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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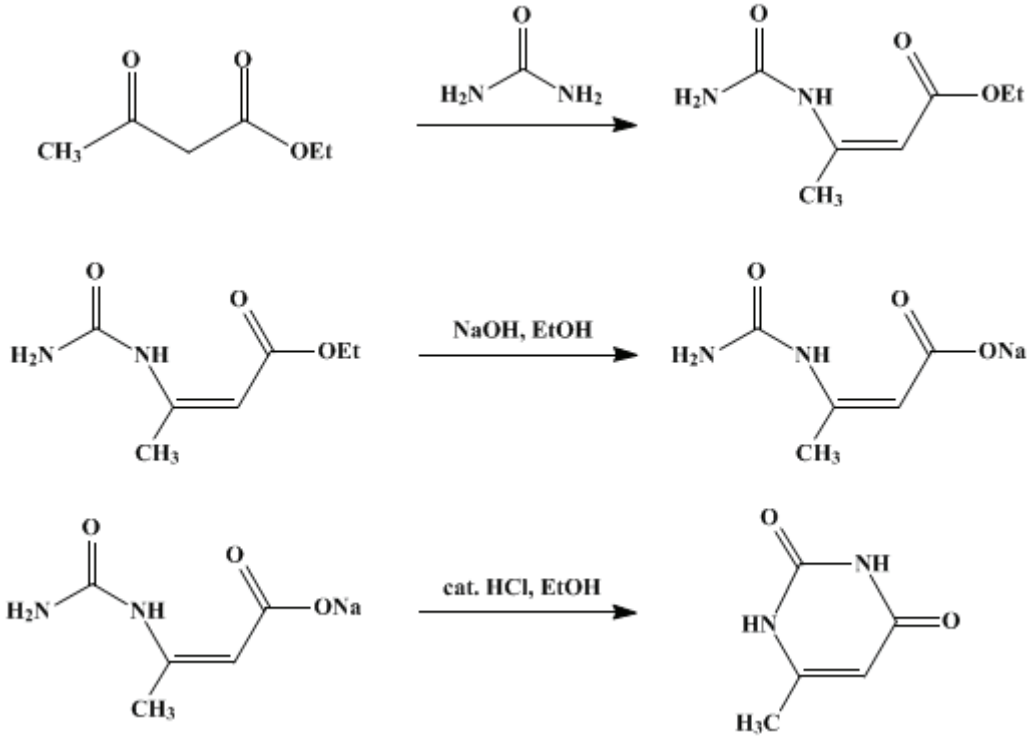
Organic Syntheses, Coll. Vol. 2, p.422 (1943); Vol. 17, p.63 (1937).

6-METHYLURACIL

[Uracil, 6-methyl-]



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1. Procedure

Eighty grams (1.33 moles) of finely powdered urea is stirred into a mixture of 160 g. (155 cc., 1.23 moles) of ethyl acetoacetate (Note 1), 25 cc. of absolute alcohol (Note 2), and ten drops of concentrated hydrochloric acid in a 5-in. crystallizing dish. The reagents are mixed well, and the dish is covered loosely with a watch glass and placed in a vacuum desiccator over concentrated sulfuric acid. The desiccator is evacuated continuously with a water pump until the mixture has gone to dryness (Note 3), which usually requires from five to seven days (Note 4). The crude β-uraminocrotonic ester when thoroughly dry weighs 200–205 g.

The dry, finely powdered, crude β-uraminocrotonic ester is stirred into a solution of 80 g. (2 moles) of sodium hydroxide in 1.2 l. of water at 95°. The clear solution is then cooled to 65° and carefully acidified, while stirring, by the slow addition of concentrated hydrochloric acid. The 6-methyluracil precipitates almost immediately, and after the mixture is cooled the product is collected on a filter, washed with cold water, alcohol, and ether, and air-dried. The substance is obtained as a colorless powder of a high degree of purity, and the yield is 110–120 g. (71–77 per cent of the theoretical amount). For further purification the pyrimidine may be crystallized from glacial acetic acid. 6-Methyluracil decomposes above 300°.

2. Notes

1. Commercial ethyl acetoacetate can be used with satisfactory results. Directions for preparing this ester are given in Org. Syn. Coll. Vol. I, **1941**, 235.
2. Larger amounts of alcohol increase the period of drying without improving the yield. When no

alcohol is used, the condensation proceeds slowly and the yields are low.
3. If the condensation product is used before it is dry, a large amount of carbon dioxide is evolved later in the acidification, indicating incomplete utilization of the ethyl acetoacetate.
4. It is usually advisable to change the sulfuric acid at least daily. Any lumps should be disintegrated occasionally to aid in the drying process.

3. Discussion

The synthesis of 6-methyluracil from ethyl acetoacetate and urea was described first by Behrend.[1] The substance has been obtained also by the action of lead hydroxide on methylthiouracil in an alkaline medium;[2] by boiling benzal-2-(4-hydroxy-6-methyl) pyrimidylhydrazine with hydrochloric acid;[3] and from urea and diketene.[4]

References and Notes

1. Behrend, Ann. **229**, 5 (1885); Behrend and Roosen, ibid. **251**, 238 (1889) Biltz and Heyn, ibid. **413**, 109 (1917).
2. List, ibid. **236**, 23 (1886).
3. Thiele and Bihan, ibid. **302**, 308 (1898).
4. Carbide and Carbon Chemicals Corporation, U. S. pat. 2,138,756 [C. A. **33**, 2152 (1939)]; Standard Oil Development Company, U. S. pat. 2,174,239 [C. A. **34**, 450 (1940)]; Boese, Ind. Eng. Chem. **32**, 16 (1940).

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

β-uraminocrotonic ester

benzal-2-(4-hydroxy-6-methyl) pyrimidylhydrazine

alcohol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

lead hydroxide

carbon dioxide (124-38-9)

diketene (674-82-8)

urea (57-13-6)

Ethyl acetoacetate (141-97-9)

6-Methyluracil,
Uracil, 6-methyl- (626-48-2)

pyrimidine (289-95-2)

methylthiouracil