9-BORABICYCLO[3.3.1]NONANE A MOST UNUSUAL HETEROCYCLIC DIALKYLBORANE

Herbert C. Brown

The Richard B. Wetherill Laboratory of Chemistry

Purdue University, West Lafayette,

Indiana 47907, U.S.A.

Clinton F. Lane

Aldrich-Boranes, Inc., a Subsidiary of

Aldrich Chemical Company, Inc., Milwaukee,

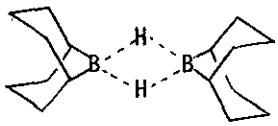
Wisconsin 53233, U.S.A.

The cyclic hydroboration of 1,5-cyclooctadiene provides 9-borabicyclo[3.3.1]nonane, an unusual boraheterocycle, with interesting chemical properties and unusual characteristics as a hydroborating and reducing agent.

CONTENTS

A. INTRODUCTION

The formation of organoborane heterocycles *via* cyclic hydroboration of dienes was the subject of a recent review in this journal.[1] As described previously, many interesting organoborane heterocycles are known. However, the most exciting and useful cyclic organoborane is undoubtedly bis-9-borabicyclo[3.3.1]nonane (9-BBN, 1).

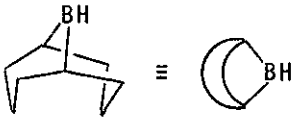


1

First characterized by Köster,[2] 9-BBN was found to exist as a stable crystalline dimer, mp 142°, which could even be sublimed. Subsequently, Knights and Brown reported that the direct reaction of 1,5-cyclooctadiene with borane in tetrahydrofuran (BH_3-THF) provides a highly convenient synthetic

route to 9-BBN.[3] This development opened the door to the application of 9-BBN for the hydroboration of alkenes.[4] The resulting *B*-alkyl-9-BBN compounds then found numerous applications in the rapidly expanding synthetic chemistry of organoboranes.[5]

9-BBN exists as the dimer 1, both in solution and as a crystalline solid. However, for purposes of discussion and for reaction stoichiometries, it is usually more convenient to treat it as the monomer. As a further convenience, the monomer can be represented in the shorthand notation shown (2).

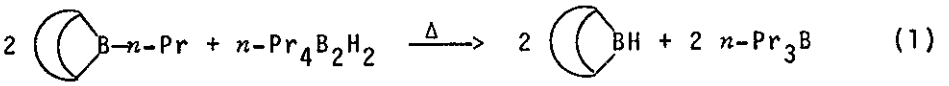


2

9-BBN is a truly unique dialkylborane. In this review, we will limit the discussion to the unusual chemistry of 9-BBN and to how the properties of 9-BBN are a direct consequence of the heterobicyclic structure. Obviously, 9-BBN is a highly useful synthetic reagent. Because of its commercial availability,[6] 9-BBN has become an important tool for the preparation of many organic compounds. A detailed discussion of the synthetic applications of 9-BBN and of *B*-R-9-BBN derivatives is beyond the scope of this review. These synthetic applications will be reviewed by us elsewhere.[7]

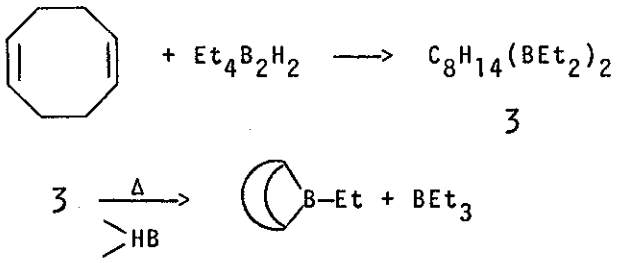
B. Preparation of 9-BBN

The first reported preparation of 9-BBN involved the thermal disproportionation of tetra-*n*-propyldiborane and *B*-*n*-propyl-9-BBN (eq 1).[2]



$$2\ \text{B}\text{—}n\text{-Pr} + n\text{-Pr}_4\text{B}_2\text{H}_2 \xrightarrow{\Delta} 2\ \text{BH} + 2\ n\text{-Pr}_3\text{B} \qquad (1)$$

The required *B*—R—9-BBN was prepared by Köster *via* a 2-step process.[8] For example, direct hydroboration of 1,5-cyclooctadiene with tetraethyldiborane gives 3, converted to *B*-ethyl-9-BBN by a thermal disproportionation in the presence of boron hydride catalyst (eq 2).[8] The direct thermal treatment

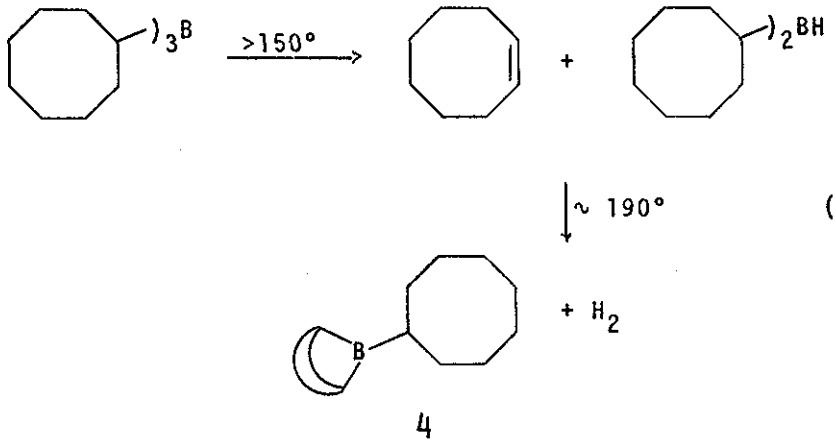


$$+\ \text{Et}_4\text{B}_2\text{H}_2 \longrightarrow \underset{3}{\text{C}_8\text{H}_{14}(\text{BEt}_2)_2} \qquad (2)$$

$$3 \xrightarrow[>\text{HB}]{\Delta} \text{B—Et} + \text{BEt}_3$$

of 1,5-cyclooctadiene with tetraethyldiborane results in extensive polymer formation.[9]

