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Similarity Models for Solvation Effects on Reactivity. The Dissociative Reaction Channel for Solvolyses of Sulphonyl Chlorides in Binary Aqueous Mixtures*

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Rate constants and product selectivities (*S*) are reported for solvolyses of pentamethylchroman and tri-isopropylbenzene sulphonyl chlorides in acetone/, ethanol/, and methanol/water mixtures, and rate constants for solvolyses of 1-adamantyl methanesulphonate are reported for aqueous binary mixtures with acetonitrile and dioxane. *S* values show maxima in plots *versus* % water in alcohol, consistent with the competing reaction channels discussed previously. Y_{OMs} derived from rate constants for solvolyses of 1-adamantyl mesylate correlate with Grunwald-Winstein *Y* values; there is a small dispersion into separate correlation lines for the various binary mixtures, so the solvation requirements of the sulphonate group in these aqueous mixtures are similar to those for chloride.

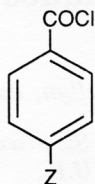
INTRODUCTION

Trifluoroethanolyses of benzoyl chloride (**1**) and substituted derivatives occur by a dissociative mechanism,^{1,2} with a similar substituent effect to solvolyses of mesitoyl derivatives, which show common ion rate depression.³ Hydrolyses of dimethylamino-benzoyl fluoride also show common ion rate depression,² but solvolyses of *p*-methoxybenzoyl chloride (**1**, Z = OMe) do not; although the reaction is dissociative, product formation probably occurs *via* a solvent separated ion pair.^{2,4} In an extension of this work, we now report studies of hindered and/or electron rich sulphonyl chlorides, which it was hoped would also react by a dissociative mechanism.

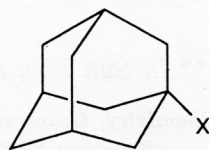
* Dedicated to Professor Dionis E. Sunko on the occasion of his seventieth birthday.

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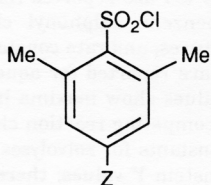
Rates and products of solvolyses of benzoyl (**1**, Z = H) and *p*-chlorobenzoyl (**1**, Z = Cl) chlorides in nucleophilic media (*e.g.* ethanol/water mixtures) can be dissected quantitatively into two competing reaction channels, one a dissociative pathway similar to solvolyses of *p*-methoxybenzoyl chloride (**1**, Z = OMe), and the other an addition-elimination reaction similar in mechanism to solvolyses of *p*-nitrobenzoyl chloride (**1**, Z = NO₂).⁴ When logarithms of observed rate constants (not dissected) for solvolyses of (**1**, Z = H and Cl) were plotted against logarithms of rate constants for solvolyses of (**1**, Z = OMe), curved plots were obtained (see Figure 4 of Ref. 5), and there were separate correlations for each of the five aqueous binary mixtures examined. In contrast, the corresponding plot for the dissected rate constants was linear (see Figure 5 of Ref. 5), and there was negligible dispersion for the five binary mixtures.



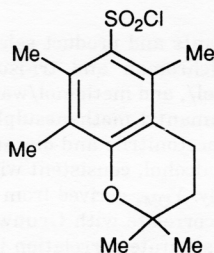
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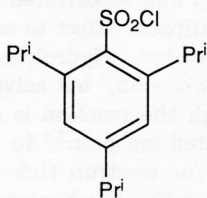
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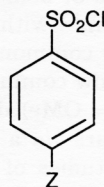
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Quantitative success depended on the choice of solvolyses of **1**, Z = OMe as a similarity model^{6,7} for the dissociative reaction channel for solvolyses of (**1**, Z = H and Cl).

