Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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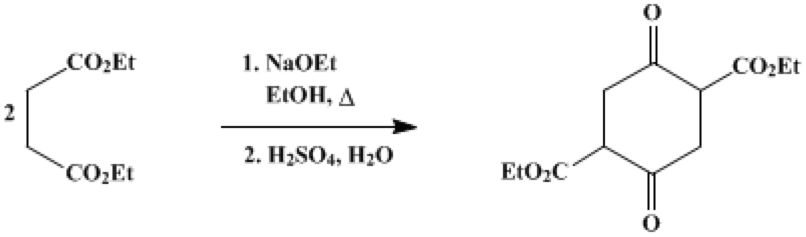
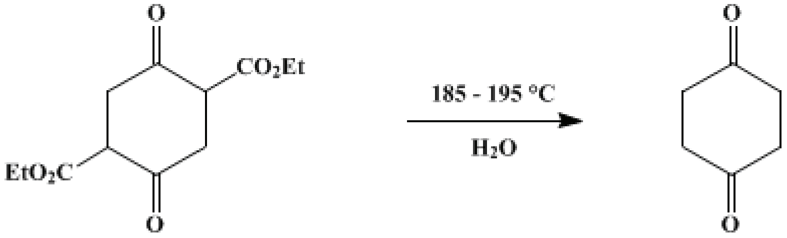
1,4-CYCLOHEXANEDIONE





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1. Procedure

A. *2,5-Dicarbethoxy-1,4-cyclohexanedione*. A solution of sodium ethoxide is prepared by adding small pieces of sodium (92 g., 4 g. atoms) as rapidly as possible to 900 ml. of commercial absolute ethanol contained in a 3-l., three-necked, round-bottomed flask equipped with two stoppers and a reflux condenser fitted with a drying tube packed with calcium chloride and soda lime. The reaction is completed by heating the mixture under reflux for 3–4 hours (Note 1). To the hot solution is added diethyl succinate (348.4 g., 2 moles) (Note 2) in one portion *(Caution! Exothermic reaction)*, and the mixture is heated under reflux by maintaining the original bath temperature for 24 hours. A thick pink-colored precipitate is formed almost immediately and remains throughout the reaction.

At the end of the 24-hour period, the ethanol is removed under reduced pressure on a steam bath. A 2*N* sulfuric acid solution (2 l.) is added to the warm residue, and the mixture is stirred vigorously for 3–4 hours (Note 3). The solid is removed by suction filtration and washed several times with water. The air-dried product is a pale-buff powder weighing 180–190 g., m.p. 126–128°. The solid is added to 1.5 l. of ethyl acetate, the mixture is heated to boiling and is filtered rapidly while hot (Note 4). The filtrate is chilled, and it yields cream to pink-cream colored crystals of 2,5-dicarbethoxy-1,4-cyclohexanedione, 160–168 g., m.p. 126.5–128.5°. The filtrate is concentrated to one-tenth of its original volume in order to obtain a second crop of crystals, 5–7 g., m.p. 121–125°. The total yield is 165–175 g. (64–68%).

B. *1,4-Cyclohexanedione*. The purified 2,5-dicarbethoxy-1,4-cyclohexanedione (170 g., 0.66 mole) (Note 5) and 170 ml. of water are placed in a glass liner (vented) of a steel pressure vessel of 1.5-l. capacity (fitted with a pressure-release valve). The vessel is sealed, heated as rapidly as possible to 185–195°, and kept at this temperature for 10–15 minutes (Note 6). The reaction vessel is immediately removed from the heater, placed in a large tub of ice water, and cooled to room temperature. The gas pressure then is carefully released. The resulting yellow to orange liquid is transferred to a distillation flask with the aid of a minimum volume of ethanol, and most of the water and ethanol is removed under reduced pressure by means of a rotary evaporator. The flask is attached to a short heated column fitted with a short air condenser. The remainder of the water and ethanol is removed under reduced pressure, and the 1,4-cyclohexanedione is distilled, b.p. 130–133° (20 mm.). The product solidifies to a white to pale-yellow solid, m.p. 77–79°, yield 60–66 g. (81–89% yield from 2,5-dicarbethoxy-1,4-cyclohexanedione). The compound may be conveniently recrystallized from carbon tetrachloride (7 ml.

per gram of dione); the purified product is obtained as white plates, m.p. 77–79° (90% recovery).

