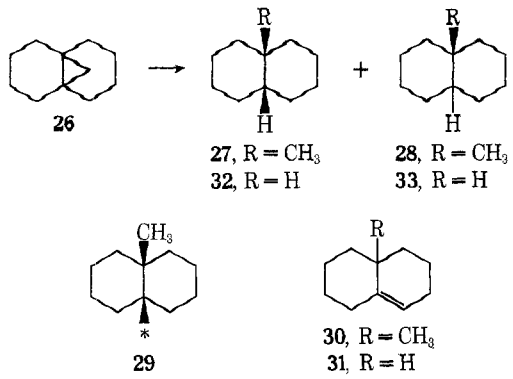

state, **29**, predominant formation of the cis decalin **27** would be expected. As shown for **3** in diagram **21**, the C_1 equatorial hydrogen bond in **26** is perpendicular to the cyclopropane bond which is adsorbed on the catalyst. Thus, the formation of the olefin **30** could occur by a process similar to that described for the formation of **22**. While the product stereochemistry obtained from the hydrogenation of **30** is not available, it has been reported that the hydrogenation of the demethyl compound **31** over platinum in acetic acid at room temperature and 1 atm gives a 60:40 mixture of the cis and trans decalins **32** and **33**.[18] Further work is currently underway in an attempt to establish whether the hydrogenolysis of cyclopropyl compounds such as **3** and **26** does, indeed, take place through an olefin intermediate as proposed here.

Registry No.—**3**, 2506-66-3; **7**, 51267-72-2; **9a**, 51231-35-7; **9b**, 51231-36-8; **11**, 51231-37-9; **12a**, 26605-74-3; **13a**, 51267-73-3; **14**, 51231-38-0; **16a**, 5986-74-3; **17**, 21496-61-7; **18**, 51267-74-4; **19a**, 26606-26-8; **19b**, 51231-39-1.

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Selective Reductions. XX. Stereochemistry of the Reduction of Cyclic, Bicyclic, and Polycyclic Ketones by Dialkylboranes. A Simple, Convenient Procedure for the Reduction of Ketones to the Corresponding Alcohols with Exceptionally High Steric Control[1]

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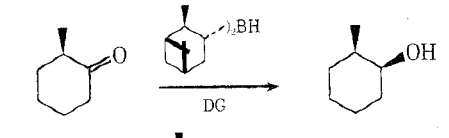
The introduction of two alkyl substituents into borane provides a simple, convenient means of modifying the steric requirements and reducing properties of this reagent. Dialkylboranes are found to be consistent reagents for steric control of reduction in monocyclic, bicyclic, and steroidal systems. 2-Alkylcycloalkanones of various ring size are reduced to 2-alkylcycloalkanols to give predominantly the less thermodynamically stable of the two possible alcohols (cis). In the case of bicyclic and steroidal ketones, which are analogs of 2-alkylcyclohexanones (such as 1-, 4-, or 6-keto steroids), dialkylboranes provide the less stable of the two possible alcohols in high isomeric purity. Unlike the conventional reagents, such as lithium aluminum hydride, borane, etc., the remarkable consistency exhibited by dialkylboranes in directing the reduction of these ketones from the less hindered direction provides a simple, convenient method for distinguishing the less hindered side of the molecule and for establishing the configurations of a pair of epimeric alcohols. Dialkylboranes provide the basis for a highly convenient synthetic procedure to achieve steric control of reduction of cyclic ketones where such control is required in synthetic operations such as the essentially quantitative conversion of 2-cyclohexylcyclohexanone to *cis*-2-cyclohexylcyclohexanol in 96% stereochemical purity.

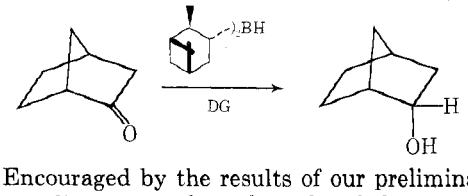
The stereochemistry of the reduction of cyclic ketones by complex metal hydrides and metal hydrides has attracted considerable attention, both from the synthetic as well as mechanistic viewpoint.[3] These extensive studies, in addition to providing simple procedures for the stereoselective synthesis of alcohols, have resulted in many fundamental theoretical concepts concerning nucleophilic additions to the carbonyl group. Since their discovery, the complex metal hydrides, such as lithium aluminum hydride and sodium borohydride, have been widely utilized for the conversion of ketones to alcohols. However, there is a major disadvantage in applying these reagents to cyclic ketones. Thus, reduction of cyclic ketones such as 2-methylcyclohexanone with lithium aluminum hydride appears

to involve the attack of the reagent from the more hindered direction (from the side of the methyl group) yielding predominantly the thermodynamically more stable of the two possible alcohol epimers (trans). However, in the case of rigid bicyclic ketones such as norcamphor, this reagent attacks the carbonyl group from the less hindered side to yield the less stable of the two possible epimers. Even among the monocyclic ketones, the behavior of lithium aluminum hydride is not consistent. Thus, 2-methylcycloheptanone[4] and 2-methylcyclooctanone yield the cis alcohol preferentially (73%).

