Characterization of Torsional Angle Effects as the Dominant Steric Effect in the Hydroxymercuration of Substituted Cyclohexenes[1]

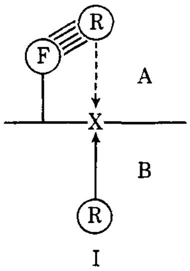
Daniel J. Pasto* and John A. Gontarz

Contribution from the Department of Chemistry, University of Notre Dame, Notre Dame, Indiana 46556.

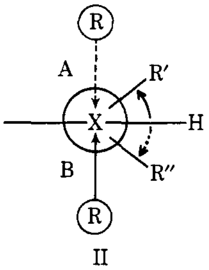
Received March 8, 1971

Abstract: The dominant steric effect operative in the oxymercuration of substituted cyclohexenes is shown to involve torsional angle effects (eclipsing strain energy) generated between the C_1–H, C_6-pseudoequatorial bond and the C_2–H, C_3-pseudoequatorial bond. The magnitude of the torsional angle effect is directly related to the size of the functional group at the C_3 position in the *cis*-3-alkyl-5-*tert*-butylcyclohexenes. Remote steric effects are shown to be relatively unimportant.

The study of steric effects on the course of organic reactions has attracted the attention of many organic chemists and has resulted in a vast body of chemical information. In general, there are basically two different types of steric effects which are manifest in both reaction rates and the stereochemistry of product formation. These two categories of steric effects can be classified as: (1) remote steric effects and (2) torsional angle effects. These effects are illustrated in I and II, respectively. In I the approach of a reagent R toward the reaction center X from side A involves the generation of a steric interaction between the incoming reagent R and a remote functional group F. In general this effect is repulsive in nature and results in a retardation in the rate of attack from side A. In contrast, the approach of R from side B toward X is unimpeded by the remote functional group F, and thus is the favored direction of attack. Remote steric effects of this type may be apparent very early along the reaction coordinate, *i.e.*, involving very little bond formation between R and the reaction center X, as well as very late along the reaction coordinate, *i.e.*, involving extensive bond formation between R and the reaction center X. The former case is generally referred to as involving “steric approach control,” and the latter extreme as involving “product development control.”[2]



I



II

Torsional angle effects arise in transition states in which a change in configuration occurs resulting in the generation, or reduction, of bond-bond eclipsing interactions. This effect is illustrated in II. Attack of the reagent R from side A (along the dotted line) at the reaction center X (arbitrarily a trigonal carbon atom) results in a change in the hybridization at the reaction center from sp^2 to sp^3. During this change the C–H bond moves along an arc denoted by the dotted arrow resulting in the generation of an eclipsing strain energy between the C–H and C–R″ bonds. Alternatively, attack of R from side B (along the solid line) results in movement of the C–H bond along the arc described by the solid arrow resulting in the generation of eclipsing strain energy between the C–H and C–R′ bonds. If the eclipsing strain energy developed between the C–H and C–R′ bonds is greater than that developed between the C–H and C–R″ bonds, attack from side B will be favored. Although we illustrate torsional angle effects in a reaction proceeding from sp^2 to sp^3 hybridization, torsional angle effects should be observable in reactions proceeding from sp^3 to sp^2 hybridization (elimination reactions), and in nucleophilic displacement reactions (sp^3 to pentavalent intermediate or transition state to sp^3 hybridization). Torsional angle effects are expected to be maximal when the transition state and the point of maximum eclipsing coincide,[3] and may occur at any point along the reaction coordinate depending on the structure of the reactant species. The distinction between remote steric effects and torsional angle effects can be made by the careful selection of substrates for study, although in many cases both effects may be operative.

Although remote steric effects have been the subject of study for a considerable period of time, torsional angle effects have received attention only recently. In 1965 Garbisch and coworkers[4] suggested that the diimide reduction of substituted cyclohexenes was subject to torsional angle effects, and in 1967 Schleyer[5] suggested that torsional angle effects might account for the observed preference for exo reactivity in norbornyl and norbornene systems. Schleyer suggested that torsional angle effects could be used to explain the high exo:endo addition ratios in the oxymercuration, epoxidation, hydroboration, and cyclopropanation of norbornene.

More recently, Bartlett and coworkers[3] have attributed the exo–endo stereoselectivity of the atom abstraction reactions of the 2-norbornyl radical to torsional angle effects.

In a detailed study on the stereochemistry of attack and direction of addition of borane and substituted

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(1) Submitted by J. A. G. in partial fulfillment of the requirements for the Ph.D., University of Notre Dame, Notre Dame, Ind., 1970.

(2) For the original introduction of these terms see W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Amer. Chem. Soc.*, **78**, 2579 (1956).

