



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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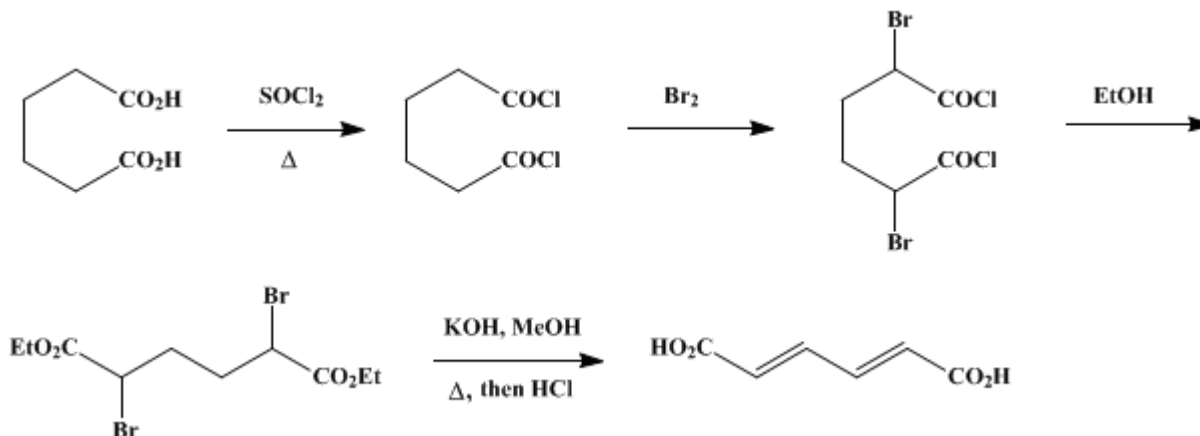
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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MUCONIC ACID



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1. Procedure

A. *Diethyl α,δ -dibromoadipate*. In a 3-l. three-necked flask (Note 1) fitted with a reflux condenser, a dropping funnel, and a mechanical stirrer are placed 1 kg. (6.85 moles) of adipic acid and 2 kg. (1220 ml., 16.8 moles) of thionyl chloride (Note 2) and (Note 3). The mixture is stirred and heated gently on the steam bath until solution is effected, and the evolution of hydrogen chloride (Note 4) ceases after about 3 hours. The excess thionyl chloride is distilled by heating on a steam bath, the last portion of the reagent being taken off under reduced pressure.

To the acid chloride, mechanically stirred and heated on the steam bath, is added 2.5 kg. (805 ml., 15.6 moles) of dry bromine (p. 124) as rapidly as it will react (Note 5). The addition requires about 12 hours. The contents of the flask are stirred and heated an additional 2 hours, transferred to a dropping funnel (Note 6), and added in a thin stream to 5 l. of absolute ethanol, which has previously been placed in a 12-l. flask provided with a stopper carrying an efficient reflux condenser, a separatory funnel, and a mechanical stirrer. The resulting vigorous reaction is controlled by external cooling. After the dibromoacid chloride has been added, the reaction mixture is allowed to stand at room temperature overnight and is then poured into 5 l. of cold water. The top ethanolic aqueous layer is decanted and extracted once with 8 l. of ether. The oily bottom layer is dissolved in the ether extract and washed first with 1 l. of a 2% sodium bisulfite solution, then with two 1-l. portions of 3% sodium carbonate solution, and finally with several portions of water. The ether solution is dried over 175 g. of potassium carbonate; the solvent is distilled on the steam bath. The yield of residual ester (Note 7) amounts to 2260–2400 g. (91–97%).

B. *Muconic acid*. To a solution of 3 kg. of potassium hydroxide and 5 l. of methanol (Note 8) in a 12-l. flask, equipped as described above, is added in a thin stream from a separatory funnel (Note 6), and with stirring, 1130 g. (3.14 moles) of diethyl α,δ -dibromoadipate. The ester is heated on the steam bath to nearly 100° before it is added. The addition is so regulated as to permit rather vigorous refluxing and requires 45 minutes. Heating on the steam bath and stirring are continued an additional 2 hours. The mixture is allowed to stand at room temperature overnight and is cooled. The potassium muconate and potassium bromide are filtered (Note 9), washed on the funnel with two 350-ml. portions of methanol and 400 ml. of ether, transferred without further drying to an enameled 11- to 12-l. pail, and dissolved in 8 l. of hot water. The aqueous solution, to which is added 30 g. of Norit, is heated to boiling by introduction of steam, filtered through a Norit filter pad by suction, and cooled in an ice-salt bath. The muconic acid is precipitated by the addition of a large excess (1.5 l.) (sp. gr. 1.18) of concentrated hydrochloric acid to the cold solution. The acid is added in a thin stream to the well-stirred solution.

