CHAPTER I

HYDRATION OF OLEFINS, DIENES, AND ACETYLENES VIA HYDROBORATION

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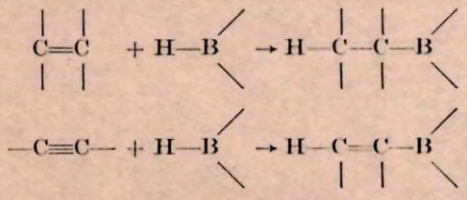
CONTENTS

INTRODUCTION

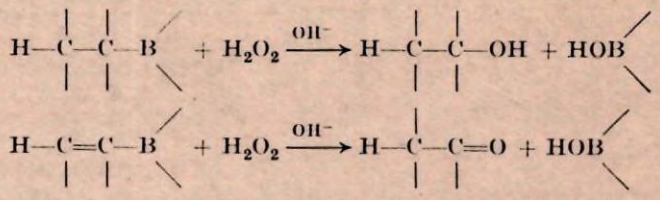
The hydroboration of olefins, dienes, and acetylenes involves the addition of a boron-hydrogen bond to the carbon-carbon multiple bond.[1,2] This



[1] Brown and Subba Rao, *J. Am. Chem. Soc.*, **78**, 5694 (1956); **81**, 6423, 6428 (1959); *J. Org. Chem.*, **22**, 1136 (1957).

[2] Brown and Zweifel, *J. Am. Chem. Soc.*, **81**, 1512 (1959); **83**, 3834 (1961).

reaction provides a new convenient route to the corresponding organoboranes and makes them readily available as intermediates in organic synthesis. One of the important reactions which the organoboranes undergo is the rapid and essentially quantitative oxidation with alkaline hydrogen peroxide.



The hydroboration of olefins involves a *cis* addition of the boron-hydrogen bond, the boron atom becoming attached to the less substituted of the two olefinic carbon atoms of the double bond. Furthermore the oxidation occurs with retention of configuration, placing the hydroxyl group at the precise position occupied by the boron atom in the initial organoborane. Both the hydroboration and the oxidation reactions appear to be free of the carbon skeleton rearrangements that occasionally accompany other hydration procedures. As a result, hydroboration followed by oxidation with alkaline hydrogen peroxide has become an important new synthetic method for the anti-Markownikoff, *cis* hydration of double bonds.

This chapter surveys the available information on the hydration of olefins, dienes, acetylenes, and their derivatives by the hydroboration-oxidation procedure.*

Early observations on the reaction of diborane with olefins indicated that the reaction required elevated temperatures and long reaction periods[3] and did not provide a convenient route to organoboranes. Later it was observed that anhydrous aluminum chloride enhanced the reducing power of sodium borohydride to the point where the reagent at room temperature readily reduced substances such as nitriles and esters, groups which are normally resistant to sodium borohydride itself.[4] Even more unexpected was the observation that olefins reacted with the reagent, utilizing one B-H equivalent per molecule of olefin and forming an organoborane.[4]

$$9RCH{=}CH_2 + 3NaBH_4 + AlCl_3 \rightarrow 3(RCH_2CH_2)_3B + AlH_3 + 3NaCl$$

* Another survey is to be found in an article by Brown, *Tetrahedron*, **12**, 117 (1961), and a detailed treatment of the hydroboration reaction and of the synthetic applications of the resulting organoboranes is given by Brown, *Hydroboration*, W. A. Benjamin, New York, 1962.

[3] Hurd, *J. Am. Chem. Soc.*, **70**, 2053 (1948); Stone and Emeléus, *J. Chem. Soc.*, **1950**, 2755; Whatley and Pease, *J. Am. Chem. Soc.*, **76**, 835 (1954); Stone and Graham, *Chem. & Ind. (London)*, **1955**, 1881.

[4] Brown and Subba Rao, *J. Am. Chem. Soc.*, **78**, 2582 (1956); **81**, 6423 (1959).

This discovery led to the search for alternative procedures for hydroboration. It was found that hydroboration could readily be achieved by treating an olefin with sodium borohydride and boron trifluoride in an appropriate solvent.

$$12RCH{=}CH_2 + 3NaBH_4 + 4BF_3{:}O(C_2H_5)_2 \rightarrow 4(RCH_2CH_2)_3B + 3NaBF_4 + 4(C_2H_5)_2O$$

It was also discovered that, contrary to the impression given by the earlier reports, diborane itself adds rapidly and quantitatively to olefins in ether solvents.[1]

$$6RCH{=}CH_2 + B_2H_6 \rightarrow 2(RCH_2CH_2)_3B$$

The reaction appears to be as general as the addition of hydrogen or bromine to multiple carbon-carbon bonds.

Johnson and Van Campen had noted that alkaline hydrogen peroxide effected a complete dealkylation of tri-*n*-butylborane and related organoboranes to form alcohols and boric acid.[5] A detailed study of this reaction revealed that the oxidation is essentially quantitative at 25°, that the solvents utilized for the hydroboration do not interfere with the oxidation and hence the reaction can be performed without isolating the organoborane, and that the reaction is of very wide generality.[6]

The subject matter of this chapter is limited to hydroboration-oxidation as a specific combination for the hydration of multiple carbon-carbon bonds under mild conditions. It may be noted, however, that organoboranes undergo protonolysis in the presence of carboxylic acids, providing a non-catalytic means of hydrogenating multiple carbon-carbon bonds.[7] Organoboranes also undergo coupling on treatment with alkaline silver nitrate, and this reaction provides a new synthesis for carbon-carbon bonds.[8]

HYDROBORATION OF OLEFINS

As a result of the developments outlined above, two convenient procedures are available for the hydroboration of olefins under mild conditions: (1) treatment of a mixture of the unsaturated compound and an alkali metal borohydride in a suitable solvent with boron trifluoride etherate (or other acid), and (2) external generation of diborane followed by its reaction with the unsaturated compound in an appropriate solvent. Each of these procedures possesses advantages that will lead to its selection for specific reactions. Both procedures are described in the section on Experimental Procedures.

[5] Johnson and Van Campen, *J. Am. Chem. Soc.*, **60**, 121 (1938).

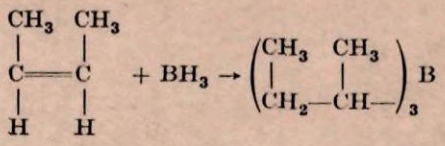
[6] H. C. Brown, C. H. Snyder, B. C. Subba Rao, and G. Zweifel, to be published.

[7] Brown and Murray, *J. Am. Chem. Soc.*, **81**, 4108 (1959).

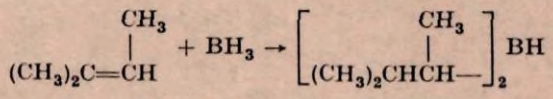
[8] Brown, Hébert, and Snyder, *J. Am. Chem. Soc.*, **83**, 1001 (1961); Brown and Snyder, *ibid.*, **83**, 1001 (1961); Brown, Verbrugge, and Snyder, *ibid.*, **83**, 1002 (1961).

Scope and Stoichiometry

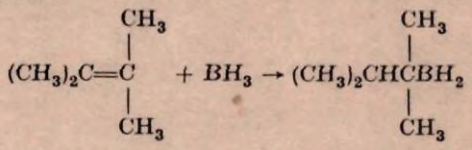
The hydroboration reaction has been applied to a large number of olefins of widely different structures. In practically all cases the reaction proceeds simply and rapidly. Only the most hindered olefins exhibit any resistance to addition. Simple olefins commonly utilize all the hydrogen atoms of diborane and form the trialkylborane.



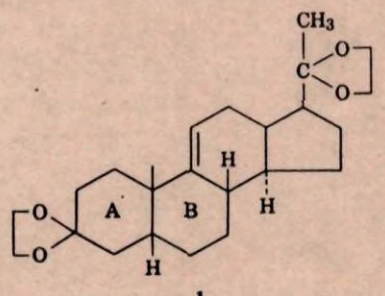
However, trisubstituted olefins, such as 2-methyl-2-butene and 1-methylcyclohexene, utilize only two of the three hydrogen atoms of the borane group forming a dialkylborane.



Further reaction to form a trialkylborane is very slow at room temperature. Finally, tetrasubstituted olefins, such as tetramethylethylene, react rapidly to utilize only one hydrogen atom of the borane group and form the monoalkylborane.



Up to the present time only two olefins, the steroids **1** and **2** (Refs. 9 and 10, respectively), have been reported not to undergo hydroboration.



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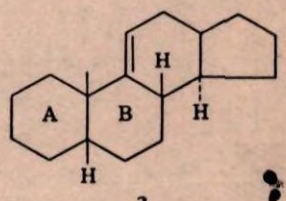


2

[9] Wechter, *Chem. & Ind. (London)*, **1959**, 294.

[10] Nussim and Sondheimer, *Chem. & Ind. (London)*, **1960**, 400.

On the other hand, the analogous compounds with the A/B-*trans* junction do undergo hydroboration.

The stoichiometry of the hydroboration reaction for a number of representative olefins is summarized in Table I.

TABLE I

STOICHIOMETRY OF HYDROBORATION OF REPRESENTATIVE OLEFINS[1,11]

	Acyclic Olefins	Cyclic Olefins
(*a*)	3 Olefin + $BH_3 \xrightarrow{20°}$ Trialkylborane, R_3B	
	2-Methyl-1-butene	Cyclopentene
	3-Methyl-1-butene	Cyclohexene
	1-Hexene	Cycloheptene
	2-Hexene	Norbornene
	3-Hexene	β-Pinene
	4-Methyl-2-pentene	
	3,3-Dimethyl-1-butene	
	2,4,4-Trimethyl-1-pentene	
	Styrene	
	α-Methylstyrene	
	1-Tetradecene	
(*b*)	2 Olefin + $BH_3 \xrightarrow{20°}$ Dialkylborane, R_2BH	
	2-Methyl-2-butene	1-Methylcyclopentene
	4,4-Dimethyl-2-pentene	1-Methylcyclohexene
	2,4,4-Trimethyl-2-pentene	α-Pinene
(*c*)	1 Olefin + $BH_3 \xrightarrow{20°}$ Monoalkylborane, RBH_2	
	2,3-Dimethyl-2-butene	1,2-Dimethylcyclopentene
	2,2,5,5-Tetramethyl-3-hexene[12]	1,2-Dimethylcyclohexene

Directive Effects[13]

The oxidation of an organoborane to an alcohol by alkaline hydrogen peroxide is essentially quantitative and proceeds without rearrangement. Consequently, the structure of the alcohol formed serves to locate the position of the boron atom in the organoborane.

Terminal olefins, $RCH{=}CH_2$, give predominantly addition of the boron atom to the terminal carbon atom (93–94%). Thus hydroboration of 1-hexene yields an organoborane which, upon oxidation with alkaline hydrogen peroxide, is converted to a mixture composed of 94% 1-hexanol and 6% 2-hexanol. Similar results are observed with 1-butene, 1-pentene,

[11] Brown and Zweifel, *J. Am. Chem. Soc.*, **83**, 2544 (1961).
[12] Logan and Flautt, *J. Am. Chem. Soc.*, **82**, 3446 (1960).
[13] Brown and Zweifel, *J. Am. Chem. Soc.*, **82**, 4708 (1960).

and 1-octene, establishing the predominantly *anti*-Markownikoff direction of addition.[1] Branching of the alkyl chain as in 3-methyl-1-butene, 3,3-dimethyl-1-butene, and 4,4-dimethyl-1-pentene makes no essential difference in the direction of addition.

The presence of an alkyl substituent in the 2 position increases the directive effect. The boron atom adds to the terminal position of olefins such as 2-methyl-1-butene to the extent of 99%.

TABLE II

DIRECTIVE EFFECTS IN THE HYDROBORATION OF TERMINAL OLEFINS AT 20°

Olefin	Alcohol Distribution,[a] %	
	1-ol	2-ol
1-Butene	93	7
1-Pentene	94	6
2-Methyl-1-butene	99	1
3-Methyl-1-butene	94	6
1-Hexene	94	6
3,3-Dimethyl-1-butene	94	6
4,4-Dimethyl-1-pentene	93	7
Styrene	80	20
p-Chlorostyrene	65	35
2,4,4-Trimethyl-1-pentene	99	1
α-Methylstyrene	100	Trace
p-Methylstyrene	82	18
p-Methoxystyrene	91	9
Allylbenzene	90	10

[a] The yields by gas-liquid partition chromatography were 90 ± 10%.

The addition to styrene is less selective; 80% of the boron becomes attached to the terminal position and 20% to the secondary carbon atom. Moreover, the direction of addition is strongly modified by substituents in the *para* position of the aromatic nucleus.

The results are summarized in Table II.

The data in Table II—specifically the facts that ethylene, isopropylethylene, and *t*-butylethylene give 93%, 94%, and 94%, respectively, of primary alcohol—clearly show that an increase in the bulk of the alkyl group attached to the double bond does not influence the direction of addition. These results argue against steric control of the direction of addition. The marked influence of *para* substituents on the direction of addition to styrene supports the contention that the direction of addition is controlled primarily by electronic factors.

Dialkyl ethylenes, RCH=CHR′, such as 2-pentene and 2-hexene, undergo addition to place the boron atom in approximately equal

amounts on the 2- and 3-carbon atoms. This is true even for molecules such as *trans*-4-methyl-2-pentene and *trans*-4,4-dimethyl-2-pentene, where the two alkyl groups differ markedly in their steric requirements. Only in *trans*-1-phenylpropene, where the phenyl group is opposed to a methyl group, is a marked directive effect indicated; the boron atom becomes attached to the carbon atom holding the phenyl substituent to the extent of 85% (Table III).

TABLE III

DIRECTIVE EFFECTS IN THE HYDROBORATION OF INTERNAL OLEFINS AT 20°

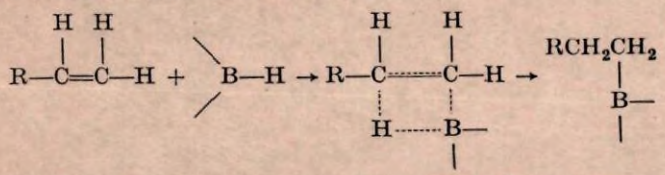
Olefin	Alcohol Distribution,[a] %	
	2-ol	3-ol
cis-2-Pentene	55	45
trans-2-Pentene	51	49
2-Methyl-2-butene[b]	98[c]	2
cis-2-Hexene	50	50
trans-2-Hexene	46	54
trans-4-Methyl-2-pentene	57	43
trans-4,4-Dimethyl-2-pentene[b]	58	42
2,4,4-Trimethyl-2-pentene[b]	2	98[d]
trans-1-Phenylpropene	85[e]	15[f]

[a] The yields by gas-liquid partition chromatography were 90 ± 10%.
[b] The addition yields a dialkylborane.
[c] The product is 3-methyl-2-butanol.
[d] The product is 2,2,4-trimethyl-3-pentanol.
[e] The product is 1-phenyl-1-propanol.
[f] The product is 1-phenyl-2-propanol.

