The Kinetics of Hydrogen Isotope Exchange Reactions. Part II. The Reaction between* para-*Substituted* [*o*-^{2}H]*Phenols and Aqueous Sulphuric Acid.*

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The loss of deuterium from *p*-nitro[*o*-^{2}H]phenol, *p*-chloro[*o*-^{2}H]phenol, and [*o*-^{2}H]*p*-cresol has been examined kinetically in various sulphuric acid–water mixtures. The logarithms of the rate constants of the reactions are found to vary linearly with Hammett's acidity function H_0, except at the highest acidities ($H_0 < -8$) where the rate increase is less steep.

The results are held to indicate that the rate-determining step of the exchange reaction is an intramolecular rearrangement of a conjugate acid of the phenol.

It is well established that the velocity of hydrogen isotope exchange between aromatic compounds and aqueous acid, under heterogeneous conditions, increases rapidly with the concentration of acid in the aqueous phase and, more generally, that the kinetic efficiency of acids is qualitatively related to their acidity (Ingold, Raisin, and Wilson, *Nature*, 1934, 134, 734; *J.*, 1936, 915, 1637). The object of the present study was to examine the dependence of reaction velocity on acidity over a wider range, in a more quantitative fashion, in the hope of gaining a better insight into the mechanism of the reaction. In particular, it was thought at the outset that the acidity dependence might throw light on the nature and kinetic efficiency of the different acidic (H_3O^+, H_2SO_4, HSO_4^-, etc.) and basic (H_2O, HSO_4^-, SO_4^{2-}, etc.) species known to be present in sulphuric acid–water mixtures. Earlier two-phase experiments (Gold and Long, Part I*) on the exchange between [9-$^2H_1$]anthracene and sulphuric acid (84—90 wt.%) had indicated the promise of such an investigation, but the need for experiments on the distribution of the organic substrate between the two phases diminished the accuracy of the results and complicated their interpretation. For this reason single-phase experiments were adopted in the present work. In the event, experimental results provided diagnostic information about the mechanism of the reaction in a form different from that expected.

The choice of *para*-substituted phenols for this study was governed by practical considerations concerning properties such as solubility, basicity, exchange reactivity, and resistance to sulphonation or oxidation by sulphuric acid. Useful substrates must also have only one type of exchanging position if kinetic complexity is to be avoided. Some information about the exchange behaviour of *p*-nitrophenol was available (Koizumi and Titani, *Bull. Chem. Soc. Japan*, 1938, **13**, 318) which suggested appropriate experimental conditions for the preparation of *p*-nitrophenol deuterated practically exclusively at the position *ortho* to the hydroxyl group. Analogous information was not available in the cases of *p*-cresol and *p*-chlorophenol, but there was some evidence which implied that it would be possible to achieve selective exchange in these cases also (Kistiakowsky and Tichenor, *J. Amer. Chem. Soc.*, 1942, **64**, 2302; Tryon, Brown, and Kharasch, *ibid.*, 1948, **70**, 2003; Brodskii, *Izvest. Akad. Nauk S.S.S.R.*, 1949, 3).

The reaction rates studied all refer to dilute solutions of an aromatic compound in aqueous sulphuric acid. The reaction observed was the replacement of deuterium initially present in the aromatic compound by protium derived from a completely light solvent. Under these conditions the exchange kinetics assume a particularly simple form (Harris, *Trans. Faraday Soc.*, 1951, **47**, 716) and the greatest economy in the use of deuterium is achieved.

EXPERIMENTAL

Isotope Analysis.—The method used has been described by Bryce-Smith, Gold, and Satchell (*J.*, 1954, 2743). The percentages of deuterium are relative to the natural abundance of deuterium and are based on the assumption that the suppliers' (Norsk Hydro) analysis of

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* Part I, *J. Amer. Chem. Soc.*, 1953, **75**, 4543.

99·73% D_2O was correct. A sample containing $G\%$ by weight of this commercial deuterium oxide and $(100 - G)\%$ by weight of laboratory distilled water is then described as containing $0{\cdot}9973G\%$ of D_2O by weight. All the analyses reported were obtained by comparison with the densities of standard samples prepared in this manner. A more rigorous expression of the analytical figures is unnecessary for our present purpose. Atom percentages ($\equiv 100F$) were calculated from these weight percentages (W) by the expression

$$\text{Atom percentage} = 100W/[W + 1{\cdot}1111(100 - W)]$$

Solvents.—The concentrations of the sulphuric acid–water mixtures were determined by titration and/or density measurements.

Experiments on the Preparation of ortho-*Deuterated Phenols.*—All the deuterated specimens were prepared by direct substitution, an enriched acid being used. This method depends on the directional properties of the substituents already present in the molecule. Since the products, unlike those from other aromatic substitution reactions, cannot be freed from unwanted isomers, great care has to be taken in the choice of experimental conditions in order to avoid their formation. The following exploratory experiments indicated that suitable conditions could be found for our compounds. The deuterium oxide sample used in them contained 99·7% of D_2O.