(3) P. D. Bartlett, G. N. Fickes, F. C. Haupt, and R. Helgeson, *Accounts Chem. Res.*, 3, 177 (1970).

(4) E. W. Garbisch, S. M. Schildkraut, and D. M. Patterson, *J. Amer. Chem. Soc.*, **87**, 2932 (1965).

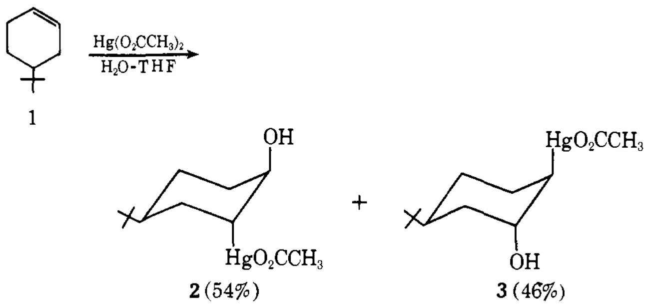
(5) P. von R. Schleyer, *ibid.*, **89**, 699 (1967).

boranes to substituted cyclohexenes, Pasto and Klein[6] concluded that torsional angle effects were not important in the hydroboration reaction. By comparison of relative rates and the stereochemistry of attack on substituted cyclohexenes Pasto and Klein also concluded that torsional angle effects were not important in diimide reductions and epoxidation reactions. The dominant steric effects in the substituted cyclohexenes were remote steric effects imposed by functional groups in the 4- and 5-pseudoaxial positions and exocyclic syn-axial positions. In a more recent study Pasto and Rao have discussed the reversal of the thermodynamic stability-reactivity relationship for tosylate solvolyses and alcohol oxidations in the cyclohexyl series, observed with the 2,5-di-*tert*-butylcyclohexyl derivatives, in terms of torsional angle effects.[7]

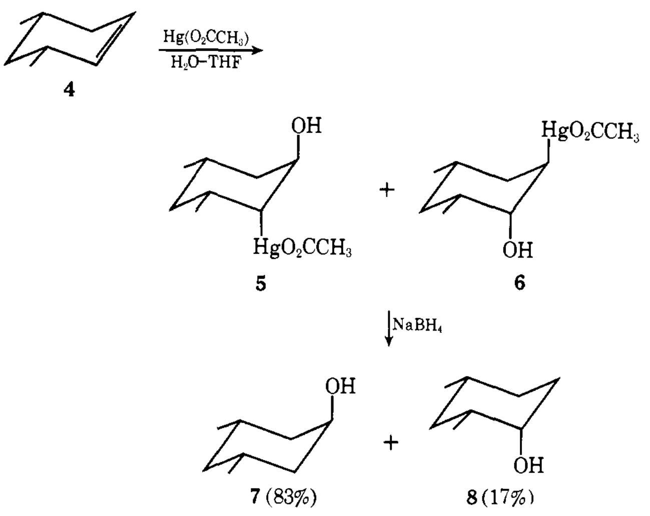
In a continuation of our studies of steric effects in organic reactions we have evaluated the steric effects in the oxymercuration of substituted cyclohexenes. In the preceding article the mechanism of the oxymercuration of substituted cyclohexenes was shown to occur *via* mercurinium ion intermediates.[8] In the present article we wish to present the results of a study designed to evaluate remote steric effects *vs.* torsional angle effects in the oxymercuration of substituted cyclohexenes.

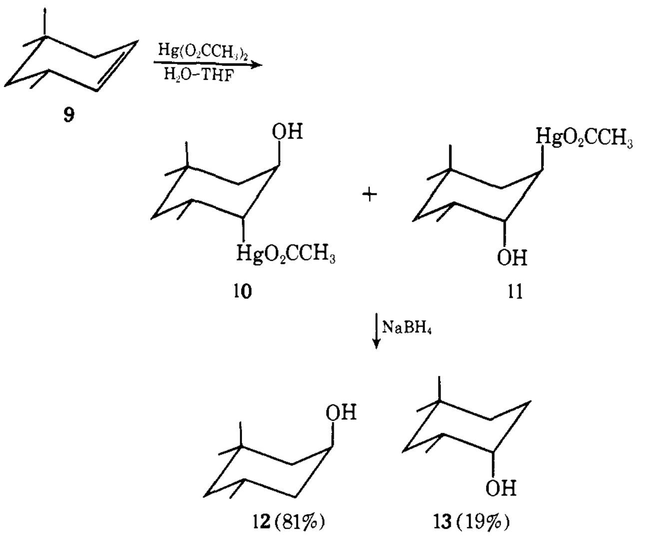
Results and Discussion

The oxymercuration of 4-*tert*-butylcyclohexene (**1**) proceeds to give the trans diaxial adducts **2** and **3** in a 54:46 ratio.[8] The ratio of attack by water on the mercurinium ion cis and trans to the 4-*tert*-butyl group is essentially the same as that for attack by borane on **1**, the borane cis-trans attack ratio being 55:45.[6] This is, however, as far as any similarity between the oxymercuration and hydroboration reactions of substituted cyclohexenes goes.



