To the Graduate Council:

I am submitting herewith a thesis written by Chanda L. Elam entitled "The Effect of Solid and Solution Phase Lewis Acids on Acetal Formation and the Diels-Alder Reaction." 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 Organic 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

THE EFFECT OF SOLID AND SOLUTION PHASE LEWIS ACIDS ON ACETAL FORMATION AND THE DIELS-ALDER REACTION

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Chanda L. Elam

May 1997

DEDICATION

I wish to dedicate this thesis to my parents Mr. Robert Elam and the late Mrs. Lillian Elam. There are no words that could possible express my appreciation, love, and gratitude for so many years of being understanding, patient, and loving. Both of you have taught me that perseverance will always make dreams come true. Thank you for having faith in me when I felt as though I could not make it. I love you both.

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To my sisters, Dedrey and Sabrina, I wish to thank you for always making me laugh when I needed cheering up.

To my niece and nephew, Ashley and Kyle, thank you for reminding me of the joys of learning.

To the rest of my friends and family I wish to say thank you for always being there for me.

ABSTRACT

Previous research has employed activated alumina as a catalyst for acetal formation. Although the alumina converted aldehydes to acetals in high yields, the conversion of ketones was poor. The goal of a portion of this thesis is to use *B*-bromoboronated alumina to convert aldehydes and ketones to acetals. A comparison of these results with previous research will determine the effectiveness of this catalyst on the conversion of ketones to acetals.

The second portion of this thesis will focus on the effect of solid and solution phase Lewis acids on the Diels-Alder reaction of methyl acrylate and *trans*-piperylene. Research by Inukai demonstrates that highly acidic Lewis acids such as aluminum trichloride readily catalyzed this reaction and yield a regioselective product in the process. The effectiveness of activated (dehydrated) and modified aluminas, as well as the catalyst lithium perchlorate in diethyl ether will determine which of these catalyst exhibits regioselective capabilities.

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CHAPTER I

INTRODUCTION

The focus of this thesis is a study of the catalytic activity of alumina, modified aluminas, and lithium perchlorate in diethyl ether (LPDE) on selected reactions which include acetal formation and the Diels-Alder reaction. Alumina[1,2] has already been used to induce acetal formation from aldehydes and ketones. Ordinarily the acetal reaction proceeds well with aldehydes but poorly with ketones[1]. Other solid catalysts which have been studied extensively by Kabalka, Pagni and coworkers [3,4] may be more effective than alumina. For example, boronated aluminas (BX_n/Al_2O_3) are strong Lewis acids which may catalyze the acetalization of both aldehydes and ketones. Boronated aluminas are the focus of one part of this thesis. This report begins with an examination of the nature of alumina and then proceeds to an evaluation of the effectiveness of LPDE.

A. Alumina

Surface chemistry has evolved over the last century to become an important part of chemistry. In the late 1800s Gibbs[5,6] showed that the concentrations of substances at an interface will differ from those in the bulk phase.[7] There are many solids whose surfaces are of interest to chemists. Solids such as alumina (Al_2O_3), zeolite ($Na_2[(Al_2O_3)\cdot 6(SiO_2)]12H_2O$), silica ($SiO_2$) and zinc sulfide ($ZnS_2$) all have proven useful. However, in recent years, alumina has received much attention because of its catalytic properties.

Initially, alumina's catalytic properties were not fully understood. Much of the early

research on alumina as a catalyst in the dehydration of ethanol, which was done by Bondt[8], was overlooked. Later work performed by Peri[9] and Knözinger and Ratnasamy[10] led to a number of studies on the nature of alumina. Studies pertaining to optimum activation was the focus of Peri's work, while Knözinger's study of the catalytic activity of exposed sites led to the work of Gibbs and Bayer[11] who discussed ways of preparing Al_2O_3, (Figure 1).

The process, known as the Bayer Process, could be used to extract alumina from bauxite. Aluminum hydroxide ($Al(OH)_3$) also comes from the bauxite ore. Figure 1 outlines how sodium hydroxide reacts with bauxite to form caustic sodium aluminate ($NaAlO_2$) (step 3) which is then washed to remove impurities and leave behind crystalline alumina (step 4). The crystalline alumina is dissolved to form pure crystals of Gibbsite ($Al(OH)_3$) (step 5). These crystals are dried, or calcined, for metallurgical-grade alumina (step 8).

Equation 1, step 5 (Figure 1), shows how caustic sodium aluminate ($NaAlO_2$) is neutralized with carbonic acid or water. This process leads to the production of Gibbsite ($Al(OH)_3$), the main ingredient in the synthesis of γ-alumina, a form widely used for catalysis. Equation 2 summarizes the conversion of Gibbsite to Boehmite which is then dehydrated to γ-alumina. Further dehydration over 1200 °C (Figure 2) leads to corundum (α-alumina).

Gibbsite has a structure in which aluminum ions exist between two layers of tightly packed hydroxide ions. A side view of Gibbsite (Figure 3) shows the oxygen layers shift positions between layers (A and B) leaving a closely packed system. Instead of the oxygens layering one atop the other, they fall into pockets created by oxygens adjacent to one

Equation 1

$$2NaAlO_2 + CO_2 + 3H_2O \xrightarrow{40\,^{\circ}C} 2Al(OH)_3 + Na_2CO_3$$

and

$$NaAlO_2 + H_2O \xrightarrow{75\,^{\circ}C} Al(OH)_3 + NaOH$$

Equation 2

$$2Al(OH)_3 \xrightarrow{\Delta} \underset{\text{Boehmite}}{2AlOOH} \longrightarrow \gamma\text{-}Al_2O_3 + H_2O$$

$$\text{Gibbsite} \xrightarrow{250\,^{\circ}C} \chi \xrightarrow{900\,^{\circ}C} \kappa \xrightarrow{1200\,^{\circ}C} \alpha$$

$$\text{Gibbsite} \longrightarrow \text{Boehmite} \xrightarrow{450\,^{\circ}C} \gamma \xrightarrow{600\,^{\circ}C} \delta \xrightarrow{1050\,^{\circ}C} \theta \xrightarrow{1200\,^{\circ}C} \alpha$$

$$\text{Pseudoboehmite} \xrightarrow{300\,^{\circ}C} \text{Pseudogamma} \xrightarrow{900\,^{\circ}C} \delta \xrightarrow{1000\,^{\circ}C} \theta \xrightarrow{1200\,^{\circ}C} \alpha$$

Figure 2 Decomposition of aluminum hydroxide

another. This distortion is shown in an overall view of gibbsite.

Peri[10] theorized that the ideal surface of γ-alumina has two distinct layers. One layer, the surface layer, contains the hydroxyl ions created when water is desorbed from Boehmite (AlOOH). The next layer contains oxides and aluminum ions which lie directly below the hydroxyl ions. The layer below the surface is supposedly unaffected by dehydrating Boehmite. Figure 4 contains the Peri model for the ideal surface of γ-alumina, activated and hydrated. However, Knözinger and Ratnasamy[11] theorized that the layers below the initial two layers would also be affected by activation (dehydration) of alumina (Figure 5). These

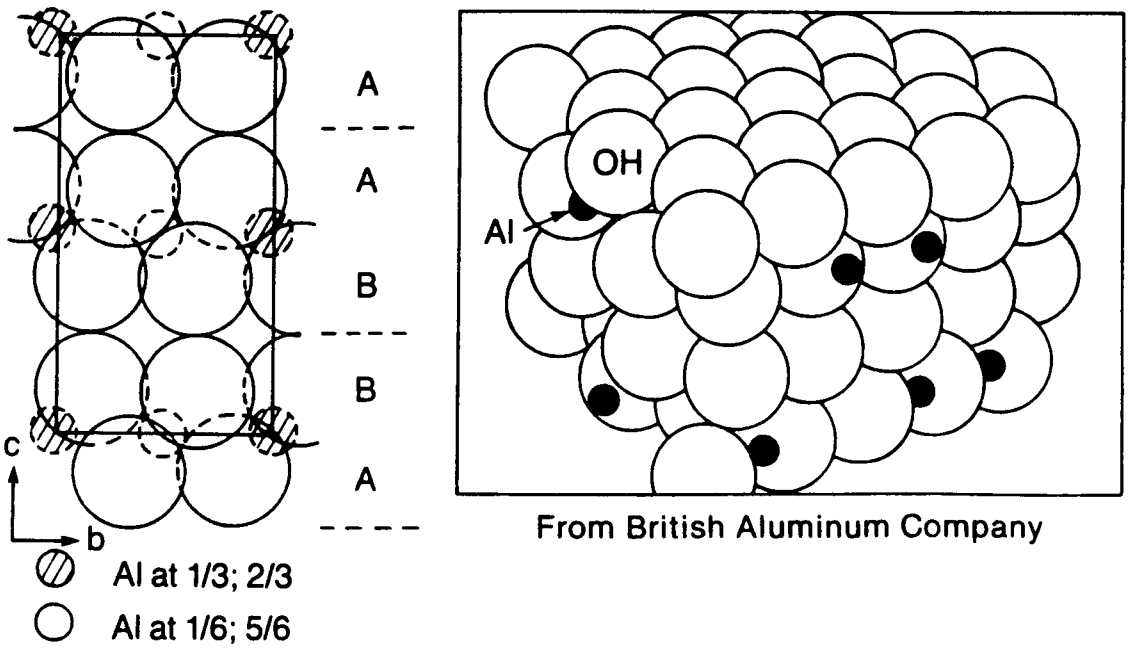


Figure 3 Gibbsite structure

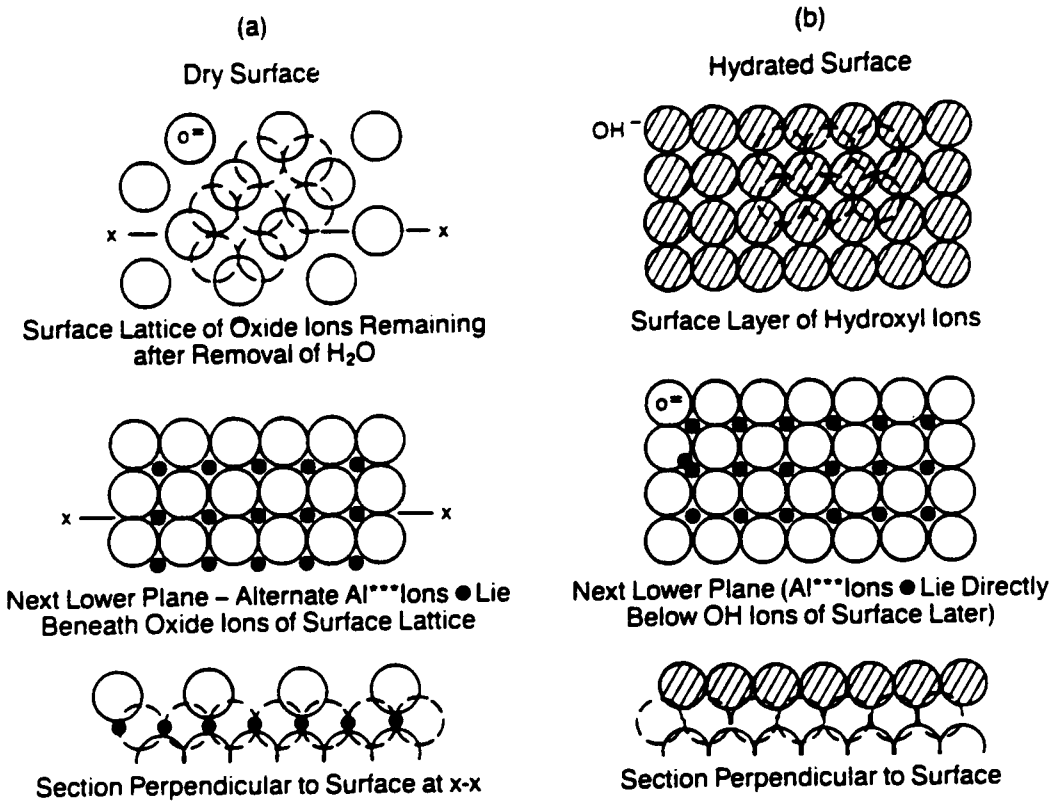


Figure 4 Ideal surface of γ-alumina, activated and hydrated.

