660. *The Reactions of Organic Phosphates. Part III.* The Hydrolysis of Dimethyl Phosphate.*

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The hydrolysis of dimethyl phosphate has been investigated over a range of acidities, pH 5 to solution in 5M-perchloric acid. Two hydrolytic mechanisms have been identified, both proceeding largely with carbon–oxygen bond fission but involving respectively the neutral species and the conjugate acid. Hydrolysis in strongly alkaline solution also proceeds with carbon–oxygen fission. The mechanisms of these reactions are discussed.

PART I of this series * reported a study of the mechanisms of hydrolysis of monomethyl dihydrogen phosphate. This paper is concerned with a similar study of dimethyl hydrogen phosphate.

It has been known for some time that dialkyl phosphates are hydrolysed readily only in strongly acidic solutions.[1] The only quantitative studies so far reported, however, are those of Westheimer and his co-workers.[2,3,4] They investigated the hydrolyses of dibenzyl phosphate [2] in some detail, and found that in the range of acidity pH 8 to 1·0M-acid there were two hydrolytic reactions, involving, respectively, the neutral and the conjugate acid species. The monoanion species, unlike that of phosphate monoesters, was relatively unreactive. The hydrolysis of dimethyl phosphate in strongly alkaline solution was also investigated.[3] Under these conditions hydrolysis was found to be of the first order in hydroxide ion and exceedingly slow, which is consistent with the generalisation [5] that alkaline lability in dialkyl hydrogen phosphates occurs only when the molecule contains a hydroxyl group in proximity to the phosphoryl function.

EXPERIMENTAL

Sodium dimethyl phosphate was prepared by refluxing pure trimethyl phosphate (35 g.), obtained by fractionation of a commercial sample, with sodium iodide (40 g.) in acetone (200 c.c.). The precipitate was filtered off, washed with dry acetone until free from iodide ions, and dried at 160° (Found: C, 16·4; H, 4·0. Calc. for $C_2H_6NaO_4P$: C, 16·2; H, 4·1%). The free acid was obtained by the use of Amberlite resin I.R-120(H) (Found: equiv., 148·1. Calc. for $C_2H_7O_4P$: equiv., 148).

Determination of the Dissociation Constant.—The dissociation constant of dimethyl hydrogen phosphate was obtained by pH measurements as described in Part I. At 0°, 25°, and 50° the

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* Parts I and II, *J.*, 1958, 3574, 3588.

[1] Plimmer and Burch, *J.*, 1929, 279, 292.

[2] Kumamoto and Westheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 2515.

[3] Kumamoto, Cox, and Westheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 4858.

[4] Westheimer, *Chem. Soc. Spec. Publ.*, 1957, No. 8, p. 1.

[5] Brown and Todd, *J.*, 1952, 52.

values obtained were 0·62, 0·76, 1·00. Graphical extrapolation to 100° gave the value 1·60. The value at 25° was also determined conductometrically:

Concn. (10^{-4} mole/l.)	337·5	168·7	84·4	42·2	33·7	21·1	13·5	6·7	3·4
Equiv. cond. (ohm^{-1})	323·6	343·3	354·9	362·0	358·4	365·3	367·8	374·5	374·8

from which the equivalent conductance at infinite dilution is obtained as 379·9. Application of the Onsager equation led to pK = 0·50.

The agreement between these two methods is as good as expected.

TABLE 1.

Time (min.)	Spekker reading	G	c'	$(c' + c_p)$	k_0 (min.$^{-1}$ × 10^4)
0	0·000	—	—	—	—
600	0·048	1·25	0·539	0·587	3·45
1000	0·105	1·75	0·755	0·860	3·23
1400	0·185	2·19	0·946	1·131	3·19
1800	0·275	2·46	1·063	1·338	3·09
2100	0·348	2·59	1·117	1·465	3·02
2400	0·432	2·81	1·210	1·642	3·12
2700	0·518	2·99	1·290	1·808	3·18
3000	0·607	2·95	1·275	1·882	3·05
3300	0·702	1·96	1·277	1·979	3·02
∞ (Calc.)	3·137	—	—	3·137	—

Buffer Solutions.—Buffer solutions for the kinetic experiments were those for which the pH values have been given at 20° and 150° by Stene.[6] The values of the pH at intermediate temperatures were found by interpolation (see Part I).