2. Notes

1. A heating bath containing a liquid heat exchanger such as hydrogenated cottonseed oil should be used. Employment of an electric heating mantle may cause extreme charring in the later stages of the reaction.
2. The diethyl succinate was obtained from Eastman Organic Chemicals and used without purification.
3. The lumps of the sodium salt of 2,5-dicarbethoxy-1,4-cyclohexanedione should be completely reacted before the filtration step. If desired, the mixture may be stirred overnight at this point. The checkers found that in some runs a rock-like precipitate persisted on the bottom of the flask, and it had to be broken up manually by using a spatula with care.
4. A large fluted filter paper and a heated funnel are recommended for the filtration. The dark insoluble material which is removed by this process quickly fills the pores of the filter paper; more than one filter paper may be required. If a large amount of material remains in the filter, the material should be treated with additional ethyl acetate, the mixture filtered, and the filtrate combined with the first filtrate.
5. Use of unpurified ester results in a much lower yield of 1,4-cyclohexanedione.
6. An electrically heated pressure bomb, 4.5 in. in diameter, of 1.5-l. capacity, was employed (American Instrument Company, Model E 1143, cold-tested to 23,000 p.s.i.). About 90 minutes was required to raise the temperature from 25° to 185°.

3. Discussion

2,5-Dicarbethoxy-1,4-cyclohexanedione has been prepared by the self-condensation of diethyl succinate by use of sodium or sodium ethoxide catalyst (with or without a solvent)[2,3,4,5,6,7,8,9,10] and by reaction of ethyl 4-bromo-3-ketobutanoate[11] or ethyl 4-chloro-3-ketobutanoate[12,13] with sodium ethoxide in ethanol.

1,4-Cyclohexanedione has been prepared by hydrolysis and decarboxylation of 2,5-dicarbethoxy-1,4-cyclohexanedione by using concentrated sulfuric acid,[14] aqueous alcoholic phosphoric acid,[15] or water at 195–200°,[7,8,16] and by peroxyvanadic acid oxidation of cyclohexanone.[17]

4. Merits of the Preparation

The present procedure is simpler than others previously described and gives equally good yields. It is easily adapted to the preparation of large quantities of either the diester or the diketone. It can be extended to the preparation of various alkylated 1,4-cyclohexanediones[18] and bicyclic diketodicarboxylic esters such as diethyl bicyclo[2.2.2]octane-2,5-dione-1,4-dicarboxylate.[19,20] 1,4-Cyclohexanedione is a useful intermediate for the preparation of 1,4-substituted cyclohexanes such as the dioxime,[21] diamine,[22] 1,4-dichloro-1,4-dinitrosocyclohexane,[23] and 1,4-dinitrocyclohexane.[24] It is also the precursor of 7,7,8,8-tetracyanoquinodimethan.[25]

References and Notes

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

sodium salt of 2,5-dicarbethoxy-1,4-cyclohexanedione

ethanol (64-17-5)

sulfuric acid (7664-93-9)

ethyl acetate (141-78-6)

Cyclohexanone (108-94-1)

carbon tetrachloride (56-23-5)

sodium (13966-32-0)

phosphoric acid (7664-38-2)

sodium ethoxide (141-52-6)

ethyl 4-bromo-3-ketobutanoate

Diethyl succinate (123-25-1)

1,4-Cyclohexanedione (637-88-7)

2,5-dicarbethoxy-1,4-cyclohexanedione (787-07-5)

ethyl 4-chloro-3-ketobutanoate (638-07-3)

peroxyvanadic acid

diethyl bicyclo[2.2.2]octane-2,5-dione-1,4-dicarboxylate

1,4-dichloro-1,4-dinitrosocyclohexane

1,4-dinitrocyclohexane

7,7,8,8-tetracyanoquinodimethan