Directive Effect of a Carboxylate Group in the Hydroboration of Cyclohexenes

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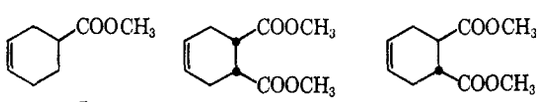
Hydroboration of methyl cyclohexene-3-carboxylate (I) yields mostly methyl *trans*-3-hydroxycyclohexanecarboxylate and that of dimethyl *cis*-tetrahydrophthalate (II) gives exclusively the *trans* alcohol (IV). Dimethyl *trans*-tetrahydrophthalate (III), trimethylcyclohexene (XVIII), and 4-methylcyclohexene (XXIV) were also studied.

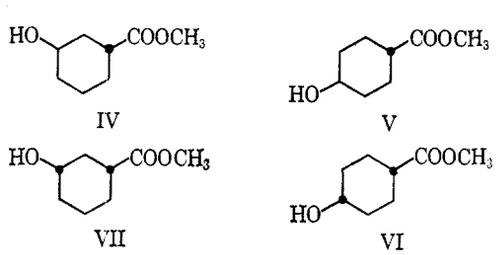
A directive effect of carboxylate on addition of diborane to a double bond in a heterocyclic ring was found in Witkop's laboratory.[2] The influence of polar substituents[3,4] in the allyl position on the position of attachment of boron was also demonstrated. In our laboratory,[1] the study of the influence of a remote carboxylate on the addition of diborane to cyclohexenes has started with methyl cyclohexene-3-carboxylate (I). It was extended then to the dimethyl esters of *cis* II and *trans*-tetrahydrophthalic acid (III) for two reasons: first, only one positional isomer can be formed in each case owing to symmetry, and secondly, the cumulative or opposite action of the two carboxylate groups should give more information on the nature of the directing effect. In addition, 4-methylcyclohexene and 3,5,5-trimethylcyclohexene were also studied to evaluate the influence of nonpolar substituents.



I II III

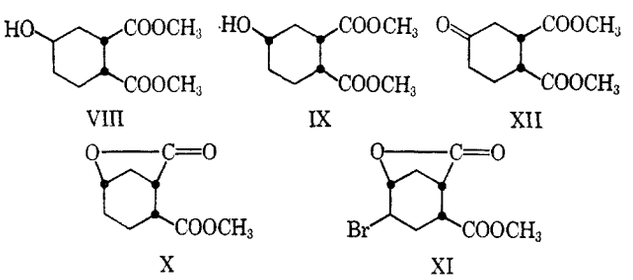
Results

Hydroboration and subsequent oxidation of I yielded a mixture of difficultly separable isomers. Gas–liquid partition chromatography (glpc) showed that the isomers were formed in an approximate ratio IV/V/VI/VII = 4:2:1:1.



IV V VII VI

A single hydroxy diester was obtained in 75% yield on hydroboration of II with subsequent oxidation. This substance was different from its isomer (IX) obtained by the action of methanol in presence of acid on the ester lactone (X), which was prepared by reduction of XI with triphenyltin hydride. The alcohol obtained in hydroboration of II is therefore VIII. Both isomers VIII and IX were obtained on reduction of the keto diester (XII) with diborane.[5] The same isomer

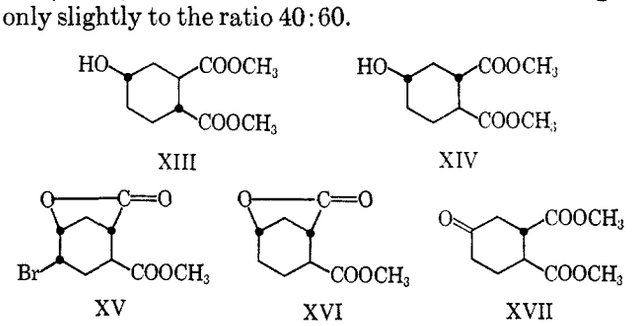


VIII IX XII X XI

(VIII) was formed in the hydroboration of the anhydride of II and subsequent oxidation and esterification.