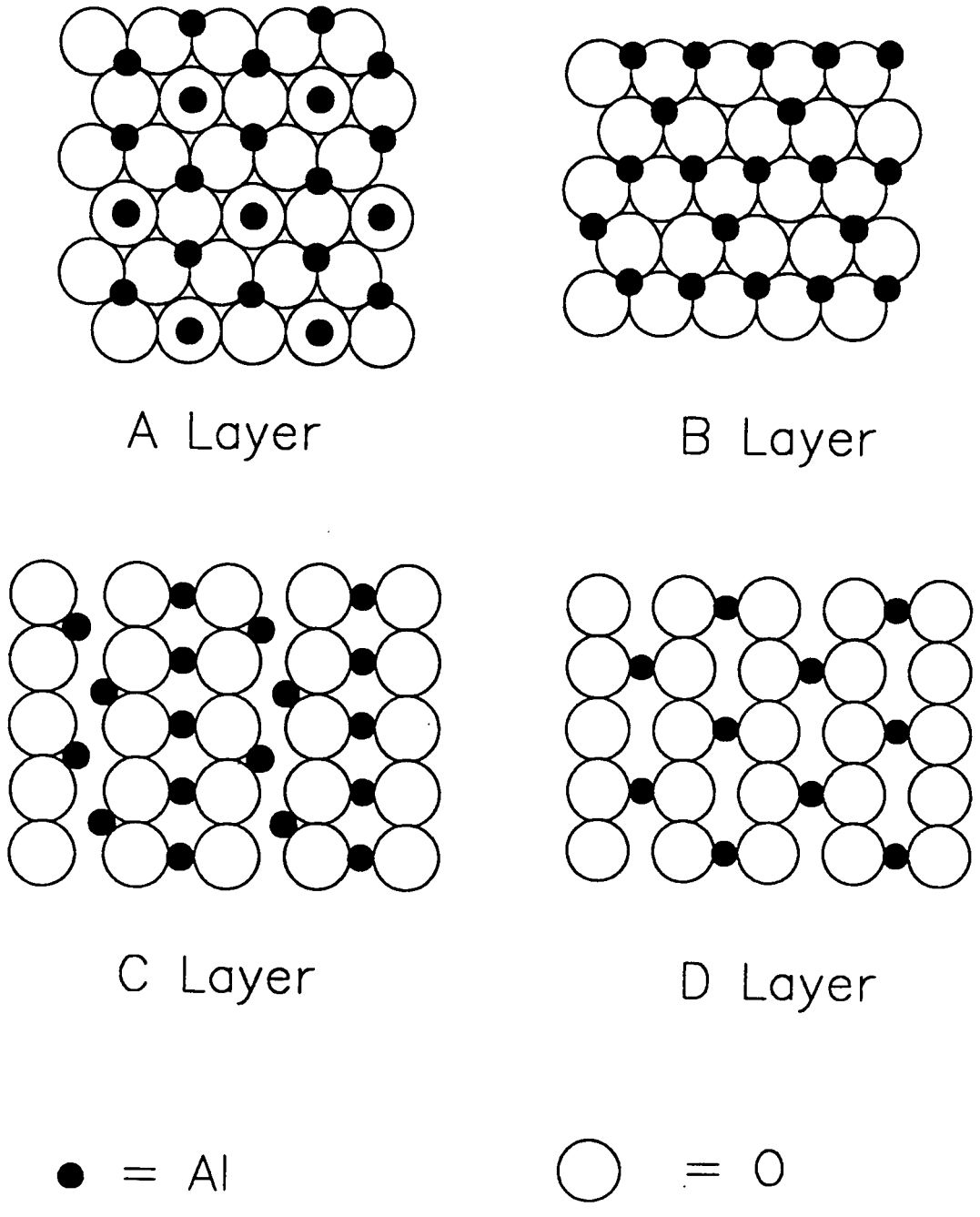


Figure 5 The Knözinger and Ratnasamy Layers of γ-Alumina

layers could in fact create spatial pockets on the surface which make γ-alumina highly catalytic. They then theorized that the layers stacked upon one another to form anion vacancies (Figure 6).

Also, due to the lattice structure of alumina, Peri[10] and Knözinger and Ratnasamy[11] believed that there are five configurations of hydroxyl groups on the surface which is supported by IR and NMR studies. Aluminum cations, in octahedral or tetrahedral environments, or a mixture of the two geometries, can coordinate to the hydroxyl ion (Figure 7) to yield the five types of hydroxyl groups. Upon activation, this packing can expose more acidic (Al^{+3}) and basic (O^{-2}) sites (Figure 8) creating many reservoirs where catalytic sites are located.

Because of γ-alumina's packing, it has been used as a catalyst in many organic reactions over the years. Posner[12] has shown that γ-alumina has excellent catalytic abilities. Consider, for example, the applications of alumina as a catalyst shown in equations 3 and 4. In the first case, alumina is functioning as a Brönsted acid, while in the second it is functioning as a Lewis acid. Also alumina (Woelm, 200°C activated, Neutral) can be selective when used to dehydrate certain alcohols (Equation 5).

In some cases, the alumina does not have to be activated to catalyze a reaction. Surface hydroxide ions can function as weak Brönsted acids and bases. Equation 6 contains a representative example of an isomerization. However, by varying the temperature at which the alumina is activated, different types and numbers of catalytic sites are formed. Higher temperatures will expose more Al^{+3} sites. Studies by Knözinger and Ratnasamy[11] on the catalytic of activity alumina activated at varying temperatures showed that alumina

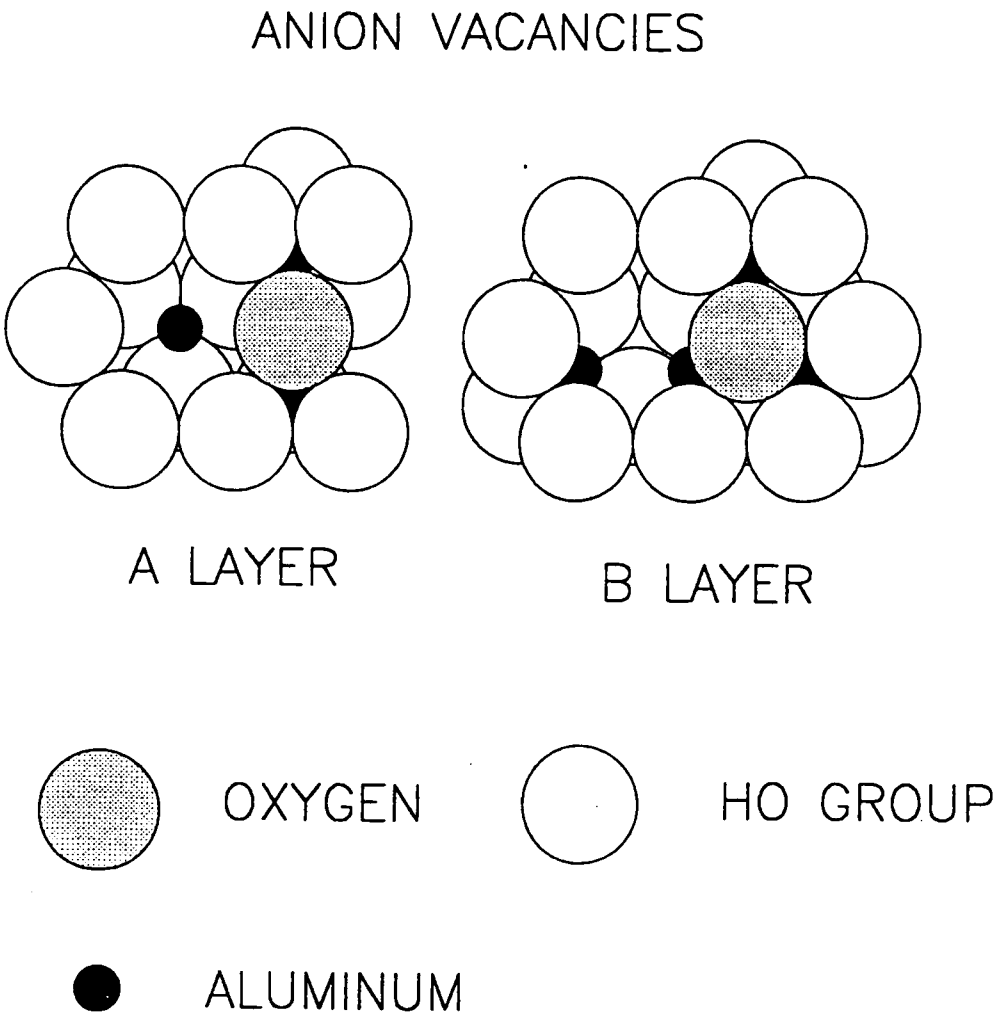
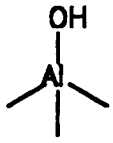
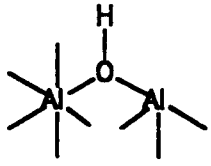


Figure 6 Surface Anion Vacancies of Alumina

TYPE	A LAYER	⁻OH STRETCHING FREQUENCIES IN CM^{-1}
Ia		3760-3780
IIa		3730-3735

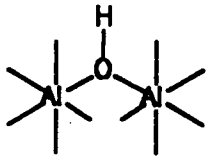
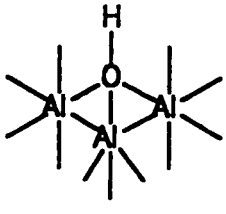
TYPE	B LAYER	⁻OH STRETCHING FREQUENCIES IN CM^{-1}
Ib		3785-3800
IIb		3740-3745
III		3700-3740

Figure 7 Hydroxyl Types and IR Stretching Patterns

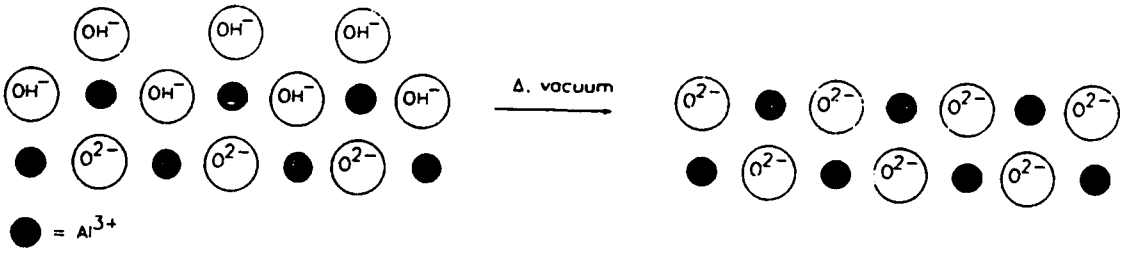
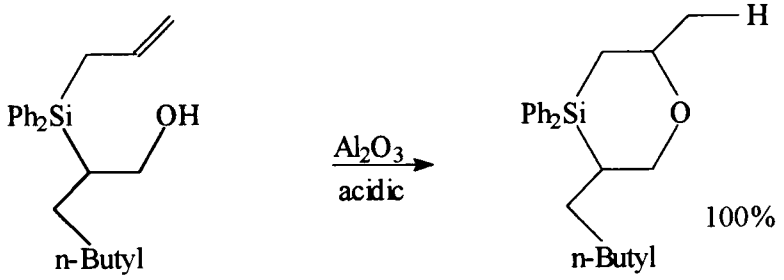
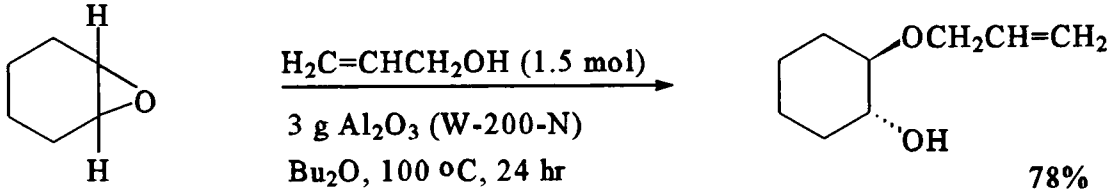


Figure 8 Activation of γ-Alumina by Dehydration

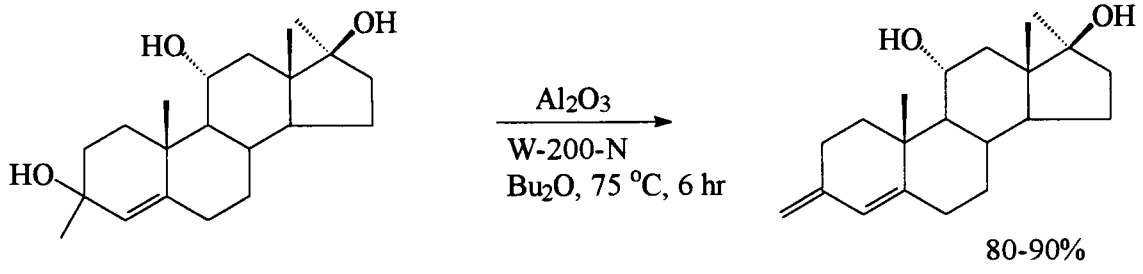
Equation 3



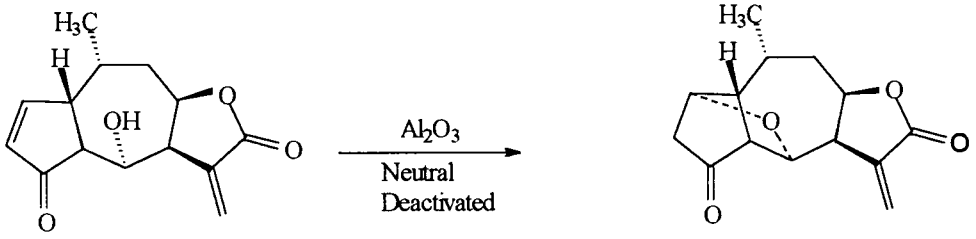
Equation 4



Equation 5



Equation 6



activated below 300°C created normal acidic sites, while activation above 300 °C generate small numbers of highly active defect sites.

In a study of particular importance in connection with the present study, Hojo[1] et al. showed that alumina (Woelm Acid TLC) which had been dried at 170-190 °C catalyzes the conversion of aldehydes to acetals (1,3-dioxoranes) using ethylene glycol (Eq. 7). Silica gel was also utilized to catalyze the reactions; however, both reaction media and substituent groups affected yields. Alumina, on the other hand, was successful in all solvents with aliphatic and aromatic aldehydes (Table 1-1). Acetalization of aldehydes afforded yields greater than 60%, but the acetalization of ketones was unsuccessful. The yield of acetophenone acetal (16%) suggests that it is possible to produce the acetals of ketones, but not on alumina. In the presence of a different Lewis acid, the reaction might go to completion.

As inferred from the data in Table 1-1, alumina is a weak catalyst. However, by treating alumina with boron trifluoride (BF_3), and other boronating agents, stronger Lewis acids and potentially better catalysts are created.[13] The properties of these boronated aluminas have been reported by Pagni and Kabalka et al.[4] Table 1-2 contains a summary of the properties of representative boronated aluminas and the structures of the boronated aluminas are shown in Figure 9.