The kinetically controlled oxymercuration[8] of *cis*-3,5-dimethylcyclohexene (**4**) followed by reductive demercuration of the intermediate adducts **5** and **6** with sodium borohydride produces the axial alcohols **7** and **8** in an 83:17 ratio. The preferential formation of **5** over **6** is at first somewhat surprising. From a remote steric effect basis, the two equatorial methyl groups of **4** should offer very little steric inhibition to formation of either **5** or **6**. (It is considered that **4** reacts in the conformation shown and not in a conformation having one or both of the methyl groups pseudoaxial involving a twist-boat conformation in the transition state.)





To further assess remote steric effects in a molecule similar to **4**, the oxymercuration of 3,5,5-trimethylcyclohexene (**9**) was studied. The oxymercuration of **9**, followed by reductive demercuration, produces only the axial alcohols **12** and **13**, which must be derived from the intermediate adducts **10** and **11**, in an 81:19 ratio. Surprisingly, the introduction of the 5-axial methyl group imposes essentially no remote steric effect on the steric course of the oxymercuration of **9** relative to **4**. The presence of the 5-axial methyl group is expected to have little effect on the formation of the two possible mercurinium ions in that the *A* value for mercury is essentially zero.[9] However, in the rate-determining attack by water on the intermediate mercurinium ions, the molecule of water undergoing nucleophilic attack at C-1 must enter the transition state past the C-5 axial methyl group in **14**, yet the major product is formed in this manner. That the remote steric effect between the C-5 axial methyl group and the incoming molecule of solvent is in fact not the dominant steric effect is supported by the results of the acetoxymercuration of **9**. Acetic acid is a considerably larger molecule than water, and hence should develop a greater steric interaction with the C-5 axial methyl group in mercurinium ion **14**. The distribution of products in the acetoxymercuration of **4** and **9** is different from that observed in hydroxymercuration; how-

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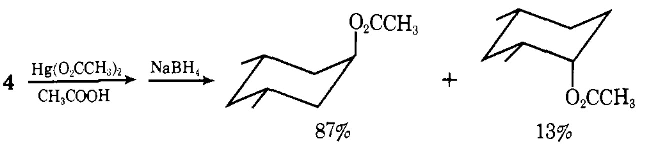
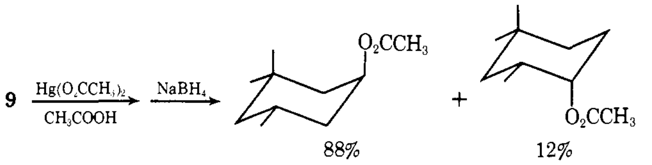
[6] D. J. Pasto and F. M. Klein, *J. Org. Chem.*, 33, 1468 (1968).

[7] D. J. Pasto and D. R. Rao, *J. Amer. Chem. Soc.*, **92**, 5151 (1970).

[8] D. J. Pasto and J. A. Gontarz, *ibid.*, **93**, 6902 (1971).

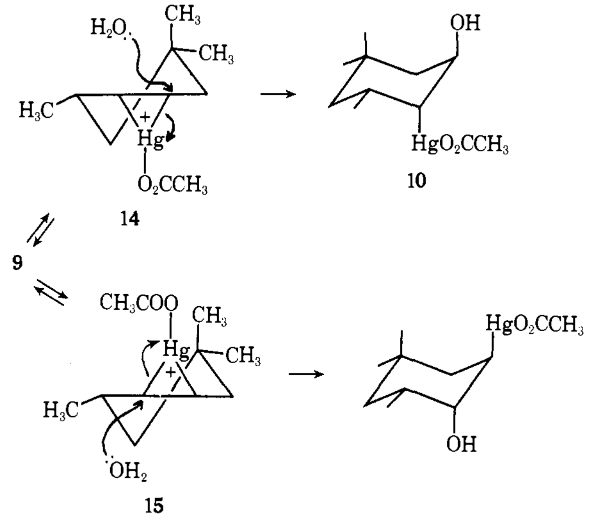
[9] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1966, p 44.

