Stereochemical Studies. Part XLVI.* The 2-Alkylcyclohexyl Tosylate Solvolysis Problem: The Solvolysis of the 2-Methyl-4-t-butylcyclohexyl Tosylates †

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Hypotheses formerly suggested to explain the solvolytic behaviour of the 2-alkylcyclohexyl tosylates are briefly reviewed. A study is reported of the acetolysis and ethanolysis of the four stereoisomeric 2-methyl-4-t-butylcyclohexyl tosylates. A comparison with analogous data for the *cis*- and *trans*-4-*t*-butylcyclohexyl tosylates clarifies the effects of a vicinal methyl group, in all four positions relative to the tosyloxy-group, on rate and product composition. The ethanolysis rate of (axial) *cis*-4-*t*-butylcyclohexyl tosylate is reduced by an axial 2-methyl group by a factor of 1·15 but accelerated by a factor of 9·5 by an equatorial 2-methyl group; the reaction of (equatorial) *trans*-4-*t*-butylcyclohexyl tosylate is slowed by a factor of about 3 by an equatorial 2-methyl but accelerated by factor of 30 by an axial 2-methyl group. The rate relationships for the acetolysis are quite similar. Olefins form 73—87% of the total product in acetolysis of all the four 2-methyl-4-t-butyltoluenesulphonates. The two isomers in which the toluenesulphonyloxy- and the methyl group are *cis* to each other afford a significantly higher proportion of rearranged products than do the others in which the tosyloxy- and the methyl groups are *trans* to each other. Further, the percentage of inverted unrearranged substitution products is notably lower in the '*cis*'- than in the '*trans*'-isomers. These results substantiate and extend former findings on conformationally less well-defined 2-alkylcyclohexyl tosylates (*e.g.*, the menthyl tosylate series) and are best rationalised (*a*) by postulating rate acceleration through hydrogen participation in the case of *both* '*cis*'-isomers and (*b*) by assuming that the isomers with an equatorial tosyloxy-group react mainly, or exclusively, by way of a non-chair transition state.

THE solvolysis of a large number of 2-alkylcyclohexyl tosylates has been investigated.[1-12] The most interesting features in the solvolysis of these compounds are the very considerably higher rates of the *cis*- than of the *trans*-isomers. Thus, for the 2-methylcyclohexanols (VI and V) the *cis*-to-*trans* rate ratio is 68, for the 2-isopropylcyclohexanols it is 44, and for the isomenthol–menthol pair it is about 100.

Winstein and his co-workers have suggested [2] that the high rates of the *cis*-isomers relative both to the *trans*-isomers and to cyclohexyl tosylate are due to assistance, in the ionisation step, by the hydrogen on the carbon carrying the alkyl group. This 'nucleophilic' hydrogen can become anti-periplanar to the leaving tosyloxy-group in the case of the 2-*cis*-isomer but not in the corresponding 2-*trans*-isomer, whatever the conformation of the six-membered ring. This interpretation has been questioned by Goering and Reeves [3] on the grounds that the rate constants of the solvolysis of *cis*- and *trans*-2-t-butylcyclohexyl tosylate differ only by a factor of about 2, it being 'difficult to see why hydrogen participation should result in increased reactivity with an adjacent equatorial methyl or isopropyl group but not with a t-butyl group.' The hydrogen-participation hypothesis has also been attacked by Moritani, Nishida, and Murakami [4] on the basis of data on the product composition of the solvolysis of *trans*,*cis*-α-decalyl tosylate. In the preceding paper,[13] however, it has been shown that the experimental findings of the Japanese authors are erroneous.§

Hückel [1,14] visualised the difference in rates to result from the following steric feature: In the course of the chair–chair transition (ring flipping) only *cis*-placed vicinal substituents pass through a 'true syn-planar position,' *trans*-placed substituents do not. The reaction in the case of the *cis*-isomers is visualised as taking place 'in the moment of syn-planarity' and its rate as depending on the 'frequency of flipping' (or mobility of the ring).

Wohl [15] and, subsequently, Grob and Tam [16] suggested that the much higher solvolysis rates of the *cis*-isomers can be ascribed mainly to the difference in the direct steric interactions between the substituents in the two isomers. Since the cyclohexane ring is a slightly

* Part XLV, M. Tichý and J. Sicher, *Coll. Czech. Chem. Com.*, 1968, **33**, 68.

† Presented in part at the International Symposium on Reaction Mechanisms, Cork, Ireland (June 1964).

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§ Hückel had earlier [1] criticised the hydrogen participation hypothesis but later considered [5] it as *one* of the causes contributing towards the high rates of the *cis*-isomers.

