Nucleophilic Substitution at Sulphonyl Sulphur. Part 1. Reactivity of Thiophen-2-sulphonyl Halides in Water and Methanol–Acetonitrile

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The reaction kinetics of substituted thiophen-2-sulphonyl chlorides and fluorides (5-OMe, 5-Me, H, 5-Cl, 4-NO_2, 5-NO_2) with anionic and neutral nucleophiles were studied in water at 25 °C. For the reactions of chlorides with H_2O, AcO^-, and N_3^- and for the hydrolysis of fluorides U shaped Hammett plots were observed. For the reaction of sulphonyl chlorides with aniline, pyridine, imidazole, and OH^- an approximately linear Hammett correlation is found. Common chloride ion effects on the hydrolysis rate constants appear to be absent. Nucleophilic substitution reactions of substituted thiophen-2-sulphonyl chlorides were also studied in MeOH–MeCN, where the Hammett equation is obeyed. The data appear consistent with an S_N2-type mechanism which can shift toward an S_N1 or an S_AN process depending on the nucleophile, on the ring substituent, and on the leaving group ability. The application of the More O'Ferrall and Thornton approaches for the prediction of substituent effects on the transition state structure seems to support the above interpretation.

SEVERAL studies on the hydrolysis of benzenesulphonyl chlorides have been made both in water and in mixed aqueous solvents.[1-7] Substituent effects,[8-10] the effect of co-solvents,[11] the volume of activation, the heat capacity of activation,[12] solvent isotope effects,[13] and nucleophilic catalysis [14-16] have been examined. An interpretation of the reaction mechanism differing from those previously accepted has been given [4,5,17,18] and curvature of the Hammett plot claimed.[8,9] Recently, a study of this reaction for a large number of substituted benzenesulphonyl chlorides was reported.[19]

Despite this work in the benzene series, hydrolysis reactions of thiophensulphonyl chlorides have not been studied.

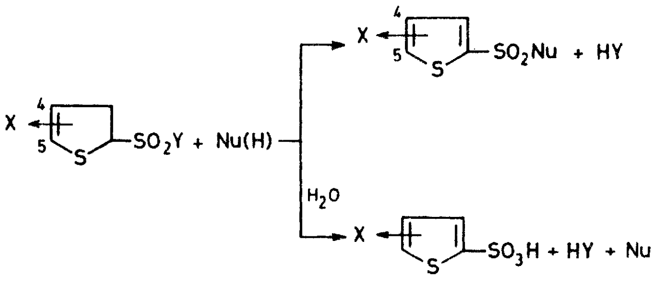
In previous papers we have studied the reactions of heterocyclic sulphonyl halides extensively and postulated an S_AN mechanism (a two-step addition–elimination leading to a metastable intermediate along the reaction co-ordinate) in which the rate-determining step involved attack of a nucleophile on the sulphonyl group or S–halogen bond-breaking depending on the substrate and on the solvent.[20-24]

The nucleophilic reactivity order, studied by means of the Brönsted, Ritchie, and Edwards equations, was found to depend mainly on basicity, although there may well be some dependence on polarizability and solvation.[24] To extend our investigation to pure water as solvent and compare the behaviour of thiophen with that of benzene, we report here a kinetic study of the hydrolysis of substituted thiophen-2-sulphonyl chlorides and the rate constants at various temperatures of the reactions with aniline and *p*-anisidine in MeOH–MeCN.

Moreover, reactivity data for thiophensulphonyl fluorides are very scarce,[20] owing to the lack of a convenient method for the synthesis of these derivatives. A ready conversion of the more readily available sulphonyl chlorides into the corresponding fluorides under phase-transfer catalysis conditions has recently been reported.[25] The application of this crown ether catalysed fluorine–chlorine exchange reaction provided a suitable route for the preparation of thiophen-2-sulphonyl fluorides under very mild conditions. We also report here the synthesis of substituted thiophen-2-sulphonyl fluorides and the rate constants for their reactions with nucleophiles in water.

RESULTS

The reaction kinetics of thiophen-2-sulphonyl halides in water and MeOH–MeCN in the presence of excess of nucleophile were followed by potentiometric acid–base titrations (Scheme). Table 1 reports the rates of hydrolysis of substituted thiophen-2-sulphonyl chlorides and fluorides in water, together with the chlorine–fluorine relative reactivities, and Table 2 the common ion effect on the hydrolysis rate constants of substituted thiophen-2-sulphonyl chlorides by NaCl.



SCHEME X = 5-OMe, 5-Me, H, 5-Cl, 5-NO_2, 4-NO_2; Y = Cl; solvent = water; nu(H) = aniline, pyridine, imidazole, water, AcO^-, NO_2^-, N_3^-, OH^-

X = H; Y = F; solvent = water; Nu(H) = aniline, *p*-anisidine, imidazole, n-butylamine, morpholine, piperidine

X = 5-Me, H, 5-Cl, 5-NO_2, 4-NO_2; Y = F; solvent = water; Nu(H) = water

X = 5-OMe, 5-Me, H, 5-Cl, 5-NO_2; Y = Cl; solvent = MeOH–MeCN; Nu(H) = aniline, *p*-anisidine

The Hammett plot (Figure 1) is a curve with an upward concavity, the minimum being the *p*-Cl derivative for chlorides and the unsubstituted compound for fluorides.