Kinetic Experiments.—Hydrolysis of dimethyl hydrogen phosphate is difficult to investigate kinetically since there are no convenient methods of estimation of either the substrate or the primary products. However, one of the products, monomethyl phosphate, itself undergoes hydrolysis to inorganic phosphate, and this can be estimated as described in Part I:

$$(\mathrm{MeO})_2\mathrm{PO{\cdot}OH} + \mathrm{H_2O} \xrightarrow{k_0} \mathrm{MeO{\cdot}PO(OH)_2} + \mathrm{MeOH}$$

$$\mathrm{MeO{\cdot}PO(OH)_2} + \mathrm{H_2O} \xrightarrow{k_0'} \mathrm{PO(OH)_3} + \mathrm{MeOH}$$

Since the first-order coefficients k_0 and k_0' are of similar size progressive estimation of the inorganic phosphate enables k_0 to be found if k_0' is known.

If c_0 is the initial concentration of dimethyl phosphate, and c' and c_p are the concentrations of monomethyl phosphate and inorganic phosphate respectively at time t, then

$$k_0 = \frac{2{\cdot}303}{t} \log \frac{c_0}{c_0 - (c' + c_p)}$$

and since $dc_p/dt = k_0'c'$ we have

$$k_0 = \frac{2{\cdot}303}{t} \log \frac{c_0}{c_0 - \left\{\dfrac{dc_p}{dt} \cdot \dfrac{1}{k_0'} + c_p\right\}}$$

Since only first-order processes are involved and since the intensity of colour developed in the phosphate determination obeys Beer's law, the equation may be written as:

$$k_0 = \frac{2{\cdot}303}{t} \log \frac{D_\infty - D_0}{\left(D_\infty - D_t - \dfrac{dD_t}{dt} \cdot \dfrac{1}{k_0'}\right)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \tag{1}$$

where D_0, D_t, and D_∞ are the colour intensities at zero time, time t, and complete reaction respectively. The method requires dD_t/dt to be determined graphically: nevertheless, it was found that the spread in the values of the rate coefficients in any one run was not larger than is

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[6] Stene, *Rec. Trav. chim.*, 1930, **49**, 1133.

usually found with simple first- or second-order processes. k_0 can also be found from the equation:

$$c_p = \frac{1}{(k_0 - k_0')} \{c_0(k_0' - k_0) - c_0[k_0' \exp(-k_0 t) - k_0 \exp(-k_0' t)]\} \quad . \quad . \quad (2)$$

but the labour involved appears to be greater.

The following experimental details of a run at 100° with $4{\cdot}8 \times 10^{-3}$M-dimethyl phosphate and 0·50M-perchloric acid are typical. Aliquot parts (6·00 c.c.) were sealed in glass tubes, placed in a thermostat until thermal equilibrium was reached, removed at appropriate intervals, and cooled. Analysis for inorganic phosphate was carried out as described in Part I. The results are shown in Table 1, where

$$G = dD_t/dt, \quad c' = \frac{dD_t}{dt} \cdot \frac{1}{k_0'}, \quad (c' + c_p) = \left\{\frac{dD_t}{dt} \cdot \frac{1}{k_0'} + (D_t - D_0)\right\}.$$

G is in Spekker units × min.$^{-1}$ × 10^4, c' and $(c' + c_p)$ are in Spekker units.

For summarised results see Tables 2 and 3.

Isotope Experiments.—Experiments with ^{18}O are also more difficult than with monomethyl phosphate. It is practicable to examine isotopically only one of the products (*i.e.*, methanol), and, unfortunately, this arises partly from the secondary hydrolysis of monomethyl phosphate.

