



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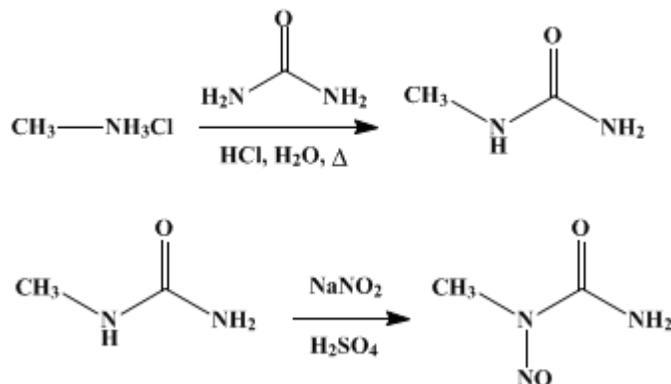
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.461 (1943); Vol. 15, p.48 (1935).

NITROSOMETHYLUREA

[Urea, α -methyl- α -nitroso-]

[I. (From Methylamine Hydrochloride)]



Submitted by F. Arndt

Checked by C. R. Noller and S. Lieberman.

1. Procedure

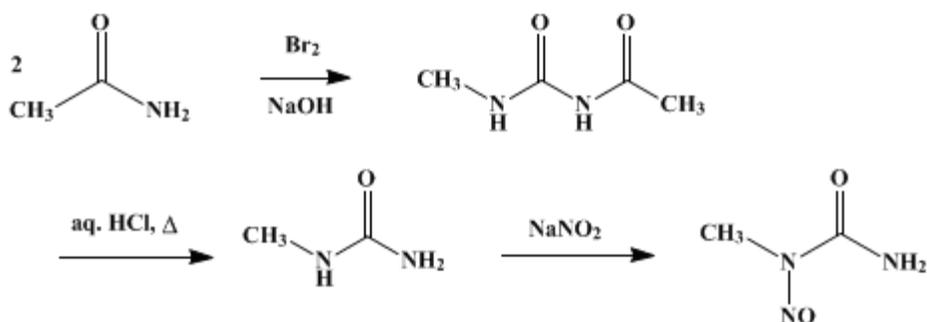
In a tared 1-l. flask is placed 200 g. (1.5 moles) of 24 per cent aqueous methylamine solution (Note 1), and concentrated hydrochloric acid is added until the solution is acid to methyl red; about 155 cc. of acid is required. Water is added to bring the total weight to 500 g., 300 g. (5 moles) of urea is added, and the solution is boiled gently under reflux for two and three-quarters hours and then vigorously for one-quarter hour. The solution is cooled to room temperature, 110 g. (1.5 moles) of 95 per cent sodium nitrite is dissolved in it, and the whole is cooled to 0°. A mixture of 600 g. of ice and 100 g. (1 mole) of concentrated sulfuric acid in a 3-l. beaker is surrounded by an efficient freezing mixture, and the cold methylurea-nitrite solution is run in slowly with mechanical stirring at such a rate that the temperature does not rise above 0° (Note 2).

The nitrosomethylurea rises to the surface as a crystalline foamy precipitate which is filtered at once with suction and pressed well on the filter. The crystals are stirred to a paste with about 50 cc. of cold water, sucked as dry as possible (Note 3), and dried in a vacuum desiccator to constant weight. The yield is 105–115 g. (66–72 per cent of the theoretical amount) (Note 4).

2. Notes

1. The methylamine content of the commercial aqueous solution (Röhm and Haas) was determined by titration with standard acid using methyl red as indicator. If the methylamine content is found to be different an equivalent quantity is used.
2. It is convenient to keep the methylurea-nitrite solution in an ice-salt bath and to siphon it into the acid solution, the end of the siphon dipping below the surface. About one hour is required for the addition.
3. A sample of the moist product should dissolve completely in boiling methyl alcohol. If an appreciable residue remains, which is not usually the case, the washing process is repeated. Each successive washing decreases the yield somewhat.
4. The preparation obtained in this way may be kept indefinitely in a refrigerator. It should not be kept above 20° for more than a few hours. At temperatures in the neighborhood of 30° it may undergo a sudden decomposition without explosion but with the evolution of irritating fumes. It has been reported that the stability is increased by the addition of a few drops of acetic acid.

[II. (From Acetamide)]



Submitted by E. D. Amstutz and R. R. Myers.

Checked by C. F. H. Allen and J. Dec.

