

Stoichiometric Solvation Effects. Part 2. A New Product–Rate Correlation for Solvolyses of *p*-Nitrobenzenesulfonyl Chloride in Alcohol–Water Mixtures

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For reactions involving nucleophilic attack in alcohol–water mixtures, a linear relationship between the reciprocal of product selectivities (S) and the molar ratios of alcohol and water solvents can be derived, if it is assumed that the reactions are second-order in protic solvent (*e.g.*, with one molecule of solvent acting as a nucleophile and the other as a general base). The relationship $\{1/S = (\text{slope})([\text{alcohol}]/[\text{water}]) + \text{intercept}\}$ fits the products of solvolyses of *p*-nitrobenzenesulfonyl chloride in aqueous ethanol and methanol at 25 °C (determined by refrigerated RP–HPLC) within the range from water to 80% v/v alcohol–water. From the slopes and intercepts of these product plots and the one observed rate constant for hydrolysis in pure water, the observed first-order rate constants in alcohol–water mixtures up to 90% (v/v) can be calculated satisfactorily, further supporting the validity of the derived linear relationship; the kinetic model includes three third-order rate constants: k_{ww} , where water acts as both nucleophile and general base; k_{wa} , water acts as a nucleophile and alcohol acts as a general base; k_{aw} , alcohol acts as a nucleophile and water acts as a general base. Inclusion of a fourth rate constant, k_{aa} , where the alcohol acts as a nucleophile and a second molecule of alcohol acts as a general base, is necessary to account for solvolyses in 90–99% alcohol–water; k_{aa} can be calculated from the observed first-order rate constants in pure alcohols. Independent values of k_{aw} and k_{wa} can be obtained from k_{aa} and the slopes and intercepts of linear relationships between S and the molar solvent ratio $[\text{water}]/[\text{alcohol}]$ within the range 90–99% alcohol–water. The dominant effect of solvent stoichiometry and the absence of other substantial medium effects is confirmed by the approximately constant third-order rate constants, calculated from the observed first-order rate constants in acetonitrile–, acetone– and dioxane–water mixtures.

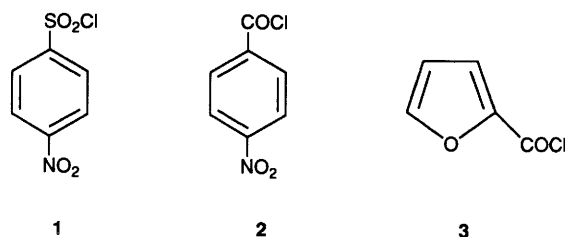
Competing nucleophilic substitution reactions in alcohol–water mixtures are interpreted in terms of product selectivities (S), defined from molar ratios of products and of solvents [eqn (1)]. If these reactions simply involved competition between attack by one molecule of water or one molecule of alcohol, S values would be independent of the solvent. However, many reactions show solvent-dependent S values,¹ for which, until recently, no convincing explanation had been given. Contrary to the reactivity–selectivity principle,² S often increases in more aqueous media when reactivity also increases.

$$S = \frac{[\text{alcoholysis prod}][\text{water solv}]}{[\text{hydrolysis prod}][\text{alcohol solv}]} \quad (1)$$

$$1/S = (\text{slope})([\text{alcohol solv}]/[\text{water solv}]) + (\text{intercept}) \quad (2)$$

We recently reported a new eqn. (2), accounting for the solvent dependence of product selectivities in alcohol–water mixtures;³ eqn. (2) is successful both for the product-forming step of reactions of free cations^{3,4} and also for concerted nucleophilic substitution reactions.^{3,5,6} In the latter case, from the derivation given below, it is predicted that there should be a relationship between the product selectivities and the observed rate constants. We now show that eqn. (2) leads *directly* to a new product–rate correlation for solvolyses of *p*-nitrobenzenesulfonyl chloride (1) in aqueous ethanol and methanol, in support of the kinetic model used to derive eqn. (2).

Sulfonyl chlorides are important reagents in organic chemistry for activating alcohol groups,⁷ and their substitution reactions bridge inorganic and organic chemistry.⁸ In basic



media, reactions occur by direct substitution with the possibility of nucleophilic catalysis,⁹ and alkanesulfonyl chlorides also react *via* sulfenes.¹⁰ Under neutral or acidic conditions, solvolyses of electron-rich arenesulfonyl chlorides in alcohol–water mixtures show surprising maxima in S values [eqn. (1)] in about 40% alcohol,¹¹ revealing mechanistic changes which depend on the water content or on the polarity of the solvent. These effects were hidden in previous investigations restricted to hydrolyses in mixtures with aprotic solvents¹² or in sulfuric acid,¹³ where only one product is formed.

Maxima in S observed for solvolysis of carboxylic acid chlorides have been explained by competing reaction channels, with an S_N1 -like reaction channel favoured by more aqueous media.^{11,14} However, S_N1 reactions are unfavourable even for electron-rich sulfonyl chlorides;^{11,15} the reaction channel favoured in more aqueous media is probably S_N2 ,¹¹ as proposed previously,¹² but the mechanism of the second reaction channel favoured in less aqueous media is not yet clear. To understand further these mechanistic changes, we investigated rate constants and product selectivities for solvolyses of the electron-deficient arenesulfonyl chloride (1) in ethanol– and methanol–water mixtures, for which the second reaction channel should be dominant.

