mization, every effort was made to ensure that, other than those products resulting from decomposition of the starting materials,[10] no reaction products isomeric with those isolated were present in the crude reaction-product mixtures. In all cases greater than 95% of the material balance has been accounted for.

(8) F. Zymalkowski and J. Rimek, *Naturwissenschaften*, **47**, 83 (1960).
(9) The air was dried by passage through successive drying towers of concentrated H_2SO_4, solid KOH, and silica gel.
(10) Cf. E. L. Esmans and F. C. Alderweireldt, *Bull. Soc. Chim. Belg.*, **82**, 435 (1973).

The Effect of Lewis Acids on Stereoselectivities in Ketone Reductions. The Principle of Complexation-Induced Conformational Perturbation. Energy Minimization in the Transition States for Hydride Transfer[1]

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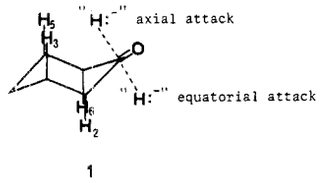
Stereochemical results from reductions of alkyl-substituted cyclohexanones by organosilanes in boron trifluoride etherate and in aqueous sulfuric acid demonstrate that Lewis acid complexation with the carbonyl oxygen plays a major role in determining product stereoselectivity. These results, together with similar changes in stereoselectivity due to variations in the metal ion employed in Meerwein–Ponndorf–Verley, borohydride, and aluminum hydride reductions, lead to the proposal that stereoselectivity in ketone reductions is a function of the size of the complexing agent and the degree of association between the carbonyl oxygen and the complexing agent in the transition state for hydride transfer. To explain the "4-methyl, 4-*tert*-butyl effect" and the "2-methyl effect" the principle of complexation-induced conformational perturbation is introduced. According to this tenet, the reacting complexed ketone adopts a conformation that minimizes steric (or torsional) interactions in the transition state for hydride transfer. Stereochemical and kinetic data are consistently explained by application of this principle. Stereochemical results from reductions of model ketones, *trans*-1-decalone and *trans*-2-decalone, are reported; these results are consistent with the transition state model for complexation-induced conformational perturbation but are opposite to those predicted from the conformational equilibrium model. The effects of the postulate that hydride transfer preferentially occurs to minimize interactions between the incoming hydride and the complexed ketone on the currently held models for stereoselectivity in nucleophilic addition reactions are discussed.

The predominance of one stereoisomeric product in nucleophilic additions to ketones depends on the nature of the nucleophile, on the stereochemical relationship between the reactants during addition, and on the intricate details of the reaction pathway.[3] The evolution of current understanding of stereoselectivity in these reactions has occurred primarily through studies of cyclic ketones.[4,5] A wealth of data on stereoselective hydride reductions of cyclic ketones exists and is interpreted with general acceptance[5] in terms of a combination of steric and torsional interactions between the substrate and the reducing agent in the transition state for hydride transfer as well as by electronic influences emanating from polar substituents remote from the carbonyl group. Conformational[6] and molecular orbital[7] influences on stereoselectivity in cyclic ketone reductions have recently been proposed.

Steric approach control,[4b] which implies that the transition state resembles the reactants in geometry, is widely believed to govern the course of ketone reductions by hydride reducing agents. Furthermore, hydride transfer is understood to preferentially occur when the ketone is in its most stable conformation and, to effect maximum overlap in the transition state, hydride approaches the carbonyl carbon along a line perpendicular to the plane of the carbonyl group.[7e,8]

When these criteria are applied to reductions of substituted cyclohexanones, for example, a distinct picture of stereoselective control emerges (structure 1). Axial hydride attack is subject to steric interactions from atoms or groups of atoms on the axial 3,5 positions. Equatorial hydride attack is subject to torsional interference with the axial 2,6 hydrogens. The stereoselectivity of hydride transfer to substituted cyclohexanones is believed to be determined by the relative magnitude of these steric and torsional interactions.[5]



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Recent stereochemical data on reductions of cyclohexanones by numerous aluminum hydride,[4h,9] borohydride,[10] and organosilane[1,6d,11] reagents have generated several questions that cannot be explained by the account of stereoselective control outlined in structure **1**. The "2-methyl effect",[6a] in which the relative yields of the less stable cis isomer from reductions of 2-methylcyclohexanone are substantially greater than those from 4-*tert*-butylcyclohexanone, requires modification of the currently held view of stereoselectivity. The complex "4-methyl, 4-*tert*-butyl effect" is even more difficult to understand. Here, the relative yield of the less stable cis alcohol from reductions of 4-methylcyclohexanone is greater than that from 4-*tert*-butylcyclohexanone when sterically small reducing agents are employed, but this phenomenon is reversed when sterically large reducing agents are used.

In the course of our investigations of stereoselectivity in ketone reductions by organosilanes we have found that the nature of the Lewis acid catalyst has a major effect.[1] In this paper we assign to Lewis acid complexation an integral role in the control of reduction stereoselectivity. We will describe the stereochemical relationship between the reactants in the process of reduction in terms of "complexation-induced conformational perturbation" of the ketone in the transition state. This new principle of stereoselective control unravels the "2-methyl effect" and the "4-methyl, 4-*tert*-butyl effect", satisfactorily explains the results from hydride reductions and nucleophilic additions of cyclic ketones, and predicts the stereochemical course of these reactions more successfully than previous theories.

Table I. Stereoselectivities of Organosilane Reductions of Alkyl-Substituted Cyclohexanones in Aqueous Sulfuric Acid and in Boron Trifluoride Etherate[a]

Registry no.	Cyclohexanone	Relative yield, % less stable alcohol from reduction by: n-$BuSiH_3$		Et_2SiH_2		Et_3SiH	
		BF_3·Et_2O[b]	H_2SO_4[c]	BF_3·Et_2O[b]	H_2SO_4[c]	BF_3·Et_2O[d]	H_2SO_4[c]
98-53-3	4-*tert*-Butyl-	17	10	36	20	61	32
589-92-4	4-Methyl-	19	18	39	26	60	35
591-24-2	3-Methyl-	24	19	48	29	67	39
583-60-8	2-Methyl-	34	31	52	41	64	54
873-94-9	3,3,5-Trimethyl-	87	74	91	85	95	90

[a] Reactions were run at room temperature (25 ± 2 °C). [b] Molar ratio of boron trifluoride etherate to ketone was 1:1. Alcohols were the only products observed after basic hydrolysis. [c] Data taken from ref 6d. [d] Data taken from ref 1.

