Mechanism of Iodination of Some Substituted Thiophens

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The mechanism of aromatic iodination proposed previously has been confirmed by a study of the reactions of substituted thiophens. For 2-phenylthiophen the kinetic hydrogen isotope effect depends upon the substrate concentration, which is consistent with the reaction scheme.

In a previous paper[1] we proposed that the mechanism of aromatic iodination by iodine and nitric acid involves the illustrated sequence of reactions. To explain the variation of rate with concentration of aromatic compound it was necessary to postulate that k_{-3} and k_4 should be of comparable magnitude. The rate equation (i) then applies. The results obtained with a number of substituted benzenes were entirely consistent with this scheme. However, one necessary consequence is that with a highly activated substrate at high concentration, the term $k_4[\mathrm{ArH}]$ might be large enough to make k_{-3} negligible, and then k_{obs} should be independent of the substrate concentration. This situation has been realised with 2-phenylthiophen.

$$\mathrm{N_2O_4} \underset{}{\overset{K_1}{\rightleftharpoons}} \mathrm{2NO_2}$$

$$\mathrm{NO_2} + \mathrm{H^+} \overset{K_2}{\rightleftharpoons} \mathrm{NO_2H^+}$$

$$\mathrm{NO_2H^+} + \tfrac{1}{2}\mathrm{I_2} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{HNO_2I^+}$$

$$\mathrm{ArH} + \mathrm{HNO_2I^+} \xrightarrow{k_4} \mathrm{ArI} + \mathrm{HNO_2} + \mathrm{H^+}$$

$$k_{\mathrm{obs}} = k_4k_3K_2K_1^{\frac{1}{2}}[\mathrm{N_2O_4}]^{\frac{1}{2}}[\mathrm{H^+}][\mathrm{ArH}]/(k_{-3} + k_4[\mathrm{ArH}]) \quad \text{(i)}$$

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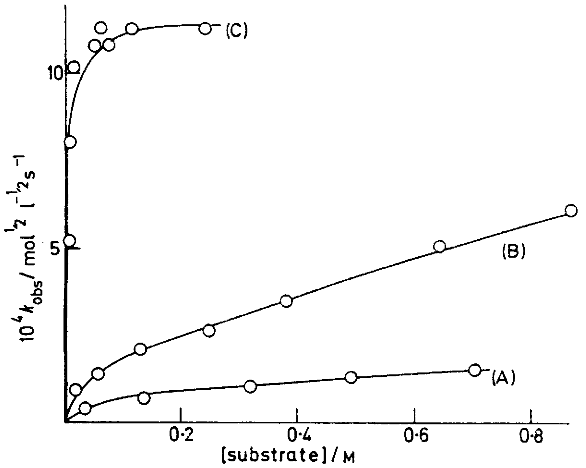
[1] A. R. Butler and A. P. Sanderson, *J. Chem. Soc.* (*B*), 1971, 2264.

RESULTS AND DISCUSSION

The variation of k_{obs} with concentration of substrate for 2-chlorothiophen, thiophen, and 2-phenylthiophen, is shown in the Figure. The results for the first two compounds are very similar to those for the substituted benzenes described previously.[1] There is no reason to doubt that the mechanism is the same for both sets of compounds. With 2-phenylthiophen, the most reactive of the three, it is seen that above 0·01M the rate is essentially independent of the substrate concentration, which is exactly what is expected from the scheme proposed previously; thus confirmation is provided.



Variation of rate constant with substrate concentration for the iodination of some substituted thiophens: (A) 2-chlorothiophen, (B) thiophen, (C) 2-phenylthiophen; $[I_2]_0$ 1·23 × 10^{-3} M; $[NaNO_2]$ 0·0050M; $[HNO_3]$ 0·16M

Iodine and nitric acid are known [2] to iodinate thiophen at the 2-position. By analogy with bromination studies,[3] iodination of 2-chlorothiophen will give 2-chloro-5-iodothiophen. However, with 2-phenylthiophen it is possible that iodination of the phenyl ring may occur; for this reason, product analysis was undertaken. In fact, 2-iodo-5-phenylthiophen was found to be the only product and so the three reactions under consideration are strictly comparable.