The *trans* diester (III) yielded on hydroboration and oxidation a mixture of two isomers (XIII and XIV) in the ratio 7:3. The same two isomers were obtained from the *trans* anhydride in the ratio 3:2. The reference substances were prepared as above by reduction of bromo lactone XV with triphenyltin hydride to ester lactone XVI, which gave XIV on treatment with methanol and acid. The other isomer (XIII) was identified by gas chromatography as the second isomer formed on reduction[5] of the carbonyl group in XVII. An attempt to prepare XIV by converting first bromo lactone XV to the hydroxybromo diester by treatment with methanol and subsequent debromination of the obtained diester with triphenyltin hydride yielded instead lactone XVI. A similar lactonization occurred when this sequence was tried on bromo lactone XI. In the latter case, lactone X was formed.

Isomeric fractionation did not occur during the oxidation step and alkaline treatment. This was proved by submitting a mixture of XIII and XIV to the conditions of the oxidation and work-up steps after hydroboration. The proportion of the two isomers did not change after this treatment. A mixture of VIII and IX (37:63) submitted to this same treatment changed only slightly to the ratio 40:60.



XIII XIV XV XVI XVII

The cyclic olefin (XVIII) was prepared from isophorone by the method of Caglioti[6] and submitted to hydroboration yielding a mixture of the four isomeric products (XIX, XX, XXI, and XXII) in the ratio

(1) Taken in part from the M.S. thesis of D. Avrahami, The Hebrew University, 1962.

(2) Y. Fujita, F. Irreverre, and B. Witkop, *J. Am. Chem. Soc.*, **86**, 1844 (1964).

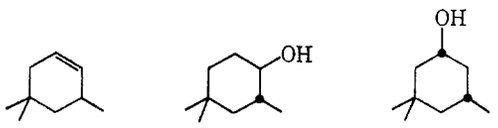
(3) H. C. Brown and K. A. Keblys, *ibid.*, **86**, 1791, 1795 (1964).

(4) H. C. Brown and O. J. Cope, *ibid.*, **86**, 1801 (1964).

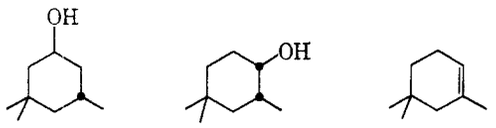
(5) J. Klein and E. Dunkelblum, *Tetrahedron*, **23**, 205 (1967).

(6) L. Caglioti, G. Cainelli, G. Maina, and A. Selva, *ibid.*, **29**, 957 (1964).

16:34:3:47. The alcohols of reference XX and XXI were obtained by reduction of dihydroisophorone.[5] Compound XIX was obtained by hydroboration of XXIII, which was prepared by reduction of isophorone with lithium aluminum hydride–aluminum chloride.[7]



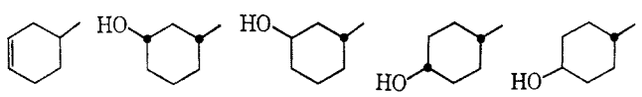
XVIII XIX XX



XXI XXII XXIII

The tosylate of XIX gave on treatment with sodium acetate an acetate with the opposite configuration, from which the *cis* alcohol (XXII) was obtained by saponification.

4-Methylcyclohexene (XXIV) was also submitted to the standard hydroboration–oxidation procedure. The separation of the products was difficult, but their



XXIV XXV XXVI XXVII XXVIII

quantitative analysis could be made by glpc of the alcohols and the ketones obtained by oxidation of their mixture. An almost equal amount of all the four isomeric alcohols (XXV, XXVI, XXVII, and XXVIII) was obtained (the ratio was 28:27:20:25, respectively).

Discussion

The site of boron attack on I can be explained by a polar factor. It is reasonable that the partial positive charge developed on the olefinic carbon next to the one forming a bond with boron, should tend to be as remote as possible from the electron-attracting carboxylate group. The predominant formation of the *trans*-3-product from I can be explained in several ways: (1) the carboxylate keeps the molecule in a conformation in which this group is equatorial and the borane attacks the double bond in a perpendicular manner, as it is known for many additions; (2) the carboxylate can also exercise a polar effect, which makes the trans attack more favorable; (3) a purely steric effect can be conceived, in which a *cis* approach to the ring system is more difficult than an approach *trans* to the carboxylate.

No appreciable polar effect[5] occurs in the reduction of substituted cyclohexanones with diborane, and substituents in a cyclohexene ring are known[8] not to affect the ratio of positional isomers or stereoisomers in the hydroboration reaction. Thus, 3-methylcyclohexene and 3,3-dimethylcyclohexene give almost equal amounts of all possible isomers.[8] In contrast, the steric course of the hydroboration of steroids is selective.[9-11]

Our results with 4-methylcyclohexene support the view[8] that methyl groups have no visible steric influence in hydroboration. The reason for this may lie in an ability of diborane to add to the double bond to give with almost equal ease an equatorial or axial product. An assumption that each isomer is formed from a different conformation of the reacting substance would demand the ratio of the rate constants of the conformers to be always equal to the inverted ratio of their mole fractions.

