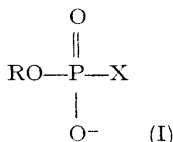


The Methyl Phosphorazidate Anion: a Selective Phosphorylating Agent

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IONIC phosphate esters of the type (I) (where X is a potential leaving group) have, with the notable exception of phosphoramidic acid derivatives ($X = \overset{+}{N}H_3$, *etc.*), been little studied as phosphorylating agents. Such species have been postulated in, but not isolated in, the reactions of monoalkyl



phosphates in the presence of condensing agents such as aryl sulphonyl halides on carbodiimides.¹ However, the anions of a simple diester of

phosphoric acid are rather resistant to external nucleophilic attack at the phosphorus atom, which in many cases fails to compete with nucleophilic attack elsewhere in the molecule. We report the first preparation of the methyl phosphorazidate anion (I; $X = N_3$) and find that it undergoes nucleophilic attack exclusively at phosphorus.

Unlike carboxylic acid hydrazides the readily available phosphorohydrazidates (I; $X = NH-NH_2$)² evolved nitrogen with cold aqueous nitrous acid and gave none of the corresponding phosphorazidates. Dimethyl phosphorazidate,³ however, reacted smoothly with sodium iodide in acetone to give the stable, crystalline sodium methyl phosphorazidate, m.p. 146—148° (decomp.). Elemental analysis was consistent with the proposed

formula and the compound had a strong absorption at 2144 cm.^{-1} (MeOH) characteristic of the azide group.

The rate of hydrolysis in aqueous solution at 50° ($\mu = 0.20$) was independent of pH over the range 3.5–11.5 and second order rate constants for attack by various nucleophiles under the above conditions are shown.

k (l. mol. ⁻¹ hr. ⁻¹)			
n-Butylamine	..	3.7	HO ⁻ 0.60
Benzylamine	..	2.0	F ⁻ 0.03
Pyridine	..	0.52	HPO ₄ ²⁻ 0.00
2,6-Lutidine	..	0.00	H ₂ O 5.4×10^{-5}

Reactions were followed by the liberation of azide ion⁴ (which was quantitative) and by the appearance of methyl dihydrogen phosphate (in the first two cases the appropriate phosphoramidate ester was formed quantitatively) on paper chromatograms.

It is clear that the methyl phosphorazidate ion is a highly selective phosphorylating agent for amines—even in dilute aqueous solution—and that it, and similar compounds, may be potentially useful in the phosphorylation of alkoxides in nonaqueous solution. Unlike the monoesters of

phosphoramidic acid and other methods which involve activation of a monoalkyl phosphate, competing nucleophilic attack by other anions, particularly those leading to pyrophosphates, are likely to be negligible.

One final point of interest is that the rate of aqueous hydrolysis is much slower (a factor of 10^3 at 50°) than either methyl phosphoramidate or its *N*-cyclohexyl derivative.⁵ Since nucleophilic displacements on the latter compounds are believed to proceed on the zwitterion form (I; R = Me, X = $-\text{NH}_3^+$) it would appear that the neutral amine molecule is a better leaving group than azide ion despite the fact that pK_a values of the conjugate acid predict the opposite. While further investigation is necessary to determine in detail the factors responsible for this apparently large discrepancy it seems clear that the validity of equations correlating rates of hydrolysis of phosphate esters with the pK_a of the displaced anion⁶ cannot be assumed for the prediction of rates when the potential leaving group bears a positive charge adjacent to phosphorus.

Studies on the mechanism and uses of phosphorylating agents containing a P–N bond are in progress.

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