Neighbouring Group-Induced Phosphorus-Oxygen Fission in Acidic Hydrolysis of Phosphonates

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Summary Anchimeric assistance by the neighbouring oxime function in acid hydrolysis of alkyl α-hydroxyimino-*p*-nitrobenzyl alkylphosphonates (III), besides increasing the rate of de-esterification by *ca.* 10^7 compared with simple phosphonates (I), leads to P–O fission, normally associated with alkaline hydrolysis of the latter.

ACIDIC hydrolysis of dialkyl alkylphosphonates (I) gives alkyl hydrogen alkylphosphonates *via* alkyl–oxygen fission,[1,2] *e.g.* that of ethyl pinacolyl methylphosphonate (I; R^1 = Et, R^2 = Bu^tCHMe, R^3 = Me) proceeds *via* the pinacolyl carbonium ion, which gives the three possible C_6 alkenes by elimination of a proton.[2]

We now report cases, brought about by neighbouring-group participation, where acidic hydrolysis proceeds *via* P–O fission, similar to the behaviour of simple phosphonates (I) in alkaline solution. Thus, hydrolysis at pH 2—3·5 of α-hydroxyimino-*p*-nitrobenzyl pinacolyl methylphosphonate (III; R^2 = Bu^tCHMe, R^3 = Me), from *p*-nitrobenzonitrile oxide and pinacolyl hydrogen methylphosphonate,[3]

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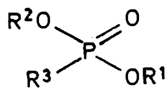
Relative rates at hydrolysis of $R^1R^2P(O)OC(Ar){=}NOH$ *at* pH 2.75 *at* 25° *in aqueous dioxan* (2% *v/v*)

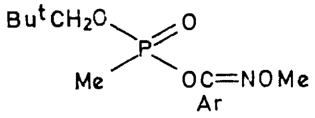
			$R^2 = Me$			
R^1	MeO	EtO	PrO	Pr^iO	Bu^tCH_2O	Bu^tCHMeO[a]
Rel. rate	87	71	45	14	10	1
			$R^1 = EtO$			
R^2	Me	Et . .	Bu^t			
Rel. rate	71	4	$<0{\cdot}4$			

[a] $k_1 = 0{\cdot}01\ min^{-1}$.

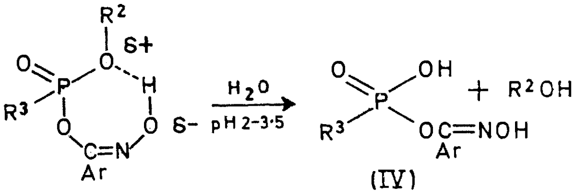
proceeds exclusively with the formation of pinacolyl alcohol and the corresponding hydrogen phosphonate (IV; $R^3 = Me$). C_6 Alkenes, which would have been indicative of the pinacolyl carbonium ion and hence of alkyl–oxygen fission were absent (by g.l.c.). The reaction, first order in phosphonate, is very fast, being complete in a few minutes at room temperature (Table) and the rate is independent of pH in the range 2—3·5. These facts suggest intramolecular catalysis involving the acid form of the oxime ($=NOH$ rather than $=NO^-$ or $=NOH_2^+$) *via* protonation of the ester oxygen as shown in (III), which then decomposes *via* bimolecular reaction of water at phosphorus with resulting P–O fission and loss of ROH as the leaving group.



(I)

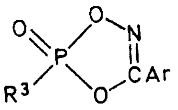


(II)



(III)

(IV)



(V)

Ar = p-$NO_2{\cdot}C_6H_4$

In accord with this are the observations: (i) α-methoxyimino-*p*-nitrobenzyl neopentyl methylphosphonate (II), where the oxime proton is replaced by methyl, is not hydrolysed after a period equal to seven half life-times for the hydrolysis of the free oxime (III; $R^2 = Bu^tCH_2$, $R^3 = Me$), thus confirming the participation of the free oxime in the fast hydrolysis; (ii) a hundred-fold decrease in rate was observed (Table) on hydrolysis of the *P*-t-butyl- rather than the *P*-methyl-phosphonate. Since substitutions at phosphorus are sensitive to steric crowding, [1,4] this indicates the occurrence in these instances (III) of bimolecular attack at phosphorus rather than at the ester α-carbon atom. Unimolecular decomposition of (III) is thus also ruled out. (iii) In a series of alkyl methylphosphonates (III) the rate constants (Table) fall in the order $R = Me > Et > Pr^n > Pr^i > Bu^tCH_2 > Bu^tCHMe$, thus parallelling the order observed[1] for alkaline hydrolysis, *via* P–O fission, of simple phosphonates (I; $R^1 = R^2$, $R^3 = Me$), and is contrary to the known[1] order of reactivity ($Pr^i > Me \sim Bu^tCH_2$) of the latter in acid solution, involving alkyl–oxygen fission; (iv) α-hydroxyimino-*p*-nitrobenzyl propyl methylphosphonate (III; $R^2 = Pr$, $R^3 = Me$) undergoes quantitative *trans*-esterification in methanol at room temperature to give the corresponding methyl ester (III; $R^2 = R^3 = Me$). This is explicable only on the basis of anchimerically assisted methanolic attack on phosphorus, with P–O fission, normal *trans*-esterifications of (I) being very slow (6 days at 130°).[5]

A possible refinement of the postulated route (III)—(IV), not affecting the important fact of P–O fission, involves the formation from (III) of a cyclic intermediate (V), with synchronous loss of R^2OH, followed by fast ring opening by water. There is evidence, however,[3,6] from studies of alkaline hydrolysis, of a reaction which proceeds *via* a similar cyclic intermediate formed by intramolecular attack of the oximate anion on phosphorus, which is against the intermediacy of (V) at low pH. In particular, there is no parallellism between the rates of hydrolyses at high and low pH of the series of phosphonates (III).

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