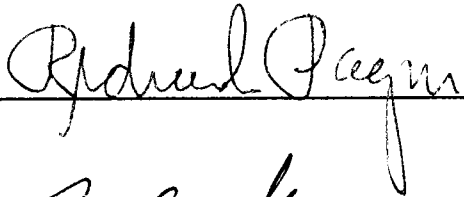


To the Graduate Council:

I am submitting herewith a thesis written by Kurt Edric Vagle entitled "Organic Reactions with Boronated Alumina. I. The Diels-Alder Reaction. II. Amidolysis of Esters". I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Chemistry.


George W. Kabalka, Major Professor

We have read this thesis
and recommend its acceptance:




Accepted for the Council:


Associate Vice Chancellor
and Dean of the Graduate School

Organic Reactions with Boronated Alumina

I. The Diels-Alder Reaction

II. Amidolysis of Esters

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Kurt Edric Vagle

May, 1995

*To my wife, Senta, for her constant encouragement, understanding
and faith in my abilities. I love you.*

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Thanks to Mom and Dad who sacrificed so much to make sure that I always had the best opportunities available, without them, none of this would have been possible. I love you both.

Thanks to Mom and Dad Jorgensen who gave me Senta and continue to give us love and support.

Finally, I must thank our zoo. Homer, our dog, has been with us the longest and has put up with quite a bit of moving and cramped living arrangements. Kitty, our cat, puts up with us. Herbie, our youngest dog, loves us almost as much as he loves Kitty and a heated waterbed.

ABSTRACT

Boronated aluminas were used as Lewis acid catalysts in the Diels-Alder reaction of methyl acrylate and isoprene. The results were compared to the methyl acrylate and isoprene Diels-Alder reaction that is catalyzed by dissolved Lewis acids. The amidolysis reaction of methyl phenylacetate and aniline was carried out using bromo-boronated alumina as the Lewis acid catalyst.

The complexes of B-bromo and B-chlorocatecholborane with crotonaldehyde were studied using proton NMR. The approximate conformation of the complexes were determined using rotating frame Overhauser enhancement spectroscopy (ROESY).

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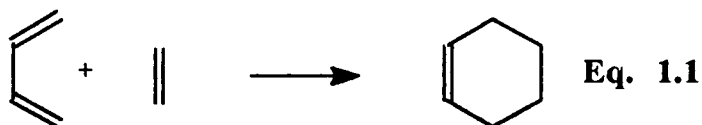
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CHAPTER 1

Introduction

The Diels-Alder reaction, which is an example of a [4 + 2] cycloaddition reaction, is one of the most important reactions in chemistry (eq. 1.1). The formation of two carbon-carbon sigma bonds and one carbon-carbon pi bond makes it very attractive to synthetic chemists who need to form functionalized six-membered rings. The reaction requires a 1,3-diene and an olefin which is often referred to as the dienophile.



The attractiveness of the Diels-Alder reaction in synthesis is enhanced by its predictability.¹ Even though the Diels-Alder often gives mixtures of products when unsymmetrical reactants are used, usually one predominates over the others. There are four variables of the Diels-Alder reaction that contribute to the nature of the reaction and distribution of products.²

Firstly, acyclic 1,3-dienes exist in *s-cis* or *s-trans* conformations (Fig. 1.1). The Diels-Alder reaction demands that the diene adopt the *s-cis* conformation.³ Dienes that are fixed *s-trans* do

not give Diels-Alder adducts because this would require that the resultant product, a six-membered ring, contain a *trans* double bond, a molecule that would be energetically unfavorable.

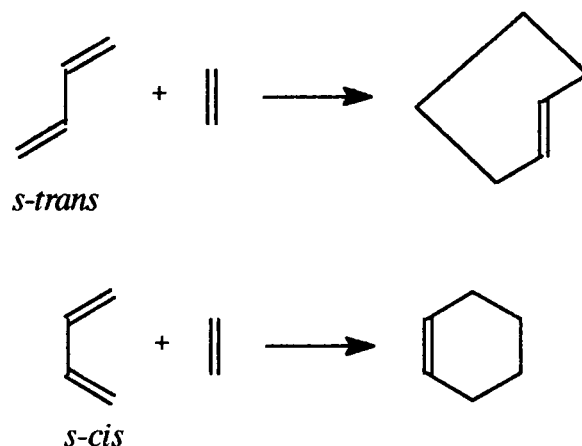
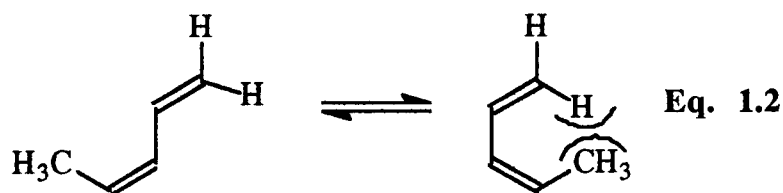
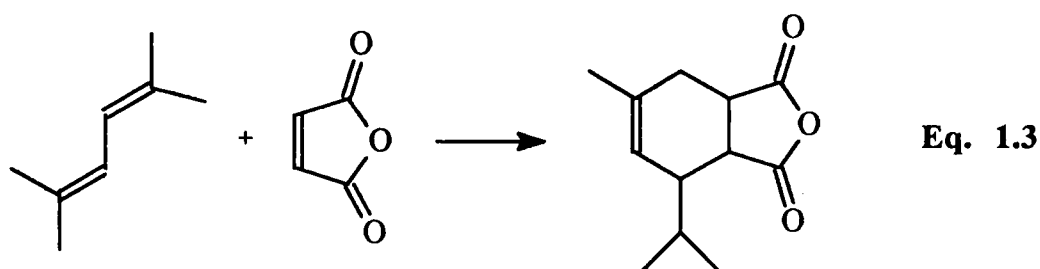


Fig. 1.1 *s-Cis* and *s-trans* butadienes and their respective Diels-Alder products. The concerted nature of the Diels-Alder would require that the *s-trans* butadiene produce a thermally unstable *trans* double bond within a cyclohexene ring.

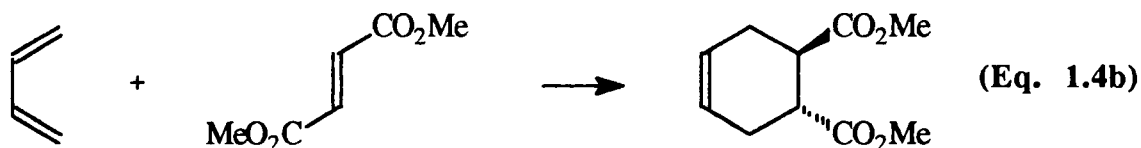
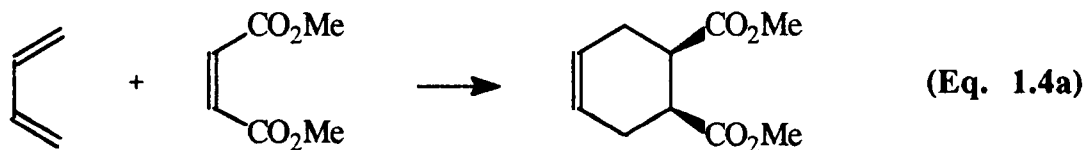
Fixed *s-trans* dienes such as 3-methylenecyclohexene do not react with dienophiles to afford Diels-Alder adducts.¹ Similarly, acyclic dienes that are *cis*-1-substituted or *cis,cis*-1,4-substituted often have pronounced reductions in reaction rates with respect to their *trans*-substituted counterparts.¹ Steric strain does not allow the *cis* dienes to assume the *s-cis* conformation; therefore, the reaction rates are greatly reduced.



2,5-Dimethyl-2,4-hexadiene is an example of a diene for which the *s-cis* conformation is extremely strained. It reacts with maleic anhydride, a very reactive dienophile, only at high temperatures after rearranging to a less strained diene, 2,5-dimethyl-1,3-hexadiene.¹ (Eq. 1.3).



The second factor affecting the nature of the reaction occurs during the approach of the reactants. Once the proper diene conformation is achieved, the reactants may approach on parallel planes, one over the other. The positioning of the reactants in this manner and the concerted, suprafacial nature of this cycloaddition allow the relative stereochemistry of the diene and dienophile to be retained in the cyclization process.⁴ This phenomenon was recognized early in the history of the Diels-Alder reaction by Alder and Stein and is often referred to as the *cis* principle.⁵ The reaction of 1,3-butadiene and dimethyl maleate gives the *cis* adduct, for example, while dimethyl fumarate gives the *trans* adduct.⁶ (Eq. 1.4a,b)



The third variable deals with the regioselectivity of the reaction when unsymmetrical reactants are used. When the reactants both are mono-substituted, two products are often generated. These products are usually called *ortho*-, *para*- and *meta*-like. Frontier orbital interactions between the reactants account for both the distribution of products and the rates of these reactions.² There are three basic types of Diels-Alder reactions that have three distinct frontier orbital interactions. The three types of Diels-Alder reactions are classified as normal, inverse and neutral electron demand reactions.⁷ These classifications are defined by the observed increase in rate when the reactants are substituted with electron-withdrawing or releasing groups. The rate increases in normal demand reactions when the diene bears an electron-releasing group (ERG) and the dienophile has an electron-withdrawing group (EWG). The predominate HOMO-LUMO interaction is between the HOMO of the diene and the LUMO of the dienophile. In an inverse demand reaction, the rate is increased by the EWG on the diene and the ERG on the dienophile. The predominate HOMO-LUMO interaction is between the HOMO of the

dienophile and the LUMO of the diene. The rate is not affected by substituents in neutral demand reactions, and both HOMO-LUMO interactions influence regioselectivity. The predominant HOMO-LUMO interactions are illustrated in Figure 1.2.

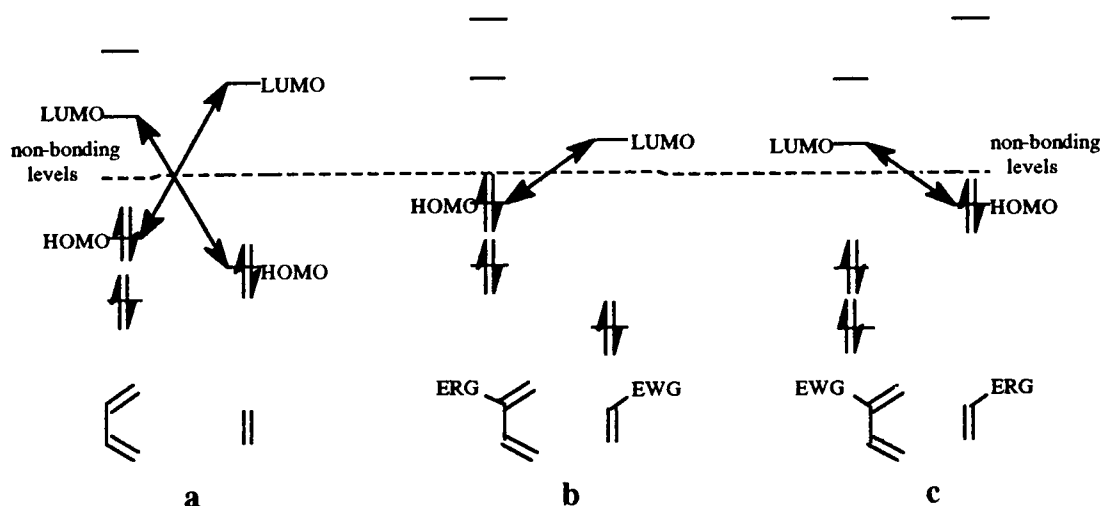


Fig. 1.2 Predominant frontier orbital interactions in a) neutral, b) normal and c) inverse demand Diels-Alder reactions. Adapted from Lowry, T.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry, Third ed.* Harper Collins, 1987. p. 922

There is equal probability of the formation of the meta-substituted and the para-substituted adducts in the normal demand reaction if only the HOMO-LUMO energy gap or the phases of the molecular orbitals are considered. This applies to any HOMO-LUMO Diels-Alder interaction (Fig. 1.3). The trends seen in most data, however, suggest that there is usually a preference for one adduct over any other possibilities.¹

The coefficients of the four carbons that form the two new σ -bonds largely account for this observed regiochemical preference.⁸ In the case of a normal demand Diels-Alder, a butadiene with an

