477. *The Hydrolysis of Phosphonate Esters.*

By R. F. Hudson and L. Keay.

Measurements of the rate of hydrolysis of a series of esters of methylphosphonic acid in water have established the rate order Me > Et > Pr^i > *neo*pentyl in alkaline solution, and Me > Et = *neo*pentyl < Pr^i in acid solution. Substitution at the phosphorus atom has little effect on the reactivity in acid but reduces the rates considerably in alkaline solution, indicating that the latter reaction normally occurs at the phosphorus atom. The acid hydrolysis of di*neo*pentyl methylphosphonate leads to the formation 2-methylbut-2-ene. This ester therefore reacts by preliminary ionisation of the C–O bond and the relative reactivities in acid solution suggest that the ethyl and *iso*propyl esters react similarly.

Few quantitative measurements of the rate of hydrolysis of esters of quinquevalent phosphorus have been reported,[1] and the effect of structure on the reactivity appears not to have been studied systematically. It is well known [2] that substitution normally occurs at the acidic centre of esters of weak acids, whereas esters of strong acids are usually more reactive at the saturated carbon atom. Phosphates and phosphonates are therefore of interest in view of the " medium " strength of the corresponding acids.

The effect of changing the ester group on the rate and activation energy of acid and alkaline hydrolysis of a series of methylphosphonates is shown in Table 1. The order of reactivity towards hydroxide ions is characteristic of a bimolecular reaction proceeding either at the carbon atom [3] or at the phosphorus atom [4] (termed S_N2P below). In the latter case the decreases in rate with substitution may be due to increasing conjugation with the P=O group,  R—O–P=O, and possibly to increasing steric hindrance by the alkoxy-group. The latter effect is indicated by the reduced reactivity of the *neo*pentyl ester. In contrast to the S_N2 reactions of *neo*pentyl halides,[5] no increase in activation energy is observed in the alkaline hydrolysis of di*neo*pentyl methylphosphonate, which suggests that this reaction at least proceeds at the P atom.

Table 1. *The effect of changing the ester group on the rate of acid and alkaline hydrolysis of dialkyl methylphosphonates.*

	Me	Et	Pr^i	*neo*Pentyl		Me	Et	Pr^i	*neo*Pentyl
Acid hydrolysis					*Alkaline hydrolysis*				
Relative rate ...	1·2	1	25	1	Relative rate ...	600	40	1	0·33
E^* (kcal./mole)	26·7	26·7	25·6	—	E^* (kcal./mole)	13·5	14·0	14·9	13·6
$10^{-12}PZ$	3·6	2·4	0·26	—	$10^{-4}PZ$	1900	360	27	1·5

There are some indications that the phosphorus atom in esters of quinquevalent phosphorus is more reactive towards hydroxyl ion than the saturated carbon atom. Thus ^{18}O exchange experiments have shown [6] that P–O fission occurs in the alkaline hydrolysis of trimethyl phosphate, whereas in acid solution C–O fission predominates. In addition, alkyl phosphonates of optically active alcohols are hydrolysed with complete retention of configuration in alkaline and extensive racemisation in acid solution.[7] The low activation energies observed in the alkaline reaction (Table 1) are also indicative of the S_N2P mechanism, since higher values (~20 — 23 kcal./mole) are normally observed in reactions of water and hydroxyl ion at the saturated carbon atom, *e.g.*, alkyl halides [3] and sulphonates.[8]

[1] Cavalier, *Compt. rend.*, 1898, **127**, 114.

[2] Anbar, Dostrovsky, Samuel, and Yoffe, *J.*, 1954, 3604.

[3] Hughes, *Trans. Faraday Soc.*, 1941, **37**, 603.

[4] Dostrovsky and Halmann, *J.*, 1953, 502.

[5] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 157.

[6] Blumenthal and Herbert, *Trans. Faraday Soc.*, 1945, **41**, 611; Barnard, Bunton, Llewellyn, Oldham, Silver, and Vernon, *Chem. and Ind.*, 1953, 761.

