To the Graduate Council:

I am submitting herewith a dissertation written by Ann Marie Scott Fabirkiewicz entitled "Reactions of Boranes with Carbonyl Compounds: An Investigation." I have examined the final copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

George W. Kabalka, Major Professor

We have read this dissertation and recommend its acceptance:

John F. Fellers

Accepted for the Council:

Vice Provost
and Dean of The Graduate School

REACTIONS OF BORANES WITH CARBONYL COMPOUNDS: AN INVESTIGATION

A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Ann Marie Scott Fabirkiewicz

August 1987

DEDICATION

For their love, support, encouragement and understanding the author wishes to dedicate this work to her parents, Eugene and Barbara Scott, her grandparents, Max and Ann Mallow, and her husband, Stephen. The author also wishes to extend a special dedication to her mother.

ACKNOWLEDGMENTS

The author wishes to thank Dr. George Kabalka for his advice and support through the course of this work. The author also wishes to thank the University of Tennessee for financial support, in the form of a teaching assistantship, during her graduate work.

ABSTRACT

The reaction of trialkylboranes with carbonyl reagents has not yet been reported. Trialkylboranes are nonnucleophilic, and thus do not participate in reactions with typical organic electrophiles. Modifications of the Lewis acidity of the borane are reported. Polarization of the carbonyl moiety was also investigated. Solvents, Lewis acids, and several carbonyl derivatives were investigated for their ability to polarize the carbonyl group.

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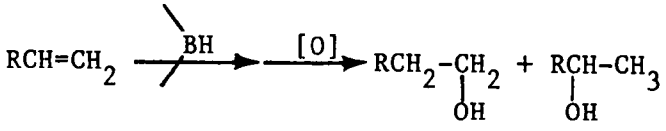
CHAPTER I

INTRODUCTION

A. General Considerations

The hydroboration reaction, discovered in 1956[1], involves a facile addition of a boron-hydrogen moiety to the carbon-carbon double bond of alkenes and the carbon-carbon triple bond of alkynes. Originally carried out using sodium borohydride and boron trifluoride diethyl etherate to generate diborane in situ, the reaction has since been simplified experimentally by the commercial availability of several hydroborating agents, including borane-tetrahydrofuran, borane-dimethyl sulfide and 9-borabicyclononane (9-BBN).

The hydroboration reaction is generally quantitative and instantaneous and occurs in a syn, anti-Markovnikov fashion (equation 1-1).[2] Hydroboration with borane-tetrahydrofuran gives approximately 6%

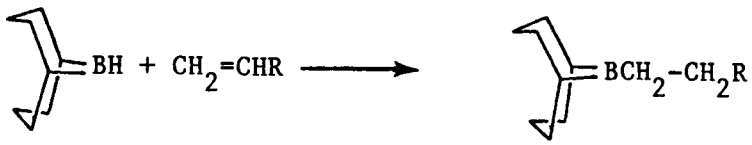


(1-1)

BH_3	94%	6%
9-BBN	99.9%	<0.1%

of the branched isomer whereas 9-BBN, due to its steric bulk, is more selective. Other hydroborating agents, such as dicyclohexylborane, disiamylborane, and diisopinocampheylborane follow this trend.[3]

Dialkylboranes, such as 9-BBN, are often used as hydroborating agents for reactions in which only one of the alkyl groups participates. The advantage of these reagents, in addition to their higher regioselectivity, lies in the need for only one equivalent of alkene to form the desired organoborane (equation 1-2). In cases where the alkene



(1-2)

is a valuable synthetic intermediate, the use of a dialkylborane eliminates the loss of two moles of a desired, or expensive, alkene. Another advantage for these reagents is found in the hydroboration of hindered alkenes, in which case, hydroboration with BH_3 to form the desired triorganoborane may become very difficult. Hydroboration with appropriate, moderately hindered dialkylboranes presents a less sterically hindered boron atom to the alkene, permitting successful hydroborations. Thus, 9-BBN will hydroborate more effectively in some cases than BH_3.

Triorganoboranes are of great synthetic utility in a variety of organic syntheses. They participate in a number of reactions in which the boron is replaced by other atoms. The alkaline hydrogen peroxide oxidation is perhaps the most well known (equation 1-3). This reaction

$$R_3B + H_2O_2 + NaOH \longrightarrow 3\ ROH \qquad (1\text{-}3)$$

provides a means whereby an alkene can be converted to the corresponding anti-Markovnikov alcohol.[4]

The amination of organoboranes is accomplished by a variety of procedures,[5-8] perhaps the most convenient of which is the treatment of the trialkylborane with ammonium hydroxide and sodium hypochlorite (equation 1-4).[7]

$$R_3B + NH_4OH + NaOCl \longrightarrow RNH_2 \qquad (1\text{-}4)$$

The reaction proceeds via in situ formation of chloramine, which then reacts to form the amine. Only one of the three alkyl groups participates in this reaction (equation 1-5).

$$[CH_3(CH_2)_7]_3B + NH_4OH + NaOCl \longrightarrow CH_3(CH_2)_7NH_2 \qquad (1\text{-}5)$$

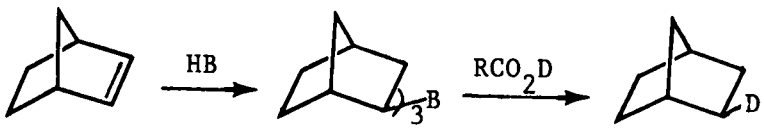
The boron atom in a triorganoborane can also be replaced by halogens.[9,10] Treatment of the borane with electropositive iodine in the presence of a base provides a rapid, convenient method of forming the alkyl iodide from the corresponding alkene (equation 1-6).[11]

$$H_2C{=}CH(CH_2)_{15}CO_2H \xrightarrow{HB} \xrightarrow[NaOH]{ICl} ICH_2(CH_2)_{16}CO_2H \qquad (1\text{-}6)$$

Protonolysis of triorganoboranes provides a noncatalytic method for hydrogenating a double bond. While stable to water and aqueous inorganic acids, triorganoboranes are readily cleaved by carboxylic acids (equation 1-7).[12] The reaction can be utilized to synthesize

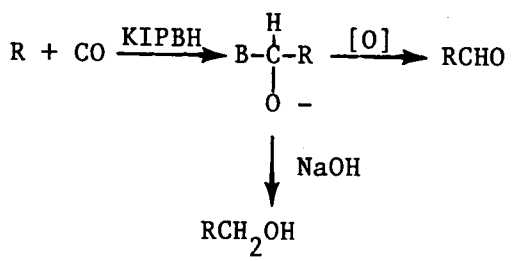
$$R_3B + 3\ HOAc \longrightarrow 3\ RH + B(OAc)_3 \qquad (1\text{-}7)$$

stereochemically defined alkanes and alkenes, including deuterated products (equation 1-8).[13]



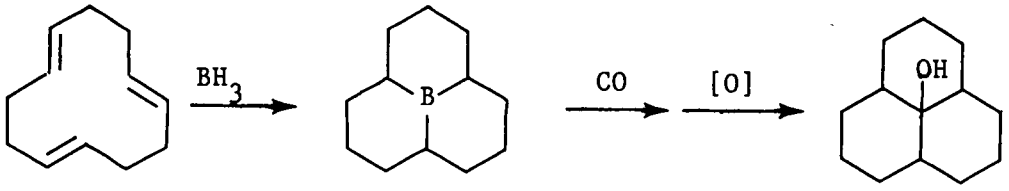
(1-8)

Organoboranes are also capable of participating in carbon-carbon bond forming reactions. The carbonylation reaction is a well-known example. The reaction with carbon monoxide can yield any of several products depending on the reaction conditions. Treatment of the organoborane in the presence of a mild hydride reagent, such as potassium triisoproxyborohydride (KIPBH), leads to an intermediate which can be oxidized to the aldehyde or hydrolyzed to the homologous alcohol (equation 1-9).



(1-9)

The carbonylation reaction can also be used to synthesize ketones and tertiary alcohols from organoboranes. The reaction can occur with transfer of all three alkyl groups, so that subsequent oxidation produces the tertiary alcohol (equation 1-10).[14,15] If the reaction is

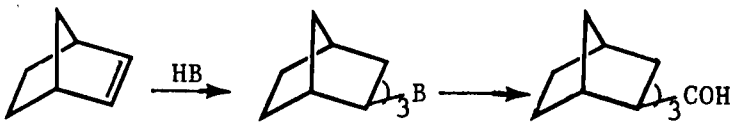


(1-10)

carried out in the presence of water, only two alkyl groups are transferred, and oxidation provides the ketone (equation 1-11).[16] A

$$R_3B + CO \xrightarrow{H_2O} R_2C(OH) - BR(OH) \xrightarrow{[O]} R_2C{=}O \qquad (1\text{-}11)$$

variety of organoboranes participate in this reaction including those for which R is alkyl, cyclohexyl or norbornyl (equation 1-12).[14]



(1-12)

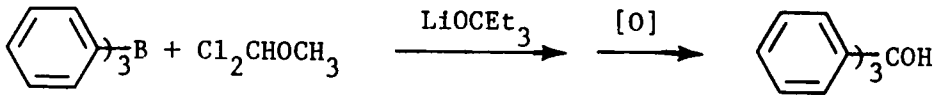
Organoboranes react with cyanide salts in a similar fashion. The reactions require the addition of an electrophile, such as trifluoroacetic anhydride, since the complex initially formed between the organoborane and the cyanide anion does not react further. Addition of the electrophile induces migration of the three alkyl groups to give, on oxidation, the tertiary alcohol (equation 1-13).[17]

$$R_3B + NaCN \longrightarrow R_3BCN \xrightarrow{(CF_3CO)_2O} \xrightarrow{[O]} R_3COH \qquad (1\text{-}13)$$

Organoboranes also react with α,α-dichloromethyl methyl ether in the presence of a sterically hindered base to give the tertiary alcohols, following oxidation (equation 1-14).[18] This reaction occurs

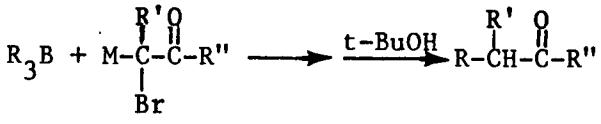
$$R_3B + Cl_2CHOMe \xrightarrow{LiOCEt_3} \xrightarrow{[O]} R_3COH \qquad (1\text{-}14)$$

for a variety of organoboranes, including those with high steric requirements, such as tricyclohexylborane, tri-exo-norbornylborane and triphenylborane (equation 1-15).[18]



(1-15)

Anionotropic rearrangements of suitably substituted organoborates also serve as carbon-carbon bond forming reactions. The examples that follow are representative. Treatment of a trialkylborane with the alkali metal salt of an α-bromo substituted carbonyl compound leads to an intermediate borate which undergoes rearrangement and, following hydrolysis, leads to the α-alkylated carbonyl derivative. A number of carbonyl compounds are known to undergo this reaction, including α-bromo esters, α-bromo ketones and α-chloro nitriles (equation 1-16).[19,20]

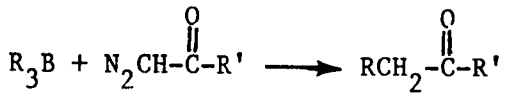


(1-16)

R', R" = H, alkyl

R" = alkoxy

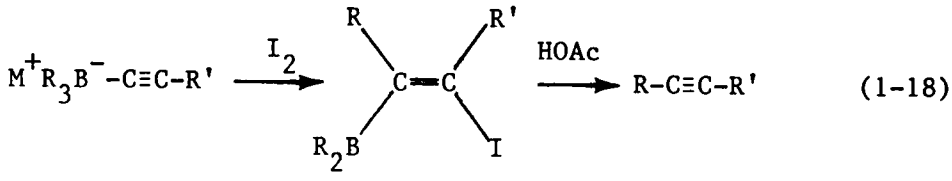
Diazo compounds also participate in a similar rearrangement. Initial coordination, followed by migration, loss of nitrogen, then hydrolysis leads to the alkylated product (equation 1-17).[21]



(1-17)

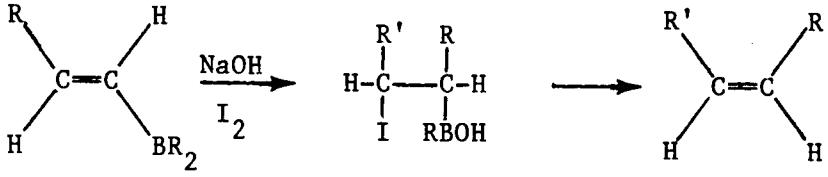
R' = H, alkyl

Triorganoboranes form alkynylborates upon treatment with the alkali metal salt of the alkyne. Migration is then induced by the addition of molecular iodine. Deiodoboration leads to the alkylated alkyne (equation 1-18).[22]



(1-18)

Migration can also be induced in vinyl dialkylboranes by the addition of a base and molecular iodine. Deiodoboration leads to the cis-alkene exclusively (equation 1-19).[23]



(1-19)

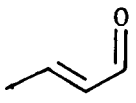
B. Conjugate Addition Reactions

While organoboranes are known to undergo a variety of organic reactions, they are rather nonnucleophilic. There are, however, several known examples of 1,4 addition to α,β-unsaturated aldehydes and ketones.

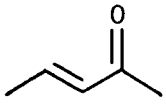
A variety of functionally substituted trialkylboranes undergo a remarkably fast 1,4 addition to methyl vinyl ketone[24] and acrolein.[25]

The reaction was shown to proceed via free radical, rather than ionic intermediates.[26]

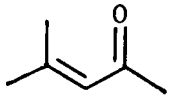
The reaction was found to be spontaneous only for methyl vinyl ketone, propenal and related derivatives. Several enones do not undergo spontaneous reaction, including trans-2-butenal (I), trans-3-penten-2-one (II), mesityl oxide (III), 2-cyclohexen-1-one (IV) and 1-cyclohexenyl methyl ketone (V), but the addition of a free radical



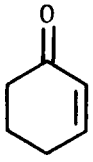
I



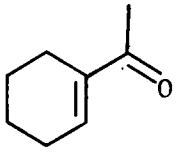
II



III



IV

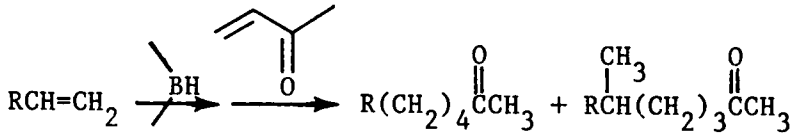


V

initiator allows these reagents to participate in the conjugate addition reaction with trialkylboranes.[27] In all cases, only one alkyl group of the trialkylborane is utilized in the reaction.

The reaction mechanism involves displacement of an alkyl radical from the trialkylborane. The alkyl group which leads to the most stable free radical is generally displaced preferentially in mixed organoboranes.[28] Diphenylalkylboranes provide an exception in that the alkyl group is transferred exclusively in conjugate addition reactions.[29] An additional advantage in using this reagent is found in the product

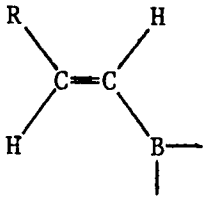
distribution: the hydroboration of a terminal olefin (with BH_3) places 6% of the boron atoms at the secondary position. Secondary groups transfer more readily, thus 15% of the branched isomer is obtained. Diphenylalkylboranes form only 2% of the branched isomer in the conjugate addition reaction (equation 1-20).



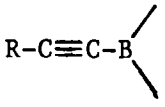
BH_3	85%	15%
Ph_2BH	98%	2%

(1-20)

The 1,4 addition reactions of simple, saturated trialkylboranes are believed to proceed via a free radical mechanism, as discussed above. Unsaturated boranes, however, such as the alkenyl (VI) and alkynyl (VII) boranes apparently react via a different mechanism.

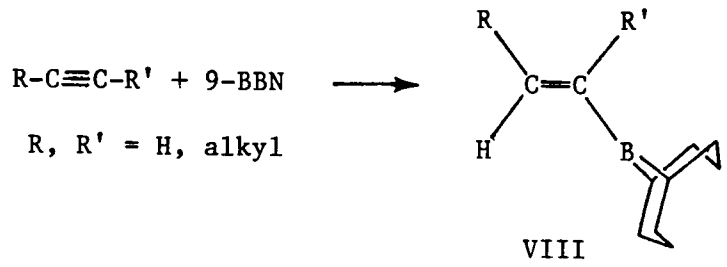


VI



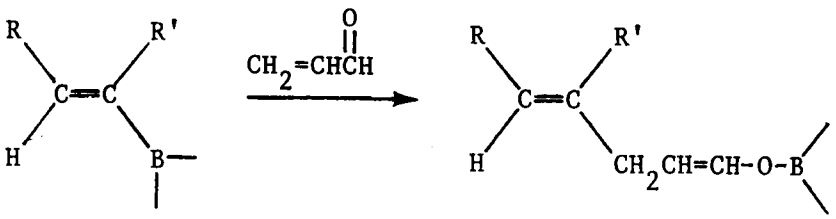
VII

Alkenylboranes are synthesized by monohydroboration of the corresponding alkynes. (Dihydroboration is minimized by using an excess of the alkyne.) Hydroboration occurs in a trans, anti-Markovnikov fashion to give the alkenylborane (VIII) (equation 1-21). Conjugate addition occurs with retention of stereochemistry: that is, the boron atom is replaced, in a stereospecific manner, by carbon (equation 1-22).[30]



(1-21)

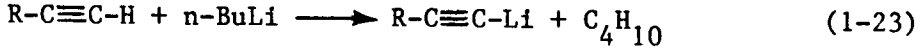
VIII



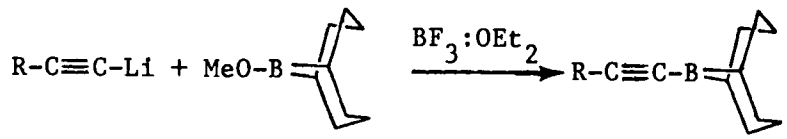
(1-22)

The stereochemistry of the products is one of the factors supporting a concerted mechanism for this reaction. Other supporting evidence for a concerted mechanism includes the fact that, unlike other conjugate additions of boranes, this reaction is unaffected by the addition of free radical initiators. Also, ketones and aldehydes which cannot assume a cisoid conformation, such as cyclohexenone, are unreactive, even at high temperatures over long periods of time.

Alkynylboranes are synthesized by treating a terminal alkyne with n-butyllithium. The salt thus formed is treated with B-methoxy-9-BBN, followed by treatment with boron trifluoride diethyl etherate, to give the alkynylborane (equation 1-23, 1-24). As is the case for the

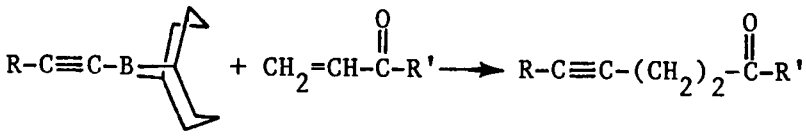


(1-23)



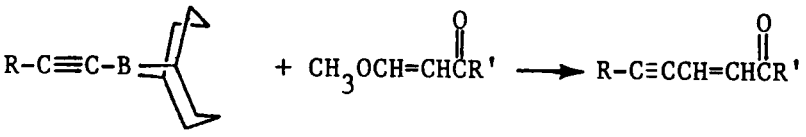
(1-24)

alkenylboranes, these reagents also undergo what is believed to be a concerted, conjugate addition to give the δ,γ-acetylenic ketone (equation 1-25).[31]



(1-25)

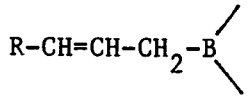
It is also possible to obtain the conjugated enynones via conjugate addition to an α,β-unsaturated carbonyl group with a leaving group, such as the methoxy moiety, in the β position (equation 1-26).[32]



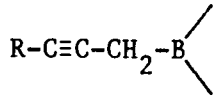
(1-26)

C. Reactions of Unsaturated Boranes

Unsaturated boranes, including the alkenylboranes (VI), alkynylboranes (VII), allylboranes (IX) and propargylboranes (X), are known to undergo carbonyl addition reactions, in addition to most of the reactions outlined earlier.



IX

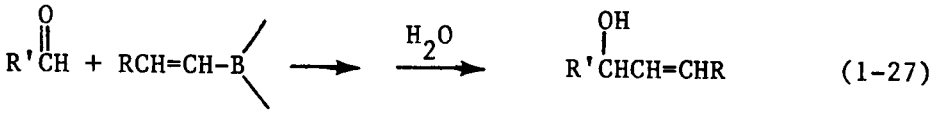


X

As noted earlier, the alkenyl- and alkynylboranes participate in a 1,4 addition reaction with α,β-unsaturated aldehydes and ketones. In these cases, no 1,2 addition product is observed. Allylboranes and propargylboranes (IX and X) are exceptions and do add to α,β-unsaturated carbonyl

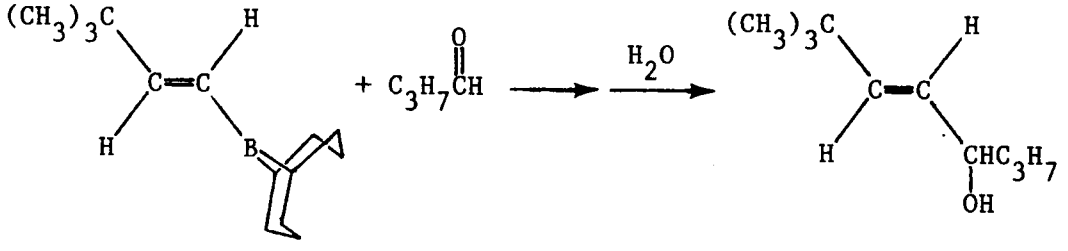
compounds in a 1,2 fashion, as will be discussed later. (No 1,4 addition products have been reported.)

