### 203. *The Exchange of Oxygen-18 between Water and Phosphorous Acid.*

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The rate of isotopic exchange of oxygen between phosphorous acid and water was measured over the range from pH 10 to $9.4N$-$HClO_4$. The observed rate of exchange increases continuously with increasing acidity. The rate constants for the exchange between water and the various ionic species present at different pH's were calculated and the mechanisms of the exchange discussed.

THE exchange of oxygen-18 between water and phosphorous acid has been examined by Brodskii and Sulima,[1] who reported that the exchange of the monosodium salt $NaH_2PO_3$ at 100° is retarded by the addition of acid or base; that the disodium salt $Na_2HPO_3$ gave no exchange during 10 hours at 100°, and that phosphorous acid at 63° has a half-life for exchange of 6.5 hours.

In connection with our work on the mechanism of isotopic exchange of hydrogen bonded to phosphorus,[2] data on the isotopic exchange of oxygen between phosphorous acid and water was needed. Since results from preliminary experiments differed somewhat from those reported by Brodskii and Sulima, we have studied the kinetics of this exchange

[1] Brodskii and Sulima, *Doklady Akad. Nauk. S.S.S.R.*, 1953, **92**, 589 (*Chem. Abs.*, 1954, **48**, 5620).
[2] Luz and Silver, *J. Phys. Chem.*, 1962, **66**, 1356; Reuben, Samuel, and Silver, *J. Amer. Chem. Soc.*, 1963, **85**, 3093.
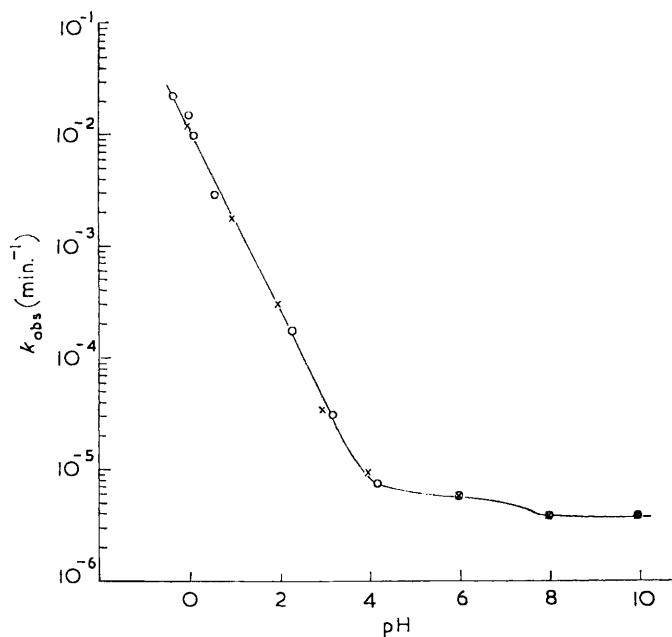
FIG. 1.   Observed (circles) and calculated (crosses) rate constants for the isotopic exchange of oxygen between phosphorous acid and water at $100 \pm 0.1°$.
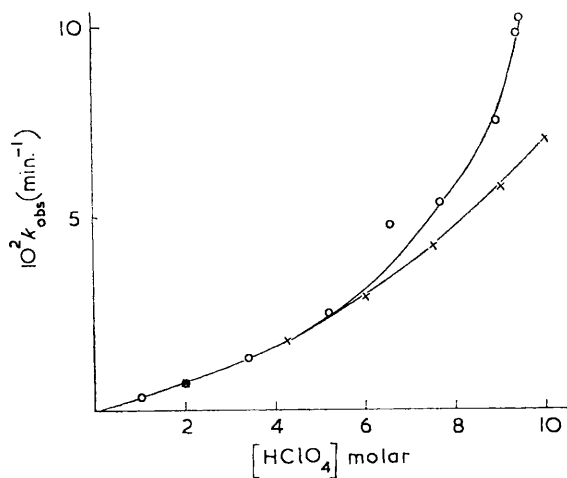


FIG. 2.   Observed (circles) and calculated (crosses) rate constants for the isotopic exchange of oxygen between phosphorous acid and water in perchloric acid solution at $80 \pm 0.1°$.

reaction over the range from 9·4 N-$HClO_4$ to pH 10.   The variation of the observed first-order rate constant $k_{obs}$ for isotopic oxygen exchange with pH is shown in Tables 1 and 2 and plotted in Figs. 1 and 2.   The results can be discussed in terms of two distinct ranges of acidity.