[7] Gerrard, Green, and Nutkins, *J.*, 1952, 4076.

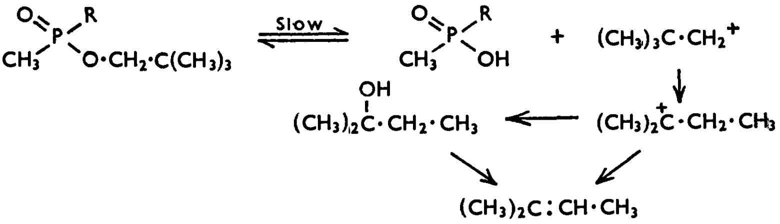
[8] Grunwald, Winstein, and Jones, *J. Amer. Chem. Soc.*, 1951, **74**, 2700; Robertson, *Canad. J. Chem.*, 1953, **31**, 589; Marshall, Ph.D. Thesis, London, 1954.

On the other hand, the activation energies of the bimolecular reactions of carboxylic esters proceeding with acyl–oxygen fission [9] are considerably lower both in acid and alkaline solution. The activation energy rises, however, to 23·2 kcal./mole in the acid hydrolysis of *tert.*-butyl acetate [10] where alkyl–oxygen fission occurs. In view of the similar reactivity of carbonyl and phosphonyl halides,[4] the high reactivity of the phosphonates towards the hydroxyl ion resulting from these low activation energies indicates that the reaction occurs at the P=O centre.

In acid solution the rate order is almost reversed, the *iso*propyl ester reacting about 25 times faster than the ethyl ester. If the protonation equilibrium is assumed to increase with the basicity of the alcohol,[11] *i.e.*, Me < Et = *neo*pentyl < Pr^i, the observed rate sequence might be explained by assuming a bimolecular reaction between water and the protonated ester, the rate of which increases in the same order as in the alkaline reaction. The resultant effect of this reactivity order and the protonation equilibrium could conceivably lead to a minimum rate. The high reactivity of the secondary ester suggests, however, that this reaction proceeds by the alternative S_N1 mechanism, in agreement with the extensive racemisation obtained on acid hydrolysis of phosphonates of optically active alcohols.[7] The greater reactivity of the methyl ester than of the ethyl ester shows that the former reacts predominantly by an S_N2 or S_N2P mechanism, since protonation and the S_N1 reactivity both favour the reverse order.

In order to investigate further the possibility of ionisation in acid solution, the products of reaction of the di*neo*pentyl ester were analysed. The only product detected was 2-methyl-2-butene. On solvolysis of *neo*pentyl halides, a mixture of *tert.*-amyl alcohol and olefin has been reported,[5] *e.g.*, at 125° 36% of olefin was obtained in 50% aqueous alcohol. In the present reaction, any *tert.*-amyl alcohol would be converted rapidly into olefin, owing to the high acidity of the medium (p. 2468). No such re-arrangement of *neo*pentyl alcohol occurs even under the drastic conditions used in the ester hydrolysis.

These observations suggest therefore that the olefin is produced mainly from the alcohol, and not directly from the carbonium ion :



It follows that the di*neo*pentyl ester is hydrolysed by the S_N1 mechanism in N-aqueous benzenesulphonic acid at a rate almost equal to that for the diethyl ester. As the basicities of the two alcohols are probably similar [11] this equality suggests that the diethyl ester also reacts predominantly by this mechanism. Reference to the rate of solvolysis of analogous esters shows that in aqueous solution ethyl sulphonates [12] and halides [13] are considerably more reactive than the corresponding *neo*pentyl esters. In formic acid, however, *i.e.*, in a strongly ionising medium, the rates of the ethyl and the *neo*pentyl compounds are similar. There is some doubt concerning the nature of the reaction mechanism of primary sulphonates in formic acid [14] and, moreover, according to Marshall and Winstein,[12] β-group participation may accelerate somewhat the rate of solvolysis of *neo*pentyl sulphonates. The above interpretation of the equal rates of the two esters must therefore be regarded as tentative at present.

