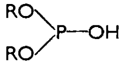
258. *Ionisation of the* P–H *Bond. Deuterium-exchange Studies with Diethyl and Ethyl Hydrogen Phosphonate.*

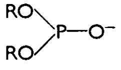
By P. R. Hammond.

Peaks assigned to the hydrogen of the P–H bond in the nuclear magnetic resonance spectrum of diethyl phosphonate $PHO(OEt)_2$ have been found to disappear in a number of deuterium oxide buffer solutions. The exchanges are of the first order in phosphonate and are catalysed by acid and base. In basic solutions the rate constants are best expressed as a linear function of base-catalyst concentration, whereas in acid solutions a decrease in catalytic coefficient with increasing deuterium-ion concentration or a fractional order applies. The exchanges are ascribed to ionisation of the P–H bond. The phosphorus-bound hydrogen of ethyl hydrogen phosphonate EtO·PHO·OH undergoes exchange in acid deuterium oxide whereas in solutions of the salts exchange does not occur.

Reactions of diesters of phosphorous acid in which the phosphorus acts as a nucleophilic centre [1] may be understood in terms of a triply-connected central atom. However, neither dialkyl hydrogen phosphite (I) nor the dialkyl phosphite anion (II) has been detected in neutral solution,[2] and vigorous conditions, *e.g.*, reaction with metallic sodium or a sodium alkoxide, are necessary to remove the phosphorus-bound hydrogen.

Evidence for the phosphonate structure (III) has come from infrared spectra [3] showing frequencies attributable to P–H and $P \simeq O$ groups, and from nuclear magnetic resonance spectra.[4] The spectrum for the pure diethyl phosphonate showed a triplet centred at τ 8·7 (methyl–hydrogen), an indistinct [*] quadruplet centred at τ 5·9 (methylene–hydrogen), and two peaks τ —5·5 and 11·9. No obvious change occurred in deuterium oxide solutions


(I)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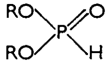
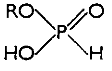

(III)


(IV)

except that the last two peaks together slowly disappeared. These are assigned to the *P*-H hydrogen. The coupling between the ^{31}P–H nuclei is calculated to be 697 cycles.

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[*] For a more detailed examination of the spectrum, see Mavel, *Compt. rend.*, 1959, **248**, 3699 and ref. 8.

[1] Michaelis and Becker, *Ber.*, 1897, **30**, 1003; Abramov, *Zhur. obshchei Khim.*, 1952, **22**, 647; Pudovik and Arbusov, *ibid.*, 1951, **21**, 382; Atherton and Todd, *J.*, 1947, 674; Andrews and Atherton, *J.*, 1960, 4682.

[2] Doak and Freedman, *Chem. Rev.*, 1961, **61**, 31.

[3] Wolf, Mathis-Noël, and Mathis, *Bull. Soc. chim. France*, 1960, 124; Daasch, *J. Amer. Chem. Soc.*, 1958, **80**, 5301.

[4] Callis, Van Wazer, Shoolery, and Anderson, *J. Amer. Chem. Soc.*, 1957, **79**, 2719; Finegold, *Ann. N.Y. Acad. Sci.*, 1958, **70**, 875.

Information on the stability of the various species was to be expected from a kinetic study of the deuterium exchange and this was undertaken.

Hydrogen-isotope exchanges in hypophosphorous acid[5] have shown that the phosphorus-bound hydrogen undergoes slow exchange in acid solution but that there is no exchange in solutions of the salts. Similarly with phosphorous acid[6] the exchange occurs at a measurable rate, but not with its salts. Exchange of deuterium between dibutyl phosphonate and butyl [^{2}H]alcohol has been shown to be catalysed by both acid and base.[7]

The infrared spectra of thin films, between silver chloride plates, of diethyl phosphonate and deuterium oxide mixtures therewith were observed on a Perkin–Elmer Infracord spectrophotometer. A band at 1775 cm.$^{-1}$, assigned to the P–D stretching vibration, appeared within a few minutes. The rate of exchange was catalysed by both acid and base, and with 0·1M-sodium hydrogen carbonate was complete before the readings could be taken. The high concentrations (5M) of the ester and the uncertainty of the temperature in the liquid detracted from the value of the measurements.

