



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](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.*

*Organic Syntheses, Coll. Vol. 5, p.602 (1973); Vol. 46, p.42 (1966).*

## HEXAMETHYLPHOSPHOROUS TRIAMIDE

### [Phosphorous triamide, hexamethyl-]



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### 1. Procedure

A solution of phosphorus trichloride (137.3 g., 1.0 mole) in 1.5 l. of dry ether (Note 1) is added to a 3-l., three-necked, round-bottomed flask equipped with an efficient stirrer, thermometer, a gas-inlet tube (Note 2), and a reflux condenser vented through a nitrogen reservoir (a T-tube under slight positive nitrogen pressure) into a well-functioning hood (Note 3). The flask is cooled in an ice bath to 0–5°, and an excess of anhydrous dimethylamine (Note 4) is introduced at such a rate that the temperature does not exceed 15°. The addition requires about 3–4 hours. At the end of this period the flask contains the white stirrable slurry of the amine hydrochloride and the ethereal solution of the phosphorous triamide (Note 5). The reaction mixture is allowed to warm to room temperature overnight while still being protected by nitrogen. Filtration of the slurry and thorough washing of the filter cake with three 100-ml. portions of dry ether afford dimethylamine hydrochloride, quantitatively (Note 6). The clear filtrate is concentrated on a rotary evaporator connected to a water aspirator in a bath not exceeding 40° to give 152–154 g. (94–95%) of hexamethylphosphorous triamide as a light yellow oil. The product can be purified by distillation at atmospheric pressure, b.p. 162–4°, or under reduced pressure, b.p. 49–51° (12 mm.),  $n_D^{25}$  1.4636 (Note 7). Hexamethylphosphorous triamide is best stored in a nitrogen atmosphere (Note 8).

### 2. Notes

1. An equal volume of a hydrocarbon solvent (pentane, hexane, benzene) can be substituted for ether without affecting the yield of the triamide.
2. The lower part of the gas-inlet tube, which reaches below the surface of the liquid, should be wide enough that it will not be clogged by the amine hydrochloride. A 12-mm. I.D. glass tube was found satisfactory.
3. Carbon dioxide is not satisfactory because it reacts with hexamethylphosphorous triamide.
4. Available from the Matheson Company. The checkers used Rohm & Haas anhydrous dimethylamine.
5. The water extract of the clear solution should give, after acidification with dilute nitric acid, no white precipitate with silver nitrate. When free of chloride ion, the water extract gives only a dark coloration or precipitate.
6. The use of a large (9.5 cm. in diameter, 8 cm. high or larger), coarse grade, sintered-glass funnel, which permits the slurring and thorough rinsing of the filter cake, is recommended. Since the conversion of the phosphorous trichloride to the triamide is quantitative, the major cause of lower yields is the retainment of the liquid product by the salt cake.
7. As a safety precaution the exposure of the hot material in the flask to air should be avoided. The checkers recovered 134 g. (82%) of distillate from 153 g. of crude product.
8. Essentially the same procedure can be used to obtain the higher alkyl homologs of hexamethylphosphorous triamide. Since the higher dialkylamines are liquid at room temperature, the gas-inlet tube is replaced by an addition funnel. Alternatively, the mode of addition may be reversed (*i.e.*, phosphorus trichloride may be added to the amine) without affecting the subsequent workup or yield. The higher homologs of hexamethylphosphorous triamide such as the ethyl, *n*-propyl, and *n*-butyl can also be prepared in 95–100% conversion when a slight excess (5–10%) of the amine is employed.

### 3. Discussion

The described procedure is a modification of the method of Carmody and Zletz<sup>2</sup> and of Burg and Slota.<sup>3</sup> The higher homologs were reported by Stuebe and Lankelma.<sup>4</sup>

#### 4. Merits of the Preparation

This is a general method of preparing hexaalkylphosphorous triamides from the corresponding dialkylamines. The procedure is simple, and the yields are high. Hexaalkylphosphorous triamides are powerful nucleophiles.<sup>5</sup> This feature can be used in a rather unique way to synthesize epoxides directly from aldehydes.<sup>5,6</sup> More recently the methyl and ethyl derivatives have been used in desulfurization reactions to prepare thiolactones<sup>7</sup> and thietanes.<sup>8</sup>

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 5, 358](#)
- [Org. Syn. Coll. Vol. 9, 711](#)

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#### References and Notes

1. Hooker Chemical Corporation, Niagara Falls, New York.
2. D. R. Carmody and A. Zletz, U.S. Patent 2,898,732 (1959).
3. A. B. Burg and P. J. Slota, Jr., *J. Am. Chem. Soc.*, **80**, 1107 (1958).
4. C. Stuebe and H. P. Lankelma, *J. Am. Chem. Soc.*, **78**, 976 (1956).
5. V. Mark, *J. Am. Chem. Soc.*, **85**, 1884 (1963).
6. [V. Mark, this volume, p. 358.](#)
7. J. H. Markgraf, C. I. Heller, and N. L. Avery, *J. Org. Chem.*, **35**, 1588 (1970).
8. D. N. Harpp and J. G. Gleason, *J. Org. Chem.*, **35**, 3359 (1970).

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

[Benzene \(71-43-2\)](#)

[ether \(60-29-7\)](#)

[nitric acid \(7697-37-2\)](#)

[silver nitrate \(7761-88-8\)](#)

[nitrogen \(7727-37-9\)](#)

[amine hydrochloride](#)

[carbon dioxide \(124-38-9\)](#)

[phosphorus trichloride,  
phosphorous trichloride \(7719-12-2\)](#)

[dimethylamine \(124-40-3\)](#)

Pentane (109-66-0)

dimethylamine hydrochloride (506-59-2)

chloride ion

hexane (110-54-3)

Hexamethylphosphorous triamide,  
Phosphorous triamide, hexamethyl- (1608-26-0)

phosphorous triamide