The alkoxy derivatives of lithium aluminum hydride are equally unreliable, as there is no correlation between the steric bulk of the alkoxy substituent and the degree of steric approach control induced. Thus, lithium trimethoxyaluminohydride (LTMA) behaves as a more hindered reducing agent than lithium tri-*tert*-butoxyaluminohydride (LTBA).[3e] This phenomenon has been attributed to the aggregation in THF of LTMA into dimeric and trimeric species, whereas LTBA remains monomeric.[5] Accordingly, it appeared desirable to search for a reagent with well-defined steric requirements capable of reducing both monocyclic and bicyclic ketones consistently, with unambiguous stereochemistry.

The discovery of the hydroboration reaction has made available a wide variety of dialkylboranes with varying steric requirements around the boron atom.[6] These derivatives are far superior to the parent borane molecule as regioselective hydroborating agents. Consequently, we undertook an estensive investigation of the reducing ability of representative alkyl-substituted boranes,[7a] such as thexylborane,[7c] disiamylborane,[7b] 9-borabicyclo[3.3.1]nonane,[7d] etc., as reflected by the reaction in THF with selected organic molecules containing representative functional groups. During the course of this investigation, it was observed that dialkylboranes, such as disiamylborane and di-3-pinanylborane, exhibit remarkable consistency in directing the reduction of both α-substituted cycloalkanones and bicyclic ketones from the less hindered side to yield predominantly the less stable of the two possible epimers[8] (eq 1 and 2).





Encouraged by the results of our preliminary exploratory studies, we undertook a detailed examination of the various alkyl-substituted boranes with representative monocyclic, bicyclic, and polycyclic ketones. The results of these investigations are reported in the present paper.

Results and Discussion

General Procedure for the Reduction of Ketones. Standard solutions of borane–THF, disiamylborane–THF, and thexylborane–THF, prepared and stored at 0°, were utilized. Dicyclohexylborane and di-3-pinanylborane were prepared *in situ* by hydroborating the corresponding olefins at 0°, fresh for each run.

In the procedure developed for monocyclic and bicyclic ketones, a known quantity of the reagent (BH_3, RBH_2, or R_2BH) was placed or generated in the reaction flask in tetrahydrofuran (THF) or diglyme (DG) and cooled to 0°. A measured quantity of ketone was injected and stirred for a period of 8–24 hr (the time utilized depends on the particular ketone and the reagent used). Water was added to hydrolyze the reaction mixture, the boronic acid or borinic acid moiety was oxidized with alkaline hydrogen peroxide, and the product was extracted with ether and analyzed by glpc for the total yield (>85%) and isomer ratio using an internal standard.

Table I
Reduction of 2-Methylcyclohexanone with Borane and Its Alkyl Derivatives at 0°

Reagent, solvent	Mmol	Ketone, mmol	Time, hr	Cis epimer,[a] %
BH_3–THF	10	10	6	26
BH_3–THF	10	20	6	26
BH_3–THF	10	30	24	26
t-HexBH_2–THF	10	10	8	47
t-HexBH_2–THF	10	20	8	47
Sia_2BH–THF[b]	40	40	8	79
$CHex_2BH$–THF[c]	20	20	8	86
$CHex_2BH$–DG[c]	20	20	8	94
IPC_2BH–THF[c,d]	20	20	8	66
IPC_2BH–DG[c,e]	20	20	8	94

[a] Analysis by glpc. [b] Excess (5%) reagent was used to cover the initial loss. [c] Reagent was prepared *in situ*. [d] 12 mmol of α-pinene was formed by displacement. [e] 7 mmol of α-pinene was detected. However, a separate control experiment indicated that IPC_2BH in DG is formed only to 87.5% (17.5 mmol).

The procedure was tested for the material balance and for possible equilibration during the reaction by subjecting a standard mixture of *cis*- and *trans*-2-methylcyclohexanol of known cis/trans ratio to the reagent under identical conditions and work-up procedures. Both the yield and the cis/trans ratio corresponded to the standard mixture initially added. Consequently, equilibration is not a factor under these conditions.

In the study of polycyclic systems, involving steroidal ketones such as cholestan-6-one, the epimer ratio was determined by integrating the characteristic pmr signal of the axial or equatorial α-methine protons (–CHOH).

