METALATED ORGANOBORANES

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RONALD KOW
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This is to certify that the

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Metalated Organoboranes

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Ronald Kow

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Major professor

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ABSTRACT

METALATED ORGANOBORANES

By

Ronald Kow

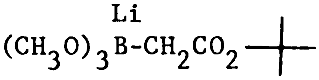
The formation of metalated organoboranes by base-promoted α-proton removal from organoboranes has never been previously reported. In large part, this must be due to the tendency of bases to coordinate to the boron atom. The use of a sterically-congested base, lithium 2,2,6,6-tetramethylpiperidide, overcomes this difficulty, and with the use of this base metalated organoboranes can be prepared from trialkylboranes. The metalated derivatives react with alkyl halides to give alcohols after oxidation, and with cyclohexanone to give alkenes after elimination.

The yields of metalation with the trialkylboranes seldom exceeded 50 percent and a search for more acidic boron compounds was undertaken. Vinyldialkylboranes (from hydroboration of alkynes) were found to react with lithium 2,2,6,6-tetramethylpiperidide to furnish the metalated derivatives in good yields. The reactions of these metalated derivatives with a variety of electrophilic reagents were investigated.

Attempts were made to metalate other boron compounds. The results of the studies with diphenylmethylborane, geminal diboraalkanes, and o-phenylene methylboronate are presented.

The reaction of trimethyl borate with lithium t-butylacetate gives

the salt XXXIX. The reactions and properties of this salt were investigated.



$$\mathrm{(CH_3O)_3\overset{Li}{B}\text{-}CH_2CO_2}\!-\!\!\!+\!\!-$$

XXXIX

METALATED ORGANOBORANES

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A THESIS

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To

Helen, With Love

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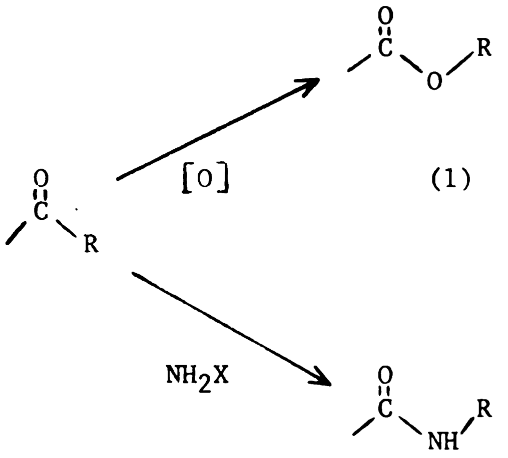
CHAPTER I

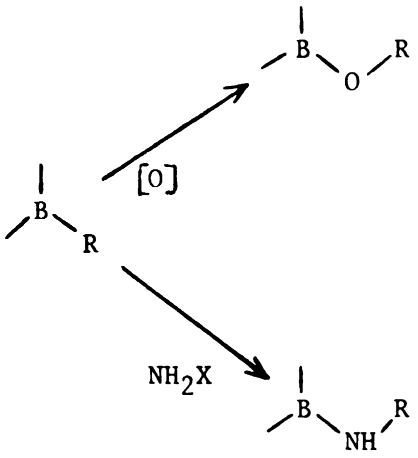
THE PREPARATION AND REACTIONS OF METALATED TRIALKYLBORANES

INTRODUCTION

The electronic configuration of trivalent boron is similar to that of carbon in a carbonyl grouping. Because of this similarity many of the reactions of aldehydes and ketones have counterparts in the reactions of trialkylboranes. For example, the Baeyer-Villiger[1] and Beckmann rearrangements[2] (eq. 1) of ketones are analogous to the oxidation[3] and amination reactions (eq. 2) of organoboranes.[4]

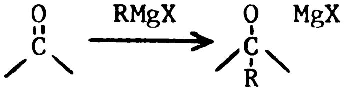


(1)

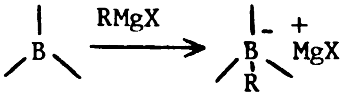


(2)

The addition of Grignard reagents to aldehydes and ketones (eq. 3) is also duplicated with boron compounds (eq. 4).[5]



(3)



(4)

Enolate anions, anions stabilized by an adjacent carbonyl group, (Figure 1), are well-known and provide the organic chemist with many

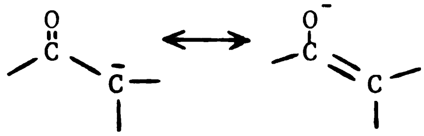


Figure 1. Enolate Anion

useful and versatile synthetic procedures. Carbanions stabilized by an adjacent boron atom, the organoborane counterpart of enolate anions (Figure 2), are less well-characterized and have not been as widely

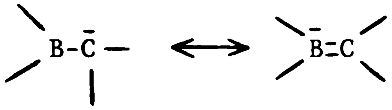


Figure 2. Organoborane Anion

used as the enolate anions. Since the boron atom is one of the easiest of all functional groups to introduce within a molecule (through the hydroboration reaction of olefins),[6] carbanions derived from trialkylboranes have the potential of being useful synthetic intermediates.

Literature Review.

In 1956 and 1957 H. C. Brown and B. C. Subba Rao reported that olefins can be readily and quantitatively converted into organoboranes under mild conditions (eq. 5), thus providing a new route to organoboranes:[7,8] the hydroboration reaction.

$$6RCH{=}CH_2 + B_2H_6 \longrightarrow 2(RCH_2CH_2)_3B \qquad (5)$$

Further study of the hydroboration reaction revealed that the addition is controlled in part by steric factors. Simple 1-alkenes, such as 1-pentene and 1-hexene, react to place 94 percent of the boron on the terminal carbon, the remaining 6 percent is placed on carbon 2.[9] The use of sterically hindered dialkyboranes $[(R_2BH)_2]$ as hydroborating reagents with 1-alkenes permits even greater regiospecificity, giving hydroborated products with more than 99 percent of the boron attached to the terminal carbon. A few of the sterically hindered organoborane reagents currently used are shown in Figure 3.[10]

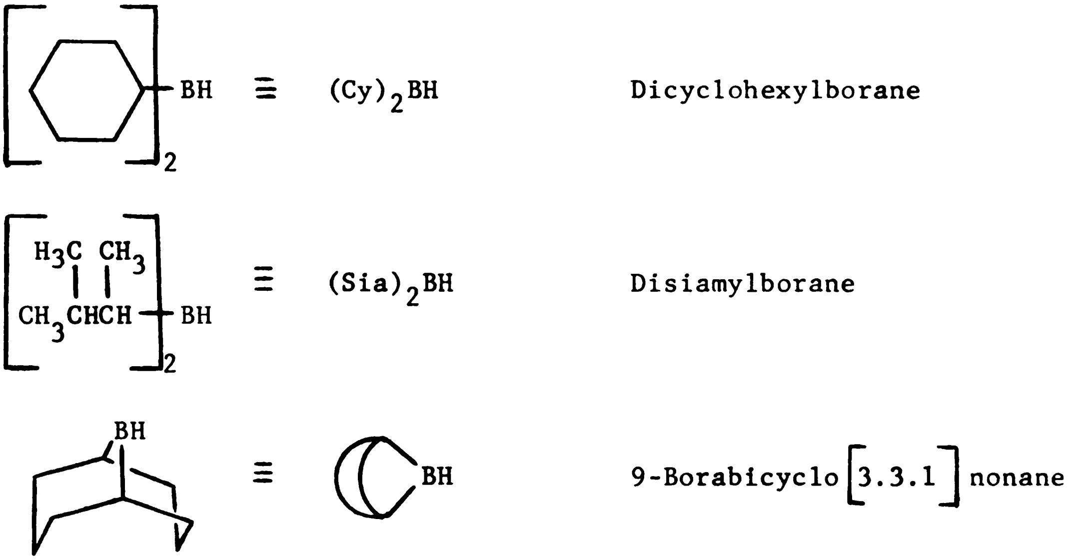
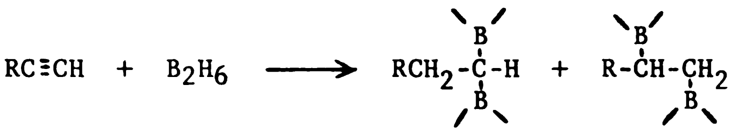


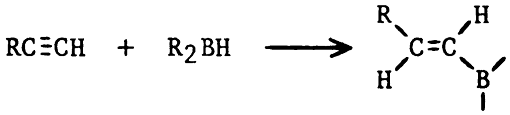
Figure 3. Sterically Hindered Organoboranes

The addition of diborane to terminal alkynes produces mixtures of addition products, both 1,1- and 1,2- addition (eq. 6).



$$RC\equiv CH + B_2H_6 \longrightarrow RCH_2-\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{C}}-H + R-\overset{\diagdown B \diagup}{C}H-\underset{\diagup B \diagdown}{C}H_2 \qquad (6)$$

The use of two equivalents of a sterically hindered organoborane as the hydroborating reagent with an alkyne will give an almost quantitative yield of only the 1,1- addition product,[11] while the addition of only one equivalent of the same reagent to an alkyne will give a vinylborane derivative (eq. 7).[12]

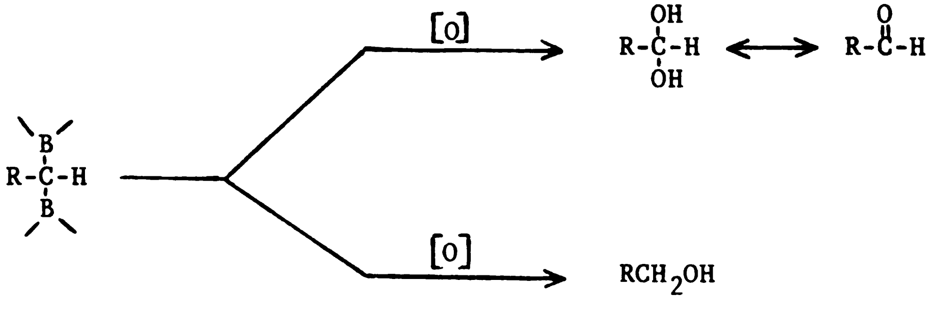


(7)

Oxidation of trialkylboranes with alkaline hydrogen peroxide gives alcohols (eq. 8) in essentially quantitative yields.[3]

$$R_3B + 3H_2O_2 + NaOH \longrightarrow 3ROH + NaB(OH)_4 \qquad (8)$$

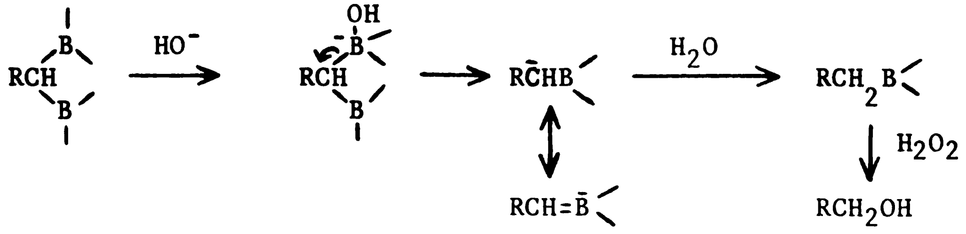
The expected product of oxidation with alkaline hydrogen peroxide of the dihydroborated derivative with both borons on the same carbon, was the carbonyl derivative (eq. 9). Surprisingly, oxidation of the dihydroborated 1- and 3-hexynes did not give any carbonyl compounds, but yielded 1- and 3-hexanol as a major product in each case (eq. 10).



(9)

(10)

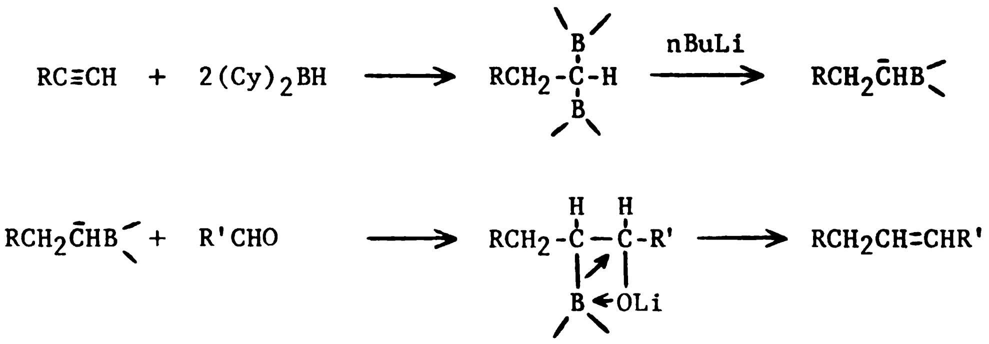
Brown suggested that the geminal diboroalkane was unstable to sodium hydroxide and proposed the following mechanism (eq. 11):[13]


(11)

I

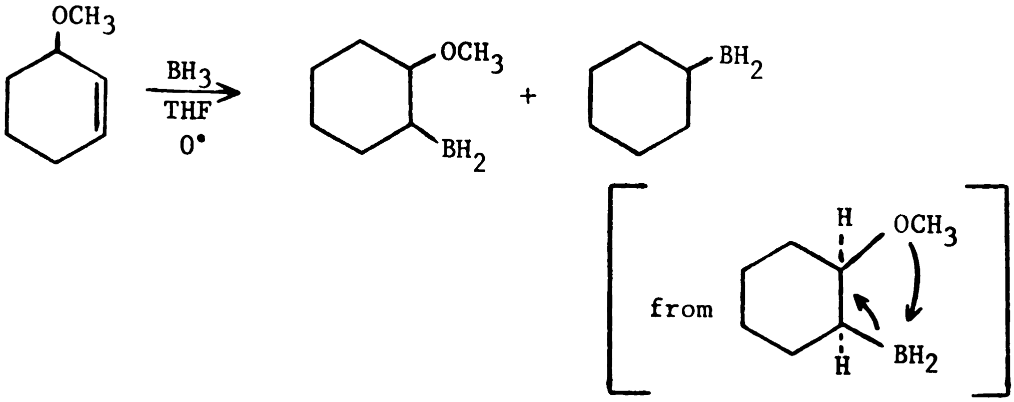
The carbanion, which is formed by attack of the base on one of the electrophilic boron atoms, is stabilized through resonance by the vacant orbital of the second boron atom. Thus, in 1961, Brown was the first to propose the possibility of an organoboron carbanion intermediate (I).

Although Brown was the first to suggest the existence of an organoboron carbanion intermediate, other researchers began to explore the possibility of using these anions as useful intermediates in synthetic reactions. One of the first reports to appear (submitted by Cainelli and co-workers in 1965-1966)[14,15] described the reaction of metalated organoboranes with carbonyl compounds (eq. 12) to give olefin derivatives.[14] Generation of the metalated derivative was accomplished by reaction of the base, n-butyllithium, with a geminal diboron compound:


(12)

II

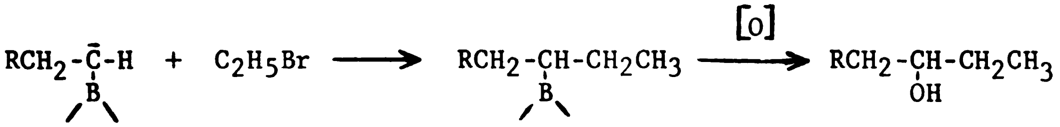
After formation of the metalated derivative, the reaction involves a nucleophilic attack of the anion at the carbonyl grouping, leading to the intermediate II. II then undergoes a 1,2-elimination to give the olefin. 1,2-eliminations are fairly common for β-halo, β-hydroxy, and β-acetoxyalkylboranes.[16] One of the examples given by House is shown below (eq. 13):



(13)

The yields of olefins from the metalated organoboranes ranged from 20 to 50 percent for various carbonyl compounds (i.e. benzaldehyde, cyclohexanone, cholestanone).

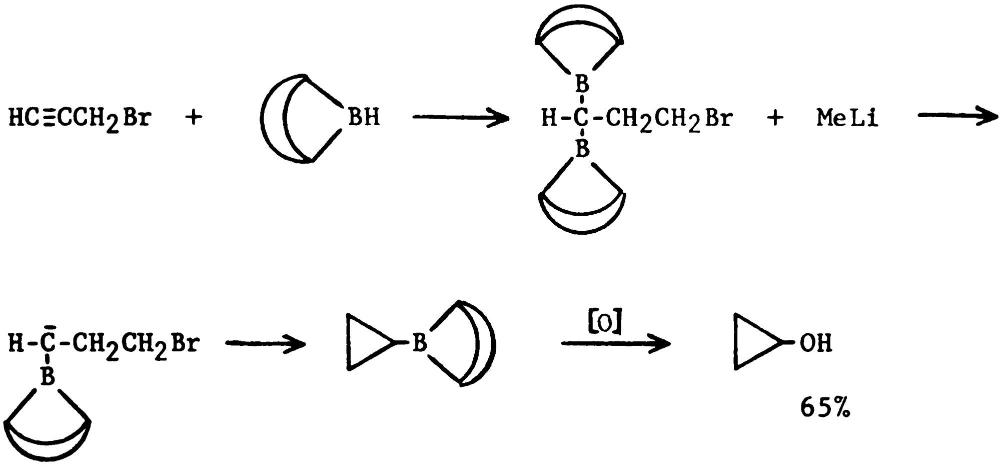
During the same period, George Zweifel and H. Arzoumanian investigated the reaction of metalated organoboranes with ethyl bromide.[17] Zweifel used essentially the same method as Cainelli to generate the metalated organoboranes for his study. The base induced cleavage of geminal dihydroborated intermediates was accomplished with a variety of bases including sodium methoxide, lithium methoxide, n-butyllithium, methyllithium . After reaction of the anion with ethyl bromide and oxidation with alkaline hydrogen peroxide, Zweifel obtained the alcohol in yields of 35 to 90 percent, depending on the reaction conditions (eq. 14).



$$\mathrm{RCH_2\text{-}\underset{B}{\bar{C}}\text{-}H} + \mathrm{C_2H_5Br} \longrightarrow \mathrm{RCH_2\text{-}\underset{B}{CH}\text{-}CH_2CH_3} \xrightarrow{[O]} \mathrm{RCH_2\text{-}\underset{OH}{CH}\text{-}CH_2CH_3} \qquad (14)$$

The best results were obtained with methyllithium as the base.

In 1969 Brown used metalated organoborane intermediates to synthesize cyclopropane (eq. 15) and cyclobutane derivatives (eq. 16).[18]



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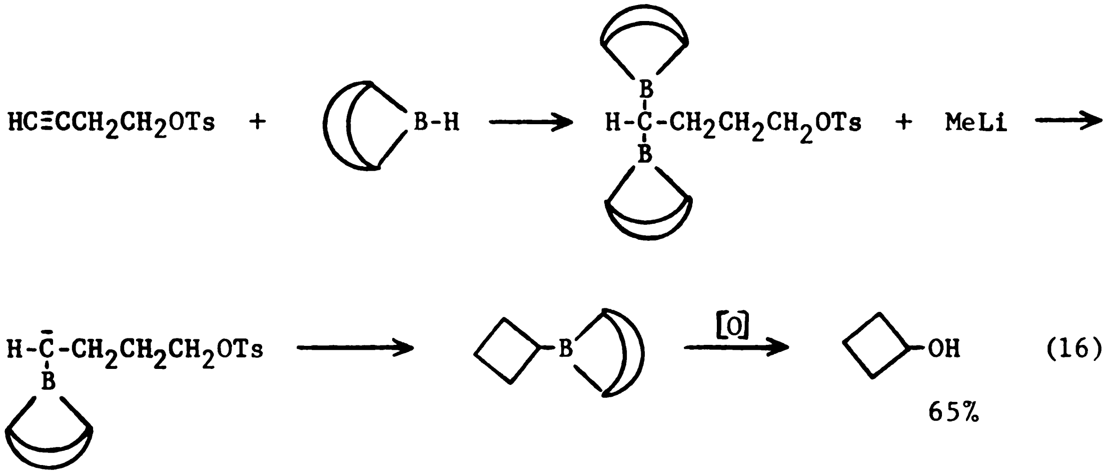
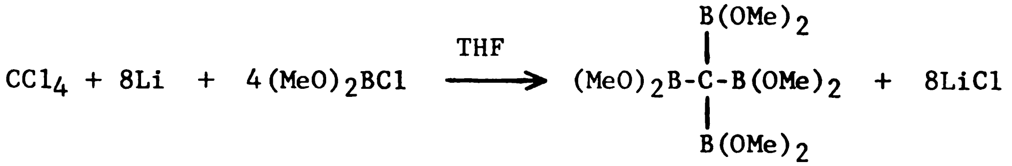


(16)

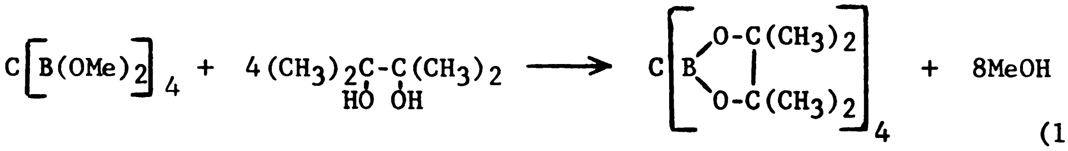
Generation of metalated organoborane intermediates was again accomplished by the addition of a base, methyllithium, to geminal dihydroborated derivatives. The intermediates then cyclized through an intramolecular nucleophilic substitution.

D. S. Matteson, working along the same lines but using a different set of organoboron substrates, also studied the formation and reactions of metalated organoboranes.[19-29] The substrates Matteson chose to work with were the methanetetraboronic esters, $C[B(OR)_2]_4$. These boronic esters were synthesized by Matteson's group by a difficult process (eq. 17).[19,23]



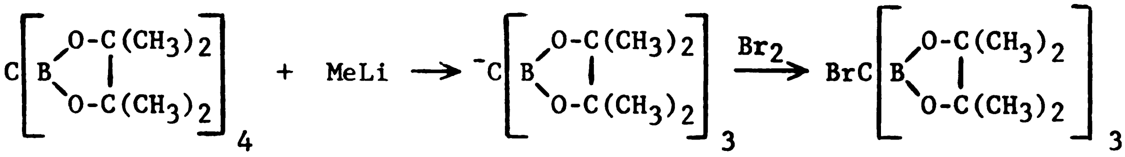
$$CCl_4 + 8Li + 4(MeO)_2BCl \xrightarrow{THF} (MeO)_2B\text{-}\overset{B(OMe)_2}{\underset{B(OMe)_2}{C}}\text{-}B(OMe)_2 + 8LiCl \qquad (17)$$

Tetrakis(dimethoxyboryl)methane III can be converted into other boronic esters by a transesterification reaction (eq. 18).[25,26]



III IV (18)

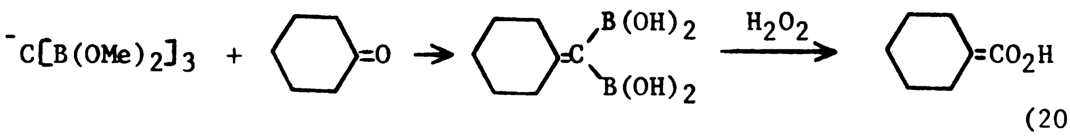
The boronic esters react readily with alkyllithium to form triborylmethide anions. For example, treatment of the pinacol boronic ester IV with methyllithium yields the corresponding triborylmethide anion V.[26] The anion reacts with bromine to give the bromomethanetriboronic ester VI (eq. 19).