[1] W. Hückel, R. Bross, O. Fechtig, H. Feltkamp, S. Geiger, M. Hanack, M. Heinzel, A. Hubele, J. Kurz, M. Maier, D. Maucher, G. Näher, R. Neidlein, and R. B. Rashingkar, *Annalen*, 1959, **624**, 142.

[2] S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan, and H. Marshall, *J. Amer. Chem. Soc.*, 1952, **74**, 1127.

[3] H. L. Goering and R. L. Reeves, *J. Amer. Chem. Soc.*, 1956, **78**, 4931.

[4] I. Moritani, S. Nishida, and M. Murakami, *J. Amer. Chem. Soc.*, 1959, **81**, 3420.

[5] W. Hückel and P. Heinzelmann, *Annalen*, 1965, **687**, 82.

[6] W. Hückel, H. Feltkamp, and S. Geiger, *Annalen*, 1960, **637**, 1.

[7] W. Hückel and W. Sommer, *Annalen*, 1965, **687**, 102.

[8] W. Hückel and H. D. Sauerland, *Annalen*, 1955, **592**, 190.

[9] W. Hückel, D. Maucher, O. Fechtig, J. Kurz, M. Heinzel, and A. Hubele, *Annalen*, 1961, **645**, 115.

[10] H. L. Goering, H. H. Espy, and W. D. Closson, *J. Amer. Chem. Soc.*, 1959, **81**, 329.

[11] A. P. Krapcho, J. E. McCullough, and K. V. Nahabedian, *J. Org. Chem.*, 1965, **30**, 139.

[12] C. W. Shoppee and G. A. R. Johnston, *J. Chem. Soc.*, 1961 3261.

[13] N. C. G. Campbell, D. A. Muir, R. R. Hill, H. Parish, R. M. Southam, and M. C. Whiting, *J. Chem. Soc.* (*B*), 1968, preceding paper.

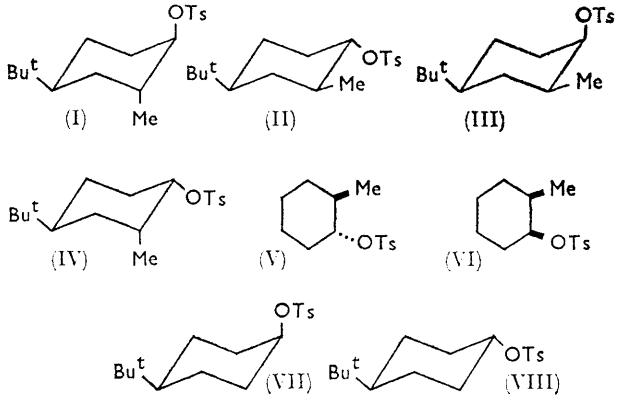
[14] W. Hückel, *Bull. Soc. chim. France*, 1960, 1369.

[15] R. A. Wohl, *Chimia*, 1964, **18**, 219.

[16] C. A. Grob and S. W. Tam, *Helv. Chim. Acta*, 1965, **48**, 1317.

flattened, rather than a perfect, chair,[17] a *cis*-2-alkyl substituent is closer to the leaving group than the *trans*-2-alkyl substituent and, therefore, the former produces greater steric acceleration on ionisation.

Most of the compounds studied hitherto, including the four stereoisomeric menthyl[1,2,6] and carvomenthyl tosylates,[5] have the serious disadvantage of conformational ambiguity. This ambiguity in the last two series essentially arises from the variable effective steric bulk of the isopropyl group. As stated by Stolow:[18] '*While* the methyl group *is* small, and the t-butyl group *is* large, the isopropyl group is anywhere intermediate in its effect.' Thus, *e.g.*, the 4-isopropyl group in the carvomenthols is effectively only slightly larger than the methyl and hence does not act as a conformation-holding group; by contrast, the 2-isopropyl group in the neomenthol in an axial position next to an equatorial hydroxyl becomes effectively extremely bulky, making the conformation of this compound again uncertain.



We felt, therefore, that a study of the solvolysis of a set of conformationally homogeneous 2-alkylcyclohexyl tosylates could help to clarify the complex and still confused situation. The four isomeric 2-methyl-4-t-butylcyclohexyl tosylates (I)—(IV) seemed to fulfil these requirements very well and a rate study of the acetolysis and ethanolysis, as well as a product study of the former, was therefore undertaken.*

RESULTS AND DISCUSSION

The outcome of the product analysis study of the acetolysis of the compounds (I)—(IV) is summarised in Table 1.