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Results

After competing hydrolysis and alcoholysis [eqn. (3)] of *p*-nitrobenzenesulfonyl chloride (1), the ester (ArSO₂OR) is slowly converted into ArSO₃H by S_N2 attack at carbon.^{16a} To avoid



Table 1 *S* [eqn. (1)] for solvolyses of *p*-nitrobenzenesulfonyl chloride (1) in alcohol–water mixtures (after one half-life at 25 °C)^a

Vol%	Ethanol–water		Methanol–water	
	[Ester]/[Acid]	<i>S</i>	[Ester]/[Acid]	<i>S</i>
99 ^{b,c,d}	4.18	0.13	22.0	0.47
98 ^{b,c,e}	2.86	0.18	10.9	0.51
95 ^{b,c}	1.64	0.28	5.58	0.66
92 ^{b,c}	0.31	0.37	4.35	0.85
90 ^b	1.11	0.40	3.51	0.88
85 ^b	1.03	0.59	2.92	1.16
80 ^b	0.84	0.68	2.14	1.20
70 ^b	0.68	0.94	1.68	1.62
60 ^b	0.56	1.21	1.30	1.94
50 ^f	0.45	1.47	1.00	2.27
40 ^f	0.35	1.71	0.76	2.57
30 ^f	0.25	1.91	0.54	2.86
20 ^g	0.15	2.00	0.36	3.19
10 ^g	0.069	2.03	0.17	3.39
5 ^h	0.034	2.07	0.079 ⁱ	3.4

^a Determined by duplicate HPLC analyses of two solutions of each solvent composition; average deviation < ±2%, typically ±1%. ^b Injected 10 μl of a 10% solution of sulfonyl chloride in acetonitrile into 5 cm³ of solvent. ^c Corrected for 0.2% acid impurity in the sample of 1. ^d Actual compositions by Karl–Fischer analysis: 99% MeOH = 99.06%; 99% EtOH = 99.05% EtOH; *S* is corrected for these compositions. ^e Actual compositions by Karl–Fischer analysis: 98% MeOH = 97.98%; 98% EtOH = 98.09% EtOH; *S* is corrected for these compositions. ^f Injected 10 μl of a 3% solution of sulfonyl chloride in acetonitrile into 5 cm³ of solvent. ^g Injected 20 μl of a 1% solution of sulfonyl chloride in acetonitrile into 5 cm³ of solvent. ^h Injected 30 μl of a 0.4% solution of sulfonyl chloride in acetonitrile into 5 cm³ of solvent. ⁱ Average deviation ±10%.

this complication, selectivity data were obtained from initial product ratios determined by reversed-phase high performance liquid chromatography (HPLC) after one half-life of reaction of the sulfonyl chloride (Table 1). Solvolysis of the unchanged sulfonyl chloride during HPLC analysis was avoided by refrigerating the HPLC column and by making 50–100 preliminary injections of the sulfonyl chloride to condition the column; we assume that some of the free silanol groups on the ODS column initially react with the sulfonyl chloride, and prevent reproducible analyses. Product selectivities [*S*, eqn. (1)] are shown in Table 1.

Most of the rate constants were determined conductometrically over 2–3 half-lives of reaction, under the same conditions (10⁻³–10⁻⁴ mol dm⁻³ substrate) as for the product studies. Results for ethanol– and methanol–water mixtures are shown in Table 2, and for acetonitrile–, acetone–, and dioxane–water mixtures are shown in Table 3.

Discussion

Development of the Kinetic Model.—Alcoholyses of carboxylic acid chlorides (e.g., 2^{17b,17e}) in mixtures of aprotic solvents containing small concentrations of protic solvent, are known to be second order in the protic solvent, presumably with one molecule of protic solvent acting as a nucleophile and the other acting as a general base.^{5,17} The high kinetic solvent isotope effect (KSIE) of 2.27 ± 0.1 (this work) for solvolyses of 2 in methanol supports proton transfer to the solvent (*i.e.*, a general-base catalysis mechanism). Methanolysis of 1 has the same KSIE (2.3,¹⁸ cf. 1.82 in water^{19a}), and a similar third-order mechanism (second order in alcohol) can reasonably be assumed in agreement with previous studies of hydrolyses of sulfonyl chlorides.^{12a,12b,19}

Kinetic order in solvent was previously determined^{12a,12b} from a plot of log *k* vs. [water] in aqueous binary mixtures containing aprotic solvents. In this procedure, it is assumed that solvent effects on reactivity can be ignored. Since a plot of log

Table 2 Product–rate correlations for solvolyses of *p*-nitrobenzenesulfonyl chloride (1) in alcohol–water mixtures

