Sulphonyl Transfer Reactions: Solvolysis of Arenesulphonyl Chlorides in Aqueous Trifluoroethanol

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Activation parameters for the solvolysis in aqueous trifluoroethanol of arenesulphonyl chlorides with electron-supplying substituents have been determined; the results are not in accord with earlier proposals that such compounds react by an S_N1 mechanism.

Nucleophilic substitution reactions of arenesulphonyl halides and related compounds (eqn. 1) are clearly analogous to acyl transfer reactions (eqn. 2).

$$ArSO_2X + Y^-(H–Y) \rightarrow ArSO_2Y + X^-(H–X) \quad (1)$$

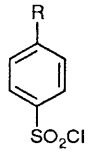
$$RCOX + Y^-(H–Y) \rightarrow RCOY + X^-(H–X) \quad (2)$$

The reactions of eqn. (2) have been intensively investigated over many years owing to their occurrence in many important biological processes, and the mechanisms are reasonably well understood.[1] Over a similar period, there have been many fewer investigations into the mechanisms of the reactions of eqn. (1) and, in spite of some classic work, our understanding of these reactions remains superficial.[2] It has been recognised more recently that these sulphonyl transfer reactions are akin not only to the acyl transfers of eqn. (2) but also to other reactions including phosphoryl transfer. Together, they constitute a family of reactions in which a group, bonded through an atom (sulphur, carbon or phosphorus in these examples) that is unsaturated owing to multiple bonding to one or more oxygen atoms, is transferred as a Lewis acid from one Lewis base to another.

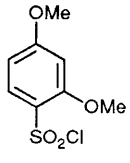
Three mechanisms have been proposed for the reactions of eqn. (1) and are indicated in Scheme 1:[2] (*i*) heterolysis of the S–X bond (with or without prior protonation at X) to give a planar trigonal intermediate sulphonylium cation which then suffers nucleophilic capture by Y^- (or HY), (*ii*) concerted displacement of X^- (or its conjugate acid) from the sulphur atom by Y^- (or HY) *via* a trigonal bipyramidal activated complex, and (*iii*) addition of Y^- (or HY) at the sulphur atom to give a trigonal bipyramidal intermediate from which X^- departs (with or without prior protonation) following, if necessary, a conformational change to allow the nucleofuge to occupy an apical position.

The corresponding mechanisms for the acyl transfers of eqn. (2) have all been characterized.

As far as the sulphonyl transfers of eqn. (1) are concerned, there is presently an uneasy consensus that a single mechanism, the concerted bimolecular S_N2 process (*ii*), can account for all the experimental evidence so far available.[3] The S_N2 mechanism, however, allows considerable variation in the degree of synchroneity in the bond breaking and making, and does not imply a single invariable transition state structure. The sense and the degree of the curvature of the diagonal across the reaction map[4] of Scheme 2 which best describes the mechanism in any particular reaction of eqn. (1) will be determined principally by the nucleofuge, the nucleophile, and the substituents in the arene ring. There are, however,



1a; R = Me
b; R = OMe
c; R = NMe_2



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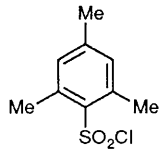

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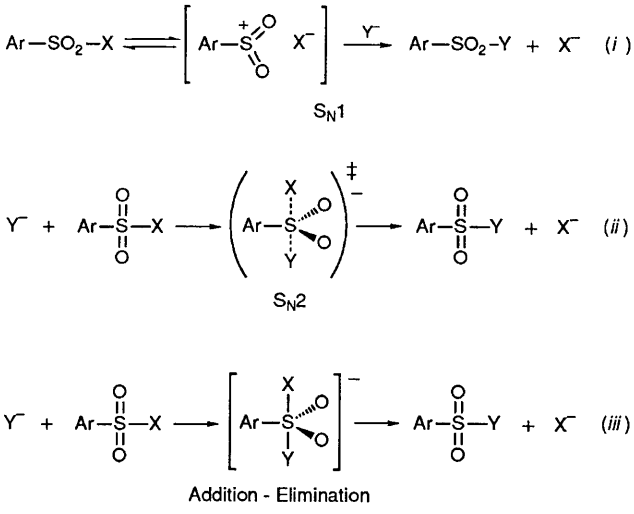
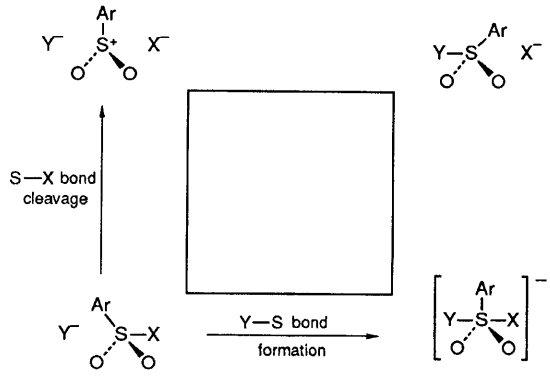


Scheme 1



Scheme 2

reports of evidence allegedly requiring stepwise mechanisms (*i*) and (*iii*).[5–7] These may be represented by very strongly curved paths *via* intermediates located near either the upper left (S_N1) or the lower right (addition–elimination) in Scheme 2.

