

Reactivity of Thiophenoxide Ion toward *o*- and *p*-Halogenonitrobenzenes

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Kinetic data for the thiophenoxy-dehalogenation of *o*- and *p*-fluoro- and -bromo-nitrobenzene in methyl and *t*-butyl alcohols in the absence or presence of dicyclohexyl-18-crown-6 at 50° are reported. In methyl alcohol the *ortho* : *para* ratios were found to be 1.46 (fluoro-substrates) and 0.32 (bromo-substrates) in the absence of crown ether, and 1.37 (fluoro-substrates) and 0.32 (bromo-substrates) in the presence of crown ether. In *t*-butyl alcohol the *ortho* : *para* ratios were found to be 28.1 (fluoro-substrates) and 5.33 (bromo-substrates) in the absence of crown ether, and 1.44 (fluoro-substrates) and 0.43 (bromo-substrates) in the presence of crown ether. The rates of reaction of fluoro- and bromo-substrates in methanol with lithium thiophenoxide were also measured but no change in reactivity with respect to potassium thiophenoxide was detected in this solvent. The reasons for the increase in the *ortho* : *para* ratio on going from methyl to *t*-butyl alcohol as solvent are discussed.

ALTHOUGH it has long been known that thiophenoxide ion readily displaces halogens from *o*- and *p*-halogenonitrobenzenes^{1a-e} giving nitrophenyl phenyl sulphides, chemists have paid relatively little attention to the factors governing the reactivity of *o*- as compared to *p*-halogenonitrobenzenes toward thiophenoxide ion. Recently the question of the *ortho* : *para* ratio in aromatic nucleophilic substitutions involving reactions of anionic species as nucleophiles and halogenonitrobenzenes has been the subject of increasing attention. Generally alkoxides in their respective lyate solvent are used as nucleophiles.^{1f-j} In the present work we report kinetic data on the effect of the leaving group, solvent, and counterion on the reaction of thiophenoxide ion toward *o*- and *p*-halogenonitrobenzenes.

RESULTS AND DISCUSSION

The reaction of thiophenoxide ion with *o*- and *p*-fluoro- and -bromo-nitrobenzene in methyl and *t*-butyl alcohol, in the absence or presence of crown ether proceeds quantitatively according to the stoichiometric equation (1).



An addition-elimination mechanism with rapid decomposition of the tetrahedral intermediate complex into products is generally suggested^{1b-e} for these reactions.

In Table 1 the rate constants and the *ortho* : *para* ratios for the reactions of *o*- and *p*-fluoro- and -bromo-nitrobenzene with potassium thiophenoxide in methyl and *t*-butyl alcohol at 50° are listed. In the case of the bromo-substrates rates at different concentrations of thiophenoxide (in the range 2×10^{-3} – 2×10^{-2} M) were measured in order to check the effect of the concen-

¹ (a) J. Miller, 'Aromatic Nucleophilic Substitution,' Elsevier, Amsterdam, 1968; (b) J. F. Bunnett and W. D. Merritt, jun., *J. Amer. Chem. Soc.*, 1957, **79**, 5967; (c) C. W. Bevan and J. Hirst, *J. Chem. Soc.*, 1956, 254; K. C. Ho, J. Miller, and K. W. Wong, *J. Chem. Soc. (B)*, 1966, 310; (d) G. Bartoli, L. Di Nunno, L. Forlani, and P. E. Todesco, *Internat. J. Sulfur Chem. C*, 1971, 77; (e) J. F. Bunnett and R. F. Snipes, *J. Amer. Chem. Soc.*, 1955, **77**, 5422; (f) T. O. Bamkole, J. Hirst, and E. I. Udossien, *J.C.S. Perkin II*, 1973, 2114; (g) C. W. L. Bevan, A. J. Foley, J. Hirst, and W. O. Uwamu, *J. Chem. Soc. (B)*, 1970, 794 and previous papers in the series; (h) K. Masaru, S. Shizen, and M. Kokji, *Kogyo Kagaku Zasshi*, 1970, **73**(3), 513 (*Chem. Abs.*, 1973, **73**, 44,563); (i) M. Takayoshi, K. Masaru, S. Yoshio, S. Hiroshi, S. Shizen, M. Kokji, *ibid.*, 516 (*Chem. Abs.*, 1973, **73**, 44,564); (j) F. Del Cima, G. Biggi, and F. Pietra, *J.C.S. Perkin II*, 1973, 55 and previous papers in the series.

