[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

Kinetics of Aromatic Halogenation. V. The Iodination of 2,4-Dichlorophenol and Anisole with Iodine Monochloride[1]

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The kinetics of iodination of 2,4-dichlorophenol and anisole with iodine monochloride has been studied in water containing an excess of hydrogen and chloride ions. The experimental results satisfy the rate expression $-dx/dt = k_5(\mathrm{ArH})(\mathrm{H_2OI^+})$, where ArH stands for the 2,4-dichlorophenoxide ion or anisole. Similar results had previously been obtained in the iodination of *p*-chloroaniline with iodine monochloride. Various mechanisms, conforming to the observed kinetics, are discussed.

The iodination of *p*-chloroaniline with iodine monochloride in water can be presented by the rate law

$$-dx/dt = k_{\mathrm{obs}}(p\text{-}\mathrm{ClC_6H_4NH_2})_{\mathrm{st}}(\mathrm{ICl})_{\mathrm{st}} = k(p\text{-}\mathrm{ClC_6H_4NH_2})(\mathrm{HOI})(\mathrm{H^+}) = k_5(p\text{-}\mathrm{ClC_6H_4NH_2})(\mathrm{H_2OI^+}) \quad (1)$$

where the subscript st refers to stoichiometric concentrations.[2] It is compatible with a reaction between the free amine and either the conjugate acid of hypoiodous acid, $\mathrm{H_2OI^+}$, or the hydrogen ion catalyzed reaction of hypoiodous acid. In order to test the generality of this kinetic expression in the iodination of fairly reactive compounds, the study has been extended to two more types of aromatic compounds, one acidic, 2,4-dichlorophenol, and the other neutral, anisole. The preparative iodination of these two compounds by iodine monochloride has been described before and affords 6-iodo-2,4-dichlorophenol and 4-iodoanisole, respectively.[3] The conditions of the iodination were the same as for *p*-chloroaniline; the compounds were iodinated in water containing an excess of hydrogen ion and chloride ion, in order to prevent rapid hydrolysis of iodine monochloride and to minimize the effect of the small amount of chloride ion formed during substitution.

Experimental

Materials and Kinetic Determinations.—2,4-Dichlorophenol was a commercial sample which was recrystallized three times from ligroin (30–40°); it formed white needles of m.p. 42–43° (cor.). A commercial sample of anisole was washed with sodium hydroxide solution and water, and was then dried and distilled *in vacuo*. It was redistilled from metallic sodium through a small column and boiled at 154.0° at 757.5 mm.; it was then redistilled *in vacuo* at 43° and 11 mm.; $n^{25}\mathrm{D}$ 1.5141, lit.[4] 1.5143. The inorganic materials were best reagent grade chemicals; the purified ICl sample was one that had been used previously.[2] The kinetic determinations were carried out as described before.[2] Anisole solutions were made up on the same day on which they were used, because on longer standing they developed an impurity which somewhat interfered with the kinetics. The solubility of *p*-iodoanisole in water is very small, and iodination solutions became cloudy when the concentration of product was about 0.0004–0.0005 *M*, depending somewhat on electrolyte concentration. Whenever that happened, rate constants fell off, probably because of absorption of ICl on the product, and reaction was usually only followed to 40–50% conversion (with ICl $\simeq$ 0.001 *M*). Precipitation of 6-iodo-2,4-dichlorophenol only occurred at fairly high concentration of reactants, but rate constants were not appreciably disturbed. All runs were conducted at least in duplicate, and the agreement between duplicate runs was usually better than 1.5%. Within one run, average deviations were rarely greater than 1.5% and usually less, particularly for the phenol. Runs in buffers (anisole) had somewhat greater errors. Errors obtained from least square calculations are probable errors in the least square constants.

An isolation run for the iodination of 2,4-dichlorophenol was carried out on a 1-l. scale, 0.008 *M* in phenol, 0.6 *M* in NaCl, 0.5 *M* in $\mathrm{HClO_4}$ and 0.004 *M* in ICl. A crystalline precipitate formed after about 30 minutes. The solution was allowed to stand overnight in the cold. The filtered material was dried and crystallized from 50% aqueous ethanol. The yield of the known 6-iodo-2,4-dichlorophenol was 1.034 g. (89.5%) of white material of m.p. 60.4–61.0° (cor.). One more crystallization from petroleum ether afforded white needles of m.p. 60.7–61.2° (lit. 61°,[3] 63°[5]).