Substitution at the phosphorus atom also produces rate changes of different orders of

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[9] Bunton, *Research*, 1951, **4**, 383; Stimson, *J.*, 1955, 2010.

[10] Skrabal, *Monatsh.*, 1924, **45**, 148; 1926, **47**, 17, 30; Tommila and Hinshelwood, *J.*, 1938, 867.

[11] Conant and Wheland, *J. Amer. Chem. Soc.*, 1936, **58**, 1124.

[12] Marshall and Winstein, *ibid.*, 1952, **74**, 1120.

[13] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 164.

[14] Streitwieser, *J. Amer. Chem. Soc.*, 1955, **77**, 1117.

magnitude in the acid and the alkaline reactions. In acid solution, progressive alkyl substitution in the methylphosphonate has a small retarding effect, whereas in alkaline solution the rate changes are considerable (Table 2). For example, the *tert.*-butylphosphonate is one-third as reactive as the corresponding methylphosphonate in acid solution but has 1/500th of the reactivity in alkaline solution. The considerable difference in rate in alkaline solution of the *n*- and *tert.*-butylphosphonates shows the pronounced effect of steric hindrance since the electronic changes are expected to be small. Electronic changes probably have a considerable effect in the other cases, as shown by the general increase in activation energy with decrease in reactivity (Table 2). The differentiation between electronic and steric effects on the reactivity is difficult to explain,[15] but the magnitude of the rate changes in alkaline solution suggest that substitution probably occurs at the phosphorus atom, in agreement with previous indications.

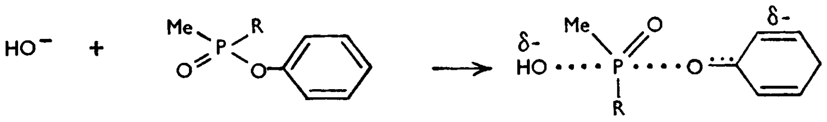
TABLE 2. *The effect of substitution at the phosphorus atom on the rate of hydrolysis of dialkyl phosphonates.*

	Me	Et	Pr^n	Bu^n	Bu^t
Acid hydrolysis (N) *of di-isopropyl esters*					
Relative rate	1	0·5	0·5	0·33	0·33
E^* (kcal./mole)	25·6	26·0	26·0	25·1	—
$10^{-11}PZ$	2·6	2·6	1·9	—	—
Alkaline hydrolysis of di-isopropyl esters					
Relative rate	1	0·16	0·062	0·039	0·002
E^* (kcal./mole)	14·9	16·2	15·9	16·2	—
$10^{-5}PZ$	2·7	2·8	0·75	0·69	—
Alkaline hydrolysis of diethyl esters					
Relative rate	1	0·5	—	0·10	—
E^* (kcal./mole)	14·0	14·2	—	14·7	—
$10^{-5}PZ$	36	22	—	8·9	—

TABLE 3. *Rates of hydrolysis in water of aromatic and aliphatic methylphosphonates.*

	Temp.	k_2 (l. mole^{-1} hr.$^{-1}$)	E^* (kcal. mole^{-1})		Temp.	k_2 (l. mole^{-1} hr.$^{-1}$)
Alkaline hydrolysis				*Acid hydrolysis*		
Ph_2	21·5°	122	12·0	Et p-$NO_2 \cdot C_6H_4$	110·4°	0·055
Me_2	50·0	52·6	13·5	Et_2	109·9	0·0737
Et p-$NO_2 \cdot C_6H_4$	25·0	144	12·0	Ph_2	110·0	~0·0018
Et_2	50·0	9·36	14·0			

Finally the reactivities of aliphatic and aromatic phosphonates may be compared in acid and alkaline solution (Table 3). In view of the usual inactivity of the benzene nucleus towards substitution, the greater reactivity of the aromatic esters is probably due to conjugation in the displaced group :



