



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.

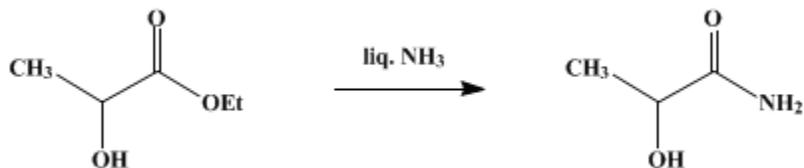
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.516 (1955); Vol. 21, p.71 (1941).

LACTAMIDE



Submitted by J. Kleinberg and L. F. Audrieth.
Checked by Homer Adkins and William H. Bateman.

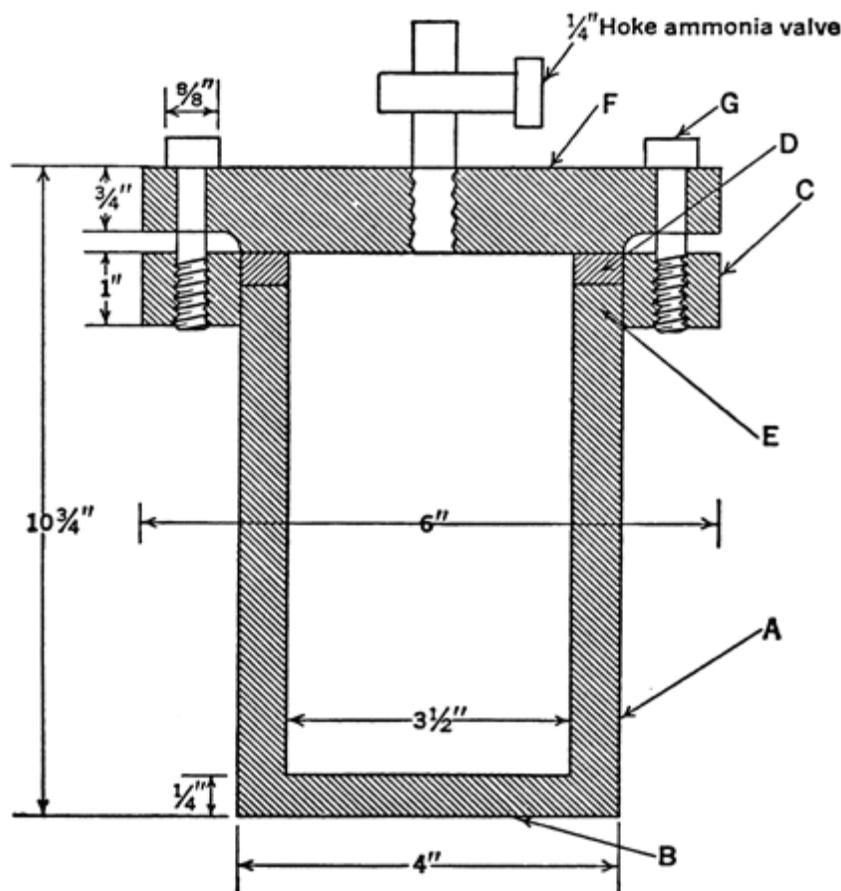
1. Procedure

One hundred and twenty-five grams (1.06 moles) of [ethyl lactate](#) is placed in a suitable Pyrex container which is subsequently cooled in a Dry Ice-acetone bath. When the ester has been cooled below the boiling point of [ammonia](#) ([Note 1](#)), 125 ml. of liquid [ammonia](#) ([Note 2](#)) is added. The mixture is then placed in a specially constructed steel pressure apparatus ([Note 3](#)) and permitted to come to room temperature. After 24 hours ([Note 4](#)) the excess of [ammonia](#) is allowed to escape slowly through the gas outlet of the bomb. The last traces of [ammonia](#) are removed under reduced pressure. The reaction product is stirred with 200 ml. of absolute [ether](#) to dissolve unchanged ester and [ethanol](#). The residue is filtered, washed with [ether](#), and air-dried. The yield of [lactamide](#) melting at 74–75° amounts to 65–70 g. (70–74%) ([Note 5](#)).

2. Notes

- Care must be taken to cool the ester below the boiling point of [ammonia](#) before addition of the [ammonia](#), to avoid loss of ester by spattering.
- For manipulative procedures employing liquid [ammonia](#) see Franklin, *The Nitrogen System of Compounds*, A.C.S. Monograph 68, Appendix, Reinhold Publishing Corporation, New York, 1935; also, Fernelius and Johnson, *J. Chem. Education*, 6, 441 (1929).
- The steel bomb in which the reaction is carried out is depicted in [Fig. 16](#). It consists of a cylindrical tube (A) of ordinary steel to which a steel bottom (B) has been welded. A 1-in. flange (C) is welded to the top of the container extending about 3/16 in. above the top of the bomb. The lead gasket (D) is pressed into the groove (E) when the cover of stainless steel is tightened by means of six steel bolts (G). The top (F) is machined to make a tight seal on the gasket (D). A 1/4-in. steel Hoke ammonia valve serves as the gas outlet. The cross-sectional dimensions are noted in the diagram. The checkers carried out the reaction in a glass beaker which was set in a steel reaction vessel such as is used for hydrogenations at pressures of 50–500 atm.¹

Fig. 16.



4. Increase in reaction time causes no appreciable increase in yield of amide.
5. This method has been used for the preparation of numerous amides.² However, with many esters it is necessary to heat the reaction mixture to 200–250° for a few hours. Ethyl mandelate is like ethyl lactate in that it gives a good yield (75–80%) of mandelamide at room temperatures.

3. Discussion

Lactamide has been prepared by the action of ammonia on ethyl lactate,³ methyl lactate,⁴ lactic anhydride,⁵ lactide,⁶ and the condensation product of lactic acid with acetone.⁷ In general, amides have been prepared by the reaction of liquid ammonia with esters at temperatures varying from –33° to 250°.^{2,8,9}

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 85

References and Notes

1. Adkins, *Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts*, p. 31, University of Wisconsin Press, Madison, Wisconsin, 1937; *Ind. Eng. Chem., Anal. Ed.*, **4**, 342 (1932).
2. Wojcik and Adkins, *J. Am. Chem. Soc.*, **56**, 2421 (1934), Paden and Adkins, *J. Am. Chem. Soc.*, **58**, 2497 (1936).
3. Brüning, *Ann.*, **104**, 197 (1857).
4. Ratchford, *J. Org. Chem.*, **15**, 326 (1950).

5. Wurtz and Friedel, *Ann. chim. phys.*, (3) **63**, 108 (1861).
 6. Wislicenus, *Ann.*, **133**, 259 (1865).
 7. Oeda, *Bull. Chem. Soc. Japan*, **11**, 385 (1936).
 8. Glattfeld and MacMillan, *J. Am. Chem. Soc.*, **58**, 898 (1936).
 9. Audrieth and Kleinberg, *J. Org. Chem.*, **3**, 312 (1938).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

ethanol (64-17-5)

ammonia (7664-41-7)

ether (60-29-7)

acetone (67-64-1)

ethyl lactate (687-47-8)

lactic acid (50-21-5)

Methyl lactate (547-64-8)

Lactamide (2043-43-8)

Ethyl mandelate (4358-88-7)

Mandelamide (4410-31-5)

lactic anhydride

lactide (95-96-5)