Phosphorylation of Alcohols through the Acid-catalysed Fragmentation of α-Oxyiminophosphonates†

Eli Breuer,*[a] Rafik Karaman,[a] Haim Leader,[b] and Amiram Goldblum[a]

[a] *Department of Pharmaceutical Chemistry, The Hebrew University School of Pharmacy, Jerusalem, Israel*
[b] *The Israel Institute for Biological Research, Ness Ziona, Israel*

The acid-catalysed fragmentation of monoalkyl α-oxyiminophosphonates results in the formation of (mixed) phosphodiesters and a nitrile in high yields.

Although α-oxyiminophosphonates are easily accessible from acylphosphonates,[2] their chemistry had hardly been studied, apart from their reduction to α-aminophosphonates,[2,3] in spite of the interesting possibilities presented by the proximity of the oxime and phosphoryl functions. In this communication we report that monoesters of α-oxyiminophosphonic acids [*e.g.* methyl hydrogen (hydroxyiminobenzyl)phosphonate, (**1**)] undergo acid-catalysed fragmentation to give a nitrile, and in the presence of an alcohol, to give a (mixed) phosphodiester, equation (1).

Dimethyl hydroxyiminobenzylphosphonate, (**2**) [obtained by treating dimethyl benzoylphosphonate with hydroxylamine[2] as a mixture of (*Z*) and (*E*) isomers, the structures of which are not assigned] could be monodealkylated by treating with lithium bromide in acetonitrile at ambient temperature to

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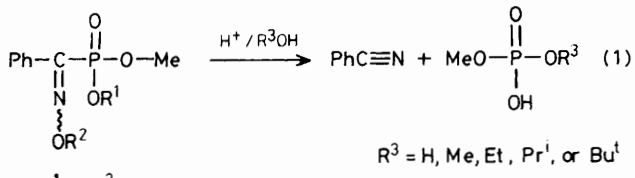


R^3 = H, Me, Et, Pr^i, or Bu^t

(1) $R^1 = R^2 = H$

(2) R^1 = Me, R^2 = H

(3) R^1 = Li, R^2 = H

(4) R^1 = H, R^2 = Me

Table 1. Fragmentation of methyl hydrogen (hydroxyiminobenzyl)-phosphonate ($Z + E$) 0.20 M in alcoholic hydrogen chloride solution at ambient temperature.

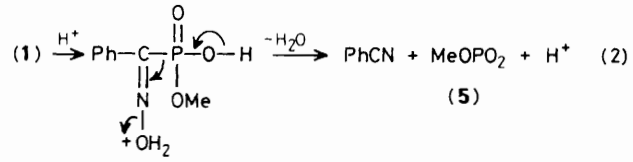
Alcohol	Concentration of HCl/M	$t_{1/2}$/min of product formation	^{31}P N.m.r. data[a] of product δ/p.p.m., coupling pattern (P–O–CH)
MeOH	0.20	1500	−0.416, septet
MeOH	0.55	405	−0.416, septet
MeOH	1.67	250	−0.416, septet
EtOH	0.55	525	−2.527, sextet
Pr^iOH	0.55	550	−4.278, d. quartet
Bu^tOH	0.55	500	−3.517, quartet

[a] ^{31}P Spectra were determined in the respective alcoholic solution and chemical shifts are with respect to 85% phosphoric acid.

give lithium methyl hydroxyiminobenzylphosphonate (**3**)‡ [also as a mixture of (*Z*) and (*E*) isomers in similar ratio to the dimethyl ester].

While solutions of the salt (**3**) were found to be stable at alkaline pH values up to pH 14, liberation of the free acid, (**1**), by acidification of aqueous solutions of (**3**) causes it to decompose to give benzonitrile (85%) and methyl dihydrogen phosphate, identified by ^{31}P n.m.r. spectroscopy [−0.10 p.p.m. (q)] as the sole phosphorus-containing product.

Similarly, methyl hydrogen (methoxyiminobenzyl)phosphonate (**4**) yields in water methyl dihydrogen phosphate, and in methanol dimethyl hydrogen phosphate, in addition to benzonitrile.



Oxime (**1**) behaves analogously in alcoholic hydrogen chloride solutions (in different alcohols) yielding, in addition to benzonitrile (80—90% determined by gas chromatography), the corresponding alkyl methyl hydrogen phosphate. These reactions were monitored by ^{31}P n.m.r. spectroscopy and their $t_{1/2}$ values are listed in Table 1. From Table 1 it can be seen that the reaction is catalysed by acid and that its rate is not affected by the alcohol structure.

Such behaviour indicates that the alcohol is not involved in the rate-determining step of the reaction, excluding an associative mechanism that would involve expansion of the phosphorus co-ordination. On the other hand, the data are compatible with a dissociative mechanism that consists of a slow, acid-catalysed fragmentation of the oxime (**1**) to give benzonitrile and monomeric methyl metaphosphate (**5**), equation (2), which is rapidly trapped by the solvent.[4]

Another conceivable mechanism involving a Beckmann type migration of the phosphoryl group from C to N is excluded by the complete stability of diester (**2**) under the reaction conditions. This novel fragmentation reaction is of interest with regard to the relationship between the steric structure of the oximes and their tendency to undergo fragmentation and the involvement of monomeric methyl metaphosphate as an intermediate.

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‡ Satisfactory elemental (C, H) analyses were obtained for $C_8H_9NO_4PLi{\cdot}H_2O$. N.m.r. spectra (D_2O): ^{1}H δ 7.20 (br., 5H), 3.29 (d, *J* 10.94 Hz, 2/3 of 3H) (major isomer), 3.11 (d, *J* 11.2 Hz, 1/3 of 3H) (minor isomer); ^{31}P δ 6.42 (1/3 of 1P, q, *J* 11.24 Hz), 1.83 (2/3 of 1P, q, *J* 10.94 Hz) p.p.m. M.p. > 270 °C.

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