Supporting Information

Catalytic Decarboxylative Fluorination for the Synthesis of Tri- and Difluoromethyl Arenes

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1. General Experimental Information

All solvents and chemicals were used as purchased unless stated otherwise. All NMR spectra were recorded on Bruker DPX200, DPX250, AV400, AVIII400 or AVII 500 spectrometers. NMR data were processed using TOPSPIN 3.1 software. Proton and carbon-13 NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to residual undeuterated solvent peak using the Bruker internal referencing procedure (edlock). Fluorine-19 NMR spectra are referenced relative to $CFCl_3$ in $CDCl_3$. Coupling constants (*J*) are reported in units of hertz (Hz). The following abbreviations are used to describe multiplets: s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), m (multiplet), br (broad). High resolution mass spectra (HRMS, *m*/*z*) were recorded on a Bruker MicroTOF spectrometer using positive electrospray ionization (ESI+) or on a Micromass GCT spectrometer using chemical ionization (CI+). Infrared spectra were recorded as neat compound using a Bruker Tensor 27 FT-IR spectrometer. Absorptions are reported in wavenumbers (cm^{-1}) and only peaks of interest are reported. Melting points of solids were measured on a Griffin apparatus and are uncorrected. IUPAC names were obtained using the ACD I-Lab 2.0 service. All reactions were performed in flame-dried apparatus with magnetic stirring under an inert atmosphere of argon or nitrogen. Thin layer chromatography (TLC) was performed using Merck aluminium-foil baked plates precoated with Kieselgel 60 F_{245}. The products were visualized using UV fluorescence (254 nm) or potassium permanganate stain. Flash column chromatography was performed over Merck silica gel C60 (40-60 μm) using eluent systems as described for each experiment. Known compounds have been checked against literature references and only two pieces of

analytical data are given. Silver nitrate was purchased from Sigma Aldrich® and F-TEDA-BF_4 (Selectfluor®) supplied by Apollo Scientific Ltd. Unless otherwise specified, other reagents were obtained from commercial suppliers.

2. Experimental Procedures and Characterisation Data

2-1. Synthesis of α,α-difluoroaryl acetic acids

General procedure for Cu-promoted cross-coupling of aryl iodide with ethyl bromodifluoroacetate (GP A) [1]**:**

In a 50 mL round bottom flask under an atmosphere of N_2, the appropriate aryl iodide (10 mmol, 1.0 equiv) and ethyl bromodifluoroacetate (1.3 mL, 10 mmol, 1.0 equiv) were added to a suspension of activated Cu powder (1.7 g, 26 mmol, 2.6 equiv) in DMSO (26 mL, 0.4 M). The reaction mixture was stirred at 60 °C for 12 h, after which time it was poured into a mixture of ice and sat. aq. NH_4Cl, the aqueous phase was extracted with Et_2O (3 × 50 mL). The combined organic phases were washed with sat. aq. NH_4Cl (2 × 50 mL) and brine (2 × 50 mL), then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography.

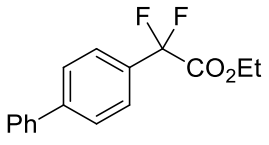
Activation of Cu powder:

Copper powder (< 424 μm , 26 mmol) was stirred vigorously in diluted aq. HCl (1 M, 10 mL) for 10 minutes at room temperature and filtered. This procedure was repeated with water (10 mL), MeOH (10 mL) and acetone (10 mL), respectively. Finally, the copper powder was dried under vacuum for 15 minutes before use.

***General procedure for hydrolysis of ethyl α,α-difluoroaryl acetate (GP B)*:**

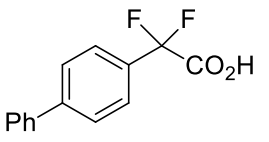
In a 50 mL round bottom flask, ethyl α,α-difluoroaryl acetate (5 mmol, 1.0 equiv) obtained by GP A was added to a mixture of MeOH (15 mL, 0.3 M) and 1 M K_2CO_3 aq. (15 mL) and stirred for 2 h at room temperature. The reaction was then poured into 1 M HCl aq. to acidify to pH 1, and the aqueous phase was extracted with EtOAc (3 × 10 mL), washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Products were purified by washing with petroleum ether 30/40.

Ethyl biphenyl-4-yl(difluoro)acetate[2]



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 5% Et_2O in petroleum ether 30/40) to give 2.05 g (79 % yield) of the title compound as a colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.0 Hz, 3H), 4.18 (q, J = 7.0 Hz, 2H), 7.22−7.26 (m, 1H), 7.30−7.33 (m, 2H), 7.44−7.47 (m, 2H), 7.52−7.58 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 63.3, 113.6 (t, J = 251.5 Hz), 126.0 (t, J = 6.0 Hz), 127.3, 127.4, 128.1, 129.0, 131.7 (t, J = 26.0 Hz), 140.0, 144.0, 164.3 (t, J = 25.5 Hz); **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ −103.5 (s, 2F). Characterization data consistent with reported data.[2]

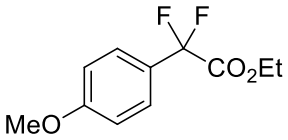
Biphenyl-4-yl(difluoro)acetic acid[3] **(1a)**



Synthesised following GP B (7.4 mmol scale), yielding 1.75 g (85 % yield) of **1a** as an off-white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 7.43 (m, J = 1.5 Hz, 7.5 Hz, 1H), 7.49−7.57 (m, 2H), 7.67−7.73 (m, 4H), 7.84 (d, J = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 114.1 (t, J = 248.5 Hz), 126.2 (t, J = 6.0 Hz), 127.4, 127.7, 128.7, 129.5, 132.1 (t, J = 24.5 Hz), 139.4, 143.4, 165.4 (t, J = 34.0 Hz); **^{19}F NMR** (376.5 MHz, $(CD_3)_2SO$) δ −102.4 (s, 2F); **IR** (neat) ν 3516, 1702, 1324, 1263, 1143, 1125, 1102,

840, 739, 697 cm^{-1}; **HRMS** (ESI) calc for $C_{14}H_9F_2O_2$ $[M-H]^-$ 247.0576, found 247.0577; **Mp** 114−117 °C. Characterization data consistent with reported data.[3]

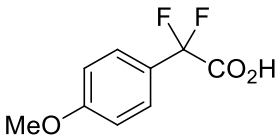
Ethyl difluoro-2-(4-methoxyphenyl)acetate[4]



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 5% EtOAc in petroleum ether 30/40) to give 846 mg (37% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.1 Hz, 3H), 3.86 (s, 3H), 4.32 (q, *J* = 7.1 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 9.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 55.4, 63.0, 113.6 (t, *J* = 251.9 Hz), 114.0, 124.9 (t, *J* = 26.6 Hz), 127.1 (t, *J* = 6.1 Hz), 161.6, 164.5 (t, *J* = 36.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −102.6 (s, 2F). Characterization data consistent with reported data.[4]

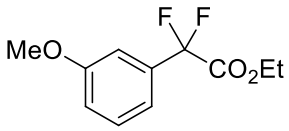
Difluoro(4-methoxyphenyl)acetic acid (1b)



Synthesised following GP B (3.7 mmol scale), yielding 588 mg (79% yield) of **2b** as a yellow solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 3.80 (s, 3H), 7.07 (d, *J* = 8.8 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 55.8, 114.2 (t, *J* = 250.9 Hz), 114.7, 125.1 (t, *J* = 25.9 Hz), 127.3 (t, *J* = 6.0 Hz), 161.7, 165.7 (t, *J* = 34.7 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −101.0 (s, 2F); **IR** (neat) ν 1739, 1610, 1514, 1439, 1252, 1177, 1141, 1098, 1030, 988, 890, 829, 744, 693, 638 cm^{-1}; **HRMS** (ESI) calc for $C_9H_7F_2O_3$ $[M-H]^-$ 201.0369, found 201.0361; **Mp** 72−74 °C.

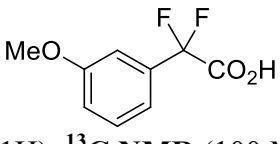
Ethyl difluoro(3-methoxyphenyl)acetate



Synthesised following GP A (5 mmol scale). Purified by flash column chromatography (eluent: 5% EtOAc in petroleum ether 30/40) to give 897 mg (78% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.1 Hz, 3H), 3.84 (s, 3H), 4.31 (q, *J* = 7.1 Hz, 2H), 7.03 (dd, *J* = 8.4 Hz, J = 2.3 Hz, 1H), 7.14 (s, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 8.1 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 55.4, 63.2, 110.7 (t, *J* = 6.4 Hz), 113.2 (t, *J* = 253.4 Hz), 116.9, 117.7 (t, *J* = 6.2 Hz), 129.8, 134.1 (t, *J* = 25.3 Hz), 159.7, 164.2 (t, *J* = 35.2 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.8 (s, 2F); **IR** (neat) ν 1764, 1605, 1493, 1456, 1278, 1218, 1101, 1047, 1019, 859, 792, 747, 693 cm^{-1}; **HRMS** (ESI) calc for $C_{11}H_{12}F_2NaO_3$ $[M+Na]^+$ 253.0647, found 253.0642.

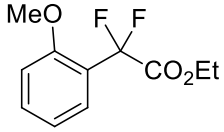
Difluoro(3-methoxyphenyl)acetic acid (1c)



Synthesised following GP B (3.9 mmol scale), yielding 436 mg (55% yield) of **1c** as a pale yellow solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 3.81 (s, 3H), 7.07 (t, *J* = 1.9 Hz, 1H), 7.13−7.15 (m, 1H), 7.15−7.17 (m, 1H), 7.46 (t, *J* = 8.0 Hz, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 55.8, 111.0 (t, *J* = 6.3 Hz), 113.8 (t, *J* = 250.8 Hz), 117.1, 117.6 (t, *J* = 6.1 Hz), 130.8, 134.6 (t, *J* = 25.4 Hz), 159.8, 165.3 (t, *J* = 33.7 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −102.4 (s, 2F); **IR** (neat) ν 1743, 1602, 1493, 1466, 1329, 1294, 1274, 1215, 1145, 1113, 1082, 1039, 1012, 917, 847, 790, 734, 686 cm^{-1}; **HRMS** (ESI) calc for $C_9H_8F_2NaO_3$ $[M+Na]^+$ 225.0334, found 225.0326; **Mp** 63−66 °C.

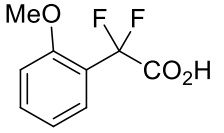
Ethyl difluoro(2-methoxyphenyl)acetate



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: EtOAc/*n*-hexane = 95/5 to 90/10) to give 1.5 g (66% yield) of the product as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.0 Hz, 3H), 3.80 (s, 3H), 4.32 (q, *J* = 7.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.8, 55.6, 62.6, 111.4, 112.3 (t, *J* = 248.0 Hz), 120.6, 121.9 (t, *J* = 24.0 Hz), 126.2 (t, *J* = 7.5 Hz), 132.4, 156.7 (t, *J* = 5.0 Hz), 164.1 (t, *J* = 34.0 Hz); **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ −102.6 (s, 2F); **IR** (neat) ν 2360, 1773, 1495, 1468, 1283, 1257, 1101, 1071, 1048, 1020, 755, 672 cm^{-1}; **HRMS** (ESI) calc for $C_{11}H_{12}F_2NaO_3$ $[M+Na]^+$ 253.0647, found 253.0649.

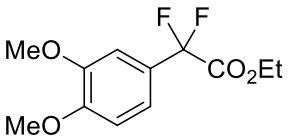
Difluoro(2-methoxyphenyl)acetic acid (1d)



Synthesised following GP B (5.8 mmol scale), yielding 1.15 g (98% yield) of **1d** as a pale yellow solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 3.79 (s, 3H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 7.51−7.58 (m, 2H); **^{13}C NMR** (125 MHz, $(CD_3)_2SO$) δ 55.9, 112.2, 112.5 (t, *J* = 246.0 Hz), 120.4, 121.6 (t, *J* = 24.0 Hz), 125.6 (t, *J* = 7.0 Hz), 132.5, 156.6 (t, *J* = 4.5 Hz), 164.6 (t, *J* = 28.0 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −101.8 (s, 2F); **IR** (neat) ν 1775, 1606, 1495, 1470, 1298, 1261, 1213, 1109, 1080, 1048, 995, 843, 774, 748, 731, 663, 608 cm^{-1}; **HRMS** (ESI) calc for $C_9H_7F_2O_3$ $[M-H]^-$ 201.0369, found 201.0365; **Mp** 96−99 °C.

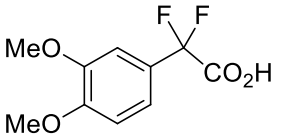
Ethyl (3,4-dimethoxyphenyl)(difluoro)acetate[5]



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 10% EtOAc in petroleum ether 30/40) to give 1.63 g (63% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.1 Hz, 3H), 3.93 (s, 3H), 3.93 (s, 3H), 4.32 (q, *J* = 7.1 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 7.18−7.22 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 56.0, 56.0, 63.0, 108.3 (t, *J* = 5.9 Hz), 110.8, 113.4 (t, *J* = 253.3 Hz), 118.5 (t, *J* = 6.6 Hz), 125.1 (t, *J* = 26.4 Hz), 149.0, 151.1, 164.4 (t, *J* = 35.9 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −102.7 (s, 2F). Characterization data consistent with reported data.[5]

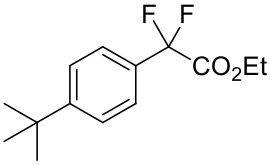
(3,4-Dimethoxyphenyl)(difluoro)acetic acid (1e)



Synthesised following GP B (6.3 mmol scale), yielding 1.16 g (80% yield) of **1e** as an off-white solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 3.80 (s, 3H), 3.81 (s, 3H), 7.06 (d, *J* = 1.8 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.13 (dd, *J* = 1.8 Hz, *J* = 8.4 Hz, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 56.1, 56.1, 108.6 (t, *J* = 5.5 Hz), 112.0, 114.1 (t, *J* = 253.8 Hz), 118.6 (t, *J* = 6.3 Hz), 125.2 (t, *J* = 26.0 Hz), 149.2, 151.3, 165.6 (t, *J* = 34.6 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −100.8 (s, 2F); **IR** (neat) ν 1770, 1521, 1466, 1452, 1297, 1267, 1208, 1173, 1151, 1102, 1046, 1019, 865, 801, 767, 729, 641 cm^{-1}; **HRMS** (ESI) calc for $C_{10}H_9F_2O_4$ $[M-H]^-$ 231.0474, found 231.0476; **Mp** 62−65 °C.

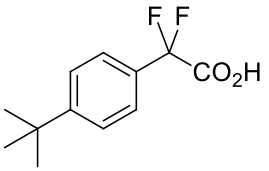
Ethyl (4-*tert*-butylphenyl)(difluoro)acetate



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 2% EtOAc in petroleum ether 30/40) to give 1.21 g (47% yield) of the title compound as a colourless oil.

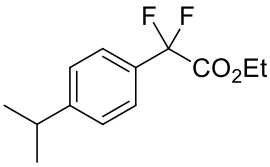
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.2 Hz, 3H), 1.34 (s, 9H), 4.31 (q, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 31.2, 34.9, 63.0, 113.6 (t, *J* = 251.8 Hz), 125.2 (t, *J* = 6.0 Hz), 125.6, 129.9 (t, *J* = 25.8 Hz), 154.3, 164.4 (t, *J* = 35.5 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.2 (s, 2F); **IR** (neat) ν 2966, 1765, 1271, 1144, 1098, 1013, 991, 834, 706 cm^{-1}; **HRMS** (ESI) calc for $C_{14}H_{18}F_2NaO_2$ $[M+Na]^+$ 279.1167, found 279.1162.

(4-*tert*-Butylphenyl)(difluoro)acetic acid (1f)



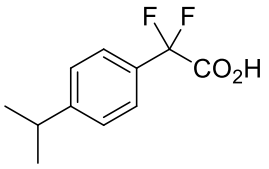
Synthesised following GP B (4.7 mmol scale), yielding 713 mg (66% yield) of **1f** as an off-white solid.
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 1.29 (s, 9H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 31.3, 35.1, 114.1 (t, *J* = 249.8 Hz), 125.4 (t, *J* = 5.9 Hz), 126.2, 130.3 (t, *J* = 25.6 Hz), 154.3, 165.5 (t, *J* = 34.1 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −102.1 (s, 2F); **IR** (neat) ν 1740, 1269, 1148, 1106, 992, 916, 840, 691 cm^{-1}; **HRMS** (EI/FI) calc for $C_{12}H_{14}F_2O_2$ $[M]^+$ 228.0962, found 228.0962; **Mp** 80−82 °C.

Ethyl difluoro[4-(propan-2-yl)phenyl]acetate



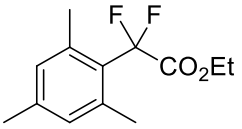
Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 2% EtOAc in petroleum ether 30/40) to give 1.07 g (44% yield) of the title compound as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (d, *J* = 6.9 Hz, 6H), 1.34 (t, *J* = 7.1 Hz, 3H), 2.98 (sept, *J* = 6.9 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 23.8, 34.0, 63.0, 113.6 (t, *J* = 251.0 Hz), 125.5 (t, *J* = 6.1 Hz), 126.7, 130.3 (t, *J* = 25.4 Hz), 152.0, 164.4 (t, *J* = 35.5 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.2 (s, 2F); **IR** (neat) ν 1764, 1269, 1096, 1056, 1013, 992, 835 cm^{-1}; **HRMS** (ESI) calc for $C_{13}H_{16}F_2NaO_2$ $[M+Na]^+$ 265.1011, found 265.1007.

Difluoro[4-(propan-2-yl)phenyl]acetic acid (1g)



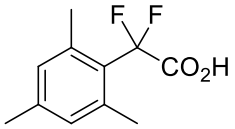
Synthesised following GP B (4.4 mmol scale), yielding 707 mg (75% yield) of **1g** as a white solid.
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 1.21 (d, *J* = 6.9 Hz, 6H), 2.94 (sept, *J* = 6.9 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H); **^{13}C NMR** (100.6 MHz, $(CD_3)_2SO$) δ 24.0, 33.8, 114.1 (t, *J* = 251.6 Hz), 125.6 (t, *J* = 5.8 Hz), 127.3, 130.7 (t, *J* = 25.6 Hz), 152.1, 165.6 (t, *J* = 34.1 Hz); **^{19}F NMR** (376.6 MHz, $(CD_3)_2SO$) δ −102.0 (s, 2F); **IR** (neat) ν 1739, 1268, 1143, 1113, 1058, 993, 916, 836, 750, 695 cm^{-1}; **HRMS** (EI/FI) calc for $C_{11}H_{12}O_2F_2$ $[M]^+$ 214.0805, found 214.0804; **Mp** 32−34 °C.

Ethyl 2,2-difluoro-2-mesitylacetate



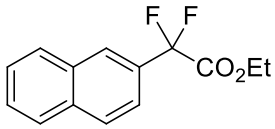
Synthesised following GP A (6 mmol scale). Purified by flash column chromatography (eluent: 2% EtOAc in petroleum ether 30/40) to give 950 mg (65% yield) of the title compound as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.1 Hz, 3H), 2.29 (s, 3H), 2.44 (t, *J* = 4.3 Hz, 6H), 4.32 (q, *J* = 7.2 Hz, 2H), 6.88 (s, 2H); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 13.9, 20.8, 21.6 (t, *J* = 5.8 Hz), 63.0, 116.3 (t, *J* = 253.1 Hz), 126.9 (t, *J* = 23.0 Hz), 131.1, 137.6 (t, *J* = 3.3 Hz), 139.9, 164.6 (t, *J* = 35.6 Hz); **^{19}F NMR** (376.6 MHz, $CDCl_3$) δ −94.7 (s, 2F); **IR** (neat) ν 1762, 1278, 1242, 1170, 1093, 1017, 986, 956, 855, 835 cm^{-1}; **HRMS** (ESI) calc for $C_{13}H_{16}F_2NaO_2$ $[M+Na]^+$ 265.1011, found 265.1010.

Difluoro(2,4,6-trimethylphenyl)acetic acid (1h)



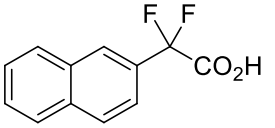
Synthesised following GP B (3.9 mmol scale), yielding 336 mg (40% yield) of **1h** as a white solid.
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 2.23 (s, 3H), 2.37 (t, *J* = 4.2 Hz, 6H), 6.93 (s, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 20.7, 21.5 (t, *J* = 5.6 Hz), 116.8 (t, *J* = 251.5 Hz), 127.4 (t, *J* = 22.4 Hz), 131.3, 137.2 (t, *J* = 3.1 Hz), 139.9, 165.8 (t, *J* = 34.0 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −94.2 (s, 2F); **IR** (neat) ν 1739, 1426, 1284, 1236, 1128, 1102, 688 cm^{-1}; **HRMS** (EI/FI) calc for $C_{12}H_{14}F_2F_2O_2$ $[M]^+$ 265.1011, found 214.0802; **Mp** 97−99 °C.

Ethyl difluoro(naphthalen-2-yl)acetate



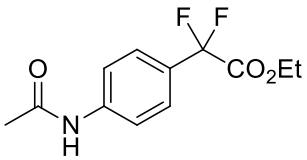
Synthesised following GP A (5 mmol scale). Purified by flash column chromatography (eluent: 5% Et_2O in petroleum ether 30/40) to give 420 mg (34% yield) of the title compound as a yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.0 Hz, 3H), 4.24 (q, *J* = 7.0 Hz, 2H), 7.46-7.53 (m, 2H), 7.58 (dd, *J* = 2.0 Hz, 9.0 Hz, 1H), 7.79−7.89 (m, 3H), 8.05 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 13.9, 63.2, 113.6 (t, *J* = 252.0 Hz), 121.9 (t, *J* = 5.5 Hz), 125.7 (t, *J* = 7.0 Hz), 126.9, 127.7, 127.8, 128.8 (2C), 130.0 (t, *J* = 25.5 Hz), 132.4, 134.2, 164.2 (t, *J* = 35.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.6 (s, 2F); **IR** (neat) ν 2361, 1764, 1280, 1098 cm^{-1}; **HRMS** (CI) calc for $C_{14}H_{12}O_2F_2$ $[M]^+$ 250.0805, found 250.0802.

Difluoro(naphthalen-2-yl)acetic acid (1i)



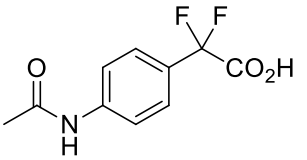
Synthesised following general procedure B (1.6 mmol scale), yielding 241 mg (68% yield) of **1i** as an off-white solid.
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.61−7.68 (m, 3H), 8.02 (d, *J* = 7.0 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 7.0 Hz, 1H), 8.23 (s, 1H); **^{13}C NMR** (125 MHz, $(CD_3)_2SO$) δ 121.7 (t, *J* = 4.5 Hz), 125.2 (t, *J* = 6.0 Hz), 127.2, 127.7, 127.9, 128.7, 128.9, 130.0 (t, *J* = 25.0 Hz), 132.0, 133.7; **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −102.1 (s, 2F); **IR** (neat) ν 1740, 1227, 1194, 1163, 1126, 1106, 1015, 906, 868, 827, 747, 717 cm^{-1}; **HRMS** (ESI) calc for $C_{12}H_7F_2O_2$ $[M-H]^-$ 221.0420, found 221.0410; **Mp** 120−121 °C.

Ethyl [4-(acetylamino)phenyl](difluoro)acetate



Synthesised following GP A (5 mmol scale). Purified by flash column chromatography (eluent: 30% EtOAc in petroleum ether 30/40) to give 1.10 g (86% yield) of the title compound as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.0 Hz, 3H), 2.11 (s, 3H), 4.22 (q, *J* = 7.0 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.96 (br. s, N*H*); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 24.5, 63.2, 113.3 (t, *J* = 252.0 Hz), 119.7, 126.4 (t, *J* = 6.0 Hz), 128.1 (t, *J* = 26.0 Hz), 140.5, 164.3 (t, *J* = 35.0 Hz), 169.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.2 (s); **IR** (neat) ν 1763, 1672, 1603, 1533, 1409, 1371, 1317, 1265, 1184, 1142, 1099, 1028, 1011, 992, 834, 761, 689 cm^{-1}; **HRMS** (ESI) calc for $C_{12}H_{13}F_2NNaO_3$ $[M+Na]^+$ 280.0756, found 280.0749.

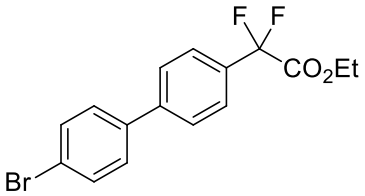
[4-(Acetylamino)phenyl](difluoro)acetic acid (1j)



Synthesised following GP B (4 mmol scale), yielding 576 mg (48% yield) of **1j** as a pale yellow solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 2.07 (s, 3H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 10.2 (s, N*H*); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 24.5, 114.1 (t, *J* = 251.5 Hz), 119.2, 126.4 (t, *J* = 6.0 Hz), 127.6 (t, *J* = 26.0 Hz), 142.2, 165.5 (t, *J* = 33.8 Hz), 169.2; **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −101.5 (s, 2F); **IR** (neat) ν 3347, 1924, 1715, 1592, 1540, 1411, 1375, 1257, 1187, 1116, 1073, 996, 969, 838, 785, 755, 726, 688, 629, 609 cm^{-1}; **HRMS** (ESI) calc for $C_{10}H_8F_2NO_3$ $[M-H]^-$ 228.0478, found 228.0487; **Mp** 154−156 °C.

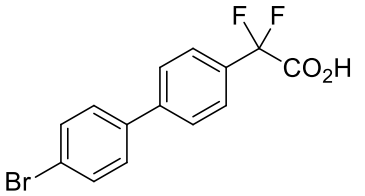
Ethyl (4'-bromobiphenyl-4-yl)(difluoro)acetate



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 2% EtOAc in petroleum ether 30/40) to give 1.91 g (54% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, *J* = 7.1 Hz, 3H), 4.35 (q, *J* = 7.1 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 63.2, 113.4 (t, *J* = 255.5 Hz), 122.5, 126.1 (t, *J* = 5.9 Hz), 127.2, 128.8, 132.1 (t, *J* = 25.6 Hz), 132.1, 138.9, 142.7, 164.1 (t, *J* = 35.4 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.7 (s, 2F); **IR** (neat) ν 1762, 1484, 1266, 1099, 1034, 1003, 856, 815, 772, 758, 679 cm^{-1}; **HRMS** (EI/FI) calc for $C_{16}H_{13}F_2BrO_2$ $[M]^+$ 354.0067, found 354.0063.

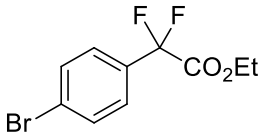
(4'-Bromobiphenyl-4-yl)(difluoro)acetic acid (1k)



Synthesised following GP B (1.6 mmol scale), yielding 241 mg (68% yield) of **1k** as an off-white solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.65−7.72 (m, 6H), 7.83 (d, *J* = 8.3 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 114.0 (t, *J* = 252.2 Hz), 122.3, 126.3 (t, *J* = 5.9 Hz), 127.6, 129.5, 132.4, 132.4 (t, *J* = 25.4 Hz), 138.6, 142.1, 165.3 (t, *J* = 34.7 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −102.5 (s, 2F); **IR** (neat) ν 1751, 1268, 1152, 1110, 1075, 991, 897, 852, 815, 747, 671 cm^{-1}; **HRMS** (ESI) calc for $C_{14}H_8F_2BrO_2$ $[M-H]^-$ 324.9681, found 324.9689; **Mp** 150−153 °C.

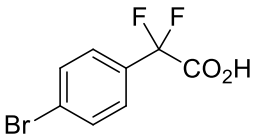
Ethyl (4-bromophenyl)(difluoro)acetate[4]



Synthesised following GP A (5 mmol scale). Purified by flash column chromatography (eluent: 3% EtOAc in petroleum ether 30/40) to give 433 mg (31% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 7.41 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 63.4, 113.0 (t, *J* = 252.3 Hz), 125.7, 127.2 (t, *J* = 6.0 Hz), 131.8 (t, *J* = 26.2 Hz), 132.0, 163.8 (t, *J* = 34.9 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −104.1 (s, 2F). Characterization data consistent with reported data.[4]

(4-Bromophenyl)(difluoro)acetic acid (1l)

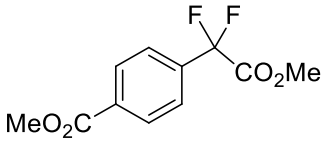


Synthesised following GP B (1.5 mmol scale), yielding 286 mg (76% yield) of **1l** as an off-white solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.54 (d, *J* = 8.6 Hz, 2H), 7.76 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 113.6 (t, *J* = 250.2 Hz), 125.3, 127.8 (t, *J* = 5.8 Hz), 132.5 (t, *J* = 26.6 Hz), 132.5, 165.0 (t, *J* = 33.4 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −102.7 (s); **IR** (neat) ν 1748, 1595, 1486, 1437, 1398, 1263, 1139, 1100, 1071, 989, 898, 828, 746, 721, 673 cm^{-1}; **HRMS** (ESI) calc for $C_8H_4BrF_2O_2$ $[M-H]^-$ 248.9368, found 248.9358; **Mp** 95−97 °C.

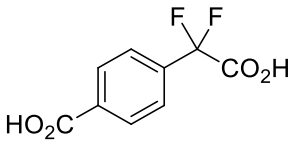
Methyl 4-(1,1-difluoro-2-methoxy-2-oxoethyl)benzoate

To a solution of 1.2 g crude 4-(2-ethoxy-1,1-difluoro-2-oxoethyl)benzoic acid (synthesised following GP A, 5 mmol scale) in MeOH (22 mL) was added dropwise thionyl chloride (1.8 mL) at 0 °C. The mixture was allowed to warm to room temperature while stirring overnight, after which it was concentrated *in vacuo* and the crude product was purified by flash column chromatography (eluent: 10% EtOAc in *n*-hexane) to give 725 mg (59% yield) of the title compound as a white solid.



^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.88 (s, 3H), 7.62 (d, *J* = 8.5 Hz, 2H), 8.06 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 52.5, 53.8, 113.0 (t, *J* = 253.0 Hz), 125.7 (t, *J* = 6.0 Hz), 129.9, 132.7, 136.8 (t, 25.5 Hz), 164.2 (t, *J* = 35.0 Hz), 166.1; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −104.3 (s, 2F); **IR** (neat) ν 1770, 1729, 1281, 1193, 1002 cm^{-1}; **HRMS** (ESI) calc for $C_{11}H_{10}F_2NaO_4$ $[M+Na]^+$ 267.0439, found 267.0442; **Mp** 40−42 °C.

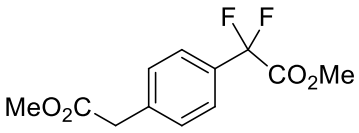
4-[Carboxy(difluoro)methyl]benzoic acid (1n)



In a 50 mL round bottom flask, methyl 4-(1,1-difluoro-2-methoxy-2-oxoethyl)benzoate (600 mg, 2.6 mmol, 1.0 equiv) was added to a mixture of MeOH (8 mL, 0.3 M) and 1M NaOH (15 mL, 15 mmol, 3.0 equiv) and stirred for 5 h at room temperature. The reaction mixture was then poured into 1M HCl to acidify to pH 1, extracted with EtOAc (× 3), washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give 418 mg (74% yield) of **1n** as a white solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.72 (d, *J* = 8.5 Hz, 2H), 8.09 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (125 MHz, $(CD_3)_2SO$) δ 113.2 (t, *J* = 252.5 Hz), 125.5 (t, *J* = 5.5 Hz), 129.8, 133.3, 136.6 (t, *J* = 25.5 Hz), 164.5 (t, *J* = 33.0 Hz), 166.5; **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −103.0 (s, 2F); **IR** (neat) ν 1721, 1581, 1425, 1309, 1281, 1264, 1148, 1108, 993, 955, 865, 729, 704 cm^{-1}; **HRMS** calc for $C_9H_5F_2O_4$ $[M-H]^-$ 215.0161, found 215.0162; **Mp** 240−241 °C.

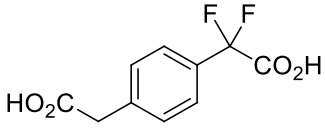
Methyl 2,2-difluoro-2[4-(2-methoxy-2-oxoethyl)phenyl]acetate



To a solution of the crude of 2-[4-(2-ethoxy-1,1-difluoro-2-oxoethyl)phenyl]acetic acid (synthesised following GP A, 10 mmol scale), in MeOH (25 mL) was added dropwise thionyl chloride (2.6 mL) at 0 °C. The mixture was allowed to warm to room temperature while stirring overnight, after which time it was concentrated *in vacuo* and the crude product was purified by flash column chromatography (eluent: 10% EtOAc in *n*-hexane) to give 900 mg (37% yield) of the title compound as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 2H), 3.69 (s, 3H), 3.83 (s, 3H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 40.7, 52.1, 53.5, 113.3 (t, *J* = 250.3 Hz), 125.7 (t, *J* = 6.3 Hz), 129.6, 131.5 (t, 26.1 Hz), 137.1, 164.5 (t, *J* = 35.5 Hz), 171.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −103.6 (s, 2F); **IR** (neat) ν 2360, 2170, 1735, 1487, 1435, 1253. 1158, 1009, 800 cm^{-1}; **HRMS** (ESI) calc for $C_{12}H_{12}F_2NaO_4$ $[M+Na]^+$ 281.0596, found 281.0604.

2-[4-(Carboxymethyl)phenyl]-2,2-difluoroacetic acid (1o)

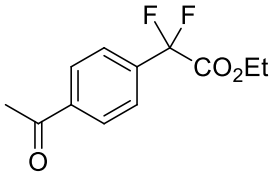


In a 50 mL round bottom flask, methyl 2,2-difluoro-2[4-(2-methoxy-2-oxoethyl)phenyl]acetate (900 mg, 7 mmol, 1.0 equiv) was added to a mixture of MeOH (10 mL, 0.3 M) and

1M NaOH aq. (15 mL, 6 mmol, 6.0 equiv) and stirred for 5 h at room temperature. The reaction mixture was then poured into 1M HCl to acidify to pH 1, extracted with EtOAc (3 ×), washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give 700 mg (43% yield) of **1o** as a white solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 3.61 (s, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 40.3, 113.6 (t, J = 248.7 Hz), 125.1 (t, J = 6.0 Hz), 130.0, 131.1 (t, J = 25.3 Hz), 165.0 (t, J = 34.0 Hz), 172.3; **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −102.2 (s, 2F); **IR** (neat) ν 2900, 2675, 1703, 1421, 1293, 1266, 1144, 1120, 994, 940, 829, 724, 670 cm^{-1}; **HRMS** calc for $C_{10}H_7F_2O_4$ $[M-H]^-$ 229.0318, found 229.0314; **Mp** 107−108 °C.

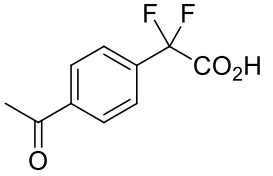
Ethyl difluoro(4-acetophenone)acetate



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 10% Et_2O in petroleum ether 30/40) to give 2.2 g (92% yield) of the title compound as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 3H), 2.60 (s, 3H), 4.28 (q, J = 7.0 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 8.01 (d, J = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.8, 26.7, 63.4, 112.9 (t, J = 252.0 Hz), 125.9 (t, J = 6.0 Hz), 128.5, 136.9 (t, J = 25.5 Hz), 139.0, 163.2 (t, J = 35.0 Hz), 197.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −104.5 (s, 2F); **IR** (neat) ν 2361, 1763, 1690, 1408, 1360, 1264, 1142, 1098, 1011, 993, 959, 833, 770, 752, 702, 628 cm^{-1}; **HRMS** (ESI) calc for $C_{12}H_{12}O_3F_2$ [M+Na]+ 265.0755, found 265.0697.

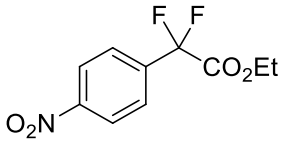
Difluoro(4-acetophenone)acetic acid (1p)



Synthesised following GP B (9.0 mmol scale), yielding 1.02 g (53% yield) of **1p** as a pale red solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 2.63 (s, 3H), 7.73 (d, J = 8.0 Hz, 2H), 8.10 (d, J = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 27.4, 113.7 (t, J = 251.0 Hz), 126.1 (t, J = 6.0 Hz), 129.2, 137.1 (t, J = 25.0 Hz), 139.3, 165.0 (t, J = 33.0 Hz), 197.9; **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −103.8 (s, 2F); **IR** (neat) ν 2623, 1766, 1650, 1407, 1246, 1141, 1117, 1097, 994, 969, 845, 830, 778, 740, 689, 635 cm^{-1}; **HRMS** (ESI) calc for $C_{10}H_8O_3F_2$ $[M-H]^-$ 213.0369, found 213.0452. **Mp** 129−131°C

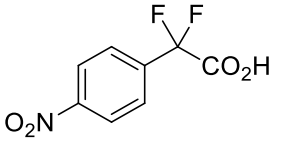
Ethyl difluoro-2-(4-nitrophenyl)acetate[2]



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 9% EtOAc in petroleum ether 30/40) to give 1.63 g (66% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 4.35 (q, J = 7.1 Hz, 2H), 7.84 (d, J = 8.8 Hz, 2H), 8.35 (d, J = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 13.9, 63.8, 112.4 (t, J = 253.4 Hz), 123.9, 127.0 (t, J = 6.1 Hz), 138.8 (t, J = 26.3 Hz), 149.6, 163.1 (t, J = 33.9 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −104.5 (s, 2F). Characterization data consistent with reported data.[2]

Difluoro(4-nitrophenyl)acetic acid (1q)

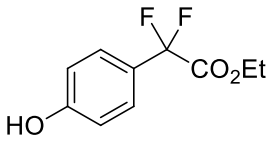


Synthesised following GP B (6.6 mmol scale), yielding 1.24 g (87% yield) of **1q** as a pale yellow solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.89 (d, J = 8.8 Hz, 2H), 8.38 (d, J = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 113.2 (t, J =

252.3 Hz), 124.6, 127.5 (t, J = 6.1 Hz), 139.1 (t, J = 25.9 Hz), 149.7, 164.6 (t, J = 32.7 Hz); **^{19}F NMR** (377 MHz, $(CD_3)_2SO$) δ −103.2 (s, 2F); **IR** (neat) ν 1755, 1525, 1348, 1291, 1262, 1153, 1122, 1106, 992, 865, 851, 706 cm^{-1}; **HRMS** (CI) calc for $C_8H_5NO_4F_2$ $[M]^+$ 217.0187, found 217.0181; **Mp** 162−164 °C.

Ethyl difluoro(4-hydroxyphenyl)acetate



Synthesised following GP A (10 mmol scale). Purified by flash column chromatography (eluent: 15% EtOAc in petroleum ether 30/40) to give 820 mg (38% yield) of the title compound as a colourless oil.

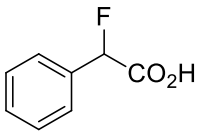
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, J = 7.1 Hz, 3H), 4.31 (q, J = 7.1 Hz, 2H), 5.60 (br. s, OH), 6.89 (d, J = 8.6 Hz), 7.49 (d, J = 8.6 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 13.9, 63.2, 113.5 (t, J = 251.8 Hz), 115.5, 125.0 (t, J = 26.2 Hz), 127.3 (t, J = 6.1 Hz), 157.9, 164.7 (t, J = 36.3 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ –102.6 (s, 2F); **IR** (neat) ν 3411, 1740, 1598, 1518, 1444, 1266, 1210, 1164, 1139, 1095, 1021, 839, 760, 646 cm^{-1}; **HRMS** (EI/FI) calc for $C_{10}H_{10}O_3F_2$ [M]+ 216.0598, found 216.0601.

2-2. Synthesis of α-onofluoroaryl acetic acids

General procedure for the synthesis of α-monofluoroaryl acetic acids (GP C)[6]:

To a solution of arylacetic acid (5.0 mmol) and TBSCl (1.73 g, 11.5 mmol) in THF (10 mL) at 0 °C was added LiHMDS (1M in THF, 11.0 mL, 11.0 mmol) slowly. The reaction was stirred overnight, during which time it was allowed to warm to room temperature, before concentrating *in vacuo*. The crude bis-silylketeneacetal was dissolved in hexane (25 mL) and the LiCl was filtered off and washed with hexane (25 mL) before evaporating the combined solution under reduced pressure. The residue was redissolved in acetonitrile (10 mL) and added to a solution of Selectfluor (2.30 g, 6.5 mmol) in acetonitrile (20 mL) at room temperature. After stirring for 15 minutes the reaction mixture was poured into a 1 M aq. HCl (50 mL) and extracted into ether (2 × 50 mL). The combined ether layers were extracted with 1 M NaOH (2 × 30 mL) and the combined basic phases were subsequently washed with ether (2 x 100 mL). The organic extracts were discarded and the aqueous phase was acidified with 6 M aq. HCl to pH 1. The acidic phase was then extracted with ether (2 × 100 mL) and the combined ether layers were dried over $MgSO_4$ and evaporated under reduced pressure to afford the corresponding α-monofluoroaryl acetic acids.

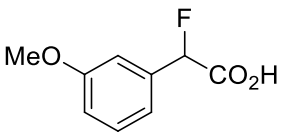
Fluoro(phenyl)acetic acid[6] (6a)



Synthesised following GP C, yielding 650 mg (84% yield) of **6a** as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (d, J = 47.5 Hz, 1H), 7.22−7.27 (m, 3H), 7.28−7.33 (m, 2H), 9.52 (br. s, 1H, COO*H*); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 88.8 (d, J = 187.0 Hz), 126.7 (d, J = 6.0 Hz), 128.9, 130.0 (d, J = 2.0 Hz), 133.4 (d, J = 20.5 Hz), 174.2 (d, J = 28.0 Hz). Characterization data consistent with reported data.[6]

Fluoro(3-methoxyphenyl)acetic acid[6] (6b)

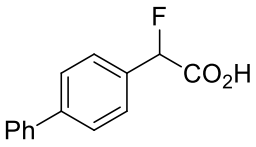


Synthesised following GP C, yielding 800 mg (87% yield) of **6b** as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 5.82 (d, J = 47.5 Hz, 1H), 6.96−7.01 (m, 1H), 7.05 (s, 1H), 7.09 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 10.8 (br. s, 1H, COO*H*); **^{13}C NMR** (100

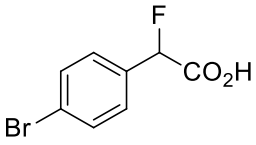
MHz, $CDCl_3$) δ 55.4, 88.7 (d, *J* = 187.0 Hz), 111.9 (d, *J* = 6.5 Hz), 115.7 (d, *J* = 2.0 Hz), 118.9 (d, *J* = 6.0 Hz), 130.0, 134.8 (d, *J* = 20.5 Hz), 159.9, 173.9 (d, *J* = 28.0 Hz). Characterization data consistent with reported data.[6]

Biphenyl-4-yl(fluoro)acetic acid (6c)



Synthesised following GP C, yielding 926 mg (80% yield) of **6c** as a pale yellow solid.
^{1}H NMR (400 MHz, CD_3CN) δ 5.74 (d, *J* = 47.5 Hz, 1H), 7.21 (m, *J* = 1.5 Hz, *J* = 7.4 Hz, 1H), 7.26−7.32 (m, 2H), 7.36 (dd, *J* = 1.5 Hz, *J* = 8.0 Hz, 2H), 7.46−7.50 (m, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 9.56 (br. s, 1H, COO*H*); **^{13}C NMR** (100 MHz, CD_3CN) δ 89.3 (d, *J* = 182.0 Hz), 127.6, 128.0, 128.1 (d, *J* = 5.5 Hz), 128.5, 129.5, 134.3 (d, *J* = 20.0 Hz), 140.5, 142.9, 169.4 (d, *J* = 28.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −177.6 (d, *J* = 47.0 Hz, 1F); **IR** (neat) ν 3029, 1757, 1687, 1180, 1047, 1008, 831, 756, 732, 694 cm^{-1}; **HRMS** (EI/FI) calc for $C_{14}H_{11}FO_2$ $[M]^+$ 230.0743, found 230.0739; **Mp** 133−134 °C.

Fluoro(4-bromo)acetic acid (6d)



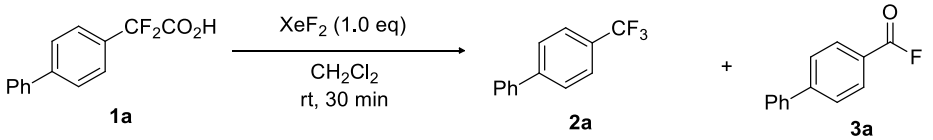
Synthesised following GP C, yielding 959 mg (82% yield) of **6d** as a pale yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (d, *J* = 47.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 9.82 (br. s, 1H, COO*H*); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 88.1 (d, *J* = 188.0 Hz), 124.3 (d, *J* = 2.5 Hz), 128.2 (d, *J* = 6.0 Hz), 132.2, 132.3 (d, *J* = 21.0 Hz), 173.6 (d, *J* = 28.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −182.3 (d, *J* = 48.0 Hz, 1F); **IR** (neat) ν 3029, 1759, 1686, 1490, 1406, 1171, 1048, 818, 745, 669 cm^{-1}; **HRMS** (ESI) calc for $C_8H_5BrFNa_2O_2$ $[M+Na]^+$ 276.9238, found 276.9247; **Mp** 84−85 °C.

2-3. Control Experiments

(a) Reaction in the presence of 1-fluoro-3-nitro-benzene

Control experiments confirmed that the decarboxylative fluorination of the model substrate **1a** did not proceed when the reaction following GP D was performed with the addition of 1-fluoro-3-nitro-benzene (1 equiv). This result suggests that 1-fluoro-3-nitro-benzene might act as a radical quencher.

(b) Decarboxylative fluorination of biphenyl-4-yl(difluoro)acetic acid with XeF_2



To a solution of XeF_2 (25.4 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL) was added biphenyl-4-yl(difluoro)acetic acid (37.2 mg, 0.15 mmol) at room temperature. The mixture was stirred for 30 min before quenching with sat. aq. $NaHCO_3$ (5.0 mL). The reaction mixture was extracted with DCM (3 ×), dried over $MgSO_4$ and concentrated *in vacuo*. Analysis of the crude mixture by ^{19}F NMR showed the formation of **2a** (−62.4 ppm as a diagnostic peak)

and **3a** (18.1 ppm as a diagnostic peak), in 23% and 11% yield respectively. The yield was determined using benzotrifluoride as an internal standard.

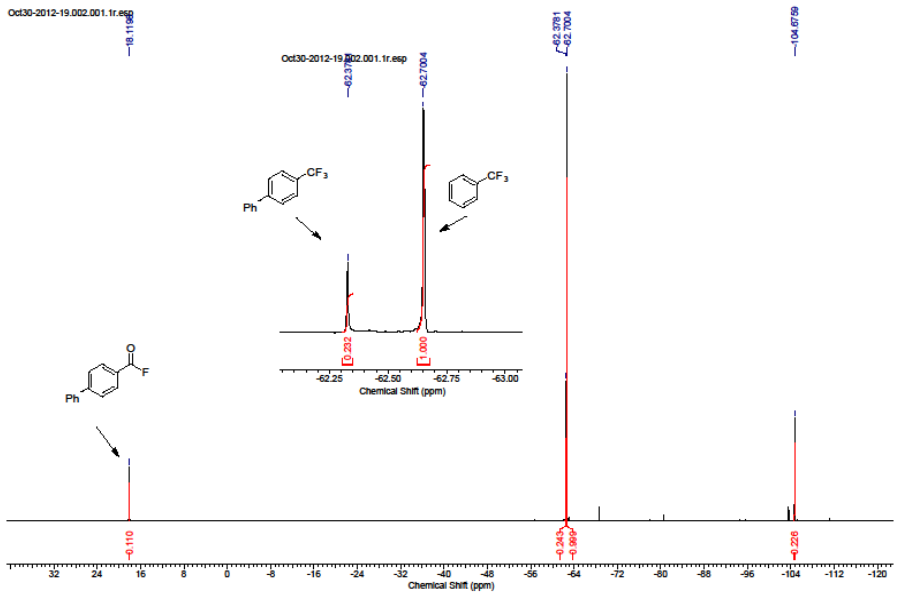
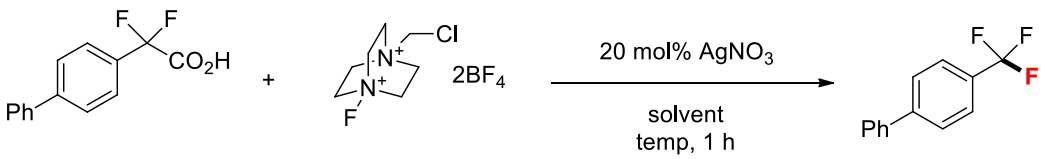


Figure 2. ^{19}F NMR spectrum.