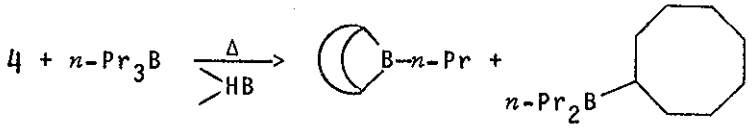
Alternatively, Köster found that tricyclooctylborane could be converted directly to *B*-cyclooctyl-9-BBN (4) by a thermal displacement reaction (eq 3).[10]



(3)

4

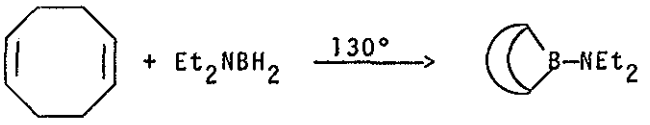
B-Cyclooctyl-9-BBN can be used to prepare other *B*-R-9-BBN compounds by a boron hydride catalyzed disproportionation (eq 4).[11]



(4)

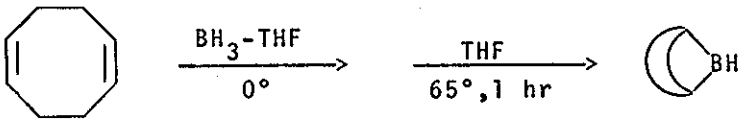
These thermal transformations of organoboranes have been reviewed by Köster.[12] Although of limited synthetic utility for the preparation of 9-BBN, these processes developed by Köster indicate that the 9-BBN heterocyclic ring system possesses remarkable thermal stability. In all cases involving a cyclooctylboron compound, the thermodynamically controlled product contains the 9-BBN moiety. For example, hydroboration of 1,5-cyclooctadiene with diborane followed by thermal isomerization apparently gives *B*-cyclooctenyl-9-BBN.[13] Similarly, the thermal reaction of diethylaminoborane with 1,5-cyclooctadiene gives a 68% isolated yield of *B*-diethylamino-9-BBN (eq

5).[14]



(5)

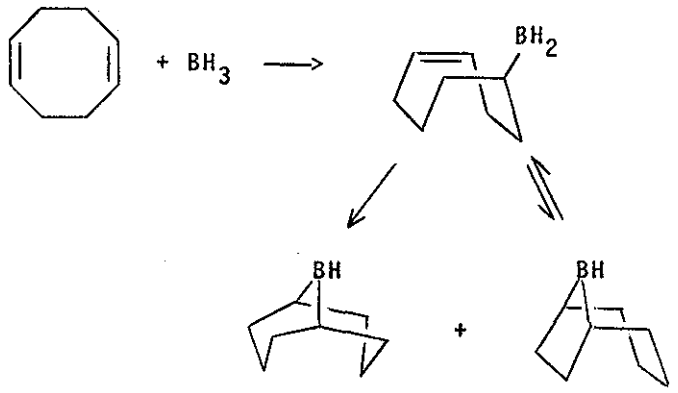
The first convenient synthesis of 9-BBN was reported by Knights and Brown.[3] In this greatly improved process, 1,5-cyclooctadiene is treated with BH_3-THF with ice bath cooling. A mild isomerization at 65° of the initial product then gives 9-BBN as a solution in THF in essentially quantitative yield (eq 6).[3] Upon cooling, 9-BBN can be isolated as the crystal-



(6)

line material in ∿ 65% yield.

A detailed examination of the hydroboration of dienes with BH_3-THF in a molar ratio of 1:1 revealed that 1,5-cyclooctadiene is a special case.[15] Thus, in marked contrast to all other dienes examined, the hydroboration of 1,5-cyclooctadiene appears to be essentially a simple cyclization (eq 7).



(7)

5 70%

6 30%

Oxidation of the reaction mixture produces a 70:30 mixture of *cis*-1,5- and *cis*-1,4-cyclooctanediols in 92% yield.[16] Obviously, the thermal treatment (1 hr at 65°) converts 6 to 5. The 1,5 isomer (5), with two fused six-membered rings, would be expected to be the thermodynamically controlled product.

C. Physical Properties of 9-BBN

High-purity, crystalline 9-BBN shows mp 152-155° (in a sealed, evacuated capillary).[17]

The boiling point of 9-BBN, 195° (12 mm), is unusually high. It should be contrasted to the boiling point of di-*n*-butylborane, 98° (12 mm). This marked difference in boiling points suggests that in contrast to $(n\text{-}Bu_2BH)_2$, $(9\text{-BBN})_2$ resists dissociation and distills as the dimer.[3]

The infrared spectrum of 9-BBN exhibits a strong absorption at 1567 cm^{-1}, either as a mineral oil mull of the solid or in solution.[17] This indicates the presence of a B–H–B bridge. Therefore, 9-BBN must exist as the dimer 1, in the solid state, in solution, and as the vapor (during distillation at 12 mm).

The mass spectrum of 9-BBN exhibits a prominent cluster of peaks at m/e 242, 243, and 244 in the approximate ratio of 1:8:16.[17] This corresponds to the peaks expected for the *molecular ion derived from the dimer* 1.

The chair-chair conformation shown in 1, as well as the boron-hydrogen bridge, has been confirmed by a crystal structure determination.[18]

A very useful property of 9-BBN is its solubility in a wide variety of common solvents, as shown in Table I. At 0°, the solubility of 9-BBN in THF is only 0.28 *M*.[19] Obviously, commercial 9-BBN in THF (0.5 *M*) should be stored at room temperature. Storage in a cold room will result in crystallization of 9-BBN.

D. Chemical Properties of 9-BBN

The most remarkable property of 9-BBN is its thermal stability. 9-BBN can be distilled at 195° (12 mm) or heated for 24 hr at 200° under nitrogen without loss of hydride activity.[3] In sharp contrast, disiamylborane isomerizes at 75°.[20] Obviously, 9-BBN is stable at room temperature. The

TABLE I. Solubility of 9-BBN

Solvent	Solubility at 25° (moles per liter)
Pentane	0.48
Hexane	0.52
Heptane	0.43
Decane	0.36
Benzene	0.81
Toluene	0.72
o-Xylene	0.63
Diethyl ether	0.39
Tetrahydrofuran	0.62
Diglyme	0.09
Methylene chloride	0.56
Chloroform	1.01
Carbon tetrachloride	0.71
Methyl sulfide	1.20

reagent can be stored, either as the solid or in solution, for indefinite periods (>4 years) without any noticeable change in activity, provided oxygen and water are rigorously excluded by maintaining an inert atmosphere.

