# 1100. *The Kinetics of Aromatic Protio- and Deuterio-deiodination.*

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The deiodination of iodo-2,4,6-trimethoxybenzene by mineral acids has been kinetically studied in aqueous solution at 25°. The reaction is catalysed by chloride ions according to a complex pattern, which indicates the simultaneous occurrence of two alternative reaction paths, both involving hydrogen and chloride ions, as well as an acid-catalysed path not involving halide ions. The rate constants characterising these processes, and the deuterium isotope effect on them, have been evaluated. The implications of the findings concerning the mechanism of aromatic iodination are indicated.

THE replacement of iodine by hydrogen can be effected by the action of certain acids on aromatic iodo-compounds. Gold and Whittaker,[1] from a study of substituent effects on the reaction velocity of iodophenol with a hydriodic acid–acetic acid–water reagent, concluded that this was an electrophilic aromatic substitution. In discussing the nature of the acidic entity responsible for the reaction under these conditions, they drew attention to the superior effectiveness of hydriodic acid compared to other acids, and therefore concluded that iodine was a constituent of the transition state of the reaction. Choguill and Ridd[2] have stressed that the iodide component of the system has another function in the reaction: it serves to prevent reversal of the reaction (*i.e.*, iodination) by binding the iodine produced in the form of tri-iodide ions. They concluded that, in aqueous solvent mixtures, the rate-limiting step is attack of hydrogen ions on the aryl iodide. This reaction would be the exact analogue of the kinetically important attack of hydrogen ions on a deuterium- or tritium-labelled aromatic compound, which leads to hydrogen-isotope exchange. In this formulation of the deiodination mechanism, the entering proton replaces $I^+$ (which leaves in combination with a suitable residue), whereas in detritiation, the entering proton displaces $T^+$ (which leaves in combination with water as a solvated $H_2TO^+$ ion). It therefore appeared important to test the correctness of these conclusions and the extent of the analogy in isotope effects. The substrate chosen in the present work, iodo-2,4,6-trimethoxybenzene, is therefore exactly comparable with the compound used in our corresponding exchange studies (1,3,5-trimethoxybenzene).[3] These molecules are unlikely to be significantly protonated in the media employed, which means that the dependence of the deiodination on the acidity of an aqueous medium can be examined without referring to the protolytic equilibria of the substrate, as had to be done in the study of iodoanilines.[2] The reaction naturally possesses added interest by the circumstance that its reversal is aromatic iodination, and, by the principle of microscopic reversibility, it is possible to draw conclusions about iodination from information about deiodination.

In both previous kinetic studies[1,2] of protio-deiodination, considerable experimental difficulty was experienced because of the oxidation of iodide ions (or hydriodic acid) in acid solutions by dissolved or atmospheric oxygen. This reaction sets a severe limit to the accuracy of rate measurements based on the determination of iodine. In the present study, this

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[1] V. Gold and M. Whittaker, *J.*, 1951, 1184.
[2] H. S. Choguill and J. H. Ridd, *J.*, 1961, 822.
[3] B. D. Batts and V. Gold, *J.*, 1964, 4284.

difficulty was circumvented by using a reagent other than iodide, namely, 1,1-dimethylcyclohexane-3,5-dione (dimedone), to combine with the iodine generated during the reaction, and the reaction velocity was followed by spectrophotometric observation of the formation of iododimedone.

The reaction did not provide the simple model system which we had hoped to find. An investigation indicated an intricate pattern of mechanisms, which was elucidated by means of detailed kinetic study.

## EXPERIMENTAL

*Iodo-2,4,6-trimethoxybenzene.*—This was prepared by the iodination of 1,3,5-trimethoxybenzene[3] with an equimolar quantity of iodine monochloride[4] in glacial acetic acid solution. At the completion of reaction, the product was precipitated from solution by the addition of water. The precipitate was filtered off, dissolved in chloroform, and washed with aqueous sodium hydroxide solution and water. The layers were separated, the chloroform was distilled off, and the crude product recrystallized several times from ethanol; it had m. p. 122·5° (lit.,[5] m. p. 121°) (Found: C, 36·8; H, 3·9; I, 43·5; OMe, 31·85. Calc. for $C_9H_{11}IO_3$: C, 36·75; H, 3·8; I, 43·2; OMe, 31·7%).

*Dimedone.*—Hopkin and Williams Laboratory Reagent grade was recrystallized several times from water; it had m. p. 148°.

*Inorganic Salts.*—These were recrystallized where necessary and dried overnight at 140° before use.

*Perchloric Acid.*—The AnalaR grade (72%), with a specified maximum chloride content of 0·0001%, was used.

