Insensitivity to Steric Hindrance of a Nucleophilic, Neighbouring-group Substitution at Pentavalent Phosphorus

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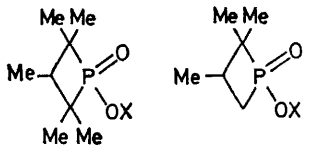
Summary The reactions of ethyl α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (III; R = Me, Et, Bu^t), and the α-hydroxyimino-*p*-nitrobenzyl esters of 1-hydroxy-2,2,3,4,4-pentamethyl- and -2,2,3-trimethyl-1-oxo-phosphetans [I, II; X=C(:NOH)·C_6H_4·NO_2-*p*] at pH 8–9 proceed at rates independent of steric factors to give *p*-nitroaniline and the corresponding phosphonic or phosphinic acid, in marked contrast to the corresponding alkyl esters.

WHEREAS it is known that attack of external nucleophiles on phosphonates and phosphinates is subject to steric hindrance depending on the size of the alkyl groups attached



(I) (II)

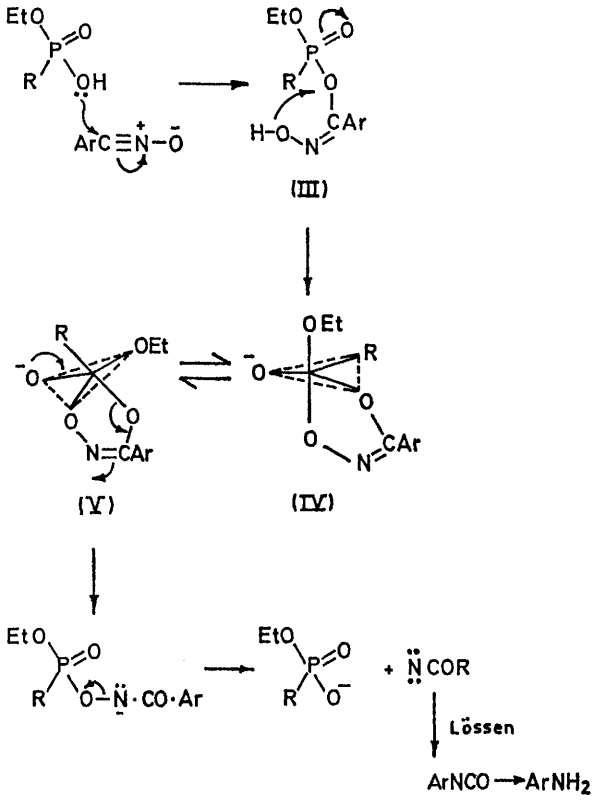
to phosphorus, we now report the observation that intramolecular attack by a neighbouring nucleophile on phosphorus is not sterically inhibited, *e.g.*, in (III) which involves intramolecular attack of the oxime function on phosphorus. Thus, di-isopropyl methylphosphonate

TABLE. *Relative rates of hydrolysis of α-hydroxyimino-p-nitrobenzyl esters* [X=C(:NOH)·C_6H_4·NO_2-p] (pH 8·45, 25°)

R in R(EtO)·P(O)·OX	Me	Et	Bu^t
Rel. rate	1·5	1·1	1·0[a]
	(I)		(II)
Rel. rate	1·0[b]		0·7
Rel. rate (X=Me)	1·0		4×10^3

[a] E_{act} = 93 kJ mol^{-1}; $\Delta S^{\ddagger} = +0{\cdot}5$ e.u.; $k_1 = 0{\cdot}065$ min^{-1} at 25°. [b] E_{act} = 81·7 kJ mol^{-1}; $\Delta S^{\ddagger} = -8{\cdot}8$ e.u.; $k_1 = 0{\cdot}005$ min^{-1} at 25°.

[$(Pr^iO)_2P(O)Me$] is hydrolysed in alkali 500 times more readily than the corresponding t-butyl analogue [$(Pr^iO)_2$-P(O)Bu^t].[1] Hawes and Trippett[2] have shown that the trimethylphosphetan derivative (II; X = Me) is hydrolysed, *via* apical OH^- attack on phosphorus, some 4×10^3 times faster than the more sterically hindered pentamethyl analogue (I: X = Me) (see Table). In contrast, we have now shown that at pH 8—9 the compounds (III), readily formed from *p*-nitrobenzonitrile oxide and the corresponding ethyl hydrogen alkylphosphonates,[3] as shown in the Scheme, quantitatively give the latter phosphonates and *p*-nitroaniline at rates which are almost independent of the *P*-alkyl group (Table). These results indicate that these reactions, which are very fast ($t_{\frac{1}{2}}$ *ca.* 10 min at 25°), proceed as shown in the Scheme, wherein attack by the well-positioned neighbouring oximate anion is not subject to the steric barriers implicit in apical bimolecular attack by an external nucleophile. Indeed, inspection of models suggests that such intramolecular attack is not purely apical. Such reaction would give the pentacovalent intermediate (IV) and hence, by pseudorotation, (V) Subsequent departure of the hydroxamate function from the apical position in (V), followed by rapid fission and subsequent Lössen rearrangement then leads to the observed products.



SCHEME. Ar = *p*-NO_2·C_6H_4

In accord with these observations, the α-hydroxyimino-*p*-nitrobenzyl analogues [I, II; X=C(:NOH)·C_6H_4·NO_2-*p*] of Hawes and Trippett's phosphetans (I, II; X = Me)[2] also hydrolyse at almost identical rates, in marked contrast to the methyl esters (Table).

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[1] L. Keay and R. F. Hudson, *J. Chem. Soc.*, 1956, 2463.
[2] W. Hawes and S. Trippett, *Chem. Comm.*, 1968, 577.
[3] J. I. G. Cadogan, J. A. Challis, and D. T. Eastlick, *J. Chem. Soc.* (*B*), 1971, 1988.