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(1) (a) For a discussion and leading references, see H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, New York, N.Y., 1972, pp 89–96. (b) As an illustration of the divergence of product distributions from cyclic enones which may be obtained with different hydride reagents, see H. C. Brown and H. M. Hess, *J. Org. Chem.*, **34**, 2206 (1969). (c) Recently, exclusive 1,4 reduction of α,β-unsaturated systems to saturated ketones has been achieved using copper(I) hydride complexes; see R. K. Boeckman, Jr., and R. Michalak, *J. Am. Chem. Soc.*, **96**, 1623 (1974).

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(6) The increase in 1,2 addition by borohydride with increasing solvent polarity has been attributed to the ability of polar solvents (such as methanol) to more effectively stabilize the more charge-localized transition state of 1,2 addition.[3b] However, the rapid reaction of $NaBH_4$ with methanol[7] and the demonstrated preponderance of carbonyl attack by trialkoxyborohydride[3a] may account for much of the selectivity shown by borohydride. In addition, 1,4 attack of β-aryl conjugated systems involves loss of conjugation with the phenyl ring while no such loss occurs upon 1,2 addition.

(7) See H. C. Brown, "Boranes in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 1972, p 214, and references cited therein.

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(9) See H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 89–97, and references cited therein.

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(11) The absence of allylic hydrocarbons in the reductions of alicyclic carbonyl compounds reinforces the previous suggestion that the allylic ethers formed from these systems in acidic methanol did not arise from acid-catalyzed reactions of the allylic alcohols; otherwise the corresponding reductions in HMPT should have produced some allylic hydrocarbons (compare entries 1 and 8 with entries 12, 13, 23, and 24).

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Notes

Evidence of Significant Participation of the Less Stable Conformation in the Reduction of 2-Methylcyclohexanone by Sodium Borohydride

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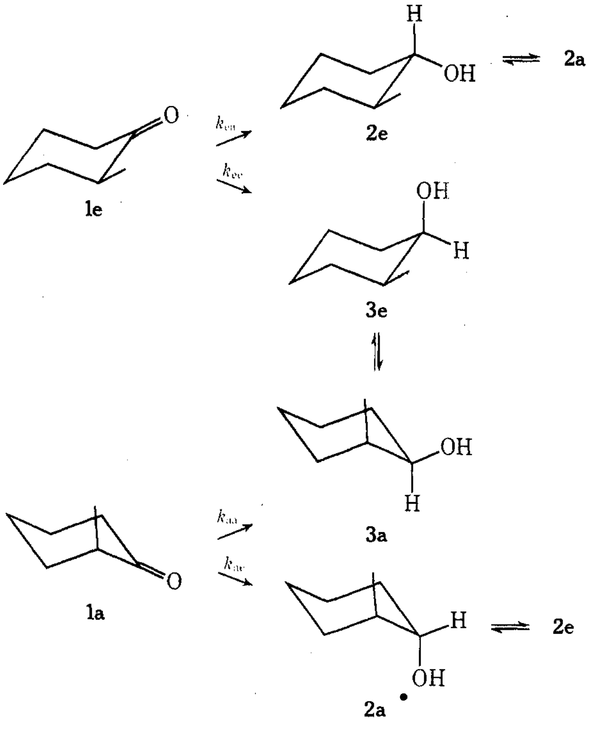
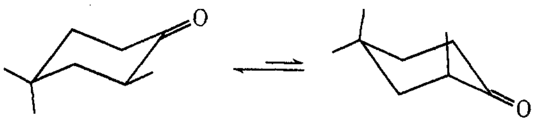
The reduction of conformationally mobile 2-alkylcyclohexanones by complex metal hydrides can, in principle, occur through two conformations: one with the alkyl group equatorial and the other with the alkyl group axial. Thus it is possible that both cis and trans alcohols may arise via two different routes, i.e., axial or equatorial attack on a given conformation (Scheme I).