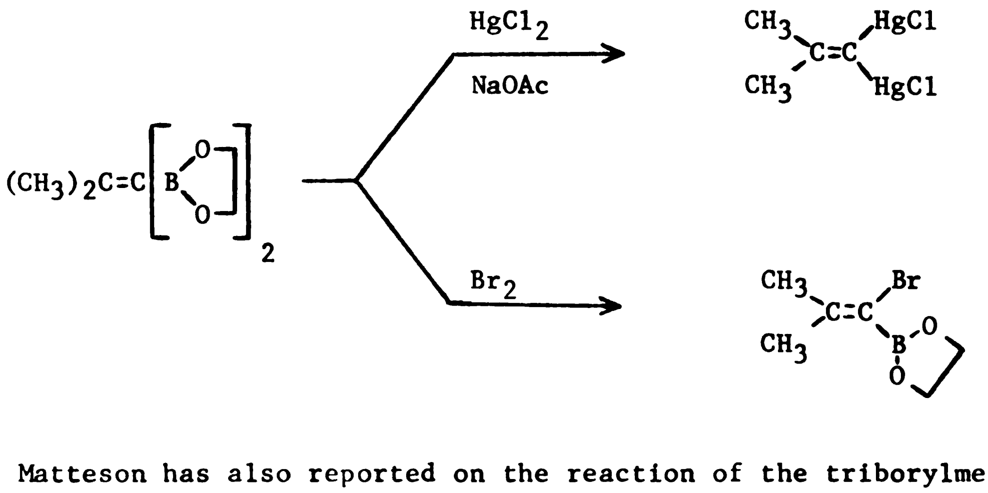
IV V VI (19)

Matteson also discovered that the bromomethanetriboronic ester VI can react with more alkyllithium to form the carbanion, $^{-}CBr(BO_2C_2Me_4)_2$. This carbanion reacted with bromine to give the dibromomethanediboronic ester, $Br_2C(BO_2C_2Me_4)_2$.

Triborylmethide ions, $[(RO)_2B]_3C^{-}$, condense readily with ketones to form alkene-1,1-diboronic esters, $R_2'C{=}C[B(OR)_2]_2$.[27] This reaction is general and functional groups, such as α-chloro, carbethoxy, and tertiary amino substituents, on the ketone do not affect it adversely. Matteson also found that alkene-1,1-diboronic esters are potentially useful synthetic intermediates. He was able to convert the alkenes to carboxylic acids (eq. 20), α-bromoalkeneboronic esters (eq. 22), and alkenyl-1,1-dimercuric chlorides (eq. 21).



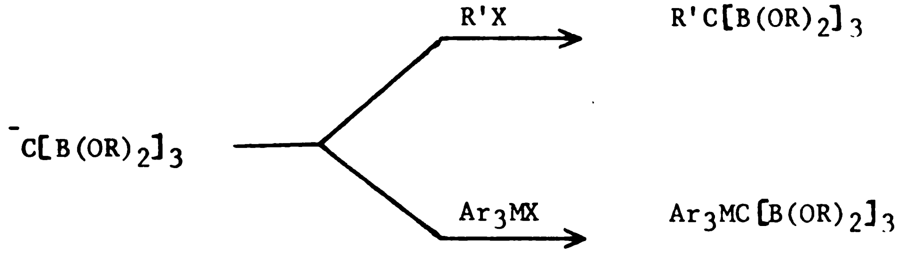
(20)



(21)

(22)

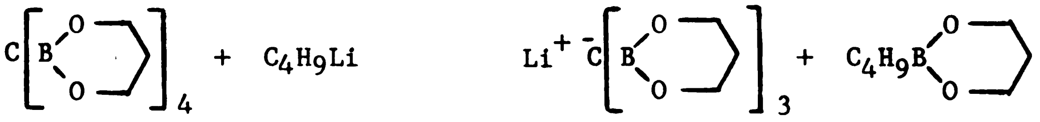
Matteson has also reported on the reaction of the triborylmethide ions with alkyl halides (eq. 23),[22] and the metalation of the anions with group IV triarylmetal halides (eq. 24).[24,25]



(23)

(24)

One of the more interesting aspects of Matteson's work is the fact that he was able to isolate a boron-substituted carbanion.[28] The lithium salt of tris(trimethylenedioxyboryl)methide ion VII was isolated in yields of 75 to 100 percent from the reaction of butyllithium and tetrakis(trimethylenedioxyboryl)methane in tetrahydrofuran at -70°C (eq. 25).



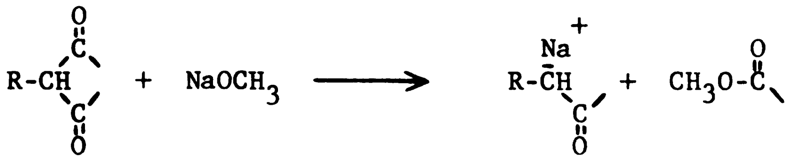
VII

(25)

Since VII chars in air and reacts very rapidly with water, it must be handled under argon. This salt is very reactive and undergoes all the reactions of triborylmethide ions discussed earlier.

Discussion of the Problem and an Outline of the Research.

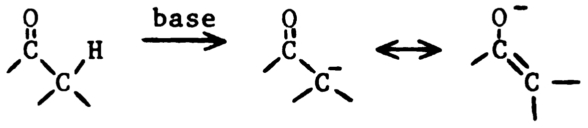
In all the cases of metalated organoboranes discussed above the metalated derivative was generated by the base-promoted cleavage of a carbon compound containing two or more boron atoms on the same carbon. This process is analogous to the cleavage of β-diketones by base (eq. 26).[30]



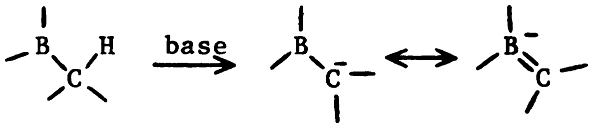
(26)

The disadvantage of base-cleavage for the formation of metalated organoboranes is that one is limited to alkynes for the formation of dihydroborated derivatives, or to a difficult and expensive synthesis to obtain the tetraborylmethane or triborylmethane compounds.[23]

In most synthetically useful examples of enolate anion formation, the anions are generated by the removal of an α-hydrogen by a base (eq. 27). It was thought that a similar reaction might be possible with organoboranes, and a study was undertaken on the feasibility of α-proton removal from organoboranes by the action of strong bases (eq. 28).

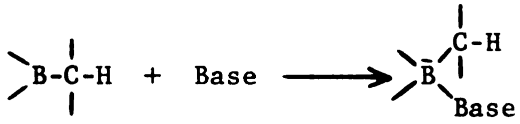


(27)



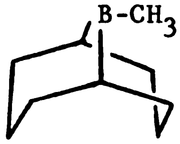
(28)

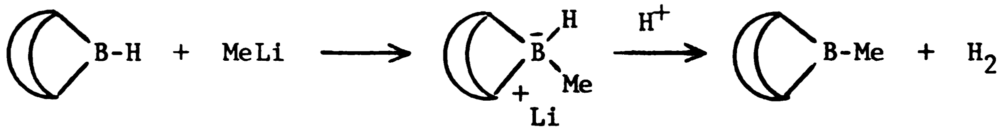
A major obstacle to this base-promoted deprotonation of organoboranes is their strong Lewis acidity. Normally, addition of a base to an organoborane results in coordination of the base to the boron atom (eq. 29).[5] In some cases organoboranes can even be titrated quantitatively with alkoxide bases.[31]


(29)

This acid-base reaction (eq. 29) ties up the base and is undoubtedly the major reason why alpha metalation of organoboranes by base has not previously been observed (eq. 28).

Our study began with B-methyl-9-borabicyclo[3.3.1]nonane (B-methyl-BBN) VIII as the organoboron substrate. B-methyl-BBN was chosen because it is easily synthesized (eq. 30)[32] and because of the expected differences in the rate of α-proton abstraction between the methyl and tertiary protons.


VIII


(30)

We assumed the methyl protons to be more acidic than the tertiary-bridgehead protons because primary carbanions are more stable than tertiary carbanions,[33] and because resonance stabilization by the boron atom of the tertiary carbanion would involve a double bond to a bridgehead carbon (Figure 4), which is expected to be much less stable than the corresponding contributor for the methyl anion.

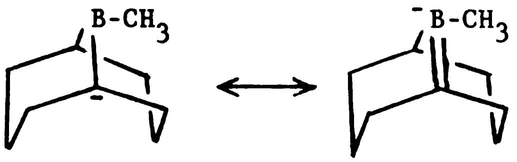
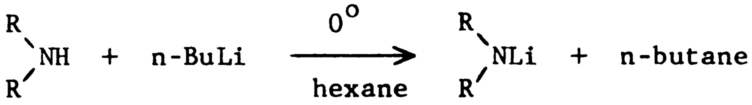


Figure 4. Poor resonance contributor

Once VIII was prepared we began a search for a base so sterically hindered that coordination to the boron atom of VIII would be difficult or impossible, thereby preventing the unwanted neutralization reaction of eq. 29. Once such a base was found, studies were undertaken to prove that a metalated organoborane was formed, and to find the optimum conditions necessary for complete metalation. Another aspect of this research was to search for useful synthetic reactions of the metalated organoboranes. Lastly, studies were conducted to learn if other organoboranes, besides B-methyl-BBN, form metalated derivatives. The results of these studies are presented in the following section.

RESULTS

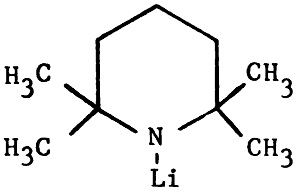
Metalation of organoboranes was studied with B-methyl-BBN and a variety of lithium dialkyl amides. The lithium dialkyl amides were prepared by the reaction of the corresponding secondary amine at 0° with n-butyllithium in hexane (eq. 31).



$$\mathrm{R(R')NH} + \text{n-BuLi} \xrightarrow[\text{hexane}]{0^{\circ}} \mathrm{R(R')NLi} + \text{n-butane} \qquad (31)$$

Initial Studies Using PMR.

Early studies consisted of proton nmr examination of the reaction mixtures of VIII and the lithium amides in benzene. Benzene was chosen as the initial solvent because the resonance signals from the benzene protons would not interfere with the signals from B-methyl-BBN, and because benzene is relatively inert to the amide bases. The first three bases tried, lithium diisopropyl amide, lithium diethyl amide, and lithium isopropylcyclohexyl amide, appeared to coordinate to the boron atom of VIII. In the pmr spectra, the methyl group of B-methyl-BBN was shifted from a δ value of 0.90 (TMS internal reference) to a δ value of 0.2-0.4 in the presence of the base. Refluxing the reaction mixture for a few hours produced no change in the pmr spectra. Addition of B-methyl-BBN to the hindered base IX, lithium 2,2,6,6-tetramethylpiperidide (LiTMP), in benzene resulted in a pmr spectrum which

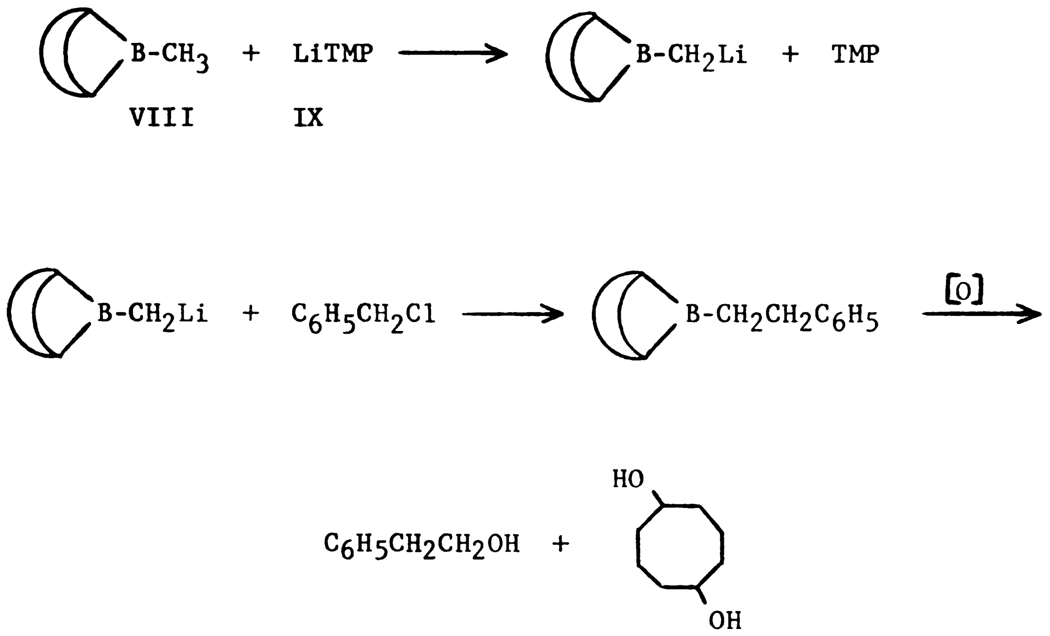


IX

corresponded closely to a mixture of the two components. Apparently this base is too hindered for coordination with the boron atom of VIII to take place. After refluxing, this reaction mixture exhibited a significant change in its pmr spectrum. The methyl signal of VIII disappeared and new signals appeared at fields higher than TMS.[34] From these results, we assumed that LiTMP was the sterically crowded base that we were searching for.

Use of Benzyl Chloride as a Probe.

Since the pmr spectra did not provide unambiguous evidence for the formation of a metalated organoborane, more conclusive proof was needed. We decided to quench the reaction mixture with an alkyl halide and then oxidize the resulting organoborane with alkaline hydrogen peroxide. If a metalated organoborane were formed, this sequence of reactions, with benzyl chloride as the alkylating agent, would yield β-phenylethanol (eq. 32).



VIII IX

(32)

In the initial experiment, VIII was refluxed with one equivalent of IX for 24 hours, following which the reaction mixture was quenched with benzyl chloride at room temperature. After oxidation, β-phenylethanol was detected in 7 percent yield. In an attempt to improve the yield of β-phenylethanol, various reaction conditions were tried. The effect of solvents, temperature of reaction mixture, time, and quantity of reagents used were studied. The optimum conditions, using one equivalent of base, occurred when the reaction mixture of the organoborane and the base was allowed to stir for one hour at room temperature. The yield of β-phenylethanol obtained in this case, as determined by glpc, was 21.4 percent. An excess of base increased the yield of alcohol to 46 percent; however, the use of more polar solvents did not improve the yield. Table 1 summarizes a few of the reactions studied.

The effect of different size bases was also studied with the

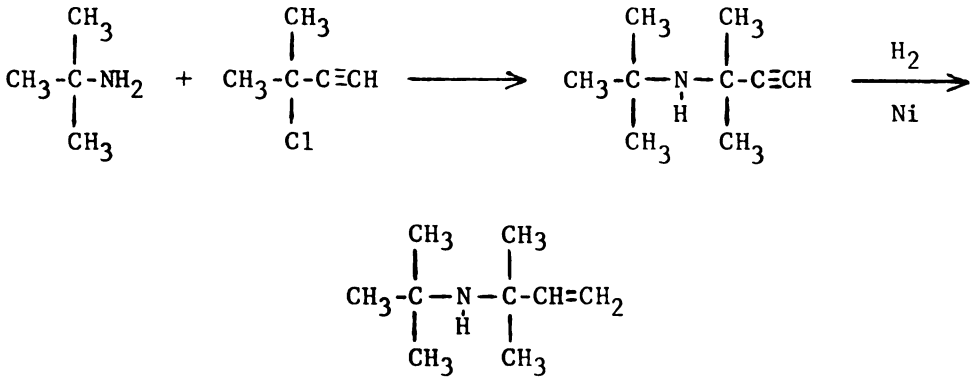
TABLE 1

Effect of solvent on the formation of metalated B-methyl-BBN.

Ratio of LiTMP/VIII	Reaction Time	Temperature of Reaction Mixture	Solvent	% Yield[a] of β-phenylethanol
1/1	24 hrs.	Reflux	Toluene	6
1/1	24 hrs.	Reflux	Benzene	7
1/1	24 hrs.	Reflux	HMPA	7
1/1	24 hrs.	Reflux	Ethyl Ether	9
1/1	15 min.	Reflux	THF	20
1/1	1 hr.	R. T.	Benzene	21
2/1	1 hr.	R. T.	Benzene	46

[a] Yield determined by glpc with an internal standard.

benzyl chloride alkylation reaction. As expected, the less hindered bases gave little or no β-phenylethanol after quenching with the halide. 3-t-butylamino-3-methyl-1-butene (X) appears to be as sterically hindered as IX and gave comparable results. X was obtained through a substitution reaction (eq. 33).[35]



$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-NH_2 + CH_3-\overset{CH_3}{\underset{Cl}{C}}-C\equiv CH \longrightarrow CH_3-\overset{CH_3}{\underset{CH_3}{C}}-\underset{H}{N}-\overset{CH_3}{\underset{CH_3}{C}}-C\equiv CH \xrightarrow[Ni]{H_2} \quad (33)$$

$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-\underset{H}{N}-\overset{CH_3}{\underset{CH_3}{C}}-CH=CH_2$$

X

LiTMP was used in most of these experiments because the amine is commercially available and relatively inexpensive. The results of using different bases to accomplish metalation are presented in Table 2.

Several reactions were tried in which the amines were removed by distillation. If the formation of the metalated organoborane is an equilibrium reaction (eq. 34), the removal of the amine should force the equilibrium to the right.

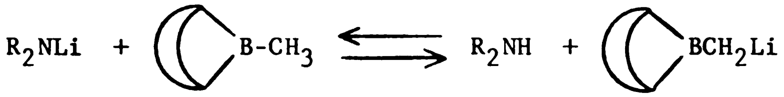
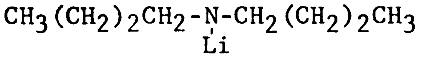
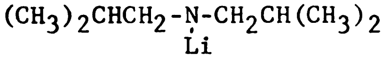
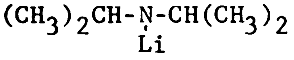
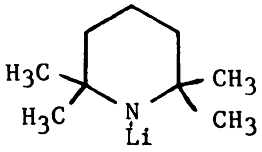
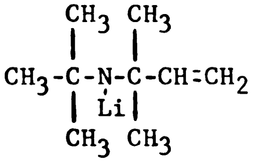
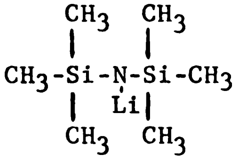
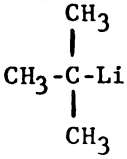

(34)

TABLE 2

Effect of different bases on the formation of metalated B-methyl-BBN.[a]

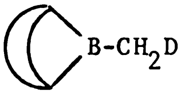
Base	% Yield of β-phenylethanol
 $CH_3(CH_2)_2CH_2\text{-}\underset{Li}{N}\text{-}CH_2(CH_2)_2CH_3$	0
 $(CH_3)_2CHCH_2\text{-}\underset{Li}{N}\text{-}CH_2CH(CH_3)_2$	0
 $(CH_3)_2CH\text{-}\underset{Li}{N}\text{-}CH(CH_3)_2$	3
	18
 $CH_3\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}\underset{Li}{N}\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}CH{=}CH_2$	20
 $CH_3\text{-}\overset{CH_3}{\underset{CH_3}{Si}}\text{-}\underset{Li}{N}\text{-}\overset{CH_3}{\underset{CH_3}{Si}}\text{-}CH_3$	5
 $CH_3\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}Li$	0

[a] B-methyl-BBN was added to the base in benzene and the mixture refluxed for 15 min. before the addition of benzyl chloride.

The results from these experiments were usually very poor, giving little or no β-phenylethanol after quenching.

Use of Deuterium Oxide as a Probe.

Since the yields of the alkylation reactions using benzyl chloride were not large, the possibility existed that the alkylation reaction was not going to completion and therefore, gave an incomplete picture of the extent of metalation. Clearly, another method for determining the amount of metalation was needed. A few experiments showed that B-methyl-BBN was fairly stable to water for short periods. Consequently, the decision was made to use deuterium oxide as a quenching reagent to establish the proportion of starting organoborane that was being converted to the metalated derivative. The final product of this quenching experiment would be the deuterated B-methyl-BBN (XI). The resulting mixture was analyzed by mass spectrometry.



XI

Since the best results with the benzyl chloride alkylations were obtained when the base and the boron compound were reacted at room temperature, all the reactions with deuterium oxide were done at this temperature. In each reaction, the boron compound was added to one equivalent of the base suspended in benzene, quenched with deuterium oxide after an appropriate reaction period, and isolated by glpc for mass spectral analysis. The results of mass spectral analysis confirmed the findings of the benzyl chloride alkylations, that the less hindered bases do not effect metalation. The results from the reactions of three different bases are given in Table 3.

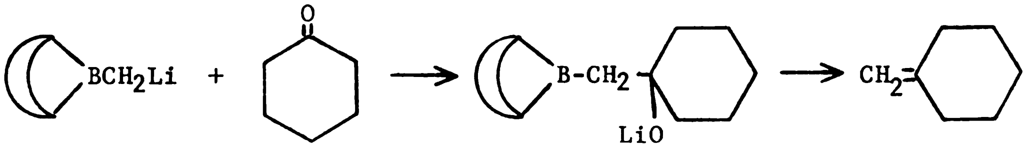
Since the use of different solvents in the alkylation reactions did not improve the yields of β-phenylethanol, only a brief study of solvent effects was undertaken for the deuterium oxide reaction. The results were quite similar to those from the benzyl chloride reaction, and the data are summarized in Table 4.

The effect of different quantities of base on the reaction was also studied. The results are given in Table 5.

Reactions of Metalated B-methyl-BBN.

The results of quenching with deuterium oxide seemed to indicate that the metalation of B-methyl-BBN was not quantitative. For this reason only a few reactions of the metalated derivative were studied.

Reaction of the metalated derivative of B-methyl-BBN with cyclohexanone gave a 55 percent yield of methylenecyclohexane (XII), based on the quantity of B-methyl-BBN used (eq. 35).



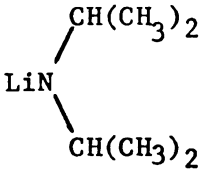
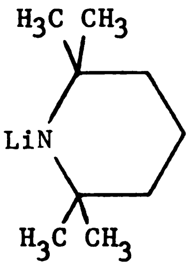
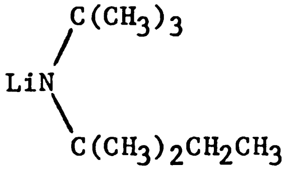
XII

(35)

With a 50 percent excess of base, the yield of XII was increased to 66 percent. This reaction is similar to the reaction of organoboron carbanions and carbonyl compounds reported by Cainelli[14] and Matteson.[27]

TABLE 3

Amount of deuterium incorporation in B-methyl-BBN with different bases.[a]

Lithium amide	Reaction time (hours)	Deuterium Incorporation, %[b]
 $\mathrm{LiN}\begin{array}{l}\diagup\mathrm{CH(CH_3)_2}\\ \diagdown\mathrm{CH(CH_3)_2}\end{array}$	12	0
	1	40
	12	50
	24	60
	48	65
	7 days	62
 $\mathrm{LiN}\begin{array}{l}\diagup\mathrm{C(CH_3)_3}\\ \diagdown\mathrm{C(CH_3)_2CH_2CH_3}\end{array}$	12	40
	4 days	50

---

[a] Reaction mixtures are 1M in boron compound. Equivalent amounts of base and boron compound were utilized.

