175. *The Mechanism of Protodeiodination of* p-*Iodoaniline.*

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The rate of protodeiodination of *p*-iodoaniline in aqueous solutions of mineral acids (0·025—6·0M) is shown to be of first order with respect to the stoicheiometric concentration of *p*-iodoaniline, but independent of the concentration of hydrogen ions and of iodide ions. The rate in aqueous solutions is greater than that in deuterium oxide by a factor of about 6. These results indicate: (1) that the transition state for deiodination is similar to that for the uncatalysed mechanism of iodination at lower acidities where the iodinating agent has been shown to be a positive iodine species; (2) that deiodination is therefore a S_E2 reaction of the free amine with a solvated proton; and (3) that the rate of deiodination of the free amine depends on the H_0 acidity function, not on the concentration of hydrogen ions.

THE iodination of aromatic compounds has long been recognised as a reversible process, but recent kinetic investigations have been largely limited to the forward reaction.[1] The only detailed kinetic study of deiodination appears to be that of Gold and Whittaker [2] on the reaction of substituted phenols with hydriodic acid in aqueous acetic acid. In this medium, the kinetics of deiodination are too complex to be easily interpreted in terms of the reaction mechanism. To facilitate comparison with the kinetics of iodination, the experiments reported below were all carried out in water or deuterium oxide as solvent, and this change in medium appears greatly to simplify the kinetic form.

    [1] Berliner, *J. Amer. Chem. Soc.,* 1950, **72**, 4003; cf. de la Mare and Ridd, " Aromatic Substitution," Butterworths, London, 1959, p. 120.
    [2] Gold and Whittaker, *J.,* 1951, 1184.

At 100°, p-iodoaniline reacts at a convenient rate with dilute aqueous acids (~0·1M) containing potassium iodide (~0·5M) to give aniline and iodine, the latter as tri-iodide ions. This reaction has been followed by spectrometric and titrimetric estimation of the iodine formed. Some concurrent oxidation of iodide ions to iodine occurs in the medium. The

TABLE 1. *The dependence of the initial rate* (v_0 *in mole l.$^{-1}$ sec.$^{-1}$) on the concentration of* p-*iodoaniline.*

[HCl] = 0·05M. [KI] = 0·25M. Temp. 98°.

| [NH$_2$·C$_6$H$_4$I] * (M)	0·0025	0·005	0·01	0·02
$10^8 v_0$	17·1	34·8	65·5	134·0
$10^6 k_1$ (sec.$^{-1}$)	68·4	69·6	65·5	67·0

* In this and the following Tables the listed amine concentration is the stoicheiometric value, not the molecular concentration of the free amine.

rate of this " blank reaction " has been studied by preparing reaction mixtures equivalent to those used in the deiodination experiments but containing no p-iodoaniline. Under the conditions used, the initial rate of the blank reaction was about 5—30% of that of the total reaction. Because of certain complications in comparing the blank reaction and the total reaction (see p. 826), this investigation was based on the difference in the initial rates of formation of iodine in the presence and in the absence of p-iodoaniline, and this value is referred to in the Tables as the initial rate of deiodination. Where the blank reaction was unimportant, rate coefficients were also calculated from integrated rate equations and an example is given on p. 826.

The variation of the initial rate of deiodination with the stoicheiometric concentration of p-iodoaniline is indicated in Table 1. The last line shows the values of a rate coefficient (k_1) obtained by dividing the initial rate by the concentration of p-iodoaniline; the constancy of k_1 indicates that the reaction is of first order with respect to the amine.

The effect of acids on the initial rate of deiodination is shown in Table 2; over the range studied the reaction rate is effectively independent of the nature and concentration of the acid. Concentrations of perchloric acid above 0·1M caused some precipitation of potassium perchlorate from the reaction mixture, and some cloudiness also appeared in the solution containing M-sulphuric acid. Experiments with these acids were therefore limited to the lower acidities.

The results in Table 3 show that the initial reaction rate is effectively independent of the concentration of potassium iodide, and no significant difference could be detected at later stages of the kinetic runs. Under the conditions of the experiments, it follows that a 0·25M-concentration of iodide ions is sufficient to displace the equilibrium in equation (1)

$$^+NH_3·C_6H_4I + H^+ + 2I^- = {}^+NH_3·C_6H_5 + I_3^- \qquad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
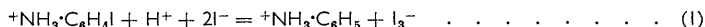
in favour of almost complete deiodination. The iodide ions have no kinetic effect on the reaction rate, and so the superior efficiency of hydriodic acid over other mineral acids in aqueous deiodination appears to arise only from the mass-law effect on the above equilibrium. The results in Table 3 also show that potassium chloride has no significant effect on the reaction rate.

