

COMPARISON OF β -DEUTERIUM EFFECTS IN SOLVOLYSIS OF PERHYDRO-*as*-INDACENYL AND VARIOUS 2-ALKYLCYCLOHEXYL *p*-TOLUENESULPHONATES*

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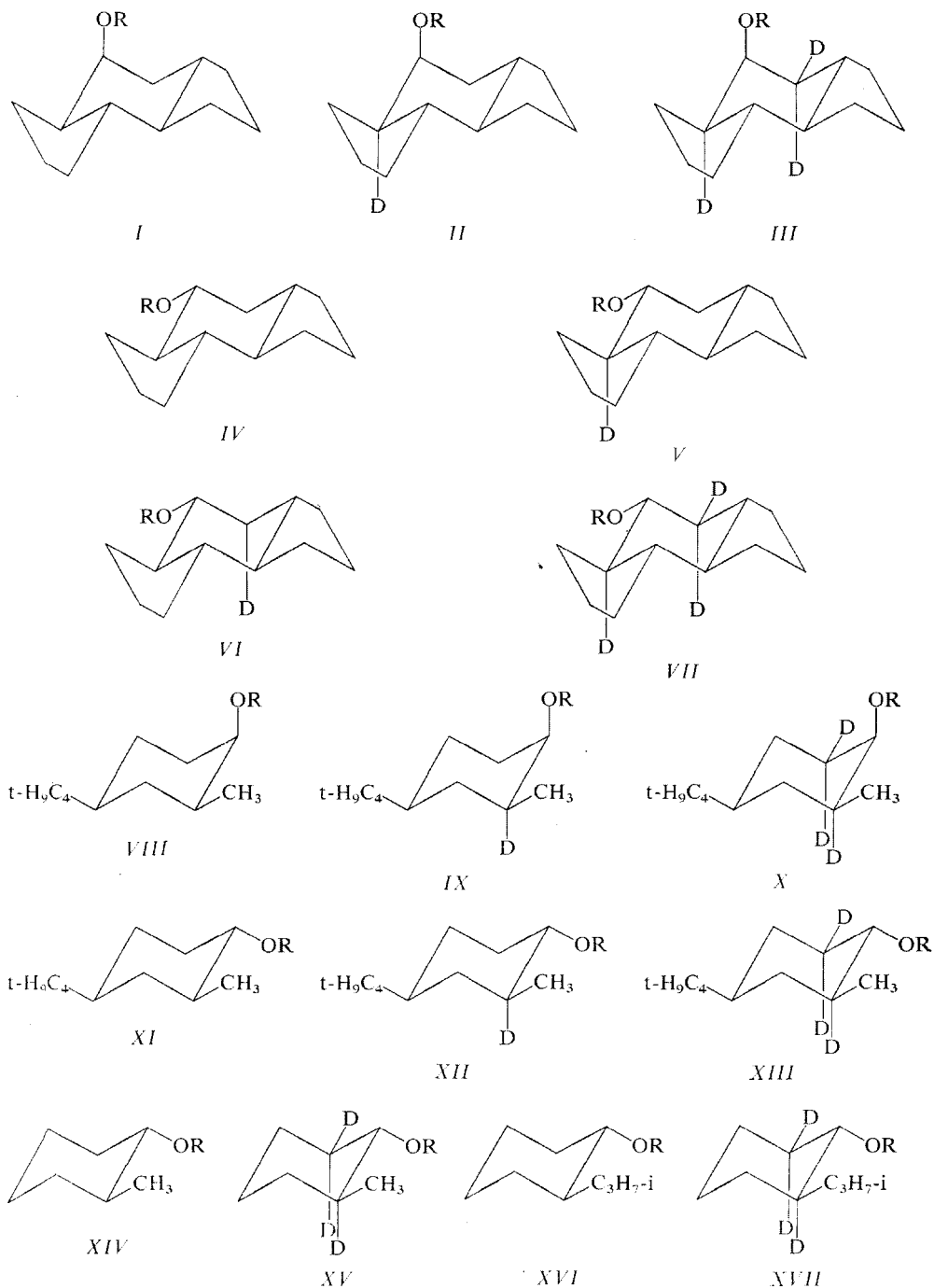
Epimeric 3-deuterio- and 3,5,5-trideuterio 4-*p*-toluenesulphonyloxy-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacenes, as well as 4-*tert*-butyl-2-methyl-, *trans*-2-methyl- and *trans*-2-isopropyl-2,6,6-trideuteriocyclohexyl *p*-toluenesulphonates, were synthesized and their β -deuterium effects in trifluoroethanolysis were determined. The equatorial perhydro-*as*-indacetyl *p*-toluenesulphonate *IVb* was found to be a model of "limiting" equatorial solvolysis. A discrepancy was found between the order of isotope effects for the individual 2-alkylcyclohexyl systems and the assumed ease of ring distortion in the transition state.

The question of the transition states in the solvolysis of variously substituted cyclohexyl *p*-toluenesulphonates has attracted considerable attention and has been tackled from many sides (see refs¹⁻¹⁴ and references therein). In spite of this effort our knowledge of the real geometry of the cyclohexane ring in the transition state and of the effects of substituents is only fragmentary.

Perhaps the most promising approach was the study of isotope effects. Shiner and Jewett investigated β -isotope effects in the solvolysis of stereospecifically deuterated 4-*tert*-butylcyclohexyl *p*-bromobenzenesulphonates⁴. The isotope effects were consistent with a chair-like transition state with participation of the axial β -hydrogen in the case of the axial leaving group whereas the results obtained for the compound with the equatorial tosyloxy group indicated a non-chair transition state. Also, the investigations of Saunders⁵ on cyclohexyl *p*-toluenesulphonate were interpreted in terms of a non-chair transition state.

