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

Kinetics of Aromatic Halogenation. III.[1] The Iodination of *p*-Chloroaniline with Iodine Monochloride

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The kinetics of iodination of *p*-chloroaniline with iodine monochloride has been studied in water containing an excess of chloride and hydrogen ions. The results are in agreement with a reaction involving the free amine and the hypoiodous acidium ion, H_2OI^+.

Although iodine monochloride has been used as an iodinating agent for over 100 years,[2] the only kinetic study of ICl substitution is that of Lambourne and Robertson, who used glacial acetic acid or chlorobenzene as solvent for the iodination of various aromatic compounds.[3] The authors found that iodination by ICl in these solvents is inhibited by the HCl formed during the reaction and the consequent formation of $HICl_2$ and that, like bromination in acetic acid, it is a complex reaction, which is first order with respect to aromatic compound and second order in ICl. At higher temperatures the order with respect to ICl approaches one.

Most of the preparative methods for ICl iodination follow with a slight modification the procedure of Michael and Norton,[2] who used either acetic acid or hydrochloric acid solutions for the iodination of amines and acetanilide.[4] In order to approximate one of these preparative procedures, a study of the iodination with ICl of *p*-chloroaniline in water containing an excess of both chloride and hydrogen ions has been carried out. These conditions were considered desirable in order to prevent hydrolysis of ICl[5] and to supply a constant, large excess of chloride ions, which act as a buffer for the chloride ions formed during the reaction

$$p\text{-}ClC_6H_4NH_2 + ICl \longrightarrow p\text{-}Cl\text{-}o\text{-}IC_6H_3NH_2 + H^+ + Cl^-$$

One of the specific aims of the investigation was to gain some insight into the nature of the substituting agent in iodination by ICl.

Experimental

Materials.—A sample of *p*-chloroaniline (Eastman Kodak Co.) was distilled *in vacuo* (3 mm., 75–77°) and recrystallized first from 50% ethanol and then three times from benzene–ligroin (60–70°). The colorless, crystalline product was dried in a vacuum desiccator, ground in a mortar and stored in an amber bottle; m.p. 70.0–70.7° cor. (lit.[6] 70–71°). All inorganic materials were best commercial Reagent Grade chemicals and, with the exception of ICl, were used without further purification.

The purest sample of ICl was obtained by high-vacuum sublimation, in which about one-half of the material was discarded and the ICl remaining in the middle trap was used.[7,8] With this sample iodinations proceeded practically to completion. Other samples contained an impurity, easily corrected for in the kinetic runs, which liberated iodine from KI, but did not give a starch test and did not iodinate; it was probably iodic acid. Whether or not a non-iodinating residue remained (never more than 1–2%) depended also on the way in which the ICl stock solution was prepared. The following method yielded solutions with which no corrections were necessary. The ICl was heated in a thermostat at 28–29° until most of it had liquified. About 100 mg. (10–11 drops) was pipetted with a syringe into a suspension of 0.2 mole of NaCl and about 10–20 ml. of water. The material was mixed by swirling, transferred quantitatively to a 100-ml. volumetric flask and diluted to volume. This stock solution was light yellow and turned slightly orange; it contained enough chloride ion to prevent hydrolysis. With $HClO_4$ present the solution was lemon-colored. The stock solution was stable for a long time and did not change in titer for several weeks.

Kinetic Runs.—Stock solutions of *p*-chloroaniline in perchloric acid and of all other reagents were prepared, and appropriate amounts were pipetted into a 250-ml. flask. Enough water was pipetted into the mixture to bring the solution to 95 ml., and this solution, as well as the ICl stock solution, were thermostated at the desired reaction temperature. A 5-ml. sample of the ICl was pipetted into the flask with vigorous swirling, and a 10-ml. sample was immediately withdrawn from the reaction mixture for the initial titer. This operation required about 20–30 seconds. The 10-ml. sample was pipetted into a solution of 15 ml. of 1 *N* sulfuric acid and 5 ml. of a 5% KI solution and titrated to the starch end-point with 0.02 *N* thiosulfate from a 5-ml. microburet graduated in hundredths. With very fast runs, the initial titer was determined by a blank. Usually 8 samples were withdrawn for one run and, when necessary, one sample was allowed to stand for at least 10 half-lives to determine the final ICl titer. Rate constants were calculated from the integrated form of the second-order rate equation. All runs were conducted at least in duplicate. The average deviations within each run were rarely more than 1.5% and the duplicate runs also agreed within 1.5% and usually better. Where constants were obtained by least square plots, the quoted errors are the probable errors in the least square constants. All runs were conducted in a dimmed-out room, although it was not demonstrated that light influenced the reaction. Rate constants for the activation energies are corrected for volume changes.

