methylene chloride at 0° for 1.0 minute in a separatory funnel. The layers were separated, and the aqueous portion extracted several times with 5-ml. portions of methylene chloride. The combined methylene chloride extracts were washed with water, dried over magnesium sulfate and concentrated. The residual 2-chloro-2,3,3-trimethylbutane was purified by sublimation under reduced pressure. The recovery was 0.60 g.

The following procedures were used to convert the chloride samples to silver chloride for radioactive assay. A portion of the aqueous hydrochloric acid solution containing about 1–2 millimoles of chloride ion was diluted to 5 ml. with water containing 1 ml. of 6 *N* nitric acid. The solution was warmed to about 50° and 10 ml. of 10% silver nitrate solution added rapidly with stirring. The precipitate of silver chloride was collected on a sintered-glass funnel, rinsed several times with acetone and dried in an evacuated desiccator over phosphorus pentoxide. The organic chloride (about 0.1–0.2 g.) was dissolved in 5 ml. of ethanol, warmed to 50–60° and a warm solution of 10 ml. of 10% silver nitrate containing 1 ml. of 6 *N* nitric acid was added with stirring. The precipitated silver chloride was collected and dried as above.

The samples for counting were prepared by weighing out identical amounts of silver chloride on copper dishes previously checked for radioactive contamination. The samples were counted in a methane-filled proportional counter ("Nucleometer," Radiation Counter Laboratories). Trials indicated that the manner of spreading of the samples in the sample dish was not critical provided the samples were spread reasonably evenly. In the experiment described above, the measured activities for 29.0-mg. samples of silver chloride corrected for background with standard deviations were 1309 ± 44 and 15 ± 10 counts per minute for the silver chloride from the original aqueous solution and the organic chloride from the reaction mixture, respectively.

In this experiment, the initial reaction mixture contained 98.5 millimoles of hydrochloric acid and 7.4 millimoles of organic chloride. If complete equilibration had occurred, the activity of the organic chloride would be (98.5/106) × 1310 ± 44 = 1220 ± 41 counts per minute. The extent of exchange was thus (15 ± 10/1220) × 100 or 1.2 ± 0.8%. Further experimental results regarding the exchanges are presented in Table II.

CAMBRIDGE 39, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XIX. *t*-Butylcyclohexyl Derivatives. Quantitative Conformational Analysis

BY S. WINSTEIN AND N. J. HOLNESS[1]

RECEIVED JANUARY 22, 1955

The *cis*- and *trans*-4-*t*-butylcyclohexanols represent a pair of conformationally pure *equatorial* and *axial* cyclohexanols with no α- or β-substituents. The *t*-butyl group serves as a compelling but remote control of conformation. Thus the rates of reaction and other chemical behavior of the cyclohexanols and their derivatives supply information on the differences to be expected simply from the *equatorial* or *axial* disposition of the reactive group on the chair form of the cyclohexane ring. Also, the observed rates are useful as the basis of a quantitative conformational analysis of conformationally less homogeneous cyclohexyl derivatives. At 50°, the *axial*-4-*t*-butylcyclohexanol is oxidized by chromic anhydride in 75% acetic acid more rapidly, its acid phthalate is saponified more slowly in water and its toluenesulfonate solvolyzes more rapidly in acetic acid than the *equatorial*-4-*t*-butylcyclohexyl isomers by factors of 2.55, 9 and 3.24, respectively. The cyclohexyl derivatives display intermediate rates, closer to the *equatorial*-4-*t*-butylcyclohexyl derivatives. The data shed light on the conformational distribution of the cyclohexyl derivatives, and also other substituted cyclohexanols. Rough values of *A*, the free energy of preference for the equatorial position, have been derived for the OH, acid phthalate, OTs, *n*-Bu, *n*-Pr and Et groups. In solvolysis, the *equatorial*-4-*t*-butylcyclohexyl toluenesulfonate yielded 67–76% olefin and nearly completely inverted *axial*-4-*t*-butylcyclohexanol or its ester, in aqueous acetone, acetic acid or formic acid as solvents. The *axial*-4-*t*-butylcyclohexyl toluenesulfonate yielded 83–87% olefin and the rest alcohol, largely inverted *equatorial*-4-*t*-butylcyclohexanol in aqueous acetone, but containing increasing amounts of *axial*-4- and rearranged *axial*-3-*t*-butylcyclohexanols. The *axial*-4- and 3-alcohols are thought to arise from hydrogen-bridged cations, and the bearing of the results on the role, nature and behavior of carbonium ions in addition, solvolysis and rearrangement, is discussed.

In connection with investigations involving participation of neighboring groups in solvolysis of compounds containing cyclohexyl[2,3] or steroidal[4,5] ring systems, it was desirable to have available a pair of conformationally pure *equatorial* and *axial*[6–9] simple cyclohexanols with no α- or β-substituents. The 4-*t*-butylcyclohexanols were anticipated as an ideal pair of such isomers, and the preparation and various reactions of these materials and some of their derivatives are described in the present article along with some comparable observations on the 3-*t*-butylcyclohexanols which it became advisable to make during the course of the work.

The data collected on the *t*-butylcyclohexyl derivatives are helpful in understanding the rates of conformationally less homogeneous materials. In this paper the connection between rate and the distribution of a substance among conformational isomers is discussed. Also, a method of quantitative conformational analysis based on rate measurements is developed and applied.

Conformation and Reactivity.—For a better understanding of the relation of reactivity to structure and configuration we must explicitly recognize that both ground states and transition states may exist in more than one conformation. Such conformational heterogeneity is reduced[8,10] in alicyclic systems, but one must pass over 3-, 4- and 5-rings[10,11] to the cyclohexane ring to avoid angle strain and eclipsing strain as in acyclic materials.

(1) Hercules Powder Co. Fellow, 1953–1954.

(2) S. Winstein, *et al.*, THIS JOURNAL, **74**, 1127 (1952).

(3) R. Heck, unpublished work.

(4) S. Winstein and R. Adams, THIS JOURNAL, **70**, 838 (1948).

(5) N. J. Holness, E. Kosower and A. H. Schlesinger, unpublished work.

(6) O. Hassel, *et al.*, *Acta Chem. Scand.*, **1**, 149, 929 (1947).

(7) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

(8) (a) D. H. R. Barton, *Experientia*, **6**, 316 (1950); (b) *J. Chem. Soc.*, 1027 (1953).

(9) D. H. R. Barton, O. Hassel, K. S. Pitzer and V. Prelog, *Nature*, **172**, 1096 (1953).

(10) V. Prelog, *J. Chem. Soc.*, 420 (1950).

(11) H. C. Brown, R. S. Fletcher and R. B. Johannesen, THIS JOURNAL, **73**, 212 (1951).

In general, without considering possible exceptions, the rates of the rate-determining steps in typical reactions are slower than rates of equilibration among conformational isomers.[12] Also, transition states still resemble the original molecules sufficiently for a transition state conformation to be related to a corresponding ground state conformation. While the term conformation is employed both for rotational isomer in acyclic cases and *equatorial* or *axial* isomer in chair cyclohexane derivatives, we shall employ a chair cyclohexyl derivative for illustration. The free energy diagram in Fig. 1 shows two conformations of the ground state, *e* for *equatorial* and *a* for *axial*, differing in free energy F by an amount A, defined by equation 1. Figure 1 also depicts two corresponding conformations of the transition state, $e^{\pm}$ and $a^{\pm}$, differing in free energy by an amount $A^{\pm}$, defined by equation 2.

As Hammett[13] has pointed out, the relative amounts of reaction through the transition states $e^{\pm}$ and $a^{\pm}$ are independent of A or the relative proportions of the ground state conformations *e* and *a*, and they depend only on the free energy difference $A^{\pm}$

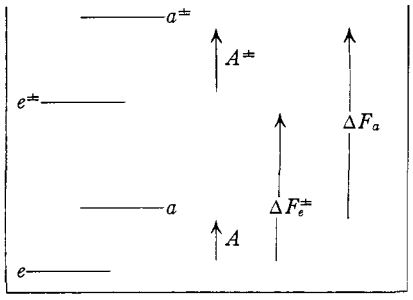
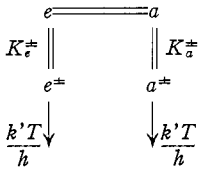


Fig. 1.—Free energy diagram for reaction of two conformations of ground state, *e* and *a*, through two conformations of the transition state, $e^{\pm}$ and $a^{\pm}$.

between the conformationally isomeric transition states $e^{\pm}$ and $a^{\pm}$. However, we must notice that the observed rates are related to the conformational distribution of the ground state. For unimolecular reactions, transition state theory[15] leads to the formulation



On this basis, the rate of formation of products, dx/dt, is given by equation 3, using brackets to indicate concentration of a species. The constants, $K_e^{\pm}$ and $K_a^{\pm}$, are related to the free energies of activation, $\Delta F_e^{\pm}$ and $\Delta F_a^{\pm}$, respectively, indicated in Fig. 1. Division by the total concentration of reacting species, $[e + a]$, converts equation 3 to 4. The left-hand side of equation 4 is simply a first-order rate constant, k, as ordinarily evaluated without regard

$$A \equiv F_a - F_e = 2.303RT \log (N_e/N_a) \quad (1)$$

$$A^{\pm} \equiv F_a^{\pm} - F_e^{\pm} \quad (2)$$

$$\frac{dx}{dt} = \frac{k'TK_e^{\pm}}{h}[e] + \frac{K'TK_a^{\pm}}{h}[a] \quad (3)$$

$$\frac{dx}{dt}\Big/[e + a] = \frac{[e]}{[e + a]}\frac{k'T}{h}K_e^{\pm} + \frac{[a]}{[e + a]}\frac{k'T}{h}K_a^{\pm} \quad (4)$$

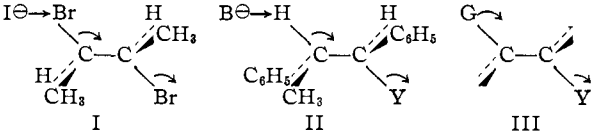
$$k = N_e k_e + N_a k_a \quad (5)$$

to conformational questions; $[e]/[e + a]$ and $[a]/[e + a]$ may be replaced by N_e and N_a, mole fractions of each of the conformations of the ground states; $k'TK_e^{\pm}/h$ and $k'TK_a^{\pm}/h$ may be replaced by k_e and k_a, rate constants that correspond to pure *e* reacting through an *e*-type transition state and pure *a* reacting through an *a*-type transition state. This leads to the convenient equation 5, k being a weighted average of the rate constants characteristic of the conformational isomers *e* and *a*.

Equation 5 applies to a reaction of the substance being used in Fig. 1 if the kinetics are cleanly of one order, k, k_e and k_a all being constants of the same order. If the reaction is of mixed order, for example, first and second order, then it must be dissected in terms of a first-order rate constant, k_1 and a second-order rate constant, k_2. Each of these constants may then be conformationally dissected, at least in principle, by the application of equation 5.

Even if k, k_e and k_a are all of the same order, both k_e and k_a may still be composite and may refer largely to reactions of different mechanism. For example, in solvolysis, k_e may be the sum of k_{Δ}^{e}, relating to anchimerically assisted ionization, and k_s^e, relating to anchimerically unassisted solvolysis.[16]

Considering equation 5, we see that rate, just as other properties such as infrared absorption,[12] dipole moment[12] and optical activity,[17] may be expressed in terms of the characteristics of the pure conformational isomers. In specific cases, the structure of the molecule and the nature of the reaction may make only one of the conformational rate constants, for example k_a, different from zero. Under these conditions, k is $N_a k_a$, rate being determined by the proportion[2,18c] of conformation *a* and the intrinsic rate constant, k_a, associated with this conformation. Examples of this situation are the E2 elimination of bromine from 2,3-dibromobutane[18] by iodide ion (I) or of hydrogen halide from 1,2-diphenylpropyl halide[19] by base (II). In each



case, each diastereomer reacts through a transition

(12) (a) J. C. McCoubrey and A. R. Ubbelohde, *Quart. Revs.*, **5**, 364 (1951); (b) S. Mizushima, "Internal Rotation, Reilly Lectures," **5**, 1 (1951).

(13) Quoted by D. Curtin in an excellent discussion[14] of related matters.

(14) D. Y. Curtin, *Record Chem. Progress*, **15**, 111 (1954).

(15) S. Glasstone, K. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 14.

(16) S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, THIS JOURNAL, **75**, 147 (1953).

(17) W. W. Wood, W. Fickett and J. G. Kirkwood, *J. Chem. Phys.*, **20**, 561 (1952).

(18) (a) R. Dillon, W. G. Young and H. J. Lucas, THIS JOURNAL, **52**, 1953 (1930); (b) S. Winstein, D. Pressman and W. G. Young, *ibid.*, **61**, 1645 (1939); (c) W. G. Young, Eighth Nat. Org. Symposium, St. Louis, Mo., Dec., 1939, p. 92 of Abstracts.

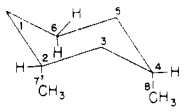
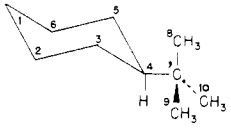
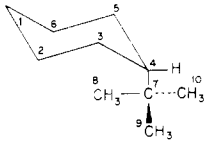
(19) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5851 (1952).

state which corresponds to only one of the three conformational minima of the ground state. Another example is represented by a reaction which is solely the one which is anchimerically assisted by a neighboring group[20] G(III). Considering equation 5 further, we see that one could solve for N_e and N_a, whose sum is unity, if k_e and k_a could be estimated from other sources. In this way, rate measurements could be made the basis of a quantitative method of conformational analysis.

Conformational Preference of the *t*-Butyl Group. —With 4-*t*-butylcyclohexyl derivatives, there is considerable compulsion for the *t*-butyl group to be *equatorial*. Thus the *t*-butyl group serves as a compelling but remote handle, effective in controlling conformational position of a 1-substituent. Any *a priori* estimate of the energy quantity which compels the *t*-butyl group to be *equatorial* on the chair form of the cyclohexane ring is rough, but the quantity is clearly quite large. The estimate is summarized in Table I.

