ORGANOBORANE HETEROCYCLES VIA CYCLIC HYDROBORATION OF DIENES

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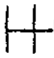
Hydroboration of dienes can give rise to heterocyclic organoboron derivatives or polymers depending upon the hydroborating agent and conditions used. It is advantageous to use bifunctional hydroborating agents such as thexylborane (BH_2) or monochloroborane etherate ($BH_2Cl \cdot OEt_2$) for such cyclic hydroboration.

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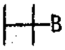
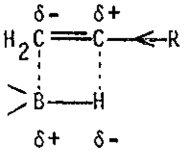
A. INTRODUCTION

The organoborane heterocycles may be defined as those cyclic species which contain at least one boron atom in the ring structure. Although a number of boron-containing heterocycles have been known for a long time,[1] the discovery of hydroboration and the recent developments in organoborane chemistry[2,3] have remarkably widened this field. The chemistry of organoboranes containing boron-hetero atom bonds[4] and that of carboranes[5] has been extensively reviewed elsewhere. In this review, we restrict ourselves to the chemistry of organoborane heterocycles which contain one or more endocyclic boron atoms incorporated into the cyclic system *via* boron-carbon bonds.

Methods available for the preparation of organoborane heterocycles include cyclic hydroboration of dienes and polyenes,[2,3] transmetallation,[6] disproportionation,[6,7] displacement reactions,[7,8] substitution,[7] and allylboration.[9] However, in cases where cyclic hydroboration is applicable, it is usually the method of choice, since it is simpler and more convenient than other methods. Therefore, we primarily deal with those heterocyclic organoboranes obtainable *via* the cyclic hydroboration of acyclic α,ω-dienes, mixed dienes and cyclic dienes with borane (BH_3) itself, or with monosubstituted boranes, such as thexylborane ( BH_2)[10] and monochloroborane etherate ($BH_2Cl \cdot OEt_2$).[11] Some overlap with our previous review[8] is inevitable. However, much progress has been made since that review was prepared, especially in the development of chloroborane as a versatile reagent for cyclic hydroboration of dienes.[12]

Hydroboration involves the interaction of the carbon-carbon multiple bonds with the electrophilic boron-hydride species (Chart 1).

Chart 1

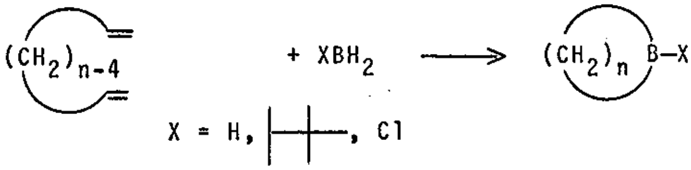


The reaction is influenced by the inductive, resonance and steric effects of the interacting molecules. The boron-containing moiety, being sterically more demanding than the hydrogen atom, prefers attachment to the less substituted carbon atom in simple alkenes and alkynes. When two carbon-carbon double bonds are isolated, the difference between the observed regiochemistry and that predicted from the findings with monoenes is attributable to the intervention of a cyclic process of hydroboration.[13] In conjugated dienes, the reactivity of one double bond is greatly influenced by the inductive and resonance effects of the other, resulting in other complications.

B. HYDROBORATION OF ACYCLIC α,ω-DIENES

Hydroboration of acyclic α,ω-dienes with suitable reagents under appropriate conditions leads to the formation of boracycloalkanes (Chart 2).

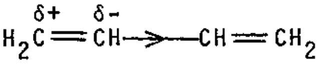
Chart 2



1. Hydroboration with Borane-THF

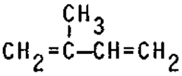
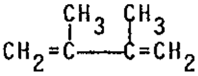
Among acyclic α,ω-dienes, 1,3-butadiene is unique in that it is a simple conjugated diene, and its hydroboration has been investigated in great detail.[8,14-17] The course of hydroboration with borane does not follow the usual 94:6 regioselectivity in favor of the terminal position observed in simple terminal olefins. Instead, the usual hydroboration-oxidation sequence reveals a 30:70 mixture of 1,3- and 1,4-butanediols respectively. Since it is highly unlikely that four-membered ring formation in the hydroboration reaction is competitive with five-membered ring formation, this abnormal alcohol ratio is attributed to the electron-withdrawing effect of the carbon-carbon double bond favoring increased attachment of the boron to the 2-position in the initial reaction. This electronic effect can be circumvented by the introduction of methyl groups in the 2-positions[16] (Chart 3).