TABLE I

KINETIC DATA FOR THE IODINATION WITH IODINE MONOCHLORIDE AT 25°

2,4-Dichlorophenol 0.004 *M*, $\mathrm{HClO_4}$ 0.4 *M*, NaCl 0.5 *M*, $\mathrm{NaClO_4}$ 0.3 *M*, ICl $\simeq$ 0.001 *M*			Anisole 0.004004 *M*, $\mathrm{HClO_4}$ 0.3 *M*, NaCl 0.5 *M*, $\mathrm{NaClO_4}$ 0.2 *M*, ICl $\simeq$ 0.001 *M*		
Time, min.	0.02 *N* thiosulfate, ml.	$10^2 k_{\mathrm{obs}}$, l. mole^{-1} sec.$^{-1}$	Time, min.	0.02 *N* thiosulfate, ml.	$10^2 k_{\mathrm{obs}}$, l. mole^{-1} sec.$^{-1}$
0	0.992		0	0.990	
15	.888	3.12	8	.898	5.14
30	.794	3.17	16	.812	5.28
45	.715	3.15	23	.748	5.24
63	.628	3.18	30	.688	5.26
81	.559	3.14	38	.629	5.23
102	.488	3.12	46	.576	5.20
124	.419	3.16	54	.528	5.18
146	.366	3.14	1767	...	..

THE DEPENDENCE OF THE RATE ON THE INITIAL CONCENTRATION OF REACTANTS AT 25°

$\mathrm{HClO_4}$ 0.5 *M*, NaCl 0.6 *M*			$\mathrm{HClO_4}$ 0.05 *M*, NaCl 0.5 *M*, $\mathrm{NaClO_4}$ 0.05 *M*		
2,4-Dichlorophenol moles/l. × 10^3	ICl moles/l. × 10^3	k_{obs} × 10^2, l. mole^{-1} sec.$^{-1}$	Anisole moles/l. × 10^3	ICl moles/l. × 10^3	k_{obs} × 10^2, l. mole^{-1} sec.$^{-1}$
2.00	0.990	1.89	4.63	0.748	3.94
4.00	.988	1.88	2.05	1.00	4.01
8.00	.986	1.88	4.00	0.994	4.02
1.97	1.97	1.89	7.18	.990	4.05
4.00	1.97	1.89	4.01	1.59	4.07
8.00	1.97	1.89	4.06	2.00	3.97
12.0	2.44	1.87			
2.00	4.07	1.87			
8.00	4.06	1.87			
12.0	4.06	1.85			
4.00	8.14	1.90			

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(1) Presented in part before the Symposium on Aromatic Substitution at the 130th Meeting of the American Chemical Society in Atlantic City, N. J., September, 1956.

(2) E. Berliner, THIS JOURNAL, **78**, 3632 (1956).

(3) B. Jones and E. N. Richardson, *J. Chem. Soc.*, 713 (1953).

(4) J. Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publishing Co., Inc., New York, N. Y., 1950, p. 470.

(5) M. Kohn and S. Sussmann, *Monatsh.*, **46**, 575 (1925).

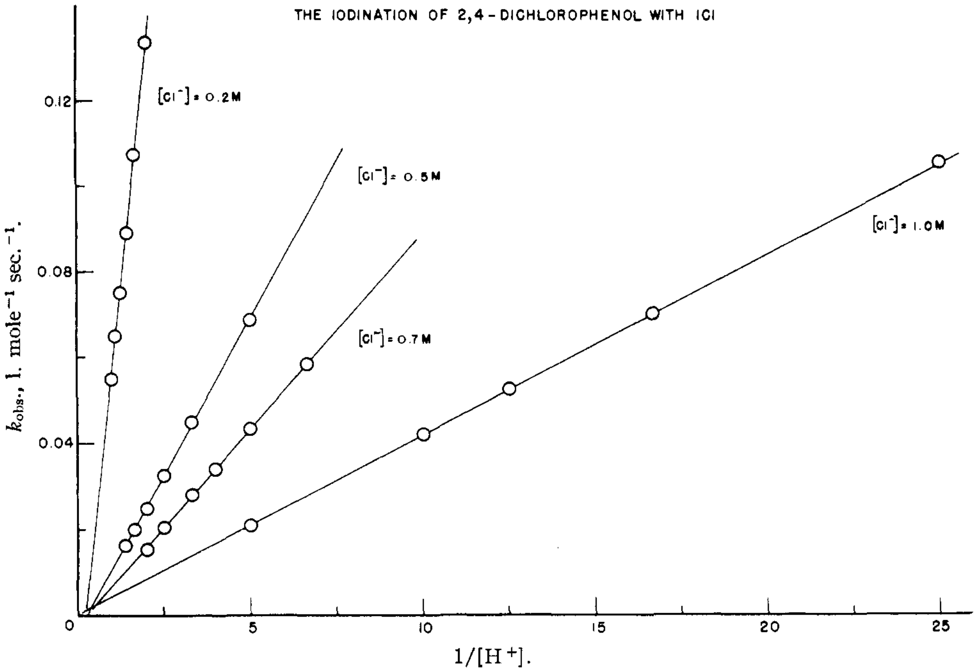

Fig. 1.—The dependence of the rate on the hydrogen ion concentration at 25°. The hydrogen ion concentration is taken equal to the concentration of perchloric acid. The slopes have the values ($\times 10^{-3}$): 77.9 ± 0.46, 14.7 ± 0.08, 9.11 ± 0.04, 4.21 ± 0.002. A point corresponding to (H^+) = 0.02 *M* is not shown on the last line.