Isolation Runs.—The main isolation run, which was conducted under conditions similar to those used in the kinetic determinations, was carried out on a 1-l. scale. The final solution was 0.01 *M* in amine, 0.5 *M* in both NaCl and $HClO_4$, and 0.00265 *M* in ICl, the last value being determined by titration of a separate sample. The solution, which soon became colorless, was allowed to stand for two days at room temperature and for two more days in the

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(1) For previous publications in this series see E. Berliner, THIS JOURNAL, **72**, 4003 (1950); **73**, 4307 (1951).

(2) J. F. Brown, *Ann.*, **92**, 321 (1854); *Phil. Mag.*, [4] **8**, 201 (1854); P. Schuetzenberger, *Jahresber.*, 349 (1861); 251, 413 (1862); J. Stenhouse, *J. Chem. Soc.*, **17**, 327, 366 (1864); A. Michael and L. M. Norton, *Ber.*, **11**, 107 (1878); C. Willgerodt and E. Arnold, *ibid.*, **34**, 3343 (1901); A. E. Bradfield, K. J. P. Orton and I. C. Roberts, *J. Chem. Soc.*, 782 (1928); B. Jones and E. N. Richardson, *ibid.*, 713 (1953).

(3) L. J. Lambourne and P. W. Robertson, *ibid.*, 1167 (1947).

(4) For instance: "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 196, 343, 349.

(5) P. Schuetzenberger, *Cómpt. rend.*, **84**, 389 (1877); E. C. Sullivan, *Z. physik. Chem.*, **28**, 523 (1899); A. E. Gillam and R. A. Morton, *Proc. Roy. Soc. (London)*, **132**, 152 (1931); J. H. Faull, THIS JOURNAL, **56**, 522 (1934); F. A. Philbrick, *ibid.*, **56**, 1257 (1934). For recent general reviews of the properties of ICl see N. V. Sidgwick, "The Chemical Elements and Their Compounds," Oxford Press, Oxford, Vol. II, 1950, pp. 1151, 1190; A. G. Sharpe, *Quart. Revs.*, **4**, 115 (1950).

(6) I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1943.

(7) G. G. Palmer and E. O. Wiig, THIS JOURNAL, **74**, 2785 (1952).

(8) I am greatly indebted to Dr. G. Zimmerman of this Department for his help in the fractional high-vacuum sublimation of the ICl sample.

ice-box. The diiodo compound which precipitated directly from the acid solution was filtered and recrystallized from aqueous ethanol. The crystallized material melted at 127.2–127.8° (lit.[9] 129°) and was obtained in 7.1 and 6.1% yield in duplicate runs. The mother liquor from the first precipitation of the diiodo compound was made strongly alkaline with solid NaOH, and the monoiodo compound which precipitated at this point was filtered on a sintered-glass funnel, after being stored in the ice-box for two days. The crude 2-iodo-4-chloroaniline, obtained in duplicate runs in 76.5 and 67.1% yield, melted at 39.2–40.2° and was crystallized from petroleum ether. The crystallized material (67.8 and 59.7%) formed long needles and melted at 40.0–41.0°. A further recrystallization from petroleum ether did not change the m.p. (lit. m.p. 46° from water[9]). The acetyl derivative formed white long needles from aqueous ethanol and melted at 148.2–149.2° (lit.[9] 150°); mixed m.p. with an authentic sample[9] was undepressed. All melting points are corrected. The isolation runs recorded in Table VII were conducted exactly as above, except that hydrochloric acid was used to provide both hydrogen and chloride ions. The solutions were all 0.5 *M* in HCl.

Results

The Order of the Reaction.—With an excess of hydrogen ions and chloride ions, the iodination reaction is strictly second-order over-all within one run, as shown by two examples in Table I.

TABLE I

THE IODINATION OF *p*-CHLOROANILINE WITH IODINE MONOCHLORIDE AT 25°

p-Chloroaniline 0.005 *M*, $HClO_4$ 0.405 *M*, NaCl 0.4 *M*, $NaClO_4$ 0.4 *M*, ICl ≌0.001 *M*			*p*-Chloroaniline 0.004 *M*, $HClO_4$ 0.05 *M*, NaCl 0.9 *M*, $NaClO_4$ 0.25 *M*, ICl ≌ 0.001 *M*		
Time, min.	0.02 *N* thiosulfate, ml.	10^2k_{obs}, l. mole^{-1} sec.$^{-1}$	Time, min.	0.02 *N* thiosulfate, ml.	10^3k_{obs}, l. mole^{-1} sec.$^{-1}$
0	1.070	...	0	1.036	...
7	0.964	5.02	5	0.900	12.1
14	.871	5.00	10	.788	12.0
22	.777	5.00	15	.691	12.0
30	.695	5.00	21	.590	12.1
40	.604	5.03	27	.510	12.1
51	.521	5.02	34	.430	12.1
67	.421	5.02	41	.366	12.1
			∞	.014	