In strongly acidic solutions an additional complication arises since methanol undergoes direct isotopic exchange with the solvent. Under these conditions, therefore, it is desirable to work with methanol isolated after ~10% of reaction. Above pH 1 the isotopic exchange of methanol is too slow to be important, and since, in this range the hydrolysis of monomethyl phosphate is faster than that of dimethyl phosphate, a considerable proportion of the isolated methanol arises from the secondary hydrolysis of the primary ester. The procedure for correcting for this is as follows:

TABLE 2. *Rates of hydrolysis of dimethyl phosphate at* pH 0—5 (100° *unless specified*).

pH	10^6k_0 (sec.$^{-1}$)	Medium	pH	10^6k_0 (sec.$^{-1}$)	Medium
0·02	6·62	1·0M-$HClO_4$	3·33	0·072	0·05M-$KHC_8H_4O_4$, 0·0147M-HCl
0·32	4·93	0·5M-$HClO_4$			
0·72	3·93	0·2M-$HClO_4$	4·17	0·01	0·05M-$KHC_8H_4O_4$
1·02	3·15	0·1M-$HClO_4$	1·24 [1]	0·463	0·0645M-HCl, 0·05M-KCl
1·24	3·13	0·0645M-HCl, 0·05M-KCl	1·24 [2]	6·12	,, ,,
2·51	0·532	0·05M-$KHC_8H_4O_4$, 0·0396M-HCl	1·24 [3]	15·2	,, ,,

$KHC_8H_4O_4$ is potassium hydrogen phthalate.

[1, 2, 3] At 80°, 106·6°, and 117·6° respectively.

The Arrhenius parameters for the reaction at pH 1·24 are 25·5 kcal. mole^{-1} and $1{\cdot}2 \times 10^{13}$ sec.$^{-1}$.

TABLE 3. *Rates of hydrolysis of dimethyl phosphate in strongly acidic solutions at* 100° (concns. refer to room temperature).

[$HClO_4$] (M)	1·00	2·00	3·00 [3]	4·00 [2]	5·00 [1]	2·00 [1]	3·00 [1]
[$NaClO_4$] (M)	—	—	—	—	—	3·00	2·00
10^6k_0 (sec.$^{-1}$)	6·62	10·8	14·7	23·3	35·6	21·2	25·7
[$HClO_4$] (M)	3·50 [1]	4·00 [1]	2·00 [2]	3·00 [2]	1·00 [3]	2·00 [3]	2·50 [3]
[$NaClO_4$] (M)	1·50	1·00	2·00	1·00	2·00	1·00	0·50
10^6k_0 (sec.$^{-1}$)	28·8	29·3	16·9	19·8	11·2	13·3	14·6

[1, 2, 3] Solutions of total ionic strength (μ), 5·00, 4·00, and 3·00 respectively.

Let c_0, c', and c_p have the same significance as above. Then, at any time, t, the concentrations of methanol produced by hydrolysis of di- and mono-methyl phosphate are, respectively, $(c' + c_p)$ and c_p. The fraction (f) of the total methanol which arises from hydrolysis of monomethyl phosphate is then $f = c_p/(c' + 2c_p)$. It can be shown that c' and c_p are given, respectively, by the expressions:

$$c' = [c_0k_0/(k_0 - k_0')]\{\exp(-k_0 t) - \exp(-k_0' t)\}$$

$$c_p = [c_0/(k_0 - k_0')]\{(k_0' - k_0) - [k_0' \exp(-k_0 t) - k_0 \exp(-k_0' t)]\}$$

and hence, f is given by:

$$f = \frac{k_0[\exp(-k_0' t) - 1] - k_0'[\exp(-k_0 t) - 1]}{k_0[\exp(-k_0' t) - 2] - 2k_0'[\exp(-k_0 t) - 1] + k_0 \exp(-k_0 t)]}$$

Table 4 gives the results obtained in the experiments with water enriched in the isotope ^{18}O. The techniques involved and the methods of isotopic analysis are described in Part I. N_s and N_m refer to the excess abundance of ^{18}O in the solvent (water) and in the isolated methanol respectively. Q_c is the proportion of the hydrolysis of dimethyl phosphate which proceeds with carbon–oxygen bond fission.