We studied⁷ some 4-*tert*-butyl-2-methylcyclohexyl *p*-toluenesulphonates deuterated at the tertiary carbon C₍₂₎ (such as *IXb* and *XIIb*) and have shown that, whereas both stereoisomers with methyl and *p*-toluenesulphonyloxy groups in the *cis*-relation exhibit a large isotope effect, indicating thus hydrogen participation, in isomers where methyl and the leaving group are *trans* to each other the effect of the β -deuterium is almost negligible, irrespective whether the *p*-toluenesulphonyloxy and the methyl groups are diaxial or diequatorial.

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In the formulae: a. R = H; b. R = Tos

Recently, Sunko and collaborators¹³, on the basis of a small β -deuterium effect found for solvolysis of menthyl *p*-toluenesulphonates, stated that one conformation holding group cannot prevent a "distortion of the chair conformation in the transition state" whereas two bulky substituents in positions 2,5 or 2,4 relative to the reacting center can hinder such distortion effectively. The simple diagnostics of such distortion suggested¹³ is based on the study of the isotope effect of fully β -deuterated compounds. Accordingly, a small β -deuterium effect (k_H/k_{D_3} or $k_H/k_{D_4} \sim 1.3$) indicates that the molecule reacts in a true "undistorted" chair transition state, whereas in the case of a large (2.2–2.4) isotope effect the chair is distorted.

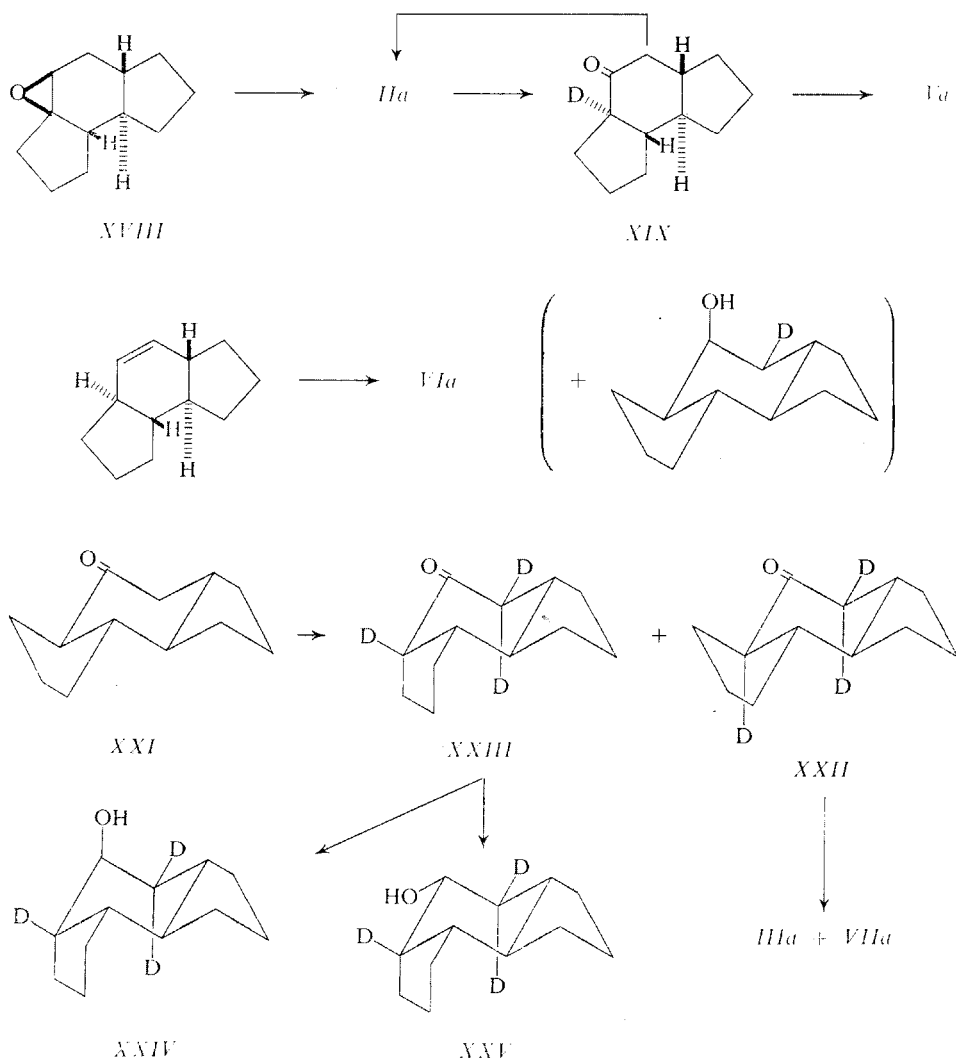
The models hitherto used in the β -deuterium effect studies can more or less be subjected to a ring deformation in the transition state, and therefore a "limiting" model of a rigid β -perdeuterated cyclohexyl *p*-toluenesulphonates would be of great value. Such a model could be found in *trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene derivatives¹⁵ in which the rigidity of the ring makes any distortion in the transition state highly improbable. We therefore prepared some compounds of this type, investigated the solvolysis of the epimeric 4-*p*-toluenesulphonyloxy derivatives of this system (*Ib* and *IVb*), measured β -deuterium effects for the corresponding β -mono (*Iib*, *Vb* and *VIb*) and β -trideuterated (*IIIb*, *VIIb*) *p*-toluenesulphonates and compared these values with other β -deuterated systems such as *trans*-4-*tert*-butyl-*trans*-2-methylcyclohexyl, *trans*-2-methylcyclohexyl and *trans*-2-isopropylcyclohexyl *p*-toluenesulphonates (*XIIIb*, *XVb* and *XVIIb*, respectively).