The high lability of the aromatic group is shown by the exclusive release of *p*-nitrophenol from ethyl *p*-nitrophenyl methylphosphonate in alkaline solution (Table 4). In acid solution, ethanol is exclusively released at a rate very similar to that of acid hydrolysis of diethyl methylphosphonate. The reduced rate of the acid hydrolysis of diphenyl methylphosphonate may be attributed partly to increased acidity of the ester. The rates for the corresponding aliphatic and aromatic carboxylic esters are, however, almost equal,[16] and

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[15] Evans, *Trans. Faraday Soc.*, 1946, **42**, 718; de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3200.

[16] Tommila and Hinshelwood, *J.*, 1938, 1801.

consequently the large rate difference observed in the present case (Table 3) suggests that a change in mechanism occurs, as with the sulphonates.[17]

EXPERIMENTAL

Materials.—The diakyl phosphonates were prepared by refluxing the corresponding trialkyl phosphite with an equivalent amount of the alkyl halide (Arbusov reaction[18]). The trialkyl phosphites were prepared by the action of phosphorus oxychloride (1 mole) on the alcohol (3 moles) and triethylamine (3 moles) in light petroleum (b. p. 40—60°) (cf. Ford-Moore and Williams,[19] and McCombie, Saunders, and Stacey[20]). The following esters were prepared, the b. p.s in parentheses being those given by Ford-Moore and Williams:[19] dimethyl methylphosphonate, b. p. 98°/50 mm. (60°/10 mm.); diethyl methylphosphonate, b. p. 189° (192—194°); di*iso*propyl methylphosphonate, b. p. 87—88°/22 mm. (66°/3 mm.); diethyl ethylphosphonate, b. p. 92—93°/20 mm.; diethyl *n*-butylphosphonate, b. p. 85°/2 mm.; di-*n*-propyl *n*-propylphosphonate, b. p. 130°/20 mm.; di*iso*propyl ethylphosphonate, b. p. 56—57°/1 mm.; di*iso*propyl *n*-propylphosphonate, b. p. 75—76°/3 mm.; di*iso*propyl *n*-butylphosphonate, b. p. 86—88°/4 mm.

Diphenyl methylphosphonate, previously prepared by the Arbusov reaction,[18,21] was prepared by amine-catalysed esterification of the dichloride, and had b. p. 140°/0·2 mm., m. p. 33—34° (lit., b. p. 190—195°/11 mm., m. p. 35—36°).

Diethyl phenylphosphonate was prepared by the Friedel–Crafts reaction between phosphorus trichloride and benzene, followed by chlorination at 0° in tetrachloroethane to give $Ph{\cdot}PCl_4$. The solution was then treated with excess of absolute ethanol, and the hydrogen chloride was removed under reduced pressure.[22] The yield was 51%, and the b. p. 116—118°/1·5 mm. (lit., b. p. 117—118°/1·5 mm.). A higher-boiling fraction (b. p. 181—183°/2 mm.) was found to be ethyl diphenylphosphinate (yield 15%).

Di*iso*propyl *tert.*-butylphosphonate was prepared from the dichloride, itself obtained by the Friedel–Crafts reaction between *tert.*-butyl chloride and phosphorus trichloride.[23] Crystallised from ligroin (b. p. 60—80°), it had m. p. 121° (lit., m. p. 123°). Reaction of the dichloride with propan-2-ol in the presence of a tertiary base was slow, and the alternative reaction of the *iso*propoxide was used. Sodium (9·2 g.) was dissolved in absolute propan-1-ol (50 ml.), then *tert.*-butylphosphonyl dichloride (36 g.) in propan-2-ol (100 ml.) was added slowly. The whole was refluxed for 4 hr., the solution evaporated at the water-pump, a little water was added, and the mixture extracted twice with ether. The extract was dried ($MgSO_4$), the ether removed, and the *ester* vacuum-distilled (23 g., 50%; b. p. 62°/1 mm.) (Found: C, 53·1; H, 10·5; P, 13·7. $C_{10}H_{23}O_3P$ requires C, 54·0; H, 10·3; P, 14·0%).

