21.1. Anal. Calcd for $C_{16}H_{15}BrCl_2$: C, 53.66; H, 4.22. Found: C, 53.90; H, 4.19.

1-(2-Bromophenyl)-1,3-Dichloro-3-(*p*-tolyl)propane (628): The reaction of 2-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3

(3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.86 g (80%) 1-(2-bromophenyl)-1,3-dichloro-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.59-7.09 (m, 8H), 5.79 (dd, 0.6H, J = 10.5, 3.1 Hz), 5.24 (dd, 0.6H, J = 10.6, 3.1 Hz), 5.10-4.99 (m, 0.8H), 2.80-2.42 (m, 2H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 139.8, 139.5, 138.7, 138.4, 137.8, 136.4, 132.9, 129.8, 129.4, 128.7, 128.1, 128.0, 127.3, 126.8, 122.7, 122.6, 60.6, 59.7, 58.9, 48.6, 48.4, 21.1. Anal. Calcd for $C_{16}H_{15}BrCl_2$: C, 53.66; H, 4.22. Found: C, 53.84; H, 4.23.

1,3-Dichloro-1,3-di(*p*-tolyl)propane (629): The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.60 g (68%) 1,3-dichloro-1,3-di(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.25-7.11 (m, 8H), 5.14 (t, 1H, J = 6.8 Hz), 4.76 (t, 1H, J = 7.3 Hz), 2.99-2.88 (m, 0.5H), 2.69-2.61 (m, 1.5H), 2.32 (s, 6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 138.6, 138.4, 137.8, 137.2, 129.5, 126.9, 60.7, 49.4, 49.3, 21.1. Anal. Calcd for $C_{17}H_{18}Cl_2$: C, 69.63; H, 6.19. Found: C, 69.78; H, 6.22.

1,3-Dichloro-1-(*o*-tolyl)-3-(*p*-tolyl)propane (630): The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.64 g (70%) 1,3-dichloro-1-(*o*-tolyl)-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.46-7.09 (m, 8H), 5.49 (t, 0.5H, J = 7.2 Hz), 5.23 (t, 0.5H, J = 7.2 Hz), 5.00 (dd, 0.5H, J = 8.3, 6.4 Hz), 4.88 (t, 0.5H, J = 7.4 Hz), 3.02-2.89 (m, 0.5H), 2.76-2.62 (m, 1.5H), 2.36 (s, 1.5H), 2.33 (s, 1.5H), 2.32 (s, 1.5H), 2.21 (s, 1.5H);

^{13}C NMR ($CDCl_3$/TMS) δ ppm, 138.7, 138.5, 138.1, 137.9, 137.1, 135.6, 135.2, 130.7, 130.6, 129.5, 129.4, 128.4, 128.3, 126.9, 126.8, 126.7, 126.6, 126.5, 126.4, 60.9, 60.1, 57.1, 56.2, 48.6, 48.4, 21.1, 19.0. Anal. Calcd for $C_{17}H_{18}Cl_2$: C, 69.63; H, 6.19. Found: C, 69.78; H, 6.18.

4-[1,3-Dichloro-3-(*p*-tolyl)propyl]benzonitrile (631): The reaction of 4-cyanobenzaldehyde (3.0 mmol, 0.39 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.44 g (48%) 4-[1,3-dichloro-3-(p-tolyl)propyl]benzonitrile, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.68-7.12 (m, 8H), 5.26-5.15 (m, 1H), 4.75 (t, 1H, J = 7.5 Hz), 2.99-2.87 (m, 0.5H), 2.68-2.57 (m, 1.5H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 145.8, 145.2, 139.0, 138.8, 137.4, 136.6, 132.6, 129.6, 129.5, 127.9, 127.8, 126.9, 126.8, 118.2, 112.5, 60.3, 59.6, 59.5, 58.8, 49.4, 49.2, 21.1. Anal. Calcd for $C_{17}H_{15}Cl_2N$: C, 67.12; H, 4.52; N, 4.60. Found: C, 67.14; H, 5.02; N, 4.51.

1,3-Dichloro-1-(4-nitrophenyl)-3-(*p*-tolyl)propane (632): The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.45 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BCl_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.62 g (64%) 1,3-dichloro-1-(4-nitrophenyl)-3-(*p*-tolyl)propane, a yellow oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 8.19 (d, 2H, J = 8.5 Hz), 7.55 (d, 2H, J = 8.5 Hz), 7.28-7.15 (m, 4H), 5.31-5.26 (m, 0.5H), 5.22-5.16 (m, 0.5H), 4.83-4.73 (m, 1H), 3.00-2.88 (m, 0.5H), 2.70-2.659 (m, 1.5H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 147.8, 147.7, 147.5, 146.9, 138.9, 138.7, 137.3, 136.5, 129.6, 129.5, 128.0, 127.9, 126.9, 126.8, 123.9,

60.3, 59.6, 59.1, 58.4, 49.3, 49.1, 21.1. Anal. Calcd for $C_{16}H_{15}Cl_2NO_2$: C, 59.28; H, 4.66; N, 4.32. Found: C, 58.88; H, 4.65; N, 4.32.

1,4-Di[1′,3′-dichloro-3′-(*p*-tolyl)propyl]benzene (633): The reaction of benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g), 4-methylstyrene (6.0 mmol, 0.71 g) and BCl_3 (6.0 mmol, 6.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.14 g (79%) 1,4-di[1′,3′-dichloro-3′-(*p*-tolyl)lpropyl]benzene, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.60-7.15 (m, 12H), 5.20-5.14 (m, 2H), 4.83-4.71 (m, 2H), 3.00-2.88 (m, 1H), 2.68-2.60 (m, 1H), 2.34 (s, 6H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 141.3, 141.2, 140.7, 140.6, 138.7, 138.6, 137.7, 136.9, 129.5, 127.5, 126.9, 126.8, 60.6, 60.2, 59.9, 59.6, 49.5, 49.2, 21.1. Anal. Calcd for $C_{26}H_{26}Cl_4$: C, 65.02; H, 5.46. Found: 65.38; H, 5.38.

1,3-Dibromo-1,3-diphenylpropane (634):[178] The reaction of benzaldehyde (3.0 mmol, 0.32 g), styrene (3.0 mmol, 0.31 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.80 g (75%) 1,3-dibromo-1,3-diphenylpropane, a white solid, mp 111.0–112.0 °C (lit. 111.5–112.5 °C). ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.33-7.25 (m, 10H), 5.18 (t, 1H, J = 7.2 Hz), 4.79 (t, 1H, J = 7.7 Hz), 3.26-3.14 (m, 0.5H), 2.94-2.83 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.9, 140.3, 128.9, 128.7, 127.4, 53.0, 51.8, 49.2, 49.1.

1,3-Dibromo-1-(4-fluorophenyl)-3-phenylpropane (635): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), styrene (3.0 mmol, 0.31 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.09 g (98%) 1,3-dibromo-1-(4-fluorophenyl)-3-phenylpropane, a colorless oil. ^{1}H NMR

($CDCl_3$/TMS) δ ppm, 7.34-7.25 (m, 7H), 7.03-6.96 (m, 2H), 5.16 (t, 1H, J = 7.1 Hz), 4.83 (dd, 1H, J = 14.9, 7.2 Hz), 3.24-3.11 (m, 0.5H), 2.90-2.78 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.4, 160.5, 140.7, 140.1, 136.9, 136.2, 129.3, 129.1, 128.9, 128.7, 127.4, 116.0, 115.7, 52.8, 52.0, 51.6, 50.6, 49.3, 49.1. Anal. Calcd for $C_{15}H_{13}Br_2F$: C, 48.42; H, 3.52. Found: 48.48; H, 3.51.

1,3-Dibromo-1-phenyl-3-(*p*-tolyl)propane (636): The reaction of methylbenzaldehyde (3.0 mmol, 0.36 g), styrene (3.0 mmol, 0.31 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.66 g (60%) 1,3-dibromo-1-phenyl-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.31-7.10 (m, 9H), 5.15 (t, 1H, J = 7.0 Hz), 4.90-4.81 (m, 1H), 3.25-3.13 (m, 0.5H), 2.93-2.81 (m, 1.5H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.9, 140.4, 138.7, 138.6, 137.9, 137.3, 129.5, 128.8, 128.6, 127.3, 127.2, 53.0, 52.9, 52.0, 51.9, 49.2, 49.0, 21.2. Anal. Calcd for $C_{16}H_{16}Br_2$: C, 52.21; H, 4.38. Found: 52.31; H, 4.34.

