Reactions of Thiolsulphonates with Amines

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The equilibrium constants for the reaction of morpholine with methyl or t-butyl toluene-*p*-thiolsulphonates have been measured in acetonitrile–water (7:1, v/v) at 25 °C. Contrary to previous data they are $2{\cdot}5 \times 10^{-3}$ and 3·4 for the methyl and t-butyl substrates respectively. In the same solvent medium have been measured the reaction rates and the activation parameters of the nucleophilic displacement reaction of morpholine with the same substrates. The overall mechanism is discussed.

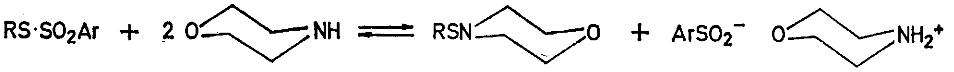
In a first approach to the problem of determining sulphur basicities[1,2] we turned our attention to the reactions of thiolsulphonates with morpholine which have been reported as equilibria in aqueous solvents.[3] In so doing we realized that some of the reported equilibrium constants are in error and that the simple reaction scheme represented by equations (3a) and (3b) is inadequate.

RESULTS

The rates of reaction between morpholine and methyl or t-butyl toluene-*p*-thiolsulphonates have been measured in acetonitrile–water (7 : 1, v/v). The data are in the Table. The stoicheiometry and the products were determined previously.[3] The reactions were followed conductimetrically. The conductivity of the product salt was proportional to its concentration up to at least 1×10^{-3}M. Under pseudo-first-order conditions, with the substrate concentration *ca.* 1×10^{-3}M, all kinetic runs followed good linear semilogarithmic plots. A sufficiently large amine : substrate ratio was necessary in order to displace the equilibrium (1) far to the right. The equilibrium constant for the reaction (1) of morpholine with methyl toluene-*p*-thiolsulphonate was measured conductimetrically in acetonitrile–water (7 : 1, v/v) at 25 °C after careful calibration of the conductivity of reagents and products and computed by use of equation (2). The equilibrium constant for the reaction of morpholine with t-butyl toluene-*p*-thiolsulphonate was similarly measured at 60 and 70 °C in the same solvent medium. The methane sulphenamide is very unstable in aqueous solution. It is hydrolysed autocatalytically in a few min to give unidentified acidic products. In the presence of an excess of base the rate of hydrolysis is low enough to permit measurement of the equilibrium constants, even though not very accurately, after *ca.* 20 min

$$K_{eq} = \frac{[\text{Sulphenamide}][\text{Morpholinium ion}]\,\dfrac{}{[\text{Sulphinate ion}]}}{[\text{Thiolsulphonate}][\text{Morpholine}]^2} \quad (2)$$

from mixing of the reagents. The values measured at constant initial concentration of morpholine (10^{-2}M) and seven initial concentrations of methyl toluene-*p*-thiolsulphonate ranging from 5×10^{-4} to 1×10^{-2}M displayed only a maximum deviation of *ca.* 25%; $K_{eq} = (2{\cdot}5 \pm 0{\cdot}6) \times 10^{-3}$ at 25 °C. The equilibrium constant for the t-butyl toluene-*p*-thiolsulphonate is much more accurate owing to the greater stability of the corresponding sulphenamide; $K_{eq} = 2{\cdot}38 \pm 0{\cdot}14$ at 60 and $2{\cdot}26 \pm 0{\cdot}13$ at 70 °C. These


(1)

Kinetic data for the reaction of morpholine with methyl and t-butyl toluene-*p*-thiolsulphonates[a,b,c]

	t/°C	10^3k / l mol^{-1} s^{-1}	No. of runs	$\Delta H^{\ddagger}$ / kcal mol^{-1}	$\Delta S^{\ddagger}$ / cal mol^{-1} K^{-1}
Me	0·0	9·5	5		
	25·0	35·0	4	7·8	−38·9
Bu^t	25·0	0·00034[d]		23·0	−11·4
	80·0	0·148	1		
	90·0	0·399	1		
	100·0	0·824	3		
	110·0	2·14	1		

[a] Substrate concentration *ca.* 1×10^{-3}M. [b] Morpholine concn., 0·05—0·23M. [c] In acetonitrile–water (7 : 1, v/v). [d] Extrapolated from higher temperatures.

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[1] A. J. Parker, *Proc. Chem. Soc.*, 1961, 371.

[2] J. Hine and R. D. Weimar, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 3387.

[3] J. E. Dunbar and H. Rogers, *J. Org. Chem.*, 1966, **31**, 2842.

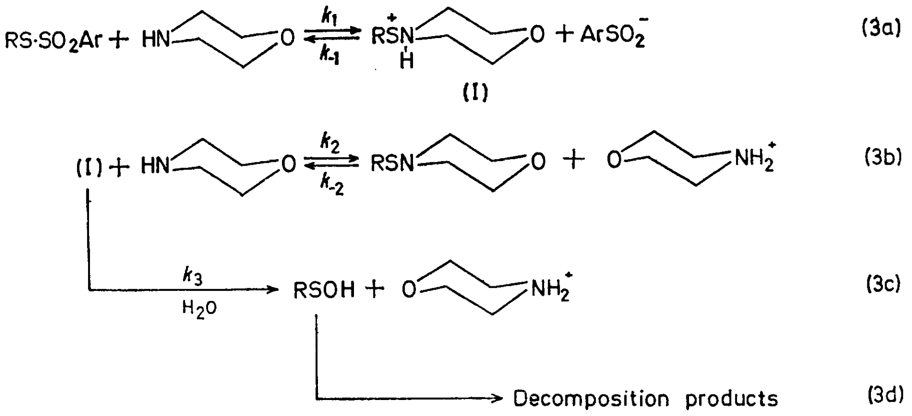
experiments were performed starting from constant initial concentration of morpholinium sulphinate (10^{-3}M) and varying initial concentrations of sulphenamide (six concentrations at each temperature ranging from 1 × 10^{-3} to 1 × 10^{-2}M). The extrapolated value at 25 °C suffers a maximum deviation of *ca.* 50%; $K_{\mathrm{eq}} = 3{\cdot}4 \pm 1{\cdot}5$.

