318. *The Reactions of Organic Phosphates. Part IV.* Oxygen Exchange between Water and Orthophosphoric Acid.*

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The rates of oxygen exchange of inorganic orthophosphate have been measured over a wide range of pH. A plot of exchange rate against pH has a maximum at pH *ca.* 5 and a minimum at pH *ca.* 1; the curve steepens rapidly with increasing hydrogen-ion concentration. This pH dependence is very similar to that observed for the hydrolysis of methyl dihydrogen phosphate. The mechanisms of the two processes are very similar and we compare their rates.

POTASSIUM DIHYDROGEN ORTHOPHOSPHATE slowly exchanges its oxygen atoms with water by a reaction which does not involve formation and hydrolysis of higher phosphates.[1] There have been several qualitative investigations of the oxygen exchange of inorganic phosphates,[1,2] but the only kinetic study has been on concentrated solutions of orthophosphoric acid.[3] In this special system it seems that condensed phosphoric acids are intermediates.

The work now described has been with dilute solutions of phosphate, and shows that the oxygen exchange of orthophosphoric acid, and its anions, proceeds by mechanisms which are analogous to those which give phosphorus–oxygen bond fission in the hydrolysis of monoalkyl phosphates. These hydrolytic mechanisms are now well characterised, and the main reactive species are the conjugate acid and the monoanion of the ester.[4,5] Preliminary accounts of our exchange results have been given elsewhere.[6]

The variation, with acidity, of the first-order rate constant, k_E, for the oxygen exchange of orthophosphoric acid, is shown in Figs. 1 and 2. The forms of the plots are very similar to those observed for the hydrolyses of the monoesters.[4,5]

Oxygen Exchange at pH 1—9.—The kinetics of the oxygen exchange in this pH range (Fig. 1) can be analysed by the procedures applied to the hydrolyses of monoalkyl phosphates.[5] The rate of exchange has a maximum value at pH 4·5—5·5, where the monoanion, $H_2PO_4^-$, is the predominant species. Thus we conclude that, as for the ester hydrolysis, reaction is by attack of water upon the monoanion (other possible mechanisms can be excluded for reasons given elsewhere [4,5]). The value of the rate at pH *ca.* 5 gives us an approximate value for the rate coefficient, k_M, for the reaction between the monoanion and water. A more exact value can be obtained by correction for the small amount of exchange which comes from reaction between the undissociated acid, H_3PO_4, and water. The first-order rate constant, k_N, for this exchange can be estimated by two methods.

(*a*) The plot of k_E against the hydrogen-ion concentration can be extrapolated to zero acidity. This gives a value of $10^6k_N \approx 1·3$ sec.$^{-1}$. (*b*) From the rates of exchange at two different pH's, 2·21 and 4·00, and the relative amounts of H_3PO_4 and $H_2PO_4^-$ at these pH's, we can calculate $10^6k_M = 4·03$ sec.$^{-1}$, and $10^6k_N = 1·28$ sec.$^{-1}$. The values of k_N agree well and, as a further test of our method, we have calculated the extents of exchange by reaction of H_3PO_4 and $H_2PO_4^-$. These are plotted in Fig. 1 (broken lines). The full line is their sum, together with the contribution of the acid-catalysed exchange which becomes significant only below pH 0·5.†

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* Part III, *J.*, 1960, 3293.

† Dissociation constants and pH values were measured at 20°. The error involved in using these data to interpret the kinetic results, obtained at 100°, appears to be small.

[1] Winter and Briscoe, *J.*, 1942, 631.

[2] Brodskii and Sulima, *Doklady Akad. Nauk S.S.S.R.*, 1953, **92**, 589; *Chem. Abs.*, 1954, **48**, 5620.

[3] Keisch, Kennedy, and Wahl, *J. Amer. Chem. Soc.*, 1958, **80**, 4778.

[4] Butcher and Westheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 2420; Kumamoto and Westheimer, *ibid.*, p. 2515; Westheimer, *Chem. Soc. Special Publ.*, No. 8, 1957, 1.

[5] Bunton, Llewellyn, Oldham, and Vernon, *J.*, 1958, 3574.

[6] Vernon, *Chem. Soc. Special Publ.*, No. 8, 1957, 17.

Acid-catalysed Exchange.—When the pH is low we can neglect the exchange of the monoanion. Exchange is then due to reaction of the undissociated species, H_3PO_4, and its conjugate acid. The value of k_N has already been estimated. By subtracting this value from k_E we obtain $(k_E - k_N)$, the first-order rate constant for the acid-catalysed exchange. The rate increases sharply with increasing hydrogen-ion concentration (Fig. 2). However, this exchange fits neither of the limiting forms of acid-catalysis predicted by the Zucker–Hammett hypothesis,[7] *i.e.*, linear dependence of rate on [H$^+$] or upon Hammett's acidity function, h_0. A plot of log $(k_E - k_N)$ against log [H$^+$] is a straight line of slope 1·9, and against $-H_0$ it is a curve of continuously decreasing slope (Fig. 3). Since the rates with hydrochloric and perchloric acids are almost the same (Table 1), it appears that nucleophilic catalysis by anions of the strong acids is absent.

