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ORGANOBORANES FOR SYNTHESIS. 11.[1] PREPARATION OF ALKYL BROMIDES IN THE DARK REACTION OF BROMINE WITH ORGANOBORANES.[2,3] EXCEPTIONAL REACTIVITY TOWARD RADICAL BROMINATION OF THE ALPHA HYDROGEN IN TRIALKYLBORANES

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Abstract - The reaction of the three isomeric tributylboranes (tri-*n*-butyl, triisobutyl and tri-*sec*-butyl) with bromine in the dark gives rise to both butyl bromide and hydrogen bromide when carbon tetrachloride is used as a solvent. The rate of disappearance of the borane and bromine are essentially equal and decreases in the order *sec*-butyl > *n*-butyl > isobutyl. However, the corresponding butyl bromide appears at a much slower rate and the formation of hydrogen bromide is quite rapid during the initial stages of the reaction. The amount of hydrogen bromide produced in the reaction reaches a peak in 1 h and then decreases with time. Similar results are obtained in cyclohexane. In methylene chloride, the rate of initial disappearance of bromine and tributylborane compares closely to the results obtained in carbon tetrachloride and cyclohexane. However, butyl bromide is formed with essentially the same rate as the rate of disappearance of the borane. Moreover, hydrogen bromide is formed in only minor amounts and the yields of alkyl bromides are high. In tetrahydrofuran, tri-*n*-butylborane and tri-*sec*-butylborane react at a rate similar to the rate similar to the rate of formation of the corresponding bromobutanes. This reaction is proposed to involve a slow, direct electrophilic attack of bromine, or its complex with THF, on tributylborane. Whereas in carbon tetrachloride, cyclohexane and methylene chloride, a fast, initially free-radical bromination, followed by a slow cleavage of the resulting α–bromoorganoborane with hydrogen bromide, takes place. Evidence supporting this mechanism is given. Competitive bromination studies reveal that the α–hydrogen in trialkylboranes is highly reactive toward free-radical bromination in the dark reaction. As an important synthetic application of this new reaction, the preparation of alkyl bromides is presented.

In general, organometallic compounds react with halogens with great ease to form the corresponding halides.[5] Consequently, the apparent sluggishness in the reaction of organoboranes with halogens, such as iodine[6,7] or bromine,[8,9] constitutes a unique characteristic. Accordingly, we undertook a detailed study of the reaction of organoboranes with bromine with an aim to finding a simple means of facilitating the reaction, thereby achieving a convenient new synthesis of organic bromides from alkenes *via* hydroboration. The base-induced bromination of organoboranes provides a convenient synthesis of primary alkyl bromides from terminal alkenes[1] (eq 1).

$$(RCH_2CH_2)_3B + 3\,Br_2 + 3\,NaOCH_3 \xrightarrow{THF,\ 0^oC} 3\,RCH_2CH_2Br + 3\,NaBr + B(OCH_3)_3 \qquad (1)$$

However, in view of the unusual inversion of configuration in this reaction,[1] it was felt necessary to examine in detail the reaction of bromine with trialkylboranes in the absence of base. The simplest possible reaction conditions

were chosen for this study. Thus, the brominations were carried out in the absence of added electrophile or nucleophile in various solvents that are inert to bromine and in the dark in order to minimize any radical reactions.

RESULTS AND DISCUSSION

Structural Effects. Three isomeric tributylboranes (10 mmol) (*n*-butyl, *sec*-butyl, isobutyl) in 20 mL of carbon tetrachloride were treated in the dark at 25°C with 10 mmol of bromine. At the end of appropriate intervals of time, cyclohexene (20 mmol) was added to convert the residual bromine into 1,2-dibromocyclohexane. An internal standard (1 mL of a hydrocarbon) was added and the reaction mixture was analyzed directly by GC. Hydrogen bromide that escaped from the reaction mixture was trapped in a known amount of standard aqueous sodium hydroxide and determined by titration. The results are summarized in Table 1 and those obtained for tri-*sec*-butylborane are illustrated in Figure 1.

Table 1. The dark reaction of bromine with tributylboranes in carbon tetrachloride[a]

Tributylborane	Time min	R_3B, mmol	Br_2,[b] mmol	RBr,[c] mmol	HBr,[d] mmol	HBr,[e] mmol
n-butyl	5	8.4	6.9	0.4	3.3	
	30	5.2	5.4	0.7	3.2	
	60	3.1	4.4	0.9	2.8	
	480	1.2	4.1	1.9	1.4	
sec-butyl	5	6.1	6.6	trace	1.4	2.2
	30	2.2	1.6	0.8	5.3	2.0
	60	2.0	1.7	1.5	4.4	1.0
	240	0.3	0.4	2.3	1.9	1.2
	480			2.8	0.5	1.8
isobutyl	5	10.0	9.8		1.2	
	30	10.0	9.6	trace	1.4	
	60	10.0	9.3	trace	1.6	
	480	8.2	7.2	1.4	1.6	
	24 h	6.9	7.1	2.3	0.7	

[a]Bromine (10 mmol) allowed to react in 20 mL of CCl_4 with 10 mmol of R_3B for time indicated at 20-25°C. Excess cyclohexene then added and reaction mixture analyzed by GC. [b]Analysis by GC *via* 1,2-dibromocyclohexane. [c]Corresponding butyl bromide from the tributylborane. [d]Analysis by GC *via* bromocyclohexane. [e]Amount trapped in gas bubbler containing aqueous sodium hydroxide.

