The Ready Hydrolysis of *syn-p*-Nitrophenyl Phenacyl Methylphosphonate Oxime

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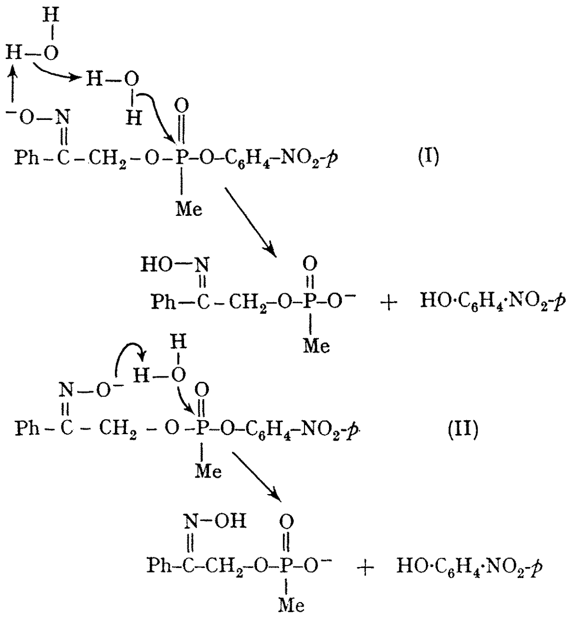
Summary Both *syn*- and *anti-p*-nitrophenyl phenacyl methylphosphonate oximes are hydrolysed very rapidly, which suggests strongly that the reaction involves a water-mediated reaction of the oximate anion.

OUR earlier work[1] established the very large rate increase in phosphonate ester hydrolysis which results from the incorporation of a suitably placed oxime group into the molecule. We now report that the anchimeric assistance by a neighbouring oxime group in phosphonate ester hydrolsis is not predominantly a result of oxime configuration. That is, the *anti*- and *syn*-configurations both function with remarkable efficacy. The *p*-nitrophenyl phenacyl methylphosphonate oxime of our previous communication,[1] which hydrolyses *ca.* 10^7 times faster than ethyl *p*-nitrophenyl methylphosphonate, was assigned the *syn*-configuration, primarily on the basis of its ready hydrolysis reaction. Based on n.m.r. spectral evidence, it has recently been designated[2] *anti-p*-nitrophenyl phenacyl methylphosphonate oxime (I). Compound (I) can be isomerized to *syn-p*-nitrophenyl phenacyl methylphosphonate oxime (II) *in situ* by several procedures, the most convenient of which is in solution in glacial acetic acid. A further increase of *ca.* 120 times in hydrolysis rate is exhibited by the *syn*-isomer. The hydrolysis of (II) under pseudo-first-order conditions in aqueous solution over the pH range 2·10—2·48 at 25.0° is first-order in $[OH^-]$ with a rate constant $k_{OH} = 1{\cdot}27 \times 10^9 \mathrm{M}^{-1}\,\mathrm{sec.}^{-1}$. Excellent first-order plots were obtained to >3 half-lives and the production of *p*-nitrophenol, determined spectrophotometrically at 330 nm., is stoicheiometric. At pH 2·48, the half-life is 163 sec. ± 2·3%†.

The rapid hydrolysis of both (I) and (II) has reinforced our position that the mechanistic pathway operating under the conditions studied involves a water-mediated reaction of the oximate anion:[1]



It is particularly significant that anchimeric assistance in the hydrolysis of (I) and (II) is *not predominantly* a result

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† The kinetic experimental evidence on (I) and (II) is compatible with that of a simple reaction preceded by an equilibrium. As such, it is recognized that the observed rate constant is a product of (a) the actual rate constant for the rate-determining process and (b) the equilibrium constant of the preceding equilibrium.

of oxime configuration. The relative similarity in rates between the two isomers compared with the large rate enhancement exhibited by each supports a common mechanism. This makes it impossible to accommodate either (i) a mechanism involving direct attack by hydroxide ion on phosphorus facilitated by hydrogen-bonding assistance in undissociated oxime, or (ii) a mechanism involving direct attack by the oximate anion on phosphorus.[1] For steric reasons the *anti*-isomer (I) cannot react by either of these pathways. In conjunction with these conclusions, it should be noted that we have unequivocally established that an isomerization step is *not* involved in the hydrolysis data reported. To wit, a mixture of the *syn*- and *anti*-isomers (75% *syn*/25% *anti*) was prepared and analysed by n.m.r. Subsequent spectrophotometric kinetic analysis on this sample (monitoring *p*-nitrophenol production) was then carried out at pH 2·48 and 4·50. At pH 2·48, *p*-nitrophenol production corresponded to the same percentage of the *syn*-isomer reflected in the n.m.r. analysis. Under these conditions the *anti*-isomer is virtually inert. Raising the pH to 4·50 resulted in a further increase in *p*-nitrophenol production corresponding to the same percentage of *anti*-isomer reflected in the n.m.r. analysis. This experiment was, of course, made possible by the *ca.* 100 fold difference in hydrolysis rates between the two isomers.

Finally, it should be noted that while the Arrhenius equation is obeyed by compound (I), it is not obeyed by compound (II). The significance of this finding is currently being investigated.

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[1] C. N. Lieske, J. W. Hovanec, G. M. Steinberg, and P. Blumbergs, *Chem. Comm.*, 1968, 13.

[2] P. Blumbergs, C. B. Thanawalla, A. B. Ash, C. N. Lieske, and G. M. Steinberg, Abstracts, First Northeast Regional Meeting of the American Chemical Society, Boston, Mass., Oct. 1968, p. 98. (*syn* and *anti* refer to the oxime hydrogen in relation to phosphorus).