In Table II are recorded rate constants for runs in which both the amine and the ICl concentrations were varied at constant hydrogen and chloride ion concentration. The constancy of k_{obs} confirms the second-order nature of the reaction, and establishes the reaction as strictly first order with respect to both *p*-chloroaniline and ICl. For reasons mentioned later, it was important to look for a possible reaction, zeroth-order in aromatic compound, and the kinetics was therefore investigated over a fairly wide range of concentrations, but a tenfold change in either component does not materially alter the value of the second-order rate constant. At high concentrations the constants tend to become somewhat larger, possibly because some diiodo compound precipitates. In runs in which the ratio of amine to ICl is 2:1 or 1:1, the amount of the diiodo compound, 2,6-diiodo-4-chloroaniline, is not negligible, and rate constants calculated for monosubstitution show a slight upward drift as reaction progresses. The last three entries show that at a lower hydrogen ion concentration the reaction is also second order.

TABLE II

THE DEPENDENCE OF THE RATE ON THE INITIAL CONCENTRATION OF REACTANTS

p-Chloroaniline × 10^3	10^3 ICl	10^2k_{obs}, l. mole^{-1} sec.$^{-1}$
$HClO_4$ 0.4 *M*, NaCl 0.5 *M*, *T* = 25°		
2.5	0.76	3.72
5.0	0.76	3.70
2.0	1.28	3.72
5.0	1.28	3.70
8.0	1.28	3.68
12.0	1.28	3.70
2.0	1.99	3.80[a]
5.0	2.56	3.80
10.0	2.56	3.72
15.0	1.97	3.72
5.0	4.94	3.82[a]
10.0	4.92	3.80
15.0	4.92	3.82
20.0	4.92	3.82[b]
25.0	7.87	3.87[b]
$HClO_4$ 0.04 *M*, NaCl 1.5 *M*		
2.0	0.918	5.82
6.0	0.910	6.13
6.0	2.715	6.08

[a] Taken to only about 45% reaction. [b] Some material precipitated as reaction progressed.

Dependence on Hydrogen Ion Concentration.—The rate of the reaction is inversely proportional to the hydrogen ion concentration at constant chloride ion concentration and constant ionic strength. This was demonstrated over three ranges of hydrogen ion concentration (0.8 to 0.1, 0.08 to 0.02 and 0.02 to 0.008 *M*), for which the chloride ion concentrations were 0.4, 0.9 and 1.4 *M*, respectively. In Fig. 1 is shown one plot of k_{obs} against $1/H^+$ for which the least square slope has the value (23.7 ± 0.05) × 10^{-3}, and slopes obtained from the other data have similarly small de-

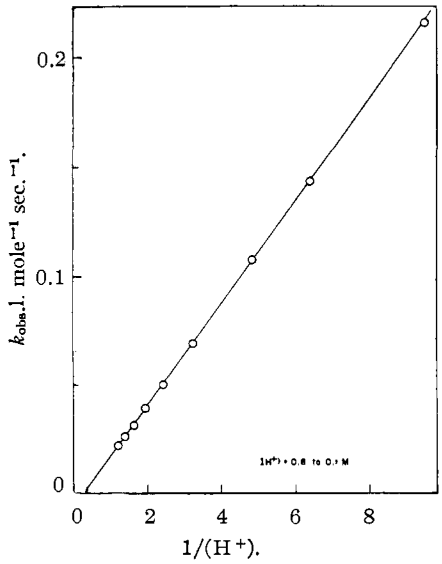

Fig. 1.—The dependence of the rate on the hydrogen ion concentration; (H^+) = 0.8 to 0.1 *M*.

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[9] F. B. Dains, T. H. Vaughan and W. M. Janney, THIS JOURNAL, **40**, 930 (1918); F. B. Dains and A. W. Magers, *ibid.*, **52**, 1572 (1930).

viations from linearity. Since the dependence of the rate on the chloride ion concentration is known (see below), the three sets can be recalculated to one chloride ion concentration, and in Fig. 2 are shown the combined data, where log k_{obs} is plotted against log 1/H$^+$. The slope has the value 1.06 ± 0.0034, instead of unity, demanded by the inverse relationship. Furthermore, at very high acid concentrations (1–5 M), log k_{obs} is linear in Hammett's acidity function,[10] rather than the logarithm of the acid concentration, with a slope of 1.17 ± 0.011 (Table III). Such deviations from unit slope have been observed in other cases, and have been ascribed to salt effects.[11]

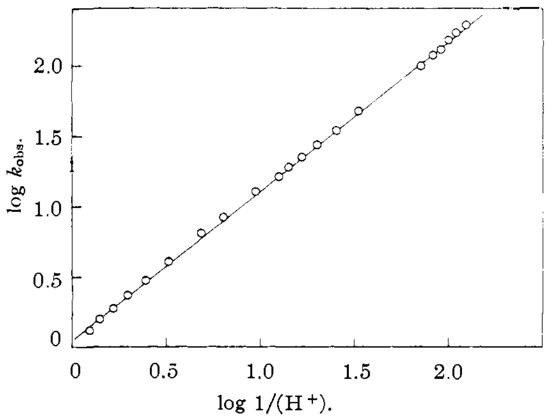

Fig. 2.—The dependence of the rate on the hydrogen ion concentration.