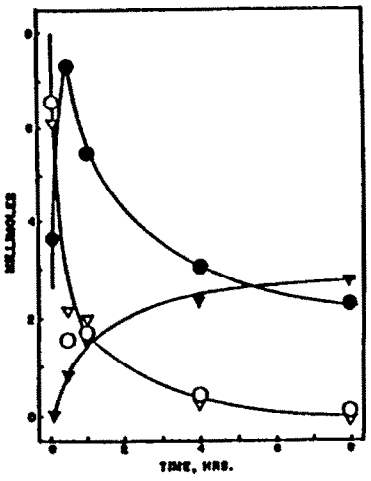


Figure 1. The dark reaction of tri-*sec*-butylborane (10 mmol) with bromine (10 mmol) in 20 ml of carbon tetrachloride solvent: ○, Br_2; ▽, R_3B; ●, total HBr; ▼, 2-bromobutane.

As is apparent from Table 1, the rate of reaction of bromine with organoboranes is in the order tri-*sec*-butyl > tri-*n*-butyl > triisobutyl. For a given system, the bromine and tributylborane disappear at essentially the same rate, but the corresponding butyl bromide appears at a much slower rate. Also, hydrogen bromide is formed rapidly, followed by a slower disappearance. In all cases, the amount of hydrogen bromide present in the reaction mixture reaches a peak during the first hour of the reaction and then decreases with time. These results are clearly incompatible with a mechanism involving the direct rupture of carbon-boron bond by bromine. On the contrary, they require that the initially fast reaction of bromine with organoborane to produce an intermediate and hydrogen bromide should be followed by a slow step to produce alkyl bromide.

Solvent Effects. Since the bromination of trialkylboranes in carbon tetrachloride follows an unexpected course, this reaction was examined in more detail. By following essentially the same procedure,[10] bromination was carried out in cyclohexane, a hydrocarbon solvent. The results (Table 2) are essentially the same as those obtained with carbon tetrachloride as the solvent. However, bromocyclohexane was never observed in any more than a trace amount, indicating that the bromination of cyclohexane, even when present as a solvent, is insignificant.

Table 2. The dark reaction of bromine with tributylboranes in cyclohexane[a]

Tributylborane	Time,, min	R_3B mmol	Br_2,[b] mmol	RBr,[c] mmol	HBr,[d] mmol	HBr[e] mmol
n-butyl	5	7.1	7.6	trace	1.7	
	30	4.6	5.0	0.6	3.0	0.1
	60	3.5	5.0	0.6	1.8	0.1
	480	1.0	1.3	1.3	1.5	
sec-butyl	5	6.6	6.3	trace	2.7	0.4
	30	2.7	2.5	0.5	4.3	0.5
	60	1.9	1.6	0.5	4.4	0.6
	480	trace		1.3	2.6	1.4

[a]Bromine (10 mmol) allowed to react in 20 mL of cyclohexane with 10 mmol of R_3B for the time indicated, at 20-25°C. Excess cyclopentene then added and the reaction mixture analyzed by GC. [b]Analysis by GC *via* 1,2-dibromocyclopentane. [c]Corresponding butyl bromide from the tributylborane. [d]Analysis by GC *via* bromocyclopentane. [e]Amount trapped in gas bubbler containing aqueous sodium hydroxide.

Bromination in methylene chloride proved to be significantly different. In this solvent, butyl bromide appears in the reaction medium at the same rate as the disappearance of bromine and organoborane. Only minor amounts of hydrogen bromide were observed. Moreover, the yields of butyl bromide were relatively high, suggesting that one mole of organoborane reacted with one mole of bromine to produce one mole of alkyl bromide (Table 3).

Table 3. The dark reaction of bromine with tributylboranes in methylene chloride[a]

Tributylborane	Time, min	R_3B, mmol	Br_2,[b] mmol	RBr,[c] mmol	HBr,[d] mmol	HBr,[e] mmol
n-butyl	5	7.0	5.1	1.1(0.6)[f]	1.1	
	30	3.3	2.9	4.2(1.0)	1.3	
	60	3.3	3.3	5.4(1.2)	0.6	
	480	1.2	1.2	6.4(1.2)	trace	
sec-butyl	5	6.6	6.7	3.1	0.5	0.1
	30	1.4	1.9	6.2	1.0	0.1
	60	0.6	1.6	7.4	0.4	0.1
	480		0.7	7.4	0.1	0.1

[a]Bromine (10 mmol) allowed to react in 20 mL of methylene chloride with 10 mmol of R_3B for time indicated at 20-25°C. Excess cyclohexane then added and reaction mixture analyzed by GC. [b-e]See corresponding footnotes in Table 1. [f]Amount of 2-bromobutane given in parentheses.

Although these results are consistent with a direct reaction of bromine with the organoborane to rupture the carbon-carbon bond (eq 2), the rates of disappearance of bromine and tributylboranes are essentially the same as in

$$R_3B + Br_2 \xrightarrow[25°C]{CH_2Cl_2,\ dark} RBr + R_2BBr \qquad (2)$$

cyclohexane or carbon tetrachloride.[11] Consequently, the results are best interpreted as involving the same initial step in these three solvents, with methylene chloride evidently accelerating the second step in which the α-bromoborane intermediate reacts with hydrogen bromide. Since the hydroboration reaction is commonly carried out in ether solvents such as tetrahydrofuran (THF), the reaction of bromine with tri-*n*-butyl and tri-*sec*-butylborane was examined using THF as the solvent in order to develop a one-pot synthesis of alkyl bromides.

The dark reaction of bromine with boranes in THF was followed with time by adding an alkene at appropriate intervals of time and then analyzing for any butyl bromide formed and for the amount of unreacted trialkylborane.