However, only equatorial methyls do not affect the steric course of the reaction. The stereoselective course of hydroboration of steroids,[9-11] which proceeds mostly *trans* to the angular methyl, suggested the importance of this substituent. Our results with 3,5,5-trimethylcyclohexene (XVIII) stress the influence of the conformation of a methyl in monocyclic systems.

The most simple explanation of the ratio of isomers formed during the hydroboration of XVIII is founded on the very reasonable assumption that for this olefin conformation XXIX is energetically preferred and that the reaction of this conformer is favored. No information is available on the energy of XXIX relative

XXIX XXX

to that of the other possible conformation of this olefin, *e.g.*, XXX. It is known that the difference in conformational energy between an axial and equatorial bromine in the 4 position of cyclohexene[12] is only 0.1 kcal/mole, whereas in bromocyclohexane the *A* value is about 0.5 kcal/mole[13] owing to larger axial–axial interactions and to the presence of two such interactions instead of one in bromocyclohexene. Because interactions between axial substituents rise steeply with their size, it can be admitted that a methyl group with an *A* value of 1.8 will have, when axially disposed, a much stronger interaction with a pseudo-axial methyl than with a pseudo-axial hydrogen (compare CH_3H diaxial interaction of 0.9 kcal and CH_3CH_3 interaction of 3.7 kcal in cyclohexane), and a much higher one than between an axial bromine and pseudo-axial hydrogen. A conformational energy difference of 2 kcal/mole is enough to confine 95% of all molecules to conformation XXIX.

The nmr spectrum of XVIII shows that the two geminal methyls and the two geminal hydrogens at position 5 are not equivalent. The signals of the methyls are observed at τ 9.16 (singlet, attributed to the axial geminal methyl), 9.12 (singlet, equatorial geminal methyl), 9.09 (doublet, J = 7 cps, allylic methyl). The geminal protons at position 4 show three signals (τ 8.94, 8.76, 8.67) which correspond to 1.5 protons and may be due to three signals of a doublet of doublets owing to geminal splitting, the fourth singlet being

(7) E. L. Eliel, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **22**, 129 (1961).

(8) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 2544 (1961).

(9) F. Sondheimer and M. Nussim, *J. Org. Chem.*, **26**, 630 (1961).

(10) A. Hassner and C. Pillar, *ibid.*, **27**, 2914 (1962).

(11) W. J. Wechter, *Chem. Ind.* (London), 294 (1959).

(12) F. R. Jensen and C. H. Bushweller, *J. Am. Chem. Soc.*, **87**, 3285 (1965).

(13) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co. Inc., 1962, New York, N. Y., Chapter 8.

hidden under other bands, or to the AB part of a more complex AMB spectrum, where weaker signals account for the remaining half-proton. Additional signals are at τ 8.26 (geminal allylic protons, multiplet), a broad multiplet at 8 (CHMe), and at 4.5 (olefinic protons). However this spectrum cannot be considered as a proof for the presence of one conformation, since the methyls are not magnetically equivalent even for a dynamic mixture of conformers.

Although the dangers in attempting to correlate reaction products with conformational populations of the ground state of reacting molecules are well known,[14,15] it seems to us justifiable to do so in the case of hydroborations. This reaction is very fast and the transition state is probably very near in structure and energy to the reagents.

The energies of the ground-state conformations have to be taken into consideration. The transition state is constituted of the hydrocarbon with a structure similar to that of the starting olefin and the borane, that has to be situated perpendicular to the plane of the double bond, to ensure overlap of the π electrons with the unoccupied orbital of boron. A similar situation is found in the bromination and protonation of enols and enolates, although the analogy cannot be complete, the hydroboration being a four-center reaction. The interaction between borane and the olefin in the transition state has to be taken into consideration, since two perpendicular modes of approach to XVIII are possible.

With this in mind it may be observed that diborane attacks the molecule in conformation XXIX preponderantly *trans* to the axial methyl group (81%), which is *cis* to the single methyl in position 3. This influence of an axial methyl, which is not observed in the case of the equatorial ones supports the hypothesis of a perpendicular attack of diborane. This perpendicular attack is particularly hindered in position 1, where a 1,3-diaxial interaction is developing between the methyl and diborane in case of a *cis* attack (*trans* to the methyl in 3).

