# Selective Reductions. XXI. 9-Borabicyclo[3.3.1]nonane in Tetrahydrofuran as a New Selective Reducing Agent in Organic Synthesis. Reaction with Selected Organic Compounds Containing Representative Functional Groups[1]

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The approximate rates, stoichiometry, and products of the reaction of 9-borabicyclo[3.3.1]nonane (9-BBN) with selected organic compounds containing representative functional groups under standard conditions (tetrahydrofuran, 25 °C) were determined in order to establish the utility of the reagent as a selective reducing agent. Primary, secondary, and tertiary alcohols and simple phenols evolve hydrogen rapidly and quantitatively. However, 2,6-di-*tert*-butylphenol is inert to this reagent even at 65 °C. Reaction with *n*-hexylamine and thiols is quite sluggish. Aldehydes and ketones of diverse structure are reduced rapidly and quantitatively to give the corresponding alcohols in excellent yields. However, the highly hindered ketone 2,2,4,4-tetramethyl-3-pentanone is quite inert even at 65 °C. Reduction of 2-methylcyclohexanone gives 40% *cis*- and 60% *trans*-2-methylcyclohexanol, respectively. Cinnamaldehyde is rapidly and cleanly reduced to cinnamyl alcohol; it undergoes further hydroboration very slowly. Anthraquinone is cleanly reduced to 9,10-dihydro-9,10-anthracenediol in 79% yield. Carboxylic acids liberate hydrogen rapidly and quantitatively and further reduction is very slow. However, in refluxing THF *n*-octanoic acid is reduced to *n*-octyl alcohol quantitatively in 24 h. Acid chlorides are reduced rapidly and quantitatively to the corresponding alcohols. Esters are reduced at a moderate rate at room temperature. However, at 65 °C complete reduction can be achieved in 4 h. γ-Butyrolactone is reduced to 1,4-butanediol at a moderate rate whereas the reduction of phthalide is very slow. Both *n*-octyl bromide and *p*-bromotoluene are inert toward his reagent. Epoxides such as 1,2-butylene oxide react very sluggishly. However, the presence of a catalytic quantity of borohydride enhances the rate dramatically. Primary amides evolve one hydrogen and further reaction is very slow. Tertiary amides are rapidly reduced to give alcohols as the major product. Nitriles are reduced slowly. 1-Nitropropane is inert, whereas nitrobenzene reacts very slowly. Azobenzene is inert whereas azoxybenzene is slowly reduced to the azobenzene stage. Cyclohexanone oxime liberates hydrogen rapidly and undergoes slow reduction to *N*-cyclohexylhydroxylamine. Phenyl isocyanate is rapidly reduced to the imine stage and further reduction is very slow. Pyridine and pyridine *N*-oxide undergo slow reduction. Dimethyl sulfoxide is reduced at a moderate rate, whereas the other sulfur compounds tested—disulfides, sulfide, sulfone tosylate, and sulfonic acids—are inert to this reagent under standard conditions. Kinetics of the reaction of 9-BBN with various readily reacting functional groups indicate that the dissociation of dimeric 9-BBN is the rate-determining step in these reactions. Relative reactivity studies on functional groups by competition experiments reveal that cyclohexanone can be reduced without significant attack on cyclopentene, cyclopentene can be hydroborated with total exclusion of ester, and acid chlorides can be reduced quantitatively without significant attack on esters.

The discovery of the hydroboration reaction in 1956 has made available a number of partially alkylated borane derivatives.[3] Among them 9-borabicyclo[3.3.1]nonane (9-BBN), a bicyclic dialkylborane obtained by the cyclic hydroboration of 1,5-cyclooctadiene, exhibits certain remarkable physical and chemical characteristics quite distinct from those of borane and other mono- and dialkylboranes.[4] It is a white, crystalline solid (mp 154–155 °C), exceptionally stable thermally, relatively insensitive to air, and soluble in a variety of organic solvents. It hydroborates olefins with exceptionally high regio- and stereoselectivity, far greater than those observed with borane and other dialkylboranes.[5] *B*-alkyl and *B*-aryl derivatives of 9-BBN have proved highly effective in the stereoselective synthesis of carbon structures through the selective migration of the alkyl or aryl group on boron.[3]

We recently reported an extensive investigation of the approximate rates and stoichiometry of the reaction in tetrahydrofuran (THF) at 0 °C of borane, thexylborane, and disiamylborane with organic compounds containing representative functional groups.[6] The remarkable properties of 9-BBN discussed earlier together with its commercial availability[7] persuaded us of the desirability of making a related systematic study of the reducing characteristics of this new reagent.

Accordingly, we undertook a detailed examination of the rate, stoichiometry, and products of the reaction of 9-BBN with representative functional groups and its applicability for selective reductions in organic synthesis. The results of these investigations are reported in the present paper.

## Results and Discussion

**Standard Solution of 9-BBN.** Solutions of 9-BBN in tetrahydrofuran were prepared either by the stoichiometric hydroboration of 1,5-cyclooctadiene with borane–THF at 0 °C and refluxing the resulting mixture for 2 h or by dissolving a calculated amount of commercial 9-BBN powder in dry THF to give the desired concentration. The concentration was determined by hydrolyzing a known aliquot of the solution with methanol–THF (1:1) at 25 °C and measuring the hydrogen evolved.

Such solutions are stable indefinitely under dry nitrogen atmosphere.

**Procedure for Rate and Stoichiometry Studies.** In order to define the reduction characteristics of 9-BBN, we undertook to examine the reaction of 70 organic compounds containing representative functional groups with excess 9-BBN. The procedure adopted was to add 5 mmol of the organic compound containing a representative functional group to 20 mmol of 9-BBN in sufficient tetrahydrofuran to give 40 ml solution. This made the reaction mixture 0.5 M in 9-BBN and 0.125 M in the compound under examination.[8] The solutions were maintained at constant temperature (ca. 25 °C) and the aliquots were removed at appropriate intervals of time and analyzed for "residual hydride" by hydrolysis.[9]

In this manner it was possible both to establish the rate at which reduction proceeds and the stoichiometry of the reaction, i.e., the number of hydrides utilized per mole of compound when the reaction comes to an effective halt.

**Product Analysis by GLC.** Having established the approximate rate and stoichiometry of the reaction, it was desirable to establish the nature of the products (and the intermediates in some typical cases) wherever it is interesting and offers possibility for selective reduction. Further, even with functional groups which are inert it was of interest to examine whether the compound can be recovered without any loss after prolonged contact with 9-BBN.

Accordingly, separate reactions on a 5-mmol scale were carried out. Either essentially a stoichiometric amount of 9-BBN or excess was utilized depending upon the functional group. In some instances, the temperature was raised to refluxing THF to shorten the reaction time.

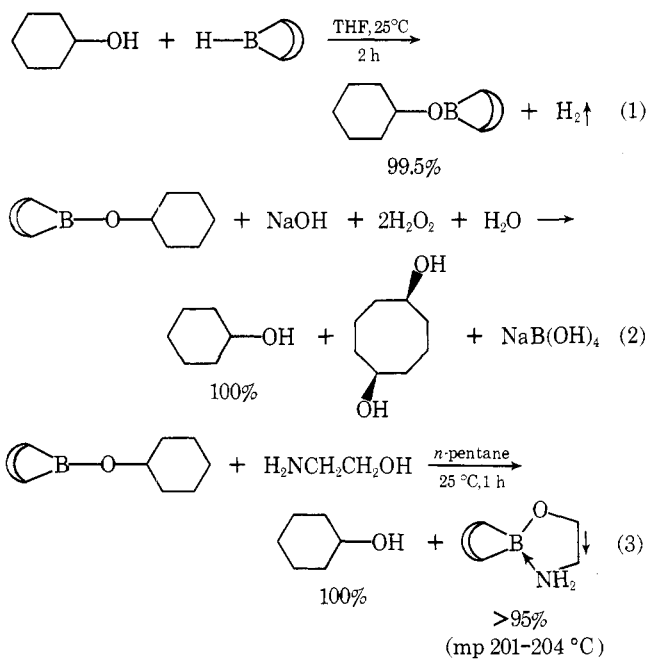
The products were identified by GLC comparison with authentic samples. Yields were determined, also by GLC analysis, utilizing internal standards and standard synthetic mixtures.

**Procedures for the Isolation of the Reaction Products. Removal of 9-BBN Moiety from the Reaction Mixture.** A large number of organic functional groups, such as alcohol, aldehyde, ketone, carboxylic acid, ester, acid chloride, amide, epoxide, etc., after reduction with 9-BBN end up as the *B*-alkoxy-9-BBN derivative. Consequently, a convenient separation of the alcohol from the 9-BBN moiety is highly desirable. We prepared *B*-cyclohexyloxy-9-BBN and explored various procedures for the recovery of cyclohexanol from 9-BBN moiety (eq 1).

Initially, we explored the feasibility of simply extracting from the organic phase *B*-hydroxy-9-BBN, produced on hydrolysis, with various complexing agents, such as sodium hydroxide, mannitol, etc. Various proportions of solvent mixtures were also examined (pentane–THF). However, these procedures were not satisfactory.

Finally, further research in this direction led to the development of two convenient workup procedures. The reaction mixture can be treated with alkaline hydrogen peroxide[10] to oxidize the 9-BBN moiety and the product separated by distillation from the *cis*-1,5-cyclooctanediol (procedure A) (eq 2).

Alternatively and more conveniently, the THF can be removed under vacuum from the reaction mixture and pentane added. The addition of 1 mol of ethanolamine precipitates the 9-BBN as the adduct. Removal of the pentane solution followed by distillation yields the product (procedure B)[11] (eq 3).

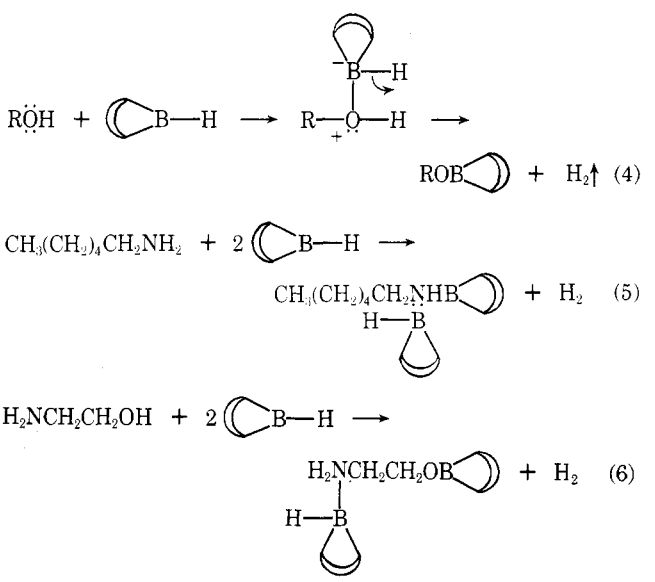



In addition to pentane, ether and benzene also work quite satisfactorily, as revealed by the recovery of cyclohexanol in yields of 100 and 97%, respectively. In a typical experiment utilizing ether as the solvent, the 9-BBN adduct of ethanolamine was isolated in 94% yield. Unfortunately, this adduct is soluble in THF.[12]

This serves as an excellent neutral workup procedure for compounds containing acid- and base-sensitive groups. Utilizing this procedure, a variety of products were isolated in 78–86% yield.

