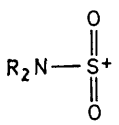
Kinetics of Hydrolysis of *NN'*-Diarylsulphamides

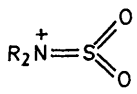
By **William J. Spillane,*** Chemistry Department, University College, Galway, Ireland
James A. Barry and **Francis L. Scott,** Chemistry Department, University College, Cork, Ireland

The kinetics of hydrolysis of five *para*-substituted NN'-diarylsulphamides, p-$XC_6H_4NHSO_2NHC_6H_4X$-p (X = H, Me, MeO, Cl, or NO_2) in 9:1 v/v water–acetone containing added hydrochloric acid have been measured at 50 and 75°. The Hammett ρ for the hydrolysis reaction is +1·03. The effect on rate of varying the pH from 3·05 to 1·05 has been studied for both *NN'*-diphenylsulphamide and *N*-phenylsulphamic acid. The rate of hydrolysis of phenylsulphamic acid is *ca.* 100 times faster than the rate of hydrolysis of diphenylsulphamide under identical conditions. Thus the intermediacy of phenylsulphamate in the hydrolysis of diphenylsulphamide does not complicate the kinetics and first-order kinetics have been observed. The major hydrolytic pathway involves bimolecular water attack on unprotonated diarylsulphamide.

Because of the stabilization afforded by the amino-function the possibility exists that sulphamyl halides can ionize $R_2NSO_2Cl \longrightarrow R_2NSO_2^+ + Cl^-$. The resulting sulphamylium ions could experience charge delocalization *e.g.* (1) and (2) and in fact such resonance



(1)



(2)

stabilized species have been suggested as being involved in the solvolysis of dimethylsulphamyl chloride.[1a] Later, Hall and Lueck [1b] examined the reaction by two methods. First, by promoting the ionization mechanism using mercuric perchlorate as a powerful electrophilic reagent and second, by attempting to trap the intermediate sulphamylium ions produced. Dimethylsulphamyl chloride reacts very rapidly with the mercuric salt, a reaction which they concluded involved sulphamylium ions, though these could not be trapped by a variety of nucleophiles, such as amines, oximes, azides, and sulphide ions. More recently, Rogne [2] has studied the solvolysis of dimethylsulphamyl chloride in water and aqueous acetone and he interprets his results in favour of an S_N2 rather than the S_N1 mechanism previously suggested by Hall.[1] However, in current work Robertson,[3] who has measured the heat capacities of activation and secondary deuterium isotope effects for the hydrolysis of dimethylsulphamyl chloride and other sulphamyl chlorides, explains his results in terms of an S_N1 mechanism involving steric hindrance to the approach of water.

We have examined other systems capable of forming sulphamylium ions to see whether such capacity is realized. The most promising starting materials for such a study would be the synthetically inaccessible arylsulphamyl halides, $ArNHSO_2X$. Accordingly, we have previously examined the hydrolysis of the corresponding arylsulphamic acids,[4a] which follow an *A*-2 type mechanism and alkylsulphamic acids,[4b] which display *A*-2 and borderline mechanisms. The present study examines the hydrolysis of the amides of the arylsulphamic acids.

EXPERIMENTAL

M.p.s are uncorrected. Microanalyses were carried out by Dr. Pascher (Bonn) and by Messrs. Weiler and Strauss (Oxford).

Preparation of Sulphamides.—The syntheses of the sulphamides, p-$XC_6H_4NHSO_2NHC_6H_4X$-p was carried out either by the method of Kirsanov [5] (X = H or MeO) which involved an amine exchange reaction with sulphamide itself in dry pyridine or by the Parnell method [6] (X = NO_2, Cl or Me), namely the reaction of sulphuryl chloride with the amine in dry pyridine: X = H, m.p. 109—110° (lit.,[5] 111—112°); X = MeO, m.p. 99—101° (lit.,[5] 99—101°); X = NO_2, m.p. 195—197° (lit.,[6] 195—197°); and X = Cl; m.p. 119—120° (lit.,[6] 120—121°). All gave correct analyses. NN'-*Di*-p-*tolylsulphamide* has not been previously reported, m.p. 98—100° [from chloroform–light petroleum (b.p. 40—60°)] (Found: C, 60·5; H, 6·0. $C_{14}H_{16}N_2O_2S$ requires C, 60·9; H, 5·8%).