1,3-Dibromo-1,3-di(4-fluorophenyl)propane (637): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.12 g (96%) 1,3-dibromo-1,3-di(4-fluorophenyl)propane, colorless crystals, m.p. 74.0-75.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomers: 7.38-7.31 (m, 4H), 7.09-7.00 (m, 4H), 5.17 (t, 2H, J = 7.2 Hz), 2.86 (t, 2H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.6, 136.8, 129.3, 116.1, 115.7, 51.9, 49.4. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, S; S, R*)-isomers: 7.37-7.32 (m, 4H), 7.06-6.99 (m, 4H), 4.83 (t,

2H, J = 7.4 Hz), 3.23-3.10 (m, 1H), 2.88-2.76 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 160.6, 136.1, 129.1, 116.1, 115.7, 50.6, 49.5. Anal. Calcd for $C_{15}H_{12}Br_2F_2$: C, 46.19; H, 3.10. Found: 46.15; H, 3.11.

1,3-Dibromo-1-(2-fluorophenyl)-3-(4-fluorophenyl)propane (638): The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.37 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 M solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.11 g (95%) 1,3-dibromo-1-(2-fluorophenyl)-3-(4-fluorophenyl)-propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.40-6.96 (m, 8H), 5.49 (dd, 0.5H, J = 8.7, 5.7 Hz), 5.20 (dd, 0.5H, J = 8.7, 5.5 Hz), 5.08-4.94 (m, 1H), 3.24 (m, 0.5H), 2.98-2.81 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.5, 164.4, 161.5, 160.6, 160.5, 157.5, 136.8, 135.9, 135.8, 130.5, 130.4, 129.3, 129.2, 129.1, 128.9, 128.0, 127.8, 127.4, 124.7, 124.6, 116.2, 116.9, 115.9, 115.7, 115.6, 51.9, 50.3, 48.0, 47.9, 44.9, 44.8, 43.8. Anal. Calcd for $C_{15}H_{12}Br_2F_2$: C, 46.19; H, 3.10. Found: 46.31; H, 3.19.

1,3-Dibromo-1-(4-bromophenyl)-3-(4-fluorophenyl)propane (639): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 M solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.03 g (76%) 1,3-dibromo-1-(4-bromophenyl)-3-(4-fluorophenyl)-propane, colorless crystals, m.p. 68.0-69.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.46 (d, 2H, J = 8.3 Hz), 7.38-7.31 (m, 2H), 7.23 (d, 2H, J = 8.3 Hz), 7.06-6.99 (m, 2H), 5.13 (dd, 1H, J = 15.2, 7.5 Hz), 4.79 (dd, 1H, J = 7.6, 7.4 Hz), 3.21-3.28 (m, 0.5H), 2.86-2.74 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.5, 160.6, 160.5, 139.8, 139.2, 136.7, 132.1,

129.2, 129.1, 129.0, 122.8, 122.7, 116.1, 115.7, 51.8, 51.7, 50.5, 50.4, 49.2, 49.0. Anal. Calcd for $C_{15}H_{12}Br_3F$: C, 39.95; H, 2.68. Found: 40.15; H, 2.73.

1,3-Dibromo-1-(3-bromophenyl)-3-(4-fluorophenyl)propane (640): The reaction of 3-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 1.22 g (90%) 1,3-dibromo-1-(3-bromophenyl)-3-(4-fluorophenyl)-propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.52-6.98 (m, 8H), 5.21-5.10 (m, 1H), 4.86 (t, 0.5H, J = 7.5 Hz), 4.72 (t, 0.5H, J = 7.1 Hz), 3.20-3.09 (m, 0.5H), 2.86-2.75(m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.5, 160.5, 143.0, 142.3, 136.7, 131.9, 131.8, 130.4, 129.2, 129.1, 126.0, 125.9, 125.8, 116.1, 116.0, 115.7, 51.9, 51.5, 50.4, 50.1, 49.1, 49.0. Anal. Calcd for $C_{15}H_{12}Br_3F$: C, 39.95; H, 2.68. Found: 39.82; H, 2.72.

1,3-Dibromo-1-(4-fluorophenyl)-3-(*p*-tolyl)propane (641): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.88 g (76%) 1,3-dichloro-1-(4-fluorophenyl)-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.36-6.98 (m, 8H), 5.18-5.11 (m, 1H), 4.88-4.81 (m, 1H), 3.24-3.12 (m, 0.5H), 2.91-2.78 (m, 1.5H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.5, 160.6, 138.9, 137.3, 136.9, 136.4, 129.6, 129.3, 129.2, 127.3, 116.0, 115.7, 52.9, 52.0, 51.8, 50.9, 49.3, 49.2, 21.1. Anal. Calcd for $C_{16}H_{15}Br_2F$: C, 49.77; H, 3.92. Found: C, 49.55; H, 3.92.

1,3-Dibromo-1-(4-chlorophenyl)-3-(*p*-tolyl)propane (642): The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BBr_3

(3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.92 g (76%) 1,3-dibromo-1-(4-chlorophenyl)-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.31-7.11 (m, 8H), 5.14-5.08 (m, 1H), 4.85-4.79 (m, 1H), 3.22-3.09 (m, 0.5H), 2.89-2.76 (m, 1.5H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 139.4, 138.9, 138.8, 137.7, 137.1, 134.4, 134.3, 129.5, 129.0, 128.7, 127.2, 52.8, 51.7, 50.6, 49.0, 48.9, 21.1. Anal. Calcd for $C_{16}H_{15}Br_2Cl$: C, 47.74; H, 3.76. Found: C, 48.20; H, 3.80.

1,3-Dibromo-1-(4-bromophenyl)-3-(*p*-tolyl)propane (643): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.99 g (74%) 1,3-dibromo-1-(4-bromophenyl)-3-(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.47 (d, 2H, J = 8.2 Hz), 7.26-7.22 (m, 4H), 7.14 (d, 2H, J = 8.2 Hz), 5.10 (dd, 1H, J = 7.0, 11.7 Hz)), 4.81 (d, 1H, J = 7.4 Hz), 3.22-3.10 (m, 0.5H), 2.90-2.77 (m, 1.5H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 140.0, 139.4, 138.9, 138.8, 137.8, 137.2, 132.1, 129.6, 129.1, 127.2, 122.7, 52.8, 51.7, 50.7, 49.1, 48.9, 21.2. Anal. Calcd for $C_{16}H_{15}Br_3$: C, 42.99; H, 3.38. Found: C, 42.99; H, 3.77.

1,3-Dibromo-1,3-di(*p*-tolyl)propane (644): The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), 4-methylstyrene (3.0 mmol, 0.36 g) and BBr_3 (3.0 mmol, 3.0 mL 1.0 *M* solution in CH_2Cl_2) was carried out as described in **6.4.2.1** and produced 0.97 g (85%) 1,3-dibromo-1,3-di(*p*-tolyl)propane, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 7.19 (dd, 8H, J = 7.8 Hz), 5.13 (t, 1H, J = 7.2 Hz), 4.86 (t, 1H, J = 7.5 Hz), 3.22-3.13 (m, 0.5H), 2.95-2.81 (m, 1.5H), 2.33 (s, 6H); ^{13}C NMR ($CDCl_3$/TMS)

δ ppm, 138.7, 138.0, 137.5, 129.6, 127.3, 53.1, 52.1, 49.1, 21.2. Anal. Calcd for $C_{17}H_{18}Br_2$: C, 53.43; H, 4.75. Found: C, 53.74; H, 4.80.

3-Chloro-1,3-diphenylpropanol (645): The reaction of benzaldehyde (3.0 mmol, 0.32 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.56 g (76%) 3-chloro-1,3-diphenyl-propanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.38-7.21(m, 10H), 5.20 (dd, 1H, J = 9.7, 4.5 Hz), 5.09 (dd, 1H, J = 8.8, 4.4 Hz), 2.44 (s, 1H), 2.33-2.27 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 143.8, 141.6, 128.6, 128.5, 128.3, 127.8, 126.9, 125.7, 71.2, 60.5, 48.8. Anal. Calcd for $C_{15}H_{15}ClO$: C, 73.02; H, 6.13. Found: C, 73.07; H, 6.24.

3-Chloro-1-(4-fluorophenyl)-3-phenylpropanol (646): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.37 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.69 g (87%) 3-chloro-1-(4-fluorophenyl)-3-phenylpropanol, a colorless solid. m.p. 75.0-76.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.26-7.04 (m, 7H), 7.05-6.98 (m, 2H), 5.21 (dd, 1H, J = 14.2, 4.8 Hz), 5.09 (dd, 1H, J = 8.6, 4.4 Hz), 2.34-2.28 (m, 2H), 2.15 (s, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 164.2, 160.3, 141.5, 139.7, 128.7, 128.4, 127.5, 127.4, 126.9, 115.6, 115.3, 70.7, 60.5, 48.9. Anal. Calcd for $C_{15}H_{14}ClFO$: C, 68.06; H, 5.33. Found: C, 68.26; H, 5.25.