The olefin : acetate ratio for all the four isomers is rather similar, being very roughly 4 : 1. One significant difference between the two '*cis*'- and the two '*trans*'-isomers (that is, isomers having the 2-alkyl group *cis*- and *trans*- to the sulphonate residue) is that in the former pair there is a greater proportion of products which must have arisen by rearrangement.†

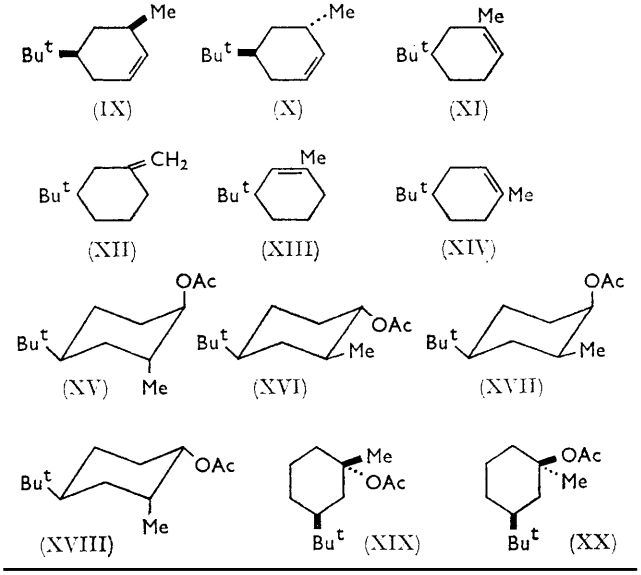
* Hückel and Sommer[7] recently reported a study of the solvolysis of the 5-methyl-2-t-butylcyclohexyl tosylates. As is apparent from an earlier study of Goering and Reeves,[3] the 2-t-butylcyclohexyl tosylates represent a somewhat special case, suggesting that the conclusions are not immediately relevant to those of 2-alkylcyclohexyl tosylates with other, less bulky, groups.

TABLE 1

Products of the acetolysis of the tosylates (I)—(IV) (see Scheme 1)

Product	(I)	(II)	(III)	(IV)
(IX)	—	16·1	1·1	—
(X)	26·0	—	—	0·8
(XI) [c]	41·4	35·0 [a]	58·9	54·7
(XII)	1·5	2·8 [a]	3·2	6·1
(XIII)	5·1	11·2	9·8	25·3
(XIV) [b]	1·1	0·9	—	—
Unidentified	4·2	11·3	0·2	—
Total elimination ...	79·3	77·3	73·2	86·9
(XV)	0·7	—	—	0·4
(XVI)	—	3·2	0·2	—
(XVII)	—	13·9	—	—
(XVIII)	5·8	—	—	0·1
(XIX)	7·2	1·1 [a]	21·8	7·7
(XX)	3·0	3·2 [a]	4·0	4·8
Unidentified	4·0	1·3	0·8	0·1
Total substitution ...	20·7	21·7	26·8	13·1

[a] Corrected for isomerisation of the olefins and for addition of acetic acid to them, as estimated on the basis of experiments involving heating the appropriate olefins under the reaction conditions. [b] Prepared according to Cross and Whitham (*J. Chem. Soc.*, 1960, 3892). [c] Synthesised from 5-t-butylcyclohex-1-enecarboxylic acid as will be described subsequently.



† An uncertainty is introduced by the fact that the cyclohexene derivative (XI), which is the principal product in the reaction, could be formed either directly or by rearrangement. However, some indications as to the origin of (XI) may be obtained by reference to the relative proportions of (XIII) formed from the isomeric tosylates (I)—(IV). The compound (XI), when it is formed by rearrangement, arises from the same carbonium ion precursor as (XII) or (XIII). Since the ratio (XIII) to (XII) is reasonably constant (3·4), it is probable that the ratio of (XI) *formed by rearrangement* to (XIII) or (XII) will also be reasonably constant. Since the overall percentage of the olefin (XI) formed from the '*cis*'-isomers (III) and (IV) is considerably higher than from the '*trans*'-isomers (I) and (II), it follows that the proportion of olefin (XI) formed by rearrangement from the '*cis*'-isomers will be larger than that formed *via* by rearrangement from the '*trans*'-isomers. Thus the products from the '*cis*'-isomers (III) and (IV) are probably nearer to the upper limits given than are those from the '*trans*'-isomers (I) and (II).

[17] J. Fridrichson and A. McL. Mathieson, *Acta Cryst.*, 1962, **15**, 119; O. Hassel and M. Davis, *Acta Chem. Scand.*, 1963, **17**, 1181; P. Groth and O. Hassel, *ibid.*, 1965, **19**, 1709; H. J. V. H. Greise, Thesis, Leiden, 1964.

[18] R. D. Stolow, *J. Amer. Chem. Soc.*, 1964, **86**, 2170.

