



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.

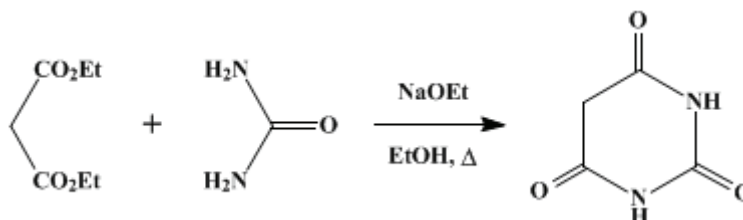
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior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

Organic Syntheses, Coll. Vol. 2, p.60 (1943); Vol. 18, p.8 (1938).

BARBITURIC ACID



Submitted by J. B. Dickey and A. R. Gray.
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1. Procedure

In a 2-l. round-bottomed flask fitted with a reflux condenser protected by a calcium chloride tube, 11.5 g. (0.5 gram atom) of finely cut **sodium** is dissolved in 250 cc. of absolute **alcohol**. To this solution is added 80 g. (0.5 mole) of **ethyl malonate** followed by 30 g. (0.5 mole) of dry **urea** dissolved in 250 cc. of hot (70°) absolute **alcohol**. After being well shaken the mixture is refluxed for seven hours on an oil bath heated to 110°. A white solid separates rapidly. After the reaction is completed, 500 cc. of hot (50°) water is added and then enough **hydrochloric acid** (sp. gr. 1.18) to make the solution acidic (about 45 cc.). The resulting clear solution is filtered and cooled in an ice bath overnight. The white product is collected on a Büchner funnel, washed with 50 cc. of cold water, and then dried in an oven at 105–110° for three to four hours. The yield of **barbituric acid** is 46–50 g. (72–78 per cent of the theoretical amount).

3. Discussion

Barbituric acid has been prepared by the action of **phosphorus oxychloride** on **malonic acid** and **urea**;¹ by treating an **acetic acid** solution of **urea** and **malonic acid** with **acetic anhydride**;² from **ethyl malonate** and **urea** using **sodium ethoxide** as a condensing agent;³ and from **ethyl malonate** and the sodium derivative of urea prepared from **urea** and **sodium** in liquid **ammonia**.⁴

The procedure described is an adaption of that of Michael.³

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 2*, 440
- *Org. Syn. Coll. Vol. 3*, 37

References and Notes

1. Grimaux, *Compt. rend.* **87**, 752 (1878); Conrad and Guthzeit, *Ber.* **14**, 1643 (1881); Grimaux, *Bull. soc. chim.* (2) **31**, 146 (1879); Matignon, *Ann. chim. phys.* (6) **28**, 289 (1893).
 2. Biltz and Wittek, *Ber.* **54**, 1035 (1921).
 3. Michael, *J. prakt. Chem.* (2) **35**, 456 (1887); Tafel and Weinschenk, *Ber.* **33**, 3383 (1900); Gabriel and Colman, *ibid.* **37**, 3657 (1904).
 4. Jacobson, U. S. pat. 2,090,594 [C. A. **31**, 7068 (1937)].
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(Registry Number)

sodium derivative of urea

alcohol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ammonia (7664-41-7)

acetic anhydride (108-24-7)

Phosphorus Oxychloride (21295-50-1)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

urea (57-13-6)

ethyl malonate (1071-46-1)

Malonic acid (141-82-2)

Barbituric acid (67-52-7)