TABLE I

STERIC ENERGIES IN *t*-BUTYLCYCLOHEXANE

Compound	Interactions	Partial sums
	(C_6-C_7); (C_6-C_8)	2α
	(C_2-C_8); (C_4-C_7)	2α
	(C_7-C_8)	2α
IV	Total	6α
	(C_3-C_8); (C_3-C_9)	2α
	(C_5-C_8); (C_5-C_{10})	2α
V	Total	4α
	(C_3-C_8); (C_3-C_9)	2α
	(C_5-C_8); (C_5-C_{10})	2α
	(C_2-C_7); (C_6-C_7)	2α
	(C_2-C_8); (C_6-C_8)	4α
VI	Total	10α

For the *equatorial* position of the *t*-butyl group on a cyclohexane ring (V), there are four interactions of the *gauche* butane variety, using Pitzer's procedure for methylcyclohexane. Using Pitzer's parameter α,[7] 4α is the sum of the repulsive interactions indicated. For the *axial* position of the *t*-butyl group on the cyclohexane ring (VI), the same repulsive interactions are present which were present in the *equatorial* position. In addition, there are the extra repulsions involving the C_2- and C_6-ring methylene groups, especially large because the *axial* group on C_4 is a *t*-butyl group. A problem akin to this occurs in the case of *cis*-1,3-dimethylcyclohexane with two axial methyl groups (IV). Here Pitzer[7] chose 6α, admittedly arbitrarily, for the sum of the repulsive interactions. This amounts to assigning 2α to the $(C_6-C_7) + (C_6-C_8)$ interactions, and then treating the rest of the repulsive interaction as though 2α was assigned to the $(C_2-C_8) + (C_4-C_7)$ interactions and an additional 2α added on for the C_7-C_8 interaction. An analogous treatment for *axial* *t*-butylcyclohexane adds 6α to the 4α already mentioned for a sum of 10α. This crude estimate makes the *axial* position for the *t*-butyl group less stable than the *equatorial* position by 6α or 5.4–5.8 kcal./mole. Thus the *axial* position of the *t*-butyl group in simple *t*-butylcyclohexane is as prohibited as the boat form of cyclohexane, estimated by Pitzer[7] to be 5.6 kcal./mole less stable than the chair.

(20) See ref. 16, footnote 10, for previous comment on the relation of conformation to participation and driving forces.

The energy quantity by which a *t*-butyl group favors the *equatorial* position is sufficiently large to guarantee conformational homogeneity to most 4-*t*-butylcyclohexyl derivatives. For illustration, consider a derivative with the second group one whose preference for the *equatorial* position is measured by 1.6 kcal./mole. Then, for the *trans*-4-*t*-butylcyclohexyl derivative, the *equatorial* position for the second group is favored by 5.6 + 1.6 or 7.2 kcal./mole. In other words, $A = 7.2$ kcal./mole, and N_e is essentially unity. For the *cis*-4-*t*-butylcyclohexyl derivative, the *axial* position for the second group is favored by 5.6 − 1.6 or 4.0 kcal./mole. Here $A = -4.0$ kcal./mole, and N_a is essentially unity. A similar argument can be employed on the transition states for reaction of the two diastereomers as long as the preference for the *equatorial* position which the transition state group displays is not sufficiently higher than 1.6, to begin to compare with the 5.6. Under such conditions, the measured rate constants for the diastereomeric 4-*t*-butylcyclohexyl derivatives would be k_e in one case and k_a in the other. Any observed chemical behavior could be taken to be characteristic of the pure conformation.

The *t*-butyl group is so distant from the reaction zone that polar effects due to the *t*-butyl group tend to be small or negligible. Also, even if there are more subtle additional effects on rate due to the *t*-butyl group, some types of effects will be cancelled out in the ratio of rates of the two diastereomeric materials. Thus the factor between rates of the diastereomeric materials tends to be solely a measure of the intrinsic difference between the *equatorial* and *axial* positions of the reactive group on the cyclohexane ring.

To the extent all effects of the *t*-butyl group are negligible, the observed rate constants are identical to the k_e and k_a applicable in equation 5 for a quantitative conformational analysis of the unsubstituted and therefore conformationally less homogeneous cyclohexyl derivative. To the extent this procedure is successful, information on conformationally homogeneous diastereomers provides an analysis of similar but conformationally inhomogeneous substances.

Conformational considerations render very easy the assignment of configuration to the 4- and 3-*t*-butylcyclohexanols. The *cis*-4- and *trans*-3-*t*-butylcyclohexanols VII and XI can be expected to have *axial* and therefore more congested hydroxyl groups, corresponding to relatively easy elution in chromatography, due to steric hindrance to absorption, and to relatively slow[8] saponification of the corresponding acid phthalates. On the other hand,

the *trans*-4- and *cis*-3-*t*-butylcyclohexanols VIII and X have *equatorial* hydroxyl groups and thus will be more difficult to elute and give rise to more easily saponified acid phthalates.

Results

Preparation of Isomers.—A convenient starting point for the 4-*t*-butylcyclohexanols VII and VIII was available commercial material[21] which proved to be predominantly *trans*-VIII. The latter isomer was obtained readily in 64% yield by several crystallizations and then saponification of the acid phthalate, m.p. 146.2–146.7°. The *cis*-alcohol VII could be obtained in low yield by chromatographing the residual alcohol after removal of most of the *trans* isomer. However, hydrogenation of 4-*t*-butylcyclohexanone, obtained in high yield by chromic acid oxidation of the commercial alcohol, was more satisfactory. Hydrogenation, either with platinum oxide in acetic acid or Raney nickel in ethanol, gave rise to sufficiently high proportions of *cis* isomer to allow isolation of substantial amounts of pure *cis* material either as the acid phthalate or by chromatography.

The melting point behavior of mixtures of *cis*- and *trans*-4-*t*-butylcyclohexanols is such that melting point may be a misleading guide to purity or composition. The two pure isomers have nearly identical melting points, and, as the detailed data in the Experimental Part show, apparently form a *ca.* 2:1 material melting as high as either pure isomer. To be useful as a guide to purity or composition mixed melting points need to be performed on quantitatively weighed-out mixtures of correctly chosen composition.

In chromatography, the *cis*-alcohol is eluted before the *trans*, a distinct and reproducible separation occurring whether weakly or strongly activated alumina is employed. Under standardized conditions (30 g. of alumina per gram of alcohol), the *cis* isomer was eluted with pentane whereas elution of the *trans*-alcohol required a solvent containing 10 to 20% ether. In this way a synthetic mixture of *cis*- and *trans*-alcohols was separated into its components with an accuracy of *ca.* 1%.

The 3-*t*-butylcyclohexanols X and XI were prepared from 3-*t*-butylcyclohexanone which was derived from 1,4-addition of the *t*-butyl Grignard reagent to Δ^2-cyclohexenone, a reaction previously investigated by Whitmore and Pedlow.[22] Reduction of the 3-*t*-butylcyclohexanone with lithium aluminum hydride gave the *cis*-3-*t*-butylcyclohexanol X in good yield. Chromatography of the alcohol suggested the presence of some of the more easily eluted *trans* isomer XI. The predominant alcohol fraction was less easily eluted material, and this led to pure acid phthalate of *cis*-3-*t*-butylcyclohexanol X. The convenient route to the *trans* isomer XI lay in reduction of the ketone with Raney nickel. The more easily eluted fraction of the alcohol led to acid phthalate of *trans*-3-*t*-butylcyclohexanol XI after recrystallization.

Table II summarizes the physical properties of the 3- and 4-*t*-butylcyclohexanols and their acid phthalates and *p*-toluenesulfonates.

TABLE II

PROPERTIES OF THE 3- AND 4-*t*-BUTYLCYCLOHEXANOLS AND DERIVATIVES

	3-*t*-Butylcyclohexyl		4-*t*-Butylcyclohexyl	
Isomer	*cis*	*trans*	*trans*	*cis*
Alcohol, m.p., °C.	40–41	48–49	81–82	82–83
Position of OH	(*equat.*)	(*axial*)	(*equat.*)	(*axial*)
Formula	X	XI	VIII	VII
Acid phthalate, m.p., °C.	136.0–136.8	154.5–155.5	146.2–146.7	141–142
Toluenesulfonate, m.p., °C.	58–59.5	33–35	89.4–90.0	79–80

Rate Measurements.—All four of the *t*-butylcyclohexyl acid phthalates displayed good second-order behavior in saponification in aqueous sodium hydroxide, and the results of the rate measurements are summarized in Table III. This Table includes also the results of rate measurements carried out

TABLE III

RATES OF SAPONIFICATION OF ACID PHTHALATES IN AQUEOUS SODIUM HYDROXIDE

Acid phthalate	Temp., °C.	Phthalate, 10^2 *M*	NaOH, 10^2 *M*	$10^5 k_2$, l. mole^{-1} sec.$^{-1}$	$\Delta H^{\neq}$, kcal./mole	$\Delta S^{\neq}$, e.u.
Cyclohexyl	39[a]			56		
	50.20	3.29	6.54	123 ± 1		
	50.02	3.29	6.89	120 ± 3		
	50.14	4.83	5.43	120 ± 3		
	50.00			120 ± 1	13.2	−31
	75.00	3.34	6.66	551 ± 10		
	75.00	3.39	6.62	581 ± 17		
	75.20	4.85	5.41	564 ± 11		
	75.00			563 ± 12		
trans-4-*t*-	39[a]			52		
Butyl	50.14	4.35	5.69	115 ± 5		
	50.02	3.80	6.39	117 ± 3		
	50.20	3.48	6.35	125 ± 6		
	50.00			118 ± 4	14.4	−28
	69[a]			433		
	75.12	3.35	6.48	636 ± 17		
	75.12	2.85	6.97	641 ± 13		
	75.00	2.00	8.19	656 ± 6		
	75.00	3.36	6.47	617 ± 10		
	75.00			634 ± 11		
cis-3-*t*-	39[a]			56.8		
Butyl	50.00	3.15	6.73	121 ± 2		
	50.00	2.88	6.99	121 ± 2	13.2	−31
	75.00	3.33	6.55	559 ± 14		
	75.00	3.03	6.84	575 ± 8		
	75.00			567 ± 8		
cis-4-*t*-	39[a]			5.2		
Butyl-	50.02	3.75	6.44	13.0 ± 0.8		
	50.10	3.61	6.57	13.1 ± 0.2		
	50.00			13.0	15.9	−27
	69[a]			54.4		
	75.00	3.77	6.41	82.5 ± 4.0		
	75.00	3.59	6.60	83.1 ± 1.2		
	75.00			82.8		
trans-3-*t*-	39[a]			5.46		
Butyl-	50.00	2.65	7.22	13.5 ± 0.1	15.8	−27
	75.00	2.62	7.25	85.1 ± 0.6		

[a] Extrapolated or interpolated from data at the other temperatures.

(21) Kindly supplied by the Dow Chemical Co. through the courtesy of Dr. E. C. Britton.

(22) F. C. Whitmore and G. W. Pedlow, Jr., THIS JOURNAL, **63**, 758 (1941).

with cyclohexyl acid phthalate for comparison. In the case of both the 3-*t*-butyl and 4-*t*-butyl pairs of isomers, one of each pair is much more reactive than its mate, so the kinetic behavior of the materials in saponification constitutes the best proof of configurational purity.

The *cis*- and *trans*-4-*t*-butylcyclohexanols and, for comparison, cyclohexanol displayed satisfactorily second-order kinetics[23,24] in oxidation at low concentration with chromium trioxide in 75% acetic acid. Table IV summarizes the collected data.

In acetolysis and formolysis, the four *t*-butylcyclohexyl *p*-toluenesulfonates displayed good first-order behavior, the data being summarized in Table V along with some collected for cyclohexyl *p*-toluenesulfonate.

The *cis*- and *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonates displayed good first-order behavior in ethanolysis, the pertinent rate constants together with those for cyclohexyl *p*-toluenesulfonate being summarized in Table VI. The addition of 0.065 *M* sodium ethoxide to the 0.03 *M* solution of the toluenesulfonate in ethanol gave rise to a greatly increased rate obeying second-order kinetics in the case of the *cis*-4-*t*-butylcyclohexyl and cyclohexyl esters. The second-order rate constants are summarized in Table VI, and a sample run for *cis*-4-*t*-butylcyclohexyl toluenesulfonate is illustrated in Table VII. With *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate the inclusion of 0.065 *M* sodium ethoxide in the ethanol gave only a slightly increased rate which still obeyed good first-order kinetics. This is illustrated in Table VIII. First-order rate constants at still higher concentrations of sodium ethoxide are summarized in Table VI.

TABLE IV

RATES OF OXIDATION OF CYCLOHEXANOLS WITH CHROMIC ACID IN 75% ACETIC ACID

Cyclohexanol	Temp., °C.	[ROH], 10^2 *N*	[CrO_3], 10^2 *N*	10^3 k_2, l. mole^{-1} sec.$^{-1}$
Cyclohexanol	25.00	1.75	1.13	5.85 ± 0.18
	25.00	1.84	0.98	5.62 ± .17
	25.00	1.69	1.00	6.06 ± .05
	25.00			5.84
	49.90[b]	1.18	0.95	4.1 ± .1
	50.32	1.50	1.12	42.9 ± 1.0
	50.32	1.50	1.12	43.2 ± 0.9
	50.00[a]			42.1
trans-4-*t*-Butyl-	25.00	1.59	0.93	4.83 ± 0.03
	25.00	1.59	0.93	4.60 ± 0.13
	25.00			4.72
	50.16	1.60	1.05	30.7 ± 0.8
	50.22	1.69	1.16	29.7 ± 0.5
	50.0[a]			29.9
cis-4-*t*-Butyl-	25.00	1.49	1.11	13.80 ± 0.30
	25.00	1.49	1.11	14.10 ± 0.15
	25.00			14.0
	50.22	1.53	1.16	76.5 ± 3.6
	50.22	1.53	1.16	76.2 ± 3.3
	50.10	1.55	0.98	77.3 ± 1.7
	50.00[a]			76.3

[a] Interpolated from the data at the other temperatures. [b] 50% acetic acid as solvent.

