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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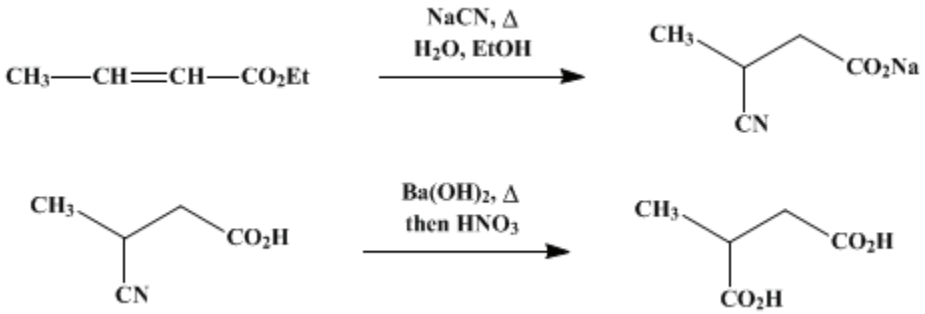
METHYLSUCCINIC ACID

[Pyrotartaric acid]



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1. Procedure

The procedure should be carried out under a hood since the poisonous hydrogen cyanide may be evolved.

In a 3-l. flask provided with a reflux condenser are placed 114 g. (1.0 mole) of ethyl crotonate (Note 1), 460 ml. of 95% ethanol, and a solution of 54 g. (1.06 moles) of 95% sodium cyanide in 128 ml. of water. The solution is refluxed on a steam bath for 5 hours, during which time some ammonia is evolved and the solution becomes dark yellow. A suspension of 150 g. of barium hydroxide octahydrate in 286 ml. of hot water is added to the solution, and the mixture is concentrated under reduced pressure (about 30 mm.) to a volume of about 400 ml. It is again refluxed on the steam bath for 4 hours or until the evolution of ammonia almost ceases (Note 2). The solution is then concentrated to a thick paste under reduced pressure.

The residue is cooled and dissolved in 171 ml. of nitric acid (sp. gr. 1.4) (Note 3), and the solution is warmed for 30 minutes on the steam bath. It is immediately concentrated to complete dryness under reduced pressure (Note 4). The flask is cooled, 300 ml. of benzene is added, and the mixture is refluxed for a short time to render the cake friable. The benzene is removed by decantation, and the cake is pulverized and extracted six times by refluxing it briefly with 300-ml. portions of ether. The combined benzene and ether extracts are filtered and concentrated to a volume of about 225 ml. In the mean-time the residual salts are extracted twice by refluxing them vigorously for a short time with 300-ml. portions of benzene. The benzene solutions are separated by decantation and added to the ether concentrate. The distillation is then continued until about two-thirds of the benzene has been removed, when the benzene solution is poured into a beaker and allowed to cool. The methylsuccinic acid is collected on a filter and is washed by shaking a suspension of it in 150 ml. of chloroform (Note 5). The yield of air-dried product, melting at 110–111°, amounts to 87–93 g. (66–70%) (Note 6).

2. Notes

1. Ethyl crotonate may be prepared readily from technical crotonic acid by action of sulfuric acid and ethanol. The checkers obtained 72% yield both by the ordinary procedure and by the method of azeotropic distillation.
2. The checkers refluxed the mixture for 8 hours at this point; traces of ammonia were still present. Most of the ammonia was evolved in 4 hours, however.
3. The excess nitric acid is used in order to oxidize unchanged crotonic acid. Since hydrocyanic acid may be evolved the operation should be carried out under a hood.

4. The residue must be dry because methylsuccinic acid is extremely soluble in water.
5. If a series of runs is to be made, the chloroform may be used repeatedly.
6. The submitter states that the same percentage yield is obtained when four times the above quantities of reagents are used.

3. Discussion

Methylsuccinic acid has been prepared by the pyrolysis of tartaric acid;[1] from 1,2-dibromopropane or allyl halides by the action of potassium cyanide followed by hydrolysis;[2] by reduction of itaconic citraconic, and mesaconic acids;[3] by hydrolysis of ketovalerolactonecarboxylic acid;[4] by decarboxylation of 1,1,2-propanetricarboxyl acid;[5] by oxidation of β-methylcyclohexanone;[6] by fusion of gamboge with alkali;[7] by hydrogenation and condensation of sodium lactate over nickel oxide;[8] from acetoacetic ester by successive alkylation with a methyl halide and a monohaloacetic ester;[9] by hydrolysis α-methyl-α'-oxalosuccinic ester[10] or α-methyl-α'-acetosuccinic ester;[11] by action of hot, concentrated potassium hydroxide upon methylsuccinaldehyde dioxime;[12] from the ammonium salt of α-methylbutyric acid by oxidation with hydrogen peroxide;[13] from β-methyllevulinic acid by oxidation with dilute nitric acid[14] or hypobromite;[15] fro, β-methyladipic acid;[16] from the decomposition products of glyceric acid[17] and pyruvic acid;[18] and by the action of methylmagnesium bromide on ethylene tetracarboxylic ester, followed by hydrolysis and decarboxylation.[19] The method described above is a modification of that of Higginbotham and Lapworth.[20]

References and Notes

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

itaconic citraconic, and mesaconic acids

ketovalerolactonecarboxylic acid

1,1,2-propanetricarboxyl acid

α-methyl-α'-oxalosuccinic ester

α-methyl-α'-acetosuccinic ester

ethylene tetracarboxylic ester

ethanol (64-17-5)

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

Benzene (71-43-2)

ether (60-29-7)

chloroform (67-66-3)

nitric acid (7697-37-2)

sodium cyanide (143-33-9)

hydrogen cyanide,
hydrocyanic acid (74-90-8)

1,2-dibromopropane (78-75-1)

potassium cyanide (151-50-8)

potassium hydroxide (1310-58-3)

hypobromite

hydrogen peroxide (7722-84-1)

tartaric acid (87-69-4)

barium hydroxide octahydrate (12230-71-6)

Pyruvic acid (127-17-3)

glyceric acid (600-19-1)

methylmagnesium bromide (75-16-1)

crotonic acid (3724-65-0)

Methylsuccinic acid,
Pyrotartaric acid (498-21-5)

ethyl crotonate (623-70-1)

β-methylcyclohexanone (583-60-8)

sodium lactate (72-17-3)

nickel oxide

methylsuccinaldehyde dioxime

β-methyllevulinic acid (6628-79-1)

β-methyladipic acid (3058-01-3)

ammonium salt of α-methylbutyric acid