Hydrolysis of Secondary Alkyl Sulphonates. S_N2 Reactions with High Carbocation Character

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Rate constants for hydrolysis of various secondary methanesulphonates (mesylates. ROMs) in water have been determined, and rate constants for 2-adamantyl mesylate (I: X = OMs) in <0.1% v/v acetone–water have been used to estimate a rate constant for 2-adamantyl mesylate in pure water at 25°. Rate ratios for selected tosylates and mesylates have been evaluated and range from *ca*. 0.8 in 50% v/v ethanol–water to 2.1 in water but do not appear to depend markedly on the nature of the secondary alkyl group. The estimated rate constant for 2-adamantyl tosylate in water is $3.1(5) \times 10^{-4}$ s^{-1} and leads to values of the following solvent parameters: solvent ionizing power, Y_{OTs} (4.1) and solvent nucleophilicity, N_{OTs} (−0.44). The magnitudes of nucleophilic solvent assistance, calculated using $[k_{ROMs}/k_{2-AdOMs}]_{H_2O}/[k_{ROTs}/k_{2-AdOTs}]_{CF_3CO_2H}$, range from 48 for propan-2-yl † to 9 for cyclohexyl, and are very similar to those calculated for formic acid. The unbranched substrates (propan-2-yl, butan-2-yl, pentan-2-yl, pentan-3-yl, and heptan-4-yl) give a good correlation with $\Sigma\sigma^*$ with a slope (−4.03), slightly greater than that for formic acid (−3.35) but much less than that for trifluoroacetic acid (−7.21). These and other results suggest that these unbranched substrates hydrolyse *via* S_N2 like transition states with high carbocation character. The rate ratio (*exo*/*endo*) for hydrolysis of 2-norbornyl systems (IV) and (V) is 2 550, the highest reported at 25°. By comparison with cyclopentyl mesylate as a model system it is suggested that 2-*exo*-norbornyl systems are solvolysed anomalously rapidly and 2-*endo*-norbornyl systems anomalously slowly.

IT has recently been proposed that the apparently conflicting evidence for S_N2 character and for ion pair formation in the solvolysis of many secondary alkyl sulphonates can be rationalised by formation of nucleophilically solvated ion pairs,[1] or ' ion sandwiches '.[2] These interpretations imply that intermediates, similar to the usual S_N2 transition state but having appreciable carbocation character, may be formed. There is independent evidence that intermediates present in solution can lead to ^{18}O scrambling [3] and racemization,[4] in ' unreacted ' starting material, and this can be interpreted as a lower-limit estimate of ' internal return ' from ion pair intermediates. Unfortunately, it is not known whether ^{18}O-scrambling, racemization, and solvolysis occur *via* the same ion pair intermediates. Consequently, it has been difficult to evaluate the importance of internal ion pair return in solvolytic reactions.‡ In parallel research, mechanistic information has been deduced from comparisons of rates of solvolyses in various media, particularly solvents of high ionizing power and low nucleophilicity. By comparison with trifluoroacetic acid and hexafluoropropan-2-ol, it appears

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† Although application of the IUPAC rules would lead to the numbering of the radical position in an alkyl radical as 1, for reasons of clarity this rule has not been strictly followed.

‡ Mechanistic interpretations are further complicated by the possibility of ' hidden return,' *i.e.* return of contact ion pairs to covalent starting material without ^{18}O-scrambling and/or racemization.[5] Recent evidence suggests that hidden return is not appreciable for solvolyses of simple secondary arenesulphonates.[1,6]

[1] T. W. Bentley and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1976, **98**, 7658.

[2] F. G. Bordwell and T. G. Mecca, *J. Amer. Chem. Soc.*, 1975, **97**, 123, 127; F. G. Bordwell, P. F. Wiley, and T. G. Mecca, *ibid.*, p. 132.

[3] A. F. Diaz, I. Lazdins, and S. Winstein, *J. Amer. Chem. Soc.*, 1968, **90**, 1904.

[4] S. Winstein, B. Appel, R. Baker, and A. Diaz, Chem. Soc. Spec. Publ., No. 19, 1965, pp. 109—130.

[5] V. J. Shiner, jun., R. D. Fisher, and W. Dowd, *J. Amer. Chem. Soc.*, 1969, **91**, 7748.