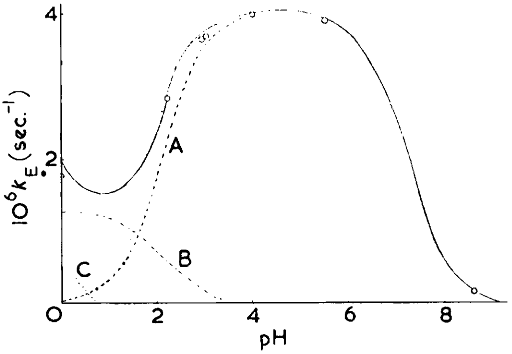

FIG. 1. *Oxygen exchange of orthophosphate at* pH 0—9 *and* 100·1°.

Contribution of (A) *exchange of monoanion,* (B) *neutral exchange, and* (C) *acid-catalysed exchange. Full line is calculated curve* (*see text*).

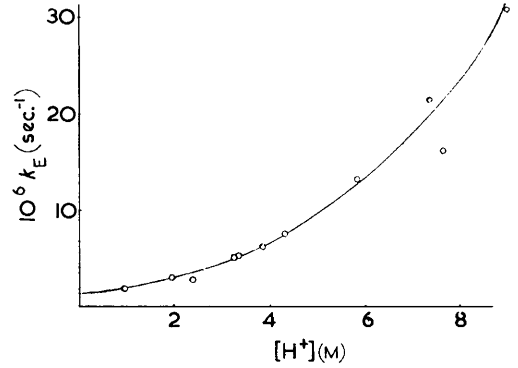

FIG. 2. *Dependence of rate of oxygen exchange of orthophosphate on acidity.*

TABLE 1. *Perchloric-acid catalysed exchange at* 100·1°.

[H$^+$] (M)	0·99	1·97	2·40	3·26 *	3·34	3·86 †	4·31	5·82	7·35	7·61	8·93
[KH_2PO_4] (M)	0·38	0·37	0·76	0·40	0·37	0·74	0·38	0·38	0·37	0·38	0·37
$10^6 k_E$ (sec.$^{-1}$)	1·76	2·91	2·71	5·00	5·26	6·17	7·48	13·1	21·4	16·1	30·9
$10^6(k_E - k_N)$ (sec.$^{-1}$)	0·48	1·63	1·43	3·72	3·98	4·90	6·20	11·9	20·1	14·8	29·6

* HCl. † Two-point run.

TABLE 2. *Effect of added sodium perchlorate.*

[H$^+$] (M)	1·05			4·00	
μ (mole l.$^{-1}$)	1·05	3·05	5·05	4·00	7·00
$10^6 k_E$ (sec.$^{-1}$)	1·78 *	1·66	2·18	6·38 *	11·0

* Interpolated values.

The acid-catalysed exchange is strongly catalysed by added sodium perchlorate (Tables 1 and 2), although this salt does not increase the rate at pH 0, where the undissociated

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[7] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.

acid, H_3PO_4, is the reactive species. It seems, therefore, that the lack of proportionality between the rate and acid concentration (Figs. 2 and 3) may arise from a salt effect of the fully ionised perchloric acid since, at a constant ionic strength, $\mu = 7$, the rate is approximately proportional to the hydrogen-ion concentration. For reactions in not very dilute solutions, the dependence of rate on ionic strength has the form [8]

$$v = v_0 \exp \beta\mu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where v and v_0 are the rates at ionic strengths μ and zero respectively. Therefore, the first-order rate constant for the acid-catalysed exchange should be given by

$$(k_E - k_N) = k_A[H^+] \exp \beta\mu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The values of k_A and β were calculated from the rates of exchange in 4M-perchloric acid and in that acid plus 3M-sodium perchlorate: $10^7 k_A = 5{\cdot}45$ sec.$^{-1}$ mole^{-1} l., and $\beta = 0{\cdot}212$.

The line of Fig. 2 is a plot calculated from equation (2) by using the calculated values of k_A and β. The agreement with experiment is good, and, therefore, the kinetic form of the acid-catalysed exchange can be explained in terms of a positive salt effect superimposed upon the acid catalysis; this implies that the salt effects of perchloric acid and sodium perchlorate are very similar.