A Grignard-like 1,2 addition to the carbonyl moiety is known in only a few cases for the alkenylboranes. While a reaction with ketones has not yet been reported, the B-alkenyl-9-BBN derivatives participate in a 1,2 addition with aromatic and aliphatic aldehydes (equation 1-27).[33] This reaction provides a means for synthesis of trans-allylic



(1-27)

alcohols. While yields in the reaction are modest (36 to 86%), the trans stereochemistry of the B-alkenylborane is retained (greater than 99% by GC) (equation 1-28).

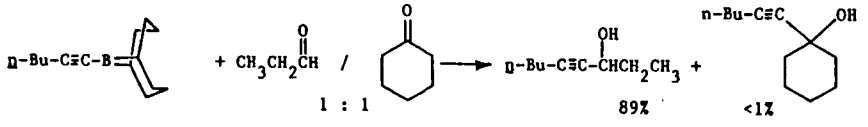


(1-28)

B-alkynyl-9-BBN compounds also undergo 1,2 addition reaction with carbonyl compounds. The reaction is very sensitive to steric factors, with more hindered aldehydes and ketones requiring longer reaction times and/or higher temperatures.[34] For example, reaction occurs at 25° in ten minutes with propionaldehyde to give an 85% yield of the desired

product. An 85% yield is obtained in the reaction with acetone only after sixteen hours at 65°.

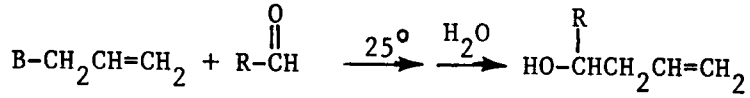
B-alkynyl-9-BBN reagents are not ionic and they demonstrate a remarkable chemoselectivity in comparison with other alkynyl metals. Due to their sensitivity to steric factors, the B-alkynyl-9-BBN derivatives can distinguish, and react selectively with, the least hindered carbonyl moiety (equation 1-29).



(1-29)

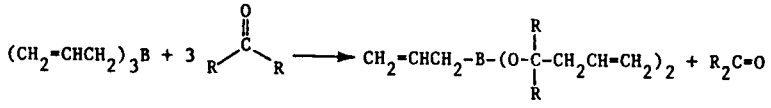
At 25°, B-alkynyl-9-BBN compounds are inert to a variety of functional groups including acid chlorides, amides, anhydrides, nitriles, acetals and ketals. They are also nonbasic and thus do not undergo many of the side reactions which are a drawback for other alkynyl metals. B-alkynyl-9-BBN compounds provide a facile, mild synthesis of propargyllic alcohols in moderately high yield.

The reactions of allylic boranes with aldehydes and ketones have been studied extensively. Triallylboranes react with aldehydes to form the homologous boric esters. Utilization of all three alkyl groups requires temperatures above 100°, however. It is more convenient to use monoallyldialkylboranes and carry out the reaction at more moderate temperatures (equation 1-30).[35]



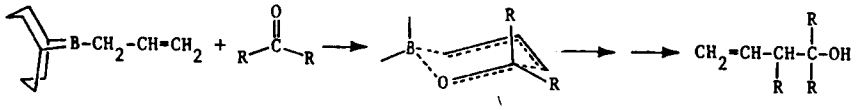
(1-30)

Triallylboranes react with ketones to form the boronic or borinic esters. The third allyl moiety does not react, presumably due to steric crowding around the boron atom (equation 1-31).[36]



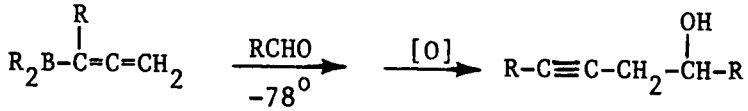
(1-31)

The reactions of allylboranes are presumed to proceed via a six-membered chair intermediate and accompanied by allylic rearrangement. Terminally substituted B-allyl-9-BBN derivatives were shown to undergo rearrangement, and unrearranged products were not detected in any case studied (equation 1-32).[37]



(1-32)

Treatment of the allenylborane (XI) with an aldehyde leads to the homopropargylic alcohol (equation 1-33).[38] If the borane is allowed to

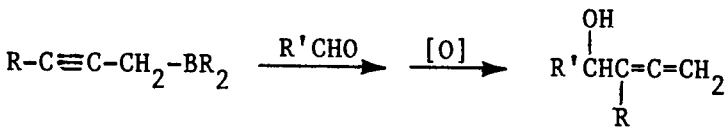


(1-33)

XI

warm and equilibrate before aldehyde addition, the propargylborane (XII)

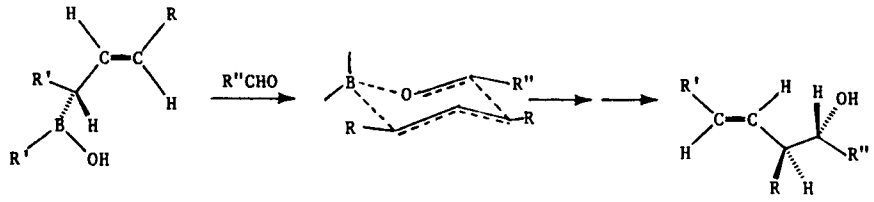
is formed, and the product obtained is the allenic alcohol (equation 1-34).[38] Yields for the reaction are good, ranging from 75 to 89%, but



(1-34)

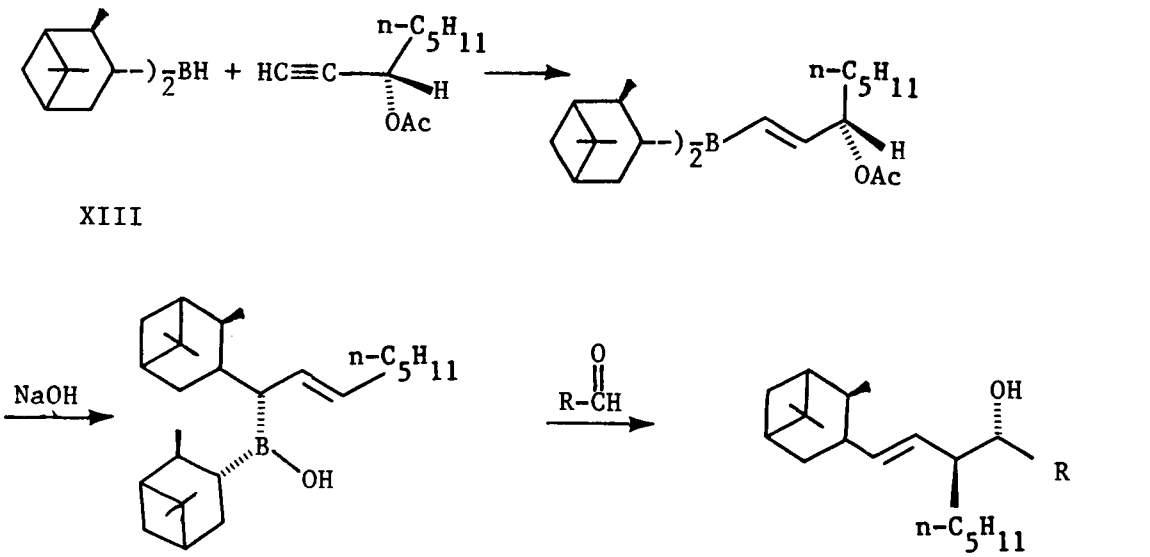
only one of the alkyl groups on the borane is utilized. Furthermore, only the 1,2 addition product is observed upon treatment of either XI or XII with α,β-unsaturated aldehydes. Preliminary studies indicate that ketones give a mixture of products arising from reaction with both XI and XII.

Enantiomerically enriched allylboranes are capable of undergoing reaction with aldehydes to give enantiomerically enriched products (percent enantiomeric excess ranging from 50.2% to 85%). The enantioselectivity of this reaction is attributed to preferential formation of the most stable chair intermediate in the transition state (equation 1-35).[39] A large increase in enantiomeric purity is observed with an



(1-35)

increase in the steric bulk of the alkyl substituents attached to the borane, thus diisopinocampheylborane (XIII) is the hydroborating agent of choice. In addition, this reaction provides a facile, one pot synthesis of the less commonly produced threo isomer of the homoallylic alcohol (equation 1-36).



XIII

(1-36)

D. Organoborate Additions to the Carbonyl

Tetraorganoborate salts are generally synthesized via treatment of a trialkylborane with an alkyl lithium salt (equation 1-37).

$$R_3B + R'Li \longrightarrow Li^+ \bar{B}R_3R' \qquad (1\text{-}37)$$

Only one reaction of simple saturated tetraalkylborates with carbonyl derivatives is known. Lithium tetraalkylborates undergo a smooth intermolecular transfer to acid halides to give the corresponding ketones in moderate yields (51 to 86%). In addition, the

triorganoborane can be recovered almost quantitatively (greater than 95%) (equation 1-38).[40]

$$LiB(\underline{n}Bu)_4 + CH_2{=}CH(CH_2)_8\overset{O}{\overset{\|}{C}}Cl \longrightarrow B(\underline{n}Bu)_3 + CH_2{=}CH(CH_2)_8\overset{O}{\overset{\|}{C}}\text{-}\underline{n}Bu \qquad (1\text{-}38)$$

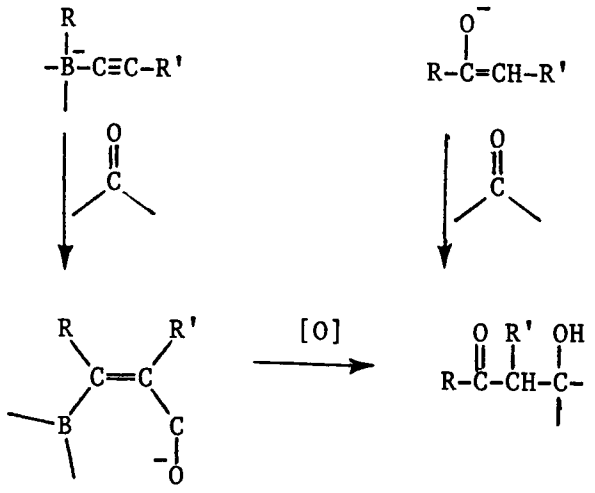
Vinyltrialkylborates are known to undergo intramolecular transfer reactions of synthetic interest, in the presence of an electrophile.[41] The reaction occurs when the electrophile is formaldehyde (equation 1-39).[42]

$$R\text{-}\overset{R}{\underset{R}{\overset{|}{\underset{|}{B^-}}}}\text{-}CH{=}CH_2 + CH_2{=}O \longrightarrow R\text{-}\overset{R}{\underset{R}{B}}\text{-}CH\text{-}CH_2\text{-}CH_2\text{-}O^- \xrightarrow{[O]} R\text{-}CH(OH)CH_2CH_2OH \qquad (1\text{-}39)$$

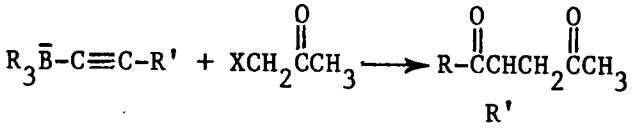
Similar reactions with more highly substituted boranes have not been reported, although the reaction is known for benzaldehyde and 2-methylpropanal.[43]

Alkynyl borates function as enolate anion equivalents in their reactions with carbonyls, as illustrated in Scheme I.[44]

Scheme I:



The reactions of alkynyl borates with carbonyl compounds are similar to the vinyl borate reactions described above. Intramolecular 1,2 migration is followed by attack on the carbonyl moiety to give the aldol-like product (equation 1-40).[45]



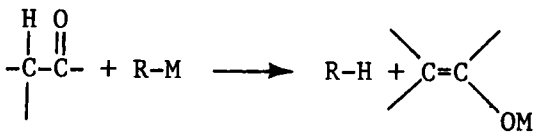
(1-40)

The organoboranes participate in a number of useful synthetic transformations. However, the reaction of simple organoboranes with carbonyl compounds in a Grignard like fashion has never been reported. It is this reaction which was investigated.

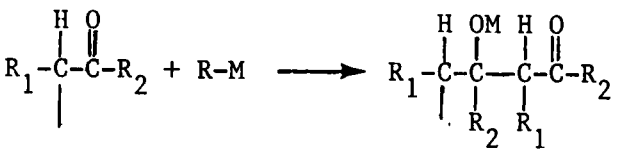
CHAPTER II

DISCUSSION OF THE PROBLEM

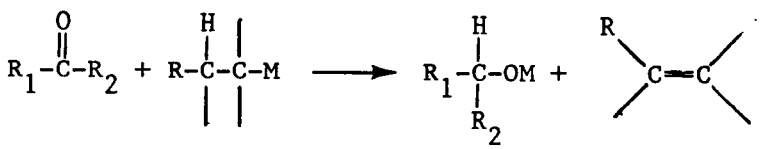
The development of a Grignard-like carbonyl addition reaction utilizing organoboranes would be of interest to synthetic chemists. Such a reaction would eliminate many of the disadvantages involved in the use of traditional organometallic reagents. For example, one of the principle drawbacks of organometallic compounds is their basicity, which leads to side reactions such as enolization (equation 2-1), condensation (equation 2-2) and reduction (equation 2-3):



(2-1)



(2-2)



(2-3)

Organoboranes are weak bases and would not be expected to participate in these reactions.

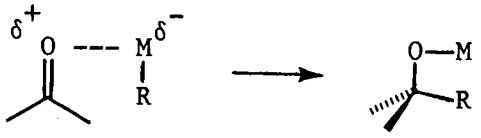
The reaction of trialkylboranes with simple carbonyl compounds has never been reported. The apparent lack of reactivity of trialkylboranes toward the carbonyl moiety can best be rationalized by considering the mechanism of organometallic carbonyl addition reactions. The initial

step for this reaction is a coordination between the carbonyl oxygen and the metal atom to give a complex (equation 2-4). This step is followed



(2-4)

by migration of the alkyl group to the carbonyl carbon (equation 2-5).



(2-5)

The reaction then depends on two factors: coordination and alkyl group migration. Both of these apparently play a role in the nonreactivity of organoboranes toward carbonyls.

When compared with other organometallic reagents, organoboranes are found to be substantially less polar than reagents which do undergo a carbonyl addition reaction. Table 2-1 shows the percent ionic character for some representative organometallic reagents.[46] Lower percent ionic character of the carbon metal bond leads to a lower reactivity of the organometallic reagent.

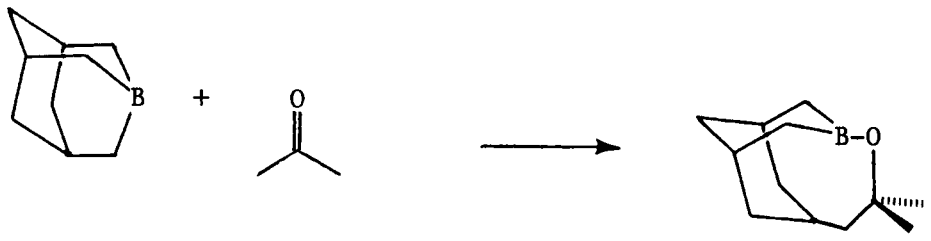
The principal disadvantage in the use of many of the reactive organometallic reagents, as was stated earlier, is their high basicity (a consequence of too great an ionic character) leading to side reactions, such as enolization, reduction and condensation. This is the case with the alkyl sodium reagents, for which enolization is the major reaction observed with carbonyl compounds. Organomagnesium compounds

Table 2-1: Percent Ionic Character of the Carbon-Metal Bond

C-M	Percent Ionic Character	Reaction with Carbonyl Moiety
C-Na	47	enolization
C-Li	45	1,2 addition
C-Mg	35	1,2 addition
C-Al	22	1,2 addition many side reactions
C-Zn	18	1,2 addition in some cases
C-Cd	15	no reaction
C-Hg	9	no reaction
C-B	6	no reaction

are also subject to these side reactions, although to a lesser extent. Less polarized agents usually do not participate in these side reactions, but as can be seen from Table 2-1, reagents such as the organomercurials and organocadmiums do not undergo 1,2 carbonyl addition reactions. The organoboranes are not expected to participate in the side reactions that limit the usefulness of many organometallic reagents, but their low polarity is expected to affect their ability to react with the carbonyl moiety.

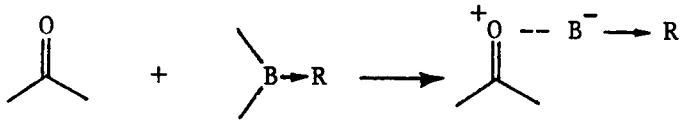
The 1,2 carbonyl addition reaction of organoboranes is thermodynamically favored. The bonds that are forming in the 1,2 addition reaction (the boron to oxygen bond and the carbon to carbon bond) have energies of approximately 120 kcal/mole[47] and 80 kcal/mole, respectively. The bonds broken in the addition reaction have energies of approximately 60 kcal/mole[48] (for the carbon to oxygen bond) and 80 kcal/mole[49] (for the carbon to boron bond). The reaction is favored by approximately 60 kcal/mole. In fact, the reaction is known in only one case. Adamantylborane (XIV) has a tetrahedral geometry about the boron atom, and thus an increased coordinating ability is anticipated. Mikhailov and coworkers have observed a 1,2 carbonyl addition reaction between acetone and adamantylborane (equation 2-6).[50]



(2-6)

XIV

One approach to achieving a successful Grignard like reaction would be to increase the polarity of the organoborane. Polarization of the boron-carbon bond can be accomplished by replacing one or more of the alkyl groups with an electron withdrawing group. This substitution would increase the electron deficiency on boron, thus increasing the likelihood of coordination (equation 2-7).



(2-7)

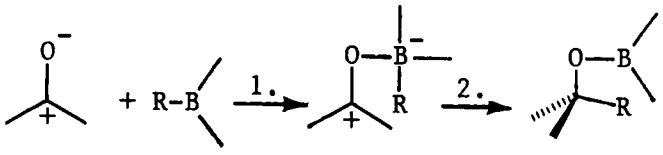
An alternate approach to the problem would be to make the alkyl group more anion-like, so as to increase its reactivity toward carbonyls. This could be accomplished by replacement of an alkyl group with an electron donating group, which would also have the effect of increasing the electron density on the borane, and increase the likelihood of migration of the alkyl group, as shown in step two of the proposed mechanism (equation 2-8).



(2-8)

An ideal group to be substituted on the boron atom would be one which had both electron-donating and electron-withdrawing properties. Such a group would be sufficiently electron-withdrawing to allow coordination to occur between the boron atom and the carbonyl oxygen, and yet, once coordination occurred, could donate electron density to boron so as to encourage migration from boron to the carbonyl carbon.

A third approach to the problem would involve polarization of the carbonyl bond. A more electronegative oxygen is more likely to attack the borane (step one), and a more electropositive carbon would make a better receptor site for the migrating alkyl group (step two) (equation 2-9).



(2-9)

To assist the reaction, the borate complex could be preformed by addition of methoxide or acetate ion to the trialkylborane. This would insure the formation of the borate and eliminate the need for coordination, shown in step one of the proposed mechanism. The addition of a preformed borate to the carbonyl group in a polar medium might allow a 1,2 carbonyl addition reaction. This approach was used with some success by Negishi et al., in the intramolecular organoborate rearrangements discussed earlier.

Each of these approaches were investigated in detail. The experiments were monitored by NMR spectroscopy, as described in Chapter 3. The results of investigations into the modification of organoboranes are outlined in detail in Chapter 4. Approaches to polarization of the carbonyl moiety and the results of these experiments are discussed in Chapter 5.

CHAPTER III

USE OF BORON-11 AND CARBON-13 NMR TO MONITOR REACTIONS

A. General Discussion

Nuclear Magnetic Resonance (NMR) spectroscopy has been widely used in the structural elucidation of organic compounds. This technique has also found considerable application in organoboron chemistry. As in carbon and proton NMR spectroscopy, it is possible to determine the chemical environment around each boron atom based on its resonance frequency in an NMR spectrum (commonly referred to as "chemical shift").

In the simplest case, when placed in a magnetic field (H_o), a spinning nucleus will align with or against the magnetic field. The magnetic moment (μ) will precess about the force line of the applied magnetic field (Figure 3-1a).[51] The NMR experiment is performed by exposing the sample to an additional, perpendicular magnetic field (H_1). The two magnetic fields add to produce an effective magnetic field (H_{eff}), which the spinning nucleus then precesses about (Figure 3-1b). Resonance absorption of energy occurs when the frequency of the magnetic field H_1 is identical to the frequency of precession, known as the Larmor frequency (ν), and results in a spin flip from the lower energy state, in which the nuclei are aligned with H_o, to the higher energy state, in which the nuclei are aligned against H_o (Figure 3-1c).

