702. *The Mechanism of Hydrolysis of Phosphorochloridates and Related Compounds. Part III.* *Phosphoramidochloridates.*

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A kinetic investigation of the mechanism of hydrolysis involving P–Cl fission of phosphoramidochloridates is reported. The effect of substitution, solvents, and anionic reagents on the reactivity show that the reaction is a bimolecular displacement rather than an ionisation process, although bond-breaking is more important than in the hydrolysis of phosphorochloridates. Nitrite ions increase the rate of hydrolysis of tetra-alkylphosphorodiamidic chlorides, whereas the considerably more basic hydroxide ions have no effect. 2,6-Lutidine catalyses the hydrolysis of *NN'*-diethylphosphoro-diamidic chloride but not that of diethyl phosphorochloridate which is sterically similar, suggesting that the former reacts by preliminary removal of a proton from the nitrogen atom.

IN a previous paper,[1] a comparison of the influence of steric and electronic effects on the rate of acylation and phosphylation was made, with particular reference to phosphono-chloridates. The investigation is now extended to phosphoramidochloridates and phosphoramidic chlorides of the kind $NR_2 \cdot PClO \cdot OR'$, $(NR_2)_2PClO$, $R' \cdot PClO \cdot NR_2$, and $(NHR)_2PClO$. The effects of changes in R and R', in the reaction medium, and in the nature of the attacking reagent have been investigated with a view to elucidating the mechanism involved in the fission of the P–Cl bond.

The suggestion [2] that the hydrolysis of *NNN'N'*-tetramethylphosphorodiamidic chloride occurs by an ionisation mechanism is based on a comparison with di-isopropyl

* Part II, *J.*, 1960, 1865.

[1] Hudson and Keay, *J.*, 1960, 1859.

[2] Hall, *J. Org. Chem.*, 1956, **21**, 248.

phosphorochloridate, and on the absence of a rate increase on addition of hydroxide ions, m-tolyloxide ions, and pyrrolidine. The corresponding fluorides[3] probably react by a bimolecular displacement mechanism as hydroxide ions increase the rate of reaction significantly, although the reactivities of the compounds are greatly modified by steric effects. Thus the ratio of the rate of alkaline hydrolysis[4] to the rate of solvolysis of di-isopropyl phosphorofluoridate is *ca.* 10^7, whereas for tetra-alkylphosphorodiamidic chlorides the ratio is reduced to *ca.* 10^3. This difference may be attributed partly to conjugation between nitrogen and phosphorus, but steric hindrance is probably more important.[5]

Rate of P–Cl fission:
I, acid formed; II, amine liberated.
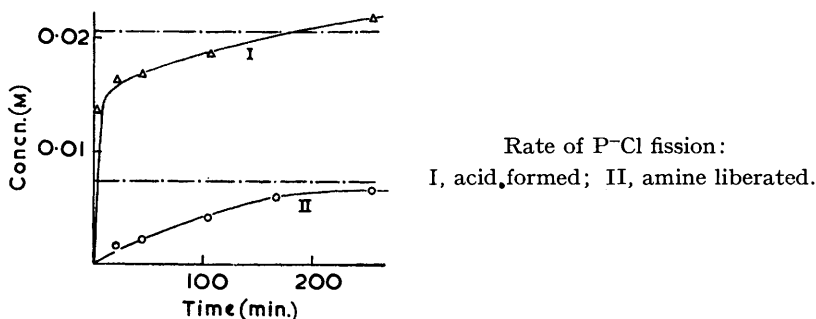
In view of the possibility that P–N fission occurs in dilute acid, as for fluorides,[6] the relative rates of deamination and solvolysis of ethyl *NN*-diethylphosphoramidochloridate were determined as described on p. 3598. The initial rapid hydrolysis is followed by a
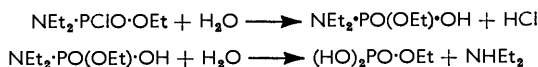
TABLE 1.

