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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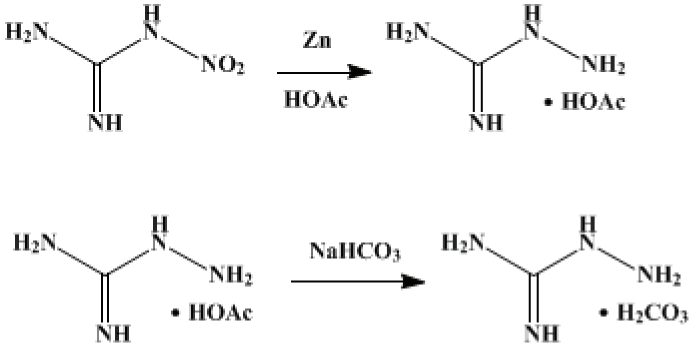
Organic Syntheses, Coll. Vol. 3, p.73 (1955); Vol. 26, p.7 (1946).

AMINOGUANIDINE BICARBONATE

[Guanidine, amino-, bicarbonate]



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1. Procedure

Two hundred and sixteen grams (2.07 moles) of nitroguanidine[1] and 740 g. (11.3 moles) of purified zinc dust (Note 1) are thoroughly ground together in a mortar, and then enough water (about 400 ml.) is added with stirring with the pestle to form a thick paste. The paste is transferred to a 3-l. enameled can or beaker surrounded by an ice bath. A solution of 128 g. (2.14 moles) of glacial acetic acid in 130 ml. of water is cooled to 5° in another 3-l. beaker, which is fitted with a strong mechanical stirrer and surrounded by an ice bath. The paste of nitroguanidine and zinc dust, cooled to 5°, is added slowly with mechanical stirring, the temperature of the reaction mixture being kept between 5° and 15°. A total of about 1 kg. of cracked ice is added to the mixture from time to time as the mixture becomes too warm or too thick to stir. The addition of the paste takes about 8 hours, and the final volume of the mixture is about 1.5 l. (Note 2). The mixture is then slowly warmed to 40° on a water bath with continued stirring, and this temperature is maintained for 1–5 minutes, until reduction is complete (Note 3).

The solution is immediately separated from the insoluble material by filtration on a 20-cm. Büchner funnel, and the cake is sucked as dry as possible. The residue is transferred to the 3-l. beaker, triturated well with 1 l. of water, and then separated from the liquid by filtration. In the same manner, the residue is washed twice more with two 600-ml. portions of water. The filtrates are combined and placed in a 5-l. round-bottomed flask. Two hundred grams of ammonium chloride is added, and the solution is mechanically stirred until solution is complete (Note 4). The stirring is continued, and 220 g. (2.62 moles) of sodium bicarbonate is added during a period of about 10 minutes. The aminoguanidine bicarbonate begins to precipitate after a few minutes, and the solution is then placed in a refrigerator overnight. The precipitate is collected by filtration on a Büchner funnel. The cake is removed to a 1-l. beaker and mixed with a 400-ml. portion of a 5% solution of ammonium chloride and filtered. It is again washed with two 400-ml. portions of distilled water, the wash solution being removed each time by filtration. Finally the solid is pressed down on the Büchner funnel; the mat is broken up with a spatula and washed while on the funnel with two 400-ml. portions of 95% ethanol and then with one 400-ml. portion of ether. After air drying, the aminoguanidine bicarbonate amounts to 180–182 g. (63–64%) of a white solid, melting at 172° with decomposition (Note 5) and (Note 6).

2. Notes

1. The zinc is purified by stirring 1.2 kg. of commercial zinc dust with 3 l. of 2% hydrochloric acid for 1 minute. The acid is removed by filtration, and the zinc is washed in a 4-l. beaker with one 3-l. portion of 2% hydrochloric acid, three 3-l. portions of distilled water, two 2-l. portions of 95% ethanol, and finally with one 2-l. portion of absolute ether, the wash solutions being removed each time by filtration. Then

the material is thoroughly dried and any lumps are broken up in a mortar.

2. The solution becomes basic to litmus after one-half to three-fourths of the paste has been added. Lower yields are obtained if a larger excess of acetic acid is employed.