Differently from the chlorides, for which a 5-NO_2 : 5-Me ratio of 0.25 is observed, sulphonyl fluorides show a 5-NO_2 : 5-Me ratio of 17 and a larger dependence on substituent effects.

In water all the nucleophiles yield sulphonic acids by nucleophilic catalysis, except N_3^-, aniline, and imidazole for which the corresponding substitution products are obtained, in analogy to the observations for the benzene series.[15] The reaction was first order in the sulphonyl halides and also first order in the nucleophile. The overall second-order rate constants were obtained from a plot of $k_{obs.}$ *versus* nucleophile concentration. The uncatalysed hydrolysis was in all cases negligible, as indicated by the zero intercept of this plot. k_2 Values are collected in Table 3.

TABLE 1

Rate constants for the neutral hydrolysis of substituted thiophen-2-sulphonyl halides in water at 25 °C

Substituent	Chloride $10^3\ k_{obs.}{}^a/s^{-1}$	Fluoride $10^7\ k_{obs.}{}^a/s^{-1}$	k_{Cl}/k_F
5-OMe	3.00		
5-Me	1.27	6.169	2 054
H	0.478 [b]	1.754	2 723
5-Cl	0.164	4.515	362
5-NO_2	0.301	104.5	29
4-NO_2	0.270	30.45	89

[a] $k_{obs.}$ Values accurate to ±6% (90% confidence limit); k_2 value can be obtained by dividing $k_{obs.}$ by 55.5. [b] From ref. 24.

The reactions of sulphonyl chlorides with aniline, pyridine, imidazole, and NO_2^- show almost linear Hammett plots with positive ρ values (Figure 2), while for the reactions with H_2O, AcO^-, and N_3^- U shaped Hammett plots with a minimum value for 5-Cl derivative are observed (Figure 1).

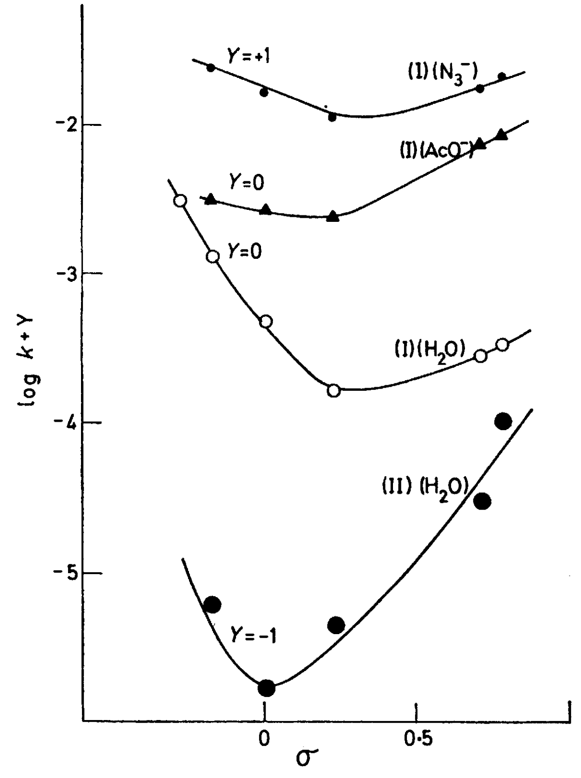


FIGURE 1 Hammett plots for the reactions of substituted thiophen-2-sulphonyl chlorides (I) and fluorides (II) with nucleophiles in water at 25 °C; N_3^-, AcO^- ($k = k_2$), H_2O ($k = k_{obs.}$)

The logarithms of the rate constants of thiophen-2-sulphonyl fluoride are linearly correlated with the pK_a of the nucleophiles in water (Figure 3) over a range of 8 log k units and 13 pK_a units.

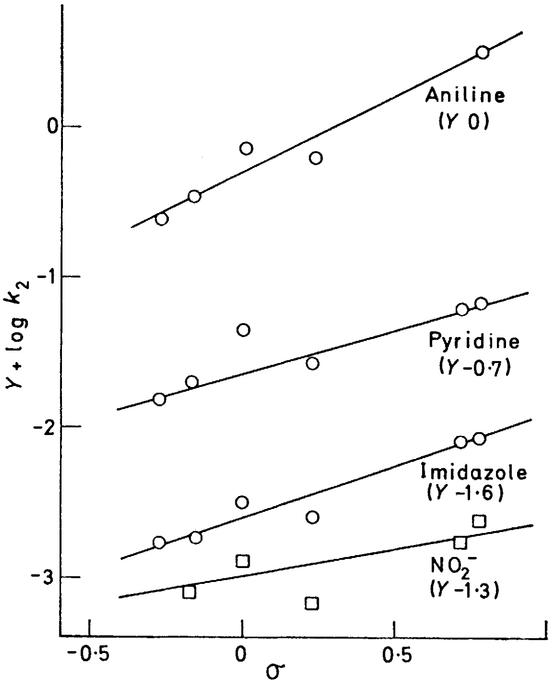


FIGURE 2 Hammett plots for the reactions of substituted thiophen-2-sulphonyl chlorides with nucleophiles in water at 25 °C

Second-order rate constants for the reactions of thiophen-2-sulphonyl chlorides with aniline and *p*-anisidine in

TABLE 2

Common-ion effect on hydrolysis rate constants of substituted thiophen-2-sulphonyl chlorides by NaCl in water at 25 °C