TABLE V

SUMMARY OF RATES OF ACETOLYSIS AND FORMOLYSIS

OTs	Solvent	Temp., °C.	Concn., 10^2 *M*	10^5 *k*, sec.$^{-1}$	$\Delta H^{\neq}$, kcal./mole	$\Delta S^{\neq}$ e.u.
Cyclohexyl	HCOOH	25.00	3.02	3.87 ± 0.12	23.8	+1.0
	HCOOH	50.00	3.03	93.0 ± 2.1		
trans-4-*t*-Butyl-	AcOH	50.00[a]		0.148		
	AcOH	75.00	1.68	3.62 ± 0.12		
	AcOH	75.14	1.80	3.89 ± .08		
	AcOH	74.78	1.62	3.68 ± .05		
	AcOH	75.00[a]		3.75		
	AcOH	99.63	1.79	60.4 ± 0.4		
	AcOH	99.58	2.12	59.6 ± 2.8		
	AcOH	99.87	1.92	58.8 ± 0.7		
	AcOH	100.0[a]		61.4	28.1	+1.7
	HCOOH	25.02	1.67	3.35 ± 0.22		
	HCOOH	25.02	1.75	3.65 ± .12		
	HCOOH	25.00	2.10	3.56 ± .12		
	HCOOH	25.00[a]		3.51	22.9	−2.0
	HCOOH	51.10	1.55	82.4 ± 2.6		
	HCOOH	51.10	1.92	87.0 ± 3.5		
	HCOOH	50.55	1.53	83.2 ± 3.4		
	HCOOH	50.00[a]		75.6		
cis-4-*t*-Butyl-	AcOH	50.18	2.08	0.488 ± 0.007		
	AcOH	50.18	1.59	.491 ± 0.007		
	AcOH	50.00[a]		.479	26.7	−0.5
	AcOH	75.02	1.99	10.28 ± 0.13		
	AcOH	75.02	1.78	10.06 ± 0.16		
	AcOH	75.00[a]		10.2		
	AcOH	100.0[a]		144 ± 2		
	HCOOH	25.00	1.80	14.2 ± 0.4	22.0	−2.4
	HCOOH	50.00	1.75	271 ± 12		
cis-3-*t*-Butyl-	AcOH	50.00[a]		0.142		
	AcOH	75.00	1.30	3.33 ± 0.04		
	AcOH	99.59	1.52	49.0 ± 0.5		
	AcOH	100.0[a]		51.1	27.5	−0.5
trans-3-*t*-Butyl-	AcOH	50.00	1.36	0.510 ± 0.008	26.6	−0.6
	AcOH	75.00	1.59	10.9 ± 0.4		
	AcOH	100.0[a]		153		

[a] Extrapolated or interpolated from data at the other temperatures.

Solvolysis.—The products of solvolysis were investigated for both *trans*- and *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonates XII and XIX in 60% aqueous acetone with suspended calcium carbonate and in acetic and formic acids containing sodium acetate or formate, respectively. In the case of the latter two solvents, the product was treated with lithium aluminum hydride before chromatography to separate olefin from alcohol. The results of the solvolyses are summarized in Table IX.

From the *trans*-4-*t*-butylcyclohexyl toluenesulfonate XII in either aqueous acetone, acetic acid or formic acid at high sodium formate concentration (0.566 *M*), the product was two-thirds to three-quarters olefin, the rest being almost entirely pure inverted *cis*-4-*t*-butylcyclohexanol XV. There was no more difficultly eluted *trans*-alcohol in evidence.

When the sodium formate concentration was low (0.04 *M*) in the formolysis of the *trans*-4-*t*-butylcyclohexyl toluenesulfonate XII, nearly no olefin was isolated and the entire alcohol product obtained in high yield was a low melting easily eluted mixture. Quite clearly, 0.04 *M* sodium formate was insufficient to render the conditions irreversible. This was verified by the behavior of the olefin in formic acid. Olefin, obtained from solvolysis of the toluenesulfonate, was converted to the low melting easily eluted mixture in formic acid, very substantially at low sodium formate concentration but only slightly at 0.33 *M*.

(23) G. Vavon and C. Zaremba, *Bull. soc. chim.*, **49**, 1853 (1931).

(24) F. H. Westheimer and A. Novick, *J. Chem. Phys.*, **11**, 506 (1943).

TABLE VI

SUMMARY OF ETHANOLYSIS RATES

Cyclohexyl OTs	Temp., °C.	ROTs concn., 10^2 *M*	[NaOEt], 10^2 *M*	$10^5 k_1$, sec.$^{-1}$	$10^5 k_2$, l. mole^{-1} sec.$^{-1}$	$\Delta H^{\ddagger}$, kcal./mole	$\Delta S^{\ddagger}$, e.u.
Cyclohexyl OTs	50.18	3.52	...	0.141 ± 0.003		25.5	−6
	50.00[a]			0.138			
	75.20	3.13	...	2.63 ± 0.09			
	75.00[a]			2.58			
	75.20	3.76	6.46		247 ± 11		
	75.00[a]				241		
trans-4-*t*-Butyl-	50.18	3.67	...	0.110 ± 0.003		26.6	−4
	50.00[a]			0.107			
	75.20	3.16	...	2.30 ± 0.13			
	75.00[a]			2.25			
	51.10	3.00	6.56	0.184 ± 0.004		25.3	−7
	50.00[a]			0.160			
	75.20	3.12	6.56	2.96 ± 0.11			
	75.00[a]			2.89			
	75.35	3.02	12.56	4.18 ± 0.07			
	75.00[a]			4.03			
	75.20	5.64	28.06	5.71 ± 0.11			
	75.00[a]			5.60			
cis-4-*t*-Butyl-	50.18	3.88	...	0.427 ± 0.006		24.4	−8
	50.00[a]			0.418			
	75.20	3.32	...	7.03 ± 0.16			
	75.00[a]			6.89			
	51.10	3.02	6.56		61.5 ± 2.2	22.2	−5
	50.00[a]				54.6		
	75.20	2.85	6.56		713 ± 16		
	75.00[a]				700		

[a] Extrapolated or interpolated from data at other temperatures.

TABLE VII

REACTION OF 0.0285 *M* *cis*-4-*t*-BUTYLCYCLOHEXYL *p*-TOLUENESULFONATE IN 0.0656 *M* ETHANOLIC SODIUM ETHOXIDE AT 75.20°

Time, 10^{-3} sec.	Ml. of acid per aliquot	$10^3 k_2$, l. mole^{-1} sec.$^{-1}$
0	6.253	
1.380	5.093	6.89
2.345	4.629	7.02
4.020	4.161	7.08
6.060	3.848	7.33
8.280	3.704	7.33
∞	3.509	
	Mean	7.13 ± 0.16

TABLE VIII

REACTION OF 0.0300 *M* *trans*-4-*t*-BUTYLCYCLOHEXYL *p*-TOLUENESULFONATE IN 0.0656 *M* ETHANOLIC SODIUM ETHOXIDE AT 51.10°

Time, 10^{-3} sec.	Ml. of acid per aliquot	$10^5 k_1$, l. mole^{-1} sec.$^{-1}$
0	6.254	
0.356	6.067	0.186
1.191	5.663	.190
2.520	5.189	.181
5.962	4.352	.180
∞	3.347	
	Mean	0.184 ± 0.004

Authentic 4-*t*-butylcyclohexene XIV, prepared from pyrolysis of the pure crystalline methyl xanthate from *trans*-4-*t*-butylcyclohexanol VIII, also was subjected to several hydration experiments. In formic acid at 25° in 94 hr., a 50% yield of the low melting alcohol mixture was obtained, an analogous result being obtained with cyclohexene[25] (Table IX). At a concentration of sodium formate equal to 0.38 *M* *t*-butylcyclohexene was only 2.5% converted to the low melting alcohol mixture. In acetic acid, perchloric acid catalyst was necessary to cause addition to the olefin.

The *cis*-4-*t*-butylcyclohexyl toluenesulfonate XIX gives even more olefin, namely, 83–87%, in solvolysis in aqueous acetone, and in dry acetic and formic acids under irreversible conditions. The substitution product from the *cis*-toluenesulfonate consists almost entirely of *trans*-4-*t*-butylcyclohexanol XXI in aqueous acetone solvent, and it still contains substantial amounts of the *trans*-alcohol when the product is obtained from solvolysis in acetic or formic acids. However, with the *cis*-4-*t*-butylcyclohexyl toluenesulfonate XIX, formation of the low melting alcohol mixture begins to be important even under irreversible conditions. The low melting alcohol mixture constitutes a minor fraction of the substitution product in aqueous acetone, but it becomes the predominant product in formic acid.

The low melting alcohol mixtures, which tended to be eluted in chromatography after *cis*-4-*t*-butylcyclohexanol VII and before *trans*-4-*t*-butylcyclohexanol VIII, obviously contained *cis*-4-*t*-butylcyclohexanol. For example, a fraction, m.p. 59–60°, of the low melting product from solvolysis of *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate XII in formic acid at low sodium formate concentration gave rise to a toluenesulfonate which, on recrystallization,

(25) See H. B. Knight, R. E. Koos and D. Swern, THIS JOURNAL, **75**, 6212 (1953), for the recent conversion of cyclohexene to cyclohexyl formate in 69% yield by refluxing in formic acid in the presence of perchloric acid catalyst.

TABLE IX

SUMMARY OF SOLVOLYSES

Compound	Solvent	Temp., °C.	Concn., 10^3 M	Base or acid	Time, hr.	Products, % Total Rec.	Olefin	ROH cis-4	Oily ROH	trans-4	Other
trans-4-t-Butylcyclohexyl OTs	60% acetone	Reflux	6.53	$CaCO_3$	55	100	67	31	1.3		1[a]
	AcOH	100	4.04	0.0481 M NaOAc	7.5	83	72	24.3			2.9[b]
	HCOOH	50.5	3.29	.04 M NaOCHO	20		7		93		
	HCOOH	25	3.07	.566 M NaOCHO	75	97	76.2	20.6	2.4		0.8[a]
cis-4-t-Butylcyclohexyl OTs	60% acetone	Reflux	6.53	$CaCO_3$	28	98	83		2.3	12.7	1.8[c]
	AcOH	100	3.57	.0481 M NaOAc	2	100	83		9.9	7.1	
	AcOH	100	3.22	.049 M NaOAc	2.25		87.9		7.8	4.3	
	HCOOH	50.5	2.97	.040 M NaOCHO	12	100	20		80	..	
	HCOOH	25	3.29	.566 M NaOCHO	18.5	97	87.3		8.3	4.4	
Chugaev 4-t-butylcyclohexene	AcOH	25	8.58	.045 M $HClO_4$	103	78	81		19		
	AcOH	100	8.58	.045 M $HClO_4$	0.5	83	46		54		
	HCOOH	25	7.24	.....	94	71	30		70		
	HCOOH	25	9.66	.381 M NaOCHO	94	80	97		3		
Solvolysis 4-t-butylcyclohexene	HCOOH	50	5.59	.007 M NaOCHO	12		41		59		
	HCOOH	25	4.89	.334 M NaOCHO	60	74	88		12[d]		
Cyclohexene	HCOOH	25	32.5	.....	96				45[e]		

[a] Eluted before cis-4-t-butylcyclohexanol. [b] Estimated 2.3 and 0.6 of cis- and trans-4-t-butylcyclohexanols, respectively. [c] Eluted after trans-4-t-butylcyclohexanol. [d] Some pure cis-4-t-butylcyclohexanol sublimed from this material. [e] Based on theoretical yield. Cyclohexanol was characterized as the acid phthalate, m.p. 96–97°, undepressed by authentic cyclohexyl acid phthalate.

proved to be pure *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate XIX by melting point and first-order solvolysis rate. The low melting alcohol mixtures quite obviously contained *trans*-3-*t*-butylcyclohexanol XVIII also. From one fraction, pure *trans*-3-*t*-butylcyclohexanol XVIIII actually crystallized. Further, the low melting alcohol mixtures were composed nearly exclusively of axial alcohols XV and XVIII. This could be judged by the rate behavior of acid phthalates of the alcohol mixtures since the equatorial acid phthalates were so much more reactive than the axial isomers toward saponification. When some of the fractions of low melting alcohol from formic acid addition to *t*-butylcyclohexene were examined in this way, no reactive *equatorial* material was detected in the intermediate fractions and only small amounts (*ca.* 10%) in a late pair of fractions.

The low melting alcohol which was obtained along with pure *trans*-4-*t*-butylcyclohexanol from acetolysis of *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate XIX was shown to consist of an approximately 50:50 mixture of 3- and 4-*t*-butylcyclohexanols by oxidation to the mixture of ketones and examination of the infrared spectrum of the ketone mixture.

A synthetic 1:1 mixture of the *axial* 3- and 4-*t*-butylcyclohexanols behaved in chromatography just as the low melting alcohol mixtures from solvolysis or addition to olefin. The higher melting chromatographic fraction was identical in m.p. with and undepressed by the analogous fraction from solvolysis alcohol mixture.

Discussion

First we can consider the relative behavior of the *axial* and *equatorial* *t*-butylcyclohexyl derivatives.

Oxidation.—The oxidation of the alicyclic alcohols by chromium trioxide in aqueous acetic acid presumably involves a reaction of the acid chromate ester[24] in equilibrium with the reagents. For convenience, the reaction may be formulated as in

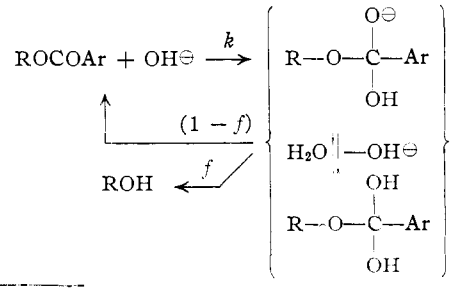
$$ROH + CrO_3 \overset{K}{\rightleftharpoons} ROCrO_3H \qquad (6)$$

$$ROCrO_3H \xrightarrow{k} \text{ketone} \qquad (7)$$

equations 6 and 7. It is apparent that the measured second-order rate constant, k_2, is composite, being Kk, the product of an equilibrium constant and a rate constant. For the *axial* isomer we have $k_2^a = K_a k_a$, and for the *equatorial* one we have $k_2^e = K_e k_e$. We can anticipate that $K_e > K_a$, and also[8] that $k_a > k_e$. However, it is not obvious what the net balance of opposing effects will be.

As summarized in Table X, the *cis*-4-*t*-butylcyclohexanol, with an *axial* hydroxyl group, oxidizes more rapidly than the *trans* isomer with its *equatorial* hydroxyl group by the small factor of *ca.* 2.5 to 3 at 50 and 25°, respectively. Thus, the sequence of rates is the one which has come to be taken as qualitatively typical[8] of *axial* and *equatorial* isomers. Clearly k_a exceeds k_e by more than K_e exceeds K_a. However, the net balance leaves only a small factor characteristic of the *axial–equatorial* difference.