Trisubstituted olefins, $R_2C{=}CHR$, such as 2-methyl-2-butene and 2,4,4-trimethyl-2-pentene, add the boron atom predominantly at the less substituted ethylenic carbon atom.

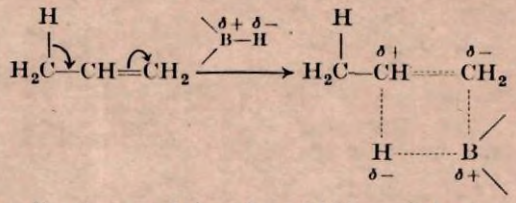
The data are summarized in Table III

Diborane undergoes *cis* addition to cyclic olefins and to acetylenes, which will be discussed later. Consequently, the addition very likely involves a four-center transition state.

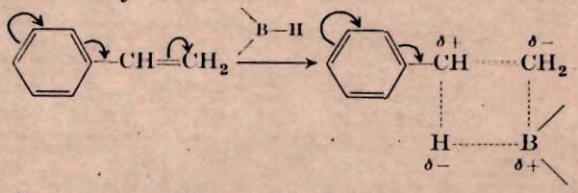


The boron-hydrogen bond is presumably polarized, the hydrogen having some hydridic character. The addition of the boron atom to the terminal position is then readily understood on the basis of the electronic shifts

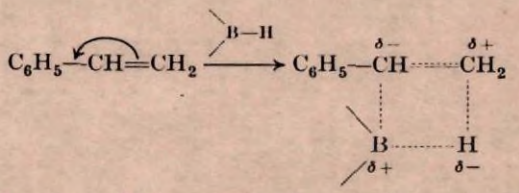
generally assumed in order to account for the normal ionic addition to propylene.



A similar rationalization explains the addition of the boron atom to the terminal position of styrene.



It is generally recognized that a phenyl group can supply electrons to an electron-deficient center or serve as an electron sink. This provides a simple explanation for the increased substitution in the α position observed in styrene.



Electron-withdrawing substituents, such as p-chloro, should stabilize and electron-supplying substituents, such as *p*-methoxy, should destabilize such a transition state. This conclusion is in accord with the influence of the *p*-chloro and the *p*-methoxyl group on the hydroboration of substituted styrenes (Table II).

Little quantitative information is available concerning the influence of other substituents on the direction of the addition reaction. It is evident that major effects will be encountered. Trimethylvinylsilane undergoes hydroboration to place 37% of the boron atoms at the secondary position[14] as compared to 6% for 3,3-dimethyl-1-butene.[13]

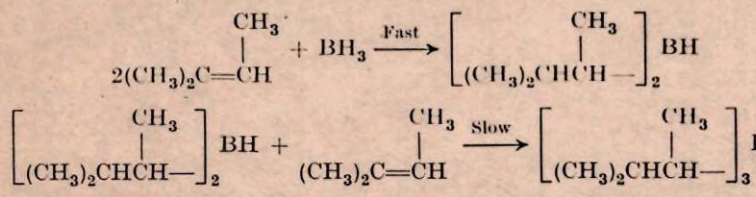
Bis-(3-methyl-2-butyl)borane as a Selective Hydroborating Agent[15]

It was pointed out earlier that highly substituted olefins, such as 2-methyl-2-butene, undergo hydroboration rapidly to the dialkylborane

[14] Seyferth, *J. Inorg. Nucl. Chem.*, **7**, 152 (1958).

[15] Brown and Zweifel, *J. Am. Chem. Soc.*, **83**, 1241 (1961).

stage, further reaction to the trialkylborane stage being relatively slow.



The slowness of the last stage, in contrast to the high speed with which other olefins form the trialkylboranes, is presumably a result of the large steric requirement of the intermediate dialkylborane. It therefore

TABLE IV

DIRECTIVE EFFECTS IN THE HYDROBORATION OF UNSYMMETRICAL OLEFINS WITH DIBORANE AND WITH BIS-(3-METHYL-2-BUTYL)BORANE

Olefin	Hydroborating Agent	Temp., °C.	Time, hr.	Alcohol Distribution, % 1-ol	2-ol	3-ol
1-Hexene	Diborane	25	1	94	6	
	R_2BH[a]	0	1	99	1	
cis-4-Methyl-2-pentene	R_2BH[a]	25	12		97	3
trans-4-Methyl-2-pentene	Diborane	25	1		57	43
	R_2BH[a]	25	12		95	5
Styrene	Diborane	25	1	80	20	
	R_2BH[a]	25	2	98	2	
p-Methoxystyrene	Diborane	25	1	91	9	
	R_2BH[a]	25	2	98	2	

[a] R_2BH is $\left[(CH_3)_2CHCH(CH_3)-\right]_2BH$.

appeared that this dialkylborane might exhibit an enhanced sensitivity to the steric requirement of the substituents on double bonds of other olefins and thereby exert a steric influence on the direction of hydroboration.

The reagent, bis-(3-methyl-2-butyl)borane, reacted rapidly with 1-hexene, and oxidation of the product yielded 1-hexanol in an isomeric purity of at least 99%, in contrast to the 94% isomeric purity realized with diborane itself. Similarly, styrene yielded less than 2% of the secondary alcohol, in contrast to 20% formed in the corresponding reaction with diborane. Finally, *cis*-4-methyl-2-pentene gave 97% of the less hindered isomer, 4-methyl-2-pentanol.

The experimental data are summarized in Table IV.

In these studies the ease with which different olefins reacted with bis-(3-methyl-2-butyl)borane was found to vary enormously. Thus the reaction with 1-hexene was complete in a matter of minutes at 0°, whereas

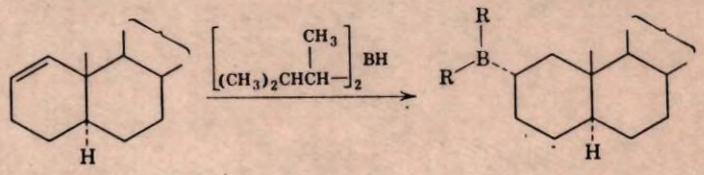
internal olefins reacted much more slowly, cyclopentene reacting faster than *cis*-2-hexene and the latter reacting considerably faster than cyclohexene. *cis*-2-Hexene also reacted considerably faster than the *trans* isomer. Trisubstituted olefins, such as 2-methyl-2-butene and 1-methylcyclohexene, reacted very slowly.

The results may be expressed in the following series of relative rates of reaction: 1-hexene $\geq$ 3-methyl-1-butene $>$ 2-methyl-1-butene $>$ 3,3-dimethyl-1-butene $>$ *cis*-2-hexene $\geq$ cyclopentene $>$ *trans*-2-hexene $>$ *trans*-4-methyl-2-pentene $>$ cyclohexene $\geq$ 1-methylcyclopentene $>$ 2-methyl-2-butene $\geq$ 1-methylcyclohexene $\geq$ 2,3-dimethyl-2-butene.

The differences in reactivities are quite large and can be utilized for the selective hydroboration of a more reactive olefin in the presence of a less reactive one. Thus treatment of a mixture of 1-pentene and 2-pentene with a controlled quantity of bis-(3-methyl-2-butyl)borane yielded pure 2-pentene. Similar treatment of a mixture of 1-hexene and cyclohexene afforded essentially pure cyclohexene, while an equimolar mixture of cyclopentene and cyclohexene gave a product containing only minor amounts of the more reactive cyclopentene. A commercial mixture of *cis*- and *trans*-2-pentene (18% *cis* and 82% *trans*) with the reagent gave a product that contained more than 97% of the *trans* isomer.

In contrast to the results achieved with acyclic olefins, no significant directive effect was noted in the hydroboration of 3-methylcyclopentene, 3-methylcyclohexene, or 3,3-dimethylcyclohexene.[11]

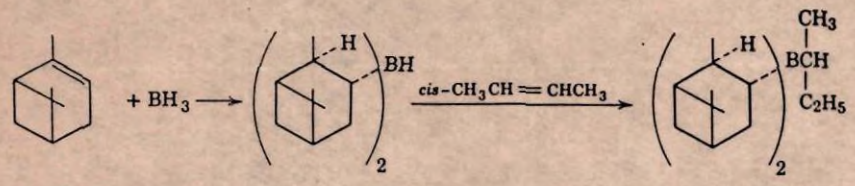
In a rigid cyclic system, selective reaction was observed. Treatment of 1-cholestene with bis-(3-methyl-2-butyl)borane resulted in the predominant formation of cholestan-2α-ol, in contrast to the nearly 1:1 mixture of cholestan-1α-ol and cholestan-2α-ol obtained with diborane.[16]



Asymmetric Synthesis

The remarkable selectivity of a dialkylborane in hydroboration is further illustrated by the conversion of olefins to optically active alcohols.[17] Hydroboration of α-pinene ($[\alpha]_D + 47°$) gives diisopinocampheylborane.[11] This reagent was utilized for the hydroboration of *cis*-2-butene, *cis*-3-hexene, and norbornene. Oxidation of the resulting organoborane with

[16] Sondheimer and Nussim, *J. Org. Chem.*, **26**, 630 (1961).
[17] Brown and Zweifel, *J. Am. Chem. Soc.*, **83**, 486 (1961).

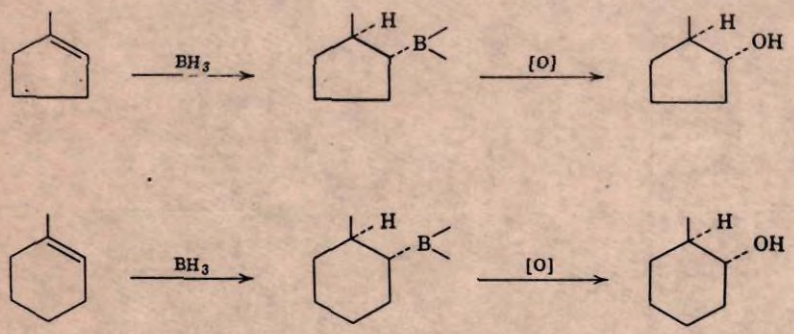


alkaline hydrogen peroxide produced the corresponding alcohols in optical purities of 70–90%. It is noteworthy that the alcohols obtained from the hydroboration of acyclic *cis*-olefins with the diisopinocampheylboranes derived from (+) or (−) α-pinene have the R and S configurations, respectively. *trans*-Olefins and hindered olefins react only slowly with diisopinocampheylborane.

Negligible racemization of the asymmetric organoborane was observed when it was kept for several hours at room temperature.[18]

Stereochemistry

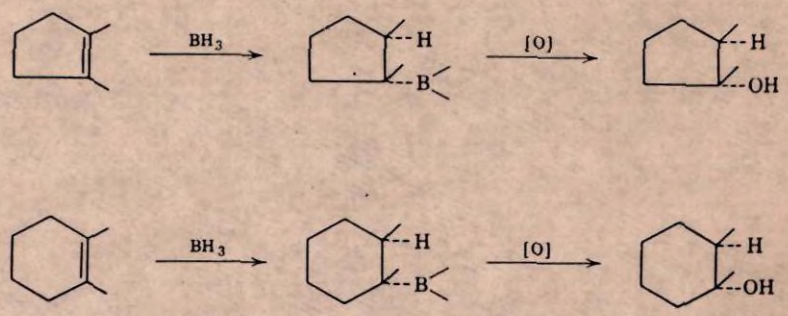
The hydroboration of cyclic olefins provides a means of determining the stereochemistry of the reaction.[11] Thus the hydroboration of 1-methylcyclopentene and 1-methylcyclohexene, followed by oxidation with alkaline hydrogen peroxide, results in the formation of almost pure *trans*-2-methylcyclopentanol and *trans*-2-methylcyclohexanol, respectively. The available evidence indicates that the hydrogen peroxide oxidation proceeds with retention of configuration. Consequently, the hydroboration must involve a *cis* addition of the hydrogen-boron bond to the olefinic linkage.



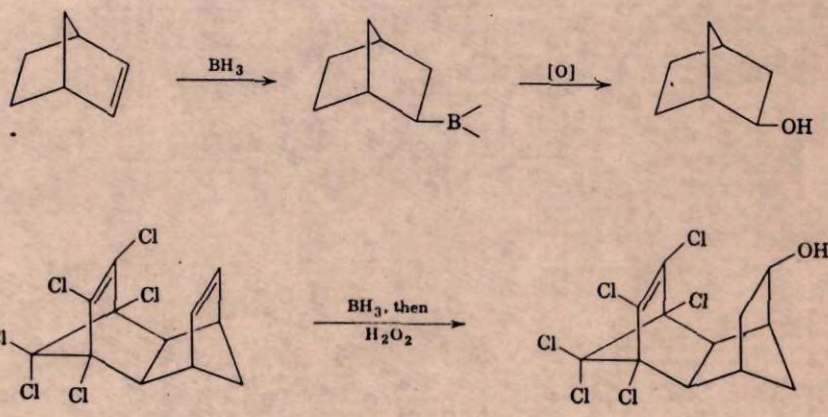
The products of these reactions are the thermodynamically more stable isomers. However, thermodynamic stability of the product cannot be

[18] H. C. Brown, N. R. Ayyangar and G. Zweifel, to be published.

the controlling factor in the reaction because the hydroboration of 1,2-dimethylcyclopentene and 1,2-dimethylcyclohexene produces the thermodynamically less stable isomers, pure *cis*-1,2-dimethylcyclopentanol and *cis*-1,2-dimethylcyclohexanol, respectively.



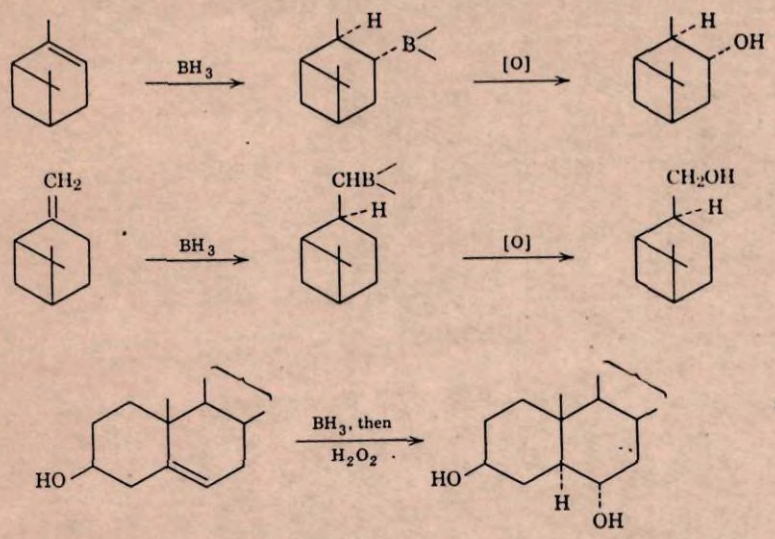
The hydroboration of norbornene proceeds to give *exo*-norborneol almost exclusively. Similarly the hydroboration-oxidation of isodrin occurs from the less hindered side.[19,20]



The generalization that hydroboration proceeds by *cis* addition from the less hindered side of the double bond is now supported by a considerable number of observations. α-Pinene is readily converted to isopinocampheol, β-pinene to *cis*-myrtanol, and cholesterol to cholestane-3β,6α-diol.[9]

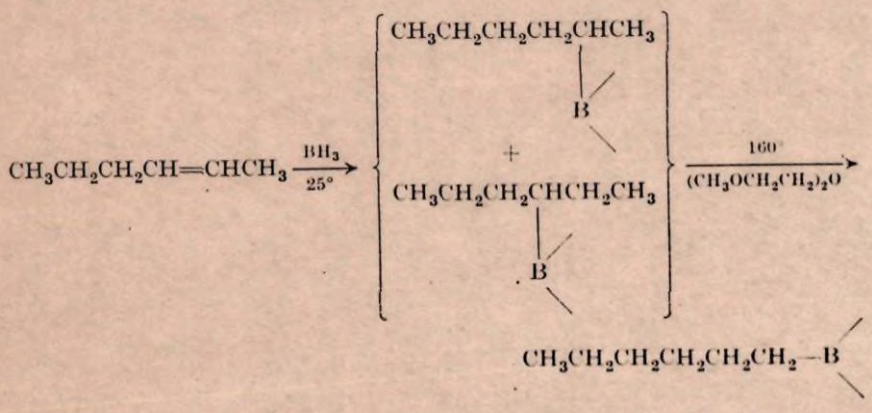
[19] Cookson and Crundwell, *Chem. & Ind. (London)*, **1959**, 703; Bird, Cookson, and Crundwell, *J. Chem. Soc.*, **1961**, 4809.