Effect of Structure of the Alkylborane and Solvent on Stereoselectivity. In order to understand the influence of the reagent structure on stereoselectivity, 2-methylcyclohexanone was treated with borane (BH_3), thexylborane (*t*-HexBH_2), disiamylborane (Sia_2BH), dicyclohexylborane ($CHex_2BH$), and di-3-pinanylborane (IPC_2BH) at 0° in THF. The resulting product was analyzed for the cis/trans ratio in the 2-methylcyclohexanol product. No change in the isomer distribution is observed as the ketone:reagent ratio is varied (ketone:BH_3 ratio of 1:1, 2:1, and 3:1 all gave 26% cis isomer), clearly indicating that the presence of excess reagent (B–H bond) does not change the cis/trans ratio. The results also revealed that the transfer of the first two hydrides in borane is rapid, whereas the transfer of the third is very slow.

Introduction of one bulky alkyl substituent, such as the thexyl group, enhances the relative amount of cis isomer (*t*-HexBH_2, 47% cis), the isomer which is less stable thermodynamically. Introduction of two alkyl substituents in borane has an even more dramatic effect, resulting in an enhanced stereoselectivity with the preferential formation of cis isomer (Sia_2BH, 79%; $CHex_2BH$, 86%; IPC_2BH, 66%). This clearly indicates that the introduction of hindered alkyl substituents in borane increases the stereoselectivity of the reduction.

Dialkylboranes, such as di-3-pinanylborane and dicyclohexylborane, exhibit greater stereoselectivity in diglyme than in THF. Thus, both IPC_2BH and $CHex_2BH$ gave 94% cis isomer in diglyme (DG). This can be attributed to two factors: (a) increased solubility of IPC_2BH in THF

Table II
Reduction of Representative 2-Methylcycloalkanones by Dialkylboranes at 0°

Registry no.	Ketone	cis-2-Methylcycloalkanol,[a] % (reaction time, hr) LiAlH4 in THF	BH3[c] in THF	Sia2BH[d] in THF	CHex2BH[e] in THF	IPC2BH[f] in DG
1517-15-3	2-Methylcyclobutanone	25 (1)	41 (1)	74 (4)	71 (8)	83 (8)
1120-72-5	2-Methylcyclopentanone	21 (1)	25 (2)	78 (8)	80 (8)	94 (8)
583-60-8	2-Methylcyclohexanone	25 (1)	26 (6)	79 (8)	94 (8)	94 (8)
932-56-9	2-Methylcycloheptanone	73 (2)	74 (8)	64 (24)	97 (24)	98 (24)
10363-27-6	2-Methylcyclooctanone	73 (2)	82 (8)	*b* (24)		

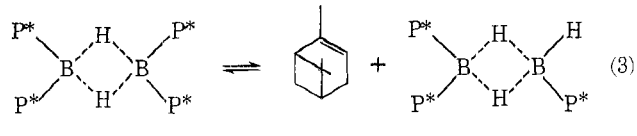
[a] Analysis by glpc. [b] Very slow reaction. [c] Registry no., 13283-31-3. [d] Registry no., 1069-54-1. [e] Registry no., 1568-65-6. [f] Registry no., 1091-56-1.

Table III
Reduction of 2-, 3-, and 4-Alkylcyclohexanones by Dialkylboranes at 0°

Registry no.	Cyclohexanone	Less stable epimer,[a] % LiAlH4 in THF	BH3 in THF	Sia2BH in THF	CHex2BH in DG	IPC2BH in DG
	2-Methyl[b]	25	26	79	94	94
4423-94-3	2-Ethyl[b]	33	49	91	94	93
1004-77-9	2-Isopropyl[b]	37	69	100	96	97
1728-46-7	2-*tert*-Butyl[b]	58	77	100	96	88
90-42-6	2-Cyclohexyl[b]				96	96
591-24-2	3-Methyl[c]	15	23	8	28	35
936-99-2	3-*tert*-Butyl[c]	18	30	11	13	28
589-92-4	4-Methyl[b]	17	21	13	24	33
98-53-3	4-*tert*-Butyl[b]	11	18	8	14	37
89-80-5	2-Isopropyl-5-methyl			84	79	

[a] Analysis by glpc. [b] Less stable epimer cis alcohol. [c] Less stable epimer trans alcohol.

over that in DG with greater dissociation in THF, resulting in a less sterically hindered reagent; (b) possible displacement of some olefin from dialkylborane during the addition to hindered ketones such as 2-methylcyclohexanone, camphor, etc.[9] (eq 3). Indeed, we were able to demonstrate that, during the reduction of hindered ketones with IPC_2BH, some formation of α-pinene occurs.



(3)

IPC_2BH tri-3-pinanyldiborane (less hindered reagent)

These results point out clearly that dicyclohexylborane and di-3-pinanylborane in diglyme possess remarkable ability to introduce steric control into the reduction of ketones. The results are summarized in Table I.