Modified aluminas, known as the haloboronated alumina (BX_n/Al_2O_3) where X= F, Cl, Br, and I and n= 1-3, are more potent Lewis acids than activated aluminas. Kabalka, Pagni et al.[14] have found that boron trifluoride (BF_3) and boron trichloride (BCl_3) modified

Table 1-2. Properties of Boronated Alumina

Solid	Color	^{11}B NMR Chemical Shift[a,b]	Acidity Function (H_o)[c]
BF_3/Al_2O_3	white	6.5 (strong), 10.0 weak	$+0.8 \leq H_0 \leq -3.0$[d]
$BCl_{1.5}/Al_2O_3$	light brown	7.0	$-3.0 \leq H_0 \leq -8.2$[e]
BBr/Al_2O_3	reddish brown	7.0	$H_0 \leq -13.2$
BI/Al_2O_3	mustard yellow	8.1	$H_0 \leq -13.2$

a. After complexation to pyridine relative to $NaB(C_6H_5)_4$ at $\delta = 0$. b. Value for solids prepared with 400 °C Al_2O_3. c. Determined use indicator dyes. d. Solid prepared with 400 °C Al_2O_3. e. Solid prepared with 200 °C Al_2O_3.

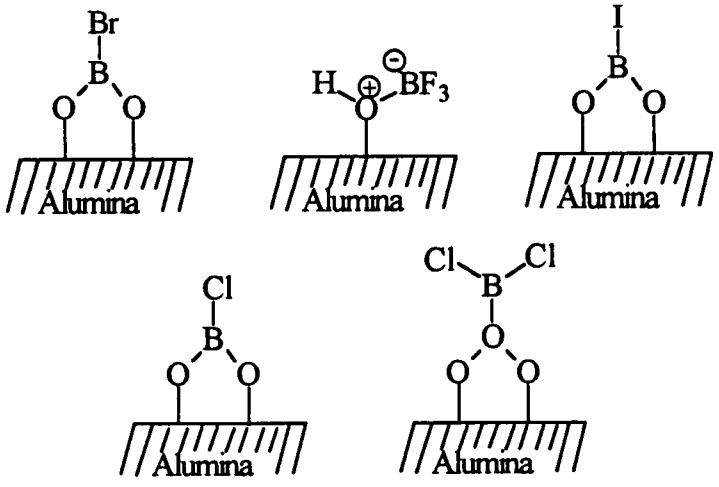


Figure 9. Structure of boron trihalides chemisorbed to the surface of alumina.

alumina are not as catalytically active as the boron tribromide (BBr_3) modified alumina. The synthesis of the boronated aluminas is shown in equations 8 and 9. This study concerns the use of the modified alumina *B*-bromoboronated alumina, as a catalyst for protecting ketones and aldehydes.

The properties of these boronated aluminas have been reported by Pagni and Kabalka et al.[4] Table 1-2 contains a summary of some of the properties, while the structures of the boronated aluminas are shown in Figure 9.

Equation 8

$$BF_3 \cdot EtO_2 + Al_2O_3 \longrightarrow BF_3/Al_2O_3$$

$$BX_3 + Al_2O_3 \longrightarrow HX + BX_n/Al_2O_3$$

$$X = Cl, Br \qquad n = 1.5\ (Cl),\ n = 1\ (Br)$$

Equation 9

$$BH_3 \cdot Me_2S + Al_2O_3 \longrightarrow BH/Al_2O_3$$

$$2BH_3/Al_2O_3 + I_2 \longrightarrow 2BI/Al_2O_3 + H_2$$

The research described in this portion of the thesis involves the Diels-Alder reaction of trans-piperylene ((*E*)-1,3-pentadiene) and methyl acrylate (MA). Previous studies of this reaction by Inukai et al.[15] and Bazyl'chik[16] suggest that the acid-catalyzed reaction is more regio- and diastereoselective than the uncatalyzed reaction. Because boronated aluminas are strong Lewis acids, it was of interest to study their effect and those of the activated alumina on this Diels-Alder reaction. It was also of interest to investigate the effect of lithium perchlorate in ether (LPDE), a catalyst extensively studied by Pagni and Kabalka[3].

B. Lithium Perchlorate in Diethyl Ether

The chemistry of perchlorates began with the accidental discovery of potassium perchlorate ($KClO_4$) by Count Friederich von Stadion in 1816.[17] For the next eighty years the development of perchlorate chemistry intrigued chemists around the European continent. Then in 1895, Carlson experimented with the production of explosives containing ammonium perchlorate. During World War I, there was increased production of the explosive perchlorates due in part to the lack of nitric acid during this time. In 1945, perchlorate salts were found to be useful in the manufacturing of solid rocket propellants. By the middle 1950s, Eastham[18] et al. reported that lithium perchlorate ($LiClO_4$), in pyridine, catalyzed the mutarotation of glucose. By the late 50s, Winstein[19] had noted that $LiClO_4$ in an organic solvent appreciably enhanced the polarity of the solution. Scientists such as Flohr[20] believed that the polarity effect could be a driving force for Diels-Alder reactions.

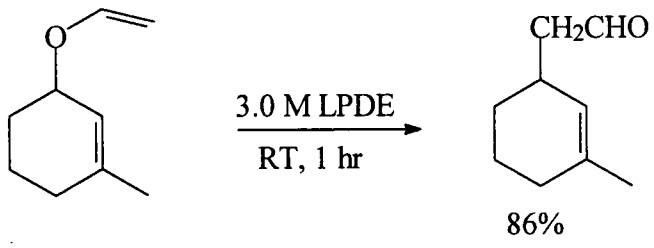
Leading studies on the nature of LPDE have been carried out by Grieco[21], Dailey[22],

as well as Pagni and Kabalka[23]. Grieco has theorized, for example, that LPDE confines solute movement and hence retains solvent ordering, compressing the reactants in much the same manner as the macroscopic application of external pressure.

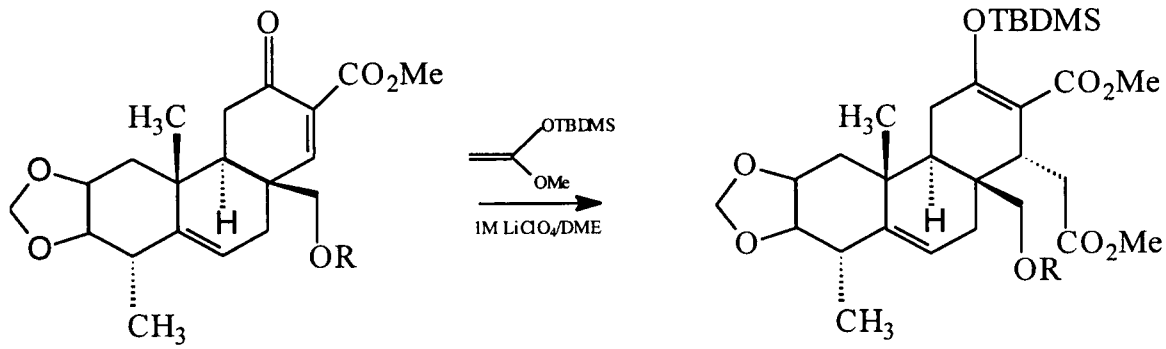
Grieco, et al. noted that when LPDE is used to catalyze a Claisen rearrangement, a typical reaction becomes atypical. The expected [3,3] sigmatropic reaction did not occur, but instead an exclusive [1,3] sigmatropic reaction occurred (Eq. 10).

Also, Grieco[24] showed that lithium perchlorate can act as a catalyst in forming protecting groups for ketones (Eq. 11). Although lithium perchlorate is useful in the reactions previously described, it is also useful in Diels-Alder reactions.

Equation 10



Equation 11



Equation 13 contains an example of a LPDE catalyzed Diels-Alder reaction. Without a catalyst, this reaction proceeds very sluggishly. Only at high temperatures and elevated pressures does the reaction yield the products shown. One reason for this sluggishness is due in part to the loss of the aromaticity of the furan moiety during the reaction.[21] Grieco speculated that $LiClO_4$ in ether might be a suitable medium for this reaction because its cohesive energy density (internal pressure) is high; in fact the reaction works well in LPDE.

Guy[25] and his group showed that $LiClO_4$ improved the efficiency of intramolecular Diels-Alder reactions at room temperature. This is the case when comparing the results of equation 14 (84%) to that in which the uncatalyzed reaction was carried out in toluene. The reaction in toluene was heated at 80 °C for 65 hours, afforded only a 22% yield of product.

Bains[23] reported that LPDE catalyzed the reaction of methyl acrylate (MA) and cylcopentadiene (CP), as do the modified and activated aluminas (Table 3). Although the product ratios for LPDE were no as large as the modified and activated aluminas, they were comparable to other unactivated, uncatalyzed reactions with and without solvent.

Previous works by Inukai[15] and his group showed that alumina trichloride ($AlCl_3$) catalyzed the reaction of *trans*-piperylene and methyl acrylate stereo- and regioselectively. The uncatalyzed reaction yielded four products (Eq. 12). In Inukai's study of trans-piperylene and MA, there was a dramatic change in the ortho:endo/-exo ratio between the catalyzed and uncatalyzed reaction. Instead of four products, the ortho products become the observed product with traces of the meta products. Table 1-4 shows the ratios and product yields for the Diels-Alder reactions performed by Inukai. The catalyzed reaction afforded the more regio- and stereoselective product. However, the study described in this thesis will

Table 1-3 Selectivities in the Reactions of Methyl Acrylate and Cyclopentadiene[a]

Catalyst	Methyl Acrylate and Cyclopentadiene	
	N:X	Percent (%) Yield
BF_3/Al_2O_3 - toluene	24	31[b]
$BCl_{1.5}/Al_2O_3$ - toluene	12	78[b]
BBr/Al_2O_3 - toluene	13	88[b]
BBr/Al_2O_3 - no solvent	8	18[c]
BI/Al_2O_3 - toluene	16	47[b]
Uncatalyzed	4.9[d]	--
Al_2O_3, Unactivated	5.8	--
Al_2O_3 - 400 °C	52	--
$AlCl_3$	99[e]	--
$LiClO_4$ - ether	8[f,g]	--

(a) All reactions were run at ambient temperature. (b) 1 hr reaction time. (c) 4 hr reaction time. (d) In CH_3CN. (e) Isaacs, N.S. *Phys. Org. Chem.;* Wiley, New York, **1987**; p. 705. (f) Pagni, R.M.; Kabalka, G.W.; Bains, S.; Plesco, M.; Wilson, J.; Bartmess, J *J. Org. Chem.* **1993**, 58, 3130. (g) 6M $LiClO_4$.

Equation 12

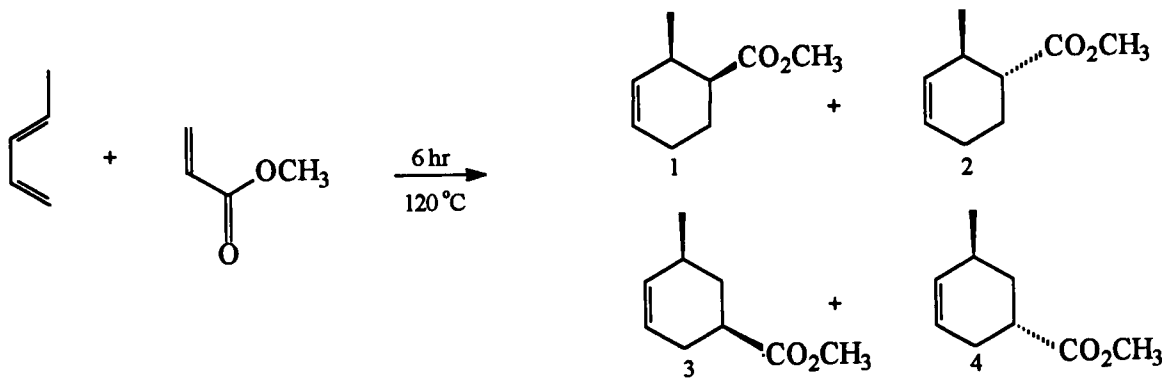


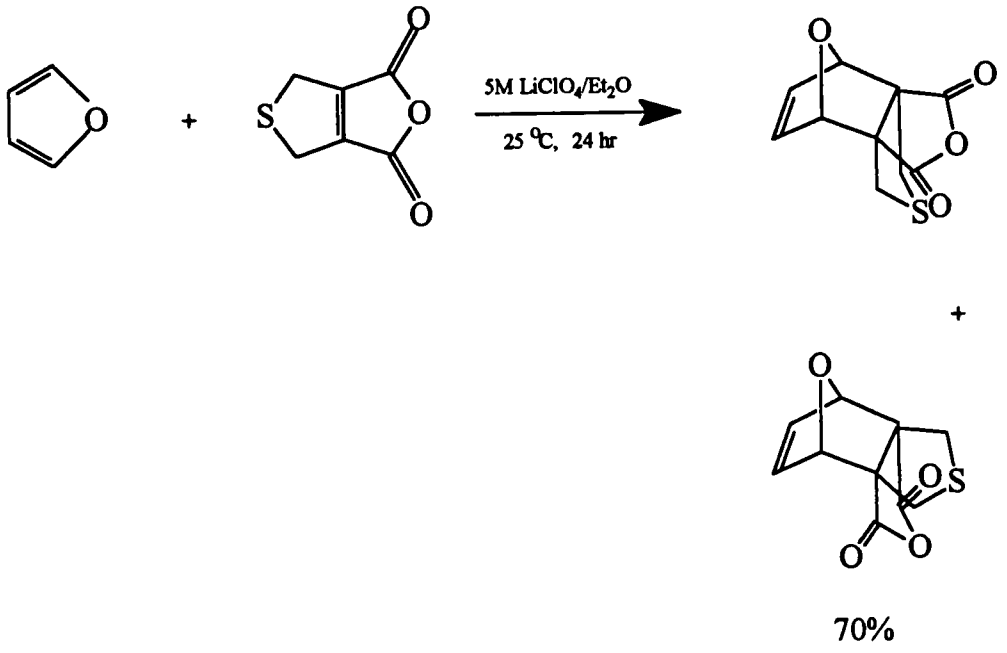
Table 1-4. Isomer Distributions of the Products from Reagents of *trans*-Piperylene and Methyl Acrylate (or Acrylic Acid)