Solvent	<i>k</i> /10 ⁻³ s ⁻¹		Contribution to <i>k</i> _{calc} ^a				% Ester	
	<i>k</i> _{obs}	<i>k</i> _{calc} ^b	<i>k</i> _{aa}	<i>k</i> _{aw}	<i>k</i> _{wa}	<i>k</i> _{ww}	Calc ^c	Obs ^d
100E ^e	0.054		0.54					
90E	0.376	0.37	0.44	1.65	1.38	0.26	56.0	52.6
80E	0.674	0.68	0.35	2.94	2.45	1.05	48.4	45.6
70E	0.954	0.97	0.26	3.85	3.21	2.35	42.5	40.3
60E	1.30	1.24	0.19	4.40	3.67	4.19	37.9	35.9
50E	1.67	1.51	0.13	4.59	3.83	6.54	31.3	31.2
40E	2.32	1.76	0.086	4.40	3.67	9.42	25.5	26.0
30E	2.90	1.99	0.049	3.85	3.21	12.82	19.6	20.2
20E	2.96	2.21	0.022	2.94	2.45	16.74	13.4	13.3
10E	2.76	2.42	0.005	1.66	1.38	21.23	6.9	6.5
Water ^e	2.62					26.2		
100M ^e	0.171 ^f		1.71					
90M	0.572	0.65	1.38	3.67	1.21	0.26	77.7	77.9
80M	0.982	1.08	1.09	6.54	2.15	1.05	70.6	68.2
70M	1.69	1.46	0.84	8.59	2.82	2.35	64.6	62.8
60M	2.22	1.78	0.61	9.80	3.22	4.18	58.5	56.6
50M	2.80	2.05	0.43	10.22	3.36	6.54	52.0	50.0
40M	3.22	2.27	0.27	9.81	3.22	9.42	44.4	43.3
30M	3.22	2.44	0.15	8.59	2.82	12.82	35.8	35.3
20M	3.20	2.61	0.068	6.54	2.15	16.74	25.3	26.4
10M	2.98	2.61	0.017	3.68	1.21	21.23	14.2	14.3
Water ^e	2.62					26.2		

^a Third-order rate constants *k*_{ww} [eqn. (6)], *k*_{aw} [eqn. (7)], *k*_{wa} [eqn. (8)], and *k*_{aa} [eqn. (11)], summarised in Table 5, are multiplied by the appropriate solvent concentrations to give the first-order values. ^b Eqn. (12). ^c Eqn. (13). ^d Calculated from the product ratios given in Table 1; error estimate ±1%. ^e Experimental data. ^f Literature value 0.166 [ref. 16(b)].

Table 3 Rate constants (k) for solvolyses of *p*-nitrobenzenesulfonyl chloride (**1**) in aqueous binary mixtures at 25 °C^{a,b}

Solvent % v/v	$k/10^{-3} \text{ s}^{-1}$		
	Acetone	Acetonitrile	Dioxane
90	0.134 ^c	0.083 ^d	0.059 ^e
80	0.383 ^c	0.23 ^d	0.23 ^e
70	0.708 ^c	0.39 ^d	0.71 ^{e,f}
60	1.11 ^c	0.59 ^d	1.34 ^e
50	1.60 ^c		2.20 ^e
40	2.12 ^c	0.94	
30	2.59	1.47	3.74 ^g
20	2.85	2.21	3.33 ^g
10	2.58	2.67	3.01 ^g
Water ^h	2.62	2.62	2.62

^a Determined conductimetrically in duplicate. ^b Average deviation typically $\pm 3\%$. ^c In satisfactory agreement with ref. 12(a). ^d Data interpolated from ref. 12(b). ^e Ref. 12(a). ^f Also, $k = 0.89 \times 10^{-3}$ [ref. 12(f)]—data extrapolated from 30 and 50 °C. ^g Data interpolated from ref. 12(c). ^h Solvent contained 0.2–0.4% acetonitrile; six previous literature values range from 2.37–2.82 [ref. 12(d)].

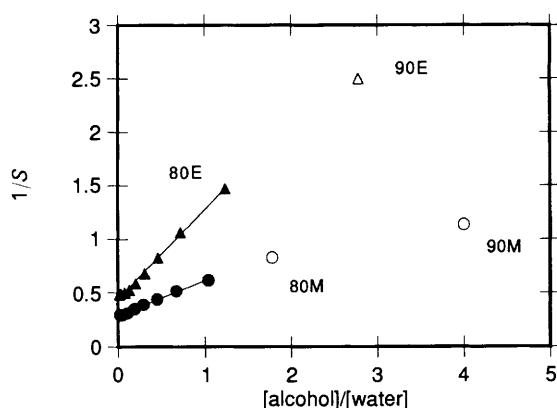


Fig. 1 Correlation of $1/S$ [eqn. (5)] and alcohol–water molar ratio for solvolyses of *p*-nitrobenzenesulfonyl chloride (**1**); S values from Table 1; for ethanol–water (\blacktriangle): slope = 0.836 ± 0.020 , intercept = 0.440 ± 0.011 , $r = 0.998$ (excluding 90E—the same slope is obtained if the point for 80E is also removed); for methanol–water (\bullet): slope = 0.329 ± 0.009 , intercept = 0.285 ± 0.004 , $r = 0.998$ (excluding 80M and 90M)

$\{1/[\text{water}]\}$ vs. Grunwald–Winstein Y values (a measure of the solvent effect) is approximately linear, it is not possible to identify separately the kinetic order in solvent (mass law effect) without additional independent evidence.

