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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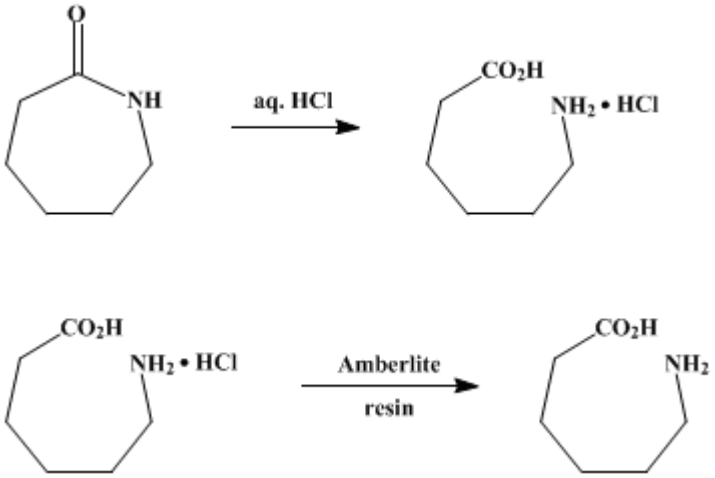
ε-AMINOCAPROIC ACID

[Hexanoic acid, 6-amino-]



Submitted by Cal Y. Meyers and Leonard E. Miller[1].
Checked by Richard T. Arnold and William R. Hasek.

1. Procedure

Into a 500-ml. round-bottomed flask containing 50 g. (0.44 mole) of 2-ketohexamethylenimine (ε-caprolactam) is poured a solution containing 45 ml. of concentrated hydrochloric acid (sp. gr. 1.19) dissolved in 150 ml. of water. The mixture is boiled for 1 hour, and the resulting yellow solution is decolorized with Norit and evaporated to dryness under reduced pressure on a steam bath (Note 1).

The resulting ε-aminocaproic acid hydrochloride is converted into the amino acid by means of a column containing Amberlite IR-4B resin (Note 2):

1. Construct the column as shown in Fig. 2.

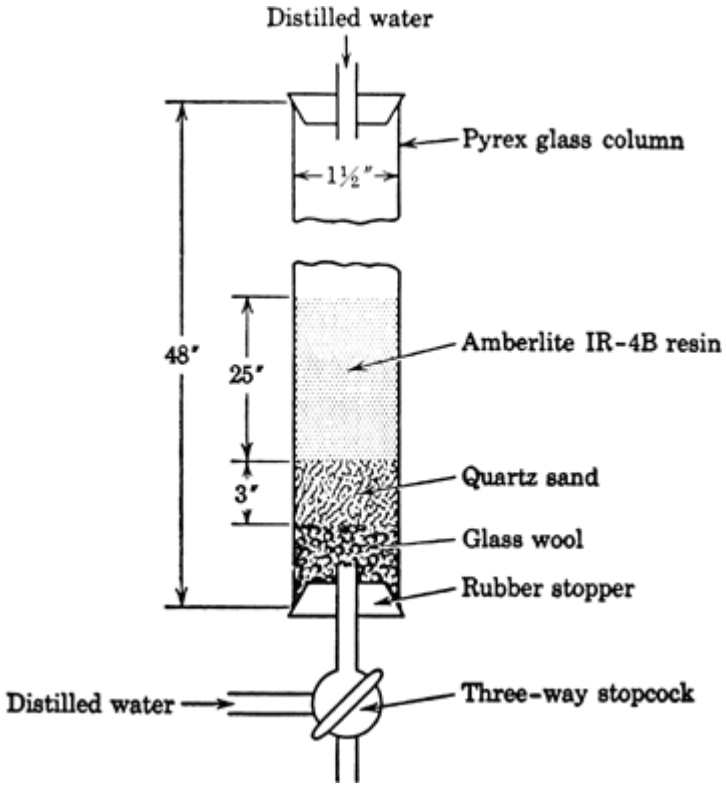
2. *Exhaustion.* Pass a 1% aqueous hydrochloric acid solution through the column (downflow) until the pH of the solution leaving the column decreases from 5.5–6.5 to about 2.

