Solvolysis of *endo*- and *exo*-Bicyclo[3.2.1]octan-3-yl Toluene-*p*-sulphonates. Part 2.[1] Rates and Deuterium Kinetic Isotope Effects

By **Mrs R. M. Banks** and **H. Maskill,*** Department of Chemistry, University of Stirling, Stirling FK9 4LA

Rates and secondary deuterium kinetic isotope effects for the solvolysis of *endo*-and *exo*-bicyclo[3.2.1]octan-3-yl toluene-*p*-sulphonates [(4a and c) and (5a and c)] have been measured. Rate constants, rate ratios, and apparent *m* values, when compared with results for model compounds, suggest that the solvolyses of (4a) and (5a) are close to the limiting (S_N1) extreme in all solvents. The α-deuterium kinetic isotope effects are high (*ca.* 1.19—1.20 at 25 °C) for (5c) in formic and acetic acids, aqueous 50, 80, and 98% ethanol, and aqueous 97% 2,2,2-trifluoroethanol, and for (4c) in all these solvents except aqueous 98% ethanol (1.141 at 60.4 °C). The β-$^2H_4$ kinetic isotope effects are also high for both (4a) and (5a). The results are interpreted in terms of a principal mechanism involving rate-determining formation of intimate ion-pair intermediates. For the solvolysis of (4a) in aqueous 98% ethanol some direct S_N2 reaction of solvent with covalent tosylate is also invoked. Mechanisms of solvolysis generally are discussed including the roles of intimate and solvent-separated ion-pairs, and solvent-induced S_N2.

THE chemistry of derivatives of bicyclo[3.2.1]octane is important in two respects. First, bicyclo[3.2.1]octan-2-yl arenesulphonates are homologues of the corresponding norbornan-2-yl compounds. Both have bridging alkyl substituents at the β-carbon atoms and are potentially capable of carbon hyperconjugation during ionization with subsequent formation of non-classical ions in solvolysis.[2] Investigations of the higher homologues have helped the chemistry of norbornan-2-yl compounds to be seen in a wider context.[3-5] Secondly, bicyclo[3.2.1]octan-3-yl halides [6] and arenesulphonates [7] do not have carbon branching at the β-carbon atoms and relate to other simple secondary alkyl halides and arenesulphonates. Comparative studies of these different secondary alkyl compounds provide insight into the steric and stereochemical requirements of particular reaction types in the absence of complicating features such as proximal alkyl substituents.

A spectacular illustration of the effect of a bridging alkyl substituent at the β-carbon atom is seen in the products of acetolysis of toluene-*p*-sulphonates (tosylates). Compound (1a) gives very predominantly (1b), and (2a) gives a mixture of (2b) plus (3b); [3] the same

[1] Part 1, R. M. Banks and H. Maskill, *J.C.S. Perkin II*, 1976, 1506.
In Table 3 of this paper, the ratios of inversion to retention from formolysis of *endo*-bicyclo[3.2.1]octan-3-yl tosylate and acetolysis of the *exo*-isomer are given as 227 and 883, respectively. These should be 22.7 and 88.3.

[2] G. D. Sargent, *Quart. Rev.*, 1966, **20**, 301; P. D. Bartlett, 'Nonclassical Ions,' Benjamin, New York, 1965.

[3] H. L. Goering and G. N. Fickes, *J. Amer. Chem. Soc.*, 1968, **90**, 2848, 2856, 2862; H. L. Goering and M. F. Sloan, *ibid.*, 1961, **83**, 1397, 1992.

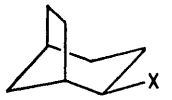
[4] H. Maskill, *J. Amer. Chem. Soc.*, 1976, **98**, 8482; *J.C.S. Perkin II*, 1976, 1889.

[5] H. Maskill, *J.C.S. Perkin II*, 1975, 1850.

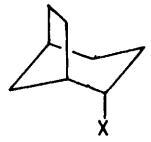
[6] C. A. Grob and A. Weiss, *Helv. Chim. Acta*, 1966, **49**, 2605.

[7] C. W. Jefford, D. T. Hill, and J. Gunsher, *J. Amer. Chem. Soc.*, 1967, **89**, 6881.

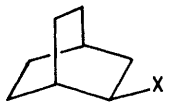
products are obtained from (3a) as from (2a).[3] These results are readily interpretable on the basis of stereospecific formation of isomeric non-classical cations from (1a) and (2a).[3,5] On the other hand, bicyclo[3.2.1]oct-2-ene plus the inverted unrearranged substitution



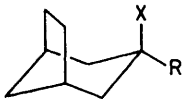
(1) a; X=OTs
b; X=OAc



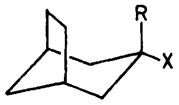
(2) a; X=OTs
b; X=OAc



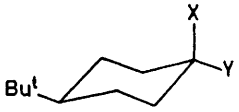
(3) a; X=OTs
b; X=OAc



(4) a; X=OTs, R=H
b; X=OAc, R=H
c; X=OTs, R=D
d; X=OH, R=H,D

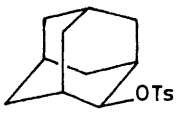


(5) a; X=OTs, R=H
b; X=OAc, R=H
c; X=OTs, R=D
d; X=OH, R=H,D



(6) a; X=OTs, Y=H
b; X=OBs, Y=H

(7) a; X=H, Y=OTs
b X=H, Y=OBs



(8)

products (4b) and (5b) are the major products from (5a) and (4a), respectively.[1] These results are accommodated by a mechanism involving classical intimate ion-pairs (each ion-pair within a single solvation shell), and are closely analogous to the results obtained from the 4-t-butylcyclohexyl arenesulphonates (6) and (7).[8]

We have already described [1] the detailed analysis of the products of solvolysis of (4a) and (5a) and now report the rates and α-deuterium kinetic isotope effects (α-k.i.e.) for the solvolysis of (4a and c) and (5a and c) in buffered formic and acetic acids, buffered 50% aqueous ethanol, unbuffered aqueous 80 and 98% ethanol, and aqueous 97% 2,2,2-trifluoroethanol, and of (5a and c) in unbuffered 50% aqueous ethanol. We also present the kinetic isotope effects of β-$^2H_4$ substitution upon the solvolysis of (4a) and (5a) in buffered formic and acetic acids, buffered 50% aqueous ethanol, and unbuffered aqueous 98% ethanol.

