

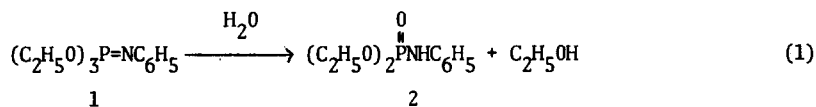
THE HYDROLYSIS OF AN IMINOPHOSPHORANE. EVIDENCE FOR AN INTERMEDIATE

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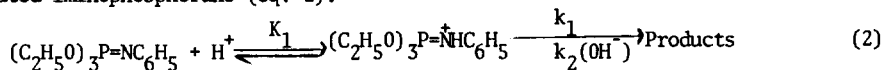
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The transformation of trialkoxy iminophosphoranes to phosphoramidate dialkyl esters (e.g. eq. 1) has received little mechanistic attention (1-7). In the hope that its study might be relevant to the problem of pentacovalent intermediates in nucleophilic substitution at the phosphoryl group, we have examined some aspects of this reaction. We report herein evidence for the occurrence of an intermediate in the hydrolysis of triethoxy N-phenyl-iminophosphorane 1.



The pH-rate profile for the hydrolysis of 1 (1) in 50% CH₃CN-H₂O, 30°, is given in Figure 1. Experiments at pH > 3 were carried out in buffered solution, and the rate constants, determined spectrophotometrically, were extrapolated to zero buffer concentration at constant pH to correct for the considerable catalytic effects of acetate and phosphate buffers on the rate of hydrolysis. More limited data were also obtained in unbuffered solution, using the pH-stat (closed circles, Fig. 1).

The kinetic data are consistent with rate-determining attack of water or of hydroxide ion on the protonated iminophosphorane (eq. 2).



The solid line in Figure 1 is calculated from the rate equation based on this mechanism (eq. 3),

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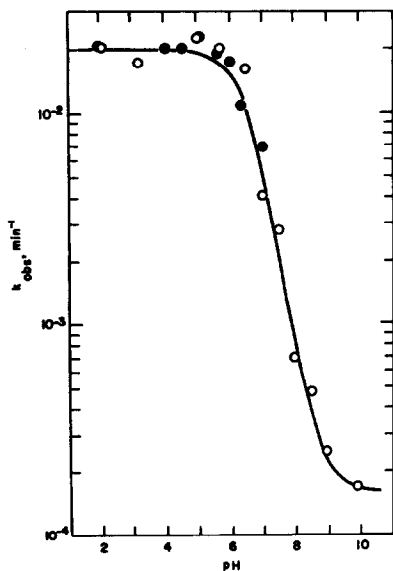


Figure 1.

an acid of pK_a 5.6.***

Any mechanism for the hydrolysis of 1 must account for the independent influences of pH on the rate of hydrolysis and on the incorporation of oxygen-18 into the reaction product. Put another way, the incorporation of O^{18} into the hydrolysis product 2 varies markedly in a pH region

* Final ultraviolet spectra of reaction mixtures indicated the formation of 2 in yields of $100 \pm 2\%$. Isolated yields of 2 from pH-stat experiments were in the range of 80-95%.

** Samples of 2 were combusted and the resulting CO_2 analysed by mass spectrometry. We are indebted to Dr. M. Caplow for making available to us the mass spectrophotometer facilities.

*** Solutions of 2 underwent no O^{18} exchange when kept in 50% CH_3CN-H_2O at pH 1.3 or 7.8 for 24 hrs., under conditions where as little as 3% exchange would have been easily detected.

with $k_1 = 0.02 \text{ min}^{-1}$, $k_2 = 5000 \text{ M}^{-1}$, $K_w = 10^{-14}$ and $pK_1 = 6.5$. The latter value is in reas-

$$k_{\text{obs}} = (k_1[H^+] + k_2K_w)/([H^+] + K_1) \quad (3)$$

onable accord with $pK_1 = 6.3$ determined by spectrophotometric titration of 1.

The phosphoramidate 2 is the exclusive product of the hydrolysis of 1 at pH 2-8.* To ascertain the origin of the phosphoryl oxygen atom of 2, the phosphoramidate was isolated from hydrolyses of 1 carried out in O^{18} -enriched water at constant pH in the range 2-8.** The extent of incorporation of oxygen-18 varies from 0.22 mole at low pH to 0.81 mole at high pH (Figure 2). In the intermediate range the variation in isotope content of 2 with pH follows approximately the ionization curve of

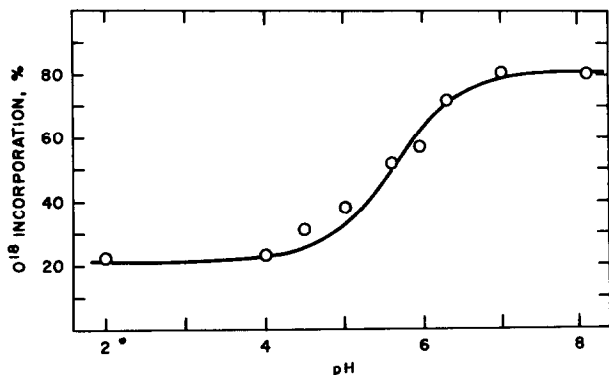
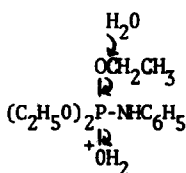


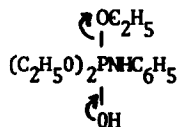
Figure 2.

where the rate of hydrolysis follows essentially a single rate law, i.e., rate = k_1 (protonated iminophosphorane) (H_2O)*. These observations appear to require the postulation on the reaction path of an intermediate whose formation is rate-determining; furthermore, the conversion of the intermediate to 2 must occur by at least two competing, pH-dependent pathways, which lead to the introduction of different amounts of O^{18} into the product.

The structure of the intermediate is still uncertain. Possibly a cationic pentacovalent adduct formed by addition of water to the protonated iminophosphorane undergoes dealkylation by solvent attack on an ethyl substituent, with concerted or consecutive expulsion of the original nucleophilic water molecule (3). At higher pH, a neutral form of the intermediate (4) might collapse with expulsion of ethoxide ion, with consequent retention of solvent oxygen in the phosphoramidate. Clearly, this tentative mechanism predicts that O^{18} incorporation into 2 will vary in sigmoid fashion between 0.0



3



* At pH 7, the reaction with hydroxide ion contributes no more than 2% of the total rate of reaction.

and 1.0 mole, and does not, in this simplified form, explain the observed variation from 0.22 to 0.81 mole at the extremes of pH.

References

1. M.I. Kabachnik and V.A. Gilyarov, *Bull. Acad. Sci. USSR, Div. Chem. Sci. English Transl.*, 809 (1956).
2. I.N. Zhmurova and A.V. Kirsanov, *J. Gen. Chem. USSR, Eng. Transl.*, 29, 1864 (1959).
3. I.N. Zhmurova, I. Yu. Voitsekhovskaya, and A.V. Kirsanov, *ibid.*, 31, 3495 (1961).
4. P.J. Bunyan and J.I.G. Cadogan, *J. Chem. Soc.*, 42 (1963).
5. R. J. Sundberg, *J. Org. Chem.*, 30, 3604 (1965).
6. R. J. Sundberg, *J. Am. Chem. Soc.*, 88, 3781 (1966).
7. J.I.G. Cadogan, D.J. Sears, D.M. Smith, and M.J. Todd, *J. Chem. Soc., C*, 2813 (1969).