tration of the nucleophile on the rate coefficient. As it emerges from Table 1 small changes of the rate constant occurred. For practical reasons a thiophenoxide ion concentration of 5×10^{-3} M was chosen for all comparative experiments.

TABLE I

Second-order rate coefficients for the reactions of *o*- and *p*-fluoro- and -bromo-nitrobenzene with potassium thiophenoxide in methyl and *t*-butyl alcohol at 50°

Solvent	[Substrate]/[Nucleophile] ^{a/}		10 ⁴ k/ 1 mol ⁻¹ s ⁻¹	k _o /k _p	
	M	M			
MeOH	<i>o</i> -F, 0.03	0.005	38.5	1.46	
	<i>p</i> -F, 0.03	0.005	26.4		
	<i>o</i> -F, 0.03	0.005 ^b	38.3	1.46	
	<i>p</i> -F, 0.03	0.005 ^b	26.3		
	<i>o</i> -Br, 0.01	0.005	2.40	0.32	
	<i>p</i> -Br, 0.01	0.005	7.40		
	<i>o</i> -Br, 0.01	0.01	2.55	0.34	
	<i>p</i> -Br, 0.01	0.01	7.55		
	<i>o</i> -Br, 0.01	0.02	2.70	0.36	
	<i>p</i> -Br, 0.01	0.02	7.60		
	Bu ^t OH	<i>o</i> -F, 0.005	0.005	6720	28.1
		<i>p</i> -F, 0.005	0.005	239	
<i>o</i> -F, 0.005		0.005 ^b	6570	27.4	
<i>p</i> -F, 0.005		0.005 ^b	240		
<i>o</i> -Br, 0.01		0.002	278	4.63	
<i>p</i> -Br, 0.002		0.002	60.0		
<i>o</i> -Br, 0.01		0.005	289	5.33	
<i>p</i> -Br, 0.03		0.005	54.2		
<i>o</i> -Br, 0.01		0.01	292	5.73	
<i>p</i> -Br, 0.03		0.01	51.0		

^a The potassium thiophenoxide concentrations are equal to those of the alkoxides. The concentration of free thiophenol was in four-fold excess over that of alkoxide. ^b The concentration of free thiophenol was in ten-fold excess over that of alkoxide.

The main points which emerge from examination of the data of Table 1 are the following.

(1) The fluoro-substrates are always more reactive than the bromo-compounds. The rise in reactivity with the change of leaving group from bromine to fluorine is more pronounced in the *ortho*- ($k_F : k_{Br}$ ca. 15–20) than in the *para*-derivatives ($k_F : k_{Br}$ 3–4) and scarcely affected by the change of solvent.

(2) Considering the *ortho*- and the *para*-series individually, the change of the solvent from methyl to *t*-butyl alcohol always causes an increase in the rate of thiophenoxy-dehalogenation. The magnitude of the rise is more pronounced for the *ortho*- than for the *para*-isomers.

(3) An examination of the *ortho* : *para* ratio reveals that in *t*-butyl alcohol the *ortho*-derivatives are more reactive than the *para*-compounds (a factor of ca. 5 for

bromo-substrates and *ca.* 30 for fluoro-substrates); in methyl alcohol the reactivity of the *ortho*-fluoro-derivative is still larger, although only slightly, than that of the *para*-compound (*ortho* : *para* *ca.* 1.5), whereas for the bromo-substrates the *para*-isomer is the more reactive (*ortho* : *para* *ca.* 0.3).