[8] N. C. G. Campbell, D. M. Muir, R. R. Hill, J. H. Parish, R. M. Southam, and M. C. Whiting, *J. Chem. Soc.* (*B*), 1968, 355.

RESULTS AND DISCUSSION

Preparations of the non-deuteriated compounds have already been described; [1,7] the deuteriated analogues were made by standard methods. Our sources of deuterium were lithium aluminium deuteride (>99% $^2H_4$) or sodium borodeuteride (>98% $^2H_4$) for the α-deuteriated compounds, and deuterium oxide (>99.8% $^2H_2$) for the β-deuteriated materials, but the deuterium contents of our substrates were independently established by g.l.c.–mass spectrometry.[9] Alcohols (4d) and (5d) were unsuitable, as the intensities of parent ions were too low. The corresponding trimethylsilyl ethers showed intense $(M - 15)^+$ peaks (loss of methyl) but calculations based upon this region gave results of 88—90% isotopic purity; similarly low results were obtained from the mass spectra of the acetates. These values were disconcerting as no protium could be detected at C-3 in the integrated n.m.r. spectra of the alcohols. Mass spectra of the trimethylsilyl ethers of the β-$^2H_4$ alcohols were analysed in the same way. The tetradeuteriated diastereoisomeric alcohols had been prepared simultaneously from the same tetradeuteriated ketone and had been subjected to a common work-up procedure. Surprisingly, the deuterium incorporation results were not only low, but different for the two diastereoisomers. We conclude that the fragmentation patterns of deuteriated and undeuteriated trimethylsilyl ethers are different, owing to substantial kinetic isotope effects. These results are in contrast to those we obtained for *cis*- and *trans*-4-t-butylcyclohexyl [10] and bicyclo[2.2.2]-octan-2-yl [4] trimethylsilyl ethers. Deuteriated bicyclo-[3.2.1]oct-2-ene, isolated from the acetolysis of (5c), was shown by mass spectroscopy to be of high isotopic purity (>98% $^2H_1$); consequently (5c) must have contained an equally acceptable level of deuterium. Undeuteriated bicyclo[3.2.1]oct-2-ene [1] itself gave an intense parent peak and negligible $(M - 1)^+$ and $(M - 2)^+$ peaks so this method is suitable for an accurate determination of deuterium content using the parent ion region. The integrated n.m.r. spectrum of a concentrated solution of 3-deuterio-*exo*-bicyclo[3.2.1]octan-3-yl tosylate showed no vestige of a signal due to protium at C-3, a result which corroborates the indirect mass spectrometric result from the deuteriated alkene. We conclude that the reliability of mass spectrometry for the direct determination of deuterium in alcohols, esters, and trimethylsilyl ethers is dependent upon the structure of the alkyl residue. Consequently, other investigators using such compounds may have made unwarranted adjustments to their subsequent kinetic isotope effect results on the basis of inaccurately low deuterium incorporation measurements.

[9] K. Biemann, 'Mass Spectrometry,' McGraw–Hill, New York, 1962; A. F. Thomas, 'Deuterium Labelling in Organic Chemistry,' Appleton–Century–Crofts, 1971, New York.

[10] R. M. Banks, Ph.D. Thesis, Stirling University, 1975.

Although a conductance technique [11,12] would have given more precise rate measurements in aqueous ethanol and trifluoroethanol, an adaptation of the spectrophotometric method of Swain and Morgan [13] was used which allowed rates to be measured in strongly conducting acidic solutions with high salt concentrations. The results are shown in Table 1.

Rates of Solvolysis.—The rates of acetolysis of (4a) and (5a) at 25 °C have already been compared with those of cyclohexyl, 4-t-butylcyclohexyl, and bicyclo[3.2.1]oct-6-en-3-yl tosylates.[14] There is no convincing evidence of any large rate enhancements from this comparison or from the application of the Foote–Schleyer equations.[7,15] The k_{endo}/k_{exo} values for (4a) and (5a) range from 14 formic acid than in acetic acid, and in aqueous ethanol the rates increase as the proportion of water increases. If a solvolytic reaction involves rate-determining ionization followed by more rapid reactions of ions or ion-pairs (the classical S_N1–$E1$ mechanism), the reaction rate should be only marginally affected by different solvents of varying nucleophilicities at constant Y value (ionizing power).[19] A commonly used test of this is the rate in 98E compared with the rate in acetic acid.[20,21] Values are 0.56 (60 °C) for (4a) and 0.35 (70 °C) for (5a), which may be compared with 7.8, 4.3, and 0.13 for isopropyl, cyclohexyl, and 2-adamantyl tosylates (25 °C).[22] The complementary effect of the solvent ionizing power at constant nucleophilicity upon the

TABLE 1

Rates [a] and secondary kinetic isotope effects for the solvolysis of (4a) and (5a)

		HCO_2H [b]	AcOH [c]	97 TFE [i]	50E [d,i]	80E [i]	98E [i]
$k_H \times 10^5/s^{-1}$ (T/°C)	(4a)	333	63.4	119	48.3	164	35.4
		∓2	∓0.6	∓1	∓0.2 [f]	∓2	∓0.3
		(24.8°)	(60.6°)	(41.4°)	(24.8°)	(55.0°)	(60.4°)
	(5a)	10.6	14.4	6.32	4.26	5.12	4.98
		∓0.2	∓0.2 [e]	∓0.06	∓0.08 [g,h]	∓0.06	∓0.05
		(24.8°)	(70.6°)	(41.4°)	(36.0°)	(55.0°)	(70.1°)
α-^{2}H-k.i.e. (T/°C)	(4a)	1.17	1.169	1.188	1.194	1.177	1.141
		∓0.01	∓0.008	∓0.006	∓0.004 [f]	∓0.009	∓0.002
		(24.8°)	(60.6°)	(41.4°)	(24.8°)	(55.0°)	(60.4°)
	(5a)	1.20	1.163	1.203	1.198	1.178	1.183
		∓0.01	∓0.008 [e]	∓0.007	∓0.008 [h]	∓0.007	∓0.007
		(24.8°)	(70.6°)	(41.4°)	(36.0°)	(55.0°)	(70.1°)
β-$^2H_4$-k.i.c. (T/°C)	(4a)	2.75	2.43		2.58		2.23
		∓0.05	∓0.03		∓0.02		∓0.02
		(28.3°)	(61.4°)		(30.0°)		(60.0°)
	(5a)	2.36	2.14		2.19		1.93
		∓0.02	∓0.03		∓0.02		∓0.03
		(36.0°)	(70.5°)		(46.6°)		(69.8°)