Results and Discussion

The results of the iodination of 2,4-dichlorophenol and of anisole are completely analogous to that of *p*-chloroaniline and can be discussed in terms of the previous results[2] and in terms of the above rate expression 1, to which they conform.

Kinetic Order.—The iodination of 2,4-dichlorophenol or of anisole is first order in aromatic compound and in iodine monochloride, and second order over-all (Table I). 2,4-Dichlorophenol could be studied over a fairly wide range of concentration, because only monosubstitution is possible. The range over which anisole could be investigated is more limited, because of the possibility of disubstitution and a more limited solubility of substrate and product. For that reason also, rate constants in the latter case were usually only determined up to 40–50% reaction.

Dependence on Acid Concentration.—The rate of iodination of the phenol is inversely proportional to the hydrogen ion concentration, as shown in Fig. 1, where observed rate constants at various chloride ion concentrations are plotted against 1/H^+ at a constant ionic strength. In three cases perchloric acid was used as the source of hydrogen ions and sodium chloride of chloride ions (μ 1.2); in one, a combination of sodium chloride and hydrochloric acid (μ 0.7). The hydrogen ion concentration range is from 0.02 to 1.00 *M*.[6] The inverse dependence of the rate on the hydrogen ion concentration is interpreted to mean that the species iodinated is not the phenol but the 2,4-dichlorophenoxide ion, and that the iodination itself is independent of *p*H. While this cannot be unambiguously proved, it is likely by analogy to other substitution reactions of phenols,[7,8] and is strengthened by the behavior of anisole in solutions of varying acid concentrations (Table II, Fig. 2). For anisole the rate is independent of *p*H over a wide range of concentration; at very high acid concentration the rate decreases somewhat, probably because of hydrogen bonding of the ether oxygen, and the formation of a hydrogen-bonded complex which is less susceptible to electrophilic attack.

The experiments with anisole at low acid concentration point toward the reason why only reactive compounds can be iodinated with iodine monochloride and provide a justification for the established practice of conducting such iodinations in acid solution. Up to a hydrogen ion concentration of 0.02 *M*, the reactions go to completion, and no oxidizing material is left in the solution. At H^+ = 0.02 *M*, there is left 1.6% of a material which is colorless in solution, does not iodinate or give a starch test, but which liberates iodine from potassium iodide. This is believed to be iodic acid, HIO_3, formed by disproportionation of hypoiodous acid or hypoiodite. The disproportionation is known to proceed faster in alkaline solution, because it takes place partly through the hypoiodite ion; a similar iodination, the iodination of tyrosine by molecular iodine, has been used to study the kinetics of iodate formation.[9] In the present case,

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(6) The least square lines do not go through the origin, as they are expected to, except in the series for the lowest acid concentration range (H^+ = 0.02 to 0.2 *M*). Similar negative intercepts have been observed with *p*-chloroaniline (ref. 2), and they may be connected with the high acid or, generally, the high salt concentrations.

(7) E. Berliner, This Journal, **73**, 4307 (1951).

(8) C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. I. Minkoff and R. I. Reed, *J. Chem. Soc.*, 2628 (1950); B. S. Painter and F. G. Soper, *ibid.*, 342 (1947); R. Wistar and P. D. Bartlett, This Journal, **63**, 413 (1941); F. G. Soper and G. F. Smith, *J. Chem. Soc.*, 1582 (1926); see also ref. 24.

(9) C. H. Li and C. F. White, This Journal, **65**, 335 (1943).

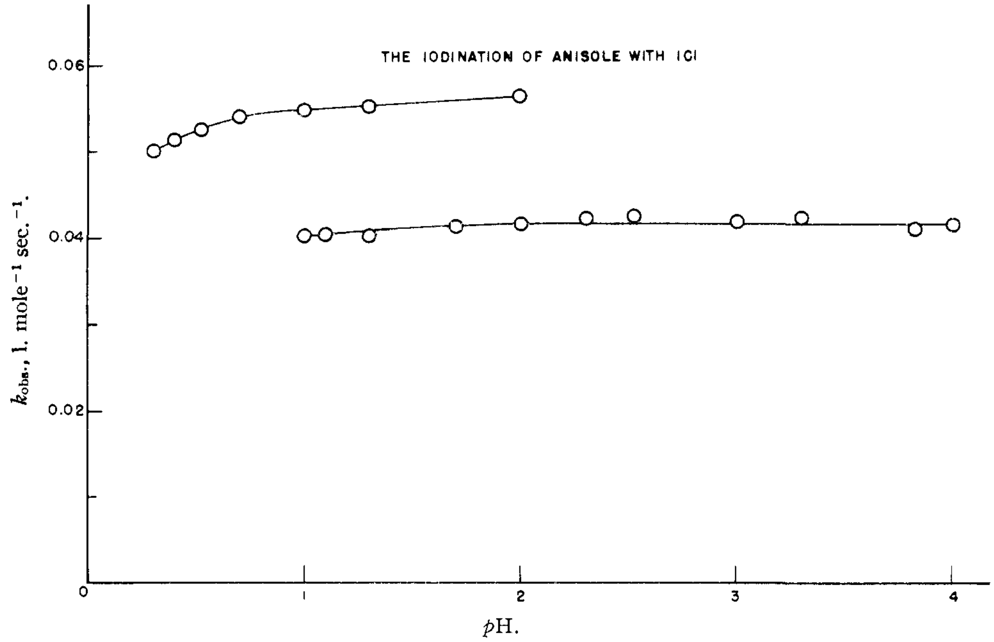

Fig. 2.—The dependence of the rate on the hydrogen ion concentration at 25° The upper curve represents runs at a total salt concentration 1.0 M, the lower 0.6 M.