Chart 3



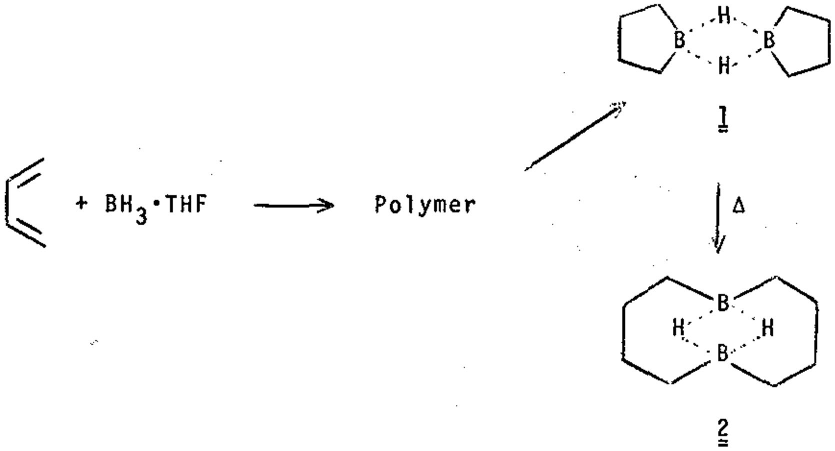
$$H_2\overset{\delta+}{C}=\overset{\delta-}{CH}\rightarrow CH=CH_2$$

Hydroboration-oxidation of substituted
1,3-butadienes

	$CH_2=CH-CH=CH_2$	 $CH_2=\overset{CH_3}{C}-CH=CH_2$	 $CH_2=\overset{CH_3}{C}-\overset{CH_3}{C}=CH_2$
1,4-diol	70%	87%	100%
1,3-diol	30%	13%	0%

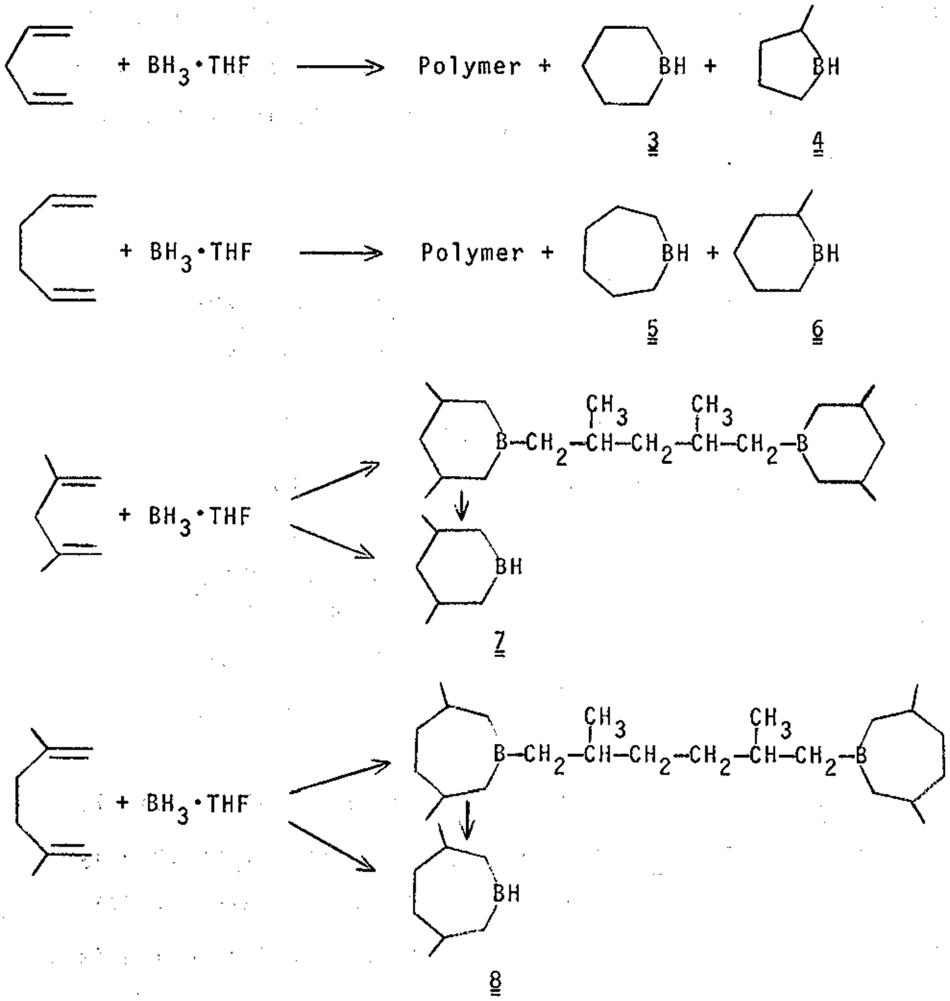
The primary hydroboration product of 1,3-butadiene with borane-THF is mainly polymeric. Thermal treatment converts the polymer into highly stable 1,6-diboracyclodecane (2) *via* a relatively labile intermediate, bisborolane (1) (Chart 4).

Chart 4



The reaction of 1,4-pentadiene[15,18] with borane-THF gives 70% polymer and 30% monomer. The cyclic monomeric product is chiefly borinane (3) along with a small quantity of 2-methylborolane (4). Hydroboration of 1,5-hexadiene yields 78% cyclic product which is a 70:30 mixture of borepane (5) and 2-methylborinane (6) respectively.[15] Placement of two methyl groups at the two internal olefinic carbons of 1,4-pentadiene and 1,5-hexadiene greatly simplifies the course of hydroboration to achieve the synthesis of boron heterocycles (7 and 8)[19,20] (Chart 5). In these cases, the mixture undergoes redistribution on standing for a number of hours, yielding improved conversion to the desired boron heterocycles, 3, 5, 7, and 8.