We are investigating the limit of the concerted process in the direction of the upper left corner of the reaction map of Scheme 2, and whether, at some stage, the mechanism switches over to become a stepwise S_N1 as has been suggested.[5,7] We reasoned that this requires substrates with electron-supplying substituents in the arene ring to stabilise developing electron deficiency at the sulphonyl group, a good nucleofuge, no added nucleophile and a highly-ionizing but weakly-nucleophilic solvent. We sought evidence for a change in mechanism by determining the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ and the disappearance of the second-order term in the rate law for compounds with increasingly effective electron-supplying substituents. In view of an increasing interest in sulphonyl transfer reactions,[8] we report here our initial results for compounds **1, 2** and **3** which cause some earlier mechanistic proposals to be no longer tenable.

In order to provide data for an authentic S_N2 mechanism in the medium that we were to use for more reactive substrates, we first investigated the reaction of 4-toluenesulphonyl chloride (tosyl chloride, **1a**)[2] in 1:1 (v/v) trifluoroethanol–water. The results are shown in Table 1 and include the low standard enthalpy of activation and the very negative standard entropy of activation characteristic of a solvent-induced bimolecular process. As expected, the reaction showed a second-order rate law with added sodium hydroxide.

The solvolysis of 4-methoxybenzenesulphonyl chloride **1b** has also been investigated previously. Tonnet and Hambly,[7] in a very thorough study, suggested that whilst it underwent hydrolysis by a solvent-induced S_N2 mechanism, substrates with more effective electron-donating substituents, *e.g.* 2,4-dimethoxybenzenesulphonyl chloride **2**, should react by the S_N1 mechanism that had been proposed earlier for mesitylene-2-sulphonyl chloride **3** and related compounds,[5] and which has been identified for the hydrolysis of an arenecarbonyl fluoride.[9] As our results in Table 1 show, there is no evidence that any of these compounds react by a mechanism different from that of tosyl chloride in 1:1 (v/v) TFE–water. Further, we established that the dimethoxy compound **2** showed no common-ion rate retardation, but that it did show a second-order rate term in the presence of increasing concentrations of sodium hydroxide. Interestingly, whilst **2** is more reactive than tosyl chloride **1a** in its solvolytic reaction with aqueous TFE

Table 1 Rate and activation parameters for the solvolysis of arenesulphonyl chlorides

Compound	Solvent	$k(25\,^{\circ}C)/s^{-1}$ [a]	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
1a	50:50TFE[b]	4.65×10^{-5} [c]	71	−91
1b	50:50TFE[b]	8.32×10^{-5}	71	−85
2	50:50TFE[b]	15.5×10^{-5} [d]	70	−82
3	50:50TFE[b]	43.7×10^{-5}	65	−93
3	97:3TFE[e]	4.27×10^{-5}	53	−150
1c	100TFE[f]	5.54×10^{-3}	28	−193

[a] Calculated from results obtained at other temperatures. [b] 1:1 by volume, trifluoroethanol–water. [c] At 25 °C and the ionic strength maintained constant with $NaClO_4$, a second-order rate law was obtained with increasing concentrations of NaOH (k_2 = 2.76 dm^3 mol^{-1} s^{-1}). [d] At 25 °C and the ionic strength maintained constant with $NaClO_4$, a second-order rate law was obtained with increasing concentrations of NaOH (k_2 = 0.167 dm^3 mol^{-1} s^{-1}). Addition of increasing concentrations of chloride at constant ionic strength had no rate-retarding effect. [e] 97:3 by weight, trifluoroethanol–water. [f] Anhydrous trifluoroethanol.

(rate ratio = 3.3 at 25 °C), the latter is more reactive with the nucleophilic solute NaOH (or, in view of the relative acid strengths of water and trifluoroethanol,[4] with $NaOCH_2CF_3$) by a factor of about 17. We also investigated the solvolysis of **3** in the less nucleophilic 97:3 (w/w) TFE–water. The results show that the reaction is slower than in the more aqueous medium due wholly to a more negative $\Delta S^{\ddagger}$, and $\Delta H^{\ddagger}$ is actually lower than in the 1:1 medium. The most reactive substrate that we investigated, 4-(dimethylamino)benzenesulphonyl chloride **1c**, was too reactive in aqueous TFE and we had to use the very weakly nucleophilic but highly ionizing anhydrous TFE. Even here, we see no evidence of a change in mechanism. In all cases, there is a very substantial negative entropy of activation characteristic of a loss of translational degrees of freedom upon formation of the activated complex. Correspondingly, the enthalpies of activation are lower than typical S_N1 values for these media[10] owing to compensation of bond breaking by bond making in the activated complex.

It would appear, therefore, that although the incipient sulphonylium cation and the transition state for its formation are stabilized by the introduction of electron-donating substituents, there is still no barrier to its subsequent nucleophilic capture by even a weakly nucleophilic solvent. This mechanism corresponds to a concerted bimolecular substitution mechanism in which the bond breaking is ahead of bond forming in the transition state. Evidence which actually requires the fully stepwise S_N1 mechanism with an appreciable

barrier to nucleophilic capture of the intermediate sulphonylium cation is still lacking.

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