TABLE II

DEPENDENCE OF RATE ON ACID CONCENTRATION IN THE IODINATION OF ANISOLE WITH IODINE MONOCHLORIDE AT 25°

Anisole ~ 0.004 M, ICl ≃ 0.001 M, NaCl 0.5 M, μ 0.6[a]			Anisole ≃ 0.004 M, ICl ≃ 0.001 M NaCl 0.5 M, μ 1.0[a]		
$HClO_4$, mole/l.	10^2k_{obs}, l. mole^{-1} sec.$^{-1}$	Residual ICl, %	$HClO_4$, mole/l.	10^2k_{obs}, l. mole^{-1} sec.$^{-1}$	Residual ICl, %
0.1	4.01	..	0.5	5.00	..
.08	4.03	..	.4	5.13	..
.05	4.02	..	.3	5.26	..
.02	4.12	1.6	.2	5.41	..
.01	4.15	2.6	.1	5.48	..
.005	4.21	3.0	.05	5.54	..
.003	4.25	3.2	.01	5.66	2.6
.001	4.19	3.6			
.0005	4.25	3.6			
.0001	4.16	3.8			

pH[b]	HAc, mole/l.	NaAc, mole/l.	10^2k_{obs}, l. mole^{-1} sec.$^{-1}$	Residual ICl, %
3.83	0.50	0.10	..[c]	7.8
3.83	.35	.07	..	8.6
3.83	.25	.05	3.81	8.6
3.83	.10	.02	4.02	8.0
3.83	.05	.01	4.11	7.0
4.54	.05	.05	..	34.5
4.54	.02	.02	..	29.0
4.54	.01	.01	..	24.0
4.54	.005	.005	(3.97)[d]	18.0
5.21	.002	.01	..	45.0
5.21	.001	.005	..	38.0
	Na_2HPO_4, mole/l.	KH_2PO_4, mole/l.		
6.45	0.01	0.01	(4.81)[d]	63.7
6.45	0.005	0.005	(5.00)[d]	63.0

[a] The ionic strength was maintained with $NaClO_4$. [b] Measured with a Beckman model G pH meter. [c] Leaders indicate that no rate constants were calculated because of a considerable downward drift. [d] Approximate value because of a downward drift.

the amount of iodic acid or iodate increases with pH, as shown in Table II, where it is listed as residual ICl (infinity) titer. The transformation seems to be catalyzed also by general bases, because in acetate or phosphate buffers the residual titer is greater and reaches over 50% of the initial ICl in phosphate buffers at pH 6.45.[10] At the same pH, but different buffer concentrations, the residual titer increases with the buffer concentration. If the aromatic compound is not very reactive, the rate of formation of iodic acid will compete successfully with substitution, and the usefulness of iodine monochloride probably has reached its limit with anisole in acid solution.[11] With the much more reactive 2,4-dichlorophenol, the infinity titer in acetate or phosphate buffers at pH 5.21 and 6.45 is only about 2% of the initial titer, while with anisole the amounts are 45 and 63%, respectively.

When the residual titer was low (as in all runs represented in Fig. 2), rate constants were corrected by deducting this infinity titer from the initial ICl titer, but at higher pH and high buffer concentrations the competing kinetics interfered, and the rate constants drifted strongly. However, even at pH 4.54 (HAc = Ac^- = 0.005 M) the corrected rate constant for iodination is 3.97 l. mole^{-1} sec.$^{-1}$, the same as at lower pH; and at a pH of 6.45 (Na_2PO_4 = KH_2PO_4 = 0.005 M) it is somewhat higher, 5.00 l. mole^{-1} sec.$^{-1}$, so that the rate of anisole iodination is essentially independent of pH over more than five pH units.

Dependence on Chloride Ions.—The rates of both reactions are decreased with an increase in the chloride ion concentration, and vary linearly with the expression $K_1/(K_1 + Cl^-)(Cl^-)$, where K_1 is the equilibrium constant for iododichloride disso-

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[10] See also R. M. Chapin, THIS JOURNAL, **56**, 2211 (1934).