3-Chloro-1-(2-fluorophenyl)-3-phenylpropanol (647): The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.37 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.63

g (79%) 3-chloro-1-(2-fluorophenyl)-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.42-7.00 (m, 9H), 5.37 (d, 1H, J = 9.3 Hz), 5.25 (dd, 1H, J = 10.6, 3.5 Hz), 2.43-2.30 (m, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 161.1, 157.7, 141.6, 129.2, 129.1, 128.6, 128.3, 127.2, 127.1, 126.9, 124.4, 115.6, 115.3, 65.7, 60.4, 47.3. Anal. Calcd for $C_{15}H_{14}ClFO$: C, 68.06; H, 5.33. Found: C, 68.06; H, 5.23.

3-Chloro-1-(4-chlorophenyl)-3-phenylpropanol (648): The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.67 g (79%) 3-chloro-1-(4-chlorophenyl)-3-phenylpropanol, a colorless solid. m.p. 81.0-82.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.39-7.22 (m, 9H), 5.21 (dd, 1H, J = 10.0, 4.2Hz), 5.02 (dd, 1H, J = 8.9, 3.9 Hz), 2.35-2.14 (m, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 142.4, 141.4, 133.4, 128.7, 128.4, 127.1, 126.9, 70.7, 60.4, 48.8. Anal. Calcd for $C_{15}H_{14}Cl_2O$: C, 64.07; H, 5.02. Found: C, 64.02; H, 5.13.

3-Chloro-1-(4-bromophenyl)-3-phenylpropanol (649): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.81 g (82%) 3-chloro-1-(4-bromophenyl)-3-phenylpropanol, a colorless solid, m.p. 86.0-87.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.42 (d, 2H, J = 8.4 Hz), 7.31-7.23 (m, 2H), 7.17 (d, 2H, J = 8.4 Hz), 5.18 (dd, 1H, J = 10.0, 4.2Hz), 4.97 (dd, 1H, J = 9.2, 3.7 Hz), 2.45 (s, 1H), 2.33-2.20 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-

isomer): 142.7, 141.1, 131.5, 128.5, 128.2, 127.3, 126.7, 121.4, 70.5, 60.2, 48.5. Anal. Calcd for $C_{15}H_{14}BrClO$: C, 55.33; H, 4.33. Found: C, 55.32; H, 4.32.

3-Chloro-1-(*o*-tolyl)-3-phenylpropanol (650): The reaction of 2-methylbenzaldehyde (3.0 mmol, 0.36 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.44 g (56%) 3-chloro-1-(*o*-tolyl)-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.42-7.13 (m, 9H), 5.35-5.29 (m, 2H), 2.35 (s, 3H), 2.30 (m, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 141.7, 134.2, 130.4, 128.6, 128.2, 127.4, 126.9, 126.3, 124.9, 67.8, 61.0, 47.8, 18.9. Anal. Calcd for $C_{16}H_{17}ClO$: C, 73.70; H, 6.57. Found: C, 73.85; H, 6.78.

3-Chloro-1-(*p*-tolyl)-3-phenylpropanol (651): The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.47 g (60%) 3-chloro-1-(*p*-tolyl)-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.40-7.07 (m, 9H), 5.20 (dd, 1H, J = 8.9, 5.7 Hz), 4.97 (dd, 1H, J = 7.9, 4.9 Hz), 2.37-2.30 (m, 5H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 141.7, 140.9, 137.6, 129.3, 128.6, 128.2, 127.0, 125.7, 71.2, 60.6, 48.7, 21.1. Anal. Calcd for $C_{16}H_{17}ClO$: C, 73.70; H, 6.57. Found: C, 73.45; H, 6.64.

4-(3-Chloro-1-hydroxy-3-phenylpropyl)benzonitrile (652): The reaction of 4-cyanobenzaldehyde (3.0 mmol, 0.40 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.79 g (96%) 4-(3-chloro-1-hydroxy-3-phenylpropyl)benzonitrile, a pale-yellow solid, m.p.

54.0-55.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 7.60-7.26 (m, 9H), 5.26 (dd, 1H, J = 10.7, 3.3 Hz), 5.15 (d, 1H, J = 9.6 Hz), 2.94 (s, 1H), 2.40-2.15 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 149.5, 141.1, 132.3, 128.9, 128.4, 126.8, 126.2, 118.6, 111.0, 70.4, 60.2, 48.8. Anal. Calcd for $C_{16}H_{14}ClNO$: C, 72.72; H, 5.19; N, 5.15. Found: C, 72.63; H, 5.34; N, 4.95.

3-Chloro-1-(4-nitrophenyl)-3-phenylpropanol (653): The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.45 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.81 g (92%) 3-chloro-1-(4-nitrophenyl)-3-phenylpropanol, a yellow solid. m.p. 50.0-51.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 8.18 (d, 2H, J = 8.6 Hz), 7.54 (d, 2H, J = 8.6 Hz), 7.41-7.24 (m, 5H), 5.30-5.21 (m, 2H), 2.45 (s, 1H), 2.32-2.19 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 151.3, 147.4, 141.1, 128.6, 128.5, 126.9, 126.4, 123.8, 70.6, 60.3, 48.9. Anal. Calcd for $C_{15}H_{14}ClNO_3$: C, 61.76; H, 4.84; N, 4.80. Found: C, 61.84; H, 4.84; N, 4.55.

4-(3-Chloro-1-hydroxy-3-phenylpropyl)benzaldehyde (654): The reaction of benzene-1,4-dicarbaldehyde (3.0 mmol, 0.40 g), styrene (6.0 mmol, 0.62 g) and phenylboron dichloride (6.0 mmol, 0.96 g) was carried out as described in **6.4.2.2** and produced 0.37 g (45%) 4-(3-Chloro-1-hydroxy-3-phenylpropyl)benzaldehyde, a yellow solid, m.p. 43.0-44.5 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 9.97 (s, 1H), 7.81 (d, 2H, J = 8.1 Hz), 7.51 (d, 2H, J = 8.1 Hz), 7.36-7.24 (m, 5H), 5.27 (dd, 1H, J = 10.7, 3.5 Hz), 5.16 (d, 1H, J = 9.1 Hz), 2.95 (s, 1H), 2.43-2.20 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*-isomer): 192.0, 151.0, 141.3, 135.6, 130.0, 128.8,

128.4, 126.8, 126.2, 70.8, 60.4, 48.8. Anal. Calcd for $C_{16}H_{15}ClO_2$: C, 69.95; H, 5.50. Found: C, 69.82; H, 5.45.

3-Chloro-1-(3-pyridinyl)-3-phenylpropanol (655): The reaction of 3-pyridinecarbaldehyde (3.0 mmol, 0.32 g), styrene (3.0 mmol, 0.31 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.67 g (90%) 3-chloro-1-(3-pyridinyl)-3-phenylpropanol, a yellow wax. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 9.26 (s, 1H), 9.14 (s, 1H), 8.28-8.18 (dd, 1H, J = 15.0, 8.1 Hz), 7.75 (t, 1H, J = 7.2 Hz), 7.38-7.24 (m, 5H), 5.35-5.25 (m, 1H), 5.01 (t, 0.5H, J = 7.5 Hz), 4.61 (dd, 0.5 H, J = 8.5, 4.8 Hz), 2.89 (s, 1H), 2.74-2.62 (m, 0.5H), 2.46-2.23 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 143.7, 143.5, 143.3, 142.7, 142.3, 142.1, 141.6, 141.4, 140.4, 139.6, 129.0, 128.9, 128.8, 128.6, 127.0, 126.8, 126.0, 68.6, 68.2, 59.7, 59.3, 46.4, 46.1. Anal. Calcd for $C_{14}H_{14}ClNO$: C, 67.88; H, 5.70; N, 5.65. Found: C, 67.98; H, 5.43; N, 5.58.

3-Chloro-1-(3-pyridinyl)-3-(4-fluorophenyl)propanol (656): The reaction of 3-pyridinecarbaldehyde (3.0 mmol, 0.32 g), 4-fluorostyrene (3.0 mmol, 0.37 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.67 g (84%) 3-chloro-1-(3-pyridinyl)-3-(4-fluorophenyl)propanol, a yellow oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, 9.30 (s, 1H), 9.16 (s, 1H), 8.27 (t, 1H, J = 10.0 Hz), 7.81 (t, 1H, J = 7.5 Hz), 7.43-7.35 (m, 2H), 7.09-6.89 (m, 2H), 5.41-5.27 (m, 1H), 5.07 (t, 0.5H, J = 7.8 Hz), 4.68 (t, 0.5 H, J = 8.5 Hz), 2.84 (s, 1H), 2.78-2.67 (m, 0.5H), 2.48-2.24 (m, 1.5H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, 164.6, 164.4, 160.6, 160.5, 143.8, 143.7, 143.3, 142.7, 142.4, 142.2, 141.6, 141.4, 136.4, 135.8, 127.0, 126.8, 126.6, 126.0, 116.1,

115.9, 115.8, 115.5, 68.8, 68.2, 58.9, 58.5, 46.6 46.3. Anal. Calcd for $C_{14}H_{13}ClFNO$: C, 63.28; H, 4.93; N, 5.27. Found: C, 63.60; H, 5.01; N, 5.57.