TABLE 1.

Rate of isotopic exchange in perchloric acid solution at $80 \pm 0.1°$.

| $[H^+]$ (M) | 1.00 | 2.00 | 3.39 * | 3.67 | 5.22 | 6.55 | 7.60 | 8.95 | 9.35 | 9.42 |
|---|---|---|---|---|---|---|---|---|---|---|
| $[H_3PO_3]$ (M) | 0.1 | 0.1 | 0.1 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.2 |
| $10^3 k_{obs}$ (min.$^{-1}$) | 3.45 | 6.90 | 13.8 | 15.2 | 25.5 | 48.0 | 54.5 | 76.5 | 100 | 104 |

\* In HCl solution.

TABLE 2.

Rate of isotopic exchange in the range 2N-$HClO_4$ to pH at $100 \pm 0.1°$ (0.1M $H_3PO_3$).

| pH | | | | 0.59 | 2.3 | 3.2 | 4.2 | 6.0 | 8.0 | 10.0 |
|---|---|---|---|---|---|---|---|---|---|---|
| *or* N of $HClO_4$ | 2.12 | 1.06 | 0.74 | | | | | | | |
| $k_{obs}$ (min.$^{-1}$) | 2.25 $\times 10^{-2}$ | 1.45 $\times 10^{-2}$ | 1.00 $\times 10^{-2}$ | 2.90 $\times 10^{-3}$ | 1.75 $\times 10^{-4}$ | 3.05 $\times 10^{-5}$ | 7.6 $\times 10^{-6}$ | 5.7 $\times 10^{-6}$ | 3.8 $\times 10^{-6}$ | 3.8 $\times 10^{-6}$ |

## RESULTS

*The Range* pH 10 *to* 0.—The dissociation constants of phosphorous acid are [3] $K_1 = 5.1 \times 10^{-2}$ and $K_2 = 1.8 \times 10^{-7}$ at 18°. The observed first-order rate constants for isotopic exchange at pH 8 and 10 (Table 2) are virtually the same, the value being $k_2 = 3.8 \times 10^{-6}$ min.$^{-1}$. Above pH 8 the acid is entirely dissociated and hence the observed rate constant can be considered to be that for the isotopic exchange of oxygen between the di-anion and water. At pH 6 where both di- and mono-anion exist in significant concentrations, the proportion of each can be calculated from the dissociation constants given above. From the concentration of the di-anion and its partial rate constant ($k_2$) the contribution of this species to the total rate of exchange can be calculated. The balance of the rate at pH 6 can be assumed to be due to exchange with the mono-anion, $H_2PO_3^-$, and hence the first-order rate constant of the latter, found by difference, is $k_1 = 6 \times 10^{-6}$ min.$^{-1}$.

Between pH 0 and 3, a plot of log (observed rate constant) against pH has a slope of $\sim 1.2$ (Fig. 1). This deviation from direct proportionality of rate with stoicheiometric acidity may indicate that two mechanisms occur in this range, an acid-catalysed exchange and a "water reaction" of the neutral species. From the measured values of the rate constants at pH 0 and 1, the pseudo-first-order rate constants for these reactions are found to be $k_a = 9.9 \times 10^{-3}$ min.$^{-1}$ for the acid-catalysed reaction and $k_w = 1.77 \times 10^{-3}$ min.$^{-1}$ for the "water reaction." From the calculated values for $k_1$, $k_2$, $k_a$, and $k_w$, the total rate of exchange was calculated for various points in the range pH 0 to 10. As seen in Fig. 1 the agreement between the experimental and observed results is excellent. This type of analysis is that commonly in use for calculating the profile of pH against rate for the hydrolysis of phosphate esters.[4]