Other Materials.—*p*-Toluidine was recrystallized from carbon tetrachloride and *p*-chloroaniline from chloroform before use. Pyridine was dried by refluxing over barium oxide for several hours. Sulphamide (Eastman), m.p. 90—92° (decomp.) was used as obtained. Sulphuryl chloride (B.D.H.) was used as obtained. The syntheses of the salts of phenylsulphamic acid has been described.[7]

Hydrochloric acid of the strength required for the kinetic studies was prepared from Volucon standards. The strengths of such acids were checked by titration with standard sodium hydroxide using Methyl Red as indicator. Acetone (Pronalys) was redistilled before use. The hydrochloric acid–acetone mixtures were prepared by equilibration at 20° of 9 : 1 v/v acid–acetone, followed by mixing. Barium chloride, potassium sulphate, sodium chloride, hydrochloric acid, and glycerol (all AnalaR) were used as obtained. Ethanol (analytical grade) was purified by the method of Smith.[8]

Solutions for Turbidimetric and Nephelometric Analysis.[9]—The details of the preparation of solutions used in turbidimetric and nephelometric analyses are as follows: (a)

[1] (*a*) H. K. Hall, jun., *J. Amer. Chem. Soc.*, 1956, **78**, 1450; (*b*) H. K. Hall, jun., and C. H. Lueck, *J. Org. Chem.*, 1963, **28**, 2818.
[2] O. Rogne, *J. Chem. Soc.* (*B*), 1969, 663.
[3] E. C. F. Ko and R. E. Robertson, *J. Amer. Chem. Soc.*, 1972, **94**, 573; *Canad. J. Chem.*, 1972, **50**, 946.
[4] (*a*) F. L. Scott and W. J. Spillane, *Chem. and Ind.*, 1967, 1999; W. J. Spillane, C. B. Goggin, N. Regan, and F. L. Scott, *Internat. J. Sulfur Chem.* (*A*), submitted for publication; (*b*) W. J. Spillane, F. L. Scott, and C. B. Goggin, *ibid.*, 1971, **4**, 223.
[5] A. V. Kirsanov, *Zhur. obschchei Khim.*, 1953, **23**, 223.
[6] E. W. Parnell, *J. Chem. Soc.*, 1960, 4366.
[7] W. J. Spillane and F. L. Scott, *J. Chem. Soc.* (*B*), 1968, 779.
[8] A. Smith, *J. Chem. Soc.*, 1927, 1288.
[9] A. I. Vogel, 'Quantitative Inorganic Analysis,' 3rd edn., Longmans, London, 1962, pp. 847 *et seq.*

standard potassium sulphate was prepared by dissolving potassium sulphate (1·814 g) in water (1 l) giving 1·0 mg of sulphate per ml; (b) sodium chloride–hydrochloric acid reagent was prepared by dissolving sodium chloride (60 g) in water (200 ml) adding concentrated hydrochloric acid (5 ml) and diluting the solution to 250 ml; (c) glycerol–alcohol solution was prepared by mixing glycerol (150 ml) with ethanol (300 ml); and (d) barium chloride reagent was prepared by dissolving barium chloride (30 g) in water (100 ml) to give a 1·44M solution.