After 2 hours the **muconic acid** is filtered, washed first with two 400-ml. portions of cold water and then with 200 ml. of **methanol**, and dried at 85°. The yield of nearly colorless product melting at 296–298°, with decomposition, amounts to 165–195 g. (37–43%).

2. Notes

1. Apparatus with ground-glass joints is preferable.
2. The yield obtained in molar-sized runs is also about 40% of the theoretical.
3. The submitters used 1 mole of **adipic acid** and added 2 moles of **phosphorus pentachloride** in 20-g. portions over an interval of 30 minutes.
4. The considerable quantities of **hydrogen chloride** and **hydrogen bromide** evolved are best handled by means of a gas-absorption trap. The insertion of a **calcium chloride** tube between the trap and the reflux condenser is recommended.
5. The **bromine** is added as rapidly as it will react but not so rapidly that loss occurs through the condenser. A photoflood lamp accelerates the rate of bromination.
6. The dibromoacid chloride solidifies at room temperature. It is advisable to heat the funnel by means of a coil of **copper** tubing through which steam is passed.
7. Two isomers, a solid and a liquid, are formed during the bromination and subsequent esterification.
8. A commercial grade of **methanol** was used; absolute **methanol** did not result in an increased yield.
9. A pad of Filter-Cel aids in the slow filtration. About 100 g. is needed with a 30-cm. funnel.

3. Discussion

Muconic acid has been obtained in a variety of ways. The procedures that seem most important from a preparative point of view are by treatment of **ethyl α,δ -dibromoadipate** with ethanolic **potassium hydroxide**,^{1,2} by condensation of **glyoxal** (as the **sodium bisulfite** addition product) with **malonic acid**,^{3,4} by heating ethyl 1-acetoxy-1,4-dihydromuconate (obtained by condensing **ethyl oxalate** and **ethyl crotonate**, acetylating, and reducing),^{5,6} by oxidation of **phenol**⁷ or **catechol**⁸ with **peracetic acid**, and by hydrolysis of the half-ester obtained by the condensation of **ethyl fumaraldehyde** with **malonic acid**.⁹

Three stereoisomeric muconic acids are known.¹⁰

References and Notes

1. Ingold, *J. Chem. Soc.*, **119**, 967 (1921).
2. Guha and Sankaran, *Ber.*, **70**, 2110 (1937).
3. Doebner, *Ber.*, **35**, 1147 (1902).
4. Behrend and Koolman, *Ann.*, **394**, 244 (1912).
5. Kuhn and Grundmann, *Ber.*, **69**, 1759 (1936).
6. Brit. pat. 477,774 [*C. A.*, **32**, 4174 (1938)].
7. Boeseken and Engelbert, *Proc. Acad. Sci. Amsterdam*, **34**, 1292 (1931) [*C. A.*, **26**, 2970 (1932)].
8. U. S. pat. 2,534,212 [*C. A.*, **45**, 3415 (1951)].
9. Funke and Karrer, *Helv. Chim. Acta*, **32**, 1016 (1949).
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Appendix

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

dibromoacid chloride

ethyl 1-acetoxy-1,4-dihydromuconate

muconic acids

ethanol (64-17-5)

calcium chloride (10043-52-4)

potassium carbonate (584-08-7)

hydrogen chloride,
hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

glyoxal (107-22-2)

phosphorus pentachloride (10026-13-8)

thionyl chloride (7719-09-7)

Adipic acid (124-04-9)

phenol (108-95-2)

hydrogen bromide (10035-10-6)

sodium carbonate (497-19-8)

bromine (7726-95-6)

sodium bisulfite (7631-90-5)

copper (7440-50-8)

potassium hydroxide (1310-58-3)

potassium bromide (7758-02-3)

Catechol (120-80-9)

Ethyl oxalate

Malonic acid (141-82-2)

peracetic acid (79-21-0)

ethyl crotonate (623-70-1)

Muconic acid (505-70-4)

Diethyl α,δ -dibromoadipate (869-10-3)

potassium muconate

ethyl α,δ -dibromoadipate

ethyl fumaraldehydate (2960-66-9)