2-Alkylcycloalkanones. Previously, we had observed that disiamylborane and di-3-pinanylborane reduce 2-methylcyclopentanone and 2-methylcyclohexanone to give the cis alcohol preferentially.[10] These results encouraged us to extend this study to representative 2-methylcycloalkanones of various ring sizes (C_4–C_8). Accordingly, 2-methylcycloalkanones of C_4 to C_8 were reduced with $LiAlH_4$–THF, BH_3–THF, Sia_2BH–THF, $CHex_2BH$–DG, and IPC_2BH–DG at 0°.

It is clearly evident from these results that both lithium aluminum hydride and borane are not consistent in their direction of attack. Thus, C_4, C_5, and C_6 ketones yield trans alcohol (more stable, attack from the more hindered side) preferentially with both $LiAlH_4$ and BH_3, whereas C_7 and C_8 ketones yield the cis alcohol (less stable, attack from the less hindered side) preferentially. However, with all of these ketones dialkylboranes exhibit remarkable consistency in approaching from the less hindered direction to give predominantly *cis*-2-methylcycloalkanol (C_4–C_8). The results are summarized in Table II.

Finally, the stereoselectivity of the reaction is strongly dependent on the steric bulk of the 2-alkyl substituent present in the ketone. The increase in the steric requirements of the alkyl substituent in 2-alkylcyclohexanone from methyl to *tert*-butyl dramatically enhances the stereoselectivity. Thus, 2-methylcyclohexanone with Sia_2BH yields 79% cis alcohol, whereas 2-isopropylcyclohexanone and 2-*tert*-butylcyclohexanone yield 100% cis alcohol (Table III).

3- and 4-Alkylcyclohexanones. With 3- and 4-alkylcyclohexanones, where the alkyl substituent is relatively remote from the reaction center, the dialkylboranes exert only a minor influence on the direction taken by the reduction. In all cases the product is predominantly the more stable of the two possible epimers. Thus, 3-*tert*-butyl- and 4-*tert*-butylcyclohexanone yield the more stable alcohols, *cis*-3-*tert*-butylcyclohexanol and *trans*-4-*tert*-butylcyclohexanol, to the extent of 72 and 64%, respectively. The results are summarized in Table III.

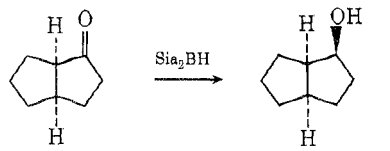
Bicyclic Ketones. Reduction of bicyclic ketones such as norcamphor and camphor by lithium aluminum hydride and lithium trimethoxyaluminohydride have been shown to proceed with preferential attack of the hydride reagent from the less hindered side, yielding the less stable of the two epimers predominantly.[3e] Extension of dialkylborane reductions to representative bicyclic ketones reveals their remarkable preference to attack from the less hindered direction. With norcamphor, Sia_2BH, $CHex_2BH$, and IPC_2BH all gave over 90% of *endo*-norborneol (from exo attack). However, the direction of attack was inverted by the steric influence of the *gem*-dimethyl substituents of camphor, yielding 93% isoborneol with $CHex_2BH$ and 100% isoborneol with IPC_2BH (endo attack).

We decided to test the generality of these results in other bicyclic systems that are prevalent in the naturally occurring molecules. Accordingly, bicyclo[3.3.0]octan-2-one, isopinocamphone, and isocarone were reduced with disiamylborane in THF. With all of these ketones, the reagent exhibits remarkable consistency in directing the reduction from the less hindered side, confirming the wide general applicability of the reaction (eq 4–6). The results are summarized in Table IV.

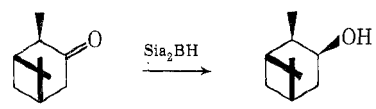
Table IV
Reduction of Representative Bicyclic Ketones by Dialkylboranes at 0°

Registry no.	Ketone	Less stable alcohol epimer	Less stable epimer,[a] % (reaction time, hr) BH_3 in THF	Sia_2BH in THF	$CHex_2BH$ in DG	IPC_2BH in DG
497-38-1	Norcamphor	endo	98 (6)	92 (8)	94 (8)	94 (8)
464-49-3	Camphor	exo	52 (6)	65 (8)	93 (24)	100 (24)
19915-11-8	Bicyclo[3.3.0]octan-2-one	endo		98 (8)		
15358-88-0	Isopinocamphone	exo		99 (8)		
4176-01-6	Isocarone	exo		87 (8)		

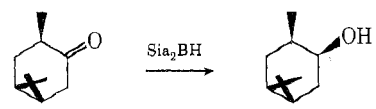
[a] Analysis by glpc.