The rate increase observed on going from methyl to *t*-butyl alcohol as solvent is parallel to the decreasing polarity of the solvent. Such solvent effects are in accord with that expected on the basis of the Hughes-Ingold theory² (reaction between anion and neutral molecule which leads to an intermediate with charge dispersion). But at this point a question emerges. Why is the effect of the solvent different in the *ortho*- and *para*-series? Before answering this problem it must be remembered that analogous behaviour toward the change of the solvent has been noticed by other authors for similar reactions and different interpretations have been proposed. Hirst *et al.*¹⁰ have interpreted the increase in the *ortho* : *para* ratio on going from methyl, through ethyl, to isopropyl alcohol in the reaction of *o*- and *p*-fluoronitrobenzene with sodium alkoxides in their respective lyate solvents and with sodium phenoxide in terms of steric inhibition of solvation of the transition state of the *ortho*-isomer. Pietra *et al.*¹¹ have invoked another factor to explain the very high *ortho* : *para* ratio found (3.6×10^2) in the reactions of *o*- and *p*-fluoronitrobenzene with potassium *t*-butoxide in *t*-butyl alcohol, *viz.* special stabilization of the transition state relative to the *ortho*-substituted substrate due to potassium ion bridging between the alkoxide and the nitro-group oxygen atoms. Certainly support for this view was given by the recent results of Pietra,¹¹ who obtained an *ortho* : *para* ratio of *ca.* 1 when the aforementioned reactions were carried out in the presence of dicyclohexyl-18-crown-6. The crown ether is known³ to be a very strong cation-binding complexing agent and therefore when it is added to potassium *t*-butoxide in *t*-butyl alcohol it traps potassium and removes the cause of the preferential stabilization of the *ortho*-transition state.

In order to check the role played by the counterion in our reaction, the rates of the thiophenoxy-dehalogenation of fluoro- and bromo-substrates were measured with lithium thiophenoxide and with potassium thiophenoxide in the presence of dicyclohexyl-18-crown-6. The data are summarized in Table 2. The change of the cation from potassium to lithium was limited to methyl alcohol owing to the low solubility of lithium thiophenoxide in *t*-butyl alcohol. As Table 2 shows the use of lithium instead of potassium as cation has practically no effect on the reactivity in methyl alcohol. Much more interesting data are those concerning the reactivity of potassium thiophenoxide in the presence of crown ether. Comparison of these data with those obtained in the absence of crown ether reveals the following points.

(1) In *t*-butyl alcohol the presence of crown ether

² E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, 1941, **37**, 6.

³ C. J. Pedersen, *J. Amer. Chem. Soc.*, (a) 1967, **89**, 7017; (b) 1970, **92**, 386, 391.

generally causes an increase of reactivity of the thiophenoxide ion; the effect is slight for *ortho*-substrates (factor of *ca.* 2—3), but a larger effect occurs in the reaction of *para*-substrates (factor of 30—40). From this the *ortho* : *para*-ratios which were *ca.* 30 (fluoro-substrates) and *ca.* 5 (bromo-substrates) in the absence of crown ether drop to *ca.* 1.5 and 0.4 respectively, values not much different from those obtained for methyl alcohol.

