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Lewis acid-catalyzed tri- and difluoromethylation reactions of aldehydes

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General Remarks: All reactions were performed in oven- and flame-dried glassware under a positive pressure of argon. Air- and moisture-sensitive reagents and solvents were transferred with a syringe or cannula, and were introduced into the reaction vessels through a rubber septum. All of the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel plate (60F-254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid in ethanol/heat. Column chromatography was carried out on a column packed with KANTO KAGAKU silica gel 60N 37571. ^{1}H NMR (200 MHz) and ^{19}F NMR (188 MHz) spectra for solutions in $CDCl_3$ were recorded on a Varian Gemini-200. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane for ^{1}H NMR and $CFCl_3$ for ^{19}F NMR. Infrared spectra were recorded on a JASCO FT/IR-200 spectrometer. Mass spectra were recorded on a SHIMADZU GCMS QP5050A gas chromatograph mass spectrometer.

Typical procedure for Lewis Acid-catalyzed trifluoromethylation of aldehyde (Procedure A): Trimethyl[2,2,2-trifluoro-1-(2-naphthalenyl)ethoxy]silane (2a).[1] To a mixture of **1a** (30 mg, 0.19 mmol) and TiF_4 (2.4 mg, 0.019 mmol) in DMF (0.6 mL) was added Me_3SiCF_3 (57 μL, 0.38mmol) at room temperature. The reaction mixture was stirred for 2 hours, followed by quenching with sat. $NaHCO_3$ aqueous solution (5 mL). The mixture was extracted with ethyl acetate (5 mL x 2) and combined organic phase was dried with $MgSO_4$ and evaporated. The residue was purified by silica chromatography (hexane) to afford **2a** as a colorless solid (96 %). In case of reaction catalyzed by $Ti(O\textit{i}Pr)_4$ (5.7 μL, 0.019 mmol) afforded **2a** (55 mg, 96 %) as a white solid; ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 9H), 5.07 (q, J = 7.0 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^+).

Typical procedure for ligand-contolled trifluoromethylation (Procedure B)

Trimethyl[2,2,2-trifluoro-1-(2-naphthalenyl)ethoxy]silane (2a).[1] A mixture of $Cu(OAc)_2$ (3.5 mg, 0.019 mmol), dppe (7.6 mg, 0.019 mmol) and toluene (0.6 mL) was stirred for 30 min at room temperature. Then, to the stirred mixture was added **1a** (30 mg, 0.19 mmol) and Me_3SiCF_3 (57 μL,

0.38mmol). The reaction was complete in less than 1 hour, followed by quenching with sat. $NaHCO_3$ aqueous solution (5 mL). The mixture was extracted with ethyl acetate (5 mL x 2) and the combined organic phase was dried with $MgSO_4$ and evaporated. The residue was purified by silica-gel column chromatography (hexane) to give **2a**, yield 99%.

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

Using the procedure **A**, reaction of **1b** (30mg, 0.28 mmol) with Me_3SiCF_3 (84 μL, 0.56 mmol) catalyzed by TiF_4 (3.5 mg, 0.028 mmol) in DMF (0.6 mL) gave **2b** (53 mg, 76 %) as a colorless oil, in case of reaction catalyzed by Ti(O*i*Pr)$_4$ (8.4 μL, 0.028 mmol) afforded **2b** (63 mg, 89 %). Using the procedure **B**, reaction of **1b** (30 mg, 0.28 mmol) with Me_3SiCF_3 (84 μL, 0.56 mmol) catalyzed by $Cu(OAc)_2$ (5.1mg, 0.028 mmol) and dppe (11 mg, 0.028 mmol) in toluene (0.6 mL) gave **2b** (67 mg, 96 %); ^{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* = 6.6 Hz, 3F); IR (neat) 3069, 3036, 2961, 2898, 1497, 1456, 1369, 1271, 1172, 1133, 1031, 882, 756, 701, 634, 552; MS (EI) *m/z* 248 (M^+).

