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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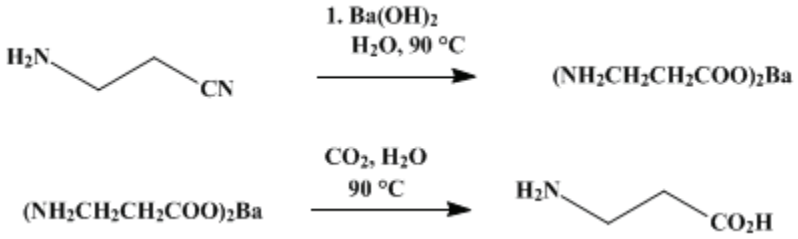
β-ALANINE



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1. Procedure

In a 2-l. three-necked flask equipped with a mechanical stirrer, a thermometer, and a dropping funnel is placed 185 g. (0.55 mole) of technical barium hydroxide octahydrate. The flask is heated on a steam bath in a hood. When the barium hydroxide has dissolved in its water of crystallization, the stirrer is started and 70.1 g. (1.00 mole) of β-aminopropionitrile (p. 93) is added dropwise over a period of 40 minutes. The temperature is maintained at 90–95° during the addition and for 40 minutes thereafter. Forty grams of asbestos filter aid (Note 1) and 1 l. of hot water are added, and the mixture is saturated with carbon dioxide (Note 2) while the temperature is held at 85–90°. The mixture is filtered with suction, the precipitate is returned to the flask with 500 ml. of hot water, and the mixture is heated and stirred for 20 minutes. After the barium carbonate has been filtered the washing procedure is again repeated with a second 500 ml. of hot water. The combined filtrates and washings are concentrated under reduced pressure on the steam bath (Note 3) until solid material separates. To the residue are added 200 ml. of hot water and 0.5 g. of decolorizing carbon (Note 4). The resulting solution is warmed on the steam bath for a few minutes and then filtered into a weighed 500-ml. Erlenmeyer flask. The flask is heated on a steam bath, and a jet of clean compressed air is directed at the surface of the solution. When the total weight of the solution is 130 g., it is cooled to 15–20° and diluted slowly with 400 ml. of methanol. After the solution has stood for several hours in the refrigerator, the product is filtered with suction and washed with two 100-ml. portions of methanol. The yield of β-alanine melting at 197–198° (dec.) is 75–80 g. (85–90%).

2. Notes

1. Standard Super-Cel (Johns-Manville, Inc.) was used.
2. Either carbon dioxide gas or Dry Ice may be used, and the saturation may be completed in 15–20 minutes by either method. The *p*H of the saturated solution is about 8–9 when tested with a universal indicator paper, such as Alkacid or Hydrion.
3. The submitter used a special apparatus suitable for the rapid evaporation of water under reduced pressure. The checkers used standard flasks.
4. The solution is nearly colorless at this point, but the carbon aids in the removal of finely divided insoluble material.

3. Discussion

β-Alanine has been prepared by the catalytic reduction of cyanoacetic acid,[1] esters,[2] or salts;[3] by heating acrylonitrile,[4] β-aminopropionitrile,[5] bis-(β-cyanoethyl) amine,[6] β-hydroxypropionitrile,[7] β-alkoxypropionitriles,[8] bis-(β-cyanoethyl) ether,[9] or bis-(β-cyanoethyl) sulfide[9] with aqueous ammonia at 150–225°; by the hydrolysis of β-aminopropionitrile with concentrated hydrochloric acid and subsequent removal of the acid with anion-exchange resins;[10] by hydrolysis of β-phthalimidopropionitrile prepared from phthalimide and acrylonitrile;[11] from β,β'-iminodipropionic acid, β,β'-iminopropionitrile, or diethyl-β,β'-iminopropionate through preliminary conversion with phthalic

anhydride at 200° to the corresponding phthalimide and subsequent hydrolysis.[12] The method as described above has been published.[13] Additional references to methods of preparation are given in connection with a procedure for making β-alanine from succinimide through the action of potassium hypobromite.[14,15]

References and Notes

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13. Ford, *J. Am. Chem. Soc.*, **67**, 876 (1945).
14. *Org. Syntheses* Coll. Vol. **2**, 20 (1943).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

β,β'-iminopropionitrile

diethyl-β,β'-iminopropionate

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

methanol (67-56-1)

carbon dioxide (124-38-9)

phthalic anhydride (85-44-9)

carbon (7782-42-5)

Phthalimide (85-41-6)

β-hydroxypropionitrile (109-78-4)

cyanoacetic acid (372-09-8)

barium hydroxide (17194-00-2)

barium carbonate (513-77-9)

barium hydroxide octahydrate (12230-71-6)

β-Alanine (107-95-9)

Succinimide (123-56-8)

β-Aminopropionitrile (151-18-8)

acrylonitrile (107-13-1)

bis-(β-cyanoethyl) amine (111-94-4)

bis-(β-cyanoethyl) ether (1656-48-0)

bis-(β-cyanoethyl) sulfide (111-97-7)

β-phthalimidopropionitrile

potassium hypobromite

β,β'-iminodipropionic acid