Substituent	$10^3\ k_{obs.}/s^{-1}\ {}^a$	10[NaCl]/M
CH_3	1.27	0.0000
	1.21	0.04081
	1.27	0.3908
	1.27	0.6035
	1.23	1.7840
	1.18	2.6791
	1.07	3.6050
	1.09	4.4165
H	0.478	0.0000
	0.503	0.04226
	0.507	0.2135
	0.498	0.8875
	0.501	4.3633
	0.503	5.3303
	0.505	9.0602
	0.497	1.2074
Cl	0.164	0.0000
	0.167	0.1991
	0.186	0.4374
	0.177	0.5406
NO_2	0.301	0.0000
	0.292	0.01626
	0.290	0.4473
	0.295	0.6333
	0.294	1.7392
	0.280	1.9037
	0.274	5 3486

[a] Values of $k_{obs.}$ are accurate to ±6% (90% confidence limit).

MeOH–MeCN mixtures are reported in Tables 4 and 5, together with the activation parameters.

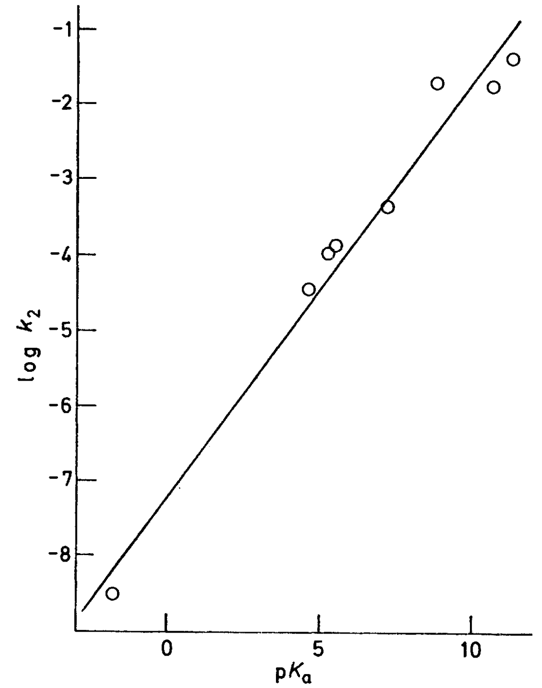


FIGURE 3 Brönsted plot for the reaction of thiophen-2-sulphonyl fluoride with nucleophiles in water. pK_a from A. Albert and E. P. Serjeant, ' Ionization Constants of Acids and Bases ', Wiley, New York, 1962, p. 144.

DISCUSSION

Hammett Correlations.—Hammett plots (Figures 1 and 2) give an indication that continuous modification of the nature of the transition state takes place as both the nucleophile and the substituents are changed.

For the reaction of thiophen-2-sulphonyl chlorides with aniline, pyridine, imidazole, and NO_2^- the Hammett equation is not accurately obeyed (Figure 2). A treatment using σ values gives the following results: r (correlation coefficient) 0.97, ρ (slope) 0.98; r 0.85, ρ 0.53; r 0.97, ρ 0.64; and r 0.73, ρ 0.43, respectively, for aniline, pyridine, imidazole, and NO_2^-. The positive ρ values are indicative of nucleophilic substitution with bond-making more advanced than bond-breaking in the transition state. The failure to obtain good correlations can be ascribed to the possibility of the substituent changing the transition state structure considerably.

TABLE 3

Second-order rate constants k_2 for the reactions of substituted thiophen-2-sulphonyl halides with nucleophiles in water at 25 °C

		$10^3 k_2$[a]/l mol^{-1}s^{-1} nucleophile						
Substituent	Halide	AcO^-	NO_2^-	Aniline	Pyridine	Imidazole	N_3^-	OH^-
5-OCH_3	Cl			246	75.9	68.0		
5-CH_3	Cl	3.00	16.2	340	98.9	73.6	235	2 820
H	Cl	2.55 [b]	25.9 [b]	709 [b]	220 [b]	125 [b]	163 [b]	5 280
5-Cl	Cl	2.22	13.3	613	133	99.6	110	12 400
5-NO_2	Cl	7.76	48.0	3 079	331	341	193	80 500
4-NO_2	Cl	6.76	34.7		306	332	162	
H	F [c]			0.0350	0.107	0.469		
k_{Cl}/k_F				20 300	2 056	74		

[a] Values of k_2 are accurate to $\pm 6\%$ (90% confidence limit). [b] Ref. 24. [c] Nucleophile, $10^3 k_2$, k_{Cl}/k_F: *p*-anisidine, 0.321, 7 220; n-butylamine, 17.9, —; morpholine, 20.3, —; piperidine, 40.8, —.

Poor Hammett correlations seem to be feature of hydrolysis reactions of the sulphonyl group, because on changing the substituents or the solvents a change in the transition state can occur. In fact for the hydrolysis of benzenesulphonyl chlorides an inversion of effect of substituents on the rate as the solvent became poorer in water has been observed.[2] Hambly and his coworkers [10] found a region of solvent composition in which all the substituents other than *p*-NO_2 produce similar hydrolysis rates. Their interpretation, also based on the magnitudes of $\Delta C_p^\ddagger$ and $\Delta V^\ddagger$, is that in pure water the transition state has appreciable stretching of and production of a charge on the S–Cl bond, while in solvent mixtures of low dielectric constant bond-making will be dominant. This interpretation seems to be supported by our data, as a very good Hammett correlation with a high positive ρ value is found for the reactions of aniline with thiophensulphonyl chlorides in methanol,[23,26] while in water the correlation is not so good and the slope is smaller. This could be ascribed to better solvation of the leaving chlorine group by water compared with methanol.