3-Chloro-1-(3-pyridinyl)-3-(4-chlorophenyl)propanol (657): The reaction of 3-pyridinecarbaldehyde (3.0 mmol, 0.32 g), 4-chlorostyrene (3.0 mmol, 0.42 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.72 g (85%) 3-chloro-1-(3-pyridinyl)-3-(4-chlorophenyl)propanol, a yellow solid, m.p. 97.0-98.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomer: 9.36 (s, 1H), 9.24 (s, 1H), 8.38 (t, 1H, *J*= 10.4 Hz), 7.76 (t, 1H, *J* = 8.0 Hz), 7.42-7.22 (m, 4H), 5.74 (dd, 1H, *J* = 10.0, 4.5 Hz), 5.34 (t, 1 H, *J* = 9.0 Hz), 2.88 (s, 1H), 2.43-2.27 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomer: 145.6, 144.5, 138.3, 137.8, 136.3, 131.2, 128.9, 127.1, 123.2, 69.2, 54.9, 46.8. Anal. Calcd for $C_{14}H_{13}Cl_2NO$: C, 59.59; H, 4.64; N, 4.96. Found: C, 59.80; H, 4.47; N, 5.11.

3-Chloro-1-(3-pyridinyl)-3-(2-chlorophenyl)propanol (658): The reaction of 3-pyridinecarbaldehyde (3.0 mmol, 0.32 g), 2-chlorostyrene (3.0 mmol, 0.42 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.77 g (90%) 3-chloro-1-(3-pyridinyl)-3-(2-chlorophenyl)propanol, a pale-yellow solid, m.p. 128.0-129.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomer: 9.34 (s, 1H), 9.24 (s, 1H), 8.34 (t, 1H, *J*= 8.0 Hz), 7.61 (t, 1H, *J* = 7.4 Hz), 7.60 (d, 1H, *J* = 10.0 Hz), 7.39-7.25 (m, 3H), 5.83 (dd, 1H, *J* = 8.0, 5.0 Hz), 5.42 (t, 1H, *J* = 7.4 Hz), 2.78 (s, 1H), 2.39-2.33 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomer: 143.6, 143.5, 142.2, 141.5, 137.7, 132.2, 129.7, 128.5, 127.8, 127.6, 125.9, 68.1, 55.9,

47.3. Anal. Calcd for $C_{14}H_{13}Cl_2NO$: C, 59.59; H, 4.64; N, 4.96. Found: C, 59.76; H, 4.62; N, 5.02.

3-Chloro-1-(3-pyridinyl)-3-(*p*-tolyl)propanol (659): The reaction of 3-pyridinecarbaldehyde (3.0 mmol, 0.32 g), 4-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.51 g (64%) 3-chloro-1-(3-pyridinyl)-3-(*p*-tolyl)propanol, a yellow oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomer: 9.28 (s, 1H), 9.17 (s, 1H), 8.25 (t, 1H, J = 7.7 Hz), 7.76 (t, 1H, J = 7.3 Hz), 7.30-7.03 (m, 4H), 5.34 (d, 1H, J = 7.5 Hz), 5.21 (dd, 1H, J = 7.5, 3.2 Hz), 2.74-2.68 (m, 2H), 2.47-2.25 (m, 4H); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*R, R; S, S*)-isomer: 143.7, 143.4, 142.3, 138.7, 137.5, 136.7, 129.5, 127.3, 126.8, 126.0, 68.4, 59.8, 48.5, 21.1. Anal. Calcd for $C_{15}H_{16}ClNO$: C, 68.83; H, 6.16; N, 5.35. Found: C, 68.93; H, 6.42; N, 5.48.

3-Chloro-1-(4-fluorophenyl)-2-methyl-3-phenylpropanol (660): The reaction of 4-fluorobenzaldehyde (3.0 mmol, 0.40 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.79 g (94%) 3-chloro-1-(4-fluorophenyl)-2-methyl-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 7.33-7.26 (m, 7H), 7.01-6.95 (m, 2H), 5.52 (s, 1H), 5.00 (d, 1H, J = 10.8 Hz), 2.53 (s, 1H), 2.37-2.20 (m, 1H), 0.50 (d, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 163.7, 159.1, 140.6, 139.1, 128.6, 128.1, 127.5, 127.1, 127.0, 115.1, 114.8, 71.9, 64.7, 48.1, 9.9. Anal. Calcd for $C_{16}H_{16}ClFO$: C, 68.94; H, 5.79. Found: C, 68.85; H, 5.63.

3-Chloro-1-(2-fluorophenyl)-2-methyl-3-phenylpropanol (661): The reaction of 2-fluorobenzaldehyde (3.0 mmol, 0.40 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.80 g (95%) 3-chloro-1-(2-fluorophenyl)-2-methyl-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 7.41-7.04 (m, 9H), 5.45 (s, 1H), 5.10 (d, 1H, J = 10.6 Hz), 2.46 (s, 1H), 2.32-2.19 (m, 1H), 0.50 (d, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 162.7, 158.1, 140.9, 129.5, 129.2, 128.6, 128.5, 128.1, 127.4, 127.2, 126.9, 124.8, 115.4, 115.0, 70.8, 62.7, 48.6, 9.9. Anal. Calcd for $C_{16}H_{16}ClFO$: C, 68.94; H, 5.79. Found: C, 68.98; H, 5.82.

3-Chloro-1-(4-chlorophenyl)-2-methyl-3-phenylpropanol (662): The reaction of 4-chlorobenzaldehyde (3.0 mmol, 0.42 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.58 g (65%) 3-chloro-1-(4-chlorophenyl)-2-methyl-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 7.32-7.18 (m, 9H), 5.50 (d, 1H, J = 2.1 Hz), 4.98 (d, 1H, J = 10.4 Hz), 2.45-2.39 (m, 1H), 2.37 (s, 1H), 0.58 (d, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 141.8, 140.5, 132.6, 128.6, 128.3, 127.4, 126.9, 71.9, 66.5, 48.0, 9.9. Anal. Calcd for $C_{16}H_{16}Cl_2O$: C, 65.10; H, 5.46. Found: C, 64.88; H, 5.40.

3-Chloro-1-(4-bromophenyl)-2-methyl-3-phenylpropanol (663): The reaction of 4-bromobenzaldehyde (3.0 mmol, 0.56 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and

produced 0.61 g (60%) 3-chloro-1-(4-bromophenyl)-2-methyl-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 7.42-7.21 (m, 9H), 5.48 (s, 1H), 5.02 (d, 1H, J = 10.4 Hz), 2.66-2.47 (m, 1H), 2.28 (s, 1H), 0.52 (d, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 142.0, 140.8, 131.1, 128.6, 128.3, 127.3, 126.9, 122.5, 70.9, 64.2, 48.4, 9.9. Anal. Calcd for $C_{16}H_{16}BrClO$: C, 56.58; H, 4.75. Found: C, 56.91; H, 4.71.

3-Chloro-1-(*p*-tolyl)-2-methyl-3-phenylpropanol (664): The reaction of 4-methylbenzaldehyde (3.0 mmol, 0.36 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.30 g (36%) 3-chloro-1-(*p*-tolyl)-2-methyl-3-phenylpropanol, a colorless oil. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 7.37-7.14 (m, 9H), 5.51 (s, 1H), 5.00 (d, 1H, J = 10.3 Hz), 2.35-2.28 (m, 4H), 2.15 (s, 1H), 0.53 (d, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 140.9, 140.5, 136.6, 128.9, 128.6, 128.2, 126.9, 125.5, 72.4, 66.6, 48.1, 10.0. Anal. Calcd for $C_{17}H_{19}ClO$: C, 74.31; H, 6.97. Found: C, 74.12; H, 6.83.

