The Reactivity of Organophosphorus Compounds. Part XXVII.[1] Reactions of Alkyl Hydrogen Alkylphosphonates with *p*-Nitrobenzonitrile Oxide: Anchimerically Assisted P–O Fission in Acidic Hydrolysis of the Resulting α-Hydroxyimino-*p*-Nitrobenzyl Alkylphosphonates ‡

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p-Nitrobenzonitrile oxide reacts readily with alkyl hydrogen alkylphosphonates (I; R^1 = Me, R^2 = Me, Et, Pr, Pr^i, Bu^tCH_2, or Bu^tCHMe) and (I; R^1 = Et, Bu^t, or Ph; R^2 = Et), diethyl hydrogen phosphate, and hydrogen diethylphosphinate to give the corresponding 1:1-adducts, alkyl α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (II; R^1 = Me; R^2 = Me, Et, Pr, Pr^i, Bu^tCH_2, or Bu^tCHMe) and (II; R^1 = Et, Bu^t or Ph; R^2 = Et), diethyl α-hydroxyimino-*p*-nitrobenzyl phosphate (II; R^1 = EtO, R^2 = Et), and α-hydroxyimino-*p*-nitrobenzyl diethylphosphinate (III), respectively. Except for the last case, which is stable in acid, the adducts undergo very fast, anchimerically assisted, P–O fission at pH 2—3·5 in dilute aqueous dioxan (*ca.* 10^7 faster, as shown by a kinetic study, than corresponding hydrolysis of simple esters which undergo alkyl–oxygen fission under similar conditions). Transesterification, also very fast, proceeds similarly, while the *O*-methyl derivative of (II; R^1 = Me; R^2 = Bu^tCH_2) is stable at pH 2—4·5. The results point to a novel neighbouring-group acceleration involving the proton of the oxime group in (II).

HYDROLYSES of simple esters of phosphorus acids, *e.g.* dialkyl alkylphosphonates, are relatively slow processes. In acid or neutral solution they proceed *via* alkyl–oxygen fission [2-4] while in alkaline solution P–O fission results *via* a five-co-ordinate transition-state rather than a five-co-ordinate intermediate of finite lifetime.[4] We have investigated the hydrolyses of a series of phosphinates, phosphonates, and phosphates where one ester group is a α-hydroxyimino-*p*-nitrobenzyl [·OC(:N·OH)-$C_6H_4NO_2$-*p*]. As will be shown, the reactions proceed very quickly in the range pH 2—9 as a result of participation by the neighbouring oxime function. In acid solution, reported in this paper, novel P–O fission occurs, while in alkaline solution, reported in the succeeding Part, a novel rearrangement involving the intermediate formation of a five-co-ordinate species takes place.

*Preparation of α-Hydroxyimino-*p*-nitrobenzyl Esters of Phosphorus Acids.*—Alkyl α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (II; R^1 = Me; R^2 = Me, Et, Pr, Pr^i, Bu^tCH_2, or Bu^tCHMe) and (II; R^1 = Et, Bu^t or Ph, R^2 = Et), diethyl α-hydroxyimino-*p*-nitrobenzyl

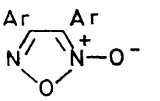
$$R^2O{\cdot}(R^1)P(:O)OH + ArC{\equiv}\overset{+}{N}{-}\overset{-}{O} \longrightarrow R^2O{\cdot}(R^1)P(:O){\cdot}O{\cdot}C(:NOH)Ar$$

(I) (II)

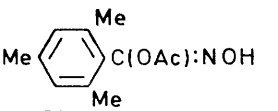
phosphate (II; R^1 = EtO; R^2 = Et), and α-hydroxyimino-*p*-nitrobenzyl diethylphosphinate (III), were readily obtained by reaction of the corresponding alkyl hydrogen alkylphosphonates (I), diethyl hydrogen phosphate, or hydrogen diethylphosphinate with *p*-nitrobenzonitrile oxide in dioxan under rigorously dry conditions (Scheme 1). Separation of the product from di-*p*-nitrophenylfuroxan (IV; Ar = *p*-$NO_2C_6H_4$), formed competitively by dimerization of *p*-nitrobenzonitrile oxide was easily achieved. The α-hydroxyimino-*p*-nitrobenzyl esters of phosphorus acids were characterised by analysis, titration, and p.m.r. and i.r. spectroscopy as described in the Experimental section, and are analogous to the previously described adduct (V) of acetic acid and 2,4,6-trimethylbenzonitrile oxide [5]

$$Et_2P(:O){\cdot}O{\cdot}C(:NOH)Ar$$

(III)



(IV)



(V)

It is noteworthy that the i.r. spectrum of ethyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate (II; R^1 = Me, R^2 = Et) exhibited the P–O–Et bond at 1030 cm^{-1} in Nujol which shifted to 1000 cm^{-1} in dioxan (4% w/v)

‡ Preliminary communications: J. I. G. Cadogan and (Miss) J. A. Maynard, *Chem. Comm.*, 1966, 854; J. I. G. Cadogan and D. T. Eastlick, *ibid.*, 1970, 1546.

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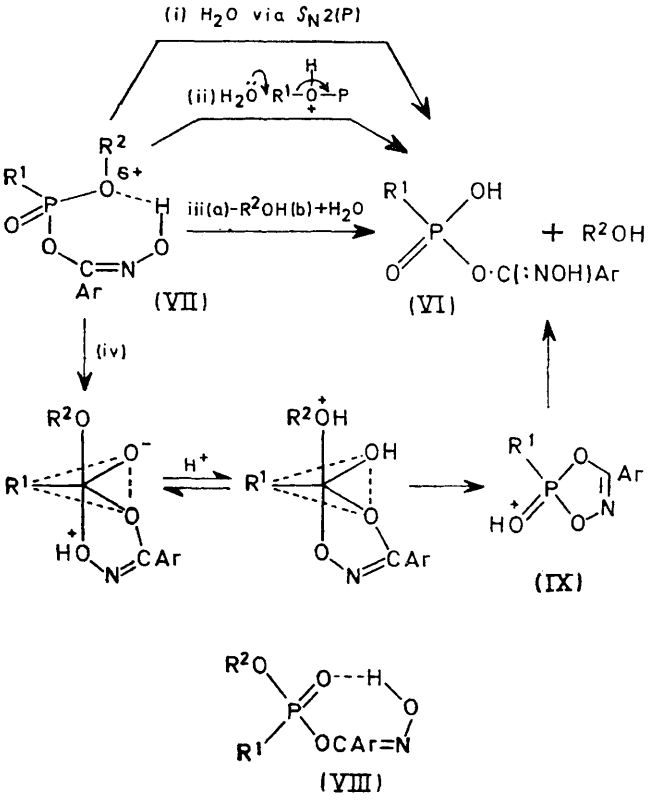
[1] Part XXVI, J. I. G. Cadogan and D. T. Eastlick, *J. Chem. Soc.* (*B*), 1970, 1314.
[2] J. I. G. Cadogan, D. T. Eastlick, F. Hampson, and R. K. Mackie, *J. Chem. Soc.* (*B*), 1969, 144.
[3] R. F. Hudson and L. Keay, *J. Chem. Soc.*, 1956, 2463.
[4] A. J. Kirby and S. G. Warren, 'The Organic Chemistry of Phosphorus,' Elsevier, London, 1967.
[5] C. Grundmann and H. D. Frommeld, *J. Org. Chem.*, 1966, **31**, 157.

