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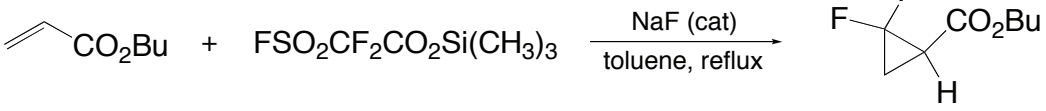
September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.080.0172
Organic Syntheses, Vol. 80, p. 172-176 (2003); Coll. Vol. 11, p. 469-472 (2009).

PREPARATION AND USE OF A NEW DIFLUOROCARBENE REAGENT. TRIMETHYLSILYL 2-FLUOROSULFONYL-2,2-DIFLUOROACETATE: *n*-BUTYL 2,2-DIFLUOROCYCLOPROPANECARBOXYLATE

[(Cyclopropanecarboxylic acid, 2,2-difluoro-, butyl ester and Acetic acid, difluoro(fluorosulfonyl)-, trimethylsilyl ester)]

A. $FSO_2CF_2CO_2H + (CH_3)_3SiCl \xrightarrow{0^\circ \text{ to RT}} FSO_2CF_2CO_2Si(CH_3)_3$

B. 

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1. Procedure

Caution: Trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate should be handled with care. Skin contact, which will cause painful burns and blistering, should be avoided. If such contact occurs, the affected area should be washed thoroughly with water and with sodium bicarbonate solution.

A. Trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate. All glassware is oven-dried for about 1 h prior to use. A 1-L, three-necked, round-bottomed flask is equipped with a magnetic stirrer, addition funnel with a nitrogen (N_2) inlet, and water-cooled condenser with gas outlet. The gas outlet is connected by Tygon tubing to an empty 500-mL back-up trap, and then to an inverted 75-mm glass funnel outlet positioned just above a 1-L beaker containing 75 g of sodium bicarbonate ($NaHCO_3$) in 500 mL water (to neutralize HCl and chlorotrimethylsilane from the reaction vessel) (Note 1). The flask is charged with 150 g of 2-fluorosulfonyl-2,2-difluoroacetic acid (0.84 mol) (Note 2). Then, with a slow N_2 flow and cooling with an ice bath, 363 g of chlorotrimethylsilane (3.2 mol) (Notes 3, 4) is added dropwise with stirring over a 2 h period. Upon completion of the addition, the mixture is allowed to warm to room temperature and is stirred with N_2 bubbling for 24

h. The product mixture is distilled to give 175 grams (83%) of trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate (bp 52 °C at 15 mm) (Notes 5, 6).

B. n-Butyl 2,2-difluorocyclopropanecarboxylate. A 500-mL, round-bottomed, three-necked flask is fitted with a magnetic stirrer, condenser, addition funnel, gas dispersion tube extending to the bottom of the flask, and gas outlet with a paraffin oil bubbler. The flask is charged with 200 mL of toluene, 0.4 g of sodium fluoride (0.06 eq), and 20 g of *n*-butyl acrylate (0.156 mol) (Notes 7, 8). The solution is heated to reflux and slow N_2 bubbling is initiated with stirring for 1 h. Trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate (62.5 g, 0.31 mol, 1.6 eq) (Note 5) is added dropwise (Note 9). The mixture is heated for 8 h, then cooled and filtered under vacuum filtration through a Celite pad (Note 10). Toluene is removed by simple distillation at atmospheric pressure, and the residue distilled at reduced pressure to obtain 15.4 g of *n*-butyl 2,2-difluorocyclopropanecarboxylate (55%) (bp 99-101 °C at 58 mm) as a colorless liquid (Note 11).

2. Notes

1. In order to avoid suction of the $NaHCO_3$ solution into the trap, the mouth of the funnel should not be submerged in the $NaHCO_3$ solution.

2. 2-Fluorosulfonyl-2,2-difluoroacetic acid can be obtained from Aldrich Chemical Co., Inc., Oakwood Products, Inc., or from FluoroTech, LLC (PO Box 13135, Gainesville, FL 32604).

