cholesteryl o-benzoylbenzoate isomer A, 62930-26-1; pseudo cholesteryl o-benzoylbenzoate isomer B, 62961-06-2.

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Hydroboration. 47. Unique Stereospecificity of the Hydroboration of 1,3-Dimethylcycloalkenes with 9-Borabicyclo[3.3.1]nonane

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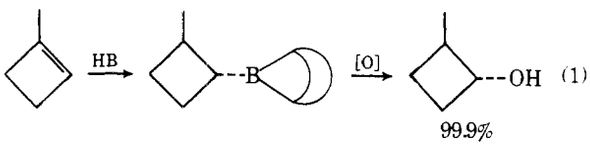
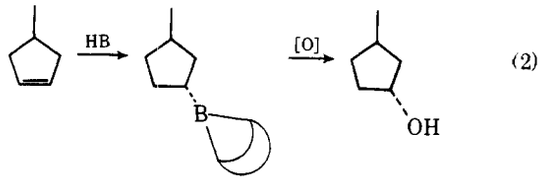
The hydroboration of 1,3-dimethylcycloalkenes **1–4** with 9-borabicyclo[3.3.1]nonane (9-BBN) proceeds with exceptionally high stereospecificity, affording only 2,ω-dimethylcycloalkyl-9-borabicyclo[3.3.1]nonane with both methyl groups trans to the 9-BBN moiety. For example, 1,3-dimethylcyclopentene is converted exclusively into *trans*-2,*trans*-5-dimethylcyclopentyl-9-borabicyclo[3.3.1]nonane. Stereochemical assignments are based on ^{13}C NMR spectra of the resulting organoboranes produced as well as on characterization of the alcohols derived from their oxidation. The synthetic utility of this remarkable stereospecific reaction is indicated by the ready conversion of the organoborane intermediates into the corresponding *cis*-2,ω-dimethylcycloalkanones and *trans*-2,*trans*-ω-dimethylcycloalkanols.

The hydroboration of cyclic olefins with 9-borabicyclo[3.3.1]nonane (9-BBN) proceeds with exceptionally high regio- and stereoselectivity.[2] Such hydroborations of 1-substituted cycloalkenes cleanly produce the *trans*-2-alkylcycloalkyl-9-borabicyclo[3.3.1]nonane. For example, hydroboration–oxidation of 1-methylcyclobutene yields 99.9% *trans*-2-methycyclobutanol (eq 1). Similarly, treatment of 3- or 4-



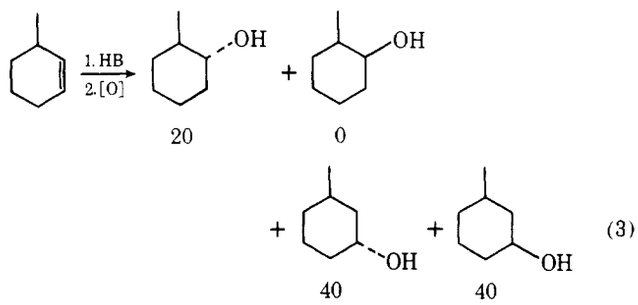
99.9% (1)

alkyl-substituted, 1,4-dialkyl-substituted cyclic olefins or of related exocyclic olefins with 9-BBN affords predominantly those products arising from addition to the least hindered side of the double bond. For example, 4-*tert*-butylcyclopentene is converted into *trans*-3-*tert*-butylcyclopentyl-9-borabicyclo[3.3.1]nonane, (99%), while 4-methylcyclopentene gives 3-methylcyclopentyl-9-borabicyclo[3.3.1]nonane (95%) (eq 2).



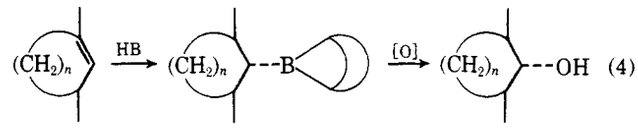
(2)

We recently reported the results of an extensive investigation into the regio- and stereochemistry of the hydroboration of representative cyclic olefins with 9-BBN.[2] During the course of this investigation, it was observed that hydroboration of 3-methylcyclopentene or 3-methylcyclohexene with 9-BBN produces no cis-1,2 isomer (eq 3). This unanticipated



(3)

result, coupled with the behavior of 1-methylcycloalkenes, led us to predict that 1,3-dimethylcycloalkenes should hydroborate to form exclusively the *trans*-2,*trans*-ω-dialkylcycloalkyl-9-borabicyclo[3.3.1]nonane derivatives (eq 4). Accordingly, we examined the stereochemistry of hydroboration of representative 1,3-dialkylcycloalkenes with 9-BBN.



