



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](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.

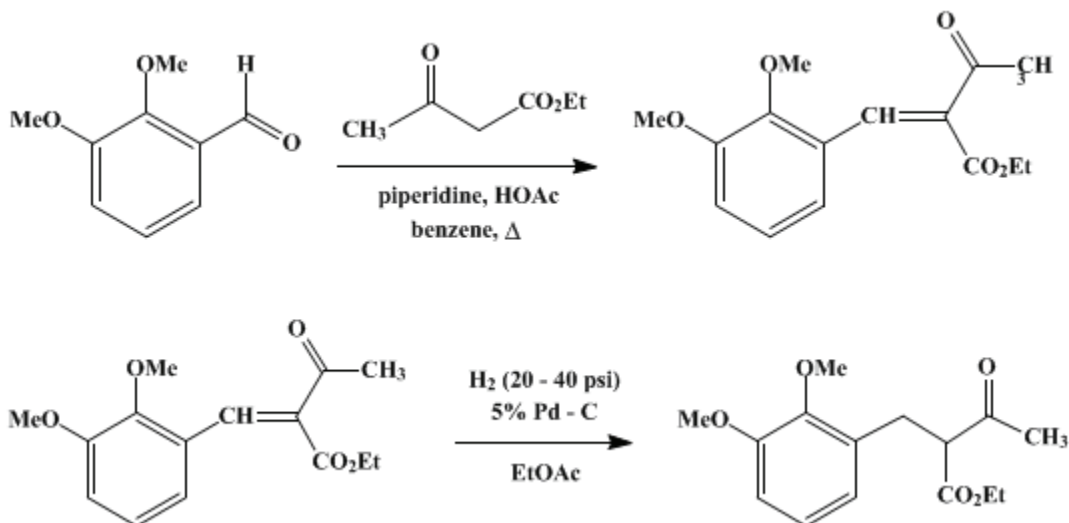
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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.*

*Organic Syntheses, Coll. Vol. 4, p.408 (1963); Vol. 31, p.56 (1951).*

## ETHYL $\alpha$ -ACETYL- $\beta$ -(2,3-DIMETHOXYPHENYL)-PROPIONATE

[Hydrocinnamic acid,  $\alpha$ -acetyl-2,3-dimethoxy-, ethyl ester]



Submitted by E. C. Horning, J. Koo, M. S. Fish, and G. N. Walker<sup>1</sup>.

Checked by T. L. Cairns and Charles W. Todd.

### 1. Procedure

A. *Ethyl  $\alpha$ -acetyl- $\beta$ -(2,3-dimethoxyphenyl)acrylate.* In a 1-l. round-bottomed flask fitted with a water-benzene separator<sup>2</sup> and a reflux condenser are placed 183 g. (1.1 moles) of 2,3-dimethoxybenzaldehyde (Note 1) and 130 g. (1.0 mole) of ethyl acetoacetate. The water-benzene separator is filled with benzene, an additional 70 ml. of benzene is added to the mixture, and the 2,3-dimethoxybenzaldehyde is brought into solution by warming. Piperidine (4 ml.) and glacial acetic acid (12 ml.) are added, and the mixture is heated under reflux for 2–3 hours (Note 2). The mixture is cooled, poured into a separatory funnel with 800 ml. of ether, and washed successively with 200-ml. portions of 5% hydrochloric acid, 5% sodium bicarbonate solution, and 5% acetic acid, and twice with water. The extract is dried over anhydrous magnesium sulfate (about 250 g.). After filtration, the ether and benzene are distilled under atmospheric pressure, and the residue is distilled under reduced pressure. The yield of viscous, yellow oil collected at 186–190°/2 mm. (Note 3) is 180–199 g. (64–72%),  $n_D^{25}$  1.5507–1.5508.

B. *Ethyl  $\alpha$ -acetyl- $\beta$ -(2,3-dimethoxyphenyl)propionate.* The product obtained in Part A is divided into two approximately equal portions, and to each are added 125 ml. of ethyl acetate and 5 g. of 5% palladium-on-carbon catalyst (Note 4). Each solution is shaken with hydrogen at pressures between 20 and 40 lb. in a low-pressure apparatus. About 45 minutes is usually needed for complete reduction. The two solutions are then combined, and the catalyst is removed by filtration and washed with 20 ml. of ethyl acetate. The ethyl acetate is distilled at atmospheric pressure, and distillation of the residue under reduced pressure yields 158–176 g. (56–63% over-all) of a colorless product collected at 175–177°/3 mm.,  $n_D^{25}$  1.5042–1.5044 (Note 3) and (Note 5).

