An Unusual Entropy Effect in the Sovolysis of some Steroidal Toluene-*p*-sulphonates

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SOLVOLYSES of the axial and equatorial epimers of a number of 3-steroidal toluene-*p*-sulphonates have been studied in order to investigate the influence of conformational transmission.[1] The axial–equatorial rate-ratio, observed to increase substantially from acetic to acetic–formic acid, was found to be associated with a change in the entropy of activation.

Axial alcohols, from which 5α-cholest-6-en-3α-yl and 5α-cholest-7-en-3α-yl toluene-*p*-sulphonates (III) and (V) were prepared, were most conveniently obtained by inversion of the corresponding 3β-esters [(IV) and (VI)] with tetrabutylammonium acetate in acetone.[2] Reduction of the acetates with lithium aluminium hydride gave alcohols which, analysed as the trimethyl silyl ethers, contained 95—98% of the 3α-epimer. Cholestan-3α-yl and cholestan-3β-yl toluene-*p*-sulphonates [(I) and (II)] were prepared by the usual method.

Rates of solvolysis of the pairs of axial and equatorial compounds were determined in both acetic and a 1 : 1 (v/v) formic–acetic acid† mixture and Arrhenius parameters obtained (Tables 1 and 2). The greater rate of solvolysis of the axial compounds in acetic acid and the greater rate increase for the axial epimers with change in solvent arises primarily from a difference in the entropy of activation. Entropies of activation associated with the equatorial epimers are negative and are little affected by the change in solvent, showing, if anything, a trend to more negative values. For the axial epimers, entropies of activation are more positive in acetic acid than those for the equatorial epimers and show a marked increase in acetic–formic acid. This effect probably originates from participation of the β-axial hydrogen at the transition state. In a less nucleophilic and more dissociating solvent (acetic–formic mixture) orbital overlap between the neighbouring carbon–hydrogen band and the developing *p*-orbital competes favourably with solvent participation. Similar entropy changes have been noted for systems considered to involve participation.[3] Rate effects consistent with methyl participation were reported recently for the solvolysis of neopentyl toluene-*p*-sulphonate.[4] No Arrhenius parameters were published but we would expect a similar trend in the $\Delta S^{\ddagger}$ values in acetic and formic acid. A contribution to the more positive entropy of activation for the axial epimers, other than by β-hydrogen participation, may be the greater degree of rotational freedom of the toluene-*p*-sulphonate group at transition than in the more sterically hindered ground state.

TABLE 1

*Rate constants for the solvolysis of the toluene-*p*-sulphonates* ($\times 10^5$ sec.$^{-1}$).

	Acetolysis			Acetolysis: formolysis		
Temp.	50°	74·7	100	34·1	51·0	74·7
(I)	0·685	16·5			64·0	
(II)		2·75	40·2		4·22	58·7
Temp.	49·9°	75·1		36·9	49·9	73·5
(I)				9·62	60·0	
(III)	0·485	12·3		7·25	52·2	
(IV)		2·14[a]			2·58	34·6
(V)	0·203	4·18		2·45	17·7	
(VI)		1·22[a]			1·35	17·5

[a] Ref. 1.

TABLE 2

*Arrhenius parameters for solvolysis of axial and equatorial toluene-*p*-sulphonates*

	Rate ratios		$\Delta H^{\ddagger}$ (Kcal.)		$\Delta S^{\ddagger}$ (e.u.)	
	AcOH	AcOH–HCO_2H	AcOH	AcOH–HCO_2H	AcOH	AcOH–HCO_2H
(I)			28·07	27·4	+4·35	+11·4
(II)	6·00	15·2	26·62	24·11	−3·19	−4·32
(III)			28·0	29·6	+3·65	+17·9
(IV)	5·75	20·2	(27·6)	23·7	(−0·87)	−6·32
(V)			26·2	29·7	−3·66	+16·0
(VI)	3·43	13·1	(26·7)	23·5	(−4·57)	−8·25

Products from the solvolyses (in 10 : 1 buffer to substrate) have been investigated by g.l.c. and mass spectroscopy. Both axial and equatorial toluene-*p*-sulphonates gave a substantial amount of olefin (50—70% for the equatorial epimers, *ca.* 90% for the axial epimers) which increased in acetic–formic acid. Some differences were noted in the elimination to substitution ratios which could be accounted for in terms of conformational transmission. Inversion: retention ratios (at the 3-position) varied considerably, but tended to be much higher for the equatorial epimers than for the axial. In formic acid, all inversion : retention ratios measured diminished. The results for the product analysis differ considerably from that obtained for the corresponding *cis*- and *trans* 4-t-butylcyclohexyl toluene-*p*-sulphonates, which suggests that this system is distorted and, therefore, not a suitable model for cyclohexane systems.[5]

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† The mixed solvent was used because the toluene-*p*-sulphonates were almost insoluble in formic acid.

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