The rate of P–N fission of ethyl hydrogen *NN*-diethylphosphoramidate compared with the rate of P–Cl fission of ethyl *NN*-diethylphosphoramidochloridate.

Concn. of P compound (M)	Concn. of HCl (M)	$10^5 k_1$ (sec.$^{-1}$) (at 41°)
0·00690	—	19·4
0·00923	—	15·0
0·166	—	13·3
0·00950	0·01	15·4
0·00601	0·50	43·5

Rate of P–Cl fission at 39° = 43 × 10^{-4} sec.$^{-1}$.

slower reaction producing acid (see Figure), the rate of which is equal to the rate of removal of amine. Table 1 shows that the rate of P–Cl fission is *ca.* 25 times that of the subsequent deamination of the acid, establishing the following reactions:

$$\text{NEt}_2\cdot\text{PClO}\cdot\text{OEt} + \text{H}_2\text{O} \longrightarrow \text{NEt}_2\cdot\text{PO(OEt)}\cdot\text{OH} + \text{HCl}$$

$$\text{NEt}_2\cdot\text{PO(OEt)}\cdot\text{OH} + \text{H}_2\text{O} \longrightarrow \text{(HO)}_2\text{PO}\cdot\text{OEt} + \text{NHEt}_2$$

As in the case of *NNN′N′*-tetramethylphosphorodiamidic acid,[6] the rate of de-amination of ethyl hydrogen *NN*-diethylphosphoramidate is approximately independent of acid concentration below pH 1 (Table 1), and consequently a first-order relation was observed in all cases. The abnormally high pK_a's of these acids, *e.g.*, 6·76 for $(\text{NMe}_2)_2\text{PO}_2\text{H}$[6] and 7·2 for $\text{NEt}_2\cdot\text{PO(OEt)}\cdot\text{OH}$, suggest that they exist in the zwitterion form, like the corresponding inorganic amides,[7] *e.g.*, $\text{NaH(PO}_3\cdot\text{NH}_2)$ and $^+\text{NH}_3\cdot\text{PO}_3^-$.

In more concentrated acidic solution, the rates of deamination increase, presumably
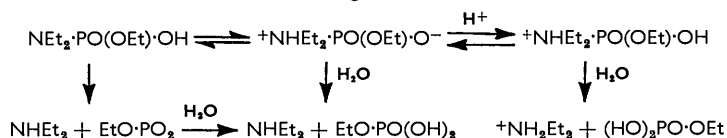
[3] Heath, *J.*, 1956, 3796, 3804.
[4] Green, Sainsbury, Saville, and Stansfield, *J.*, 1958, 1583.
[5] Dostrovsky and Halmann, *J.*, 1953, 511.
[6] Heath and Casapieri, *Trans. Faraday Soc.*, 1951, **47**, 1093.
[7] Corbridge and Lowe, *J.*, 1954, 493; Hobbs, Corbridge, and Raistrick, *Acta Cryst.*, 1953, **6**, 621.

owing to incursion of a normal acid-catalysed amide hydrolysis. These hydrolysis mechanisms are summarised in the following scheme:

$$NEt_2 \cdot PO(OEt) \cdot OH \rightleftharpoons {}^+NHEt_2 \cdot PO(OEt) \cdot O^- \overset{H^+}{\underset{}{\rightleftharpoons}} {}^+NHEt_2 \cdot PO(OEt) \cdot OH$$

$$\downarrow \qquad\qquad \downarrow H_2O \qquad\qquad \downarrow H_2O$$

$$NHEt_2 + EtO \cdot PO_2 \overset{H_2O}{\longrightarrow} NHEt_2 + EtO \cdot PO(OH)_2 \qquad {}^+NH_2Et_2 + (HO)_2PO \cdot OEt$$

Effect of Substituents on the Rate of Solvolysis (P–Cl *Fission*).—Having established that P–Cl fission precedes P–N fission in the hydrolysis of ethyl *NN*-diethylphosphoramido-chloridate, we assume that this is also the case for the more reactive phosphorodiamidic chlorides. The solvolysis rates of such chlorides, recorded in Tables 2 and 8, decrease

TABLE 2.

