2-Trifluoromethoxyethyl Triflate: A Versatile Trifluoromethoxyethyl Carrier

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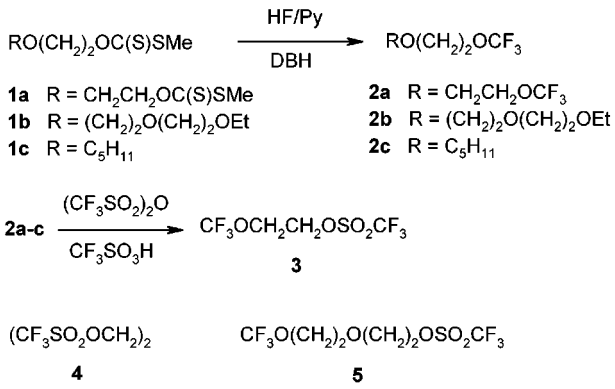
Introduction

On the basis of its electronic properties, which are close to those of a chlorine or a fluorine atom,[1] the trifluoromethoxy group has been referred to as a super-[2] or a pseudo-halogen.[3] On the other hand, the fluorination of carbon adjacent to oxygen atoms increases lipophilicity as shown by the high value of the OCF_3 hydrophobic substituent parameter.[4] Molecules bearing this group should be more able to traverse lipid membranes than their non fluorinated analogues. Unlike aromatic trifluoromethyl ethers,[5] there are few examples of aliphatic trifluoromethyl ethers;[6] mainly because there is no general direct method for the introduction of the OCF_3 unit in organic molecules.[7] We here report the preparation of 2-trifluoromethoxyethyl triflate **3** from ethylene glycol derivatives **1a**−**c** and its use as a useful aliphatic trifluoromethyl ether carrier for the preparation of substituted aliphatic trifluoromethyl ethers **6a**−**f** by its ready reaction with various nucleophiles.

Results and Discussion

Recent advances in the fluorodesulfurization reaction[8] enabled the preparation of aromatic as well as aliphatic trifluoromethyl ethers by treatment of dithiocarbonates (xanthate esters) with 1,3-dibromo-5,5-dimethylhydantoin (DBH) in an HF−pyridine medium.[9] This transformation may be interpreted as involving successive bromonium formation with sulfur atoms followed by nucleophilic introduction of fluorine substituents. To our knowledge, no functional fluorinated ether has been prepared using this methodology. Our own work in this area has shown that a functional group (e.g., ester) close to the xanthate ester does interfere (or even participate) with the fluorination process.[10] We thought that an ether function could survive the fluorination conditions while enabling further chemical transformations.

Scheme 1



For our purpose, xanthate esters of ethylene glycol derivatives **1a**−**c** were readily obtained using minor variations of the standard phase transfer procedure.[11] Fluorination of the xanthates **1a**−**c** using the HF−pyridine, DBH method (Scheme 1) proceeds uneventfully to give the corresponding trifluoromethyl ethers **2a**−**c** in good yields.

To obtain other functional trifluoromethyl ethers from compounds **2a**−**c**, the nonfluorinated group has to be transformed selectively. Various methods are described in the literature for the cleavage of simple ethers. THF, for example, is known to be cleaved symmetrically by trifluoromethanesulfonic anhydride ($(CF_3SO_2)_2O$) to give 1,4-butaneditriflate.[12] It has been claimed that the same behavior is observed with diethyl ether.[13]

