Axial:Equatorial Rate Ratios. 1. Eliminations Leading to the Exocyclic Methylene Group

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Phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfoxide (**4**) thermolyzes to 1-*t*-butyl-4-methylenecyclohexane (**5**) at 116 and 130° about five to six times faster than its *trans* (equatorial) epimer **6**. *cis*-4-*t*-Butylcyclohexanemethyl bromide (**7**) undergoes elimination with potassium *t*-butoxide in *t*-butyl alcohol at 100° about nine times faster than its *trans* (equatorial) epimer **8**. The rate difference found for the sulfoxides **4** and **6** is the first clear demonstration of steric acceleration (without any contribution from any reagent repulsion effect) in the formation of an exocyclic carbon–carbon double bond in a simple anchored cyclohexane system. The faster elimination from **7** (*vs.* **8**) is ascribed primarily to steric acceleration; the experiment neither requires nor excludes the influence of non-bonding repulsions between the substrate and the attacking base.

Le phényl *t*-butyl-4 *cis* cyclohexaneméthyl sulfoxyde (**4**) se transforme par thermolyse à 116 et 130° en *t*-butyl-1 méthylène-4 cyclohexane (**5**); la vitesse est de cinq à six fois plus grande que pour l'épimère (équatorial) *trans* **6**. Le *t*-butyl-4 bromométhyl-1 cyclohexane (**7**) subit une réaction d'élimination sous l'action du *t*-butoxyde de potassium dans l'alcool *t*-butylique à 100° et la vitesse est de neuf fois plus grande que pour l'épimère (équatorial) *trans* **8**. La différence de vitesse trouvée pour les sulfoxydes **4** et **6** constitue la première preuve d'une accélération stérique (sans aucune contribution d'effets de répulsion du réactif) dans la formation d'une double liaison carbone–carbone exocyclique appartenant à un système cyclohexanique rigide. L'élimination plus rapide dans **7** (*vs.* 8) est due principalement à une accélération stérique; les résultats obtenus n'impliquent et n'excluent pas l'influence des répulsions de non-liaison entre le substrat et la base qui vient d'attaquer.

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Introduction

Since the appearance of Barton's pioneering paper two decades ago (1), conformational analysis has become part of the very fabric of organic chemistry, being used routinely to explain or predict both the products and relative rates of reactions. Rationalization of relative rates in conformational terms requires some kind of description of the geometry of transition states, and it seemed to us that if we only knew enough about how conformational factors affect reaction rates, we could apply this knowledge to learn about transition state geometry, *i.e.* as a tool in the general problem of elucidating reaction mechanisms.

We have begun our attempts to apply conformational phenomena to mechanistic study using reactions of substituted cyclohexyl compounds because these appeared to be the best understood of any in conformational terms. In this, the first paper of a projected series, we describe our experiments on reactions of the type **1** → **2** ← **3**, as in Scheme 1.[1] Prior to this study, what was known about the system **1** → **2** ← **3** derived from study of the chromic acid oxidation of cyclohexanols (3–8). The work described in this account was done primarily to see if the analysis that had evolved from the cyclohexanol oxidations was general, *i.e.* could be extended to include reactions in which the central atom of A, A^+, and A′ was something other than oxygen. We also sought

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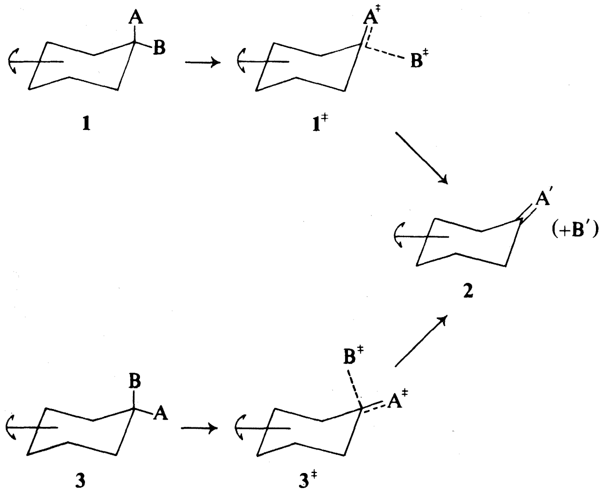
[1] We use the symbol (i) below to indicate a rigid or anchored (2) cyclohexane ring. This symbol makes it easy to depict reaction schemes involving anchored six-membered rings without further specifying the structure, *i.e.* whether it is part of a simple *trans*-decalin, a more complex fused ring (*e.g.* steroid), or 4-*t*-butylcyclohexyl system. At the same time the symbol (i) diminishes the likelihood of misunderstanding by clearly distinguishing between a simple cyclohexyl system, which is normally readily converted to the other chair conformation, from an anchored cyclohexyl system, which is not.

(i)

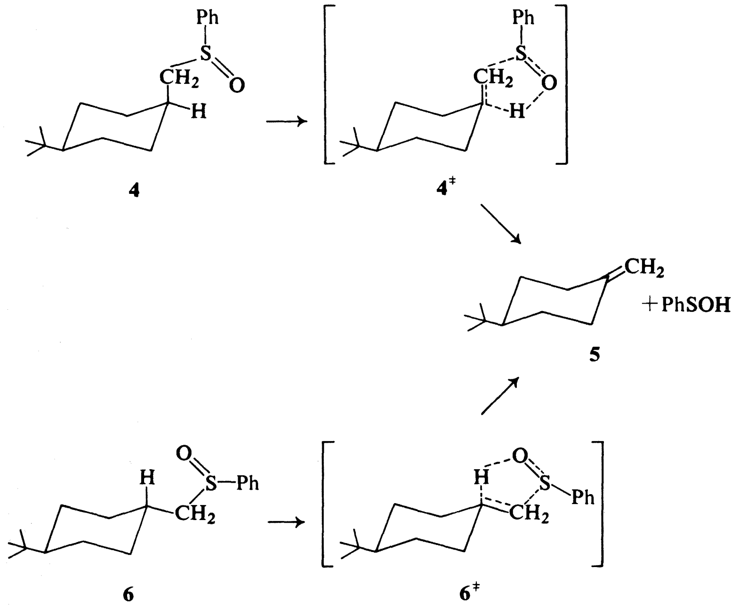


SCHEME 1

to obtain clear demonstration of the "steric acceleration effect" in a simple axial cyclohexyl compound in which the only other axial functions are hydrogens, and in addition to determine the significance, if any, of the "reagent repulsion effect" (see below). The second, and accompanying paper demonstrates the application of this "method of axial:equatorial rate ratios" to a reaction in which we have been interested, for entirely independent reasons, for some time, namely the formation of sulfenes by dehydrohalogenation of sulfonyl chlorides.