The hydrolysis of phosphate esters [4] and the isotopic exchange oxygen between phosphoric acid [5] and water both show a maximum in the rate at about pH 4. In contrast to this behaviour and to Brodskii and Sulima's [1] results, we have not observed a maximum in the rate of isotopic exchange of oxygen between phosphorous acid and water, which would indicate that the mono-anion of phosphorous acid has no special reactivity, as it has in the case of phosphates. The rate of hydrolysis of monoalkyl hydrogen phosphonates, RHP(:O)OH, also shows no maximum in the pH–rate profile.[6]

*The Strong Acid Range.*—The plot of $k_{obs}$ against stoicheiometric acidity deviates upward from linearity in strongly-acid solution (Fig. 2). A similar relationship was found [4] in the isotopic exchange of oxygen between water and phosphoric acid. The run in hydrochloric acid indicates that there is no specific effect of chloride or perchlorate ion. The effect of added sodium perchlorate is shown in Table 3.

The interpretation of the rates of reaction in strong acid is at present not entirely clear. Various functions have been put forward for deriving mechanistic information from experimental data. Bunton *et al.*[4] in their study of the isotopic exchange of phosphoric acid, accounted quantitatively for the upward curve of the rate curve in strong acid by assuming the observed rate to be the sum of an acid-catalysed rate, a neutral rate, and a salt effect. They used the relationship, $v = v_0 \exp\beta\mu$, where $v$ and $v_0$ are the rates at ionic strength $\mu$ and zero, respectively, the

[3] Takahashi and Yui, *Bull. Inst. Phys. Chem. Research (Tokyo)*, 1941, **20**, 521.
[4] Bunton, Llewellyn, Oldham, and Vernon, *J.*, 1958, 3574.
[5] Bunton, Llewellyn, Vernon, and Welch, *J.*, 1961, 1636.
[6] Nylen, *Svenks. kem. Tidskr.*, 1936, **48**, 2.

first-order rate constant for the acid-catalysed exchange being given by [4] $k_{obs} = k_A[A^+]\exp\beta\mu$. In the case of the present results, with the rates of exchange in 4·24M-perchloric acid plus sodium

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TABLE 3.

Effect of added sodium perchlorate on the rate of isotopic exchange in perchloric acid solution at 80 ± 0·1°.

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| [H⁺] | 1·16 | | | 4·24 | |
|---|---|---|---|---|---|
| $\mu$ (mole l.⁻¹) | 1·16 | 3·16 | 5·16 | 4·24 | 7·24 |
| $10^3 k_{obs}$ (min.⁻¹) | 3·60 | 4·30 | 4·10 | 18·0 | 23·5 |

perchlorate as a basis for calculation, values were found for $k_A = 2\cdot9 \times 10^{-3}$ min.⁻¹ and $\beta = 0\cdot09$. The lower line in Fig. 2 is a plot of the rate constant for exchange calculated on the basis of these values. The agreement with experiment is not good and one must therefore conclude that a simple salt effect cannot account for the experimental data of the exchange reaction in phosphorous acid. Bunton *et al.*[4] also took into account the rate of exchange due to the neutral "water reaction." In the present case this reaction can be ignored since the neutral rate (see above) is several orders of magnitude lower than the rates measured in the range under discussion.

The rate constants for exchange were also plotted by the method developed by Bunnett.[7] Plots of (log $k + H_0$) against log $a_{H_2O}$, and (log $k - [HClO_4]$) against log $a_{H_2O}$, have a negative curvature as in many of the cases cited by Bunnett. The approximate slopes $w$ and $w^*$, respectively, using Bunnett's nomenclature, are very similar to those (+3·4 and 0·7) found for the isotope exchange of oxygen between phosphoric acid and water. The values of $w$ and $w^*$ were used by Bunnett to determine the role of water in the transition state in a large number of reactions. In the case of the hydrolysis of phosphate esters and in the isotopic exchange of oxygen between orthophosphate and water, the values of $w$ and $w^*$ were not consistent with other chemical evidence, and the mechanism of oxygen exchange is unknown. The same situation applies to the results of the present work.