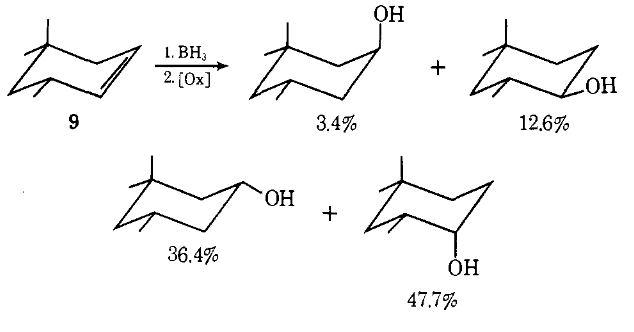




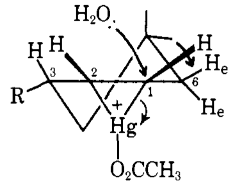
ever, the change is in the direction *opposite* that expected on the basis of a dominant remote steric effect.

The steric role of the C-5 axial methyl group in **9** is completely different from that observed in the hydroboration of **9**, in which case 85% of the hydroboration occurs trans to the C-5 axial methyl group.[6] As the C-5 equatorial methyl group in **4** and **9** is in the same relative position to the carbon–carbon double bond as the 4-*tert*-butyl group is in **1**, *we must conclude that the C-3 pseudoequatorial methyl groups in* **4** *and* **9** *exert the dominant steric effect in the oxymercuration of* **4** *and* **9**.





The observed steric effect imposed on the oxymercuration of **4** and **9** can be explained by invoking the presence of torsional angle effects in the transition states for the attack of solvent on the mercurinium ions **16** and **17**.



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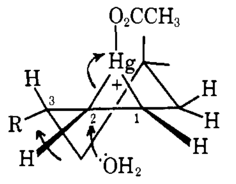


17

In the attack of water at C-1 of **16** the C_1–H bond is forced past the C_6–H_e bond, thus introducing eclipsing strain energy. Attack by water at C_2 in **17** forces the C_2–H bond past the C_3–R bond also introducing torsional strain energy. As in **15**, the C_3–R,C_2–H torsional strain energy must be greater than the C_6–H_e,-C_2–H torsional strain energy in **14**; product formation *via* **14** is favored.[10]

If the foregoing proposal is correct, the torsional strain energy created in **17** should be a function of the size of the R functional group.[11] We accordingly prepared a series of *cis*-3-alkyl-5-*tert*-butylcyclohexenes, as illustrated below, and subjected these olefins to kinetically controlled oxymercuration. The oxymercuration products were reductively demercurated with sodium borohydride and the resulting alcohol mixtures were analyzed by glpc by comparison of retention times with authentic samples. The peak areas were converted to weight ratios by the use of response ratios. The results are given in Table I. The observed trend

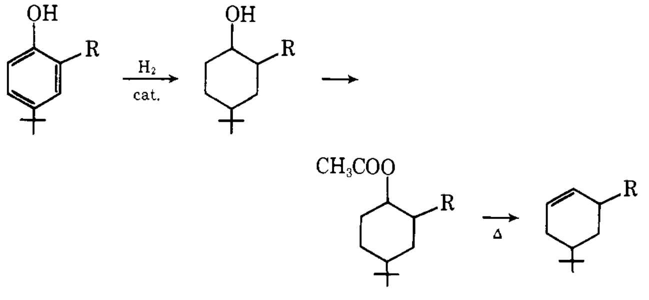
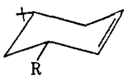
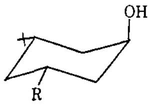
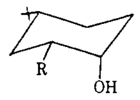


Table I. Results of Oxymercuration–Reductive Demercuration of *cis*-3-Alkyl-5-*tert*-butylcyclohexenes at 25°

 R =		
H	46.4	53.6
CH_3	89.8	10.2
C_2H_5	90.5	9.5
$CH(CH_3)_2$	94.2	5.8
$C(CH_3)_3$	99.06	0.94

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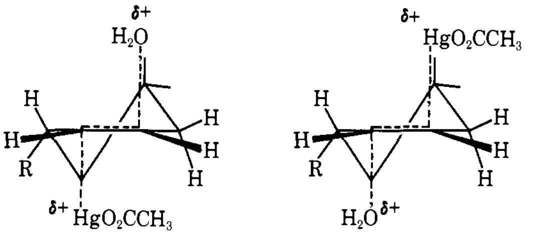
(10) The steric effects observed in the oxymercuration of **4** and **9**, as well as the other *cis*-3-alkyl-5-*tert*-butylcyclohexenes reported in this study, cannot be accounted for in Ad_E3-type transition states. The C_1–H and C_2–H bonds remain between the C–H_e and C–H_a bonds of C_3 and C_6 throughout the course of the reaction. These results further support the conclusions presented in the foregoing article that the oxymercuration of substituted cyclohexenes proceeds *via* the reversible formation of mercurinium ion intermediates.



