



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.

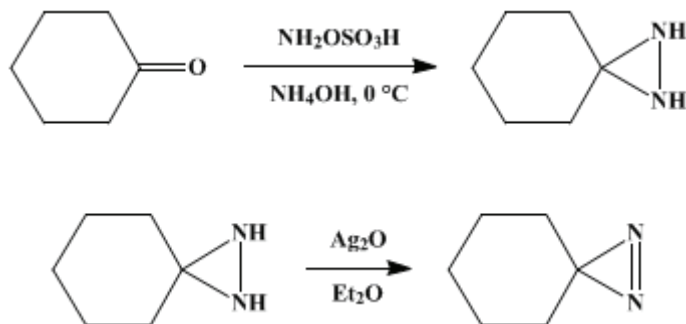
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

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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.*

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### 3,3-PENTAMETHYLENEDIAZIRINE



Submitted by Ernst Schmitz and Roland Ohme<sup>1</sup>.  
Checked by E. J. Corey and Richard Glass.

## 1. Procedure

A. *3,3-Pentamethylenediaziridine*. A solution of 147 g. (1.5 moles) of **cyclohexanone** in 400 ml. of 15*N* aqueous **ammonia** (6.0 moles) in a 1-l. beaker is stirred mechanically and cooled to 0° with an ice-salt mixture. Maintaining the temperature of the solution between 0° and +10°, 124 g. (1.0 mole) of 90% **hydroxylamine-O-sulfonic acid** (Note 1) is added in portions of about 1 g. The addition requires about 1 hour, and the mixture is stirred for another hour at 0° and allowed to stand overnight at -15° in a refrigerator. The precipitated crystalline cake is filtered and pressed tight with a glass stopper. The solid is washed with 50-ml. portions of ice-cold **ether**, **toluene**, and finally **ether**. There is obtained 110–115 g. of product which is 70–90% pure (Note 2) and (Note 3). The product is divided into two portions, each of which is boiled briefly with a 50-ml. portion of **toluene**; the solutions are decanted from small salt residues and cooled to 0° for 2 hours. The precipitates are filtered with suction and washed with 50 ml. of ice-cold petroleum ether. The combined yield of **3,3-pentamethylenediaziridine** is 68–78 g. (61–70%), m.p. 104–107°. The purity is 96–100% (Note 4).

B. *3,3-Pentamethylenediazirine*. **Caution!** See (Note 5). A solution of 34.0 g. (0.2 mole) of **silver nitrate** in 100 ml. of water is treated dropwise, with shaking, with 100 ml. of 2*N* **sodium hydroxide**. The precipitate is filtered with suction and washed thoroughly with water, **methanol**, and lastly **ether**. A mixture of 10.0 g. (0.089 mole) of **3,3-pentamethylenediaziridine** (Note 5) and 220 ml. of **ether** is warmed, the resulting solution cooled to room temperature, and within a 5-minute period the **silver oxide** prepared above is added in small portions, with shaking, to the cooled solution. During the addition the reaction mixture is cooled with tap water and then is shaken without cooling until an aliquot does not liberate **iodine** from an acidified iodide solution; the reaction is normally complete in 30–60 minutes. The mixture is filtered through a fluted filter, the solid residue washed with a small volume of **ether**, and the filtrate dried over **potassium carbonate**. The **ether** is distilled at a bath temperature of 45° through a 30-cm. Vigreux column. The last 20 ml. of the solvent is removed at a pressure of 30 mm. and a bath temperature of 10°. Using a protective shield, the residue is distilled at 33° (30 mm.) to yield 6.4–7.4 g. (65–75%) of **3,3-pentamethylenediazirine**. In order to prevent decomposition of the product on storage, it is diluted with ether and kept in a refrigerator.

## 2. Notes

1. **Hydroxylamine-O-sulfonic acid** is prepared according to the method of Gösl and Meuwesen,<sup>2</sup> or of Matsuguma and Audrieth.<sup>3</sup> The material is available from Eastman Organic Chemicals. Analysis of this substance, just prior to use, is carried out in the following manner. A sample is dissolved in water and treated with a solution of **potassium iodide** in 2*N* **sulfuric acid**. After 5 minutes the solution is titrated with thiosulfate solution; near the end of the titration the solution is boiled to ensure completeness of **iodine** liberation. Instead of the 90% product, a correspondingly greater amount of the 80% product can be employed.

