

[171] PHENYL DIHYDROGEN PHOSPHATE

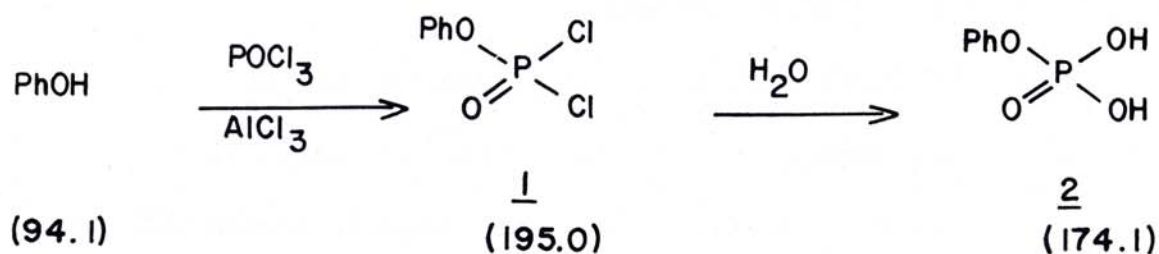
Conversion of Phenols into Aryl Dihydrogen Phosphates

Jyoti B. Chattopadhyaya, Geoffrey R. Owen, and Colin B. Reese

*Department of Chemistry, King's College, Strand, London WC2R 2LS,
England*

INTRODUCTION

We have advocated¹ the use of phenyl and other aryl esters of orthophosphoric acid as the source of phosphate in the synthesis of oligonucleotides by the phosphoric triester approach. Such aryl dihydrogen phosphates (e.g., 2) may readily be prepared² from the corresponding aryl phosphorodichloridates (e.g., 1). In nearly all of the procedures described in the literature, the latter are hydrolyzed under basic conditions, and an extra step is necessary if the free acid is needed. The procedure³ described here for the preparation of phenyl dihydrogen phosphate (2) is based on that of Hoeflake⁴ and simply involves heating phenyl phosphorodichloridate (1) with a small excess of water. The method is applicable to the preparation of other aryl dihydrogen phosphates, and high yields of crystalline products are generally obtained.³ Phenyl phosphorodichloridate (1) is conveniently prepared⁵ by heating phenol with an excess of phosphoryl chloride in the presence of a catalytic amount of aluminum(III) chloride.



PROCEDURE

Phenyl Dihydrogen Phosphate (2)

Phenol^a (47.0 g, 0.50 mol), phosphoryl chloride^b (78 ml, 0.85 mol), and anhydrous aluminum(III) chloride (0.1 g) are heated together^c under gentle reflux with the exclusion of moisture for 13 hr.^d Distillation^e of the cooled products gives phenyl phosphorodichloridate (1), b.p. 68° to 70°/0.07 torr; yield 87 g (89%).

Compound 1 is stirred and heated while water (31.7 ml, 1.76 mol) is added dropwise during 1 hr.^f After a further 1 hr the products are cooled and evaporated under diminished pressure^g to

^aLaboratory-grade reagent (>98% purity).

^bLaboratory-grade reagent is used without redistillation.

^cThe reactants, contained in a 500-ml, single-necked, round-bottomed flask fitted with a reflux condenser and a calcium chloride drying-tube, are heated in an oil bath (bath temperature 110° to 114°). The reaction is conducted in an efficient hood.

^dIf a fourfold excess of phosphoryl chloride is used, the reaction proceeds to completion in 4 hr.

^eThe excess of phosphoryl chloride is removed at water-pump pressure.

^fThe reaction is conducted in a 250-ml, two-necked flask fitted with a reflux condenser and a 50-ml dropping-funnel. The reactants are magnetically stirred, and heated by an oil-bath (bath temperature 90° to 93°). The reaction is conducted in a hood.

give a crystalline residue. Recrystallization from chloroform (100 ml) gives 2 as colorless crystals, yield (in two crops), 67.0 g (77%), m.p. 99° to 100° (lit.² m.p. 97° to 98°).

REFERENCES

1. J. H. van Boom, P. M. J. Burgers, G. R. Owen, C. B. Reese, and R. Saffhill, *Chem. Commun.*, 869 (1971); N. J. Cusack, C. B. Reese, and J. H. van Boom, *Tetrahedron Lett.*, 2209 (1973); C. B. Reese, *Phosphorus and Sulfur*, 1, 245 (1976).
2. For a review, see K. Sasse, in E. Müller (ed.), Houben-Weyl, *Methoden der Organischen Chemie*, Vol 12/2, Georg Thieme Verlag, Stuttgart, 1964, pp. 172 to 175.
3. G. R. Owen, C. B. Reese, C. J. Ransom, J. H. van Boom, and J. D. H. Herscheid, *Synthesis*, 704 (1974).
4. J. M. A. Hoeflake, *Recl. Trav. Chim. Pays-Bas*, 36, 24 (1916).
5. V. V. Katyshkima and M. Ya. Kraft, *Zh. Obshch. Khim.*, 26, 3060 (1956); *C. A.*, 51, 8028 (1957).