(a) p-*Nitrophenol.* The behaviour of *p*-nitrophenol in acid solution was examined by heating samples of " enriched " perchloric acid [60·0% perchloric acid (2·96 g.) together with deuterium oxide (0·0877 g.)] with a comparable amount of *p*-nitrophenol (1·20 g.) in sealed ampoules at 100°. At intervals the ampoules were cooled and opened, their contents were diluted with a little distilled water, and the solid nitrophenol was filtered off. This was recrystallised from water in such a way as to remove deuterium from the hydroxyl group without disturbing the deuterium atom attached to the nucleus. The admissibility of this procedure follows from Koizumi and Titani's experiments (*loc. cit.*). The nitrophenol was then subjected to isotopic analysis with the following results :

Duration of expt. (hr.)	70	140	190	430	1100
Wt. % of D_2O in combustion water	2·07	2·03	2·07	2·07	2·11

These figures indicate that the amount of deuterium taken up by the compound had reached a constant value after <70 hr. The deuterium percentage is consistent with the assumption that two nuclear hydrogen atoms (in addition to the hydroxylic hydrogen) are concerned in the exchange and that the partition ratio (ρ_{C-H}) for the deuterium exchange between nuclear hydrogen and perchloric acid

$$\rho_{C-H} = \frac{\text{Atoms \% D in C–H bonds of nitrophenol}}{\text{Atoms \% D in aqueous perchloric acid}}$$

has a value of $0{\cdot}98_2 \pm 0{\cdot}01$ at 100°. This value agrees with other determinations of distribution coefficients for similar exchange equilibria (cf. Gold and Satchell, *Quart. Rev.*, 1955, **9**, 51). In this calculation of ρ_{C-H} we used the result of a separate experiment which showed that the corresponding constant for the O–H bond in *p*-nitrophenol (ρ_{O-H}) had a value of 1·06 (cf. Koizumi and Titani, *loc. cit.*). It seems legitimate to assume that the two nuclear positions concerned in the exchange are those *ortho* to the hydroxyl group and that, under the conditions stated, it is possible to prepare *p*-nitro[*o*-^{2}H]phenol with a suitable content of deuterium and essentially free from deuterium in the *meta*-positions.

The main batch of material was accordingly prepared by this method [*p*-nitrophenol (40 g.), deuterium oxide (4 ml.), 60% perchloric acid (20 ml.) heated at 100° in a sealed glass flask for 100 hr]. After several crystallisations from water the specimen contained 6·00 atoms % of D. This sample was used in all the kinetic experiments with this compound.

(b) p-*Chlorophenol.* An exploratory experiment was carried out at 100°. Sealed ampoules each containing 60·0% perchloric acid (37·37 g.), deuterium oxide (0·801 g.), and *p*-chlorophenol (1·20 g.) were heated to 100°. After an appropriate length of time an ampoule was cooled and opened, and its contents diluted with water and extracted with ether. The ethereal extract was shaken with barium carbonate to remove any acid, and then dried ($MgSO_4$). After filtration the ether was removed by evaporation under reduced pressure. The residue was redissolved in sufficient water to free the hydroxyl group from detectable deuterium. This aqueous solution was again extracted with ether, the ethereal extract dried, and the ether removed as before. The residue was distilled rapidly in a semimicro-apparatus. This procedure was adopted in order to minimise possible errors arising from isotope exchange between the hydroxyl group and the nucleus at high temperatures. The occurrence of such a reaction was reported for phen[^{2}H]ol at 200° (Brodskii and Kukhtenko, *Dopovidi Akad. Nauk Ukrain.*, 1950, 279) and, for this reason, prolonged heating of the substance was avoided. The only distillation in the above procedure occurred in the final stage immediately before combustion, at which stage this type of exchange reaction should be of no consequence. The results were :

Duration of expt. (hr.)	24	70	90
Wt. % of D_2O in combustion water	2·00	2·53	2·60

These figures correspond to an increasing number of nuclear hydrogen atoms being involved in the exchange. If the values of ρ for the C–H and O–H bonds of this compound are assumed to be similar to those found for *p*-nitrophenol, the lowest value corresponds to an average participation of about 2·3 and the highest value to about 3·0 nuclear hydrogen atoms per molecule. It is therefore apparent that the positions *ortho* to the hydroxyl group, which are expected to be the most reactive, are not the only positions involved in the exchange under these conditions. It was therefore attempted to discover conditions for more selective substitution. An experiment, by the same procedure, was carried out at 25° with *p*-chlorophenol (0·80 g.), 73·81 wt.% sulphuric acid (182·0 g.), and deuterium oxide (2·20 g.) in each ampoule :

Duration of expt. (hr.)	16	40	64
Wt. % of D_2O in combustion water	1·06	1·16	1·16

The last two figures correspond to the occurrence of exchange at exactly two positions (as desired) if ρ_{C-H} has a value of $0{\cdot}98_6$.

Because of the low solubility of *p*-chlorophenol in acid, the main batch of material was prepared by a two-phase process in which *p*-chlorophenol (50 g.) in carbon tetrachloride (50 ml.) was shaken (40 hr. at 20°) with sulphuric acid (200 ml., 80% by wt.) and deuterium oxide (12 ml.). The time of shaking was selected by consideration of the volumes of the phases and the distribution of *p*-chlorophenol between them. The figures for the deuterium content, given below, show that exchange equilibrium was not reached even at two nuclear positions, and the product may therefore be considered to be reasonably free from *p*-chloro[*o*, *m*-^{2}H]-phenol. After separation of the phases, the carbon tetrachloride layer was shaken several times with water and then dried ($MgSO_4$). The carbon tetrachloride was distilled off under reduced pressure. The residue crystallised. It was considered inadvisable to subject the sample to distillation in case an isotope rearrangement occurred. The chief impurity likely in the sample is a trace of carbon tetrachloride, which is of no consequence in the isotope assay or the kinetic exchange experiments. The specimen contained 2·98 atoms % of D.