(c) Solvent screening



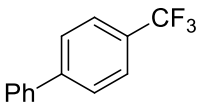
Entry	solvent	temp	con. (%)	yield (%)
1	Acetone	reflux	—	—
2	Acetone/H_2O 1 :1	55 °C	>99	> 95%
3	MeCN	55 °C	—	—
4	MeCN/H_2O 1 :1	55 °C	13	—
5	DCM	reflux	8	—
6	THF	55 °C	<1%	—

2-3. Silver-catalyzed Fluorodecarboxylation

General Procedure for the fluorodecarboxylation of di- and monofluoroaryl carboxylic acids (GP D)[7]:

To a Schlenk tube containing a magnetic stirrer bar was added the carboxylic acid (49.6 mg, 0.2 mmol, 1.0 equiv), Selectfluor (141.7 mg, 0.4 mmol, 2.0 equiv) and silver nitrate (13.6 mg, 0.08 mmol, 20 mol%). The Schlenk tube was closed with a rubber septum and equipped with a nitrogen balloon, and the system was purged with nitrogen. Acetone (2 mL) and water (2 mL) were added and the reaction was stirred at 55 °C for 1 h, before diluting with water. The reaction mixture was extracted with DCM (3 × 5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Crude ^{19}F NMR yields were determined by comparing the integration of the product peak with the integration of 1.0 equiv (0.2 mmol, 21 μL) 1-fluoro-3-nitrobenzene which was added to the reaction after workup as the internal standard. The crude mixture was purified by flash column chromatography using the indicated solvent system.

4-(Trifluoromethyl)biphenyl[8] (2a)

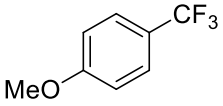


Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 38 mg (85 % yield) of **2a** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, *J* = 7.5 Hz, 2.0 Hz, 1H), 7.36−7.40 (m, 2H), 7.49−7.52 (m, 2H), 7.60 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 124.4 (q, *J* = 273.0 Hz), 125.7 (q, *J* = 4.0 Hz), 127.3, 127.4, 128.2, 129.0, 129.4 (q, *J* = 32.0 Hz), 139.8, 144.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.4 (s, 3F). Characterization data consistent with reported data.[8]

*The reaction performed on a 2 mmol scale afforded **2a** in 86% yield.

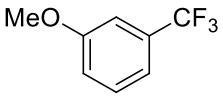
1-Methoxy-4-(trifluoromethyl)benzene[9] (2b)



Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 29 mg (82% yield) of the product as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 6.88 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 54.4, 112.9, 123.4 (q. *J* = 270.0 Hz), 121.8 (q, *J* = 33.0 Hz), 125.8 (q, *J* = 4.0 Hz), 161.0; **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ −61.5 (s, 3F). Characterization data consistent with reported data.[9]

1-Methoxy-3-(trifluoromethyl)benzene[9] (2c)

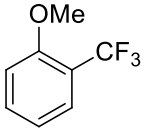


Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40 to 10% Et_2O in petroleum ether) to give 30 mg (86% yield) of **2c** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 6.99 (d, *J* = 8.0 Hz, 1H), 7.05 (br. s, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 55.4, 110.6 (q, *J* = 4.0 Hz), 117.4 (q, *J* = 4.0 Hz), 117.6, 124.0 (q, *J* = 272.5 Hz), 129.9, 131.8 (q, *J* = 33.0 Hz), 159.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.7 (s, 3F). Characterization data consistent with reported data.[9]

*The reaction performed on a 2 mmol scale afforded **2c** in 85% yield.

1-Methoxy-2-(trifluoromethyl)benzene[10] (2d)



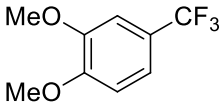
Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40 to 10% Et_2O in petroleum ether) to give 31 mg (88% yield) of **2d** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 3H), 6.82-6.86 (m, 2H), 7.33 (t, *J* =

8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 55.7, 111.9, 118.7 (q, J = 31.0 Hz), 120.0, 123.9 (q, J = 272.0 Hz), 127.0 (q, J = 5.5 Hz), 133.4, 157.5 (q, J = 1.5 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.4 (s, 3F). Characterization data consistent with reported data.[10]

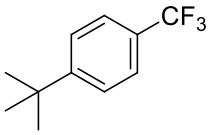
*The reaction performed on a 2 mmol scale afforded **2d** in 85% yield.

1-Methoxy-2-(trifluoromethyl)benzene (2e)



The reaction following GP D gave a complex reaction mixture.

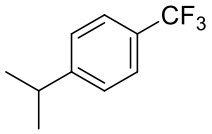
1-*tert*-Butyl-4-(trifluoromethyl)benzene[9] (2f)



Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 31 mg (77% yield) of **2f** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 9H), 7.41 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 31.1, 35.0, 124.4 (q, J = 272.0 Hz), 125.0 (q, J = 3.5 Hz), 125.6, 127.7 (q, J = 32.5 Hz), 155.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.30 (s). Characterization data consistent with reported data.[9]

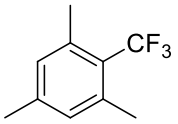
1-Isopropyl-4-(trifluoromethyl)benzene (2g)



Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 25 mg (66%) of the product as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.20 (s, 3H), 2.89 (sept, J = 7.0 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 23.7, 34.1, 124.4 (q, J = 271.0 Hz), 125.3 (q, J = 3.5 Hz), 126.7, 128.2, 152.9; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.3 (s, 3F); **IR** (neat) ν 2923, 2361, 2341, 1261, 1019, 800, 669 cm^{-1}; **HRMS** (CI) calc for $C_{10}H_{11}F_3$ $[M]^+$ 188.0813, found 188.0817.

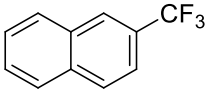
1,2,4-Trimethyl-5-(trifluoromethyl)benzene[8] (2h)



Synthesised following GP D. Purified by flash column chromatography (eluent: 5% Et_2O in n-hexane) to give 21 mg (56% yield) of **2h** as a yellow oil. (Note: 93% NMR yield. **2h** is very volatile.)

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.36 (q, J = 3.5 Hz, 6H), 6.82 (s, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 20.6, 21.1 (q, J = 4.0 Hz), 124.6 (q, J = 28.5 Hz), 126.0 (q, J = 276.0 Hz), 130.7, 137.1 (q, J = 2.0 Hz), 140.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −53.7 (sept, J = 3.5 Hz, 3F). Characterization data consistent with reported data.[8]

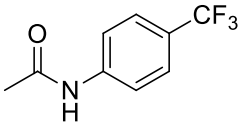
2-(Trifluoromethyl)naphthalene[9] (2i)



Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 20 mg (51% yield) of **2i** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.58 (m, 3H), 7.81−7.88 (m, 3H), 8.07 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 121.4 (q, J = 3.0 Hz), 124.4 (q, J = 270.0 H), 125.7 (q, J = 4.5 Hz), 127.2, 127.8 (q, J = 27.0 Hz), 127.9, 128.0, 128.8, 129.0, 132.2, 134.6; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.2 (s, 3F). Characterization data consistent with reported data.[9]

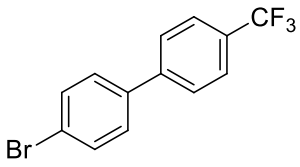
***N*-[4-(Trifluoromethyl)phenyl]acetamide[10] (2j)**



Synthesised following GP D. Purified by flash column chromatography (eluent: 30% to 50% EtOAc in petroleum ether 30/40) to give 35 mg (86 %) of **2j** as an off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (s, 3H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 24.7, 119.3, 124.1 (q, *J* = 271.5 Hz), 126.0 (q, *J* = 33.0 Hz), 226.3 (q, *J* = 4.0 Hz), 140.9, 168.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.1 (s, 3F). Characterization data consistent with reported data.[10]

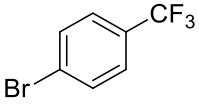
4-Bromo-4'-(trifluoromethyl)biphenyl[8] (2k)



Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 50 mg (83% yield) of **2k** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dt, *J* = 8.5 Hz, 2.0 Hz, 2H), 7.51 (dt, J = 8.5 Hz, 2.0 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 122.6, 124.2 (q, *J* = 272.5 Hz), 125.9 (q, *J* = 4.0 Hz), 127.2, 128.8, 129.7 (q, *J* = 32.0 Hz), 132.2, 138.7, 143.5; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.5 (s, 3F). Characterization data consistent with reported data.[8]

1-Bromo-4-(trifluoromethyl)benzene[11] (2l)

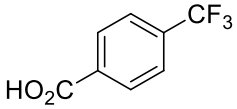


Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 15 mg (33% yield) of **2l** as a white solid.

The reaction with 4.0 eq. Selectfluor and in the mixture of H_2O/acetone 1:4 following GP D gave **2l** in 49% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 123.8 (q, *J* = 272.5 Hz), 125.9 (q, *J* = 4.0 Hz), 126.4, 129.5 (q, *J* = 33.5 Hz), 131.1; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −62.7 (s). Characterization data consistent with reported data.[11]

4-(Trifluoromethyl)benzoic acid (2n)



Synthesised following GP D. Purified by flash column chromatography to give 7 mg (18% yield) of **2n** as a white solid.

Analysis of the crude mixture with ^{19}F NMR showed the formation of **2n** (−63.6 ppm as a diagnostic peak) in 49% yield. The yield was determined using 1-fluoro-3-nitrobenzene as an internal standard.

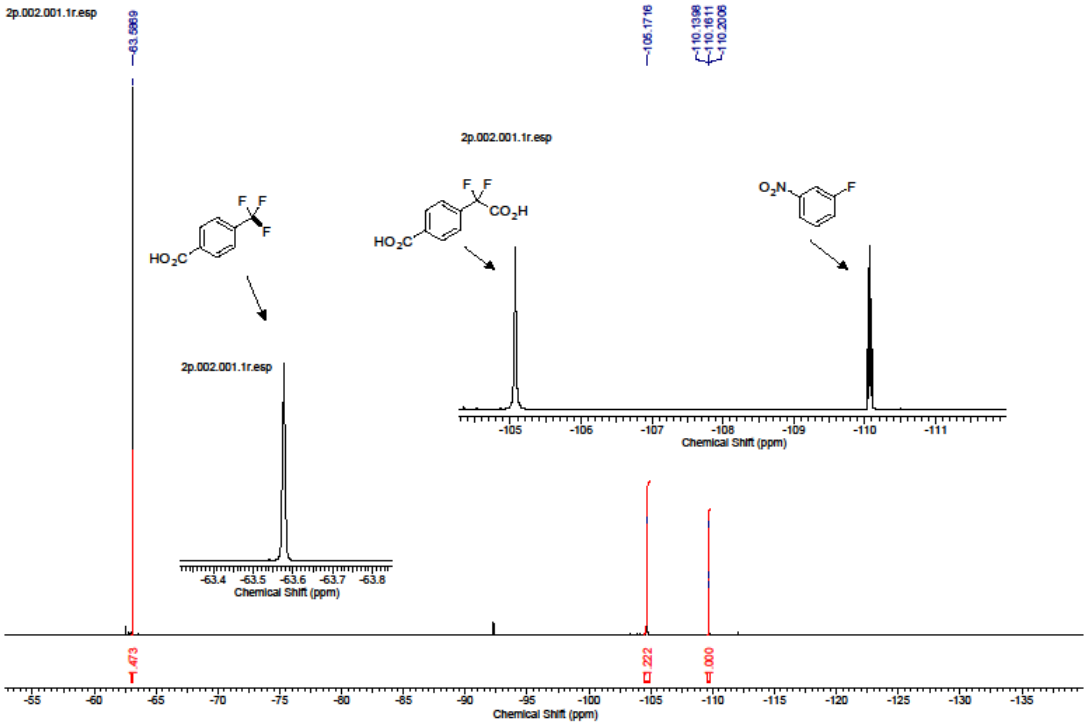
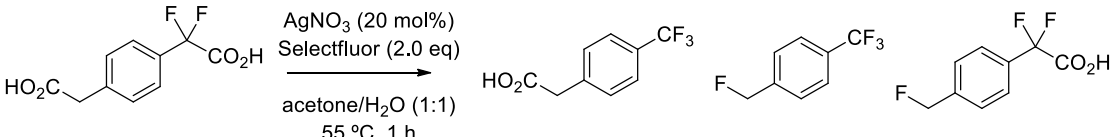


Figure 3. ^{19}F NMR spectrum.

2-[4-(Trifluoromethyl)phenyl]acetic acid (2o)



1o

2o 17%

4o 24%

5o 2%

1o was recovered in 57% yield.

Synthesised following GP D. Analysis of the crude mixture with ^{19}F NMR showed the formation of **2o** (−63.0 ppm as a diagnostic peak) in 17% yield along with the formation of side-products **4o** (−63.0 and −212.1 ppm as diagnostic peaks) and **5o** (−213.6 ppm as a diagnostic peak) in 24% and 2% yield, respectively. The yield was determined using 1-fluoro-3-nitrobenzene as an internal standard.

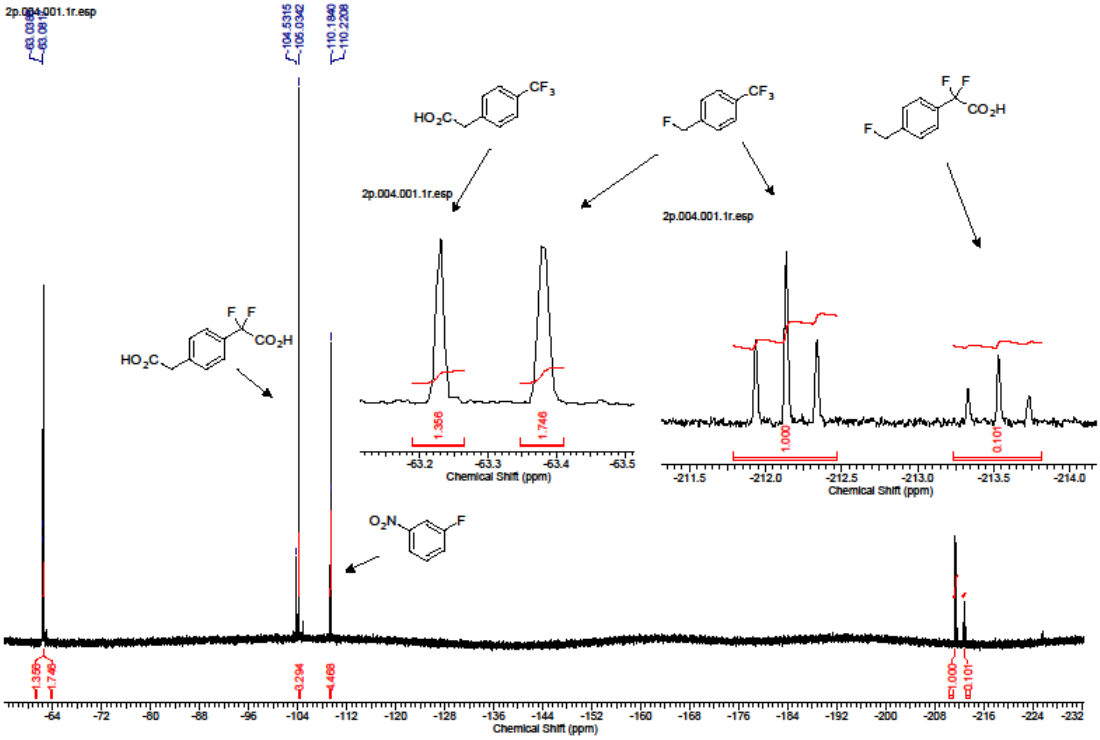
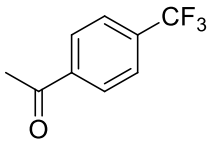


Figure 4. ^{19}F NMR spectrum.

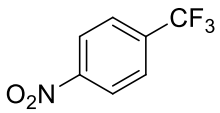
1-[4-(Trifluoromethyl)phenyl]ethanone[12] (2p)



Synthesised following GP D. Purified by flash column chromatography (eluent: 5% Et_2O in *n*-hexane) to give 8 mg (21% yield) of **2p** as a white solid.

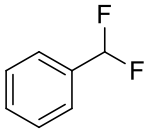
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (s, 3H), 7.73 (d, J = 7.5 Hz, 2H), 8.08 (d, J = 7.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 26.8, 123.6 (q, J = 271.6 Hz), 125.7 (q, J = 4.0 Hz), 128.6, 134.4 (q, J = 32.3 Hz), 139.6, 197.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ −63.1 (s, 3F). Characterization data consistent with reported data.[12]

1-nitro-4-(trifluoromethyl)benzene (2q)



The reaction of **1q** under standard conditions (GP D) did not proceed.

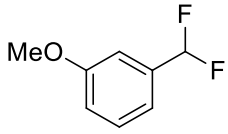
(Difluoromethyl)benzene[11] (7a)



Synthesised following GP D, to give **7a** in 72% yield by ^{19}F NMR. The compound was not isolated due to its high volatility.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (t, J = 56.6 Hz, 1H), 7.35–7.44 (m, 5H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ –110.9 (d, J = 56.5 Hz). Characterization data consistent with reported data.[11]

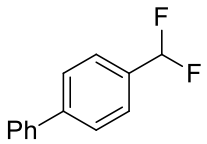
1-(Difluoromethyl)-3-methoxybenzene[13] (7b)



Synthesised following GP D. Purified by flash column chromatography (eluent: 5% Et_2O in petroleum ether 30/40) to give 26 mg (83% yield) of **7b** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 6.53 (t, *J* = 56.5 Hz, 1H), 6.91–6.94 (m, 1H), 6.96 (s, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 55.4, 110.6 (t, *J* = 6.0 Hz), 114.6 (t, *J* = 236.0 Hz), 116.6 (t, *J* = 2.0 Hz), 117.8 (t, *J* = 6.0 Hz), 129.9, 135.7 (t, *J* = 22.0 Hz), 159.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –110.6 (d, *J* = 56.5 Hz). Characterization data consistent with reported data.[13]

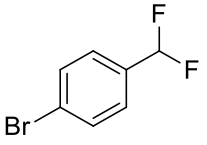
4-(Difluoromethyl)biphenyl[14] (7c)



Synthesised following GP D. Purified by flash column chromatography (eluent: 5% Et_2O in petroleum ether 30/40) to give 37 mg (91% yield) of **7c** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (t, *J* = 56.5 Hz, 1H), 7.29–7.33 (m, 1H), 7.35–7.40 (m, 2H), 7.48–7.52 (m, 4H), 7.59 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 114.8 (t, *J* = 238.5 Hz), 126.1 (t, *J* = 6.0 Hz), 127.3, 127.5, 127.8, 128.9, 133.2 (t, *J* = 22.5 Hz), 140.2, 143.7 (t, *J* = 2.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ –110.3 (d, *J* = 56.5 Hz). Characterization data consistent with reported data.[14]

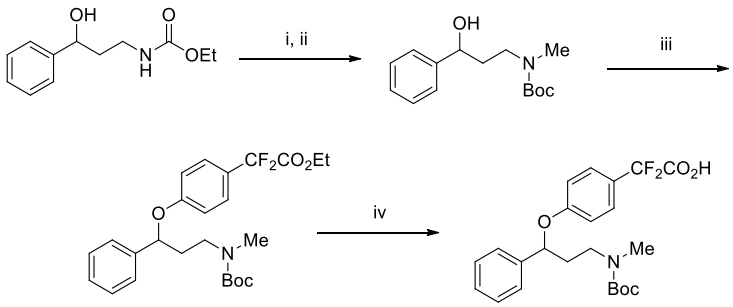
1-Bromo-4-(difluoromethyl)benzene[2] (7d)



Synthesised following GP D. Purified by flash column chromatography (eluent: petroleum ether 30/40) to give 34 mg (82% yield) of the product as a white solid.

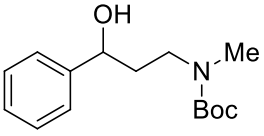
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (t, *J* = 56.0 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 114.1 (t, *J* = 239.0 Hz), 125.1 (t, *J* = 2.5 Hz), 127.2 (t, *J* = 6.0 Hz), 132.0, 133.3 (t, *J* = 23.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ –111.06 (d, *J* = 56.0 Hz). Characterization data consistent with reported data.[2]

2-5. Synthesis of Fluoxetine: *N*-Methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine trifluoroacetic acid salt (2m)



Reagents (i) LAH, THF; (ii) Boc_2O, Et_3N, MeOH; (iii) ethyl difluoro(4-hydroxyphenyl)acetate, DIAD, PPh_3, diethyl ether; (iv) K_2CO_3, MeOH.

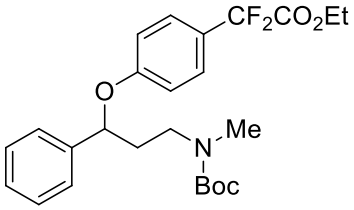
***tert*-Butyl (3-hydroxy-3-phenylpropyl)methylcarbamate**



To a solution of $LiAlH_4$ (112 mg, 3.0 mmol) in dry THF (5.0 mL) under N_2 at room temperature was added a solution of *N*-(ethoxycarbonyl)-3-amino-1-phenyl-1-propanol[15] (300 mg, 1.3 mmol) in dry THF (10.0 mL) dropwise, the mixture was heated under reflux and stirred for 1 h. After completion of the reaction mixture was cooled to room temperature and ethyl acetate (1.0 mL) was slowly added. The resultant reaction mixture was filtered, and then the residue was treated with ethyl acetate and filtered three times. The filtrates were combined and evaporated under reduced

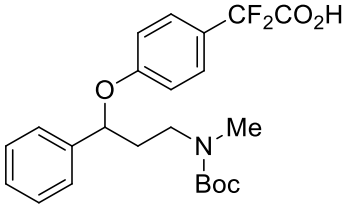
pressure. The residue was added to a 50 mL three-necked flask, to which was added 10 mL of MeOH, di-*tert*-butyl carbonate (308 µL, 1.3 mmol) and Et_3N (37 µL, 0.13 mmol). The mixture was heated under reflux and stirred for 6 h. After completion of the reaction as indicated by the TLC, the reaction mixture was cooled to room temperature. The solvent was evaporated and the residue was purified by flash column chromatography on silica gel (eluent: 30% EtOAc in *n*-hexane) to afford *tert*-butyl (3-hydroxy-3-phenylpropyl)methylcarbamate (113 mg, 32% yield) as a pale yellow oil.
^{1}H NMR (200 MHz, $CDCl_3$) δ 1.48 (s, 9H), 1.69–2.05 (m, 2H), 2.89 (s, 3H), 3.00–3.16 (m, 1H), 3.68–4.03 (m, 1H), 4.62 (dd, J_1 = 3.2 Hz, J_2 = 9.6 Hz, 1H), 7.28–7.41 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 28.4, 34.3, 37.2, 45.1, 69.9, 80.1, 125. 6, 127.0, 128.3, 144.1, 157.2; **IR** (neat) ν 3419, 2976, 1667, 1482, 1452, 1394, 1366, 1248, 1166, 1061, 880, 670 cm^{-1}; **HRMS** (ESI) calc for $C_{15}H_{23}N_2NaO_3$ $[M+Na]^+$ 288.1566, found 288.1570.

Ethyl (4-{3-[(*tert*-butoxycarbonyl)(methyl)amino]-1-phenylpropoxy}phenyl) (difluoro)acetate



The title compound was prepared according to literature procedures:[15] Diisopropyl azodicarboxylate (44.5 µL, 0.23 mmol) in dry ether (0.1 mL) was slowly added to a solution of triphenyl phosphine (59.3 mg, 0.23 mmol) in dry ether (0.6 mL) at 0 °C, after 20 min at 0 °C ethyl difluoro(4-hydroxyphenyl)acetate (38.9 mg, 0.18 mmol) taken in dry ether (0.2 mL) was added. To this resultant mixture was added *tert*-butyl (3-hydroxy-3-phenylpropyl)methylcarbamate (40.0 mg, 0.15 mmol) in dry ether (0.5 mL) and allowed to warm to room temperature . After completion of the reaction as indicated the TLC (1 hr), the solvent was evaporated and the residue was purified by flash column chromatography on silica gel (eluent: 15% EtOAc in *n*-hexane) to afford the title compound (34.6 mg, 50% yield) as colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J = 7.1 Hz, 3H), 1.38 (br. s, 9H), 2.03–2.23 (m, 2H), 2.85 (s, 3H), 3.27–3.53 (m, 2H), 4.26 (q, J = 7.1 Hz, 2H), 5.15 (dd, J_1 = 3.7 Hz, J_2 = 8.6 Hz, 1H), 6.87 (d, J = 9.0 Hz, 2H), 7.29–7.35 (m, 5H), 7.42 (d, J = 9.0 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 13.9, 28.3, 34.5, 37.2, 45.7, 62.9, 78.2, 79.4, 113.4 (t, J = 250.2 Hz), 115.7, 124.9 (t, J = 26.5 Hz), 125.6, 126.9 (t, J = 5.7 Hz), 127.8, 128.8, 141.0, 155.7, 160.0, 164.4 (t, J = 36.0 Hz); **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ –102.5 (s, 2F); **IR** (neat) ν 2978, 1764, 1691, 1611, 1512, 1454, 1393, 1366, 1245, 1175, 1142, 1098, 1024, 987 cm^{-1}; **HRMS** (ESI) calc for $C_{25}H_{31}F_2NNaO_5$ $[M+Na]^+$ 486.2055, found 486.2063.

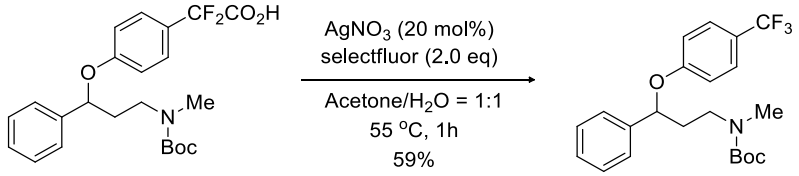
(4-{3-[(tert-Butoxycarbonyl)(methyl)amino]-1-phenylpropoxy}phenyl)(difluoro)acetic acid (1m)



In a 50 mL round bottom flask, ethyl (4-{3-[(tertbutoxycarbonyl)(methyl)amino]-1-phenylpropoxy}phenyl) (difluoro)acetate (80.0 mg, 0.17 mmol) was added to a mixture of MeOH (0.5 mL) and 1M K_2CO_3 aq. (0.5 mL, 0.51 mmol) and stirred for 2 hrs at room temperature. The reaction was then poured into 0.5M HCl to acidify to pH 1, extracted with EtOAc, washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give **1m** (57.0 mg, 77% yield) as a white solid.
^{1}H NMR (500 MHz, toluene-d_8, 367K) δ 1.29 (s, 9H), 1.88–1.99 (m, 1H), 2.07–2.09 (m, 1H), 2.56 (s, 3H), 3.15–3.30 (m, 2H), 5.09 (dd, J_1 = 3.8 Hz, J_2 = 7.9 Hz, 1H), 6.77 (d, J = 8.5 Hz,2 H), 7.06–7.10 (m, 3H), 7.20 (d, J = 7.3 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 8.45 (br. s, CO_2H); **^{13}C NMR** (125 MHz, toluene-d_8, 367K) δ 28.6, 34.5, 37.3, 46.3, 78.7, 80.5, 116.53, 126.3, 127.7 (t, J = 5.5 Hz), 129.1, 141.8, 156.7, 160.8, 165.6 (t, J = 34.7 Hz).

(Note: The CF_2 carbon was not observed); **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ –103.5 (m, 2F); **IR** (neat) ν 2930, 1760, 1612, 1152, 1243, 1368, 1243, 1176, 1106, 989, 835, 757, 735, 701 cm^{-1}; **HRMS** (ESI) calc for $C_{23}H_{27}F_2NNaO_5$ $[M+Na]^+$ 458.1729, found 458.1750; Mp 32 °C.

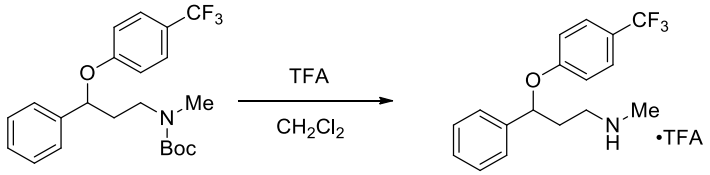
***tert*-Butyl methyl{3-phenyl-3-[4-(trifluoromethyl)phenoxy]propyl}carbamate**



Synthesised following GP D (0.06 mmol scale), yielding 13.2 mg (59% yield) of the title compound as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): (both rotamers) δ 1.38 (br. s, 9H), 2.05–2.24 (m, 2H), 2.86 (s, 3H), 3.30–3.53 (m, 2H), 5.17 (dd, J_1 = 3.6 Hz, J_2 = 8.3 Hz, 1H), 6.89 (d, J = 8.3 Hz, 2H), 7.28–7.37 (m, 5H), 7.43 (d, J = 8.3 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): (both rotamers) δ 27.7, 28.4, 34.6, 36.2, 36.6, 37.2, 45.2, 47.2, 79.4, 82.9, 118.2, 118.4, 125.7, 125.9, 127.7, 127.8, 128.6, 128.8, 138.0, 138.1, 141.0, 141.2, 153.3, 155.7, 157.8, 158.0. (Note: The CF_3 carbon was observed); **^{19}F NMR** (376.5 MHz, $CDCl_3$): (both rotamers) δ –61.6 (s, 3F); **IR** (neat) ν 2930, 2360, 1693, 1324, 1249, 1159, 1111, 1068, 1050, 1010, 835, 760, 701 cm^{-1}; **HRMS** (ESI) calc for $C_{22}H_{26}F_3NNaO_3$ $[M+Na]^+$ 432.1756, found 458.1757.

***N*-Methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine trifluoroacetic acid salt (2m)**



To a solution of *tert*-butyl methyl{3-phenyl-3-[4-(trifluoromethyl)phenoxy]propyl}carbamate (120 mg, 0.29 mmol) in dichloromethane (250 µL) was added 250 µL of TFA at room temperature, and then the mixture was stirred for 1 hr. The excess TFA was evaporated and the residue was dried in *vacuo* to give title compound (122.0 mg, quant.) as a colourless oil.

^{1}H NMR (250 MHz, $CDCl_3$) δ 2.19–2.46 (m, 2H), 2.63(s, 3H), 3.08–3.26 (m, 2H), 5.32 (dd, J_1 = 4.3 Hz, J_2 = 8.2 Hz, 1H), 6.87 (d, J = 8.8 Hz, 2H), 7.25–7.37 (m, 5H), 7.42 (d, J = 8.8 Hz, 2H), 9.22 (br, s, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 33.1, 34.6, 46.3, 77.1, 115.7, 123.3 (q, J = 32.2 Hz), 124.2 (q, J = 269.1 Hz), 125.5, 126.8 (q, J = 3.8 Hz), 128.4, 129.1, 139.0, 159.6, 161.7 (q, J = 30.3 Hz): (Note: The CF_3 carbon of TFA was not observed); **^{19}F NMR** (377 MHz, $CDCl_3$) δ –75.8 (s, 3F), –61.7 (s, 3F); **IR** (neat) ν 2821, 1670, 1614, 1517, 1325, 1245, 1109, 1067, 835, 722, 701 cm^{-1}; **HRMS** (ESI) calc for $C_{17}H_{19}F_3NO$ $[M+H]^+$ 310.1405, found 310.1413.

3. Fluorine gas experiments

General procedure for fluorine-promoted fluorodecarboxylation:

The substrate (0.5 mmol) and $AgNO_3$ (17 mg, 0.1 mmol) were dissolved in MeCN (5 mL) and placed in a PTFE reaction vessel fitted with a stirrer bar. The reaction vessel was connected to a gas inlet and outlet fitted to the elemental fluorine apparatus which allows for safe introduction of F_2. The reaction vessel was cooled to the appropriate temperature using an ice bath or an acetone/dry ice bath and the system was purged with nitrogen gas for 10 minutes before allowing 10 % fluorine gas in nitrogen (v/v) to flow through the system at a constant rate set by a mass flow control apparatus (15 mL/min). The reaction was rapidly stirred under these conditions for the time calculated to correspond to a known amount of F_2. Afterwards, the system was again purged with nitrogen gas for 10 minutes and warmed to room temperature. The reaction mixture was concentrated under reduced pressure and the residue was redissolved in CD_3CN and 1-fluoro-3-nitrobenzene (0.5 mmol, 1 equiv) was added as an internal reference to calculate ^{19}F NMR yields.

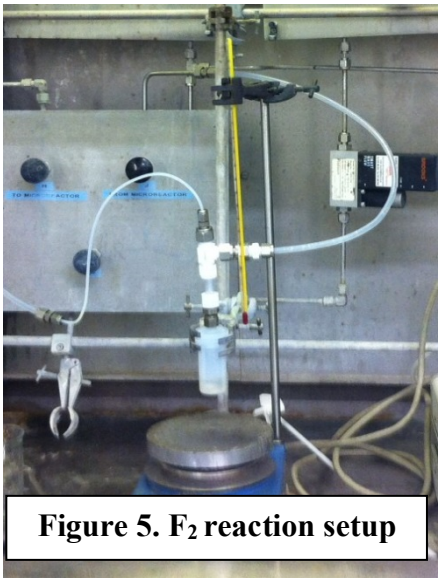
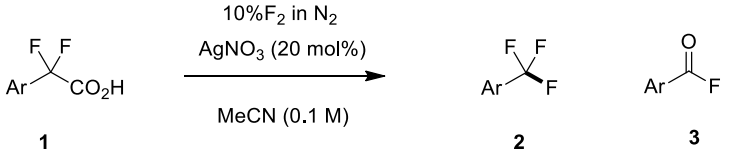
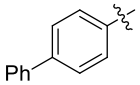
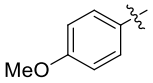
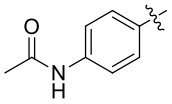
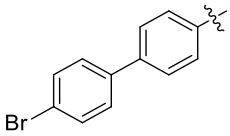
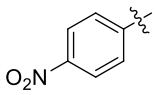


Figure 5. F_2 reaction setup

Table 1. Fluorodacarboxylation of α,α-difluoroaryl acetic acid



Entry	Substrate	F_2 (eq.)	Temp. (°C)	Yield of **2** (%)[a]	Comments[b]
1	 **1a**	3	−35	17	**1a** (60%), multiple peaks
2		3	−10	10	**1a** (54%), multiple peaks
3		5	−35	36	**1a** (55%), multiple peaks
4	 **1b**	2	−35	2	**1b** (36%), −126 ppm (29%), −133 ppm (14%)
5[c]		2	−35	0	**1b** (45%), −126 ppm (14%), −133 ppm (40%)
6	 **1j**	2	−35	0	**1j** (45%), −127 ppm (20%), multiple peaks
7		2	0	0	**1j** (65%), −127 ppm (24%), multiple peaks
8		5	−35	0	multiple peaks
9	 **1k**	3	rt	13	**1k** (60%), multiple peaks
10		6	rt	14	**1k** (5%), multiple peaks
11[d]		6	rt	18	multiple peaks
12	 **1q**	2	−35	13	**1q** (38%), **3q** (25%), multiple peaks
13		3	−35	15	**1q** (14%), **3q** (10%), multiple peaks
14		3	−10	24	**3q** (23%), multiple peaks

[a] ^{19}F NMR yield using 1-fluoro-3-nitrobenzene as internal reference. [b] Detected peaks in ^{19}F NMR analysis, the value in parentheses is the ^{19}F NMR yield for the reaction. [c] The reaction in MeCN (0.05 M) was carried out. [d] 40 mol% of $AgNO_3$ was used.

4. Radiochemistry

***General protocols for synthesis of [^{18}F]fluorine*:**

[^{18}F]F^- was obtained in the nuclear reaction $^{18}O(p,n)^{18}F$ by irradiating oxygen-18 enriched water (2.2 mL) for 5 minutes with a 17 MeV proton beam of 35 μA produced with a CC-18/9 cyclotron (Efremov Institute of Electrophysical Apparatuses, St Petersburg, Russia).

At the end of bombardment, the $[^{18}F]F^-$ was solubilised in a potassium carbonate/acetonitrile aqueous solution and transferred into the reaction vessel in the hot cell, followed by the standard azeotropic drying procedure using $Kryptofix_{222}$ and acetonitrile. $[^{18}F]F_2$ gas was prepared following the post-target synthesis described by Bergman and Solin.[16]

***Measurement of Radiochemical Yield*:**
Radiochemical yield and radiochemical purity were determined by radio-HPLC. High performance liquid chromatography (HPLC) was performed on a Spectra SYSTEM P2000 with a Spectra SYSTEM UV2000 detector and a Bioscan flow-count radioactivity detector in series, or a VWR-Hitachi L-2130 HPLC pump (VWR Hitachi, VWR International GmbH, Darmstadt, Germany) combined with a VWR- Hitachi L-2400 UV-absorption detector (λ=254 or 280 nm) and a 2 x 2 inch NaI-crystal for radioactivity detection. HPLC studies of all reactions were performed using a reverse phase analytical column (Waters Atlantis dC18 Column, 5 µm, 150 mm x 3.9 mm). Elution was performed at a gradient of MeCN/H_2O (gradient: 5:95 to 80:20 % 15 min) with a flow rate of 1 mL/min.

***Measurement of specific activity*:**
Determination of the specific activities for $[^{18}F]$**1a**, $[^{18}F]$**1j** and $[^{18}F]$**6a** was carried out by HPLC. The fraction corresponding to the $[^{18}F]$product was collected and its activity was measured. The mass of the $[^{18}F]$product in the collected fraction was calculated by comparing HPLC retention times and peak intensities to the $[^{19}F]$reference compound of known concentration. The specific activities were decay corrected to the E.O.S of $[^{18}F]$Selectfluor *bis*(triflate).
Decay corrected values for specific activities of $[^{18}F]F_2$, $[^{18}F]$Selectfluor and compounds radiolabeled with these are:

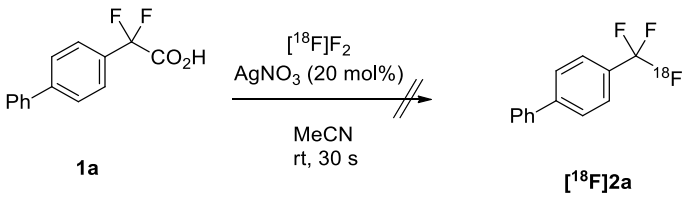
$$\mathbf{m}F_2 + \mathbf{n}[^{18}F]CH_3F \xrightarrow[\mathbf{m} >> \mathbf{n}]{h\nu} (\mathbf{m-3n})[^{18}F]F_2 + \mathbf{n}[^{18}F]CF_4 + \mathbf{3n}[^{18}F]HF$$

$SA_{[18F]F2} = k*A_{[18F]CH3F} / M_{F2}$ [GBq/µmol]
$SA_{[18F]CH3F} > 5$ TBq /µmol
$M_{F2} = 1.1 \pm 0.1$µmol
$0.3 < k < 0.6$
$SA_{[18F]SF} = 0.5* SA_{F2}$
SA compound = $0.5* SA_{F2}$
SA compound = $SA_{[18F]SF}$

Table 2. Amount of $[^{18}F]CH_3F$ used in production of $[^{18}F]F_2$ and subsequently in synthesis of $[^{18}F]$Selectfluor for labelling of compounds, resulting in measured SA

Compound	A$[^{18}F]CH_3F$ [GBq]	SA of compound [GBq/µmol]
$[^{18}F]$**2a**	–	3.54
	–	3.20
	–	3.22
$[^{18}F]$**2j**	3.22	0.442
	1.83	0.298
	1.83	0.297
$[^{18}F]$**7a**	12.8	2.19
	12.8	2.54
	12.8	2.65

4-1. Reaction with $[^{18}F]F_2$



1a **[^{18}F]2a**

$[^{18}F]F_2$ was bubbled into a Wheaton vial containing **1a** (0.5 µmol) and silver nitrate (0.1 µmol) in dry MeCN (500 µL) for 30 seconds at room temperature, before the reaction mixture was analysed by HPLC. In this reaction no desired product was observed at 17.4 minutes. A complex group of radioactive peaks (bottom chromatogram) were observed from 5.0 to 9.3 minutes corresponding to the expected retention time of the carboxylic acid starting material as seen in the top UV chromatogram. Hence, it is believed that the labelling reaction lead to unspecific $[^{18}F]$fluorination on the aromatic moiety of the starting material.

Chromatogram of Radio-HPLC trace

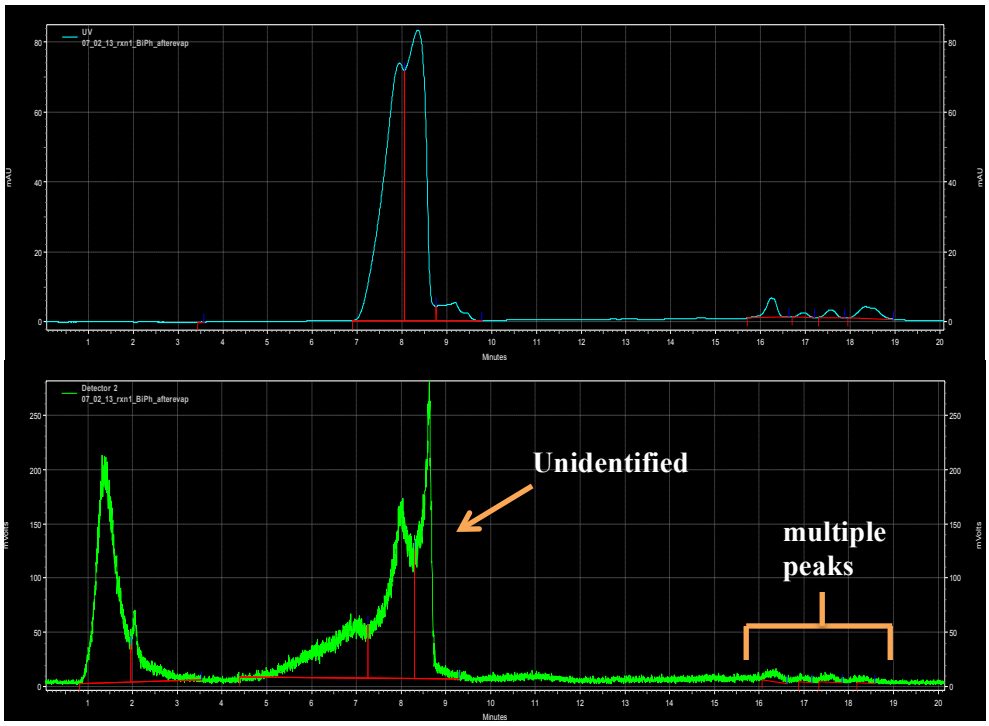
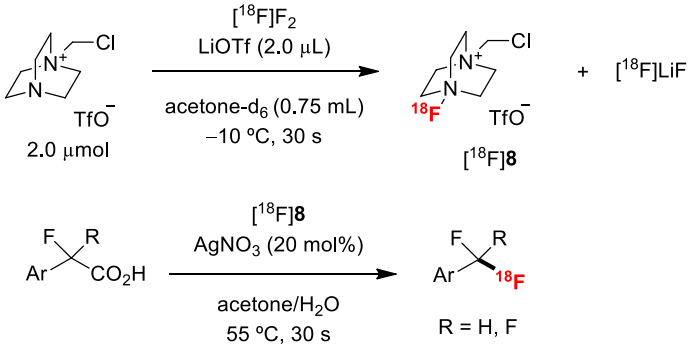
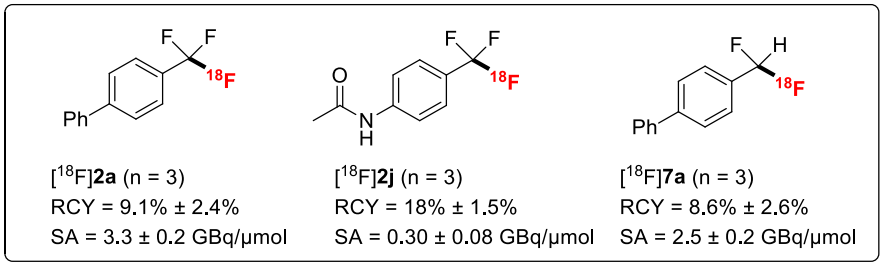


Figure 6. Top: UV HPLC chromatogram, side-product retention time = 8.0 to 9.2 min (starting material also included in this group of peaks). Bottom: Radio-HPLC chromatogram, side-product retention time = 5.0 to 9.3 min.

4-2. Reactions using [^{18}F]Selectfluor *bis*(triflate)





[^{18}F]Selectfluor *bis*(triflate) [^{18}F]**8** was prepared as described previously.[17] The [^{18}F]F_2 gas was bubbled into a vial containing a mixture of 1-chloromethyl-4-aza-1-azoniabicyclo[2.2.2]octane triflate (2 μmol (0.003 M)) and lithium triflate (1 equiv) in acetone-d_6 (0.75 mL) at room temperature for ~ 30 seconds. Aliquots (220 μL) of this crude stock solution were used directly in labelling reactions.

A stock solution of the precurosr (10 μmol) and silver nitrate (2 μmol) in water (10 mL) was prepared. An aliquot (100 μL) was added to a Wheaton vial and [^{18}F]**8** (220 μL) was added. At 55 ^{o}C the reaction volume was concentrated to ~ 15 μL under a flow of helium and the reaction stirred at this temperature for 30 minutes in total. The reaction mixture was analysed by radio-HPLC and radio-TLC.

Chromatogram of radio-HPLC trace of [^{18}F]2a

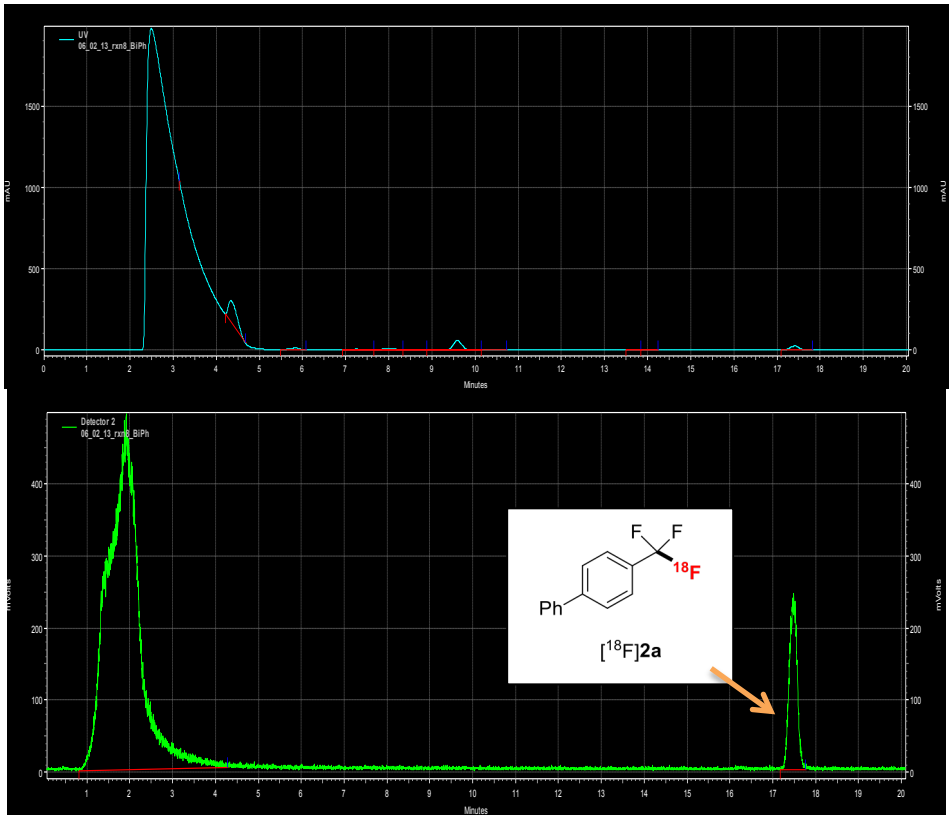
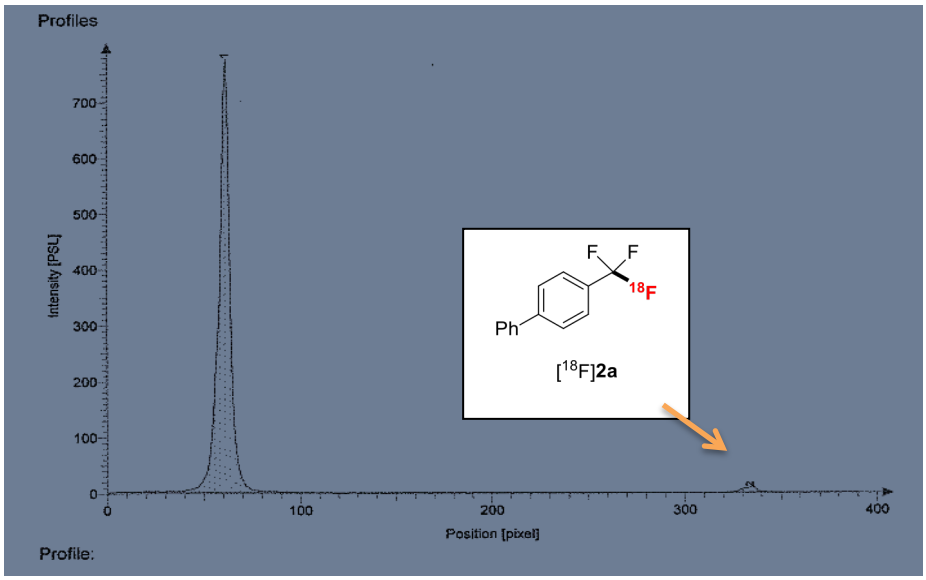


Figure 7. Top: UV HPLC chromatogram, product retention time = 17.4 min. Starting material retention time = 9.6 min. Bottom: Radio-HPLC chromatogram, product retention time = 17.49 min.