**Rate and Stoichiometry. Alcohols, Phenols, Amines, and Thiols.** All of the simple alcohols examined (primary, secondary, and tertiary) liberate hydrogen rapidly and quantitatively. While the primary and secondary alcohols require only 10 min for complete hydrogen evolution, tertiary alcohol requires 30 min. However, the highly hindered alcohol 2,2,4,4-tetramethyl-3-pentanol requires 6 h for complete hydrogen evolution under standard conditions. The product in all of these cases is the *B*-alkoxy-9-BBN. Thus, stoichiometric reaction of 9-BBN with 1-hexanol liberates hydrogen quantitatively in 60 min to give 100% yield of *B*-*n*-hexyloxy-9-BBN as determined by NMR using benzene as internal standard. The alcohol can be regenerated quantitatively either by simple hydrolysis or by treating with 2-aminoethanol in *n*-pentane. Phenol, 2,6-dimethylphenol, and 2,6-diisopropylphenol evolve hydrogen quantitatively in 30 min. However, 2,6-di-*tert*-butylphenol is completely inert toward 9-BBN; even under reflux (65 °C) no hydrogen evolution is observed in 24 h. This could be attributed to the inability of 9-BBN to coordinate with the oxygen atom of this phenol, presumably the first step in the protonolysis reaction (eq 4).

Both *n*-hexanethiol and benzenethiol are sluggish in their reactions. *n*-Hexylamine evolves only 1 equiv of hydrogen at 65 °C. However, hydrolysis of the reaction mixture with methanol–THF protonolyzes only 2 of the 3 equiv of 9-BBN remaining. The addition of 6 N HCl protonolyzes the third equivalent. Presumably we are forming an amine–borane complex (eq 5). Similarly, 9-BBN evolves hydrogen rapidly with 2-aminoethanol. Here again the hydrolysis of the third equivalent of 9-BBN requires 6 N HCl, indicating the formation of amine–borane complex (eq 6).




The results are summarized in Table I.

**Aldehydes and Ketones.** Simple aldehydes and ketones, both alkyl and aryl, consume 1 equiv of hydride, indicating clean reduction to the corresponding *B*-alkoxy-9-BBN (eq 7). Indeed, stoichiometric reduction of *n*-hexanal with 9-BBN gives a quantitative yield of *B*-*n*-hexyloxy-9-BBN (deter-

**Table I. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Alcohols, Phenols, Amines, and Thiols in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, min | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 67-56-1 | Methanol | 1 | 0.68 | 0.68 | 0.00 |
| | | 2 | 0.88 | 0.88 | 0.00 |
| | | 5 | 0.98 | 0.98 | 0.00 |
| | | 10 | 1.00 | 1.00 | 0.00 |
| 111-27-3 | 1-Hexanol | 5 | 0.95 | 0.95 | 0.00 |
| | | 10 | 1.00 | 1.00 | 0.00 |
| | | 30 | 1.00 | 1.00 | 0.00 |
| 100-51-6 | Benzyl alcohol | 30 | 1.03 | 1.03 | 0.00 |
| | | 60 | 1.03 | 1.03 | 0.00 |
| 623-37-0 | 3-Hexanol | 2 | 0.93 | 0.93 | 0.00 |
| | | 5 | 0.97 | 0.97 | 0.00 |
| | | 10 | 1.00 | 1.00 | 0.00 |
| | | 30 | 1.00 | 1.00 | 0.00 |
| 597-49-9 | 3-Ethyl-3-pentanol | 5 | 0.61 | 0.61 | 0.00 |
| | | 10 | 0.77 | 0.77 | 0.00 |
| | | 15 | 0.89 | 0.89 | 0.00 |
| | | 30 | 1.00 | 1.00 | 0.00 |
| | | 60 | 1.00 | 1.00 | 0.00 |
| 14609-79-1 | 2,2,4,4-Tetramethyl-3-pentanol | 15 | 0.20 | 0.20 | 0.00 |
| | | 30 | 0.29 | 0.29 | 0.00 |
| | | 180 | 0.76 | 0.76 | 0.00 |
| | | 360 | 1.00 | 1.00 | 0.00 |
| 108-95-2 | Phenol | 5 | 0.64 | 0.64 | 0.00 |
| | | 10 | 0.79 | 0.79 | 0.00 |
| | | 15 | 0.88 | 0.88 | 0.00 |
| | | 30 | 1.00 | 1.00 | 0.00 |
| 576-26-1 | 2,6-Dimethylphenol | 2 | 0.48 | 0.48 | 0.00 |
| | | 5 | 0.70 | 0.70 | 0.00 |
| | | 10 | 0.96 | 0.96 | 0.00 |
| | | 15 | 0.99 | 0.99 | 0.00 |
| | | 30 | 1.05 | 1.06 | 0.01 |
| 2078-54-8 | 2,6-Diisopropylphenol | 2 | 0.50 | 0.50 | 0.00 |
| | | 5 | 0.74 | 0.74 | 0.00 |
| | | 10 | 0.98 | 0.98 | 0.00 |
| | | 15 | 1.03 | 1.03 | 0.00 |
| | | 360 | 1.03 | 1.03 | 0.00 |
| 128-39-2 | 2,6-Di-*tert*-butylphenol | 60 | 0.00 | 0.00 | 0.00 |
| | | 720 | 0.00 | 0.00 | 0.00 |
| | | 1440 | 0.02 | 0.02 | 0.00 |
| | | 60[c] | 0.00 | 0.00 | 0.00 |
| | | 360[c] | 0.00 | 0.00 | 0.00 |
| | | 1440[c] | 0.00 | 0.00 | 0.00 |
| 111-31-9 | 1-Hexanethiol | 60 | 0.40 | 0.40 | 0.00 |
| | | 180 | 0.81 | 0.81 | 0.00 |
| | | 360 | 0.99 | 0.99 | 0.00 |
| | | 1440 | 1.00 | 1.00 | 0.00 |
| 108-98-5 | Benzenethiol | 180 | 0.68 | 0.68 | 0.00 |
| | | 360 | 0.84 | 0.84 | 0.00 |
| | | 720 | 0.95 | 0.95 | 0.00 |
| | | 1440 | 1.00 | 1.00 | 0.00 |
| 111-26-2 | *n*-Hexylamine[d] | 180 | 0.09 | 0.09 | 0.00 |
| | | 900 | 0.11 | 0.11 | 0.00 |
| | | 1440[c] | 1.00 | 1.00 | 0.00 |
| 141-43-5 | 2-Aminoethanol[d] | 2 | 0.96 | 0.96 | 0.00 |
| | | 5 | 1.04 | 1.04 | 0.00 |
| | | 10 | 1.04 | 1.04 | 0.00 |

[a] 5.0 mmol of compound was added to 20 mmol of 9-BBN (20 mmol of hydride in 40 ml of solution; 0.125 M in compound and 0.5 M in hydride). [b] mmol/mmol of compound. [c] Refluxing tetrahydrofuran. [d] Hydrolysis with 6 N hydrochloric acid.

mined by NMR using benzene as the internal standard), identical with the product obtained by the reaction of 9-BBN with 1-hexanol.

$$R_2CO + H{-}B\bigcirc \xrightarrow[25^\circ]{THF} R_2CHOB\bigcirc \qquad (7)$$

R = H, alkyl, aryl 95–100%

Cyclic and bicyclic ketones, such as cyclohexanone, 2-methylcyclohexanone, 4-*tert*-butylcyclohexanone, and norcamphor, are reduced completely in 30–60 min.

Hindered ketones, such as diisopropyl ketone and camphor, required 6 h for complete reduction. Highly hindered ketones, such as 2,2,4,4-tetramethyl-3-pentanone, proved inert toward 9-BBN. Even in refluxing THF, this ketone failed to react and was recovered in 96% yield after 24 h.

Cinnamaldehyde utilizes one hydride rapidly (<30 min) and the uptake of the second hydride is very slow and incomplete. An experiment carried out using a stoichiometric amount of

**Table II. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Aldehydes and Ketones in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 66-25-1 | *n*-Hexanal | 0.5 | 0.05 | 1.02 | 0.97 |
| | | 1.0 | 0.05 | 1.05 | 1.00 |
| 100-52-7 | Benzaldehyde | 0.5 | 0.01 | 0.96 | 0.95 |
| | | 1.0 | 0.01 | 1.01 | 1.00 |
| 110-43-0 | 2-Heptanone | 0.5 | 0.07 | 1.08 | 1.01 |
| | | 1.0 | 0.07 | 1.08 | 1.01 |
| 98-86-2 | Acetophenone | 0.5 | 0.06 | 1.03 | 0.97 |
| | | 1.0 | 0.06 | 1.05 | 0.99 |
| | | 3.0 | 0.06 | 1.05 | 0.99 |
| 119-61-9 | Benzophenone | 0.5 | 0.00 | 0.65 | 0.65 |
| | | 1.0 | 0.00 | 0.93 | 0.93 |
| | | 3.0 | 0.00 | 0.98 | 0.98 |
| | | 12.0 | 0.00 | 0.98 | 0.98 |
| 565-80-0 | Diisopropyl ketone | 0.5 | 0.05 | 0.41 | 0.36 |
| | | 1.0 | 0.05 | 0.62 | 0.57 |
| | | 6.0 | 0.05 | 1.06 | 1.01 |
| 815-24-7 | 2,2,4,4-Tetrameth- | 1.0 | 0.00 | 0.00 | 0.00 |
| | yl-3-pentanone | 12.0 | 0.00 | 0.00 | 0.00 |
| | | 24.0 | 0.00 | 0.00 | 0.00 |
| | | 24.0[c] | 0.00 | 0.00 | 0.00 |
| 108-94-1 | Cyclohexanone | 0.5 | 0.00 | 1.00 | 1.00 |
| 583-60-8 | 2-Methylcyclohexa- | 0.25 | 0.00 | 1.00 | 1.00 |
| | none | 1.0 | 0.00 | 1.00 | 1.00 |
| 1728-46-7 | 4-*tert*-Butylcyclo- | 0.25 | 0.00 | 1.00 | 1.00 |
| | hexanone | 1.00 | 0.00 | 1.00 | 1.00 |
| 497-38-1 | Norcamphor | 0.5 | 0.05 | 0.93 | 0.88 |
| | | 1.0 | 0.05 | 0.98 | 0.93 |
| | | 3.0 | 0.05 | 0.99 | 0.94 |
| 76-22-2 | Camphor | 0.5 | 0.00 | 0.67 | 0.67 |
| | | 1.0 | 0.00 | 0.82 | 0.82 |
| | | 3.0 | 0.00 | 0.94 | 0.94 |
| | | 6.0 | 0.00 | 1.01 | 1.01 |
| 104-55-2 | Cinnamaldehyde | 0.5 | 0.02 | 0.98 | 0.96 |
| | | 1.0 | 0.02 | 1.00 | 0.98 |
| | | 3.0 | 0.02 | 1.05 | 1.03 |
| | | 24.0 | 0.02 | 1.32 | 1.30 |
| | | 48.0 | 0.02 | 1.52 | 1.50 |

[a-c] See the corresponding footnotes in Table I.

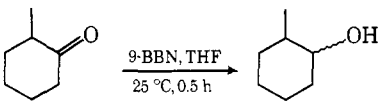
**Table III. Stereochemistry of the Reduction of Representative Cyclic and Bicyclic Ketones with 9-Borabicyclo[3.3.1]nonane in Tetrahydrofuran at 25 °C**

| Registry no. | Ketone | Total yield, % | Less stable isomer | Percentage |
|---|---|---|---|---|
| 591-24-2 | 2-Methylcyclohexanone | 100 | Cis | 40 |
| | 3-Methylcyclohexanone | 98 | Trans | 12 |
| | 4-*tert*-Butylcyclohexanone | 99 | Cis | 8 |
| | Norcamphor | 100 | Endo | 91 |
| | Camphor | 100 | Exo | 75 |

9-BBN (1 equiv) gave a quantitative yield of cinnamyl alcohol. Consequently, we are achieving the rapid reduction of the aldehyde group followed by the very sluggish hydroboration of the double bond. The results are summarized in Table II.