*Kinetic Procedure.*—The reaction was mainly studied spectrophotometrically, the solution being contained in a 3-cm. quartz cell placed inside the thermostatted (25°) cell compartment of a Unicam S.P. 500 spectrophotometer; the increase in absorption at 292 mμ, due to iododimedone, was observed as a function of time. To check that the function of dimedone was confined to its intended rôle of "mopping up" the iodine in a rapid and kinetically insignificant reaction, the reaction velocities under a series of conditions were measured as a function of the dimedone concentration. The rate was found to be constant for dimedone concentrations in the range (8—40) × $10^{-5}$M (Table 1). For all other runs, the concentration of dimedone was kept at 4 × $10^{-4}$M, and the concentration of iodotrimethoxybenzene at *ca.* 2 × $10^{-5}$M. Runs in which this technique was used in the presence of bromide ions were less reproducible, and the one result quoted is not as reliable as are the other rate constants obtained.

TABLE 1.

Observed rate of reaction as a function of dimedone concentration at 25°.
[Iodo-2,4,6-trimethoxybenzene] = 2 × $10^{-5}$M.

| Acid | [Acid] (M) | $10^5$[Dimedone] (M) | $10^5k$ (sec.$^{-1}$) | Acid | [Acid] (M) | $10^5$[Dimedone] (M) | $10^5k$ (sec.$^{-1}$) |
|---|---|---|---|---|---|---|---|
| HCl | 0·1736 | 8 | 77·6 | DCl | 0·1681 | 40 | 39·6 |
| HCl | 0·1736 | 16 | 78·2 | $HClO_4$ | 0·1404 | 20 | 1·03 |
| HCl | 0·1736 | 24 | 76·9 | $HClO_4$ | 0·1404 | 40 | 1·03 |
| HCl | 0·1736 | 32 | 78·2 | $DClO_4$ | 0·1404 | 20 | 1·42 |
| HCl | 0·1736 | 40 | 77·5 | $DClO_4$ | 0·1404 | 40 | 1·39 |
| DCl | 0·1681 | 20 | 39·0 | | | | |

In iodide solution, the above technique could not be used, because of the high absorption of iodide ions at 292 mμ. The course of the reaction was followed, in the absence of dimedone, by noting the increase in absorption of the $I_3^-$ anion at 353 mμ. The results were plotted according to the method of Swinbourne,[6] in order to avoid relying on an infinity reading, which would be most in error owing to atmospheric oxidation of the iodide anions. A potassium iodide concentration of at least 4·0 × $10^{-2}$M was to be found necessary to ensure that the deiodination reaction went to completion. The attempted deiodination in neutral solution in the presence of sodium

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[4] A. E. Bradfield, J. P. Orton, and I. C. Roberts, *J.*, 1928, 782.
[5] H. Kauffmann and F. Kieser, *Ber.*, 1913, **46**, 3788.
[6] E. S. Swinbourne, *J.*, 1960, 2371.

chloride (expt. 20, Table 4) was studied by extraction of iodotrimethoxybenzene from the reaction medium, after this has been made alkaline, into cyclohexane (spectroscopic grade). No change in the concentration of iodotrimethoxybenzene in this extract was detectable spectrophotometrically over a period of 2 days.

TABLE 2.

Observed rate of reaction and solvent isotope effect as a function of perchloric acid concentration at 25°.

[Iodo-2,4,6-trimethoxybenzene] = $2 \times 10^{-5}$M; [dimedone] = $4·0 \times 10^{-4}$M.

| [$HClO_4$] (M) | $10^6 k_H$ (sec.$^{-1}$) | [$DClO_4$] (M) | $10^6 k_D$ (sec.$^{-1}$) | | $k_H/k_D$ |
|---|---|---|---|---|---|
| 0·000 | 0·00 | 0·000 | 0·00 | | — |
| 0·035 | 2·98 | 0·035 | 4·05 | | 0·74 |
| 0·070 | 5·70 | 0·070 | 7·60 | | 0·75 |
| 0·105 | 8·09 | — | — | | — |
| 0·140 | 10·3 | 0·140 | 13·9 | | 0·74 |
| 0·176 | 11·7 | 0·176 | 15·4 | | 0·76 |
| | | | | Average | 0·75 |

TABLE 3.

Observed rate of reaction and solvent isotope effect as a function of hydrochloric acid concentration at 25°.

[Iodo-2,4,6-trimethoxybenzene] = $2 \times 10^{-5}$M; [dimedone] = $4·0 \times 10^{-4}$M.

| [HCl] (M) | $10^5 k_H$ (sec.$^{-1}$) | [DCl] (M) | $10^5 k_D$ (sec.$^{-1}$) | $k_H/k_D$ |
|---|---|---|---|---|
| 0·0331 | 9·04 | 0·0331 | 5·99 | 1·51 |
| 0·0654 | 23·2 | 0·0654 | 12·9 | 1·76 |
| 0·1001 | 39·9 | 0·0994 | 21·2 | 1·87 |
| 0·1346 | 56·7 | 0·1321 | 29·7 | 1·87 |
| 0·1736 | 77·7 | 0·1681 | 39·3 | 1·91 |

TABLE 4.

Observed rate of reaction as a function of salt concentration (in M) at 25° in $H_2O$ solution.