[6] T. W. Bentley, S. H. Liggero, M. A. Imhoff, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1974, **96**, 1970.

that even acetic and formic acids are relatively nucleophilic and both kinetic and stereochemical data are consistent with the S_N2 character of many acetolyses and formolyses.[1,7]

We now report kinetic data for hydrolysis of secondary alkyl sulphonates. Water has a unique combination of ionizing power and nucleophilicity. It is more nucleophilic than acetic and formic acids, but has an ionizing power comparable with that of hexafluoropropan-2-ol.[7] Also the high dielectric constant and high dissociating power of water may lead to unusual reaction rates for solvolyses of substrates which undergo internal ion pair return (*e.g.* 2-*exo*-norbornyl mesylate, discussed later).

Hydrolysis rate constants for many alkyl halides, and methyl, ethyl, and propan-2-yl sulphonates have been determined in pure water and in binary solvents, *e.g.* acetone–water, dioxan–water, and alcohol–water mixtures.[8a,9] The rate of hydrolysis of 3-methylbutan-2-yl mesylate in pure water has also been examined,[10] but no previous systematic study of the hydrolysis rates for simple secondary sulphonates has been carried out.*

TABLE 1

Solvolytic rate constants for secondary alkylsuphonates [a]

Parent alcohol	Leaving group [b]	Solvent [d]	T/°C	k/s^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} k^{-1}	$k_{\mathrm{OTs}} : k_{\mathrm{OM}}$
Propan-2-ol	OMs	H_2O	25.0 [e]	$(2.09 \pm 0.06) \times 10^{-4}$			
	OTs	H_2O	25.0 [e]	$(4.13 \pm 0.02) \times 10^{-4}$			1.98
	OMs	H_2O	25.0 [f]	1.965×10^{-4}	22.13	−1.3	
	OTs	H_2O	25.0 [f]	4.106×10^{-4}	22.05	−0.08	2.09
	OMs	50% E	50.08	$(3.00 \pm 0.01) \times 10^{-4}$			
			25.08	$(1.75 \pm 0.01) \times 10^{-5}$	21.2	−9.3	0.87 [g]
	OMs	80% E	50.0	$(4.84 \pm 0.03) \times 10^{-5}$			1.14 [g]
Butan-2-ol	OMs	H_2O	25.0 [e]	$(5.00 \pm 0.06) \times 10^{-4}$			
Pentan-2-ol	OMs	H_2O	0.25	$(2.04 \pm 0.02) \times 10^{-5}$			
			25.0	$(6.03 \pm 0.02) \times 10^{-4}$	21.6	−0.9	
Octan-2-ol	OMs	H_2O	25.0 [e]	$(6.23 \pm 0.14) \times 10^{-3}$			
Pentan-3-ol	OMs	H_2O	25.0 [e]	$(1.41 \pm 0.02) \times 10^{-3}$			
Heptan-4-ol	OMs	H_2O	0.1	$(8.00 \pm 0.02) \times 10^{-5}$			
			25.0	$(1.89 \pm 0.04) \times 10^{-3}$	20.0	−3.9	
3-Methylbutan-2-ol (II)	OMs	H_2O	25.0 [e]	$(2.05 \pm 0.01) \times 10^{-3}$			
			25.0 [h]	2.022×10^{-3}	20.37	−2.51	
3,3-Dimethylbutan-2-ol (III)	OMs	H_2O	0.3	$(3.94 \pm 0.03) \times 10^{-5}$			
			25.0	$(1.33 \pm 0.01) \times 10^{-3}$	22.5	+3.8	
Cyclopentanol	OMs	H_2O	0.05	$(2.16 \pm 0.12) \times 10^{-4}$			
			9.95 [i]	8.49×10^{-4}			
			15.75	$(1.77 \pm 0.01) \times 10^{-3}$	20.3	−0.7	
			25.0	$(5.46 \pm 0.06) \times 10^{-3}$			
Cyclohexanol	OMs	H_2O	0.0	$(1.24 \pm 0.04) \times 10^{-5}$			
			25.0 [j]	$(4.26 \pm 0.20) \times 10^{-4}$	22.3	+0.9	
	OMs	5% A	25.0	$(2.98 \pm 0.02) \times 10^{-4}$			
	OTs	5% A	25.0	$(5.90 \pm 0.03) \times 10^{-4}$			1.98
exo-Norbornan-2-ol (IV)	OMs	H_2O	0.22	$(1.49 \pm 0.01) \times 10^{-2}$			
			10.63 [i]	6.37×10^{-2}	19.4	+4.4	
			15.36	$(9.98 \pm 0.03) \times 10^{-2}$			
			25.0 [c]	3.26×10^{-1}			
			25.04	$(3.27 \pm 0.17) \times 10^{-1}$			
	OMs	50% E	25.18	$(6.34 \pm 0.05) \times 10^{-3}$			
	OTs	50% E	25.18	$(4.33 \pm 0.05) \times 10^{-3}$			0.68
endo-Norbornan-2-ol (V)	OMs	H_2O	25.0 [e]	$(1.28 \pm 0.05) \times 10^{-4}$			
	OMs	50% E	25.0 [e]	$(3.94 \pm 0.16) \times 10^{-6}$			
	OTs	50% E	25.0 [e]	$(3.15 \pm 0.05) \times 10^{-6}$			0.80
Adamantan-2-ol (I)	OMs	0.025% A	25.0 [e, i]	1.46×10^{-4}			
	OMs	0.07% A	25.0 [e]	$(1.38 \pm 0.02) \times 10^{-4}$			
	OMs	5% A	50.07	$(2.37 \pm 0.01) \times 10^{-3}$			
			40.05 [i]	7.15×10^{-4}	23.9	+3.2	
			25.0	$(9.68 \pm 0.20) \times 10^{-5}$			
	OMs	50% E	75.0	$(4.39 \pm 0.05) \times 10^{-4}$			0.84 [g]
	OMs	80% E	75.0	$(1.95 \pm 0.05) \times 10^{-5}$			0.98 [k]