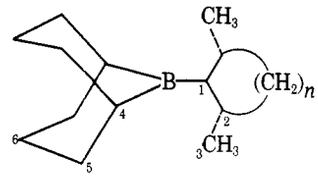
(4)

The 1,3-dimethylcycloalkenes, **1–4**, were selected as representative for the examination of the validity of the high stereospecificity predicted for this reaction with 9-BBN.

Results and Discussion

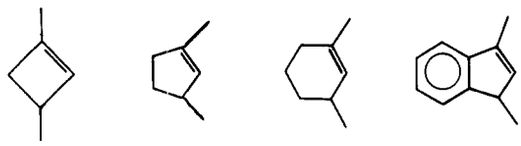
General Procedure for Stereochemical Assignments. The hydroboration of olefins **1–4** was carried out to comple-

Table I. ^{13}C Chemical Shifts of Organoboranes



Registry no.	Starting olefin	1	2	3	4	5	6
1489-61-8	1	52.0	29.1	23.5*	30	33.2	23.4*
62184-82-1	2	55.1	35.8	22.3	31.5	33.1	23.3
2808-76-6	3	54.0	33.1	24.6	31.7	34.1	23.8
2177-48-2	4	56.5	40.2	20.9	31.3	33.0	23.3

[a] In parts per million relative to Me_4Si. Assignment of chemical shifts for close-lying peaks marked with an asterisk may be reversed.

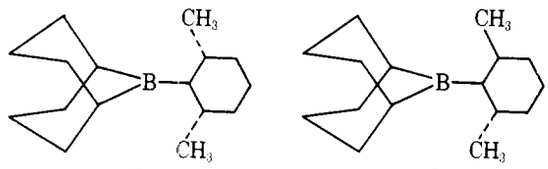


1 2 3 4

tion by allowing solid 9-BBN to react with an equivalent amount of olefin (as a 1 M solution in carbon tetrachloride) at 50 °C for 12 h. Removal of the solvent under reduced pressure afforded the corresponding *B*-cycloalkyl-9-borabicyclo[3.3.1]nonane derivative.

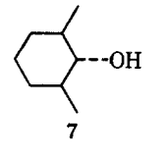
Both the isomeric purity of the product borane and the stereochemical assignment were based on the ^{13}C NMR spectra.[3] The symmetry of the products produced simplified application of this procedure and the interpretation of the data.

For example, hydroboration of **3** yielded a product which exhibited eight different resonances in its decoupled ^{13}C NMR spectrum. This is consistent with the symmetrical structure **5**.



5 6

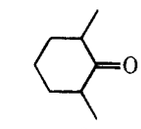
The other possible isomer **6** should display a spectrum characteristic of a molecule lacking a plane of symmetry, i.e., more than eight nonequivalent carbon atoms. The data are summarized in Table I. In all cases the NMR data established the hydroboration product to be a single isomer with the symmetry required for the proposed *trans*-2,*trans*-ω-dimethylcycloalkyl-9-borabicyclo[3.3.1]nonane structure such as is shown in Table I. This stereochemical assignment was confirmed by oxidation of the intermediate with alkaline hydrogen peroxide[4] to the known alcohol **7**.[5]



7

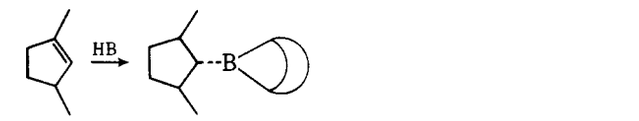
It is evident that the remote methyl group in olefins **1–4** exerts the same stereochemical control of the hydroboration stage as was observed in the monoalkylated olefins.[2]

Synthetic Applicability. The availability of intermediates, such as **5**, with high isomeric purity suggested a new route to *cis*-2,ω-dimethylcycloalkanones which have been previously difficult to prepare in pure form.[6] Thus, oxidation of **5** with alkaline hydrogen peroxide followed by chromic acid oxidation of the intermediate alcohol **7** using the Brown–Garg–Liu procedure[7] yielded ketone **8** with high isomeric purity.