Kinetic Procedure.—An ampoule technique was used in all rate measurements. The appropriate amount of sulphamide or phenylsulphamate was dissolved in the water–acetone so as to give a 1×10^{-4}M solution. In the case of the sulphamides all the material did not dissolve until the water–acetone mixture was at the temperature of the rate run. Reasonably good first-order rates were obtained, the precision of mean rate constants being ±7%. However, two difficulties were encountered in the sulphamide rate runs. First, infinity values tended to drift somewhat. This difficulty was solved by taking infinities at periods varying from 7 to 12 half-lives until two consecutive values were identical. Second, earlier points on a rate (up to 20% reaction in some cases) varied somewhat randomly. For example, instantaneous rate constants calculated for the first two points (out of nine) generally differed substantially from the remaining seven. A referee has suggested that these initial segments of the rate may have significance. We feel because of their random character, and their non-reproducibility that they are due to the presence of small quantities of contaminants in the diarylsulphamides. Certainly these segments do not invalidate conclusions based on the major remaining portions of each run which are reproducible. The first few points were therefore ignored or alternatively points were not taken until after 10% reaction. The increase in the concentration of sulphate with the progress of the rate was measured either as a galvanometer deflection reading (nephelometric determination) or, more frequently, as the optical density (turbidimetric determination). The rate of hydrolysis of *NN'*-bis-*p*-nitrophenylsulphamide was followed by colorimetric determination of the liberated *p*-nitroaniline. This rate could not be followed turbidimetrically because of the change in the intensity of colour of the solution during the rate. Each run was carried out in duplicate or triplicate and in some cases runs were repeated four or five times.

Turbidimetric and Nephelometric Measurements.—Turbidimetric measurements were carried out on a Hilger–Spekker absorptiometer model H760 (fitted with two neutral filters) and cells with a 1 cm path length. This instrument was also used for colorimetric measurements. The correct pair of colour filters was chosen by plotting for each pair the optical density (on transmittance) *vs.* concentration.[10] Nephelometric measurements were made with a B & T EEL nephelometer using the optical test tubes (diam. $\frac{5}{8}$ in, length 6 in) supplied with the instrument. Measurement techniques are described in refs. 9 and 11—13. Details of experiments can be had from the authors on request. Nephelometric determinations are accurate to ±7%, turbidimetric determinations to ±5—6%.

[10] Ref. 9, p. 757.

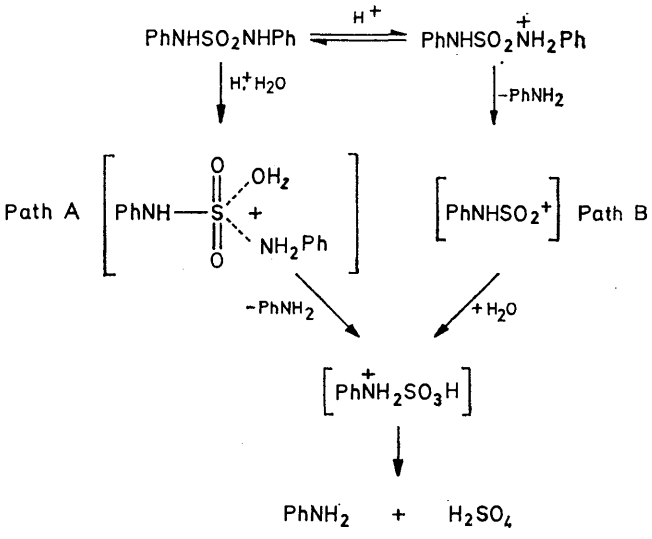
[11] (*a*) F. P. Hochgesang, in ' Treatise on Analytical Chemistry,' eds. I. M. Kolthoff and P. J. Elving, Wiley-Interscience, New York, 1964, part I, vol. 5, p. 3289; (*b*) E. J. Meenan and G. Chiu, *Analyt. Chem.*, 1964, **36**, 536.

Product Runs.—Products were determined for the examples *NN'*-diphenyl-, *NN'*-bis-*p*-methoxyphenyl-, and *NN'*-bis-*p*-nitrophenyl-sulphamide. In each case the sole product identified was the corresponding aniline (by m.p. of the picryl chloride derivative [14]).