Extending the above evidence, we assume that solvolyses in alcohol–water mixtures also obey third-order kinetics, and there are then four contributing reaction pathways. If the pathway in water is denoted by a third-order rate constant k_{ww} , where water acts as nucleophile and acts also as general base, the other pathways are: k_{wa} , water acts as a nucleophile and the alcohol acts as a general base; k_{aw} , the alcohol acts as nucleophile and water acts as a general base; k_{aa} , the alcohol acts as nucleophile and a second molecule of alcohol acts as a general base. By restricting the range of solvents to the more aqueous regions, the k_{aa} term can be ignored;^{3,5} S [eqn. (1)] is then given by eqn. (4), and the reciprocal of eqn. (4) simplifies to eqn. (5).

$$S = \left(\frac{k_{aw}[\text{alcohol}][\text{water}]}{k_{wa}[\text{alcohol}][\text{water}] + k_{ww}[\text{water}]^2} \right) \times [\text{water}]/[\text{alcohol}] \quad (4)$$

$$1/S = (k_{wa}/k_{aw})([\text{alcohol}]/[\text{water}]) + k_{ww}/k_{aw} \quad (5)$$

If the three rate constants in eqn. (5) are independent of the solvent or (more generally) if the rate ratio k_{wa}/k_{aw} in eqn. (5) is

independent of the solvent, it is predicted that a plot of $1/S$ vs. $[\text{alcohol}]/[\text{water}]$ should be linear [eqn. (2)]. Values of $1/S$ for solvolyses of **1** correlate well with the molar solvent ratio up to at least 70% alcohol–water mixtures (Fig. 1), with the neglected k_{aa} term causing a significant deviation for 90% compositions. Slopes and intercepts of the correlations are given in Table 4. We previously observed deviations from eqn. (5) for solvolyses of **2** between water and 40% alcohol–water.⁵ In contrast, eqn. (2) is very successful for solvolyses of **1** between 20 and 80% alcohol–water, but there may be minor deviations in more highly aqueous media for which it is more difficult to obtain precise data.

The above derivation of eqn. (5) implies that it may be possible to calculate the observed first-order rate constants if one of the three third-order rate constants is known. We calculated k_{ww} from the observed first-order rate constant in water divided by square of the molar concentration of water [eqn. (6)], next obtained k_{aw} from the intercepts of Fig. 1 [eqn. (7)], and then obtained k_{wa} from the slopes of Fig. 1 [eqn. (8)]. The third-order rate constants are summarised in Table 5.

$$k_{ww} = k_{\text{obs}}/[\text{water}]^2 \quad (6)$$

$$k_{aw} = k_{ww}/(\text{intercept}) \quad (7)$$

$$k_{wa} = k_{aw} \times (\text{slope}) \quad (8)$$

Observed first-order rate constants in alcohol–water mixtures are then given by eqn. (9), and the % ester product is given by eqn. (10).

$$k_{\text{calc}} = k_{ww}[\text{water}]^2 + (k_{wa} + k_{aw})[\text{water}][\text{alcohol}] \quad (9)$$

$$\text{mol\% ester} = (k_{aw}[\text{water}][\text{alcohol}])/k_{\text{calc}} \quad (10)$$

Although eqn. (9) is derived from the product data and *only one* observed rate constant [k_{ww} obtained from rate data in pure water—eqn. (6)], with no adjustment of parameters apart from the two obtained by linear regression to correlate the product data [Fig. 1, eqns. (7) and (8)], the calculated first-order rate constants [eqn. (9)] agree well with the observed results over most of the water–alcohol solvent range: e.g. even in 90% ethanol–water, a solvent composition remote from the calibrating data point for pure water, k_{calc} is $0.33 \times 10^{-3} \text{ s}^{-1}$, whereas k_{obs} $0.37 \times 10^{-3} \text{ s}^{-1}$, and the calculated % ester [eqn. (10)] is 50.2 (observed, 52.6); in 90% methanol–water, k_{calc} is $0.51 \times 10^{-3} \text{ s}^{-1}$, whereas k_{obs} $0.57 \times 10^{-3} \text{ s}^{-1}$, and the calculated % ester [eqn. (10)] is 71.4 (observed, 77.9). Other predictions based on eqn. (9) can be obtained from the k_{aw} , k_{wa} and k_{ww} contributions to k_{calc} shown in Table 2.

More complete calculations include a k_{aa} term, defined from the observed first-order constants in pure alcohol, divided by the square of the molar concentration of alcohol [eqn. (11)].

$$k_{aa} = k_{\text{obs}}/[\text{alcohol}]^2 \quad (11)$$

Eqns. (9) and (10) are then modified to eqns. (12) and (13). Product–rate correlations then require two first-order rate constants as input data, and predictions for alcohol–water mixtures are then based on experimental data in both pure water and pure alcohol. As would be expected when an important additional piece of experimental data is included before predictions are made, the results (Table 2) give improvements, particularly for solvolyses in 90–99% alcohol–water mixtures when the k_{aa} term is quite significant. A comparison of observed and calculated first-order rate constants for ethanol–water mixtures, calculated from eqn. (12), is given in Fig. 2.

