Substituent Effects on the Kinetics of Pyridine-catalysed Hydrolysis of Aromatic Sulphonyl Chlorides; Brønsted and Hammett Correlations

By **O. Rogne**, Norwegian Defence Research Establishment, Division for Toxicology, N-2007 Kjeller, Norway

The rates of hydrolysis of substituted benzenesulphonyl chlorides, catalysed by substituted pyridines, have been determined. Substituent effects in acid chloride and pyridine are correlated by Hammett and Brønsted equations, respectively. The Hammett plots are curved because of an abnormal low reactivity of *m*- and *p*-nitrobenzenesulphonyl chloride. The sensitivity parameters, β and ρ (excluding the nitro-compounds), obtained from the free-energy relations, are dependent upon the reactivity of the system. Thus β, which varies from 0·406 for *p*-methoxy- to 0·557 for *p*-nitro-benzenesulphonyl chloride, are linearly related to the σ values for the sulphonyl chloride substituents. Likewise the ρ values are linearly related to pK_a of the pyridines. These results show that bond formation in the transition state increase with electron-attracting substituents in the acid chloride, whereas such substituents in the nucleophile leads to increased bond stretching relative to bond formation.

In a previous paper [1] the rates of reaction in methanol of substituted benzenesulphonyl chlorides with various substituted anilines were reported. It was shown that substituent effects in the sulphonyl chloride and aniline could be correlated by Hammett and Brønsted equations, respectively. It was further shown that the sensitivity parameters, ρ and β, obtained from the free-energy relations, were themselves sensitive to the reactivity of the system. Thus, ρ and β varied linearly with the basicity of the anilines and the σ values for the sulphonyl chloride substituents, respectively. To confirm and extend these results, the rates of hydrolysis of some substituted benzenesulphonyl chlorides catalysed by various substituted pyridines have been measured. This reaction, which has been investigated for benzenesulphonyl chloride [2] (R^1 = Ph in Scheme), was shown to occur by a nucleophilic catalysis mechanism involving rate-determining formation of an unstable sulphonylpyridinium intermediate, as shown in the Scheme.

$$\mathrm{R^1SO_2Cl + R^2C_5H_4N \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^1SO_2{\cdot}\overset{+}{N}C_5H_4R^2 + Cl^-}$$

$$\mathrm{\xrightarrow[H_2O]{k_2} R^1SO_2{\cdot}OH + R^2C_5H_4N}$$

EXPERIMENTAL

Materials.—All compounds were commercial samples. The sulphonyl chlorides were fractionally distilled or recrystallised from light petroleum (b.p. 60—80 °C). The pyridines were dried (KOH) and fractionally distilled or recrystallised (light petroleum). B.p.s or m.p.s agreed satisfactorily with literature values.[3,4] G.l.c. showed only a single peak in each case.

Rate Measurements.—The rate of hydrolysis of the sulphonyl chlorides, in the presence of various pyridines, was measured by continuous titration at constant pH of the acid produced by means of the Radiometer Titrator. The apparatus has been described.[2] The procedure was also as described [2] except for the initial concentration of sulphonyl chlorides which was *ca.* 8 × 10^{-5}M, and the concentration of sodium hydroxide which was 0·025N.

All runs were done in water containing 0·05M-sodium chloride at a pH at least 3 units greater than the pK_a of the pyridine.[2] The concentration ranges used for the various pyridines varied from 1·0—10·0 × 10^{-4}M for the fastest reactions to 0·025—0·10M for the slowest.

Reactions were generally run to *ca.* 3 to 4 half-lives. The observed first-order rate constants were calculated from the recorded curve of amount of alkali added against time by Guggenheim's method.[5] Reactions were also occasionally run to completion (10 half-lives) and tested for first-order kinetics by means of conventional plots of log $(a—x)$ against time. Second-order rate constants were calculated from the slopes of plots of the observed first-order rate constants against the pyridine concentration. Rate constants are estimated to be accurate ±5% or better. Activation parameters were calculated from a least-squares treatment of $\ln(k/T)$ against T^{-1}. The estimated precision is *ca.* ±0·5 kcal mol^{-1} in $\Delta H^{\ddagger}$ and *ca.* ±2 cal mol^{-1} K^{-1} in $\Delta S^{\ddagger}$.

