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Hydroboration. 48. Effect of Structure on Selective Monohydroboration of Representative Nonconjugated Dienes by 9-Borabicyclo[3.3.1]nonane

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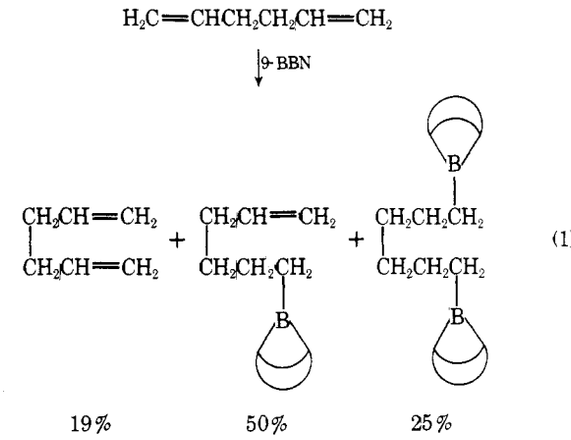
The exceptionally high sensitivity toward structure exhibited by 9-borabicyclo[3.3.1]nonane (9-BBN) in the hydroboration of simple olefins carries over to the hydroboration of nonconjugated dienes. In this way many such dienes can be selectively monohydroborated and thereby converted into synthetically useful intermediates. For example, dienes containing one terminal double bond and one internal double bond can be selectively hydroborated at the terminal position. Whereas 2-methyl-1,4-pentadiene is selectively hydroborated by disiamylborane at the less substituted double bond, the greater reactivity of 9-BBN for the 2-methyl-1-alkene structure permits the preferential hydroboration of the other position. The hydroboration of certain symmetrical cyclic dienes, such as 1,4-cyclohexadiene and 1,5-cyclooctadiene, with 9-BBN (1:1 mole ratio) is readily controlled to produce the monoadducts. The observation that the relative reactivities of simple olefin structures toward hydroboration with 9-BBN can be carried over so reliably to predict the point of hydroboration of nonconjugated dienes greatly facilitates the utilization of such dienes as intermediates in organic synthesis.

9-Borabicyclo[3.3.1]nonane is an interesting hydroborating agent which exhibits unusual regio-[2] and stereospecificities.[3] It also exhibits a remarkable sensitivity to the structure of individual olefins.[4] The question arose as to whether this knowledge could be carried over to predict the course of the monohydroboration of representative dienes. If so, such dienes could be selectively monohydroborated and the products utilized in the many transformations now available for organoboranes.[5] Accordingly, we undertook to study the monohydroboration of a number of representative nonconjugated dienes with this reagent and to compare the results with those realized in an earlier study utilizing disiamylborane.[6]

Results and Discussion

The reaction procedure involved the addition of a standard solution of 9-BBN in tetrahydrofuran (THF) to an equivalent amount of the diene in the same solvent. An internal standard suitable for GC analysis was present. The reaction was allowed to proceed to completion at 25 °C. The reaction product was oxidized by alkaline hydrogen peroxide in the usual manner.[5] GC examination for residual diene established the extent of monohydroboration (0% diene = 100% monohydroboration; 50% diene = 0% monohydroboration). The mono-ol product revealed the point or points of attack.

Symmetrical Acyclic Dienes. The reaction of 9-BBN with symmetrical dienes, such as 1,4-pentadiene and 1,5-hexadiene, would be expected to proceed in an essentially statistical manner, giving 25% residual diene, 50% of the monohydroboration products, and 25% of the dihydroboration product. Indeed, the data for 1,6-hexadiene closely follow this prediction for statistical behavior, with a minor discrepancy in the residual 1,5-hexadiene (eq 1).