The number of energy states available to a nucleus is given by its nuclear spin number, I. This number is determined by the number of

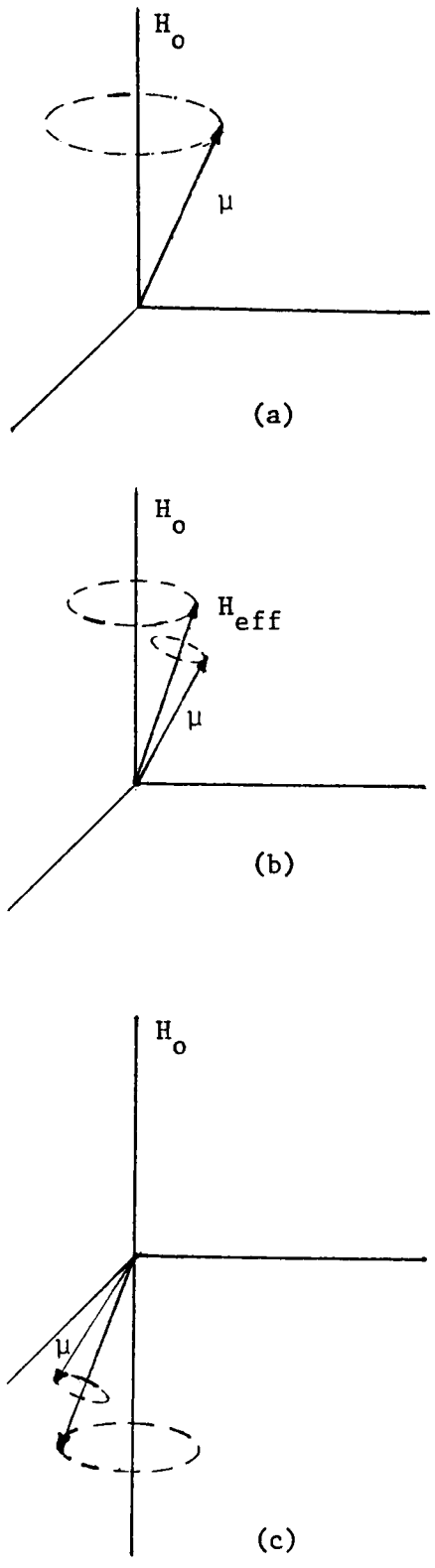


Figure 3-1. Various Configurations of the Nucleus in an NMR Experiment.

protons and neutrons in the nucleus and is described by the following rules:

1. If the sum total of protons and neutrons in the nucleus is odd, I is an half-integral, i.e., 1/2, 3/2, 5/2, etc.

2. If the sum total of the protons and neutrons in the nucleus is even and the number of protons is odd, I is integral, i.e., 1, 2, 3, etc.

3. If the sum total is even and the number of protons is even, there is no net nuclear spin, i.e., I equals zero and the nucleus is nonmagnetic.

There are 2I+1 discrete energy levels available to a given nucleus, separated by an energy E, which is dependent on the Larmor frequency and characteristic of the nucleus and its chemical environment (Figure 3-2).[51] It is this energy that is measured by the NMR spectrometer.

Energy absorption to the higher energy states is followed by relaxation back to the lower energy state. There are two mechanisms by which this occurs. The first mechanism is referred to as spin-lattice relaxation, a process whereby energy is diffused to the lattice, or environment around the nucleus. Its efficiency is described by T_1, the reciprocal of the first order rate constant for the relaxation process. Another mode of relaxation, spin-spin relaxation, occurs by transfer of energy from an excited nucleus to a nearby nucleus. The efficiency of this mode is given the symbol T_2.

The importance of relaxation modes is two fold. Line width is inversely proportional to relaxation time, such that nuclei with long

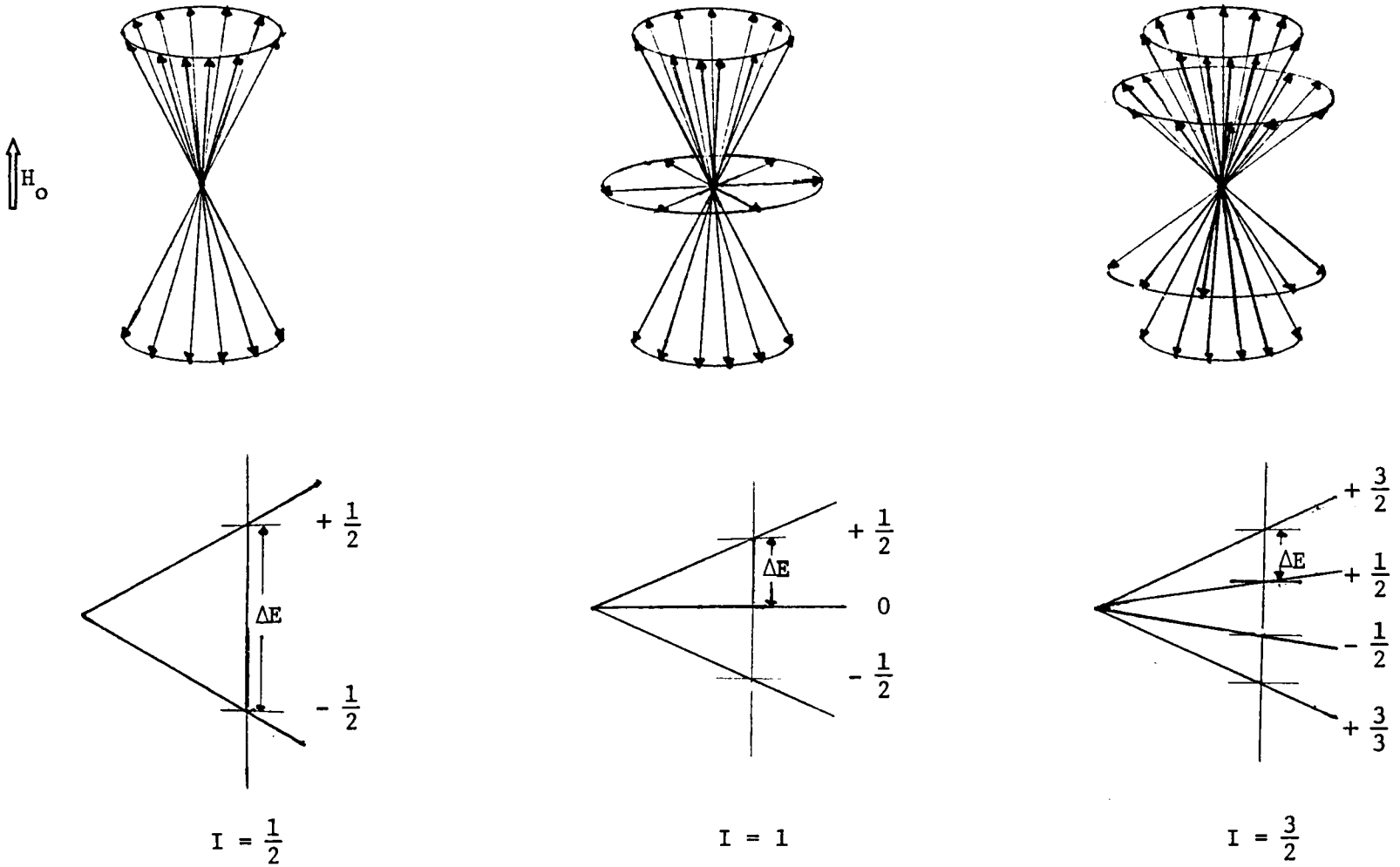
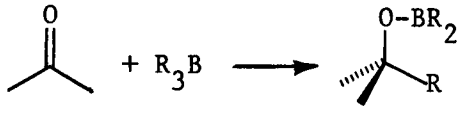


Figure 3-2. Energy Levels of Nuclei in an Applied Magnetic Field.

relaxation times, such as ^{13}C, give very narrow lines, and nuclei with short relaxation times have very broad NMR signals. In addition, relaxation to the ground state is essential for experiments which require multiple excitation/relaxation sequences, and will be discussed later.

In the current study, both ^{13}C and ^{11}B NMR spectroscopy were used extensively. Proton NMR (PMR) was not generally useful, due to line broadening that occurs in proton spectra in the presence of boron. In addition, we wished to monitor a reaction (equation 3-1) in



(3-1)

which no significant changes in the PMR spectra were expected, since the carbonyl carbon under investigation has no attached protons, in either reactants, intermediates or products. Minor changes in the alkyl region of the PMR spectra would be expected, due to changes in the chemical environment of the methyl groups in acetone and the alkyl group attached to the boron, but the changes would not be dramatic, and possibly not observed due to the complexity of the spectrum in the alkyl region. Specifically, the methyl protons of acetone show a single peak in the PMR spectrum at 2.1 ppm. The methyl protons adjacent to the developing tertiary center would be expected to show a single peak at approximately 1.2 ppm. When the PMR spectrum of tributylborane is superimposed on the

spectra of these two compounds, any distinction in this region is lost. For these reasons, PMR was used only sparsely.

B. Carbon-13 Nuclear Magnetic Resonance

The most abundant of the carbon nuclei, ^{12}C, is nonmagnetic and thus of no use in NMR experiments. Carbon-13, with a natural abundance of about 1%, has a nuclear spin of one-half and, like ^{1}H, is useful for NMR studies. The low abundance of ^{13}C does require the use of special techniques, such as Fourier Tranform NMR (FT-NMR).

FT-NMR first became practical in the early 1970s. In a typical experiment, all the nuclei are excited to a higher energy spin state by a short, high-energy radio-frequency pulse, and the energy released as they return to the ground state is measured. After a delay time which allows most of the nuclei to return to the ground state, the sample is pulsed again. Repetitive pulsing and data acquisition result in signals which are then processed by a computer to provide the ^{13}C spectrum of the sample. Carbon-13 relaxation times are relatively long, so the lines in these spectra are narrow. Wideband noise decoupling to eliminate the magnetic interactions with the attached protons results in a single sharp line for each chemically nonequivalent carbon.

Each of the experiments reported was monitored by ^{13}C NMR. The ^{13}C NMR spectrum of acetone has two single sharp lines at 206.0 ppm and 30.6 ppm (Figure 3-3). During the course of the proposed reaction, the peak at 206.0 ppm, due to the carbonyl carbon would be expected to shift downfield upon coordination to the boron atom and to disappear as the

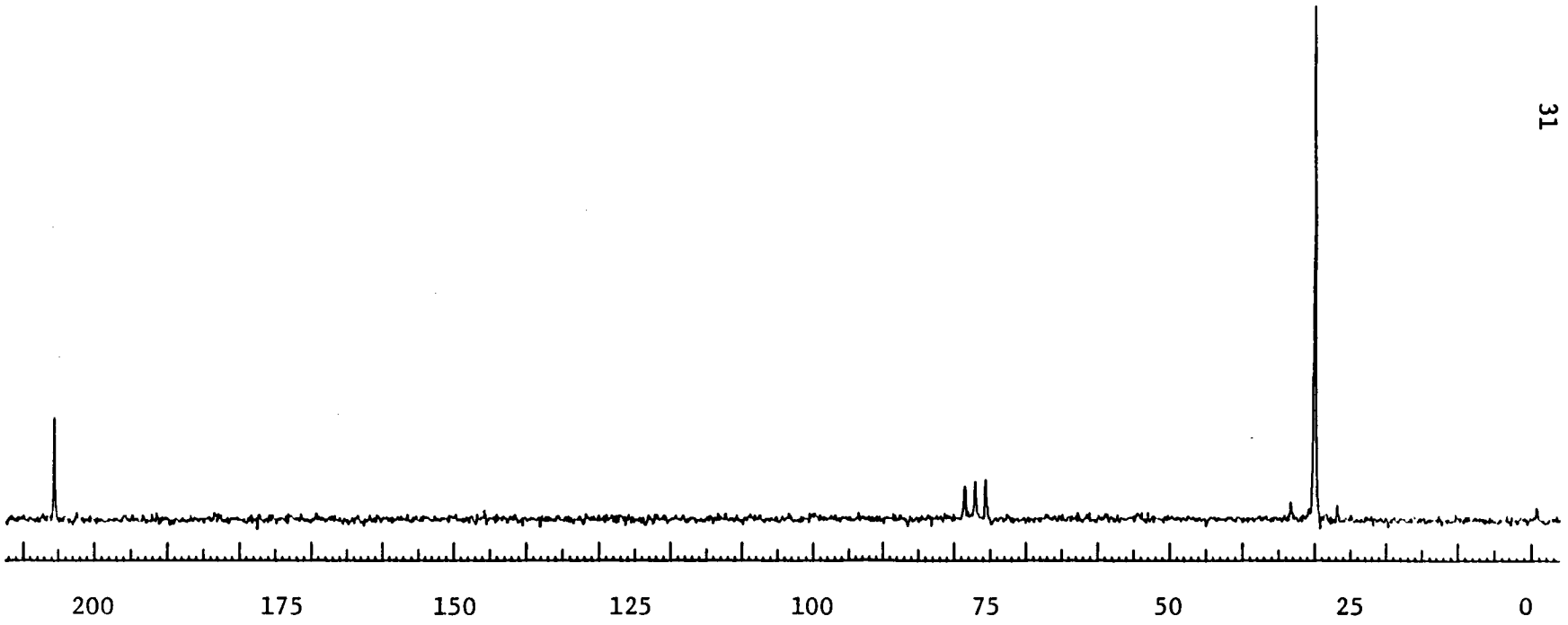


Figure 3-3. Carbon-13 NMR Spectrum of Acetone.

tertiary center is formed. Figures 3-4 and 3-5 show the ^{13}C NMR of tertiary alcohols which would result from successful carbonyl addition of tricyclohexylborane and tributylborane to acetone. Because of the length of time required to obtain a ^{13}C spectrum (thirty minutes or more) the coordination step is not likely to be observed.

Carbon-13 NMR spectra were monitored during the course of the reactions described in this thesis. The developing tertiary center is expected to have a chemical shift near 70 ppm. This peak is due to a tertiary carbon with no attached hydrogens and would be expected to be small. Since the ethereal solvents used in many of these reactions could potentially interfere in the analysis of the 70 ppm region, the region between 40 and 50 ppm was also monitored for resonance due to the carbon adjacent to the alcohol carbon. This region of the ^{13}C spectrum is relatively free of extraneous peaks, and thus would be a more reliable source of information about the spectrum.

C. Boron-11 Nuclear Magentic Resonance

The reactions described in this thesis were also monitored by ^{11}B NMR. Unlike carbon, both of the common isotopes of boron are magnetically active. Boron NMR studies are most often performed on ^{11}B for several reasons. Boron-11 has a natural abundance of 80%, a nuclear spin number of 3/2, and a low electric quadrupole moment (0.0355×10^2 m^2).[52] In contrast, ^{10}B has a nuclear spin number of three and a high electric quadrupole moment (0.111×10^2 m^2),[52] and thus its spectra are much more complicated.

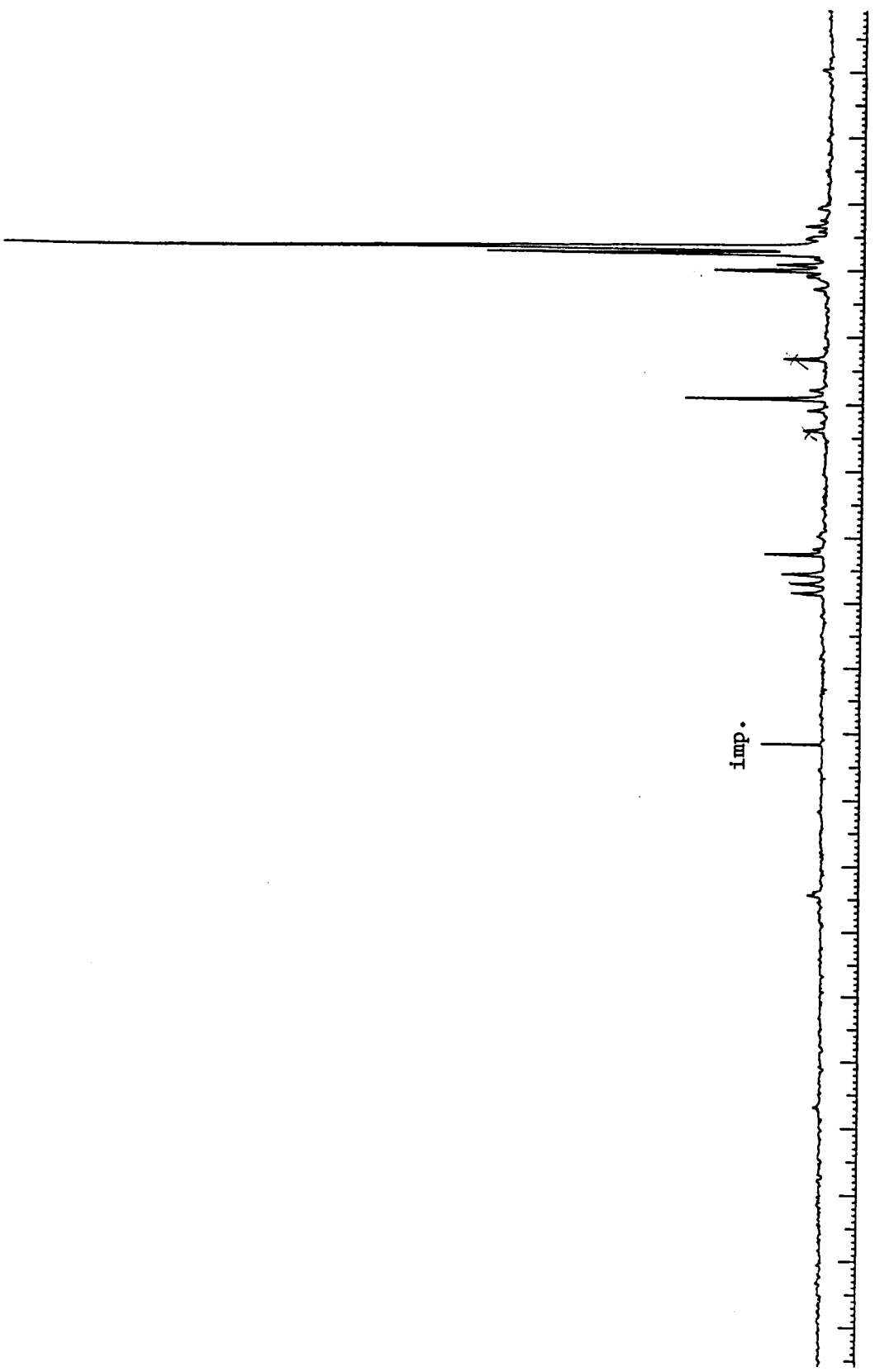


Figure 3-4. Carbon-13 NMR Spectrum of 2-Cyclohexyl-2-Propanol.

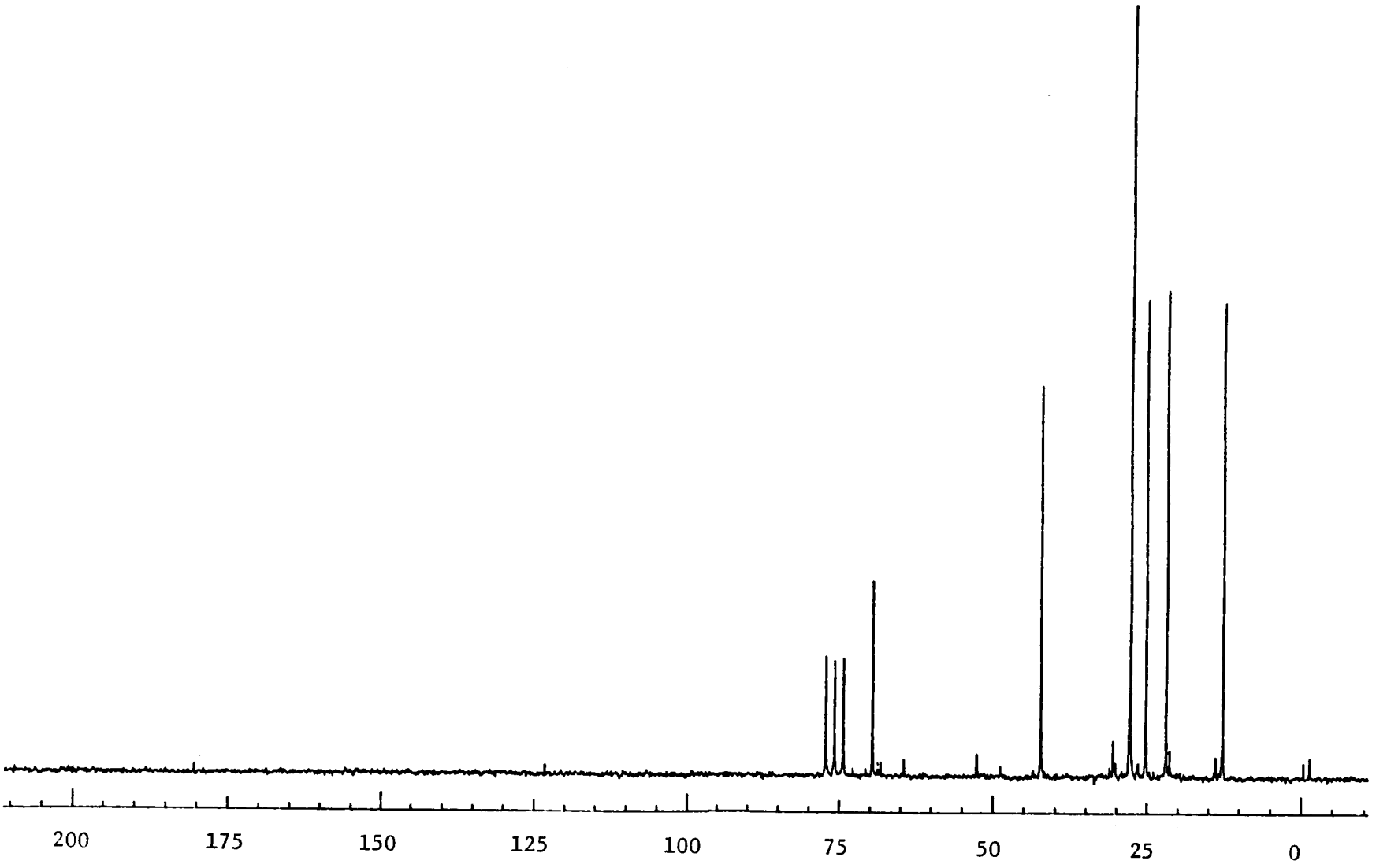
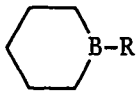


Figure 3-5. Carbon-13 NMR Spectrum of 2-Methyl-2-hexanol.