[Iodo-2,4,6-trimethoxybenzene] = $2 \times 10^{-5}$M; [dimedone] = $4·0 \times 10^{-4}$M.

| | Cations | | Anions | | | | |
|---|---|---|---|---|---|---|---|
| Expt. no. | A | [A] | B | [B] | C | [C] | $10^6 k$ (sec.$^{-1}$) |
| | | | [$H^+$] = 0·035M | | | | |
| 1 | — | — | $ClO_4^-$ | 0·035 | — | — | 2.98 |
| 2 | $Na^+$ | 0·010 | $Cl^-$ | 0·010 | $ClO_4^-$ | 0·035 | 62·1 |
| 3 | $Na^+$ | 0·025 | $Cl^-$ | 0·025 | $ClO_4^-$ | 0·035 | 91·0 |
| 4 | — | — | $Cl^-$ | 0·035 | — | — | 103 |
| 5 | $Na^+$ | 0·100 | $Cl^-$ | 0·035 | $ClO_4^-$ | 0·100 | 103 |
| 6 | $Na^+$ | 0·200 | $Cl^-$ | 0·035 | $ClO_4^-$ | 0·200 | 106 |
| 7 | $Na^+$ | 0·040 | $Cl^-$ | 0·040 | $ClO_4^-$ | 0·035 | 106 |
| 8 | $Na^+$ | 0·040 | $Cl^-$ | 0·075 | — | — | 127 |
| 9 | $Na^+$ | 0·080 | $Cl^-$ | 0·115 | — | — | 146 |
| 10 | $Na^+$ | 0·120 | $Cl^-$ | 0·155 | — | — | 156 |
| 11 | $Na^+$ | 0·200 | $Cl^-$ | 0·235 | — | — | 172 |
| 12 | $K^+$ | 0·200 | $Cl^-$ | 0·235 | — | — | 174 |
| 13 | $Li^+$ | 0·200 | $Cl^-$ | 0·235 | — | — | 174 |
| 14 | $Na^+$ | 0·320 | $Cl^-$ | 0·355 | — | — | 195 |
| 15 | $Na^+$ | 0·400 | $Cl^-$ | 0·435 | — | — | 213 |
| 16 | $K^+$ | 0·200 | $Cl^-$ | 0·035 | $Br^-$ | 0·200 | 211* |
| | | | [$H^+$] = 0·1736M | | | | |
| 17 | — | — | $Cl^-$ | 0·1736 | — | — | 776 |
| 18 | $K^+$ | 0·040 | $Cl^-$ | 0·1736 | $I^-$ | 0·040 | 1030 |
| 19 | — | — | $ClO_4^-$ | 0·1736 | — | — | 11·4 |
| | | | [$H^+$] ~ $10^{-7}$M | | | | |
| 20 | $Na^+$ | 0·50 | $Cl^-$ | 0·50 | — | — | <0·1 |

* Not accurate.

To test for the possible incursion of demethylation in some experiments (particularly those at high chloride concentrations) as an additional reaction path, a solution of iodotrimethoxybenzene ($2 \times 10^{-5}$M) in 1·0M-hydrochloric acid was allowed to react (23 hr.). A portion of this solution was then rendered alkaline with sodium hydroxide, and non-acidic (non-phenolic) organic compounds were extracted with cyclohexane. The residual aqueous layer was examined spectrophotometrically in the 210-mμ region for the presence of phenolic compounds. None was detected, although *ca.* 3% of hydrolysis would have produced a noticeable absorption at that wavelength. The conclusion that demethylation is not important under our conditions is the expected one, since this reaction in similar compounds is known to require more drastic conditions.[7]

The reaction rates were systematically studied, in both ordinary water and deuterium oxide as solvent: (*a*) as a function of acid concentration, hydrochloric and perchloric acids being used (Tables 2 and 3); and (*b*) as a function of the concentration of various alkali-metal halides, especially sodium chloride, at constant hydrogen-ion concentration (Tables 4 and 5). Experiments in deuterium oxide (Norsk Hydro > 99·5% D) are indicated by the formula ($DClO_4$ or DCl) given to the catalysing acid. Rate constants in water and deuterium oxide are given by the symbols $k_H$ and $k_D$, respectively.

TABLE 5.

Observed rate of reaction as a function of chloride concentration at 25° in $D_2O$ solution.

[Iodo-2,4,6-trimethoxybenzene] = $2 \times 10^{-5}$M; [dimedone] = $4{\cdot}0 \times 10^{-4}$M; [$DClO_4$] = 0·035M.

| Expt. no. | [$ClO_4^-$] (M) | [$Cl^-$] (M) | $10^6k$ (sec.$^{-1}$) | Expt. no. | [$Cl^-$] (M) | $10^6k$ (sec.$^{-1}$) |
|---|---|---|---|---|---|---|
| 1 | 0·035 | 0·000 | 4·05 | 6 | 0·115 | 77·2 |
| 2 | — | 0·010 | 43·1 | 7 | 0·155 | 78·9 |
| 3 | — | 0·025 | 56·1 | 8 | 0·195 | 81·5 |
| 4 | — | 0·035 | 61·2 | 9 | 0·235 | 83·2 |
| 5 | — | 0·075 | 72·6 | 10 | 0·355 | 89·4 |

## DISCUSSION

The main findings may be summarised as follows:

(i) The velocity increases with concentration of perchloric acid at a rate slightly less than strict proportionality would require (Fig. 1). There is an isotope effect, $k_H/k_D = 0{\cdot}75$. In the absence of acid, no reaction is observable.