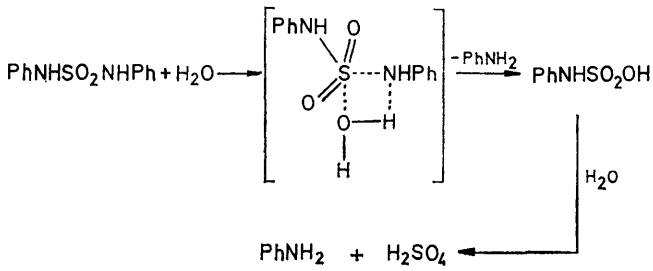
Hydrolysis of Barium N-*Phenylsulphamate*—Barium N-phenylsulphamate (0·962 g, 0·02 mol) was dissolved in 9 : 1 v/v water–acetone (100 ml) containing 0·09M-hydrochloric acid. The solution was maintained at 100° for 10 half-lives. A precipitate of barium sulphate formed and the solution turned light brown due to the formation of aniline. Barium sulphate (98%) was determined by standard gravimetric methods. Aniline was determined by formation of the picryl chloride adduct [14] as before.

RESULTS AND DISCUSSION

Several mechanisms may be envisaged for the hydrolysis of *NN'*-diarylsulphamides (exemplified for *NN'*-diphenylsulphamide in Schemes 1 and 2). Irrespective



SCHEME 1



SCHEME 2

of whether the first step is an acid-catalysed displacement at sulphur (path A, Scheme 1), an acid-catalysed heterolysis to yield substituted sulphamylium ions (Path B, Scheme 1), or a spontaneous bimomecular hydrolysis of unprotonated sulphamide (Scheme 2), phenylsulphamic acid is a likely intermediate. Table 1

[12] A. Steinbergs, *Analyst*, 1953, **78**, 47.

[13] G. Toennies and B. Bakay, *Analyt. Chem.*, 1953, **25**, 160.

[14] ' Organic Reagents for Organic Analysis,' Hopkin and Williams, Chadwell Heath, 1956.

compares the rates of hydrolysis of diphenylsulphamide and phenylsulphamic acid under identical conditions. The data in Table 1 show that a 10-fold increase in the acid concentration speeds the phenylsulphamate hydrolysis by a factor of ten while the rate of hydrolysis of the

TABLE 1

Comparison of rates for the hydrolysis of *NN'*-diphenylsulphamide and phenylsulphamic acid [a] in 10% aqueous acetone at 75°

[HCl]/M	0·0009	0·009	0·09
Sulphamide (10^6k/s^{-1})	4·45	6·2	8·42
Sulphamate (10^6k/s^{-1})	7·50	84·3	734

[a] As the barium salt.

diphenylsulphamide is only increased by *ca.* 1·4. A 100-fold increase in acid concentration increases the rate of hydrolysis of the phenylsulphamate by a factor of 100 while the rate of hydrolysis of the diphenylsulphamide is barely doubled. In 0·0009M-acid the complication of consecutive kinetics arises and the system would be of the type, $X \xrightarrow{k_1} Y \xrightarrow{k_2} Z$ where k_1 and k_2 are comparable. In 0·09M-acid the ratio $k_2 : k_1$ approaches 100 and under these conditions the first-order rate constants (Table 2) are 'overall' rate constants for the hydrolysis of diarylsulphamide to amine and sulphate.[15] The rate-determining step is thus the formation of phenylsulphamic acid.

TABLE 2

Rates and activation parameters for the hydrolysis of *NN'*-diarylsulphamides *p*-$XC_6H_4NHSO_2NHC_6H_4X$-*p* in 10% aqueous acetone [a]

Substnt. (X)	10^7k_{50}/s^{-1}	10^6k_{75}/s^{-1}	$\Delta H^{\ddagger}$/ kJ mol^{-1}	$\Delta S^{\ddagger}$/ J mol^{-1} K^{-1}
p-NO_2	57·4	41·3	71	−126
p-Cl	18·0	14·6	76	−122
H	9·9	8·42	76	−122
p-CH_3	6·1	5·58	80	−118
p-CH_3O	4·04	3·66	80	−122

[a] Containing 0·09M-hydrochloric acid.