(c) p-*Cresol.* The investigation concerning the preparation of [*o*-^{2}H]*p*-cresol proceeded along lines similar to those described for *p*-chlorophenol. A high-temperature (100°), one-phase experiments, using *p*-cresol (1·00 g.), perchloric acid (60 %; 37·37 g.), and deuterium oxide (0·801 g.) per ampoule and a separation technique similar to that used in the corresponding experiment with *p*-chlorophenol, showed an increasing amount of deuterium uptake by the aromatic compound with time :

Duration of expt. (hr.)	24	70	90
Wt. % of D_2O in combustion water	1·52	1·94	2·00

These figures indicate the average participation of 2·9—3·8 hydrogen atoms per molecule, and show that the experimental conditions are two drastic. In a low-temperature (25°), one-phase experiment, using *p*-cresol (0·80 g.), perchloric acid (60%, 123·2 g.), and deuterium oxide (2·20 g.) per ampoule, it was possible to confine isotope equilibration to two positions :

Duration of expt. (hr.)	1	24	48
Wt. % of D_2O in combustion water	0·90	0·91	0·93

These figures are consistent with the effective participation of 2·00, 2·02, and 2·05 nuclear positions, respectively, if the value of ρ_{C-H} is assumed to be $0{\cdot}95_2$.

The main batch of *p*-cresol was deuterated in a two-phase experiment. *p*-Cresol (40 g.), in carbon tetrachloride (30 ml.), was shaken (10 hr., 20°) with perchloric acid (60%; 200 ml.) and deuterium oxide (25 ml.). The product was isolated by the route described for *p*-chlorophenol. Analysis showed that exchange equilibrium was by no means reached even at the positions *ortho* to the hydroxyl group. The total hydrogen in the product contained 2·56 atoms % of D.

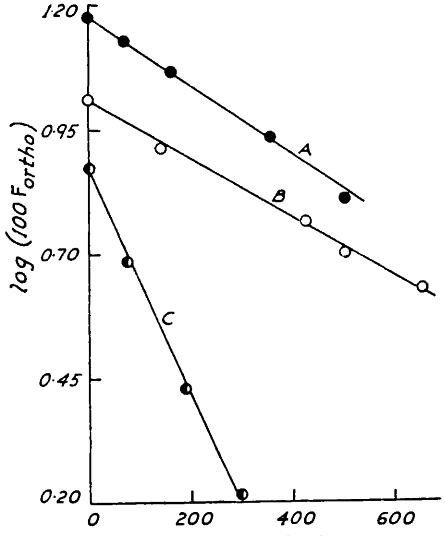
Kinetic Experiments on the Loss of Deuterium from the ortho-*Positions*.—Samples of the deuterated phenols (0·6 g.) were dissolved in portions of sulphuric acid (220 ml.) contained in flasks which were then sealed off and kept at 25° (thermostat). After various time intervals the flasks were removed and opened. Their contents, after dilution with water when necessary (the temperature being kept below 25°), were extracted with ether. The extract was kept over barium carbonate and anhydrous magnesium sulphate for several hours, then filtered, and the ether distilled off. The residual *p*-nitrophenol was analysed without further treatment; *p*-cresol and *p*-chlorophenol were first distilled to free them from the last traces of ether.

The percentage of deuterium in the system being so small, the exchange kinetics should not deviate detectably from first-order behaviour (Harris, *loc. cit.*) and should obey a relation of the form

$$\ln (F_0/F) = \lambda t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

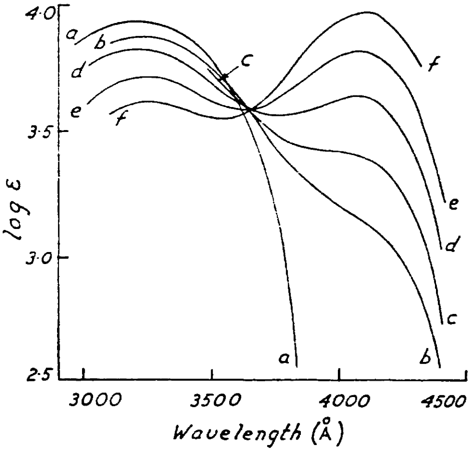
where F_0 and F are the fractional abundances of deuterium present initially and after a time t respectively. This was found to be the case, and examples of the plots of log (F_0/F) against t obtained for the three compounds are shown in Fig. 1. The linearity of these graphs serves to confirm that all the deuterium atoms in the samples occupy kinetically equivalent positions.

FIG. 1. *Examples of first-order exchange behaviour.*



A, p-*Nitrophenol*; *B*, p-*cresol*; *C*, p-*chlorophenol*.

FIG. 2. *Absorption spectra illustrating basic ionisation of* p-*nitrophenol in* H_2SO_4.



Concn. of H_2SO_4: *a*, 5; *b*, 89·62; *c*, 92·22; *d*, 94·52; *e*, 96·25; *f*, 98% by wt.