1. Procedure

(A) *Acetyl Methylurea*.—To a solution (Note 1) of 59 g. (1 mole) of acetamide in 88 g. (0.55 mole) of bromine in a 4-l. beaker is added, dropwise and with hand stirring, a solution of 40 g. (1 mole) of sodium hydroxide in 160 cc. of water. The resulting yellow reaction mixture is heated on a steam bath until effervescence sets in (Note 2), after which heating is continued for an additional two to three minutes. Crystallization of the product from the yellow to red colored solution usually commences immediately (Note 3) and is completed by cooling in an ice bath for one hour. The weight of the white crystalline acetyl methylurea obtained by filtration and air drying is 49–52 g. (84–90 per cent of the theoretical amount) (Note 4)(Note 5). It melts at 169–170°.

(B) *Nitrosomethylurea*.—A mixture of 49 g. (0.42 mole) of acetyl methylurea (Note 6) and 50 cc. of concentrated hydrochloric acid is heated, with hand stirring, on a steam bath until it is apparent that no more solid (Note 5) is dissolving. Heating is continued for three or four minutes longer (total time on steam bath—eight to twelve minutes), after which the solution is diluted with an equal volume of water and cooled below 10° in an ice bath. A cold saturated solution of 38 g. (0.55 mole) of sodium nitrite in 55 cc. of water is then run in slowly with stirring. The mixture is allowed to remain in the ice bath for several minutes, after which the nitrosomethylurea is filtered and washed with about 8–10 cc. of ice-cold water. Air drying gives 33–36 g. (76–82 per cent of the theoretical amount) of nitrosomethylurea as pale yellow crystals melting at 123–124°.

2. Notes

1. Gentle heating on a steam bath assists in dissolving the acetamide. Care is necessary, however, to see that only the minimum amount of bromine is lost during the heating.
2. Occasionally this effervescence becomes quite brisk, and for this reason a large container is used.
3. If the solution at this point is perfectly colorless, the product is usually slower in crystallizing, it contains more sodium bromide, and the yield is somewhat lower. For these reasons, the slight excess of bromine used is necessary.
4. When the crude yield is the lower figure given, the remainder of the product can be secured by long cooling of the filtrate in ice.
5. The crude acetyl methylurea contains some sodium bromide, which appears as a white crystalline material insoluble in concentrated hydrochloric acid in Part (B). The sodium bromide dissolves when the solution is diluted and has no effect upon the subsequent treatment with sodium nitrite.
6. The acetyl methylurea prepared in Part (A) may be used without drying.

3. Discussion

Nitrosomethylurea is always prepared by the nitrosation of methylurea. Methylurea, in turn, can be prepared from (a) methylamine hydrochloride and potassium cyanate;¹ (b) methyl sulfate, ammonia, and potassium cyanate;¹ (c) methylamine hydrochloride and urea;² and (d) acetamide, bromine, and alkali.³ Checked directions for preparing methylurea, and for its subsequent nitrosation, according to (a) and (b)

are described on p. 48 of Volume 15 of *Organic Syntheses*. The preparation of methylurea, and its subsequent nitrosation, according to (c) and (d) are given in procedures I and II, above. The preparations using potassium cyanate suffer because of the difficulty and the expense of obtaining that reagent. Arndt, Loewe, and Avan² have discussed the merits of the different methods of preparing nitrosomethylurea.

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 2*, 165

References and Notes

1. Arndt and Amende, *Z. angew. Chem.* **43**, 444 (1930); Arndt and Scholz, *ibid.* **46**, 47 (1933).
 2. Arndt, Loewe, and Avan, *Ber.* **73**, 606 (1940); Eistert, *Angew. Chem.* **54**, 124 (1941).
 3. Owen, Ramage, and Simonsen, *J. Chem. Soc.* **1938**, 1213.
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Methyl Red

Urea, α -methyl- α -nitroso-
sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

Acetamide (60-35-5)

acetic acid (64-19-7)

ammonia (7664-41-7)

methyl alcohol (67-56-1)

sodium hydroxide (1310-73-2)

bromine (7726-95-6)

sodium bromide (7647-15-6)

sodium nitrite (7632-00-0)

urea (57-13-6)

methyl sulfate (75-93-4)

Methylamine hydrochloride (593-51-1)

[methylamine \(74-89-5\)](#)

[potassium cyanate \(590-28-3\)](#)

[Nitrosomethylurea](#)

[methylurea-nitrite](#)

[Acetyl methylurea \(623-59-6\)](#)

[methylurea \(598-50-5\)](#)