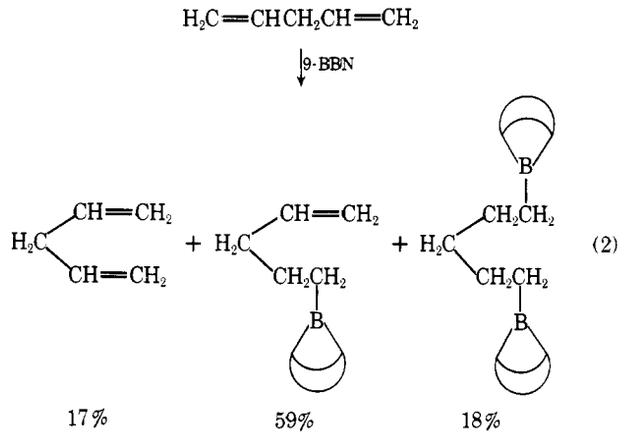


(1)

The results for 1,4-pentadiene are similar, but reveal a moderate displacement from the purely statistical distribution (eq 2). Conceivably there could be a small interaction of the double bond with the boron atom in the monohydroboration product sufficiently significant as to retard slightly its conversion into the dihydroboration product.

Similar results are realized with disiamylborane.[6]

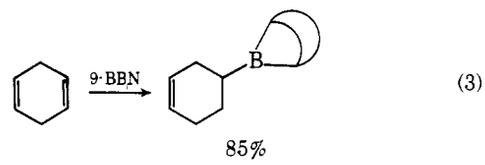
Symmetrical Cyclic and Bicyclic Dienes. In contrast to the behavior of the symmetrical acyclic dienes, the hydroboration of certain symmetrical cyclic dienes with 9-BBN can be controlled to yield the monohydroboration product predominantly. In the case of 1,5-cyclooctadiene, the results differ



(2)

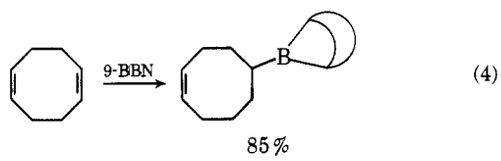
in major respect from those attainable with disiamylborane.[6]

Thus, the treatment of 1,4-cyclohexadiene with 1 equiv of 9-BBN proceeds predominantly to form the monoadduct (eq 3).



(3)

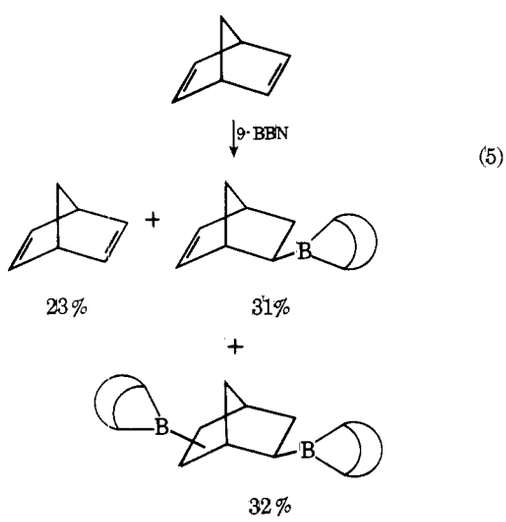
Similarly, the hydroboration of 1,5-cyclooctadiene with 9-BBN in the usual 1:1 molar ratio produces the monoadduct preferentially (eq 4). In sharp contrast, treatment of 2 mol of



(4)

1,5-cyclooctadiene (excess) with 1 mol of disiamylborane gives predominantly (86%) the dihydroboration product.[6] Consequently, the present procedure provides a valuable new synthetic route to 4-cycloocten-1-ol and other 4-cycloocten-1-yl derivatives.[5]

Norbornadiene behaves much more like a simple symmetrical diene, yielding a product distribution approaching that predicted for a statistical reaction (eq 5).