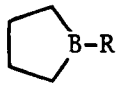
Both ^{10}B and ^{11}B have an electric quadrupole moment, that is, a nonspherical distribution of charge around the nucleus. This allows a more efficient interaction with adjacent nuclei for energy transfer processes, thus a more efficient relaxation of the nucleus to the ground state which produces broad lines in the NMR spectra.

As with ^{13}C and ^{1}H NMR spectroscopy, the chemical shift of organoboranes is dependent on the chemical environment around each boron atom. The ^{11}B chemical shift is strongly dependent on the π-donor ability and/or the σ polarizing ability of the substituent groups on the boron. Good and Ritter[53] developed a method to justify ^{11}B chemical shifts based on the additive relationship of these two effects. This theory has been extended to include anisotropic effects by Noth and Vahrenkamp.[54]

Trialkylboranes are not expected to experience either of these effects very strongly. Between sp^3 carbon and sp^2 boron, π-bonding is at a minimum, and, consequently, these boranes appear in the NMR spectrum at very low field (83-93 ppm). Very little change is observed as the carbon chain length is increased. The alkyl groups surround the boron in a trigonal planar arrangement, and only when the steric effects become great enough to disrupt this geometry is a shift to higher field observed (R = t-butyl, Δ = 3 ppm). The borinanes (XV), six membered ring boron heterocycles, appear at approximately the same position as other trialkylboranes (approximately 87 ppm). When boron is part of a five membered ring, however (the borolanes, XVI), the bond angles are



XV



XVI

altered and a 6 ppm shift to low field is observed. These effects are relatively small, however, and in general, chemical shifts for simple trialkylboranes are observed in the range stated earlier.

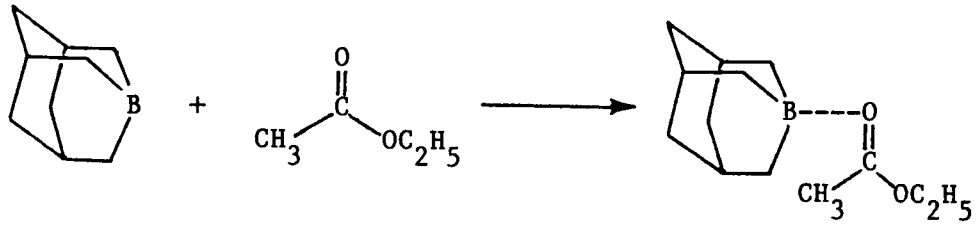
As the alkyl groups on boron are substituted with electron donating groups or electronegative groups (such as halogens), chemical shifts to higher field are always observed. For weak donors, such as vinyl groups, successively increasing the number of donors produces a nearly constant shift to higher field. Strong π-donors, such as methoxy groups, do not produce this linear relationship, because of the σ polarizing effect they have on the alkyl-carbon to boron bond.

A dialkylborane substituted with a single π-donating substituent exhibits a resonance at approximately 50 ppm (relative to $BF_3{:}OEt_2$). A second substitution results in a shift to even higher field (to approximately 30 ppm). A third substitution of an alkyl group by a π-donating group produces a further shift (to 18 ppm).[52]

$(CH_3)_3B$	$(CH_3)_2BOCH_3$	$CH_3B(OCH_3)_2$	$B(OCH_3)_3$
86 ppm	53 ppm	29 ppm	18 ppm

There are very little data available concerning the chemical shifts of organoboranes complexed with carbonyl compounds. The chemical shift

of adamantylborane is 82 ppm, while its complex with ethyl acetate has a reported shift of 15 ppm (equation 3-2).[55] (Adamantylborane is known

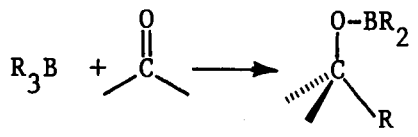


82 ppm 15 ppm

(3-2)

to undergo a 1,2 carbonyl addition reaction.)[50]

Many of the reactions reported in this thesis were performed in the NMR instrument and were followed by NMR. A mechanism analogous to that of a typical organometallic addition to the carbonyl was postulated. A chemical shift to higher field was anticipated for the carbonyl-borane complex compared to the chemical shift of the starting borane. Because of the sparsity of literature data on these complexes and the possibility that the complexation-alkyl transfer sequence would occur too fast on the NMR time scale to be observed, the product from the alkyl transfer reaction (equation 3-3) was of primary interest. As noted



85 ppm 55 ppm

(3-3)

earlier, monooxygenated boranes are observed in the region near 55 to 45 ppm. A second coordination-transfer sequence, resulting in a dioxygenated borane, would also be readily diagnosed (via the appearance of a resonance near 30 ppm).

Boron-11 NMR has been used to monitor the progress of a number of organoborane rearrangements. In particular, studies of disproportionation reactions have been aided by the development of this area of spectroscopy.[56-58] The principal advantage encountered was the ability to examine reactions on a small scale (1-2 mmol) to determine if preliminary results were promising. Only in cases where NMR indicated that a reaction had taken place were the reactions repeated on a larger scale.

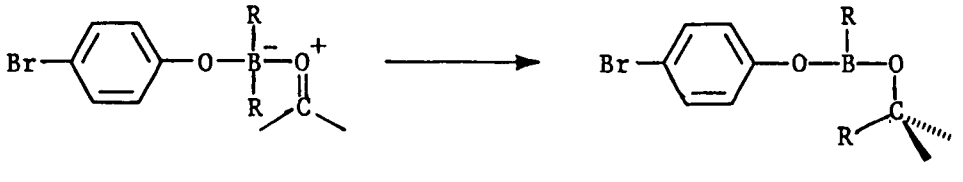
CHAPTER IV

MODIFICATION OF THE ORGANOBORANE

A. Results and Discussion

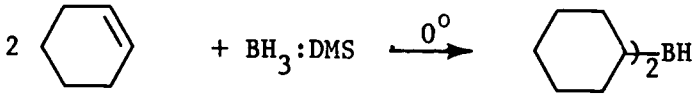
The mechanism of the addition of organometallic reagents to the carbonyl moiety is a two step process, involving an initial coordination between the metal atom and the carbonyl oxygen, followed by migration of the alkyl group to the carbonyl carbon. As noted earlier, organoboranes do not generally undergo reactions with carbonyl groups. The likelihood of a successful reaction might be increased by substituting an electron withdrawing group on the borane, thus making the borane appear electron poor and increasing the coordination between boron and the carbonyl oxygen. Conversely, substituting an electron donating group on the borane would make it more electron rich and increase the likelihood of an alkyl migration.

To test these hypotheses, the p-bromophenoxy group was substituted for a hydride in a borane molecule. It was felt that a phenyl ring bearing electron withdrawing substituents might fulfill both requirements. The phenyl ring is electron withdrawing in nature and could aid in the coordination reaction; once coordination occurred, the lone electron pairs on oxygen could assist migration of the alkyl group by making the borane appear electron rich (equation 4-1). To this end,



(4-1)

p-bromophenyl dicyclohexylborinate was synthesized. The cyclohexyl moiety was chosen as the alkyl group because dicyclohexylborane is one of the few dialkylboranes which can be synthesized directly via the reaction of BH_3 with alkenes. For steric reasons, it is possible to stop the hydroboration reaction once two cyclohexyl groups are attached to the borane (equation 4-2). Dicyclohexyl borane then precipitates



(4-2)

from the reaction mixture as a dimer. Treatment with p-bromophenol provided p-bromophenyl dicyclohexylborinate (equation 4-3). A single

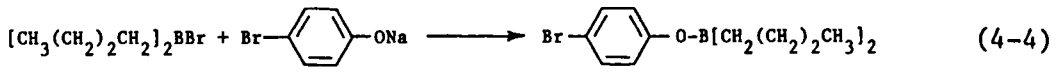


(4-3)

peak in the boron NMR spectrum of the borane was observed at 55 ppm relative to boron trifluoride diethyl etherate, which is consistent with the structure indicated for p-bromophenyl dicyclohexylborinate. The reagent was treated with acetone and the reaction monitored by NMR. Complexation of the reagent with a carbonyl group should result in an increase in electron density around the boron atom shifting the boron resonances upfield. Boron-11 NMR analyses revealed no shift in the boron resonance demonstrating that no coordination occurred. Following workup in aqueous base, the mixture was analyzed by ^{13}C NMR for product peaks, especially a peak at 75 ppm, which is characteristic of the

desired carbinol product. No resonances coinciding with the desired product, 2-cyclohexyl-2-propanol, were observed.

In an anionotropic rearrangement, it is expected that primary groups would migrate faster than secondary alkyl groups. Thus a method was sought for synthesizing phenyl dialkylborinates in which the alkyl groups were primary, rather than secondary groups such as cyclohexyl. The commercial availability of monobromoborane as the dimethyl sulfide (DMS) complex solved the problem. The hydroboration of 1-butene was carried out at 0^{o} over four hours to yield di-n-butylbromoborane complexed with DMS. In order to remove the DMS complexing agent, an equimolar amount of tribromoborane was added to the cooled reaction mixture. After stirring for several hours, the solvent (dichloromethane) was removed, allowing the solid tribromoborane:DMS to precipitate. Filtration to remove the solid was carried out under nitrogen. The product, di-n-butylbromoborane, which has a chemical shift of 70 ppm in the ^{11}B NMR, was obtained with a slight contamination of tribromoborane:DMS (δ = -10.1 ppm), and was used without further purification, due to its hydrolytic instability. p-Bromophenyl dibutylborinate (δ = 55.1 ppm) was formed by treating dibutylbromoborane with sodium p-bromophenoxide (equation 4-4). p-Bromophenyl

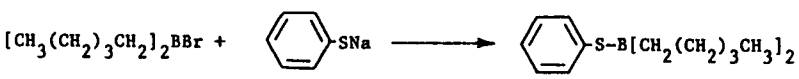


(4-4)

dibutylborinate was treated with acetone and the reaction monitored by NMR. Reaction times and temperatures were varied, but no change was observed, either in the ^{13}C or ^{11}B NMR spectrum (Figures 4-1, 4-2).

No coordination or reaction was observed with bromophenyl dibutylborinate presumably due to the proximity of the oxygen atom and its lone pairs of electrons. Molecular orbital theory predicts that the probability of π-backbonding is high, because the empty p-orbital of the boron atom and the orbitals which contain oxygen's lone pairs should be approximately the same size. For this reason, thiophenyl dialkylborinates were then examined. Sulfur has the same valence shell electron configuration as oxygen, but the orbitals which contain the lone pairs are predicted by quantum theory to be larger than those of oxygen, and thus should not overlap as effectively with the empty p-orbital of boron.

Thiophenyl dipentylborinate was synthesized by treating dipentylbromoborane with sodium thiophenoxide at room temperature (equation 4-5). The product exhibited one peak at 54 ppm in the ^{11}B



(4-5)

NMR. Another, smaller peak, at 11 ppm, was attributed to thiophenyl borate, arising from the reaction of sodium thiophenoxide with the tribromoborane:DMS complex, present in the starting material (equation 4-6).

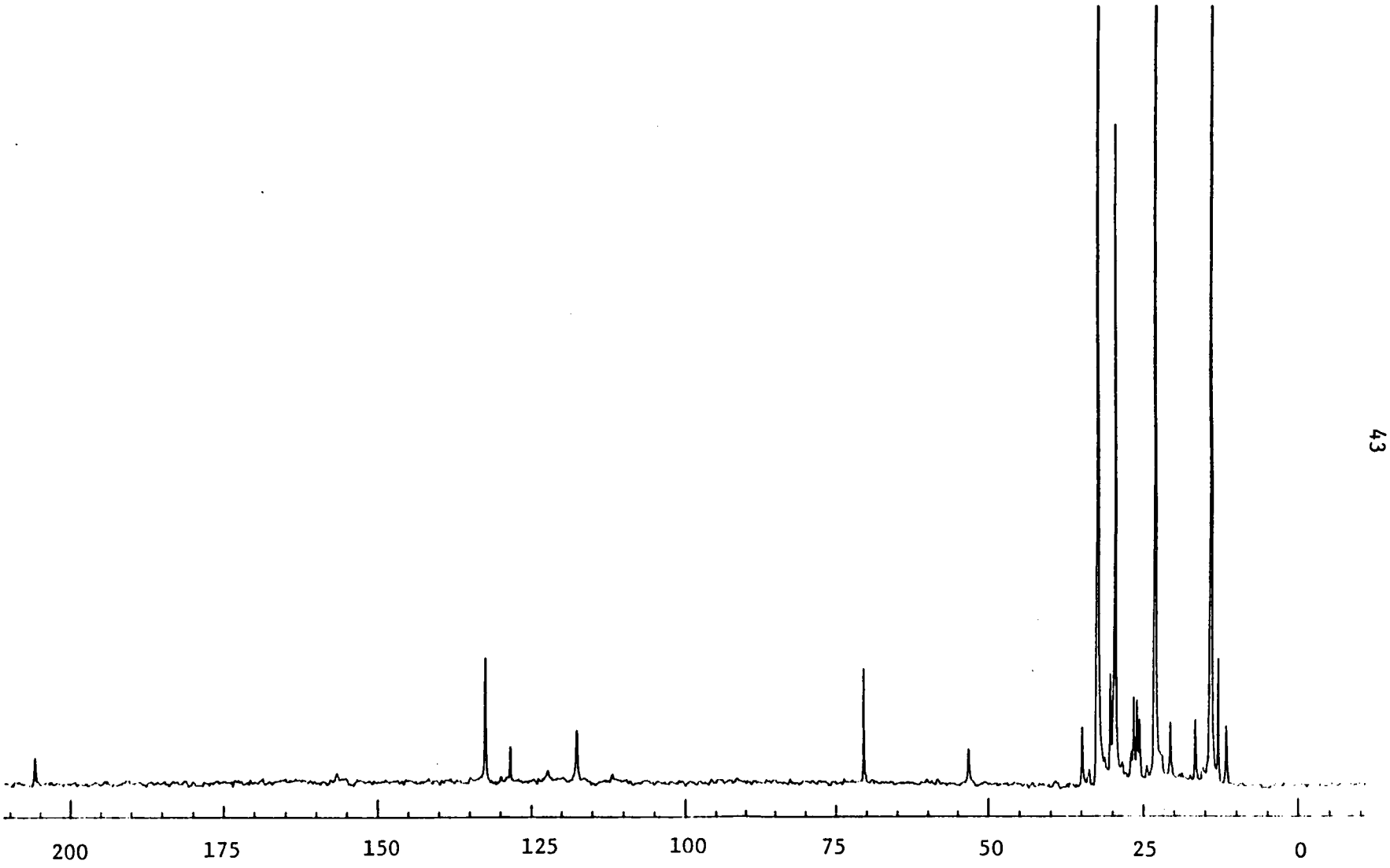


Figure 4-1. Carbon-13 NMR Spectrum of p-Bromophenyl Dibutylborinate and Acetone Reaction Mixture.

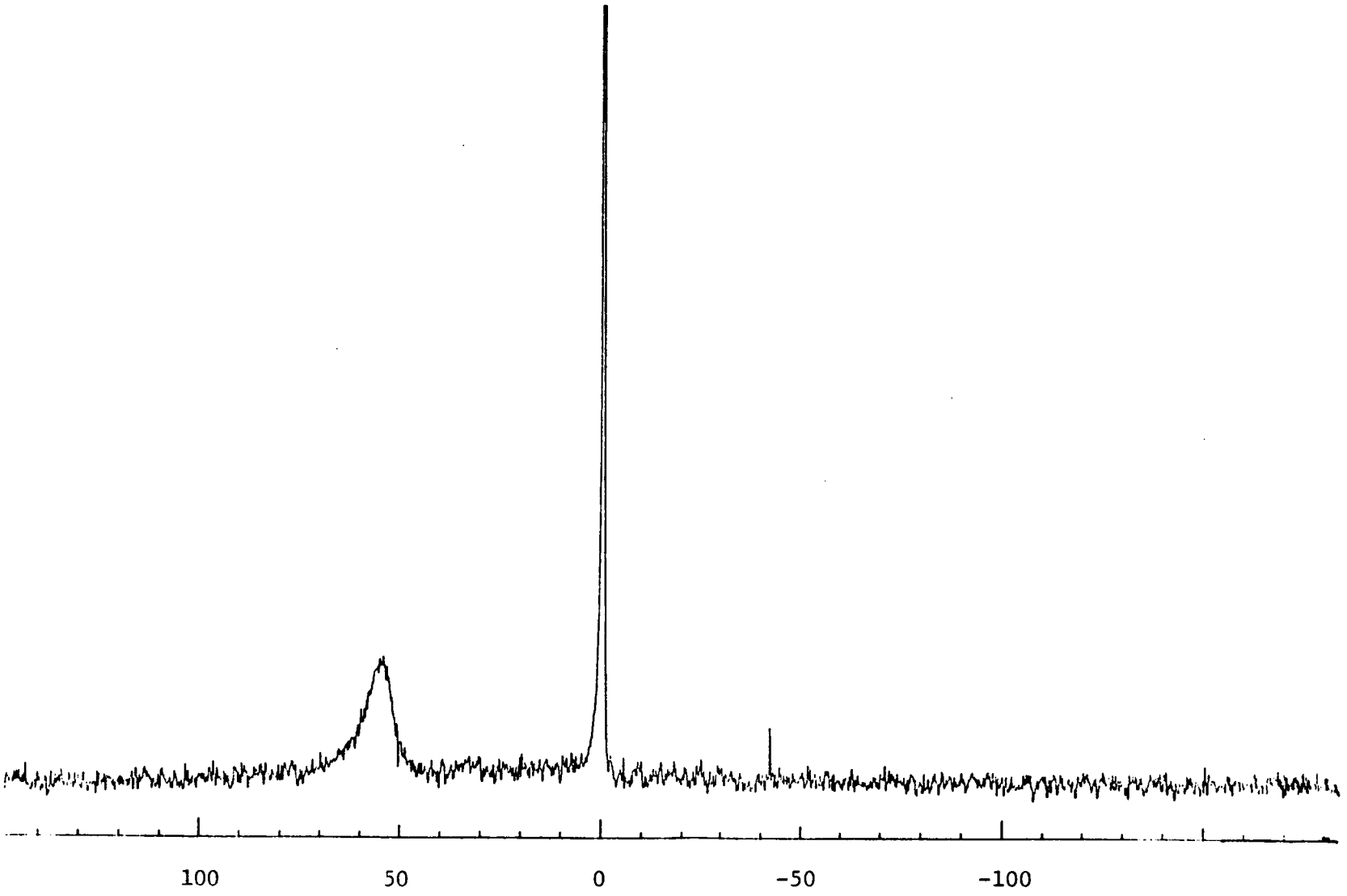
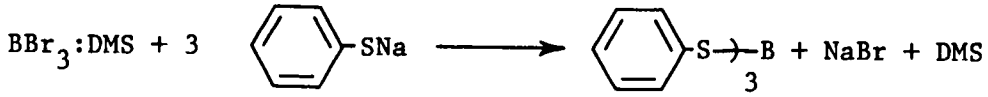


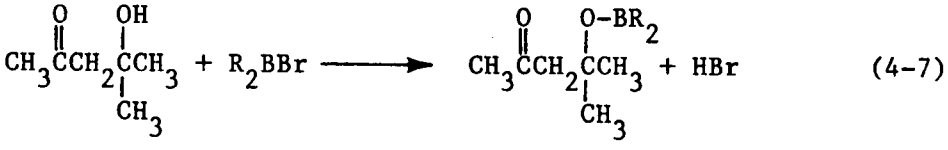
Figure 4-2. Boron-11 NMR Spectrum of p-Bromophenyl Dibutylborinate and Acetone Reaction Mixture.



(4-6)

Acetone was added to the borane, and the reaction was monitored by NMR with no observable change in either the ^{13}C or ^{11}B NMR spectrum (Figure 4-3). Heating the reaction mixture also failed to bring about reaction. Apparently the electron density around the boron atom is still too great to allow initial coordination to occur.

The reaction of dialkylbromoborane with the carbonyl moiety was then examined. Bromoboranes are better Lewis acids than alkoxyboranes, and, thus, coordination is more likely to occur. Instead of the desired 1,2 addition reaction, an aldol reaction, apparently catalyzed by the bromoborane, was observed (Figure 4-4). One peak was observed in the ^{11}B NMR at 55 ppm (Figure 4-5). The shift from 70 ppm can be rationalized by assuming condensation of the borane with the alcohol formed in the aldol reaction (equation 4-7). The reaction was worked up



(4-7)

in aqueous base, which led to dehydration of the aldol product, to form mesityl oxide. Unfortunately, the desired product was not observed.