The logarithms of the rate constants for the reaction of thiophen-2-sulphonyl chlorides with nucleophiles like H_2O, AcO^-, and N_3^- and thiophen-2-sulphonyl fluorides with H_2O show U shaped Hammett plots (Figure 1), which could indicate a changeover of mechanism. The lack of a common-ion effect on the hydrolysis rate constants by NaCl (Table 2) seems to rule out the possibility of an S_N1 mechanism and a more plausible hypothesis calls for an S_N2 mechanism leading to both ' loose ' and ' tight ' S_N2 type transition states depending on the substituent. For electron-donating groups a loose transition state would be energetically favoured in water, which has both high ionizing power and provides strong electrophilic assistance to the leaving group by hydrogen-bonding.*

On the other hand a tight transition state in which

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* In a previous study of solvent effects we advanced the possibility of electrophilic solvation of the leaving group at the transition state.[23,24] More recently, Kamlet and Taft [27] applied their solvatochromic comparison method to our data, claiming a ' push–pull ' mechanism where the lower the nucleophilicity of the attacking group, the greater the importance of electrophilic assistance to the leaving group by the protic solvent.

bond-making is advanced with respect to bond-breaking would be expected for electron-attracting groups. This interpretation is supported by the selectivity order (which is expressed as k_{Nu}/k_{H_2O} and can be calculated from values in Tables 1 and 3) which increases from 5-OMe to 5-NO_2 as expected for a more covalent structure in a tight transition state.

TABLE 4

Second-order rate constants for the reaction of thiophen-2-sulphonyl chloride with $XC_6H_4NH_2$ in MeOH–MeCN and activation parameters

MeOH [a]	X	10^3k_2 [b]/l mol^{-1} s^{-1}				k_2(p-OMe) [c] / k_2 (H)	$\Delta H^‡_{298}$ [d]/kcal mol^{-1}	$-\Delta S^‡_{298}$ [d]/cal mol^{-1} K^{-1}
		15°	25°	35°	45°			
1.0	H [e]	2.62	5.62	11.0	20.8	5.8	11.9 ± 0.40	28.7 ± 1.3
	p-OMe [e]	19.0	32.8	56.5	87.3		8.7 ± 0.34	36.0 ± 1.1
0.96	H	3.21	5.12	9.52	18.2	7.5	10.0 ± 2.2	35.4 ± 7.3
	p-OMe	21.3	38.3 [f]	75.2	121		10.1 ± 1.1	30.9 ± 3.7
0.88	H	3.41	5.70	10.1	17.6	8.1	9.4 ± 1.0	37.2 ± 3.4
	p-OMe	22.8	46.0 [f]	79.0	126		9.8 ± 1.4	32.0 ± 4.7
0.56	H	2.94	5.41	8.95	14.7	7.3	9.1 ± 0.5	38.3 ± 1.7
	p-OMe	22.8	39.6 [f]	67.2	106		8.8 ± 0.3	35.5 ± 1.1
0.19	H	1.40	2.45	3.88	5.59	11.5	7.8 ± 1.1	44.3 ± 3.7
	p-OMe	15.9	28.2 [f]	42.3	62.9		7.7 ± 1.1	39.9 ± 3.8
0.0	H [g]	—	1.20	1.93	2.60	13.7	6.9 ± 2.4	48.9 ± 7.9
	p-OMe	9.39	16.4 [f]	25.1	35.5		7.5 ± 1.3	41.7 ± 4.4

[a] Molar fraction. [b] Measured under pseudo-first-order conditions from at least three kinetic runs at different nucleophile concentrations, accurate to ±6% (90% confidence limits). [c] Second-order rate constants ratio at 25 °C. The ratio in water is equal to 3.3 (see Table 1 in ref. 24). [d] 90% confidence limit. [e] Ref. 21. [f] Ref. 23. [g] A. Arcoria, E. Maccarone, G. A. Tomaselli, R. Cali, and S. Gurrieri, *J. Heterocyclic Chem.*, 1975, **12**, 333.

The Hammett ρ value calculated for the H, 5-Cl, and 5-NO_2 substituted sulphonyl fluoride (ρ 2.31, r 0.998) * is very large and comparable with that found for the alkaline hydrolysis of benzenesulphonyl fluorides (ρ 2.78).[29] Such a large value in substitution at sulphonyl sulphur was claimed to be indicative of an S_AN mechanism, with appreciable participation of the empty d orbital of the sulphur atom in the bond-making process.[29]

TABLE 5

Second-order rate constants k_2 for the reaction of 5-substituted thiophen-2-sulphonyl chlorides with aniline at 25 °C in MeOH–MeCN.

