



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.

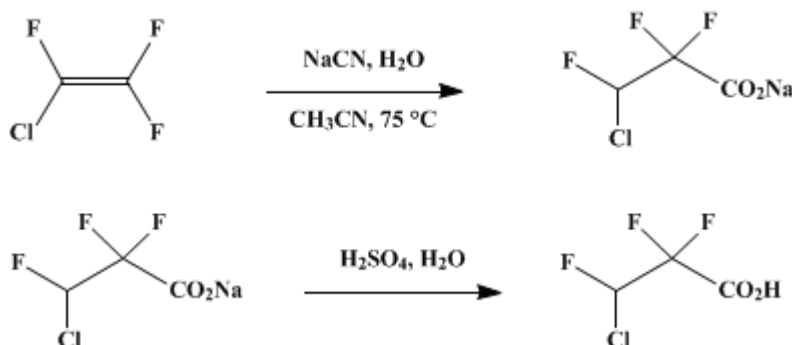
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.239 (1973); Vol. 40, p.11 (1960).

3-CHLORO-2,2,3-TRIFLUOROPROPIONIC ACID

[Propionic acid, 3-chloro-2,2,3-trifluoro-]



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1. Procedure

Caution! This is a strongly exothermic reaction. The reaction should be carried out in a hood. A protective shield should be placed between the operator and the reaction bottle.

A modified Parr low-pressure hydrogenation apparatus is used for this preparation.² The bottle is fitted with a two-holed rubber stopper through which is passed a thermocouple well made of 5-mm. glass tubing and a gooseneck made of 8-mm. heavy-walled glass tubing. The thermocouple well extends into the bottle within about 2 cm. of the bottom. The gooseneck extends 1 cm. into the bottle, and the other end is connected directly to a manifold system with heavy-walled pressure tubing using screw clamps. Also attached to the manifold system through needle valves are a vacuum line, a storage cylinder of chlorotrifluoroethylene, a pressure gauge, and a bleed line.

The bottle is charged with 52 g. (1.0 mole) of 95% sodium cyanide, 100 ml. of water, and 100 ml. of acetonitrile, giving a two-phase liquid system. After the bottle is clamped in the metal cage of the shaking apparatus, the bottle is evacuated and filled to a gauge pressure of 10 lb. (0.68 atm.) with chlorotrifluoroethylene. This procedure is repeated twice to purge the system of air. Finally, the bottle is pressured to 40 lb. (2.7 atm.), chlorotrifluoroethylene leaving the valve open to maintain this pressure (Note 1). The thermocouple is fitted into place and shaking is started. The temperature steadily increases, and in 10–15 minutes it is about 75° and rising more rapidly. It is kept at 75–80° by cooling and/or slowing the rate of chlorotrifluoroethylene addition. *Caution! Careful control of the reaction is mandatory. If the reaction rate cannot be controlled, it is imperative to shut the gas addition valve and to stop the agitation immediately.* Cooling is accomplished by packing ice inside the wire cage holding the bottle and/or pouring ice water on the bottle. When cooling is used, it is possible to complete the reaction in 1 hour. When the rate of chlorotrifluoroethylene absorption is negligible and the temperature is about 30°, pressure is released through the bleed line and the bottle is removed. The gain in weight is 130–135 g. (about 1.1 moles).

The product is a dark-colored solution which is poured slowly into sulfuric acid (100 ml. of concentrated sulfuric acid in 100 ml. of water) with cooling (Note 2). *This operation should be conducted in a hood because some hydrogen cyanide may be evolved from unreacted sodium cyanide.* The mixture is then extracted four times with 100-ml. portions of ether (Note 3). The first 100 ml. of ether yields about 260 ml. of organic material, and succeeding portions about 95 ml. each. The extract is dried over about 20 g. of magnesium sulfate and distilled (Note 4). After removal of low-boiling materials, there is obtained 124–128 g. (76–79%) of crude 3-chloro-2,2,3-trifluoropropionic acid, b.p.