In experiments with *p*-nitrophenol in sulphuric acid of concentration greater than 50 moles %, when sulphonation might be expected, the rate of sulphonation was always small compared with that of exchange. In all cases the amount of phenol recovered was greater than 60% of the amount used. Therefore, errors which might result from selective sulphonation caused by the isotope effect on the reaction velocity of that reaction (Berglund-Larsson and Melander, *Arkiv Kemi*, **1953**, **6**, 219) are considered to be negligible.

Basic Ionisation Constant of p-*Nitrophenol*.—Solutions of *p*-nitrophenol in concentrated sulphuric acid have a marked yellow-green colour which is removed on dilution. This suggests a basic ionisation of the nitro-group similar to that found in other nitro-compounds (cf. Brand, Horning, and Thornley, *J.*, 1952, 1374). By using spectrophotometric methods essentially similar to those described by Brand *et al.*, and a series of five acids in the 90—98 wt.% region, the extinction coefficient and the pK_a values for the conjugate acid of *p*-nitrophenol were determined (see Fig. 2):

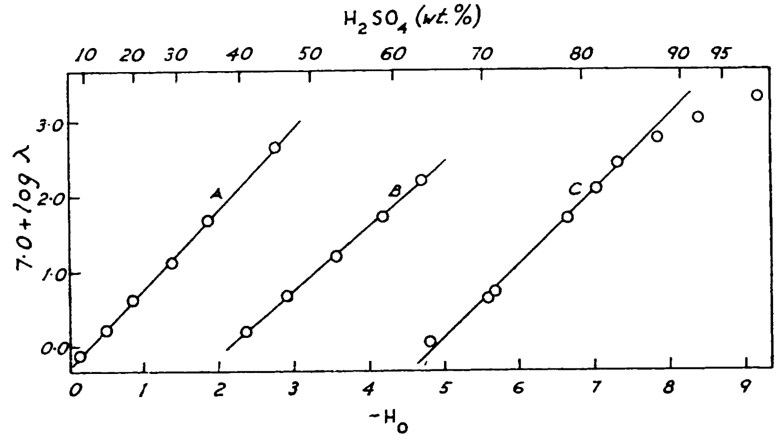
$$\varepsilon_{\max.} = 15{,}430 \ (4100 \ \text{Å}); \quad -pK_a = 9{\cdot}06$$

In calculating the exchange rate constant it was assumed, as seems reasonable, that the fraction of the phenol present as its conjugate acid did not undergo exchange. These rate constants are therefore maximum values for the un-ionised phenol. No such ionisation is considered likely for the other two compounds. In these cases, too, the quoted rate constants are considered to apply to the un-ionised phenol.

RESULTS AND DISCUSSION.

Dependence of Reaction Velocity on Acid Composition.—The kinetic results are tabulated below, and their dependence on acidity is shown in Fig. 3. It is seen that, over a considerable range of acidities (covering ~8 logarithmic units of acidity), log λ is a linear function of Hammett's acidity function H_0. The slopes of these graphs are 1·08, 0·90, and *ca.* 0·94 for *p*-cresol, *p*-chlorophenol, and *p*-nitrophenol respectively.

FIG. 3. *Dependence of exchange rate on acidity.*



A, p-*Cresol*; *B*, p-*chlorophenol*; C, p-*nitrophenol.*

H_2SO_4 (wt. %)	$-H_0$	$10^7\lambda$ (sec.$^{-1}$) p-$C_6H_4Me{\cdot}OH$	$10^7\lambda$ (sec.$^{-1}$) p-$C_6H_4Cl{\cdot}OH$
9·8	0·15	0·61	—
14·5	0·50	1·73	—
19·3	0·85	4·00	—
27·0	1·35	13·3	—
34·5	1·85	47·0	—
40·5	2·36	—	1·57
45·3	2·75	438·3	—
47·0	2·90	—	4·73
53·0	3·56	—	15·9
59·0	4·18	—	53·2
63·5	4·69	—	159·0

H_2SO_4 (wt. %)	$-H_0$	$10^7\lambda$ (sec.$^{-1}$) p-$C_6H_4(NO_2){\cdot}OH$
64·3	4·80	1·16
70·3	5·58	4·40
71·1	5·68	5·33
78·8	6·65	48·5
81·3	7·03	123·0
82·9	7·31	270
87·2	7·85	508
92·2	8·40	1012
97·6	9·17	1933

As previously mentioned, an alternative method of analysis of the data was *ca.* also attempted in terms of the concentrations of the different Brönsted acids present in aqueous sulphuric acid, the absence of strong kinetic effects due to the medium being assumed, *i.e.*, on the basis of a rate equation of the form

$$(1/t)\ \ln\ (F_0/F) = \Sigma k_i A_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