The rate of hydrolysis of phosphorodiamidic chlorides, R_2PClO, in water at 18°.

R	Et_2N	$EtNH$	Me_2N
pK_b	2·90	3·25	3·29
10^5k (sec.$^{-1}$), at 18°	280	350	420

with increasing basicity of the corresponding amine. This suggests that the rate decreases with increase in electron-release to the reaction centre, which is the reverse of the rate sequence expected for an ionisation process. The observations are in agreement with a bimolecular mechanism, since the rate changes may be produced by steric hindrance and by reduced bond-forming energy with increase in electron-density at the phosphorus atom.

A comparison of the reactivities of a wider range of phosphorus compounds shows that the effect of substitution is complex, and that the electronic effect of a particular group is very sensitive to the nature of the other groups. Thus the replacement of one alkoxy-group by an amino-group leads to a decrease in reactivity, as shown by the following relative values, obtained from the rate data in Table 8 and in Part I of this series: Me·PClO·OEt is *ca.* 20 times more reactive than Me·PClO·NEt$_2$; and PClO(OEt)$_2$ is *ca.* 13 times more reactive than NEt$_2$·PClO·OEt. Since changes in the alkyl groups attached to the nitrogen atom produce only small changes in rate, thus indicating small steric effects (Table 2), these rate decreases may be attributed almost entirely to conjugation between the nitrogen and the phosphorus atom.

The corresponding rate decrease is much greater for the corresponding fluorides.[3,8] Thus PFO(OPr^i)$_2$ is solvolysed *ca.* 50 times faster than PFO(NHPr^i)$_2$, and 140 times faster than the morpholine derivative O<[CH$_2$·CH$_2$]$_2$>N·PFO·OEt. This is probably due to the high electronegativity of the fluorine atom, which produces a low electron-density on the phosphorus atom. This increases the conjugation energy between the nitrogen and phosphorus atoms since the $3d_\pi$–$2p_\pi$ overlap is very sensitive to the magnitude of the positive charge on the phosphorus atom.[9] In addition, the more electronegative fluorine atom will increase the bond-forming energy term in the transition state, owing to the increased inductive effect. This influence is also shown by the effect of hydroxide ions on the rate.

Substitution of a second amine group, however, increases the rate of hydrolysis of both phosphoramidic chlorides and the corresponding fluorides. Thus (NEt$_2$)$_2$PClO is *ca.* 4 times more reactive than NEt$_2$·PClO·OEt, and (NHPr^i)$_2$PFO is *ca.* 6 times more reactive than O<[CH$_2$·CH$_2$]$_2$>N·PFO·OEt. Again these differences could be due to an increase in P–N conjugation on the introduction of a more electronegative OR group, so that the total conjugation energy in NR$_2$·PClO·OEt is greater than that in (NR$_2$)$_2$PClO. Alternatively the second NR$_2$ group could conjugate so strongly that the decrease in bond-breaking energy is greater than the decrease in bond-forming energy in the transition

[8] Kilpatrick and Kilpatrick, *J. Phys. Colloid Chem.*, 1949, **53**, 1371.
[9] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332; Jaffé, *J. Phys. Chem.*, 1954, **58**, 185.

state. This would mean that the amino-groups produce a gradual change in the transition state towards an ionisation mechanism, similar to that which has been observed in S_N1–S_N2 reactions of alkylating agents.[10]

In order to examine this possibility, the influence of changes of medium on the rate of solvolysis was examined.

Effect of Solvent Changes.—The effect on the rate of solvolysis of changing from an acidic to a more basic (nucleophilic) solvent of comparable ionising power may also indicate the extent of covalent-bond formation in the transition state. Thus S_N1 ionisations of alkyl halides proceed at similar rates in formic acid and in 50% aqueous ethanol,[11] whereas primary and secondary halides are more reactive (by factors of $\sim10^2$) in the aqueous ethanol. Since this solvent is more nucleophilic, the increased reactivity shows that the reaction in the more aqueous solvent is a bimolecular (S_N2) displacement involving bond-formation in the transition state.