Preparation of the Compounds

The preparation of the axial and equatorial alcohols *Ia* and *IVa* was already described¹⁵. The 3a-monodeuterio alcohol *IIa* was prepared by lithium borodeuteride opening of the corresponding epoxide *XVIII*, as described¹⁵ for the non-deuterated compounds (Scheme 1). The epimeric alcohol *Va* was prepared by a careful oxidation of *IIa* to the ketone *XIX* which was immediately reduced to a mixture of *IIa* and *Va* and the pure compounds were obtained by chromatography. No loss of the deuterium content was observed during these operations. The 5a-monodeuterio alcohol *VIa* was prepared by deuterioboration of the olefin *XX* (ref.¹⁶), followed by chromatographic separation.

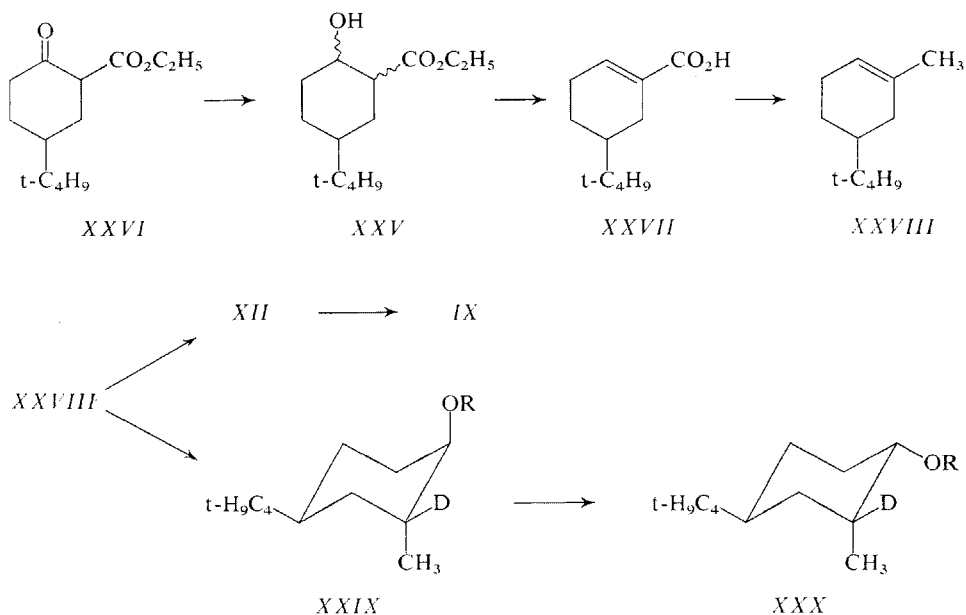
The β -trideuterio compounds *IIIa* and *VIIa* were prepared by reduction of the ketone *XXII*, which was obtained from *XXI* by a base-catalysed deuterium exchange in deuterium oxide. The exchange reaction was accompanied by epimerisation of the ketone *XXII* to its epimer *XXIII* which preponderated in the mixture. The crude mixture of the trideuterio ketones *XXII* and *XXIII* was reduced to the four epimeric alcohols *IIIa*, *VIIa*, *XXIV* and *XXV* and these were separated chromatographically (Scheme 1).

The monodeuterated 4-*tert*-butyl-2-methylcyclohexyl alcohols *IXa*, *XIIa*, *XXIXa* and *XXXa* (mentioned in⁷) were prepared by deuterioboration of 4-*tert*-butyl-2-methylcyclohexene (*XXVIII*) which in turn was obtained from 5-*tert*-butylcyclohex-1-ene-carboxylic acid (*XXVII*) (Scheme 2). Deuterioboration afforded the two “*trans*” alcohols *XIIa* and *XXIXa* which were separately transformed by fusion of their *p*-toluenesulphonates with tetrabutylammonium acetate into the “*cis*” alcohols *IXa* and *XXXa*. The compounds *Xa* and *XIIIa* were obtained by lithium aluminium reduction



SCHEME 1

of a mixture of epimeric 4-*tert*-butyl-2-methyl-2,6,6-trideuteriocyclohexanones and subsequent chromatographic purification. Also the alcohols *XVa* and *XVIIa* were prepared analogously from the corresponding trideuterio ketones.



In the formulae: *a*; R = H, *b*; R = Tos

SCHEME 2

Solvolysis of the Tricyclic *p*-Toluenesulphonates

Since the *p*-toluenesulphonate *IVb* can flip neither into another chair form nor into a boat, the participation of the solvent from the rear side of the carbon bearing the equatorial leaving group is hindered, similarly as (and perhaps still more effectively than) in 2-adamantyl *p*-toluenesulphonate. The perhydro-*as*-indacene system therefore can be regarded as another model for a limiting solvolysis¹⁷ in which the preferred reaction path is a front-side attack by the solvent. Moreover, this model has a secondary carbon in the vicinal position to the reacting center which allows realization of some situations which are not possible in adamantane derivatives, hitherto used as models¹⁷.