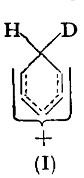
where F_0 and F have the same meaning as in equation (1) and A_i represents the concentration of the *i*th Brönsted acid in the system. The concentrations of the acidic species have been deduced from the intensities of Raman spectra of aqueous sulphuric acid (Young, *Record of Chem. Progress*, Spring Issue, 1951, p. 81, and personal communication). The concentrations of H_3O^+ and HSO_4^- are appreciable and reasonably well known over the acidity range with which we are concerned. It is evident from the data that the rate at which these concentrations increase with the stoicheiometric concentration of sulphuric acid in the medium is far smaller than the corresponding increase in the reaction velocity. If, therefore, equation (2) were to describe the dependence of the exchange rate on the acid composition, the terms involving H_3O^+ and HSO_4^- cannot make a very significant contribution to the reaction velocity. The data concerning the concentration of the species H_2SO_4 refer only to the highest stoicheiometric concentrations and, on the basis of the Raman spectra, $[H_2SO_4]$ is indistinguishable from zero if the stoicheiometric concentration is less than 14M (80 wt. %). It would therefore be consistent with these data to postulate that, at any rate over most of the range, H_2SO_4 is, in fact, the only species which gives rise to a significant term in equation (2) and that its concentration decreases from the measured value of 3M at $[H_2SO_4]_{\text{stoich.}} = 15{\cdot}18$M to about 10^{-7}M at $[H_2SO_4]_{\text{stoich.}} = 1{\cdot}2$M, in such a way as to parallel the falling off in reaction velocity with dilution. It would be a corollary of this postulate that the species H_2SO_4 would have to be of the order of 10^8 times more reactive in effecting proton transfer than H_3O^+. There is no evidence from any other acid-catalysed reaction in moderately concentrated sulphuric acid that a minute and highly reactive amount of H_2SO_4 competes as a catalytic species with H_3O^+. Further circumstantial evidence against this postulate is the analogous behaviour of hydrochloric and phosphoric acid. As is shown in Part IV (*J.*, 1955, 3622), these acids behave very similarly to sulphuric acid in regard to both the dependence of reaction velocity on H_0 and the absolute values of the velocity constants. To accommodate these observations it would be necessary to postulate, in these cases also, a single active species whose decrease in concentration parallels h_0 (h_0 = antilog $-H_0$) and which again is many powers of 10 more reactive than H_3O^+, yet is of closely similar reactivity to H_2SO_4. We do not believe that an analysis requiring such a combination of improbable postulates can reasonably be defended and therefore regard the dependence of reaction velocity on H_0 as established, in spite of the disparity between the observed slopes of the log λ–H_0 plots and the ideally expected slope of -1.

Acid–Base Pre-equilibrium Hypothesis.—Following Hammett, a proportionality between a rate constant and h_0 has usually been interpreted as implying a rate-determining reaction of the conjugate acid of a substrate (either a unimolecular reaction or a bimolecular reaction with a second substance other than water), the initial protonation occurring rapidly and only to a small extent, *e.g.*:

$$HA + S \overset{\text{Fast}}{\rightleftharpoons} SH^+ + A^-$$

$$SH^+ + \cdots \xrightarrow{\text{Slow}} \text{Products}$$

In applying this idea to the loss of deuterium from a substrate in an acidic medium we must be careful to note that we cannot identify SH^+ with a species (I) in which the entering hydrogen and the leaving deuterium atom occupy equivalent positions. This intermediate is the obvious one to formulate by analogy with the intermediates thought to occur in other electrophilic aromatic substitution reactions (Melander, *Arkiv Kemi*, 1950, 2, 213; Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Son, Ltd., London, 1953, pp. 279—281). If SH^+ were identical with (I), the rate law would require a dependence of reaction velocity on acidity analogous to that required by equation (2) [cf. equation (32) given by Gold and Satchell, *loc. cit.*], and this has already been dismissed as inconsistent with the observed dependence on H_0.


(I)

For this reason, if we accept the basic principles of the Hammett interpretation, we must identify SH^+ with a conjugate acid of the aromatic molecule of a structure such that the added proton does not occupy an equivalent position to the deuterium nucleus to be replaced. The entering hydrogen must (i) be linked less tightly than the deuterium to the carbon atom at which substitution occurs, or, (ii) be attached elsewhere in the same molecule, or (iii) be attached to a different phenol molecule from the one undergoing deuterium loss.

Intermolecular Mechanism.—The third of these possibilities would arise if a conjugate acid of the phenol (formed, say, by proton attachment at the oxygen atom) were to be the only acidic species effective in attacking the deuterium-carrying nucleus. Writing RD and RH for the deuterated and light phenol molecules and ϕ for the phenol irrespective of its isotopic composition (*i.e.*, $[\phi] = [\mathrm{RH}] + [\mathrm{RD}]$), we can represent this mechanism as :

$$\phi + \mathrm{H_3O^+} \rightleftharpoons \phi\mathrm{H^+} + \mathrm{H_2O} \text{ (Equilibrium constant } = K_a^{\phi\mathrm{H^+}})$$

$$\phi\mathrm{H^+} + \mathrm{RD} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{RDH^+} + \phi \xrightarrow{k'_-} \mathrm{RH} + \phi\mathrm{D^+}$$

where $\mathrm{RDH^+}$ stands for the conjugate acid of structure (I), and $\phi\mathrm{D^+}$ and $\phi\mathrm{H^+}$ are conjugate acids in which the hydrion attachment is of the looser kind mentioned above. This mechanism leads to the rate law

$$\lambda = \frac{k_+ \, . \, k'_-}{k_- + k'_-}[\phi\mathrm{H^+}] \, . \, \frac{f_{\phi\mathrm{H^+}}f_{\mathrm{RD}}}{f_{(\phi \cdots \mathrm{H} \cdots \mathrm{RD})^+}} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Since for a small extent of conversion of phenol into its conjugate acid

$$\frac{[\phi\mathrm{H^+}]}{[\phi]} = \frac{h_0}{K_\mathrm{a}^{\phi\mathrm{H^+}}} \, . \, \frac{f_\phi f_{\mathrm{BH^+}}}{f_{\phi\mathrm{H^+}}f_{\mathrm{B}}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $K_a^{\phi\mathrm{H^+}}$ is the acidity constant of $\phi\mathrm{H^+}$, we have, if the activity coefficient ratio is unity

$$\lambda = \frac{k_+k'_-}{(k_- + k'_-)K_a^{\phi\mathrm{H^+}}} \, . \, h_0[\phi] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

This equation involves a dependence of reaction rate on acidity compatible with our results. It was not practicable to test the dependence of the velocity on the total concentration of phenol which is implied in this equation. However, the following considerations lead us to reject this mechanism on quite general grounds.

