Some Studies of Substituent Effects on the Nucleophilic Reactivities of Thiophenoxide Ions

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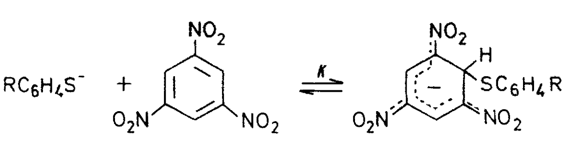
The rate constants have been measured for reaction of a series of 16 substituted thiophenoxides with 1-chloro-2,4-dinitrobenzene in 95% (v/v) ethanol–water at 25° using a stopped-flow spectrophotometric method. The values obtained which give a measure of the nucleophilic reactivites of the thiophenoxides correlate very well with the corresponding carbon basicities.

A DISTINCTION has been drawn[1,2] for nucleophiles between *basicity*, which relates to equilibria, and *nucleophilic reactivity*, which relates to rate phenomena. The basicities of nucleophiles are usually compared by measuring their thermodynamic affinities for protons in the Brönsted sense [equation (1)]. However it was shown recently[3] that carbon basicities, thermodynamic affinity for carbon, of a series of substituted thiophenoxide ions could be compared using equation (2) in which stable Meisenheimer-type complexes are formed. The results indicated a somewhat greater susceptibility to change in substituent for the carbon basicities than for the proton basicities so that a plot of log K *versus* pK_a had a slope of 1·24.

$$RC_6H_4S^- + H^+ \overset{(K_a)^{-1}}{\rightleftharpoons} RC_6H_4SH \qquad (1)$$



(2)

There have been some reports of the effects of ring substituents on the nucleophilic reactivities of thiophen-

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

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

[3] M. R. Crampton, *J. Chem. Soc.* (*B*), 1971, 2112.

oxide,[4-8] but measurements have been made in a variety of solvents and sometimes using only a few polar substituents. In the present work we report substituent effects on the nucleophilic reactivities of thiophenoxide ions for 1-chloro-2,4-dinitrobenzene in 95% (v/v) ethanol–water, the solvent system previously employed to measure carbon basicities.

EXPERIMENTAL

1-Chloro-2,4-dinitrobenzene was a recrystallised commercial specimen, m.p. 51°. Thiophenols were either commercial specimens or were prepared as before [3] from the corresponding anilines *via* the xanthate esters.[9,10] Liquid thiols were purified by g.l.c. in the temperature range 150—220° on a column packed with 17% 2-cyanoethylmethylsilicone on Chromosorb P. ^{1}H N.m.r. spectra of the liquid thiols or of solutions in carbon tetrachloride indicated the expected structures and the absence of major impurities.

Kinetic Measurements.—All measurements were made in a solvent system of 95% (v/v) ethanol–water. A stock solution of 1-chloro-2,4-dinitrobenzene in ethanol was prepared and was diluted before use to the required solvent composition. Solutions of variously substituted sodium thiophenoxides were prepared just before use by dissolving a weighed amount of the required thiol in a known volume of ethanol, adding the required quantity of standardised sodium hydroxide solution in water, and diluting to the required solvent composition. A sufficient excess of thiol over base was used to ensure virtually complete conversion of hydroxide and ethoxide ions into thiophenoxide.

Rate constants were measured using a 'Canterbury' stopped-flow apparatus (N.P. Consulting). Monochromatic light was brought by means of silica light-guides to a 2 mm silica measuring cell and from thence to a photomultiplier. The output from this was fed to a Tektronix storage oscilloscope. Solutions of 1-chloro-2,4-dinitrobenzene and sodium thiophenoxide were allowed separately to attain a temperature of 25° in a thermostatted bath before being mixed by pressure on drive syringes. The resultant change with time of the light intensity emergent from the measuring cell was measured on the oscilloscope. In all cases described here only a very small relative change in light intensity (corresponding to a change in optical density of $<0{\cdot}02$) occurred during any one kinetic run. Because of this the scale readings from the oscilloscope give directly the relative concentrations of absorbing species to an accuracy $>1\%$.

Measurements were usually made by following the increase with time of the concentrations of the reaction products, the substituted phenyl 2,4-dinitrophenyl sulphides. The absorption maxima of these compounds are in the region of 350 nm but they show significant absorption at longer wavelengths. Owing to interference from absorption by the substituted thiophenoxide ions at 350 nm measurements were generally made in the range 400—410 nm. In this wavelength region 1-chloro-2,4-dinitrobenzene shows no absorption and most of the substituted thiophenoxides show very little absorption.

In all cases the concentration of thiophenoxide was in large excess (>10) of that of the 1-chloro-2,4-dinitrobenzene and first order kinetics were observed. A typical data set is given in Table 1.