[11] Although anisole can be iodinated with ICl in acetic acid, p-bromoanisole or anisic acid are reported not to react appreciably; ref. 3.

ciation (2)

$$\mathrm{ICl_2^-} \rightleftarrows \mathrm{ICl} + \mathrm{Cl^-} \quad K_1 \qquad (2)$$

This linear relationship is shown for 2,4-dichlorophenol in Fig. 3, where values for k_{obs} are plotted against $K_1/(K_1 + \mathrm{Cl^-})(\mathrm{Cl^-})$ at various acid concentrations and at a constant ionic strength, and for anisole in Fig. 4. Some relevant data are listed in Table III. As in the iodination of *p*-chloroaniline, the reaction is thus inversely proportional to the chloride ion concentration, after allowing for the initial complexing of iodine monochloride with chloride ion,[2] and, as in the previous case, the least square plots all have a small positive intercept, which is either kinetically insignificant, or indicates a small amount of iodination by $\mathrm{ICl_2^-}$.

TABLE III

DEPENDENCE OF RATE ON THE CHLORIDE ION CONCENTRATION IN IODINATIONS WITH IODINE MONOCHLORIDE AT 25°

2,4-Dichlorophenol 0.004 *M*, $\mathrm{HClO_4}$ 0.5 *M*, ICl $\simeq$ 0.001 *M*, μ 1.2[a]		Anisole $\simeq$ 0.004 *M*, $\mathrm{HClO_4}$ 0.1 *M*, ICl $\simeq$ 0.001 *M*, μ 1.0[a]	
NaCl, mole/l.	$10^2 k_{\text{obs}}$, l. mole^{-1} sec.$^{-1}$	NaCl, mole/l.	$10^2 k_{\text{obs}}$, l. mole^{-1} sec.$^{-1}$
0.70	1.37	0.90	1.86
.60	1.81	.80	2.28
.50	2.49	.70	2.98
.40	3.73	.60	3.88
.30	6.34	.50	5.48
.25	8.85	.40	8.13
.20	13.40	.30	14.24
Slope 0.901 ± 0.004		Slope 2.12 ± 0.01	
Intercept (3.56 ± 0.30) × 10^{-3}		Intercept (3.47 ± 0.29) × 10^{-3}	

[a] Constant ionic strength was maintained with $\mathrm{NaClO_4}$.

Dependence on Ionic Strength.—The iodination of the phenol shows a strong linear dependence on salt concentration, and the rates *decrease* with an increase in ionic strength, as is also the case with *p*-chloroaniline. The rate of iodination of anisole *increases* almost linearly with salt concentration, but the rate constants at very high ionic strength become irregular and drift, probably because of salting-out phenomena (Table IV). In both cases, the salt concentrations had to be very high, so that not much significance can be attached to these linear relationships, except to say that they are frequent in reactions between neutral molecules and ions at high ionic strength.[12]

TABLE IV

DEPENDENCE OF RATE ON THE IONIC STRENGTH IN IODINATIONS WITH IODINE MONOCHLORIDE AT 25°

2,4-Dichlorophenol 0.004 *M*, $\mathrm{HClO_4}$ 0.5 *M*, NaCl 0.5 *M*, ICl $\simeq$ 0.001 *M*			Anisole $\simeq$ 0.004 *M*, $\mathrm{HClO_4}$ 0.05 *M*, NaCl 0.5 *M*, ICl $\simeq$ 0.001 *M*		
$\mathrm{NaClO_4}$, mole/l.	μ	$10^2 k_{\text{obs}}$, l. mole^{-1} sec.$^{-1}$	$\mathrm{NaClO_4}$, mole/l.	μ	$10^2 k_{\text{obs}}$, l. mole^{-1} sec.$^{-1}$
..	1.00	2.69	0.05	0.60	4.02
0.20	1.20	2.52	.25	0.80	4.70
.40	1.40	2.33	.45	1.00	5.54
.60	1.60	2.14	.60	1.15	6.06
.80	1.80	1.95	.70	1.25	6.60
1.00	2.00	1.77	.90	1.45	7.26

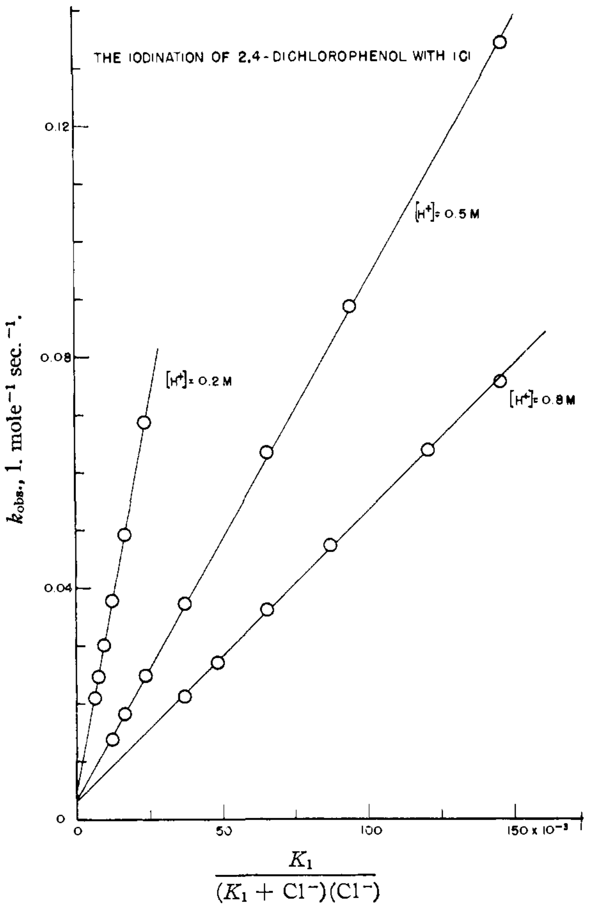

Fig. 3.—The dependence of the rate on the chloride ion concentration at 25°. The slopes have the values: 2.69 ± 0.002, 0.901 ± 0.004, 0.502 ± 0.004.