Thus, whereas the '*trans*'-isomer (I) gives 26·1—67·5% of rearrangement products, the corresponding (tosyloxy-axial) '*cis*'-isomer (III) gives 39·8—98·7% of rearrangement product. Analogously, the '*trans*'-isomer (II) gives 31·8—66·8%, the '*cis*'-isomer (IV) gives 44·0—98·7% of rearrangement products.

The difference between the '*cis*'- and the '*trans*'-isomers is even more strikingly evident from a comparison of the percentage of 'inverted' (*i.e.*, inverted, unrearranged) substitution products: whereas the '*trans*'-isomers (I) and (II) yielded 5·8 and 13·9% of the 'inverted' acetates, respectively, the '*cis*'-isomers (III) and (IV) yielded as little as 0·2 and 0·4% of the corresponding products. A comparison of these figures with the corresponding data [13] from the acetolysis of *cis*- and *trans*-4-t-butylcyclohexyl tosylate is also instructive. *cis*-4-t-Butylcyclohexyl tosylate gives 7·5% of the 'inverted' acetate (4-t-butylcyclohexyl acetate) and *trans*-4-t-butylcyclohexyl tosylate gives 19% of the 'inverted' acetate. The extent of 'inverted' acetate formation from the '*cis*'-isomers (III) and (IV) hence represents only some 2—3% of the extent of substitution in the corresponding non-methylated analogues; by contrast, in the case of the '*trans*'-isomers (I) and (II) the extent of 'inverted' acetate formation represents as much as 75% of the extent of 'inverted' acetate formation in the parent compounds (VII) and (VIII). Thus, while a methyl group *trans* to the tosyloxy-group has only a very small effect on the course of the substitution reaction, a methyl placed *cis* to the tosyloxy-group has a very pronounced effect (suppressing the formation of inverted, unrearranged substitution product).

The rate results (Scheme 1) show that the isomers in which the methyl and the tosyloxy-groups are *cis* to each other [compounds (III) and (IV)] react considerably more rapidly than the compounds in which these groups are *trans* to each other [compounds (I) and (II)], irrespective of the conformational relationship of the two groups. Of particular interest is the very high rate of the '*cis*'-isomer (IV) in which the main conformer has an equatorial tosyloxy-group. By comparing the rates of *cis*- and *trans*-4-t-butylcyclohexyl tosylates (VII) and (VIII) with those of the appropriate isomers of the four 2-methyl-4-t-butylcyclohexyl tosylates (I)—(IV) we now, for the first time, can estimate the effect of a vicinal methyl group in all the four mutual steric positions to the tosyloxy-group on solvolysis rate. The appropriate figures, expressed as the ratios of rates (k_{Me}/k_H) of the 2-methylcyclohexyl tosylate (k_{Me}) to those of the corresponding cyclohexyl tosylates (k_H), are also given in Scheme 1.

The effect of introducing a methyl *trans* to the tosyloxy-group has a small rate-retarding effect in the case of the mainly equatorial tosyloxy-group ($k_{Me}/k_H = 1/3$) and only a negligible effect in the case of the axial tosyloxy-group (k_{Me}/k_H = *ca.* 1). On the other hand, introduction of a methyl *cis* to the tosyloxy-groups leads to a notable rate enhancement, by a factor of *ca.* 10 in the case of the axial tosyloxy-group, and by a factor of *ca.* 30 in the case of the equatorial tosyloxy-group.

There is thus far-reaching similarity in the behaviour of the two '*cis*'-isomers (III) and (IV), both with respect to product composition (high proportion of rearrangement products), as well as with respect to rate

SCHEME 1

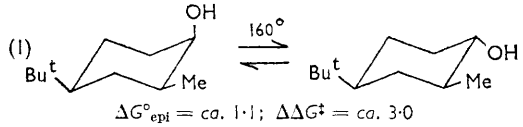
		(I)	(II)	(III)	(IV)
10^6k (70°)	Ethanolysis	29·9	3·76 [a]	367	363
	Acetolysis ...	62·5	7·88	619	617
$\frac{k_{Me}}{k_H}$	Ethanolysis	1/1·25	1/3·19	9·84	30·3
	Acetolysis ...	1·14	1/2·68	11·2	29·3
		(V)	(VI)	(VII)	(VIII)
10^6k (70°)	Ethanolysis	3·70 [b]	280	37·3	12·0
	Acetolysis ...	7·87	404	54·8	21·1

[a] $\Delta H^{\ddagger} = 26·4$, $\Delta S^{\ddagger} = -7·0$; [b] $\Delta H^{\ddagger} = 26·6$, $\Delta S^{\ddagger} = -6·0$. Rates of ethanolysis and/or acetolysis of these compounds have already been determined by other authors (see refs. 1, 8, 25) though not at 70°. A computation of k_{70} from the literature data shows fair to good agreement with the rate constants now determined.