Table II. Stereoselectivity in Triethylsilane Reductions of 4-*tert*-Butylcyclohexanone Promoted by Lewis Acid Catalysts

Registry no.	Acid	Alcohol derivative	% cis isomer	$k_{axial}/k_{equatorial}$
76-05-1	CF_3COOH[6d]	Trifluoroacetate	32	0.47
7664-93-9	H_2SO_4, H_2O[6d]	Alcohol	32	0.47
64-18-6	$HCOOH$[1]	Formate	38	0.61
7772-99-8	$SnCl_2$[1]	Alkyl silyl ether	42	0.72
7446-70-0	$AlCl_3$[1]	Alkyl silyl ether	60	1.50
7637-07-2	BF_3[1]	Borate ester[b]	61	1.56
56889-93-1	*trans*-4-*tert*-Butylcyclohexyl[6d,a]	Symmetrical ether	63	1.7
56889-94-2	*cis*-4-*tert*-Butylcyclohexyl[6d,a]	Symmetrical ether	84	5.2

[a] Reduction of $R_2C{=}^+OR'$ leading to symmetrical ethers during triethylsilane reduction of 4-*tert*-butylcyclohexanone in trifluoroacetic acid. [b] Analyzed as alcohol.

Results and Discussion

Effect of Lewis Acid Complexation on Stereoselectivity in Cyclic Ketone Reductions. Table I presents the stereochemical results from reductions of alkyl-substituted cyclohexanones by alkylsilanes in boron trifluoride etherate and compares these results with those from the corresponding reactions in aqueous sulfuric acid. Cyclohexanones are rapidly reduced by organosilanes in BF_3·Et_2O to borate esters

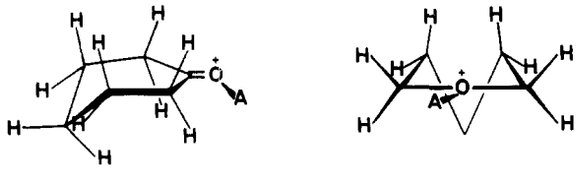
$$3R_2C{=}O + 3R'_3SiH + BF_3 \rightarrow (R_2CHO)_3B + 3R'_3SiF \quad (1)$$

which are, in turn, conveniently hydrolyzed to alcohols during product isolation from aqueous base. The mechanism of ketone reductions in BF_3·Et_2O is suggested to involve hydrosilylation of the boron trifluoride activated carbonyl group followed by fluoride displacement at silicon and has been previously discussed.[1]

Table I clearly shows that stereoselectivity depends on the acid employed in cyclic ketone reductions by organosilanes. Not only do the relative yields of the less stable alcohol isomers increase with increasing size of the reducing agent (steric approach control) but, also, a substantial increase in the relative yield of the less stable alcohol isomer is obtained when the size of the Lewis acid is increased from "H^+" (aqueous H_2SO_4) to BF_3 (BF_3·Et_2O). A similar effect on stereoselectivity has been noted in $AlCl_3$-, $ZnCl_2$-, and $SnCl_2$-catalyzed organosilane reductions of 4-*tert*-butylcyclohexanone.[1] In addition, reductions of oxonium ions of the type $R_2C{=}^+OR'$ ($R_2C{=}O$ = 4-*tert*-butylcyclohexanone, R′ = *cis*- and *trans*-4-*tert*-butylcyclohexyl) to ethers by organosilanes are highly sensitive to the nature of R′.[6d] Table II summarizes the dependence of reduction stereoselectivity on Lewis acids by presenting the ratio of the relative rates for axial and equatorial attack by triethylsilane on Lewis acid complexed 4-*tert*-butylcyclohexanone. Clearly the Lewis acid plays an integral role in the control of stereoselectivity in organosilane reductions.

The increase in equatorial attack in cyclohexanone reductions that is caused by changes in the Lewis acid is not limited to organosilane reagents. Recent stereochemical results from several laboratories, involving a wide range of hydride reducing agents, point to the same dependence. In the Meerwein–Ponndorf–Verley reductions of substituted cyclohexanones and steroidal ketones, changing from lithium to sodium to potassium isopropoxide substantially increases the yields of the less stable alcohol isomers.[12] Similarly, in cyclic ketone reductions by tri-*sec*-butyl borohydride, the potassium salt[13] favors the less stable alcohol isomer more than does the lithium salt;[10c] similar results are reported for lithium and sodium borohydride reductions of alkylcyclohexanones.[14] Stereoselectivity in aluminum hydride reductions is likewise subject to the nature of the metal salt.[6a] Although these results can be explained by proposing changes in the effective sizes of the individual reducing agents, we believe that they are more properly and harmoniously ascribed to conformational changes in the reacting ketone due to complexation of the Lewis acid (or metal ion) with the carbonyl oxygen in the transition state for hydride transfer. This complexation activates the carbonyl group for hydride transfer and stabilizes the resulting alkoxide.

Complexation-Induced Conformational Perturbation. Three basic postulates underlie the theories that have been developed to explain stereoselectivity in ketone reductions: (a) that steric approach control governs the course of ketone reductions by hydride reducing agents, (b) that the hydride approaches perpendicular to the carbonyl group,[8] and (c) that hydride transfer preferentially occurs when the ketone is in its most stable conformation (which is usually defined as the most stable ground state conformation[4,5]). When laid upon these foundations at least four reaction parameters are identified as controlling stereoselectivity during hydride attack at the carbonyl carbon of cyclic ketones: (1) the size of the nucleophile, (2) the "nucleophilicity" of the attacking reagent, (3) steric interactions between the cyclic ketone and the attacking reducing agent, and (4) torsional strain (or gauche hydrogen–hydrogen interactions[15]) between the incoming hydride and suitably positioned α hydrogens.[4,5] Except for the recent proposal of a conformational equilibrium



3a 3b

Figure 1. Complexation-induced ring flattening of cyclohexanone: view from the side (**3a**) and view along the carbonyl group (**3b**).

model to explain the 2-methyl effect,[6] the attributes of complexation between the carbonyl oxygen of ketones and a Lewis acid or metal ion in effecting stereochemical control of hydride transfer have been generally overlooked.