[20] Bruck, Thompson, and Winstein, *Chem. & Ind. (London)*, **1960**, 405.



Isomerization of Organoboranes

A simple synthetic route to primary organoboranes involves the isomerization of organoboranes derived from internal olefins. Secondary and tertiary organoboranes, synthesized by means of the Grignard reaction, slowly isomerize at 200–215° to yield primary organoboranes.[21] The isomerization is far more rapid under hydroboration conditions. Thus tri-2-hexylborane is almost completely isomerized to tri-*n*-hexylborane in one hour at 160° in diglyme solution.[1,22]

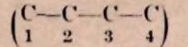
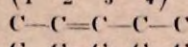
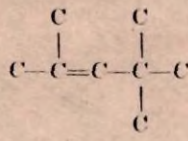
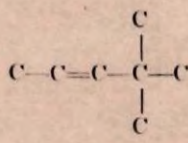
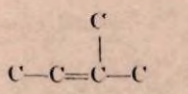
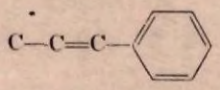


[21] Hennion, McCusker, Ashby, and Rutkowski, *J. Am. Chem. Soc.*, **79**, 5190 (1957).
[22] Brown and Subba Rao, *J. Am. Chem. Soc.*, **81**, 6434 (1959).

The small quantities of excess diborane produced in the hydroboration stage markedly catalyze the isomerization.[23] Typical results are summarized in Table V.

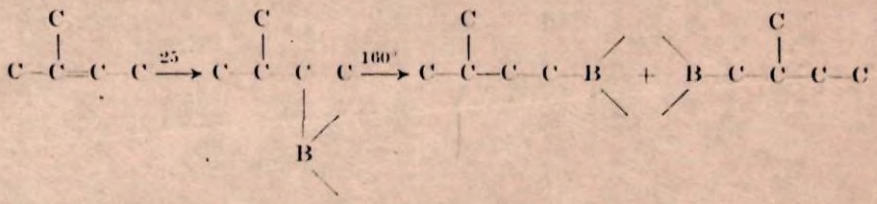
TABLE V

ISOMERIZATION OF ORGANOBORANES AT 160°[23]

Olefin	Location of the Boron[a] Initially at 25°, %		After 1 hr. at 160°, %			
	2	3	1	2	3	4
	52	48	95	4	1	
	46	54	91	6	3	
	1	99	97	1	2	
	57	43	96	2	2	
	98	2	52	1	Tr.	47
	15	85	76	10	14	

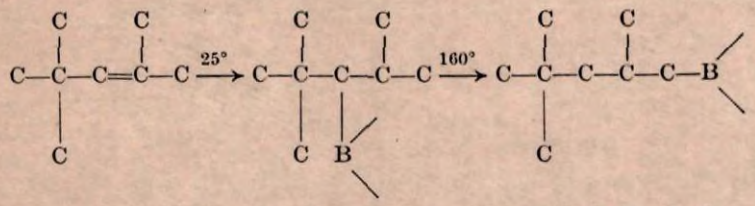
[a] The numbers indicate the position of the boron atom, counting from the left-hand end of the chain.

The results indicate that the boron atom not only moves readily down a straight chain, but also encounters no difficulty in moving past a single alkyl branch.

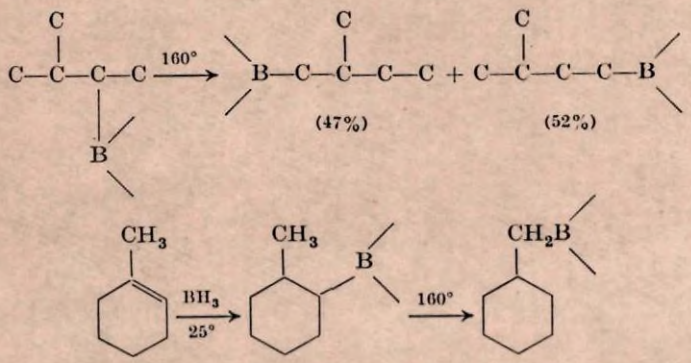


However, under the mild conditions generally used, the boron atom does not migrate past a double branch.

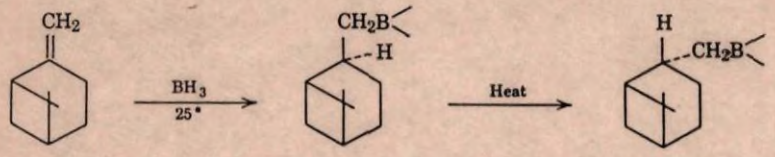
[23] Brown and Zweifel, *J. Am. Chem. Soc.*, **82**, 1504 (1960); *ibid.*, to be published.



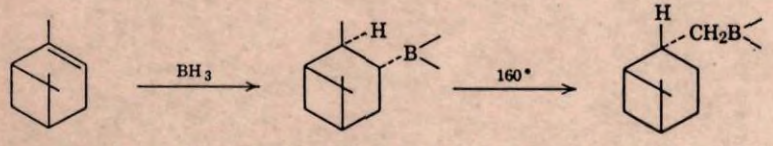
In these isomerizations, the boron atom migrates preferentially to the least hindered position in the molecule.



It is noteworthy that hydroboration of β-pinene yields the *cis*-organoborane.[11] However, on heating, the *cis*-organoborane is converted to the more stable *trans* derivative.[24,25]

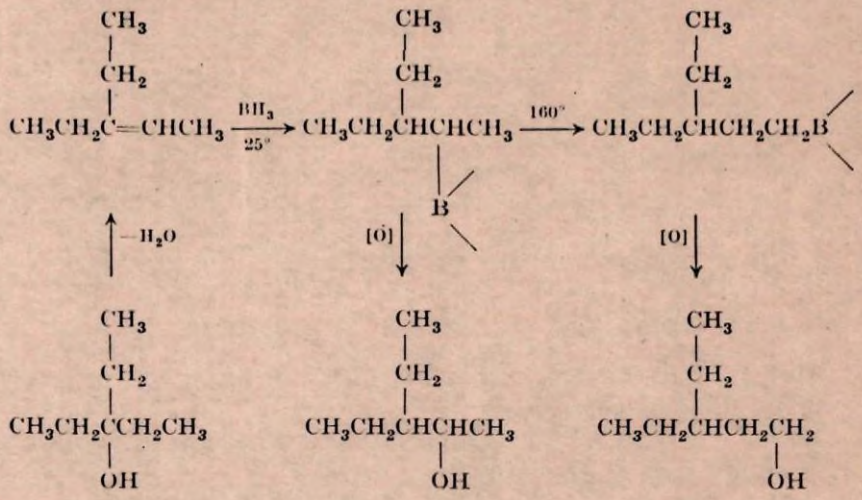


Moreover, the *trans* derivative is obtained from the hydroboration of α-pinene followed by isomerization.[24]



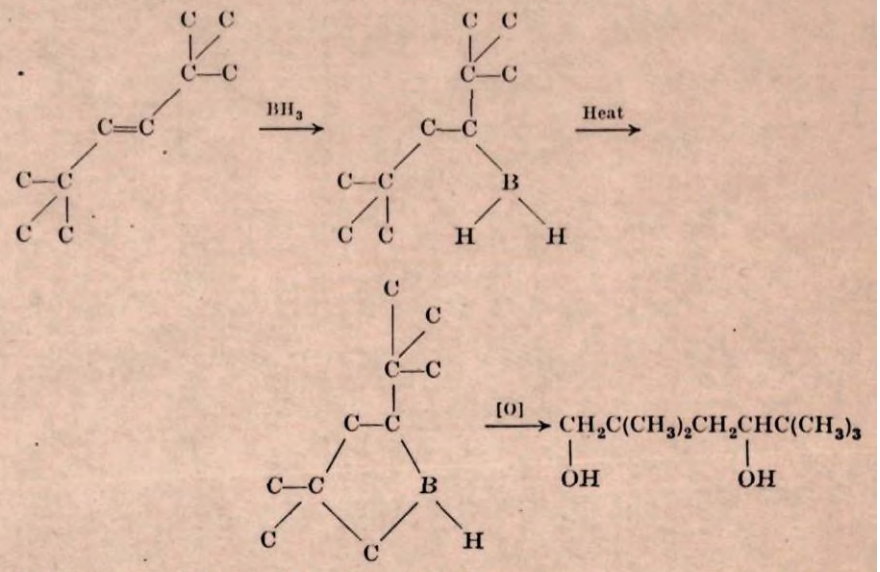
The versatility of the hydroboration reaction when coupled with thermal isomerization is illustrated by the following transformations, all of which proceed readily in yields of approximately 90%.

[24] H. C. Brown, M. V. Bhatt, and G. Zweifel. Unpublished research.
[25] Braun and Fisher, *Tetrahedron Letters*, No. 21, 9 (1960).



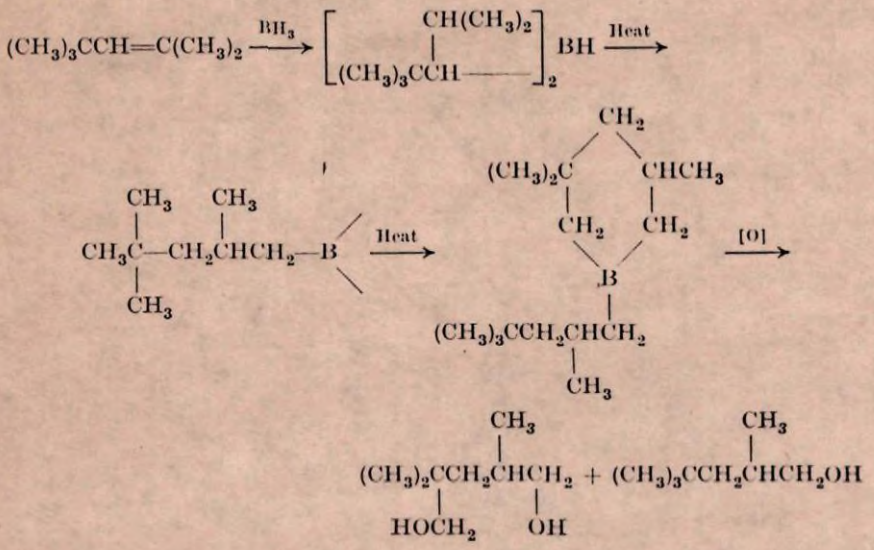
Thermal Cyclization of Organoboranes

Certain organoboranes cyclize at elevated temperatures.[12,26-28] Thus the monoalkylborane derived from *trans*-di-*t*-butylethylene loses hydrogen above 100° to form a cyclic organoborane. Oxidation of this cyclic product gives 2,2,5,5-tetramethyl-1,4-hexanediol.[12]



[26] Winternitz and Carotti, *J. Am. Chem. Soc.*, **82**, 2430 (1960).
[27] Köster and Rotermund, *Angew. Chem.*, **72**, 138 (1960); **72**, 563 (1960).
[28] H. C. Brown, K. J. Murray, and G. Zweifel. Unpublished research.

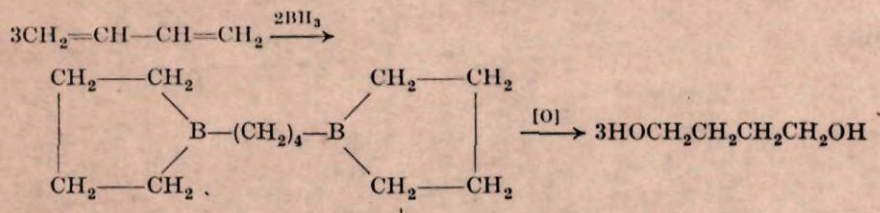
Similarly, at 160° in refluxing diglyme, bis-(2,4,4-trimethyl-1-pentyl)-borane undergoes cyclization. Oxidation of the product yields 2,4,4-trimethyl-1,5-pentanediol and 2,4,4-trimethyl-1-pentanol.[28]



HYDROBORATION OF DIENES

Hydroboration with Diborane

Dihydroboration of dienes followed by oxidation of the organoborane provides a route to diols.[29–32] 1,3-Butadiene is transformed into a 4:1 mixture of 1,4- and 1,3-butanediol. Köster has assigned a cyclic structure to the organoborane derived from 1,3-butadiene.[30]



By similar procedures 1,5-hexadiene[29] and cyclopentadiene[31,32] are converted to 1,6-hexanediol and *trans*-1,3-cyclopentanediol, respectively.

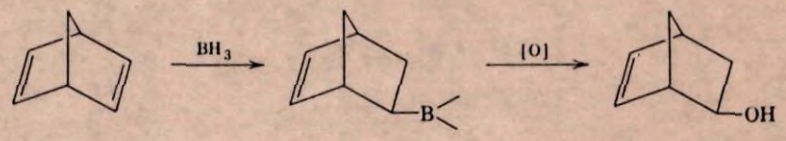
[29] Brown and Zweifel, *J. Am. Chem. Soc.*, **81**, 5832 (1959); Zweifel, Nagase, and Brown, *ibid.*, **84**, 183 (1962).

[30] Köster, *Angew. Chem.*, **71**, 520 (1959).

[31] Saegebarth, *J. Am. Chem. Soc.*, **82**, 2081 (1960); *J. Org. Chem.*, **25**, 2212 (1960).