Dependence on Temperature.—Activation energies, log *A* factors and activation entropies were obtained from measurements of rate constants at four temperatures (Table V) and are listed with their least square errors, and the coresponding data for *p*-chloroaniline. The values are not true parameters for substitution, because they contain ΔH for all equilibria, including that for the dissociation of the phenol. No value is available for the latter,

TABLE V

DEPENDENCE OF RATE ON TEMPERATURE IN IODINATIONS WITH IODINE MONOCHLORIDE

2,4-Dichlorophenol 0.004 *M*, $\mathrm{HClO_4}$ 0.5 *M*, NaCl 0.5 *M*, ICl $\simeq$ 0.001 *M*		Anisole $\simeq$ 0.004 *M*, $\mathrm{HClO_4}$ 0.05 *M*, NaCl 0.5 *M*, $\mathrm{NaClO_4}$ 0.05 *M*, ICl $\simeq$ 0.001 *M*	
T, °C.	$10^2 k_{\text{obs}}$,[a] l. mole^{-1} sec.$^{-1}$	*T*, °C.	$10^2 k_{\text{obs}}$,[a] l. mole^{-1} sec.$^{-1}$
34.95	5.59	38.00[b]	10.84
25.00	2.69	32.00	6.95
18.00	1.57	25.00	4.02
11.00	0.836	18.00	2.14

	E, kcal.	log *A*	ΔS^*, e.u.	$k_{\mathrm{H_2OI^+}}$
2 4-Dichlorophenol	13.8 ± 0.16	8.52 ± 0.12	−21.5	~5.4 × 10^9
Anisole	14.7 ± .18	9.33 ± .13	−17.8	~6.4 × 10^3
p Chloroaniline[2]	16.5 ± .05	10.84 ± .035	−10.9	~1.8 × 10^6

[a] Corrected for volume changes. [b] Anisole was 0.00299 *M* in this run.

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(12) R. P. Bell, "Acid Base Catalysis," Oxford University Press, Oxford, Eng., 1941, pp. 32–34.

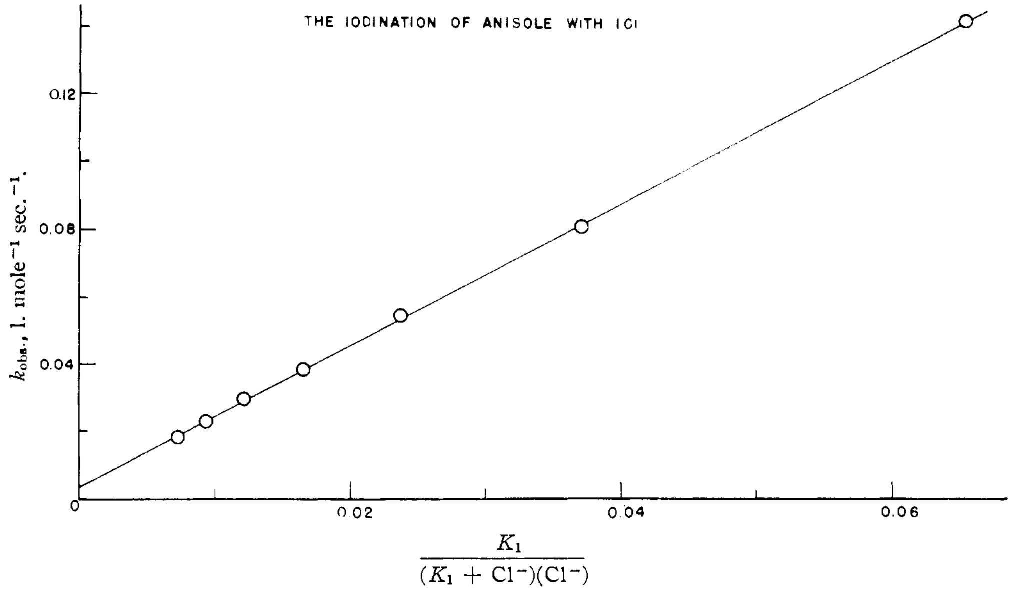

Fig. 4.—The dependence of the rate on the chloride ion concentration at 25°. The slope has the value 2.12 ± 0.01.