Example of radio-TLC scan of [^{18}F]2a



Chromatogram of radio-HPLC trace of [^{18}F]2j

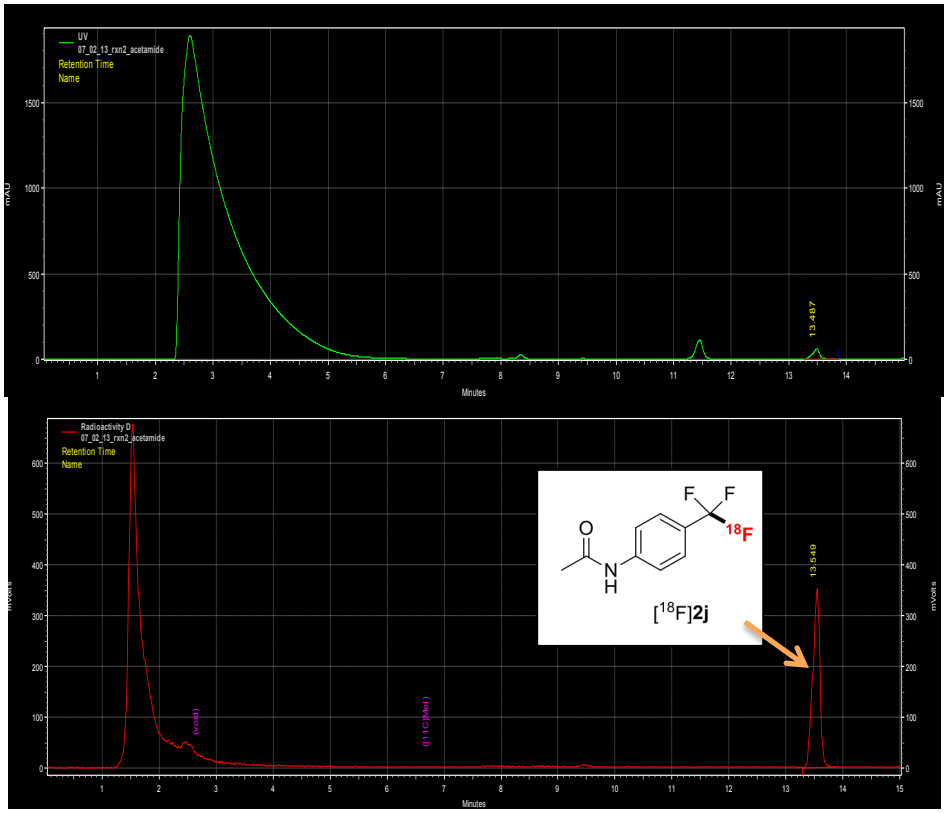
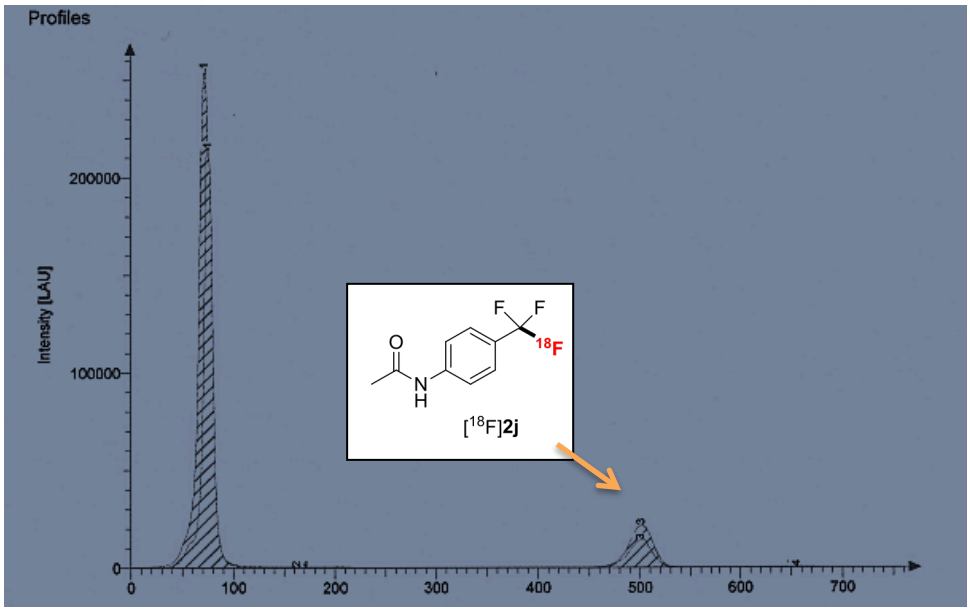


Figure 8. Top: UV HPLC chromatogram, product retention time = 13.5 min. Starting material retention time = 8.3 min. Bottom: Radio-HPLC chromatogram, product retention time = 13.6 min.

Example of radio-TLC scan of [^{18}F]2j



Chromatogram of radio-HPLC trace of [^{18}F]7c

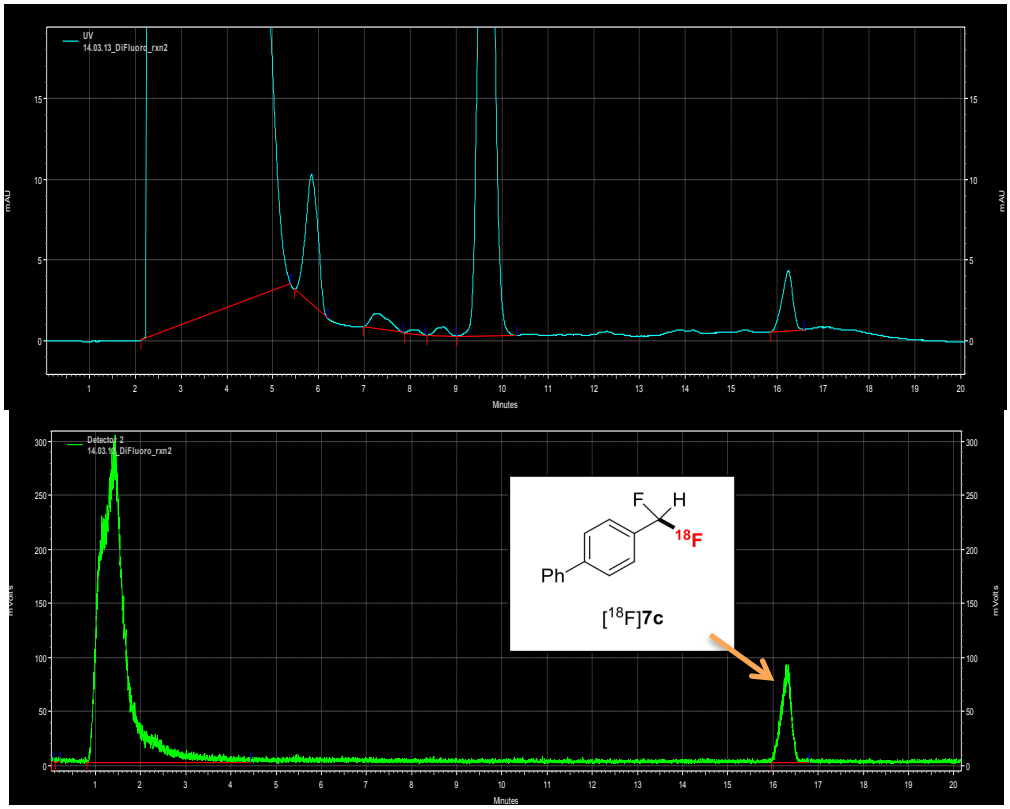
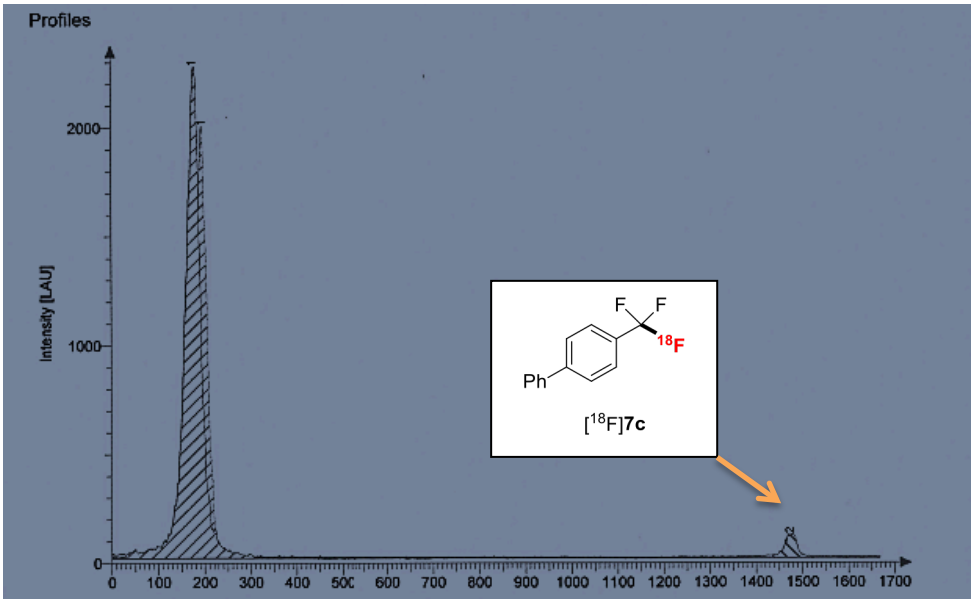


Figure 9. Top: UV HPLC chromatogram, product retention time = 16.3 min. Starting material retention time = 9.78 min. Bottom: Radio-HPLC chromatogram, product retention time = 16.4 min.

Example of radio-TLC scan of [^{18}F]7c



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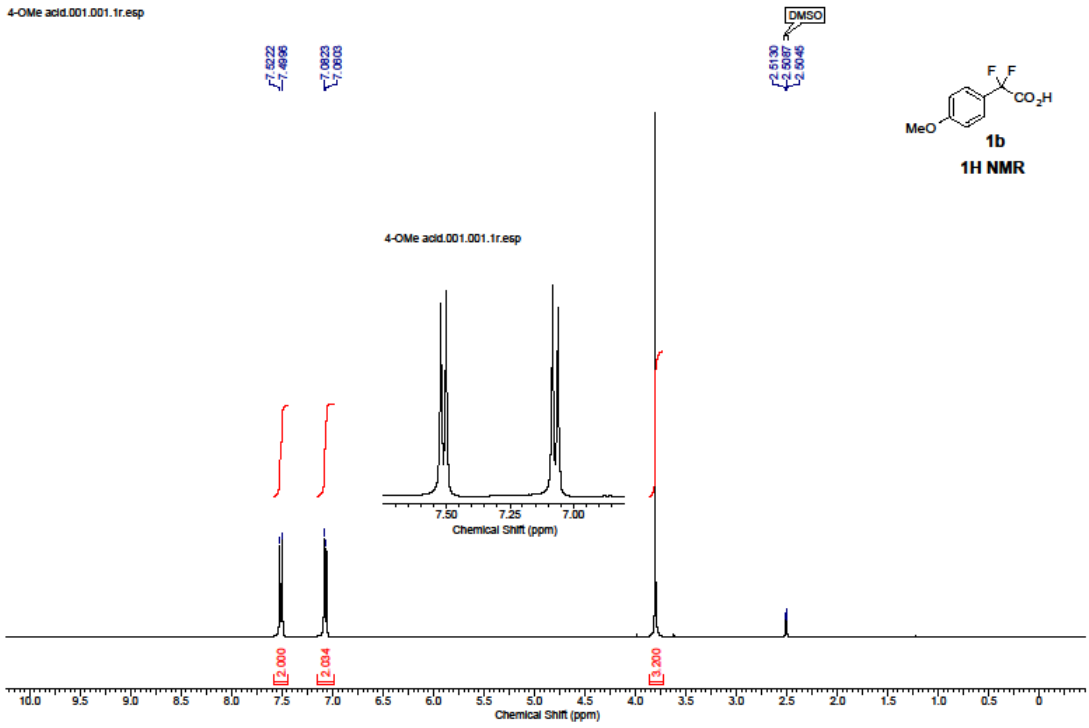
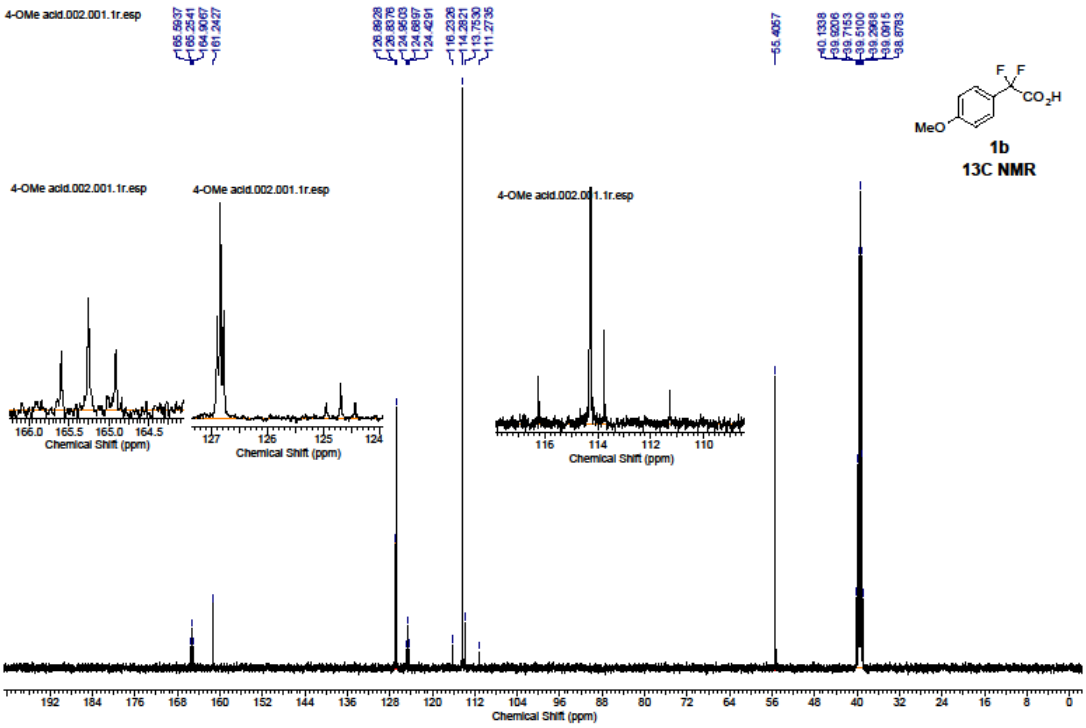
6. NMR Spectra

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113.7530
111.2735
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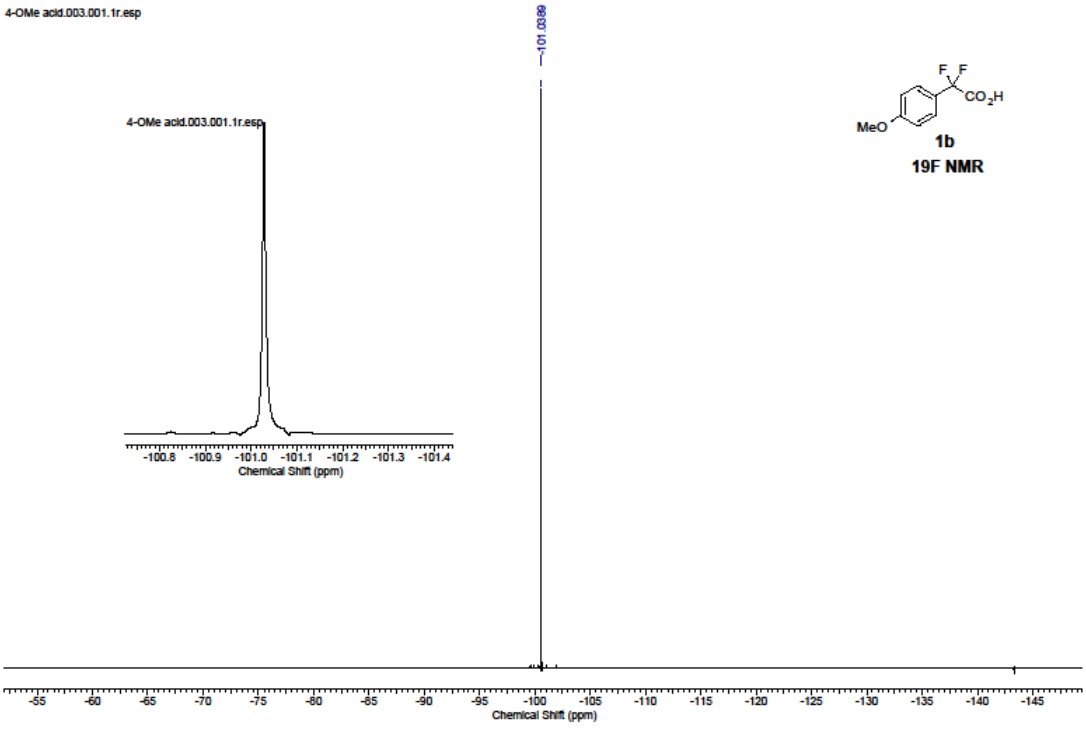
38.8783
F F
CO2H
MeO
1b
13C NMR
Chemical Shift (ppm)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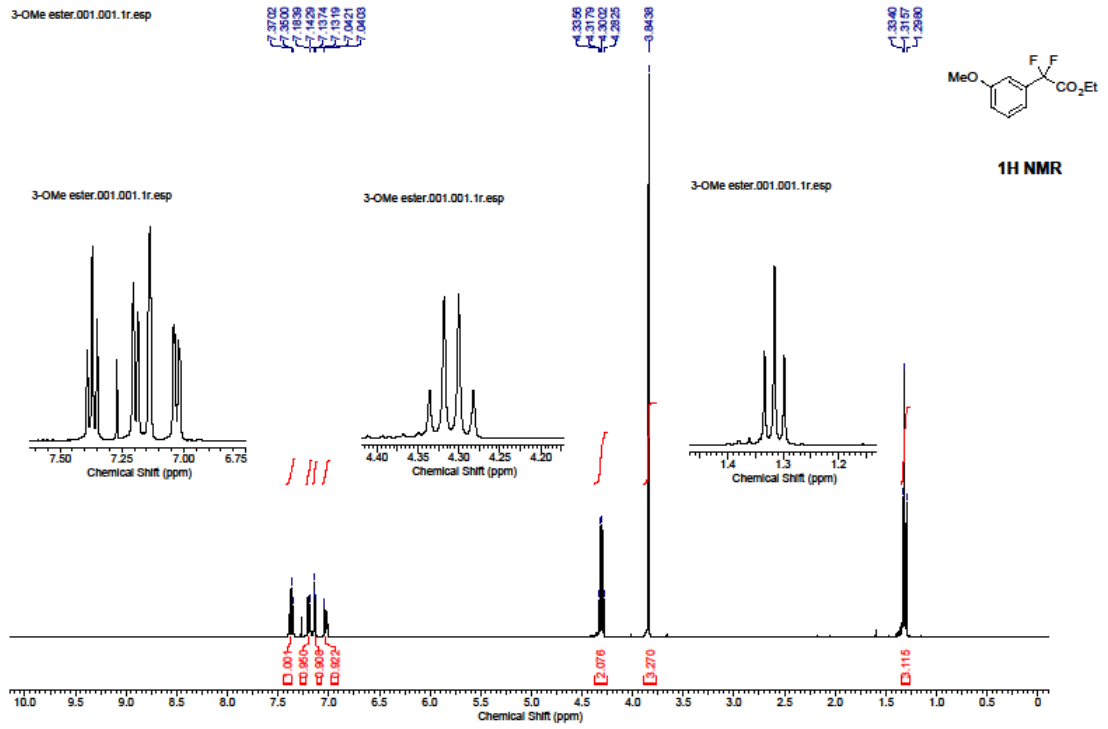
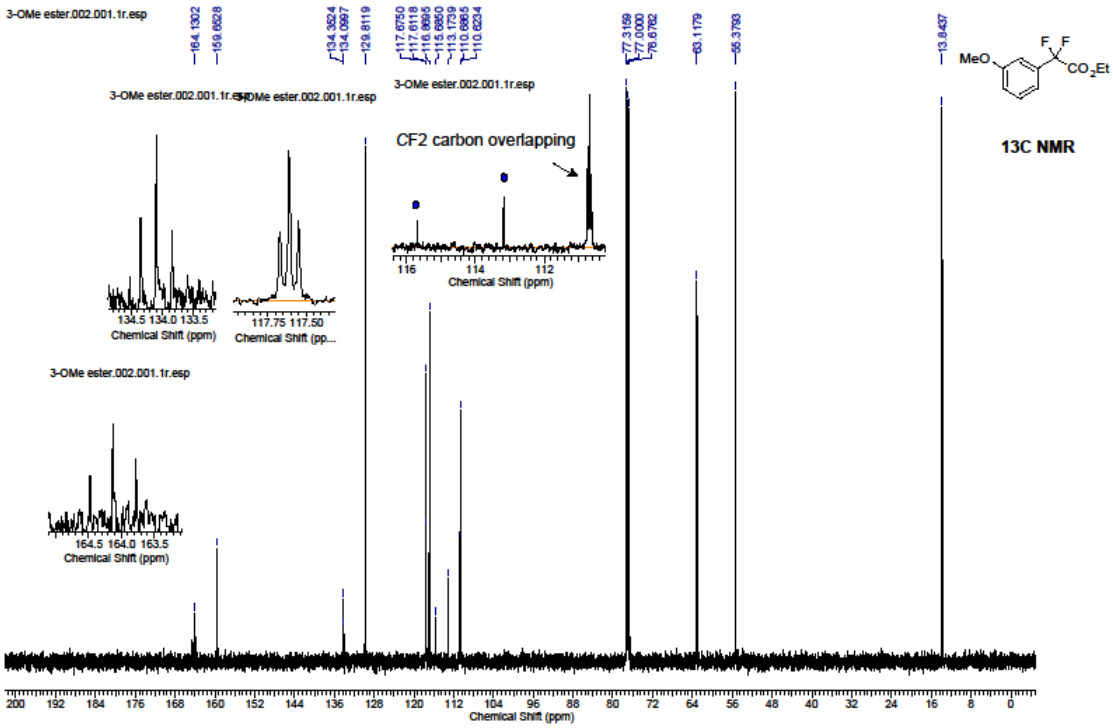
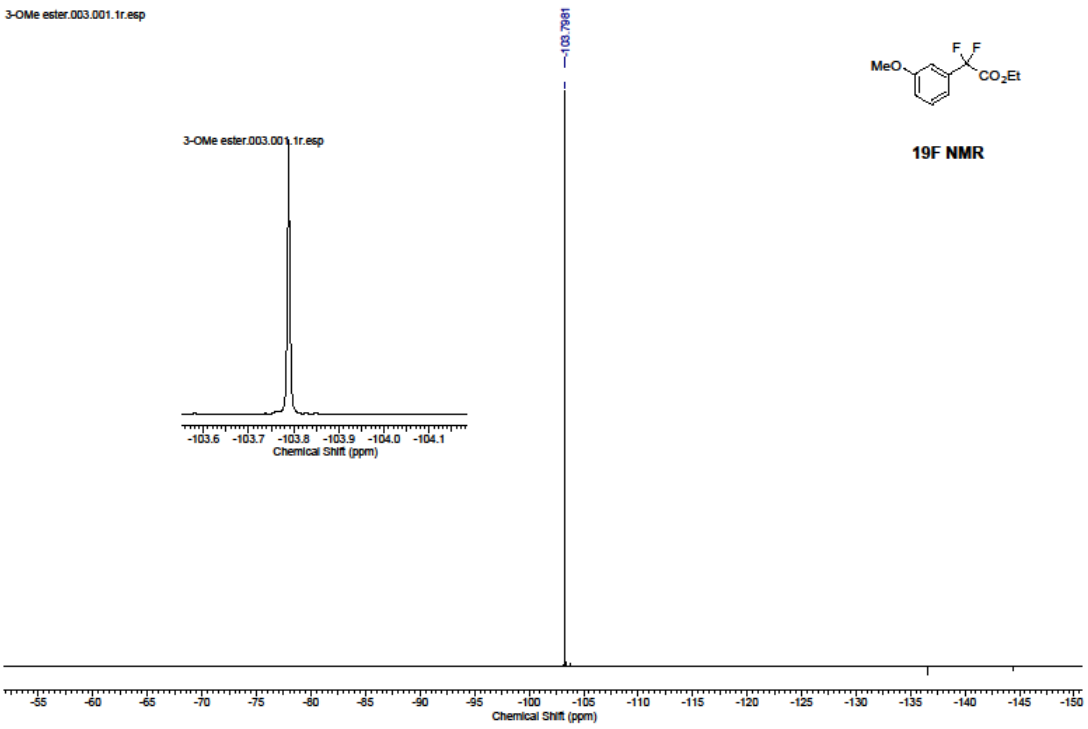
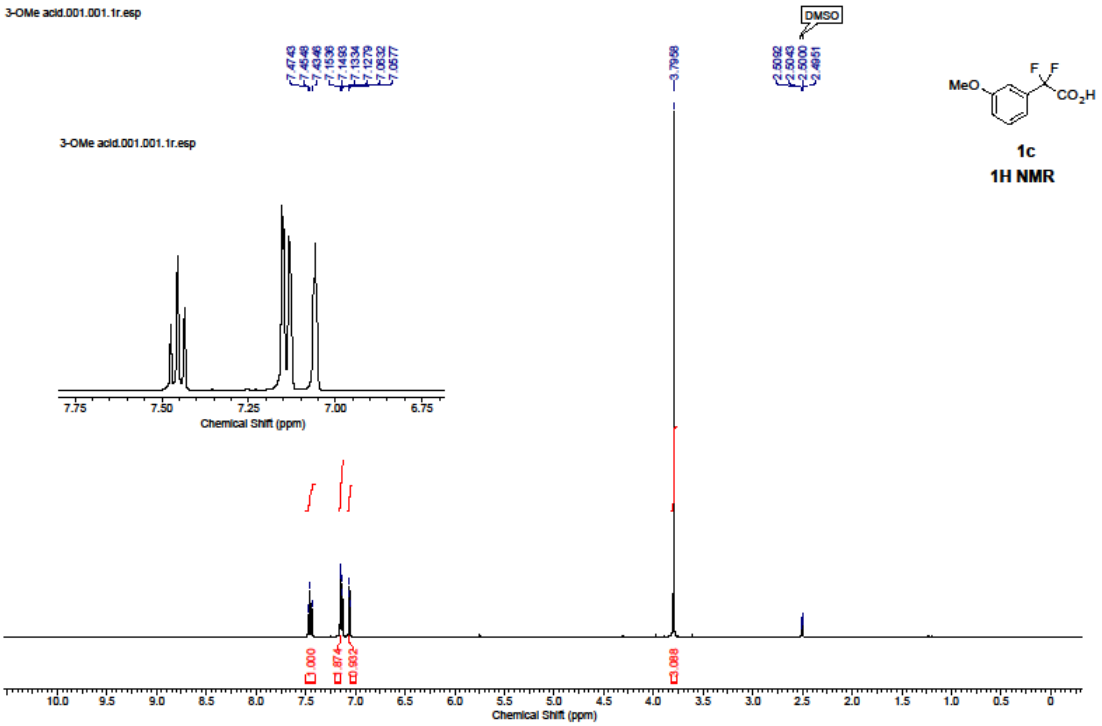
19F NMR
Chemical Shift (ppm)


3-OMe ester.001.001.1r.esp
MeO
F F
CO2Et
1H NMR
Chemical Shift (ppm)

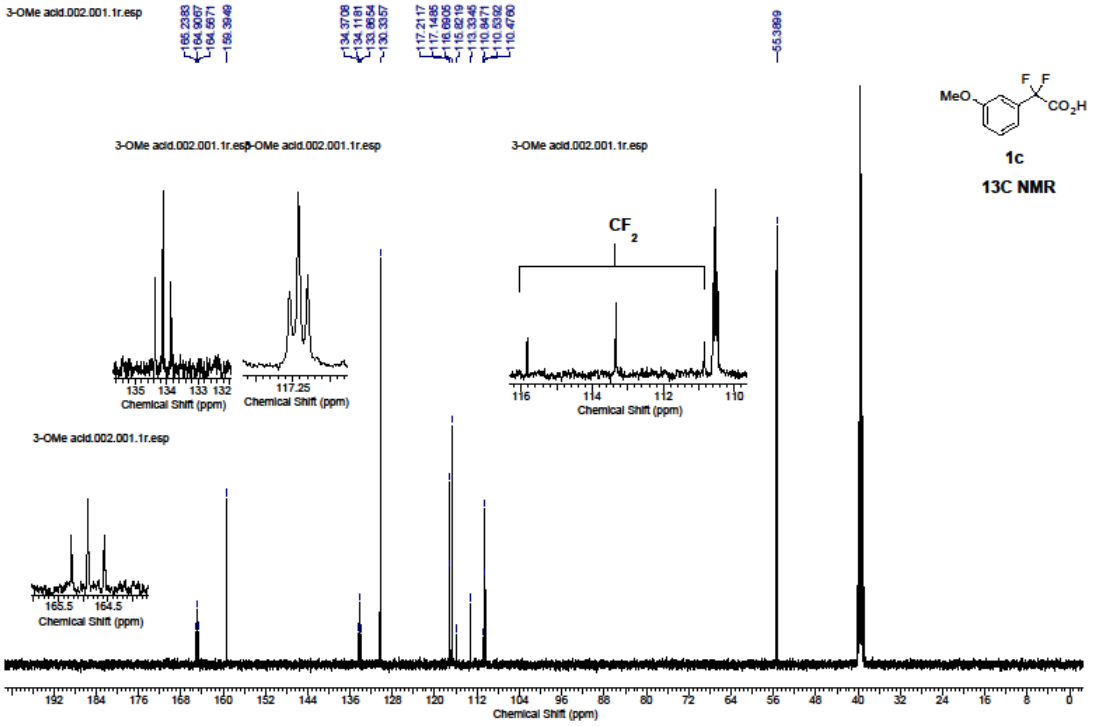

3-OMe ester.002.001.1r.esp
MeO
F F
CO2Et
13C NMR
CF2 carbon overlapping
Chemical Shift (ppm)

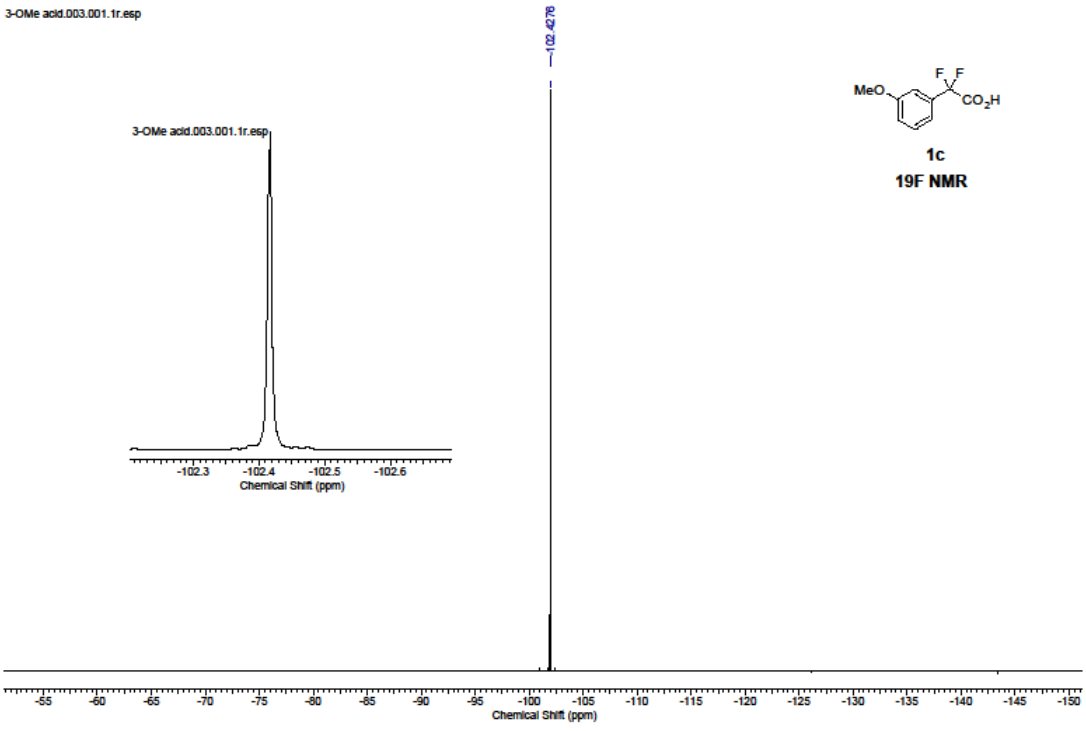


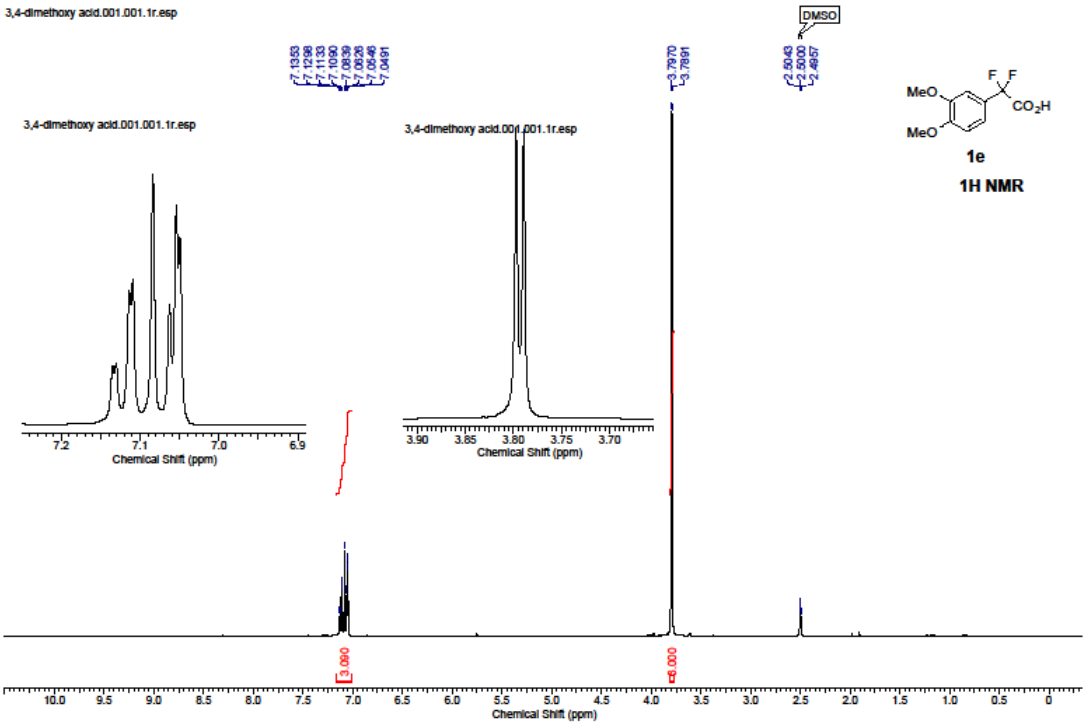
19F NMR

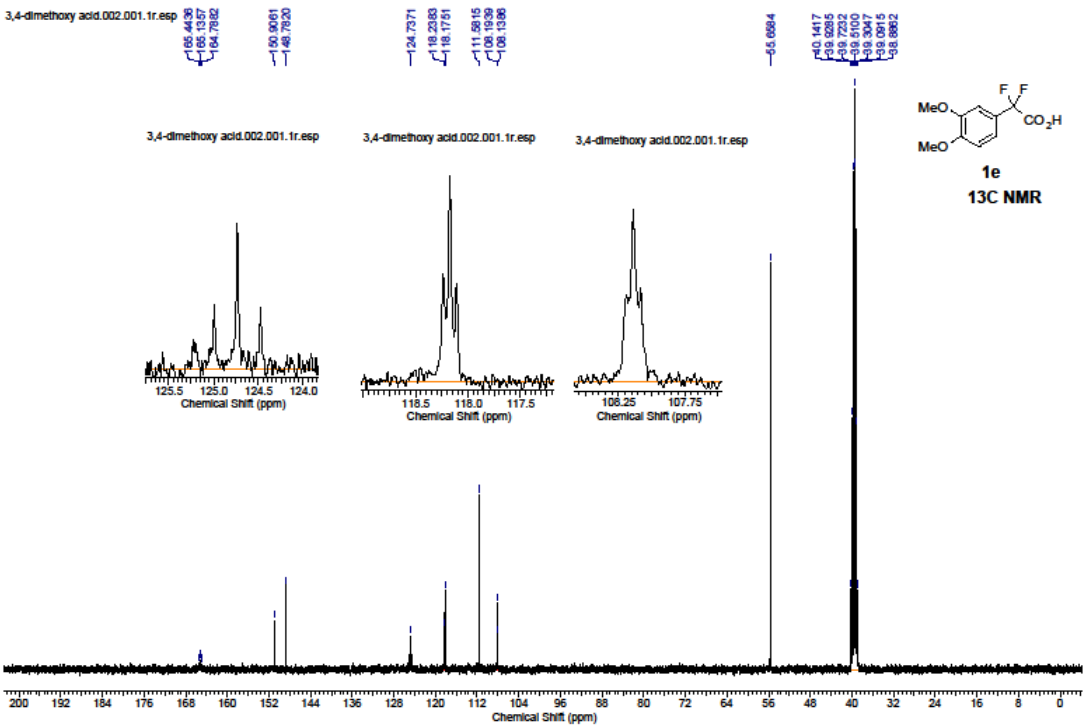


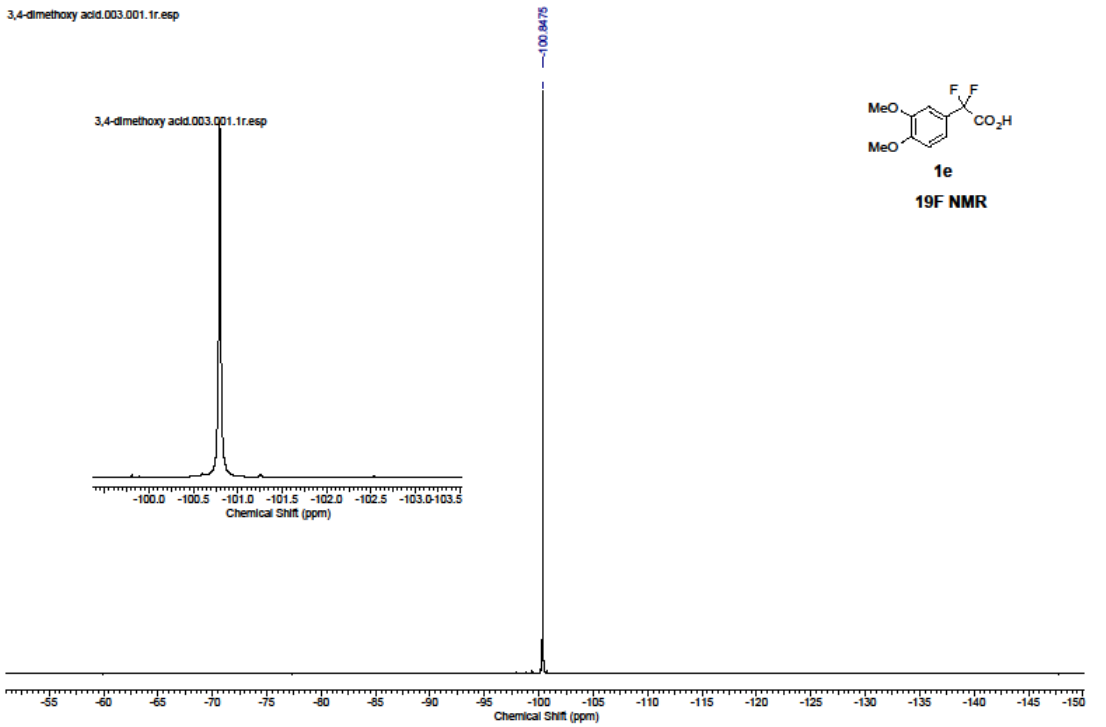
1c
1H NMR

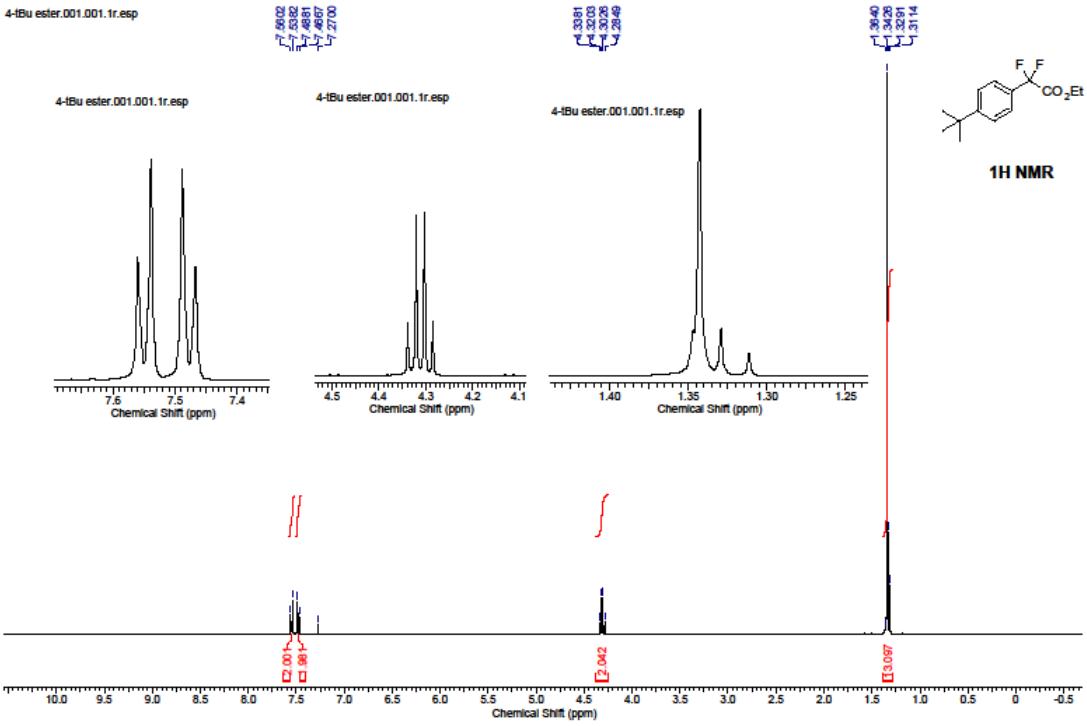

3-OMe acid.002.001.1r.esp
MeO
F F
CO2H
1c
13C NMR
CF2
Chemical Shift (ppm)

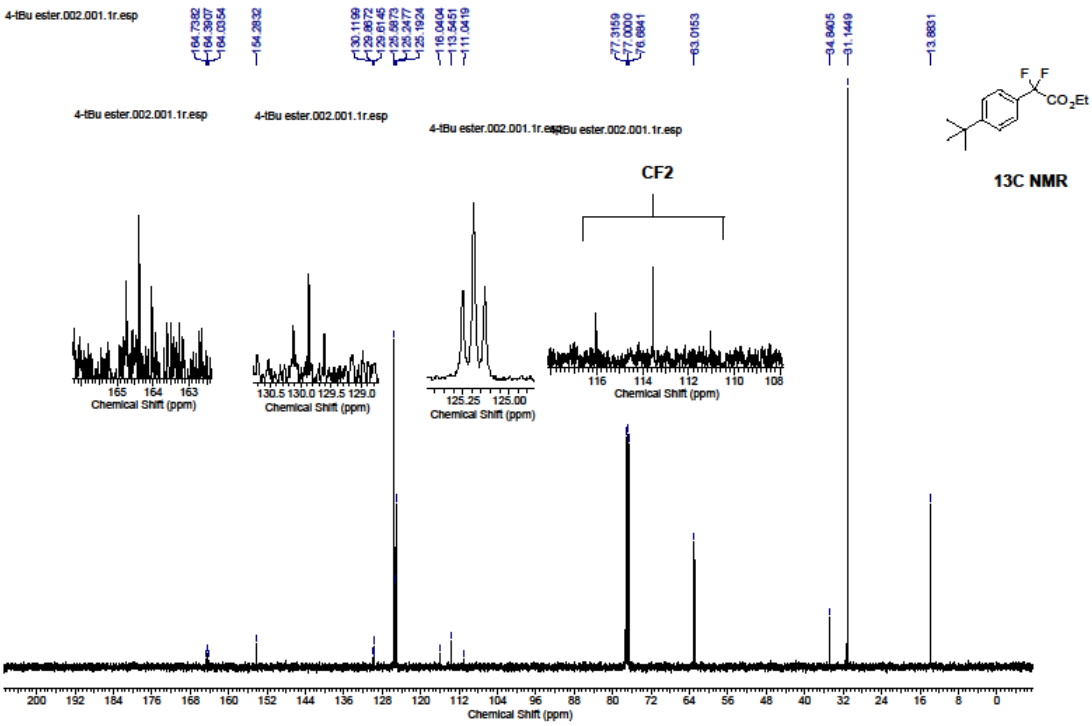

3-OMe acid.003.001.1r.esp
MeO
F F
CO2H
1c
19F NMR
Chemical Shift (ppm)

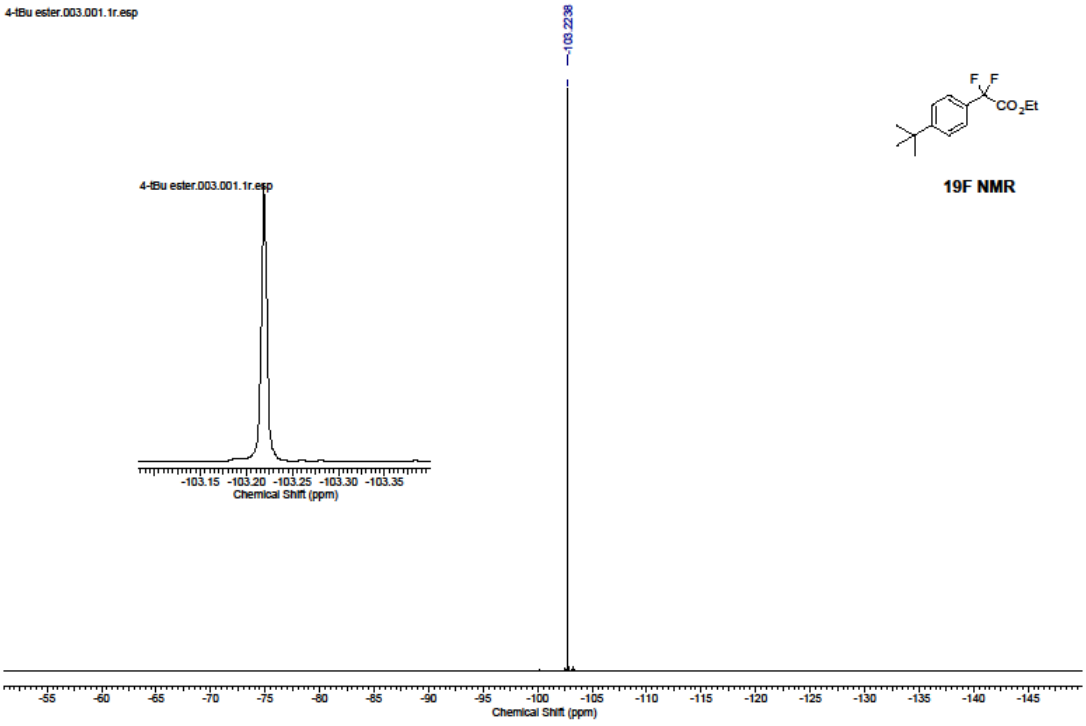

3,4-dimethoxy acid.001.001.1r.esp
DMSO
7.1353
7.1298
7.1133
7.1090
7.0939
7.0626
7.0545
7.0491
3.7970
3.7891
2.5043
2.5000
2.4957
3,4-dimethoxy acid.001.001.1r.esp
3,4-dimethoxy acid.001.001.1r.esp
Chemical Shift (ppm)
3,4-dimethoxy acid.001.001.1r.esp
Chemical Shift (ppm)
MeO
MeO
F F
CO2H
1e
1H NMR
3.090
6.000
Chemical Shift (ppm)

