Supplementary Material (ESI) for Green Chemistry

Supporting Information

Solkane® 365mfc is an environmentally benign alternative solvent for trifluoromethylation reactions

*Akihiro Kusuda, Hiroyuki Kawai, Shuichi Nakamura, Norio Shibata**

Department of Applied Chemistry, Graduate School of Engineering, Nagoya Institute of Technology,
Gokiso, Showa-ku, Nagoya 466-8555, Japan

Experimental Section

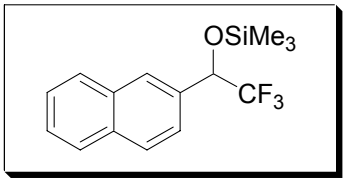
General Methods:

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Solvents were transferred *via* syringe and were introduced into the reaction vessles though a rubber septum. All of the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or $KMnO_4$ in water/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. The ^{1}H-NMR (200 MHz), ^{19}F-NMR (188 MHz) spectra for solution in $CDCl_3$ was recorded on a Varian Mercury 200. Chemical shifts (δ) are expressed in ppm downfield from internal TMS or $CHCl_3$. Mass spectra were recorded on a SHIMADZU GCMS-QP5050A. Infrared spectra were recorded on a JASCO FT/ IR-200 spectrometer.

1. General experimental procedure for the trifluoromethylation of carbonyl compounds:

To a stirred solution of **1** (0.20 mmol) and KOH (2.2 mg, 0.040 mmol) in Solkane® 365mfc (0.5 mL), Me_3SiCF_3 (59.1 μL, 0.40 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature. Then the solvent was removed in vacuo, and the product was purified by column chromatography (*n*-hexane: ethyl acetate=90:10) to give trifluoromethylated compounds **2**.

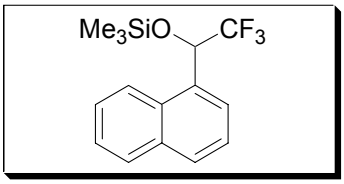
Trimethyl[2,2,2-trifluoro-1-(2-naphthalenyl)ethoxy]silane (2a).[1]



Reaction of **1a** (31.2 mg, 0.20 mmol), KOH (2.2 mg, 0.040 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol)

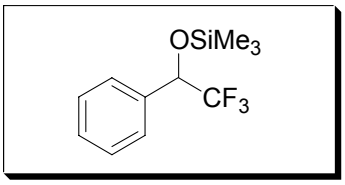
in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2a** (57.3 mg, 96%) as a white solid. ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 9H), 5.07 (q, *J* = 6.6 Hz, 1H), 7.45–7.58 (m, 3H), 7.83–7.88 (m, 4H); ^{19}F NMR ($CDCl_3$) δ –78.2 (d, *J* = 7.0 Hz, 3F); IR (KBr) 3066, 2958, 2927, 2856, 1363, 1262, 1177, 1128, 969, 900, 853, 818, 748, 697, 575, 548 cm^{-1}; MS (EI, *m/z*) 298 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl[2,2,2-trifluoro-1-(1-naphthalenyl)ethoxy]silane (2b).[1]



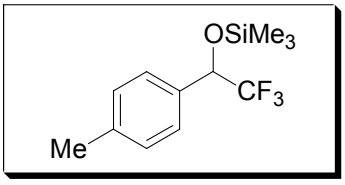
Reaction of **1b** (27.2 μL, 0.20 mmol), KOH (2.2 mg, 0.040 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 30 min gave **2b** (54.7 mg, 92%) as a white solid. ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 9H), 5.74 (q, *J* = 6.2 Hz, 1H), 7.46–7.52 (m, 3H), 7.79–7.89 (m, 3H), 8.08 (d, *J* = 8.0 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ –77.4 (d, *J* = 6.0 Hz, 3F); IR (KBr) 3066, 2962, 1599, 1514, 1354, 1272, 1172, 1131, 1008, 875, 850, 798, 776, 751, 696, 633, 536, 442 cm^{-1}; MS (EI, *m/z*) 298 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl[(2,2,2-trifluoro-1-phenylethoxy)]silane (2c).[1]