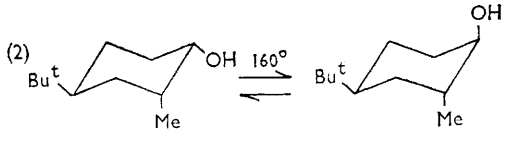
(large rate enhancement as a result of introduction of methyl *cis* to the tosyloxy-group, regardless whether the latter is axial or equatorial). It therefore is tempting to conclude that whatever interpretation is correct for the reaction of the '*cis*'-isomer (III) will probably also apply to the other '*cis*'-isomer (IV).

We now consider the hypothesis [15,16] that the much higher rates of solvolysis of the *cis*- than of the *trans*-isomers are due to the difference in the direct steric interactions between the vicinal substituents in the two isomers. The difference between the ground-state strain in the isomeric '*cis*' and '*trans*' tosylates (III) and (II) as well as (IV) and (I) should be close to those of the corresponding parent alcohols, as reflected in the free energies ($\Delta G°_{epi}$) corresponding to the equilibria (1) and (2) (Scheme 2). In a parallel study [19] we have determined the equilibria (1) and (2), *i.e.*, the values of $\Delta G°_{epi}$.*

SCHEME 2



$\Delta G°_{epi}$ = *ca.* 1·1; $\Delta\Delta G^{\ddagger}$ = *ca.* 3·0



$\Delta G°_{epi}$ = *ca.* 0·0; $\Delta\Delta G^{\ddagger}$ = *ca.* 1·7

Considering the '*cis*'–'*trans*' pair of Equilibrium 1 we see that the free energy corresponding to it is about 1·1 kcal. mole^{-1}; the differences in the free energies of

* The rate and the equilibration data refer to different temperatures; simple consideration suggests, however, that this cannot affect the validity of our semi-quantitative conclusions.

[19] J. Sicher and M. Tichý, *Coll. Czech. Chem. Comm.*, 1967, **32**, 3687.

activation of the solvolyses of the corresponding tosylates, (III) and (II), $\Delta\Delta G^{\ddagger}_{III-II}$ (*i.e.*, $\Delta G^{\ddagger}_{III}-\Delta G^{\ddagger}_{II}$), however, is as large as 3 kcal. mole^{-1}. Similarly, for the second '*cis*'–'*trans*' isomer pair (Equilibrium 2), the free-energy difference of the epimerisation is close to zero, whereas the difference in the free energies of activation of the corresponding tosylates (IV) and (I), $\Delta\Delta G^{\ddagger}_{IV-I}$, corresponds to about 1·7 kcal. mole^{-1}. Further, the differences in the direct steric interactions cannot account for the observed considerable differences in product composition. From this it seems that differences in direct steric interactions, though probably contributing to the observed large differences between the '*cis*'- and the '*trans*'-isomers, can hardly be the dominating factor responsible.

The solvolytic behaviour of the '*cis*'-isomers (III) and (IV) (*i.e.*, the high percentage of rearrangement as well as the relatively high rates) could be accounted for by postulating participation of the C(2)–H hydrogen. Now, hydrogen participation is readily visualised as operating in the '*cis*'-isomer (III), since here the tosyloxy-group is anti-periplanar to the potentially participating hydrogen in the chair form. If, in accordance with current theory, it is accepted that hydrogen participation requires anti-periplanarity of the hydrogen and the tosyloxy-group, a stereochemical difficulty arises in the case of the '*cis*'-isomer (IV) because in a chair-type transition state, anti-planarity cannot be attained, though it could be met in a non-chair transition state. A non-chair transition state for the reaction of the '*cis*'-isomer (IV) would also account for the surprising fact that the rate acceleration resulting from the introduction of the 2-methyl group (expressed as k_{Me}/k_{H}, Scheme 2) is higher in (IV) than in (III) (30 as compared with 10). In the solvolysis of (IV) there should be strain relief on going from the chair ground state (with the axial methyl) to the non-chair transition state; there is no analogous strain relief [relative to the 'non-methylated' compound (VII)] in the solvolysis of the '*cis*'-isomer (III).

A non-chair transition state has recently been suggested for the solvolysis of *trans*-4-t-butylcyclohexyl tosylate (VIII) by Shiner and Jewett [20] on the basis of the secondary deuterium isotope effects and their conclusions have found support in studies of solvolysis products reported in the preceding paper.[13] We also postulated a non-chair transition state for an intramolecular substitution in a cyclohexane system.[21]

Quite recently, Jones, Squires, and Lynn [22] discussed a non-chair transition state for a bimolecular elimination process.