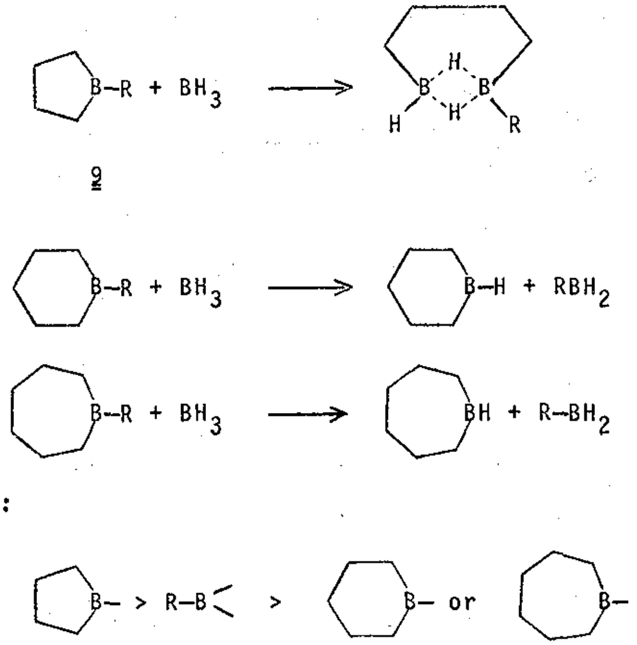
Chart 5



Cyclic hydroboration of 1,6-heptadiene, 1,8-nonadiene and higher α,ω-dienes with borane has not been reported in the literature. However, 1,7-octadiene gives essentially a polymeric material.[15]

The order of reactivity of the boron-carbon bond toward borane-THF can be summarized[15] as shown in Chart 6, based on the representative reactions. The remarkable reactivity of borolane ring toward borane is indicated by a facile addition of borane to B-alkylborolane (**9**).[17]

Chart 6

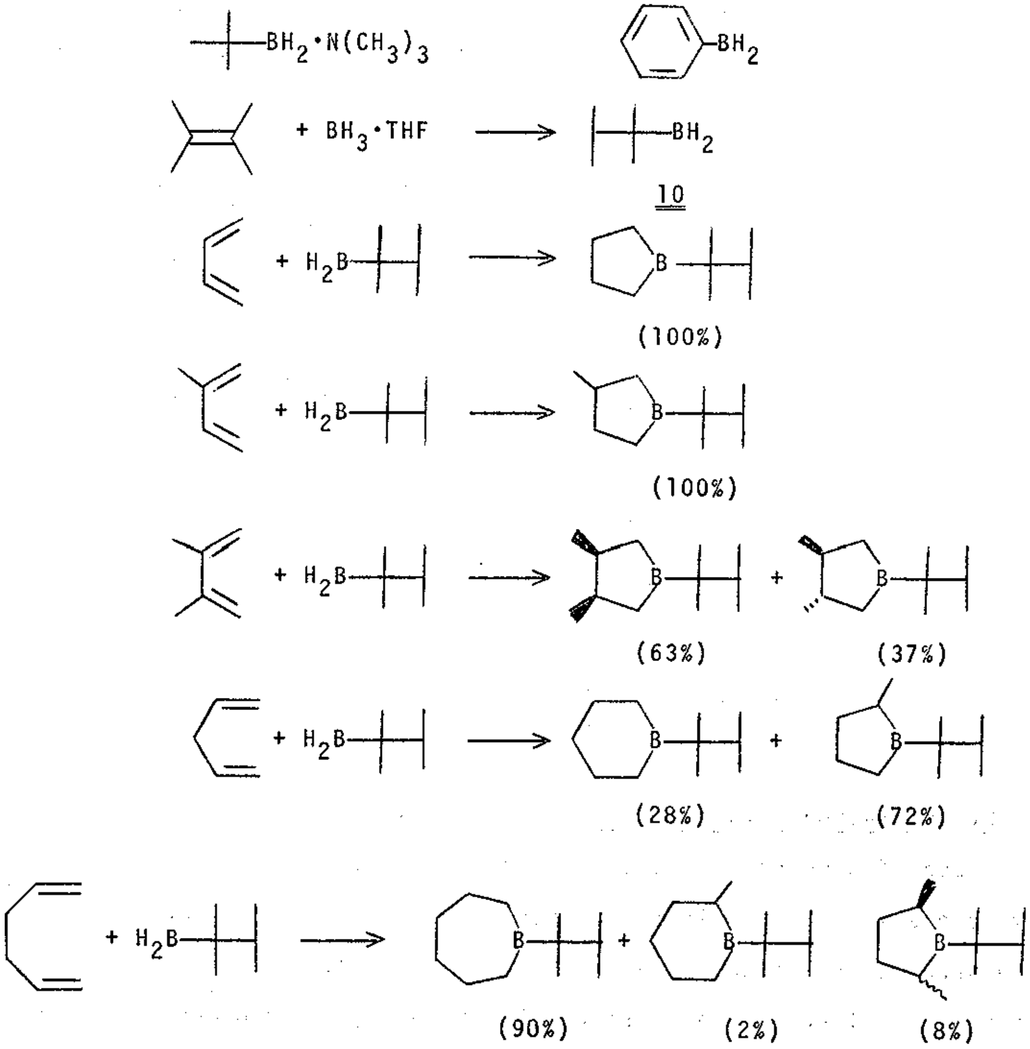


2. Hydroboration with Thexylborane

Use of a monosubstituted borane is expected to simplify the hydroboration of acyclic α,ω-dienes. Hawthorne[21] and Mikhailov[22] prepared several organoborane heterocycles by the hydroboration of dienes with t-butylborane-trimethylamine and phenylborane respectively.

