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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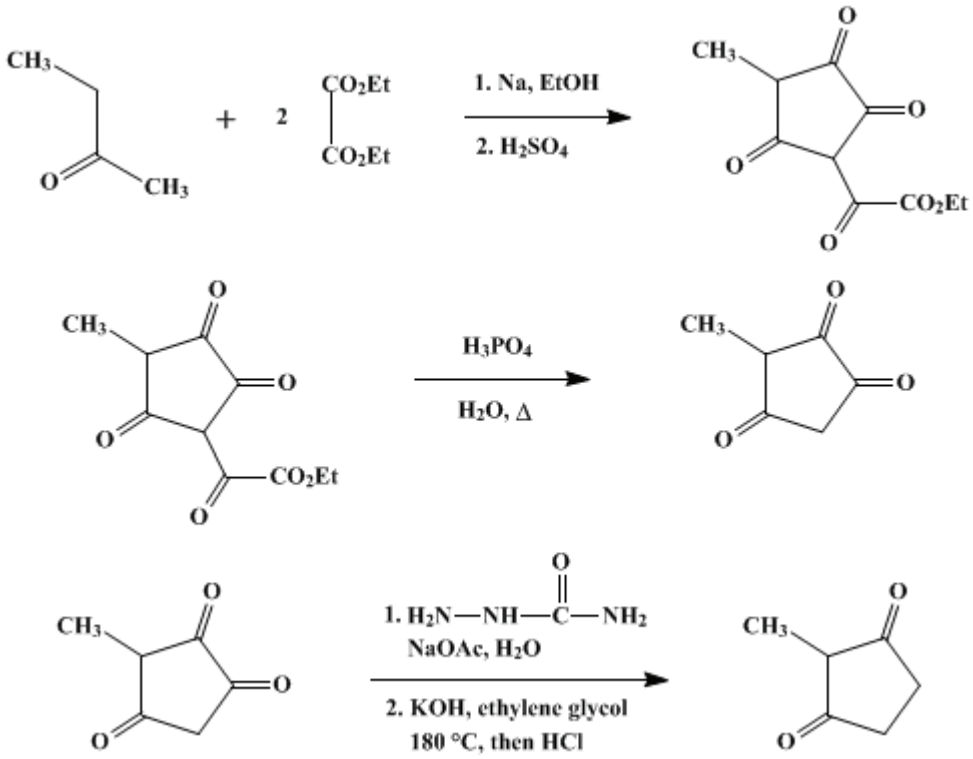
2-METHYLCYCLOPENTANE-1,3-DIONE

[1,3-Cyclopentanedione, 2-methyl-]



Submitted by Joseph P. John, S. Swaminathan, and P. S. Venkataramani[1].
Checked by J. A. Berezowsky and Peter Yates.

1. Procedure

A. *2-Methyl-4-ethoxalylcyclopentane-1,3,5-trione*. A solution of sodium ethoxide is prepared in a 2-l. three-necked, round-bottomed flask fitted with a mercury-sealed stirrer, a reflux condenser carrying a drying tube, and a stopper by the addition of 69.0 g. (3 moles) of sodium to 950 ml. of absolute ethanol. The solution is cooled to 0–5° in an ice bath and stirred. The stopper is replaced by a dropping funnel, and a cold mixture (5–15°) of 108 g. (1.50 moles) of freshly distilled 2-butanone and 482 g. (3.30 moles) of diethyl oxalate (Note 1) is added gradually over a period of 30 minutes. After the addition is complete, the thick, orange-red mixture is allowed to warm with continued stirring to room temperature, heated under reflux for 30 minutes, and cooled again to 0° in an ice bath. The mixture is decomposed by stirring with 165 ml. of sulfuric acid (1:1 by volume) added in portions. The sodium sulfate formed is filtered by suction and washed with ethanol (150–200 ml.) (Note 2). The washings and filtrate are combined and concentrated by evaporation at room temperature for 3–4 days in two wide-mouthed (6-in.) 1-l. crystallizing basins (Note 3). The yellowish brown product which accumulates by slow crystallization is collected by filtration, washed with small quantities of ice-cold water, and dried in air. The crude product weighs 140–150 g. Further evaporative concentration of the mother liquor followed by cooling furnishes an additional 40–50 g. of the keto ester, bringing the total yield to 180–200 g. (53–59%) (Note 2). This crude material (m.p. 120–130°) is used in the next step. A pure sample can be obtained by crystallization from ethyl acetate after treatment with Norit activated carbon, m.p. 160–162°.

B. *2-Methylcyclopentane-1,3,5-trione hydrate*. A mixture of 200 g. (0.89 mole) of the keto ester prepared above, 910 ml. of water, and 100 ml. of 85% phosphoric acid is heated under reflux for 4 hours

and then cooled in an ice-salt bath to −5°. The trione mixed with oxalic acid separates and is collected by filtration and dried under reduced pressure. The dried material is extracted with boiling ether (250–300 ml.) under reflux, and the ethereal extract is separated from the undissolved oxalic acid. The original aqueous filtrate is also extracted with ether in a continuous extractor. The two extracts are combined, and ether is removed by distillation. The crude trione separates as a dark brown solid and is crystallized from *ca.* 250 ml. of hot water. The once-crystallized, faintly yellow product weighs 95–105 g. (74–82%), m.p. 70–74°. This product is used in the next step without further purification. A better specimen, m.p. 77–78°, which is almost colorless, can be obtained by recrystallization from hot water after treatment with Norit activated carbon.