The solvolysis rates of the *p*-toluenesulphonates *Ib*–*VIIIb* in 70% ethanol and in 97% trifluoroethanol are given in Table I. We see that in 70% ethanol the reaction rate of the axial isomer *Ib* is similar to the corresponding monocyclic derivative

TABLE I

Rate Constants for Solvolysis of *p*-Toluenesulphonates *Ib*–*XIIIb* in 70% (vol) Ethanol (E) and 97% (wt/wt) Trifluoroethanol (TFE) at Various Temperatures

<i>p</i> -Toluene-sulphonate	Solvent	$k \cdot 10^5, s^{-1}$ (temperature, °C)
<i>Ib</i>	70% E	2.795 (25.0), 5.427 (30.0), 18.85 (40.0), 33.99 (45.0), 848 ± 17 (75.0) ^{a,b}
<i>IIb</i>	70% E	2.540 (30.0), 9.100 (40.0), 16.52 (45.0), 431 ± 11 (75.0) ^{a,c}
<i>IIIb</i>	70% E	2.285 (30.0), 8.194 (40.0), 15.01 (45.0), 404 ± 10 (75.0) ^{a,d}
<i>IVb</i>	70% E	2.346 (75.0)
	97% TFE	10.06 (70.0)
<i>Vb</i>	70% E	2.201 (75.0)
	97% TFE	0.993 (70.0)
<i>VIb</i>	97% TFE	10.00 (70.0)
<i>VIIb</i>	70% E	2.110 (75.0)
	97% TFE	9.68 (70.0)
<i>VIIIb</i>	70% E	2.126 (20.0), 4.170 (25.0), 8.066 (30.0), 27.75 (40.0), 1230 ± 20 (75.0) ^{a,e}
<i>IXb</i>	70% E	1.902 (25.0), 3.721 (30.0), 13.33 (40.0), 656 ± 10 (75.0) ^{a,f}
<i>Xb</i>	70% E	1.630 (25.0), 3.195 (30.0), 11.41 (40.0), 562 ± 8 (75.0) ^{a,g}
<i>XIb</i>	70% E	4.237 (65.0), 7.617 (70.0), 13.51 (75.0), 23.56 (80.0), 0.169 ± 0.002 (40.0) ^{a,h}
	97% TFE	20.10 (70.0), 6.477 (60.0)
<i>XIIb</i>	70% E	3.618 (65.0), 6.524 (70.0), 11.61 (75.0), 0.142 ± 0.003 (40.0) ^{a,i}
	97% TFE	5.438 (60.0), 16.96 (70.0)
<i>XIIIb</i>	70% E	2.594 (65.0), 4.705 (70.0), 8.434 (75.0), 0.098 ± 0.003 (40.0) ^{a,j}
	97% TFE	13.64 (70.0)

^a Extrapolated value, the errors are given as 95% confidence limits; ^b $\Delta H^\ddagger = 22.92 \pm 0.1$ kcal . mol⁻¹, $\Delta S^\ddagger = -2.5 \pm 0.3$ e.u.; ^c $\Delta H^\ddagger = 23.3 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -2.6 \pm 0.4$ e.u.; ^d $\Delta H^\ddagger = 23.6 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -2.7 \pm 0.3$ e.u.; ^e $\Delta H^\ddagger = 22.8 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -2.0 \pm 0.2$ e.u.; ^f $\Delta H^\ddagger = 23.4 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -1.5 \pm 0.2$ e.u.; ^g $\Delta H^\ddagger = 23.5 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -1.7 \pm 0.2$ e.u.; ^h $\Delta H^\ddagger = 26.5 \pm 0.05$ kcal mol⁻¹, $\Delta S^\ddagger = -0.5 \pm 0.2$ e.u.; ⁱ $\Delta H^\ddagger = 26.6 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -0.5 \pm 0.3$ e.u.; ^j $\Delta H^\ddagger = 26.9 \pm 0.1$ kcal mol⁻¹, $\Delta S^\ddagger = -0.2 \pm 0.4$ e.u.

VIIIb whereas the solvolysis of the equatorial isomer *IVb* is nearly six-times slower than that of the equatorial monocyclic derivative *XIb*.

The low reactivity of *IVb* is remarkable: the solvolysis rate of this compound is less than half of that of 2-adamantyl *p*-toluenesulphonate (estimated from ref.¹⁸

$k_{75^\circ} \sim 6 \cdot 10^{-5} \text{ s}^{-1}$ in 70% ethanol) which was suggested by Schleyer and collaborators¹⁷ as a model for "limiting" solvolysis.

The deuterium effect for the monodeuterated axial isomer *I**b*** is 2.07 at 40°C (70% ethanol); this is nearly the same value as found⁷ for the monocyclic analogue *IXb*. The tricyclic system is thus, in this respect, similar to other *cis*-2-alkylcyclohexyl *p*-toluenesulphonates where a *trans*- β -deuterium atom on the tertiary carbon atom exhibits a great isotope effect (about 2). Also the values of $k_{\text{H}}/k_{\text{D}_3}$ for the compounds *IIIb* and *Xb* are very similar (2.30 and 2.43, respectively, at 40°C in 70% ethanol). On the other hand, the effect of introduction of one deuterium atom into the tricyclic equatorial isomer *IVb* is very small, as illustrated by the rates of *Vb* and *VIb* ($k_{\text{H}}/k_{\text{D}} = 1.013$ and 1.006, respectively; 75°C, 97% trifluoroethanol). Under the same conditions, the deuterium effect in the tert-butyl compound *XIIb* is 1.18. Also the deuterium effect in the trideuterated equatorial isomer *VIIb* is unexpectedly small; in fact this is apparently the smallest effect found for a β -trideuterated cyclohexyl *p*-toluenesulphonate: $k_{\text{H}}/k_{\text{D}_3} = 1.11$ in 70% ethanol and even 1.04 in 97% trifluoroethanol.

