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Preparation of Aluminum Enolates and
Boron Enolates Via Aluminum Amides
and Boron Phosphides

presented by

Robert Elghanian

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of the requirements for

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Michael Rathke
Major professor

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PREPARATION OF ALUMINUM ENOLATES AND BORON ENOLATES VIA ALUMINUM AMIDES AND BORON PHOSPHIDES

By

Robert Elghanian

A DISSERTATION

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ABSTRACT

PREPARATION OF ALUMINUM ENOLATES AND BORON ENOLATES VIA ALUMINUM AMIDES AND BORON PHOSPHIDES

By

Robert Elghanian

The main objective of this dissertation is to investigate the reactivity of aluminum and boron bases to carbonyl substrates. For this purpose a series of aluminum amides, boron amides, and boron phosphides were synthesised and tested to determine whether enolate formation can be accomplished using these reagents. This work provides the first observation of an aluminum enolate prepared using an aluminum amide. This work also provides the first observation of a boron enolate prepared via a boron phosphide.

A series of dimeric and monomeric aluminum amides (compounds **I-XV**) were synthesized and evaluated for their ability to react in an acid/base reaction using a variety of ketones. Compounds **I**, **II**, and **XV** were unreactive to ketones. Compounds **III-XIV** reacted with ketones to generate the corresponding aluminum enolates. Enolates generated from the reaction of **III** with pinacolone and 3-pentanone were selected as model systems and condensed with benzaldehyde. The stereoselectivity of the enolate formation and the aldol reaction were investigated using ^{1}H-NMR spectroscopy.

Likewise, a series of boron amides and phosphides (**II-III,V-XI**) were synthesized and evaluated for their ability to react in acid/base reactions using a variety of carbonyl substrates. Boron amides (**II-III**) were unreactive to ketones. Boron phosphides reacted to a variety of carbonyl substrates. The stereoselectivity of the aldol condensation of 3-pentanone was determined to be the *syn* stereoisomer using ^{1}H-NMR

spectroscopy. ^{31}P-NMR spectroscopy was used to determine the extent of enolization throughout this study.

To:My Parents

Acknowledgments

I would like to express my deepest appreciation to Dr. Rathke for helping me and guiding me throughout the course of this study. He is an example of a great teacher, a great researcher, and a great advisor. I would also like to thank the other members of my guidance committee, Drs. Reusch, Eick, Watson, Schwendeman, and Malechka. Thanks to Dr. Azadnia for his friendship and many hours of conversation, chemistry as well as Farsi. I would like to thank members of the Reusch and Baker labs for their friendship. Many thanks to Dr. Long Le and Kermit Johnson for help with NMR experiments and training. Thank you much to Lisa Dillingham and Diane Frost for their friendship and excellent secretarial skills. I would like to thank Kyung Il Kim (a.k.a. Mr. Kim) and family for their friendship. To Phil and Karen (Schultz & Inman), thanks for endless hours of "fun".

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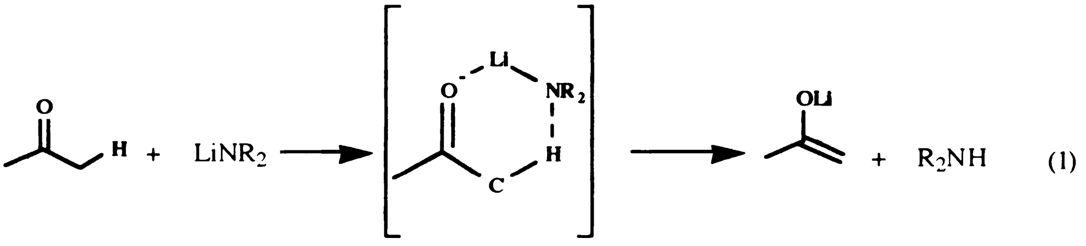
List of Abbreviations

9-BBN	Borabicyclo[3.3.1]nonyl
^{11}B-NMR	Boron(^{11}B) NMR
i-Bu	iso-Butyl
t-Bu	Tertiary Butyl
^{13}C NMR	Carbon (^{13}C) NMR
Chex	cyclohexyl
d	doublet
δ	chemical shift
Et	Ethyl
eq	equation
ether	Diethyl ether
HMDS	1,1,1,3,3,3-Hexamethyldisilazane
^{1}H NMR	Proton (^{1}H) NMR
Hz	hertz
LAH	Lithium aluminum hydride
LDA	Lithium diisopropylamide
LICA	Lithium isopropyl cyclohexylamide
m	Multiplet
Me	Methyl
NEE	N-ethylethanolamine
NONEE	N-silyl, O-silyl, N-ethylethanolamine

MEK	Methyl ethyl ketone
NMR	Nuclear Magnetic Resonance Spectroscopy
NTE	N-tosylethanolamine
^{31}P NMR	Phosphorous (^{31}P) NMR
c-pentyl	cyclopentyl
Ph	Phenyl
i-Pr	Isopropyl
q	quartet
s	singlet
t	triplet
TMP	Tetramethyl pipridine
TMSCl	Trimethylchlorosilane
Tos	Tosyl

Introduction

Carbon-carbon bond formation is the fundamental step in the construction of organic molecules in the laboratory. Many carbon-carbon bond forming processes involve the reaction between a nucleophilic carbon species and an electrophilic carbon species. The nucleophilic species generated upon deprotonation of the carbon alpha to a carbonyl functional group is called an enolate. The most useful method for the preparation of enolates is the enolization of the appropriate carbonyl compound via the acid-base reaction of the carbonyl acid with a lithium dialkylamide base (eq.1). (1)



I

The resulting enolate in equation 1 is a lithium enolate. The regioselectivity and the stereoselectivity of this reaction are rationalized by the six centered transition state **I**.(2) There are several considerations in this acid-base reaction: a)-coordination of the metal cation is known to enhance the acidity of the carbonyl ligand(3), b)-the amide anion is a powerful base (pKa~40) c)- the concurrent coordination of oxygen and nitrogen atoms in the cyclic transition state allows for stereoselective deprotonation of the substrate. This rationale has scarcely been applied to the development of bases other than lithium and in particular boron or aluminum bases have not been explored as potential bases for enolate chemistry.

The chemical literature on the reactivity of metal bases analogous to the lithium amides is rather scanty and little is known about their reactivity to carbonyl compounds. However lithium dialkylamides have been extensively studied due to the prominent role they play in organic synthesis. Studies based on the colligative properties(3a) and solution NMR(3b)spectroscopy on the structure of lithium dialkyl amides have shown that cyclic oligomers exist in both donor and non donor solvents. The structure of LDA is believed to be the THF solvated dimer shown by Willard's X-ray structure in **Figure 1**.(4)

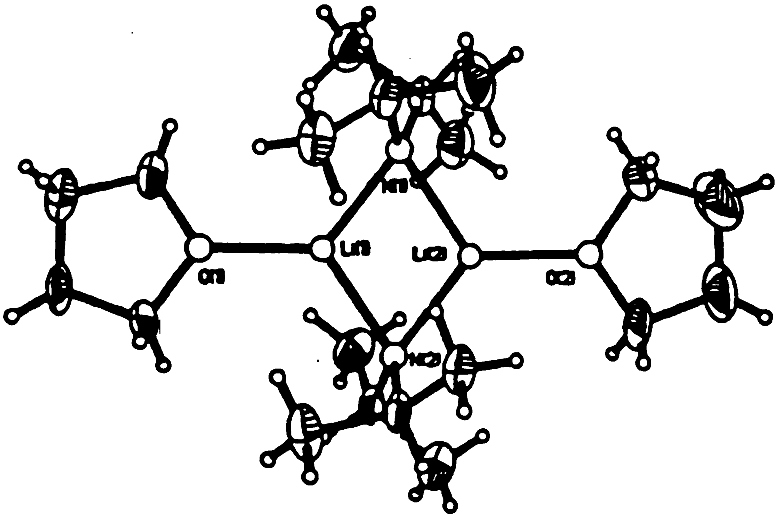
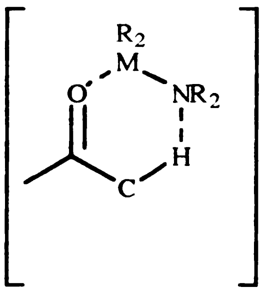


Figure 1. X-Ray structure of LDA after Willard *et al.*

The solution NMR studies have also revealed that for lithium isopropylcyclohexylamide (LICA) an equilibrating set of stereoisomeric dimers (*cis,trans*) is present.(5) The latter study suggests the presence of weak intermolecular interactions and their dynamic nature in solution. Studies on other metal amides have demonstrated that magnesium, zinc and aluminum amides are strongly associated in solution through nitrogen bridges.(6) Magnesium and zinc amides are known to react only sluggishly(7) or incompletely (8) with simple carbonyl compounds.

The rationale for our research centers on the consideration of transition states analogous to **I** for a generalized metal amide, (R_2M-NR_2) **II** shown in **Figure 2.**



II

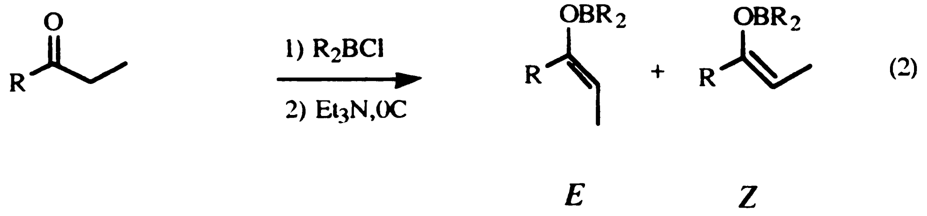
Figure 2. Generalized Transition State Structure For Metal Amides

The objective of our study was to discover bases which can be used in an analogous manner to lithium amides to prepare enolates of metals more electronegative than lithium. The advantage of such bases would be that in contrast to lithium, aluminum and boron are more powerful Lewis acids. From previous work performed in our laboratory it is known that metal complexation with carbonyl compounds enhances the alpha proton acidity; hence a weaker base can be effective (eq 1a, 1b).(9)

$$EtO_2CCH_2CO_2Et \xrightarrow[\text{2) PhCOCl}]{\text{1) } MgCl_2,\ Et_3N} \underset{85\%}{(EtO_2C)_2CHCOPh} \qquad (1a)$$

$$EtO_2CCH_2CO_2Et \xrightarrow[\text{2) PhCOCl}]{\text{1) } Et_3N} \underset{0\%}{(EtO_2C)_2CHCOPh} \qquad (1b)$$

In our review of the literature on the preparation of boron enolates, we found the current methodology for the preparation of boron enolates uses a dialkylboron halide (Lewis acid), a hindered tertiary amine (base) and a carbonyl substrate to prepare boron enolates with good success. This methodology has now been extensively studied by Brown *et al.* (eq2).(10, 11)



Our approach would simplify this procedure by incorporating both features of a base and a Lewis acid into one molecule and reducing the number of reagents employed in the reaction from three to two. In contrast to the general method available for the preparation of boron enolates, we did not encounter an analogous method of preparation for aluminum enolates. This prompted us to undertake our search for aluminum amides hoping that we could emulate the success achieved with lithium amides.

We envision that in addition to the simplification of the current methodology, the advantage of such bases may be that in contrast to lithium, aluminum and boron are capable of accommodating ligands on the metal center due to their multivalency. This property allows one to carry out double stereodifferentiation on the stereochemical outcome of the aldol condensation reaction in the presence of appropriate chiral ligands on the metal center. The other attractive feature of such metal amides is that if a direct route to enolization of the carbonyl substrate can be devised then this route may be a general and useful one for the preparation of enolates.

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CHAPTER I: Preparation of Boron Enolates From Boron Phosphides

Literature review of boron enolates

Several metal enolates have been prepared and studied in the past three decades including B, Al, Mg, Sn, Ti, Zr, Cu, and Zn. The studies on these enolates have revealed that boron enolates are among the most stereoselective agents in organic synthesis.(1) Goodman *et al.* have carried out theoretical calculations on the structure of boron enolates.(2) S-trans structures for boron enolates having hydrogen ligands on boron were found to be the more stable conformation and S-cis the less favored (**Figure1.1**).

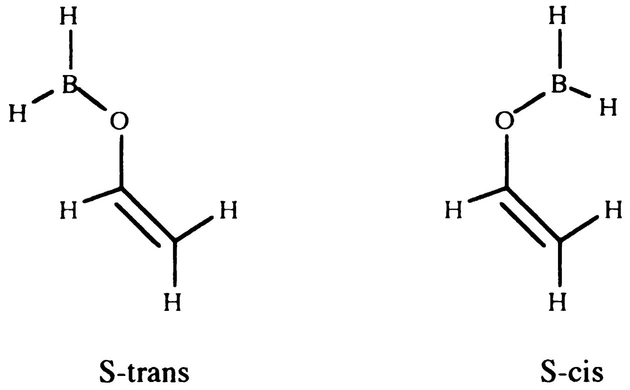
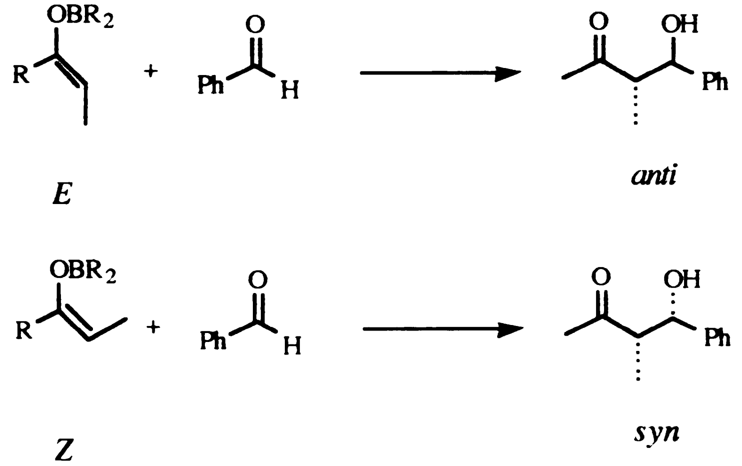


Figure 1.1 S-trans and S-cis conformations of boron enolates after Goodman *et al.*

These calculations have also revealed planar enolate structures resulting from the conjugative delocalization of 4 pi electrons over the olefinic carbon, the enol oxygen, and the coordinatively unsaturated trivalent boron. The most useful reaction of these enolates is the aldol condensation of the enolate with an aldehyde. Evans and coworkers have determined that the enolate stereochemistry and the resulting aldol product stereochemistry are intimately related.(3) Evans has shown that the reaction of *E* boron enolates produces *anti* aldol products, while *Z* enolates react to give *syn* aldol products stereoselectively (**Scheme 1.1**).

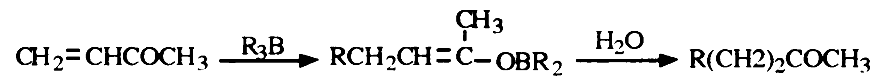


Scheme 1.1 Stereoselectivity of boron enolates

It was also found that the enolate stereochemistry is dependent on the structure of the ketone. However, regardless of the structure of the ketone consistent correlation was observed between the enolate stereochemistry and the aldol product stereochemistry (Table 6). As a result of these studies and studies done by other workers in this area several routes have become available for the synthesis of boron enolates.

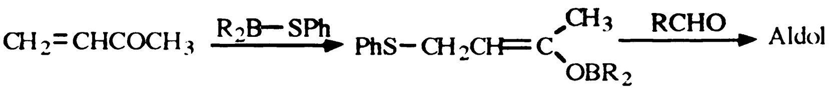
1-Conjugate Addition

Suzuki and Brown *et al.* have prepared unsymmetrical ketones via the conjugate addition of trialkylboranes to methyl vinyl ketone(4a)(eq2). It was later demonstrated that this reaction proceeds via a free radical mechanism to the enolate.(4d) The stereochemistry of the enolate depends on the enone substituents but without useful trends in stereochemical control.(5)



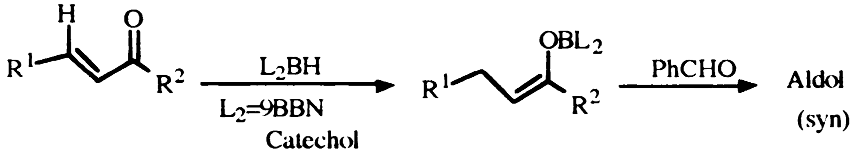
$$CH_2{=}CHCOCH_3 \xrightarrow{R_3B} RCH_2CH{=}\overset{CH_3}{\overset{|}{C}}{-}OBR_2 \xrightarrow{H_2O} R(CH2)_2COCH_3 \qquad (2)$$

Mukaiyma *et al.* have prepared boron enolates via the 1,4 addition of a dialkyl boron thiolate to methyl vinyl ketone (eq3).(6) The aldol product was isolated in 92% yield in reaction with benzaldehyde. The intermediate enolate was quenched with methanol and the β-phenylthiobutan-2-one was recovered in 86% yield.



$$CH_2{=}CHCOCH_3 \xrightarrow{R_2B-SPh} PhS-CH_2CH{=}C\overset{CH_3}{\underset{OBR_2}{}} \xrightarrow{RCHO} \text{Aldol} \quad (3)$$

Boldrini and Matsumoto *et al.* have utilized the 1,4 addition of borane reagents to α,β unsaturated ketones in order to prepare *Z* boron enolates using a variety of ligands on boron (eq 4).(7)



(4)

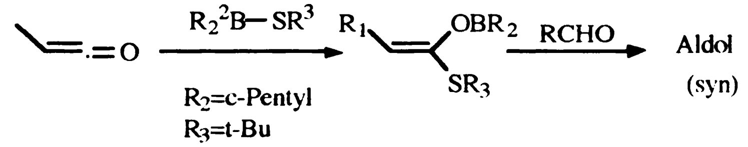
This is a particularly useful method since regioselectivity and stereoselectivity can be achieved in absence of byproducts other than the ligands on boron. The stereoselectivity of the enolate formation was reported to be greater than 99:1, in all cases in favor of the Z enolate. Representitive results are shown in **Table 1.1**.

Table 1.1. Representative results for the reaction of alkylboranes with unsaturated ketones after Matsumoto *et al.*

		9BBN		**Catechol**	
R^1	R^2	%Yield	*Z/E*	%Yield	syn/anti
H	Ph	97	96/4	98	
Me	Ph	99	99/1	98	75/25
Ph	Ph	92	97/3	97	78/12

2)-1,2 Addition

Mukaiyama and Masamune *et al.* have prepared boron enolates of thioesters via the acyl addition of an alkyl boron thiolate to a ketene (eq 5).(8,6) Representative results are shown in **Table 2.1**. This method complements the stereoselective preparation of tert-butyl thioester enolates available through enolization of the thioester by using boron triflate reagents that are known to produce the *E* enolate stereoselectively.(8)



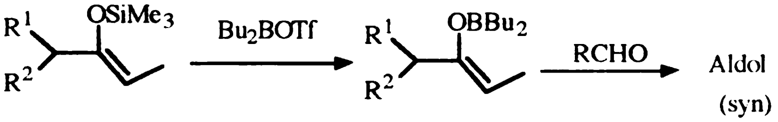
(5)

Table 2.1. Representative results for the reaction of boron sulfides with ketene after Masamune *et al.*

Aldehyde	%Yield	*syn/anti*
R=C_6H_5	78	7/93
C_3H_7	75	5/95
$(CH_2)_2Ph$	65	5/95

Transmetallation

This method takes advantage of the exchange of a previously formed metal or metalloid enolate with the metal of choice in order to prepare the desired enolate. Kuwajima and coworkers have shown that treatment of (Z)-trimethylsilylenol ethers with dibutyl boryl trifluoromethane sulphonate generates the corresponding *Z* boron enolate after a short time at low temperature. This enolate was then reacted with a variety of aldehydes in order to produce aldol condensation products with excellent *syn* selectivity (eq 6).(9a)



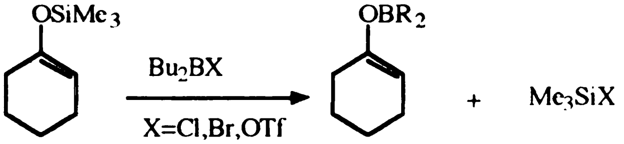
(6)

The disadvantage of this method is that trimethylsilyltriflate has to be removed prior to the aldol reaction since it also participates in the reaction via a silicon mediated aldol. **Table 3.1** provides some representative examples.

Table 3.1 Representative results of the reaction of dibutylboron triflate with silylenolethers after Kuwajima *et al.*

R^1	R^2	*E/Z*	R	%aldol	*syn/anti*
CH_3	H	96/4	Ph	63	95/5
C_4H_9	H	95/5	Ph	74	94/6
C_8H_{17}	H	91/9	Ph	80	91/9
$C_6H_5CH_2$	H	95/5	Ph	82	95/5

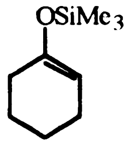
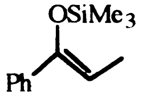
Wada has compared the reaction of dialkylboron triflates and dialkylboron halides with silylenolethers to give the corresponding boron enolates under mild conditions (eq 7).(9b)



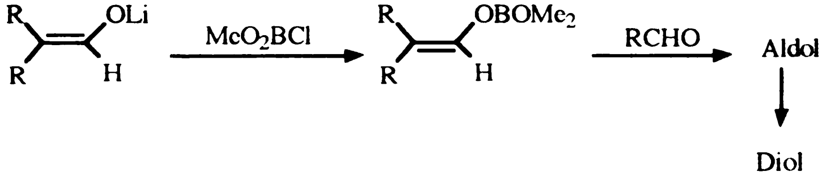
(7)

The reaction of the triflates was the faster reaction in the cases studied and produced exellent yields and good selectivity. Representitive results are shown in **Table 4.1.**

Table 4.1 Representative results for the reaction of dibutylborontriflate with silylenolethers. After Wada *et al.*

Silylenol ether	%Aldol	*syn/anti*
	90	25/75
	88	70/30

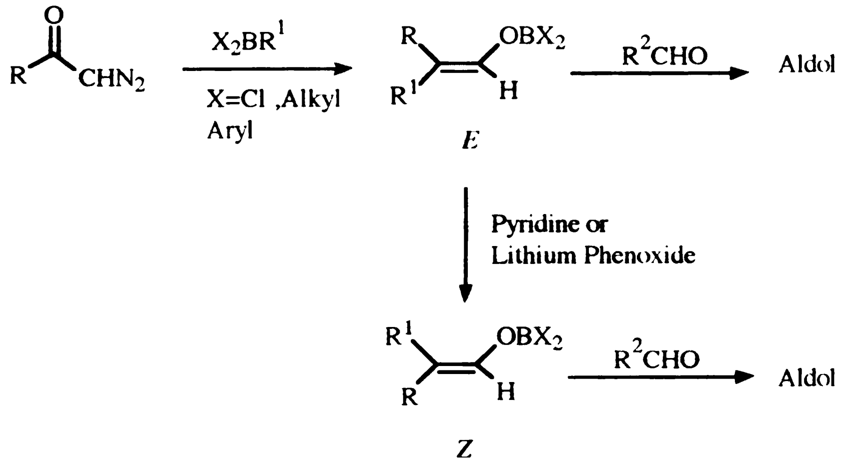
Hoffmann and Froech generated the lithium enolate of acetaldehyde and transmetallated it with chlorodimethoxyborane to give the enolborate (eq 8).(10) These enolborates were reacted with aldehydes to generate a protected aldol-acetal product. These enolates are not stable at room temperature and polymerize rapidly, and the aldol-acetal product was then allylated with allylmagnesium bromide to prepare diols in 62-77% overall yield and 70/30 *anti/syn* selectivity.



(8)

4)-1,2 Hydride or Alkyl Transfer

Transfer of a hydride or an alkyl group from a boron reagent to an alpha diazo ketone in a 1,2 manner has also been utilized as a method to prepare enolates of boron. Hooz, Brown, and Masamune *et al.* have prepared boron enolates by the reaction of α-diazoketones with a variety of organoboron reagents (eq 9).(11) This method allows one to prepare both *E* and *Z* stereoisomers of the enolate. This reaction proceeds with the liberation of molecular nitrogen and no other byproduct. The enolate produced in this method has the *E* stereochemistry and it can be isomerized to the *Z* enolate by addition of a catalytic amount of pyridine or lithium phenoxide.



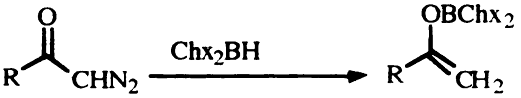
(9)

Representative results from the method developed by Masamune are shown in **Table 5.1**

Table 5.1 Representative results of the reaction of alkylboranes with diazo ketones after Masamune *et al.*

Isomer	R	R^1	R^2	% Aldol	*syn/anti*
E	Me	Bu	Ph	92	1/3
	$PhCH_2$			88	1/4
	Ph			86	1/3
Z	Me	Bu	Ph	90	>20/1
	$PhCH_2$			84	>20/1
	Ph			85	>20/1

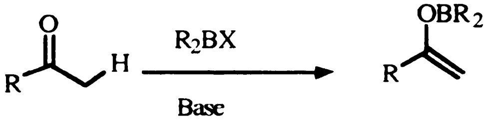
Hooze has also modified this method in order to synthesize enolates of methyl ketones regioselectively using dicyclohexyl borane (eq10).(11d)



(10)

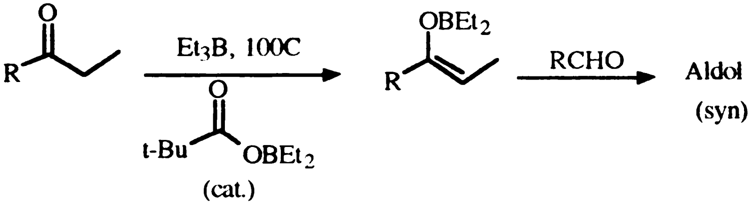
5)-Carbonyl Enolization

This method is probably the most common and convenient method used to prepare boron enolates. Several reagents have been used with varying results. The general equation for this transformation is shown in equation 11a.