The stability of colorless, crystalline 9-BBN toward air oxidation is unique among dialkylboranes. A fresh, unopened bottle of commercial, crystalline 9-BBN can be opened in the air and the entire contents transferred rapidly to a nitrogen flushed flask with only very minor loss of activity. Small amounts should NOT be removed in air at frequent intervals with the bottle being repeatedly opened and closed. Such a

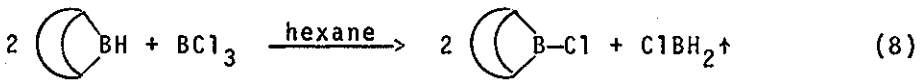
practice can, at worst, result in significant deterioration of the 9-BBN.[21] Consequently, for quantitative small-scale studies, manipulations of solid 9-BBN is best carried out under a nitrogen atmosphere, in order to maintain maximum hydride activity and purity. Solutions of 9-BBN, on the other hand, are quite reactive to both oxygen and water. Such solution should be rigorously protected from the atmosphere for both preparative and quantitative studies in the manner utilized in handling other organoboranes and reactive organometallics.[5]

The unusual inertness of crystalline 9-BBN toward oxygen may be a reflection of the unusual stability of the B—H—B bridge in the dimer. Support for this reasoning is evidenced by the observation that *B*—X—9-BBN compounds are very reactive toward oxygen. For example, neat *B*-methoxy-9-BBN, solid *B*-chloro-9-BBN, and solid *B*-hydroxy-9-BBN are all pyrophoric. Also, *B*-alkyl-9-BBN derivatives are quite reactive toward oxygen--more so than the corresponding trialkylboranes.[22] Hence, with the B—H—B bridge no longer present, the exposed position of the boron atom in the heterobicyclic bridge makes the derivatives of 9-BBN unusually reactive toward oxygen.

The reactions of 9-BBN in THF at 25° with water and alcohols afford quantitative yields of hydrogen and the corresponding *B*-hydroxy- and *B*-alkoxy-9-BBN derivatives.[17] For example, methanolysis of 9-BBN provides a convenient synthesis of *B*-methoxy-9-BBN.[23] However, these reactions are by no

means instantaneous, requiring 10-60 min for complete evolution of hydrogen. This is much slower than comparable solvolyses of disiamylborane.[24] Again, this sluggishness is probably a reflection of the unusual stability of the B–H–B bridge in the 9-BBN dimer.

9-BBN reacts readily with anhydrous hydrogen chloride in diethyl ether.[23] The *B*-chloro-9-BBN product must be isolated immediately since it cleaves ethers readily. *B*-Chloro-9-BBN is stable indefinitely in hydrocarbon solution.[23] Thus, an improved yield of *B*-chloro-9-BBN is possible *via* the reaction of 9-BBN with boron trichloride in hexane (eq 8).[25] A similar



(8)

91% isolated yield

reaction can be used to prepare *B*-bromo-9-BBN from 9-BBN and boron tribromide.[25] Also, protonolysis of 9-BBN with hydrogen bromide and treatment of 9-BBN with half an equivalent of bromine both yield *B*-bromo-9-BBN.[26]

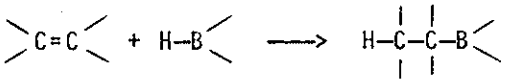
Alkaline hydrogen peroxide oxidation of 9-BBN proceeds cleanly, giving an essentially quantitative yield of *cis*-1,5-cyclooctanediol.[27] However, chromic acid oxidation of 9-BBN has resulted in conflicting reports. Bishop claims that 9-BBN can be converted to 1,5-cyclooctanedione by Jones oxidation.[28] On the other hand, Devaprabhakara and coworkers found that Brown-Garg oxidation of 9-BBN gives mainly cyclooctanone.[29]

Unfortunately, neither group has provided experimental details.

Two research groups have found that the reaction of 9-BBN with alkaline silver nitrate results in a mixture of products.[30,31] In both cases, cyclooctanone was reported to be the major product. Interestingly, one group reported the detection of *cis*-bicyclo[3.3.0]octane as a minor product.[31]

E. 9-BBN as a Hydroboration Reagent

Hydroboration of alkenes is a broadly applicable reaction which makes organoboranes readily available for applications in organic synthesis (eq 9).[5] BH_3—THF is the most widely used



(9)

hydroboration reagent. However, the polyfunctional nature of BH_3, its relatively low selectivity, and its low steric requirements sometimes cause difficulties. Various borane derivatives have been developed to overcome these problems associated with selective hydroborations.[32] Unfortunately, the limited stability of many of these borane derivatives means that they must be used relatively soon following their preparation.

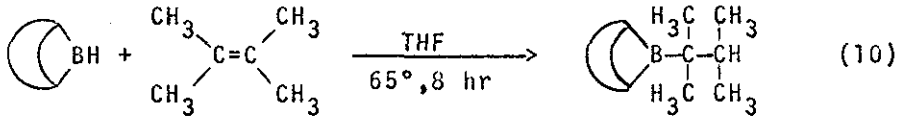
A detailed study proved that 9-BBN is a uniquely selective reagent for the hydroboration of alkenes.[4,17,33] Thus, the unusual stability and commercial availability makes 9-BBN an exceptionally convenient selective hydroboration reagent.

1. Hydroboration of Alkenes, Reactivity and Regioselectivity

The rate of reaction of 9-BBN with simple unhindered alkenes is considerably slower than that of disiamylborane. The earlier kinetic studies with disiamylborane indicated that hydroboration is second order, first order in alkene, and first order in the disiamylborane dimer.[34] Thus, the rate-determining step apparently involves the direct reaction of dimeric disiamylborane with the alkene. In sharp contrast, first order kinetics are observed for hydroboration of terminal alkenes with 9-BBN in THF.[35] This result is consistent with rapid trapping of a small, equilibrium concentration of monomeric 9-BBN by the reactive terminal alkene, causing dissociation of 9-BBN (dimer) to become the rate-determining step. Indeed, good agreement was realized between the first order rate constants obtained in studies of five different reactive alkenes.[35] This striking difference in mechanism may be a result of the unusually strong B—H—B bridge in the heterocyclic structure of 9-BBN (dimer).