TABLE III

THE DEPENDENCE OF THE RATE ON THE ACIDITY FUNCTION

p-Chloroaniline 0.005 M, NaCl 0.1 M, ICl ≌0.001 M, T = 25°

$HClO_4$, moles/ liter	$10^2 k_{obs}$, l. mole^{-1} sec.$^{-1}$	H_0[a]
1.0[b]	22.7	−0.11
2.0	5.80	−0.66
3.0	1.61	−1.13
4.0	0.427	−1.60
5.0	0.107	−2.10

[a] Recalculated to moles per liter from the values of L. P. Hammett and A. J. Deyrup, THIS JOURNAL, 54, 2721 (1932), and L. P. Hammett and M. A. Paul, *ibid.*, 56, 827 (1934), and densities listed in "Int. Crit. Tab.," Vol. 3, 1927. [b] p-Chloroaniline was 0.004 M in this run.

The Effect of Chloride Ions.—The chloride ions formed during the reaction react with unused ICl to form the ICl_2^- ion, and the second-order rate constants within one run decrease, unless the initial chloride ion concentration is large enough to swamp the amount of chloride ion formed. In the present runs the initial chloride ion concentration was always over 100 times larger than the initial ICl concentration, large enough to give no indication of a drift within one run. Since ICl also complexes with the initial chloride ions, the over-all reaction depends on the initial chloride ion concentration (Table IV). Because of the equilibrium 1[12]

$$ICl_2^- \rightleftharpoons ICl + Cl^- \quad K_1 \qquad (1)$$

and the relation

$$(ICl)_{eq} = (ICl)_{st} - ICl_2^- \qquad (1a)$$

where the subscripts eq and st refer to equilibrium (actual) and to stoichiometric (titratable) concentrations, respectively, the relation holds

$$(ICl)_{eq} = (ICl)_{st} \times K_1/(K_1 + Cl^-)$$

When reactions were conducted with different initial chloride ion concentrations, the rate was found to be proportional to $K_1/(K_1 + Cl^-)(Cl^-)$. In Fig. 3 is shown a plot of the observed rate constants at constant hydrogen ion concentration and constant ionic strength against the expression $K_1/(K_1 + Cl^-)(Cl^-)$. Over the fourfold variation in chloride ion concentration, the straight line has a slope of 2.85 ± 0.0068 (and an intercept of 0.00915 ± 0.00043). In Table IV are listed the data from which the line is obtained together with the calculated rate constants.

TABLE IV

THE DEPENDENCE OF THE RATE ON THE CHLORIDE ION CONCENTRATION

p-Chloroaniline 0.005 M, $HClO_4$ 0.205 M, ICl ≌0.001 M, μ 1.005, T = 25.0 ± 0.05°

Cl^-, mole/ liter	k_{obs} × 10 l. mole^{-1} sec.$^{-1}$	k(calcd.) × 10[a] l. mole^{-1} sec.$^{-1}$
0.2	4.23	4.24
.3	1.97	1.95
.4	1.16	1.14
.5	0.768	0.767
.6	.555	.562
.7	.435	.437
.8	.343	.357

[a] Calculated from the least square constants of the straight line.

Effect of Ionic Strength.—The rates decrease almost linearly with an increase in ionic strength (Table V). These runs were conducted at the rather high ionic strength of 0.8–2.0 M and at constant hydrogen and chloride ion concentrations. The over-all decrease within that range is about 35%. Because of this effect, the ionic strength in all other runs was kept constant by the addition of $NaClO_4$.

Activation Energies and Entropies.—From the least-square plot of log k_{obs} against 1/T at four

TABLE V

THE DEPENDENCE OF THE RATE ON IONIC STRENGTH

p-Chloroaniline 0.004 M, NaCl 0.4 M, $HClO_4$ 0.4 M, ICl ≌ 0.001 M, temp. is 25.0 ± 0.05°

μ, mole/l.	$10^2 k_{obs}$, l. mole^{-1} sec.$^{-1}$
0.8	5.62
1.0	5.35
1.2	5.05
1.4	4.70
1.6	4.35
1.8	3.98
2.0	3.65

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(10) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 267 ff.

(11) R. P. Bell and A. H. Brown, *J. Chem. Soc.*, 774 (1954); D. McIntyre and F. A. Long, THIS JOURNAL, **76**, 3240 (1954); V. Gold and J. Hilton, *J. Chem. Soc.*, 843 (1955).

