MECHANISMS OF SUBSTITUTION REACTIONS AT SULFINYL SULFUR.

CONCOMITANT ELECTROPHILIC AND NUCLEOPHILIC CATALYSIS OF

THE HYDROLYSIS OF p-TOLUENESULFINYL p-TOLYL SULFONE

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In investigating further the role of a sulfinyl sulfone (I) as an

intermediate in the disproportionation of an aryl sulfinic acid (1,2) we

have measured the rate of hydrolysis of Ia (eq. 1) in acetic acid-1% water

as solvent. In the course of this work we have discovered that the rate

$$\text{Ar}\overset{O}{\underset{\underset{O}{\|}}{\overset{\|}{S}}}-\text{SAr} + H_2O \longrightarrow 2 \ \text{ArSO}_2H \tag{1}$$
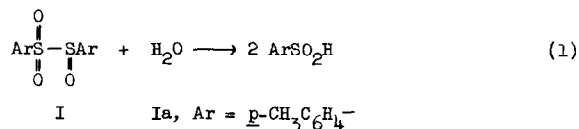
I   Ia, Ar = p-CH$_3$C$_6$H$_4$-

of acid-catalyzed hydrolysis of Ia is profoundly accelerated by the

presence of very small amounts of certain alkyl sulfides. This phenomenon

bears a striking resemblance to several earlier examples (3,4) of

concomitant nucleophilic and electrophilic catalysis of the scission of a

sulfur-sulfur bond. These other cases, however, involved nucleophilic

attack on a sulfenyl rather than a sulfinyl sulfur. The present results

thus suggest that this type of catalysis of sulfur-sulfur bond scission is

even more general than was previously suspected and is not restricted

merely to reactions involving divalent sulfur.

The hydrolysis of Ia in acetic acid-1% water solvent containing various

amounts of added sulfuric acid can be conveniently followed by observing the

arance of the strong absorption at 300 mμ (ϵ = 8,000) due to Ia.

Provided the initial concentration of Ia is kept low ($<10^{-3}\underline{M}$) the reverse reaction--formation of Ia from p-toluenesulfinic acid--can be neglected. Both in the presence and absence of added sulfide the hydrolysis of Ia follows good first-order kinetics. Table I summarizes the experimental first-order rate constants, k_1, for the hydrolysis under the various

Table I

Kinetics of Hydrolysis of Ia in Acetic Acid-0.56 $\underline{M}$ Water at 21.0°

Sulfide	(H_2SO_4),$\underline{M}$	$(R_2S) \times 10^3$, $\underline{M}$	$k_1 \times 10^4$, sec^{-1} [a]	$k_S = \left[\dfrac{k_1-k_1^\circ}{(R_2S)}\right]$ [b]
none	0.10	0.00	1.9	
	0.20	0.00	3.5	
	0.30	0.00	5.6	
	0.40	0.00	8.3	
$(PhCH_2)_2S$	0.10	0.69	5.1	0.46
	0.10	1.38	8.3	0.46
	0.10	2.07	10.7	0.43
	0.20	0.69	10.8	1.1
	0.30	0.69	19	1.9
	0.40	0.69	32	3.5
$\underline{n}$-Bu_2S	0.10	0.24	19	7.1
	0.10	0.48	39	7.8
	0.10	0.69	54	7.5
	0.20	0.24	55	21
	0.30	0.24	83	32
$(HOOCCH_2CH_2)_2S$	0.10	83	122	0.14
	0.10	42	56	0.13
tetrahydro-thiophene	0.10	0.127	50	38
	0.10	0.076	30	37
Et_2S	0.10	0.334	25	6.8
	0.10	0.167	13.2	6.8
$(HOOCCH_2)_2S$	0.20	62	6.03	0.0041
	0.20	93	6.75	0.0035

[a] Initial concentration of Ia in the range 0.86-2.6×10^{-4} $\underline{M}$. [b] k_1° equals the rate of hydrolysis in the absence of sulfide under otherwise identical conditions.

reaction conditions. That the sulfide-catalyzed reaction is first order in sulfide is shown by the fact that for a given sulfide at a given sulfuric acid concentration $(k_1 - k_1^0)/(R_2S)$ is a constant independent of sulfide concentration.