**Stereochemistry of the Reduction of Cyclic and Bicyclic Ketones with 9-BBN.** A detailed study of the reaction of various dialkylboranes with representative monocyclic, bicyclic, and polycyclic ketones[13] revealed that dialkylboranes, such as disiamylborane and di-3-pinanylborane, exhibit remarkable consistency in directing the reduction of both $\alpha$-substituted cycloalkanones and bicyclic ketones from the less hindered side to yield predominantly the less stable of the two possible epimers. Unfortunately, 9-BBN was not known when this study was carried out in our laboratory. Consequently, it was of interest to examine the ability of 9-BBN to introduce steric control into the reduction of such systems. Reactions were carried out at 25 °C utilizing essentially a stoichiometric quantity of 9-BBN (3–5% excess). The results are summarized in Table III.

2-Methylcyclohexanone gives only 40% cis isomer, significantly less than that observed with other dialkylboranes previously examined (eq 8). With 3-methyl- and 4-*tert*-




100% (40% cis) (8)

butylcyclohexanones, 9-BBN exerts little influence on the direction taken by the reduction. The product is predominantly the more stable of the two possible isomers. Reduction of bicyclic ketones, such as norcamphor and camphor, proceeds with preferential attack of the 9-BBN from the less hindered side, yielding the less stable of the two possible isomers predominantly (91% *endo*-2-norbornanol and 75% iso-

**Table IV. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Quinones in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 106-51-4 | *p*-Benzoquinone[c] | 1.0 | 0.37 | 0.40 | 0.03 |
| | | 6.0 | 0.39 | 0.46 | 0.07 |
| 84-65-1 | Anthraquinone[d] | 0.5 | 0.00 | 0.72 | 0.72 |
| | | 1.0 | 0.00 | 1.55 | 1.55 |
| | | 3.0[e] | 0.00 | 2.00 | 2.00 |

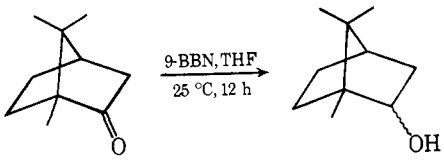
[a,b] See the corresponding footnotes in Table I. [c] White, gelatinous precipitate. [d] Reverse addition. After 2 h no solid anthraquinone was observed. [e] After methanolysis the resulting solution was fluorescent.

**Table V. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 142-62-1 | Hexanoic acid | 0.5 | 1.03 | | |
| | | 6.0 | 1.03 | 1.13 | 0.10 |
| | | 24.0 | 1.03 | 1.38 | 0.35 |
| | | 72.0 | 1.03 | 1.83 | 0.80 |
| | | 6.0[c] | 1.03 | 2.39 | 1.36 |
| | | 24.0[c] | 1.03 | 3.13 | 2.10 |
| 65-85-0 | Benzoic acid | 0.5 | 1.04 | 1.04 | 0.00 |
| | | 12.0 | 1.04 | 1.15 | 0.11 |
| | | 24.0 | 1.04 | 1.22 | 0.18 |
| | | 6.0[c] | 1.04 | 1.84 | 0.80 |
| 108-24-7 | Acetic Anhydride | 0.5 | 0.06 | 1.93 | 1.87 |
| | | 1.0 | 0.06 | 2.01 | 1.95 |
| | | 3.0 | 0.06 | 2.01 | 1.95 |
| | | 24.0 | 0.06 | 2.10 | 2.04 |
| 108-30-5 | Succinic anhydride | 1.0 | 0.03 | 0.35 | 0.32 |
| | | 3.0 | 0.03 | 0.58 | 0.55 |
| | | 24.0 | 0.03 | 1.31 | 1.28 |
| | | 48.0 | 0.03 | 1.70 | 1.67 |
| 85-44-9 | Phthalic anhydride | 6.0 | 0.04 | 0.41 | 0.37 |
| | | 24.0 | 0.04 | 0.92 | 0.88 |
| | | 48.0 | 0.04 | 1.52 | 1.48 |
| 142-61-0 | Hexanoyl chloride | 0.5 | 0.08 | 1.63 | 1.55 |
| | | 1.0 | 0.08 | 1.96 | 1.88 |
| | | 3.0 | 0.08 | 2.06 | 1.98 |
| | | 6.0 | 0.08 | 2.08 | 2.00 |
| 98-88-4 | Benzoyl chloride | 0.5 | 0.00 | 0.79 | 0.79 |
| | | 1.0 | 0.00 | 1.19 | 1.19 |
| | | 3.0 | 0.00 | 1.86 | 1.86 |
| | | 6.0 | 0.00 | 2.01 | 2.01 |

[a-c] See the corresponding footnotes in Table I.

borneol, respectively) (eq 9). This is comparable to the stereoselectivity achieved with disiamylborane.



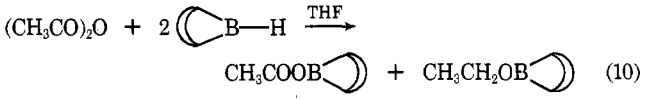

100% (75% exo) (9)

The lower stereoselectivity observed with 9-BBN in these transformations is attributed to two factors: (1) a decrease in the steric crowding around boron attributed to the rigid bicyclic structure; (2) a possible change in the nature of the species involved in the reduction (discussed later).

**Quinones.** *p*-Benzoquinone rapidly consumed 0.46 hydride per mole of compound of which 85% was utilized for hydrogen evolution and the remaining 15% for reduction, a value which did not change with time. A white, gelatinous precipitate was observed. The value does not correspond either to reduction to hydroquinone or 1,4-dihydroxycyclohexadiene. However, the reaction with anthraquinone is quite simple. It reacts fairly rapidly (3 h) with 2 equiv of reagent, without any hydrogen evolution, to give cleanly 9,10-dihydro-9,10-anthracenediol. Anthraquinone itself is only sparingly soluble in THF. After 2 h all of it went into solution. The results are summarized in Table IV.

**Carboxylic Acids and Derivatives.** Both hexanoic acid and benzoic acid liberate hydrogen rapidly and quantitatively (<5 min). Further reduction with hexanoic acid is very slow; however, complete reduction can be achieved at 65 °C in 24 h. The corresponding reaction with benzoic acid is very slow.

Acetic anhydride consumes two hydrides very rapidly for reduction with only a slow reduction thereafter, presumably to give ethanol and acetic acid (eq 10). Both succinic anhydride and phthalic anhydride react only at a moderate rate.




(10)

Surprisingly, both hexanoyl chloride and benzoyl chloride undergo reduction utilizing 2 equiv of hydride with remarkable ease (3–6 h). This was quite unexpected since both borane and thexylborane react sluggishly with acid chlorides and disiamylborane is inert. The results are summarized in Table V.

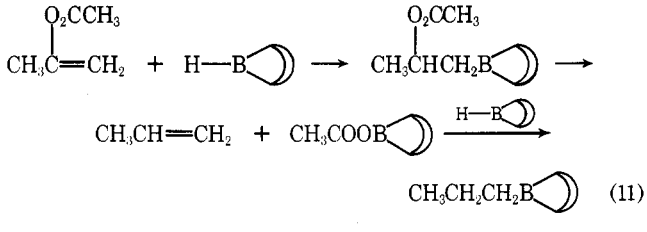
**Esters and Lactones.** Both ethyl hexanoate and phenyl acetate undergo reduction at a moderate rate and the reduc-

**Table VI. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Esters and Lactones in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 123-66-0 | Ethyl hexanoate | 1.0 | 0.00 | 0.09 | 0.09 |
| | | 3.0 | 0.00 | 0.36 | 0.36 |
| | | 6.0 | 0.00 | 0.70 | 0.70 |
| | | 12.0 | 0.00 | 1.15 | 1.15 |
| | | 24.0 | 0.00 | 1.60 | 1.60 |
| 93-89-0 | Ethyl benzoate | 24.0 | 0.00 | 0.45 | 0.45 |
| | | 48.0 | 0.00 | 0.68 | 0.68 |
| 122-79-2 | Phenyl acetate | 24.0 | 0.10 | 0.99 | 0.89 |
| | | 96.0 | 0.10 | 1.78 | 1.68 |
| | | 192.0 | 0.10 | 2.03 | 1.93 |
| 96-48-0 | γ-Butyrolactone | 0.5 | 0.00 | 0.87 | 0.87 |
| | | 1.0 | 0.00 | 1.30 | 1.30 |
| | | 3.0 | 0.00 | 1.85 | 1.85 |
| | | 6.0 | 0.00 | 2.00 | 2.00 |
| 87-41-2 | Phthalide | 6.0 | 0.00 | 0.71 | 0.71 |
| | | 24.0 | 0.00 | 1.56 | 1.56 |
| | | 48.0 | 0.00 | 2.07 | 2.07 |
| | | 72.0 | 0.00 | 2.08 | 2.08 |
| 591-87-7 | Isopropenyl acetate | 0.5 | 0.03 | 1.60 | 1.57 |
| | | 1.0 | 0.03 | 1.88 | 1.85 |
| | | 3.0 | 0.03 | 2.05 | 2.02 |
| | | 6.0 | 0.03 | 2.08 | 2.05 |
| | | 24.0 | 0.03 | 2.40 | 2.37 |

[a,b] See the corresponding footnotes in Table I.

tion of ethyl benzoate is slow. Ethyl hexanoate can be reduced rapidly in refluxing THF. Of the lactones γ-butyrolactone undergoes reduction at a moderate rate, with an uptake of two hydrides in 6 h. The reduction of phthalide is slow, requiring 48 h. Isopropenyl acetate consumes two hydrides rapidly and the further reduction proceeds only slowly. Presumably the reaction involves an initial hydroboration, followed by rapid elimination and the hydroboration of 1-propene produced in the elimination step (eq 11).



(11)

The results are summarized in Table VI.

**Epoxides and Halides.** Both *n*-octyl bromide and *p*-bromotoluene are completely inert toward 9-BBN and are recovered essentially in quantitative yield after 24 h. The reactions of 1,2-butylene oxide and cyclohexene oxide with 9-BBN are quite sluggish, requiring 3 and 8 days for completion, respectively (one hydride uptake). Styrene oxide proceeds beyond the utilization of one hydride, revealing 1.36 hydride uptake in 48 h. This is quite similar to the observations made with borane and other alkyl-substituted boranes, attributed to the attack of the aromatic nucleus.[6] The reaction of 1-methylcyclohexene oxide also proceeds slowly, accompanied by hydrogen evolution. One hydride is utilized for hydrogen evolution and one hydride is utilized for reduction, a behavior similar to that observed with borane, thexylborane, and disiamylborane indicating the formation of 2-hydroxymethylcyclohexanol following oxidation.

Although the reaction of epoxides with 9-BBN is quite slow, introduction of a catalytic amount of lithium borohydride has a dramatic effect on the rate of the reaction. Thus in the presence of 7.5 mol % of lithium borohydride, 1,2-butylene oxide is reduced completely in 30 min at 25 °C to give 98% of butanols (98% of 2- and 2% of 1-butanol).[14] Thus, the 9-BBN–borohydride combination provides yet another method for the rapid reduction of the epoxides. The results are summarized in Table VII.

**Amides and Nitriles.** Primary amides react to liberate only one of the two possible hydrogens; while the hydrogen evolution with the benzamide is complete in 0.5 h, hexanamide requires 24.0 h. Further reduction of benzamide is very slow. Hexanamide consumes one hydride at a moderate rate in 48 h and no further reduction is observed. Both the tertiary amides undergo rapid reduction consuming two hydrides to give alcohols as the major product. Reaction with nitriles is sluggish. However, in refluxing tetrahydrofuran the reduction of hexanenitrile is complete in 24 h. The results are summarized in Table VIII.