### 2. Notes

1. A practical grade of 2,3-dimethoxybenzaldehyde, although discolored, is satisfactory. It is best handled and weighed as a liquid. This is done by warming the container on a steam bath for several minutes.

2. The time of reflux is determined by the rate at which water separates from the reaction mixture. In general, the theoretical amount of water (18 ml.) is collected in the water separator after about 1 hour, but additional refluxing usually results in the separation of another 4–5 ml. Anhydrous materials are not

necessary for the reaction.

3. Using a 6-in. Vigreux column with a wide side arm, the checkers observed a boiling point of 166–168°/3 mm. for [ethyl  \$\alpha\$ -acetyl- \$\beta\$ -\(2,3-dimethoxyphenyl\)propionate](#) and 176–179°/2 mm. for the [acrylate](#).

4. These quantities are convenient for hydrogenation in a Parr low-pressure apparatus; if a larger apparatus is available, it is unnecessary to divide the material. The palladium-on-carbon catalyst is prepared by Hartung's method,<sup>3</sup> using sufficient [Norit](#) to give a 5% catalyst. A few chips of Dry Ice should be placed in the bottle before the catalyst is added to provide an inert atmosphere. The checkers used a catalyst obtained from Baker and Company, Inc., 113 Astor Street, Newark, New Jersey.

5. The same procedure may be used with other aromatic aldehydes. The acrylate ester prepared from [veratraldehyde](#) is a crystalline compound melting at 82.5–84.5°. It may be purified by distillation under reduced pressure, b.p. 190–196°/0.8 mm. The yield is 53–63%. The hydrogenated product is obtained as a colorless oil, b.p. 180–183°/1.0 mm., in 38–44% over-all yield.

### 3. Discussion

Substituted  $\alpha$ -benzylacetoacetic esters have usually been prepared by the general method of Leuchs,<sup>4</sup> in which [ethyl acetoacetate](#) is alkylated in [ethanol](#) solution with [benzyl chloride](#) and [sodium ethoxide](#). The present method is based upon Cope's<sup>5</sup> procedure for the condensation of carbonyl compounds with [ethyl acetoacetate](#), followed by catalytic reduction of the condensation product.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 5, 550](#)

---

### References and Notes

1. University of Pennsylvania, Philadelphia, Pennsylvania.
2. [Org. Syntheses Coll. Vol. 3, 382 \(1955\)](#).
3. [Org. Syntheses Coll. Vol. 3, 685 \(1955\), Method D](#).
4. Leuchs, *Ber.*, **44**, 1510 (1911).
5. Cope and Hofmann, *J. Am. Chem. Soc.*, **63**, 3456 (1941).

---

### Appendix

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

palladium-on-carbon

$\alpha$ -benzylacetoacetic esters

[ethanol](#) (64-17-5)

[hydrochloric acid](#) (7647-01-0)

[acetic acid](#) (64-19-7)

[Benzene](#) (71-43-2)

[ethyl acetate](#) (141-78-6)

ether (60-29-7)

hydrogen (1333-74-0)

sodium bicarbonate (144-55-8)

Norit (7782-42-5)

piperidine (110-89-4)

sodium ethoxide (141-52-6)

benzyl chloride (100-44-7)

Ethyl acetoacetate (141-97-9)

magnesium sulfate (7487-88-9)

Veratraldehyde (120-14-9)

acrylate

2,3-dimethoxybenzaldehyde (86-51-1)

ETHYL  $\alpha$ -ACETYL- $\beta$ -(2,3-DIMETHOXYPHENYL)-PROPIONATE,  
Hydrocinnamic acid,  $\alpha$ -acetyl-2,3-dimethoxy-, ethyl ester,  
Ethyl  $\alpha$ -acetyl- $\beta$ -(2,3-dimethoxyphenyl)propionate (53608-80-3)

Ethyl  $\alpha$ -acetyl- $\beta$ -(2,3-dimethoxyphenyl)acrylate (19411-81-5)