



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.

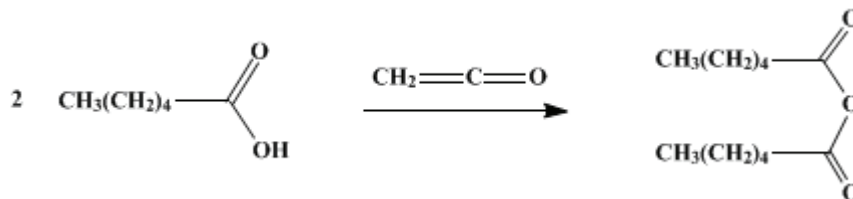
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

Organic Syntheses, Coll. Vol. 3, p.164 (1955); Vol. 21, p.13 (1941).

***n*-CAPROIC ANHYDRIDE**



Submitted by Jonathan W. Williams and John A. Krynitsky.
Checked by Nathan L. Drake and Joseph Lann.

1. Procedure

One hundred and sixteen grams (126 ml., 1 mole) of *n*-caproic acid is placed in a 250-ml. gas-washing bottle. The bottle is supported in an ice bath, and 0.50 to 0.55 mole of ketene is passed into the acid at a rate of approximately 0.45 mole per hour (Note 1) and (Note 2).

The resulting mixture is transferred to an apparatus for fractional distillation, and carefully fractionated, an oil bath being used for heating (Note 3). A low-boiling fraction, consisting of acetone containing some ketene, acetic acid, and a small quantity of acetic anhydride, is removed at atmospheric pressure. As the distillation progresses the temperature of the oil bath is raised to 220° over a period of about 1 hour and held there until 3 hours has elapsed from the time distillation started (Note 4).

The distillation at atmospheric pressure is then discontinued, the liquid is allowed to cool somewhat, and distillation is continued at a pressure of 3–10 mm. After a fore-run of less than 20 g., *n*-caproic anhydride is collected (b.p. 109–112°/3 mm., 118–121°/6 mm.). The yield is 86–95 g. (80–87%) (Note 5).

2. Notes

1. Ketene may be generated conveniently, at the proper rate, in the apparatus described by Williams and Hurd.¹
2. Addition of 1 mole of ketene per mole of acid does not increase the yield. Under these conditions more acetic anhydride is found in the low-boiling fraction.
3. Submitters and checkers used a column of the Whitmore-Lux type,² 12 mm. in diameter, 50 cm. long, packed with glass helices, and provided with the usual jackets for heating. A less efficient column will serve in the preparation of caproic anhydride but not in the preparation of propionic anhydride or butyric anhydride by the same method.
4. It is imperative to continue the distillation at atmospheric pressure until conversion of any mixed anhydride to caproic anhydride is complete. The acetic acid formed by this conversion comes off very slowly, and approximately 3 hours is necessary to complete the distillation at atmospheric pressure.
5. According to the submitters, equally good yields can be obtained in the preparation of propionic anhydride and *n*-butyric anhydride.

3. Discussion

n-Caproic anhydride has been prepared by heating caproic acid with acetic anhydride,³ by heating sodium caproate and acetic anhydride in a sealed tube,⁴ by the action of phosphorus oxychloride on barium caproate,⁵ by the action of acetyl chloride on caproic acid,⁶ and by treating a mixture of sodium caproate and sulfur with chlorine.⁷ The method used in the present synthesis was first described by Hurd and Dull.⁸

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 176
- Org. Syn. Coll. Vol. 3, 181

References and Notes

1. Williams and Hurd, *J. Org. Chem.*, **5**, 122 (1940).
 2. Whitmore and Lux, *J. Am. Chem. Soc.*, **54**, 3451 (1932).
 3. Autenrieth, *Ber.*, **34**, 168 (1901).
 4. Michael, *Ber.*, **34**, 918 (1901).
 5. Chiozza, *Ann.*, **86**, 359 (1853).
 6. Fournier, *Bull. soc. chim. France*, (4), **5**, 920 (1909).
 7. Brit. pat. 24,842 (1908) [*C. A.*, **4**, 2190, 2719 (1910)].
 8. Hurd and Dull, *J. Am. Chem. Soc.*, **54**, 3427 (1932).
-

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

acetic acid (64-19-7)

acetic anhydride (108-24-7)

acetyl chloride (75-36-5)

sulfur (7704-34-9)

acetone (67-64-1)

Phosphorus Oxychloride (21295-50-1)

chlorine (7782-50-5)

Caproic acid,
n-caproic acid (142-62-1)

butyric anhydride,
n-butyric anhydride (106-31-0)

Ketene (463-51-4)

propionic anhydride (123-62-6)

caproic anhydride,
n-CAPROIC ANHYDRIDE (2051-49-2)

sodium caproate (10051-44-2)

barium caproate