The rule of perpendicular attack by diborane is not linked with a conformational demand for a chairlike transition state. Since formation of the *cis* alcohol (XX) is not due to an equatorial attack, it has to be admitted that both attacks, the antiparallel with a chairlike and the parallel with a boatlike transition state[16] are almost equally favored. The highest amount of alcohol XXII formed confirms once more the insensitivity of the reaction to an equatorial methyl. A much larger amount of *cis* attack on the 2 position than on the 1 position is in agreement with less interaction between the axial methyl and diborane attacking axially a *para* than a *meta* position.

It is interesting that the *cis* alcohol (XX), probably the most stable of all isomers, is formed in a somewhat lesser proportion than *cis* alcohol XXII (34:47), where an *ortho-cis* methyl group is present. Although all results support the view that the transition states have structures like the starting materials, the chairlike is probably energetically somewhat more favored than the boatlike one.

(14) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.* **77**, 5562 (1955).
(15) D. J. Curtin, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **15**, 111 (1954).
(16) J. Valls and E. Toromanoff, *Bull. Soc. Chim. France*, 758 (1961).

A carbomethoxy group has a smaller A value than a methyl. The exclusive formation of the *trans* hydroxy ester (VIII) in the hydroboration of II cannot be ascribed to the axial carbomethoxy group, since XVIII, having an axial methyl, reacts with diborane *cis* and *trans* to this methyl in the ratio 1:4. The directive effect observed in hydroboration of II cannot be therefore of pure steric origin and is probably due, at least partly, to the polar influence of the carbomethoxy group.

The steric course of the hydroboration of *trans*-diester III is more difficult to interpret, because of the existence of two conformers, a diaxial and a diequatorial one. The ratio 7:3 in favor of the 4-*trans* isomer (XIII) obtained in the hydroboration of III can be explained either by stereoselective reaction of the diequatorial isomer, or by the reaction of both conformers, the diaxial being stereoselective and the diequatorial not. It seems that the first explanation is the correct one, since the anhydride of III, in which the carbonyl groups are constrained to equatorial positions, is also selective, giving the ratio 3:2. The lower stereoselectivity of the anhydride relative to the ester suggests that the polar effect of the substituent may also depend on its arrangement in space.[17] The polar effect of the closer carbomethoxy group is stronger than that of the more remote one.

The exact nature of the hydroborating agent in these reactions is not known. Both borane and alkylboranes may react since an excess of diborane was used. The steric result should not be much different in both cases. It is known that diborane and disiamylborane give similar ratios of positional and stereoisomers in nonterminal olefins.[8]

Experimental Section

Methyl Cyclohexene-4-carboxylate (I).—Methyl acrylate (155 g), 250 g of butadiene, 200 ml of benzene, and 1 g of hydroquinone were heated at 150–160° for 5 hr in an autoclave. Distillation gave 235 g of I, boiling at 80° (25 mm). This ester contains some vinylcyclohexene. It was purified by saponification with sodium hydroxide solution, isolation of the acid, boiling at 128–132° (18 mm), and esterification with sulfuric acid–methanol.

***cis*-Δ^4-Tetrahydrophthalic anhydride** (monomer–polymer) was crystallized from benzene–hexane, mp 101–102°.[18]

Dimethylcyclohexene *cis*-4,5-Dicarboxylate (II).—*cis*-Δ^4-Tetrahydrophthalic anhydride (50 g) was dissolved in 250 ml of methanol and the monoester formed after 12 hr at room temperature was esterified directly in the methanolic solution with diazomethane. Distillation of the solvent and then of the diester yielded 40 g boiling at 108–113° (1 mm).

Dimethylcyclohexene *trans*-4,5-Dicarboxylate (III).—The dichloride[19] (20 g) prepared from butadiene and fumaroyl dichloride was added in portions to 100 ml of cold methanol. The reaction mixture was poured, after 12 hr at room temperature, on ice water, the product was extracted three times with ether, and the ether was washed with sodium bicarbonate solution. Distillation gave 17 g of the diester, bp 102–105° (2 mm).

