

Novel Fluorination of Small-ring Tertiary Cycloalkanols: Reaction of Diethylaminosulfur Trifluoride with Tertiary Cyclobutanols†

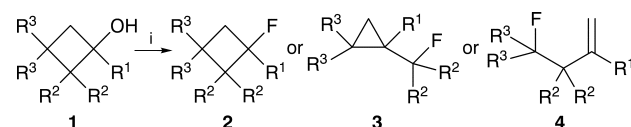
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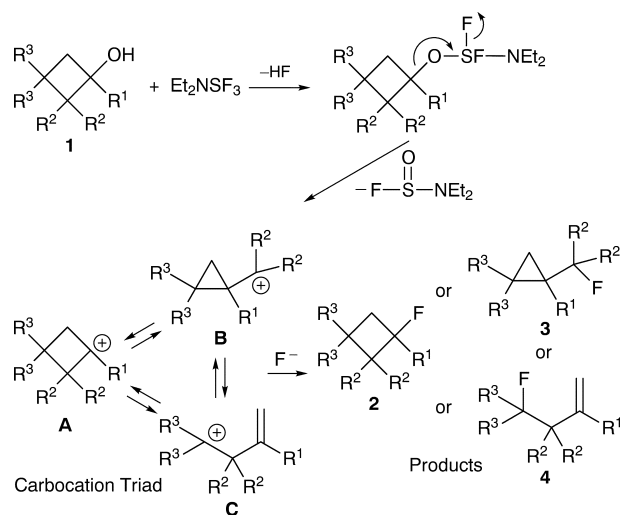
The reaction of diethylaminosulfur trifluoride with a tertiary cyclobutanol afforded a fluorocyclobutane, a (fluoromethyl)-cyclopropane or a homoallylic fluoride.

There has been much effort to develop novel methods of fluorination, because fluorine-containing molecules have become increasingly important in scientific and industrial fields.¹ Diethylaminosulfur trifluoride (DAST), an agent converting aliphatic alcohols or silyl ethers into alkyl fluorides under mild conditions, is one of the most convenient reagents in organic synthesis.² There have been several reports concerning new fluorinating methods using DAST.^{3–15} Among these methods, we reported that the reaction of DAST with tertiary cyclopropyl silyl ethers causes ring opening to give allylic fluorides.¹¹



Scheme 1 Reagents and conditions: i, DAST, CH₂Cl₂, room temperature

We now report that a tertiary cyclobutanol reacts with DAST to afford a fluorocyclobutane, a (fluoromethyl)-cyclopropane or a homoallylic fluoride, Scheme 1. The results of this reaction are summarized in Table 1. Fluorocyclobutanes **2** were obtained from the substrates **1a**, **1b** bearing electron-donating substituents at C-1 (R¹ = *n*-C₈H₁₉ or Ph). (Fluoromethyl)cyclopropanes **3** resulted with the electron-withdrawing group at C-1 (R¹ = CN or CO₂Me)



Scheme 2

*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1

Entry	Starting material	Products
1		 2a (72%)
2		 2b (91%)
3		 3c 82% (8 : 1)* 4c
4		 3d (82%)
5		 3e (82%)
6		 2f (17%) 4f (67%)

*An inseparable mixture. The ratio of the products was determined on the basis of the ¹H and ¹⁹F NMR spectral data.

(**1c–1e**). The compound **1f** bearing both an electron-withdrawing group at C-1 and electron-donating substituents at C-3 (R¹ = CN, R³ = Ph) gave a homoallylic fluoride **4** as the main product.

A plausible reaction mechanism is depicted in Scheme 2. The first step is nucleophilic displacement of a fluorine atom in DAST by the oxygen of the substrate **1**. Next, the elimination of sulfinyl dimethylamide fluoride generates a carbocation triad (equilibrium mixture of **A**, **B** and **C**).¹⁶ In the cases of compounds bearing electron-donating substituents at C-1, cyclobutyl cations (**A**) were predominant. On the other hand, cyclopropylmethyl cations (**B**) predominated in the cases of compounds bearing an electron-withdrawing group at C-1. The homoallylic cation (**C**) predominated only in the case of the compound having an electron-withdrawing group at C-1 and electron-donating substituents at C-3. Finally, the fluoride ion attacks the carbocations to afford the final products.