[a] Determined conductometrically in duplicate, except where otherwise noted; errors shown are average deviations. [b] OMs = mesylate, OTs = tosylate. [c] Calculated from data at other temperatures. [d] %E = % v/v ethanol–water; %A = % v/v acetone–water. [e] Calculated from a value of the rate constant at an accurate temperature close (±0.2°) to 25 °C. [f] Ref. 8*a*. [g] Tosylate data from ref. 1. [h] Ref. 10. [i] One measurement of rate constant. [j] Average of four independent runs using two different cells. [k] Tosylate data from ref. 13.

RESULTS

Kinetic data are summarised in Table 1. Some of the rate constants were determined in aqueous acetone to reduce experimental difficulties due to the poor solubility of sulphonates in water. Our results are in good agreement with independent measurements by Robertson and his co-

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* See also ref. 27.

[7] F. L. Schadt, T. W. Bentley, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1976, **98**, 7667.

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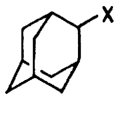
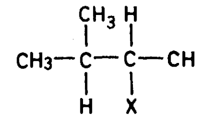
[9] E. Tommila, *Ann. Acad. Sci. Fennicae*, 1967, IIA, 139; *Suomen Kemi.*, 1960, **33**, 37.

[10] Y. Inomoto, R. E. Robertson, and G. Sarkis, *Canad. J. Chem.*, 1969, **47**. 4599.

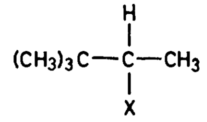
workers for hydrolysis of propan-2-yl[8] and 3-methylbutan-2-yl mesylates.[10]

DISCUSSION

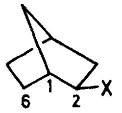

(I)

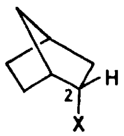

(II)

$CH_3-CH(CH_3)-CH(X)-CH_3$


(III)

$(CH_3)_3C-CH(X)-CH_3$


(IV)


(V)