To circumvent the inconvenience associated with the preparation of these reagents, we used a readily available monoalkylborane, thexylborane (10) for the cyclic hydroboration of dienes[23] (Chart 7).

Chart 7



(Isomer distribution is shown in parentheses)

The formation of boracyclanes (Chart 7) is more efficient when thexylborane is used for the hydroboration of α,ω-dienes. Even in the case of 1,3-butadiene, 100% B-thexylborolane is formed.[23] The results obtained with thexylborane indicate a strong kinetic preference for the formation of the five-membered ring over the corresponding six-membered ring.[23]

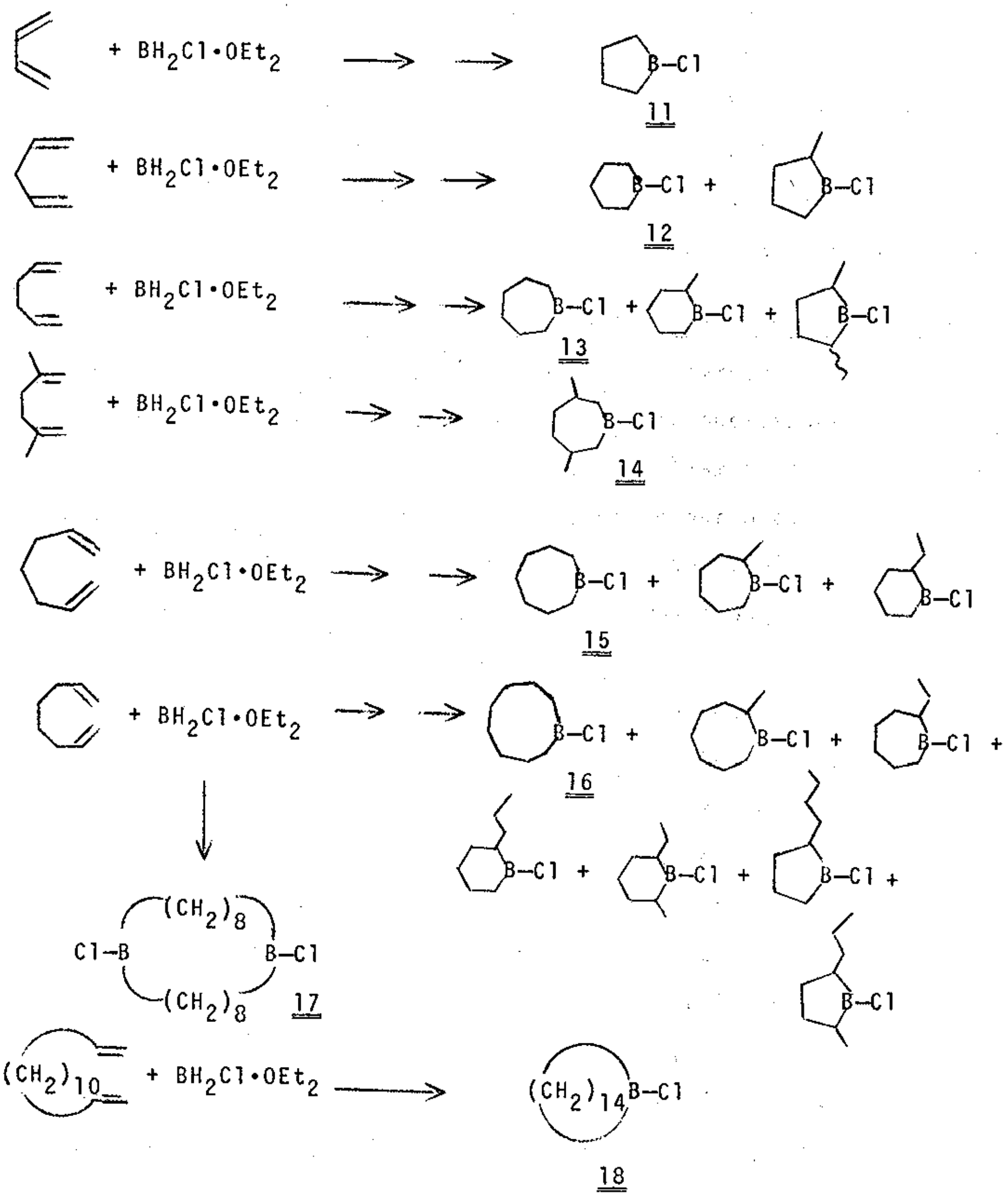
3. Hydroboration with Monochloroborane-Etherate

Preliminary observations on cyclic hydroboration of 1,4-pentadiene and 1,5-hexadiene with monochloroborane appeared promising.[24] Consequently, a systematic study was undertaken recently.[12] Application of monochloroborane etherate ($BH_2Cl \cdot OEt_2$) in the cyclic hydroboration of acyclic α,ω-dienes appears to offer considerable advantage for remarkable progress toward the synthesis of organoborane heterocycles (Chart 8).