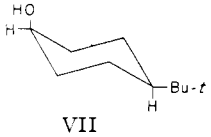
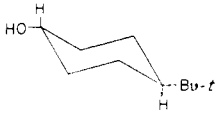
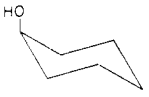
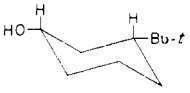
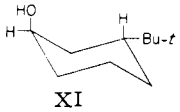
Saponification.—The basic saponification of the acid phthalates very probably is not a direct substitution[26] but involves successive addition and elimination reactions[26] formulated as



(26) M. L. Bender, THIS JOURNAL, **73**, 1626 (1951); **75**, 5596 (1953); M. L. Bender, R. D. Ginger and K. C. Kemp, *ibid.*, **76**, 3350 (1954).

TABLE X

SUMMARY OF RATE COMPARISONS

	Rel. rates of sapn. of acid phthalates 50°	Rel. rates of Oxidn. of ROH by CrO_3 in 75% AcOH 25°	50°	Solvolysis of ROTs at 50° Rel. rates EtOH	AcOH	HCOOH	Solvent rate sequence EtOH < AcOH < HCOOH			Rel. rates of dehydration[29] 140–160°	Rel. rates of E2 ROTs NaOEt, EtOH 75°
 VII	0.11	2.97	2.55	3.90	3.24	3.58	0.87	1.00	570	3.5	1.00
 VIII	1.00	1.00	1.00	1.00	1.00	1.00	0.72	1.00	510	1.0	<0.01
 IX	1.02 0.94[a]	1.24	1.41	1.29	1.24[b]	1.23				1.16	0.26
 X	1.03				0.96						
 XI	0.11				3.45						

[a] Based on the value of $k_2 = 111 \times 10^{-5}$ reported by W. Hückel, *Ber.*, **67**, 129 (1934). [b] First-order rates of acetolysis taken as 1.83×10^{-6} sec.$^{-1}$ and 4.14×10^{-5} sec.$^{-1}$ at 50 and 75°, respectively, from work of A. Fainberg.

Thus the second-order rate constants for saponification, k_2, are equal to kf, the product of a rate constant and a factor f, the fraction of intermediate which enters into alcohol-producing elimination. For different materials, not only may k differ, but some variation in f also contributes to the variation in k_2 with structure. The present results supply the magnitude of the difference in k_2 due merely to the *axial* or *equatorial* position of the acid phthalate group. As summarized in Table X, the equatorial acid phthalates are *ca.* 10 times as reactive as the axial esters, whether a *t*-butyl group is in the 3- or 4-position. The corresponding 3- and 4-*t*-butylcyclohexyl esters possess nearly identical saponification rates. The factor of 10 between *equatorial* and *axial* conformations is the largest one observed for any reaction we have investigated where neither of the conformations is essentially precluded from participating in a certain mechanism by stereoelectronic considerations.

The factor of 10 at 39° between saponification rates of the *equatorial* and *axial* acid phthalates corresponds to a difference in free energy of activation ($\Delta\Delta F^{\ddagger}$) of 1.4 kcal./mole. This $\Delta\Delta F^{\ddagger}$ may be identified with $A^{\ddagger} - A$ in the terminology of Fig. 1, if e and $e^{\ddagger}$ correspond to the equatorial diastereomer and a and $a^{\ddagger}$ to the axial diastereomer. The factor of 10 is too small to make a reliable separation of the $\Delta\Delta F^{\ddagger}$ into $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$, but it is clear from Table III that the more hindered acid phthalates tend to have the higher $\Delta H^{\ddagger}$ but also higher values of $\Delta S^{\ddagger}$. The direction of change of $\Delta S^{\ddagger}$ with increasing hindrance is opposite to that observed with increasing hindrance due to change of R in neutral esters RCOOR′, the data for which Taft[27] recently has utilized in the separation of steric effects into repulsion and "steric hindrance to motion." It is not clear whether the difference is due to the presence of an already charged phthalate ion group in work, but the present sign of $\Delta\Delta S^{\ddagger}$ is more often than not the one observed by Hückel and co-workers in saponification of various pairs of isomeric acid phthalates[28] or acid succinates.[28]

(27) R. W. Taft, Jr., THIS JOURNAL, **75**, 4534 (1953). Taft has written $\Delta\Delta F^{\ddagger}$ composed of an electrical contribution, $\Delta\Delta E_e^{\ddagger}$ and a steric contribution, $\Delta\Delta E_s^{\ddagger}$, as in equation 8, and has dissected $\Delta\Delta E_s^{\ddagger}$ into

$$\Delta\Delta F^{\ddagger} = \Delta\Delta E_e^{\ddagger} + \Delta\Delta E_s^{\ddagger} \quad (8)$$

$$\Delta\Delta F^{\ddagger} = \Delta\Delta E_e^{\ddagger} + \Delta\Delta E_r^{\ddagger} - RT \ln IIQ \quad (9)$$

$$\Delta\Delta H^{\ddagger} = \Delta\Delta E_e^{\ddagger} + \Delta\Delta E_r^{\ddagger} + RT^2 \frac{\mathrm{d} \ln IIQ}{\mathrm{d}T} \quad (10)$$

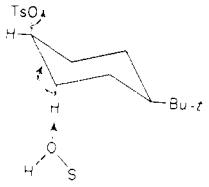
$$T\Delta\Delta S^{\ddagger} = RT \ln IIQ + RT^2 (\mathrm{d} \ln IIQ/\mathrm{d}T) \quad (11)$$

a steric strain term and one due to "steric hindrance to motion," as in equation 9. The last term, $-RT \ln IIQ$, has been called equal to $-T\Delta\Delta S^{\ddagger}$ in the belief that the term RT^2 (d ln IIQ/dt) in equation 11 for $T\Delta\Delta S^{\ddagger}$ is negligible. This belief is based on the apparent constancy of $\Delta H^{\ddagger}$ values (and therefore $\Delta\Delta H^{\ddagger}$ values) over temperature ranges of 30 or 40°. However, this apparent constancy cannot validly be made the basis of the proposed separation of $\Delta\Delta E_s^{\ddagger}$ into the two components. This is because the apparent constancy of $\Delta\Delta H^{\ddagger}$ tells us merely, if we refer to equation 10, that the quantity RT^2 (d ln IIQ/dt) does not change by an amount visibly above experimental error in 30 or 40°. It does not show that the quantity is zero, as is being assumed. To put the matter another way, consider the change in $\Delta\Delta H^{\ddagger}$ as temperature increases from absolute zero. If the change between 300 and 330° is small, we may not conclude that the total change to 330° is small.

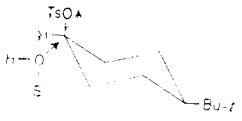
(28) W. Hückel, *et al.*, *Ann.*, **533**, 128 (1937).

(29) G. Vavon and M. Barbier, *Bull. soc. chim.*, [4] **49**, 567 (1931).

Solvolysis, Elimination and Addition.—As is summarized in Table X, the difference in solvolysis rate between the *axial* and *equatorial* toluenesulfonates is considerably smaller and in the reverse direction from that observed with the acid phthalates in saponification. The *axial* 4-*t*-butylcyclohexyl toluenesulfonate solvolyzes more rapidly than the equatorial isomer at 50° by factors of 3.90, 3.24 and 3.58 in ethanol, acetic acid and formic acid solvents, respectively. The rates of the *axial* and *equatorial* 3-*t*-butylcyclohexyl derivatives match those of the corresponding 4-*t*-butyl derivatives within a few per cent. in acetic acid, the only solvent in which the 3-derivatives were investigated. Not only are the rates similar for *axial* and *equatorial* isomers, but no definite difference in $\Delta S^{\ddagger}$ is visible (Table V). The small difference in rate between the *axial* and *equatorial* isomers is not to be ascribed appreciably to nucleophilic attack by solvent on β-hydrogen (XXIV) or carbon (XXV). For the former, only the *axial* isomer is stereoelectronically suitable, and for the latter, the *axial* isomer is more favorable judging by SN2 displacement rates.[30]



XXIV



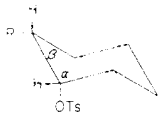
XXV

However, nucleophilic solvents should accentuate such solvent behavior and increase the gap in rate between *axial* and *equatorial* isomers. Instead, the *axial–equatorial* rate ratio is very similar in ethanol, acetic acid and formic acid (Table X). To put it another way, as also is done in Table X, the solvent rate sequences, EtOH < AcOH < HCOOH, are very similar for the two conformational isomers.

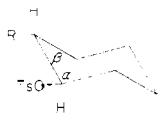
At least one contributing cause of the somewhat higher rate of the *axial* over the *equatorial* isomers is steric acceleration.[31] Considering that a factor of three in rate is equivalent to 700 cal. in $\Delta F^{\ddagger}$, and that an *axial* methyl group, for example, is sterically strained relative to an *equatorial* one by *ca.* 1800 cal.,[7] the order of magnitude of the rate acceleration is proper for steric acceleration. There may be other contributing reasons having to do with hyperconjugation, for example, but the total effect of all contributing causes is certainly small.

The rough analogy between relative solvolysis rates of toluenesulfonates and acid-catalyzed dehydration rates of the alcohols, previously[2] referred to, is also apparent with the 4-*t*-butylcyclohexanols. As summarized in Table X, Vavon's dehydration[29] experiments showed the *axial* isomer to be *ca.* 3.5 times as reactive as the *equatorial* isomer.

The small solvolysis rate factor between *axial* and *equatorial* toluenesulfonates XIX and XII provides a useful standard for the consideration of *axial–equatorial* ratios for systems with C_β more suitably[32] substituted to promote hydrogen participation in the rate-determining ionization. Thus, with 2-alkylcyclohexyl toluenesulfonates, the *cis* isomer tending to be *axial* (XXVI) and the *trans equatorial* (XXVII), the *cis–trans* solvolysis rate factor is of the order of 10^2 for R equal to *i*-Pr[2] or Me[3]

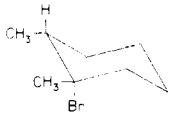


XXVI

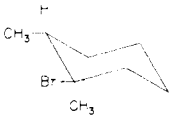


XXVII

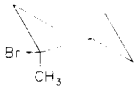
With an α-methyl group, making C_α tertiary, k_s, the rate constant for ionization without anchimeric assistance, is so much more increased than k_Δ, the anchimerically assisted ionization rate constant, that the *axial–equatorial* solvolysis rate factor can be expected to be small again. An illustration of this is provided by the relative rates of solvolysis at 25° in aqueous 2-butanone of *trans*-1,2-dimethylcyclohexyl bromide (largely XXVIII), *cis*-1,2-dimethylcyclohexyl bromide (largely XXIX) and 1-methylcyclohexyl bromide recently reported by Nevitt and Hammond.[33,34]



XXVIII, 1.09



XXIX, 1.12



1.00

On inclusion of sodium ethoxide in the solvent ethanol, the *axial*-4-*t*-butyl cyclohexyl *p*-toluenesulfonate is subject to a second-order reaction, whereas any increase in rate with the *equatorial* isomer could not be distinguished from a salt effect. Even if all the increase in the latter case at 75° is ascribed to a second-order reaction, an upper limit to k_2 is obtained of *ca.* 10^{-4} l. mole^{-1} sec.$^{-1}$. Thus the minimum factor between *axial* and *equatorial* isomers in second-order rate is 70, but this number is obviously only a poor minimum figure.

While the products of the second-order reaction of the *axial*-4-*t*-butylcyclohexyl *p*-toluenesulfonate with ethoxide ion were not investigated, the reaction is presumed to consist largely of stereoelectronically favored E2 elimination. Attack of ethoxide ion on sulfur leading to sulfur–oxygen cleavage, important with bornyl toluenesulfonate,[35] should be faster with the *equatorial* than the *axial* isomer. (Compare the behavior of the acid phthalates.) The SN2 reaction with ethoxide ion, exceptionally slow with cyclohexyl[30,36] derivatives, would be somewhat faster with the *axial* than *equatorial* isomer, but by only a small factor. Neither of these competing processes therefore can contribute significantly to the reaction.

For consideration of the products from solvolysis of the *equatorial*- and *axial*-4-*t*-butylcyclohexyl toluenesulfonates, the results given in Table IX have been summarized in Table XI. Traces of unac-

(30) N. J. Holness, unpublished work.

(31) (a) H. C. Brown, *Science*, **103**, 385 (1946); (b) P. D. Bartlett 10th Nat. Org. Symposium, Boston, Mass., p. 22 of Abstracts, June, 1947.

(32) S. Winstein, *et al.*, THIS JOURNAL, **74**, 1113 (1952).

(33) T. D. Nevitt and G. S. Hammond, *ibid.*, **76**, 4124 (1954).

(34) See reference 11 for 1,2-dimethylcyclohexyl chloride.

(35) W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940).

(36) (a) J. B. Conant and R. E. Hussey, THIS JOURNAL, **47**, 476 (1925); (b) P. D. Bartlett and L. Rosen, *ibid.*, **64**, 543 (1942).

counted-for materials have been neglected in the percentage compositions. Also, although the low melting mixtures of *axial*-4- and 3-*t*-butylcyclohexanols were not all analyzed and undoubtedly varied somewhat in composition, these were arbitrarily split in two. Thus the percentage of *cis*-4-*t*-butylcyclohexanol in the substitution product, when much rearranged *trans*-3-*t*-butylcyclohexanol is present, is not precise, but the broad trends are perfectly clear.