TABLE 4. *Isotope experiments at* 100°.

Medium	Time (hr.)	10^6k_0 (sec.$^{-1}$)	$10^6k_0'$ (sec.$^{-1}$)	f (%)	N_s	N_m	Q_c (%)
5M-$HClO_4$	2	35·6	18·5	9	0·58	0·50	87
5M-$HClO_4$	2	35·6	18·5	9	0·60	0·50	84
pH 1·24	500	3·13	3·52	50	0·85	0·37	79
pH 1·24	500	3·13	3·52	50	0·85	0·40	85
pH 1·24	500	3·13	3·52	50	0·77	0·31	72
pH 1·24	500	3·13	3·52	50	0·77	0·33	76

The method of calculation of Q_c may be illustrated for the first experiment cited in Table 4. The ratio N_m/N_s has the value 0·864. This is not equal to Q_c because 9% of the isolated methanol is derived from hydrolysis of monomethyl phosphate. Of this methanol, 73% has the same excess abundance of ^{18}O as the solvent (*i.e.*, in 5M-$HClO_4$ at 100°, monomethyl phosphate undergoes hydrolysis with 73% carbon–oxygen bond fission). Hence, the true ratio $(N_m/N_s)_D$, for the methanol derived from the hydrolysis of dimethyl phosphate is given by $(0{\cdot}864 - 0{\cdot}09 \times 0{\cdot}73)/0{\cdot}91 = 0{\cdot}877$. This still differs from Q_c since some of the isotopic enrichment in the methanol arises from the direct oxygen exchange between methanol and water. Q_c may be calculated from the equation (derived in Part I):

$$Q_c = \frac{\left[\left(\frac{N_m}{N_s}\right)_D \cdot (R - 1)\right](k_0 - k_E^M) - k_E^M \exp(-k_0t) + k_0 \exp(-k_E^M t)}{k_0\,[\exp(-k_E^M t) - \exp(-k_0 t)]}$$

where k_E^M is the first-order rate coefficient for the oxygen exchange of methanol, $7{\cdot}58 \times 10^{-6}$ sec.$^{-1}$, and R is the fraction of dimethyl phosphate hydrolysed at time t (0·226 under the stated conditions).

Q_c, for the first experiment, is found to have the value 87%. It can be seen that both corrections, *i.e.*, for the secondary hydrolysis of monomethyl phosphate and for the methanol exchange, are small under the relevant conditions.

At pH 1·24, however, although the second correction is zero, the first correction is large, because, under the conditions chosen, 50% of the methanol is derived from methyl phosphate. Of this methanol, 8·7% has the same excess abundance of ^{18}O as the solvent (calculated from data given in Part I). Calculation as above gives the values of Q_c quoted in Table 4.

Some isotope experiments were also carried out in strongly alkaline conditions. Sodium dimethyl phosphate was heated in *ca.* M-sodium hydroxide in sealed silver tubes for 6 days at 140°. Methanol was isolated and analysed in the usual way. The values of N_m/N_s obtained in separate experiments were 0·90, 0·82, and 0·79.

DISCUSSION

(a) *Hydrolysis of the Neutral Species.*—The variation of rate of hydrolysis with pH in the region 0—5 is quite different from that observed with monomethyl phosphate. In the latter case maximum reactivity occurs where the bulk component is the monoanion species. With dimethyl phosphate, on the other hand, reactivity is low at pH's where the monoanion is in high concentration and rises progressively as the monoanion is converted into the neutral species. This suggests that, at least, in solutions which are not more acidic than pH 0, the only substrate involved in hydrolysis is the neutral species. If this is so then the specific rate coefficient is given by $k_N = k_0c_p/c_N$, where k_0 is the observed rate coefficient at any pH and c_N/c_p is the fraction of the dimethyl phosphate present in the neutral form. Table 5 gives the values of k_N calculated in this way, the fractions c_N/c_p having been derived by using the value pK = 1·60.

