The S_N3–S_N2 spectrum. Rate constants and product selectivities for solvolyses of benzenesulfonyl chlorides in aqueous alcohols

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Rate constants for a wide range of binary aqueous mixtures and product selectivities (*S*) in ethanol–water (EW) and methanol–water (MW) mixtures, are reported at 25 °C for solvolyses of benzenesulfonyl chloride and the 4-chloro-derivative. *S* is defined as follows using molar concentrations: $S = ([\text{ester product}]/[\text{acid product}]) \times ([\text{water solvent}]/[\text{alcohol solvent}])$. Additional selectivity data are reported for solvolyses of 4-Z-substituted sulfonyl chlorides (Z = OMe, Me, H, Cl and NO₂) in 2,2,2-trifluoroethanol–water. To explain these results and previously published data on kinetic solvent isotope effects (KSIEs) and on other solvolyses of 4-nitro and 4-methoxybenzenesulfonyl chloride, a mechanistic spectrum involving a change from third order to second order is proposed. The molecularity of these reactions is discussed, along with new term 'S_N3–S_N2 spectrum' and its connection with the better established term 'S_N2–S_N1 spectrum'. Copyright © 2009 John Wiley & Sons, Ltd.

Keywords: solvolysis; solvent effects; alcohols; product selectivity; mechanistic spectrum; general base catalysis

INTRODUCTION

Investigations of the rates and product selectivities for solvolyses in binary alcohol–water mixtures have provided new insights into reaction mechanisms and into solvent effects on reactivity. A solvolysis reaction of a substrate (RX) in an alcohol–water mixture (R'OH—H₂O) gives two substitution products (Eqn (1)) and product selectivities (*S*, Eqn (2), in which square brackets refer to molar concentrations[1]), provide information about the product-determining steps;[1] e.g. for S_N1 reactions, *S* values can indicate whether the products are formed from a solvent-separated ion pair[1–3] or from more dissociated cations.[3]

$$RX + R'OH/H_2O \rightarrow ROR'/ROH + HCl \qquad (1)$$

$$S = ([ROR']/[ROH]) \times ([H_2O]/[R'OH]) \qquad (2)$$

Solvent effects on rate constants can be interpreted using the Grunwald–Winstein (GW) equation (Eqn (3))[4] and the various extended GW equations (e.g. Eqn (4)).[5–8]

$$\log(k/k_0) = mY + c \qquad (3)$$

$$\log(k/k_0) = mY + lN + c \qquad (4)$$

In Eqns (3) and (4), log *k* refers to the rate constant in any solvent relative to 80% ethanol–water (EW) (k_0), *m* is the sensitivity of the substrate (RX) to the solvent ionizing power (*Y*) and *c* is a small residual term. In Eqn (4), *l* is the sensitivity of the substrate to solvent nucleophilicity (*N*). Solvolyses of adamantyl substrates have led to the modified GW equation, in which Y_X values replace *Y* to minimise nucleophilic solvation effects and to allow for differences in solvation effects of leaving groups.[6] There are also various *N* scales,[7] and an additional parameter (*I*) can be included to allow for solvation effects in conjugated substrates: e.g. when the developing positive charge can be delocalised onto aromatic rings.[8]

Equations such as Eqn (3), having one solvent parameter, are very useful for detecting mechanistic changes which occur as the solvent composition changes (e.g. solvolyses of benzoyl chloride[9] and 4-dimethylaminobenzoyl fluoride[10] in alcohol–water mixtures). Equation (4) provides some of the best evidence for a spectrum of mechanisms from bimolecular to unimolecular (S_N2 to S_N1).[5,11–14]

Evidence for third order solvolytic reactions can be obtained directly from rate laws for mixtures of aprotic solvents and very small amounts of alcohol.[15] By combining rate and selectivity data, rate-product correlations for the whole range of alcohol–water mixtures have been shown to be consistent with third order reactions for pseudo-first order solvolyses of 4-nitrobenzenesulfonyl chloride (**1**, Z = NO₂),[16] and of other acid chlorides.[17–19] Recently, we contrasted the third order solvolyses of **1**, Z = NO₂ with the second order solvolyses of 4-nitrobenzyl tosylate (**2**).[20] The second order solvolyses of **2** correlated linearly with Y_{OTs} (in the appropriately modified version of Eqn (3)), whereas the correlation for **1**, Z = NO₂ curved downwards at high values of Y_{OTs}. Also, **1**, Z = NO₂ showed a much higher kinetic solvent isotope effect (KSIE) than **2**.[16,20]

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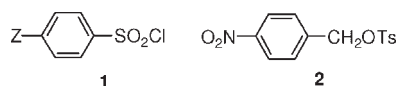
We now show that published kinetic data for solvolyses of 4-methoxybenzene sulfonyl chloride (**1**, Z = OMe) correlate well with data for **2**, and we report new rate and product data for solvolyses of (**1**, Z = OMe, Me, H, Cl and NO$_2$). These and other published results for these solvolyses (particularly KSIEs[21,22]) are consistent with a spectrum of reactivities from second order for **1**, Z = OMe to third order for **1**, Z = NO$_2$. The concept of an S$_N$3–S$_N$2 spectrum of mechanisms will be discussed.