In the event, however, only trace amounts of triflate **3** were formed during attempted cleavage of the bis-ether **2a** with $(CF_3SO_2)_2O$ under strictly anhydrous conditions (sealed tube, 60 °C, 4 days). Under more forcing conditions (80 °C reflux, 2 days) and using an excess of $(CF_3SO_2)_2O$, the main product formed was the bis triflate **4**.[14] We suspected that in this case trace amounts of trifluoromethanesulfonic acid may have catalyzed the reaction. Trifluoromethanesulfonic acid itself is also known to cleave diethyl ether to give ethylene and ethyl triflate.[15] Attempted cleavage of the ether **2a** with CF_3SO_3H alone (60 °C, 3 days) gave an incomplete reaction (50% conversion) and resulted in a complex mixture of fluorinated products. After some trials, it turned out that when ether **2a** was held at 60 °C for 2 days with a mixture comprising $(CF_3SO_2)_2O$ (4 equiv) and CF_3SO_3H (0.1 equiv) a clean reaction was observed leading to triflate **3** in 50% isolated yield.[16] These experimental conditions were then applied to ethers **2b** and **2c** giving triflate **3** in 27 and 73% isolated yield, respectively. The lower yield encountered

(1) Olah, G. A.; Yamamoto, T.; Hashimoto, T.; Shih, J. G.; Trivedi, N.; Singh, B. P.; Piteau, M.; Olah, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 3708.
(2) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *85*, 1314.
(3) Haas, A. *Adv. Inorg. Chem. Radio Chem.* **1984**, *28*, 167.
(4) Smart, B. E. In *Chemistry of Organic Fluorine Compounds II*; Hudlický, M., Pavlath, A. E., Eds.; ACS Monograph 187; American Chemical Society: Washington, DC, 1997; p 986.
(5) Clarck, J. H.; Wails, D.; Bastock, T. W. *Aromatic fluorination*; CRC Press: Boca Raton, 1996; Chapter 7.
(6) Ben-David, I.; Rechavi, D.; Mishani, E.; Rozen, S. *J. Fluorine Chem.* **1999**, *97*, 75.
(7) McClinton, M. A.; McClinton, D. A. *Tetrahedron* **1992**, *48*, 6555.
(8) Kollonitsch, J.; Marburg, S.; Perkins, L. M. *J. Org. Chem.* **1976**, *41*, 3107. See also: Sondej, S. C.; Katzenellenbogen, J. A. *J. Org. Chem.* **1986**, *51*, 3508.
(9) Kanie, K.; Tanaka, Y.; Suzuki, K.; Kuroboshi, M.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 471.
(10) Lequesne, C. Thesis, University of Versailles, 1997.
(11) Lee, A. W. M.; Chan, W. H., Wong, H. C.; Wong, M. S. *Synth. Commun.* **1989**, *19*, 547.
(12) Beard, C. D.; Baum, K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3673.
(13) Forbus, T. R., Jr.; Taylor, S. L.; Martin, J. C. *J. Org. Chem.* **1987**, *52*, 4156. This specific example does not appear, however, in the cited publication (ref 12).
(14) Katsuhara, Y.; Desmarteau, D. D. *J. Fluorine Chem.* **1980**, *16*, 257.
(15) Gramstad, T.; Haszeldine, R. N. *J. Org. Chem.* **1957**, *22*, 9.
(16) Based on the expectation that cleavage of **2a** should give two molecules of **3**.

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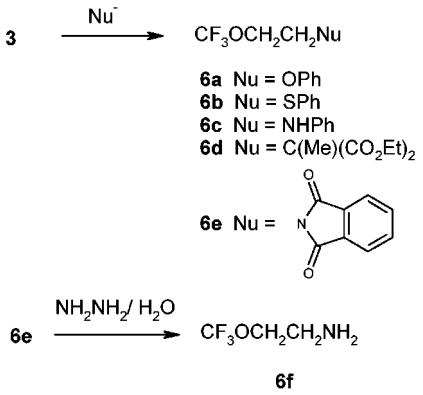
Scheme 2



in the cleavage of ether **2b** was not unexpected because of the various protonation sites possible. In this specific case we also isolated triflate **5**.