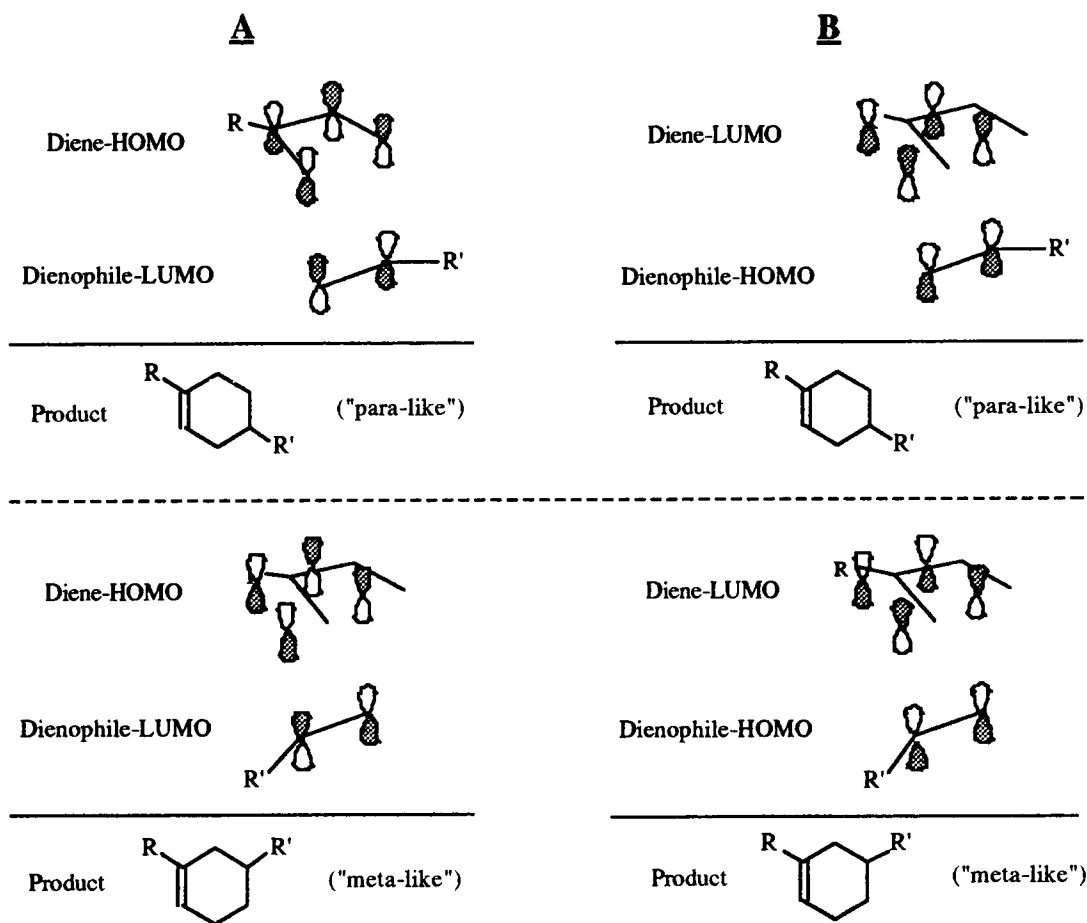


Fig. 1.3 Possible orientations of 2-substituted dienes and 1-substituted dienophiles in A) normal and B) inverse demand Diels-Alder reactions. There is equal probability of either the *"meta-like"* or *"para-like"* products being formed in any Diels-Alder reaction, however, equal distribution of products is not usually observed.

electron-releasing substituent on carbon-1 has a large positive coefficient on carbon-1 and a very small negative coefficient on carbon-4. A 2-substituted butadiene has the large positive coefficient at the 4 position and a small negative coefficient on

carbon-1. The dienophile, which has an electron withdrawing group, has a large positive coefficient on carbon-1 with a small negative coefficient on carbon-2.⁸ (Fig. 1.4)

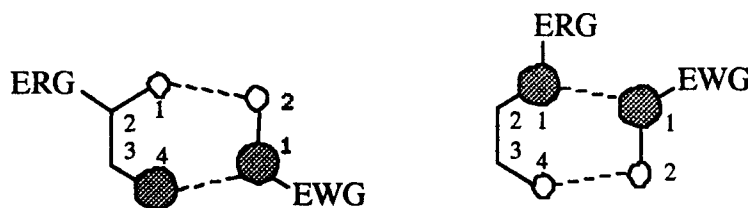
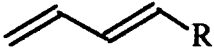
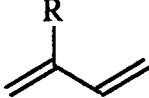


Fig. 1.4 Qualitative representation of HOMO and LUMO orbital coefficients for normal demand Diels-Alder reactions.

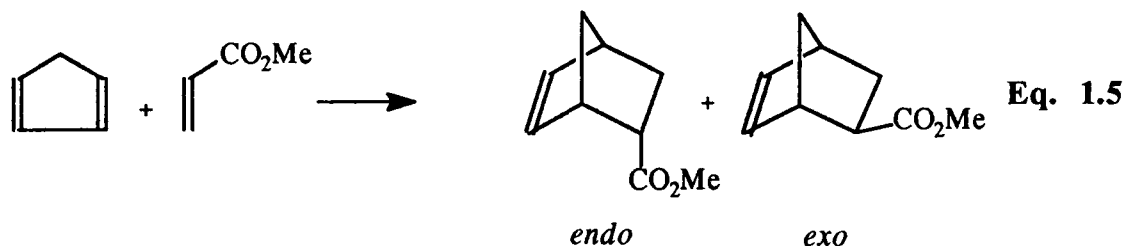
Ortho-substituted adducts are favored for 1-substituted butadienes and para-substituted adducts for 2-substituted butadienes in normal demand Diels-Alder reactions because of these coefficients (Table 1.1).

Table 1.1 Regioselectivity of Diels-Alder reactions with substituted butadienes with methyl acrylate.

R	 (% ortho)	 (% para)
Me	88	70
Ph	>98	>96
COOH	83	
NHCO ₂ Et	98	
OMe	88	70
SPh	>98	80
SiR _i	75(R _i =Me)	77(R _i =Et)

Adapted From Fringuelli, F.; Taticchi, A. Dienes in the Diels-Alder Reaction. John Wiley and Sons, Inc. 1990. p. 49.

The fourth variable deals with the diastereoselectivity of the reaction. When the diene is either 1-substituted or 1,4-disubstituted, *endo* and *exo* addition is possible.



The *endo* mode of addition has the more sterically demanding transition state. The dienophile is required to approach the diene on a parallel plane in a manner where the substituent is closest to the unsaturation of the diene. *Exo* addition is sterically less demanding, but surprisingly, this mode of addition is usually less favored than *endo*. This is especially true when the electron-withdrawing substituent is unsaturated, such as with carbonyl-containing groups. This is often referred to as the Alder rule and is most likely due to secondary orbital effects between the substituent and the diene (Fig. 1.5).^{5,9}

Until 1960, the Diels-Alder reaction was synthetically useful only for a few dienophiles which had high reactivity.⁴ Because the reaction is thermally activated, the reaction was limited to reagents that could withstand thermal conditions for long periods of time without breaking down. Yeats and Eaton reported that the Lewis acid, aluminum trichloride, considerably increased the rate of

reaction for many Diels-Alder reactions.¹⁰ Synthetic chemists increased their attention on the Lewis acid-catalyzed Diels-Alder reaction because a wider variety of less reactive dienophiles could be used under milder conditions. Furthermore, the reactions gave enhanced regio- and stereoselectivity.^{11,12} (Eq. 1.6 a and b)

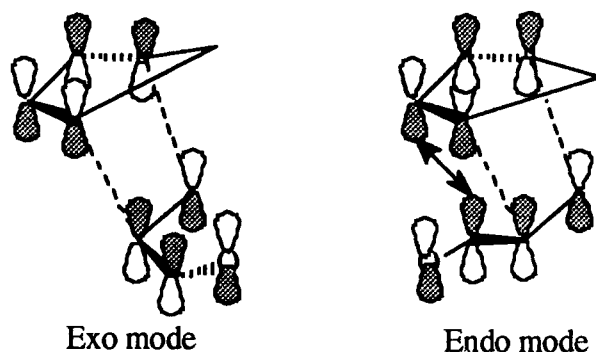
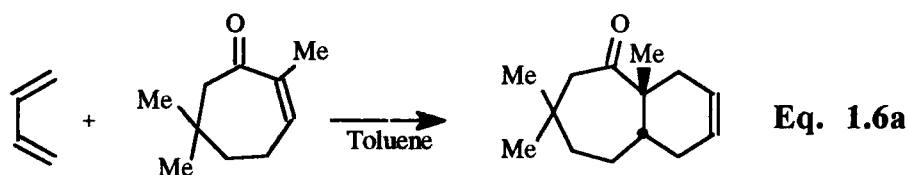
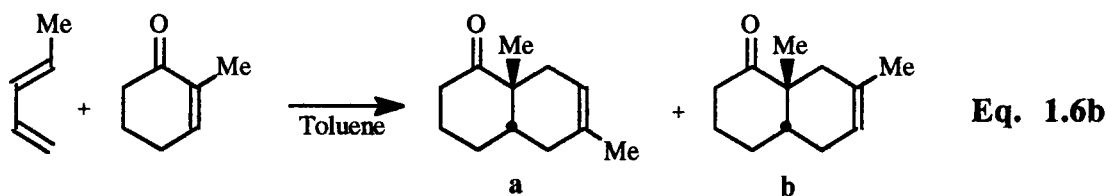


Fig. 1.5 Secondary orbital overlap may account for the endo mode of addition being favored over the sterically less demanding exo mode. The double-headed arrow shows the points of secondary orbital interaction.



	Conditions	Yield
Thermal	150°C, 144 h.	6%
Catalyzed	25°C, 18 h, AlCl ₃	95%



	Conditions	Yield	a/b
Thermal	150°C, 142 h.	20%	1.9
Catalyzed	25°C, 17 h., AlCl ₃	79%	32

α,β -Unsaturated carbonyl compounds are probably the most widely used dienophiles in normal Diels-Alder reactions.^{2,4} It is believed that Lewis Acids increase the rate of these Diels-Alder reactions by complexation to the Lewis basic carbonyl oxygen (Fig. 1.6).² This lowers the energy of the dienophile HOMO and LUMO and increases the reactivity of the carbon-carbon double bond by polarizing the double bond even more than it was initially.

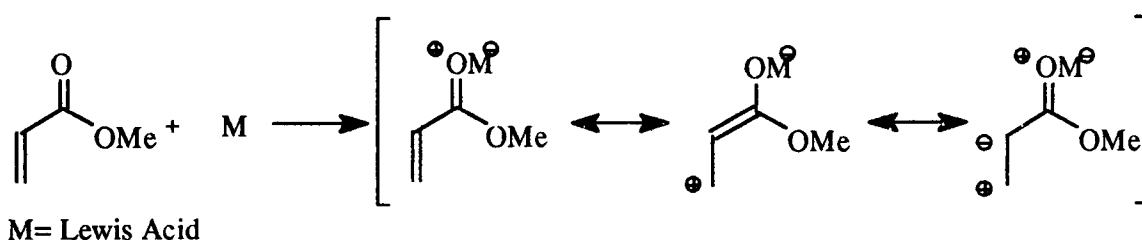


Fig. 1.6 Resonance structures of complexed α,β -unsaturated carbonyl compounds.

It has been shown that many inorganic solids such as silica gel¹³, alumina¹⁴, and zeolites¹⁵ catalyze the Diels-Alder reaction. Often, the Diels-Alder reaction is not of primary interest, but rather it is a probe that provides evidence about the nature of the surface being studied.^{14e} However, these solids may also be synthetically useful catalysts that give better regio- and stereoselectivity than traditional Lewis acid catalysts in solution.

Alumina has been the focus of much attention in this area. Models of the surface of alumina have been proposed by Knozinger and Ratnasamy.¹⁶ The surface of unactivated γ -alumina is covered by hydroxy groups which may be removed by heating. Heating

causes adjacent hydroxy groups to form H_2O and O^{2-} (Fig 1.7). This exposes the underlying Al^{3+} sites, the sites responsible for the solid's catalytic activity in the Diels-Alder reaction. The activation of alumina at higher temperatures exposes even more of these Lewis acid sites.