TABLE XI

SUMMARY OF RESULTS OF SOLVOLYSIS OF *cis*- AND *trans*-4-*t* BUTYLCYCLOHEXYL *p*-TOLUENESULFONATES

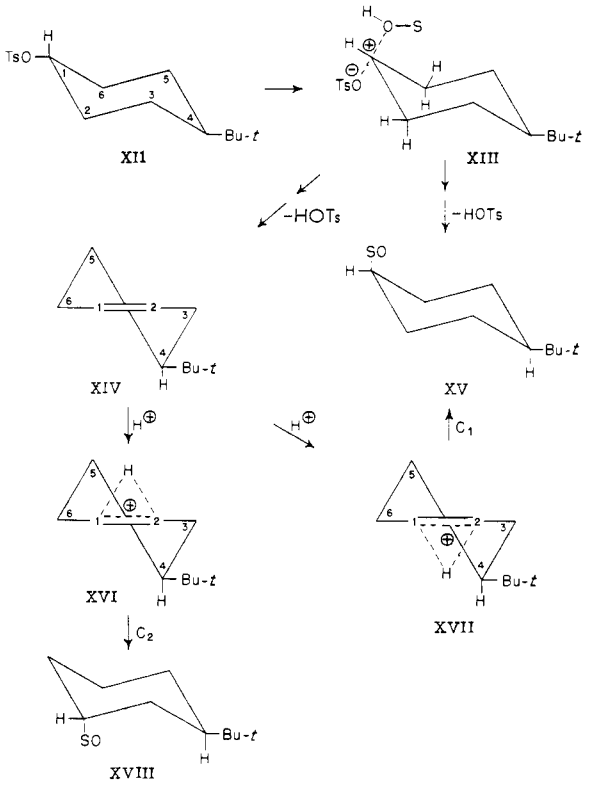
Isomer	Solvent	Temp., °C.	Olefin, %	Composition of ROH, % *trans*-4 (*equatorial*)	*cis*-4 (*axial*)	*trans*-3 (*axial*)	H shift, %
trans (*equatorial*)	60% Me_2CO	Reflux	67		98		
	AcOH	100	72		98		
	HCOOH	25	76		97	3	
cis (*axial*)	60% Me_2CO	Reflux	83	85	8	7	15
	AcOH	100	86	40	30	30	60
	HCOOH	25	87	35	33	32	65

From the *equatorial*-4-*t*-butylcyclohexyl toluenesulfonate XII under the solvolytic conditions, the proportion of olefin (67–76%) produced is not too far below that obtained from the *axial* isomer. It is instructive that so much olefin is produced even from an enforced *equatorial* derivative, since olefin formation cannot be ascribed to an E2 type[35] elimination reaction involving solvent as depicted in XXIV for the *axial* isomer. It must stem from a carbonium ion intermediate, depicted as XIII, an intimate[37] ion pair, showing explicitly only one nearest solvent molecule. This is shown giving rise to olefin, symbolized by XIV, employing the representation recently suggested by Barton, *et al.*[38] While the low percentages of other products than *cis*-4-alcohol XV from *trans*-4-tosylate XII are admittedly unreliable, it is clear that the substitution product is nearly completely inverted and that essentially no rearranged product is formed even in formic acid. In the latter solvent, where the most rearrangement is observed, the alcohol product is *ca.* 3% *trans*-3-*t*-butylcyclohexanol XVIII, after making a small correction for the trace of reaction of olefin in formic acid even under these conditions.

From the *axial*-4-*t*-butylcyclohexyl toluenesulfonate XIX under solvolytic conditions the substitution product is largely the inverted *equatorial*-4-alcohol XXI in aqueous acetone. The proportion of *axial*-4- and rearranged 3-alcohols XV and XVIII in the substitution product, small in aqueous acetone, is large in acetic and formic acids.

There is a striking difference between the stereochemical outcome of solvolysis of the toluenesulfonates in the present study and that observed in the presumably carbonium ion deamination of cyclohexyl- and decalylamines.[39] In nitrous acid deamination, the *equatorial*-alcohol is obtained very predominantly from *axial*-amine and essentially exclusively from *equatorial*-amine. It seems, in the case of solvolysis of the *equatorial*-4-*t*-butylcyclohexyl *p*-toluenesulfonate XII, essentially the whole substitution product must stem from an intermediate no further along in the ionization–dissociation process[37] than the first intimate ion pair XIII. In the case of the *axial*-4-*t*-butylcyclohexyl *p*-toluenesulfonate XIX we would anticipate that collapse of the intimate ion pair XX to give inverted alcohol XXI would compete with formation of solvent-separated ion pair or dissociated ions just as well as in the case of the *equatorial*-tosylate. Thus we would anticipate just as high a degree of inversion at the 4-carbon atom in solvolysis of *axial*-tosylate as for *equatorial*-tosylate, were it not for another mode of formation of *axial*-4-alcohol XV. This other mode is thought to involve the hydrogen-bridged carbonium ion XVII or XXII, also responsible for rearrangement. On this basis, the percentage hydrogen shift connected with the alcohol from the *axial*-tosylate XIX may be calculated as the sum of the *axial*-4- and the 3-*t*-butylcyclohexanols. These are listed in Table XI, running 15, 60 and 65% in aqueous acetone, acetic acid and formic acid, respectively.

The exact stage where the competition between β-hydrogen and solvent occurs is not definite. It may be as late as but no later than the intimate ion pair XX. At a carbonium ion center formed with the least modification of the chair structure of a cyclohexyl derivative, the axis of the so-called vacant *p* orbital is much more nearly parallel to the β-C–H bonds to the originally *axial*-hydrogen atoms than to the *equatorial* ones. Probably, then, the



(37) *E.g.* (a) S. Winstein, *et al.*, THIS JOURNAL, **74**, 1147 (1952); (b) *Chemistry and Industry*, 664 (1954).

(38) D. H. R. Barton, R. C. Cookson, W. Klyne and C. W. Shoppee, *ibid.*, 21 (1954).

(39) (a) J. A. Mills, *J. Chem. Soc.*, 260 (1953); (b) A. K. Bose, *Experientia*, **9**, 256 (1953); (c) W. G. Dauben, R. C. Tweit and C. Mannerskantz, THIS JOURNAL, **76**, 4420 (1954).

axial-hydrogen atoms would be the ones to shift. If they shift in the intimate ion pair form, ion pairs XX and XIII from *axial* and *equatorial* materials, respectively, may have sufficiently different ratios of hydrogen shift to collapse to account for the greater rearrangement of the *axial* isomer.

The observed increasing proportion of hydrogen shift in the solvent sequence, aqueous acetone < acetic acid < formic acid, is to be expected[40] from the decreasing nucleophilic character and increasing ionizing power. Also, the trend in the present data is in line with analogous observations on other systems.[40]

The present results have some bearing on the role, nature and behavior of carbonium ion intermediates in addition, elimination, solvolysis and rearrangement. Idealized carbonium ion theory, involving dissociated carbonium ions, visualizes the carbonium ion as a common intermediate for all these reactions, although it is difficult to point to illustrative examples. In recent years, structures for the carbonium ions involving Br, R, H, etc., in the bridged[41] position have become important along with the classical open structures. Figure 2 depicts olefin, addition product, $R\overset{\oplus}{O}HS$ or RY, and both classical and bridged forms of the carbonium ion intermediate for the specific case of addition of SOH or HY, analogous formulations being possible for addition of BrY, RY, etc.

Much recent evidence is available on acid-catalyzed hydration of olefins to tertiary alcohols. On the basis of specific hydronium ion catalysis,[42] dependence of hydration rate on Hammett's acidity function,[43,44] lack of isomerization of 2-methyl-2-butene and 2-methyl-1-butene during hydration,[45] and the behavior of trimethylethylene and methylenecyclobutane in heavy water,[44] Taft has interpreted[43,44] the hydration–dehydration with the aid of both a π-complex and classical carbonium ion[46] as in Fig. 2. Stage 1, the protonation of the double bond to a π-complex, and stage 3, the conversion of classical carbonium ion to conjugate acid of alcohol or the reverse, are labeled equilibria, while stage 2, the interconversion of π-complex and classical carbonium ion is regarded rate-determining. In other words, $k_{-1} >> k_2$, and $k_3 >> k_{-2}$.

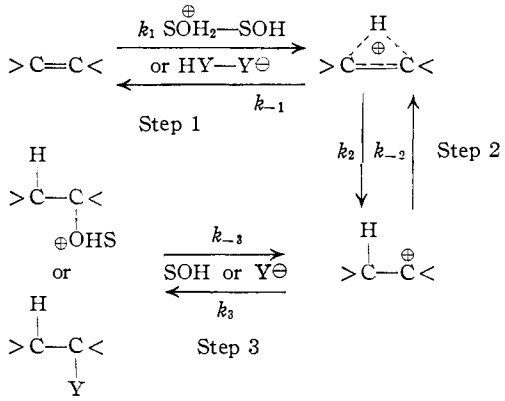
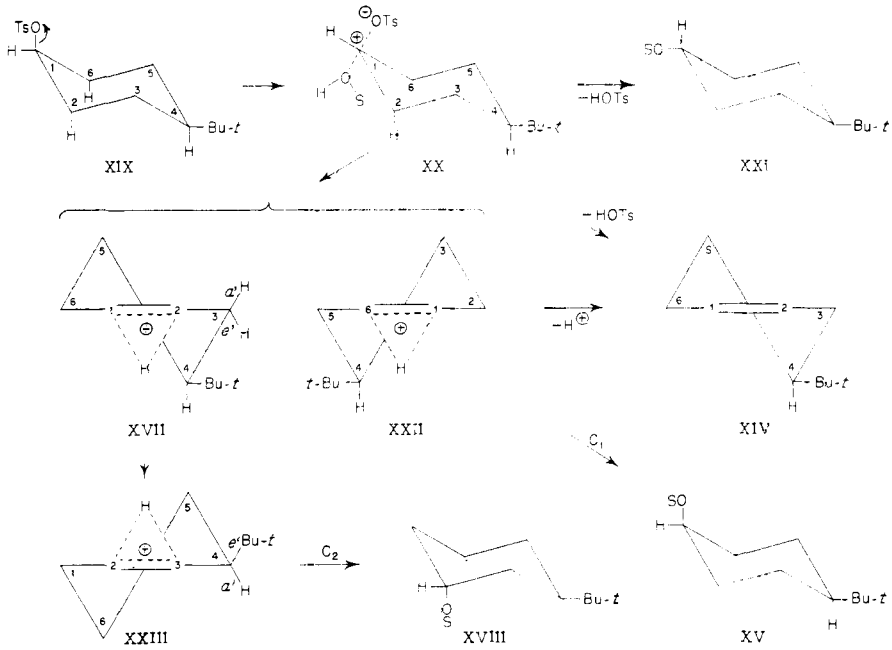


Fig. 2.—Idealized carbonium ion formulation of addition, elimination and solvolysis.



While this general scheme, with the specified relationships among the rate constants, was not intended to be applied promiscuously to other reactions, structures and solvents, it makes a convenient reference point for comparison in the present discussion. We already have seen that stereochemistry of substitution during solvolysis of the diastereomeric 4-*t*-butylcyclohexyl tosylates would

(40) (a) S. Winstein, paper at Symposium on Reaction Mechanisms, 120th Meeting of American Chemical Society, New York, N. Y., Sept., 1951, page 25M of Abstracts; (b) S. Winstein, M. Brown, H. C. Schreiber and A. H. Schlesinger, THIS JOURNAL, **74**, 1140 (1952); (c) J. D. Roberts, W. Bennett, R. E. McMahon and E. W. Holroyd, Jr., THIS JOURNAL, **74**, 4283 (1952).

(41) See, *e.g.*, (a) I. Roberts and G. Kimball, *ibid.*, **59**, 947 (1937); (b) S. Winstein and H. J. Lucas, *ibid.*, **61**, 1576, 2845 (1939); (c) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford Univ. Press, Oxford, 1949, p. 144, etc.; (d) S. Winstein and B. K. Morse, THIS JOURNAL, **74**, 1133 (1952).

(42) (a) H. J. Lucas and W. F. Eberz, *ibid.*, **56**, 460 (1934); (b) F. G. Ciapetta and M. Kilpatrick, *ibid.*, **70**, 639 (1948).

(43) R. W. Taft, Jr., *ibid.*, **74**, 5372 (1952).

(44) R. W. Taft, Jr., Paper at Symposium on Mechanisms of Homogeneous and Heterogeneous Hydrocarbon Reactions," Divisions of Petroleum and Physical and Inorganic Chemistry, Kansas City, Mo., March, 1954.

(45) J. B. Levy, R. W. Taft, Jr., and L. P. Hammett, THIS JOURNAL, **75**, 1253 (1953).

(46) See P. B. D. De La Mare, E. D. Hughes, C. K. Ingold and Y. Pocker, *J. Chem. Soc.*, 2930 (1954), for an alternative formulation of the process of hydration of the olefin involving slow conversion of the olefin to an ordinary carbonium ion by addition to the olefin of an unspecified form of the proton, freer than covalent $H_3O^{\oplus}$ and in rapid equilibrium with it.

not be understandable on the basis of a dissociated carbonium ion (the same from each diastereomer).

There are a number of places where it is clear that additions of HY and carbonium ion reactions of RY do not involve largely the same intermediates. One example which can be cited is the addition of hydrogen bromide or chloride to conjugated dienes, such as butadiene[41c,47] or isoprene.[47] Butadiene,[48] for example, gives, as kinetically controlled product, mainly α-methylallyl halide, while α- or γ-methylallyl alcohols, on treatment with hydrochloric or hydrobromic acids, yield, as kinetically controlled product, mainly γ-methylallyl halide.[49] Another example is the recently reported[50] cleanly *trans* addition of hydrogen bromide to 1,2-dimethylcyclohexene under conditions leading to kinetically controlled product. Judging by the rates of ionization[33] of the two diastereomeric bromides, RY in Fig. 2, and the position of equilibrium between them, addition and solvolysis cannot involve entirely the same intermediates. Without knowledge of the kinetics of the addition and the nature of the various hydrogen bromide species involved, a possible mechanism for the hydrogen bromide addition involves[50] the bridged carbonium ion whose opening is sufficiently concerted to give *trans* addition product.

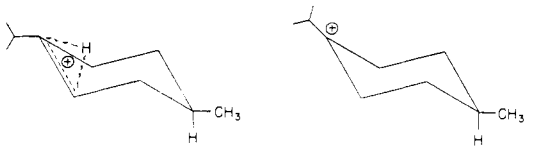
In the present work it also is clear that solvolysis of the toluenesulfonates and addition of formic acid to *t*-butylcyclohexene do not involve substantially the same intermediates. In the addition of formic acid to the olefin, both the 4- and 3-*t*-butylcyclohexanols are certainly very predominantly *axial*. A possible mechanism for the addition reaction involves the hydrogen-bridged species XVI and XVII, these opening stereospecifically. Judging by the behavior in opening of epoxides[51] and in halogen addition,[51] one might, *a priori*, expect that direction of opening to predominate which leads to *axial* alcohol. On this basis, species XVII would yield *axial*-4-derivative by attack on C_1 and species XVI would yield *axial*-3-derivative by attack on C_2.

