The Absence of Free Sulphur Trioxide as an Intermediate in the Hydrolysis of Isoquinoline *N*-Sulphonate

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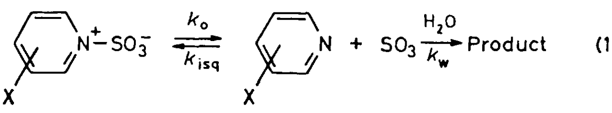
Mass–law experiments using added nucleofuge exclude the existence of free sulphur trioxide as an intermediate in the solvolysis of isoquinoline *N*-sulphonate in 80% acetonitrile solution (v/v) containing 4.4M-water.

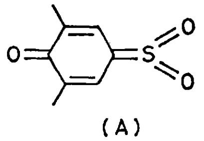
This communication describes classical 'mass–law' effect studies[1] of the hydrolysis of isoquinoline *N*-sulphonate in aqueous acetonitrile solution with added isoquinoline.

Classical methods for demonstrating unsaturated intermediates in solvolysis are very difficult to apply in sulphonate group transfer reactions where sulphur trioxide is a possible intermediate [equation (1)]. The powerful technique where a trapping agent yields trapped product by attack *after* rate-



(1)

limiting expulsion of a leaving group cannot be applied successfully using amine or hydroxy nucleophiles because of the competition by an alternative process which leads to a theoretical yield of the same product. The trapping technique has been applied successfully to reactions involving intermediates analogous to sulphur trioxide, namely sulphenes,[2] aminosulphene (MeN=SO_2),[3] and the *para*-oxosulphene (A).[4]



(A)

Decomposition of isoquinoline *N*-sulphonate in 80% acetonitrile–water shows no variation in first-order rate constant (which is larger than that obtained when the solvent is water alone). The rate constant (k_{calc}) expected for each isoquinoline concentration has been calculated [using equation (2)] for a reaction presumed to proceed by the

$$k_{calc} = k_0\,[H_2O]/\{(k_{isq}/k_w)\,[\text{isoquinoline}] + [H_2O]\} \qquad (2)$$

mechanism of equation (1), using the value k_w/k_{isq} determined later for the reaction of SO_3, and with the assumption that the rate constant observed in the absence of isoquinoline corresponds to k_0. The expected rate decrease with increasing isoquinoline concentration (Table 1) is very much greater than our experimental error and, since no dependence on isoquinoline concentration is actually observed, we must conclude that the mechanism is different from that depicted in equation (1).

The relative reactivity of water and isoquinoline towards sulphur trioxide ($k_w/k_{isq} = 0.71$) was obtained by measuring the total inorganic sulphate and isoquinoline *N*-sulphonate formed when SO_3 was passed through a solution (at −15 °C) in acetonitrile–water (80:20) of isoquinoline (1.02 M). The isoquinoline *N*-sulphonate produced in the reaction was assayed by observing the change in absorbance at 350 nm ($\Delta\epsilon_{350}$ 490) of an aliquot of the stock solution in buffer at pH 8.02. Total sulphate analysis of the completely hydrolysed product gives the inorganic sulphate (produced by reaction of water with SO_3 in competition with isoquinoline) by difference with the isoquinoline *N*-sulphonate formed.†

Table 1. Solvolysis of isoquinoline *N*-sulphonate[a] in acetonitrile–water (80:20 v/v) in the presence of increasing concentrations of isoquinoline.[b]

[Isoquinoline]/M	$k_{obs} \times 10^3/s^{-1}$ [c]	$k_{calc} \times 10^3/s^{-1}$ [d]
pH 8.00		
0	9.9	9.9
0.34	10.2	<8.9
0.51	9.96	<8.5
0.68	9.9	<8.1
1.02	9.96	<7.5
pH 9.27		
0	10.0	<10.0
1.02	10.0	<7.6

[a] Isoquinoline *N*-sulphonate was obtained by passing sulphur trioxide into a solution of isoquinoline in 1,2-dichloroethane and it gave satisfactory analytical data. [b] 25 °C, 0.05 M ionic strength, tris [$(HOCH_2)_3CNH_2$] buffer (0.01 M). The varying volumes of isoquinoline were compensated by dioxan which was shown to have no effect on the rate constant for hydrolysis of the sulphonate up to 12% (v/v). [c] Kinetics measured at 350 nm; results of several runs; errors $< \pm 0.5\ 10^{-3}\ s^{-1}$. [d] Calculated from equation (2); k_0 is the rate constant at zero added isoquinoline and the value quoted is an *upper* limit.

We conclude that sulphur trioxide or its complex with acetonitrile does not participate in the solvolysis reaction.‡

Trapping experiments of Benkovic[5] where methanol competes on an equal footing with water for sulphur trioxide and salicyl sulphate are consistent with the conclusion that the controlling transition-state in sulphonate group transfer has preponderant sulphur trioxide character.

It is impossible to apply the 'mass–law' technique to reactions of the sulphonate in pure water because this would swamp any partitioning of the intermediate to the added nucleofuge. Benkovic[6] finds that the water term (divided by 55.5 M) fits the Brønsted type relationship for second-order reaction of nucleophiles with 4-nitrophenyl sulphate. We observe a similar relationship for attack of nucleophiles on pyridine *N*-sulphonate in water and for reactions with the isoquinoline analogue.[7] Since powerful nucleophiles react with these sulphonates in a bimolecular mechanism it is unlikely that the mechanism would change for water to a dissociative path where the bonding to the nucleophile would be non-existent. It is unreasonable that the mechanism of the present reaction should change to a dissociative process going from organic to aqueous solvent.

The present studies do not exclude a stepwise pre-association mechanism for transfer of the sulphur trioxide group.[8] The symmetry of the controlling transition-state derived from a complete structure reactivity study of the transfer of sulphonate between nitrogen and oxyanions[7] supports the concerted as opposed to the stepwise pre-association mechanism which requires an unsymmetrical transition-state. The bonding between sulphur and the entering and leaving group is very weak compared with a full single bond.

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† Sulphur trioxide is a very reactive species and mixing probably masks the true selectivity (P. Rys, *Angew. Chem.*, 1977, **16**, 807) towards water–isoquinoline. The value obtained for the selectivity should be taken as an upper limit as it is unreasonable that water is more reactive than isoquinoline towards an electrophile.

‡ The possibility that the zero change in rate constant is due to a cancellation of effects was shown not to be the case by checking the reactivity of isoquinoline *N*-sulphonate in the same system with different solutes in place of the added isoquinoline.