As is mentioned above, the oxidation of cyclohexanols with chromic acid has been studied extensively (3–8). It was found that axial alcohols react faster than their equatorial epimers, and further, that, except for an extremely hindered hydroxyl group (8), the greater the steric compression on the hydroxyl group the faster the reaction (4). This was explained (4) as deriving from a *steric acceleration effect*, which may be described in terms of the structures in Scheme 1. When A = OH and B = H, **1** has higher energy than **3** (*i.e.* $G(\mathbf{1}) > G(\mathbf{3})$), because of the higher total non-bonding interaction energy associated with the axial disposition of the hydroxyl function compared with the equatorial. On going from the starting material to the transition state, the non-bonding interaction energy difference, $G(\mathbf{1}^{\ddagger}) - G(\mathbf{3}^{\ddagger})$, is reduced as the geometries of $\mathbf{1}^{\ddagger}$ and $\mathbf{3}^{\ddagger}$ approach that of the product **2**; *i.e.* $G(\mathbf{1}^{\ddagger}) - G(\mathbf{3}^{\ddagger}) < G(\mathbf{1}) - G(\mathbf{3})$. Hence $G(\mathbf{1}^{\ddagger}) - G(\mathbf{1}) < G(\mathbf{3}^{\ddagger}) - G(\mathbf{3})$, or, since $G(\mathbf{1}^{\ddagger}) - G(\mathbf{1})$ is simply $\Delta G_1^{\ddagger}$, the free energy of activation for **1**, and $G(\mathbf{3}^{\ddagger}) - G(\mathbf{3})$ is $\Delta G_3^{\ddagger}$, the free energy of activation for **3**, this is more simply stated: $\Delta G_1^{\ddagger} < \Delta G_3^{\ddagger}$, *i.e.* the axial isomer **1** reacts faster than its equatorial epimer **3**.

Barton (1) had previously pointed out that "if the rate determining step is attack upon the carbon–hydrogen bond rather than upon the carbon–oxygen bond" then reaction of axial alcohols would be subject to smaller steric hindrance than that of the equatorial epimers. In terms of Scheme 1 (A = OH, B = H, and $B^{\ddagger}$ = a hydrogen partially bonded to the hydrogen-abstracting reagent), this would mean that in the process $\mathbf{3} \rightarrow \mathbf{3}^{\ddagger}$, the total non-bonding energy increases more than it does in process $\mathbf{1} \rightarrow \mathbf{1}^{\ddagger}$. This basic notion has been applied in numerous contexts for some time; for the purposes of specific reference in this paper we shall call this the *reagent repulsion effect*. As data on the cyclohexanol oxidation became available it grew apparent that for that reaction at least, the steric acceleration effect was definitely the more important, and perhaps the only significant, steric effect. In general, however, until the magnitude of the putative reagent repulsion effect in all reactions of the type $\mathbf{1} \rightarrow \mathbf{2} \leftarrow \mathbf{3}$ can be estimated, it would appear advisable to keep it in mind as a possibility which requires consideration. Alternatively, of course, one could design a system in which reagent repulsion is clearly impossible or



SCHEME 2

obviously of no consequence. This is, in fact, the approach adopted in the first of the reactions discussed in this paper.

Evidence available when this work was begun (9–12), and added to subsequently (13–15), strongly indicates that the thermolysis of simple alkyl (or aryl alkyl) sulfoxides with at least one β-hydrogen atom leads to the olefin and the sulfenic acid via a cyclic concerted process in which the sulfoxide oxygen acts as the proton-abstracting agent. Reactions **4** → **5** ← **6** in Scheme 2 illustrate the specific example of the sulfoxide thermolysis corresponding to the general system in Scheme 1. The transition states for the *cis*-sulfoxide **4** and the *trans*-sulfoxide **6** are depicted by $\mathbf{4}^{\ddagger}$ and $\mathbf{6}^{\ddagger}$, respectively. It is evident that the contribution of any reagent repulsion effect in this system would be inconsequential, whereas the steric acceleration effect would be predicted to show up undiminished. On the basis of the foregoing analysis it would be expected that relative rates of the thermolysis of **4** and **6** would be a direct measure of the steric acceleration in this system, and hence could give some notion of the significance of this effect in the general system **1** → **2** ← **3** in which the central atom of A and A′ is carbon.

A second system of the general type **1** → **2** ← **3** was also studied briefly, namely the dehydrohalogenation of the axial and equatorial cyclohexanemethyl bromides **7** and **8** to 1-*t*-butyl-4-methylenecyclohexane (**5**). It was hoped that in addition to providing another example of the Scheme 1 system in which A is carbon and B is hydrogen, that it might also lead to definite information concerning the reagent repulsion effect.

After our work was well underway another effect relevant to our study of axial:equatorial rate ratios was suggested in order to account for the products of hydride reduction and Grignard addition to carbonyl compounds (16, 17); for the specific example of additions to cyclohexanones this would be an example of the reaction **1** ← **2** → **3**, *i.e.* the *reverse* of the general reaction that we are concerned with in this paper. Felkin and co-workers (16–18) have postulated the existence of torsional strain in the transition state between the partial bond joining the attacking nucleophile to the erstwhile carbonyl carbon and any bonds to the α-carbons that eclipse (or nearly eclipse) this partial bond. This hypothesis, which we shall call the "Felkin postulate", was used to account, among other things, for the well-known predominance of the equatorial alcohol in the hydride reduction of unhindered anchored cyclohexanones, the torsional strain in this instance being between the hydride hydrogen to carbon bond and the two C—H bonds between the α-carbons

TABLE 1. Rates of thermolysis of the phenyl *cis*- and *trans*-4-*t*-butylcyclohexanemethyl sulfoxides (**4** and **6**) in benzene

Compound	Configuration	Temperature (°C)	$k \times 10^6$ (s^{-1})	k_{Ax}/k_{Eq}
cis-**4**	Axial	129.9	32	5.4
trans-**6**	Equatorial	129.9	5.9	
cis-**4**	Axial	116.4	6.4	5.8
trans-**6**	Equatorial	116.4	0.11	

and their axial hydrogens. These authors specifically suggest that the torsional strain is significant even in transition states in which the partial bond is weak; in terms of Scheme 1 this refers to that situation in which $1^{\ddagger}$ is close to **2** on the reaction coordinate.