[a] Rate constants are means of 5—8 values and kinetic isotope effects are means of 5—8 ratios except where otherwise stated. Errors are standard errors. See refs. 4 and 5 for further details. [b] Contains 0.15M-sodium formate. [c] Contains 0.15M-potassium acetate. [d] Contains 0.008 9M-borax unless otherwise stated. [e] At 60.6 °C $k_H = 4.46 \mp 0.08 \times 10^{-5}$ s^{-1}, α-k.i.e. = 1.16 ∓ 0.02 (means of 4 runs). [f] Mean of 11 runs. With 0.003 5M-borax, $k_H = 49.1 \mp 0.6 \times 10^{-5}$ s^{-1}; α-k.i.e. = 1.214 ∓ 0.007. [g] k_H = 1.04 ∓ 0.03 × 10^{-5} s^{-1} at 24.7 °C. [h] [Borax] = 0.003 5M. With no borax, $k_H = 3.74 \mp 0.05 \times 10^{-5}$ s^{-1}, α-k.i.e. = 1.188 ∓ 0.008 (means of 4 runs). [i] Aqueous 50, 80, and 98% ethanol and aqueous 97% trifluoroethanol = 50E, 80E, 98E, and 97TFE, respectively.

(AcOH; 61 °C) to *ca.* 50 (50E; 25 °C). These values are larger than comparable results for unbridged cyclohexyl systems, *e.g.* 3.01 (AcOH) and 4.35 (EtOH) for *trans*-2-decalyl tosylates (50 °C),[16] and 3.24 (AcOH; 50 °C) [17] and 4.55 (50E; 35 °C) [18] for 4-t-butylcyclohexyl arenesulphonates [(6a), (7a) and (6b), (7b)]. The present ratios also increase as the nucleophilicity of the solvent is increased, a tendency not found in the unbridged systems.

The qualitative effects of solvents upon these rates of solvolysis are unexceptional: the reactions are faster in solvolysis rate is reflected in the m value (aqueous ethanol [19]) or the apparent m value (carboxylic acids [21,23]) of the reactant in terms of the Grunwald–Winstein equation in the form $\log k_2/k_1 = m(Y_2 - Y_1)_N$. From our results and Jefford's, we calculate approximate apparent m values of 0.76 for (4a) and 0.63 for (5a) at 25 °C. These may be compared with values reported for isopropyl (0.65), 1,2-dimethylpropyl (0.75), and 1,2,2-trimethylpropyl (0.83) brosylates (25 °C),[23] and 1.0 for 2-adamantyl tosylate (25 °C).[24,25b]

[11] V. J. Shiner, W. E. Buddenbaum, B. L. Murr, and G. Lamaty, *J. Amer. Chem. Soc.*, 1968, **90**, 418.
[12] V. J. Shiner, W. Dowd, R. D. Fisher, S. R. Hartshorn, M. A. Kessick, L. Milakowsky, and M. W. Rapp, *J. Amer. Chem. Soc.*, 1969, **91**, 4838.
[13] C. G. Swain and C. R. Morgan, *J. Org. Chem.*, 1964, **29**, 2097.
[14] N. A. LeBel and R. J. Maxwell, *J. Amer. Chem. Soc.*, 1969, **91**, 2307.
[15] C. S. Foote, *J. Amer. Chem. Soc.*, 1964, **86**, 1853; P. von R. Schleyer, *ibid.*, p. 1854.
[16] H. Tanida, S. Yamamoto, and K. Takeda, *J. Org. Chem.*, 1973, **38**, 2792.
[17] S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.
[18] V. J. Shiner and J. G. Jewett, *J. Amer. Chem. Soc.*, 1964, **86**, 945; 1965, **87**, 1382, 1383.
[19] E. Grunwald and S. Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 846; A. H. Fainberg and S. Winstein, *ibid.*, 1956, **78**, 2770.
[20] S. Winstein, E. Grunwald, and H. W. Jones, *J. Amer. Chem. Soc.*, 1951, **73**, 2700.
[21] A. Streitwieser, 'Solvolytic Displacement Reactions,' McGraw–Hill, New York, 1962.
[22] J. L. Fry, C. J. Lancelot, L. K. M. Lam, J. M. Harris, R. C. Bingham, D. J. Raber, R. E. Hall, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1970, **92**, 2538.
[23] S. Winstein and H. Marshall, *J. Amer. Chem. Soc.*, 1952, **74**, 1120.
[24] J. M. Harris, R. E. Hall, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1971, **93**, 2551.
[25] (*a*) J. L. Fry, J. M. Harris, R. C. Bingham, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1970, **92**, 2540; P. von R. Schleyer, J. L. Fry, L. K. M. Lam, and C. J. Lancelot, *ibid.*, p. 2542; (*b*) T. W. Bentley and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1976, **98**, 7658.

The implicit standard reaction in these empirical correlations is the solvolysis of t-butyl chloride in 80E.[19,20] A compound to which (4a) and (5a) are more closely related structurally, and which is believed to react in the common solvents by an entirely limiting (S_N1) mechanism, is 2-adamantyl tosylate (8).[22,25a] A comparison is shown in Table 2.

