

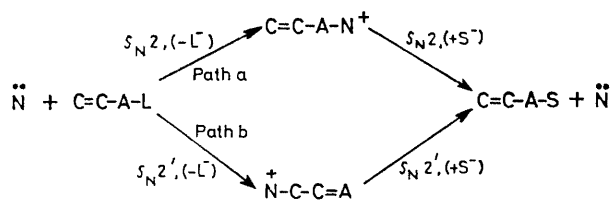
Vinylogous Nucleophilic Catalysis: Hydrolysis of Ethenesulphonyl Chloride in the Presence of Pyridine Bases

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Summary Evidence is presented that hydrolysis of ethenesulphonyl chloride (**2a**) in the presence of pyridine bases takes place by the route (**2a**) → (**5**) → (**3a**), *i.e.* by vinylogous nucleophilic catalysis.

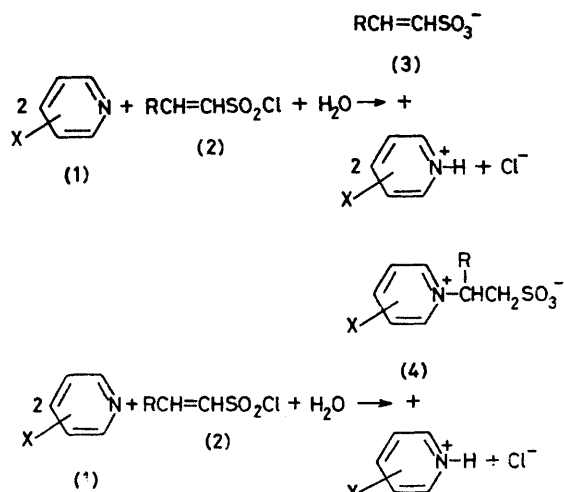
SINCE bimolecular nucleophilic substitution at a centre bearing a 1-alkenyl group may proceed either by a direct (S_N2) or a vinylogous (S_N2') attack, it is to be expected that nucleophilic catalysis of displacement at such a centre should have the same potential for mechanistic duality (Scheme 1).



SCHEME 1. Path a: conventional nucleophilic catalysis. Path b: vinylogous nucleophilic catalysis.

We have recently proposed[†] 'vinylogous nucleophilic catalysis'[†] or ' S_N2' catalysis' as a key feature in the mechanism of the formation of esters when ethenesulphonyl (**2a**) and prop-1-ene-1-sulphonyl chlorides (**2b**) are treated

with alcohols in the presence of tertiary amines in CH_2Cl_2 . Because such a process was unprecedented and the particular system not well suited to a more extensive mechanistic study, we sought clearer proof of the existence of such a mechanism by examining the reactions of (**2a**) and (**2b**) with water in the presence of pyridine bases and now report the results of these investigations.



SCHEME 2. a, R = H; b, R = Me.

[†] We now prefer this name to the previously used ' S_N2' catalysis' to avoid completely any connotations of concertedness sometimes attached to the designation S_N2' (see also ref. 1, footnote †).

TABLE. Rate constants and products of the reactions of alkenesulphonyl chlorides (2) with substituted pyridine bases (1) in aqueous solution^a

Substituents in (1)	p <i>K</i> _a ^b	(2a)		(2b)	
		<i>k</i> _B /l mol ⁻¹ s ⁻¹	<i>q</i> ^c	<i>k</i> _B /l mol ⁻¹ s ⁻¹	<i>q</i> ^c
3,4-Dimethyl	6.65	91.5	0.91	8.28	0.76
3,5-Dimethyl	6.15	61.6	0.85	5.50	0.70
4-Methyl	6.15	57.3	0.88	3.92	0.74
4-Ethyl	6.15	57.2	0.83	—	—
3-Methyl	5.68	38.4	0.86	3.47	0.68
None	5.35	27.3	0.80	1.96	0.58
3-Ethanamido	4.50	24.6	0.66	1.25	0.43
3-Carbamoyl	3.47	6.18	0.5	0.57	—
3-Methoxycarbonyl	3.25	6.66	0.55	0.41	0.27
3-Cyano	1.45	1.90	0.17	0.12	0.08
2-Methyl	6.15	15.6	0.57	0.30	0.40
2-Ethyl	6.00	3.51	0.75	0.10	0.25
2,6-Dimethyl	6.87	4.17	0.65	0.12	(<0.05)
2,4,6-Trimethyl	7.40	0.04	—	—	—
Benzo[<i>b</i>] ^d	4.80	2.58	0.51	0.10	0.10

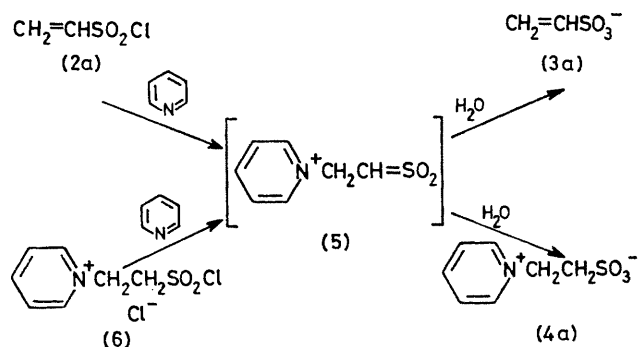
^a At 25.0 °C in 0.1 mol l⁻¹ KCl solution; rate constants were determined by the pH-stat technique. ^b Determined in 0.1 mol l⁻¹ KCl except for the 3-cyanopyridine value which was estimated from the literature value in water. ^c *q* = (amount of betaine)/(total of betaine plus alkenesulphonate) in the reaction product as estimated by n.m.r. integration. ^d *I.e.*, quinoline.