The stereochemical outcome of the solvolysis of *IVb* is also instructive. The composition of the solvolysis products in 70% ethanol and 70% trifluoroethanol is given in Table II. Unlike the monocyclic tert-butyl derivative *XIb* and menthyl *p*-toluene-

TABLE II
Products (%) of Solvolysis of the *p*-Toluenesulphonates *IVb* and *XIb*

Products ^a	70% Ethanol		70% Trifluoroethanol	
	<i>IVb</i>	<i>XIb</i>	<i>IVb</i>	<i>XIb</i>
Olefins	11.9	62.2	7.6	43.4
Tertiary ethers ^b	^c	4.1	^c	1.4
Axial ethers	14.6 (<i>I</i>) ^d	6.9 (<i>VIII</i>) ^d	24.5 (<i>I</i> + <i>IV</i>) ^{e,f}	4.7 (<i>VIII</i> + <i>XI</i> + tertiary) ^{e,g}
Equatorial ethers	15.3 (<i>IV</i>) ^d	1.0 (<i>XI</i>) ^d		
Tertiary alcohols	0.9	9.1	0.7	28.9
Axial alcohols	25.7 (<i>I</i>) ^h	12.9 (<i>VIII</i>) ^h	5.5 (<i>I</i>) ^h	10.8 (<i>VIII</i>) ^h
Equatorial alcohols	31.6 (<i>IV</i>) ^h	2.7 (<i>XI</i>) ^h	61.7 (<i>IV</i>) ^h	10.6 (<i>XI</i>) ^h
Other alcohols	—	1.1	—	1.6

^a From 0.01 mmol *p*-toluenesulphonate and 0.01 mmol collidine in 1 ml solvent, 125°C, 10 half-lives; the products were analysed by gas-liquid chromatography, using 2.1 m column packed with 5% 1,2,3-tris(cyanoethoxy)propane on Chromosorb W 100/120; ^b assigned to the remaining peak in the ether region in the chromatogram; ^c no additional peak in the ether region; ^d $\text{R} = \text{C}_2\text{H}_5$, the standards were prepared from the corresponding alcoholate and ethyl iodide in hexamethylphosphoric triamide and were used in the gas-liquid analysis without purification; ^e $\text{R} = \text{CF}_3\text{CH}_2$; ^f not separated; ^g three peaks in the ether region: 1.7%, 1.6% and 1.4%, they were not identified; ^h $\text{R} = \text{H}$.

sulphonate¹³ which afford under similar conditions about 40% to 60% of olefins, the solvolysis of *IVb* results in the formation of only about 10% of olefins. The most interesting is the ratio of the substitution products with inverted configuration to the products with retained configuration. Whereas compounds with inverted configuration predominate in the products of reaction of the monocyclic derivative *XIb*, the solvolysis of *IVb* proceeds with predominant retention of configuration. In 70% trifluoroethanol the ratio of equatorial to axial alcohols *IVa* : *Ia* is about 11; this ratio is practically the same as found by Sunko and coworkers¹³ for the products of trifluoroethanolysis of menthyl *p*-toluenesulphonate (about 10) and higher than found¹⁹ for the adamantyl system. Also this fact shows the "limiting" nature of the perhydro-*as*-indacene model.

Comparison of β -Deuterium Effects in Various Systems

The relatively large difference (1.04 vs 1.27, see Table III) in the deuterium effects found for the tricyclic derivative *VIIb* and trideuterated menthyl *p*-toluenesulphonate, which is supposed also not to be capable of distortion in the transition state, is interesting and it was evidently desirable to measure the isotope effects in other cyclohexyl compounds. We determined therefore deuterium effects for *XIIIb*, *XVb* and *XVIIb*. The first compound contains two substituents in the positions 2 and 4 relative to the reacting center and therefore, according to the conclusions of Sunko and coworkers¹³, it should not be distorted in the transition state and should exhibit a small deuterium effect, similar to that of menthyl *p*-toluenesulphonate. On the

TABLE III

Rate Constants and β -Deuterium Effects ($k_{\text{H}}/k_{\text{D}_3}$) for Solvolysis of Some Non-Deuterated (k_{H}) and β -Trideuterated (k_{D_3}) Cyclohexyl *p*-Toluenesulphonates in 97% (wt/wt) Trifluoroethanol

Non-deuterated	Temp., °C	$k_{\text{H}} \cdot 10^4$	Trideuterated	$k_{\text{D}_3} \cdot 10^4$	$k_{\text{H}}/k_{\text{D}_3}$
<i>IVb</i>	70	1.006	<i>VIIb</i>	0.968 ^a	1.04
<i>XIb</i>	70	2.010	<i>XIIIb</i>	1.364 ^a	1.47
<i>XIVb</i>	70	1.753	<i>XVb</i>	1.144 ^a	1.53
<i>XVIIb</i>	60	4.913	<i>XVIIb</i>	2.846 ^a	1.73
Menthyl <i>p</i> -toluenesulphonate ^b	45	0.552	2,6,6-trideuterio- menthyl <i>p</i> -toluenesulphonate ^b	0.435 ^a	1.27

^a Corrected for the isotopic purity; ^b ref.¹³.

other hand, the compounds *XVb* and *XVIIb* should be capable of distortion and their deuterium effects should be greater than those found for the rigid compounds.