[b] From mass spectral analysis of recovered boron compound.

TABLE 4

Amount of deuterium incorporation in B-methyl-BBN with different solvents.[a]

Solvent	% Deuterium Incorporation
Benzene	60
THF	32
4% HMPA/Benzene	58
20% HMPA/Benzene	26

[a] Reaction conditions: B-methyl-BBN was stirred with one equivalent of LiTMP at room temperature for 24 hours before quenching.

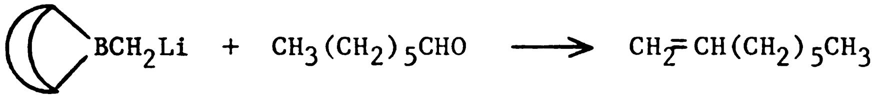
TABLE 5

Reaction of B-methyl-BBN with varying amounts of lithium 2,2,6,6-tetramethylpiperidide in benzene.[b]

Base/Boron Compound	% Deuterium Incorporation
0.5	36
0.75	49
1.0	60
2.0	75
4.0	73

[b] Reaction times are 24 hours.

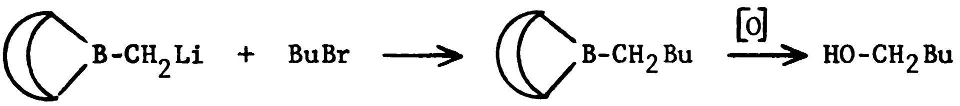
A reaction of metalated B-methyl-BBN with an aldehyde, heptanal, was also attempted (eq. 36).



(36)

The yield of 1-octene was very low. Aldehydes have a tendency to undergo condensation reactions in the presence of strong bases. Since the metalated B-methyl-BBN and the unreacted LiTMP are strong bases, self-condesation of the aldehyde must be a competing reaction in this case. Cainelli[14] also commented on the fact that competing condensation reactions were probably a factor in the low yields of some of the olefins formed in his studies.

Other alkyl halides (butyl bromide, pentyl chloride, and octyl chloride) were also studied as alkylating agents (Table 6). In the case of butyl bromide, a 42 percent yield of n-pentanol was obtained (eq. 37).



(37)

Cyclohexane was also tested as a solvent with butyl bromide as the alkylating agent, the results were the same as when benzene was the solvent (38 percent of n-pentanol was detected).

TABLE 6

Alkylation of metalated B-methyl-BBN.[a]

Alkyl halide	Alcohol obtained	% Yield of Alcohol[b]
Butyl bromide	Pentanol	42[c]
Pentyl chloride	Hexanol	37
Octyl chloride	Nonanol	36
Benzyl chloride	2-phenylethanol	21

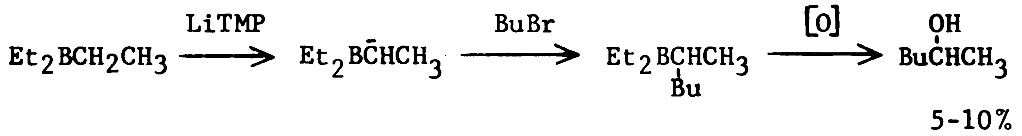
[a] Reaction conditions for formation of metalated B-methyl-BBN: One equivalent of LiTMP in benzene at room temperature for one hour.

[b] Yields determined by glpc analysis.

[c] B-methyl-BBN and LiTMP were stirred for 12 hours at room temperature before addition of butyl bromide.

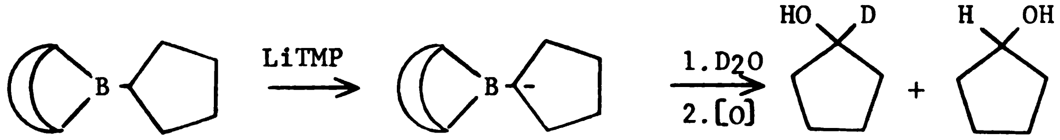
Formation of Metalated Derivatives from Other Organoboranes.

The success of B-methyl-BBN in forming a metalated compound could not be duplicated with other alkylboranes. Triethyl boron, on reaction with LiTMP, followed by alkylation with butyl bromide and oxidation by alkaline hydrogen peroxide, gave very low yields of 2-hexanol (eq. 38).



$$\mathrm{Et_2BCH_2CH_3} \xrightarrow{\text{LiTMP}} \mathrm{Et_2B\bar{C}HCH_3} \xrightarrow{\text{BuBr}} \mathrm{Et_2B\underset{Bu}{C}HCH_3} \xrightarrow{[O]} \underset{5\text{-}10\%}{\mathrm{Bu\overset{OH}{C}HCH_3}} \qquad (38)$$

Another trialkyborane, B-cyclopentyl-9-borabicyclo[3.3.1]nonane (XIII) also gave poor conversions to the corresponding metalated derivative. The amount of metalation was determined by deuterium oxide quenching (eq. 39).



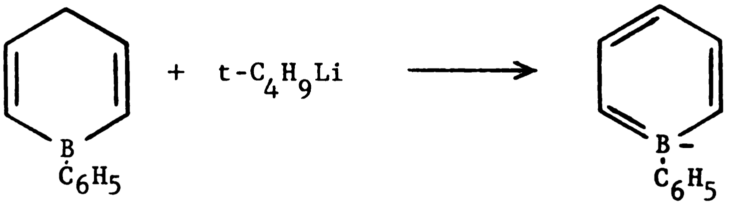
XIII

(39)

After oxidation of the organoborane the cyclopentanol was collected by glpc and analyzed by pmr. The amount of deuterium incorporation in the product ranged from 10-15 percent.

DISCUSSION

The results presented in the previous section represent the first example of base-promoted α-proton removal from organoboranes to produce metalated organoboranes. The removal of a γ-proton from 1-phenyl-1,4-dihydroborabenzene by a base to furnish a metalated organoborane has been reported recently (eq. 40).[36]



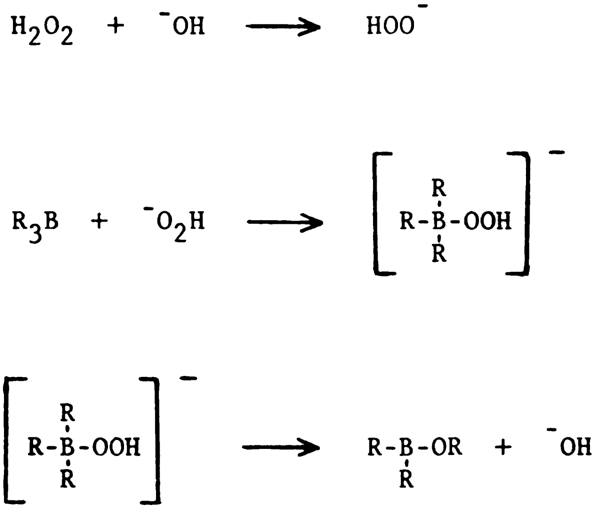
XIV

(40)

The metalated derivative XIV is probably stabilized by aromatic resonance and therefore represents a special case of metalated organoboranes. This section will include a discussion of some of the ideas behind this research and on the results of the study.

Use of Sterically Hindered Reagents in Reactions of Organoboranes.

Because the boron atom of trialkylboranes has only six electrons in its outer shell and can accomodate eight, trialkylboranes are classified as Lewis acids. Many of the reactions of trialkylboranes are assisted by this empty orbital of boron. For example, oxidation of organoboranes by alkaline hydrogen peroxide probably involves an initial coordination of a hydroperoxy anion to the boron atom (eq. 41).[3]



$$H_2O_2 + {}^-OH \longrightarrow HOO^-$$

$$R_3B + {}^-O_2H \longrightarrow \left[R-\overset{R}{\underset{R}{B}}-OOH \right]^-$$

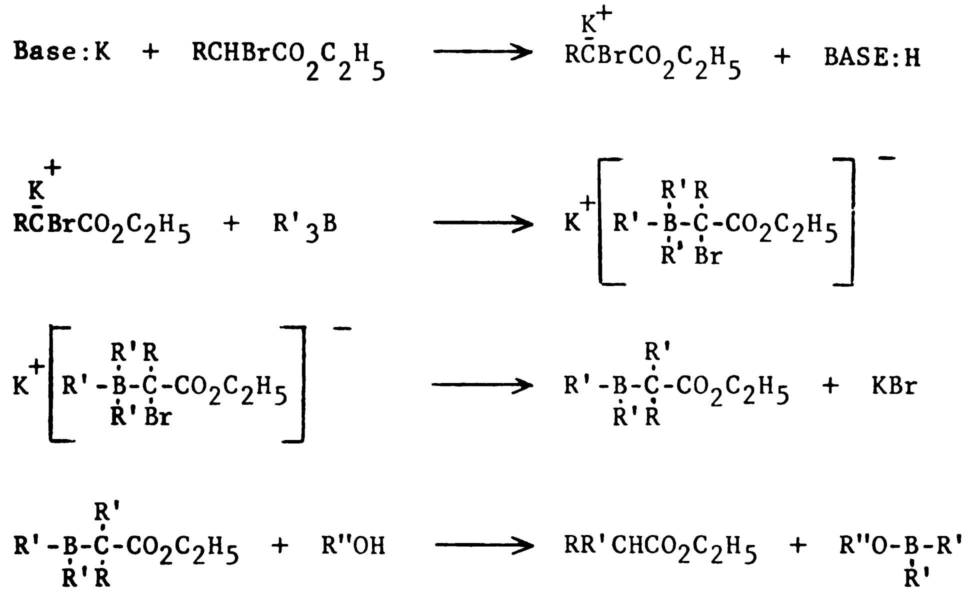
$$\left[R-\overset{R}{\underset{R}{B}}-OOH \right]^- \longrightarrow R-\underset{R}{B}-OR + {}^-OH \qquad (41)$$

The initial coordination of a nucleophilic reagent with organoboranes may be of assistance in some of their reactions, but can be a major obstacle to a base-promoted metalation of trialkylboranes. This undesired coordination of a nucleophile with boron can usually be prevented by using a reagent that is so sterically crowded that coordination becomes impossible.

The use of a sterically hindered reagent in reactions with organoboranes to prevent coordination to the boron atom is not a new concept. For example, the alkylation reaction of α-haloalkanoic esters with organoboranes utilizes a sterically hindered base (eq. 42).[37]

$$R_3'B + RCHBrCO_2C_2H_5 \xrightarrow{\text{Base}} RR'CHCO_2C_2H_5 \qquad (42)$$

The mechanism proposed for the above reaction is given in eq. 43.



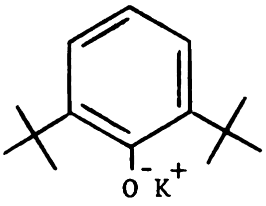
$$\text{Base:K} + \text{RCHBrCO}_2\text{C}_2\text{H}_5 \longrightarrow \text{R}\overset{\text{K}^+}{\bar{\text{C}}}\text{BrCO}_2\text{C}_2\text{H}_5 + \text{BASE:H}$$

$$\text{R}\overset{\text{K}^+}{\bar{\text{C}}}\text{BrCO}_2\text{C}_2\text{H}_5 + \text{R'}_3\text{B} \longrightarrow \text{K}^+\left[\text{R'-}\underset{\text{R'}}{\overset{\text{R'}}{\text{B}}}\text{-}\underset{\text{Br}}{\overset{\text{R}}{\text{C}}}\text{-CO}_2\text{C}_2\text{H}_5\right]^-$$

$$\text{K}^+\left[\text{R'-}\underset{\text{R'}}{\overset{\text{R'}}{\text{B}}}\text{-}\underset{\text{Br}}{\overset{\text{R}}{\text{C}}}\text{-CO}_2\text{C}_2\text{H}_5\right]^- \longrightarrow \text{R'-}\underset{\text{R'}}{\text{B}}\text{-}\underset{\text{R}}{\overset{\text{R'}}{\text{C}}}\text{-CO}_2\text{C}_2\text{H}_5 + \text{KBr}$$

$$\text{R'-}\underset{\text{R'}}{\text{B}}\text{-}\underset{\text{R}}{\overset{\text{R'}}{\text{C}}}\text{-CO}_2\text{C}_2\text{H}_5 + \text{R''OH} \longrightarrow \text{RR'CHCO}_2\text{C}_2\text{H}_5 + \text{R''O-}\underset{\text{R'}}{\text{B}}\text{-R'} \qquad (43)$$

Optimum results were obtained by using the base, potassium 2,6-di-t-butylphenoxide (XV). According to Brown the reason why this phenoxide



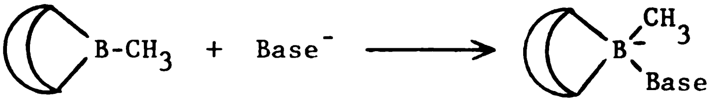
XV

is so effective is because "the large steric requirements of the base prevents coordination to the trialkylboranes. Coordination would be unfavorable for the rapid capture of the α-halocarbanions"[37] by the organoboranes. In our own case coordination of the base to the organoboranes would tie up the base and prevent it from removing a proton from the organoborane.

Steric Effect of the Bases.

For our studies on the ionization reaction we needed a variety of bases having different steric requirements. We chose the lithium dialkyl amides as bases because they are easy to prepare and because they are very strong bases, pKa of these amines is approximately 36 pKa units.[38] Furthermore a variety of secondary amines of different sizes are readily available. We tested a number of amides of increasing size until we found one that gave satisfactory results with B-methyl-9-borabicyclononane.

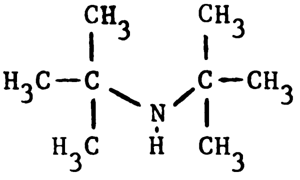
The lithium amides of di-n-butyl, diisobutyl, and diethyl amine, the bases with the least steric requirements in the series tested, do not give a metalated derivative with B-methyl-BBN. Another base, t-butyllithium, is also unsuccessful in the base-promoted ionization reaction of trialkylboranes. These bases are undoubtedly too small and are coordinating to the boron atom (eq. 44).



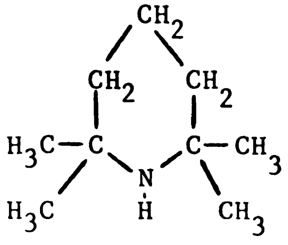
(44)

Lithium diisopropylamide and lithium isopropylcyclohexylamide are bulkier bases, but still do not form a metalated compound on reaction with organoboranes.

The next base that we wanted to try was lithium di-t-butylamide, which is more sterically hindered than lithium diisopropylamide, but the amine was not readily available.



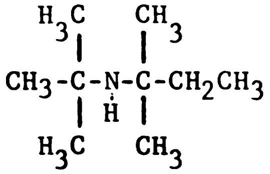
XVI



XVII

The only difference between the two amines XVI and XVII is an extra methylene group in the cyclic compound joining the two t-butyl groups together. Since XVII is probably as sterically hindered as XVI and is commercially available, we chose the piperidide as the next amide to study. The piperidide gives satisfactory results for metalation and therefore must be hindered enough to prevent coordination to organoboranes.

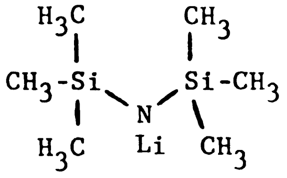
Another amine, which is approximately the same size as the tetramethylpiperidine, is 2-t-butylamino-2-methylbutane (XVIII). The lithium amide of XVIII gave satisfactory metalation with B-methyl-BBN.



$$CH_3\text{-}\underset{H_3C}{\overset{H_3C}{C}}\text{-}\underset{H}{N}\text{-}\underset{CH_3}{\overset{CH_3}{C}}\text{-}CH_2CH_3$$

XVIII

Surprisingly, lithium bis(trimethylsilyl)amide (XIX), which appears to be as bulky as the tetramethylpiperidide, gave very poor yields of metalated organoboranes. No data on the pKa of the bis(trimethylsilyl)amine could be found in the literature, but we assume the pKa to be

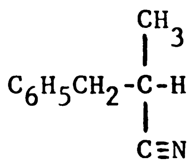


XIX

lower than that of the dialkyl amine, since the silicon can provide charge delocalization with its empty 3d orbital.[39] The lower basicity of the silyl amide could be a factor in the poor yields of organoborane metalation. It is also possible that the Si-N bond length is longer than the C-N length. This would make XIX actually less hindered than it appears.

Solvent Effects.

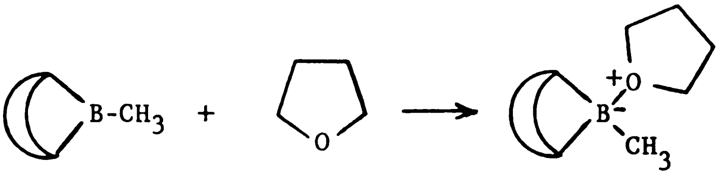
Solvents can play a large part in determining the rate of carbanion formation. Thus, an increase in the rate of carbanion generation is usually observed when more polar solvents are used. For example, the base-catalyzed racemization of optically active 2-methyl-3-phenylpropionitrile (XX) is much faster in DMSO than in alcohol solvents.[40]



$$\begin{array}{r} CH_3 \\ | \\ C_6H_5CH_2\text{-}C\text{-}H \\ | \\ C\equiv N \end{array}$$

XX

Because the lithium amides and the metalated organoboranes are extremely basic reagents, we were limited to non-proton-donating solvents in our own studies. Although lithium 2,2,6,6-tetramethylpiperidide is much more soluble in more polar solvents (tetrahydrofuran, ethyl ether, and HMPA) than in benzene or cyclohexane, the rate of organoborane metalation in these solvents is usually the same or lower in comparison to benzene. Possibly, the more polar solvents coordinate to the organoborane and in this manner, as shown for tetrahydrofuran (eq. 45), hinder the desired ionization reaction.

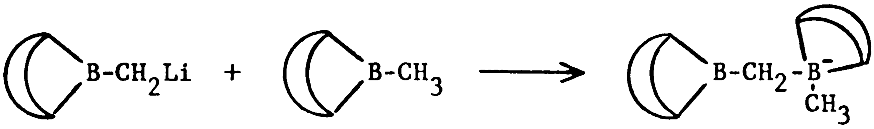


(45)

Matteson has indicated the possibility of metalated organoboranes, $^{-}C[B(OR)_2]_3$, abstracting protons from supposedly "aprotic" solvents, such as tetrahydrofuran and dimethyl sulfoxide.[26,27] We do not have any evidence for proton abstraction from tetrahydrofuran in our own investigations, but this possibility cannot be ruled out.

Reactions of Metalated Organoboranes.

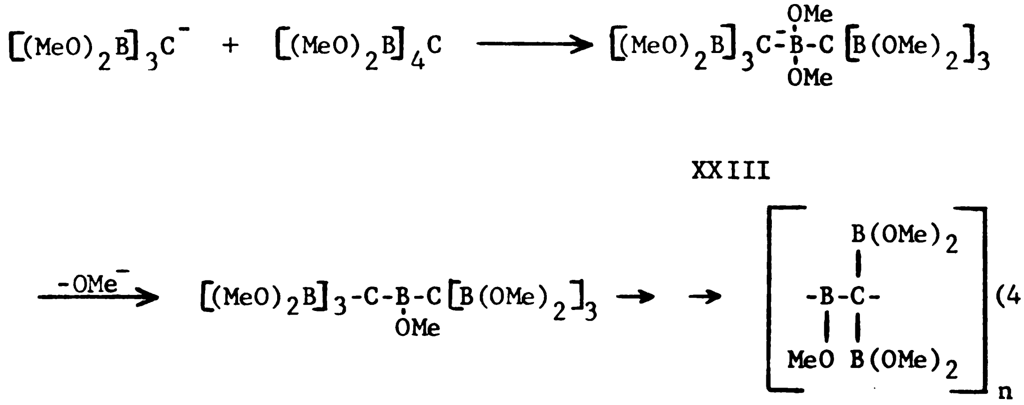
The yields of the alkylation, deuteration, and condensation reactions with the metalated derivatives of B-methyl-9-borabicyclononane, obtained with one equivalent of base, seldom exceeded 50 percent, showing incomplete formation of the metalated derivative. One possible reason for the incomplete formation of the metalated organoborane may be the formation of a complex. The newly formed metalated organoborane XXI can attack the boron atom of unreacted starting material to form an addition complex (eq. 46).



(46)

XXI VIII XXII

If formed, the complex XXII would prevent at least half of the starting organoborane from reacting with the amide. Matteson reported a similar problem in his own studies (eq. 47).[23]



$$[(MeO)_2B]_3C^- + [(MeO)_2B]_4C \longrightarrow [(MeO)_2B]_3C\text{-}\overset{OMe}{\underset{OMe}{B^-}}\text{-}C[B(OMe)_2]_3$$

XXIII

$$\xrightarrow{-OMe^-} [(MeO)_2B]_3\text{-}C\text{-}\underset{OMe}{B}\text{-}C[B(OMe)_2]_3 \rightarrow \rightarrow \left[\begin{array}{c} \quad B(OMe)_2 \\ -B-C- \\ MeO \; B(OMe)_2 \end{array}\right]_n \quad (47)$$

In Matteson's case, the resulting complex XXIII can lose a methoxide group, add another carbanion, and continue the process to form a polymer. There are no good leaving groups in XXII and consequently, formation of a polymer is prevented. Formation of the complex XXII, if it occurs, is probably an equilibrium reaction, as excess base usually increases the amount of metalation to greater than 50 percent, and because the metalated organoborane can be alkylated.

Alkylation of metalated organoboranes takes place readily with alkyl halides. We found that benzyl chloride gave lower yields of substitution product compared with the primary alkyl halides and the deuteration studies. Matteson also found the benzyl halides to be poor alkylating agents with his triborylmethide anions.[20,23] The difficulty with the benzyl halides could be due to a competing metal-halogen exchange between the halide and the metalated organoborane (eq. 48).

$$\gt B\text{-}\overset{Li}{\underset{|}{C}}\text{-} + C_6H_5CH_2X \longrightarrow \gt B\text{-}\overset{X}{\underset{|}{C}}\text{-} + C_6H_5CH_2Li \qquad (48)$$

Matteson examined one of the reaction mixtures of benzyl bromide and a triborylmethide anion by treatment with carbon dioxide, and verified the metal-halogen side reaction (eq. 49).

$$Li^{+-}C(BO_2C_3H_6)_3 + PhCH_2Br \longrightarrow BrC(BO_2C_3H_6)_3 + PhCH_2Li \qquad (49)$$

$$\xrightarrow[2.\ H_3O^+]{1.\ CO_2} PhCH_2CO_2H$$

58%

Limitations of Metalated Organoboranes.

Although B-methyl-9-borabicyclononane gives reasonable yields of metalated organoborane, other trialkylboranes do not form metalated derivatives readily. Part of the difficulty could rest in the difference in the acidity of the α-protons present in the different organoboranes. The pKa's of the α-protons of organoboranes are not known, but if we assume that the effect of the boron atom is equal in all organoboranes and that the pKa's for methane, ethane, and cyclopentane are 40, 42, 44 respectively,[41] then the methyl protons of B-methyl-BBN should be more acidic than the α-protons of triethylboron, which should be more acidic than the α-proton in B-cyclopentyl-BBN. Triethylboron and B-cyclopentyl-BBN could be such weak acids that lithium 2,2,6,6-tetramethylpiperidide is not sufficiently strong as a base to give good yields of metalation.