Nuclear magnetic resonance, on the other hand, permitted from 1·5 to 0·1M-diethyl phosphonate to be measured, and the sample temperature, taken as room temperature, had a maximum variation of 1°.

EXPERIMENTAL AND RESULTS

Diethyl phosphonate, fractionally distilled through a Vigreux column, had b. p. 78·0—78·5°/15 mm., and was used directly or stored at 0°.

Nuclear magnetic resonance spectra at 20° were obtained at 40 Mc./sec. by a Varian Associates 4300 B spectrometer with the usual flux stabilisation and sample spinning.

The height of the peak at τ 11·9 was used as a measure of the P–H concentration. Other studies[8] had shown that the peak height was proportional to concentration. The peak width did not alter during the experiments, and could be compared with the average of the lower peaks of the neighbouring ethyl triplet as internal standard.

The height and structure of the triplet did not alter during exchange, and no increase in complexity, which could be attributed to formation of an intermediate, was observed.

For each point, at least four comparisons of the peak heights were made and the average ratio R was assumed to occur at the average time t at which the peaks were recorded. 5—7 Points per run were obtained.

A series of deuterium oxide (99·9% purity) buffer solutions of acids whose dissociation constants in this solvent were known[9] were prepared by dissolving weighed amounts of the dried salts.* No previous deuterium exchange was performed with hydrogen-containing materials. The molar percentage of protium in deuterium thus introduced, together with the total fraction coming from the diethyl phosphonate, never exceeded 2·0%, and at the beginning of the experiment, where the measurements were the most reliable, the molar percentage was frequently as low as 0·1%. Sodium chloride was added to bring all to constant ionic strength.

Results.—For the reactions, the pseudo-first-order relation $\log R = -0{\cdot}434kt + \log R_0$ was found to hold. The first-order rate constants were calculated from the regression of log R on t, and the results are shown in the accompanying Tables. The standard errors of these were $\pm\sim$10%. Rate constants were plotted for buffer solutions against concentrations (0·15M, 0·10M, and 0·05M) of both acid and anion (Table 1). Similarly, for buffers containing acetic and

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* Dissociation constants of acetic and cacodylic acid have not been reported in deuterium oxide for 20°, but the variations in K_A with temperature are small and imply a negligible change in deuterium oxide.

[5] Erlenmeyer, Schoenauer, and Schwarzenbach, *Helv. Chim. Acta*, 1937, **20**, 726; Jenkins and Yost, *J. Inorg. Nuclear Chem.*, 1959, **11**, 297; Brodskii and Sulima, *Doklady Akad. Nauk S.S.S.R.*, 1952, **85**, 1277.

[6] Martin, *J. Amer. Chem. Soc.*, 1959, **81**, 1574.

[7] Fox, N.R.L. Report 5242, Jan. 1959, Washington, D.C.

[8] Hammond, Univ. California Radiation Lab. Report, UCRL–9652, 1961.

[9] Schwarzenbach, *Z. Elektrochem.*, 1938, **44**, 46; La Mer and Chittum, *J. Amer. Chem. Soc.*, 1936, **58**, 1642; Hornel and Butler, *J.*, 1936, 1361.

TABLE 1.

Disappearance of the P–H hydrogen peak in buffer solutions at 20°.

Run no.	Acid in buffer	Acid (M)	Anion (M)	NaCl (M)	10^4k (sec.$^{-1}$)	Run no.	Acid in buffer	Acid (M)	Anion (M)	NaCl (M)	10^4k (sec.$^{-1}$)
1	Acetic	0·15	0·15	0·05	2·6	7	Phosphoric	0·15	0·15	0·05	0·86
2		0·10	0·10	0·10	1·9	8		0·10	0·10	0·10	0·65
3		0·05	0·05	0·15	1·2	9		0·05	0·05	0·15	0·39
4	Cacodylic	0·15	0·15	0·05	87	10	Hydrochloric	0·10	—	0·10	1·4
5		0·10	0·10	0·10	53	11		0·20	—	—	2·0
6		0·05	0·05	0·15	34	12		0·02	—	0·18	0·55

TABLE 2.