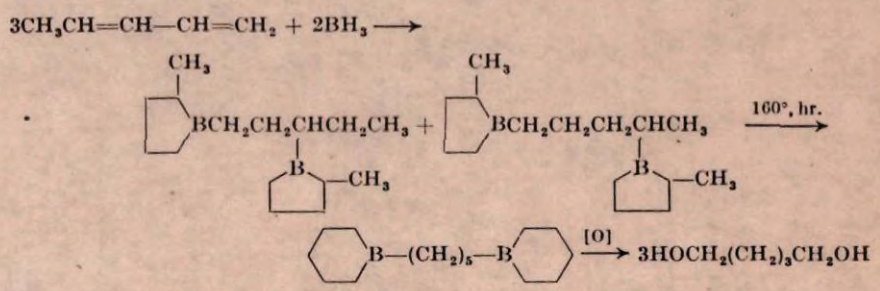
[32] Brown and Zweifel, *J. Org. Chem.*, in print.

The partial hydroboration of dienes (monohydroboration) followed by oxidation gives the corresponding alcohols in modest yields.[29] 1,5-Hexadiene is transformed into 5-hexene-1-ol, and cyclopentadiene[33] into 3-cyclopenten-1-ol. Bicycloheptadiene yields *exo*-dehydronorborneol (87% *exo* and 13% *endo*).[29]



Isomerization

Dihydroboration of acyclic dienes with diborane followed by isomerization yields cyclic organoboranes. The preferred product appears to be the 6-membered heterocycle.[31] Hydroboration of 1,3-pentadiene yields what was considered to be a mixture of bis-1,3- and bis-1,4-(1-bora-2-methylcyclopentyl)pentane, for on oxidation it furnished a 1:9 mixture of 1,3- and 1,4-pentanediol. However, the product obtained after thermal isomerization and oxidation was essentially pure 1,5-pentanediol.[31]

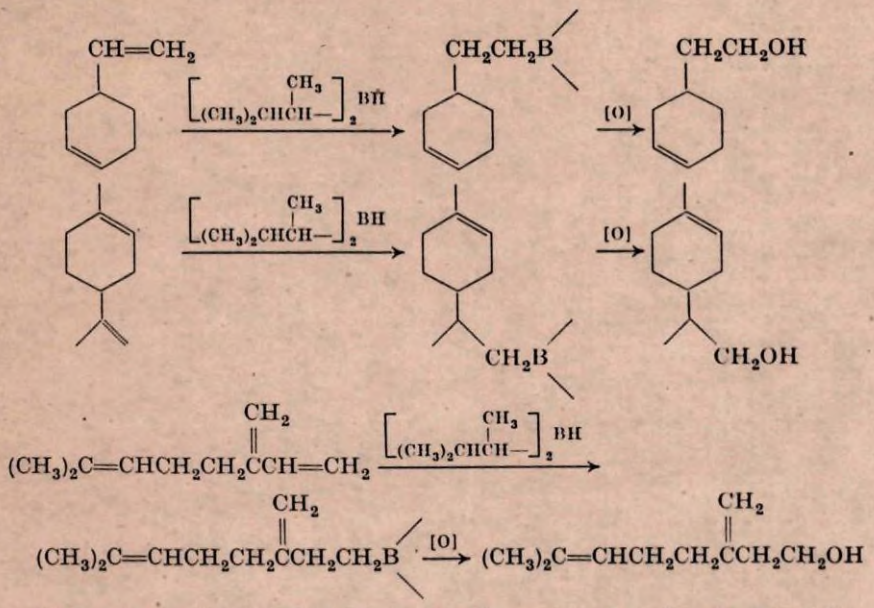


Hydroboration with Bis-(3-methyl-2-butyl)borane

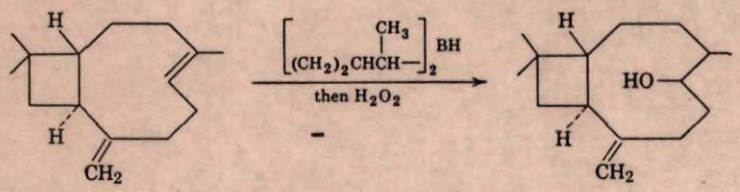
Bis-(3-methyl-2-butyl)borane has been applied to the selective hydroboration of dienes with excellent results.[15,34] 2-Methyl-1,5-hexadiene was converted in good yield to 5-methyl-5-hexen-1-ol, and 1,3-cyclohexadiene furnished a mixture consisting of 90% 2-cyclohexen-1-ol and 10% 3-cyclohexen-1-ol. Also, the more reactive double bonds in vinylcyclohexene, *d*-limonene, and myrcene[35] are hydrated without attack on the less reactive double bond(s).

[33] Winstein, Allred, and Sonnenberg, *J. Am. Chem. Soc.*, **81**, 5833 (1959); Allred, Sonnenberg, and Winstein, *J. Org. Chem.*, **25**, 26 (1960).

[34] Zweifel, Nagase, and Brown, *J. Am. Chem. Soc.*, **84**, 190 (1962).

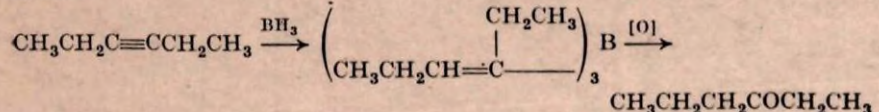


It is noteworthy that hydroboration of caryophyllene involves a preferential attack at the highly reactive *trans* internal double bond.[35]



HYDROBORATION OF ACETYLENES

Hydroboration of disubstituted acetylenes with diborane proceeds readily and can be controlled to give predominantly the vinylorganoborane. Oxidation of the latter with hydrogen peroxide affords the ketone.[2]

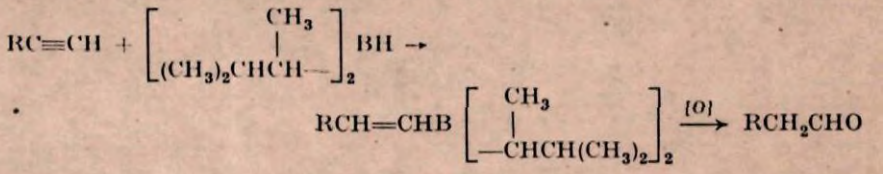


The corresponding reaction with 1-alkynes yields predominantly the dihydroboration product. However, use of either bis-(3-methyl-2-butyl)-borane or trimethylamine-*t*-butylborane[36] circumvents this difficulty and

[35] H. C. Brown and K. P. Singh. Unpublished research.

[36] Hawthorne, *J. Am. Chem. Soc.*, **83**, 2541 (1961).

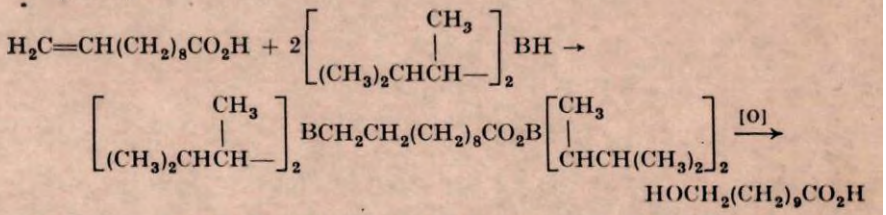
results in the formation of the monohydroborated product. Oxidation of the vinylorganoborane gives the corresponding aldehyde.



HYDROBORATION OF OLEFINS CONTAINING OTHER FUNCTIONAL GROUPS

Up to the present the hydroboration-oxidation reaction has been applied primarily to olefins, dienes, and acetylenes. Extension of the reaction to functional derivatives of such compounds is complicated by the reduction of many functional groups by diborane.[37,38] Fortunately, this is not an insurmountable difficulty. The hydroboration of carbon-carbon double or triple bonds is so rapid that they can frequently be converted to organoboranes in excellent yield in the presence of such functions as acid chlorides, esters, or nitro groups. In some cases a group which is reduced very rapidly, such as the carboxyl group, can be tolerated.

For example, methyl oleate has been converted to 9- and 10-hydroxystearic acid via hydroboration.[39] Similarly bis-(3-methyl-2-butyl)borane, which reacts with but does not reduce the carboxyl group under hydroborating conditions, has been utilized to convert 10-undecenoic acid to 11-hydroxyundecanoic acid.[38]



Numerous alcohols have been hydroborated, especially steroid alcohols. The presence of one or more free hydroxyl groups requires a corresponding excess of the hydroborating agent. The boric esters formed do not interfere with the hydroboration.

$$3ROH + BH_3 \rightarrow (RO)_3B + 3H_2$$

Finally, there are many functional groups that are relatively inert toward diborane or other hydroborating agents. Hydroboration of

[37] Brown and Subba Rao, *J. Am. Chem. Soc.*, **82**, 681 (1960); Brown and Korytnyk, *ibid.*, **82**, 3866 (1960).

[38] Brown and Bigley, *J. Am. Chem. Soc.*, **83**, 486 (1961).

[39] Fore and Bickford, *J. Org. Chem.*, **24**, 920 (1959).

unsaturated derivatives containing these substituents appears to offer no difficulty. The following examples are illustrative.

Vinyltrimethylsilane was readily hydroborated and converted to the corresponding alcohol.[14] Both *p*-chlorostyrene and *p*-methoxystyrene were converted to the corresponding alcohols; the *p*-substituents merely affected the ratio of the two isomeric alcohols produced.[13] Ethyl vinyl ether,[40] allyl methyl sulfide,[7] and allyl chloride[41] have been hydroborated. The organoborane derived from allyl chloride yields 3-chloropropanol on oxidation.[41] On treatment with base, however, it cyclizes to cyclopropane.[42]

OXIDATION OF ORGANOBORANES

Whereas alkylboranes of low molecular weight are spontaneously flammable in air, tri-*n*-butylborane and higher homologs react with oxygen but do not inflame. Since air oxidation has not proved valuable in synthesis, it will not be discussed here.

Perbenzoic acid reacts practically quantitatively with tri-*n*-butylborane in chloroform solution. All three alkyl groups are cleaved with the formation of *n*-butyl alcohol and boric acid.[5]

$$R_3B + 3C_6H_5CO_3H \rightarrow B(OR)_3 + 3C_6H_5CO_2H$$
$$B(OR)_3 + 3H_2O \rightarrow 3ROH + H_3BO_3$$

Aqueous hydrogen peroxide in the presence of dilute alkali effects a complete dealkylation of tri-*n*-butylborane.[43] The reaction was suggested as the basis of a convenient method for the determination of boron in organoboranes[5] and was later developed as an analytical procedure.[44] However, the vigorous conditions used involved heating the organoborane with excess hydrogen peroxide and concentrated sodium hydroxide under reflux.

Early applications of this reaction in the hydroboration-oxidation studies also utilized more vigorous conditions[1] than were subsequently found necessary. Hydrogen peroxide concentration, base concentration, and oxidation temperature can be varied widely without affecting the yield significantly.[6] The results are summarized in Table VI.

Standard conditions for the oxidation were defined as follows: 16.6 mmoles of tri-*n*-hexylborane in 40 ml. of diglyme was treated with 15 mmoles of sodium hydroxide (5 ml. of 3*N* solution), followed by the

[40] Mikhailov and Shchegoleva, *Bull. Acad. Sci. USSR., Div. Chem. Sci.* (*English Transl.*), **1959**, 518.

[41] H. C. Brown and K. Keblys. Unpublished research.

[42] Hawthorne and Dupont, *J. Am. Chem. Soc.*, **80**, 5830 (1958); Hawthorne, *ibid.*, **82**, 1886 (1960).

[43] Snyder, Kuck, and Johnson, *J. Am. Chem. Soc.*, **60**, 105 (1938).

[44] Belcher, Gibbons, and Sykes, *Mikrochim. Acta.*, **40**, 76 (1952).

TABLE VI

EFFECT OF HYDROGEN PEROXIDE CONCENTRATION, BASE CONCENTRATION, AND TEMPERATURE IN THE OXIDATION OF TRI-*n*-HEXYLBORANE

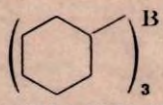
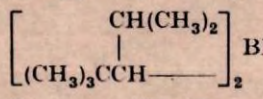
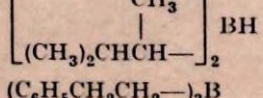
Hydrogen Peroxide Added, % of Theory	NaOH, mmoles	Temp., °C.	Yield, % of 1-hexanol
72	45	25–35	80
95	45	25–35	97
120	45	25–35	98
150	45	25–35	97
100	45	25–35	97
100	30	25–35	92
100	15	25–35	94
100	0	25–35	57
100	45	0–5	89
100	45	25–35	97
100	45	50–55	96
100	45	75–80	97

slow addition of 60 mmoles of hydrogen peroxide, 20% excess (6.0 ml. of a 30% solution). The amount of 1-hexanol obtained was determined by gas-liquid partition chromatography. The oxidation was achieved equally well in tetrahydrofuran. In diethyl ether, however, reaction was more sluggish, presumably because of the immiscibility of the solvent with water. The addition of ethanol as a cosolvent circumvented this difficulty and the yield under these conditions was 98%.[6]

As indicated in Table VII, wide variations in the structure of the organoborane do not affect the oxidation greatly.

TABLE VII

EFFECT OF STRUCTURE UPON OXIDATION

Organoborane	Yield, % of alcohol
	97
$[(CH_3)_3CCH_2CH(CH_3)CH_2—]_3B$	95
	79
	98
$(C_6H_5CH_2CH_2—)_3B$	99

Numerous substances, such as olefins, dienes, acetylenes, esters, ketones, and nitriles, may be present without influencing the yield of alcohol or undergoing any reaction themselves. The results with such additives present are summarized in Table VIII.

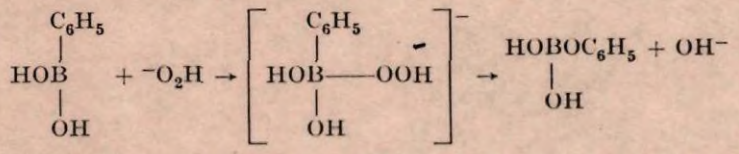
TABLE VIII

EFFECT OF ADDED SUBSTANCES (50 MMOLES) ON THE OXIDATION OF TRI-*n*-HEXYLBORANE (16.6 MMOLES)

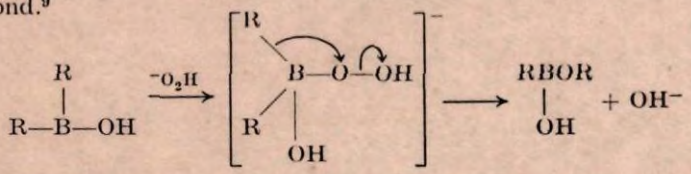
Substance Added	Recovery of Added Substance After Oxidation, %	Yield, % of *n*-hexanol
1-Hexene	96	95
1,3-Cyclohexadiene	96	95
1-Hexyne	92	100
Isobutyraldehyde	63	97
Ethyl acetate	92	95
n-Butyl bromide	93	99
Acetonitrile	97	99

Although no detailed kinetic studies of the oxidation reaction of alkylboranes have been reported, Kuivila and co-workers have studied the related reaction of benzeneboronic acid with hydrogen peroxide.[45] The following mechanism was proposed.

$$H_2O_2 + {}^-OH \rightleftharpoons HO_2^- + H_2O$$



Wechter proposed an identical mechanism for the oxidation of the alkylboron bond.[9]



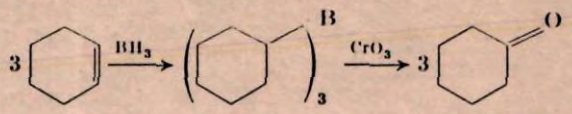
In this mechanism the group R shifts with its pair of electrons from boron to oxygen. This is consistent with the retention of configuration observed in the hydroboration-oxidation of cyclic olefins.