Recent work has established that solvolyses of electron-rich benzenesulphonyl chlorides (e.g. **3**, Z = OMe) are *qualitatively* similar to solvolyses of **1**, Z = H.⁸ Appropriate similarity models should allow a *quantitative* dissection of solvolyses into competing reaction pathways, which was a major aim of this work. Our previous attempts⁸ were limited by the lack of available data for appropriate model compounds: e.g. 1-adamantyl mesylate (**2**, X = OSO₂CH₃), for which additional data are now reported, contains a sulphonyl group.

RESULTS

Pentamethylchroman sulphonyl chloride (**4**) is recommended for the protection of peptides, because of its ease of removal in a trifluoroacetic acid deprotection step;⁹ the structure was designed to give the maximum resonance interaction between the methoxy group and the benzene ring, and hence the possibility of a dissociative mechanism should be enhanced. A dissociative reaction could also be favoured sterically, so tri-isopropylbenzene-sulphonyl chloride (**5**) was also examined.¹⁰ Rate constants for acetone/, ethanol/ and methanol/water mixtures are given in Tables I and II, and product selectivities (S, equation 1) in ethanol/ and methanol/water mixtures are

$$S = [\text{ester}]_{\text{prod}} [\text{water}]_{\text{soln}} / [\text{acid}]_{\text{prod}} [\text{alcohol}]_{\text{soln}} \quad (1)$$

TABLE I

Rate constants (k) for solvolyses of pentamethylchroman sulphonyl chloride (4) in aqueous mixtures at 25 °C

solvent composition ^b	acetone	ethanol <i>k</i> /10 ⁻³ s ⁻¹	methanol
100		0.386 ± 0.002	2.81 ± 0.03
80	0.036 ± 0.002	1.48 ± 0.01	10.3 ± 0.1
60	0.373 ± 0.001	3.57 ± 0.02	31.2 ± 0.6
40	4.09 ± 0.01	15.7 ± 0.2 ^c	102 ± 2 ^c
20 ^c	61.7 ± 0.4 ^c	187 ± 3 ^c	280 ± 30 ^d

^a Determined conductimetrically in duplicate, except where stated otherwise; errors shown are average deviations. ^b Solvent contained up to 0.5% acetonitrile.

^c Determined in triplicate. ^d Determined in quadruplicate.

TABLE II

Rate constants (k) for solvolyses of tri-isopropylbenzenesulphonyl chloride (5) in aqueous mixtures at 25 °C^a

solvent composition ^b	acetone	ethanol <i>k</i> /10 ⁻³ s ⁻¹	methanol
100		0.038 ± 0.001	0.247 ± 0.003
80	0.0091 ± 0.0005	0.126 ± 0.001	0.75 ± 0.02
60	0.054 ± 0.001	0.223 ± 0.001	1.95 ± 0.10
40	0.31 ± 0.02	0.646 ± 0.012	4.9 ± 0.21

^a Determined conductimetrically in duplicate, errors shown are average deviations.

^b Solvent contained up to 0.5% acetonitrile.

TABLE III

Selectivity values (*S*, equation 1) for solvolyses of pentamethylchroman sulphonyl chloride (4) and tri-isopropylbenzenesulphonyl chloride (5) in aqueous alcohols at 25 °C^a

solvent composition ^b	ethanol/water		methanol/water	
	4	4	4	5 ^c
90	2.1		3.6	2.2
80	2.7		3.8	2.9
60	4.0		4.4	4.5
50	4.3			
40	4.0		4.0	
20	2.7		3.2	
10	2.2		2.9	
5	2.2			

^a Determined by duplicate analyses of duplicate samples by reversed phase HPLC.

^b Solvent composition are %v/v. ^c Availability of data limited by low solubility of substrate.

given in Table III. In equation (1), the observed product ratio is divided by the molar concentrations of alcohol and water in the solvent.