but a heat of dissociation of about 6 kcal. at 25° is reported for phenol itself.[13] Assuming a value of a similar order of magnitude for 2,4-dichlorophenol, an activation energy of less than 10 kcal. is required for the phenoxide ion substitution, or considerably less than for anisole under comparable conditions, in spite of the two deactivating chlorine atoms on the phenol. Since *p*-chloroaniline was iodinated under such conditions that it was present almost completely as the *p*-chloroanilinium ion, a similar[14] correction would probably also bring the activation energy for *p*-chloroaniline substitution below that of anisole, but not of 2,4-dichlorophenol. As in similar reactions, the activation entropies are negative, because ions are formed from neutral molecules in the formation of H_2OI^+. The decrease is most for the phenol reaction because of the additional formation of the 2,4-dichlorophenoxide ion.[15]

The Mechanism.—The above results are in agreement with a reaction between the 2,4-dichlorophenoxide ion (3), or of anisole (4), with the hypoiodous acidium ion or with a hydrogen ion catalyzed reaction of hypoiodous acid.

$$-dx/dt = k(2,4\text{-}Cl_2C_6H_3O^-)(HOI)(H^+) = k_5(2,4\text{-}Cl_2C_6H_3O^-)(H_2OI^+) \quad (3)$$

$$-dx/dt = k(C_6H_5OCH_3)(HOI)(H^+) = k_5(C_6H_5OCH_3)(H_2OI^+) \quad (4)$$

In the case of the phenol, the kinetic results are not distinguishable from a reaction between free 2,4-dichlorophenol and hypoiodous acid (5), but by

$$-dx/dt = k(2,4\text{-}Cl_2C_6H_3OH)(HOI) \quad (5)$$

analogy with *p*-chloroaniline and anisole the expression H_2OI^+ is preferred, and all three compounds are considered to be substituted by the same species. The same substituting agent also has been assumed to be responsible for iodination of phenol and aniline by molecular iodine.[7,16]

Since all equilibrium constants are known,[17,18] although some only approximately, the specific rate constants for iodination by H_2OI^+ can be calculated. Sufficient kinetic data are available for 2,4-dichlorophenol to use the following procedure: if H_2OI^+ is the substituting agent, k_{obs} is equal to $k_5K_IK_2K_5/(H^+)\ (K_I + Cl^-)(Cl^-)$, where K_5 is the equilibrium constant for (6), and K_2 that for the

$$ICl + H_2O \rightleftharpoons H_2OI^+ + Cl^- \quad K_5 \quad (6)$$

dissociation of 2,4-dichlorophenol.[19] The slopes in Fig. 1 have therefore the values $k_5K_IK_2K_5/(K_I + Cl^-)(Cl^-)$, and by plotting all slopes against $K_I/(K_I + Cl^-)(Cl^-)$, a new slope equal to $k_5K_2K_5$ is obtained, and the specific rate constant k_5 can be calculated. Likewise, on plotting the slopes from Fig. 3 against $1/H^+$, the same product is obtained.[20] These two methods afford values for k_5 of 5.1×10^9 and 5.7×10^9, respectively. Their average and the values for anisole and *p*-chloroaniline are listed in Table V as $k_{H_2OI^+}$. Because of the uncertainties in the equilibrium constants, the specific rate constants are perhaps uncertain by a power of ten, but their relative magnitudes should be correct. The 2,4-dichlorophenoxide ion, in spite of two deactivating chlorine atoms, reacts about 10^7 times faster than anisole and about 10^3 times faster than *p*-chloroaniline. This relative order is in accord with the electronic effect of the substituents ($O^- > NH_2 > OCH_3$).

The substitution process can be represented by the sequence I

$$ArH + H_2OI^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArHI^+ + H_2O \quad (I)$$

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[13] H. Lunden, *Z. physik. Chem.*, **70**, 249 (1910).

[14] Landoldt-Börnstein, "Physikalisch-Chemische Tabellen," Verlag von Julius Springer, Berlin, 1923, Vol. II, p. 1579.

[15] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 122 ff.

[16] E. Berliner, This Journal, **72**, 4003 (1950).

[17] J. H. Faull, *ibid.*, **56**, 522 (1934).

[18] R. P. Bell and E. Gelles, *J. Chem. Soc.*, 2734 (1951).

[19] G. J. Tiessen, *Rec. trav. chim.*, **48**, 1066 (1929).