Disappearance of the P–H hydrogen peak in buffer solutions at 20°.

Run no.	Acid in buffer	Acid (M)	Anion (M)	NaCl (M)	10^4k (sec.$^{-1}$)	Run no.	Acid in buffer	Acid (M)	Anion (M)	NaCl (M)	10^4k (sec.$^{-1}$)
13	Acetic	0·15	0·05	0·15	1·0	17	Cacodylic	0·15	0·05	0·15	28
14		0·09	0·03	0·17	0·7	18		0·09	0·03	0·17	19
15		0·05	0·15	0·05	3·1	19		0·05	0·15	0·05	110
16		0·03	0·09	0·11	2·2	20		0·03	0·09	0·11	85

TABLE 3.

Influence of sodium chloride on the disappearance of the P–H hydrogen peak at 20° (buffers 0·1M in acid and in anion).

Run no.	Acid in solution	NaCl (M)	10^4k (sec.$^{-1}$)	Run no.	Acid in solution	NaCl (M)	10^4k (sec.$^{-1}$)
21	Acetic	0·00	2·0	23	Cacodylic	0·00	61
2		0·10	1·9	5		0·10	53
22		0·30	1·9	24		0·30	44
10	Hydrochloric	0·10	1·4				
25	(0·10M)	0·30	1·4				

cacodylic acid, plots were made for solutions containing the acid and anion in proportions other than 1 : 1 (Table 2). The influence of sodium chloride on acetate, cacodylate, and hydrochloric acid systems was found to be small, in the region of the accuracy of the experiments (Table 3). The rates of hydrolysis of the ester [10] in basic protium oxide solutions are approximately one-thousandth of the rates of P–H disappearance reported here, and in acid solutions are approximately one-twentieth. Corrections needed for hydrolysis are therefore negligible in basic solutions and are small in hydrochloric acid.

Extrapolating graphs I and II and the plots for the phosphate buffer to zero buffer concentrations gives the catalysis by the water species OD^-, D^+, and D_2O. A rate constant of $0·1 \times 10^{-4}$ sec.$^{-1}$ was obtained for solutions containing 0·15, 0·10, and 0·05M-acetic acid. This was taken as the neutral water rate.

These graphs show linear relationships between rate constants and catalyst concentrations. Also plots of rate constants against base-catalyst concentrations for the two chosen ratios acid : anion [plots IA, B, and IIA, B)] give lines reasonably parallel to (I) or (II). Thus in these solutions catalysis by acid is very small, and the rates may be best expressed as a linear function of base-catalyst concentration:

$$k = k_W + k_B(B) + k_{OD}(OD^-). \qquad (1)$$

From the OD^- concentrations [9,11] and the intercepts of Figs. 1 and 2 the values of k_{OD} and k_B could be determined. Correcting for the uncatalysed rate, and using a value of 0·7 for the activity coefficient of all univalent ions, gave $2·5 \times 10^5$ and $1·5 \times 10^5$ l. mole^{-1} sec.$^{-1}$ for k_{OD} in acetate and cacodylate buffer, respectively. In view of the inaccuracy of the measurement this is good agreement. The intercepts for the other lines (IA, B, and IIA, B) favour the higher value. Also k_B values of $1·3 \times 10^{-3}$ and $4·5 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ were estimated for the acetate and cacodylate buffers. For the fast rates (runs 4, 19, and 20), as many readings of peak

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[10] Nylen, *Svensk kem. Tidskr.*, 1937, **49**, 79.