If this mechanism were correct it would imply that $\phi\mathrm{H^+}$ is more effective than $\mathrm{H_3O^+}$ (or any other acid) in transferring a proton to the aromatic ring to form the conjugate acid (I). Let us consider the equilibrium between RH and its conjugate acid $\mathrm{RH_2^+}$ which has the same structure as (I). We may reasonably assume that the basicities of RH and RD are the same. If the only acidic and basic species present in the system are ϕ, $\phi\mathrm{H^+}$, $\mathrm{RH_2^+}$, $\mathrm{H_3O^+}$, and $\mathrm{H_2O}$, the following conditions of equilibrium must obtain :

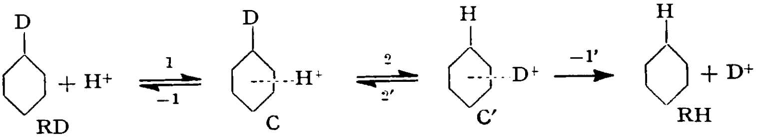
$$\frac{[\mathrm{RH_2^+}]}{[\mathrm{RH}]} = \frac{k_+^{\mathrm{H_3O^+}}[\mathrm{H_3O^+}]}{k_-^{\mathrm{H_2O}}[\mathrm{H_2O}]} = \frac{k_+^{\phi\mathrm{H^+}}[\phi\mathrm{H^+}]}{k_-^{\phi}[\phi]} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and

$$\frac{[\mathrm{RH_2^+}]}{[\mathrm{RH}]} = \frac{(k_+^{\mathrm{H_3O^+}}[\mathrm{H_3O^+}] + k_+^{\phi\mathrm{H^+}}[\phi\mathrm{H^+}]}{(k_-^{\mathrm{H_2O}}[\mathrm{H_2O}] + k_-^{\phi}[\phi]} \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The equations (6) follow from the condition that each of the acid–base pairs must separately be in equilibrium with the pair $\mathrm{RH_2^+}$, RH. Equation (7) is a consequence of the requirement that, at equilibrium, the rate of attachment of a proton, from whatever source, to RH must equal the total rate of detachment. It follows that, if the acid $\phi\mathrm{H^+}$ is, in preference to $\mathrm{H_3O^+}$, responsible for most of the reaction converting RH into $\mathrm{RH_2^+}$ then its conjugate base ϕ must be responsible for an equal share of the reverse reaction. Therefore, it would be necessary to say that ϕ is more effective than $\mathrm{H_2O}$ for proton (and deuteron) abstraction, in spite of the fact that $\mathrm{H_2O}$ is a stronger base and present in much greater concentration. For this reason, the intermolecular mechanism appears untenable and we have to consider that the initial proton attachment occurs in the molecule which subsequently loses deuterium—the slow step being intramolecular.

Intramolecular Mechanism.—On this basis we formulate the reaction mechanism as involving a rapid, reversible, loose attachment of a proton to the deuterated molecule which is then followed by a slow rearrangement of this species :



We may write the reaction velocities of the various steps in the form $v = k \times$ (activity of the organic species/activity coefficient of the transition state), so that the specific reaction rates k are functions of the solvent acidity. Assuming the concentrations of C and C′ to be very small, and applying Bodenstein's " stationary state " treatment, we obtain for the overall rate constant λ an expression of the approximate form

$$\lambda = \frac{k'_{-1}k_1k_2}{(k_{-1}k'_2 + k_{-1}k'_{-1} + k'_{-1}k_2)} \cdot \frac{f_{\mathrm{RD}}}{f_{\mathrm{X}^+}} \quad . \; . \; . \; . \; . \; . \; . \quad (8)$$

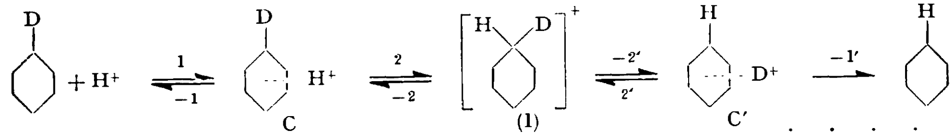
and, if $k'_{-1} \gg k'_2$ and $k_{-1} \gg k_2$,

$$\lambda = k_1k_2f_{\mathrm{RD}}/k_{-1}f_{\mathrm{X}^+} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (9)$$

or

$$\lambda = h_0k_2(f_{\mathrm{RD}}f_{\mathrm{BH}^+})/K_a^{\mathrm{C}}(f_{\mathrm{X}^+}f_{\mathrm{B}}) \quad . \; . \; . \; . \; . \; . \; . \; . \quad (10)$$