Another factor that may account for the lower yields of metalated derivatives with other organoboranes could be that the anion of B-methyl-BBN forms a complex (XXII) with unreacted starting material, and that such complexation helps to stabilize the metalated compound. The metalated derivatives of the other trialkylboranes might be too hindered to form such complexes.

Since the formation of metalated derivatives from organoboranes is not a quantitative reaction, the use of the metalated organoboranes as a synthetic intermediate will be limited. Unreacted base in the reaction mixture will react with other reagents and contaminate the desired reaction. For example, the addition of enolizable ketones and aldehydes to the metalated organoborane mixture will undergo self-condensation because of the unreacted amide. Because the formation of metalated organoboranes is not quantitative, much of the starting material is also lost in a synthetic process.

EXPERIMENTAL SECTION

I. General

Spectra.

Proton magnetic resonance spectra were measured using a Varian T-60 spectrometer. The mass spectra were determined by Mrs. Lorraine Guile of this department with a Hitachi-Perkin-Elmer model RMU-6 spectrometer.

Gas Chromatography.

Vapor phase chromatographic analysis and preparative work were carried out on a Varian Aerograph A-90 thermal conductivity chromatograph. Relative peak areas were determined by a Varian disc chart integrator-model 255.

II. Materials

Handling of Materials.

All reactions were carried out under a nitrogen atmosphere and all liquids were transferred in glass syringes under nitrogen. All solvents were carefully dried and stored under a nitrogen atmosphere over molecular sieves. Extra precautions must be taken with the organoboranes, as they tend to oxidize quite rapidly in the presence of oxygen.

Amines.

All amines, except for 2-t-butylamino-2-methylbutane, were commercially available and were distilled before use.

Preparation of 3-chloro-3-methyl-1-butyne.

84 gms. of dimethylethynylcarbinol (1 mole) was stirred with 420 ml. of concentrated hydrochloric acid (5 moles) containing 1 gm. of hydroquinone while the reaction flask was cooled with a water bath. After 1 hour of stirring the two layers were separated and the organic layer dried over anhydrous potassium carbonate. The organic layer was distilled and the fraction boiling at 73-80°C was collected, this fraction was redistilled using a Vigreaux column and the product collected at 74-75°C.

Preparation of 2-t-butylamino-2-methylbutane.

A solution of 33.6 gms. (.6 moles) of potassium hydroxide, 30 milligrams of powdered copper, and 126 ml. (1.2 moles) of t-butyl amine in 50 ml. of water was placed in a 500 ml. three-necked flask equipped with a mechanical stirrer and addition funnel. 45.3 ml. (.4 moles) of 3-chloro-3-methyl-1-butyne was then added through the addition funnel over a 2 hour period with vigorous stirring. After stirring for an additional two hours the mixture was allowed to stand overnight. The organic layer was then separated and the aqueous portion extracted with pentane, which was added to the organic layer. The combined organic extracts were washed four times with 100 ml. of water and then dried over potassium carbonate. After removal of the solvent by a rotary evaporator , the remaining organic mixture was added to a hydrogenation flask with 30 ml. of ethanol and 1 gm. of RaNi. The mixture was hydrogenated for 24 hours at room temperature. After the hydrogenated mixture was filtered distillation gave 16 gms. of product (28%), b.p. 140°C.

Preparation of 9-Borabicyclo[3.3.1] nonane.

A 500 ml. flask equipped with a reflux condenser, an addition funnel, a magnetic stirring bar, and a side-arm fitted with a rubber serum stopper was flushed with nitrogen and maintained under a static nitrogen atmosphere. In the flask was placed 163 ml. of .61M borane (.1 mole) in tetrahydrofuran and the flask was immersed in an ice bath. In the dropping funnel was placed 12.2 ml. (.1 mole) of 1,5-cyclooctadiene. The diene was added dropwise to the $BH_3 \cdot THF$ solution with vigorous stirring. The mixture was then heated under reflux for one hour. The 9-borabicyclo[3.3.1] nonane was left in the flask in the THF solution for subsequent steps.

Preparation of B-methyl-9-borabicyclo[3.3.1] nonane.

The same set-up as that used for the preparation of 9-BBN was used for the preparation of the methyl derivative. 100 ml. of a .1M solution of methyllithium (.1 mole) in ether was placed in the cleaned dropping funnel and added dropwise to the solution of 9-BBN at 0°C over a period of one hour. This was immediately followed by dropwise addition of 6.5 ml. of methanesulfonic acid (.1 mole) and approximately .1

mole of hydrogen was rapidly evolved. The salt was allowed to settle, and the clear solution was transferred under nitrogen to a distilling flask and the product distilled. A 70 percent yield of B-methyl-9-BBN, b.p. 67-68°C/14 mm., was obtained.

Preparation of B-cyclopentyl-9-borabicyclo[3.3.1]nonane.

9.8 ml. of cyclopentane (.1 mole) was added to a solution of 9-BBN (.1 mole) dropwise at 0°C. The mixture was allowed to stir for 2 hours at room temperature. After removal of the solvent by a vacuum the product was distilled, 110-114°C/7mm. (78%).

Triethylborane.

Triethylborane was commercially available and was used without further purification.

Cyclohexanone.

Cyclohexanone was commercially available and was distilled before use.

Alkyl halides.

All the alkyl halides were commercially available and were used without further purification.

III. Bases

All the lithium amides were prepared in the manner to that illustrated below for lithium 2,2,6,6-tetramethylpiperidide. t-butyllithium was commercially available as a solution in pentane.

Preparation of lithium 2,2,6,6-tetramethylpiperidide.

A 50 ml. round-bottomed flask equipped with a side-arm fitted with a rubber serum stopper was attached to a gas connection tube and mercury bubbler. The apparatus was flame dried under nitrogen and allowed to cool to room temperature. To this flask was added 2.07 ml. (5 mmoles) of 2.4M BuLi in hexane. At 0°, 0.85 ml. of 2,2,6,6-tetramethylpiperidine was added dropwise over a period of a few minutes to the butyllithium. As the reaction proceeded, butane was evolved and the temperature of the reaction mixture increased. After the addition of the amine the mixture was stirred for a few minutes and the solvent removed with a water aspirator to give a whitish-yellow solid of the lithium amide. The base was left in the flask for subsequent reactions.

IV. Studies with Metalated Organoboranes

PMR Studies of the Reaction Mixtures.

In the pmr studies of the reaction mixtures 5 ml. of benzene or tetrahydrofuran was added to the solid lithium amide (5 mmoles) in the 50-ml. round-bottomed flask equipped with a reflux condenser under a nitrogen atmosphere. 0.75 ml. of B-methyl-BBN (5 mmoles) was then added to the mixture and the solution refluxed. Although the amides are not soluble in the benzene the amides did disolve after the addition of the organoborane and the application of heat. 0.4 ml. aliquots of the reaction mixtures are removed at intervals and transferred to a pmr tube under nitrogen, at which point pmr spectra are taken.

Deuterium Oxide Quenching of the Reaction Mixture of B-methyl-BBN.

5 ml. of benzene, or whatever solvent was being tested, was added to the lithium amide (5 mmoles). 0.75 ml. of B-methyl-BBN (5 mmoles) was then added to the reaction mixture and stirred for the appropriate time interval at room temperature. The mixture was quenched with 1 ml. of deuterium oxide, followed by the addition of 1.0 ml. 3N hydrochloric acid a few minutes later. The water layer was removed with a syringe and the remaining organic layer was saturated with anhydrous potassium carbonate. The B-methyl-BBN was collected by preparative glpc using a ¼ inch by 6 ft. SE-30 column. The collected organoborane was then analyzed by mass spectrometer.

Deuterium Oxide Quenching of the Reaction Mixtures of B-cyclopentyl-BBN.

5 ml. of benzene was added to the lithium amide (5 mmoles), and was followed by the addition of 0.99 ml. of B-cyclopentyl-BBN (5 mmoles). After stirring for 1 hour at room temperature, 1 ml. of deuterium oxide was added to the reaction mixture and then stirred for a few minutes. 2 ml. of ethanol was then added to the mixture, and was followed by 1.9 ml. of 3 N sodium hydroxide. After cooling the reaction flask to 0^oC with an ice bath, 1.7 ml. of a 30% solution of hydrogen peroxide was added to the solution dropwise. After 10 minutes the organic layer was washed successively with 3 N hydrochloric acid, water, and saturated sodium chloride solution. After drying the organic layer with anhydrous magnesium sulfate, cyclopentanol was collected by preparative glpc using a ¼ inch by 6 ft. carbowax column. The collected cyclopentanol was then analyzed by pmr.

Stability of B-methyl-BBN to Reaction Conditions and Water.

The stability of B-methyl-BBN to the reaction conditions was tested by stirring the B-methyl-BBN (5 mmoles) at room temperature in benzene containing the lithium amide (5 mmoles) and 5 mmoles of undecane (for glpc analysis). Aliquots were removed at appropriate intervals and added to water. The water was removed and the organic layer dried with anhydrous potassium carbonate. The mixture was then analyzed by glpc. Aliquots at the end of 4 days showed the B-methyl-BBN present in 90-100 percent quantities.

Refluxing of the reaction mixture and testing of the aliquots for B-methyl-BBN showed the organoborane stable for short periods of reflux, but only 30 percent of the organoborane could be recovered after 22 hours of reflux.

Removal of Amine by Distillation from Reaction Mixture.

Sixty ml. of xylene was added to the lithium amide IX (5 mmoles) in a 100 ml. round-bottomed flask equipped with a distilling head and a side arm fitted with a rubber serum cap. B-methyl-BBN (5 mmoles) was added to the mixture and the solvent and amine were distilled at 40°C/22 mm. Fresh xylene was added periodically to the flask as the distillation proceeded. A total of 180 ml. of xylene was distilled and the recovered xylene was analyzed by glpc for 2,2,6,6-tetramethylpiperidine (4.3 mmoles recovered). The reaction flask, containing approxmately 10 ml. of solution, was cooled to room temperature and 0.58 ml. of benzyl chloride (5 mmoles) was added to the reaction flask and stirred for 15 minutes. The reaction flask was then cooled to 0^{o} with an ice bath and 3 ml. of ethanol was added, followed by 1.9 ml. of 3N sodium hydroxide. 1.7 ml. of 30% hydrogen peroxide was added dropwise to complete the oxidation of the organoborane. The mixture was saturated with potassium carbonate and analyzed by glpc for β-phenylethanol (6 percent).

V. Preparation and Reactions of Metalated Organoboranes.

The preparation given below is representative of the many reaction procedures used.

Preparation of Metalated B-methyl-BBN.

5 ml. of benzene was added to the lithium amide (5 mmoles) in the 50 ml. round-bottomed flask. The B-methyl-BBN (5 mmoles) was added to the undissolved amide at room temperature. The amide gradually dissolves over a period of an hour to give a clear yellow solution. The mixture was stirred for 12 hours, during which time a yellow precipitate forms. The metalated derivative was left in the flask for subsequent reactions.

Reaction of Metalated Organoboranes with Alkyl Halides.

The procedure given below is representative.

1.1 ml. of n-butyl bromide (10 mmoles) was added to the solution of metalated B-methyl-BBN (5 mmoles) and the mixture stirred for one hour at room temperature. The reaction flask was cooled to $0^{o}C$ by an ice bath and 2 ml. of ethanol and 1.9 ml. of 3N sodium hydroxide was added. 1.7 ml. of 30% hydrogen peroxide was added dropwise and the mixture stirred an additional 15 minutes at room temperature. The solution was saturated with potassium carbonate and the organic layer removed. 0.3 ml. of ethylbenzene was added to the organic layer as an internal standard for glpc analysis. The mixture was analyzed by glpc on a carbowax column; yield of n-pentanol was 42 percent.

All alcohols from the alkylation reactions had identical nmr spectra compared with the commercially available product.

Reaction of Cyclohexanone with Metalated B-methyl-BBN.

0.75 ml. of cyclohexanone (7.5 mmoles) was added to metalated B-methyl-BBN (5 mmoles) dropwise at room temperature and the mixture stirred for an hour. 2 ml. of ethanol was added to the reaction mixture and the flask was cooled to 0^o with an ice bath. 1.9 ml. of 3N sodium hydroxide was added to this solution, followed by 1.7 ml. of 30% hydrogen peroxide added dropwise. The mixture was stirred for an additional fifteen minutes at room temperature. 0.35 ml. of cumene was added as an internal standard for glpc analysis, and this organic layer was washed successively with 3N hydrochloric acid, water, and saturated sodium chloride. After drying over anhydrous magnesium sulfate the mixture was analyzed by glpc using an SE-30 column. 53 percent methylenecyclohexane was detected.

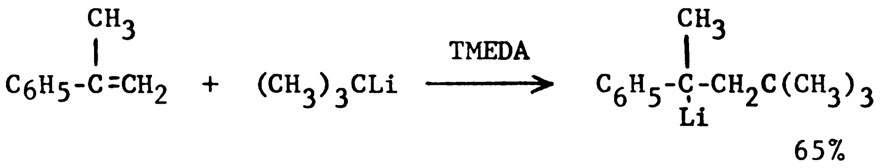
CHAPTER II

THE PREPARATION AND REACTIONS OF METALATED VINYLBORANES

INTRODUCTION

The formation of metalated derivatives of trialkylboranes using lithium amide bases is not a quantitative reaction. This limits its usefulness in organic synthesis. One of the reasons suggested for the poor yields of metalation is the weak acidity of the alpha protons in the trialkylboranes. There are two possible solutions to this problem: 1) a stronger base (for example, an alkyllithium compound) could be used for the proton abstraction, or 2) the metalated organoboranes could be made from more acidic boron compounds (for example, the vinylboranes).

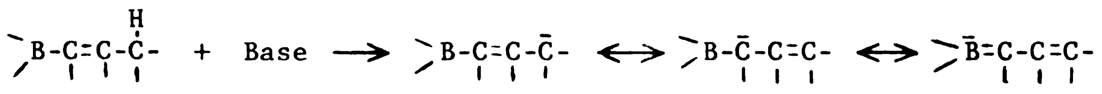
Initially, we worked on the first solution, but the synthesis of alkyllithium compounds of large steric requirements gave poor yields of alkyllithium reagents (for example, eq. 50),[42] and after a few



$$C_6H_5\text{-}\overset{CH_3}{\overset{|}{C}}{=}CH_2 \;+\; (CH_3)_3CLi \xrightarrow{TMEDA} C_6H_5\text{-}\underset{Li}{\overset{CH_3}{\overset{|}{C}}}\text{-}CH_2C(CH_3)_3 \qquad (50)$$

65%

experiments we decided to explore the possibility of using the more acidic vinylboranes to form metalated organoboranes. The vinylboranes are expected to be more acidic than trialkylboranes because of increased delocalization of charge in the anion (eq. 51).[43]



$$>B\text{-}C{=}C\text{-}\overset{H}{C}\text{-} \;+\; \text{Base} \longrightarrow\; >B\text{-}C{=}C\text{-}\bar{C}\text{-} \;\longleftrightarrow\; >B\text{-}\bar{C}\text{-}C{=}C\text{-} \;\longleftrightarrow\; >\bar{B}{=}C\text{-}C{=}C\text{-}$$

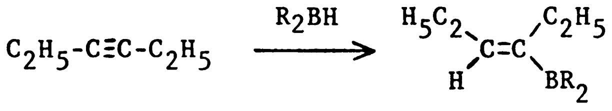
(51)

The vinylboranes are easy to prepare and react quite readily with lithium 2,2,6,6-tetramethylpiperidide to form metalated vinylboranes in good yields. The metalated vinylboranes were reacted with a number of electrophilic reagents to give a variety of products. The results of these studies are presented in the following section.

RESULTS

Synthesis of Vinylboranes.

Vinylboranes can be prepared by the addition of dialkylboranes to alkynes.[12] For example, the hydroboration of 3-hexyne with disiamylborane or dicyclohexylborane goes quantitatively to the vinyldialkylborane (eq. 52).



$$C_2H_5\text{-}C{\equiv}C\text{-}C_2H_5 \xrightarrow{R_2BH} (H_5C_2)(H)C{=}C(C_2H_5)(BR_2) \qquad (52)$$

(R = cyclohexyl or siamyl)

This reaction proceeds by a cis addition to the triple bond. Terminal alkynes react with these dialkylborane reagents to give a vinyl derivative with the boron on the terminal carbon (eq. 53).

$$R'C{\equiv}CH \ + \ R_2BH \longrightarrow R'CH{=}CHBR_2 \qquad (53)$$

(R = cyclohexyl or siamyl)

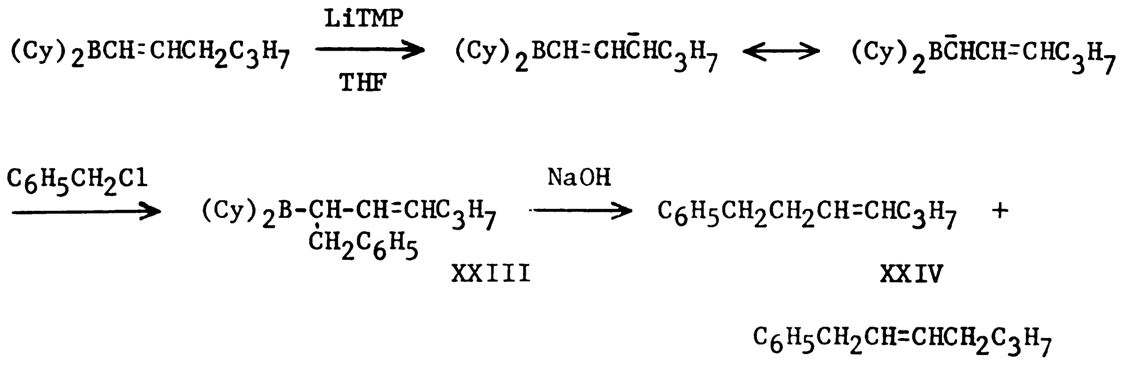
The preparation of these vinylboron compounds was carried out in tetrahydrofuran and the compounds were not isolated.[12] In our studies the solutions of the vinylboron compounds were added directly to the base.

Studies with 2-lithio-2-phenyl-4,4-dimethylpentane.

The addition of one equivalent of t-butyllithium in pentane to one equivalent of α-methylstyrene in the presence of TMEDA gave a 65 percent yield of 2-lithio-2-phenyl-4,4-dimethylpentane (eq. 50). The yield of alkyllithium reagent was determined by quenching the reaction mixture with water and analyzing for 4-phenyl-2,2-dimethylpentane by glpc. A solution of hexenyldicyclohexylborane in tetrahydrofuran was added to this alkyllithium reagent and the mixture was stirred for an hour. Analysis of the mixture by glpc, after quenching with n-octyl bromide and oxidation with alkaline hydrogen peroxide, did not reveal any products from the reaction of n-octyl bromide with metalated hexenyldicyclohexylborane. Possibly, the alkyllithium reagent is not bulky enough to prevent coordination to the boron atom in the vinylborane.

Initial Studies of Vinylboranes with LiTMP.

The addition of hexenyldicyclohexylborane in tetrahydrofuran to lithium 2,2,6,6-tetramethylpiperidide at room temperature produced a light red solution. After stirring for 15 minutes the mixture was quenched with benzyl chloride. Oxidation of the quenched reaction mixture with sodium hydroxide and hydrogen peroxide gave a 50 percent yield of two $C_{13}H_{18}$ alkenes. The two alkenes, XXIV and XXV were assumed to be formed through the following mechanism (eq. 54).



$$(Cy)_2BCH{=}CHCH_2C_3H_7 \xrightarrow[THF]{LiTMP} (Cy)_2BCH{=}CH\bar{C}HC_3H_7 \longleftrightarrow (Cy)_2B\bar{C}HCH{=}CHC_3H_7$$

$$\xrightarrow{C_6H_5CH_2Cl} \underset{\textstyle CH_2C_6H_5}{(Cy)_2B\text{-}CH\text{-}CH{=}CHC_3H_7} \xrightarrow{NaOH} C_6H_5CH_2CH_2CH{=}CHC_3H_7 + C_6H_5CH_2CH{=}CHCH_2C_3H_7$$

XXIII XXIV XXV (54)

The formation of the alkenes was surprising, as we had expected the allyl portion of XXIII to be oxidized to the corresponding allyl alcohol. A search of the literature revealed that allyldialkylboranes (e.g. XXIII) are very reactive and hydrolyze rapidly in water[44] and therefore, XXIII must be undergoing hydrolysis faster than oxidation.

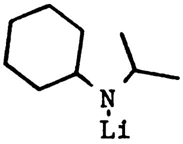
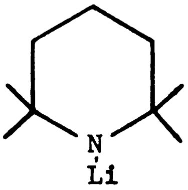
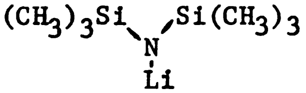
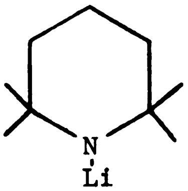
Since benzyl chloride did not give very good results in our earlier studies we decided to use other alkyl halides to quench the reaction mixture. Under the same conditions as those used for benzyl chloride, n-octyl bromide gave a 70 percent yield of $C_{14}H_{28}$ alkenes.

Hexenyldicyclohexylborane was reacted with a variety of bases to determine their relative effectiveness in forming metalated derivatives. No bases, other than LiTMP, produced a red solution when added to the vinylboranes and only the reaction mixtures with LiTMP gave alkenes on quenching with an alkyl halide (Table 7).

Reaction conditions were varied in an attempt to increase the yield of alkenes. Formation of the metalated compounds was essentially complete in 15 minutes at room temperature. Reactions ran at lower temperatures (e.g. 0°C) usually gave poorer yields of alkenes

TABLE 7

Effect of different bases on the metalation of hexenyldicyclohexylborane.

Base	Alkyl Halide	% Yield of Alkenes[a]	Conditions[b]
	$C_6H_5CH_2Cl$	0	15 minutes/r.t.
	$C_6H_5CH_2Cl$	50	15 minutes/r.t.
 $(CH_3)_3Si\text{-}N(Li)\text{-}Si(CH_3)_3$	$n\text{-}C_8H_{17}Br$	0	20 hours/r.t.
	$n\text{-}C_8H_{17}Br$	70	15 minutes/r.t.
$(CH_3)_3CLi$	$n\text{-}C_8H_{17}Br$	0	15 minutes/r.t.

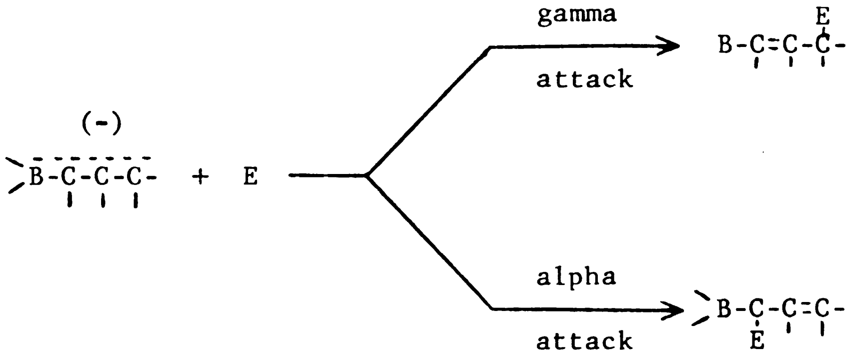
[a] Yields determined by glpc.