Alkyldiphenylboranes were also of interest, due to the effects on the alkyl-to-boron bond due to the proximity of the π-systems of the two

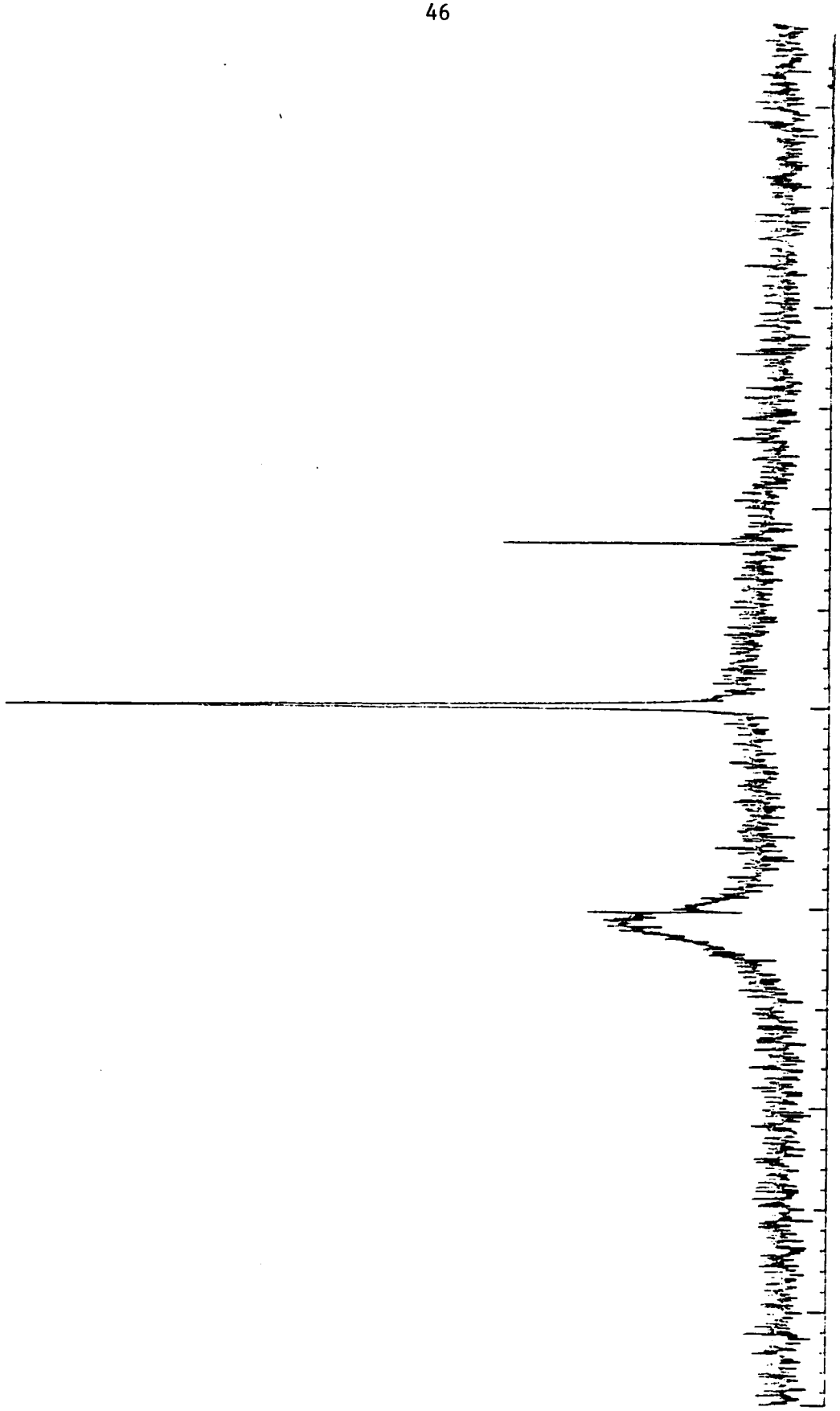


Figure 4-3. Boron-11 NMR Spectrum of Thiophenyl Dipentylborinate and Acetone Reaction Mixture.

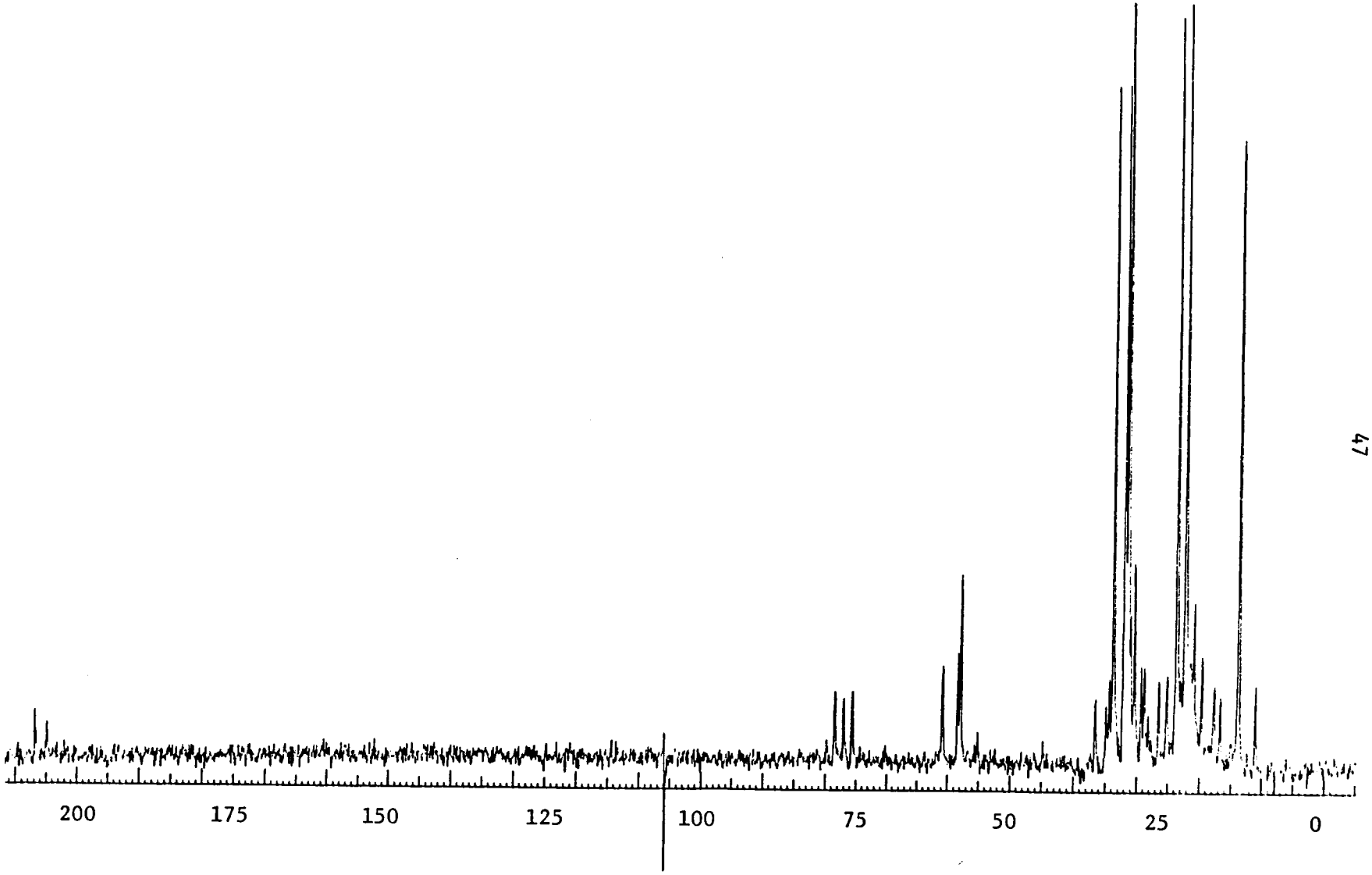


Figure 4-4. Carbon-13 NMR Spectrum of Dihexylbromoborane and Acetone Reaction Mixture.

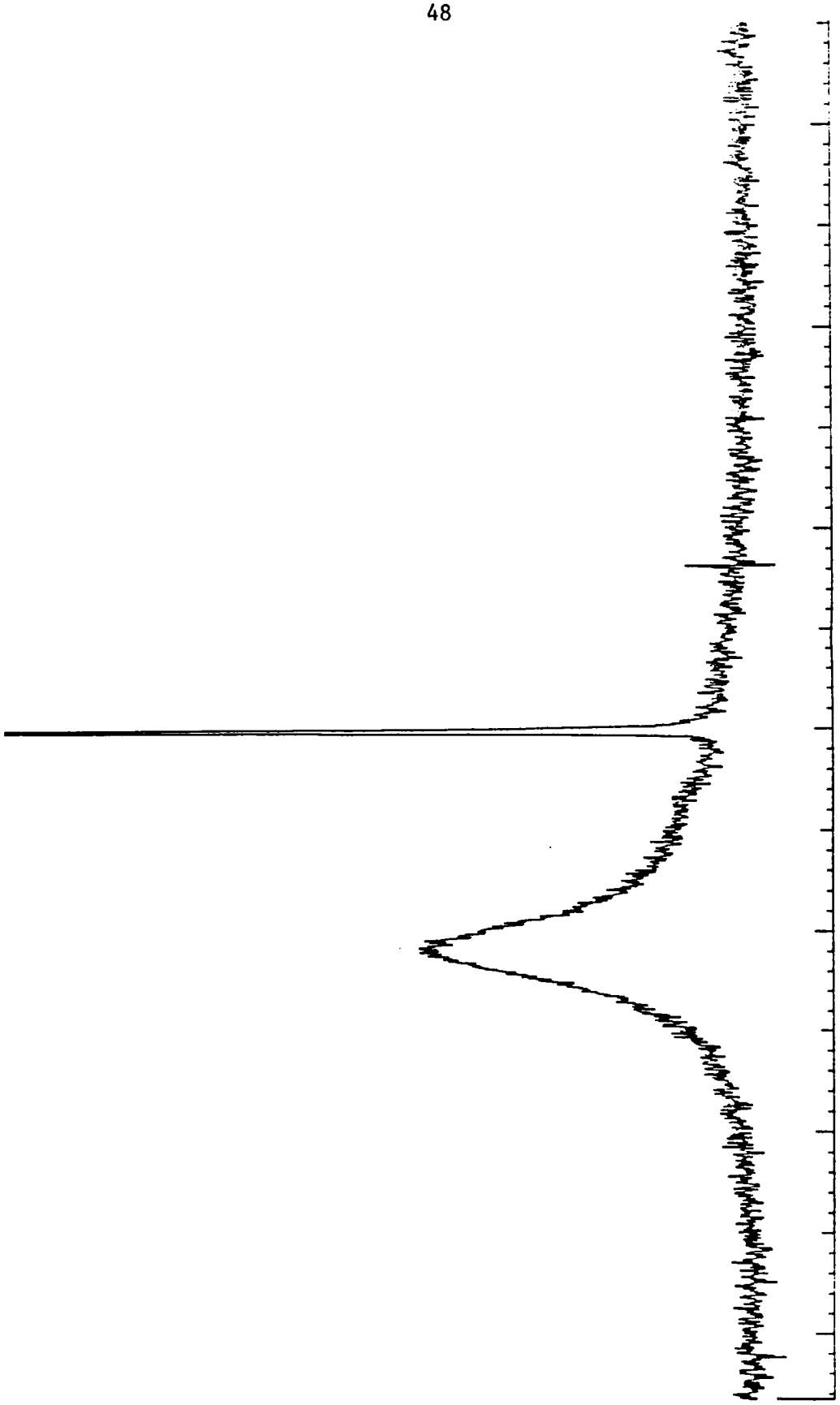
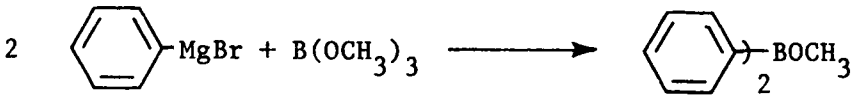


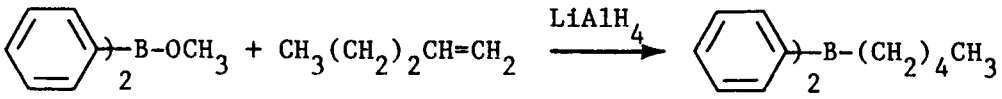
Figure 4-5. Boron-11 NMR Spectrum of Dihexylbromoborane and Acetone Reaction Mixture.

phenyl rings. An effort was made to synthesize pentyldiphenylborane by the method reported by Jacobs.[29] Methyl diphenylborinate was formed by the transmetallation reaction of phenyl magnesium bromide with trimethyl borate (equation 4-8). Methyl diphenylborinate was then treated with



(4-8)

lithium aluminum hydride in the presence of pentene to give pentyldiphenylborane (equation 4-9). At this point, the formation of the

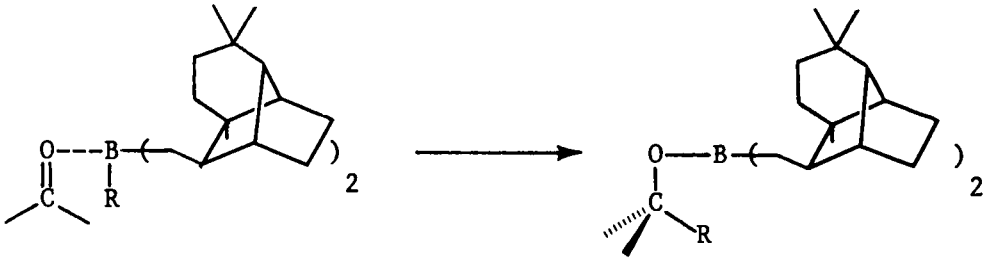


(4-9)

expected borane was not observed. Attempts to synthesize diphenylborohydride (δ = -15.4 ppm) were successful, but the hydroboration step did not occur. The alkene was still present in the reaction mixture (as evidenced by ^{13}C NMR) and the acetone added to destroy excess hydride was reduced to 2-propanol by the borohydride, as evidenced by a peak that developed in the ^{11}B NMR at 54 ppm. Numerous attempts were made to duplicate the published procedure, but failed due to the lack of detail in the original paper.

Dilongifolylborane is a hydroborating agent with unique steric restraints. The bulky longifolyl group is separated from the borane by a methylene unit, such that coordination with carbonyl groups should be

possible. Once the carbonyl group coordinated to the borane (XVIII), the steric hindrance might be great enough to force a migration of the alkyl group (equation 4-10). Dilongifolylborane can be obtained in



XVIII (4-10)

crystalline form, if the correct procedure is followed. Addition of approximately half the required amount of longifolene was carried out at 0^{o}, with stirring. Then stirring was discontinued and the mixture allowed to warm to room temperature, the remaining longifolene was added slowly, and the mixture allowed to stand overnight. The cessation of stirring and warming of the mixture was essential for obtaining crystalline product. The desired trialkylborane reagent was formed by reaction of dilongifolylborane with an alkene, as evidenced both by the disappearance of the solid dilongifolylborane and by NMR. However, no reaction was observed between acetone and alkyldilongifolylborane.

B. Conclusion

Modification of the boron-to-alkyl bond, via substitution on the boron atom, initially appeared to be the most convenient and generalized approach to the problem of carbonyl additions of organoboranes. In fact, it was determined that boranes which are strong enough Lewis acids

to coordinate to the carbonyl serve only to catalyze the aldol condensation reaction. The oxygen and sulfur atoms in the phenyl borinates and thiophenyl borinates apparently made the borane too electron rich and thus nonreactive towards the carbonyl group. At this point, it was concluded that polarization of the carbonyl bond would be a better approach to the problem. These experiments will be discussed in chapter five.

C. Experimental

1. General

All NMR spectra were recorded on a Jeol FX-90Q pulsed FT-NMR spectrometer. Carbon-13 NMR spectra were referenced to either deuteriocholorform, $CDCl_3$, (δ = 77.1 ppm), or boron trifluoride diethyl etherate, $BF_3{:}OEt_2$, (δ = 69.7 ppm). Boron-11 NMR spectra were referenced to boron trifluoride diethyl etherate (δ = 0.00 ppm). The commercially available chemicals are listed in Table 4-1.

2. 2-Cyclohexyl-2-propanol

A 250-mL round-bottomed flask equipped with a condenser, nitrogen inlet (and outlet) and magnesium turnings (2.4 g, 0.1 mole) was flame-dried and cooled under a nitrogen flow. The flask was charged with 20 mL of diethyl ether and a small amount of bromocyclohexane. Once the Grignard reaction had begun, evidenced by the formation of a grey precipitate, then bromocyclohexane (16.8 g, 0.1 mole) in 20 mL diethyl ether was added at such a rate as to maintain reflux. The mixture was allowed to stir at room temperature for two hours, then heated at reflux

Table 4-1: Manufacturer and Methods of Purification of Commercially Available Chemicals

Reagent	Manufacturer[a]	Method of Purification[b]
Acetone	M	
BH_3:DMS	A	
BF_3:OEt_2	A	
Bromobenzene	F	1
Bromobutane	E	1
Bromocyclohexane	E	1
p-Bromophenol	E	
1-Butene	MG	
Chloroform	M	
Cyclohexene	F	2
Deuteriochloroform	A	
Diethyl ether	M	3
1-Hexene	A	2
Hydrogen peroxide (30%)	F	
Lithium Aluminum Hydride (1M in diethyl ether)	A	
Longifolene	C	2
Magnesium turnings	F	
Methanol	M	
Monobromoborane:DMS (1M in dichloromethane)	A	
1-Pentene	A	

Table 4-1 (continued)

Reagent	Manufacturer[a]	Method of Purification[b]
Sodium	F	
Sodium hydroxide	M	
Sodium sulfate, anhydrous	M	
Thiophenol	A	1
Tribromoborane	A	
Trimethyl borate	A	

[a]Manufacturers
A = Aldrich
C = Camphor and Allied Products, Ltd., India
E = Eastman Organics
F = Fisher Scientific
M = Mallinckrodt
MG = MG Scientific Gases

[b]Methods of Purification
1. distilled
2. distilled from Na
3. distilled from Na /benzophenone

for an additional two hours until all the magnesium was gone. The mixture was then cooled in an ice-salt bath, and acetone (5.8 g, 0.1 mole) in 20 mL diethyl ether was added over 30 minutes. The mixture was stirred and then allowed to come slowly to room temperature overnight. Water was added to the reaction mixture to decompose the solid which formed. The ether layer was separated, dried over sodium sulfate, and the solvent removed under reduced pressure. The crude product was analyzed by ^{13}C NMR: ($CDCl_3$)δ 72.65 ppm, 49.12 ppm, 30.00 ppm, 27.45 ppm, 26.69 ppm.

3. 2-Methyl-2-hexanol

The above procedure paralleled that used for synthesizing 2-cyclohexyl-2-propanol, except the reagents were bromobutane (6.9 g, 0.05 mole), magnesium turnings (1.2 g, 0.05 mole), and acetone (2.9 g, 0.05 mole). The crude product was analyzed by ^{13}C NMR: ($CDCl_3$)δ 69.68 ppm, 42.43 ppm, 27.86 ppm, 25.31 ppm, 21.98 ppm, 12.80 ppm.

4. p-Bromophenyl Dicyclohexylborinate

A 250-mL round-bottomed flask equipped with a nitrogen inlet (and outlet) and a magnetic stirring bar was flame-dried and cooled under nitrogen flow. The flask was charged with cyclohexene (16.4 g, 0.2 mole) in 75 mL diethyl ether. The solution was cooled to 0° and borane:DMS (0.1 mole, 10 mL of a 10 M solution) was added over 30 minutes. Stirring was continued at 0° for three hours, during which time dicyclohexylborane precipitated as a white powder. p-Bromophenol (17.4 g, 0.1 mole) was added dropwise over 30 minutes at 0° and the

reaction mixture was then allowed to warm to room temperature over two hours. Ether was removed under nitrogen flow, and the product analyzed by ^{11}B and ^{13}C NMR: ($CDCl_3$)δ 55 ppm. ($CDCl_3$)δ 155 ppm, 132 ppm, 122 ppm, 115 ppm, 30-25 ppm (m).

5. Dialkylbromoborane: General Procedure

A 100-mL round-bottomed flask, equipped with a nitrogen inlet (and outlet) was flame-dried and cooled under nitrogen flow. Monobromoborane:DMS (25 mmole, 25 mL of a 1 M solution in dichloromethane) was added to the flask and cooled to 0^{o}. 1-Butene (3.57 g, 64 mmole) was condensed into a separate, dried, nitrogen-flushed flask, and then allowed to warm and distill into the monobromborane solution via a double ended needle. The mixture was stirred and allowed to warm slowly to room temperature over four hours. The mixture was then cooled to 0^{o}, and tribromoborane (2.4 mL, 25 mmole), contained in a graduated cylinder, was added to the flask via a double ended needle. The mixture was allowed to stir while warming to room temperature over four hours. Dichloromethane was removed under vacuum and the tribromoborane:DMS precipitated. The mixture of solid tribromoborane:DMS and liquid dibutylbromoborane was passed through a syringe barrel that had been capped with a septum and packed with glass wool, via a 12 gauge double ended needle (Figure 4-6). Dibutylbromoborane was obtained with a slight contamination of tribromoborane:DMS in 35% yield and was analyzed by ^{11}B and ^{13}C NMR: (CH_2Cl_2)δ 70 ppm, (CH_2Cl_2)δ 28 ppm, 25 ppm, 14 ppm.