RESULTS

Rate constants for solvolyses of 4-chlorobenzenesulfonyl chloride (**1**, Z = Cl) are shown in Table 1 and those for benzenesulfonyl chloride (**1**, Z = H) are in Table 2. Product selectivities (*S*, Eqn (2)) for solvolyses of five substrates (**1**, Z = OMe, Me, H, Cl and NO$_2$) in ethanol-, methanol- and 2,2,2-trifluoroethanol–water are in Table 3.

DISCUSSION

There is a general consensus that solvolyses of typical sulfonyl chlorides are S$_N$2 reactions with dominant bond making to the incoming solvent nucleophile.[29–32] Although the possibility of some extent of addition to the sulfonyl group cannot be excluded,[21,33] there is currently little support for this proposal.

Table 2. Rate constants (*k*) for solvolyses of benzenesulfonyl chloride (**1**, Z = H) in aqueous binary mixtures at 25 °C[a]

Solvent % v/v	$k/10^{-3}$ s^{-1}			
	EtOH	MeOH	Me$_2$CO	MeCN
100	0.021[b]	0.103[b]		
90	0.077	0.272	0.0077[c]	0.012[d]
80	0.136	0.478	0.026[e]	0.041[d]
70			0.063[f]	0.080[d]
60	0.299	1.14	0.12[e]	0.143[d]
40	0.882	2.01	0.517[e]	0.266
20	2.73[g]	3.08	1.67	1.34
Water	3.07[h]	3.07[h]	3.07[h]	3.07[h]

[a] Determined conductimetrically in duplicate; average deviation typically ±3%; additional data at 25 °C for dioxan–water are as follows: calculated from data in Reference [26], 90% (0.0033), 80% (0.019), 60% (0.136), 40% (0.675); interpolated from data in Reference [27], 70% (0.065), 50% (0.31); interpolated from data in Reference [23], 30% (1.17), 20% (1.80), 10% (2.45).
[b] Data from Reference. [24]
[c] Reference [26] reports $10^3 k = 0.0058$.
[d] Calculated from data in Reference [28].
[e] In satisfactory agreement with Reference. [26]
[f] Reference. [26]
[g] Quadruplicate determination of rate constant.
[h] Solvent contained 0.2–0.4% acetonitrile; six previously published value of *k* range from 2.97 to 3.10 (Reference [25]).

Table 1. Rate constants (*k*) for solvolyses of 4-chlorobenzenesulfonyl chloride (**1**, Z = Cl) in aqueous binary mixtures at 25 °C[a]

Solvent % v/v	$k/10^{-3}$ s^{-1}			
	EtOH	MeOH	Me$_2$CO	MeCN
100	0.022[b]	0.083		
90	0.094	0.255	0.017	0.0089
80	0.171	0.467	0.051	0.0324
70	0.249	0.733	0.111	0.0633
60	0.357	1.05	0.203	0.0985
50	0.526	1.44	0.370	0.160
40	0.85	1.87	0.598	0.286
30	1.41	2.15	0.975	0.547
20	1.87	2.29	1.38	0.99
10	2.02	2.01	1.65	1.55
Water	2.00[c]	2.00[c]	2.00[c]	2.00[c]

[a] Determined conductimetrically in duplicate; average deviation typically ±3%; additional data at 25 °C for dioxan–water interpolated from data in Reference [23] are as follows: 30% (1.14), 20% (1.40), 10% (1.66).
[b] Literature value: 0.0237 (Reference [24]).
[c] Solvent contained 0.2–0.4% acetonitrile; literature value 2.02 (Reference [25]).

Also, the possible involvement of *one* additional solvent molecule as a general base is often considered,[16,21,22,31,33] and even higher kinetic orders in solvent have also been suggested.[34] Highly electron rich sulfonyl chlorides (e.g. **1**, Z = NMe$_2$ and mesitylene sulfonyl chloride, **3**) undergo a mechanistic change to a more polar 'exploded' S$_N$2 transition state.[35–37] The main focus of the following discussion is the mechanistic role of only *one* additional solvent molecule for solvolyses of the less electron rich substrates.
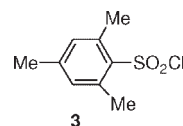
Product selectivities (S)

As is often observed,[1] values of *S* increase in more aqueous solvents and are greater for EW mixtures than for corresponding methanol–water (MW) mixtures (Table 3). Also *S* increases gradually as the substituent (Z) becomes more electron donating; the effect is largest for 97% TFE and for the less aqueous EW and MW mixtures (the results for **1**, Z = Me may be slightly low because of uncertainties in the ester/acid response factor).