(12) J. H. Faull, ref. 5; K_1 is 0.006.

different temperatures, the activation energy for the over-all substitution reaction is calculated to be 16.5 ± 0.05 kcal. Log PZ has the value 10.84 ± 0.035 l. mole^{-1} sec.$^{-1}$, and the over-all activation entropy has the negative value, $\Delta S^* = -10.91$ e.u.[13] (Table VI).

TABLE VI

THE DEPENDENCE OF THE RATE ON TEMPERATURE

p-Chloroaniline 0.004 M, $HClO_4$ 0.4 M, NaCl 0.4 M, ICl $\cong$ 0.001 M

T, °C.	k_{obs},[a] l. mole^{-1} sec.$^{-1}$
35.0	0.137
25.0	.0561
17.98	.0286
11.49	.0148

[a] Corrected for volume changes.

Product Isolation.—In a large scale kinetic run, in which the ratio of amine to ICl was 4:1, there was isolated a 67.8% yield of once-crystallized 2-iodo-4-chloroaniline and a 7.1% yield of once-crystallized 2,6-diiodo-4-chloroaniline. No other products could be detected. The kinetic runs were usually conducted with a four- to fivefold excess of amine, and the small amount of disubstitution product did not noticeably alter the rate constants.

Since the mono- and disubstitution products are easily separated by virtue of their different basicities, several experiments were conducted with a view of establishing the amount of disubstitution as a function of the amine-to-ICl ratio. The yields listed in Table VII refer to once-crystallized product. With an 8-fold excess of amine, the amount of diiodo compound is about 2%, and it gradually increases to become the predominant product when the ICl is twice the concentration of the amine. Since the method of separation is simple, these figures might be of some value for the preparation of these compounds, which had previously been made by iodination with iodine.[9]

TABLE VII

THE AMOUNT OF DISUBSTITUTION IN THE IODINATION OF *p*-CHLOROANILINE

p-Chloroaniline, mole/liter	ICl, mole/liter	*p*-Chloroaniline: ICl	2,6-Diiodo-4-chloroaniline, %
0.02	0.0025	8:1	1.4
.02	.0025	8:1	2.4
.01	.002	5:1	3.9
.02	.004	5:1	4.8
.01	.0025	4:1	4.1
.02	.005	4:1	5.3
.01	.005	2:1	14.9
.02	.01	2:1	11.6
.01	.01	1:1	33.5
.02	.02	1:1	28.6
.005	.01	1:2	92.0
.005	.01	1:2	91.5

Discussion

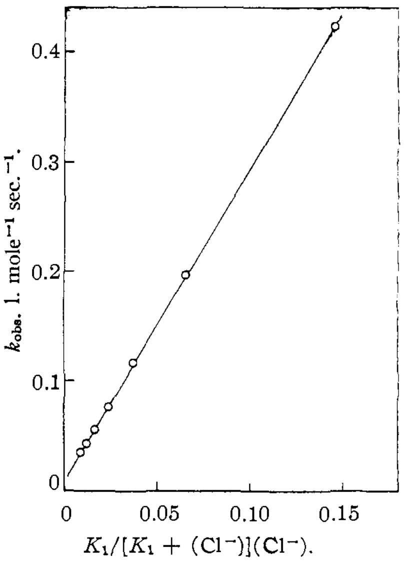

Fig. 3.—The dependence of the rate on the chloride ion concentration.

The important results of the iodination studies are that the reaction rate is inversely proportional to the hydrogen ion concentration and that it is proportional to the term $K_1/(K_1 + Cl^-)(Cl^-)$. The latter is equivalent to saying that it is inversely proportional to the chloride ion concentration after allowing for the complexing of ICl with chloride ion.

The inverse dependence of the rate on the first power of the hydrogen ion concentration is best explained by assuming that the species which is iodinated is the free amine. At the high acid concentrations used, the base is present almost completely as the salt, and the concentration of the free base will be given by $(ArNH_2)_{free} = (ArNH_2)_{st} \times K_2/(K_2 + H^+)$, where $(ArNH_2)_{st}$ is the stoichiometric concentration of amine used. Because the equilibrium constant for (2) is of the order of 10^{-4},[14]

$$p\text{-Cl-}C_6H_4NH_3^+ \rightleftarrows p\text{-Cl-}C_6H_4NH_2 + H^+ \quad K_2 \qquad (2)$$

it can be neglected in the denominator at the hydrogen ion concentrations used, and the concentration of free base will be inversely proportional to the H^+ concentration, *i.e.* $= (ArNH_2)_{st}(K_2/H^+)$, as found. This is, of course, anticipated by the chemical evidence, because the amine is exclusively substituted *ortho* to the amino group, whereas *meta* substitution should have resulted if the *p*-chloroanilinium ion were involved. The conclusion is justified that the reaction takes place on the free amine and that it is otherwise independent of the hydrogen ion concentration.[15] Because the acid dependence of the

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(13) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 417.