We propose that stereoselectivity in ketone reductions is a function of the size of the complexing agent and of the degree of association between the carbonyl oxygen of the ketone and the complexing agent in the transition state for hydride transfer. This complexation initially results in steric (or torsional) interference between the complexing agent and α substituents of the ketone. With cyclohexanone in particular, the complexing agent (A) and substituents on the equatorial 2,6 positions are nearly eclipsed or sterically encumbered when cyclohexanone is in its chair conformation (structure **2a**). To relieve this strain *the complexed ketone adopts a conformation that minimizes steric (or torsional) interactions in the transition state for hydride transfer.* In the case of cyclohexanone, complexation induces a flattening of the ring about the carbonyl group (structure **2b**). The extent of ring flat-

2a 2b

tening in the transition state is dependent on the flexibility of the ketone, on the size and degree of association of A with the carbonyl oxygen, on the nature and size of α substituents, and on the reactivity of the hydride reducing agent. Complexation may occur prior to hydride transfer, as in organosilane reductions,[1,11] or be concurrent with hydride transfer, as appears likely in ketone reductions by lithium aluminum hydride.[16] In either case, *complexation activates the carbonyl group for hydride transfer, stabilizes the developing alkoxide ion, and induces a change in the conformation of flexible*[17] *ketones.*

Ground state flattening of cyclohexane rings from the idealized model having bond angles of 109.5° and torsional angles of 60° is well documented.[18-20] Electron diffraction and x-ray analyses of substituted cyclohexane derivatives suggest that the cyclohexane ring is flexible to conformational distortions. Torsional angles around the bonds adjacent to the carbonyl group are contracted appreciably in comparison with the idealized model.[20] Further flattening of the cyclohexanone ring is, therefore, a reasonable consequence of complexation between the carbonyl group and a Lewis acid in the transition state for hydride transfer.

Structures **3a** and **3b** in Figure 1 exemplify the consequences of complexation-induced ring flattening for hydride attack on cyclohexanones. In structure **3** C_5, C_6, C_1, C_2, and C_3 all lie in the same plane; however, this conformation is but one complexation-induced conformational possibility between the chair and boat conformational extremes for cyclohexanone. Flattening of the cyclohexanone ring produces increased "gauche → eclipsed" interactions between hydrogens on 2,6 and 3,5 positions and between C_1–C_2, C_1–C_6 and C_3–C_4, C_5–C_4, but these effects are counteracted by the decreased interactions between A and "equatorial" 2,6 hydrogens. Structure **3** represents that conformation in which interactions between A and substituents on the 2 and 6 positions are minimized. Noteworthy is the inward compression of axial 3,5 hydrogens which leads to an increase in this long-range 1,3-diaxial interaction but effects a decrease in short-range torsional strain between "equatorial" 2,6 hydrogens and axial 3,5 hydrogens. For axial hydride attack flattening of the cyclohexanone ring leads to increased interactions of the incoming hydride with "equatorial" 2,6 hydrogens and to decreased interactions with axial 3,5 hydrogens (steric interference[4e]). Likewise, for equatorial hydride attack there is an increase in the long-range interaction between the incoming hydride and the axial 4 hydrogen but, also, a slight decrease in interactions with "axial" 2,6 hydrogens (torsional strain[4f,g,15]).

Ring flattening of cyclohexanones during reduction or nucleophilic addition reactions has recently been promoted by Anh and co-workers as a factor favorable to axial attack.[21] Our analysis does not provide such a clear-cut distinction. Indeed, the protraction of "axial" 2,6 hydrogens due to ring flattening leads to little change or a slight decrease in interactions of these hydrogens with an incoming hydride, while contraction of the "equatorial" 2,6 hydrogens suggests that an incoming hydride will encounter increased interactions with these hydrogens.

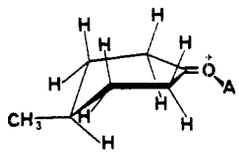
Participation of the flexible conformation of cyclohexanones in chemical reductions has also been suggested to explain reaction stereoselectivities.[22] However, the flexible cyclohexanone conformation does not offer any advantage over the chair conformation in minimizing interactions between α substituents and A.

The postulate of complexation-induced flattening of the cyclohexanone ring in the transition state for hydride transfer retains those four reaction parameters that were previously discussed as playing an integral role in controlling stereoselectivity. However, our proposal modifies one of the basic postulates that underlies stereoselectivity arguments—that hydride transfer preferentially occurs when the ketone is in its most stable conformation. Application of the modified postulate, that *hydride transfer preferentially occurs to minimize interactions between the incoming hydride and the complexed ketone,* leads to the inference that as the transition state for hydride transfer approaches structure **3** the forces between the reducing agent and the substrate can be divided into two categories: short-range effects and long-range effects. Interactions of the incoming hydride with "axial" 2,6 hydrogens and with "equatorial" 2,6 hydrogens comprise short-range effects and are responsible for the stereoselectivities obtained in reductions of cyclohexanones by small reducing agents such as sodium borohydride, lithium aluminum hydride, and *n*-butylsilane. Interactions with axial 3,5 hydrogens and with the axial 4 hydrogen comprise long-range effects which, together with short-range effects, affect the stereoselectivities in reductions of cyclohexanones by bulky reducing agents such as the tri-*sec*-butyl borohydrides[10c,13] or di-*tert*-butylmethylsilane.[11a] This stereochemical model is significantly different from that used by Marshall[4e] and, as will be discussed next, provides a uniform explanation for the "4-methyl, 4-*tert*-butyl effect".

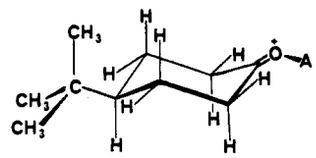
Table III compares the relative yields of the less stable cis-alcohol isomers from reductions of 4-*tert*-butylcyclohexanone and 4-methylcyclohexanone by representative aluminum hydride, borohydride, and organosilane reagents. With small reducing agents such as diborane, *n*-butylsilane, lithium aluminum hydride, and sodium borohydride,[24] the relative yields of the less stable cis alcohol isomer from reductions of 4-*tert*-butylcyclohexanone are less than those from reductions of 4-methylcyclohexanone. However, as the steric bulk of the

reducing agent is increased, there is a reversal in the relative yields of the cis-alcohol isomers; reductions of 4-*tert*-butylcyclohexanone by bulky trialkyl borohydrides and trialkylsilanes give a greater percentage of cis alcohol than do reductions of 4-methylcyclohexanone.