RESULTS

The observed rates of reaction were, under conditions of constant pH, always of the first order. Plots of the observed first-order rate constants against concentration of pyridine were also in all cases linear, showing that the reactions are of the first order in pyridine. The second-order rate constants at 25 °C obtained from the slope of these plots are in Table 1. The reactions of the unsubstituted pyridine were also studied at several temperatures. These rate constants are in Table 2 together with the calculated activation parameters.

TABLE 1

Second-order rate constants for the reaction of substituted benzenesulphonyl chlorides with pyridines in water (0·05M-sodium chloride) at 25 °C

	k/l mol^{-1} s^{-1}				
Pyridine	*p*-MeO	*p*-Me	H	*m*-NO_2	*p*-NO_2
3,4-Dimethylpyridine	4·65	9·16	11·5	14·1	31·4
4-Methylpyridine	2·85	5·30	6·54	7·80	15·9
3-Methylpyridine	2·55	4·73	5·65	5·82	11·7
Pyridine	1·52	2·53	3·08	3·03	5·84
3-Acetylpyridine	0·238	0·356	0·405	0·254	0·502
4-Cyanopyridine	0·0675	0·0900	0·0949	0·0475	0·0845
3-Cyanopyridine	0·0395	0·0510	0·0531	0·0240	0·0447

The hydrolysis of the various sulphonyl chlorides produced, at constant pH, 2 equivalents of acid per equivalent acid chloride consumed. This stoicheiometric amount of

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[1] O. Rogne, *J. Chem. Soc.* (*B*), 1971, 1855.

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

[3] 'Handbook of Chemistry and Physics,' The Chemical Rubber Co., Ohio, 45th edn., 1964.

[4] A. R. Katritzky and J. M. Lagowski, 'Heterocyclic Chemistry,' Methuen, London, 1960.

[5] E. A. Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

Table 2

Rate constants and activation parameters for the reaction of pyridine with sulphonyl chlorides in water (0·05M-NaCl)

Sulphonyl chloride	k/l mol^{-1} s^{-1} 15 °C	20 °C	30 °C	35 °C	ΔH/kcal mol^{-1}	$\Delta S^‡$/cal mol^{-1} K^{-1}
p-$NO_2 \cdot C_6H_4 \cdot SO_2Cl$	2·87	4·02	8·50	11·6	11·9	−15
m-$NO_2 \cdot C_6H_4 \cdot SO_2Cl$	1·32	2·01	4·27	5·81	12·5	−14
$PhSO_2Cl$ *	1·48	2·14		6·31	12·2	−15
p-$MeC_6H_4 \cdot SO_2Cl$	1·15	1·73	3·73	5·15	12·7	−14
p-$MeO \cdot C_6H_4 \cdot SO_2Cl$	0·632	1·00	2·09	3·17	13·4	−13

* Data from ref. 2.

Table 3

Slopes (β) and correlation coefficients (r) of the Brønsted plots (Figure 1) for the reaction of pyridines with sulphonyl chlorides

Sulphonyl chloride	σ †	β	r
p-$NO_2 \cdot C_6H_4 \cdot SO_2Cl$	0·78	0·557 ± 0·006 *	0·999
m-$NO_2 \cdot C_6H_4 \cdot SO_2Cl$	0·71	0·545 ± 0·005	0·999
$PhSO_2Cl$	0·00	0·457 ± 0·007	0·999
p-$MeC_6H_4 \cdot SO_2Cl$	−0·17	0·441 ± 0·007	0·999
p-$MeO \cdot C_6H_4 \cdot SO_2Cl$	−0·45	0·406 ± 0·007	0·999

* Standard deviation. † σ Values, from ref. 6, except for *p*-MeO which is from ref. 7.

Table 4

Slopes (ρ), based on the *p*-methoxy, *p*-methyl, and unsubstituted compound, of the Hammett plots in Figure 3

Pyridine	pK_a *	ρ
3,4-Dimethylpyridine	6·46	0·89
4-Methylpyridine	6·02	0·82
3-Methylpyridine	5·68	0·78
Pyridine	5·21	0·69
3-Acetylpyridine	3·18	0·52
4-Cyanopyridine	1·90	0·34
3-Cyanopyridine	1·39	0·30

* In aqueous solution at 25°, from D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965.