Triflate **3** proved to be a valuable intermediate for the formation of substituted trifluoromethyl ethers. It thus reacted readily with various common nucleophiles under mild conditions (THF, rt) to give the products **6a**−**e** in good yields (Scheme 2). Further deprotection of the phthalimide derivative **6e** using hydrazine hydrate[17] afforded the potentialy useful amine **6f**, isolated as its hydrochloride salt in 70% yield.

Conclusions

It appears that ether substituents are compatible with the experimental conditions of the fluorodesulfurization reaction of alkyl dithiocarbonates. Starting from the xanthate ester **1a**, it is possible to obtain by this way the hemifluorinated glyme **2a**. A regioselective cleavage of the non fluorinated ether group allows the preparation of the trifluoromethoxy substituted triflate **3** from ethylene glycol derivatives. Its ready reaction with nucleophiles open the way to the easy introduction of the 2-trifluoromethoxyethyl moiety into organic molecules. This substituent should increase the lipophilicity of the products and consequently their bioavailability.

Experimental Section

General Methods. NMR spectra were recorded as $CDCl_3$ solutions. The reported coupling constants and chemicals shifts were based on a first-order analysis. Internal reference was the residual peak of $CHCl_3$ (δ 7.27) for ^{1}H (300 MHz), central peak of $CDCl_3$ (δ 77) for ^{13}C (75 MHz) spectra and internal $CFCl_3$ (0 ppm) for ^{19}F (282 MHz) NMR spectra. Elemental analyses were obtained at ICSN, Gif-sur-Yvette, France. The hydrogen fluoride−pyridine complex used was purchased from Aldrich and contains ca. 70% HF.

General Procedure for the Preparation of Xanthates As Described by the Preparation of [MeSC(S)O(CH$_2$)$_2$]$_2$O (1a). A two-necked 1 L round-bottomed flask equipped with a magnetic stirbar and a reflux condenser was charged with 15.0 g of diethyleneglycol (140 mmol) and 3.0 g of tetrabutylammonium sulfate (8.8 mmol). A 50% solution of sodium hydroxide (282 mL) was added via a dropping funnel. After the mixture was stirred for 10 min, CS_2 (282 mL) was added dropwise, followed by 43.7 g of iodomethane (310 mmol). The mixture was stirred for 4 h at room temperature. Water (40 mL) was added. The organic layer was removed, and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The pooled organic layers were washed with brine (2 × 20 mL) and dried over $MgSO_4$. After removal of the solvents, the solid residue was eluted on a silica gel column using first 20% CH_2Cl_2/pentane as eluent to remove less polar impurities (mainly dimethyl trithiocarbonate). Further elution with CH_2Cl_2 gave 35.1 g (87% yield) of [MeSC(S)O(CH$_2$)$_2$]$_2$O as pale yellow crystals: mp 62.5−62.9 °C; ^{1}H NMR ($CDCl_3$) δ 4.6 (m, 4 H), 3.8 (m, 4 H), 2.5 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 215.8, 72.5, 68.7, 19.0; FTIR (CCl_4) 1197, 1079 cm^{-1}; CIMS (NH_3) *m*/*z* 304 (M + NH_4^+, 5), 135 (75), 70 (100). Anal. Calcd for $C_8H_{14}O_3S_4$: C, 33.54; H, 4.93; O, 16.76; S, 44.78. Found: C, 33.59; H, 4.91; O, 16.81; S, 44.75.