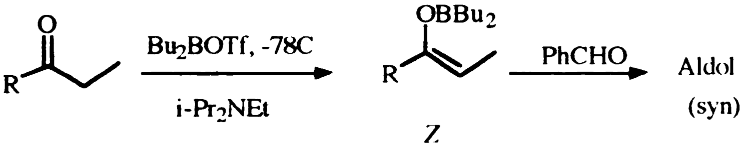
(11a)

Fenzel and Koster used triethylborane and a catalytic amount of diethyl boronpivalate to effect the enolization of a variety of ketones. This reaction proceeds with the liberation of ethane under vigorous conditions (eq11).(12a)



(11)

A milder method was introduced by Mukaiyama and coworkers using a dialkyl boron triflate and a hindered tertiary amine (eq 12).(13)



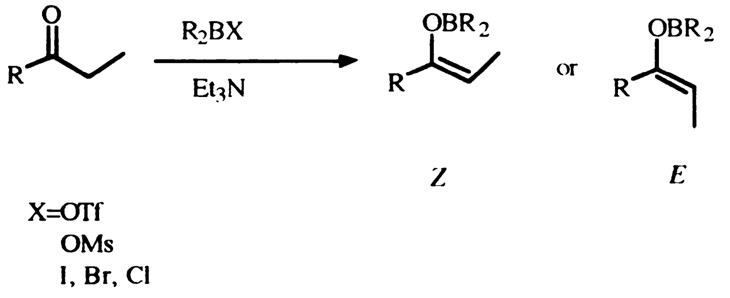
(12)

Several dialkylborontriflates have since been studied by other investigators.(14) Evans has shown that a variety of factors affect the stereoselectivity of this reaction.(3) The proposed mechanism of the reaction by Evans involves initial coordination of the boron triflate to the ketone carbonyl with subsequent deprotonation by the amine in a cyclic six centered transition state in analogy to the Zimmerman model. Evans observed consistent correlation between enolate geometry and aldol product stereochemistry for acyclic ketones. Simple esters and amides cannot be enolized by these reagents, but thioesters are enolized readily. Representitive results of their experiments are shown in **Table 6.1**.

Table 6.1 Representative results for the enolization of ketones and a thioester after Evans *et al.*

R	*Z*/*E*	% Aldol	*syn*/*anti*
Et	>99/1	77	>97/3
Ph	>99/1	82	>97/3
^{i}Pr	>99/1	82	>97/3
^{t}BuS	5/95	80	10/90

Another class of boron reagents used for the enolization of carbonyl compounds has been the substituted boron halides. Preparation of various reagents with moderate success has been reported in the literature.(12) However the most useful and versatile method has been recently developed by Brown and coworkers. Brown has shown that dicyclohexylchloroborane reacts with aldehydes, ketones, and carboxylic acids to produce a near quantitative yield of boron enolates under mild conditions (eq 13).(16)



(13)

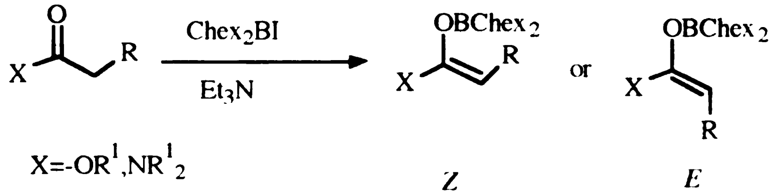
This method allows one to prepare either *E* or *Z* boron enolates of ketones by varying either the leaving group on the boron atom of the reagent or the reaction conditions.

Representitive results are shown in **Table 7.1** along with the reagents developed for enolization.

Table 7.1 Representative results for the enolization of ketones with **B-X-9-BBN** and **Chex$_2$-B-X** after Brown *et al.*

		B-X-9-BBN		**Chex$_2$-B-X**	
Ketone	X	Z/E	%Yield	Z/E	%Yield
R					
i-Pr	OTf	88/12	96	25/75	96
	OMs	82/18	94	23/77	93
	I	27/97	97	32/68	98
	Br	57/43	96	11/89	95
	Cl	46/54	95	3/97	97
Et	OTf	97/3	97	80/20	96
	OMs	93/3	95	80/20	93
	I	97/3	97	56/44	96
	Br	97/3	97	30/70	96
	Cl	97/3	95	21/79	97
t-Bu	OTf	10/90	90	3/97	85
	OMs	3/97	87	3/97	66
	I	97/3	95	97/3	96
	Br	3/97	94	10/90	82
	Cl	3/97	94	3/97	60

This method has been extended to the preparation of the enolates of esters and tertiary amides by using dicyclohexylboron iodide and a tertiary amine (eq 14).(17a,b) Brown has demonstrated that the stereochemical correlation for the reaction of ketone enolates as shown by Evans does not hold for amide enolates and in fact it is the exact opposite. For the reaction of esters they observed a dependence of the stereochemistry of enolization on the R substituent.(17a) For example, bulky R groups produced *anti* aldols but methyl and ethyl produced *syn* aldols stereoselectively. One unusual feature of enolization of amides is the solvent dependence of enolization. Alkane solvents produced aldols with *syn* stereochemistry whereas chlorinated or aromatic solvents produced aldols with *anti* stereoselectivity.(17b). Representative results for the enolization of ethylesters and tertiaryethylamides are shown in **Table 8.1**.



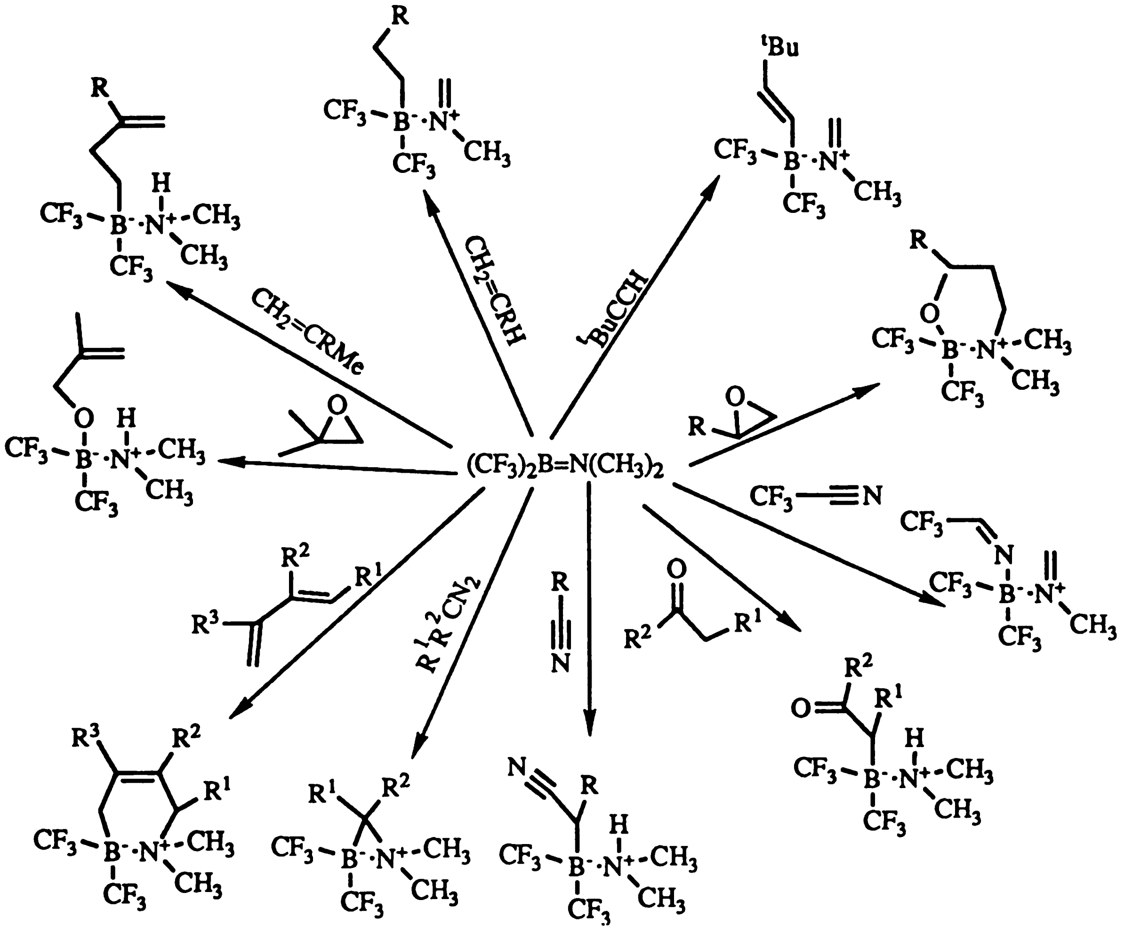
(14)

Table 8.1 Representative results for the enolization of ethylesters and tertiaryethylamides after Brown *et al.*

			Temperature		aldol%	
X	R	Solvent	enol	aldol	*syn/anti*	Yield
$N(CH_2)_5$	Me	CCl_4	0	0	3/97	95
		Hexane	0	-78	97/3	93
NEt_2		CCl_4	0	0	5/95	96
		Hexane	0	-78	97/3	96
OEt	Me	CCl_4	0	0	97/3	96
			0	-78	94/6	96
			25	25	88/12	97
	Et		0	0	95/5	95
	i-Pr		0	0	3/97	94
	i-Bu		0	0	3/97	84
	t-Bu		0	0	3/97	96

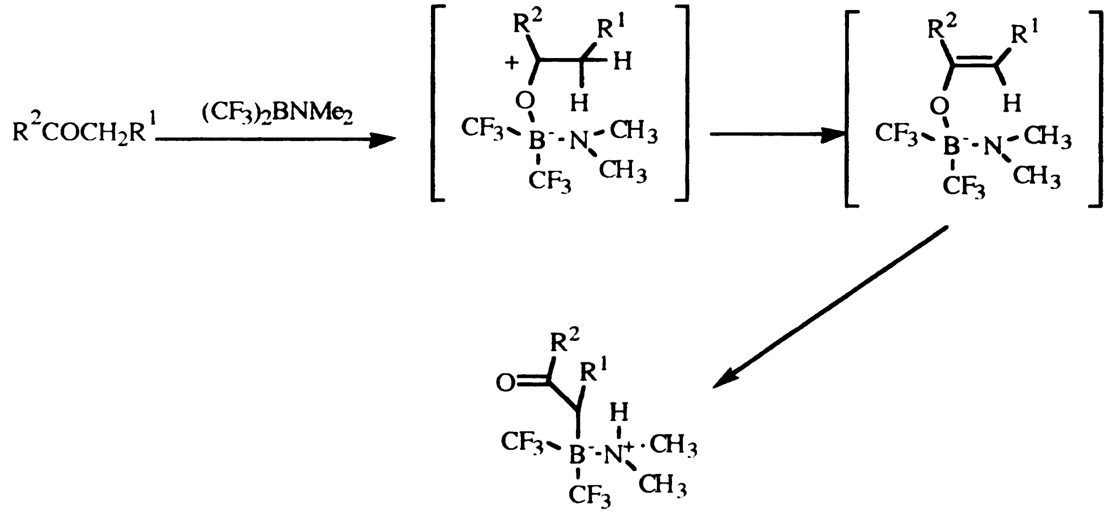
Structure, physical properties, and preparation of boron amides

Boron amides (also known as aminoboranes) are compounds in which boron is attached to one or more nitrogen ligands. These compounds have been a focus of attention in the chemical literature for the past thirty years and several reviews have appeared on their structures and their physical properties.(18) Boron amides have been used as ligands for transition metal catalysts(19), reducing agents(20), and precursors to boron-nitrogen cage compounds.(21) One recent example of the reactivity of an unusual nature is the compound dimethylaminobis(trifluoromethyl)borane reported by Burger *et al*(22). This compound has been shown to display a variety of reactions not observed before with boron amides.(23) **Scheme 2.1** shows a compilation of reactions carried out to date with this complex.



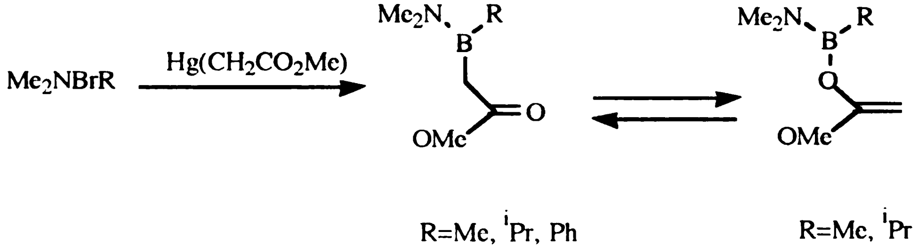
Scheme 2.1 Reactions of $(CF_3)_2BN(CH_3)_2$

The reaction of this reagent with carbonyl compounds is noteworthy. Although this aminoborane has been shown to react with ketones, boron-carbon bond formation is favored over boron-oxygen bond formation in an equilibrium exchange involving the enolate (**Scheme 3.1**). The rearrangement of the enolate produced as an intermediate has been suggested as a possible pathway to the formation of the boron-carbon bond.



Scheme 3.1 Proposed mechanism for the rearrangement of boron enolate after Burger *et al.*.

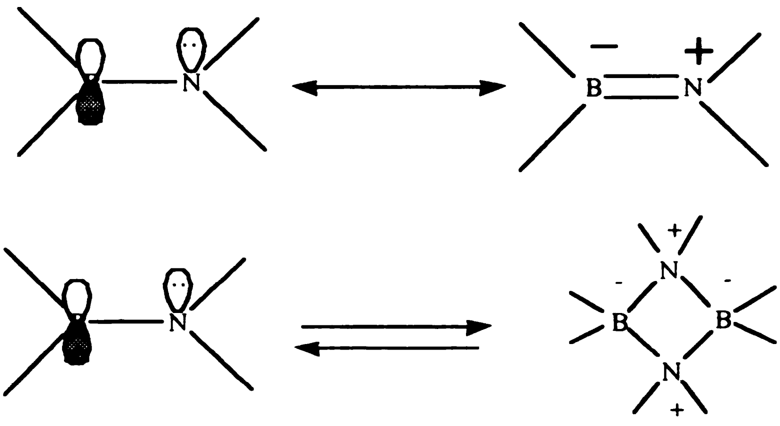
The alkyl boron products in this reaction are generally isolated in 70% to 90% yield. Burger has suggested that the rearrangement of the enolate to the alkyl boronate is too fast to be observed by NMR in the case of amides, esters, and methyl ketones. The only enolate reported in this study was a diethyl ketone enolate of unknown stereochemistry. In a related reaction reported by Paetzold and Biermann alpha mercury methylesters react with boron amides bearing a bromine substituent to produce boron enolates through transmetallation.(24) This reaction has been shown to be an equilibrium, the direction of which is dominated by the alkyl substituent on the boron atom (**scheme 4.1**).



Scheme 4.1 Carbon to oxygen rearrangement for alkylaminoborane

The general features of boron amides are: 1)-they are mostly monomeric and dimerize slowly at room temperature and faster if heated,; 2)-they are weak Lewis Acids; 3)-boron and nitrogen both possess trigonal geometry when monomeric; 4)-the boron-nitrogen bond is isoelectronic with the carbon-carbon double bond of alkenes and regarded as such; 5)-these compounds are air and moisture sensitive and are handled by using inert atmosphere techniques.

The monomeric nature of boron amides requires special attention. Since these compounds harbor both donor and acceptor sites within one molecular entity, conjugation, and oligomerization both play a role as stabilizing effects in these compounds (**Scheme 5.1**).



Scheme 5.1 Resonance stabilization of boron amides

The association of boron amides is highly dependent on the nature of the substituent on the boron. For example, amino difluoroboranes dimerize rapidly, but the analogous chlorides and bromides dimerize slowly.(25) Variable temperature NMR investigations (^{13}C,^{1}H) have demonstrated that conjugation may be a dominant stabilizing force. The rotation barrier around the boron nitrogen bond is in the order of 17-24 kcal/mol for monoaminoboranes.(26) Of course, one cannot entirely rule out steric effects due to the small size of boron. Electron diffraction data also support sp^2 hybridization around the boron nitrogen bond with bond angles of approximately 120 degree for a variety of boron amides.(27)

Preparation of boron amides

There are five routes available for the preparation of boron amides. However, the most useful and direct method for simple amides of boron is the reaction of amines with boron trihalides. These methods generally produce boron amides in excess of 80% yield.

1)-Displacement reactions of haloboranes

Boron halides(28)or their amine complexes(29) react in the presence of excess amines to cleave boron halogen bonds (eqs 1 and 2). Reaction of amines with boron trichloride is highly exothermic; hence, these reactions are often carried out at low temperatures initially.

$$Cl_3B.NH_2Ph \quad + \quad 5NH_2Ph \longrightarrow B(NHPh)_3 \quad + \quad 3PhNH_3Cl \qquad (1)$$

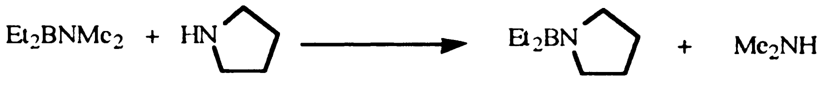
$$Cl_3B \quad + \quad 6NH_2Me \longrightarrow B(NHMe)_3 \quad + \quad 3MeNH_3Cl \qquad (2)$$

Displacement of chlorides and bromides is most often used since displacement of fluoride is more difficult.(30) Steric effects have been shown to prevent complete displacement of halide in the case of hindered amines (eq 3).(31)

$$Cl_3B \xrightarrow[\text{Excess}]{\text{i-Pr}_2\text{NH}} ClB(Ni\text{-}Pr_2)_2 + Ni\text{-}Pr_2HCl \qquad (3)$$

2)-Transamination

Boron amides can be transaminated in the presence of amines. Transamination reactions of boron amides are particularly prone to steric problems (eq 4).(32) The displacement order follows the sequence $NH_2 > NHR > NR_2$, and $NMe_2 > NBu_2 > NH^tBu > N^iPr_2$.(33, 31b)

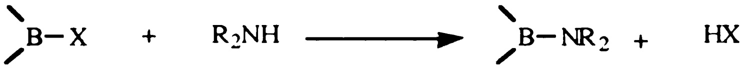

(4)

This method is also useful for the preparation of hindered unsymmetrical aminoboranes (eq 5).(34)

$$B(NMe_2)_3 \xrightarrow{PhNH_2} PhNHB(NMe_2)_2 + Me_2NH \qquad (5)$$

3)-Displacement reactions of hydrido -alkyl -alkoxy -hydroxy or alkylthio-boranes

The general reaction for these transformations is depicted in equation (6). The driving force for these reactions is the formation of the strong boron-nitrogen bond.

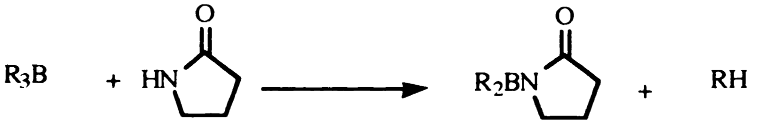

(6)

X=R, OR, OH, SR, H

When a borane and an amine are reacted together at elevated temperatures, hydrogen evolution is the result and the boron amide is prepared in good yield (eq 7).(35)

$$BH_3 + NHMe_2 \longrightarrow (H_2BNMe_2)_2 + 2H_2 \qquad (7)$$

In contrast to the aluminum alkyls, elimination of alkane from boron alkyls is difficult and requires severe conditions. However in the presence of coordinating functional groups (i.e. carbonyl grouping of amides) elimination occurs under milder conditions (eq 8).(36)


(8)

Reaction of alkyl borates or alky thioborates with amines is an equilibrium reaction. Removal of the leaving group from the reaction by using volatile or cheating ligands(37) results in successful preparation of boron amides (eq 9,10).(28,38,37a)

$$B(OR)_3 + 3RNH_2 \longrightarrow B(NHR)_3 + 3ROH \quad (9)$$

$$B(SR)_3 + 3RNH_2 \longrightarrow B(NHR)_3 + 3RSH \quad (10)$$

The alternative to this method is the use of an alkali metal amide instead of the amine (eq 11).(39)

$$B(OMe)_3 + 3NaNHBu \longrightarrow B(NHBu)_3 + 3NaOMe \quad (11)$$

4)-Disproportionation and metathetical exchange

Some unsymmetrical halogeno, alkoxy-, alkylthio-, or alkyl-aminoboranes are prone to disproportionation when heated. As a result symmetrical trisubstituted boron amides have been made inadvertently. For example bis(dibutylamino)fluoroborane disproportionates upon distillation (eq 12).(40,38)

$$2FB(NBu_2)_2 \longrightarrow B(NBu_2)_3 + F_2BNBu_2 \quad (12)$$

Metathetical exchange has been used to prepare boron amides from a mixture of an aluminum tris amide and an alkyl borane or phenyldiethylborate (eq 13,14).(41)

$$2R_3B + Al(NMe_2)_3 \longrightarrow 2R_2BNMe_2 + R_2AlMe_2 \quad (13)$$

$$PhB(OEt)_2 + Al(NMe_2)_3 \longrightarrow PhB(NMe_2)_2 + (EtO)_2AlNMe_2 \quad (14)$$

A reaction analogous to eq 13 can be carried out with tris diethylaminoborane and triethyl borane to prepare ethyl substituted diethyl boron amide (eq 15).(42) This reaction requires the use of borane THF complex as a catalyst. The boron amide is obtained in high yield.

$$Et_3B + B(NEt_2)_3 \xrightarrow{BH_3.THF} Et_2BNEt_2 \quad (15)$$

5)-Insertion reactions

Boron amides have been prepared by the insertion of isocyanates into boron-nitrogen(38d), boron-chlorine(43), boron-carbon,(43,38d) and boron-oxygen bonds (eq 16,17,18,19). The advantage of insertion reactions is the lack of any by products since both reaction partners combine to form one product.

$$Pr_2BNHPh \quad + \quad PhNCO \longrightarrow Pr_2BNPhCONHPh \qquad (16)$$

$$PhBCl_2 \quad + \quad 2PhNCO \longrightarrow PhCONPhB(Cl)NPhCOCl \qquad (17)$$

(18)

(19)

Insertion of carbodiimides into boron-chloride and boron-carbon bonds has been reported (eq 20).(44)

$$PhBCl_2 \quad + \quad 2RN{:}C{:}NR \longrightarrow RN{:}CPhNRB(Cl)NRClC{:}NR \qquad (20)$$

Other examples of insertion reactions for the preparation of boron amides are the reaction of borane(45) or a trialkylborane(46) or trialkylboronate(47) complexes with imines (eq 21,22,23).

$$B_2H_6 \quad + \quad 2PhN{:}CHAr \longrightarrow 2H_2BNPhCH_2Ar \qquad (21)$$

$$BR_3 \quad + \quad MeN{:}CHPh \longrightarrow R_2BN(Me)CHRPh \qquad (22)$$

$$Li[BR_3BH_4] \quad + \quad 6Ar^1N{:}CHAr \longrightarrow 2B[N(Ar^1)CH_2Ar]_3 \qquad (23)$$

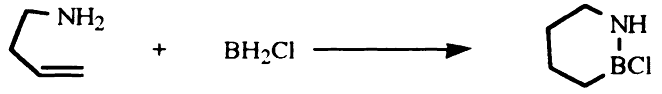
Other examples of insertion reactions include carbon-oxygen or carbon-sulfur insertions into the boron-nitrogen bond of a tris boron amide to produce oxygen(48) or sulfur(49) substituted boron amides (eqs 24, 25).

$$B(NMe_2)_3 \quad + \quad 2COS \longrightarrow [Me_2NC(S)O]_2BNMe_2 \qquad (24)$$

$$XCNB(NMe_2)_2 + \text{p-TolNCX} \longrightarrow XNCB(NMe_2[N(Tol\text{-}p)C(NTol\text{-}p)NMe_2] \qquad (25)$$

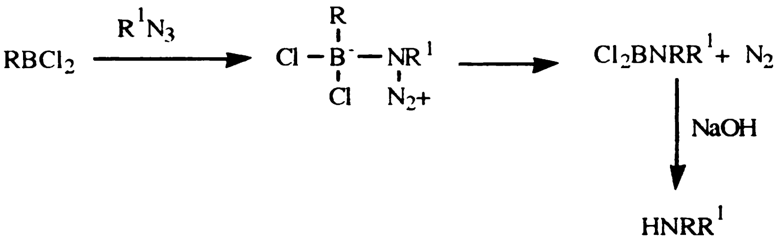
X=O or S

Hydroboration followed by amine insertion into the boron hydrogen bond provides a route for the formation of aminoalkylhaloboranes (eq 26).(50)



(26)

Dialkyl chloroboranes or trialkylboranes may be employed to prepare secondary amines by the reaction of alkylazides in a manner analogous to hydroboration. However, the aminoborane has not been isolated though it is believed to be an intermediate in this reaction (eq 27).(51)

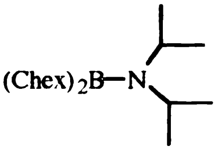


$$RBCl_2 \xrightarrow{R^1N_3} Cl-\overset{\overset{R}{|}}{\underset{\underset{Cl}{|}}{B^-}}-\underset{\underset{N_2+}{|}}{NR^1} \longrightarrow Cl_2BNRR^1 + N_2 \xrightarrow{NaOH} HNRR^1 \qquad (27)$$

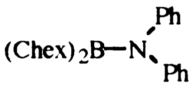
Reaction of secondary chloroamines with trialkylboranes produces boron amides with elimination of alkylhalide (eq 28).(52)

$$BR_3 \xrightarrow{ClNR_2} RCl \quad + \quad R_2BNR_2 \qquad (28)$$

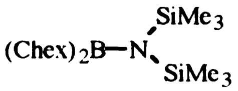
We began our initial studies by the design of boron amides that may act as bases. Compounds I, II, and III were proposed as our first model compounds.