Table 4 Ratios of third-order rate constants k_{aw}/k_{wa} derived from $1/S$ and S plots for solvolyses of *p*-nitrobenzenesulfonyl chloride (**1**) in alcohol–water mixtures at 25 °C

Plot	Solvent range	Slope	k_{aw}/k_{wa}	Eqn.
$1/S^a$	5–80% EtOH	0.836 ± 0.020	1.20 ± 0.03	5
S^b	95–99% EtOH	1.04 ± 0.12	1.04 ± 0.12	15
$1/S^a$	5–70% MeOH	0.329 ± 0.009	3.04 ± 0.1	5
S^b	90–99% MeOH	1.93 ± 0.16	1.93 ± 0.16	15

^a Fig. 1. ^b Fig. 3.

Table 5 Calculated third-order rate constants ($\text{dm}^6 \text{mol}^{-2} \text{s}^{-1}$) for the product–rate correlations for solvolyses of *p*-nitrobenzenesulfonyl chloride (**1**) in alcohol–water mixtures^a

Rate constant	Ethanol–water	Methanol–water
	$1/S$ eqn. (5) [S eqn. (15)]	$1/S$ eqn. (5) [S eqn. (15)]
k_{ww}^b	8.49×10^{-7}	8.49×10^{-7}
k_{wa}^c	1.61×10^{-6} [1.74×10^{-6}]	9.80×10^{-7} [6.5×10^{-7}]
k_{aw}^d	1.93×10^{-6} [1.81×10^{-6}]	2.98×10^{-6} [1.26×10^{-6}]
k_{aa}^e	1.84×10^{-7}	2.80×10^{-7}

^a The slopes and intercepts necessary for these calculations are given in the legends to Figs. 1 and 3. ^b From eqn. (6). ^c Data for $1/S$ eqn. from eqn. (8). ^d Data for $1/S$ eqn. from eqn. (7). ^e From eqn. (11).

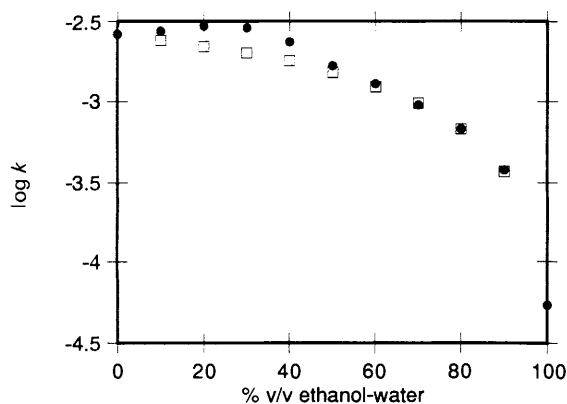


Fig. 2 Comparison of logarithms of calculated (\square) [eqn. (12)] and observed (\bullet) first-order rate constants for solvolyses of *p*-nitrobenzenesulfonyl chloride (**1**) in ethanol–water at 25 °C

$$k_{\text{calc}} = k_{ww}[\text{water}]^2 + (k_{wa} + k_{aw})([\text{water}][\text{alcohol}]) + k_{aa}[\text{alcohol}]^2 \quad (12)$$

$$\text{mol\% ester} = (k_{aw}[\text{water}][\text{alcohol}] + k_{aa}[\text{alcohol}]^2)/k_{\text{calc}} \quad (13)$$

The 54-fold increase in first-order rate constants from ethanol to water can be explained with a maximum error of 30% by eqn. (12) (see Fig. 2) and the maximum difference between the % ester calculated [eqn. (13)] and the % ester observed is only 4% (Table 2). Agreement between calculated and observed results for methanol–water mixtures is similarly good: e.g., in 90% methanol–water, the error in the first-order rate constant is only 10% and the calculated % ester agrees with the observed value, despite the deviation of the 90M point from the $1/S$ plot (Fig. 1). However, the shape of the rate–composition profile for solvolyses of **1** involves a shallow rate maximum with a 10–20% reduction in rate constants between 30% alcohol–water and water; this subtle feature was not reproduced by eqn. (12) (see Fig. 2). In contrast, the solvent compositions (70% ethanol–

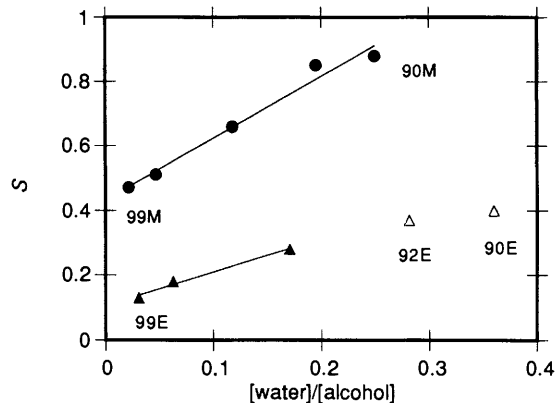


Fig. 3 Correlation of S [eqn. (15)] and water/alcohol molar ratio for solvolyses of *p*-nitrobenzenesulfonyl chloride (**1**); S values from Table 1; for 99–95% ethanol–water (\blacktriangle): slope = 1.04 ± 0.12 , intercept = 0.106 ± 0.013 , $r = 0.994$ (if the data point for 92% ethanol–water is included the slope is 0.94 ± 0.06 ($r = 0.995$)); for 90–99% methanol–water (\bullet): slope = 1.93 ± 0.16 , intercept = 0.431 ± 0.025 , $r = 0.990$

water and 40% methanol–water) corresponding to the unusual and more marked rate maxima for solvolyses of **2** were well reproduced by eqn. (12).⁵ Hence, additional special solvation effects in alcohol–water solvent mixtures are *not essential* to explain these rate maxima, but small additional effects cannot be ruled out (see later discussion).