Preparation of EtO(CH$_2$)$_2$O(CH$_2$)$_2$OC(S)SMe (1b). Similarly, **1b** was prepared by the general procedure from 5.0 g (37.3 mmol) of diethyleneglycol monoethyl ether, 0.5 g (1.4 mmol) of ^{n}Bu$_4$NHSO$_4$, 40 mL of 50% NaOH, 40 mL of CS_2, and 6.4 g (45 mmol) of MeI. The reaction mixture was purified as described above and gave 5.9 g (71% yield) of EtO(CH$_2$)$_2$O(CH$_2$)$_2$OC(S)SMe as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 4.11 (t, J = 4.9 Hz, 2 H), 3.73 (t, J = 4.9 Hz, 2 H), 3.68 (m, 2 H); 3.61 (m, 2 H), 3.54 (q, J = 7.0 Hz, 2 H), 2.54 (s, 3 H), 1.22 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 215.8, 72.6, 70.7, 69.7, 68.4, 66.5, 18.9, 15.0; FTIR (CCl_4) 1170, 1090 cm^{-1}; LRMS *m*/*z* 224 (M$^+$, 1), 116 (45), 72 (100). Anal. Calcd for $C_8H_{16}S_2O_3$: C, 42.83; H, 7.19; S, 28.59. Found: C, 42.73; H, 7.18; S, 28.46.

Preparation of C$_5$H$_{11}$O(CH$_2$)$_2$OC(S)SMe (1c). Similarly **1c** was prepared by the general procedure from 4.6 g (35 mmol) of ethyleneglycol monopentyl ether, 0.5 g (1.4 mmol) of ^{n}Bu$_4$NHSO$_4$, 40 mL of 50% NaOH, 40 mL of CS_2, and 6.4 g (45 mmol) of MeI. The reaction mixture was purified as described above and gave 7.0 g (91% yield) of C$_5$H$_{11}$O(CH$_2$)$_2$OC(S)SMe as a yellow oil: bp 252−254 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 4.73 (m, 2H), 3.77 (m, 2H), 3.46 (t, J = 6.7 Hz, 2H), 2.57 (s, 3 H), 1.59 (m, 2 H), 1.34 (m, 4 H), 0.9 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 216.0, 72.8, 71.5, 67.9, 29.2, 28.1, 22.4, 19.0, 14.0; FTIR (CCl_4) 1192, 1095 cm^{-1}; LRMS *m*/*z* 223 (M$^+$ + 1, 1), 114 (63), 99 (100). Anal. Calcd for $C_9H_{18}O_2S_2$: C, 48.61; H, 8.16. Found: C, 48.49; H, 8.30.

General Procedure for the Preparation of Trifluoromethyl Ethers As Described by the Preparation of [CF$_3$O(CH$_2$)$_2$]$_2$O (2a). A two-necked 500 mL round-bottomed flask equipped with a magnetic stirbar, a septum port, and a reflux condenser connected to a silica gel guard was charged with 60.0 g (210 mmol) of 1,3-dibromo-5,5-dimethylhydantoin (DBH) and 300 mLof CH_2Cl_2, The flask was immersed in a dry ice/acetone cooling bath and the HF/pyridine complex (50 mL) was added via a polyethylene syringe followed by 10.0 g (35 mmol) of the bis-xanthate **1a**. The cooling bath was removed and the reaction mixture was allowed to reach rt over 2 h. The mixture was poured into 500 mL of ice water, diluted with 100 mL of CH_2Cl_2, and saturated with NaCl. The organic layer was removed, and the aqueous phase was extracted with 3 × 200 mL of CH_2Cl_2. The organic layers were pooled and washed successively with 250 mL of a cold 37% $NaHSO_3$ solution and then with 2 × 250 mL of cold brine. After drying ($MgSO_4$) and removal of the solvents, short-path distillation of the residue (0.01 mmHg) to a cold (−78 °C) trap gave 6.7 g (79% yield) of [CF$_3$O(CH$_2$)$_2$]$_2$O as a colorless oil: bp 132−134 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 4.0 (m, 4 H), 3.7 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 121.6 (q, J = 255 Hz), 66.5 (q, J = 3.3 Hz), 68.8 (s); ^{19}F NMR ($CDCl_3$) δ −61,5; LRMS *m*/*z* 241 (M$^+$ − H, 1), 143 (60), 113 (86), 69 (100). Anal. Calcd for $C_6H_8O_3F_6$: C, 29.76; H, 3.33. Found: C, 29.88; H, 3.31.

