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.

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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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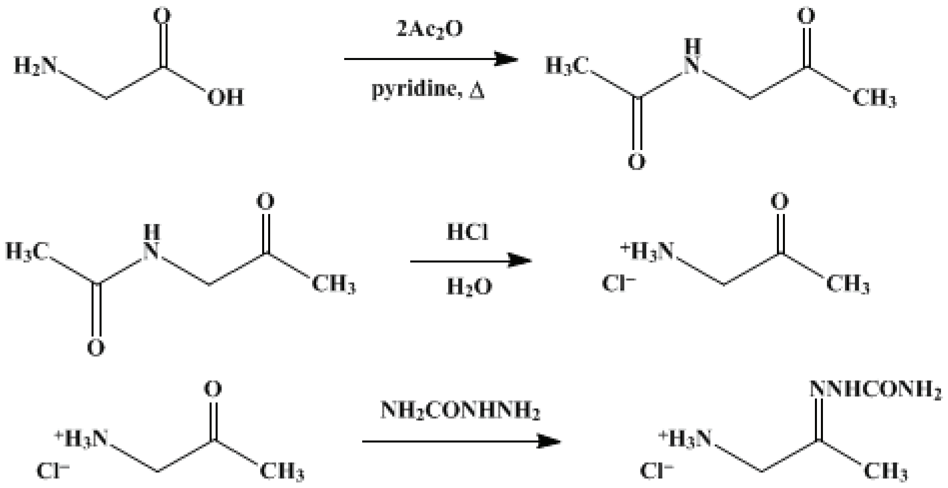
AMINOACETONE SEMICARBAZONE HYDROCHLORIDE

[Amino-2-propanone, semicarbazone hydrochloride]



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1. Procedure

A. *Acetamidoacetone*. A mixture of 75.0 g. (1.0 mole) of glycine (Note 1), 475 g. (485 ml., 6 moles) of pyridine (Note 1), and 1190 g. (1.1 l., 11.67 moles) of acetic anhydride (Note 1) and (Note 2) is heated under reflux with stirring for 6 hours (Note 3) in a 3-l., three-necked, round-bottomed flask. The reflux condenser is replaced by one set for downward distillation, and the excess pyridine, acetic anhydride, and acetic acid are removed by distillation under reduced pressure. The residue is transferred to a simple distillataion apparatus such as a Claisen flask and is distilled to give 80–90 g. (70–78%) of a pale yellow oil, b.p. 120–125° (1 mm.). This product is of satisfactory purity for use in step B.

B. *Aminoacetone hydrochloride*. A mixture of 175 ml. of concentrated hydrochloric acid and 175 ml. of water is added to 52 g. (0.45 mole) of the acetamidoacetone from step A contained in a 1-l. round-bottomed flask. The mixture is boiled under reflux under a nitrogen atmosphere (Note 4) for 6 hours. The resulting solution is concentrated using a flash evaporator held below 60° and with the condensation trap for solvent being cooled by a dry ice-acetone bath. The dark red oily residue (40–45 g.) is satisfactory for use in step C (Note 5).

C. *Aminoacetone semicarbazone hydrochloride*. The product from step B is dissolved in 250 ml. of absolute alcohol in a 1-l. Erlenmeyer flask, and to this solution is added a solution of 48 g. of semicarbazide hydrochloride (Note 1) in 100 ml. of water. The mixture is allowed to stand at room temperature for 2 hours, the crystalline precipitate is collected by suction filtration, and the off-white product is washed on the filter with absolute alcohol. The crystals, after air-drying, amount to 54–58 g. (72–78%) and melt at 208–210°. The product is essentially pure and can be used for most purposes without further purification (Note 6).

2. Notes

1. The glycine, pyridine, acetic anhydride, and semicarbazide hydrochloride employed were of reagent grade and were used directly as supplied.
2. This ratio of pyridine to acetic anhydride has been found to be the most satisfactory.
3. It is necessary that the mixture actually boil under reflux or the yield may drop to 25–30%.
4. The checkers used high-purity nitrogen. If ordinary commercial nitrogen is employed, the oxygen

should be removed by passing the gas through Fieser's solution.
5. Aminoacetone hydrochloride is very hygroscopic and is best stored as the semicarbazone. If the compound itself is desired, however, the dark red oil is dried under reduced pressure over phosphorus pentoxide. The resulting crystalline aminoacetone hydrochloride can be purified by dissolving it in absolute ethanol and precipitating it by the addition of dry ether.
6. For further purification, the semicarbazone hydrochloride may be recrystallized from aqueous ethanol to give colorless crystals, m.p. 212°.

3. Discussion

This preparation is based on the procedure used to synthesize 3-acetamido-2-butanone.[2] Aminoacetone hydrochloride has been prepared from isopropylamine via the N,N-dichloroisopropylamine,[3] from hexamethylenetetramine and chloroacetone,[4] by reduction of nitroacetone[5] or isontirosoacetone,[6] and from phthalimidoacetone by acid hydrolysis,[6] cited as the most convenient method of preparation.[7] The semicarbazone has been prepared previously in the same manner.[8].

4. Merits of the Preparation

Aminoacetone is a versatile starting material for many syntheses, particularly for the preparation of heterocycles. The present procedure describes a convenient method for its preparation in a form suitable for storage. The aminoacetone can be generated from aminoacetone semicarbazone hydrochloride *in situ* as needed.

References and Notes

1. Department of Chemistry, College of Technology, Huddersfield, England; present address, North Lindsey Technical College, Scunthorpe, England.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

semicarbazone

semicarbazone hydrochloride

isontirosoacetone

alcohol,
ethanol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

acetic anhydride (108-24-7)

oxygen (7782-44-7)

nitrogen (7727-37-9)

pyridine (110-86-1)

aminoacetone (298-08-8)

Glycine (513-29-1)

hexamethylenetetramine (100-97-0)

chloroacetone (78-95-5)

isopropylamine (75-31-0)

3-Acetamido-2-butanone (6628-81-5)

Aminoacetone semicarbazone hydrochloride,
Amino-2-propanone, semicarbazone hydrochloride (10469-70-2)

Acetamidoacetone (7737-16-8)

semicarbazide hydrochloride (563-41-7)

Aminoacetone hydrochloride

N,N-dichloroisopropylamine

nitroacetone (10230-68-9)

phthalimidoacetone (3416-57-7)

phosphorus pentoxide (1314-56-3)