[11] Wynne-Jones, *Trans. Faraday Soc.*, 1936, **32**, 1397.

heights were taken as for the others by increasing chart speed and speed of scan, but the loss of sensitivity under these conditions makes these rates suspect.

The intercept for the phosphate buffers, $0{\cdot}15 \times 10^{-4}$ sec.$^{-1}$ at a deuterium-ion concentration of $2{\cdot}6 \times 10^{-3}$ mole l.$^{-1}$, together with runs 10—12 show that a relation of the form $k = k_W + k_D(D^+)$ does not apply. This effect can be attributed only partly to the small amount of hydrolysis, and further experiments are in progress. For the time being, the results may be best expressed as a fractional-order relation or as a decrease in catalytic coefficient with increasing deuterium-ion concentration.

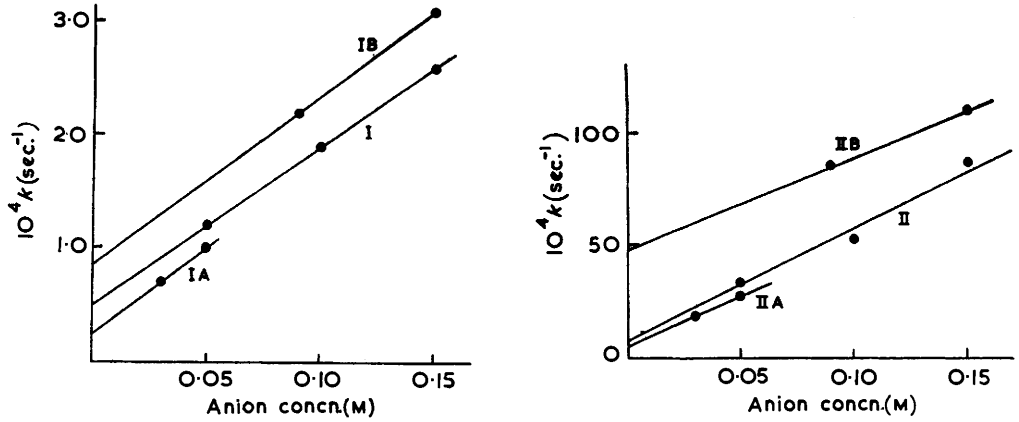

FIG. 1. FIG. 2.

Disappearance of the P–H peak in (Fig. 1) acetate buffers, and (Fig. 2) cacodylate buffers.

DISCUSSION

The stability of the rest of the diethyl phosphonate spectrum supports the view that the reaction is the exchange of the P–H hydrogen for deuterium.

Equation (1) expresses the rates of exchange in acetic and cacodylic acid buffers. The second-order coefficients for the acetate, cacodylate, and deuteroxide ion ($1{\cdot}3 \times 10^{-3}$, $4{\cdot}5 \times 10^{-2}$, and $2{\cdot}0 \times 10^{5}$ l. mole^{-1} sec.$^{-1}$) may be compared with the same second-order coefficients for the reaction of the ester with iodine[12] ($1{\cdot}5 \times 10^{-3}$, $3{\cdot}0 \times 10^{-2}$, and $1{\cdot}2 \times 10^{5}$ * l. mole^{-1} sec.$^{-1}$). The rates, which were independent of iodine concentration, were measured in protium oxide solutions. Thus, since acetate, cacodylate, and deuteroxide anion species are slightly stronger bases than their counterparts in protium oxide, the agreement in catalytic coefficients for the two reactions is within experimental error.

The base-catalysed iodine reaction obeyed a Brönsted relation, and a similar relation is strongly implied for the deuterium exchange. Thus the rate-determining steps are likely to be proton transfers. The following mechanism is sufficient to explain the kinetics:

$$k_2(\mathrm{DB}) \gg k_1(\mathrm{B})$$

The iodine reaction may be represented by fast removal of the anion.