Preparation of CF$_3$O(CH$_2$)$_2$O(CH$_2$)$_2$OEt (2b). Similarly, **2b** was prepared by the general procedure from 5.0 g (22.3 mmol) of xanthate **1b**, 32.0 g (112 mmol) of DBH, and 37 mL of HF/pyridine complex in 150 mL of CH_2Cl_2. Column chromatography of the crude reaction mixture (SiO_2, CH_2Cl_2) gave 3.13 g (70% yield) of CF$_3$O(CH$_2$)$_2$O(CH$_2$)$_2$OEt as a colorless oil: bp 152−154 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 4.11 (m, 2 H), 3.75 (m, 2 H), 3.67 (m, 2 H), 3.61 (m, 2 H), 3.54 (q, J = 7 Hz, 2 H), 1.22 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 121.6 (q, J = 254 Hz), 70.9, 69.7, 68.6, 66.6, 66.5 (q, J = 3.3 Hz), 15.0; ^{19}F NMR ($CDCl_3$) δ −61.4; LRMS *m*/*z* 202 (M$^+$, 1), 73 (71), 69 (91), 59 (100). Anal. Calcd for $C_7H_{13}O_3F_3$: C, 41.59; H, 6.48. Found: C, 41.56; H, 6.64.

Preparation of CF$_3$O(CH$_2$)$_2$OC$_5$H$_{11}$ (2c). Similarly, **2c** was prepared by the general procedure from 5.0 g (22.5 mmol) of xanthate **1c**, 19.3 g (67.6 mmol) of DBH, and 37 mL of HF/pyridine complex in 150 mL of CH_2Cl_2. Column chromatography of the crude reaction mixture (SiO_2, 30% CH_2Cl_2/pentane) gave 3.1 g (69% yield) of CF$_3$O(CH$_2$)$_2$OC$_5$H$_{11}$ as a colorless oil:

(17) Sheehan, J. C.; Bolhofer, W. A. *J. Am. Chem. Soc.* **1950**, *72*, 2786.

bp 142−144 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 4.07 (t, J = 4.7 Hz, 2 H), 3.64 (t, J = 4.7 Hz, 2 H), 3.47 (t, J = 6.6 Hz, 2 H), 1.59 (m, 2 H), 1.33 (m, 4 H), 0.89 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 121.7 (q, J = 254 Hz), 71.6, 68.0, 66.5 (q, J = 3.2 Hz), 29.2, 28.1, 22.5, 13.9; ^{19}F NMR ($CDCl_3$) δ −61.4; LRMS m/z 201 (M^+ + 1, 1), 71 (100). Anal. Calcd for $C_8H_{15}O_2F_3$: C, 48.00; H, 7.55. Found: C, 47.95; H, 7.71.

General Procedure for the Preparation of $CF_3O(CH_2)_2OSO_2CF_3$ (3) As Described by the Reaction of Ether 2a with $(CF_3SO_2)_2O$ and CF_3SO_3H. A mixture of 14 mL of $(CF_3SO_2)_2O$ (82 mmol), 0.5 mL of CF_3SO_3H (5.6 mmol), and 5.0 g of trifluoromethyl ether **2a** (21 mmol) was stirred at 60 °C over 48 h in a two-necked 50 mL round-bottomed flask equipped with a magnetic stirbar and a reflux condenser under an argon atmosphere. Volatile compounds were removed under reduced pressure (40 mmHg), and the residue was diluted with 50 mL of CH_2Cl_2, washed with water, and dried ($MgSO_4$). After removal of the solvent under reduced pressure (40 mmHg), short-path distillation (0.1 mmHg) of the residue gave 5.41 g (50% yield) of $CF_3O(CH_2)_2OSO_2CF_3$ as a colorless oil: bp 140−142 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 4.69 (m, 2 H), 4.27 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 121.3 (q, J = 256 Hz), 118.5 (q, J = 319 Hz), 72.6, 64.0 (q, J = 3.6 Hz); ^{19}F NMR ($CDCl_3$) δ −75.1 (s, 3F), −62.1 (s, 3F); CIMS (CH_4) m/z 263 (M^+ + 1, 2), 243 (37), 177 (100). No satisfactory combustion analysis could be obtained for this compound. Anal. Calcd for $C_4H_4F_6O_4S$: C, 18.33; H, 1.54. Found: C, 16.96, H, 1.27. The derivatives, however (vide infra), are well characterized.

