



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.

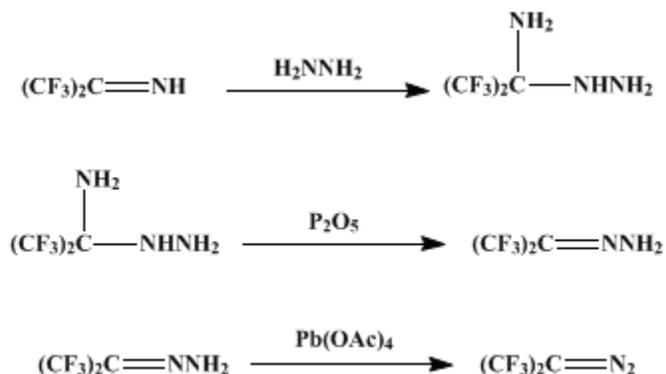
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.161 (1988); Vol. 50, p.6 (1970).

BIS(TRIFLUOROMETHYL)DIAZOMETHANE

[Propane, 2-diazo-1,1,1,3,3,3-hexafluoro-]



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1. Procedure

Caution! This procedure should be carried out in a good hood and behind a shield to avoid exposure to the toxic compounds, hexafluoroacetone imine and hydrazine.

A. *Hexafluoroacetone hydrazone*. A 100-ml., three-necked, round-bottomed flask fitted with a thermometer, a gas-inlet tube, a Dewar condenser, and a magnetic stirring bar is charged with 16 g. (0.50 mole) of anhydrous hydrazine [*Org. Synth., Coll. Vol. 6, 10 (1988)*] and cooled in an ice-methanol bath. The condenser is filled with a cooling mixture of ice and methanol, the magnetic stirrer is started, and 82.5 g. (0.500 mole) (Note 1) of hexafluoroacetone imine [*Org. Synth., Coll. Vol. 6, 664 (1988)*] is slowly distilled into the flask through the gas-inlet tube, while the temperature is maintained below 10°. After the addition, which requires about 1 hour, the cooling bath is removed and the reaction mixture is allowed to warm to room temperature, then poured rapidly into a 500-ml., single-necked, round-bottomed flask containing 150 g. of phosphorus pentoxide. A spatula is used to partially mix the liquid with the phosphorus pentoxide (Note 2); the flask is quickly fitted with a simple still head with condenser and heated with a heating mantle until no further distillation occurs (Note 3). The crude distillate is redistilled through a 45-cm. spinning-band column, giving 48–53 g. (53–59% conversion) of hexafluoroacetone hydrazone as a colorless liquid, b.p. 95.5–96°, n_D^{25} 1.3298.

B. *Bis(trifluoromethyl)diazomethane*. A 1-l., three-necked, round-bottomed flask is equipped with a sealed mechanical stirrer and a 100-ml., pressure-equalizing dropping funnel. The third neck is connected with pressure tubing to a 50-ml. capacity cold trap immersed in an acetone-dry ice cooling bath and protected from the atmosphere with a calcium chloride drying tube. The system is purged with nitrogen, and 375 ml. of benzonitrile and 120 g. (0.271 mole) of lead tetraacetate (Note 4) are placed in the flask. Stirring is started and the flask is cooled with an ice bath before a solution of 45 g. (0.25 mole) of hexafluoroacetone hydrazone in 50 ml. of benzonitrile is added with the dropping funnel over a period of 1 hour. The ice bath is removed and the reaction mixture is stirred for an additional hour at room temperature. During this time some product collects in the cold trap. The remaining product is distilled into the trap at 10 mm. pressure by removing the drying tube and connecting the trap to a pump or aspirator (a small amount of acetic acid and other impurities can be removed by trap-to-trap distillation), yielding 20–21 ml. or 34–35 g. (76–79%) (Note 5) of bis(trifluoromethyl)diazomethane as a yellow liquid, b.p. 12–13°. The product is neither impact- nor static-sensitive (Note 6) and is stable to long storage at –78°; however, it partly decomposes with loss of nitrogen after several weeks at room temperature.

2. Notes

1. If it is inconvenient to distill the **hexafluoroacetone imine** directly from a cylinder, it may be condensed first in a calibrated cold trap cooled to -10° , then distilled from the trap into the reaction mixture. About 55 ml. of the imine, measured at -10° , corresponds to 0.5 mole.
2. *Caution! A spontaneous reaction may result if mixing is prolonged beyond 1 minute. Rubber gloves should be worn to avoid exposure to hydrazine vapors.*
3. About 14 g. (17%) of **hexafluoroacetone imine** can be recovered during the redistillation step if the receivers for both distillations are cooled to -10° or lower. The yield of the hydrazone is about 67% if the recovered imine is taken into account.
4. Since **acetic acid** does not interfere with this reaction, a grade of **lead tetraacetate** that has been stabilized with **acetic acid** may be used.
5. The submitters have obtained yields as high as 90% on runs two times this scale.
6. *Caution! Toxicity data on this material are not available; therefore, it should be assumed to be as toxic as other diazo compounds and handled only in an efficient hood. Although it has been stored in stainless-steel cylinders at autogenous pressure and handled without incident, contact with reagents likely to initiate rapid evolution of nitrogen should be carried out with caution.*

3. Discussion

Bis(trifluoromethyl)diazomethane has been prepared by the nitrosation of 1,1,1,3,3,3-hexafluoroisopropylamine² and by the present procedure,³ which gives higher yields. **Bis(perfluoroethyl)diazomethane** has also been prepared by an extension of this method.²

Bis(trifluoromethyl)diazomethane is a reactive, electrophilic compound, in that it forms adducts with nucleophiles such as amines and phosphines³ and adds to olefins, acetylenes,³ and thiocarbonyl compounds, forming heterocycles. It has been used as a source of **bis(trifluoromethyl)carbene** in reactions with **benzene**,³ saturated hydrocarbons,⁴ **carbon disulfide**,⁵ and transition metal compounds,⁶ and it undergoes a unique radical chain reaction with saturated hydrocarbons, giving hydrazone and azine adducts.⁴

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 6, 392*

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References and Notes

1. Central Research and Development Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898.
2. E. P. Mochalina and B. L. Dayatkin, *Izv. Akad. Nauk SSSR Ser. Khim.*, **5**, 926 (1965).
3. D. M. Gale, W. J. Middleton, and C. G. Krespan, *J. Am. Chem. Soc.*, **88**, 3617 (1966).
4. W. J. Middleton, D. M. Gale, and C. G. Krespan, *J. Am. Chem. Soc.*, **90**, 6813 (1968).
5. M. S. Raasch, *Chem. Commun.*, 577 (1966).
6. J. Cooke, W. R. Cullen, M. Green, and F. G. A. Stone, *Chem. Commun.*, 170 (1968).
7. W. J. Middleton, *J. Org. Chem.*, **34**, 3201 (1969).

Appendix

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

1,1,1,3,3,3-hexafluoroisopropylamine

acetic acid (64-19-7)

Benzene (71-43-2)

methanol (67-56-1)

benzonitrile (100-47-0)

nitrogen (7727-37-9)

carbon disulfide (75-15-0)

hydrazine (302-01-2)

Bis(trifluoromethyl)diazomethane,
Propane, 2-diazo-1,1,1,3,3,3-hexafluoro- (684-23-1)

Hexafluoroacetone imine (1645-75-6)

Hexafluoroacetone hydrazone (1588-41-6)

Bis(perfluoroethyl)diazomethane

bis(trifluoromethyl)carbene

phosphorus pentoxide (1314-56-3)

lead tetraacetate (546-67-8)