98% (4)



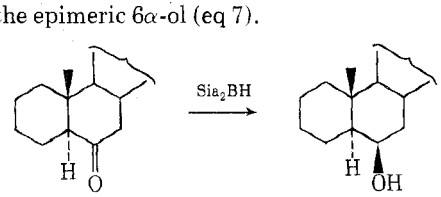
99% (5)



87% (6)

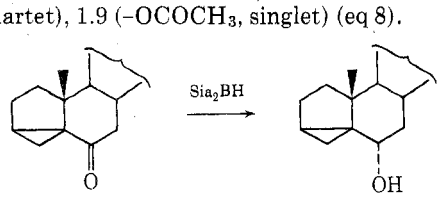
Polycyclic (Steroidal) Systems. Polycyclic ketones such as steroidal ketones possess a highly rigid conformation and undergo hydride reduction from the less hindered side of the carbonyl group. It was of interest to examine their behavior toward dialkylboranes. Accordingly, we reduced cholestan-6-one and 3,5-cyclocholestan-6-one with disiamylborane in THF.

Reduction of cholestan-6-one with Sia_2BH yielded an alcohol whose pmr spectrum exhibited the following absorptions: δ 3.6 (-CHOH, broad, equatorial hydrogen)[11] and 4.15 (-OH, disappearing with D_2O). Scanning the spectrum at higher amplitude at δ 3.0–4.2 did not reveal any additional absorption, indicating the essential absence of the epimeric 6α-ol (eq 7).



(7)

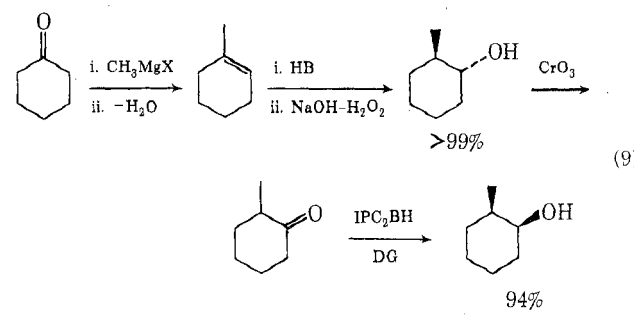
However, the reduction of 3,5-cyclocholestan-6-one with Sia_2BH yielded exclusively 3,5-cyclocholestan-6α-ol, as revealed by the pmr spectrum of the reduction product, δ 3.81 (-CHOH, broad) and 2.73 (-OH, disappearing with D_2O), and 6α-acetate derivative,[12] δ 5.07 (-CHOAc, unresolved quartet), 1.9 (-$OCOCH_3$, singlet) (eq 8).



(8)

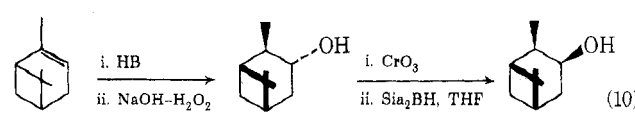
Scope and Applicability. For achieving the conversion of the keto group to the >CHOH grouping, dialkylborane reduction offers many unique advantages over the conventional reagents such as lithium aluminum hydride and its alkoxy derivatives, aluminum hydride, borane, etc. Extensive study of the reaction of typical organic functional groups with excess disiamylborane in THF indicates that the reagent is a mild reducing agent and can tolerate the presence of many functional groups such as nitro, halogen (alkyl and aryl), epoxide, carboxylic acid, acid chloride, ester, nitrile, oxime, sulfide, disulfide, sulfone, tosylate, etc. Consequently, dialkylboranes should be highly useful for achieving the selective steric control reduction of the ketones in the presence of these functional groups.

From the synthetic point of view, dialkylborane can be coupled with hydroboration–oxidation of many 1-alkylcycloalkenes (prepared from the unsubstituted ketone *via* Grignard addition and dehydration) and bicyclic olefins to yield the two isomeric alcohols in high stereochemical purity. For example, hydroboration–oxidation of 1-methylcyclohexene yields *trans*-2-methylcyclohexanol in isomeric purity of >99%. Oxidation to the ketone by chromic acid followed by reduction with di-3-pinanylborane yields the epimer, *cis*-2-methylcyclohexanol, in isomeric purity of 94% (eq 9). Similarly, α-pinene can be converted to pure



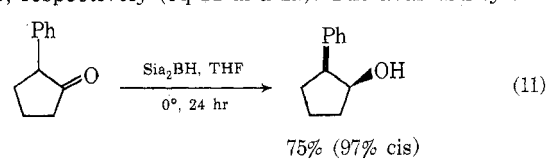
(9)

isopinocampheol *via* hydroboration–oxidation. This on further oxidation with chromic acid and reduction by disiamylborane yields neoisopinocampheol in 99% isomeric purity (eq 10).