The byproduct $(CF_3SO_2OCH_2)_2$ **(4)** was isolated by column chromatography (SiO_2, CH_2Cl_2) from the residue left after the short path distillation, and had the following properties: ^{1}H NMR ($CDCl_3$) δ 4.78 (s); ^{13}C NMR ($CDCl_3$) δ 118.5 (q, J = 319 Hz), 71.7; ^{19}F NMR ($CDCl_3$) δ −74.8 (s); CIMS (NH_3) m/z 344 (M + NH_4^+, 100), 177 (98).

Preparation of $CF_3O(CH_2)_2OSO_2CF_3$ (3) from Ether 2b. Similarly, **3** was prepared by the general procedure from 3.5 mL of $(CF_3SO_2)_2O$ (20 mmol), 0.1 mL of CF_3SO_3H (1.13 mmol), and 1.0 g of trifluoromethyl ether **2a** (5 mmol). Short-path distillation was not performed. Instead, column chromatography of the crude residue (SiO_2, 10% Et_2O/ pentane) gave 0.36 g (28% yield) of $CF_3O(CH_2)_2OSO_2CF_3$ **3**, 0.43 g (27% yield) of $(CFSO_2OCH_2)_2$ **4**, and 0.29 g (19% yield) of a new byproduct $CF_3O(CH_2)_2O(CH_2)_2OSO_2CF_3$ **(5)** with the following characteristics: bp 156−158 °C (Siwoloboff, dec); ^{1}H NMR ($CDCl_3$) δ 4.63 (m, 2 H), 4.11 (m, 2 H), 3.83 (m, 2 H), 3.76 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 121.6 (q, J = 255 Hz), 118.6 (q, J = 319 Hz), 75.3, 68.8, 68.5, 66.4 (q, J = 3.2 Hz); ^{19}F NMR ($CDCl_3$) δ −75.2 (s, 3F), −61.6 (s, 3F); CIMS (NH_3) m/z 324 (M + NH_4^+, 100). Anal. Calcd for $C_8H_{15}O_2F_3$: C, 23.54; H, 2.63. Found: C, 23.56; H, 2.65.

Preparation of $CF_3O(CH_2)_2OSO_2CF_3$ (3) from Ether 2c. Similarly **3** was prepared by the general procedure from 3.5 mL of $(CF_3SO_2)_2O$ (20 mmol), 0.1 mL of CF_3SO_3H (1.13 mmol), and 1.0 g of trifluoromethyl ether **2c** (5 mmol) and gave after Kugelrohr distillation (75 °C, 15 mmHg) 0.96 g (73% yield) of $CF_3O(CH_2)_2OSO_2CF_3$.