In contrast, solvolyses of 4-substituted benzoyl chlorides (**4**, Table 4 of Reference[38]) and 4-substituted benzyl chlorides (**5**,

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Table 3. Product selectivities (*S*, Eqn (2)) for solvolyses of 4-Z substituted benzenesulfonyl chlorides (**1**) in aqueous alcohol mixtures at 25 °C

Alcohol % v/v	Substituent (Z)				
	OMe[a]	Me[a]	H[b]	Cl[b]	NO$_2$[c]
Ethanol					
90	1.6	1.0	0.92	0.61	0.40
80	2.3	1.5	1.5	1.0	0.68
70			2.0	1.5	0.94
60	3.8	2.6	2.6	1.8	1.2
50	3.9		3.1	2.4	1.5
40	4.2	3.0	3.4	2.9	1.7
30	3.9		3.5[d]	3.3[d]	1.9
20	3.6	2.9	3.5[d]	3.2[d]	2.0
10	3.4	3.0	2.9[e]	2.6[e]	2.0
5	3.2	2.7	2.9[f]	2.8[f]	2.1
Methanol					
90	2.5		1.3	0.86	0.88
80	4.2	2.2	2.2	1.4	1.2
70			3.2	2.1	1.6
60	4.4	3.5	3.9	2.9	1.9
50			4.5	3.3	2.3
40	6.0	4.5	5.0	3.9	2.6
30			5.2[d]	4.1[d]	2.9
20	5. 9	4.2	4.8[d]	3.7[d]	3.2
10	5.2	4.5	4.7[e]	3.6[e]	3.4
5	5.1	4.4	4.7[f]	3.7[f]	3.4
2,2,2-trifluoroethanol–water (% w/w) at 75 °C					
97	0.2	0.09	0.07	0.05	0.02

[a] Data from Reference [21].
[b] This work determined by at least duplicate analyses of two independent solutions; substrate injected as a 10% solution in acetonitrile (10 μl) into 5 ml of thermostatted solvent, except where stated otherwise; typical errors 2–6%.
[c] Data from Reference [16].
[d] Injected 20 μl of a 5% solution of the substrate.
[e] Injected 30 μl of a 1% solution of the substrate.
[f] Injected 30 μl of a 0.5% solution of the substrate.

Table 1 of Reference[20]) do not show consistent trends in either substituent or solvent effects. These more complex trends are explained by larger substituent effects leading to mechanistic changes. Consequently, the simpler pattern of substituent effects on *S* for solvolyses of sulfonyl chlorides (**1**, Z = OMe, Me, H, Cl, NO$_2$) is in agreement with the accepted[29–32] S$_N$2 mechanism.

Z—〈benzene ring〉—C(=O)Cl **4**   Z—〈benzene ring〉—CH$_2$Cl **5**
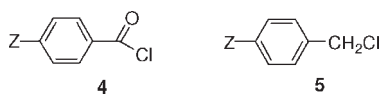
Although the selectivity data for sulfonyl chlorides (Table 3) do not show any clear evidence for mechanistic changes, it is not unusual for values of *S* to decrease slightly (*ca.* 10%) from 40 to 5% alcohol–water solvents – in Table 3, only solvolyses of **1**, Z = NO$_2$ do not show this effect, and **1**, Z = OMe shows a larger effect. The decrease in *S* may indicate a mechanistic change (e.g.

to a process lacking significant general base catalysis[21,39]), but reasonable doubts have already been raised[40] about our interpretation[21] of rate and product data in highly aqueous media. The new selectivity data (Table 3) support the possibility that a small decrease in *S* can occur in the absence of a mechanistic change, but rate–rate profiles still support our viewpoint[21] (refer to last paragraph of this discussion).

Rate–rate profiles and the correlation of solvolysis rates with solvent parameters

Very recent work[41] on correlations for various sulfonyl chlorides utilising Eqn (4) gave *m* values of 0.6–0.7 and *l* values of 1.1–1.3 for aromatic sulfonic acid chlorides. When compared with earlier correlations,[40] lower errors in the quoted parameters were found by including additional data[42] for fluorinated alcohols; the importance of a diversity of solvents can be illustrated by solvolyses of **1**, Z = OMe and Me, for which the error in *l* was halved by the addition of only one data point for 97% TFE to a data set for over 30 other aqueous mixtures. Even with the improved data set, it is difficult to make a case for mechanistic changes using Eqn (4), and the reactions were all classified as S$_N$2.[41]

For solvolysis reactions, some the most important evidence for mechanistic changes is obtained by comparing solvolysis rates with the rates of 'well understood' reference reactions for substituent or solvent effects. In the case of solvent effects, it is sometimes difficult to distinguish between solvation effects and changes in mechanism,[43] and multi-parameter treatments are not helpful in resolving these difficulties because they are relatively insensitive.[44]

Solvolyses of methyl, ethyl and 4-nitrobenzyl tosylate (**2**) are suitable 'well understood' reference reactions for S$_N$2 solvolyses.[5,13,20] Log (*k/k$_0$*) for solvolyses of **2** correlate linearly with log (*k/k$_0$*) for solvolyses of methyl tosylate with only small deviations for weakly nucleophilic solvent such as formic acid and 97% TFE (Fig. 2 of Reference[13]); importantly, there are no large deviations for other aqueous mixtures such as acetonitrile–water. In contrast, the data point for 90% acetonitrile–water deviates over one order of magnitude from the correlation line for aqueous ethanol in a plot *versus* Y_{OTs} (Fig. 1 of Reference[13]). The deviation can be explained by the relatively low nucleophilicity of acetonitrile–water mixtures, reflected in the values of N_{OTs}, which decrease as the percentage acetonitrile increases.[12]