**Nitro Compounds and Their Derivatives.** 1-Nitropropane is inert to 9-BBN. However, nitrobenzene is reduced very slowly. Azobenzene is completely inert whereas azoxybenzene undergoes reduction, presumably to azobenzene, consuming two hydrides, one for the hydrogen evolution and the other for reduction. These results are similar to those observed with disiamylborane. The results are summarized in Table IX.

**Other Nitrogen Compounds.** Cyclohexanone oxime liberates one hydrogen rapidly and then slowly utilizes one hydride for reduction slowly (3 days), indicating reduction to the *N*-cyclohexylhydroxylamine. Phenyl isocyanate consumes two hydrides rapidly, with consumption of a third hydride proceeding sluggishly. Pyridine undergoes very slow reduction. Pyridine *N*-oxide utilizes two hydrides in total, 0.34 hydride for the hydrogen evolution and 1.67 hydride for the reduction. Borane and thexylborane liberate no hydrogen, consuming three hydrides at a moderate rate. Disiamylborane reduction utilizes two hydrides, one for the hydrogen evolution and the other for reduction. Based on these, we are now in a position to offer plausible explanations (Scheme I). The results are summarized in Table X.

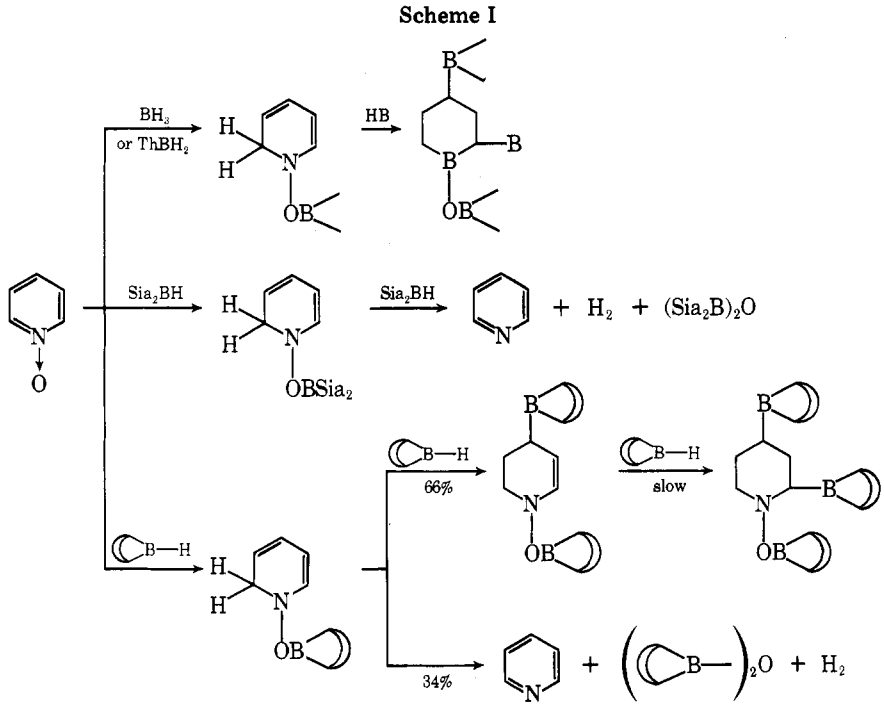
**Sulfur Compounds.** Among the sulfur compounds examined only dimethyl sulfoxide was reduced (presumably to dimethyl sulfide) by 9-BBN consuming one hydride for hydrogen evolution and one hydride for reduction. Both

**Table VII. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Halides and Epoxides in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 111-83-1 | *n*-Octyl bromide | 3.0 | 0.00 | 0.00 | 0.00 |
| | | 12.0 | 0.00 | 0.00 | 0.00 |
| | | 24.0 | 0.00 | 0.00 | 0.00 |
| 106-38-7 | *p*-Bromotoluene | 3.0 | 0.00 | 0.00 | 0.00 |
| | | 12.0 | 0.00 | 0.00 | 0.00 |
| | | 24.0 | 0.00 | 0.00 | 0.00 |
| 106-88-7 | 1,2-Butylene oxide | 12.0 | 0.03 | 0.46 | 0.43 |
| | | 24.0 | 0.03 | 0.67 | 0.64 |
| | | 48.0 | 0.03 | 0.86 | 0.83 |
| | | 96.0 | 0.03 | 1.04 | 1.01 |
| 286-20-4 | Cyclohexene oxide | 3.0 | 0.00 | 0.10 | 0.10 |
| | | 6.0 | 0.00 | 0.17 | 0.17 |
| | | 12.0 | 0.00 | 0.24 | 0.24 |
| | | 24.0 | 0.00 | 0.43 | 0.43 |
| 96-09-3 | Styrene oxide | 1.0 | 0.03 | 0.21 | 0.18 |
| | | 6.0 | 0.03 | 0.80 | 0.77 |
| | | 24.0 | 0.03 | 1.13 | 1.10 |
| | | 48.0 | 0.03 | 1.39 | 1.36 |
| 1713-33-3 | 1-Methylcyclohex-ene oxide | 12.0 | 0.81 | 1.36 | 0.65 |
| | | 24.0 | 0.90 | 1.66 | 0.76 |
| | | 48.0 | 0.96 | 1.92 | 0.96 |
| | | 72.0 | 1.03 | 2.00 | 0.97 |

[a,b] See the corresponding footnotes in Table I.

**Scheme I**




methanesulfonic acid and *p*-toluenesulfonic acid liberated hydrogen quantitatively. However, no reduction was observed. Disulfide, sulfide, sulfone, and cyclohexyl tosylate were all inert to 9-BBN. These observations are very similar to those previously realized with borane, thexylborane, and disiamylborane. The results are summarized in Table XI.

**Mechanistic Considerations. Kinetics of the Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Substrates. Mode of Action of 9-BBN.** Our preliminary exploration of the reaction of 9-BBN with hydroxylic compounds revealed certain interesting features. For example, the reactions of excess 9-BBN with simple alcohols such as methanol, ethanol, *tert*-butyl alcohol, and 3-ethyl-3-pentanol did not exhibit any significant difference in their rates. The reactions of 9-BBN with a stoichiometric quantity of methanol, 1-hexanol, 3-hexanol, etc., were also quite insensitive to the structure of the alcohol, requiring 1 h for completion. This was puzzling. The rates of reactions of disiamylborane with various alcohols have been studied.[6b] Hydrogen evolution was instantaneous with primary and secondary alcohols. However, no hydrogen evolution was observed with the tertiary alcohol, 3-ethyl-3-pentanol. Consequently, 9-BBN is evidently less sterically hindered than disiamylborane.

How can we account for the slower rates of reactions of 9-BBN with simple alcohols? Presumably, the sluggish reaction of 9-BBN with simple alcohols may be a reflection of the unusual stability of the boron–hydrogen bridge in the 9-BBN dimer. It would be desirable to have an understanding of the mechanism of these reactions which would provide a reasonable explanation for the marked difference in the behavior of 9-BBN and $Sia_2BH$.

Accordingly, we undertook to measure precisely the rates

**Table VIII. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Amides and Nitriles in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 628-02-4 | Hexanamide | 3.0 | 0.62 | 1.29 | 0.67 |
| | | 6.0 | 0.68 | 1.38 | 0.70 |
| | | 24.0 | 0.96 | 1.74 | 0.78 |
| | | 48.0 | 0.98 | 2.02 | 1.04 |
| 55-21-0 | Benzamide | 3.0 | 1.01 | 1.01 | 0.00 |
| | | 24.0 | 1.12 | 1.18 | 0.06 |
| 5830-30-8 | *N,N*-Dimethyl-hexanamide | 1.0 | 0.25 | 1.88 | 1.63 |
| | | 3.0 | 0.27 | 2.12 | 1.85 |
| 611-74-5 | *N,N*-Dimethyl-benzamide | 0.25 | 0.00 | 1.35 | 1.35 |
| | | 1.0 | 0.00 | 1.98 | 1.98 |
| | | 3.0 | 0.00 | 2.00 | 2.00 |
| | | 6.0 | 0.00 | 2.01 | 2.01 |
| 628-73-9 | Hexanenitrile | 3.0 | 0.00 | 0.10 | 0.10 |
| | | 6.0 | 0.00 | 0.22 | 0.22 |
| | | 24.0 | 0.00 | 0.40 | 0.40 |
| | | 48.0 | 0.00 | 0.88 | 0.88 |
| | | 3.0[c] | 0.00 | 1.43 | 1.43 |
| | | 6.0[c] | 0.00 | 1.74 | 1.74 |
| | | 24.0[c] | 0.00 | 2.16 | 2.16 |
| 100-47-0 | Benzonitrile | 1.0 | 0.00 | 0.23 | 0.23 |
| | | 3.0 | 0.00 | 0.36 | 0.36 |
| | | 24.0 | 0.00 | 0.74 | 0.74 |
| | | 48.0 | 0.00 | 0.78 | 0.78 |
| | | 3.0[c] | 0.01 | 1.04 | 1.03 |
| | | 6.0[c] | 0.01 | 1.23 | 1.22 |
| | | 24.0[c] | 0.01 | 1.55 | 1.54 |
| | | 48.0[c] | 0.01 | 1.60 | 1.59 |

[a,b] See the corresponding footnotes in Table I. [c] Refluxing THF.

**Table IX. Reaction of 9-Borabicyclo[3.3.1]nonane with Nitro Compounds and Their Derivatives in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 108-03-2 | 1-Nitropropane | 1.0 | 0.00 | 0.00 | 0.00 |
| | | 12.0 | 0.00 | 0.00 | 0.00 |
| 98-95-3 | Nitrobenzene | 1.0 | 0.00 | 0.00 | 0.00 |
| | | 12.0 | 0.00 | 0.00 | 0.04 |
| | | 24.0 | 0.00 | 0.08 | 0.08 |
| 103-33-3 | Azobenzene | 1.0 | 0.00 | 0.02 | 0.02 |
| | | 24.0 | 0.00 | 0.02 | 0.02 |
| 495-48-7 | Azoxybenzene | 24.0 | 0.66 | 1.32 | 0.66 |
| | | 72.0[c] | 0.86 | 1.89 | 1.03 |
| | | 96.0[c] | 0.91 | 2.00 | 1.09 |

[a,b] See corresponding footnotes in Table I. [c] Solution color changed from light yellow to orange.

**Table X. Reaction of 9-Borabicyclo[3.3.1]nonane with Other Nitrogen Compounds in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 100-64-1 | Cyclohexanone oxime | 6.0 | 1.01 | 1.27 | 0.26 |
| | | 24.0 | 1.01 | 1.77 | 0.76 |
| | | 36.0 | 1.01 | 1.86 | 0.85 |
| | | 86.0 | 1.01 | 2.04 | 1.03 |
| 103-71-9 | Phenyl isocyanate | 0.5 | 0.01 | 1.76 | 1.75 |
| | | 1.0 | 0.01 | 2.00 | 1.99 |
| | | 24.0 | 0.01 | 2.29 | 2.28 |
| 110-86-1 | Pyridine[c] | 1.0 | 0.00 | 0.06 | 0.06 |
| | | 24.0 | 0.00 | 0.09 | 0.09 |
| 694-59-7 | Pyridine *N*-oxide[c] | 1.0 | 0.21 | 0.53 | 0.32 |
| | | 3.0 | 0.32 | 1.19 | 0.87 |
| | | 12.0 | 0.34 | 1.75 | 1.49 |
| | | 24.0[d] | 0.34 | 1.87 | 1.53 |
| | | 48.0 | 0.34 | 2.01 | 1.67 |

[a,b] See the corresponding footnotes in Table I. [c] Yellow color was observed when compound was added. [d] Solution became colorless.

