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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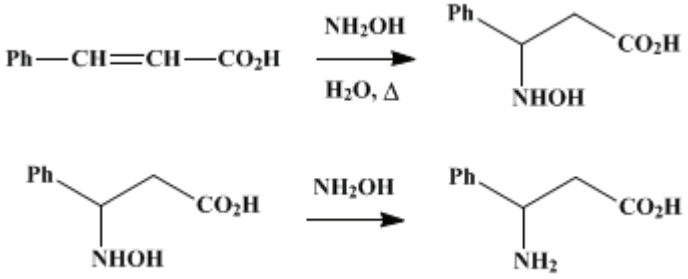
dl-β-AMINO-β-PHENYLPROPIONIC ACID

[Hydrocinnamic acid, β-amino-*dl*-]



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1. Procedure

A hot solution of sodium ethoxide is prepared, in a 3-l. round-bottomed flask, from 46 g. (2 gram atoms) of sodium and 1.6 l. of absolute ethanol. With shaking, a solution of 139 g. (2 moles) of hydroxylamine hydrochloride in 100 ml. of hot water is added. The resulting suspension is cooled quickly by placing the flask in an ice-water mixture and is then filtered with suction through a Büchner funnel. The residue of sodium chloride is washed with small portions (total 200 ml.) of absolute ethanol. The filtrate is returned to the 3-l. flask, and to it is added 148 g. (1 mole) of cinnamic acid, whereupon a voluminous precipitate forms. The mixture is refluxed on a steam bath for 9 hours (Note 1). The amino acid begins to separate after 5–6 hours; the suspended solid causes the mixture to bump (Note 2). The suspension is allowed to remain overnight at room temperature, and the crystals are then collected on a Büchner funnel (Note 3). The product is washed with 300 ml. of absolute ethanol, then with some ice-cold water to remove all the sodium chloride, and finally with 300 ml. of absolute ethanol, always in small portions. The colorless crystals of amino acid are dried in a vacuum desiccator over flake sodium hydroxide. The yield is 56 g. (34%).

If a purer product is desired, the amino acid is dissolved in 16 times its weight of boiling water, and to the solution is added absolute ethanol (46 ml. per g. of acid). The solution is stirred mechanically while it is cooled in an ice-water mixture. After 3 hours, the snow-white crystals are collected on a Büchner funnel and are washed with 300 ml. of 95% ethanol, in small portions, and dried as before. The recovery of amino acid, melting at 221° with decomposition (Note 4), is 81%.

2. Notes

1. The solution becomes clear when the boiling point is reached. It is important that the mixture be boiled for the specified time in order to ensure complete conversion of the hydroxylamino acid into the amino acid. The solubilities of these two acids are nearly the same.
2. It may happen that the hot solution remains supersaturated, and crystallization does not take place, until the solution is cooled. The checkers obtained a poor yield when this occurred. They, therefore, seeded other runs during the boiling process in order to bring about crystallization. Posner[1] had to concentrate the solution to about half its volume in order to bring about crystallization.
3. The mother liquors from the crystallization appear to be free of amino acid if the yield mentioned is obtained. Among other products they contain at least 19 g. of acetophenoneoxime (14%), which is formed by the secondary reaction:

The acetophenoneoxime may be isolated by evaporating the mother liquors almost to dryness, adding water repeatedly to remove the alcohol, and then treating the oily residue with 1 *N* sodium carbonate solution.

4. The melting point varies considerably with the rate and duration of heating. Values ranging from 215° to 231° have been reported in the literature. The product obtained appears to be perfectly stable and shows no tendency to assume the pink coloration reported by Posner.[1]

3. Discussion

The procedure described is that given by Posner,[1] with some modifications and additions. The amino acid has also been prepared by boiling the oxime hydrate of β-hydroxylaminohydrocinnamohydroxamic acid with water;[2] by decarboxylation of β-amino-β-phenylethane-α,α-dicarboxylic acid;[3] and by the reaction of cinnamic acid with ammonia under pressure in the presence of anhydrous stannic chloride.[4]

References and Notes

1. Posner, *Ber.*, **38**, 2320 (1905); *Ann.*, **389**, 120 (1912). Fischer, Scheibler, and Groh, *Ber.*, **43**, 2024 (1910).
2. Posner, *Ber.*, **40**, 227 (1904).
3. Rodionow and Malewinskaja, *Ber.*, **59**, 2956 (1926); Rodionow, *J. Am. Chem. Soc.*, **51**, 851 (1929); Evans and Johnson, *J. Am. Chem. Soc.*, **52**, 5001 (1930); Johnson and Livak, *J. Am. Chem. Soc.*, **58**, 301 (1936).
4. Enkvist, Monoven, and Soderlund, *Finska Kemistsamfundets Medd.*, **53**, No. ¾, 66 (1944); [*C. A.*, **41**, 4103 (1947)].

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

oxime hydrate of β-hydroxylaminohydrocinnamohydroxamic acid

ethanol (64-17-5)

ammonia (7664-41-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

Hydroxylamine hydrochloride (5470-11-1)

cinnamic acid (621-82-9)

stannic chloride (7646-78-8)

acetophenoneoxime

β-amino-β-phenylethane-α,α-dicarboxylic acid

DL-β-Amino-β-phenylpropionic acid,
Hydrocinnamic acid, β-amino-dl- (614-19-7)

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