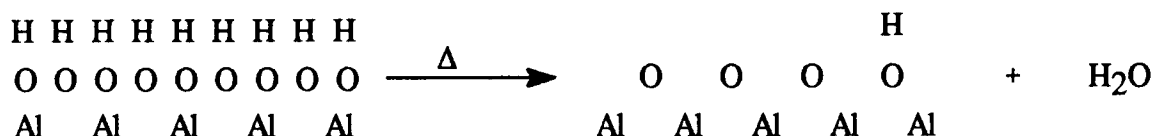


Fig 1.7 Activation of alumina by heat

Even stronger Lewis acids can be created using alumina as a solid support for other Lewis acids. This has been done using aluminum (III) chloride and titanium chloride.^{13d} The boron trihalides also modify the surface of alumina in a similar fashion (Fig. 1.8).^{15d}

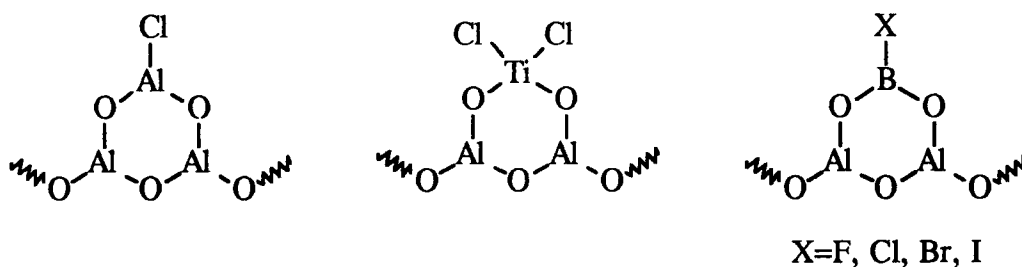


Fig. 1.8 Lewis acid modified aluminas

A comparison of the acid strength (H_0) of alumina at different levels of activation and the four BX_3 -modified aluminas reveals the modified aluminas to have markedly greater acidity. The trend

indicates that the two Lewis acid sites now present on the surface work to create an even more acidic medium. (Table 1.2)

Table 1.2 H_0 measurements of various alumina and modified alumina surfaces using Hammet base indicators

Solid	H_0	Solid	H_0
Al_2O_3 (unact'd)	$> +6.8^b$	Al_2O_3/BF_3	$+0.8 \rightarrow -3.0^b$
Al_2O_3 (100 °C) ^a	$+4.8 \rightarrow +2.0^b$	Al_2O_3/BCl_3	$-3.0 \rightarrow -8.2^b$
Al_2O_3 (200 °C) ^a	$-3.0 \rightarrow -8.2^b$	Al_2O_3/BBr_3	$< -13.2^b$
Al_2O_3 (300 °C) ^a	$-3.0 \rightarrow -8.2^b$	Al_2O_3/BI_3	$< -13.2^c$
Al_2O_3 (400 °C) ^a	$-3.0 \rightarrow -8.2^b$		

^a Activation Temperature

^b Data from Lee Tan, L.C., *Studies of Organic Reactions on Alumina*. Doctor of Philosophy Dissertation, University of Tennessee, Knoxville, TN, 1992.

^c Data from unpublished work of McGinnis, M.

Modified aluminas are unique systems in which to observe the Diels-Alder reaction. Significant yields of products are attained even in the absence of solvents which raises the possibility of environmentally safer processes that use fewer carcinogenic solvents and eliminates serious and expensive cleanup of acidic water.

CHAPTER 2

Results and Discussion

Alumina that is activated by heating to 400°C catalyzes the Diels-Alder reaction between acrylate esters and 1,3-dienes because activation exposes Lewis acid sites which are able to coordinate with the Lewis basic carbonyl oxygen of the dienophile.^{14c} The boronated aluminas which show even greater Lewis acidity may have even better catalytic activity resulting in higher yields and selectivities. The reaction of methyl acrylate with isoprene on various boron trihalide-modified aluminas was chosen to examine this possibility.

The fluoro-boronated alumina was prepared in a dry flask under argon by adding 1 mmol of $\text{BF}_3 \cdot \text{etherate}$ to 1 gram of Brockmann Activity I neutral alumina stirring in a hexanes slurry. The slurry was allowed to stir for 3 hours. The solvent was removed *in vacuo* leaving a white solid that was air sensitive. Heat was applied to the flask to eliminate the complexed ether. The solid was then used immediately or transferred, under argon, to a flame-dried flask for storage.

The chloro- and bromo-boronated aluminas were prepared in a dry flask under argon by adding 1 mL of 1 M BCl_3 or BBr_3 in hexanes to 1 gram of Brockmann Activity I neutral alumina stirring

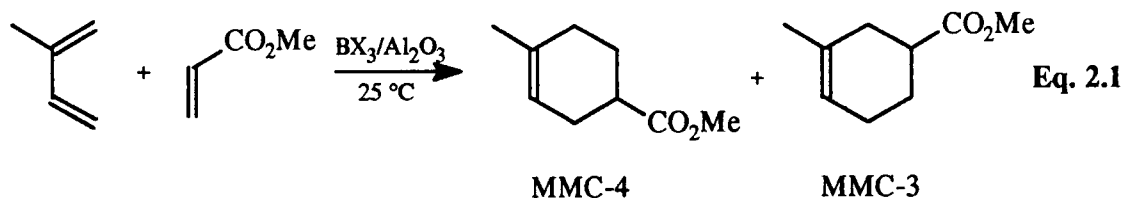
in a hexanes slurry. The slurry was allowed to stir for 3 hours. The solvent was removed *in vacuo* in each case, leaving a white solid in the case of $\text{BCl}_3/\text{Al}_2\text{O}_3$ and a light beige solid in the case of $\text{BBr}_3/\text{Al}_2\text{O}_3$. Each solid was air sensitive, releasing HX. The solids were then used immediately or transferred, under argon, to a flame-dried flask for storage.

The iodo-boronated alumina was prepared in a dry flask under argon by adding 1 mmol $\text{BH}_3\cdot\text{DMS}$ to 1 gram of Brockmann Activity I neutral alumina stirring in a hexanes slurry. The slurry was allowed to stir for 3 hours. Iodine (1 equivalent) dissolved in hexanes was added to the slurry. The solvent was removed *in vacuo* leaving a dark amber solid that reacted violently when exposed to air. The solid was then used immediately or transferred, under argon, to a flame-dried flask for storage.

A. Diels-Alder Reaction of Methyl Acrylate and 2-Methyl-1,3-Butadiene on Boronated Alumina.

The Diels-Alder reactions of methyl acrylate and isoprene (Eq. 2.1) were run using a 1:1 mole ratio of catalyst to dienophile. The modified alumina had a loading of 1.0 mmol of BX_3 ($\text{X} = \text{F}, \text{Cl}, \text{Br}, \text{I}$) per gram of alumina. Therefore, 5.0 mmol of methyl acrylate was added to a slurry of 5.0 g of boronated alumina in 10 mL of toluene. The reaction mixture was allowed to stir for 10 minutes before 5.0

mmol of isoprene was added. The reaction was allowed to run for 3 hours at room temperature before workup.



The products, a mixture of methyl 3-methylcyclohex-3-enecarboxylate (MMC-3) and methyl 4-methylcyclohex-3-enecarboxylate (MMC-4), were extracted from the surface with three aliquots of 50% methanol and hexanes after which the solution was filtered through celite and a glass-fritted filter and the solvent was removed *in vacuo*. Decane (2.0 mL) was added as an internal standard for analysis via GC/MS. The results of these reactions are tabulated on Table 2.1.

Table 2.1 Reaction of methyl acrylate (MA) and isoprene (IP) on boronated aluminas in the presence of toluene.

BX ₃ /Al ₂ O ₃	g BX ₃ /Al ₂ O ₃	MA(mMol)	IP(mMol)	Meta:Para	Yield
X=F	5.00	9.19	22.29	1 : 5.8	0.80%
X=Cl	5.12	5.58	16.44	1 : 34.7	79.5%
X=Br	6.25	6.16	16.03	1 : 49.0	75.5%
X=I	7.12	5.70	15.32	1 : 22.6	56.0%

The chloro- and bromo-boronated aluminas afforded the best yields, while the bromo-boronated alumina showed the greatest selectivity with a meta : para ratio of 1 : 49.0. These effects could be due to the greater acidity of the $\text{BBr}_3/\text{Al}_2\text{O}_3$. The fluoro-boronated alumina, however, is relatively inactive as a catalyst for the methyl acrylate and isoprene reaction. This inactivity may be a direct result of its lack of Lewis acidity compared to the other boronated aluminas.

It is interesting to note that the ratio of meta to para adducts increased even more when no solvent was used (Table 2.2). The alumina should provide an environment that is more sterically demanding for the meta transition state (Fig. 2.1). The solvent may increase the mobility of the complexed dienophile, thus allowing the diene to form more of the meta adduct.

The $\text{BBr}_3/\text{Al}_2\text{O}_3$ catalyst exhibits turnover, i.e., the ability of one Lewis acid center to facilitate more than one reaction. This is demonstrated by the fact that similar yields are obtained using 0.5 grams of 1.0 mmol BBr_3/g of alumina per 1 mmol of diene (Table 2.2). This shows that the boron-bromine bond isn't broken during the course of complexation and reaction, but rather it is maintained over more than one reaction cycle. If the Lewis acid center were destroyed during the course of the reaction, the yield would be less than 50% because only half of the dienophiles would undergo

complexation before all of the Lewis acid centers were destroyed. However, the meta : para ratios do decline appreciably.

The trends seen in the boronated alumina catalyzed methyl acrylate and isoprene reaction are similar to trends seen in other boronated alumina catalyzed Diels-Alder reactions. The $\text{BF}_3/\text{Al}_2\text{O}_3$ gives little, if any, product. The yields increase with the $\text{BCl}_3/\text{Al}_2\text{O}_3$ and $\text{BBr}_3/\text{Al}_2\text{O}_3$ and then decrease again with the $\text{BI}_3/\text{Al}_2\text{O}_3$ (Table 2.3).

B. Diels-Alder Reaction of Methyl Acrylate and 2-Methyl-1,3-Butadiene with B-Halocatecholboranes.

Aluminum trichloride was one of the first Lewis acids to be studied in detail as a Diels-Alder catalyst.¹⁰ For the AlCl_3 -catalyzed reaction of methyl acrylate and isoprene, the meta to para ratio has been reported to be 1 : 20;¹¹ this was confirmed in this laboratory. The $\text{BX}_3/\text{Al}_2\text{O}_3$ catalysts give even better selectivity. There are two explanations for this. First, the environment of the boronated alumina may be interfering sterically with the formation of the meta isomer. AlCl_3 and similar dissolved catalysts do not have the steric bulk that alumina does, in fact, alumina can be thought of as one

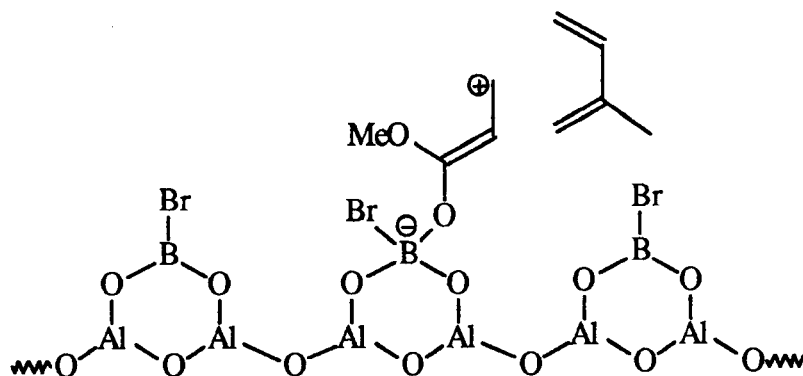


Fig. 2.1 Required approach of isoprene to the complexed methyl acrylate.

Table 2.2 Diels-Alder reaction of methyl acrylate and isoprene, catalyzed by $\text{BBr}_3/\text{Al}_2\text{O}_3$, under various conditions.

$\frac{\text{mMol BBr}_3}{\text{gram Al}_2\text{O}_3}$	g $\text{BBr}_3/\text{Al}_2\text{O}_3$	Solvent	mMol MA	mMol IP	Meta:Para	Yield
0.5	5.42	Toluene	3.97	3.95	1 : 28.2	46.6%
1.0	2.50	Toluene	5.11	14.83	1 : 22.5	66.9%
1.0	5.06	Toluene	6.16	16.03	1 : 50.2	75.5%
1.0	6.25	none	5.08	17.13	1 : 56.4	62.0%

Table 2.3 Results of methyl acrylate + cyclopentadiene reaction (Eq. 1.2) on boronated alumina.^a

$\text{Al}_2\text{O}_3/\text{BX}_3$	Endo/Exo	Yield
X=I	24.0 : 1	31.1%
X=Br	11.5 : 1	77.8%
X=Cl	13.3 : 1	88.0%
X=F	15.7 : 1	47.1%

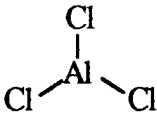
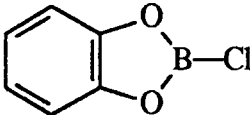
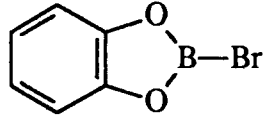
^a Results from unpublished work of McGinnis, M.

extremely large molecule that can easily block other approaching molecules out. The second possibility is the electronic effect of the Lewis acid complex. The acidity of the complexing boron may be great, thus effecting the coefficients of the dienophile's reactive carbons. To get a better grasp of the catalyst and its effect, a small molecule analog was chosen. *B*-Halocatecholborane was chosen because of its structural similarity to the modified alumina, the Lewis acid center attached to two oxygens and a halide.