MeOH [b]	10^3k_2 [a]/l mol^{-1} s^{-1} substituent					ρ
	OCH_3	CH_3	H	Cl	NO_2	
1.0	4.80	5.05 [c]	5.62 [c]	10.98 [c]	167.1 [c]	1.06
0.96	5.46	6.13	5.12 [d]	10.08	441.8	1.36
0.88	3.84	5.55	5.70 [d]	14.19	360.2	1.30
0.66		4.22	5.59	10.12	583.2	1.54
0.41		4.01	4.20	7.82	335.1	1.38
0.19	1.60	2.22	2.45 [d]	4.31	186.1	1.36
0.0	0.758	0.899 [e]	1.20 [e]	1.81 [e]	14.8 [e]	0.88

[a] Measured under pseudo-first-order conditions, accurate to ±6% (90% confidence limit). [b] Molar fraction. [c] From ref. 26. [d] From Table 4. [e] From ref. 23.

Lyate Ion Effects.—The effect of added sodium hydroxide on the rates of hydrolysis of thiophensulphonyl chlorides is to enhance the rates strongly (Table 3). Differently from the previous nucleophiles, OH^- gives a good linear Hammett plot (r 0.999 7, ρ 1.53) which indicates that in this case bond-making predominates. Our results are in agreement with those obtained previously for the hydrolysis of benzenesulphonyl chlorides by Rogne,[9] who found a balanced effect between bond-making and bond-breaking in the transition state for neutral hydrolysis, but dominant bond formation for alkaline hydrolysis.

Brönsted Relationships.—Previously for the reactions of thiophen-2-sulphonyl chloride with nucleophiles in water we found a good Brönsted relationship with a β_E value of 0.68.[24] In the present work we studied the reactions of thiophen-2-sulphonyl chlorides with fewer nucleophiles and the number of points does not allow suitable statistical correlations. However, even if the results are less accurate in this case, the β_E values obtained (Table 6) give a rough indication that the sensitivity to the nucleophile change increases with the electron-attracting character of the substituent, according to the previous mechanistic interpretation. However, if the log k values for the reactions of each sulphonyl chloride with the nucleophiles are plotted, according to Hudson and Klopman,[30] against the log k values for the corresponding reactions of the unsubstituted thiophensulphonyl chloride with the same nucleophiles, a series with good correlation is obtained. The slopes of such correlations (ρ_N, Table 6) give the

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* The analogous values for sulphonyl chlorides hydrolysis are ρ 0.46, r 0.998. McLennan[28] supported the use of ρ values as indicative of transition-state structure variations, if allowance is made for the different efficiency of charge transmission for different reaction series. The comparison between the ρ value of sulphonyl fluorides and that of sulphonyl chlorides is meaningful and would indicate a structure with more advanced bond-making in the former case.

sensitivity of the reaction rate to changes in charge distribution in the nucleophile (as do β_E values). Also in this case, in which it is possible to consider all the nucleophiles, the ρ_N pattern is analogous to the β_E pattern.

The Brönsted value for the reaction of thiophen-2-sulphonyl fluoride with nucleophiles in water (β_N 0.54, see Figure 3) is comparable with that reported for the reactions of thiophen-2-sulphonyl chlorides with aniline in methanol.[21]

If the log *k* values for the reactions of substituted sulphonyl chlorides with water are plotted against the log *k* values for the corresponding reactions of thiophensulphonyl fluorides, we obtain β_L values (Table 6) which indicate decreasing sensitivity to the leaving group effect upon decreasing the electron-donor character of the substituent.

Leaving Group Mobilities.—Fluorides are hydrolysed more slowly than the corresponding chlorides and the relative reactivity ratios are strongly affected by the substituent in the aromatic framework. The k_{Cl}/k_F ratios show a regular trend in decreasing with increasing electron-withdrawing character of the substituent.

The data for the hydrolysis of sulphonyl chlorides and fluorides are consistent with an S_N2 type mechanism leading to a range of transition states with different degrees of bond-making and bond-breaking depending on the substituent. For electron-releasing substituents bond-breaking would be more advanced than bond formation and a high k_{Cl}/k_F ratio would be expected, owing to the larger energy required for the cleavage of the S–F bond with respect to S–Cl. For electron-withdrawing substituents bond-making would be dominant and small k_{Cl}/k_F values would be expected. Experimental results confirm this prediction (Table 1). However, the possibility that an intermediate is formed along the reaction co-ordinate, according to an *S*–N mechanism, especially for powerful electron-attracting substituents such as 5-NO_2, cannot be completely ruled out in this case.

The relative leaving-group mobilities in the neutral and alkaline hydrolysis of benzenesulphonyl chloride and fluoride, have been related by Swain and Scott[31] to the degree of bond-breaking, which is higher on increasing the k_{Cl}/k_F ratio. According to this interpretation, the decreasing k_{Cl}/k_F ratios on increasing the basicity of the nucleophile in thiophen-2-sulphonyl fluoride reactions (Table 3) indicate a variable transition state structure with decreasing S–F bond cleavage along the series.

Reactions of Substituted Thiophen-2-sulphonyl Chlorides in Mixed Solvents.—Second-order rate constants for the reactions of thiophen-2-sulphonyl chlorides with aniline and *p*-anisidine in CH_3OH–CH_3CN are reported in Tables 4 and 5 together with the activation parameters. An inversion of the substituent effect with respect to water is observed in CH_3OH, CH_3CN, and in mixed solvents. These findings suggest the possibility that bond-making is the predominant process in these solvents, owing to the lower electrophilic assistance to the leaving group by hydrogen bonding. The increasing ratio $k_{p\text{-anisidine}}/k_{aniline}$ in the solvent series H_2O, CH_3OH, CH_3OH–CH_3CN, CH_3CN (Table 4) seem to support the idea of an increasing predominance of bond-making leading to a tighter transition state along the series.