70–85°/30 mm.; the bulk of this fraction distills at 83°/30 mm., n_D 1.3708–1.3717. This product is of sufficient purity for most purposes (Note 5). About 25–30 g. of high-boiling residue remains which is chiefly chlorotrifluoropropionamide (Note 6).

2. Notes

1. The chlorotrifluoroethylene cylinder is fitted with a pressure-reduction valve which is set at a maximum pressure of 40 lb. (2.7 atm.).
2. The amount of product was not changed by cooling, but the acidification reaction is very exothermic and cooling is necessary before extraction with ether.
3. The checkers encountered troublesome emulsions in the extraction step. It was found helpful to filter the acidified reaction mixture through a sintered-glass funnel before ether extraction.
4. A precision distillation column is not necessary. The submitters have used an 80-cm. spinning-band column with a 10 mm. inside diameter or a 25-cm. helix-packed column of about 10 mm. inside diameter.
5. The neutral equivalent of this material is 169–173 (theory is 162.5). It is readily purified by mixing it thoroughly with 10% of its weight of phosphorus pentoxide and redistilling. The purified acid boils at 82–83°/30 mm. (159–160°/760 mm.), n_D^{25} 1.3695, N.E. 163.5. Recovery from the crude is 92%.
6. The higher-boiling material is largely 3-chloro-2,2,3-trifluoropropionamide, and some fractions crystallize at room temperature. The amide can be purified by redistillation, b.p. 111–112°/30 mm. (198–200°/760 mm.) or recrystallization from carbon tetrachloride. The pure amide melts at 41–42°. The amount of amide formed is not changed by running the above charge at a lower temperature. However, when the amount of water is reduced to 50 ml. and the temperature kept below 50°, the yield of crude acid is 38% and of amide, 21%. When the same charge is run at 80° maximum temperature, the yield of crude acid is 78% and of amide, 7%.

3. Discussion

3-Chloro-2,2,3-trifluoropropionic acid has been prepared by permanganate oxidation of 3-chloro-2,2,3-trifluoropropanol³ which is one of the telomerization products of chlorotrifluoroethylene with methanol. The present procedure is a modification of one reported earlier⁴ and is undoubtedly the method of choice for making propionic acids containing 2–4 fluorine atoms, i.e., 2,2,3,3-tetrafluoropropionic acid, 3,3-dichloro-2,2-difluoropropionic acid, and 3-bromo-2,2,3-trifluoropropionic acid. When preparing 2,2,3,3-tetrafluoropropionic acid from tetrafluoroethylene, it is desirable to use an additional 50 ml. of acetonitrile and externally applied heat to initiate the reaction.

References and Notes

1. Contribution No. 554 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company.
 2. R. Adams and V. Voorhees, *Org. Syntheses*, Coll. Vol. 1, 66 (Fig. 6) (1941). Later models of this apparatus use a larger-mouthed bottle which is more easily adapted to this preparation.
 3. R. M. Joyce, U. S. pat. 2,559,628 (1951) [C.A., 46, 3063 (1952)].
 4. D. C. England, L. R. Melby, and R. V. Lindsey, Jr., *J. Am. Chem. Soc.*, 80, 6422 (1958).
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Appendix

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

sulfuric acid (7664-93-9)

methanol (67-56-1)

ether (60-29-7)

acetonitrile (75-05-8)

sodium cyanide (143-33-9)

hydrogen cyanide (74-90-8)

carbon tetrachloride (56-23-5)

magnesium sulfate (7487-88-9)

Chlorotrifluoroethylene (79-38-9)

tetrafluoroethylene (9002-84-0)

3-Chloro-2,2,3-trifluoropropionic acid,
Propionic acid, 3-chloro-2,2,3-trifluoro- (425-97-8)

chlorotrifluoropropionamide,
3-chloro-2,2,3-trifluoropropionamide

3-chloro-2,2,3-trifluoropropanol

3-bromo-2,2,3-trifluoropropionic acid

2,2,3,3-tetrafluoropropionic acid (756-09-2)

phosphorus pentoxide (1314-56-3)

3,3-dichloro-2,2-difluoropropionic acid