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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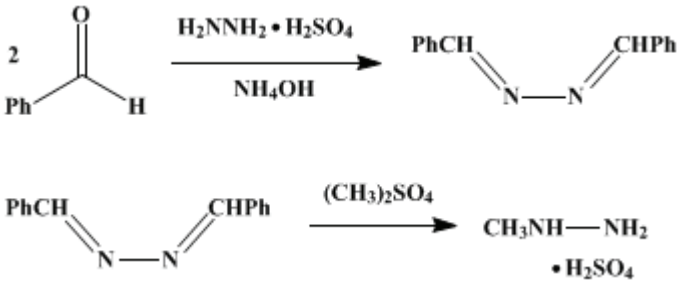
METHYLHYDRAZINE SULFATE

[Hydrazine, methyl-, sulfate]



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1. Procedure

(*A*) *Benzalazine*.—In a 5-l. round-bottomed flask, provided with a stout glass mechanical stirrer, are placed 240 g. (1.85 moles) of powdered hydrazine sulfate (Org. Syn. Coll. Vol. I, **1941**, 309), 1.8 l. of water, and 230 cc. (207 g., 3.4 moles) of 28 per cent aqueous ammonia (sp. gr. 0.90). The mixture is stirred, and, when the hydrazine sulfate has dissolved, 440 cc. (460 g., 4.35 moles) of benzaldehyde (Note 1) is added from a separatory funnel during the course of four to five hours (Note 2). After the mixture has been stirred for a further two hours, the precipitated benzalazine is filtered with suction, washed with water, and pressed thoroughly on a Büchner funnel. The product is dissolved in 800 cc. of boiling 95 per cent ethyl alcohol, and, on cooling, the azine separates in yellow needles melting at 92–93°. The yield is 350–360 g. (91–94 per cent of the theoretical amount); an additional 10–15 g. of less pure material can be isolated from the mother liquors. The azine is freed of ethyl alcohol by drying in a vacuum desiccator over calcium chloride.

(*B*) *Methylhydrazine Sulfate*.—Two hundred grams (0.96 mole) of benzalazine, 350 cc. of dry, thiophene-free benzene, and 100 cc. (133 g., 1.05 moles) of methyl sulfate (Note 3) are mixed in a 3-l. round-bottomed flask, provided with a reflux condenser bearing a calcium chloride tube. The mixture is heated continuously, with occasional shaking, on a water bath to gentle refluxing for five hours. The mixture is cooled, and the solid addition product is decomposed by adding 600 cc. of water and shaking until all the solid material has disappeared. The benzene and benzaldehyde are removed by steam distillation; the residual liquor, after cooling, is treated with 15–20 cc. of benzaldehyde and left overnight. The resin and benzalazine are separated by filtration (Note 4).

The filtrate is evaporated under reduced pressure on a water bath until a semi-crystalline mass remains; this is further desiccated by evaporating twice under reduced pressure with 50-cc. portions of absolute ethyl alcohol. The resulting crystalline cake is crushed with 50 cc. of absolute ethyl alcohol, filtered, and the process repeated. The white, crystalline product is almost pure methylhydrazine sulfate and contains very little hydrazine sulfate. After drying in a vacuum desiccator over calcium chloride, the yield is 105–110 g. (76–80 per cent of the theoretical amount). For purification, the sulfate is dissolved in about 250 cc. of boiling 80 per cent ethyl alcohol, and any undissolved material (chiefly hydrazine sulfate) is filtered. On cooling, the methylhydrazine sulfate separates in white plates, which are filtered with suction and washed with a little absolute alcohol. After drying over calcium chloride, the first fraction, m.p. 141–142°, weighs 70–75 g. (51–54 per cent of the theoretical amount) (Note 5).

2. Notes

1. The benzaldehyde should be freed of benzoic acid by shaking with aqueous sodium carbonate solution.

2. The mixture is stirred vigorously during the reaction, and one or two stout glass rods are clamped in the flask to act as baffles and to break up the lumps of benzalazine.
3. Methyl sulfate is extremely toxic. It should not be spilled; neither should the vapor be inhaled. Ammonia is a specific antidote.
4. Unreacted hydrazine sulfate is removed by conversion to benzalazine. The filtrate should not give an appreciable precipitate when mixed with 5 cc. of benzaldehyde and left for four hours.
5. From the mother liquors about 12 g. of less pure material, m.p. 133–136°, can be recovered.

3. Discussion

The procedure given above is essentially the method of Thiele.[1] Methylhydrazine has also been prepared by reduction and subsequent hydrolysis of nitrosomethylurea,[2] nitromethylurethane,[3] and nitrosomethylamine sulfonic acid;[4] and by methylation of hydrazine hydrate with methyl iodide[5] or diazomethane.[6]

References and Notes

1. Thiele, Ann. **376**, 244 (1910).
2. Brüning, ibid. **253**, 7 (1889).
3. Backer, Rec. trav. chim. **31**, 193 (1912).
4. Traube and Brehmer, Ber. **52**, 1286 (1919).
5. Harries and Haga, ibid. **31**, 56 (1898).
6. Staudinger and Kupfer, ibid. **45**, 501 (1912).

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

Benzalazine

ethyl alcohol,
alcohol (64-17-5)

calcium chloride (10043-52-4)

ammonia (7664-41-7)

Benzene (71-43-2)

sodium carbonate (497-19-8)

Benzoic acid (65-85-0)

benzaldehyde (100-52-7)

Methyl iodide (74-88-4)

methyl sulfate (75-93-4)

hydrazine hydrate (7803-57-8)

Hydrazine sulfate (10034-93-2)

Diazomethane (334-88-3)

Nitrosomethylurea

Methylhydrazine sulfate,
Hydrazine, methyl-, sulfate (302-15-8)

Methylhydrazine (60-34-4)

nitromethylurethane

nitrosomethylamine sulfonic acid