This "4-methyl, 4-*tert*-butyl effect", although reflecting small energy differences, is adequately explained by application of the principle of complexation-induced conformational perturbation. Ring flattening of complexed 4-*tert*-butylcyclohexanone during hydride transfer is hindered by steric interactions between the *tert*-butyl group and axial 3,5 hydrogens. No such hindrance to ring flattening can be expected from the methyl group of 4-methylcyclohexanone. Thus from our earlier consideration of short-range effects in reductions of complexed ketones, we can predict that the yield of the less stable alcohol isomer will be less in reductions of 4-*tert*-butylcyclohexanone than in reductions of 4-methylcyclohexanone—exactly what is observed. However, the stereoselectivities in reductions of 4-methylcyclohexanone by bulky reducing agents, in which long-range effects are also operative, are influenced by decreased interaction between the incoming hydride and axial 3,5 hydrogens and by increased interference from the axial 4 hydrogen, relative to reductions of 4-*tert*-butylcyclohexanone (structures **4a** and **4b**).[20a] Compared to reductions of 4-*tert*-butylcyclohexanone



4a



4b

by the same bulky reducing agents both of these long-range interactions favor axial hydride attack leading to the equatorial alcohol.[20b]

Similar considerations of complexation-induced ring flattening of cyclohexanones explain the general observation of higher yields of the less stable alcohol isomer in reductions of 3-methylcyclohexanone when compared to reductions of 4-*tert*-butylcycohexanone. Although ring flattening of 3-methylcyclohexanone causes increased interaction between the "axial" 2-hydrogen and the equatorial 3-methyl group and leads to further inward compression of the axial 3,5 hydrogens compared to cyclohexanone, in the chair conformation for 3-methylcyclohexanone the equatorial 3-methyl substituent increases steric interference of the equatorial 2 hydrogen with the complexing agent ("gauche-butane"-like interactions[15,26,27]) and promotes ring flattening.

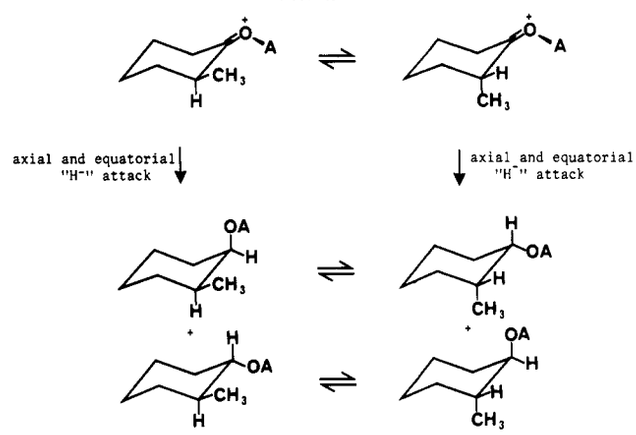
2-Methyl Effect. The "2-methyl effect" in reductions of 2-methylcyclohexanones has received considerable attention in recent years.[6] Evidence has been presented to suggest that there is significant participation of the less stable chair conformer in the transition state for reduction of 2-methylcyclohexanone.[6a-c] Model compounds for the equatorial chair conformer of 2-methylcyclohexanone, *cis*-4-*tert*-butyl-2-methylcyclohexanone,[6a] and 2,4,4-trimethylcyclohexanone[6c] have been used to determine the extent of involvement of the equatorial and axial chair conformers in the transition state for reduction by hydride reagents. To explain the accumulated data the reduction of 2-methylcyclohexanone is represented as occurring through hydride attack on both the axial and equatorial conformers (conformational equilibrium model, Scheme I). Prior or concurrent association of the complexing agent (A) with the carbonyl group increases the relative proportion of the associated axial conformer in the transition state for hydride transfer.[6a] This interpretation for the

Table III. Stereoselectivities in Hydride Reductions of 4-*tert*-Butylcyclohexanone and 4-Methylcyclohexanone

Reducing agent	Relative % cis isomer from reduction of 4-*tert*-Butyl cyclohexanone	Relative % cis isomer from reduction of 4-Methyl-cyclohexanone
B_2H_6[23]	10	15
$LiAlH(O\text{-}t\text{-}Bu)_3$[9a]	10	14
n-$BuSiH_3$, H^+[6d]	10	18
$LiAlH_4$, Et_2O[9b,10b]	11	17
$NaBH_4$, i-PrOH	12, 14[10g]	15,[10f] 14[10g]
n-$BuSiH_3$, BF_3	17	19
Et_2SiH_2, H^+[6d]	20	26
Et_3SiH, H^+[6d]	32	35
Et_2SiH_2, BF_3	36	39
$1PC_2BH$[a,10b,25]	37	33
LiPBPH[b,10b]	54	52
Et_3SiH, BF_3-Et_2O[1]	61	60
$(t\text{-}Bu)_2MeSiH$, H^+[11a]	72	67
Li-*sec*-Bu_3BH, 0 °C[10c]	93	80
$LiSia_3BH$, −78 °C[10h]	>99.5	99.0

[a] Diisopinocampheylborane. [b] Lithium perhydro-9b-borophenalylhydride.

Scheme I



stereoselectivities that are observed in reductions of 2-methylcyclohexanone differs markedly from our proposal of complexation-induced conformational perturbation.

The principle of complexation-induced conformational perturbation predicts that ring flattening of 2-methylcyclohexanone will occur in the transition state for hydride transfer. Ring flattening decreases steric interactions between the complexing agent and the "equatorial" 2-methyl group but, also, increases steric interactions between the incoming hydride and the "equatorial" 2-methyl group in the transition state for axial attack (structure **5**). Increasing the size of the

5

complexing agent magnifies these steric interactions by increasing the CH_3–C_2–C_1=$^+$OA dihedral angle and leads to an increase in the relative yield of the less stable cis alcohol—exactly what is observed. However, although both this model and the conformational equilibrium model predict the same stereochemical results for reductions of 2-methylcyclohexa-

Table IV. Stereoselectivities in Reductions of 2-Methylcyclohexanone and Conformational Models for 2-Methylcyclohexanone

Reducing agent	Relative % less stable alcohol from reduction of 2-Methylcyclohexanone	*trans*-1-Decalone	4-*tert*-Butylcyclohexanone	*cis*-4-*tert*-Butyl-2-methylcyclohexanone
$LiAlH_4$, THF[6a]	24	26[a,b]	10	17 (17)[a,b]
$ClMgAlH_4$, THF[6a]	36		10	21
$Mg(AlH_4)_2$, THF[6a]	49		13	27
$NaBH_4$, *i*-PrOH	31[6c]	37[a] (32)[c,d]	12[a]	21[a]
n-$BuSiH_3$, H^+ [6d]	31	34[a]	10	19[a]
n-$BuSiH_3$, BF_3[a]	34	42	17	25
Et_2SiH_2, H^+ [6d]	41	44[a]	20	31[a]
Et_2SiH_2, BF_3[a]	52	58	36	43
Et_3SiH, H^+ [6d]	48	48[a]	32	39[a]
Et_3SiH, BF_3[1]	64	65[a]	61	54[a]

[a] This work. [b] Ethyl ether solvent, 0 °C. [c] Reduction in methanol, ref 28. [d] Reduction of 2,4,4-trimethylcyclohexanone yields 18% of the less stable cis isomer.