In the present context the Felkin postulate would suggest that as $1^{\ddagger}$ and $3^{\ddagger}$ become more and more like **2** (as one changes the reaction conditions or the nature of A or B), the energy difference between $1^{\ddagger}$ and $3^{\ddagger}$ will not become negligible because of the differences in torsional strain. If this be the case then the axial:equatorial rate ratio will not reduce to a simple reflection of the difference in energy between the two starting materials ($G(\mathbf{1}) - G(\mathbf{3})$).

The work described in this paper neither alters the status of the Felkin postulate nor makes specific use of it. The topic is mentioned as a possible effect which could influence axial:equatorial rate ratios in general and also as an illustration of the complexities and uncertainties that may still surround even semi-quantitative theoretical interpretation of axial:equatorial rate ratios. We wish to emphasize that application of the method of axial:equatorial rate ratios at present is an essentially empirical procedure in which the validity of the argument is directly related to the similarity between the unknown and model systems. In order to make non-trivial application of the method, the unknown and model reactions must be chemically different but sterically analogous. Obviously, enough must be known of the important factors governing axial:equatorial rate ratios to be sure that unknown and model reactions are really sterically analogous and that the unknown system will not be controlled by a hitherto unknown effect. The primary aim of our study (which is described in part in this paper) was to assemble an array of carefully chosen model systems for comparison with reactions of unknown course. It was hoped that we might also either uncover any further influences of importance in anchored cyclohexyl systems, or else reduce the likelihood of their existence to the point that useful mechanistic conclusions could be drawn by applying the method of axial:equatorial rate ratios.

Results and Discussion

Thermolysis of cis and trans Phenyl 4-t-Butylcyclohexanemethyl Sulfoxides (4 and 6)

The axial and equatorial sulfoxides **4** and **6** were obtained in a straightforward manner from the corresponding 4-*t*-butylcyclohexylcarbinols, via the methanesulfonates and the phenyl sulfides (see Experimental). Model experiments with phenyl cyclohexanemethyl sulfoxide showed that thermolysis in benzene at 130° gave, in addition to methylenecyclohexane, a second material (perhaps 1-methylcyclohexene) running slightly more slowly on v.p.c.; formation of this second material was completely suppressed by addition of calcium carbonate to the reaction. The rates of the thermolyses were followed by v.p.c. determination of the 1-*t*-butyl-4-methylenecyclohexane (**5**). The reactions were found to be cleanly first order to >60% reaction; variation in the amount of calcium carbonate had no effect on the rate.

As may be seen in Table 1, the axial sulfoxide **4** reacts five to six times faster than its equatorial epimer **6** in benzene solution in the temperature range 116–130°. By way of comparison it should be noted that Eliel and co-workers (7) found that the oxidation of *cis*-4-*t*-butylcyclohexanol with chromic acid in 75% acetic acid at 25° proceeds 3.23 times faster than the *trans* (equatorial) epimer. The increase in the ratio k_{Ax}/k_{Eq} on going from 129.9 to 116.4° with the sulfoxides suggests that the ratio at 25° might well be distinctly greater than 6; the data, however, are probably not accurate enough to justify extrapolation to lower temperatures (or estimation of enthalpies and entropies of activation).

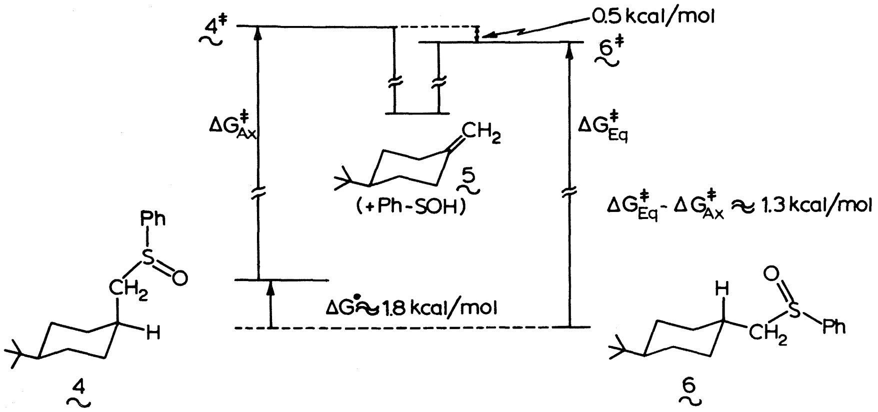


FIG. 1. Energy diagram for the thermolyses of the *cis*- and *trans*-phenyl 4-*t*-butylcyclohexanemethyl sulfoxides (**4** and **6**) at 130°.

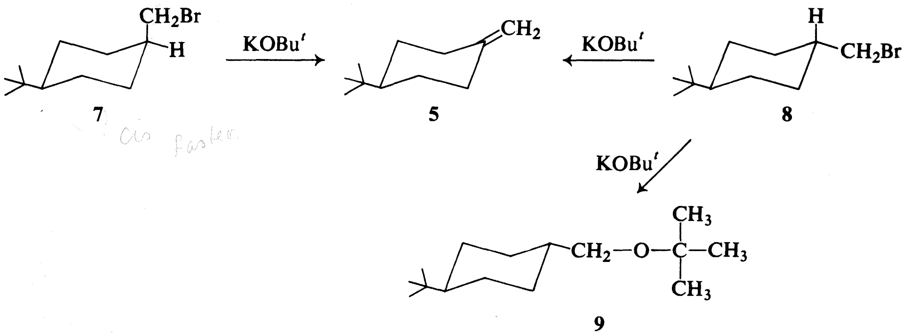
The approximate relative free energies in the thermolyses of the sulfoxides **4** and **6** are summarized in Fig. 1. The $\Delta G°$ value (*i.e.* $G_{\mathrm{Ax}} - G_{\mathrm{Eq}}$) for the —$CH_2SO$—Ph group is assumed to be about 1.8 kcal/mol, *i.e.* comparable to that found with other —CH_2X groups, *e.g.* —CH_2CH_3, 1.75 kcal/mol (19) and CH_2OCH_3, 1.80 kcal/mol (20); it is also further assumed that the value is not much different at 130°. At that temperature the rate ratio, $k_{\mathrm{Ax}}/k_{\mathrm{Eq}}$, is 5.9, corresponding to a difference in free energy of activation ($\Delta G^{\ddagger}_{\mathrm{Eq}} - \Delta G^{\ddagger}_{\mathrm{Ax}}$) of 1.3 kcal/mol, indicating a roughly 0.5 kcal/mol difference in energy between the two transition states $\mathbf{4}^{\ddagger}$ and $\mathbf{6}^{\ddagger}$.