In order to discuss the data for sulfonyl chlorides, we can now select **2** as a reference system for S$_N$2 reactions, knowing that a link to methyl tosylate is established.[13] Also, we showed recently that rate constants for solvolyses of **2** in EW and MW mixtures could be correlated with the product compositions, assuming that the reactions were second order.[20] Logarithms of rate constants for solvolyses of **1**, Z = OMe correlate linearly (slope = 1.09 ± 0.04, *r* = 0.981) with those for **2**, in all solvents including 97% TFE (Fig. 1), showing that their responses to changes in solvent nucleophilicity are almost identical; using Eqn (4), *l* values of 0.94 ± 0.03[13] and 1.07 ± 0.08[41] were reported for **2** and **1**, Z = OMe, respectively.

In previous work on sulfonyl chlorides,[21,39–41,45] the Y_{Cl} parameter was employed in Eqns (3) and (4) to investigate the responses to changes in solvent ionising power. Substituent effects on rates of solvolyses of sulfonyl chlorides are small, even in weakly nucleophilic media such as TFE,[42] supporting the judgement made earlier[21] that relatively little positive charge is delocalised onto the benzene ring during typical S$_N$2 solvolyses
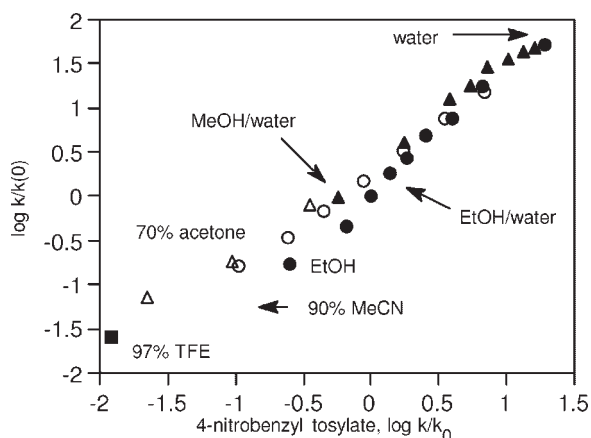
Table 4. Statistical data for correlations of logarithms of rate constants for solvolyses of 4-Z substituted benzenesulfonyl chlorides (**1**) with those for 4-methoxybenzoyl chloride (**4**, Z=OMe) in binary aqueous mixtures at 25 °C[a]

| (Cosolvent) m, c, r[b]	Substituent				
	OMe	Me	H	Cl	NO$_2$
(Ethanol)					
m	0.468 (0.011)	0.424 (0.013)	0.410 (0.025)	0.352 (0.026)	0.266 (0.047)
$-c$	0.037 (0.025)	0.063 (0.029)	0.088 (0.054)	0.106 (0.058)	0.171 (0.105)
r	0.997	0.996	0.991	0.976	0.885
n[c]	11	11	7	11	11
(Methanol)					
m	0.404 (0.028)	0.370 (0.030)	0.346 (0.042)	0.305 (0.043)	0.249 (0.050)
c	0.326 (0.066)	0.295 (0.068)	0.206 (0.095)	0.136 (0.101)	−0.10 (0.12)
r	0.979	0.974	0.964	0.921	0.854
n[c]	11	10	7	11	11
(Acetone)					
m	0.496 (0.013)	0.508 (0.014)	0.452 (0.018)	0.355 (0.019)	0.213 (0.029)
$-c$	0.268 (0.029)	0.329 (0.032)	0.256 (0.037)	0.138 (0.041)	0.004 (0.064)
r	0.997	0.997	0.996	0.989	0.932
n[c]	10	10	7	10	10
(Acetonitrile)					
m	0.567 (0.021)		0.472 (0.020)	0.467 (0.015)	0.301 (0.026)
$-c$	0.566 (0.048)		0.448 (0.045)	0.654 (0.034)	0.428 (0.058)
r	0.996		0.996	0.997	0.982
n[c]	7		6	7	7

[a] Equation (3) was used, with the following modified Y values derived from log (k/k_0) for 4-methoxybenzoyl chloride (**4**, Z=OMe) from Reference:[43] EtOH, −1.34; 90% EtOH, −0.56; 80% EtOH, 0.0 (by definition); 70% EtOH, 0.48; 60% EtOH, 0.94; 50% EtOH, 1.40; 40% EtOH, 2.08; 30% EtOH, 2.81; 20% EtOH, 3.20; 10% EtOH, 3.59; water, 3.86; MeOH, −0.31; 90% MeOH, 0.22; 80% MeOH, 0.71; 70% MeOH, 1.17; 60% MeOH, 1.60; 50% MeOH, 2.04; 40% MeOH, 2.44; 30% MeOH, 2.93; 20% MeOH, 3.29; 10% MeOH, 3.59; 90% acetone, −2.02; 80% acetone, −0.99; 70% acetone, −0.25; 60% acetone, 0.39; 50% acetone, 1.02; 40% acetone, 1.65; 30% acetone, 2.31; 20% acetone, 2.81; 10% acetone, 3.39; 90% acetonitrile, −1.15; 80% acetonitrile, −0.22; 60% acetonitrile, 0.76; 40% acetonitrile, 1.78; 30% acetonitrile, 2.50; 20% acetonitrile, 2.94.
[b] Slope (m) and intercept (c), with associated ± errors in brackets, and r is the correlation coefficient.
[c] n = Number of data points in each set of data, including the data for pure water.