The initial hydroboration product is partially polymeric in the case of 1,4-pentadiene and 1,5-hexadiene, and essentially polymeric in the case of higher dienes. Careful distillation of the polymeric material gives B-chloroboracycloalkanes in excellent yields. A great advantage is that no extensive isomerization was observed during the depolymerization of products derived from the C_5—C_7 olefins.

Pure B-chloroborinane (**12**), B-chloroborepane (**13**), and B-chloro-3,6-dimethylborepane (**14**) were readily isolated. An eight-membered ring boracycloalkane, B-chloroborocane (**15**), was prepared for the first time by the hydroboration-depolymerization of 1,6-heptadiene. However, 1,7-octadiene, under similar experimental conditions, gave

Chart 8


+ $BH_2Cl \cdot OEt_2$
B–Cl
11
+ $BH_2Cl \cdot OEt_2$
B–Cl + B–Cl
12
+ $BH_2Cl \cdot OEt_2$
B–Cl + B–Cl + B–Cl
13
+ $BH_2Cl \cdot OEt_2$
B–Cl
14
+ $BH_2Cl \cdot OEt_2$
B–Cl + B–Cl + B–Cl
15
+ $BH_2Cl \cdot OEt_2$
B–Cl + B–Cl + B–Cl +
16
B–Cl + B–Cl + B–Cl +
B–Cl
$(CH_2)_8$
Cl–B
B–Cl
$(CH_2)_8$
17
$(CH_2)_{10}$
+ $BH_2Cl \cdot OEt_2$
$(CH_2)_{14}$B–Cl
18

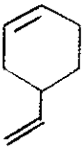
a mixture of products varying from five- to nine-membered rings of which only 1% was nine-membered ring (16). When high dilution technique was used for the hydroboration of 1,7-octadiene, a small quantity of 1,10-dichloro-1,10-diboracyclooctadecane (17) was produced. Under similar conditions, 1,13-tetradecadiene gave B-chloroboracyclopentadecane (18). These were characterized by conversion to the corresponding ketones by the DCME reaction.[25]

C. HYDROBORATION OF MIXED DIENES

The dienes containing one exocyclic and one endocyclic carbon-carbon double bond are referred to as mixed dienes. Cyclic hydroboration of mixed dienes under suitable conditions lead to the bicyclic systems.

1. Hydroboration with Borane-THF

The hydroboration-oxidation of 4-vinylcyclohexene (19) with borane-THF is neither stereoselective nor regioselective.[15] Introduction of methyl groups in strategic positions greatly simplifies the results as observed in the hydroboration-oxidation of D-(+)-limonene (20).[13] No other mixed dienes were tried with borane.



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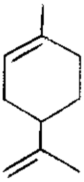

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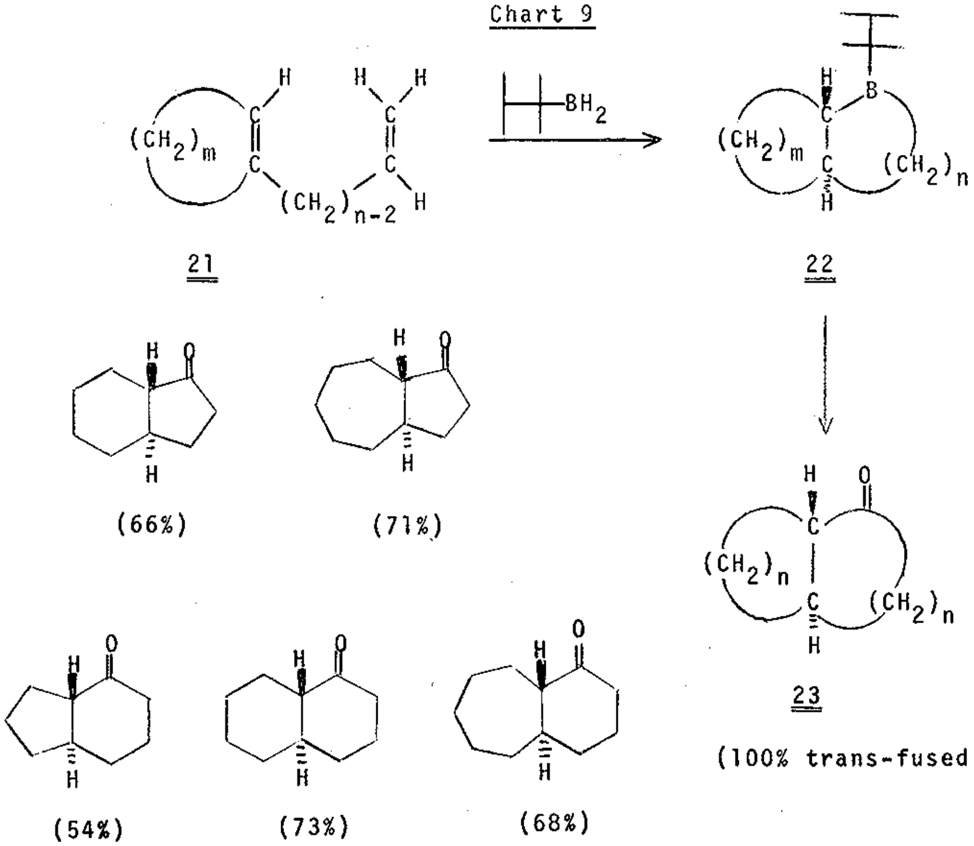
2. Hydroboration with Thexylborane