Reaction of **1c** (20.3 μL, 0.20 mmol), KOH (2.2 mg, 0.040 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 15 min gave **2c** (45.4 mg, 91%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H), 4.90 (q, *J* = 6.6Hz, 1H), 7.26–7.50 (m, 5H) ; ^{19}F NMR ($CDCl_3$) δ –78.5 (d, *J* = 6.0 Hz, 3F); IR (neat) 3069, 3036, 2961, 2898, 1497, 1456, 1369, 1271, 1172, 1133, 1031, 882, 756, 701, 634, 552 cm^{-1}; MS (EI, *m/z*) 248 (M^+). These assignments are in good accord with those in the litireture.[1]

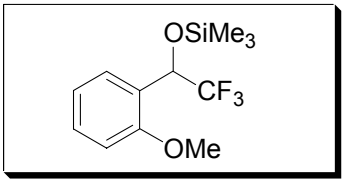
Trimethyl[2,2,2-trifluoro-1-(4-methylphenyl)ethoxy]silane (2d).[1]



Reaction of **1d** (23.4 μL, 0.20 mmol), KOH (2.2 mg, 0.040 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol)

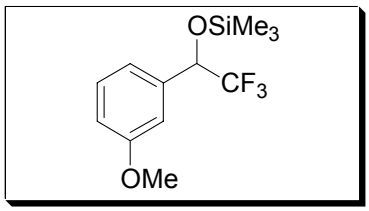
in Solkane® 365mfc (0.5 mL) at room temperature for 1 h gave **2d** (47.2 mg, 90%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H), 2.36 (s, 3H), 4.86 (q, *J* = 6.2 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –78.6 (d, *J* = 6.0 Hz, 3F); IR (neat) 2961, 1368, 1271, 1256, 1171, 1133, 883, 845, 755, 681 cm^{-1}; MS (EI, *m/z*) 262 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl[2,2,2-trifluoro-1-(2-methoxyphenyl)ethoxy]silane (2e).[2]



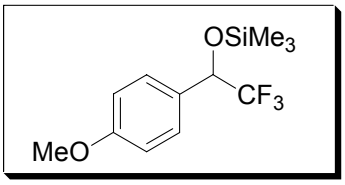
Reaction of **1e** (27.2 mg, 0.20 mmol), $CsOH·H_2O$ (3.4 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 1 h gave **2e** (44.5 mg, 80%) as a colorless oil.. ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 9H), 3.84 (s, 3H), 5.53 (q, *J* = 6.6 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.98 (dt, *J* = 1.8, 7.4 Hz, 1H), 7.31 (dt, *J* = 1.8, 8.4 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ –78.3 (d, *J* = 6.6 Hz, 3F) ; IR (neat) 2961, 2843, 1605, 1592, 1494, 1467, 1442, 1378, 1250, 1173, 1134, 1090, 1050, 1030, 885, 847, 756, 685, 628 cm^{-1}; MS (ESI, *m/z*) 301 (M + Na^+). These assignments are in good accord with those in the litireture.[2]

Trimethyl[2,2,2-trifluoro-1-(3-methoxyphenyl)ethoxy]silane (2f).



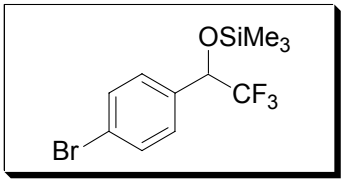
Reaction of **1f** (24.4 μL, 0.20 mmol), KOH (2.2 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 1 h gave **2f** (51.1 mg, 92%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H), 3.81 (s, 3H), 4.88 (q, *J* = 6.6 Hz, 1H), 6.86–6.92 (m, 1H), 6.98–7.01 (m, 2H), 7.27 (t, *J* = 14.4 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ –78.1 (d, *J* = 5.3 Hz, 3F); IR (neat) 2960, 2902, 2839, 1604, 1492, 1467, 1457, 1438, 1366, 1257, 1171, 1133, 1086, 1050, 920, 879, 845, 785, 763, 709 cm^{-1}; MS (EI, *m/z*) 278 (M).

