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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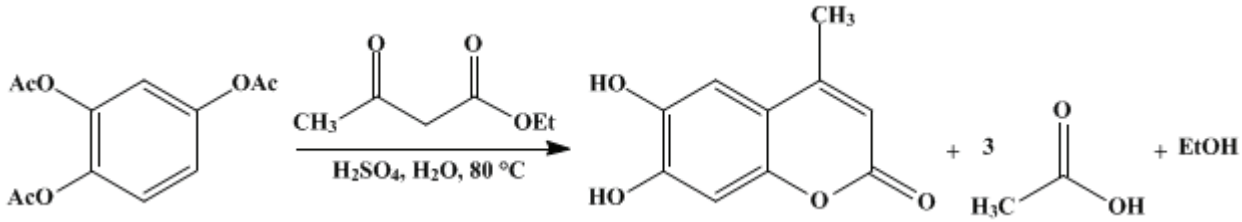
4-METHYLESCULETIN

[Esculetin, 4-methyl-]



Submitted by E. B. Vliet
Checked by Roger Adams and E. E. Dreger.

1. Procedure

A smooth, uniform paste is made by thoroughly mixing 60 g. (0.45 mole) of ethyl acetoacetate (p. 235) (Note 1) and 114 g. (0.45 mole) of hydroxyhydroquinone triacetate (p. 317). This requires several minutes of stirring. To this mixture is added 450 cc. of 75 per cent sulfuric acid (Note 2). The paste slowly dissolves with the evolution of heat, giving a deep red solution; the latter is heated on a warm bath with occasional stirring until it reaches 80°, at which temperature it is maintained for one-half hour. It is then allowed to cool to room temperature and poured into 1850 cc. of cold water. The resulting mixture is cooled to room temperature, filtered with suction, and the precipitate washed with cold water to free it from excess acid. The 4-methylesculetin thus obtained is dried at 100° and is generally gray in color. The yield is about 80 g. (92 per cent of the theoretical amount).

A pure product may be obtained by dissolving, with the aid of heat and stirring, 100 g. of 4-methylesculetin in a solution of 200 g. of borax in 700 cc. of water. The solution obtained is filtered while hot and then cooled, whereupon the esculetin borate separates (Note 3). This is filtered off and dissolved in 1800 cc. of water, and the solution thus obtained added to 50 g. (27.2 cc.) of concentrated sulfuric acid in 500 cc. of water. 4-Methylesculetin separates and, after the mixture has been cooled, is filtered, washed, and dried. From 100 g. of the crude material, 85 g. of pure product melting at 272–274° (uncorr.) is obtained. This is generally nearly colorless but occasionally possesses a slight grayish tinge.

2. Notes

1. In order to obtain a fairly pure product without recrystallization, the intermediate ethyl acetoacetate and hydroxyhydroquinone triacetate must be pure.
2. It is important to use 75 per cent sulfuric acid in this reaction, because more concentrated acid gives a very dark product and a lower yield, while more dilute acid will not induce the reaction.
3. The exact nature of the precipitate has not been determined.

3. Discussion

4-Methylesculetin can be prepared by condensing hydroxyhydroquinone triacetate and ethyl acetoacetate with sulfuric acid or zinc chloride.[1]

References and Notes

1. v. Pechmann and v. Krafft, Ber. **34**, 423 (1901); Bargellini and Martegiani, Gazz. chim. ital. **41** (2), 613 (1911).

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

sulfuric acid (7664-93-9)

zinc chloride (7646-85-7)

Ethyl acetoacetate (141-97-9)

Hydroxyhydroquinone triacetate (613-03-6)

4-Methylesculetin,
Esculetin, 4-methyl- (529-84-0)

esculetin borate

borax (1303-96-4)