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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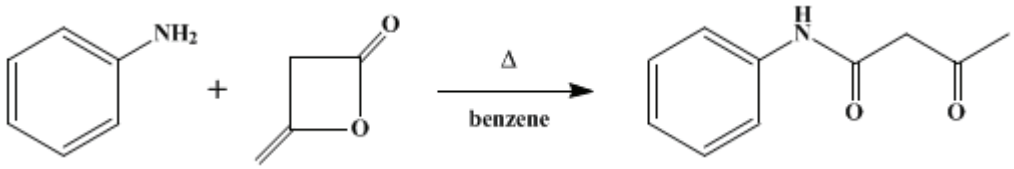
ACETOACETANILIDE



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1. Procedure

In a 500-ml. round-bottomed three-necked flask fitted with a reflux condenser, a dropping funnel, and a mercury-sealed stirrer (Note 1) is placed a solution of 46 g. (0.5 mole) of dry aniline in 125 ml. of pure dry benzene. Stirring is started, and a solution of 42 g. (0.5 mole) of ketene dimer (p. 508) in 75 ml. of pure dry benzene is added dropwise over a period of 30 minutes. The reaction mixture is then heated under reflux on the steam bath for 1 hour. After the major portion of the benzene has been removed by distillation from the steam bath, the remainder is removed under reduced pressure. The residue is dissolved in 500 ml. of hot 50% aqueous ethanol from which the acetoacetanilide separates on cooling. The mixture is cooled to 0° before filtration. A second crop of crystals can be obtained by adding 250 ml. of water to the mother liquor and cooling again (Note 2). The total yield of product, m.p. 82–83.5°, is 65 g. (74%). Further purification by recrystallization from 300 ml. of 50% ethanol yields 55 g. of a product that melts at 84–85°.

2. Notes

1. A seal of rubber tubing lubricated by glycerol is satisfactory.
2. If the second mother liquor is evaporated to about half of its original volume, a small third crop of very impure crystals may be obtained.

3. Discussion

Acetoacetanilide has been prepared by the reaction of aniline with ethyl acetoacetate[1,2,3,4,5] or acetoacetyl chloride,[6] and by the reaction of ketene dimer with aniline.[7,8]

References and Notes

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2. Roos, *Ber.*, **21**, 624 (1888).
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4. Mizuno, *J. Pharm. Soc. Japan*, **69**, 126 (1949).
5. U. S. pat. 2,416,738 [*C. A.*, **41**, 3485 (1947)].
6. Hurd and Kelso, *J. Am. Chem. Soc.*, **62**, 1548 (1940).
7. Chick and Wilsmore, *J. Chem. Soc.*, **1908**, 946.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Ketene dimer

ethanol (64-17-5)

Benzene (71-43-2)

aniline (62-53-3)

glycerol (56-81-5)

Ethyl acetoacetate (141-97-9)

Acetoacetanilide (102-01-2)

acetoacetyl chloride