Trimethyl[2,2,2-trifluoro-1-(4-methylphenyl)ethoxy]silane (2c).[3]

Using the procedure **A**, reaction of **1c** (30mg, 0.25 mmol) with Me_3SiCF_3 (74 μL, 0.50 mmol) catalyzed by TiF_4 (3.1 mg, 0.025 mmol) in DMF (0.6 mL) gave **2c** (41 mg, 62 %) as a colorless oil, in case of reaction catalyzed by Ti(O*i*Pr)$_4$ (7.4 μL, 0.025 mmol) afforded **2c** (56 mg, 86 %). Using the procedure **B**, reaction of **1c** (30 mg, 0.25 mmol) with Me_3SiCF_3 (74 μL, 0.50 mmol) catalyzed by $Cu(OAc)_2$ (4.5 mg, 0.025 mmol) and dppe (10 mg, 0.025 mmol) in toluene (0.6 mL) gave **2c** (63 mg, 96 %); ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H), 2.36 (s, 3H), 4.86 (q, *J* = 6.6 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ –78.6 (d, *J* = 6.6 Hz, 3F); IR (neat) 2961, 1368, 1271, 1256, 1171, 1133, 883, 845, 755, 681; MS (EI) *m/z* 262 (M^+).

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

Using the procedure **A**, reaction of **1d** (30mg, 0.25 mmol) with Me_3SiCF_3 (74 μL, 0.50 mmol) catalyzed by TiF_4 (3.1 mg, 0.025 mmol) in DMF (0.6 mL) gave **2d** (41 mg, 62 %) as a colorless oil, in case of reaction catalyzed by Ti(O*i*Pr)$_4$ (7.4 μL, 0.025 mmol) afforded **2d** (40 mg, 71 %). Using the procedure **B**, reaction of **1c** (30 mg, 0.25 mmol) with Me_3SiCF_3 (74 μL, 0.50 mmol) catalyzed by $Cu(OAc)_2$ (4.5 mg, 0.025 mmol) and dppe (10 mg, 0.025 mmol) in toluene (0.6 mL) gave **2d** (69 mg, 99 %); ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 9H), 3.81 (s, 3H), 4.84 (q, *J* = 6.6 Hz, 1H), 6.88 (d t, *J* = 8.4 Hz, *J* = 2.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 4H); ^{19}F NMR ($CDCl_3$) δ –7.88 (d, *J* = 6.6 Hz, 3F); IR (neat) 2960, 2840, 1614, 1516, 1466, 1368, 1254, 1172, 1131, 1036, 882, 845, 754, 682, 623, 587, 527; MS (EI) *m/z* 278 (M^+).

Trimethyl[2,2,2-trifluoro-1-(4-nitrophenyl)ethoxy]silane (2e).[5]

Using the procedure **A**, reaction of **1e** (30mg, 0.20 mmol) with Me_3SiCF_3 (59 μL, 0.40 mmol) catalyzed by TiF_4 (2.5 mg, 0.020 mmol) in DMF (0.6 mL) gave **2e** (58 mg, 99 %) as a colorless oil, in case of reaction catalyzed by $Ti(OiPr)_4$ (5.3 μL, 0.020 mmol) afforded **2e** (49 mg, 84 %). Using the procedure **B**, reaction of **1e** (30 mg, 0.20 mmol) with Me_3SiCF_3 (59 μL, 0.36 mmol) catalyzed by $Cu(OAc)_2$ (3.6 mg, 0.018 mmol) and dppe (7.9 mg, 0.020 mmol) in toluene (0.6 mL) gave **2e** (55 mg, 94 %); ^{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 = 8.2 Hz, J = 2.0 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –78.2 (d, J = 6.4 Hz, 3F); IR (neat) 2961, 2900, 1528, 1351, 1269, 1176, 1138, 1016, 879, 848, 753, 710, 623, 554, 533; MS (EI) *m/z* 293 (M^+).

[1-(4-Bromophenyl)-2,2,2-trifluoroethoxy]trimethylsilane (2f).[1]