Reaction Conditions				
	Catalyzed[a]	Uncatalyzed[b]		
Temp (°C)	10-20	25	120	120
Piperylene (mole)	1.47	0.2	0.3	0.56
Methyl acrylate (mole)	1.47	0.16	0.3	0.78
Time	3 hr	70 days	6 hr	7 hr
Yield (%)	50	39	53	52
Product Distribution				
(1 + 2) : (3 +4)[d]	50:1.0	10:1.1	6.3:1.2	9.1:1.1
(1 + 2) : (3 +4)[e]	50:1.0	10:1.1	5.9:1.2	8.3:1.1
1:2[e]	20:1.1	2.3:1.8	2.2:1.9	2.8:1.6
3:4[f]	Mostly *cis*	3.7:1.4	2.9:1.5	2.6:1.6

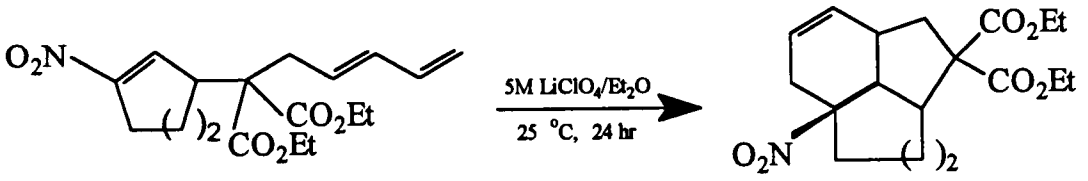
a. In benzene (150 ml) in the presence of 0.15 mole of anhydrous aluminum chloride. b. Room-temperature (*ca.* 25°) reaction in a scaled tube, and 120° reactions in a stainless steel autoclave. Hydroquinone was added. c. Reaction of free acrylic acid. d. By glpc analysis of the aromatization products. e. By glpc analysis of the cyclohexenecarboxylates. f. By glpc analysis of the cyclohexanecarboxylates.

determine yields and product distribution using the catalyst (LPDE) discussed earlier.

Equation 13



Equation 14



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CHAPTER II

ACETAL FORMATION CATALYZED BY *B*-BROMOBORONATED ALUMINA

A. Introduction

The ability to protect carbonyl functionalities has been of interest to chemists for many years. The interest arises from the basic need to carry out chemical reactions without destroying the carbonyl group. This portion of the thesis will focus on the protection of aldehydes and ketones using *B*-bromoboronated alumina.

B. Catalyst

Previous research by Hojo and Masuda[1] revealed that alumina (Al_2O_3) is a good catalyst for acetal formation. As noted in Chapter 1, alumina was effective in converting aldehydes to acetals in very high yields, but the conversion of ketones to acetals was difficult. For example, an attempt to produce acetophenone acetal using alumina as a catalyst afforded only a 16% overall yield. This study demonstrated that producing the ketal was possible but that a stronger catalyst was needed to achieve acceptable yields. Research has shown that the modified aluminas, especially *B*-bromoboronated alumina, are powerful catalysts (Chapter 1). For this reason, *B*-bromoboronated alumina was investigated as a catalyst for acetal formation.

C. Acetal Formation of Cinnamaldehyde in the Presence of BBr/Al_2O_3

Aryl aldehydes tend to form acetals quite readily in the presence of *B*-bromonated

alumina. Benzaldehyde (100% overall yield) is representative[1]. However once substituent groups are added to the ring, the reaction is not as efficient. This is the case with cinnamaldehyde, which was used as a representative aldehyde in this study. Initial studies of the formation of the cinnamaldehyde acetal provided information (amount of catalyst, reaction time, etc.) (Table 2-1) that proved to be useful in developing a general procedure for the production of acetals.

The overall reaction of cinnamaldehyde was carried out as shown in Equation 16. Scheme 1 shows a possible intermediate during the initial stages of the reaction where the aldehyde will chemically bond with the modified alumina and create a positive charge on the carbonyl carbon. Based on the fact that the vinyl group is an electron-releasing group (ERG) which will stabilize the positive charge, the reaction will proceed quickly and unincumbered.

Equation 16

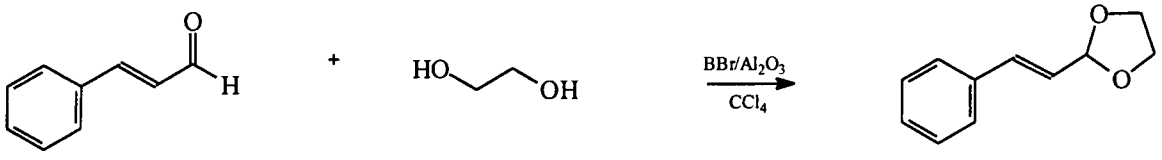
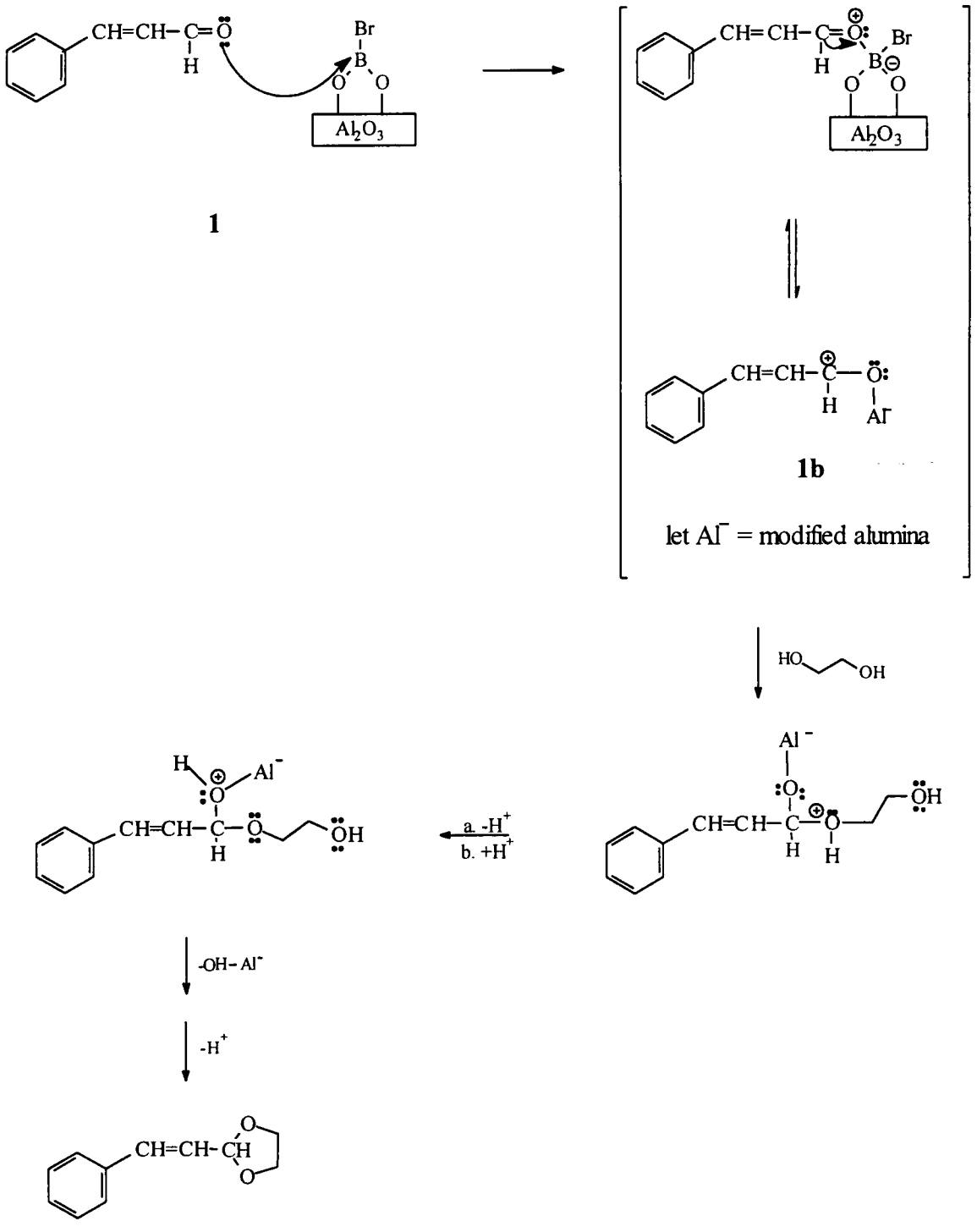


Table 2-1 Acetalization of Cinnamaldehyde with BBr/Al_2O_3 catalyst.[a,b]			
Aldehyde	**$HOCH_2CH_2OH$(mmol)**	**Catalyst (g)**	**Yield (%)**
Cinnamaldehyde	5.0	0.5	84
Cinnamaldehyde	5.0	1.0	95
a. All reaction refluxed for 24 hrs. b. Anhydrous CCl_4 used as solvent.			

Scheme 1


CH=CH–C=O
H
Br
B
O
O
Al2O3
1
CH=CH–C=O
H
Br
B
O
O
Al2O3
CH=CH–C
H
O:
Al⁻
1b
let Al⁻ = modified alumina
HO
OH
Al⁻
:O:
CH=CH–C
H
O
H
OH
a. -H+
b. +H+
H
Al⁻
O
CH=CH–C
H
O
H
OH
-OH-Al⁻
-H+
CH=CH-CH
O
O

D. Acetalization of Aldehydes and Ketones in the Presence of BBr/Al_2O_3

As noted earlier, a study was carried out to determine the effect of modified alumina on the formation of acetals. A standard reaction in which cinnamaldehyde was used showed that high yields were possible. One explanation was that the vinyl group, an electron releasing group (ERG), stabilized the charge by delocalizing it (the positive charge) into the ring. This would lead to conversion of most of the aldehyde to the corresponding acetal. For this reason, it was thought that aldehydes containing electron-releasing groups (ERG) such as methyl, methoxy, and vinyl groups would produce high yields of the acetal; while electron-withdrawing groups (EWG) which destabilize a cation would produce lower yields. Table 2-2 reveals that is indeed the case for aldehydes, with one exception.

The exception was 1-naphthaldehyde in which the additional ring led to a lower than expected yield. The ring system has the capability of stabilizing a positive charge by

Table 2-2 *B*-bromoboronated Alumina Catalyzed Formation of Acetals.[a,b,c]

Aldehyde	Amount (g)	$HOCH_2CH_2OH$ (mmol)	Yield (%)
Benzaldehyde	0.21	10	100
1-Naphthaldehyde	0.31	10	58
p-Tolualdehyde	0.24	10	85
p-Anisaldehyde	0.27	10	84
5-Chlorosalicylaldehyde	0.31	10	87
3-Nitrobenzaldehyde	0.25	10	51

a. All reactions refluxed for 24 hrs. b. Anhydrous CCl_4 used as solvent. c. All reactions used 1 gram of catalyst.

delocalization into the ring. Because of this it would be expected that yields should be as high as benzaldehyde or cinnamaldehyde, but only 58% of the acetal was formed. Perhaps longer reaction times would lead to enhanced yields.

This study also highlighted the effect of the modified alumina on ketones. cause ketones are more sterically hindered than aldehydes, the acetal yields (Table 2-3) were expected to be lower than those obtained from aldehydes. In the case of acetophenone, the ERG (methyl) stabilizes the charge on the carbonyl carbon. Also, the aromatic ring can stabilize the charge by delocalization . However, when other substituents such as methoxy groups are placed on the ring, the yields are reduced. The *para*-methoxy group in 3,4-dimethoxyacetophenone can delocalize the positive charge onto the oxygen of the methoxy group, but it only afforded a 28% of the ketal. Even though the oxygen is present in the strong ERG (CH_3O-), it is highly electronegative. Perhaps this is responsible for the low yields.

2-Heptanone was also studied with respect to acetal formation. The alkyl ERG were able to stabilize the positive charge providing reasonable yields consistent with those obtained for other ketones. Further experiments utilizing 1,3-diphenyl-2-propanone were carried out. The benzyl groups replaced the alkyl groups in 2-heptanone, but the benzyl groups apparently stabilized the positive charge. However, when benzophenone was used, the yields diminished drastically. The inductive effect of the phenyl ring apparently dictated the course of the reaction. This study demonstrated that ketones are capable of forming acetals.

Cyclopentanone, cyclohexanone and cyclooctanone were also investigated. All

Table 2-3 Acetal Formation of Ketones Catalyzed by BBr/Al_2O_3.[a,b,c]			
Ketones	**Amount (g)**	**$HOCH_2CH_2OH$ (mmol)**	**Yield (%)**
Acetophenone	0.24	10	56
3,4-Dimethoxyacetophenone	0.36	10	28
2-Heptanone	0.23	10	57
1,3-Diphenyl-2-Propanone	0.42	10	56
Benzophenone	0.36	10	5
Cyclopentanone	0.17	10	43
Cyclohexanone	0.20	10	55
Cyclooctanone	0.25	10	58
a. All reactions run for 24 hours. b. CCl_4 used as solvent. c. 1.0 g of catalyst used			

produced reasonable yields of the corresponding acetals. From this study it is clear that substituents affect yields in acetal formation.