Bearing in mind the uncertainties associated with the values of pH and of pK of dimethyl phosphate at 100° it can be said that k_N is sensibly constant over the range pH 0·72—4·17. The maximum difference between individual values (*ca.* 20% of the mean) is, in the circumstances, acceptable, especially since the range of values of the fraction c_N/c_P covered is large (about 350-fold).

TABLE 5.

pH	c_N/c_P	k_N	k_0 (obs.)	k_0 (calc.)	pH	c_N/c_P	k_N	k_0 (obs.)	k_0 (calc.)
0·02	0·975	6·79	6·62	4·13	1·24	0·697	4·49	3·13	2·96
0·32	0·951	5·18	4·93	4·04	2·51	0·109	4·96	0·532	0·462
0·72	0·883	4·45	3·93	3·74	3·33	0·018	3·93	0·072	0·077
1·02	0·792	3·98	3·15	3·36	4·17	0·0027	3·73	0·01	0·011

Rate coefficients are 10^6 sec.$^{-1}$.

From the mean value of k_N ($4·2 \times 10^{-6}$ sec.$^{-1}$) the expected values of k_0 at each pH can be obtained. The agreement between these and the observed values is good except below pH 0·72, where an acid-catalysed reaction obviously becomes important. It may be concluded, therefore, that in solutions, other than strongly acidic ones, dimethyl phosphate undergoes hydrolysis *via* the neutral species and that the monoanion is unreactive.

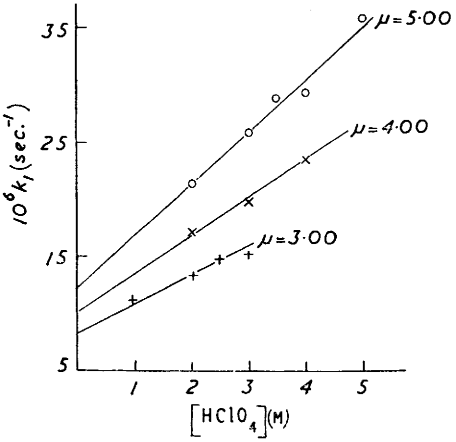

FIG. 1. *Hydrolysis of dimethyl phosphate in perchloric acid at constant ionic strengths, at* 100°.

The difference between the reactivities of the monoanions of mono- and di-substituted phosphates has been discussed, in structural terms, elsewhere.[7] It is of interest, however, to estimate the difference. The slope of the line obtained by plotting the logarithm of the rate coefficients for dimethyl phosphate against pH over the range pH 2·51—4·17 is almost exactly 1·0. Incursion of a reaction involving the monoanion would have decreased this slope. At pH 4·17, any monoanion reaction must, therefore, be a small component of the observed rate, certainly not amounting to more than 10%. Hence the reactivity ratio for the monoanions of methyl and dimethyl phosphate must be at least 1 : 10^4 and may be much larger. Hydrolysis *via* the monoanion can be observed, as Kumamoto, Cox, and Westheimer found, in strongly alkaline solution. This reaction, however, involves hydroxide ions and not water molecules as nucleophiles, and, as shown in the present investigation, proceeds largely * with carbon–oxygen bond fission.

The specific rate coefficients for the hydrolysis of the neutral species may also be estimated from the rates of hydrolysis in strongly acidic solutions. Fig. 1 shows plots of

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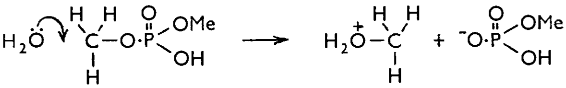
* The isotope results do not indicate complete carbon–oxygen bond fission. Since, however, the hydrolysis of monomethyl phosphate has not been investigated under these conditions, the significance of this is doubtful.