Using the procedure **A**, reaction of **1f** (30mg, 0.16 mmol) with Me_3SiCF_3 (48 μL, 0.32 mmol) catalyzed by TiF_4 (2.0 mg, 0.016 mmol) in DMF (0.6 mL) gave **2f** (47 mg, 89 %) as a colorless oil, in case of reaction catalyzed by $Ti(OiPr)_4$ (4.8 μL, 0.016 mmol) afforded **2f** (48 mg, 90 %). Using the procedure **B**, reaction of **1f** (30 mg, 0.16 mmol) with Me_3SiCF_3 (48 μL, 0.32 mmol) catalyzed by $Cu(OAc)_2$ (2.9 mg, 0.016 mmol) and dppe (6.5 mg, 0.016 mmol) in toluene (0.6 mL) gave **2f** (49 mg, 92 %); ^{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 = 8.2 Hz, J = 2.0 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ –78.6 (d, J = 6.4 Hz, 3F); IR (neat) 2960, 2900, 1594, 1489, 1407, 1367, 1257, 1173, 1135, 1012, 880, 846, 755, 725, 667, 622; MS (EI) *m/z* 328 (M^++1), 328 (M^+–1).

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

Using the procedure **A**, reaction of **1g** (30mg, 0.23 mmol) with Me_3SiCF_3 (67 μL, 0.45 mmol) catalyzed by TiF_4 (2.8 mg, 0.023 mmol) in DMF (0.6 mL) gave **2g** (57 mg, 91 %) as a colorless oil, in case of reaction catalyzed by $Ti(OiPr)_4$ (6.7 μL, 0.023 mmol) afforded **2g** (61 mg, 98 %). Using the procedure **B**, reaction of **1g** (30 mg, 0.23 mmol) with Me_3SiCF_3 (67 μL, 0.45 mmol) catalyzed by $Cu(OAc)_2$ (4.1 mg, 0.023 mmol) and dppe (9.0 mg, 0.023 mmol) in toluene (0.6 mL) gave **2g** (62 mg, 99 %); ^{1}H NMR ($CDCl_3$) δ 0.20 (s, 9H), 4.54 (ddq, J = 6.4 Hz, J = 6.4 Hz, J = 1.2 Hz, 1H), 6.16 (dd, J = 15.8 Hz, J = 6.4 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 = 6.4 Hz, 3F); IR (neat) 3030, 2961, 1373, 1271, 1132, 970, 893, 847, 749, 694; MS (EI) *m/z* 274 (M^+).

Trimethyl(1-trifluoromethyloctyloxy)silane (2h).[6]

Using the procedure **A**, reaction of **1h** (30mg, 0.23 mmol) with Me_3SiCF_3 (69 μL, 0.46 mmol) catalyzed by TiF_4 (2.9 mg, 0.023 mmol) in DMF (0.6 mL) gave **2h** (47 mg, 75 %) as a colorless oil, in case of reaction catalyzed by $Ti(OiPr)_4$ (6.9 μL, 0.023 mmol) afforded **2h** (42 mg, 67 %). Using

the procedure **B**, reaction of **1h** (30 mg, 0.23 mmol) with Me_3SiCF_3 (69 μL, 0.46 mmol) catalyzed by $Cu(OAc)_2$ (4.3 mg, 0.023 mmol) and dppe (9.3 mg, 0.023 mmol) in toluene (0.6 mL) gave **2h** (60 mg, 95 %); ^{1}H NMR ($CDCl_3$) δ 0.16 (s, 9H), 0.89 (t, J = 6.6 Hz, 3H), 1.28 (br.s, 9H), 1.60 (m, 2H), 3.86 (m, 1H); ^{19}F NMR ($CDCl_3$) δ –78.8 (d, J = 6.6 Hz, 3F); IR (neat) 2957, 2928, 2859, 1467, 1392, 1281, 1254, 1166, 1146, 844, 754, 722, 689; MS (EI) *m/z* 270 (M^+).

Trimethyl-(2,2,2-trifluoro-1-furan-2-yl-ethoxy)silane (2i).[4]
Using the procedure **B**, reaction of **1i** (30 mg, 0.31 mmol) with Me_3SiCF_3 (92 μL, 0.62 mmol) catalyzed by $Cu(OAc)_2$ (5.7 mg, 0.031 mmol) and dppe (12 mg, 0.031 mmol) in toluene (0.6 mL) gave **2i** (41 mg, 55 %) as a colorless oil; H NMR ($CDCl_3$) δ 0.13 (s, 9H), 4.98 (q, J = 6.4 Hz, 1H), 6.37-6.47(m, 2H), 7.42-7.43 (m, 1H); ^{19}F NMR ($CDCl_3$) δ -77.8 (d, J = 6.4 Hz, 3F); IR (neat) 2963, 2902. 1502, 1364, 1278, 1240, 1155, 1136, 1014, 953, 872, 845, 744, 699; MS (EI) *m/z* 238 (M^+).