(ii) Hydrochloric acid is a much better catalyst than is perchloric acid (at 0·176M-acid, $k(HCl)/k(HClO_4) \sim 70$). The rate increases with acid concentration slightly more rapidly than proportionality would require (Fig. 2). The isotope effect on the rate is now in the opposite direction ($k_H/k_D = 1{\cdot}51$, at an acid concentration of 0·0331M), and increases with rising acid concentration (Table 3).

(iii) The addition of alkali-metal chlorides, at a constant concentration of hydrogen ions, causes a rapid increase with rate up to a chloride concentration of *ca.* 0·15M; beyond that point, the rate increase is approximately linear. Lithium, sodium, and potassium chlorides have the same effect; addition of sodium perchlorate does not influence the rate. There is a large isotope effect on the chloride effect: $k_H/k_D > 1$, increasing with chloride concentration.

(iv) The rate increase caused by potassium chloride is less than that produced by potassium bromide, which, in turn, is much less than that caused by potassium iodide.

It follows from (ii) and (iii) that chloride and other halide ions are important catalysts in the reaction, although a very slow reaction can take place in the absence of halide ions. The shape of the chloride catalysis (Fig. 3) suggests that there is superposition of at least two effects. One of these increases rapidly in importance, and then reaches a limiting value as the concentration of chloride is reached. This limit is met at the point where the catalytic curve assumes a linear form. Another effect is linear in chloride concentration, and is the only effect responsible for the further rate increase from this point onwards. The small intercept indicates that there is also a reaction path not involving halide intervention, but its contribution to the total reaction rate, at the chloride concentrations used, is small. At a fixed

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[7] W. M. Schubert and R. H. Quacchia, *J. Amer. Chem. Soc.*, 1963, **85**, 1284.

hydrogen-ion concentration, the contributions of the three postulated simultaneous processes are easily evaluated, since one of them is given by this small intercept ($k'$), and that due to the linear chloride effect ($k'''$) is obtained as the product of the slope of the linear portion and the chloride concentration. The non-linear contribution $k''$ is then obtained by difference from the total rate constant ($k'' = k - k' - k'''$). This dissection is shown in Table 6 for the experiments with sodium chloride given in Tables 4 and 5.

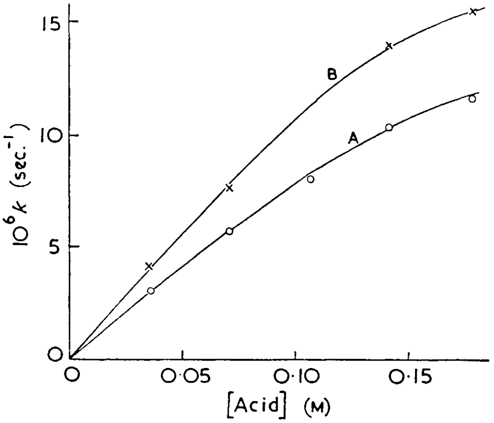

Fig. 1.

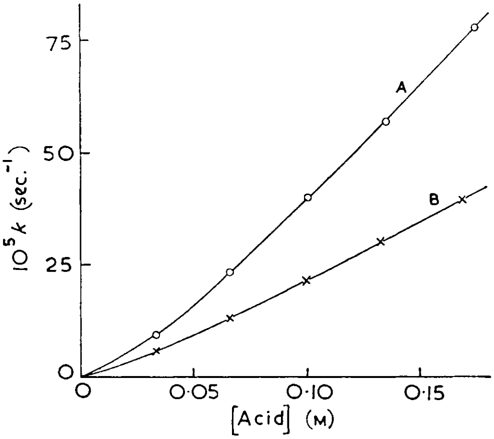

Fig. 2.

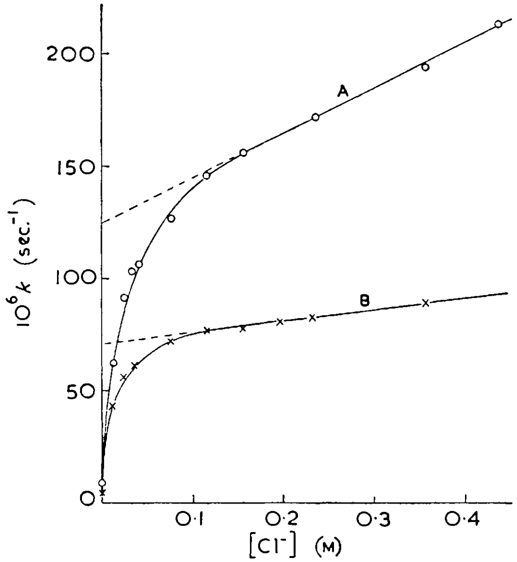

Fig. 3.