For any reaction in which the rate difference between two epimers derives exclusively from steric acceleration as defined here, it is evident from Fig. 1 that the rate difference cannot be greater than ΔG^0, the difference in the free energies of the starting materials; *i.e.* as the two transition states approach the same energy, $\Delta G^{\ddagger}_{\mathrm{Eq}} - \Delta G^{\ddagger}_{\mathrm{Ax}}$ tends toward $\Delta G°$, or, taking the Felkin postulate into account, $\Delta G°$ less the energy of the torsional strain difference. With the sulfoxide thermolysis the maximum possible difference in $\Delta G^{\ddagger}$ would be ~1.8 kcal/mol, whereas the difference that is actually observed is 1.3 kcal/mol or about 70% of this value. For the chromic acid oxidation of cyclohexanols the rate ratio of 3.23 at 25° quoted earlier corresponds to a diffence in $\Delta G^{\ddagger}$ of about 0.7 kcal/mol or about 80% of 0.87 kcal/mol, the $\Delta G°$ value for the hydroxyl groups in hydroxylic media (19). If the extent of the reaction in the transition state in the thermolysis and oxidation reactions should happen to be roughly comparable, then the difference in rate between the axial and equatorial alcohols in chromic acid oxidation would seem almost entirely ascribable to steric acceleration, with little or no room for contribution by reagent repulsion. Alternatively the difference between $\Delta\Delta G^{\ddagger}$ and $\Delta G°$ could be ascribed entirely to Felkin's torsional strain in the transition state $\mathbf{1}^{\ddagger}$; this would still leave very little leeway for any effect of reagent repulsion.

E2 Reaction of cis- and trans-4-t-Butylcyclohexanemethyl Bromides (7 and 8)

With the aim of obtaining further data on $k_{\mathrm{Ax}}/k_{\mathrm{Eq}}$ for exocyclic eliminations, we briefly investigated the reaction of the *cis*- and *trans*-4-*t*-butylcyclohexanemethyl bromides (**7** and **8**) with strong base. These compounds were readily prepared from the cyclohexylcarbinols via the *p*-nitrobenzenesulfonate esters (see Experimental).

Each bromide was found to react with potassium *t*-butoxide in *t*-butyl alcohol at 100°. As shown in Scheme 3 the axial bromide (**7**) gave 1-*t*-butyl-4-methylenecyclohexane 5 (**6**) (~80% yield) with no sign of any of the *t*-butyl ether. The equatorial isomer (**8**) however, gave a mixture estimated to contain about 30% of **6** and about 70% of *t*-butyl 4-*t*-butylcyclohexanemethyl ether (**9**) (total yield of this mixture also 80%), the product of a presumed S_N2 displacement at the equatorial primary carbon. As will be described in a subsequent paper in this series, we have observed that the formation of **8** from the *p*-nitrobenzenesulfonate takes place about 20 times faster than



cis faster

SCHEME 3

that of the axial isomer **7** under the conditions studied. For the S_N2 reaction of **7** and **8** with potassium *t*-butoxide we estimate $k_{Ax}/k_{Eq} < 0.3$; only an upper limit was obtainable because of the absence of any detectable amount of the ether from **7**.

The rate of the reaction of the bromides **7** and **8** with a large excess of potassium *t*-butoxide was obtained by following the rate of release of bromide ion. With **7** this gives the rate of elimination directly, but with **8** this yields the sum of the rates of substitution and elimination. At 100° with a base concentration of 0.76 *M* in *t*-butyl alcohol the rate of bromide ion release from the axial bromide **7** corresponded to a second order rate constant of $9.4 \times 10^{-4}\,l\,mol^{-1}\,s^{-1}$. With the equatorial bromide (**8**) the corresponding rate constant was $3.5 \times 10^{-4}\,l\,mol^{-1}\,s^{-1}$, which, from the product ratio given above, corresponds to a second order rate constant for the *elimination* of $1.1 \times 10^{-4}\,l\,mol^{-1}\,s^{-1}$. To show that the reaction rate depended on base concentration, another pair of determinations was carried out with the solution 0.41 *M* in potassium *t*-butoxide; this led to rate constants for the elimination of 9.0×10^{-4} and $1.0 \times 10^{-4}\,l\,mol^{-1}\,s^{-1}$ for **7** and **8** respectively.

Approximate though these measurements are, they clearly show that the axial bromide **7** undergoes elimination (evidently bimolecular) distinctly more rapidly than its equatorial epimer **8**, by about nine times, in fact. This value corresponds to a difference in $\Delta G^{\ddagger}$ of about 1.6 kcal/mol, which is close to, but still less than, the maximum difference derivable exclusively from steric acceleration, which may be estimated as detailed above to be about 1.8 kcal/mol. It had been hoped that the considerable bulk of the *t*-butoxide ion might lead to a difference in $\Delta G^{\ddagger}$ of more than 1.8 kcal/mol, thereby requiring the postulation of another effect, *viz.* reagent repulsion, in addition to steric acceleration. In the absence of further data it is not unreasonable to ascribe the faster elimination of the axial bromide (**7**) primarily to steric acceleration; reagent repulsion is neither required nor entirely excluded.