DISCUSSION

Both the direct and the reverse reaction of equilibrium (1) are so slow at 25 °C for the more bulky substrate ($\mathrm{R = Bu^t}$) that the equilibrium constant can be measured only at temperatures above 60 °C. The extrapolated equilibrium constant at 25 °C is 3·4. The value of the equilibrium constant previously measured,[3] 6·1 × 10^{-3}, at room temperature, was probably due to contamination by atmospheric carbon dioxide which yielded a small amount of salt whose conductivity was measured and attributed to the formation of morpholinium sulphinate.

The previously reported[3] equilibrium constant for the methyl derivative, 0·2, is on the contrary larger than the average value at 25 °C, 2·5 × 10^{-3}, reported here. The larger value might have resulted because of the instability of the methyl sulphenamide (see Results section) which is thus subtracted from the equilibrium to yield acidic products which present a conductivity similar to that of morpholinium sulphinate.

The large discrepancy found between the equilibrium constants given earlier and those herein reported casts doubt on the equilibrium constants reported for other thiolsulphonates[3] and the mechanistic conclusions resting on them.



The experimental observations made during the rate and equilibrium experiments permit the formulation of mechanism (3a)—(3d), whose features are not generally recognized. Such is the case of the equilibrium rate constants measured by Dunbar and Rogers.[3] They did not take into account that both steps of equilibrium (3a) must be slow for the t-butyl derivatives as is the case for all nucleophilic substitutions of sulphenyl derivatives.[4] They also disregarded the possibility that (I) might undergo fast hydrolysis [followed by decomposition (3d) of the sulphenic acid].[5] Only a large excess of morpholine displaces equation (3b) far to the right so that the concentration of the sulphenylmorpholinium ion (I) becomes too small for reaction (3c) to be relevant. This step is less important for the more bulky substrate since nucleophilic attack by water is much more sensitive to steric hindrance than proton transfer. The scheme of reactions (3) is also valid when tertiary amines are the nucleophiles except for the deprotonation step (3b). However, it was not taken into account by Oae *et al.* who state that aryl benzenethiolsulphonates do not react with a buffer made up of *N*-ethylmorpholine and *N*-ethylmorpholinium sulphate in aqueous dioxan.[6] A fast reaction can in fact be followed conductimetrically when *N*-methylmorpholine is added to an aqueous solution of methyl or *p*-tolyl toluene-*p*-thiolsulphonate.[7] Besides, tertiary amine-catalysed hydrolysis of sulphenyl esters[8] and sulphonyl chloride in aqueous solvents[9,10] have been reported. Therefore, the conclusion that the hydrolysis of aryl benzenethiolsulphonates[6] at pH values around 7 in the presence of *N*-ethylmorpholine occurs by direct attack of $\mathrm{OH^-}$ has yet to be proven and the reported ρ value cannot be attributed with certainty to the alkaline hydrolysis of benzenethiolsulphonates.[6]

The observation that equilibrium (3c) is displaced to the right only by a large excess of morpholine suggests that the basicity of methanesulphenamide is similar to that of morpholine, that is, much larger than usually thought.

EXPERIMENTAL

Materials.—Reagent grade acetonitrile was refluxed over potassium carbonate and fractionated. Morpholine was

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[4] (*a*) E. Ciuffarin and A. Fava, *Progr. Phys. Org. Chem.*, 1968, **6**, 81; (*b*) W. A. Pryor and K. Smith, *J. Amer. Chem. Soc.*, 1970, **92**, 2731.

[5] D. R. Hogg and P. W. Vipond, *J. Chem. Soc.* (*B*), 1970, 1242.

[6] S. Oae, R. Nomura, Y. Yoshikawa, and W. Tagaki, *Bull. Chem. Soc. Japan*, 1969, **42**, 2903.

[7] L. Senatore and E. Ciuffarin, unpublished results.

[8] L. Senatore, E. Ciuffarin, and L. Sagramora, *J. Chem. Soc.* (*B*), 1971, 2191.

[9] O. Rogne, *J. Chem. Soc.* (*B*), 1970, 727.

[10] O. Rogne, *J. Chem. Soc.* (*B*), 1970, 1056.

refluxed over KOH pellets and fractionated. t-Butyl toluene-*p*-thiolsulphonate,[11] methyl toluene-*p*-thiolsulphonate,[12] 4-(t-butylthio)morpholine,[3] 4-(methylthio)morpholine,[3] and morpholinium toluene-*p*-sulphinate [3] were prepared according to general procedures and gave good elemental analyses.

Kinetics.—The reactions of methyl and t-butyl thiosulphonates with morpholine were followed conductimetrically with a Metrohm E 101 apparatus. The reaction of the methyl derivative was followed directly in the conductivity cell at 0 or 25 °C. The reaction of the t-butyl derivative was followed by sealing portions of the reacting solution in ampoules which were heated in a thermostatted bath at the appropriate temperature, withdrawn at intervals, and rapidly cooled to 25 °C at which temperature the conductivity of the solution was recorded. Care was taken to avoid contact with atmospheric carbon dioxide.

The procedure used to determine the equilibrium constants is similar to that described above for the kinetic runs.

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