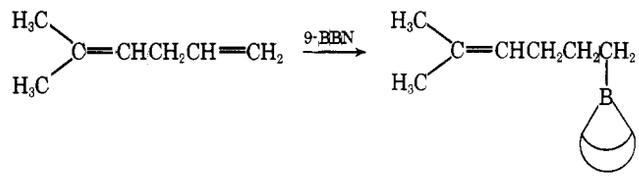


(5)

The monohydroboration product is entirely the exo derivative. GC examination of the alcohol produced via the usual oxidation revealed no trace of the endo isomer. In this respect, the reaction establishes a major advantage over hydroboration with disiamylborane.[6] Here the monohydroboration product yielded *exo*-dehydronorbornenol containing 13% of the endo isomer. The major difficulties in separating such isomers make the present procedure strongly preferable. By utilizing an excess of norbornadiene in the hydroboration stage, a considerably more favorable conversion to the desired *exo*-dehydronorbornenol and other derivatives should be realized.

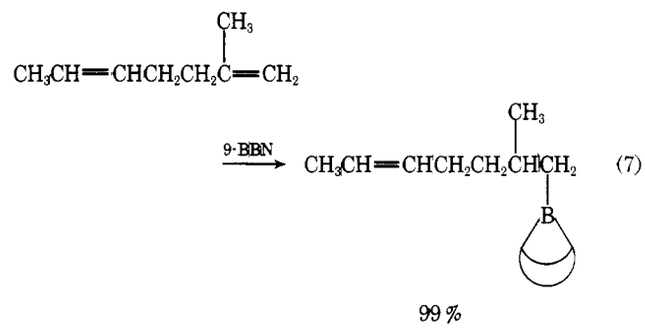
Unsymmetrical Acyclic Dienes. The presence in a diene of two different double bonds, which may differ greatly in reactivity, greatly facilitates monohydroboration.[5] A major question was whether the relative reactivities we had earlier established for the isolated olefin structures[4] could be utilized to predict the behavior of nonconjugated dienes containing related structures.

For example, 1-hexene is 116 times more reactive than 2-methyl-2-butene toward 9-BBN. It appears reasonable to predict that 5-methyl-1,4-hexadiene should undergo hydroboration by 9-BBN predominantly at the 1 position. Indeed, the monohydroboration reaction is remarkably clean—the predicted product is realized essentially isomerically pure (eq 6).



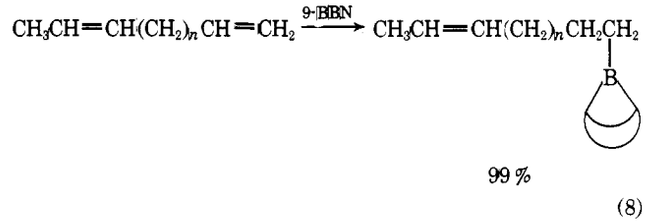
(6)

Similarly, 2-methyl-1-pentene is 194 times more reactive toward 9-BBN than *cis*-2-pentene. Accordingly, 2-methyl-1,5-heptadiene would be predicted to undergo hydroboration predominantly at the 1 position. The observed product is that predicted (eq 7).



(7)

1-Hexene is 100 times more reactive toward 9-BBN than *cis*-2-pentene. Consequently, both 1,4-hexadiene and 1,5-heptadiene would be predicted to undergo monohydroboration cleanly at the 1 position. In fact, the product is cleanly that predicted (eq 8).



(8)

In certain of these cases (eq 6, 8), the direction taken by the monohydroboration process is similar to that predicted for disiamylborane.[6,7] In the case of eq 7, the relative reactivities of the two olefin structures toward disiamylborane are very

similar.[7] Consequently, a selectivity of the kind achieved with 9-BBN cannot be anticipated. In the following case, it appeared from the reactivities of the parent olefins toward disiamylborane[7] and 9-BBN[4] that the regioselectivity of the monohydroboration of certain dienes could be reversed. We undertook to check this possibility.