**Table XI. Reaction of 9-Borabicyclo[3.3.1]nonane with Representative Sulfur Derivatives in Tetrahydrofuran at 25 °C[a]**

| Registry no. | Compd | Time, h | Hydrogen evolved[b] | Hydride used[b] | Hydride used for redn[b] |
|---|---|---|---|---|---|
| 629-45-8 | Di-*n*-butyl disulfide | 1.0 | 0.00 | 0.00 | 0.00 |
| | | 6.0 | 0.00 | 0.00 | 0.00 |
| | | 24.0 | 0.00 | 0.00 | 0.00 |
| 882-33-7 | Diphenyl disulfide | 1.0 | 0.00 | 0.00 | 0.00 |
| | | 6.0 | 0.00 | 0.02 | 0.02 |
| | | 48.0 | 0.00 | 0.01 | 0.01 |
| 623-13-2 | Methyl *p*-tolyl sulfide | 1.0 | 0.00 | 0.00 | 0.00 |
| | | 6.0 | 0.00 | 0.02 | 0.02 |
| | | 24.0 | 0.00 | 0.04 | 0.04 |
| 67-68-5 | Dimethyl sulfoxide | 6.0 | 0.34 | 0.63 | 0.29 |
| | | 24.0 | 0.76 | 1.51 | 0.75 |
| | | 48.0 | 0.96 | 1.94 | 0.98 |
| | | 72.0 | 1.00 | 2.00 | 1.00 |
| 127-63-9 | Diphenyl sulfone | 1.0 | 0.01 | 0.02 | 0.01 |
| | | 6.0 | 0.01 | 0.02 | 0.01 |
| | | 48.0 | 0.01 | 0.03 | 0.02 |
| 75-75-2 | Methanesulfonic acid | 0.5 | 1.07 | 1.07 | 0.00 |
| | | 48.0 | 1.07 | 1.07 | 0.00 |
| 104-15-4 | *p*-Toluenesulfonic acid monohydrate | 1.0 | 3.03 | 3.07 | 0.04 |
| | | 24.0 | 3.03 | 3.07 | 0.04 |
| 953-91-3 | Cyclohexyl tosylate | 1.0 | 0.00 | 0.00 | 0.00 |
| | | 12.0 | 0.00 | 0.00 | 0.00 |

[a,b] See the corresponding footnotes in Table I.

**Table XII. Rates of Reaction of 9-Borabicyclo[3.3.1]nonane with Various Substrates in Tetrahydrofuran at 25 ± 0.5 °C**

| | | | Reaction, % | | | | | | | | | | | | First order |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Compd | M | M | 2 min | 4 min | 5 min | 8 min | 10 min | 12 min | 15 min | 20 min | 25 min | 30 min | 45 min | 60 min | $10^{-3}k^1$, $s^{-1}$ |
| Methanol[a] | 0.2 | 0.1 | 33 | 45 | 50 | 62 | 69 | 74 | 80 | 88 | 92 | 95 | 98 | 99 | 1.56 |
| | 0.4 | 0.1 | 33 | 41 | 50 | 61 | 68 | 74 | 80 | 87 | 91 | 95 | | | 1.52 |
| Methanol-*O*-*d*[a] | 0.2 | 0.1 | 32 | 44 | 48 | 61 | 69 | 73 | 80 | 87 | 91 | 94 | | | 1.53 |
| 1-Hexanol[a] | 0.2 | 0.1 | 32 | 42 | 47 | 59 | 65 | 70 | 76 | 85 | 90 | 93 | 96 | 98 | 1.39 |
| | 0.4 | 0.1 | 31 | 41 | 47 | 57 | 65 | 71 | 79 | 85 | 90 | 93 | 98 | | 1.44 |
| | 0.6 | 0.1 | 32 | 42 | 47 | 57 | 63 | 67 | 74 | 82 | 88 | 91 | 97 | 98 | 1.24 |
| 3-Hexanol[a] | 0.2 | 0.1 | 31 | 43 | 48 | 59 | 66 | 70 | 77 | 86 | 90 | 95 | 98 | | 1.42 |
| | 0.4 | 0.1 | 30 | 42 | 46 | 59 | 65 | 70 | 77 | 83 | 89 | 92 | | | 1.34 |
| Hexanoic acid[a] | 0.25 | 0.125 | 32 | 44 | 48 | 60 | 66 | 73 | 79 | 85 | 91 | 95 | 99 | | 1.77 |
| | 0.50 | 0.125 | 32 | 42 | 47 | 58 | 65 | 70 | 77 | 85 | 90 | 94 | 98 | | 1.37 |
| Methanesulfonic acid[a] | 0.2 | 0.1 | 34 | 44 | 50 | 61 | 67 | 73 | 79 | 86 | 92 | 95 | 98 | | 1.46 |
| | 0.4 | 0.1 | 34 | 44 | 50 | 61 | 67 | 73 | 78 | 86 | | 93 | 98 | | 1.44 |
| Cyclohexanone[b] | 0.2 | 0.1 | 32 | 43 | 48 | 57 | 61 | | 73 | | | | | | 1.15 |
| | 0.4 | 0.1 | 34 | | 49 | 58 | 64 | | | | | | | | 1.22 |
| Cyclopentene[c] | 0.2 | 0.1 | | 36 | | 51 | | 59 | | 75 | | | | | 1.06 |
| | 0.4 | 0.2 | | | | | | | | | | | | | 1.07 |

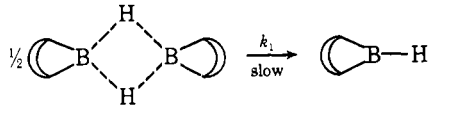
[a] Reaction was monitored by measuring the hydrogen evolved with time. [b] Monitored by GLC using an internal standard. [c] Data taken from ref 5c.

of reactions of 9-BBN with various proton sources as well as with other typical functional groups, such as ketones and olefins at 25 ± 0.5 °C at various concentrations. The results are summarized in Table XII.

It is clearly evident that methanol, 1-hexanol, and 3-hexanol, alcohols in the order of increasing steric requirements, all protonolyze 9-BBN at essentially the comparable rates. Even stronger acids, such as methanesulfonic acid and hexanoic acid, protonolyze 9-BBN, at essentially the same rate. Increasing the concentration of the proton source two- or threefold did not alter the rate. Even more important is the observation that the rate of reaction of cyclohexanone and the rate of hydroboration of reactive olefins, such as cyclopentene, with 9-BBN are comparable to the protonolysis rate. These rates also were independent of the reactant concentration. All of these reactions gave excellent first-order kinetic plots.

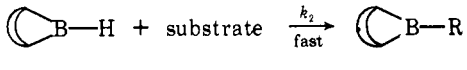
It was previously pointed out that 9-BBN exists as an exceptionally tightly bound dimer in solid as well as in solution. Thus, the above experimental observations can be attributed to the following steps (eq 12 and 13).

(a) A slow rate-determining dissociation of the dimer to the monomer.




(12)

(b) Rapid capture of the monomer by reactive substrates.




(13)

Consequently, we must be measuring the rate of dissociation of dimer to the monomer, and dimeric 9-BBN does not react. This is in contrast to the behavior of disiamylborane.

**Table XIII. Relative Reactivities of Various Functional Groups toward 9-Borabicyclo[3.3.1]nonane in Tetrahydrofuran at 25 °C[a]**

| Expt | Compd used | mmol | 9-BBN, mmol | Products[b] | Mol % | $K_{rel}$[c] |
|---|---|---|---|---|---|---|
| 1 | Hexanal | 5.0 | | Hexanal | 5.0 | |
| | | | 5.0 | 1-Hexanol | 44.3 | 27.0 |
| | 2-Heptanone | 5.0 | | 2-Heptanone | 45.9 | |
| | | | | 2-Heptanol | 3.8 | |
| 2 | Cyclohexanone | 5.0 | | Cyclohexanone | 23.5 | |
| | | | 5.0 | Cyclohexanol | 26.5 | 1.2 |
| | Methanol | 5.0 | | Methanol | 26.8 | |
| | | | | *B*-Methoxy-9-BBN | 23.2 | |
| 3 | Cyclohexanone | 5.0 | | Cyclohexanone | 25.0 | |
| | | | 5.0 | Cyclohexanol | 25.5 | 1.1 |
| | 2-Cyclohexen-1-one | 5.0 | | 2-Cyclohexen-1-one | 27.0 | |
| | | | | 2-Cyclohexen-1-ol | 22.5 | |
| 4 | Cyclohexanone | 5.0 | | Cyclohexanone | 15.0 | |
| | | | 5.0 | Cyclohexanol | 37.0 | |
| | Cyclopentanone | 5.0 | | Cyclopentanone | 34.5 | 3.2 |
| | | | | Cyclopentanol | 13.0 | |
| 5 | Cyclohexanone | 5.0 | | Cyclohexanone | 6.0 | |
| | | | 5.0 | Cyclohexanol | 43.5 | |
| | Cyclopentene | 5.0 | | Cyclopentene | 47.3 | 37.5 |
| | | | | *B*-Cyclopentyl-9-BBN | 3.2 | |
| 6 | Cyclopentene | 5.0 | | Cyclopentene | 1.5 | |
| | | | 5.0 | *B*-Cyclopentyl-9-BBN | 50.0 | |
| | Ethyl hexanoate | 5.0 | | Ethyl hexanoate | 50.0 | |
| | | | | 1-Hexanol | 0.0 | |
| 7 | Cyclopentene | 5.0 | | Cyclopentene | 5.5 | |
| | | | 10.0 | *B*-Cyclopentyl-9-BBN | 43.5 | |
| | Caproic acid[d] | 5.0 | | Caproic acid[e] | 49.0 | |
| | | | | 1-Hexanol | 1.0 | |
| 8 | Cyclopentene | 5.0 | | Cyclopentene | 2.5 | |
| | | | 5.0 | *B*-Cyclopentyl-9-BBN | 50.0 | |
| | Epoxycyclohexane | 5.0 | | Epoxycyclohexane | 46.5 | |
| | | | | Cyclohexanol | 0.0 | |
| 9 | Hexanoyl chloride | 5.0 | | Hexanoyl chloride[e] | <2.5 | |
| | | | 10.5 | 1-Hexanol | 47.5 | |
| | Methyl heptanoate | 5.0 | | Methyl heptanoate | 49.8 | |
| | | | | 1-Heptanol | <0.1 | |
| 10 | Hexanoyl chloride | 5.0 | | Hexanoyl chloride[e] | 5.5 | |
| | | | 10.0 | 1-Hexanol | 44.5 | |
| | 2-Hexyl acetate | 5.0 | | 2-Hexyl acetate | 49.0 | |
| | | | | 2-Hexanol | <1.0 | |

[a] Unless otherwise indicated, reaction mixtures were 0.2 M in both 9-BBN and the substrates. [b] Analysis by GLC using an internal standard. [c] $K_{rel} = k_A/k_B$. [d] An additional 1 equiv of 9-BBN was used to correct for quantitative hydrogen evolution, 9-BBN concentration 0.4 M. [e] Not determined directly; estimated by difference.

Kinetics of the hydroboration of olefins with disiamylborane indicate the dimer to be the hydroborating agent, not the monomer.[15] Accordingly, this is the basis for differences observed with $Sia_2BH$ and 9-BBN. Further, protonolysis of 9-BBN with methanol and methanol-*O*-*d* shows no significant difference in their rates ($k_{MeOH}/k_{MeOD} = 1.02$), indicating that O–H bond breaking is not involved in the rate-determining step, supporting the above mechanism.