***trans*-Δ^4-Tetrahydrophthalic anhydride** was prepared from the acid and acetic anhydride, mp 182–184°.[19]

Hydroboration of I.—To a solution of 7 g of I in 20 ml of THF, cooled in an ice bath, was added dropwise during 1 hr 45 ml of a 1 *M* solution of diborane in THF.[20] The reaction mixture was then left for 1 hr at room temperature and the excess

(17) H. Kwart and L. J. Miller, *J. Am. Chem. Soc.*, **83**, 4552 (1961).
(18) O. Diels and K. Alder, *Ann.* **460**, 113 (1928).
(19) K. Alder and M. Schumacher, *ibid.*, **564**, 96 (1949).
(20) G. Zweifel, K. Nagase, and H. C. Brown, *J. Am. Chem. Soc.*, **84**, 183 (1962).

diborane was destroyed by dropwise addition of water. Sodium hydroxide (10 ml of 3 *N*) was added with stirring, followed by dropwise addition during 1 hr of 10 ml of 30% hydrogen peroxide, and the mixtue was stirred for 1 additional hr. Addition of an aqueous sodium chloride solution, repeated extractions with ether, and distillation yielded 4.5 g, bp 147–150° (25 mm). This product was analyzed by glpc on a 5 ft × 0.25 in. column of 10% polyethylene glycol adipate on Silocel. The hydroxy esters of reference were prepared by known methods: catalytic hydrogenation of the hydroxybenzoic acids, separation of the isomers,[21] and esterification with diazomethane.[22]

Hydroboration of II.—Diborane generated by addition of a solution of 14 g of $BF_3 \cdot Et_2O$ in 25 ml of diglyme to 1.9 g of sodium borohydride in 50 ml of diglyme[23] was passed during 75 min into a stirred solution of 9.5 g of II in 50 ml of THF, cooled in an ice bath. The solution was then left for 75 min at room temperature, excess diborane was decomposed with water (15 ml), 15 ml of 3 *N* sodium hydroxide was added, and 15 ml of 30% hydrogen peroxide was added dropwise. The reaction mixture was then stirred for 1 hr at room temperature and extracted repeatedly with ether and dichloromethane. Distillation yielded 7.5 g of product VIII, boiling at 130–132° (0.3 mm); $n^{30}D$ 1.4703; $\bar{\nu}_{max}$ (neat) 3400, 1735 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.5; H, 7.5. Found: C, 55.2; H, 7.4.

Hydroboration of III was performed similarly as for II. There was obtained 7.5 g of the mixture of isomers, boiling at 130–132° (0.5 mm); $n^{30}D$ 1.4685; $\bar{\nu}_{max}$ (neat) 3400, 1740 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.5; H, 7.5. Found: C, 55.6; H, 7.6.

Hydroboration of *cis*-Δ^4-tetrahydrophthalic anhydride was carried out on 7.6 g as for II. The solution was acidified with cooling with sulfuric acid to pH 1, after oxidation with hydrogen peroxide, and a diazomethane solution was added until the yellow coloration of diazomethane persisted. The product was then extracted with ether and dichloromethane and the organic layer was washed with 10% sodium carbonate solution. Distillation yielded 5 g of the diesters, boiling at 130–140° (1 mm); $\bar{\nu}_{max}$ (neat) 3400, 1735 cm^{-1}.

Hydroboration of *trans*-Δ^4-tetrahydrophthalic anhydride was carried out as for the *cis* anhydride; 7.6 g of starting material yielded 4.5 g of the product boiling at 130–140° (1 mm); $\bar{\nu}_{max}$ (neat) 3400, 1735 cm^{-1}.

Methyl *cis*-2,4-γ-Lactocyclohexanecarboxylate (X).—Bromo lactone XI,[24] (5.2 g) and 7 g of triphenyltin hydride[25] were refluxed in 100 ml of dry toluene for 6 hr under nitrogen and with stirring. Distillation gave 2.8 g of X: bp 115–120° (0.5 mm); $n^{30}D$ 1.4828; $\bar{\nu}_{max}$ (neat) 1800, 1740 cm^{-1}.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.7; H, 6.5. Found: C, 59.0; H, 6.8.

Methyl *trans*-2,4-γ-lactocyclohexanecarboxylate (XVI) was prepared as isomer X; 5.2 g of bromo lactone XV[26] yielded 3 g of lactone XVI boiling at 120° (0.5 mm); mp 48–49° (hexane); $\bar{\nu}_{max}$ (neat) 1790, 1740 cm^{-1}.

Anal. Calcd for $C_9H_{12}O_4$; C, 58.7; H, 6.5. Found: C, 58.8; H, 6.4.