(11) Eclipsing strain energy is generally believed to be due to a combination of atom or functional group nonbonded interactions and electrostatic repulsion between the electrons comprising the eclipsed bonds. As one changes the nature of the R functional group in **17**, both the nonbonded interactions and the electronic repulsion contributions will change; however, when R is constrained to a series of alkyl groups the dominant change in the eclipsing strain energy should be the nonbonded interaction term.

in product ratios is consistent with the proposed torsional angle effects.

The magnitude of the torsional angle effect is directly proportional to the *A* value for the 3-alkyl groups.[9] As the products are formed in competitive reactions, the difference in transition-state free energies ($\Delta\Delta G^{\ddagger}$) is directly calculable from the product ratios. The $\Delta\Delta G^{\ddagger}$ values for the oxymercuration of **4**, **9**, and the *cis*-3-alkyl-5-*tert*-butylcyclohexenes, along with the appropriate *A* values, are given in Table II. The reduced value of $\Delta\Delta G^{\ddagger}$ for **9** relative to **4** is consistent with the contribution of a small amount of a remote steric effect generated between the C-5 axial methyl group and the attacking molecule of water. The higher $\Delta\Delta G^{\ddagger}$ value obtained for *cis*-3-methyl-5-*tert*-butylcyclohexene is probably due to a distortion of the cyclohexene and/or mercurinium ion structures caused by the 5-*tert*-butyl group[12] resulting in increased torsional angle effects. A linear correlation exists between the $\Delta\Delta G^{\ddagger}$ values and the *A* values for the methyl, ethyl, and isopropyl systems; $\Delta\Delta G^{\ddagger} = 0.67A$. The $\Delta\Delta G^{\ddagger}$ value for the oxymercuration of *cis*-3,5-di-*tert*-butylcyclohexene does not follow the trend exhibited by the other *cis*-3-alkyl-5-*tert*-butylcyclohexenes. This may be due to a further distortion of the system by the 3-*tert*-butyl group.

Table II. $\Delta\Delta G^{\ddagger}$ Values for the Competitive Pathways in the Oxymercuration of 3-Substituted Cyclohexenes

Olefin	3-Alkyl group	$\Delta\Delta G^{\ddagger}$, kcal/mol	A_R
4	Methyl	0.95	1.7
9	Methyl	0.85	1.7
	Methyl	1.28	1.7
	Ethyl	1.33	1.8
	Isopropyl	1.65	2.1
	tert-Butyl	2.75	~5

Experimental Section

Preparation of Olefins. ***cis*-3,5-Dimethylcyclohexene.** Phosphorus oxychloride (0.29 mol) was slowly added to a solution of 19.2 g (0.15 mol) of a mixture of *cis,cis*- and *trans,trans*-3,5-dimethylcyclohexanol in 220 ml of pyridine at 0°. The reaction mixture was stirred for 2 hr at 0° and then at 25° for 24 hr. The reaction mixture was cooled and the excess phosphorus oxychloride was hydrolyzed by the cautious addition of water. The hydrolyzed mixture was acidified by the addition of 20% hydrochloric acid, and was extracted with three 200-ml portions of pentane. The pentane extract was washed with water and dried ($MgSO_4$), and the solvent was removed by distillation. The residue was distilled under reduced pressure giving *cis*-3,5-dimethylcyclohexene: bp 72° (130 mm) [lit.[13] 121° (760 mm)].

***cis*-3,5-Di-*tert*-butylcyclohexene.** *cis*-3,5-Di-*tert*-butylcyclohexene was prepared from a mixture of *cis,cis*- and *trans,trans*-3,5-di-*tert*-butylcyclohexanol as described above for **4**. The product was purified by preparative glpc; however, the oxymercuration of the olefin gave inconsistent results and indicated the presence of very minor amounts of impurities. As it appeared that the impurities underwent oxymercuration at a faster rate than the desired olefin, the di-*tert*-butylcyclohexene was purified by repeated partial oxymercuration (see later in this section for the details of the oxymercuration procedure) until consistently reproducible oxymercuration results were obtained. The purified *cis*-3,5-di-*tert*-butylcyclohexene gave bp 48° (0.2 mm) [lit.[14] 110–112° (21 mm)].

***cis*-3-Methyl-5-*tert*-butylcyclohexene.** Acetyl chloride (0.35 mol) was slowly added to a solution of 1.17 mol of *cis*-2-methyl-*cis*-4-*tert*-butylcyclohexanol in 100 ml of dimethylaniline at 0°. The reaction mixture was stirred at 25° for 15 hr and was then heated on a steam bath for 3 hr. The reaction mixture was then poured onto 60 g of ice in 200 ml of 10% hydrochloric acid and was extracted with three 100-ml portions of pentane. The pentane extract was washed with 10% hydrochloric acid until neutral and was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was distilled giving *cis*-2-methyl-*cis*-4-*tert*-butylcyclohexyl acetate (77%): bp 69–71° (0.8 mm).