8

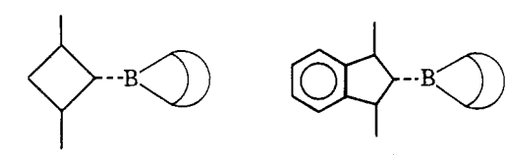
Applying the same sequence to 1,3-dimethylcyclopentene (**2**) provided the corresponding *cis*-2,5-dimethylcyclopentanone **9** (eq 5). This new synthesis of isomerically pure dialkylated cycloalkanones offers distinct advantages by proceeding through a series of reactions with high yields and stereochemical control, eliminating the need for difficult separation from significant amounts of isomeric by-products.



(5)

9

Although we did not convert the cyclobutenyl and idenyl derivatives into other products, the ^{13}C NMR spectra clearly establish the isomeric purity of the products (**10**, **11**).

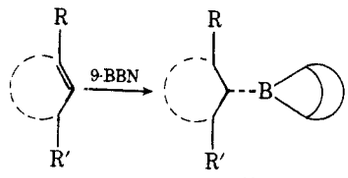


10 11

It is evident that it is possible to take advantage of the unique hydroboration characteristics of 9-BBN[2,8] to produce boron derivatives with clearly defined stereochemistry. The large number of substitution reactions of organoboranes[9] provides a valuable entry into such stereochemically defined products.

The present study was restricted to the 1,3-dimethylcycloalkenes because of their more ready availability and greater convenience in characterization. However, there is no reason

to question the general utility of this procedure for converting related cyclic olefins containing more complex substituents into related organoboranes (12) and many derivatives into which such organoboranes can be transformed (eq 6).



12 (6)

Conclusions

The results of this work confirm our prediction on the stereochemical outcome of the described hydroboration reactions. They also provide an example of a practical application of the known sensitivity[2,10] of 9-BBN to subtle differences in steric environment to achieve stereospecific synthesis.

Experimental Section

The organoboranes were always handled under an atmosphere of prepurified nitrogen with careful exclusion of both oxygen and water. All glassware, syringes, and needles were oven dried at 150 °C before use. ^1H NMR spectra were obtained with a Varian T-60. The ^{13}C NMR spectra were recorded at 35 °C on a Varian CFT-20 (20 M Hz FT) instrument with the following parameters: 1.024-s acquisition time, ~45° pulse angle, 100-ms pulse delay, 4000-Hz sweep width, 8K data points, >50 000 transients. The neat samples were contained in a 5-mm tube mounted coaxially in an 8-mm tube containing the lock sample ($CDCl_3$) and Me_4Si reference. The chemical shifts are reported relative to the Me_4Si reference (δ 0). The GLC analyses of alcohols, ketones, and olefins were carried out using a Hewlett-Packard 5752B chromatograph, and a Perkin-Elmer Model 226 FID capillary chromatograph, each instrument equipped with the appropriate column.

Materials. The preparation of solid 9-BBN was carried out as described previously.[8,11] 1,3-Dimethylcyclohexene was used as received (Chemical Samples). The rest of the olefins were prepared as follows.

1,3-Dimethylcyclobutene (1). Following the procedure in the literature,[12] 1-methyl-3-methylenecyclobutane[13] was treated with sodium on alumina to yield a mixture of olefins from which 1,3-dimethylcyclobutene was separated pure by preparative GLC (20% β,β-oxydipropionitrile, 10 ft × 0.25 in.).

1,3-Dimethylcyclopentene (2). 3-Methylcyclopentanone (12.2 g, 120 mmol) was dissolved in 100 mL of anhydrous ether and the resulting solution cooled to −79 °C. To the vigorously stirred solution, 95 mL (142.5 mmol) of a 1.5 M solution of methyllithium in ether was added slowly. The resulting mixture was allowed to warm up to room temperature and stirred for an additional 2 h. After addition of 6 mL of ethyl alcohol and 100 mL of water, the organic layer was separated. The aqueous layer was extracted with two 60-mL portions of ether and the combined ether solutions washed with water and dried with magnesium sulfate. Evaporation of the solvent afforded a liquid residue which was used for the next step without purification.