The scope of this work was limited by the poor solubility of the alkyl arenesulphonates in water. Satisfactory results for the hydrolysis of propan-2-yl toluene-*p*-sulphonate (tosylate) were obtained (Table 1) but not for cyclohexyl tosylate. By first dissolving the tosylate in acetone it was possible to study hydrolyses of cyclohexyl tosylate in 5% v/v acetone–water, but this procedure was unsatisfactory for 2-adamantyl tosylate (I; X = OTs). Satisfactory results for alkyl mesylates up to C_7 were obtained in pure water, but small amounts (<0.1%) of acetone were required to assist in the preparation of homogeneous solutions of 2-adamantyl mesylate (I; X = OMs). Extrapolation of our results for 0.025, 0.07, and 5% v/v acetone–water (Table 1) suggests that a reasonable estimate of the rate constant for hydrolysis of 2-adamantyl mesylate in pure water is 1.5×10^{-4} s^{-1} at 25 °C. To compare this value with the results for tosylates, discussed earlier,[1,7] it is necessary to estimate reaction rates for tosylates from those for mesylates. Various tosylate : mesylate rate ratios ($k_{\mathrm{OTs}} : k_{\mathrm{OMs}}$) are shown in Table 1 and others for cyclobutyl solvolyses in acetic acid (0.7), trifluoroethanol (1.06), and ethanol (1.3) have been reported.[11] All values are within the range 0.68—2.1 and appear to depend more on the solvent composition than on the substrate, *e.g.* in 50% v/v ethanol–water $k_{\mathrm{OTs}} : k_{\mathrm{OMs}}$ ratios in the range 0.68—0.87 were observed for propan-2-yl, 2-adamantyl, 2-*exo*-norbornyl, and 2-*endo*-norbornyl mesylates, whereas in water propan-2-yl gives $k_{\mathrm{OTs}} : k_{\mathrm{OMs}}$ 2.09 and in 5% v/v acetone–water cyclohexyl gives a ratio of 1.98; the latter is likely to be lower than the corresponding value for pure water. These values are in line with results for methyl (1.6) and ethyl (2.1) in pure water.[8a] Consequently a $k_{\mathrm{OTs}} : k_{\mathrm{OMs}}$ ratio of 2.1 for hydrolyses in pure water will be assumed for all of the secondary substrates discussed. This ratio leads to an estimate of $3.1(5) \times 10^{-4}$ s^{-1} for the rate constant for hydrolysis of 2-adatantyl tosylate in water at 25°, which leads to values of 4.1 for Y_{OTs}, a scale of solvent ionizing power for sulphonates alternatively referred to as $Y_{2\text{-AdOTs}}$,[7,12c] and to N_{OTs} −0.44,[7] a measure of solvent nucleophilicity. The Y_{OTs} value is almost as high as that of trifluoroacetic acid (4.57) and higher than that of 97% hexafluoropropan-2-ol–water (3.67) and formic acid (3.04).[7] Most of the following discussion requires the less specific assumption that, in water, $k_{\mathrm{OTs}} : k_{\mathrm{OMs}}$ ratios are constant, *i.e.* independent of the nature of the alkyl group.

Using 2-adamantyl tosylate (I) as a model for S_N1 or limiting behaviour and assuming that trifluoroacetolyses of all secondary sulphonates are S_N1 processes, it has been proposed that the S_N2 character of a secondary solvolysis can be calculated using equation (1).[13] The

$$\text{nucleophilic solvent assistance} = [k_{\mathrm{ROTs}}/k_{2\text{-AdOTs}}]_{\text{any solvent}}/[k_{\mathrm{ROTs}}/k_{2\text{-AdOTs}}]_{\mathrm{CF_3CO_2H}} \quad (1)$$

assumptions and limitations of this equation have been discussed elsewhere,[7,12a,14] and the equation is expected to lead to *minimum* estimates of the magnitude of nucleophilic solvent assistance. It is suggested that the equation gives an estimate of the rate effects due to the kinetically significant involvement of the solvent as nucleophile or base by partial bonding (as distinct from general electrostatic solvation) to any atom of the substrate (*e.g.* α-carbon, β-hydrogen). Values of nucleophilic solvent assistance > *ca.* 10 are associated with S_N2 processes and this is consistent with stereochemical evidence for acetolyses and formolyses.[7,12b] Estimates of the magnitude of nucleophilic solvent assistance for hydrolyses of secondary tosylates are given in Table 2.