The acetate was pyrolyzed in a stream of nitrogen by slowly dropping through a 2 × 30 cm glass helices packed column maintained at 450 ± 10°. The pyrolysate was collected in Dry Ice–acetone cooled traps. The pyrolysate was poured into 50 ml of water and extracted with 50 ml of pentane. The pentane extract was washed with water and saturated sodium bicarbonate and dried ($MgSO_4$). The pentane was removed under reduced pressure and the residue was distilled giving *cis*-3-methyl-5-*tert*-butylcyclohexene: bp 71–73° (15 mm).

Anal. Calcd for $C_{11}H_{20}$: C, 86.76; H, 13.24. Found: C, 86.68; H, 13.32.

***cis*-3-Ethyl-5-*tert*-butylcyclohexene.** *cis*-3-Ethyl-5-*tert*-butylcyclohexene was prepared from *cis*-2-ethyl-*cis*-4-*tert*-butylcyclohexanol as described above for *cis*-3-methyl-5-*tert*-butylcyclohexene: bp 98° (25 mm).

Anal. Calcd for $C_{12}H_{22}$: C, 86.67; H, 13.33. Found: C, 86.83; H, 13.33.

***cis*-3-Isopropyl-5-*tert*-butylcyclohexene.** *cis*-3-Isopropyl-5-*tert*-butylcyclohexene was prepared as described above for the 3-methyl and 3-ethyl isomers: bp 97–99° (20 mm).

Anal. Calcd for $C_{13}H_{24}$: C, 86.59; H, 13.41. Found: C, 86.68; H, 13.23.

Preparation of Alcohols. ***cis,cis*-2,4-Dimethylcyclohexanol.** 2,4-Dimethylphenol (0.74 mol) in 150 ml of glacial acetic acid was hydrogenated over 2.0 g of platinum at an initial pressure of 50 psig in a Paar hydrogenation apparatus. After hydrogenation, the reaction mixture was poured into 400 ml of water and was extracted with three 200-ml portions of ether. The ether extract was washed with saturated bicarbonate until neutral and was dried ($MgSO_4$). The solvent was removed under reduced pressure giving a mixture of isomeric 2,4-dimethylcyclohexanols (by glpc).

The mixture of alcohols was oxidized with chromic acid according to the procedure of Hussey and Baker[15] giving a mixture of isomeric 2,4-dimethylcyclohexanones (87% cis by glpc).

The mixture of 2,4-dimethylcyclohexanones was reduced with iridium tetrachloride in the presence of trimethyl phosphite, hydrochloric acid, and 2-propanol according to the procedure of Eliel, *et al.*[16] The alcohol mixture was separated by preparative glpc giving pure *cis,cis*-2,4-dimethylcyclohexanol: nmr δ 3.76 (m, 1 H, >C*H*OH).

***trans,trans*-3,5-Dimethylcyclohexanol.** *cis*-3,5-Dimethylcyclohexanone was isolated from a mixture of isomeric 3,5-dimethylcyclohexanones (Aldrich Chemical Co.) by fractional distillation on a Nester/Faust annular spinning band column. Reduction of *cis*-3,5-dimethylcyclohexanone with "Henbest's catalyst"[16] produced *trans,trans*-3,5-dimethylcyclohexanol: bp 83.5° (23 mm) [lit.[17] 77–79° (17 mm)]; mp 38.3–39.0° [lit.[18] 40–41°].

***trans*-3,3,5-Trimethylcyclohexanol.** *trans*-3,3,5-Trimethylcyclohexanol was prepared by reduction of 3,3,5-trimethylcyclohexanone with "Henbest's catalyst."[16] The product was purified by preparative glpc: mp 53–54° [lit.[19] 56°].

***cis*-2,4,4-Trimethylcyclohexanol** was obtained from Professor E. L. Eliel.

***cis*-2-Methyl-*cis*-4-*tert*-butylcyclohexanol.** 2-Methyl-4-*tert*-butylphenol was hydrogenated as described above. The mixture of isomeric alcohols was chromatographed on 400 g of alumina using 70:30 benzene–ether as eluent giving >99% pure *cis*-2-methyl-*cis*-4-*tert*-butylcyclohexanol: mp 78–79° [lit.[20] 78–79°].

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[12] Distortions of the cyclohexene ring system by the *tert*-butyl group have been proposed previously; see ref 6 and references contained therein.

[13] F. Johnson and A. Whitehead, *Tetrahedron Lett.*, 3825 (1964).

[14] B. Rickborn and J. H.-H. Chan, *J. Org. Chem.*, **32**, 3576 (1967).