3-Chloro-1-(4-cyanophenyl)-2-methyl-3-phenylpropanol (665): The reaction of 4-cyanobenzaldehyde (3.0 mmol, 0.40 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.83 g (97%) 3-chloro-1-(4-cyanophenyl)-2-methyl-3-phenylpropanol, a colorless crystal, m.p. 153.0-154.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 7.65 (d, 2H, J = 8.4 Hz), 7.52 (d, 2H, J = 8.4 Hz), 7.39-7.31 (m, 5H), 5.65 (s, 1H), 5.02 (d, 1H, J = 10.3 Hz), 2.40-2.30 (m, 1H), 1.87 (s, 1H), 0.49 (d, 3H, J =

6.9 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 149.1, 140.3, 132.1, 128.7, 128.5, 127.5, 126.3, 118.8, 110.7, 71.9, 66.4, 48.1, 9.9. Anal. Calcd for $C_{17}H_{16}ClNO$: C, 71.45; H, 5.64; N, 4.90. Found: C, 71.17; H, 5.63; N, 4.84.

3-Chloro-1-(4-nitrophenyl)-2-methyl-3-phenylpropanol (666): The reaction of 4-nitrobenzaldehyde (3.0 mmol, 0.45 g), (*E*)-β-methylstyrene (3.0 mmol, 0.36 g) and phenylboron dichloride (3.0 mmol, 0.48 g) was carried out as described in **6.4.2.2** and produced 0.87 g (95%) 3-chloro-1-(4-nitrophenyl)-2-methyl-3-phenylpropanol, a yellow crystal, m.p. 121.0-122.0 °C. ^{1}H NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 8.17 (d, 2H, J = 8.6 Hz), 7.57 (d, 2H, J = 8.6 Hz), 7.43-7.24 (m, 5H), 5.05 (d, 1H, J = 10.4 Hz), 2.84 (s, 1H), 2.46-2.34 (m, 1H), 0.49 (d, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ ppm, (*1R, 2R, 3R; 1S, 2S, 3S*)-isomer: 151.3, 146.7, 128.6, 128.2, 127.4, 126.3, 123.3, 71.8, 66.3, 47.91, 9.8. Anal. Calcd for $C_{16}H_{16}ClNO_3$: C, 62.85; H, 5.27; N, 4.58. Found: C, 62.65; H, 5.11; N, 4.55.

LIST OF REFERENCES

List of references

1. Gay-Lussac, J. L.; Thenard, J. L. *Ann. Chim. (Phys.)* **1809**, 69, 204.

2. (a) Brown, H. C.; Holmes, R. R. *J. Am. Chem. Soc.* **1956**, 78, 2173. (b) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry* John Wiley & Sons: New York, **1980**.

3. Ishihara, K. In *Lewis acids in organic synthesis* Yamamoto, H. Ed.; Vol. 1, Wiley: New York; **2000**, pp. 89-130.

4. Guindon, Y.; Therine, M.; Girard, Y.; Yoakim, C. *J. Org. Chem.* **1987**, 52, 1680.

5. Benton, F.; Dillon, T. *J. Am. Chem. Soc.* **1942**, 64, 1128.

6. Toshima, K.; Nagai, H.; Ushiki, Y.; Matsumura, S. *Synlett.* **1998**, 1007.

7. (a) Yamoga, S.; Machii, D.; Nakamura, E.; *J. Org. Chem.* **1991**, 56, 2098. (b) Wulf, W. D.; Gilbertson, S. R. *J. Am. Chem. Soc.* **1985**, 107, 503.

8. (a) Hyatt, J. A.; Raynolds, P. W. *J. Org. Chem.* **1984**, 49, 384. (b) Walker, H. G.; Sanderson, J. J.; Hauser, C. R. *J. Am. Chem. Soc.* **1953**, 75, 4109.

9. (a) Frankland, E.; Duppa, B. F. *Proc. Roy. Soc.* **1859**, 10, 568. and *Annalen*, **1860**, 115, 319. (b) Frankland, E. *J. Chem. Soc.* **1862**, 15, 363. and *Proc. Roy. Soc.*, **1863**, 12, 123.

10. (a) Massey, A. G. *Adv. Inorg. Chem. Radiochem.* **1968**, 10, 1. (b) Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem.* **1982**, 239, 23. (c) Hubbard, J. L.; Fuller, J. C.; Jackson, T. C.; Singaram, B. *Tetrahedron* **1993**, 49, 8311. (d) Brown, H. C.; Murali, D.; Singaram, B. *J. Organomet. Chem.* **1999**, 581, 116.

11. (a) Schlesinger, H. I.; Burg, A. B. *J. Am. Chem. Soc.* **1931**, 53, 4321. (b) Burg, A. B. *J. Am. Chem. Soc.* **1934**, 56, 499.

12. Koester, R.; Wolfgang, F. *Angew. Chem. Int. Ed. Engl.* **1967**, 6, 802.

13. Brown, H. C. *Organic Synthesis via Boranes* John Wiley & Sons: New York, **1975**.

14. Brown, H. C. *Boranes in Organic Chemistry* Cornell University Press: Ithaca, New York, **1972**.

15. Brown, H. C. *Hydroboration* W. A. Benjamin: New York, **1962**.

16. Cragg, G. M. L. *Organoboranes in Organic Synthesis*, Marcel Dekker: New York, **1973**.

17. Patterson, I. *Pure & Appl. Chem.* **1992**, 64, 1821.

18. (a) Brown, H. C.; Ramachandran, P. V. *Pure & Appl. Chem.* **1991**, 63, 307. (b) Singh, V. K. *Synthesis* **1992**, 605.

19. (a) Crane, S. N.; Burnell, D. J. *J. Org. Chem.* **1998**, 63, 5708. (b) Geier, G. R.; Giringh, Y.; Li, F.; Haynes, D. M. Lindsey, J. S. *Org. Lett.* **2000**, 2, 1745. (c) Pelletier, J. D.; Poirier, D. *Tetrahedron Lett.* **1994**, 35, 1051.

20. (a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, 11, 513. (b) Suzuki, A.; Miyaura, N. *Chem. Rev.* **1995**, 95, 2457.

21. Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents* Academic Press: San Diego, CA, **1988**.

22. Brown, H. C.; Ichikawa, K. *J. Am. Chem. Soc.* **1961**, 83, 4372.

23. Gensler, W. J.; Johnson, F.; Sloan, D. B. *J. Am. Chem. Soc.* **1960**, 82, 6074.

24. Lansbury, P. T.; Macleay, R. E. *J. Am. Chem. Soc.* **1965**, 87, 831.

25. Pierre, J.-L.; Handel, H. *Tetrahedron Lett.* **1974**, 15, 2317.

26. Lefour, J. M.; Loupy, A. *Tetrahedron* **1978**, 34, 2597.

27. Sorell, T. N.; Pearlman, P. S. *Tetrahedron Lett.* **1980**, 21, 3963.

28. Hutchins, R. O.; Hoke, D.; Keogh, J. *Tetrahedron Lett.* **1969**, 10, 3495.

29. Hutchins, R. O.; Kandasamy, D.; Maryanoff, C. A. *J. Org. Chem.* **1977**, 42, 82.

30. Brown, H. C.; Krishnamurthy, S. *Tetrahedron* **1979**, 35, 567.

31. (a) Yoon, N. M.; Pak, C. S.; Brown, H. C.; Krishnamurthy, S.; Stocky, T. P. *J. Org. Chem.* **1973**, 38, 2786. (b) Brown, H. C.; Heim, P. *J. Org. Chem.* **1973**, 38, 912.

32. Lane, C. F. *Aldrchimica Acta* **1974**, 7, 7.

33. Subba Rao, B. C.; Thalar, G. P. *Cur. Sci.* **1963**, 404.

34. McCorkindale, N. J.; Roy, T. P.; Hutchinson, S. A.; *Tetrahedron* **1972**, 28, 1107.

35. Curran, W. V.; Angier, R. B. *J. Org. Chem.* **1966**, 31, 3867.

36. Brown, H. C.; Bigley, D. B. *J. Am. Chem. Soc.* **1961**, 83, 3166.

37. Andrews, G. C.; Crawford, T. C. *Tetrahedron Lett.* **1980**, 21, 693.

38. Brown, H. C.; Bigley, D. B.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, 92, 7161.

39. Brown, H. C.; Krishnamurthy, S.; Yoon, N. M. *J. Org. Chem.* **1976**, 41, 1778.

40. Brown, H. C.; Ramachandran, P. V. *Acc. Chem. Res.* **1992**, 25, 16.

41. Mikhailov, B. M.; Bubnov, Yu. N.; Kiselev, V. G. *J. Gen. Chem. USSR*, **1966**, 36, 65.

42. (a) Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Am. Chem. Soc.* **1979**, 101, 2352. (b) Midland, M. M. *Chem. Rev.* **1989**, 89, 1553.

43. Brown, H. C.; Ramachandran, P. V.; Weissman, S. A.; Swaminathan, S. *J. Org. Chem.* **1990**, 55, 6328.

44. Brown, H. C.; Ramachandran, P. V.; Chandrasekharan, J. *Organometallics* **1986**, 5, 2138.

45. Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, 110, 1539.

46. Chandrasekharan, J.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1985**, 50, 5446.

47. Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1976**, 98, 1785.