3. *Regeneration.* Now pass a 1% aqueous sodium hydroxide solution through the column (downflow) until the solution leaving the column is strongly alkaline.

4. *Classification.* Wash the resin (upflow) with 10 l. of distilled water.

5. Wash the resin with distilled water (downflow) (Note 3) until the salts are all washed out and the pH of the washings is 5.6–6.5. The column is now ready for use (Note 4).

Fig. 2.



The solid ε-aminocaproic acid hydrochloride is dissolved in 1 l. of distilled water. This solution is passed through the column (downflow) and followed by at least 2 l. of distilled water (Note 5).

The collected solution (pink) is concentrated by distillation, under reduced pressure, to a volume of about 100 ml. (Note 6), and the resulting orange-colored solution is decolorized with Norit. After the addition of 300 ml. of absolute ethanol and 500 ml. of ether, followed by vigorous shaking, a white solid forms within a few minutes. The ε-aminocaproic acid is collected on a Büchner funnel and dried in a vacuum desiccator until no more ether-alcohol odor is detected. A yield of 52 g. (90%) is obtained; m.p. 202–203°.

2. Notes

1. This hydrolysis is similar to that utilized previously.[2]
2. Obtained from the Resinous Products Division, Rohm and Haas Company, Philadelphia, Pennsylvania. The checkers found that this resin sometimes liberates carbon dioxide when treated with 1% hydrochloric acid. In such cases the total resin sample may be pretreated in a beaker with 1% hydrochloric acid until no more gas is evolved, and then a 30-in. (rather than 25-in.) column containing 1% hydrochloric acid is packed with resin. Further treatment of the resin is continued as described by the submitters.
3. Intermittent silver nitrate tests will indicate whether the solution is free of salts.
4. The liquid level of the column should always be above the resin when the column is not in use.
5. To assure the user that the resin is functioning, the eluant should be tested frequently for pH and the presence of salts. If the test for chloride ion becomes positive, or if the pH falls below 5.6, regeneration procedures are necessary; generally the column is good for two runs.
6. Excessive heating and excessive evaporation may result in peptide formation.

3. Discussion

ε-Aminocaproic acid has been prepared by the hydrolysis of ε-benzoylaminocapronitrile,[3] by the hydrolysis of diethyl ω-phthalimidobutylmalonate,[4] from cyclohexanone oxime by rearrangement and hydrolysis,[5] by hydrochloric acid hydrolysis of ε-caprolactam and removal of the acid by the use of

litharge, silver oxide, etc.,[2] by alkaline hydrolysis of ε-caprolactam[6] or by hydrolysis of ε-caprolactam in the presence of a cation exchange resin,[7] by the reduction of δ-cyanovaleric acid[8] or the corresponding ethyl ester,[9] and by the hydrogenation of ε-oximinocaproic acid.[10]

References and Notes

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6. Shpital'nyi, Shpital'nyi, and Yablochnik, *Zhur. Priklad. Khim.*, **32**, 617 (1959) [*C. A.*, **53**, 16005 (1959)].
7. Itin and Kahr (to Inventa A.-G. für Forschung und Patentverwertung), Brit. pat. 774,468 [*C. A.*, **52**, 2056 (1958)].
8. Shono and Hachihama, *Chem. High Polymers (Japan)*, **8**, 504 (1951) [*C. A.*,**48**, 10581 (1954)].
9. Chrétien, *Ann. chim. (Paris)*, [13] **2**, 682 (1957).
10. Chiusoli and Minisci, *Gazz. chim. ital.*, **88**, 261 (1958).

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

alcohol,
ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

silver oxide (20667-12-3)

silver nitrate (7761-88-8)

carbon dioxide (124-38-9)

Norit (7782-42-5)

ε-AMINOCAPROIC ACID,
Hexanoic acid, 6-amino- (60-32-2)

2-Ketohexamethylenimine,
ε-caprolactam (105-60-2)

ε-aminocaproic acid hydrochloride

ε-benzoylaminocapronitrile

Cyclohexanone oxime (100-64-1)

diethyl ω-phthalimidobutylmalonate

δ-cyanovaleric acid (5264-33-5)

ε-oximinocaproic acid