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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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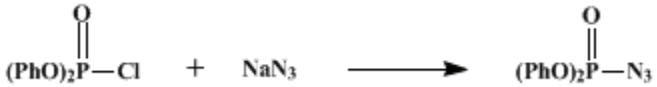
DIPHENYL PHOSPHORAZIDATE

[Phosphorazidic acid, diphenyl ester]



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1. Procedure

A mixture of 56.8 g (0.21 mol) of diphenyl phosphorochloridate (Note 1), 16.3 g (0.25 mol) of sodium azide, and 300 mL of anhydrous acetone (Note 2) in a 500-mL round-bottomed flask fitted with a calcium chloride tube is stirred at 20–25°C for 21 hr. The lachrymatory mixture is filtered in a hood, and the filtrate is concentrated under reduced pressure. The residue is distilled through a short Vigreux column (Note 3). The yield of diphenyl phosphorazidate, bp 134–136°C (0.2 mm), is 49–52 g (84–89%) (Note 4).

2. Notes

1. Diphenyl phosphorochloridate (diphenyl chlorophosphate), from Aldrich Chemical Company, Inc., was used after purification by distillation at 165–168°C (5 mm).
2. Commercial acetone was dried over anhydrous potassium carbonate and distilled.
3. The bath temperature should be kept below 200°C to minimize decomposition of diphenyl phosphorazidate.[3]
4. Diphenyl phosphorazidate is a colorless nonexplosive oil that can be kept for a long time without decomposition if it is protected against light[3] and moisture.

3. Discussion

The procedure described is essentially that of Shioiri and Yamada.[4] Diphenyl phosphorazidate is a useful and versatile reagent in organic synthesis.[5] [6] It has been used for racemization-free peptide syntheses,[4,7,8] thiol ester synthesis,[9] a modified Curtius reaction,[7,10,11] *C*-acylation of active methylene compounds,[12] esterification of an α-substituted carboxylic acid,[13] formation of diketopiperazines,[14] an alkyl azide synthesis,[15] phosphorylation of alcohols and amines,[16] and polymerization of amino acids and peptides.[17] Furthermore, diphenyl phosphorazidate acts as a nitrene source[3] and as a 1,3-dipole.[18,19] An example of the ring contraction of cyclic ketones to form cycloalkanecarboxylic acids is presented on page 135 in this volume.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 7, 135
- Org. Syn. Coll. Vol. 8, 612

References and Notes

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spectral data: ^{1}H NMR ($CDCl_3$), δ: 7.0–7.3 (br, s, C_6H_5-); IR (neat) cm^{-1}: 3060 (w, C-H), 2170 (s, $-N_3$), 1590 (m), 1490 (s, arene C=C), 1270 (m, P=O), 960 (s, P-O-aryl).

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

Diphenyl phosphorochloridate (diphenyl chlorophosphate)

potassium carbonate (584-08-7)

acetone (67-64-1)

sodium azide (26628-22-8)

diphenyl phosphorochloridate (2524-64-3)

Diphenyl phosphorazidate,
Phosphorazidic acid, diphenyl ester (26386-88-9)