Experimental

Melting points, which were determined on a Kofler hot stage, and boiling points are uncorrected. Unless otherwise stated, i.r. and n.m.r. spectra were determined in carbon tetrachloride solution (Fisher Spectranalyzed grade), and were determined on a Beckman IR-10 instrument and a Varian A-60 spectrometer, respectively; the chemical shifts are recorded in p.p.m. downfield from internal tetramethylsilane. The u.v. spectra were determined on a Jasco model O.R.D./U.V.5 spectropolarimeter. The t.l.c. was carried out using Camag silica gel DF 5. The refractive indices were determined with a thermostatically controlled Bausch and Lomb refractometer. Organic extracts were dried with anhydrous magnesium sulfate. The silica gel used for column chromatography was B.D.H. (for Chromatographic Adsorption). Dry ether refers to ether (Mallinckrodt anhydrous) freshly distilled from lithium aluminum hydride (Metal Hydrides). Petroleum ether refers to the fraction of b.p. 30–60°. The v.p.c. was carried out on F and M model 700 apparatus; *I* refers to injector temperature, *O* to oven temperature, and *D* to detector temperature; helium (40 ml/s) was used as the carrier gas. The degassing and sealing of Carius tubes was carried out according to the following procedure. Then tube was placed in liquid nitrogen until the sample was frozen, and then evacuated with a vacuum pump (10^{-2}–10^{-3} mm). The direction connection to the pump was closed and the sample removed from the liquid nitrogen and allowed to thaw and let stand for about 10 min with occasional gentle shaking. The tube was then put back in the liquid nitrogen, pumped, warmed, shaken as before, and then cooled and evacuated for a third time, after which the tube was sealed off at the torch.

cis-4-t-Butylcyclohexanemethyl Methanesulfonate

cis-4-*t*-Butylcyclohexylcarbinol (2.3 g) prepared as described by Buchanan *et al.* (21), and methanesulfonyl chloride (1.3 ml, Eastman, redistilled) were dissolved in methylene chloride (15 ml, Fisher Spectranalyzed grade) and cooled in an ice bath. To this cooled solution, triethylamine (3 ml, Fisher Reagent grade, redistilled) in methylene chloride (5 ml) was added slowly. The reaction mixture was left standing at room temperature for 10 min, then poured into water, and extracted twice with methylene chloride. The combined methylene chloride layers were washed successively with water, sulfuric acid (10%) and water, and dried. Evaporation of the methylene chloride gave a white solid (2.1 g). Crystallization from methylene chloride – pentane gave *cis*-4-*t*-butylcyclohexanemethyl methanesulfonate as fine plates, m.p. 45.5–46°. The i.r. bands were found at ν_{max} 1370 (s), 1350 (s), 1250 (vw), 1180 (s), 990 (sh), 970 (sh), 950 (s), 940 (sh) cm^{-1}. The n.m.r. spectrum had bands at 0.84 (s, —C(CH_3)$_3$), 2.90 (s, —OSO$_2$CH_3), and 4.12 p.p.m. (d, —CH_2OSO$_2$CH$_3$, J 7.5 Hz).

Anal. Calcd. for $C_{12}H_{24}O_3S$: C, 58.01; H, 9.74; S, 12.89. Found: C, 57.82; H, 9.93; S, 13.05.

trans-4-Butylcyclohexanemethyl Methanesulfonate

This was prepared from *trans*-4-*t*-butylcyclohexylcarbinol (21) by the same procedure as for *cis*-4-*t*-butylcyclohexanemethyl methanesulfonate. Crystallization from methylene chloride – pentane gave *trans*-4-*t*-butylcyclohexanemethyl methanesulfonate as large plates, m.p. 71.5–72°. The i.r. bands were found at ν_{max} 1370 (s), 1350 (s), 1240 (vw), 1180 (s), 995 (sh), 980 (sh), 950 (s), 910 (vw) cm^{-1}. The n.m.r. spectrum had bands at 0.84 (s, —C(CH_3)$_3$), 2.85 (s, —OSO$_2$CH_3), and 3.90 p.p.m. (d, —CH_2OSO$_2$CH$_3$, J 5.5 Hz).

Anal. Calcd. for $C_{12}H_{24}O_3S$: C, 58.01; H, 9.74; S, 12.89. Found: C, 58.20; H, 9.88; S, 12.98.

Cyclohexanemethyl Methanesulfonate

This was prepared from cyclohexylcarbinol (Aldrich) by the same procedure as for *cis*-4-*t*-butylcyclohexanemethyl methanesulfonate. Crystallization from methylene chloride – pentane gave cyclohexanemethyl methanesulfonate as needles, m.p. 45–46.5°. The i.r. bands were found at ν_{max} 1350 (vs), 1180 (s), 980 (s), 945 (s), 900 (m) cm^{-1}. The n.m.r. spectrum had bands at 2.96 (s, —OSO$_2$CH_3) and 3.92 p.p.m. (d, —CH_2OSO$_2$CH$_3$, J 6 Hz).

Anal. Calcd. for $C_8H_{16}O_3S$: C, 49.97; H, 8.39; S, 16.67. Found: C, 50.14; H, 8.32; S, 16.56.

Phenyl cis-4-t-Butylcyclohexanemethyl Sulfide

cis-4-*t*-Butylcyclohexanemethyl methanesulfonate (1.3 g) was dissolved in dioxane (5 ml, Fisher Reagent grade, redistilled) and added to a solution of sodium thiophenoxide prepared by mixing sodium (0.5 g), ethyl alcohol (15 ml, 95%), thiophenol (2.5 g, Fisher Reagent grade) in dioxan (50 ml). This mixture was refluxed for 12 h under a nitrogen atmosphere and then poured into a mixture of ether and 5% aqueous sodium hydroxide. The ethereal layer was washed with 10% sulfuric acid (until the washings were acidic), then with water, and dried. Evaporation of the ether gave a white solid (1.3 g). Crystallization from pentane gave phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfide as spars, m.p. 48–49°. The i.r. bands were found at ν_{max} 3060 (vw), 1585 (w), 1240 (w), 1090 (vw), 1030 (w) cm^{-1}. The n.m.r. spectrum had bands at 0.82 (s, —C(CH_3)$_3$), 2.86 (d, —CH_2SC$_6$H$_5$, J 7.5 Hz), and 7.1 p.p.m. (m, —SC$_6H_5$).