Currently, only two *B*-halocatecholboranes are commercially available, the *B*-chloro- and *B*-bromocatecholborane. The *B*-bromocatecholborane was previously identified as a good Lewis acid catalyst for the Diels-Alder reaction of several dienes and carbonyl containing dienophiles.¹⁷ The reactions were run at room temperature in dry methylene chloride for three hours with a catalytic amount of *B*-halocatecholborane. The reaction was

quenched with 50% water in methanol and extracted with methylene chloride. The methylene chloride was dried over anhydrous MgSO_4 and filtered through Celite using a glass fritted filter. The solvent was reduced *in vacuo* and decane was added as an internal standard for GC analysis. The results are summarized in Table 2.4.

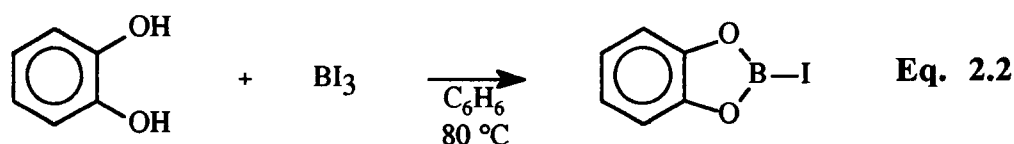
Table 2.4 Reaction of methyl acrylate (MA) and isoprene (IP) in the presence of various catalysts.

Catalyst	MA(mmol)	IP(mmol)	Meta:Para	Yield
	9.19	22.29	1 : 20	84.0%
	9.63	18.48	1 : 22.9	93.8%
	9.57	19.48	1 : 25.3	63.4%

The meta : para ratios obtained using *B*-halocatecholboranes are comparable to the ratios observed using AlCl_3 , but less than those obtained using $\text{BX}_3/\text{Al}_2\text{O}_3$. This demonstrates that the increase in regioselectivity with the boronated aluminas is due largely to steric effects since there are no appreciable steric effects with the *B*-halocatecholboranes when compared to the boronated aluminas.

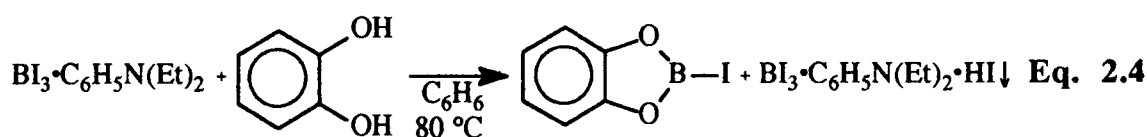
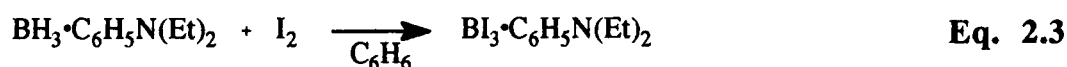
Attempts were also made to synthesize the *B*-fluoro- and *B*-iodocatecholboranes in order to compare the activity of all of the boronated solids and the *B*-halocatecholboranes. The synthesis of *B*-fluorocatecholborane had not been previously reported. The route chosen was to prepare the disodium or dilithium salt of catechol and then attempt a displacement reaction with $\text{BF}_3 \cdot \text{Et}_2\text{O}$. The disodium salt of catechol was not soluble in hydrocarbon solvents. The dilithium salt was insoluble in both ethereal and hydrocarbon solvents. When BF_3 was added, no noticeable reaction occurred and attempts at extraction were unsuccessful.

The synthesis of *B*-iodocatecholborane had been previously reported by Siebert, Gast and Schmidt in 1970.¹⁸ The method used involved a displacement reaction between boron triiodide and catechol in benzene at reflux (Eq.2.1). They isolated *B*-iodocatecholborane, a clear liquid, in 61% yield after vacuum distillation. This method was attempted, a dark purple oil remained after removal of the solvent. When vacuum distillation was attempted, no product distilled before charring occurred.



The same method was used with the BI_3 generated *in situ* by adding I_2 , dissolved in toluene, to $\text{BH}_3 \cdot \text{C}_6\text{H}_5\text{N}(\text{Et})_2$. This mixture was

added to dry catechol and allowed to react for 2 hours at 80 °C (Eq. 2.2, 2.3). The $\text{C}_6\text{H}_5\text{N}(\text{Et})_2 \cdot \text{HI}$ precipitated from the reaction mixture and the solvent was removed *in vacuo*. The resultant products were vacuum distilled but only the precipitate, $\text{C}_6\text{H}_5\text{N}(\text{Et})_2 \cdot \text{HI}$, distilled before charring occurred.

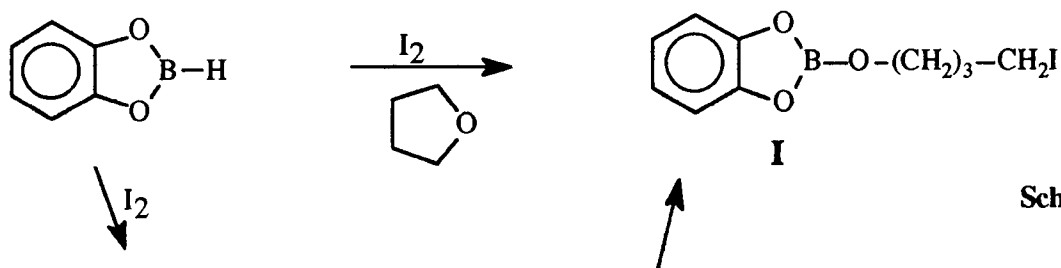


The method used to successfully synthesize mono-iodoorganoboranes involved a displacement reaction using one equivalent of iodine added to a dialkylborane.¹⁹ The same method was attempted in the synthesis of *B*-iodocatecholborane using different solvents (Table 2.5). The iodine was dissolved in the dry solvent and added to a pressure-equalizing dropping funnel. The iodine was then added to neat catecholborane while stirring. The reaction was performed under a number of conditions in a variety of solvents. No reaction was observed in any hydrocarbon solvent, as gauged by disappearance of the iodine color. A reaction did occur in ethereal solvents such as THF and diethyl ether. The solvent was removed when the reactions were complete, leaving white solids. The structure of the resultant product, in ether, was determined to be *B*-ethoxycatecholborane while the product of the reaction run in THF was *B*-(4-iodobutoxy)-catecholborane. The *B*-

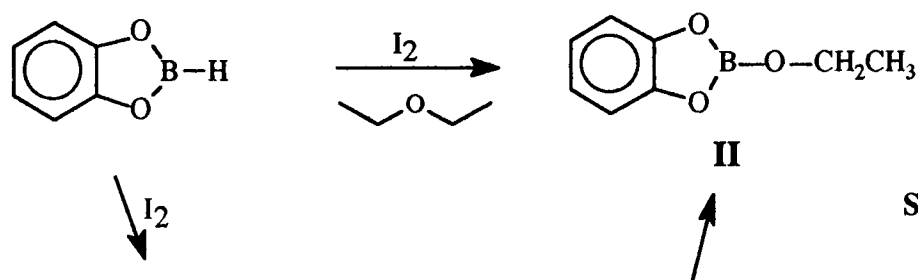
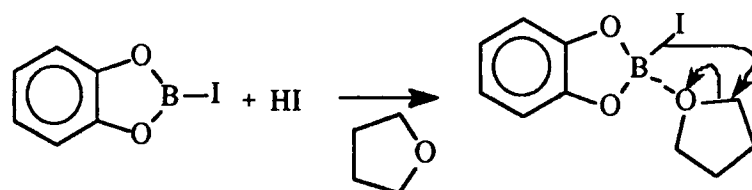
halocatecholboranes are known to cleave ethers readily, suggesting that *B*-iodocatecholborane was being formed but that the conditions required for the formation of *B*-iodocatecholborane also lead to the destruction of the desired product (Schemes 2.1 and 2.2).

Table 2.5 Reaction conditions of I₂ + catecholborane reactions

Solvent System	Temperature(°C)	Results
DMS	25	N.R.
CH ₂ Cl ₂ /DMS	25	N.R.
CH ₂ Cl ₂ /HMPA	25	N.R.
CH ₂ Cl ₂ /HMPA	Reflux	N.R.
CH ₂ Cl ₂	25	N.R.
CH ₂ Cl ₂ /THF	25	I
THF/Hexanes	25	I
Hexanes/C ₆ H ₆	25	N.R.
C ₆ H ₆	Reflux	N.R.
C ₆ H ₆ /1,2-Dichloroethane	25	N.R.
CH ₃ I(no I ₂ added in reaction)	25	N.R.
CH ₃ I	25	N.R.
Et ₃ N	25	N.R.
Et ₂ O	25	II
Pentane	0	N.R.
Pentane	25	N.R.
Pentane	Reflux	N.R.



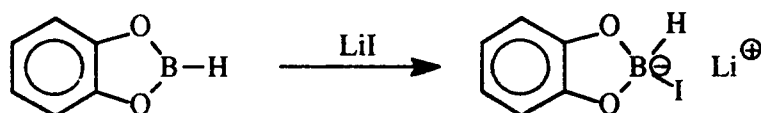
Scheme 2.1



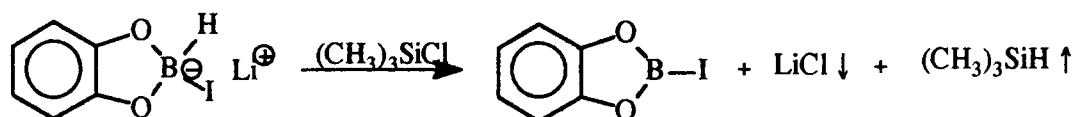
Scheme 2.2

A two step method for synthesizing the B-iodocatecholborane was also attempted (Scheme 2.3). Neat catecholborane was first complexed to anhydrous LiI followed by the addition of trimethylchlorosilane. When neat catecholborane was added to LiI, a white solid was formed. The solid forms a slurry on addition of the liquid trimethylchlorosilane. This mixture was then heated to 60 °C for two hours. Benzene was then added to dissolve any B-iodocatecholborane. The solvent was then decanted and removed *in*

vacuo leaving a clear liquid which was inactive when exposed to air or water, suggesting that the B-iodocatecholborane was not present.



Scheme 2.3



C. Low Temperature NMR Studies of B-Halocatecholborane complexes of Crotonaldehyde.

Lewis acids catalyze Diels-Alder reactions by complexation to the carbonyl oxygen of the dienophile which polarizes the double bond of the α,β -unsaturated carbonyl compound.^{2,4} ¹H NMR is a good method for investigating changes in charge distribution because chemical shift is related to electron density around a particular nucleus and, therefore, changes in charge distribution. Childs developed a method for measuring Lewis acidity based on the change in chemical shift ($\Delta\delta$) of H^c of *E*-crotonaldehyde when complexed to the Lewis acid (Fig. 2.2).²⁰ Childs found that when various Lewis acids were complexed at low temperatures to crotonaldehyde in CH₂Cl₂, all of the H^b, H^c, and H^d proton peaks shifted downfield, the chemical shift for the aldehydic proton, H^a, varied randomly.

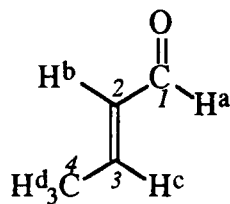


Fig. 2.2 Crotonaldehyde

Chemical shifts (δ), in ^1H NMR spectroscopy, have a strong relationship to the electron density near a given proton. The greater the electron density near a proton, the more the proton is shielded from the applied magnetic field. The more a proton is shielded, the more upfield its ^1H NMR signal lies. Conversely, when a proton is deshielded, it has a chemical shift which lies farther downfield. The acidic proton of a carboxylic acid, for example, normally appears the farthest downfield, $\delta=10-12$, with respect to TMS ($\delta=0.0$). This is due to the fact that the $-\text{OH}$ hydrogen has little electron density to shield it. A hydride, a proton with two electrons, on the other hand, often has a negative chemical shift; its signal lies upfield from TMS.

H^c generally had the largest $\Delta\delta$ values in Childs' study. $\Delta\delta$ was defined as $\delta_{(\text{complexed})} - \delta_{(\text{uncomplexed})}$, thus giving a positive $\Delta\delta$ for a downfield shift. When the Lewis base, *E*-crotonaldehyde, is complexed, H^c would be expected to shift farther downfield because the electron density would decrease at the carbon to which it is bonded. This can be rationalized by the predominant resonance structures expected for Lewis acid complexed crotonaldehyde (Fig. 2.3). For the strongest Lewis acids, such as BBr_3 and BCl_3 , the $\Delta\delta$ for H^c was over +1.3 ppm.