Figure 1. Logarithms of relative rate constants log k/k_0 (log k_0 refers to 80% ethanol–water) for solvolyses of 4-methoxybenzene sulfonyl chloride (**1**, Z = OMe) at 25 °C *versus* log k/k_0 for solvolyses of 4-nitrobenzyl tosylate (**2**) at 45 °C; data from References [13,20,21]
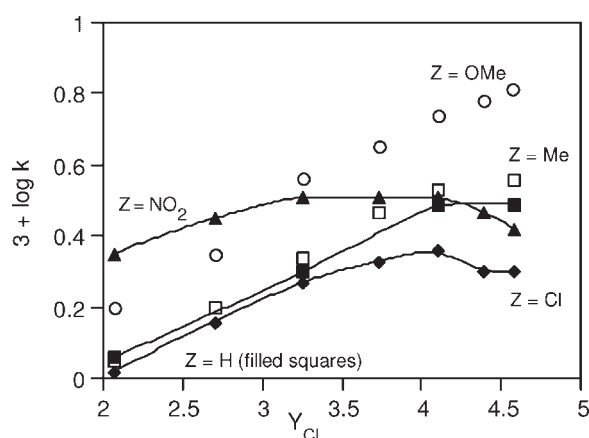
Figure 2. Logarithms of rate constants for solvolyses of 4-Z substituted benzene sulfonyl chlorides (**1**) at 25 °C *versus* Y_{Cl}[6] for a range of binary mixtures between 60% methanol–water and water; kinetic data from Tables 1 and 2 and References [16,21]

of benzenesulfonyl chlorides. Consequently, it may not be necessary to make any allowances for solvation effects adjacent to the reaction site (e.g. using the *I* parameter[8] or alternative similarity models). Nevertheless, an alternative *Y* scale, based on solvolyses of 4-methoxybenzoyl chloride (**4**, Z = OMe), was chosen to investigate substituent effects on *m* values for the sulfonyl chlorides (**1**) – one practical reason is that insufficient Y_{Cl} values were available for acetonitrile–water mixtures.

The results (Table 4) show slopes (*m*) and intercepts (*c*) for each substrate in each binary mixture (note: all intercepts are shown as – *c*, except for methanol). Good correlations are observed for **1**, Z = OMe. As the substituents (Z) become less electron-donating (changing from OMe to NO$_2$), *m* decreases significantly, and the correlations become progressively less precise. Also, more precise correlations are observed for acetonitrile–water mixtures, the least nucleophilic solvent mixture.[7,12] Correlations for acetone–water, EW and MW become progressively less precise. An alternative plot (Fig. 2) for MW, showing log *k* (not log *k/k*$_0$) clearly shows that curvature is significant for solvolyses of **1**, Z = NO$_2$, Cl and H.

Molecularity, S$_N$1, S$_N$2 and S$_N$3

Before discussing the concept of an S$_N$3–S$_N$2 spectrum of mechanisms, some general comments are appropriate. The agreed definition of an S$_N$2 reaction is 'two molecules simultaneously undergoing covalency change'[46] during the rate-determining step of the reaction, and the reaction is bimolecular.[46] When a substrate RX reacts with an anionic nucleophile, a second order rate law provides good evidence for an S$_N$2 reaction.

Ingold's definition of the molecularity of a reaction stage is 'the number of molecules necessarily undergoing covalency change'. It is not expected that the reactions in solution will be 'termolecular', with a meaning that requires simultaneous collision between three molecules. By analogy with the S$_N$2 transition state as an assembly of two separate molecules, an 'S$_N$3 reaction' could occur when two molecules preassociate prior to reaction with the third (followed by the covalency changes). Many reactions are thought to proceed in this way, including hydrolytic reactions of anhydrides,[47] acid chlorides,[15–19] esters[48–51] and amides.[52] Although the label '3' is relatively rare, the Ad$_E$3 electrophilic addition reaction is the reverse of the E2 elimination.[53,54]

Research[55,56] on methoxymethyl substrates was important in establishing the idea that some S$_N$2 reactions occur via relatively cationic transition states – these may be referred to as 'S$_N$2 reactions with high carbocation character'[57] or the more graphic equivalent 'exploded S$_N$2 transition states'.[56] In other words, it is also agreed that there can be varying extents of (and even quite small) rate enhancements due to nucleophilic attack, although the terminology may vary.