Anal. Calcd. for $C_{17}H_{26}S$: C, 77.79; H, 9.99; S, 12.21. Found: C, 78.01; H, 10.18; S, 12.16.

Phenyl trans-4-t-Butylcyclohexanemethyl Sulfide

This was prepared from *trans*-4-*t*-butylcyclohexanemethyl methanesulfonate by the same procedure as for phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfide. Crystallization from pentane gave phenyl *trans*-4-*t*-butylcyclohexanemethyl sulfide as fine needles, m.p. 40–41°. The i.r. bands were found at ν_{max} 3060 (vw), 1585 (w), 1270 (vw), 1240 (vw), 1090 (vw), 1070 (sh), 1030 (vw) cm^{-1}. The n.m.r. spectrum had bands at 0.82 (s, —C(CH_3)$_3$), 2.70 (d, —CH_2SC$_6$H$_5$, J 6 Hz), and 7.1 p.p.m. (m, —SC$_6H_5$).

Anal. Calcd. for $C_{17}H_{26}S$: C, 77.79; H, 9.99; S, 12.21. Found: C, 78.04; H, 10.10; S, 12.18.

Phenyl Cyclohexanemethyl Sulfide

This was prepared from cyclohexanemethyl methanesulfonate by the same procedure as for phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfide. Crystallization from pentane gave phenyl cyclohexanemethyl sulfide as spars m.p. 19–21°. The i.r. bands were found at ν_{max} 3070 (w), 1585 (m), 1260 (w), 1240 (w), 1090 (w), 1070 (sh), 1030 (w) cm^{-1}. The n.m.r. spectrum had bands at 2.70 (d, —CH_2SC$_6$H$_5$, J 6 Hz) and 7.1 p.p.m. (m, —SC$_6H_5$).

Phenyl cis-4-t-Butylcyclohexanemethyl Sulfoxide (4)

To a solution of phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfide (2.9 g) in glacial acetic acid (200 ml) at 15° was added aqueous hydrogen peroxide (10 ml, 30%). The reaction mixture was left standing at 15° for 1 h and then poured into water. The resulting mixture was extracted twice with ether. The combined ethereal layers were washed with water and then with a saturated solution of sodium bicarbonate and dried. Evaporation of the ether gave an oil (3.0 g). Crystallization from pentane gave phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfoxide (**4**) as fine needles, m.p. 60–61°. The i.r. bands were found at ν_{max} 3060 (vw), 1580 (vw), 1370 (m), 1240 (w), 1090 (m), 1070 (sh), 1050 (vw), 1025 (sh), 1000 (sh) cm^{-1}. The n.m.r. spectrum had bands at 0.84 (s, —C(CH_3)$_3$), 2.70 (m, —CH_2SOC$_6$H$_5$), and 7.5 p.p.m. (m, —SOC$_6H_5$).

Anal. Calcd. for $C_{17}H_{26}OS$: C, 73.31; H, 9.41; S, 11.51. Found: C, 73.61; H, 9.59; S, 11.71.

Phenyl trans-4-t-Butylcyclohexanemethyl Sulfoxide (6)

This was prepared from phenyl *trans*-4-*t*-butylcyclohexanemethyl sulfide by the same procedure as for phenyl *cis*-4-*t*-butylcyclohexanemethyl sulfoxide (**4**). Crystallization from methylene chloride – pentane gave phenyl *trans*-4-*t*-butylcyclohexanemethyl sulfoxide (**6**) as fine plates, m.p. 107–108°. The i.r. bands were found at ν_{max} 3060 (vw), 1580 (vw), 1370 (m), 1260 (w), 1240 (w), 1090 (m), 1070 (sh), 1050 (vs), 1030 (sh), 1000 (sh) cm^{-1}. The n.m.r. had bands at 0.84 (s, —C(CH_3)$_3$), 2.50 (m, —CH_2SOC$_6$H$_5$), and 7.5 p.p.m. (m, —SOC$_6H_5$).

Anal. Calcd. for $C_{17}H_{26}OS$: C, 73.31; H, 9.41; S, 11.51. Found: C, 73.63; H, 9.45; S, 11.50.

Phenyl Cyclohexanemethyl Sulfoxide

This was prepared from phenyl cyclohexanemethyl sulfide by the same procedure as for phenyl *cis*-4-*t*-

butylcyclohexanemethyl sulfoxide (**4**). Crystallization from methylene chloride – pentane gave phenyl cyclohexanemethyl sulfoxide as fine needles, m.p. 56–57°. The i.r. bands were found at ν_{max} 3060 (w), 1580 (vw), 1270 (vw), 1100 (sh), 1080 (m), 1070 (sh), 1050 (s), 1020 (sh), 1000 (sh) cm^{-1}. The n.m.r. spectrum had bands at 2.71 (d, —$CH_2SOC_6H_5$, J 6 Hz) and 7.5 p.p.m. (m, —SOC_6H_5).

Anal. Calcd. for $C_{13}H_{18}OS$: C, 70.20; H, 8.16; S, 14.41. Found: C, 70.38; H, 8.09; S, 14.37.

1-t-Butyl-4-methylenecyclohexane (5)

This was prepared from 4-*t*-butylcyclohexane following the general procedure of Greenwald *et al.* (22). The i.r. bands were found at ν_{max} 3080 (w), 1650 (m), 1370 (m), 1245 (w), 1225 (w), 990 (w), 910 (sh), 900 (s) cm^{-1}. The n.m.r. spectrum had bands at 0.86 (s, —$C(CH_3)_3$) and 4.5 p.p.m. (broad s, $C{=}CH_2$).