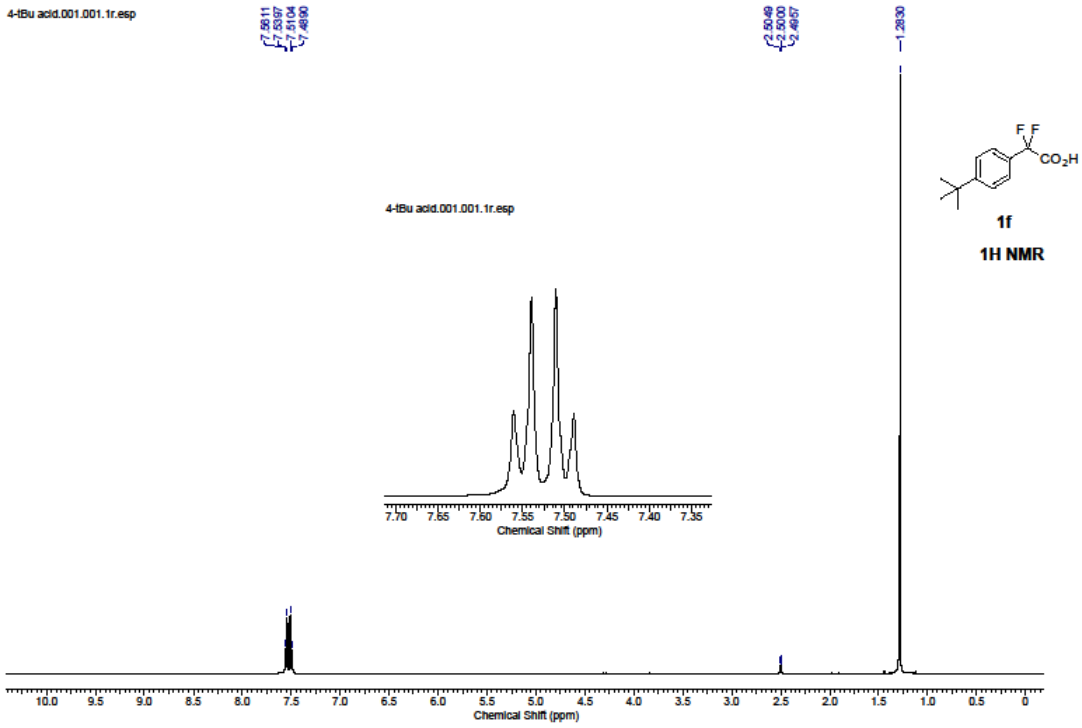

3,4-dimethoxy acid.002.001.1r.esp
165.4436
165.1357
164.7882
150.9061
148.7820
124.7371
118.2383
118.1751
111.5815
108.1939
108.1386
55.6884
40.1417
39.9285
39.7232
39.5100
39.3047
39.0915
38.8862
3,4-dimethoxy acid.002.001.1r.esp
3,4-dimethoxy acid.002.001.1r.esp
3,4-dimethoxy acid.002.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
MeO
MeO
F F
CO2H
1e
13C NMR
Chemical Shift (ppm)

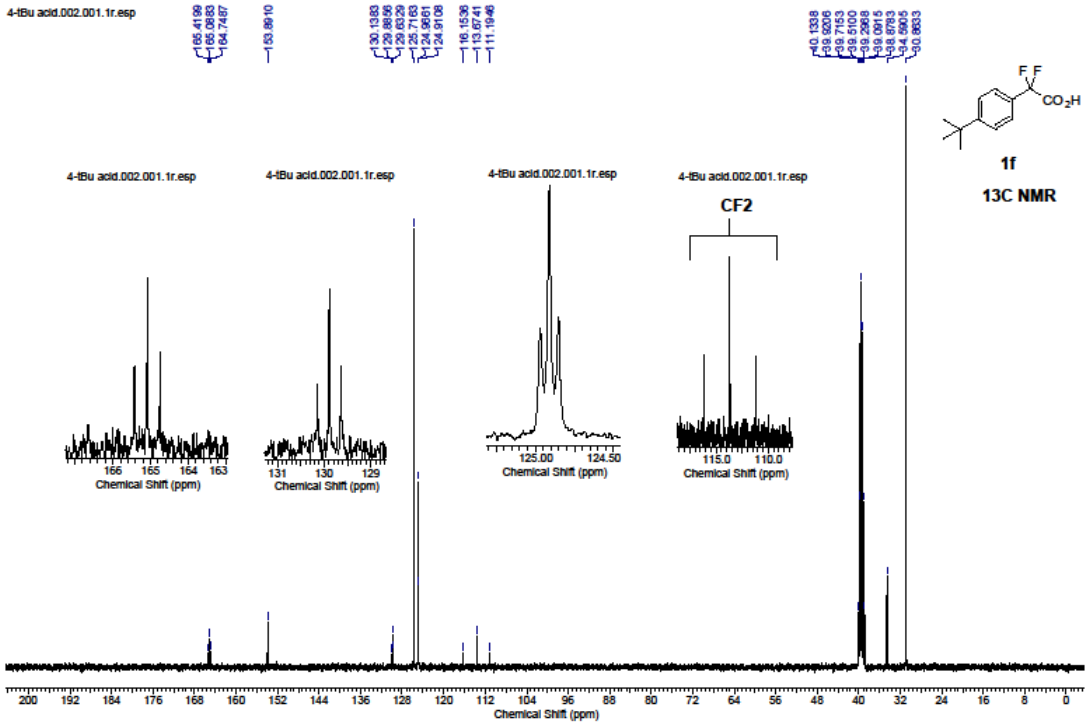

3,4-dimethoxy acid.003.001.1r.esp
-100.8475
3,4-dimethoxy acid.003.001.1r.esp
-100.0 -100.5 -101.0 -101.5 -102.0 -102.5 -103.0-103.5
Chemical Shift (ppm)
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
Chemical Shift (ppm)
F F
MeO
MeO
CO2H
1e
19F NMR

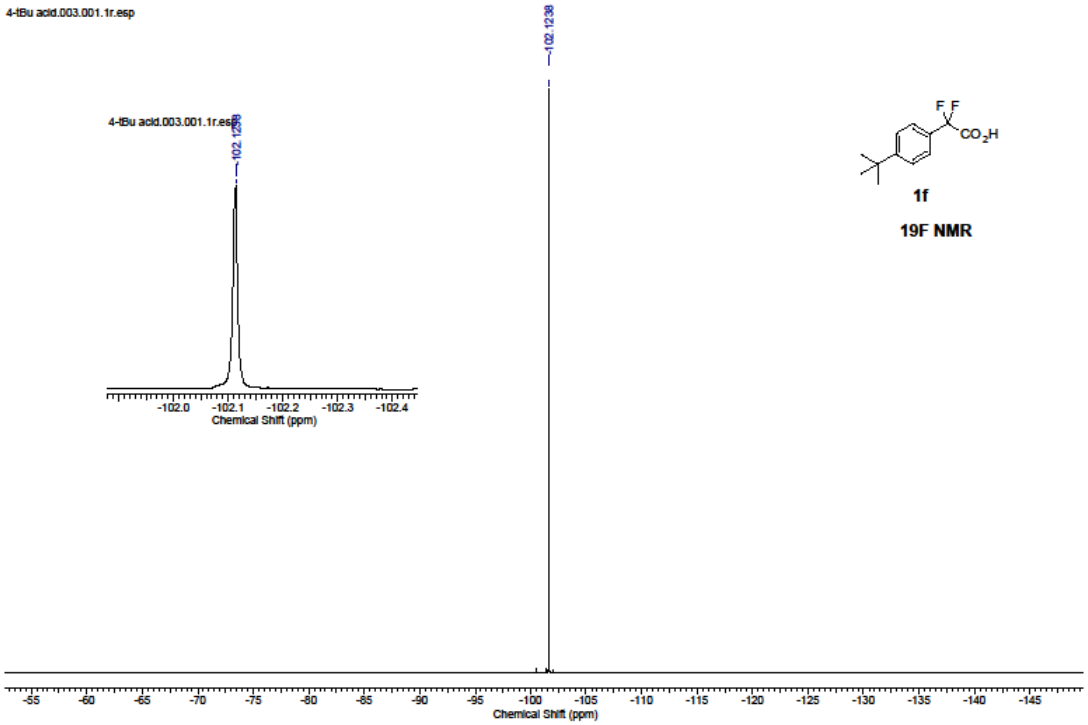

4-tBu ester.001.001.1r.esp
7.7602
7.7382
7.4861
7.4657
7.2700
4.3381
4.3203
4.3026
4.2849
3.1640
3.1426
3.1291
3.1114
4-tBu ester.001.001.1r.esp
7.6 7.5 7.4
Chemical Shift (ppm)
4-tBu ester.001.001.1r.esp
4.5 4.4 4.3 4.2 4.1
Chemical Shift (ppm)
4-tBu ester.001.001.1r.esp
1.40 1.35 1.30 1.25
Chemical Shift (ppm)
F F
CO2Et
1H NMR
2.001
1.961
2.042
3.097
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

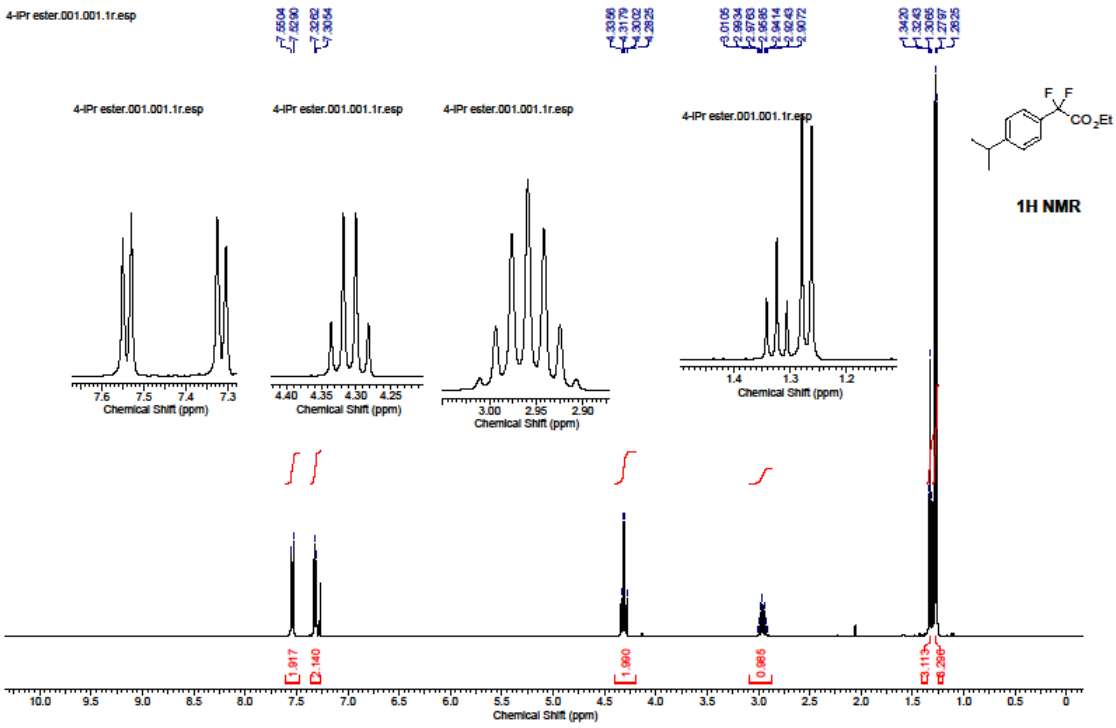

4-tBu ester.002.001.1r.esp
164.7382
164.3807
164.0354
154.2832
130.1199
129.8672
129.6145
126.5873
125.2477
125.1924
116.0404
113.5451
111.0419
77.3159
77.0000
76.6841
63.0153
34.8405
31.1449
13.8831
CF2
13C NMR
Chemical Shift (ppm)

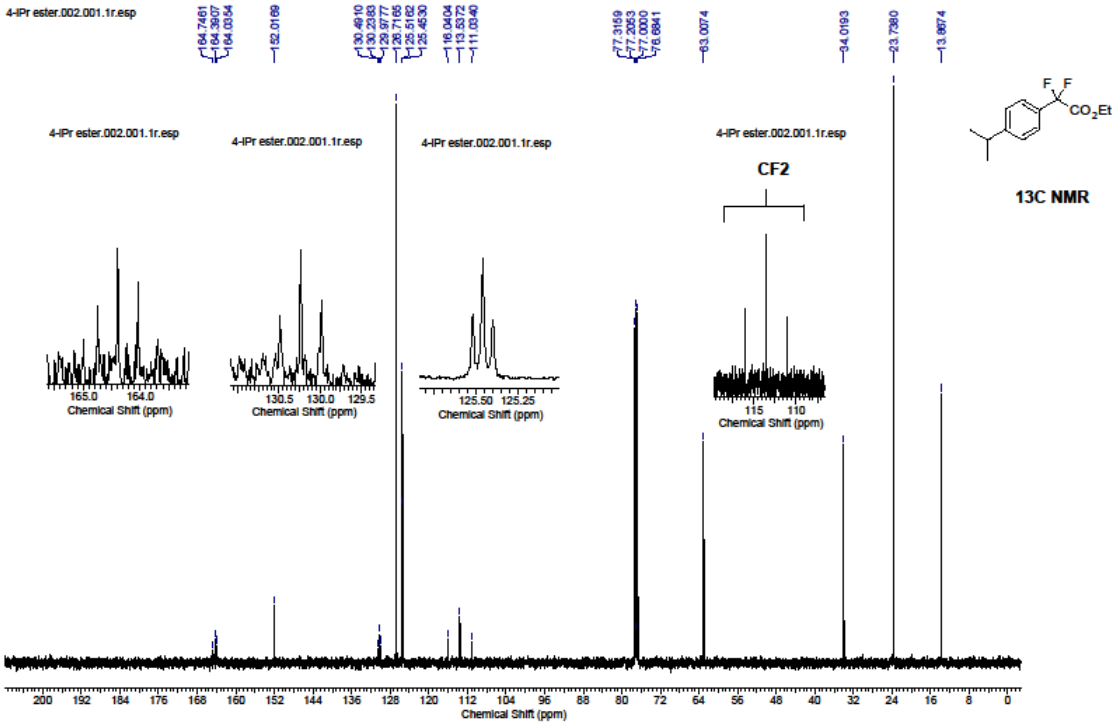

4-tBu ester.003.001.1r.esp
-103.2236
19F NMR
Chemical Shift (ppm)

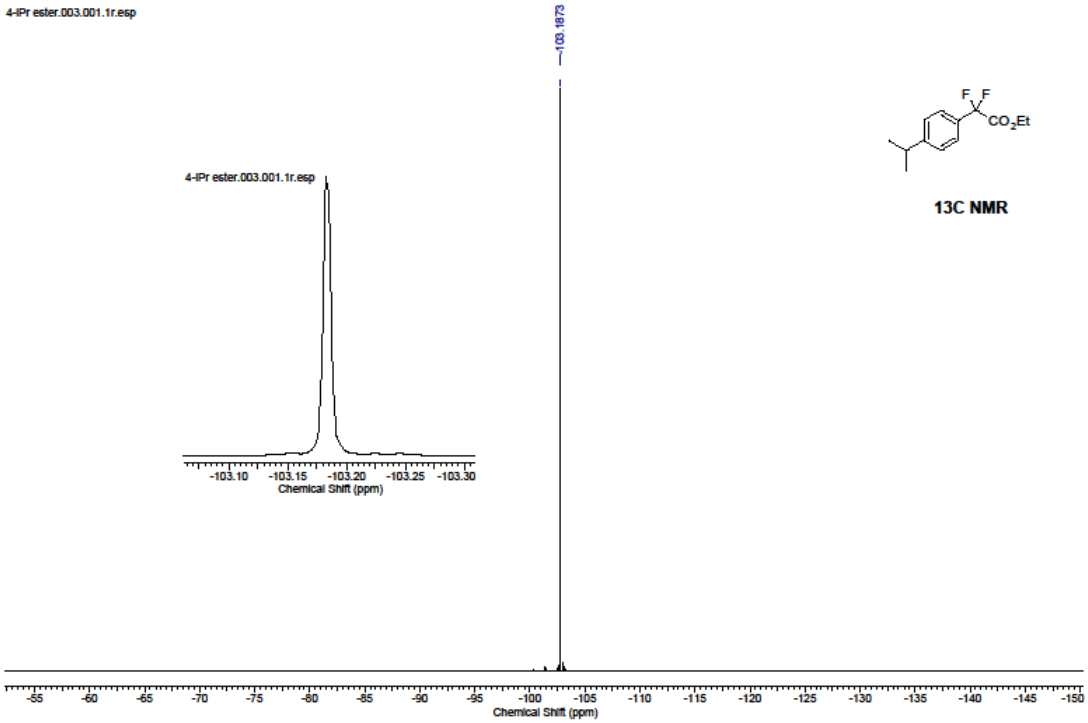

4-tBu acid.001.001.1r.esp
7.5611
7.5397
7.5104
7.4890
2.5049
2.5000
2.4957
1.2830
F F
CO2H
1f
1H NMR
4-tBu acid.001.001.1r.esp
7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35
Chemical Shift (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


4-tBu acid.002.001.1r.esp
165.4199
165.0883
164.7487
153.8910
130.1383
129.8896
129.6329
125.7163
124.9661
124.9108
116.1536
113.6741
111.1946
40.1338
39.9206
39.7153
39.5100
39.2968
39.0915
38.8783
34.5905
30.8833
F F
CO2H
1f
13C NMR
4-tBu acid.002.001.1r.esp
166 165 164 163
Chemical Shift (ppm)
4-tBu acid.002.001.1r.esp
131 130 129
Chemical Shift (ppm)
4-tBu acid.002.001.1r.esp
125.00 124.50
Chemical Shift (ppm)
4-tBu acid.002.001.1r.esp
CF2
115.0 110.0
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


4-tBu acid.003.001.1r.esp
-102.1238
4-tBu acid.003.001.1r.esp
-102.1288
F F
CO2H
1f
19F NMR
-102.0 -102.1 -102.2 -102.3 -102.4
Chemical Shift (ppm)
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145
Chemical Shift (ppm)


4-iPr ester.001.001.1r.esp
7.5504
7.5290
7.3262
7.3054
4.3396
4.3179
4.3032
4.2825
3.0105
2.9934
2.9763
2.9585
2.9414
2.9243
2.9072
1.3420
1.3243
1.3065
1.2797
1.2625
4-iPr ester.001.001.1r.esp
4-iPr ester.001.001.1r.esp
4-iPr ester.001.001.1r.esp
4-iPr ester.001.001.1r.esp
F F
CO2Et
1H NMR
7.6 7.5 7.4 7.3
Chemical Shift (ppm)
4.40 4.35 4.30 4.25
Chemical Shift (ppm)
3.00 2.95 2.90
Chemical Shift (ppm)
1.4 1.3 1.2
Chemical Shift (ppm)
1.917
2.140
1.990
0.985
3.113
6.296
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


4-IPr ester.002.001.1r.esp
164.7461
164.3607
164.0354
152.0169
130.4910
130.2383
129.9777
126.7165
125.5152
125.4530
116.0404
113.5372
111.0340
77.3159
77.2053
77.0000
76.6841
63.0074
34.0193
23.7980
13.8674
CF2
13C NMR
Chemical Shift (ppm)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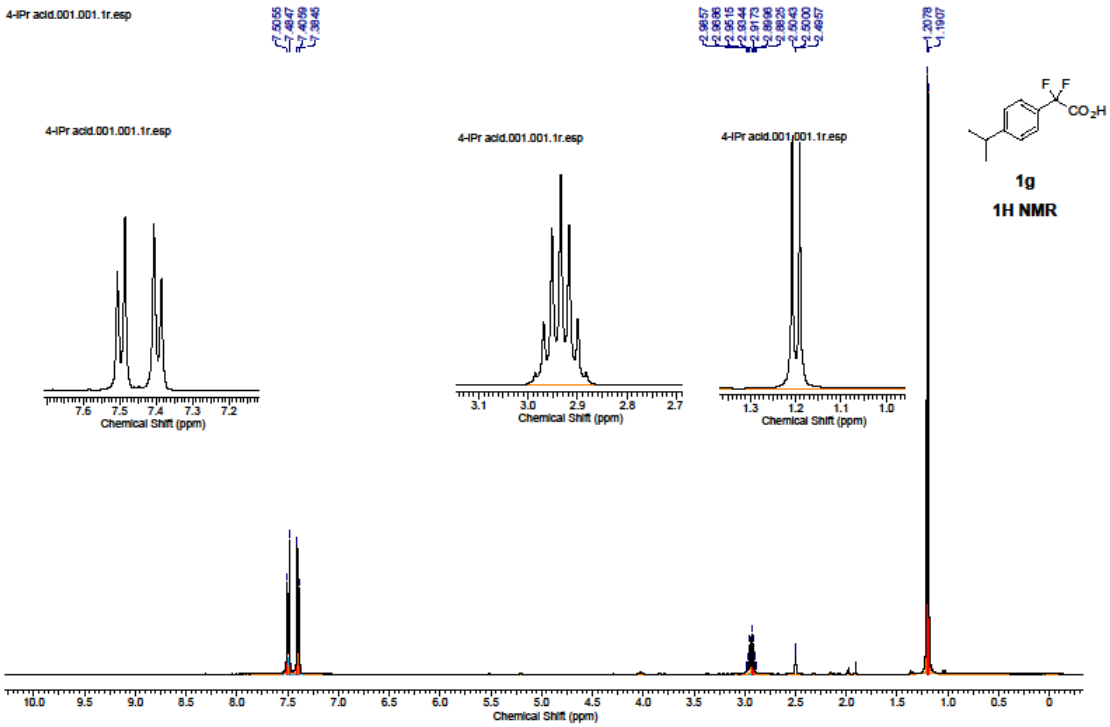
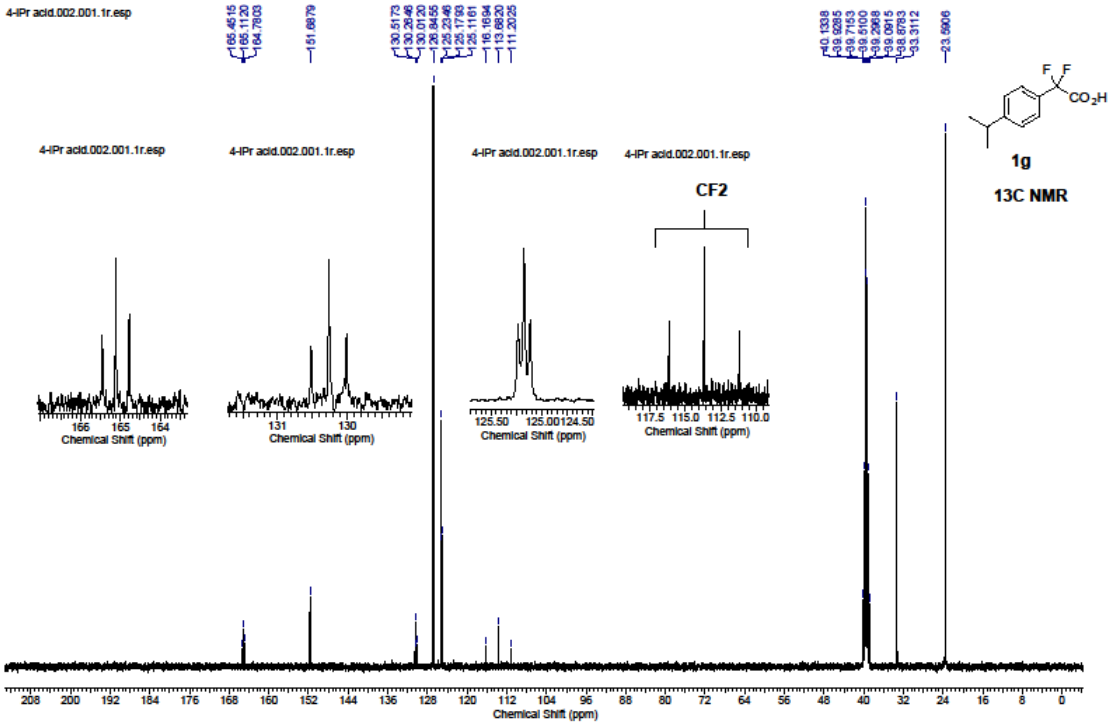
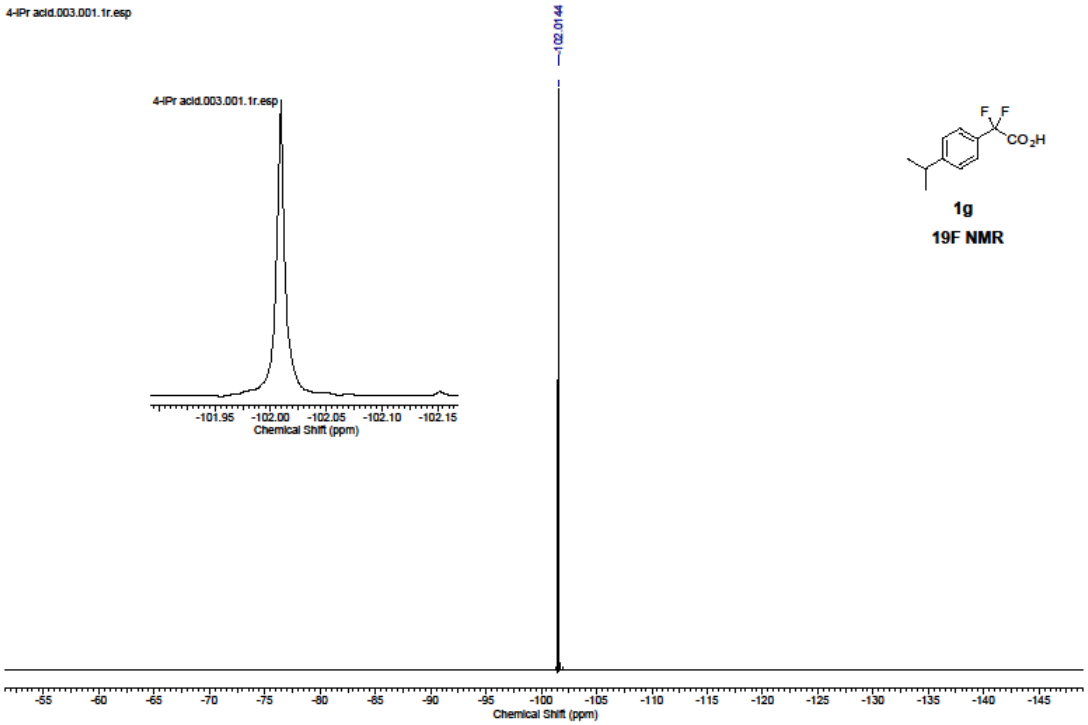
-103.1873
13C NMR
Chemical Shift (ppm)

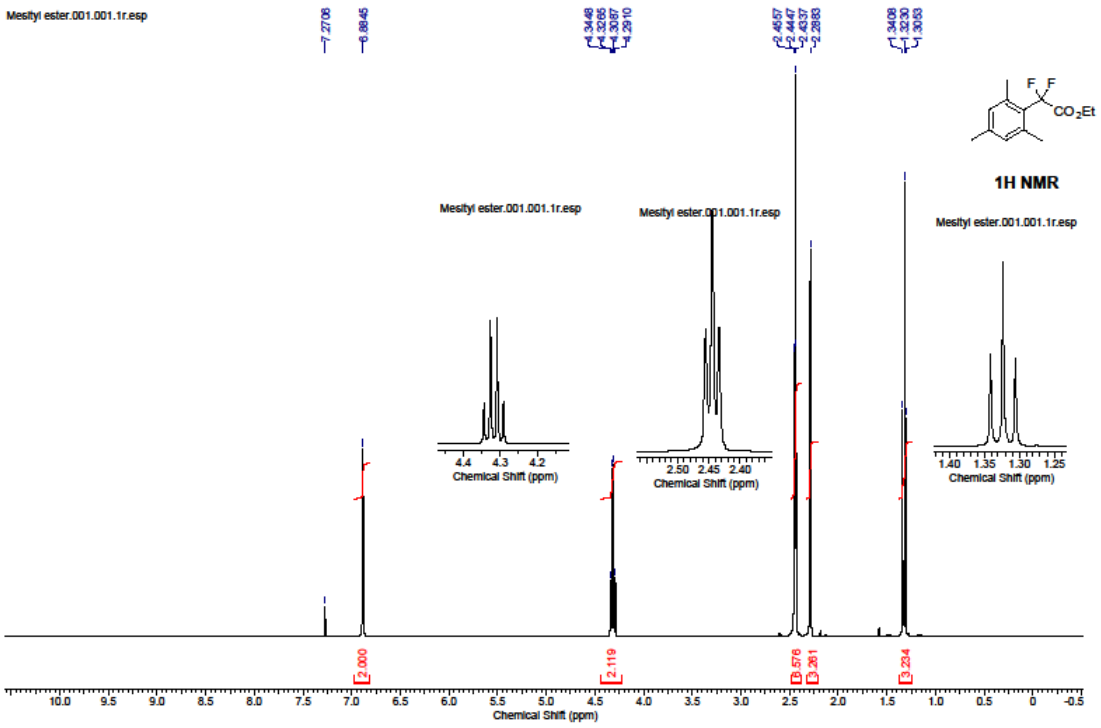

4-IPr acid.001.001.1r.esp
7.5055
7.4847
7.4059
7.3845
2.9957
2.9696
2.9515
2.9344
2.9173
2.8996
2.8825
2.5043
2.5000
2.4957
1.2078
1.1907
F F
CO2H
1g
1H NMR
Chemical Shift (ppm)


4-IPr acid.002.001.1r.esp
166.4515
166.1120
164.7803
151.6879
130.5173
130.2646
130.0120
126.8455
125.2346
125.1793
125.1161
116.1694
113.6820
111.2025
40.1338
39.9295
39.7153
39.5100
39.2958
39.0815
38.8673
33.3112
23.6906
F F
CO2H
1g
13C NMR
CF2
Chemical Shift (ppm)

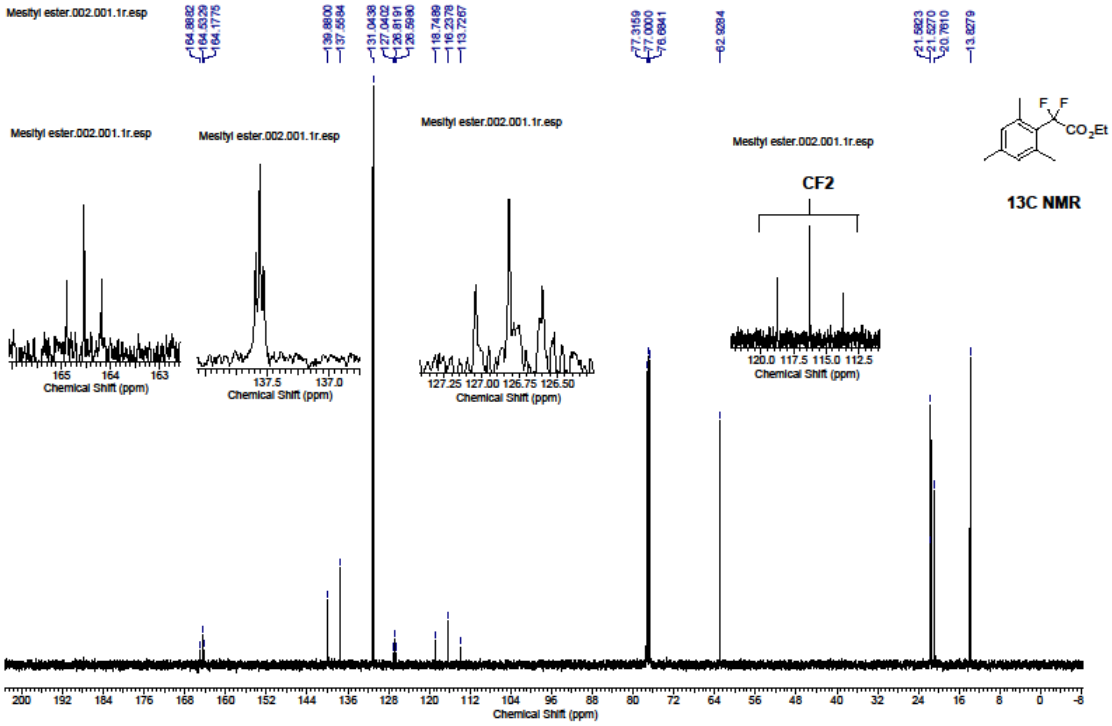


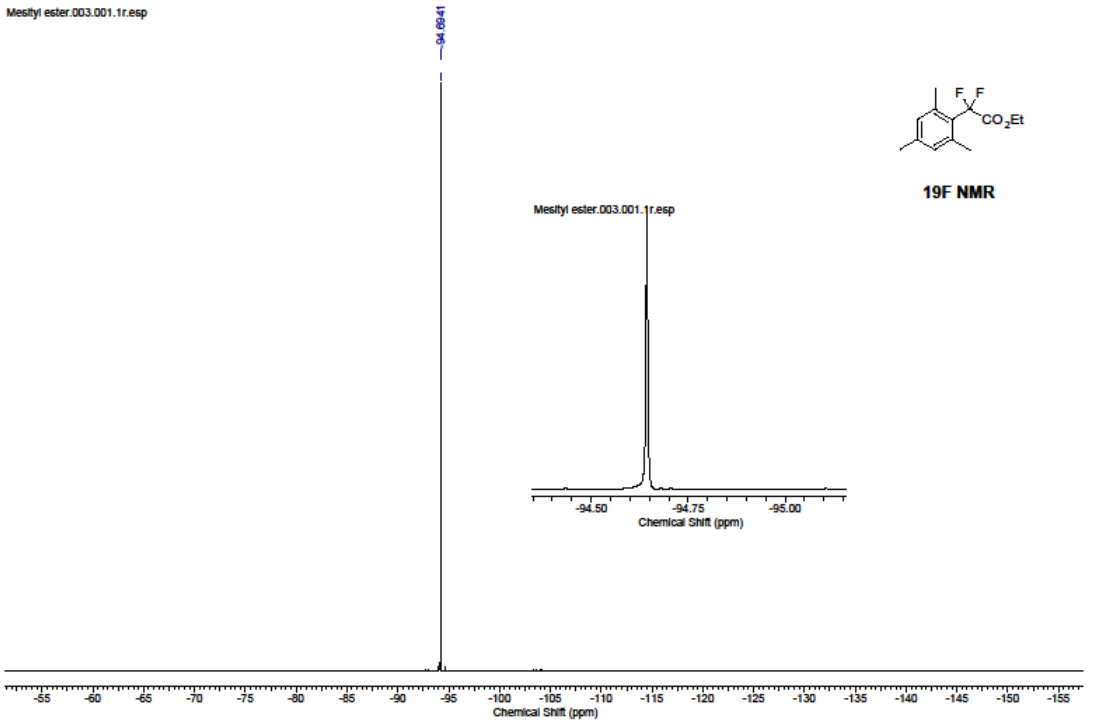
1g

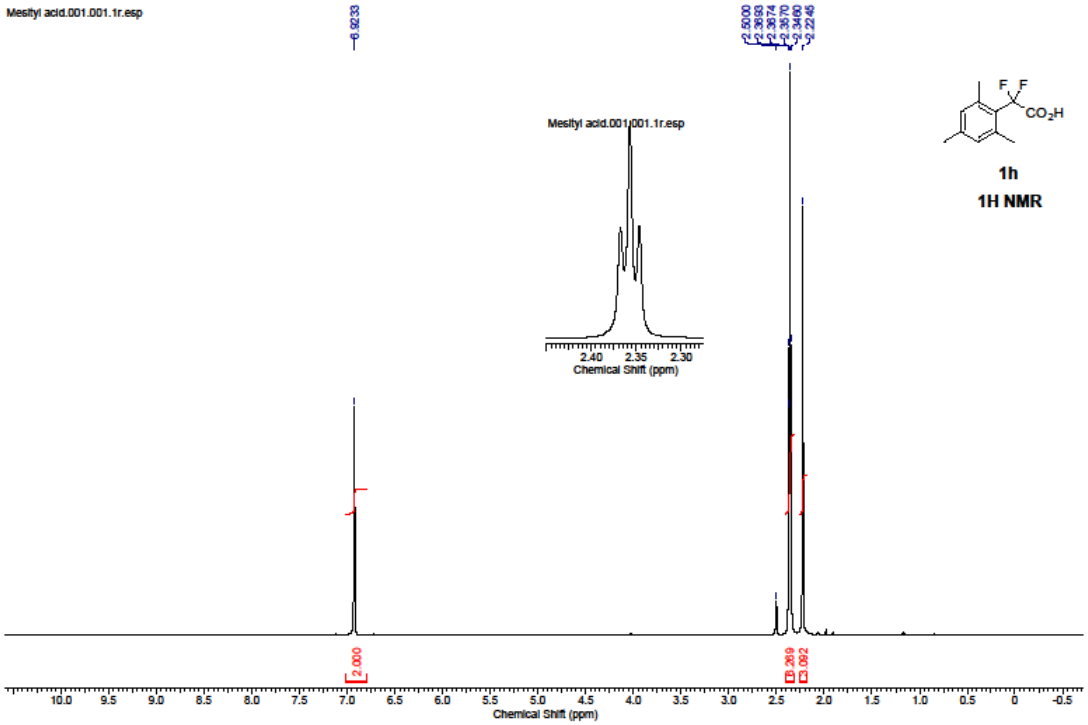
19F NMR

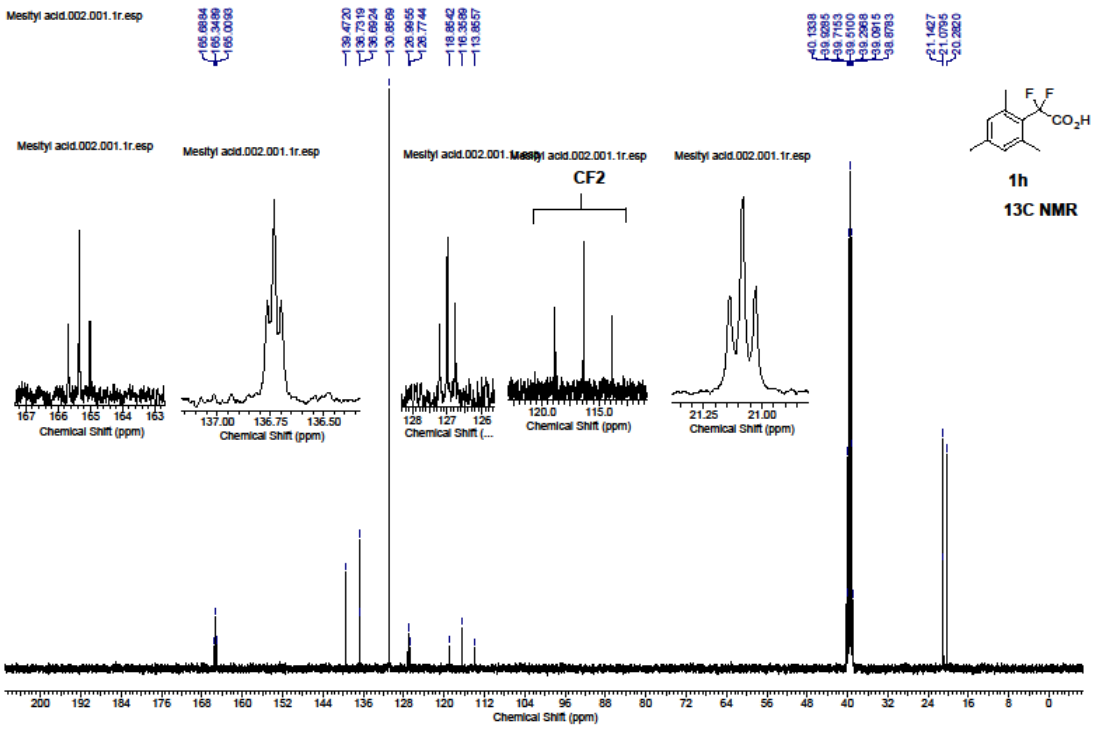


1H NMR


Mesityl ester.002.001.1r.esp
164.8882
164.5329
164.1775
139.8600
137.3584
131.0438
127.0402
126.8191
126.5980
118.7489
116.2378
113.7267
77.3159
77.0000
76.6841
62.9284
21.5823
21.5270
20.7610
13.9279
CF2
13C NMR
Chemical Shift (ppm)


Mesityl ester.003.001.1r.esp
94.6941
19F NMR
Chemical Shift (ppm)


Mesityl acid.001.001.1r.esp
6.9233
2.6000
2.3693
2.3674
2.3570
2.3460
2.2245
Mesityl acid.001.001.1r.esp
2.40
2.35
2.30
Chemical Shift (ppm)
F F
CO2H
1h
1H NMR
2.000
2.269
3.092
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)


Mesityl acid.002.001.1r.esp
165.6884
165.3489
165.0093
139.4720
138.7319
136.6924
130.8569
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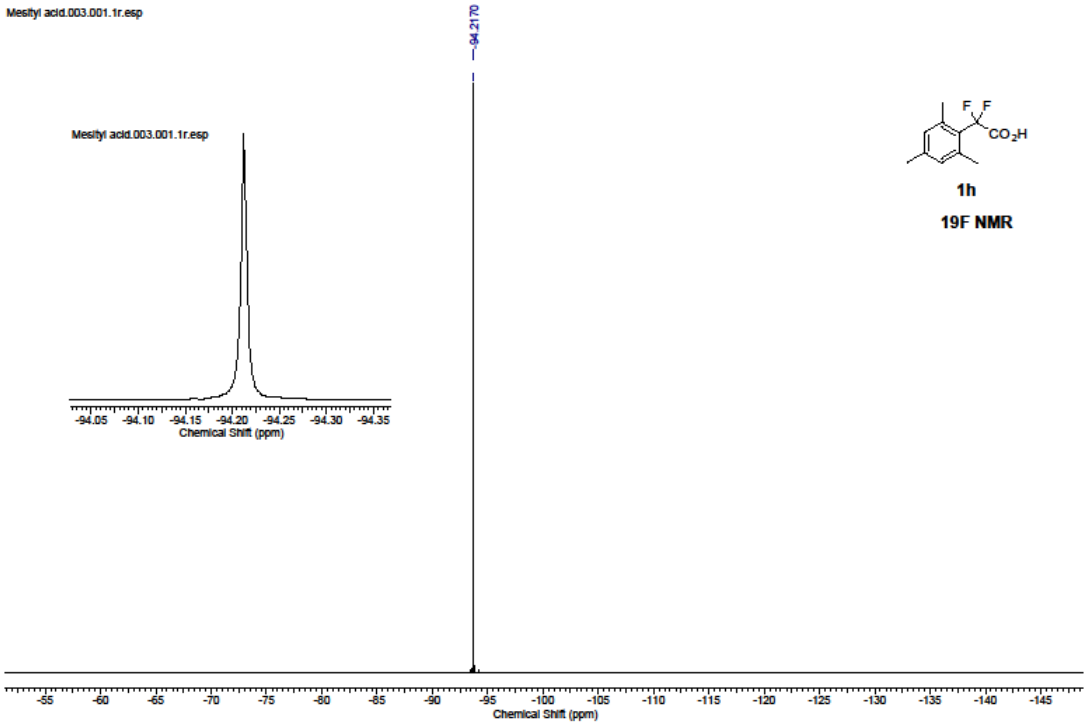
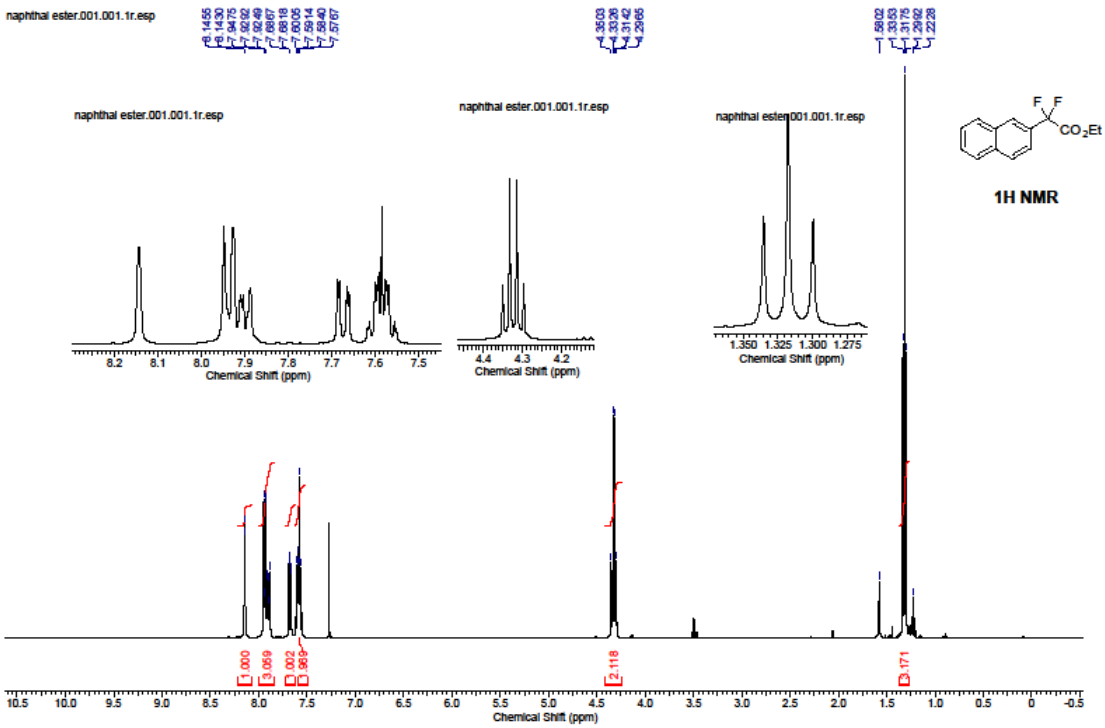
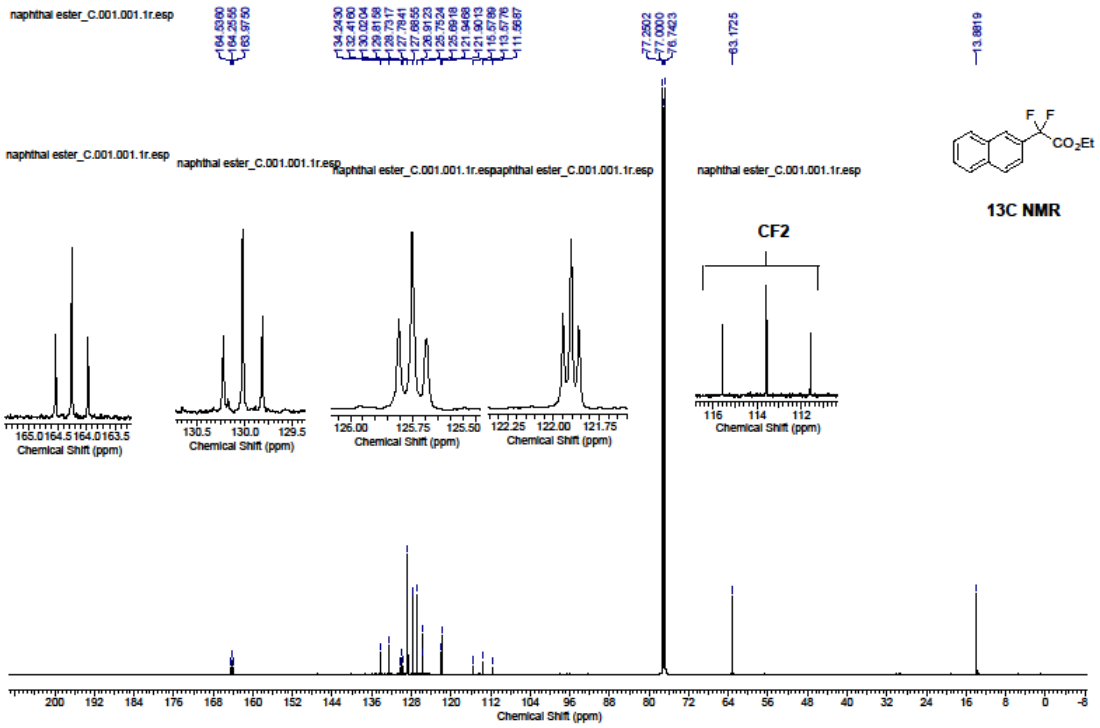
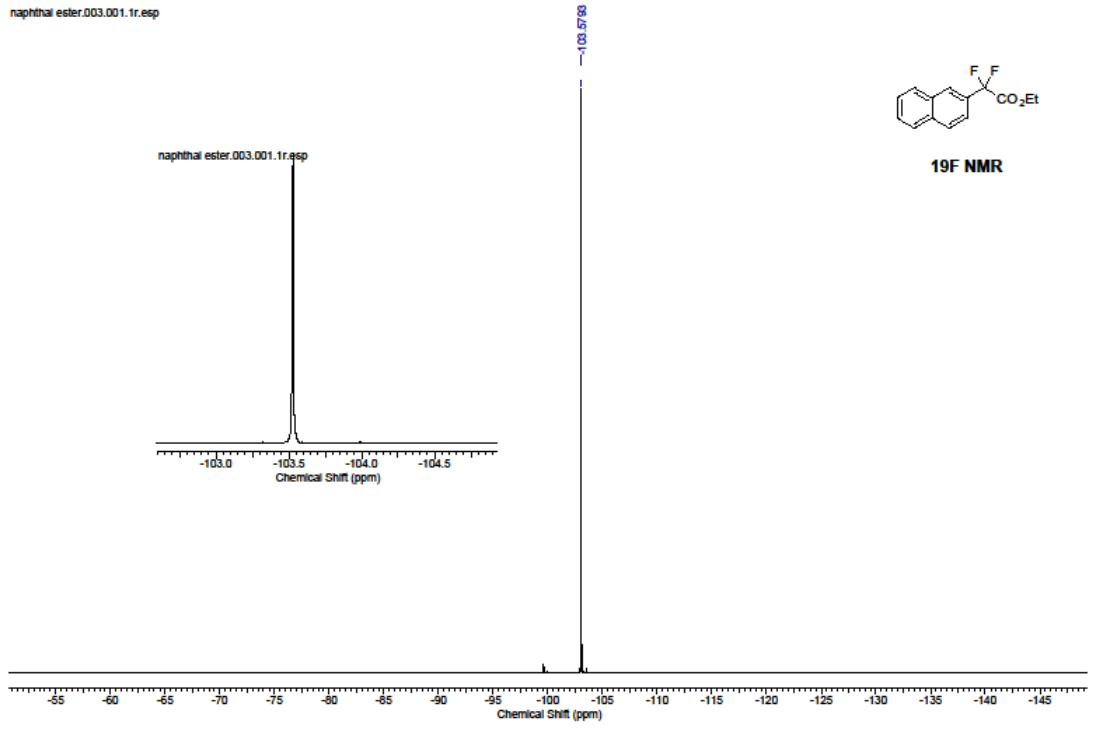
128.7744
119.8542
119.3589
113.8857
40.1338
39.9285
39.7153
39.5100
39.2968
39.0915
38.8783
21.1427
21.0795
20.2820
Mesityl acid.002.001.1r.esp
167
166
165
164
163
Chemical Shift (ppm)
Mesityl acid.002.001.1r.esp
137.00
136.75
136.50
Chemical Shift (ppm)
Mesityl acid.002.001.1r.esp
128
127
126
Chemical Shift (...
Mesityl acid.002.001.1r.esp
CF2
120.0
115.0
Chemical Shift (ppm)
Mesityl acid.002.001.1r.esp
21.25
21.00
Chemical Shift (ppm)
F F
CO2H
1h
13C NMR
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