Unfortunately, THF interfered with the reaction of bromine with alkene. Therefore, an accurate analysis of bromine was not possible. Table 4 summarizes these results. The reaction in THF apparently proceeds by a different

Table 4. The dark reaction of bromine with tributylboranes in tetrahydrofuran[a]

Tributylborane	Time, min	R_3B, mmol	1-Bromobutane mmol	Bromobutane mmol
n-butyl	5	10.0		
	30	10.0	trace	
	60	8.4	1.2	trace
	480	6.6	3.9	0.3
sec-butyl	5	9.7		trace
	30	8.9		0.7
	60	9.0		1.2
	480	6.2		3.1

[a]Bromine (10 mmol) allowed to react in 20 mL of THF with 10 mmol of R_3B for time indicated at 20-25°C. Excess cyclohexane then added and reaction mixture analyzed directly by GC.

pathway than those in carbon tetrachloride, cyclohexane or methylene chloride. In THF, the rate of disappearance of tributylborane corresponds very closely to the rate of formation of butyl bromide. Also, the rate of reaction, as measured by the disappearance of organoboranes, is markedly slower in THF. One can easily see this pronounced solvent effect by noting that the reaction half-lives for both tri-*n*-butyl- and tri-*sec*-butylborane in either carbon tetrachloride or cyclohexane are $\leq$ 30 min, while in THF, they are both > 8 h. Furthermore, the rates of disappearance of tri-*n*-butylborane and tri-*sec*-butylborane were essentially equal in THF solvent. The low reactivity of bromine with trialkylboranes in THF, as compared to those in inert solvents, such as cyclohexane, carbon tetrachloride and methylene chloride, apparently results from its strong complexation with THF.

Table 5. The dark reaction of bromine with trialkylboranes in methylene chloride solvent[a]

Trialkylborane from Alkene	Product	Yield,[b] %
1-butene	1-bromobutane	80
	2-bromobutane	11
2-butene	2-bromobutane	88
isobutylene[c]	isobutyl bromide	85
1-octene	1-bromooctane	63
	2-bromooctane	12
	n-octane	21
2,4,4-trimethyl-1-pentene	1-bromo-2,4,4-trimethylpentane	82
cyclopentene	bromocyclopentane	84
cyclohexene	bromocyclohexane	99
norbornene	*exo*-bromonorbornane	88

[a]Reactions were allowed to proceed for 24 h at ~ 25°C in a closed system using a 10% excess of bromine. [b]By GC analysis. The yield is based on a maximum production of 1 mol of RBr from 1 mol of R_3B (eq 2). [c]After 48 h at ~ 25°C. [d]The absence of the endo isomer was indicated by GC analysis (< 1%).

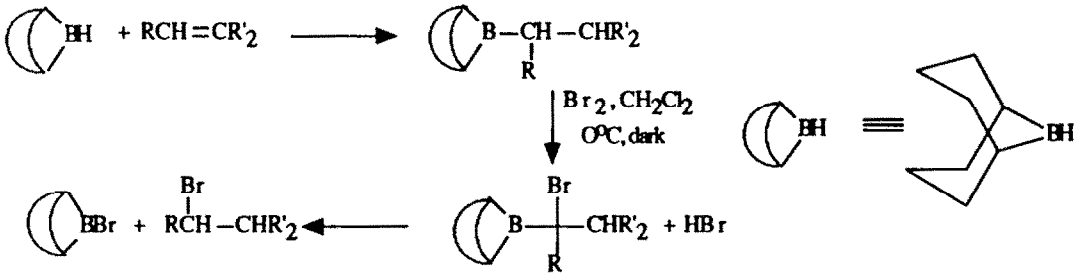
It is felt that the bromination reaction in THF does not involve a prior bromination of the trialkylborane with the formation of hydrogen bromide. Instead, the reaction is assumed to proceed through a slow direct electrophilic attack of bromine or its THF complex on boron-carbon bond to provide the corresponding alkyl bromides. This reaction was not studied any further.

Synthetic Applications. Bromination of Trialkylboranes. The tributylboranes react readily in the dark with bromine in methylene chloride solution to give the corresponding butyl bromide and dibutylboron bromide (eq 2). Mild reaction conditions and high yield of alkyl bromide indicated that this reaction might be very useful in certain

synthetic applications. Consequently, the dark reaction of bromine with organoboranes in methylene chloride was applied to a series of representative trialkylboranes, the results of which are summarized in Table 5.

The reaction is general and the yields are moderate. However, it suffers from the disadvantage of utilizing only one of the three alkyl groups in trialkylborane. A number of new reactions of trialkylboranes are limited in their synthetic utility for the same reason.[12] Thus, when a valuable alkene is to be converted into the desired product, the maximum yield obtainable is only 33%. This difficulty was circumvented by using a blocking group on boron so that the desired alkyl group is utilized effectively.

Bromination of Alkyl-9-borabicyclo[3.3.1]nonanes. Hydroboration of alkenes with 9-borabicyclo[3.3.1]nonane (9-BBN) provides *B*-alkyl-9-BBN compounds.[13] These derivatives show selectivity in the migration of the *B*-alkyl bonds in preference to the *B*-cyclooctyl bonds in a number of reactions.[12] Therefore, maximum utilization of the alkene is possible if such selectivity is exhibited in this reaction. In the base-induced bromination of *B*-alkyl-9-BBN derivatives, the selective migration of alkyl groups was realized.[1] Consequently, the dark reaction of bromine with *B*-alkyl-9-BBN derivatives in methylene chloride was investigated. Particularly, *B-sec*-alkyl-9-BBN compounds, conveniently prepared *via* hydroboration of internal alkenes with 9-BBN, readily undergo the bromination reaction to afford the corresponding alkyl bromides in high yields (Scheme 1).



Scheme 1

A wide range of internal alkenes can be accommodated in this reaction, as shown in Table 6.