indicating a considerable weakening of the P–OEt bond, perhaps due to hydrogen bonding with the oxime proton, a point which has significance in connection with the discussion, below, of the mechanism of the hydrolysis of the adducts (II). This observation also implies a *cis*-configuration of the adduct II [*i.e.* as depicted in (VII)]. This is in accord with the formation of the corresponding *cis*-adduct from the addition of thiols to arene nitrile oxides.[6]

*Acidic Hydrolysis of α-Hydroxyimino-*p*-nitrobenzyl Esters of Phosphorus Acids.*—(i) *Products.* The case of ethyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate (II; $R^1 = Me$; $R^2 = Et$) is typical. Hydrolysis in aqueous dioxan (2%) at pH 2—3·5 at room temperature occurred within a few minutes with formation of ethanol and hydrogen α-hydroxyimino-*p*-nitrobenzyl methylphosphonate (VI; R = Me), which was characterised by titration, analysis, and spectroscopy. The reaction could be followed either by carrying it out in an automatic titration assembly, the procedure which was selected for the kinetic study (v.i.), or in the n.m.r. tube (using dry deuteriochloroform or hexadeuteriodimethyl sulphoxide with a trace of deuterium oxide). Other α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates behaved similarly and in each case the p.m.r. spectrum of the hydrolysed product exhibited signals attributable only to the alcohol (R^2OH) after removal by filtration of the hydrogen phosphonate (VI). In the case of pinacolyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate (II; $R^1 = Me$; $R^2 = Bu^tCHMe$) the presence of pinacolyl alcohol was established by g.l.c. and by characterisation as the *p*-chlorophenylurethane. C_6 Alkenes, which would have been indicative [2] of the pinacolyl carbonium, if present, were shown to be absent by g.l.c., a point which will be shown below to have particular mechanistic significance.

At high pH, as discussed in the succeeding Part, the products of the hydrolysis are quite different and include *p*-nitroaniline and the corresponding hydrogen phosphonates (I). At intermediate pH mixtures of products arise.

(ii) *Kinetic results and discussion.* The kinetic results of the acidic hydrolysis of the α-hydroxyimino-*p*-nitrobenzyl esters of phosphorus acids in 2% aqueous dioxan or ethanol are summarised in Tables 6 and 7. In the case of alkyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate adducts (II) studied, the kinetics obeyed the first-order rate equation, the hydrolyses being performed with a large excess of water thus giving pseudo unimolecular conditions. The reaction was remarkably fast ($k_1 = 0{\cdot}65$ min^{-1} at pH 3·5; $E_a = 62{\cdot}3$ kJ mol^{-1}) being *ca.* 2×10^7 faster than the hydrolysis of ethyl *p*-nitrophenyl methylphosphonate to give ethanol.[3] Such an acceleration and observed constancy of the rate in the range pH 2—3·5 suggest intramolecular catalysis involving the free oxime (*i.e.* =NOH rather than $=NO^-$ or $=NOH_2^+$) and that further protonation of the phosphonate (II; $R^1 = Me$; $R^2 = Et$) is not necessary for the rapid reaction to occur. In theory the above catalysis could involve participation of the alkoxy-oxygen (VII), where internal protonation of the alkoxyl oxygen is implied, or (VIII) involving protonation of the phosphoryl oxygen. The latter alternative can be discounted, not only on lack of precedent, but because it can be argued that subsequent reaction should involve elimination of the better of the two possible leaving groups, in the case of (VIII) this would be the hydroxamate, rather than the alkoxide ion, whereas in the case of (VII) the leaving group would be the alcohol (R^2OH), as observed. The intermediate (VII) also implies a certain lack of rotation in the transition state which is in accord with the observed negative entropy of activation (−19 e.u.). The intermediate (VII) could then, in theory, give the products *via* several possible routes (Scheme 1): (i) bimolecular reaction of water at phosphorus with displacement of the alcohol *via* P–O fission; (ii) bimolecular reactions of water at the ester α-carbon atom to give the alcohol *via* alkyl-oxygen fission; (iii) unimolecular loss of the alcohol; (iv) the formation of a cyclic intermediate (IX), with concomitant formation of the alcohol, which would then undergo fast hydrolysis. Of these, routes (i) and (iv) are the most satisfactory for the reasons discussed below.

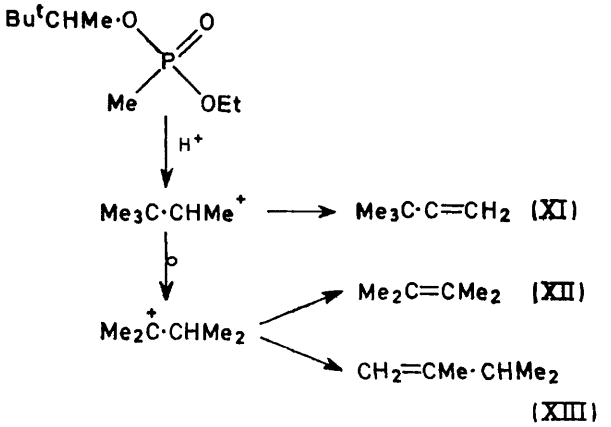


SCHEME 1

Route (i) requires the occurrence of P–O fission, hitherto unobserved in acidic hydrolysis of non cyclic phosphates and phosphonates.[2,3] Thus, ethyl pinacolyl

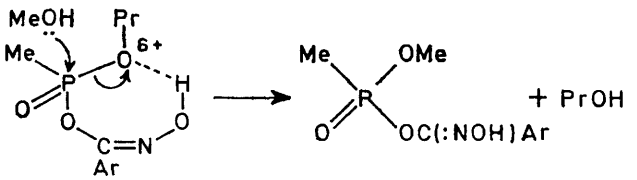
[6] M. H. Benn, *Canad. J. Chem.*, 1964, **42**, 2393; J. Waser and W. H. Watson, *Nature*, 1963, **198**, 1297.

methylphosphonate (X) hydrolyses in acid solution to give three C_6 alkenes (XI), (XII), (XIII),[2] indicating the formation and rearrangement of the pinacolyl carbonium ion (Scheme 2). Acidic hydrolysis of alkyl α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (II), however, always proceeds with the formation of the corresponding alcohol, and in the case of the pinacolyl derivative (II; R^1 = Me; R^2 = Bu^tCHMe) pinacolyl alcohol was isolated and no C_6 alkenes were detected (by g.l.c.)