Mesityl acid.003.001.1r.esp
-94.2170
Mesityl acid.003.001.1r.esp
-94.05 -94.10 -94.15 -94.20 -94.25 -94.30 -94.35
Chemical Shift (ppm)
F F
CO2H
1h
19F NMR
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145
Chemical Shift (ppm)


naphthal ester.001.001.1r.esp
8.1455
8.1430
7.9475
7.9292
7.9249
7.8667
7.8618
7.6005
7.5914
7.5840
7.5767
4.3503
4.3326
4.3142
4.2965
1.5802
1.3353
1.3175
1.2992
1.2228
naphthal ester.001.001.1r.esp
8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5
Chemical Shift (ppm)
naphthal ester.001.001.1r.esp
4.4 4.3 4.2
Chemical Shift (ppm)
naphthal ester.001.001.1r.esp
1.350 1.325 1.300 1.275
Chemical Shift (ppm)
F F
CO2Et
1H NMR
1.000
3.059
2.002
0.969
2.118
3.171
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


naphthal ester_C.001.001.1r.esp
164.5360
164.2255
163.9150
134.2430
132.4160
130.0204
129.8156
128.7317
127.7841
127.6855
126.8723
125.7524
125.6918
121.9468
121.9013
115.5789
113.5776
111.5687
77.2502
77.0000
76.7423
63.1725
13.8819
F F
CO2Et
13C NMR
CF2
Chemical Shift (ppm)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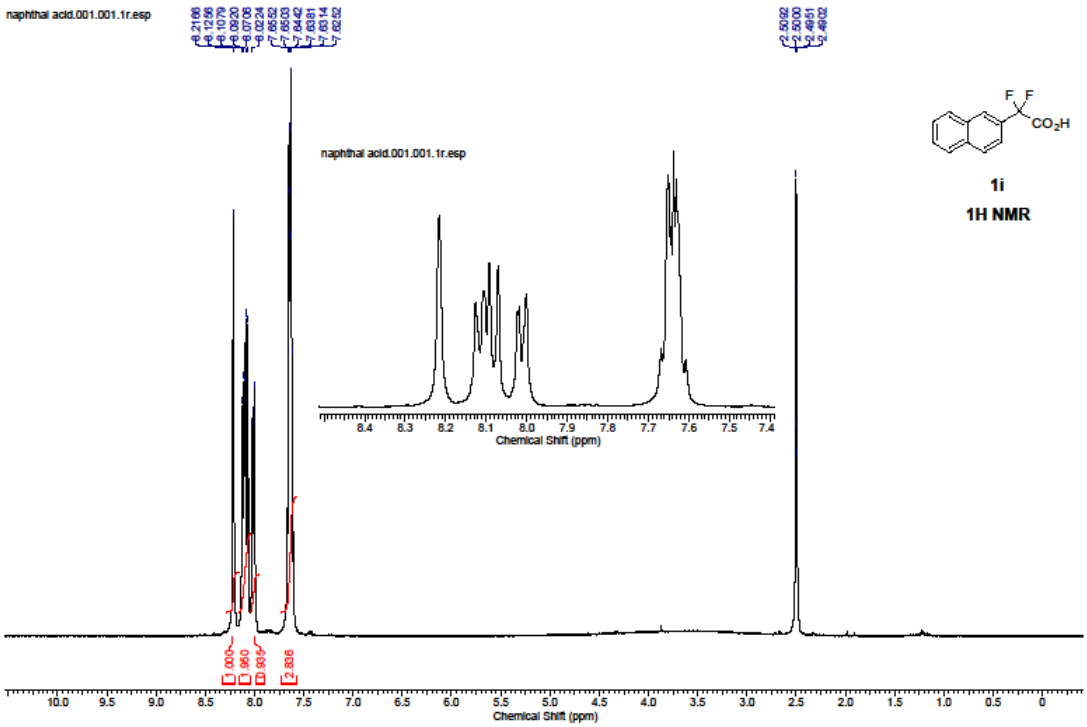
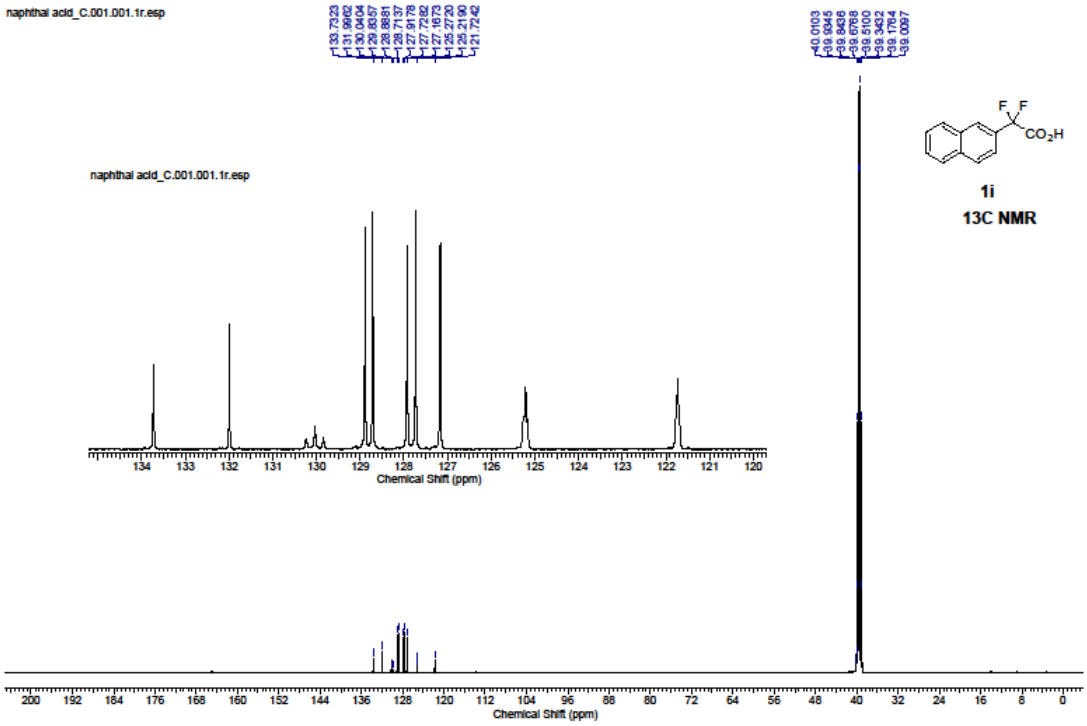
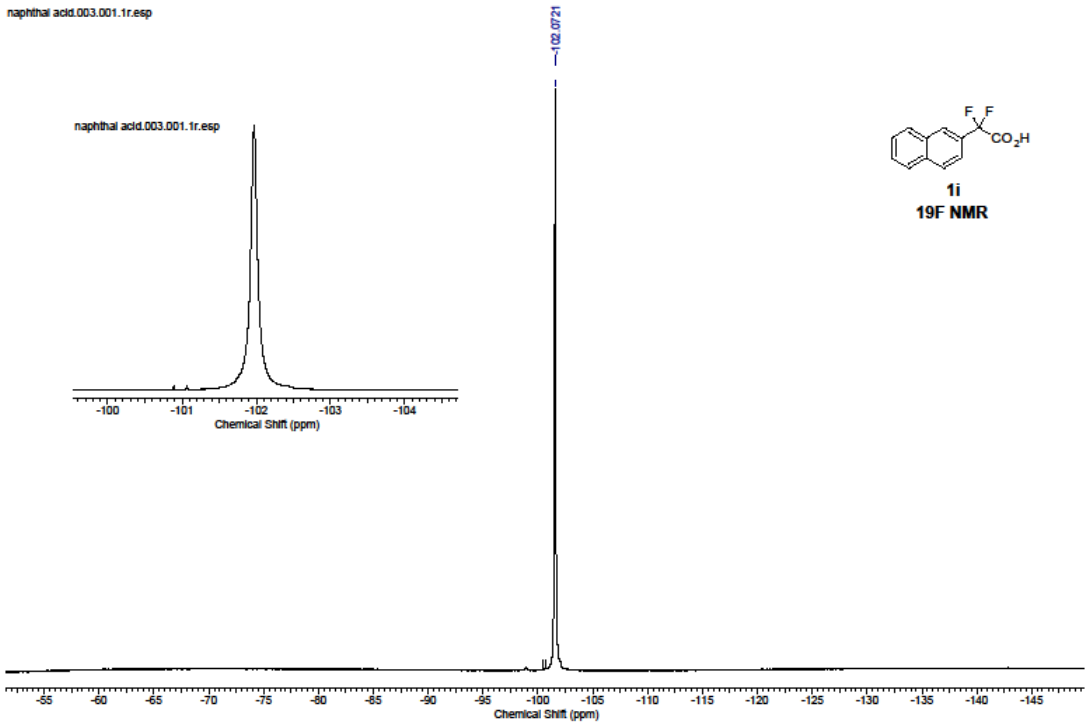
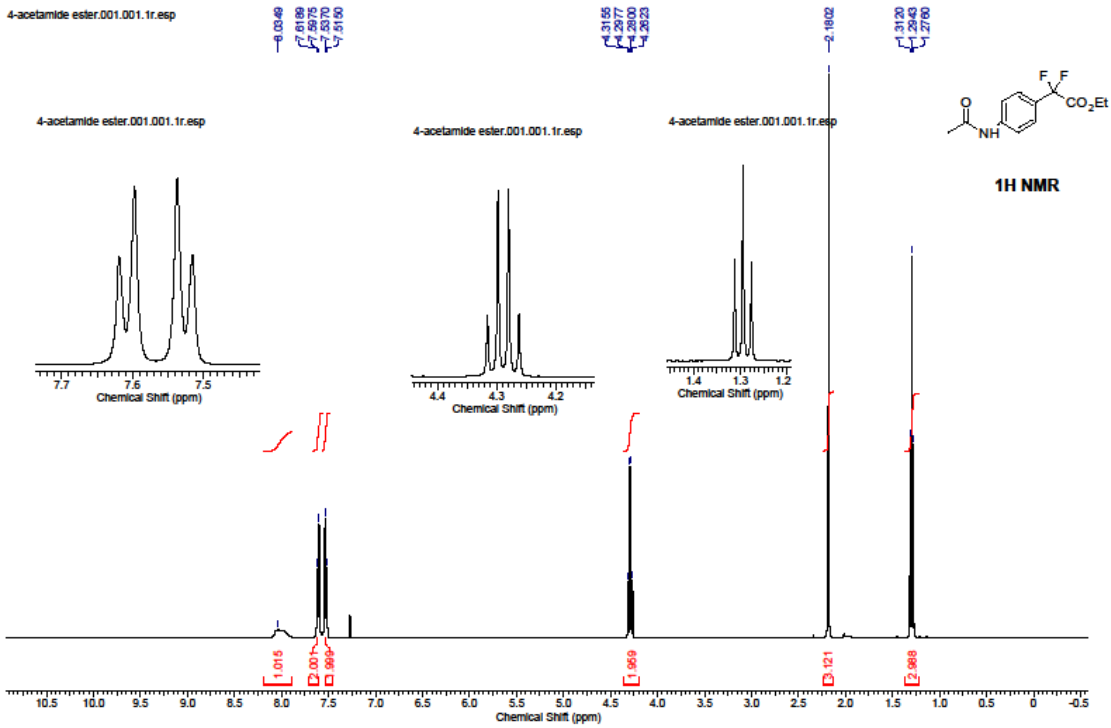
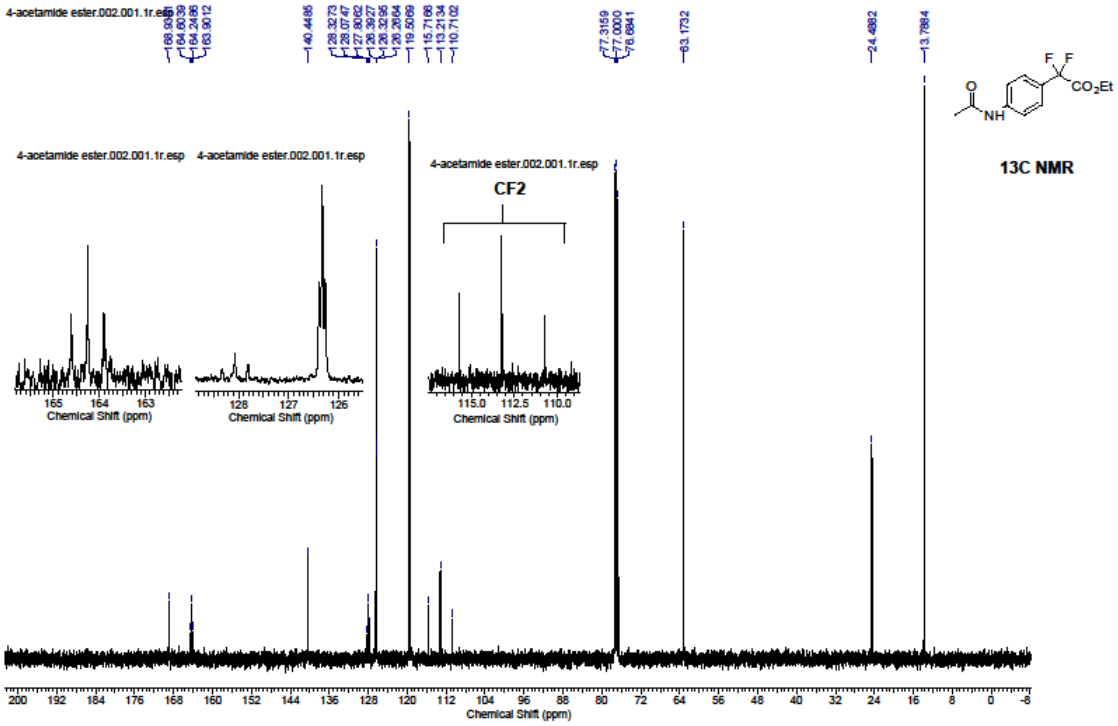
-103.5793
F F
CO2Et
19F NMR
Chemical Shift (ppm)

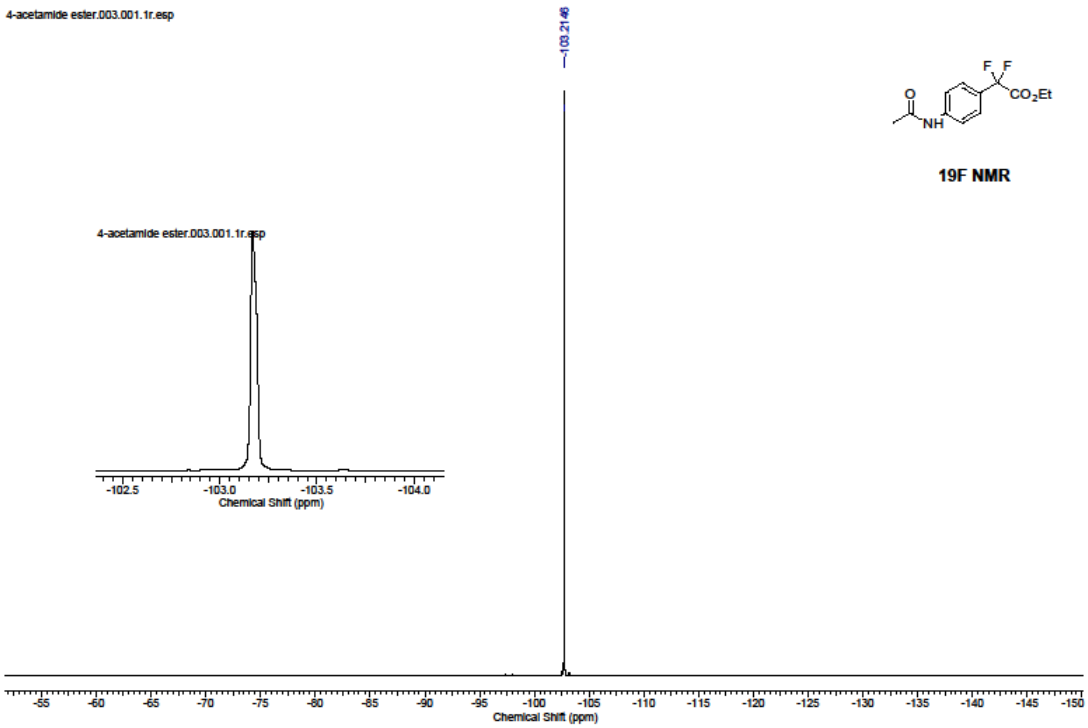

naphthal acid.001.001.1r.esp
naphthal acid.001.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
1i
1H NMR


naphthal acid_C.001.001.1r.esp
naphthal acid_C.001.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
1i
13C NMR


naphthal acid.003.001.1r.esp
-102.0721
naphthal acid.003.001.1r.esp
F F
CO2H
1i
19F NMR
Chemical Shift (ppm)


4-acetamide ester.001.001.1r.esp
8.0349
7.6189
7.6075
7.5370
7.5150
4.3155
4.2977
4.2800
4.2623
2.1802
1.3120
1.2943
1.2760
4-acetamide ester.001.001.1r.esp
4-acetamide ester.001.001.1r.esp
4-acetamide ester.001.001.1r.esp
F F
CO2Et
O
NH
1H NMR
1.015
2.001
0.998
1.959
3.121
2.988
Chemical Shift (ppm)


4-acetamide ester.002.001.1r.esp
CF2
Chemical Shift (ppm)
13C NMR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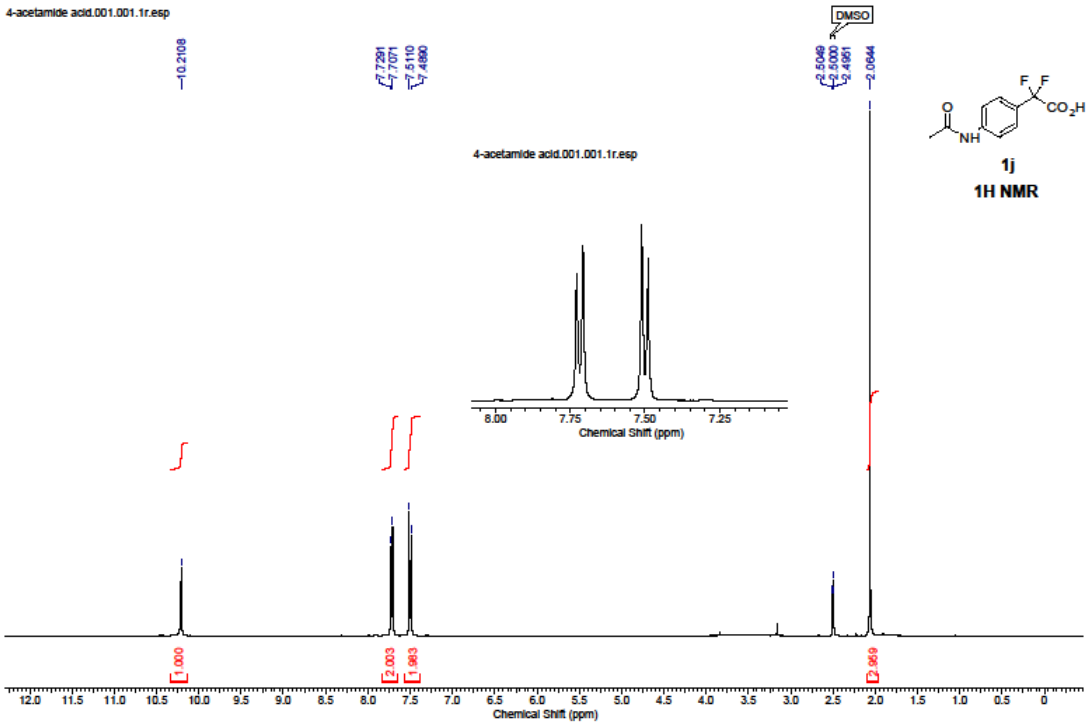
-103.2146
Chemical Shift (ppm)
19F NMR


4-acetamide acid.001.001.1r.esp
DMSO
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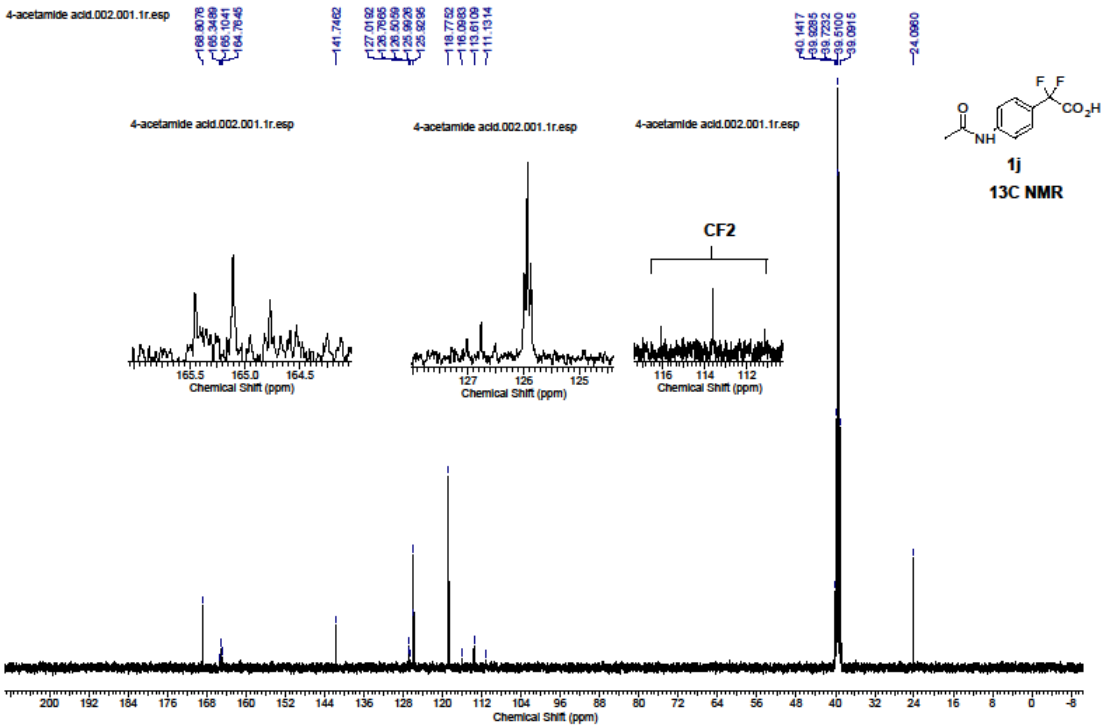
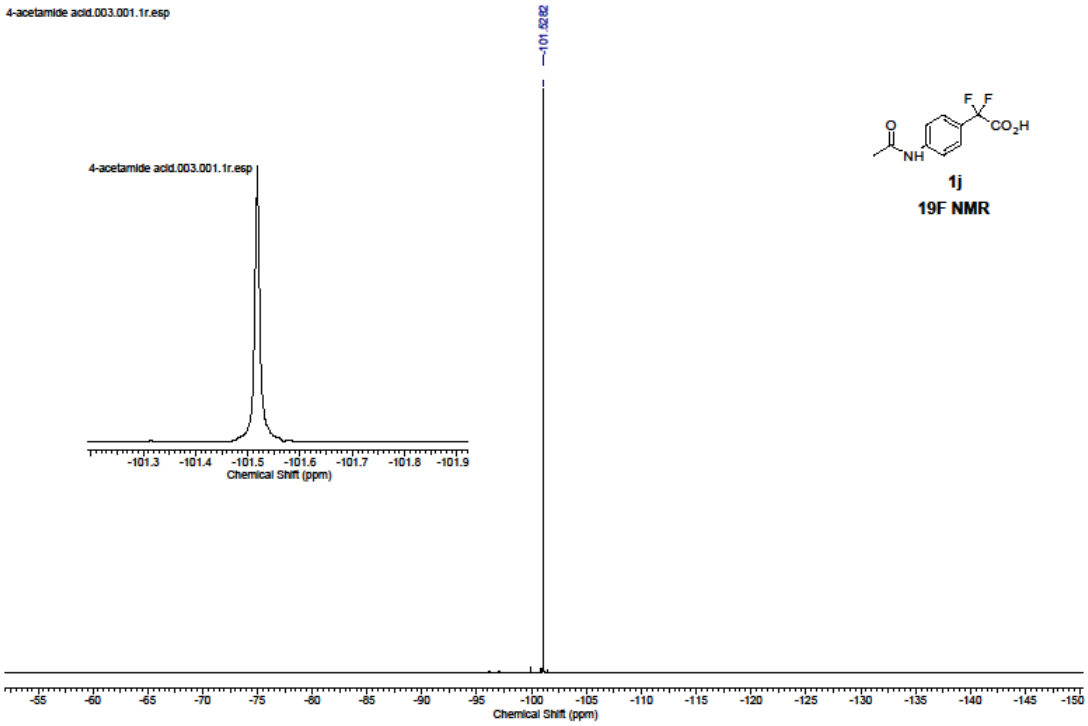
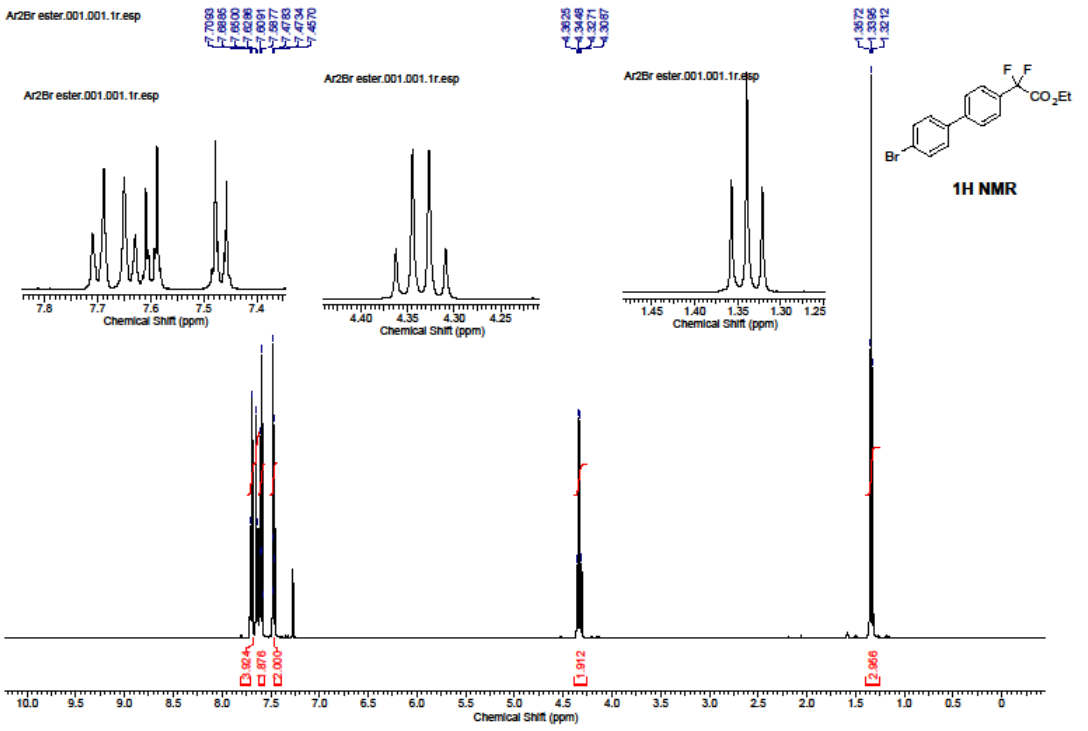
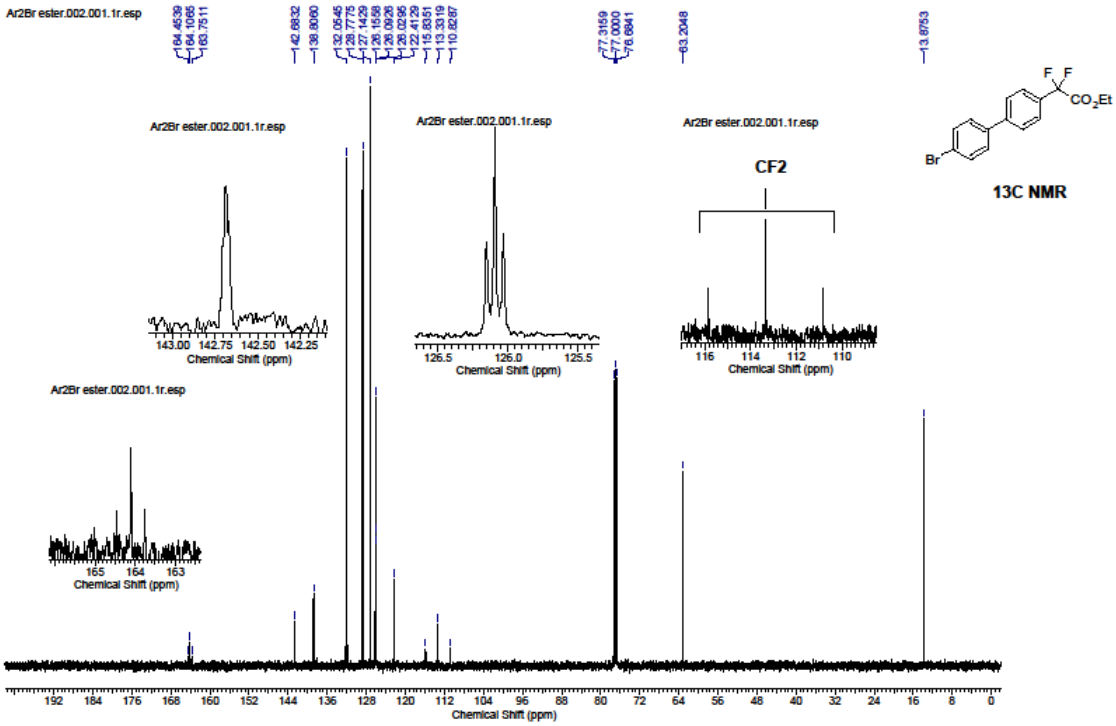
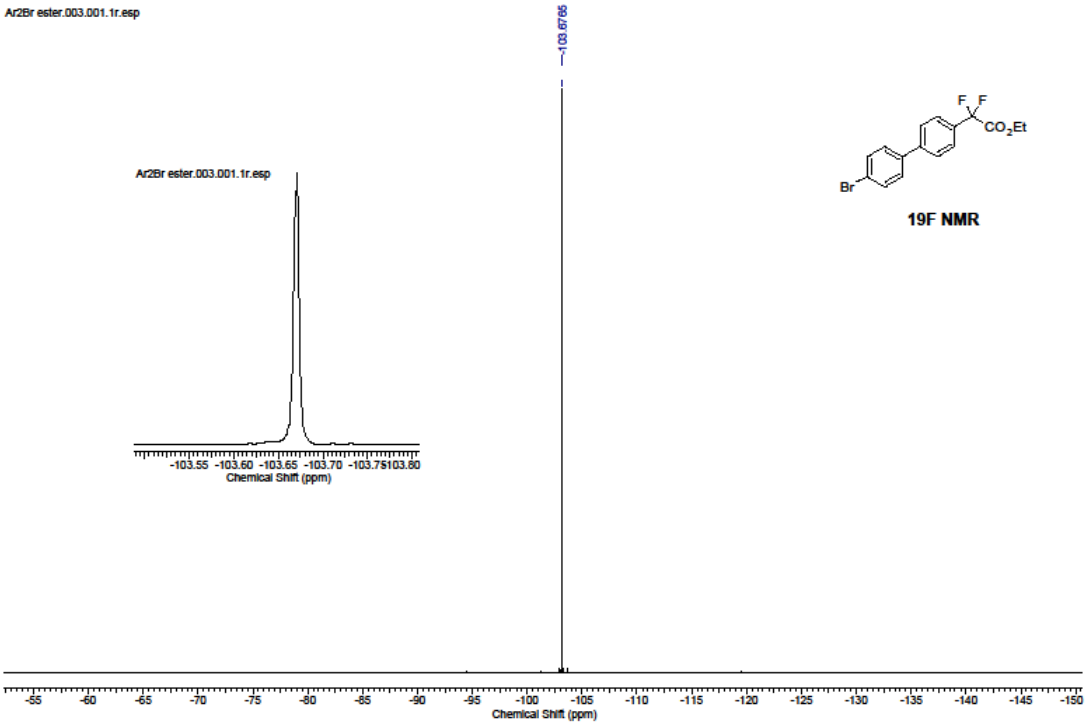
7.7291
7.7071
7.5110
7.4880
2.5049
2.5000
2.4951
2.0644
1.000
2.003
1.983
2.959
Chemical Shift (ppm)
1j
1H NMR

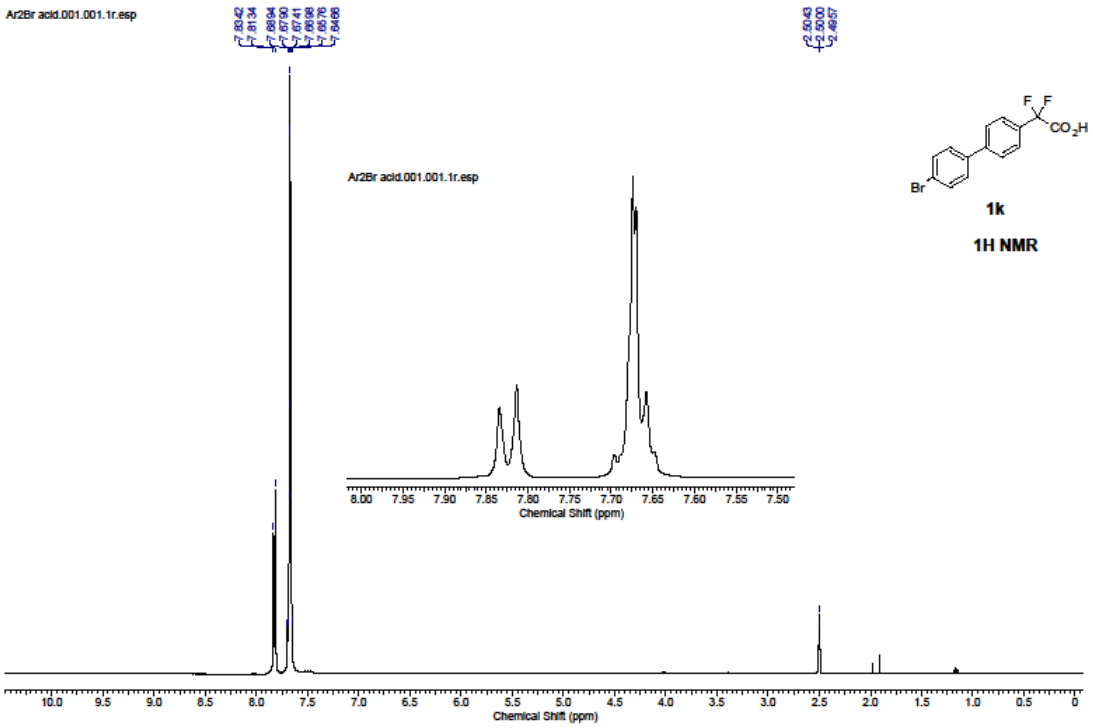

4-acetamide acid.002.001.1r.esp
168.9078
166.3469
166.1041
164.7845
141.7462
127.0192
126.7765
126.5099
125.9938
125.9295
118.7752
116.0983
113.6109
111.1314
40.1417
39.9285
39.7232
39.5100
39.0915
24.0960
CF2
Chemical Shift (ppm)
1j
13C NMR

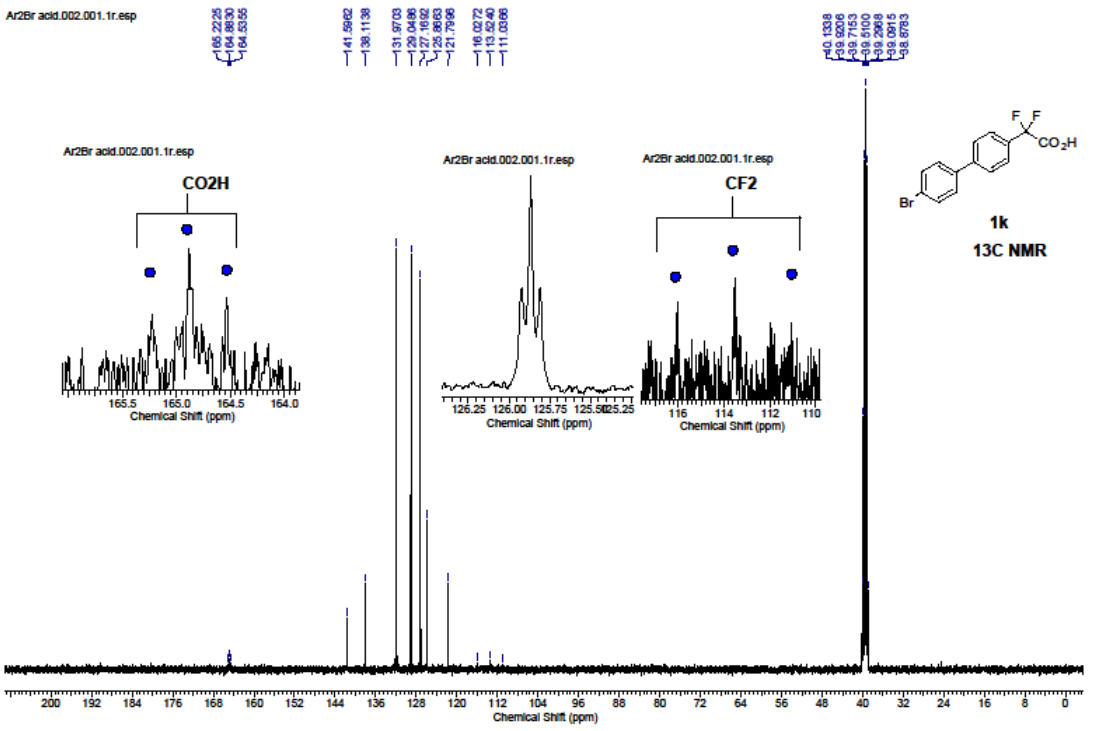

4-acetamide acid.003.001.1r.esp
-101.5282
4-acetamide acid.003.001.1r.esp
-101.3 -101.4 -101.5 -101.6 -101.7 -101.8 -101.9
Chemical Shift (ppm)
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
Chemical Shift (ppm)
F F
CO2H
O
NH
1j
19F NMR

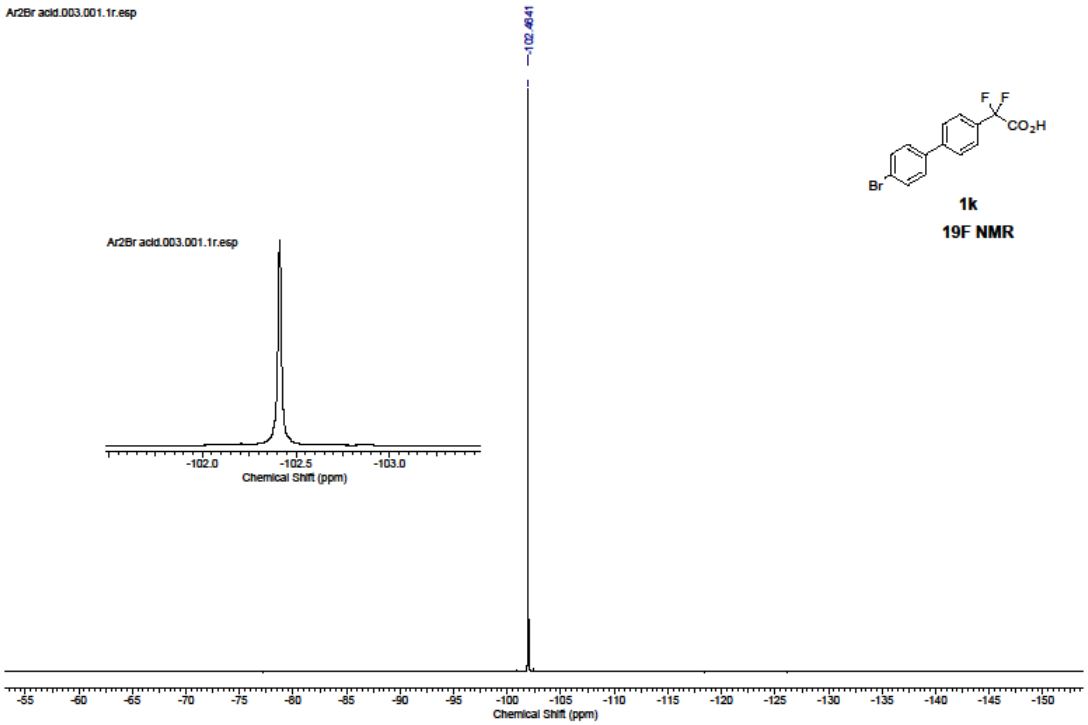

Ar2Br ester.001.001.1r.esp
7.7093
7.6885
7.6500
7.6286
7.6091
7.5877
7.4783
7.4734
7.4570
4.3625
4.3448
4.3271
4.3097
1.3672
1.3495
1.3312
Ar2Br ester.001.001.1r.esp
7.8 7.7 7.6 7.5 7.4
Chemical Shift (ppm)
Ar2Br ester.001.001.1r.esp
4.40 4.35 4.30 4.25
Chemical Shift (ppm)
Ar2Br ester.001.001.1r.esp
1.45 1.40 1.35 1.30 1.25
Chemical Shift (ppm)
3.924
3.876
2.000
1.912
2.866
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)
F F
CO2Et
Br
1H NMR

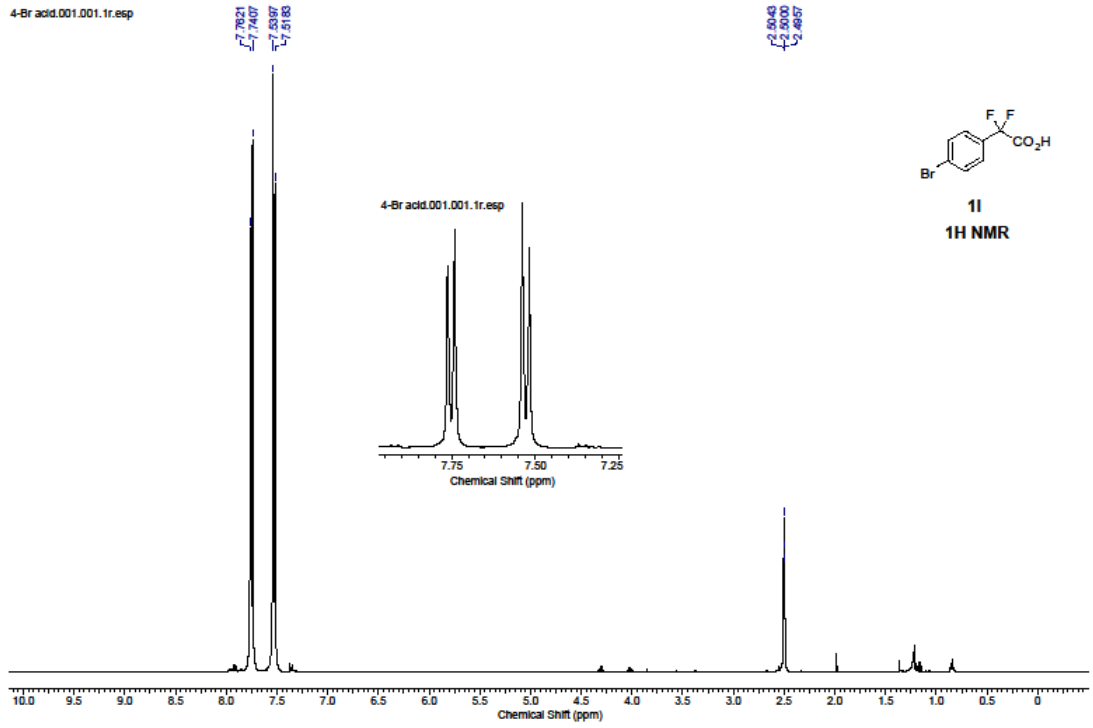

Ar2Br ester.002.001.1r.esp
CF2
13C NMR
Chemical Shift (ppm)

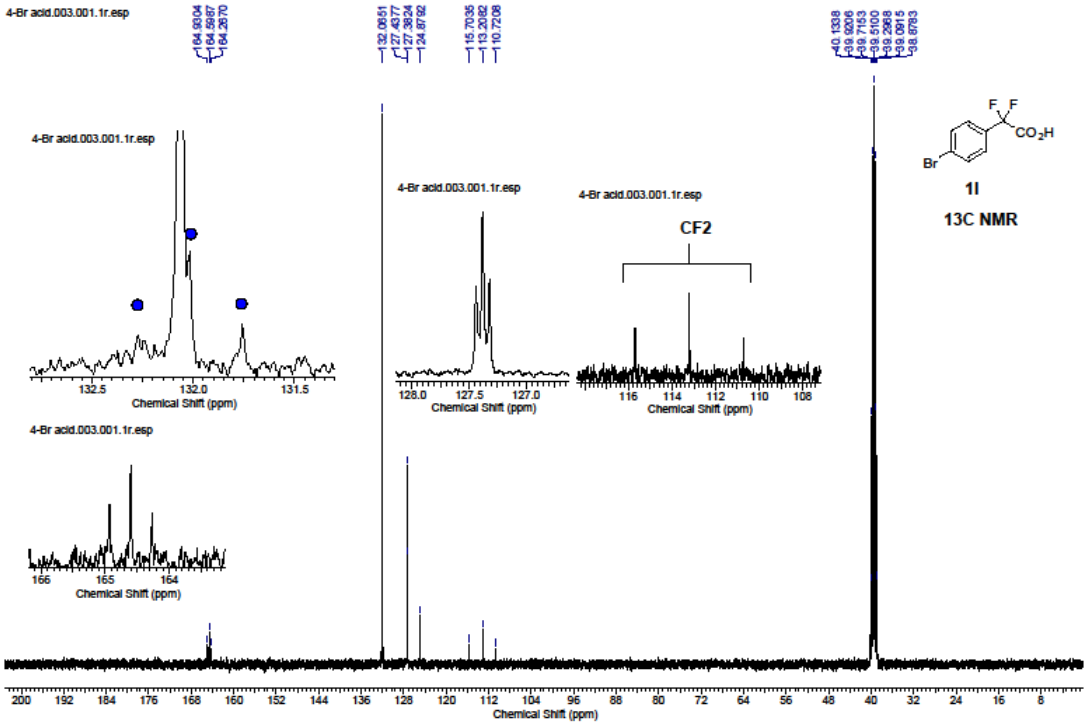

Ar2Br ester.003.001.1r.esp
19F NMR
Chemical Shift (ppm)

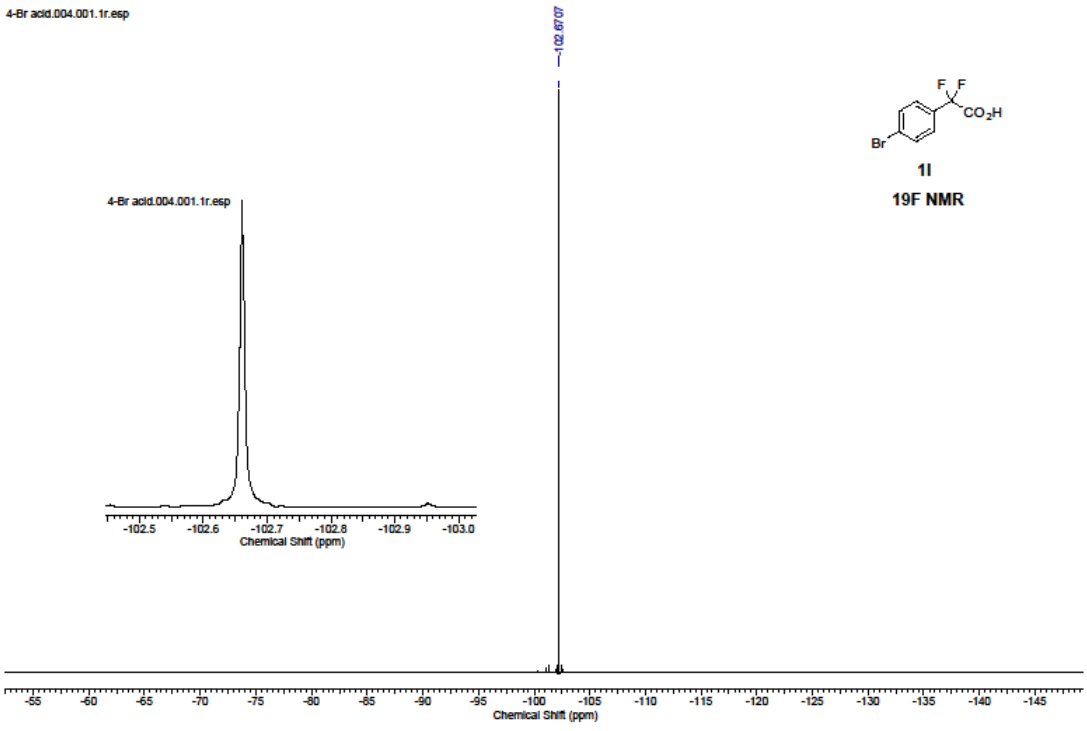

Ar2Br acid.001.001.1r.esp
Ar2Br acid.001.001.1r.esp
Chemical Shift (ppm)
1k
1H NMR