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[16] E. L. Eliel, T. W. Doyle, R. O. Hutchins, and E. C. Gilbert, *Org. Syn.*, **50**, 13 (1970).

[17] A. Skita and W. Faust, *Ber. Deut. Chem., Ges. B*, **72**, 1124 (1939).

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[19] E. L. Eliel and H. Haubenstock, *J. Org. Chem.*, **26**, 3504 (1966).

***trans*-3-Methyl-*trans*-5-*tert*-butylcyclohexanol.** Hydrogenation of 3-methyl-5-*tert*-butylphenol as described above followed by chromatographic separation of the mixture of alcohols on alumina eluting with 70:30 hexane–ether gave >99% pure *trans*-3-methyl-*trans*-5-*tert*-butylhexanol (9% yield): bp 54° (0.1 mm); nmr δ 4.15 (>C*H*OH).

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.46; H, 13.08.

***cis*-2-Ethyl-*cis*-4-*tert*-butylcyclohexanol.** In a 1-l. three-necked flask equipped with a condenser, dropping funnel, and magnetic stirrer was mixed 100 g (0.82 mol) of 2-ethylphenol, 134 g of *tert*-butyl chloride, and 11.0 g of aluminum chloride. The reaction mixture was stirred at 25° for 2.5 hr and then an additional 45 g of *tert*-butyl chloride was added. The reaction mixture was then maintained at 55° for 3.5 hr and a final 27.0 g of *tert*-butyl chloride was added and the heating was continued for another 3.5 hr. The reaction mixture was poured into 600 ml of water and extracted with ether. The ether extract was dried ($MgSO_4$) and the solvent was removed under reduced pressure giving 70.0 g (48%) of 2-ethyl-4-*tert*-butylphenol: bp 145° (127 mm).

The 2-ethyl-4-*tert*-butylphenol was hydrogenated as described above. The resulting mixture of alcohols was chromatographed on 500 g of alumina eluting with 70:30 hexane–ether giving *cis*-2-ethyl-*cis*-4-*tert*-butylcyclohexanol: bp 78–80° (1.1 mm); nmr δ 3.89 (>C*H*OH).

Anal. Calcd for $C_{12}H_{24}O$: C, 78.20; H, 13.12. Found: C, 78.34; H, 13.01.

***trans*-3-Ethyl-*trans*-5-*tert*-butylcyclohexanol.** *trans*-3-Ethyl-*trans*-5-*tert*-butylcyclohexanol was prepared by the hydroxymercuration–demercuration of *cis*-3-ethyl-5-*tert*-butylcyclohexene (as described under the general procedure for the hydroxymercuration–reductive demercuration of olefins) followed by chromatographic separation on alumina eluting with hexane–ether mixtures: mp 47.5–48.5°; nmr δ 4.24 (>C*H*OH).

Anal. Calcd for $C_{12}H_{24}O$: C, 78.20; H, 13.12. Found: C, 78.13; H, 13.00.

***cis*-2-Isopropyl-*cis*-4-*tert*-butylcyclohexanol.** 2-Isopropyl-4-*tert*-butylphenol was prepared by the Friedel–Crafts alkylation of 2-isopropylphenol with *tert*-butyl chloride as described above for the preparation of 2-ethyl-4-*tert*-butylphenol.

The crude 2-ethyl-4-*tert*-butylphenol was catalytically hydrogenated as described above to give a mixture of isomeric alcohols rich in the all-cis isomer. The mixture of isomeric alcohols (12 g) was separated by column chromatography on 450 g of alumina eluting with 90:10 benzene–ether to give pure *cis*-2-isopropyl-4-*tert*-butylcyclohexanol: bp 68° (0.15 mm); mp 41–42°; nmr δ 4.05 (>C*H*OH).

Anal. Calcd for $C_{13}H_{16}O$: C, 78.72; H, 13.21. Found: C, 78.57; H, 13.06.

***trans*-3-Isopropyl-*trans*-5-*tert*-butylcyclohexanol.** *trans*-3-Isopropyl-*trans*-5-*tert*-butylcyclohexanol was prepared by the hydroxymercuration–reductive demercuration procedure (outlined in the general procedure for the hydroxymercuration–reductive mercuration of olefins) followed by separation of the axial alcohol mixture (1.2 g) by chromatography on 40 g of alumina eluting with hexane and hexane–ether mixtures to give pure alcohol: mp 47.5–48.5°; nmr δ 4.24 (>C*H*OH).

Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.52; H, 13.12.

***cis*,*cis*-2,4-Di-*tert*-butylcyclohexanol.** *cis*,*cis*-2,4-Di-*tert*-butylcyclohexanol was prepared by the catalytic hydrogenation of 2,4-di-*tert*-butylphenol, as described above, followed by column chromatographic separation of the resulting isomeric mixture of alcohols (8.0 g) on 350 g of alumina eluting with 95:5 benzene–ethyl acetate to give the pure cis,cis alcohol: bp 85–86° (1.2 mm); mp 41–42°; nmr δ 4.17 (>C*H*OH).