If the above mechanism of addition of formic acid were the correct one, it would involve opening of the bridged carbonium ion without prior rearrangement to the classical carbonium ion, that is, contrary to the scheme in Fig. 2. We can anticipate that the occurrence of such rearrangement prior to attack will depend on structure and solvent.

If the hydrogen bridged species tend to react stereospecifically to yield only *axial*-alcohols, there would appear to be a difficulty with the nature of the 3-*t*-butylcyclohexanol from rearrangement accompanying solvolysis of 4-*t*-butylcyclohexyl toluenesulfonate under irreversible conditions. While the 3-*t*-butylcyclohexanol from solvolysis was not scrutinized as thoroughly, the chromatographic behavior of the 4- and 3-*t*-butylcyclohexanol mixtures suggests a largely *axial* conformation for the 3-alcohol from rearrangement. If only originally *axial*-hydrogen atoms move into the bridging positions, bridged species XVII or XXII would be formed in solvolysis of *axial*-4-*t*-butylcyclohexyl toluenesulfonate XIX. These might be expected to yield only *axial*-4-*t*-butylcyclohexanol XV and not *axial*-3-*t*-butylcyclohexanol XVIII. The formation of so predominantly *axial*-3-*t*-butylcyclohexanol by rearrangement seems to demand either: (i) originally equatorial hydrogen atoms bridge, after all; or (ii) the first bridged species, *e.g.*, XVII, rearranges by further hydrogen shift. For example, movement of the *a'*-hydrogen atom on C_3 in XVII into the bridging position would yield species XXIII which would yield *axial*-3-*t*-butylcyclohexanol XVIII by attack on C_2. Hydrogen shifts in the cyclohexane[52] ring accompany other reactions to a sufficient extent to lend credence to this possibility.

The reaction scheme in Fig. 2 depicts proton loss from the bridged π-complex, classical carbonium ion isomerizing to π-complex before proton loss. Such a situation is clearly not general. That a proton may be lost from a carbonium ion without its isomerization to a bridged species may be illustrated from the present results. Thus the *equatorial*-4-*t*-butylcyclohexyl tosylate XII in formic acid gives 76% olefin and no more than 3% rearrangement in the alcohol product. On the other hand, the *axial*-tosylate XIX gives 87% olefin and 32% rearrangement in the alcohol product. Obviously, if elimination involved a hydrogen bridged species which also gave rise to rearranged product, the amount of rearrangement with the *equatorial* isomer should rival that observed with the *axial* isomer. At least most of the olefin observed in solvolysis of the *equatorial*-tosylate must proceed without bridging of the carbonium ion. Some, but an unknown fraction, of the olefin observed from solvolysis of the *axial* isomer could stem from bridged ion.

The relationship, $k_{-1} >> k_2$, associated with the reaction scheme in Fig. 2, which states that proton loss from the π-complex is much faster than isomerization to a classical carbonium ion, cannot be general, either. If this condition applied, then, since 1,2-hydrogen shifts pass through such bridged species along the way, no rearranged product derived from rearranged classical carbonium ion ever would be obtained under irreversible solvolytic conditions. This is clearly not true in general. Actually k_{-1}/k_2 can become very small, for example in the case of the bridged ion XXX from neomenthyl[2] toluenesulfonate solvolysis. In this case, the hydrogen shift, in formic acid solvent, is complete to species XXXI



XXX XXXI

(47) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 657.

(48) M. S. Kharasch, J. Kritchevsky and F. R. Mayo, *J. Org. Chem.*, **2**, 489 (1938).

(49) W. G. Young and J. Lane, THIS JOURNAL, **60**, 847 (1938).

(50) G. S. Hammond and T. D. Nevitt, *ibid.*, **76**, 4121 (1954).

(51) (a) A. Furst and Pl. A. Plattner, page 409 of Abstracts, 12th International Congress of Pure and Applied Chemistry, New York, N. Y., 1951; (b) L. F. Fieser, *Experientia*, **6**, 312 (1950); (c) D. H. Barton, E. Miller and H. T. Young, *J. Chem. Soc.*, 2598 (1951).

(52) (a) L. Schmerling, THIS JOURNAL, **69**, 1121 (1947); (b) J. H. Simons and A. C. Meunier, *ibid.*, **65**, 1269 (1943); (c) C. D. Nenitzescu and D. Curcaneanu, *Ber.*, **70B**, 346 (1937).

before proton loss occurs; in other words, k_{-1}/k_2 is essentially zero.[53]

Consideration of Other Structures.—The behavior of the conformationally homogeneous *t*-butylcyclohexyl derivatives supplies a starting point for the scrutiny of the behavior of other materials, whether conformationally inhomogeneous or not. Unsubstituted cyclohexyl derivatives may be considered first.

In chromic acid oxidation of cyclohexanols and in solvolysis of the toluenesulfonates, orbital hybridization at C_I changes to trigonal with 120° preferred for the C_6–C_1–C_2 angle. Brown[11] has stressed the increase in total strain attending reactions of this type, and he has labeled cyclohexyl "slow" in the two reactions mentioned, as well as in S_N2 displacements. However, a more detailed quantitative analysis would be necessary to assess the strain involved. At any rate, in nucleophilic substitution on cyclohexyl, S_N2 reactions[36] are extremely slow, but solvolytic ionization is not unduly slow, the rate being comparable to isopropyl.[2] The important point here is not the assessment of the exact size of the small effect of cyclohexane ring-produced strain effects on solvolysis rate but whether a 4-*t*-butyl group contributes appreciably to such strain effects. Again, it would require detailed quantitative calculations which have not been performed. Superficial examination of models shows that making planar the 1-carbon atom of the cyclohexane ring does not have any large effect on the disposition of a 4-*t*-butyl group. Thus the effect of a 4-*t*-butyl group must at least be very small. In the present work, the 3-*t*-butyl group was found to have effects on rate identical to the 4-*t*-butyl group, suggesting that both polar effects and sterically induced effects are both very close to negligible for 3- and 4-*t*-butyl groups in solvolysis. On this basis the rate constants for the 4-*t*-butylcyclohexyl derivatives have been employed in equation 5 for a conformational analysis of cyclohexanol and cyclohexyl toluenesulfonate.

Both in oxidation of the alcohol and in solvolysis of the toluenesulfonate, cyclohexyl displays a rate intermediate between that of *equatorial*- and *axial*-4-*t*-butylcyclohexyl but closer to that of the equatorial isomer (Table X). Because of the small spread in rate constants the conformational analysis is crude and cannot be employed to scrutinize temperature variation of the conformational distribution. From oxidation rate, N_a, the fraction of *axial* conformation, is 0.19 ± 0.07 at 25–50° for cyclohexanol, and it is 0.10 ± 0.01 for the toluenesulfonate at 50° in ethanol, acetic acid and formic acid solvents. From these values of N_a, values of A may be calculated with the aid of equation 1, and these are listed in Table XII. For the cyclohexyl toluenesulfonate, the value of A in Table XII is a grand average, using the values for the three solvents at the various temperatures, 25, 50 or 75°.

TABLE XII

GROUP A VALUES

Group	Solvent	Temp., °C.	Group A, kcal./mole
t-Bu	..	..	>5.4
i-Pr	H_2O	39	>3.3
± {$OCOC_6H_4CO_2^{\ominus}$, $OH^{\ominus}$}	H_2O	39	2.6
n-C_4H_9	H_2O	39	2.1
n-C_3H_7	H_2O	39	2.1
C_2H_5	H_2O	39	2.1
CH_3	..	..	1.8
OTs	EtOH, AcOH HCOOH	50	1.7
$OCOC_6H_4CO_2^{\ominus}$	H_2O	39	1.2
OH	75% AcOH	40	0.8

As far as information is available, the disposition of products in solvolysis of cyclohexyl toluenesulfonate is similar to that with the 4-*t*-butylcyclohexyl derivatives. Roberts and Chambers[54] have reported predominantly olefin together with some acetate as products of acetolysis.

In absolute alcohol, cyclohexyl toluenesulfonate is much more subject to a second-order reaction than is the *equatorial*-4-*t*-butylcyclohexyl ester. The apparent second-order constant for the total reaction of 241 × 10^{-5} at 0.0646 M NaOEt at 75° may be corrected for solvolysis to yield a value of *ca.* 180 × 10^{-5}. This is about one-fourth the value of *axial*-4-*t*-butylcyclohexyl toluenesulfonate (Table X). A conformational analysis with the aid of equation 5 would yield a value of N_a of 0.26, higher than the values obtained from solvolysis. Although only one measurement was made of the rate of reaction of cyclohexyl toluenesulfonate with sodium ethoxide and this problem requires more study, it seems that cyclohexyl is too reactive relative to *axial*-4-*t*-butylcyclohexyl and a likely value of N_a. It seems probable that the rate of *axial*-4-*t*-butylcyclohexyl toluenesulfonate is not a valid standard, being too low because of an effect of the *t*-butyl group.

The saponification rate of cyclohexyl acid phthalate resembles that of the *equatorial*-4- and 3-*t*-butylcyclohexyl esters, as summarized in Table X. Available[28,55] saponification rates on other alicyclic acid phthalates and acid succinates, summarized in Table XIII, gain new significance in the light of the present results on the conformationally homogeneous 4-*t*-butylcyclohexyl esters. Looking first at conformational control by 3- or 4-substituents, we see that the 4-isopropyl group in the 4-isopropylcyclohexyl acid phthalates is already quite effective. The rate factor between the diastereomeric esters is 7.7 at 39° instead of 10.0 observed with the 3- and 4-*t*-butyl derivatives. Actually, the factor in the 4-*i*-Pr case may be higher than 7.7, since the rate of the slow *cis* isomer has been reported the same as,

(53) (a) J. Schwartz, unpublished work; (b) S. Winstein, "1,2- and 1,3-Hydrogen Shift," Symposium on Molecular Rearrangements, Queen Mary College, Univ. of London, April 6, 1954. (c) NOTE ADDED IN PROOF.—The above discussion presupposes Dewar's use of the term, π-complex, for a common bridged carbonium ion intermediate in certain addition and rearrangement reactions. L. G. Cannell and R. W. Taft, Jr. [page 34N of Abstracts of American Chemical Society Meeting, Cincinnati, Ohio, March 29 to April 7, 1955] have recognized that the π-complex intermediate employed in the interpretation of isobutylene hydration cannot be the bridged ion (if one is involved) in the isobutyl → *t*-butyl rearrangement attending deamination of isobutyl amine.

(54) J. D. Roberts and V. C. Chambers, THIS JOURNAL, **73**, 5034 (1951).

(55) G. Vavon, *Bull. soc. chim.*, [4] **49**, 989 (1931).

that of the *trans* isomer somewhat lower than, those of the corresponding 4-*t*-butyl derivatives. The situation is summarized in Table XIII.

TABLE XIII

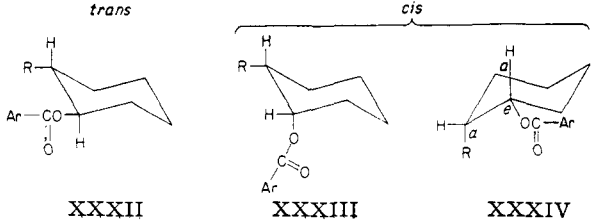
RELATIVE RATES OF SAPONIFICATION OF ESTERS

Type ester	Compound	Rel. rate of epimer *A*	*B*	Ratio
P[a,b]	4-*t*-Bu-C[c]	1.00	0.10	10
				8.0[d]
P	3-*t*-Bu-C	1.09	.10	10
P[55]	4-*i*-Pr-C	0.74	.10	7.7
P[55]	2-Me-C	.42	.15	2.8
P[55]	2-Et-C	.20	.055	3.7
P[55]	2-Pr-C	.12	.032	3.7
P[55]	2-Bu-C	.042	.012	3.5
P[55]	2-*i*-Pr-C			34[d]
P[55]	2-C-C			11[d,e]
A[28f,g]	Cyclohexyl	1.00		
A[28]	*trans*-β-D[h]	(II)1.23	(I)0.16	7.9
A[28]	*cis*-β-D	(I)1.17		
		(II)0.71		
A[28]	*cis*-α-D	(I) .46		
		(II) .13		
A[28]	*trans*-α-D	(II) .25	(I) .0117	21
A[56]	2-*i*-Pr, 5-Me-C	.026[e]	.00081[e]	32[e]

[a] P is acid phthalate. [b] Data on acid phthalates are at 39° unless otherwise indicated. [c] C is cyclohexyl. [d] Temp. is 69°. [e] Solvent is 75% EtOH instead of water. [f] A is acid succinate. [g] Data on acid succinates are at 40° unless otherwise indicated. [h] D is decalyl.

With the *trans*-β-decalol-II, *cis*-β-decalol-I and *cis*-β-decalol-II, the *equatorial* position is highly favored for the hydroxyl or ester group on the chair–chair decalin ring system. In line with this, the reported relative saponification rates of acid succinates, 1.04 ± 0.22, are nearly equal to that of the cyclohexyl ester, 1.00. In the case of *trans*-β-decalol-I, there is great compulsion on the hydroxyl or ester group to be *axial*, since an *equatorial* position on a chair form of ring A demands that ring B be fused *axial–axial* to ring A. The hindrance in the *axial–trans*-β-decalol-I is, in models, identical to that in *axial*-4-*t*-butylcyclohexanol, and, in line with this, the factor between *trans*-β-decalols-II and -I in saponification rate of acid succinates is 7.9, comparable to the value 10 observed with the 4-*t*-butylcyclohexyl acid phthalates.

Now we shift our attention to conformational control by vicinal 2-substituents which differ from more distant ones by the introduction of an additional steric effect, and by a polar effect which is now not so nearly negligible. If the polar effect of an alkyl substituent R were the same in both conformations of both diasteromeric 2-alkylcyclohexyl esters, and if steric effects were simply additive as the sum of the various group–group interactions, the rate factor between *equatorial*- and *axial*-esters XXXII and XXXIII, each with an *equatorial*-2-R group, would be the same as for the *equatorial* and *axial*-4-*t*-butylcyclohexanols since all additional interactions would cancel out. The available data show the difference between the actual situation and the expectations based on simple additivity.



