CCCLXVII.—*The Halogenation of Phenols. Part II. Iodination.*

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THE relative ionisation constants of chlorine and hypochlorous acid to give a positive halogen ion (Soper and Smith, J., 1926, 1582) express qualitatively the ease with which these substances chlorinate phenols. A study of the chlorination by hypochlorous acid showed, however, that the hypochlorous acid *molecule* was the chlorinating agent, so that the parallelism between the ease of chlorination and the ionisation constant of the chlorinating molecule is not due to preliminary ionisation into a reactive positive halogen ion. The ionisation constant of the halogenating agent may be regarded as a measure of the number of polarised molecules present and collisions between these and other molecules may be effective. It was of interest to extend this line of argument to iodination by iodine and by hypoiodous acid, the relative ionisation constants of which, given by the ratio K_h/K_w (K_h being the hydrolysis constant, $C_{\mathrm{H}^{\cdot}} C_{\mathrm{I}'} C_{\mathrm{HOI}}/C_{\mathrm{I}_2} = 3 \times 10^{-13}$, of iodine in water; Bray and Connolly, *J. Amer. Chem. Soc.*, 1911, **33**, 1485), are as 30 to 1. It might be expected from this ratio that the ease of halogenation by iodine would be comparable with that by hypoiodous acid.

The mechanism of the iodination of phenols was investigated by Cofman (J., 1919, **115**, 1040), who showed that in acid solution iodine does not iodinate, whilst the active iodine in an alkaline solution was equal to the concentration of hypoiodous acid, as calculated from the known kinetics of iodate formation (Skrabal, *Monatsh.*, 1911, **32**, 171). It might appear from these facts that iodine is incapable of iodination and that hypoiodous acid or (as Cofman suggests as an alternative) the positive iodine ion is the halogenating agent. As, however, in acid solution the phenol would be mainly un-ionised, whilst in alkaline solution the very much more highly reactive phenoxide ions would be present, the mechanism has been further examined in order to determine whether iodine is capable of reacting with phenoxide ions.

Examination of the speed of iodination of phenol was carried out by the use of a solution of iodine in potassium iodide in the presence of a neutral phosphate buffer. If molecular iodine is involved in the interaction, then the speed will be proportional, on the classical reaction-velocity equation, to the concentration of free iodine in the mixture. The equilibrium concentration of free iodine can be calculated from the expression $C_{I_2}C_{I'}/C_{I_3'} = K_1$ (Bray and MacKay, *J. Amer. Chem. Soc.*, 1910, **32**, 914), using the appropriate value for K_1 which depends on the iodide concentration. The speed of iodination at constant phenol concentration will thus be given by $v = k_{I_2}K_1C_{I_3'}/C_{I'}$, and since, in the presence of excess of iodide ions, $C_{I_3'}$ is represented sufficiently accurately by the thiosulphate titre of the solution, the velocity coefficient, k_1, of the reaction calculated from the equation

$$v = k_1 \times \text{thiosulphate titre} \quad . \quad . \quad . \quad . \quad (1)$$

should vary inversely as the iodide-ion concentration.

If the iodination is caused by hypoiodous acid, the velocity coefficient k_1 should vary approximately as the inverse of the square of the concentration of the iodide ion at constant hydrogen-ion concentration, for $C_{\text{HOI}}a_{\text{H}^\cdot}a_{I'}/C_{I_2} = K_h = 3 \times 10^{-13}$, a denoting the appropriate activity * of the ion, and hence

$$v = k_{\text{HOI}} \, . \, C_{\text{HOI}} = k_{\text{HOI}}K_hK_1C_{I_3'}/a_{\text{H}^\cdot}a_{I'}C_{I'} \quad . \quad . \quad . \quad (2)$$

The results obtained are given in Table I. The values of the activity of the iodide ion, $a_{I'}$, have been interpolated for the appropriate ionic strength, μ, from a table of the activities of the chloride ion (Lewis and Randall, "Thermodynamics," 1924, p. 351). The concentrations of iodine and of hypoiodous acid given in cols. 4 and 6, respectively, are the initial equilibrium concentrations of these substances in the reaction mixture. The unimolecular coefficient k_1 (the mean of two experiments agreeing to within 1%) is seen to

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* The activity of a neutral molecule has been equated to its concentration, in the absence of other information.

be proportional to the initial concentration of the hypoiodous acid. Although the concentration of the iodine is between 10^4 and 10^5 times that of the hypoiodous acid, there is no appreciable iodination by iodine.