SCHEME 2

(Scheme 2), thus pointing to route (i) involving P–O fission. This mechanism also accounts for the very fast and quantitative conversion, by transesterification, of propyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate (II; R^1 = Me; R^2 = Pr) into the corresponding methyl ester (II; R^1 = Me, R^2 = Me), which occurs in methanol during a few minutes at room temperature. This is to be compared with ' normal ' transesterification of phosphates which takes six days at 130°.[7] The former observation is explicable in terms of anchimerically assisted methanolic attack on phosphorus, with P–O fission (Scheme 3) analogous to route (i).



SCHEME 3

Hitherto, P–O fission has been observed only during *alkaline* hydrolysis of simple phosphonates.[3] In the series of α-hydroxyimino-*p*-nitrobenzyl esters (II) it is therefore in accord with the postulated route (i) that the rate constants (Table 1) should fall in the order R^1 (in R^1O) = Me > Et > Pr > Pr^i > Bu^tCH_2 > Bu^tCHMe, thus paralleling the order observed for alkaline hydrolysis, *via* P–O fission, of simple phosphonates $[(R^1O)_2P(:O)Me]$,[3]

[7] H. M. Bell, *J. Org. Chem.*, 1969, **34**, 681.
[8] H. Christol and C. Marty, *J. Organometallic Chem.*, 1968, **12**, 471.

TABLE 1

Relative rate constants for hydrolysis of $R^1R^2P(:O)\cdot O\cdot C(:NOH)Ar$ at pH 2·75

R^2 = Me

R^1	MeO	EtO	PrO
Rel. rate	87	71	45
	Pr^iO	Bu^tCH_2O	Bu^tCHMeO
Rel. rate	14	10	1

R^2 = EtO

R^1	Me	Et	Bu^t
Rel. rate	71	41	<0·4

but contrary to the known [3] order of reactivity (Pr^i > Me ≈ Bu^tCH_2) of the latter in acid solution, involving alkyl-oxygen fission.

The postulated implication of the oxime proton in the anchimeric assistance observed in these reactions is supported by the results of the acidic hydrolysis of neopentyl α-methoxyimino-*p*-nitrobenzyl methylphosphonate [$Bu^tCH_2O(Me)P(O)OCAr{=}NOMe$], in which the oxime proton is replaced by methyl. This ester was unaffected by acid during a period equal to seven half-lives for the hydrolysis of the corresponding free oxime (II; R^1 = Me; R^2 = Bu^tCH_2).

Route (i) postulates bimolecular attack of water at phosphorus. Since it is well established that such substitutions are sensitive to steric crowding [3,8-10] a decrease in rate of hydrolysis of α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (II) with increase of the size of the *P*-alkyl group should therefore be, and is, observed (Table 1). This confirms bimolecular attack at phosphorus (route i) as well as telling against bimolecular attack on α-carbon (route ii) and unimolecular loss of the alcohol (route iii), neither of which would be expected to be influenced by steric crowding at phosphorus.

Route (iv) still remains a possibility, however, because it is in accord with the above observations. At this time we cannot distinguish between these possible routes.

It has already been established that it is valid directly to compare alkaline hydrolysis of simple dialkyl alkylphosphonates $[(R^2O)_2P(:O)R^1]$ with acidic hydrolysis of the α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (II), both of which occur with P–O fission. Following this it is noteworthy that the reactivity range in the latter case (Table 1) is much compressed compared with the former. Thus Hudson and Keay [3] and Christol and Marty [8] reported a much greater reactivity range, encompassing a factor of 1800, for alkaline hydrolysis of dineopentyl and dimethyl methylphosphonates [*cf.* 9 for the corresponding (II) (Table 1)]. Such a decrease in reactivity with increasing size of the ester alkyl group was attributed to steric hindrance [3,8] and also to reduced electrophilicity of the phosphorus atom resulting from the greater ease of π-interactions involving oxygen induced by the inductive effect of the ester alkyl group.[3,11]

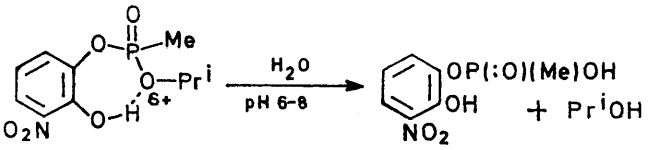
[9] M. Ikehara and E. Ohtsuka, *Chem. Pharm. Bull* (*Japan*), 1963, **11**, 1353.
[10] W. Hawes and S. Trippett, *Chem. Comm.*, 1968, 577.
[11] R. F. Hudson and L. Keay, *J. Chem. Soc.*, 1960, 1859.

In the adducts (II), the oxime proton provides an alternative electron sink, however, so that the proton can receive part of the above π-interaction, normally participating with the phosphorus atom in simple phosphonates. Thus, the observed smaller decrease in rate in the series of adducts (II) (Table 1) can then be attributed to the operation of the effects of steric hindrance of the ester moiety only.

This explanation is strengthened by the observed magnitude (k_{Me}/k_{But} = 180) of the diminution in rate of hydrolysis of the adducts (II) caused by increasing the size of the *P*-alkyl group. The observed ratio is more nearly that observed for the alkaline hydrolysis of the corresponding di-isopropyl alkylphosphonates (k_{Me}/k_{But} = 500).[11] In this case the phosphorus atom in the adducts (II; R^1 = Me; R^2 = Et and R = Bu^t; R^2 = Et) receives in full the steric and electronic effects of the alkyl groups, because protonation of the ester moiety can have little influence on effects transmitted directly to phosphorus.

The diethyl hydrogen phosphate adduct (II; R^1 = EtO, R^2 = Et) and that from ethyl hydrogen t-butylphosphonate (II; R^1 = Bu^t, R^2 = Et) are two cases where the normal acidic hydrolysis is complicated by the much greater rate of alkaline hydrolysis. Both adducts hydrolysed by both routes at pH 2·5 to give both ethanol and *p*-nitroaniline. In spite of there being only a low concentration of the anion at pH 2·5, in each case, the rate of the competing intramolecular attack on phosphorus by oxime was sufficient to produce a measurable quantity of *p*-nitroaniline. In accord with the foregoing, α-hydroxyimino-*p*-nitrobenzyl diethylphosphinate (iii), on the other hand, was stable in acid solution, having no alkoxy-groups available for hydrolysis by this route. This enabled the pK_a (4·65) to be determined.