E. Conclusion

Based on the percent yields, aldehydes produce more product than ketones. This is due in part to the electronic effect of the substituent on the ring system.

F. Experimental Method

i. Analytical Methods

Gas chromatography was performed using a Hewlett-Packard 5890 Gas Chromatograph equipped with a 30 m x 1/8" column packed with 30% SE-30 by weight utilizing Chromosorb W support. Gas chromatography with mass spectrometery was performed using a Hewlett Packard 5890 GC fitted with a 5970 mass spectrometer.

Nuclear Magnetic Resonance (NMR) spectra were obtained using a Bruker AC 250 spectrometer. Samples were dissolved in $CDCl_3$ with 1% tetramethylsilane (TMS) as the internal standard (δ = 0.0 ppm).

ii. Manipulation of Reagents

Due to the nature of the modified alumina, transfers of the catalyst were performed using a glove bag in an inert, dry argon atmosphere. Glassware, syringes and needles were oven-dried (or flame-dried) and assembled under argon. With a stream of argon and bubbler attached to relieve pressure, all glassware was allowed to cool to room temperature. The reactions were carried out under argon or nitrogen atmospheres.

G. Experimental Procedures

i. Acetalization of Benzaldehyde To a flame-dried, argon flushed 100-mL roundbottomed flask containing 1.0 g of *B*-bromoboronated alumina, and 10 mL of carbon tetrachloride was added, while stirring, 0.20 mL (0.21 g) of dry benzaldehyde (2.0 mmol). A color change was noted as the mixture turned

purple. After the mixture was allowed to stir at room temperature for 10 minutes, 0.62 g (0.56 mL) of ethylene glycol (10 mmol) was added. Then the purple color disappeared. The reaction mixture was refluxed for 24 hours and then allowed to cool. Neutralization of the solution was achieved using two 10-mL washes of saturated aqueous sodium bicarbonate. The two layers were separated and the aqueous layer washed with anhydrous ethyl ether. The organic layers were combined in a 100 mL round bottomed flask and the solvent was removed under reduced pressure using a rotary evaporator to yield an oily residue (0.29g, 100% overall product yield). Using a silica gel column with 14% ethyl acetate in hexane as eluent, the pure acetal was isolated. Analysis was performed via proton (^{1}H) and carbon (^{13}C) NMR spectroscopy and gas chromotography (GC). mp. 192-195 °C ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 8.06 (2H, *d*, J = 7.2 Hz), 7.89 (1H, *d*, J = 7.0 Hz), 7.52 (2H, *m*), 5.80 (1H, *s*), 4.03 (4H, *m*). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 134.44, 129.73, 129.18, 128.98, 128.34, 126.40, 103.74, 65.29.

ii. **Acetalization of Cinnamaldehyde** was carried out as described in section i utilizing cinnamaldehyde (0.13g, 1.0 mmol) to produce an isolated yield of 0.16g, 95%. The final step produced an oily product. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.40 (5H, *m*), 6.74 (1H, *d*, J = 9.2 Hz), 6.21 (1H, *dd*, J = 6.1 Hz), 5.44 (1H, *d*, J = 6.2 Hz), 4.07 (4H, *m*). ^{13}C NMR ($CDCl_3$) (ppm) acetal: δ 152.71, 135.77, 134.77, 131.22, 129.04, 128.53, 128.43,

126.88, 125.10, 103 , 64.35 .

iii. **Acetalization of Benzophenone** was carried out as described in section i utilizing benzophenone (0.36g, 2.0 mmol) to produce an isolated yield of 0.022g, 5%: mp. 86-88 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.79 (4H, *d*, J = 6.9 Hz), 7.50 (2H, *m*), 7.47 (4 H, *dt*, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 142.12, 137.59, 132.35, 130.01, 128.07, 126.11, 64.84.

iv. **Acetalization of *p*-Anisaldehyde** was carried out as described in section i utilizing *p*-anisaldehyde (0.27g, 2.0 mmol) to produce an isolated yield of 0.30g, 84%. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.25 (2H, *d*, J = 8.5 Hz), 6.92 (2H, *d*, J = 6.7 Hz), 4.10 (4 H, *m*), 3.80 (3H, *s*). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 136.10, 129.74, 128.89, 126.54, 114.42, 103, 64.

v. **Acetalization of 5-Chlorosalicylaldehyde** was carried out as described in section i utilizing 5-chlorosalicylaldehyde (0.31g, 2.0 mmol) to produce an isolated yield of 0.34g, 87%: mp. 72-75 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.71 (1H, *s*), 6.85 (1H, *d*, J = 8.4 Hz,) 5.92 (1 H, *s*), 4.12 (4H, *m*). ^{13}C NMR ($CDCl_3$) (ppm) acetal: 153.88, 130.43, 127.9, 118.58, 103.17, 64.84.

vi. **Acetalization of 2-Heptanone** was carried out as described in section i utilizing 2-heptanone (0.23g, 2.0 mmol) to produce an isolated yield of 0.18g, 57%: mp. 163-166 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: 3.39 (4H, *m*), 2.45 (2H, *d*t, J = x Hz), 1. 31 (4H, *m*). 0.89 (3H *t*, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 110.18, 64.56, 39.17, 32.74, 23.74.

vii. **Acetalization of *p*-Tolualdehyde** was carried out as described in section i utilizing *p*-tolualdehyde (0.24g, 2.0 mmol) to produce an isolated yield of 0.28g, 85%: mp. 211-215 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.34 (2H, *d*,J = 8.1 Hz), 7.19 (2H, *d*, J = 7.9 Hz), 5.77 (1H, *s*), 4.051 (4H, *m*), 2.34 (3H, *s*). ^{13}C NMR ($CDCl_3$)(ppm) acetal: 138.92, 134.87, 129.74, 128.92, 103.70, 65.14, 21.16.

viii. **Acetalization of 1-Naphthaldehyde** was carried out as described in section i utilizing 1-naphthaldehyde (0.31g, 2.0 mmol) to produce an isolated yield of 0.22g, 58%: mp. 170-175 °C ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 9.25 (1H, *d*, J = 8.4 Hz), 8.3 - 7.4 (6H, *m*), 4.15 (4H, *m*). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 136.60, 135.25, 129.55, 129.04, 128.52, 128.43, 126.92, 126.25, 125.67, 124.83, 103.78, 65.13.

ix. **Acetalization of 3,4-Dimethoxyacetophenone** was carried out as described in section i utilizing 3,4-dimethoxyacetophenone (0.36g, 2.0 mmol) to

produce an isolated yield of 0.12g, 28%. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.53 (1H, *d*, J = 7.1 Hz), 6.91 (1 H, *d*, J = 8.3), 3.94 (6H, *s*), 2.57 (3H, *s*). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 130.43, 123.22, 110.66, 110.05, 109.90, 64.35, 55.98, 26.13.

x. **Acetalization of 1,3-Diphenyl-2-propanone** was carried out as described in section i utilizing 1,3-diphenyl-2-propanone (0.42g, 2.0 mmol) to produce an isolated yield of 0.30g, 58%: mp. 62-67 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 7.26 (6H, *m*), 7.18 (4H, *d*, J = 4.5 Hz) 3.44 (4 H, s). ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 133.95, 129.43, 128.62, 126.96, 64.6, 49.05, 29.12.

xi. **Acetalization of Cyclohexanone** was carried out as described in section i utilizing cyclohexanone (0.20g, 2.0 mmol) to produce an isolated yield of 0.16g, 55%: mp. 176-179 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm): δ 3.84 (4H, *m*), 2.34 (4H, *dt*, J = 5.3 Hz), 1.59 (4H, *t*, J = 3.0 Hz). ^{13}C NMR ($CDCl_3$) (ppm) acetal: δ 98.07, 64.53, 36.75, 29.95, 25.62.

xii. **Acetalization of Cyclopentanone** was carried out as described in section i utilizing cyclopentanone (0.17g, 2.0 mmol) to produce an isolated yield of 0.11g, 43%: mp. 151-156 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 3.85 (4H, *m*), 2.29 (4H, *t*, J = 7.5 Hz), 1.75-1.54 (4H, *m*). ^{13}C NMR

($CDCl_3$)(ppm) acetal: δ 110.65, 64.28, 35.27, 27.58.

xiii. **Acetalization of Cyclooctanone** was carried out as described in section i utilizing cyclooctanone (0.25g, 2.0 mmol) to produce an isolated yield of 0.20g, 58%: mp. 210-211 °C. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) acetal: δ 3.85(4H, *m*), 2.39(4H, *t*, 6.3 Hz), 1.73(4H, *m*), 1.56(4H, *m*) ^{13}C NMR ($CDCl_3$)(ppm) acetal: δ 110.98, 63.15, 42.07, 32.22, 29.59, 23.85.

xiv. **Preparation BBr/Al_2O_3** To a 250-mL roundbottomed flask with a septum-sealed, side arm and magnetic stirrer was added 25 g of unactivated Grade I neutral alumina. A vacuum adapter was attached and the vessel was flame-dried. The flask was cooled while maintaining an argon flow. Hexanes (30-mL) was added to make a slurry, then BBr_3 (25 mmol, 25 mL of 1M solution in hexanes) was introduced using a double-ended needle. HBr gas was released as the BBr_3 solution was added. The mixture was allowed to stir for 3 hours. The solvent was removed *in vacuo*. The solid was transferred in a glove bag to a flame-dried Erlenmeyer flask.

H. Materials

i. Solvents

Anhydrous Ethyl Ether, Fisher Scientific
Ethyl Acetate, Fisher Scientific
Carbon Tetrachloride, Aldrich Chemical Co.
Hexanes, Fisher Scientific
Toluene, Fisher Scientific

ii. Gases

Prepurified Argon, National Welders Supply Company
Prepurified Nitrogen, National Welders Supply Company

iii. Reagents

Acetophenone, Fisher Scientific
Alumina (modified and activated), Fisher Scientific, Neutral Brockman Activity Grade I, was prepared according to the procedure described by Pagni, et al. [2]
para-Anisaldehyde, Aldrich Chemical Company
Benzaldehyde, Aldrich Chemical Company
Benzophenone, Fisher Scientific
5-Chlorosalicyaldehyde, Eastman Kodak Co.
trans-Cinnamaldehyde, Aldrich Chemical Co.
Cyclohexanone, Aldrich Chemical Co.
Cyclooctanone, Aldrich Chemical Co.
Cyclopentanone, Eastman Kodak
para-Dibromobenzene, Eastman Chemical Co.
3,4-Dimethoxyacetophenone, Aldrich Chemical Co.
1,3-Diphenyl-2-propanone, Mathes, Coleman and Bell Division
Ethylene Glycol, Fisher Scientific
2-Heptanone, Eastman Chemical Co.
1-Naphthaldehyde, Eastman Organic Co.
Silica Gel, Baxter
para-Tolualdehyde, Eastman Kodak
Undecane, Aldrich Chemical Co.

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CHAPTER III

DIELS-ALDER REACTIONS

A. Introduction

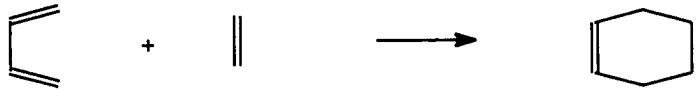
Diels-Alder reactions have been known for a number of years. The use of catalyst to accelerate the reaction has also been known for almost as long. This chapter will focus on the catalytic effect of Lewis acids on the Diels-Alder reaction of *trans*-piperylene and methyl acrylate (MA).

B. Diels-Alder Reaction of Methyl Acrylate and *trans*-Piperylene

The Diels-Alder reaction, a cycloaddition reaction, is widely used to form carbon-carbon bonds. Occurring either inter- or intramolecularly, the reaction is a concerted process which yields a six-membered ring and as many as four stereogenic centers. Equation 16 shows a hypothetical Diels-Alder reaction.

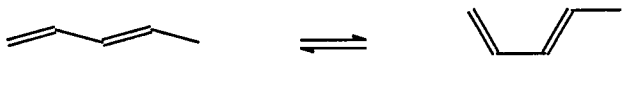
The diene (**5**) must be in a s-cis conformation for the reaction to occur. This conformation is necessary so that the appropriate overlap between its p orbitals and those of the dienophile can occur. As with diene **5**, *trans*-piperylene (Eq 17) can rotate about the central sigma (σ) bond to yield s-trans (the more stable conformation) (**8**).

Equation 16



5 **6** **7**

Equation 17

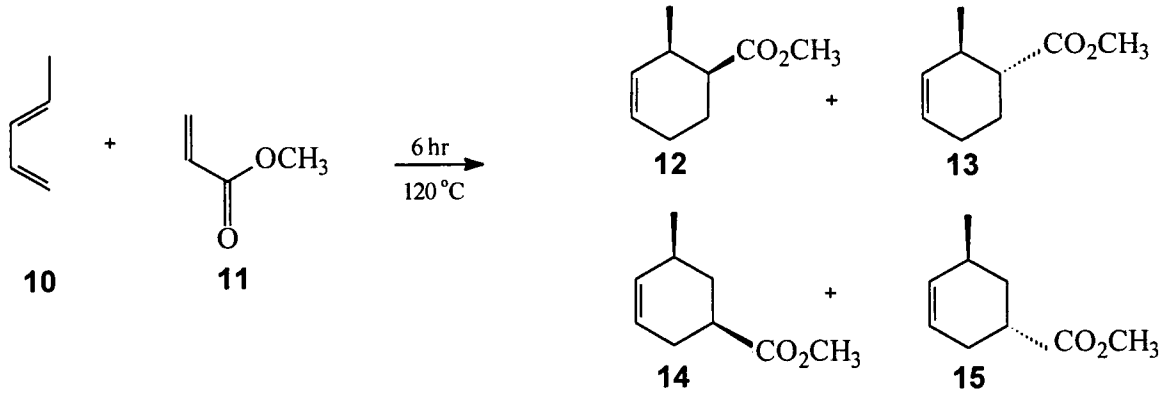


8 **9**

The uncatalyzed reaction of MA and *trans*-piperylene was carried out in a sealed quartz tube at 120 °C and afforded four products (Equation 18).[1] Figure 10 shows the GC/MS spectrum of the product mixture. The three GC peaks were easily assigned based on the prior published work. All peaks afforded similar mass spectra, all consistent with the expected products. The ortho-endo (the first peak) and the ortho-exo (the last peak) were very easy to distinguish. However, it was impossible to separate the meta-endo and -exo isomers which eluted as one small peak. Because of the difficulty in distinguishing the four products an alternative technique was used to analyze the product mixture.