TABLE I.

Ph·OH = 0·010; I_2 added = 0·001M; Temp. = 25·0°; $a_{H^\cdot} = 10^{-7}$.

μ.	$C_{I'}$.	$K_1 \,.\, 10^3$.	$C_{I_2} \,.\, 10^5$.	$a_{I'}$.	$C_{HOI} \,.\, 10^{10}$.	k_1.	$\frac{10^{-4} \,.\, k_1}{C_{I_2}}$.	$\frac{10^{-8} . k_1}{C_{HOI}}$.
0·2092	0·1	1·31	1·295	0·0745	5·231	0·1926	1·486	3·685
0·3092	0·2	1·21	0·605	0·1434	1·287	0·0477	0·788	3·75
0·5092	0·4	1·00	0·250	0·2724	0·2752	0·0102	0·407	3·71

It is now necessary to differentiate between the interaction of hypoiodous acid and that of positive iodine ion with the phenol molecule or with the phenoxide ion. This is possible by an examination of the speed of iodination in solutions containing a constant concentration of iodide ion and various hydrogen-ion concentrations. Since the reaction is examined over the hydrogen-ion concentration range from $0·5 \times 10^{-7}$ to 4×10^{-7}, the phenol exists mainly in the un-ionised condition, its ionisation constant, K_a, being $1·1 \times 10^{-10}$. The concentration of phenoxide ions is thus inversely proportional to the hydrogen-ion concentration.

For a reaction between hypoiodous acid and phenol, the speed will be given by

$$\begin{aligned} v &= k_2\, C_{HOI} C_{Ph\cdot OH} = k_2\, K_1 K_h C_{Ph\cdot OH}\, C_{I_3'}/a_{H^\cdot} a_{I'} C_{I'} \\ &= k_2\, K_I K_h C_{Ph\cdot OH}\, C_{I_3'}/a_{H^\cdot} f_{I'} {C_{I'}}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3) \end{aligned}$$

where $f_{I'}$ is the activity coefficient of the iodide ion. The velocity coefficient, k_1, of equation (1) should vary inversely as $f_{I'} a_{H^\cdot}$, or, since the ionic strength is nearly constant in the different mixtures, inversely as the hydrogen-ion activity. If the reaction is between the phenoxide *ion* and hypoiodous acid,

$$\begin{aligned} v &= k_3\, C_{HOI}\, C_{Ph\cdot O'} \\ &= k_3\, K_1 K_h K_a C_{Ph\cdot OH} C_{I_3'}/{a_{H^\cdot}}^2 f_{Ph\cdot O'}\, f_{I'} {C_{I'}}^2 \quad . \quad . \quad (4) \end{aligned}$$

and k_1 should vary approximately as the inverse of the square of the hydrogen-ion activity.

For iodination by positive iodine ions, the concentration of which is controlled by the equilibrium constant $K_2 = a_{I^\cdot} a_{I'}/C_{I_2} = a_{I'} C_{I^\cdot} f_{I^\cdot}/C_{I_2}$, the velocity equation will be $v = k_4\, C_{Ph\cdot OH}\, C_{I^\cdot} = k_4 K_1 K_2 C_{Ph\cdot OH} C_{I_3'}/C_{I'} a_{I'} f_{I^\cdot}$, and k_1 would be independent of the hydrogen-ion concentration, whilst for an interaction of positive iodine ion with the phenoxide ion the constant k_1 would be inversely proportional (approximately) to the hydrogen-ion concentration. Actually, experiments carried out at the hydrogen-ion activities of 0·5, 1·0, 2·0, and 3·98 × 10^{-7} showed that the velocity coefficient k_1 varied more rapidly than the inverse of the hydrogen-ion activity of the mixture, but less rapidly than its inverse square. The results are summarised in Table II.

TABLE II.

Ph·OH = 0·010; KI = 0·100; temp. = 25·0°.