Table V. Stereoselectivities in Reductions of *trans*-2-Decalone and 3- and 4-Methylcyclohexanones

Reducing agent	Relative % less stable alcohol from reduction of 3-Methylcyclohexanone	4-Methylcyclohexanone	*trans*-2-Decalone
$LiAlH_4$	16[10b]	17[10b]	18[a]
n-$BuSiH_3$, H^+	19[6d]	18[6d]	18
Et_3SiH, H^+	39[6d]	35[6d]	39
Et_3SiH, BF_3	67[1]	60[1]	64

[a] Ethyl ether solvent, 0 °C.

none, they differ significantly in their predictions of the stereochemical outcome for reductions of *trans*-1-decalone.

The stereoselectivities for reductions of *trans*-1-decalone are predicted by the conformational equilibrium model to be nearly identical with those of *cis*-2-methyl-4-*tert*-butylcyclohexanone or 2,4,4-trimethylcyclohexanone, since in each of these three ketones the 2-alkyl group is essentially locked in the equatorial position. The yield of the less stable alcohol isomer from reductions of *trans*-1-decalone is, therefore, predicted to be significantly less than that found in reductions of 2-methylcyclohexanone.

In contrast, the principle of complexation-induced conformational perturbation predicts that the relative yield of the less stable alcohol isomer from reductions of *trans*-1-decalone will be at least as great as the relative yield of *cis*-2-methylcyclohexanol from reductions of 2-methylcyclohexanone. Ring flattening about the carbonyl group of *trans*-1-decalone is not restricted by the ring fusion and should occur to nearly the same extent as in reductions of 2-methylcyclohexanone. However, because of the "3-alkyl" substituent on the cyclohexanone ring of *trans*-1-decalone, which also promotes ring flattening in the transition state for hydride transfer, the relative yield of the less stable axial isomer from *trans*-1-decalone reductions is expected to be slightly greater than the relative yield of *cis*-2-methylcyclohexanol.

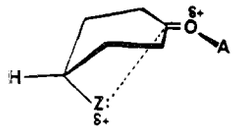
Table IV presents the stereochemical results from reductions of *trans*-1-decalone and 2-methylcyclohexanone and compares these yields with those from reductions of 4-*tert*-butylcyclohexanone and *cis*-4-*tert*-butyl-2-methylcyclohexanone. Clearly, the relative yields of the less stable alcohol isomer from reductions of *trans*-1-decalone are at least as great as or greater than those from reductions of 2-methylcyclohexanone. The data in Table IV are consistent with the predictions of stereoselectivity that are based on the complexation-induced ring flattening model but markedly disagree with those based on the conformational equilibrium model.

Hydride reduction of *cis*-4-*tert*-butyl-2-methylcyclohexanone gives lower yields of the less stable alcohol isomer than does hydride reduction of 2-methylcyclohexanone because the 4-*tert*-butyl group restricts ring flattening. Indeed, it is noteworthy that the yield of the less stable alcohol from reductions of *cis*-4-*tert*-butyl-2-methylcyclohexanone falls approximately midway between the corresponding alcohol yields from reductions of 2-methyl- and 4-*tert*-butylcyclohexanones. For reductions of complexed *cis*-4-*tert*-butyl-2-methylcyclohexanone the effects on energy minimization by the 4-*tert*-butyl and 2-methyl groups are opposed in the transition state for hydride transfer: the 2-methyl group promotes ring flattening while the 4-*tert*-butyl group hinders ring flattening.

Consideration of the principle of complexation-induced conformational perturbation for reductions of 2,4,4-trimethylcyclohexanone also results in the prediction that the relative yield of the cis-alcohol product will be less than the relative yield of *cis*-2-methylcyclohexanol from reductions of 2-methylcyclohexanone. The axial 4-methyl substituent does not restrict ring flattening. However, ring flattening presses the axial 4-methyl group close to the carbonyl group and leads to an increase in steric hindrance to hydride attack that results in the less stable alcohol isomer.

The conformational equilibrium model has also been used to explain the stereoselectivities in reductions of 3-alkylcyclohexanones.[6d,10a] However, as can be seen from the stereochemical data in Table V, there is little or no difference in the percent yields of the less stable alcohol isomers from reductions of 3-methylcyclohexanone and *trans*-2-decalone. Thus, the conformational populations of the reactant ketones do not measurably influence reduction stereoselectivity. The complexation-induced conformational perturbation model correctly predicts the observed stereochemical results.

The principle of complexation-induced conformational perturbation unifies diverse results that have been previously explained by the conformational equilibrium model or by electrostatic effects from remote substituents.[5,28,29] Application of this principle to the kinetic and stereochemical results obtained by Kwart and Takeshita on the sodium borohydride reductions of cyclohexanones with polar substituents at the 4 position, for example, adequately explains the observed increases in percent cis alcohol and in the relative rate for reduction. Association of the polar Z group with the metal ion complexed carbonyl group (structure 6) stabilizes the transition state for hydride transfer and, at the same time, effectively blocks hydride attack from the direction that would lead to the less stable trans alcohol. Indeed, results such as



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these suggest a corollary to the principle of complexation-induced conformational perturbation: that the *conformation of the reacting ketone in the transition state for hydride transfer is altered by remote polar substituents in order to maximize stabilization of the complexed carbonyl group and minimize interference between the complexing agent and substituent groups on α positions.*[30]

It must be emphasized that those same factors that influence conformational equilibration and the rates for conformational interchange[15,26,27] are integrated in the principle of complexation-induced conformational perturbation. Theories of stereoselectivity that are based on conformational rigidity present an unwarranted oversimplification of energy minimization in the transition state for nucleophilic addition reactions. Complexation with the carbonyl group modifies the conformation of the reacting ketone. Only conformationally rigid ketones such as norcamphor can be expected to be relatively insensitive to the complexing agent. The stereochemical course in nucleophilic additions to flexible ketones, particularly cyclohexanones, is demonstrably affected by both the complexing agent and the nucleophile. In our survey of nucleophilic addition reactions with cyclic ketones we have found no stereochemical results that could not be explained by application of the principle of complexation-induced conformational perturbation.[31,32] We expect that this same principle can also be applied to nucleophilic additions to acyclic ketones and, with suitable modifications, can be used to explain the stereochemical course of other stereoselective processes.[35]