I



II



III

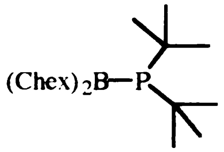
The purpose of this study was to determine the effect of bulky substituent and electron deficient substituents on the back bonding of nitrogen to boron. The rationale behind this initial proposal was to maximize steric interactions of the ligands on both boron and nitrogen centers. This was accomplished by placing sterically demanding substituents on boron (cyclohexyl), and nitrogen (i-Pr, TMS, Ph). At the same time we wished to minimize the boron-nitrogen back bonding that may interfere with the reagent acting as a base. Hence conjugating substituents on nitrogen were chosen for compounds **II** and **III**. The proposed reagents were synthesized via salt elimination from the haloborane and lithium amide precursors according to equation 29.

$$(\mathrm{Chex})_2\mathrm{BCl} \xrightarrow{\mathrm{LiNR_2}} (\mathrm{Chex})_2\mathrm{BNR_2} \quad + \quad \mathrm{LiCl} \qquad (29)$$

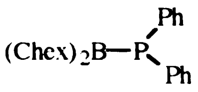
These reagents were then tested by the addition of one equivalent of pinacolone to an NMR tube and the recording of the ^{1}H-NMR spectrum at room temperature. After three hours at room temperature the methyl resonance (alpha) of pinacolone persisted and no vinylic resonances were observed in the spectra of **II** and **III**. It was then apparent to us that minimizing the boron-nitrogen conjugation present in boron amides without destroying either the Lewis acidity of boron or the basicity of the nitrogen ligand presents a more formidable problem. We assume that either significant boron-nitrogen back bonding is still present in these compounds (**II-III**) or else the nitrogen lone-pair is rendered so weakly basic by the conjugating substituents that proton transfer is unfavorable.

We hypothesized that if pi bonding of boron with the second-row element, phosphorus, is unfavorable, then the use of boron phosphides (R_2B-PR_2) rather than boron amides might provide acceptable base strength.

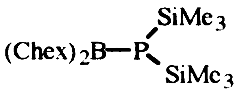
Boron phosphides (also known as phosphinoboranes) are compounds in which boron is attached to one or more phosphorus ligands. Boron phosphides are normally associated molecules, with phosphorus bridges.(53) The presence of donor and acceptor sites in these molecules may provide conjugation and association as stabilizing mechanisms for their structure. In contrast to boron amides these compounds are rarely monomeric in the absence of bulky substituents or donor ligands such as nitrogen, and dimerise rapidly. For example Me_2BPH_2 is dimeric at room temperature whereas Me_2BNH_2 is only dimeric at low temperatures and a monomer at ambient temperature. At the least this implies that for boron phosphides B-P pi bonding (present in the monomer) is less favorable than B-P sigma bonding present in the oligomer. Furthermore, it has been noted that boron phosphide-amides are monomeric and pi bonding occurs from the nitrogen atom rather than the phosphorus atom.(54) Finally the nature of the B-P bond in the rare monomeric boron phosphides has been examined by spectral methods.(55) Power has concluded that while there is no inherent weakness in the B-P pi bonds, the presence of a large inversion barrier often prohibits the necessary planar configuration at phosphorous.(56) Other workers in this field have determined that $Me_2BP(TMS)_2$ is in a fast monomer-dimer equilibrium above 17 degrees Celsius.(57) Encouraged by these considerations, we synthesized a number of boron phosphides and examined their reaction with simple ketones. Our first model compounds were compounds **IV**, **V**, and **VI**. These compounds were proposed with the same considerations in mind as previously mentioned for corresponding amides compounds **I**, **II**, and **III**.



IV



V



VI

Synthesis Of Boron Phosphides

Several monomeric boron phosphides have been prepared and characterized in the past five years.(58) Alkyl boron phosphides have previously been prepared for chemical vapour deposition applications(59). There are three main routes available to the synthesis of boron phosphides. These routes are generally elimination reactions and provide good to excellent yields of the boron phosphide.

1)Elimination of hydrogen halide

Phosphines react with boron halides in the presence of a stoichiometric amount of tertiary amine bases to produce boron phosphides (eq 1).(60)

$$PH_3 + Me_2BBr \xrightarrow{Et_3N} \underset{\text{Dimer}}{Me_2BPH_2} + Et_3NHBr \quad (1)$$

2)Elimination of trimethylsilylhalide

Alkylsilyl phosphines react with boron halides to eliminate trimethylsilylchloride and produce the corresponding boron phosphide. This reaction is a slow reaction and requires heating for completion (eq 2).(60) The attractive feature of this method is the generation of volatile trimethylsilylchloride.

$$Me_3SiPEt_2 \xrightarrow[\text{120 C}]{BCl_3} Et_2PBCl_2 + Me_3SiCl \quad (2)$$

3)Elimination of metal salts

Alkylhaloboranes react with alkali metal phosphides with elimination of alkali metal halide (eq 3).(60) This method is probably the most convenient route since alkali metal phosphides can be prepared from either deprotonation of phosphines or metallation of halophosphines.

$$LiPEt_2 \xrightarrow{Ph_2BCl} Et_2PBPh_2 + LiCl \quad (3)$$

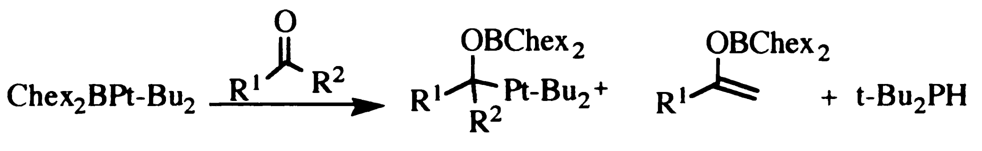
Results and Discussion

Our studies began with the preparation of dicyclohexyl(di-t-butylphosphino)borane (**IV**). This compound has been previously prepared via the elimination of lithium chloride from lithium di-t-butylphosphide and dicyclohexylchloroborane and characterized by Noth *et al*. (eq 1).(61)

$$\mathrm{Chex_2BCl} + \quad \mathrm{LiPt\text{-}Bu_2} \xrightarrow[\text{Hexane}]{\text{0C}} \mathrm{Chex_2BPt\text{-}Bu_2} + \quad \mathrm{LiCl} \qquad (1)$$

We found ^{31}P-NMR spectroscopy to be an extremely useful and invaluable method for the direct analysis of the course of the reactions throughout our studies. Since the evolution of dialkylphosphine can be directly monitored, it can be used as a means of estimating the extent of enolization. We chose the non-donor solvent toluene to eliminate any complexation of the solvent to the reagent. Addition of 100 μmol of methyl ethyl ketone (MEK) to an NMR tube containing 100 μmol of **IV** (δ 36.11ppm), (**Figure 2.1**) in hexane resulted in complete consumption of **IV** at room temperature and appearance of two new resonances at 64.69 ppm. and 21.17 ppm. in 8:1 ratio, (**Figure 3.1**).

We attribute these resonances to the addition product resulting from the nucleophilic addition of the phosphide to the carbonyl carbon and enolization of the carbonyl substrate to release di-t-butylphosphine, respectively (eq 2).



(2)

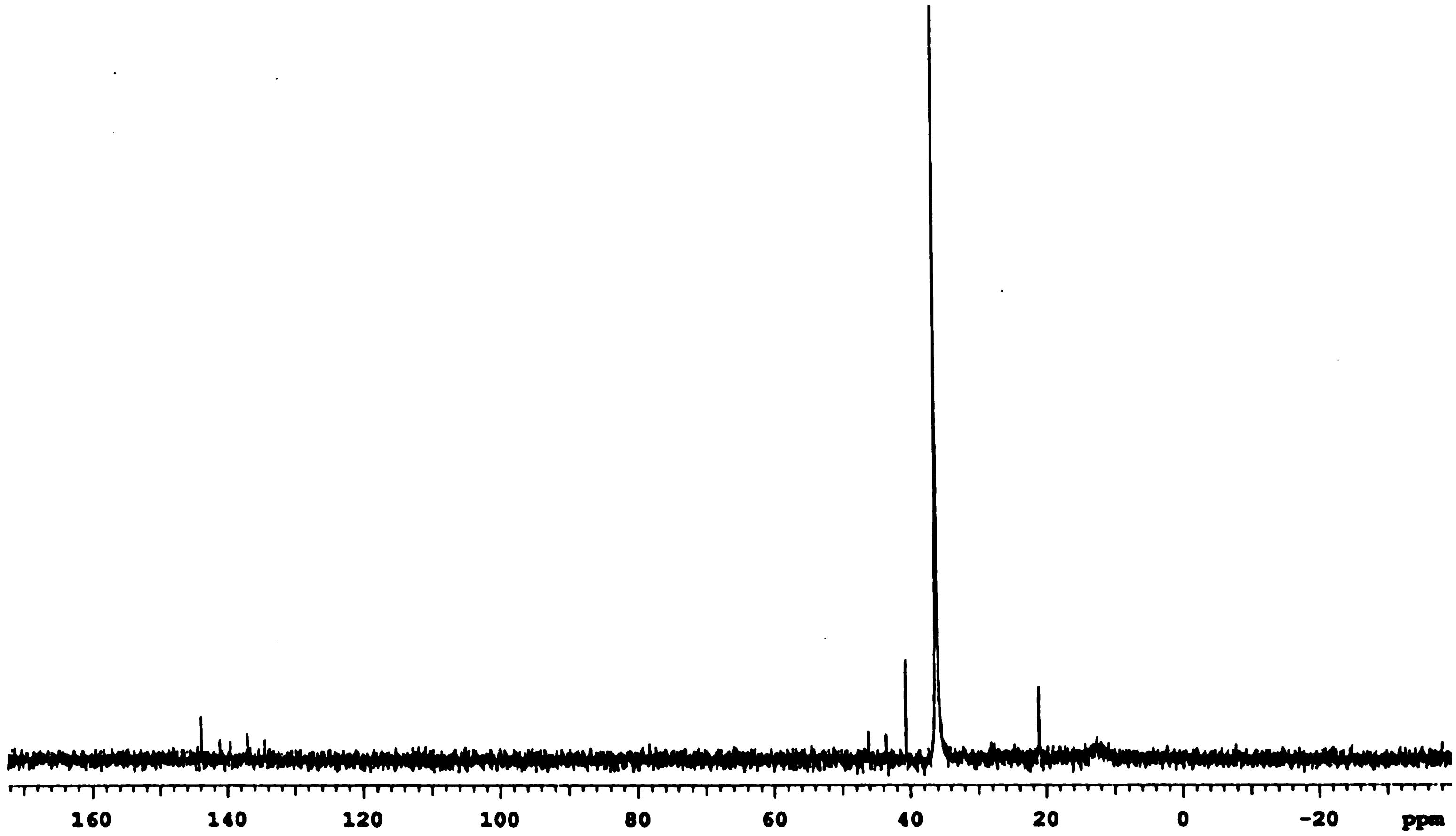


Figure 2.1 ^{31}P-NMR spectrum of Dicyclohexyl(di-t-butylphosphino)borane

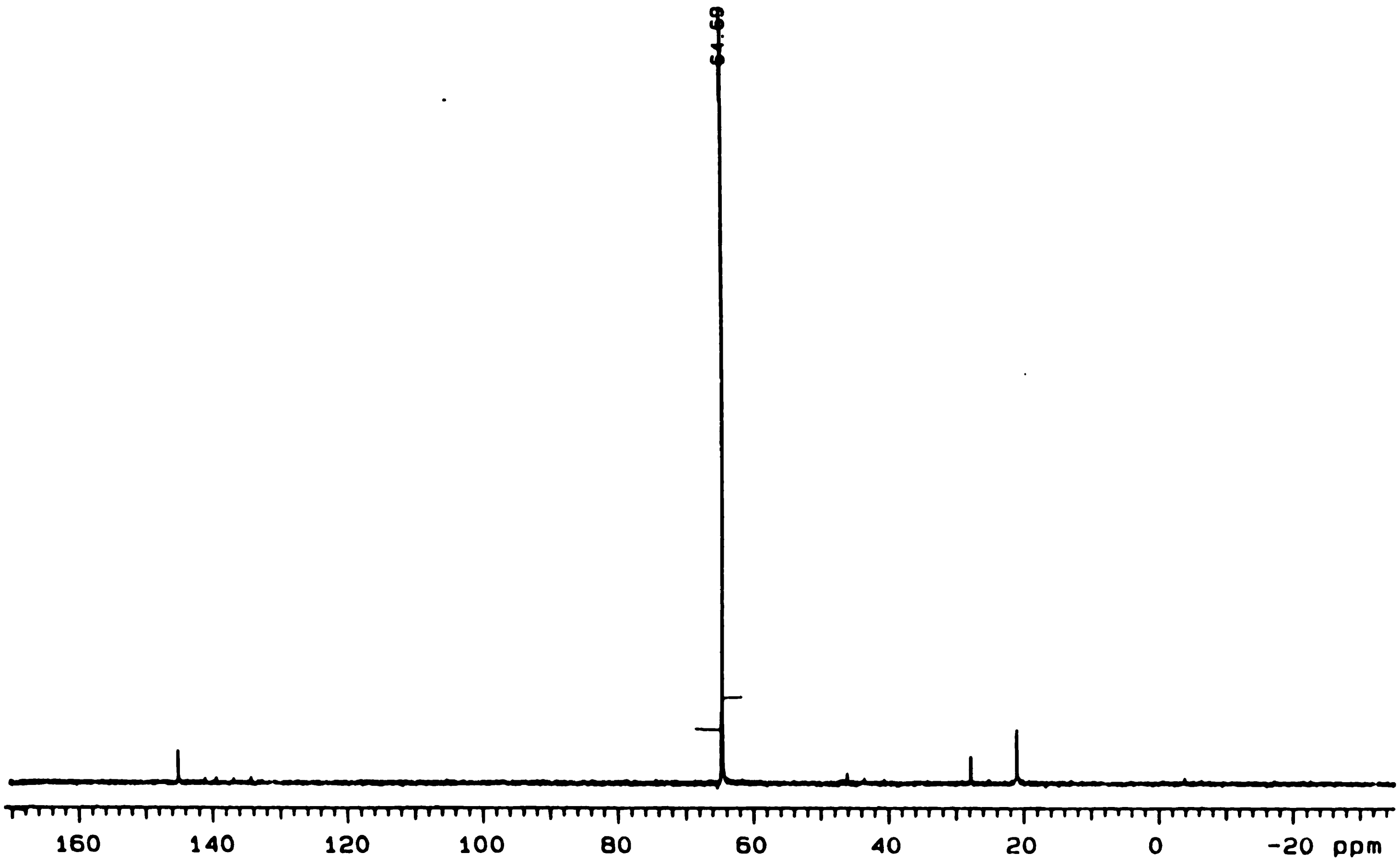


Figure 3.1 ^{31}P-NMR spectrum of Dicyclohexyl(di-t-butylphosphino)borane after addition of MEK and standing at 25C for 1 hour

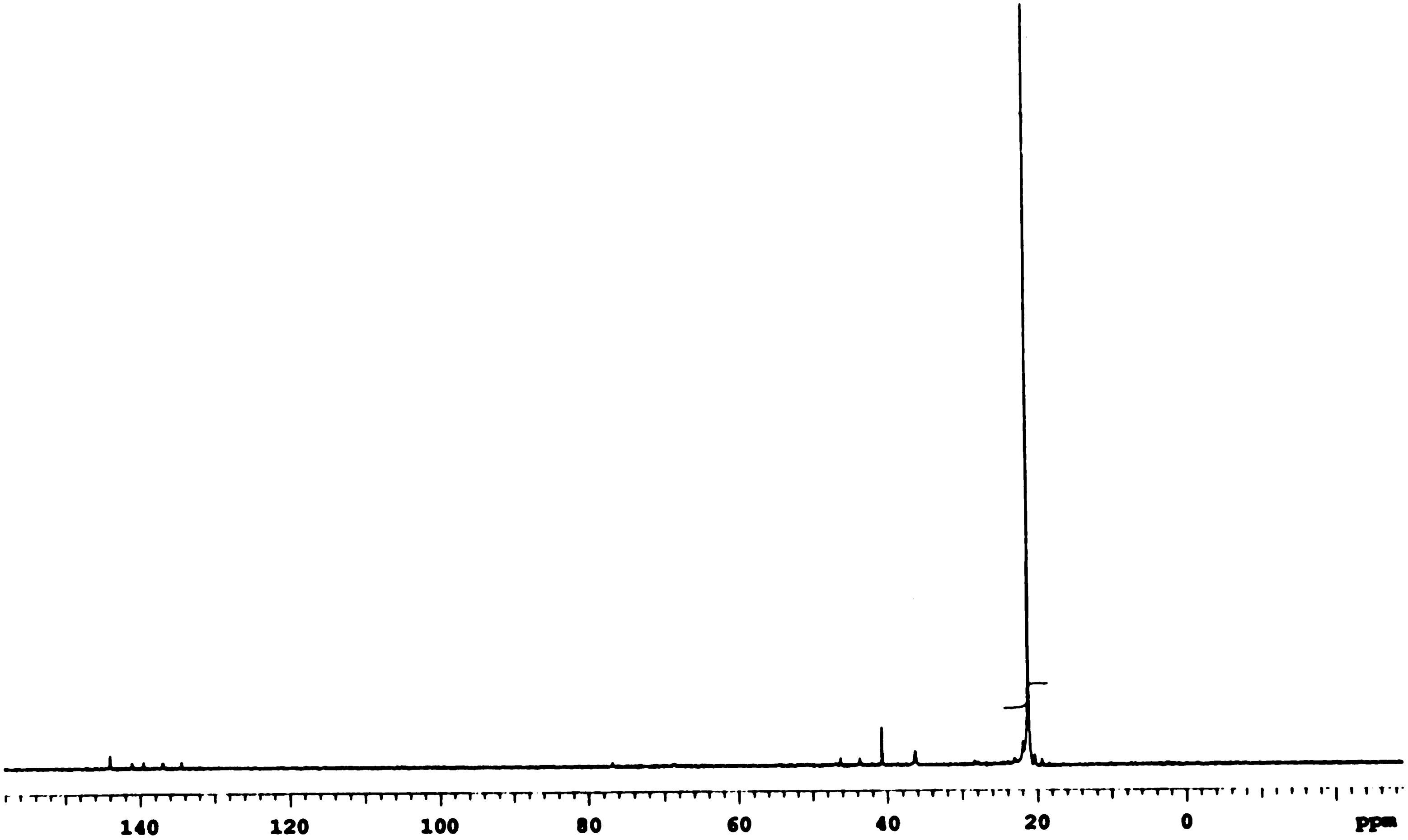


Figure 4.1 ^{31}P-NMR spectrum of Dicyclohexyl(di-t-butylphosphino)borane after addition of diisopropyl ketone and standing at 25C for 24 hours

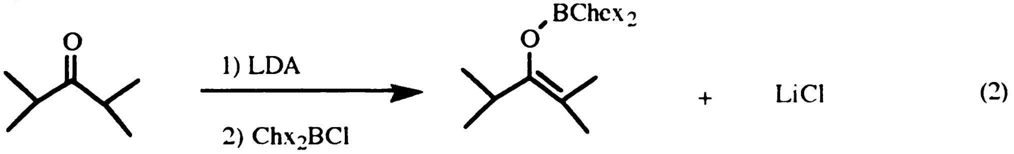
Table 9.1 summarizes the results obtained with this reagent with a variety of carbonyl compounds. The control experiment was the reaction of lithium di-t-butylphosphide with pinacolone and MEK which produced di-t-butylphosphine as the sole product.

Table 9.1. Reaction of Dicyclohexyl(di-t-butylphosphino)borane with carbonyl substrates

R^1	R^2	% addition	% enolization	Temperature	Time
Me	Et	89	11	25	1 hr
Me	Et	78	20	-78	1 hr
^{t}Bu	Me	3	19	25	1 hr
^{i}Pr	^{i}Pr	<1	>98	25	24 hr
Me	OEt	6	5	25	17 hr
Me	NMe_2	25	52	25	4 hr

The results in **Table 9.1** demonstrate the effect of bulky substituents on the ability of the phosphide to partition between the deprotonation pathway and the addition pathway. When the addition of the phosphide is suppressed, deprotonation is the prefered pathway as demonstrated in the cases of pinacolone and diisopropyl ketone, (**Figure 4.1**). Esters and amides appear to be less reactive due to their lower acidities.

We wished to verify the formation of enolate in these reactions by synthesizing the enolate via a different route. For that purpose the lithium enolate of diisopropyl ketone was prepared and transmetalated with dicyclohexylchloroborane to generate the corresponding boron enolate (eq 3).



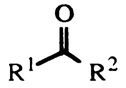
(2)

Comparison of the ^{13}C-NMR spectra obtained on the products generated via the two different methods showed identical chemical shifts. This is the first observation of enolization of a ketone with a boron phosphide.

Encouraged by the above observations, and in an effort to reduce the nucleophilicity of the phosphorus ligand, the dicyclohexyl(diphenylphosphino)borane **V** was synthesized. Addition of dicyclohexylchloroborane to a suspension of lithium diphenylphosphide resulted in an insoluble and chalk like precipitate. ^{31}P and ^{11}B NMR analysis of the supernatant did not show any phosphorus or boron resonances.

We attribute this behaviour to the formation of the insoluble phosphinoborane dimer in toluene. For this reason THF was chosen to carryout the synthesis of **V**, and slow down the dimerization by serving as a Lewis base. A series of low temperature NMR experiments were carried out in THF to verify the presence of one or more reactive species in THF solutions of the boron phosphide. Addition of a THF solution of lithium diphenyl phosphide (red solution) to dicyclohexylchloroborane resulted in the disappearence of the red color upon each drop at -78 C. As the reaction mixture was allowed to warm up a pale yellow solution containing a fine white precipitate (LiCl) formed. Analysis of this solution by ^{31}P NMR spectroscopy revealed the presence of two resonances. Addition of pinacolone to the NMR tube resulted in the disappearence of both resonances and appearence of diphenylphosphine over a period of one hour at ambient temperature. Based on these observations a solution of the phosphinoborane was then reacted with pinacolone, 3-pentanone, ethylacetate, and N,N-dimethylpropionamide in four separate reactions. Results of these reactions are provided in **Table 10.1**.

Table. 10.1 Reaction of $Chex_2BPPh_2$ with Carbonyl substrates



R^1	R^2	Time	Temperature	% Phosphine
^tBu	Me	2hr	25	80
Et	Et	2hr	25	92
Et	NMe_2	2hrs	25	46
		4hrs	25	46
Me	OEt	4hrs	25	48

We determined the stereoselectivity of this acid/base reaction with 3-pentanone. The stereochemistry of enolate formation for 3-pentanone was investigated in an indirect manner since ^{1}H-NMR of the *E* and the *Z* enolates of boron bearing cyclohexyl substituents are indistinguishable as previously reported by Brown *et al.*(2) Hence the enolate of 3-pentanone was reacted with benzaldehyde at -78C as prescribed by Brown.

We determined the configuration of the enolate to be of *Z* configuration since the aldol product isolate has the *syn/anti* ratio of 9:1.

These results show that conjugating substituents on phosphorus reduce the nucleophilicity of the phosphorus ligand, and due to the reduced basicity of the phosphorus thermodynamic enolate formation is favored because of a slow reaction.

In another set of experiments the effects of donor ligand(s) on the efficiency of enolate formation were examined. These experiments were carried out by substitution of the cyclohexyl ligand for oxygen, nitrogen, electron dificient nitrogen, electron deficient oxygens, and combinations of both characteristics. The diphenyl phosphide ligand was chosen based on our previous observations that it is less nucleophilic than the di t-Butyl phosphide ligand. Results of these studies are provided in **Table 11.1**.

Table 11.1 Survey of the Reaction of heteroatom substituted boron diphenylphosphides ($R^1R^2BPPh_2$)with pinacolone

R^1	R^2	% addition	% enolization	Temperature	Time	Solvent	Compound
N^{i}Pr	N^{i}Pr	0	0	25	24hrs	THF	**VII**
Catechol		>90	<10	25	15min	THF	**VIII**
NEE		25	75	25	30min	Ether	**IX**
		34	66	25	30min	THF	
NTE			0.3	25	30min	THF	**X**
C_4H_8N	Cl	0	1	25	30min	Hexane	**XI**

These results show that steric effects as well as electronic effects play a major role in the activity of these reagents. The presence of two pi donors in the absence of any steric effects increase the reactivity of the reagent towards a carbonyl substrate as evident from the NEE phosphide (**IX**). In contrast the presence of one pi donor ligand and one electon deficient ligand (**XI**) or two electron deficient pi donors (catechol ligand **VIII**) diminish the activity of the boron complex towards deprotonation as evident from last two enteries in the table (**X**, **XII**). The lack of reactivity in the latter case (**XI**) may be attributed to significant back bonding contribution from phosphorus resulting in the unavailability of the lone pair on the phosphorus. Another explanation in the latter case may be the presence of strong boronphosphide aggregates (dimers) that are unreactive. We attribute the lack of reactivity of the phosphide having two diisopropylamine ligands (**VII**) to steric effects contributed from the diisopropylamido ligands.