TABLE 2. *The dependence of the initial rate* (v_0, *in mole l.$^{-1}$ sec.$^{-1}$) on acidity.*

[NH$_2$·C$_6$H$_4$I] = 0·01M. [KI] = 0·25M. Temp. 98°.

Acid concn. (M) ...	0·025	0·05	0·10	0·50	1·0	2·0	4·0	6·0
$10^8 v_0$: HCl	71·7	65·5	71·7	65·5	70·4	70·5	67·0	79·2
HClO$_4$	69·1	69·1	70·1	—	—	—	—	—
H$_2$SO$_4$	—	—	—	—	67·6	—	—	—

The pK_a of p-iodoaniline is 3·18,[3] and so, under the conditions listed in Tables 1—3, the stoicheiometric concentration of the amine is effectively equal to the concentration of its conjugate acid. The kinetic form of the reaction is therefore as indicated in equation

[3] Bennett, Brooks, and Glasstone, *J.*, 1935, 1821.

(2), and, in particular, the kinetic equation does not include the concentration of hydrogen ions or that of iodide ions. This result would not have been expected from other published data on deiodination [2] but it can be understood by comparing the transition states for iodination and deiodination.

$$\text{Rate} = k_1[\overset{+}{\text{NH}_3} \cdot \text{C}_6\text{H}_4\text{I}] \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad (2)$$

Kinetic studies on the deiodination of other aromatic compounds have shown that the reaction is an electrophilic displacement of iodine,[2] and hence, at the acid concentrations listed in Tables 1—3, almost certainly involves the free amine. The single term in equation
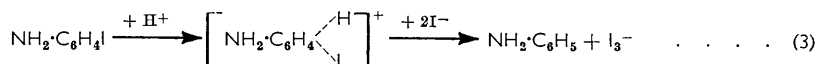
TABLE 3. *The dependence of the initial rate* $(v_0,$ *in mole* $l.^{-1}$ *sec.*$^{-1})$ *on the concentration of potassium iodide and potassium chloride.*

$[\text{H}^+]$ * $= 0.05\text{M}.$ $[\text{NH}_2 \cdot \text{C}_6\text{H}_4\text{I}] = 0.01\text{M}.$ Temp. 98°.

[KI]	0.25	0.50	1.0	2.0	0.25	0.25
[KCl]	—	—	—	—	1.0	4.0
$10^8 v_0$	65.5	60.2	70.4	69.8	71.8 73.9 †	64.6

* Set by either hydrochloric acid or perchloric acid; the difference is not kinetically significant.
† Carried out in the presence of M-hydrochloric acid.

(2) shows that the transition state contains only a free iodoaniline molecule and a proton or hydroxonium ion. The course of substitution in the free iodoaniline can therefore be written as in (3), where the possible hydration of the proton is ignored.

$$\text{NH}_2 \cdot \text{C}_6\text{H}_4\text{I} \xrightarrow{+\ \text{H}^+} \left[\text{NH}_2 \cdot \text{C}_6\text{H}_4 \overset{\text{H}}{\underset{\text{I}}{<}}\right]^+ \xrightarrow{+\ 2\text{I}^-} \text{NH}_2 \cdot \text{C}_6\text{H}_5 + \text{I}_3^- \qquad . \qquad . \qquad . \qquad (3)$$

The kinetic equation of the reverse reaction has been obtained from studies involving buffer solutions [1] and contains several terms, one or more arising from base-catalysis from the components of the buffer. There is also one uncatalysed term and this corresponds to a transition state containing only a free aniline molecule and an iodine cation (possibly hydrated). This is the same composition as the transition state in equation (3) and it therefore appears that the iodination and deiodination experiments involve the same reaction path, despite the considerable difference in the experimental conditions.

This similarity also extends to kinetic isotope effects. Comparison of the aqueous iodination of aniline and 2,4,6-trideuteroaniline shows a k_H/k_D ratio [4] of about 4, and the evidence from other iodinations [5] suggests that this isotope effect appears equally in the uncatalysed and the base-catalysed kinetic terms. This isotope effect must correspond to a considerable weakening of the C–H bond in the transition state, which suggests that proton loss to a water molecule is largely rate-determining. By the principle of microscopic reversibility, deiodination under the same conditions should involve a rate-determining proton transfer to p-iodoaniline from a hydroxonium ion. Electrophilic substitutions of this type, involving slow proton transfers from Brönsted acids, have been termed [6] $A\text{-}S_\text{E}2$.