Hydroborations with disiamylborane are normally carried out at 0°. Higher temperatures cannot be used to drive sluggish reactions to completion because of the instability of disiamylborane. Fortunately, both 9-BBN and *B*-R-9-BBN compounds exhibit remarkable thermal stabilities. Thus, hydroborations with 9-BBN can be carried out at 25° or higher to achieve essentially complete hydroboration for alkenes of widely different structural types.[17]

In general, the hydroborations of terminal alkenes with an equimolar amount of 9-BBN in THF are complete in 2 hr at 25°.[17] Internal alkenes vary widely in reactivity, but these hydroborations can be carried out without difficulty in THF at reflux. Under these conditions, almost all alkenes are quantitatively converted to *B*-R-9-BBN derivatives within 1 hr. Even the most sluggish alkene studied, 2,3-dimethyl-2-butene, is completely hydroborated in 8 hr at 65° (eq 10).[17]



(10)

The relative reactivities of a large number of alkenes containing various structural features toward hydroboration by 9-BBN in THF were recently determined.[36] Where comparable data were available, a comparison was made between 9-BBN and disiamylborane. Both reagents display large steric requirements, reacting preferentially with less hindered double bonds. However, 9-BBN is far more sensitive to electron influences. For example, *p*-methoxystyrene is 67 times as reactive as *p*-trifluoromethylstyrene toward 9-BBN, but is only 1.5 times as reactive toward disiamylborane.[36] This greater sensitivity to electronic influences could be attributed to a greater electronic demand by the B—H moiety in the strained 9-BBN *monomer* structure.

9-BBN exhibits a remarkable regiospecificity in the hydroboration of many alkenes.[17,33] The regioselectivity

obtained surpasses that obtained with all other hydroboration reagents. For example, terminal alkenes react to place the boron at the terminal position with a selectivity of at least 99.9% (eq 11).[17] Even more remarkable is the regioselectivity exhibited upon hydroboration of *cis*-4-methyl-2-pentene (eq 12).[17]

$$CH_3(CH_2)_3CH{=}CH_2 \xrightarrow[2)\ [O]]{1)\ HB} CH_3(CH_2)_3CH_2\underset{OH}{CH_2} + CH_3(CH_2)_3\underset{OH}{CH}CH_3 \quad (11)$$

HB Agent:		
BH_3	94%	6%
Sia_2BH	99%	1%
9-BBN	> 99.9%	

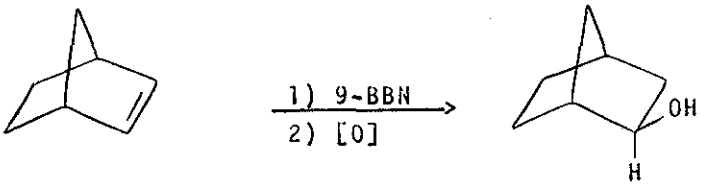
$$(CH_3)_2CH \quad CH_3 \;\; C{=}C \;\; H \quad H \xrightarrow[2)\ [O]]{1)\ HB} (CH_3)_2CHCH_2\underset{OH}{CH}CH_3 + (CH_3)_2CH\underset{OH}{CH}CH_2CH_3 \quad (12)$$

HB Agent:		
BH_3	57%	43%
Sia_2BH	97%	3%
9-BBN	99.8%	0.2%

The origin of this surprisingly high regioselectivity observed with 9-BBN is not clear.[33] The facile reaction of 9-BBN with highly substituted alkenes seems to indicate that the reagent is sterically less demanding than disiamylborane. However, the heterobicyclic structure of 9-BBN is rigid and steric crowding in the transition state cannot be relieved by internal rotation. Thus, the rigid bicyclic 9-BBN reagent may be more sensitive to subtle differences in steric environment than the more flexible, acyclic disiamylborane.

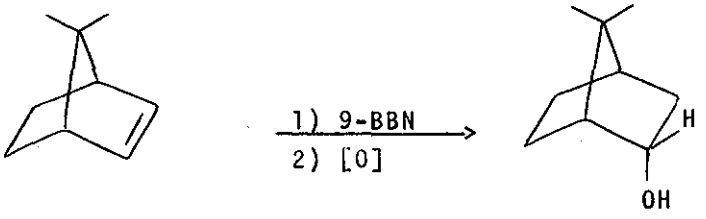
2. Hydroboration of Cyclic Alkenes, Regio- and Stereoselectivity

As expected, excellent stereoselectivity is shown for the hydroboration of cyclic alkenes with 9-BBN. For example, norbornene reacts to give the exo isomer almost exclusively (eq 13),[17] while 7,7-dimethylnorbornene gives the endo isomer predominantly (eq 14).[37] 1-Methylcyclohexene provides > 99.8% of the trans isomer (eq 15).[17]



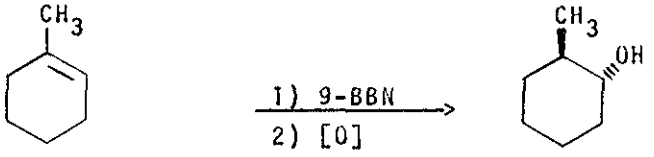
(13)

99.5% *exo*



(14)

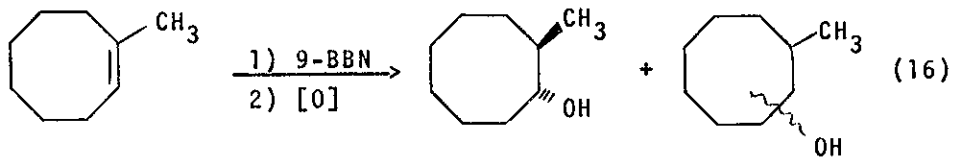
97% *endo*



(15)

>99.8% *trans*

In general, hydroboration of 1-alkylcycloalkenes with 9-BBN produces the corresponding *trans*-2-alkylcycloalkyl-9-BBN in essentially quantitative yield.[38] Even 1-methylcyclooctene (7) can be converted to the trans isomer in high isomeric purity (eq 16).[39] This is in sharp contrast to borane