Measurement of the Rate of the Reaction of the Pyrolysis of Phenyl cis- and trans-4-t-Butylcyclohexanemethyl Sulfoxides (4 and 6)

The phenyl 4-*t*-butylcyclohexanemethyl sulfoxide (*ca.* 250 mg) and naphthalene (*ca.* 140 mg, B.D.H. laboratory reagent, added as a standard for the v.p.c. assay) were weighed and dissolved in benzene (Fisher Spectranalyzed Grade, freshly distilled from calcium hydride) and the resulting solution made up to 10 ml at 25 °C. Aliquots (1 ml) of this solution with solid calcium carbonate (*ca.* 20 mg) were degassed and sealed under vacuum. These aliquots were then put into an oil bath whose temperature was controlled by a Fisher "Proportional Temperature Control" thermostat to ±0.2°. Timing was started at the time of immersion in the oil bath. After an appropriate time interval the aliquot was removed from the oil bath and placed under rapidly running cold water. The aliquot was then cooled in Dry Ice – acetone and opened. The thawed solution was then poured down a column of silica gel (*ca.* 5 g) and the column washed with 10 ml of benzene – *n*-pentane (1:1). This short column removed any unpyrolysed sulfoxide but did not alter the ratio of 1-*t*-butyl-4-methylenecyclohexane to naphthalene (known mixture ratios being the same before as after the above work-up). The resulting solution was then analyzed by v.p.c. using a 10% silicon rubber GE.SE.33 on Chromosorb WAW.DMSC 80–100 mesh column (6′ × $\frac{1}{4}$″ diameter) v.p.c. *I*, 165°; *O*, 120°; *D*, 178°). The amount of 1-*t*-butyl-4-methylenecyclohexane produced in the reaction was estimated by a comparison of the areas under the peak corresponding to naphthalene. This ratio was compared to ratios of known composition analyzed under the same conditions.

Two samples, one of the *cis*-sulfoxide **4**, the other of the *trans*-epimer **6** were sealed in ampoules as described above (except that the naphthalene was omitted), heated at 130° for 50 h, chromatographed as above, and the solvent evaporated. The n.m.r. spectra of the two materials were identical with that of an authentic specimen of 1-*t*-butyl-4-methylenecyclohexane (**5**) except for the presence of a small amount of an impurity containing hydrogens on an aromatic ring.

cis-4-t-Butylcyclohexanemethyl p-Nitrobenzenesulfonate

cis-4-*t*-Butylcyclohexylcarbinol (3.0 g) was dissolved in pyridine (5 ml, redistilled) and the resulting solution cooled in an ice bath. To this cooled solution *p*-nitrobenzenesulfonyl chloride (4.0 g, Eastman Organic) in dry pyridine (5 ml) was added slowly. The resulting solution was left standing in the ice bath for 20 min. The mixture was then poured into water and extracted twice with methylene chloride. The combined methylene chloride layers were washed with 10% sulfuric acid until the washings were acidic and then washed with water and dried. Evaporation of the methylene chloride gave a yellow solid. Crystallization from methylene chloride – carbon tetrachloride gave *cis*-4-*t*-butylcyclohexanemethyl *p*-nitrobenzenesulfonate as yellow needles, m.p. 108–109°. The i.r. bands were found at ν_{max} 3100 (vw), 1605 (w), 1535 (s), 1405 (sh), 1380 (vs), 1365 (vs), 1350 (vs), 1315 (m), 1240 (vw), 1185 (vs), 1100 (m), 1020 (vw), 975 (m), 950 (s), 930 (sh), 900 (sh), 685 (m), 615 (m) cm^{-1}. The n.m.r. spectrum had bands at 0.78 (s, —$C(CH_3)_3$), 4.20 (d, —CH_2OSO_2—, J 8 Hz), and 8.10 to 8.55 (q, —OSO_2-$C_6H_4NO_2$, J_{AB} 9 Hz, δ_A 8.22, δ_B 8.47).

Anal. Calcd. for $C_{17}H_{25}NO_5S$: C, 57.44; H, 7.09; N, 3.94; S, 9.02. Found: C, 57.47; H, 7.04; N, 3.88; S, 8.91.

trans-4-t-Butylcyclohexanemethyl p-Nitrobenzenesulfonate

This was prepared from *trans*-4-*t*-butylcyclohexylcarbinol by the same procedure as for *cis*-4-*t*-butycyclohexanemethyl *p*-nitrobenzenesulfonate. Crystallization from methylene chloride – carbon tetrachloride gave *trans*-4-*t*-butylcyclohexanemethyl *p*-nitrobenzenesulfonate as fine needles, m.p. 138–139°. The i.r. bands were found at ν_{max} 3100 (vw), 1650 (w), 1535 (s), 1360 (sh), 1350 (s), 1310 (m), 1230 (w), 1185 (vs), 1095 (m), 985 (w), 950 (s), 685 (m), 615 (m) cm^{-1}. The n.m.r. had bands at 0.81 (s, —$C(CH_3)_3$), 3.98 (d, —CH_2OSO_2—, J 6 Hz), and aromatic absorption from 8.0 to 8.53 analyzed as an AB quartet: δ_A 8.15, δ_B 8.45 p.p.m. (J_{AB} 9 Hz).

Anal. Calcd. for $C_{17}H_{25}NO_5S$: C, 57.44; H, 7.09; N, 3.94; S, 9.02. Found: C, 57.35; H, 7.16; N, 3.93; S, 9.08.

cis-4-t-Butylcyclohexanemethyl Bromide (7)

cis-4-*t*-Butylcyclohexanemethyl *p*-nitrobenzenesulfonate (2.0 g) was dissolved in dry acetone (100 ml). Lithium bromide (1.5 g) and calcium carbonate (1.0 g) were added to the solution and the resulting mixture refluxed for 24 h. The reaction mixture was then poured into water and extracted twice with petroleum ether and the extract dried. Evaporation of the petroleum ether gave an oil (1.3 g). The oil was adsorbed onto silica gel (40 g). Elution with petroleum ether afforded the crude bromide as an oil. Distillation (b.p. 58–60°/0.6 mm) gave *cis*-4-*t* butylcyclohexanemethyl bromide as an oil, n_D^{25} 1.5900. The i.r. bands were found at ν_{max} 1300 (w), 1240 (sh), 1230 (m), 1030 (broad, w), 960 (w), 680 (m) cm^{-1}. The n.m.r. spectrum had bands at 0.85 (s, —$C(CH_3)_3$) and 3.41 p.p.m. (d, —CH_2Br, J 8 Hz).