The kinetic hydrogen isotope effect for the iodination of 2-phenylthiophen was determined and the results are given in the Table. At a substrate concentration of 0·01M, k_H/k_D = 1·35, a value which is consistent with a mechanism in which the substrate is involved in the rate-determining step. However, at a higher substrate concentration (0·06M), where attack of the substrate is no longer one of the slow steps, the kinetic isotope effect is reduced to 1·06. These results further confirm the reaction scheme proposed previously.

Iodination of 2-deuterio-5-phenylthiophen and 2-phenylthiophen at 25°

$[I_2]_0$ 1·24 × 10^{-3}M $[HNO_3]$ 0·16M $[NaNO_2]$ 0·0050M

Substrate	Concentration (M)	$10^4 k_{obs}/\text{mol}^{\frac{1}{2}}\,\text{l}^{-\frac{1}{2}}\,\text{s}^{-1}$
2-Phenylthiophen	0·011	8·4 (±0·2)
	0·062	11·0 (±0·3)
2-Deuterio-5-phenylthiophen	0·010	6·2 (±0·2)
	0·061	10·4 (±0·3)

EXPERIMENTAL

Materials.—Thiophen and 2-chlorothiophen were distilled before use. 2-Phenylthiophen was prepared according to a literature method.[4]

2-*Iodo-5-phenylthiophen*. 2-Phenylthiophen (1 g) was added to thallium(III) trifluoroacetate (3·4 g) in acetonitrile (8 ml) [5] and the mixture was stirred for 20 min. Potassium iodide (7·9 g) in water (100 ml) was added and the mixture was stirred for 15 min. Sodium hydrogen sulphite was then added and the mixture was stirred for 15 min, then made alkaline (4M-NaOH). Thallium(I) iodide was filtered off and the mixture was extracted with ether. The extracts were dried ($MgSO_4$) and evaporated to give 2-iodo-5-phenylthiophen (75%), m.p. 81° (from ethanol) (lit.,[6] 81·5°).

2-*Deuterio-5-phenylthiophen*. A solution of 2-phenylthiophen (3·5 g) in dry ether (50 ml) was cooled to 0° and butyl-lithium in hexane (15%; 15 ml) was added during 30 min under dry nitrogen. The mixture was stirred for 30 min, then deuterium oxide (5 ml) was added, with the temperature kept below 20°, and the mixture was stirred for a further 90 min, dried (Na_2SO_4), and evaporated. The residue was crystallised from ethanol (charcoal) to give 2-deuterio-5-phenylthiophen. The presence of more than 90% deuterium at the 2-position was confirmed by n.m.r. spectroscopy.

Product Analysis.—2-Phenylthiophen (0·1 g) and iodine (0·006 g) were dissolved in acetic acid (18 ml), and 0·05M-sodium nitrite (2 ml) and concentrated nitric acid (0·2 ml) were added. The mixture was stirred for 10 min, then poured into dilute aqueous sodium hydroxide and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated. T.l.c. of the residue (CCl_4–C_6H_6 as solvent) showed only one spot, which had an R_F value identical with that of authentic 2-iodo-5-phenylthiophen.

Kinetic Method.—This has been described previously.[1] The half-order rate constants were calculated by the use of a specially written program (details available on request).

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[4] A. I. Kosak, R. Palchak, W. A. Steele, and C. M. Selwitz, *J. Amer. Chem. Soc.*, 1954, **76**, 4450.

[5] A. McKillop and E. C. Taylor, *Chem. in Britain*, 1973, **9**, 4.

[6] A. Chrzaszczewska, *Chem. Zentr.*, 1926, 2905.