(14) J. C. James and J. G. Knox, *Trans. Faraday Soc.*, **46**, 254 (1950).

(15) The plots of k_{obs} against $1/H^+$ should, strictly, go through the origin, but all three have actually an experimentally real negative intercept. For instance, for the above quoted case (H^+ = 0.8 to 0.1 M) the intercept is $(-7.18 \pm 0.23) \times 10^{-3}$. These intercepts have probably no mechanistic significance and might be due to specific effects or deviations because of the high ionic concentrations used. If any physical meaning be given to the intercepts, it would mean that iodination of the amine ceases before all of it has been completely converted to the salt. The situation might then be similar to the nitration of nitrobenzene in sulfuric acid, where hydrogen bonding between nitrobenzene and sulfuric acid has been suggested as an explanation for the decrease in rate with increasing sulfuric acid.[16]

(16) R. J. Gillespie and D. J. Millen, *Quart. Revs.*, **2**, 277 (1948).

reaction is due only to the spurious choice of an amine as the aromatic compound, the proportionality between log k_{obs} and H_0 has probably no other meaning than that the ratio $\log f_{\text{BH}^+}/f_{\text{B}}$ for *p*-chloroaniline is affected by the medium in the same way as the corresponding expression for the indicator base that was used in defining H_0.

The observed rate constant should be proportional to $K_1/(K_1 + \text{Cl}^-)$ if molecular ICl were the iodinating agent. This relationship is not observed, and molecular iodine monochloride must therefore be ruled out. Taking account of the chloride ion dependence only, the substituting agent could be HOI. Because of (3) k_{obs} should be equal

$$\text{ICl} + \text{H}_2\text{O} \rightleftarrows \text{HOI} + \text{H}^+ + \text{Cl}^- \quad K_3 \qquad (3)$$

to $k_3K_1K_2K_3/(K_1 + \text{Cl}^-)(\text{Cl}^-)(\text{H}^+)^2$, assuming the free amine to be involved. While this expression gives the correct chloride ion dependence, it demands an inverse square relationship of hydrogen ions, which is not observed; hypoiodous acid must therefore also be ruled out. The observed dependence is obtained if (3) is followed by (4)

$$\text{HOI} + \text{H}^+ \rightleftarrows \text{H}_2\text{OI}^+ \quad K_4 \qquad (4)$$

or if the hydrolysis is represented by (3) plus (4) to give (5).[17]

$$\text{ICl} + \text{H}_2\text{O} \rightleftarrows \text{H}_2\text{OI}^+ + \text{Cl}^- \quad K_5 \qquad (5)$$

For the reaction between the free amine and the hypoiodous acidium ion (the conjugate acid of hypoiodous acid) the relation holds

$$\text{rate} = k_{\text{obs}}\,(\text{amine})_{\text{st}}(\text{ICl})_{\text{st}} = k_5\,(\text{amine})_{\text{eq}}(\text{H}_2\text{OI}^+) = \frac{k_5K_1K_2K_5(\text{amine})_{\text{st}}(\text{ICl})_{\text{st}}}{(K_1 + \text{Cl}^-)(\text{Cl}^-)(\text{H}^+)}$$

and therefore

$$k_{\text{obs}} = \frac{k_5K_1K_2K_5}{(K_1 + \text{Cl}^-)(\text{Cl}^-)(\text{H}^+)}$$

as observed.[18] The experimental results can also be reproduced by the ionization (6) or (7) in which

$$\text{ICl} \rightleftarrows \text{I}^+ + \text{Cl}^- \quad K_6 \qquad (6)$$

$$2\text{ICl} \rightleftarrows \text{I}^+ + \text{ICl}_2^- \quad K_7 \qquad (7)$$

case for (6) $k_{\text{obs}} = k_6K_1K_2K_6/(K_1 + \text{Cl}^-)(\text{Cl}^-)(\text{H}^+)$.[18] Because H_2OI^+ and I^+ differ only by a molecule of water they are kinetically not distinguishable.

Another possibility, allowed by the kinetics, involves a reaction between hypoiodous acid and the *p*-chloroanilinium ion, but, as in the iodination of aniline by iodine,[1] this possibility can be rejected on chemical grounds. A cationic species of iodine is thus left as the most plausible substituting agent, and the iodination is suitably represented by

$$-\text{d}x/\text{d}t = k(p\text{-chloroaniline})(\text{HOI})(\text{H}^+) = k_5(p\text{-chloroaniline})(\text{H}_2\text{OI}^+)$$

an expression which is similar to that obtained for the iodination of aniline and phenol by molecular iodine.[1,19] The term $(\text{HOX})(\text{H}^+)$ has also been observed in the chlorination and bromination by the hypohalous acids.[20]

The iododichloride ion, ICl_2^-, has been ruled out as the iodinating agent. However, in the plot of k_{obs} against $K_1/(K_1 + \text{Cl}^-)(\text{Cl}^-)$ (Fig. 3) there is obtained a very small, but finite positive intercept. If this is real and mechanistically significant, it would indicate a very small amount of iodination by ICl_2^-.[21] While ICl_2^- is not an impossible iodinating agent, it is not a very likely one and, with the iodine in the middle,[22] has an unfavorable geometry for substitution. The small positive intercept might equally well be a kinetic artifact, perhaps due to the very high ionic strength of the solutions. The latter explanation is preferred, but the question should be left open.