More O'Ferrall Plot.—More O'Ferrall diagrams[32] have been recently used to examine the nucleophilic substitution reactions of benzyl halides.[33,34] The data for sulphonyl halides seem to have some affinity with these reactions.

The predictions which can be made by applying this kind of approach are related to the placement of the transition state along the reaction co-ordinate. Supposing that in the sulphonyl chlorides hydrolysis the transition state lies at the midway point A on the S_N2 path when the ring substituent is 5-Cl (which represents a minimum in the Hammett plot), we can test the hypothesis by analysing substituent effects. Substituents with a larger electron-donor character than 5-Cl will have a stabilizing effect on the $\overset{+}{N}\ \overset{-}{S}\ \overset{-}{X}$ structure (upper left corner, Figure 4).

TABLE 6

β_E and ρ_N values for the reactions of substituted thiophensulphonyl chlorides with nucleophiles in H_2O at 25 °C and β_L values for the leaving group for the neutral hydrolysis of substituted thiophensulphonyl halides in H_2O at 25 °C

	Substituent					
	5-OCH_3	5-CH_3	H	5-Cl	4-NO_2	5-NO_2
β_E	0.50[a]	0.59[b]	0.68[b]	0.73[b]	0.70[c]	0.75[b]
γ[d]	0.98	0.98	0.98	0.98	0.998	0.97
ρ_N[e]	0.73	0.87	1.00	1.10	1.08	1.34
γ[d]	0.999	0.994		0.997	0.999	0.991
β_L[f]		−0.36	−0.38	−0.28	−0.21	−0.16

[a] Obtained with $C_6H_5NH_2$, C_5H_5N, and H_2O as nucleophiles. [b] Obtained with $C_6H_5N_2H$, C_5H_5N, NO_2^-, N_3^-, and H_2O as nucleophiles. [c] Obtained with C_5H_5N, NO_2^-, N_3^-, and H_2O as nucleophiles. [d] Correlation coefficient. [e] See text. For the nucleophiles we used the following pK_a values:[24] $C_6H_5NH_2$, 4.58; C_5H_5N, 5.23; NO_2^-, 3.37; N_3^-, 4.74; AcO^-, 4.75; imidazole, 7.10; OH^-, 15.7; H_2O, −1.74. [f] Obtained from the relationship $\log[k(XC_4H_2S\text{–}SO_2Cl)/k(XC_4H_2S\text{–}SO_2F)] = \beta_L \Delta pK_a$ where $\Delta pK_a = pK_{aCl}\ (-5.7) - pK_{aF}\ (3.45)$.

The corresponding transition state B will lie in a reaction co-ordinate lying between S_N1 and S_N2 paths and will involve more S–X cleavage, less N–S formation, more positive charge development on S, and more negative charge development on X. Consequently for electron-donating ring substituents high k_{Cl}/k_F ratios are expected together with less selectivity, as observed from the k_{Cl}/k_F ratios in Table 1 and from the ratios k_{AcO^-}/k_{H_2O} or $k_{NH_3^-}/k_{H_2O}$, taken as selectivity measurements, which can be calculated from the data in Table 3.

On the other hand an electron-attracting substituent will stabilize the structure $\overset{+}{N}\text{–}S\text{–}\overset{-}{X}$ (lower right corner, Figure 4). The new transition state C will be tighter with increased bond formation and reduced bond cleavage with respect to A. This prediction is in agreement with the increasing sensitivity to the entering group basicity (increasing β_E or ρ_N values, Table 6) or with the decreasing sensitivity to the leaving group effect (decreasing β_L values, Table 6) on increasing the electron-attracting character of the substituent.

Both an early, D, and a late, F, transition state would not be consistent with the experimental results. In fact, in this case the upper left corner of Figure 4 is essentially parallel to the reaction co-ordinate (Hammond effect) and a more electron-releasing group than 5-Cl will affect the position of the transition state little, because part of the motion is helped (allowing X to depart more easily) and part is hindered (making N less eager to bond).