Cyclic hydroboration of mixed dienes, especially 1-alkenylcycloalkenes (21) have produced very interesting bicyclic organoboranes (22) which have been converted to trans-fused bicyclic ketones (23) in good overall yields.[26] The conversion of *B*-thexylboracyclanes (22) to the corresponding ketones (23) can be carried out either by carbonylation[27] or by the cyanoborate process.[28] The general reaction scheme and the ketones obtained[26] are shown in Chart 9.

Chart 9

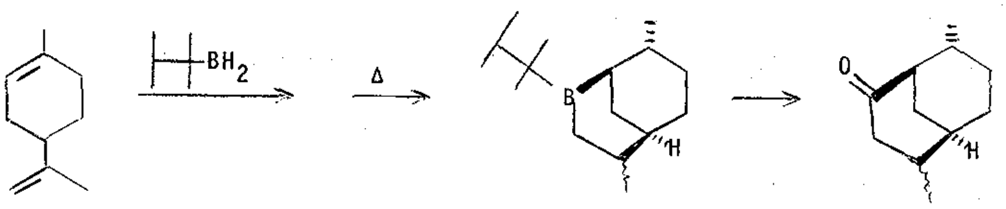


(The overall yields from the diene are shown in parentheses)

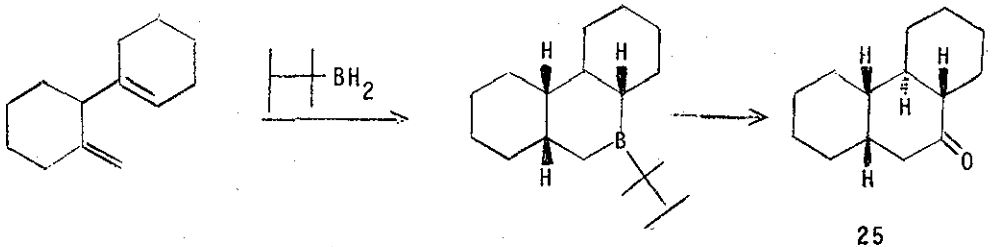
The trans geometry of these bicyclic organoboranes is anticipated from the exclusively cis nature of hydroboration reaction.

Hydroboration of D-(+)-limonene followed by distillation gives the bicyclic product, thexyllimonylborane (24).[13] Another interesting application is the synthesis of perhydrophenanthren-9-one (25) *via* cyclic hydroboration[28] (Chart 10).

Chart 10



24 (85% yield)



25 (80% yield)

(The overall yields from diene are shown in parentheses)

3. Hydroboration with Monochloroborane Etherate

Cyclic hydroboration of mixed dienes with monochloborane etherate is presently under investigation in this laboratory.

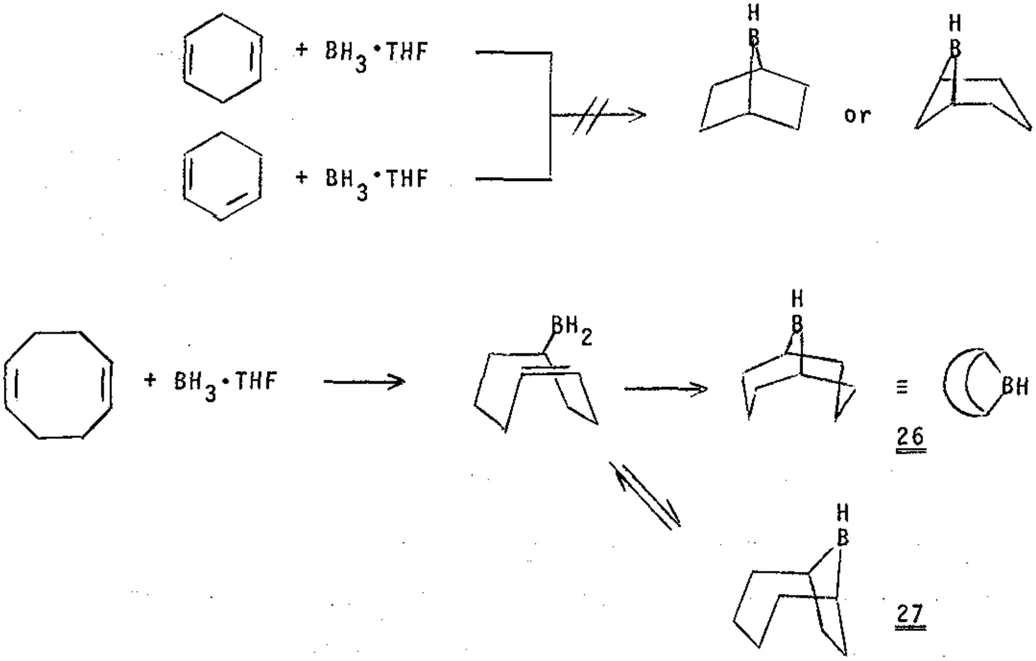
D. HYDROBORATION OF CYCLIC DIENES

Cyclic dienes, which contain two endocyclic carbon-carbon double bonds, have been an interesting class frequently used for building borabicycloalkanes.