Previously Reported Reactions Relevant to the Hydrolysis of the Adducts (II).—A number of fast intramolecular alkaline- and acid-catalysed hydrolyses of the esters of phosphorus acids have been reported,[12-18] but only that of isopropyl 3-nitro-2-hydroxyphenyl methylphosphonate (XIV) described by Mlodozenic [13] is comparable with that reported in this paper. The phosphonate (XIV) was readily dealkylated at pH 6—8 under acid catalysis from the neighbouring hydroxy-group (Scheme 5). The half-life (30 min at 30°) for this unimolecular reaction was slightly longer (×10) than observed by us for the analogous α-hydroxyimino-derivative (II; R^1 = Me, R^2 = Pr^i) and the activation parameters were similar [(XIV E_a = 58·1 kJ mol^{-1}; $\Delta S^{\ddagger}$ = −30 e.u. (II; R^1 = Me, R^2 = Et): E_a = 62·3 kJ mol^{-1}; $\Delta S^{\ddagger}$ = −19 e.u.). In the former case (XIV) it was not established, however, whether the effect of the neighbouring hydroxy-



SCHEME 5

group involved anchimeric assistance of the solvolysis of the isopropyl group *via* P–O fission.

EXPERIMENTAL

Preparation of Reagents.—Alkyl methylphosphonochloridates. These compounds were in general prepared by adding ing the appropriate alcohol (1 mol) with triethylamine (1 mol) to a vigorously stirred solution of the methylphosphonic dichloride (1 mol) in ether at 0°. After standard work-up the chloridate was obtained by distillation under reduced pressure. Pinacolyl methylphosphonochloridate was prepared as described previously.[19] *Ethyl t-butylphosphonochloridate* was prepared by adding sodium ethoxide (80 mmol, 5·44 g) in suspension-solution (150 ml benzene) to t-butylphosphonic dichloride [12·9 g, 74 mmol, m.p. 112° (lit.,[20] m.p. 110°)], with vigorous stirring in boiling benzene during 1 h. After removal of benzene, the ether solution was filtered through Hyflo-supercel and the *product* was obtained by distillation (Found: C, 38·6; H, 7·8. $C_6H_{14}ClO_2P$ requires C, 39·0; H, 7·6%). *Ethyl isopropylphosphonochloridate,* was prepared analogously from isopropylphosphonic dichloride [20] [b.p. 75—76°/23 mm (lit.,[21] b.p. 76°/23 mm)].

TABLE 2

Physical constants of some chloridates, $R^1R^2P(O)Cl$

R^1	R^2	B.p.°/mm	n_D^{25}	Lit. b.p.°/mm n_D^{18}	Ref.
OMe	Me	54/4	1·4322 *	73/22, 1·4395	22
OEt	Me	44/2·5	1·4320	32/1, 1·4385	22, 23
OPr	Me	52/2	1·4320	94/21, 1·4378	22
OPr^i	Me	44/0·6	1·4290	83/22, 1/4285 †	22
OCH_2Bu^t	Me	68/1	1·4309	51/0·08	24
$OCHMeBu^t$	Me	52/0·01	1·4413 †	52—54/0·02, 1·4430	19
OEt	Ph	98/0·05	1·5368	103/0·3	23
OEt	OEt	80—81/9	1·4143	93—95/18	25
OEt	Bu^t	32/0·5	1·4352	New compound	
OEt	Pr^i	89/23	1·4355	53/1·9, 1·4357 ‡	26

* At 22°. † At 23°. ‡ At 25°.

Physical constants of the phosphorochloridates used are summarised in Table 2.

[12] J. Epstein, H. O. Michel, D. H. Rosenblatt, R. E. Plapinger, R. A. Stephani, and E. Cook, *J. Amer. Chem. Soc.*, 1964, **86**, 4959.
[13] A. R. Mlodozenic, *Diss. Abs.*, 1964, **25**, 1157.
[14] L. E. Tammelin, *Acta Chem. Scand.*, 1957, **11**, 859.
[15] C. E. Griffin, M. Gordon, and V. A. Notaro, *J. Amer. Chem. Soc.*, 1964, **86**, 1898; G. M. Blackburn and M. J. Brown, *J. Amer. Chem. Soc.*, 1969, **91**, 525.
[16] M. L. Bender and J. M. Lawlor, *J. Amer. Chem. Soc.*, 1963, **85**, 3010.
[17] V. M. Clark and A. J. Kirby, *J. Amer. Chem. Soc.*, 1963, **85**, 3705.
[18] C. Lieske, J. Hovanec, G. Steinberg, and P. Blumbergs, *Chem. Comm.*, 1968, 13.
[19] J. I. G. Cadogan, R. K. Mackie, and J. A. Maynard, *J. Chem. Soc.* (*C*), 1967, 1359.
[20] A. M. Kinnear and E. A. Perren, *J. Chem. Soc.*, 1952, 3437.
[21] J. P. Clay, *J. Org. Chem.*, 1951, **16**, 892.
[22] Z. Pelchowicz, *J. Chem. Soc.*, 1961, 238.
[23] R. F. Hudson and L. Keay, *J. Chem. Soc.*, 1957, 3604.
[24] M. Green and D. M. Thorp, *J. Chem. Soc.* (*A*), 1967, 731.
[25] H. McCombie, B. C. Saunders, and G. J. Stacey, *J. Chem. Soc.*, 1945, 380.
[26] F. W. Hoffmann, T. C. Simmons, and L. J. Glunz, *J. Amer. Chem. Soc.*, 1957, **79**, 3570.

Alkyl hydrogen alkylphosphonates and related acids. In general, these compounds were obtained by hydrolysis of the corresponding chloridate (Table 4). Alkyl methylphosphonochloridates and diethyl phosphorochloridate were hydrolysed by their dropwise addition to vigorously stirred ice–water mixtures. More forcing conditions were used for chloridates whose structure would lead to slow rates of hydrolysis in ice–water mixtures. Standard work and distillation was employed to isolate the acids (Table 3).

TABLE 3

Hydrolyses of chloridates, $(R^2O)R^1POCl$

R^1	R^2	Conditions of hydrolysis
Me	Bu^tCH_2	Sodium hydroxide (2M), 60°, 2 h
Me	Bu^tCHMe	Sodium hydroxide (2M), 60°, 2 h
Pr^i	Et	Sodium hydroxide (2M), 40°, 1/2 h
Bu^t	Et	Sodium hydroxide (2·7M), 40°, 14 h followed by 5M, 70°, 4 h

Diethyl ethylphosphonate and ethyl diethylphosphinate (see below) were hydrolysed in sodium hydroxide solution (4·5M) at 80° for 3 h. The cooled alkaline solutions were acidified and water was removed with rotatory evaporator at $>35°$. The residue was extracted with chloroform and the extract was dried (Na_2SO_4 for 12 h); the acids were obtained by distillation (Table 4). The equivalent weights of the acids were determined by titration and agreed within 3% of the calculated value.