Dimethyl *cis,cis*-4-Hydroxycyclohexane-1,2-dicarboxylate (IX).—The lactone (X, 2 g) was dissolved in 50 ml of methanol and the cooled (ice bath) solution was saturated with hydrogen chloride gas. The methanol was removed after 24 hr at room temperature *in vacuo* without heating. The solution was poured on ice and sodium bicarbonate and the product was extracted with ether and distilled to yield 1.5 g: bp 130–135° (0.5 mm); $n^{30}D$ 1.4749; $\bar{\nu}_{max}$ (neat) 3450, 1725 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.5; H, 7.5. Found: C, 55.3; H, 7.3.

Dimethyl *cis*-4-Hydroxycyclohexane-*trans*-1,2-dicarboxylate (XIV).—The lactone (XVI, 3 g) was treated as above and yielded 2.5 g XIV: bp 125–130° (0.5 mm); $n^{30}D$ 1.4670; $\bar{\nu}_{max}$ (neat) 3400, 1725 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.5; H, 7.5. Found: C, 55.1; H, 7.3.

Analysis of the products of hydroboration of II, III, and their anhydrides was carried out by glpc on a 7 ft × 0.25 in. copper column of 20% Neopentylglycol succinate on Chromosorb W at 200 or 250°.

3,5,5-Trimethycyclohexene (XVIII).—Diborane generated by addition of a solution of 60 g of boron trifluoride etherate in 50 ml of diglyme to 11.5 g of sodium borohydride in 75 ml of diglyme, was bubbled during 1 hr at 0° through a solution of 14 g of isophorone in 100 ml of diglyme, with stirring. The solution was left for 1 hr at room temperature. Acetic anhydride (60 ml) was then added dropwise and the solution was refluxed for 1 hr under nitrogen. The mixture was distilled directly and a fraction boiling not higher than 145° (690 mm) was collected. This distillate was poured slowly into a solution of 90 g of potassium hydroxide in 200 ml of water and stirred during 15 hr. The product was extracted several times with hexane and the organic layer was washed with water, Distillation gave 6.5 g of XVIII: bp 135° (690 mm), $\bar{\nu}_{max}$ (neat) 1650 cm^{-1}, $n^{24}D$ 1.4380.

Anal. Calcd for C_9H_{16}: C, 87.1; H, 12.9. Found: C, 86.9; H, 12.6.

2,4,4-Trimethylcyclohexene (XXIII).—Aluminum chloride (55 g) was added slowly to 100 ml of anhydrous ether and this was followed by a careful addition of 6 g of lithium aluminum hydride. To this mixture a solution of 13.8 g of isophorone in 100 ml of ether was added dropwise during 15 min. The solution was then refluxed for an additional 0.5 hr and excess hydride was decomposed by ethyl acetate. The mixture was poured on ice and sulfuric acid and the product was extracted several times with ether. The ethereal solution was washed with 10% sodium carbonate solution, then with water, dried on magnesium sulfate and distilled. There were obtained 6.5 g of XXIII: bp 130–135° (690 mm), $n^{24}D$ 1.4519.

Anal. Calcd for C_9H_{16}: C, 87.1; H, 12.9. Found: C, 87.0; H, 12.8.

2-*trans*-Methyl-4,4-dimethylcyclohexanol (XIX).—The olefin (XXIII) was hydroborated with externally generated diborane, and then oxidized as described for the diesters; 5 g of XXIII yielded 3.5 g of XIX: bp 92–94° (25 mm), $n^{24}D$ 1.4570, $\bar{\nu}_{max}$ (neat) 3330 cm^{-1}.

Anal. Calcd for $C_9H_{18}O$: C, 76.0; H, 12.7. Found: C, 76.3; H, 12.8.

Tosylate of XIX.—*p*-Toluenesulfonyl chloride (6 g) was added to a solution of 4 g of XIX in 30 ml of pyridine cooled to 0°. The solution was then left for 5 days in the refrigerator, then poured on ice and hydrochloric acid and extracted with dichloromethane. Evaporation of the solvent left a residue, which was crystallized from ethanol, mp 94° (6.5 g).

Anal. Calcd for $C_{16}H_{24}O_3S$: C, 64.9; H, 8.1; S, 10.8. Found: C, 64.6; H, 7.9; S, 10.4.