TABLE 2

Comparison of rate constants of secondary alkyl tosylates (25 °C) [a]

	$k_{Pr^i}/k_{2\text{-Ad}}$	$k_{Pin}/k_{2\text{-Ad}}$ [b]	k_{exo} [d]$/k_{2\text{-Ad}}$	k_{endo} [d]$/k_{2\text{-Ad}}$
HCO_2H	3.2	20.3	9.1	287
AcOH	13.0	32.2	43 (60.6 °C) [b]	610 (60.6 °C) [b]
50E	19.1	36.1	13.5	627
80E	122	72.5	31 (55.0 °C) [c]	982 (55.0 °C) [c]

[a] Rate constants for isopropyl and 2-adamantyl tosylates taken from ref. 25a; rate ratios for pinacolyl tosylate/2-adamantyl tosylate taken from ref. 26. [b] k(60.6 °C) for 2-adamantyl tosylate calculated to be 1.04×10^{-6} s^{-1} from results in ref. 25a. [c] k(55.0 °C) for 2-adamantyl tosylate calculated to be 1.67×10^{-6} s^{-1} from results in ref. 25a. [d] k_{exo} and k_{endo} are rate constants for (5a) and (4a), respectively.

Whereas the rate ratios for isopropyl and 2-adamantyl tosylates change by a factor of *ca.* 38, over the same range of solvents, the respective rate ratios for (4a) and (5a) with (8) change by less than five-fold. The range for this ratio for 1,2,2-trimethylpropyl (pinacolyl) tosylate with (8) is 3.6.[26]

These several criteria indicate that (4a) and (5a) undergo solvolysis by mechanisms which are more closely related to the mechanisms of solvolysis of 2-adamantyl tosylate and t-butyl chloride than to the more nucleophilically assisted mechanisms attributed to the solvolysis of simple acyclic secondary systems such as isopropyl arenesulphonates.[21,22,25]

α-Deuterium Kinetic Isotope Effects.—When the known temperature dependence of the α-k.i.e. is taken into account,[27a] the results for (4a) and (5a) are seen to be remarkably insensitive to the nature of the solvent, and close to 1.19—1.20 (25 °C) with the exception of the results for (4a) in formic acid and 98E. The result in formic acid is less precise than most of the others and so should not be regarded as significantly different. The value for (4a) in the strongly nucleophilic, weakly ionizing 98E,[28] however, is reasonably precise and genuinely low at 1.141 (60.4 °C).

These results, with the exception of that for (4a) in 98E, are higher than those for simple acyclic secondary alkyl arenesulphonates in the common solvents,[27a] and are comparable with the result for *cis*-4-t-butylcyclohexyl brosylate (1.202; 50E; 35 °C).[18] They are consistently lower than the values recorded for 2-adamantyl tosylate [24] and tresylate (2,2,2-trifluoroethanesulphonate) [29] in the common solvents, and for simple secondary alkyl arenesulphonates [24] in the very weakly nucleophilic trifluoroacetic acid (*ca.* 1.22—1.23; 25 °C) by an amount which is outside experimental error.

The close similarity of the results for (4a) and (5a), with the exception of that for (4a) in 98E, supports the mechanistic conclusion based upon the stereospecificities of the product analyses:[1] (4a) and (5a) react by very similar mechanisms. The magnitudes, 1.19—1.20 (25 °C), and the absence of any variation with solvent indicates that these mechanisms are close to the limiting (S_N1) extreme, a conclusion supported by the above considerations of rates and rate ratios.

The low result for the α-k.i.e. of (4a) in 98E implicates a mechanism which is different in some crucial way from the mechanisms of (4a) and (5a) in other solvents. One possibility is that the solvolysis of (4a) in 98E involves a greater extent of solvent-induced S_N2 reaction either upon covalent tosylate,[25b,30,31] or upon pre-formed intimate ion-pairs.[12,32] Another possibility is that ion-pair formation is rate-determining for (4a) in 98E whereas in the other solvents [and for (5a) in all the solvents] a subsequent step is rate-determining, the solvent-separation of the ion-pairs (ions remain paired but become separately solvated).[29,33,34]

β-Deuterium Kinetic Isotope Effects.—The results are seen to be high; this is expected for reactions in which ionization is strongly assisted by hydrogen hyperconjugation.[27a,35] They support the general mechanistic contention that (4a) and (5a) react largely by a limiting mechanism, and that (5a) reacts through a non-chair cyclohexane conformation.[1,8,18] As β-k.i.e.s are strongly stereospecific [18,36] and the temperature dependence is not fully understood,[27a] our composite values do not allow a more detailed interpretation at present.

Conclusions.—The analysis of the products from (4a) and (5a) facilitated a molecular description of those steps of the solvolysis mechanism subsequent to the formation of ion-pair intermediates, the rearrangement and product-determining steps.[1] Substitution without rearrangement from both (4a) and (5a) is strongly stereospecific in favour of inversion. We believe that this implicates intimate ion-pairs as the principal inter-

[26] J. E. Nordlander, R. R. Gruetzmacher, and F. Miller, *Tetrahedron Letters*, 1973, 927.

[27] 'Isotope Effects in Chemical Reactions,' eds. C. J. Collins and N. S. Bowman, Amer. Chem. Soc. Monograph 167, Van Nostrand–Reinhold, New York, 1970, (*a*) ch. 2 by V. J. Shiner; (*b*) ch. 3 by D. E. Sunko and S. Borcic.

[28] P. E. Peterson and F. J. Waller, *J. Amer. Chem. Soc.*, 1972, **94**, 991; T. W. Bentley, F. L. Schadt, and P. von R. Schleyer, *ibid.*, 1972, **94**, 992.

[29] V. J. Shiner and R. D. Fisher, *J. Amer. Chem. Soc.*, 1971, **93**, 2553.

[30] D. J. Raber, J. M. Harris, R. E. Hall, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1971, **93**, 4821.

[31] V. J. Shiner, M. W. Rapp, and H. R. Pinnick, *J. Amer. Chem. Soc.*, 1970, **92**, 232.

