Nucleophilic Substitution at Two-co-ordinate Sulphur. Effect of the Basicity of the Nucleophile and Structural Effects on the Sulphur Substrate

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The rate of reaction of *p*-nitrobenzenesulphenyl chloride with substituted anilines has been measured in benzene at 20 °C with a stopped-flow spectrophotometer. The kinetic data, plotted in a Brønsted fashion against the pK_a of the conjugated acid of the nucleophile, yield good linear relationships characterized by $\beta = 1{\cdot}250$ in absence of additives and by $\beta = 1{\cdot}256$ in the presence of tetra-n-butylammonium perchlorate. The large effect of the basicity of the nucleophile is interpreted in terms of almost complete bond forming in the transition state and *d*-orbital participation is suggested. In contrast, the effect of *para*-substitution on the sulphur substrate is almost nil.

EVIDENCE for the participation of sulphur *d*-orbitals in nucleophilic substitutions at sulphur has long been sought.[1] However, only recently has some positive evidence been presented.[2,3] For two-co-ordinate sulphur much evidence is against *d*-orbital participation.[1,4-6] The formation of relatively stable ' five-co-ordinate ' sulphur intermediates † along the reaction path has been suggested in the chlorination of sulphenyl chlorides,[2] while for simple nucleophilic displacements with amines there is only one report which presents data suggestive of *d*-orbital participation in the transition state.[7] However, in that case it was not clearly established whether the intermediate which was kinetically detected [8] is an addition complex or the ion pair which can also be postulated.[8,9]

Two of the probes which yielded results in contrast with the idea of the expansion of the sulphur valence shell are the effect of the basicity of the nucleophile [6] and the structural effect on the sulphur substrate.[5] The basicity of the nucleophile has a small effect on the rate for the reaction of oxygen bases with *p*-nitrophenyl triphenylmethanesulphenate.[6] The nucleophilic Brønsted component is small ($\beta = 0{\cdot}25$) and similar to that for nucleophilic substitutions at saturated carbon.[10,11] The small structural effects on the sulphur substrate usually found for displacements at two-co-ordinate sulphur have also been discussed in terms of very little bond-formation in the transition state.[5]

The above two criteria have never been considered together: *i.e.*, for the same type of substrate and the same type of nucleophile in the same solvent. We suggested [6] that a change in these variables could bring about a change in the mechanism and that the likelihood of finding *d*-orbital participation is greatest with neutral amines since the data for anionic nucleophiles are always consistent with a synchronous direct displacement. We now report a study of the effect of the basicity of the nucleophile and that of the substituents on the reaction centre for the reaction of *para*-substituted benzenesulphenyl chlorides with *para*-substituted anilines in benzene.

RESULTS AND DISCUSSION

The rate of reaction of *p*-nitrobenzenesulphenyl chloride with *p*-methoxy-, *p*-methyl-, and *p*-chloroaniline was measured in benzene at 20 °C. In all kinetic runs the concentration of the substrate was *ca.* 2—3 × 10^{-5}M. At low amine concentration autocatalysis was observed owing to the hydrochlorides produced.[9] Thus, under these circumstances, only initial rates were measured. However, when the amine concentration is higher than 10^{-2}M the catalytic effect of salt is negligible

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† Lone pairs are considered as ligands; see footnote 6 in R. Tang and K. Mislou, *J. Amer. Chem. Soc.*, 1969, **91**, 5644.

[1] E. Ciuffarin and A. Fava, ' Progress in Physical Organic Chemistry,' ed. A. Streitwieser, jun., and R. W. Taft, Interscience Publishers, New York, 1968, vol. **6**.

[2] E. N. Givens and H. Kwart, *J. Amer. Chem. Soc.*, 1968, **90**, 378, 386.

[3] (*a*) B. M. Trost, R. LaRochelle, and R. C. Atkins, *J. Amer. Chem. Soc.*, 1969, **91**, 2175; (*b*) B. W. Christiansen and Anders Kjæn, *Chem. Comm.*, 1969, 934; (*c*) S. Oae, M. Yokoyama, M. Kise, and N. Furukawa, *Tetrahedron Letters*, 1968, 4131.

[4] A. Fava and A. Iliceto, *J. Amer. Chem. Soc.*, 1958, **80**, 3478.

[5] J. L. Kice and J. M. Anderson, *J. Org. Chem.*, 1968, **33**, 3331.

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

[7] E. Ciuffarin and G. Guaraldi, *J. Org. Chem.*, 1970, **35**, 2006.