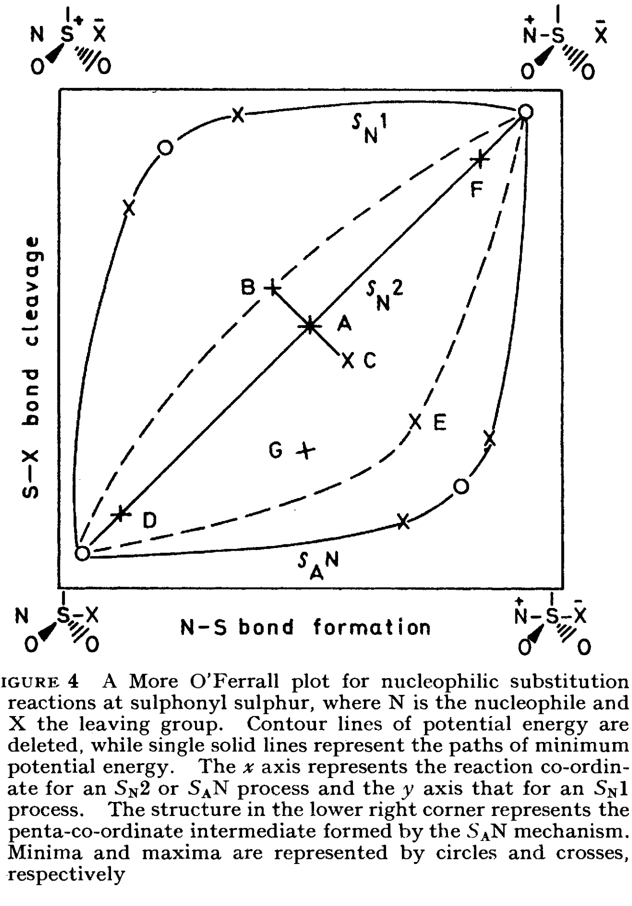

FIGURE 4 A More O'Ferrall plot for nucleophilic substitution reactions at sulphonyl sulphur, where N is the nucleophile and X the leaving group. Contour lines of potential energy are deleted, while single solid lines represent the paths of minimum potential energy. The *x* axis represents the reaction co-ordinate for an S_N2 or S_AN process and the *y* axis that for an S_N1 process. The structure in the lower right corner represents the penta-co-ordinate intermediate formed by the S_AN mechanism. Minima and maxima are represented by circles and crosses, respectively

The larger positive ρ values observed in sulphonyl fluorides hydrolysis for electron-withdrawing substituents with respect to that of sulphonyl chlorides indicates a transition state structure with more bond formation and less S–X cleavage (negative charge development on the sulphur atom) than that represented by C, in which less negative charge development on the sulphur atom occurs. In this case the reaction co-ordinate would lie between S_N2 and S_AN processes and closer to the latter one. The transition state could lie, say, at a midway point, such as E, or on the co-ordinate for the S_AN reaction depending on the length of the motion (which depends on the symmetry of the energy surface at the saddle point).

Moreover, every change making X a worse leaving group (change of Cl to F, solvents with low electrophilic assistance ability, *etc.*) will move the transition state, say, G, in order to give a new transition state with more N–S formation, essentially unchanged S–X cleavage, and more dispersal of positive charge from sulphur to the nucleophile. This prediction is in accord with the increasing ρ values in the reactions of substituted anilines with thiophen-2-sulphonyl chloride upon changing the solvent from water to alcohols and to aprotic solvents.*

EXPERIMENTAL

General.—Potentiometric titrations were carried out by a digital pH meter, Amel model 333, equipped with a motorized burette, Amel 233.

Materials.—Aniline, *p*-anisidine, imidazole, n-butylamine, morpholine, pyridine, and piperidine were purified by distillation or crystallization. Reagent grade inorganic sodium salts were used. Commercial methanol and acetonitrile were used without further purification. Thiophen-2-sulphonyl chloride and 5-substituted thiophen-2-sulphonyl chlorides were obtained by literature procedures.[26] Thiophen-2-sulphonyl fluoride was prepared by a literature method,[35] b.p. 75—76° at 1 mmHg. Substituted thiophen-2-sulphonyl fluorides were synthesized by the procedure described by Bianchi and Cate.[25] All new fluorides analysed correctly for C, H and N.

5-*Methylthiophen*-2-*sulphonyl fluoride* (60%) had b.p. 44° at 0.1 mmHg, $\nu_{max.}$ 1 325 (SO_2 asym. str.) and 1 155 cm^{-1} (SO_2 sym. str.); *m/e* 180 (M^+). 5-*Chlorothiophen*-2-*sulphonyl fluoride* formed yellow prisms (50%), m.p. 111—113°; $\nu_{max.}$ 1 335 (SO_2 asym. str.) and 1 160 cm^{-1} (SO_2 sym. str.); *m/e* 200 (M^+). 5-*Nitrothiophen*-2-*sulphonyl fluoride* afforded yellow prisms (52%), m.p. 35—37°, $\nu_{max.}$ 1 350 (SO_2 asym. str.) and 1 130 cm^{-1} (SO_2 sym. str.); *m/e* 211 (M^+). 4-*Nitrothiophen*-2-*sulphonyl fluoride* yielded prisms (52%), m.p. 58—60°, $\nu_{max.}$ 1 330 (SO_2 asym. str.) and 1 180 cm^{-1} (SO_2 sym. str.); *m/e* 211 (M^+).

Kinetic Procedures.—Second-order rate constants were measured potentiometrically, under pseudo-first-order conditions, following the procedure already described.[1,2]

Rates for thiophen-2-sulphonyl chlorides with azide were determined by titration. In a typical experiment, a solution of sodium azide (9.5 ml, 10^{-3}M) was added to each of 12 volumetric flasks (10 ml) and the volume was brought to the mark with a solution of thiophensulphonyl chloride in acetone (0.5 ml). Flasks were removed from a constant temperature bath at approximately equal percentage intervals of completed reaction and were quenched by swirling in a cold acetone bath. Two infinity flasks were removed and quenched after 10 half-lives. The solutions were titrated with standardized aqueous sodium hydroxide using Bromothymol Blue as indicator.

Pseudo-first-order rate constants were calculated using a least-squares computer program by relationship (1) where V

$$k_1 = \frac{1}{t} \ln \frac{V - V_0}{V - V_t} \qquad (1)$$

is the experimental infinity titre, V_0 the initial titre, and V_t the titre at time t.

The second-order rate constant k_2 was obtained from at least three determinations of k_1 according to relationship (2).