Trimethyl-(2,2,2-trifluoro-1-thiophen-2-yl-ethoxy)-silane (2j).[7]
Using the procedure **B**, reaction of **1j** (30 mg, 0.27 mmol) with Me_3SiCF_3 (79 μL, 0.53 mmol) catalyzed by $Cu(OAc)_2$ (4.8 mg, 0.027 mmol) and dppe (11 mg, 0.027 mmol) in toluene (0.6 mL) gave **2j** (67 mg, 99 %) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9H), 5.18 (q, J = 6.4Hz, 1H), 6.97-7.34 (m, 3H); ^{19}F NMR ($CDCl_3$) δ -78.9 (d, J = 6.4 Hz, 3F); IR (neat) 2961, 2900, 1436, 1361, 1276, 1256, 1175, 1135, 1044, 878, 846, 764, 706, 637; MS (EI) *m/z* 254 (M^+).

Typical procedure for ligand-contolled difluoromethylation of aldehydes: 2,2-Difluoro-1-naphthalen-2-yl-2-phenylselanyl-ethanol (4a). A mixture of $Cu(OAc)_2$ (2.3 mg, 0.0128 mmol), dppe (5.0 mg, 0.0128 mmol) and DMF (0.25 mL) was stirred for 10 min at room temperature. Then, to the stirred mixture was added **1a** (20 mg, 0.128 mmol) and Me_3SiCF_2SePh **3a** (89 mg, 0.32mmol). The reaction mixture was stirred for 20 hour, followed by quenching with sat. $NaHCO_3$ aqueous solution (5 mL). The mixture was extracted with ethyl acetate (5 mL x 2) and the combined organic phase was dried with $MgSO_4$ and evaporated. The redidue was added 1N HCl (1 mL), and THF (1 mL) ,and stirred for 1hour at room temperature. After stirring, reaction mixture was diluted with ethyl acetate (5 mL), extracted and washed with sat. NaCl aqueous. A combined organic phase was dried with $MgSO_4$ and evaporated. The redidue was purified by silica-gel colum chromatography (Hexane / AcOEt = 9/1) to give **4a**, yield 94%. as a pale yellow solid; ^{1}H NMR ($CDCl_3$) δ 2.85 (brs, 1H), 5.07-5.20 (m, 1H), 7.24-7.65 (m, 8H), 7.81-7.93 (m, 4H): ^{19}F NMR ($CDCl_3$) δ -78.0 (dd, J_{FF} = 208 Hz, J_{FH} = 8.6 Hz, 1F), -82.1 (dd, J_{FF} = 208 Hz, J_{FH} = 12.0 Hz,1F); IR(KBr); 3293, 3056, 1600, 1577, 1508, 1476, 1438, 1366, 1273, 1157, 1125, 1061, 960, 941, 795, 783, 740, 690, 479: MS (EI) *m/z* 364(M^++1).

2,2-Difluoro-1-phenyl-2-phenylselanyl-ethanol (4b).[8] Using the same method, reaction of **1b** (20 mg, 0.19 mmol) with **3a** (131 mg, 0.47 mmol) catalyzed by $Cu(OAc)_2$ (3.4 mg, 0.019 mmol) and dppe (7.5 mg, 0.019 mmol) in DMF (0.25 mL) gave **4b** (59 mg, 99 %) as a pale yellow solid; ^{1}H NMR ($CDCl_3$) δ 2.68 (d, J = 4.2 Hz 1H), 4.89-5.02 (m, 1H), 7.24-7.44 (m, 8H), 7.62-7.66 (m, 2H): ^{19}F NMR ($CDCl_3$) δ -78.3 (dd, J_{FF} = 208 Hz, J_{FH} = 7.7 Hz, 1F), -82.7 (dd, J_{FF} = 208 MHz, J_{FH} = 12.5 Hz, 1F): IR (KBr) 3468, 3064, 2893, 1495, 1477, 1453, 1440, 1390, 1291, 1236, 1197, 1142, 1062, 1011, 966, 945, 844, 758, 741, 701, 657: MS (EI) *m/z* 314(M^++1).