Figure 11 contains a portion of the high field proton (^{1}H) NMR of the product mixture. To distinguish the four products, the doublets representing the methyl groups on

Equation 18



10 **11** **12** **13** **14** **15**

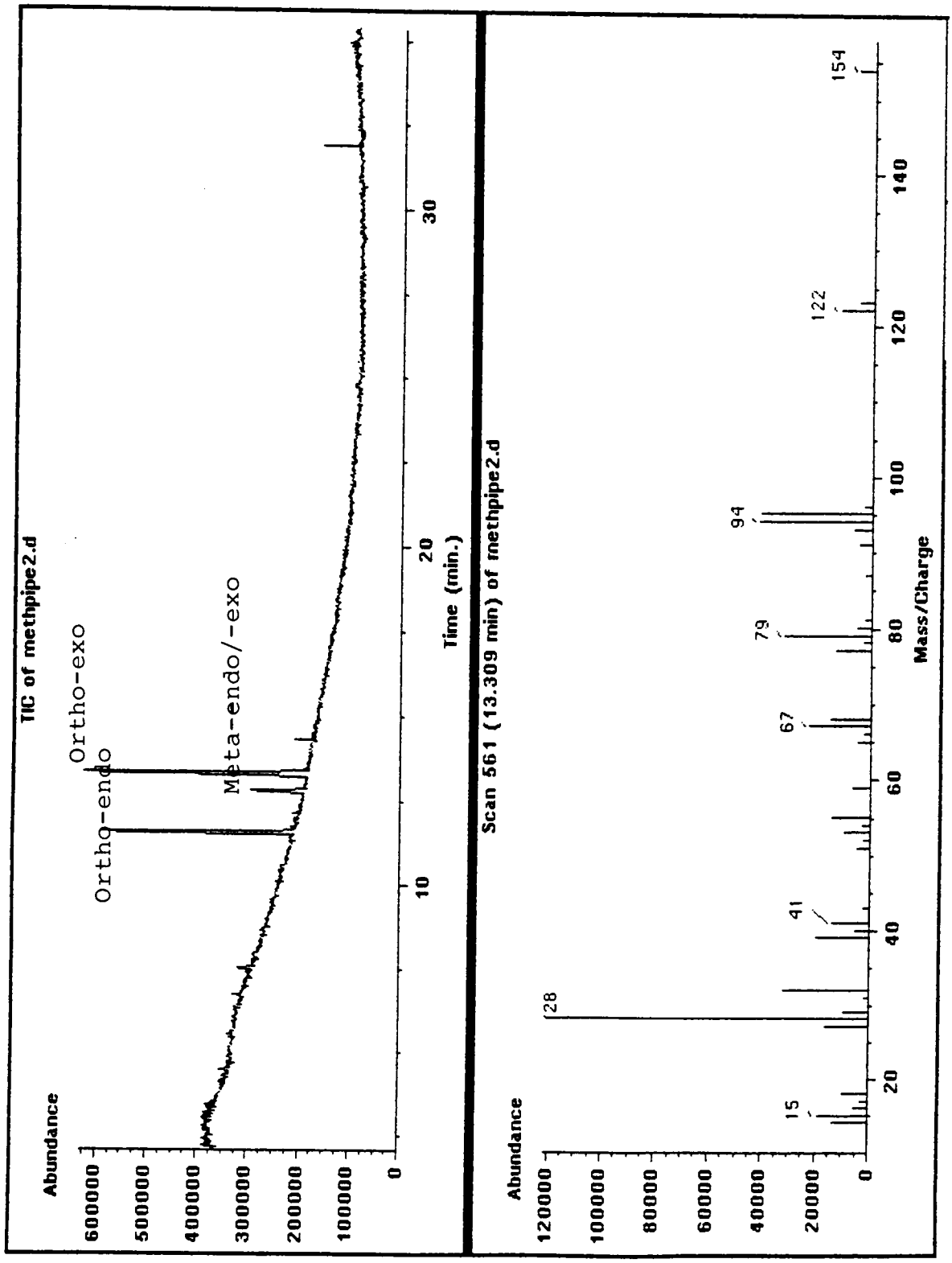


Figure 10 GC/MS of Uncatalyzed Diels-Alder Reaction

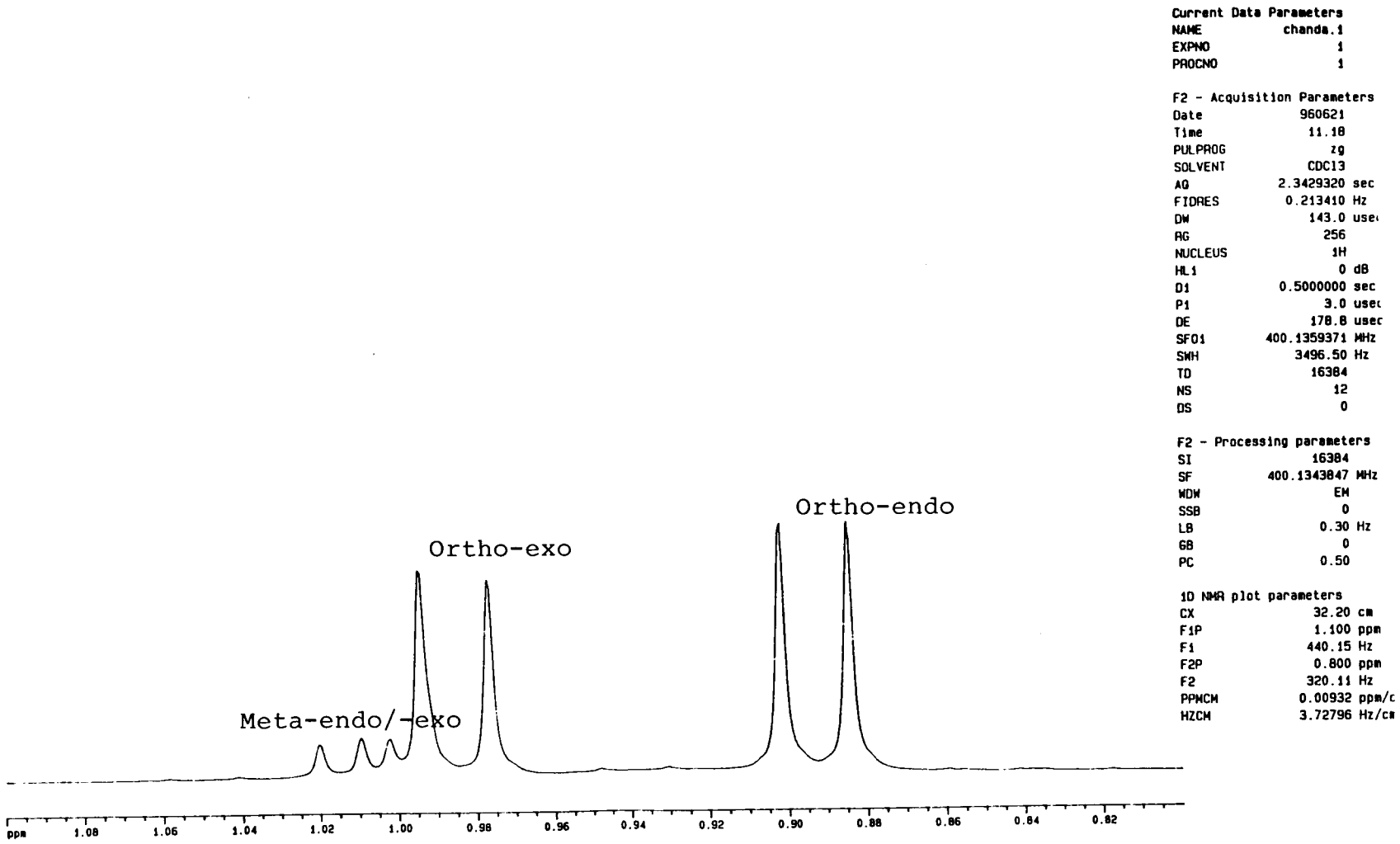


Figure 11 Proton NMR of Uncatalyzed Diels-Alder Reaction

the six-membered ring were examined. As can be seen, the four doublets are almost completely resolved. To determine which doublet represented which isomer, the GC and NMR results for the uncatalyzed and catalyzed reactions were compared.

The aluminum trichloride-catalyzed reaction of MA and *trans*-piperylene yielded the ortho-endo product in excess and traces of the others compounds. This aided in distinguishing between the ortho-endo and -exo products in the uncatalyzed reaction. Once the assignments for the uncatalyzed reaction were completed, a study of the effect of lithium perchlorate in diethyl ether (LPDE) on this reaction was performed.[2,3]

The reactions were carried out by adding varying amounts of dried lithium perchlorate to a volumetric flask, then a 1:1 mole ratio of MA (0.33 ml) and *trans*-piperylene (0.37 ml) was added to the volumetric flask followed by ether. The flask was shaken to dissolve the lithium perchlorate and the ether added to the mark. The solutions were then transferred to a flame-dried container (EXPERIMENTAL XI - XVI). Table 3-1 contains the ortho-endo to ortho-exo ratio obtained from the proton (^{1}H) NMR of the product mixtures; no meta products were formed in the reactions.

When the Diels-Alder reaction of MA and *trans*-piperylene was carried out in the presence of the LPDE at varying reaction times, the ortho-endo adduct was the major product, with only trace amounts of the ortho-exo and the meta products being formed. Similarly, in the presence of varied concentrations of LPDE, the endo to exo ratios remained essentially the same. Table 3-2 contains the results of the Diels-Alder reactions run in LPDE for 12 hours. Only the ortho products were formed. Meta products were not detected by GC.

Table 3-1 Endo:Exo Ratio for the Diels-Alder Reaction of MA and *trans*-piperylene in the presence of LPDE		
Entry	**Reaction Conditions[g,h]**	**Ortho (Endo:Exo)**
1	1M[a]	3.5:1
2	2M[b]	3.9:1
3	3M[c]	3.9:1
4	4M[d]	4.7:1
5	5M[e]	3.9:1
6	6M[f]	4.2:1
Each concentration varied its time to obtain maximum yield of product: a. Reaction stirred for 144 hrs. b. Reaction stirred for 68 hrs. c. Reaction stirred for 72 hrs. d. Reaction stirred for 48 hrs. e. Reaction stirred for 36 hrs. f. Reaction stirred for 12 hrs. g. Degradation takes place if the reactions are not neutralized after this time period. h. Reactions run at room temperature.		

Table 3-2 Product Yields of Diels-Alder Reaction in the presence of LPDE. [a,b]		
Entry	**Products (%) Yield**	
	Endo	**Exo**
1	1	--
2	3	--
3	9	2
4	18	4
5	35	7
6	40	11
a. Analysis taken via Gas Chromatograph. Parameters set at initial temperature of 50°C for 2.00 minutes. A ramp of 2 °C/min was used to reach the final temperature of 200 °C. The GC remained at 200 °C for 2 minutes, then cooled to 50 °C. b. All reactions were run for 12 hours at room temperature.		

Because the reactions in LPDE were not particularly impressive, other Lewis acids were used to catalyze the Diels-Alder reaction of *trans*-pipierylene and MA. When the Diels-Alder reaction was carried out on aluminas of varying activity, the results were interesting. The ortho-endo to -exo ratio increased as the activation temperature of alumina increased. This is consistent with the idea that as more acidic sites are exposed to the surface the selectivity will increase. The data in Table 3-3 indicated that the ratio of the 200 °C activated alumina was existent. The 800°C activated alumina yielded a ratio of adducts of 4.6 to 1. The 400 °C activated alumina afforded the ortho-endo product with traces of the meta product. However, GC analysis did not show any of the minor products. Only trace amounts of the ortho-exo were detected. Figure 12 contains the ^{1}H NMR spectrum of the product mixture obtained from the 800 °C activated alumina. As with the lithium perchlorate reactions, there were mixtures of the ortho-endo

Table 3-3 Ortho Endo:Exo Ratio of Diels-Alder Reaction using the Activated Aluminas[a,b,c]

Entry	Activated Alumina	Endo:Exo	Product (%) Yield
1	200 °C	0	1
2	400 °C	2.2:1.0	4
3	600 °C	3.1:1.0	55
4	800 °C	4.6:1.0	47

a. Reaction carried out neat. b. Reaction temperature of 75°C for 4 hours. c. 15 ml of methanol added to reaction and stirred overnight. Vacuum filtration used to collect organic layer.