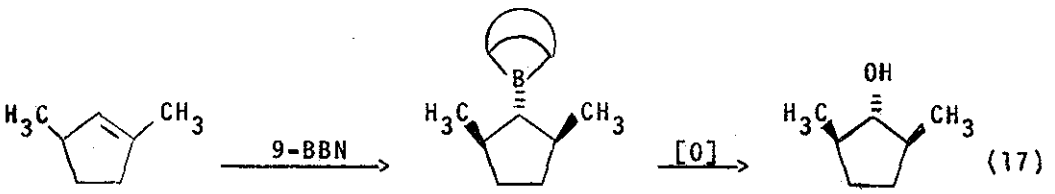


(16)

7 98% 2%

and disiamylborane where the organoborane initially derived from 7 undergoes a rapid isomerization.[40] This reluctance of *B*-alkyl-9-BBN derivatives to undergo thermal isomerization is probably a reflection of the smaller steric crowding in these organoboranes, as compared with other trialkylboranes.

Hydroboration of 3-alkylcycloalkenes with 9-BBN produces none of the *cis*-1,2-isomer.[38] Both diborane and disiamylborane form significant amounts of this isomer when 3-alkylcycloalkenes are hydroborated. The amazing selectivity exhibited by 9-BBN with regard to the hydroboration of 1-methyl- and 3-methylcycloalkenes lead to the prediction that 1,3-dimethylcycloalkenes should form exclusively the *trans,trans*-dimethylcycloalkyl-9-BBN derivative.[38] Indeed, this proved to be the case.[41] For example, 1,3-dimethylcyclopentene is converted exclusively into *t*-2,*t*-5-dimethylcyclopentanol (eq 17).[41]

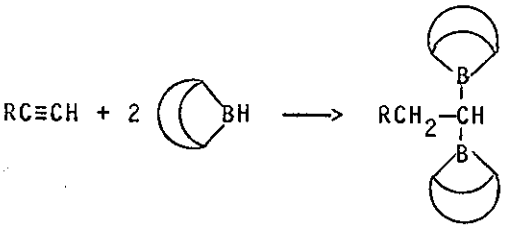


(17)

The results obtained for the hydroboration of cyclic alkenes clearly indicate that the regio- and stereoselectivity of 9-BBN surpasses that obtained with other hydroboration reagents. Also, these results provide additional evidence that 9-BBN is indeed very sensitive to subtle differences in the steric environment of the alkene.

3. Hydroboration of Alkynes

Terminal alkynes are readily converted to the 1,1-dibora derivative (eq 18).[42] To achieve monohydroboration of terminal



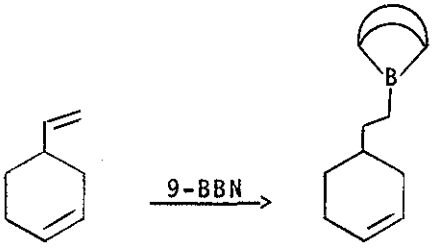
(18)

alkynes with 9-BBN, it is necessary to use a two-fold excess of the alkyne.[35] On the other hand, monohydroboration of internal alkynes occurs readily with an equimolar amount of 9-BBN in THF at 0°.[35] The corresponding *B*-alkenyl-9-BBN derivatives are formed in yields of 90-95%.

4. Hydroboration of Dienes

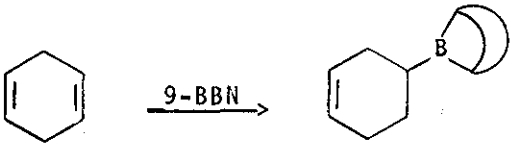
The data available[36] for the relative reactivities of representative alkenes toward 9-BBN are consistent with the results realized in the monohydroboration of dienes.[43] Dienes containing one terminal double bond and one internal double bond can be selectively hydroborated at the terminal position, as shown by the following examples (eq 19, 20).[43]

$$CH_3CH{=}CHCH_2CH{=}CH_2 \xrightarrow{9\text{-BBN}} CH_3CH{=}CHCH_2CH_2\overset{1}{C}H_2 \quad (19)$$



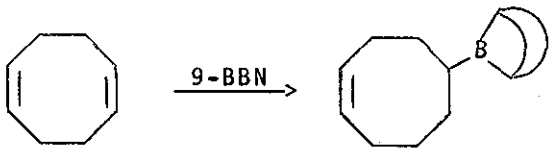
(20)

The symmetrical acyclic diene, 1,5-hexadiene, reacts with 9-BBN in a nearly statistical manner giving 17% unreacted diene, 50% monohydroboration, and 25% dihydroboration.[43] On the other hand, the symmetrical cyclic dienes, 1,4-cyclohexadiene and 1,5-cyclooctadiene, react with one equivalent of 9-BBN to form predominantly the mono- adduct (eq 21, 22).[43] Norbornadiene



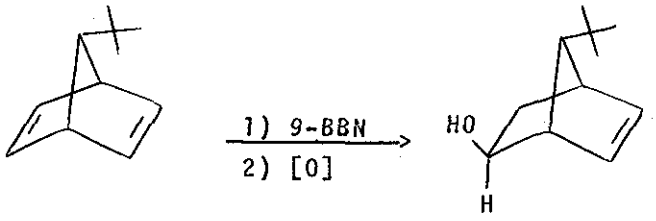
(21)

85%



85% (22)

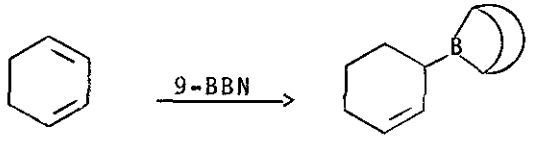
behaves much more like a simple symmetrical diene, yielding a product distribution approaching that predicted for a statistical reaction.[43] In contrast, 7-*tert*-butylnorbornadiene undergoes a relatively clean monohydroboration giving entirely the *exo* derivative 8 (eq 23).[44]



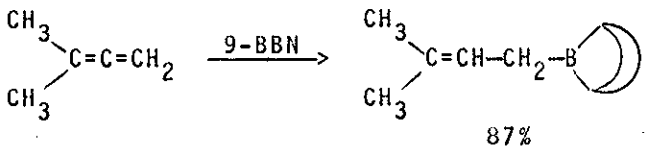
(23)

8

Monohydroboration of a limited number of conjugated dienes and allenes with 9-BBN can be controlled to give *B*-allyl-9-BBN compounds.[26] The monohydroboration of 1,3-cyclohexadiene (eq 24)[26] and 3-methyl-1,2-butadiene (eq 25)[26,45] provides two specific examples.