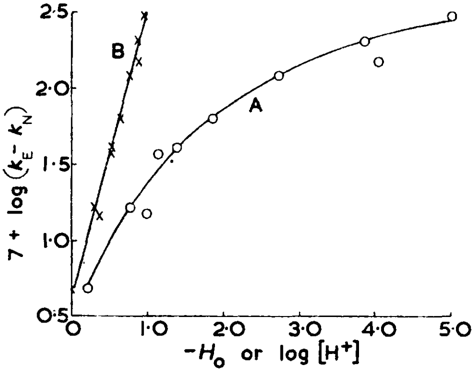

FIG. 3. *Dependence of rate of oxygen exchange on Hammett's acidity function.*

Plot of log (k_E − k_N) *against* (A) − H_0 *and* (B) log [H$^+$].

It has recently been suggested that explicit account should be taken of the activity of water in interpreting the catalytic effect of strong acids. For several reactions it is found [9] that plots of log $(k + H_0)$ against the activity of water have non-zero slopes, *i.e.*, $w \neq 0$. The value of w is often nearly integral and is thought to represent the differing numbers of water molecules in the initial and the transition states. A plot of $\log [(k_E - k_N) + H_0]$ against $\log a_{H_2O}$ is a straight line of slope $w = 3{\cdot}9$. For the acid hydrolysis of methyl phosphate, $w = 6$. The significance of this value is, however, uncertain because this hydrolysis proceeds by two distinct reactions with different positions of bond fission.[5]

Mechanisms of Exchange.—The oxygen exchange of phosphoric acid is a reaction which is analogous to the hydrolysis of a monoalkyl phosphate proceeding with phosphorus–oxygen bond fission [4,5] (*i.e.*, the reactions involve the separation from the phosphorus atom of the groups OH and OR respectively). For reactions of the mono-negative anions, the values of k_M are $4{\cdot}03 \times 10^{-6}$ sec.$^{-1}$ and $8{\cdot}23 \times 10^{-6}$ sec.$^{-1}$ for phosphate exchange and hydrolysis of methyl phosphate, respectively.[5] Hydrogen-bonded intermediates are thought to be important in the hydrolysis of the monoanion,[4,5] and intermediates of similar structure can be postulated for the oxygen exchange of the mono-negative anion, $H_2PO_4^-$.

Although the exchange of the monoanion is very similar to the hydrolysis of the

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[8] Long and McDevitt, *Chem. Rev.*, 1952, **51**, 119.

[9] Bunnett, *J. Amer. Chem. Soc.*, 1960, **82**, 499.

monoanion of methyl phosphate, there are marked differences between the mechanisms for the neutral molecules. The hydrolysis of undissociated methyl dihydrogen phosphate is almost swamped by the hydrolyses of the monoanion and the conjugate acid,[5] whereas the exchange of the undissociated orthophosphoric acid can be easily observed. The overall rate constants, k_N, are $1{\cdot}3 \times 10^{-6}$ sec.$^{-6}$ and *ca.* $0{\cdot}5 \times 10^{-6}$ sec.$^{-1}$ for oxygen exchange and hydrolysis of methyl phosphate, respectively, but these values are not strictly comparable because the ester hydrolysis is by predominant alkyl–oxygen bond fission and, moreover, is subject to a large positive salt effect.[5] Thus, oxygen exchange is much faster than hydrolysis with phosphorus–oxygen bond fission. This may be because hydrolysis requires breaking of the bond between the alkoxy-group and the phosphorus atom, whereas formation of a quinquecovalent intermediate, followed by a rapid proton-transfer, will give oxygen exchange. (We assume both processes to be bimolecular.)

The values of the rate constants for the acid-catalysed oxygen exchange of orthophosphoric acid and the corresponding values for the hydrolysis of the monomethyl ester are similar: $10^6k_A = 5{\cdot}47$ for the exchange and $3{\cdot}08$ l. mole^{-1} sec.$^{-1}$ for hydrolysis.[5] However, there are differences between the two processes, because for the component of hydrolysis by phosphorus–oxygen bond fission $10^6k_A \approx 1$ l. mole^{-1} sec.$^{-1}$. Further, whereas the oxygen exchange shows a positive salt effect, there is no salt effect upon the acid-hydrolysis of the ester. The acid-hydrolysis of methyl phosphate is accompanied by an oxygen exchange of the ester, presumably by a mechanism similar to that of the exchange of orthophosphoric acid itself. These reactions may be formulated as synchronous displacements of a water molecule by a water molecule from the solvent, or as the formation of a quinquecovalent intermediate.[5] A unimolecular decomposition of the conjugate acids seems improbable, because of the kinetic form of the acid catalysis.