Trimethyl[2,2,2-trifluoro-1-(4-methoxyphenyl)ethoxy]silane (2g).[1]



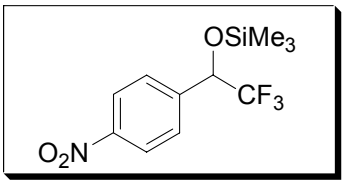
Reaction of **1g** (24.2 μL, 0.20 mmol), KOH (2.2 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 25 min gave **2g** (52.5 mg, 94%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 9H), 3.81 (s, 3H), 4.84 (q, J = 6.6 Hz, 1H), 6.88 (dt, J = 2.4, 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –78.8 (d, J = 6.0 Hz, 3F) ; IR (neat) 2960, 2840, 1614, 1516, 1466, 1368, 1254, 1172, 1131, 1036, 882, 845, 754, 682, 623, 587, 527 cm^{-1}; MS (EI, *m/z*) 278 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl[2,2,2-trifluoro-1-(4-bromophenyl)ethoxy]silane (2h).[1]



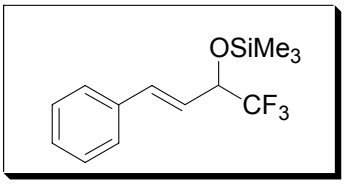
Reaction of **1h** (37.0 mg, 0.20 mmol), $CsOH{\cdot}H_2O$ (3.4 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2h** (57.6 mg, 88%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H), 4.86 (q, J = 6.4 Hz, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.50 (dt, J = 2.0 8.2, Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –78.6 (d, J = 7.0 Hz, 3F); IR (neat) 2960, 2900, 1594, 1489, 1407, 1367, 1257, 1173, 1135, 1012, 880, 846, 755, 725, 667, 622 cm^{-1}; MS (EI, *m/z*) 328 (M^+ + 1), 328 (M^+ – 1). These assignments are in good accord with those in the litireture.[1]

Trimethyl[2,2,2-trifluoro-1-(4-nitrophenyl)ethoxy]silane (2i).[1]



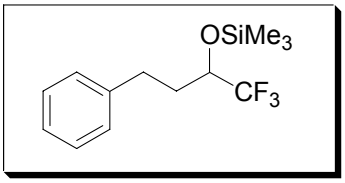
Reaction of **1i** (30.2 mg, 0.20 mmol), CsF (6.1 mg, 0.040 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2i** (55.1 mg, 94%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9H), 5.01 (q, J = 6.4 Hz, 1H), 7.64 (d, J = 8.2 Hz, 2H), 8.24 (dt, J = 2.0, 8.2 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –78.2 (d, J = 7.0 Hz, 3F); IR (neat) 2961, 2900, 1528, 1351, 1269, 1176, 1138, 1016, 879, 848, 753, 710, 623, 554, 533 cm^{-1}; MS (EI, *m/z*) 293 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl[[(2*E*)-3-phenyl-1-(trifluoromethyl)-2-propenyl]oxy]silane (2j).[1]



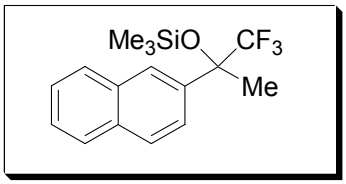
Reaction of **1j** (25.2 μL, 0.20 mmol), $CsOH \cdot H_2O$ (3.4 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2j** (46.0 mg, 84%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.20 (s, 9H), 4.54 (ddq, *J* = 6.2, 6.2, 1.4 Hz, 1H), 6.16 (dd, *J* = 6.2, 15.8 Hz, 1H), 6.74 (d, *J* = 15.8 Hz, 1H) 7.24–7.43 (m, 5H); ^{19}F NMR ($CDCl_3$) δ –78.5 (d, *J* = 6.6 Hz, 3F); IR (neat) 3030, 2961, 1373, 1271, 1132, 970, 893, 847, 749, 694 cm^{-1}; MS (EI, *m/z*) 274 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl[3-phenyl-1-(trifluoromethyl)propoxy]silane (2k).[1]



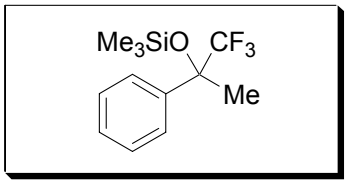
Reaction of **1k** (26.3 μL, 0.20 mmol), CsF (6.1 mg, 0.040 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2k** (45.3 mg, 82%) as a colorless oil. ^{1}H NMR ($CDCl_3$,) δ 0.11 (s, 9H), 1.91–2.00 (m, 2H), 2.52–2.68 (m, 1H), 2.76–2.91 (m, 1H), 3.83–3.99 (m, 1H), 7.16–7.33 (m, 5H); ^{19}F NMR ($CDCl_3$) δ –78.5 (d, *J* = 6.6 Hz, 3F); IR (neat) 2961, 1279, 1255, 1164, 1132, 977, 845, 752, 699 cm^{-1}; MS (EI, *m/z*) 276 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl(2,2,2-trifluoro-1-methyl-1-naphthylethoxy)silane (2l).