TABLE 1

Rate data for reaction of 1-chloro-2,4-dinitrobenzene (5×10^{-5}M) with sodium 3-methylthiophenoxide ($1{\cdot}03 \times 10^{-2}$M) in 95% (v/v) ethanol–water at 25°

t/s	Scale reading (405 nm)	k_{obs}/s^{-1}
0	1·95	—
0·05	2·80	3·32
0·10	3·57	3·46
0·15	4·21	3·48
0·20	4·75	3·50
0·25	5·20	3·50
0·35	5·85	3·46
0·40	6·10	3·44
0·50	6·50	3·43
0·65	6·91	3·45
∞	7·50	

For each set of reaction conditions at least five separate kinetic runs were made. First order rate constants were reproducible within 2%. In all cases measurements were made at 1×10^{-2} and 5×10^{-3}M-base and in the presence of different excesses of substituted thiophenol. Second order rate constants k ($= k_{obs}/[NaSC_6H_4R]$) were within experimental error independent of the concentration of base and of the excess concentration of thiol present. This is illustrated in the case of 4-bromothiophenol by the data in Table 2.

TABLE 2

Invariance of second order rate constant k with conditions for the reaction of 1-chloro-2,4-dinitrobenzene with sodium 4-bromothiophenoxide

[4-Bromothiophenol]$_{Stoich}$/M	[HO$^-$]$_{Stoich}$/M	k_{obs}/s^{-1}	k/l mol^{-1} s^{-1}
0·02	0·005	0·44 ± 0·01	88 ± 2
0·03	0·005	0·43 ± 0·01	86 ± 2
0·02	0·010	0·85 ± 0·02	85 ± 2
0·04	0·010	0·86 ± 0·02	86 ± 2

Some difficulty was encountered for thiophenoxide ions containing 3-acetyl, 4-acetyl, and 4-nitro-substituents. In these cases the thiophenoxide ions show considerable absorption in the visible region where the reaction products absorb. In order to obtain sufficient light intensity and a measureable change in optical density it was necessary to work at wavelengths in the range 450—500 nm and with comparatively high concentrations of 1-chloro-2,4-dinitrobenzene (5×10^{-4}M), although these were still an order of magnitude smaller than the thiophenoxide concentrations. In fact with the 4-nitro-substituted compound the reaction product 2,4-dinitrophenyl 4-nitrophenyl sulphide shows smaller absorption at the wavelength of measurement, 503 nm, than does 4-nitrothiophenoxide, so that in this case optical densities decreased with time. Because of the slowness of the reaction in this case some difficulty was found in obtaining a stable baseline (infinity value) and rate constants were evaluated using Guggenheim's method. The error associated with the rate constant (±30%) for this compound is much larger than for other substituents.

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[8] G. Bartoli, L. di Nunno, L. Forlani, and P. E. Todesco, *Internat. J. Sulfur Chem. C*, 1971, 77.

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RESULTS AND DISCUSSION

The reaction of 1-chloro-2,4-dinitrobenzene with substituted sodium thiophenoxides is known to produce substituted phenyl 2,4-dinitrophenyl sulphides.[11,12] Our results indicate that the second order rate constants k are independent of the thiophenoxide concentration and of the excess of thiol present. Values are collected in Table 3 where, for comparison, values of the equilibrium constant K relating to equation (2) are also given.

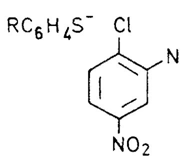
TABLE 3

Rate constants for the reaction of substituted thiophenoxides with 1-chloro-2,4-dinitrobenzene in 95% (v/v) ethanol–water at 25°

No.	Substituent	$10^{-2}k$/l mol^{-1} s^{-1}	K/l mol^{-1} [a]
1	4-NH_2	21·0 ± 0·6	2·65 × 10^3
2	4-OMe	9·6 ± 0·2	450
3	4-Me	6·4 ± 0·1	143
4	3-Me	3·4 ± 0·1	69
5	H	1·90 ± 0·05	43·2
6	4-F	1·82 ± 0·04	34
7	3-OMe	1·96 ± 0·04	29·5
8	4-Cl	0·98 ± 0·02	6·0
9	3-Ac	1·20 ± 0·02	4·9
10	4-Br	0·86 ± 0·02	4·8
11	3-Cl	0·56 ± 0·01	2·2
12	3-Br	0·61 ± 0·01	2·0
13	4-Ac	0·32 ± 0·02	0·5
14	2-Me	2·15 ± 0·03	70
15	2-NH_2	3·4 ± 0·1	59
16	4-NO_2	0·03 ± 0·01	

[a] Equilibrium constants relating to reaction (2) from ref. 3.