Finally, the above mechanism suggests that if two rapidly reacting substrates of different reactivities are allowed to compete for the limited quantity of 9-BBN, then the monomer 9-BBN should be able to distinguish them. Indeed, $k_{cyclohexanone}/k_{cyclopentene}$ was found to be 37.5 (discussed in the next section) when the reaction was carried out in the same flask as a competitive reaction; when the relative reactivities were compared kinetically, the ratio was 1.08.

**Relative Reactivity Studies. Competition Experiments.** Extensive study of the reaction of typical organic functional groups with 9-BBN gave a rough indication of the relative ease of reduction by this reagent of representative functional groups.

However, functional groups which react rapidly with 9-BBN did not show any significant difference in their reactivity, since dissociation of the dimer is the rate-determining step. Consequently, it was desirable to examine the relative reactivities of certain functional groups by means of competition experiments. Accordingly, equimolecular amounts of two compounds containing representative functional groups were allowed to compete for a limited quantity of 9-BBN in THF. The 9-BBN was added slowly to the reaction mixture maintained at 25 °C. After appropriate time intervals, the mixture was analyzed by GLC using an internal standard. The results are summarized in Table XIII.

The competitive reduction of a mixture of hexanal and 2-heptanone resulted in the preferential reduction of the aldehyde of over 85% ($k_{hexanal}/k_{2\text{-heptanone}} = 27$). The reactivity of ketone and alcohol are essentially identical as evident from the cyclohexanone–methanol pair ($k_{cyclohexanone}/k_{methanol} = 1.2$). Further, there is no significant difference between conjugated 2-enones and a saturated ketone ($k_{cyclohexanone}/k_{2\text{-cyclohexenone}} = 1.1$). Cyclohexanone is reduced at a faster rate than cyclopentanone by a factor of 3.2.

The ease of reduction of aldehydes and ketones by this reagent is remarkable. Thus, 9-BBN reacts with cyclohexanone in preference to cyclopentene ($k_{cyclohexanone}/k_{cyclopentene} = 37.5$). This is complementary to the behavior of borane, which

exhibits greater reactivity toward olefins. This led to the detailed systematic exploration of 9-BBN for the selective reduction of $\alpha,\beta$-unsaturated aldehydes and ketones to the corresponding allylic alcohols.[16]

Cyclopentene reacts completely to the total exclusion of an ester, an acid, and an epoxide.

Finally, acid chlorides are reduced rapidly and preferentially without any significant attack on the esters (≤2%).

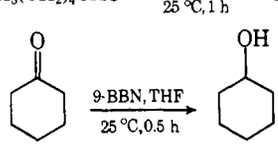
With certain pairs the relative reactivity $k_{rel} = k_A/k_B$ was calculated using the expression of Ingold and Shaw.[17]

$$k_{rel} = \frac{\log A_0 - \log A}{\log B_0 - \log B}$$

**Synthetic Utility.** In order to establish the synthetic utility of this new reducing agent product studies for the reduction of selected compounds containing representative functional groups were carried out. We utilized essentially stoichiometric quantity of 9-BBN (as defined by stoichiometric studies) with most of the functional groups examined. With carboxylic acids, a modest excess of 9-BBN, 4.00 9-BBN per mole of RCOOH (33% excess), was utilized. Reductions were carried out either at 25 or 65 °C (refluxing THF) depending upon the ease with which the functional group undergoes reduction. As already discussed earlier, the products were identified by GLC or by isolation.

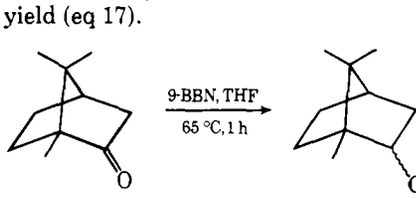
Simple aldehydes and ketones such as hexanal, cyclohexanone, 2-methylcyclohexanone, etc., were reduced rapidly to their corresponding alcohols in excellent yield (>95%) (eq 14 and 15). Even the hindered ketone camphor was reduced

$$CH_3(CH_2)_4CHO \xrightarrow[25\ °C,1\ h]{9\text{-BBN, THF}} CH_3(CH_2)_4CH_2OH\ 100\% \quad (14)$$



100% (78% isolated) (15)

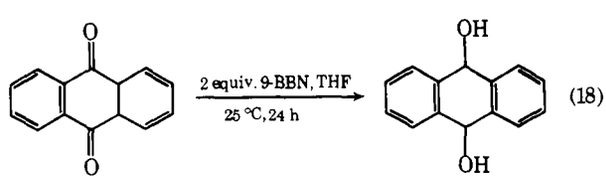
to borneols in quantitative yield in 12 h at 25 °C. In refluxing THF the complete reduction can be achieved in 1 h (eq 16). Cinnamaldehyde was converted into cinnamyl alcohol in 98% yield (eq 17).



100% (81% isolated) (16)

$$C_6H_5CH{=}CH\cdot CHO \xrightarrow[0\ °C,2\ h]{9\text{-BBN, THF}} C_6H_5CH{=}CHCH_2OH\ 98\% \quad (17)$$

Anthraquinone was converted into 9,10-dihydro-9,10-anthracenediol in 79% yield (eq 18).



(18)

(79% isolated)

Carboxylic acids such as *n*-hexanoic acid and *n*-octanoic acid were converted into *n*-hexyl alcohol and *n*-octyl alcohol, respectively, in 92% yield in refluxing THF (eq 19).

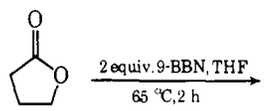
$$CH_3(CH_2)_6COOH \xrightarrow[65\ °C,18\ h]{4\ \text{equiv. 9-BBN, THF}} CH_3(CH_2)_6CH_2OH \quad (19)$$
92% (83% isolated)

Acid chlorides, such as hexanoyl chloride and benzoyl chloride, were converted into *n*-hexyl alcohol and benzyl alcohol in yields of 92 and 90%, respectively (eq 20).

$$CH_3(CH_2)_4COCl \xrightarrow[25\ °C,12\ h]{2\ \text{equiv. 9-BBN, THF}} CH_3(CH_2)_4CH_2OH \quad (20)$$
92% (81% isolated)

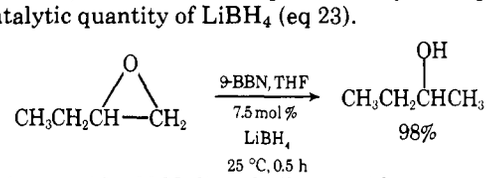
Esters such as ethyl hexanoate and methyl heptanoate were reduced in reflux using THF to 1-hexanol and 1-heptanol in yields of 100 and 99%, respectively (eq 21). γ-Butyrolactone was reduced to 1,4-butanediol in 98% yield (eq 22).

$$CH_3(CH_2)_5COOCH_3 \xrightarrow[65\ °C,4\ h]{2\ \text{equiv. 9-BBN, THF}} CH_3(CH_2)_5CH_2OH \quad (21)$$
99% (77% isolated)



$HOCH_2CH_2CH_2CH_2OH$ (22)
98%

Epoxides such as 1,2-butylene oxide reacted sluggishly with 9-BBN alone, but were reduced quantitatively in the presence of a catalytic quantity of $LiBH_4$ (eq 23).



(23)

Tertiary amide, *N,N*-dimethylbenzamide, was converted into benzyl alcohol and *N,N*-dimethylbenzylamine (eq 24). The results are summarized in Table XIV.

$$C_6H_5CON(CH_3)_2 \xrightarrow[25\ °C,4\ h]{9\text{-BBN, THF}} \underset{80\%}{C_6H_5CH_2OH} + \underset{20\%}{C_6H_5CH_2N(CH_3)_2} \quad (24)$$

**Scope and Applicability.** Detailed and systematic explorations on the reducing characteristics of 9-BBN have revealed many interesting and unusual features of this reagent, quite different from those observed for borane and other partially alkylated boranes previously studied. The reactivity of various functional groups toward 9-BBN can be classified into five broad categories as follows: (1) very rapid reduction—aldehyde and ketone; (2) rapid reduction—olefin, quinone, tertiary amide, acid anhydride, acid chloride, and lactone; (3) slow reduction—ester, epoxide, and oxime; (4) very slow reduction—carboxylic acid, sulfoxide, and azoxy; (5) inert (no reaction)—nitro (both aliphatic and aromatic), azo, sulfide, disulfide, sulfone, sulfonic acid, tosylate, halogen (aryl and alkyl).

9-BBN has four major advantages over borane and other partially alkylated boranes. First, solid 9-BBN is relatively insensitive to air and can be handled with no more hazard than lithium aluminum hydride. Second, as solid and solution, it is indefinitely stable. One such solution prepared in THF did not lose any of its activity even after 6 years. Third, unlike $BH_3$–THF and other dialkylboranes, its thermal stability is exceptional. This permits the reduction of even difficultly reducible groups, such as carboxylic acids. Fourth, 9-BBN is soluble in a variety of organic solvents.

Reduction of aldehydes and ketones with 9-BBN proceeds rapidly and quantitatively. Consequently, this permits the ready reduction of such groups in the presence of almost any other functional group listed in the categories 2–5. The feasibility of utilizing elevated temperatures with this reagent renders possible the smooth reduction of even hindered ketones such as camphor in a short period (1 h, 65 °C).

Selective reduction of $\alpha,\beta$-unsaturated aldehydes and ketones to the corresponding allylic alcohols represents one of the major application of this new reducing agent. Indeed, a detailed study underway in our laboratory has revealed a considerable number of interesting applications of this reagent for this purpose (especially with the functionalized $\alpha,\beta$-unsaturated system[16]).

**Table XIV. Products of Reduction of Selected Organic Compounds Containing Representative Functional Groups with 9-Borabicyclo[3.3.1]nonane in Tetrahydrofuran**

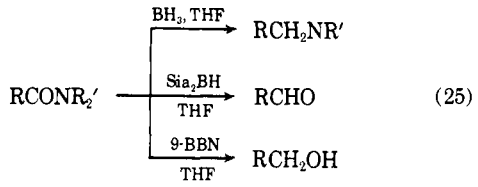
| Compd | Time, h | Temp, °C | Ratio 9-BBN/compd | Products | Yield,[a] % |
|---|---|---|---|---|---|
| Hexanal | 0.5 | 25 | 1.0 | 1-Hexanol | 100 |
| Cyclohexanone | 1.0 | 25 | 1.0 | Cyclohexanol | 100 (78) |
| 2-Methylcyclohexanone | 1.0 | 25 | 1.0 | 2-Methylcyclohexanol | 100 |
| 2,2,4,4-Tetramethyl-3-pentanone | 24.0 | 65 | 4.0 | 2,2,4,4-Tetramethyl-3-pentanol | <1.0 |
| | | | | 2,2,4,4-Tetramethyl-3-pentanone | 96 |
| Camphor | 12.0 | 25 | 1.0 | Borneols | 100 |
| | 1.0 | 65 | 1.0 | Borneols | 100 (81) |
| Cinnamaldehyde | 2.0 | 0 | 1.0 | Cinnamyl alcohol | 98 |
| Anthraquinone | 24.0 | 25 | 2.0 | 9,10-Dihydro-9,10-anthracenediol | (79) |
| Hexanoic acid | 18.0 | 65 | 4.0 | 1-Hexanol | 92 |
| Octanoic acid | 18.0 | 65 | 4.0 | 1-Octanol | 92 (83) |
| Benzoyl chloride | 6.0 | 25 | 4.0 | Benzyl alcohol | 90 |
| Hexanoyl chloride | 18.0 | 25 | 2.0 | 1-Hexanol | 92 (81) |
| Ethyl hexanoate | 24.0 | 25 | 4.0 | 1-Hexanol | 75 |
| | 4.0 | 65 | 2.0 | 1-Hexanol | 100 |
| Methyl heptanoate | 4.0 | 65 | 2.0 | 1-Heptanol | 99 (77) |
| γ-Butyrolactone | 2.0 | 65 | 2.0 | 1,4-Butanediol | 98 |
| Cyclohexene oxide | 24.0 | 25 | 4.0 | Cyclohexanol | 30 |
| 1,2-Butylene oxide | 0.5 | 25 | 4.0 | 2-Butanol | 98 |
| | | | | 1-Butanol | 2 |
| *n*-Octyl bromide | 24.0 | 25 | 4.0 | *n*-Octane | 0 |
| | | | | *n*-Octyl bromide | 100 |
| *p*-Bromotoluene | 24.0 | 25 | 4.0 | Toluene | 0 |
| | | | | *p*-Bromotoluene | 96 |
| *N,N*-Dimethylbenzamide | 3.0 | 25 | 4.0 | Benzyl alcohol | 80 |
| | | | | *N,N*-Dimethylbenzylamine | 20 |
| Nitrobenzene | 24.0 | 25 | 4.0 | Nitrobenzene | 90 |
| Di-*n*-butyl disulfide | 24.0 | 25 | 4.0 | Di-*n*-butyl disulfide | 98 |

[a] Yields were determined by GLC using a suitable internal standard. Numbers in parentheses indicate the isolated yield.