We have used this comparison in investigations of the mechanism of solvolysis of acid chlorides[12] and phosphonochloridates.[13] In the latter case, the ratio of the reactivity in 65% aqueous acetone * to that in formic acid were found to be $\sim10^4$ (Table 3). The
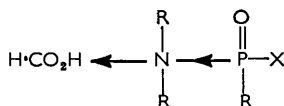
TABLE 3.

Hydrolysis of phosphorus acid chlorides in formic acid and in acetone.

Compound	Temp.	In $H \cdot CO_2H$, $10^5 k_F$ (sec.$^{-1}$)	In 65% aq. $COMe_2$, $10^5 k_A$ (sec.$^{-1}$)	k_A/k_F
Me·PClO·OOct *	−21°	0·036 †	327	9000
Me·PClO·OEt	0	0·312 †	3504	11,000
$(NMe_2)_2PClO$	20	0·296 †	60 ‡	200
$(NHEt)_2PClO$	45	13·1	1000 ‡	77
$NEt_2 \cdot PClO \cdot OEt$	50	2·68	81·9	30

* Oct = 1-methylheptyl. † Extrapolated by using experimental activation energies. ‡ Extrapolated by using the Grunwald–Winstein equation (*J. Amer. Chem. Soc.*, 1948, **70**, 846).

ratios for several phosphorodiamidic chlorides (although less by factors of $\sim10^2$ than those for the chloridates) are considerably greater than unity, showing the reaction to be predominantly bimolecular. The smaller ratios suggest that bond-breaking is more significant in the transition state of the phosphorodiamidic chlorides, as discussed above, owing to the smaller charge on the phosphorus atom and increased conjugation with the amino-groups. An alternative explanation is, however, possible. Hydrogen bonding between the acid and the amino-groups would decrease the electron-density on the phosphorus atom, thus assisting the displacement in formic acid:

$$H \cdot CO_2H \longleftarrow \underset{\underset{R}{|}}{\overset{\overset{R}{|}}{N}} \longleftarrow \underset{\underset{R}{|}}{\overset{\overset{O}{\|}}{P}} - X$$

The rate ratios given in Table 3 are therefore regarded as minimum values for the phosphorodiamidic chlorides.

In a further investigation, the influence of changing the water content of the medium on the rate of solvolysis was determined. The rate, k_1, may be represented semiquantitatively by the Grunwald–Winstein equation:[14] $\log k_1/k_0 = mY + $ Constant, where Y is the (empirical) solvating power of the medium and m a parameter related to the polarity of the transition state. Although the application of this equation should be restricted

* In this paper $x\%$ aqueous acetone refers to a mixture of x ml. of water and $(100 - x)$ ml. of acetone.

[10] Cf. Gold, *J.*, 1956, 4633.
[11] Bateman and Hughes, *J.*, 1940, 945; Dostrovsky and Hughes, *J.*, 1946, 172.
[12] Crunden and Hudson, *J.*, 1956, 501.
[13] Hudson and Keay, *J.*, 1960, 1865.
[14] Grunwald and Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 846.

to ionisation processes, the magnitude of m over a particular solvent-composition range may be compared with the limiting value (*ca.* 1·0 for a chloride) for an ionisation.

The m value of 0·36 (see Table 4) is similar to the value of 0·43 for isopropyl methylphosphonochloridate [13] over the same water-concentration range, again suggesting that hydrolysis of both compounds proceeds by a bimolecular mechanism.

TABLE 4.

Values of Y and m in the Grunwald–Winstein equation for the solvolysis of $(NMe_2)_2PClO$ in aqueous acetone at $21\cdot2° \pm 0\cdot7°$.