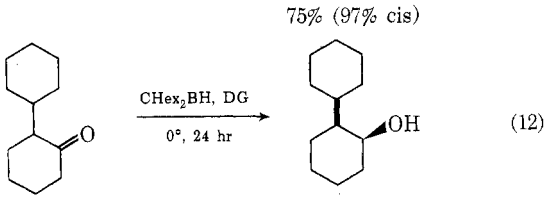


(10)

The synthetic utility of these reagents is further evidenced by the conversion of 2-phenylcyclopentanone and 2-cyclohexylcyclohexanone into *cis*-2-phenylcyclopentanol and *cis*-2-cyclohexylcyclohexanol in isolated yields of 75 and 99%, respectively (eq 11 and 12). The availability of a



(11)
75% (97% cis)



(12)
99% (96% cis)

variety of hindered dialkylboranes for such transformations renders possible the use of proper reagent, depending upon the difference in the physical properties of the

alcohol formed and the alcohol generated from the dialkylboranes by oxidation.

The remarkable consistency exhibited by dialkylboranes in their approach from the less hindered side of the carbonyl group provides a more reliable tool for exploring the stereochemical environments of carbonyl groups and for establishing the configurations of a pair of epimeric alcohols. Thus, as already pointed out, disiamylborane reduces cholestan-6-one from the α side to give exclusively cholestan-6β-ol, but reduces 3,5-cyclocholestan-6-one from the β direction to give exclusively 6α-ol.[13] These results clearly show that in 3,5-cyclocholestan-6-one the bottom side is more hindered and in the cholestan-6-one the top side is more hindered. The reduction of cholestan-6-one and 3,5-cyclocholestan-6-one by lithium aluminum hydride has been previously observed to proceed from opposite directions in these two systems.[14] However, the inconsistencies which have been observed for such reductions with lithium aluminum hydride make it dangerous to rely upon such reductions for conclusions as to the stereochemical environments of carbonyl group.

Finally, the results of this investigation clearly indicate that the 2-alkyl substituent in the 2-alkylcyclohexanones exerts a dominant steric effect on the direction taken in the reductions involving the highly hindered dialkylboranes. This can be explained by the increase in the transition-state energy as the size of the α substituent increases (owing to steric interactions) thereby hindering axial (topside) attack, whereas the torsional strain between the reagent and the two α-axial hydrogens remains relatively insensitive to the steric bulk of the reagent, thereby facilitating equatorial attack (bottom side) to give the cis isomer.[3i,j,k]

Experimental Section

Materials. Tetrahydrofuran was dried with excess lithium aluminum hydride and distilled under nitrogen. Diglyme was first dried over calcium hydride and distilled under reduced pressure. Again it was treated with a small quantity of lithium aluminum hydride and distilled under reduced pressure, bp 63° (14 mm), in a nitrogen atmosphere. Borane–THF solution was prepared from sodium borohydride and boron trifluoride etherate.[15,16] Standard solutions of thexylborane[7c] and disiamylborane[7b] were prepared from the borane and the respective olefins by stoichiometric reaction. These solutions were standardized by hydrolyzing a known aliquot of the solution with glycerine–water–THF mixture and measuring the hydrogen evolved. Dicyclohexylborane and di-3-pinanylborane were prepared *in situ* by hydroboration of the corresponding olefins in tetrahydrofuran and in diglyme.[9b] Some of the ketones used were the commercial products of the highest purity. They were further purified by distillation or sublimation. 2-Alkylcycloalkanones of very high purity were prepared by subjecting 1-alkylcycloalkenes to hydroboration–oxidation to yield the pure *trans*-2-alkylcycloalkanol[17] and further oxidation by the chromic acid–ether procedure.[18] 1-Alkylcycloalkenes were prepared by the Grignard addition to cycloalkanone followed by dehydration. Similar sequences of steps were utilized for the preparation of certain bicyclic ketones, for example, the synthesis of isopinocamphone from α-pinene.[3e] Hydroboration–oxidation of cholest-5-ene[19] gave cholestan-6α-ol, which on chromic acid oxidation yielded cholestan-6-one, mp 93–99°. 3,5-Cyclocholestan-6-one was prepared by the solvolysis of cholesteryl tosylate, followed by chromic acid oxidation.[14b] In the case of all of the compounds synthesized, physical constants agreed satisfactorily with constants in the literature. For further details, the thesis should be referred to.[20]

Glpc Analyses. Glpc analyses of the reduction products were carried out on the Perkin-Elmer 226 temperature-programmed instrument fitted with a Golay column. Authentic samples of isomeric alcohols were utilized to identify the products.