The found deuterium effects, together with the pertinent solvolysis rates, are given in Table III. It is seen on the first glance that the tert-butyl *p*-toluenesulphonate *XIIIb* exhibits a greater deuterium effect (1.47) than menthyl *p*-toluenesulphonate (1.27). On the other hand, whereas *XIIIb* has practically the same deuterium effect as the 2-methyl derivative *XVb* (1.53), the effect found for the 2-isopropyl derivative *XVIIb* (1.73) is substantially higher than that for menthyl *p*-toluenesulphonate. The stereochemical relation of the compound *XVb* to *XIIIb* and *XVIIb* to menthyl *p*-toluenesulphonate is very similar: both compounds in each pair have the same substituent in the position 2 (methyl or isopropyl) and differ only in the substituent at C₍₄₎, which no doubt has a conformation stabilizing effect. It is therefore somewhat surprising that in the first pair the deuterium effect is practically the same whereas in the second one it differs significantly.

This discrepancy might indicate either that in the transition state the 4-tert-butyl-2-methylcyclohexyl system can undergo the same distortion as the 2-methylcyclohexyl system, whereas for some reason this is not possible for the menthyl-2-isopropylcyclohexyl pair, or that the suggested relationship between the isotope effect and the ease of conformational distortion in the transition state is not so clearcut as originally anticipated.

EXPERIMENTAL

The alcohols *Ia*, *IVa*, *VIIIa*, *XIa*, *XIVa* and *XVIa*, as well as their *p*-toluenesulphonates (with the exception of *Ib* and *IVb*), were already described^{6,13,20-23}.

The *p*-toluenesulphonates of all monodeuterio and trideuterio alcohols exhibited the same melting points as the corresponding non-deuterated compounds. Their identity and purity was moreover checked by mass spectrometry.

r-3a-Deuterio-*trans*-4-hydroxy-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (*IIa*)

To a stirred solution of lithium borodeuteride (1.3 g) in tetrahydrofuran (40 ml) was added boron trifluoride etherate (1.5 g) in tetrahydrofuran (15 ml) under nitrogen. After 30 min the epoxide¹⁵ *XVIII* (4.5 g) was added dropwise, the mixture stirred for another 2 h, cooled and decomposed with cold 1M-H₂SO₄ (14 ml). Potassium carbonate was added, the organic solution decanted, taken down *in vacuo* and the residue shaken between water and pentane. The pentane layer was dried, taken down and the product chromatographed on silica gel (200 g). Elution with pentane-ether (5 : 1) afforded pure *IIa*, m.p. 59–60°C (2.1 g, 46%), containing 95.2% d₁ species.

r-3a-Deuterio-*cis*-4-hydroxy-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (*Va*)

The alcohol *IIa* (1.3 g) was oxidized in acetone with Jones reagent, the resulting ketone was isolated and without purification immediately reduced with lithium aluminium hydride (0.27 g) in ether (10 ml). The product was worked up as usual and the alcohol *Va*, m.p. 121–122°C,

was obtained (0.45 g) after four crystallisations from ligroin. A further amount (0.3 g) of this compound was isolated from the mother liquors by chromatography on silica gel. The product contained 94.5% of d_1 species.

cis-5-Deuterio-*cis*-4-hydroxy-(*r*-3aH)-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (VIa)

The olefin¹⁶ *XX* (0.56 g) was treated with sodium borodeuteride (65 mg) and boron trifluoride etherate (290 mg) in diglyme (5 ml) at 0°C for 1 hour and then with sodium hydroxide (70 mg) in water (0.6 ml), followed by 30% hydrogen peroxide (0.7 ml), for another hour. The usual isolation procedure afforded 0.5 g of a mixture of *VIa* and its epimer (66 : 34) from which the desired *VIa* was obtained by chromatography on silica gel (60 g) with ether-pentane (1 : 4) as eluant. The product contained 90% d_1 species.

r-3a,5,5-Trideuterio-*trans*-4-hydroxy-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (*IIIa*) and *r*-3a,5,5-Trideuterio-*cis*-4-hydroxy-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (*VIIa*)

The ketone¹⁵ *XXI* (2.9 g) was refluxed with 20 ml of a solution of NaOD (prepared²⁴ from 0.2 g sodium, 15 ml deuterium oxide and 50 ml dioxane) for 3 h, the mixture poured into 0.1% acetic acid, extracted four times with pentane, the organic layer washed with water, dried and taken down *in vacuo*. After repeating this procedure four times, the mixture of ketones (*XXII* : *XXIII* = 1 : 9) contained 97% d_3 and 3% d_2 species. Reduction with lithium aluminium hydride (0.3 g), followed by repeated chromatography of the product on silica gel (400 g), afforded all the four trideuterated alcohols in the pure state. Elution with pentane-ether (4 : 1) gave successively: *IIIa*, m.p. 59–60°C (68 mg), *XXIV*, m.p. 84°C (86 mg), *VIIa*, m.p. 121–122°C (58 mg) and *XXVa*, m.p. 87–88°C (110 mg), together with large intermediate fractions. All the alcohols contained 97% d_3 species.

trans-4-*p*-Toluenesulphonyloxy-(*r*-3aH)-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (*Ib*) was prepared from *Ia* and *p*-toluenesulphonyl chloride in pyridine and crystallized from methanol (–10°C); m.p. 89–90°C (dec.). For $C_{19}H_{26}O_3S$ (334.4) calculated: 68.24% C, 7.84% H; found: 67.93% C, 7.76% H.

cis-4-*p*-Toluenesulphonyloxy-(*r*-3aH)-*trans*-8a-*transoid*-8a,8b-*trans*-8b-perhydro-*as*-indacene (*IVb*) was prepared analogously from *IVa*; m.p. 83–85°C (methanol). For $C_{19}H_{26}O_3S$ (334.4) calculated: 68.24% C, 7.84% H; found: 67.98% C, 7.76% H.