The estimation of the corresponding isotope effect for deiodination by the same reaction path but under the conditions reported in this paper is complicated by the absence of information on the effective zero-point energy of the solvated proton. Some recent work suggests [7] that this is less than that of an aromatic proton, and so the primary isotope effect in deiodination should be less than the factor of 4 observed in iodination, and should be further reduced by the higher temperature of the deiodination runs. However, in addition, the change to a deuterated medium should decrease [8] the free amine concentration by a factor of 4 at 25° and rather less (possibly 3) at 100°. These factors, taken together, suggest that the $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$ ratio for deiodination should be between 3 and 9.

[4] Shilov and Weinstein, *Nature*, 1958, **182**, 1300; *Doklady Akad. Nauk S.S.S.R.*, 1958, **123**, 93.
[5] Grimison and Ridd, *J.*, 1959, 3019.
[6] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.
[7] Gold, Lambert, and Satchell, *J.*, 1960, 2461.
[8] Högfeldt and Bigeleisen, *J. Amer. Chem. Soc.*, 1960, **82**, 15.

TABLE 4. *Comparison of the rate of deiodination in water and in deuterium oxide* *(containing* 2·5% *of* H_2O).

[HCl] = 0·05M.   [$NH_2 \cdot C_6H_4I$] = 0·01M.   [KI] = 0·25M.   Temp. 98°.

	$10^3[I_2]$ in H_2O			$10^3[I_2]$ in D_2O		
Time (min.)	Total	Blank	Diff.	Total	Blank	Diff.
30	1·25	0·08	1·17	0·27	0·04	0·23
60	2·39	0·12	2·27	0·56	0·09	0·48
90	3·65	0·16	3·49	0·79	0·13	0·66
120	4·52	0·23	4·29	1·03	0·19	0·84
150	5·21	0·27	4·94	1·26	0·23	1·03
180	5·93	0·32	5·61	1·52	0·28	1·24
Mean values of k_1	$76·6 \times 10^{-6}$ sec.$^{-1}$			$13·1 \times 10^{-6}$ sec.$^{-1}$		

$$k_{H_2O}/k_{D_2O} = 5·8.$$

Deiodinations in water and in 97·5% deuterium oxide are compared in Table 4. The conditions were adjusted so that the blank reaction was small, and rate coefficients were calculated from a logarithmic plot of the *p*-iodoaniline concentration. The ratio k_{H_2O}/k_{D_2O} is about 6. This is consistent with the expected mechanism. The conclusion that the primary isotope effect persists in dilute solutions of mineral acids is supported by a recent study [9] of the iodination of anisole, where the k_H/k_D ratio remains constant over the pH range 1—4.

This correspondence between iodination and deiodination has been stressed because it strongly reinforces the argument that deiodination, under the above conditions, occurs by an A-S_E2 mechanism, and therefore permits the kinetic data to be used as evidence of the dependence of A-S_E2 reactions on acidity. The results in Table 2 show that the overall rate of iodination remains effectively independent of acidity, even in the region where the H_0 acidity function deviates from pH. Since the concentration of the free amine is then inversely proportional to h_0 it follows that the rate of substitution in the free amine must be proportional to h_0. If the rate of this substitution were instead proportional to the concentration of the hydroxonium ions then the consideration of the product [$NH_2 \cdot C_6H_4I$][H_3O^+] shows that, in hydrochloric acid, the overall rate of deiodination would decrease by a factor of 17 in going from [H^+] = 0·05 to [H^+] = 6·0. It is impossible to explain the discrepancy between this calculated result and the experimental data by including a large salt effect or chloride-ion catalysis since, as shown in Table 3, potassium chloride has no effect on the overall reaction rate. It seems therefore that, at least for this reaction, the rate of proton transfer from the medium * depends on the acidity function and not on the concentration of hydroxonium ions. This supports the view, recently put forward by other workers,[6,10] that criteria based on acidity functions do not distinguish between prototropic pre-equilibria (mechanism A-1) and rate-determining proton transfer (mechanism A-S_E2).

It is hoped that current studies on the deiodination of other substituted anilines will provide evidence on the factors determining the detailed mechanism of substitution.

