Rearrangement of Phosphylated Amidoximes

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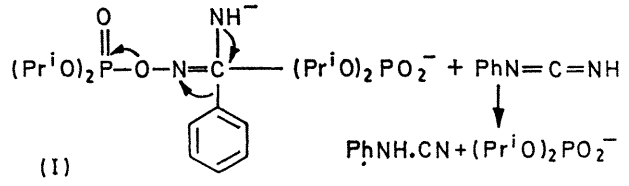
Summary Phosphorylated benzamidoximes undergo the Tiemann rearrangement in alkaline solution whereas the phosphinylated amidoxime hydrolyses rapidly, and the phosphonylated amidoxime undergoes an intramolecular rearrangement with simultaneous dealkylation.

AMIDOXIMES are readily *O*-phosphorylated[1] in neutral solution to give products which, unlike the corresponding *O*-acylated amidoximes, react in alkaline solution in a variety of ways.

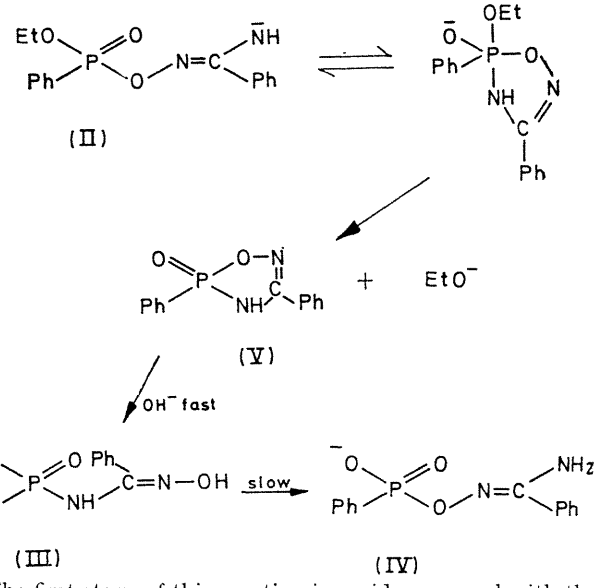


(I)

Thus the *O*-phosphorylated benzamidoxime (I) gives phenyl cyanamide in a reaction which may proceed by mechanism similar to that of the Tiemann rearrangement.[2]

The phosphonylated amidoxime (II), however, gives *ethanol* and an intermediate (III) in a fast second-order reaction in alkaline solution (Table). The u.v. spectrum of this intermediate with a maximum at 265 nm, which is close to that found for benzamidoxime, slowly changes in a first-order process to give a final product with $\lambda_{max} \simeq 245$ nm, *i.e.* close to the maximum shown by (II).

This produces ethanol and a cyclic ester (V), which presumably would open rapidly in alkaline solution to give (III). This then slowly isomerises to (IV), the thermodynamically stable isomer.



The first stage of this reaction is rapid compared with the direct hydrolysis, since the *N*-dimethyl analogue (VI) hydrolyses slowly in alkaline solution (Table).

Rates of alkaline hydrolyses of O-phosphylated amidoximes and the corresponding p-nitrophenyl esters, in water at 25° (Ar = *p*-$O_2N.C_6H_4$).

	k_2 (l.mole^{-1}min.$^{-1}$)		k_2 (l.mole^{-1}min.$^{-1}$)	
(Pr^{i}O$_2$)P(:O)O·N:C(Ph)NH$_2$ (I)	0·19	(Pr^{i}O)$_2$P(:O)OAr	0·06	(ref. 4)
EtO(Ph)P(:O)O·N:C(Ph)NH$_2$ (II)	70	EtO(Ph)P(:O)OAr	60	
EtO(Ph)P(:O)O·N:C(Ph)NMe (VI)	0·54	Ph$_2$P(:O)OAr	350	
Ph$_2$P(:O)O·N:C(Ph)NH$_2$ (VII)	44			

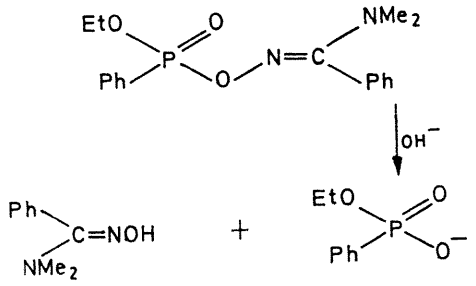
This product which was isolated as its sodium salt analyses correctly for (IV), and cannot be acylated under mild conditions. Treatment with dilute acid leads to the rapid formation of benzamidoxime and phenylphosphonic acid.

We explain these results by the rapid cyclisation of the ionised form of (II) to give an intermediate (or transition state) with an axial ethoxy-group, in agreement with the stereoelectronic requirements advanced by Westheimer.[3]

The *O*-phosphinylated benzamidoxime (VII) hydrolyses rapidly in this way to give diphenylphosphinic acid and benzamidoxime.

The different reaction courses followed by these various phosphylated amidoximes depend on the relative rates of phosphylation (*e.g.* as shown in the Table by the rates of alkaline hydrolysis of the *p*-nitrophenyl esters), and on the leaving-group tendency of the phosphorus moiety.

Thus, the Tiemann rearrangement is promoted by a good



leaving group, *e.g.* $(RO)_2PO_2^-$ and a phosphorus atom of relatively low electrophilic power. The phosphonate (II) is a stronger electrophile, but the $RO(Ph)PO_2^-$ group is a poorer leaving group, hence intramolecular attack on phosphorus is preferred in this case.

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[1] R. E Plapinger and O. O. Owens, *J. Org. Chem.*, 1956, **21**, 1186.
[2] S. M. Partridge and H. A. Turner, *J. Pharm. Pharmacol.*, 1953, **5**, 103.
[3] F. H. Westheimer, *Accounts Chem. Res.*, 1968, **1**, 70.
[4] L. Ginjaar, Ph.D. Thesis, Leiden, 1960.