3. The state of reduction can be determined by placing 3 drops of the reaction mixture in a test tube containing 5 ml. of a 10% solution of sodium hydroxide and then adding 5 ml. of a freshly prepared saturated solution of ferrous ammonium sulfate. A red coloration indicates incomplete reduction; when the reduction is complete, only a greenish precipitate is observed. The mixture should not be heated after this test shows that reduction is complete.

4. The presence of the ammonium chloride prevents the coprecipitation of zinc salts when sodium bicarbonate is added to the solution to precipitate the aminoguanidine as the bicarbonate. If the solution is not clear at this step, it should be filtered.

5. The aminoguanidine bicarbonate is pure enough for most purposes. It should not be recrystallized from hot water, since decomposition will occur.

6. W. W. Hartman and Ross Philips have submitted a procedure suitable for the preparation of aminoguanidine bicarbonate on a larger scale. The sulfates of methylisothiourea and of hydrazine are allowed to react with the evolution of methyl mercaptan. In a 30-gal. crock are placed 10 l. of water and 5760 g. (20 moles) of methylisothiourea sulfate.[2] In a 22-l. flask, 5.2 kg. (40 moles) of hydrazine sulfate[3] is stirred with 12 l. of water, and 40% sodium hydroxide is added until all the hydrazine sulfate has dissolved and the solution is just neutral to Congo paper. The exact amount of alkali is noted and a duplicate amount added. The hydrazine solution is then added to the 30-gal. crock with stirring, as fast as possible, without allowing the foam to overflow the crock. The mixing is done out-of-doors, or in an efficient hood, since large volumes of methyl mercaptan are evolved. If the reaction is carried out on a smaller scale in 12- or 22-l. flasks, using appropriate amounts of material, the methyl mercaptan evolved may be absorbed in cold sodium hydroxide solution and isolated if desired. The solution is stirred until evolution of mercaptan stops, and then a few liters of water are distilled off under reduced pressure to free the solution entirely from mercaptan. The residual liquor is chilled in a crock, and a crop of hydrated sodium sulfate is filtered off, washed with ice water, and discarded. The filtrate is warmed to 20–25°, 25 ml. of glacial acetic acid is added, then 4 kg. of sodium bicarbonate, and the solution is stirred vigorously for 5 minutes and thereafter occasionally during an hour, or until the precipitate no longer increases. The precipitate is filtered with suction and washed with ice water and then with methanol, and is dried at a temperature not above 60–70°. The yield is 3760 g. (69% of the theoretical amount). Hydrazine sulfate may be recovered from the final filtrate, if the filtrate is strongly acidified with sulfuric acid and allowed to cool.

3. Discussion

Numerous references for the preparation of aminoguanidine bicarbonate and other salts can be found in an excellent review article by Lieber and Smith.[4] It has also been prepared by treating a cyanamide solution at 20–50° with hydrazine and carbon dioxide,[5] and by the electrolytic reduction of nitroguanidine.[6]

References and Notes

1. *Org. Syntheses* Coll. Vol. **1**, 399 (1941).
2. *Org. Syntheses* Coll. Vol. **2**, 411 (1943).
3. *Org. Syntheses* Coll. Vol. **1**, 309 (1941).
4. Lieber and Smith, *Chem. Revs.*, **25**, 213 (1939)
5. Ger. pat. 689,191 [*C. A.*, **35**, 3650 (1941)].
6. Shreve and Carter, *Ind. Eng. Chem.*, **36**, 423 (1944).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number);

(Registry Number)

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

methanol (67-56-1)

ether (60-29-7)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

sodium sulfate (7757-82-6)

carbon dioxide (124-38-9)

zinc (7440-66-6)

Nitroguanidine (556-88-7)

Hydrazine sulfate (10034-93-2)

hydrazine (302-01-2)

methyl mercaptan (74-93-1)

Aminoguanidine bicarbonate,
Guanidine, amino-, bicarbonate (2582-30-1)

ferrous ammonium sulfate (10045-89-3)

aminoguanidine

bicarbonate (71-52-3)

methylisothiourea

methylisothiourea sulfate

cyanamide (420-04-2)