



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.

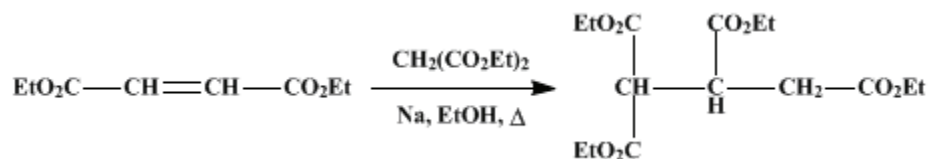
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.272 (1941); Vol. 4, p.29 (1925).

ETHYL PROPANE-1,1,2,3-TETRACARBOXYLATE

[1,1,2,3-Propanetetracarboxylic acid, tetraethyl ester]



Submitted by H. T. Clarke and T. F. Murray.

Checked by C. S. Marvel and M. M. Brubaker.

1. Procedure

In a 5-l. flask, fitted with a stirrer, a reflux condenser, and a dropping funnel, is placed 1 kg. (1266 cc.) of absolute [ethyl alcohol](#) (p. 249 and p. 259); 92 g. (4 atoms) of [sodium](#), cut into strips, is then added through the condenser at such a rate that the alcohol does not boil too vigorously. When all the [sodium](#) is in solution, the flask is cooled and 800 g. (754 cc., 5 moles) of [diethyl malonate](#) added through the condenser, with stirring. The mixture is warmed gently on the steam bath and 700 g. (658 cc., 4.1 moles) of [diethyl fumarate](#) ([Note 1](#)) added from the dropping funnel. During this addition the solution is kept boiling gently, heat being applied if necessary ([Note 2](#)). The mixture is boiled for one hour after the [diethyl fumarate](#) has been added. It is then cooled and 250 g. (238 cc., 4.2 moles) of glacial [acetic acid](#) is added.

Most of the alcohol is distilled off under slightly reduced pressure on the steam bath and the residue is poured into sufficient distilled water to dissolve all the solid. The water layer is separated and extracted four times with [carbon tetrachloride](#), which is added to the ester layer. The ester-carbon tetrachloride mixture is washed twice with water and the water washings extracted once with [carbon tetrachloride](#). The [carbon tetrachloride](#) is distilled off under atmospheric pressure through a column, the moisture being carried over simultaneously.

The residue is then distilled under reduced pressure, when the [ethyl propane-1,1,2,3-tetracarboxylate](#) comes over at 182–184°/8 mm. The yield is 1261–1273 g. (93–94 per cent of the theoretical amount).

2. Notes

1. The [diethyl malonate](#) and [diethyl fumarate](#) should be redistilled under reduced pressure, and the material boiling over a 2° range collected. Directions for the preparation of [diethyl fumarate](#) are given in [Org. Syn. 10](#), 48, and for [fumaric acid](#) in [Org. Syn. 11](#), 46.
2. Heat is developed during the reaction, and the mixture may be kept boiling by adding the [ethyl fumarate](#) at a suitable rate.

3. Discussion

[Ethyl propane-1,1,2,3-tetracarboxylate](#) can be prepared by condensing malonic ester with [ethyl chlorosuccinate](#),¹ [ethyl ethoxysuccinate](#),² [diethyl fumarate](#)³ or [diethyl maleate](#).⁴ The last two methods are now most convenient because of the commercial availability of fumaric and maleic acids.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 523](#)

References and Notes

1. Emery, Ber. **23**, 3759 (1890).
 2. Staudinger, Z. Naturw. **75**, 385 (1903) [Chem. Zentr. II, 943 (1903)]; Ann. **341**, 104 (1905).
 3. Auwers, Köbner and v. Myenburg, Ber. **24**, 2889 (1891); Michael and Schulthess, J. prakt. Chem. (2) **45**, 56 (1892); Ruhemann and Cunningham, J. Chem. Soc. **73**, 1007 (1898); Staudinger, Ann. **341**, 102 (1905).
 4. Michael and Schulthess, J. prakt. Chem. (2) **45**, 56 (1892).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

ester-carbon tetrachloride

fumaric and maleic acids

ethyl alcohol (64-17-5)

acetic acid (64-19-7)

carbon tetrachloride (56-23-5)

sodium (13966-32-0)

ethyl fumarate (2459-05-4)

diethyl malonate (105-53-3)

Fumaric acid (110-17-8)

Ethyl propane-1,1,2,3-tetracarboxylate

1,1,2,3-Propanetetracarboxylic acid, tetraethyl ester (635-03-0)

diethyl fumarate (623-91-6)

ethyl chlorosuccinate

ethyl ethoxysuccinate

diethyl maleate (141-05-9)