48. (a) Soundararajan, R.; Matterson, D. S. *J. Org. Chem.* **1990**, 55, 2274. (b) Soundararajan, R.; Matterson, D. S. *Organometallics* **1995**, 14, 4157.

49. Ramachandran, P. V.;Gong, B.; Brown, H. C. *Chirality* **1995**, 7, 103.

50. Midland, M. M.; Zderic, S. A. *J. Am. Chem. Soc.* **1982**, 104, 525.

51. (a) Kharasch, M. S.; Reinmuth, O. *Grignard Reactions of Non-Metallic Substances* Prentice-Hall: New York, **1954**. (b) Blomberg, C.; Hartog, F. A. *Synthesis* **1977**, 18. (c) Larock, R. C. *Comprehensive Organic Transformations* VCH: New York, **1989**, pp 553–567. (d) Sweeny, J. B. In *Comprehensive Organic Functional Group Transformations* Katrizky, A. R.; Meth-Cohn, O.; Rees, C. W.; Ley, S. V. Eds.; Pergamon: Cambridge, **1995**, Vol. 2, pp 37.

52. Wakefield, B. J. *Organolithium Method* Academic: New York, **1988**.

53. (a) Knochel, P.; Singer, R. D. *Chem. Rev.*, **1993**, 93, 2117. (b) Furukawa, J.; Kawabata, N. *Adv. Organomet. Chem.*, **1974**, 12, 103.

54. (a) Reetz, M. T.; Steinbach, R.; Westermann, J.; Urz, R.; Wenderoth, B.; Peter, R. *Angew. Chem. Int. Ed. Engl.* **1982**, 21, 135. (b) Kauffmann, T.; Hopp, G.; Laarmann, B. *Tetrahedron Lett.* **1990**, 31, 511. (c) Kataoka, Y.; Makihira, I.; Utsunomiya, M.; Tani, K. *J. Org. Chem.* **1997**, 62, 8540.

55. (a) Reformatsky, *Chem. Ber.* **1887**, 20, 1210 and **1895**, 28, 2842. (b) Fikstner, A. *Synthesis* **1989**, 571.

56. Shibata, T.; Tabira, H.; Soai, K. *J. Chem. Soc., Perkin Trans.1* **1998**, 117.

57. (a) Negishi, E. *Organometallics in Organic Synthesis* Vol. 1; Wiley-Interscience: New York, **1980**, pp. 304. (b) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, 93, 2207.

58. Roush, W. R.; Grover, P. T. *J. Org. Chem.* **1995**, 60, 3806.

59. Brown, H. C.; Randad, R. A.; Bhatt, K. S.; Zaidlewicz, M.; Racherla, U. S. *J. Am. Chem. Soc.* **1990**, 112, 2389.

60. (a) Jacob, P. III; Brown, H. C. *J. Org. Chem,* **1977**, 42, 579. (b) Kramer, G. W.; Brown, H. C. *J. Org. Chem.* **1977**, 42, 2292.

61. Brown, H. C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, 96, 7765.

62. (a) Wang, Z.; Meng, X. J.; Kabalka, G. W. *Tetrahedron Lett.* **1991**, 32, 1945. (b) Wang, Z.; Meng, X. J.; Kabalka, G. W. *Tetrahedron Lett.* **1991**, 32, 5677 and **1991**, 32, 4619.

63. Brown, H. C.; Rogic, M. M.; Rathke, M. W. *J. Am. Chem. Soc.* **1968**, 90, 6218.

64. Hooz, J.; Linke, S. *J. Am. Chem. Soc.* **1968**, 90, 6891.

65. Brown, H. C.; Kabalka, G. W.; Rathke, M. W.; Rogic, M. M. *J. Am. Chem. Soc.* **1968**, 90, 4165-4166 and 4166-4168.

66. (a) Kabalka, G. W.; Brown, H. C.; Suzuki, A.; Homma, S.; Arase, A.; Itoh, M. *J. Am. Chem. Soc.* **1970**, 92, 710. (b) Kabalka, G. W.; Brown, H. C. *J. Am. Chem. Soc.* **1970**, 92, 712.

67. Mikhailov, B. M.; Baryshnikova, T. K.; Shashkov, A. S. *J. Organomet. Chem.* **1981**, 219, 301.

68. Kabalka, G. W. *Intra-Sci. Chem. Rep.* **1973**, 7, 57.

69. Miyaura, N.; Itoh, M.; Suzuki, A.; Brown, H. C.; Midland, M. M.; Jacob, P. III. *J. Am. Chem. Soc.* **1972**, 94, 6549

70. Kabalka, G. W.; Maddox, J. T.; Bogas, E.; Kelly, S. W. *J. Org. Chem.* **1997**, 62, 3688.

71. Okada, K.; Hosoda, Y.; Oda, M. *Tetrahedron Lett.* **1986**, 27, 6213.

72. (a) Polivka, Z.; Ferles, M. *Chemicke Lisky* **1968**, 62, 869. (b) Suzuki, A.; Hara, S. *Trends Org. Chem.* **1990**, 1, 77. (c) Suzuki, A. *Pure & Appl. Chem.* **1986**, 58, 629. (d) Suzuki, A. *Rev. Heteroat. Chem.* **1997**, 17, 271.

73. Lappert, M. F.; Prokai, B. *J. Organomet. Chem.* **1964**, 1, 384.

74. (a) Blackborow, J. R. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1989. (b) Blackborow, J. R. *J. Organomet. Chem.* **1977**, 128, 161.

75. (a) Suzuki, A. In *Boron Chemistry* Hermanek, S. Ed., World Scientific: New Jersey, **1987**, pp. 273. (b) Suzuki, A. In *Reviews on Heteroatom Chemistry 1*, Oae, S. Ed., MY, Tokyo, **1988**, pp. 291.

76. Hara, S.; Satoh, Y.; Ishiguro, H.; Suzuki, A. *Tetrahedron Lett.* **1983**, 24, 731. and Hara, S.; Dojo, H.; Takinami, S.; Suzuki, A. *Tetrahedron Lett.*,**1983**, 24, 735.

77. (a) Miyaura, N.; Serizawa, H.; Hara, S.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, 107, 972. (b) Satoh, Y.; Serizawa, H.; Hara, S.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, 107, 5225.

78. Hyuga, S.; Takinami, S.; Hara, S.; Suzuki, A. *Tetarhedron Lett.* **1986**, 27, 977.

79. Satoh, Y.; Serizawa, H.; Miyaura, N.; Hara, S.; Suzuki, A. *Tetarhedron Lett.* **1988**, 29, 1811.

80. (a) Lappert, M. F. *Angew. Chem.* **1960**, 72, 36. (b) Joy, F.; Lappert, M. F. *Proc. Chem. Soc.* **1960**, 353. (c) Joy, F.; Lappert, M. F.; Prokai, B. *J. Organomet. Chem.* **1966**, 5, 506.

81. Kabalka, G. W.; Wu, Z. *Tetrahedron Lett*. **2000**, 41, 579.

82. Lansinger, J. M.; Ronald, R. C. *Syn. Commun*. **1979**, 9, 341.

83. (a) Mikhailov, B. M.; Kiselev, V. G.; Bubnov, Yu. N. *Bull. Acad. Sci. USSR Div. Chem. Sci.* **1965**, 865. (b) Mikhailov, B. M.; Bubnov, Yu. N.; Kiselev, V. G. *J. Gen. Chem. USSR*, **1966**, 36, 62.

84. Brwon, H. C.; Ramachandran, P. V. In *Advances in Asymmetric Synthesis* Hassner, A. Ed.; JAI press: Greenwich, CT, **1995**, Vol. 1, 147-210. (b) Brwon, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **1995**, 500, 1.

85. (a) Beardsley, D. A.; Fisher, G. B.; Goralski, C. T.; Nicolson, L. W.; Singaram, G. *Tetrahedron Lett.*, **1994**, 35, 1511. (b) Barrett, A. G. M.; Seefeld, M. A.; Williams, D. J. *J. Chem. Soc., Chem. Commun*., **1994**, 1053.

86. Amrollah-Madidababi, A.; Pham, T. N.; Ashby, E. C. *Synthesis* **1989**, 614.

87. Corre, M. L.; Gheerbrant, E.; Deit, H. L. *J. Chem. Soc. Chem. Commun.* **1989**, 313.

88. Aizpurua, J. M.; Palomo, C. *Tetrahedron lett.* **1984**, 25, 1109.

89. Midland, M. M.; Tramantano, A.; Aderic, S. A. *J. Organomet. Chem.* **1978**, 156, 203.

90. Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetradedron Lett.* **2000**, 41, 5161.

91. Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem*. **1980**, 45, 384.

