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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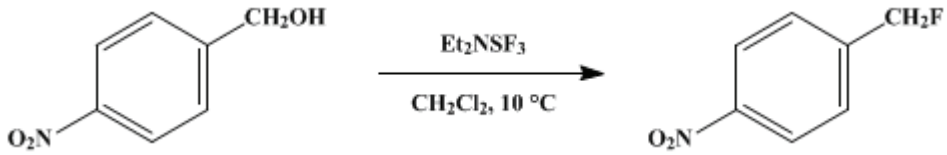
Organic Syntheses, Coll. Vol. 6, p.835 (1988); Vol. 57, p.72 (1977).

4-NITROBENZYL FLUORIDE

[Benzene, 1-(fluoromethyl)-4-nitro-]



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1. Procedure

Caution! Protective gloves should be worn when handling diethylaminosulfur trifluoride because this material can cause severe HF burns.

A dry, 1-l., three-necked, round-bottomed flask is fitted with a 500-ml. dropping funnel, thermometer, a magnetic stirrer, and a reflux condenser protected from the atmosphere with a drying tube. The apparatus is flushed with dry nitrogen, and 150 ml. of dry dichloromethane and 21 ml. (0.16 mole) of diethylaminosulfur trifluoride [*Org. Synth.*, **Coll. Vol. 6**, 440 (1988)] are added to the flask. The contents of the flask are cooled to 10°, and a solution of 23.0 g. (0.150 mole) of 4-nitrobenzyl alcohol (Note 1) in 450 ml. of dichloromethane is added dropwise at a fast rate (45 minutes). The reaction mixture is allowed to come to room temperature and poured into a beaker containing 300 g. of ice, decomposing any unreacted diethylaminosulfur trifluoride. The organic layer is separated, and the water layer is extracted twice with 45-ml. portions of dichloromethane. The organic layer and extracts are combined, washed with 150 ml. of water, and dried over anhydrous magnesium sulfate. Evaporation to dryness under reduced pressure gives 20.9–22.1 g. (90–95%) of crude product. Recrystallization from 500 ml. of pentane yields 15.5 g. (67%) of 4-nitrobenzyl fluoride as colorless needle-shaped crystals, m.p. 36–37° (Note 2).

2. Notes

1. 4-Nitrobenzyl alcohol is available from Eastman Organic Chemicals or Aldrich Chemical Company, Inc.
2. An additional quantity of product of lesser purity can be obtained as a second crop by evaporation of the pentane.

3. Discussion

This procedure is an example of a broadly applicable, simple method for replacing the hydroxyl group of functionally substituted and unsubstituted primary, secondary, and tertiary alcohols with fluorine. Diethylaminosulfur trifluoride,[2] the fluorinating reagent used in this procedure, is less likely to cause rearrangements or dehydration than other reagents sometimes used for this purpose (SF_4, HF, HF·pyridine, SeF_4·pyridine, and $(C_2H_5)_2NCF_2CHClF$).[3] Furthermore, diethylaminosulfur trifluoride is a liquid that can be measured easily and used in standard glass equipment at moderate temperatures and atmospheric pressure.

Some alcohols that have been converted into the corresponding fluorides by reactions with diethylaminosulfur trifluoride include 1-octanol, 2-methyl-2-butanol, 2-butanol, cycloöctanol, ethylene glycol, crotyl alcohol, 2-phenylethanol, 2-bromoethanol, ethyl lactate, and ethyl α-hydroxynaphthaleneacetate.[3]

4-Nitrobenzyl fluoride has also been prepared in 40–60% yield by the reaction of 4-nitrobenzyl bromide with mercuric fluoride[4] and in mixture with the *ortho* and *meta* isomers by the nitration of benzyl fluoride.[5]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 440
- Org. Syn. Coll. Vol. 6, 628

References and Notes

1. Central Research and Development Department, Experimental Station, E. I. duPont deNemours and Co., Wilmington, Del. 19898.
2. W. J. Middleton and E. M. Bingham, *Org. Synth.*, **Coll. Vol. 6**, 440 (1988).
3. W. J. Middleton, *J. Org. Chem.*, **40**, 574 (1975).
4. J. Bernstein, J. S. Roth, and W. T. Miller, *J. Am. Chem. Soc.*, **70**, 2310 (1948).
5. C. K. Ingold and C. H. Ingold, *J. Chem. Soc.*, 2249 (1928).

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

nitrogen (7727-37-9)

2-BROMOETHANOL (540-51-2)

ethylene glycol (107-21-1)

Pentane (109-66-0)

dichloromethane (75-09-2)

2-phenylethanol (60-12-8)

ethyl lactate (687-47-8)

magnesium sulfate (7487-88-9)

1-Octanol (111-87-5)

2-Methyl-2-butanol (75-85-4)

Fluorine (7782-41-4)

mercuric fluoride (7783-39-3)

Crotyl alcohol

2-Butanol (78-92-2)

Diethylaminosulfur trifluoride (38078-09-0)

4-NITROBENZYL FLUORIDE,
Benzene, 1-(fluoromethyl)-4-nitro- (500-11-8)

4-nitrobenzyl alcohol (619-73-8)

ethyl α-hydroxynaphthaleneacetate

4-nitrobenzyl bromide (100-11-8)

benzyl fluoride (350-50-5)

cyclooctanol