Comparison with Rates of trans- *and* cis-2-*Methylcyclohexyl Tosylates* (V) *and* (IV) *with Rates of Corresponding 'Biased' Compounds* (I)—(IV).—*trans*-2-Methylcyclohexyl tosylate will, at the temperatures employed, exist essentially in the 'di-equatorial' conformation. The rates as well as thermodynamic parameters in both ethanolysis and acetolysis of *trans*-2-methylcyclohexyl tosylate are essentially identical with those of *trans*-2-methyl-*trans*-4-t-butylcyclohexyl tosylate (II), the all-equatorial isomer. Detailed conformational considerations and the marked discrepancies found recently for the rates and thermodynamic parameters for the solvolysis of the 4-t-butylcyclohexyl tosylates (VII) and (VIII) and cyclohexyl tosylate,[23] as well as other data,[24] make us feel that the agreement now observed is probably due to a fortuitous cancellation of effects rather than reflecting the near identity in ground and transition-state behaviour between the 'biased' and the 'mobile' compound postulated by the Winstein–Holness hypothesis.[25] Indeed, a comparison of the rates of the two 'biased' '*cis*'-isomers (III) and (IV) with that of *cis*-2-methylcyclohexyl tosylate (VI) (Scheme 1) supports this conclusion since the rate constant of the latter is lower than that of the biased derivatives (III) and (IV) by factors of 1·3 and 1·5, and thus falls outside the range within which it is supposed to lie.

EXPERIMENTAL

Synthesis of Tosylates.—The synthesis of the four isomeric 2-methyl-4-t-butylcyclohexanols has been reported; [26] the tosylates (II) and (IV) have been described.[27] By the same procedures were prepared cis-4-*t-butyl*-trans-2-*methylcyclohexyl* p-*toluenesulphonate* (I), m. p. 81—82° (from light petroleum) (Found: C, 66·70; H, 8·55. $C_{18}H_{28}O_3S$ requires C, 66·6; H, 8·7%) and cis-4-*t-butyl*-cis-2-*methylcyclohexyl* p-*toluenesulphonate* (III), m. p. 97—98° (from methanol) (Found: C, 66·7; H, 8·6. $C_{18}H_{28}O_3S$ requires C, 66·6; H, 8·7%).

Kinetic Measurements.—Solutions (0·0005M in tosyl ester in ethanol) (containing 0·17% of water according to a Karl Fischer titration) or acetic acid (containing about 0·05% water) were made up and 10 c.c. aliquot portions heated in sealed glass tubes in a constant-temperature bath, and quenched at intervals.

In ethanolysis, the reaction was quenched by rapidly cooling in an ice-bath and the contents were added to 100 c.c. of water. The toluenesulphonic acid liberated was titrated with aqueous 0·02N-sodium hydroxide with bromothymol blue–phenol red (1 : 1) in ethanol as indicator.

In the acetolysis runs 10 c.c. were pipetted from the 11—12 c.c. contents of each of the quenched ampoules and titrated with sodium acetate in glacial acetic acid with bromothymol blue in acetic acid as indicator.

A typical run is reproduced in Table 2.

[20] V. J. Shiner and J. G. Jewett, *J. Amer. Chem. Soc.*, 1965, **87**, 1382.
[21] J. Sicher, M. Tichý, F. Šipoš, and M. Pánková, *Coll. Czech. Chem. Comm.*, 1961, **26**, 2418.
[22] W. M. Jones, T. G. Squires, and M. Lynn, *J. Amer. Chem. Soc.*, 1966, **89**, 318.
[23] J. L. Mateos, C. Perez, and H. Kwart, *Chem. Comm.*, 1967, 125.
[24] H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, 1964, **86**, 1161; E. L. Eliel and F. J. Biros, *ibid.*, 1966, **88**, 3339; F. Shah-Malak and J. H. P. Utley, *Chem. Comm.*, 1967, 69.
[25] S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.
[26] F. Šipoš, J. Krupička, M. Tichý, and J. Sicher, *Coll. Czech. Chem. Comm.*, 1962, **27**, 2079.
[27] J. Sicher, M. Tichý, and F. Šipoš, *Coll. Czech. Chem. Comm.*, 1966, **31**, 2238.