Experimental

Infrared spectra were measured with a Perkin-Elmer 1600 series FT-IR spectrophotometer, ¹H and ¹⁹F NMR spectra on a JEOL GX270 instrument with tetramethylsilane (for ¹H) and chlorotrifluoromethane (for ¹⁹F) as an internal standard, mass (MS) and high-resolution mass spectra (HRMS) on a JEOL JMS D-200 spectrometer.

General Procedure for the Reaction of DAST with Tertiary Cyclobutanols.—To a solution of tertiary cyclobutanol (1.0 mmol) in dichloromethane (3 ml) was added DAST (1.0 mmol) at room temperature under an inert atmosphere, and the mixture was stirred for 30 min. A saturated sodium hydrogencarbonate solution was added, and the resulting mixture extracted with dichloromethane. The extract was dried over anhydrous sodium sulfate, filtered, and evaporated to afford the crude product. Purification by chromatography (silica gel, hexane–dichloromethane) gave a pure sample.

1-Fluoro-1-nonylcyclobutane 2a.—Colorless oil; δ_{H} (CDCl_3) 0.88 (3 H, t, J 7.0 Hz), 1.22–1.35 (12 H, m), 1.35–1.41 (2 H, m), 1.41–1.50 (1 H, m), 1.61–1.72 (2 H, m), 1.75–1.84 (1 H, m), 2.02–2.15 (2 H, m), 2.20–2.34 (2 H, m); δ_{F} (CDCl_3) –130.8 to –131.1 (m); IR 2882, 1556, 1538, 1504, 1392, 1336, 1200, 1116, 1057, 980, 803, 707, 666 cm^{-1} ; MS m/z 199 ($[M - \text{H}]^+$), 180 ($[M - \text{HF}]^+$); HRMS Calc. for $\text{C}_{13}\text{H}_{24}\text{F}$ ($[M - \text{H}]^+$) 199.1993, Found 199.1929.

1-Fluoro-1-phenylcyclobutane 2b.—Colorless oil; δ_{H} (CDCl_3) 1.16–1.19 (1 H, m), 1.69–1.80 (1 H, m), 2.02–2.17 (1 H, m), 2.52–2.74 (3 H, m), 7.30–7.35 (1 H, m), 7.37–7.42 (2 H, m), 7.46–7.50 (2 H, m); δ_{F} (CDCl_3) –126.8 to –127.1 (m); IR 3047, 3018, 2970, 1567, 1556, 1538, 1484, 1360, 1270, 1200, 1093, 1036, 972, 926, 902, 834, 794, 723, 677, 660 cm^{-1} ; MS m/z 149 ($[M - \text{H}]^+$); HRMS Calc. for $\text{C}_{10}\text{H}_{10}\text{F}$ ($[M - \text{H}]^+$) 149.0887, Found 149.0845.

Inseparable mixture of 1-(fluoromethyl)cyclopropanecarbonitrile 3c and 2-(2-fluoroethyl)prop-2-enitrile 4c.—Colorless oil; δ_{H} (CDCl_3) 1.08–1.11 (16/9 H, m), 1.39–1.42 (16/9 H, m), 2.50 (2/9 H, dt, J_{HF} 25.0, J_{HH} 6.0), 4.34 (16/9 H, d, J_{HF} 47.0), 4.62 (2/9 H, dt, J_{HF} 47.0, J_{HH} 6.0 Hz), 5.88 (1/9 H, s), 6.01 (1/9 H, s); δ_{F} (CDCl_3) –212.09 (8/9 F, t, J 47.0), –220.15 (1/9 F, tt, J 47.0 and 25.0 Hz); IR 2970, 2248, 1654, 1617, 1435, 1387, 1289, 1041, 1010 cm^{-1} ; MS m/z 100 ($[M + \text{H}]^+$), 79 ($[M - \text{HF}]^+$).

Methyl 1-(fluoromethyl)cyclopropanecarboxylate 3d.—Colorless oil; δ_{H} (CDCl_3) 0.99–1.00 (2 H, m), 1.37–1.38 (2 H, m), 3.73 (3 H, s), 4.52 (2 H, d, J_{HF} 49.0 Hz); δ_{F} (CDCl_3) –213.10 (t, J 49.0 Hz); IR 2956, 1732, 1438, 1356, 1283, 1248, 1200, 1167, 1003, 755 cm^{-1} ; MS m/z 133 ($[M + \text{H}]^+$), 132 (M^+), 113 ($[M - \text{F}]^+$); HRMS Calc. for $\text{C}_6\text{H}_9\text{O}_2\text{F}$ (M^+) 132.0586, Found 132.0584.

