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.

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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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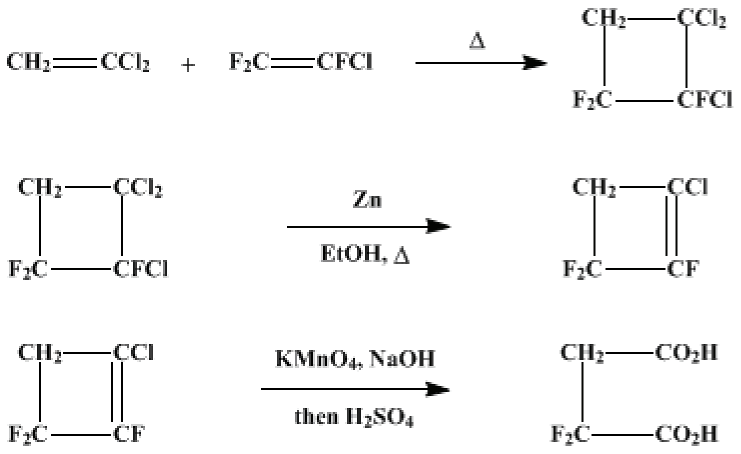
2,2-DIFLUOROSUCCINIC ACID

[Succinic acid, 2,2-difluoro-]



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1. Procedure

Caution! In the absence of toxicity data, the fluorine compounds should all be treated as though they were toxic materials.

A. *1,1,2-Trichloro-2,3,3-trifluorocyclobutane*. In a 1-l. rocker bomb are placed 350 g. (3.6 moles) of 1,1-dichloroethylene (Note 1) are 1 g. of hydroquinone. The bomb is cooled in a mixture of Dry Ice and acetone and evacuated. The vacuum is released with nitrogen and the bomb is again evacuated. The bomb is then charged with 300 g. (2.6 moles) of chlorotrifluoroethylene (Note 1) from a cylinder. The bomb is heated at 180° for 7 hours behind a barricade (Note 2) and is then cooled, vented, and unloaded. The solid polymer (about 45 g.) is removed by filtration and is rinsed with 50 ml. of ether. The combined filtrate and rinse are concentrated and then distilled through a 30-cm. packed column to give 242–262 g. (44–48%) of 1,1,2-trichloro-2,3,3-trifluorocyclobutane, b.p. 120–121°, n_{D}^{25} 1.4139–1.4141.

B. *1-Chloro-2,3,3-trifluorocyclobutene*. A 1-l. three-necked flask fitted with mercury-sealed stirrer, dropping funnel, reflux condenser, and heater is charged with 150 ml. of absolute ethyl alcohol and 76 g. (1 mole) of 95% zinc dust. The alcohol is heated to boiling, and 235 g. (1.1 moles) of 1,1,2-trichloro-2,3,3-trifluorocyclobutane is added through the dropping funnel during 40 minutes. After the reaction has started, external heating is decreased. The mixture is heated under reflux for 1 hour after the end of the addition. It is then cooled below reflux temperature, 15 g. (0.2 mole) more of zinc powder is added, and the heating under reflux is continued for 30 minutes more. The mixture is again cooled below reflux temperature, and a simple still head arranged for downward distillation is attached in place of the condenser. Distillation is carried out until 165 ml. of distillate has been collected. The still head reaches a temperature of about 90°. The distillate is washed with two 250-ml. portions of water and dried by shaking gently for 5 minutes with 5 g. of 8-mesh calcium chloride. The product is decanted from the calcium chloride and distilled through a 30-cm. packed column to give 107–113 g. (68–72%) of 1-chloro-2,3,3-trifluorocyclobutene, b.p. 52–53°, n_{D}^{25} 1.3614–1.3619.