Table 6. The dark reaction of *B-sec*-alkyl-9-borabicyclo[3.3.1]nonanes with bromine[a]

B-Alkyl-9-BBN from Alkene	Product	Yield,[b] %
2-butene	2-bromobutane	85
2-methyl-2-butene	2-bromo-3-methylbutane	88
2,3-dimethyl-2-butene	2-bromo-2,3-dimethylbutane	0[c]
4-methyl-2-pentene	2-bromo-4-methylpentane	88
cyclohexene	bromocyclohexane	84
norbornene	*exo*-bromonorbornane[d]	90
1-methylcyclopentene	1-bromo-2-methylcyclopentane[e]	80

[a]Reactions were allowed to proceed for 30 min at 0-5°C, then 1 h at 20-25°C in a closed system using a 10% excess of bromine and methylene chloride as solvent. [b]By GC analysis. The yields are based on the amount of starting alkene. [c]The alkyl group does not contain an α–hydrogen; therefore, α–bromination cannot occur. [d]The absence of the endo isomer was indicated by GC analysis (< 1%). [e]Stereochemistry was not established.

This reaction provides a convenient procedure for the *anti*-Markovnikov hydrobromination of internal alkenes and nicely complements the base-induced bromination reaction,[1] which provides a procedure for the hydrobromination of terminal alkenes.

Mechanistic Considerations. The mechanism we wish to propose for the reactions in inert solvents involves a free-

radical chain bromination at the α–position of organoborane, a free-radical bromination that proceeds rapidly, even in the dark (eqs 3-5).[14]

$$Br_2 + R_3B \xrightarrow{\text{slow}} Br\cdot + R_2BBr + R\cdot \tag{3}$$

$$R_2B-\underset{\displaystyle H}{\overset{\displaystyle |}{C}}- + Br\cdot \longrightarrow R_2B-\underset{\displaystyle \cdot}{\overset{\displaystyle |}{C}}- + HBr \tag{4}$$

$$R_2B-\underset{\displaystyle \cdot}{\overset{\displaystyle |}{C}}- + Br_2 \longrightarrow R_2B-\underset{\displaystyle Br}{\overset{\displaystyle |}{C}}- + Br\cdot \tag{5}$$

The remarkably high reactivity of organoborane toward attack by bromine[15] is indicated by the observation that even the use of cyclohexane as a solvent results in insignificant diversion of bromine atoms to this possible reactant. A further evidence in support of the activation of the α–position by boron atom in organoboranes is given in a later section.

The precise nature of the initiation step is uncertain, but may involve the attack of bromine on the organoborane (eq 3).[16] The hydrogen bromide produced in the substitution step can then react preferentially with α–bromoorganoborane to form alkyl bromide (eq 6), or competitively with an alkyl group on the α–bromoorganoborane to afford an alkane (eq 7).

$$R_2B-\underset{\displaystyle Br}{\overset{\displaystyle |}{C}}- + HBr \longrightarrow R_2BBr + H-\underset{\displaystyle Br}{\overset{\displaystyle |}{C}}- \tag{6}$$

$$R-B\begin{matrix}/\\ \\ \backslash\end{matrix} + HBr \longrightarrow RH + Br-B\begin{matrix}/\\ \\ \backslash\end{matrix} \tag{7}$$

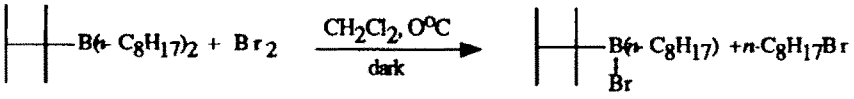
This mechanism is capable of accounting for all of the available experimental observations.

In inert solvent, the rate of loss of bromine decreases in the order: *sec*-butyl > *n*-butyl > isobutyl. This is consistent with the greater reactivity of a tertiary hydrogen, as compared to a secondary hydrogen, towards abstraction by a free-radical. In carbon tetrachloride and cyclohexane solvents, considerable hydrogen bromide was formed in the reaction mixture in the initial stages of the reaction. This hydrogen bromide disappeared as the butyl bromide appeared, indicating that the α–bromination is occurring at a much faster rate than the subsequent cleavage of the α–bromoorganoborane by hydrogen bromide. In methylene chloride, however, the cleavage reaction must be greatly facilitated.

Indeed, the addition of methylene chloride to a reaction mixture from bromine and tri-*sec*-butylborane in carbon tetrachloride at a time when most of the bromine had reacted, but little *sec*-butyl bromide had appeared, resulted in a rapid increase in the formation of *sec*-butyl bromide with a corresponding decrease in the amount of hydrogen bromide present in the reaction mixture. For example, in the reaction of bromine (10 mmol) with tri-*sec*-butylborane (10 mmol) in carbon tetrachloride, 1.5 mmol of 2-bromobutane and 5.4 mmol of hydrogen bromide was formed in 1 h, while 2.0 mmol of borane and 1.7 mmol of bromine remained unreacted. This reaction was repeated and methylene chloride (20 mL) was added after 1 h. After 7 h, the reaction was quenched with cyclohexene. The results show that only a trace of bromine and borane remained, while 8.5 mmol of α–bromobutane was formed with only a trace of hydrogen bromide remaining in the solution.

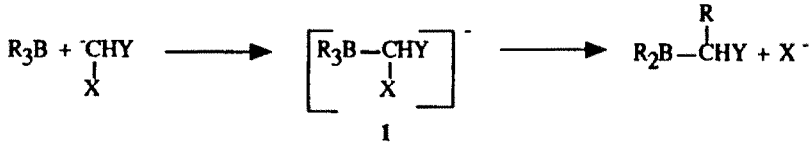
Further support for this mechanism is provided by the interesting observation that when the reaction was carried out under reduced pressure to facilitate escape of the hydrogen bromide the amount of butyl bromide present in the reaction mixture decreased with a corresponding increase in the amount of hydrogen bromide trapped in the gas bubbler containing aqueous sodium hydroxide. For example, when bromine (10 mmol) was allowed to react for 1 h in the dark with 10 mmol of tri-*n*-butylborane in 20 mL of methylene chloride at atmospheric pressure, there was present in the reaction mixture 6.1 mmol of bromobutane and 0.8 mmol of hydrogen bromide. However, when the reaction was repeated under exactly the same conditions, except for a partial vacuum of 130 mm of mercury, the yield of bromobutane decreased to 1.5 mmol and the total amount of hydrogen bromide increased to 8.8 mmol! The results for a similar experiment using tri-*sec*-butylborane were not quite as striking, but still the yield of 2-bromobutane decreased and the yield of hydrogen bromide increased when the reaction was run under reduced pressure. Thus, even in the methylene chloride solvent system where the hydrogen bromide cleavage reaction is apparently greatly facilitated, the application of a partial vacuum has removed hydrogen bromide from the reaction mixture before it could react with an α–bromoalkyldialkylborane to produce an alkyl bromide. Consequently, the formation of alkyl bromides in the dark reaction of bromine with trialkylboranes must be due in part, if not entirely, to cleavage of an α–bromoorganoborane intermediate by hydrogen bromide.