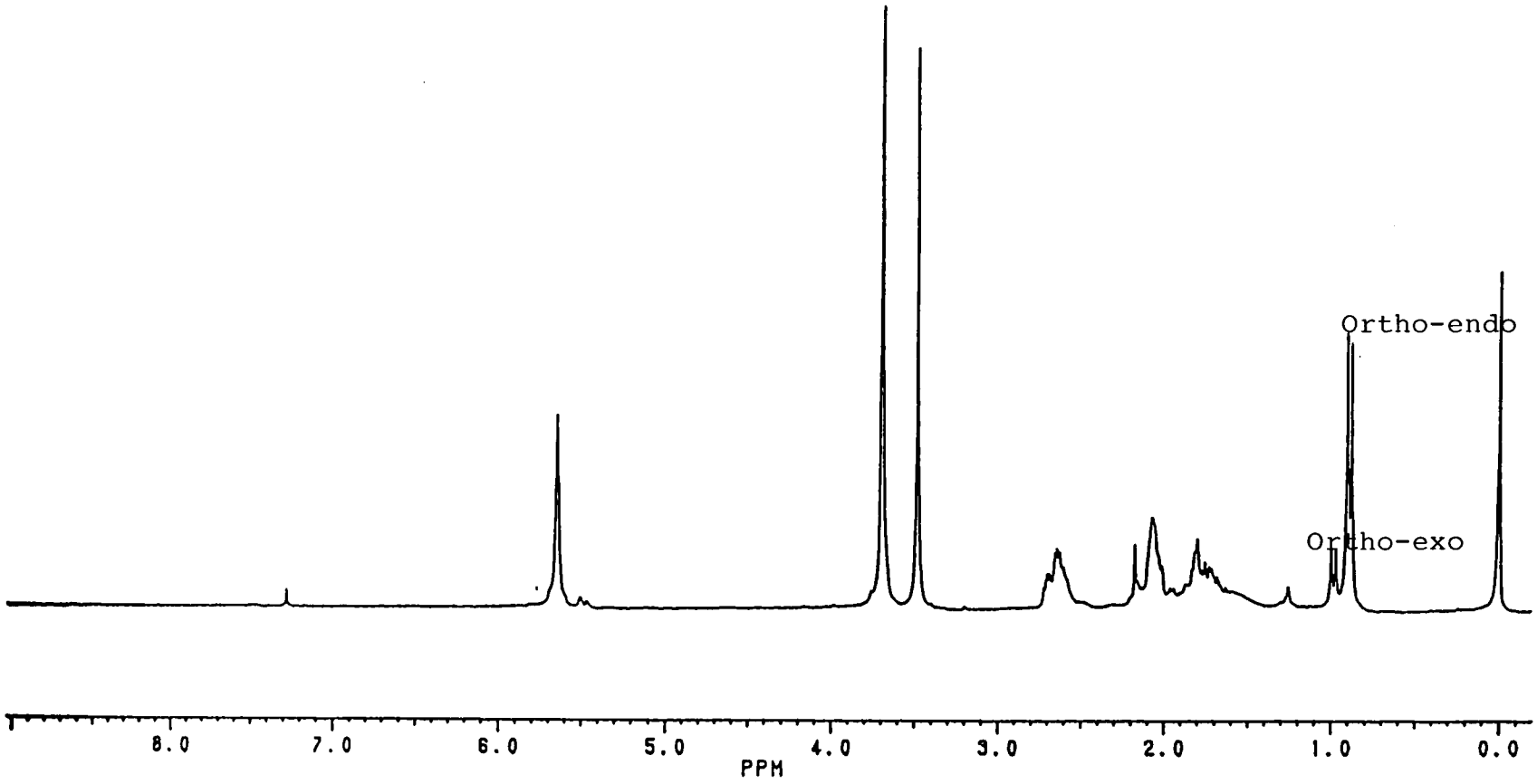


Figure 12 Diels-Alder Reaction on the 800 °C Alumina

and -exo products. Although the more activated γ-alumina created more acidic sites, it was not enough to produce one diastereomer exclusively. A more acidic Lewis acid perhaps would do better. As discussed earlier (CHAPTER 1), the halo-boronated aluminas could fill this role.

Because *B*-bromoboronated alumina, as discussed in Chapter 1, is more acidic than the *B*-fluoro and -chloro modified alumina, it may be a more selective catalyst for this Diels-Alder reaction. This is also true of BI/Al_2O_3. Figure 13 is the H^1 NMR of the product obtained from the BBr/Al_2O_3 catalyzed reaction of MA and *trans*-piperylene and indicates that the ortho-endo product and trace amounts of the ortho-exo diastereomer were formed. Analysis of the BI/Al_2O_3 catalyzed by ^1H NMR, shows that the ortho-endo to ortho-exo ratio is even larger than th reaction on BBr/Al_2O_3. Table 3-4 contains a summary of the product ratios obtained for all the boronated aluminas.

Table 3-4 Ratio of Ortho-Endo:Ortho-Exo in the Presence of the B-HaloBoronated Aluminas. [a,b,c]

Entry	Modified Alumina	Endo:Exo
1	BF_3/Al_2O_3	--
2	$BCl_{1.5}/Al_2O_3$	--
3	BBr/Al_2O_3	8.2:1
4	BI/Al_2O_3	47.4:1

a. Reaction run in toluene for 1 hour. b. Reactions neutralized with 15 ml of methanol, then left to stir overnight. c. Analysis done using Bruker 250 MHz NMR.

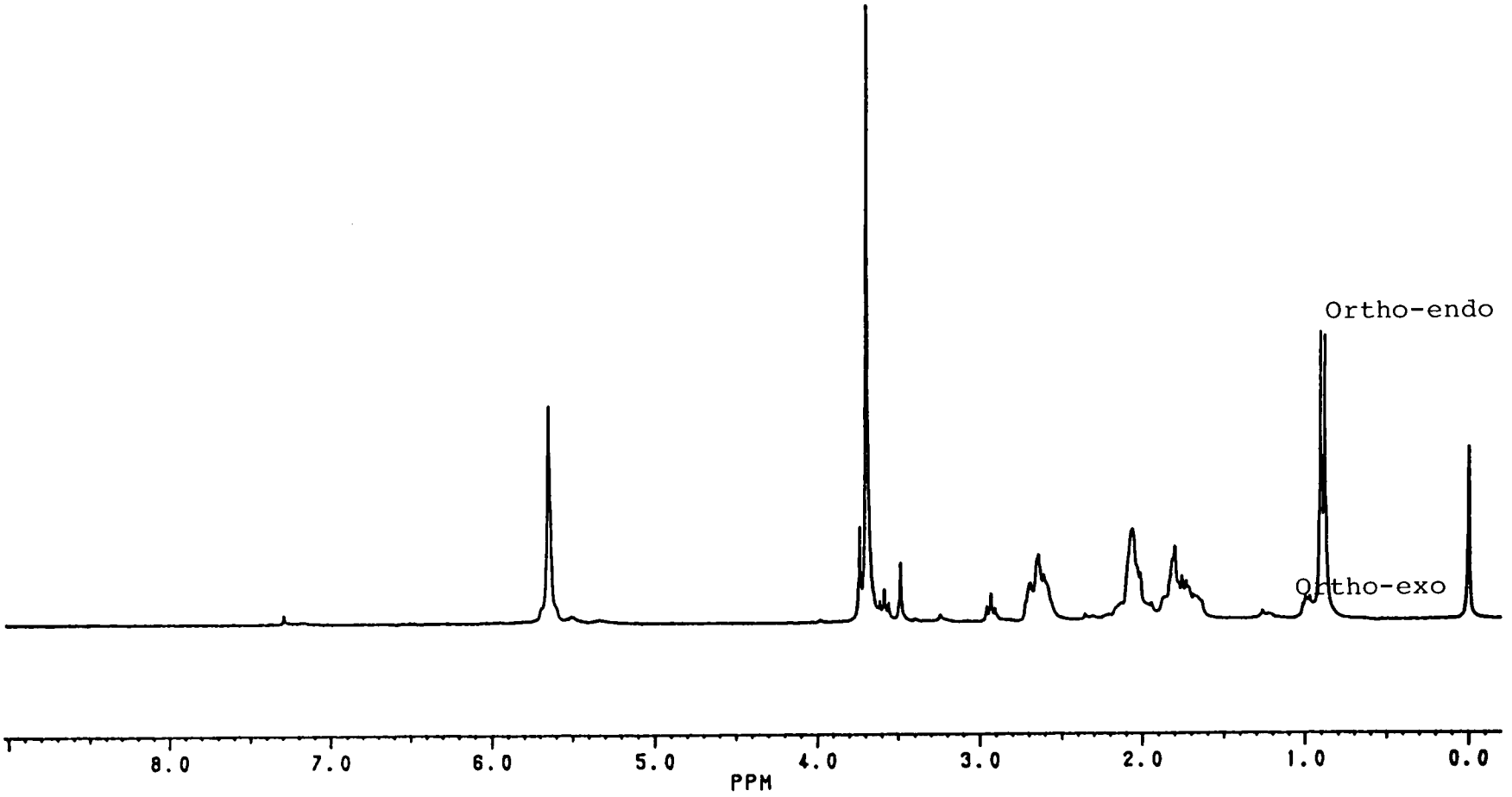


Figure 13 Diels-Alder Reaction on BBr/Alumina

During the allotted reaction time of one hour both the B-fluoro and -chloro alumina did not yield adequate amounts of products for ^{1}H NMR analysis. However, gas chromatography revealed trace amounts (2% product yield) for the B-chloro-modified alumina-catalyzed reaction. GC analysis was carried out on the other reactions to determine percent yields (Table 3-5). From the product distribution it is clear that *B*-iodoboronated alumina produced predominantly one diastereomer (ortho-endo) and the overall percent yield was greater than the *B*-bromo catalyzed reaction.

Table 3-5. Product Distribution for Diels-Alder Reaction of MA and *trans*-piperylene.[a,b,c]

Entry	Modified Alumina	Product (%) Yield	
		O-endo	O-exo
1	BF_3/Al_2O_3	--	--
2	BCl/Al_2O_3	2	--
3	BBr/Al_2O_3	8.8	1
4	BI/Al_2O_3	33.5	1

a. Analysis done using GC. b. All reaction run for 1 hr in toluene. c. Reactions neutralized with 15 ml of methanol, then left to stir overnight.

C. Conclusion

It is clear that LPDE and the activated aluminas produce the ortho endo:exo products in lower ratios. From the data collect by NMR and GC, only the highly acidic modified alumina could produce a regioselective product.

D. Experimental Method

i. Analytical Methods

Gas chromotography (GC) was performed using a Hewlett-Packard 5890 GC instrument equipped with a 30 m x 1/8" column packed with 30% SE-30 by weight on a Chromosorb W support. Gas chromatograph with mass spectrometer was performed using a Hewlett-Packard 5890 GC with 5970 mass spectrometer.

Nuclear Magnetic Resonance (NMR) spectra were obtained on Bruker AC 250 and 400 MHz spectrometers. Samples were dissolved in $CDCl_3$ with 1% tetramethylsilane (TMS) as the internal standard (δ = 0.0 ppm).

ii. Manipulation of Reagents

Due to the fact that the activated and modified aluminas react with water, transfers of the catalysts were performed in a glove bag under an inert, dry argon atmosphere. Glassware, syringes and needles were oven-dried or flame-dried and assembled, under a stream of argon. All glassware was allowed to cool to room temperature under an inert atmosphere. The reactions were done under an argon or nitrogen atmosphere.

E. Experimental Procedures

i. Diels-Alder of *trans*-Piperylene and Methyl Acrylate (MA) in a Sealed Quartz Tube.

To a 50-mL quartz tube in the shape of a bulb, 0.66 mL of methyl acrylate (7.4 mmol) was added via syringe. After adding 10 mg of

hydroquinone, 0.73mL of *trans*-piperylene (7.3 mmol) was added by syringe. A septum was placed atop the tube for transfer to an evacuating system. An adapter was used to connect the tube to the evacuating system. The tube was cooled using liquid nitrogen, then purged of oxygen by pumping. Several times the tube was heated, cooled, then purged. Using a welder torch, the neck of the tube was sealed while under vacuum. After the neck of the sealed tube had cooled, it was placed in an oven at 120 °C for 6 hours. The tube was then cooled in liquid nitrogen and opened. An aliquot of a yellow oil was immediately taken for analysis via ^{1}H and ^{13}C NMR spectroscopy and GC/MS. ^{1}H NMR ($CDCl_3$ w/TMS) (ppm): δ: 6.40 (1H, dd, J = 1.5 Hz), 6.13 (1H , dd, J = 10 Hz), 5.82 (1H , dd, J = 1.5 Hz), 3.70 (3H, *s)*, *ortho endo*: δ: 0.902 (3H, *d*, J = 7.0 Hz); *ortho exo*: δ: 0.994 (3H, *d*, J = 7.0 Hz); *meta- endo* and *-exo*: 1.02 and 1.00 (3H, *d*, J = 7.0 Hz). GC Yield: 49% yield of ortho-endo; 1% yield of ortho-exo; 3% yield of meta-endo and -exo.

ii. Acid-Catalyzed Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate.