2,2-Difluoro-1-(4-methoxy-phenyl)-2-phenylselanyl-ethanol (4d). Using the same method, reaction of **1d** (26 mg, 0.19 mmol) with **3a** (131 mg, 0.47 mmol) catalyzed by $Cu(OAc)_2$ (3.4 mg, 0.019 mmol) and dppe (7.5 mg, 0.019 mmol) in DMF (0.25 mL) gave **4d** (45 mg, 70 %) as a pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 2.70 (brs, 1H), 4.83-5.00 (m, 1H), 6.86-6.91 (m, 2H), 7.24-7.42 (m, 5H), 7.62-7.66 (m, 2H): ^{19}F NMR ($CDCl_3$) δ -78.9 (dd, J_{FF} = 206 Hz, J_{FH} = 8.1 Hz, 1F), -82.3 (dd, J_{FF} = 207 MHz, J_{FH} = 12.0 Hz, 1F); IR (neat); 3435, 3059, 3003, 2935, 2838, 1612, 1586, 1514, 1476, 1463, 1440, 1306, 1252, 1177, 1158, 1060, 1026, 968, 948, 833, 789, 742, 691, 601, 572: MS (EI) *m/z* 344 (M^++1).

2,2-Difluoro-1-(4-nitro-phenyl)-2-phenylselanyl-ethanol (4e). Using the same method, reaction of **1e** (28 mg, 0.19 mmol) with **3a** (131 mg, 0.47 mmol) catalyzed by $Cu(OAc)_2$ (3.4 mg, 0.019 mmol) and dppe (7.5 mg, 0.019 mmol) in DMF (0.25 mL) gave **4b** (63 mg, 94 %) as a pale yellow solid; ^{1}H NMR ($CDCl_3$) δ 2.89 (d J = 4.0 Hz, 1H), 4.97-5.08 (m, 1H), 7.29-7.45 (m, 3H), 7.61-7.65 (m, 4H), 8.18-8.22 (m, 2H): ^{19}F NMR ($CDCl_3$) δ -77.4 (dd, J_{FF} = 213 Hz, J_{FH} = 6.8 Hz, 1F), -83.8 (dd, J_{FF} = 213 MHz, J_{FH} = 12.4 Hz, 1F) ; IR(KBr); 3461, 3115, 2924, 1605, 1523, 1346, 1197, 1156, 1085, 1040, 1014, 937, 854, 838, 799, 744, 700, 691, 596: MS (EI) *m/z* 359 (M^++1).

1,1-Difluoro-4-phenyl-1-phenylselanyl-but-3-en-2-ol (4g). Using the same method, reaction of **1g** (25 mg, 0.19 mmol) with **3a** (131 mg, 0.47 mmol) catalyzed by $Cu(OAc)_2$ (3.4 mg, 0.019 mmol) and dppe (7.5 mg, 0.019 mmol) in DMF (0.25 mL) gave **4g** (56 mg, 88 %) as a pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 2.44 (d J = 5.0 Hz, 1H), 4.49-4.63 (m, 1H), 6.20 (dd, J = 16.0 Hz, 6.2Hz, 1H), 6.80 (d, J = 16.0 Hz, 1H), 7.24-7.43 (m, 8H), 7.68-7.72 (m, 2H): ^{19}F NMR ($CDCl_3$) δ -79.6 (dd, J_{FF} = 304 Hz, J_{FP} = 103 Hz, 1F), -82.5 (dd, J_{FF} = 208 MHz, J_{FH} = 9.5 Hz, 1F); IR (neat); 3396, 3059, 1654, 1578, 1496, 1477, 1449, 1439, 1159, 1062, 968, 943, 857, 742, 690: MS (EI) *m/z* 340 (M^++1).