The dark reaction of bromine with thexyldi-*n*-octylborane provides only 1-bromooctane and no detectable amount of thexyl bromide (eq 8). This provides an additional support for the proposed mechanism because α–bromination of the thexyl(2,3-dimethyl-2-butyl) group is not possible.



(8)

Finally, the most convincing evidence for the formation of an α–bromoorganoborane during the dark reaction of bromine with trialkylboranes was obtained through a study of the products formed upon alkaline hydrogen peroxide oxidation. α–Haloalkyltrialkylborates (**1**) have been postulated as intermediates in the reaction of trialkylboranes with α–halocarbanions[17] (eq 9).



(9)

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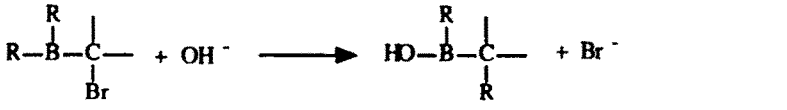
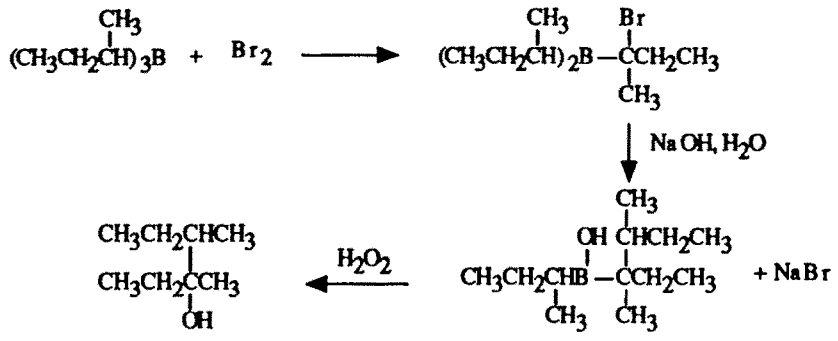
Y = –COOR, –COR, or –CN X = Br or Cl

The intermediate **1** was then thought to undergo a rapid rearrangement of an alkyl group from boron to carbon with loss of the halide ion.[18-20] One would expect a similar type of rearrangement to occur if an α–bromoorganoborane was treated with an appropriate nucleophile, such as hydroxide ion (eq 10).



(10)

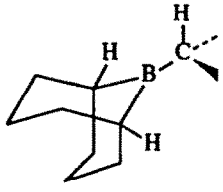
Consequently, the reaction mixture from the bromination of tri-*sec*-butylborane in carbon tetrachloride after 30 min was treated with aqueous sodium hydroxide.[21] Alkaline hydrogen peroxide oxidation then gave a 32% yield of 3,4-dimethyl-3-hexanol, the product anticipated for the transfer of a *sec*-butyl group from boron to the α–carbon position (Scheme 2).



Scheme 2

The results obtained for the dark reaction of bromine with tri-*n*-butyl and tri-*sec*-butyl and triisobutylborane indicate that the reaction is extremely dependent upon the degree of substitution and steric environment of the α–carbon. This suggested that a high degree of selectivity should be possible in the dark reaction of bromine with organoboranes.

The *B*-alkyl-9-BBN derivatives appeared to be uniquely structured for the desired selectivity. The α–hydrogen on the alkyl group in **2** should be more susceptible to free-radical abstraction than the bridgehead hydrogens because the



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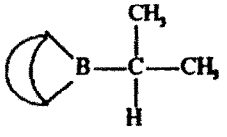
resulting α–boro free-radical would be able to interact with the vacant *p*-orbital on boron, while a bridgehead free-radical would presumably not be able to interact with the boron atom. This is because the odd electron in the bridgehead free-radical would necessarily occupy an orbital which is orthogonal to the vacant *p*-orbital on boron and the rigid bicyclic structure prevents the bond rotation required for maximum interaction.

Remarkable Selectivity and Enhanced Reactivity of α–Hydrogen. The high yields (~ 90%) of alkyl bromides realized in the bromination of *B*-*sec*-alkyl-9-BBN derivatives (Table 6) suggest that the α–position of the alkyl group is exceptionally activated to achieve such a selective substitution at this position.[21,15] This conclusion has been tested by examining the competitive bromination of *B*-isopropyl-9-BBN and cumene. Treatment of an equimolar solution of *B*-*i*-Pr-9-BBN (**3**), cumene (**4**) and cyclohexane in methylene chloride with bromine at 0°C revealed that the relative reactivity of **3**:**4** is 5.5, as shown by the GC analysis of the residual **3** and **4**. No substitution of cyclohexane occurs. If we utilize the literature value of 120 for the relative reactivities[22] of cumene and isobutane (**5**), this results in a relative reactivity of the tertiary hydrogen in **3** to that of isobutane of 660. Clearly, the activation toward attack by bromine atoms of the tertiary position provided by the 9-BBN moiety in **3** exceeds that provided by the phenyl group in **4**.

