

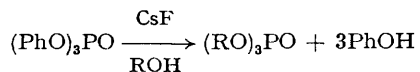
Fluoride Ion-promoted Transesterification in Phosphate Triesters

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Summary Phenyl groups are readily replaced in phosphate triesters by alcohols in general in the presence of caesium fluoride.

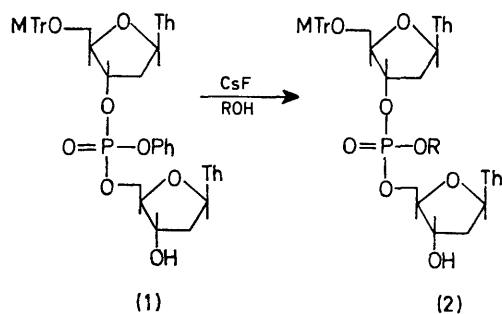
TRIESTERS of phosphoric acid have important uses ranging from plasticisers to key intermediates in nucleotide synthesis. We have observed that triphenyl phosphate is rapidly



converted into trialkyl phosphates when dissolved in

anhydrous alcohols containing an excess (10 mol. equiv.) of CsF. The yields are quantitative and the alcohols tested include methanol, ethanol, n-propanol, propan-2-ol, n-butanol, and n-pentanol. The reaction appears (by g.l.c.) to be complete within 8 h. The displacement of ordinary alkyl groups does not occur under these conditions. Thus, for example, trimethyl phosphate and tributyl phosphate were not affected by CsF after 24 h when dissolved in anhydrous butanol and methanol respectively.

Triphenyl phosphate was also converted into the above trialkyl phosphates using tetra-(n-butyl)ammonium fluoride (TBAF). In these experiments triphenyl phosphate was



a; R = Cl₃CCH₂

b; R = MeCH₂

c; R = Me

Th = thymine; MTr = monomethoxytrityl

dissolved in tetrahydrofuran containing 10 mol. equiv. of TBAF. An equal volume of the alcohol was added and the reactions were complete within 8 h.

This reaction is of particular value in nucleotide chemistry where phosphate triesters in oligonucleotides¹ and cyclic nucleotides² are of current interest. For example, compound (1)† is converted into compounds (2a–c) in 8 h by dissolving the nucleotide in the appropriate alcohol containing CsF.‡ These compounds can be isolated by silica gel chromatography in >90% yields. Compounds (1) and (2) were fully characterized including their conversion into authentic thymidylyl-(3'-5')-thymidine.

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† Prepared by condensing 5'-O-monomethoxytritylthymidine 3'-(phenyl phosphate) (1 mmol) with 3'-O-t-butyldimethylsilylthymidine (1.5 mmol) in pyridine using tri-isopropylbenzenesulphonyl chloride (2 mmol) followed by work-up on silica gel thick-layer plates.

‡ Note that the silyl group is unaffected under these conditions.

¹ R. L. Letsinger and K. K. Ogilvie, *J. Amer. Chem. Soc.*, 1967, **89**, 4803; N. J. Cusack and C. B. Reese, *Tetrahedron Letters*, 1974, 3785; F. Eckstein, and I. Rizk, *Angew. Chem. Internat. Edn*, 1967, **79**, 939; P. S. Miller, K. N. Fang, N. S. Kondo, and P. O. P. Ts'O, *J. Amer. Chem. Soc.*, 1971, **93**, 6657.

² J. Engels and W. Pfeleiderer, *Tetrahedron Letters*, 1975, 1661; R. N. Gohil, R. G. Gillen, and J. Naggyvary, *Nucleic Acids Res.*, 1974, **1**, 1691.