For the uncatalysed reactions, the first-order rate constants $0{\cdot}1 \times 10^{-4}$ sec.$^{-1}$ for the deuterium exchange and $0{\cdot}07 \times 10^{-4}$ sec.$^{-1}$ for the reaction with iodine are of the order

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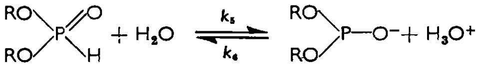
* The value quoted is Nylen's hydroxide-catalysed reaction in cacodylic acid buffers. For the deuterium exchange studies it can be said that the same values of k_{OD} for acetate and cacodylate solutions apply.

[12] Nylen, *Z. anorg. Chem.*, 1938, **235**, 161.

predicted from the quoted Brönsted coefficients, if water is assumed to function as a base in the ionisation:



The reverse reaction, k_6, one between oppositely charged ions, will be rapid, and close to the limiting velocity for a diffusion-controlled reaction ($k_6 = 10^{10}$ l. mole^{-1} sec.$^{-1}$). This gives an estimate ($K_A = k_5/k_6$) for the acid strength of diethyl phosphonate in water at pK_a 15. A direct measurement in water is not possible owing to the rapid hydrolysis [10] of the ester. In contrast with acids of the electronegative nitrogen and oxygen, phosphorus acids may well resemble those of carbon [13] in that ion recombination in all but the weakest members will be below the predicted limiting velocity. For this reason, k_6 and hence pK_a given above may be too high.

Deuterium Exchange in Ethyl Hydrogen Phosphonate.—The hydrogen of the P–H bond in ethyl hydrogen phosphonate (IV) was also found to undergo exchange with deuterium. Evidence for the existence of the P–H bond in a number of alkyl hydrogen phosphonates was obtained from nuclear magnetic resonance spectra, where signals appearing in the region of τ 10·8 and —4·9 for strong solutions of the acids and the ammonium salts in water were assigned to ^{31}P–H spin coupling (*J* 630 cycles). *E.g.*, ethyl ammonium phosphonate showed a triplet centred at τ 8·4, a quadruplet at 5·8, and two single peaks at 10·8 and —4·9. In addition, an absorption at 2360 cm.$^{-1}$ for the infrared spectra of the ammonium salts was assigned to the P–H vibration frequency.

Again, the P–H peak at high field in molar solutions of the ester was compared with the lower two peaks of the ethyl triplet. The procedure developed above was repeated and first-order rate constants for the disappearance of the P–H bond at 23° were obtained. No increase in the complexity of the spectra, which would be expected if hydrolysis occurred at a comparable rate, was observed.

Solution	Rate constant (sec.$^{-1}$)	Molar percentage of protium in deuterium
Ethyl hydrogen phosphonate	$0·56 \times 10^{-4}$	2
,, ,, ,, in 0·86N-HCl	$0·79 \times 10^{-4}$	8
Ammonium ethyl phosphonate Potassium ethyl phosphonate	$<3·0 \times 10^{-8}$	1

Thus, exchange occurs under acid conditions where the undissociated acid [14] (IV) (p*K* 0·8) is present in solution. The stability of the anion is in accord with a very weak secondary dissociation of a dibasic acid, where the second proton is released from a centre already adjacent to a negative charge.

The reactivity of the P–H proton in acids (III) and (IV) parallels the ease with which the compounds may be oxidised.[15] Similarly, deuterium exchange of the P–H bond in phosphorous and hypophosphorous acid [5,6] corresponds to their reactivity towards carbonyl compounds.[16] It is likely that these reactions require ionisation of the P–H bond.

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[13] Bell, *Quart. Rev.*, 1959, **13**, 169.

[14] Farr, " Phosphorus, Properties of the Element and Some of its Compounds," Tennessee Valley Authority, Wilson Dam, Ala., 1950 (TVA Chem. Eng. Rept., No. 8).

[15] Dimroth and Ploch, *Chem. Ber.*, 1957, **90**, 801; Brown and Hammond, *J.*, 1960, 4229.

[16] Ville, *Ann. Chim. Phys.*, 1891, **23**, 289; Marie, *Chem. Zentr.*, 1904, **8**, II, 1708.