[7] Vernon, *Chem. Soc. Spec. Publ.*, 1957, No. 8, p. 17.

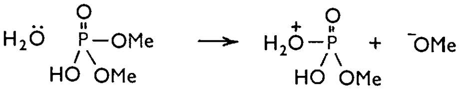
the observed rate coefficients against stoicheiometric perchloric acid concentration at a series of constant ionic strengths. Each intercept (at $HClO_4 = 0$) gives the rate coefficient (k'_N) for the neutral species at a particular ionic strength. As with methyl phosphate, the reaction shows a positive salt effect,* and the data can be represented by the equation $k_N' = k_N \exp b\mu$, where $k_N = 4{\cdot}92 \times 10^{-6}$ sec.$^{-1}$ and $b = 0{\cdot}182$.

This value of k_N is larger (by about 15%) than that obtained from the result for pH 0—5. It is difficult to know which value is the more accurate. The higher value will be in error if the dependence of rate on acid concentration at fixed ionic strength is not exactly linear. On the other hand, the accuracy of the lower value depends on the precision with which pK of dimethyl phosphate † and the pH's of the various solutions are known. Considering the complexities of the system, the agreement between the two values of k_N, obtained in quite different ways, is surprisingly good.

Experiments at pH 1·24 in water enriched in the isotope ^{18}O show that, under conditions where the neutral species is the only effective substrate, reaction proceeds largely with carbon–oxygen bond-fission (78%). As with the neutral species of monomethyl phosphate, this process is best formulated as bimolecular, since (*a*) the alternative formulation involving a methyl cation is energetically unlikely, and (*b*) in the presence of chloride ions (or other halide nucleophiles) a rapid second-order process proceeding by carbon–oxygen fission may be observed.[7]



The isotope results also show, however, the presence of a process proceeding with phosphorus–oxygen bond fission. This process, which constitutes about 20% of the whole reaction, can, in the absence of evidence pointing to the existence of an intermediate, be formulated in an analogous way:



The corresponding process for monomethyl phosphate has not been detected (see Part I). This probably arises, however, for purely experimental reasons, since the reaction of the neutral species of monomethyl phosphate is difficult to separate from that of the monoanion, and the isotope results are, therefore, correspondingly less easy to interpret. With aryl phosphates, on the other hand, reactions involving the neutral species and proceeding with phosphorus–oxygen bond fission are readily observed. For example, the reaction

$$H_2{}^{18}O + PhO\text{–}\ PO(OH)_2 \longrightarrow H^{18}O{\cdot}PO(OH)_2 + PhOH$$

has,[7] at 100°, a first-order rate coefficient of $2{\cdot}7 \times 10^{-5}$ sec.$^{-1}$, and is, therefore, some 32 times faster than the corresponding reaction with dimethyl phosphate [k_N(P) is *ca.* $4{\cdot}24 \times 0{\cdot}18 \times 10^{-6}$ sec.$^{-1}$ = *ca.* $0{\cdot}85 \times 10^{-6}$ sec.$^{-1}$]. The greater reactivity of the aryl phosphates in this reaction probably arises from the greater stability of the departing anions.

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* The salt effect is considerably smaller than with methyl phosphate ($b = 0{\cdot}182$ compared with $b = 0{\cdot}423$). In trimethyl phosphate the salt effect is further reduced.[8] The significance of this will be discussed in a subsequent paper which will deal primarily with the hydrolysis of trimethyl phosphate.

† When pK is taken as 1·50 instead of 1·60, the data from the range pH 0—5 yield $k_N = 4{\cdot}87 \times 10^{-6}$ instead of $4{\cdot}2 \times 10^{-6}$ sec.$^{-1}$. The validity of the conclusions drawn are obviously not critically dependent on the value of pK chosen, but the absolute value of k_N is.

[8] Barnard, Ph.D. Thesis, London, 1956.