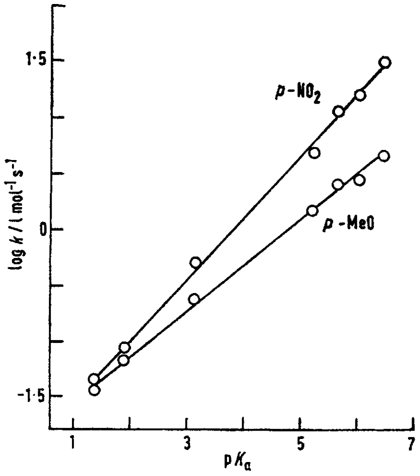

Figure 1 Relationships of log k to pK_a for the reaction of *p*-nitro- and *p*-methoxy-benzenesulphonyl chloride with substituted pyridines in water. From left to right, the points represent pyridines with the substituents 3-CN, 4-CN, 3-Ac, H, 3-Me, 4-Me, and 3,4-Me_2, respectively

acid produced remained unchanged in the presence of the various pyridines.

The rate constants for the reaction of each sulphonyl chloride with the various pyridines are related to the pK_a (Table 4) in water of the corresponding pyridines as exemplified by the Brønsted plots in Figure 1. The slopes, standard deviations, and correlation coefficients for these Brønsted plots, calculated by a least-squares treatment of log k against pK_a, are in Table 3. The slope, β, of the Brønsted plots is linearly related to the σ values [6] (Table 3) for the sulphonyl chloride substituents as shown in Figure 2. The σ values used in this correlation are the ordinary values except that for *p*-MeO (= −0·45) which was determined as a ' best ' value in the reaction of *para*-substituted benzenesulphonyl

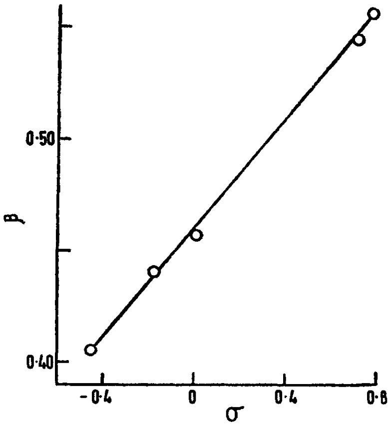

Figure 2 Dependence of the Brønsted slopes, β (Table 3), upon the σ values for the sulphonyl chloride substituents. The line has a slope of 0·122 ± 0·002 (r = 0·999)

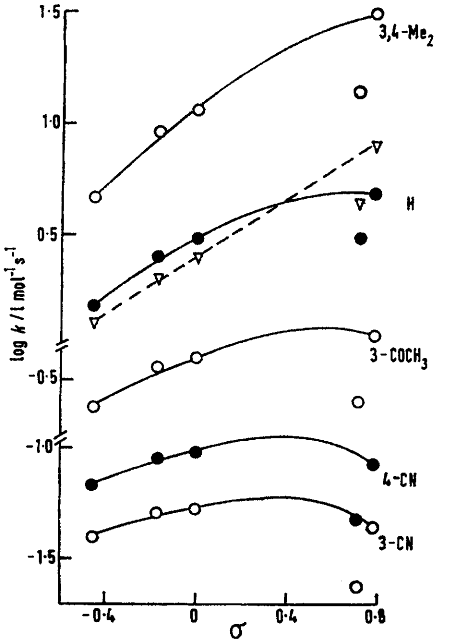

Figure 3 Hammett plots for the reaction of substituted benzenesulphonyl chlorides with pyridines. The sulphonyl chloride substituents are, with increasing σ: *p*-MeO, H, *m*-NO_2, and *p*-NO_2. The broken line represents the reaction of pyridine with the sulphonyl chlorides in methanol at 25 °C; rate constants from ref. 7 except for the *m*-NO_2 compound which was measured to $4 \cdot 47 \times 10^{-2}$ l mol^{-1} s^{-1}

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[6] P. R. Wells, *Chem. Rev.*, 1963, **63**, 171.

chlorides with pyridine in methanol.[7] This value was used here since it gave significantly better correlation than either σ or σ^{+}. A similar σ value for p-MeO was also used in Hammett correlations for the reactions of aromatic sulphonyl chlorides with anilines in methanol.[1] The significance of this σ value, which is about midway between σ^{0} and σ^{+} [6] was attributed to a certain amount of resonance stabilisation of the ground state of p-methoxybenzenesulphonyl chloride.[7]

The rate constants for the reactions of each pyridine with the various sulphonyl chlorides are expected to correlate with σ to give a family of Hammett plots similar to that found in the reaction of sulphonyl chlorides with anilines in methanol.[1] Plots of log k against σ (Table 3) are, however, curved as shown in Figure 3. The plots for 4-methyl- and 3-methyl-pyridine are, for the sake of clarity, not shown. These follow the same pattern, falling between the plots for 3,4-dimethylpyridine and pyridine. If the two nitro-compounds are excluded, a series of ρ values can be obtained. These ρ values, which are given in Table 4, show a linear correlation with the basicity of the pyridines, as shown in Figure 4.