TABLE 2

Acetolysis of the tosylate (III) at 70·01°

Time (sec.)	C.c. of base per aliquot portion	10^4k (sec.$^{-1}$)
	0·30	
180	0·53	6·28
360	0·74	6·42
540	0·90	6·10
720	1·10	6·61
900	1·19	6·02
1080	1·29	5·80
1260	1·44	5·95
∞	2·42	

Mean 6·19 ± 0·09

cis-3-*Methyl*-5-*t*-*butylcyclohex*-1-*ene* (IX).—A mixture *cis*-2-methyl-*cis*-4-t-butylcyclohexyldimethylamine [28] was shaken with 30% hydrogen peroxide (3 c.c.) and methanol (4 c.c.) until a clear solution was obtained; another 1 c.c. of hydrogen peroxide was added and the mixture was allowed to stand for 48 hr., when it no longer gave a colour with phenolphthalein. The excess of hydrogen peroxide was destroyed by adding platinum black under nitrogen, the mixture was filtered, and the filtrate taken to dryness under reduced pressure. The pyrolysis was carried out in a Hickman flask whose receiver was cooled with solid carbon dioxide–acetone. The distillate was taken up in ether, extracted with dilute hydrochloric acid, then water, the extract was dried, and the residue was distilled; yield 0·4 g. (65%), b. p. 85—87°/35 mm., n_D^{20} 1·4580 (Found: C, 86·0; H, 13·05. $C_{11}H_{20}$ requires C, 86·75; H, 13·25%).

trans-3-*Methyl*-5-*t*-*butylcyclohex*-1-*ene* (X).—The same procedure when applied to *cis*-2-methyl-*trans*-4-t-butylcyclohexyldimethylamine [28] afforded the olefin (X) in 56% yield, b. p. 63°/10 mm., n_D^{20} 1·4566 (Found: C, 86·55; H, 13·25%).

3-*t*-*Butylmethylenecyclohexane* (XII).—A solution of butyllithium (10 mmoles) in ether was added to a suspension of triphenylmethylphosphonium bromide (4·04 g,. 10 mmoles) in ether (50 c.c.) and the mixture shaken for 2 hr. The resulting yellow solution was treated with 3-t-butylcyclohexanone [29] (1·54 g., 10 mmoles), the mixture was shaken for 2 hr., and allowed to stand overnight. The inorganic material was removed on the centrifuge, the ethereal supernatant liquid was washed with water, dried, and evaporated. The residue was chromatographed on alumina (30 g., grade II—III) from pentane which gave 0·8 g. (52·5%) of the pure olefin, b. p. 68—69°/10 mm., n_D^{20} 1·4603 (Found: C, 87·15; H, 13·0%).

cis- *and* trans-1-*Methyl*-3-*t*-*butylcyclohexanol*.—3-t-Butylcyclohexanone [30] (2·0 g.) was allowed to react with the Grignard reagent, prepared from methyl iodide (4·0 g.) and magnesium (0·7 g.) in ether (50 c.c.), for 1 hr. at room temperature. The mixture was then treated with saturated aqueous ammonium chloride (50 c.c.) and water, dried, and evaporated. The solid residue (2·0 g.) was chromatographed on alumina (grade II—III, 250 g.). The light petroleum–ether eluates afforded 1·5 g. of pure trans-*isomer*, m. p. 84—85·5°, ν_{OH} (stretch) 3612 cm.$^{-1}$ (5×10^{-3}M in CCl_4) (Found: C, 77·6; H, 12·97. $C_{11}H_{22}O$ requires C, 77·6; H, 13·0%).

The ethereal eluates afforded 0·2 g. of the pure cis-*isomer*, m. p. 65—67°, ν_{OH} (stretch) 3612 cm.$^{-1}$ (5×10^{-3}M in CCl_4) (Found: C, 77·7; H, 12·85%).

[28] J. Krupička, J. Sicher, J. Závada, and M. Tichý, to be published.

The configurations were assigned on the basis of the OH stretching frequencies and the order of elution in the absorption as well as gas–liquid chromatography.

Mixture of 1-*Methyl*-3-*t*-*butylcyclohexene* (XIII), 2-*Methyl*-5-*t*-*butylcyclohexene* (XI), *and* 1-*Methylene*-3-t-*butylcyclohexane* (XII).—A solution of *trans*-1-methyl-3-t-butylcyclohexanol (0·2 g.) and phosphorus oxychloride (0·5 c.c.) in pyridine (5 c.c.) was left for 48 hr., then treated with water, the mixture was extracted with pentane, the extracts were washed with dilute hydrochloric acid, sodium hydrogen carbonate, and water, dried, and evaporated. The residue was chromatographed on alumina (15 g., grade II). The pentane eluates were directly analysed by gas chromatography on the silver nitrate column; the chromatogram exhibited only three peaks of which two were identical with those of the olefins (XI) and (XII), independently prepared by other methods (see above); the third peak was therefore assigned to the olefin (XIII).