1-Hexene is preferentially hydroborated by disiamylborane in the presence of 2-methyl-1-pentene. Indeed, the relative reactivity of 1-hexene toward this reagent is some 20 times greater.[7]

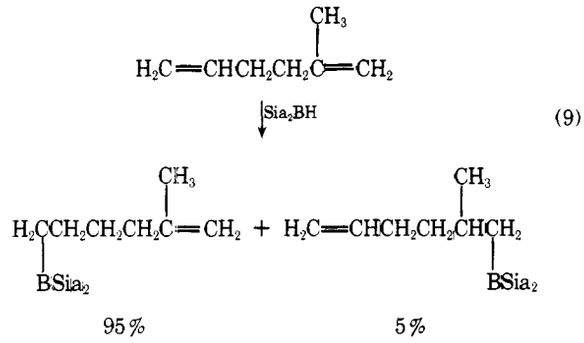
$$\frac{k_{\text{1-hexene}}}{k_{\text{2-methyl-1-pentene}}} = 20.4$$

On the other hand, toward 9-BBN 2-methyl-1-pentene is more reactive than 1-hexene.[4]

$$\frac{k_{\text{1-hexene}}}{k_{\text{2-methyl-1-pentene}}} = 1.94$$

It is believed that disiamylborane is more sensitive to steric effects than is 9-BBN, whereas the latter is more sensitive to electronic contributions.[4] In the case of disiamylborane, the steric contributions of the 2-methyl substituent dominate the reaction, whereas with 9-BBN, its electronic contributions facilitate the reaction.

On this basis, it is not unexpected that 2-methyl-1,5-hexadiene is hydroborated by disiamylborane predominantly at the 6 position[6] (eq 9), whereas this diene is hydroborated by 9-BBN preferentially at the 1 position (eq 10).



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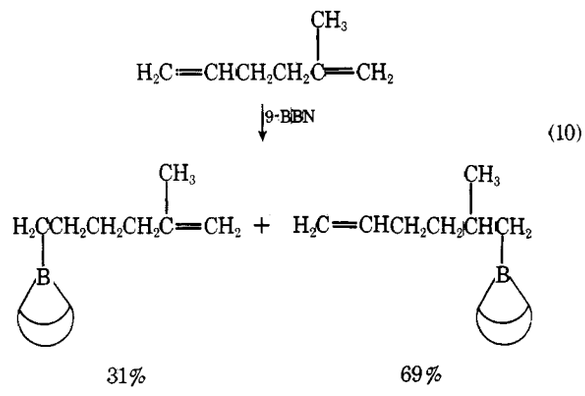
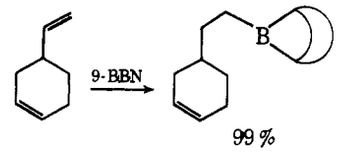


(10)

Consequently, by an appropriate choice of the hydroborating agent, 9-BBN or disiamylborane, it is possible in some cases to achieve a reversal of the particular double bond in a diene which undergoes hydroboration.

Unsymmetrical Alicyclic Dienes. This procedure of predicting the point of attack by 9-BBN in dienes from the reactivity data for the related olefins[4] also works well for "mixed" dienes, such as 4-vinylcyclohexene. 1-Hexene is 1500 times more reactive than cyclohexene toward 9-BBN. With such a large difference in the relative reactivities of the respective double bonds, it would be anticipated that 4-vinylcyclohexene should undergo hydroboration regiospecifically at the vinyl group. That is indeed observed (eq 11).

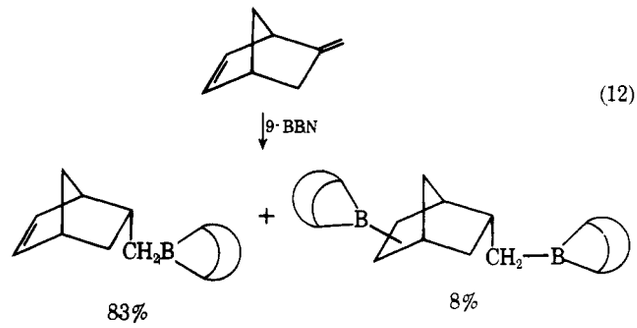


(11)

2-Methylenenorbornane is 3.8 times more reactive than norbornene with respect to 9-BBN hydroboration. This is not a large difference in relative reactivity and considerable competitive attack at the norbornene double bond might have been anticipated. However, 9-BBN adds to the exocyclic double bond preferentially (eq 12).