The facile and clean reduction of anthraquinone to 9,10-dihydro-9,10-anthracenediol in 79% yield represents another promising area of application, useful in the area of synthetic dyes. Currently available hydride reducing agents, such as lithium aluminum hydride and its alkoxy derivatives, borane–THF, etc., yield a mixture of 9,10-dihydro-9,10-anthracenediol and 9,10-dihydroxyanthracene.[6,18]

The rapid and quantitative reduction of acid chlorides with 9-BBN provides a convenient entry to the corresponding alcohols. This was quite unexpected since borane and disiamylborane are inert to acid chlorides and thexylborane reacts only sluggishly.[6] Even more important is the observation that the acid chlorides can be selectively reduced in the presence of esters, with no significant attack on the ester group. No other hydride reagent currently available exhibits such a unique selectivity.

The reduction of tertiary amides to alcohols represents yet another promising area of applications that requires detailed exploration. It should be pointed out that the reduction with borane–THF proceeds to give amines and with disiamylborane yields aldehydes. Consequently, we are now in a position to control the course of this reaction using various reagents to get three different products (eq 25).




(25)

Recently, 9-BBN has been found to exhibit good selectivity for the γ-carboxyl group of the glutamate and unhindered C-terminal carboxylate group with only marginal reduction of the β-carboxyl group of aspartate in proteins.[19] Borane–THF also reduces the carboxyl groups in proteins, but will not differentiate between γ-, β-, and C-terminal carboxyl groups.[20] Further, unlike $BH_3$–THF, 9-BBN does not cleave the disulfide bonds which are responsible for the tertiary structure of the protein (and their enzymatic activity). Consequently, 9-BBN should be highly useful for the specific chemical modification of proteins and as a valuable conformational probe.

## Conclusions

9-Borabicyclo[3.3.1]nonane hydroborates olefins with very high regio- and stereoselectivity, thus providing a convenient route to the synthesis of various 9-alkyl-9-BBN derivatives. These derivatives are finding numerous applications in the synthesis of carbon structures. The subject of the present study, the reducing characteristics of 9-BBN, reveals that 9-BBN is also a highly selective and unique reducing agent and should find major applications in organic synthesis.

## Experimental Section

**Materials.** Tetrahydrofuran was dried with excess lithium aluminum hydride, distilled under nitrogen, and stored over 5-Å molecular sieves. Borane solution in THF was prepared from sodium borohydride and boron trifluoride etherate and standardized by hydrolyzing a known aliquot of the solution with glycerine–water–THF mixture and measuring the hydrogen evolved.[21,22]

Most of the organic compounds utilized in this study were the commercial products of the highest purity. They were further purified by distillation or recrystallization when necessary. Some compounds were synthesized using standard procedures. In all of the cases, physical constants agreed satisfactorily with constants in the literature. All glassware was dried thoroughly in a drying oven and cooled under a dry stream of nitrogen. All reduction experiments were carried out under a dry nitrogen atmosphere. Hypodermic syringes were used to transfer the solution.[23]

**Standard Solution of 9-Borabicyclo[3.3.1]nonane in Tetrahydrofuran.**[5b,c] A 2-l. flask, oven dried, equipped with a side arm

fitted with a silicone rubber stopple, was cooled down under a dry stream of nitrogen. It was fitted with a magnetic stirring bar and a reflux condenser connected to a mercury bubbler. The flask was maintained under a static nitrogen pressure and immersed in an ice bath (ca. 0 °C). Into the flask was introduced 338 ml (800 mmol) of 2.36 M borane solution in THF. After 15 min, 86.4 g (98 ml, 800 mmol) of 1,5-cyclooctadiene was added dropwise with vigorous stirring over a period of 1 h. The ice bath was removed and the mixture was refluxed for 1 h. Then it was cooled to room temperature and 9-BBN crystallized out as a white solid.

9-BBN was purified by repeatedly washing with *n*-pentane (freshly distilled over $LiAlH_4$) at −10 °C. After drying at 50 °C in vacuo, a snow-white solid of 9-BBN was obtained, 73.5 g (75%), mp 152.5–153.5 °C. This was dissolved in 900 ml of THF. The concentration was determined by hydrolyzing 5-ml aliquot solutions with THF–MeOH mixture at 25 °C and measuring the hydrogen evolved (requires 45 min). It was found to be 0.67 M in 9-BBN.

Alternatively, commercial 9-BBN powder was dissolved in THF to give the solutions of required concentration.[7]

**Procedure for Rate and Stoichiometry.** Reduction of ethyl hexanoate is representative. A 100-ml flask was dried in an oven and cooled down in a dry stream of nitrogen. The flask was equipped with a rubber syringe cap, a magnetic stirring bar, and a reflux condenser connected to a gas buret through a dry ice trap. The flask was immersed in a water bath (ca. 25 °C) and 1.7 ml of THF was introduced into the reaction flask, followed by 35.7 ml (20 mmol) of 0.56 M solution of 9-BBN in THF and 0.57 ml (2.5 mmol) of *n*-dodecane to serve as the internal standard. Finally, 2 ml (5 mmol) of 2.5 M solution of ethyl hexanoate in THF was injected into the reaction flask. Now the reaction mixture was 0.5 M in 9-BBN and 0.125 M in ester. No hydrogen evolution was observed.

At the end of 3 h, an 8.0-ml aliquot of the reaction mixture (1 mmol of the compound) was removed with a hypodermic syringe and injected into a hydrolyzing mixture of THF–MeOH (1:1). The hydrogen evolved was measured. This indicated that 0.36 mmol of hydride had reacted per millimole of the ester (18% reduction). The reaction was monitored at 6 (35%), 12 (58%), and 24 h (80%).

At the end of 24 h, the remaining mixture was hydrolyzed, oxidized, and analyzed on a 5% Carbowax 20M column, 6 ft × 0.125 in., indicating the presence of 75% *n*-hexyl alcohol.

The results for other compounds are summarized in Tables I–XI.

**Representative Procedure for Product Analysis by GLC. Reduction of Methyl Heptanoate to 1-Heptanol.** A clean, oven-dried, 25-ml flask, equipped with a side arm fitted with a silicone rubber stopple, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler, was cooled down to room temperature with nitrogen. Then 10.1 ml (5.5 mmol) of a 0.55 M solution of 9-BBN in THF was injected into the reaction flask, followed by 0.285 ml (1.25 mmol) of *n*-dodecane as the internal standard. The flask was heated carefully to reflux temperature. Then 2.5 mmol (0.42 ml) of methyl heptanoate was introduced by a syringe. The mixture was stirred well and at appropriate intervals of time the reaction was monitored by GLC: 2 h (93% reaction), 4 h (99% reaction).

At the end of 4 h, the mixture was allowed to cool down to room temperature and the excess hydride destroyed with MeOH. The boronic acid derivative was oxidized by the addition of 2 ml (6 mmol) of 3 N aqueous sodium hydroxide followed by 1.5 ml (13 mmol) of 30% hydrogen peroxide and heating at 50 °C for 1 h. The aqueous layer was saturated with 2 g of potassium carbonate and the dry THF layer was subjected to GLC analysis on 5% Carbowax 20M column, 6 ft × 0.125 in., indicating the presence of 99% 1-heptanol and 1.5% methyl heptanoate.

Similar procedure was employed for examining the stereochemistry of the reduction of cyclic and bicyclic ketones with 9-BBN.

The results for other compounds are summarized in Tables III and XIV.

**General Kinetic Procedures. A. Rate of Protonolysis of 9-BBN with Methanol.** A 100-ml flask, with a side arm, a magnetic stirring bar, and a reflux condenser connected to an inverted gas buret via a dry ice trap, was flame dried and cooled down to room temperature under a dry stream of nitrogen. The flask was immersed in a water bath (25 ± 0.5 °C). Then 13.9 ml of dry THF was injected into the reaction flask followed by 9.1 ml (5 mmol) of 0.55 M 9-BBN solution in THF. The mixture was stirred for 20 min to equilibrate to the bath temperature. The reaction was initiated by adding 2 ml (5 mmol) of a 2.5 M solution of methanol in THF (a timer started when half the syring was empty). Now the reaction mixture was 0.1 M in 9-BBN dimer and 0.2 M in methanol. Reaction was monitored by measuring the hydrogen evolved with time. After the reaction came to an effective halt (120 min, 130 ml, 5.02 mmol), the infinity reading was taken. The first-order plot gave a good straight line ($k_1 = 1.56 \times 10^{-3}$ s$^{-1}$). Additional kinetic runs in which methanol concentrations were increased to 0.4 M (concentration of 9-BBN dimer being the same, 0.1 M) also gave an excellent first-order plot, $k_1 = 1.52 \times 10^{-3}$ s$^{-1}$.

An identical run carried out with methanol-*O*-*d* (99.5% + deuterium content), 0.1 M in $(9\text{-BBN})_2$ and 0.2 M in MeOD, gave $k_1 = 1.53 \times 10^{-3}$ s$^{-1}$; $k_{MeOH}/k_{MeOD} = 1.02$.

**B. Rate of Reduction of Cyclohexanone with 9-BBN.** The experimental setup was the same as in the previous experiments. To the reaction flask was added 27.9 ml of dry THF, followed by 18.1 ml (10 mmol) of 0.55 M solution of 9-BBN in THF. The mixture was stirred for 30 min and allowed to equilibrate to the bath temperature (25.0 ± 0.5 °C). The reaction was initiated by rapidly injecting 4 ml of the THF solution containing 10 mmol of cyclohexanone and 5 mmol of *n*-dodecane (internal standard) into the reaction flask. Now the reaction mixture was 0.1 M in 9-BBN dimer and 0.2 M in cyclohexanone. Samples (5 ml) were withdrawn periodically via syringe and injected into separate flasks containing 3 ml of MeOH + 3 ml of THF to quench the reaction.[24] After stirring for at least 1 h, quenched samples were oxidized with $NaOH–H_2O_2$ and analyzed by GLC on a 5% Carbowax 20M column, 6 ft × 0.125 in., for the remaining cyclohexanone and cyclohexanol formed. The contents of the main reaction flask were stirred for 6 h, then hydrolyzed, oxidized, and analyzed for infinity reading. Reaction gave a good first-order plot, $k_1 = 1.15 \times 10^{-3}$ s$^{-1}$. Another experiment performed at 0.4 M cyclohexanone and 0.1 M 9-BBN dimer gave $k_1 = 1.22 \times 10^{-3}$ s$^{-1}$.