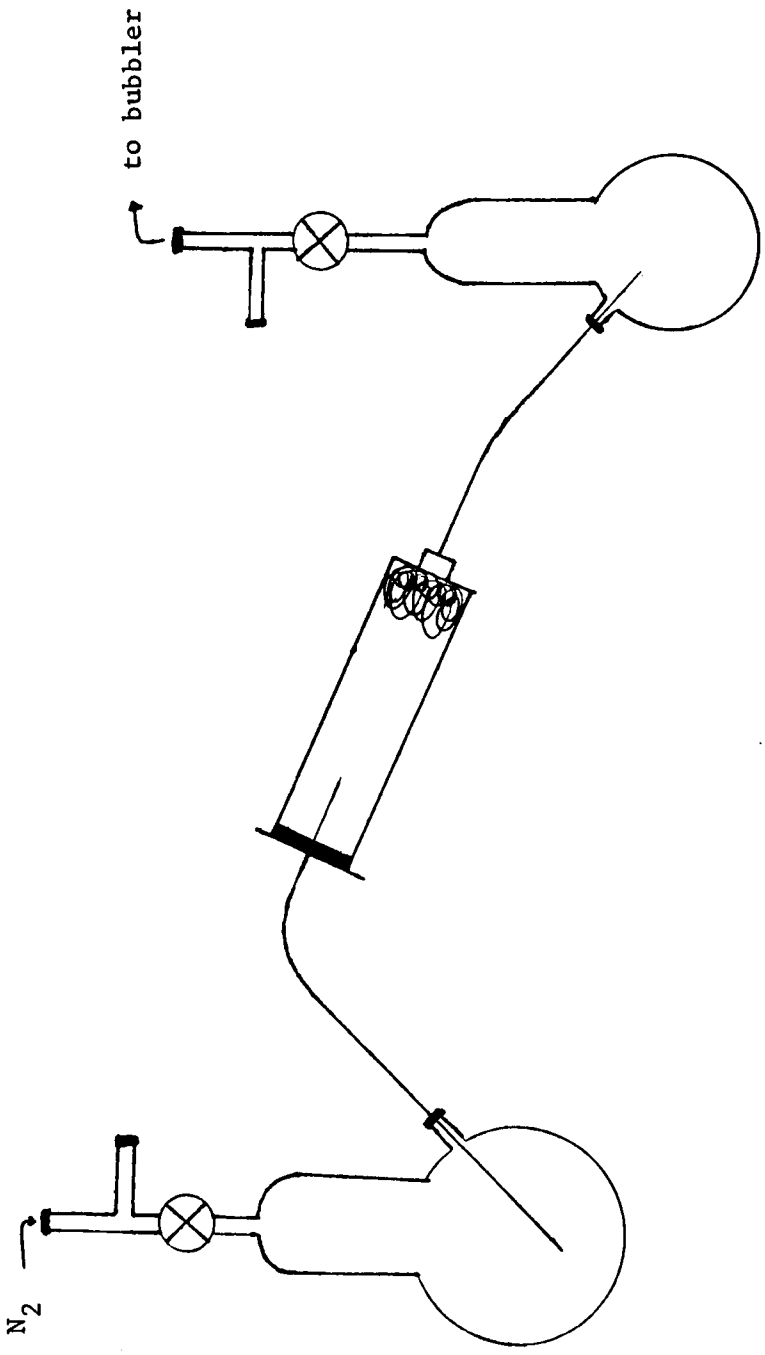


Figure 4-6. Apparatus Used for Filtration of Air Sensitive Liquids.

6. p-Bromophenyl Dibutylborinate

Dibutylbromoborane (0.73 g, 3.5 mmole) in a dry, nitrogen-flushed flask, was cooled to 0°, and a suspension of sodium p-bromophenoxide (4 mmole) in 5 mL benzene was added. The mixture was allowed to warm to room temperature over several hours. The product was analyzed by ^{11}B and ^{13}C NMR: ($CDCl_3$)δ 55 ppm, ($CDCl_3$)δ 154 ppm, 132 ppm, 131 ppm, 125 ppm, 26 ppm, 25 ppm, 14 ppm.

7. Thiophenyl Dipentylborinate

Dipentylbromoborane (5.04 g, 21.6 mmole) in a dry, nitrogen-flushed flask equipped with a nitrogen inlet (and outlet) was stirred with a suspension of sodium thiophenoxide (4.9 g, 37 mmole) in 25 mL dichloromethane at room temperature for thirty-six hours. The reaction was followed by ^{11}B NMR and was judged to be complete when all starting material had disappeared. The solid was removed by filtration through a syringe barrel packed with glass wool. The product was analyzed by ^{11}B and ^{13}C NMR: (CH_2Cl_2)δ 54 ppm, (CH_2Cl_2)δ 130-125 ppm (m), 39.5 ppm, 34.4 ppm, 23.4 ppm, 22.2 ppm, 13.8 ppm.

8. Methyl Diphenylborinate

A flask equipped with a condenser, nitrogen inlet and outlet, magnetic stirring bar and magnesium turnings (12.5 g, 0.05 mole) was flame-dried and cooled under nitrogen flow. Monobromobenzene (7.85 g, 0.05 mole) in 10 mL diethyl ether was added to the flask over 20 minutes, at such a rate as to maintain a gentle reflux. The mixture was stirred at room temperature for two hours, then heated at reflux for an

additional two hours. The reaction was judged to be complete when most of the magnesium was gone. Trimethyl borate (2.83 mL, 25 mmole) in 50 mL bis (2-methoxyethyl) ether was placed in a separate, dry, nitrogen-flushed flask and cooled to -7^{o} in an ice salt bath. Phenyl magnesium bromide was added dropwise to the stirring solution. The mixture was allowed to warm slowly to room temperature over four hours, during which time a precipitate formed. Aqueous hydrochloric acid (12.5 mL, 6 M) was then added to the cooled solution to destroy the "borate" complexes. The organic layer was separated and the solvent removed under reduced pressure. Diphenylborinic acid was then converted to the methyl borinate by azeotropic distillation with methanol (2.72 mL, 67 mmol) in chloroform (9.16 mL, 11 mmole). Methyl diphenylborinate was analyzed by ^{11}B NMR: ($CHCl_3$)δ 45 ppm.

9. Diphenylalkylboranes: General Procedure

To a flame-dried nitrogen-flushed flask equipped with a nitrogen inlet (and outlet) was added crude methyl diphenylborinate (5.17 g, 25 mmole) in 10 mL tetrahydrofuran. The solution was cooled to 0^{o} and 2.19 mL (20 mmole) pentene was added. A solution of lithium aluminum hydride in diethyl ether (6.67 mL, 6.67 mmole, 1 M) was then added dropwise to the stirring solution. Stirring was continued for one hour, then 2 mL acetone was added to destroy excess hydride. The mixture was analyzed by ^{11}B NMR: ($CDCl_3$)δ 45 ppm. Carbon-13 NMR showed alkene still present in all cases.

10. Dilongifolylborane

A flame-dried, nitrogen-flushed flask was charged with borane:DMS (10 mmole, 10 mL of a 10 M solution) in 10 mL diethyl ether. Longifolene (7.0 mL, 31.79 mmole) was added in two portions. Approximately 3.5 mL was added dropwise to borane:DMS at 0°, with stirring. The ice bath was removed and stirring stopped, and the mixture allowed to warm to room temperature. The remaining portion was added dropwise, and the mixture allowed to stand overnight, during which time the crystalline dilongifolylborane precipitated. The liquid was removed by filtration, and the crystals washed several times with 10 mL portions of diethyl ether. All remaining traces of solvent were removed under vacuum to give 2.62 g (6.23 mmole, 62.3%) of crystalline dilongifolylborane.

11. Alkyldilongifolylborane: General Procedure

To the flask containing dilongifolylborane (2.62 g, 6.23 mmole) was added 20 mL diethyl ether. 1-Hexene (0.48 g, 5.7 mmole) was added to the stirred suspension and the stirring continued overnight to insure complete hydroboration. NaOH (2.19 mL, 3 N) and H_2O_2 (2.1 mL, 30%) were added to the clear solution at 0°. The mixture was warmed slowly and then refluxed for two hours. The organic layer was separated and dried over Na_2SO_4. The solvent was removed under reduced pressure and the mixture analyzed by GC. A mixture of the two alcohols was obtained in 89% yield.

12. Reactions with Acetone: General Procedure

To a measured amount of the borane in a flask, or NMR tube, was added a slight excess of acetone. The reaction was followed by NMR over the course of a day or longer, with heating or sonication if no reaction was observed in the first few hours. In instances where a reaction was indicated, the experiments were repeated on a scale which would permit product identification.

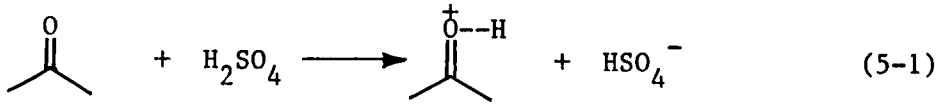
CHAPTER V

POLARIZATION OF THE CARBONYL BOND

A. Results and Discussion

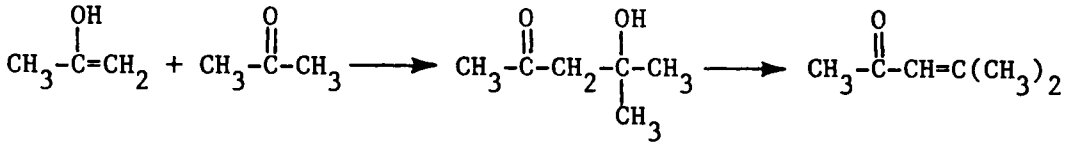
The 1,2 addition of organometallic reagents to the carbonyl moiety generally proceeds via initial coordination of the metal atom to the carbonyl oxygen followed by transfer of an alkyl group to the carbonyl carbon. Modification of the borane reagent, as described in the previous chapter, was limited by the synthetic methods available. It was desired to make the proposed reaction between organoboranes and carbonyl compounds a general one, so that it would be applicable to a broad range of aldehydes and ketones. This requirement guided the attempts to polarize the carbonyl moiety.

The first approach to the problem was to investigate the effect of various solvents on the reaction of tributylborane with acetone. Solvents with a range of polarities were studied, including hexane, benzene, diethyl ether, acetone and acetonitrile. In all cases, no change in chemical shift was observed, either in the ^{13}C or ^{11}B NMR spectrum. Oxidative workup of the reaction mixture with alkaline hydrogen peroxide gave only starting ketone and butanol, the expected product from oxidation of the borane. It is known that aliphatic and aromatic ketones are almost completely protonated in concentrated sulfuric acid (equation 5-1).[59] The conjugate acid of the ketone is strongly polarized



(5-1)

and might be intercepted by a trialkylborane to achieve alkyl migration to the carbonyl carbon. There were two difficulties with this approach. Enolization of the conjugate acid was quickly followed by aldol condensation to give mesityl oxide (equation 5-2). This reaction was followed



(5-2)

by monitoring changes in the ^{13}C NMR spectrum over time, and by examination of the reaction products. A second difficulty is the fact that the formation of the conjugate acid is concentration dependent. Thus, in absolute sulfuric acid, nearly 100% of the acetone (pKa = -7.2) is in its conjugate acid form, but only 50% of the acetone is protonated in 82% sulfuric acid.[60] Consequently, dilution of the sulfuric acid-acetone mixture with the trialkylborane served only to deprotonate the ketone, and no reaction, aside from aldol condensation, was observed.

Liquid carbon dioxide was also investigated as a solvent for the reaction between acetone and tributylborane. This unusual solvent behaves like a typical hydrocarbon solvent, but has a low polarizing effect.[61] The carbonyl stretching frequency in the infrared is a measure of the degree to which a carbonyl group is polarized. Table 5-1 shows the effect of liquid carbon dioxide on the carbonyl stretching frequency of acetone as compared to other solvents.[61]

Table 5-1: Solvent Effects on $\nu_{C=O}$ of Acetone

Solvent	ν_{co}, cm^{-1}	$\Delta\nu_{co}$
none (gas phase)	1736	0
n-hexane	1722	14
CO_2 (liquid)	1720	16
benzene	1716	20
chloroform	1712	24
methanol	1709	27

The reaction was performed by placing approximately thirty grams of Dry Ice in a high pressure reaction vessel (Parr) with acetone and tributylborane (in equimolar amounts), sealing the unit, and allowing the mixture to stir overnight. The pressure was released and an NMR spectrum of the reaction mixture was obtained under inert atmosphere. It was determined that the borane underwent oxidation presumably caused by the oxygen present in the Dry Ice. No reaction with acetone was observed.

In order to avoid the presence of oxygen, Dry Ice was condensed from a cylinder of pure (99.99%) carbon dioxide gas into the high pressure vessel. Tributylborane and acetone were added in equimolar amounts, the vessel sealed and the mixture stirred overnight. Little oxidation of the borane was observed under these conditions. However, following oxidative workup (in alkaline hydrogen peroxide), none of the desired 1,2 addition product was observed, and acetone and butanol were recovered.

Polarization of the carbonyl moiety was then attempted via complexation with cations, such as lithium. A saturated solution of lithium chloride in acetone was prepared by warming the acetone gently while stirring over excess lithium chloride. A 1 ppm shift to higher field was observed in the ^{13}C NMR spectrum for both the carbonyl and methyl peaks. Because of complexation with the lithium ion, the carbonyl group would not be available to complex with tributylborane and an alkyl migration would not be expected. (Experiments involving lithium chloride-acetone mixtures with an equimolar amount of tributylborane confirmed this postulation.) In an effort to supply a more nucleophilic alkylation reagent, a tetraalkylborate was utilized instead of tributylborane.

Lithium tetra-n-butylborate was synthesized by treating tributylborane in diethyl ether with an equimolar amount of n-butyllithium in hexane (equation 5-3). After stirring for two hours in the cold, the

$$(n\text{-Bu})_3B + n\text{-BuLi} \longrightarrow (n\text{-Bu})_4B^-Li^+ \qquad (5\text{-}3)$$

mixture was transferred to a septum-capped erlenmeyer flask for storage. Boron-11 NMR indicated a major peak at -17.9 ppm, which corresponds to the chemical shift reported in the literature for lithium tetrabutylborate.[52] A minor peak at -16.6 ppm was also observed. This peak is due to the organoborate salt formed by reaction of n-butyllithium with a small amount of butyl dibutylborinate present as an impurity in the commercially available tributylborane (equation 5-4). Addition of the

$$\underline{n}\text{-BuLi} + \text{BuO-B}(\underline{n}\text{-Bu})_2 \longrightarrow [\text{BuO-B}(\underline{n}\text{-Bu})_3]^-\text{Li}^+ \qquad (5\text{-}4)$$

lithium chloride-acetone mixture to the tetra-n-butylborate resulted in a color change, but the NMR spectra showed no reaction. While it is clear that lithium chloride has a polarizing effect on the carbonyl, it is apparent that this effect is not sufficient to allow the carbonyl addition reaction to occur.

In an effort to polarize the carbonyl moiety to a greater degree, boron trifluoride diethyl etherate was then utilized as a complexing agent. Polarization was observed (a downfield shift in the NMR spectrum for the carbonyl carbon). Further reaction in the presence of either tributylborane or lithium tetra-n-butylborate resulted only in the formation of the aldol condensation product, as is evident in the ^{13}C NMR spectrum (Figure 5-1). While formation of the aldol product is not unexpected, it was desired to intercept the intermediate, polarized carbonyl with lithium tetra-n-butylborate. Unfortunately, the aldol addition product appears to form faster than the desired migration reaction. An additional complication involves the fact that lithium tetra-n-butylborate disproportionates in the presence of boron trifluoride diethyl etherate to give tributylborane and lithium tetrafluoroborate (equation 5-5) as is apparent in the ^{11}B NMR spectrum (Figure 5-2).

$$4\ BF_3 + 3\ (n\text{-Bu})_4B^-Li^+ \rightarrow 4\ (n\text{-Bu})_3B + 3\ LiBF_4 \qquad (5\text{-}5)$$

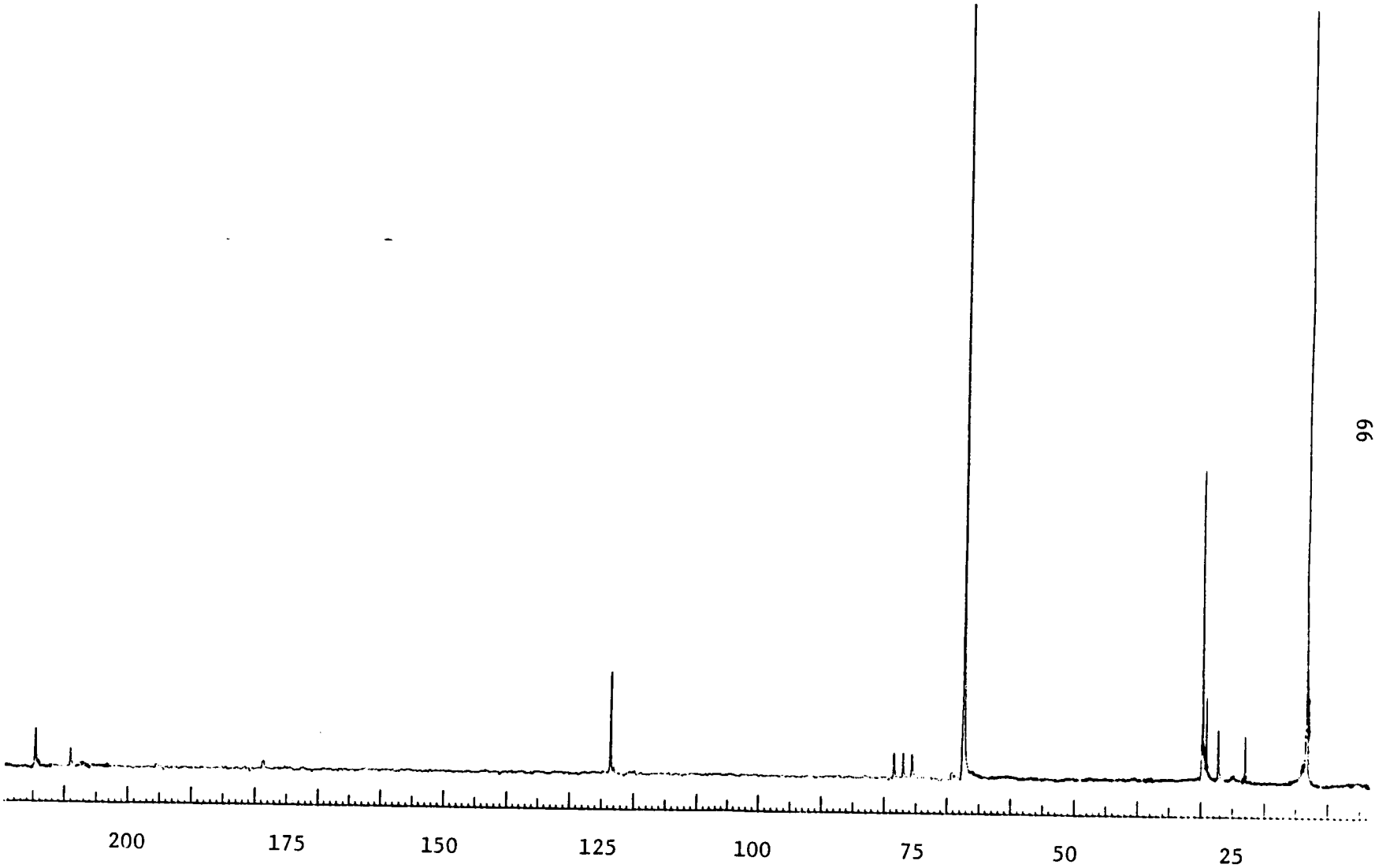


Figure 5-1. Carbon-13 NMR Spectrum of Acetone and Boron Trifluoride Diethyl Etherate Reaction Mixture.

