



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.

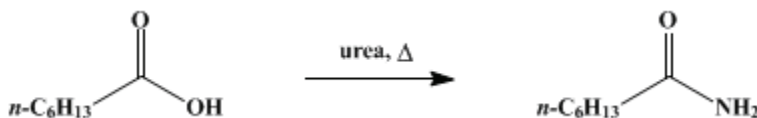
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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***n*-HEPTAMIDE**

[Heptanamide]



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Checked by William S. Johnson and Duane Zinkel.

1. Procedure

In a 1-l. round-bottomed flask, fitted with a thermometer extending nearly to the bottom, are placed 60 g. (1 mole) of **urea** and 69 g. (0.5 mole) of 95% *n*-heptanoic acid (Note 1). A condenser (Note 2) is attached to the flask, and the mixture is heated by means of an electric mantle. When the temperature reaches 140°, the **urea** is in solution, and a rather vigorous evolution of gas occurs which continues for several minutes. The temperature is maintained at 170–180° for 4 hours (Note 3), and then the mixture is allowed to cool.

As soon as the temperature drops to 110–120°, 400 ml. of 5% **sodium carbonate** solution is added carefully through the condenser, and the mixture is shaken vigorously (Note 4). The mixture is cooled in an ice bath, and the product is collected on a Büchner funnel. The solid, when dry, is slightly colored, and weighs 57–64 g., m.p. 85–91°.

The crude material is boiled for a few minutes with 200 ml. of 95% **ethanol** and a small amount of **decolorizing carbon** (Note 5). The mixture is filtered by gravity, and 800 ml. of water is added to the filtrate. The resulting slurry is cooled in an ice-salt bath and the solid is collected by filtration on a Büchner funnel. The product, which is almost colorless is air-dried. It weighs 44–48 g. (68–74%) and melts at 91–94° (Note 6). Evaporation of the filtrate under reduced pressure and reprecipitation of the residue from 20 ml. of 95% **ethanol** and 80 ml. of water affords an additional 3–4 g. (5–6%) of material which melts at 90–93°.

2. Notes

1. Eastman Kodak Company, yellow label brand (95%), *n*-heptanoic acid was used.
2. A condenser should be chosen which has an inside diameter of at least 1.5 cm.; otherwise frequent loosening of the sublimate is required to prevent clogging. A 3-ft., air-cooled tube with an internal diameter of about 2.5 cm. serves as a satisfactory condenser.
3. Temperatures below 170° lead to slightly lower yields, and temperatures above 180° cause excessive sublimation of **urea**. Although the reaction is nearly complete after 2 hours, the yield appears to be improved by additional heating.
4. Failure to make the mixture basic leads to the formation of a greasy, colored product.
5. A small amount of solid does not dissolve in the alcohol.
6. Recrystallization from dilute **ethanol** affords colorless material, m.p. 94–95°.

3. Discussion

Heptamide has been prepared by heating **heptanoic acid** with **ammonia** in a sealed tube² at 230°, by treating **heptanoic anhydride** with **ammonia**,³ by passing **ammonia** through **heptanoic acid**⁴ at 125–190°, by the rearrangement of heptaldehyde oxime in the presence of **Raney nickel** in a quartz tube at 150° for 5 minutes,⁵ by the Willgerodt reaction with 2-, 3-, or 4-heptanone or **heptanal**,^{6,7} and by the action of **ammonia** on **heptanoyl chloride**.⁸

The procedure described is based on the method of E. Cherbuliez and F. Landolt,⁹ by which formic

and acetic acids were converted into the corresponding amides.

References and Notes

1. University of Missouri, Columbia, Missouri.
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 3. Chiozza and Malerba, *Ann.*, **91**, 103 (1854).
 4. Mitchell and Reid, *J. Am. Chem. Soc.*, **53**, 1879 (1931).
 5. Paul, *Bull. soc. chim.*, [5]**4**, 1115 (1937).
 6. Cavalieri, Pattison, and Carmack, *J. Am. Chem. Soc.*, **67**, 1783 (1945).
 7. King and McMillan, *J. Am. Chem. Soc.*, **68**, 1369 (1946).
 8. Philbrook, *J. Org. Chem.*, **19**, 623 (1954).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Heptamide

heptaldehyde oxime

2-, 3-, or 4-heptanone

[ethanol](#) (64-17-5)

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

[sodium carbonate](#) (497-19-8)

[Raney nickel](#) (7440-02-0)

[decolorizing carbon](#) (7782-42-5)

[urea](#) (57-13-6)

[Heptanoic acid,
n-HEPTANOIC ACID](#) (111-14-8)

[Heptanal](#) (111-71-7)

[heptanoic anhydride](#) (626-27-7)

[heptanoyl chloride](#) (2528-61-2)

[Heptanamide](#) (628-62-6)