



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.

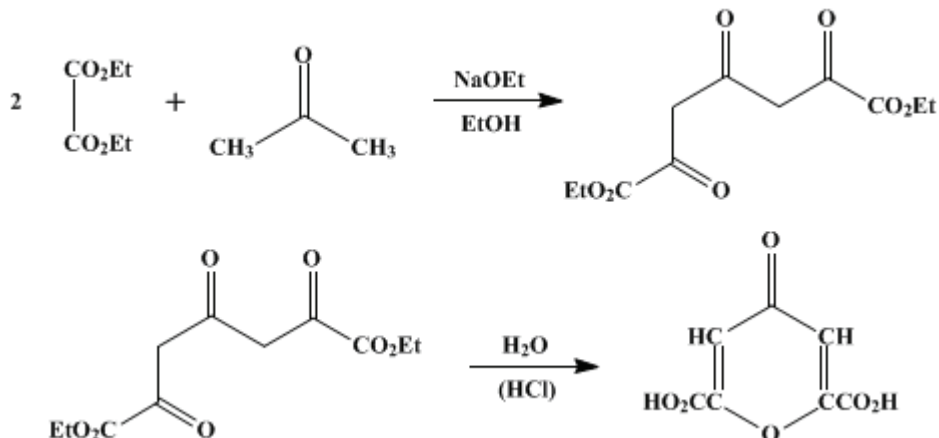
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.126 (1943); Vol. 17, p.40 (1937).

CHELIDONIC ACID



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1. Procedure

In a 1-l. round-bottomed flask, fitted with a reflux condenser protected by a calcium chloride tube, 46 g. (2 gram atoms) of **sodium** is dissolved in 600 cc. of absolute **alcohol** (Note 1). About one hour is required for the addition of the **sodium**, and another hour for its complete solution. Toward the end of the reaction the flask may be heated with a small smoky flame. While the **sodium** is being dissolved, the following materials are weighed in dry, stoppered containers: 58 g. (1 mole) of dry **acetone** (Note 2), 150 g. (1.03 moles) of freshly distilled **ethyl oxalate** (*Org. Syn. Coll. Vol. I, 1941, 261*), and 160 g. (1.1 moles) of **ethyl oxalate**.

About half of the **sodium ethoxide** solution is poured into a 3-l. round-bottomed, three-necked flask provided with a liquid-sealed stirrer and a reflux condenser; the other half is kept warm by a small flame. The first half of the solution is allowed to cool until a solid begins to appear, then 58 g. of dry **acetone** mixed with 150 g. of **ethyl oxalate** is added at once and the stirrer is set in motion. Heat is evolved, and the liquid turns brown but remains clear. As soon as any turbidity appears, the other half of the hot **sodium ethoxide** solution is poured into the mixture together with 160 g. of **ethyl oxalate**, the two streams being allowed to mix as they flow into the flask. The liquid initially is clear and of a deep brown color, but after stirring for about thirty minutes the mixture becomes practically solid. The flask is then connected with a condenser for distillation and heated in an oil bath at 110° until 150 cc. of alcohol has distilled. The flask is protected by a calcium chloride tube and the reaction mixture is cooled to 20°. The sodium derivative is removed to a 3-l. beaker by means of a glass rod and treated with a mixture of 300 cc. of concentrated **hydrochloric acid** (sp. gr. 1.19) and 800 g. of cracked ice (Note 3). All lumps are carefully crushed, and the creamy yellow suspension of acetonedioxydicarboxylic ester is collected on a 15-cm. Büchner funnel. The ester is removed from the filter, stirred with about 100 cc. of ice water, and again collected (Note 4). For hydrolysis the crude material is heated with 300 cc. of concentrated **hydrochloric acid** in a 5-l. flask (Note 5) on the steam bath for twenty hours. After cooling to 20° the solid hydrated acid is collected on a 10-cm. Büchner funnel, washed with two 50-cc. portions of ice water, and dried, first at 100° for two hours, and then at 160° to constant weight to remove the water of crystallization. The yield of product decomposing at 257° (corr.) is 140–145 g. (76–79 per cent of the theoretical amount).

2. Notes

1. A good grade of absolute **alcohol** should be used (*Org. Syn. Coll. Vol. I, 1941, 259*).
2. The **acetone** is dried for several days over **calcium chloride**, filtered, and distilled. Some **acetone** is

lost in this operation by combination with the [calcium chloride](#).¹

3. The temperature must be kept as low as possible during the neutralization, for any undue rise in temperature results in a darkening of the product.

4. The crude ester, after a further washing and after drying in a vacuum desiccator over [sulfuric acid](#), melts at 98–100° and weighs 220 g. (85 per cent of the theoretical amount).

5. A large flask is used because the mixture froths seriously at first. If the frothing becomes troublesome it may be stopped by adding a little [ether](#).

3. Discussion

Natural [chelidonic acid](#) is obtained from the herb celandine (*Chelidonium majus*). The synthesis from [ethyl oxalate](#) and [acetone](#) was first described by Claisen;² the process was simplified by Willstätter and Pummerer³ and further improved by Ruzicka and Fornasir.⁴ The present procedure is modeled after that of the last-mentioned investigators.

References and Notes

1. Bagster, J. Chem. Soc. **111**, 494 (1917).
 2. Claisen, Ber. **24**, 111 (1891).
 3. Willstätter and Pummerer, *ibid.* **37**, 3744 (1904).
 4. Ruzicka and Fornasir, Helv. Chim. Acta **3**, 811 (1920).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

[alcohol](#) (64-17-5)

[calcium chloride](#) (10043-52-4)

[sulfuric acid](#) (7664-93-9)

[hydrochloric acid](#) (7647-01-0)

[ether](#) (60-29-7)

[acetone](#) (67-64-1)

[sodium](#) (13966-32-0)

[sodium ethoxide](#) (141-52-6)

[Ethyl oxalate](#)

[Chelidonic acid](#) (99-32-1)