It was hoped to synthesise a more sterically hindered substrate, 1,3,5-tri-*t*-butylbenzenesulphonyl chloride, but chlorosulphonation of 1,3,5-tri-*t*-butylbenzene resulted in loss of a *t*-butyl group.¹¹ Had this synthesis been successful, it now appears that the tri-*t*-butyl compound would have been too insoluble for this work – even the tri-iso-

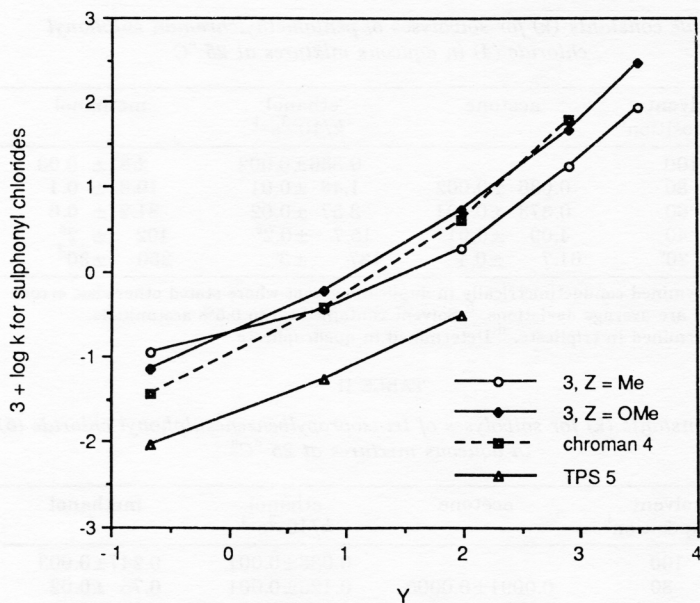


Figure 1. Correlation of logarithms of rate constants for solvolyses of sulphonyl chlorides in acetone/water with *Y* values; kinetic data from Table I and II and Ref. 8, and *Y* values from Ref. 14.

TABLE IV

Rate constants (k) for solvolyses of 1-adamantyl methanesulphonate (**2**, $X = \text{OSO}_2\text{CH}_3$) in aqueous mixtures^a

solvent ^b	temp/°C	k/s^{-1}	$\frac{\Delta H^\ddagger}{\text{kcal/mol}}$	$\frac{\Delta S^\ddagger}{\text{cal mol}^{-1} \text{K}^{-1}}$
99An	25.0 ^d	$(4.55 \pm 0.04) \times 10^{-6}$		
90An	25.0 ^e	$(2.51 \pm 0.03) \times 10^{-4}$		
80An	40.1	$(1.28 \pm 0.03) \times 10^{-2}$	17.4	-11.8
	25.0	$(2.96 \pm 0.01) \times 10^{-3}$		
70An	25.0 ^f	$(1.26 \pm 0.01) \times 10^{-2}$	17.8	-7.4
	7.0	$(1.71 \pm 0.02) \times 10^{-3}$		
60An	40.1	$(1.73 \pm 0.01) \times 10^{-1}$		
	25.0 ^f	$(4.01 \pm 0.07) \times 10^{-2}$	18.2	-4.1
	10.0	$(7.06 \pm 0.06) \times 10^{-3}$		
40An	25.0 ^f	$(3.45 \pm 0.13) \times 10^{-1}$		
	10.5	$(6.96 \pm 0.14) \times 10^{-2}$	17.2	-2.9
	-9.9	$(6.40 \pm 0.12) \times 10^{-3}$		
20An	25.0 ^c	5.4		
	10.5	1.09 ± 0.13	17.9	4.8
	0.0	$(3.10 \pm 0.01) \times 10^{-1}$		
90D	25.0	$(1.18 \pm 0.05) \times 10^{-5}$		
80D	50.0	$(3.4 \pm 0.1) \times 10^{-3}$		
	25.0	$(2.28 \pm 0.02) \times 10^{-4}$	20.1	-7.9
70D	25.0	$(1.50 \pm 0.01) \times 10^{-3}$		
60D	25.0	$(1.04 \pm 0.01) \times 10^{-2}$	18.7	-4.7
	7.0	$(1.28 \pm 0.02) \times 10^{-3}$		
40D	25.0	$(2.69 \pm 0.02) \times 10^{-1}$		
	10.8	$(5.49 \pm 0.04) \times 10^{-2}$	18.1	-0.3
	-9.0	$(4.63 \pm 0.04) \times 10^{-3}$		
20D	25.0 ^c	4.6		
	7.7 ^f	$(6.3 \pm 0.3) \times 10^{-1}$	18.6	7.0
	0.8	$(2.65 \pm 0.02) \times 10^{-1}$		