There is no difficulty in accepting the species H_2OI^+. Its existence has been justified thermodynamically by Bell and Gelles, who confirmed their calculations by direct electrometric measurements.[23] Spectral evidence has since also been adduced.[24] Using the appropriate equilibrium constants from the literature,[14,12,23] the specific rate constant for the reaction of *p*-chloroaniline with H_2OI^+, at a 0.1 *M* concentration of hydrogen and chloride ions (and neglecting the effect of the ionic strength), is about 5×10^5 times the observed rate constants.

Inasmuch as there exists a difference between the hypoiodous acidium ion H_2OI^+ and the iodinium ion I^+ (which would be electrostatically hydrated), and the two are separated by an energy barrier,[25] it is of importance to distinguish between the two. Such a distinction has been made for the pair $\text{H}_2\text{O-Cl}^+$ and Cl^+ on kinetic grounds, based on the occurrence of a zeroth-order reaction.[25,26] No such reaction of zeroth-order with respect to aromatic compound was observed in the present iodination over the investigated concentration range (Table II). The lack of a zeroth-order reaction could be explained by assuming that in the case of the more electropositive iodine an equilibrium concentration of I^+ is built up, which is not used up as fast as it is formed, leading to the dependence of the rate on the aromatic compound. This argument, however, is not in agreement with the thermodynamic calculations, which show that the bare I^+ must have such a low equilibrium concentration that it would seem to be a very unlikely kinetic intermediate.[23] For that reason, and in the absence of other compelling evidence, the hypoiodous acidium ion H_2OI^+ is at

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(17) For instance, see K. J. Morgan, *Quart. Revs.*, **8**, 123 (1954).

(18) Because the complete expression for total ICl_{st} (1a) should also contain terms for H_2OI^+ and HOI, the strict derivation for k_{obs} contains the terms K_1K_5 and K_1K_3/H^+ in the denominator. These have been considered negligibly small compared to $(K_1 + \text{Cl}^-)(\text{Cl}^-)$, which is justified under the present conditions, where in the least favorable case they contribute only about 0.2%, and usually less than 0.1%, to the denominator.

(19) B. S. Painter and F. G. Soper, *J Chem. Soc.*, 342 (1947).

(20) E. A. Shilov and N. P. Kaniaev, *Compt. rend. acad. Sci. U.R.S.S.*, **24**, 890 (1939) [*C. A.*, **34**, 4062 (1940)]; W. J. Wilson and F. G. Soper, *J. Chem. Soc.*, 3376 (1949); D. H. Derbyshire and W. A. Waters, *ibid.*, 564, 574 (1950); 73 (1951); P. B. D de la Mare, E. D. Hughes and C. A. Vernon, *Research*, **3**, 192, 242 (1950); P. B. D. de la Mare, A. D. Ketley and C. A. Vernon, *J. Chem. Soc.*, 1290 (1954).

(21) If this were the case, the specific rate constant for iodination by ICl_2^- can be calculated to be only about 0.001% of the specific rate constant for iodination by H_2OI^+.

(22) R. W. G. Wyckoff, THIS JOURNAL, **42**, 1100 (1920).

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

(24) T. L. Allen and R. M. Keefer, THIS JOURNAL, **77**, 2957 (1955); L. I. Katzin, *J. Chem. Phys.*, **21**, 490 (1953).

(25) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 292–294.

(26) P. B. D. de la Mare, *et al.*, ref. 20.

the moment preferred as the substituting entity.

A hydrogen ion catalyzed reaction between amine and hypoiodous acid, *i.e.* $-\mathrm{d}x/\mathrm{d}t = k(\text{amine})\cdot(\mathrm{HOI})(\mathrm{H}^+)$, is another possibility which is kinetically identical with, but mechanistically slightly different from, the above. The proton could be visualized as attaching itself to the oxygen atom of hypoiodous acid at the moment of substitution and as weakening, through hydrogen bonding, the oxygen–iodine bond. This picture would not require the actual formation of $\mathrm{H_2OI^+}$ prior to substitution.