Organoboranes can be oxidized to ketones by chromic acid.[46] The use

[45] Kuivila, *J. Am. Chem. Soc.*, **76**, 870 (1954); **77**, 4014 (1955); Kuivila and Wiles, *ibid.*, **77**, 4830 (1955); Kuivila and Armour, *ibid.*, **79**, 5659 (1957).

[46] Pappo, *J. Am. Chem. Soc.*, **81**, 1010 (1959).

of this reagent makes it possible to go from a cyclic olefin such as cyclohexene to the corresponding ketone, cyclohexanone, in satisfactory yield without isolating the secondary alcohol.[47]



EXPERIMENTAL CONDITIONS

The preparation and handling of organoboranes require techniques and precautions similar to those used for the Grignard reaction. Although the necessity for a nitrogen atmosphere has not been established, hydroboration reactions are normally carried out under nitrogen. It is convenient to transfer solutions of diborane and dialkylboranes by means of a hypodermic syringe.

Earlier reports have stressed the hazardous nature of diborane. However, during the exploration of the hydroboration reaction no difficulties have been encountered in the preparation and handling of dilute solutions of diborane and dialkylboranes. Even when solutions of diborane or dialkylboranes in tetrahydrofuran or diglyme were exposed to air, they did not inflame spontaneously but were slowly oxidized. Nevertheless, adequate ventilation is recommended.

Hydroboration With Diborane Generated *in Situ*

In this procedure an acid is added slowly in an inert atmosphere to a mixture of the unsaturated compound and the hydride in an appropriate solvent. Since no diborane is liberated, the method possesses many advantages for large-scale preparations where the presence of the hydride and the inorganic reaction product, e.g., sodium borofluoride, offers no difficulty. Therefore it is most useful when the organoborane is desired simply as an intermediate for further reaction.

Sodium borohydride is essentially insoluble in common ether solvents, but readily soluble in diglyme (dimethyl ether of diethylene glycol) and triglyme (dimethyl ether of triethylene glycol). Consequently, these solvents are used with sodium borohydride.[48] However, numerous procedures have been developed for utilizing metal hydrides and complex hydrides in the preparation of diborane and related reactions so as to avoid the necessity for a particular solvent or reagent.[49]

[47] Brown and Garg, *J. Am. Chem. Soc.*, **83**, 2951 (1961).

[48] Brown, Mead, and Subba Rao, *J. Am. Chem. Soc.*, **77**, 6209 (1955).

[49] Brown, K. J. Murray, L. J. Murray, Snover, and Zweifel, *J. Am. Chem. Soc.*, **82**, 4233 (1960).

Lithium borohydride is readily soluble in diethyl ether and tetrahydrofuran as well as in other ether solvents. In diethyl ether the essentially quantitative hydroboration of 1-octene was achieved with boron trifluoride etherate, hydrogen chloride, and sulfuric acid. Lithium borohydride requires only sufficient boron trifluoride to convert the lithium to lithium fluoride.

$$12RCH{=}CH_2 + 3LiBH_4 + BF_3 \rightarrow 4(RCH_2CH_2)_3B + 3LiF$$
$$9RCH{=}CH_2 + 3LiBH_4 + 3HCl \rightarrow 3(RCH_2CH_2)_3B + 3LiCl + 3H_2$$

Sodium borohydride is soluble in diglyme and triglyme, and the hydroboration reactions with boron trifluoride etherate, hydrogen chloride, or sulfuric acid proceed rapidly and quantitatively at room temperature.

Although the solubility of sodium borohydride in tetrahydrofuran is small, the hydroboration of an olefin is readily achieved by treating with boron trifluoride a suspension of sodium borohydride in tetrahydrofuran containing the olefin.[49,50] Alternatively, a solution of diborane in tetrahydrofuran can be prepared by treating a suspension of sodium borohydride in that solvent at 0° with hydrogen chloride. Hydroboration is then accomplished by adding the olefin to this solution.

Finally, it is possible to utilize diethyl ether as the solvent by introducing 10 mole % of anhydrous zinc chloride to catalyze the reaction between sodium borohydride and boron trifluoride etherate.

$$12RCH{=}CH_2 + 3NaBH_4 + 4BF_3 \xrightarrow{10\%\,ZnCl_2} 4(RCH_2CH_2)_3B + 3NaBF_4$$

Potassium borohydride, although only slightly soluble in triglyme and in tetrahydrofuran, can be utilized as a suspension in these solvents. A potassium borohydride suspension in triglyme will react directly with boron trifluoride etherate, while a suspension in tetrahydrofuran will react with lithium chloride to form the soluble lithium borohydride.[51] The latter can be utilized for the hydroboration.[49]

$$KBH_4\ (susp.) + LiCl \rightarrow LiBH_4 + KCl$$
$$12RCH{=}CH_2 + 3LiBH_4 + BF_3 \rightarrow 4(RCH_2CH_2)_3B + 3LiF$$

Lithium aluminum hydride with boron trifluoride etherate appears to be a convenient reagent for hydroboration in diethyl ether.[52,53]

$$12RCH{=}CH_2 + 3LiAlH_4 + 4BF_3 \rightarrow 4(RCH_2CH_2)_3B + 3LiAlF_4$$

[50] Schubert and Lang, *Angew. Chem.*, **72**, 994 (1960).
[51] Paul and Joseph, *Bull. Soc. Chim. France*, **1952**, 550.
[52] Wolfe, Nussim, Mazur, and Sondheimer, *J. Org. Chem.*, **24**, 1034 (1959).
[53] Sondheimer and Wolfe, *Can. J. Chem.*, **37**, 1870 (1959).

TABLE IX

CONVENIENT PROCEDURES FOR HYDROBORATION WITH VARIOUS HYDRIDE REAGENTS[49]

Solvent	Hydride Source	Acid	Molar Ratio Hydride : Acid : Olefin			1-Octene, % reacted in 1 hr. at 25°
Diglyme	$NaBH_4$	BF_3	3	4	12	99
		BCl_3	3	4	12	98
		$AlCl_3$	3	1	9	50
		HCl	2	2	6	94
		H_2SO_4	2	1	6	91
		CH_3I	2	2	6	95
THF[a]	$NaBH_4$	BF_3	3	4	12	99
Diethyl ether	$NaBH_4/ZnCl_2$	BF_3	3	4	12	94
THF	$KBH_4/LiCl$	BF_3	3	1	12	83
Diglyme	$LiBH_4$	BF_3	3	4	12	98
		BCl_3	3	1	12	92
THF	$LiBH_4$	BF_3	3	1	12	99
		HCl	2	2	6	95
		H_2SO_4	2	1	6	99
Diethyl ether	$LiBH_4$	BF_3	3	1	12	87
		HCl	2	2	6	95
		H_2SO_4	2	1	6	92
	$LiAlH_4$	BF_3	3	4	12	80[b]
		BCl_3	3	4	12	95
Diglyme	NaH	BF_3	6	8	6	99
THF	NaH	BF_3	6	8	6	99
Diglyme	LiH	BF_3	6	8	6	95
THF	LiH	BF_3	6	8	6	95
Diethyl ether	LiH	BF_3	6	8	6	93
Benzene	$C_5H_5N:BH_3$	BF_3	1	1	3	90[c]

[a] THF is tetrahydrofuran.

[b] Cyclohexene was the olefin in this experiment.[53]

[c] This experiment was run for 16 hours at 75°.

The most convenient hydroboration procedures are summarized in Table IX. It is to be noted that lithium borohydride in tetrahydrofuran or in diethyl ether requires less boron trifluoride than does sodium borohydride or lithium aluminum hydride.

Hydroboration With Diborane Generated Externally

Hydroboration with diborane produces the organoborane in essentially quantitative yield and free of inorganic salt or other by-products. In this

procedure, diborane, prepared by the addition of sodium borohydride in diglyme to boron trifluoride etherate, is passed into a solution of the olefin in an ether solvent. Tetrahydrofuran has two distinct advantages as a reaction medium: it is an excellent solvent for diborane, and it is readily distilled from the reaction products.

Sodium borohydride in diglyme absorbs a half-molar equivalent of diborane, forming sodium diborohydride ($NaBH_4 \cdot BH_3$ or NaB_2H_7).[54] Because of the formation of this species, the addition of boron trifluoride etherate to a diglyme solution of sodium borohydride does not liberate diborane until nearly half of the acid has been added. Consequently, to generate diborane smoothly it is preferable to add the solution of sodium borohydride to an excess of boron trifluoride in diglyme.

$$3NaBH_4 + 4BF_3 \rightarrow 2B_2H_6 + 3NaBF_4$$
$$12RCH{=}CH_2 + 2B_2H_6 \rightarrow 4(RCH_2CH_2)_3B$$

Alternatively, a 1*M* solution of diborane in tetrahydrofuran may be prepared and then utilized for the hydroboration. Such solutions can be kept at 0–5° for several weeks without significant change in the diborane concentration.

Solvents

In order to avoid losses of active hydride in the hydroboration stage, it is important that the solvents be free of water and peroxides.

Diglyme (dimethyl ether of diethylene glycol, b.p. 162°) (Ansul Chemical Co.) is purified in the following way: 1 l. of diglyme is stored over 10 g. of small pieces of calcium hydride for 12 hours. The diglyme is then decanted into a distilling flask and sufficient lithium aluminum hydride is added to ensure an excess of active hydride. The solvent is distilled at 62–63°/15 mm.

Triglyme (dimethyl ether of triethylene glycol, b.p. 212°) is purified as described for diglyme. The solvent is distilled at 107–108°/15 mm.

Tetrahydrofuran (pure grade) is treated with lithium aluminum hydride as just described, then distilled at atmospheric pressure; b.p. 66–67°.

Diethyl ether (anhydrous reagent grade) is utilized without purification.

In order to inhibit peroxidation during storage of these solvents, it is advantageous to add 0.01% of sodium borohydride.

Boron Trifluoride Etherate

Boron trifluoride diethyl etherate, 500 ml., is treated with 10 ml. of anhydrous diethyl ether (to ensure an excess of this component) and

[54] Brown and Tierney, *J. Am. Chem. Soc.*, **80**, 1552 (1958).

distilled in an all glass apparatus at 46°/10 mm. from 2 g. of granular calcium hydride. The hydride removes small quantities of volatile acids and greatly reduces bumping during the distillation. The density of the product at 25° is 1.125.

Metal Hydrides

Sodium borohydride (98%) from Metal Hydrides, Inc., may be used without purification. Commercial lithium borohydride and potassium borohydride were used without purification after analysis for active hydrogen.

EXPERIMENTAL PROCEDURES

Procedures in Which Diborane Is Generated *in Situ*

The apparatus consists of a three-necked flask equipped with a condenser fitted with a calcium chloride tube, a pressure-equalizing dropping funnel, a thermometer, and a stirrer (a magnetic stirrer may be utilized for small-scale experiments). The apparatus is dried in an oven and assembled under dry nitrogen. Alternatively, it can be flamed dry in a stream of dry nitrogen.

To the flask are added the olefin and the hydride in an appropriate solvent. A 10–20% excess of the hydride is generally used. A quantity of acid, equivalent to the hydride used and generally in a solvent, is added dropwise in a nitrogen atmosphere. After completion of the addition, the excess hydride is *carefully* decomposed by water or ethylene glycol. The organoborane obtained can be oxidized *in situ* with alkaline hydrogen peroxide.

Isopinocampheol from α-Pinene (Use of Sodium Borohydride and Boron Trifluoride Etherate in Diglyme).[11,55] In a 300-ml. flask are placed 82.5 ml. of a 1*M* solution of sodium borohydride in diglyme

(10% excess) and 27.2 g. of α-pinene (0.20 mole; n_D^{20} 1.4648, $[\alpha]_D^{20}$ +46.8°) in 20 ml. of diglyme. The flask is immersed in a water bath (~20°). From the dropping funnel 14 ml. of boron trifluoride etherate (15.62 g., 0.11 mole) is added dropwise to the stirred reaction mixture over a period

[55] H. C. Brown, K. P. Singh, and G. Zweifel. Unpublished research.

of 30 minutes, while the temperature is maintained at 20–25°. The flask is kept for 1 hour at this temperature. Excess hydride is then decomposed by the careful dropwise addition of 20 ml. of water.

The organoborane (R_2BH) is oxidized at 30–50° by the immediate addition of 22 ml. of 3*N* sodium hydroxide, followed by the dropwise addition of 22 ml. of 30% hydrogen peroxide. The reaction mixture is left for 1 hour at room temperature and is then extracted with 150 ml. of ether. The ethereal extract is washed five times with equal amounts of ice water to remove diglyme, and dried over anhydrous magnesium sulfate. The product obtained after removal of the solvent is crystallized from a small amount of petroleum ether (35–37°). There is obtained 24.3 g. (79%) of isopinocampheol: m.p. 55–57°, $[\alpha]_D^{20}$ −32.8° (*c*, 1% in benzene).

4-Methyl-1-pentanol from 4-Methyl-1-pentene (Use of Sodium Borohydride and Boron Trifluoride Etherate in Tetrahydrofuran).[49] To a well-stirred suspension of 3.4 g. (90 mmoles) of pulverized sodium borohydride in 150 ml. of tetrahydrofuran containing 25.2 g. of 4-methyl-1-pentene (0.30 mole; n_D^{20} 1.3830) is added 15.1 ml. of boron trifluoride etherate (17.0 g., 0.120 mole) in 20 ml. of tetrahydrofuran over a period of 1 hour, while the temperature is maintained at 25°. The flask is kept an additional hour at 25° before the excess hydride is decomposed with water.

The organoborane is oxidized at 30–40° (water bath) by the addition of 32 ml. of a 3*N* solution of sodium hydroxide, followed by the dropwise addition of 32 ml. of 30% hydrogen peroxide. The reaction mixture is saturated with sodium chloride. The tetrahydrofuran layer formed is separated, and then washed with saturated aqueous sodium chloride. The extract is dried over anhydrous magnesium sulfate.

Distillation furnished, after removal of the tetrahydrofuran, 24.5 g. (80%) of 4-methyl-1-pentanol, b.p. 151–153°/735 mm; n_D^{20} 1.4140.

2,4,4-Trimethyl-1-pentanol from 2,4,4-Trimethyl-1-pentene (Use of Lithium Borohydride and Sulfuric Acid in Tetrahydrofuran).[49] In a 500-ml. flask are placed 2.62 g. of lithium borohydride (0.12 mole), 33.6 g. of 2,4,4-trimethyl-1-pentene (0.30 mole, n_D^{20} 1.4807), and 170 ml. of tetrahydrofuran. Concentrated sulfuric acid (5.88 g., 60 mmoles) in 42 ml. of diethyl ether is added over a period of 1 hour to the lithium borohydride-olefin solution, the temperature being maintained at 25°. The reaction is permitted to proceed for an additional hour at room temperature, and then the excess hydride is decomposed with water.