^a Determined conductimetrically in duplicate except where stated otherwise; errors shown are average deviations. ^b Solvent compositions are % *v/v*; solvent codes are acetonitrile (An) and dioxane (D). ^c Calculated from data at other temperatures. ^d Determined by titrating liberated acid with NaOMe utilizing Lacmoid indicator (Ref. 12). ^e One measurement in the presence of excess lutidine. ^f Triplicate measurement of rate constant.

propyl compound **5** presented severe problems due to its low solubility in aqueous media. (An alternative hindered substrate is 1,3,5-tribromobenzenesulphonyl chloride¹¹).

Another possible similarity model for solvolyses of sulphonyl chlorides is 1-adamantyl methanesulphonate (**2**, $X = \text{OSO}_2\text{CH}_3$),¹³ for which rate constants in acetonitrile/water and dioxane/water are shown in Table IV.

DISCUSSION

The Grunwald-Winstein equation (2) relates changes in solvolysis rate constant (k) in any solvent, relative to the rate constant in 80% ethanol/water (k_0), to the solvent ionizing power (Y);¹⁴ for solvolyses of *t*-butyl chloride at 25 °C, the slope (m) is defined as unity and the intercept (c) as zero.

$$\log(k/k_0) = mY + c \quad (2)$$

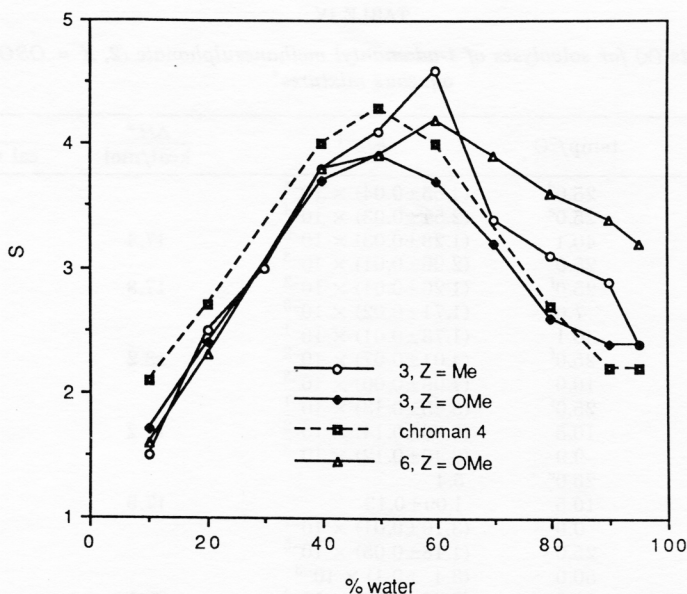


Figure 2. Plot of S values (Table III) for solvolyses of sulphonyl chlorides in ethanol/water *versus* solvent composition.

Solvolyses of the chroman **4** are more sensitive to solvent ionizing power in acetone/water mixtures than other sulphonyl chlorides (**3**, $Z = \text{OMe}$, Me , and **5**); slopes of plots (Figure 1) are very similar in the more aqueous media (high Y values), but the plot for **4** is the least curved. These results can be explained if **4** solvolyses to a greater extent by a dissociative, nucleophilically-assisted^{8a} reaction channel, and hence of these compounds, it would be the most appropriate similarity model. However, the selectivity data show maxima (Figure 2), which we associate with mechanistic complexity due to competing reaction channels.^{4,8} Although steric hindrance apparently reduced the reactivity of **5**, the solvent effect was similar to solvolyses of (**3**, $Z = \text{Me}$), and nucleophilic attack may occur perpendicular to the plane of the benzene ring.

