



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.

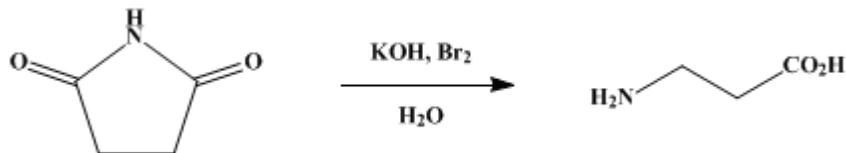
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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β-ALANINE



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1. Procedure

To a cold (0–5°) solution of 302 g. of potassium hydroxide sticks in 2720 cc. of distilled water is added slowly, with stirring, 96.6 g. (30.8 cc., 0.6 mole) of bromine. This solution is chilled to 0°, and 59.4 g. (0.6 mole) of succinimide (p. 562) is added with hand stirring. The mixture is warmed in a water bath to 55–60°, when it becomes colorless, and is held at that temperature for two hours (Note 1). After standing overnight at room temperature, it is acidified to Congo red with concentrated hydrochloric acid (about 380 cc., sp. gr. 1.18) (Note 2) and evaporated to dryness on a steam bath under reduced pressure. The residue is treated with 1 l. of warm 95 per cent alcohol; the undissolved potassium bromide is filtered and washed with 150–200 cc. of cold alcohol in small portions. The filtrate and washings are combined and evaporated to dryness under reduced pressure, and the residue is extracted with 100 cc. of 95 per cent alcohol. The resulting solution is again evaporated to dryness and the residue finally extracted with 140 cc. of hot absolute alcohol (Note 3). After distilling the bulk of the alcohol, this extract is diluted with about 200 cc. of distilled water and shaken out twice with 80-cc. portions of ether. The ether extracts are discarded (Note 4).

The aqueous solution is freed of ether and alcohol and then boiled under reflux for one to one and a half hours in order to hydrolyze any β-alanine ester. After evaporating under reduced pressure to remove as much as possible of the excess hydrochloric acid, the residue is dissolved in water and diluted to exactly 1 l. A 5-cc. portion of this solution is withdrawn for determination of total halides. A suspension of silver oxide prepared from 10 per cent more than the equivalent quantity of silver nitrate (Note 5) is added to the remaining portion of the solution, and the mixture is stirred well in order to bring about complete precipitation of the halides. After standing overnight the precipitate is filtered and washed with water. The filtrate and washings are concentrated under reduced pressure to about 400 cc., saturated with hydrogen sulfide, and filtered through a thin layer of decolorizing carbon. The colorless filtrate is evaporated to a volume of about 100 cc., treated with decolorizing carbon if necessary, concentrated on the steam bath until crystallization begins, and chilled. The crystals are filtered with suction, washed with a little cold alcohol, and dried. A further crop is obtained by concentrating the mother liquor and again chilling (Note 6). The combined crops (28–30 g., m.p. 189–192°) are recrystallized from water, employing the same procedure, and yield 22–24 g. (41–45 per cent of the theoretical amount) of pure β-alanine, which melts at 197–198° (corr.) with decomposition. About 2 g. of less pure product can be secured from the final mother liquors.

2. Notes

1. The odor of ammonia is perceptible, indicating some hydrolysis.
2. On acidification a small amount of bromine may be liberated; this is removed rapidly during the subsequent evaporation.
3. In the last extraction the alcohol-insoluble material may be removed advantageously with a centrifuge.
4. This ether extraction removes small quantities of succinic acid and its esters.
5. The silver oxide is prepared by dissolving the silver nitrate in about five parts of cold water and adding a slight excess of pure sodium hydroxide in 10 per cent solution. The precipitate is well stirred, collected by filtration or centrifuging, and washed free of sodium salts. It should not be dried before use.

6. The final mother liquor consists of a rather viscous solution containing uncrystallizable by-products.

3. Discussion

The above directions are based upon the methods of Hoogewerff and Van Dorp,¹ as modified by Holm² and by Hale and Honan.³ β -Alanine has also been prepared by the action of hypobromite upon succinamide and hydrolysis of the resulting β -ureidopropionic acid;⁴ by the action of ammonia upon β -iodopropionic acid;⁵ by the hydrolysis of methyl carbomethoxy- β -aminopropionate, obtained by the action of sodium methoxide on succinbromimide;⁶ by the reduction of β -nitrosopropionic acid;⁷ by heating ethyl acrylate with alcoholic ammonia;⁸ from succinylglycine ester by the azide synthesis;⁹ by the action of liquid ammonia upon methyl acrylate;¹⁰ and by the reduction of cyanoacetic acid,¹¹ or its ethyl ester followed by hydrolysis.¹²

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 34](#)

References and Notes

1. Hoogewerff and Van Dorp, *Rec. trav. chim.* **10**, 5 (1891).
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3. Hale and Honan, *J. Am. Chem. Soc.* **41**, 774 (1919).
4. Weidel and Roithner, *Monatsh.* **17**, 172 (1896).
5. Heintz, *Ann.* **156**, 25 (1870); Mulder, *Ber.* **9**, 1902 (1876); Abderhalden and Fodor, *Z. physiol. Chem.* **85**, 114 (1913).
6. Lengfeld and Stieglitz, *Am. Chem. J.* **15**, 215, 504 (1893).
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9. Curtius and Hechtenberg, *J. prakt. Chem. (2)* **105**, 289 (1923).
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Appendix

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

β -alanine ester

succinic acid and its esters

succinylglycine ester

[alcohol \(64-17-5\)](#)

[hydrochloric acid \(7647-01-0\)](#)

[ammonia \(7664-41-7\)](#)

ether (60-29-7)

sodium hydroxide (1310-73-2)

silver oxide (20667-12-3)

hydrogen sulfide (7783-06-4)

silver nitrate (7761-88-8)

bromine (7726-95-6)

sodium methoxide (124-41-4)

decolorizing carbon (7782-42-5)

potassium hydroxide (1310-58-3)

potassium bromide (7758-02-3)

hypobromite

cyanoacetic acid (372-09-8)

ethyl acrylate (140-88-5)

β -Alanine (107-95-9)

Succinimide (123-56-8)

succinamide (110-14-5)

β -ureidopropionic acid (462-88-4)

β -iodopropionic acid (141-76-4)

methyl carbomethoxy- β -aminopropionate

succinbromimide

β -nitrosopropionic acid

methyl acrylate (96-33-3)