Fig. 1. Catalysis by perchloric acid in the absence of chloride ions: A, in $H_2O$; B, in $D_2O$.

Fig. 2. Catalysis by hydrochloric acid: A, in $H_2O$; B, in $D_2O$.

Fig. 3. Catalysis by chloride ions at constant hydrogen-ion concentration (0·035M): A, in $H_2O$; B, in $D_2O$.

By analogy with the accepted mechanism of aromatic halogenation reactions, the reverse reaction studied in this work is considered to be a two-step reaction.[8] The function of chloride ions, with their "less-than-linear" effect on $k''$, suggests that their rôle in that component of the reaction is analogous to the effect of base in the pyridine-catalysed diazo-coupling

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[8] H. Zollinger, *Experientia*, 1956, **12**, 165.

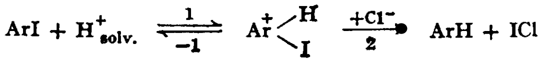
TABLE 6.

The components of the total rate as a function of chloride concentration.

| | In $H_2O$ | | | | In $D_2O$ | | | |
|---|---|---|---|---|---|---|---|---|
| [Cl⁻] (M) | $10^6k$ | $10^6k'$ | $10^6k''$ | $10^6k'''$ | $10^6k$ | $10^6k'$ | $10^6k''$ | $10^6k'''$ |
| 0 | 3·0 | 3·0 | 0 | 0 | 4·1 | 4·1 | 0 | 0 |
| 0·010 | 62·1 | 3·0 | 57·1 | 2·0 | 43·1 | 4·1 | 38·5 | 0·5 |
| 0·025 | 91·0 | 3·0 | 82·9 | 5·1 | 56·1 | 4·1 | 50·7 | 1·3 |
| 0·035 | 103 | 3·0 | 92·9 | 7·1 | 61·2 | 4·1 | 55·3 | 1·8 |
| 0·040 | 106 | 3·0 | 94·8 | 8·2 | — | — | — | — |
| 0·075 | 127 | 3·0 | 108·7 | 15·3 | 72·6 | 4·1 | 64·7 | 3·8 |
| 0·115 | 146 | 3·0 | 119·5 | 23·5 | 77·2 | 4·1 | 67·3 | 5·8 |
| 0·155 | 156 | 3·0 | 121·4 | 31·6 | 78·9 | 4·1 | 67·0 | 7·8 |
| 0·195 | — | — | — | — | 81·5 | 4·1 | 67·6 | 9·8 |
| 0·235 | 172 | 3·0 | 121·0 | 48·0 | 83·2 | 4·1 | 67·3 | 11·8 |
| 0·355 | 195 | 3·0 | 119·5 | 72·5 | 89·5 | 4·1 | 67·6 | 17·8 |
| 0·435 | 213 | 3·0 | 121·3 | 88·7 | — | — | — | — |

Notes: (1) Rate constants in sec.$^{-1}$ throughout. (2) Concentrations of other species, and reaction conditions, are given in Tables 4 and 5. (3) $10^6k'''$ is evaluated as 204[Cl⁻] in $H_2O$, and as 50[Cl⁻] in $D_2O$; the constants are the linear slopes in Fig. 3. (4) The asymptotic values of $10^6k''$ at infinite chloride concentration are calculated from the intercepts of the broken lines in Fig. 3 as 121 sec.$^{-1}$ for $H_2O$ and 67·4 sec.$^{-1}$ for $D_2O$.

reaction between *p*-chlorobenzenediazonium and 2-naphtholate-6,8-disulphonate ions. The following analysis is therefore based on the scheme



$$\mathrm{ArI} + \mathrm{H}^+_{\mathrm{solv.}} \underset{-1}{\overset{1}{\rightleftharpoons}} \mathrm{Ar}^{+}\!\overset{\mathrm{H}}{\underset{\mathrm{I}}{<}} \xrightarrow[2]{+\mathrm{Cl}^-} \mathrm{ArH} + \mathrm{ICl} \qquad \text{(A)}$$

for the $k''$ component. If the concentration of $(\mathrm{HArI})^+$ remains small throughout, it follows that

$$k'' = \frac{k_1k_2\,[\mathrm{H}^+]\,[\mathrm{Cl}^-]}{k_{-1}+k_2\,[\mathrm{Cl}^-]}, \qquad (1)$$

and that the limiting value of $k''$, as $[\mathrm{Cl}^-] \to \infty$, is given by

$$k_\infty'' = k_1\,[\mathrm{H}^+], \qquad (2)$$

the rate of proton transfer from aqueous hydrogen ions to the iodo-compound. Similar mechanistic steps have recently been mentioned for the iodide-catalysed protio-debromination of 2,4,6-tri-t-butyliodobenzene.[9] By combining equations (1) and (2) and rearranging, we obtain

$$\frac{k_{-1}}{k_2} = \left(\frac{k_\infty''}{k''}-1\right)[\mathrm{Cl}^-] \qquad (3)$$

Values of $k_{-1}/k_2$ calculated from equation (3) are given in Table 7. The constancy of this ratio for different chloride concentrations supports the correctness of equation (3).