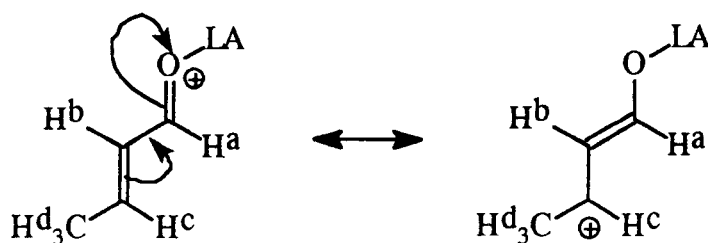


Fig. 2.3 Resonance structures of crotonaldehyde.

When the *B*-halocatecholboranes were studied using Childs' technique, H^a , H^b , H^c and H^d shifted upfield (Fig. 2.4, 2.5; Table 2.6). This means that the protons are *more* shielded than normal. *B*-Halocatecholboranes are disubstituted benzene rings which may possibly stabilize the complex by interacting with the pi orbitals of the double bond of *E*-crotonaldehyde. The pi-complex is most likely responsible for this behavior.

Additionally, in the one-dimensional spectrum, there are double the number of proton resonances. The integration of these peaks suggests that there are two species present in nearly equal quantity. The uncomplexed crotonaldehyde spectrum shows two sets of peaks with a 95 : 5 area ratio, corresponding to the *E* : *Z* ratio reported by the manufacturer. The coupling constants of the complexed crotonaldehyde peaks suggest that there are two separate species (Fig. 2.6). There are two possibilities which could lead to two species being observed: Either an equilibrium exists

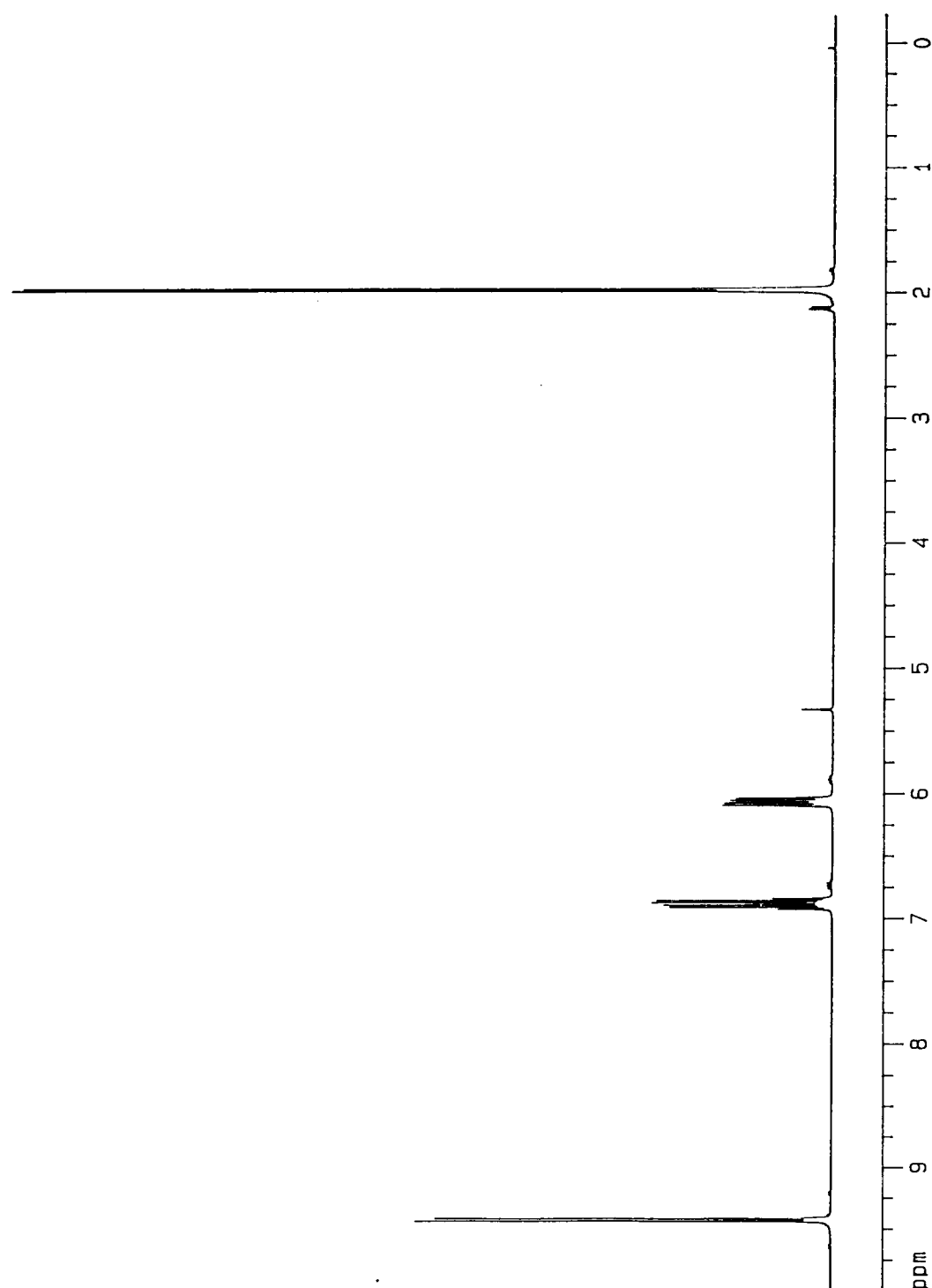


Fig. 2.4 ^1H NMR spectra of crotonaldehyde.

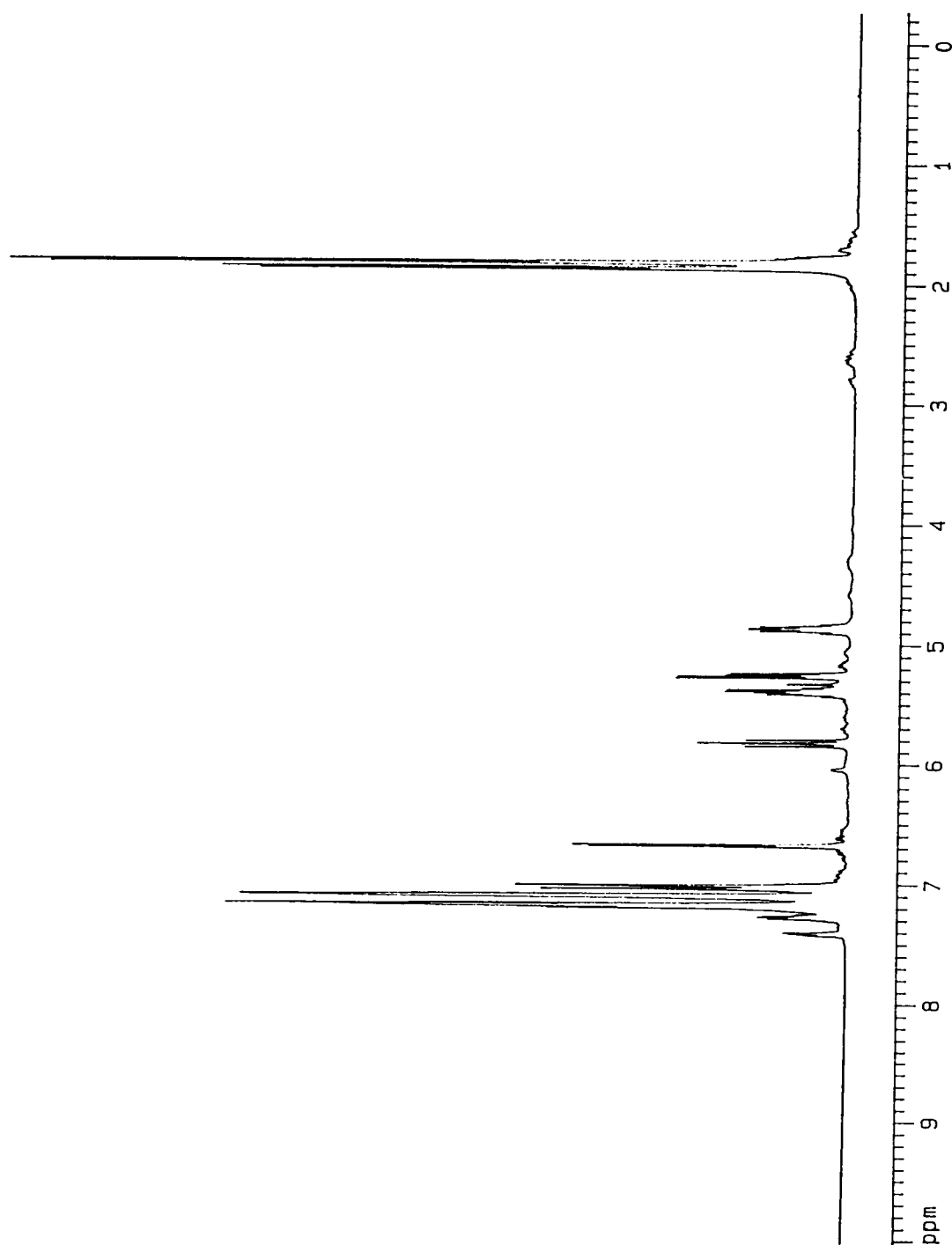
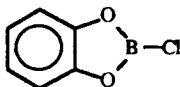
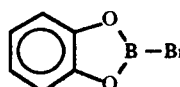


Fig. 2.5 ^1H NMR spectra of an equimolar solution of crotonaldehyde and *B*-bromocatecholborane.

Table 2.6 Change in ^1H chemical shifts of Lewis acid complexed crotonaldehyde at -20°C

Lewis Acid	$\Delta\delta\text{H}^{\text{a}}$	$\Delta\delta\text{H}^{\text{b}}$	$\Delta\delta\text{H}^{\text{c}}$	$\Delta\delta\text{H}^{\text{d}}$
BBr_3^{a}	0.11	0.93	1.49	0.51
BCl_3^{a}	-0.65	0.85	1.35	0.49
AlCl_3^{a}	-0.20	0.76	1.32	0.47
BF_3^{a}	-0.27	0.74	1.23	0.44
	-2.32	-0.35	-2.19	-0.29
	-2.69	-0.85	-1.57	0.34
	-2.39	-0.23	-2.02	-0.11
	-2.75	-0.80	-1.49	-0.16

^a Data from Ref. 22

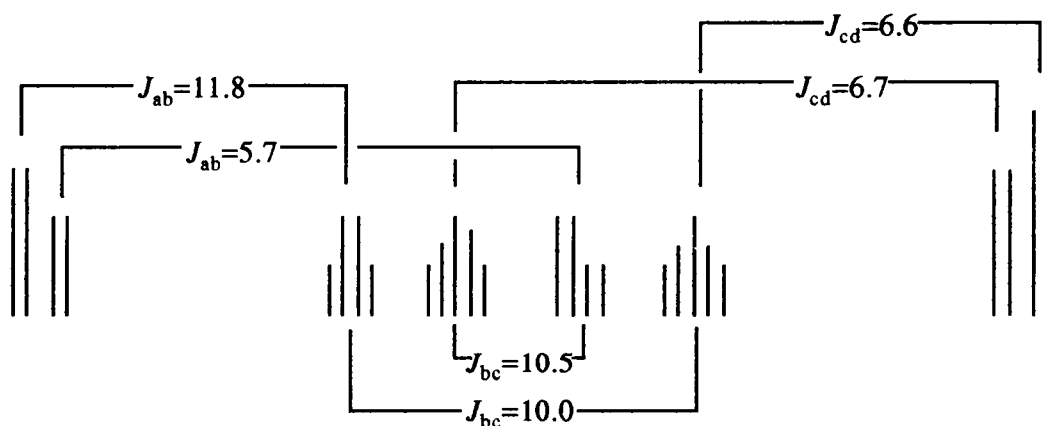


Fig. 2.6 Coupling constants and connectivity of the ^1H NMR spectrum of crotonaldehyde complexed with *B*-bromocatecholborane.

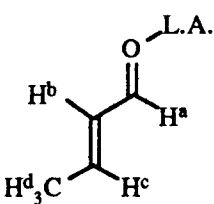
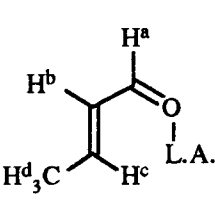
between the *cis* and *trans* (*E* and *Z*) complexed crotonaldehyde or there is an equilibrium between the *s-cis* and *s-trans* conformations of the complexed *E*-crotonaldehyde.

The latter possibility was supported when the complex was quenched with H₂O. The GC/MS analysis of the organic phase showed that the hydrolyzed complex gave only crotonaldehyde and its HBr-addition product, 3-bromobutanal. ¹H NMR analysis of the organic phase showed that only one form of crotonaldehyde, the *E*-isomer, was present (catechol and 3-bromobutanal were also present). There should have been a 1 : 1 mixture of *Z* and *E* isomers after hydrolysis if rapid interconversion between *Z*- and *E*-crotonaldehyde occurred when complexation took place. This demonstrates that there is no rapid interconversion between *cis* and *trans* isomers of crotonaldehyde when complexed with *B*-bromocatecholborane.

