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.*
1. Procedure

In a 5-1. round-bottomed flask, 500 g. (5.3 moles) of chloroacetic acid (Note 1) is dissolved in 700 cc. of water. The solution is warmed to 50°, neutralized with 290 g. (2.7 moles) of anhydrous sodium carbonate, and again cooled to room temperature. Meanwhile, 294 g. (6 moles) of sodium cyanide (97 per cent) is dissolved in 750 cc. of water warmed to 55°; the solution is cooled to room temperature and then added to the sodium chloroacetate solution, with rapid mixing of the two solutions and cooling under the water tap. When the solutions are completely mixed, cooling is stopped and the temperature allowed to rise. When it reaches 95°, the solution is cooled by adding 200 cc. of ice water, and this is repeated, if necessary, until the temperature no longer rises (Note 2). The solution is then heated on the steam bath for one hour to ensure completion of the reaction.

At the end of this time, the solution is cooled to room temperature and 240 g. (6 moles) of solid u.s.p. sodium hydroxide is slowly dissolved in it. When solution is complete, the reaction mixture is again heated on the steam bath under a hood. When the temperature reaches 60–70°, evolution of ammonia begins and becomes more vigorous with rise in temperature. Most of the ammonia is evolved in forty-five minutes, but the solution is heated for at least three hours, and the last traces of ammonia are removed by bubbling steam through the hot solution for forty-five to sixty minutes more.

A solution of 600 g. of anhydrous calcium chloride in 1.8 l. of water warmed to 40° is added slowly with rapid mixing to the hot sodium malonate solution. A cheese-like precipitate of calcium malonate is formed immediately and becomes coarsely crystalline on standing for twenty-four hours. After the supernatant solution is decanted, the calcium malonate is washed by decantation four or five times with 500-cc. portions of cold water. It is then transferred to a filter, sucked as dry as possible, and dried in the air, or at 45–50°, to constant weight. The yield is 800–900 g.

The dry calcium malonate is placed in a 3-1. round-bottomed flask with sufficient (750–1000 cc.) alcohol-free ether (Note 3) to make a paste which can be stirred. The flask is surrounded by an ice bath, and the well-stirred salt is treated with 1 cc. of 12 N hydrochloric acid for each gram of salt. After the acid has been added slowly through a dropping funnel, the solution is transferred to a continuous extractor (Note 4) and extracted with ether until no more malonic acid is obtained. The product, as obtained from the undried ether solution by concentration, filtration, and drying in the air, melts at 130° or higher and is sufficiently pure for most purposes. The yield is 415–440 g. (75–80 per cent of the theoretical amount).

2. Notes

1. A freshly distilled product boiling over a 3° range was used.
2. If the reaction between the cyanide and the chloroacetate becomes too vigorous, hydrogen cyanide is liberated and partly changed to a brown material, and a corresponding quantity of glycolate is formed. If the temperature of the reaction mixture is allowed to go above 95° spontaneously, the liquid may boil so vigorously and suddenly as to escape from the flask despite the large extra volume provided.
3. Ether is used to avoid unnecessarily increasing the volume of aqueous solution to be extracted. This ether may be used for further extraction. It is necessary to use alcohol-free ether to avoid esterifying the malonic acid during the protracted extraction period.
4. A convenient type of extractor used in this preparation was made as follows by modifying that described by J. Friedrichs: A 20-cm. calcium chloride tower, or other narrow-necked cylinder with a volume of about 1.3 l., was used as an extraction chamber. The mantle-tube, conducting the ether vapors to an Allihn condenser, was made of 25-mm. tubing and was about 50 cm. long. The goose-neck to the extraction flask, of 14-mm. tubing, was sealed to the mantle-tube about 8 cm. from the bottom end. The inner tube was of 14-mm. tubing, about 65 cm. long, flanged at the top to a diameter of about 20 mm. A Witt filter plate of the proper diameter may be sealed into the bottom of the tube to make the ether pass up through the water in a stream of fine bubbles, or this can also be accomplished by sealing off the bottom of the tube and piercing it with 3–6 pinholes. The mantle-tube was fitted to the chamber by a properly bored rubber stopper, the condenser to the top of the mantle-tube, and the 500-cc. extraction flask to the goose-neck by charred cork stoppers. With this apparatus 395–400 g. of malonic acid was extracted in seventy-two hours, the ether being changed every twenty-four hours, and the final traces were extracted after an additional twenty-four hours. The extractor as described by Friedrichs is shown in Fig. 12.

Fig. 12

3. Discussion

Malonic acid has been prepared by the hydrolysis of malononitrile with concentrated hydrochloric acid; by the hydration of carbon suboxide; and from an alkali cyanide and ethyl bromoacetate, ethyl chloroacetate, or chloroacetic acid followed by hydrolysis. The preparation using sodium cyanide and chloroacetic acid is the most convenient and economical.

This preparation is referenced from:

References and Notes

1. Friedrichs, Chem. Fabrik 1, 91 (1928).
2. Henry, Compt. rend. 102, 1396 (1886).
4. Franchimont, ibid. 7, 216 (1874).
5. Kolbe, Ann. 131, 349 (1864); Müller, ibid. 131, 352 (1864); Petriev, J. Russ. Phys.-Chem. Soc. 10, 64 (1878).
6. v. Miller, J. prakt. Chem. (2) 19, 326 (1879); Grimaux and Tcherniak, Bull. soc. chim. (2) 31, 338 (1879); Bourgoin, ibid. (2) 33, 574 (1880); Conrad, Ann. 204, 126 (1880).

Appendix

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

- carbon suboxide
- calcium chloride (10043-52-4)
- hydrochloric acid (7647-01-0)
- ammonia (7664-41-7)
- ether (60-29-7)
- sodium hydroxide (1310-73-2)
- sodium cyanide (143-33-9)
- hydrogen cyanide (74-90-8)
- sodium carbonate (497-19-8)
- chloroacetic acid (79-11-8)
- sodium chloroacetate (3926-62-3)
- Ethyl chloroacetate (105-39-5)
- Malonic acid (141-82-2)
- sodium malonate (141-95-7)
- calcium malonate
- Malononitrile (109-77-3)