Ethyl hydrogen phenylphosphonate was not distilled, but used immediately to form the adduct with *p*-nitrobenzonitrile oxide (see below), as Kosolapoff [27] reported the compound to be unstable. The structure of the acid was confirmed by n.m.r. spectroscopy, (CCl_4/$CDCl_3$) τ −2·96 (s, PO*H*, 1H), 2·0—2·8 (complex multiplet, P-*Ph*, 5H), 6·02 $POCH_2CH_3$, 2H), and 8·79 (t, $-CH_2CH_3$, 3H).

Ethyl diethylphosphinate. Kosolapoff and Watson's method [28] using thiophosphoryl chloride and ethylmagnesium bromide gave poor yields (3%) of the silver salt of diethylphosphinic acid. A more successful preparation was that of Sander [29] based on the reaction of ethyl phosphorodichloridite [b.p. 116—118°; n_D^{20} 1·4625 (lit.,[30] $n_D^{19.5}$ 1·4628)] and ethylmagnesium chloride to give ethyl diethylphosphinite [b.p. 42°/20 mm; n_D^{25} 1·4351 (lit.,[29] b.p. 51°/67 mm; n_D^{20} 1·4403), 18%]. Ethyl diethylphosphinate was obtained by oxidation of the phosphinite (3 g) with 10% v/v hydrogen peroxide (10 ml) in aqueous solution at 0°. The solution was stirred for 0·5 h and was then allowed to warm to room temperature. The ester was not isolated but hydrolysed *in situ* to the sodium salt of diethylphosphinic acid.

p-*Nitrobenzonitrile oxide.* *p*-Nitrobenzhydroxamoyl chloride (m.p. 125—126°, lit.[33] m.p. 116°) in dry ether solution (200 ml), was treated with an equimolar quantity of triethylamine (4·5 g) at 0°, with vigorous mechanical stirring. The precipitate was washed thoroughly with water to remove base hydrochloride and the remaining light-yellow nitrile oxide was dried repeatedly over phosphorus pentoxide under high vacuum, until the i.r. spectrum showed an absence of hydroxylic stretching frequencies at 3500 cm^{-1}. The m.p. depended on the rate of heating. Thermal dimerization to the furoxan [m.p. 185—195° (lit.,[34] m.p. 199—201°)] sometimes occurred on slow heating of the compound. Rapid heating of the nitrile oxide gave m.p. 93° (lit.,[34] m.p. 95°).

TABLE 4

Alkyl hydrogen alkylphosphonates and related compounds, $R^1R^2PO_2H$

R^1	R^2	B.p.°/mm	n_D^{25}	Lit. b.p.°/mm; n_D^{20}	Ref.
MeO	Me	92/0·1	1·4250 [a]	104/0·1; 1·4248	31
EtO	Me	110/0·05	1·4219	106—107/0·1; 1·4258	31
PrO	Me	106/0·05	1·4259	104—105/0·05; 1·4282	31
Pr^iO	Me	88/0·02	1·4210	97—98/0·08; 1·4228	31
Bu^tCH_2O	Me	110/0·02	1·4250	New compd. [d]	
Bu^tCHMeO	Me	98/0·05	1·4320	116—118/0·1; 1·4322 [b]	19
EtO	EtO	120/0·06	1·4140		
EtO	Et	92/0·04	1·4281		
EtO	Bu^t	72—76/0·03	1·4253	New compd.[e]	
EtO	Ph		1·5223		
EtO	Pr^i	80—82/0·05	1·4199	New compd.[f]	
Et	Et	160/0·03	1·4551 [c]	194—195/21	32

[a] 18°. [b] 25°. [c] 20°. [d] Found: C, 43·9; H, 9·0. $C_6H_{15}O_3P$ requires C, 43·4; H, 9·1%. [e] Found: C, 43·3; H, 9·6. $C_6H_{15}O_3P$ requires C, 43·4; H, 9·1%. [f] Found: C, 39·1; H, 8·7. $C_5H_{13}O_3P$ requires C, 39·5; H, 8·6%.

*Alkyl α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates and related compounds.* It was essential for the preparation of these 1 : 1 adducts of *p*-nitrobenzonitrile oxide and phosphorus acid for all chemicals, solvents, and apparatus to be rigorously dry. A dry box, in which weighing and filtration operations could be carried out, was used throughout the preparation of these adducts.

The preparation of pinacolyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate was typical of the procedure followed. Pinacolyl hydrogen methylphosphonate [3·24 g, 18 mmol dried in dioxan solution (20 ml) over sodium sulphate] was mixed with *p*-nitrobenzonitrile oxide (5·5 g, 34 mmol) in dioxan (150 ml), the mixture was set aside for 24 h at room temperature in a light-protected flask. The dioxan was then removed at room temperature ($>25°$) and 0·05 mm pressure to leave a solid residue. This residue was extracted with pinacolyl alcohol to leave a pale yellow residue, which was washed with ether and dried by drawing nitrogen through it in the dry box. The solid was identified as bis-*p*-nitrophenylfuroxan (3·2 g, 58% based on the nitrile oxide) by its i.r. spectrum (identical with that of an authentic sample).

The alcohol solution was evaporated at room temperature and 0·05 mm pressure, and ether (25 ml) with a little light petroleum (40—60°, 5 ml) was added to precipitate a light yellow solid. The solid adduct (2·3 g, 37% based on acid taken) was washed with ether, and again dried by drawing nitrogen through it in the dry box.

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The structure of the resultant *pinacolyl α-hydroxyimino-p-nitrobenzyl methylphosphonate* was confirmed by n.m.r. and i.r. spectroscopy. The i.r. spectrum showed the presence of NOH (3100—3140 cm^{-1}), aromatic ring (1600 and 850 cm^{-1}), NO_2 (1515 and 1350 cm^{-1}), phosphorus bonding [ν(P=O) 1230, ν(POEt) 1035 cm^{-1}] and oxime [ν(C=N), 1635 cm^{-1}] moieties.

The n.m.r. spectrum showed the correct integral for each of the proton species and each of the absorptions to be expected for the 1 : 1 adduct: τ ($CDCl_3$) 1·78 (centre of AA'BB' quartet, 4H), 5·58 (quintet, methine C–*H*, 1H), 8·21 (centre of doublet, P–CH_3, J_{PMe} 18 Hz, 3H), 8·65 (quartet, lone methyl, HC–CH_3, 3H), and 9·05 (singlet, *t-Bu*, 9H).

Other adducts of the benzonitrile oxide and hydrogen phosphorus esters were prepared similarly. In general, the ratio of nitrile oxide : acid of 2 : 1 was found to give the optimum yield bearing in mind the competing dimerization of the nitrile oxide and the formation of the adduct as a clean, dry solid. It was also necessary to use the alcohol corresponding to the ester moiety for the work-up to prevent transesterification. When the corresponding alcohol was a solid, the initial residue was extracted with ether (4 × 75 ml).