The rate factors (Table 2) are not large in terms of energy,[14] but they represent rate enhancements due to nucleophilic solvent assistance compared with processes assisted only by electrostatic solvation. Such rate enhancements will only be observed when the energy gained by nucleophilic solvent assistance is in excess of the energy required to attract a solvent molecule from the bulk

TABLE 2

Estimates of nucleophilic solvent assistance [equation (1)]

Tosylate	Water [a]	HCO_2H [b]	CH_3CO_2H [b]	80% EtOH [b]
2-Adamantyl (I)	1.0 [c]	1.0 [c]	1.0 [c]	1.0 [c]
3,3-Dimethylbutan-2-yl (III)	1.9	2.4	8.6	12
Cyclohexyl	9	5	28	104
Cyclopentyl	13	10	105	455
Heptan-2-yl	9	3.9	28	146
Pentan-3-yl	10	6.2	46	310
Pentan-2-yl	18	9.6	88	616
Butan-2-yl	20	13	140	979
Propan-2-yl	48	32	472	4 430

[a] Kinetic data from Table 1 and ref. 1 and assuming $k_{\mathrm{OTs}}:k_{\mathrm{OMs}}$ ratios are constant in water (see text). [b] Ref. 7. [c] By definition.

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[11] D. D. Roberts, *J. Org. Chem.*, 1972, **37**, 1510.

[12] T. W. Bentley and P. v. R. Schleyer, *Adv. Phys. Org. Chem.*, 1977, **14**, (*a*) 8; (*b*) 15; (*c*) 36.

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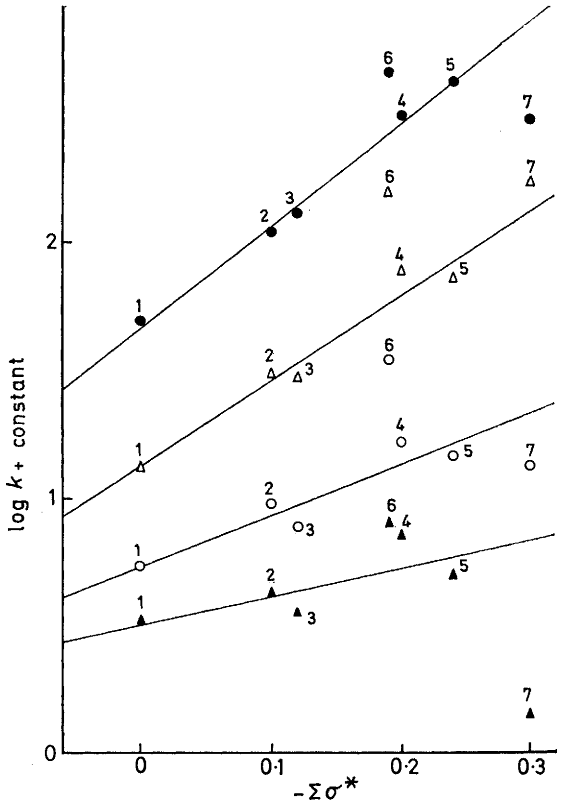
[14] J. R. Pritt and M. C. Whiting, *J.C.S. Perkin II*, 1975, 1458.

medium to act as nucleophile.* As only the excess energy is responsible for rate increases the extent of covalent interactions in the transition states for these hydrolyses may correspond to much larger rate factors than those given in Table 2. Similarly, addition of hydroxide ion does not lead to large rate enhancements, presumably because the hydroxide ion needs to be desolvated, partially, before it can act as an effective nucleophile.[16]

Recent work[7] has shown the importance of solvent nucleophilicity in determining the rates of many secondary solvolyses but the results for water and formic acid (Table 2) are very similar, even though water is much more nucleophilic than formic acid. Because water has a high ionizing power, formation of transition states would require less nucleophilic solvent assistance than reactions in an equally nucleophilic solvent having lower ionizing power (*e.g.* 80% ethanol, Table 2). Therefore it is not unreasonable that formic acid, having a lower nucleophilicity and a lower ionizing power than water, undergoes solvolyses with nucleophilic solvent assistance of comparable magnitude to hydrolyses.