Experimental Section

Methods and Materials. Instrumentation has been previously described.[6d] The Varian Model 485 digital integrator and the Varian CDS 101 data system were used to determine peak areas in GLC analyses. Commercial samples of 3- and 4-methylcyclohexanones and of *trans*-1-decalone were used without further purification. 2-Methylcyclohexanone and 4-*tert*-butylcyclohexanone were purified by distillation prior to use. 3,3,5-Trimethylcyclohexanone was prepared by a standard Jones oxidation procedure from commercially available 3,3,5-trimethylcyclohexanol; 2-decalol was similarly oxidized to 2-decalone. Isomeric alcohol mixtures were either commercially available or were prepared from the corresponding ketones by lithium aluminum hydride reduction. Diethyl- and triethylsilane were commerically available and were used without further purification. *n*-Butylsilane was prepared by lithium aluminum hydride reduction of *n*-butyltrichlorosilane.[36] Commercial boron trifluoride etherate was purified by distillation from calcium hydride through a 10-cm Vigreux column under a slow flow of nitrogen and was stored over calcium hydride and under nitrogen in a refrigerator at 5 °C.

***cis*-4-*tert*-Butyl-2-methylcyclohexanone.** A solution of 32.9 g of 4-*tert*-butyl-2-methylphenol in 175 mL of glacial acetic acid was hydrogenated at room temperature and 45 psi of initial pressure according to the procedure of Allinger and co-workers,[37] using 1.0 g of platinum oxide. The resulting 4-*tert*-butyl-2-methylcyclohexanol, which was isolated in 80% yield, was then oxidized by chromic acid in aqueous acetone to *cis*-4-*tert*-butyl-2-methylcyclohexanone in 75% yield by the procedure of Djerassi et al.,[38] with the workup procedure similar to that used in standard Jones oxidation procedures. The resulting dark orange solution was distilled to give a clear, colorless liquid, bp 82–84 °C (1.1 Torr) [lit.[39] 110–113 °C (14 Torr)]. The isolated ketone was free of alcohol and isomerically pure by ^{1}H NMR[37,40] and GLC analysis (6 ft 10% DEGS on Chromosorb W).

General Organosilane Reduction Procedure in Boron Trifluoride Etherate. Boron trifluoride etherate (5.0 mmol) was added dropwise by syringe to an ice-bath cooled and rapidly stirred solution of the ketone (5.0 mmol) and organosilane (5.5 mmol) that were contained in a round-bottom flask fitted with a gas inlet tube, septum, and drying tube. The reaction system was flushed with dry nitrogen or argon prior to the addition of BF_3·Et_2O. After the addition was complete the homogeneous solution was allowed to warm to room temperature. Generally a white precipitate formed as the reaction progressed. Although reaction times for >95% reduction were less than 1 h, the reaction was allowed to continue for 24 h. An excess of 3 N sodium hydroxide was then slowly added to the reaction mixture and stirring was continued for an additional 30 min. The hydrolyzed mixture was then extracted three times with ether, the combined ether extract was passed through anhydrous magnesium sulfate, and the magnesium sulfate filter cake was rinsed several times with small portions of ether. The combined ether washes and extract was concentrated under reduced pressure, and the products were subjected to GLC analyses. Yields of recovered alcohol products, determined by GLC analyses through reference to an internal standard and corrected for detector response, were 65–82%. Aldol condensation competes with reduction in reactions that employ BF_3·Et_2O.[1]

Effect of BF_3·Et_2O Concentration on Stereoselectivity. Since BF_3·Et_2O is a reactant in the reductive conversion of ketones to borate esters,[1] stereoselectivity in reductions of alkyl-substituted cyclohexanones may be expected to be sensitive to the boron trifluoride to ketone ratio. Organosilane reductions of 2-methylcyclohexanone, 4-*tert*-butylcyclohexanone, *trans*-1-decalone, and *cis*-4-*tert*-butyl-2-methylcyclohexanone were, therefore, performed at two different molar ratios of boron trifluoride to ketone. The results from reductions of these ketones using a molar ratio of BF_3:ketone of 1.0 were given in Tables I–V. Reductions using a molar ratio of BF_3:ketone equal to 0.38 were performed in the manner previously described. Reaction times for complete reduction were generally 24 h. Alcohol products were obtained in 84–89% isolated yield. Stereoselectivities in the formation of the less stable alcohol isomer from reductions of 4-*tert*-butylcyclohexanone, *trans*-1-decalone, and *cis*-4-*tert*-butyl-2-methylcyclohexanone by *n*-butylsilane, diethylsilane, and triethylsilane with a BF_3:ketone molar ratio of 0.38, and from the reduction of 2-methylcyclohexanone by triethylsilane under the same conditions, were 1–3% less than those from reductions with a BF_3:ketone molar ratio of 1.0. For reductions of 2-methylcyclohexanone with *n*-butylsilane and diethylsilane using a BF_3:ketone molar ratio of 0.38, the percent yield of *cis*-2-methylcyclohexanol was 2% greater than in reductions using a BF_3:ketone molar ratio of 1.0. Thus, the variations in stereoselectivity by changing the BF_3·Et_2O concentration are not large, particularly when compared to those observed in sodium borohydride reductions,[10a] and the results obtained for organosilane reductions using 1:1 BF_3:Et_2O accurately reflect the effect of boron trifluoride complexation with alkyl-substituted cyclohexanones.

Other Reduction Procedures. Organosilane reductions in trifluoroacetic acid were performed as previously described.[6d] Sodium borohydride reductions in isopropyl alcohol were performed according to the procedure of Wigfield and Phelps[6b,c,41] with a twofold molar excess of sodium borohydride over ketone. Reductions by lithium aluminum hydride were run in anhydrous ethyl ether using equimolar amounts of $LiAlH_4$ and ketone. Control experiments that were run for procedural comparison with published results duplicated literature values for stereoselectivities in reduction.