TABLE 7.

Values of $k_1/k_2$ calculated from equation (3).

| | $10^4k_{-1}/k_2$ | |
|---|---|---|
| $10^3$[Cl⁻] (M) | in $H_2O$ | in $D_2O$ |
| 10 | 112 | 75 |
| 25 | 115 | 82 |
| 35 | 106 | 77 |
| 40 | 110 | — |
| Mean | 111 | 78 |

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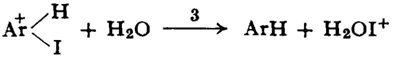
[9] P. C. Myhre, S. L. Murov, R. C. Clark, and L. Armi, Abstracts of Papers, 19M, Division of Organic Chemistry, 144th Meeting, Amer. Chem. Soc., Los Angeles, 1963.

The reaction which occurs in the absence of chloride ions (using perchloric acid), contributing $k'$ to the total rate constant, is regarded as an analogous process with the same first step, but with water functioning as the reagent of the second step, *e.g.*,



$$\overset{+}{\mathrm{Ar}}\left\langle{}^{\mathrm{H}}_{\mathrm{I}}\right. + \mathrm{H_2O} \xrightarrow{3} \mathrm{ArH} + \mathrm{H_2OI^+} \qquad \text{(B)}$$

Combining the concentration of water with the rate constant for that step, the expression

$$k' = \frac{k_1 k_3}{k_{-1}+k_3}[\mathrm{H}^+] \qquad (4)$$

is obtained as the analogue of equation (1). This reaction is expected to make an independent (though small) contribution to the rate in the presence of chloride. Equation (4) and, as we shall show below, equation (1) do not accurately reproduce the dependence of the reaction velocity on the hydrogen-ion concentration. Fig. 1 indicates that the reaction rate is not strictly proportional to acid concentration and the limiting slope at low acid concentration ($9 \times 10^{-5}$ sec.$^{-1}$ M$^{-1}$) is a maximum value. Exactly the same effect is found in the deuteriated medium, so that the isotope effect remains constant (Table 2). At the highest concentration used (0·174M), the rate is *ca.* 25% less than the value calculated from the limiting slope. We are not certain of the cause of this effect. It is unlikely to be a general ionic-strength effect, since, even though the experiments were performed without regulation to constant ionic strength, added sodium perchlorate was found not to have any detectable influence on the rate (of the chloride-catalysed reaction, it must be noted). The effect may be due to a complication which occurs in the reactions carried out in the strong perchloric acid solutions, but not in those carried out in the weaker acid solutions.

In equation (1), the two terms in the denominator are of comparable magnitude at low concentrations of chloride, but the second term is dominant at high chloride concentrations. This is implied by the values of $k_{-1}/k_2$ given in Table 7. The foregoing scheme requires that, in equation (4), the first term of the denominator must be dominant throughout, since, from the experimental values

$$k' = 9 \times 10^{-5}\,[\mathrm{H}^+] \quad \text{(at low acid concentration)}$$

and

$$k_\infty'' = 3{\cdot}46 \times 10^{-3}\,[\mathrm{H}^+] \text{ (from Table 6),}$$

and equations (2) and (4), we can calculate the ratio $k_{-1}/k_3 = 37$. From the corresponding results for the deuteriated solvent system,

$$k' = 11{\cdot}5 \times 10^{-5}\,[\mathrm{D}^+] \text{ and } k_\infty'' = 1{\cdot}92 \times 10^{-3}\,[\mathrm{D}^+],$$

we obtain $(k_{-1}/k_3)_{\mathrm{D}} = 16$.

Since there is no reaction in solutions of sodium chloride without added acid, the reaction which appears as the linear contribution to the total rate ($k'''$), at constant hydrogen-ion concentration, is concluded to be likewise an acid-catalysed process, *i.e.*,

$$k''' = k_4[\mathrm{H}^+][\mathrm{Cl}^-], \qquad (5)$$

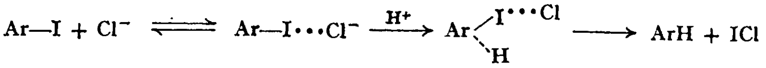
with $k_4 = 5{\cdot}82 \times 10^{-3}$ sec.$^{-1}$ mole$^{-2}$ for ordinary water, and $k_4^{\mathrm{D}} = 1{\cdot}43 \times 10^{-3}$ sec.$^{-1}$ mole$^{-2}$ for deuterium oxide.

Except for the possible presence of water molecules in one or both of the two transition states, the composition of the transition state for process (5), (ArI, H$^+$, Cl$^-$), is therefore the same as that for the $k''$ component at low chloride concentration, since, from equation (1), it is deduced that

$$k'' = \frac{k_1 k_2}{k_{-1}}[\mathrm{H}^+][\mathrm{Cl}^-], \qquad (6)$$

the quotient $k_1 k_2/k_{-1}$ being $311 \times 10^{-3}$ sec.$^{-1}$ mole$^{-1}$ in ordinary water, and $247 \times 10^{-3}$ sec.$^{-1}$ mole$^{-1}$ in deuterium oxide. The value of $k_4$ is much smaller than that of $k_1 k_2/k_{-1}$. This follows from the smallness of the contribution of the $k'''$ component at low chloride concentrations (Table 6).