Coupling constants of the complexes also corresponded to the model of a *s-cis/s-trans* conformational equilibrium. It is possible that, once complexed with *B*-bromocatecholborane, crotonaldehyde has more pi character between carbons 1 and 2 (Fig. 2.3). This would lead to coupling that acts more alkene-like than aldehyde-like. J_{ab} for conformation I (Table 2.7) is very large (11.8 Hz) compared to the normal J_{ab} that would be expected for an α,β -unsaturated aldehyde (≈ 6 Hz), but very close to the range for a *trans* double-bond (12-18 Hz). The J_{ab} for conformation II is 5.7 Hz,

within the range for an α,β -unsaturated aldehyde, but also very close to the range of a *cis* double-bond.

Table 2.7 Coupling constants (J) of A) *B*-bromocatecholborane and B) *B*-chlorocatecholborane complexed *s-trans* and *s-cis* crotonaldehyde.

							
I				II			
A				B			
	J_{ab}	J_{bc}	J_{cd}		J_{ab}	J_{bc}	J_{cd}
I	11.8	10.0	6.7	I	11.9	9.7	6.6
II	5.7	10.6	6.6	II	5.8	10.1	6.6

Rotating frame Overhauser enhancement spectroscopy (ROESY) is used to determine spatial arrangements of medium-sized molecules.²¹ Normal 1-D ^1H NMR and 2-D correlated spectroscopy (COSY) have signals which are split by scalar coupling, coupling which is caused by protons on adjacent carbons, and through space coupling. Scalar coupling is so pronounced, however, that the through space coupling is often impossible to see. ROESY, in effect, eliminates scalar coupling which uncovers the through space interactions. ROESY spectra can also be used to calculate through space distances, thus giving a complete picture of the configuration of a molecule while in solution.

The ROESY signals that are of interest are those which have only negative cross signals with respect to the diagonals.^{21c} Other 2-D methods such as correlated spectroscopy (COSY) give four signals which form a square, two of which are positive and two of which are negative. ROESY spectra often have combinations of both ROESY and COSY signals, but the COSY peaks are referred to as artifacts, giving little useful information outside of connectivities. The ROESY peaks are usually a set of two negative peaks, side-by-side, which indicate a through-space interaction.

The ROESY spectrum of the *B*-bromocatecholborane complex of crotonaldehyde shows several through space interactions of interest (Fig 2.7). There is an interaction between H^a and H^c of conformation I, consistent with an *s-trans* conformation. There is no interaction between the same protons of conformation II, consistent with an *s-cis* conformation.

The most notable characteristic of the ROESY spectra is the interaction between the phenyl ring of the *B*-bromocatecholborane and the methyl groups of the two crotonaldehyde conformers. This supports the postulation that the pi electrons of the phenyl ring are stabilizing the complex, thus the ¹H NMR signals lie much farther upfield than would be expected. The most likely conformation of the complex would be for the two molecules to lie flat, one over the other (Fig. 2.5)

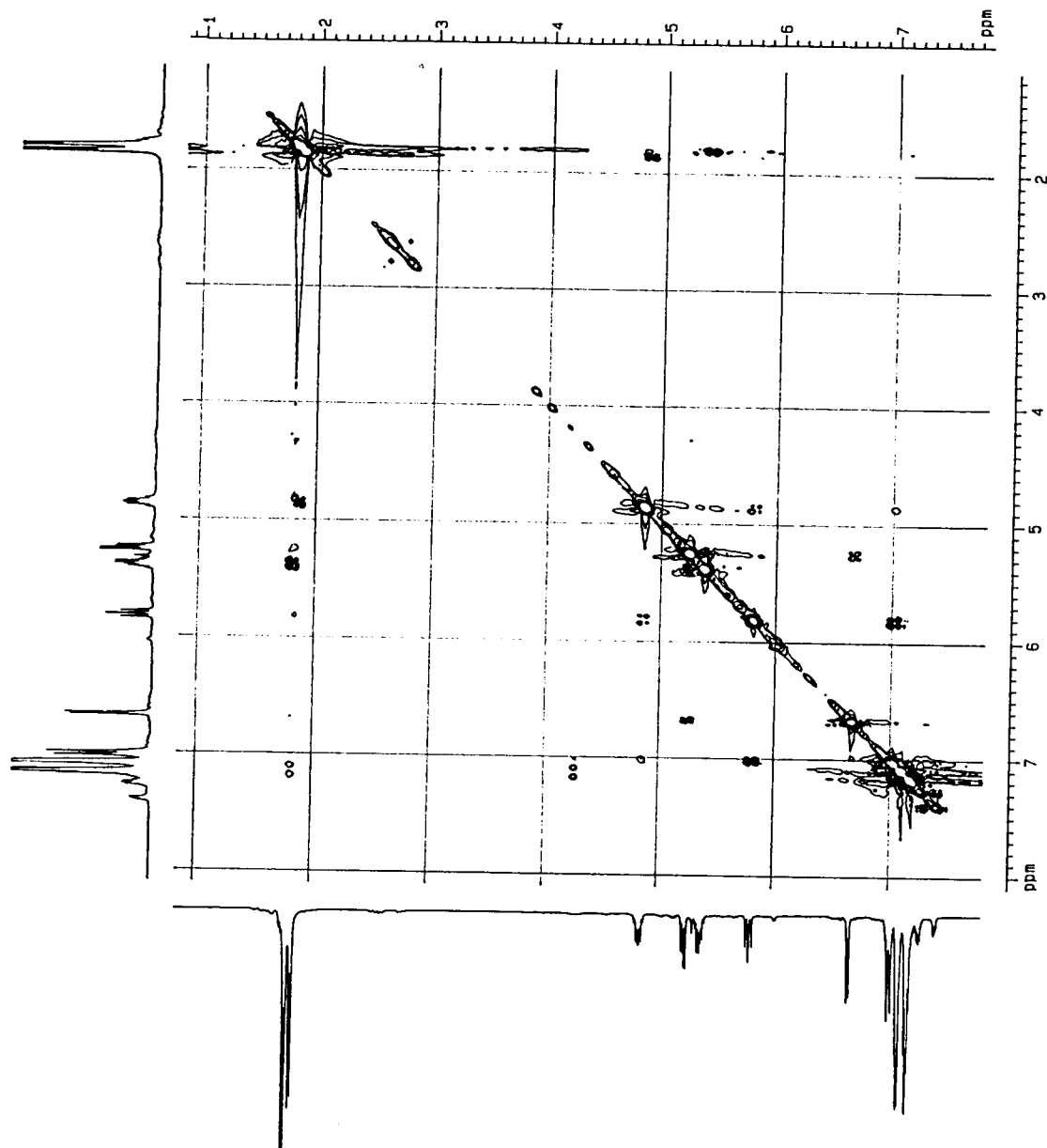


Fig. 2.7 ROESY spectra of an equimolar solution of crotonaldehyde and *B*-bromocatecholborane.

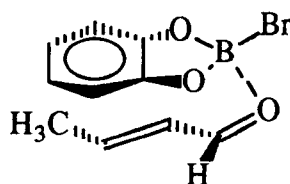


Fig. 2.8 Possible conformation of the *B*-bromocatecholborane-crotonaldehyde π -complex.

D. Amidolysis of Esters on Boronated Alumina.

The conversion of carboxylic esters to amides using boron tribromide under mild conditions was first reported in 1974.²² Amides were obtained from corresponding carboxylic esters in excellent yields and even unstable amines, such as 7-aminocephalosporanic acid, and amino acids gave good yields. The formation of an ester-boron trihalide complex was suggested by Gerrard as an important intermediate in this reaction.²³ Since $\text{BBr}_3/\text{Al}_2\text{O}_3$ is known to form similar complexes with carbonyl containing groups, it was of interest to examine this conversion using $\text{BBr}_3/\text{Al}_2\text{O}_3$.

The amidolysis of methyl phenylacetate with aniline was run using a 1:1 mole ratio of catalyst to ester. The modified alumina had a loading of 1.0 mmol of BX_3 per gram of alumina. Therefore, 5.0 mmol of methyl phenylacetate was added to a slurry of 5.0 g of boronated alumina in 10 mL of benzene. The reaction mixture was allowed to stir for 10 minutes before 5.0 mmol of aniline was added.

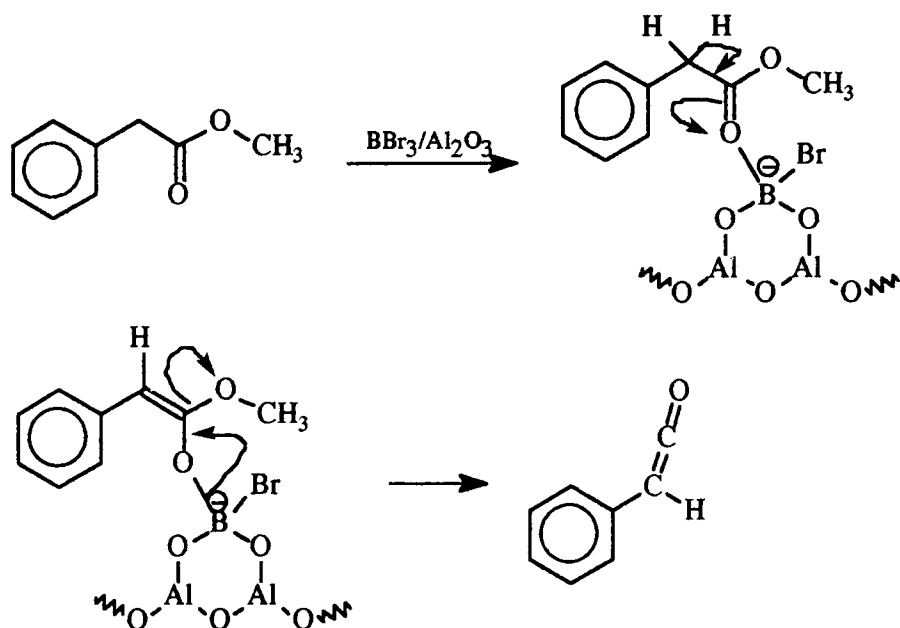
The reaction was allowed to proceed for 3 hours at room temperature before workup.

The product, *N*-phenyl phenylacetamide, was extracted from the surface with three aliquots of ethyl acetate which were then dried with 5.0 g. of anhydrous MgSO_4 . The reaction mixture was filtered through celite and a glass fritted filter. The solvent was removed in vacuo and the reaction mixture was purified via flash chromatography and characterized via ^1H NMR spectroscopy. The yield was 10.2%.

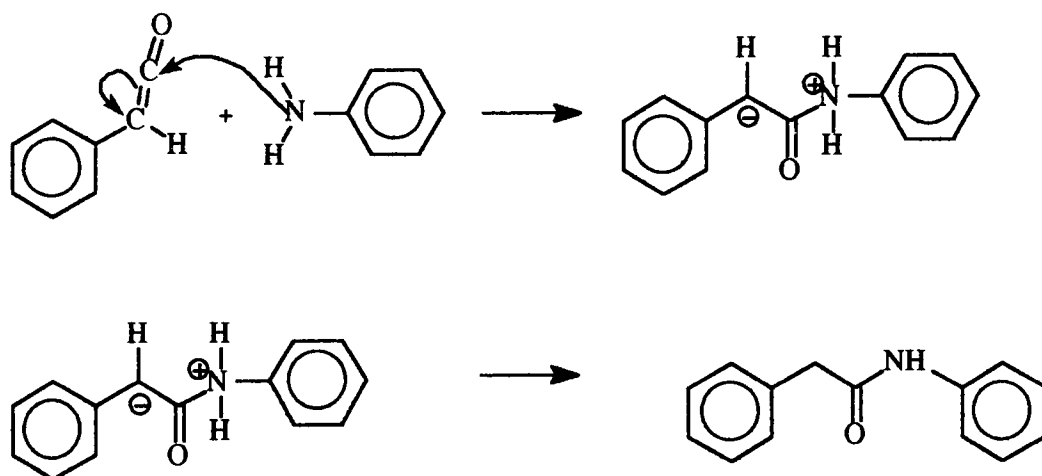
The amidolysis of methyl benzoate with aniline was carried out using a 1:1 mole ratio of catalyst to ester. The modified alumina had a loading of 1.0 mmol of BX_3 per gram of alumina. Therefore, 5.0 mmol of methyl phenylacetate was added to a slurry of 5.0 g of boronated alumina in 10 mL of benzene. The reaction mixture was allowed to stir for 10 minutes before 5.0 mL of aniline was added. The reaction was allowed to run for 6 hours at 70 °C before workup. The mixture was then extracted from the surface with three aliquots of ether which were then dried with 5.0 g. of MgSO_4 . The mixture was analyzed by thin layer chromatography which showed no product.

