



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.

Organic Syntheses, Coll. Vol. 4, p.325 (1963); Vol. 31, p.33 (1951).

DIISOPROPYL METHYLPHOSPHONATE

[Phosphonic acid, methyl-, diisopropyl ester]



Submitted by A. H. Ford-Moore and B. J. Perry¹.

Checked by William S. Johnson and James Ackerman.

1. Procedure

A 2-l. round-bottomed flask containing 284 g. (113 ml., 2 moles) of [methyl iodide](#)² is fitted with an efficient water-cooled condenser and a dropping funnel which is charged with 416 g. (453 ml., 2 moles) of [triisopropyl phosphite](#) (Note 1). A few pieces of porous plate are added to the [methyl iodide](#), and about 50 ml. of the [phosphite](#) is introduced. The mixture is heated over a gauze with a free flame until an exothermic reaction begins. The flame is then withdrawn and the remainder of the phosphite is added at such a rate that the mixture keeps boiling briskly. Towards the end of the addition it may be necessary to reapply heat. After the addition is complete, the mixture is boiled under reflux for 1 hour. The condenser is replaced by a 50–75 cm. Vigreux column attached to a condenser set for distillation, and the bulk of the [isopropyl iodide](#) is distilled at 85–95° (atmospheric pressure). The residue is transferred to a pear-shaped flask for distillation through a 75-cm. Vigreux column under reduced pressure. The remainder of the [isopropyl iodide](#) is distilled at water-pump pressure, a Dry Ice trap being interposed between the receiver and the pump in order to effect complete condensation. A total of 310 g. (91%) of [isopropyl iodide](#) is thus recovered. The residue is then fractionated at vacuum-pump pressure. Except for a small fore-run and residue, the product distils almost entirely at 51°/1.0 mm. (46°/0.8 mm.). The yield of colorless product is 308–325 g. (85–90%); n_D^{20} 1.4101, n_D^{25} 1.4081; d_4^{24} 0.985, d_4^{40} 0.997 (Note 2).

2. Notes

1. The [triisopropyl phosphite](#) is prepared according to the procedure for [triethyl phosphite](#) (p. 955) and should be free from any [diisopropyl hydrogen phosphite](#). The latter substance does not enter into the reaction but is difficult to remove from the final product. The starting material was supplied to the submitters by Messrs. Albright, Wilson and Company, Oldbury, Birmingham, England.

2. [Diisopropyl ethylphosphonate](#) can be obtained by a similar procedure, using the appropriate amount of [ethyl iodide](#) in place of [methyl iodide](#). [Ethyl iodide](#) is less reactive, and it is necessary to apply heat during the addition of the phosphite and to allow the mixture to reflux for 7 hours after the addition. On a 2M scale the yield is 354 g. (91%), b.p. 61°/0.7 mm., n_D^{25} 1.4108, d_4^{25} 0.968. The recovery of [isopropyl iodide](#) is 317 g. (93%).

[Diethyl ethylphosphonate](#) may be obtained by refluxing 332 g. (348 ml., 2 moles) of [triethyl phosphite](#) and 250 g. (1.6 moles) of [ethyl iodide](#), for 3 hours. After distillation of 231 g. (92%) of [ethyl iodide](#), the residue is fractionated under reduced pressure, giving 329 g. (98.5%) of product, b.p. 56°/1 mm. (58.5°/1.8 mm.); n_D^{25} 1.4141, n_D^{20} 1.4161; d_4^{25} 1.022.

[Diethyl methylphosphonate](#) may be prepared similarly by refluxing one molar equivalent of [triethyl phosphite](#) with one mole of [methyl iodide](#), but it is very difficult to separate the product from the small amount of [diethyl ethylphosphonate](#) that is formed simultaneously by the interaction of the phosphite with the [ethyl iodide](#) liberated in the reaction. The pure substance boils at 51°/1 mm., n_D^{25} 1.4117, d_4^{25} 1.050.

3. Discussion

[Diisopropyl methylphosphonate](#) has been prepared from [diisopropylethyl phosphite](#) and [methyl](#)

iodide,³ and by treating sodium diisopropylphosphonate with methyl chloride.⁴ The method described here for the preparation of diisopropyl methylphosphonate is a modification of the Arbusov rearrangement.⁵

References and Notes

1. Chemical Defence Experimental Station, Porton, Nr. Salisbury, Wilts, England.
 2. *Org. Syntheses Coll. Vol. 2*, 404 (1943).
 3. Landauer and Rydon, *J. Chem. Soc.*, **1953**, 2224.
 4. Smith, U. S. pats. 2,853,507 [*C. A.*, **53**, 7989 (1959)], 2,880,224 [*C. A.*, **53**, 15978 (1959)].
 5. Arbusov, *Chem. Zentr.*, [II] **77**, 1640 (1906); Ford-Moore and Williams, *J. Chem. Soc.*, **1947**, 1465.
-

Appendix

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

methyl chloride (74-87-3)

Methyl iodide (74-88-4)

Ethyl iodide (75-03-6)

isopropyl iodide (75-30-9)

Diisopropyl methylphosphonate,
Phosphonic acid, methyl-, diisopropyl ester (1445-75-6)

triisopropyl phosphite (116-17-6)

phosphite

Triethyl phosphite (122-52-1)

diisopropyl hydrogen phosphite

Diisopropyl ethylphosphonate (1067-69-2)

Diethyl ethylphosphonate (78-38-6)

Diethyl methylphosphonate (683-08-9)

diisopropylethyl phosphite

sodium diisopropylphosphonate