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.
ADIPCIC ACID

Submitted by B. A. Ellis
Checked by Roger Adams and C. D. Thompson.

1. Procedure

In a 5-l. round-bottomed flask fitted with a mechanical stirrer, a thermometer, and a 1-l. separatory funnel, is placed 2100 g. (16.6 moles) of 50 per cent nitric acid (sp. gr. 1.32) (Hood). The acid is heated nearly to boiling, and 1 g. of ammonium vanadate (Note 1) is added. The stirrer is started, and 500 g. (5 moles) of cyclohexanol (Note 2) is introduced slowly through the separatory funnel. At first 40–50 drops of cyclohexanol are admitted and the reaction mixture is stirred until the reaction has started (four to five minutes) as is indicated by the evolution of oxides of nitrogen (Note 3). Then the reaction flask is placed in an ice-water bath and cooled until the temperature of the oxidizing mixture is 55–60°. The cyclohexanol is then added as rapidly as possible while the temperature of the mixture is kept within these limits. Toward the end of the oxidation (after about 475 g. of cyclohexanol has been added) the ice bath must be removed and sometimes heat must be applied in order to maintain the temperature and avoid crystallization of adipic acid.

Stirring is continued for about one hour after the addition of the last of the cyclohexanol. Then the mixture is cooled to about 0° and the adipic acid is collected on a suction filter, washed with 500 cc. of ice water, and dried in the air overnight. The yield is 395–410 g. of white crystals which melt at 146–149°. Evaporation of the nitric acid mother liquors yields an additional 30–40 g. of product which melts at 141–144° (Note 4). The total yield of crude adipic acid is 425–440 g. (58–60 per cent of the theoretical amount) (Note 5). This product is pure enough for most purposes. However, a purer product may be obtained by recrystallizing this crude material from 700 cc. of concentrated nitric acid (sp. gr. 1.42). The loss in this purification is about 5 per cent. The recrystallized acid melts at 151–152° (Note 6) and (Note 7).

2. Notes

1. It is suggested that no catalyst is necessary if the temperature of the reaction mixture, once the reaction has started, is maintained at 85–90°. (W. W. Hartman, private communication.)
2. The cyclohexanol used was a commercial grade, which contained practically no phenol. Over 90 per cent of the product boiled between 158–163°.
3. It is important that the oxidation start before a large amount of cyclohexanol has been added or the reaction will become violent. The reaction must be carried out in a good hood.
4. The nitric acid mother liquors contain considerable amounts of adipic acid mixed with glutaric and succinic acids. It has not proved practicable to separate these acids by crystallization. However, if the nitric acid is removed by evaporation and the resulting mixture of acids is esterified with ethyl alcohol, a mixture of ethyl succinate (b.p. 121–126°/20 mm.), ethyl glutarate (b.p. 133–138°/20 mm.), and ethyl adipate (b.p. 142–147°/20 mm.) can be obtained. These esters can be separated quite satisfactorily by distillation.
5. The following modified procedure is reported to give better yields. In a 3-l. three-necked flask provided with a stirrer, reflux condenser, and dropping funnel set in asbestos-sodium silicate stoppers, are placed 1900 cc. of 50 per cent nitric acid (1262 cc. of nitric acid, sp. gr. 1.42, diluted to 1900 cc.) and 1 g. of ammonium vanadate. The flask is surrounded by a water bath heated to 50–60°, and, while the mixture is stirred, 357 g. (3.5 moles) of commercial cyclohexanol is added very slowly so that the temperature of the bath is maintained at 50–60°. This requires about six to eight hours. The reaction is
completed by heating the water bath to boiling until the evolution of nitrogen oxides has ceased (about one hour). The hot reaction mixture is siphoned off and allowed to cool. The yield of crude adipic acid
is 372 g. (72 per cent of the theoretical amount). (Duncan G. Foster, private communication.)
The asbestos-sodium silicate stoppers are prepared by cutting thin asbestos paper into strips about 2.5
cm. wide, moistening the strips in water-glass solution, and then winding them around the end of the
condenser, for example, until a stopper of the correct size is obtained. After the apparatus is assembled
the stoppers are coated with water-glass and allowed to harden overnight.
6. The nitric acid mother liquors from the crystallization may be used as part of the acid for a
subsequent oxidation.
7. Adipic acid may also be recrystallized from 2.5 times its weight of water or 50 per cent alcohol.
However, these solvents are less satisfactory than nitric acid.

3. Discussion

Adipic acid can be prepared by the oxidation of cyclohexanol and cyclohexanone with nitric acid\(^1\)
or potassium permanganate.\(^2\) The procedure described is adapted from the patent of the Deutsche
Hydrierwerke A.-G.\(^1\)

Other methods of preparing adipic acid are the oxidation of cyclohexene with dichromate and
sulfuric acid\(^3\) and the interaction of \(\gamma\)-bromobutyric ester with sodium malonic ester followed by
hydrolysis and decarboxylation of the resulting triethyl 1,4,4-butanetricarboxylate.\(^4\)

This preparation is referenced from:


References and Notes

Hollemann, Van Der Laan and Slijer, Rec. trav. chim. \textbf{24}, 23 (1905); Bouveault and Locquin, Bull.
soc. chim. (4) \textbf{3}, 438 (1908); Chavanne and Simon, Compt. rend. \textbf{168}, 1326 (1919); Thorpe
(1933)].
2. Rosenlew, Ber. \textbf{39}, 2202 (1906); Mannich and Hâncu, Ber. \textbf{41}, 575 (1908); Blaise and Koehler,
Bull. soc. chim. (4) \textbf{5}, 682 (1909); v. Braun and Lemke, Ber. \textbf{55B}, 3529 (1922); Wagner, J.
Chem. Education \textbf{10}, 114 (1933); D. A. Howes (private communication) prepared adipic acid in
quite satisfactory yields by the permanganate oxidation method.
3875 (1937).

Appendix

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

oxides of nitrogen
glutaric
succinic acids
asbestos-sodium silicate
nitrogen oxides
γ-bromobutyric ester
sodium malonic ester
ethyl alcohol,
alcohol (64-17-5)
sulfuric acid (7664-93-9)
Adipic acid (124-04-9)
nitric acid (7697-37-2)
ammonium vanadate (7803-55-6)
Cyclohexanol (108-93-0)
phenol (108-95-2)
ethyl succinate
ethyl glutarate (1070-62-8)
Ethyl adipate (626-86-8)
Cyclohexanone (108-94-1)
potassium permanganate (7722-64-7)
Cyclohexene (110-83-8)
dichromate
triethyl 1,4,4-butanetricarboxylate