[1,1-Difluoro-2-hydroxy-2-(4-nitro-phenyl)-ethyl]-phosphonic acid diethyl ester (5e). Using the same method, reaction of **1e** (28 mg, 0.19 mmol) with $Me_3SiCF_2P(O)OEt_2$ **3b** (122 mg, 0.47 mmol) catalyzed by $Cu(OAc)_2$ (3.4 mg, 0.019 mmol) and dppe (7.5 mg, 0.019 mmol) in DMF (0.25

mL) gave **5e** (50 mg, 78 %) as a white solid; ^{1}H NMR ($CDCl_3$) δ 1.31-1.43 (m, 6H), 4.11-4.38 (m, 4H), 5.13-5.30 (m, 1H), 7.67 (d, J = 8.4 Hz, 2H), 8.24 (d, J = 8.6 Hz, 2H): ^{19}F NMR ($CDCl_3$) δ -114 (ddd, J_{FF} = 208 Hz, J_{FH} = 102 Hz, 1F), -126 (ddd, J_{FF} = 208 Hz, J_{FH} = 103 Hz, J_{FH} = 21 Hz, 1F): ^{31}P NMR (81 MHz, $CDCl_3$) δ 7.82 (dd, J = 102 Hz, J = 103Hz , 1P); IR(KBr); 3280, 2996, 916, 1611, 1529, 1348, 1243, 1183, 1089, 1065, 1043, 1024, 765, 731, 561: MS (EI) *m/z* 311 (M^+-Et)

2,2-Difluoro-1-(4-nitro-phenyl)-2-phenylsulfanyl-ethanol (6e). Using the same method, reaction of **1e** (28 mg, 0.19 mmol) with Me_3SiCF_2SPh **3c** (109 mg, 0.47 mmol) catalyzed by $Cu(OAc)_2$ (3.4 mg, 0.019 mmol) and dppe (7.5 mg, 0.019 mmol) in DMF (0.25 mL) at 85 °C gave **5e** (35 mg, 60 %) as a yellow solid; ^{1}H NMR ($CDCl_3$) δ 2.86 (d, J = 1.5 Hz, 1H), 5.03-5.14 (m, 1H), 7.31-7.69 (m, 7H), 8.21-8.25 (m, 2H); ^{19}F NMR ($CDCl_3$) δ -80.3 (dd, J_{FF} = 212 Hz, J_{FH} = 7.0 Hz, 1F), -85.7 (dd, J_{FF} = 212 MHz, J_{FH} = 11.3 Hz, 1F); IR (KBr); 3489, 3120, 3081, 1607, 1521, 1345, 1195, 1144, 1086, 1053, 853, 829, 746, 709, 687, 637, 622, 499 : MS (EI) *m/z* 311 (M^+)

2,2-Difluoro-1-naphthalen-2-yl-ethanol (7a).[9] A mixture of **4a** (28 mg, 0.081 mmol) and toluene (2 mL) was heated at 100 °C, followed by addition of a catalytic amount of AIBN (4.0 mg, 0.024 mmol) and tributyltin hydride[8] (109 μL, 0.41 mmol). After being kept at 100 °C for 30 min, the mixture was cooled to room temperature and the solvent was evaporated, diluted with saturated NaF solution (10 mL), and filtered. The aqueous layer was extracted with AcOEt (3 x 10 mL). The combined organic extracts were washed with water (3 x 10 mL) and brine (10 mL), dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography [hexane/AcOEt, 4/1 (v/v)] to gave **7a** (15 mg, 99 %) as a white solid; ^{1}H NMR ($CDCl_3$) δ 2.49 (d, J = 3.4 Hz, 1H), 5.00 (m, 1H), 5.85 (td, J_{FH} = 56 Hz, J_{HH} = 4.8 Hz, 1H), 7.48-7.53 (m, 3H) 7.83-7.90 (m, 4H): ^{19}F NMR ($CDCl_3$) δ -127 (dt, J = 56 Hz, J = 9.0 Hz, 2F); IR (KBr); 3367, 3053, 2921, 1600, 1508, 1363, 1274, 1139, 1122, 1051, 860, 825, 782, 765, 739, 481; MS (EI) *m/z* 208 (M^+).

2,2-Difluoro-1-phenyl-ethanol (7b).[10] Using the same radical reaction procedure described above, the radical reduction of **4b** (25 mg, 0.080 mmol) with tributyltin hydride (107 μL, 0.40 mmo) iniciated by AIBN (3.9 mg, 0.024 mmol) in toluene (2.0 mL) at 100 °C gave **7b** (15 mg, 99 %) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 1H), 4.83 (m, 1H), 5.76 (td, J_{FH} = 56 Hz, J_{HH} = 4.8 Hz, 1H), 7.37-7.40 (m, 5H); ^{19}F NMR ($CDCl_3$): -127 (dt, J = 56 Hz, J = 7.0 Hz, 2F); IR (neat); 3409, 2975, 2925, 1380, 1259, 1202, 1120, 1070, 845, 763, 701, 644, 606, 549, 494; MS (EI) *m/z* 158 (M^+).