[32] R. A. Sneen, *Accounts Chem. Res.*, 1973, **6**, 46; R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, 1969, **91**, 6031; H. Weiner and R. A. Sneen, *ibid.*, 1965, **87**, 292; R. A. Sneen and H. M. Robbins, *ibid.*, 1972, **94**, 7868.

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

[34] J. M. Harris, D. C. Clark, A. Becker, and J. F. Fagan, *J. Amer. Chem. Soc.*, 1974, **96**, 4478; J. M. Harris, A. Becker, J. F. Fagan, and F. A. Walden, *ibid.*, p. 4484.

[35] V. J. Shiner and J. O. Stoffer, *J. Amer. Chem. Soc.*, 1970, **92**, 3191.

[36] M. Tarle, S. Borcic, and D. E. Sunko, *J. Org. Chem.*, 1975, **40**, 2949, 2954.

mediates from which product partitioning occurs. Such ion-pairs are not unsolvated;[25a] the intimate ion-pair is within a shell of orientated solvent molecules and the interaction between each ion with specific solvent molecules will be affected by the structural features and electronic properties of cation, anion, and solvent molecules.

The very small amount of substitution with retention of configuration could arise from material which has undergone internal return[37] with inversion of configuration[38,39] as proposed earlier,[1] or it could be derived from a small proportion of solvent-separated ion-pairs, intermediates which should react with lower stereospecificity.[37,38,40] However, the amount of substitution with retention is very low and is not significantly dependent upon the nature of the solvent. We conclude that solvent-separated ion-pairs are not major intermediates in any of these reactions and therefore the low α-k.i.e. for (4a) in 98E cannot be due to the suppression of ion-pair solvent-separation by the most nucleophilic medium.

If the formation of ion-pairs is rate-determining in acetic acid (and the less nucleophilic media) as should be the case,[21,40,41] the change to 98E at constant Y can only facilitate processes which occur *after* the slow step and consequently could not affect the α-k.i.e. The depressed α-k.i.e. for (4a) in 98E, therefore, is most satisfactorily ascribed primarily to the intrusion of an appreciable extent of S_N2 by solvent upon covalent tosylate.[24,25b,31,42]

It is significant that this manifestation of an S_N2 reaction occurs for (4a) but not for (5a). The former reacts exclusively through its ground state conformation and a nucleophile has a relatively uninhibited equatorial approach to the correct side of C-3. Evidently the partial rate constant in the generalized Winstein–Holness equation[8,17] for the unstable conformer of (5a) which is stereochemically able to undergo bimolecular reaction is not high enough to compensate for the low concentration of that conformer. The extra concurrent mode of reaction for (4a) also satisfactorily accounts for the high k_{endo}/k_{exo} values which increase with increasing solvent nucleophilicity, and the higher k_{98E}/k_{AcOH} value for (4a) than for (5a).

The principal remaining question concerns the mechanism for (4a) and (5a) in solvents other than 98E with which, for (4a) but not (5a), a solvent-induced S_N2 mechanism competes in 98E. The mechanism must be different in some essential detail from that for the solvolysis of (8) to account for the consistent difference in the α-k.i.e.s. It must also allow for the virtually identical and high α-k.i.e.s of simple secondary alkyl arenesulphonates in trifluoroacetic acid.[24,27a] An unacceptable explanation is that whereas (8) reacts exclusively *via* the S_N1 mechanism, (4a) and (5a) react in all the modestly nucleophilic media by the same proportion of two concurrent mechanisms (or a kinetically equivalent single intermediate mechanism),[25b] the classical S_N1 with rate-determining ionization and solvent-induced S_N2. The solvent dependence of the k_{endo}/k_{exo} values, the different stereochemistries of (4a) and (5a) in the context of the S_N2 mechanism which is known to have stringent stereochemical requirements,[40,43] and the constant α-k.i.e. values in a wide range of solvolytic conditions, taken together, are incompatible with such a simple explanation. The simple Sneen[12,32] ion-pair mechanism is equally unable to provide an acceptable explanation of the α-k.i.e.s for (4a) and (5a) being less than 1.23, and of their constancy across a wide range of solvents.

Application of the complete Winstein–Shiner[29,33,34,37] range of solvolysis mechanisms accounts completely for our results; it also fits a much wider body of experimental evidence. Besides the S_N1–S_N2 mechanistic dichotomy, this overall scheme includes a further bifurcation within the S_N1 mechanism: product formation from either intimate or solvent-separated ion-pairs. This requires that the conversion of intimate into solvent-separated ion-pairs, a process which involves the insertion of one or more solvent molecules *between* cation and anion, has a free energy of activation, and that both types of ion-pair correspond to free energy minima.

The existence of both intimate and solvent-separated ion-pairs has long been recognised when the cation has some special stabilizing feature.[37,44] Acknowledgement that either formation of the intimate ion-pairs or their conversion into the solvent-separated ion-pairs may be rate-determining in the solvolysis of secondary alkyl systems (or, expressed alternatively, that either intimate or solvent-separated ion-pairs may be the principal intermediates from which the product-forming paths diverge in carbocation processes) has been resisted. The general scheme is illustrated.

The limiting extreme of the S_N1 mechanism which obtains for (8) in all common solvents, and simpler secondary alkyl substrates in trifluoroacetic acid, has an α-k.i.e. of *ca.* 1.23 which is largely independent of the

[37] A. F. Diaz, I. Lazdins, and S. Winstein, *J. Amer. Chem. Soc.*, 1968, **90**, 1904; S. Winstein, B. Appel, R. Baker, and A. Diaz, *Chem. Soc. Special Publ.*, 1965, **19**, 109; S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck, and G. C. Robinson, *J. Amer. Chem. Soc.*, 1956, **78**, 328; S. Winstein, J. S. Gall, M. Hojo, and S. Smith, *ibid.*, 1960, **82**, 1010.

[38] H. L. Goering and H. Hopf, *J. Amer. Chem. Soc.*, 1971, **93**, 1224.

[39] K. Okamoto, S. Saito, and H. Shingu, *Bull. Chem. Soc. Japan*, 1970, **43**, 3008.