The structures of all the 1 : 1 adducts were confirmed by spectroscopy and the compounds had satisfactory elemental analyses (Table 5).

N.m.r. spectra were run in deuteriochloroform on approximately 5% (saturated) solutions. τ Values quoted in Table 5 are that of the multiplet centre. Average coupling constants (*J*) were observed as follows: P–CH_3 18 Hz; $POCH_3$ 11 Hz; $POCH_2$ 7 Hz; and CH_3–CH_2 7 Hz. In a few cases, signals due to the oxime proton were recorded, thus compound 10, τ = −2·3; 7, −1·8; 15, −2·5; 12, −2·2.

The i.r. spectra of the adducts were obtained from Nujol mulls and confirmed the structures. The principal groups in the adducts showed frequencies at 3100 (w, NOH), 1600 (m—s, aromatic ring), 1520 and 1350 (s, NO_2), 1180—1250 (s, P=O), and 850 cm^{-1} (s, NO_2). The phosphoryl group absorption was generally around 1230 cm^{-1}, but lower values were observed for the phosphinate adducts.[35]

Variation in the position of the oxime C=N stretching frequency was observed. The alkyl methylphosphonate adducts had ν(C=N) values of *ca.* 1630 cm^{-1}, which is at the lower end of the generally accepted range of oxime stretching values. All of the other adducts showed values of ν(C=N) of 1690—1700 cm^{-1}, which is at the upper limit of observed oxime stretching frequencies.[35] Methyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate was unique in that it showed values at 1630 and 1700 cm^{-1}. Concomitant with the increase in the ν(C=N) frequency was the increase in the intensity of the NOH absorption at 3100 cm^{-1} from being of previously weak intensity to weak—medium intensity.

TABLE 5

Preparation of 1 : 1 adducts [$R^1R^2P(:O)O{\cdot}C(:NOH)C_6H_4NO_2$-*p*] from *p*-nitrobenzonitrile oxide and hydrogen phosphylates †

Compd.	R^1	R^2	Analysis (%) * C	H	N	Yield (%)	M.p.°	N.m.r. τ
(1)	MeO	Me	39·2 39·4	4·0 4·0	10·4 10·2	40	115	1·78 (q, Ar, 4H), 6·10 (d, POCH_3, 3H), and 8·20 (d, P-*Me*, 3H)
(2)	EtO	Me	41·6 41·7	4·7 4·5	10·1 9·7	27	130	1·73 (q, Ar, 4H), 5·77 (quintet, POCH_2CH$_3$, 2H), 8·21 (d, P-*Me*, 3H) and 8·64 (t, $POCH_2CH_3$, 3H)
(3)	PrO	Me	42·9 43·8	5·0 5·0		46	88—90	1·79 (q, Ar, 4H), 5·84 (q, POCH_2CH$_2$, 2H), 8·21 (d, P-*Me*, 3H) and 9·04 (t, –CH_2CH_3, 3H)
(4)	Pr^iO	Me	43·0 43·8	5·0 5·0	8·9 9·3	30	112—114	1·78 (q, Ar, 4H), 5·1 (quintet of doublets, POC*H*, 1H), 8·25 (d, P–CH_3, 3H) and 8·43 (dd, POCH–CH_3, 6H)
(5)	Bu^tCH_2O	Me	47·0 47·3	5·5 5·8	8·7 8·9	50	110	1·80 (q, Ar, 4H), 6·19 (dd, POCH_2, 2H), 8·21 (d, P-*Me*, 3H) and 9·07 (s, C–$(CH_3)_3$, 9H)
(6)	Bu^tCHMeO	Me	49·0 48·8	6·0 6·1	8·4 8·1	55	110—113	1·78 (q, Ar, 4H), 5·59 [quintet, POC(Me)*H*, 1H], 8·21 (d, P-*Me*, 3H), 8·65 (q, POCHCH_3, 3H) and 9·05 [s, $C(CH_3)_3$, 9H]
(7)	EtO	EtO	40·6 41·5	4·5 4·7	8·8 8·7	20	94·5—95	1·77 (q, Ar, 4H), 5·62 (quintet, POCH_2CH$_3$, 4H) and 8·85 (t, $POCH_2CH_3$, 6H)
(8)	EtO	Et	44·0 43·7	5·0 5·0	9·6 9·3	27	98—100	1·83 (q, Ar, 4H), 5·75 (quintet, POCH_2CH$_3$, 2H), 7·79 (septet, PCH_2CH$_3$, 2H), 8·52 (t, PCH_2CH_3, 3H) and 8·90 (t, $POCH_2CH_3$, 3H)
(9)	Et	Et	45·6 46·1	5·2 5·3	10·0 9·8	17	112	1·82 (q, Ar, 4H), 8·04 (septet, PCH_2CH$_3$, 2H) and 8·64 (t, PCH_2CH_3, 6H)
(10)	EtO	Bu^t	47·6 47·3	5·6 5·8		19	114	1·80 (unresolved, Ar, 4H), 5·77 (quintet, POCH_2CH$_3$, 4H) and 8·52—8·80 ($POCH_2$-CH_3 and $C(CH_3)_3$, 12H)
(11)	EtO	Ph	51·4 51·3	4·3 4·3		24	142—143	1·95 (q, Ar, $C_6H_4NO_2$) and 2·0—2·8 (complex multiplets, P–C_6H_5, total Ar protons, 9H), 5·68 (quintet, POCH_2CH$_3$, 2H) and 8·62 (t, POCH_2CH$_3$, 3H)

* New compounds: top row 'Found,' bottom row 'Required'.
† The furoxan (see text) (20—50%) was also obtained in most cases.

[35] L. J. Bellamy, 'The Infra-red Spectra of Complex Molecules,' Methuen, London, 1962.

In the case of ethyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate, the POEt band at 1030 cm^{-1} in Nujol had shifted to 1000 cm^{-1} in dioxan (4% w/v) indicating a considerable weakening of the PO bond, perhaps due to hydrogen bonding involving the oxime.

Products of Acidic Hydrolysis of Arenenitrile Oxide–Phosphorus Ester Adducts.—This reaction is exemplified by the case of ethyl α-hydroximino-*p*-nitrobenzyl methylphosphonate. The adduct (10 mg) in ethanol (0·5 ml) was added to water (25 ml) and kept at pH 3·6 by addition of sodium hydroxide (0·1N) by means of a Radiometer Automatic Titrimeter. Reaction was complete in 15 min. Titration of the resultant solution with sodium hydroxide (0·1N) showed that two equivalents of acid had been produced, end points at pH 4·9 and 9·5 corresponding to equivalent weights of 299 and 147·5 respectively. The initial adduct requires equivalent weights of 288 and 144. The titration curve was similar to that of hydrogen α-hydroxyimino-*p*-nitrobenzyl methylphosphonate.