Conclusions

A new procedure has been developed for the preparation of enolates of boron via an acid/base reaction previously unknown for phosphinoboranes. Our results provide the first example of a boron base capable of forming ketone enolates. We have demonstrated that the reactivity of these complexes is very sensitive to both the nature of ligands on boron as well as the nature of ligands on phosphorus. Bulky alkyl substituents on phosphorus increase the nucleophilicity of the reagent. In contrast, phenyl substituents decrease the nucleophilicity of the phosphorus center to the extent that an acid/base reaction can occur efficiently when non-pi donor ligands are present on the boron center.. We have determined that the enolates prepared from the reaction of phosphinoboranes with ketones are a thermodynamically favod product due to the slowness of the reaction of these bases. Although the basicity of phosphide ligands used in this study is not currently sufficient for the formation of a kinetic product, development of new phosphide ligands in the future studies may overcome this limitation.

Experimental

All operations were carried out under an argon or nitrogen atmosphere. Diphenylamine, diisopropylamine, 1,1,1,3,3,3-hexamethyldisilazane (HMDS), hexane, chlorotrimethylsilane, N-ethylethanolamine, ethanolamine, and toluene were obtained from Aldrich Chemical Company and distilled from calcium hydride prior to use. Deuterated benzene, toluene, and chloroform were dried over calcium hydride and purged with nitrogen. Ketones were obtained from Aldrich Chemical Company and dried over calcium hydride and purified by distillation. n-Butyllithium was obtained from Aldrich Chemical Company as a 1.6 M solution in hexane and was used directly. Tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone prior to use. Lithium metal was obtained as rods from Aldrich Chemical Company and handled in a dry box. D_2O inserts were prepared by sealing the open end of a 12 cm thick walled glass tube with 1mm internal diameter. To this tube was added approximately 100 μL of D_2O via a syringe and the glass tube was sealed over a bunsen burner. This tube served as the source for the deuterium lock signal for the instrument. ^{1}H-, ^{31}P-, ^{13}C-, ^{11}B-NMR data were recorded on a Varian (VXR) spectrometer operating at 300, 121.4, 75.4, 96.2 MHz respectively. Phosphorous and boron NMR data are reported with respect to 85% phosphoric acid and borontrifluoride etherate external standards. NMR tubes and D_2O inserts were dried at 150C in an electric oven, fitted with a septum, and purged with nitrogen using a long needle for at least one hour prior to use.

General Method for Examination of Boron Phosphides

To an NMR tube fitted with a septum and a D_2O insert was added 1 ml of a boron phosphide solution. Ketone was added to the tube via a gas tight Hamilton syringe and the spectrum recorded.

Preparation of Phosphines

Di-t-Butylphosphine (^{31}P NMR δ 20.7 s) was prepared according to the procedure by Timmer *et al.* by reduction of di-t-butylchlorophosphine with LAH(62). Diphenylphosphine (^{31}P NMR δ -39.9 s) was prepared by lithiation of triphenylphosphine followed by aqueous workup under nitrogen as described by Wittenberg and Gilman(63).

Preparation of Lithium Phosphides

Lithium di-t-Butylphosphide was prepared by deprotonation of the phosphine precursor with n-Butyllithium. Lithium diphenylphosphide was also prepared by deprotonation of the corresponding phosphine.

Preparation of Chloroboranes

Bis-(diiopropylamino)chloroborane was prepared from borontrichloride and excess diisopropylamine according to the procedure by Davies *et al.*(63) Dicyclohexylchloroborane was prepared from dicyclohexyl borane and phosphorus pentachloride according to the procedure by Brown *et al.*(64) Catecholchloroborane was prepared by disproportionation of boron trichloride and 2,2'-o-Phenylenedioxybis(1,3,2-benzodioxaborole) according to the procedure by Mannig and Noth *et al.*(65) Pyrolidinodichloroborane was prepared according to the procedure by Musgrave.(66)

General Method for The Survey and Preparation of Phosphinoboranes

Phosphinoboranes were prepared by addition of a stoichiometric amount of the desired chloroborane to a stoichiometric amount of freshly prepared lithium diphenylphosphide (^{31}P NMR THF δ -24.6 s insoluble in hexane) or lithium di-t-butylphosphide (^{31}P NMR THF δ 36.71 s insoluble in hexane) at -78C. A precipitate (LiCl) was observed in all cases upon warming to room temperature. The suspension was allowed to settle, and cannula transfered into a 10 ml volumetric flask. The precipitate was washed with two small portions (1ml) of solvent and transfered to the volumetric flask. The survey of the reagents prepared in this manner (typically 0.5 M) was conducted based on the appearrance of phosphine upon addition of a stoichiometric amount of pinacolone to a 0.7 mL (0.35 mmol) aliquot NMR sample. ^{31}P-NMR of all boron phosphides prepared in this manner showed the absence of the corresponding lithium phosphide resonances and appearance of new phosphorous resonanance(s). Percent yield of reagents are based on intergration of total phosphorous resonances.

Preparation of N-Tosyl Ethanolamine (NTE)

To a 1L Erlenmeyer flask was added 200 mL of dichloromethane and 70 mL of ethanolamine (1.2 mole). This solution was cooled using an ice bath. 91.1 grams of tosylchloride (0.47 mole) was dissolved in 300 ml of dichloromethane and transfered to a 500 ml addition funnel. This solution was then added to the Erlenmeyer flask over an hour and allowed to reach room temperature after the completion of addition. Aquous workup with saturated bicarbonate solution and evaporation of dichloromethane resulted in 80 grams (74% yield) of a clear thick liquid that crystallized upon standing. m.p.54-55 C

^{1}H NMR(300MHz;CDCl$_3$) : δ 2.42(s, 3H), 2.83(br s, 1H), 3.06(m, 2H), 3.67(br s, 2H), 5.57(s, 1H), 7.30(d, 2H), 7,75(d, 2H).

^{13}C NMR(75.4MHz; CDCl$_3$) : 21.46, 45.16, 61.20, 127.05, 129.73, 136.25, 143.54.

Preparation of N-silyl,O-silyl, N-Ethylethanolamine (NONEE)

Lithium metal 13.32 g (1.92 mole 20% excess) was shaved from lithium rods inside a dry box and transfered to a three neck 1L round bottom flask. The flask was kept under an atmosphere of argon and equipped with an addition funnel, a thermometer, and a water cooled condenser. The flask was charged with 250 ml of dry ether and cooled to

-10C (internal temperature) with stirring using a CO_2/acetone bath. The addition funnel was charged with 150 mL of ether, followed by 103 mL (0.96 mole) of n-butylbromide. The butylbromide solution was added to the lithium suspension over a 30 minute period, after which it was allowed to warm up to 10C and kept at this temperature for an hour. The vessel was cooled down to 0C and 39.0 mL (0.4 mole) of N-ethylethanolamine was added dropwise through the addition funnel over 20 minutes while keeping the internal temperature at 0C. After one hour 101.5 mL (0.8 mole) of TMSCl was added over an hour while maintaining the reaction temperature at 0C. The reaction was allowed to come to room temperature over an additional hour and filtered to give a clear solution. Ether was distilled and 80 g of a liquid product (86%) was isolated by vaccum distillation (bp. 62C, 0.1 mm Hg).

^1H NMR(300MHz;$CDCl_3$) : δ -0.01(s, 9H), 0.08(s, 9H), 0.95(t, J=6.6Hz, 3H), 2.75(q, J=7.1Hz, 2H), 2.82(t, J=7.0, 2H), 3.45(t, J=7.0, 3H)

^{13}C NMR(75.4MHz; $CDCl_3$) : -0.51, 0.00, 16.10, 41.69, 48.77, and 62.30.

Preparation of N-Ethylethanolaminechloroborane

To a 250 mL round bottom flask was added 50 mL of a 1M solution (50 mmol) of borontrichloride in hexane, and diluted with an additional 50 mL of hexane. The vessel was cooled using an ice water bath. To this solution was added 11.65 grams of NONEE (50 mmol) in a dropwise fashion, over a 10 minute period. Upon dropwise addition, a white precipitate appeared. Removal of solvent and TMSCl by a water aspirator produced 6.7 grams of a pale red solid. The solid was washed with two-10 mL portions of hexane and residual hexane was removed under reduced pressure to produce 6.57 g of a sticky solid (96% yield).

^{11}B-NMR analysis in CCl_4 showed presence of two singlets at 27.7 ppm and 8.70 ppm in 1:1 ratio. Heating the sample to 80C changes the ratio to 6:1. When the sample was cooled to room temperature, a 1:1 ratio was re-established. This data suggests the presence of a monomer and dimer in solution.

^{13}C NMR(75MHz; CCl_4, 80C) : 16.76, 41.69, 50.25, 67.63

Preparation of N-Tosyl-Ethanolaminechloroborane

To a 10 mL round bottom flask was added 1.07 g (5.0 mmol) of N-Tosyl-Ethanolamine. 5 ml of dichloromethane was added and the solid dissolved. To this solution was added 5 ml of a 1M borontrichloride solution (5 mmol) in dichloromethane. After half an hour standing at room temperature the solvent was removed under a stream of nitrogen leaving behind a white solid.(1.27 g 97%)

^{1}H NMR(300MHz;$CDCl_3$) : δ 2.45(s, 3H), 3.80(ddd, J=7.5Hz, 2H), 0.95(ddd, J=6.6Hz, 2H), 7.82(d, J=8.4Hz, 2H), 7.35(d, J=8.7, 2H).

^{13}C NMR(75.4MHz; $CDCl_3$) : 21.55, 47.74, 65.23, 127.15, 129.86, 136.01, 144.54.

^{11}B NMR(96.2MHz; $CDCl_3$,) : 25.66

Preparation Of N-Tosylethanolamine(diphenylphosphino)borane **X**

In a 25 mL round bottom flask 5 mmol of N-Tosylethanolaminechloroborane was prepared. The solid was dissolved in 10 mL of THF at -78C. To this solution was added 5 mmols of a diphenylphosphine solution and the reaction was allowed to warm up to room temperature. A pale yellow solution resulted. A 0.5 mL sample was transfered to a NMR tube. ^{31}P-NMR analysis showed presence of a major resonance at -61.2 ppm (69%). Addition of pinacolone to the tube resulted in the release of 0.3% phosphine over 30 minutes.

Preparation of N-Ethylethanolamine(diphenylphosphino)borane **IX**

To a 10 mL round bottom flask was added 0.51 mL of diphenyphosphine (3.0 mmol) followed by 2 mL of THF. 2 mL of a 1.5 M Butyllithium solution in hexane (3.0 mmol)was added at OC in a dropwise manner. A deep orange solution resulted. To this solution was added 4.3 mL of a 0.7 M solution of N-ethylethanolaminechloroborane (3.0 mmol). After half an hour a pale yellow solution resulted with appearance of a precipitate. The solid was allowed to settle and the supernatant was transfered to a 10 ml volumetric flask. The solid was washed with two portions (1 mL) of THF and the resulting solution transfered to the volumetric flask. A one mL aliquot (0.3 mmol) of this solution was transfered to a NMR tube. ^{31}P NMR analysis of the sample showed a broad singlet at -65 ppm that accounted for 73% with other resonances at -40 ppm (11% diphenylphosphine), -19.4 ppm (13%), and -14.4 ppm (3%). Addition of 35 μL of pinacolone (0.3 mmol) at room temperature resulted in disappearance of the resonance at -65 ppm and increase in the amount of diphenylphosphine in addition to appearance of a new resonance at 7.2 ppm (34%).

Examination of Catechol(diphenylphosphino)borane **VIII**

A 5ml round bottom flask was charged with 0.8 ml of n-Butyllithium (1.25 mmol). 217 μL of diphenylphosphine (1.25 mmol) was added via a syringe at zero degrees. After standing for 10 minutes a white slury resulted. To this slurry was added 2 ml of a 0.6 M solution of catecholchloroborane (1.2 mmol) in benzene. The solution was then allowed to settle and an aliquot was removed for NMR analysis. ^{31}P NMR of the sample showed a major broad singlet at -65.4 ppm which dissapeared upon addition of pinacolone without the release of diphenylphosphine. A new singlet appeared at 7.1 ppm which may account for addition of phosphorous to the ketone.

Examination of Pyrolidinechloro(Diphenylphosphino)borane **XI**

In a 5 ml round bottom flask 1.6 mmol of lithium diphenyl phosphide was prepared by the addition of 1 ml of a 1.6 M n-Butyllithium to 278 μL of diphenylphosphine in 2 ml of hexane at zero degrees. To this suspension was added 213 μL of pyrolidinedichloroborane (1.6 mmol). After 30 minutes a 0.5 ml sample was removed for NMR analysis. ^{31}P NMR showed presence of two new resonances at -35.5 ppm and -46.1 ppm. Upon addition of pinacolone no significant changes were observed.

Examination of bis-diisopropylamine(diphenylphosphino)borane **VII**

1.05 mmole of bis-diisopropylaminechloroborane (0.256 g) was transfered to a 5 ml round bottom flask and dissolved in 1 ml of THF. To this solution was added 1 ml of a 1M lithium diphenylphosphide solution in THF in a dropwise manner at -78. The cooling bath was removed and the reaction mixture was allowed to stirr at room temperature for one hour. A pale yellow suspension was the result. An aliquot was removed for NMR analysis. ^{31}P NMR of the sample showed a single resonance at -36.5 ppm. Addition of pinacolone to this sample did not show any significant change. Reexamination of the sample after 24 hours produced the same spectrum.

Examination of dicyclohexyboron(hexamethyldisilazino)borane **III**

A 25 mL round bottom flask was charged with 8 mL of hexane and 2mL of a 1.6M n-butyllithium (3.2 mmol). The flask was then cooled to 0C and 0.65 mL of HMDS (3.2 mmol) was added dropwise. After 30 minutes a viscous liquid resulted. To this suspension was added 680 μL (3.2 mmol) of dicyclohexylchloroborane in a dropwise manner. During the addition of the boron chloride a salt precipitated and persisted. Upon completion of addition the ice bath was removed. The mixture was stirred at room temperature fo an hour and allowed to settle. ^{1}H-NMR examination of a sample of the supernatant after evaporation of hexane showed broad resonances between 0.8 and 1.8 ppm(ring resonances) and a singlet at 0.17 ppm (TMS resonances). Addition of pinacolone to this sample did not result in any observable reaction (no change in the ratio of TMS resonances and the pinacolone methyl resonance at 2.1 ppm).

Examination of dicyclohexyl(diphenylamino)borane **II**

A 25 mL round bottom flask was charged with 0.54 g of diphenylamine and 8 mL of benzene. The flask was then cooled to 0C and 2mL of a 1.6M n-butyllithium (3.2 mmol) was added dropwise. After 30 minutes a slurry resulted. To this suspension was added 680 μL (3.2 mmol) of dicyclohexylchloroborane in a dropwise manner. During the addition of the boron chloride a salt precipitate persisted. Upon completion of addition the ice bath was removed. The mixture was stirred at room temperature for an hour and allowed to settle. ^{1}H-NMR examination of a sample of the supernatant after evaporation of benzene showed broad resonances between 0.8 and 1.8 ppm(ring resonances) and a set of multiplets above 7.0 ppm. Addition of pinacolone to this sample did not result in any observable reaction (no change in the ratio of aromatic resonances and the pinacolone methyl resonance at 2.1 ppm).

Preparation of dicyclohexylboron enolate of diisopropyl ketone

To a 25 mL round bottom flask was added 5 mL of hexane at 0C followed by 3.2 mL of a 1.6M n-Butyllithium (5mmol). Diisopropylamine (700 μL) was added dropwise and the solution became more viscous. The vessel was allowed to come to room temperature to complete the reaction. After 15 minutes the reaction vessel was cooled to 0 C and 708 μL of diisopropyl ketone (5.0 mmol) was added. Upon standing at room temperature for half an hour a white precipitate appeared. The solvent was evaporated at reduced pressure where a white solid remained. The solid was resuspended in 5 ml of benzene, cooled to 0C, and 1mL of dicyclohexylchloroborane (5 mmol) was added dropwise with stirring. The reaction was stirred at room temperature for an hour. Benzene was evaporated at reduced pressure and replaced with $CDCl_3$.

^{13}C NMR(75.4MHz; $CDCl_3$) : 18.06, 18.23, 20.14, 27.06, 27.41, 27.84, 28.09, 28.68, 29.49, 107.89, 149.38.

^{11}B NMR(96.2MHz; $CDCl_3$,) : 49.32

Reaction of Dicyclohexyl(di-t-butylphosphino) borane With Diisopropylketone

To a 10 mL round bottom flask was added 3.12 mL of a 1.6 M n-butyllithium solution in hexane (5.0 mmol) followed by 0.9 mL of di-t-butyhlphosphine (5.0 mmol). The mixture was then heated at 50C and after 30 minutes a slurry resulted. The flask was then cooled with an ice bath. To this slurry was added 1.1 mL of dicyclohexylchloroborane (5.0 mmol) at 0C in a dropwise manner. After one hour a sample was removed for NMR analysis. ^{31}P-NMR showed a major resonance at 36.11 ppm which accounted for a 91% yield.

A 1 mL sample was removed from the flask and hexane was evaporated under reduced pressure, 0.181 g of a clear pale yellow oil remained (0.56 mmol). Based on this determination, 80 μL of diisopropyl ketone (0.56 mmol) was added to an NMR tube after transfer of the sample in hexane. ^{31}P-NMR analysis revealed slow release of di-t-butylphosphine. After completion of the reaction (24 hours), the sample was evaporated to remove excess phosphine and ^{13}C NMR recorded.

^{13}C NMR(75.4MHz; CDCl$_3$) : 18.07, 18.23, 20.13, 27.03, 27.38, 27.81, 27.94, 28.64, 29.48, 107.89, 149.36.

^{11}B NMR(96.2MHz; CDCl$_3$,) : 49.32

Examination of the reaction of dicyclohexyl(di-t-butylphosphino)borane

N,N-dimethylpropionamide

A 0.5 M stock solution of dicyclohexyl(di-t-butylphosphino)borane was prepared in d^8 toluene in a 10 mL volumetric flask according to the general procedure. To an NMR tube was added 700 μL of the stock solution (0.35 mmol). To this tube was added 38 μL of N,N-dimethylpropionamide via a syringe. Examination of the sample after 4 hours showed complete consumption of the starting material (^{31}P 32.4 ppm) and appearance of two major resonances at 18.1 ppm (52% phosphine) and 29.36ppm(25%).

Ethylacetate

A 0.5 M stock solution of dicyclohexyl(di-t-butylphosphino)borane was prepared in d^8 toluene in a 10 mL volumetric flask according to the general procedure. To an NMR tube was added 700 μL of the stock solution (0.35 mmol). To this tube was added 28 μL of ethylacetate via a syringe. Examination of the sample after 17 hours showed lack of consumption of the starting material (^{31}P 32.4 ppm) and appearance of two minor resonances at 18.1 ppm (5% phosphine) and 56.13 ppm(6%).

Pinacolone

A 0.5 M stock solution of dicyclohexyl(di-t-butylphosphino)borane was prepared in hexane in a 10 mL volumetric flask according to the general procedure. To an NMR tube was added 700 μL of the stock solution (0.35 mmol). To this tube was added 43 μL of pinacolone via a syringe. Examination of the sample after one hour showed slow consumption of the starting material and appearance of two resonances at 21.1 ppm (19% phosphine) and 61.8ppm (3%).

MEK

A 0.5 M stock solution of dicyclohexyl(di-t-butylphosphino)borane was prepared in hexane in a 10 mL volumetric flask according to the general procedure. To an NMR tube was added 700 μL of the stock solution (0.35 mmol). To this tube was added 35 μL of MEK via a syringe. Examination of the sample after 30 minutes showed complete consumption of the starting material (^{31}P 36.1ppm) and appearance of one minor resonance at 21.2 ppm (2% phosphine) and a major resonance at 64.64 ppm(98%).

Examination of reaction of dicyclohexy(diphenylphosphino)borane

Diethylketone

A solution of dicyclohexylchloroborane in THF was prepared by addition of 1.25 mmoL (270 μL) of dicyclohexylchloroborane to 5 mL of THF at -78C in a 25 mL round bottom flask. In a 10 mL round bottom flask 1.25 mmol of lithiumdiphenylphosphide was prepared by the addition of 1.25 mmol (217 μL) of diphenylphosphine to 0.8 mL of n-butyllithium in THF (5 mL) at -78C. A bright orange solution resulted and the flask was allowed to warm up to room temperature. The phosphide solution was added to the chloride solution via a syringe in three portions in a dropwise manner. Complete discoloration of the lithium phosphide solution occured upon addition of each drop. The reaction vessel was then allowed to warm up to 0C where a white precipitate appeared To this suspension was added 125 μL of diethylketone (1.25 mmol) in a dropwise manner. After 1.5 hours the flask was cooled to -78C and 127 μL of benzaldehyde was added and the mixture was stirred for 2 hours. The reaction was worked up using 680 μL of 30% hydrogen peroxide after 3 hours. A 1 mL sample was removed and THF was evaporated. This sample was extracted with hexane, washed with dilute HCl then water , and dried over anhydrous Na_2SO_4. The product was analysed by ^{1}H NMR to determine the syn/anti ratio of 9:1 and the percent yield (92%).The percent yield is based on the amount of aldehyde recovered.

N,N-Dimethylpropionamide

A solution of dicyclohexylchloroborane in THF was prepared by addition of 1.25 mmoL (270 μL) of dicyclohexylchloroborane to 5 mL of THF at -78C in a 25 mL round bottom flask. In a 10 mL round bottom flask 1.25 mmol of lithiumdiphenylphosphide was prepared by the addition of 1.25 mmol (217 μL) of diphenylphosphine to 0.8 mL of n-butyllithium in THF (5 mL) at -78C. A bright orange solution resulted and the flask was allowed to warm up to room temperature. The phosphide solution was added to the chloride solution via a syringe in three portions in a dropwise manner. Complete discoloration of the lithium phosphide solution occured upon addition of each drop. The reaction vessel was then allowed to warmed up to 0C where a white precipitate appeared To this suspension was added 137 μL of N,N-dimethylpropionamide (1.25 mmol) in a dropwise manner. ^{1}H NMR analysis after 2 hours showed presence of starting amide (two methyl resonances at 2.92 and 3.0 ppm)and a singlet at 2.60 belonging to the enolate (vinylic protons appeared at 4.85 ppm as 2 sets of overlaping quartets) which accounted for 46% enolate formation. Re-examination of the reaction at 4 hours did not show any changes.

Ethylacetate

A solution of dicyclohexylchloroborane in THF was prepared by addition of 1.25 mmoL (270 μL) of dicyclohexylchloroborane to 5 mL of THF at -78C in a 25 mL round bottom flask. In a 10 mL round bottom flask 1.25 mmol of lithiumdiphenylphosphide was prepared by the addition of 1.25 mmol (217 μL) of diphenylphosphine to 0.8 mL of n-butyllithium in THF (5 mL) at -78C. A bright orange solution resulted and the flask was allowed to warm up to room temperature. The phosphide solution was added to the chloride solution via a syringe in three portions in a dropwise manner. Complete discoloration of the lithium phosphide solution occured upon addition of each drop. The reaction vessel was then allowed to warmed up to 0C where a white precipitate appeared To this suspension was added 122 μL of ethylacetate (1.25 mmol) in a dropwise manner. ^{31}P analysis after 4 hours showed 48% release of diphenylphosphine and another major resonance at 1.24 ppm (30%), the remainder was 9% starting material and two other resonances at 17.6 and 14.2 ppm.

Pinacolone

A solution of dicyclohexylchloroborane in THF was prepared by addition of 1.25 mmoL (270uL) of dicyclohexylchloroborane to 5 mL of THF at -78C in a 25 mL round bottom flask. In a 10 mL round bottom flask 1.25 mmol of lithiumdiphenylphosphide was prepared by the addition of 1.25 mmol (217 μL) of diphenylphosphine to 0.8 mL of n-butyllithium in THF (5 mL) at -78C. A bright orange solution resulted and the flask was allowed to warm up to room temperature. The phosphide solution was added to the chloride solution via a syringe in three portions in a dropwise manner. Complete discoloration of the lithium phosphide solution occured upon addition of each drop. The reaction vessel was then allowed to warmed up to 0C where a white precipitate appeared To this suspension was added 156 μL of pinacolone (1.25 mmol) in a dropwise manner. ^{31}P analysis after 2 hours showed 80% release of diphenylphosphine and other minor resonances, the remainder was 14% starting material and two other resonances at 19.6 and 14.1 ppm.

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Chapter II:Preparation of Aluminum Enolates From Aluminum Amides

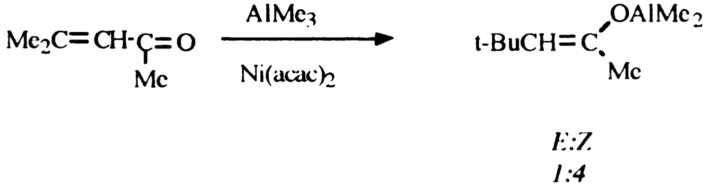
Literature review of Aluminum Enolates Structure, Properties, and Methods of Synthesis

A review of the literature shows that descriptions of aluminum enolates are rare, and no general method is available for their preparation. The best example for the structure of aluminum enolates is the work by Jeffery *et al.* According to molecular weight determinations in benzene, aluminum enolates tend to be associated in solution with oxygen bridges.(10)

Work in this area during the past three decades has resulted in the preparation of aluminum enolates via several indirect routes. These routes are in many ways analogous to the routes to boron enolates described in chapter I.

1)-Conjugate addition.