92. Putokhin, N. I.. *J. Gen. Chem. (USSR)*, **1945**, 15, 332.

93. Krohnke, F.; A Wander, A.-G.; *Ber. Chem.* **1950**, 83, 35.

94. Olah, G. A.; Pavlath, A. E.; Olah, J. A.; Herr, F. *J. Org. Chem.* **1957**, 22, 879.

95. Campbell, J. J.; Glover, S. A.; Hammond, G. P.; Rowbottom, C. A.; *J. Chem. Soc. Perkin Trans. 2* **1991**, 12, 2067.

96. Roberts, B. P.; Wilson, *J. Chem. Soc. C. Chem. Commun*. **1978**, 17, 752.

97. Raucher, S. *Tetrahedron Lett.* **1977**, 18, 3909.

98. Chaintreau, A.; Adrian, G.; Couturier, D. *Syn. Commun*., **1981**, 11, 669.

99. Tait, J. M. S.; Shannon, T. W.; Harrison, A. G. *J. Am. Chem. Soc.* **1962**, 84, 4.

100. Ouertani, M.; Girard, P.; Kagan, H. B. *Bulletin de la Societe Chimique de France* **1982**, 9-10, Pt. 2, 327.

101. Kolker, P. L.; Waters, William A. *J. Chem. Soc.* **1964**, Mar., 1136.

102. (a) Bentley, M. D.; Dewar, M. J. S. *J. Am. Chem. Soc.* **1970**, 92, 3991. (b) Bentley, M. D.; Dewar, M. J. S. *J. Org. Chem*. **1970**, 35, 2707.

103. (a) Sket, B.; Zupan, M. *J. Org. Chem*. **1986**, 51, 929. (b) Anderson, S. N. Ballard, D. H.; Johnson, M. D. *J. Chem. Soc. Perkin Trans. 2* **1972**, 311.

104. Majumdar, S.; Mukhopadhyay, R.; Bhattacharjya, A. *Tetrahedron* **2000**, 56, 8945.

105. Batey, R. A.; Mackay, D. B.; Santhakumar, V. *J. Am. Chem. Soc.* **1999**, 121, 5075.

106. Kabalka, G. W.; Wu, Z.; Trotman, S. E.; Gao, X. *Org. Lett.* **2000**, 2, 255.

107. Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron* **2001**, 57, 1663.

108. Bhatt, M. V.; Kulkarni, S. U. *Synthesis* **1983**, 249.

109. Brown, H. C.; Dhar, R. K.; Ganesan, K.; Singaram, B. *J. Org. Chem.* **1992**, 57, 499.

110. (a) Brown, H. C.; Midland, M. M.; Kabalka, G. W. *Tetrahedron* **1986**, 42, 5523. (b) Brown, H. C.; Midland, M. M. *Tetrahedron* **1987**, 43, 4059. (c)

Bieber, L. W.; Rolim Neto, P. J.; Generino, R. M. *Tetrahedron Lett.* **1999**, 40, 4473. (d) Miyabe, H.; Ueda, M.; Yoshioka, N. Naito, T. *Synlett.* **1999**, 465.

111. (a) Suzuki, A.; Matsumoto, H.; Itoh, M.; Brown, H. C.; Rogic, M. M.; Rathke, M. W. *J. Am. Chem. Soc.* **1967**, 89, 5708. (b) Ollivier, C.; Renaud, P. *Chem. Eur. J.* **1999**, 5, 1468. (c) Brown, H. C.; Kabalka, G. W. *J. Am. Chem. Soc.* **1970**, 92, 714.

112. Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron Lett.* **2000**, 41, 5161.

113. Brown, H. C.; Ravindran, N.; Kulkarni, U. *J. Org. Chem.* **1979**, 44, 2417.

114. Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, 60, 3218.

115. Huitric, A. C.; Kumler, W. D. *J. Am. Chem. Soc.* **1956**, 78, 1147.

116. Cervinka, O.; Belovsky, O. *Collect. Czech. Chem. Commun.* **1967**, 32, 4149.

117. Kristic, V.; Muskatirovic, M. *Liebigs Ann. Chem.* **1980**, 11, 1637.

118. Szmuszkovicz, J.; Skaletzky, L. L. *J. Org. Chem.* **1967**, 32, 3300.

119. Barcus, R. L.; Hadel, L. M.; Johnston, L. J.; Platz, M. S.; Savino, T. G.; Scaiano, J. C. *J. Am. Chem. Soc.* **1986**, 108, 3928.

120. Geigy Chem. Corp. US 34,448,200; 1963; *Chem. Abstr.* **1969**, *71*, 60981.

121. Kasper, F.; Muller, H.-G. *J. Prakt. Chem.* **1966**, 34, 283.

122. Blanch, A. I.; Fernandez, G. F.; Perez, O. R.; Plumet, J. *An. Quim.* **1978**, 74, 70.

123. Owen, J. R.; Saunders Jr., W. H. *J. Am. Chem. Soc.* **1966**, 88, 5809.

124. Kabalka, G. W.; Maddox, J. T.; Bogas, E. *J. Org. Chem.* **1994**, 59, 5530.

125. Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, 106, 3693.

126. Eprova, Ltd., GB 1,014,668; *Chem Abstr.* **1965**, *62*, 14635f.

127. Franks, S.; Hartley, F. R. *J. Chem. Soc. Perkin Trans. 1* **1980**, 2233.

128. Buu-Hoi, N. P.; Xuong, N. D.; Diep, B. K. *J. Org. Chem.* **1961**, 26, 1673.

129. Nicolaus, R. *Ann. Chim (Rome)*, **1953**, 43, 488.

130. Stoll, W. G. (Geigy Chemical Corp.). US 3,448,200; 1963; *Chem. Abstr.* **1969**, 71, 60981.

131. Levene, M. J. *Biol. Chem.* **1926**, 70, 377.

132. Coleman, J. P.; Shah-Malak, F. I.; Utley, J. H. P. *J. Chem. Soc.* **1970**, 666.

133. Hamlin, K. E.; Weston, A. W.; Fischer, F. E.; Michaels, J. R. J. *J. Am. Chem. Soc.* **1949**, 71, 2731.

134. (a) Macquire, A. R. In *Comprehensive Organic Functional Group Transformations*, Katristzky, A. R.; Meth-Cohn, O.; Rees, C. W., Eds; Pergamon Press, New York, **1995**, Vol. 1, p. 719. (b) Hurdlick, P. F.; Peterson, D. J. *J. Am. Chem. Soc.* **1975**, 1464. (c) Julia, M. *Pure Appl. Chem.* **1985**, 57, 763.

135. Mcmurry, J. E.; Fleming, M. P. *J. Am. Chem. Soc.* **1974**, 96, 4708.

136. Engman, L. *J. Org. Chem.* **1984**, 49, 3559.

137. Vedejs, E.; Dolphin, J. M.; Stolle, W. T. *J. Am. Chem. Soc.* **1979**, 101, 249.

138. Katritzky, A. R.; Tymoshenko, D. O.; Belyakov, S. A. *J. Org. Chem.* **1999**, 64, 3332.

139. (a) Kabalka, G. W.; Hutchina, R. O.; Natale, N. R.; Yang, D. T. C.; Broach, V. *Org. Synth*esis **1979**, 59, 42. (b) Kabalka, G. W.; Simmers, S. T. *J. Org. Chem.* **1981**, 46, 1217.

140. Courtney, S. H.; Balk, M. W.; Philips, L. A.; Webb, S. P.; Yang, D.; Levy, D. H.; Fleming, G. R. *J. Chem. Phys.* **1988**, 89, 6697.

141. (a) Mitchell, P. J.; Phillips, L. *J. Chem. Soc. Chem. Commun.* **1975**, 908. (b) Giger, T.; Wigger, M.; Audetat, S.; Benner, S. A. *Syn. Lett.* **1998**, 6, 688.

142. Sengupta, S.; Bhattacharyya, S.; Sadhukhan, S. K. *J. Chem. Soc. Perkin Trans.1* **1998**, 2, 275.

143. Mitsumori, T.; Koga, N.; Iwamura, H. *J. Phys. Org. Chem.* **1994**, 7, 43.

144. (a) Wallace, T. W.; Wardell, I.; Li, K. –D.; Leeming, P.; Redhouse, A. D.; Challand, S. R. *J. Chem. Soc. Perkin Trans. 1* **1995**, 18, 2293. (b) Terfort, A.; Brunner, H. *J. Chem. Soc. Perkin Trans. 1* **1996**, 12, 1467.

145. Warner, P.; Sutherland, R. *J. Org. Chem.* **1992**, 57, 6294.

146. (a) Howard, L. B.; Hilbert, G. E.; Wiebe, R.; Gaddy, V. L. *J. Am. Chem. Soc.* **1932**, 54, 3628. (b) Silverman, M.; Bogert, M. T. *J. Org. Chem.* **1946**, 11, 34.