General Procedure for the Alkylation of Nucleophiles with $CF_3O(CH_2)_2OSO_2CF_3$ (3) As Described by the Preparation of $CF_3O(CH_2)_2OPh$ (6a). Sodium phenoxide (0.42 g, 3.6 mmol) was added to a stirred solution of 0.86 g (3.3 mmol) of $CF_3O(CH_2)_2OSO_2CF_3$ **3** in 25 mL of THF. The mixture was stirred for 48 h. After addition of water (20 mL) and basification with saturated $NaHCO_3$ solution, the mixture was extracted with Et_2O (3 × 20 mL). Drying of the organic layer ($MgSO_4$) followed by concentration under vacuum and flash chromatography of the residue (SiO_2, CH_2Cl_2) gave 0.67 g (90% yield) of $CF_3O(CH_2)_2OPh$ as a colorless oil: bp 182−184 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 7.43 (t, J = 8.0 Hz, 2 H), 7.13 (t, J = 7.4 Hz, 1 H), 7.04 (d, J = 8.0 Hz, 2 H), 4.36 (m, 2 H), 4.23 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 158.2, 129.5, 121.7 (q, J = 254 Hz), 121.4, 114.6, 65.6 (q, J = 3.3 Hz), 65.2; ^{19}F NMR ($CDCl_3$) δ −61.4; LRMS m/z 206 (M^+, 64), 106 (30), 94 (100), 77 (42), 69 (31). Anal. Calcd for $C_9H_9F_3O_2$: C, 52.43; H, 4.40. Found: C, 52.41; H, 4.51.

Preparation of $CF_3O(CH_2)_2SPh$ (6b). Similarly, **6b** was prepared by the general procedure from 0.57 g (3.8 mmol) potassium thiophenoxide and 0.86 g (3.3 mmol) of $CF_3O(CH_2)_2OSO_2CF_3$ **3** and gave 0.49 g (66% yield) of $CF_3O(CH_2)_2SPh$ as a colorless oil: bp 204−206 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 7.41 (m, 2 H), 7.31 (m, 3 H), 4.09 (t, J = 7.2 Hz, 2 H), 3.19 (t, J = 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 134.1, 130.5, 129.2, 127.1, 121.5 (q, J = 255 Hz), 65.5 (q, J = 3.0 Hz), 32.5; ^{19}F NMR ($CDCl_3$) δ −61.1; LRMS m/z 222 (M^+, 45), 123 (100), 109 (22), 69 (30). Anal. Calcd for $C_9H_9F_3O_2$: C, 48.64; H, 4.08. Found: C, 48.28; H, 4.01.

Preparation of $CF_3O(CH_2)_2NHPh$ (6c). Similarly **6c** was prepared by the general procedure from 0.4 g (4.3 mmol) of aniline, 0.32 g (3.2 mmol) of triethylamine, and 0.86 g (3.3 mmol) of $CF_3O(CH_2)_2OSO_2CF_3$ **3** and gave after column chromatography (SiO_2, 20% CH_2Cl_2/pentane) 0.54 g (80% yield) of $CF_3O(CH_2)_2NHPh$ as a colorless oil: bp 184−186 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 7.30 (t, J = 7.9 Hz, 2 H), 6.87 (t, J = 7.4 Hz, 1 H), 6.71 (t, J = 7.9 Hz, 2 H), 4.19 (t, J = 5.4 Hz, 2 H), 3.96 (br s, 1H), 3.49 (t, J = 5.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 147.1, 129.3, 121.6 (q, J = 254 Hz), 118.2, 113.1, 65.8 (q, J = 3.0 Hz), 42.4; ^{19}F NMR ($CDCl_3$) δ −61.2; FTIR (CCl_4) 3422, 3465 cm^{-1}; LRMS m/z 205 (M^+, 24), 106 (100. Anal. Calcd for $C_9H_{10}F_3ON$: C, 51.69; H, 4.91; N, 6.83. Found: C, 51.66; H, 4.88; N, 6.71.