where K_a^{C} is the acidity constant of C and hence $[C]/[\mathrm{RD}] = k_1f_{\mathrm{RD}}/k_{-1}f_{\mathrm{C}} = h_0f_{\mathrm{RD}}f_{\mathrm{BH}^+}/K_a^{\mathrm{C}}f_{\mathrm{C}}f_{\mathrm{B}}$. Equation (10) correctly represents the proportionality of the reaction rate to h_0 (on making the usual assumption that $f_{\mathrm{RD}}f_{\mathrm{BH}^+}/f_{\mathrm{X}^+}f_{\mathrm{B}} = 1$) and appears to be the simplest interpretation of this observation in accordance with Hammett's principle mentioned. However, by analogy with the case of aromatic nitration we consider it likely that the hydrogen isotope exchange also involves an intermediate of structure (I) and, for this reason, we prefer to formulate the reaction mechanism as :



. . . . (11)

where C and C′ and (I) are low-concentration intermediates. On this basis the expression for λ analogous to (8) becomes :

$$\lambda = \frac{k_1k'_{-1}k_2k'_{-2}}{k_{-1}k'_{-1}k'_{-2} + k_{-1}k'_{-1}k_2 + k'_{-1}k_2k'_{-2} + k_{-1}k_{-2}k'_2} \cdot \frac{f_{\mathrm{RD}}}{f_{\mathrm{X}^+}} \quad . \; . \; . \quad (12)$$

or, if k_{-1} and k'_{-1} are very much greater than the other k values,

$$\lambda = \frac{k_1}{k_{-1}} \cdot k_2 \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot \frac{f_{\mathrm{RD}}}{f_{\mathrm{X}^+}}$$

$$= \frac{h_0}{K_a^{\mathrm{C}}} \cdot k_2 \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot \frac{f_{\mathrm{RD}}f_{\mathrm{BH}^+}}{f_{\mathrm{X}^+}f_{\mathrm{B}}} \quad . \; . \; . \; . \; . \; . \quad (13)$$

which is identical with equation (10) except for the numerical factor $k'_{-2}/(k_{-2} + k'_{-2})$, the value of which is expected to lie in the range 0·09—0·33 (Gold and Satchell, *loc. cit.*). A comparison of the rate of deuterium and tritium loss from RD and RT may afford a test for the existence of an intermediate of structure (I) in these exchange reactions.

Examination of the Acid-freer Proton Pre-equilibrium Hypothesis.—Recently, during a discussion of the mechanism of hydration of olefins (de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930), a more general formulation of this type of mechanism was proposed. This formulation envisages a rapid equilibrium between acidic species and protons in a " freer form." The rate-determining step is the reaction between the protons and the substrate, *e.g.*,

$$\mathrm{HA} \xrightleftharpoons{\text{Fast}} \mathbf{H}^+ + \mathrm{A}^-$$

$$\mathbf{H}^+ + \mathrm{S} \xrightarrow{\text{Slow}} \text{Products}$$

where $\mathbf{H}^+$ represents the " freer " proton.

The difference between such a description of the mechanism and that given in equation (11) is that the structurally less specific " freer " protons replace the conjugate acids C and C′ as reaction intermediates. If the proton is attached, however loosely, to S, then the two formulations are indistinguishable and, in our case, the " freer " proton is the proton attached to the aromatic molecule, in the complex C (or C′). If, on the other hand, the " freer " protons are not associated with the particular molecule undergoing exchange then, strictly speaking, the mechanism is chemically different, although a distinguishing experimental test has not yet been devised. For the hydrogen isotope exchange reaction the " freer " proton formulation can be written :

$$H_3O^+ \text{ (or } H_2SO_4) \underset{-1}{\overset{1}{\rightleftharpoons}} H_2O \text{ (or } HSO_4^-) + \mathbf{H}^+ \quad \text{(fast)}$$

$$RD + \mathbf{H}^+ \underset{-2}{\overset{2}{\rightleftharpoons}} RDH^+ \xrightarrow{-2'} RH + \mathbf{D}^+$$

$$\mathbf{D}^+ + H_2O \text{ (or } HSO_4^-) \underset{1'}{\overset{-1'}{\rightleftharpoons}} H_2DO^+ \text{ (or } HDSO_4) \quad \text{(fast)}$$

On this basis

$$\lambda = k_2 \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot (\mathbf{H}^+) \cdot \frac{f_{RD}}{f_{X^+}} \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where X^+ is the transition state of reaction (2), or, since $(\mathbf{H}^+) = \mathbf{K}(H^+)$ and $(H^+) = h_0 f_{BH^+}/f_B$,

$$\lambda = k_2\mathbf{K} \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot h_0 \cdot \frac{f_{RD}f_{BH^+}}{f_{X^+}f_B} \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

which is formally identical with (13).

The experimental results of the present study are compatible with any type of " freer proton." However, the following discussion, during which the term " freer protons " is taken to refer to those " freer protons " which exist in some state *other* than that of a loose attachment to the reacting molecule, seems to us to argue against their kinetic intervention and that, therefore, it is justifiable to represent the reaction mechanism by the specific picture proposed in the preceding section.