The organoborane is oxidized at 20–40° (water bath) by the addition of 32 ml. of a 3*N* solution of sodium hydroxide, followed by the dropwise addition of 32 ml. of 30% hydrogen peroxide. The tetrahydrofuran-ether layer is separated, washed with water, and dried over anhydrous magnesium sulfate.

The product obtained after removal of the solvent furnishes on distillation 31.6 g. (81%) of 2,4,4-trimethyl-1-pentanol, b.p. 165–166°/748 mm., n_D^{20} 1.4274.

Cyclohexanol from Cyclohexene (Use of Lithium Aluminum Hydride and Boron Trifluoride Etherate in Diethyl Ether).[53] In a flask are placed 3.4 g. of boron trifluoride etherate (24 mmoles), 4 g. of cyclohexene (49 mmoles), and 100 ml. of diethyl ether. A solution of 0.7 g. (18 mmoles) of lithium aluminum hydride in 70 ml. of ether is added to the olefin-boron trifluoride mixture during 20 minutes. The mixture is stirred at room temperature for 2 hours, and then the excess hydride is decomposed by slowly adding 20 ml. of acetone. A saturated solution of sodium sulfate is added, followed by solid sodium sulfate. The mixture is filtered, and the clear filtrate evaporated.

The residue is dissolved in 30 ml. of 90% ethanol containing 0.8 g. of sodium hydroxide, and 10.2 ml. of 20% hydrogen peroxide is added with stirring during 5 minutes. The temperature of the reaction mixture rises to about 70°. It is maintained at this temperature for 5 minutes longer by external heating, and the flask is then cooled. Water and ether are added, and the ether extract is washed with water, dried, and evaporated. On distillation there is obtained 4.0 g. (82%) of cyclohexanol; b.p. 161–162°, n_D^{20} 1.4656.

Procedures in Which Diborane Is Generated Externally (Fig. 1)

***exo*-Norborneol from Norbornene.**[11,56] A dry 500-ml. three-necked flask is equipped with a thermometer, a condenser connected to a mercury bubbler containing acetone (T-tube dipping in mercury), and a sintered glass dispersion tube. A tube from the condenser outlet dips below the surface of some mercury in a side-arm test tube. Above the mercury is a layer of acetone which serves to destroy escaping diborane by reacting with it to form diisopropoxyborane, $[(CH_3)_2CHO]_2BH$.

A solution of 28.2 g. (0.30 mole) of norbornene, m.p. 45°, in 100 ml. of tetrahydrofuran is placed in the flask. The dispersion tube (completely immersed in the tetrahydrofuran-olefin solution) is connected with Tygon tubing to a 300-ml. two-(or three-)necked flask serving as the diborane generator.

The generator is equipped with a pressure-equalizing dropping funnel (serving alternatively as an inlet for nitrogen) containing 90 ml. of a 1*M* solution of sodium borohydride in diglyme (3.4 g., 20% excess). In the generator is placed 23 ml. of boron trifluoride etherate (25.5 g., 0.18 mole, 50% excess) in 20 ml. of diglyme.

[56] H. C. Brown, S. Nishida, and G. Zweifel, Unpublished research.

Diborane is generated by the dropwise addition of the sodium borohydride solution to the stirred boron trifluoride etherate-diglyme solution. The gas is passed into the olefin-tetrahydrofuran solution (maintained at 20°) by applying a slight flow of dry nitrogen through the generator.

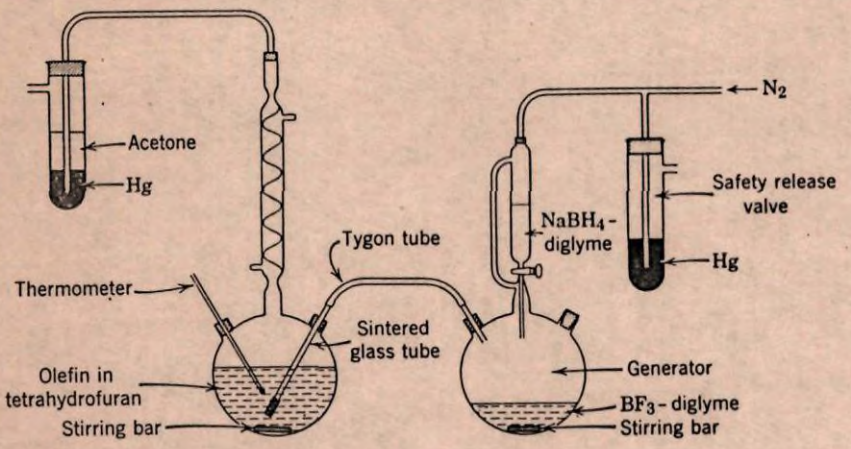


FIG. 1.

After completion of the sodium borohydride addition (1 hour), the generator is heated for 1 hour at 70–80°, the nitrogen flow being maintained to ensure the complete transfer of the diborane to the hydroboration flask. The generator is allowed to cool to room temperature and is then disconnected from the hydroboration flask.

The excess hydride in the hydroboration flask is decomposed by the careful addition of 20 ml. of water. The organoborane is oxidized at 30–50° (water bath) by the addition of 32 ml. of 3*N* sodium hydroxide, followed by dropwise addition of 32 ml. of 30% hydrogen peroxide. During the oxidation, efficient stirring is maintained. The reaction mixture is stirred for an additional hour, then 100 ml. of diethyl ether is added. The organic phase is separated, the aqueous phase is saturated with sodium chloride and then extracted twice with 50-ml. portions of ether. The combined extracts are washed twice with 50-ml. portions of saturated sodium chloride solution and dried over anhydrous magnesium sulfate.

The product obtained after removal of the solvent is crystallized from a small amount of petroleum ether to furnish 24.4 g. (74%) of *exo*-norborneol, m.p. 126–127° after sublimation.

2,3-Dimethyl-1,4-butanediol from 2,3-Dimethylbutadiene (Preparation and Use of a Solution of Diborane in Tetrahydrofuran).[29] *A. Preparation of a Solution of Diborane in Tetrahydrofuran.* The

experimental conditions and the apparatus utilized are described on p. 32.

In a 1-l. flask with a side arm capped by a rubber septum to permit the removal of material is placed 500 ml. of tetrahydrofuran. The flask is immersed in an ice bath. Diborane, generated by the addition of 950 ml. of a 1*M* solution of sodium borohydride in diglyme to 1.90 moles of boron trifluoride etherate (50% excess), is passed through a solution of sodium borohydride (to remove traces of boron trifluoride) into the tetrahydrofuran.

Determination of the boron by titration and hydride by hydrolysis shows that the solution is ~1.0*M* in diborane. The concentration of the diborane does not change significantly over a period of several weeks when the solution is kept under nitrogen at 0°.

B. Hydroboration-Oxidation. In a 300-ml. flask is placed 8.2 g. (0.10 mole) of 2,3-dimethyl-1,3-butadiene in 100 ml. of tetrahydrofuran. The flask is immersed in an ice bath. Fifty milliliters of a 1*M* solution of diborane in tetrahydrofuran is added slowly to the diene-tetrahydrofuran solution. After the addition the flask is kept for 30 minutes at room temperature, and the excess hydride is decomposed by the careful addition of water.

The organoborane is oxidized at 30–50° (water bath) by the addition of 24 ml. of 3*N* sodium hydroxide, followed by the dropwise addition of 24 ml. of 30% hydrogen peroxide. After 1 hour at room temperature, 75 g. of potassium carbonate is added with moderate stirring. The tetrahydrofuran layer is separated, and the aqueous phase extracted twice with 30-ml. portions of tetrahydrofuran. The extracts are combined and dried over anhydrous magnesium sulfate.

The solvent is removed and the product is distilled. The yield of 2,3-dimethyl-1,4-butanediol (b.p. 105–106°/2 mm., n_D^{20} 1.4563) is 7.8 g. (66%).

n-Octanal from 1-Octyne [Preparation and Use of Bis-(3-methyl-2-butyl)borane].[2] *A.* In a three-necked flask are placed 33.6 g. of 2-methyl-2-butene (0.48 mole) and 180 ml. of a 1*M* solution of sodium borohydride in diglyme. The flask is immersed in an ice bath. Boron trifluoride etherate, 0.24 mole, is added dropwise to the reaction mixture, efficient stirring being maintained. The flask is permitted to remain for 2 hours at 0° and is then placed in an ice-salt bath.

B. To the reagent (0.24 mole) prepared in *A*, 22.0 g. (0.20 mole) of 1-octyne in 20 ml. of diglyme is added as rapidly as possible while the temperature is maintained at 0–10°. The reaction mixture is permitted to warm to room temperature to complete the hydroboration.

The organoborane is oxidized at 0° by the addition of 150 ml. of a 15%

solution of hydrogen peroxide, while the *p*H of the reaction mixture is maintained at 7–8 by the controlled addition of 3*N* sodium hydroxide. The reaction mixture is then neutralized and steam distilled. The distillate is extracted with ether and the extract dried over anhydrous magnesium sulfate. Distillation yields 18.0 g. (70%) of *n*-octanal, b.p. 83–85°/33 mm., n_D^{20} 1.4217.

(+)-2-Butanol from *cis*-2-Butene (Preparation of Diisopinocampheylborane and Use in Asymmetric Synthesis).[17,57] *A.* In a 500-ml. flask fitted with a condenser, a pressure-equalizing dropping funnel, and a thermometer are placed 75 ml. of 1*M* sodium borohydride (2.85 g.) in diglyme and 27.2 g. (0.2 mole) of (−)-α-pinene, $[\alpha]_D^{20}$ −47.8°) in 100 ml. of diglyme. The flask is immersed in an ice bath and 12.6 ml. (14.2 g., 0.10 mole) of boron trifluoride etherate is added dropwise to the well-stirred reaction mixture. Stirring is continued for 4 hours at 0–5°. The diisopinocampheylborane separates as a thick white precipitate.

B. cis-2-Butene (8.5 ml., 6.1 g., 0.11 mole) is condensed at −78° and then introduced to the well-stirred diisopinocampheylborane. The reaction flask is equipped with a cold trap in order to minimize the loss of *cis*-2-butene. The reaction mixture is stirred for 2 hours at 0–5°, then allowed to warm to room temperature (2 hours). The excess hydride is decomposed by the addition of 10 ml. of water.

The organoborane is oxidized at 30–50° (water bath) by the addition of 32 ml. of 3*N* sodium hydroxide and 32 ml. of 30% hydrogen peroxide. The temperature is maintained at 45° for an additional hour.

The reaction mixture is extracted with three 100-ml. portions of ether. The combined extracts are washed with saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. The ether is removed and the product distilled. There is obtained 6.15 g. (83%) of 2-butanol; b.p. 98°/725 mm., n_D^{20} 1.3970 $[\alpha]_D^{20}$ +11.6°.

The isopinocampheol formed in this reaction is obtained in 92% yield by distillation.

3-Ethyl-1-pentanol from 3-Ethyl-2-pentene (Preparation and Isomerization of an Alkylborane).[58] *A.* To 50 ml. of diglyme

$$(C_2H_5)_2C{=}CHCH_3 \xrightarrow{BH_3} \left[\begin{array}{c} CH_3 \\ | \\ (C_2H_5)_2CHCH- \end{array}\right]_2 BH \xrightarrow{\text{Heat}}$$

$$[(C_2H_5)_2CHCH_2CH_2-]_2BH \xrightarrow{[O]} (C_2H_5)_2CHCH_2CH_2OH$$

cooled in an ice bath is added 25 ml. of boron trifluoride etherate. The ether is removed by applying a vacuum of 5–10 mm. for 20 minutes while the flask is kept at 20–25°. The resulting boron trifluoride diglymate is

[57] H. C. Brown, N. R. Ayyangar, and G. Zweifel. Unpublished research.

[58] H. C. Brown and G. Zweifel. Unpublished research.

approximately 3.65*M*. Since the material darkens relatively rapidly, it is prepared in small quantities and used soon after preparation.

B. In a 100-ml. flask are placed 45 ml. of a 1*M* solution of sodium borohydride in diglyme and 14.7 g. (0.15 mole) of 3-ethyl-2-pentene (n_D^{20} 1.4148). The flask is immersed in a water bath. Boron trifluoride diglymate (16.2 ml. of a 3.65*M* solution) is added dropwise to the well-stirred reaction mixture over a period of 30 minutes. The apparatus is kept under a static pressure of nitrogen.

C. The organoborane obtained in *B* is heated for 2 hours at 160°. The solution is cooled, and water is added to decompose residual hydride. After addition of 16 ml. of a 3*N* solution of sodium hydroxide, the organoborane is oxidized at 30–40° by the dropwise addition of 16 ml. of 30% hydrogen peroxide.

The reaction mixture is extracted with diethyl ether, and the extract is washed five times with equal volumes of ice water to remove diglyme. The ether extract is dried over anhydrous magnesium sulfate. The residue left after removal of the solvent is distilled. The yield of 3-ethyl-1-pentanol is 15.4 g. (88%); b.p. 169–170°/740 mm., n_D^{20} 1.4296.

2-Methylcyclohexanone from 1-Methylcyclohexene (Preparation and Oxidation of an Organoborane).[47] To 4.8 g. (50 mmoles) of 1-methylcyclohexene and 22.5 mmoles of lithium borohydride in 30 ml. of diethyl ether in a 200-ml. flask fitted with a stirrer, condenser, addition funnel, and thermometer are added 0.95 ml. (7.5 mmoles) of boron trifluoride etherate in 4 ml. of diethyl ether over a period of 15 minutes at 25–35°. After 2 hours, excess hydride is destroyed with 5 ml. of water. A chromic acid solution, prepared from 11.0 g. (36.9 mmoles) of sodium dichromate dihydrate and 8.25 ml. (147.4 mmoles) of 96% sulfuric acid and diluted with water to 45 ml., is added to the stirred solution over a period of 15 minutes, the temperature being maintained at 25–30°. After heating under reflux for 2 hours, the upper layer is separated and the aqueous phase extracted with diethyl ether. The ether is removed and the product distilled. There is obtained 4.36 g. (78%) of 2-methylcyclohexanone; b.p. 63–64°/24 mm., n_D^{20} 1.4487.

TABULAR SURVEY

In Tables X–XVII are listed examples of the hydration of olefins, dienes, and acetylenes by the hydroboration reaction reported in the literature up to March 1962.

The following abbreviations are used: Diglyme for the dimethyl ether of diethylene glycol; Triglyme for the dimethyl ether of triethylene glycol; THF for tetrahydrofuran.