[8] E. Ciuffarin and F. Griselli, *J. Amer. Chem. Soc.*, in the press.

[9] E. Ciuffarin and G. Guaraldi, *J. Amer. Chem. Soc.*, 1969, **91**, 1745.

[10] R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1962, 1062.

[11] R. F. Hudson and G. Loveday, *J. Chem. Soc.*, 1962, 1068.

and linear pseudo-first-order plots are obtained. The kinetic features of these reactions are identical with those discussed for the reaction of *p*-nitrobenzenesulphenyl chloride with aniline.[8] The pseudo-second-order rate coefficient depends on the amine concentration in a non-linear fashion and tends to a limiting value with increasing amine concentration. The data are in Table 1.

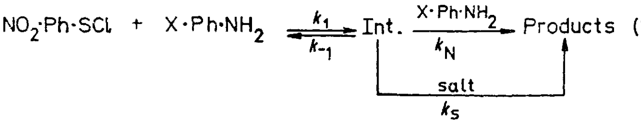
TABLE 1

Pseudo-first-order rate constant (k') and pseudo-second-order rate coefficient ($k_2 = k'/[X\cdot Ph\cdot NH_2]$) for the reaction between *p*-nitrobenzenesulphenyl chloride and substituted anilines in benzene at 20 °C [a]

Substnt.	$10^3[X\cdot Ph\cdot NH_2]$ (M)	$10^2k'$ (sec.$^{-1}$)	k_2 (l. mole^{-1} sec.$^{-1}$)
p-MeO	3·28	18·2	55·3 [b]
p-MeO	7·88	72·5	92·0 [b]
p-MeO	8·50	80·7	95·0 [b]
p-MeO	9·16	92·9	101 [b]
p-MeO	18·3	229	125
p-MeO	27·5	371	135
p-MeO	31·2	436	140
p-MeO	35·8	550	154
p-Me	4·50	8·92	19·8 [b]
p-Me	10·3	38·9	37·8 [b]
p-Me	17·0	76·7	45·0
p-Me	38·3	234	61·1
p-Me	95·7	890	93·0
p-Cl	8·32	0·968	1·16 [b]
p-Cl	9·87	1·23	1·25 [b]
p-Cl	16·6	3·06	1·84
p-Cl	41·6	12·9	3·10
p-Cl	55·2	17·8	3·22
p-Cl	83·2	30·1	3·61

[a] The substrate concentration is *ca.* 2—3 × 10^{-5}M. [b] Initial rate.

In the presence of tetra-n-butylammonium perchlorate ($\geqslant 1{\cdot}5 \times 10^{-4}$M) the second-order rate constant is independent of the amine concentration. Table 2 gives results for the reaction of *p*-nitrobenzenesulphenyl chloride with *p*-methoxy-, *p*-methyl-, *p*-chloro-, and unsubstituted aniline in the presence of Bu_4NClO_4. The above-mentioned kinetic features have been discussed in terms of intermediate formation as expressed by equation (1).[8] Steady-state treatment of mechanism (1) yields equation (2).



$$\begin{tikzcd} NO_2\cdot Ph\cdot SCl + X\cdot Ph\cdot NH_2 \arrow[r, shift left, "k_1"] & Int. \arrow[l, shift left, "k_{-1}"] \arrow[r, "X\cdot Ph\cdot NH_2", "k_N"'] \arrow[r, bend right=60, "salt", "k_s"'] & Products \end{tikzcd} \qquad (1)$$

$$k_2 = \frac{k_1(k_N[X\cdot Ph\cdot NH_2] + k_s[salt]^m)}{k_{-1} + k_N[X\cdot Ph\cdot NH_2] + k_s[salt]^m} \qquad (2)$$

Whilst in the presence of salt, equation (2) simplifies to $k_2 = k_{1,salt}$, in the absence of additives it simplifies to equation (3). [Besides the specific effect shown in equation (1), the salt exerts also a strong medium effect on the rate constants;[8,9] $k_{1,salt}$ is thus larger than k_1 which is measured in absence of additives (see Table 3).]

$$k_2 = \frac{k_1k_N[X\cdot Ph\cdot NH_2]}{k_{-1} + k_N[X\cdot Ph\cdot NH_2]} \qquad (3)$$

TABLE 2

Second-order rate constants for the reaction between *p*-nitrobenzenesulphenyl chloride [a] and substituted anilines in the presence of tetra-n-butylammonium perchlorate [b] in benzene at 20 °C