Anal. Calcd. for $C_{11}H_{21}Br$: C, 56.66; H, 9.08; Br, 34.27. Found: C, 56.65; H, 9.16; Br, 34.31.

trans-4-t-Butylcyclohexanemethyl Bromide (8)

This was prepared from *trans*-4-*t*-butylcyclohexanemethyl *p*-nitrobenzenesulfonate by the same procedure as for *cis*-4-*t*-butylcyclohexanemethyl bromide, except that the reaction mixture was refluxed for only 2 h. Column chromatography (silica gel, elution with petroleum ether) followed by distillation (b.p. 58–60°/0.6 mm) gave *trans*-4-*t*-butylcyclohexanemethyl bromide as an oil, n_D^{25} 1.4858. The i.r. bands were found at ν_{max} 1300 (w), 1255 (m), 1235 (m), 1200 (vw), 1150 (vw), 980 (w), 900 (w), 655 (m) cm^{-1}. The n.m.r. spectrum had bands at 0.84 (s, $—C(CH_3)_3$) and 3.29 p.p.m. (d, $—CH_2Br$, *J* 5.5 Hz).

Anal. Calcd. for $C_{11}H_{21}Br$: C, 56.66; H, 9.08; Br, 34.27. Found: C, 56.67; H, 9.31; Br, 34.38.

t-Butyl trans-4-t-Butylcyclohexanemethyl Ether (9)

trans-4-*t*-butylcyclohexanemethyl bromide (215.5 mg) was dissolved in potassium *t*-butoxide – *t*-butyl alcohol (0.412 *M*, 20 ml) and the resulting solution degassed three times and sealed under vacuum (.001 mm). This sealed ampoule was then left standing at 100° for 24 h. The reaction mixture was poured into water and extracted with methylene chloride and then with ether. The methylene chloride and ether layers were neutralized with 2% sulfuric acid, washed with water, combined, and then dried. Evaporation of the solvent gave an oil (152 mg). Separation (t.l.c. cyclohexane–ether (4:1)) gave the crude ether (100 mg) as a solid. Recrystallization from pentane gave *t*-butyl *trans*-4-*t*-butylcyclohexanemethyl ether as fine needles, m.p. 31–32°. The i.r. bands were found at ν_{max} 1230 (w), 1200 (s), 1075 (m), 1020 (w) cm^{-1}. The n.m.r. spectrum had bands at 0.84 (s, $—C(CH_3)_3$), 1.10 (s, $—OC(CH_3)_3$), and 3.30 p.p.m. (d, $—CH_2OC(CH_3)_3$, *J* 5 Hz).

Anal. Calcd. for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.29; H, 13.20.

Measurement of the Rate of the Reaction of cis- and trans-4-t-Butylcyclohexanemethyl Bromide (7 and 8) with Potassium t-Butoxide in t-Butyl Alcohol at 100°

(a) Titration of the Bromide Ion Produced

Potassium *t*-butoxide was prepared by dissolving freshly cut potassium (free of the oxide crust and washed three times in pentane) in *t*-butyl alcohol (freshly distilled from calcium hydride) under a nitrogen atmosphere. The solution was standardized by titration with hydrochloric acid (0.1 *N*, B.D.H., concentrated Volumetric Solution). The *cis*- or *trans*-4-*t*-butylcyclohexanemethyl bromide solution was prepared by weighing the bromide (*ca.* 200 mg) and dissolving it in *t*-butyl alcohol (freshly distilled from calcium hydride) and making the solution up to 50 ml at 30°.

To a solution of the bromide (5 ml) was added the *t*-butoxide solution (5 ml), this mixture was then degassed three times and sealed under vacuum. The sealed solutions were then thoroughly mixed and placed in an oil bath whose temperature was controlled by a Fisher "Proportional Temperature Control" thermostat to 100.0 ± 0.2°. Timing was started at the time of immersion in the oil bath. After an appropriate time interval the aliquot was removed from the oil bath and placed in an ice bath. The sample was then opened and poured into water containing nitric acid (5 ml, 6 *N*) and the bromide ion titrated with silver nitrate. The pseudo first order rate constant was calculated from the slope of a plot of log (100 − % reaction) *vs.* time for six such determinations varying from <20 to >60% reaction; the apparent second order rate constant for bromide ion formation was obtained by dividing the pseudo first order rate constant by the potassium *t*-butoxide concentration. The apparent second order rate constants so obtained for the reaction of the *cis* bromide **7** were 9.4×10^{-4} l mol^{-1} s^{-1} (KOBu^t 0.76 and substrate 1.96×10^{-2} *M*) and 9.0×10^{-2} l mol^{-1} s^{-1} (KOBu^t 0.41 and substrate 1.66×10^{-2} *M*); for the *trans* bromide **8** the apparent second order rate constants for bromide ion release were 3.2×10^{-4} (KOBu^t 0.41 and substrate 1.81×10^{-2} *M*) and 3.5×10^{-4} l mol^{-1} s^{-1} (KOBu^t 0.76 and substrate 1.96×10^{-2} *M*).

(b) Product Analysis of the Reaction of cis- and trans-t-Butylcyclohexanemethyl Bromide with Potassium t-Butoxide

The bromide (*ca.* 250 mg) was dissolved in the *t*-butoxide solution (20 ml, 0.412 *M*), degassed three times, sealed under vacuum, and left at 100° for 24 h. The ampoule was cooled, opened, poured into water, and extracted with methylene chloride and ether. The methylene chloride and ethereal layers were neutralized with 2% sulfuric acid, washed with water, combined, and dried.

cis-4-*t*-Butylcyclohexanemethyl bromide (250 mg) gave an oil (130 mg), the n.m.r. spectrum of which showed a band at 4.45 ($C{=}CH_2$) and no bands in the region 2.5–4.4 p.p.m. ($—CH_2Br$ and $—CH_2OC(CH_3)_3$). *trans*-4-*t*-Butylcyclohexanemethyl bromide (215.5 mg) gave an oil (152 mg), the n.m.r. spectrum of which showed bands at 3.03 (d, $—CH_2OC(CH_3)_3$) and 4.45 ($C{=}CH_2$) in the ratio of 2.24:1 (*i.e.* 69:31%), but no band at 3.38 p.p.m. (CH_2Br). The apparent second order rate constants for the bromide ion formation from the *cis*-bromide (**7**) were therefore taken directly as the rate constants for the bimolecular elimination. The rate constants for the bimolecular elimination for the *trans*-bromide **8** were taken as 31% of the rate constants for the bromide ion release *i.e.* 1.0×10^{-4} and 1.1×10^{-4} l mol^{-1} s^{-1}, respectively.

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