Because Y values include a significant contribution from solvent nucleophilicity,^{12,15} a range of Y_X scales of solvent ionizing power, based on solvolyses of 2- or 1-adamantyl substrates (**2**), has been defined (equation 3);¹⁶ for a substrate RX , specific solvation of the

$$\log (k/k_o)_{\text{AdX}} = Y_X \quad (3)$$

leaving group (X) can then also be accounted for. However, many aqueous mixtures have similar nucleophilicities, so Y values are still useful. Plots of Y_{OMe} *versus* Y (Figure 3) are linear (r values are in the range 0.997–0.999), but show some deviations into separate correlation lines for the various binary mixtures (dispersion). Slopes vary from 0.98 ± 0.01 for acetonitrile/water (excluding the data point for 20% acetonitrile) to 1.13 ± 0.03 for dioxane/water, and dispersion is in the order dioxane > acetone > methanol.

Rate constants for solvolyses of electron rich benzenesulphonyl chlorides (**3**, $Z = \text{Me}$, OMe) were previously⁸ correlated with Y_{Cl} , based on solvolyses of 1-adamantyl

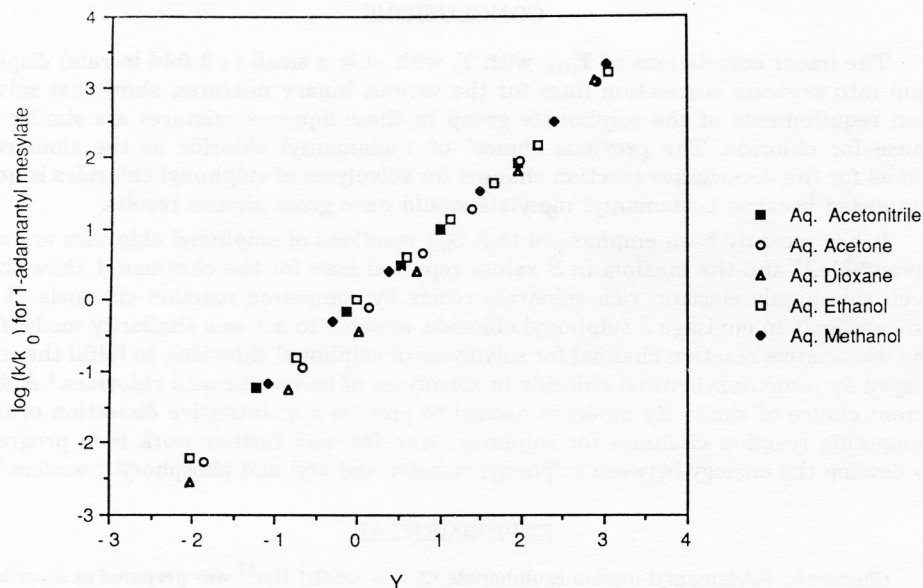


Figure 3. Correlation of rate constants ($\log k/k_0$) for solvolyses of 1-adamantyl mesylate with Y values; kinetic data from Table IV, and Y values from Refs. 6 and 14.

chloride ($2, X = \text{Cl}$);^{15a,16} a plot of Y_{Cl} versus Y is also close to linear,^{15a} so an implication from Figure 3 is that there would not be major changes in the rate-rate profiles if 1-adamantyl mesylate were chosen instead of 1-adamantyl chloride as the similarity model for the dissociative reaction channel.⁸ New Y_{OMs} values are calculated (Table V) from the kinetic data in Table IV, and the Y_{OMs} value of -2.96 for 99% acetonitrile/water is in satisfactory agreement with the Y_{OTs} value of -3.21 for pure acetonitrile.^{16,17}

TABLE V

Y_{OMs} values (equation 3) for solvolyses of 1-adamantyl methanesulphonate ($2, X = \text{OSO}_2\text{CH}_3$) in aqueous mixtures^a

composition (% v/v)	cosolvent	
	acetonitrile	dioxane
99	-2.96	-2.55
90	-1.22	-1.26
80	-0.15	-0.44
70	0.48	0.40
60	0.98	1.20
50 ^b	1.46	1.81
40	1.91	2.44
30 ^b	2.37	3.09
20	3.24	

^aKinetic data from Table IV and Ref. 13. ^b Interpolated from a plot versus Y (Figure 3).

