Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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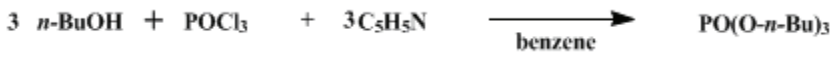
n-BUTYL PHOSPHATE



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1. Procedure

In a 2-l. round-bottomed flask, fitted with a reflux condenser, liquid-sealed mechanical stirrer, dropping funnel (Note 1), and thermometer, are placed 222 g. (274 cc., 3 moles) of dry *n*-butyl alcohol, 260 g. (265 cc., 3.3 moles) of pyridine, and 275 cc. of dry benzene (Note 2). The solution is stirred and the flask is cooled in an ice-salt mixture until the temperature has fallen to −5°. With efficient stirring (Note 3), 153 g. (91 cc., 1 mole) of phosphorus oxychloride (b.p. 106–107°) is added dropwise at such a rate that the temperature does not exceed 10°. After the addition is completed the reaction mixture is heated slowly to the reflux temperature and held there for two hours. The mixture is cooled to room temperature, and 400–500 cc. of water is added to dissolve the pyridine hydrochloride (Note 4). The benzene layer is separated, washed with 100–150 cc. of water (Note 5), and dried over 20 g. of anhydrous sodium sulfate.

The benzene and other low-boiling materials are removed by distillation at 40–50 mm. pressure until the temperature of the distilling vapor reaches 90°. The *n*-butyl phosphate fraction is collected at 160–162°/15 mm., or 143–145°/8 mm., and weighs 190–200 g. (71–75 per cent of the theoretical amount) (Note 6).

2. Notes

1. The tip of the funnel should be placed sufficiently high above the surface of the reaction mixture of avoid encrustation with pyridine hydrochloride. It is advantageous to use a thermometer on which the scale above −5° is visible above the stopper; otherwise, the fog in the flask and the pyridine salt may obscure the scale.
2. The reactants and solvent were dried by distillation; fractions boiling over an interval of 1° were used.
3. The first 10–15 cc. of phosphorus oxychloride must be added very slowly to avoid vigorous reaction and overheating. It is essential to avoid an initial temperature so low that unreacted phosphorus oxychloride accumulates and then suddenly reacts with violence. The mechanical stirrer should be of such dimensions and operated at such speeds that the heat of reaction is dissipated rapidly without throwing solid material (and occluded reactants) against the upper walls of the flask.
4. About 50 per cent of the pyridine may be recovered by concentrating this aqueous solution over a steam bath, treating with strong caustic soda solution, and distilling the pyridine layer.
5. The solution should be neutral before distillation. The presence of hydrogen chloride promotes decomposition of phosphoric esters.[1] The benzene solution should not be washed with alkaline reagents, such as sodium carbonate solution, since alkaline reagents also cause decomposition during distillation.
6. This is a general method for preparing alkyl phosphates. Using a similar procedure, the *n*-propyl ester may be obtained in 60–65 per cent yields, the *sec.*-butyl ester in 40–45 per cent yields, and the *n*-amyl ester in 60–65 per cent yields.[2]

3. Discussion

n-Butyl phosphate has been prepared by the action of phosphorus pentachloride or oxychloride on butyl alcohol;[3] by the action of phosphorus oxychloride on aluminum butoxide[4] or sodium butoxide;[5] and by the oxidation of butyl phosphite.[6] The procedure described above[2] is similar to one which has been used for the preparation of alkyl phosphites.[7]

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

caustic soda

phosphorus pentachloride or oxychloride

n-propyl ester

sec.-butyl ester

n-amyl ester

hydrogen chloride (7647-01-0)

Benzene (71-43-2)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

butyl alcohol,
n-butyl alcohol (71-36-3)

Phosphorus Oxychloride (21295-50-1)

pyridine (110-86-1)

aluminum butoxide

pyridine hydrochloride (628-13-7)

sodium butoxide

butyl phosphite

n-BUTYL PHOSPHATE (12788-93-1)