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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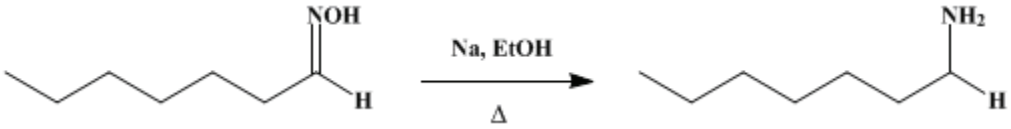
n-HEPTYLAMINE



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1. Procedure

A solution of 258 g. (2 moles) of heptaldoxime (p. 313) in 4 l. of absolute alcohol (Note 1) is heated to boiling in a 12-l. round-bottomed flask on a steam bath. The flask is equipped with a 150-cm. reflux condenser in which the inner tube is very wide (2.5 cm.). As soon as the alcohol begins to boil, the steam is shut off and the temperature is maintained by introducing strips of sodium through the top of the condenser. The total amount of sodium added is 500 g., and it should be added as rapidly as is possible without loss of alcohol (Note 2). The last 150 g. of sodium melts in the hot mixture and may be added very rapidly without loss of alcohol or amine.

As soon as the sodium has dissolved, the contents of the flask are cooled and diluted with 5 l. of water. The flask is equipped at once with a condenser set for distillation, and the distillate is carried below the surface of a solution of 300 cc. of concentrated hydrochloric acid in 300 cc. of water in a 12-l. flask. The distillation is continued as long as any basic material passes over. When frothing interferes toward the end of the distillation an additional 3 l. of water is added to the distillation flask. The total distillate is 8–9 l.

The alcohol, water, and unreacted oxime are removed by heating the acid distillate on the steam cone under reduced pressure (about 20–30 mm.); the amine hydrochloride crystallizes in the flask. The flask is then cooled and equipped with a reflux condenser through which 1 l. of 40 per cent potassium hydroxide solution is introduced. The hydrochloride is washed down from the sides of the flask, and the resulting mixture is cooled and transferred to a separatory funnel. The lower alkaline layer is removed and solid potassium hydroxide is added to the amine in the funnel. The aqueous layer is removed and fresh sticks of potassium hydroxide are added from time to time until no further separation of an aqueous alkaline solution occurs. Twenty-four to thirty hours is required for complete drying. The amine is then decanted through the top of the funnel into a 250-cc. modified Claisen flask and distilled. The *n*-heptylamine is collected at 152–157°. The yield is 140–170 g. (60–73 per cent of the theoretical amount) (Note 3).

2. Notes

1. The yields are poor if the alcohol is not completely dehydrated. A very satisfactory grade of alcohol is obtained by distilling ordinary absolute alcohol from magnesium methoxide (Org. Syn. Coll. Vol. I, **1941**, 249).
2. The best yields are obtained when the reduction is carried out rapidly.
3. Using essentially the same method the following amines have been prepared in 50–60 per cent yields: *n*-butylamine, b. p. 75–80°, from butyraldoxime; *sec.*-butylamine, b. p. 59–65°, from ethyl methyl ketoxime; cyclohexylamine, b. p. 133–135°, from cyclohexanone oxime. Greater care must be observed in drying the butylamines.

3. Discussion

n-Heptylamine can be prepared by the reduction of heptaldoxime with sodium amalgam and acetic acid,[1] with ammonium amalgam,[2] with sodium and an alcohol,[3] and catalytically;[4] by the reduction of 1-nitroheptane with iron and acetic acid;[5] by the reduction of heptanonitrile with sodium and an alcohol[3], [6]

or catalytically;[7] by the reduction of heptanoamide with sodium and an alcohol[8] or catalytically;[9] by the reduction of heptaldehyde phenylhydrazone with sodium amalgam and acetic acid;[10] and by the catalytic reduction of heptaldehyde and ammonia in alcohol.[11] [12] The formation of a secondary amine, which is a serious limitation in the catalytic reduction of heptanonitrile, can be almost completely suppressed by reducing in the presence of a large amount of ammonia.[12]

Other methods which also lead to *n*-heptylamine are the reaction between 1-bromoheptane and ammonia;[13] the Hofmann rearrangement of the amide of caprylic acid;[14] and the Beckmann rearrangement of methyl *n*-heptyl ketoxime, followed by hydrolysis.[15]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 313

References and Notes

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

Heptaldoxime

heptaldehyde phenylhydrazone

amide of caprylic acid

alcohol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ammonia (7664-41-7)

iron (7439-89-6)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

magnesium methoxide

n-butylamine (109-73-9)

Cyclohexanone oxime (100-64-1)

Ammonium (14798-03-9)

heptanonitrile (629-08-3)

butyraldoxime

ethyl methyl ketoxime

cyclohexylamine (108-91-8)

1-nitroheptane

heptanoamide

1-bromoheptane (629-04-9)

heptaldehyde (111-71-7)

n-heptylamine (111-68-2)

sec.-butylamine (13952-84-6)

methyl n-heptyl ketoxime