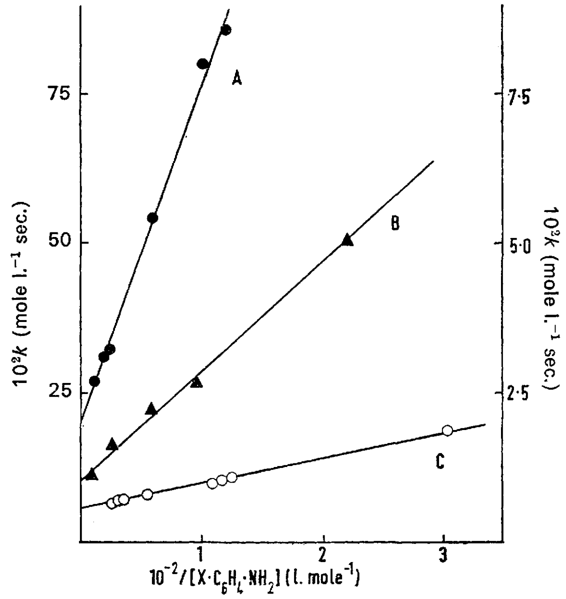
Substnt.	$10^2[X\cdot Ph\cdot NH_2]$ (M)	k_2 (l. mole^{-1} sec.$^{-1}$)
p-MeO	4·23	555
p-Me	4·73	174
None	0·90	54·6
None	2·26	53·8
None	5·66	54·0
p-Cl	1·01	10·2
p-Cl	2·52	10·8
p-Cl	6·30	10·1

[a] The substrate concentration is *ca.* 2—3 × 10^{-5}M. [b] $[Bu_4NClO_4] = 1{\cdot}79 \times 10^{-4}$M.

By reversing equation (3), we obtain equation (4).

$$1/k_2 = 1/k_1 + k_{-1}/k_1k_N \,.\, (1/[X\cdot Ph\cdot NH_2]) \qquad (4)$$

Thus, by plotting $1/k_2$ against $1/[X\cdot Ph\cdot NH_2]$ we can determine k_1 and k_1k_N/k_{-1} in the absence of additives. In the Figure the data of Table 1 are plotted in such fashion and the results are summarized in Table 3. The averages of k_2 measured in the presence of salt ($k_{1,salt}$) and the pK_a of the nucleophiles measured in water[12] are also summarized in Table 3.



Plots of the inverse of the pseudo-second-order rate constants against the inverse of the amine concentration for the reaction of *p*-nitrobenzenesulphenyl chloride with substituted anilines; A, *p*-Cl (left-hand axis); B, *p*-Me (right-hand axis); and C, *p*-MeO (right-hand axis)

The reactivities of the amines are very sensitive to their basicities. The nucleophilic Brønsted exponents, calculated by the least-squares method from Table 3, are 1·250 and 1·256 for k_1 and $k_{1,salt}$ respectively. Even though the number of points is limited to four for each

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[12] D. D. Perrin, 'Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965.

TABLE 3

Summary of the rate constants for the reaction between *p*-nitrobenzenesulphenyl chloride and substituted anilines in benzene at 20 °C

Nucleophile	k_1 (l. mole^{-1} sec.$^{-1}$)	$10^3 k_1 k_N/k_{-1}$, (l.^{2} mole^{-2} sec.$^{-1}$)	$k_{1,\text{salt}}$ [a] (l. mole^{-1} sec.$^{-1}$)	pK_A [b]
p-Chloroaniline	5·00	0·175	10·3	4·00
Aniline	41·43 [c]	1·426 [c]	54·1	4·60
p-Toluidine	95·20	6·12	174	5·07
p-Anisidine	175·5	24·0	555	5·33

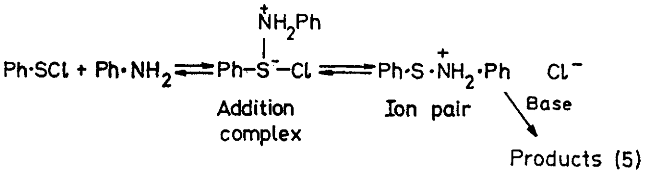
[a] $[Bu_4NClO_4] = 1{\cdot}79 \times 10^{-4}$M. [b] Acid dissociation equilibrium constants of the conjugate acid of the nucleophile measured in water; taken from ref. 12. [c] Data from ref. 8.

plot, the fits are quite good and the error on the slope is very small. Such values are among the largest ever found for Brønsted relationships and lead to the conclusion that bond-forming has proceeded to a large extent in the transition state. It might be objected that pK_a values in water are being compared with reaction rates in benzene where the pK_a values of substituted anilines are not known. However, data show that Brønsted slopes are not largely effected by a change in solvent even though the absolute pK_a values are greatly affected by the solvent.[13a] To this we can add data (to be published) from our own laboratory for the reaction of *p*-nitrophenyl triphenylmethanesulphenate with substituted anilines in water–dioxan where the pK_a's are only slightly different from those measured in pure water. The slope is again quite large, $\beta = 1{\cdot}5$, the difference in substrate and solvent notwithstanding.