This remarkable activation can be attributed to stabilization of the free-radical produced in the hydrogen abstraction step (eq 4) by the interaction of the old electron with the vacant *p*-orbital of the boron atom. Attack on the other two α–positions (bridgehead) of 9-BBN moiety is apparently much less facile, because in these positions, the odd electron would occupy an orbital which is orthogonal to the vacant *p*-orbital on boron. In fact, 2-bromo-2-propyl-9-

BBN has been isolated and characterized.



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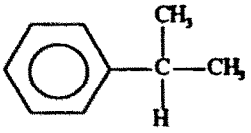

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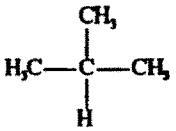

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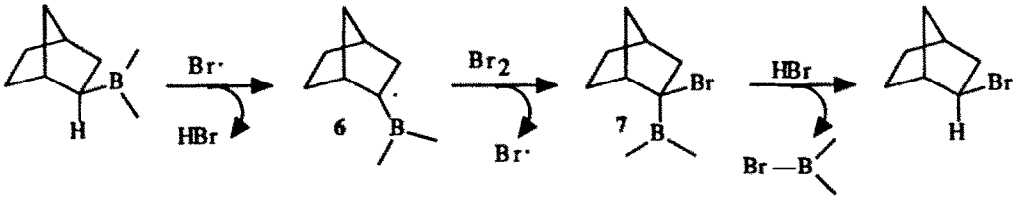
1.00

Stereochemistry. The bromonorbornane obtained *via* the dark reaction of bromine with either tri-*exo*-norbornylborane or *B*-*exo*-norbornyl-9-BBN is predominantly (> 99%) exo. This is interpreted as indicating that bromine attacks the α–boronorbornyl free-radical (6) from the sterically less hindered side (exo) to give α–*exo*-bromoborane (7). The



Scheme 3

subsequent hydrogen bromide cleavage then proceeds with clean retention of configuration to produce stereochemically pure *exo*-bromonorbornane (Scheme 3).

Irrespective of the precise reasons for the clean retention of configuration, the dark reaction of bromine with *B*-*sec*-alkyl-9-BBN should find numerous synthetic applications because the reaction proceeds under extremely mild conditions.[23]

CONCLUSIONS

Undoubtedly, the reaction of bromine with trialkylboranes involves, as the first step, a facile α–bromination of the organoborane when the reaction is carried out in an inert solvent, such as carbon tetrachloride, cyclohexane, or methylene chloride. This proposed free-radical chain bromination occurs readily, even in the dark at room temperature, to produce an α–bromoalkyldialkylborane and hydrogen bromide. Apparently, the hydrogen bromide then reacts slowly with the α–bromoorganoborane to give the alkyl bromide plus dialkylboron bromide. To explain the results observed in methylene chloride, it was assumed that the HBr cleavage reaction is greatly facilitated in this solvent.

The dark reaction in methylene chloride appeared to be synthetically useful and was used in the development of a highly convenient, new procedure for the *anti*-Markovnikov hydrobromination of internal alkenes. This new synthesis of *sec*-alkyl bromides nicely complements the method reported in the previous paper,[1] which provides a highly convenient procedure for the overall *anti*-Markovnikov hydrobromination of terminal olefins.

A number of interesting possibilities for further study have come about as a result of this investigation. The remarkably facile rearrangement of α–bromoorganoboranes appeared to have enormous implications for the formation of carbon-carbon bonds and the synthesis of carbon structures. Consequently, a new and convenient method for the synthesis of highly branched tertiary alcohols was developed.[24] Equally important is the implication that possibly α–bromoorganoboranes may now be prepared, isolated and studied.[25] Eventually, a whole series of new and important synthetic reactions may be discovered for the α–bromoorganoboranes,[25] which could presumably make them one of the most important synthetic intermediates of the already highly useful organoboranes.

EXPERIMENTAL SECTION

General Comments. The purification of the hydroboration solvents, the preparation and standardization of the borane·THF and 9-BBN·THF solutions and the GC analysis procedure are described elsewhere.[12] Carbon tetrachloride was distilled prior to use; cyclohexane was allowed to stir for at least 24 h over concentrated sulfuric acid, washed with water, dried over anhydrous potassium carbonate and distilled from a small amount of lithium aluminum hydride before using. The methylene chloride was also treated with concentrated sulfuric acid and then distilled from anhydrous potassium carbonate. The alkenes used in this study were all commercially available. In general, they were distilled from lithium aluminum hydride and stored under nitrogen prior to use. Tri-*n*-butylborane was obtained from Callery Chemical Company, redistilled [bp 69-70° (5 mm)] and stored under nitrogen. Tri-*sec*-butylborane [bp 70-71° (4.5 mm)] and triisobutylborane [bp 65-66° (5.5 mm)] were obtained in the usual manner by hydroboration of the appropriate alkene with borane·THF. The THF solvent was then distilled off under reduced pressure and the tributylborane was isolated by vacuum distillation under a nitrogen atmosphere. The three isomeric tributylboranes were all of > 99% purity by GC analysis and by oxidation to the butanols with alkaline hydrogen peroxide. All other organoboranes were obtained in the usual manner *via* hydroboration and were used directly as obtained following removal of THF by distillation. The majority of THF was removed by distillation at atmospheric pressure with the final traces being removed at reduced pressure. The organoboranes were always handled under nitrogen with careful exclusion of oxygen.