According to the above procedure, two of the required third-order rate constants are calculated from the observed first-order rate constants in the pure solvents [eqns. (6) and (11)] and two third-order rate constants (k_{wa} and k_{aw}) are obtained from the product ratios in 5–70% alcohol–water and the observed rate constant in pure water [eqn. (5)]. Independent measures of k_{wa} and k_{aw} can be obtained from the product ratios in 90–99% alcohol–water and the observed rate constant in pure alcohol because, if the k_{ww} term is ignored, S is given by eqn. (14) which simplifies to eqn. (15).⁵

$$S = \frac{(k_{aa}[\text{alcohol}]^2 + k_{aw}[\text{alcohol}][\text{water}])}{k_{wa}[\text{alcohol}][\text{water}] \times [\text{water}]/[\text{alcohol}]} \quad (14)$$

$$S = (k_{aw}/k_{wa})([\text{water}]/[\text{alcohol}]) + k_{aa}/k_{wa} \quad (15)$$

Experimental tests of eqn. (15) plotted in Fig. 3 show deviations in 90% alcohol–water mixtures because the k_{ww} term is about a sixth of the k_{wa} term (see Table 2), i.e., it is not negligible, as required for and assumed in the derivation of eqn. (15). The slopes of these plots give ratios of k_{aw}/k_{wa} which for ethanol–water mixtures are in close agreement (almost within statistical errors) with independent measures of the same rate ratio derived from eqn. (5)—see Table 4. Agreement is less good for methanol–water mixtures, and a 50% higher slope of the S plot (Fig. 3) would be required for exact agreement. The same trends were observed for solvolyses of **2**,⁵ with lower slopes (k_{aw}/k_{wa}) for ethanol–water mixtures than for methanol–water mixtures, and with the two independent values of the slopes for ethanol–water mixtures being in better agreement than for methanol–water mixtures. Possibly, the rate ratio (k_{aw}/k_{wa}) is slightly solvent dependent in methanol–water mixtures.

Slopes and intercepts of eqn. (15) provide independent measures of the absolute values of k_{aw} and k_{wa} (Table 5), which for ethanol–water mixtures are in excellent agreement with those derived totally independently from the $1/S$ eqn. (5). As k_{wa} is determined by the intercept of Fig. 3, it is not surprising that the two values of k_{wa} for methanol–water (Table 5) are in better agreement than the two values of k_{aw} , which for the S plot [Fig. 3, eqn. (15)] is determined by both the slope and the intercept.

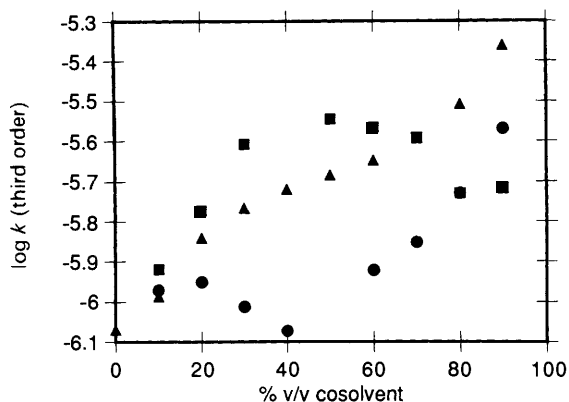


Fig. 4 Plot of logarithms of third-order rate constants [eqn. (6)] for solvolyses of *p*-nitrobenzenesulfonyl chloride (1) in acetone- (▲), acetonitrile- (●) and dioxane-water mixtures (■) against vol% cosolvent; kinetic data from Table 3

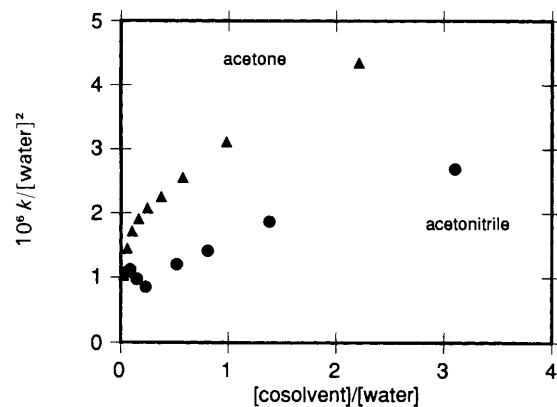


Fig. 5 Plot of third-order rate constants [eqn. (6)] for solvolyses of *p*-nitrobenzenesulfonyl chloride (1) in acetone- (▲) and acetonitrile-water (●) mixtures against molar ratio of cosolvent/water (eqn. (16)); kinetic data from Table 3

However, even if the slope of the *S* plot were increased by 50%, so that the slopes (k_{aw}/k_{wa}) given in Table 4 were in agreement, the two independent absolute values of k_{aw} would still not agree (Table 5). Hence, it appears that there is a small solvent effect for methanol-water mixtures on the rate ratio (k_{aw}/k_{wa}).