The values of the Brønsted slopes given above could hardly be interpreted in terms of concerted displacement at sulphur. They are much higher not only than those found for nucleophilic substitutions at carbon, but also than those measured for nucleophilic substitutions at sulphur with oxygen bases as nucleophiles ($\beta = 0{\cdot}25$).[6] There is no precedent for concerted displacements presenting very high values of the Brønsted exponent. On the contrary, it was suggested that for the aminolysis of *N*-phosphorylated pyridines values as low as 0·2—0·3 might be consistent with a transition state resembling an adduct of the amine to the phosphoryl group.[14]

There seems to be no way to interpret the data for reactions of sulphenyl chlorides with anilines other than that of considering bond-forming as very advanced in the transition state, unless one wants to remove any meaning from the nucleophilic Brønsted exponent, which is largely used as a mechanistic probe even though it has relative and not absolute significance.

Large bond-forming suggests *d*-orbital participation and this is in agreement with recent data relative to the leaving group mobilities (element effect [15]).[7] (Consistency with 3*d*-orbital participation does not exclude other models which might include 4*s* and 4*p* orbitals.[16]) One might conclude that the intermediate shown in equation (1) is an addition complex and not the ion pair which can also be suggested [8,9] because presumably an unstable intermediate should be similar in energy and structure to the transition state. However, a mechanism such as that shown by equation (5) is also consistent with the data since the addition complex intermediate could not be kinetically detected.



The structural effect on the sulphur substrate has also been investigated by measuring the rate of reaction of *p*-nitrobenzene-, *p*-chlorobenzene-, benzene-, and *p*-methylbenzene-sulphenyl chloride with aniline in benzene at 20 °C in the presence of Bu_4NClO_4. The general behaviour is similar to that described for the *p*-nitro-derivative. However, the spectral characteristics of these substrates, compared with those of the products, are not very favourable for accurate kinetic measurements with a stopped-flow apparatus except for the *p*-nitro-derivative. The lowest convenient substrate concentration is *ca.* 10^{-4}M. At such concentration the reactions are strongly autocatalytic and thus the data are affected by large errors. Even though we could not collect results worth reporting, all substrates seemed to react at about the same rate at any given amine concentration. Since, however, in the presence of added Bu_4NClO_4 all reactions follow good first-order kinetics, we measured (Table 4) the values of k_1 in the presence of salt. The differences in rate are very small and there is no definite trend with the σ value of the substituent. These results are consistent with all the structural effects so far measured for nucleophilic substitutions at dico-ordinated sulphur. They have always been found to be small. Small ρ values or irregular trends have been interpreted in terms of concerted diplacement. On

TABLE 4

Second-order rate constants for the reaction between substituted benzenesulphenyl chlorides and aniline in the presence of tetra-n-butylammonium perchlorate [a] in benzene at 20 °C

Substituent	10^2[Aniline] (M)	$k_{1,\text{ salt}}$ (l. mole^{-1} sec.$^{-1}$)
p-Me [b]	4·45	50·4
p-Me [b]	8·69	48·3
None [b]	4·45	40·8
None [b]	8·69	39·9
p-Cl [b]	4·45	44·0
p-Cl [b]	8·69	44·8
p-NO_2 [c]	4·45	47·5
p-NO_2 [c]	8·69	48·7

[a] Concn. $= 1{\cdot}5 \times 10^{-4}$M. [b] Concn. = *ca.* 1×10^{-4}M. [c] Concn. = *ca.* 2×10^{-5}M.

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[13] J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' John Wiley and Sons, Inc., New York, 1963, (*a*) p. 242; (*b*) p. 325.

[14] G. W. Jameson and J. M. Lawlor, *J. Chem. Soc.* (*B*), 1970, 53.

[15] J. F. Bunnett, E. W. Garbish, jun., and K. M. Pruitt, *J. Amer. Chem. Soc.*, 1957, **79**, 385.