No detectable amounts of methylenenorbornanols arising from attack at the internal norbornene double bond were observed in the GC examination of the oxidized products. Perhaps the huge strains in this rigid diene cause this minor deviation from the predicted behavior.

In eq 12, the monohydroboration product is indicated to be



(12)

the endo isomer. However, we were unable to separate the exo and endo alcohols on the columns we had available. Consequently, the assignment must be considered tentative, based on the marked preference for exo attack by hydroborating agents in norbornadiene (present study), norbornene,[3] and methylenenorbornane.[8]

The data for the hydroboration of these nonconjugated dienes with the results for the GC examination of the oxidized reaction products are summarized in Table I.

Conclusion

The present study establishes that the data available for the relative reactivities of representative olefins toward 9-BBN[4] can be used with considerable confidence to predict the point of hydroboration of nonconjugated dienes and, possibly, of polyenes. This development makes possible the selective reaction of a particular double bond in a complex structure containing more than one such bond. Moreover, by a judicious choice of disiamylborane[7] or 9-BBN it is on occasion possible to hydroborate one double bond structure in the presence of another or to invert the process. With the large and growing arsenal of organoborane transformations,[5] this development should add to the utility of hydroboration as a synthetic route for synthetic operations.

Experimental Section

General Comments. All glassware, syringes, and needles were oven dried at 150 °C before use. The glassware was assembled hot and cooled under a flow of nitrogen. Syringes were assembled and fitted with needles while hot, then cooled as assembled units. They were flushed out with nitrogen immediately before use.

Materials. The *n*-alkanes (Phillips), employed as internal standards, were used as received. Technical grade pentane was stirred over concentrated sulfuric acid to remove any olefinic impurities, washed with aqueous base, dried over anhydrous magnesium sulfate (Mallinckrodt), and distilled under nitrogen from lithium aluminum hydride. Bicyclo[2.2.1]hepta-2,5-diene and 5-methylene-2-norbornene

Table I. Hydroboration–Oxidation Product Distribution of Nonconjugated Dienes (0.5 M) with 1 Molar Equiv of 9-BBN (0.5 M) in THF at 25 °C

Registry no.	Diene	Residual diene,[a] %	Unsaturated alcohols, %	Diols,[b] %
592-42-7	1,5-Hexadiene	19	5-Hexen-1-ol, 50	1,6-Hexanediol, 25
591-93-5	1,4-Pentadiene	17	4-Penten-1-ol, 59	1,5-Pentanediol, 18
628-41-1	1,4-Cyclohexadiene	Tr	3-Cyclohexen-1-ol, 85	7[c]
111-78-4	1,5-Cyclooctadiene	9	4-Cycloocten-1-ol, 85	8[c]
121-46-0	Norbornadiene	23	*exo*-Dehydronorborneol,[d] 31	32[c]
763-88-2	5-Methyl-1,4-hexadiene	Tr	5-Methyl-4-hexen-1-ol, 99	0
	2-Methyl-1,5-heptadiene[e]	0	2-Methyl-5-hepten-1-ol,[e] 99	0
	1,4-Hexadiene[e]	Tr	4-Hexen-1-ol,[e] 99	0
	1,5-Heptadiene[e]	0	5-Hepten-1-ol,[e] 99	0
4049-81-4	2-Methyl-1,5-hexadiene	20	2-Methyl-5-hexen-1-ol, 35.8 5-Methyl-5-hexen-1-ol, 15.7	2-Methyl-1,6-hexanediol, 22
100-40-3	4-Vinylcyclohexene	0	2-(4-Cyclohexenyl)ethanol, 99	0
694-91-7	Methylenenorbornene	7	5-(Hydroxymethyl)norbornene,[f] 83	8.2[c]