More serious disagreements arise for solvolytic reactions, in which the only external nucleophile present in the reaction mixture is the solvent. Most show pseudo-first order kinetics, and the assignment of molecularity has been controversial for decades. As a large dynamic pool of solvent molecules contributes to the observed solvent effect, molecularity is much more difficult to assign.

Consider the distinction between uni- and bimolecular reactions. For a substrate (RX), when nucleophilic assistance to heterolysis of the RX bond by solvent is negligible, the reaction is unimolecular and S$_N$1 (a situation approached with solvolyses of

adamantyl derivatives[6]). The remaining difficult questions are how sensitive or reliable are the tests for nucleophilic solvent assistance (NSA). One recurring criticism of the tests based on *I* values (Eqn (4)) is that nucleophilic effects of solvents are overestimated because they have not been adequately separated from electrophilic effects; this complex issue was discussed in detail recently, and we concluded that the various criticisms based on multi-parameter correlations were unreliable, partly because the parameters used for solvent nucleophilicity were too insensitive.[44] Another test for NSA, the apparent absence of rate enhancements by 'strong' anionic nucleophiles, is insensitive because the energy required to desolvate a nucleophile is significant;[58] (e.g. the nucleophilicity of halide ions is inversely related to the *Y* value of the solvent – see Figs 6 and 7 of Reference[59]).

Even when evidence for NSA is established, it is not agreed that the evidence for molecularity follows automatically, although we then apply the term 'S$_N$2 character' to all cases.[5,57,58] Others[60,62] try to distinguish between: (i) 'nucleophilic solvation' in a transition state leading to a nucleophilically solvated cationic intermediate and (ii) a conventional S$_N$2 reaction. Another possibility is to refer to the effects simply as 'solvation'.[62] Our viewpoint is now supported by recent DFT calculations, indicating that NSA does involve the formation of a weak covalent bond for solvolyses of *t*-butyl substrates.[63,64] Consequently, it is reasonable to propose that the molecularity of the reaction has increased from 1 to 2.

Evidence supporting S$_N$3 reactions and a spectrum of mechanisms

Solvolyses of typical primary substrates occur by S$_N$2 reactions (e.g. the product ratios for solvolyses of **2** in alcohol–water mixtures[20]) can be explained by two competing second order reactions, and a medium effect. Third order solvolyses of carboxylic acid chlorides are well established directly from the rate equations for alcoholyses in a large excess of relatively inert solvents such as ether and acetonitrile, because the alcohol is not present in large excess.[15] Corresponding reactions of various acid chlorides (including **1**, Z = NO$_2$) in pure methanol, show large KSIEs[22] – the rate ratio (k_{MeOH}/k_{MeOD}) is 2.3 (Table 5), whereas S$_N$1 solvolyses and S$_N$2 solvolyses of methyl and (**2**) show a KSIEs of <1.3.[20] In MW and EW mixtures, four competing third order reactions explain the product compositions quantitatively for **1**, Z = NO$_2$, consistent with a transition state in which three molecules simultaneously undergo covalency change (i.e. an S$_N$3 mechanism – Scheme 1).

Various comparisons between solvolyses of **1**, Z = OMe and **2** (Table 5) further illustrate the strong similarities (also refer Fig. 1). In contrast to solvolyses of **1**, Z = OMe, solvolyses of **1**, Z = NO$_2$ show:

 (i) higher solvent kinetic isotope effects;
 (ii) higher rate ratios for 90% alcohol/pure alcohol despite overall lower *m* values (Table 4) and lower selectivities (Tables 3 and 5);
 (iii) a greater response to changes in solvent nucleophilicity (compare 40% ethanol and 97% trifluoroethanol – k_{40E}/k_{97T} ratios – Table 5 or *I* values Eqn (4))[40,41].

Numerical values of the above mechanistic indicators for solvolyses of **1**, Z = Me, H and Cl are consistent with a spectrum of

Table 5. Comparisons of various mechanistic indicators for solvolyses of 4-nitro and 4-methoxybenzenesulfonyl chlorides (**1**, Z = NO$_2$ and OMe) and 4-nitrobenzyl tosylate (**2**) in alcohol–water mixtures

|	Substrate		
Indicator	**1**, Z = NO$_2$[a]	**1**, Z = OMe[b]	**2**[c]
$k_{MeOH/MeOD}$	2.31[d]	1.58[d]	1.27
$k_{H2O/D2O}$	1.76[d]	1.37[d]	1.17[e]
$k_{90M/MeOH}$	3.3	2.4	2.0[f]
S_{90M}	0.88	2.5	2.1
$k_{90E/EtOH}$	7.0	2.7	2.6
S_{90E}	0.4	1.6	1.1
$k_{40E/97T}$[g]	1.5×10^4	3.0×10^2	3.3×10^2

[a] Data at 25 °C from Reference [16].
[b] Data at 25 °C from Reference [21].
[c] Data at 45 °C from References [13,20].
[d] Data from Reference [22].
[e] Refers to mesylate.
[f] Interpolated.
[g] Data for **1**, Z = OMe and NO$_2$ from Reference [42].