The nucleophilic displacement of chloride ion by thiophenoxide will proceed by the two step intermediate complex mechanism [13] and Bunnett's studies [12,14] have shown that in the present reaction the first step, intermediate complex formation, is rate limiting. The transition state for formation of the intermediate complex will have a structure (III) somewhere between the reactants (II) and the intermediate complex (IV). The intermediate complex (IV) might be expected to resemble the 1,3,5-trinitrobenzene adduct (I). A plot (Figure 1) of log k *versus* log K gives an excellent straight line with slope 0·51 ± 0·02 (correlation coefficient r 0·99). A similar plot (Figure 2) of log k *versus* pK_a values for the corresponding thiols in the same solvent shows considerably more scatter and has slope 0·65 ± 0·05 (r 0·97). One interpretation of these Brönsted-type plots would be that in the transition state (III) roughly half the negative charge has been transferred from the thiophenoxide ion to the 1-chloro-2,4-dinitrobenzene ring. However as has recently been pointed out [15,16] great caution must be exercised in the interpretation of Brönsted β values or Hammett ρ values, and we think it is probably not justifiable to quantify the charge transfer in the transition state from these measurements.



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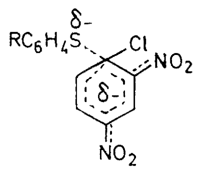

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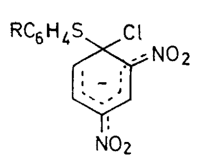

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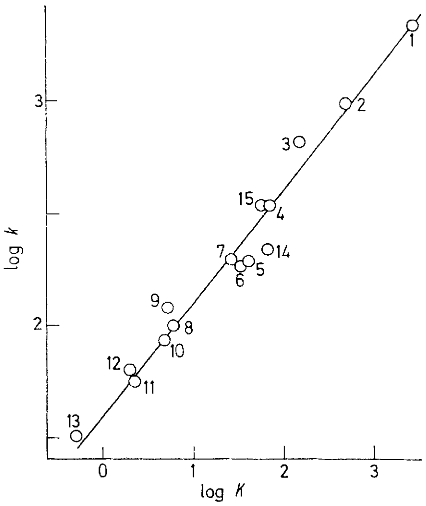

FIGURE 1 Correlation of nucleophilic reactivities and carbon basicities for substituted thiophenoxides. The numbering of substituents corresponds with Table 3

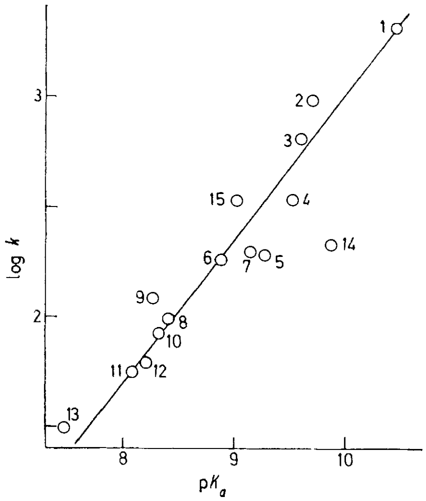

FIGURE 2 Correlation of nuclephilic reactivities and proton basicities for substituted thiophenoxides. The numbering of substituents corresponds with Table 3

It is, however, of interest that there is markedly better correlation of the nucleophilic reactivities of substituted thiophenoxide ions with their carbon basicities than with their proton basicities. This holds also of the *ortho*-substituted thiophenoxides where steric effects may be important. Thus in Figure 1 the points for 2-methyl- and 2-amino-thiophenoxides fall close to the line. The considerably reduced reactivity of 2-methylthiophen-

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[12] J. F. Bunnett and W. D. Merritt, *J. Amer. Chem. Soc.*, 1957, **79**, 5967.

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[14] J. F. Bunnett and N. S. Nudelman, *J. Org. Chem.*, 1969, **34**, 2038.

[15] F. G. Bordwell and W. J. Boyle, *J. Amer. Chem. Soc.*, 1972, **94**, 3907.

[16] C. D. Johnson and K. Schofield, *J. Amer. Chem. Soc.*, 1973, **95**, 270.

oxide compared with that expected from its proton basicity (Figure 2) is likely to result from steric interaction in the transition state (III). The fact that no such effect is observed in 2-aminothiophenoxide may result from the stabilising effect of hydrogen bonding between the amino-protons and a nitro-group in the transition state.

More generally it is of interest to see how well the nucleophilic reactivities of substituted thiophenoxide ions in other types of reaction correlate with their carbon basicities. We find that for the limited data available good correlations are obtained, better than, for example, with Hammett σ values. For example a plot of the data of Todesco *et al.*[8] for the reaction of substituted thiophenoxides with 1-chloro-4-nitrobenzene in methanol *versus* carbon basicities (log K) gives an excellent straight line with slope 0·48 (r 0·99). Incidentally the similarity of this slope to that, 0·51, observed by us for reaction with 1-chloro-2,4-dinitrobenzene, where rate constants are six orders of magnitude higher, adds weight to the argument [15,16] that such slopes do not give a good estimate of the charge transfer in the transition state. Again the rate constants for reaction of substituted thiophenoxides with benzyl bromides [7] or with ethyl phenylpropiolate [4] correlate well with carbon basicities although naturally different slopes are obtained. The similar effects of substituents in these examples probably reflects the fact that in each case reaction involves formation of a sulphur–carbon bond.

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