The transition state corresponding to equation (5) is considered to be isomeric with that for equation (6), although it would equally be possible to consider that the two transition states differ in their degree of hydration. A plausible view of the alternative reaction path (5) seems to be that, in it, the timing of attack by hydrogen and chloride ions is reversed, *i.e.*, that we have



$$\mathrm{Ar{-}I + Cl^-} \rightleftharpoons \mathrm{Ar{-}I\cdots Cl^-} \xrightarrow{\mathrm{H^+}} \mathrm{Ar}\!\begin{smallmatrix}\diagup\mathrm{I\cdots Cl}\\ \diagdown\mathrm{H}\end{smallmatrix} \longrightarrow \mathrm{ArH + ICl} \qquad \text{(C)}$$

in which the first stage is a pre-equilibrium, and steps following the proton attachment are rapid and not kinetically significant. Probably one or more intermediates in this scheme could be designated as $\pi$-complexes, though this does not appear to be necessary.

The dissection of the total rate into three simultaneous contributions, and the evaluation of rate constants characteristic of each of these processes, were carried out entirely without reference to the rate measurements at various concentrations of hydrochloric acid in the absence of added salts. As a test of our kinetic analysis, it is shown, in Table 8, that these results (taken from Table 3) can be predicted from the rate constants evaluated. The complete set of rate constants deduced and used in these calculations, together with the derived isotope effects, is summarised in Table 9.

TABLE 8.

Comparison of experimental and calculated rate constants in catalysis by hydrochloric acid.

| [HCl] (M) | $10^6k'_{\text{calc.}}$ | $10^6k''_{\text{calc.}}$ | $10^6k'''_{\text{calc.}}$ | $10^6k^{\text{total}}_{\text{calc.}}$ | $10^6k_{\text{expt.}}$ | $100(k_{\text{expt.}}-k^{\text{total}}_{\text{calc.}})/k_{\text{expt.}}$ |
|---|---|---|---|---|---|---|
| | | | In $H_2O$ | | | |
| 0·0331 | 3 | 82 | 6 | 91 | 90 | −1 |
| 0·0654 | 7 | 193 | 25 | 225 | 232 | +3 |
| 0·1001 | 10 | 312 | 58 | 380 | 399 | +5 |
| 0·1346 | 13 | 430 | 105 | 548 | 567 | +3 |
| 0·1736 | 17 | 565 | 175 | 757 | 777 | +3 |
| | | | In $D_2O$ | | | |
| [DCl] (M) | | | | | | |
| 0·0331 | 4 | 49 | 2 | 55 | 60 | +8 |
| 0·0654 | 8 | 112 | 6 | 126 | 129 | +2 |
| 0·0994 | 12 | 177 | 14 | 203 | 212 | +4 |
| 0·1321 | 17 | 240 | 25 | 282 | 297 | +5 |
| 0·1681 | 21 | 308 | 40 | 369 | 393 | +6 |

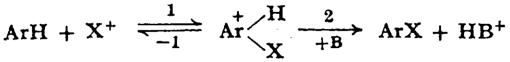
TABLE 9.

Summary of rate constants and isotope effects.

| | In $H_2O$ | In $D_2O$ | $k_H/k_D$ |
|---|---|---|---|
| $k_1$ (sec.$^{-1}$ mole$^{-1}$) | $3{\cdot}46\times10^{-3}$ | $1{\cdot}92\times10^{-3}$ | 1·80 |
| $k_{-1}/k_2$ (mole$^{-1}$) | 0·0111 | 0·0078 | 1·4 |
| $k_{-1}/k_3$ | 37 | 16 | 2·3 |
| $k_4$ (sec.$^{-1}$ mole$^{-2}$) | $5{\cdot}82\times10^{-3}$ | $1{\cdot}43\times10^{-3}$ | 4·1 |
| $k_{-1}$* (sec.$^{-1}$) | — | — | 1·4 |
| $k_3$* (sec.$^{-1}$) | — | — | 0·61 |
| $k_1/k_{-1}$* (mole$^{-1}$) | — | — | 1·3 |

* Calculated from preceding values on the assumption that there is no isotope effect on $k_2$.