2. For the analysis an ethanolic solution of the 3,3-pentamethylenediaziridine is treated with a solution of potassium iodide in 2N sulfuric acid. It liberates two equivalents of iodine instantaneously.
3. The crude product is recrystallized without additional drying; it undergoes partial decomposition on standing.
4. If subsequent treatment is not to be performed within a few days, it is recommended that the preparation be recrystallized a second time to obtain a stable product. Smaller amounts can be advantageously purified by vacuum sublimation.
5. It is recommended that the dehydrogenation be done with small amounts if the dehydrogenation product is to be isolated. Although decomposition was never observed with the preceding procedure, *diazirines should be handled with caution. Explosions were reported when working with 3-methyldiazirine<sup>4</sup> and 3-n-propyldiazirine<sup>4</sup> as well as when overheating pentamethylenediazirine.<sup>5</sup>* Most of the reactions of diazirines, especially the reaction with Grignard compounds,<sup>5</sup> can be done without purification of the diazirine.

### 3. Discussion

Diazirines have been prepared by dehydrogenation of diaziridines with mercuric oxide,<sup>6</sup> silver oxide,<sup>5</sup> or dichromate-sulfuric acid.<sup>4</sup> The present procedure corresponds to that of Schmitz and Ohme.<sup>5</sup> The procedure for the preparation of the 3,3-pentamethylenediaziridine has been reported by H. J. Abendroth.<sup>7</sup>

### 4. Merits of the Preparation

Diazirines are the cyclic isomers of the aliphatic diazo compounds. Both the diaziridines and the diazirines are starting materials for the synthesis of alkyl hydrazines. 3,3-Pentamethylenediaziridine can be hydrolyzed quantitatively to hydrazine. Methylamine<sup>8</sup> may be substituted for ammonia in the procedure resulting in 1-methyl-3,3-pentamethylenediaziridine (m.p. 35–36°, yield 62% of theoretical) and then methyl hydrazine. Use of ethylenediamine leads to ethylene bis-hydrazine<sup>9</sup> via a bifunctional diaziridine (m.p. 143–144°, yield 48% of theoretical). Ammonia can also be replaced by n-propylamine<sup>7</sup> or cyclohexylamine<sup>9</sup>; cyclohexanone by acetone.

3,3-Pentamethylenediazirine and other diazirines easily add Grignard reagents to the N—N double bond. The reaction leads to N-alkyl diaziridines which can be hydrolyzed to alkyl hydrazines. Cyclohexylhydrazine (85% yield), n-propylhydrazine (88%), isopropylhydrazine (95%), and benzylhydrazine were prepared from 3,3-pentamethylenediazirine and the corresponding Grignard reagent.<sup>10</sup>

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### References and Notes

1. Institute for Organic Chemistry of the German Academy of Sciences, Berlin-Adlershof, East Germany.
  2. R. Gösl and A. Meuwesen, *Ber.*, **92**, 2521 (1959).
  3. H. J. Matsuguma and L. Audrieth, *Inorg. Syn.*, **5**, 122 (1957).
  4. E. Schmitz and R. Ohme, *Ber.*, **95**, 795 (1962).
  5. E. Schmitz and R. Ohme, *Ber.*, **94**, 2166 (1961).
  6. S. R. Paulsen, *Angew. Chem.*, **72**, 781 (1960).
  7. H. J. Abendroth, *Angew. Chem.*, **73**, 67 (1961).
  8. E. Schmitz, R. Ohme, and R. D. Schmidt, *Ber.*, **95**, 2714 (1962).
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  10. E. Schmitz and R. Ohme, *Angew. Chem.*, **73**, 220 (1961).
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## (Registry Number)

petroleum ether

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

Cyclohexanone (108-94-1)

silver oxide (20667-12-3)

silver nitrate (7761-88-8)

potassium iodide (7681-11-0)

mercuric oxide (21908-53-2)

iodine (7553-56-2)

acetone (67-64-1)

toluene (108-88-3)

hydrazine (302-01-2)

methylamine (74-89-5)

cyclohexylamine (108-91-8)

methyl hydrazine (60-34-4)

ethylenediamine (107-15-3)

Hydroxylamine-O-sulfonic acid (2950-43-8)

3,3-Pentamethylenediazirine (930-82-5)

3,3-Pentamethylenediaziridine (185-79-5)

3-methyldiazirine

3-n-propyldiazirine

pentamethylenediazirine

1-methyl-3,3-pentamethylenediaziridine (61008-71-7)

ethylene bis-hydrazine

Cyclohexylhydrazine

isopropylhydrazine (2257-52-5)

benzylhydrazine (555-96-4)

n-propylamine (107-10-8)

n-propylhydrazine (5039-61-2)