[40] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' Bell, London, 2nd edn., 1969.

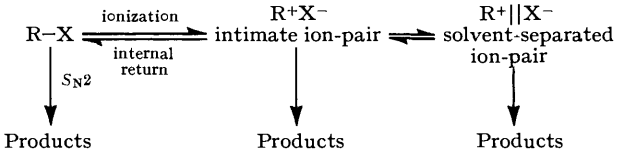
[41] A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 2780; S. Winstein, E. Grunwald, and L. L. Ingraham, *ibid.*, 1948, **70**, 821.

[42] A. Pross and R. Koren, *Tetrahedron Letters*, 1974, 1949.

[43] R. L. Julian and J. W. Taylor, *J. Amer. Chem. Soc.*, 1976, **98**, 5238; H. S. Mosher, *Tetrahedron*, 1974, **30**, 1733; B. Stephenson, G. Solladié, and H. S. Mosher, *J. Amer. Chem. Soc.*, 1972, **94**, 4184, 8646.

[44] S. Winstein and K. C. Schreiber, *J. Amer. Chem. Soc.*, 1952, **74**, 2165; S. Winstein and G. C. Robinson, *ibid.*, 1958, **80**, 169; S. Winstein and D. Trifan, *ibid.*, 1952, **74**, 1154; S. Winstein, E. Clippinger, R. Howe, and E. Vogelfanger, *ibid.*, 1965, **87**, 376.

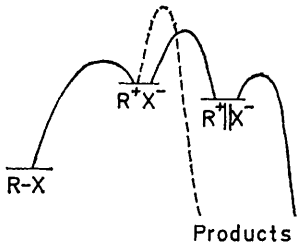
structure of the secondary alkyl group. Rate-determining solvent-separation of intimate ion-pairs has been



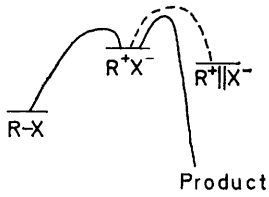
General scheme for solvolysis of R–X.

This scheme is possibly incomplete to the extent that dissociated ions are not included.

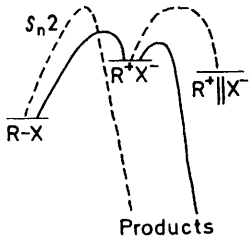
ascribed to this mechanism,[29,33,34] which is depicted in the free energy profile A.



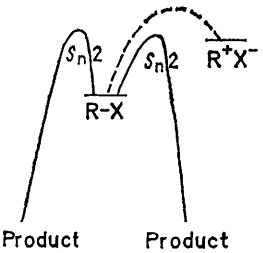
A, Rate-determining solvent-separation of intimate ion-pair



B, Rate-determining product formation (shown as a single weighted mean process) from intimate ion-pair



C, Rate-determining ionization (classical S_N1)



D, S_N2 Reactions on R–X by solvent and added nucleophile

Free energy profiles for solvolysis mechanisms of R–X; dotted lines represent reaction paths not followed

Internal return,[37] a phenomenon which the simple S_N1–S_N2 dichotomy cannot satisfactorily accommodate,[21,40] becomes a necessary concomitant of reaction *via* rate-determining ion-pair solvent-separation. The independent generation of intimate ion-pairs from propene and *p*-bromobenzenesulphonic acid in trifluoroacetic acid, and production of covalent isopropyl brosylate faster than formation of isopropyl trifluoroacetate is strong evidence in support of this mechanism.[45]

The stereochemical course of solvolysis of (8), which cannot be reconciled with nucleophilic capture of simple intimate ion-pairs as the ratio of inversion to retention is very low (*ca.* 0.5),[46] is further evidence of product formation from solvent-separated ion-pairs.

As the solvent becomes more nucleophilic (basic), or as the cation becomes more electrophilic or otherwise unstable, product-forming steps from the intimate ion-pair become faster and, at some stage, overtake the solvent-separation of the ion-pair. If the ionization step has not been affected by the changes which have caused product formation from the intimate ion-pair to have become faster than solvent-separation, this mechanism corresponds to Sneen's proposal [12,32] for S_N2 upon ion-pairs and is illustrated in profile B. (The rate-determining process would really be a weighted mean of several product-forming steps including β-proton abstraction and rearrangement as well as substitution.) Sneen's proposal for the S_N2 mechanism encountered a hostile reception. It is now seen to be expected for only a narrow range of conditions, *i.e.* where product formation, including solvent capture of the intimate ion-pair, is faster than solvent-separation, but not so fast as internal return. Pross and Aronovitch [47] have presented recent evidence that the Sneen mechanism is operative for aqueous ethanolysis of octyl derivatives in the absence of added strongly nucleophilic reagents.

Most changes in the solvent or in the structure of the substrate which would cause product formation from the intimate ion-pair to compete effectively with solvent-separation of the ion-pair, would also cause the initial ionization to become slower; consequently product formation from the intimate ion-pair will usually have become faster than internal return. This corresponds to the classical S_N1 mechanism, rate-determining ionization followed by rapid product-forming steps including, perhaps, some small extent of ion-pair separation. This mechanism is illustrated in profile C and, we propose, is the mechanism for (4a) and (5a) in the modestly nucleophilic solvents and the major mechanism for (4a) in 98E. It has an α-k.i.e. of *ca.* 1.19—1.20 (25 °C).

Solvent-induced S_N2 mechanism, which is included in profile D, will begin to intervene with further increase in solvent nucleophilicity or with an increase in substrate electrophilicity.[31] In the present investigation, this was detected with (4a) in 98E, and would be more extensive for simpler, more open secondary alkyl arene-

[45] V. J. Shiner and W. Dowd, *J. Amer. Chem. Soc.*, 1969, **91**, 6528.

[46] J. A. Bone and M. C. Whiting, *Chem. Comm.*, 1970, 115; J. A. Bone, J. R. Pritt, and M. C. Whiting, *J.C.S. Perkin II*, 1975, 1447.