Anal. Calcd for $C_{14}H_{28}O$: C, 79.18; H, 13.29. Found: C, 79.48; H, 13.21.

***trans*,*trans*-2,4-Di-*tert*-butylcyclohexanol.** A mixture of the isomeric 2,4-di-*tert*-butylcyclohexanols, prepared immediately above, was oxidized with chromic acid[13] to a mixture of 2,4-di-*tert*-butylcyclohexanones.

A solution of 6.8 g (0.032 mol) of a mixture of the *cis*- and *trans*-2,4-di-*tert*-butylcyclohexanones (cis rich) in 50 ml of ether was added to a slurry of 1.0 g (0.03 mol) of lithium aluminum hydride in 50 ml of ether. After addition of the ketone, the reaction mixture was refluxed for 1 hr. The excess hydride was decomposed by the cautious addition of water. The hydrolyzed mixture was acidified with 20% hydrochloric acid, and was extracted with three 20-ml portions of ether. The ether extract was washed with saturated bicarbonate and dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was recrystallized from benzene–hexane mixtures and was sublimed at 60° (0.1 mm) to give pure alcohol: mp 109–110°; nmr δ 3.42 (>C*H*OH).

Anal. Calcd for $C_{14}H_{28}O$: C, 79.18; H, 13.29. Found: C, 78.98; H, 13.35.

***trans*,*trans*-3,5-Di-*tert*-butylcyclohexanol.** 3,5-Di-*tert*-butylphenol was catalytically hydrogenated as described above to give a mixture of isomeric 2,5-di-*tert*-butylcyclohexanols. The alcohol mixture was oxidized directly with chromic acid[15] and the resulting mixture of ketones was reduced with Henbest's catalyst.[16] The resulting alcohol mixture (5.0 g) was separated by column chromatography on 200 g of alumina eluting with 95:5 benzene–ethyl acetate giving pure trans,trans alcohol: mp 100.5–101.8° [lit.[21] 100.8–101.7°]; nmr δ 4.25 (>C*H*OH).

***cis*,*cis*-3,5-Di-*tert*-butylcyclohexanol.** *cis*,*cis*-3,5-Di-*tert*-butylcyclohexanol was prepared by the "mixed hydride" equilibration of the alcohol mixture derived from the hydrogenation of 3,5-di-*tert*-butylphenol (immediately above) as described by Eliel and Biros.[18] The equilibrated mixture (9.0 g) was chromatographed on 550 g of alumina eluting with a 6:3:1 ether–benzene–ethyl acetate mixture giving pure cis,cis alcohol: mp 114.5–115.5° [lit.[21] 115.9–116.5°].

Hydroxymercuration of the Substituted Cyclohexenes. In a 20-ml flask equipped with a magnetic stirrer was placed 2.0 mmol of mercuric acetate, 2.0 ml of water, and 2.0 ml of tetrahydrofuran. The olefin (2.0 mmol) was added and the reaction mixture was stirred at 25 ± 1°. Aliquots were periodically removed and reduced by the addition of 0.5 *M* sodium borohydride dissolved in 3.0 *M* aqueous sodium hydroxide. The mercury was allowed to settle and the aqueous phase was saturated with sodium chloride. The aqueous layer was then extracted with three 2-ml portions of ether. The combined ether extracts were analyzed directly by glpc on a 46-ft 5% Carbowax 20 M on Chromosorb G (AW-DCMS) column at temperatures ranging from 150 to 190°. The products were identified by comparison of retention times of authentic samples. The peak area ratios were converted to weight ratios by the use of response ratios. The results are given in the text and Table I, and are averages of at least two, and generally more, independent runs. The correspondence between individual runs was approximately 1%.

The rate of reaction of the *cis*-3-alkyl-5-*tert*-butylcyclohexenes decreased quite markedly in the order methyl, ethyl, isopropyl, and *tert*-butyl, the last undergoing very slow oxymercuration. As a result of the decreasing rate of hydroxymercuration, the formation of thermodynamically controlled products became noticeable at an earlier stage of reaction than with 4-*tert*-butylcyclohexene.[7] The data reported in Table I are for reactions in which none of the thermodynamically controlled products (equatorial alcohols) were evident by glpc. In the case of the hydroxymercuration of *cis*-3,5-di-*tert*-butylcyclohexene the incursion of thermodynamically controlled products occurred at ~5% reaction.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work (PRF-1225-A1,3), and to the Alfred P. Sloan Foundation for partial support of this work.

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