2,2-Difluoro-1-(4-methoxy-phenyl)-ethanol (7d). Using the same radical reaction procedure described above, the radical reduction of **4d** (28 mg, 0.081 mmol) with tributyltin hydride (109 μL, 0.41 mmo) iniciated by AIBN (4.0 mg, 0.024 mmol) in toluene (2.0 mL) at 100 °C gave **7d** (13 mg, 99 %) as a colorless oil; 1H NMR (CDCl3) δ 2.31 (d, J = 3.2 Hz, 1H), 4.70-4.84 (m, 1H), 5.73 (td, J_{FH}

= 56 Hz, J_{HH} = 4.8 Hz, 1H), 6.89-6.94 (m, 2H), 7.31-7.36 (m, 2H)**,** ^{19}F NMR (CDCl3) δ -127.4 (dd, *J* = 56 Hz, *J* = 10.3 Hz, 2F); IR (neat); 3435, 2967, 2841, 1614, 1516, 1253, 1179, 1115, 1070, 833, 783, 553; MS (EI) *m/z* 158 (M^+).

1,1-Difluoro-4-phenyl-but-3-en-2-ol (7g). Using the same radical reaction procedure described above, the radical reduction of **4b** (25 mg, 0.073 mmol) with tributyltin hydride (99 μL, 0.37 mmo) iniciated by AIBN (3.6 mg, 0.021 mmol) in toluene (2.0 mL) at 100 °C gave **7g** (13 mg, 99 %) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.15 (brs, 1H), 4.40-4.52 (m, 1H), 5.71 (td, J_{FH} = 56 Hz, J_{HH} = 3.8 Hz, 1H), 6.20 (dd, *J* = 15.8 Hz, 6.2 Hz, 1H), 6.81 (d, *J* = 15.8 Hz, 1H), 7.26-7.42 (m, 5H); ^{19}F NMR ($CDCl_3$) δ -127.5 (ddd, *J* = 284 Hz, 56 Hz, 11.3 Hz, 1F), -129.4 (ddd, *J* = 284 Hz, 57 Hz, 9.6 Hz, 1F); IR (neat) ; 3380, 3029, 1496, 1450, 1386, 1144, 1065, 970, 751, 692; MS (EI) *m/z* 184 (M^+).

References

[1] G. K. S. Prakash, M. Mandal, C. Panja, T. Mathew, G. A. Olah, *J. Fluorine Chem.* 2003, **123**, 61-63.

[2] T. Billard, B. R. Langlois, G. Blond, *Eur. J. Org. Chem.* 2001, **8**, 1467-1471.

[3] Desilylated form; S. Sibille, S. Mcharek, J. Perichon, *Tetrahedron* 1989, **45**, 1423-1428.

[4] Desilylated form; B. Folléas, I. Marek, J.-F. Normant, L. Saint-Jalmes, *Tetrahedron* 2000, **56**, 275-283.

[5] Desilylated form; G. Kaur, V. L. Narayanan, P. A. Risbood, M. G. Hollingshead, S. F. Stinson, R. K. Varma, E. A. Sausville, *Bioorg. Med. Chem.* 2005, **13**, 1749-1761.

[6] Desilylated form; H. Hamada, M. Shiromoto, M. Funahashi, T. Itoh, K. Nakamura, *J. Org. Chem.* 1996, **61**, 2332-2336.

[7] Desilylated form; Gong, Y.; Kato, K.; Kimoto, H. *Bull. Chem. Soc. Jpn.*, 2000, **73**, 249.

[8] Y.-Y. Qin, X.-L. Qui, Y.-Y. Yang, W.-D. Meng, F.-L, Qing, *J. Org. Chem.* 2005, **70**, 9040.

[9] C. Ni, J. Hu, *Tetrahedron Lett.* 2005, **46,** 8273.

[10] G. K. S. Parakash, J. Hu, Y. Wang, G. A. Olah, *Eur. J. Org. Chem,* 2005, **11**, 2218.