General Procedure for the Reduction of Ketones. Rate of Reduction and Product Analysis. Reduction of 2-methylcyclohexanone with disiamylborane in THF is representative. An oven-dried, 100-ml, two-necked flask equipped with a side arm fitted with a silicone rubber stopple, a magnetic stirring bar, a reflux condenser, and a thermometer was flamed out and cooled in a dry nitrogen atmosphere. The flask was immersed in an ice bath and cooled to 0°. Then 4.4 ml of THF was introduced into the reaction flask followed by 25.6 ml (40 mmol) of 1.56 *M* disiamylborane solution in THF. To this stirred solution maintained at 0°, 10 ml (40 mmol) of a 4 *M* solution of 2-methylcyclohexanone was slowly added over a period of 5 min. Now the resulting reaction mixture was 1 *M* in both Sia_2BH and ketone.

At the end of 1 hr, a 5.0-ml aliquot of the reaction mixture was removed with a hypodermic syringe and injected into a hydrolyzing mixture containing a 1:1:1 mixture of glycerine–water–THF, and the hydrogen evolved was measured with a gas buret. This indicated the completion of 73% reduction. The reaction was monitored at 2 (79%), 6 (88%), 8 (92%), and 24 hr (98%).

Simultaneously, another run of the reaction was carried out under identical conditions. This was hydrolyzed at the end of 8 hr by adding slowly 2 ml of a 1:1 mixture of THF–water. The boronic acid derivative was oxidized by the addition of 13.3 ml (40 mmol) of 3 *N* sodium hydroxide followed by 11 ml (96 mmol) of 30% hydrogen peroxide. To this, 10 ml (40 mmol) of a 4 *M* solution of 3-hexanol was added to serve as an internal standard. The aqueous phase was saturated with 5–6 g of potassium carbonate, the THF layer was separated, and the aqueous phase was extracted with two 15-ml portions of ether. The combined organic extracts were dried over magnesium sulfate. Glpc examination of the organic extract indicated an 88% yield of 2-methylcyclohexanols (cis, 79%; trans, 21%) and 12% of unreacted 2-methylcyclohexanone.

Reduction of Cholestan-6-one with Disiamylborane in THF. Reduction was carried out on a 3-mmol scale for 24 hr at 0°, and the reaction mixture was worked up as in the previous experiment. The siamyl alcohol was removed under reduced pressure. Unreacted cholestan-6-one was removed by column chromatography on basic alumina (activity II) and elution with petroleum ether (no alcohol is eluted with this solvent as revealed by the ir spectrum). The alcohol (0.98 g) was totally eluted with ether–methanol and analyzed by pmr to be exclusively cholestan-6β-ol, nmr (CCl_4, TMS) δ 3.6 (s, 1, -CHOH), 4.15 (s, 1, -OH). Scanning of the spectrum at higher amplitude at δ 3.0–4.17 did not show any additional absorption, indicating the absence of 6α-ol. Cholestan-6α-ol has a characteristic -CHOH absorption at δ 3.47 (broad doublet, $J \cong 20$ Hz).

Reduction of 3,5-Cyclocholestan-6-one with Disiamylborane in THF. A 2.7-mmol portion of the ketone was reduced with excess disiamylborane in the THF. The reaction mixture, after the usual work-up and removal of siamyl alcohol under reduced pressure, yielded a glassy material which could not be crystallized. Tlc examination of this material on a silica gel plate using 10% ether in benzene revealed that the alcohol product obtained in this reaction is different and completely free from the 3,5-cyclocholestan-6β-ol, obtained by the solvolysis of cholesteryl tosylate. The alcohol was purified by column chromatography on basic alumina (activity I) and elution with 1:1 benzene–pentane mixture. It was found to be pure 3,5-cyclocholestan-6α-ol by nmr and tlc, nmr (CCl_4, TMS) δ 3.81 (s, 1, -CHOH, broad). 2.73 (s, 1, -OH). 3.5-Cyclocholestan-6β-ol exhibits the following spectrum: δ 3.15 (s, 1, -CHOH, sharp), 2.08 (s, 1, -OH).

Comparison of the nmr spectrum of the acetate of the reduction product with that of the acetate of the 6β-ol also revealed their nonidentity: 6α-acetate δ 5.07 (q, 1, -CHOAc); 6β-acetate, δ 3.4 (s, 1, -CHOAc).

General Preparative Procedure for the Steric Control Reduction of Ketones to Alcohols. The following general procedures illustrated for the reduction of 2-cyclohexylcyclohexanone to *cis*-2-cyclohexylcyclohexanol and 2-phenylcyclopentanone to *cis*-2-phenylcyclopentanol are representative. Depending upon the other substituents present in the ketone, the hydride to ketone ratio and the time required may require an increase or decrease.