The amidolysis reaction on the boronated alumina may follow a unique pathway. The absence of product from the methyl benzoate reaction may be due to the lack of α -hydrogens. All of the

esters studied by Yazawa and co-workers also contained α -hydrogens.²² This reaction may proceed by way of a ketene intermediate which then reacts with the primary amine to form the amide (Scheme 2.4).



Scheme 2.4



CHAPTER 3

Experimental

A. Materials

Solvents

- Anhydrous Diethyl Ether¹, Mallinckrodt, ACS grade
- Anhydrous Methanol¹, Mallinckrodt
- Anhydrous Methyl Sulfide¹, Aldrich Chemical Company
- Benzene², Mallinckrodt
- Chloroform-*d*¹, Aldrich Chemical Company
- 1,2-Dichloroethane¹, Aldrich Chemical Company
- Dichloromethane¹, Mallinckrodt
- Dichloromethane-*d*2¹, Aldrich Chemical Company
- Ethyl Acetate¹, Mallinckrodt
- Hexamethylphosphoramide¹, Aldrich Chemical Company
- Hexanes³, Mallinckrodt
- Iodomethane¹, Aldrich Chemical Company
- Pentane⁴, Mallinckrodt

•Triethylamine⁴, Mallinckrodt

•Toluene², Mallinckrodt

•Tetrahydrofuran², Mallinckrodt

¹ Used without further purification

² Distilled over Sodium metal and Benzophenone. Stored under argon

³ Dried over molecular sieves and stored under argon

⁴ Distilled over calcium hydride, stored under argon

Reagents

•Alumina, Brockmann Activity Grade I (neutral)

•Aluminum Trichloride, Aldrich Chemical Company

•Anhydrous Magnesium Sulfate, Mallinckrodt

•Aniline, Fisher Scientific Company

•Borane, 1M solution in Methyl Sulfide, Aldrich
Chemical Company

•Boron Trifluoride Etherate, Aldrich Chemical
Company

•Boron Trichloride 1M Solution in Hexanes, Aldrich
Chemical Company

•Boron Tribromide 1M Solution in Hexanes, Aldrich
Chemical Company

•Boron Triiodide, Aldrich Chemical Company

•*B*-Bromocatecholborane, Aldrich Chemical Company

•*n*-Butyllithium, Aldrich Chemical Company

•Catechol, Aldrich Chemical Company

•Catecholborane, 98%, Aldrich Chemical Company

•Catecholborane, 1M solution in THF, Aldrich Chemical
Company

- *B*-Chlorocatecholborane, Aldrich Chemical Company
- Decane, Aldrich Chemical Company
- Iodine, Fisher Scientific Company
- Isoprene, Aldrich Chemical Company
- Lithium Iodide, Aldrich Chemical Company
- Methyl Acrylate, Aldrich Chemical Company
- Phenylacetyl Chloride, Eastman Chemical Company
- Pyridine, Fisher Scientific Company
- Trimethylchlorosilane, Aldrich Chemical Company

B. Analytical Methods

GC Methods

All yields reported, except where noted, were calculated from peak areas measured using a Hewlett-Packard 5790 gas chromatograph fitted with a mass spectrometer detector or a Hewlett-Packard 5790 gas chromatograph. Decane was used as an internal standard for all reactions. Correction factors were calculated using a pure 20 : 19 : 1 standard of decane, methyl 4-methylcyclohex-3-ene carboxylate (MMC-4) and methyl 3-methylcyclohex-3-ene carboxylate (MMC-3). Eq. 3.2 was used for calculating the correction factor.

$$\frac{(\text{mMol Decane})}{(\text{Area Decane})} = C * \frac{(\text{mMol MMC-4} + \text{mMol MMC-3})}{(\text{Area MMC-4} + \text{Area MMC-3})} \quad \text{Eq. 3.1}$$

$$\frac{(\text{mMol Decane}) * (\text{mMol MMC-4} + \text{mMol MMC-3})}{(\text{Area Decane}) * (\text{Area MMC-4} + \text{Area MMC-3})} = C \quad \text{Eq. 3.2}$$

NMR Methods

NMR spectra were measured using Bruker 250 MHz and Bruker 400 MHz instruments. CDCl_3 and CD_2Cl_2 were used as solvents. CDCl_3 was used with 1% v/v TMS ($\delta=0.00$) as the NMR standard.

Apparatus

All syringes and needles were oven dried and purged with argon prior to use with air sensitive materials. Glassware for all reactions was oven dried. All reactions were run in glassware that was flame dried while being flushed with argon. Argon was delivered to the flask from a pressure regulated argon tank and expelled through a mercury bubbler.

C. Methods

Synthesis of Bromo- and Chloroboronated Aluminas

In a 250-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was placed 50 g of Brockmann grade I neutral alumina. The flask was then fitted with a vacuum adapter, flushed with argon, and flame dried. The flask was allowed to cool while maintaining the argon purge. After the flask was charged with hexanes (30 mL) to make a slurry, BX_3 (50 mmol; 50 mL of 1 M solution in hexanes) was then added via double-ended needle. The slurry was then allowed to stir for three hours. The solvent was removed *in vacuo* and the solid was transferred, under argon, to a flame-dried, septum-sealed Erlenmeyer flask for later use.

Synthesis of Fluoroboronated Alumina

In a 250-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was placed 50 g of Brockmann grade I neutral alumina. The flask was then fitted with a vacuum adapter, flushed with argon, and flame dried. The flask was allowed to cool while maintaining the argon purge. After the flask was charged with hexanes (30 mL) to make a slurry, $BF_3 \cdot Et_2O$ (7.1 g; 6.1 mL, 50 mmol) was added via syringe. The slurry was

allowed to stir for three hours. The solvent was removed *in vacuo*. Heat was applied to the flask, while still under vacuum, until the solid was completely dry. The solid was transferred, under argon, to a flame-dried, septum-sealed Erlenmeyer flask for later use.

Synthesis of Iodoboronated Alumina

In a 250-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was placed 50 g of Brockmann grade I neutral alumina. The flask was then fitted with a vacuum adapter, flushed with argon, and flame dried. The flask was allowed to cool while maintaining the argon purge. After the flask was charged with hexanes (30 mL) to make a slurry, $\text{BH}_3 \cdot \text{Me}_2\text{S}$ (3.8 g; 4.7 mL; 50 mmol) was added via syringe. After the slurry stirred for three hours, iodine (25 mmol; 6.3 g) in hexanes (50 mL) was added via double-ended needle. The solvent was removed *in vacuo*. The solid was transferred, under argon, to a flame-dried, septum-sealed Erlenmeyer flask for later use.

Reaction of Methyl Acrylate and Isoprene on Boronated Aluminas

To a flame-dried 250-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was transferred, under argon, $\text{BX}_3/\text{Al}_2\text{O}_3$ (5 g). The flask was sealed with

a septum and charged with toluene (10 mL). Methyl acrylate (0.43 g; 5 mmol) was then added via syringe and the reaction flask allowed to stir for 5 minutes. Isoprene (1.0 g; 15.0 mmol.) was then added via syringe. After the reaction was stirred for 3 hr, methanol (15 mL) was added and the mixture allowed to stir for 15 min. The product was then removed from the alumina by washing with methanol (2 x 15 mL), hexanes (2 x 15 mL) and filtered through a glass fritted filter packed with Celite. The mixture was concentrated *in vacuo* and decane (0.2 g; 1.4 mmol) was added as an internal standard for GC analysis.

Reaction of Methyl Acrylate and Isoprene with AlCl_3

To a flame-dried 250-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was transferred, under argon, AlCl_3 (0.25 g; 1.9 mmol). The flask was sealed with a septum and charged with benzene (20 mL) and then with methyl acrylate (3.0 g; 35 mmol) the mixture was allowed to stir for 5 min. Isoprene (7.1 g; 110 mmol) was then added to the flask. After the reaction mixture was stirred for 3 hr, H_2O (10 mL) was added. The reaction mixture was extracted with methylene chloride (3 x 15 mL). The organic phase was dried over anhydrous MgSO_4 (5 g) and filtered through a glass fritted filter packed with Celite. The solvent was removed *in vacuo* and the residue purified

via flash chromatography. Isolated yield, 3.15 g (20.5 mmol) of MMC-3 and MMC-4, 58.6%. 95:5 para:meta, determined via GC.

Reaction of MA and IP with *B*-Halocatecholboranes

B-Halocatecholborane (0.25 g) was transferred, under argon, to a flame-dried 100-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar. After the flask was sealed with a septum, it was charged first with methylene chloride (20 mL) and then with methyl acrylate (3.0 g; 35 mmol). After the mixture was stirred for 5 min, isoprene (7.1 g; 110 mmol.) was added. After 3 h, 10 mL of cold 50% aqueous methanol was added to the reaction mixture. The reaction mixture was extracted with methylene chloride (3 x 15 mL). The organic phase was dried over anhydrous MgSO₄ (5 g) and filtered (through a glass fritted filter packed with Celite). The mixture was concentrated *in vacuo*, decane (0.20 g; 1.4 mmol) was added as an internal standard for GC analysis.

B-(4-Iodobutoxy)-Catecholborane

A 250-mL round-bottomed flask equipped with a septum sealed side arm, magnetic stir bar, and a septum sealed pressure equalizing dropping funnel was flame dried and flushed with argon.

After the apparatus had cooled to room temperature (while maintaining the argon purge), it was charged with catecholborane (10 mmol; 10 mL of a 1 M solution in THF) with stirring. Iodine (1.3 g; 5 mmol) was transferred to a septum sealed Erlenmeyer flask which was then flame dried under argon purging. The iodine was dissolved in dry toluene (15 mL) and transferred via double-ended needle to the dropping funnel. The iodine solution was then added to the stirred catecholborane solution, dropwise. When the purple iodine color disappeared (about 10 minutes), the solution was transferred via double-ended needle to a flame-dried, argon-purged, 250-mL round-bottomed flask that was septum sealed and fitted with a three-way vacuum adapter. The solvent was removed in vacuo, leaving a white solid. The solid was dissolved in CDCl_3 and transferred to an NMR tube.

^1H NMR spectral characteristics of B-(4-iodobutoxy)-catecholborane (CDCl_3): 3.15 ppm (t, 2 H); 3.45 (m, 2 H); 3.85 (t, 2 H); 4.15 (t, 2 H), 7.0 (m, 4 H).

B-Ethoxycatecholborane

A 250-mL round-bottomed flask equipped with a septum-sealed side arm, magnetic stir bar, and a septum-sealed pressure-equalizing dropping funnel was flame dried and flushed with argon. After the apparatus had cooled to room temperature under argon, it was charged with neat catecholborane (1.07 mL; 10 mmol) with

stirring. Iodine (1.27g; 5 mmol) was transferred to a septum-sealed Erlenmeyer flask which was then flame dried and similarly purged with argon. The iodine was dissolved in dry methylene chloride (30 mL) and transferred via double-ended needle to the dropping funnel. The iodine solution was then added to the stirred catecholborane dropwise over 2 h. The reaction was monitored for 2 h, after all the iodine solution was added, for the disappearance of the iodine. When the iodine color had not disappeared, diethyl ether (1.04 mL; 10 mmol) was added to the solution. After the purple iodine color disappeared (about 20 minutes), the solution was transferred via double-ended needle to a flame-dried, argon-purged 250-mL round-bottomed flask that was septum sealed and fitted with a three-way vacuum adapter. The solvent was removed *in vacuo*, leaving a white solid. The solid was dissolved in CDCl_3 and transferred to an NMR tube.

^1H spectral characteristics of B-ethoxycatecholborane (CDCl_3): 1.35 ppm (t, 3 H); 4.20 ppm (q, 2 H); 7.05 ppm (m, 4 H).

B-Iodocatecholborane; Method 1

A 100-mL round-bottomed flask equipped with a septum-sealed side arm, magnetic stir bar, and a septum-sealed pressure-equalizing dropping funnel was flame-dried and flushed with argon. After the apparatus had cooled to room temperature under argon purge, the flask was charged with catecholborane (3.3 g; 20 mmol)

with stirring. Iodine (7.6 g; 30 mmol) was transferred to a septum-sealed Erlenmeyer flask which was then flame-dried and similarly purged with argon. The iodine was dissolved in benzene (25 mL) and transferred via double-ended needle to the dropping funnel. The iodine solution was then added to the stirring borane complex dropwise over 2 h. The mixture was allowed to stir for 4 h at 80 °C. The benzene was removed *in vacuo* and the flask was fitted with a fractional distillation apparatus. The remaining oil was vacuum distilled at 0.25 mm Hg. No product was isolated due to charring.