Comparing these values with the corresponding results for proton attachment to trimethoxybenzene, and its reversal, obtained from a study of hydrogen-isotope exchange, we find proton attachment to the iodo-compound to be a much more rapid process. This conclusion is unexpected from electronic effects, but can be explained by the release of steric strain, between the iodine atom and its flanking methoxyl groups, which will accompany protonation at that position with formation of a tetrahedral complex in which the iodine atom is out of the plane of the aromatic system. A similar, though not exactly analogous, situation is met in the formation of Meisenheimer complexes from picryl derivatives.[10] The isotope effects on $k_1$ and $k_{-1}$ in the present system are considerably smaller than the corresponding $k_H/k_D$ ratios for trimethoxybenzene (3·0 and 8·05, respectively[3]). The small effect on $k_{-1}$ is particularly noteworthy. It may be connected with the steric strain, in that the gain in potential energy at the transition state for proton detachment may be due more to steric compression than to weakening of the C–H bond. Bearing in mind the connection between an aromatic substitution reaction and its reversal, we may note that there is no deuterium-isotope effect (or base catalysis) in the attack of the even more bulky *p*-chlorobenzenediazonium ions on trimethoxybenzene.[11] This dependence on steric effects is opposed to the sequence recognised by Zollinger, who has pointed out that steric effects due to the bulkiness of X are expected to accelerate reaction −1 relative to 1 in the scheme:[12]



$$\mathrm{ArH} + \mathrm{X}^+ \underset{-1}{\overset{1}{\rightleftharpoons}} \overset{+}{\mathrm{Ar}}\begin{matrix}\diagup\mathrm{H}\\ \diagdown\mathrm{X}\end{matrix} \xrightarrow[+\mathrm{B}]{2} \mathrm{ArX} + \mathrm{HB}^+$$

thereby making step 2 rate-limiting. Our suggestion implies that, with some structures, the steric hindrance on stage 1 may have a decisive influence on the isotope effect.

Another possible analogy for the small isotope effect on $k_{-1}$ is proton abstraction from haloforms by hydroxide ions. This group of reactions, which resembles our system in involving a hydrogen atom attached to the same carbon atom as a halogen atom, has deuterium-isotope effects[13] in the range 1·4—2·0.

What seems even more unusual is the isotope effect on the acid dissociation constant ($k_{-1}/k_1$) of the intermediate $(\mathrm{HArI})^+$. This appears to be the first example of an acid dissociation constant being increased by deuteriation of the system, instead of the usual reduction[14] by a factor in the range 2—4. The anomaly may point to an unusually weak C–H bond in the cationic intermediate, but it should be pointed out that this last isotope effect in Table 9 carries low accuracy, owing to the accumulation of errors. It is also conceivable that reaction (2) might have an isotope effect, owing to the special stereochemical situation, in which case the asterisked isotope effects in Table 9 could be wrong. No cases with transition-state structures analogous to reactions (3) and (4) seem to be on record, and no firm deductions are possible.

By the principle of microscopic reversibility, the kinetic analysis presented allows some detailed conclusions about the iodination reaction in aqueous solution. In the absence of dimedone, some iodination would occur under our experimental conditions; the unidirectional deiodination in the present experiments is due to iodine removal by dimedone. When no halide ions are present, the iodination in acid solution will appear to be first-order in $\mathrm{H_2OI^+}$; in the presence of chloride ions, the reaction will be first-order in iodine monochloride. A kinetic order does not by itself indicate the timing of processes leading up to the transition state, it merely indicates the stoicheiometric composition of the transition state. It does, however, seem reasonable that iodine monochloride itself would be the reagent under these conditions, in view of the stability of this substance in acidic chloride solutions.[15] In the presence of a high concentration of chloride, reaction −1 will become the rate-limiting step

[10] V. Gold and C. H. Rochester, *J.*, 1964, 1692.

[11] E. Helgstrand and B. Lamm, *Arkiv Kemi*, 1963, **20**, 193.

[12] H. Zollinger, "Advances in Physical Organic Chemistry," Vol. 2, ed. V. Gold, Academic Press, London and New York, 1964, p. 163; H. Zollinger, *Helv. Chim. Acta*, 1955, **38**, 1597, 1623.

[13] J. Hine, "Physical Organic Chemistry," 2nd edn., McGraw Hill, New York, 1962, ch. 24, and references therein.

[14] R. P. Bell, "The Proton in Chemistry," Methuen, London, 1959, ch. 11.

[15] J. H. Faull, jun., *J. Amer. Chem. Soc.*, 1934, **56**, 522.

in iodination according to Scheme (A), and the reaction will show the isotope effect appropriate to that C–H rupture (which, in the case of iodotrimethoxybenzene, is unusually small). At low chloride concentration, the step $-2$ will be rate-limiting. Our experiments thus resolve, for 1,3,5-trimethoxybenzene, the mechanistic ambiguity in aromatic iodination by iodine monochloride pointed out by Berliner.[16]

Our suggestions concerning the simultaneous occurrence of processes (A) and (C) in deiodination are an unusual refinement in kinetic analysis, which is indicated by the characteristic detailed features of the kinetics of this reaction. It follows, in turn, that there are two transition states in aromatic iodination, which are both composed of one molecule each of aromatic compound and iodine chloride; they correspond to the reversal of equations (A) and (C). This finding appears to add yet another mechanistic subtlety which can be probed by suitable kinetic investigation.

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[16] E. Berliner, *J. Amer. Chem. Soc.*, 1960, **82**, 5435.