Dark Reaction of Bromine with Tri-*n*-butylborane in Carbon Tetrachloride. The procedure that is described here for the bromination of tri-*n*-butylborane in carbon tetrachloride was used in general for the study of all three isomeric tributylboranes in the solvents, carbon tetrachloride, cyclohexane,[10] methylene chloride and THF. A dry, 50-mL flask equipped with a septum inlet, magnetic stirrer, 20-25°C water bath and a gas outlet tube was flushed with nitrogen and connected to a gas bubbler containing a known amount of standard aqueous sodium hydroxide solution. The reaction flask was charged with 20 mL of dry carbon tetrachloride and 2.42 mL (10 mmol) of tri-*n*-butylborane. After completely covering the reaction flask with two layers of aluminum foil, bromine (0.5 mL, 10 mmol) was added through the septum inlet at a fast rate (~ 30 sec) using an all-glass syringe equipped with a Teflon needle. Following a given time interval (5 min, 30 min, 1 h and 8 h, *i.e.*, a total of 5 separate reactions run), cyclohexene (2 mL, ~ 20 mmol) was added to destroy any unreacted bromine and to react with any hydrogen bromide dissolved in the reaction mixture. Two internal standards, such as *n*-nonane and *n*-decane (Phillips, 99 mol %), were then added and the reaction mixture was analyzed directly on a Hewlett-Packard Model 5750 gas chromatograph equipped with a 6 ft x 1/4 in column of Dow 710, 10% on AW/DMCS Chromosorb W. The sodium hydroxide remaining in the trap was titrated with a standard potassium acid phthalate solution to determine the amount of hydrogen bromide lost from the reaction vessel. The results of this study are summarized in Table 1.

Dark Reaction of Bromine with Tri-*sec*-butylborane in Methylene Chloride. The experimental procedure described here for the bromination of tri-*sec*-butylborane is representative of the general method used in the study of the preparation of alkyl bromides *via* the dark reaction of bromine with trialkylboranes in methylene chloride. A dry, 50-mL flask equipped with a septum inlet, gas outlet tube with stopcock, magnetic stirrer and 20-25°C water bath was flushed with nitrogen and charged with 20 mL of dry methylene chloride and 2.35 mL (10 mmol) of tri-*sec*-butylborane. After the outlet tube stopcock was closed, the reaction system was covered completely with two layers of aluminum foil. Bromine (0.55 mL, 11 mmol) was then added as described in the previous experiment and the reaction was allowed to stir for 24 h at 20-25°C. Following the addition of 1 mL of cyclohexene and 1 mL each of *n*-nonane and *n*-decane (internal standards), direct GC analysis of the clear, colorless reaction mixture showed the presence of 8.8 mmol (88%) of 2-bromobutane. The results obtained when the above procedure was applied to various representative trialkylboranes are summarized in Table 5.

Dark Reaction of Bromine with Tri-*sec*-butylborane in Carbon Tetrachloride Followed by the Addition of Methylene Chloride. Two separate dark reactions were run at 20-25°C using 0.5 mL (10 mmol) of bromine and 2.35 mL (10 mmol) of tri-*sec*-butylborane in 20 mL of carbon tetrachloride. The general procedure followed was exactly the same as described above for the dark reaction of bromine with tri-*n*-butylborane in carbon tetrachloride. After each reaction had stirred for 1 h at 20-25°C in the dark, cyclohexene (2 mL) was added to reaction A and methylene chloride (20 mL) was added to reaction B. Two internal standards were added to reaction A and direct GC analysis showed that 2.0 mmol of tri-*sec*-butylborane and 1.7 mmol of bromine remained unreacted, while 1.5 mmol of 2-bromobutane and 5.4 mmol of hydrogen bromide were formed. Reaction B was allowed to stir for 7 additional hours. At that time, cyclohexene and the internal standards were added. Direct GC analysis showed that only trace amounts of tri-*sec*-butylborane, bromine, and hdyrogen bromide remained in solution. However, the yield of 2-bromobutane had increased to 8.5 mmol.

Dark Reaction of Bromine with Tri-*n*-butylborane in Methylene Chloride Under Reduced Pressure. A 100-mL flask was equipped with a septum inlet (septum inlet A), Dewar condenser, magnetic stirrer and 20-25°C water bath. The Dewar condenser was equipped with a gas outlet tube with stopcock (stiopcock A) and connected to a gas bubbler containing 25 mL of a 0.488 *M* aqueous solution of sodium hydroxide. A septum inlet (septum inlet B) was placed in the line immediately after stopcock A and a by-pass tube equipped with a 2-way stopcock (stopcock B) was placed around the gas bubbler. The entire apparatus was then connected through a 3-way stopcock (stopcock C) to a mercury bubbler and a water aspirator. With stopcocks A and B open and with stopcock C turned to the mercury bubbler, the reaction apparatus was flamed and flushed with nitrogen. Tri-*n*-butylborane (2.42 mL, 10 mmol) and

methylene chloride (20 mL) were then added to the reaction flask *via* septum inlet A and the Dewar condenser was charged with Dry Ice-acetone. At this point, the entire reaction apparatus up to stopcock A was covered with two layers of aluminum foil. The blank experiment was run first. After closing stopcock B, bromine (0.5 mL, 10 mmol) was added rapidly to the reaction flask *via* septum inlet A. The reaction mixture was then stirred for 1 h at 20-25°C. After closing stopcock A, cyclohexene (2 mL) was added through septum inlet A. The reaction was stirred and shaken for 5 min and the internal standards were added. Analysis of the reaction mixture by GC showed that 5.0 mmol of 1-bromobutane, 1.2 mmol of 2-bromobutane and 0.8 mmol of hydrogen bromide had been formed. Nitrogen was flushed through septum inlet B and titration of the sodium hydroxide solution with potassium acid phthalate showed that no hydrogen bromide had been lost from the reaction vessel. The above reaction was then repeated under reduced pressure. The apparatus was assembled, charged with methylene chloride and tri-*n*-butylborane and covered with aluminum foil, as described above. Stopcocks A and B were opened and 3-way stopcock C was turned to the water aspirator by-passing the mercury bubbler. The reaction mixture was then magnetically stirred in a 25°C water bath as a pressure of 130 mm was established. It was previously found that at 130 mm the bp of methylene chloride is less than 25°C. Consequently, the Dry Ice-acetone condenser was necessary to keep the methylene chloride and bromine from being lost. Stopcock B was then closed and the bromine (0.5 mL, 10 mmol) was added rapidly through septum inlet A. After 1 h, stopcocks A and C were closed, stopcock B was opened, and nitrogen was added through septum inlets A and B to return the reaction apparatus to atmospheric pressure. Cyclohexene was then added immediately to the reaction flask, followed by the internal standards. After 5 min stirring, the reaction mixture was analyzed directly by GC, which showed that only 1.5 mmol of 1-bromobutane and no detectable amount of 2-bromobutane had been formed. However, the reaction mixture did contain 3.1 mmol of hydrogen bromide and titration of the base remaining in the gas bubbler showed that 5.7 mmol of hydrogen bromide had been trapped in the aqueous sodium hydroxide. Therefore, by the simple application of a partial vacuum, the yield of butyl bromide decreased from 62% to 15% and the total yield of hydrogen bromide increased from 8% to 88%.