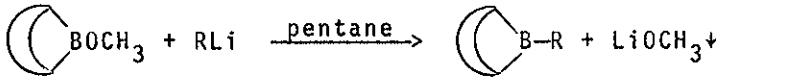
71% (24)



87% (25)

The most important result derived from the study of diene reactivity toward 9-BBN is that the remarkable sensitivity of 9-BBN to the structure of individual alkenes can be utilized, in many cases, to achieve a selective monohydroboration.[43] Thus, the known relative reactivities of simple alkene structures toward hydroboration with 9-BBN can be used directly to predict the point of hydroboration of nonconjugated dienes.

Hydroboration of alkenes, alkynes, and dienes with 9-BBN provides a highly convenient synthetic route to various *B*-alkyl-9-BBN derivatives. These *B*-R-9-BBN compounds are extremely useful intermediates for various synthetic organic transformations.[5] Unfortunately, a limited number of widely used alkyl groups cannot be attached to the 9-BBN moiety by direct hydroboration. Obvious examples include methyl, isopropyl, and *tert*-butyl. Also, *B*-aryl-9-BBN compounds must be prepared by an indirect route. These useful 9-BBN derivatives were originally prepared from 9-BBN and organolithium reagent by a two-step process.[46] Subsequently, an improved process was developed which involves the reaction of *B*-methoxy-9-BBN with organolithium reagents in pentane (eq 26).[23] Similarly, *B*-allyl-9-BBN



(26)

derivatives are readily prepared by the reaction of *B*-methoxy-9-BBN with allylic aluminum reagents.[26]

The development of 9-BBN as a hydroboration reagent provides a highly convenient synthetic route to *B*-alkyl-9-BBN compounds. Subsequent investigations revealed that 9-BBN is a remarkably regio-, stereo-, and chemoselective hydroboration reagent. Thus, an area of intense research activity has developed in recent years to utilize fully these readily available *B*-R-9-BBN derivatives for organic syntheses. Much progress has been made, and it is now possible to replace the boron-alkyl bond by many substituents or by new carbon-carbon bonds.[5,47,48]

Many of the new reactions of trialkylboranes result in the utilization of only one group on boron. Consequently, for the conversion of a valuable alkene, the yield is limited to 33%. In many cases, the alkyl group in a *B*-alkyl-9-BBN compound reacts preferentially, providing a much higher yield based on alkene. Equally important, 9-BBN is both an exceptionally convenient and a remarkably selective hydroboration reagent. Thus, 9-BBN has been used extensively as a selective reagent for synthetic transformations.[5,47,48] A discussion of these reactions of *B*-R-9-BBN compounds is beyond the scope of the present review and will be presented elsewhere.[7]

F. 9-BBN as a Reducing Agent

9-BBN exhibits certain remarkable physical and chemical properties quite distinct from those of borane and other mono-

and dialkylboranes (see sections C and D). It is a crystalline solid, exceptionally stable thermally, and soluble in a variety of solvents. It hydroborates alkenes with exceptionally high regio- and stereoselectivity, far greater than those observed for borane and other dialkylboranes (see section E). These remarkable properties of 9-BBN indicated that a systematic study of the reducing characteristics would be highly desirable. Such a study was recently completed and revealed that 9-BBN possesses many interesting and unusual features for a boron hydride reducing agent.[49]

The original article[49] should be consulted for details, but the overall results are summarized in Table II. These results should be useful both for predicting possible selective reductions and for deciding when a selective hydroboration of a functionally substituted alkene is possible.

The exceptional thermal stability of 9-BBN permits its use at higher temperatures, making practical the reduction of even difficultly reducible groups, such as carboxylic acids, esters, and lactones.[49] The reduction of octanoic acid (eq 27), methyl heptanoate (eq 28), and γ-butyrolactone (eq 29) provide specific examples.

$$CH_3(CH_2)_6COOH \xrightarrow[65°,18\ hr]{9\text{-BBN, THF}} CH_3(CH_2)_6CH_2OH \quad (27)$$

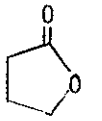
92% yield

$$CH_3(CH_2)_5COOCH_3 \xrightarrow[65°,4\ hr]{9\text{-BBN, THF}} CH_3(CH_2)_5CH_2OH \quad (28)$$

92% yield

TABLE II. Reaction of 9-BBN with Various Functional Groups in THF at 25°C

Compounds	Results
1°, 2°, and 3° Alcohols	Rapid H_2 evolution, no reduction
Simple phenols	—— " ——
Sulfonic acids	—— " ——
Carboxylic acids, 1° amides	Rapid H_2 evolution, very slow reduction
Oximes	Rapid H_2 evolution, slow reduction
Sulfoxides, azoxy compounds	Slow H_2 evolution, very slow reduction
Amines, thiols	Very slow H_2 evolution, no reduction
Aldehydes, ketones	Very rapid reduction
Alkenes, quinones	Rapid reduction
3° amides, acid anhydrides	—— " ——
Acid chlorides, lactones	—— " ——
Esters, epoxides	Slow reduction
Nitro compounds	Inert
Azo compounds, sulfides	—— " ——
Disulfides, sulfones	—— " ——
Tosylates, halides	—— " ——