C. *2,2-Difluorosuccinic acid*. In a 3-l. three-necked flask fitted with stirrer, thermometer, and dropping funnel, 80 g. (2 moles) of sodium hydroxide is dissolved in 2 l. of water and 158 g. (1 mole) of potassium permanganate is then added. The mixture is cooled to 15–20° with an ice-salt bath, and 107 g. (0.75 mole) of 1-chloro-2,3,3-trifluorocyclobutene is added through the dropping funnel during 1 hour while the permanganate solution is stirred and maintained at 15–20°. After the solution has been stirred for 2 hours more at this temperature, the manganese dioxide is removed by filtration and rinsed with three 300-ml. portions of water. The combined filtrate and washings are concentrated to a volume of 500 ml. by evaporation on a steam bath (Note 3). The solution is then cooled and 85 ml. of concentrated sulfuric acid is added slowly with stirring. The cold solution is extracted with four 250-ml. portions of ether (Note 4). Drying of the ether extract is accomplished by agitating it for 5 minutes with 30 g. of anhydrous magnesium sulfate. When the drying agent has been removed by filtration and rinsed with ether, the filtrate and the ether washings are combined and concentrated to give 91–97 g. (79–84%) of 2,2-difluorosuccinic acid. The acid is recrystallized by dissolving it in hot nitromethane (1.25 ml. per g.), filtering the solution through a layer of filter aid if necessary, and cooling the solution to 3°. The crystals are collected by suction filtration and rinsed with 30 ml. of cold nitromethane. After drying, this gives 85–92 g. (74–80%) of 2,2-difluorosuccinic acid, m.p. 144–146°.

2. Notes

1. The checkers employed 1,1-dichloroethylene supplied by Dow Chemical Co., Midland, Michigan, and chlorotrifluoroethylene supplied by the Matheson Company, Joliet, Illinois.
2. This reaction has been carried out many times without incident in a 1-l. stainless-steel rocker bomb. A pressure gauge was attached during two runs and recorded a maximum of 750 p.s.i. However, an attempt in another laboratory to scale up the reaction using a 3-l. autoclave resulted in a bulged vessel. Uncontrolled polymerization may be hazardous.
3. Evaporation may be carried out in porcelain or glass dishes, but the fluoride present will cause some etching.
4. The amounts removed in the third and fourth extractions are about 5.4 g. and 1.5 g., respectively.

3. Discussion

The procedure described is the method of Raasch[3,4] and is the only one published so far.

4. Merits of Preparation

The first step illustrates a very general reaction, the addition of fluoroalkenes to alkenes to give fluorocyclobutanes.[5] The subsequent steps illustrate the synthetic possibilities of fluorocyclobutanes as intermediates. 1,1,2-Trichloro-2,3,3-trifluorocyclobutane may also be converted into chlorotrifluorosuccinic acid, trifluorosuccinic acid, fluoromaleic acid, fluorofumaric acid, difluoromaleic acid, and difluorofumaric acid.[4,6]

References and Notes

1. Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware.
2. Mead Johnson Research Center, Evansville, Indiana.
3. M. S. Raasch, U. S. pat. 2,824,888 [*C.A.*, **52**, 12901 (1958)].
4. M. S. Raasch, R. E. Miegel, and J. E. Castle, *J. Am. Chem. Soc.*, **81**, 2678 (1959).
5. D. D. Coffman, P. L. Barrick, R. D. Cramer, and M. S. Raasch, *J. Am. Chem. Soc.*, **71**, 490 (1949); J. D. Roberts and C. M. Sharts, *Org. Reactions*, **12**, 1 (1962).
6. M. S. Raasch, U. S. pat. 2,891,968 [*C. A.*, **54**, 1323 (1960)].

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

ethyl alcohol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

ether (60-29-7)

sodium hydroxide (1310-73-2)

hydroquinone (123-31-9)

potassium permanganate (7722-64-7)

nitrogen (7727-37-9)

acetone (67-64-1)

zinc,
zinc powder (7440-66-6)

manganese dioxide (1313-13-9)

Nitromethane (75-52-5)

magnesium sulfate (7487-88-9)

Chlorotrifluoroethylene (79-38-9)

2,2-Difluorosuccinic acid,
Succinic acid, 2,2-difluoro- (665-31-6)

1,1,2-Trichloro-2,3,3-trifluorocyclobutane (697-17-6)

1-Chloro-2,3,3-trifluorocyclobutene (694-62-2)

difluorofumaric acid

Fluorine (7782-41-4)

fluoride (16984-48-8)

1,1-dichloroethylene (75-35-4)

chlorotrifluorosuccinic acid

trifluorosuccinic acid

fluoromaleic acid

fluorofumaric acid

difluoromaleic acid