It is known that hydrolysis of optically active octan-2-yl mesylate proceeds with complete inversion of configuration,[17] and the rate constant is almost the same as for pentan-2-yl mesylate (Table 1). Thus the magnitudes of nucleophilic solvent assistance for pentan-2-yl and octan-2-yl tosylates should be similar. Combination of the estimates of nucleophilic solvent assistance (Table 2) with the stereochemical data suggests that hydrolyses of these secondary sulphonates are S_N2 processes, but closer to the S_N1 limits than acetolyses.

The above arguments are supported by the ρ^* correlations shown in the Figure. The rates of hydrolyses of unbranched secondary acyclic sulphonates correlate well with $\Sigma\sigma^*$.† Water and trifluoroacetic acid[24] are the only solvents in which pentan-2-yl systems have been shown to solvolyse faster than butan-2-yl, and heptan-4-yl reacts faster than pentan-3-yl. This suggests that appreciable positive charge develops on the secondary carbon atom in the transition state for these solvolyses.[25] Although the ρ^* value (see Figure) for hydrolysis is high (−4.03), compared with acetolysis (−2.01) and 80% ethanolysis (−1.10), it is substantially less than the value observed in trifluoroacetic acid (ρ^* −7.21).[6,24] As trifluoroacetolyses are assumed to be S_N1 processes,[6,13,24] the ρ^* value for hydrolysis is consistent with an S_N2 process in which appreciable positive charge (carbocation character) has developed in the transition state.



Rates constants for solvolyses at 25° of secondary alkyl sulphonates *versus* $\Sigma\sigma^*$:[18] 1, propan-2-yl; 2, butan-2-yl; 3, pentan-2-yl; 4, pentan-3-yl; 5, heptan-4-yl; 6, 3-methylbutan-2-yl; 7, 3,3-dimethylbutan-2-yl. Correlation lines for points 1—5 only: ●, mesylates in water, ρ^* −4.03 ± 0.13, r 0.998; △, tosylates in formic acid, ρ^* −3.35 ± 0.32, r 0.979; ○, tosylates in acetic acid, p^* −2.10 ± 0.32, r 0.942; ▲, tosylates in 80% v/v ethanol–water, p^* −1.10 ± 0.041, r 0.766. Kinetic data taken from ref. 1 and Table 1

The branched systems, 3-methylbutan-2-yl (II) and 3,3-dimethylbutan-2-yl (pinacolyl) (III), do not fit the ρ^* correlations well (see points 6 and 7 in the Figure). The kinetic isotope effect for [3-^{2}H]-3-methylbutan-2-yl sulphonates (k_H/k_D *ca.* 2) and the formation of rearranged

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* This could be very important in the interpretation of borderline solvolyses, which will be discussed in detail elsewhere. As solvent isotope effects ($k_{H_2O} : k_{D_2O}$) are small, it appears that extensive O–H stretching does not occur during nucleophilic solvation.[8b,15] This implies that ionization of water is not involved in the rate-determining step.

† Despite continued criticisms of aspects of σ^* or σ_I correlations,[19] there is good evidence from gas-phase data[20–22] that σ^* does reflect the inherent ability of alkyl groups to stabilize positive charge by polar effects; steric effects cannot be important factors determining ionization potentials.[20–22] Also there are close similarities between carbocation reactivity in solution and in the gas phase.[23]

[15] P. M. Laughton and R. E. Robertson, in 'Solute–Solvent Interactions,' eds. J. F. Coetzee and C. D. Ritchie, Dekker, New York, 1969, vol. 1, ch. 7.

[16] S. Hartman and R. E. Robertson, *Canad. J. Chem.*, 1960, **38**, 2033.

[17] H. Weiner and R. A. Sneen, *J. Amer. Chem. Soc.*, 1965, **87**, 287.

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[19] M. Charton, *J. Amer. Chem. Soc.*, 1975, **97**, 3691; F. G. Bordwell and H. E. Fried, *Tetrahedron Letters*, 1977, **1121**; see however A. J. MacPhee and J. E. Dubois, *ibid.*, 1976, 2471.

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[22] R. W. Taft and L. S. Levitt, *J. Org. Chem.*, 1977, **42**, 916.

[23] E. W. Bittner, E. M. Arnett, and M. Saunders, *J. Amer. Chem. Soc.*, 1976, **98**, 3734.