Water content (%, v/v)	5	20	50	100
10^5k (sec.$^{-1}$)	0·730	4·05	29·4	500
Y	−2·76	−0·67	1·40	3·49
m		0·36	0·42	0·58

The increasing value for $(NMe_2)_2PClO$, however, suggests that the polarity of the transition state gradually increases with the ionising power of the medium, for in some bimolecular reactions the value of m decreases with increasing water content.[14] The value of 0·58 is appreciably greater than the value (0·33) for diethyl phosphorochloridate and is similar to that for secondary halides, but is considerably less than that normally obtained for ionisation reactions. These studies on the solvent influence support the general conclusion of the previous section that the solvolysis of phosphorodiamidic chlorides proceeds by a predominantly bimolecular mechanism, although bond-breaking is probably more important than in the solvolysis of the phosphorochloridates.

Effect of the Substituting Agent.—In contrast to the phosphorochloridates, tetra-alkylphosphorodiamidic chlorides are unreactive towards hydroxide ions in aqueous solution,[2] and we find that ammonia is similarly unreactive (Table 8). This resistance suggests that solvolysis proceeds by an ionisation mechanism which is assisted by P−N conjugation. Part of the rate decrease may, however, be due to steric hindrance produced by the four alkyl groups. By way of comparison, chlorotri-isopropylsilane is also inert towards hydroxide ions, although the solvolysis undoubtedly proceeds by a bimolecular displacement.[15] In view of the similar configurations of the dimethylamino- and isopropyl groups, and the similar radii of silicon and phosphorus, the steric effects should be of a comparable magnitude. By comparing the rates of reaction of tetramethylphosphorodiamidic fluoride and di-isopropyl phosphorofluoridate (p. 3592), it is found that the steric effect could account for a difference of *ca.* 10^4 in the rate.

It is of interest, therefore, to investigate the reactivity of tetra-alkylphosphorodiamidic chlorides towards other nucleophilic reagents. The importance of the steric form of the nucleophile in substitution at the phosphorus atom is shown by the lack of reaction of diethyl phosphorochloridate with 2,6-lutidine and the rapid reaction with less basic amines (*e.g.*, aniline). Other amines exhibit strong steric effects.[5]

The effective radius of the hydroxide ion is large owing to the strongly bound hydration shell. It is likely that ions with reduced solvation energies will, *ceteris paribus*, be more reactive, since the steric hindrance will be less. In agreement with this prediction the nitrite ion was found to increase the rate of hydrolysis appreciably (Table 5) according to the reaction

$$(NMe_2)_2PClO + NO_2^- \longrightarrow (NMe_2)_2P(O)\cdot O\cdot NO \xrightarrow{\ H_2O\ } (NMe_2)_2PO\cdot OH + HNO_2$$
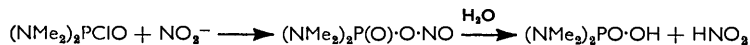
The nucleophilic power of the nitrite ion towards acylating agents [16] approaches that of the hydroxide ion in spite of the large difference in basicity. We have attributed this to the conjugation in the ion which produces charges of the order of $0\cdot5e$ on each oxygen atom. The solvation energy and hence the effective radius of the oxygen atom is therefore

[15] Allen, Charlton, Eaborn, and Modena, *J.*, 1957, 3668.
[16] Green and Hudson, *Proc. Chem. Soc.*, 1959, 149,

considerably reduced, thus reducing the steric hindrance to the approach of the phosphorus atom.

<p style="text-align:center">TABLE 5.</p>

<p style="text-align:center">Rate of reaction of phosphorodiamidic chlorides with sodium nitrite in water at 1·5° and pH 7·2.</p>

	k_2 (NO$_2$) (l. mole^{-1} sec.$^{-1}$)	k_2(NO$_2$)/k_2(H$_2$O)
(NMe$_2$)PClO	5×10^{-3}	715
(NHEt)$_2$PClO	$11·7 \times 10^{-3}$	1530

Samuel and Westheimer [17] observed a similar rate increase on the addition of sodium azide and isolated the azide in high yield. They also concluded that this reaction and the solvolysis proceed by bimolecular displacements, since the addition of other salts produced negligible rate increases.