1. Hydroboration with Borane-THF

The hydroboration of 1,3- and 1,4-cyclohexadiene is neither stereoselective nor regioselective. The extent of cyclic hydroboration is low. Attempts to prepare borabicyclo[2.2.1]heptane or borabicyclo-[3.1.1]heptane did not meet with significant success[29] (Chart 11).

Chart 11



In marked contrast to cyclohexadienes, the hydroboration of 1,5-cyclooctadiene with borane is highly stereoselective.[15,30] However, the reaction is not regioselective, giving a 72:28 mixture of 1,5- (26) and 1,4- (27) isomers respectively. But gentle thermal treatment forms the thermodynamically more stable isomer (26) exclusively. Thus the hydroboration of 1,5-cyclooctadiene followed by thermal treatment affords pure 9-borabicyclo[3.3.1]nonane in almost quantitative yield.

2. Hydroboration with Thexylborane

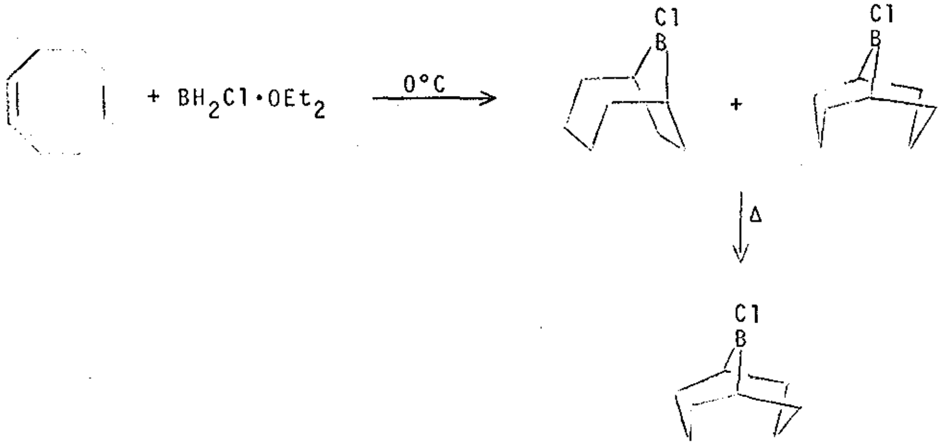
In the hydroboration-oxidation of 1,3- and 1,4-cyclohexadienes with thexylborane, a slightly larger proportion of cis-diols, compared to the case with borane, are obtained. Although this suggests that cyclic hydroboration may be responsible for this observation, B-thexylborabicycloheptanes could not be isolated.[29]

Hydroboration of 1,5-cyclooctadiene with thexylborane afforded a 22:78 mixture of 1,5- and 1,4-isomers of B-thexyl-9-borabicyclononanes. Noticeably different regiochemistry of hydroboration with thexylborane compared to borane is attributed to the steric effects of the bulky thexyl group.[31]

3. Hydroboration with Monochloroborane Etherate

Cyclic hydroboration of cyclic dienes with monochloroborane is not reported in the literature. As a representative case, the hydroboration of 1,5-cyclooctadiene with monochloroborane etherate was recently investigated.[32] Even though the stereoselectivity is as expected, the product was a 78:22 mixture of 1,4- and 1,5-isomers, which resemble thexylborane rather than borane-THF (Chart 12).

Chart 12



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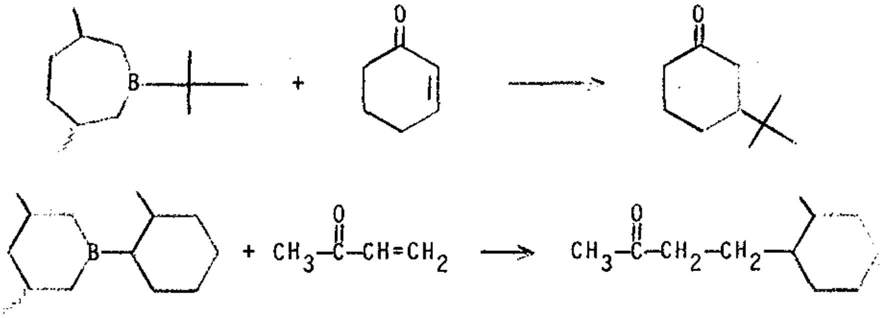
Thermal treatment after the removal of solvent, affords pure *B*-chloro-9-borabicyclo[3.3.1]nonane in excellent yield.

E. SOME REPRESENTATIVE APPLICATIONS

These syntheses of heterocyclic organoboranes are useful, both for the synthesis of reagents and for the synthesis of carbon structures, utilizing the boron derivatives as intermediates. Conversion of boracyclanes to cyclic ketones has been already mentioned.