(b) *Hydrolysis of the Conjugate Acid.*—The results in Table 3 show that in 1—5M-perchloric acid the rate of hydrolysis of dimethyl phosphate increases as the acidity increases. The relation is, at least up to 3M-perchloric acid, approximately linear and it is clear that the rate of hydrolysis is not proportional to Hammett's acidity function, h_0. However, plots of rate against stoicheiometric acidity for high values of acidity are not always particularly informative since increases in rate with increasing acidity may be partly, or even wholly, due to ionic strength effects. A more useful procedure is to plot rate against acidity at a series of constant ionic strengths. The result of doing this for the hydrolysis of dimethyl hydrogen phosphate is shown in Fig. 1. It can be seen that (i) at each ionic strength the rate increases linearly with acid concentration and can be represented by the equation $k_0 = k_N' + k_A' c_{H^+}$, where k_N' and k_N' are the rate coefficients for reaction proceeding *via* the neutral and the conjugate acid species respectively, and (ii) since the intercepts and the slopes of the lines increase as μ increases, both reactions exhibit a positive salt effect. The dependence of the rate coefficient on μ is satisfactorily represented in both cases by the second empirical term of the Debye–Hückel equation,[9] *i.e.*, $k' = k \exp b\mu$, where k is the rate coefficient at $\mu = 0$ and b is a constant. The appropriate numerical values are summarised in Table 6. At any ionic strength, the total rate of hydrolysis is given by:

TABLE 6.

μ	5·00	4·00	3·00	0 (extrap.)	
$10^6 k_N'$ (sec.$^{-1}$)	12·2	10·1	8·5	4·92	($b = 0{\cdot}182$)
$10^6 k_A'$ (l. mole^{-1} sec.$^{-1}$)	4·54	3·27	2·43	1·02	($b = 0{\cdot}306$)

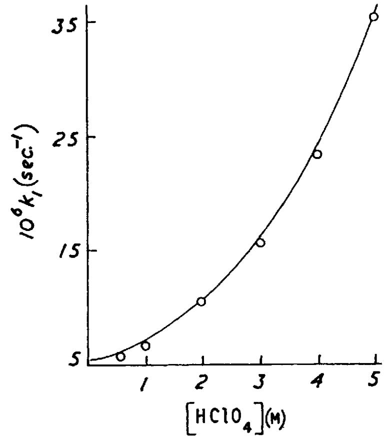

FIG. 2. *Hydrolysis of dimethyl hydrogen phosphate in perchloric acid at* 100°: *the curve corresponds to equation* 1.

$$k_0 = 4{\cdot}92 \times 10^{-6} e^{0{\cdot}182\mu} + 1{\cdot}02 c_{H+} \times 10^{-6} e^{0{\cdot}306\mu} \quad . \; . \; . \quad (3)$$

Fig. 2 shows the line obtained from this equation and the experimental values.

The experiments with ^{18}O tracer show that in 5M-perchloric acid processes involving respectively carbon–oxygen and phosphorus–oxygen bond fission occur in the ratio 0·86 : 0·14. The figures do not, however, immediately give the ratio for the acid-catalysed reaction since, from equation 3, it can be shown that under the relevant conditions 34·1% of the observed hydrolysis involves the neutral molecule as substrate. Since this process proceeds with 78% of carbon–oxygen bond fission, the proportion of carbon–oxygen bond fission (Q_c^A) for the acid-catalysed reaction is given by $Q_c^A = (0{\cdot}86—0{\cdot}78 \times 0{\cdot}341)/0{\cdot}659 =$

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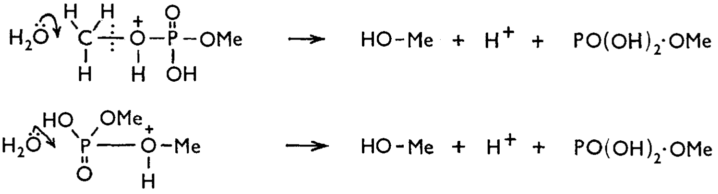
[9] Long and McDevitt, *Chem. Rev.*, 1952, **51**, 119.

