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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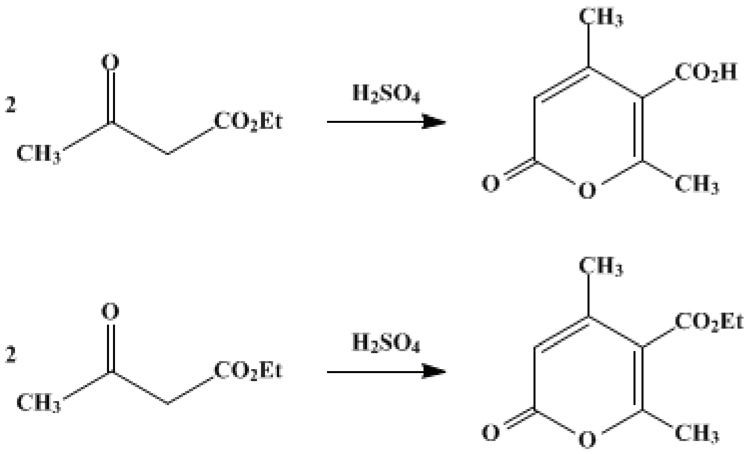
ISODEHYDROACETIC ACID AND ETHYL ISODEHYDROACETATE

[Coumalic acid, 4,6-dimethyl-, and coumalic acid, 4,6-dimethyl-, ethyl ester]



Submitted by Newton R. Smith and Richard H. Wiley[1,2].
Checked by R. S. Schreiber and H. H. Fall.

1. Procedure

In a 2-l. three-necked flask fitted with a thermometer, a stirrer, and a dropping funnel is placed 900 ml. of concentrated sulfuric acid. To the acid, cooled in an ice bath, is added, with stirring, 635 ml. (650 g., 5 moles) of ethyl acetoacetate (Note 2) at such a rate that the temperature remains between 10° and 15°. When all the ester has been added, the flask is stoppered with a calcium chloride drying tube and allowed to stand at room temperature. After 5–6 days (Note 3) the reaction mixture is poured onto 2 kg. of crushed ice while being stirred vigorously with a wooden paddle. The solid is collected on a large Büchner funnel, washed with two 200-ml. portions of cold water, and sucked as dry as possible.

The filtrate, *ca.* 4 l. in volume, is extracted with three 1.5-l. portions of ether (Note 4), and the sulfuric acid mother liquors are discarded. The ether extracts are combined and used to dissolve the solid mixture of acid and ester. If necessary, more ether can be added to assist in dissolving the solid. The ether solution is washed with 50 ml. of cold water and extracted with approximately ten 100-ml. portions of saturated sodium carbonate solution until all the isodehydroacetic acid has been removed (Note 5). The combined sodium carbonate extracts are acidified with an excess of concentrated hydrochloric acid, and the finely divided acid which precipitates is redissolved by heating to the boiling point. The hot solution is filtered with the aid of suction and is cooled in an ice bath; the solid is collected on a filter. The crude isodehydroacetic acid is dissolved in 400 ml. of hot water, and this solution is treated with decolorizing carbon, filtered, and cooled slowly to effect crystallization. The yield of isodehydroacetic acid is 91–115 g. (22–27%); m.p. 154–155°.

The ether extract, which contains ethyl isodehydroacetate, is dried for 24 hours over anhydrous sodium sulfate, and the ether is then removed by heating on a water bath. The residue is distilled from a 250-ml. Claisen flask, under reduced pressure, to give 130–175 g. (27–36%) of ethyl isodehydroacetate; b.p. 185–192°/35 mm.; m.p. 18–20° (Note 6) and (Note 7).

2. Notes

1. Two equations are written since isodehydroacetic acid is not esterified rapidly and its ester is not hydrolyzed rapidly under the conditions used here.
2. The checkers used Eastman Kodak Company white label grade ethyl acetoacetate as received.

3. If the reaction mixture is allowed to stand only 24 hours, the yields drop about 10% for both the acid and its ester.
4. Occasionally a large amount of carbon dioxide is present in the solution, and caution should be exercised in the extraction with ether.
5. The checkers found it convenient to test the pH of the extract with Hydrion papers. When the pH of the extract became the same as that of the saturated sodium carbonate solution, the color of the extract changed from green to orange. Thereafter, extraction was continued until neutralization of small aliquots with concentrated hydrochloric acid produced no solid.
6. The fore-run of 30–40 g. consists mostly of a mixture of 4,6-dimethyl-1,2-pyrone and ethyl isodehydroacetate.
7. The ester may be hydrolyzed to the acid by heating on a steam bath with 5 times its weight of concentrated sulfuric acid for 5–8 hours. The yield of acid is 40–50% with about 30% of the original ester recovered.

3. Discussion

Isodehydroacetic acid has been prepared by the action of sulfuric acid on acetoacetic ester.[3,4,5] The ethyl ester has been prepared by the action of dry hydrogen chloride on acetoacetic ester[6,7] and by the sodium-catalyzed condensation of ethyl β-chloroisocrotonate with ethyl acetoacetate.[3] The methyl ester of isodehydroacetic acid has been prepared by the thermal rearrangement of pyrazolines.[8]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 337

References and Notes

1. University of Louisville, Louisville, Kentucky.
2. The submitters wish to thank the Research Corporation for a grant under which this work was done.
3. Anshutz, Bendix, and Kerp, *Ann.*, **259**, 148 (1890).
4. Hantzsch, *Ann.*, **222**, 1 (1884).
5. Wiley and Smith, *J. Am. Chem. Soc.*, **73**, 3531 (1951).
6. Duisberg, *Ber.*, **15**, 1387 (1882).
7. Goss, Ingold, and Thorpe, *J. Chem. Soc.*, **123**, 348 (1923).
8. Büchner and Schröder. *Ber.*, **35**. 782 (1902).

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

acetoacetic ester

Isodehydroacetic acid

Ethyl isodehydroacetate

Coumalic acid, 4,6-dimethyl-

coumalic acid, 4,6-dimethyl-, ethyl ester

4,6-dimethyl-1,2-pyrone

methyl ester of isodehydroacetic acid

sulfuric acid (7664-93-9)

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

ether (60-29-7)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

carbon dioxide (124-38-9)

decolorizing carbon (7782-42-5)

Ethyl acetoacetate (141-97-9)

ethyl β-chloroisocrotonate