Dark Reaction of Bromine with Tri-*sec*-butylborane in Carbon Tetrachloride Followed by Oxidation. A dry, 100-mL flask equipped with a septum inlet, reflux condenser, magnetic stirrer and 20-25°C water bath was flushed with nitrogen and then maintained under a positive nitrogen pressure. The reaction flask was charged with 20 mL of dry carbon tetrachloride and 2.35 mL (10 mmol) of tri-*sec*-butylborane. After completely covering the reaction apparatus with two layers of aluminum foil, bromine (0.5 mL, 10 mmol) was added and the reaction was allowed to stir for 30 min. Water (5 mL) was then added, followed by 10 mL of a 3-*M*- aqueous sodium hydroxide solution. After 5 min stirring, the aluminum foil was removed and 10 mL of 30% hydrogen peroxide was added dropwise with cooling. The reaction mixture was then heated to 50°C for 3 h to ensure complete oxidation. Upon cooling to room tremperature, the lower organic layer was removed and the aqueous layer was extracted with pentane (1 x 50 mL). The combined organic layers were then dried over anhydrous potassium carbonate and analyzed by GC on a 6 ft x 1/4 in column of Carbowax 20M - 1% Armax 18D, 15% on AW/DMCS Chromosorb W, using 2-octanol as the internal standard. The GC analysis indicated that 3.2 mmol of 3,4-dimethyl-3-hexanol[27] had been produced.

Dark Reaction of Bromine with *B*-(4-Methyl-2-pentyl)-9-borabicyclo[3.3.1]nonane. The following procedure for the conversion of 4-methyl-2-pentene into 2-bromo-4-methylpentane is representative of the general method used for the dark reaction of bromine with *B*-alkyl-9-BBN compounds in methylene chloride. A dry, 500-mL flask equipped with a septum inlet, reflux condenser, gas outlet tube with stopcock and magnetic stirrer was flushed with nitrogen and then maintained under a positive nitrogen pressure. The flask was charged with 190 mL of a 0.57 *M* solution of 9-BBN (108 mmol of hydride) in THF. 4-Methyl-2-pentene (12.5 mL, 100 mmol) was added and the solution was heated to reflux and maintained at reflux for 1 h.[28] The THF was then removed *via* reduced pressure and replaced with 100 mL of methylene chloride. The solution was cooled to 0°C and the outlet tube stopcock was closed. After covering the entire reaction flask with aluminum foil, bromine (5.6 mL, 110 mmol) was added through the septum inlet over a period of 1 min using an all-glass syringe equipped with a Teflon needle. The reaction was then allowed to stir for 30 min at 0°C, followed by 1 h at 25°C. Following removal of the aluminum foil and venting the flask (HBr gas) to a trap containing alkali, the *B*-bromo-9-BBN and any excess bromine was destroyed by the dropwise addition of 75 mL of 3 *M* aqueous sodium hydroxide at 0°C. After 15 min stirring, the lower organic layer was removed, dried over anhydrous potassium carbonate, and filtered throgh Celite. Following removal of the methylene chloride on a rotary evaporator, vacuum distillation gave 12.2 g (74%) of 2-bromo-4-methylpentane, bp 58-60° (54 mm), n^{21}D 1.4415 [lit.[29] n^{24}D 1.4406].

Competitive Bromination of *B*-Isopropyl-9-BBN and Isopropylbenzene. A dry, 50-mL flask equipped with magnetic stirrer and septum inlet was flushed with nitrogen and charged with 2 mmol (0.36 mL) of *B*-isopropyl-9-BBN, 2 mmol (0.29 mL) of isopropylbenzene, 2 mmol (0.21 mL) of cyclohexane, 5 mL of methylene chloride and 5 mL of water. The mixture was cooled to 0°C and the relative ratios of *B*-isopropyl-9-BBN and isopropylbenzene to cyclohexane were measured on a clean SE-30 column. Three determinations were within 1.5% agreement for each compound. Then, 0.4 mmol (20 μL) of bromine was added all at once and instantly was decolorized. The relative ratios were then redetermined three times *via* GC and remained constant (± 1.5%) with time. Using the general equation,[30] the *B*-isopropyl-9-BBN was 5.5 ± 0.2 more reactive than isopropylbenzene. No cyclohexylbromide nor cyclohexanol was observed *via* GC. The 2-bromo-2-phenylpropane, which should have been produced, was found as 2-phenyl-2-propanol. In control experiments, *B*-isopropyl-9-BBN-cyclohexane ratio was unchanged by treatment with water or aqueous hydrogen bromide at 0°C for 1 h. When the competitive bromination experiment was repeated with no water present, using nitrogen to sweep out hydrogen bromide, the relative reactivity was 5.8.

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