The substituent effects revealed in the data in Table 2 are not consistent with the involvement of sulphamylium ions but instead correspond to solvent attack at the sulphamyl sulphur (Path A, Scheme 1 or 2) with Hammett ρ values of +1·08 (at 50°, correlation coefficient $r = 0·994$) and +0·97 (at 75°, $r = 0·989$). The high negative entropy data (Table 2) are also consistent with the participation of water in the rate-determining step.[16] In the case of the alkyl- and arylsulphamates, the entropies for their hydrolyses were in general considerably more positive so that in those cases the entropy criterion was not used as a decisive pointer in assigning mechanism. Since diarylsulphamides are weakly acidic in aqueous solution [17] the unprotonated form will probably predominate in the dilute acid which we have used for the hydrolysis.

The small magnitude of the effect of acid over the narrow range (pH 3·05 to 1·05) which we have used to study the hydrolysis of diphenylsulphamide suggests that at this acid level there is a predominant contribution to the rate from reaction of the unprotonated sulphamide (Scheme 2). If a prior protonation (as in Path A, Scheme 1) was occurring we would have expected a more pronounced effect of acid as in the case of the *N*-alkyl-[4b] and *N*-aryl-sulphamates.[4a] The small rate increase observed on changing the pH from 3·05 to 1·05 is probably an ionic strength effect.

Some related displacements at sulphonyl sulphur give a ρ of approximately +2·3 [18]; the hydrolysis of benzenesulphonyl chlorides has ρ varying from *ca.* +0·6 to *ca.* +1·7,[19] depending on (a) the substituent and (b) the solvent and ρ for the hydrolysis of benzenesulphonyl fluoride is *ca.* = 1·8.[20] However, a reduction in ρ would be expected when one inserts an additional atom between the reaction site and the substituted aromatic ring (as in going from $ArSO_2X$ to $ArNHSO_2X$). The acid hydrolysis of sulphonanilides, $C_6H_5SO_2NHC_6H_4X$-*p* (-*m*) in 50% sulphuric acid is almost insensitive to the effects of substituents and has a ρ of +0·35.[21]

We have written the processes in path A, Scheme 1 and in Scheme 2 as displacement reactions rather than as addition–eliminations on the basis of the lack of isotopic sulphur–oxygen exchange (a) in the hydrolysis of ethylene sulphite [22a] and (b) between isotopically enriched water and either diphenyl sulphone or benzenesulphonate.[22b]

The kinetic data that we have obtained show that the hydrolysis of diarylsulphamides is very much slower than the comparable hydrolysis of dimethylsulphamyl chloride (the half-life for the hydrolysis of this compound in 9 : 1 v/v water–acetone at 25° is 4·2 min,[2] possibly due to the involvement of sulphamylium ions in the case of the latter compound) and much faster than the hydrolysis of sulphonamides.[23,24] The hydrolysis of diarylsulphamides is also more rapid than the hydrolysis of their analogues, the *NN'*-diarylureas, ArNHCONHAr, which do not cleave after 2 h in concentrated hydrochloric acid at 100°. Cleavage of the nitrogen–carbon bond does occur at higher temperatures.[25]

[2/452 *Received*, 28*th February*, 1972]

[15] K. B. Wiberg, 'Physical Organic Chemistry,' Wiley, New York, 1964, p. 323.
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[18] J. F. Bunnett and J. Y. Bassett, *J. Org. Chem.*, 1962, **27**, 2345.
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[21] V. L. Levashova, N. P. Lushina, and V. F. Mandyuk, *Zhur. Org. Khim.*, 1968, **4**, 1783 (in English translation).
[22] (*a*) C. A. Bunton, P. D. B. de la Mare, P. M. Greasley, D. R. Llewellyn, N. H. Pratt, and J. G. Tillett, *J. Chem. Soc.*, 1958, 4751; (*b*) D. R. Christman and S. Oae, *Chem. and Ind.*, 1959, 1251 (see also R. E. Davis, *J. Amer. Chem. Soc.*, 1962, **84**, 599).
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