The rate constant, k_S, for a sulfide-catalyzed hydrolysis is strongly dependent on both the acidity of the solution and the nature of the sulfide. For the experiments in Table I with benzyl and butyl sulfides at several sulfuric acid concentrations one finds that a plot of log k_S for a given sulfide vs. $-H_0$ (5) is linear with a slope of about 0.95. Table II gives a comparison of k_S values for all sulfides studied. There is something over a 10,000-fold spread in reactivity between the most reactive, tetrahydrothiophene, and the least reactive, thiodiacetic acid. A plot of the log k_S values for all sulfides except tetrahydrothiophene vs. $\Sigma\sigma^*$ for R in R_2S shows excellent linearity. The apparent ρ^* value (-1.6) shows that the sulfide sulfur has a much lower electron density in the transition state than it has in the original sulfide.
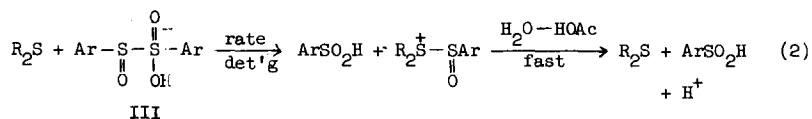
Table II

Relative Reactivity of Sulfides as Catalysts for the Hydrolysis of Ia

Sulfide	k_S, $\underline{M}^{-1}sec^{-1}$ [a]
tetrahydrothiophene	38
$\underline{n}$-Bu$_2$S	7.4
Et$_2$S	6.8
(PhCH$_2$)$_2$S	0.45
(HOOCCH$_2$CH$_2$)$_2$S	0.14
(HOOCCH$_2$)$_2$S	0.0014 [b]

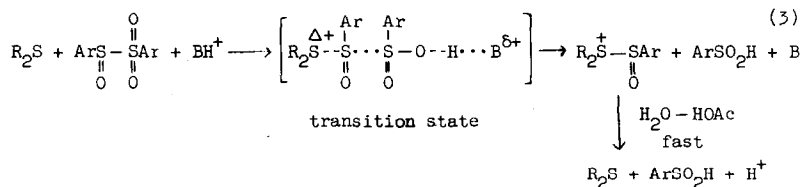[a] All data are for acetic acid-0.56 $\underline{M}$ water-0.10 $\underline{M}$ sulfuric acid at 21°.
[b] Extrapolated from 0.2 $\underline{M}$ sulfuric acid assuming same dependence of k_S on acidity as for butyl and benzyl sulfides.

At first glance a mechanism involving rate-determining nucleophilic

attack of the sulfide on the sulfonyl-protonated sulfinyl sulfone (III)

$$R_2S + Ar-\overset{\overset{O}{\underset{\|}{\|}}}{\underset{\overset{\|}{O}}{S}}-\overset{\overset{--}{}}{\underset{\overset{\|}{OH}}{S}}-Ar \xrightarrow[\text{det'g}]{\text{rate}} ArSO_2H + R_2\overset{+}{\underset{\overset{\|}{O}}{S}}-SAr \xrightarrow[\text{fast}]{H_2O-HOAc} R_2S + ArSO_2H \quad (2)$$

$$+ H^+$$

III

might seem acceptable. However, the following arguments demonstrate that

this is not the case. Sulfonyl groups represent extremely weak basic

sites (6), and one can calculate (7) that in the present solutions ($h_0 =$

13-120) the fraction of Ia present as III will be <u>less</u> than 10^{-10}. Given

k_S for the butyl sulfide-catalyzed hydrolysis, this would require that the

rate constant for reaction 2 between butyl sulfide and III be at least

10^{11}- 10^{12} $\underline{M}^{-1}sec^{-1}$, a value so large as to be patently impossible. For

this reason this mechanism and others involving III can be eliminated.

Several other mechanisms are, however, worthy of consideration.

Although no truly definitive decision can be made between them at the

present time, we are inclined to favor the one shown in eq. 3 (8). In

$$R_2S + ArS-\overset{\overset{O}{\underset{\|}{\|}}}{\underset{\overset{\|}{O}}{S}}Ar + BH^+ \longrightarrow \left[R_2\overset{\Delta+}{S}--\overset{\overset{Ar}{\|}}{\underset{\overset{\|}{O}}{S}}\cdots\overset{\overset{Ar}{\|}}{\underset{\overset{\|}{O}}{S}}-O--H\cdots B^{\delta+} \right] \longrightarrow R_2\overset{+}{\underset{\overset{\|}{O}}{S}}-SAr + ArSO_2H + B \quad (3)$$

$$\text{transition state} \qquad\qquad \downarrow \begin{array}{c} H_2O-HOAc \\ \text{fast} \end{array}$$

$$R_2S + ArSO_2H + H^+$$

this mechanism the sulfur-sulfur bond in Ia is cleaved in a single step

which involves both nucleophilic attack by the alkyl sulfide on the

sulfinyl group and, equally important, catalysis of the departure of $ArSO_2$

by donation of a proton to this group by a general acid, BH^+ (9). The

principles outlined by Bruice and Benkovic (10) lead one to expect that

such a termolecular process will have a rather low activation energy and a

rather large negative entropy of activation. We find, in agreement with

such expectations, that for the butyl sulfide-catalyzed hydrolysis E_a is

only 6.5 kcal. while $\Delta S^{\ddagger}$ is approximately -40 e.u. To those who might

feel that the correlation of log k_S with $-H_0$ is incompatible with a

mechanism involving general acid catalysis (such as eq. 3), we would point

out that other examples (11,12) are known in which the rates of general

acid catalyzed reactions correlate with $-H_0$ in strongly acid media.