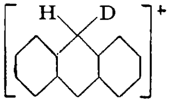
It is known that certain reactions exhibit general acid catalysis in dilute aqueous solution, *i.e.*, the total rates of these reactions can be satisfactorily represented as a sum of the contributions of catalysis by several acid species which are simultaneously present in the solvent. An example of this is the iodination of acetone. The detailed mechanism of this reaction is thought to be complex (cf. Bell, " Acid–Base Catalysis," Oxford, 1941, Chapter VII) but, for this additivity to hold, it must be true that the rate of proton uptake by acetone is the sum of the contributions to the velocity of this reaction by the individual acids. This must mean that these acids *directly* transfer protons to acetone and do not, in a pre-equilibrium, liberate " freer " protons which are then taken up by acetone, since the existence of such a pre-equilibrium is incompatible with additive catalytic effects. [This can be shown by an argument analogous to that which demonstrates that a reaction which exhibits general acid catalysis must involve a rate-determining proton transfer and cannot involve an acid–base pre-equilibrium of the reacting substrate (*idem, op. cit.*, pp. 122—127).] It follows that the reaction of any " freer protons " present with acetone must be less important than that of H_3O^+ ions and other acidic species. [The phenomenon of the simultaneous operation of proton transfer from different acids is also shown in a more direct manner in the exchange reaction between phosphine and water, although the data in this case are not as extensive as for the example quoted above (Weston and Bigeleisen, *J. Amer. Chem. Soc.*, 1954, **76**, 3074).] We may also suppose that this order of importance of the reactions will apply for any other proton acceptor. (The validity of the Brönsted catalysis law for a variety of reactions supports such a supposition.) On going from the dilute solutions for which the acetone results hold to the least acidic of the solutions studied by us, H_3O^+ and h_0 increase almost proportionately and it is expected that

(H^+) is nearly proportional to h_0. Therefore, we may expect that the relative importance of the reaction *via* " freer " protons and H_3O^+ ions will still be of the same order, the former reaction still being insignificant compared with the latter. In other words, " freer " protons do not play a part in the reaction in the dilute acids and therefore this mechanism cannot be invoked to explain the dependence of reaction velocity on h_0 in that region of acidity. Nothing seems to be gained by postulating its emergence at higher acidities. As previously mentioned, we therefore interpret our results as pointing to the occurrence of what may be regarded as a slow intramolecular rearrangement.

Chemical Formulation of the Intermediate C.—On the basis of the experiments reported in this paper at least two formulations of C seem chemically plausible. Either the proton is attached to the oxygen atom of the hydroxyl group or else there is a less localised interaction between the proton and the aromatic molecule of a type variously described as an outer complex (Mulliken, *J. Phys. Chem.*, 1952, **56**, 801) or π-complex (Dewar, " Electronic Theory of Organic Chemistry," Oxford, 1949; Brown and Brady, *J. Amer. Chem. Soc.*, 1952, **74**, 3570). This problem is more fully discussed in Part III (following paper).

Dependence of Reaction Velocity on Acidity at the Highest Concentrations of Acid.—The linear relation between log λ and H_0 breaks down at high acidity for *p*-nitrophenol. The deviation is definitely outside the limits of experimental error. In calculating these points allowance was made for the protonation of the nitro-group of nitrophenol which becomes important in this region. It was assumed that this protonated species is completely unreactive. Our determination of the pK_a value for *p*-nitrophenol is unlikely to be in error by a sufficiently large amount to make any significant difference to the result.

The deviation from linearity may be due to one or more of several causes and we cannot decide definitely between them. One possible reason is the inadmissibility of the assumption which allows equation (12) to be simplified to yield equation (13). It is conceivable that at the highest acidities the loss of a proton from C and C′ is no longer very much faster than the other reactions in view of the decreasing concentration of active bases in that composition region. Under these conditions λ will depend less strongly on h_0 and, in the limiting case of high acidities when k_{-1} and k'_{-1} are very much smaller than the other k values in equation (12), it will become independent of solvent acidity. In support of this hypothesis we may adduce that a rate of proton loss which decreases with acidity was postulated by Gold and Long (*loc. cit.*) for the ion (II) although the two cases are not strictly comparable.



(II)

An alternative explanation of the phenomenon would be along the lines of the argument suggested for the decrease in nitration rate observed over a similar range of acidities. In particular, it has been suggested by Gillespie and Norton (*J.*, 1953, 971) that the decrease is in part due to deactivation of the aromatic compound by hydrogen-bonding between potentially basic parts of the molecule with an H_2SO_4 molecule. In the case of nitro-compounds this interaction would take place at the nitro-group and deactivate the aromatic ring by electrostatic induction. This explanation could clearly be extended to the exchange reaction of *p*-nitrophenol studied by us. A similar kind of interaction was probably envisaged by Brand, Horning, and Thornley (*loc. cit.*) who suggested that the freezing-point depression of sulphuric acid by trinitrotoluene (Gillespie, Hughes, and Ingold, *J.*, 1950, 2743) could conceivably be explained by solvation of the nitro-group.

We may definitely rule out as an explanation an application of the hypothesis that at the higher acidities H_0 does not reflect an activity of protons but an activity of the Lewis acid SO_3 (Lewis and Bigeleisen, *J. Amer. Chem. Soc.*, 1943, **65**, 1144), because such an effect, if real (see Coryell and Fox, *J. Inorg. Nuclear Chem.*, 1955, **1**, 119), would only assume importance at acidities higher than those studied by us.

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