Dimethyl tert.*-butylphosphonate.* *tert.*-Butylphosphonyl dichloride (18 g.) was refluxed with sodium methoxide in methanol (8 g. of sodium in 100 ml. of methanol). After 4 hr. benzene (500 ml.) was added and the methanol distilled off. The precipitated sodium chloride was filtered off, and after removal of the benzene on the water-pump the *ester* was vacuum-distilled (5 g.; 34%; b. p. 34°/0·5 mm.; m. p. 20°) (Found: C, 41·4; H, 9·0. $C_6H_{15}O_3P$ requires C, 42·1; H, 9·0%).

Ethyl p*-nitrophenyl methylphosphonate.* This compound, mentioned by Schrader,[24] is not detailed in the literature. Methylphosphonyl dichloride was half-esterified by the action of ethanol in the presence of triethylamine in ether at 0° (yield 55%; b. p. 40—41°/1 mm.; 64°/5 mm.) (Found: C, 24·6; H, 5·5; P, 23·0; Cl, 24·2. $C_3H_8O_2ClP$ requires C, 25·3; H, 5·6; P, 21·8; Cl, 24·9%).

Ethyl methylphosphonochloridate (14·3 g.) was refluxed for 3 hr. with nitrophenol (13·9 g.) as sodium derivative in xylene. The sodium chloride was filtered off, the solvent removed on the water-pump, and the *ester* distilled *in vacuo* (yield 50%; b. p. 160°/1 mm., 190°/3 mm.; lit., b. p. 178°/1·5 mm.) (Found: C, 43·0; H, 5·1; N, 5·0. $C_9H_{12}O_5NP$ requires C, 43·7; H, 4·9; N, 5·7%).

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[17] Lapworth and Ferns, *J.*, 1912, 273; Bunton and Frei, *J.*, 1951, 1872.

[18] Arbusov, *J. Russ. Phys. Chem. Soc.*, 1906, **38**, 687.

[19] Ford-Moore and Williams, *J.*, 1947, 1465.

[20] McCombie, Saunders, and Stacey, *J.*, 1945, 380.

[21] Michaelis and Kaline, *Ber.*, 1898, **31**, 1048.

[22] Kosolapoff and Hunter, *J. Amer. Chem. Soc.*, 1947, **69**, 2020.

[23] (*a*) Crofts and Kosolapoff, *ibid.*, 1953, **75**, 3379; (*b*) Kinner and Perren, *J.*, 1952, 3437; Clay, *J. Org. Chem.*, 1951, **16**, 892.

[24] Schrader, B.I.O.S. report No. 714.

Dineopentyl methylphosphonate was prepared by the action of methylphosphonyl dichloride on *neo*pentyl alcohol obtained from *tert.*-butylmagnesium chloride and ethyl formate.[25] Methylphosphonyl dichloride (33 g. in 100 ml. of ether) was added slowly with ice-cooling to *neo*pentyl alcohol (44 g.) and triethylamine (68 g.) in ether (500 ml.). The mixture was then refluxed on the water-bath for 4 days. After filtration, the solvent was removed and the residue distilled under vacuum (yield 35%; b. p. 78—79°/0·6 mm.) (Found: C, 54·9; H, 10·3; P, 12·9. $C_{11}H_{25}O_3P$ requires C, 55·9; H, 10·6; P, 13·1%).