Ethyl 5-Tert-butyl-2-oxocyclohexanecarboxylate (*XXVI*)

The title compound was prepared from 4-tert-butylcyclohexanone (308 g), diethyl oxalate (292 g) and sodium ethoxide (from 46 g of sodium in 700 ml of ethanol) using a procedure described for the preparation of ethyl 2-cyclohexanonecarboxylate²⁵. The yield of *XXVI*, boiling at 109–109.5°C/0.5 Torr, was 280 g (62%). For $C_{13}H_{22}O_3$ (226.3) calculated: 68.99% C, 9.80% H; found: 69.09% C, 9.79% H.

5-Tert-butylcyclohex-1-enecarboxylic Acid (*XXVII*)

Hydrogenation of the ester *XXVI* (279 g) in ethanol (560 ml) over Raney nickel (28 g) at 100°C and 150 atm afforded 262 g of a mixture of hydroxy esters, boiling at 109.5°C/0.1 Torr. This

was dissolved in pyridine (1450 ml) and phosphorus oxychloride (275 ml) was added. The mixture was refluxed for 30 min, decomposed by pouring on ice and the product was extracted four times with ether. The ethereal layer was washed with dilute (1 : 1) hydrochloric acid, water, sodium hydrogen carbonate solution and again with water, dried and taken down. The unsaturated ester was distilled and then fractionated using a column, b.p. 117°C/7 Torr, yield 203 g (78%). For $C_{13}H_{22}O_2$ (210.3) calculated: 74.24% C, 10.54% H; found: 73.97% C, 10.44% H. The solution of the ester (190 g) in ethanol (350 ml) was refluxed with sodium hydroxide (200 g) in water (360 ml) for 2.5 h. The work-up afforded 137 g (83%) of the acid which was crystallized twice from ligroin, m.p. 140.5–141°C; reported 136–138°C (ref.²⁶) and 139.5–140°C (ref.²⁷).

4-Tert-butyl-2-methylcyclohexene (XXVIII)

Esterification of the acid XXVII (90 g) with diazomethane in ether afforded 94.5 g (97.5%) of the methyl ester, b.p. 92°C/0.3 Torr. For $C_{12}H_{20}O_2$ (196.3) calculated: 73.43% C, 10.27% H; found: 73.37% C, 10.39% H. The ester (93 g) was reduced with ethereal lithium aluminium hydride (20% excess), affording 74.4 g (93.3%) of 4-tert-butyl-2-hydroxymethylcyclohexene, b.p. 97°C/1.0–1.5 Torr. For $C_{11}H_{20}O$ (168.3) calculated: 78.51% C, 11.98% H; found: 78.38% C, 11.75% H. This alcohol (20.0 g) was dissolved in collidine (160 ml) and methanesulphonyl chloride (27.3 g) was added dropwise under stirring and cooling at 5–10°C. The mixture was stirred for 20 min at 0°C, decomposed with ice and the product was isolated; yield 27.9 g (95%) of the oily methanesulphonate. This was dissolved in ether and refluxed with a 40% excess of ethereal lithium aluminium hydride for 2 h. The mixture was worked up, the product dissolved in pentane and passed through an alumina column (250 g, activity II–III), yielding 13.5 g (74.7%, based on the alcohol) of XXVIII, which was fractionated on a spinning band column, b.p. 87°C/25 Torr, $n_D^{25} = 1.4610$. For $C_{11}H_{20}$ (152.3) calculated: 86.76% C, 13.24% H; found: 86.72% C, 13.20% H. IR spectrum (neat), cm^{-1} : 788, 1678, 3015, 3035; ¹H-NMR spectrum ($CDCl_3$, δ values): 0.85 s, 9 H (tert- C_4H_9); 1.65 s, 3 H ($CH_3-C=C$), 5.38 m, 1 H ($C=CH-$); 1.21 m, 1 H ($-CH-tert-C_4H_9$); 1.60–2.15 m, 6 H ($3 \times -CH_2-$).

trans-4-Tert-butyl-2-deuterio-*trans*-2-methylcyclohexanol (XIIa) and *cis*-4-Tert-butyl-2-deuterio-*trans*-2-methylcyclohexanol (XXIXa)

Boron trifluoride etherate (2.79 g) in diglyme (16 ml) was added at 0°C dropwise under nitrogen to a stirred mixture of the olefin XXVIII (5.0 g) and sodium borodeuteride (1.0 g) in diglyme (20 ml). The mixture was stirred at 0°C for 1 h and decomposed with water (6.5 ml). After addition of 3M-NaOH (6.5 ml), followed by 30% hydrogen peroxide (10 ml), the mixture was stirred for 30 min, diluted with water (600 ml) and extracted with pentane. The organic layer was washed with water and passed through an alumina column (200 g, activity II–III). The unreacted olefin and diglyme were removed by elution with pentane, elution with ether gave a mixture of XIIa and XXIXa (5.33 g; 94.8%) in the ratio 5 : 4. The alcohols (3.0 g) were separated on a silica gel column (300 g, pentane–ether 9 : 1) affording 1.15 g of XXIXa, m.p. 71°C and 0.82 g of XIIa, m.p. 71–72°C. Deuterium content: 90% of d_1 species.

trans-4-Tert-butyl-2-deuterio-*cis*-2-methylcyclohexanol (XXXa)