TABLE 2

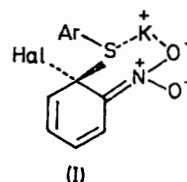
Rate constants for the reactions of *o*- and *p*-fluoro- and -bromo-nitrobenzenes with potassium thiophenoxide^a in the presence of dicyclohexyl-18-crown-6 in methyl and *t*-butyl alcohols and with lithium thiophenoxide^a in methyl alcohol at 50°

Solvent	[Substrate]/ M	Nucleophile	10 ⁴ <i>k</i> / 1 mol ⁻¹ s ⁻¹	<i>k</i> _o / <i>k</i> _p	
MeOH	<i>o</i> -F, 0.03	PhSK-c.e. ^b	36.7	1.37	
	<i>p</i> -F, 0.03		26.8		
	<i>o</i> -Br, 0.01	PhSK-c.e. ^b	2.45	0.32	
	<i>p</i> -Br, 0.01		7.54		
	Bu ^t OH	<i>o</i> -F, 0.03	PhSLi	35.4	1.38
		<i>p</i> -F, 0.03		25.6	
<i>o</i> -Br, 0.01		PhSLi	2.50	0.34	
<i>p</i> -Br, 0.01			7.40		
Bu ^t OH		<i>o</i> -F, 0.003	PhSK-c.e. ^b	14,000	1.44
		<i>p</i> -F, 0.003		9750	
	<i>o</i> -Br, 0.005	PhSK-c.e. ^b	947	0.43	
	<i>p</i> -Br, 0.005		2200		

^a In all cases 5×10^{-3} M. ^b c.e. = Crown ether. Concentration equal to that of the nucleophile (5×10^{-3} M).

In accord with the view of Pietra,¹¹ the larger increase in reactivity of the *ortho*- over the *para*-isomers on passing from methyl to *t*-butyl alcohol can be attributed to the presence of potassium as counterion. Potassium possesses good co-ordinating ability toward electronegative atoms and can give rise, in a medium of low polarity such as *t*-butyl alcohol, to intramolecular assistance favoured by the availability of the potassium thiophenoxide as ion pairs.

An approximate representation of the intermediate complex for the reaction of *ortho*-halogeno-substrates with potassium thiophenoxide in *t*-butyl alcohol is (I)



where a specific stabilization *via* the intramolecular bridging of potassium ion between the sulphur atom of the thiophenoxide and the oxygen atoms of the *o*-nitro-group occurs.

The rate increase found on adding the crown ether indicates that in *t*-butyl alcohol potassium thiophenoxide is present largely as an ion pair, species which are less efficient⁴ as nucleophiles than free ions. The crown

⁴ (a) M. Swarc, 'Ions and Ion Pairs in Organic Reactions,' Wiley-Interscience, New York, 1972, vol. 1, p. 110; (b) G. R. Burns and B. D. England, *J. Chem. Soc. (B)*, 1966, 864; (c) S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Letters*, 1960, no. 9, 24; (d) C. A. Kingsbury, *J. Org. Chem.*, 1964, **29**, 3262.

ether traps potassium ion and affords a larger amount of free thiophenoxide, therefore an increase of reactivity occurs. This effect is more evident for the *para*- than for the *ortho*-isomer, since in the latter case there is little advantage for potassium thiophenoxide in reacting as a free ion rather than as a tight ion pair because the presence of crown ether removes the cause of preferential stabilization of the *ortho*-transition state and the lack of this stabilization counterbalances the effect due to the presence of a larger amount of thiophenoxide as free ion.

A comparison of our results with those of Pietra^{1j} reveals that the *ortho* : *para* ratio is much larger when the nucleophile is potassium *t*-butoxide rather than potassium thiophenoxide (for the fluoro-substrate); these ratios are 360 and 28.1 respectively. This is not surprising if one considers that in changing from potassium *t*-butoxide to potassium thiophenoxide, sensitive differences can occur in the availability of the nucleophiles as ion pairs⁴ and in the degree of bond forming at the rate-limiting transition state: these are certainly factors which must play an important role in determining the degree of intramolecular potassium ion bridging and hence the extra stabilization of the transition state of the reactions of *o*-nitro-substituted substrates. The formation of a smaller percentage of ion pairs of potassium thiophenoxide than of potassium *t*-butoxide in *t*-butyl alcohol may be rationalized on the basis of the difference in size and in charge delocalization of the two anions.⁴ The larger increase of reactivity in *t*-butyl alcohol on addition of crown ether to the reaction of *p*-fluoronitrobenzene with *t*-butoxide than for the reaction of the same substrate with potassium thiophenoxide adds weight to this view (rate enhancements *ca.* 2000 and 40, respectively).