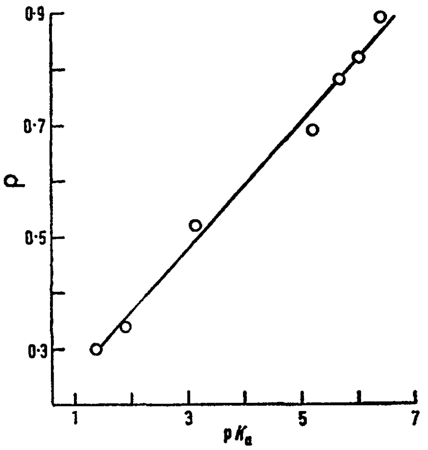
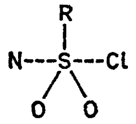


FIGURE 4 Dependence of the Hammett ρ values (Table 4) upon the basicity of the aniline. The line has a slope of 0·114 ± 0·004 (r = 0·996)

DISCUSSION

The pyridine-catalysed hydrolysis of benzenesulphonyl chloride has been shown to occur by a nucleophilic catalysis mechanism.[2] This involved rate-determining formation of a sulphonylpyridinium intermediate which rapidly hydrolyses to sulphonic acid, regenerating the pyridine, as shown in the Scheme. The kinetics, stoicheiometry, activation parameters, and substituent effects are in agreement with such a mechanism. Thus, the second-order rate constants reported here refer to a bimolecular nucleophilic substitution on sulphur. A nucleophilic substitution on tetraco-ordinate sulphur could take place by a concerted one-step process, or by an addition–elimination mechanism involving a five-co-ordinate intermediate.[8,9] Since no evidence for five-co-ordinate intermediates has been found in reactions of sulphonates [10,11] it seems less likely that they should occur in reactions of sulphonyl chlorides, which have a much better leaving group. Also since previous [1] and present results can be consistently explained by a direct S_N2 mechanism, a one-step process is preferred. The transition state for this reaction is most reasonably formulated as a trigonal bipyramidal structure.[10,12,13]



The effect of substituents in nucleophile and substrate is apparent from Table 1, the rate being increased by electron-donating substituents in the pyridine and by electron-attracting substituents in the sulphonyl chloride (except for some reactions of *meta*- and *para*-nitrobenzenesulphonyl chloride discussed below). This is as expected for nucleophilic attack of amines on the sulphur atom.

The relationship of nucleophilicity to basicity is illustrated in Figure 1 for the p-nitro- and p-methoxy-compound. The other sulphonyl chlorides gave similar plots. The slopes β (Table 3) of these plots decrease with increasingly electron-donating ability of the substituents in the sulphonyl chloride. Thus β is correlated with σ as shown in Figure 2. Since β is a measure of the degree of bond formation in the transition state,[14] it can be inferred that N · · · S bond formation decreases progressively from p-nitro- to p-methoxy-benzenesulphonyl chloride, *i.e.* with increasing electron donation to the sulphur atom. This is in agreement with predictions of substituent effects for a simple S_N2 displacement reaction.[15] A similar conclusion was reached for the reaction of anilines with sulphonyl chlorides in methanol.[1] Kinetic solvent isotope effects (k_{H_2O}/k_{D_2O}) for *para*-substituted benzenesulphonyl chlorides are also in agreement with an increase in bond-making for electron-attracting substituents.[16]

The Hammett plots for the reaction of each pyridine with the various sulphonyl chlorides are curved, as shown in Figure 3. The curvature is due to an abnormal low reactivity of the nitro-compounds (see below), and these were therefore excluded in the calculation of the ρ values (Table 4). Although the ρ values are based on

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[7] O. Rogne, *J. Chem. Soc.* (*B*), 1971, 1334.

[8] L. Senatore, E. Ciuffarin, and A. Fava, *J. Amer. Chem. Soc.*, 1970, **92**, 3035.

[9] W. A. Pryor and K. Smith, *J. Amer. Chem. Soc.*, 1970, **92**, 2731.

[10] E. Ciuffarin and A. Fava, *Progr. Phys. Org. Chem.*, 1968, **6**, 81.

