

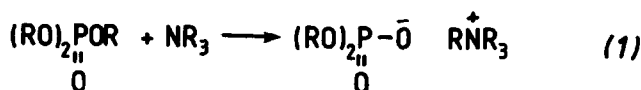
SELECTIVE DEMETHYLATION OF PHOSPHORUS ESTERS

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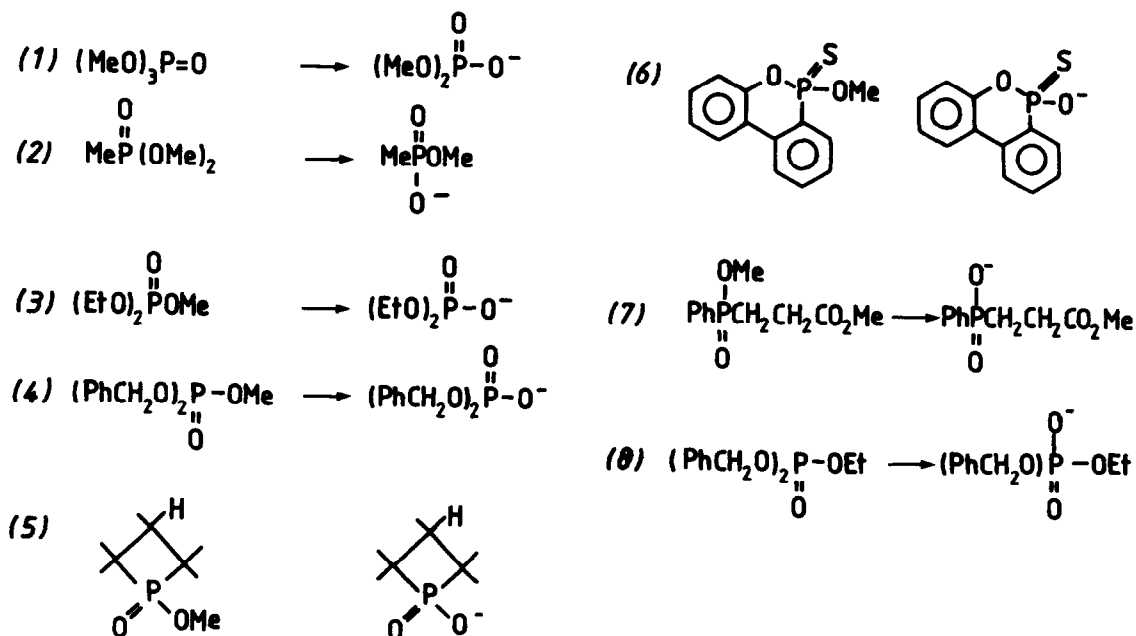
The selective cleavage of methyl phosphorus esters by t-butylamine is described.

Phosphate¹ and phosphonate esters² are well known as alkylating agents for carboxylic acids, phenols, and amines. Conversely, amines have been used for partial dealkylation of phosphoric and phosphonic esters³ as shown in equation (1).



We have found that t-butylamine is a superior reagent for this transformation. For example, using t-butylamine as solvent, ester (6) is completely demethylated within 10 min at room temperature, whereas other amines take considerably longer at their respective reflux temperatures, Pr₂NH (3 hr), Et₃N (6 hr), C₆H₁₁NH₂ (3 hr). t-Butylamine is effective in solution with solvents such as dioxan, dichloromethane and benzene, but using the amine itself as solvent is the most convenient procedure since the product, the mono t-butylamine salt (Table)⁴ can be obtained by filtration, or removal of the volatile amine.

TABLE Cleavage of Phosphorus Esters with t-Butylamine



t-Butylamine is very selective, for although it demethylates trimethyl phosphate (1) and dimethyl methylphosphonate (2) very effectively at room temperature there is no reaction with triethyl phosphate or diethyl ethylphosphonate even after 4 weeks. One obtains exclusive cleavage of the O-CH₃ bond in ester (3).

As one might expect the PhCH₂-O bond of ester (8) is cleaved by refluxing t-butylamine. However, a methyl group is lost in preference to a benzyl group, as shown by the reaction of t-butylamine with (4). Exclusive demethylation is observed; there is no trace of any products resulting from loss of the benzyl group. The mild conditions used in these reactions suggest that many functional groups can be present.⁶ For example, t-butylamine preferentially attacks the phosphorus rather than the carboxylic acid ester as shown by the product derived from (7).

We have no evidence of nucleophilic attack at phosphorus in any of these reactions. Indeed, even when the phosphorus atom is placed in a small ring, a situation known to lead to increased rates of nucleophilic attack at phosphorus⁵ one still obtains exclusive demethylation.

The use of t-butylamine for the cleavage of methyl phosphorus esters makes it possible to use the methyl group as a protecting group in the synthesis of a variety of phosphorus compounds and in particular nucleotide synthesis.⁶

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References:

1. C.A. Buchler and D.E. Pearson, Survey of Organic Synthesis, Wiley-Interscience, New York 1970.
2. P. Sutter and C.D. Weis, Phosphorus and Sulphur, 1978, 4, 335.
3. G.M. Kosolapoff and L. Maier, Organic Phosphorus Compounds, Volume 7, Wiley-Interscience 1975.
4. t-Butylmethylamine is present in solution as shown by ¹H n.m.r. and g.l.c. analysis.
5. R.F. Hudson and C. Brown, Accounts Chem. Research, 1972, 5, 204.
6. D.J.H. Smith, K.K. Ogilvie, and M.F. Gillen, following communication.

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