[24] P. E. Peterson, R. E. Kelley, jun., R. Belloli, and K. A. Sipp, *J. Amer. Chem. Soc.*, 1965, **87**, 5169.

[25] L. Radom, J. A. Pople, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1972, **94**, 5935.

products suggests that hydrogen participation occurs.[10,26] Thus it is not surprising that on all four correlations (Figure), 3-methylbutan-2-yl tosylate (II) reacts faster than expected. Pinacolyl tosylate (III) is even more highly branched and appears to solvolyse with less nucleophilic solvent assistance than the unbranched systems (see Table 1 and ref. 1). Therefore it would be expected to fall below the correlation lines (Figure), as observed for water, acetic acid, and 80% ethanol–water. In contrast the value for pinacolyl tosylate in formic acid is slightly above the correlation line drawn in the Figure, and there does not appear to be a simple explanation for this small deviation.

Kinetic data for hydrolysis of cyclopentyl, cyclohexyl, 2-*exo*-norbornyl (IV), and 2-*endo*-norbornyl (V) mesylates are also shown in Table 1. The *exo* : *endo* rate ratio for the latter pair is 2 550 at 25°, in satisfactory agreement with an independent value of 3 000 at 0°;[27] a higher *exo* : *endo* ratio of *ca.* 5 200 has been reported for CF_3-CO_2H–SO_2ClF at an unspecified temperature,[28] but our value of 2 550 is the highest reported for 25°. Lower ratios (<1 000) for mesylates in aqueous dioxan have been reported,[29] and mesylates and tosylates give similar values in 50% ethanol-water (1 600 and 1 400 respectively, Table 1). In contrast, the rate ratio for tosylates in trifluoroacetic acid at 25° is only 1 120,[30] and a value of 1 750 has been reported for 97% hexafluoropropan-2-ol-water.[31,*] Our measurements for hydrolysis of (IV, X = OMs) at 25° appear to be the highest directly determined solvolytic rate constants published to date; values up to 2.57×10^{-1} s^{-1} have been published,[32] but even faster reactions have been studied.[33]

The rates of solvolyses of (IV) and (V) have attracted considerable discussion and controversy.[28,34] From a comparison of trifluoroacetolysis titrimetric rate constants for (IV), (V), and cyclopentyl tosylates, it has been suggested that 2-*exo*-norbornyl tosylate (V) is solvolysed anomalously rapidly and 2-*endo*-norbornyl tosylate anomalously slowly.[35] It was assumed[35] that a 'normal' trifluoroacetolysis rate constant for secondary 2-norbornyl systems could be calculated from that for cyclopentyl tosylate by allowing for the *normal* inductive–hyperconjugative effects of the two extra carbon atoms in (IV) and (V). Thus in effect solvolysis rates of systems with equal numbers of carbon atoms were compared. A similar comparison can be carried out for water but it is necessary to allow for the extra nucleophilic solvent assistance in water, using estimates given in Table 2. According to this argument[35] any discrepancy between the predicted 'normal' and the experimentally observed solvolysis rates cannot be due to nucleophilic solvent assistance or to *normal* inductive–hyperconjugative effects because these have been allowed for explicitly and quantitatively. Known conformational differences[36] cannot be accounted for quantitatively, but rate ratios for tertiary systems[37,38] suggest that conformational differences between norbornyl and cyclopentyl systems do not lead to significant kinetic effects.

The results of this analysis (Table 3) show marked discrepancies between the predicted and observed rate constants (residual rate factors, Table 3) and imply that additional kinetic effects are important. For the *exo*-system (IV) it has been suggested that the enhanced reactivity is due to anchimeric assistance,[39] or that there is unusually high hyperconjugative stabilization of charge development on C(2) from the C(1)–C(6) bond.[34a] The residual rate factor of 98—260 is higher than that calculated for trifluoroacetic acid, probably because substantial internal ion pair return occurs in trifluoroacetic acid. This proposal could be checked by determining the polarimetric rate constant for trifluoroacetolysis of (IV), but unfortunately the reaction is very fast and difficult to study.[30] The *endo*-system (V) reacts slower than predicted and the residual rate factor (10—27) is in good agreement with the earlier estimate (20—60) based on trifluoroacetolysis rate constants. The minor discrepancy between the magnitudes can be explained by nucleophilic solvent assistance in (V), which is calculated [equation (1)] to be *ca.* 2. It has been