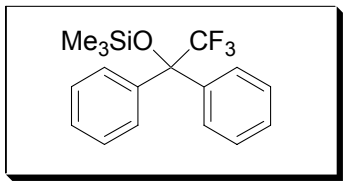
Reaction of **1l** (34.0 mg, 0.20 mmol), KOH (2.2 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 1 h gave **2l** (60.4 mg, 97%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.18 (s, 9H), 1.92 (s, 3H), 7.43–7.51 (m, 2H), 7.64–7.69 (m, 1H), 7.80–7.84 (m, 3H), 7.97 (brs, 1H); ^{19}F NMR ($CDCl_3$) δ –81.1 (s, 3F); IR (neat) 3061, 3005, 2960, 1602, 1508, 1462, 1381, 1295, 1255, 1226, 1172, 1130, 1101, 1068, 998, 950, 865, 845, 811, 746 cm^{-1}; MS (EI, *m/z*) 312 (M)

Trimethyl(2,2,2-trifluoro-1-methyl-1-phenylethoxy)silane (2m).[1]



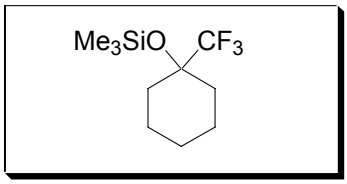
Reaction of **1m** (23.3 μL, 0.20 mmol), $CsOH \cdot H_2O$ (3.4 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2m** (46.6 mg, 89%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 9H), 1.82 (s, 3H), 7.24–7.38 (m, 2H), 7.51–7.55 (m, 2H) ^{19}F NMR ($CDCl_3$) δ –81.6 (s, 3F) ; IR (neat) 2961, 1449, 1381, 1297, 1255, 1172, 1105, 1073, 995, 864, 845, 759, 698, 653 cm^{-1}; MS (EI, *m/z*) 262 (M^+). These assignments are in good accord with those in the litireture.[1]

Trimethyl(2,2,2-trifluoro-1,1-diphenyl-ethoxy)silane (2n).[3]



Reaction of **1n** (36.4 mg, 0.20 mmol), $CsOH \cdot H_2O$ (3.4 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 2 h gave **2n** (60.5 mg, 93%) as a colorless oil. ^{1}H NMR δ 0.03 (s, 9H), 7.34–7.50 (m, 10H); ^{19}F NMR δ –73.1 (s, 3H); IR (neat) 3064, 3037, 2959, 2900, 1749, 1496, 1449, 1282, 1254, 1164, 1109, 1078, 953, 938, 914, 882, 845, 763, 723, 698 cm^{-1}; MS (EI, m/z) 324 (M). These assignments are in good accord with those in the litireture.[3]

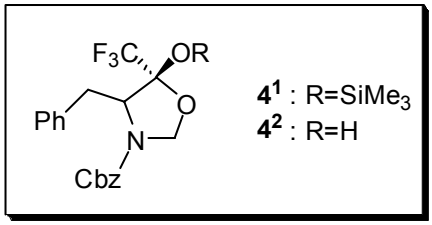
Trimethyl(1-trifluoromethylcyclohexyloxy)silane (2o).[1]



Reaction of **1o** (20.7 μL, 0.20 mmol), KOH (2.2 mg, 0.020 mmol), Me_3SiCF_3 (59.1 μL, 0.40 mmol) in Solkane® 365mfc (0.5 mL) at room temperature for 20 min gave **2o** (34.5 mg, 72%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.16 (s, 9H), 1.10–1.80 (m, 10H); ^{19}F NMR ($CDCl_3$) δ –82.3 (s, 3F); IR (KBr) 2943, 2865, 1453, 1362, 1310, 1285, 1253, 1158, 1089, 1037, 899, 845, 757, 644 cm^{-1}; MS (EI, *m/z*) 240 (M^+). These assignments are in good accord with those in the litireture.[1]