[16] (*a*) P. Palmieri and C. Zauli, *J. Chem. Soc.* (*A*), 1967, 813; (*b*) F. Bernardi and C. Zauli, *ibid.*, 1968, 2633.

the other hand, we have shown above that bond-forming seems to be much more advanced than bond-fission in the transition state and this should imply that sulphur is more negative in the transition state than in the starting material, suggesting that electron-withdrawing substituents should greatly increase the rate of reaction. It has been suggested that the negative charge on sulphur might not need to be dispersed by electron-withdrawing groups in the organic moiety since it can be very easily accommodated by low-lying *d*-orbitals [1] or that there is little conjugation between sulphur and the benzene ring.[17] It might also be possible that the structural change in the organic moiety fails to effect the reaction rate because the reactions have been studied at or near the isokinetic temperature.[13b]

EXPERIMENTAL

Materials.—4-Nitrobenzenesulphenyl chloride, m.p. 50—51 °C, 4-chlorobenzenesulphenyl chloride, b.p. 62—63°/0·4 mm., 84—85°/2 mm., 4-methylbenzenesulphenyl chloride, b.p. 68—70°/2 mm., and benzenesulphenyl chloride, b.p. 48—50°/0·8 mm., were prepared from the corresponding disulphides.[17] Commercial anilines were twice distilled from potassium hydroxide pellets or twice sublimed under vacuum. Benzene was refluxed over Na–K alloy and fractionated. The preparation of tetra-n-butylammonium perchlorate was described.[9]

Products.—The sulphenamides were prepared by the following general procedure which is similar to that for *N*-phenyl-*p*-nitrobenzenesulphenamide.[8] A solution of the aniline in dry ether was slowly added (5% excess) with stirring to an ice-cold solution of the sulphenyl chloride (*ca.* 1 g.) in dry ether. The mixture was washed several times with water and dried (Na_2SO_4). Evaporation of the solvent yielded white solids except for the *p*-nitro-derivatives which yielded deep yellow oils. The following solids were twice crystallized from the minimum of methylene dichloride–light petroleum at −15 °C; the oils were crystallized in the same way, but pure products are more difficult to obtain: p-*chloro*-N-*phenylbenzenesulphenamide*, m.p. 83—84 °C (Found: C, 61·55; H, 3·8; Cl, 15·1; N, 5·8; S, 13·4. $C_{12}H_{10}ClNS$ requires C, 61·1; H, 4·3; Cl, 15·0; N, 5·9; S, 13·6%); p-*methyl*-N-*phenylbenzenesulphenamide*, m.p. 80—81 °C (Found: C, 73·1; H, 5·6; N, 6·35; S, 14·75. $C_{13}H_{13}NS$ requires C, 72·5; H, 6·1; N, 6·5; S, 14·9%); N-*phenylbenzenesulphenamide*, m.p. 56—57 °C (Found: C, 71·5; H, 5·2; N, 6·75; S, 15·9. $C_{12}H_{11}NS$ requires C, 71·6; H, 5·5; N, 7·0; S, 15·6%); N-p-*chlorophenyl*-p-*nitrobenzenesulphenamide*, m.p. 102—103 °C (Found: C, 51·0; H, 3·15; Cl, 12·95; N, 10·0; S, 11·1. $C_{12}H_9ClN_2O_2S$ requires C, 51·3; H, 3·2; Cl, 12·6; N, 10·0; S, 11·4%); N-p-*methylphenyl*-p-*nitrobenzenesulphenamide*, m.p. 98—100 °C (Found: C, 60·7; H, 4·4; N, 10·0; S, 11·7. $C_{13}H_{12}N_2O_2S$ requires C, 60·0; H, 4·6; N, 10·8; S, 12·3%); and *N*-*p*-methoxyphenyl-*p*-nitrobenzenesulphenamide, which could not be purified and decomposed when heated.

Kinetics.—The rate of reaction was measured with a Durrum stopped-flow spectrophotometer at 350 mμ for *p*-nitrobenzenesulphenyl chloride and at 390—410 mμ for the other substrates. A Unicam SP 800 spectrophotometer was used to check the experimental infinity points against the values calculated from the extinction coefficients of the products.

All reagents were kept in a desiccator at 0 °C in the dark.

Owing to the high lability of the sulphenyl chlorides in the presence of traces of moisture, particular care was taken in the preparation of solutions. Benzene was distilled immediately before use and the solutions were prepared in a dry-box and used immediately.

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[17] L. Di Nunno, G. Modena, and G. Scorrano, *Ricerca sci.*, 1966, **36**, 825.