Figure 3. Plot of the solvent nucleophilicity parameter (N_T) versus Y_{Cl} in ethanol and methanol–water mixtures; data from References [6,7]; the two lines are drawn through the data points for methanol–water mixtures only (filled triangles)

transition state structures, as shown by the substituent effects on KSEIs,[22] as well as selectivities (Table 3) and *m* values (Table 4).
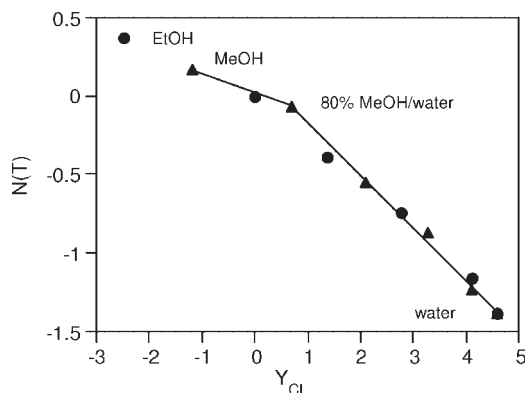
An interdependence of mechanistic indicators is established for the S$_N$2–S$_N$1 spectrum of mechanisms. As NSA increases (i.e. *l* increases), *m* decreases because the positive charge is more delocalised (e.g. by gradually changing from a hindered secondary alkyl to methyl,[5] or by gradually decreasing electron donation in substituted benzyl substrates[11–14]). An S$_N$3–S$_N$2 spectrum of mechanisms involves more subtle changes in transition state structure, but similar trends may arise. As the importance of general base catalysis increases, *l* increases and *m* decreases further (because the positive charge is more delocalised), continuing the trend from S$_N$1 to S$_N$2. The same trends may continue further to solvolyses of organo phosphorous compounds, which show high *l* values, high KSIEs and relatively low *S* values,[65] (but low *S* values have also been explained by increased steric effects[65]).

At the S$_N$2 end of the S$_N$3–S$_N$2 spectrum of mechanisms, a bimolecular (S$_N$2) reaction occurs when the extent of assistance
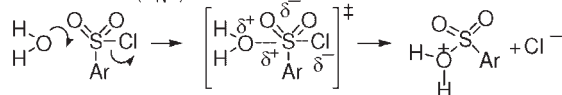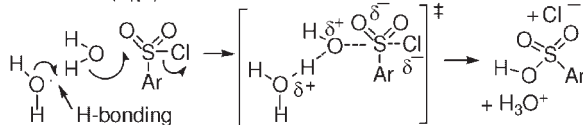
Scheme 1. A simplified picture of some differences between second (S$_N$2) and third order (S$_N$3) hydrolyses for ArSO$_2$Cl; the S$_N$3 process could alternatively be referred to as S$_N$2 with general base catalysis by a second molecule of solvent

by general base catalysis is small or negligible. Examples include most solvolyses of alkyl substrates, because deprotonation of the solvent nucleophile is relatively fast.[66] Solvolyses of **1**, Z = OMe in water appear to be close to the borderline between S$_N$2 and S$_N$3.

In contrast to the downward curvature for **1**, Z = NO$_2$ and Cl, the plot (Fig. 2) is approximately linear for **1**, Z = Me and OMe. These results are consistent with our proposal, based on upward curvature previously observed for mesitylene sulfonyl chloride (**3**),[21] that there is a mechanistic change e.g. using the terminology now proposed, from the S$_N$3–S$_N$2 spectrum for solvolyses of **1**, Z = NO$_2$ – OMe to the S$_N$2–S$_N$1 spectrum for more electron rich substrates (e.g. **3**). Whilst we accept the warning that caution is required,[40] an alternative explanation[40] of the upward curvature for **3** is incorrect as discussed below.

It was proposed[40] that the nonlinearity for **3** could be explained using Eqn (4) because of the nonlinearity of a plot of N_T (based on solvolyses of *S*-methyldibenzothiophenium ions[7]) versus Y_{Cl}; for alcohol–water mixtures, there is an increasing dependence of N_T on Y_{Cl} at higher Y_{Cl} values (Fig. 3). Plausible *l* and *m* values combined with an *l/m* ratio >3 (Eqn (4), e.g. with *l* = 1.5, *m* = 0.5) can explain the decrease in rate constant for solvolyses of **1**, Z = NO$_2$ in water (Fig. 2). As *l* decreases, the predictions from Eqn (4) more closely approach those of Eqn (3) (a linear plot *vs*. Y_{Cl}), so the increase in slope observed for solvolyses of **3** cannot be explained using Eqn (4) (assuming that only one value of *l* and one of *m* are proposed). Also, the most marked changes in slope (Fig. 3) occur between alcohol and 80% alcohol–water mixtures, whereas the changes in slopes shown in Fig. 2 occur between 40% MW and water.