[b] Conditions listed are the reaction time of the base and hexenyldicyclohexylborane.

(Table 8). No solvents other than tetrahydrofuran were tested.

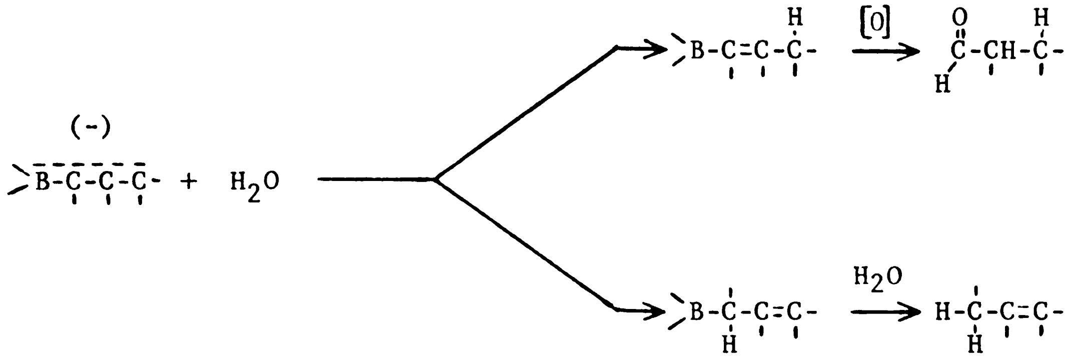
Quenching of the Reaction Mixture with Water.

Once the optimum conditions for the formation of the metalated organoboranes were established, we studied the reactions of these derivatives with different electrophilic reagents. Because they are resonance hybrids, metalated vinylboranes have two sites of reactivity (eq. 55).



(55)

Attack of a proton at the alpha carbon, followed by hydrolysis, would give an alkene (eq. 57), whereas attack at the gamma carbon, followed by oxidation would give an aldehyde (eq. 56).



(56)

(57)

TABLE 8

Effect of time and temperature on the formation of metalated hexenyldicyclohexylborane.

Conditions[a]	Alkyl Halide	% Yield of alkenes[b]
0^{o}/1 hour	$C_8H_{17}Cl$	62
0^{o}/4 hours	$C_8H_{17}Cl$	67
r.t./15 min.	$C_8H_{17}Cl$	66
r.t./15 min.	$C_8H_{17}Br$	70
r.t./1 hour	$C_8H_{17}Cl$	72

[a] Conditions listed are for the reaction of LiTMP with hexenyldicyclohexylborane.

[b] Yields determined by glpc.

In our first experiment with water as the quenching reagent, the metalated compound from octenyldicyclohexylborane was quenched with 3N sodium hydroxide, followed by hydrogen peroxide oxidation. After work-up, only a 22 percent yield of the alkene and approximately 6 percent of the aldehyde was obtained. Further analysis of the reaction mixture showed a 72 percent yield of 2-octene-1-ol. This was unexpected, since our initial studies and other reports[44] indicate that allyldialkylboranes are unstable in the oxidation mixture and are hydrolyzed before oxidation can take place. A review of the laboratory procedures for our earlier oxidations of the allyldialkylboranes showed that the sodium hydroxide solution was added at room temperature and in the later oxidations the addition of the sodium hydroxide was done at 0°C. The allyldialkylboranes must be less reactive to water at the lower temperatures and therefore can be oxidized to the allyl alcohols.

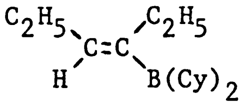
A number of experiments were conducted to determine the optimum conditions for the formation of the allyl alcohols. Refluxing of the quenched reaction mixture with 3N sodium hydroxide hydrolyzed the allylborane completely and produced a 95 percent yield of alkenes (no allyl alcohol was detected). Slow quenching of the metalated vinylboranes at low temperatures (0°C), followed by a slow oxidation (addition of the hydrogen peroxide at a slow rate) gave good yields of the allyl alcohol (Table 9).

Alkylation of Metalated Vinylboranes.

After we discovered that the oxidation of allyldialkylboranes can be controlled to give allyl alcohols, we studied the reactions of alkyl halides with the metalated vinylboranes using the new oxidation

TABLE 9

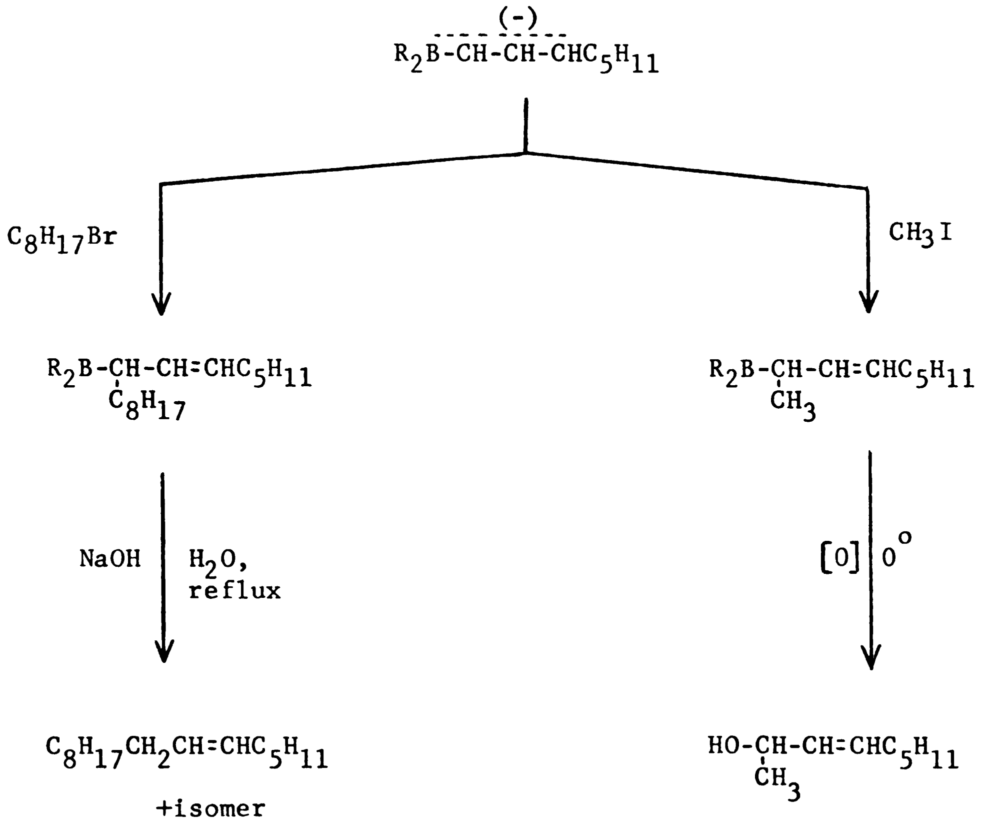
Quenching of the reaction mixtures with water.

Organoborane	Conditions[a]	Alkene (% yield)[b]	Aldehyde (% yield)	Alcohol (% yield)
$(Cy)_2BCH{=}CHC_6H_{13}$	3N NaOH/0°	1-octene + (22) 2-octene	octanal (6)	2-octene-1-ol (72)
$(Cy)_2BCH{=}CHC_6H_{13}$	3N NaOH/reflux 30 min.	1-octene + (95) 2-octene	octanal (5)	2-octene-1-ol (0)
$(Cy)_2BCH{=}CHC_6H_{13}$	3N NaOH/-78°	1-octene + (5) 2-octene	octanal (5)	2-octene-1-ol (84)
	3N NaOH/-78°			3-hexene-2-ol (71)
$(Cy)_2BCH{=}CHC_3H_7$	3N NaOH/-78°			2-pentene-1-ol (62)

[a] Conditions listed are those used for the quenching of the metalated vinylboranes. Mixtures were then oxidized with hydrogen peroxide at 0°C and analyzed by glpc.

[b] Yields of the alkenes and aldehydes for the last two vinylboranes on the list were not determined.

procedure. Thus, the reaction of n-octyl bromide with the metalated derivative of hexenyldicyclohexylborane was repeated. When the mixture was refluxed for 15 minutes with 3N sodium hydroxide following the addition of the alkyl halide, the yield of alkenes increased to 80 percent (eq. 58). Reaction of the metalated derivative of octenyldisiamylborane with methyl iodide, followed by careful oxidation at 0°C yielded 70 percent of 3-nonene-2-ol, and approximately 10 percent of isomeric nonenes from the hydrolysis reaction (eq. 59).

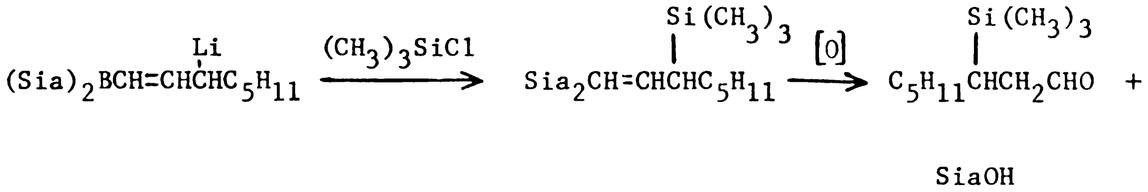


(R = cyclohexyl) (R = siamyl)

(58) (59)

Reaction of Metalated Vinylboranes with Trimethylchlorosilane.

Addition of trimethylchlorosilane to the metalated derivative of octenyldisiamylborane gave an immediate precipitate of lithium chloride, and subsequent hydrogen peroxide oxidation furnished 3-(trimethylsilyl)-octanal in 75 percent overall yields (from 1-octyne):



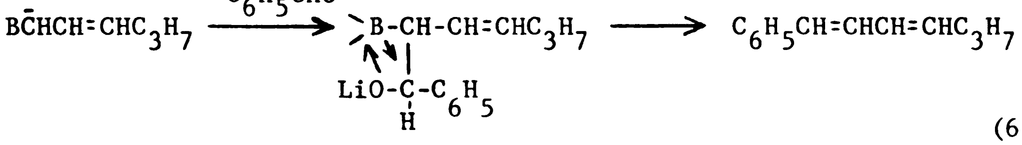
$$(\mathrm{Sia})_2\mathrm{BCH{=}CH}\overset{\mathrm{Li}}{\mathrm{C}}\mathrm{HC_5H_{11}} \xrightarrow{(\mathrm{CH_3})_3\mathrm{SiCl}} \mathrm{Sia_2CH{=}CH}\overset{\mathrm{Si(CH_3)_3}}{\mathrm{C}}\mathrm{HC_5H_{11}} \xrightarrow{[\mathrm{O}]} \mathrm{C_5H_{11}}\overset{\mathrm{Si(CH_3)_3}}{\mathrm{C}}\mathrm{HCH_2CHO} + \mathrm{SiaOH}$$

(60)

Other vinylboranes gave similar results and the yields are given in Table 10. In reactions with vinyldicyclohexylboranes the alkenes resulting from attack of trimethylchlorosilane at the gamma carbon, followed by hydrolysis, were identified, but the yields were not determined.

Reaction of Carbonyl Compounds with Metalated Vinylboranes.

The addition of benzaldehyde to hexenyldicyclohexylborane, followed by oxidation, gave a very low yield (less than 10 percent) of 1-phenyl-1,3-heptadiene. This product was probably formed by reaction of benzaldehyde at the alpha carbon of the metalated derivative (eq. 61).



$$\mathrm{B\bar{C}HCH{=}CHC_3H_7} \xrightarrow{\mathrm{C_6H_5CHO}} \mathrm{{>}B\text{-}\underset{\substack{|\\ \mathrm{LiO\text{-}\underset{H}{C}\text{-}C_6H_5}}}{CH}\text{-}CH{=}CHC_3H_7} \longrightarrow \mathrm{C_6H_5CH{=}CHCH{=}CHC_3H_7}$$

(61)

TABLE 10

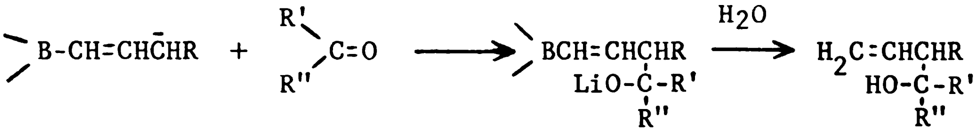
Conversion of disiamylvinylboranes to β-trimethylsilyl carbonyl compounds.

Alkyne	Silylated Product	Yield[a], %
1-pentyne	$CH_3CH_2CHSi(CH_3)_3CH_2CHO$	72
1-hexyne	$CH_3(CH_2)_2CHSi(CH_3)_3CH_2CHO$	66
1-octyne	$CH_3(CH_2)_4CHSi(CH_3)_3CH_2CHO$	75
3-hexyne	$CH_3CHSi(CH_3)_3CH_2COCH_2CH_3$	90

[a] Glpc, based on starting alkyne.

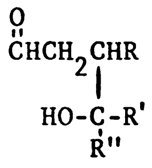
No identifiable product from reaction of benzaldehyde at the gamma carbon could be detected by gas chromatography.

The reaction of several ketones with metalated vinylboranes gave no dienes (attack at alpha carbon), although very low yields of alkenols (XXVII) were isolated from some of the reaction mixtures. These compounds were probably formed by hydrolysis of the intermediate XXVI from the reaction of the ketone at the gamma carbon of the metalated derivative (eq. 62).


(62)

XXVI XXVII

The expected product from the reaction of a carbonyl compound with the gamma carbon of a metalated vinylborane, followed by peroxide oxidation, would be a γ-hydroxyaldehyde (XXVIII), which might cyclize

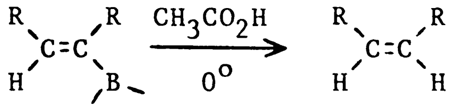

$$\overset{O}{\overset{\|}{C}}HCH_2\underset{\substack{|\\ HO-\underset{R''}{C}-R'}}{CHR}$$

XXVIII

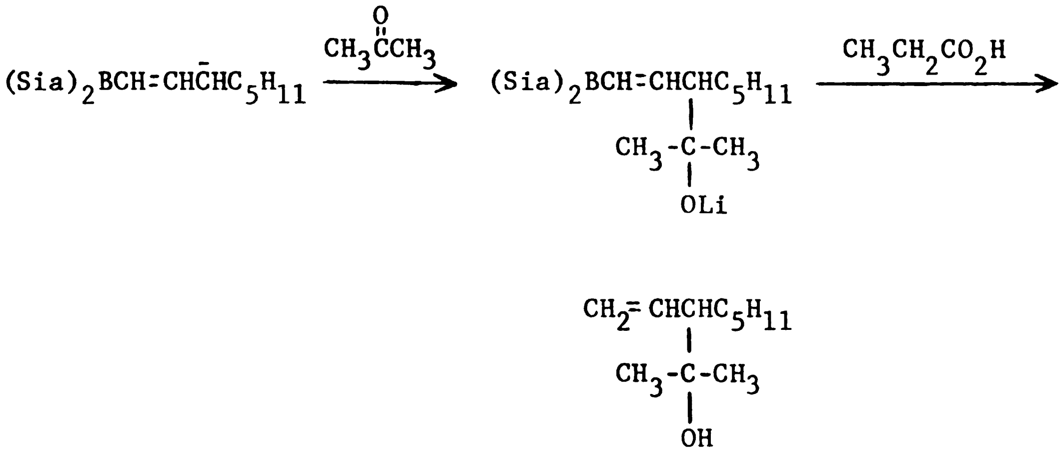
to a hemi-acetal.[45] No γ-hydroxyaldehydes or hemi-acetals could be detected in any of the reaction mixtures from carbonyl compounds and metalated vinylboranes. Possibly, XXVIII condensed in the basic solution used for the oxidations and the condensation products were not detected, or the products were lost in the work-up procedure.

Whatever the case, a new work-up procedure was needed.

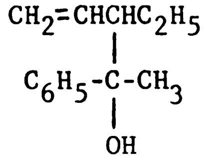
Vinylboranes readily undergo protonolysis with carboxylic acids at 0°C to give olefins (eq. 63).[12]


(63)

If XXVI is an intermediate in the reaction mixture, treatment with a carboxylic acid should give an alkenol, XXVII. To test this possibility, acetone was added to the metalated octenyldisiamylborane at room temperature. After 15 minutes propionic acid was added and the mixture was refluxed for 45 minutes, and then oxidized with alkaline hydrogen peroxide. The yield of alkenol, as determined by glpc analysis, was 72 percent (eq. 64).


$$\mathrm{(Sia)_2BCH{=}CH\overset{-}{C}HC_5H_{11}} \xrightarrow{\mathrm{CH_3\overset{O}{\overset{\|}{C}}CH_3}} \mathrm{(Sia)_2BCH{=}CH\underset{\underset{\underset{OLi}{|}}{CH_3-C-CH_3}}{\underset{|}{C}}HC_5H_{11}} \xrightarrow{\mathrm{CH_3CH_2CO_2H}} \mathrm{CH_2{=}CH\underset{\underset{\underset{OH}{|}}{CH_3-C-CH_3}}{\underset{|}{C}}HC_5H_{11}} \qquad (64)$$

A similar reaction with acetophenone and metalated pentenyldisiamylborane produced a 75 percent yield of XXIX.

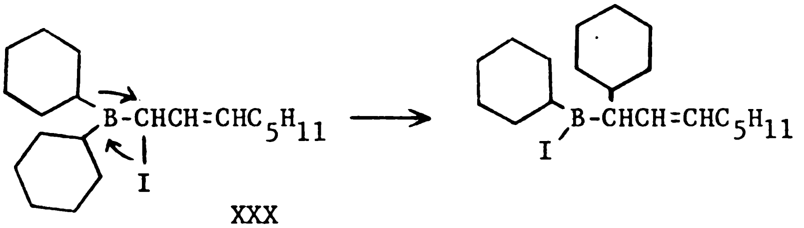


$$\begin{array}{c} CH_2{=}CHCHC_2H_5 \\ | \\ C_6H_5{-}C{-}CH_3 \\ | \\ OH \end{array}$$

XXIX

Miscellaneous Studies.

The reaction of iodine with metalated octenyldicyclohexylborane was attempted. Possibly, iodine would react at the alpha carbon of the metalated derivative to give XXX, which could then rearrange by transferring a cyclohexyl group to the octene chain (eq. 65).[46]

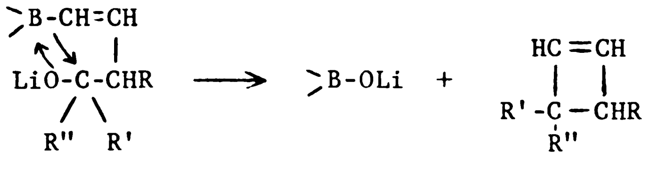


XXX

(65)

To this end, one equivalent of iodine was added to the metalated intermediate and the mixture stirred for one hour. After hydrogen peroxide oxidation at 0°C and work-up the mixture was analyzed. No products could be detected on the gas chromatograph (except for cyclohexanol and solvents). Other reaction conditions and work-up procedures were tried, but all gave the same negative results.

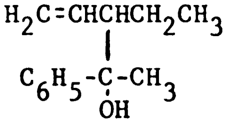
The intermediate XXVI, from the reaction of carbonyl compounds with metalated vinylboranes, is an interesting compound, which could conceivably undergo a 1,4-elimination to give a cyclobutene derivative (eq. 66).



XXVI

(66)

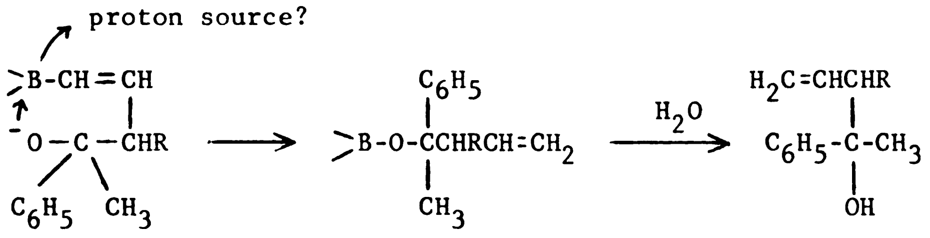
Therefore, to test this possibility, acetophenone was added to the metalated derivative of pentenyldicyclohexylborane and the mixture refluxed for one hour. After alkaline hydrogen peroxide oxidation a 70 percent yield of XXIX was obtained.



$$\begin{array}{c} H_2C{=}CHCHCH_2CH_3 \\ | \\ C_6H_5\text{-}C\text{-}CH_3 \\ OH \end{array}$$

XXIX

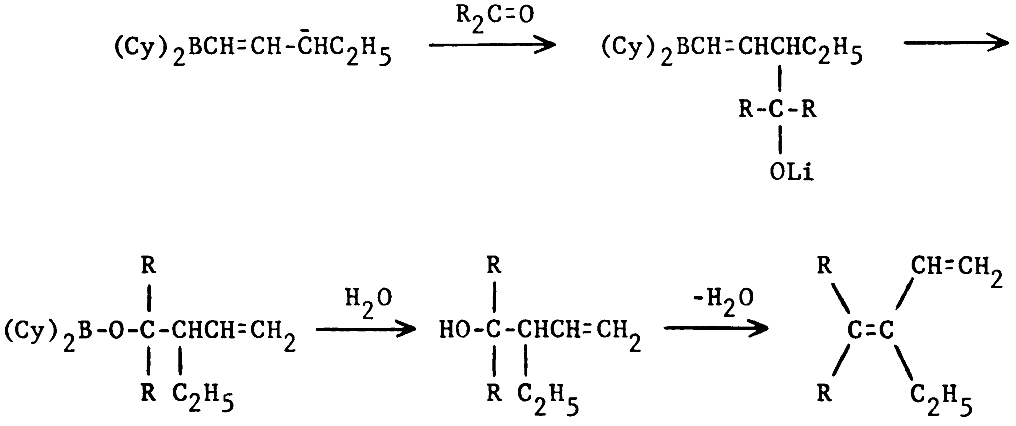
This product is the same as that obtained from the protonolysis reaction discussed earlier. Possibly the intermediate XXVI abstracts a proton from one of the reagents or solvent (eq. 67).



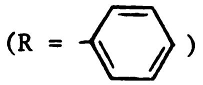
(67)

XXVI

In the same manner, the addition of benzophenone to metalated pentenyldicyclohexylborane, followed by two hours of reflux and hydrogen peroxide oxidation, gave a 90 percent yield of XXXI. The initial product is probably the alkenol, which loses water readily to give the diene (eq. 68).

