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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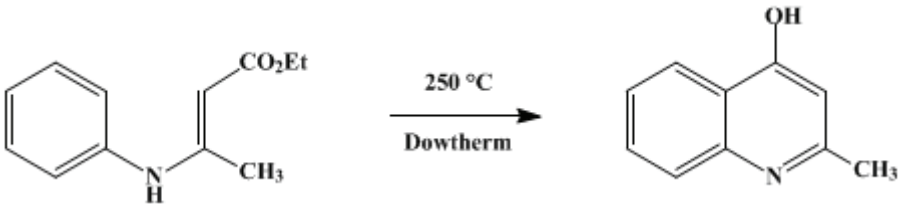
2-METHYL-4-HYDROXYQUINOLINE

[4-Quinolinol, 2-methyl-]



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1. Procedure

In a 500-ml. three-necked round-bottomed flask equipped with a dropping funnel, a sealed mechanical stirrer, and an air condenser is placed 150 ml. of Dowtherm (Note 1). The Dowtherm is stirred and heated at the reflux temperature while 65 g. (0.32 mole) of ethyl β-anilinocrotonate (p. 374) is added rapidly through the dropping funnel. Stirring and refluxing are continued for 10–15 minutes after the addition is completed. The ethanol formed in the condensation reaction may be allowed to escape from the condenser through a tube leading to a drain, or it may be collected by attaching a water-cooled condenser set for distillation to the top of the air condenser. The mixture is allowed to cool to room temperature, at which stage a yellow solid separates. Approximately 200 ml. of petroleum ether (b.p. 60–70°) is added; the solid is collected on a Büchner funnel and washed with 100 ml. of petroleum ether (b.p. 60–70°). After air drying, the crude product is treated with 10 g. of Darco or Norit in 1 l. of boiling water (Note 2). The hot solution is filtered and allowed to cool. The white, hairlike needles of 2-methyl-4-hydroxyquinoline are separated by filtration. The yield of product, melting at 235–236° (cor.), is 43–46 g. (85–90%).

2. Notes

1. Dowtherm is a mixture of diphenyl and diphenyl ether, obtainable from the Dow Chemical Company.
2. If the treatment with decolorizing carbon is omitted, the product has a low melting point after several crystallizations.

3. Discussion

The present procedure is a modification of preparations described previously.[1,2,3] The cyclization has been effected by allowing a solution of ethyl β-anilinocrotonate in concentrated sulfuric acid to stand at room temperature for several hours; by rapidly heating the ester to 240–250° without a solvent;[2] or by adding the ester to paraffin oil at 250°[3] or to refluxing diphenyl ether.[4] The procedure described has been applied to the preparation of other 2-substituted 4-hydroxyquinolines.[5]

References and Notes

1. Knorr, *Ber.*, **16**, 2593 (1883).
2. Conrad and Limpach, *Ber.*, **20**, 944 (1887).
3. Cavalito and Haskell, *J. Am. Chem. Soc.*, **66**, 1166 (1944).
4. Kaslow and Marsh, *J. Org. Chem.*, **12**, 456 (1947).
5. Hauser and Reynolds, *J. Am. Chem. Soc.*, **70**, 2402 (1948).

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

petroleum ether

Dowtherm

diphenyl

ethanol (64-17-5)

sulfuric acid (7664-93-9)

decolorizing carbon,
Norit (7782-42-5)

diphenyl ether (101-84-8)

ETHYL β-ANILINOCROTONATE (6287-35-0)

2-Methyl-4-hydroxyquinoline,
4-Quinolinol, 2-methyl- (607-67-0)