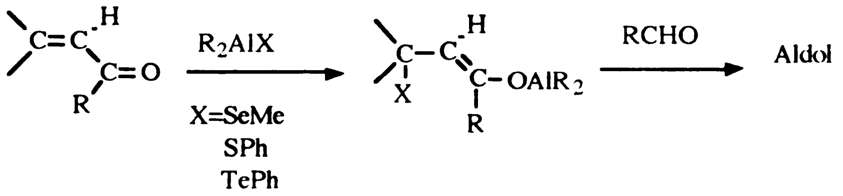
Conjugate addition of trimethylaluminum to mesityloxide in the presence of a catalytic amount of nickel acetoacetonate has been reported by Jeffery.(1b) This reaction generates the internal enolate with 4:1 selectivity in favor of the Z stereoisomer in excellent yield (eq 1).



$$\mathrm{Me_2C{=}CH{-}\underset{Me}{C}{=}O} \xrightarrow[\mathrm{Ni(acac)_2}]{\mathrm{AlMe_3}} \mathrm{t\text{-}BuCH{=}C}\begin{smallmatrix}\mathrm{OAlMe_2}\\ \mathrm{Me}\end{smallmatrix} \qquad (1)$$

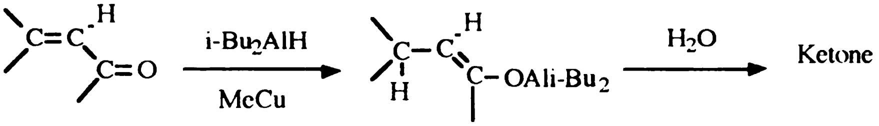
E:Z
1:4

Itoh, and Sazaki *et al.* have reported the 1,4 addition of dimethylbenzenethiolate, dimethylaluminummethyl selenide, and diisobutylaluminumphenyl telluorolate to α,β-unsaturated carbonyl compounds as a route to the preparation of internal aluminum enolates (eq 2).(2) No attempt was made to isolate or characterize the enolate in this study.



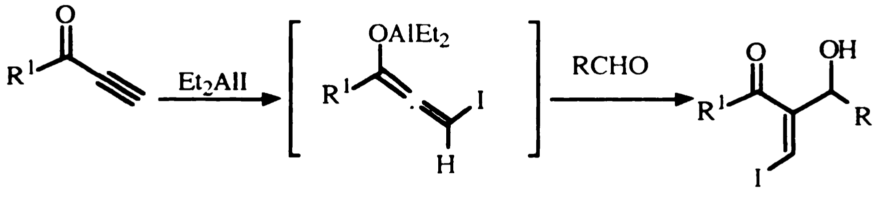
(2)

Tsuda *et al.*. have reported the conjugate addition of DIBA-H to α,β–unsaturated carbonyl compounds in the presence of catalytic amounts of methyl copper(I) (eq3).(3a) In this study the presence of enolate was verified by quenching the reaction mixture with water and the recovery of ketone.



(3)

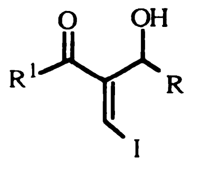
Taniguchi and coworkers have suggested the allenolate intermediate generated by the addition of diethylaluminum iodide to α,β-acetylinic ketones (eq4).(4) Subsequent reaction of this intermediate with an aldehyde provided the expected aldol product in moderate yield and selectivity.



(4)

Z

R	Z/E
Ph	64/16
Me	54/22



E

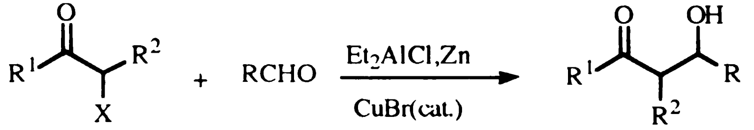
2)-Transmetallation

Zakharkin and Savina have reported the reaction of DIBA-H with silylenolethers of simple aldehydes as a means of generating the diisobutyl aluminum enolates of quenching the reaction mixture with water and recovering the aldehydes in 80% yield (eq5).

$$\mathrm{Et_3SiOCH{=}CHR} \xrightarrow{\mathrm{i\text{-}Bu_2AlH}} \mathrm{i\text{-}Bu_2AlOCH{=}CHR} + \mathrm{Et_3SiH} \qquad (5)$$

R=H or Me

Maruoka and coworkers have reported that simultaneous addition of aldehydes and α-haloketones at low temperature to a suspension of zinc dust and a catalytic amount of copper bromide and diethylaluminum chloride produced excellent yields of the expected aldol products (eq 6).(6) The involvement of a zinc enolate that may be the result of the kinetic Reformatsky reaction of 4-bromocrotonate makes the above results questionable as presented by the authors. Representative results are provided in **Table 1.2.**

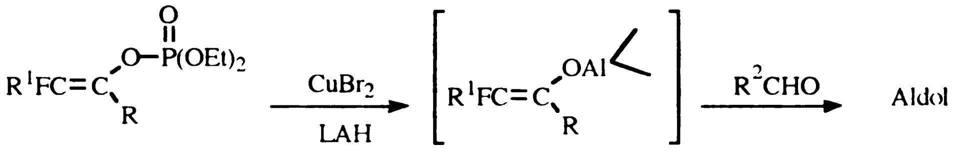


(6)

Table 1.2. Representative Results For The Reaction Of α-Haloketones With Zinc and $\mathrm{Et_2AlCl}$ After Maruoka *et al.*

Ketone	R	*syn/anti*	%Yield
2-bromocyclohexanone	Ph	1/1	97
2-Bromo-2-metylcyclohexanone	Ph	4/3	100
Methyl bromocrotonate	Ph	5/4	100

Kurobushi has suggested the presence of an aluminum enolate generated from the reaction of an a-fluoroenolphosphonate with LAH in the presence of copper (II) bromide at low temperature. The reaction of this mixture with aldehydes produces the aldol condensation product in moderate to good yields (eq 7).(7) Representative results are provided in **Table 2.2.**



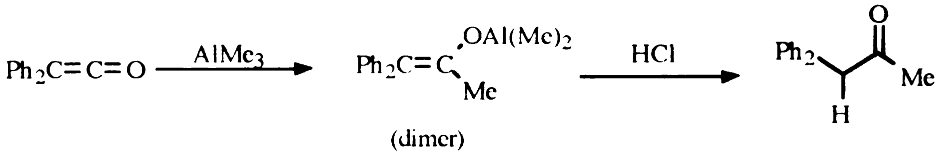
(7)

Table 2.2 Representative results for reaction of an α-fluoroenolphosphonate with LAH after Kurobushi *et al.*

R^1	R	R^2	*syn/anti*	%Yield
CF_3CF_2	c-C_6H_{11}	Ph	1.5/1	51
		(E)-$CH_3CH(CH_3)$	1/0.8	38
$CF_3(CF_2)_5$	$CH_3(CH_2)_2$	Et	1/0.8	84

3)-1,2 Addition of Metal Alkyls

The 1,2 addition of organometallic compounds to ketene is a well established method for the preparation of metal enolates.(10) Jeffrey and Meisters examined the addition of trimethylaluminum to diphenyl ketene in order to obtain an internal aluminum enolate (eq 8).(11) Ebulometric determination of the molecular weight for this enolate in benzene revealed the presence of dimeric structure in solution.

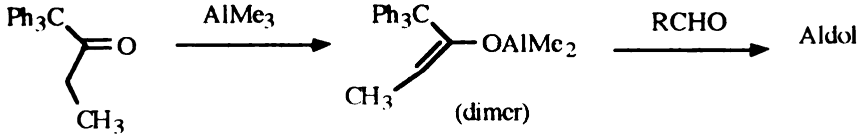


(8)

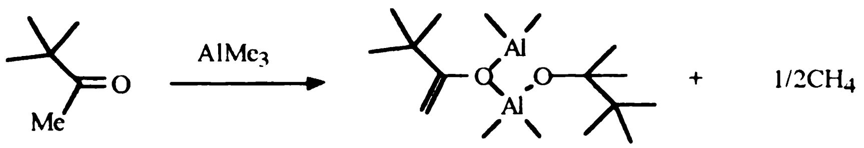
4)-Carbonyl Enolization

These methods take advantage of the acidity of the α-proton of the carbonyl compound and the use of a strong base to effect the enolization. Jeffrey and Meisters have prepared enolates of sterically hindered ketones by the reaction of trimethylaluminum with triphenylmethyl ketone or pinacolone (eq 9,10).(8a)

Etras and Seebach have prepared the enolate of ethyl trityl ketone in an analogous manner.(8b) **Table 3.2** provides a sample of the Seebach *et al.* results with representative aldehydes in an aldol reaction after 40 hours.



(9)

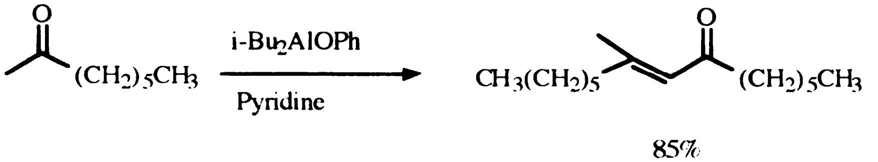


(10)

Table 3.2 Representative results for reaction of trimethylaluminum with ketones after Seebach *et al.*

R	*syn/anti*	% Aldol
Ph	5/95	96
p-CH_3OPh	7/93	95
p-NMe_2Ph	8/92	92
p-CNPh	1/99	93
p-NO_2Ph	1/99	95

Tsuji *et al.* found diisobutyl aluminum aryloxide in combination with pyridine to be an effective agent for the regioselective aldol condensation of methyl ketones at the methyl side (eq 11).(9)



(11)

To our knowledge the latter examples represent the only attempted enolizations of carbonyl compounds via an aluminum-heteroatom base and trimethylaluminum(12).

Literature review of Aluminum Amides Structure, Properties, and Methods of Synthesis

Aluminum amides are compounds in which aluminum is bonded to one or more nitrogen ligands. These compounds have been the subject of study in the past thirty years and several reviews are available on their structures and properties.(13a) They are generally air and moisture sensitive and are handled under an inert atmosphere. Their uses include reducing agents(13), polymerization catalysts(14), Diels-Alder catalysts(15), amidation agent(16), precursors to aluminum cage compounds,(17) aluminum nitride coatings for ceramics(18), reagents for the isomerisation of epoxides to allylic alcohols(19), and a reagent in the Fisher indole synthesis.(20) In contrast to boron amides, there are only a few examples of aluminum amides in which the metal and nitrogen are both tri-coordinate. These include the sterically hindered aminoalanes, such as $Al[N(i\text{-}Pr_2)_3]$, $Al[N(SiMe_3)_2]_3$, and a new monomeric azaaluminatrane Al(tert-$BuMe_2SiNCH_2CH_2)_3N$ synthesized by Verkade *et al.*(21) Other aluminum amides are dimers, oligomers, or polymers, formed as a result of intermolecular dative bonding between monomer molecules which have donor (N) as well as acceptor sites (Al). The degree of association of these amides depends on the ligands on the aluminum as well as the ligands on the nitrogen atom. For example $Me_2AlNHMe$ is trimeric(22) whereas Me_2AlNMe_2 is dimeric(23) as determined by X-ray crystallography.

Preparation of Aluminum Amides

There are several routes available to the synthesis of aluminum amides. These methods generally produce aluminum amides in excess of 90% yield. The most useful routes are the alkane elimination(24) from a trialkylaluminum precursor or hydrogen elimination(25) from an aluminum hydride precursor. Examples of these methods are demonstrated in equations 1 and 2. The reaction of aluminum hydrides provides a milder method since aluminum hydrides are more reactive than aluminum alkyls.

$$\mathrm{Me_3Al} \xrightarrow[\mathrm{100C}]{\mathrm{NHMe_2}} \mathrm{Me_2AlNMe_2} + \mathrm{CH_4} \tag{1}$$

$$\mathrm{Me_2AlH} \xrightarrow[\mathrm{25C}]{\mathrm{NHMe_2}} \mathrm{Me_2AlNMe_2} + \mathrm{H_2} \tag{2}$$

These two methods are by far the most efficient methods since the byproducts of the reactions are gases and are easily removed from the reaction vessel. The other attractive feature of these methods is the measurement of the amount of gas produced provides a means of monitoring the progress of the reaction.

A direct method for the preparation of aluminum amides is reaction of aluminum metal, hydrogen gas, and the amine in a sealed reaction vessel at 4000 psi in benzene (eq3).(26)

$$\mathrm{Al} + \mathrm{3/2H_2} \xrightarrow[\mathrm{4000\ psi}]{\mathrm{3\ NHEt_2}} \mathrm{Al(NEt_2)_3} + \mathrm{3H_2} \tag{3}$$

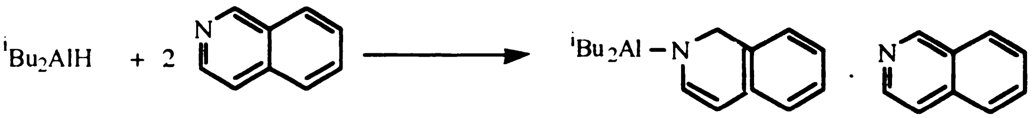
Salt elimination from the reaction of LAH and an amine hydrochloride has been used to prepare aluminum alanes (eq4).(27)

$$\mathrm{LiAlH_4} + \mathrm{Et_2NHCl} \xrightarrow{\mathrm{3Et_2NH}} \mathrm{AlNEt_3} + \mathrm{LiCl} + \mathrm{3H_2} \quad (4)$$

Metathetical exchange between trialkyl boranes and tris aluminum amides provides another method for the synthesis of dialkylaluminum amides (eq5).$^{(28)}$

$$\mathrm{2R_3B} + \mathrm{Al(NMe_2)_3} \longrightarrow \mathrm{2R_2BNMe_2} + \mathrm{R_2AlNMe_2} \quad (5)$$

Hydride insertion into the nitrogen carbon double bond of aromatic amines by DIBAL is a route to the synthesis of aluminum amides (eq6).$^{(29)}$



(6)

We used compounds **I** and **II** for our initial studies for the following reasons:

1)-Compounds **I** and **II** are easily prepared by elimination of methane from the reaction of trimethylaluminum with diethyl- and diisopropylamine.

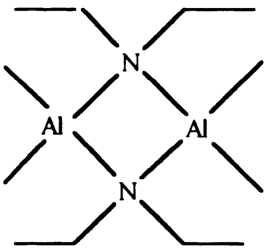
2)-Sterically hindered amines are less nucleophilic hence carbonyl addition reactions can be avoided.

3)-Methyl ligands on aluminum avoid a possible β-hydride elimination reaction commonly observed with ethyl and isobutyl ligands.

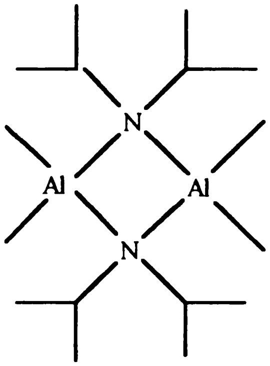
4)-Analogous lithium bases have proved to be useful for enolate chemistry.

5)-Due to the symmetry of the molecules NMR spectral interpretation would be simple.

6)-Methyl substituents on the aluminum center are converted to methane upon protic workup.



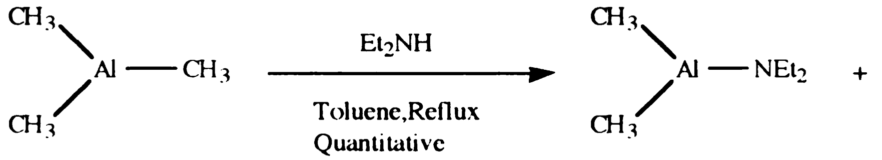
I



II

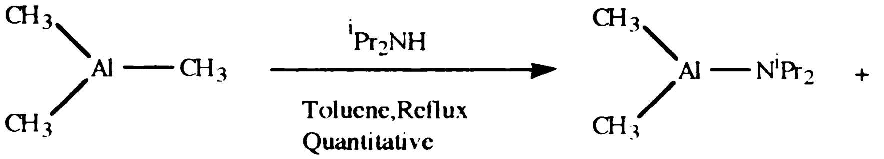
Results and Discussion

Our studies began with the preparation of compounds **I** (Dimethylaluminumdiethylamide) and **II** (Dimethylaluminumdiisopropylamide). These compounds were prepared by the reaction of trimethyl aluminum with a stoichiometric amount of the dialkylamine as previously described by Thomas *et al*. (eqs 1, 2).(30)



(eq1)

I



(eq2)

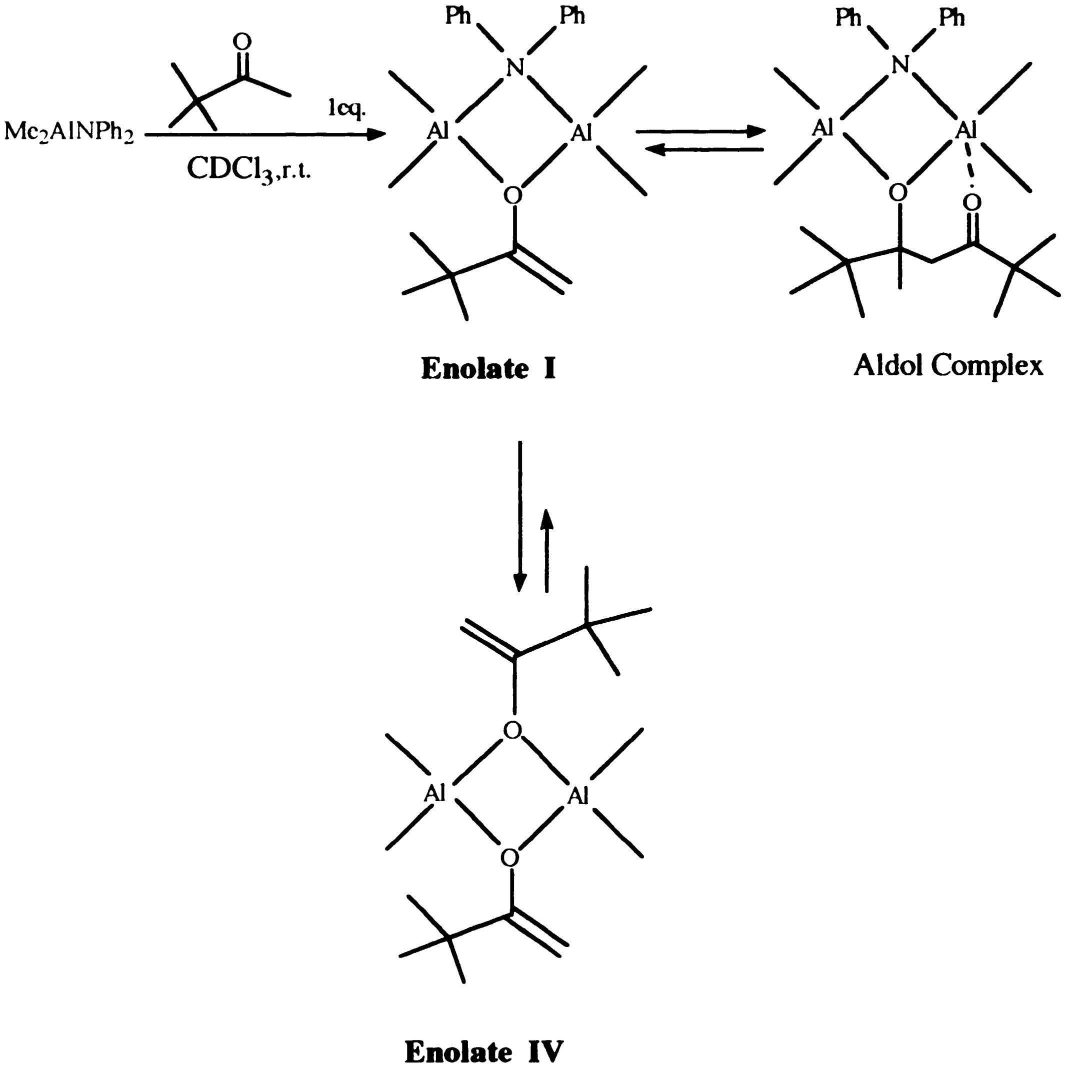
II

We found ^{1}H-NMR spectroscopy to be a powerful method for the direct analysis of the course of reaction throughout our studies. The nondonor solvent deuterated benzene was chosen to prevent complexation of the solvent to the reagent. At a later point in our studies we found deuterated chloroform to be just as useful and less costly. Hence 100 μmoles of pinacolone was injected into an NMR tube containing 100 μmoles of compound **I** in d^6-benzene at room temperature. Immediate analysis of the reaction mixture at ambient temperature showed no evidence of reaction. Upon standing at room temperature for 3.5 hours the sample was reanalysed and no change was observed, (**Figure 1.2**). In an analogous fashion compound **II** was tested and no reaction was observed after 3.5 hours.

We attribute the lack of reactivity of these complexes to the formation of strong aggregates in solution. The steric contributions of the diisopropyl ligands do not seem to have a significant effect on the reactivity of compound **II** to a carbonyl substrate. We reason that since aluminum is a strong Lewis acid and nitrogen is a strong Lewis base, association effectively neutralizes both the Lewis acidity of the aluminum and basicity of nitrogen to the extent that proton transfer to the nitrogen is prohibited on thermodynamic grounds.

We then prepared compound **III** (Dimethylaluminumdiphenylamide) to see if conjugating substituents on nitrogen can reduce the strong association of aluminum amides we previously encountered with **I** and **II** and whether enolate formation can be effected. Hence compound **III** was reacted with pinacolone at room temperature. Upon addition of 100 μmol of pinacolone to an NMR tube containing 100 μmole of compound **III** at room temperature a burst of yellow color was observed. Immediate NMR analysis showed the presence of new vinylic resonances and a complex mixture of other resonances in the aliphatic region with release of amine, (**Figure 2.2**). This experiment is the first observation of an aluminum enolate prepared via an aluminum amide. Reexamination of the NMR tube after 3.5 hours showed a very simple spectrum that had only a singlet in the aliphatic region as its major component and vinylic protons in addition to the aromatic resonances of the diphenylamine and methyl resonances on aluminum, (**Figure 3.2**).

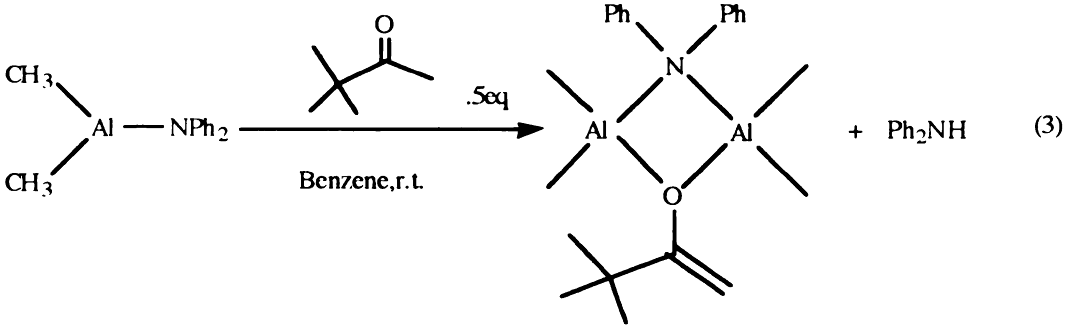
We attribute these observations to the initial formation of a nitrogen bridged enolate that is highly reactive and condenses with remaining ketone in solution. The condensed aldol product is itself unstable and hence in equilibrium with the starting **Enolate I** that dissociates to an enolate dimer, **Enolate II** (**scheme 1.2**). Collum *et al.* have spectroscopically detected (NMR) the presence of limited concentrations of mixed



Scheme 1.2 Proposed Mechanism For The Reaction Of **III** With one Equivalent of Pinacolone.

aggregates similar to Enolate I in their investigations of the reaction of LDA with pinacolone(32). Similar observations were made with addition of one equivalent of diethyl ketone to **III**. However in the case of diethyl ketone, four individual vinylic resonances were present which may be attributable to the diastereomeric enolates and their aggregates, (**figure 4.2**).

When a half equivalent of pinacolone is used the reaction can be cleanly halted at the **Enolate I** stage without any detectable amounts of the aldol complex (eq3), (**Figure 5.2**).