2-*cis*-Methyl-4,4-dimethylcyclohexanol (XXII).—A solution of 9 g of the tosylate of XIX and 20 g of fused potassium acetate in 150 ml of acetic acid was refluxed for 15 hr. The mixture was made alkaline with 30% sodium hydroxide with cooling in an ice bath. The formed acetate was extracted with dichloromethane several times and the solvent was evaporated. The residue was saponified with a solution of 5 g of potassium hydroxide in 25 ml of methanol for 4 hr at room temperature. Most of the methanol was removed *in vacuo*, 50 ml of water was added, and the product was extracted several times with dichloromethane. The solution was washed with water, dried, and distilled, giving 1 g of XXII, bp 94–96° (25 mm), which contained less than 10% of its isomer XIX (by glpc): $n^{24}D$ 1.4605, $\bar{\nu}_{max}$ (neat) 3360 cm^{-1}.

Anal. Calcd for $C_9H_{18}O$: C, 76.0; H, 12.7. Found: C, 75.8; H, 12.5.

Hydroboration of XVIII was performed on 4 g by the same procedure as for XXIII, yielding, after oxidation, 3.4 g of a mixture of alcohols boiling at 92–95° (25 mm), $\bar{\nu}_{max}$ (neat) 3350 cm^{-1}.

Anal. Calcd for $C_9H_{18}O$: C, 76.0; H, 12.7. Found: C, 75.7; H, 12.5.

Analysis of the trimethylcyclohexanols obtained in hydroboration was performed by glpc on a 17 ft × 0.25 in. copper column of 10% Diglycerol on Chromosorb P acid washed, by comparison with the reference alcohols prepared and also with a known mixture of alcohols XX and XXI.[5]

Hydroboration of 4-Methylcyclohexene (XXIV).—Compound XXIV (5 g) in 20 ml of dry THF was hydroborated at 0° with

(21) D. S. Noyce and H. J. Weingarten, *J. Am. Chem. Soc.*, **79**, 3098 (1957).
(22) H. O. House, H. Balad, R. B. Toothill, and A. W. Noltes, *J. Org. Chem.*, **27**, 4141 (1962).
(23) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.* **22**, 1136 (1957).
(24) V. F. Kucherov, A. L. Shabanov, and A. S. Onishenko, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk.*, 844, 852 (1963).
(25) G. J. M. Van der Kerk, J. G. Noltes, and J. G. A. Luijten, *J. Appl. Chem.*, **7**, 366 (1957).
(26) J. Klein and E. Dunkelblum, to be published.

40 ml of a 3 *M* solution of diborane in THF. After 1 additional hr at room temperature and oxidation with hydrogen peroxide the solution was extracted with ether and distilled yielding 5 g of a product, bp 80–82° (25 mm), $\bar{\nu}_{max}$ (neat) 3330 cm^{-1}.

Anal. Calcd for $C_7H_{14}O$: C, 73.7; H, 12.3. Found: C, 73.7; H, 12.3.

This mixture of isomers could not be separated by glpc on a series of columns. Finally, the analysis was performed by two determinations. A 17-ft column of 10% Diglycerol on acid-washed Chromosorb P separated a mixture of XXVI and XXVII from XXV and XXVIII (ratio 47:53). These two latter alcohols were separated only partially. The mixture of alcohols was therefore oxidized and the mixture of ketones was analyzed on the same column. The percentages of all the alcohols were obtained by a combination of the two determinations.

Oxidation of the Product of Hydroboration of XXIV.—A solution of 1 g of chromic acid and 1.6 g of sulfuric acid in 4 ml of water was added dropwise during 10 min to a solution of 4 g of the mixture of alcohols in 40 ml of acetone cooled to −5°; the reaction mixture was left for 1 hr at 0°. Several drops of methanol were then added to decompose excess of chromic acid. The solution was filtered and the precipitate was washed with methanol. The filtrate was concentrated *in vacuo*, water (50 ml) was added, and the product was extracted five times with 30-ml portions of dichloromethane. Evaporation of the solvent left 3.2 g of a residue, that was analyzed by glpc, showing that 60% of the alcohols were oxidized to ketones and that the ratio of peaks of the remaining alcohols changed only slightly relative to the starting material. The axial alcohols were oxidized somewhat more rapidly and the ratio of (XXVI + XXVII)/(XXV + XXVIII) was now 42:58. 3-Methylcyclohexanone (Aldrich), 4-methylcyclohexanone (Fluka), and 4-methylcyclohexene (Aldrich) of reference were commercial products. The alcohols of reference were obtained by reduction of the ketones with lithium aluminum hydride, which gave mixtures of known proportion of isomers.[27]

Registry No.—I, 6493-77-2; II, 4841-84-3; III, 7731-15-9; VIII, 7731-16-0; IX, 7775-57-7; X, 7771-14-4; XIII, 7731-17-1; XIV, 7731-18-2; XVI, 7731-19-3; XVIII, 933-12-0; XIX, 2518-25-4; XX, 933-48-2; XXI, 767-54-4; XXII, 7731-23-9; XXIII, 503-46-8; XXV, 5454-79-5; XXVI, 7443-55-2; XXVII, 7731-28-4; XXVIII, 7731-29-5.