Although the results from the *S* eqn. (15) for ethanol-water mixtures provide very strong quantitative support for the kinetic model developed here, the results are not as precise as those based on the $1/S$ eqn. (5), so detailed product-rate correlations will be restricted to predictions based on the $1/S$ eqn. (5), see Table 2.

Comments on the Kinetic Model.—Third-order rate constants derived from the above model (Table 5) vary over more than a tenfold range, and k_{aa} is small; the k_{aa} term contributes only 12% to the observed rate constant in 90% ethanol-water (Table 2), explaining why eqns. (9) and (10), which contain one term less than eqns. (12) and (13), also fit the data satisfactorily. Catalysis of nucleophilic attack by water is favoured by ethanol ($k_{wa} = 1.61 \times 10^{-6} \text{ dm}^6 \text{ mol}^{-2} \text{ s}^{-1}$, Table 5) > methanol ($k_{wa} = 9.80 \times 10^{-7} \text{ dm}^6 \text{ mol}^{-2} \text{ s}^{-1}$) > water ($k_{ww} = 8.49 \times 10^{-7} \text{ dm}^6 \text{ mol}^{-2} \text{ s}^{-1}$); as this is not the accepted order of pK_a values for these weak acids,²⁰ the second solvent molecule may not only act as a general base but may also hydrogen bond to a sulfonyl oxygen, which model calculations show carries a large negative charge.²¹ In support of this proposal, molecular-orbital calculations indicate that, at least in the gas phase, carbonyl compounds may react with water in a cyclic transition state containing two or three water molecules.²²

Interestingly, for solvolyses of 1 any combination of water and alcohol gives a higher rate constant than two water molecules or two alcohol molecules in the transition state, but solvolyses of 2 behave differently because k_{wa} is then the smallest rate constant.⁵

Water catalysis of nucleophilic attack by alcohol is favoured tenfold over alcohol catalysis (Table 5), and the rate constant for attack by methanol is about 50% larger than for attack by ethanol, as observed also for solvolyses of 2.⁵ Despite the relatively small value of k_{ww} , the water-water pathway is dominant up to about 40% methanol-water and 60% ethanol-water, after which the pathway represented by k_{aw} becomes dominant. The k_{aw} term is even more dominant for solvolyses of 2,⁵ but k_{aa} is larger than k_{ww} . Hence, for solvolyses of 2, the assumptions required for the derivation of eqn. (15) are valid over a wider solvent range, and third-order rate constants derived from eqn. (15) provided a better rate-product correlation than those derived from eqn. (5).⁵

General Implications.—The product-rate correlation (Table 2) implies that the empirical eqn. (2) can justifiably be interpreted in terms of third-order rate constants [eqn. (5)] even in pure water, providing strong experimental support for the mathematical derivation of eqn. (5) given above. Another implication of these results (Table 2) is that medium effects on the third-order rate constants [eqn. (12)] for solvolyses of 1 are relatively small. This conclusion is strongly supported for ethanol-water mixtures by the good agreement between the two independent measures of the rate constants (k_{aw} and k_{wa}) given in Table 5.

Medium effects on reactivity are associated with differences in solvation between initial and transition states, and have been dissected into contributions from these two states.^{23,24} Such dissections often show that initial-state solvation effects are substantial, but this does not prove that these effects strongly influence reactivity. Solvent reorganisation to create a cavity for relatively large organic substrates (such as 1) will be similar in initial and transition states.²³ Hydrophobic solvation of a large alkyl or aryl group will be manifest as a substantial initial-state effect, but, if it is remote from the reaction site, this solvation effect will be of very similar magnitude in the transition state and so will not significantly influence reactivity. However, initial-state solvation effects may make a small contribution to the solvolyses of 1 in aqueous alcohols. For ethanol-water mixtures, the most significant deviations from eqn. (12) between k_{obs} and k_{calc} are in the region of 30% ethanol-water. Close to these compositions, enthalpies of solution generally show endothermic maxima.²⁵ Hence, destabilisation of the initial state could account for some of the small deviations from eqn. (12) (Table 2).

Evidence given below indicates that polarities are probably similar in initial and transition states for solvolyses of 1.

(1) For acetone-, acetonitrile- and dioxane-water mixtures, calculated third-order rate constants [eqn. (6)] vary only over about a threefold range with changes in solvent composition (Fig. 4), whereas the observed first-order rate constants vary over a 44-fold range (Table 3); the complex pattern of results (Fig. 4) may be explained in part by the aprotic solvents acting as weak general bases^{12b,17b} or nucleophiles,²⁶ so accounting for the small increase in the third-order rate constant in the less aqueous mixtures. Eqn. (16) was found to be successful for

$$k_{obs}/[\text{water}]^2 = k_{ww} + k_{wc}[\text{cosolvent}]/[\text{water}] \quad (16)$$

correlating such effects for solvolyses of 2,⁵ but it is much less satisfactory for solvolyses of 1 (Fig. 5), especially for dioxane-water mixtures (Fig. 4).