To a flame-dried 100-mL round-bottomed flask containing 0.093g of aluminum chloride (0.75 mmol) under argon was added 0.75 mL of benzene (7.4 mmol). While stirring 0.66 mL of methyl acrylate (7.3 mmol) and 0.73 mL of piperylene (7.3 mmol) were then added. The reaction mixture was

cooled in ice water and left to react for 3 hours at 0-12 °C. The reaction mixture was neutralized with a saturated solution of potassium carbonate and the layers separated. The aqueous layer was washed with diethyl ether. Concentration *in vacuo* of the combined organic phase afforded the mixture of adducts. Analysis of the mixture was accomplished by ^{1}H and ^{13}C NMR spectroscopy. ^{1}H NMR ($CDCl_3$ w/TMS) (ppm) *ortho-endo*: δ: 0.90 (3H, *d*, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$ w/TMS) (ppm): δ 132, 125 , 51. GC Yield: 46% yield of ortho-endo; 2% overall yield.

iii. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on 800 °C Activated Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of 800 °C activated alumina (2.9 mmol) under argon 0.26 mL of methyl acrylate (2.9 mmol) and 0.29 mL of piperylene (2.9 mmol) were added. The reaction mixture was stirred for 4 hours at 75 °C. The reaction mixture was cooled and 15 mL of methanol was added. The methanol solution was removed from the alumina via a vacuum filtration using a fitted glass vacuum adapter and concentrated *in vacuo* on the roto-evaporator . Analysis of mixture was carried out by ^{1}H and ^{13}C NMR spectroscopy and GC. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm): δ 3.69 (3H, *s*); ortho endo: 0.906 (3H, *d*, J = 6.8Hz); ortho exo: δ 3.48 (3H, *s*), 0.999 (3H, *d*, J = 7.0). ^{13}C NMR ($CDCl_3$ w/TMS)(ppm): 175, 132, 126, 51, 43, 29, 24, 19, 17. GC Yield: 40% yield ortho-endo; 7%

yield of ortho-exo.

iv. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on 200 °C Activated Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of 200 °C activated alumina (2.9 mmol) under argon, 0.26 mL of methyl acrylate (2.9 mmol) and 0.29 mL of piperylene (2.9 mmol) were added. The reaction mixture was stirred for 4 hours at 75 °C. The reaction mixture was cooled and 15 mL of methanol was added by injection. The methanol solution was removed from the alumina via a vacuum filtration using a fitted glass vacuum adapter and concentrated *in vacuo* using the rotovap. Analysis of mixture was done by ^1H and ^{13}C NMR spectroscopy and GC. GC Yield: 1% overall yield of the ortho-endo.

v. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on 400 °C Activated Al_2O_{33}.

To a 100-mL round-bottomed flask containing 2.9 g of 400 °C activated alumina (2.9 mmol) under argon, 0.26 mL of methyl acrylate (2.9 mmol) and 0.29 mL of piperylene (2.9 mmol) were added. The reaction mixture was stirred for 4 hours at 75 °C. The reaction mixture was cooled and 15 mL of methanol was added. The methanol solution was removed from the alumina via a vacuum filtration using a fitted glass vacuum adapter

and concentrated *in vacuo* using the rotovap. Analysis of the product mixture was done by ^{1}H and ^{13}C NMR spectroscopy and GC. GC Yield: 4 % yield of ortho-exo.

vi. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on 600 °C Activated Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of 600 °C activated alumina (2.9 mmol) under argon, 0.26 mL of methyl acrylate (2.9 mmol) and 0.29 mL of piperylene (2.9 mmol) were added. The reaction mixture was stirred for 4 hours at 75 °C. The reaction mixture was cooled and 15 mL of methanol was added. The methanol solution was removed from the alumina via a vacuum filtration using a fitted glass vacuum adapter and concentrated using the rotovap. Analysis of mixture was done by ^{1}H and ^{13}C NMR spectroscopy and GC. GC Yield: 49% yield of ortho-endo; 6% ortho-exo.

vii. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on Modified BI/Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of *B*-iodoboronated alumina[4], 5 mL of toluene was added to create a slurry. Methyl acrylate (0.26 mL; 2.9 mmol) was added by syringe and the mixture was allowed to stir for 5 minutes. *Trans*-piperylene (0.29 mL, 2.9 mmol) was

then added via syringe. After the slurry stirred for one hour at room temperature, 15 mL of methanol was added and the solution was left to stir overnight. The solution was removed from the alumina via vacuum filtration and concentrated *in vacuo*. ^{1}H NMR ($CDCl_3$ w/TMS) (ppm) endo: δ 3.69 (3H, *s*), 0.905 (3H, *d*, J = 6.9 Hz). ^{13}C NMR ($CDCl_3$ w/TMS)(ppm): δ 131, 125, 51, 24; GC Yield: 67% yield of ortho-endo; 2% yield of ortho-exo.

viii. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on Modified BF_3/Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of *B*-fluoroboronated alumina, 5 mL of toluene was added to create a slurry. Methyl acrylate (0.26 mL; 2.9 mmol) was added by syringe and the mixture was allowed to stir for 5 minutes. *Trans*-piperylene (0.29 mL, 2.9 mmol) was added via syringe. After the slurry stirred for one hour at room temperature, 15 mL of methanol was added and the solution was left to stir overnight. The solution was removed from the alumina via vacuum filtration and concentrated *in vacuo*. GC Yield: 0% overall yield.

ix. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on Modified BCl/Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of *B*-

chloroboronated alumina, 5 mL of toluene was added to create a slurry. Methyl acrylate (0.26 mL; 2.9 mmol) was injected and the mixture was allowed to stir for 5 minutes. *Trans*-piperylene (0.29 mL, 2.9 mmol) was added via syringe. After the slurry stirred for one hour at room temperature, 15 mL of methanol was added and left to stir overnight. The solution was removed from the alumina via vacuum filtration and concentrated *in vacuo*. GC Yield: 2 % yield of ortho-endo.

x. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate (MA) on Modified BBr/Al_2O_3.

To a 100-mL round-bottomed flask containing 2.9 g of *B*-bromoboronated alumina, 5 mL of toluene was added to create a slurry. Methyl acrylate (0.26 mL; 2.9 mmol) was added by syringe and the mixture was allowed to stir for 5 minutes. *Trans*-piperylene (0.29 mL, 2.9 mmol) was added via syringe. After the slurry stirred for one hour at room temperature, 15 mL of methanol was added and the solution was left to stir overnight. The solution was removed from the alumina via vacuum filtration and concentrated *in vacuo*. GC Yield: 44% yield of ortho-endo; 5% yield of ortho-exo.

xi. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate in the Presence of 6M $LiClO_4$.

To a 10-ml flame-dried volumetric flask containing 6.4 g of lithium perchlorate (60 mmole), 3 ml of anhydrous diethyl ether was added. Methyl acrylate (0.33ml, 3.7 mmole) was added to the cooled ether mixture, then trans-piperylene (0.37 ml, 3.7 mmole) was added by syringe. The volumetric flask was filled with ether to its mark. The solution was shaken to dissolve the lithium perchlorate, then transferred via a double-ended needle to a septum-sealed, flame-dried test tube equipped with a magnetic stirrer. The mixture was left to stir for 12 hours at room temperature. The solution was first washed with water (2 x 10 ml), then neutralized with 5% sodium bicarbonate solution (2 x 10ml) and finally concentrated *in vacuo*. Analysis was accomplished via ^{1}H and ^{13}C NMR spectroscopy and GC. ^{1}H NMR ($CDCl_3$ w/TMS)(ppm) *ortho-endo*: δ 3.69 (3H, *s*), 0.903 (3H, *d*, J = 7.0 Hz). *Ortho-exo:* 0.990 (3H, *d*, J = 7.0 Hz). ^{13}C ($CDCl_3$ w/TMS)(ppm): δ 51, 24; GC Yield: 40% yield of ortho-endo; 11% yield of orth-exo.

xii. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate in the Presence of 1M $LiClO_4$.

To a 10-ml flame-dried volumetric flask containing 1.1 g of lithium perchlorate (10 mmole), 3 ml of anhydrous diethyl ether was added. Methyl acrylate (0.33ml, 3.7 mmole) was added to the cooled ether mixture, then trans-piperylene (0.37 ml, 3.7 mmole) was added by syringe. The volumetric flask was filled with ether to its mark. The solution was shaken to dissolve

the lithium perchlorate, then transferred via a double-ended needle to a septum-sealed, flame-dried test tube equipped with a magnetic stirrer. The mixture was left to stir for 12 hours at room temperature. The solution was first washed with water (2 x 10 ml), then neutralized with 5% sodium bicarbonate solution (2 x 10ml) and finally washed with water (2 x 10ml), after which the mixture was concentrated *in vacuo*. Analysis was accomplished via ^{1}H and ^{13}C NMR spectroscopy and GC. GC Yield: 1% yield of ortho-endo.

xiii. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate in the Presence of 2M $LiClO_4$.

To a 10-ml flame-dried volumetric flask containing 2.1 g of lithium perchlorate (20 mmole), 3 ml of anhydrous diethyl ether was added. Methyl acrylate (0.33ml, 3.7 mmole) was added to the cooled ether mixture, then trans-piperylene (0.37 ml, 3.7 mmole) was added by syringe. The volumetric flask was filled with ether. The solution was shaken to dissolve the lithium perchlorate, then transferred via a double-ended needle to a septum-sealed, flame-dried test tube equipped with a magnetic stirrer. The mixture was left to stir for 12 hours at room temperature . The solution was first washed with water (2 x 10 ml), then neutralized with 5% sodium bicarbonate solution (2 x 10ml) and finally washed with water (2 x 10ml), after which the mixture was concentrated *in vacuo*. Analysis was accomplished via ^{1}H and ^{13}C NMR

spectroscopy and GC. GC Yield: 3% yield of ortho-endo.

xiv. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate in the Presence of 3M $LiClO_4$.

To a 10-ml flame-dried volumetric flask containing 3.2g of lithium perchlorate (30 mmole), 3 ml of anhydrous diethyl ether was added. Methyl acrylate (0.33ml, 3.7 mmole) was added to the cooled ether mixture, then trans-piperylene (0.37 ml, 3.7 mmole) was added by syringe. The volumetric flask was filled with ether to its mark. The solution was shaken to dissolve the lithium perchlorate, then transferred via a double-ended needle to a septum-sealed, flame-dried test tube equipped with a magnetic stirrer. The mixture was left to stir for 12 hours at room temperature . The solution was first washed with water (2 x 10 ml), then neutralized with 5% sodium bicarbonate solution (2 x 10ml) and finally washed with water (2 x 10ml), after which the mixture was concentrated *in vacuo*. Analysis was accomplished via ^{1}H and ^{13}C NMR spectroscopy and GC. GC Yield: 9% yield of ortho-endo; 2% yield of ortho-exo.

xv. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate in the Presence of 4M $LiClO_4$.

To a 10-ml flame-dried volumetric flask containing 4.3 g of lithium perchlorate (40 mmole), 3 ml of anhydrous diethyl ether was added. Methyl

acrylate (0.33ml, 3.7 mmole) was added to the cooled ether mixture, then trans-piperylene (0.37 ml, 3.7 mmole) was added by syringe. The volumetric flask was filled with ether to its mark. The solution was shaken to dissolve the lithium perchlorate, then transferred via a double-ended needle to a septum-sealed, flame-dried test tube equipped with a magnetic stirrer. The mixture was left to stir for 12 hours at room temperature . The solution was first washed with water (2 x 10 ml), then neutralized with 5% sodium bicarbonate solution (2 x 10ml) and finally washed with water (2 x 10ml), after which the mixture was concentrated *in vacuo*. Analysis was accomplished via ^{1}H and ^{13}C NMR spectroscopy and GC. GC Yield: 18% yield of ortho-endo; 4% yield of ortho-exo.

xvi. Diels-Alder Reaction of *trans*-Piperylene and Methyl Acrylate in the Presence of 5M $LiClO_4$.

To a 10-ml flame-dried volumetric flask containing 5.3 g of lithium perchlorate (50 mmole), 3 ml of anhydrous diethyl ether was added. Methyl acrylate (0.33ml, 37 mmole) was added to the cooled ether mixture, then trans-piperylene (0.37 ml, 3.7 mmole) was added by syringe. The volumetric flask was filled with ether to its mark. The solution was shaken to dissolve the lithium perchlorate, then transferred via a double-ended needle to a septum-sealed, flame-dried test tube equipped with a magnetic stirrer. The mixture was left to stir for 12 hours at room temperature . The solution was

first washed with water (2 x 10 ml), then neutralized with 5% sodium bicarbonate solution (2 x 10ml) and finally washed with water (2 x 10ml), after which the mixture was concentrated *in vacuo*. Analysis was accomplished via ^{1}H and ^{13}C NMR spectroscopy and GC. GC Yield: 35% yield of ortho-endo; 7% yield of ortho-exo.

xvii. Dehydration of Lithium Perchlorate

To a glass boat, 30 g of unactivated lithium perchlorate was added. The glass boat was then placed in a drying pistol containing potassium pentoxide as drying agent. The side arm was connected to an evacuating system. Water was removed *in vacuo* for 24 hours. The solid was transferred in a glove bag, to a flame-dried, round bottomed flask and stored in a desicator for later use.

xviii. Activation of Brockman Grade I Neutral Alumina. General Procedure

In a 250-ml, round-bottomed flask was added 50 g of unactivated Brockman grade I neutral alumina. The flask was fitted with a vacuum adapter, then seated in a heating mantle connected to a Variac thermo-gauge. A cold-finger, which condenses liquids removed from the reaction flask, and two traps were cooled using acetone/dry-ice baths. The Variac was adjusted to obtain the activation temperature desired. Water was removed *in vacuo*

for 24 hours. The solid was then transferred in a glove bag to a flame-dried Erlenmeyer flask.

F. Materials

I. Solvents

Benzene, Fisher Scientific
Anhydrous Ethyl Ether, Fisher Scientific
Methanol, Fisher Scientific

ii. Gases

Argon, National Welders Supply Co.
Nitrogen National Welders Supply Co.

iii. Reagents

Alumina, Neutral Brockman Activity Grade I, Fisher Scientific
Alumina (modified and activated) Neutral Brockman Activity Grade I was prepared according to the procedure described by Pagni, et al.[4]
Aluminum Chloride, Fisher Scientific
Lithium Perchlorate, Aldrich Chemical Company
Methyl Acrylate, Aldrich Chemical Company
trans-Piperylene, Aldrich Chemical Company.

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VITA

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