In subsequent cases the products of hydrolysis were followed by n.m.r. spectroscopy. To a solution of the alkylphosphonate adduct in deuteriochloroform was added 4 drops of deuterium oxide; the mixture was shaken and left for a day at room temperature. The resulting mixture precipitated *hydrogen α-hydroxyimino-p-nitrobenzyl methylphosphonate*, m.p. 145—146° (decomp.) (Found: C, 36·8; H, 3·7; N, 10·6. $C_8H_9N_2O_6P$ requires C, 36·9; H, 3·5; N, 10·8%), $\nu_{max.}$ 2200 (POH) and 2650 cm^{-1} (NOH), τ[$(CD_3)_2SO$] 8·39 (d, PCH_3) 1·22 (NO*H*), 1·74 (Ar). Titration of the phosphonate (0·2N-NaOH) gave end points at pH 3·3 [P(O)OH; found equiv. wt. 260, required 260] and at pH 8·7 (NOH, found equiv. wt. 126, required 130). The i.r. spectrum was in accord with the postulated structure.

The solids filtered off from the hydrolyses of ethyl α-hydroxyimino-*p*-nitrobenzyl ethylphosphonate and phenylphosphonate had i.r. spectra similar to hydrogen α-hydroxyimino-*p*-nitrobenzyl methylphosphonate [2300 (POH, shallow), 1650 (C=N), 1600 (aromatic), 1530 and 1350 (NO_2 and P=O) 1250 (P–Ph) and 1162 cm^{-1} (P–OEt)]. They both titrated as dibasic acids and the correct equivalent weights were obtained.

In each case the p.m.r. spectrum of the filtrate showed only signals due to the alcohol resulting from hydrolysis.

In the case of pinacolyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate, the presence of pinacolyl alcohol was shown by (*a*) its retention time on two g.l.c. columns (10% PEGA, 66°, hydrolysate and authentic pinacolyl alcohol, 1 peak, retention time 10 min: 15% DNP, 56°, hydrolysate and of authentic pinacolyl alcohol, 1 peak, retention time 29·6 min). (*b*) The urethanes were made by mixing *p*-chlorophenyl isocyanate and the alcohol, and were purified by elution with 75% benzene–light petrol from an alumina column. The compounds had superimposable i.r. spectra, m.p. and mixed m.p. 101·5—102·5°. None of the olefins obtained from the acid hydrolysis of ethyl pinacolyl methylphosphonate were detected by g.l.c. using the previously established conditions.[2]

*Neopentyl α-Methoxyimino-*p*-nitrobenzyl methylphosphonate.*—Diazomethane (0·32—0·35 g) in ether solution was added to neopentyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate (0·5 g) in dioxan (20 ml). After 5 min when gas evolution had ceased, the excess of diazomethane was removed with acetic acid. After removal of dioxan, the residual oil in chloroform was washed with alkali and water and dried. The p.m.r. spectrum of the resulting yellow oil did not exhibit the NOH proton, but had a new absorption at τ 5·72 (3H) and was considered to be *neopentyl α-methoxyimino-*p*-nitrobenzyl methylphosphonate* (Found: C, 48·4; H, 6·1. $C_{14}H_{21}N_2O_6P$ requires C, 48·7; H, 6·1%). The p.m.r. spectrum (20% $CDCl_3$ solution) showed signals at τ 1·91 (q, Ar, 4H); 5·72 (s, NOCH_3, 3H), 6·20 (octet, POCH_2, 2H), 8·22 (d, P–CH_3, 3H), and 9·02 (s, Bu^t, 9H); i.r. spectrum (liquid film) peaks at: 1638 (C=N), 1598 (aromatic), 1350 and 1525 (NO_2), 1260 (P=O), 1035 and 930 ($POCH_2$), and 860 cm^{-1} (NO_2Ar).

The behaviour of this methylated compound was examined in acid and alkaline solution. The compound (*ca.* 70 mg) in dioxan (0·7 ml) was added to the Radiometer titration cell, which was maintained at constant pH 2·45. After the initial slight disturbance to the system, a continuous trace with no change was obtained during 1 h (this corresponds to 7 half-lives of reaction time of the non-methylated compound).

The adduct was also stable in alkaline solution over 10 half-lives of the reaction of the non methylated compound.

*Reaction of Propyl α-Hydroxyimino-*p*-nitrobenzyl Methylphosphonate with Methanol.*—Methanol (70 ml) was added to a solution of the phosphonate (270 mg) in dioxan (10 ml) and the mixture was set aside for 24 h at room temperature. After removal of solvents under reduced pressure at room temperature, the addition of ether precipitated a solid (70 mg). A p.m.r. spectrum of the solid showed it to be methyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate, whose n.m.r. spectrum ($CDCl_3$) showed absorptions at: τ 1·78 (q, Ar, 4H); 6·14 (d, POCH_3, J_{POMe} 11 Hz, 3H); and 8·23 (d, PCH_3, J_{PMe} 18 Hz, 3H). Signals attributable to the propyl group were absent.

*Determination of the pK_a of α-Hydroxyimino-*p*-nitrobenzyl diethylphosphinate.*—This compound was stable in acid. The pK_a was determined by Radiometer titration of the adducts in 3·5% ethanol–dioxan–water (ionic strength $\mu = 0{\cdot}1$) following the method of Albert and Sergeant.[36] The mean pK_a was 4·65 ± 0·10 (25°).

Reaction Kinetics.—Rates were determined using a Radiometer automatic titration assembly (Titrator TTT 111, Titrigraph SBR 2c, burette assembly SBU1a). The 100-ml capacity titration vessel had a thermostatically controlled jacket. The temperature control at 25° was ±0·05° and at other temperatures ±0·1°. Radiometer Type C glass and K401 saturated potassium chloride electrodes were fitted through a lid to the vessel, together with the automatic burette. A stirrer paddle was mounted through the lid and driven externally by an electric motor. The titration vessel was protected by self-indicating sodalime guard-tube.

A stock solution of ionic strength $\mu = 0{\cdot}1$ with [HCl] = 0·01M and [NaCl] = 0·09M was used. During the titration, not more than 0·5 ml of sodium hydroxide (0·1N) was added. Thus, the ionic strength of the solution was 0·1M ± 0·002M. A 25-ml aliquot of the stock solution was brought to the desired pH and allowed to come to equilibrium for 0·75 h.

The compound (0·04 mmol) in dioxan (0·5 ml) was added by way of a syringe into the titration vessel. In the acid region, sodium hydroxide solution (0·1M; B.D.H. carbonate-free) was added immediately to follow the rate of production of acid. At intermediate and alkaline pH, rapid deprotonation was corrected manually to return the pH to the desired

[36] A. Albert and E. P. Seargent, 'Ionisation constants of Acids and Bases,' Methuen, London, 1962.

value, and the automatic titrator was then allowed to follow the reaction.