[47] A. Pross and H. Aronovitch, *J.C.S. Chem. Comm.*, 1976, 817.

sulphonates such as isopropyl compounds in aqueous ethanol or acetic acid. Thus the α-k.i.e.s for isopropyl brosylate [12,33] decrease along the series 97 TFE (1.16), 70 TFE (1.140), 50 TFE (1.122), 50E (1.114), 80E (1.098), and 90E (1.083) as the proportion of solvent-induced S_N2 increases. There have recently been results [48] which suggest that solvent-induced bimolecular substitution upon an intimate ion-pair is overtaken by direct S_N2 upon covalent starting material as strongly nucleophilic reagents are added to a modestly nucleophilic solvent. This fits in very well with the presently described overall scheme.

Theory requires that the α-k.i.e. of a purely S_N2 reaction be close to unity [27] and results of this magnitude have been reported for some methyl and primary alkyl substrates.[27,49] When a secondary system contains an intramolecular nucleophile which can assume the appropriate geometrical arrangement for neighbouring group participation, the α-k.i.e. is correspondingly decreased to the value expected of an S_N2 reaction.[27b,50] Consequently, we deduce that in the solvolytic reactions of cyclohexyl and other simple secondary alkyl arenesulphonates in which the α-k.i.e. is seldom less than *ca.* 1.1, the solvent-induced S_N2 reaction never completely suppresses the unimolecular S_N1 mechanism, a conclusion reached independently by Pritt and Whiting.[51]

At the limiting extreme when solvent-separation of the ion-pair is rate-determining some feature of the intimate ion-pair, or its solvolytic environment, must stabilize the cation or hinder the otherwise rapid product-forming steps of the intimate ion-pair. It is the very low nucleophilicity and basicity of trifluoroacetic acid [28] which make nucleophilic capture and β-proton abstraction slow in this solvent compared with the rate of insertion of one molecule (or more) of solvent between cation and anion. 2-Adamantyl tosylate must also have some intrinsic feature which retards product-forming steps from the intimate ion-pair since in all the common solvents it has the same high α-k.i.e. Bimolecular processes are well known to be subject to steric hindrance [21,40,42] and 2-adamantyl tosylate, both as the covalent material and as the intimate ion-pair has an extremely hindered α-carbon.[30,46] There is also evidence, based upon stereochemistry of substitution [46] (alluded to above) and the detection of thermodynamically very unlikely products,[52] that the 2-adamantyl cation is inherently stabilized by σ-bridging.[52,53] This reinforces the resistance to nucleophilic attack at the intimate ion-pair stage already ascribed largely to steric factors. As β-proton abstraction and rearrangement by hydride [54] or alkyl migration are thermodynamically and kinetically very unfavourable processes,[52,54] the intimate ion-pair from (8) undergoes either internal return or ion-pair solvent-separation with the former being faster than the latter,[29] but their ratio being solvent dependent.

In the scheme of solvolysis mechanisms described here there is no requirement that a reactant under particular conditions be converted into products exclusively by a single mechanism. The substrate will be converted into product(s) under particular experimental conditions by one or more mechanisms according to the free energy barriers (rate constants) of the various respective mechanisms. Inevitably some mechanisms will be inoperative in particular circumstances because they correspond to prohibitively high free energy routes. But the desire to exclude a particular mechanism from the general scheme and hence in all circumstances because it is demonstrably absent in one particular case has led to avoidable controversy.

EXPERIMENTAL

Details of our routine methods and instrumentation, and of the preparation of the non-deuteriated compounds have already been described.[1,5] Mass spectrometry was done by the P.C.M.U., Harwell.

3-*Deuterio*-exo- *and* endo-*bicyclo*[3.2.1]*octan*-3-*ols*.—Mixtures of these were prepared by reduction of bicyclo-[3.2.1]octan-3-one [1] with sodium borodeuteride or lithium aluminium deuteride and were separated by chromatography of deactivated alumina (elution with light petroleum–ethyl acetate). Purification was by sublimation (80 °C; 4 Torr); *endo*-isomer, m.p. 203—204° (lit.,[55] for non-deuteriated analogue, 206—206.5°); $\nu_{max.}(CCl_4)$ 3 625, 2 930, 2 865, 2 130w, 1 445, 1 110, 1 050, and 920 cm^{-1}; $\tau(CCl_4)$ 7.6—8.8 (m) (no signal at τ *ca.* 6.1); *exo*-isomer, m.p. 108.5—109° (lit.,[55] for non-deuteriated analogue, 114—115°); $\bar{\nu}_{max.}(CCl_4)$ 3 625, 2 940, 2 880, 2 140w, 1 455, 1 170, 1 085, and 955 cm^{-1}; $\tau(CCl_4)$ 7.6—9.0 (no signal at τ *ca.* 6.2).

The tosylates were prepared from the respective alcohols by the usual procedure [1] and were recrystallized from light petroleum: *endo*-isomer, m.p. 75—76° (for non-deuteriated analogue, lit.,[7] 71—73°; lit.,[1] 75—76°); $\bar{\nu}_{max.}(CCl_4)$ 2 940, 2 870, 1 370, 1 190, 1 180, 1 170, 1 095, and 905 cm^{-1}; $\tau(CCl_4)$ 2.26 and 2.73 (4 H, ABq, *J* 8 *ca.* Hz), 7.57 (3 H, s), and 7.6—8.8 (12 H, m); *exo*-isomer, m.p. 79.5—80.5° (for non-deuteriated analogue, lit.,[7] 76—77°; lit.,[1] 80—81°); $\bar{\nu}_{max.}(CCl_4)$ 2 970, 2 880, 1 463, 1 375, 1 190, 1 180, 1 165, 1 100, and 940 cm^{-1}; $\tau(CCl_4)$ 2.31, 2.77 (4 H, ABq, *J* *ca.* 8 Hz), 7.58 (3 H, s), and 7.6—8.8 (12 H, m) (at 90 MHz, for a concentrated solution, no signal was detected at τ *ca.* 5.4).