Furthermore, because of the extensive ion pairing that occurs in acetic

acid as a result of its low dielectric constant, the significance and

generality of the acidity function in this particular medium are open to

question (12). To us it seems a solvent in which one should use the

dependence of rate on H_0 merely as an indicator of acid catalysis rather

than as a means of deciding details of mechanism.

In any event, the sulfide-catalyzed hydrolysis of Ia in acid solution

is clearly an example of concomitant electrophilic and nucleophilic

catalysis of the scission of the S-S bond in Ia. This type of catalysis

of the cleavage of a sulfur-sulfur bond has previously been observed in

two cases involving sulfenyl sulfur (3,4). The present demonstration that

it can also be important for a scission requiring nucleophilic attack at

sulfinyl sulfur shows that the phenomenon is apparently a rather general

one for sulfur-sulfur bond scissions in acid solution.

One of the most striking features of this and the previous examples

(3,4) of this type of catalysis is the extremely small concentrations

(10^{-4} - 10^{-5} $\underline{M}$) of weak sulfur nucleophiles that are able to produce

rather dramatic catalytic effects. Among other things this suggests that

in some cases in practical work the success or failure of reactions

involving sulfur-sulfur bond scission in acid solution may in actual fact

be dependent on the presence of small amounts of nucleophilic impurities

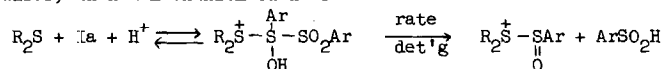in the reagent used. Furthermore, since making and breaking of S-S bonds

may be involved in the intermediate stages of reactions in which neither the original reactants or the final products themselves possess an S-S bond, this may be of wider importance than at first seems apparent.

REFERENCES AND FOOTNOTES

1. J. L. Kice and K. W. Bowers, J. Am. Chem. Soc., 84, 605 (1962).

2. J. L. Kice and N. E. Pawlowski, ibid., 86, 4898 (1964).

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4. J. L. Kice and C. G. Venier, Tetrahedron Letters, 3629 (1964).

5. D. S. Noyce and L. R. Snyder, J. Am. Chem. Soc., 80, 4324 (1958).

6. S. K. Hall and E. A. Robinson, Can. J. Chem., 42, 1113 (1964).

7. Hall and Robinson (6) give the pK_a for the conjugate acid of dimethyl sulfone as -12.3. The sulfonyl group of Ia should be less basic than that in dimethyl sulfone. Therefore, even for $H_0 = -2$ the fraction of Ia present as III should be less than 10^{-10}.

8. If one feels that valence shell expanded species such as IV are acceptable as actual intermediates in substitutions involving sulfinyl sulfur, then a mechanism such as

$$R_2S + Ia + H^+ \rightleftharpoons R_2\overset{+}{S} - \underset{\underset{OH}{|}}{\overset{\overset{Ar}{|}}{S}} - SO_2Ar \quad \xrightarrow[\text{det'g}]{\text{rate}} \quad R_2\overset{+}{S} - \underset{\underset{O}{\|}}{S}Ar + ArSO_2H$$

IV

can also be written for the sulfide-catalyzed hydrolysis. Notice, however, that in this mechanism, as in eq. 3, the sulfide acts as a nucleophile and the role of the proton in the rate-determining step is to assist the departure of the $ArSO_2$ group.

9. Because $ArS(O)\overset{+}{S}R_2$ is undoubtedly of somewhat higher free energy than Ia, we write the transition state for its formation as one in which the making of the new S-S bond and the breaking of the old one are better than half complete. This also means that transfer of the proton to the departing $ArSO_2$ group is largely complete in the transition state, a fact which, according to Kuivila and Nahabedian (11), might be particularly likely to cause a general acid catalyzed reaction to exhibit a correlation of rate with H_0 in strongly acid solution.

10. T. C. Bruice and S. J. Benkovic, J. Am. Chem. Soc., 86, 418 (1964).

11. H. G. Kuivila and K. V. Nahabedian, ibid., 83, 2159 (1961).

12. F. A. Long and M. A. Paul, Chem. Revs., 57, 935 (1957).