To the neat alcohol, a few crystals of iodine were added. The mixture was heated up to reflux temperature and then the volatile material separated. The distillate consisted of two layers. The organic layer was redistilled from $LiAlH_4$ to yield 8.05 g (70%) of a mixture of olefins which was separated by preparative GLC (silver nitrate) and the resulting pure products identified as 1,4-dimethylcyclopentene (52% of mixture, shorter retention time) and 1,3-dimethylcyclopentene (2) (48% of mixture) by comparison with authentic samples.

1,3-Dimethylindene (4). This olefin was prepared starting from indene as described elsewhere.[14]

Hydroboration of Olefins. The following procedure is representative. In a 25-mL flask, equipped with a septum inlet and a condenser connected to a mercury bubbler, was added 610 mg (5 mmol) of solid 9-BBN. To this was added 5 mL of a 1 M solution of 1,3-dimethylcyclopentene in CCl_4. The reaction mixture was stirred at 50 °C for 12 h. Evaporation of the CCl_4 under reduced pressure afforded a viscous residue which was used for ^{13}C NMR analysis. The NMR data are summarized in Table I. In all cases, the conversion of the olefins to alcohols by the hydroboration–oxidation procedure was essentially quantitative.[2]

***trans*-2,*trans*-6-Dimethylcyclohexanol (7).** Hydroboration of olefin 3 with 9-BBN was carried out as described above. The resulting organoborane was dissolved in THF and oxidized with alkaline hydrogen peroxide following the standard procedure[9] to yield after workup a low-melting solid residue. GLC analysis (SE-30) revealed the presence of two components in a 97:3 ratio. The major component was separated by preparative GLC (SE-30) and identified as *trans*-2,*trans*-6-dimethylcyclohexanol (7) by formation of its 3,5-dinitrobenzoate, mp 165–167 °C (lit.[5] 168–169 °C).

***cis*-2,6-Dimethylcyclohexanone (8).** This ketone was obtained by chromic acid oxidation of the corresponding alcohol (previous experiment) following the Brown–Garg–Liu procedure.[7] GLC analysis (FFEP, 300-ft capillary column) of the resulting ketone revealed the presence of 8 in more than 97% isomeric purity by comparison with a commercial sample containing both cis and trans isomers.

***trans*-2,*trans*-5-Dimethylcyclopentanol.** This alcohol was obtained applying the same sequence of hydroboration–oxidation and was further converted to its Me_3Si ether by reaction with *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA). GLC analysis (PPE, 300-ft capillary column) revealed the presence of a single product. This ether was identical with one of the two major components of a mixture of Me_3Si ethers obtained via $LiAlH_4$ reduction–BSTFA treatment of a commercial mixture of *cis*- and *trans*-2,5-dimethylcyclopentanone. Since the cis ketone greatly predominates in the commercial mixture, the two major components of the reduction mixture are believed to be *cis*-2,*cis*-5- and *trans*-2,*trans*-5-dimethylcyclopentanols and therefore the alcohol derived from the hydroboration (cis addition) must be the trans-2,trans-5 isomer.

***trans*-2,5-Dimethylcyclopentanone (9).** This ketone was obtained in 95% isomeric purity following the same procedure indicated for the cyclohexanone analogue.

Registry No.—5, 62587-11-5; 9-BBN, 280-64-8; *B-trans*-2,*trans*-ω-dimethylcyclobutyl-9-borabicyclo[3.3.1]nonane, 62587-12-6; *B-trans*-2,*trans*-ω-dimethylcyclopentyl-9-borabicyclo[3.3.1]nonane, 62587-13-7; *B-trans*-1,*trans*-3-dimethylindan-2-yl-9-borabicyclo[3.3.1]nonane, 62587-17-1; 3-methylcyclopentanone, 1757-42-2; 3-methylcyclopentanol, 18729-48-1.

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