[a] Analysis after oxidation. [b] % based on diene. [c] Unresolved mixture. [d] None of the endo isomer present. [e] Mixture of cis and trans. [f] Unresolved mixture of epimer.

were obtained from the Aldrich Chemical Co. 1,5-Cyclooctadiene was purchased from Cities Service. All other nonconjugated dienes were purchased from Chemical Samples. These purchased dienes were used after checking ^{1}H NMR, index of refraction, and GC retention time on a Varian Model 1200 gas chromatograph with an appropriate column.

Hydroboration of Nonconjugated Dienes. The following nonconjugated dienes were hydroborated, oxidized, and analyzed in precisely the same manner: 5-methyl-1,4-hexadiene, 2-methyl-1,6-heptadiene (mixture of cis and trans), 1,6-heptadiene, 1,4-hexadiene (mixture of cis and trans), 2-methyl-1,5-hexadiene, 1,5-hexadiene, 5-methylene-2-norbornene, and bicyclo[2.2.1]hepta-2,5-diene.

General Reaction Procedure. A dry 100-mL round-bottom flask equipped with a septum side arm and reflux condenser was connected to a mercury check valve through an adapter. The system was purged of air by nitrogen and the inert atmosphere was maintained until the oxidation stage. Normally, 10.0 mmol of diene was added via syringe along with 3 mmol of a suitable internal standard. 9-BBN (0.5 M in THF), 10.0 mmol, was added to the reaction flask slowly via syringe. After sufficient time for complete reaction, the mixture was oxidized. Sodium hydroxide solution (3 M, 3 mL) was injected into the flask, followed by 3 mL of hydrogen peroxide (30% solution), added dropwise over 10–15 min (exothermic reaction). The reaction mixture was heated to 50 °C for 1 h to complete the oxidation, then cooled to room temperature. The water layer was saturated with anhydrous potassium carbonate and the THF layer was separated and dried over anhydrous magnesium sulfate. The water layer was extracted with 15 mL of pentane. This was dried over magnesium sulfate and combined with the first extract. A small aliquot (~3 mL) was removed by disposable pipet and stored over 3 Å molecular sieves (Matheson Coleman and Bell). This aliquot was used for GC analysis. Then about 25–50 mL of pentane was added to the remaining organic fraction to precipitate *cis*-1,5-cyclooctanediol. The pentane was decanted off from the diol, which separated either as a viscous oil or a crystalline solid in the bottom of the flask. Purification by preparative gas chromatography (XE-60, 6 ft × 0.5 in.) of the organic material afforded essentially pure (>98%) unsaturated alcohol. ^{1}H NMR (Varian T-60) and IR (PE-137 and/or PE-700) were run to confirm the identity of the product. The GC correction factor was determined. The product distributions are summarized in Table I.

The hydroboration–oxidation of 4-vinylcyclohexene, 1,5-cyclooctadiene, 1,4-pentadiene, 1,3-cyclohexadiene, 5-methylene-2-norbornene, and bicyclo[2.2.1]hepta-2,5-diene were performed following the same general procedure described above, except that the products were not isolated. In these cases, authentic samples were available for comparison. These results are likewise presented in Table I.

Registry No.—9-BBN, 280-64-8; *cis*-2-methyl-1,5-heptadiene, 41044-64-8; *trans*-2-methyl-1,5-heptadiene, 41044-63-7; *cis*-1,4-hexadiene, 7318-67-4; *trans*-1,4-hexadiene, 7319-00-8; *cis*-1,5-heptadiene, 7736-34-7; *trans*-1,5-heptadiene, 7736-22-3.

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