TABLE X

Hydroboration-Oxidation of Olefins

No. of C Atoms	Olefin	Hydroborating Agent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
C_4	1-Butene	$NaBH_4$-BF_3-Diglyme	1-Butanol	93	90–95*	13
			2-Butanol	7		
C_5	1-Pentene	$NaBH_4$-BF_3-Diglyme	1-Pentanol	94	90–95*	1, 13
			2-Pentanol	6		
	2-Pentene (*cis* or *trans*)	$NaBH_4$-BF_3-Diglyme	2-Pentanol	51–55	90–95*	13
			3-Pentanol	45–49		
	2-Methyl-1-butene	$NaBH_4$-BF_3-Diglyme	2-Methyl-1-butanol	99	90–95*	13
			2-Methyl-2-butanol	1		
	2-Methyl-2-butene	$NaBH_4$-BF_3-Diglyme	3-Methyl-2-butanol	98	98*	6, 13
			2-Methyl-2-butanol	2		
	3-Methyl-1-butene	$NaBH_4$-BF_3-Diglyme	3-Methyl-1-butanol	94	90–95*	13
			3-Methyl-2-butanol	6		
	Cyclopentene	$NaBH_4$-$AlCl_3$-Diglyme	Cyclopentanol		80	4
		B_2H_6-Triglyme	Cyclopentanol		90	1
C_6	1-Hexene	$NaBH_4$-$AlCl_3$-Diglyme	1-Hexanol		90	4
		B_2H_6-Diglyme	1-Hexanol		87	1
		$NaBH_4$-BF_3-Diglyme	1-Hexanol	94	95	1, 13
			2-Hexanol	6		
		$\left[\begin{array}{l}\quad\quad CH_3 \\ \quad\quad\quad | \\ (CH_3)_2CHCH— \end{array}\right]_2$ BH-Diglyme	1-Hexanol	99	85–90*	15
			2-Hexanol	1		
C_6	2-Hexene (*cis* and *trans*)	B_2H_6-Diglyme	2- and 3-Hexanol		80	1
		$NaBH_4$-BF_3-Diglyme	2-Hexanol	46–50	90	1, 13
			3-Hexanol	50–54		
	cis-3-Hexene	$NaBH_4$-BF_3-Diglyme	3-Hexanol	100	90–95*	13
	3,3-Dimethyl-1-butene	$NaBH_4$-$AlCl_3$-Diglyme	3,3-Dimethyl-1-butanol		67	4
		B_2H_6-Triglyme	3,3-Dimethyl-1-butanol		62	1
		$NaBH_4$-BF_3-Diglyme	3,3-Dimethyl-1-butanol	94		1, 13
			3,3-Dimethyl-2-butanol	6		

	4-Methyl-1-pentene	$NaBH_4$-BF_3-THF	4-Methyl-1-pentanol	80	49
	trans-4-Methyl-2-pentene	$NaBH_4$-BF_3-Diglyme	4-Methyl-2-pentanol 57 2-Methyl-3-pentanol 43		13
		$\left[\begin{array}{c}CH_3\\ \vert \\ (CH_3)_2CHCH-\end{array}\right]_2 BH$	4-Methyl-2-pentanol 95 2-Methyl-3-pentanol 5	85–90*	15
	cis-4-Methyl-2-pentene	$\left[\begin{array}{c}CH_3\\ \vert \\ (CH_3)_2CHCH-\end{array}\right]_2 BH$	4-Methyl-2-pentanol 97 2-Methyl-3-pentanol 3	85–90*	15
	Cyclohexene	$LiAlH_4$-BF_3-diethyl ether	Cyclohexanol	80	53
	1-Methylcyclopentene	B_2H_6-THF	*trans*-2-Methylcyclopentanol	86	11
C_7	4,4-Dimethyl-1-pentene	$NaBH_4$-BF_3-Diglyme	4,4-Dimethyl-1-pentanol 93 4,4-Dimethyl-2-pentanol 7	85–90*	13
	trans-4,4-Dimethyl-2-pentene	$NaBH_4$-BF_3-Diglyme	4,4-Dimethyl-2-pentanol 58 2,2-Dimethyl-3-pentanol 42		13
	3-Ethyl-1-pentene	$NaBH_4$-BF_3-Diglyme	3-Ethyl-1-pentanol 90 3-Ethyl-2-pentanol 10	85	23
	3-Ethyl-2-pentene	$NaBH_4$-BF_3-Diglyme	3-Ethyl-2-pentanol	83	23
	1-Methylcyclohexene	B_2H_6-THF	*trans*-2-Methylcyclohexanol	85	11
	3-Methylcyclohexene	$\left[\begin{array}{c}CH_3\\ \vert \\ (CH_3)_2CHCH-\end{array}\right]_2 BH$	2-Methylcyclohexanol (*cis* and *trans*) 48 3-Methylcyclohexanol (*cis* and *trans*) 52	—	11
	1,2-Dimethylcyclopentene	B_2H_6-THF	*cis*-1,2-Dimethylcyclopentanol	80	11
	Norbornene	B_2H_6-THF	*exo*-Norborneol 99	75–85	11
		$LiBH_4$-BF_3-diethyl ether	*exo*-Norborneol	70	49
C_8	1-Octene	$LiAlH_4$-BF_3-diethyl ether	1-Octanol	80	53
		$NaBH_4$-HCl-THF	1-Octanol	80	49
	2,4,4-Trimethyl-1-pentene	$LiBH_4$-H_2SO_4-THF	2,4,4-Trimethyl-1-pentanol	81	49
		$NaBH_4$-BF_3-Diglyme	2,4,4-Trimethyl-1-pentanol 99 2,4,4-Trimethyl-2-pentanol 1	—	13
	2,4,4-Trimethyl-2-pentene	$NaBH_4$-BF_3-Diglyme	2,4,4-Trimethyl-2-pentanol 2 2,4,4-Trimethyl-3-pentanol 98	79*	6,13

Note: References 59 to 70 are on p. 54.

* The yield was determined by vapor-phase chromatography.

TABLE X—*Continued*

HYDROBORATION-OXIDATION OF OLEFINS

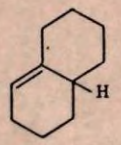
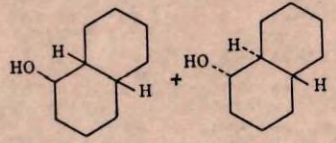
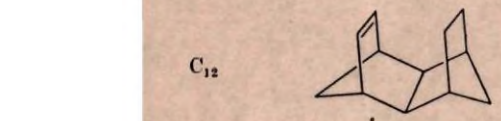
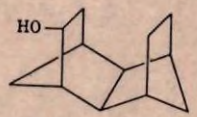
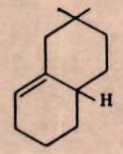
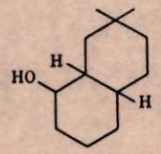
No. of C Atoms	Olefin	Hydroborating Agent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
C_8 (*contd.*)	1,2-Dimethylcyclohexene	B_2H_6-THF	*cis*-1,2-Dimethylcyclohexanol		82	11
	3,3-Dimethylcyclohexene	B_2H_6-THF	2,2-Dimethylcyclohexanol	50	—	11
			3,3-Dimethylcyclohexanol	50		
		$\left[\begin{array}{c}CH_3\\ \vert\\ (CH_3)_2CHCH-\end{array}\right]_2 BH$	2,2-Dimethylcyclohexanol	40	—	11
			3,3-Dimethylcyclohexanol	60		
	Styrene	$NaBH_4$-$AlCl_3$-*Diglyme*	2-Phenyl-1-ethanol		81	4
		$LiBH_4$-BF_3-diethyl ether	1-Phenyl-1-ethanol	20	94*	13
			2-Phenyl-1-ethanol	80		
		B_2H_6-Diglyme	1-Phenyl-1-ethanol	18	95*	13
			2-Phenyl-1-ethanol	82		
		$NaBH_4$-BF_3-Diglyme	1-Phenyl-1-ethanol	20	94*	13
			2-Phenyl-1-ethanol	80		
C_9	α-Methylstyrene	$NaBH_4$-BF_3-Diglyme	2-Phenyl-1-propanol	100	92	1, 13
	p-Methylstyrene	$NaBH_4$-BF_3-*Diglyme*	1-*p*-Tolyl-1-ethanol	18	—	13
			2-*p*-Tolyl-1-ethanol	82		
	Allylbenzene	$NaBH_4$-BF_3-Diglyme	1-Phenyl-2-propanol	10	—	13
			3-Phenyl-1-propanol	90		
	trans-1-Phenylpropene	$NaBH_4$-BF_3-*Diglyme*	1-Phenyl-1-propanol	85	—	13
			1-Phenyl-2-propanol	15		
C_{10}	1-Decene	$NaBH_4$-BF_3-Diglyme	1-Decanol		85	1
		B_2H_6-Diglyme	1-Decanol		92	1
	1,1-Di-*t*-butylethylene	B_2H_6†	$[(CH_3)_3C]_2CHCH_2OH$			60
	1,2-Di-*t*-butylethylene	B_2H_6-Diglyme	$(CH_3)_3CCHOHCH_2C(CH_3)_3$		82	12
	1-Phenylcyclobutene	B_2H_6-THF	2-Phenylcyclobutanol		82	59

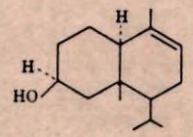
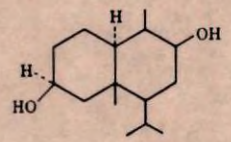
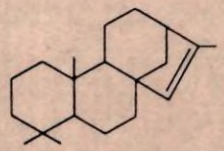
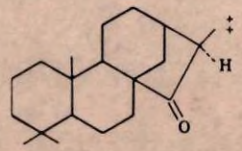
	$NaBH_4$-BF_3-Diglyme	81	11	
	B_2H_6-THF	89	11	
	B_2H_6-THF-diethyl ether	77	61	endo
	B_2H_6-Diglyme	28	82	exo

Note: References 59 to 70 are on p. 54.
* The yield was determined by vapor-phase chromatography.
† The conditions for hydroboration were not reported.

TABLE X—*Continued*

HYDROBORATION-OXIDATION OF OLEFINS

No. of C Atoms	Olefin	Hydroborating Agent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
C_{11}		$LiAlH_4$-BF_3-*diethyl ether*			—	53
C_{12}		B_2H_6†			—	20
C_{13}		$LiAlH_4$-BF_3-diethyl ether			—	53

C_{14}	1,1-Diphenylethylene	$NaBH_4$-$AlCl_3$-Diglyme	2,2-Diphenylethanol	71	4
		$NaBH_4$-BF_3-Diglyme		35	63
C_{20}		$LiAlH_4$-BF_3-diethyl ether		—	64

Note: References 59 to 70 are on p. 54.
† The conditions for hydroboration were not reported.
‡ The alcohol was oxidized directly to the ketone.

TABLE XI

HYDROBORATION-OXIDATION OF STEROIDS

Name	Hydroborating Agent	Oxidation Product(s)	Yield, %	Reference
Cholesterol	B_2H_6*	Cholestane-3β,6α-diol	45	9
		Coprostane-3β,6β-diol		
	$LiAlH_4$-BF_3-diethyl ether	Cholestane-3β,6α-diol diacetate	70	52
		Coprostane-3β,6β-diol diacetate	10–20	
1-Cholestene	$LiAlH_4$-BF_3-diethyl ether	Cholestan-1α-ol	35	16
		Cholestan-2α-ol	40	
		Cholestan-2α-ol	75	16
2-Cholestene	$LiAlH_4$-BF_3-diethyl ether or B_2H_6-THF	Cholestan-2α-ol	35	16
		Cholestan-3α-ol	45	
		Cholestan-2α-ol	35	16
		Cholestan-3α-ol	45	
3-Cholestene	$LiAlH_4$-BF_3-diethyl ether	Cholestan-3α-ol	40	16
		Cholestan-4α-ol	45	
		Cholestan-3α-ol	45	16
		Cholestan-4α-ol	35	

4-Cholestene	$LiAlH_4$-BF_3-diethyl ether	Cholestan-4α-ol	60	52
5-Cholestene	$LiAlH_4$-BF_3-diethyl ether	Cholestan-6α-ol	75	52
Androst-9(11)-ene	$LiAlH_4$-BF_3-diethyl ether	Androstan-11α-ol	90	10
	B_2H_6-THF	Androstan-11α-ol	55	10
Δ^{16}-Androstene-3β,17-diol diacetate	B_2H_6-THF (Diglyme)	Androstane-3β,16α,17β-triol	44	65
$\Delta^{1.3.5.16}$-Estratetraene-3,17-diol-3-methyl ether 17-acetate	B_2H_6-THF (Diglyme)	Estriol-3-methyl ether	50	65
$\Delta^{1.3.5.16}$-Estratetraene-3,17-diol diacetate	B_2H_6-THF (Diglyme)	Estriol	40	65
3,20-Bicycloethylenedioxy-5α-pregn-9(11)-ene	B_2H_6-THF	11-α-Hydroxy-5α-pregnane-3,20-dione	55	10
3,20-Bicycloethylenedioxy-5β-pregn-9(11)-ene	B_2H_6-THF	No reaction		9
5α-25D-Spirost-9(11)-en-3β-ol acetate	B_2H_6-THF	5α-25D-Spirostane-3β,11α-diol diacetate	60	10
5α-25D-Spirost-11(12)-en-3β-ol acetate	B_2H_6-THF	5α-25D-Spirostane-3β,11α-diol	40	16
		5α-25D-Spirostane-3β,12α-diol	40	
Test-9(11)-ene	$LiAlH_4$-BF_3-Diglyme	No reaction		10
	B_2H_6-THF	No reaction		10

Note: References 59 to 70 are on p. 54.

* The conditions for hydroboration were not reported.

TABLE XII

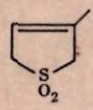
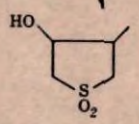
ASYMMETRIC SYNTHESES OF ALCOHOLS

Olefin	Hydroborating Agent	Optically Active Alcohol (Rotation, $[\alpha]_D^{20}$)	Optical Purity, %	Yield, %	References
cis-2-Butene	Diisopinocampheylborane from (+)-α-pinene	2-Butanol (−11.8°)	87	90	17, 18
	Diisopinocampheylborane from (−)-α-pinene	2-Butanol (+11.6°)	86	83	18
cis-3-Hexene	Diisopinocampheylborane from (+)-α-pinene	3-Hexanol (−6.5°)	91	81	17
cis-4-Methyl-2-pentene	Diisopinocampheylborane from (−)-α-pinene	4-Methyl-2-pentanol (+16.0°)	76	—	18
Norbornene	Diisopinocampheylborane from (+)-α-pinene	*exo*-Norborneol (−2.0°)	70	62	17, 18
	Diisopinocampheylborane from (−)-α-pinene	*exo*-Norborneol (+1.95°)	70	56	18

Note: References 59 to 70 are on p. 54.