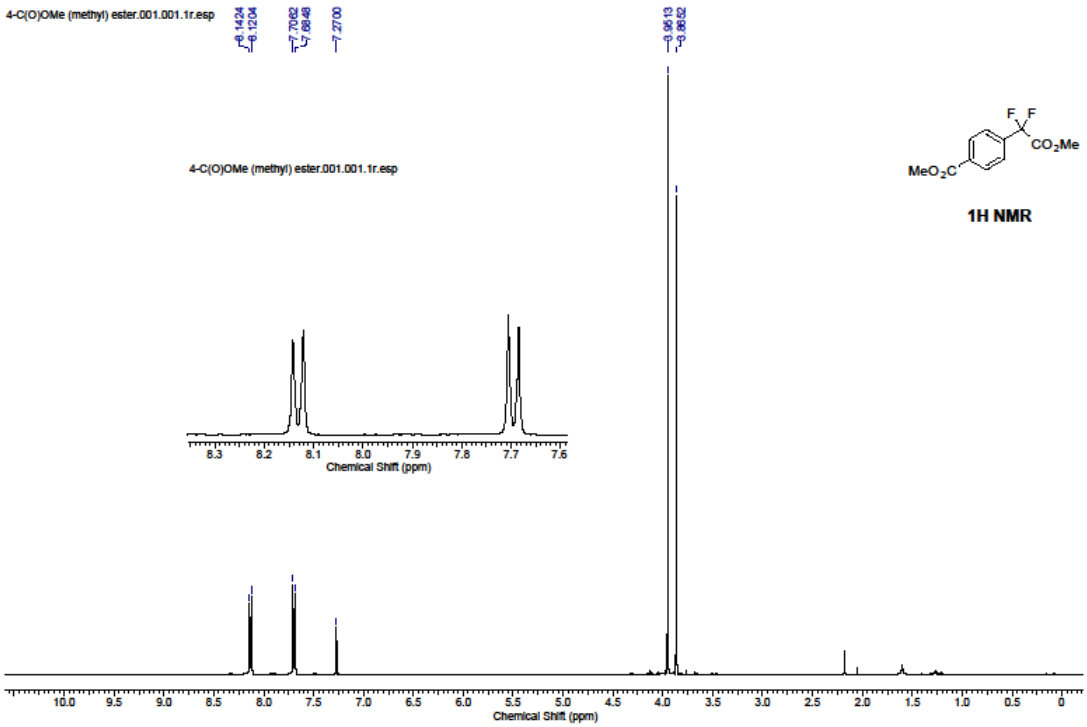

Ar2Br acid.002.001.1r.esp
CO2H
CF2
Chemical Shift (ppm)
1k
13C NMR

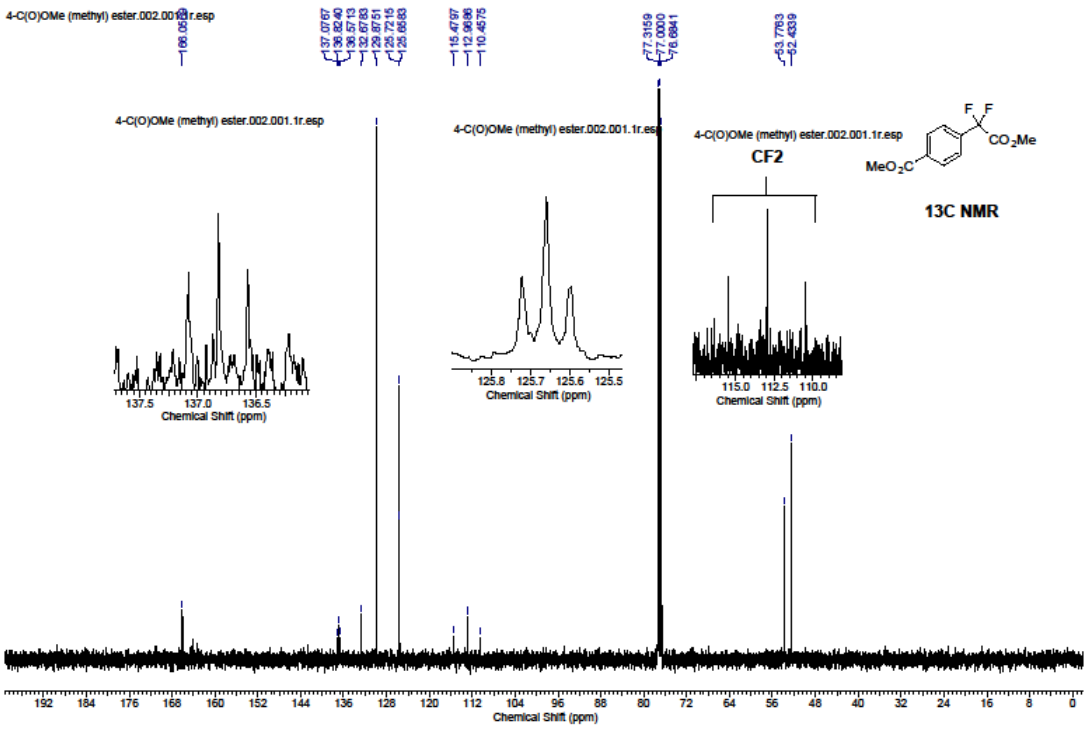

Ar2Br acid.003.001.1r.esp
-102.4641
F F
CO2H
Br
1k
19F NMR
Ar2Br acid.003.001.1r.esp
-102.0
-102.5
-103.0
Chemical Shift (ppm)
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
Chemical Shift (ppm)

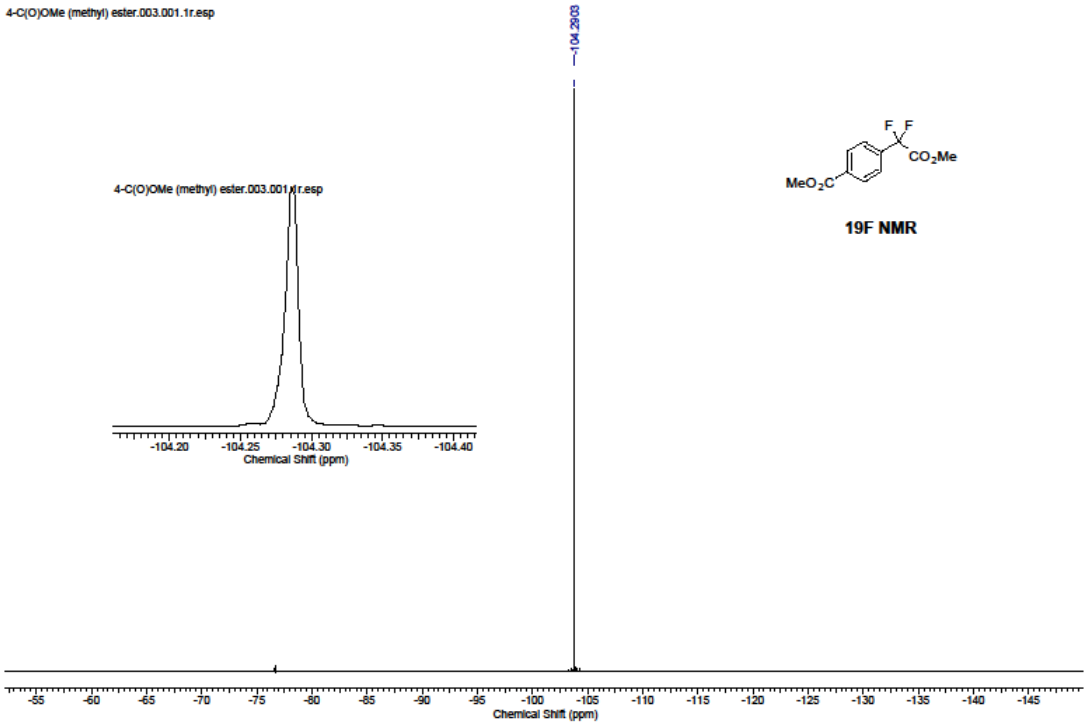

4-Br acid.001.001.1r.esp
7.7621
7.7407
7.5397
7.5183
2.5043
2.5000
2.4957
F F
CO2H
Br
1l
1H NMR
4-Br acid.001.001.1r.esp
7.75
7.50
7.25
Chemical Shift (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

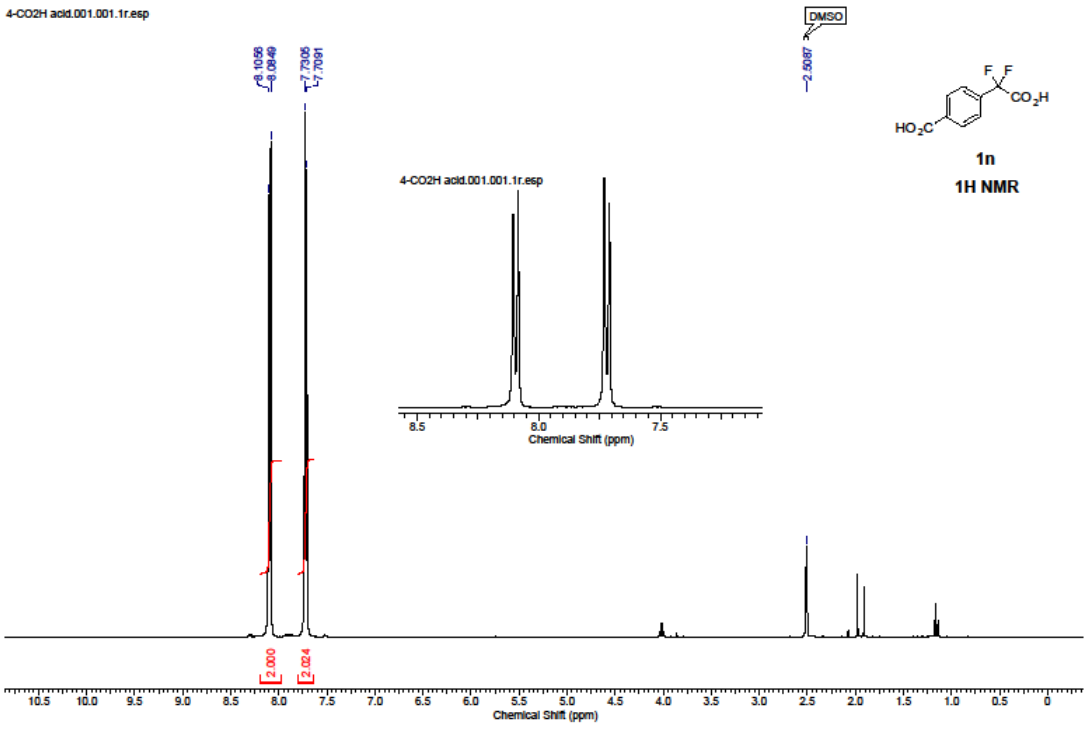

4-Br acid.003.001.1r.esp
164.9304
164.5987
164.2670
132.0651
127.4377
127.3974
124.6792
115.7035
113.2092
110.7208
40.1338
39.9206
39.7153
39.5100
39.2968
39.0915
38.8763
F F
CO2H
Br
1l
13C NMR
CF2
Chemical Shift (ppm)

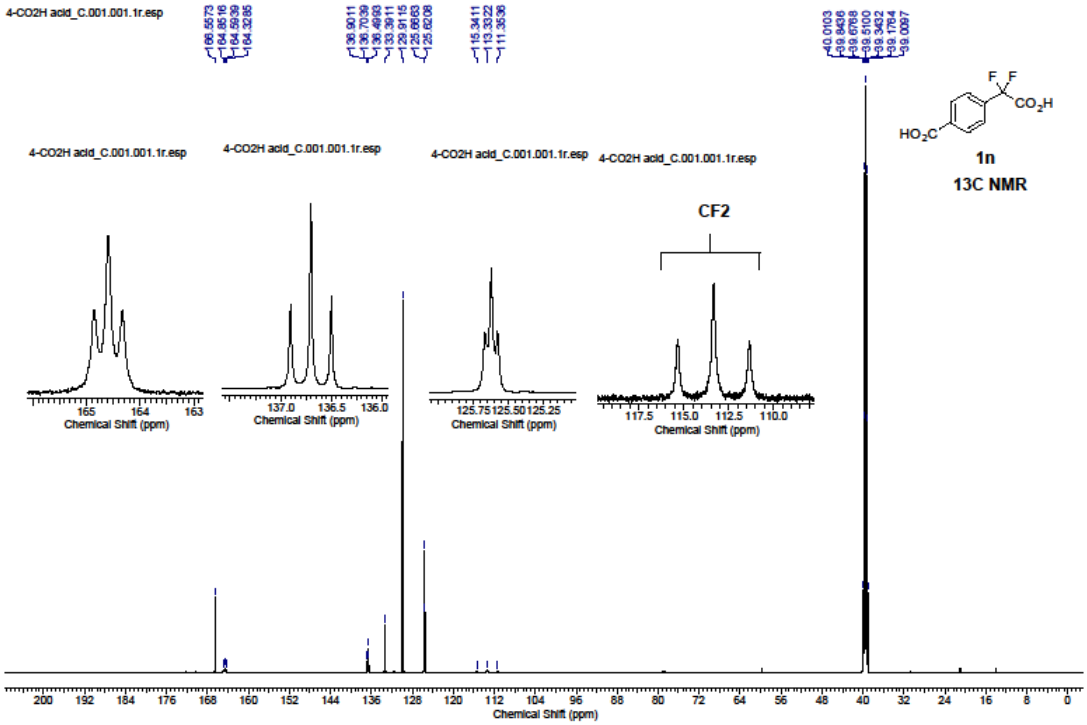

4-Br acid.004.001.1r.esp
-102.6707
F F
CO2H
Br
1l
19F NMR
Chemical Shift (ppm)

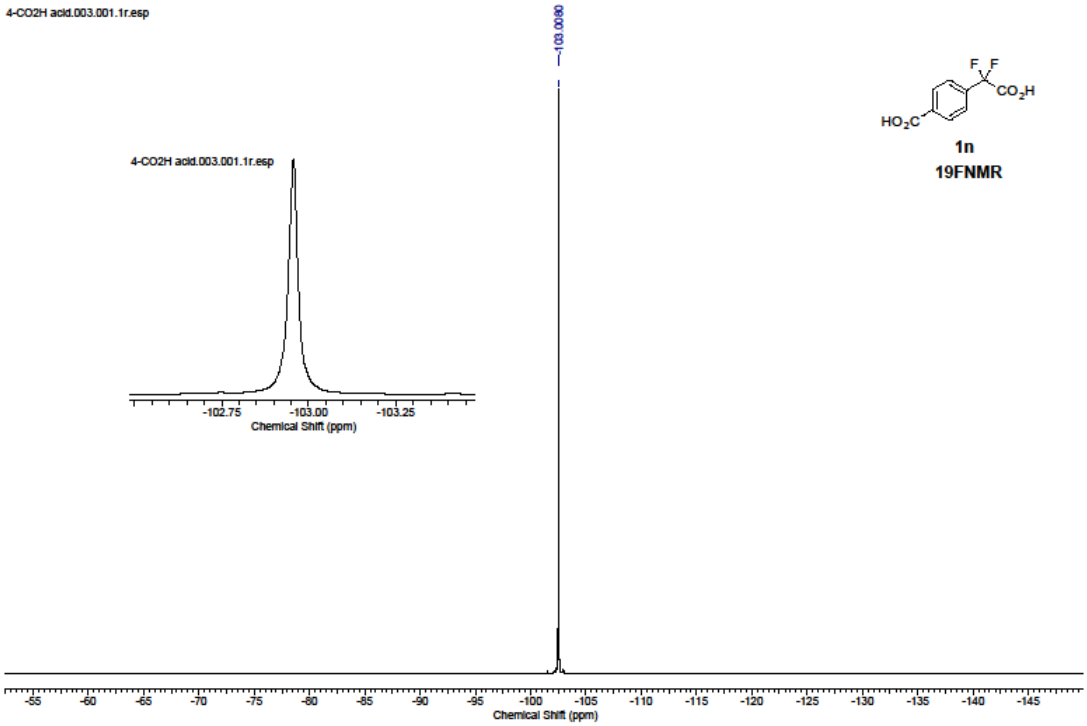

4-C(O)OMe (methyl) ester.001.001.1r.esp
8.1424
8.1204
7.7062
7.6848
7.2700
3.9613
3.8852
4-C(O)OMe (methyl) ester.001.001.1r.esp
Chemical Shift (ppm)
F F
CO2Me
MeO2C
1H NMR
Chemical Shift (ppm)

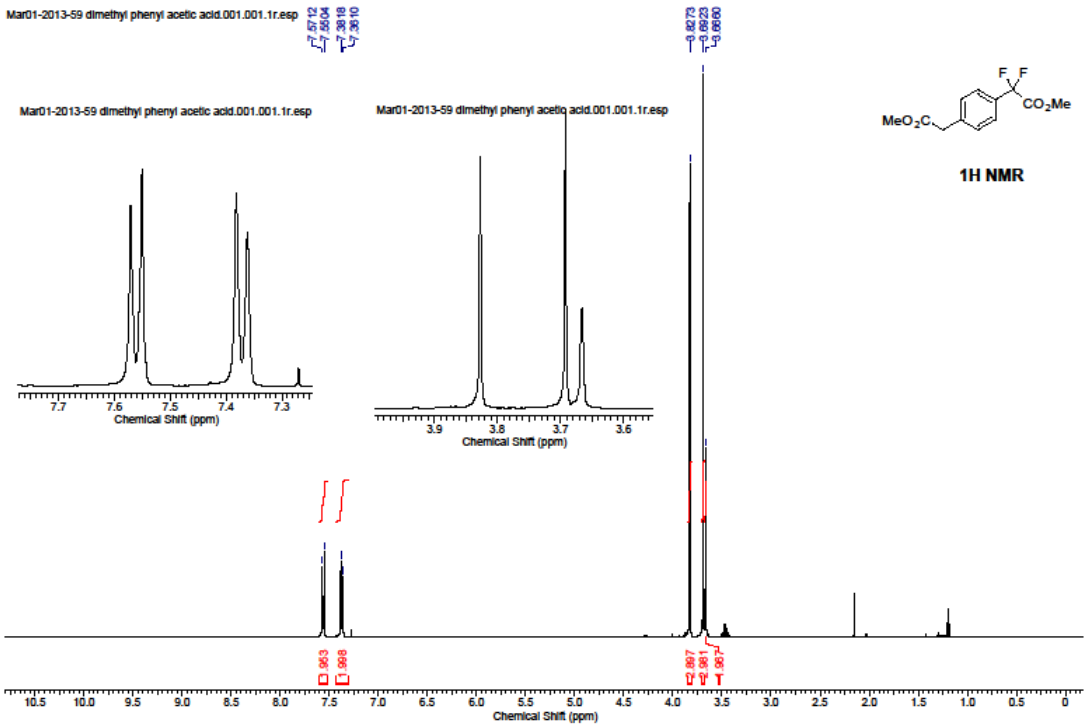

4-C(O)OMe (methyl) ester.002.001.1r.esp
166.0529
137.0767
136.8240
136.5713
132.6783
129.8751
125.7215
125.6683
115.4797
112.3696
110.4575
77.3159
77.0000
76.6841
53.7763
52.4339
4-C(O)OMe (methyl) ester.002.001.1r.esp
Chemical Shift (ppm)
4-C(O)OMe (methyl) ester.002.001.1r.esp
Chemical Shift (ppm)
4-C(O)OMe (methyl) ester.002.001.1r.esp
CF2
Chemical Shift (ppm)
F F
CO2Me
MeO2C
13C NMR
Chemical Shift (ppm)

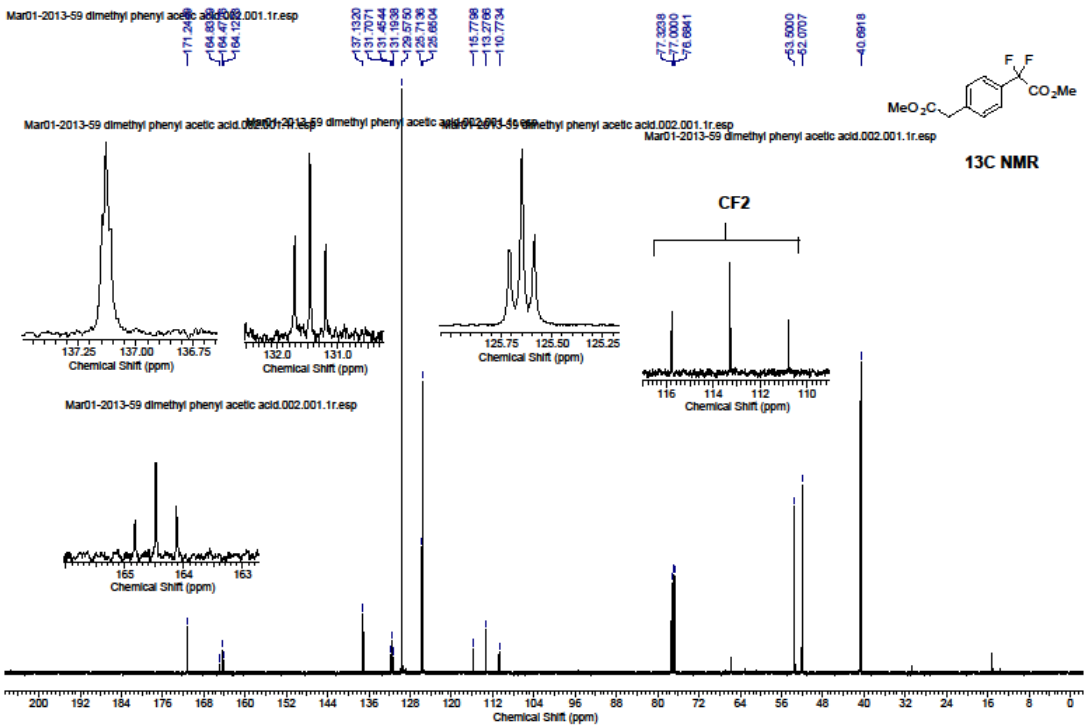

4-C(O)OMe (methyl) ester.003.001.1r.esp
-104.2903
4-C(O)OMe (methyl) ester.003.001.1r.esp
-104.20
-104.25
-104.30
-104.35
-104.40
Chemical Shift (ppm)
F F
CO2Me
MeO2C
19F NMR
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
Chemical Shift (ppm)

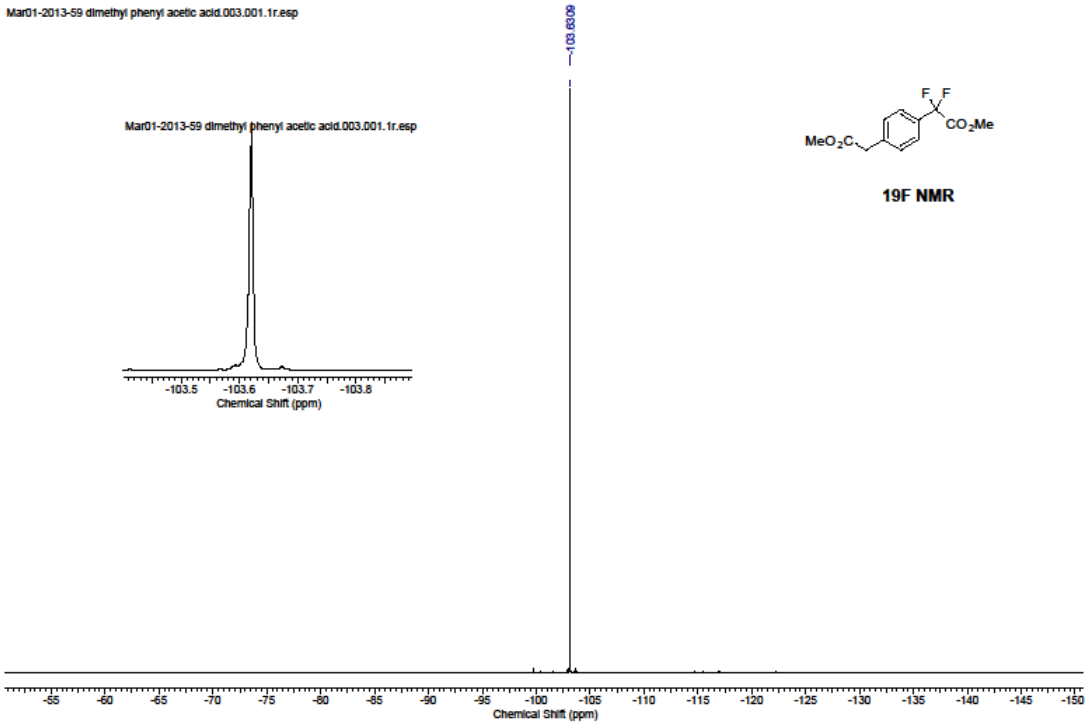

4-CO2H acid.001.001.1r.esp
8.1056
8.0849
7.7305
7.7091
DMSO
2.5087
4-CO2H acid.001.001.1r.esp
8.5
8.0
7.5
Chemical Shift (ppm)
F F
CO2H
HO2C
1n
1H NMR
2.000
2.024
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

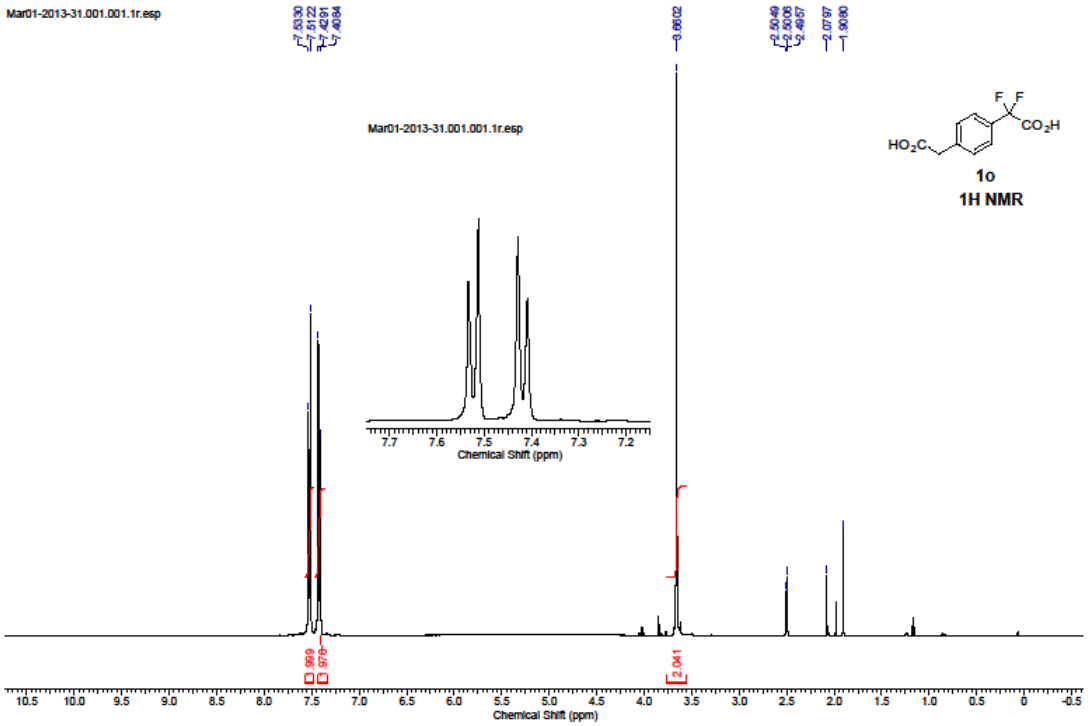

4-CO2H acid_C.001.001.1r.esp
CF2
1n
13C NMR
Chemical Shift (ppm)

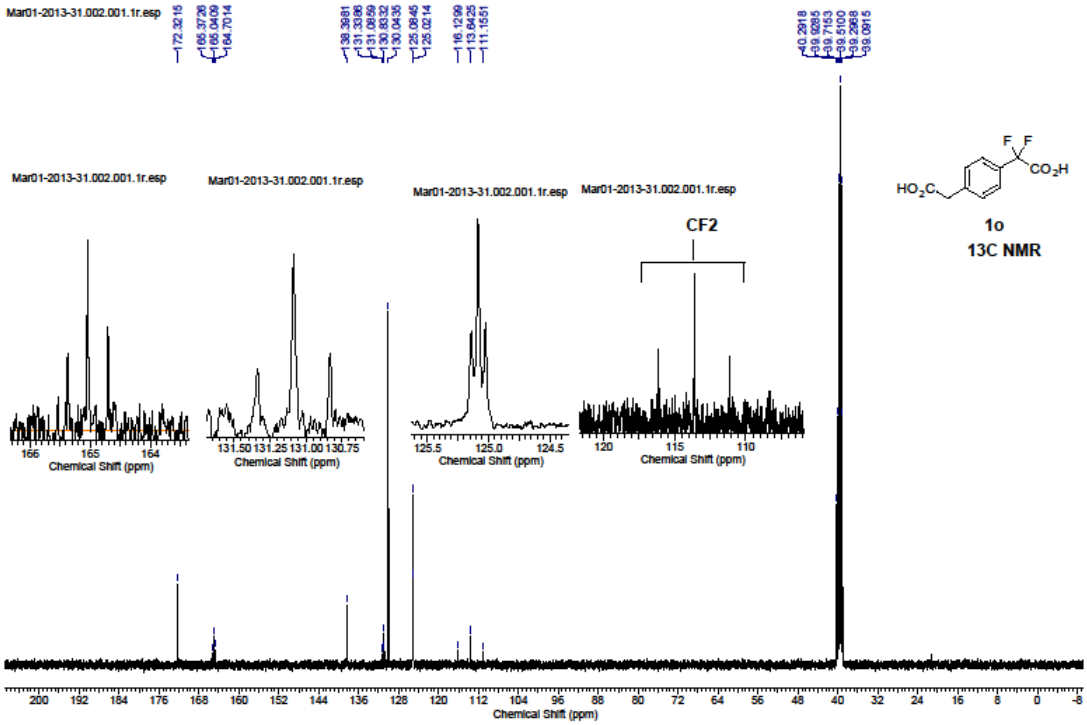

4-CO2H acid.003.001.1r.esp
1n
19FNMR
Chemical Shift (ppm)

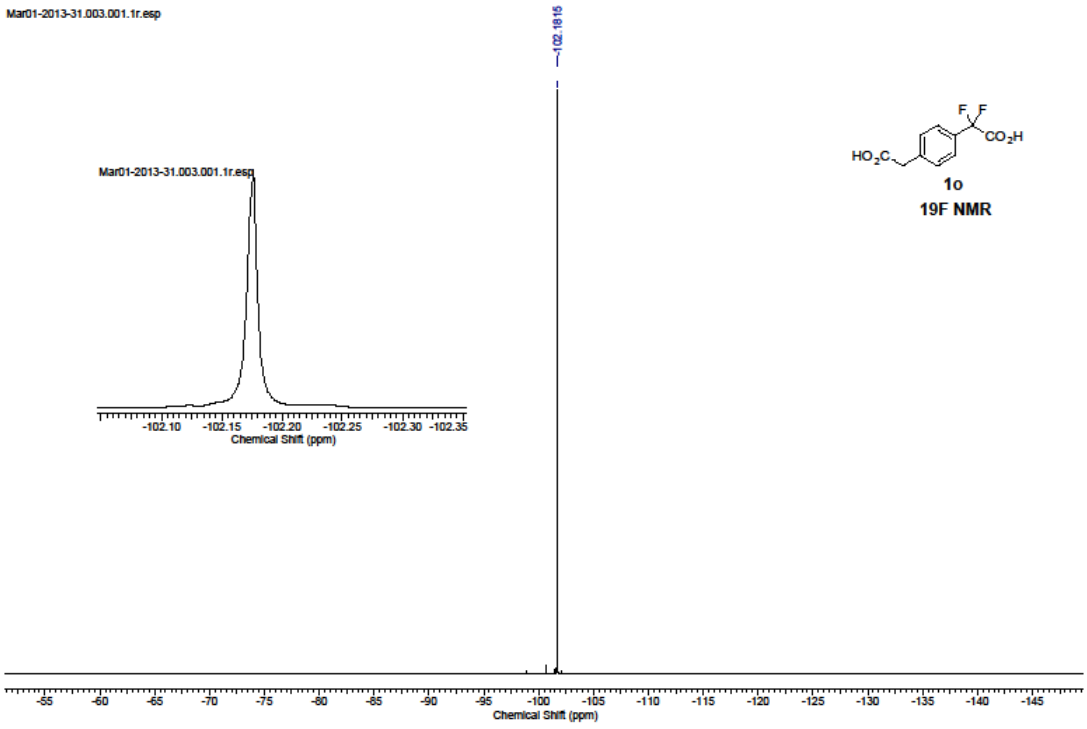

Mar01-2013-59 dimethyl phenyl acetic acid.001.001.1r.esp
1H NMR
Chemical Shift (ppm)

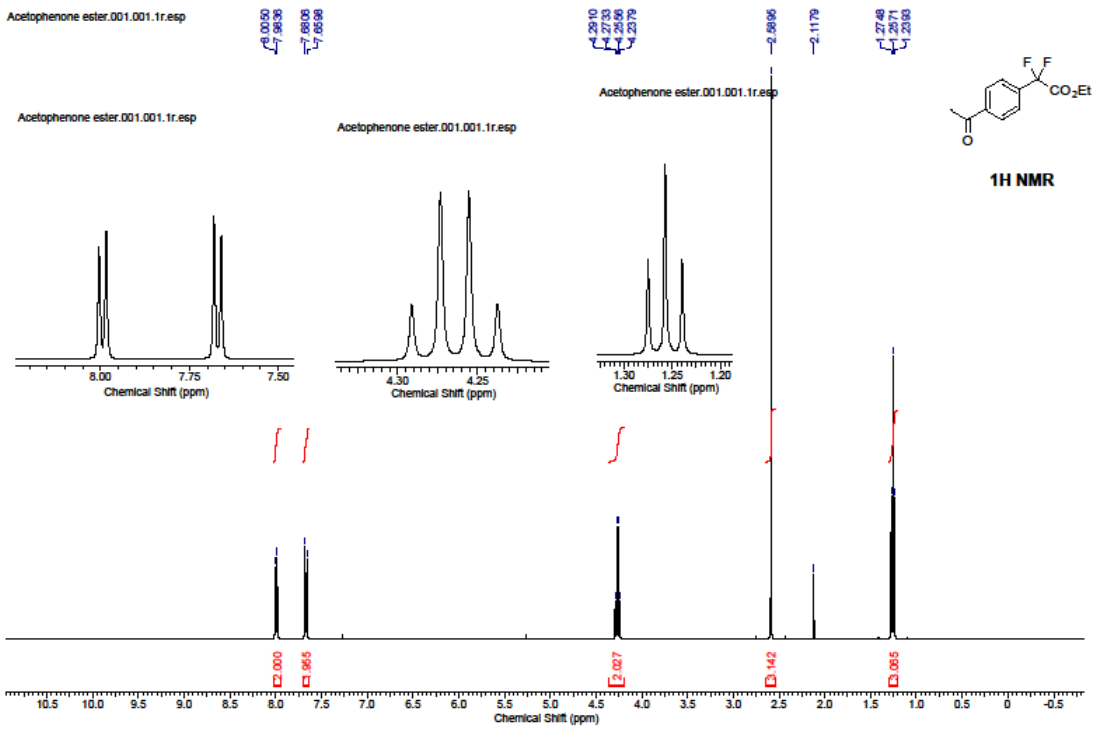

Mar01-2013-59 dimethyl phenyl acetic acid.002.001.1r.esp
13C NMR
CF2
Chemical Shift (ppm)

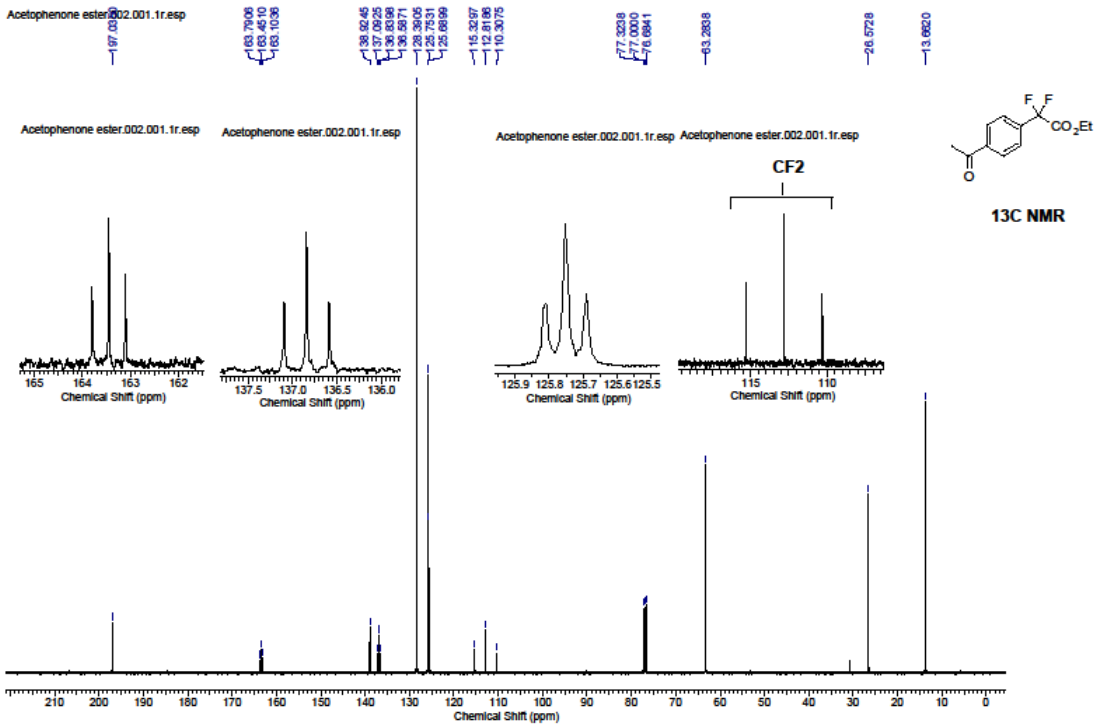

Mar01-2013-59 dimethyl phenyl acetic acid.003.001.1r.esp
-103.6309
Mar01-2013-59 dimethyl phenyl acetic acid.003.001.1r.esp
-103.5
-103.6
-103.7
-103.8
Chemical Shift (ppm)
F F
CO2Me
MeO2C
19F NMR
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
Chemical Shift (ppm)

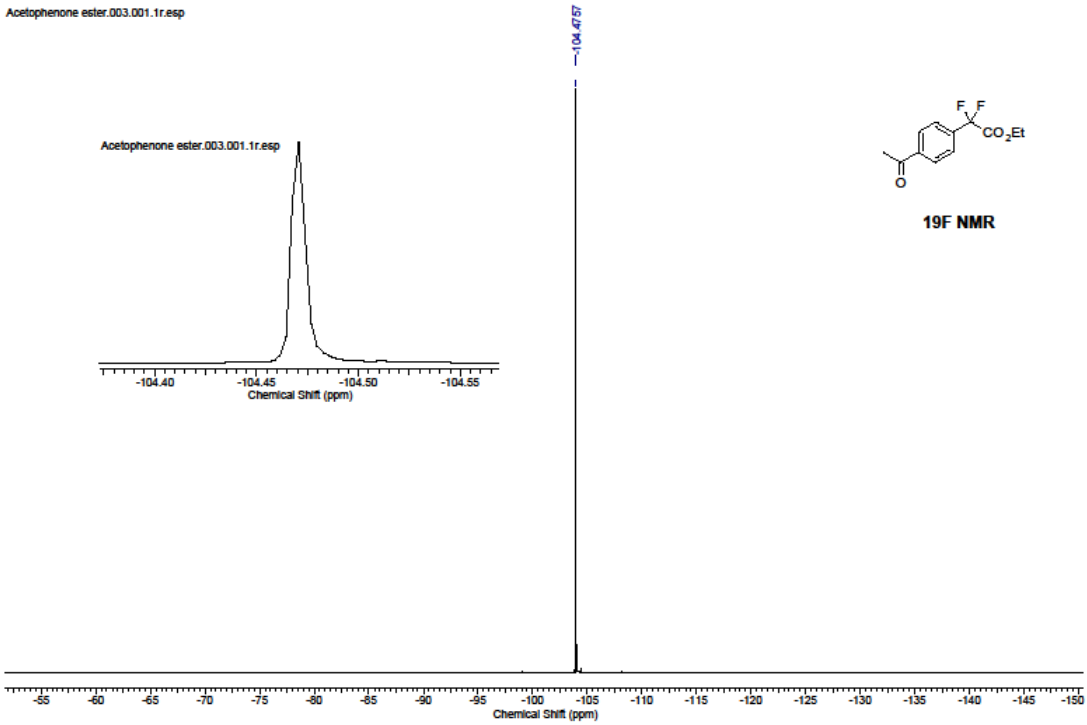

Mar01-2013-31.001.001.1r.esp
7.6330
7.6122
7.4291
7.4084
3.6602
3.5049
3.4906
3.4657
2.0797
1.9080
Mar01-2013-31.001.001.1r.esp
7.7
7.6
7.5
7.4
7.3
7.2
Chemical Shift (ppm)
F F
CO2H
HO2C
1o
1H NMR
0.999
0.976
2.041
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

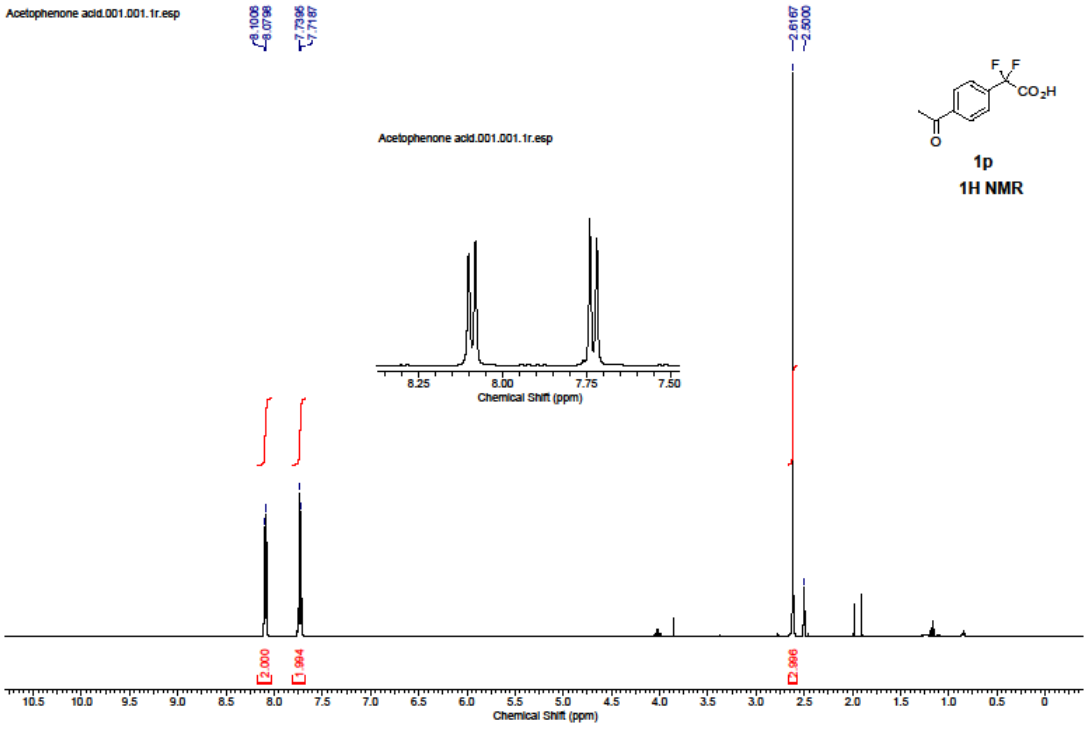

Mar01-2013-31.002.001.1r.esp
CF2
1o
13C NMR
Chemical Shift (ppm)

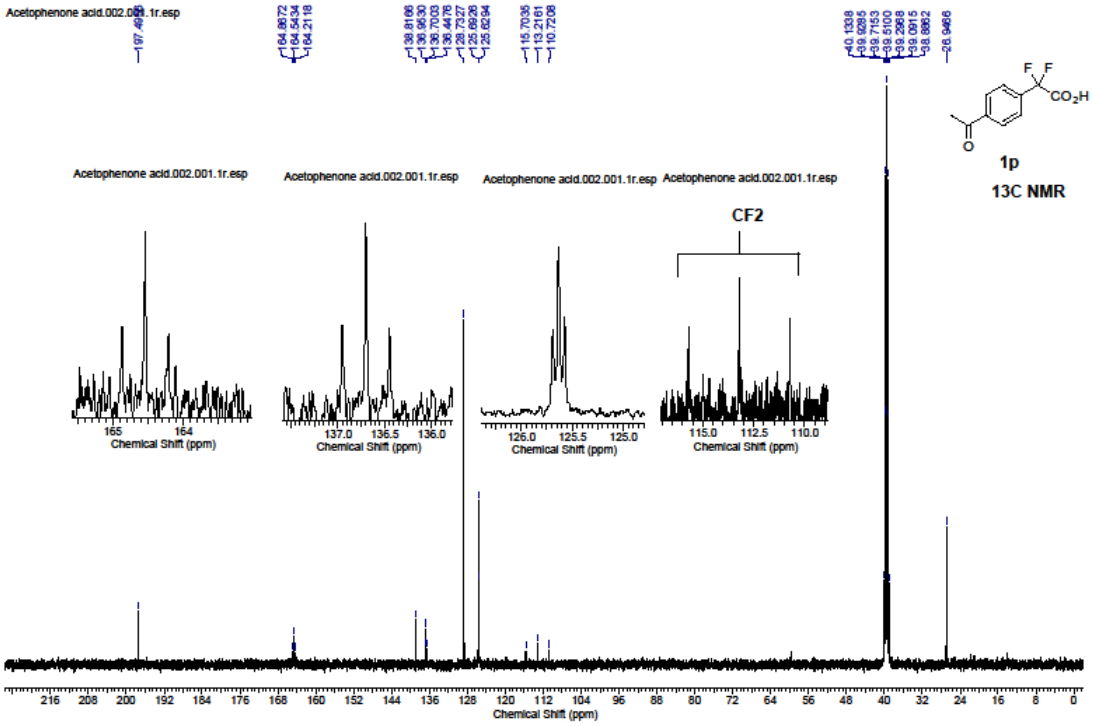

Mar01-2013-31.003.001.1r.esp
1o
19F NMR
Chemical Shift (ppm)

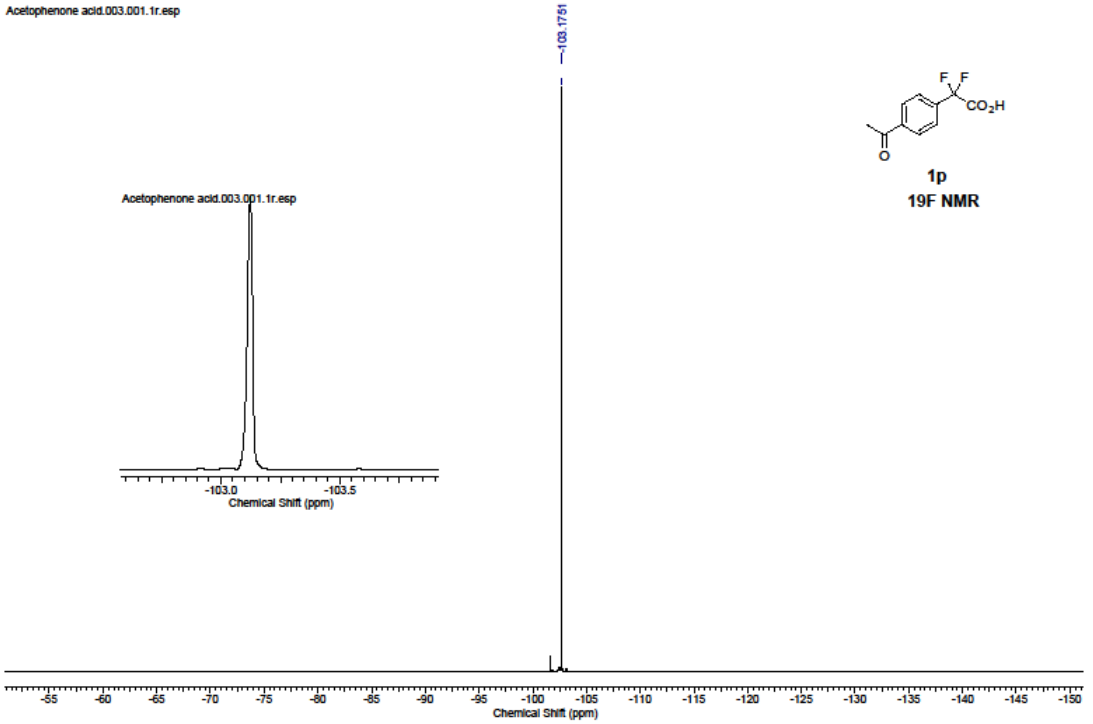

Acetophenone ester.001.001.1r.esp
8.0050
7.9836
7.8805
7.8598
4.2910
4.2713
4.2536
4.2379
2.5895
2.1179
1.2748
1.2571
1.2393
F F
CO2Et
O
1H NMR
Chemical Shift (ppm)
2.000
0.965
2.027
3.142
3.065