The reactions of (2a) and (2b) with pyridine bases in water are shown in Scheme 2. The proportions of (3) and (4) in the product vary, as may be seen from the values of *q* (the proportion of betaine in the product) in the Table. In the absence of amines, hydrolysis of (2) largely gives (3), the pH-rate profile corresponding to the equation $k_{\text{obs}} = k_{\text{H}_2\text{O}} + k_{\text{OH}}[\text{OH}^-]$, with $k_{\text{H}_2\text{O}}$ and k_{OH} being, respectively, $1.35 \times 10^{-3} \text{ s}^{-1}$ and $1.2 \times 10^2 \text{ l mol}^{-1} \text{ s}^{-1}$ for (2a), and $1.20 \times 10^{-3} \text{ s}^{-1}$ and $38 \text{ l mol}^{-1} \text{ s}^{-1}$ for (2b).[‡] In the presence of the pyridine bases (1) at pH 3–4, the pseudo-first order rate constants agree with the equation $k_{\text{obs}} = k_{\text{H}_2\text{O}} + k_{\text{B}}[\text{B}]$, where [B] is the concentration of (1). For the reaction of (2a) with (1) lacking substituents in the 2 (or 6) positions, the catalytic constants fit the expression $\log k_{\text{B}} = 0.32 \text{ p}K_{\text{a}} - 0.22$. For quinoline, 2-picoline, 2,6-lutidine, or 2,4,6-collidine, however, the k_{B} values may be 5–ca. 10^3 times lower than those predicted by this relation. The reactions of (2b) are similar except that the k_{B} values are 10–50 times lower.

Reaction of (2a) with (1) in D₂O gives the undeuterated ethenesulphonate anion (3) and betaine monodeuterated at the position α to the –SO₃⁻ group. No solvent kinetic isotope effect was observed on changing from H₂O to D₂O in the reaction of (2a) with 3-cyanopyridine.[§]

It is evident that our results are consistent with the sequence (2) → [(5)] → (3) + (4) shown in Scheme 3. One may imagine, however, an alternative mechanism in which the formation of (3) is a completely separate process from that of (4), *e.g.* if (3) were to arise by direct nucleophilic catalysis [*i.e.*, via RCH=CHSO₂py⁺ (py = pyridine)] and (4) by way of (5). With such a mechanism, however, one would expect that the replacement of the hydrogen by a methyl group at C-2 would have a much greater effect on the rate of attack at C-2 to give (4) than at the sulphur to

give (3). We found, in fact, that *q* does not change by the presence of the methyl group nearly as much as k_{B} (see Table). In other words, on the basis of this mechanism introduction of the methyl group produces a distinct lowering of the rate of attack not only at C-2 but also at the sulphur atom.[¶] When one notes that $k_{\text{H}_2\text{O}}$, the rate constant for uncatalysed hydrolysis is virtually the same for (2a) and (2b) (see above), it is apparent that these results are more simply explained by the mechanism in Scheme 3 than by the alternative route.



SCHEME 3

Confirmation of this conclusion was obtained by generating the putative common intermediate (5) from another source under similar conditions and obtaining the same product mixture. Reaction of 1-(2-chlorosulphonylethyl)-pyridinium chloride (6) with an excess of pyridine at pH 4 in water gave (3a) and (4a) in the ratio 18:82. Similar reaction of (2a) gave a 20:80 mixture of (3a) and

[‡] The mechanisms of these reactions are uncertain. Results of recent labelling and product experiments are consistent with a simple attack of water on the sulphur atom for (at least most of) the uncatalysed hydrolysis, whereas the hydroxide promoted reaction may be complex. It is likely that the $k_{\text{H}_2\text{O}}$ values indicate the relative ease of attack on the sulphur atom in (2a) and (2b), whereas the k_{OH} values may not.

[§] This base was chosen because it yields the highest proportion of (3), and hence might be expected to show most clearly any effects of general base catalysis.

[¶] Specifically, on this basis the rate constant for formation of (4) from (2) would be qk_{B} and that for (3), $(1 - q)k_{\text{B}}$; with pyridine, for example, changing from (2a) to (2b) lowers qk_{B} by 19 and $(1 - q)k_{\text{B}}$ by 7.

(4a), *i.e.* within experimental uncertainty, a ratio identical to that from (6). The possibility that the products arise simply by preliminary conversion of (6) into (2a) is excluded by our observation that the use of an excess of [²H₆]-pyridine in the reaction of (6) gives (4a) lacking any detectable incorporation of deuterium. The generation of (5) from (6) is indicated by the formation in D₂O of mono-deuteriated betaine as well as of undeuteriated (3a).

The sequence (2a) → (5) → (3a) is a specific example of vinylogous nucleophilic catalysis. Our results clearly

establish this mechanism on a sufficiently firm basis that it would be prudent to consider explicitly such a process for any catalysed substitutions at centres bearing a 1-alkenyl substituent, *i.e.* not only alkenesulphonyl groups but also allylic, αβ-unsaturated carbonyl, and other functions.

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¹ J. F. King and S. M. Loosmore, *J.C.S. Chem. Comm.*, 1976, 1011.