(2) Substituent effects on these reactions are very small: *e.g.*,

$\rho = -0.4$ in water.^{12d} Even in 97% w/w trifluoroethanol-water, ρ^+ is only -0.9 ²⁷ (*para* substituents: OMe, Me, H, Cl, NO₂) compared with -3.1 for corresponding benzoyl chlorides.²⁸

The scope of eqn. (2) is potentially very broad: *e.g.*, as well as solvolyses of **1**, reactions of the carboxylic acid chlorides **2**⁵ and **3**⁶ and S_N2 reactions of *p*-nitrobenzyl chloride have already been reported,³ and reactions of other carboxylic acid derivatives and of other alkyl halides may fit eqn. (2). Nucleophilic attack on carbocations also fit eqn. (2).⁴ Hence, eqn. (2) provides a generalisation of the expected solvent dependence of *S* for a wide range of nucleophilic substitution reactions, and it may also be applicable to nucleophilic additions (*e.g.*, to ketenes²⁹).

A second, previously established generalisation is the 'inverse', composition-independent *S* for competition between ethanol and water in some S_N1 reactions. The usual explanation is that product formation occurs from solvent-separated ion pairs,^{28b,30} possibly with general-base catalysis by the counter-anion.^{28b} *S* values which are neither in agreement with eqn. (2) nor constant may be considered as 'abnormal', warranting further investigation: *e.g.*, solvolyses of benzoyl chloride show maxima in *S* with a decrease from 80% alcohol to water, and the results can be explained quantitatively by competing reaction mechanisms.^{14,31}

Other more general implications are noted briefly. (1) Although we agree that multiparameter correlations of reactivity usually require inclusion of one or more parameters for microscopic solvent properties,²³ the macroscopic property of the molar concentration of solvent (solvent stoichiometry) is a potentially important variable. (2) Solvation effects on general-base-catalysed ester hydrolysis in aqueous mixtures of ureas^{32a} and on amide hydrolysis in aqueous alcohols^{32b} have recently been analysed successfully in terms of increments for pairwise interactions between groups present in the solvent and the substrate; inclusion of mass law effects would be a significant refinement of this work. (3) In applications of the transition-state variation model, the possibility that two or more transition states could give rise to any one product should be considered. (4) A reactivity-selectivity principle may not be required to account for complex changes in selectivity and reactivity, because in the work described here, changes in selectivity are explained directly from rate-product correlations rather than by assuming a particular relationship between reactivity and selectivity.

Conclusions

Solvolyses of **1** in aqueous binary mixtures with acetone, acetonitrile, dioxane, ethanol and methanol are third-order processes, and observed first-order rate constants are determined predominantly by the molar concentrations of protic solvent, *i.e.*, the rates of these reactions appear to be dominated by the solvent stoichiometry. Initial-state solvation effects may cancel to a large extent, and initial and transition states appear to have very similar polarities, judging from the small dependence of third-order rate constants on cosolvent (Fig. 4). In alcohol-water mixtures, there are four competing, general-base catalysed third-order processes, and observed rates and products can be calculated from the slope and the intercept of the linear plot of $1/S$ vs. alcohol/water molar ratio for 5–70% alcohol-water mixtures [eqn. (5)] with no other adjustable parameters (Table 2); this product-rate correlation strongly supports the validity of the kinetic model used to derive eqn. (5). It is likely that eqn. (5), or the empirical form [eqn. (2)], will provide a useful generalization accounting for solvent effects on *S* for a wide range of nucleophilic substitution reactions. The importance of kinetic order in solvent and associated mass law

effects is strongly supported by the selectivities obtained in 90–99% alcohol-water [eqn. (15), Fig. 3], which leads to independent values of the third-order rate constants (Table 5).

Experimental

Materials.—The *p*-nitrobenzenesulfonyl chloride (**1**) was recrystallised four times from light petroleum (b.p. 60–80 °C) (m.p. 80 °C; lit.,^{33a} 80 °C), and was shown by HPLC of methanolysis products to contain 0.2% of acid; corresponding ethyl and methyl esters were recrystallised twice from trichloromethane (both m.p. 91–92 °C, lit.,³³ 91–92 °C). Solvents for kinetic studies and for HPLC were as described previously.^{28a,31}

Chromatography by Refrigerated HPLC.—The HPLC system comprised a LDC Constametric III pump, a Rheodyne 7125 injection valve, and a Spectromonitor 3100X detector set up as usual, but the 15 cm Spherisorb ODS2 column was immersed in a 10 litre refrigerated bath along with a 1 m cooling coil (id = 0.3 mm) fitted between the pump and the valve. At 6 °C the temperature of the eluent from the detector was the same as refrigerated bath, for flow rates of 1 cm³ min⁻¹ or more.^{3b} After a suitable detector wavelength had been chosen (*e.g.*, 260 nm for solvolyses of **1**), product ratios were determined from the area ratios (integrated using an HP3390A), corrected for relative responses.

Kinetic Methods.—Rate constants were determined by standard conductimetric methods.^{28a,31}

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