TABLE 3

Relative rates of secondary hydrolyses

Mesylate	Observed [a]	Predicted [b]	Residual rate factors [c]
Cyclopentyl	1	0.077 [d]	
2-*exo*-Norbornyl	60	0.23—0.61 [e]	98—260 (20—60) too fast
2-*endo*-Norbornyl	0.023	0.23—0.61 [e]	10—27 (20—60) [f] too slow

[a] Table 1. [b] For an S_N1 reaction proceeding without anchimeric assistance. [c] See text for definition. [d] Using the estimate of 13 for nucleophilic solvent assistance (Table 2). [e] Estimated from the corresponding value for cyclopentyl using rate factors of 3—8 (see ref. 35) to allow for the normal inductive–hyperconjugative effects of the two extra carbon atoms. [f] Values in parentheses refer to a previous calculation[35] using trifluoroacetolysis rate constants.[30]

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* *Note added in proof*: Professor J. M. Harris has informed us that the ratio of 1 750 may be too low, and a revised value of *ca.* 3 000 has been obtained (J. M. Harris, D. L. Mount, and S. G. Shafer, unpublished results). The change in leaving group from brosylate[31] to tosylate seems unlikely to be the cause of this discrepancy.

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proposed that the low reactivity of (V) is due to steric hindrance to ionization[34b] or to steric hindrance to solvation of the leaving group.[35] One might have expected this effect to be greater in trifluoroacetic acid than in water because hydrogen bonding to the leaving group should be greater for the more acidic solvent. It has also been proposed that the reactivity of secondary *endo*-systems (V) is reduced because of attraction between the negative charge developing on the leaving group (X) and positive charge developing on the hydrogen atom at the 2-position.[34c]

Conclusions.—Conductometric techniques appear to give good results for hydrolysis rate constants for mesylates having up to seven carbon atoms in the alkyl chain, and the results given in Tables 1 and 2 and shown in the Figure fit well into the mechanistic framework proposed earlier for other secondary solvolyses.[1,6,7,13] The reactions examined appear to proceed *via* transition states with high carbocation character, and in most cases the solvent is implicated as a nucleophile in the rate-determining step (S_N2 reaction). Additional mechanistic information available for hydrolyses are heat capacities of activation[40] and kinetic solvent isotope effects,[15] and further work is needed to fit these into the mechanistic framework discussed above.

EXPERIMENTAL

Purification of Chemicals.—All mesylates and tosylates, prepared by reacting the alcohol with methanesulphonyl or toluene-*p*-sulphonyl chloride,[17] were purified by recrystallization from light petroleum at −78° or by column chromatography (silica gel). 2-Adamantyl mesylate is a solid, m.p. 67°,[41] but other mesylates were obtained as oils and their purity checked by t.l.c., i.r. and n.m.r.; refractive indices were in satisfactory agreement with literature values.[10,29,42]

Acetone was refluxed over $KMnO_4$, dried over 4A molecular sieves, and distilled. Ethanol was prepared as described previously.[1] Karl Fischer titration showed <0.01 wt% water in the acetone and <0.015 wt% water in the ethanol.

Kinetic Methods.—All solvolyses were followed conductometrically using a Wayne–Kerr model B331 impedance bridge or a rapid response conductivity amplifier.[43] We have established that these techniques lead to rate constants in agreement with those obtained titrimetically.[1] For each acceptable run, agreement between calculated and observed conductances after 10 or more half-lives was checked. In some cases the conductances drifted upwards, although the fit to first-order kinetics over one or two half-lives was good; these solutions, though free from visible particles, are probably not truly homogeneous. To aid in the preparation of homogeneous solutions (10^{-3}—10^{-4}M) the alkyl sulphonates were usually dissolved in acetone or ethanol before addition of water. For hydrolyses in pure water, the solutions were shaken thoroughly, and the early part of the kinetic run had sometimes to be ignored. Raw kinetic data were fitted to the first-order rate equation using a modified version of the LSKIN least-squares computer program.[44]

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