

PHOSPHINIC ACIDS AND DERIVATIVES 6. ESTERS OF DIALKYLPHOSPHINIC ACIDS¹

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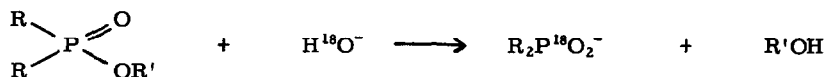
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There has been considerable recent interest in alkylphosphinate esters as substrates for study of displacement at phosphorus.²⁻⁴ Interpretation of some of this data is complicated by the problem of possible attack at alkyl carbon rather than phosphorus. We report here data on relative rates of hydrolysis in acyclic and cyclic compounds and elucidation of the position of attack by H¹⁸O⁻ in both series through use of ¹⁸O-enriched water.

The rates were studied titrimetrically in 60% dimethoxyethane-40% water solution. Some of the esters were studied at several temperatures so that relative rates at the same temperature could be obtained. The ionic strength of the reaction solution was kept constant; there is a slight negative ionic strength dependence for the reaction. The hydrolyses exhibit second order kinetics, first order in ester and first order in base.

In hydrolyses with water enriched in ¹⁸O, we observe, within experimental error, complete attack of HO⁻ at phosphorus (eq. 1). This is based upon the following ¹⁸O contents (in atom %) for experiments on methyl diethylphosphinate (1, R = CH₃): H₂O(normal, 0.203; H₂O(enriched), 1.953; starting ester, 0.202; sodium diethylphosphinate recovered from normal hydrolysis, 0.195; phosphinic acid recovered from H₂O¹⁸ hydrolysis, 0.948; ester recovered from reaction in enriched base, 0.202; phosphinic acid that was put through reaction conditions using enriched base, 0.212. The results show 88% P-O cleavage which is a lower limit because of the slightly hygroscopic nature of the sodium phosphinate.⁵



Tables 1 and 2 contain relative rates of hydrolysis of acyl substituted and alkyl substituted phosphinates. Although there is not yet enough data to separate the effects completely into steric and electronic effects,⁶ it seems clear that both must be important in displacement at phosphorus in phosphinates. Electronic effects alone will certainly not explain the relative rates in Table 1,⁷ and the effects in Table 2 are much larger than observed for acetates.⁶ We have shown that electronic effects are important in displacement at phosphinyl phosphorus.⁸ Therefore, the

complete distortion of the rate order in Table 1 from that predicted by σ^* indicates that steric effects are very important. This is probably due to the crowding due to increase of coordination number from 4 to 5 at phosphorus in the transition state for displacement.⁹ Displacements at tetrahedral carbon which would result in similar crowding generally proceed by dissociative, carbonium ion pathways rather than by the associative pathway followed for displacement at phosphorus in phosphinates.

Effects of rings are given in Tables 2 and 3. The availability of the four membered ring compound, 2, (R = CH₃)¹⁰ led us to a complete study of alkaline hydrolyses. Experiments with water enriched in ¹⁸O have established that, within experimental error HO⁻ attacks completely at phosphorus.¹¹ This proves that the speed of hydrolysis of this is truly remarkable.¹² A combination of steric effects and ring size effects would predict a very slow rate of hydrolysis if displacement were proceeding in S_N2 fashion. The fact that the rate is actually slightly faster than the corresponding 1, indicates that displacement must be possible by a pathway with geometry different from that for S_N2 at carbon, i. e., entering and leaving groups must be able to be other than co-linear with phosphorus. In the series of phosphinates with five membered rings, interpretation of the data can be based upon acceleration due to additional strain caused by a double bond¹³ and deceleration when a double bond is conjugated to phosphorus due to an increase in electron density compared to the unconjugated compound. Complete understanding of this and related data may involve pseudorotation,¹³ the steric effects of the other groups bonded to phosphorus, geometry of attack at phosphorus, etc.⁹ Further experiments on phosphinates should enable resolution of these questions.