CONCLUSIONS

The linear correlations of Y_{OMs} with Y , with only a small (<3 fold in rate) dispersion into separate correlation lines for the various binary mixtures, show that solvation requirements of the sulphonate group in these aqueous mixtures are similar to those for chloride. The previous choice⁸ of 1-adamantyl chloride as the similarity model for the dissociative reaction channel for solvolyses of sulphonyl chlorides is now supported because 1-adamantyl mesylate would have given similar results.

It has recently been emphasised that S_N1 reactions of sulphonyl chlorides are unfavourable,¹⁸ and the maxima in S values reported here for the chroman **4** show that even this highly electron rich substrate reacts by competing reaction channels. It is now difficult to envisage a sulphonyl chloride, suitable to act as a similarity model for the dissociative reaction channel for solvolyses of sulphonyl chlorides, to fulfill the role played by *p*-methoxybenzoyl chloride in solvolyses of carboxylic acid chlorides.⁴ A different choice of similarity model is needed to provide a quantitative dissection of the competing reaction channels for sulphonyl transfer, and further work is in progress to develop the analogy between sulphonyl transfer and acyl and phosphoryl transfers.¹⁹

EXPERIMENTAL

Chemicals: 1-Adamantyl methanesulphonate (**2**, $X = OSO_2CH_3$)¹³ was prepared as described previously, and was stored in cold hexane containing 2,6-lutidine.²⁰ The chroman sulphonyl chloride **4** was prepared by chlorosulphonation of the parent chroman.^{9,21} Tri-isopropylbenzene sulphonyl chloride (**5**) was a commercial sample (Lancaster), and the purity of both sulphonyl chlorides was established by HPLC analysis of methanolysis products.

Acetone, dioxane, and methanol (Fisons dried-distilled grades) were used without further purification. Acetonitrile (Fisons dried-distilled grade) was dried over phosphorous pentoxide and ethanol was dried over magnesium ethoxide, before they were distilled.^{15a}

Standard solutions of the solvolysis products (acids and esters) were prepared by injecting known amounts of sulphonyl chlorides into acetonitrile/water, dry ethanol or dry methanol, followed by HPLC analysis.^{8a} Product studies in alcohol/water mixtures required a rapid-mixing procedure; a turbostirrer was used in a 5 ml reaction vessel similar to that used for kinetics, but without the electrodes.²²

Kinetics: Conductimetric and titrimetric procedures for solvolyses of 1-adamantyl mesylate (**2**, $X = OM_s$)¹³ and rapid solvolyses ($t_{1/2} < 1$ min)²² were as described previously.

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SAŽETAK

Modeli sličnosti u opisu solvatacijskih efekata na reaktivnost. Disocijativni mehanizam u solvolizi sulfonil-klorida u binarnim vodenim smjesama.

T. William Bentley, In Sun Kon, Gareth Llewellyn i Simon J. Norman

Na osnovi analize konstanti brzina i sastava produkata solvolitskih reakcija pentametilkromana, tri-izopropilbenzen-sulfonil-klorida i 1-adamantil metansulfonata u vodenim binarnim smjesama acetonitrila i dioksana razmotreni su mogući mehanizmi reakcije, te primjenljivost 1-adamantil-klorida kao modela u studiju solvolitskih reakcija sulfonil-klorida koji reagiraju disocijativnim mehanizmom.