



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.

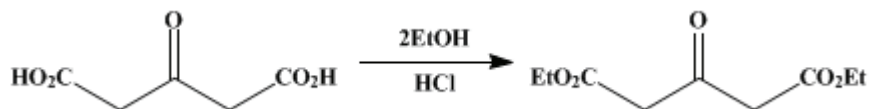
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.237 (1941); Vol. 5, p.53 (1925).

ETHYL ACETONEDICARBOXYLATE

[Glutaric acid, β -oxo-, diethyl ester]



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1. Procedure

The crude [acetonedicarboxylic acid](#) from 700 g. (3.64 moles) of [citric acid](#), as described on [p. 10](#), is treated with 700 g. (882 cc.) of absolute [ethyl alcohol](#) ([pp. 249 and 259](#)) ([Note 1](#)) to which has been added at least 130–150 g. of *dry* [hydrogen chloride](#) ([p. 293](#)). The mixture is placed in a flask fitted with a stopper holding a calcium chloride tube and then is heated to 45°. It is kept in a water bath at 45° (bath temperature) with frequent shaking until all the acid is dissolved (fifteen to twenty minutes). The solution is allowed to cool down to room temperature in the bath and finally to stand about twelve hours ([Note 2](#)).

The contents of the flask are then poured into 1300–1400 cc. of ice water, the ester layer separated, and the water-alcohol layer extracted twice with 700-cc. portions of [benzene](#). The [benzene](#) extracts are added to the original ester, which has been separated. The total solution thus obtained is washed with about 400 cc. of 10 per cent [sodium carbonate](#) solution to remove the acid, then once with dilute [sulfuric acid](#), and finally twice with 400-cc. portions of water ([Note 3](#)). The [benzene](#) is distilled on a water bath, and the ester is distilled under reduced pressure. A small low-boiling fraction comes over first, and then the ester, which boils at 131–136°/9–10 mm. or 145–148°/17 mm. ([Note 4](#)). The yield of product amounts to 284–315 g. (39–43 per cent of the theoretical amount based on the [citric acid](#)).

2. Notes

1. The directions given in the literature call for a smaller amount of alcohol than that given in the procedure, but more consistent results were obtained with the method described.
2. The ester should be isolated from the reaction mixture after twelve hours. Longer standing causes a decreased yield.
3. One of the chief precautions which must be observed, if good yields are to be obtained, is thorough and careful washing of the [benzene](#) and ester mixture. If this is not done, decomposition occurs during distillation and the yields are lowered by about one-third.
4. The ester must be distilled under low pressure (less than 20 mm.) or considerable decomposition occurs.

3. Discussion

[Ethyl acetonedicarboxylate](#) can be prepared by the esterification of [acetonedicarboxylic acid](#)¹ and of [ethyl \$\gamma\$ -cyanoacetoacetate](#).²

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 10](#)

References and Notes

1. Pechmann, Ann. **261**, 159 (1891); Jerdan, J. Chem. Soc. **75**, 809 (footnote) (1899); Ingold and Nickolls, *ibid.* **121**, 1642 (1922); Willstätter and Pfannenstiel, Ann. **422**, 6 (1921).
 2. Haller and Held, Compt. rend. **111**, 683 (1890).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

ethyl alcohol (64-17-5)

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

Benzene (71-43-2)

Acetonedicarboxylic acid

citric acid (77-92-9)

sodium carbonate (497-19-8)

Ethyl acetonedicarboxylate

Glutaric acid, β -oxo-, diethyl ester (105-50-0)

ethyl γ -cyanoacetoacetate