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.

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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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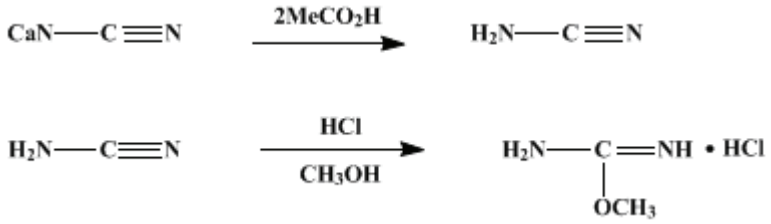
METHYLISOUREA HYDROCHLORIDE

[Pseudourea, 2-methyl-, hydrochloride]



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1. Procedure

A. *Cyanamide*. In a large mortar are placed 57 g. (54 ml., 0.75 mole) (Note 1) of glacial acetic acid and 135 ml. of water (Note 2). To this solution, 40 g. (0.5 mole) of calcium cyanamide (Note 3) is added slowly (Note 4) with good stirring and grinding. As the introduction of the calcium cyanamide proceeds, small quantities of acetylene are evolved, while the initially thin cream gradually turns into a thick, dark-gray to black paste. The mixture must remain acidic to litmus throughout the addition. After being dried at 40–50° for 12–18 hours in a vacuum oven, at a pressure of 30 mm. or less, the material is obtained as a pale-gray, dry powder. This is extracted exhaustively in a Soxhlet apparatus, for 2- to 3-hour periods, with two successive 400-ml. portions of ether (Note 5) containing a few drops of dilute acetic acid. The ethereal extracts (Note 6) are each dried over 30-g. portions of anhydrous sodium sulfate and combined, and the solvent is removed under reduced pressure (Note 7). The colorless, viscous, oily residue of cyanamide is suitable for use in the next stage. The yield of cyanamide is 10.5–15.8 g. (50–75% calculated on the basis of the formula CaNCN) (Note 8) and (Note 9).

B. *Methylisourea hydrochloride*. The crude cyanamide obtained as described above (Part A) is taken up in 100 ml. of anhydrous methanol, and the clear solution is decanted from a trace of insoluble oily material if necessary. Anhydrous hydrogen chloride is passed into the clear colorless liquid until an increase in weight amounting to 1 g. of hydrogen chloride per gram of crude cyanamide (1.15 moles) is attained. During the addition of the hydrogen chloride, the cyanamide solution is maintained at room temperature by external ice-cooling. The resulting clear liquid is set aside for 3–4 days, and the methanol is removed by distillation under reduced pressure. The residual colorless crystalline solid is dried in a vacuum desiccator containing potassium hydroxide and phosphorus pentoxide; it consists of methylisourea hydrochloride. The yield is 1.8–2.1 g. per gram of cyanamide (69–80%) (Note 10).

The material may be crystallized from boiling methanol (1 ml. per gram of crude material) and forms lustrous, colorless, thick, prismatic needles, which melt with decomposition (Note 11) and (Note 12). They are separated by suction filtration at 0° (Note 13) and quickly rinsed with a very little ice-cold methanol. The product is hygroscopic and is quickly pressed between filter paper, then dried in a vacuum desiccator over phosphorus pentoxide. The filtrates yield a further crop on partial evaporation under reduced pressure, the total recovery of recrystallized material being 85–90% (Note 14).

2. Notes

1. The exact amount of acetic acid required by a particular sample of calcium cyanamide is first determined volumetrically as follows: A weighed sample of calcium cyanamide (approximately 1 g.) is suspended in about 50 ml. of distilled water and titrated with standard hydrochloric acid (preferably of approximately normal strength), using phenolphthalein as indicator. Acid is added until the pink color of the indicator does not reappear within 2–3 minutes. From the results of the titration the amount of acetic acid required is calculated by proportion, a 10% excess being allowed to ensure that the reaction