EXPERIMENTAL

Materials.—*p*-Iodoaniline (m. p. 63°) was prepared by iodination of aniline [11] and recrystallised three times from light petroleum (b. p. 60—80°). The other components of the reaction mixtures were " AnalaR " reagents. All solids were dried before use.

Kinetic Runs.—The preliminary experiments were carried out by pipetting aliquot parts of

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* One Referee has pointed out that the proton need not come from the medium since the kinetic form is consistent with an intramolecular migration of the proton from the NH_3^+ group to the *para*-position. We consider that the proton would be transferred to the solvent before such a migration could be completed.

[9] Berliner, personal communication.
[10] Melander and Myhre, *Arkiv Kemi*, 1959, **13**, 507.
[11] *Org. Synth.*, Coll. Vol. II, John Wiley and Sons, New York, 1943, p. 347.

the reaction mixture into 50 ml. conical flasks with ground-glass stoppers secured with springs. These solutions were placed in a liquid thermostat at 98° and later withdrawn at suitable times, and the iodine was determined by titration with thiosulphate. Related experiments indicated that there was no significant catalysis by light and no loss of iodine from the stoppered flasks.

It was then found more convenient to carry out the reaction in a 1 cm. Unicam cell fitted with a B.10 stopper secured by springs. This was placed in the thermostat, removed after a suitable time, cooled at once to room temperature, cleaned, and placed in a Unicam S.P. 500 spectrophotometer. After the optical density of the solution had been measured the cell was replaced in the thermostat until the next kinetic point was required. Only the time the cell remained in the thermostat was included in the kinetic run; the rate of deiodination at room temperature is negligible. Errors associated with the time lag of heating to the thermostat temperature were partly compensated by the continuance of reaction during cooling; comparison with the method used for the preliminary experiments indicated that the intermittent heating did not cause appreciable error.

The measurements of optical density were carried out at 500 mμ with a slit width of 0·035 mm. Under the experimental conditions the only effective light absorption at this wavelength is by the I_3^- ion, and the optical density is therefore proportional to the analytical concentration of iodine. The optical density is not significantly affected by other solutes present over the range of components and concentrations listed in Tables 1—4. The extinction coefficient of the I_3^- ion under the above conditions is $2·63 \times 10^2$.

Calculation of the Rate of Deiodination.—Each kinetic experiment on deiodination was accompanied by an equivalent kinetic run carried out in the absence of p-iodoaniline but corrected where necessary to the same effective hydrogen-ion concentration. The difference between the iodine content of the solutions was attributed to deiodination. The implicit assumption that p-iodoaniline does not catalyse or anti-catalyse the oxidation of iodide ions to iodine is supported by the fact that the net rate of formation of iodine is independent of the concentration of iodide ions (see eqn. 2). Also, in a single kinetic run, the net rate of iodine formation is of first order with respect to the concentration of p-iodoaniline, when the latter is calculated on the assumption that the net iodine formed comes only from deiodination. This is illustrated by the integrated rate coefficients below, calculated for the first kinetic run listed in Table 4, where the blank reaction is not important:

Time (min.)	0	30	60	90	120	150	180
$10^3[NH_2 \cdot C_6H_4I]$ (mole l.$^{-1}$)	10	8·83	7·73	6·51	5·71	5·06	4·39
10^5k_1 (sec.$^{-1}$)	—	6·9	7·8	8·0	7·8	7·6	7·6

Since the deiodination uses up hydrogen ions, the reaction mixture and the blank solution are truly equivalent only at the start of the kinetic run, and this factor introduces considerable error into the calculation of integrated rate coefficients for some of the kinetic runs. For consistency, the results in Tables 1—3 are all quoted in terms of the initial rate of deiodination. These values in fact refer to the mean rate of deiodination over the first 10% of reaction and are therefore a little lower than the true initial rate; they are also subject to experimental errors of about ±5%. The accuracy of these results is therefore a little less than that usually reported, but more than sufficient for the mechanistic distinctions referred to above.

Analysis of Products.—A solution of p-iodoaniline (0·01 mole) in 0·05M-perchloric acid (1 l.) containing 0·5M-potassium iodide was heated to 98° for 12 hr., cooled, decolorised with sodium hydrogen sulphite, made alkaline with sodium hydroxide, and then extracted with ether. The ether layer was separated, and the ether distilled off. The remaining oil was treated with bromine water to give a 90% yield of crude 2,4,6-tribromoaniline (m. p. and mixed m. p. 121° after recrystallisation from 50% ethanol). A sample mixed with 2,6-dibromo-4-iodoaniline melted gradually, over the range 110—140°.

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