From the point of view of investigating the origin of the stereoselectivity in reductions of cyclohexanones by complex metal hydrides, the question of just how each alcohol is formed is a vital one, and in a previous study[1] we demonstrated, by analysis of the relative magnitudes of activation enthalpies, that the trans alcohol **2** is derived almost exclusively from conformation **1e**. However, we were unable to determine whether the cis alcohol was derived from conformation **1a**, **1e**, or both, owing to experimentally indistinguishable values of $\Delta H^{\ddagger}$ for the two possible processes. Since we know, however, that conformation **1a** does not

Scheme I
Reduction of 2-Methylcyclohexanone



give rise to the trans alcohol,[1,2] a very simple experiment is possible that clarifies the origin of the cis alcohol. 2,4,4-Trimethylcyclohexanone (4) serves as a model for conformation **1e** of 2-methylcyclohexanone, conformation **4a** being virtually forbidden by virtue of the 1,3-diaxial interaction of the methyl groups. Thus the stereochemical product ratio from reduction of **4** represents to a good approximation that from the *equatorial conformation of 2-methylcyclohexanone* (**1e**), and a deviation from this of the observed product ratio of 2-methylcyclohexanone (**1**) is a measure of the contribution of the axial conformation (**1a**).



4e **4a**

2,4,4-Trimethylcyclohexanone[3] is obtainable by ketone transposition of isophorone,[4,5] the penultimate intermediate providing an authentic sample of *trans*-2,4,4-trimethylcyclohexanol. Reduction of 2-methylcyclohexanone and 2,4,4-trimethylcyclohexanone under identical conditions by sodium borohydride gave 31 and 18%, respectively, of the cis isomer.

Regarding the rate of formation of the trans alcohol from 2-methylcyclohexanone as a single term E_A (that from conformation **1e**), but the rate of formation of the cis alcohol as the sum of two terms E_E and A_A arising from the conformations with equatorial and axial methyl groups respectively, the stereochemical product ratio (cis:trans) can be written as

$$(A_\mathrm{A} + E_\mathrm{E})/E_\mathrm{A} = 31.69$$

Similarly, for reduction of 2,4,4-trimethylcyclohexanone[6]

$$E_\mathrm{E}/E_\mathrm{A} = 18/82$$

From these equations it follows that $A_\mathrm{A} = 1.05E_\mathrm{E}$ or, expressing A_A and E_E as percentages of the total reaction leading to *cis*-2-methylcyclohexanol, 51% of this product arises from axial attack on **1a** while 49% of the product is derived by equatorial attack on the more stable conformation **1e.** This result is in sharp contrast with formation of *trans*-2-methylcyclohexanol, which is derived almost exclusively from **1e.**[1]

Conclusions

While some doubt must exist on the exactitude of the above figures (see ref 6), it appears that the *less* stable conformation of 2-alkylcyclohexanones plays at least a substantial role in the reduction to the cis alcohol. Any rationalization of stereochemical product ratio arising from reduction of these ketones should be consistent with this fact.

Experimental Section

2,4,4-Trimethylcyclohexanone (4) was prepared by oxidation[5] of *trans*-2,4,4-trimethylcyclohexanol, which was obtained by reduction and hydroboration of isophorone:[4] bp 191° [lit.[3] bp 191°]; $n^{21}\mathrm{D}$ 1.4485 (lit. $n^{20}\mathrm{D}$ 1.4493[3]); 2,4-dinitrophenylhydrazone mp 149–150° (lit.[9] mp 151.5° [2]). Ir and NMR spectra were in accord with published data.[9]

Reduction Procedures. Reductions were carried to completion in 2-propanol at 25° with a twofold molar excess of sodium borohydride as previously described.[1,10] GLC analyses were performed both on a Perkin-Elmer 990 gas chromatograph using a 50-ft S.C.O.T. TCEP column and on a Hewlett-Packard F & M Scientific 402 high efficiency gas chromatograph using a dual-packed column of Carbowax and TCEP, which gave base line separation of diastereomeric alcohols and ketone.[11] Both chromatographs were attached to an Infotronics CRS-208 electronic integrator for peak area determination. Reductions were performed in quadruplicate, and product ratios, which were determined both mechanically and electronically, were found to be reproducible within ±1%.

Registry No.—**1**, 583-60-8; **2**, 7443-52-9; **3**, 7443-70-1; **4**, 2230-70-8; **4** 2,4-dinitrophenylhydrazone, 2522-10-3; *trans*-2,4,4-trimethylcyclohexanol, 2518-25-4; sodium borohydride, 16940-66-2.

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(11) We are very grateful to Professor B. Rickborn for details of this column (cf. footnote 62 of ref 7).

Effects of α Substitution on the Rate of Chloromercuriolactonization of Esters of γ,δ-Unsaturated Acids[1]

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The chloromercuriolactonization of γ,δ-unsaturated acids and esters in aqueous ethanol has been studied by Rowland et al.[3] and do Amaral et al.[4] A mechanism for the reaction was proposed.[4]