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.

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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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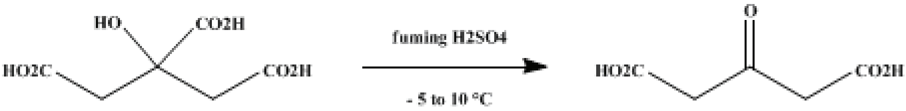
Organic Syntheses, Coll. Vol. 1, p.10 (1941); Vol. 5, p.5 (1925).

ACETONEDICARBOXYLIC ACID

[Glutaric acid, β-oxo]



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1. Procedure

In a 5-l. round-bottomed flask (Note 1), fitted with a mechanical stirrer, is placed 3 kg. (1555 cc.) of fuming sulfuric acid (20 per cent of free sulfur trioxide). Then the flask is cooled very efficiently with a thick pack of ice and salt, until the temperature of the acid reaches −5° (Note 2). The stirring is started, and 700 g. (3.64 moles) of finely powdered u. s. p. citric acid is added gradually. The speed of the addition is regulated according to the temperature of the reaction mixture. The temperature should not rise above 0° until half of the citric acid has been added, after which the temperature should not be allowed to exceed 10° until the reaction is complete. The addition requires three to four hours, provided efficient cooling is used. The citric acid should be in solution at the end of this time; if not, the stirring should be continued until it has dissolved completely.

The temperature of the reaction mixture is allowed to rise gradually until a vigorous evolution of gas commences; at this point the flask is cooled with ice water to stop the excessive frothing, but cooling is not carried far enough to stop the evolution of gas entirely (Note 3). After the more vigorous foaming has ceased, the reaction mixture is raised to about 30° and kept there until no more foaming occurs. A convenient way of determining this point is to stop the stirring for a moment and allow the mixture to remain quiet. After a minute or so, a clear brown liquid giving off very few gas bubbles should result. This general procedure requires two to three hours.

The reaction mixture is cooled down again with ice and salt until the temperature reaches 0°, then 2400 g. of finely cracked ice is added in small portions at such a rate that the temperature does not rise above 10° until one-third of the ice has been added. Then the temperature may be allowed to rise to 25–30°. The addition of the ice requires about two hours; after this, the mixture is cooled again to 0° (Note 4) and then filtered as rapidly as possible through a funnel fitted with a filtros plate (Note 5). The crystals are thoroughly pressed and sucked as dry as possible. The acetonedicarboxylic acid is light gray to white in color. After the suction and pressing have removed practically all of the sulfuric acid, the crystals are transferred to a beaker and stirred with sufficient ethyl acetate (about 200–250 cc.) to make a thick paste. The crystals are filtered with suction. If acetonedicarboxylic acid entirely free from sulfuric acid is desired, the washing with ethyl acetate should be repeated. The yield of practically dry acetonedicarboxylic acid varies from 450–475 g. (85–90 per cent of the theoretical amount) (Note 6). This may be used directly for the preparation of the ester (p. 237). The acid itself is not stable and after a few hours gradually decomposes (Note 7).

2. Notes

1. The reaction must be carried out in a good hood, since a large amount of carbon monoxide is liberated.
2. The use of a very efficient ice and salt mixture around the reaction flask is necessary if the reaction is to be carried out within the time indicated. It is very necessary to regulate the temperature as directed, since a considerably lower yield is obtained if the temperature rises.
3. Some cooling is necessary, or the rapid evolution of gas will cause the reaction mixture to foam over with consequent loss of material.
4. Vigorous cooling before final filtration of the acetonedicarboxylic acid is essential to good yields,

since the acid is fairly soluble in the reaction mixture.
5. The filtros plate for filtration can be very conveniently sealed into the Büchner funnel with a paste of water-glass and amorphous silica which is then hardened with concentrated sulfuric acid.
6. If the acid is to be esterified at once, careful drying from ethyl acetate is not necessary.
7. However, it has been observed that if the acid is purified by recrystallization from ethyl acetate and thoroughly dried it undergoes no decomposition, at least over a seven-month period, when kept at room temperature in a desiccator.[1]

3. Discussion

Acetonedicarboxylic acid can be prepared from citric acid by the action of concentrated[2] or fuming sulfuric acid.[3] The procedure described is a slight modification of that by Willstätter and Pfannenstiehl.[3] While it is more complex than the details given by Ingold and Nickolls,[3] it gives somewhat higher yields. The method of Ingold and Nickolls has been checked and found to have the advantage of requiring much less time.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 237
- Org. Syn. Coll. Vol. 1, 408
- Org. Syn. Coll. Vol. 1, 485
- Org. Syn. Coll. Vol. 4, 816

References and Notes

1. Wiig, J. Phys. Chem. **32**, 961 (1928).
2. Pechmann, Ber. **17**, 2543 (1884).
3. Pechmann, Ann. **261**, 155 (1891); Peratoner and Strazzeri, Gazz. chim. ital. **21**, I, 295 (1891) [Chem. Zentr. I, 967 (1891)]; Jerdan, J. Chem. Soc. **75**, 809 (footnote) (1889); Willstätter and Pfannenstiel, Ann. **422**, 5 (1921); Ingold and Nickolls, J. Chem. Soc. **121**, 1642 (1922); Wiig, J. Phys. Chem. **32**, 961 (1928).

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

sulfuric acid (7664-93-9)

ethyl acetate (141-78-6)

Acetonedicarboxylic acid

Glutaric acid, β-oxo (542-05-2)

sulfur trioxide (7446-11-9)

citric acid (77-92-9)

carbon monoxide (630-08-0)