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DISCUSSION

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There are four possible mechanisms for the isotopic exchange of oxygen between phosphorous acid and water: (1) reversible addition of water to the phosphoryl bond, (2) direct displacement on phosphorus by nucleophilic attack of a water molecule, a hydroxide or a hydroxonium ion, (3) ionisation giving a hydroxyl group or a water molecule by an $S_N1$ type mechanism to form a " metaphosphite " intermediate [8] which is rapidly re-hydrated, and (4) an initial rearrangement of the " phosphonate " (quadricovalent) to the " phosphite " (tervalent) form followed by reaction by mechanisms (2) or (3). These alternatives can be illustrated by the following scheme for the neutral molecule:
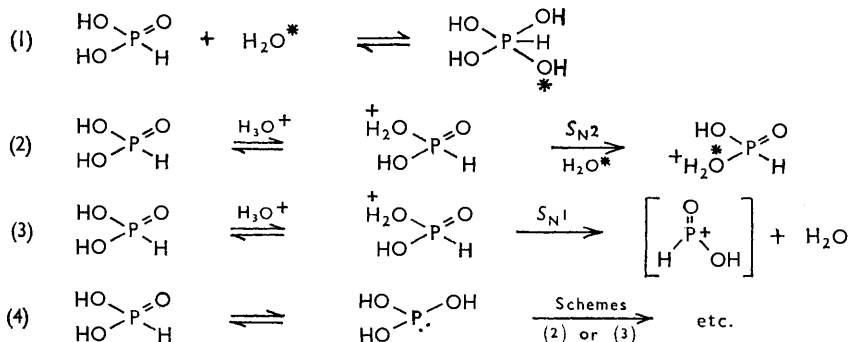


*The Di-anion and Mono-anion.*—Exchange between the di-anion and water can, in principle, occur *via* two mechanisms. Reaction between the doubly charged " phosphonate " ion and hydroxide would appear to be unlikely due to electrostatic repulsion.

[7] Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956.

[8] Van Wazer, " Phosphorus and its Compounds," Interscience Inc., New York, 1958, Vol. I, p. 413.

In fact the similarity of the rate constant at pH 8 and at pH 10 (see Table 2) demonstrates that hydroxide does not participate in the rate-determining step since a hundred-fold increase in concentration does not affect the rate of exchange. In addition, since there is only one hydrogen atom in the molecule, displacement of water by water *via* mechanism (2) is not possible. However, mechanism (4) offers a method of rearrangement to an anion which can then react by a reversible unimolecular dissociation in order to incorporate the isotopic label into the di-anion.

The mechanism for oxygen exchange by the addition of water to the phosphoryl bond (scheme 1) is also possible. The intermediate also provides a mechanism for deuterium exchange.
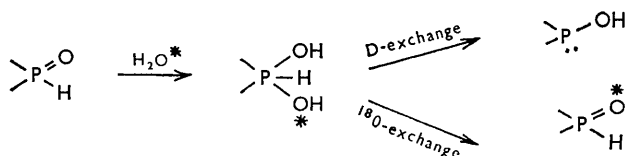


However, deuterium exchange requires the breaking of a P–H bond in the second step, whereas oxygen exchange requires the O–H bond to break. The former exchange is known to occur [2,9] at a rate two orders of magnitude faster than the latter. It therefore seems unlikely that deuterium and oxygen isotopic exchange occur by this common intermediate.

The mono-anion undergoes isotopic exchange with a rate constant of the same order as that of the di-anion, and all four mechanisms are possible.

