



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.

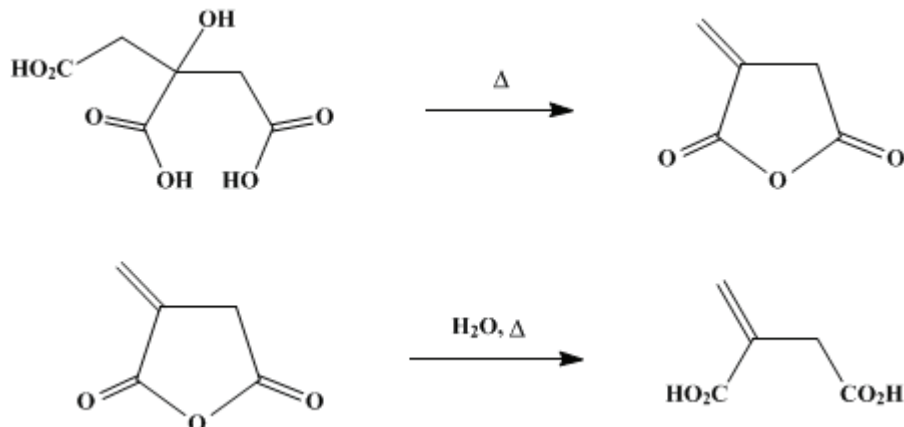
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

Organic Syntheses, Coll. Vol. 2, p.368 (1943); Vol. 11, p.70 (1931).

ITACONIC ANHYDRIDE AND ITACONIC ACID



Submitted by R. L. Shriner, S. G. Ford, and L. J. Roll.
Checked by C. R. Noller

1. Procedure

(A) *Itaconic Anhydride*.—A 500-cc. Pyrex Kjeldahl flask is fitted with an outlet tube 12 mm. in diameter bent for downward distillation and attached to a 100-cm. water-cooled condenser having an indented Pyrex inner tube (Note 1). Two 250-cc. long-necked distilling flasks, cooled in ice-water baths, are used in series as receivers; the vapors are led to the center of each flask by an adapter and glass tubing.

Two hundred grams (0.95 mole) of u.s.p. *citric acid monohydrate* is placed in the Kjeldahl flask (Note 2) and heated with a free flame until melted. Then the flask is heated very rapidly with a Meker burner, and the distillation is completed as quickly as possible (ten to twelve minutes). Superheating must be avoided (Note 3). The distillate consists of water and *itaconic anhydride*, most of which distills at 175–190°. The distillate is immediately poured into a separatory funnel and the lower layer of *itaconic anhydride* is separated (Note 4). The yield of the anhydride is 40–50 g. (37–47 per cent of the theoretical amount). It is of sufficient purity for use in the preparation of *citraconic anhydride* (p. 140) (Note 5) and (Note 6).

(B) *Itaconic Acid*.—Forty grams of *itaconic anhydride* is refluxed with 100 cc. of water for one hour. The flask is then set aside to cool, and finally placed in an ice bath. The acid crystallizes and is filtered and dried. The yield is 11–18 g. (24–39 per cent of the theoretical amount) of a product which melts at 162–165°. On concentrating the mother liquor to one-third of the original volume, an additional amount of lower-melting product may be obtained (Note 7) and (Note 8).

2. Notes

1. A Pyrex inner tube is recommended, since the rapid stream of hot vapor often cracks soft glass tubes. A suitable tube may be prepared from a piece of ordinary Pyrex tubing of the proper size by softening it in spots in the blast lamp and applying suction.
2. A clean flask should be used for each run since the presence of residue from a previous run causes excessive foaming during the first part of the decomposition. The flask is cleaned most easily by adding a 25 per cent solution of *sodium hydroxide* while the residue at the bottom is still molten. Further heating brings about complete solution.
3. Superheating tends to increase the rearrangement to *citraconic anhydride*. The flask should be heated on all sides over a considerable area, and the distillation should be stopped as soon as the vapors in the reaction flask become yellow.
4. A prompt separation of the anhydride and water layers minimizes hydrolysis of the anhydride. The

water layer may be concentrated to give a mixture of itaconic and citraconic acids.