*Attempted preparation of di-*tert.*-butyl methylphosphonate.* The action of methylphosphonyl dichloride on *tert.*-butyl alcohol in the presence of any of several tertiary amines gave *tert.*-butyl chloride and methylphosphonic acid together with an unresolved mixture of condensed phosphonates. The most promising method appeared to be through the corresponding phosphite.[26] Methyl dichlorophosphinite was prepared from phosphorus trichloride and one equivalent of methanol and converted into di-*tert.*-butyl methylphosphite by the action of the alcohol and triethylamine in light petroleum. It had b. p. 50°/2 mm. Reaction with methyl iodide was vigorous but the product decomposed on vacuum-distillation. The consistently low analytical figures for carbon are probably due to incomplete combustion, since very erratic values were obtained initially, as suggested by Ford-Moore and Williams.[19] The molecular weight, determined from the equivalent, agreed closely with the theoretical value in each case. The linearity of the graph of the appropriate rate function (see below) confirmed the purity of the esters.

Kinetic Measurements.—The rate of hydrolysis was followed by the conventional method for slow reactions by sealing 5 ml. portions of reaction mixture in ampoules and immersing them in an oil-thermostat maintained within ±0·02° in the temperature range 50—135°. Solutions were made by direct weighing into conductivity water, and the end-point was determined from the weight of pure ester taken and, when possible, from the final titration. At appropriate intervals the ampoules were removed and chilled, and, for the alkaline reaction, the contents were titrated against potassium hydrogen phthalate with phenolphthalein as indicator, under nitrogen. As only the first group is removed in alkaline solution, the rate constants could be obtained from the general equation for a second-order reaction.

In the acid reaction the products were titrated against sodium hydroxide. In the hydrolysis of ethyl *p*-nitrophenyl methylphosphonate, the *p*-nitrophenol released was determined by reaction with standard bromine solution in acid. The excess of bromine liberated iodine from potassium iodide and this was then estimated with thiosulphate.[27] These results agreed approximately with the acidimetric values (Table 4), showing the exclusive release of *p*-nitrophenol.

Evaluation of the Rate Constant of the Alkaline Reaction.—For the bromination method, k_2 was obtained from the second-order rate equation:

$$k_2 = \frac{2{\cdot}303}{(a - 2b)} \log_{10} \frac{b(a - 2x)}{a(b - x)}$$

The rate constant obtained acidimetrically was calculated from the equation:

$$\frac{2{\cdot}303V}{Ntn_\infty} \log_{10}\left(\frac{n_0 - n_\infty}{n_0} + \log_{10}\frac{n_t}{n_t - n_\infty}\right)$$

where V is the volume (5 ml.) of the aliquot portion taken, N the normality of the titrating solution (0·05N), and n the titre.

Evaluation of the Rate Constant of the Acid Reaction.—Preliminary experiments showed that both ester groups were removed at similar rates. As pK_a of the semiacid and pK_1 of the phosphonic acid are close to 2·0, and pK_2 of the phosphonic acid [23a, 28] is approximately 7·0, the rate of the first step was obtained by titration with sodium hydroxide, with methyl-orange as indicator. For the most unreactive esters, the values of the first-order rate constant could be obtained satisfactorily from the initial rates.

Products of the Acid Reaction.—In contrast to the reaction in alkaline solution, bromine

[25] Sommer, Blankman, and Miller, *J. Amer. Chem. Soc.*, 1954, **76**, 803.

[26] Arbusov and Azanovskaya, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1949, 473; Kosolapoff, *J. Amer. Chem. Soc.*, 1952, **74**, 4953.

[27] Day and Taggart, *Ind. Eng. Chem.*, 1928, **20**, 545; Scott, *Ind. Eng. Chem., Anal.*, 1931, **3**, 67.

[28] Jaffe, *J. Amer. Chem. Soc.*, 1954, **75**, 2209.

estimations failed to detect *p*-nitrophenol after hydrolysis of ethyl *p*-nitrophenyl methylphosphonate. The rate of removal of the ethyl group is slightly less than for the diethyl ester.