TABLE XIII

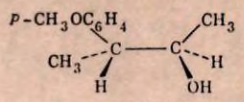
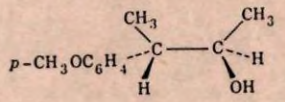
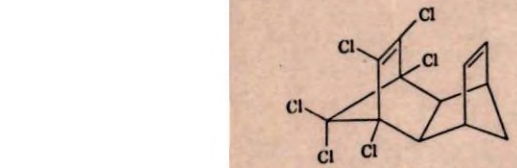
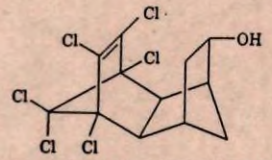
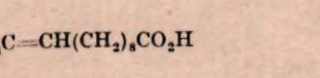
HYDROBORATION-OXIDATION OF OLEFINS CONTAINING OTHER FUNCTIONAL GROUPS

Olefin	Hydroborating Agent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
$H_2C{=}CHCH_2Cl$	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	$HOCH_2CH_2CH_2Cl$		77*	66
$H_2C{=}CHCH_2CH_2Cl$	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	$HOCH_2CH_2CH_2CH_2Cl$		88*	66
$(CH_3)_3SiCH{=}CH_2$	$NaBH_4$-$AlCl_3$-Diglyme	$(CH_3)_3SiCH_2CH_2OH$ $(CH_3)_3SiCHOHCH_3$	63 37	75	14
	B_2H_6-THF			63	67
$H_2C{=}CHCH_2CO_2C_2H_5$	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	$HOCH_2CH_2CH_2CO_2C_2H_5$		76	66
$H_2C{=}CHCH_2CH_2CO_2C_2H_5$	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	$HOCH_2CH_2CH_2CH_2CO_2C_2H_5$		78	66
p-Chlorostyrene	$NaBH_4$-BF_3-Diglyme	1-*p*-Chlorophenyl-2-ethanol 1-*p*-Chlorophenyl-1-ethanol	65 35	—	13
p-Methoxystyrene	$NaBH_4$-BF_3-Diglyme	1-*p*-Anisyl-2-ethanol 1-*p*-Anisyl-1-ethanol	91 9	—	13
	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	1-*p*-Anisyl-2-ethanol 1-*p*-Anisyl-1-ethanol	98 2	80	15
1,2-O-Isopropylidene-4-vinyl-α-D-xylotetrofuranose	B_2H_6†	5-Deoxy-1,2-O-isopropylidene-α-D-xylohexofuranose		—	68

Note: References 59 to 70 are on p. 54.

* The yield was determined by vapor-phase chromatography

TABLE XIII—*Continued*

Olefin	Hydroborating Agent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
Anetholo	B_2H_6-diethyl ether	1-*p*-Anisyl-1-propanol 1-*p*-Anisyl-2-propanol	75 25	66	33
trans-*p*-$CH_3OC_6H_4C(CH_3)=CHCH_3$	B_2H_6-diethyl ether			72	33
cis-*p*-$CH_3OC_6H_4C(CH_3)=CHCH_3$	B_2H_6-diethyl ether			77	33
	B_2H_6-diethyl ether			—	19, 20
$H_2C=CH(CH_2)_8CO_2C_2H_5$	B_2H_6-THF	$HOCH_2CH_2(CH_2)_8CO_2C_2H_5$		71	61, 66
	 BH-THF	$HOCH_2CH_2(CH_2)_8CO_2C_2H_5$		81	66
$H_2C=CH(CH_2)_8CO_2H$	 BH-THF	$HOCH_2CH_2(CH_2)_8CO_2H$		82	38
$CH_3(CH_2)_7CH=CH(CH_2)_7CO_2CH_3$	B_2H_6-Diglyme	$CH_3(CH_2)_7CH_2CHOH(CH_2)_7CO_2CH_3$ $CH_3(CH_2)_7CHOHCH_2(CH_2)_7CO_2CH_3$	50 50	—	39

Note: References 59 to 70 are on p. 54.

TABLE XIV

HYDROBORATION-OXIDATION OF DIENES

Diene	Monohydroboration, Reagent	Dihydroboration, Reagent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
1,3-Butadiene		B_2H_6-THF	1,3-Butanediol	20	74	29
			1,4-Butanediol	80		
		$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	1,3-Butanediol	10	78	34
			1,4-Butanediol	90		
2-Methyl-1,3-butadiene		B_2H_6-THF	2-Methyl-1,3-butanediol	13	69	29
			2-Methyl-1,4-butanediol	87		
1,3-Pentadiene (*cis* and *trans*)	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF		3-Pentene-1-ol (*cis* and *trans*)		74	34
1,4-Pentadiene		B_2H_6-THF	1,4-Pentanediol	62	—	29
			1,5-Pentanediol	38		
		$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	1,4-Pentanediol	15	—	34
			1,5-Pentanediol	85		
2,3-Dimethyl-1,3-butadiene		B_2H_6-THF	2,3-Dimethyl-1,4-butanediol		66	29
1,4-Hexadiene		B_2H_6-Diglyme	1,4-Hexanediol	13	78	31
1,5-Hexadiene	B_2H_6-THF		1,5-Hexanediol	87		
			5-Hexen-1-ol		26	29
	$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF		5-Hexen-1-ol		51	34
		B_2H_6-THF	1,5-Hexanediol	22	79	29
			1,6-Hexanediol	69		
			2,5-Hexanediol(?)	9		
		$[(CH_3)_2CHCH(CH_3)-]_2BH$-THF	1,6-Hexanediol		72	34

Note: References 59 to 70 are on p. 54.

TABLE XIV—*Continued*

HYDROBORATION-OXIDATION OF DIENES

Diene	Monohydroboration, Reagent	Dihydroboration, Reagent	Oxidation Product(s)	Isomer Distribution, %	Yield, %	Reference
2-Methyl-1,5-hexadiene	$\left[\begin{array}{c}CH_3\\|\\(CH_3)_2CHCH-\end{array}\right]_2$BH-THF		$CH_2{=}C(CH_3)CH_2CH_2CH_2CH_2OH$		68	34
Cyclopentadiene	B_2H_6-diethyl ether		3-Cyclopentene-1-ol		30	33
		B_2H_6-diethyl ether	*trans*-1,3-Cyclopentanediol		41	31, 32
1,3-Cyclohexadiene	B_2H_6-THF		2-Cyclohexen-1-ol 3-Cyclohexen-1-ol	60–65 35–40	—	29
	$\left[\begin{array}{c}CH_3\\|\\(CH_3)_2CHCH-\end{array}\right]_2$BH-THF		2-Cyclohexen-1-ol 3-Cyclohexen-1-ol	90 10	70	34
1,4-Cyclohexadiene	$\left[\begin{array}{c}CH_3\\|\\(CH_3)_2CHCH-\end{array}\right]_2$BH-THF		3-Cyclohexen-1-ol		75	34
Bicycloheptadiene	$LiBH_4$-BF_3-diethyl ether		*exo*-Dehydronorborneol *endo*-Dehydronorborneol	88 12	45	29
	B_2H_6-THF		*exo*-Dehydronorborneol *endo*-Dehydronorborneol	87 13	39*	29
	$\left[\begin{array}{c}CH_3\\|\\(CH_3)_2CHCH-\end{array}\right]_2$BH-THF		*exo*-Dehydronorborneol *endo*-Dehydronorborneol	87 13	45*	34
		B_2H_6-THF	Mixture of diols (?)		64	29

	$\left[\begin{matrix}CH_3\\|\\(CH_3)_2CHCH-\end{matrix}\right]_2$BH-Diglyme		72	15
	$\left[\begin{matrix}CH_3\\|\\(CH_3)_2CHCH-\end{matrix}\right]_2$BH-Diglyme		79	15
1,5-Cyclooctadiene	$\left[\begin{matrix}CH_3\\|\\(CH_3)_2CHCH-\end{matrix}\right]_2$BH-THF	Mixture of diols	85	34
$(CH_3)_2C{=}CH(CH_2)_2C(=CH_2)CH{=}CH_2$	$\left[\begin{matrix}CH_3\\|\\(CH_3)_2CHCH-\end{matrix}\right]_2$BH-THF	$(CH_3)_2C{=}CH(CH_2)_2$-$C(=CH_2)CH_2CH_2OH$		35
	B_2H_6-THF		—	69
	$\left[\begin{matrix}CH_3\\|\\(CH_3)_2CHCH-\end{matrix}\right]_2$BH-THF		—	35

Note: References 59 to 70 are on p. 54.

• The yield was determined by vapor-phase chromatography.

TABLE XV

MONOHYDROBORATION-OXIDATION OF ACETYLENES

Acetylene	Hydroborating Agent	Oxidation Product	Yield, %	Reference
1-Butyne	$t\text{-}C_4H_9BH_2\overset{-}{\underset{+}{N}}(CH_3)_3$	*n*-Butyraldehyde*	—	36
1-Hexyne	$\left[(CH_3)_2CHCH(CH_3)-\right]_2$BH-Diglyme	*n*-Hexanal*	—	2
3-Hexyne	$\left[(CH_3)_2CHCH(CH_3)-\right]_2$BH-Diglyme	3-Hexanone	62	2
1-Octyne	$\left[(CH_3)_2CHCH(CH_3)-\right]_2$BH-Diglyme	*n*-Octanal	70	2

Note: References 59 to 70 are on p. 54.

* The product was identified as the 2,4-dinitrophenylhydrazone.

TABLE XVI

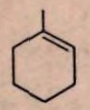
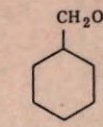
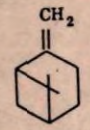
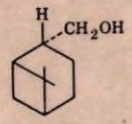
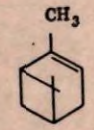
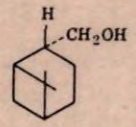
Isomerization-Oxidation of Organoboranes

Unsaturated Compound	Hydroborating Agent	Isomerization Time, hr.	Isomerization Temp., °C.	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
2-Pentene	$NaBH_4$-BF_3-Diglyme	1	160	1-Pentanol	95	82	22, 23
				2-Pentanol	4		
				3-Pentanol	1		
1,3-Pentadiene	B_2H_6*	6	160–175	1,5-Pentanediol		85	31
2-Methyl-1-butene	$NaBH_4$-BF_3-Diglyme	4	160	2-Methyl-1-butanol	43	—	23
				3-Methyl-2-butanol	1		
				3-Methyl-1-butanol	56		
2-Methyl-2-butene	$NaBH_4$-BF_3-Diglyme	4	160	2-Methyl-1-butanol	40	—	23
				3-Methyl-2-butanol	2		
				3-Methyl-1-butanol	58		
3-Methyl-1-butene	$NaBH_4$-BF_3-Diglyme	4	160	2-Methyl-1-butanol	40	—	23
				3-Methyl-2-butanol	1		
				3-Methyl-1-butanol	59		
2-Hexene	$NaBH_4$-BF_3-Diglyme	1	160	1-Hexanol	91	75	22, 23
				2-Hexanol	6		
				3-Hexanol	3		
cis-3-Hexene	$NaBH_4$-BF_3-Diglyme	1	160	1-Hexanol	90	—	23
				2-Hexanol	6		
				3-Hexanol	4		
1,4-Hexadiene	B_2H_6*	6	160–175	1,5-Hexanediol	69	82	31
				1,6-Hexanediol	31		
1,5-Hexadiene	B_2H_6*	6	160–175	1,5-Hexanediol	70	76	31
				1,6-Hexanediol	30		
4,4-Dimethyl-2-pentene	$NaBH_4$-BF_3-Diglyme	1	160	4,4-Dimethyl-1-pentanol	96	—	23
				4,4-Dimethyl-2-pentanol	2		
				2,2-Dimethyl-3-pentanol	2		

Note: References 59 to 70 are on p. 54.

* The conditions for hydroboration were not reported.

TABLE XVI—*Continued*

Unsaturated Compound	Hydroborating Agent	Isomerization Time, hr.	Isomerization Temp., °C,	Oxidation Product(s)	Isomer Distribution, %	Yield, %	References
3-Ethyl-2-pentene	$NaBH_4$-BF_3-*Diglyme*	2	160	3-Ethyl-1-pentanol		88	23
	$NaBH_4$-BF_3-Diglyme	4	160			—	23
2,4,4-Trimethyl-2-pentene	$NaBH_4$-BF_3-Diglyme	1	160	2,4,4-*Trimethyl-1-pentanol* 2,4,4-Trimethyl-2-pentanol 2,2,4-Trimethyl-3-pentanol	97 1 2	—	23
$C_6H_5CH{=}CHCH_3$	$NaBH_4$-BF_3-Diglyme	1	160	$C_6H_5CH_2CH_2CH_2OH$ $C_6H_5CH_2CHOHCH_3$ $C_6H_5CHOHCH_2CH_3$	76 10 14	—	23
Decenes (mixed)	$NaBH_4$-BF_3-Diglyme	4	160	1-Decanol		70–80	22
	$NaBH_4$-BF_3-Diglyme	4	160			80	24, 25
	$NaBH_4$-BF_3-Diglyme	4	160			80	24, 25
3-Carene	B_2H_6*	1	150	10-Hydroxycarane		—	70

Note: References 59 to 70 are on p. 54.

* The conditions for hydroboration were not reported.

TABLE XVII

Chromic Acid Oxidation of Organoboranes

Olefin	Hydroborating Agent	Oxidation Product	Yield, %	Reference
Conessine	$NaBH_4$-$AlCl_3$-Diglyme	3-β-Dimethylaminoconanin-6-one	—	46
Cyclohexene	$LiBH_4$-BF_3-diethyl ether	Cyclohexanone	60–65	47
1-Methylcyclopentene	$LiBH_4$-BF_3-diethyl ether	2-Methylcyclopentanone	83	47
1-Methylcyclohexene	$LiBH_4$-BF_3-diethyl ether	2-Methylcyclohexanone	87	47
1-Phenylcyclohexene	$LiBH_4$-BF_3-diethyl ether	2-Phenylcyclohexanone	63	47
α-Pinene	$LiBH_4$-BF_3-diethyl ether	Isopinocamphone	72	47

Note: References 59 to 70 are on p. 54.

REFERENCES FOR TABLES X–XVII

[59] Beard and Burger, *J. Org. Chem.*, **26**, 2335 (1961).
[60] Newman, Arkell, and Fukunago, *J. Am. Chem. Soc*, **82**, 2498 (1960).
[61] Dulou and Chrétien-Bessière, *Bull. Soc. Chim. France*, **1959**, 1362.
[62] Cristol, Seifert, and Soloway, *J. Am. Chem. Soc.*, **82**, 2351 (1960).
[63] Dauben, Weinstein, Lim, and Anderson, *Tetrahedron*, **15**, 217 (1961).
[64] Henderson and Hoges, *Tetrahedron*, **11**, 226 (1960).
[65] Alvarez and Arreguin, *Chem. & Ind.* (*London*), **1960**, 720.
[66] H. C. Brown and K. Keblys. Unpublished research.
[67] Krug and Boswell, *J. Org. Chem.*, **27**, 95 (1962).
[68] Wolfrom and Whiteley, *Am. Chem. Soc. Meeting, Abstr.*, April 1960, 2D.
[69] Cornforth, *J. Pure and Appl. Chem.*, **2**, 607 (1961).
[70] Arlt, Sheers, and Chamberlain, *Chem. & Ind.* (*London*), **1961**, 1409.

CHAPTER 2

HALOCYCLOPROPANES FROM HALOCARBENES

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CONTENTS