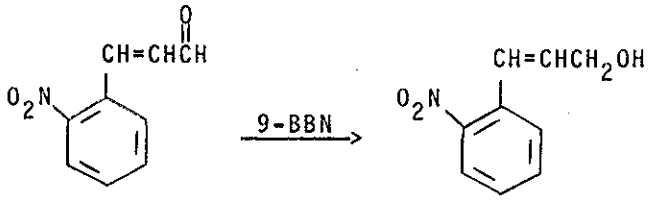


$$\xrightarrow[65°,2\ hr]{9\text{-BBN, THF}} HO(CH_2)_4OH \qquad (29)$$

98% yield

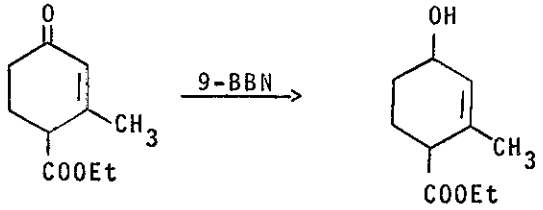
Disiamylborane is inert to acid chlorides,[24] and thexylborane reacts only sluggishly.[50] Therefore, it was somewhat unexpected that acid chlorides undergo a relatively rapid and quantitative reduction with 9-BBN.[49] As previously observed for hydroborations, this observation provides further evidence that 9-BBN is much more sensitive to electronic influences than other dialkylboranes.

Selective reduction of α,β-unsaturated aldehydes and ketones to the corresponding allylic alcohols represents one of the major applications of 9-BBN as a reducing agent.[51] The following specific examples illustrate the preparative value of the procedure for selective reductions (eq 30, 31).



(30)

75% isolated yield

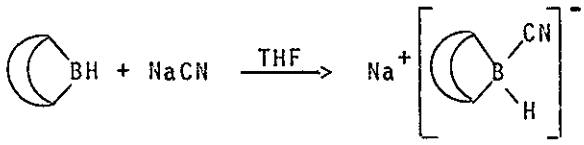


(31)

86% isolated yield

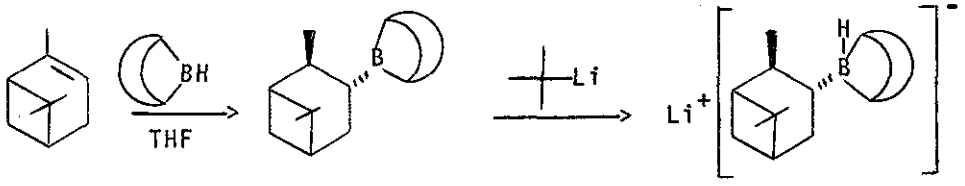
Reduction of free carboxyl groups in proteins with 9-BBN can be used to identify the *C*-terminal and other "accessible" carboxyl groups.[52] Consequently, 9-BBN should prove to be highly useful for the specific chemical modification of proteins and as a valuable conformational probe.

9-BBN "ate" complexes can also be used as reducing agents. Some applications of the cyano complex 9 were recently described, but these did not appear particularly promising.[53]



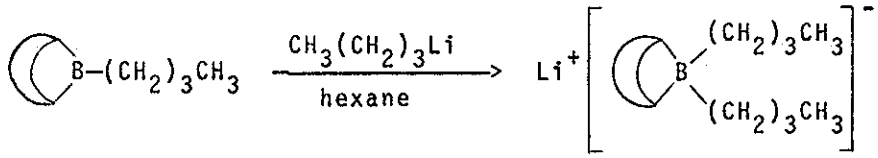
9

The isopinocampheyl borohydride 10 is much more promising. Applied to ketones, it provides optically active alcohols that are consistently enriched in the *R*-enantiomer (if (+)-α-pinene is used to prepare 10).[54]



10 +

Finally, 9-BBN "ate" complexes, such as the dibutyl compound **11**, exhibits interesting unexpected characteristics as reducing agents.[55]



11

This reducing agent reacts by a pathway which involves a truly remarkable rearrangement.[56] The fascinating chemistry of these dialkyl 9-BBN "ate" complexes will be discussed in detail in the accompanying review.[57]

G. Conclusions

It is evident from this review that the boraheterocycle, 9-BBN, possesses highly interesting characteristics and highly promising potential as a reagent. Its thermal stability is remarkable, very different from any other dialkylborane presently known. Its stability toward dissociation of the dimer to the monomer is also unique, far greater than that of any other known diborane derivative. These characteristics raise highly interesting theoretical questions as to the cause of their origin in the heterobicyclic structure.

The hydroborating characteristics of 9-BBN are also unique. It exhibits unusual regio- and stereospecificity. Compared to other hydroborating agents, it exhibits unusual sensitivity to electronic influences. *B*-Alkyl-9-BBN derivatives exhibit unusual thermal stability, resisting the facile isomerization exhibited by other organoborane derivatives.

Finally, in reductions, it also exhibits unique properties. Why is protonolysis of the reagent by various alcohols so slow compared with related organoboranes, such as disiamylborane? Why does it react so fast with acid chlorides in contrast to borane itself? Prior coordination of borane with the carbonyl group had been thought to be the initial stage in such reductions and the slow rate of reaction of acid chlorides was attributed to the low basicity of the carbonyl group in these derivatives. Yet, the fast reaction of 9-BBN is not in agreement with this interpretation. Borane reduces tertiary amides rapidly to the amines; 9-BBN reduces such amides to the alcohols. What is the cause of this major difference in behavior?

Past studies have emphasized exploration of the characteristics of 9-BBN as a reagent. Clearly there are also many interesting theoretical questions awaiting exploration.

Acknowledgement. The generous support of the National Science Foundation (CHE 76-20846), the National Institutes of Health (GM 10937), and the Army Research Office (DAAG 29-76-G-0218) in the study of the unusual characteristics of this boraheterocycle, 9-BBN, is gratefully acknowledged.

REFERENCES

1 E. Negishi, S. U. Kulkarni and H. C. Brown, *Heterocycles*, 1976, 5, 883.

2 R. Köster, *Angew. Chem.*, 1960, 72, 626.

3 E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, 1968, 90, 5280.

4 E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, 1968, 90, 5281.

5 H. C. Brown, "Organic Syntheses via Boranes," John Wiley and Sons, New York, 1975.

6 9-BBN is available from Aldrich Chemical Company as a crystalline solid and as a solution in THF or hexane.