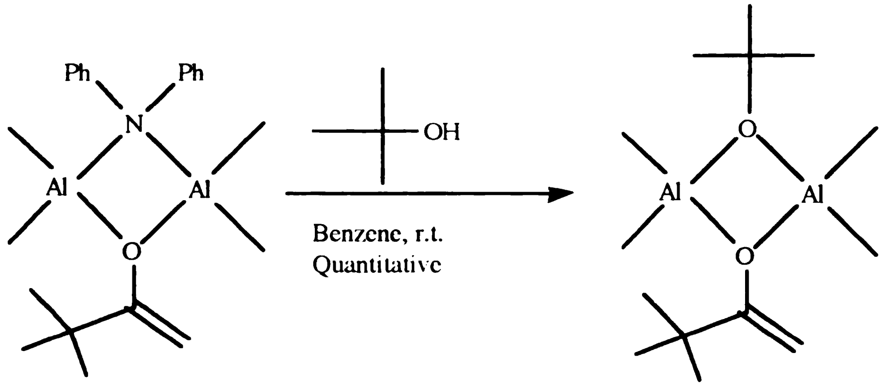
(3)

Enolate I

A series of carbonyl substrates were then tested to determine the scope of enolate formation with this reagent. The results of these experiments are shown in **Table 4.2**. These results show the formation of the kinetic enolate in all cases studied with moderate to excellent stereoselectivity and regioselectivity. The stereochemistry of the enolate of 3-pentanone was determined by nOe experiments. Irradiation of the methylene protons afforded enhancement (8.56%) at the vinylic methyl protons, whereas irradiation of the vinylic hydrogen did not show an enhancement at the methylene protons. All reactions showed complete consumption of the ketone and release of diphenylamine. The NH proton was used as an internal standard to measure the extent of the reaction. In contrast to our results reaction of esters with aluminum amides has previously been shown to produce the carboxylic acid amides by Weinreb *et al.* (eq 3a).(31)

$$Me_2AlNHPh \xrightarrow[\text{benzene, 40 hrs}]{CH_3CO_2(CH_2)_3CH_3} \underset{78\%}{CH_3CONHPh} \qquad (3a)$$

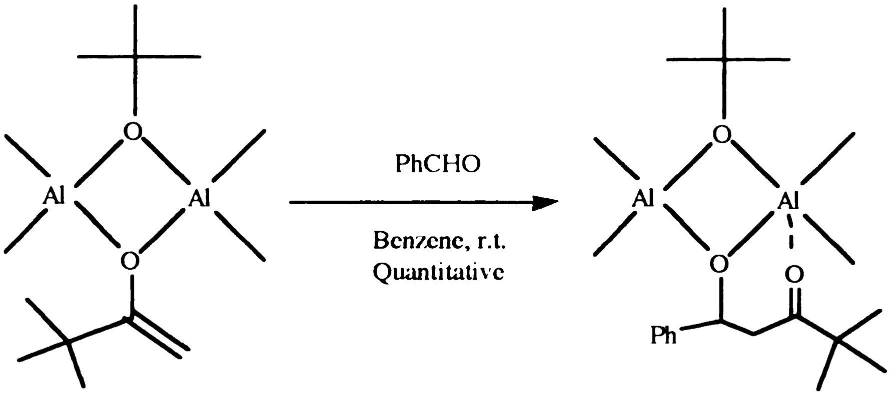
Since enolate formation had been accomplished, we wished to examine the aldol condensation reaction of the **Enolate I** with benzaldehyde using ^{1}H-NMR to follow the course of the reaction. Addition of benzaldehyde to this enolate resulted in the consumption of the aldehyde but the enolate resonances remained. The conclusion from this experiment was that the bridging diphenyl amido ligand in **Enolate I** interferes with the aldol reaction by possibly adding to the aldehyde. Hence the diphenylamido ligand in **Enolate I** was replaced with t-butylalcohol by addition of a stoichiometric amount of t-butyl alcohol to generate **Enolate II** (eq 4), (**Figure 6.2**). Other alcohols, such as methanol and ethanol reacted with **Enolate I** to produce pinacolone.



(4)

Enolate II

Addition of one equivalent of benzaldehyde to **Enolate II** resulted in complete consumption of the aldehyde with concurrent consumption of the enolate in ten minutes (eq 5), (**Figure 7.2**).



Enolate II

(5)

Four valuable conclusions were made from these sets of experiments:

1) Presence of conjugating substituents such as phenyl on the amido ligand increase the reactivity of an aluminum amide to carbonyl substrates presumably because the Lewis acidity of the metal complex is greater.

2) Enolate formation can be accomplished efficiently and cleanly with half equivalent of ketone.

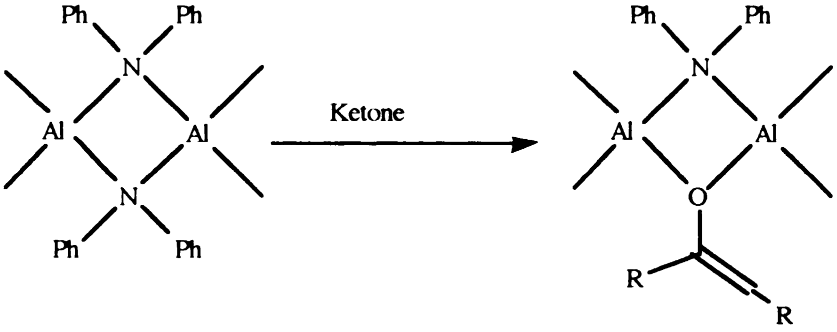
3) The self-aldol reaction following addition of stoichiometric amount of ketone is reversible.

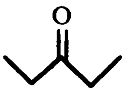
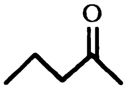
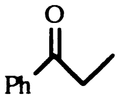
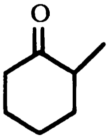
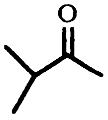
4) The bridging amido ligand can be replaced by a sterically hindered alkoxide ligand without quenching of the enolate.

Reagents Inert To **Enolate II**

Reactions of **Enolate II** with a variety of electrophiles at room temperature were examined by addition of the electrophile to NMR samples prepared from a stock standard solution of **Enolate II**. The electrophiles studied were t-butylchloride, styrene oxide, benzoylchloride, acetic anhydride, and ethylchloroformate. In all cases no reaction was observed after 24 hours at room temperature.

Table 4.2 Scope Of Enolization, Stereoselectivity and Regioselectivity Of **III.** Experiments were carried out with 50μmoles of **III** in benzene at 25C.



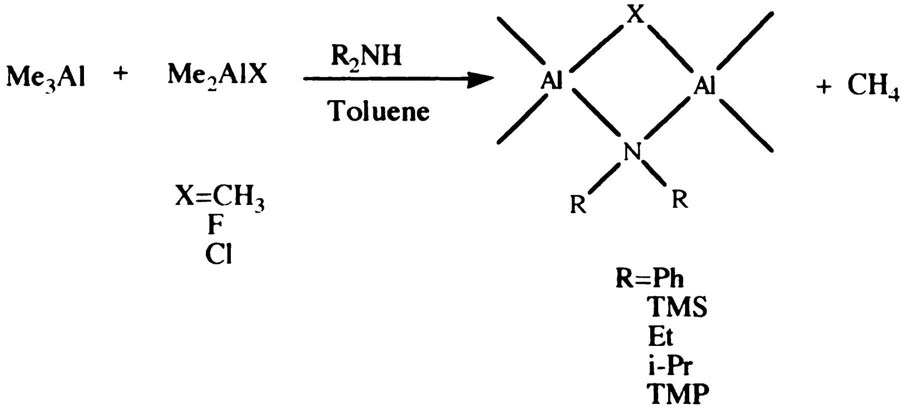
Ketone	Regioselectivity		Stereoselectivity		% Conversion
	Less Subs.	More Subs.	*E*	*Z*	
			>98		100
	4.8	1			100
			50	50	100
	>6.7[a]	<1[a]			100
	1.9	1			100

a- Due to the overlap of the ring resonances an accurate measure of the regioselectivity was not possible. Based on the amount of amine released and amount of the less substituted enolate generated an estimate of the more substituted regioisomer was made.

The lack of reactivity of **Enolate II** is attributed to the coordination of the two aluminum centers to the oxygen of the enolate. It is evident that coordination of the oxygen of the enolate to two aluminum centers reduces the nucleophilic character of the enolate towards electrophiles.

The stereoselectivity of the aldol condensation reaction was studied with the enolate of diethyl ketone prepared in an analogous manner to that used for **Enolate II** and benzaldehyde. A low temperature NMR study of the reaction mixture showed complete consumption of the enolate at -20C with the appearance of the aldol carbinol doublets in a 4:1 ratio in favor of the *anti* aldol product. Further examination after 24 hours of standing at room temperature showed isomerization of the aldol product to a 1:6 ratio in favor of the *syn* diastereomer.

The studies conducted on **Enolate II** led to the development of aluminum amides that would incorporate one basic component in a dimeric aluminum amide. At the same time we were interested in increasing the reactivity of the enolate by increasing the Lewis acidity of dimeric complexes analogous to **Enolate II**. For that purpose a series of mixed aluminum amides of the general type $Me_2AlXNR_2AlMe_2$ were synthesized (eq 5).



(6)

Reactions of these amides with pinacolone were studied to evaluate the efficiency of the acid/base reaction vs the self aldol previously observed with the symmetrical complex **III**.

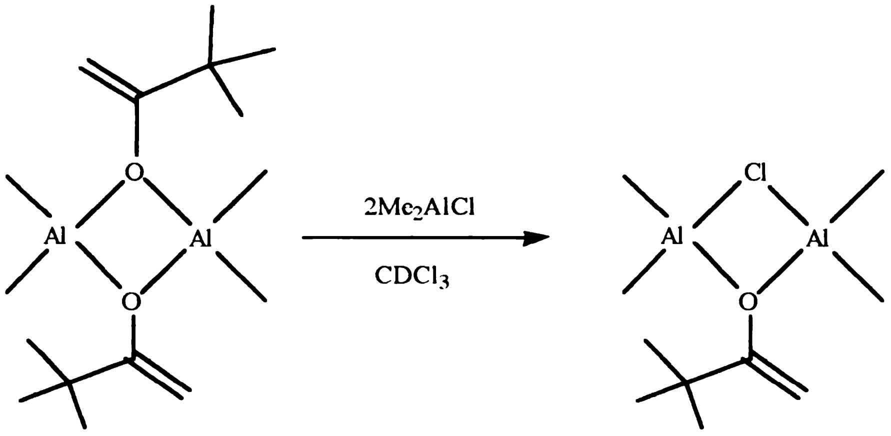
Table 5.2 provides the compilation of results of these amides with pinacolone. It is evident that the bridging atom plays an important role in the reactivity of these mixed dimers towards pinacolone.

Table 5.2. Summary Of The Reaction Of Aluminum Amides Having Non-Nitrogen Bridges With Pinacolone.

X	R	%Enolate	%Aldol	Compound
Cl	Ph	72	28	**IV**
CH_3	Ph	60	40	**V**
Cl	TMS	60	40	**VI**
F	TMS	>95		**VII**
F	^{i}Pr	>95		**VIII**
Cl	^{i}Pr	60	40	**IX**
Cl	Et	>95		**X**

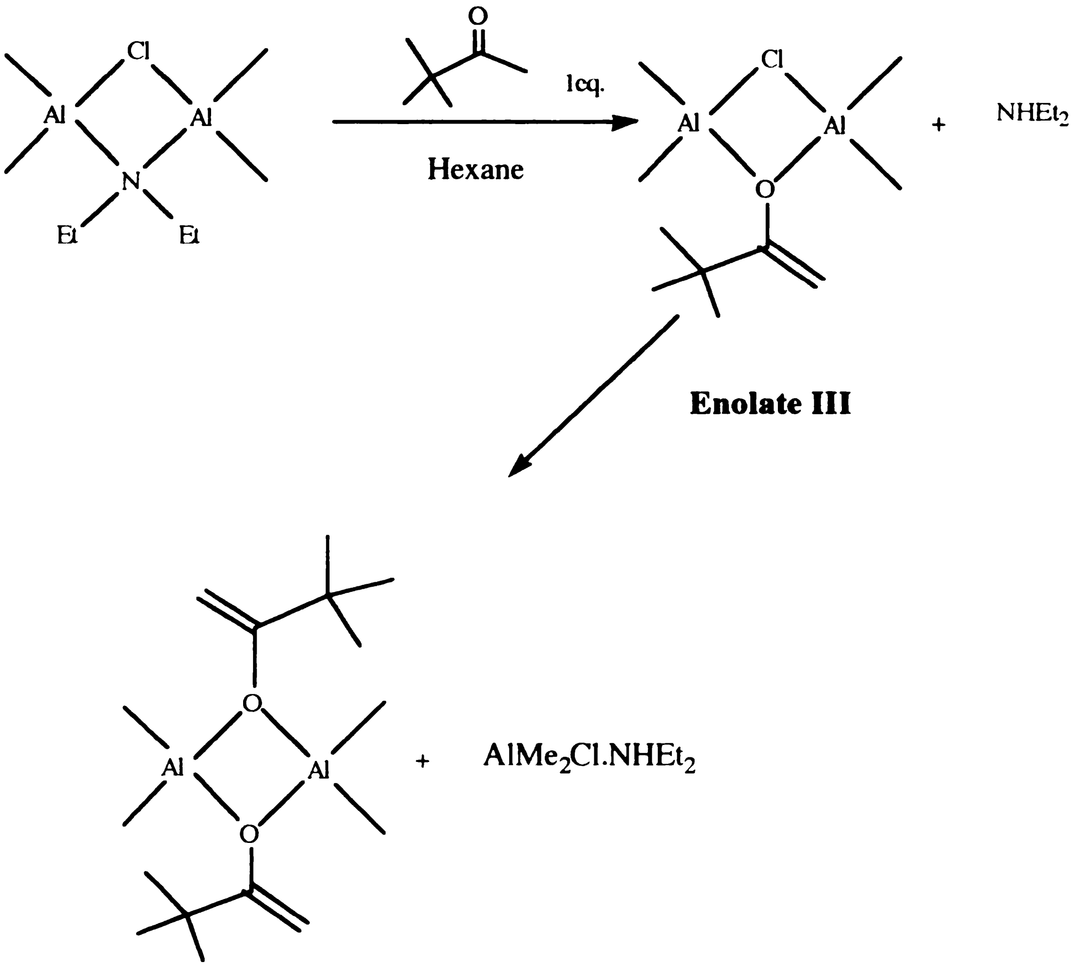
In the cases of compounds **IV** and **X** a precipitate was observed during the enolization reaction when carried out in toluene or hexane. The precipitate was isolated and dissolved in d-chloroform. ^{1}H-NMR analysis showed the absence of enolate in this solution, (**Figure 8.2**). Analysis of the supernatant showed the enolate presence in that fraction, (**Figure 9.2**). In the case of the diethylamido complex, this precipitate is formed rapidly upon addition of the ketone and persists from the beginning of the reaction only when the reaction is carried out in hexane. The latter observation may be due to the lack of solubility of the amine complex as the driving force for rapid disproportionation of the chlorine bridged enolate. We propose that upon formation of the bridging enolate disproportionation of this complex occurs, followed by the formation of an enolate dimer. The insoluble precipitate that forms is the amine complex of dimethyl aluminum chloride according to **Scheme 2.2**.

Since **Enolate IV** could be prepared amine free, we proceeded to prepare a halogen-bridged enolate by the reaction of **Enolate IV** with an equivalent of dimethylaluminum chloride (eq7). The disproportionation reaction was complete after 24 hours at ambient temperature, (**Figure 10.2**) or by heating at 80C for half an hour. These two enolate complexes display distinct chemical shifts in their NMR spectra. Acylation of both enolates was attempted in separate experiments. In contrast to **Enolate IV**, **Enolate III** can be acylated with two and a half equivalents of ethyl chloroformate to produce the ketoester of pinacolone and pinacolone in 2.3:1 ratio.



(7)

Enolate IV **Enolate III**



Enolate III

Enolate IV

Scheme 2.2 Proposed Mechanism For The Reaction Of **X** With one Equivalent of Pinacolone.

A series of other mixed amides were prepared and their reactions with 2-pentanone and 3-pentanone were studied in order to determine the generality of this methodology. Two or more sets of vinylic resonances were observed at times in most cases which may be due to disproportionation of these complexes. A compilation of these results is provided in **Table 6.2**

Table 6.2 Summary of Chemical Shift Data of Enolates Generated by the reaction of aluminum amides having Non-nitrogen bridges. Chemical shifts are reported in ppm.

X	R	3-Pentanone	2 Pentanone	Pinacolone	Compound
Cl	Ph	4.9(q)	4.3, 4.5(s) 5.0(t)	4.4, 4.6(s)	**IV**
CH_3	Ph			4.4, 4.7(s)	**V**
Cl	TMS			4.4, 4.5(s)	**VI**
F	TMS	4.9(q) 5.1(q)	4.2, 4.4(s) 4.7(t)	4.5, 4.8(s)	**VII**
F	^{i}Pr			4.5,4.5(s)	**VIII**
Cl	^{i}Pr			4.6, 4.8(s)	**IX**
Cl	Et	4.6, 4.8(q)	4.1, 4.3(s) 4.51(t)	4.3, 4.5(s)	**X**
F	Et		4.1, 4.3(s) 4.8(t)	4.4, 4.5(s)	**XI**
F	TMP	4.7,4.9(q)		4.4, 4.5(s)	**XII**
Cl	TMP			4.6, 4.8(s)	**XIII**

Examination Of The Reaction Of Monomeric Aluminum Amides With Ketones

Two monomeric aluminum amides were prepared and tested to determine their reactivity in an acid/base reaction with ketones. Tris[bis(trimethylsilyl)amino]aluminum (**XV**) was inert to the ketones tested. In contrast tris(diisopropylamino)aluminum (**XIV**) reacted with pinacolone efficiently to produce the enolate at ambient temperature.. Attempts to selectively substitute other bulky ligands for one of the amido ligands failed.

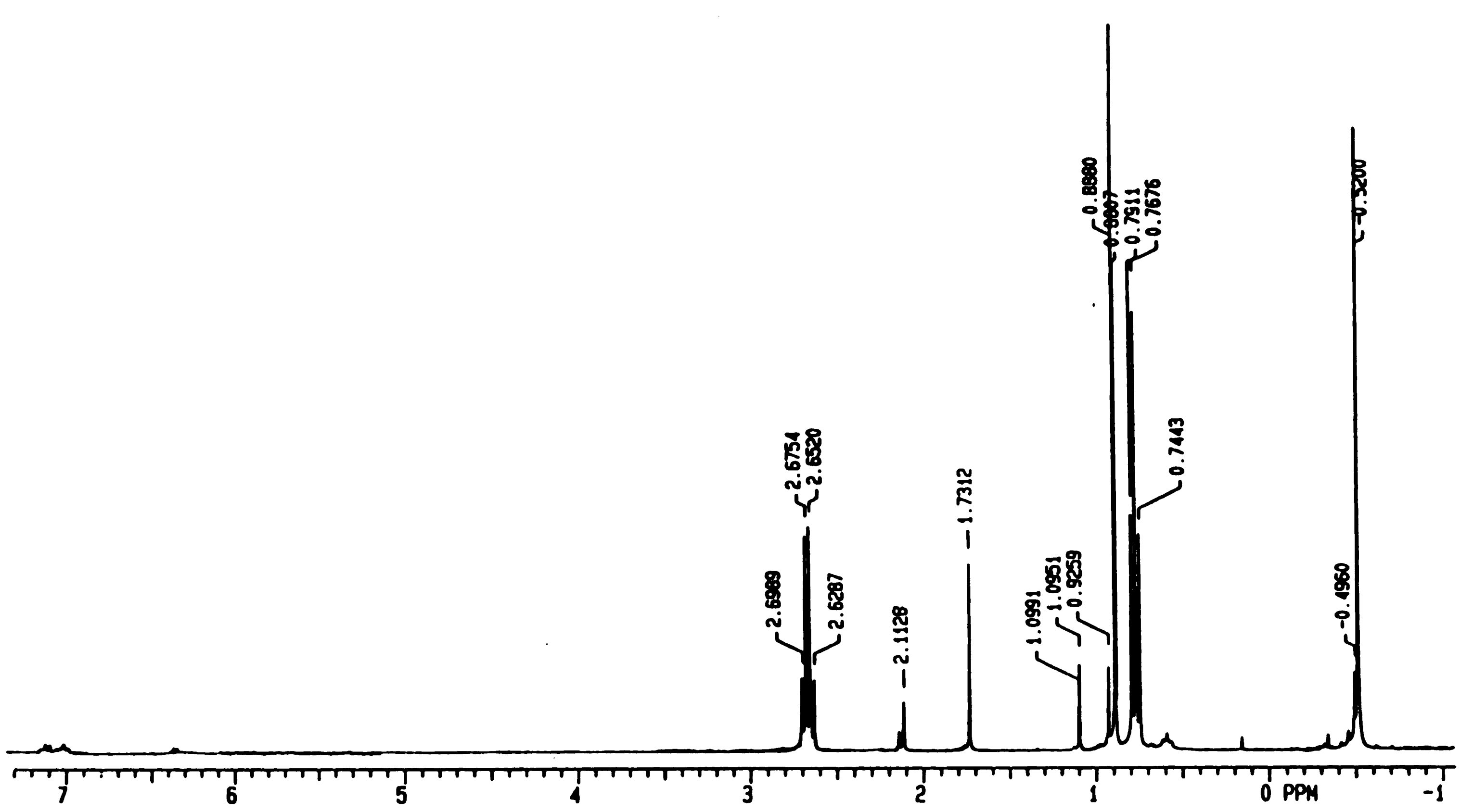


Figure 1.2 ^{1}H-NMR spectrum of Dimethylaluminumdiethylamide after addition of pinacolone and standing at 25C for 3.5 hours

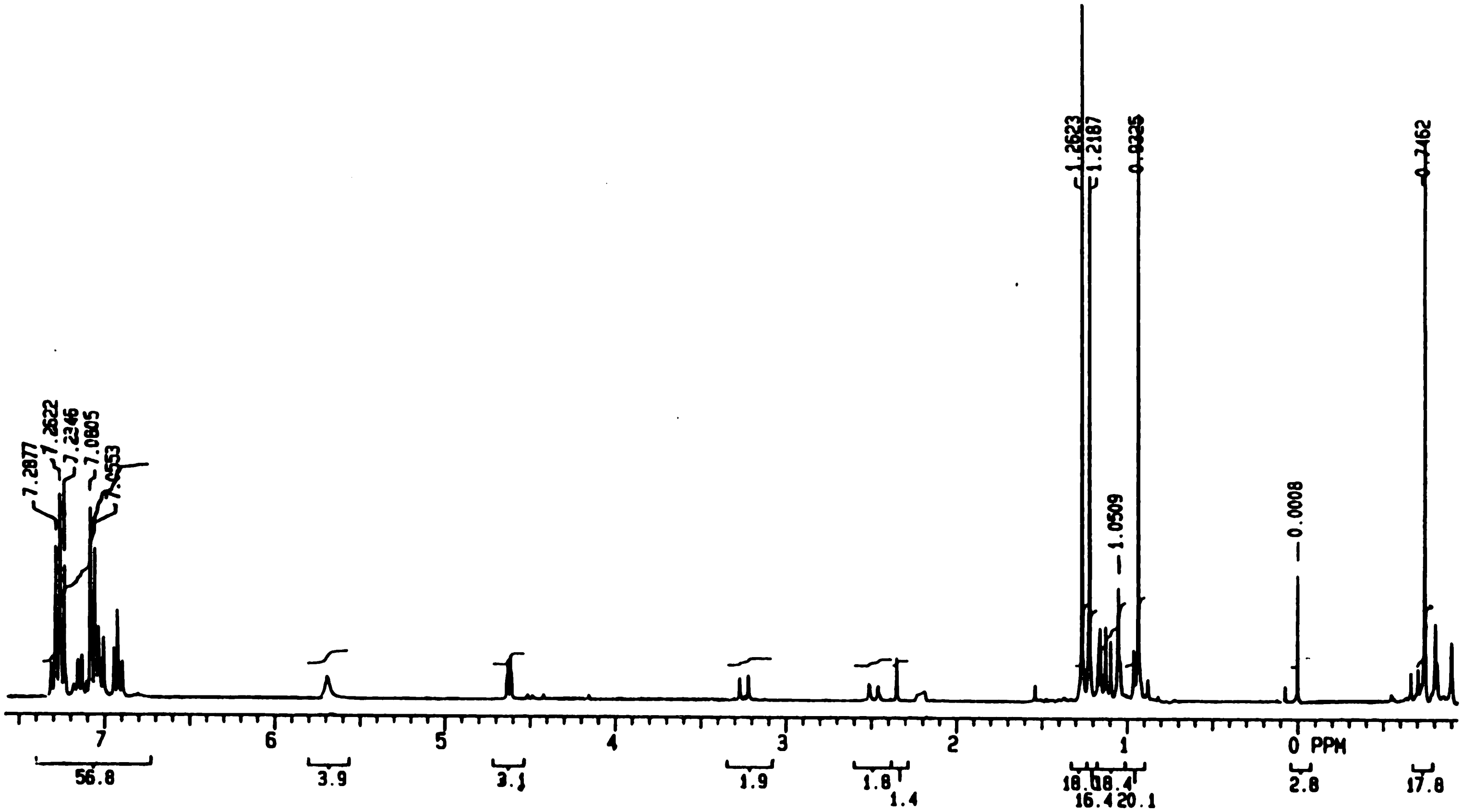


Figure 2.2 ^{1}H-NMR spectrum of Dimethylaluminumdiphenylamide after addition of one equivalent of pinacolone at 25C and immediate analysis

