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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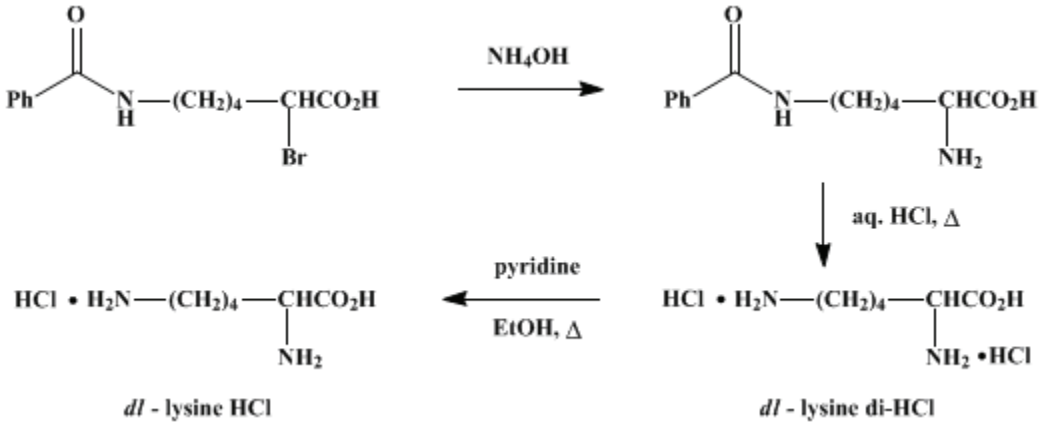
Organic Syntheses, Coll. Vol. 2, p.374 (1943); Vol. 19, p.61 (1939).

dl-LYSINE HYDROCHLORIDES



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1. Procedure

(*A*) *dl-ε-Benzoyllysine*.—A solution of 180 g. (0.57 mole) of ε-benzoylamino-α-bromocaproic acid (p. 74) in 2 l. of aqueous ammonia (sp. gr. 0.9) is filtered into a 5-l. flask and allowed to stand for two days. Any crystals which have formed at the end of this time are filtered, and the filtrate is evaporated on a steam bath at reduced pressure to about 1 l. The crystals are filtered, combined with the first crop, and washed with 100 cc. of alcohol and finally with 100 cc. of ether. The aqueous filtrate is evaporated under reduced pressure to dryness; the residue is washed with two 100-cc. portions of water to remove the ammonium bromide, and then with 50 cc. of alcohol, followed by 50 cc. of ether. The total yield of ε-benzoyllysine, melting at 265–270°, is 100–116 g. (70–81 per cent of the theoretical amount).

(*B*) *dl-Lysine Dihydrochloride*.—A solution of 100 g. (0.4 mole) of benzoyllysine in a mixture of 600 cc. of hydrochloric acid (sp. gr. 1.18) and 400 cc. of water is boiled under a reflux condenser for ten hours. The mixture is cooled and the benzoic acid removed by filtration. The filtrate is evaporated on a water bath under reduced pressure until a thick syrup remains. The syrup is transferred to a 1.5-l. beaker by means of four volumes (about 400 cc.) of hot absolute alcohol and filtered if necessary. The solution is cooled to 15–20°, and 500 cc. of ether is added slowly with stirring. The precipitate, after filtering and drying, melts at 187–189° and weighs 67–75 g. (76–85 per cent of the theoretical amount); it is analytically pure lysine dihydrochloride (Note 1).

(*C*) *dl-Lysine Monohydrochloride*.—To a solution of 55 g. (0.25 mole) of lysine dihydrochloride in 1 l. of boiling 95 per cent alcohol (Note 2) is added, with stirring, a solution of 25 g. (0.32 mole) of pyridine in 40 cc. of hot 95 per cent alcohol. The white, crystalline monohydrochloride separates immediately. After cooling overnight in a refrigerator the solid is filtered and washed with two 50-cc. portions of cold absolute alcohol. After drying, the product melts at 260–263° and weighs 42–43 g. (91–94 per cent of the theoretical amount).

For further purification to remove any pyridine hydrochloride, the above product is dissolved in 85 cc. boiling water, and 650 cc. of boiling 95 per cent alcohol added with stirring. After cooling overnight in the refrigerator the solid is filtered, and washed with one 20-cc. portion of cold absolute alcohol. There is obtained 40–42 g. (95–97 per cent recovery) of monohydrochloride melting at 263–264° (corr.).

2. Notes

1. If a product of lower melting point is obtained, it may be purified by dissolving in 1 l. of hot 95 per

cent alcohol, filtering if necessary, cooling, and, without removing any material that may have crystallized, adding slowly with stirring 1.5 l. of ether. If the product separates as an oil it will soon crystallize on standing. The checkers found that one lot of 75 g. melting at 173–178° when treated in this way gave 67 g. (89 per cent recovery) melting at 187–189°.
2. If the solution is not clear, it should be filtered before the addition of pyridine.

3. Discussion

The above procedure for *dl*-ε-benzoyllysine and *dl*-lysine hydrochloride is a modification[1] of that published by Braun.[2]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 322
- Org. Syn. Coll. Vol. 6, 90

References and Notes

1. Eck and Marvel, J. Biol. Chem. **106**, 387 (1934).
2. Braun, Ber. **42**, 844 (1909).

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

dl-LYSINE HYDROCHLORIDES

alcohol (64-17-5)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ether (60-29-7)

ammonium bromide (12124-97-9)

Benzoic acid (65-85-0)

pyridine (110-86-1)

ε-BENZOYLAMINO-α-BROMOCAPROIC ACID (1700-05-6)

pyridine hydrochloride (628-13-7)

DL-ε-Benzoyllysine,
ε-benzoyllysine (5107-18-6)

DL-Lysine dihydrochloride (617-68-5)

benzoyllysine

lysine dihydrochloride

dl-Lysine Monohydrochloride,
dl-lysine hydrochloride (26124-78-7)