Reaction of Dineopentyl Methylphosphonate.—The ester (13·12 g.) was refluxed with N-benzenesulphonic acid (60 ml.) for 7 days. An excess of sodium hydroxide was added and the mixture extracted twice with ether, the solution being then dried (Na_2SO_4), filtered, and evaporated, and the product distilled in a micro-unit. The b. p. rose sharply to 230° to give a distillate of unchanged ester, showing the absence of *neo*pentyl alcohol (b. p. 113°) and *tert.*-amyl alcohol (b. p. 102°). Further experiments showed that under these conditions amyl alcohol eliminates water rapidly, to give an olefin, whereas *neo*pentyl is unaffected. Finally, di*neo*pentyl methylphosphonate (4 g.) was heated in a sealed ampoule with N-benzenesulphonic acid (10 ml.) in 50% aqueous dioxan for 24 hr. at 140°. After cooling, the product was distilled, giving, probably, 2-methyl-2-butene (0·85 g.), b. p. 38—39° (Found : C, 86·3; H, 14·5. Calc. for C_5H_{10} : C, 85·7; H, 14·3%). It gave a dibromide, b. p. 75°/25 mm. (lit., b. p. 64°/17 mm.) (Found : C, 25·6; H, 4·4; Br, 69·8. Calc. for $C_5H_{10}Br_2$: C, 26·1; H, 4·35; Br, 69·6%).

Results.—The rate constants for the acid and alkaline hydrolyses are summarised in Tables 5 and 6.

TABLE 4.

Bromination method				Acidimetric method			
Time (min.)	n_t (ml.)	$\log \frac{a - 2x}{b - x}$	k_2 (l. mole^{-1} hr.$^{-1}$)	Time (min.)	n_t (ml.)	$\log \frac{n_t}{n_t - n_\infty}$	k_2 (l. mole hr.$^{-1}$)
0	2·30	0·3501	—	0	1·39	0·4453	—
1	2·52	0·3531	147	1	1·53	0·4729	144·5
4·5	2·92	0·3639	151	1·75	1·62	0·4927	142
6	3·02	0·3673	141·5	4	1·85	0·5528	141
9	3·22	0·3753	138	9	2·20	0·6864	140·5
13	3·47	0·3882	144·5	12	2·35	0·7715	142·5
∞	4·72	—	—	∞	2·90	—	—

Mean k_2 = 144 l. mole^{-1} hr.$^{-1}$. NaOH (*a*) = 0·05N. Ester (*b*) = 0·0236N. Temp. 25·0°.

Mean k_2 = 142 l. mole^{-1} hr.$^{-1}$. NaOH = 0·056N. Ester = 0·029N. Temp. 25·0°.

TABLE 5. *First-order rate constants for the hydrolysis of phosphonate esters* $R{\cdot}PO_3R'_2$ *in* N-*benzenesulphonic acid in water.*

R	R′	Concn. (N)	Temp.	*k* (hr.$^{-1}$)	R	R′	Concn. (N)	Temp.	*k* (hr.$^{-1}$)
Bu^t	Pr^i	0·10	115·2°	1·18	Bu^n	Et	0·20	110·0°	0·038
							0·20	119·5	0·098
Bu^n	Pr^i	0·20	96·0	0·233					
		0·20	101·0	0·299	Me	Et	0·25	101·0	0·0318
		0·10	105·3	0·668			0·26	108·8	0·0654
		0·10	110·0	1·03			0·18	109·9	0·0737
		0·20	114·7	1·22			0·25	115·3	0·112
							0·25	116·9	0·143
Pr^n	Pr^i	0·20	96·0	0·243			0·22	119·5	0·175
		0·20	101·0	0·400					
		0·20	107·3	0·675	Ph	Et	0·20	110·0	0·038
		0·18	114·0	1·17			0·25	104·4	0·0507
		0·21	114·7	1·31			0·30	105·2	0·0529
							0·28	110·2	0·0714
Et	Pr^i	0·22	92·5	0·252			0·26	114·7	0·123
		0·18	101·0	0·512			0·28	120·3	0·210
		0·20	105·3	0·702			0·30	122·6	0·235
		0·22	110·4	1·22					
		0·19	114·7	1·79	Me	Me_2	0·30	99·8	0·0412
							0·30	104·4	0·0654
Me	Pr^i	0·20	93·6	0·463			0·30	110·0	0·111
		0·20	100·6	0·907			0·20	114·3	0·164
		0·23	109·9	1·97			0·20	119·6	0·244
		0·20	110·0	2·02					
		0·21	115·0	3·10	Bu^t	Me_2	0·10	120·0	0·0809
		0·20*	88·9	0·625					
		0·17*	94·4	1·01	Me	CH_2Bu^t	0·10	103·0	0·034
		0·19*	99·7	1·72			0·10	120·0	0·158
		0·16*	104·8	3·07					
		0·18*	105·9	3·08	Ethyl *p*-nitrophenyl methylphosphonate		0·20	110·4	0·055