C. *2-Methylcyclopentane-1,3,5-trione 5-semicarbazone*. The above trione hydrate (144 g., 1.00 mole) is dissolved in a mixture of 500 ml. of water and 1 l. of ethanol. A solution of 150 g. of sodium acetate in 200 ml. of water is added with stirring to raise the pH to 5–5.5, and the precipitate formed (Note 4) is filtered and washed with a little water (*ca.* 25 ml.). The filtrate is transferred to a 4-l. beaker and warmed to 45° on a water bath. Heating is then stopped, and a solution of 112 g. (1.00 mole) of semicarbazide hydrochloride and 150 g. of sodium acetate in 250 ml. of water is added dropwise from a dropping funnel with vigorous stirring during the course of 1.5 hours (Note 5). The stirring is continued for an additional hour, and the cream-colored monosemicarbazone is collected by filtration, washed with a little aqueous ethanol, and dried at 100°. The dried material weighs 110–120 g. (60–66%) and does not melt below 300°.

D. *2-Methylcyclopentane-1,3-dione*. In a 2-l. three-necked flask equipped with a reflux condenser and a stirrer are placed 115 g. (2.00 moles) of potassium hydroxide pellets and 1150 ml. of ethylene glycol. The flask is immersed in an oil bath which is heated to 130°. To the stirred mixture is added 12 ml. of water followed by 115 g. (0.628 mole) of the semicarbazone prepared above, added in portions over 30–40 minutes through the third neck of the flask, which is kept stoppered between additions. After the addition is complete, the bath temperature is raised to 150° and kept at this temperature for 30 minutes and then raised again to 180–185°. After 2 hours at 180–185° the reaction mixture is cooled, and the ethylene glycol is removed under reduced pressure (preferably below 4 mm.) (Note 6). The dry residue remaining is dissolved in 200–225 ml. of water, and the solution is cooled and carefully (Note 7) made acidic to Congo red with concentrated hydrochloric acid. The crude dione, which separates as a brown solid, is collected by filtration and crystallized from a mixture of 250 ml. of water and 200 ml. of ethanol after treatment with Norit activated carbon. The almost colorless crystalline product weighs 40–44 g., m.p. 206–207°. The mother liquor is concentrated to furnish an additional 10–12 g. of product, m.p. 204–205°. The crops are combined and recrystallized as before to give 42–47 g. (60–67%) of colorless dione, m.p. 211–212°.

2. Notes

1. Eastman Organic Chemicals or B.D.H. Laboratory reagent grade diethyl oxalate was used.
2. The checkers washed the sodium sulfate with 500 ml. of ethanol. They obtained 202–213 g. (60–63%) of product, m.p. 140–155°.
3. The combined filtrate and washings may be concentrated to about 350 ml. under reduced pressure with a bath temperature not exceeding 40° and then worked up as described. However, the final yield of the keto ester is decreased to 120–140 g.
4. This pale yellow precipitate weighs 20–30 g. and is rejected.
5. The conditions described for the preparation of the semicarbazone are critical and should be strictly observed. Otherwise, the yield of the product in the subsequent Wolff-Kishner reduction is decreased.
6. The checkers found that it is important to remove the ethylene glycol immediately upon completion of the reaction; in a run in which the reaction mixture was allowed to stand overnight, a drastic reduction in the yield of product was observed.
7. There is considerable evolution of carbon dioxide and consequent frothing during acidification. Care must be exercised so that the contents of the flask do not spill over.

3. Discussion

2-Methylcyclopentane-1,3-dione has been prepared in 15% yield by the catalytic reduction of 2-

methylcyclopentane-1,3,5-trione over platinum.[2] The present method is based on the original procedure[3] of Panouse and Sannie with improvements as effected by Boyce and Whitehurst[4] and the submitters.[5]

4. Merits of the Preparation

2-Methylcyclopentane-1,3-dione has found increasing use as an intermediate in the synthesis of steroids.[6,7,8,9,10,11,12] The method described is the only practicable method available for the preparation of 2-methylcyclopentane-1,3-dione in large amounts.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 774
- Org. Syn. Coll. Vol. 9, 570

References and Notes

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

2-Methyl-4-ethoxalylcyclopentane-1,3,5-trione

keto ester

trione hydrate

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium acetate (127-09-3)

sodium sulfate (7757-82-6)

Oxalic acid (144-62-7)

carbon dioxide (124-38-9)

platinum (7440-06-4)

carbon,
Norit (7782-42-5)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

phosphoric acid (7664-38-2)

sodium ethoxide (141-52-6)

ethylene glycol (107-21-1)

2-butanone (78-93-3)

diethyl oxalate (95-92-1)

semicarbazide hydrochloride (563-41-7)

2-Methylcyclopentane-1,3-dione,
1,3-Cyclopentanedione, 2-methyl- (765-69-5)

2-methylcyclopentane-1,3,5-trione (4505-54-8)

2-Methylcyclopentane-1,3,5-trione hydrate

2-Methylcyclopentane-1,3,5-trione 5-semicarbazone