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(27) E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.* **79**, 5992 (1957).

Directive Effect of the Cyclopropyl Group in Hydroboration

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Vinylcyclopropane and spiro[2.5]oct-4-ene are hydroborated by diborane in dry tetrahydrofuran; the organoboranes formed are oxidized by alkaline hydrogen peroxide. An analysis of the resulting carbinol mixtures has revealed that vinylcyclopropane produces cyclopropylmethylcarbinol and 2-cyclopropylethanol in the ratio 3:97, while spiro[2.5]oct-4-ene gives a mixture of spiro[2,5]octan-4-ol and -5-ol in the ratio 22:78. Compared with the ratio of isomeric carbinols observed in ordinary terminal and internal olefins, these two olefins under consideration exhibit different product distributions, *i.e.*, a marked increase in β alcohol is to be noted. From this it may be safely assumed that the cyclopropyl group is more electron releasing than other alkyl groups.

A number of extensive studies in the directive effect of various substituents in hydroboration[1] have made it clear that the electronic effect of the substituent is one of the important factors controlling the direction of boron attack where diborane is utilized. With cyclopropyl, however, no comparable work is available as yet, but its unique double-bond character[2-4] ought to lead to significant observations and fruitful discussions about the possible behavior of cyclopropyl group in hydroboration, *e.g.*, whether it works as an alkyl group or as an unsaturated group in its influence on the direction of boron attack. The present paper aims to discuss the directive effect of cyclopropyl group from this point of view with reference to both terminal and internal olefins.

Results

Olefins investigated were vinylcyclopropane (**1**), vinylcyclohexane (**2**), and spiro[2.5]oct-4-ene (**3**). Olefin **1** was obtained by the reductive debromination[5] of 2,2-dibromo-1-vinylcyclopropane, prepared by the addition of dibromocarbene to 1,3-butadiene;[6] olefin **2** was a commercial product; olefin **3** was obtained by the thermal decomposition of spiro[2.5]oct-4-yl xanthate, the purities of these olefins being 97–98.5% on vpc analysis. The external hydroboration technique[7] was employed. The organoboranes formed were oxidized by alkaline hydrogen peroxide,[7] and the resulting alcohol mixtures were subjected to vpc analysis. The results are shown in Table I.

The major product in each case was isolated and characterized as indicated below. 2-Cyclopropylethanol was converted to crystalline phenylurethan, mp 63.9–64.1°, and β-naphthalenesulfonate, mp 26.0–27.0°. The analytical results and nmr and infrared spectra were in accordance with the 2-cyclopropylethyl structure. 2-Cyclohexylethanol was derived to the known 3,5-dinitrobenzoate, mp 71.3–71.8° (lit.[8] mp 71–72°). The structure of spiro[2.5]octan-5-ol was established by the comparison with authentic material, prepared from 3-methylenecyclohexanol *via* the Simmons–Smith reaction.[9] A mixture melting point of the 3,5-dinitrobenzoate, mp 98.4–99.4°, from both samples, showed no depression. The minor component was checked against authentic material by comparing its retention time on vpc.

In runs 1, 2, and 3, 2-cyclopropylethanol was isolated in 71–82% yield, while a mixture of spiro[2.5]-

(1) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.
(2) M. Y. Lukina, *Russ. Chem. Rev.*, **31**, 419 (1962).
(3) M. Charton, *J. Chem. Soc.*, 1205 (1964), and references cited therein.
(4) A. L. Goodman and R. H. Eastman, *J. Am. Chem. Soc.*, **86**, 908 (1964), and references cited therein.
(5) W. E. von Doering and A. K. Hoffmann, *ibid.*, **76**, 6162 (1954).
(6) R. C. Woodworth and P. S. Skell, *ibid.*, **79**, 2542 (1957).
(7) G. Zweifel and H. C. Brown, *Org. Reactions*, **13**, 1 (1963).
(8) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 1241 (1961).
(9) I. Moritani and T. Tsuji, the manuscript in preparation.