Organic Syntheses

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.

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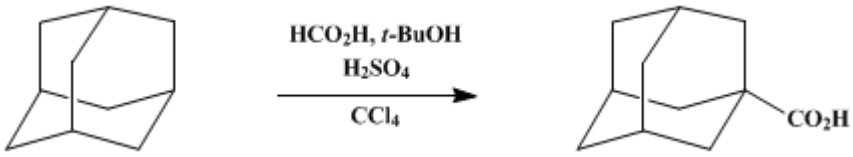
1-ADAMANTANECARBOXYLIC ACID



Submitted by H. Koch and W. Haaf[1].
Checked by W. W. Prichard and B. C. McKusick.

1. Procedure

Caution! Because carbon monoxide is evolved, the reaction should be carried out in a good hood.

A 1-l. three-necked flask equipped with stirrer, thermometer, dropping funnel, and gas-outlet tube is charged with 470 g. (255 ml., 4.8 moles) of 96% sulfuric acid (Note 1), 100 ml. of carbon tetrachloride (Note 2), and 13.6 g. (0.100 mole) of adamantane.[2] The well-stirred mixture is cooled to 17–19° in an ice bath, and 1 ml. of 98% formic acid is added. Then a solution of 29.6 g. (38 ml., 0.40 mole) of *t*-butyl alcohol in 55 g. (1.2 moles) of 98–100% formic acid is added dropwise; the rate of addition and the cooling are regulated so that the addition requires 1–2 hours, and the temperature of the reaction mixture is kept at 17–25°. The reaction mixture is stirred for an additional 30 minutes and poured onto 700 g. of crushed ice. The layers are separated, and the upper, acid layer is extracted with three 100-ml. portions of carbon tetrachloride.

The combined carbon tetrachloride layers are shaken with 110 ml. of 15*N* ammonium hydroxide (Note 3), and the crystalline ammonium 1-adamantanecarboxlate that separates is collected on a Büchner funnel having a coarse fritted disk. The salt is washed with 20 ml. of cold acetone and suspended in 250 ml. of water. The suspension is made strongly acidic with 25 ml. of 12*N* hydrochloric acid and extracted with 100 ml. of chloroform. The chloroform layer is dried over anhydrous sodium sulfate and evaporated to dryness on a steam bath (Note 4). The residue is crude 1-adamantanecarboxylic acid; weight 12–13 g. (67–72%) (Note 5); m.p. 173–174°. Recrystallization of this product from a mixture of 30 ml. of methanol and about 10 ml. of water gives 10–11 g. (56–61%) of pure acid, m.p. 175–176.5° (Note 6).

2. Notes

1. Acid concentrations of 95–98% are satisfactory. The yield falls with concentrations lower than 95%.
2. Cyclohexane or *n*-hexane can be used in place of carbon tetrachloride. Technical "normal hexane" may contain substantial amounts of methylcyclopentane and isohexane that lower the yield through formation of C_7-acids that are hard to remove.
3. A large amount of trimethylacetic acid and a small amount of at least one C_9-acid and one C_{13}-acid are formed from the *t*-butyl alcohol. The treatment with ammonia separates 1-adamantanecarboxylic acid from these acids, the ammonium salts of which remain in solution.
4. Acid that is satisfactory for most purposes may be obtained by interrupting the evaporation of the chloroform solution when crystals start to appear, cooling the concentrated chloroform solution to 0–5°, and collecting the acid on a Büchner funnel. The acid melts at 173–174°.
5. The checkers obtained similar yields when the quantity of reactants was increased fivefold.
6. As an alternative purification procedure, the checkers have esterified the crude acid by refluxing it for 2 hours with three times its weight of methanol and 2 ml. of 98% sulfuric acid. The solution is poured into 10 volumes of water and extracted with the minimum amount of chloroform required to give a clean separation of layers. The chloroform solution is washed with water, dried over calcium chloride, and distilled from a Claisen flask with an indented neck. Methyl 1-adamantanecarboxylate is collected at 77–79° (1 mm.); m.p. 38–39°. Hydrolysis of the ester with the calculated amount of 1*N* potassium

hydroxide followed by acidification yields 1-adamantanecarboxylic acid; m.p. 175–176.5°; 90% overall recovery.

3. Discussion

1-Adamantanecarboxylic acid can be prepared by carboxylation of 1-adamantanol[3] or 1-bromoadamantane[3,4] by formic acid and 96% sulfuric acid; by carboxylation of adamantane by formic acid, *t*-butyl alcohol, and 96% sulfuric acid;[5] and by carboxylation of adamantane by formic acid and 130% sulfuric acid.[6]

4. Merits of the Preparation

This procedure illustrates a general method of carboxylating saturated hydrocarbons that have a tertiary hydrogen.[7] It has been used to convert isopentane to 2,2-dimethylbutanoic acid, 2,3-dimethylbutane to 2,2,3-trimethylbutanoic acid, and methylcyclohexane to 1-methylcyclohexanecarboxylic acid. The preparation of 1-methylcyclohexanecarboxylic acid by a variation of this procedure is described on p. 739 of this volume.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 739

[8]

References and Notes

1. Max-Planck Institute für Kohlenforschung, Mülheim-Ruhr, Germany.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

ammonium 1-adamantanecarboxlate

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

methanol (67-56-1)

hydrogen (1333-74-0)

carbon monoxide (630-08-0)

chloroform (67-66-3)

sodium sulfate (7757-82-6)

formic acid (64-18-6)

carbon tetrachloride (56-23-5)

cyclohexane (110-82-7)

acetone (67-64-1)

potassium hydroxide (1310-58-3)

ammonium hydroxide (1336-21-6)

methylcyclohexane (108-87-2)

Trimethylacetic acid (75-98-9)

isopentane (78-78-4)

n-hexane (110-54-3)

t-butyl alcohol (75-65-0)

Adamantane (281-23-2)

1-Adamantanecarboxylic acid (828-51-3)

methylcyclopentane (96-37-7)

isohexane (107-83-5)

Methyl 1-adamantanecarboxylate (711-01-3)

1-Adamantanol (768-95-6)

1-bromoadamantane (768-90-1)

2,2-dimethylbutanoic acid (595-37-9)

2,3-dimethylbutane (79-29-8)

2,2,3-trimethylbutanoic acid

1-Methylcyclohexanecarboxylic acid (1123-25-7)