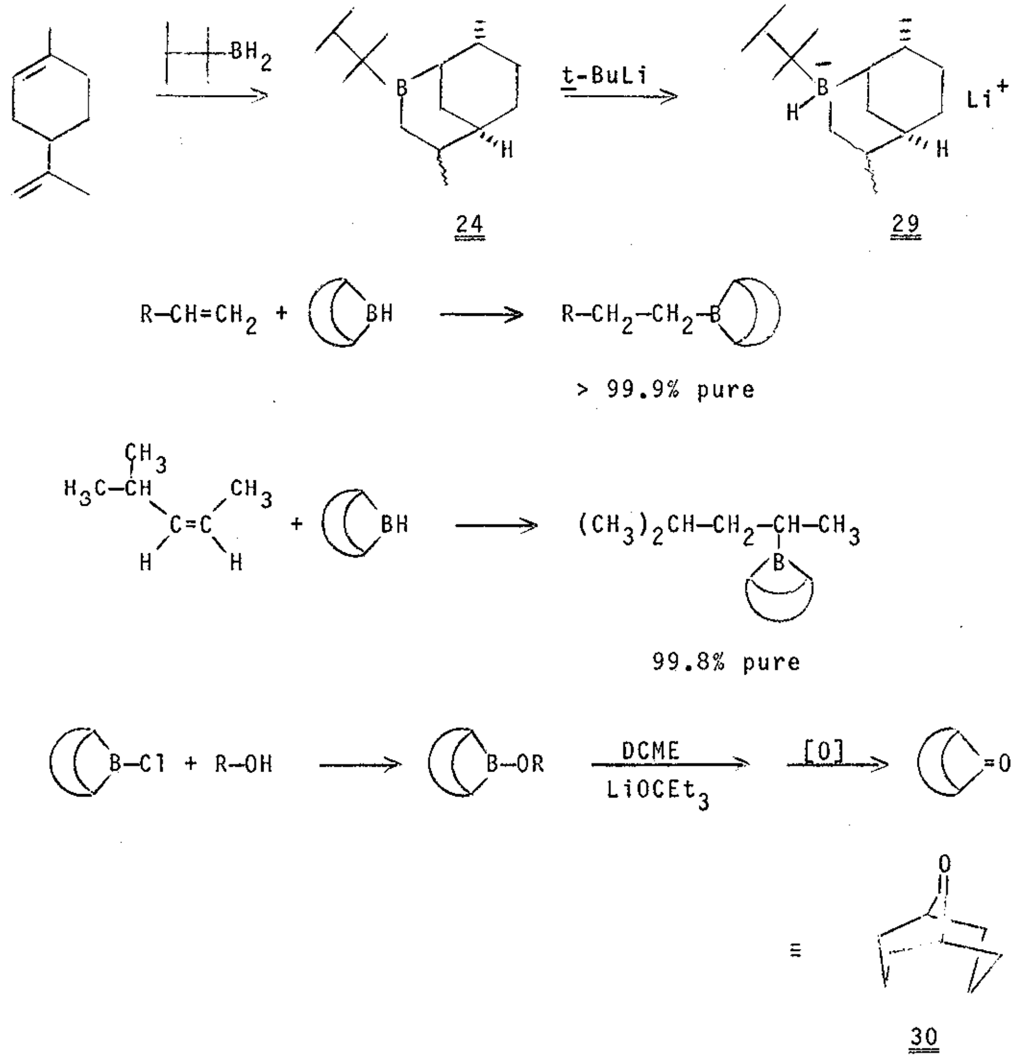
A good number of organoborane heterocycles are used as reagents. Thus 3,5-dimethylborinane (7) and 3,6-dimethylborepane (8) are useful for hydroboration and for the introduction of alkyl groups into *α,β*-unsaturated ketones[19] (Chart 13).

Chart 13



Similarly, the derivative from the cyclic hydroboration of limonene with thexylborane (24) yields thexyllimonylborohydride (29), which is highly stereospecific for the reduction of prostaglandin derivatives.[33] The product from the cyclic hydroboration of 1,5-cyclooctadiene, 9-borabicyclononane (9-BBN), is an exceptionally regiospecific hydroborating agent[30] (Chart 14), as well as a selective reducing agent.[34]

Chart 14



B-Chloro-9-BBN is readily converted into B-alkenyl-9-BBN, which can be subjected to DCME reaction leading to bicyclo[3.3.1]nonanone (30).

F. CONCLUSIONS

Cyclic hydroboration of dienes has proved to be a powerful tool in the synthesis of monocyclic and bicyclic organoboron heterocycles. Even though in the use of the trifunctional reagent, borane, polymer formation was a problem, this can be largely overcome by the use of monosubstituted boranes. With these versatile reagents, acyclic $\underline{\alpha},\underline{\omega}$-dienes can be converted to boracycloalkanes and mixed or cyclic dienes to borabicycloalkanes. Organoborane heterocycles are useful as selective hydroborating agents, selective reducing agents, reagents for 1,4-addition reactions of organoboranes and as the intermediates in the synthesis of various cyclic carbon structures. The exceptional regio- and stereoselectivity of hydroboration is reflected in the formation of isomerically pure products.

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