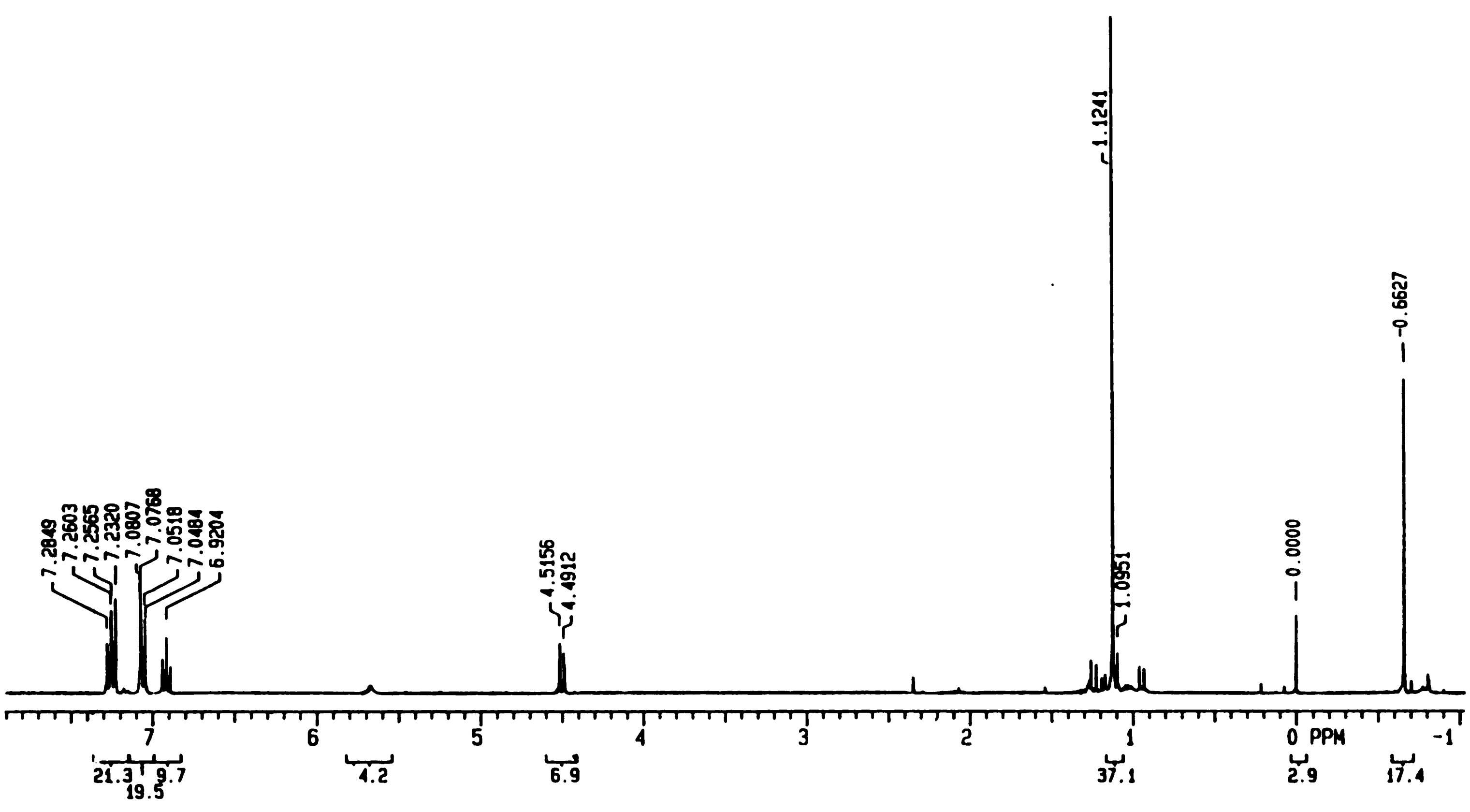


Figure 3.2 ^{1}H-NMR spectrum of Dimethylaluminumdiphenylamide after addition of one equivalent of pinacolone at 25C and standing for 4 hours

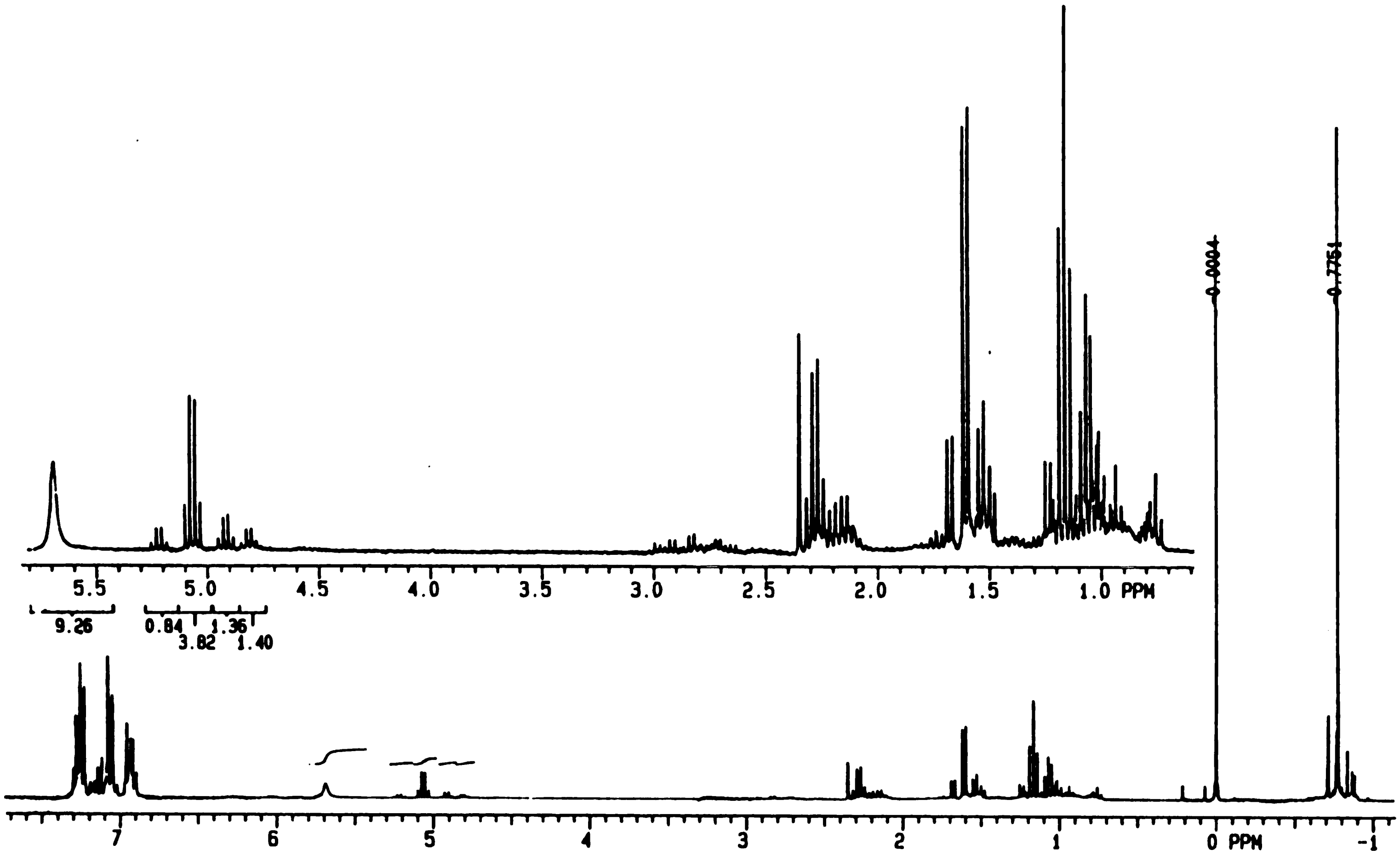


Figure 4.2 ^{1}H-NMR spectrum of Dimethylaluminumdiphenylamide after addition of one equivalent of 3-pentanone at 25C and standing for 15 minutes

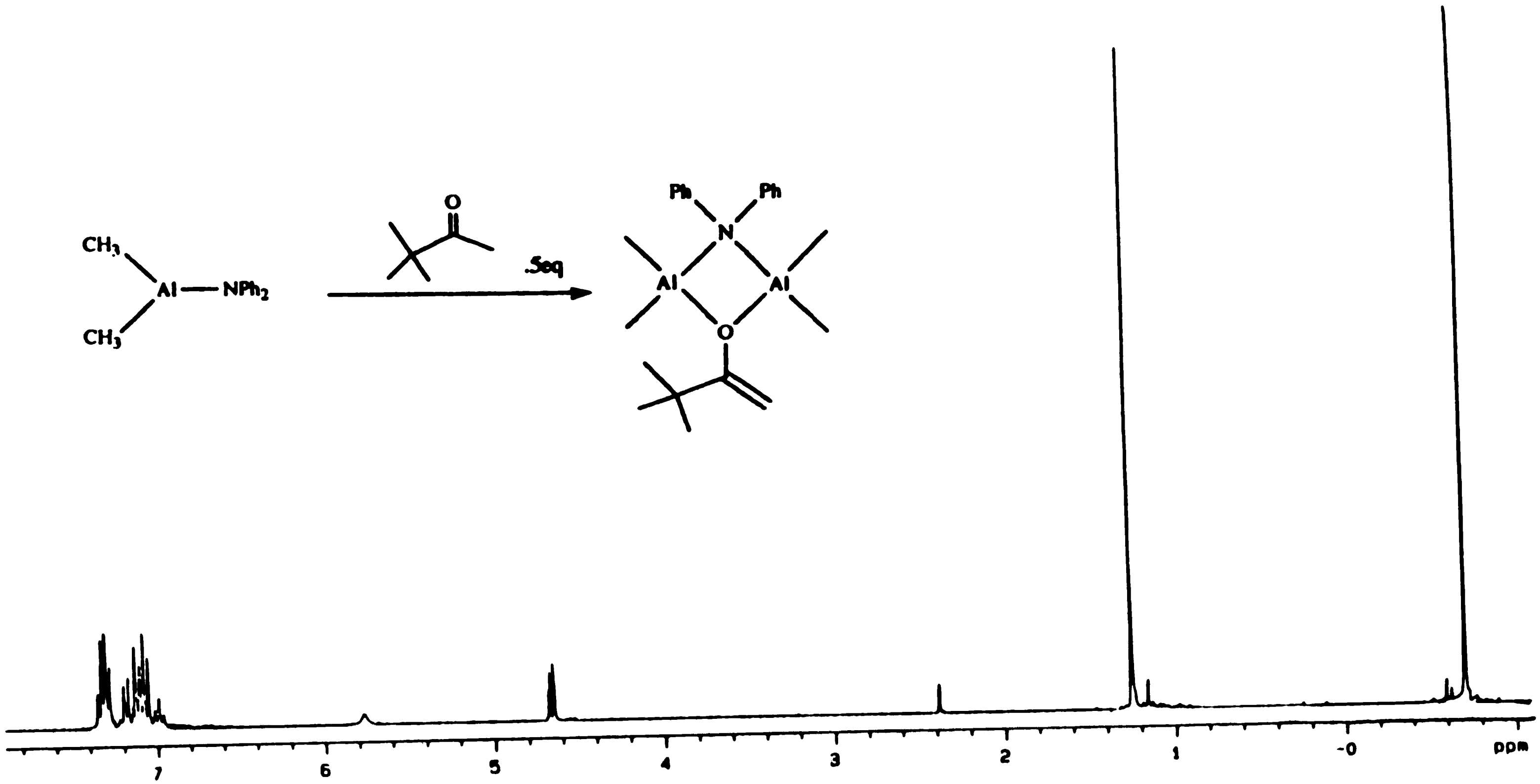


Figure 5.2 ^{1}H-NMR spectrum of Dimethylaluminumdiphenylamide after addition of one half equivalent of pinacolone at 25C and analysis

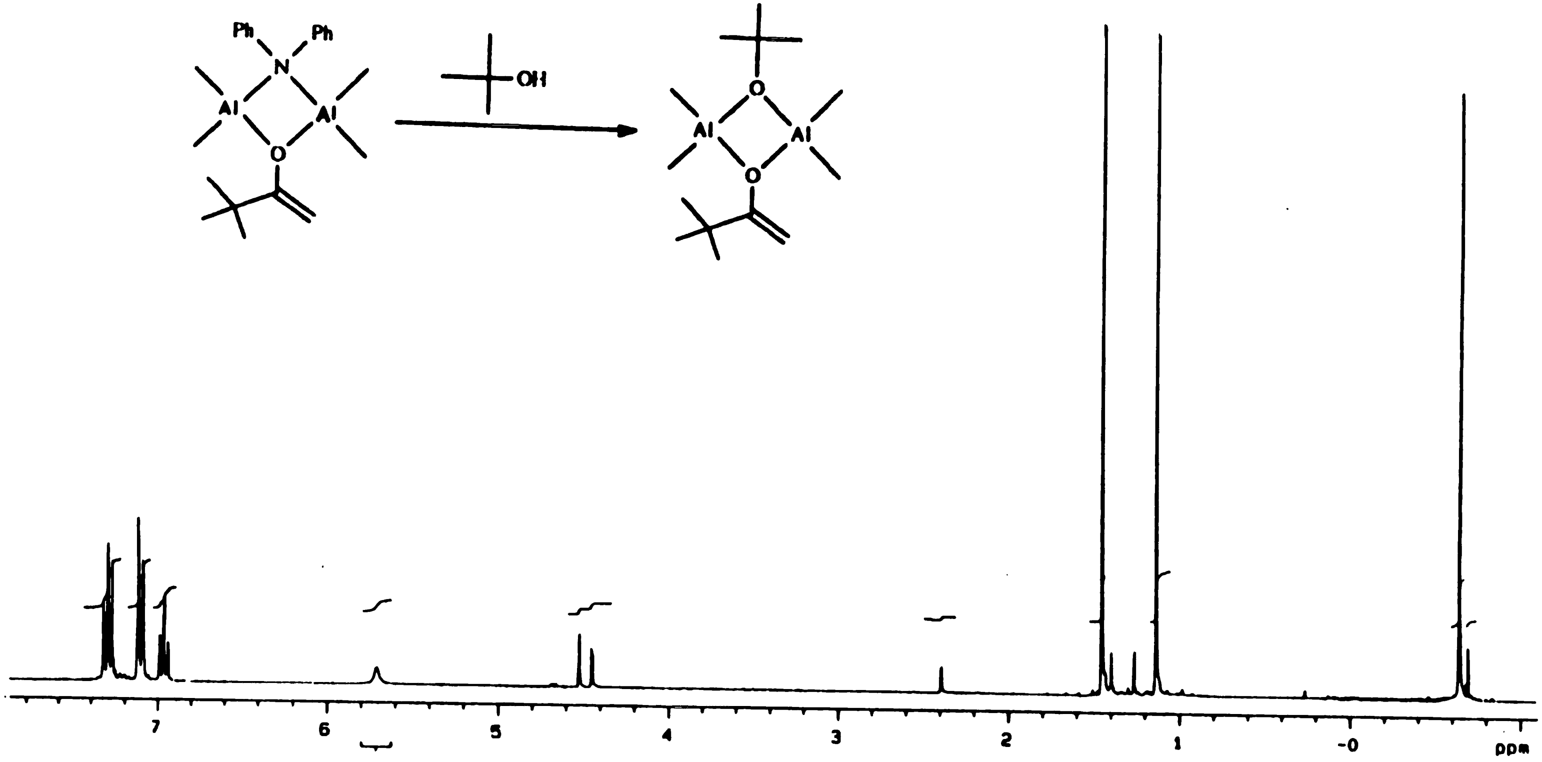


Figure 6.2 ^{1}H-NMR spectrum of **Enolate II**

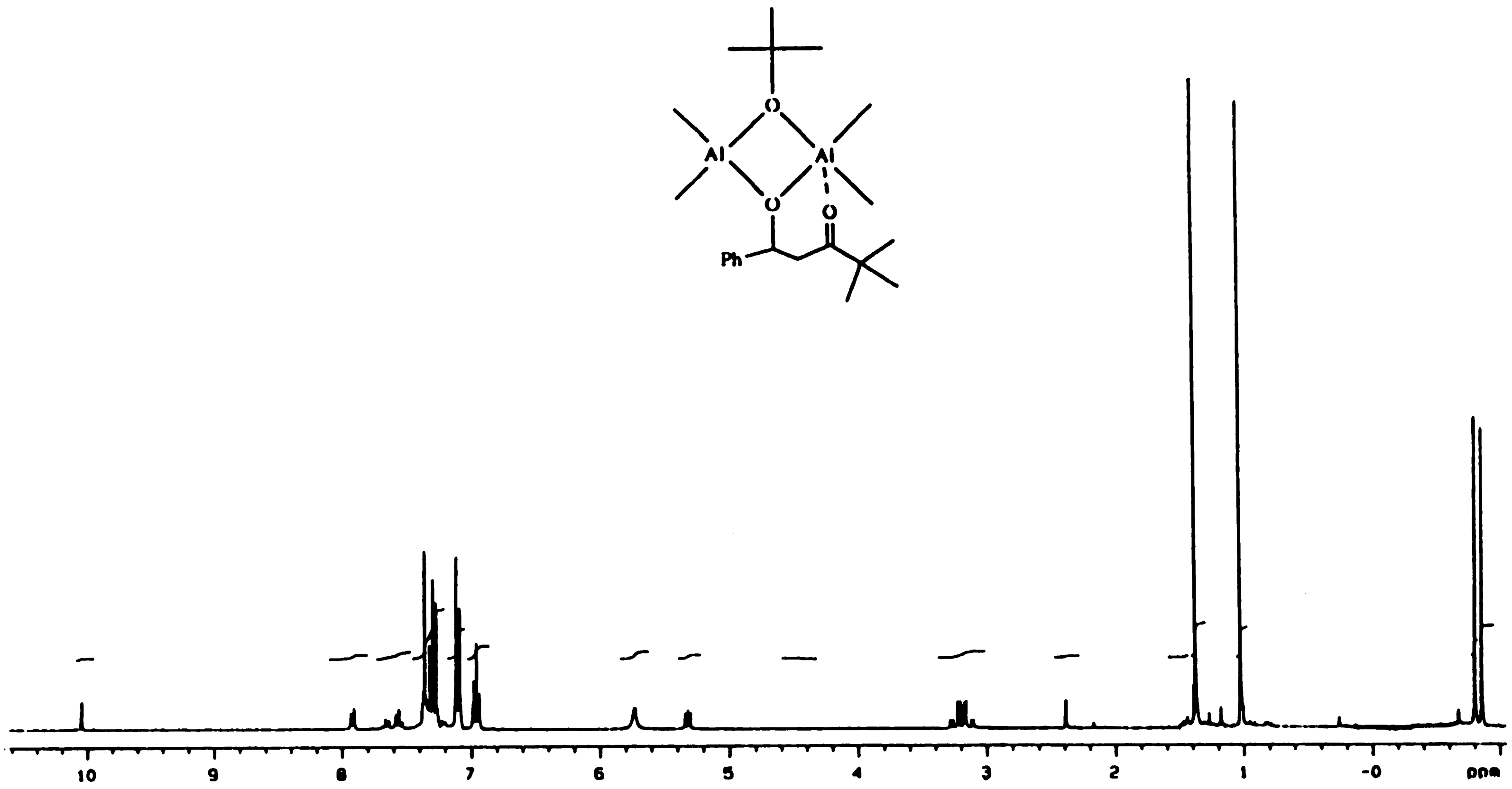


Figure 7.2 ^{1}H-NMR spectrum of the aldol condensation of **Enolate II**

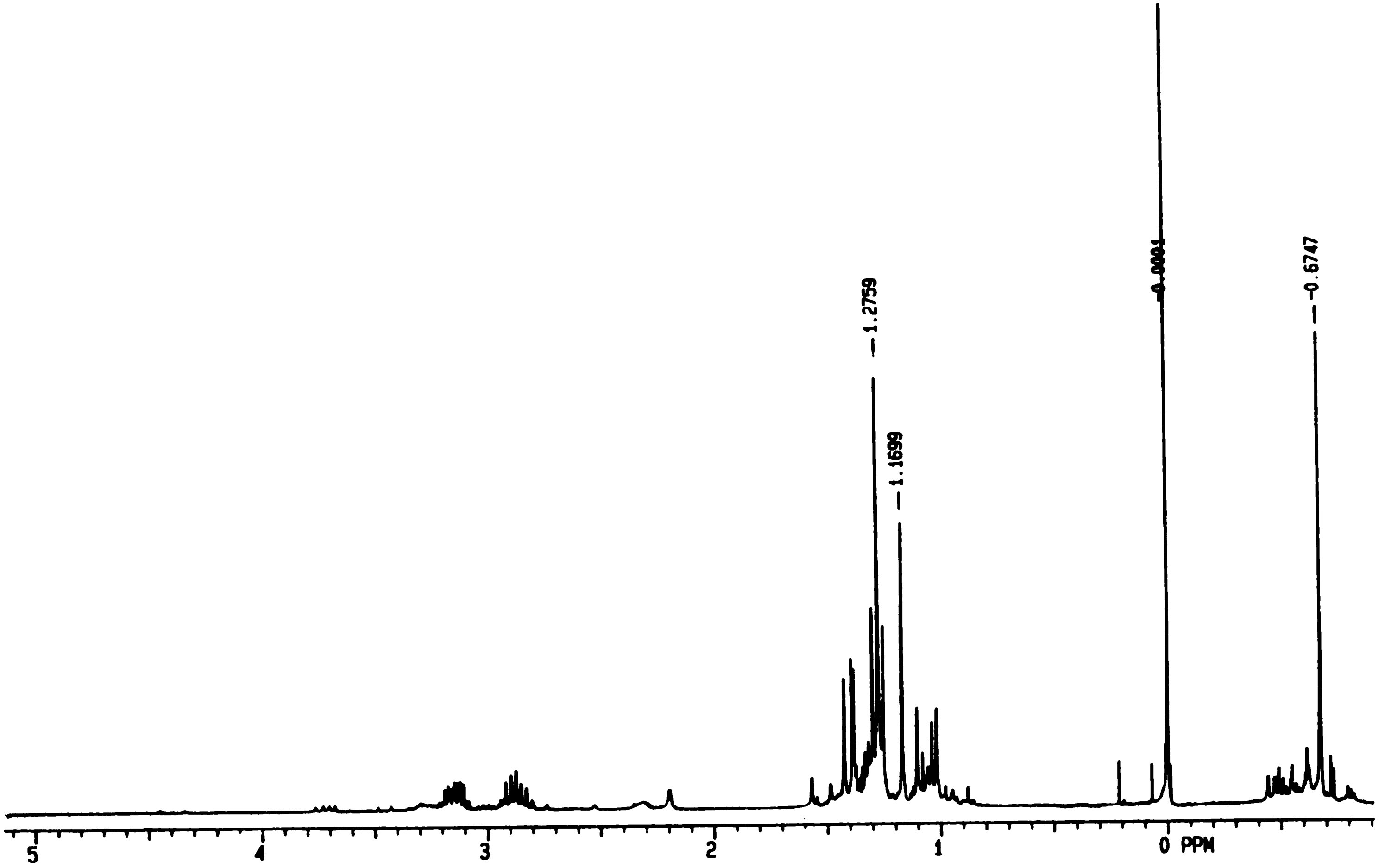


Figure 8.2 ^{1}H-NMR spectrum of the precipitate resulting from the reaction of Compound **X** with pinacolone in hexane.

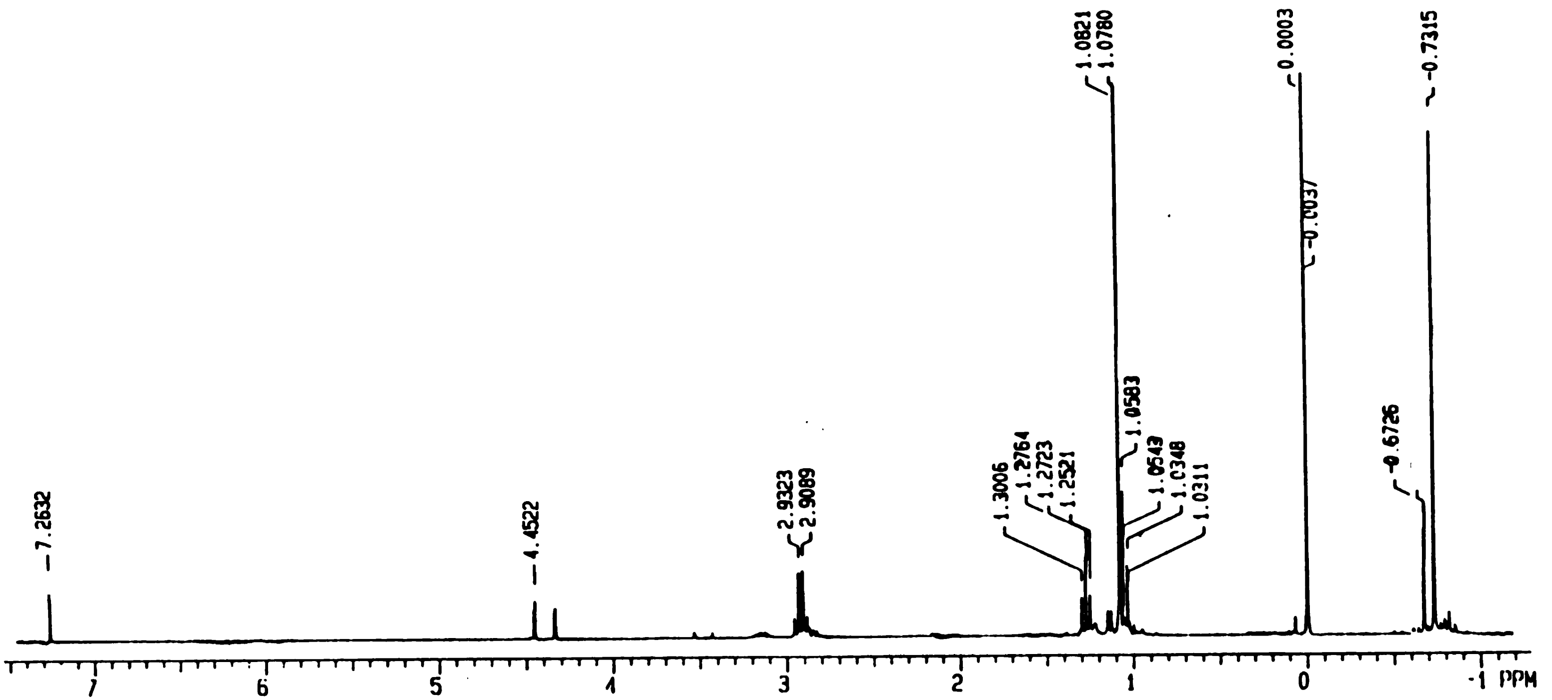


Figure 9.2 ^{1}H-NMR spectrum of the supernatent of the reaction of **X** with pinacolone.