1-(Fluorodiphenylmethyl)cyclopropanecarbonitrile 3e.—Colorless oil; δ_{H} (CDCl_3) 1.25–1.30 (2 H, m), 1.42–1.46 (2 H, m), 7.19–7.45 (10 H, m); δ_{F} (CDCl_3) –142.90 (s); IR 2926, 2240, 1780, 1654, 1600, 1493, 1449, 1277, 1191, 1078, 1049, 1011, 752, 700 cm^{-1} ; MS m/z 251 (M^+); HRMS Calc. for $\text{C}_{17}\text{H}_{14}\text{FN}$ (M^+) 251.1092, Found 251.1116.

1-Fluoro-3,3-diphenylcyclobutanecarbonitrile 2f.—Colorless oil; δ_{H} (CDCl_3) 3.34–3.43 (2 H, m), 3.61–3.68 (2 H, m), 7.16–7.37 (10 H, m); δ_{F} (CDCl_3) –143.91 to 144.17 (m); IR 3854, 3752, 3736, 3712, 3676, 3650, 3630, 3023, 2362, 1719, 1654, 1597, 1491, 1447, 1415, 1236, 1120, 1075, 1025, 928, 756, 701 cm^{-1} ; MS m/z 251 (M^+); HRMS Calc. for $\text{C}_{17}\text{H}_{14}\text{FN}$ (M^+) 251.1092, Found 251.1085.

2-(2-Fluoro-2,2-diphenylethyl)prop-2-enitrile 4f.—Colorless crystals; mp 101–102 °C; δ_{H} (CDCl_3) 3.32 (2 H, d, J_{HF} 23.0), 5.69 (1 H, s), 5.94 (1 H, s), 7.30–7.40 (10 H, m); δ_{F} (CDCl_3) –148.74 (t, J 23.0 Hz); IR 3104, 3053, 2231, 1913, 1600, 1497, 1451, 1326, 1250, 1211, 1057, 1038, 1015, 982, 958, 910, 871, 770, 774, 704, 668 cm^{-1} ; MS m/z 251 (M^+); HRMS Calc. for $\text{C}_{17}\text{H}_{14}\text{FN}$ (M^+) 251.1092, Found 251.1187.

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References

- O. A. Mascaretti, *Aldrichim. Acta*, 1993, **26**, 47; J. A. Wilkinson, *Chem. Rev.*, 1992, **92**, 505.
- M. Hudlicky, *Org. React. (N.Y.)*, 1988, **35**, 513.
- J. R. McCarthy, N. P. Peet, M. E. LeTourneau and M. Inbasekaran, *J. Am. Chem. Soc.*, 1985, **107**, 735.
- S. F. Wnuk and M. J. Robins, *J. Am. Chem. Soc.*, 1990, **55**, 4757.
- Y. Kikugawa, K. Matsumoto, K. Mitsui and T. Sakamoto, *J. Chem. Soc., Chem. Commun.*, 1992, 921.
- G. Neef, G. Ast, G. Michl, W. Schwede and H. Vierhufe, *Tetrahedron Lett.*, 1994, **35**, 8587.
- M. Kuroboshi, S. Furuta and T. Hiyama, *Tetrahedron Lett.*, 1995, **36**, 6121.
- A. J. Ratcliffe and I. Warner, *Tetrahedron Lett.*, 1995, **36**, 3881.
- S. Bildstein, J. Ducep, D. Jacobi and P. Zimmermann, *Tetrahedron Lett.*, 1996, **37**, 4941.
- S. Bildstein, J. Ducep and D. Jacobi, *Tetrahedron Lett.*, 1996, **37**, 8759.
- M. Kirihaara, T. Kambayashi and T. Momose, *Chem. Commun.*, 1996, 1103.
- D. Haigh, L. J. Jefcott, K. Magee and H. McNab, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2895.
- M. Kirihaara, K. Niimi and T. Momose, *Chem. Commun.*, 1997, 599.
- P. Borrachero-Moya, F. Cabrera-Escribano, M. Gómez-Guillén and F. Madrir-Díaz, *Tetrahedron Lett.*, 1997, **38**, 1231.
- J. M. Box, L. M. Harwood and R. C. Whitehead, *Synlett*, 1997, 571.
- G. A. Olah, V. P. Reddy and G. K. S. Prakash, *Chem. Rev.*, 1992, **92**, 69.