Table 1
Relative Rate Constants for Alkaline Hydrolysis
of Non-Cyclic Methyl Esters at 75°C

<u>Compound</u>	<u>Relative Rate</u>
(C ₂ H ₅) ₂ P(O)OCH ₃	1 ^a
(n-C ₄ H ₉) ₂ P(O)OCH ₃	.3
(C ₆ H ₅ CH ₂) ₂ P(O)OCH ₃	1.05
(C ₆ H ₅) ₂ P(O)OCH ₃	4
(C ₆ H ₅)(CH ₃)P(O)OCH ₃	36
(CH ₃) ₂ P(O)OCH ₃	53

^a Actual rate constant = $1.1 \times 10^{-2} \text{ M}^{-1} \text{ sec}^{-1}$

Table 2
Relative Rate Constants for Alkaline Hydrolysis
of Alkyl Phosphinates at 75°C







Parent Compound	R = iC_3H_7	C_2H_5	CH_3
$(C_2H_5)_2PO_2R$ (1)	1	21	160
 PO_2R (2)	9	81	333

Table 3
Relative Rates of Alkaline Hydrolyses of Cyclic Esters

Compound	R =	T(°C)	Rel. Rate Constant ^a
$(C_2H_5)_2PO_2R$	CH_3	50	1
$(C_2H_5)_2PO_2R$	C_2H_5	75	1
 PO_2R	C_2H_5	75	2.9
 PO_2R	C_2H_5	75	4.0 ^b
 PO_2R	C_2H_5	75	1.5
 PO_2R	CH_3	50	42
 PO_2R	CH_3	50	1.2

^a Relative to diethylphosphinates for which the rates of the methyl ester at 50° and the ethyl ester at 75° are set equal to 1.0.

^b E. A. Dennis and F. H. Westheimer, *J. Am. Chem. Soc.*, **88**, 3431 (1966).

REFERENCES

1. Research supported by grants from the National Science Foundation and an Alfred P. Sloan Research Fellowship to P. H. D. R. M. was a NSF Undergraduate Research Participant. Present address of R. D. C. is Department of Chemistry, American University, Beirut, Lebanon. Inquiries should be addressed to P. H. at Wesleyan University.
2. W. Hawes and S. Trippett, Chem. Comm., 577 (1968).
3. K. Bergesen, Acta Chem. Scand., 21, 1587 (1967); G. Aksnes and K. Bergesen, ibid., 20, 2508 (1966).
4. E. A. Dennis and F. H. Westheimer, J. Am. Chem. Soc., 88, 3431 (1966).
5. In these oxygen-18 experiments, control experiments were done to prove that the oxygen-18 was introduced into the phosphinate product through the hydrolysis reaction and not through some other process such as exchange of product with the solvent.
6. As done by Taft with carboxylates; R. W. Taft, Jr., in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, 1956, Chap. 13.
7. It is difficult to use previous data²⁻⁴ in comparisons with our data. Bergesen's work on the 4-membered ring showed that there is a rate difference between cis and trans isomers of the esters. However, his method for making the trans ester (from the acid, which is nonisomeric) raises questions.² It is difficult to correlate Hawes and Trippett's results² with ours because their solvent is not given and their rates were measured at several different temperatures.
8. P. Haake, D. R. McCoy, W. Okamura, S. R. Alpha, S. Wong, D. A. Tyssee, J. P. McNeal, and R. D. Cook, Tetrahedron Letters, 5243 (1968).
9. P. Haake, C. E. Diebert, and R. S. Marmor, ibid., 5247 (1968).
10. J. J. McBride, Jr., Eric Jungermann, J. V. Killheffer, and R. J. Clutter, J. Org. Chem., 27, 1833 (1962).
11. Observed result was 97% of one oxygen atom from solvent incorporated into phosphinic acid product.⁵
12. Some rates have been reported^{2, 3} although the observations could have been due to a process other than HO⁻ attack at phosphorus. The isolation of the acid (2, R = H) and its ¹⁸O analysis eliminates other reactions.
13. D. A. Usher, E. A. Dennis, and F. H. Westheimer, J. Am. Chem. Soc., 87, 2320 (1965); F. H. Westheimer, Accounts of Chemical Research, 1, 70 (1968).