Oximes are also very reactive towards acyl and phosphoryl centres,[18] and we find that acetoxime produces an appreciable increase in the solvolysis rate. In this case, however, the rate is not proportional to the concentration of ionised oxime (Table 6), and in the pH range 7—8 the reaction proceeds mainly with the un-ionised form. This suggests that the reaction proceeds either with the more basic nitrogen atom, or with the small amount of tautomer, $Me_2 \cdot C\overset{+}{:}NH \cdot O^-$ which may be present.

Hydroxyiminoacetone also reacted in aqueous solution: $Me \cdot CO \cdot CH:N \cdot OH + H_2O + R_2POX \longrightarrow R_2PO_2H + AcOH + HX + HCN$. Here some cyanide was produced and seriously affected the silver–silver chloride electrodes in the potentiometric method used to follow the rate of reaction (p. 3598), and the colorimetric method described by Saville [19] was substituted for it (p. 3598).

<p style="text-align:center">TABLE 6.</p>

<p style="text-align:center">Reaction of $NNN'N'$-tetramethylphosphorodiamidic chloride with acetoxime at 1°.</p>

Conditions	$10^5 k_1$ (sec.$^{-1}$)	Conditions	$10^5 k_1$ (sec.$^{-1}$)
Hydrolysis pH 7·2	39·0	0·05м-oxime at pH 7·0	82·7
,, pH 8·4	39·2	0·027м- ,, pH 8·4	63·4
		0·0964м- ,, pH 3·4—2·4 * ...	75·0

<p style="text-align:center">* In the absence of buffer.</p>

Reaction with 2,6-*Lutidine.*—In the course of these measurements, it was found that 2,6-lutidine increased the rate of hydrolysis of NN'-diethylphosphorodiamidic chloride but did not influence the rate of hydrolysis of diethyl phosphorochloridate (Table 7).

<p style="text-align:center">TABLE 7.</p>

<p style="text-align:center">Effect of 2,6-lutidine on the rate of hydrolysis of (NHEt)$_2$PClO and (EtO)$_2$PClO.</p>

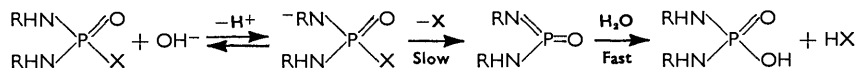| Temp.	Concn. of chloride (м)	Concn. of lutidine (м)	Solvent	$10^5 k_1$ (min.$^{-1}$)
		(NHEt)$_2$POCl		
1·2°	0·0032	0·069	Water	161
4·5	0·0028	—	,,	49·3
2·0	0·0067	0·081	4 : 1 H$_2$O–COMe$_2$	119
1·3	0·00433	—	,,	42
		(EtO)$_2$POCl		
11·0	0·0032	0·081	4 : 1 H$_2$O–COMe$_2$	251
10·0	0·0034	—	,,	231

In view of the similar stereochemistry of the two compounds, it is unlikely that the catalytic effect in the one case is produced by preliminary substitution at the phosphorus

[17] Samuel and Westheimer, *Chem. and Ind.*, 1959, 51.
[18] Hackley, Plapinger, Stolberg, and Wagner-Jauregg, *J. Amer. Chem. Soc.*, 1955, **77**, 3651; Green and Saville, *J.*, 1956, 3887.
[19] Saville, *Analyst*, 1957, **82**, 269.

atom. It was suggested by Westheimer [20] that the relatively high reactivity of NN'-dialkylphosphorodiamidic fluorides in alkaline solution is due to preliminary removal of the proton followed by a unimolecular release of the halide ion:

$$\text{RHN}{>}\!\!P({<}^{O}_{X}) + OH^{-} \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} \text{-RN}{>}\!\!P({<}^{O}_{X}) \overset{-X}{\underset{Slow}{\longrightarrow}} \text{RN}{>}\!\!P{=}O \overset{H_2O}{\underset{Fast}{\longrightarrow}} \text{RHN}{>}\!\!P({<}^{O}_{OH}) + HX$$

This reaction mechanism explains the catalytic effect of lutidine, or of the hydroxide ions in equilibrium with it, on the hydrolysis of the corresponding chloride, since interaction with the proton is not subject to steric control.