2,2,4,4-*Tetradeuteriobicyclo*[3.2.1]*octan*-3-*one*.—Bicyclo-[3.2.1]octan-3-one (1.52 g, 0.012 mol), anhydrous sodium carbonate (0.1 g), hexadeuterioacetone (1 cm^3), and deuterium oxide (20 cm^3; 99.8% ^2H_2O) were heated under reflux for 40 h. The cooled mixture was extracted three

[48] A. Pross and R. Koren, *Tetrahedron Letters*, 1975, 3613; D. G. Graczyk and J. W. Taylor, *J. Amer. Chem. Soc.*, 1974, **96**, 3255.
[49] C. M. Won and A. V. Willi, *J. Phys. Chem.*, 1972, **76**, 427.
[50] S. Richter, I. Bregovec, and D. E. Sunko, *J. Org. Chem.*, 1976, **41**, 785.
[51] J. R. Pritt and M. C. Whiting, *J.C.S. Perkin II*, 1975, 1458.
[52] M. L. Sinnott, H. J. Storesund, and M. C. Whiting, *Chem. Comm.*, 1969, 1000; H. J. Storesund and M. C. Whiting, *J.C.S. Perkin II*, 1975, 1452.
[53] D. Lenoir, R. E. Hall, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1974, **96**, 2138; D. Lenoir and P. von R. Schleyer, *Chem. Comm.*, 1970, 941.
[54] M. L. Sinnott and M. C. Whiting, *J.C.S. Perkin II*, 1975, 1446.
[55] W. Kraus, *Chem. Ber.*, 1964, 2719.

times with anhydrous ether. The combined ethereal phase was dried ($MgSO_4$), filtered, and fractionally distilled. The residual ketone was sublimed (90 °C; 10 Torr); yield 1.18 g (78%), m.p. 131—134° (lit.,[56] for non-deuteriated analogue, 135—136°); $\bar{\nu}_{max.}(CCl_4)$ 2 940, 2 880, 2 220w, 1 710, 1 450, 1 260, 1 140, 1 125, and 1 095 cm^{-1}; $\tau(CCl_4)$ 7.5br (2 H, s) and 8.1—8.7 (6 H, m).

2,2,4,4-*Tetradeuterio*-endo- *and* exo-*bicyclo*[3.2.1]*octan*-3-*ols*.—The tetradeuteriated ketone was reduced in the usual manner with lithium aluminium hydride to give a 1 : 2 mixture of *endo*- and *exo*-alcohols which were separated and purified as described above: *endo*-isomer, m.p. 202—202.5°; $\bar{\nu}_{max.}(CCl_4)$ 3 625, 2 930, 2 860, 2 200w, 2 100w, 1 450, 1 310, 1 205, 1 140, 1 083, 900, and 827 cm^{-1}; $\tau(CCl_4)$ 6.1 (1 H, s) and 7.7—8.7 (9 H, m); *exo*-isomer, m.p. 108—108.5°; $\bar{\nu}_{max.}(CCl_4)$ 3 620, 2 940, 2 875, 2 200w, 2 100w, 1 450, 1 205, 1 130, 1 078, 978, and 940 cm^{-1}; $\tau(CCl_4)$ 6.25br (1 H, s), 7.78br (3 H, s), and 8.4—8.8 (6 H, m).

The corresponding tosylates were made by the usual method [1] and were recrystallized from light petroleum: *endo*-isomer, m.p. 74—75°; $\bar{\nu}_{max.}(CCl_4)$ 2 930, 2 870, 2 200w, 2 100w, 1 365, 1 190, 1 180, 1 100, 1 000, 900, and 870 cm^{-1}; $\tau(CCl_4)$ 2.26 and 2.72 (4 H, ABq, *J ca.* 8 Hz), 5.30 (1 H, s), 7.56 (3 H, s), 7.85br (2 H, s), and 8.0—8.8 (6 H, m); *exo*-isomer, m.p. 79—80°, $\bar{\nu}_{max.}(CCl_4)$ 2 950, 2 880, 2 220w, 2 120w, 1 370, 1 190, 1 180, 1 100, 965, 933, and 870 cm^{-1}; $\tau(CCl_4)$ 2.30 and 2.76 (4 H, ABq, *J ca.* 8 Hz), 5.46br (1 H, s), 7.57 (3 H, s), 7.77br (2 H, s), and 7.9—8.8 (6 H, m).

Acetolysis of 3-*Deuterio*-exo-*bicyclo*[3.2.1]*octan*-3-*yl Tosylate*.—Compound (5c) (0.25 g) was heated in the buffered acetolysis medium (5 cm^3) at 60 °C for *ca.* 14 h. The solution was cooled, made basic, and extracted twice with pentane. The pentane solution was percolated through a short column of dry alumina and the eluate which contained deuteriobicyclo[3.2.1]oct-2-ene was analysed by g.l.c.–mass spectrometry in comparison with the authentic non-deuteriated analogue (deuterium incorporation >98%).

Solvents.—Details of the preparation of acetolysis and formolysis media and our kinetics procedures have already been described.[5] Stocks of the aqueous 80 and 98% ethanol were prepared by making water (20.0 and 2.00 cm^3, respectively, distilled from $KMnO_4$) up to 100.0 cm^3 with spectroscopic grade absolute ethanol. The aqueous 97% trifluoroethanol was made by mixing water (3.3 g; distilled from $KMnO_4$) and 2,2,2-trifluoroethanol (96.7 g; fractionally distilled from P_2O_5). Because the dissolution of the tosylates in 50% aqueous ethanol is slow, no stock solvent was prepared. The required amount of tosylate was dissolved in ethanol and an equal volume of water (or aqueous borax) was added; a fresh solution was prepared for each run. Initial tosylate concentrations were *ca.* 0.003M and buffer concentrations were 0.15M (potassium acetate in acetic acid and sodium formate in formic acid) and 0.0035M or 0.0089M (borax, when used, in 50E).

[7/455 *Received*, 14*th March*, 1977]

[56] W. Kraus, G. Klein, H. Sadlo, and W. Rothenwöhrer, *Synthesis*, 1972, 485.