HPO_4''.	H_2PO_4'.	μ.	$f_{I'}$.	$a_{H^\cdot}$. 10^7.	k_1 (obs.).	$10^7 \times$ $k_1 a_{H^\cdot}$.	$10^{14} \times$ $k_1 a_{H^\cdot}{}^2$.	k_1 (calc.).
0·0370	0·0130	0·224	0·741	0·5	0·420	0·210	0·105	0·440
0·0296	0·02037	0·209	0·745	1·0	0·193	0·198	0·193	0·182
0·0205	0·0295	0·191	0·752	2·0	0·083	0·166	0·322	0·081
0·0126	0·0374	0·175	0·759	3·98	0·036	0·143	0·570	0·038

Assigning the values 4·85 × 10^9 and 2·76 × 10^7 to k_3 and k_2 respectively, and taking the value of $f_{Ph\cdot O'}$ as equal to that of $f_{I'}$, k_1 has been calculated from the equation

$$\begin{aligned} v &= k_2 C_{HOI} C_{Ph\cdot OH} + k_3 C_{HOI} C_{Ph\cdot O'} \\ &= \frac{K_1 K_h C_{Ph\cdot OH} C_{I_3'}}{a_{H^\cdot} C_{I'}{}^2 f_{I'}} (k_2 + k_3 K_a / a_{H^\cdot} f_{Ph\cdot O'}) \quad . \quad . \quad . \quad (5) \end{aligned}$$

which, in combination with (1), gives

$$k_1 = \frac{K_1 K_h C_{Ph\cdot OH}}{a_{H^\cdot} C_{I'}{}^2 f_{I'}} (k_2 + k_3 K_a / a_{H^\cdot} f_{Ph\cdot O'}) \quad . \quad . \quad . \quad (6)$$

Bearing in mind the necessarily approximate values used for the activities of the various ions and neutral molecules, the divergencies between the observed and calculated values of k_1 are not unreasonable.

Conclusions.

It would thus appear that the iodination of phenol is not caused by the positive iodine ion, but that the main reactions are those between the hypoiodous acid and the ionised and un-ionised phenol, the reactivity of the phenoxide ion being 180 times that of the phenol molecule. Molecular iodine is a singularly poor iodinating agent, being at least 10^6 times less active than hypoiodous acid in spite of its greater ease of ionisation and, presumably, its more highly polar condition.

The behaviour of halogens and the hypohalous acids towards phenols (as illustrated by chlorine and iodine) is thus not entirely explained on a theory of reactivity governed by the polar state of the molecules, iodination indicating that some other factor can dominate. This factor may be the affinity of the residual nuclear hydrogen for the residue of the halogenating molecule. The affinity of the hydrogen ion for the hydroxyl ion is so much greater than for the iodide ion that hypoiodous acid becomes very much more reactive than iodine. In chlorination, however, the large difference in the affinities of $Cl^{\bullet}$ for OH' and for Cl' ($4{\cdot}8 \times 10^{10}$ to 1) appears to be the controlling factor.

EXPERIMENTAL.

Buffer Solutions.—The phosphate buffer solutions were prepared from potassium dihydrogen phosphate (B.D.H., A.R.) and sodium hydroxide free from carbonate; the quantities taken (Table II) were interpolated from those given by Clark (" Determination of Hydrogen Ions," N.Y., 1920, p. 76). Conductivity water was used in making up all the solutions.

Measurement of the Speed of Iodination.—The reaction was started by addition of the iodine solution in potassium iodide to the mixture of phenol (m. p. 40·0°) and phosphate buffer solution at 25·0°. 10 C.c. of the reaction mixture were removed at suitable intervals and run into 50 c.c. of 0·5*N*-sulphuric acid, whereby the reaction was stopped. Titration of the residual iodine with *N*/500-thiosulphate was carried out in an atmosphere of nitrogen, which enabled perfectly sharp end-points to be obtained. The results for a typical experiment are given in Table III.

TABLE III.

0·05M-KH_2PO_4; 0·0296M-NaOH; 0·01M-Ph·OH; 0·001M-I_2; temp. 25·0° ± 0·02°.

Time (mins.) .	0	8·70	13·97	22·80	35·58	49·90	64·93
$[I_3'] \times 10_4$ ...	9·67	8·07	7·27	5·98	4·60	3·48	2·56
$k_1/2{\cdot}303$	—	0·0208	0·0205	0·0210	0·0208	0·0205	0·0205

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