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* ρ-Value, solvent: −1.85, H_2O; −2.06, CH_3OH; −1.98, C_2H_5OH; −2.02, butan-1-ol; −3.28, acetone; −3.36, benzonitrile; −3.22, nitroethane; −3.53, nitrobenzene.[23]

Rates of reactions of thiophensulphonyl chlorides with the other nucleophiles were determined potentiometrically

$$k_1 = k_i[H_2O] + k_2[NaN_3] \qquad (2)$$

by continuous titration of the acid product with standardized aqueous NaOH, following the procedure described.[21, 24] The addition of the titrant was made using a suitable rate to keep the pH of the mixture almost constant. However preliminary measurements and Rogne's data [9] showed that the hydrolysis rates of sulphonyl chlorides are pH-independent in the pH range 3—9. In this case also the rate constants are the result of at least three determinations of $k_{obs.}$ according to relationship (3). The reagent concen-

$$k_{obs.} = k_i[H_2O] + k_2[Nu] \qquad (3)$$

trations ranged from *ca.* 0.000 2 to *ca.* 0.003M for thiophensulphonyl chlorides and from *ca.* 0.01 to *ca.* 0.2M for the nucleophiles, depending on the reaction rates.

Although not identified, some of the presumed products are well known in the benzene series.[36] Thus aromatic sulphonyl chlorides react readily in aqueous solution with NaN_3 and AcONa to yield sulphonyl azide and a mixed anhydride,[37] respectively.

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REFERENCES

[1] G. Berger and S. C. J. Olivier, *Rec. Trav. chim.*, 1927, **46**, 516.

[2] I. Hedlund, *Arkiv. Kemi Min. Geol.*, 1940, **144**, 1.

[3] H. K. Hall, *J. Amer. Chem. Soc.*, 1956, **78**, 1450.

[4] F. E. Jenkins and A. N. Hambly, *Austral. J. Chem.*, 1961, **14**, 190.

[5] R. V. Vizgert, *Russ. Chem. Rev.*, 1963, **32**, 1.

[6] C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 246.

[7] A. F. Popov, V. I. Tokarev, L. M. Litvinenko, A. I. Torganik, *Reakts. Sposobnost Org. Soedinenii*, 1957, **4**, 658 (*Chem. Abs.*, 1969, **70**, 28,266k).

[8] R. V. Vizgert and E. K. Savchuk, *Zhur. obshchei Khim.*, 1964, **34**, 3396.

[9] O. Rogne, *J. Chem. Soc.* (*B*), 1968, 1294.

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

[11] M. L. Tonnet and A. N. Hambly, *Austral. J. Chem.*, 1970, **23**, 2435.

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

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

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

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

[16] R. Foon and A. N. Hambly, *Austral. J. Chem.*, 1962, **15**, 684.

[17] R. E. Robertson, *Progr. Phys. Org. Chem.*, 1967, **4**, 213.

[18] E. Ciuffarin, L. Senatore, and M. Isola, *J.C.S. Perkin II*, 1972, 468.

[19] A. R. Haughton, R. M. Laird, and M. J. Spence, *J.C.S. Perkin II*, 1975, 637.

[20] E. Maccarone, G. Musumarra, and G. A. Tomaselli, *J. Org. Chem.*, 1974, **39**, 3286.

[21] A. Arcoria, E. Maccarone, G. Musumarra, and G. A. Tomaselli, *J. Org. Chem.*, 1973, **38**, 2457; 1974, **39**, 1689, 3595.

[22] E. Maccarone, G. Musumarra, and G. A. Tomaselli, *J.C.S. Perkin II*, 1976, 906.

[23] A. Arcoria, V. Librando, E. Maccarone, G. Musumarra, and G. A. Tomaselli, *Tetrahedron*, 1977, **33**, 105.

[24] A. Arcoria, F. P. Ballistreri, and G. A. Tomaselli, *Tetrahedron*, 1978, **34**, 2545.

[25] T. A. Bianchi and L. A. Cate, *J. Org. Chem.*, 1977, **42**, 2031.

[26] E. Maccarone, G. Musumarra, and G. A. Tomaselli, *Ann. Chim.* (*Italy*), 1973, **63**, 861.

[27] M. J. Kamlet and R. W. Taft, *J.C.S. Perkin II*, 1979, 349.

[28] D. J. McLennan, *Tetrahedron*, 1978, 2331.

[29] E. Ciuffarin and L. Senatore, *Tetrahedron Letters*, 1974, **17**, 1635.

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

[31] C. G. Swain and G. B. Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 141.

[32] R. A. More O'Ferrall, *J. Chem. Soc.* (*B*), 1970, 274. See also E. R. Thornton, *J. Amer. Chem. Soc.*, 1976, **89**, 2915; D. A. Winey and E. R. Thornton, *ibid.*, 1975, **97**, 3102; W. P. Jencks, *Chem. Rev.*, 1972, **72**, 705.

[33] P. R. Young and W. P. Jencks, *J. Amer. Chem. Soc.*, 1979, **101**, 3288.

[34] J. M. Harris, S. G. Shafer, J. R. Moffatt, and A. R. Becker, *J. Amer. Chem. Soc.*, 1979, **101**, 3295.

[35] W. Steinkopf and T. Hopner, *Annalen*, 1933, **501**, 174.

[36] C. M. Suter, 'The Organic Chemistry of Sulphur,' Wiley, New York, 1945, chs. 5 and 6.

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