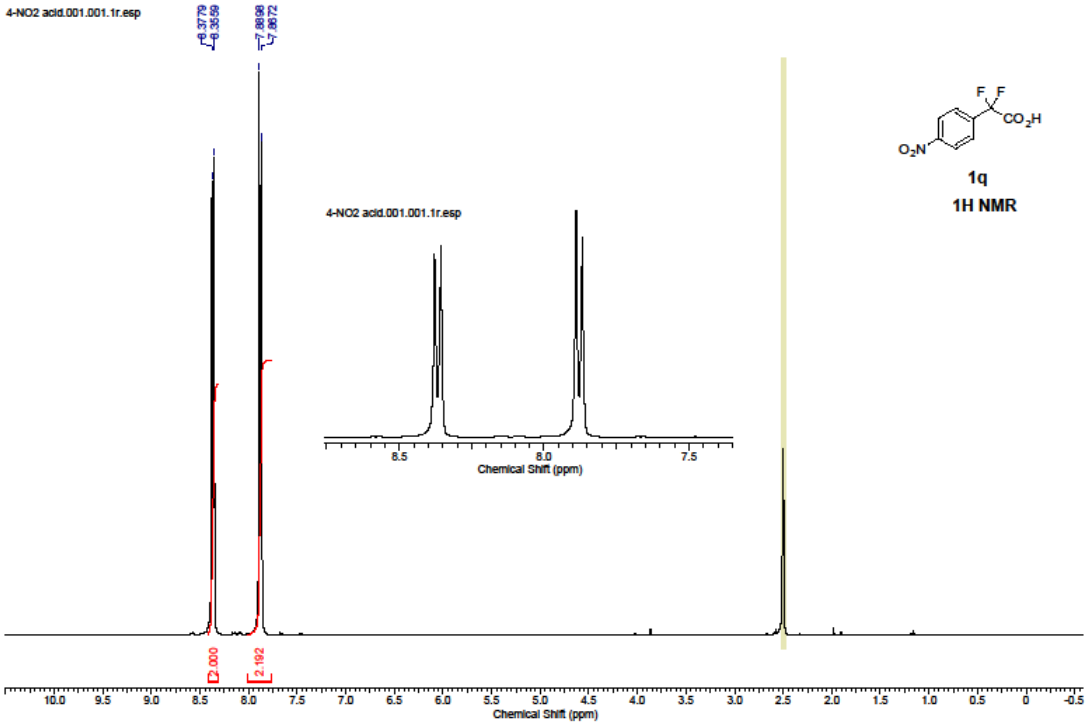

Acetophenone ester.002.001.1r.esp
197.0391
163.7906
163.4510
163.1036
138.9245
137.0925
136.8399
136.5871
128.3905
125.7531
125.6899
115.3297
112.8186
110.3075
77.3238
77.0000
76.6841
63.2838
26.5728
13.6820
F F
CO2Et
O
13C NMR
CF2
Chemical Shift (ppm)

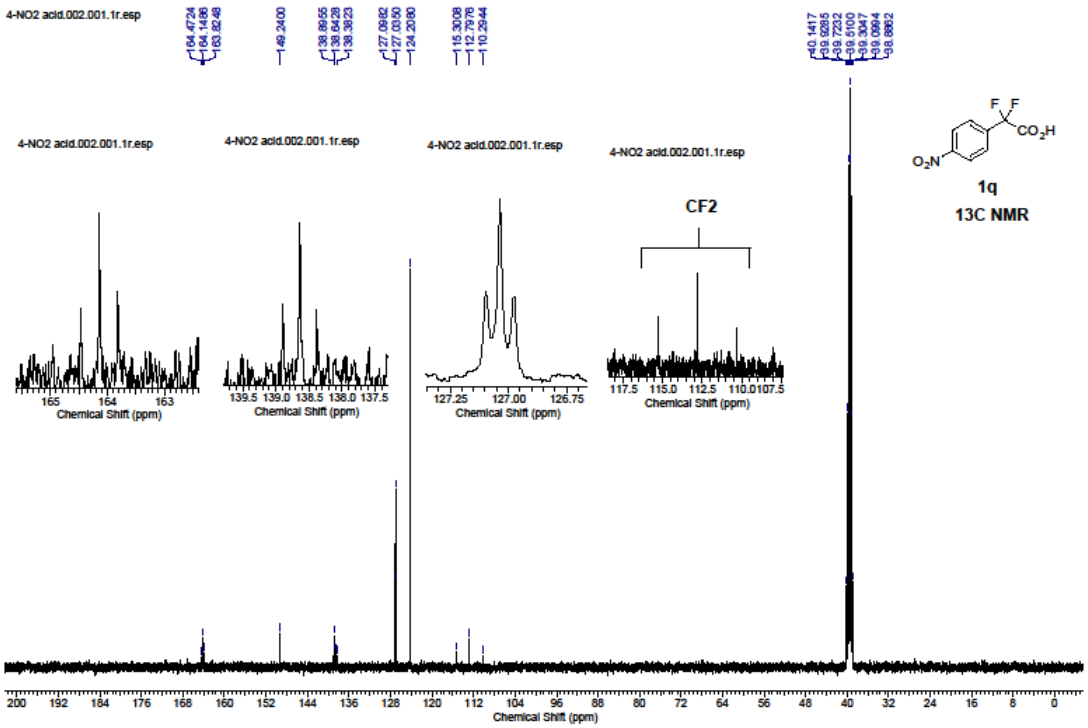

Acetophenone ester.003.001.1r.esp
-104.4757
Acetophenone ester.003.001.1r.esp
-104.40
-104.45
-104.50
-104.55
Chemical Shift (ppm)
F F
CO2Et
O
19F NMR
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
Chemical Shift (ppm)

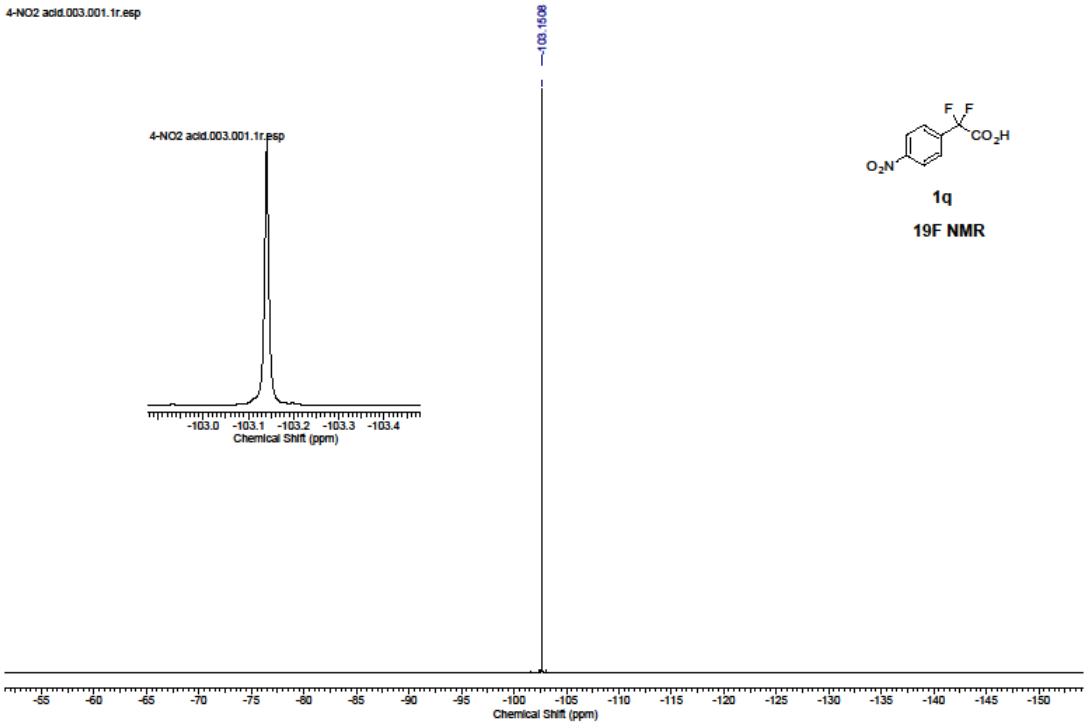

Acetophenone acid.001.001.1r.esp
8.1006
8.0798
7.7396
7.7187
2.6167
2.5000
Acetophenone acid.001.001.1r.esp
8.25
8.00
7.75
7.50
Chemical Shift (ppm)
F F
CO2H
O
1p
1H NMR
2.000
1.994
2.996
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


Acetophenone acid.002.001.1r.esp
CF2
1p
13C NMR
Chemical Shift (ppm)


Acetophenone acid.003.001.1r.esp
-103.1751
1p
19F NMR
Chemical Shift (ppm)

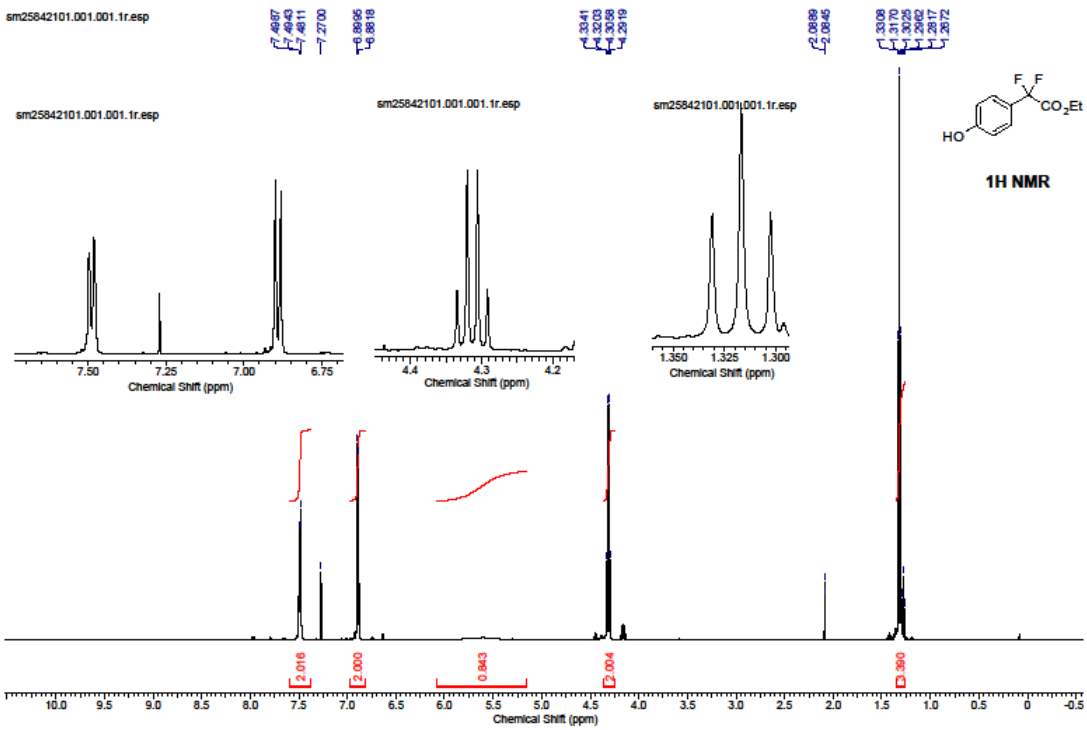

4-NO2 acid.001.001.1r.esp
8.3779
8.3559
7.8898
7.8672
4-NO2 acid.001.001.1r.esp
8.5
8.0
7.5
Chemical Shift (ppm)
F F
CO2H
O2N
1q
1H NMR
2.000
2.192
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


4-NO2 acid.002.001.1r.esp
164.4724
164.1486
163.8248
149.2400
138.8955
138.6428
138.3823
127.0982
127.0350
124.2060
115.3008
112.7976
110.2944
40.1417
39.9285
39.7232
39.5100
39.3047
39.0994
38.8862
4-NO2 acid.002.001.1r.esp
165 164 163
Chemical Shift (ppm)
4-NO2 acid.002.001.1r.esp
139.5 139.0 138.5 138.0 137.5
Chemical Shift (ppm)
4-NO2 acid.002.001.1r.esp
127.25 127.00 126.75
Chemical Shift (ppm)
4-NO2 acid.002.001.1r.esp
CF2
117.5 115.0 112.5 110.0107.5
Chemical Shift (ppm)
F F
CO2H
O2N
1q
13C NMR
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

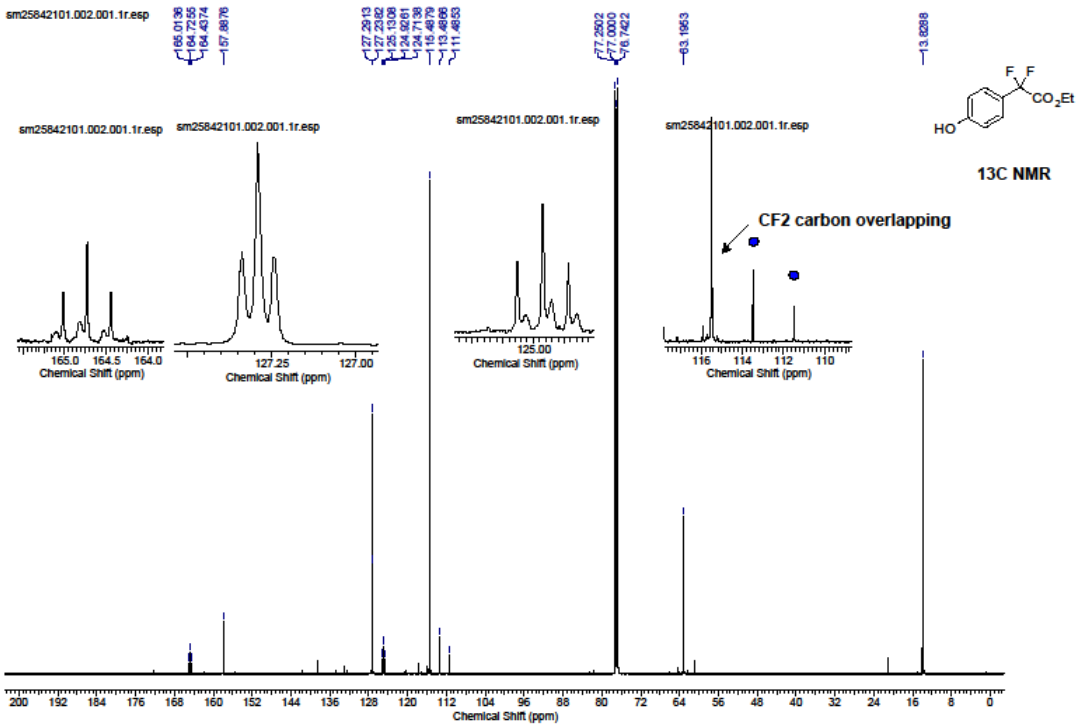


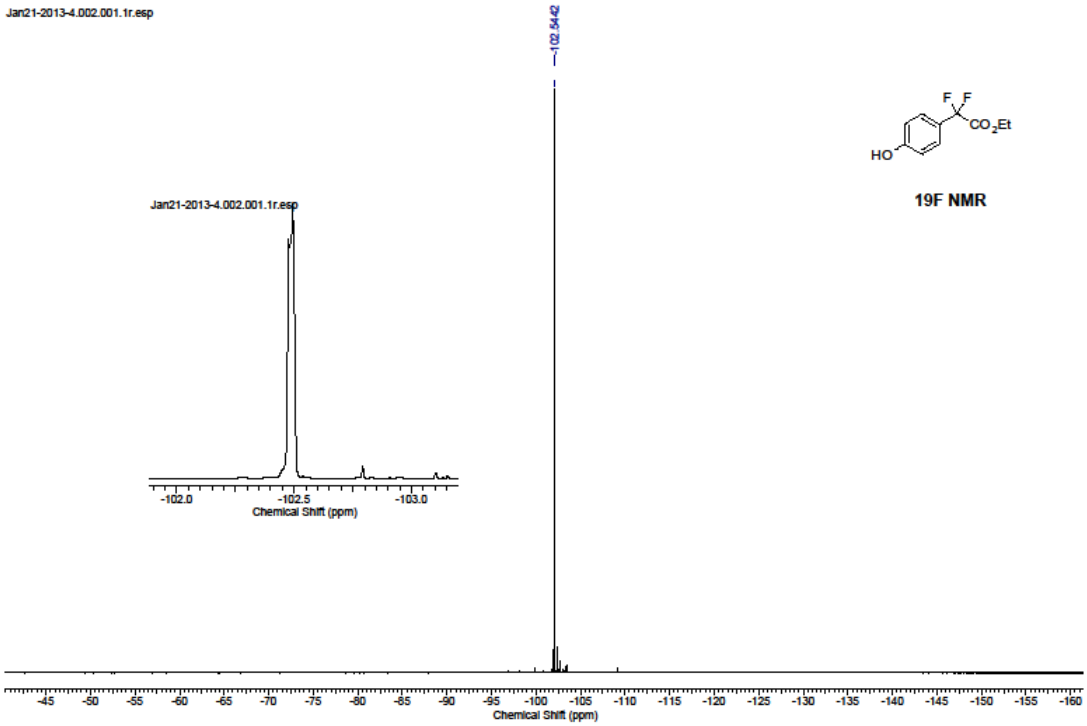
1q

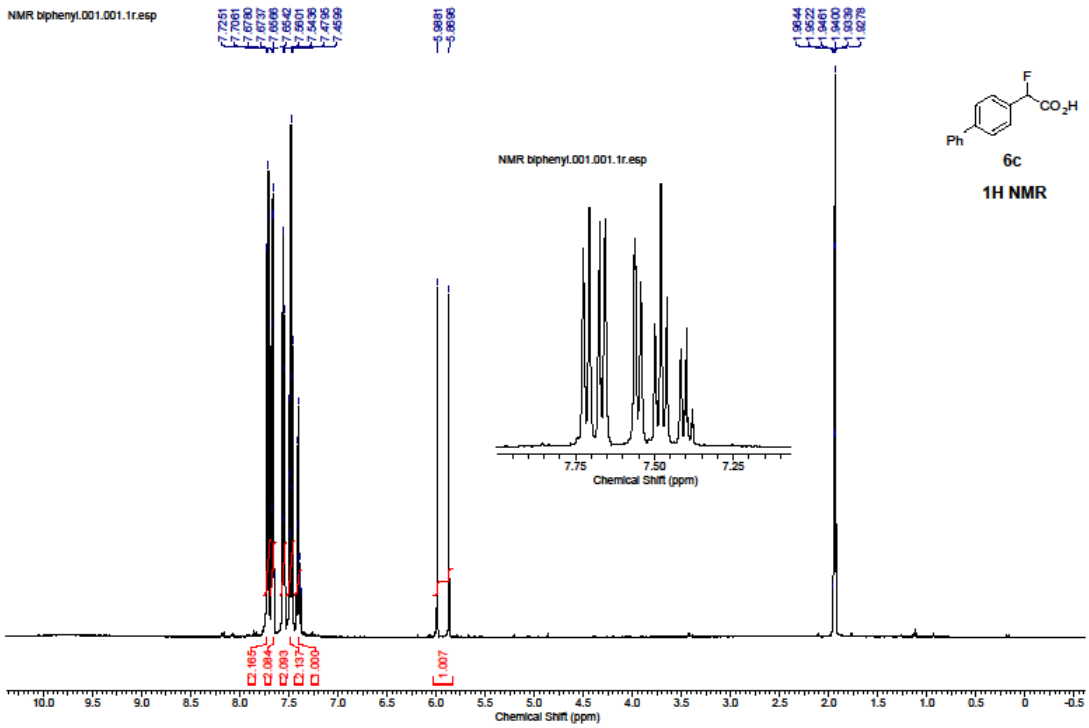
19F NMR

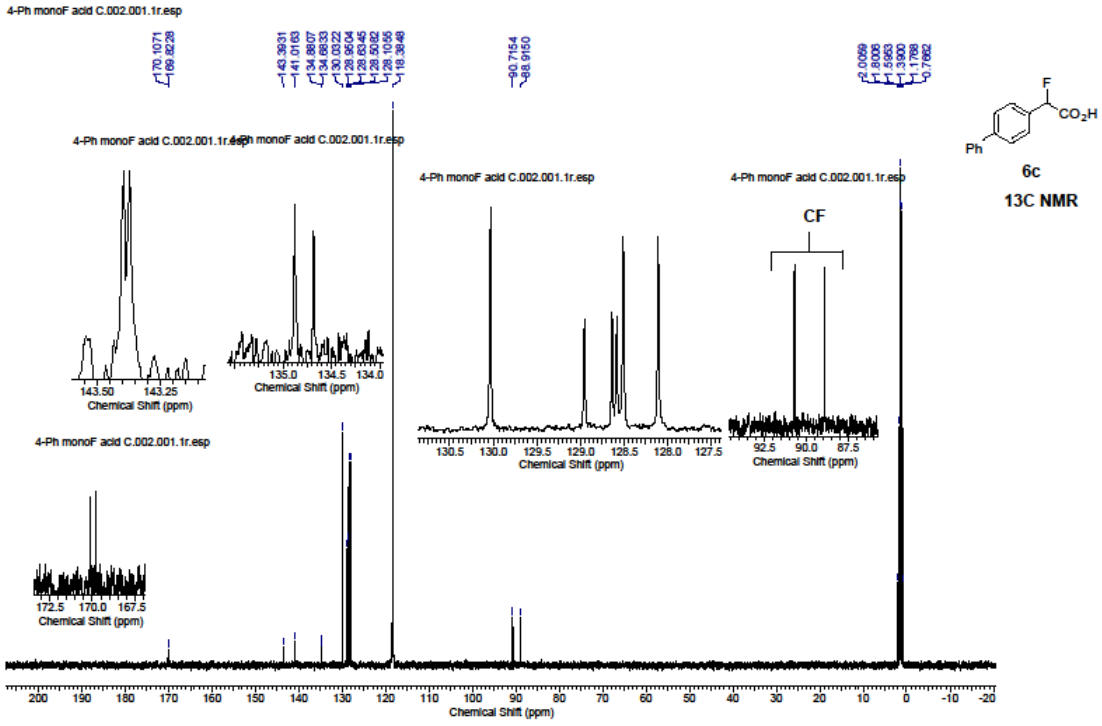


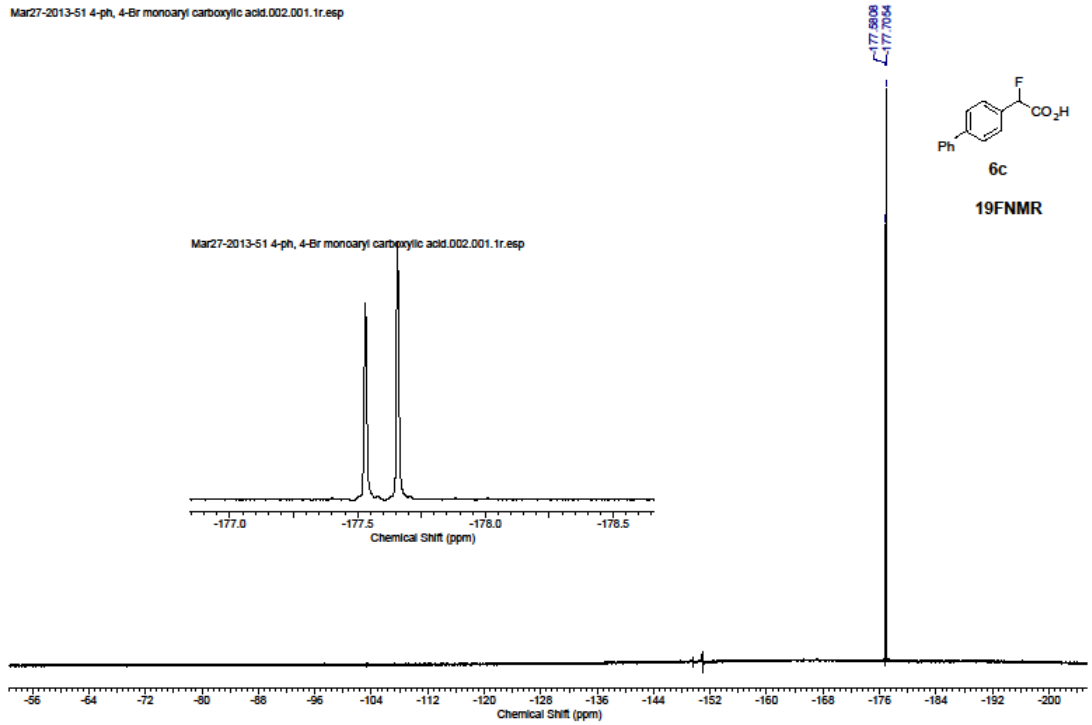
1H NMR

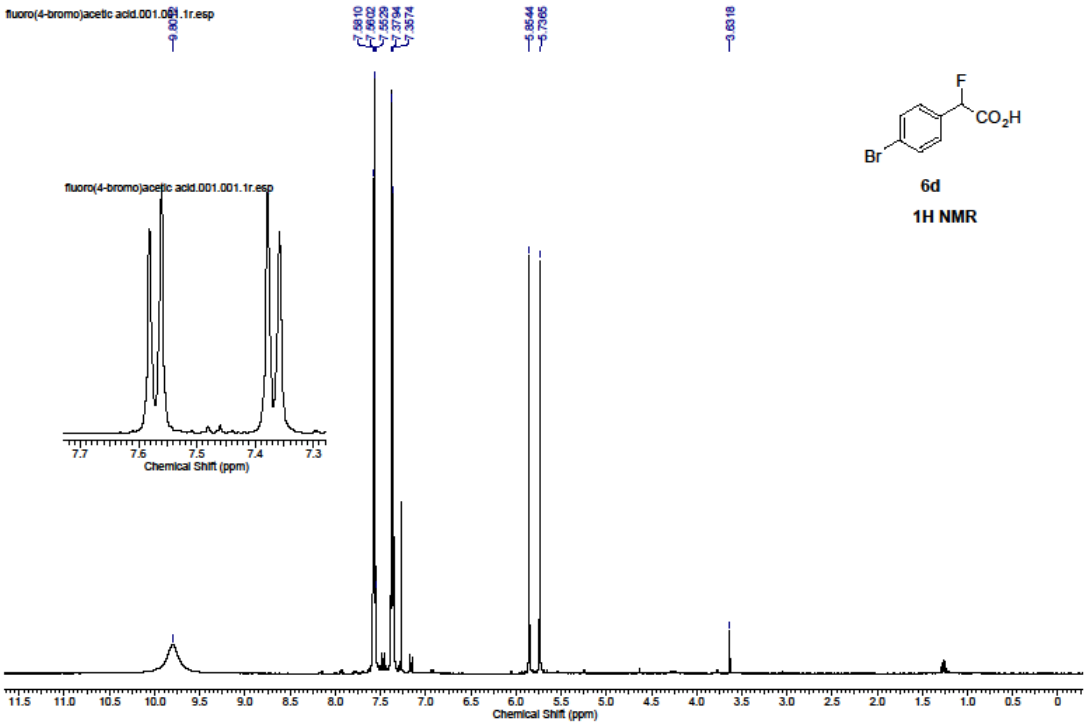

sm25842101.002.001.1r.esp
165.0136
164.7255
164.4374
157.8876
127.2913
127.2392
125.1308
124.9261
124.7138
115.4879
113.4866
111.4853
77.2502
77.0000
76.7422
63.1953
13.8288
CF2 carbon overlapping
Chemical Shift (ppm)
13C NMR

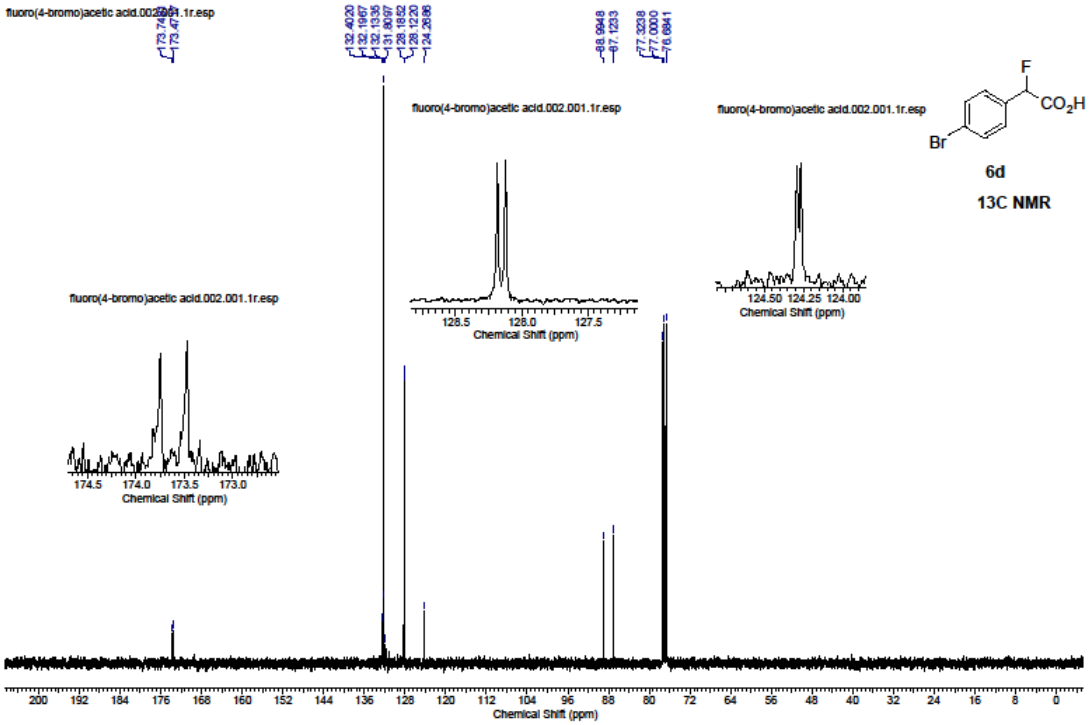

Jan21-2013-4.002.001.1r.esp
-102.5442
Chemical Shift (ppm)
19F NMR

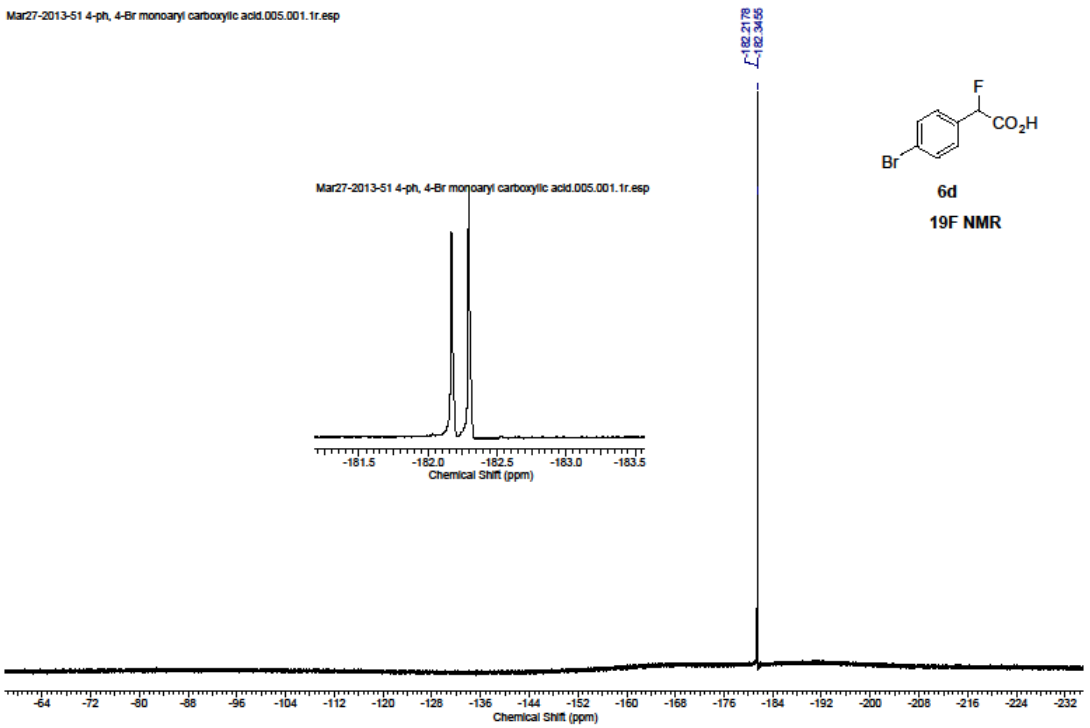

NMR biphenyl.001.001.1r.esp
7.7251
7.7061
7.6790
7.6737
7.6666
7.6542
7.5601
7.5436
7.4795
7.4599
5.9881
5.8696
1.9844
1.9622
1.9461
1.9400
1.9339
1.9278
NMR biphenyl.001.001.1r.esp
7.75
7.50
7.25
Chemical Shift (ppm)
F
CO2H
Ph
6c
1H NMR
1.65
1.004
2.093
2.137
1.000
1.007
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

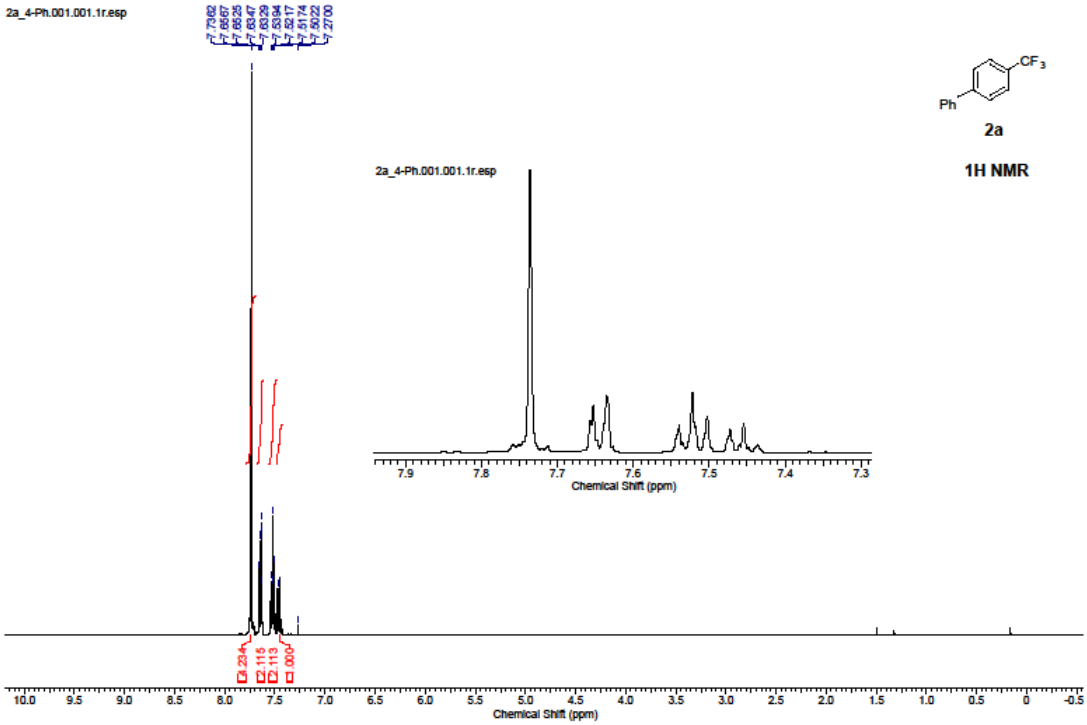

4-Ph monoF acid C.002.001.1r.esp
170.1071
169.8228
143.3931
141.0163
134.8807
134.6833
130.0322
128.9504
128.6345
128.5082
128.1056
116.3848
90.7154
88.9150
2.0099
1.8008
1.5963
1.3900
1.1788
0.7982
143.50
143.25
Chemical Shift (ppm)
135.0
134.5
134.0
Chemical Shift (ppm)
130.5
130.0
129.5
129.0
128.5
128.0
127.5
Chemical Shift (ppm)
CF
92.5
90.0
87.5
Chemical Shift (ppm)
172.5
170.0
167.5
Chemical Shift (ppm)
F
CO2H
Ph
6c
13C NMR
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

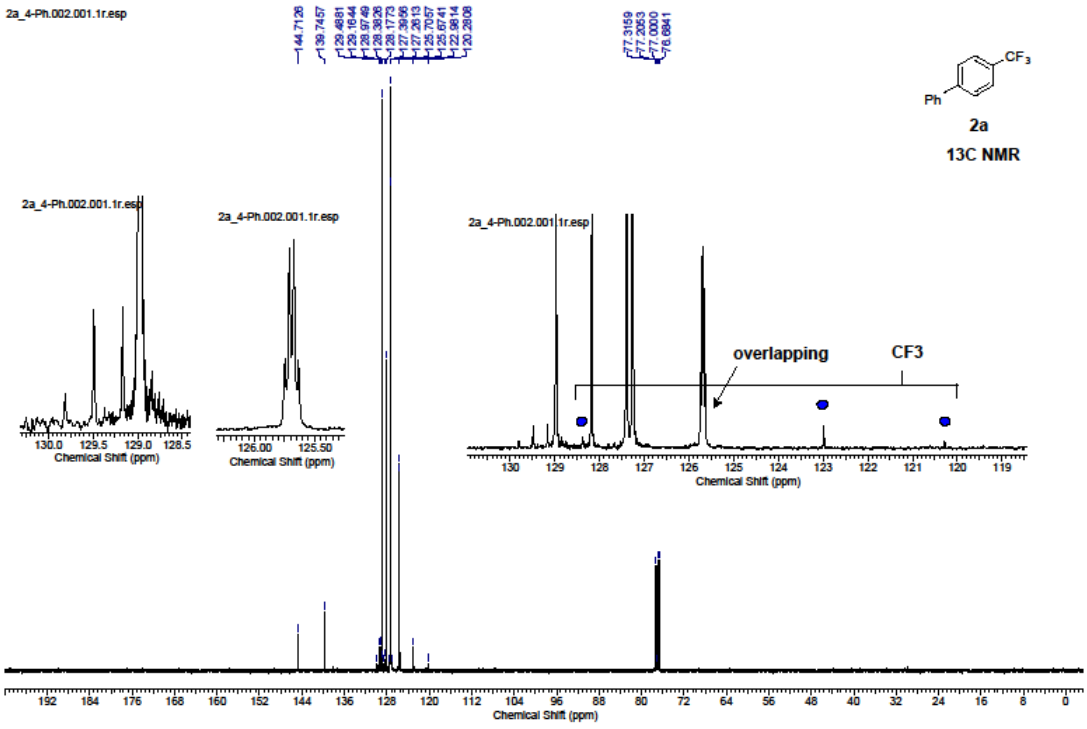

Mar27-2013-51 4-ph, 4-Br monoaryl carboxylic acid.002.001.1r.esp
-177.5908
-177.7054
F
CO2H
Ph
6c
19FNMR
Mar27-2013-51 4-ph, 4-Br monoaryl carboxylic acid.002.001.1r.esp
-177.0
-177.5
-178.0
-178.5
Chemical Shift (ppm)
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
-192
-200
Chemical Shift (ppm)

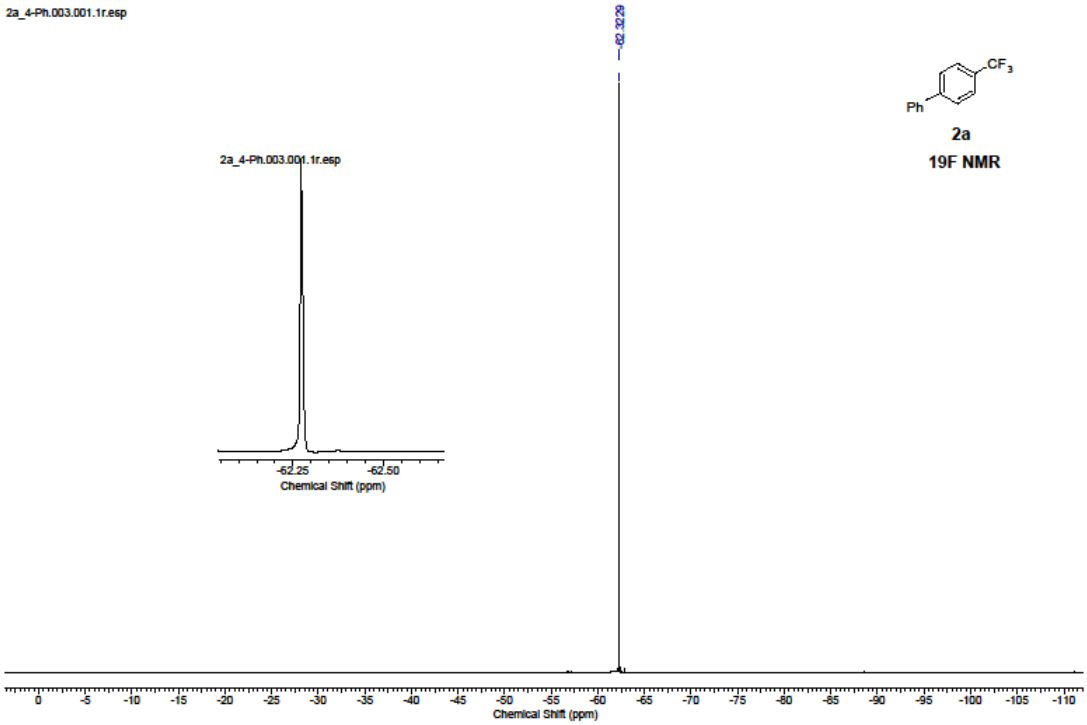

fluoro(4-bromo)acetic acid.001.001.1r.esp
7.5910
7.5602
7.5529
7.3794
7.3574
5.8544
5.7046
3.6318
F
CO2H
Br
6d
1H NMR
fluoro(4-bromo)acetic acid.001.001.1r.esp
7.7
7.6
7.5
7.4
7.3
Chemical Shift (ppm)
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

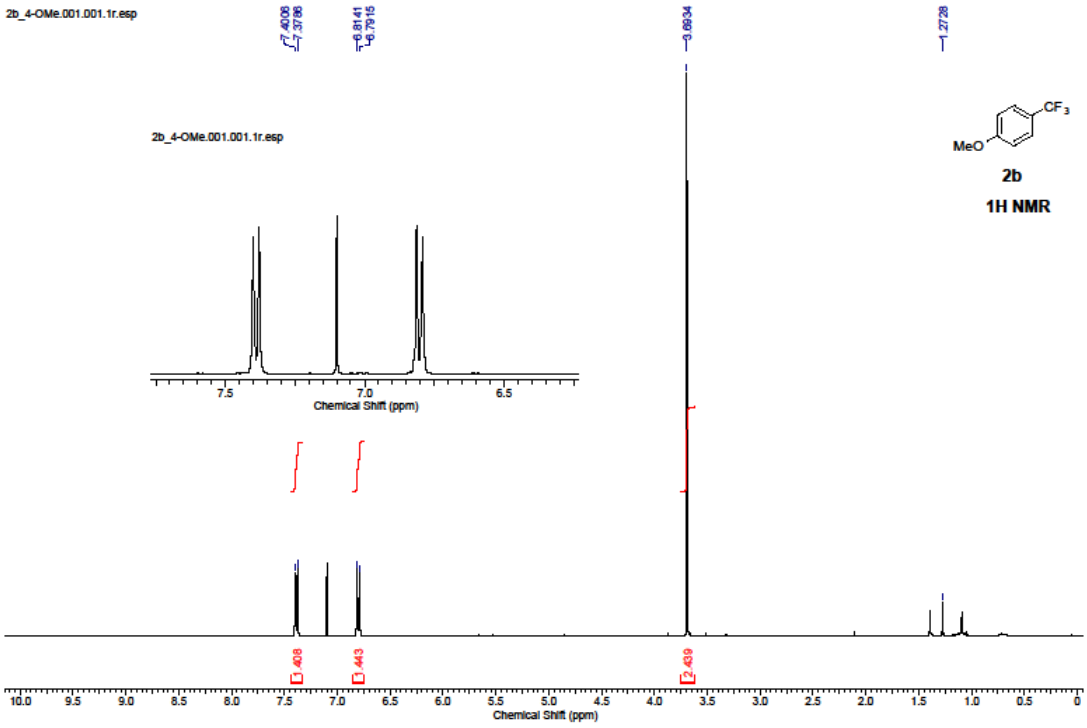

fluoro(4-bromo)acetic acid.002.001.1r.esp
132.4020
132.1967
132.1335
131.8097
128.1852
128.1220
124.2686
88.9948
87.1233
77.3238
77.0000
76.6841
fluoro(4-bromo)acetic acid.002.001.1r.esp
128.5
128.0
127.5
Chemical Shift (ppm)
fluoro(4-bromo)acetic acid.002.001.1r.esp
124.50 124.25 124.00
Chemical Shift (ppm)
fluoro(4-bromo)acetic acid.002.001.1r.esp
174.5
174.0
173.5
173.0
Chemical Shift (ppm)
F
CO2H
Br
6d
13C NMR
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

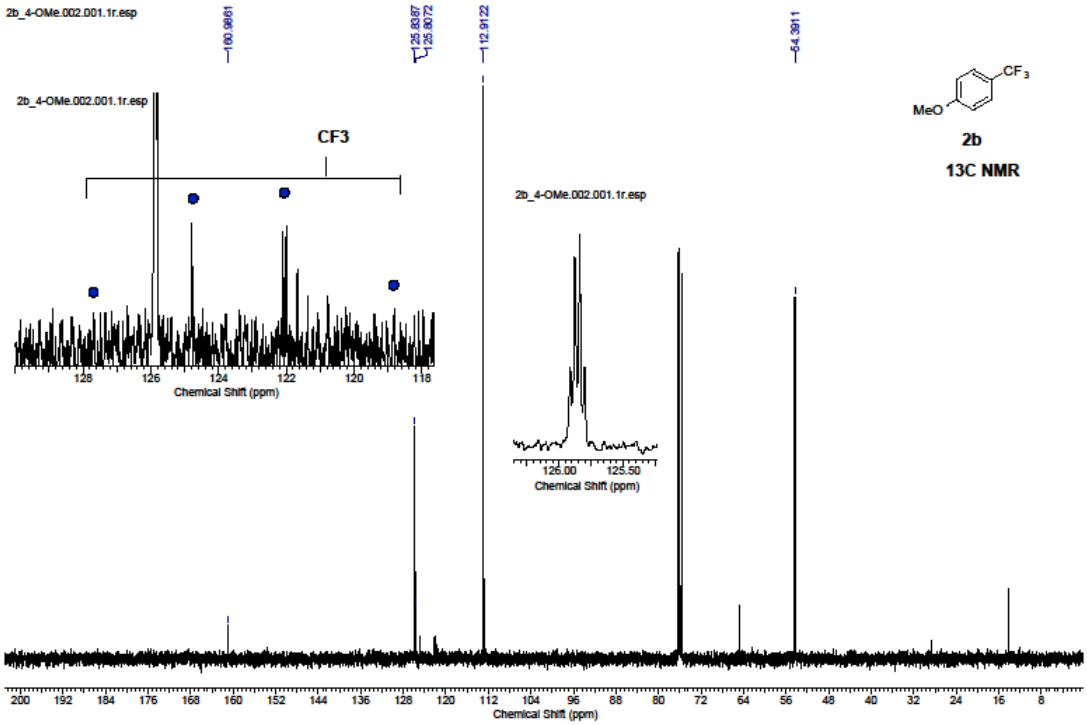

Mar27-2013-51 4-ph, 4-Br monoaryl carboxylic acid.005.001.1r.esp
182.2178
182.3455
Mar27-2013-51 4-ph, 4-Br monoaryl carboxylic acid.005.001.1r.esp
-181.5
-182.0
-182.5
-183.0
-183.5
Chemical Shift (ppm)
F
CO2H
Br
6d
19F NMR
-64 -72 -80 -88 -96 -104 -112 -120 -128 -136 -144 -152 -160 -168 -176 -184 -192 -200 -208 -216 -224 -232
Chemical Shift (ppm)