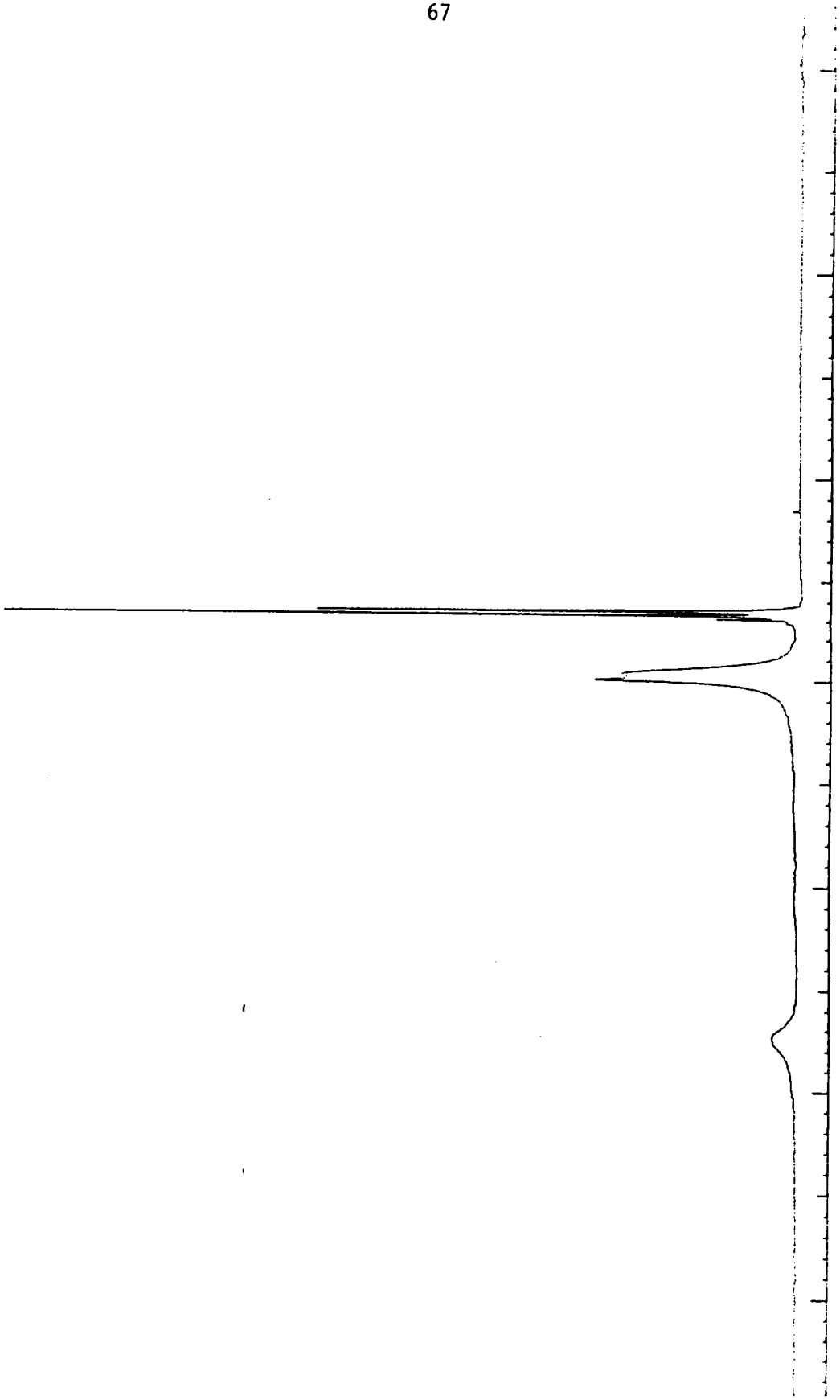
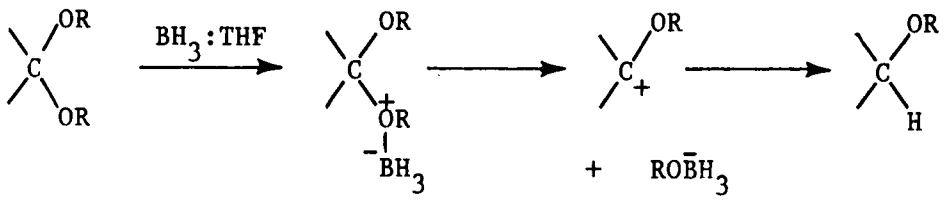


Figure 5-2. Boron-11 NMR Spectrum of Lithium Tetra-n-butylborate and Boron Trifluoride Diethyl Etherate Reaction Mixture.

Less polarizing complexing agents that would have a smaller effect on the carbonyl group were then investigated. Copper(I) chloride was added to an equimolar amount of acetone, and tributylborane (as a 1 M solution in diethyl ether) was added to the stirred suspension. No complexation or reaction was observed. The addition of zinc chloride and tin(II) chloride also failed to produce the desired 1,2 addition product.

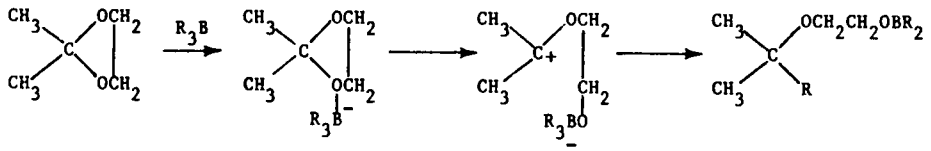
It was felt that these metal ions might also participate in transmetallation reactions, analogous to those observed in copper(I) catalyzed addition reactions of the organomagnesium reagents. This was not found to be the case for the trialkylboranes. The reaction of acetone and tetra-n-butylborate in the presence of zinc chloride or tin(II) chloride resulted in no reaction with acetone.

Polarization of the carbonyl was then attempted by preparing a number of derivatives which, in essence, are "hidden" carbonyl compounds. For example, borane:tetrahydrofuran is known to cleave acetals and ketals via complexation of the boron atom to one of the oxygen atoms, cleavage of the oxygen-carbon bond and migration of a hydride to the resultant carbocation (equation 5-6).[62] It was anticipated that the



(5-6)

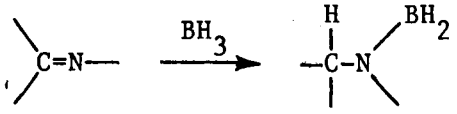
Lewis acidity of trialkylboranes could be sufficient to allow a similar reaction, resulting in an alkyl transfer to a carbonyl carbon (equation 5-7). When the ethylene glycol ketal of acetone was treated with



(5-7)

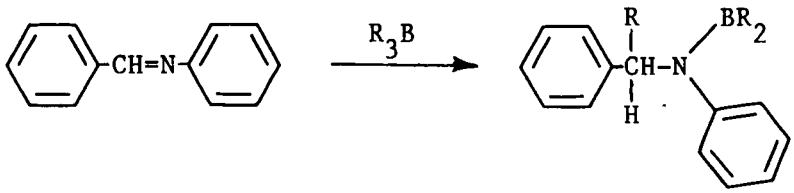
tributylborane in diethyl ether, no changes were observed in the NMR spectra and alkaline hydrogen peroxide oxidation gave only butanol (the expected product of oxidation of the starting borane) and the ketal, as evidenced in the NMR spectra. (Figure 5-3, 5-4).

Boranes are also known to reduce imines (equation 5-8).[63] Coordi-



(5-8)

nation (and polarization) is possible between the imine nitrogen and the trialkylborane, and this could then enhance the rate of alkyl group transfer (equation 5-9).



(5-9)

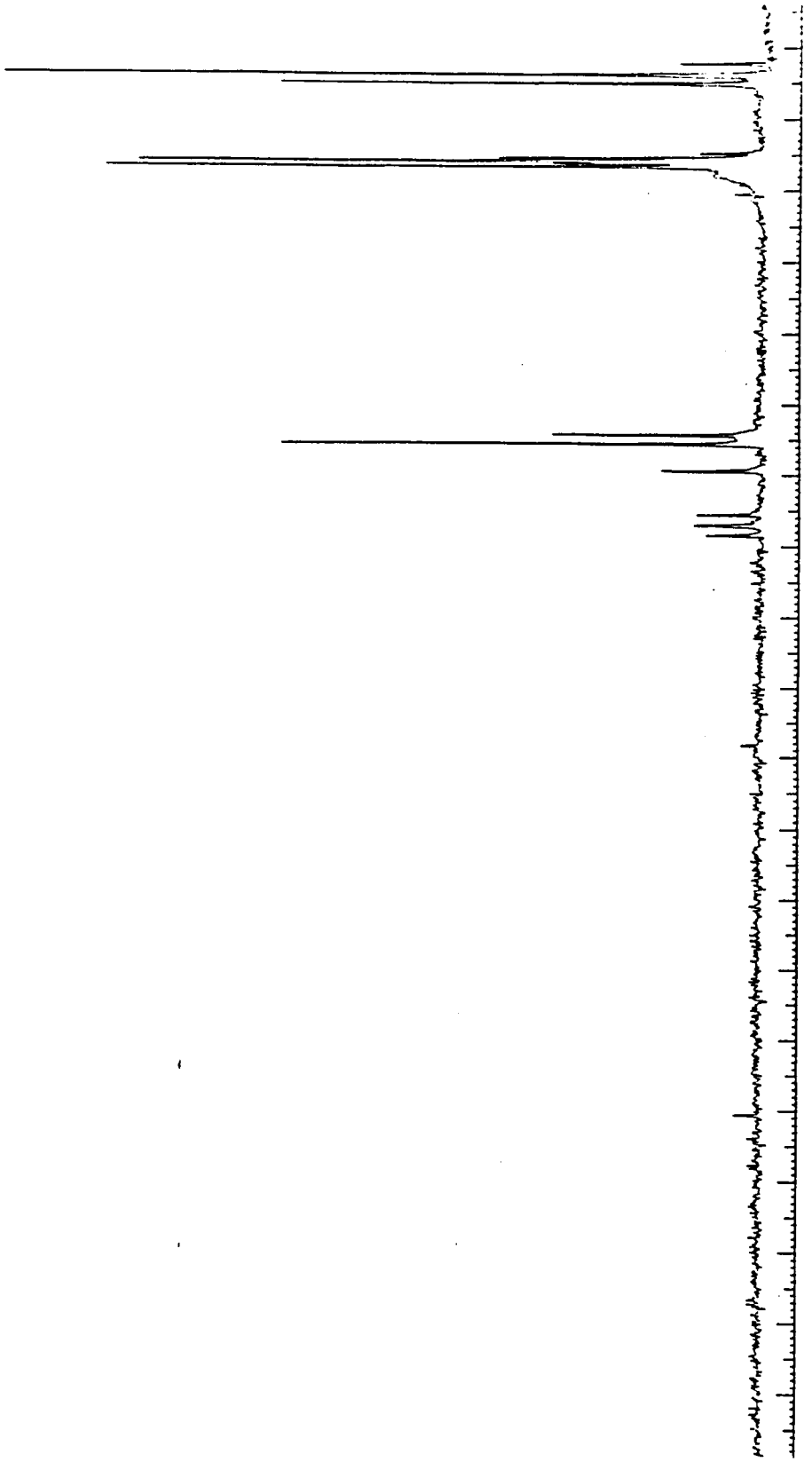


Figure 5-3. Carbon-13 NMR Spectrum of Tributylborane and 2,2-Dimethyl-1,3-Dioxolane Reaction Mixture.

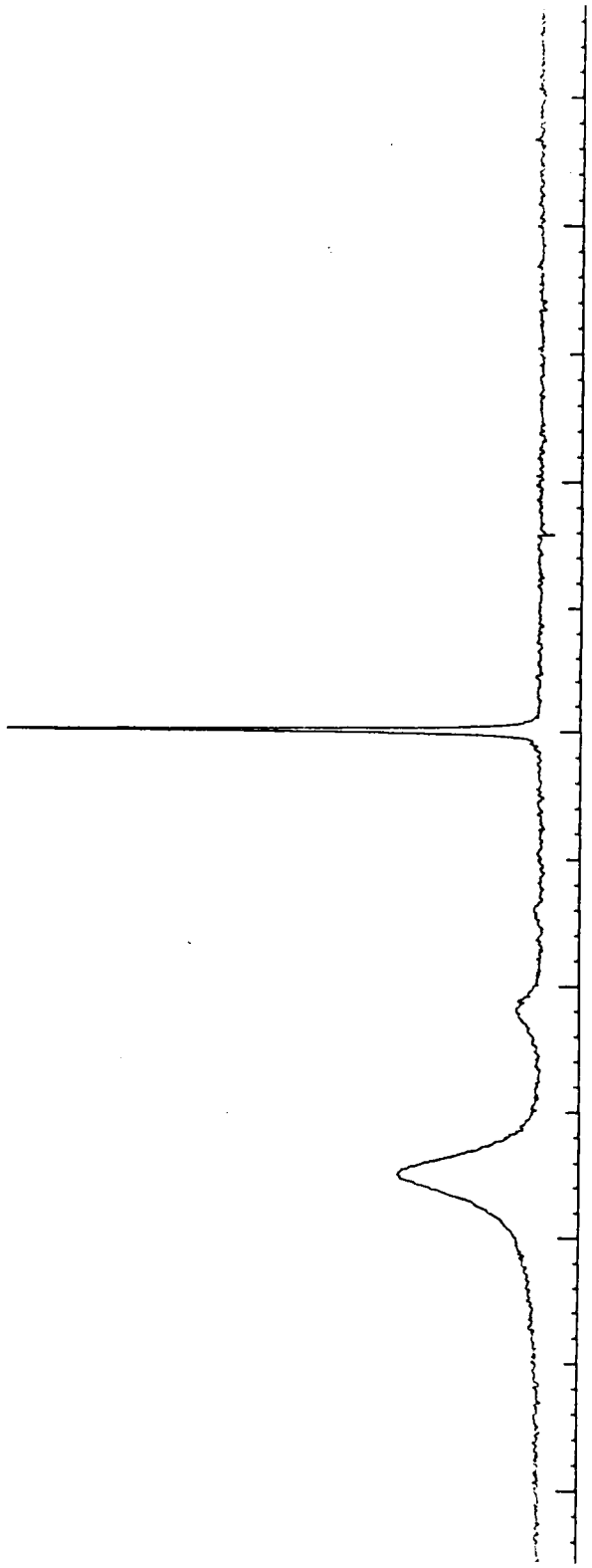
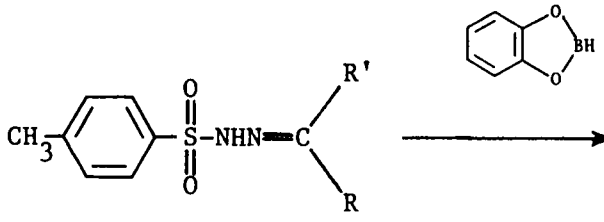


Figure 5-4. Boron-11 NMR Spectrum of Tributylborane and 2,2-Dimethyl-1,3-Dioxolane Reaction Mixture.

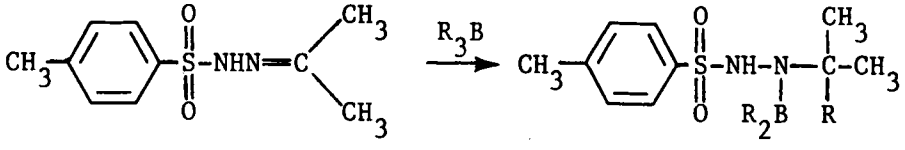
N-Benzilidene aniline was synthesized by the reported method.[64] Following treatment with tributylborane, oxidation of the reaction mixture failed to produce the desired product, the alkylated amine.

Catecholborane, a weak Lewis acid, is known to reduce p-toluenesulfonylhydrazone derivatives of ketones (equation 5-10).[65] The



(5-10)

p-toluenesulfonylhydrazone derivative of acetone was synthesized and treated with tributylborane, in an attempt to obtain the analogous alkyl migration (equation 5-11). No reaction was observed.

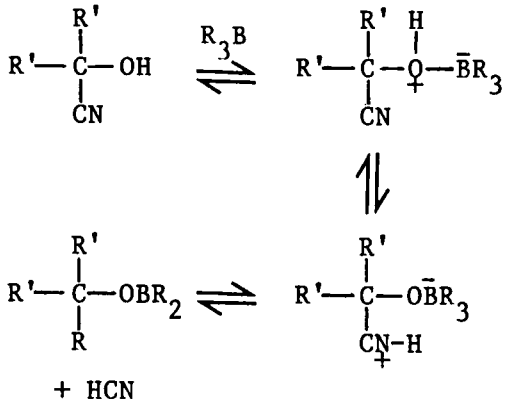


(5-11)

The 2,4-dinitrophenylhydrazone derivative of acetone was also synthesized. Treatment with tributylborane failed to bring about any reaction.

An attempt was made to achieve a 1,2 addition to the carbonyl moiety by attaching a leaving group to the original carbonyl carbon. To this end, acetone cyanohydrin was synthesized via the bisulfite addition product.[66] The proposed reaction would occur as outlined in Scheme II.

Scheme II:

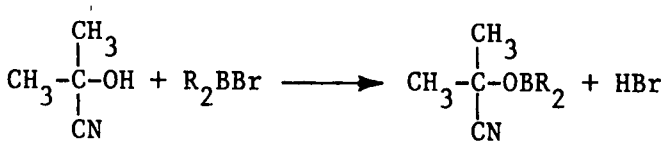


Treatment with tributylborane failed to produce the desired 1,2 addition product, and no change was observed in either the ^{13}C or ^{11}B NMR spectrum.

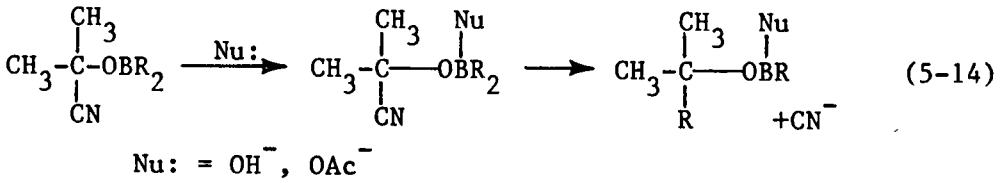
Since the lack of reaction could be due to an inefficient complexation between the trialkylborane and the cyanohydrin, the use of borinate intermediates was then investigated. Dialkylbromoboranes are known, for example, to undergo condensation reactions with alcohols (equation 5-12). This reaction was utilized to form the borinic ester

$$R'OH + R_2BBr \longrightarrow R_2BOR' + HBr \qquad (5\text{-}12)$$

(equation 5-13). Nucleophilic attack on the boron atom (accomplished



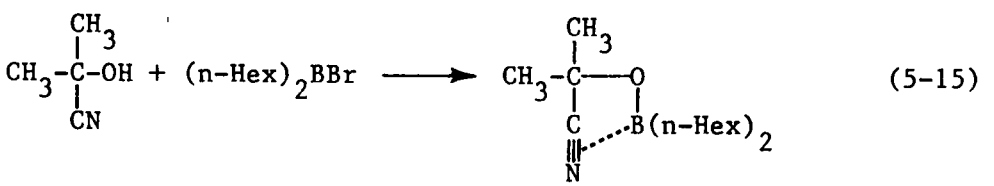
via the addition of hydroxide or acetate ion) would form the borate, which might then undergo intramolecular 1,3 migration to displace cyanide ion and form the desired product (equation 5-14).



(5-14)

Nu: = OH^-, OAc^-

Considerable changes in both the ^{13}C and ^{11}B NMR spectra were observed. Acetone cyanohydrin exhibits resonances in the ^{13}C NMR at 123 ppm, due to the nitrile carbon, at 65 ppm due to the hydroxy carbon and a single resonance at 29 ppm due to the methyl carbons (Figure 5-5). Immediately upon addition of dihexylbromoborane, the two resonances at 123 ppm and 65 ppm disappear, and two new resonances at 161 ppm and 90 ppm appear (Figure 5-6). A resonance in the ^{11}B NMR spectrum at 56 ppm (shifted from 70 ppm) can be rationalized as arising from the condensation reaction leading to the borinate ester (Figure 5-7). Initially, these results were attributed to a reaction involving the alkoxyborane and the nitrile moiety, resulting in the reduction of the nitrile bond. However, addition of water or dilute base results in the recovery of the cyanohydrin, implying that the changes observed in the NMR spectra were due to the complexation with the alkoxyborane (equation 5-15). While complexation had clearly occurred in this case, none of



(5-15)

the desired reaction was observed.

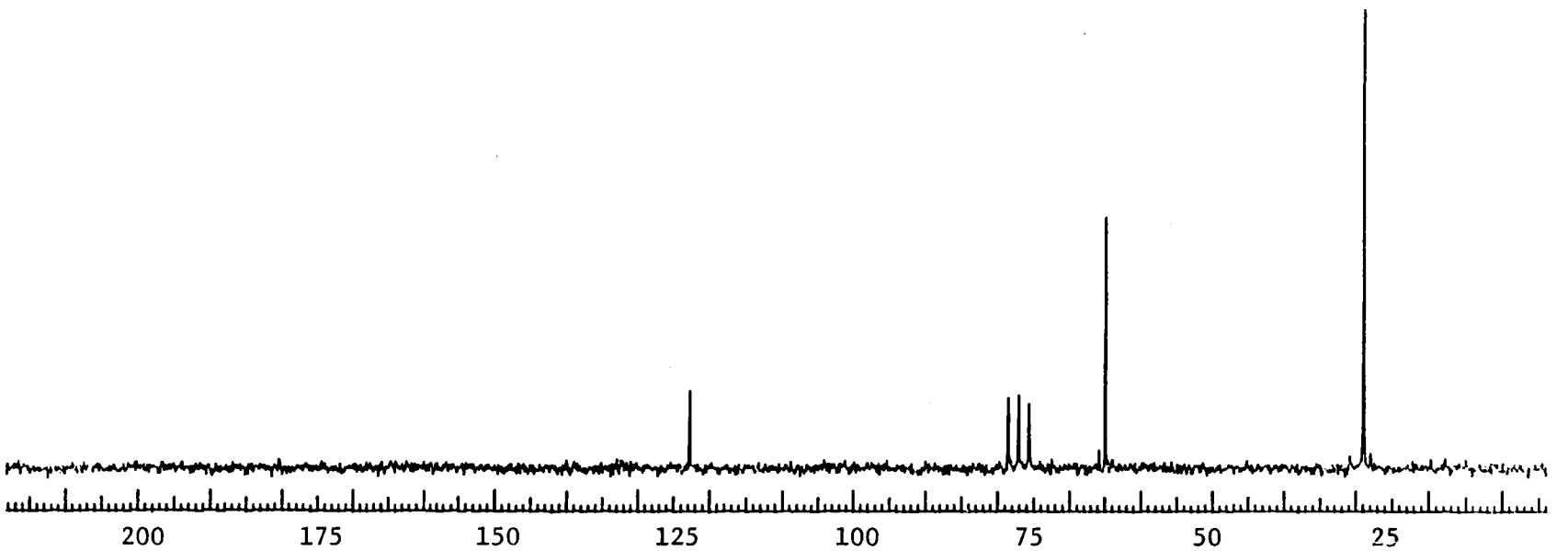


Figure 5-5. Carbon-13 NMR Spectrum of Acetone Cyanohydrin.