EXPERIMENTAL

Materials.—Ethyl NN-diethylphosphoramidochloridate was prepared by the action of diethylamine on ethyl phosphorodichloridate, b. p. 63°/19 mm., according to the general method of Michaelis [21] and had b. p. 65°/1·5 mm. (lit.,113°/18 mm.). $NNN'N'$-Tetramethylphosphorodiamidic chloride [2] was prepared by the action of dimethylamine on phosphorus oxychloride and had b. p. 98°/15 mm., n_D^{20} 1·4660. $NNN'N'$-*Tetraethylphosphorodiamidic chloride*

TABLE 8.

P–Cl fission: rates of solvolysis.

Temp.	Concn. (10³ M)	Solvent, etc.	$10^5 k_1$ (sec.⁻¹)	Temp.	Concn. (10³ M)	Solvent, etc.	$10^5 k_1$ (sec.⁻¹)
Diethyl phosphorochloridate.				*NN'-Diethylphosphorodiamidic chloride.*			
4·5°	6·42	Water	187	4·5°	2·79	Water, pH 2	49·3
18·0	3·42	20% Acetone	382	2·0	4·74	,, pH 8·4	231
2·0	6·87	50% ,,	27·2	1·8	5·03	,, pH 7·2, +0·099M-KNO₂	158
NNN'N'-Tetramethylphosphorodiamidic chloride.				1·0	0·40	,,	42·5
1·8	6·30	Water, pH 7·2	39·4	10·0	2·46	,,	112
1·2	7·08	,, pH 8·4	39·8	19·7	0·94	,,	400
1·2	6·85	,, pH 7·2, +0·106M-KNO₂	92·0	15·0		,, 0·107N-NH₃	V. fast
				1·0	0·61	,, 0·062N-KNO₂	117
17·9	4·79	,, —	421				
14·5	4·99	,, 0·106N-NH₃	289 *				
17·0	5·56	,, 0·0965N-CuSO₄	389	*Ethyl phosphoramidochloridate.*			
20·5	7·23	50% Acetone	29·4	16·8	4·07	Water	56·6
22·0	8·26	80% ,,	4·05	16·2	3·83	,, 0·0965N-CuSO₃	55·3
21·5	7·30	95% ,,	0·73	19·5	3·31	,, 1·7N-HNO₃	55·2
45·0	4·67	99·26% H·CO₂H	2·78 *	22·2	3·36	,,	117·2
60·0	6·86	,, ,,	9·20 *	27·0	3·27	,,	158
				31·0	3·34	,,	233
				39·0	3·51	,,	430
NNN'N'-Tetraethylphosphorodiamidic chloride.				17·8	3·43	20% Acetone	31·1
7·5	2·95	Water	97·8	18·4	3·93	,,	29·0
14·3	3·04	,, 1·7N-HNO₃	151	26·5	3·44	,,	65·3
14·6	3·11	,,	182	34·0	3·24	,,	123
16·2	3·18	,, 0·17N-HNO₃	249	18·5	1·68	35% ,,	7·80
16·5	4·16	,, 0·17N-NH₃	225 *				
18·7	2·98	,,	295				
28·0	2·91	,,	837				
19·9	2·96	20% Acetone	116	*NN-Diethylmethylphosphonamidic chloride.*			
28·9	2·99	,,	244				
36·0	3·00	,,	454	14·5	4·94	35% Acetone	1060

* Followed conductimetrically.

prepared from diethylamine in a similar way, had b. p. 142—144°/12 mm. (Found: C, 42·3; H, 8·8; P. 13·8; N, 12·1; Cl, 15·6. $C_8H_{20}ClN_2PO$ requires C, 42·2; H, 8·8; P, 13·6; N, 12·3;

[20] Westheimer, *Chem. Soc. Special Publ.*, No. 8, 1957, 181.
[21] Michaelis, *Annalen*, 1902, **326**, 189.