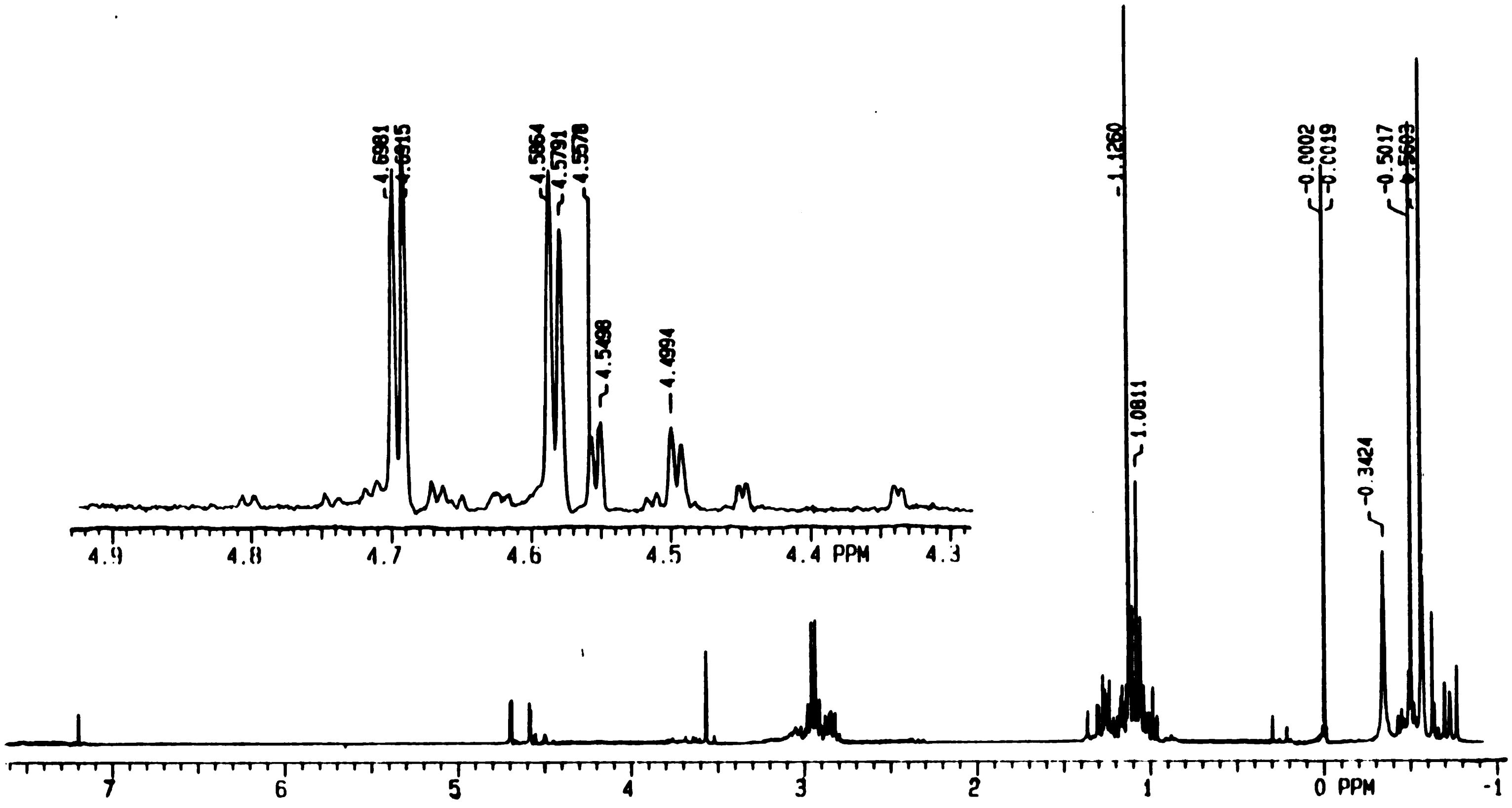


Figure 10.2 ^{1}H-NMR spectrum of the exchange of **Enolate IV** with Me_2AlCl

Conclusions

A new procedure has been developed for the preparation of aluminum enolates via an acid/base reaction previously unknown for aluminum amides. Our results provide the first observation of an aluminum enolate prepared via an aluminum amide base. The reactivities of these bases are greatly influenced by the nature of ligands on the aluminum center as well as on the nitrogen. We have demonstrated that use of conjugating substituents on the amido ligand can overcome the strong association present in aluminum amides bearing alkyl substituents on nitrogen. We have shown that weakly bridging ligands in mixed dimeric complexes provide these complexes with enough reactivity so that an acid/base reaction is favorable. We have also shown that monomeric aluminum amides react with pinacolone. Our results also provide a new mechanistic insight into the reactivity of these new bases in solution

Experimental

All operations were carried out under an argon or nitrogen atmosphere. Diphenylamine, diisopropylamine, diethylamine, 1,1,1,3,3,3-hexamethyldisilazane (HMDS), tetramethylpipridine (TMP), hexane, and toluene, were obtained from Aldrich Chemical Company and distilled from calcium hydride prior to use. Deuterated benzene, toluene, and chloroform were dried over calcium hydride and purged with nitrogen. Ketones were obtained from Aldrich Chemical Company and dried over calcium hydride and purified by distillation. Trimethylaluminum, and dimethylaluminum chloride were obtained from Aldrich Chemical Company as neat substances and stock solutions were prepared as needed inside a glove box. Sodium fluoride was obtained from Aldrich Chemical Company. ^{1}H-NMR data were recorded on a Varian spectrometer operating at 300 MHz. NMR tubes were dried at 150C in an electric oven, fitted with a septum, and purged with nitrogen using a long needle for at least one hour prior to use.

Apparatus Used For Preparation Of Aluminum Amides

Due to the pyrophoric nature of the reagents and their air and moisture sensitivity, a one step preparation of aluminum amides was developed. This method minimizes the number of transfers of the reagents and allows for a one pot synthesis of the amides as a standard stock solution. The apparatus used is shown in **Figure 11**. This apparatus also allows one to monitor the course of the reaction by measuring the amount of gas produced.The volumetric flask A (10 mL) was modified by the MSU glass blowing facility to incorporate a 14/20 ground glass joint and a sample inlet having 8 mm diameter for removal of sample aliquots. Sample removal was performed through the sample port as shown in **Figure 12**.

Preparation of Aluminum Amides

Preparation of compounds **I**, **II**, **III**,(30) **V**,(33) **XV**, **XIV**(21) have been previously reported by several investigators. Compounds **IV**, **X**, **IX**, **XIII** can be prepared via two procedures. Procedure A is a direct method and does not require the preparation of amine hydrochloride salts. In procedure B an amine hydrochloride salt is reacted with trimethylaluminum. Both procedures produce identical results except in the case of compound **VI**, where reaction of HCl gas with HMDS cannot be used to prepare the amine hydrochloride salt of this amine.

Procedure A

Trimethylaluminum, 10 mmoles (0.72g) and dimethylaluminum chloride 10 mmoles (0.92g) were weighed directly into the volumetric flask (A) in a dry box. The mixture was protected from air using a septum and cooled to -78C. Argon was introduced through the sample inlet (D). The condensor (B) and the gas burette (C) were assembled and the entire apparatus was purged with argon for 20 minutes. 10 mmoles of the desired amine was introduced through the sample inlet at -78C and the cooling bath was removed. The apparatus was then allowed to come to room temperature. The reaction vessel was immersed in an oil bath at 110C and gas burette was zeroed. Slow evolution of methane started. After 12 hours of heating gas evolution ceased (230 mL). The apparatus was disassembled under a stream of argon and the volumetric flask was fitted with a septum. The solution level was adjusted to the mark by addition of solvent. In the case of compound **VI** reaction was completed after 3 hours at room temperature.

Procedure B

The desired amine hydrochloride (5 mmoles) was weighed directly into the volumetric flask (A) inside the dry box. To this solid was added 3 mL of dry toluene and the suspension was cooled to 0C in an ice bath. The apparatus in **Figure 11** was assembled and purged with argon for 20 minutes. 5 mL of a 2M trimethylaluminum in toluene (10 mmoles) was introduced in a dropwise manner via a syringe. Gas evolution started and 5 mmoles (115 mL) of methane was produced after one hour with disappearance of the solid. The reaction vessel was then allowed to come to room temperature and immersed in an oil bath at 110C. The gas burette was zeroed after a 10 minute equilibration period, and the mixture was heated for 12 hours after which gas evolution seased. At the end of the heating period an additional 5 mmoles of methane was generated. Near quantitative amounts of methane evolved in all cases.

General Procedure For Preparation Of Fluoro-Substitiuted Aluminum Amides

Dimethylaluminum fluoride was prepared *in situ* according to the procedure by Laubengayer *et al.*(34) The volumetric flask (A) in **Figure 11** was charged with 10 mmoles (0.42g) of sodium fluoride and 10 mmoles (0.92g) of dimethylaluminum chloride inside a dry box. Toluene was added (3mL) and the apparatus in **Figure 11** was assembled under a stream of argon. This suspension was heated for 16 hours at reflux after which a fine white precipitate was present. The ^{1}H-NMR analysis of a 10uL sample after evaporation of toluene under vaccuo and resuspension in d^6 benzene showed a singlet at -0.56 ppm.(syrupy clear liquid). The vessel was then charged with 10 mmoles of a 2M trimethylaluminum solution in toluene (5 mL) at room temperature. The vessel was immersed in an oil bath at 110C, allowed to equilibrate, and gas burette was zeroed. The desired amine (10 mmol) was added. Slow evolution of methane started and ceased after 1.5-8 hours. Near quantitative amounts of methane evolved in all cases. In the case of compound **VIII** the reaction was complete after 1.5 hours.

General procedure for NMR Tube Reactions

An aliquot (50 μL) of the aluminum amide in toluene was injected into an NMR tube that had been previously purged with nitrogen. Toluene was evaporated under vaccuo, 0.7 mL of deuterated solvent was introduced via a syringe and the tube was shaken to dissolve the aluminum amide. 50 umoles of the desired ketone was injected directly into the tube, the tube was shaken and spectra recorded.

Preparation of μ-Diphenylamido, μ-Chloro, Tetramethyldialuminum Compound **IV**

The vessel described in **Figure 11** was assembled and purged with argon for 15 minutes. 10 mmoles of trimethylaluminum (5mL of a 2M solution in toluene) was added slowly at 0C to 5 mmoles (1.02g) of diphenylamine hydrochloride. Upon completion of addition a clear solution resulted with evolution of 114 mL of gas. The ice bath was removed and the reaction was allowed to come to room temperature. After stirring at room temperature for 12 hours gas evolution ceased with an additional evolution of 119 mL of methane. An aliquot (100 μL) was removed from the vessel through the sample inlet, toluene was evaporated and remaining white crystalline solid was dissolved in deutero chloroform.

^{1}H NMR(300MHz;CDCl$_3$) : δ -0.62(s, 6H), 7.17(m, 2H), 7.28(m, 4H), 7.35(m, 4H)

Preparation of μ-HMDS, μ-Chloro, Tetramethyldialuminum Compound **VI**

The vessel in **Figure 11** was assembled and purged with argon for 15 minutes. A room temperature water bath was used to cool the vessel. 5.0 mmoles of trimethylaluminum (2.5 mL of a 2M solution in toluene) and 5.0 mmoles of dimethylaluminum chloride (2.5 mL of a 2M solution in toluene) were introduced through the sample inlet via a syringe. 5.0 mmoles of HMDS (1.0 mL) was introduced via the sample inlet in a dropwise manner. Slow gas evolution was evident. After 3.5 hours 120 mL of gas was produced. An aliquot (100 μL) was removed from the vessel through the sample inlet, toluene was evaporated and remaining clear syrupy liquid was dissolved in deutero chloroform.

^{1}H NMR(300MHz;C$_6$D$_6$) : δ -0.19(s, 12H), 0.21(s, 18H)

Preparation of μ-Diethylamido,μ-Chloro, Tetramethyldialuminum compound **X**

10 mmoles of trimethylaluminum(0.72g) and 10 mmoles of dimethylaluminum chloride(0.92g) were weighed directly into the volumetric flask (A) in the dry box. The mixture was protected from air using a septum and cooled to -78 degrees. Argon was introduced through the sample inlet (D). The condenser (B) and the gas burette (C) were

assembled and the entire apparatus was purged with argon for 20 minutes. 10 mmoles of diethyl amine (1.2 mL) was introduced through the sample inlet at -78C and the cooling bath was removed. The apparatus was then allowed to come to room temperature. The reaction vessel was immersed in an oil bath at 110C and gas burette was zeroed. Slow evolution of methane started. After 12 hours of heating gas evolution ceased (231 mL). Stock solution was prepared by adding toluene to the mark. An aliquot (100uL) was removed from the vessel through the sample inlet, toluene was evaporated and remaining clear syrupy liquid was dissolved in deutero benzene.

^{1}H NMR(300MHz;C_6D_6) : δ -0.15(s, 12H), 0.78(t, J=7.1 Hz, 6H), 2.75(q, J=7.1 Hz, 4H)

Preparation of μ-Diisopropylamido, μ-Chloro, Tetramethyldialuminum compound **IX**

10 mmoles of trimethylaluminum(0.72g) and 10 mmoles of dimethylaluminum chloride(0.92g) were weighed directly into the volumetric flask (A)in the dry box. The mixture was protected from air using a septum and cooled to -78C. Argon was introduced through the sample inlet (D). The condenser (B) and the gas burette (C) were assembled and the entire apparatus was purged with argon for 20 minutes. 10 mmoles of diisopropyl amine (1.4 mL) was introduced through the sample inlet at -78 and the cooling bath was removed. The apparatus was then allowed to come to room temperature. The reaction vessel was immersed in an oil bath at 110C and gas burette was zeroed. Slow evolution of methane started. After 12 hours of heating gas evolution ceased (230 mL). Stock solution was made by adding toluene to the mark. An aliquot (100uL) was removed from the vessel through the sample inlet, toluene was evaporated and remaining clear syrupy liquid was dissolved in deutero benzene.

^{1}H NMR(300MHz;C_6D_6) : δ -0.02(s, 12H), 1.18(d, J=6.7 Hz, 12H), 3.55(m, J=6.7 Hz, 2H)

Preparation of μ-Tetramethylpipridido, μ-Chloro, Tetramethyldialuminum compound XIII

10 mmoles of trimethylaluminum(0.72g) and 10 mmoles of dimethylaluminum chloride(0.92g) were weighed directly into the volumetric flask (A) in the dry box. The mixture was protected from air using a septum and cooled to -78 degrees. Argon was introduced through the sample inlet (D). The condenser (B) and the gas burette (C) were assembled and the entire apparatus was purged with argon for 20 minutes. 10 mmoles of tetramethylpipridine (1.68 mL) was introduced through the sample inlet at -78C and the cooling bath was removed. The apparatus was then allowed to come to room temperature. The reaction vessel was immersed in an oil bath at 110C and gas burette was zeroed. Slow evolution of methane started. After 12 hours of heating gas evolution ceased (238 mL). Stock solution was made by adding toluene to the mark. An aliquot (100 μL) was removed from the vessel through the sample inlet, toluene was evaporated and remaining clear syrupy liquid was dissolved in deutero benzene.

^{1}H NMR(300MHz;$CDCl_3$) : δ -0.40(s), 1.44(s), 1.56(s), 1.9-1.2(br m)

Preparation of μ-HMDS, μ-Fluoro, Tetramethyldialuminum Compound VII

Dimethylaluminum fluoride was prepared *in situ* according to the procedure by Laubengayer *et al.*(4) Hence the volumetric flask (A) in **Figure 11** was charged with 10 mmoles (0.42g) of sodium fluoride and 10 mmoles (0.92g) of dimethylaluminum chloride inside a dry box. Dry toluene (3 mL) was added and the apparatus in **Figure 11** was assembled under a stream of argon. This suspension was heated for 16 hours at reflux after which a fine white precipitate was present. The ^{1}H NMR analysis of a 10uL sample after evaporation of toluene under vaccuo and resuspension in d^6 benzene showed a singlet at -0.56 ppm.(syrupy clear liquid). The vessel was then charged with 10 mmoles of a 2M trimethylaluminum solution in toluene (5 mL) at room temperature. The vessel was immersed in an oil bath at 110C, allowed to equilibrate, and gas burette was zeroed.

10 mmoles of HMDS (2.1 mL) was added. Rapid evolution of methane started and seased afte 1.5 hours. Near quantitative amounts of methane evolved

^{1}H NMR(300MHz;CDCl$_3$) : δ -0.56(s, 1H), 0.36(s, 1.7H),

Preparation of μ-Diisopropylamido, μ-Fluoro, Tetramethyldialuminum Compound **VIII**

Dimethylaluminum fluoride was prepared *in situ* according to the procedure by Laubengayer *et al.*(4) Hence the volumetric flask (A) in **Figure 11** was charged with 10 mmoles (0.42g) of sodium fluoride and 10 mmoles (0.92g) of dimethylaluminum chloride inside a dry box. Dry toluene (3 mL) was added and the apparatus in **Figure 11** was assembled under a stream of argon. This suspension was heated for 16 hours at reflux after which a fine white precipitate was present. The ^{1}H-NMR analysis of a 10uL sample after evaporation of toluene under vaccuo and resuspension in d^6 benzene showed a singlet at -0.56 ppm.(syrupy clear liquid). The vessel was then charged with 10 mmoles of a 2M trimethylaluminum solution in toluene (5 mL) at room temperature. The vessel was immersed in an oil bath at 110C, allowed to equilibrate, and gas burette was zeroed. 10 mmoles of diisopropylamine (1.4 mL)was added. Slow evolution of methane started and seased after 3.5 hours. Near quantitative amounts of methane evolved.

^{1}H NMR(300MHz;CDCl$_3$) : δ -0.62(br s, 6.8H), 1.31(d, J=9.0 Hz, 5.8H), 3.57(m, J=9.0 Hz, 1H).

Preparation of μ-Diethylamido, μ-Fluoro, TetramethyldialuminumCompound **XI**

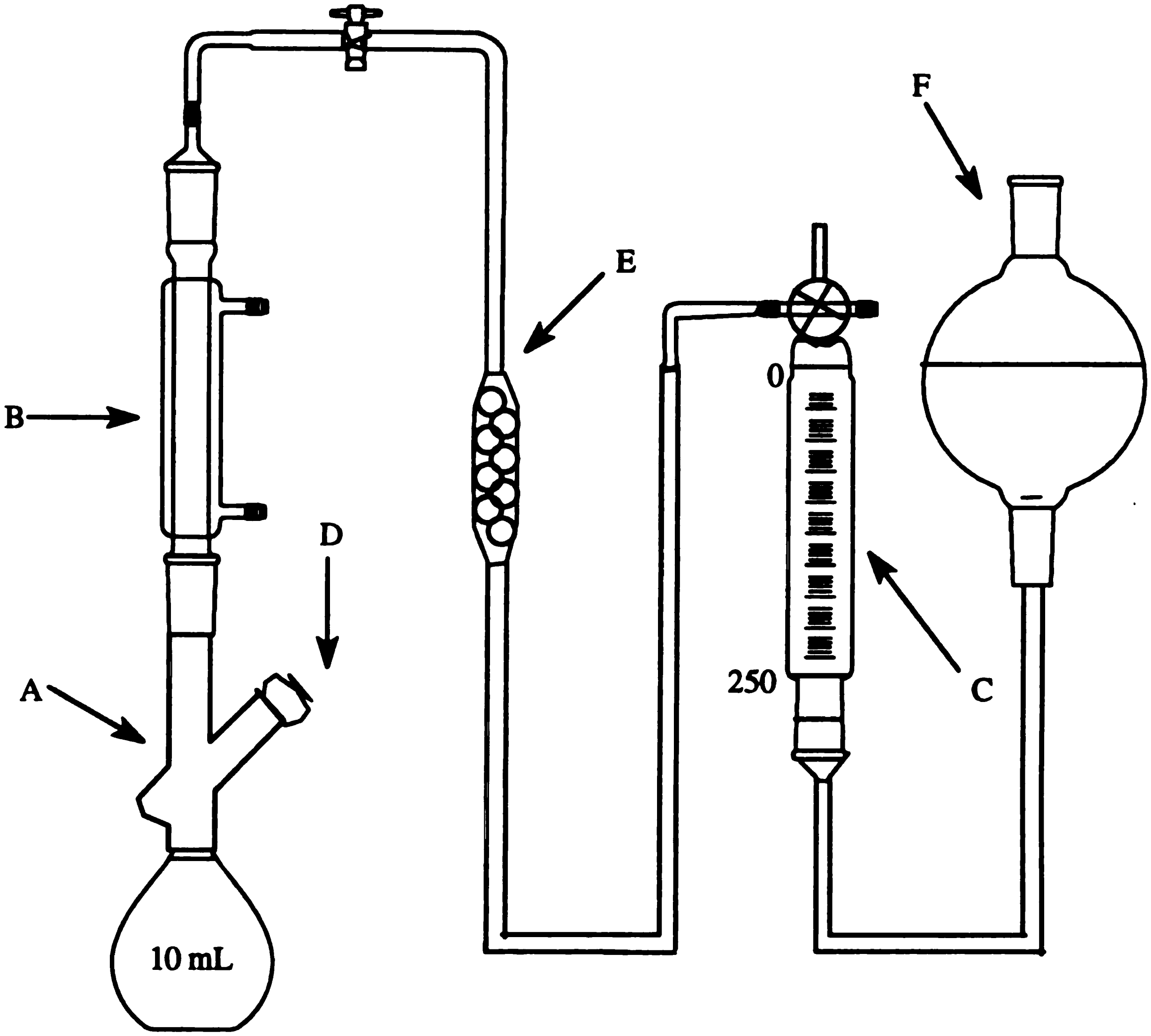
Dimethylaluminum fluoride was prepared *in situ* according to the procedure by Laubengayer *et al.*(4) The volumetric flask (A) in **Figure 11** was charged with 10 mmoles (0.42g) of sodium fluoride and 10 mmoles (0.92g) of dimethylaluminum chloride inside a dry box. Dry toluene (3 mL) was added and the apparatus in **Figure 11** was assembled under a stream of argon. This suspension was heated for 16 hours at reflux after which a fine white precipitate was present. The ^{1}H NMR analysis of a 10 μL sample after evaporation of toluene under vaccuo and resuspension in d^6 benzene showed a singlet at -0.56 ppm.(syrupy clear liquid). The vessel was then charged with 10 mmoles of a 2M trimethylaluminum solution in toluene (5 mL) at room temperature. The vessel was immersed in an oil bath at 110C, allowed to equilibrate, and gas burette was zeroed. 10 mmoles of diethylamine (1.0 mL) was added. Slow evolution of methane started and seased after 3.5 hours. Near quantitative amounts of methane evolved.

^{1}H NMR(300MHz;CDCl3) : δ -0.71(br s, 2.4H), 1.04(t, J=7.02 Hz, 1H), 2.86(q, J=7.02 Hz, 1H).

Preparation of μ-Tetramethylpipridido, μ-Fluoro, Tetramethyldialuminum Compound **XII**

Dimethylaluminum fluoride was prepared *in situ* according to the procedure by Laubengayer *et al.*$^{(4)}$ Hence the volumetric flask (A) in **Figure 11** was charged with 10 mmoles (0.42g) of sodium fluoride and 10 mmoles (0.92g) of dimethylaluminum chloride inside a dry box. Dry toluene (3 mL) was added and the apparatus in **Figure 11** was assembled under a stream of argon. This suspension was heated for 16 hours at reflux after which a fine white precipitate was present. The ^{1}H-NMR analysis of a 10 μL sample after evaporation of toluene under vaccuo and resuspension in d^6 benzene showed a singlet at -0.56 ppm.(syrupy clear liquid). The vessel was then charged with 10 mmoles of a 2M trimethylaluminum solution in toluene (5 mL) at room temperature. The vessel was immersed in an oil bath at 110C, allowed to equilibrate, and gas burette was zeroed. 10 mmoles of tetramethylpipridine (1.7 mL) was added. Slow evolution of methane started and ceased after 8 hours. Near quantitative amounts of methane evolved.

^{1}H NMR(300MHz;CDCl3) : δ -0.71(br s), 1.37(br s), 1.42(br s), 1.6-2.0(br m).



A= 10mL volumetric flask
B= condenser
C= gas burette
D= 8mm sample inlet
E= drying tube
F= reservoir

Figure 11 Apparatus used in the synthesis of aluminum amides

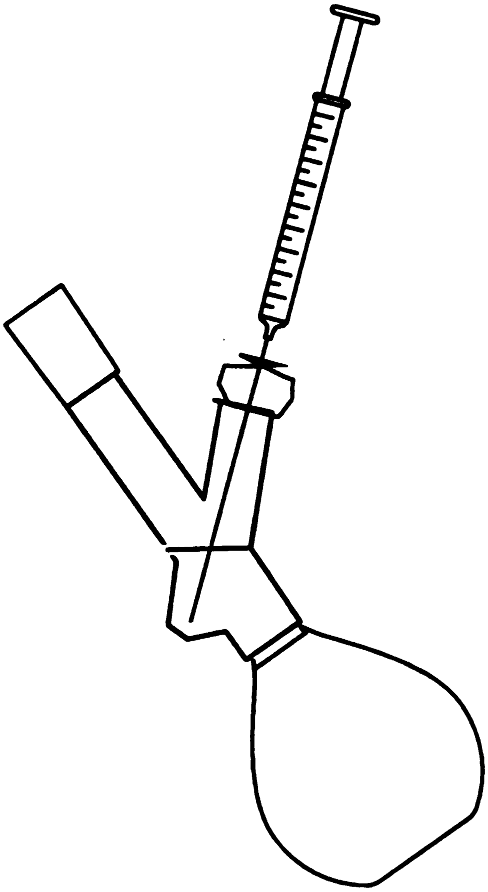


Figure 12. Sample removal from flask A

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