Exchange with the mono-anion can occur by displacement of hydroxide by hydroxide (scheme 2) which seems again unlikely for the reasons discussed above. Displacement of water is also unlikely since this would involve previous rearrangement to a species
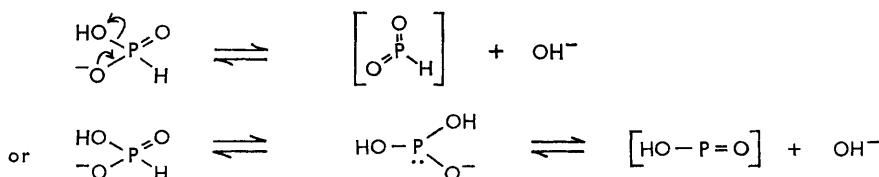


$H_2O-P(O)O^-$ with two hydrogens on one oxygen. Alternatively the mono-anion can react by a unimolecular mechanism either by direct ionisation (scheme 3) or, following previous rearrangement, by scheme (4). These mechanisms again involve a "meta-phosphite" intermediate [$HPO_2$]. Here again a hydration mechanism (scheme 1) is possible.

*The Neutral Molecule and Conjugate Acid.*—In the range pH 0 ($1_N$-HClO$_4$) to $10_N$-HClO$_4$ it is most unlikely that hydroxide is a reactant. In this range where the neutral molecule and conjugate acid occur, all four mechanisms of exchange are possible. In addition a previous rearrangement to a zwitterion form can occur which may be unlikely but not impossible. This zwitterion can then react either by ionisation or by bimolecular displacement by water.
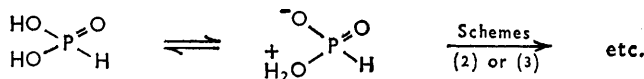


In strong acid solution, protonated species occur, but, since it is not possible to distinguish between protonation on the phosphoryl or the hydroxyl oxygens, no detailed mechanism of exchange can be determined. However, unimolecular ionisation mechanisms in strong acid are considered unlikely, since they would be expected to lead to a rough correlation between exchange rate and the Hammett acidity function. This is

[9] Samuel and Silver, unpublished results.

not found to be the case. In strong acid the rate of oxygen exchange in phosphorous acid is approximately 30 times faster than for phosphoric acid at a given acidity. In general the rate of oxygen exchange of oxyanions of a given element increases with a decrease in the number of oxygen atoms in the ion.

Finally, it should be noted that the deviation from linear relations between rate of exchange and acidity in very concentrated acid may partly be due to the possibility of multiple protonation.

## EXPERIMENTAL

*Phosphorous Acid.*—Preliminary experiments showed that phosphorous acid was not oxidised under the conditions of the exchange experiments. Rates of oxygen exchange were measured at $80 \cdot 0 \pm 0 \cdot 1°$ and $100 \cdot 0 \pm 0 \cdot 2°$, solvent water enriched in oxygen-18 being used. Weighed amounts of crystalline phosphorous acid were dissolved in known volumes of acid or buffer solutions. Samples of the solutions were kept in sealed borosilicate bulbs in a thermostat. At measured intervals a bulb was removed, cooled rapidly and, in the case of acid solutions, the contents neutralised with sodium hydroxide solution. The addition of barium chloride gave a precipitate of barium phosphite. This was dissolved in a minimum of 1N-hydrochloric acid at room temperature, filtered, and reprecipitated by the addition of sodium hydroxide solution. This procedure was repeated and the precipitate then washed throroughly with distilled water, ethanol, and finally with acetone. After being dried in a vacuum oven between 70 and 80°, the barium phosphite was analysed for its oxygen-18 content by Anbar and Guttmann's method.[10] Solvent water was analysed for oxygen-18 by the hypobromite method.[11]

The results were analysed by plotting $\log (1 - F_t)$ against time, where $F_t$ is the fraction exchange value at time $t$. The half life $t_{\frac{1}{2}}$ for exchange was taken from this graph and the pseudo-first-order rate constant $k$ for exchange calculated from the expression $k = 3 \times 0 \cdot 699/t_{\frac{1}{2}}$. The factor 3 accounts for the three exchangeable oxygen atoms in each molecule of phosphorous acid. The effect of temperature on the dissociation constants was neglected in the calculations but no large error is expected on this account.

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[10] Anbar and Guttmann, *Internat. J. Appl. Radiation Isotopes*, 1959, **4**, 233.
[11] Anbar, *Internat. J. Appl. Radiation Isotopes*, 1958, **3**, 134.