A similar procedure was employed for measuring the rate of hydroboration of cyclopentene with 9-BBN.[5c]

**Competitive Experiments. Reaction of Hexanal and 2-Heptanone with a Limited Quantity of 9-BBN in THF.** A typical reaction setup was assembled and the reaction flask was immersed in a water bath (ca. 25 °C). Then 12.7 ml of dry THF was injected into the reaction flask. Hexanal, 5 mmol (0.62 ml, freshly distilled, $n^{20}$D 1.4035), was added, followed by 2 ml (5 mmol) of 2.5 M solution of 2-heptanone in THF; 0.57 ml (2.5 mmol) of *n*-dodecane was added to serve as an internal standard. The mixture was stirred well and a minute sample withdrawn and analyzed by GLC on a 5% SE-30 column, 8 ft × 0.125 in., for the response ratio of reactants to internal standard. Reaction was initiated by the dropwise addition of 9.2 ml (5 mmol) of 0.54 M 9-BBN solution, over a period of 10 min. The resulting solution (0.2 M in each component and 9-BBN) was stirred well. After 4 h, the mixture was again analyzed, indicating the presence of 0.5 mmol of hexanal and 4.59 mmol of 2-heptanone. Then the mixture was oxidized with $NaOH–H_2O_2$ and analyzed on a 5% Carbowax 20M column, 6 ft × 0.125 in., indicating the presence of 4.43 mmol of 1-hexanol and 0.38 mmol of 2-heptanol.

The relative reactivity, $k_{rel} = k_{hexanal}/k_{2\text{-heptanone}}$, was calculated to be 27, employing the expression of Ingold and Shaw.[17] The results for the other pairs are summarized in Table XIII.

**General Preparative Procedures for the Reduction of Organic Compounds with 9-BBN.** A series of organic compounds containing representative functional groups were reduced with 9-BBN and the products were isolated to establish the synthetic utility of the reagent (depending upon the other substituents present, the time required may require an increase or decrease).

**A. Simple Ketone.** The following procedure for the reduction of cyclohexanone is representative. An oven-dried 100-ml flask with a side arm fitted with a silicone rubber stopple, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler was cooled down to room temperature under dry nitrogen. Then 40.8 ml (26 mmol) of 0.635 M 9-BBN solution in THF was introduced into the reaction flask followed by 2.6 ml (25 mmol) of cyclohexanone. After 1 h at 25°, 0.5 ml of methanol was added to destroy excess hydride. THF was removed under water aspirator and finally over the vacuum pump. Now dry *n*-pentane (25 ml) was added followed by 1.6 ml (26 mmol) of 2-aminoethanol. Immediately the ethanolamine derivative of 9-BBN began to precipitate out. The mixture was centrifuged and the clean pentane layer was separated. The precipitate was washed with 2 × 20 ml of *n*-pentane, centrifuged, and added to the main fraction. Pentane was distilled off and the residue on vacuum distillation yielded 1.93 g (78%) of cyclohexanol as a colorless liquid, $n^{20}$D 1.4650, >99% pure by GLC.

**B. Sterically Hindered Ketones.** Reduction of camphor to borneol and isoborneol is representative of the general procedure utilized.

A typical reaction setup was assembled. Then 3.8 g (25 mmol) of camphor was weighed into it. Now 41.3 ml (26 mmol) of 9-BBN solution in THF was introduced and the contents of the flask were brought to gentle reflux (65 °C). The mixture was stirred for 1 h at that temperature. Then the mixture was cooled to room temperature and the excess 9-BBN destroyed with 0.5 ml of methanol. The reaction

mixture was worked up as in the previous experiment by ethanolamine procedure. Stripping off solvent gave a white solid, which on sublimation gave 3.1 g (81%) of borneols. GLC analysis on a 5% Carbowax 20M column, 6 ft × 0.125 in., indicated 46% isoborneol and 54% borneol.

**C. Quinone.** The following procedure for the reduction of anthraquinone to 9,10-dihydro-9,10-anthracenediol is representative. A 100-ml flask with a side arm fitted with a Teflon stopcock and a magnetic stirring bar, connected to a mercury bubbler, was flame dried and cooled down to room temperature under dry nitrogen. Then 2.08 g (10 mmol) of anthraquinone was weighed into it. Now 34.1 ml (20 mmol) of 0.586 M 9-BBN solution in THF was added dropwise over a period of 10 min and the resulting mixture stirred well. After 24 h, 0.5 ml of methanol was added, followed by 3.3 ml of 6 N NaOH. THF and volatile solvents were removed under vacuum. The precipitate was filtered and washed each three times with water and cold benzene. There was obtained 1.67 g (79%) of 9,10-dihydro-9,10-anthracenediol as a white solid. A portion was recrystallized from hot benzene: mp 165–175 °C; NMR[25] ($Me_2SO$-$d_6$, $Me_4Si$) δ 5.3 and 5.44 (s, 2, >CH), 6.18 and 6.34 (s, 2, –OH), 7.2–7.9 (m, 8, aromatic).

A small quantity of the diol was converted to the corresponding diacetate by the pyridine–acetic anhydride method: 0.46 g (94%) of colorless needles, mp 171–172 °C, NMR ($CDCl_3$, $Me_4Si$) δ 2.1 (s, 6, O–$CCH_3$), 6.97 (s, 2, >CH), 7.2–7.9 (8, aromatic).

**D. Carboxylic Acid.** The following reduction of *n*-octanoic acid to *n*-octyl alcohol is representative. A 500-ml flask with a side arm fitted with a Teflon stopcock, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler was flame dried and cooled under a dry stream of nitrogen. Then 158 ml (100 mmol) of a 0.634 M solution of 9-BBN in THF was introduced into the reaction flask. Then 4.05 ml (25 mmol) of *n*-octanoic acid was injected and there was evolved 25.2 mmol of hydrogen. The resulting mixture was brought to careful reflux and stirred at that temperature for 18 h. Then it was cooled to room temperature and excess hydride destroyed with 2 ml of methanol. The boronic acid derivative was oxidized by the addition of 35 ml (105 mmol) of 3 N aqueous sodium hydroxide followed by 25 ml (225 mmol) of 30% hydrogen peroxide at 0 °C and stirring the resulting mixture at 50 °C for 1 h. The aqueous phase was saturated with anhydrous potassium carbonate. The THF layer was separated and the aqueous layer was extracted once with 20 ml of THF and twice with 20-ml portions of ether. The combined organic phase was dried over magnesium sulfate. Distillation of the solvents gave a viscous liquid which on vacuum distillation yielded 2.71 g (83%) of *n*-octyl alcohol, as a colorless liquid, bp 95–97 °C (18 mm), $n^{20}$D 1.4320.

*cis*-1,5-Cyclooctanediol, the oxidized product from the 9-BBN moiety, remains as the high-boiling residue in the pot.

**E. Acid Chloride.** The following procedure for the reduction of hexanoyl chloride to *n*-hexyl alcohol illustrates the practicality of utilizing 9-BBN for such transformations. An oven-dried 300-ml flask with a side arm and magnetic stirring bar and connected to a mercury bubbler was cooled down to room temperature under a dry stream of nitrogen. The flask was immersed in a water bath (ca. 25 °C) and 94 ml (55 mmol) of a 0.59 M solution of 9-BBN in THF injected into it. This was followed by the addition of 3.55 ml (25 mmol) of distilled hexanoyl chloride. The resulting mixture was stirred for 18 h at 25 °C. Then excess hydride was destroyed with 0.5 ml of methanol. THF was removed under water aspirator and finally over the vacuum pump, and replaced with 25 ml of dry *n*-pentane. Now 3.4 ml (55 mmol) of 2-aminoethanol was added. The ethanolamine derivative of 9-BBN precipitates down. The mixture was centrifuged and the clear pentane layer was separated. The precipitate was washed with 3 × 25 ml of *n*-pentane, centrifuged, and added to the main fraction. Pentane was removed and the residue distilled yielding 2.07 g (81%) of *n*-hexyl alcohol as a colorless liquid, bp 80 °C (62 mm), $n^{20}$D 1.4195, >98% pure by GLC.

**F. Ester.** Reduction of methyl heptanoate to *n*-heptyl alcohol is representative. A typical reaction setup was assembled. Then 101 ml (55 mmol) of 9-BBN solution in THF was introduced into the reaction flask and the flask was carefully brought to reflux temperature. Now 4.2 ml (25 mmol) of methyl heptanoate was added to the reaction mixture and stirred well. After 4 h, the mixture was cooled down to room temperature. Then the reaction mixture was worked up as described in the reduction of hexanoyl chloride. Stripping off the solvent and vacuum distillation of the residue gave 2.23 g (77%) of *n*-heptyl alcohol as a colorless liquid, bp 100 °C (40 mm), $n^{20}$D 1.4270.

**Registry No.**—2-Cyclohexen-1-one, 930-68-7; cyclopentanone, 120-92-3; cyclopentene, 142-29-0; methyl heptanoate, 106-73-0; 2-hexyl acetate, 5953-49-1; octanoic acid, 124-07-2; 9,10-dihydro-9,10-antracenediol, 58343-58-1; 9,10-dihydro-9,10-anthracenediol diacetate, 6938-79-0; octyl alcohol, 111-87-5; heptyl alcohol, 111-70-6.

## References and Notes


(1) Presented at the 8th Great Lakes Regional Meeting of the American Chemical Society, West Lafayette, Ind., June 1974.
(2) (a) Postdoctoral Research Associate on Grant DA-ARO-D-31-124-73-G148, supported by the U.S. Army Research Office (Durham); (b) Postdoctoral Research Associate on Grant DA-31-124-ARO(D)-453, supported by the U.S. Army Research Office (Durham), and a grant provided by the American Cyanamid Co.
(3) (a) H. C. Brown, "Hydroboration", W. A. Benjamin, New York, N.Y., 1962; (b) H. C. Brown, "Boranes in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 1972.
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(7) 9-BBN is now available commercially from the Aldrich Chemical Co., Milwaukee, Wis., both as the solid and the solution in tetrahydrofuran.
(8) 9-BBN is soluble only to the extent of 0.67 M in THF at 25 °C. Consequently, instead of our usual standard conditions (1.0 M in hydride, 0.25 M in compound, THF, 0 °C) we utilized the present conditions indicated.
(9) It is convenient to discuss the utilization of the reagents in terms of moles of hydride taken up per mole of the compound. However, it should not be confused that free "hydride" ion is the active species. An "active hydride" refers to one B–H bond, 1 equiv of 9-BBN.
(10) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 5694 (1956).
(11) This convenient precipitation of 9-BBN moiety was developed by Gary W. Kramer of our laboratory for a related application.
(12) It was thought that the high solubility of this adduct in THF may be due to the presence of primary amino group. However, even the complex derived from *N,N*-dimethylethanolamine was found to be highly soluble.
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(22) One molar solution of borane in tetrahydrofuran is now commercially available from Aldrich Chemical Co., Milwaukee, Wis.
(23) For a detailed review of techniques for the handling of air-sensitive substances, see H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses *via* Boranes", Wiley, New York, N.Y., 1975, pp 191–261.
(24) A control experiment carried out clearly proved the validity of using large excess of methanol for arresting the reaction.
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