Cl, 15·6%). *NN'*-Diethylphosphorodiamidic chloride, prepared by the action of ethylamine on phosphorus oxychloride,[22] had m. p. 68° (lit., m. p. 74°) (Found: C, 28·4; H, 7·3; N, 16·1; Cl, 19·7. Calc. for $C_4H_{12}ClN_2OP$: C, 28·1; H, 7·1; N, 16·4; Cl, 20·8%). *NN*-Diethyl-methylphosphonamidic chloride,[23] prepared by the action of diethylamine on methylphos-phonic dichloride, had b. p. 80—82°/0·5 mm. (lit., b. p. 135°/27 mm.) (Found, by hydrolysis, Cl, 21·5. Calc. for $C_5H_{13}ClNOP$: Cl, 20·9%).

Kinetic Measurements.—The rates of hydrolysis were measured conductimetrically with the apparatus and procedure described previously,[11] or potentiometrically with a balancing cell with silver–silver chloride electrodes.[24] These electrodes are very sensitive to added solutes, and the rate of reaction with ammonia, amines, and hydroxyiminoacetone could not be followed in this way.

In calculations of the rate constants obtained by the conductimetric method, the con-ductivity was assumed to be proportional to the concentration of hydrogen chloride released. This was verified for the solvolysis of chloroformates in formic acid over the concentration range used here.[11] A first-order reaction was assumed and the rate constant, k_1, was obtained from the relation:[11]

$$\log [R_t/(R_t - R_\infty)] = k_1 t/2\cdot303 + \log [R_0/(R_0 - R_\infty)],$$

where R_t is the resistance at time t, and R_∞ at the end and R_0 at the begining of the reaction. In all cases, good first-order plots were obtained, supporting the assumed proportionality between resistance and acid concentration.

Results are recorded in Tables 8 and 9.

TABLE 9.

Arrhenius parameters for P–Cl fission.

Compound	Solvent	E (kcal./mole)	$\log_{10} PZ$	Compound	Solvent	E (kcal./mole)	$\log_{10} PZ$
$NEt_2\cdot PClO\cdot OEt$	Water	15·8	8·74	$(NEt_2)_2PClO$	Water	17·4	10·58
	20% Acetone	15·6	8·26		20% Acetone	15·6	8·77
	35% ,,	14·2	6·57	$(NHEt)_2PClO$	Water	17·5	10·7
$(NMe_2)_2PClO$	99·26% H·CO_2H	16·7	6·96	$(OEt)_2PClO$	20% Acetone	10·2	5·27

Phosphorus–Nitrogen Fission.—The amine liberated during the hydrolysis was estimated[25] by reaction with carbon disulphide and titration of the thiocarbamic acid produced with sodium hydroxide, $Et_2NH + CS_2 \longrightarrow Et_2N\cdot CS_2H$. In a typical experiment, 5 ml. of reaction mixture were run into a standard solution of sodium hydroxide in propan-2-ol (20 ml.). The solution was titrated at 0° with standard hydrochloric acid (to phenolphthalein). Carbon disulphide (1 ml.) was added and the mixture titrated against the sodium hydroxide solution. In all cases, a control was run at the same time.

Reaction of NNN'N'-*Tetramethylphosphorodiamidic Chloride and* NN'-*Diethylphosphoro-diamidic Chloride with Hydroxyiminoacetone.*—When the reaction with this oxime was followed by the balancing-cell method, the cyanide produced seriously affected the electrodes, and so Saville's analytical method[19] was used. The intensity of the colour produced by the pyridine–pyrazolone reagent was measured by an EEL colorimeter and filter no. 608. 100 ml. of a 0·1% solution of hydroxyiminoacetone in a phosphate buffer at pH 7·2 containing *ca.* 5×10^{-7} equiv. of the phosphorus compound, known accurately by dilution were analysed: 1 equiv. of $(NMe_2)_2PClO$ gave 0·81 equiv. of CN^-; 1 equiv. of $(NHEt)_2PClO$ gave 0·47 equiv. of CN^-. These results correspond to competition factors[26] of 2×10^4 and 5×10^3, respectively, based on the un-ionised oxime.

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