Organic Syntheses

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.

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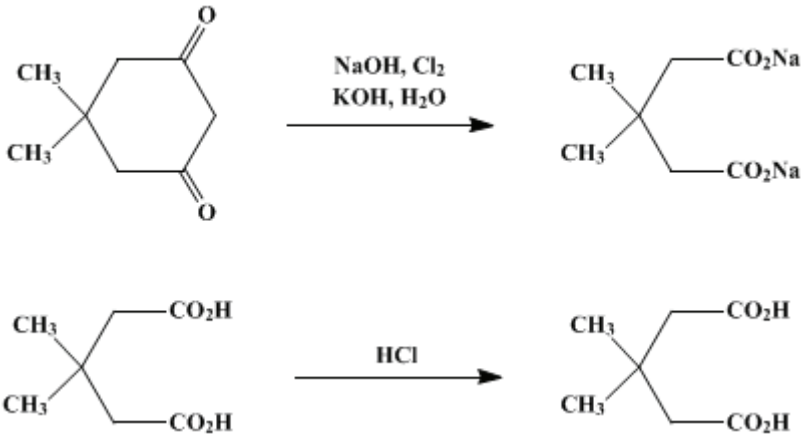
β,β-DIMETHYLGLUTARIC ACID

[Glutaric acid, 3,3-dimethyl-]



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1. Procedure

A solution of 218 g. (5.45 moles) of sodium hydroxide in 300 ml. of water in a 3-l. three-necked flask is cooled to room temperature. To this solution 1250 g. of ice is added, and a stream of chlorine is passed in rapidly through a delivery tube having a small opening and extending almost to the bottom of the liquid. The passage of the chlorine is continued until 161 g. (2.27 moles) has been absorbed. The flask is then fitted with a mechanical stirrer, a thermometer, and a 500-ml. separatory funnel.

Seventy grams (0.5 mole) of methone[2] is dissolved in a solution of 65 g. (1.16 moles) of potassium hydroxide in 525 ml. of water. The solution is cooled to room temperature, poured into the separatory funnel, and run slowly with stirring into the sodium hypochlorite solution. The temperature rises gradually to 35–40° during the addition. After the addition has been completed, the solution is stirred for 6–8 hours until the temperature drops to room temperature.

Without interrupting the stirring, 50 g. of sodium sulfite is added to decompose the excess sodium hypochlorite, and the solution is acidified to Congo red by adding concentrated hydrochloric acid slowly with stirring to avoid foaming. The acid solution is then concentrated by distillation until salts just begin to precipitate (Note 1).

The mixture is then cooled to room temperature, 300 ml. of ether and enough water are added to dissolve all of the precipitate, and the whole is transferred to a 3-l. separatory funnel. The layers are separated, and the aqueous portion is extracted with three 200-ml. portions of ether. The ether extracts are combined and dried for several hours over 15–20 g. of anhydrous magnesium sulfate. The ether is then removed by distillation. This may be conveniently carried out by fitting a 250-ml. Claisen flask with a separatory funnel in order to add the solution as the ether distils. When only 150–200 ml. of solution remains in the flask, the distillation is stopped and the residue is poured into a small beaker. The remaining ether is removed by heating on a steam bath, and the residue solidifies on cooling. The colorless, crystalline β,β-dimethylglutaric acid is dried in air. The yield is 73–77 g. (91–96%), m.p. 97–99°. Crystallization from 100–125 ml. of benzene gives 65–73 g. (81–91%) of acid, m.p. 100–102° (Note 2).

2. Notes

1. The chloroform formed in the reaction comes over during the early stages of this distillation. The

precipitation of salts usually begins after the solution has been concentrated to about one-half the original volume.
2. The melting points given in the literature are 101°,[3] 101–102°,[4] 103–104°,[5] and 98–100°.[6]

3. Discussion

β,β-Dimethylglutaric acid has been prepared by heating dimethylpropanetricarboxylic acid above its melting point;[3] by hydrolysis of the condensation product of ethyl cyanoacetate and ethyl β,β-dimethylacrylate;[7] by the action of sulfuric acid on diethyl β,β-dimethyl-α,α'-dicyanoglutarate;[8] by hydrolysis of the nitrile obtained by the action of calcium cyanide on β,β-dimethylbutyrolactone;[4] by the action of sulfuric acid on β,β-dimethyl-α,α'-dicyanoglutarimide;[9] and by the action of sodium hypobromite on methone.[5] The present procedure is essentially that of Walker and Wood.[6]

References and Notes

1. State University of Iowa, Iowa City, Iowa.
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6. Walker and Wood, *J. Chem. Soc.*, **89**, 598 (1906).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

diethyl β,β-dimethyl-α,α'-dicyanoglutarate

β,β-dimethyl-α,α'-dicyanoglutarimide

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

sodium sulfite (7757-83-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

chlorine (7782-50-5)

potassium hydroxide (1310-58-3)

Ethyl cyanoacetate (105-56-6)

calcium cyanide (592-01-8)

sodium hypochlorite (7681-52-9)

sodium hypobromite

magnesium sulfate (7487-88-9)

methone (126-81-8)

β,β-Dimethylglutaric acid,
Glutaric acid, 3,3-dimethyl- (4839-46-7)

dimethylpropanetricarboxylic acid

ethyl β,β-dimethylacrylate (638-10-8)

β,β-dimethylbutyrolactone