Product Analyses. Product yields were determined by GLC analyses. Isomeric alcohols from 3- and 4-methylcyclohexanone and from *trans*-1-decalone reductions were separated and analyzed on 6-ft, 10% DEGS columns at 75 °C (3- and 4-methylcyclohexanone reductions) and 110 °C (*trans*-2-decalone reductions). Isomeric alcohols from reductions of 4-*tert*-butylcyclohexanone and 3,3,5-trimethylcyclohexanone were separated and analyzed on 7-ft 20% Carbowax 20M columns operated at 170 and 165 °C, respectively. Isomeric alcohols from reductions of *trans*-2-decalone were analyzed on 9-ft 20% Carbowax 20M columns. Isomeric alcohols from reductions of *cis*-4-*tert*-butyl-2-methylcyclohexanone were analyzed on 6-ft 10% DEGS columns operated at 120 °C and on 7-ft 20% Carbowax 20M columns operated at 170 °C. In each separation the axial alcohol isomer was eluted first.[6d] The thermal conductivities of the geometrical isomers of each alcohol were assumed to be identical.[42]

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Registry No.—*trans*-2-Decalone, 16021-08-2; *cis*-4-*tert*-butyl-

2-methylcyclohexanone, 3211-27-6; 4-*tert*-butyl-2-methylphenol, 98-27-1; 4-*tert*-butyl-2-methylcyclohexanol, 2484-73-3.

References and Notes

(1) Silane Reductions in Acidic Media. 9. Part 8: M. P. Doyle, C. T. West, S. J. Donnelly, and C. C. McOsker, *J. Organomet. Chem.*, **117**, 129 (1976).

(2) (a) Camille and Henry Dreyfus Foundation Teacher-Scholar Grant Awardee, 1973–1978. (b) National Science Foundation Undergraduate Research Participant, summer, 1975.

(3) M. P. Doyle and C. T. West, Ed., "Stereoselective Reductions", Dowden, Hutchinson and Ross, Stroudsburg, Pa., 1976.

(4) (a) D. J. Cram and F. A. A. Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952); (b) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *ibid.*, **78**, 2579 (1956); (c) J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.*, 112 (1959); (d) H. Haubenstock and E. L. Eliel, *J. Am. Chem. Soc.*, **84**, 2363 (1962); (e) J. A. Marshall and R. D. Carroll, *J. Org. Chem.*, **30**, 2748 (1965); (f) M. Cherest, H. Felkin, and N. Prudent, *Tetrahedron Lett.*, 2199 (1968); (f) M. Cherest and H. Felkin, *ibid.*, 2205 (1968); (h) E. L. Eliel and Y. Senda, *Tetrahedron*, **26**, 2411 (1970).

(5) (a) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice-Hall, Englewood Cliffs, N.J., 1971, Chapter 3; (b) H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 2; (c) J. H. Brewster in "Elucidation of Organic Structures by Physical and Chemical Methods", Vol. III, K. W. Bentley and G. W. Kirby, Ed., Wiley-Interscience, New York, N.Y., 1972, Chapter XVII.

(6) (a) E. C. Ashby, J. R. Boone, and J. P. Oliver, *J. Am. Chem. Soc.*, **95**, 5427 (1973); (b) D. C. Wigfield and D. J. Phelps, *ibid.*, **956**, 543 (1974); (c) D. C. Wigfield, S. Feiner, and D. J. Phelps, *J. Org. Chem.*, **40**, 2533 (1975); (d) M. P. Doyle and C. T. West, *ibid.*, **40**, 3821 (1975).

(7) (a) N. T. Anh, O. Eisenstein, J.-M. Lefour, and M.-E. T. H. Dâv, *J. Am. Chem. Soc.*, **95**, 6146 (1973); (b) J. Klein, *Tetrahedron Lett.*, 4307 (1973); (c) J. Klein, *Tetrahedron*, **30**, 3349 (1974); (d) C. Agami, A. Kazakos, and J. Levisalles, *Tetrahedron Lett.*, 2035 (1975); (e) E. Toromanoff, *Bull. Soc. Chim. Fr.*, 1190 (1962).

(8) Recent ab initio calculations suggest that the angle of approach for a nucleophile to a carbonyl group in addition reactions is 105 ± 5° rather than 90°: H. B. Bürgi, J. D. Dunitz, J. M. Lehn, and G. Wipff, *Tetrahedron*, **30**, 1563 (1974). Although we advance the widely held postulate of perpendicular approach, deviations from the 90° angle to 110° do not markedly affect our proposals. Indeed, nucleophilic attack on the carbonyl group at a 110° angle serves to enhance the validity of our stereochemical arguments.

(9) (a) J.-C. Richer, *J. Org. Chem.*, **30**, 324 (1965); (b) H. C. Brown and H. R. Deck, *J. Am. Chem. Soc.*, **87**, 5620 (1965); (c) E. C. Ashby, J. P. Sevenair, and F. R. Dobbs, *J. Org. Chem.*, **36**, 197 (1971).

(10) (a) B. Rickborn and M. T. Wuesthoff, *J. Am. Chem. Soc.*, **92**, 6894 (1970); (b) H. C. Brown and W. C. Dickason, *ibid.*, **92**, 709 (1970); (c) H. C. Brown and S. Krishnamurthy, *ibid.*, **94**, 7159 (1972); (d) J. Hooz, S. Akiyama, F. J. Cedar, M. J. Bennett, and R. M. Tuggle, *ibid.*, **96**, 274 (1974); (e) S. Krishnamurthy and H. C. Brown, *ibid.*, **98**, 3383 (1976); (f) M. G. Combe and H. B. Henbest, *Tetrahedron Lett.*, 404 (1961); (g) D. C. Wigfield and D. J. Phelps, *J. Org. Chem.*, **41**, 2396 (1976); (h) S. Krishnamurthy and H. C. Brown, *J. Am. Chem. Soc.*, **98**, 3383 (1976).

(11) (a) M. P. Doyle and C. T. West, *J. Org. Chem.*, **40**, 3829 (1975); (b) *ibid.*, **40**, 3835 (1975).

(12) D. N. Kirk and A. Mudd, *J. Chem. Soc. C*, 804 (1969).

(13) C. A. Brown, *J. Am. Chem. Soc.*, **95**, 4100 (1973).

(14) (a) W. M. Jones and H. E. Wise, Jr., *J. Am. Chem. Soc.*, **84**, 997 (1962); (b) K. D. Hardy and R. J. Wicker, *ibid.*, **80**, 640 (1958).

(15) D. H. Wertz and N. L. Allinger, *Tetrahedron*, **30**, 1579 (1974).

(16) Private communication with Stanley G. Smith.

(17) "Flexible" describes cyclic ketones, such as cyclohexanone, that easily undergo conformational changes in contrast to "rigid" ketones, such as norcamphor. "Flexible" is not meant to imply the flexible cyclohexane conformation (skew-boat conformation).