XXXII XXXIII XXXIV

With the 2-alkyl-cyclohexanols the *trans* isomer tends to be *equatorial–equatorial* as in XXXII. However, the *cis* isomer tends to be distributed between conformations XXXIII, with the ester group *axial*, and XXXIV, with the ester group *equatorial*, the first of these being more predominant the more bulky R is. With the 2-isopropyl- and 2-cyclohexylcyclohexanols, and with menthol and neomenthol, the latter pair of alcohols possessing an additional preferably *equatorial*-methyl group to influence conformation, the rate of saponification is very much reduced by the 2-alkyl group. Also, this effect is somewhat larger with the *axial* ester than the *equatorial*, making the ratio of rates of the diastereomeric members of each pair larger than the factor of 10 at 39° and 8 at 69° observed with the 4-*t*-butylcyclohexyl esters. This factor is 34 for the 2-isopropylcyclohexyl acid phthalates at 69° and 32 for menthyl and neomenthyl acid succinates at 40°. These figures tend to be minimum values for the ratio since much of the observed rate of the *cis*-ester can be due to reaction of even a very small proportion of form XXXIV with the equatorial ester group.[56]

The lack of constancy of total polar and steric effects of vicinal alkyl groups is further illustrated by the *cis*- and *trans*-α-decalyl derivatives. With the *cis*-α-decalols-I and -II and with the *trans*-α-decalol-II, an acid succinate group tends to be very largely *equatorial*. In these cases, rate of saponification is reduced below that of the cyclohexyl ester by factors varying from 2 to 8. With the *trans*-α-decalol-I derivative, with the ester group constrained to the *axial* position, rate of saponification is reduced by the vicinal alkyl chain by more than for the isomer II, the factor between II and I being 21.

With the 2-alkyl cyclohexanols where alkyl is primary, the effectiveness of alkyl in constraining the *cis* isomer to the form XXXIII with an *axial* ester group is only moderate. Thus with R = Me, Et, *n*-Pr and *n*-Bu, the factor between saponification rates of *trans*- and *cis*-acid phthalates at 39° is 2.8 to 3.7. An approximate conformational analysis of the *cis*-acid phthalate may be made with the aid of equation 5 on the basis: (i) the *trans* isomer is XXXII entirely; (ii) the rate of form XXXIV is the same as that of XXXII; (iii) the rate of form XXXIII is one-tenth of that of XXXII or XXXIV.

(56) For example, in the case of *cis*-2-isopropyl-cyclohexyl acid phthalate, the whole of the saponification rate would be accounted for by 3% of the form XXXIV, with the *equatorial*-ester group and with a saponification rate *ca.* equal to that of the *trans* isomer XXXII. E. L. Eliel [*Experientia*, **9**, 91 (1953)] already has suggested for the menthols and isomenthols, in order to account for the relative rates of reaction with *p*-nitrobenzoyl chloride reported by J. Read and W. J. Grubb [*J. Chem. Soc.*, 1779 (1934)], that neoisomenthol and neomenthol react in the conformation containing equatorial hydroxyl group (like XXXIV). The relative reactivity values of Reed and Grubb do indeed suggest that most of the reaction of neoisomenthol is due to the equatorial conformation constituting *ca.* one-eighth to one-fifth of the total. On this basis, however, neomenthol, which has a methyl group opposing rather than favoring *equatorial*-hydroxyl, reacts negligibly in the *equatorial* modification.

Such analysis gives, for the percentage of *cis*-2 alkylcyclohexyl acid phthalate in the form XXXIV, with the *equatorial* ester group, 29% for 2-Me and 19.5 ± 0.7% for 2-Et, *n*-Pr and *n*-Bu.

Individual Group *A* Values.—The rough conformational analyses for the *cis*-2-alkylcyclohexyl acid phthalates lead to *A* values by application of equation 1. The assumption that these *A* values may be treated approximately as additively composed of individual group values leads to *A* values for the acid phthalate and alkyl groups. These individual *A* values represent the free energy of preference for the *equatorial* position of each individual group.

Using the value 1.8 for the methyl group, the value for the acid phthalate group may be derived from the data for the *cis*-2-methyl ester. Then, with the value for the acid phthalate group, values for Et, Pr and Bu may be derived from the data for the corresponding 2-alkyl esters. The derived group *A* values are listed in Table XII.

From the $\Delta\Delta F^{\ddagger}$ value of 1.4 kcal./mole observed in saponification of the *axial*- and *equatorial*-*t*-butylcyclohexyl acid phthalates, and the *A* value of 1.2 for the acid phthalate group, one obtains, by addition, the value of 2.6 listed in Table XII as the *A* value for the acid phthalate–hydroxide ion transition state group in saponification. A minimum value of *A* for the isopropyl group, given in Table XII, may be derived from the 7.7 as the minimum factor for saponification rates of the 4-isopropylcyclohexyl acid phthalates or the fact, pointed out in footnote 56, that there can be no more than 3% of the *cis*-2-isopropylcyclohexyl acid phthalate in the equatorial form XXXIV in saponification.

The individual group *A* values in Table XII, even though crude, are of considerable use in making discussions based on conformational analysis at least semiquantitative.

Experimental Part

***trans*-4-*t*-Butylcyclohexanol VIII and Derivatives.**—In a typical preparation, a solution of 42 g. of 4-*t*-butylcyclohexanol, m.p. 64–78°, from the Dow Chemical Co., and 42 g. (105%) of phthalic anhydride in 50 ml. of dry pyridine was kept at 100° for 1.5 hours. Working up in the usual way gave an oil which was crystallized from ethyl acetate–pentane. The first crop, m.p. 143.5–144.5°, yielded 20 g. of material, m.p. 146.2–146.7°, after two additional crystallizations.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 71.19; H, 7.80.

In two experiments 100 g. of the starting alcohol afforded 123 g. (64%) of pure *trans*-acid phthalate, m.p. 145.5–147°.

A 25-g. quantity of pure *trans*-acid phthalate, m.p. 145.5–147°, was dissolved in a solution of 20 g. of sodium hydroxide in 100 ml. of water and the solution was immediately steam distilled. The distillate was extracted four times with 100-ml. portions of pentane. The combined extracts were dried over anhydrous magnesium sulfate, and the solvent was evaporated through a Vigreux column to give 12.4 g. of the *trans*-alcohol, m.p. 81–82° (reported[29,57] m.p. 80–80.5°, 82°).

A solution of 1.6 g. of the *trans*-alcohol and 1.95 g. (102%) of *p*-toluenesulfonyl chloride in 10 ml. of dry pyridine was allowed to stand overnight at room temperature. Working up in the usual way yielded 1.8 g. of a solid, m.p. 86–89°. Crystallization from pentane with a trace of ethyl acetate gave 1.55 g. of *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate, m.p. 89.4–90.0°.

(57) H. Pines and V. Ipatieff, THIS JOURNAL, **61**, 2728 (1939).

Anal. Calcd. for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44. Found: C, 65.80; H, 8.74.

4-*t*-Butylcyclohexanone.—To a solution of 20 g. of *trans*-4-*t*-butylcyclohexanol in 100 ml. of glacial acetic acid was added a solution of 8.9 g. (103%) of chromium trioxide in 100 ml. of acetic acid in portions over 10 minutes at room temperature. After the mixture remained at room temperature overnight, 1500 ml. of water was added, and the solution was extracted successively with five 100-ml. portions of pentane. The combined extracts were washed with water and sodium bicarbonate solution and dried over anhydrous potassium carbonate. Evaporation of the pentane gave *ca.* 20 g. of an oil, which, on distillation, afforded 15.5 g. of 4-*t*-butylcyclohexanone, b.p. 90–92° (9 mm.), m.p. 47.5–48.5° (reported[52a] b.p. 106–108° (18 mm.), m.p 49–50°).

***cis*-4-*t*-Butylcyclohexanol VII and its Derivatives.**—A solution of 12 g. of 4-*t*-butylcyclohexanone in 50 ml. of glacial acetic acid was shaken with 300 mg. of Adams catalyst in an atmosphere of hydrogen until hydrogen uptake stopped. Although the hydrogen uptake was much below the theoretical amount, the product was extracted and chromatographed over commercial activated alumina. Elution with a pentane–10% ether mixture gave 4.3 g. of an alcohol, m.p. 72–75°. By the conventional procedure this alcohol afforded an acid phthalate, m.p. 139–141°, m.p. 117–120° on admixture with *trans*-4-*t*-butylcyclohexyl acid phthalate. Crystallization from ethyl acetate–pentane raised the m.p. to 141–142°.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 71.24; H, 7.99.

Hydrolysis of the acid phthalate gave *cis*-4-*t*-butylcyclohexanol, m.p. 80.5–81.5° (reported[29] 83–83.5°), m.p. 63–66° on admixture with the *trans* isomer.

Reduction of 57 g. of 4-*t*-butylcyclohexanone with hydrogen and Raney nickel catalyst in ethanol by the method of Cooke, *et al.*,[58] and careful chromatography of the product over 1.2 kg. of commercial activated alumina yielded 18.1 g. of pure *cis*-4-*t*-butylcyclohexanol, m.p. 82–83°, eluted with pentane–5% ether.

The toluenesulfonate was prepared in the conventional manner from 2.1 g. of the *cis*-alcohol and 3.75 g. of *p*-toluenesulfonyl chloride using a reaction time of 16 hours at 25°. From ethyl acetate–pentane, the product had m.p. 79–80°.

Anal. Calcd. for $C_{17}H_{26}O_3S$: C, 65.76; H, 8.45. Found: C, 65.96; H, 8.26.

Melting Point Behavior of Mixtures of *cis*- and *trans*-4-*t*-Butylcyclohexanol.—A small quantity of each of the two alcohols was weighed carefully into a small test-tube and completely melted at 100°. The melt was quickly frozen, removed from the tube and ground to a fine powder. The melting point range then was recorded in the usual way. These are listed below.

Cis, %	M.p. range, °C.	*Cis*, %	M.p. range, °C.
0	80.0–81.0	53.1	*ca.* 73–81.8[a]
4.4	60.8–70.9	59.3	80.7–83.0
9.9	61.5–69.2	66.6	78.4–82.6
17.5	62.4–66.7	77.3	75.7–82.4
25.4	62.0–63.9	84.1	75.1–80.4
29.4	62.5–70.0	90.3	76.0–77.7
35.0	61.8–75.9	95 1	76.7–80.3
45.6	62.0–79.5	100	81.0–82.0

[a] Beginning of melting range very indistinct.

Chromatographic Separation of Mixture of *cis*- and *trans*-4-*t*-Butylcyclohexanol.—A mixture of 476 mg. of the *cis*-alcohol and 738 mg. of the *trans*-alcohol was chromatographed over 36 g. of commercial activated alumina. The column was eluted with pentane and finally pentane–10% ether, 100-ml. portions being taken. Fractions 2–7, using pentane, gave 366 mg. of pure *cis*-alcohol, m.p. 81–82°, while fractions 13–15, using pentane–10% ether, gave 670 mg. of pure *trans*-alcohol, m.p. 78–79°. Intermediate fractions 8–12, using pentane, contained 165 mg. of various mixtures of *cis*- and *trans*-alcohol. On the basis of m.p. and

(58) R. G. Cooke, D. T. C. Gillespie and A. K. MacBeth, *J. Chem. Soc.*, 52 (1939).

mixed m.p., the intermediate fractions contained 96 mg. of *cis*- and 69 mg. of *trans*-alcohol. The total analysis was therefore 462 mg. of *cis*- and 739 mg. of *trans*-alcohol.

4-*t*-Butylcyclohexene.—A solution of 47 g. of *trans*-4-*t*-butylcyclohexanol in 200 ml. of dry ether was stirred for 28 hours with 10 g. of sodium hydride. To the stirred suspension of the sodium alcoholate was added 32 ml. of carbon disulfide in 2-ml. portions, followed 50 minutes later by 100 g. of methyl iodide. The reaction mixture was stirred for 14 hours, after which a further 10 ml. of methyl iodide was added and the stirring continued for one hour.

The ethereal solution of the methyl xanthate was decanted from the sodium hydride and other inorganic salts which were then washed twice with dry ether. The ether was evaporated from the combined solution and washings, and the residue was chromatographed over 300 g. of activated alumina. The first 6-g. fraction of xanthate eluted had m.p. 45–46.5°, m.p. 45.2–46.3° after recrystallization.

Anal. Calcd. for $C_{12}H_{22}OS_2$: C, 58.49; H, 8.99. Found: C, 58.70; H, 8.94.

Second and third crops, m.p. 43–44.5° and 44–46°, weighed 34.5 g., the total yield being 40.5 g. (62%).

The methyl xanthate (34 g.) was heated under vacuum (100 mm.) for one hour at 208°. The hydrocarbon then was distilled out at 20 mm. pressure and then redistilled to give a pale yellow oil, b.p. 65–66° (20 mm.), $n^{20}D$ 1.4589. Filtration through activated alumina in pentane afforded colorless 4-*t*-butylcyclohexene, $n^{20}D$ 1.4583 (reported[52b] $n^{20}D$ 1.4581).

3-*t*-Butylcyclohexanone.—Δ^2-Cyclohexenone was prepared by the method of Whitmore and Pedlow[22]; b.p. 65–66° (20 mm.), $n^{25}D$ 1.4824 [reported[22] b.p. 67° (25 mm.), $n^{20}D$ 1.4879]. Treatment of 30 g. of Δ^2-cyclohexenone with the *t*-butyl Grignard reagent afforded 17 g. (35%) of 3-*t*-butylcyclohexanone, b.p. 92–95° (10 mm.), $n^{25}D$ 1.4611, semicarbazone m.p. 204–205° dec. [reported[22] b.p. 96–98° (20 mm.), $n^{20}D$ 1.4615, semicarbazone m.p.[22] 207–208° dec., m.p.[52a] 205–206°], 3 g. of high boiling material and 17 g. of non-ketonic compound.

***cis*-3-*t*-Butylcyclohexanol X and Derivatives.**—A solution of 7 g. of 3-*t*-butylcyclohexanone in 20 ml. of dry ether was added over a period of 0.5 hour to a stirred suspension of 1 g. of lithium aluminum hydride in 50 ml. of ether. Sufficient water was added dropwise to decompose the excess reagent and to coagulate the aluminum hydroxide. The ether solution was decanted, dried over anhydrous potassium carbonate and evaporated. Chromatography of the residual oil afforded an initial fraction, eluted with pentane, which gave an impure acid phthalate, m.p. 115–120°. Of the remaining alcohol, 4.74 g. was eluted with 50% ether–pentane and this afforded an acid phthalate, m.p. 133–136°. Recrystallization from aqueous methanol gave 4.66 g. of *cis*-3-*t*-butylcyclohexyl acid phthalate, m.p. 136.0–136.8°.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 70.82; H, 8.17.