[20] The two slopes have the values of 0.521 ± 0.005 and 0.587 ± 0.007.

$$\mathrm{ArHI^+} \xrightarrow{k_2} \mathrm{ArI} + \mathrm{H^+}$$

where ArH stands for any of the three substrates. The "Pfeiffer–Wizinger" or "Melander" intermediate, $ArHI^+$, is neutral in the case of the phenoxide ion, but cationic in the other two cases. It is further assumed that the forward reaction of the first step is rate-determining and that therefore $k_2 \gg k_{-1}$, and that $ArHI^+$ is not present in stationary concentrations, but reacts faster by deprotonation than it reverts to reactants. This is the most commonly accepted form for electrophilic aromatic substitution,[21] based on the absence of a hydrogen isotope effect in various substitution reactions.[22] Although the kinetics is in agreement with this mechanism, it is also in agreement with other mechanisms differing from I in the exact timing of the bond-making and bond-breaking processes. The relative magnitude of the three rate constants will be the decisive factor, and particularly the ratio k_2/k_{-1} may vary from compound to compound.[21] If the ratio is small, the transition state for carbon–hydrogen bond-breaking will become important, and eventually the second step may become part of the rate-determining step, in which case the reaction should show a hydrogen isotope effect. Furthermore, Hammond's argument does not necessitate the formation of the intermediate,[23] since the experiments which led to its postulation only indicate that the carbon–hydrogen bond is not appreciably weakened in the transition state. Here, too, a situation may arise where bond-making and bond-breaking processes become of equal importance, leading to the kinetically indistinguishable single-step mechanism (I′)

$$\mathrm{ArH} + \mathrm{H_2OI^+} \longrightarrow \mathrm{ArI} + \mathrm{H_3O^+} \qquad (\mathrm{I}')$$

In this case, again, the reaction should show a hydrogen isotope effect, and it should be base catalyzed.

Finally, there is a mechanism which is more drastically different in that it involves a different substituting agent (II)

$$\mathrm{ArH} + \mathrm{ICl} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ArHI^+} + \mathrm{Cl^-} \qquad (\mathrm{II})$$

$$\mathrm{ArHI^+} \xrightarrow{k_2} \mathrm{ArI} + \mathrm{H^+}$$

The intermediate $ArHI^+$ is stable enough to be, in the extreme case, in equilibrium with the reactants ($k_{-1} \gg k_2$), and it reverts more often to the reactants than it goes to the products, making the second step rate-determining and also requiring a hydrogen isotope effect. Such a mechanism has been proposed for certain bromodecarboxylations and bromodesulfonations.[24,25] The kinetics of these reactions is in agreement with a steady state intermediate, and spectroscopic evidence has been adduced for the rapid formation and measurable existence of the intermediate in the bromodesulfonation of sodium 3,5-dibromo-4-hydroxybenzenesulfonate.[25] It has been proposed that such a mechanism might also hold for the direct iodination of phenols and amines by molecular iodine,[24] and Grovenstein and Kilby have recently shown that the iodination of 2,4,6-trideuterophenol by iodine is slower than that of phenol.[26] Since we have stressed the identity of substituting agents in iodinations by iodine and iodine monochloride, mechanism II must be given consideration.

The semi-stable quinonoid intermediate $ArHI^+$ in mechanism II is the same as that in I, but differs from it in stability and reactivity. In the case of 2,4-dichlorophenol it would be a neutral quinol of the type repeatedly isolated,[27] and it would be reasonable that it could be present at a stationary concentration. But this is less likely for *p*-chloroaniline, where the intermediate would be an iminoquinol hydrochloride, and even less for anisole, where it would have to be presented as an oxonium salt without any special electronic or steric[21] stabilizing features. There is kinetic evidence, based on a steady state treatment, for such intermediates in the bromodesulfonation of an aromatic amine or methoxy compound, but apparently the breaking of the $C–SO_3^-$ (and also of the $C–CO_2^-$) bond requires a greater activation energy than that of the C–H bond,[25] thus favoring k_{-1} over k_2 in these cases. Furthermore, in iodination by iodine the back reaction in the first step involves a nucleophilic attack by iodide ion on iodine, whereas in iodination by iodine monochloride the attack would have to be made by the less nucleophilic chloride ion, so that even if mechanism II should hold for the iodination by iodine, it would be less likely for iodine monochloride.

The evidence presented here therefore favors mechanism I, or one of its variants, but mechanism II cannot be ruled out.

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[21] See for instance H. Zollinger, *Helv. Chim. Acta*, **38**, 1597, 1617 (1955).

[22] L. Melander, *Acta Chem. Scand.*, **3**, 95 (1949); *Arkiv Kemi*, **2**, 211 (1950); W. M. Lauer and W. E. Noland, THIS JOURNAL, **75**, 3689 (1953); T. G. Boner, F. Bowyer and G. Williams, *J. Chem. Soc.*, 2650 (1953); P. B. D. de la Mare, T. M. Dunn and J. T. Harvey, *ibid.*, 923 (1957).

[23] G. S. Hammond, THIS JOURNAL, **77**, 334 (1955).

[24] E. Grovenstein, Jr., and U. V. Henderson, Jr., *ibid.*, **78**, 569 (1956).

[25] L. G. Cannell, *ibid.*, **79**, 2927, 2932 (1957). For a similar mechanism in the acid-catalyzed decarbonylation see W. M. Schubert and P. C. Myhre, Abstract of Papers of the 130th Meeting of the American Chemical Society, Atlantic City, N. J., September 16–21, 1956, p. 58-O.

[26] E. Grovenstein, Jr., and D. C. Kilby, *ibid.*, **79**, 2972 (1957).

[27] For literature references see ref. 24, 25, 26.