The quoted activation energy is composite of the ΔH's for all the pre-equilibria, and is therefore not a true measure of the activation energy for the substitution process. The relatively high negative entropy of activation, which is also a composite value, can be ascribed to the formation of ions (in (3) or (5)) from neutral molecules,[27] and is thus confirmatory evidence for the proposed mechanism. Reactions between neutral molecules and ions should show no salt effect at concentrations at which the limiting law applies. The almost linear relation between k_{obs} and μ is a primary salt effect characteristic of reactions between neutral molecules and ions at very high salt concentration.[28]

Acknowledgment.—The generous help afforded by a Frederick Gardner Cottrell Grant of the Research Corporation is gratefully acknowledged.

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

[28] R. P. Bell, "Acid Base Catalysis," Oxford University Press Oxford, 1941, pp. 32–34.

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The Bromination of Polymethylbenzenes in Aqueous Acetic Acid

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The bromination rates of mesitylene, isodurene and pentamethylbenzene in 90 volume % aqueous acetic acid have been measured. The reactions are first order in aromatic hydrocarbon concentration and show mixed first- and second-order dependence on free bromine concentration. Tribromide ion, which accumulates in the media during the course of the reactions, is ineffective as a brominating agent. The rate of the mesitylene reaction is much greater in the aqueous medium than in pure acetic acid. That this difference does not result entirely from the change in dielectric constant of the solvent is suggested by the results of studies of the rate of bromination of mesitylene in chlorobenzene and in acetic-*d* acid.

The effects of perchloric acid on the rate of mesitylene bromination in acetic acid and of light and heavy water on the reaction in carbon tetrachloride also have been investigated.

A series of investigations is in progress in this Laboratory to determine how variations in solvent polarity alter the mechanism of electrophilic aromatic bromination. Previous reports have described kinetic studies of the reaction of bromine and mesitylene in carbon tetrachloride[1] and in pure acetic acid.[2]

In the current investigation similar kinetic studies have been made of the reactions of several polymethylbenzenes, including mesitylene, in aqueous acetic acid (90 volume % acetic acid). The role of the hydroxylic solvent has been examined further by observing the changes in mesitylene bromination rate which occur when acetic-*d* acid or mixtures of acetic-*d* acid and heavy water are substituted for media of normal isotope content. The rates of bromination of mesitylene in chlorobenzene and in acetic acid solutions of perchloric acid also have been investigated, and the relative catalytic effects of light and heavy water in the reaction of bromine with mesitylene in carbon tetrachloride have been measured.

Experimental

Solvents.—Reagent grade acetic acid was further purified and dried by refluxing with chromic anhydride and acetic anhydride.[3] A large batch of 90% acetic acid, for use in rate runs, was prepared by mixing nine volumes of the purified acid with one volume of water.

Sulfur-free carbon tetrachloride (Eastman Organic Chemicals) was dried for several days over freshly ignited Drierite and used without distillation. Chlorobenzene (Eastman Organic Chemicals) was distilled, b.p. 131.1–132.0°, and dried for two days over Drierite.

Deuterium oxide (99.59 ± 0.1%) was obtained from the Stuart Oxygen Co. on allocation from the Atomic Energy Commission. For use in comparative rate runs on protium- and deuterium-containing solvents, samples of acetic acid and of acetic-*d* acid were prepared from acetic anhydride[4] by identical procedures. To 107.5 g. (1.051 moles) portions of distilled (b.p. 137–139°) reagent grade acetic anhydride were added 1.02 moles of deuterium oxide (20.43 g.) or water (18.43 g.). The mixtures were refluxed one hour and were distilled through a short Vigreux column. The first 4 ml. of each distillate was collected separately, and the next 100 ml. of distillate was retained for rate work.

Salts and Perchloric Acid.—Reagent grade sodium bromide and sodium acetate trihydrate were dried at 140° overnight.

A solution of perchloric acid in acetic acid was prepared by passing hydrogen chloride gas into a solution of 5.15 g. of silver perchlorate (prepared by drying the monohydrate, G. Frederick Smith Chemical Co., for four days at 120°) until silver chloride precipitation was complete. The solution was then flushed with nitrogen until it gave only faint turbidity on testing with aqueous silver perchlorate. The hydrogen chloride was generated by dropping concentrated sulfuric acid into concentrated hydrochloric acid. The gases were passed through scrubbing chambers of concentrated sulfuric acid and acetic acid before they were passed into the perchlorate solution. The solution thus prepared was 0.488 *M* in perchloric acid, as was established

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[1] (a) R. M. Keefer, J. H. Blake and L. J. Andrews, THIS JOURNAL, **76**, 3062 (1954); (b) J. H. Blake and R. M. Keefer, *ibid.*, **77**, 3707 (1955).

[2] R. M. Keefer, A. Ottenberg and L. J. Andrews, *ibid.*, **78**, 255 (1956).

[3] K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.*, 983 (1927).

[4] J. D. Roberts, C. M. Regan and I. Allen, THIS JOURNAL, **74**, 3683 (1952).