CONCLUSIONS

For solvolyses of **1**, Z = OMe, an S$_N$2 mechanistic classification is justified, e.g. on the basis of the correlation shown in Fig. 1, and previous research on 4-nitrobenzyl tosylate (**2**) and methyl tosylate.[13,20] In contrast, solvolyses of **1**, Z = NO$_2$ are consistent with third order kinetics.[16] Other mechanistic criteria such as selectivity (Table 3), changes in *m* values (Table 4) and KSIEs

(Table 5) indicate no sudden mechanistic changes for the other three compounds (**1**, Z = Me, H and Cl), so there is a mechanistic spectrum from third order for **1**, Z = NO$_2$ to second order for **1**, Z = OMe. If the third order reactions are labelled S$_N$3, referring to an S$_N$2 process with general base catalysis by a second molecule of solvent (Scheme 1), the spectrum of mechanisms due to varying extents of general base catalysis can be labelled S$_N$3–S$_N$2.

The consistent pattern of selectivities (Table 3) contrast with those observed for solvolyses of benzoyl (**4**)[38] and benzyl chlorides (**5**),[20] which show larger substituent effects and undergo more extensive mechanistic changes over the same range of substituents from Z = NO$_2$ to OMe. A mechanistic change may occur for solvolyses of more electron rich sulfonyl chlorides (**1**, Z = NMe$_2$ and **3**) in highly polar and/or weakly nucleophilic media.[35–37]

EXPERIMENTAL

Materials

Sulfonyl chlorides (**1**) and solvents were obtained and purified as described earlier.[16,42] Purified sulfonic acids were hygroscopic and so standard solutions for HPLC calibrations were prepared by solvolysing the chlorides in acetonitrile–water; ethyl and methyl esters were prepared similarly, and also by dissolving a twofold excess of sodium hydroxide in alcohol and adding the sulfonyl chloride at 0 °C (products were isolated by ether extraction after about 5 min).[67] The required 4-toluenesulfonate esters were available commercially, and were recrystallised from chloroform/petroleum spirit (40–60) at −20 °C.

2,2,2-Trifluoroethyl 4-toluenesulfonate (**6**, Z = Me, Lancaster) was recrystallised from ether at low temperature (mp 36–38). Other esters were prepared by reacting sodium hydroxide (0.0228 mol) in excess TFE (10 ml) at 0 °C with a solution of sulfonyl chloride (0.014 mol) in TFE (4 ml) added dropwise. After about 5 min, the excess TFE was removed under reduced pressure, and the products were extracted by stirring with dichloromethane (DCM, 100 ml). The mixture was then filtered and the DCM was shaken with sodium hydrogen carbonate solution, dried with magnesium sulphate and the DCM was removed. The ester was then dried overnight under vacuum in the presence of phosphorus pentoxide. Two esters (**6**, Z = H, Cl) were obtained as colourless liquids and two new solid esters were also obtained (as shown below); all were shown to be pure by HPLC and ^{1}H NMR.

6
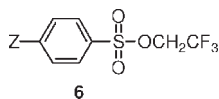
2,2,2-trifluoroethyl-4-nitrobenzenesulfonate (6, Z = NO$_2$)

Prepared as described above, yield 91%, recrystallised from ether to give pale yellow platelets, mp 80–81 °C. ^{1}H NMR: δ = 4.4 (q), 8.1 (d), 8.45 (d). Anal. Calcd for C$_8$H$_6$NO$_5$SF$_3$: C, 33.67; H, 2.12; N, 4.91. Found: C, 33.58; H, 2.24; N, 4.85.

2,2,2-trifluoroethyl-4-methoxybenzenesulfonate (6, Z = OMe)

Prepared as described above, recrystallised from ether to give long white needles, mp 56–57 °C. ^{1}H NMR: δ = 3.85 (s), 4.3 (q), 7.0(d), 7.8 (d). Anal. Calcd for C$_9$H$_8$O$_4$SF$_3$: C, 39.97; H, 3.36. Found: C, 40.13; H, 3.44.

Kinetics and product studies

Kinetic data were obtained as described earlier.[21] Product studies for rapid reactions at 25 °C were carried out by injections of μl amounts of substrate dissolved in dry acetonitrile into turbo-stirred solutions of thermostatted solvent (5 ml). Other product studies at 25 °C were performed on a 5 ml scale by suspending 8 ml sample tubes in an ultrasonic bath. Care was taken to avoid excessive reaction times, because the sulfonate ester products are further solvolysed to acid in aqueous alcohols; this side reaction becomes increasingly significant in 90–99% alcohol–water. Solvolyses in 97% TFE were performed by injecting 3.5 μl of a 10% solution of sulfonyl chloride in dry acetonitrile into 97% TFE (1 ml) in ampoules, prior to sealing and placing in a PEG 400 bath at 75 °C for 10 half-lives.

Chromatography

Products from the solvolyses of chlorides, a sulfonic acid and a sulfonate ester, were analysed using a 5 μm Spherisorb ODS2 chromatography column (15 cm × 1/4″); typical conditions were: eluent (60% MW), flow rate (1 ml/min), UV detection (λ = 259 or 218 nm for **1**, Z = H, and 265 or 226 nm for **1**, Z = Cl). Separations could also be achieved by the addition of 1% acetic acid or 0.01 M tetrabutyl ammonium bromide to the MW eluent.

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