(4*S*,5*S*)-4-Benzyl-*N*-(benzyloxycarbonyl)-5-(trifluoromethyl)-5-[(trimethylsilyl)oxy]-1,3-oxazolidine(4a[1]) and (4*S*,5*S*)-4-Benzyl-*N*-(benzyloxycarbonyl)-5-hydroxy-5-(trifluoromethyl)-1,3–oxaz

olidine (4a^2).[4]



Reaction of **3** (29.5mg, 0.095 mmol), CsF (7.6 mg, 0.050 mmol), Me_3SiCF_3 (56.2 μL, 0.38 mmol) in Solkane® 365mfc (1.0 mL) at room temperature for 15 h gave a mixture of **4^1 and 4^2** (38.4 mg, 97%, R = $SiMe_3$: H = 49 : 51) as a colorless prisms and colorless oil.

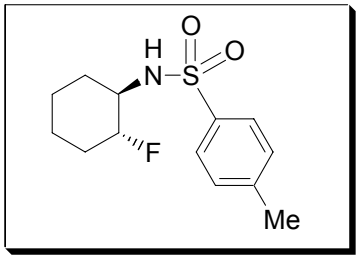
4^1 : ^{1}H NMR ($CDCl_3$) δ 0.24 (s, 9H), 2.60–2.80 (m, 1H), 3.02 (dd, *J* = 5.4, 14.0 Hz, 1H), 4.50–4.63 (m, 1H), 4.95–5.04 (m, 3H), 5.37–5.52 (m, 1H), 7.10–7.34 (m, 10H); ^{19}F NMR ($CDCl_3$) δ –84.6 (s, 3F)

4^2 : ^{1}H NMR ($CDCl_3$) δ 3.00 (dd, *J* = 7.1, 13.9 Hz, 1H), 3.04 (dd, *J* = 6.5, 14.1 Hz, 1H), 3.69 (brs, 1H) 4.61 (t, *J* = 6.6 Hz, 1H), 4.83 (d, *J* = 4.6 Hz, 1H), 4.91–5.10 (m, 2H), 5.36 (d, *J* = 4.4 Hz, 1H), 7.09–7.39 (m, 10H); ^{19}F NMR ($CDCl_3$) δ –85.0 (s, 3F). These assignments are in good accord with those in the litireture.[4]

2. General experimental procedure for the nucleophilic ring opening fluorination of aziridines:

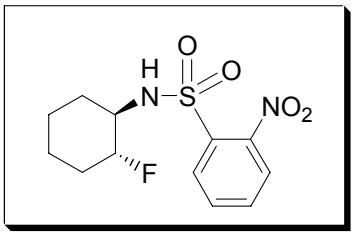
The mixture of **3** (0.10 mmol) and TBAF (31.4 mg, 0.12 mmol) in Solkane® 365mfc (1.0 mL) were stirred under nitrogen atmosphere at room temperature or 50 ºC (reflux). The reaction mixture was stirred for 15–28 h. Then the solvent was removed in vacuo, and the product was purified by column chromatography (benzene:ethyl acetate = 95:5) to give nucleophilic ring opened aziridines **4**.

***N*-(2-Fluorocyclohexyl)-4-methylbenzenesulfonamide (6a).**[5]



Reaction of **5a** (25.1 mg, 0.10 mmol) and TBAF (31.4 mg, 0.12 mmol) in Solkane® 365mfc (1.0 mL) at 50 ºC (reflux) for 15 h gave **6a** (20.8 mg, 77%) as a white solid. ^{1}H NMR ($CDCl_3$) δ 1.19–1.74 (m, 6H), 1.94–2.06 (m, 2H), 2.41 (s, 3H), 3.15–3.22 (m, 1H), 4.08 and 4.32 (dm, *J* = 48.0 Hz, 1H), 5.20 (d, *J* = 6.2 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –177.1 (dm, *J* = 48.0 Hz, 1F) ; IR (KBr) 3304, 2951, 1598, 1496 cm^{-1}; MS (EI, m/z) 271 (M^+). These assigments are in good accord with those in the litireture.[5]