Steam distillation of 3.55 g. of the *cis*-acid phthalate from 25% potassium hydroxide solution afforded 1.56 g. of *cis*-3-*t*-butylcyclohexanol, m.p. 40–41°, b.p. 103° (10 mm.), $n^{25}D$ 1.4660.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.63; H, 12.90.

The toluenesulfonate, prepared in the conventional manner from 1.27 g. of alcohol, allowing a reaction time of 24 hours at 0°, had m.p. 58–59.5° after crystallization from pentane.

Anal. Calcd. for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44. Found: C, 65.49; H, 8.39.

***trans*-3-*t*-Butylcyclohexanol XI and Derivatives.**—A solution of 8.5 g. of 3-*t*-butylcyclohexanone in ethanol was reduced with Raney nickel as described for the preparation of *cis*-4-*t*-butylcyclohexanol. Chromatography of the product afforded 3.4 g. of an easily eluted alcohol. This afforded an acid phthalate, m.p. 146–150°. Crystallization from aqueous methanol gave 3.15 g. of pure material, m.p. 154.5–155.5°.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 70.91; H, 8.19.

Saponification of 2.2 g. of the *trans*-acid phthalate furnished 1.05 g. of *trans*-3-*t*-butylcyclohexanol, m.p. 44–45°, b.p. 85° (5 mm.), $n^{25}D$ 1.4684.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.58; H, 12.90.

The toluenesulfonate was prepared in the conventional manner from 725 mg. of alcohol, allowing a reaction time of 44 hours at 0°. The toluenesulfonate was difficult to crystallize. At 0° the liquid slowly crystallized, and, after washing with pentane at −70°, it had m.p. 33–35°.

Anal. Calcd. for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44. Found: C, 65.88; H, 8.58.

Chromatography of a Mixture of *axial*-3- and 4-*t*-Butylcyclohexanols.—A 180-mg. quantity of a 1:1 mixture of the two axial alcohols was chromatographed over 8 g. of commercial activated alumina. Elution with 50-ml. portions of pentane afforded 4 oily fractions totaling 85 mg. Elution with pentane–10% ether afforded 63 mg. of a solid, m.p. 52–54°, and 30 mg. of material, m.p. 58–59°. The last fraction, on admixture with material m.p. 57–59°, from addition of formic acid to 4-*t*-butylcyclohexene, melted at 57–59°.

Kinetic Measurements on Saponification of Acid Phthalates.—The measurements were carried out with highly purified samples of the *cis*- and *trans*-3- and 4-*t*-butylcyclohexyl acid phthalates and on cyclohexyl acid phthalate, m.p. 97–98°.

Standard aqueous sodium hydroxide, carbonate free, was prepared using boiled distilled water, and it was stored in waxed bottles. The variation in titer after heating for 24 hours at 100° in Pyrex ampoules was negligible.

The acid phthalate was dissolved in excess standard aqueous sodium hydroxide, and aliquots were sealed in Pyrex ampoules which were thermostated. After suitable time intervals, the remaining sodium hydroxide was titrated with standard potassium hydrogen phthalate. In the case of the *trans*-4- acid phthalate difficulties were caused due to precipitation of the alcohol in the reaction mixture. The aliquots were therefore pipetted out through plugs of glass wool. Although the *cis*-4-alcohol also precipitated, it was in very finely divided state and did not obstruct the pipet. The other alcohols remained liquid under the experimental conditions.

The rate constants were calculated using the integrated form of the equation for a second-order reaction.

The difference in rates of saponification of *equatorial* and *axial* isomers is such that the initial rate constant for saponification of a mixture affords an analysis of the mixture. Thus a mixture of *trans*- and *cis*-4-*t*-butylcyclohexyl acid phthalates containing 15.2% *trans* gave an initial saponification rate constant of 166×10^{-5} at 75°. This corresponds to 16% *trans*.

Rates of Chromic Acid Oxidation.—J. T. Baker analyzed chromium trioxide in approximately the correct amount was dissolved in 75% acetic acid (3 volumes acetic acid to 1 volume water), and the solution was standardized against *ca.* 0.01 *N* standard sodium thiosulfate solution.

The rates of oxidation of the alcohols were followed by removing 5-ml. aliquots of thermostated reaction mixture, adding 0.5 ml. of 5% sulfuric acid and 250 mg. of potassium iodide, and titrating the liberated iodine with standard sodium thiosulfate using starch indicator.

An excess of alcohol over chromic acid was employed in the rate runs to minimize drifts due to oxidation of ketone. Rate constants were calculated using a bimolecular form and the theoretical infinity titer. Second-order rate constants, followed to 50 or 60% reaction, were quite satisfactorily constant.

Rate constants were evaluated employing oxidation–reduction normalities for alcohol and chromic acid concentrations. These rate constants were then multiplied by the factor three, the adjusted values being listed in Table IV. The units of k_2 in Table IV are such that k_2 represents the rate in moles of alcohol being oxidized per liter when concentrations of alcohol and chromic trioxide are each 1 *M*.

Kinetics of Solvolysis.—Purified samples of the four *t*-butylcyclohexyl *p*-toluenesulfonates and cyclohexyl *p*-toluenesulfonate, m.p. 43.6–44.2°, were employed for rate measurements.

Anhydrous acetic and formic acids, water content below 0.02% by Karl Fischer titration, were prepared by the usual methods.[16,32] Ethanol was dried with magnesium or calcium. Ethanolic sodium ethoxide was prepared by dissolving clean sodium in absolute ethanol and titrating with standard potassium hydrogen phthalate using phenol-

phthalein as indicator. The standard sodium ethoxide in Pyrex ampoules showed negligible variation in titer under the conditions of the ethanolyses.

Ethanolysis and acetolysis rates were followed in the conventional manner. The formolysis rates were followed by pipetting 5-ml. aliquots into 20 ml. of pure dioxane and titrating with standard sodium acetate in acetic acid using brom cresol green in acetic acid as indicator.

Solvolysis Products.—The *cis*- and *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonates and 4-*t*-butylcyclohexene were treated as summarized in Table IX and as illustrated in the detailed descriptions of several cases which follow. The olefin obtained by chromatography possessed $n^{25}D$ 1.4558 ± 0.0002 in most cases. The olefin and alcohol yields corrected to 100% recovery are listed in Table IX as well as the actual % total recovery.

Acetolysis of *trans*-4-*t*-Butylcyclohexyl *p*-Toluenesulfonate XII.—A solution of 2.50 g. of *trans*-4-*t*-butylcyclohexyl toluenesulfonate in 200 ml. of 0.0481 *M* sodium acetate in acetic acid was kept at 100° for 7.5 hours (15 half-lives for acetolysis). The solution was diluted with water to *ca.* 1 liter and extracted 6 times with 100-ml. portions of pentane. The acetate remaining after fractionation of the washed and dried pentane extract was reduced with ethereal lithium aluminum hydride. The reaction mixture was worked up in the usual way and then chromatographed over alumina.

Successive elution with the indicated solvents gave the fractions: (1) 100 ml. of pentane, 673 mg. of oil, $n^{25}D$ 1.4579; (2) 100 ml. of pentane, 6 mg. of oil; (3) 100 ml. of pentane–20% ether, 28 mg. of material, m.p. 75–77°, m.p. on admixture with *trans*-4-*t*-butylcyclohexanol 61–74°; (4) 100 ml. of pentane–50% ether, 295 mg. of material, m.p. 67–75°; (5) 100 ml. of ether, no residue.

Fraction 4 was rechromatographed on 9 g. of alumina to give the following fractions: (1) 50 ml. of pentane, no residue; (2) 50 ml. of pentane, 63 mg. of material, m.p. 79–80.5°; (3) 50 ml. of pentane, 100 mg. of material, m.p. 80.5–82°, m.p. 81.5–82.5° on admixture with pure *cis*-4-*t*-butylcyclohexanol; (4) 50 ml. of pentane, 63 mg. of solid, m.p. 80–81°, m.p. 81–82° on admixture with pure *cis*-4-*t*-butylcyclohexanol, m.p. 62–79° on admixture with *trans*-4-*t*-butylcyclohexanol; (5) 50 ml. of pentane, 30 mg. of solid, m.p. 80–81°; (6) 100 ml. of ether, 40 mg. of solid, m.p. 68–75°. Fraction 6 was rechromatographed, eluting with pentane–50% ether. There was obtained 5 mg. of colored oil and 32 mg. of solid, m.p. 72–80°, undepressed on admixture with a 77:23 mixture of *cis*- and *trans*-4-*t*-butylcyclohexanols. The combined alcohol fractions had m.p. 76–79°, m.p. 76–80° on admixture with a 95:5 mixture of *cis*- and *trans*-4-*t*-butylcyclohexanols.

Formolysis of *trans*-4-*t*-Butylcyclohexyl *p*-Toluenesulfonate XII.—A solution of 2.379 g. of *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate in 250 ml. of 0.566 *M* sodium formate in formic acid was stirred at 25° for 75 hours. The product was worked up and reduced with lithium aluminum hydride in the usual way. Chromatography over 35 g. of alumina and elution with pentane gave 870 mg. (76%) of 4-*t*-butylcyclohexene, $n^{21}D$ 1.4569. Pentane–10% ether gave 10 mg. (0.8%) of an oil followed by 255 mg. (20.6%) of pure *cis*-4-*t*-butylcyclohexanol. Further elution afforded 30 mg. (2.4%) of oily alcohol mixture.

A solution of 2.6012 g. of toluenesulfonate in 250 ml. of 0.04 *M* sodium formate in formic acid was kept at 50.55° for 20 hours. Working up and chromatography in the usual way led to elution with pentane of 83 mg. (7%) of olefin, $n^{24}D$ 1.4550. Pentane–10% ether and stronger eluting solvents afforded a series of fractions of alcohol, most of which had m.p. 59–60°.

Preparation of a toluenesulfonate from 300 mg. of the alcohol mixture, m.p. 59–60°, by the conventional procedure afforded 110 mg. of material, m.p. 76–78°, m.p. 78–80° on admixture with authentic *cis*-4-*t*-butylcyclohexyl toluenesulfonate, m.p. depressed by the *trans* isomer. This material displayed a steady first-order rate constant in acetolysis at 100° of $(154 \pm 8) \times 10^{-5}$ sec.$^{-1}$ in agreement with the value obtained with pure *cis*-4-*t*-butylcyclohexyl toluenesulfonate (Table V).

Chromic acid oxidation of 110 mg. of the alcohol mixture, m.p. 59–60°, afforded a ketone whose semicarbazone had m.p. 210–212°, m.p. 212–214° on admixture with authentic 4-*t*-butylcyclohexanone semicarbazone (m.p. 213–214°), m.p. markedly depressed on admixture with 3-*t*-butylcyclohexanone semicarbazone.

Treatment of 4-*t*-Butylcyclohexene with Formic Acid.—A solution of 2.003 g. of 4-*t*-butylcyclohexene (from the Chugaev method) in 200 ml. of dry formic acid was stirred at 25° for 94 hours. The mixture was diluted to 1500 ml. with water, and the reaction products were extracted with six 50-ml. portions of pentane. Removal of the pentane through a Vigreux column afforded a residual oil which was reduced with lithium aluminum hydride in ether in the usual manner. The product was chromatographed over 65 g. of commercial activated alumina.

Elution with pentane yielded 420 mg. (21%) of olefin, $n^{21}D$ 1.4575. Using ether–pentane (5–25% ether), a series of alcohol fractions, numbers 4 to 14, totaling 1.120 g. (50%), was eluted. These had melting points between 45 and 60°.

From fraction 5, *trans*-3-*t*-butylcyclohexanol, m.p. 47–48°, undepressed on admixture with authentic material, crystallized.

Fractions 6 and 7, m.p. 45–55°, gave an acid phthalate, the saponification rate of which indicated no equatorial material.

Fractions 10 and 11, m.p. 59°, gave an acid phthalate whose saponification appeared to indicate *ca.* 9% of a rapidly saponifying acid phthalate. The initial rate constant in saponification was *ca.* 130×10^{-5} at 75°.

Acetolysis of *cis*-4-*t*-Butylcyclohexyl *p*-Toluenesulfonate XIX.—A solution of 1.9950 g. of *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate in 180 ml. of 0.0481 *M* sodium acetate in acetic acid was kept at 100° for 2 hours. The product was worked up and reduced with lithium aluminum hydride in the usual way. Chromatography over 30 g. of alumina and elution with pentane gave 745 mg. (83%) of hydrocarbon, $n^{24}D$ 1.4563. Elution with ether afforded 180 mg. of an oily alcohol which on rechromatography yielded 100 mg. (9.9%) of oily alcohol and 72 mg. (7.1%) of pure *trans*-4-*t*-butylcyclohexanol, m.p. 78–80°, m.p. 79–80° on admixture with pure *trans*-alcohol.

On a larger scale, 10 g. of the toluenesulfonate in 1000 ml. of 0.049 *M* sodium acetate in acetic acid at 100° for 2.25 hours gave rise finally to 87.9% olefin, 7.8% of oily alcohol mixture and 4.3% of pure *trans*-4-*t*-butylcyclohexanol.

A 210-mg. quantity of the oily alcohol mixture in 5 ml. of acetic acid was oxidized to ketone by adding it to a solution of 130 mg. of chromium trioxide in 10 ml. of 95% acetic acid. The mixture was left overnight at 0° and at room temperature for 2 days. Then the ketone product was extracted with pentane and the extract was washed with sodium bicarbonate solution. The solvent was distilled through a Vigreux column and the residue was distilled at reduced pressure. The infrared spectrum of the ketone was compared with the spectrum of 3-*t*-butylcyclohexanone and 68:32 and 48:52 mixtures of 4- and 3-*t*-butylcyclohexanones. The 3-ketone shows pronounced absorption bands at 7.75, 7.85 and 8.05 μ, while the mixtures containing the 4-ketone show a band developing at 11.8 μ due to the 4-ketone. From an estimate of the relative intensities of the peaks the ketone obtained from the oily alcohol contains *ca.* 50% of the 3-ketone.

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