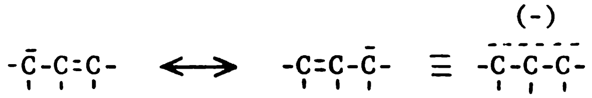


XXXI (68)



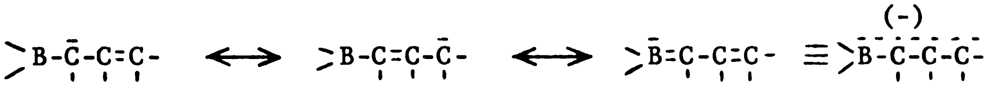
DISCUSSION

The results presented in the previous section show that vinylboranes can be metalated by lithium 2,2,6,6-tetramethylpiperidide in high yields. The yields are much higher than those obtained with the saturated organoboranes discussed in the first chapter. This change in the extent of metalation between the two groups is probably caused by the differences in the acidity of the allyl protons in vinylboranes and the alpha protons in saturated organoboranes. Allylic protons (pKa 36)[37] are more acidic than the protons on saturated hydrocarbons (pKa 40) because of the delocalization of charge in the allylic anion (Figure 5).[43] The increased acidity of the allyl protons in the vinylboranes is probably due to a similar delocalization of charge in the metalated vinylborane (Figure 6).



$$-\bar{C}-C=C- \longleftrightarrow -C=C-\bar{C}- \equiv -\overset{(-)}{\overline{C-C-C}}-$$

Figure 5. Allylic Anion



$$>B-\bar{C}-C=C- \longleftrightarrow >B-C=C-\bar{C}- \longleftrightarrow >\bar{B}=C-C=C- \equiv >\overset{(-)}{\overline{B-C-C-C}}-$$

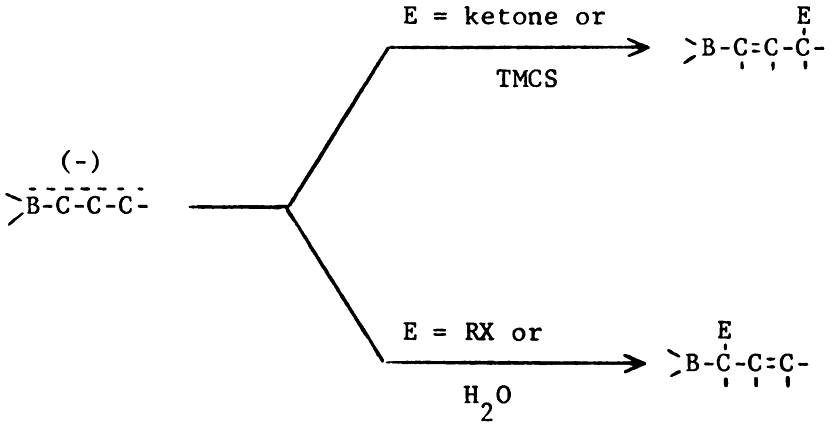
Figure 6. Metalated Vinylborane

Effect of Different Bases.

Although the protons in the vinylboranes are more acidic than the saturated organoboranes, a bulky base is still needed to effect deprotonation. Coordination of less hindered bases with boron probably takes place with the vinylboranes, since lithium diisopropylamide is still ineffective in the metalation reaction.

Sites of Reactions of Metalated Vinylboranes.

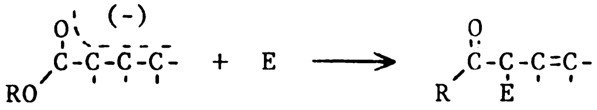
Metalated vinylboranes can conceivably react at either the alpha or gamma carbon. Our results show that metalated vinylboranes react with ketones and trimethylchlorosilane predominantly at the gamma carbon (eq. 69), and with alkyl halides and water predominantly at the alpha carbon (eq. 70).



(69)

(70)

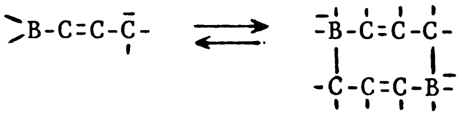
To some extent, these results may be due to steric factors. The larger reagents, because of steric repulsion by the dialkylboron group, attacks the position remote from the boron. This selectivity of reaction sites with metalated vinylboranes is different from those obtained with the enolate anions of α,β-unsaturated ketones or esters. Enolate anions derived from α,β-unsaturated ketones or esters undergo reaction almost exclusively at the carbon alpha to the carbonyl (eq. 71).[47]



(71)

The size of the dialkylboron group may also be a factor in controlling the site of reactivity. In the reaction with trimethylchlorosilane, the metalated vinyldicyclohexylboranes gave a mixture of of products (products from attack at the alpha carbon could be isolated), whereas the metalated vinyldisiamylboranes gave mostly one product (from attack at the gamma carbon). Since the disiamylboron group is probably larger than the dicyclohexylgroup, this difference is reasonable.

Because of the Lewis acidity of boron, the metalated vinylboranes can exist as dimers (for example, XXXII).

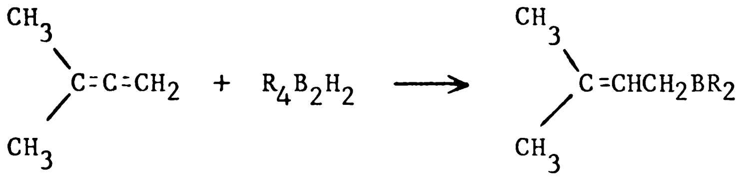


XXXII

The effect of such dimers on the preparation and reactions of metalated vinylboranes is not known, but if these dimers do exist, they certainly do not seem to stop either process.

Preparation of Allyldialkylboranes.

From this short study of metalated vinylboranes, these derivatives seem likely to have many synthetic applications. One of these is the synthesis of allyldialkylboranes. Allyldialkylborane compounds have previously been prepared by the addition of tetraalkyldiborane to allenic hydrocarbons (eq. 72).[48]

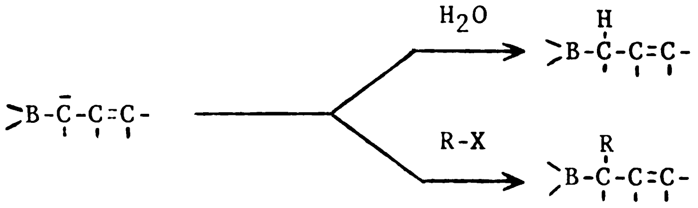


(72)

and from the addition of Grignard reagents to boron trifluoride (eq. 73).[49]

$$BF_3 + H_2C{=}CHCH_2MgBr \longrightarrow B(CH_2CH{=}CH_2)_3 \qquad (73)$$

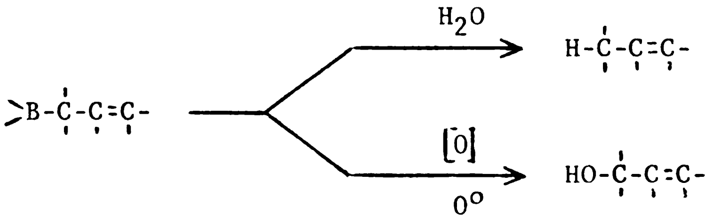
Metalated vinylboranes offer a new route to these reactive intermediates; allyldialkylboranes can be prepared from metalated vinylboranes by the addition of water (eq. 74) or by reaction with an alkyl halide (eq. 75).



(74)

(75)

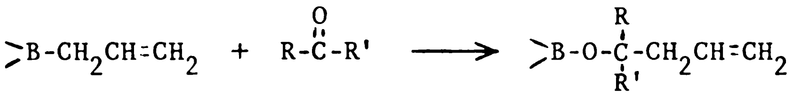
The allyldialkylboranes are very reactive intermediates and can undergo several transformations. They can be hydrolyzed to an alkene (eq. 76), or oxidized to an allyl alcohol (eq. 77).



(76)

(77)

Most trialkylboranes are inert to carbonyl compounds, but allydialkylboranes react readily with carbonyl compounds (eq. 78).[48]



$$>B-CH_2CH=CH_2 + R-\overset{O}{\overset{\|}{C}}-R' \longrightarrow >B-O-\overset{R}{\underset{R'}{C}}-CH_2CH=CH_2 \qquad (78)$$

Comparison of Metalated Vinylboranes to Metalated Trialkylboranes.

The metalation of vinylboranes not only occurs in higher yields than the metalation of trialkylboranes, but the procedure for the formation of metalated vinylboranes is much simpler. The vinyldialkylboranes are made in tetrahydrofuran and do not need to be isolated; the formation of the metalated vinylboranes occurs in the same solution, as do subsequent reactions. Also, the metalation takes only 15 minutes at room temperature, compared to several hours for the trialkylboranes. The synthesis of vinylboranes is one possible limitation in its usefulness in organic synthesis. Vinylboranes are prepared from alkynes and therefore, one is limited to alkynes for starting compounds.

EXPERIMENTAL SECTION

I. Materials

Alkyl halides.

All alkyl halides were commercially available and were used without further purification.

Alkenes.

Commercial cyclohexene and 2-methyl-2-butene were used. Both were distilled before use, cyclohexene at 82-83°C and 2-methyl-2-butene at 38-40°C.

Alkynes.

All alkynes were purchased from Chemical Samples and were used without further purification.

Carbonyls.

All carbonyl compounds were commercially available and were used without futher purification.

Trimethylchlorosilane.

Trimethylchlorosilane was commercially available and was distilled before use.

II. Vinyldialkylboranes

All preparations and reactions were conducted in flame-dried flasks and under a nitrogen atmosphere.

Preparation of Dicyclohexylborane.

In a 50 ml. round-bottomed flask equipped with a side-arm fitted with a rubber serum stopper was placed 2.03 ml. (20 mmoles) of cyclohexene and 10 ml. of tetrahydrofuran. The flask was cooled to 0^{o}, then 4.15 ml. of a 2.48M solution of borane (10 mmoles) in tetrahydrofuran was added slowly. During the borane addition, the dicyclohexylborane precipitated from solution. The mixture was stirred for an additional hour at $0^{o}C$ prior to its use.

Preparation of Disiamylborane.

Essentially the same procedure was followed for the preparation of disiamylborane as that used for the preparation of dicyclohexylborane. After addition of the borane the mixture was stirred for two hours at $0^{o}C$ before use. The disiamylborane is soluble in tetrahydrofuran and does not form a precipitate.

Preparation of Pentenyldicyclohexylborane.

The procedure given below for the preparation of pentenyldicyclohexylborane is representative of all the vinyldialkylboranes prepared.

To the dicyclohexylborane (10 mmoles) was added at $0^{o}C$ 0.98 ml. of pentyne (10 mmoles). The mixture was allowed to warm to room temperature and stirred an addition hour.

III. Studies with 2-lithio-2-phenyl-4,4-dimethylpentane

Preparation of 2-lithio-2-phenyl-4,4-dimethylpentane.

A 50 ml. round-bottomed flask equipped with a side arm fitted with a rubber serum cap was charged with 8.05 ml. of a 1.24 M solution of t-butyllithium (10 mmoles) in pentane. To this solution at $0^\circ C$ was added 1.28 ml. of TMEDA (10 mmoles). 1.29 ml. of α-methylstyrene (10 mmoles) was added dropwise to the slurry of t-butyllithium-TMEDA at $0^\circ C$. A deep red solution was obtained.

Analysis of the reaction mixture by quenching with water showed a 65 percent yield of 2,2-dimethyl-4-phenylpentane.

Attempted metalation of hexenyldicyclohexylborane with the alkyllithium reagent.

A 10 mmole solution of hexenyldicyclohexylborane was added to the solution of 2-lithio-2-phenyl-4,4-dimethylpentane and the mixture was stirred 20 minutes at room temperature. 10 mmoles of n-octyl bromide was then added to the solution. After 20 minutes the organoborane was oxidized with 4 ml. 3N sodium hydroxide and 3.4 ml. 30% hydrogen peroxide. Glpc analysis revealed no products from reaction of n-octyl bromide with metalated hexenyldicyclohexylborane.

IV. Preparation of Metalated Vinylboranes

The metalated vinylboranes were prepared in a manner similar to that illustrated for pentenyldicyclohexylborane.

Preparation of Lithium Pentenyldicyclohexylborane.

The solution of pentenyldicyclohexylborane (10 mmoles) was added at room temperature to the solid lithium 2,2,6,6-tetramethylpiperidide (10 mmoles) in a 50 ml. round-bottomed flask equipped with a side-arm fitted with a rubber serum cap. The solution became slightly warm and turned light red. The mixture was stirred for an additional 15 to 20 minutes.

V. Reactions of Metalated Vinylboranes

Product Analysis.

Most structures of products obtained were determined by PMR analysis. IR and mass spectra (molecular ion peak) data are also included for some compounds.

Reaction of Water with Metalated Vinylboranes.

Two procedures were used in the reaction of water with a metalated vinylborane. The procedures given below are representative. Internal standards are used for all glpc analysis.

(A) 4 ml. of 3N sodium hydroxide was added to 10 mmoles of lithium octenyldicyclohexylborane in THF and the mixture refluxed for 15 minutes. At 0°C 4 ml. 30% hydrogen peroxide was added dropwise. After 10 minutes of stirring 10 ml. of pentane was added and the two layers separated. The organic layer was washed successively with 10 ml. water, 10 ml. 3N hydrochloric acid, and 10 ml. saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate and the mixture analyzed by glpc using and SE-30 column. A 95 percent yield of 2- and 3-octene was obtained.

(B) The flask containing the solution of lithium octenyldicyclohexylborane was cooled to 0°C. 2 ml. H_2O was added to the solution dropwise, followed by .2 ml. 3N sodium hydroxide. After 10 minutes of stirring the two layers were separated and the organic layer washed with saturated sodium chloride solution. The organic layer was dried with anhydrous magnesium sulfate. Analysis of the reaction mixture by glpc with an SE-30 column showed a 72 percent yield of 2-octene-1-ol. PMR(CCl_4): 5.6δ(m,2H), 4.0δ(m,2H), 1.3δ(m,7H), 1.08δ(t,3H).

2-pentene-1-ol.

PMR(CCl_4): 5.6δ(m,2H), 4.0δ(m,2H), 2.1δ(m,3H), 1.0δ(t,3H). Mass Spect.: 86. IR(neat): 3350 cm^{-1}, 1680 cm^{-1}.

Alkylation of Lithium Vinyldialkylboranes.

Two methods were used to convert the product from the alkylation reaction into easily analyzable products. The first method (C) was to hydrolyze the allyldialkylboranes to alkenes, and the second method was to oxidize the allyldialkylboranes to allyl alcohols. The following procedures are representative.

(C) 1.0 ml. of n-butyl bromide (10 mmoles) was added to 10 mmoles of lithium hexenyldisiamylborane at room temperature. The mixture was then stirred for an additional 15 minutes. Procedure (A) was then followed and the mixture analyzed by glpc using an SE-30 column. An 80 percent yield of 4- and 5-decene was obtained.

Mixture of Decenes.

PMR(CCl_4): 5.4δ(m,2H), 2.0δ(m,4H), 1.0δ and 1.4δ(m,14H).
Mass Spectrum: m/e 140

(D) 0.62 ml. of methyl iodide (11 mmoles) was added to 10 mmoles of lithium octenyldisiamylborane at room temperature. The mixture was stirred for an additional 15 minutes. The flask was cooled to 0°C and 4 ml. of 3N sodium hydroxide was added slowly. 4 ml. of 30% hydrogen peroxide was then added dropwise. After 10 minutes of stirring 10 ml. of pentane was added and the two layers separated. The organic layer was washed successively with 10 ml. water, 10 ml. 3N hydrochloric acid, and 10 ml. saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate and the mixture analyzed by glpc. A 70% yield of 3-nonene-2-ol was obtained. PMR(CCl_4): 5.5δ(m,2H), 4.1δ(m,1H), 2.0δ to 1.0δ(m,15H). IR(neat): 3350 cm^{-1}, 1680 cm^{-1}.

Reaction of Trimethylchlorosilane with Metalated Vinylboranes.

1.3 ml. of trimethylchlorosilane (10 mmoles) was added to 5 mmoles of lithium octenyldisiamylborane at room temperature and the mixture stirred 30 minutes. The mixture was then oxidized using the same procedure outlined in (D). Glpc analysis with an internal standard showed a 73 percent yield of 3-(trimethylsilyl)-octanal. PMR(CCl_4): 9.9 δ(t,1H), 2.3δ(m,2H), 1.2δ(m,9H), .9δ(t,3H), 0.0δ(s,9H).

3-(trimethylsilyl)-hexanal.

PMR(CCl_4): 9.9δ(t,1H), 2.3δ(m,2H), 1.3δ and .9δ(m,8H), 0.0δ(s,9H).

Mass Spectrum: m/e 172. IR(neat): 1725 cm^{-1}.

5-(trimethylsilyl)-3-hexanone.

PMR(CCl_4): 2.3δ(m,4H), 1.0δ(m,7H), 0.0δ(s,9H).
Mass Spectrum: m/e 172. IR(neat): 1710 cm^{-1}.

3-(trimethylsilyl)-pentanal.

PMR(CCl_4): 9.9δ(t,1H), 2.3δ(m,2H), 1.3δ and 0.9δ(m,6H), 0.0δ(s,9H).
IR(neat): 1725 cm^{-1}.

Reaction of Carbonyl Compounds with Metalated Vinylboranes.

0.76 ml. of acetone (10 mmoles) was added to 5 mmoles of lithium octenyldisiamylborane at room temperature and the mixture was stirred 15 minutes. 1.5 ml. of propionic acid (20 mmoles) was then added and the mixture oxidized using the same procedure outlined in (D). Glpc analysis with an internal standard showed a 72 percent yield of 2-methyl-3-pentene-2-ol. PMR(CCl_4): 5.4δ(m,3H), 1.4δ(m,19H). IR(neat): 3400 cm^{-1}, 1670 cm^{-1}.

A similar reaction was done using acetophenone and lithium pentenyldicyclohexylborane. A 75% yield of 2-phenyl-3-ethyl-4-pentene-2-ol was obtained. PMR(CCl_4): 7.3δ(m,5H), 5.2δ(m,3H), 2.2 to 0.9δ(m, 10H). IR(neat): 3450 cm^{-1}, 1660 cm^{-1}, 1600 cm^{-1}.

Attempted Cyclization of XXVI.

1.3 gms. of benzophenone (7.5 mmoles) was added to lithium pentenyldicyclohexylborane and the mixture refluxed for two hours. The mixture was cooled to $0^{o}C$ and the solution oxidized according to procedure (D). A 90 percent yield, by glpc analysis, of 1,1-diphenyl-2-ethyl-1,3-butadiene was obtained. Mass Spectrum: m/e 234. PMR(CCl_4): 7.3δ(m,10H), 6.5 and 5.95δ(m,3H), 2.1δ(m,2H), 1.0δ(t,3H).

CHAPTER III

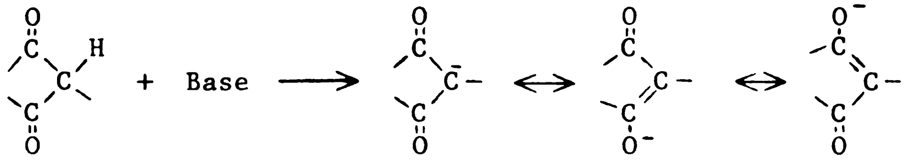
METALATED GEMINAL DIBORAALKANES AND MISCELLANEOUS STUDIES

INTRODUCTION

The results presented in the previous chapter on metalated vinylboranes encouraged us to continue our search for more acidic organoboranes. To this end, our studies of metalated organoboranes were continued with substrates such as the geminal diboraalkanes, diphenylalkylboranes, and α-borylesters. These classes of compounds are expected to be more acidic than trialkylboranes because of increased delocalization of charge in the anion or because of electron-withdrawing effects of the substituents. However, several difficulties were anticipated in the studies with these organoboron compounds.

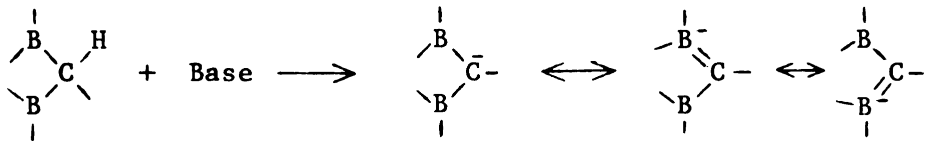
Geminal Diboraalkanes.

β-Dicarbonyl compounds are more acidic than the corresponding monocarbonyl compounds because of increased delocalization of charge in the anion (eq. 79).[43]



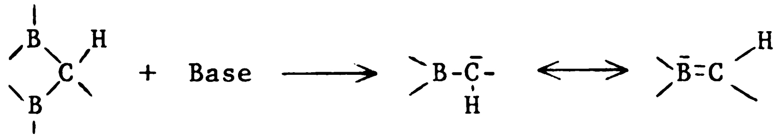
(79)

Geminal diboraalkanes are expected to be more acidic than trialkylboranes for a similar reason (eq. 80).



(80)

We expected the formation of metalated geminal diboraalkanes to be hindered by a competing base-cleavage reaction, which would give a metalated alkylborane (eq. 81).[13]

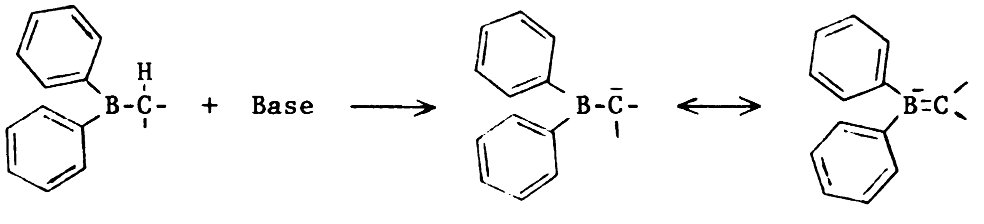


(81)

This cleavage of the geminal diboraalkanes would also hinder analysis of the reaction mixture, since the metalated alkylborane, if formed, would react with the reagents used to quench the reaction mixture.

Diphenylalkylboranes.

Diphenylalkylboranes are expected to be more acidic than trialkylboranes because phenyl substituents are electron-withdrawing[50] and are expected to stabilize the anion by an inductive effect[51] (eq. 82). For example, triphenylborane is a stronger Lewis acid than trialkylboranes.[52]



(82)

Although mixed trialkylboranes can be prepared, isolation of pure compounds is usually difficult because of the tendency of the alkyl groups of trialkylboranes to redistribute upon heating[53] (eq. 83).

$$RR'R'' \longrightarrow R_3B + R'_3B + R''_3B + \text{isomers} \qquad (83)$$

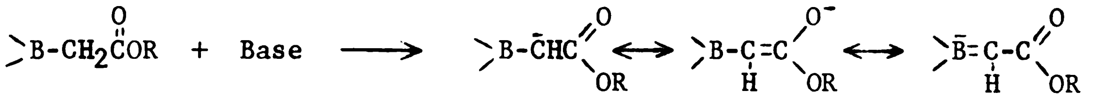
A similar problem was anticipated for the preparation of diphenylalkylboranes (eq. 84).

$$Ph_2RB \longrightarrow Ph_3B + PhR_2B + \text{isomers} \qquad (84)$$

Mixed trialkylboranes can be isolated as stable pyridine complexes.

<u>α-Borylesters.</u>

α-Borylesters (i.e. XXXIII) are expected to be more acidic than trialkylboranes because of increased delocalization of charge afforded by the carbonyl group (eq. 85).