A mixture of XXIXb (500 mg) and tetra-*n*-butylammonium acetate (2.5 g) was melted, heated to 110°C for 6 h, diluted with water, acidified with several drops of hydrochloric acid and the product was taken up into pentane. The extract was washed with water, dried and taken down. As shown by gas liquid chromatography (internal standard), the reaction afforded only 25%

of the desired acetate, the rest being products of elimination. The crude product was reduced with lithium aluminium hydride, worked up, dissolved in pentane and passed through an alumina column (10 g, activity II–III). Elution with ether gave 61.2 mg (23.3%) of *XXXa*, contaminated with 0.5% of *XXIXa*. Chromatography and crystallisation from pentane afforded pure *XXXa* (49 mg), m.p. 62.5–63°C; 90% of d_1 species.

cis-4-Tert-butyl-2-deuterio-*cis*-2-methylcyclohexanol (*IXa*)

This compound was prepared in 68% yield from *XIIb* (500 mg) and tetra-*n*-butylammonium acetate (2.5 g) using the procedure described in the preceding experiment. The product melted at 78.5–79.5°C (pentane), and contained 90% of d_1 species.

cis-4-Tert-butyl-2,6,6-trideuterio-*cis*-2-methylcyclohexanol (*Xa*)
and *trans*-4-Tert-butyl-2,6,6-trideuterio-*trans*-2-methylcyclohexanol (*XIIIa*)

A mixture of stereoisomeric 4-tert-butyl-2-methylcyclohexanones²⁸ (8.0 g) was converted into the 2,6,6-trideuterio derivatives by repeated refluxing with NaOD solution²⁴ in deuterium oxide and dioxane as described in the preparation of *IIIa* and *VIIa*. The obtained mixture of epimeric deuterio ketones (4.6 g) was distilled, b.p. 105°C/10 Torr, reduced with lithium aluminium hydride in ether and the product was isolated. A part of the product (1.5 g) was chromatographed on a silica gel column (150 g, pentane–ether 9 : 1) and the individual alcohols were crystallized from pentane, affording 145 mg of *Xa*, m.p. 77–78°C, and 300 g of *XIIIa*, m.p. 72–73°C. The alcohols contained 95% of d_3 species.

2,6,6-Trideuterio-*trans*-2-methylcyclohexanol (*XVa*)

2-Methylcyclohexanone was deuterated as described for *XXI*; the crude trideuterio ketone from the last equilibration contained 96% of d_3 species. It was reduced with lithium aluminium hydride and the resulting alcohols (0.5 g) were chromatographed on a silica gel column (100 g, pentane–ether 5 : 1), affording *XVa* as the second fraction (60 mg). The purity of the fractions was followed by gas liquid chromatography (diglycerol). Deuterium content: 95.5% d_3 species. *p*-Toluenesulphonate *XVb*, m.p. 26–27°C (ref.²² reports 27.5–28.4°C for *XIVb*).

2,6,6-Trideuterio-*trans*-2-isopropylcyclohexanol (*XVIIa*)

Introduction of deuterium into the β -positions of 2-isopropylcyclohexanone^{29,30} by the base-catalysed exchange in deuterium oxide and dioxane and the subsequent reduction of the crude trideuterio ketone was carried out as described for *XVa*. Chromatography of the reduction product (0.7 g) on silica gel (90 g, pentane–ether 5 : 1) afforded 0.3 g of pure *XVIIa*, m.p. 63–64°C (ref.²³ reports m.p. 63.8–64.4°C for *XVIIa*); 94.5% of d_3 species. *p*-Toluenesulphonate *XVIIb*, m.p. 91–92°C (ref.²³ reports m.p. 91.5°C for *XVIIb*).

Kinetic Measurements

The solvolysis rates were determined conductometrically in 50 ml cells with bright platinum electrodes³¹. The resistance was measured^{31,32} using a Metra MLL (Czechoslovakia) bridge (precision 0.02%), connected to an oscillator (2 V, 1 680 c.p.s.), the balance was detected by a phase-sensitive null detector. Time was measured by a Tesla BM 445E counter with an internal crystal time base. Temperature of the oil thermostat was maintained within $\pm 0.002^\circ\text{C}$. At least

three measurements at each temperature were carried out, the reproducibility being $\pm 0.2\%$ of the measured rate constants or better.

Usually 40–60 points were taken and fitted to the first-order rate equation $1/R_t = a - be^{-kt}$, where R_t is the resistance at the time t and a and b are constants. Späth's algorithm³³ was used and the transcendental equation in this algorithm was solved by standard *regula falsi* procedure³⁴.

The measured rate constants were corrected for the incomplete deuteration. In the case of the trideuterated compounds we arbitrarily assumed that the d_2 species, present as contaminant, have the same reaction rate as the corresponding monodeuterated compounds. Since the compounds had a high isotopic purity and the changes in rates from d_1 to d_3 species were only small, the error thus introduced was not significant.

The deuterium content of the alcohols was determined by mass spectrometry from the molecular peaks, where possible. In some equatorial alcohols where the molecular peak was too small, the $M^+ - 18$ peak was used instead. Control measurements have shown that the results obtained from these two peaks were identical. The reliability of the method was shown by the same deuterium content found for the compounds, arising from the same deuterated precursor. The deuterium content in the *p*-toluenesulphonates was assumed to be the same as in the parent alcohols. The accuracy is believed to be $\pm 1\%$ of the deuterium content. The measurements were performed on an MCH-1303 (USSR) mass spectrometer.

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