



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.

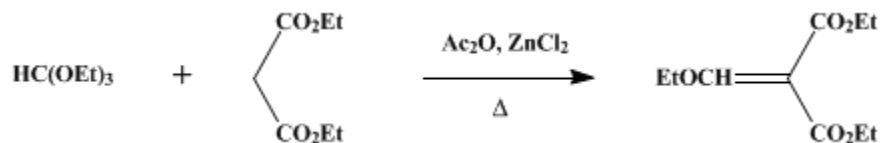
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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. 3, p.395 (1955); Vol. 28, p.60 (1948).*

## ETHYL ETHOXYMETHYLENEMALONATE

[Malonic acid, ethoxymethylene-, diethyl ester]



Submitted by W. E. Parham and L. J. Reed<sup>1</sup>.

Checked by J. R. Roland, C. W. Todd, and R. S. Schreiber.

### 1. Procedure

A mixture of 1000 g. (6.75 moles) of **ethyl orthoformate**, 1260 g. (12.3 moles) of **acetic anhydride**, 960 g. (6.0 moles) of **ethyl malonate**, and 0.5 g. of anhydrous **zinc chloride** is prepared in a 5-l. three-necked flask equipped with a thermometer, a gas inlet tube, and a 12-in. column packed with Berl Saddles (**Note 1**). The column is attached to a still head and condenser. The contents of the flask are well agitated for 5 minutes by a stream of dry air and then heated (**Note 2**) as follows: 102–115° for 2.5 hours, 115–127° for 7 hours [after the eighth hour of heating, 250 g. (2.45 moles) of **acetic anhydride** and 200 g. (1.35 moles) of **ethyl orthoformate** are added], 127–145° for 2 hours, and 145–155° for 2 hours (**Note 3**). At the end of 13.5 hours of heating the mixture is cooled to room temperature and filtered (**Note 4**). The filtrate is distilled under reduced pressure (15–20 mm.) until the temperature at the still head reaches 100° (**Note 5**). The distillation is then continued under lower pressure (0.25 mm.). The yield of **ethyl ethoxymethylenemalonate**, b.p. 108–110°/0.25 mm. (**Note 6**), is 650–780 g. (50–60% based on the **ethyl malonate** used).

### 2. Notes

1. The use of this column prevents loss of **acetic anhydride** during the heating process and permits volatile products formed during the reaction to be removed by distillation. The checkers used a 1 by 12 in. column packed with 6 by 6 mm. glass rings.
2. The **zinc chloride** dissolves, and a chlorine-free crystalline precipitate soon separates. The checkers observed only traces of this precipitate.
3. The final heating is necessary to convert unchanged **ethyl diethoxymethylmalonate**, an intermediate in the reaction, into **ethyl ethoxymethylenemalonate**. This intermediate is difficult to separate from **ethyl ethoxymethylenemalonate** by distillation, and it is important that it be converted as completely as possible during the heating process.
4. The mixture is filtered through a fluted filter paper to remove suspended zinc salts.
5. Unchanged **ethyl malonate** (as much as 15% of the amount used) can be obtained by redistillation of the fraction boiling at 70–100°/17 mm.
6. Since **ethyl diethoxymethylmalonate** is difficult to separate from **ethyl ethoxymethylenemalonate** by distillation, it is necessary to follow the course of the distillation by observation of the change in refractive index instead of the change in boiling point. After a low-boiling fraction is collected, there is obtained an intermediate fraction ( $n_D^{20}$  1.4142–1.4580), the size of which depends upon the amount of **ethyl diethoxymethylmalonate** present. Under the best of conditions it amounts to 15 g. In each of three runs, the checkers obtained about 300–400 g. of material having a refractive index in this range. The **ethyl ethoxymethylenemalonate** was collected at  $n_D^{20}$  1.4580–1.4623. The checkers used a 5-in. Vigreux column and observed that at the low pressures the boiling point of the distillate in several runs was about 10° lower than that reported by the submitters. For example, in one run at 0.25 mm. (gauge pressure) the boiling point of the distillate never rose above 97.2°; however, the refractive indices of twelve 50-ml. fractions taken in the course of this distillation were all in the proper range,  $n_D^{20}$  1.4612–1.4623. Interruption of the heating during the reaction period should be avoided. In an experiment in which the heating was discontinued after about 8 hours and resumed the next day the yield was about

50%.

### 3. Discussion

Ethyl ethoxymethylenemalonate has been prepared by heating ethyl orthoformate, ethyl malonate, and acetic anhydride in the presence of zinc chloride.<sup>2,3</sup> A higher yield of purer product is obtained by the method described above,<sup>4</sup> which is a modification of the Claisen procedure.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 272
- Org. Syn. Coll. Vol. 4, 298

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### References and Notes

1. Work done under contract with the Office of Scientific Research and Development.
  2. Claisen, *Ber.*, **26**, 2729 (1893); *Ann.*, **297**, 76 (1897).
  3. Wheeler and Johns, *Am. Chem. J.*, **40**, 237 (1908).
  4. Fuson, Parham, and Reed, *J. Org. Chem.*, **11**, 194 (1946).
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### Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

acetic anhydride (108-24-7)

zinc chloride (7646-85-7)

Ethyl orthoformate

ethyl malonate (1071-46-1)

ethyl ethoxymethylenemalonate

Malonic acid, ethoxymethylene-, diethyl ester (87-13-8)

ethyl diethoxymethylmalonate