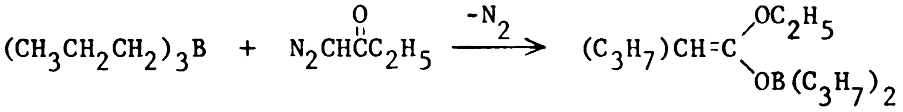


$$>B\text{-}CH_2\overset{O}{\overset{\|}{C}}OR + \text{Base} \longrightarrow >B\text{-}\bar{C}HC(=O)OR \longleftrightarrow >B\text{-}\underset{H}{C}{=}C(O^-)OR \longleftrightarrow >\bar{B}{=}\underset{H}{C}\text{-}C(=O)OR$$

XXXIII

(85)

The synthesis of these α-boryl compounds posed a major problem. Although these compounds have been postulated as intermediates in reactions, they have not been isolated. Attempts to isolate a carbon borylated derivative resulted in the isolation of an oxygen borylated compound (eq. 86).[54]



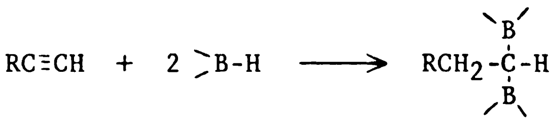
$$(CH_3CH_2CH_2)_3B \quad + \quad N_2CH\overset{\overset{\displaystyle O}{\|}}{C}C_2H_5 \xrightarrow{-N_2} (C_3H_7)CH{=}C\begin{array}{l}\diagup OC_2H_5\\ \diagdown OB(C_3H_7)_2\end{array} \qquad (86)$$

We attempted the synthesis of an α-borylester by the addition of trimethyl borate to lithium t-butylacetate.[55] The results of this reaction, along with the results of studies on geminal diboraalkanes, diphenylmethylborane and o-phenylene methylboronate are presented in the following section.

RESULTS

Preparation of Geminal Diboraalkanes.

The geminal diboraalkanes used in our experiments were prepared by the addition of 2 equivalents of a sterically hindered organoborane to an alkyne in tetrahydrofuran solution (eq. 87).[12]

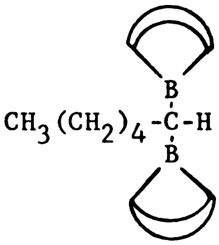


$$RC{\equiv}CH + 2\ {>}B\text{-}H \longrightarrow RCH_2\text{-}\underset{\displaystyle {\diagup}B{\diagdown}}{\overset{\displaystyle {\diagdown}B{\diagup}}{C}}\text{-}H \qquad (87)$$

These dihydroborated compounds were not isolated.

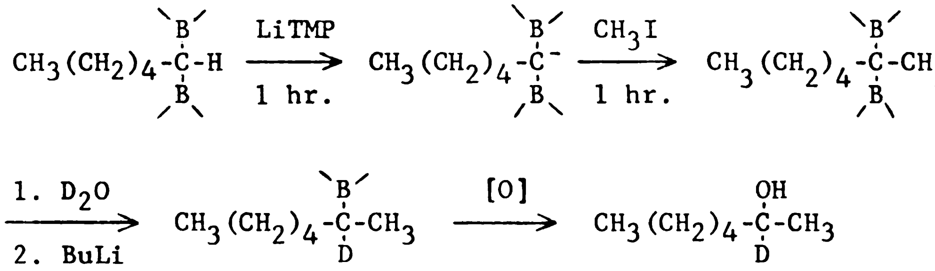
Studies with the Dihydroborated Compounds.

The dihydroborated derivative XXXIV was treated with one



XXXIV

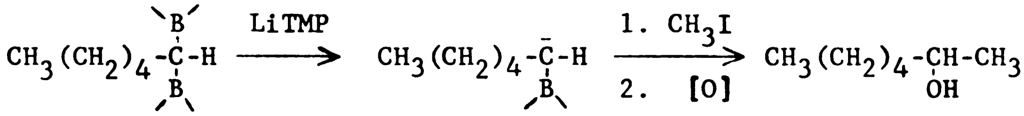
equivalent of LiTMP in tetrahydrofuran for one hour at room temperature, at which point the mixture was quenched with methyl iodide. Deuterium oxide and butyllithium were then added to hydrolyze the product of the alkylation reaction (eq. 88).



$$\mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{C}}\text{-}H} \xrightarrow[\text{1 hr.}]{\text{LiTMP}} \mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{C}}{}^{-}} \xrightarrow[\text{1 hr.}]{\mathrm{CH_3I}} \mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{C}}\text{-}CH_3}$$

$$\xrightarrow[\text{2. BuLi}]{\text{1. }\mathrm{D_2O}} \mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{D}{C}}\text{-}CH_3} \xrightarrow{[\mathrm{O}]} \mathrm{CH_3(CH_2)_4\text{-}\overset{OH}{\underset{D}{C}}\text{-}CH_3} \qquad (88)$$

After alkaline hydrogen peroxide oxidation, a 21 percent yield (glpc determination) of 2-D-2-heptanol was obtained. Since no 2-heptanol was detected in the pmr spectrum of 2-D-2-heptanol, base-cleavage of the geminal diboraalkane probably does not occur with the sterically hindered LiTMP (eq. 89).



$$\mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{C}}\text{-}H} \xrightarrow{\text{LiTMP}} \mathrm{CH_3(CH_2)_4\text{-}\overset{-}{\underset{\diagup B \diagdown}{C}}\text{-}H} \xrightarrow[\text{2. }[\mathrm{O}]]{\text{1. }\mathrm{CH_3I}} \mathrm{CH_3(CH_2)_4\text{-}\underset{OH}{CH}\text{-}CH_3}$$

0% (89)

Various reaction conditions (with the deuterium oxide and butyllithium step left out) were studied, but the yield of 2-heptanol never exceeded 32 percent (Table 11).

Benzaldehyde was added to the reaction mixture of LiTMP and XXXIV. After oxidation, 1-phenyl-2-heptanone was isolated by glpc from the reaction mixture (eq. 90).

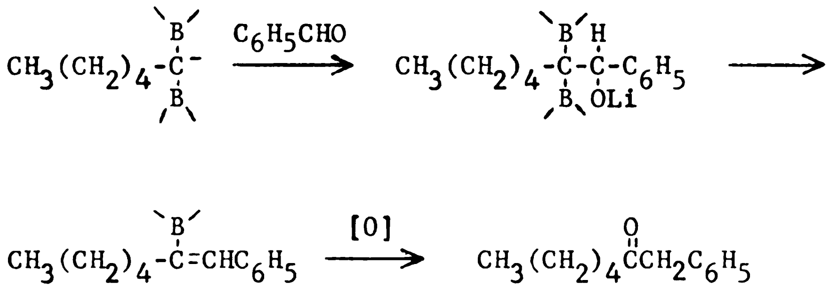
TABLE 11

Reaction of methyl iodide with metalated geminal diboraalkanes.

Reaction Conditions[a]	% Yield of 2-heptanol[b]
1 hr. r.t.	21
15 min. reflux	32
1 hr. reflux	30

[a] Reaction conditions listed for reaction of LiTMP with XXXIV in tetrahydrofuran.

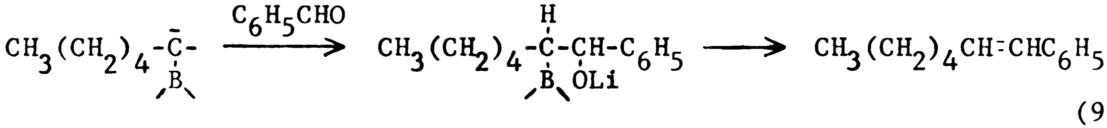
[b] Yield determined by glpc based on starting alkyne.



$$\mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{\dot{C}^-}}} \xrightarrow{\mathrm{C_6H_5CHO}} \mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{\underset{\diagup B \diagdown}{C}}\text{-}\overset{H}{\underset{OLi}{C}}\text{-}C_6H_5} \longrightarrow$$

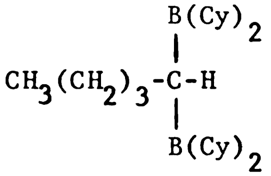
$$\mathrm{CH_3(CH_2)_4\text{-}\overset{\diagdown B \diagup}{C}{=}CHC_6H_5} \xrightarrow{[O]} \mathrm{CH_3(CH_2)_4\overset{O}{\overset{\|}{C}}CH_2C_6H_5} \qquad (90)$$

The yield of 1-phenyl-2-heptanone ranged from 30 to 39 percent for various reaction conditions with LiTMP. In some reactions a small yield (about 5 percent) of 1-phenyl-1-heptene was isolated; we assume the alkene was formed by reaction of benzaldehyde with the metalated derivative from base-cleavage of the diboraalkane (eq. 91).



$$\mathrm{CH_3(CH_2)_4\text{-}\underset{\diagup B \diagdown}{\bar{C}}\text{-}} \xrightarrow{\mathrm{C_6H_5CHO}} \mathrm{CH_3(CH_2)_4\text{-}\overset{H}{\underset{\diagup B \diagdown}{C}}\text{-}\underset{OLi}{C}H\text{-}C_6H_5} \longrightarrow \mathrm{CH_3(CH_2)_4CH{=}CHC_6H_5} \qquad (91)$$

Other bases, such as lithium diisopropylamide and lithium bis(trimethylsilyl)amide, gave poor yields of the 2-heptanone derivative (Table 12). The dihydroborated derivative from dicyclohexylborane and pentyne XXXV, on reaction with LiTMP and benzaldehyde under various reaction conditions, gave no ketone after work-up.



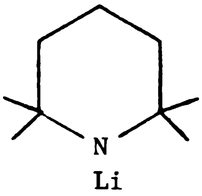
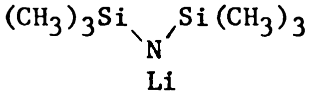
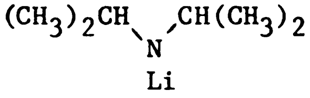
$$\mathrm{CH_3(CH_2)_3\text{-}\overset{B(Cy)_2}{\overset{|}{\underset{\underset{B(Cy)_2}{|}}{C}}}\text{-}H}$$

XXXV

The reaction of benzoyl chloride with the metalated derivative of XXXIV was also examined (eq. 92).

TABLE 12

Reaction of benzaldehyde with metalated geminal diboraalkanes.

Base	Reaction Conditions[a]	% Yield of 1-phenyl-2-heptanone[b]
	2 hr. r.t.	30
	15 min. reflux	39
	20 min. reflux	30
 $(CH_3)_3Si\underset{\substack{N\\ Li}}{\ }Si(CH_3)_3$	30 min. reflux	5
 $(CH_3)_2CH\underset{\substack{N\\ Li}}{\ }CH(CH_3)_2$	30 min. r.t.	0

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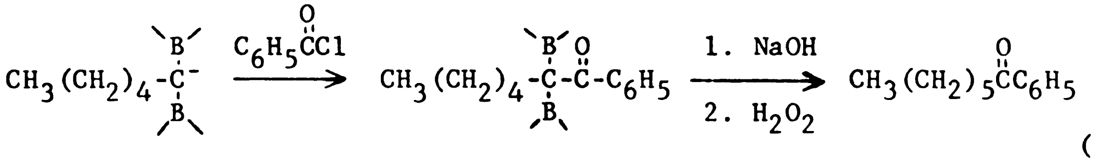
[a] Reaction conditions listed for reaction of LiTMP with XXXIV in tetrahydrofuran.

[b] Yield determined by glpc based on starting alkyne.

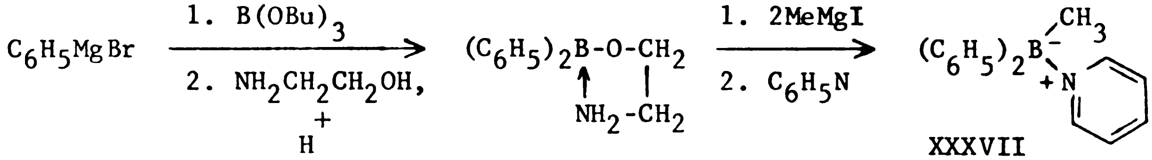

XXXVI

(92)

Since the initial product XXXVI is expected to be unstable in water, it should hydrolyze rapidly in the alkaline oxidation conditions to give a ketone. A very low yield of 1-phenyl-1-heptanone (5 percent) was obtained (glpc analysis).

Preparation of Diphenylmethylborane.

Diphenylmethylborane was prepared by the addition of methylmagnesium iodide to aminoethyl diphenylborinate, and was isolated as a pyridine complex (eq. 93).


XXXVII

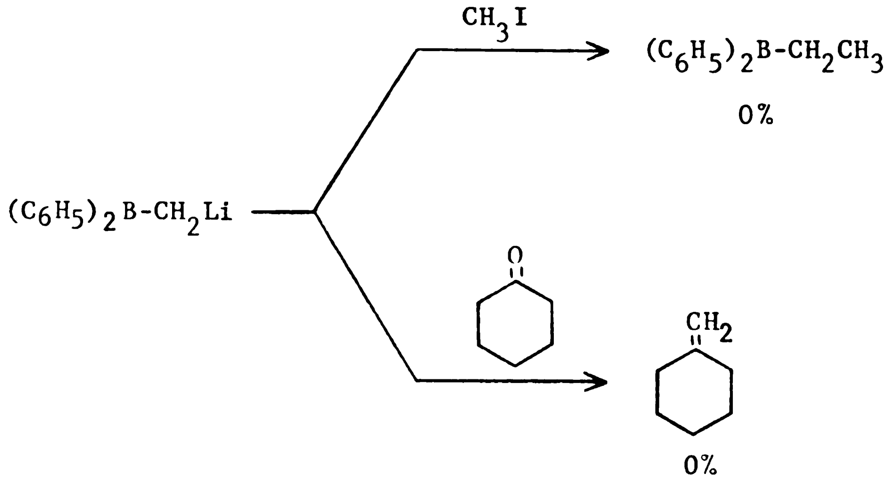
(93)

The pyridine complex XXXVII was obtained as a white crystalline solid (m.p. 145-150°C) which was fairly stable to air. The proton nmr spectrum of a sample exposed to air on a watch glass for two hours was identical to that of freshly prepared complex.

Studies with the Pyridine Complex of Diphenylmethylborane.

Pyridine-diphenylmethylborane is fairly stable to acids. XXXVII was treated with 3N hydrochloric acid, concentrated hydrochloric acid, and methanesulfonic acid under various conditions in an effort to remove the pyridine, no free diphenylmethylborane was formed. The treatment with hydrochloric acid did not cause dissociation of XXXVII, and the methanesulfonic acid seemed to react with the diphenylmethylborane to give new compounds (the methyl peak of starting boron compound disappeared from the pmr spectrum and was replaced by four new singlets).

Since the pyridine complex could not be dissociated to give pure diphenylmethylborane, several attempts were made to metalate XXXVII directly with LiTMP. Various solvents and reaction conditions were tried, but none of the products expected from the reaction of a metalated derivative with the quenching reagent were isolated (eq. 94 and 95).



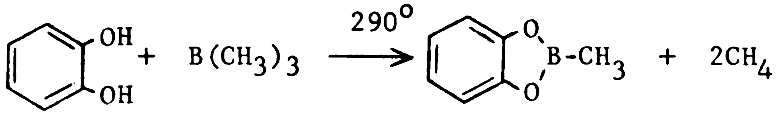
(94)

(95)

Presumably, the pyridine, by coordinating to the boron atom, hinders the formation of the metalated derivative.

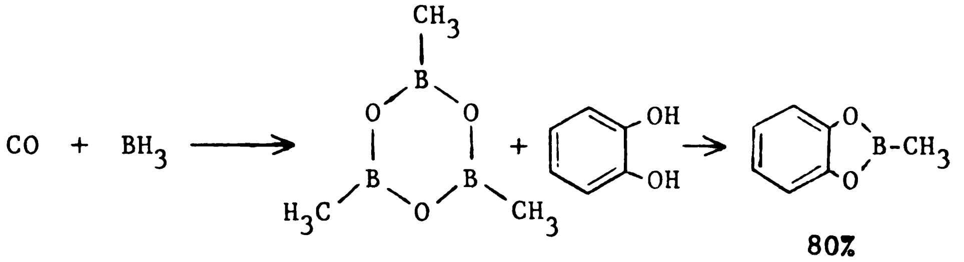
Preparation of o-phenylene methylboronate.

O-phenylene methylboronate has previously been prepared by the addition of catechol to trimethylborane (eq. 96).[56]



(96)

We were able to prepare the boronate in good yields by the addition of trimethylboroxine (from carbon monoxide and diborane)[57] to catechol (eq. 97).



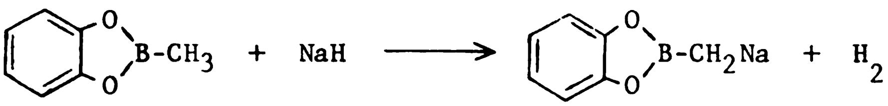
(97)

The o-phenylene methylboronate was fairly stable to air, a small sample left on a watch glass for three hours gave a pmr spectrum identical to that of a freshly distilled sample.

Attempted Metalation of o-phenylene Methylboronate.

The reaction of o-phenylene methylboronate with lithium 2,2,6,6-tetramethylpiperidide was studied using different solvents and various reaction conditions. The reaction mixtures were analyzed for possible metalation by quenching with either cyclohexanone or an alkyl halide. None of the reaction mixtures yielded any of the products expected from the reaction of a metalated o-phenylene methylboronate with the quenching reagent.

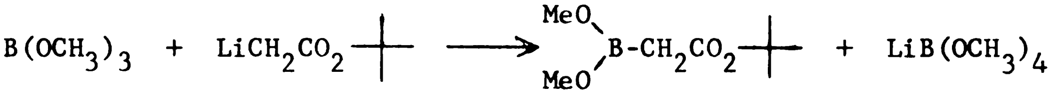
Metalation of o-phenylene methylboronate was also attempted with sodium hydride. If metalation were to occur with this reagent, hydrogen gas would be produced (eq. 98).


(98)

Therefore, to detect and measure the amount of gas produced the reaction flask was connected to a gas buret, but after 3 hours of reflux no gas collected in the buret, nor did the sodium hydride dissolve.

Reaction of Trimethyl borate with Lithium t-butylacetate.

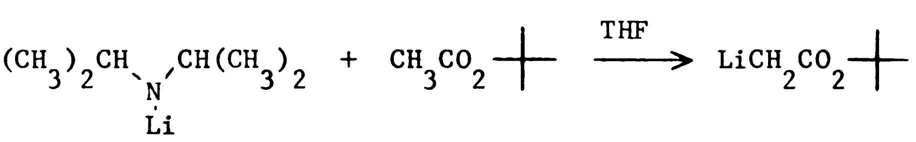
Trimethyl borate was added to lithium t-butylacetate in an attempt to synthesize dimethoxyboryl-t-butylacetate (XXXVIII) (eq. 99).



$$\mathrm{B(OCH_3)_3} + \mathrm{LiCH_2CO_2}\!-\!\!\!\!+ \longrightarrow \mathrm{(MeO)_2B\text{-}CH_2CO_2}\!-\!\!\!\!+ + \mathrm{LiB(OCH_3)_4} \qquad (99)$$

XXXVIII

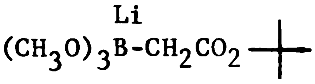
In the initial reaction, the lithium t-butylacetate, from the addition of t-butylacetate to lithium diisopropylamide in tetrahydrofuran,[58] was not isolated (eq. 100); and trimethyl borate was added directly to the metalated ester.



$$\mathrm{(CH_3)_2CH\text{-}N(Li)\text{-}CH(CH_3)_2} + \mathrm{CH_3CO_2}\!-\!\!\!\!+ \xrightarrow{\mathrm{THF}} \mathrm{LiCH_2CO_2}\!-\!\!\!\!+ \qquad (100)$$

Removal of the solvent after 45 minutes left a white precipitate. Since the precipitate produced only a red flame on ignition, we assumed the solid to be largely unreacted lithium t-butylacetate.

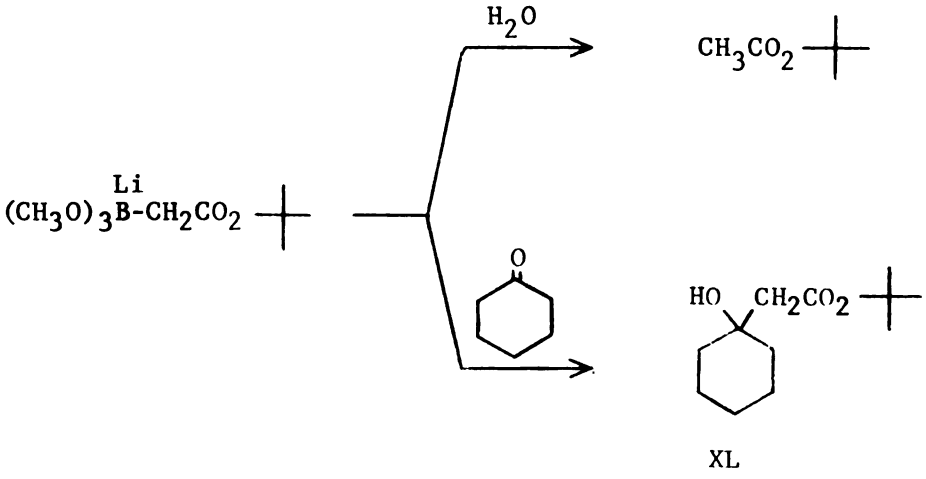
In a second attempt to synthesize XXXVIII, lithium t-butylacetate was prepared and isolated as an amine free solid[55] before the addition of trimethyl borate. The addition of trimethyl borate to lithium t-butylacetate in pentane yielded a white precipitate suspended in solution. After evaporation of the pentane, a white solid, which gave a red (lithium) and green (boron) flame on ignition, was obtained. The pmr spectrum of this solid in carbon tetrachloride solution exhibited 3 singlets: 1.4δ(9H), 1.8δ(2H), 3.1δ(9H); the ir spectrum displayed a strong band at 1660 cm^{-1} (the carbonyl stretch of t-butylacetate appears at 1740 cm^{-1}). From these data we assumed the compound has the structure XXXIX.



$(CH_3O)_3\overset{\text{Li}}{B}\text{-}CH_2CO_2+$

XXXIX

XXXIX was added to water and the resulting solution was analyzed by glpc. T-Butylacetate was detected in quantitative yield (eq. 101). The addition of cyclohexanone to XXXIX gave a 73 percent yield of the β-hydroxyester XL (eq. 102).



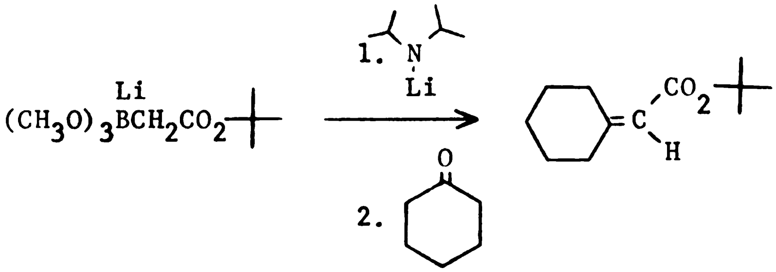
(101)

(102)

XL

A reaction of XXXIX with benzyl chloride was also attempted. After one hour at reflux, the reaction mixture of XXXIX and benzyl chloride was added to water and analyzed by glpc. Only two compounds were detected, t-butylacetate and benzyl chloride.