5. The purity of the [itaconic anhydride](#) seems to vary greatly with the conditions of the experiment. The crude anhydride always deposits crystals of [itaconic acid](#) on standing, probably due to water dissolved or suspended in the anhydride. Some idea of the purity can be obtained by the quantity of [itaconic acid](#) that is obtained from it. If the distillation proceeds at exactly the right rate, the anhydride is pure and melts at 67–68°.

6. If larger amounts of [itaconic anhydride](#) are desired, it is better to pyrolyze several 200-g. portions of [citric acid](#) than a single large portion; the percentage yield of [itaconic anhydride](#) usually decreases with larger runs.

7. In some runs no [itaconic acid](#) crystallizes. This apparently happens when the distillation of the [citric acid](#) has not been carried out rapidly enough and the [itaconic anhydride](#) contains a large amount of [citraconic anhydride](#).

8. For preparing considerable amounts of [itaconic acid](#), the following procedure is more convenient than that given above and the yields are much greater.

Nine 120-g. portions of [citric acid](#) are distilled rapidly (four to six minutes), using 300-cc. Kjeldahl flasks, and all the distillates are collected in the same receiver. The distillate, which generally does not consist of two layers, is placed in an evaporating dish, 50 cc. of water is added, and the mixture is allowed to stand on a steam bath for three hours. On cooling it sets to a semi-solid mass: this is filtered and washed with 150 cc. of water. The residue consists of 138 g. of perfectly white crystals melting at 165°. By concentrating the filtrate an additional 42 g. of product melting at 157–165° is obtained. The total yield is 26–27 per cent of the theoretical amount. (C. V. Wilson and C. F. H. Allen, private communication.)

3. Discussion

[Itaconic anhydride](#) has been made by heating [itaconic acid](#) and by distillation of [citric acid](#).¹

[Itaconic acid](#) has been prepared by the distillation of [citric acid](#),² of [aconitic acid](#),³ and of itamalic acid;⁴ by heating [citric acid](#) with dilute [sulfuric acid](#) in a closed tube;⁵ by treating [aconitic acid](#) with water at 180°;⁶ by heating [citraconic acid](#) with [sodium hydroxide](#);⁷ by heating [citraconic anhydride](#) with water at 150°;⁸ by heating a concentrated solution of [citraconic acid](#) at 120–130° in a sealed tube;⁹ and by the action of the fungus *Aspergillus itaconicus* on cane sugar.¹⁰

A mixture of citraconic and itaconic acids is obtained by flowing a concentrated aqueous solution of [citric acid](#) into a heated evacuated vessel, distilling under reduced pressure the mixture of anhydrides formed, and allowing the mixture to react with water.¹¹

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 2, 140](#)
- [Org. Syn. Coll. Vol. 4, 554](#)

References and Notes

1. Anschütz, Ber. **13**, 1541 (1880).
2. Baup, Ann. **19**, 29 (1836).
3. Crasso, ibid. **34**, 63 (1840).
4. Swarts, Zeit. für Chem. **1867**, 649.
5. Markownikow and von Purgold, ibid. **1867**, 264.
6. Pebal, Ann. **98**, 94 (1856).
7. Delisle, ibid. **269**, 86 (1892).
8. Fittig and Landolt, ibid. **188**, 72 (1877).
9. Wilm, ibid. **141**, 29 (1867).
10. Kinoshita, Acta Phytochim. **5**, 271 (1931) [C. A. **26**, 966 (1932)].
11. Boehringer Sohn A.-G., Brit. pat. 452,460 [C. A. **31**, 1045 (1937)].

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

citraconic and itaconic acids

itaconic and citraconic acids

sulfuric acid (7664-93-9)

sodium hydroxide (1310-73-2)

citric acid (77-92-9)

Aconitic acid (499-12-7)

citric acid monohydrate (5949-29-1)

Citraconic anhydride (616-02-4)

Citraconic acid (498-23-7)

Itaconic anhydride (2170-03-8)

Itaconic acid (97-65-4)