mixture remains acid throughout the experiment.
2. In order to facilitate drying at a later stage, as little water is used as will produce a paste that can still be effectively mixed.
3. Commercial calcium cyanamide (nitrolime), containing carbon and small quantities of calcium carbide, is suitable for this preparation.
4. The addition of the calcium cyanamide to the acid should be slow enough to ensure thorough mixing and to prevent the reaction mixture from becoming hot.
5. The checkers found it desirable to saturate the ether (by shaking) with water before extraction. The Soxhlet extraction should not be prolonged for more than 3–4 hours. If a longer extraction period is employed, a fresh portion of ether should be used so that the extracted material will not be subjected to heat for too long a period.
6. Cyanamide may be kept unchanged at 0° in ethereal solution in the presence of traces of acetic acid. The ethereal extracts from several runs of calcium cyanamide may therefore be combined and worked up collectively.
7. Distillation is best carried out from a previously weighed small flask, and the weighed residue of cyanamide is immediately dissolved in methanol for the next stage.
8. The yields of cyanamide from commercial calcium cyanamide vary from sample to sample but do not fluctuate greatly for one particular specimen. The present procedure was found to be satisfactory for preparing 15- to 30-g. batches of cyanamide.
9. If desired, the cyanamide may be crystallized from a mixture of ether and benzene; however, the crystallization is difficult because of the tendency of the material to oil.
10. This material is satisfactory for most synthetic purposes without further purification.
11. Methylisourea hydrochloride decomposes on heating with evolution of methyl chloride. The decomposition temperature depends on the rate of heating, but reproducible values are obtainable if the rate of heating is controlled. Samples of pure (98–99%) (Note 12) methylisourea hydrochloride, introduced into the melting-point tube without undue previous exposure to atmospheric moisture, placed in the melting-point bath at 60°, and heated at the rate of 12° per minute, sinter at 118–119° and decompose at 122–124° (the mass moving rapidly up in the melting-point tube).
12. The purity of the crystallized product, determined volumetrically by Volhard's method, exceeds 98%. In this procedure, 10 ml. of a 1% solution of methylisourea hydrochloride is acidified with a few drops of nitric acid and treated with 20 ml. of 0.1*N* silver nitrate. After removel of the silver chloride by filtration, the excess of the silver nitrate is estimated with 0.1*N* thiocyanate solution, using ferric alum as indicator. Alternatively, 10-ml. portions of 0.1*N* silver nitrate, acidified with nitric acid, may be titrated directly with the 1% methylisourea hydrochloride solution in the presence of tartrazine.
Owing to the presence of small quantities of free hydrochloric acid in the crude product, the above procedures are applicable to recrystallized specimens only.
13. It has been suggested[2] that it is best to cool the solution to −10°, cool the wash solvent to −15° in ice-salt, and to put some of the cold solvent through the funnel before filtration (the addition of a few chips of Dry Ice to this solvent on the funnel is helpful).
14. Methylisourea hydrochloride should be kept in a desiccator, even for brief storage, and especially for extended periods of time.

3. Discussion

Methylisourea hydrochloride has been prepared by the action of hydrogen chloride on a suspension of silver cyanamide[3] or a solution of cyanamide[4,5] in methanol,[4] and by the action of dimethyl sulfate on urea.[6] The free base is obtained by treating the salt with powdered potassium hydroxide in a water-ether mixture[4] or with sodium methoxide in methanol.[7]

An alternative laboratory preparation of cyanamide and a selection of references to the literature have appeared in *Inorganic Syntheses*.[8] The present method is that of Werner.[9]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 213
- Org. Syn. Coll. Vol. 5, 966

References and Notes

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6. Werner, *J. Chem. Soc.*, **1914**, 927; Janus, *J. Chem. Soc.*, **1955**, 3551.
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8. Pinck and Salisbury, *Inorg. Syntheses*, **3**, 39 (1950).
9. Werner, *J. Chem. Soc.*, **1916**, 1325; Werner, *The Chemistry of Urea*, Longmans, London, 1923, p. 184.

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

calcium cyanamide

calcium carbide

silver cyanamide

acetylene (74-86-2)

hydrogen chloride,
hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

methanol (67-56-1)

ether (60-29-7)

nitric acid (7697-37-2)

silver chloride (7783-90-6)

silver nitrate (7761-88-8)

sodium sulfate (7757-82-6)

dimethyl sulfate (77-78-1)

methyl chloride (74-87-3)

sodium methoxide (124-41-4)

carbon (7782-42-5)

potassium hydroxide (1310-58-3)

urea (57-13-6)

phenolphthalein (77-09-8)

cyanamide (420-04-2)

Methylisourea hydrochloride

Pseudourea, 2-methyl-, hydrochloride (5329-33-9)

tartrazine

phosphorus pentoxide (1314-56-3)