0·89.* The two processes which make up the acid-catalysed reaction, therefore, have specific rate coefficients, at zero ionic strength, of $k_A(C) = 0{\cdot}91 \times 10^{-6}$ and $k_A(P) = 0{\cdot}11 \times 10^{-6}$ l. mole^{-1} sec.$^{-1}$, the symbols in parentheses indicating the position of bond fission. In deriving these figures it is, of course, assumed that both reactions show the same salt effect. This may not be the case. In that event the value of $k_A(P)$ given above will be in error.

Since the total rate is approximately proportional to stoicheiometric acid concentration (and not proportional to h_0), the reactions can be formulated as a nucleophilic attack by a water molecule on a carbon or phosphorus atom of the conjugate acid of dimethyl phosphate.



(c) *General.*—Five hydrolytic mechanisms have been identified for the hydrolysis of dimethyl phosphate. Table 7 lists these and compares their rates with those found for methyl phosphate.

TABLE 7. *Summary of reaction mechanisms for hydrolysis of dimethyl phosphate.**

	Monoanion		Neutral species		Conjugate acid	
Bond fission	C–O	P–O	C–O	P–O	C–O	P–O
Me_2HPO_4	Very slow with OH^-	*ca.* 0·001 †	3·3 †	0·9 †	0·91 ‡	0·11 ‡
MeH_2PO_4	—	8·23 †	0·50 †	—	2·00 ‡	1·08 ‡

* The sums of the rates for the neutral and conjugate acid species are accurate within the accuracy of the kinetic analyses, *e.g.*, *ca.* 5%. The rates for a particular species undergoing a particular kind of bond fission are less accurately known since the errors of the isotope analysis are here also involved. For example, with the conjugate acid, the rate of reaction proceeding by C–O bond fission, will, since this reaction is the major component, be accurate within *ca.* 10%. On the other hand, the rate for the minor component, *i.e.*, the reaction proceeding by P–O bond fission, may be subject to much larger errors.

† Rate coefficients (10^6 sec.$^{-1}$) at $\mu = 0$ (100°).

‡ Rate coefficients (10^6 l. mole^{-1} sec.$^{-1}$) at $\mu = 0$ (100°).

The largest difference between the two phosphate esters occurs in the monoanions. This feature is general: monoanions of phosphate diesters are resistant to hydrolysis, those of phosphate monoesters undergo relatively rapid hydrolysis with phosphorus–oxygen bond fission.

The other differences are small and difficult to interpret. That involving the conjugate acid species is, however, worthy of note. Although the overall rate of hydrolysis of dimethyl phosphate in acid solution is greater than that of monomethyl phosphate, the true acid-catalysed rate at zero ionic strength is smaller. This arises because the reaction with the diester exhibits a considerable positive salt effect, whereas that of the monoester does not. The origin of this difference is not understood.

The behaviour of other dialkyl hydrogen phosphates can be qualitatively predicted from the above analysis. In compounds containing primary and secondary alkyl groups

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* It might be thought that, in view of the corrections which must be applied to the primary experimental data, this figure could not be said to differ significantly from unity. This view is incorrect. The corrections for (*a*) the secondary hydrolysis of methyl phosphate and (*b*) the isotopic exchange of methanol are, as shown above, negligible. The correction for the concomitant hydrolysis of the neutral species is also small since both processes proceed with approximately the same proportion of carbon–oxygen fission. Q_C^A would be unity if the neutral reaction proceeded with 41% phosphorus–oxygen bond fission, *i.e.*, about twice the observed amount.

the overall picture will be similar: the variation in the rates of the individual reactions involving carbon–oxygen bond fission will be similar to that found for other bimolecular substitutions on carbon. For compounds containing tertiary alkyl groups, rapid acid-catalysed hydrolysis involving carbon–oxygen bond fission and proceeding by a carbonium ion mechanism can be expected. In all cases reaction in solutions more alkaline than pH 3 will be very slow.

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