3. A 3.5-4 fold excess of chlorotrimethylsilane is required for full conversion of the 2-fluorosulfonyl-2,2-difluoroacetic acid. Residual acid can be difficult to separate from the ester.

4. Chlorotrimethylsilane (bp 55 °C) was obtained from Aldrich Chemical Co., Inc. and used as received.

5. Trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate is moisture-sensitive and, if possible, should be prepared immediately before use in the next step.

6. Trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate is characterized as follows: ^{1}H NMR ($CDCl_3$) δ: 0.40 ppm (s); ^{13}C NMR, δ: −1.05 ppm (s), 112.22 (dt, J = 31.5, 299.0), 155.13 (t, J = 27.0); ^{19}F NMR, δ: −103.74 ppm (2F, s), 40.58 (1F, s).[2]

7. Toluene (anhydrous), sodium fluoride (Reagent grade), and *n*-butyl acrylate (99+%) were obtained from Aldrich Chemical Co., Inc. and used as received.

8. Other acrylate esters should function equally well in this synthesis. The *n*-butyl ester was specifically chosen because the boiling point of the product is sufficiently different from that of toluene, permitting convenient separation by distillation.

9. Addition of the trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate should be slow at the beginning of the reaction, but can be gradually increased. A vigorous evolution of gas (CO_2 and SO_2) accompanies the early stages of addition, but will be barely distinguishable from the nitrogen flow at the end.

10. Filtration through the Celite pad is recommended in order to remove small amounts of acrylate polymer.

11. *n*-Butyl 2,2-difluorocyclopropanecarboxylate is characterized as follows: ^{1}H NMR ($CDCl_3$) δ: 0.91 (3H, t, J = 7.32), 1.39 (2H, m), 1.62 (2H, m), 1.72 (1H, m), 2.04 (1H, m), 2.41 (1H, m), 4.15 (2H, q, J = 6.75); ^{19}F NMR, δ: −126.50 (1F, m), −114.70 (1F, m); ^{13}C NMR, δ: 13.49, 16.30 (t, J = 10.6), 18.92, 25.51 (t, J = 10.6), 30.43, 65.31, 110.6 (m), 166.57 ppm. The product obtained by the checkers was contaminated with small amounts of *n*-butyl acrylate, which could not be removed by distillation.

Waste Disposal Information

All waste materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

The present example provides a typical procedure for difluorocyclopropanation utilizing a new and highly versatile source of difluorocarbene.[3,4] This novel reagent, trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate, provides a convenient procedure for the synthesis of difluorocyclopropane compounds via addition of difluorocarbene to alkenes

of highly variable nucleophilicity.[2] A relatively small excess of reagent is required for high yields, and even electrophilic alkenes, such as n-butyl acrylate, provide acceptable yields of the difluorocyclopropane adduct. The reactivity and preparative utility of our reagent is probably comparable to Seyferth's reagent, phenyl(trifluoromethyl)mercury,[5] but this latter substance is no longer commercially available and is both tedious and hazardous to prepare.

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

n-Butyl 2,2-difluorocyclopropanecarboxylate: Cyclopropanecarboxylic acid, 2,2-difluoro-, butyl ester (9); (260352-79-2)

Trimethylsilyl 2-fluorosulfonyl-2,2-difluoroacetate: Acetic acid, difluoro(fluorosulfonyl)-, trimethylsilyl ester (9); (120801-75-4)

Chlorotrimethylsilane: Silane, chlorotrimethyl- (8,9); (75-77-4)

2-Fluorosulfonyl-2,2-difluoroacetic acid: Acetic acid, difluoro(fluorosulfonyl)- (8,9); (1717-59-5)

n-Butyl acrylate: 2-Propenoic acid, butyl ester (9); (141-32-2)

Sodium fluoride: Sodium fluoride (NaF) (9); (7681-49-4)