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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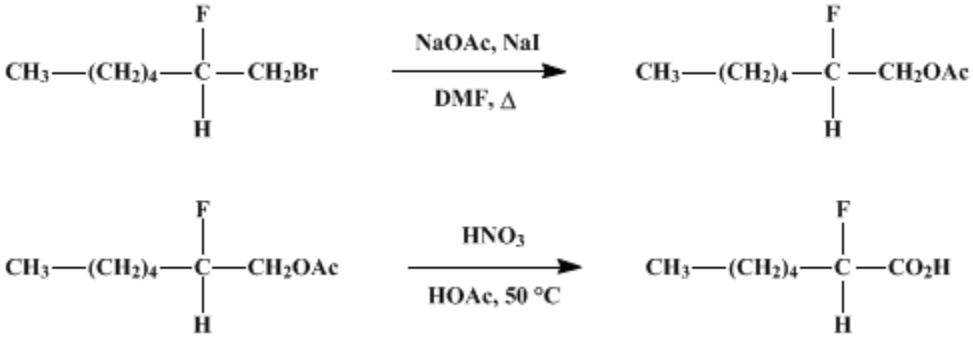
Organic Syntheses, Coll. Vol. 5, p.580 (1973); Vol. 46, p.37 (1966).

2-FLUOROHEPTANOIC ACID

[Heptanoic acid, 2-fluoro-]



Submitted by F. H. Dean, J. H. Amin, and F. L. M. Pattison[1].
Checked by Michelle Moran and B. C. McKusick.

1. Procedure

A. *2-Fluoroheptyl acetate*. A 1-l. two-necked flask is fitted with a thermometer reaching close to the bottom and a reflux condenser that has a calcium chloride tube in its end. It is charged with 29.6 g. (0.150 mole) of 1-bromo-2-fluoroheptane,[2] 22.5 g. (0.150 mole) of dry sodium iodide, 24.6 g. (0.30 mole) of anhydrous sodium acetate, and 600 ml. of dimethylformamide previously dried over anhydrous calcium sulfate. The mixture is stirred by a magnetic bar for 40 hours while being maintained at 120–130° by means of an electric heating mantle. The mixture is cooled to room temperature, diluted with 750 ml. of water, and extracted with 900 ml. of ether. The aqueous layer is extracted with two 150-ml. portions of ether, and the combined ether extracts are washed with five 150-ml. portions of water (Note 1). The ethereal solution is dried over anhydrous sodium sulfate. The ether is removed by distillation, and the residue is transferred to a Claisen flask with a 15-cm. indented neck. Fractionation under reduced pressure gives, after a small fore-run, 16.6–20.6 g. (63–78%) of 2-fluoroheptyl acetate, b.p. 83–87° (10 mm.), n^{25}D 1.4101.

B. *2-Fluoroheptanoic acid (Note 2)*. A 250-ml. two-necked flask is fitted with a thermometer and a condenser that has an outlet tube to carry oxides of nitrogen to a gas absorption trap[3] or the back of a hood. It is charged with 17.6 g. (0.100 mole) of 2-fluoroheptyl acetate, 50 ml. of glacial acetic acid, and 60 ml. of 16 *N* nitric acid. The mixture is heated at 48–50° for 25 hours by means of an electric heating mantle. It is diluted with 500 ml. of water and crushed ice and extracted with one 300-ml. portion and five 100-ml. portions of ether (Note 3). The combined ether extracts are added carefully to a slurry of 125 g. of sodium bicarbonate in 500 ml. of water in a 2-l. beaker. The aqueous alkaline solution is extracted with two 100-ml. portions of ether, which are discarded. The aqueous solution is neutralized to a pH of approximately 4 with about 300 ml. of 10% hydrochloric acid and is extracted with one 300-ml. portion and five 100-ml. portions of ether. The combined extracts are washed with four 100-ml. portions of water to remove traces of acetic acid and dried over anhydrous sodium sulfate. The ether is removed by distillation, leaving 12–13.5 g. of crude 2-fluoroheptanoic acid that soon solidifies. It is purified by distillation under reduced pressure through a short Claisen still-head with a short condenser that can be heated by steam, a burner, or a heat lamp when the acid solidifies in it. 2-Fluoroheptanoic acid, b.p. 62–64° (0.15 mm.), 78–80° (0.7 mm.), is obtained as a moist, waxy, pale yellow solid that smells faintly of acetic acid. After being dried on a porous plate, it is odorless and nearly colorless; weight 11.5–12.5 g. (78–84%), m.p. 38–39°.

2. Notes

1. Thorough washing with water is necessary to remove residual dimethylformamide.

2. 2-Fluoroheptanoic acid required no more than the usual precautions accorded organic compounds, for it and its precursors have LD_{50}>100 mg./kg. in mice. The relatively low toxicity of this and other 2-fluoroalkanoic acids is in contrast to the high toxicity of the ω-fluoro acids $F(CH_2)_nCOOH$ with *n* an odd number (if *n* = 5, LD_{50} = 1.3 mg./kg. in mice).[4]
3. The solubility of the fluoro acid in water is sufficient to require thorough ether extraction.

3. Discussion

2-Fluoroheptanoic acid[5] has been prepared only by the present procedure.

4. Merits of the Preparation

Bromofluorination[2] followed by the present procedure is a general way to convert 1-alkenes to 2-fluoroalkanoic acids; similar results have been obtained with ethylene, propylene, 1-butene, 1-hexene, 1-octene, 1-decene, and methyl 10-undecenoate.[5] It is an easy and convenient way to make 2-fluoroalkanoic acids, for it requires only conventional apparatus and readily available intermediates.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 136

References and Notes

1. Department of Chemistry, University of Western Ontario, London, Ontario, Canada.
2. F. H. Dean, J. H. Amin, and F. L. M. Pattison, this volume, p. 136.
3. C. F. H. Allen, *Org. Syntheses*, Coll. Vol. **2**, 4 (1943).
4. F. L. M. Pattison, S. B. D. Hunt, and J. B. Stothers, *J. Org. Chem.*, **21**, 883 (1956).
5. F. L. M. Pattison, R. L. Buchanan, and F. H. Dean, *Can. J. Chem.*, **43**, 1700 (1965).

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

oxides of nitrogen

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

sodium acetate (127-09-3)

sodium bicarbonate (144-55-8)

propylene (115-07-1)

nitric acid (7697-37-2)

sodium sulfate (7757-82-6)

calcium sulfate (7778-18-9)

ethylene (9002-88-4)

1-butene (106-98-9)

sodium iodide (7681-82-5)

dimethylformamide (68-12-2)

1-hexene (592-41-6)

1-Bromo-2-fluoroheptane (1786-32-9)

2-Fluoroheptanoic acid,
Heptanoic acid, 2-fluoro- (1578-58-1)

2-Fluoroheptyl acetate (1786-44-3)

methyl 10-undecenoate (111-81-9)

1-octene (111-66-0)

1-decene (872-05-9)