147. Fujio, M.; Maeda, Y.; Goto, M.; Saeki, Y.; Mishima, M.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1993**, 66, 3015.

148. Shankar, B. K. R; Shechter, H. *Tetrahedron Lett.* **1982**, 23, 2277.

149. Guesten, H.; Salzwedel, M. *Tetrahedron* **1967**, 23, 173.

150. (a) Fu, S.-C.; Sah, P. P. T. *J. Am. Chem. Soc.* **1942**, 64, 1482. (b) Barber, H. J.; Slack, R. *J. Am. Chem. Soc.* **1943**, 65, 1776.

151. Brown, H. C.; Basavaiah, D; Kulkarni, S. U. *J. Org. Chem.* **1982**, 47, 3808.

152. Brinckman, F. E.; Stone, F. G. A. *J. Am. Chem. Soc.* **1960**, 82, 6218.

153. Satoh, Y.; Tayano, T.; Koshino, H.; Hara, S.; Suzuki, A. *Synthesis* **1985**, 406.

154. Kawamura, F.; Tayano, T.; Satoh, Y.; Hara, S.; Suzuki, A. *Chem. Lett.* **1989**, 1723.

155. Satoh, Y.; Tayano, T.; Hara, S.; Suzuki, A. *Tetrahedran Lett.* **1989**, 30, 5153.

156. (a) Vieregge, H.; Bos, H. J. T.; Arens, J. F. *Rec. Trav. Chim.* Pays-Bas. **1959**, 78, 664. (b) Bos, H. J. T.; Arens, J. F. *Rec. Trav. Chim.* Pays-Bas. **1963**, 82, 845.

157. Kabalka, G. W.; Wu, Z.; Ju, Y. *Org. Lett.* **2002**, 4, 1491.

158. (a) Wagniere, G. H. *The chemistry of the carbon-halogen bond* Willey: New York, **1973**. (b) Porret, D.; Goodev, C. G. *Proc. R. Soc. London A* **1958**, 31, 165.

159. (a) Cella, J. A. *J. Org. Chem.* **1982**, 47, 2125. (b) Kaur, G.; Kaushik, M.; Trehan, S. *Tetrahedron Lett.* **1997**, 38, 2521. (c) Rubin, M.; Gevorgyan, V. *Org. Lett.* **2001**, 3, 2705.

160. (a) Mikami, K.; Shimizhu, M. *Chem. Rev.* **1992**, 92, 1021. (b) Evans, D. A.; Bargey, C. S.; Paras, N. A.; Vojkovsky, T.; Tregay, S. W. *J. Am. Chem. Soc.* **1998**, 120, 5824. (c) Snider, B. B. *Acc. Chem. Res.* **1980**, 13, 426.

161. (a) Wovkulich, P. M.; Uskokovich, M. R. *J. Org. Chem.* **1982**, 47, 1600. (b) Wovkulick, P. M.; Barcelos, F.; Batcho, A. D.; Sereno, J. F.; Baggiolini, E. G.; Hennessy, B. M.; Uskokovich, M. R. *Tetrahedron* **1984**, 40, 2283.

162. (a) Blomquist, A. T.; Himies, R. J. *J. Org. Chem.* **1968**, 33, 1156. (b) Blomquist, A. T.; Himies, R. J.; Meador, J. D. *J. Org. Chem.* **1968**, 33, 2462. (c) Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, 104, 555. (d) Malladi, R. R.; Li, N.-S.; Tejedor, D.; Kabalka, G. W. *Synth. Commun.* **2000**, 30, 3163.

163. (a) Gill, G. B.; Parrot, S. J.; Wallace, B. *J. Chem. Soc., Chem. Commun.* **1978**, 655. (b) Gill, G. B.; Wallace, B. *J. Chem. Soc. Chem. Commun.* **1977**, 380; **1977**, 382. (c) Benner, J. P.; Gill, G. B.; Parrot, S. J.; Wallace, B. *J. Chem. Soc. Perkin Trans. 1* **1984**, 291; **1984**, 331. (d) Benner, J. P.; Gill, G.;B.; Parrot, S. J.; Wallace, B.; Begley, M. *J. Chem. Soc. Perkin Trans. 1* **1984**, 315.

164. Snider, S. W.; van Straten, J. W. *J. Org. Chem.* **1979**, 44, 3567.

165. Behr, A.; Fiere, M. *Eur. J. Lipid Sci. Technol.* **2000**, 102, 212.

166. Vidari, G.; Bonicelli, M. P.; Anastasia, L.; Zanoni, G. *Tetrahedron Lett.* **2000**, 41, 3471.

167. Peidro, L.; Le Roux, C.; Laporterie, A.; Dubac, J. *J. Organomet. Chem.* 1996, 521, 397.

168. Houston, T. A.; Tanaka, A.; Koreeda, M. *J. Org. Chem.* **1993**, 58, 4287. (b) Cartaya-Marin, C. P.; Jackson, A. C.; Snider, B. B. *J. Org. Chem.* 1984, 49, 2443.

169. (a) Wada, M. *Chem. Lett.* **1981**, 153. (b) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, 103, 2127.

170. Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron Lett.* **2001**, 42, 5793.

171. (a) Mizuno, A.; Miya, M.; Kamei, T.; Shibata, M.; Tatsuoba, T.; Nakanishi, K.; Takiguchi, C.; Hadaka, T.; Yamaki, A.; Inomata, N. *Chem. Pharm. Bull.* **2000**, 48, 1129. (b) Ocal, N.; Turgut, Z.; Kaban, S. *J. Heterocyclic Chem.* **1998**, 35, 1349. (c) Yoshida, N.; Osuka, A. *Org. Lett.* **2000**, 2, 2963 (d)

Rooke, N.; Li, D. - J.; Keung, W. M. *J. Med. Chem.* **2000**, 43, 4169. (e) Grimm, F. W.; Hafner, K. *Tetrahedron* **2000**, 56, 4239. (f) Wang, Y.; Kurchan, A. N.; Barnhurst, L. A.; Kutataladze, A. G. *Org. Lett.* **2000**, 2, 1133. (g) Singh, M. S.; Singh, K. K. *Heterocycles* **2000**, 53, 851.

172. (a) Leonel, E.; Dolhem, E.; Devaud, M.; Paugam, J. P.; Nedelec, J. Y. *Electrochim. Acta* **1997**, 42, 23125. (b) Miranda, M. A.; Perez-Prieto, J.; Font-Scenchis, E.; Konya, K.; Scaiao, J. C. *J. Org. Chem.* **1997**, 62, 5713.

173. Kuck, D.; Schuster, A.; Paisdor, B.; Gestmann, D. *J. Chem. Soc., Perkin Trans. 1* **1995**, 721.

174. Buhle, E. L.; Moore, A. M.; Wiselogle, F. Y. *J. Am. Chem. Soc.* **1943**, 65, 29.

175. Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron Lett.* **2003**, 44, 1187.

176. (a) Gardner, I. J.; Noyes, R. M. *J. Am. Chem. Soc.* **1961**, 83, 2409. (b) Banks, J. T.; Garcia, H.; Miranda, M. A.; Perez-Prieto, J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1995**, 117, 5049.

177. Perez-Prieto, J.; Miranda, M. A.; Font-Sanchis, E.; Konya, K.; Scaiano, J. C.; *Tetrahedron Lett.* **1996**, 37, 4923.

178. (a) Devanathan, W.; Arumugam, J. A. *Curr. Sci.* **1965**, 34, 429. (b) LaLonde, R. T.; Ferrara, P. B.; Debboli, A. D. *J. Org. Chem.* **1972**, 37, 1094.

VITA

Yuhong Ju was born on October 2, 1965 in Lanzhou city, P. R. China. She enrolled the high school of Gansu Normal University (the best high school in Gansu Province) in 1981. She entered Lanzhou University in 1984 and got the Bachelor of Science degree majoring in polymer chemistry in 1988. She had worked in the Paint and Coating Industry Research Institute of the Ministry of the Chemical Engineering of P. R. China as a chemical engineer since 1988. In February 1998, she was awarded a scholarship from China Scholarship Council and came to Oak Ridge National Laboratory as a visiting scholar. She joined the Department of Chemistry, University of Tennessee, Knoxville in August 1999 under the direction of Dr. George W. Kabalka and received her Ph.D in August, 2003. She was awarded a postgraduate fellowship by Oak Ridge Institute for Science and Education starting July, 2003 to work in National Risk Management Research Laboratory of U.S. Environmental Protection Agency, Cincinnati, OH.

Yuhong Ju married Qifeng Tao in 1991 and they have a daughter Yuchen (Nina) Tao who was born on April 20, 1992.