



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.

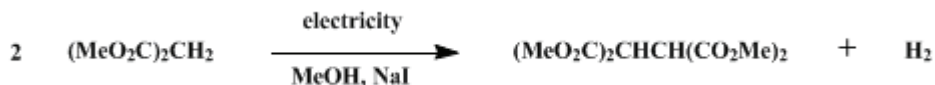
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries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

Organic Syntheses, Coll. Vol. 7, p.482 (1990); Vol. 60, p.78 (1981).

INDIRECT ELECTROLYSIS: TETRAMETHYL 1,1,2,2-ETHANETETRACARBOXYLATE

[1,1,2,2-Ethanetetracarboxylic acid, tetramethyl ester]



Submitted by Donald A. White¹

Checked by Carl R. Johnson and Robert C. Elliott.

1. Procedure

The preparation is carried out in a 500-mL, three-necked flask equipped with two graphite rod electrodes (Note 1). To the flask are added 132 g (1.0 mol) of dimethyl 1,3-propanedioate (Note 2), 15 g (0.10 mol) of sodium iodide, and 300 mL of methanol. A thermometer and reflux condenser are attached; the mixture is stirred and the solution formed is heated to 60°C. The heat source is removed. The solution is electrolyzed with a constant current of 2.0 A (Note 3) for 13.5 hr (Note 4) with gentle magnetic stirring. After a few minutes of electrolysis, the electrolyte begins to reflux gently and reflux is maintained throughout the electrolysis period by the heating effect of current passage (Note 5). Small granular crystals of the product begin to separate toward the end of the electrolysis period.

After electrolysis the reaction mixture is allowed to cool to room temperature and is filtered (Note 6). The crystalline residue is washed three times with 100-mL portions of methanol, dried by suction on the filter, and finally dried under vacuum. The product (88.4–91 g, 67–69%) is obtained as a white solid, mp 134–135°C.

2. Notes

1. The electrodes are 12 × ¼ in. graphite rods such as those used by glassblowers in shaping softened glass. They are attached as shown on page 183 via thermometer adaptors (Ace Glass Company, Vineland, NJ) and a specially made glass adaptor having two 10/18 and one 34/45 standard-taper joints. The electrodes should extend as far as possible into the electrolyte without interfering with the operation of the magnetic stirrer.
2. Dimethyl 1,3-propanedioate (dimethyl malonate) was obtained from Aldrich Chemical Company, Inc., and used as supplied.
3. A Heath/Schlumberger dc power supply, Model SP-2711, 30 V, 3 A, operating in its constant current mode, was used.
4. The current passed is 1.01F (1 faraday = 26.8 A-hr) and this is sufficient to convert 75–80% of the starting material to product. At higher conversions further oxidation occurs, leading to formation of tetramethyl ethenetetracarboxylate and hexamethyl 1,1,2,2,3,3-propanehexacarboxylate. The latter has solubility properties similar to those of the desired product. The product may be contaminated with the propanehexacarboxylate ester if the reaction is taken to higher conversions.
5. The cell voltage was initially 15 V and rose to 18 V at the end of the electrolysis. The cell voltage should be in the range 15–20 V so that the heat generated can be controlled by reflux. Since the cell voltage changes only slightly during the course of the electrolysis, a constant-voltage power supply could be used.
6. The filtrate contains only 2–5 g of the desired product; recovery is not worthwhile. The filtrate can, however, be reused as the electrolyte for conversion of further propanedioate ester.
7. The product may be recrystallized (from methanol), which gives material with mp 135–136°C.
8. The product gave an acceptable C,H analysis; the molecular weight by osmometry in chloroform was found to be 258 (C₁₀H₁₄O₈ in theory 262). The product showed ¹H NMR (CDCl₃) δ: 3.8, 4.2.

3. Discussion

The propanedioate (malonate) carbanion can be oxidized directly at an anode to give ethanetetracarboxylate esters, presumably via a radical intermediate.^{2,3,4} Competing oxidation of solvent leads to a mixture of products^{3,4} and for preparative purposes it is advantageous to carry out the reaction via indirect electrolysis as reported here. Indirect electrolysis refers to the continuous generation and regeneration of a reagent at an electrode, which interacts with substrate, as opposed to direct reaction of the substrate at the electrode. In the present case [iodine](#) is generated at the anode (1) and reacts with the cathodically generated (2) carbanion as shown (3) to give the desired overall reaction (4):

The present procedure is based on literature reports^{5,6} using indirect electrolysis involving electrogenerated halogens. Ethanetetracarboxylate esters have also been prepared by the chemical reaction of propanedioate carbanions with halogens.^{7,8,9} The present procedure has the advantage of providing in situ generation of both the carbanion and the halogen from a small amount of added sodium halide. In other work it has been shown that the anodic formation of ethanetetracarboxylate ester can be paired with cathodic conversion of propenoate (acrylate) to hexanedioate (adipate) esters^{10,11} In addition to these routes based on propanedioate esters, ethanetetracarboxylate esters have been obtained by electrocarboxylation of *cis*-butenedioate (maleate) esters.^{12,13}

14

References and Notes

1. Corporate Research Department, Monsanto Company, St. Louis, MO 63166.
2. Okubo, T.; Tsutsumi, S. *Technol. Rep. Osaka Univ.* **1963**, *13*, 495; *Chem. Abstr.* **1964**, *61*, 6637e.
3. Brettle, R.; Parkin, J. G. *J. Chem. Soc. C* **1967**, 1352–1357.
4. Brettle, R.; Seddon, D. *J. Chem. Soc. C* **1970**, 1153–1154.
5. Okubo, T.; Tsutsumi, S. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 1794–1797.
6. Osa, T.; Okhatsu, Y.; Tezuka, M. "Extended Abstracts"; 149th National Meeting of the Electrochemical Society, Washington, DC, 1976; p. 764.
7. Bischoff, C. A.; Rach, C. *Chem. Ber.* **1884**, *17*, 2781.
8. Bailey, W. J.; Anderson, W. J. *J. Am. Chem. Soc.* **1956**, *78*, 2287–2290.
9. Walker, J.; Appleyard, J. R. *J. Chem. Soc.* **1895**, *67*, 768.
10. Thomas, H. G.; Lux, E. *Tetrahedron Lett.* **1972**, 965–968.
11. Baizer, M. M.; Hallcher, R. C. *J. Electrochem. Soc.* **1976**, *123*, 809–813.
12. Tyssee, D. A.; Wagenknecht, J. H.; Baizer, M. M.; Chruma, J. L. *Tetrahedron Lett.* **1972**, 4809–4812.
13. Tyssee, D. A.; Baizer, M. M. *J. Org. Chem.* **1974**, *39*, 2819–2823.
14. Mulliken, S. P. *J. Am. Chem. Soc.* **1893**, *15*, 526.

Appendix

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

Dimethyl 1,3-propanedioate (dimethyl malonate)

[methanol](#) (67-56-1)

[chloroform](#) (67-66-3)

[iodine](#) (7553-56-2)

[sodium iodide](#) (7681-82-5)

dimethyl 1,3-propanedioate (108-59-8)

Tetramethyl 1,1,2,2-ethanetetracarboxylate,
1,1,2,2-Ethanetetracarboxylic acid, tetramethyl ester (5464-22-2)

tetramethyl ethenetetracarboxylate (1733-15-9)

hexamethyl 1,1,2,2,3,3-propanehexacarboxylate