A. Preparation of *cis*-2-Cyclohexylcyclohexanol. In a 1-l. flask equipped with a reflux condenser, a thermometer, a dropping funnel, and a magnetic stirring bar, and maintained at 0° under dry nitrogen atmosphere, were placed 660 mmol (54.12 g, freshly distilled over $LiAlH_4$) of cyclohexene in 100 ml of diglyme and 225 ml of a 1 *M* solution of sodium borohydride in diglyme (225 mmol). The flask was immersed in an ice bath. Diborane was generated by adding 37.8 ml (300 mmol) of boron trifluoride etherate diluted with 50 ml of diglyme to the well-stirred reaction mixture over a period of 15 min. During the boron trifluoride etherate addition, dicyclohexylborane precipitated from the solution. The reagent was maintained at 0° for an additional period of 3 hr.

To this stirred mixture 27 g (150 mmol) of 2-cyclohexylcyclo-

hexanone was slowly added and the resulting mixture was stirred for 24 hr at 0°. Then water was added (10–15 ml) slowly to decompose the excess hydride and to hydrolyze the reaction mixture. The boronic acid formed was oxidized by adding 66 ml of 3 *N* sodium hydroxide followed by *dropwise* addition of 66 ml of 30% hydrogen peroxide (vigorous reaction). The resulting mixture was stirred at 30–50° for 1 hr. Then the reaction mixture was extracted five times with 60-ml portions of ether and the ether extract was washed five times with equal amounts of ice water to remove diglyme. The ether extract was dried over magnesium sulfate. After the solvent was removed, the mixture was distilled at 20 mm to remove cyclohexanol (from the oxidation). The pressure was then reduced to obtain 27 g (99%) of 2-cyclohexylcyclohexanol (cis 96% by glpc analysis on a TCEP column), bp 117–118° (6 mm), mp 59–61°, *p*-nitrobenzoate mp 112–114° (lit.[21] mp 61°, *p*-nitrobenzoate mp 113°).

B. Preparation of *cis*-2-Phenylcyclopentanol. To a solution of 150 ml (150 mmol) of a 1.0 *M* solution of disiamylborane in THF in a 500-ml flask maintained at 0° under nitrogen was added 14.4 g (90 mmol) of 2-phenylcyclopentanone over a period of 15 min. The resulting mixture was stirred at 0° for 24 hr and then worked up as usual. The volatile solvents and siamyl alcohol were removed at 40–45° (10 mm). Distillation of the residue yielded 11 g (75%) of 2-phenylcyclopentanol (cis 97% by glpc), bp 118° (8 mm), n^{20}D 1.5433, *p*-toluenesulfonate mp 96–97° [lit.[22] pure cis isomer, bp 111–113° (5 mm), n^{20}D 1.5460, *p*-toluenesulfonate mp 97–98°].

Registry No.—Cholestan-6-one, 570-46-7; cholestan-6*β*-ol, 35490-51-8; 3,5-cyclocholestan-6-one, 3839-06-6; 3,5-cyclocholestan-6*α*-ol, 508-41-8; 3,5-cyclocholestan-6*α*-ol acetate, 17132-05-7; *cis*-2-cyclohexylcyclohexanol, 51175-62-3; *cis*-2-phenylcyclopentanol, 2362-73-4; 2-phenylcyclopentane, 1198-34-1; dithexylborane, 20622-63-3.

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Oxymercuration–Demercuration and Hydroboration–Oxidation of *endo*-Dicyclopentadiene (*endo*-Tricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene)[1a]

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The course of monohydration of *endo*-tricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene (1) (*endo*-dicyclopentadiene) with hydroboration–oxidation and oxymercuration–demercuration is compared and the stereochemistry of the alcohols is elucidated both by spectral studies and by acid-catalyzed and photochemical cyclizations to ethers of novel structures. The addition of nitrosyl chloride to 1 is also described.

Hydroboration–oxidation[2] and oxymercuration–demercuration[3,4] have proved to be efficient methods for the hydration of carbon–carbon double bonds without appreciable rearrangement. The hydroboration of unsymmetrical olefins normally leads to the anti-Markovnikov hydration product, while oxymercuration–demercuration is equally convenient for the preparation of Markovnikov alcohols. Synthesis of hydroxy olefins by monohydration of dienes has been accomplished using these procedures.[5,6] Previous studies of electrophilic addition to *endo*-dicyclopentadiene (1) have been concerned with the determination of the stereochemistry of addition (exo *vs.* endo, cis *vs.* trans) and the effect of the reagent upon the ring system, namely the tendency toward rearrangement to a derivative of *exo*-dicyclopentadiene (4).[7-11] Although the possibility of isomers differing only in the position of a double bond is often acknowledged, amounts have seldom been reported and specific structures have rarely, if ever, been proposed. In the present work the monohydration of 1 by these two methods is compared and the stereochemistry of the alco-