* In N-HCl.

TABLE 6. *Rate of alkaline hydrolysis of alkylphosphonates* R·PO$_3$R′$_2$ *in water.*

R	R′	[Ester] (N)	[NaOH] (N)	Temp.	k_2 (l. mole^{-1} hr.$^{-1}$)
Me	Pr^i	0·12	0·20	80·0°	0·551
		,,	,,	90·0	0·825
		,,	,,	100·0	1·735
		0·10	,,	110·0	2·77
		0·11	,,	119·2	5·69
Et	Pr^i	0·14	0·20	104·9	0·382
		0·15	,,	114·9	0·734
		0·16	,,	119·7	0·960
		0·15	,,	124·5	1·16
Pr^n	Pr	0·08	0·20	109·9	0·186
		0·16	,,	114·9	0·278
		0·17	,,	119·7	0·355
		0·10	,,	124·5	0·540
Bu^n	Pr^i	0·08	0·20	114·9	0·169
		,,	,,	119·7	0·279
		0·09	,,	124·5	0·286
Bu^t	Pr^i	0·04	0·20	125·0	0·015
Pr^n	Pr^n	0·03	0·05	95·0	1·29
		0·06	0·20	105·3	2·25
Me	Et	0·02	0·05	60·0	9·36
		0·03	,,	70·0	13·80
		,,	,,	80·0	23·64
		,,	,,	90·0	40·56
Et	Et	0·04	0·05	69·5	6·42
		,,	,,	73·9	8·25
		,,	,,	84·7	15·21
		,,	,,	91·3	22·25
Bu^n	Et	0·03	0·05	80·3	2·65
		,,	,,	91·2	4·21
		,,	,,	99·0	6·91
		,,	,,	105·1	9·27
		,,	,,	109·3	13·24
		,,	,,	116·0	16·38
Ph	Et$_2$	0·04	0·05	59·8	16·08
		,,	,,	65·7	22·80
		0·02	,,	74·9	36·24
		0·03	,,	79·4	45·30
		,,	,,	84·8	65·93
		0·04	,,	89·1	73·61
Me	Me$_2$	0·04	0·05	49·8	52·6
		0·02	,,	60·0	89·4
		0·04	,,	70·0	161·3
		0·03	,,	79·8	311·8
Me	Ph	0·02	0·05	0·1	24·1
		,,	,,	15·0	85·2
		,,	,,	21·5	122
Me	CH$_2$Bu^t	0·05	0·20	88·0	0·345
		0·10	,,	105·0	0·882
		0·05	,,	120·0	1·60
Et *p*-nitrophenyl methylphosphonate		0·04	0·05	0·0	21·6
		,,	,,	15·0	65·3
		0·02	,,	25·0	144
Me$_3$PO$_4$		0·04	0·05	60·0	7·44
Me·SO$_3$Ph		0·02	0·05	100·0	41·0*
		,,	,,	110·7	117·8*

* In 50% aqueous dioxan (v/v).

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