[11] E. T. Kaiser, *Accounts Chem. Res.*, 1970, **3**, 145.

[12] R. E. Robertson and B. Rossall, *Canad. J. Chem.*, 1971, **49**, 1441.

[13] R. M. Laird and M. J. Spence, *J. Chem. Soc.* (*B*), 1971, 1434.

[14] J. F. Bunnett, *Ann. Rev. Phys. Chem.*, 1963, **14**, 271.

[15] J. C. Harris and J. L. Kurtz, *J. Amer. Chem. Soc.*, 1970, **92**, 349.

[16] B. Rossall and R. E. Robertson, *Canad. J. Chem.*, 1971, **49**, 1451.

three points only, the relative values are believed to be significant. The ρ values, which decrease with decreasing reactivity of the pyridine, are linearly related to pK_a of the pyridine as shown in Figure 4, in agreement with that found in the reaction of anilines with sulphonyl chlorides.[1] The slope of the plot of ρ against pK_a is, within experimental error, the same as that of the plot of β against σ (Figure 2). This is as expected since the various ρ and β values are inter-related through equation (1) where C is a constant.[17,18] As ρ is related

$$\frac{\rho_1 - \rho_2}{pK_a^1 - pK_a^2} = \frac{\beta_i - \beta_o}{\sigma_i} = C \qquad (1)$$

to the extent of bond breaking relative to bond formation,[19] the conclusion[1] that stretching and charging of the S–Cl bond increases relative to the formation of the N–S bond, *i.e.* the transition state becomes more product-like, with increasingly electron-attracting substituents in the nucleophile, is confirmed. This is also in agreement with predictions of substituent effects on transition state structure for a simple S_N2 displacement reaction.[15]

The ' normal ' behaviour of the ρ values derived from the *p*-methoxy-, *p*-methyl-, and unsubstituted compound agree with the assumption that the reactivity of the nitro-compounds is too low compared with the other compounds. This is similar to the S_N2 hydrolysis in aqueous dioxan of substituted benzenesulphonyl chlorides.[20] Here the hydrolysis of compounds with electron-attracting substituents is progressively inhibited, relative to the unsubstituted compound, as the solvent approach pure water. The explanation[20] for this behaviour is that stretching and charging in the transition state of the S–Cl bond becomes more important relative to the bond-forming process with increasing dielectric constant of the solvent. Since electron-attracting substituents favour bond-making but oppose bond stretching, their effectiveness in lowering the free energy of activation is reduced as the polarity of the medium is increased.

The decreased reactivity of the nitro-compounds compared to the other compounds become more pronounced as the reactivity of the pyridine decreases, and as the solvent changes from methanol to water (Figure 3). This is consistent with the conclusion above that bond breaking increases (and thus become a more important factor) as the reactivity of the nucleophile decreases, and as the solvent become more polar.[20]

The decreased reactivity of the nitrobenzenesulphonyl chlorides is also more pronounced for *meta* than for the *para* compound, opposite to that expected from the σ values. A possible explanation may be that the highly electronegative reaction centre polarises the ring electrons away from the substituents so that the normal resonance of the *p*-nitro-group with the benzene ring is reduced. The electron-withdrawing effect of the nitro-substituents, which is then mainly inductive, is thus not adequately represented by the normal σ value which contain a resonance contribution. A similar explanation has been used in dissociation of pyridinium ions,[21] where 4-(M) substituents showed marked deviation from the Hammett line.

Although the inhibitory effect of the nitro-substituents on the reactivity decreases as the solvent changes from water to methanol, the effect is still apparent for *m*-nitrobenzenesulphonyl chloride (Figure 3). This is in contrast to the reactions of anilines with sulphonyl chlorides in methanol,[1] where no significant deviation of the *m*-nitro-compound occurred. This probably reflects a more dominating influence of the bond-forming process in the reaction of anilines as compared to pyridines, where a considerable charging and stretching of the S–Cl bond is necessary to reach the transition state.

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[17] E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, 1962, **84**, 4319.

[18] W. P. Jencks, *Progr. Phys. Org. Chem.*, 1964, **2**, 63.

[19] C. G. Swain and W. P. Langsdorf, *J. Amer. Chem. Soc.*, 1951, **73**, 2813.

[20] M. L. Tonnet and A. N. Hambly, *Austral. J. Chem.*, 1971, **24**, 703.

[21] A. Fischer, W. J. Galloway, and J. Vaughan, *J. Chem. Soc.*, 1964, 3591.