Preparation of $CF_3O(CH_2)_2C(Me)(CO_2Et)_2$ (6d). Similarly, **6d** was prepared by minor variations of the general procedure from 0.34 g (1.1 mmol) of 80% NaH in oil, 0.2 g (1.1 mmol) of $MeCH(CO_2Et)_2$, and 0.3 g (1.1 mmol) of $CF_3O(CH_2)_2OSO_2CF_3$ **3** under an argon atmosphere and gave after neutralization with NH_4Cl extraction with CH_2Cl_2 and column chromatography (Al_2O_3, 10% CH_2Cl_2/pentane), 0.25 g (77% yield) of $CF_3O(CH_2)_2C(Me)(CO_2Et)_2$ as a colorless oil: bp 210−212 °C (Siwoloboff); ^{1}H NMR ($CDCl_3$) δ 4.16 (q, J = 7.1 Hz, 4 H), 4.06 (t, J = 6.6 Hz, 2 H), 2.26 (t, J = 6.6 Hz, 2 H), 1.44 (s, 3H), 1.22 (t, J = 7.1 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 171.4, 121.4 (q, J = 255 Hz), 63.7 (q, J = 3.5 Hz), 61.5, 51.6, 34.4, 20.1, 13.8; ^{19}F NMR ($CDCl_3$) δ −61.6; FTIR (CCl_4) 1732, 1764 cm^{-1}; LRMS m/z 286 (M^+, 4), 241 (81), 214 (32), 174 (95), 128 (69), 115 (81), 100 (99), 69 (100). Anal. Calcd for $C_{11}H_{17}F_3O_5$: C, 46.16; H, 5.99. Found: C,46.47; H, 6.06.

Preparation of *N*-[2-(Trifluoromethoxy)ethyl]phthalimide (6e). Similarly, **6e** was prepared by minor variations of the general procedure from 1 g (5.4 mmol) of potassium phthalimide and 0.86 g (3.3 mmol) of $CF_3O(CH_2)_2OSO_2CF_3$ **3** and gave after extraction with CH_2Cl_2 and column chromatography (SiO_2, CH_2Cl_2 gradient/pentane), 0.71 g (84% yield) of *N*-[2-(trifluoromethoxy)ethyl]phthalimide as white crystals: mp 77.0−77.4 °C; ^{1}H NMR ($CDCl_3$) δ 7.82 (m, 2 H), 7.71 (m, 2 H), 4.19 (t, J = 5.6 Hz, 2 H), 3.98 (t, J = 5.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 167.7, 134.1, 131.7, 123.4, 121.4 (q, J = 255 Hz), 63.8 (q, J = 3.2 Hz), 36.6; ^{19}F NMR ($CDCl_3$) δ −61.4; FTIR (CCl_4) 1727 cm^{-1}; LRMS m/z 259 (M^+, 24), 190 (100). Anal. Calcd for $C_{11}H_8F_3O_3N$: C, 50.98; H, 3.11; N, 5.40. Found: C, 50.85; H, 3.11; N, 5.18.

Preparation of $CF_3O(CH_2)_2NH_2$ (6f). A solution of 0.7 g (2.7 mmol) of phthalimide **6e** and 0.16 g (3.2 mmol) of hydrazine hydrate in 25 mL of MeOH was refluxed during 2 h. The mixture was cooled to 0 °C, 3 mL of 3 M HCl was added, and the mixture was refluxed again for 1 h. After the mixture was cooled to room temperature, the solid was filtered and washed with water (2 × 5 mL). The resulting aqueous phase was extracted with Et_2O (3 × 15 mL), and the ethereal layer was dried with $MgSO_4$. After filtration, the organic phase was saturated with gaseous HCl, followed by evaporation of the solvent and gave 0.31 g (70% yield) of the hydrochloride salt of $CF_3O(CH_2)_2NH_2$ as an hygroscopic white powder: mp 189.4−191.0 °C dec; ^{1}H NMR (D_2O) δ 4.18 (br t, 2 H), 3.21 (br t, 2 H); ^{13}C NMR (D_2O) δ 123.8 (q, J = 255 Hz), 66.4 (q, J = 3.4 Hz), 41.0; ^{19}F NMR (D_2O) δ −59.9; FTIR (Nujol mull) 3037 cm^{-1}; POS ESIMS m/z 130 (M^+, 100). Anal. Calcd for $C_3H_7ClF_3NO$: C, 21.93; H, 4.17; N, 8.08. Found: C, 21.77; H, 4.26; N, 8.46.

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