(18) H. R. Buys and H. J. Geise, *Tetrahedron Lett.*, 2991 (1970), and references cited therein.

(19) P. L. Johnson and J. F. McConnell, *Tetrahedron*, **28**, 2901 (1972).

(20) (a) M. Calligaris, G. Manzini, G. Pitacco, and E. Valentin, *Tetrahedron*, **31**, 1501 (1975), and references cited therein. X-ray analyses of 2-substituted 4-*tert*-butylcyclohexanones show that there is no significant twisting of the *tert*-butyl group from the staggered arrangement depicted in structure **4b**. (b) However, although the "4-methyl, 4-*tert*-butyl effect" is adequately explained by interpretation of the principle of complexation-induced conformational perturbation, other factors, including the mechanistic changes advocated by Wigfield and Phelps[10g] or the changes in the transition state geometry for hydride attack that we have proposed,[11b] may alternatively be responsible for the differential rates for hydride attack that are observed with changes in the steric bulk of the reducing agent.

(21) J. Hust, Y. Maroni-Barnaud, N. T. Anh, and J. Seyden-Penne, *Tetrahedron Lett.*, 159 (1976).

(22) S. R. Landor and J. P. Regan, *J. Chem. Soc. C*, 1159 (1959).

(23) (a) J.Klein and E. Dunkelblum, *Isr. J. Chem.*, **5**, 181 (1967); (b) J. Klein and E. Dunkelblum, *Tetrahedron*, **23**, 205 (1967).

(24) The stereochemical results in Table III for reductions of 4-methyl- and 4-*tert*-butylcyclohexanone by sodium borohydride differ according to the source of the data and exhibit the least difference in percentage yield of the less stable isomers among the series of "small reducing agents". The absence of a significant difference may indicate that sodium ion complexation with the ketone does not occur when sodium borohydride reductions are performed in isopropyl alcohol or that complexation is weak and its effect on stereoselectivity in reductions of unhindered ketones is minor. The most extensive data for reductions of these ketones by sodium borohydride is that of Wigfield and Phelps[10g] who have suggested either mechanistic changes or differential transition states to explain their results with an extensive series of cyclic ketones. The argument which we present concerning the "4-methyl, 4-*tert*-butyl effect" does not suggest that there is but one mechanism or one transition state for hydride reductions but does state that, in increasing the steric bulk of the reducing agent, the reversal in percentage yield of the less stable isomer for reductions of 4-methyl- and 4-*tert*-butylclohexanone is due to interactions defined by the principle of complexation-induced conformational perturbation.

(25) H. C. Brown and V. Varma, *J. Am. Chem. Soc.*, **88**, 2870 (1966).

(26) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Wiley-Interscience, New York, N.Y., 1965.

(27) (a) N. L. Allinger, M. A. Miller, J. Hirsch, and I. Tyminski, *J. Am. Chem. Soc.*, **91**, 337 (1969); (b) N. L. Allinger, M. T. Tribble, and M. A. Miller, *Tetrahedron*, **28**, 1173 (1972); (c) N. L. Allinger and M. T. Tribble, *ibid.*, **28**, 1191 (1972); (d) N. L. Allinger, G. A. Lane, and G. L. Wang, *J. Org. Chem.*, **39**, 704 (1974).

(28) R. S. Monson, D. Przybycien, and A. Baraze, *J. Org. Chem.*, **35**, 1700 (1970).

(29) H. Kwart and T. Takeshita, *J. Am. Chem. Soc.*, **84**, 2833 ((1962).

(30) Cyclohexanones with polar groups at the axial 3 position cannot achieve both maximum stabilization of the complexed carbonyl group and minimum steric interference between the complexing agent and substituent groups on α positions.[7d]

(31) A decrease has recently been observed in the stereoselectivity for formation of axial or cis alcohol in trialkyl- or triarylaluminum additions to cyclic ketones,[33] due to the change in the R_3Al to $R_2C{=}O$ molar ratio.[34] This stereoselectivity has been explained as resulting from a "compression effect" in the transition state for nucleophilic addition. However, close examination of molecular models shows that in order for the bulky R_3Al complexing agent to minimize steric interference with ketone substituents α to the carbonyl group, alkylation must be directed more to the side of the carbonyl group that leads to the formation of equatorial or trans alcohol. The stereochemical results obtained by Ashby and his co-workers are not in conflict with the principle of complexation-induced conformational perturbation and, therefore, do not require a "compression effect" to explain them. Ashby's results do, however, provide unique examples of steric influences on the direction of nucleophilic attack.

(32) E. C. Ashby and J. T. Laemmle, *Chem. Rev.*, **75**, 521 (1975).

(33) J. Laemmle, E. C. Ashby, and P. V. Roling, *J. Org. Chem.*, **38**, 2526 (1973); E. C. Ashby and J. T. Laemmie, *ibid.*, **40**, 1469 (1975).

(34) H. M. Neumann, J. T. Laemmie, and E. C. Ashby, *J. Am. Chem. Soc.*, **95**, 2597 (1973); E. C. Ashby, J. T. Laemmie, and H. M. Neumann, *ibid.*, **90**, 5179 (1968); E. C. Ashby and J. T. Laemmie, *J. Org. Chem.*, **33**, 3398 (1968).

(35) The results and conclusions of J. E. Nordlander and T. J. McCrary, Jr., *J. Am. Chem. Soc.*, **94**, 5133 (1972), point to similar effects operative in solvolysis reactions.

(36) M. P. Doyle, D. J. De Bruyn, S. J. Donnelly, D. A. Kooistra, A. A. Odubela, C. T. West, and S. M. Zonnebelt, *J. Org. Chem.*, **39**, 2740 (1974).

(37) N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *J. Am. Chem. Soc.*, **88**, 2999 (1966).

(38) C. Beard, C. Djerassi, J. Sicher, F. Šipoš, and M. Tichý, *Tetrahedron*, **19**, 919 (1963).

(39) H. O. House, B. A. Tefertiller, and H. O. Olmstead, *J. Org. Chem.*, **33**, 935 (1968).

(40) K. L. Servis and D. J. Bowler, *J. Am. Chem. Soc.*, **97**, 80 (1975).

(41) D. C. Wigfield and D. J. Phelps, *Can. J. Chem.*, **50**, 388 (1972).

(42) E. L. Eliel, S. H. Schroeter, T. J. Brett, F. J. Biros, and J.-C. Richer, *J. Am. Chem. Soc.*, **88**, 3327 (1966).