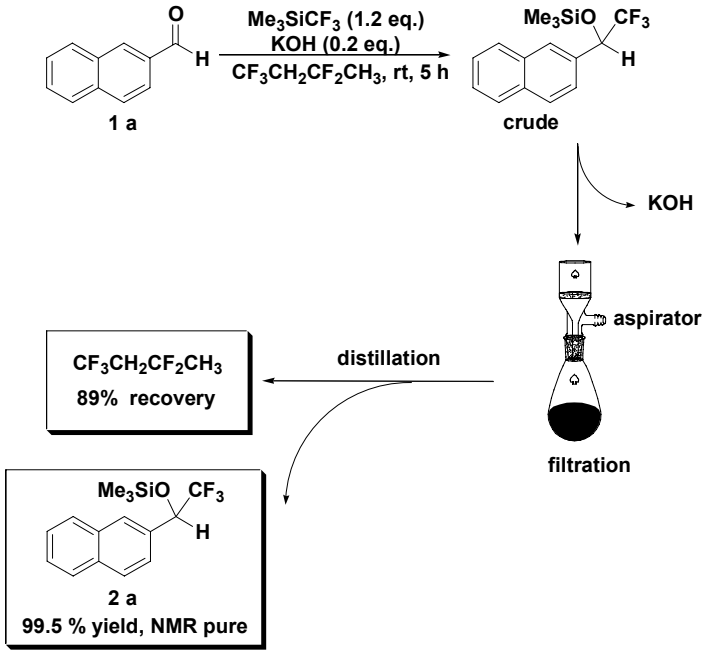
***N*-(2-Fluorocyclohexyl)-2-nitrobenzenesulfonamide (6b).**



Reaction of **5b** (28.2 mg, 0.10 mmol) and TBAF (31.4 mg, 0.12 mmol) in Solkane® 365mfc (1.0 mL) at room temperature for 28 h gave **6b** (23.0 mg, 76%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.20–2.22 (m, 6H), 1.97–2.22 (m, 2H), 3.32–3.53 (m, 1H), 4.06 and 4.31 (dm, *J* = 50.0 Hz, 1H), 5.54 (d, *J* = 7.4 Hz, 1H), 7.65–7.76 (m, 2H), 7.82–7.92 (m, 1H), 8.07–8.18 (m, 1H); ^{19}F NMR ($CDCl_3$) δ –174.7 (dm, *J* = 47.2 Hz, 1F); IR (neat) 3340, 3100, 2945, 2867, 1540, 1429, 1362, 1302, 1168, 1126, 1088, 1034, 944, 918, 896, 854, 783, 742, 731, 655 cm^{-1}; MS (EI, m/z) 302 (M).

3. Experimental procedure for the trifluoromethylation of 1a, isolation of 2a with recovering Solkane® 365mfc:

To a stirred solution of **1a** (624.7mg, 4.00 mmol) and KOH (44.9 mg, 0.80 mmol) in Solkane® 365mfc (10 mL), Me_3SiCF_3 (0.71 mL, 4.80 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 5 h, then the reaction mixture was filtered to remove KOH. Distillation of the filtrate under atmosphere pressure gave 8.86 mL (89%) of recovered Solkane® 365mfc, and 1.19 g (99.5%) of product **2a** was left which proton NMR spectrum indicated a pure **2a** compatible with the assigned structure.



References:

1) S. Mizuta, N. Shibata, T. Sato, H. Fujimoto, S. Nakamura, T. Toru, *Synlett*, 2006, 267.

2) S. Mizuta, N. Shibata, M. Hibino, S. Nagano, S. Nakamura, T. Toru, *Tetrahedron*, 2007, **63**, 8521.

3) G. K. S. Prakash, C. Panja, H. Vaghoo, V. Surampudi, R. Kultyshev, M. Mandal, G. Rasul, T. Mathew, G. A. Olah, *J. Org. Chem.*, 2006, **71**, 6806.

4) M. W. Walter, R. M. Adlington, J. E. Baldwin, C. J. Schofield, *J. Org. Chem.*, 1998, **63**, 5179.

5) S. Noritake, N. Shibata, H. Kawai, M. K. Pandey, S. Nakamura, T. Toru, *Heterocyclic Commun.*, 2009, **15**, 2.