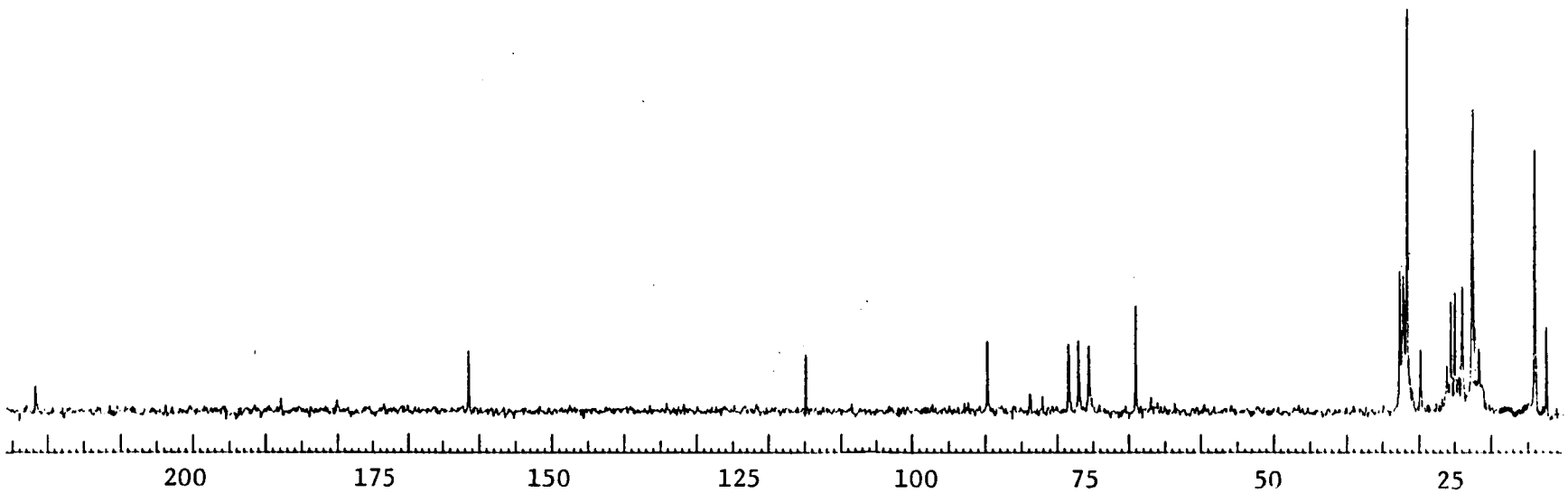


Figure 5-6. Carbon-13 NMR Spectrum of Acetone Cyanohydrin and Dihexylbromoborane Reaction Mixture.

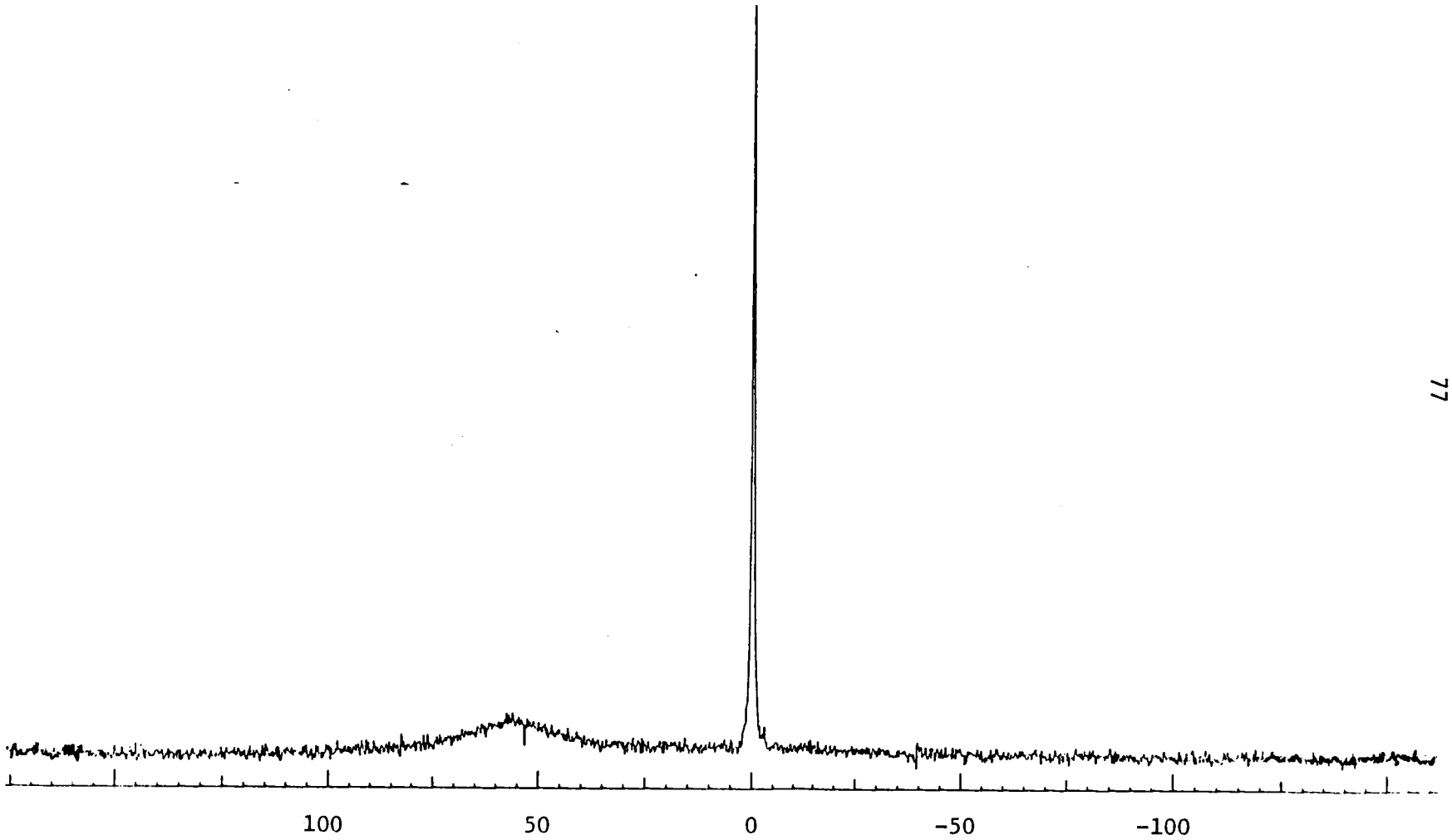
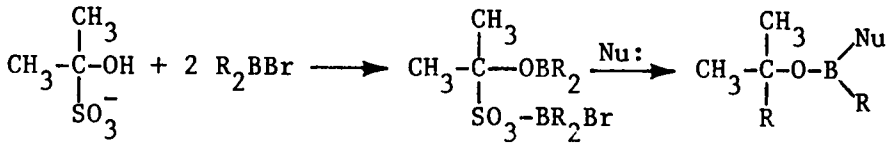


Figure 5-7. Boron-11 NMR Spectrum of Acetone Cyanohydrin and Dihexylbromoborane Reaction Mixture.

The bisulfite addition product of acetone was also treated with an excess of dialkylbromoborane in order to affect the condensation reaction with the hydroxyl function to generate the alkoxy borane. It was anticipated that nucleophilic displacement of the bisulfite group by the alkyl moiety could be induced by nucleophilic attack on the borane (equation 5-16).



(5-16)

In fact, a shift in resonance in the boron NMR from 70 ppm to 56 ppm was observed, which could correspond to formation of the borinate ester. Migration was not induced with the addition of hydroxide as the nucleophile, however.

B. Conclusion

In the series of experiments reported in this chapter, attempts were made to polarize the carbonyl by a variety of methods. From these results, it was determined that solvent has little effect on the reaction. It was also concluded that several carbonyl derivatives are stable to trialkylboranes. For example, the ketal group is known to revert to the starting ketone in the presence of acid, but is apparently stable to the weak Lewis acidity of the organoboranes. Simple cations are relatively ineffective at polarizing the carbonyl group, and yet those Lewis acids which strongly coordinate to the carbonyl group lead to aldol condensation products. It may be possible to find a complexing agent with an intermediate Lewis acidity which would catalyze the 1,2

addition reaction, without formation of the aldol product. The drawback to this approach is that the Lewis acids also catalyze organoborane disproportionation reactions. On the other hand, if not sufficiently reactive, the complexing agent will not coordinate to the carbonyl. Placing a leaving group on the carbonyl carbon, to direct the reaction via nucleophilic displacement, also has possibilities that should be explored further. The bisulfite addition product of acetone fails to undergo the desired reaction, perhaps due to insufficient nucleophilicity of the alkyl moiety. The nitrile nitrogen of the cyanohydrin is capable of coordinating with the organoborane, thus effectively blocking nucleophilic attack by another nucleophile. Unfortunately, this coordination is insufficient to bring about the desired nucleophilic displacement reaction.

There are other approaches to the 1,2 addition of organoboranes to carbonyl compounds which have not been explored in this thesis: polarization via photochemical or electrochemical excitation of the carbonyl bond; molten salt solvents; or development of a nucleophilic leaving group that would not attack the borane.

C. Experimental

1. General

All NMR spectra were recorded on a Jeol FX 90Q pulsed FT NMR spectrometer. Carbon-13 NMR spectra were referenced to deuteriochloroform ($CDCl_3$, δ = 77.1 ppm). Boron-11 NMR spectra were referenced to boron trifluoride diethyl etherate ($BF_3{:}OEt_2$, δ = 0.0 ppm). Table 5-2 contains a list of commercially available reagents, their

Table 5-2: Manufacturers and Methods of Purification of Commercially Available Chemicals

Reagent	Manufacturer[a]	Method of Purification[b]
Acetonitrile	F	1
Aniline	F	1
Benzaldehyde	F	1
Benzene	M	1
Carbon dioxide	MG	
Copper(I) chloride	A	
2,4-Dinitrophenylhydrazine	E	
Ethanol (95%)	F	
Ethylene glycol	F	1
Hexane	M	1
Lithium chloride	F	
Magnesium sulfate	M	
Sodium bisulfite	F	
Tin(II) chloride	M	
p-Toluenesulfonic acid	F	
p-Toluenesulfonylhydrazine	A	
Tributylborane (1M solution in diethyl ether)	A	
Triethyl orthoformate	E	
Zinc chloride	R	

[a] A = Aldrich
E = Eastman Organics
F = Fisher
M = Mallinckrodt
MG = MG Scientific Gases
R = Merck

[b] 1 = distilled

manufacturers and methods of purification. (Several reagents are listed in Table 4-1, p. 52, and are not repeated here.)

2. Solvent Study: General Procedure

A 50-mL flask equipped with nitrogen inlet (and outlet) and magnetic stirrer was flame-dried, and cooled under nitrogen flow. The flask was then charged with tributylborane (5 mmole, 5 mL of a 1M solution in diethyl ether). Nitrogen flow was used to remove the ether solvent, then 5 mL hexane was added. Acetone (0.37 mL, 5 mmole) was added, and the mixture stirred overnight. After an NMR spectrum was taken under inert atmosphere, the reaction mixture was oxidized via addition of NaOH (7.5 mmole, 2.5 mL of a 3N solution) and H_2O_2 (22.5 mmole, 2.5 mL of a 9M solution) at 0°. The mixture was warmed to reflux and heated for two hours. The organic layer was separated, dried briefly over anhydrous sodium sulfate, concentrated, and analyzed by NMR.

3. Solvent Study: Concentrated Sulfuric Acid

Acetone (5.8 g, 10 mmole) and concentrated sulfuric acid (10 mmole, 0.55 mL of a 98% solution) were combined at 0°, with stirring, in a nitrogen flushed flask. To this solution was added, dropwise, tributylborane (10 mmole, 10 mL of a 1 M solution in diethyl ether). NMR spectra obtained under inert atmosphere were recorded periodically throughout the course of the reaction.

4. Solvent Study: Liquid Carbon Dioxide

A 22.5 mL Parr reaction vessel equipped with magnetic stirrer was flushed with argon while cooling in a liquid nitrogen bath. Carbon dioxide (approximately 30 g) was condensed from a cylinder of the pure gas (99.99%) into the reaction vessel. Tributylborane (5 mmole, 5 mL of a 1M solution in diethyl ether) and acetone (0.37 mL, 5 mmole) were added to the reaction vessel at -78°. The vessel was then sealed, and the mixture was warmed to room temperature and stirred overnight. Pressure was released slowly to avoid loss of the borane, then the reaction vessel was opened, capped with a septum and the reaction mixture transferred to a nitrogen flushed NMR tube via a double ended needle. Carbon-13 NMR showed no change, but ^{11}B NMR showed resonances at 89 ppm, 56 ppm, 30 ppm, and 18 ppm, due to air oxidation of the borane. To confirm that this was the case, the reaction mixture was transferred to a 50-mL flask equipped with a condenser and magentic stirring bar. After cooling to 0°, NaOH (7.5 mmole, 2.5 mL of a 3N solution) and H_2O_2 (22.5 mmole, 2.5 mL of a 9M solution) were added. The mixture was then warmed to reflux, and heated for two hours. The organic layer was separated, dried briefly over sodium sulfate, and concentrated. Carbon-13 NMR indicated the presence of butanol and acetone. No product was observed.

5. Lithium Tetra-n-Butylborate

A flame-dried, nitrogen-flushed flask equipped with a nitrogen inlet (and outlet) was charged with tributylborane (25 mmole, 25 mL of a 1M solution in diethyl ether). The stirring solution was cooled to -20°

in a Dry Ice-acetone bath, and n-butyllithium (25 mmole, 15.63 mL of a 1.6M solution in hexane) was added dropwise. Stirring was continued for two hours, then the solution was transferred to a pre-calibrated, septum-capped erlenmeyer flask and the total volume diluted to 50 mL with diethyl ether, to give a 0.5M solution of lithium tetra-n-butylborate in a mixture of diethyl ether and hexane. The product was analyzed by ^{11}B NMR: (diethyl ether/hexane)δ -16.6 ppm, -17.9 ppm.

6. Cation Complexation: Lithium Chloride

Lithium chloride (0.42 g, 10 mmole) was placed in a 50-mL flask equipped with a magnetic stirrer and nitrogen inlet (and outlet). The flask was then flushed with nitrogen, and acetone (0.37 mL, 5 mmole) was added. The flask was warmed briefly, then cooled, and tributylborane (5 mmole, 5 mL of a 1M solution in diethyl ether) was added. Nitrogen flow was used to remove most of the solvent. After stirring for several hours, NMR spectra under inert atmosphere were obtained, and these indicated no change for either ^{13}C or ^{11}B.

7. Cation Complexation: Copper(I) Chloride

Copper(I) chloride (0.3 g, 3 mmole) was placed in a 50-mL flask equipped with a magnetic stirrer and nitrogen inlet (and outlet). The flask was flushed with nitrogen, and tributylborane (3 mmol, 3 mL of a 1M solution in diethyl ether) was added. Nitrogen flow was used to remove the solvent. Acetone (0.26 mL, 3 mmol) was added to the flask. Stirring was continued for several hours, and ^{13}C and ^{11}B NMR spectra were obtained, indicating no reaction.

8. Cation Complexation: Tin(II) Chloride

Tin(II) chloride (0.95 g, 5 mmole) was added to a 50-mL flask equipped with a magnetic stirrer and nitrogen inlet (and outlet). The flask was flushed with nitrogen, then tributylborane (5 mmole, 5 mL of a 1M solution in diethyl ether) was added, and nitrogen flow used to remove most of the solvent. Acetone (0.37 mL, 5 mmol) was added, and the tin(II) chloride was observed to dissolve. Two layers separated, but were miscible in $CDCl_3$ added as an NMR solvent. The mixture was stirred for several hours hours before NMR spectra were obtained under inert atmosphere. No reaction or coordination was indicated by NMR.

9. Cation Complexation: Zinc Chloride

A 50-mL flask equipped with magentic stirrer, nitrogen inlet (and outlet), and zinc chloride (0.68 g, 5 mmole) was flushed with nitrogen, then charged with tributylborane (5 mmole, 5 mL of a 1M solution in diethyl ether). The solvent was removed by nitrogen flow. Acetone (0.37 mL, 5 mmole) was added, and the zinc chloride was observed to dissolve. A second layer separated, but both layers were miscible in $CDCl_3$, added as an NMR solvent. After stirring for several hours at room temperature, NMR spectra were obtained under inert atmosphere. No reaction was indicated.

10. 2,2-Dimethyl-1,3-Dioxolane

To a 125-mL erlenmeyer flask was added, sequentially, p-toluenesulfonic acid (0.1 g), triethyl orthoformate (14.82 g, 0.1 mole), acetone (5.8 g, 0.1 mole) and freshly distilled ethylene glycol (6.2 g,

0.1 mole). (The order of addition is critical.) Heat was evolved on addition of the last reagent. The flask was allowed to stand at room temperature overnight. The acid catalyst was neutralized with several pellets of sodium hydroxide, then 25 mL of water was added. The product was extracted with 5 x 15 mL of chloroform and dried briefly over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give 2,2-dimethyl-1,3-dioxolane (1.22 g, 12%). The low yield in this reaction is due to the high water solubility of the product. 2,2-Dimethyl-1,3-dioxolane was analyzed by ^{13}C NMR: ($CDCl_3$)δ 108 ppm, 64 ppm, 26 ppm.

11. Benzalaniline

A 100-ml flask equipped with a magentic stirrer was charged with freshly distilled benzaldehyde (10.6 g, 0.1 mole). Freshly distilled aniline (9.3 g, 0.1 mole) was added dropwise with rapid stirring. Reaction occurred almost immediately with the evolution of heat and separation of water. The mixture was allowed to stand for fifteen minutes at room temperature, then poured, with stirring, in 20 mL of 95% ethanol. After 15 minutes at room temperature, during which time the product precipitated as white crystals, the solution was cooled in an ice-water bath for 20 minutes. Filtration by suction, followed by air drying gave benzalaniline (8.5 g, 47%), mp 50-51.5 , ^{13}C NMR: ($CDCl_3$)δ 160 ppm, 152 ppm, 131 ppm, 129.2 ppm, 126 ppm, 121 ppm.

12. Acetone 2,4-Dinitrophenylhydrazone

2,4-Dinitrophenylhydrazine (1 g, 5 mmole) was dissolved in 5 mL of concentrated sulfuric acid. This solution was added to a mixture of

water (7 mL) and 95% ethanol (25 mL). the dinitrophenylhydrazine reagent thus prepared was added to acetone (0.3 g, 5 mmole). Orange crystals precipitated immediately. After standing for 15 min, the reaction mixture was filtered by suction and washed with cold, 95% ethanol. The crystals were dried in air and analyzed by ^{13}C NMR: ($CDCl_3$)δ 150 ppm, 145 ppm, 136 ppm, 130 ppm, 123 ppm, 116 ppm, 25 ppm, 17 ppm.

13. Acetone p-Toluenesulfonylhydrazone

A 25-mL erlenmeyer flask was charged with acetone (1.53 g, 26.5 mmole), p-toluenesulfonylhydrazine (5.53 g, 29.7 mmole) and 17 mL of 95% ethanol. The flask was heated on a steam bath for ten minutes, then allowed to cool slowly. Acetone p-toluenesulfonylhydrazone precipitated as a white powder. The solution was suction filtered and air dried to give 4.71 g (70%) acetone p-toluenesulfonylhydrazone, m.p. 139.5°-140°. The product was analyzed by ^{13}C NMR: ($CDCl_3$)δ 156 ppm, 143 ppm, 135 ppm, 129 ppm, 128 ppm, 25 ppm, 21 ppm, 17 ppm.

14. Acetone Cyanohydrin

Acetone (5.8 g, 0.1 mole) and sodium cyanide (0.1 mole, 17 mL of a 6M solution) were combined in a 150 mL beaker. Approximately 30 g of ice was added to the stirring solution alternately with 28 mL of a saturated solution of sodium bisulfite. Stirring was continued for an additional 30 minutes, then the reaction mixture was extracted with 3 x 20 mL diethyl ether and dried briefly over sodium sulfate. The solvent was removed under vacuum to give 4.79 g (56%) of acetone cyanohydrin, which was analyzed by ^{13}C NMR: ($CDCl_3$)δ 123 ppm, 65 ppm, 29 ppm.

15. Sodium 1-Methyl-1-Hydroxyethylsulfonate

Acetone (4 g, 69 mmole) was added dropwise to 10 mL of a saturated solution of sodium bisulfite contained in an erlenmeyer flask immersed in an ice water bath. Sodium 1-methyl-1-hydroxyethylsulfonate precipitated almost immediately as a white powder. Ethanol (25 mL, 95%) was added to aid precipitation. The solution was filtered by suction and the white powder dried in air.

16. Reaction With Acetone Derivatives: General Procedure

The acetone derivative was combined with an equimolar amount of tributylborane (as a 1M solution in diethyl ether) in a flame-dried, nitrogen-flushed flask, equipped with a magnetic stirrer and nitrogen inlet (and outlet). The ethereal solvent was removed by nitrogen flow, and the reactants allowed to stir for several hours. Deuteriochloroform (1.5-2 mL) was added as an NMR solvent, and NMR spectra were obtained under inert atmosphere. In cases where a reaction was indicated, the reaction was repeated on a larger scale to allow characterization of the products.

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