trans-1-*Methyl*-3-*t*-*butylcyclohexyl Acetate* (XIX).—A solution of phenyl-lithium (from 0·15 g. lithium and 1·3 g. bromobenzene) in ether (25 c.c.) was treated with *trans*-1-methyl-3-t-butylcyclohexanol (0·7 g.) and, after the latter had all dissolved, with acetic anhydride (1·0 g.). The mixture was shaken for 20 min., treated with dilute hydrochloric acid, and the ethereal layer washed with aqueous sodium hydrogen carbonate. Distillation afforded 0·7 g. of the crude product which was freed from small amounts of the starting alcohol by chromatography on alumina (grade II). The pure *acetate* has n_D^{20} 1·4503 (Found: C, 73·7; H, 11·3. $C_{13}H_{24}O_2$ requires C, 73·55; H, 11·4%).

cis-1-*Methyl*-3-*t*-*butylcyclohexyl Acetate* (XX).—Synthesised as described above for the *trans*-isomer, the pure compound has n_D^{20} 1·4564 (Found: C, 73·45; H, 11·15%).

Synthesis of the Four Steroisomeric 2-*Methyl*-4-*t*-*butylcyclohexyl Actates* (XV)—(XVIII).—The appropriate 2-methyl-4-t-butylcyclohexanol (0·002 mole) was treated with acetic anhydride (0·002 mole) in pyridine (3 c.c.); after standing overnight, the mixture was poured into dilute hydrochloric acid, the product was extracted with ether and, after evaporation of the solvent, distilled. The refractive indices and elemental analyses of the acetates are given in Table 3.

TABLE 3

2-Methyl-4-t-butylcyclohexyl acetates

($C_{13}H_{24}O_2$ requires C, 73·55; H, 11·4%)

Compound	Configuration	n_D^{20}	C (%)	H (%)
(XV)	$OH^aCH^a_3$	1·4509	73·85	11·4
(XVI)	$OH^eCH^e_3$	1·4517	73·75	11·3
(XVII)	$OH^aCH^e_3$	1·4499	73·9	11·45
(XVIII)	$OH^eCH^a_3$	1·4541	73·8	11·45

Preparative-scale Acetolysis.—A solution of the tosylate (I)—(IV) (0·0005 mole) in 10 c.c. of anhydrous acetic acid containing dry sodium acetate (0·01 mole) and *cis*-decalin (38·39 mg.) as internal standard was heated in a sealed ampoule to 100° for 10 half-lives (30 min. to 20 hr.). The contents were shaken between pentane (5 c.c.) and an aqueous solution (35 c.c.) containing potassium monohydrogen orthophosphate (30 g.) and potassium hydroxide (9·2 g.). The organic layer (injection about 15 μl.) was

[29] M. Tichý, F. Šipoš, and J. Sicher, *Coll. Czech. Chem. Comm.*, 1962, **27**, 2907.

[30] B. Cross and G. H. Whitham, *J. Chem. Soc.*, 1960, 3892.

directly analysed by gas chromatography. The analysis was performed on a 4 m. column filled with GEO 100 on Embacel (15% w/w).[13] The olefins and acetates were analysed in a single run; the former at 80°/500 mm. of nitrogen, and the acetates at 120°/820 mm. of nitrogen. One complete run took 4 hr.

The molar response ratios olefin *vs.* *cis*-decalin, and acetate *vs.* *cis*-decalin were 1·207 and 1·198, respectively. The analyses are given in Table 1; the yields were calculated from the sum of the peak areas and their ratio to the peak area of the internal standard.

Actual yields were computed from ratios of the product areas to the area of the known amount of octalin, added before the reaction. In all cases the computed total yields were in the region 97—106%; this indicates that no significant amount of products other than those here reported was formed.

In the system GEO 100 on Embacel we were unable to separate the olefins (XIII) and (IX), and only imperfectly the *cis–trans* isomer pair (IX) and (X). In order to determine these we first separated the olefins from the acetates by chromatography on alumina (25 g., deactivated with 1·2 c.c. of 10% acetic acid); a control analysis on the GEO column showed that acetates have been completely removed and that the chromatography did not affect the olefin composition.

The *cis–trans* isomers (IX) and (X) could be separated on a 12 m. column containing 15% bis(cyanoethoxy)ethane on Embacel at 76°; the olefin (XIII) was separated from all the other isomers on a 2·5 m. column containing 4% silver nitrate–triethylene glycol (1 : 1) at 50°.

Most of the work on the analysis of acetolysis products was carried out in the Dyson Perrins Laboratory, Oxford; the remainder, and all the kinetic work, in the Institute of Organic Chemistry and Biochemistry, Czeckoslovak Academy of Science, Prague.

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