



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.

PURIFICATION OF TETRAHYDROFURAN

WARNING

It has been reported that serious explosions may occur when impure tetrahydrofuran is treated with solid potassium hydroxide or with concentrated aqueous potassium hydroxide, as has been recommended widely for the purification of tetrahydrofuran; see *Org. Syntheses*, Coll. Vol. **4**, 474, 792 (1963); Vol. **40**, 94 (1960). There is evidence that the presence of peroxides in the tetrahydrofuran being purified was causal. It is strongly recommended, therefore, that this method not be used to dry tetrahydrofuran, if the presence of peroxides is indicated by a qualitative or quantitative test with acidic aqueous iodide solution. Traces of peroxide can be removed by treatment with cuprous chloride; see p. 692. The safety of this operation should be checked first on a small scale (1-5 ml.). It is recommended that tetrahydrofuran containing larger than trace amounts of peroxides be discarded by flushing down a drain with tap water. It must be kept in mind that mixtures of tetrahydrofuran vapor and air are easily ignitable and explosive; purification is best carried out in a hood which is well exhausted and which does not contain an ignition source.

The best procedure for drying tetrahydrofuran appears to be distillation (under nitrogen) from lithium aluminum hydride. This operation should not be attempted until it is ascertained that the tetrahydrofuran is peroxide-free and also not grossly wet. A small-scale test can be carried out in which a small amount of lithium aluminum hydride is added to ca. 1 ml. of the tetrahydrofuran to determine whether a larger-scale drying operation with lithium aluminum hydride would be too vigorous for safe operation. Tetrahydrofuran so purified rapidly absorbs both oxygen and moisture from air. If not used immediately, the purified solvent should be kept under nitrogen in a bottle labeled with the date of purification. Storage for more than a few days is not advised unless 0.025% of 2,6-di-*t*-butyl-4-methyl phenol is added as an antioxidant.

There are no indications that *peroxide-free*, but moisture containing, tetrahydrofuran cannot safely be predried over potassium hydroxide. However, even this operation should be attempted only after a test-tube scale experiment to make sure that a vigorous reaction does not occur.

A peroxide-free grade of anhydrous tetrahydrofuran (stabilized by 0.025% of 2,6-di-*t*-butyl-4-methyl phenol) is available currently (1966) from Fisher Scientific Co. in 1-lb. bottles. This product as obtained from freshly opened bottles has been found to be suitable for reactions such as the formation of Grignard reagents in which purity of solvent is critical (duPont Co., unpublished observations). It is standard practice in at least one laboratory to use only tetrahydrofuran (Fisher) from freshly opened bottles and to discard whatever material is not used within 2- 3 days.

References and Notes