(2) In methyl alcohol the addition of crown ether has no particular effect on the reactivity and the *ortho* : *para* ratios are practically unchanged. This indicates that in a medium such as methyl alcohol the nucleophile is present as the free ion and that the reactivity data obtained in this solvent reflect the intrinsic nucleophilicity of the thiophenoxide ion toward the halogenonitrobenzenes investigated.

In conclusion, the most important aspect of this study is that in the reactions of *p*- and *o*-fluoro- and -bromonitrobenzenes with thiophenoxide ion, as in the reaction of the same substrates with alkoxide ions,^{1f-j} neither

inhibition of the resonance of the *o*-nitro-group, nor repulsion between the entering and the leaving group occurs to any appreciable extent in the transition state of the rate-determining step.

EXPERIMENTAL

U.v. spectra were taken on a Zeiss PM Q II spectrophotometer. Reagent grade methyl alcohol was further purified by the magnesium method;⁵ *t*-butyl alcohol was recrystallized several times and then distilled over calcium hydride.⁶ *o*-Fluoro-, *p*-fluoro-, *o*-bromo-, and *p*-bromo-nitrobenzene were commercial products which were distilled or recrystallized several times prior to use. Dicyclohexyl-18-crown-6 ether was a commercial sample (Fluka) purified by crystallization from light petroleum (b.p. 30–50°). Thiophenol was distilled under nitrogen just before use.

Kinetics.—In the concentration range used for the kinetic runs the Beer–Lambert law is strictly obeyed. Standard solutions of substrate, thiophenol, and metal alkoxides were prepared. Thiophenoxide solutions were prepared by mixing under nitrogen suitable portions of solutions of thiophenol and metal alkoxide. The concentration of thiolate anion was taken as equal to that of the alkoxide titrated with 0.1*N*-hydrochloric acid (Methyl Red–Bromocresol Green). A similar procedure was used for measurements in the absence or presence of crown ether: the only difference was that in the latter case an equimolar (to nucleophile) quantity of crown ether was present in the reaction mixture. In all cases the concentration of free thiophenol in the reaction mixture was four times that of the alkoxide. In the case of reactions of fluoro-substrates, runs with ten-fold excess of free thiophenol were also performed; no change in rate constant was found on changing the concentration of free thiophenol, thus indicating the absence of acid catalysis. Kinetics were performed under nitrogen by adding a solution of the thiophenoxide to that of the substrate kept separately at constant temperature for 15 min. Portions of the reaction mixture were removed at suitable intervals and discharged into a standard volume of dilute, alcoholic acetic or hydrochloric acid to give an assay solution for optical density measurements. A convenient wavelength (372 nm) was chosen on the basis of the absorption characteristics of the original substrates and of the sulphides. Good second-order rate coefficients were obtained.⁷ Duplicate runs were performed (error $\pm 4\%$). In all cases the absorption spectrum (300–400 nm) of the reaction mixture after several half-lives corresponded to within 4% of that of the infinity sample prepared from the appropriate nitrophenyl phenyl sulphide. In all cases no other product could be detected by t.l.c. analysis [benzene–light petroleum (b.p. 60–80°) (1 : 1) as solvent] of infinity samples of the reaction solution.

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⁵ L. F. Fieser, 'Experiments in Organic Chemistry,' Heath, Boston, 2nd edn., 1941, p. 360.

⁶ H. C. Brown and R. L. Klimisch, *J. Amer. Chem. Soc.*, 1966, **88**, 1425.

⁷ D. Spinelli, G. Guanti, and C. Dell'Erba, *J.C.S. Perkin II*, 972, 441.