Boron Triiodide

A 250-mL round-bottomed flask equipped with a septum-sealed side arm, magnetic stir bar, and a septum-sealed pressure-equalizing dropping funnel was flame-dried and flushed with argon. After the apparatus had cooled to room temperature under argon purge, it was charged with borane-*N,N'*-diethylaniline complex (3.3 g; 20 mmol) with stirring. Iodine (7.6 g; 30 mmol) was transferred to a septum sealed Erlenmeyer flask which was then flame dried and similarly purged with argon. The iodine was dissolved in dry toluene (60 mL) and transferred via double-ended needle to the dropping funnel. The iodine solution was then added to the stirring borane complex dropwise over 2 h. The mixture was allowed to stir for 2 h, leaving a colorless 2 layer system which was used later.

B-Iodocatecholborane: Method 2

A 100-mL Erlenmeyer flask was flame dried and flushed with argon. After it had cooled to room temperature under argon purge, catechol (2.2 g; 20 mmol) was added to the flask under argon. The catechol was dissolved in dry CH_2Cl_2 (50 mL) and transferred, via double-ended needle, to the $\text{BI}_3 \cdot N,N'$ -diethylaniline/toluene system (described above), releasing HI. The solution turned yellow, indicating the formation of N,N' -diethylaniline $\cdot$ HI. The solution was transferred via double-ended needle to a flame dried, argon purged 250-mL round-bottomed flask that was septum sealed and fitted with a three-way vacuum adapter. The CH_2Cl_2 was removed *in vacuo*, precipitating a white solid, presumably N,N' -diethylaniline $\cdot$ HI which is insoluble in toluene. The remaining solution was decanted via double ended needle into a 100-mL round-bottomed flask fitted with a septum sealed side arm, magnetic stir bar, and a fractional distillation apparatus. The mixture was concentrated *in vacuo*. The remaining oil was vacuum distilled at 0.25 mm Hg. No product was isolated due to charring.

B-Iodocatecholborane: Method 3

A 50-mL round-bottomed flask equipped with a septum-sealed side arm, magnetic stir bar and a three-way vacuum adapter was flame-dried and flushed with argon. After the apparatus had cooled to room temperature under argon purge, boron triiodide (2.5

g; 6.3 mmol) was transferred to it under argon and dissolved in dry CH_2Cl_2 (5 mL). Catechol (0.76 g; 6.9 mmol) was transferred under argon to a septum sealed Erlenmeyer flask which was flame dried and similarly purged with argon. The catechol was dissolved in dry CH_2Cl_2 (15 mL) and transferred via double-ended needle to the round-bottomed flask. The mixture was allowed to stir for 3 h at 80 °C. The benzene was removed *in vacuo* and the flask was fitted with a fractional distillation apparatus. The remaining oil was vacuum distilled at 0.25 mm Hg. No product was isolated due to charring.

B-Iodocatecholborane; Method 4

A 50-mL round bottomed flask equipped with a septum-sealed side arm, magnetic stir bar and a three-way vacuum adapter was flame-dried and flushed with argon. After the apparatus had cooled to room temperature under argon purge, lithium iodide (1.3 g; 10 mmol) was transferred to it under argon. Catecholborane (1.2 g; 1.1 mL; 30 mmol) was transferred via syringe to the round-bottomed flask. The mixture was allowed to stir for 30 min until a white solid was formed. Trimethylchlorosilane was transferred via syringe to the round-bottomed flask which was shaken until slurried. The flask was then charged with benzene (20 mL) and stirred for an additional 30 min. The benzene was decanted into a 50-mL round-bottomed flask which was flame dried and purged

with argon. The solvent was removed *in vacuo*, leaving a clear liquid.

Low Temperature NMR Studies

Four 5-mm NMR tubes were septum sealed, flame dried and flushed with argon. After the tubes were cooled, *B*-halocatecholborane was transferred, under argon, to each of the tubes with increasing amounts of *B*-halocatecholborane being placed in each tube (0.3 mmol, 0.6 mmol, 0.9 mmol and 1.2 mmol). CD₂Cl₂ (0.75 mL) was injected into each NMR tube which were shaken to ensure the solid was completely dissolved. The tubes were cooled to -72 °C and each was injected with crotonaldehyde (1.2 mmol; 100 µL). Spectra were taken at -20 °C on a Bruker 400 MHz NMR with a variable temperature unit.

Synthesis of Methyl Phenylacetate

To a flame-dried 100-mL, round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was added, via double-ended needle, benzene (20 mL). Phenylacetyl chloride (1.5 g; 1.3 mL; 1.9 mmol) was added to the flask and stirred. Methanol (0.3 g; 0.4 mL; 10 mmol) was then added to the flask followed by pyridine (0.8 g; 0.8 mL; 10 mmol). After the reaction mixture was stirred for 3 hr, H₂O (10 mL) was added. The reaction

mixture was extracted with methylene chloride (3 x 15 mL). The organic phase was dried over anhydrous MgSO_4 (5 g) and filtered through a glass fritted filter packed with Celite. The solvent was removed *in vacuo* and the residue purified via flash chromatography (10% ethyl acetate in hexanes).

Aminolysis of Methyl Phenylacetate with $\text{BBr}_3/\text{Al}_2\text{O}_3$

To a flame dried 250-mL round bottomed flask equipped with a septum sealed side arm and a magnetic stir bar, was transferred, under argon, $\text{BBr}_3/\text{Al}_2\text{O}_3$ (5 g). The flask was sealed with a septum and charged with 10 mL of benzene. Methyl phenylacetate (0.8 g; 5 mmol) was then added via syringe and the reaction flask allowed to stir for 1 h. Aniline (0.5 g; 5.0 mmol) was then added via syringe. After the reaction was stirred for 3 hr, a saturated solution of NaHCO_3 in water (15 mL) was added and the mixture allowed to stir for 15 min. The product was then removed from the alumina by washes with ethyl acetate (4 x 15 mL) filtered through a glass fritted filter packed with Celite. The reaction mixture was extracted with methylene chloride (3 x 15 mL) dried over anhydrous MgSO_4 (5 g) and filtered through a glass fritted filter packed with Celite. The solvent was removed *in vacuo* and the residue purified via flash chromatography (15% ethyl acetate in hexanes).

^1H spectral characteristics of *N*-phenyl phenylacetamide (DMSO- d_6): 3.65 ppm (s, 2 H); 7.30 ppm (m, 10 H); 10.15 ppm (s, 1 H).

Aminolysis of Methyl Benzoate with $\text{BBr}_3/\text{Al}_2\text{O}_3$

To a flame-dried 250-mL round-bottomed flask equipped with a septum-sealed side arm and a magnetic stir bar, was transferred, under argon, $\text{BBr}_3/\text{Al}_2\text{O}_3$ (5 g). The flask was sealed with a septum and charged with 10 mL of benzene. Methyl benzoate (0.7 g; 0.6 mL; 5 mmol) was then added via syringe and the reaction flask allowed to stir for 1 h. Aniline (5.0 mL) was then added via syringe. After the reaction was stirred for 3 hr, a saturated solution of NaHCO_3 in water (15 mL) was added and the mixture allowed to stir for 15 min. The product was then removed from the alumina by washes with ether (4 x 15 mL) filtered through a glass fritted filter packed with Celite. The organic phase was dried over anhydrous MgSO_4 (5 g) and filtered through a glass fritted filter packed with Celite. TLC indicated that no product had formed.

LIST OF REFERENCES

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1. Hill, R. K.; Martin, J. G. *Chem. Rev.* **1961**, *61*, 537.
2. Carey, F.A.; Sundberg, R.J. *Advanced Organic Chemistry*, 3rd Ed. Plenum Press: New York, **1990**.
3. Alder, K. *Ann.* **1951**, *157*, 571.
4. Fringuelli, F.; Taticchi, A. *Dienes in the Diels-Alder Reaction* Wiley-Interscience: New York, **1990**.
5. Alder, K.; Stein, G. *Angew. Chem.* **1937**, *50*, 510.
6. Bachmann, W.E.; Scott L.B. *J. Am. Chem. Soc.* **1948**, *70*, 1458.
7. Houk, K. N.; Strozier, R.W. *J. Am. Chem. Soc.* **1973**, *95*, 4094.
8. Houk, K.N., *J. Am. Chem. Soc.* **1973**, *95*, 4092.
9. Kakushima, M., *Can. J. Chem.* **1979**, *57*, 2564.
10. Yates, P.; Eaton, P., *J. Amer. Chem. Soc.* **1960**, *82*, 4436.
11. a) Inukai, T.; Kojima, T., *J. Org. Chem.* **1965**, *30*, 3567.
b) Inukai, T.; Kojima, T., *J. Org. Chem.* **1966**, *31*, 1121.
12. Fringuelli, F.; Pizzo, F.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1983**, *48*, 2802.
13. a) Hudlicky, M.J. *J. Org. Chem.* **1974**, *39*, 3460.
b) Veselovsky, V.V.; Gybin, A.S.; Lozanova, A.V.;

- Moiseenkov, A.M.; Smit, W.A.; Caple, R. *Tetrahedron Lett.* **1988**, 175. c)Conrads, M.; Mattay, J.; Runsink, J. *Chem. Ber.* **1989**, 122, 2208. d)Cativiela, C.; Fraile, J.M.; Garcia, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J. *Tetrahedron* **1993**, 49, 4073. e)Cativiela, C.; Figueras, F.; Garcia, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J. *Tetrahedron: Asymmetry* **1993**, 4, 621.
14. a)Parlar, H.; Baumann, R. *Angew. Chem. Int. Ed. Engl.* **1981**, 20, 1014. b)Koreeda, M.; Ricca, D.J.; Luengo, J.I. *J. Org. Chem* **1988**, 53, 5586. c)Hondrogiannis, G.; Pagni, R.M.; Kabalka, G.W.; Kurt, R.; Cox, D. *Tetrahedron Lett.* **1991**, 2303. d)Kabalka, G.W.; Pagni, R.M.; Bains, S.; Hondrogiannis, G.; Plesco, M.; Kurt, R.; Cox, D.; Green, J. *Tetrahedron: Asymmetry* **1991**, 2, 1283. e)Pagni, R.M.; Kabalka, G.W.; Hondrogiannis, G.; Bains, S.; Anosike, P.; Kurt, R.; *Tetrahedron* **1993**, 49, 6743. f)see also Ref 13.d. g)see also Ref. 13.e.
15. a)Ipaktschi, J.Z. *Naturforsch. B* **1986**, 41, 496. b)Pindur, V.; Haber, M. *Heterocycles* **1991**, 32, 1463. c)Narayana Murthy, Y.V.S.; Pillai, C.N. *Synth. Commun.* **1991**, 21, 783
16. Knozinger, H.; Ratnasamy, P. *Catal. Rev. Sci. Eng.* **1978**, 17, 31
17. Kelly, T.R.; Maity, S.K.; Meghani, P.; Chandrakumar, N.S. *Tetrahedron Lett.* **1989**, 30, 1357
18. Seibert, W.; Gast, E.; Schmidt, M. *J. Organometal. Chem.* **1970**, 23, 329
19. Brown, H.C.; Ganesan, K.; Dhar, R.K. *J. Org. Chem.* **1993**, 58, 147.

20. Childs, R.F.; Mulholland, D.L.; Nixon, A. *Can. J. Chem.*, **1982**, *60*, 801.
21. a)Summers, M.F.; Marzilli, L.G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285. b)Neuhaus, D.; Keeler, J. *J. Mag. Res.* **1986**, *68*, 568. c)Kessler, H.; Griesinger, C.; Kerssebaum, R.; Wagner, K.; Ernst, R.R. *J. Am. Chem. Soc.* **1987**, *109*, 607. d)Griesinger, C.; Ernst, R.R. *J. Mag. Res.* **1987**, *75*, 261. e)Kessler, H.; Gehrke, M.; Griesinger, C. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 490. d)Kessler, H.; Bats, J.W.; Griesinger, C.; Koll, S.; Will, M.; Wagner, K. *J. Am. Chem. Soc.* **1988**, *110*, 1033.
22. Yazawa, H.; Tanaka, K.; Kariyone, K. *Tetrahedron Lett.* **1974**, *46*, 3995.
23. a)Frazer, M.J.; Gerrard, W. *J. Chem. Soc.* **1955**, 2959. b)Gerrard, W.; Wheelans, M.A. *J. Chem. Soc.* **1956**, 4296.

VITA

Kurt E. Vagle was born in Edina, Minnesota on August 13, 1970. He graduated from Minneapolis Lutheran High School in June 1988. He then attended Valparaiso University in Valparaiso, Indiana until May 1992, when he earned a Bachelor of Science Degree in chemistry. In August 1992, he entered the University of Tennessee for graduate studies in organic chemistry.