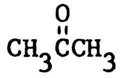
The reaction of XXXIX with lithium diisopropylamide was examined. XXXIX was added to lithium diisopropylamide in tetrahydrofuran at -78°C and the mixture was stirred for 1 hour. After the addition of cyclohexanone a very low yield (about 5 percent) of the unsaturated ester was detected (eq. 103).



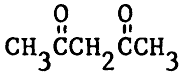
(103)

DISCUSSION

Two carbonyl groups should exert a greater stabilizing influence on an α-carbanion than a single carbonyl group (pKa of XLI is 20 vs. 11 for XLII).[38] We had hoped that two boron atoms would exert a similar effect and stabilize an α-carbanion so that metalation of geminal diboraalkanes would occur much more readily than the metalation of trialkylboranes. The results of the previous section show that metalation of geminal diboraalkanes occurs to a lesser extent than metalation of B-methyl-BBN, but to a greater extent than the metalation of other trialkylboranes.


$CH_3\overset{O}{\overset{\|}{C}}CH_3$

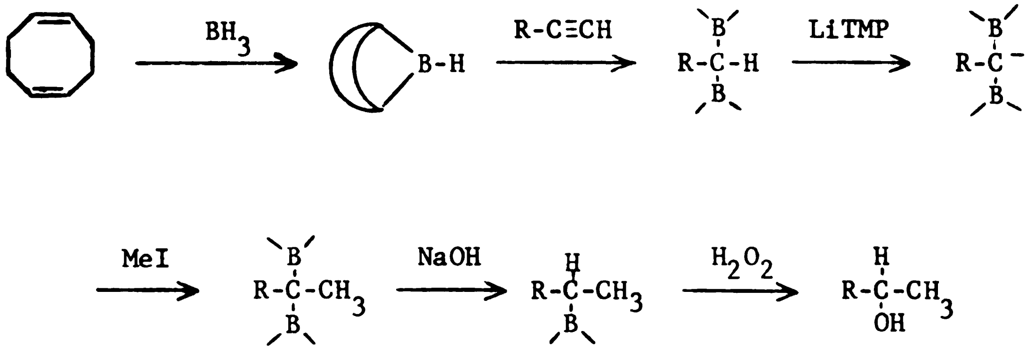
XLI


$CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}CH_3$

XLII

The poor yields of metalation with the diboraalkanes might be due to the low acidity of the α-hydrogens. Conceivably, the α-protons of geminal diboraalkanes might not be much more acidic than those of trialkylboranes.

A more likely explanation for the low yields (20 to 40 percent) of metalation could be the long sequence of reactions used, from the synthesis of the geminal diboraalkanes to the final oxidized products obtained at the end.

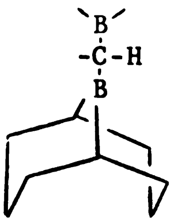


(104)

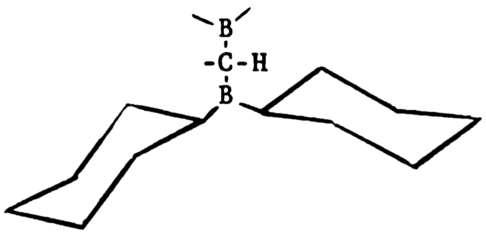
(R = pentyl)

This sequence of reactions, illustrated here for the preparation of 2-heptanol, involves six steps (eq. 104). If each step is not quantitative, the yield of 2-heptanol would be lowered accordingly.

The poor results observed with the dihydroborated derivative obtained from dicyclohexylborane XXXV, in comparison to the results from XXXIV, were somewhat surprising. The difference in the degree of metalation could possibly be attributed to the size of the alkyl groups of the dialkylboranes. In the dicyclohexylboryl derivative XXXV the cyclohexyl groups are freer to move about, whereas the alkyl groups of XXXIV are tied back in the bicyclic system. Thus, the α-protons of XXXIV are probably more accessible to the bulky LiTMP.



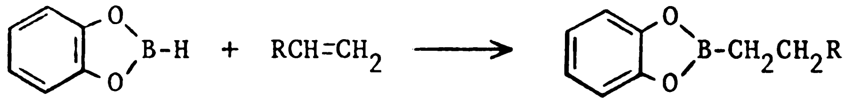
XXXIV



XXXV

O-Phenylene methylboronate.

One disadvantage of working with organoboranes is their rapid and exothermic reaction with oxygen. The study of o-phenylene methylboronate was undertaken because of the low reactivity of o-phenylene alkylboronates to oxygen and because a variety of these compounds are readily available through a simple reaction (eq. 105).[59]

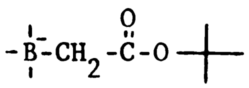


(105)

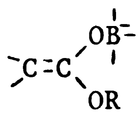
Unfortunately, o-phenylene methylboronate failed to undergo metalation. The boron atom of o-phenylene methylboronate is not as effective in the stabilization of the carbanion formed from α-proton removal because of back-coordination from oxygen to boron $(\text{-}\overset{\curvearrowright}{\ddot{\mathrm{O}}\text{-}\mathrm{B}}\langle)$.[60] Thus, the o-phenylene alkylboronates are probably weaker acids than the trialkylboranes. Another reason for the failure of o-phenylene methylboronate to undergo metalation may be that coordination of the base with the boron atom is permitted by the decreased steric hindrance in this system. Coordination of the base could even cause displacement of one of the oxygen atoms.

Reaction of Trimethylborate with Lithium t-butylacetate.

The addition of trimethyl borate to lithium t-butylacetate could have occurred at either of two sites to give the carbon XXXIX or oxygen borylated products XLIII. Compounds similar to XLIII have

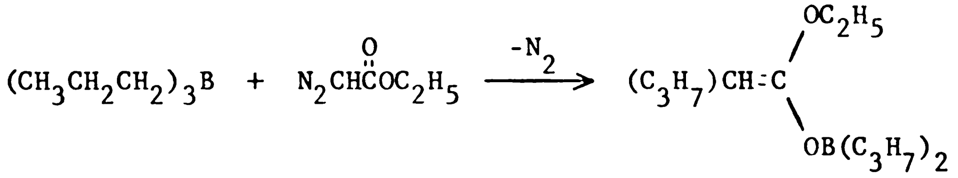


XXXIX



XLIII

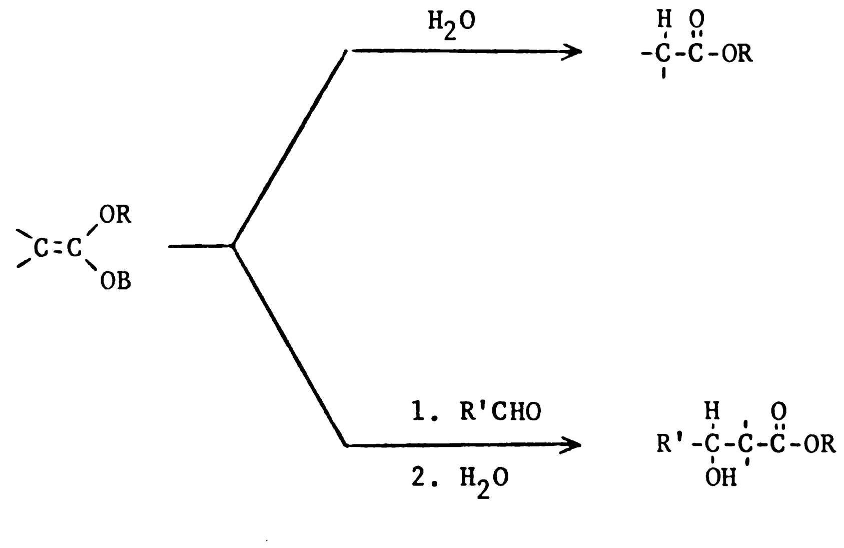
been prepared, for example, XLIV was formed in the reaction of tri-n-propylborane with ethyl diazoacetate (eq. 106).[54]



XLIV

(106)

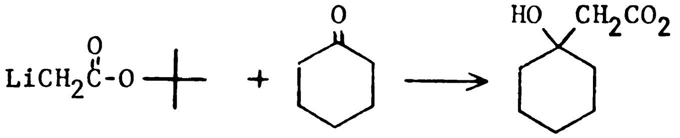
XLIV displayed no absorption in the carbonyl region of its ir spectrum. The vinyloxyboranes react with water (eq. 107)[54] and carbonyl compounds (eq. 108)[61] in a manner similar to that of XXXIX.



(107)

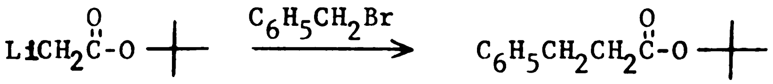
(108)

Compound XXXIX seems to be less reactive than the corresponding lithium t-butylacetate. Thus, lithium t-butylacetate reacts with cyclohexanone in 5 minutes to give a 95 percent yield of the β-hydroxyester (eq. 109),[57] whereas XXXIX, on addition of cyclohexanone,



(109)

gives only a 48 percent yield of the β-hydroxyester after 10 minutes, which then increases to 73 percent after two hours. Although lithium t-butylacetate is alkylated by benzyl bromide[58] to give a 96% yield of the ester (eq. 110), XXXIX does not react with benzyl chloride at



$$\mathrm{LiCH_2\overset{O}{\overset{\|}{C}}\text{-}O\text{-}C(CH_3)_3} \xrightarrow{C_6H_5CH_2Br} \mathrm{C_6H_5CH_2CH_2\overset{O}{\overset{\|}{C}}\text{-}O\text{-}C(CH_3)_3} \qquad (110)$$

reflux temperature. It would be interesting to study the different reactions of XXXIX and determine the usefulness of this compound for further synthetic sequences.

EXPERIMENTAL SECTION

I. Materials

Preparation of Bis-1,1-(dicyclohexylboryl)pentane.

In a 50 ml. round-bottomed flask equipped with a side-arm fitted with a rubber serum stopper under nitrogen was placed 2.03 ml. of cyclohexene (20 mmoles) in 5 ml. of tetrahydrofuran. The flask was cooled to 0°C, then 4.7 ml. of a 2.13 M solution of borane (10 mmoles) in tetrahydrofuran was added slowly. The mixture was stirred for an additional hour before its use.

To the dicyclohexylborane was added at room temperature .5 ml. of 1-pentyne (5 mmoles). The mixture was stirred for an additional 6 hours prior to its use.

Preparation of Bis-1,1-(borabicyclononyl)pentane.

In a 50 ml. round-bottomed flask equipped with a side-arm fitted with a rubber serum stopper and a reflux condenser under nitrogen was placed 4.7 ml. of 2.13 M borane (10 mmoles) in tetrahydrofuran. The flask was cooled to 0°C, then 1.22 ml. of cyclooctadiene (10 mmoles) was added dropwise through the rubber septum with a syringe. The mixture was then refluxed for an additional hour prior to its use.

To the borabicyclononane formed was added at room temperature .5 ml. of 1-pentyne (5 mmoles). The mixture was stirred for an additional 4 hours before its use.

Preparation of Trimethylboroxine.

.5 mole of borane in 200 ml. of tetrahydrofuran and .2 gms. of sodium borohydride (.005 mole) were placed in a 500 ml. round-bottomed flask. The flask was flushed with carbon monoxide and connected to a gas buret filled with the same gas. The reaction was initiated by magnetically stirring the contents of the reaction flask. Approximately 12 liters of carbon monoxide were delivered to the flask over a period of 12 hours. The trimethylboroxine was not isolated, but left in solution for the following reaction.

Preparation of o-phenylene methylboronate.

22 gms of catechol (200 mmoles) was dissolved in 40 ml. of tetrahydrofuran in a 500 ml. round-bottomed flask. 100 ml. of the trimethylboroxine solution (250 mmoles) was added to the catechol at room temperature and the reaction mixture stirred for 15 minutes. 20 gms. of sodium sulfate was then added to remove the water formed. After 15 minutes the solution was filtered and the solvent evaporated. Distillation of the remaining mixture (160-165°C) gave an 80 percent yield of o-phenylene methylboronate.

NMR (CCl_4): 7.1 (m,4H); 0.8 (s,3H)

Preparation of Aminoethyl Diphenylborinate.

52 ml. of a 1.92 M solution of phenylmagnesium bromide (100 mmoles) in ether was added dropwise over a period of 1.5 hours to a well-stirred solution of 14.5 ml. butyl borate (50 mmoles) in ether at dry ice temperature. The mixture was allowed to warm to room temperature and

stirred overnight, then hydrolyzed with 20 ml. of 3N hydrochloric acid. The ether layer was mixed with 25 ml. of 75% ethanol and 6 ml. of ethanolamine. After this solution had been warmed on the steam-bath for a short time, the ester precipitated. Recrystallization from aqueous alcohol yielded the purified ester as fine white needles, m.p. 190-192°C (50% yield).

Preparation of Pyridine-Diphenylmethylborane.

28.4 gms. of aminoethyl diphenylborinate (125 mmoles) was dissolved in 200 ml. of tetrahydrofuran in a 500 ml. round-bottomed flask equipped with an addition funnel. The flask was cooled with an ice-bath and 100 ml. of a 2.5 M solution of methylmagnesium iodide (250 mmoles) in ether was added dropwise. The mixture was stirred overnight at room temperature, then 20 ml. of pyridine was added to form the complex. 3N hydrochloric acid was then added to dissolve the magnesium salts. The layers were separated and the organic layer washed with water. Evaporation of the solvent gave white powdery crystals, which were recrystallized in carbon tetrachloride, m.p. 145-150°C (50% yield).

NMR(CCl_4): 7.6 and 8.6δ(m,5H); 7.1δ(s,10H); 0.6δ(s,3H).

II. Studies with Geminal Diboraalkanes.

Reaction of Methyl Iodide with Metalated Bis-1,-1(borabicyclononyl)-pentane.

A solution of bis-1,1-(borabicyclononyl)pentane (10 mmoles) was added to the solid LiTMP (10 mmoles) and the mixture stirred for one hour at room temperature. 1.3 ml. of methyl iodide (20 mmoles) was added to the dark red solution and the mixture stirred an additional hour. 3 ml. deuterium oxide was added to this mixture, followed by 10 mmoles of butyllithium. The reaction flask was cooled to 0°C and the organoborane oxidized by the addition of 6 ml. 3N sodium hydroxide and the dropwise addition of 8 ml. 30% hydrogen peroxide. 20 ml. of pentane was added and the two layers separated, the organic layer was washed successively with 3N hydrochloric acid, water, and saturated sodium chloride solutions. After drying over anhydrous potassium carbonate the mixture was analyzed by glpc. A 21 percent yield of 2-D-2-heptanol was detected.

Reaction of Benzaldehyde with Metalated Bis-1,1-(borabicyclononyl)pentane.

A solution of the diborapentane (5 mmoles) was added to the solid LiTMP (5 mmoles) and the mixture stirred for one hour at room temperature. 0.6 ml. of benzaldehyde (6 mmoles) was added to the dark-red solution and the mixture stirred for 3 hours at room temperature. The reaction flask was cooled to 0°C and the organoborane oxidized by the addition of 4 ml. 3N sodium hydroxide and the dropwise addition of 4 ml. 30% hydrogen peroxide. The same work-up procedure as that used above was then carried out. A 35 percent yield of 1-phenyl-2-heptanone was detected. NMR(CCl_4): 7.2δ(s,5H), 3.6δ(s,2H), 2.3δ(m,2H), 1.3 and 1.0δ(m,9H).

III. Miscellaneous Reactions

Attempted Metalation of o-Phenylene Methylboronate.

.6 ml. o-phenylene methylboronate (5 mmoles) was added to LiTMP (5 mmoles) in tetrahydrofuran and the mixture was stirred for one hour at room temperature. .5 ml. cyclohexanone (5 mmoles) was then added and the mixture stirred an additional 15 minutes. 2 ml. 3N sodium hydroxide was added and after 10 minutes the solution was saturated with anhydrous potassium carbonate. Analysis of the organic layer by glpc showed no methylenecyclohexane.

Attempted Metalation of Pyridine-Diphenylmethylborane.

1.3 gms. of pyridine-diphenylmethylborane (5 mmoles) was added to LiTMP (5 mmoles) in benzene and the mixture was stirred for one hour at room temperature. .5 ml. cyclohexanone (5 mmoles) was then added and the mixture stirred 30 minutes. The organoborane was oxidized at $0^{o}C$ by the addition of 1 ml. 6N sodium hydroxide and 2 ml. 30% hydrogen peroxide. The resulting mixture was saturated with anhydrous potassium carbonate and the organic layer analyzed by glpc. No methylenecyclohexane was detected.

Reaction of Trimethyl borate with Lithium t-butylacetate.

0.47 gms. of lithium t-butylacetate (3.9 mmoles) was added to 5 ml. of pentane in a 50 ml. round-bottomed flask under nitrogen. To this suspension was added 0.45 ml. (3.9 mmoles) of trimethyl borate. The reaction flask warmed up slightly, but no change in the suspension could be detected. After 30 minutes the pentane was evaporated to give 0.852 gms. of a white glassy solid. 3.9 mmoles of XXXIX is expected to weigh 0.884 gms. NMR and ir data are given in the results section.

Reaction of Cyclohexanone with XXXIX.

0.5 ml. of cyclohexanone (5 mmoles) was added to 5 mmoles of XXXIX in pentane. After stirring for two hours, the reaction mixture was quenched by the addition of 3N sodium hydroxide. A 73% yield of t-butyl(1-hydroxycyclohexyl)acetate was detected by glpc. The β-hydroxyester was identified by comparison of glpc retention times with authentic material.

BIBLIOGRAPHY

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1. C. H. Hassall, *Org. Reactions*, *9*, 73 (1957).
2. G. Donaruma and W. Heldt, *Org. Reactions*, *11*, 1 (1960).
3. H. C. Brown, "Hydroboration", W. A. Benjamin, Inc., New York (1962), p. 69.
4. M. W. Rathke, N. Inoue, K. Varma, and H. C. Brown, *J. Amer. Chem. Soc.*, *88*, 2870 (1966).
5. Brown, *Op. Cit.*[3], p. 56.
6. H. C. Brown, "Boranes in Organic Chemistry", Cornell Univ. Press, New York (1972).
7. H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, *22*, 1136 (1957).
8. H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, *88*, 5694 (1956).
9. Brown, *Op. Cit.*[3], p. 114.
10. Brown, *Op. Cit.*[6], p. 281.
11. G. Zweifel and H. Arzoumanian, *J. Amer. Chem. Soc.*, *89*, 291 (1967)
12. H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, *83*, 3834 (1961).
13. *Ibid.*
14. G. Cainelli, G. Bello, and G. Zubiani, *Tetrahedron Lett.*, 4315 (1966).
15. G. Cainelli, G. Bello, G. Zubiani, *Tetrahedron Lett.*, 3429 (1965).
16. H. O. House, "Modern Synthetic Reactions", 2nd edition, W. A. Benjamin, Inc., Menlo Park (1972) p. 116.
17. G. Zweifel and H. Arzoumanian, *Tetrahedron Lett.*, 2535 (1966).
18. H. C. Brown and S. Rhodes, *J. Amer. Chem. Soc.*, *91*, 4306 (1969).
19. R. Castle and D. Matteson, *J. Amer. Chem. Soc.*, *90*, 2194 (1968).

20. D. Matteson and G. Larson, J. Amer. Chem. Soc., 91, 6541 (1969).

21. D. Matteson and P. Tripathy, J. Organomet. Chem., 21, P6 (1970).

22. D. Matteson and J. Thomas, J. Organomet. Chem., 24, 263 (1970).

23. D. Matteson and R. Castle, J. Organomet. Chem., 20, 19 (1969).

24. D. Matteson and G. Larson, J. Organomet. Chem., 57, 225 (1973).

25. D. Matteson and R. Wilcseh, J. Organomet. Chem., 57, 231 (1973).

26. D. Matteson, R. Davis, and L. Hagelee, J. Organomet. Chem., 69, 45 (1974).

27. D. Matteson and P. Tripathy, J. Organomet. Chem., 69, 53 (1974).

28. D. Matteson, L. Hagelee, and R. Wilcseh, J. Amer. Chem. Soc., 95, 5096 (1973).

29. D. Matteson and M. Furve, J. Organomet. Chem., 69, 63 (1974).

30. H. Stetter and W. Dierichs, Chem. Ber., 85, 1061 (1952).

31. H. C. Brown and V. Dodson, J. Amer. Chem. Soc., 79 2302 (1957).

32. H. C. Brown and M. Rogic, J. Amer Chem. Soc., 91, 4304 (1969).

33. D. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York (1965), p. 21.

34. G. Fraenkel, D. Adams, and J. Williams, Tetrahedron Lett., 767 (1963).

35. G. Hennion and C. Digiovanna, J. Org. Chem., 30, 2645 (1965).

36. A. Ashe and P. Shu, J. Amer. Chem. Soc., 93, 1804 (1971).

37. H. C. Brown, M. Rogic, M. Rathke, and G. Kabalka, J. Amer. Chem. Soc., 90, 818 (1968).

38. House, Op. Cit.[16], p. 494.

39. Cram, Op. Cit.[33], p. 71.

40. D. Cram and M. Sahyun, J. Amer. Chem. Soc., 84, 1734 (1962).

41. Cram, Op. Cit.[33], p. 19.

42. G. Fraenkel, J. Russell and Y. Chen, J. Amer. Chem. Soc., 95, 3208 (1973).

43. Cram, Op. Cit.[33], p. 52.

44. B. M. Mikhailov, Organometal. Chem. Rev. A, 8, 1 (1972).

45. J. March, "Advanced Organic Chemistry: Reactions, Mechanisms and Structure," McGraw-Hill, Inc., New York (1968), p. 661.

46. H. C. Brown and Y. Yamamoto, J. Amer. Chem. Soc., 93, 2796 (1971).

47. M. W. Rathke and D. Sullivan, Tetrahedron Lett., 4249 (1971).

48. B. M. Mikhailov, V. N. Smirnov, and O. D. Ryazonova, Dokl. Akad. Nauk SSSR, 204, 447 (1972).

49. B. M. Mikhailov and F. B. Tutorskaya, Dokl. Akad. Nauk SSSR, 123, 479 (1958).

50. March, Op. Cit.[45], p. 21.

51. Cram, Op. Cit.[33], p. 55.

52. G. E. Coates, "Organo-Metallic Compounds," John Wiley & Sons, Inc., New York (1960), p.112.

53. W. Gerrard, "The Organic Chemistry of Boron," Academic Press, New York (1961) p. 102.

54. D. J. Pasto and P. Wojtkowski, Tetrahedron Lett., 215 (1970).

55. M. W. Rathke and D. Sullivan, J. Amer. Chem. Soc., 95, 3050 (1973).

56. D. Ulmschneider and J. Goubeau, Chem. Ber., 90, 2733 (1957).

57. M. W. Rathke and H. C. Brown, J. Amer. Chem. Soc., 89, 2737 (1967).

58. M. W. Rathke and A. Lindert, J. Amer. Chem. Soc., 93, 2318 (1971).

59. H. C. Brown and S. K. Gupta, J. Amer. Chem. Soc., 93, 1816 (1971).

60. Gerrard, Op. Cit.[53], p. 12.

61. T. Mukaiyama, K. Inomata, M. Murake, J. Amer. Chem. Soc., 95, 967 (1973).