The solutions were 2% in dioxan for all of the hydrolyses except for some of the phosphinate adducts, where it was necessary to use a 4% ethanol–dioxan–water mixture because of the reduced solubility. It was found, however, that when the reaction medium for some of the phosphonate adducts was changed to 4% aqueous dioxan, or 4% aqueous ethanol–dioxan no change in rate coefficient occurred. As the titration proceeded in alkaline solution, the contents of the Radiometer cell became bright yellow. At low pH, the solution became more yellow as the rate dropped off above pH 3.

Rate constants were calculated either by Guggenheim's method or by the use of the integrated first-order rate equation.

Values of the first-order rate constants at low pH are tabulated (Table 6), and at varying temperatures (Table 7) and are estimated to have an accuracy of ±4%. Good Arrhenius plots were obtained for all compounds. Values of the entropy of activation were calculated by the equation of Schaleger and Long.[37]

TABLE 6

Rate constants for hydrolysis of $R^1R^2P(:O)\cdot OC(:NOH)\cdot C_6H_4NO_2$-*p* at 25·0°

Compd. No. (see Table 5)		pH and Rate constants ($10k_1$ min^{-1})					
(1)	pH	2·10	2·39	2·75	3·09		
	$10k_1$	3·56	6·10	8·7	18·1		
(1) *	pH	2·31	2·40	2·46	2·50	2·54	2·59
	$10k_1$	2·11	2·17	2·38	2·55	2·67	3·04
	pH	2·66	2·73	2·80	2·90	2·94	3·00
	$10k_1$	3·21	3·27	3·15	2·94	3·00	2·89
	pH	3·16	3·42	3·62			
	$10k_1$	2·70	2·28	2·34			
(2)	pH	2·10	2·50	2·80	3·00	3·28	3·50
	$10k_1$	6·90	7·00	7·10	7·10	7·50	6·50
	pH	3·72	4·00	4·32	4·50	4·63	5·02
	$10k_1$	5·90	5·30	3·40	4·20	2·60	2·30
	pH	6·00	6·58	6·80			
	$10k_1$	1·50	1·30	1·20			
(3)	pH	2·00	2·32	2·67	3·00	3·31	3·60
	$10k_1$	4·73	4·69	4·60	3·84	3·96	3·50
(4)	pH	2·08	2·40	2·89	3·15	3·35	3·60
	$10k_1$	1·37	1·46	1·47	1·45	1·41	1·21
	pH	3·90					
	$10k_1$	1·01					
(5)	pH	2·00	2·35	2·58	3·00	3·32	3·61
	$10k_1$	0·87	0·85	1·03	1·00	0·84	0·85
	pH	3·99					
	$10k_1$	0·62					
(6)	pH	2·10	2·40	2·72	3·00	3·24	3·52
	$10k_1$	0·09	0·10	0·10	0·11	0·12	0·13
(7)	pH	2·20	2·35	2·59	2·75	2·90	3·00
	$10k_1$	3·56	3·24	3·92	4·15	4·40	5·25
	pH	3·50					
	$10k_1$	6·46					
(8)	pH	2·19	2·30	2·60	2·89	3·19	3·32
	$10k_1$	2·60	2·90	4·20	4·00	3·90	3·30
	pH	3·60					
	$10k_1$	2·90					
(10)	pH	2·5					
	$10k_1$	V. slow					
(11) *	pH	2·11	2·53	2·63	2·71	2·83	2·91
	$10k_1$	0·54	1·11	1·52	2·00	2·23	1·88
	pH	3·10	3·31	3·53			
	$10k_1$	1·67	1·54	1·37			

* At 0·00°.

TABLE 7

Rate constants and Arrhenius parameters for hydrolysis of $(EtO)MeP(:O)O\cdot C(:NOH)\cdot C_6H_4NO_2$-*p* at pH 3·0 in the range 0·4—25·0°

T°c	0·4	5·0	10·3	14·7	19·8	25·0
$10k_1$/min^{-1}	0·78	1·1	1·9	2·8	4·3	7·1

E_A = 62·3 kJ mol^{-1}. $\Delta S^{\ddagger}$ −19 e.u.

A continuous rate-pH profile was determined only for ethyl α-hydroxyimino-*p*-nitrobenzyl methylphosphonate. As the rate dropped off with increasing pH, so the colour of the reaction solution became more intensely yellow. For the adducts capable of acid hydrolysis, the rate was followed to pH 3·5 and in the alkaline region where the values were essentially constant, over the short range of pH 8—9.

The reaction of ethyl α-hydroxyimino-*p*-nitrobenzyl t-butylphosphonate was slow in acid solution, the first-order rate constant was $4{\cdot}1 \times 10^{-3}$ min^{-1} at pH 2·50. This value represents both hydrolysis to yield ethanol (detected by g.l.c., 15% D.N.P., 60°, Aerograph 1520 B) and rearrangement to yield *p*-nitroaniline. The u.v. spectrum of the hydrolysate showed the presence of *p*-nitroaniline ($\lambda_{max.}$ 380 nm) and of the 1 : 1 adduct or its hydrolysis product ($\lambda_{max.}$ 268 nm).

*Hydrolysis of Diethyl α-Hydroxyimino-*p*-nitrobenzyl Phosphate.*—The hydrolysis at low pH was complicated by the two ester groups available for hydrolysis and the greater degree of *p*-nitroaniline formation. At pH 8—9 and 25·00° the rate of formation of *p*-nitroaniline was too fast to be measured and the increase in the observed rate coefficient from pH 2—4 reflects the greater proportion of *p*-nitroaniline being formed. At pH 2·50, the solution was yellow.

The hydrolysis of the ester moieties was studied by n.m.r. spectroscopy. A solution of the compound in $(CD_3)_2SO$ had the expected spectrum of the adduct: τ 1·80 (2, Ar, 4H), τ 5·78 (quintet, $POCH_2CH_3$, 4H) and τ 8·79 (t, $POCH_2CH_3$, 6H).

Rapid hydrolysis (pseudo-unimolecular) occurred on the addition of D_2O to form a 20% aqueous solution. The p.m.r. signals due to the ester moiety at τ 5·8 declined, with increasing signal strength of the methylene protons of free ethanol at τ 6·5. The first ester moiety was completely lost after 10 min (half-life, therefore, *ca.* 1 min at 35·5°), while the second ester moiety was only 75% hydrolysed after a further 1·5 h.

The p.m.r. spectrum of the final solution (after 15 h showed that complete hydrolysis had occurred, showing absorptions at: τ 1·81 (q, Ar, 4H), 6·50 (q, CH_3CH_2OH, 4H), and 8·90 (t, CH_3CH_2OH, 6H).

The rate constants determined at 25·00° at pH 2—4 refer to the loss of one ester moiety as determined from the volume of titrant added.

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[37] L. L. Schaleger and F. A. Long, *Adv. Phys. Org. Chem.*, 1963, 7.