7 H. C. Brown and C. F. Lane, manuscript in preparation.

8 R. Köster and G. Griaznov, *Angew. Chem.*, 1961, 73, 171.

9 R. Köster, G. Griaznov, W. Larbig and P. Binger, *Ann. Chem.*, 1964, 672, 1.

10 R. Köster and G. Rotermund, *Angew. Chem.*, 1962, 74, 252; *Angew. Chem. Int. Ed. Engl.*, 1962, 1, 217.

11 R. Köster, W. Larbig and G. W. Rotermund, *Ann. Chem.*, 1965, 682, 21.

12 R. Köster, *Angew. Chem. Int. Ed. Engl.*, 1964, 3, 174.

13 R. K. Sharma, B. A. Shoulders and P. D. Gardner, *Chem. Ind.*, 1962, 2087.

14 R. Köster, H. Bellut, S. Hattori and L. Weber, *Ann. Chem.*, 1968, 720, 32.

15 H. C. Brown, E. Negishi and P. L. Burke, *J. Am. Chem. Soc.*, 1972, 94, 3561.

16 In marked contrast, hydroboration of 1,5-cyclooctadiene with an equimolar amount of thexylborane followed by oxidation gives an 80:20 mixture of *cis*-1,4- and *cis*-1,5-cyclooctanediol in 93% yield: H. C. Brown and E. Negishi, *J. Am. Chem. Soc.*, 1972, 94, 3567.

17 H. C. Brown, E. F. Knights and C. G. Scouten, *J. Am. Chem. Soc.*, 1974, 96, 7765.

18 D. J. Brauer and C. Krüger, *Acta Crystallogr., Sect. B*, 1973, 29, 1684.

19 H. C. Brown and J. A. Sinclair, unpublished results, 1972.

20 H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, 1966, 88, 1433.

21 Impure, solid 9-BBN, which has undergone partial oxidation or hydrolysis, can be pyrophoric. However, if pure, crystalline 9-BBN is left open to the atmosphere (exposed on a glass plate), the material does not become pyrophoric and only slowly decomposes.

22 H. C. Brown and M. M. Midland, *Chem. Commun.*, 1971, 699.

23 G. W. Kramer and H. C. Brown, *J. Organometal. Chem.*, 1974, 73, 1.

24 H. C. Brown, D. B. Bigley, S. K. Arora and N. M. Yoon, *J. Am. Chem. Soc.*, 1970, 92, 7161.

25 R. Köster and M. A. Grassberger, *Ann. Chem.*, 1968, 719, 169.

26 G. W. Kramer and H. C. Brown, *J. Organometal. Chem.*, in press.

27 Reference 5, pp 32, 33.

28 R. Bishop, *J. Chem. Soc., Perkin I*, 1974, 2364.

29 M. M. Bhagwat, I. Mehrotra and D. Devaprabhakara, *J. Organometal. Chem.*, 1974, 82, C27.

30 I. Mehrotra and D. Devaprabhakara, *J. Organometal. Chem.*, 1974, 82, C1.

31 R. Murphy and R. H. Prager, *Tetrahedron Lett.*, 1976, 463.

32 For a discussion of hydroboration with borane derivatives, see reference 5, pp 37-50.

33 C. G. Scouten and H. C. Brown, *J. Org. Chem.*, 1973, 38, 4092.

34 H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, 1961, 83, 3417; 1963, 85, 2063.

35 C. G. Scouten, Ph.D. Thesis, Purdue University, West Lafayette, Indiana, 1975; *Diss. Abstr. Int. B*, 1976, 36, 4495.

36 H. C. Brown, R. Liotta and C. G. Scouten, *J. Am. Chem. Soc.*, 1976, 98, 5297.

37 H. C. Brown, J. H. Kawakami and K.-T. Liu, *J. Am. Chem. Soc.*, 1973, 95, 2209.

38 H. C. Brown, R. Liotta and L. Brener, *J. Am. Chem. Soc.*, in press.

39 H. Taniguchi, L. Brener and H. C. Brown, *J. Am. Chem. Soc.*, 1976, 98, 7107.

40 H. C. Brown and R. L. Klimisch, *J. Am. Chem. Soc.*, 1966, 88, 1430.

41 L. Brener and H. C. Brown, *J. Org. Chem.*, in press.

42 H. C. Brown and S. P. Rhodes, *J. Am. Chem. Soc.*, 1969, 91, 4306.

43 R. Liotta and H. C. Brown, *J. Org. Chem.*, manuscript submitted for publication.

44 W. C. Baird, Jr. and J. H. Surridge, *J. Org. Chem.*, 1972, 37, 304.

45 L. Chevolot, J. Soulié and P. Cadiot, *Tetrahedron Lett.*, 1974, 3435.

46 H. C. Brown and M. M. Rogić, *J. Am. Chem. Soc.*, 1969, 91, 4304.

47 H. C. Brown, "Boranes in Organic Chemistry," Cornell University Press, Ithaca, New York, 1972.

48 G. M. L. Cragg, "Organoboranes in Organic Synthesis," Marcel Dekker, Inc., New York, 1973.

49 H. C. Brown, S. Krishnamurthy and N. M. Yoon, *J. Org. Chem.*, 1976, 41, 1778.

50 H. C. Brown, P. Heim and N. M. Yoon, *J. Org. Chem.*, 1972, 37, 2942.

51 S. Krishnamurthy and H. C. Brown, *J. Org. Chem.*, 1975, 40, 1864; 1977, 42, 1197; C. F. Lane, *Aldrichimica Acta*, 1976, 9, 31.

52 M. Z. Atassi, A. F. Rosenthal and L. Vargas, *Biochim. Biophys. Acta*, 1973, 303, 379.

53 R. O. Hutchins, D. Kandasamy, C. A. Maryanoff, D. Masilamani and B. E. Maryanoff, *J. Org. Chem.*, 1977, 42, 82.

54 S. Krishnamurthy, F. Vogel and H. C. Brown, *J. Org. Chem.*, in press.

55 Y. Yamamoto, H. Toi, S.-I. Murahashi and I. Moritani, *J. Am. Chem. Soc.*, 1975, 97, 2558.

56 G. W. Kramer and H. C. Brown, *J. Organometal. Chem.*, 1975, 90, C1; *J. Am. Chem. Soc.*, 1976, 98, 1964.

57 H. C. Brown and G. W. Kramer, *Heterocycles*, following paper.

Received, 30th May, 1977