Oxygen exchange does not occur to any appreciable extent by attack of one ion or molecule of a phosphate upon another (cf. ref. 1). Consistently, oxygen exchange is of the first order with respect to orthophosphate (Tables 1 and 3), and higher orders are observed only for high concentrations of orthophosphoric acid.[3]

TABLE 3. *Rate of exchange at* 100·1°, pH > 0

pH	0 *	2·21	2·96	3·1	4·00	5·51	8·61
[KH_2PO_4] (M)	0·380	0·382	0·291	0·610	0·290	0·301	0·282
10^6k_E (sec.$^{-1}$)	1·76	2·83	3·65	3·67	4·00	3·91	0·16

The pH value is that measured at 20°. * 0·99M-$HClO_4$.

EXPERIMENTAL

The rates of oxygen exchange were measured at 100·1°, $H_2{}^{18}O$ being used. A weighed amount of potassium dihydrogen phosphate was dissolved in a known volume of $H_2{}^{18}O$, and either mineral acid or alkali added. Any precipitate of potassium perchlorate was centrifuged off. For the exchange catalysed by perchloric or hydrochloric acid, the hydrogen-ion concentration was calculated on the assumption that the phosphoric acid was undissociated. The pH values, where required, were measured with a glass electrode. Portions of the solution, in sealed tubes, were heated and potassium dihydrogen phosphate was isolated by one of three methods.

(*a*) A modification of Cohn's method,[10] in which barium phosphate is first precipitated and then converted into potassium dihydrogen phosphate.[5]

(*b*) The diluted solution was neutralised with potassium hydroxide to pH 8—10. The precipitate of potassium perchlorate was removed, and the pH of the solution adjusted to pH 5 by addition of 2M-hydrochloric acid. Impure potassium dihydrogen phosphate, contaminated with the perchlorate, was precipitated by ethanol. This precipitate was treated at 0° with insufficient water to dissolve the same weight of pure potassium dihydrogen phosphate. The undissolved perchlorate was centrifuged off and the dihydrogen phosphate precipitated by ethanol.

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[10] Cohn, *J. Biol. Chem.*, 1949, **180**, 771.

(*c*) No potassium perchlorate was present in the experiments at pH 5·51 and 8·61 and, therefore, we were able to precipitate the pure phosphate by the direct addition of ethanol.

The dried potassium dihydrogen phosphate was equilibrated isotopically with carbon dioxide[5] and this gas was analysed mass-spectrometrically; a small correction was applied for isotopic dilution by carbon dioxide.

In all our experiments the water was in large excess over the phosphate, and the first-order rate constant for oxygen exchange, irrespective of tracer, is calculated from:

$$k_E = 4 \times (2{\cdot}3/t) \log N_\infty/(N_\infty - N_t)$$

where t is the time, in seconds, and N_∞ and N_t are the isotopic abundances of the phosphate at times ∞ and t respectively, expressed in atom % excess above normal. The factor of 4 arises because k_E is four times the value of the first-order rate constant for equilibration of the tracer.

N_∞ was calculated from the isotopic abundance of the water and the relative amounts of phosphate and water. For the run with 9M-perchloric acid, its value was compared with that found experimentally: N_∞ (calc.) 0·456; N_∞ (found) 0·451 and 0·450 atom % excess, at 96 and 120 hr., respectively.

In an experiment designed to test the analytical procedure, potassium dihydrogen phosphate, prepared by reaction between phosphoric oxide and a large excess of $H_2{}^{18}O$ (0·98 atom % excess), had that isotopic abundance (mean of 5 measurements).

The experimental results for an exchange in 3·34M-perchloric acid at 100·1° were:

t (hr.)	23	46	69	92	115	138	161	∞
N (atom % excess)	0·089	0·139	0·190	0·225	0·267	0·314	0·379	0·643 (calc.)

$10^6 k_E$ = 5·26 sec.$^{-1}$ (calc. graphically).

All pH measurements were made at room temperature and, therefore, the dissociation constants of orthophosphoric acid[11] at 20° were used in calculations, *viz.*, $10^3K_1 = 7{\cdot}90$ mole l.$^{-1}$, $10^8K_2 = 6{\cdot}06$ mole l.$^{-1}$.

The rate constants k_M and k_N were calculated from the values of k_E at pH 2·21 and 4·00 (at 20°), and the relative amounts of H_3PO_4 and $H_2PO_4^-$ as estimated by using the above values of K_1 and K_2. Activity effects were ignored.

The full-line curve in Fig. 1 was obtained by using the following calculated molar percentages of $H_2PO_4^-$:

pH	0	1	2	3	4	5	6	7	8	9
$H_2PO_4^-$ (%)	0·78	7·32	44·1	88·8	98·7	99·3	94·3	62·3	14·2	1·62

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[11] Nims, *J. Amer. Chem. Soc.*, 1933, **55**, 1946; 1934, **56**, 1110.