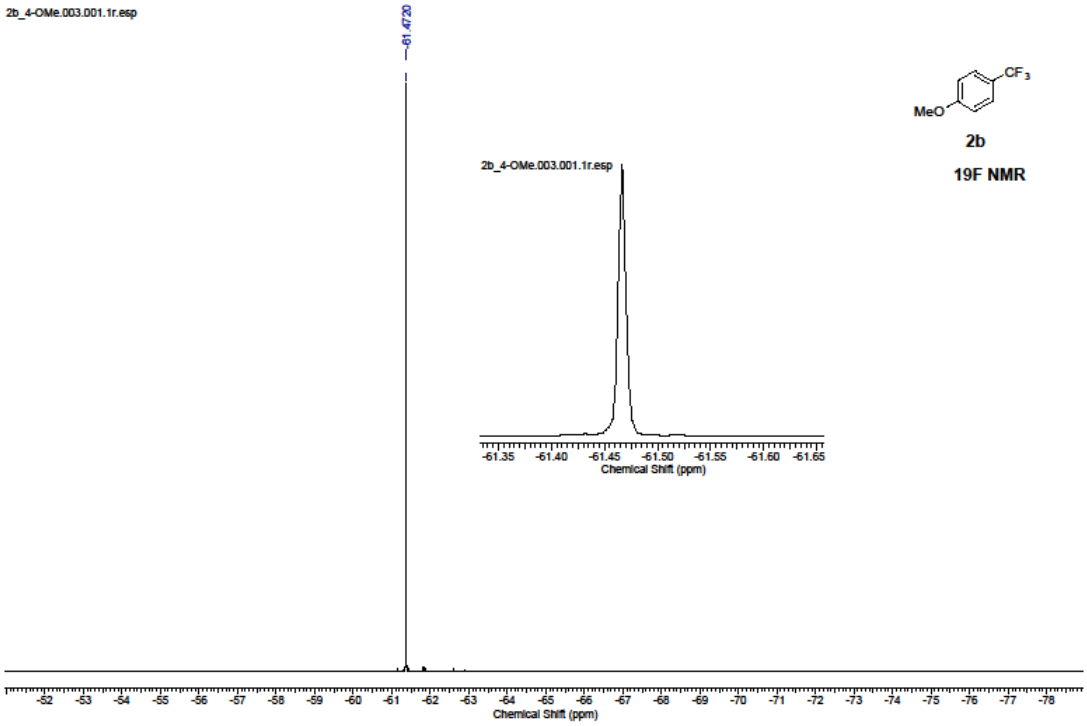

2a_4-Ph.001.001.1r.esp
7.7962
7.6567
7.6525
7.6347
7.6329
7.5394
7.5217
7.5174
7.5022
7.2700
CF3
Ph
2a
1H NMR
2a_4-Ph.001.001.1r.esp
7.9
7.8
7.7
7.6
7.5
7.4
7.3
Chemical Shift (ppm)
2.314
2.115
2.113
1.000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)

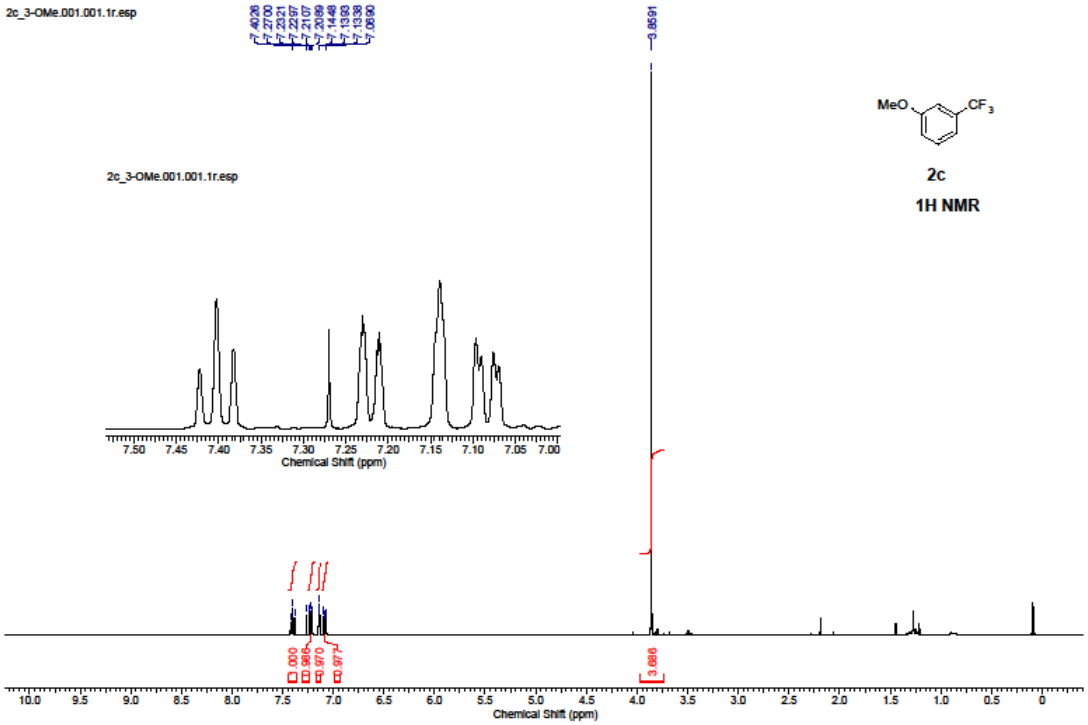

2a_4-Ph.002.001.1r.esp
144.7126
139.7457
129.4681
129.1644
128.9749
128.3826
128.1773
127.3956
127.2613
125.7057
125.6741
122.9814
120.2808
77.3159
77.2053
77.0000
76.6841
CF3
Ph
2a
13C NMR
2a_4-Ph.002.001.1r.esp
130.0
129.5
129.0
128.5
Chemical Shift (ppm)
2a_4-Ph.002.001.1r.esp
126.00
125.50
Chemical Shift (ppm)
2a_4-Ph.002.001.1r.esp
overlapping
CF3
130
129
128
127
126
125
124
123
122
121
120
119
Chemical Shift (ppm)
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

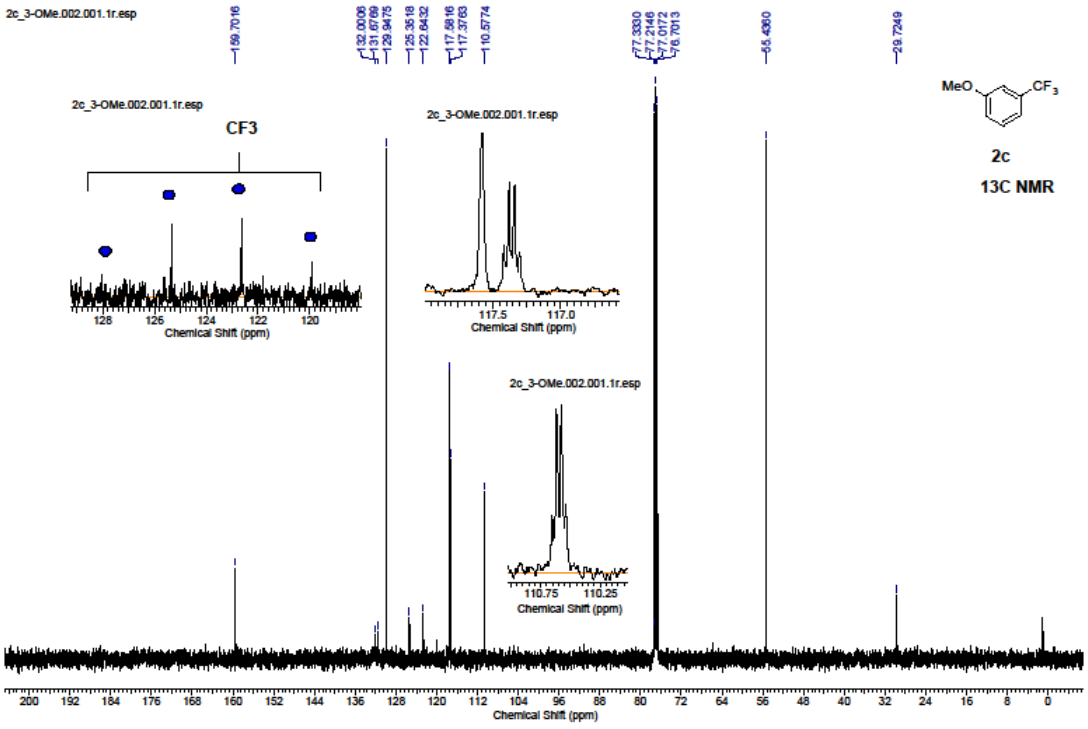

2a_4-Ph.003.001.1r.esp
-62.3229
2a_4-Ph.003.001.1r.esp
-62.25
-62.50
Chemical Shift (ppm)
CF3
Ph
2a
19F NMR
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
Chemical Shift (ppm)

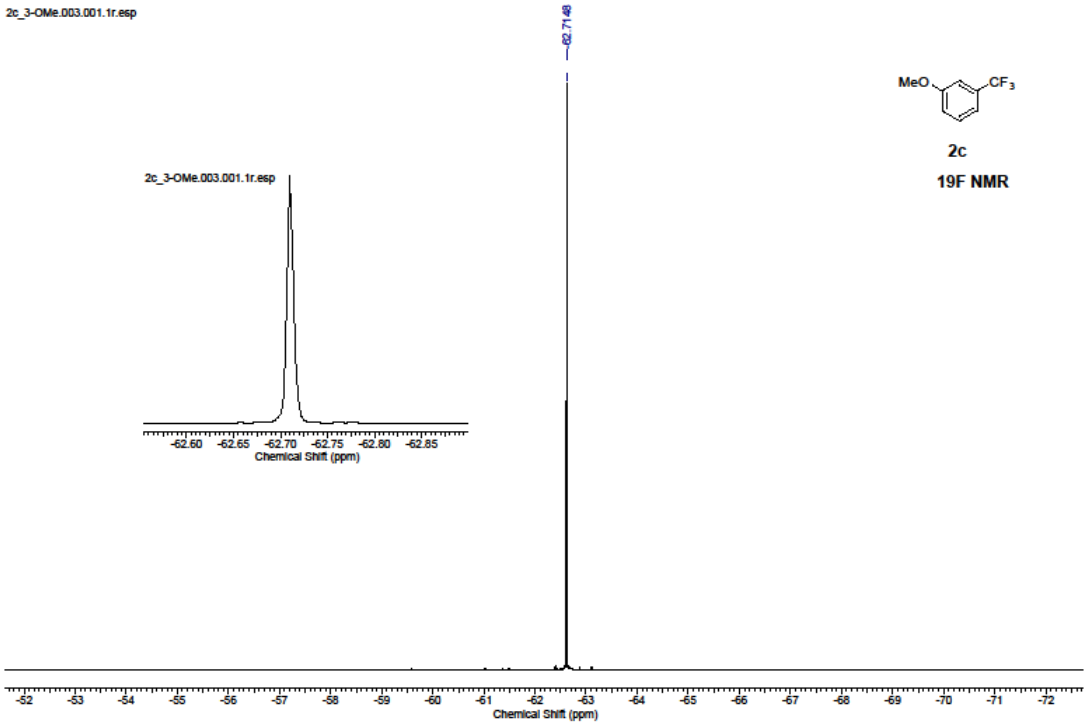

2b_4-OMe.001.001.1r.esp
7.4008
7.3788
6.8141
6.7915
3.6934
1.2728
2b_4-OMe.001.001.1r.esp
7.5
7.0
6.5
Chemical Shift (ppm)
CF3
MeO
2b
1H NMR
2.408
2.443
2.439
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

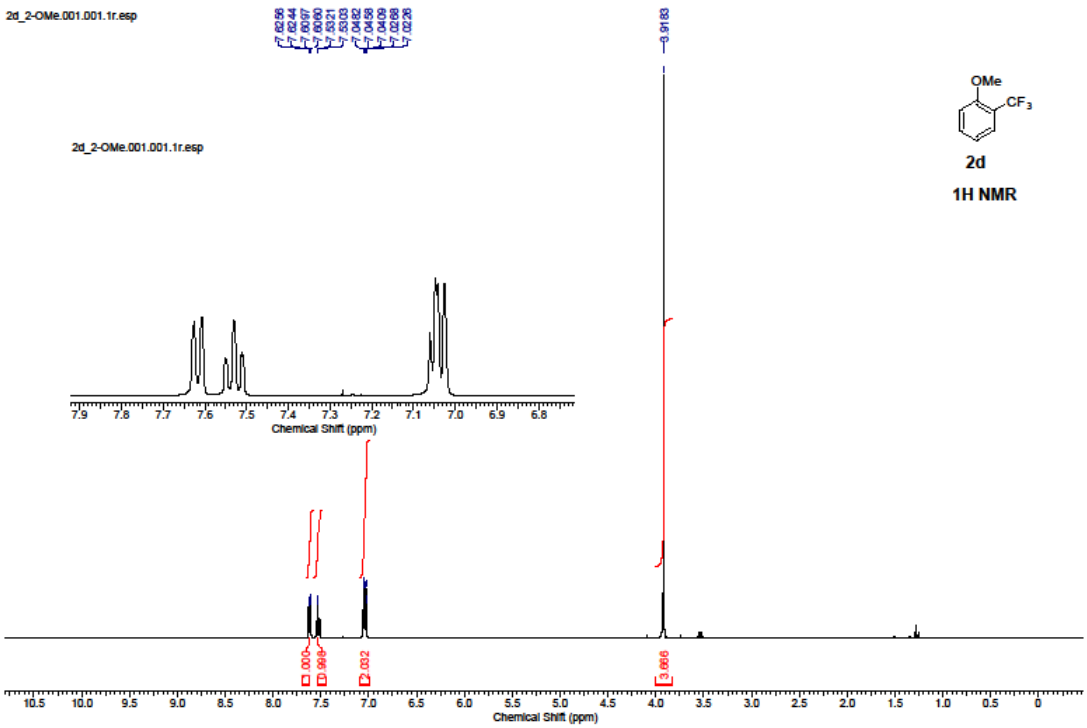

2b_4-OMe.002.001.1r.esp
160.9861
125.8387
125.9072
112.9122
54.3911
CF3
Chemical Shift (ppm)
MeO
CF3
2b
13C NMR

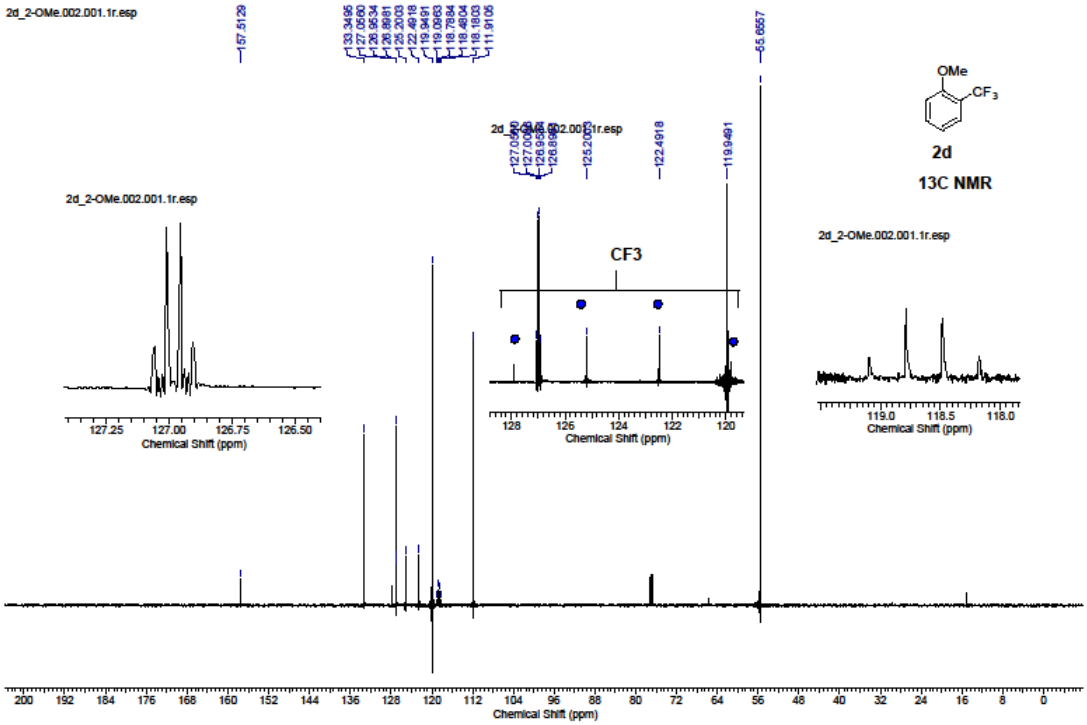

2b_4-OMe.003.001.1r.esp
61.4720
Chemical Shift (ppm)
MeO
CF3
2b
19F NMR

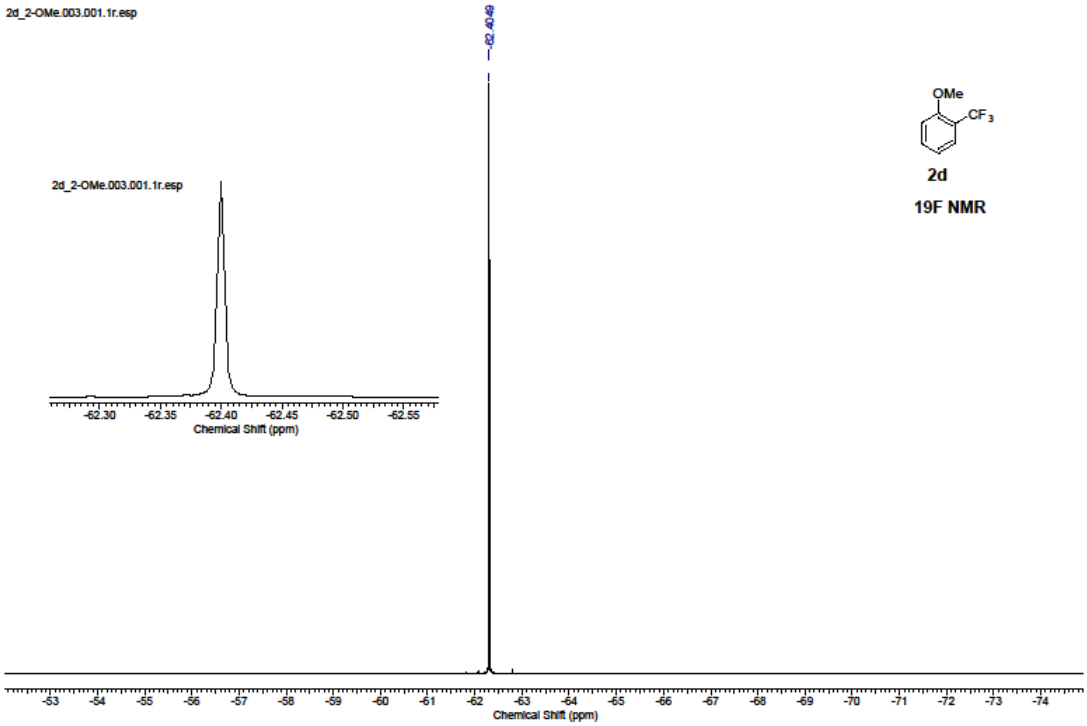

2c_3-OMe.001.001.1r.esp
7.4026
7.2700
7.2321
7.2297
7.2107
7.2069
7.1448
7.1383
7.1338
7.0890
3.8591
MeO
CF3
2c
1H NMR
2c_3-OMe.001.001.1r.esp
7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00
Chemical Shift (ppm)
1.000
0.986
0.970
0.974
3.686
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

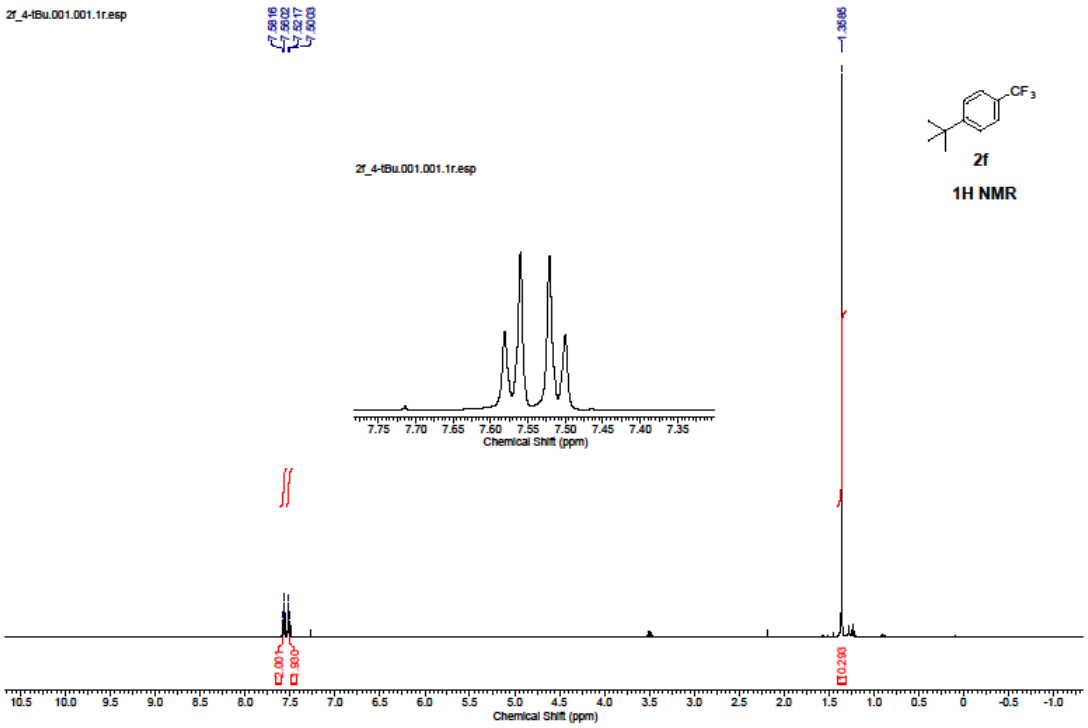

2c_3-OMe.002.001.1r.esp
159.7016
132.0006
131.6769
129.9475
125.3518
122.6432
117.5816
117.3763
110.5774
77.3330
77.2146
77.0372
76.7013
55.4360
29.7249
MeO
CF3
2c
13C NMR
2c_3-OMe.002.001.1r.esp
CF3
128 126 124 122 120
Chemical Shift (ppm)
2c_3-OMe.002.001.1r.esp
117.5 117.0
Chemical Shift (ppm)
2c_3-OMe.002.001.1r.esp
110.75 110.25
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

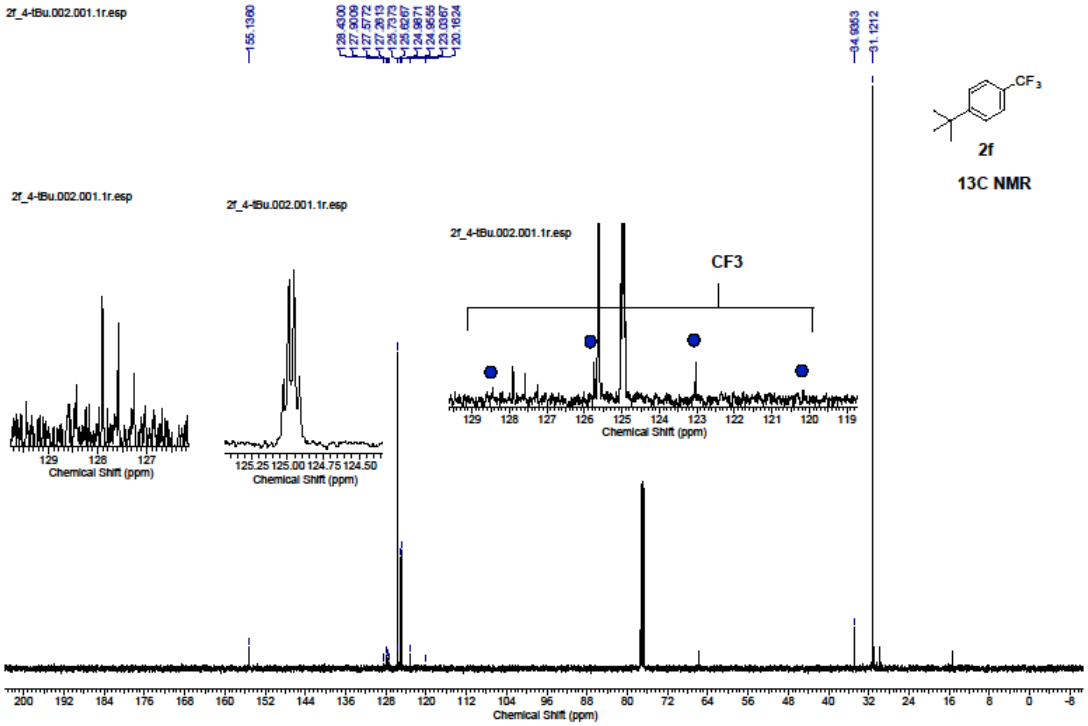

2c_3-OMe.003.001.1r.esp
-62.7148
MeO
CF3
2c
19F NMR
2c_3-OMe.003.001.1r.esp
-62.60 -62.65 -62.70 -62.75 -62.80 -62.85
Chemical Shift (ppm)
-52 -53 -54 -55 -56 -57 -58 -59 -60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72
Chemical Shift (ppm)

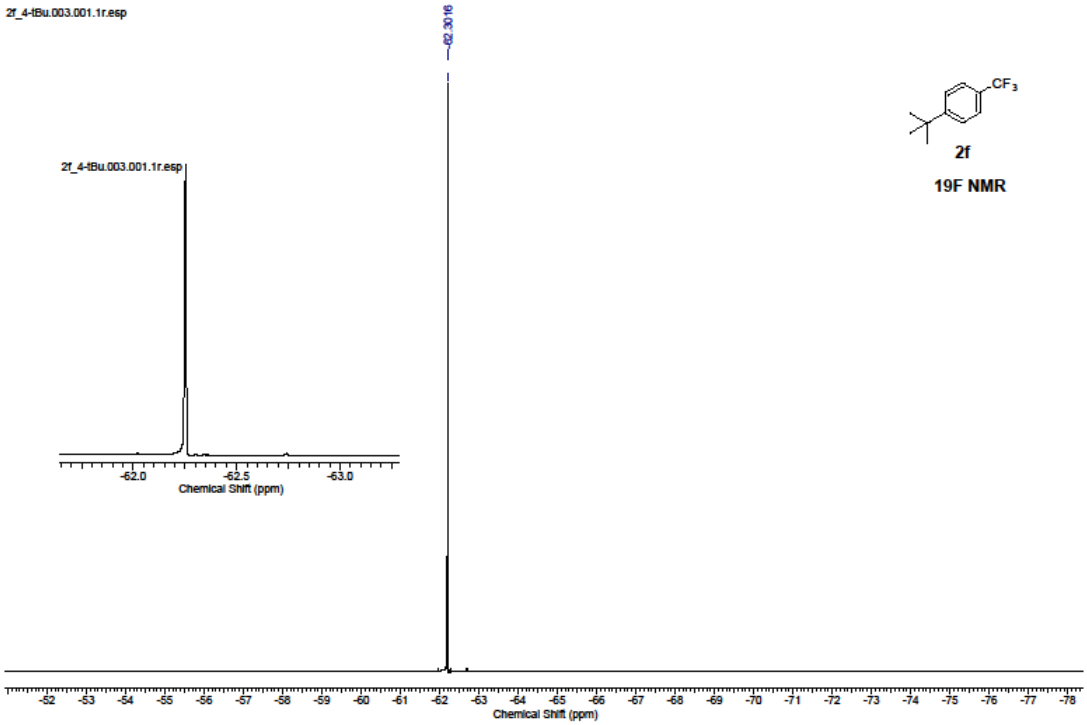

2d_2-OMe.001.001.1r.esp
7.62.96
7.62.44
7.60.97
7.60.60
7.53.21
7.53.03
7.04.82
7.04.58
7.04.39
7.02.98
7.02.26
-3.9183
OMe
CF3
2d
1H NMR
2d_2-OMe.001.001.1r.esp
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
Chemical Shift (ppm)
1.000
0.998
2.032
3.000
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

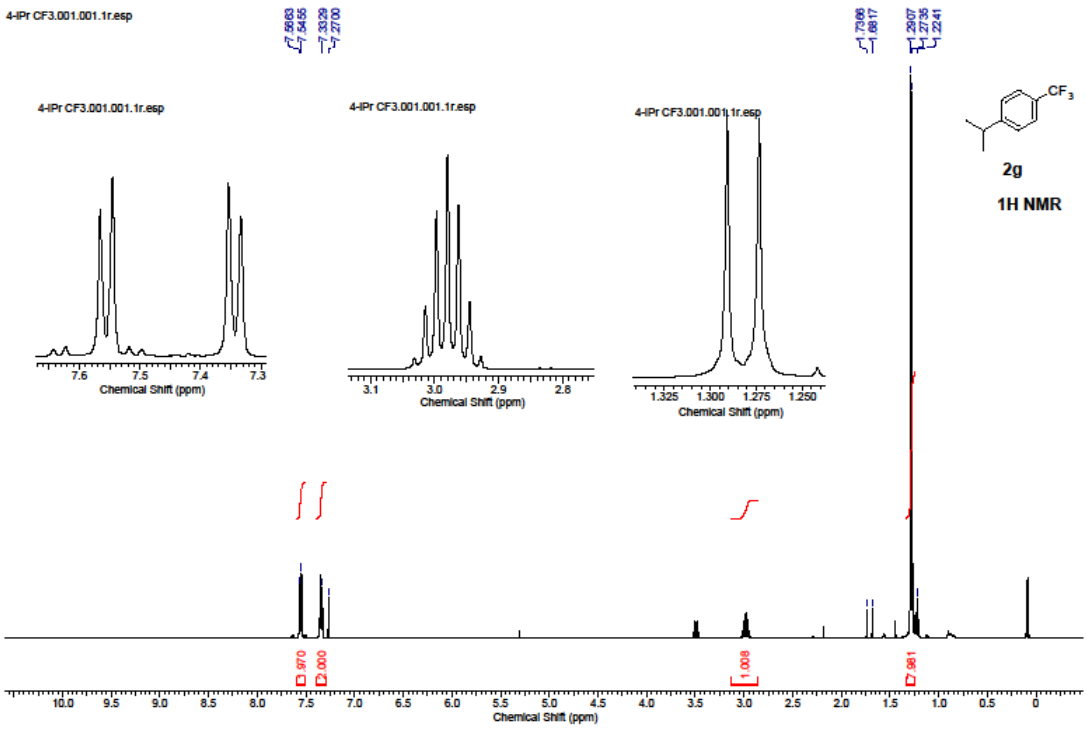

2d_2-OMe.002.001.1r.esp
157.5129
133.3495
127.0560
126.9534
126.8981
125.2003
122.4918
119.9491
118.7884
118.4804
118.1803
111.9105
55.6557
OMe
CF3
2d
13C NMR
CF3
Chemical Shift (ppm)

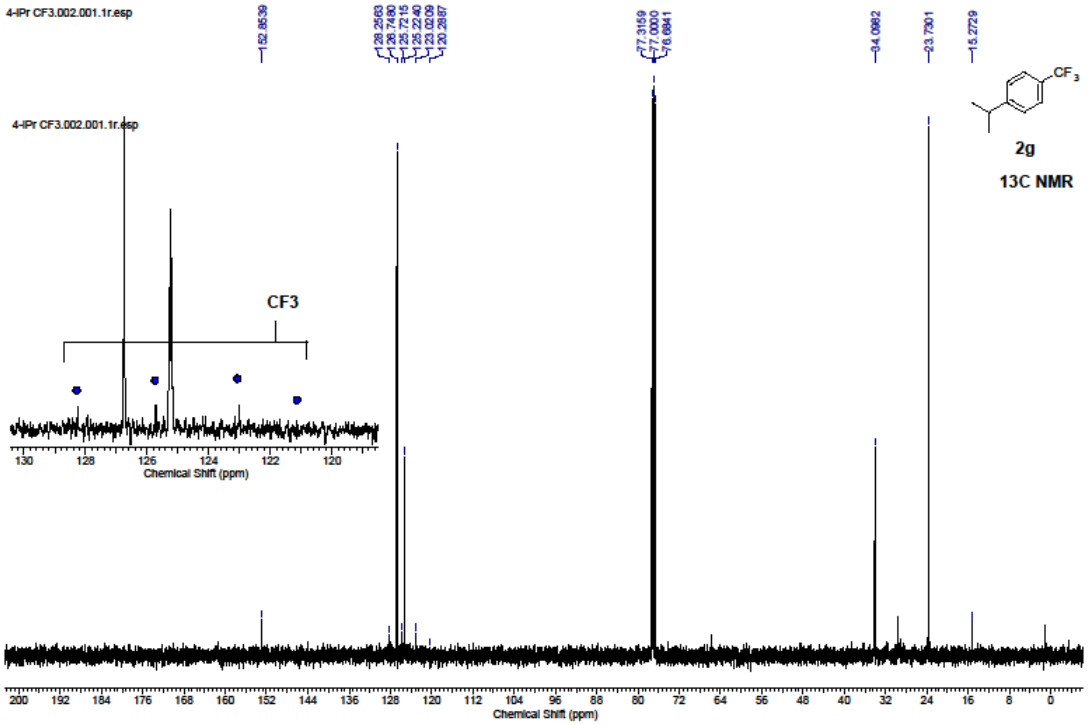

2d_2-OMe.003.001.1r.esp
62.4049
OMe
CF3
2d
19F NMR
Chemical Shift (ppm)

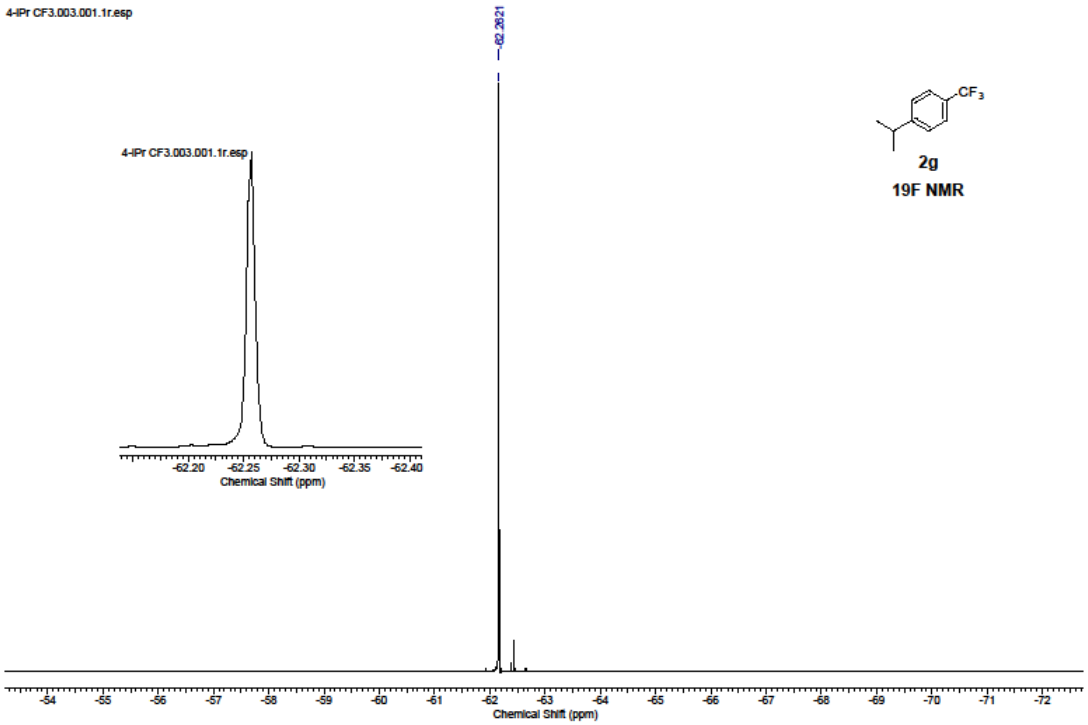

2f_4-tBu.001.001.1r.esp
7.5916
7.5802
7.5717
7.5603
1.3685
2f_4-tBu.001.001.1r.esp
7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35
Chemical Shift (ppm)
CF3
2f
1H NMR
2.001
0.980
10.293
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5 -1.0
Chemical Shift (ppm)

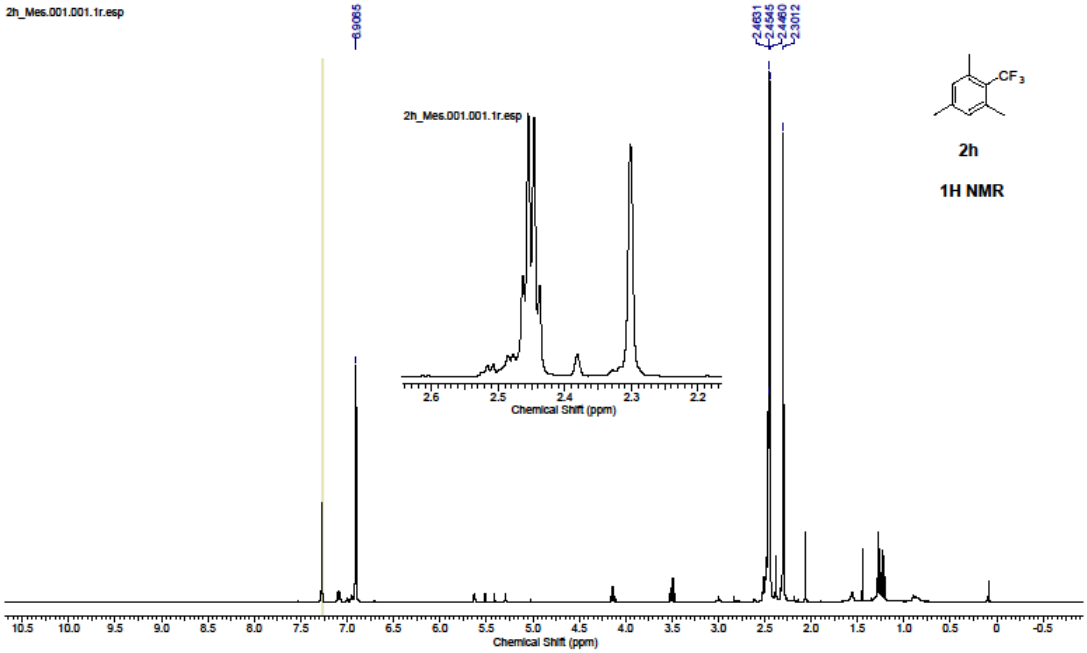

2f_4-tBu.002.001.1r.esp
155.1390
128.4300
127.0699
127.0572
127.0513
125.7373
125.6267
124.9871
124.9555
123.0367
120.1624
34.9353
31.1212
CF3
2f
13C NMR
2f_4-tBu.002.001.1r.esp
129 128 127
Chemical Shift (ppm)
2f_4-tBu.002.001.1r.esp
125.25 125.00 124.75 124.50
Chemical Shift (ppm)
2f_4-tBu.002.001.1r.esp
129 128 127 126 125 124 123 122 121 120 119
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

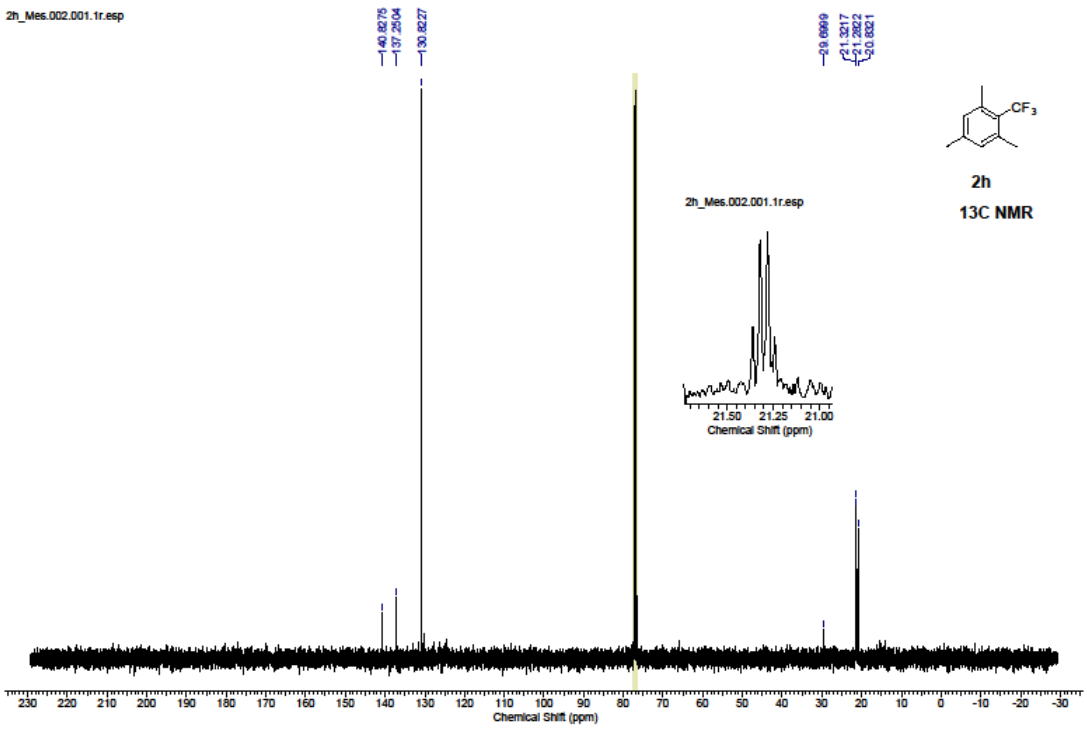

2f_4-tBu.003.001.1r.esp
-62.3016
2f_4-tBu.003.001.1r.esp
-62.0
-62.5
-63.0
Chemical Shift (ppm)
CF3
2f
19F NMR
-52 -53 -54 -55 -56 -57 -58 -59 -60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72 -73 -74 -75 -76 -77 -78
Chemical Shift (ppm)

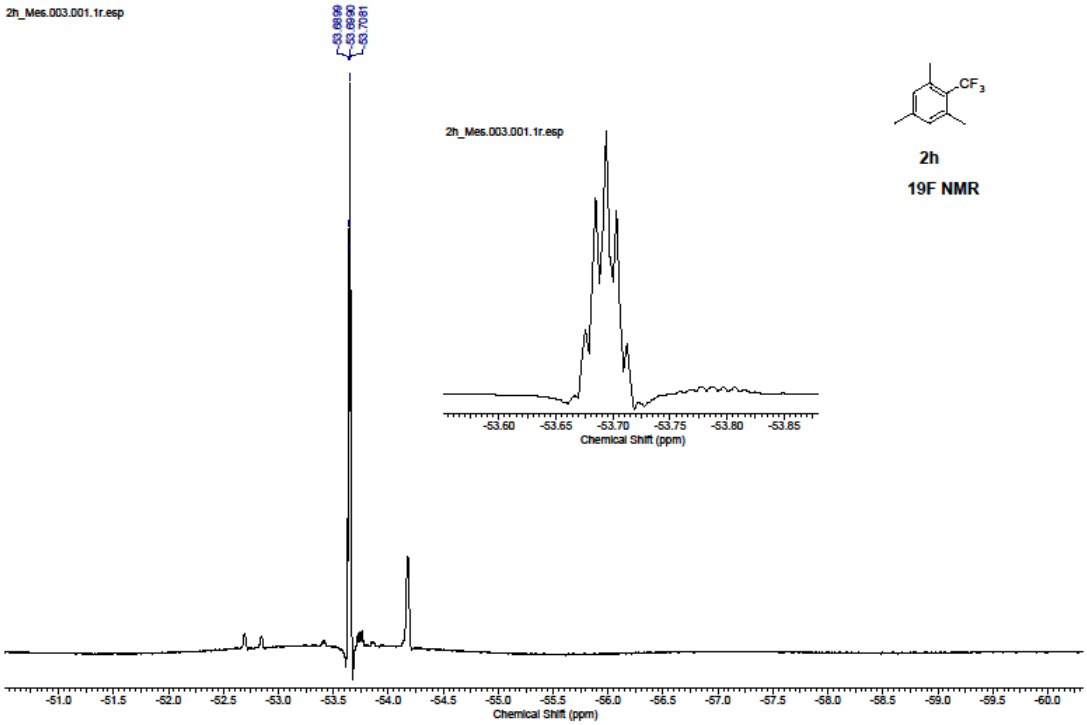

4-IPr CF3.001.001.1r.esp
7.5663
7.5456
7.3329
7.2700
1.7366
1.6817
1.2907
1.2735
1.2241
4-IPr CF3.001.001.1r.esp
7.6 7.5 7.4 7.3
Chemical Shift (ppm)
4-IPr CF3.001.001.1r.esp
3.1 3.0 2.9 2.8
Chemical Shift (ppm)
4-IPr CF3.001.001.1r.esp
1.325 1.300 1.275 1.250
Chemical Shift (ppm)
CF3
2g
1H NMR
3.970
2.000
1.008
7.981
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

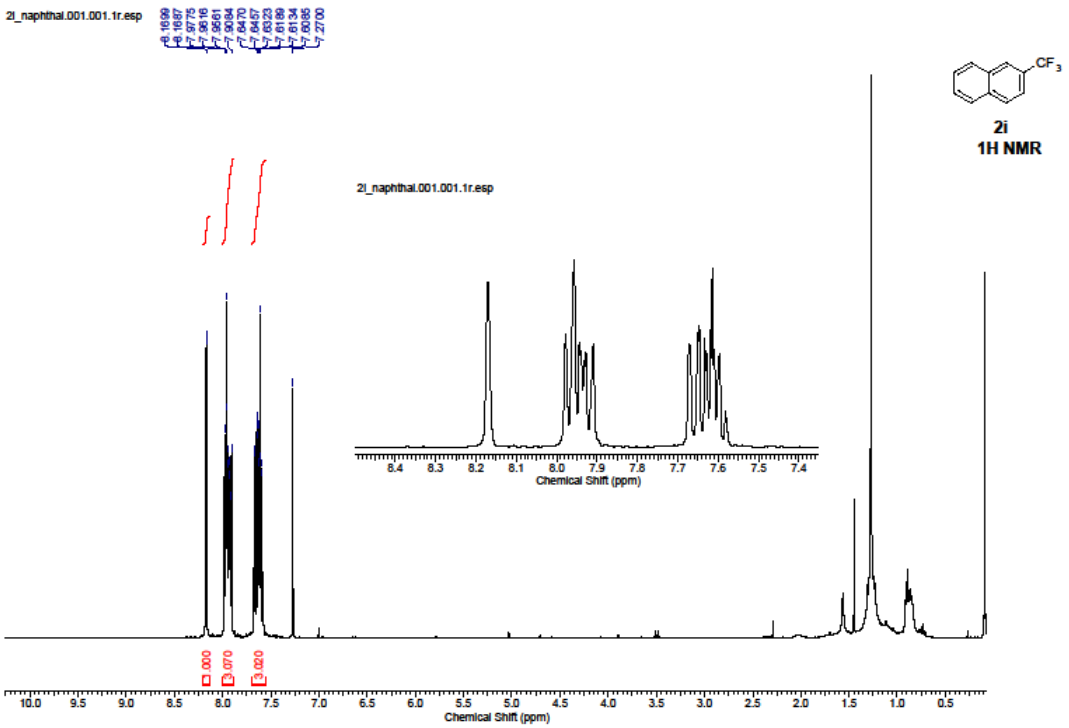

4-IPr CF3.002.001.1r.esp
152.8639
128.2563
126.7490
125.7215
125.2240
123.0209
120.2887
77.3159
77.0000
76.6841
34.0962
23.7001
15.2729
CF3
Chemical Shift (ppm)
2g
13C NMR

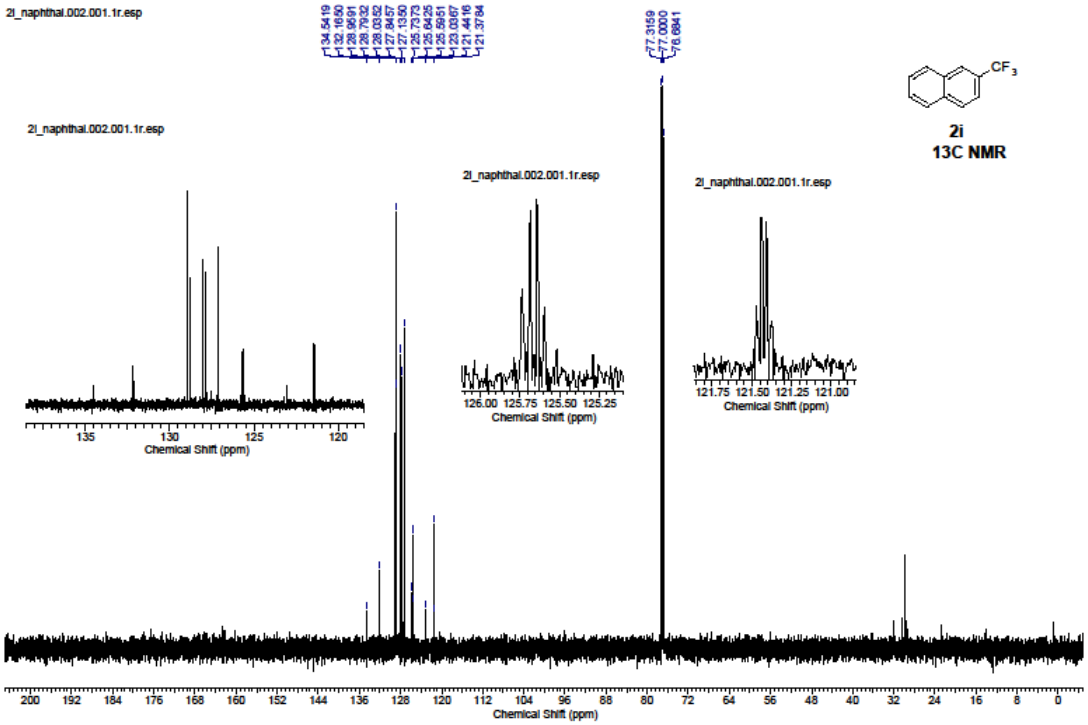

4-IPr CF3.003.001.1r.esp
-62.2621
Chemical Shift (ppm)
2g
19F NMR

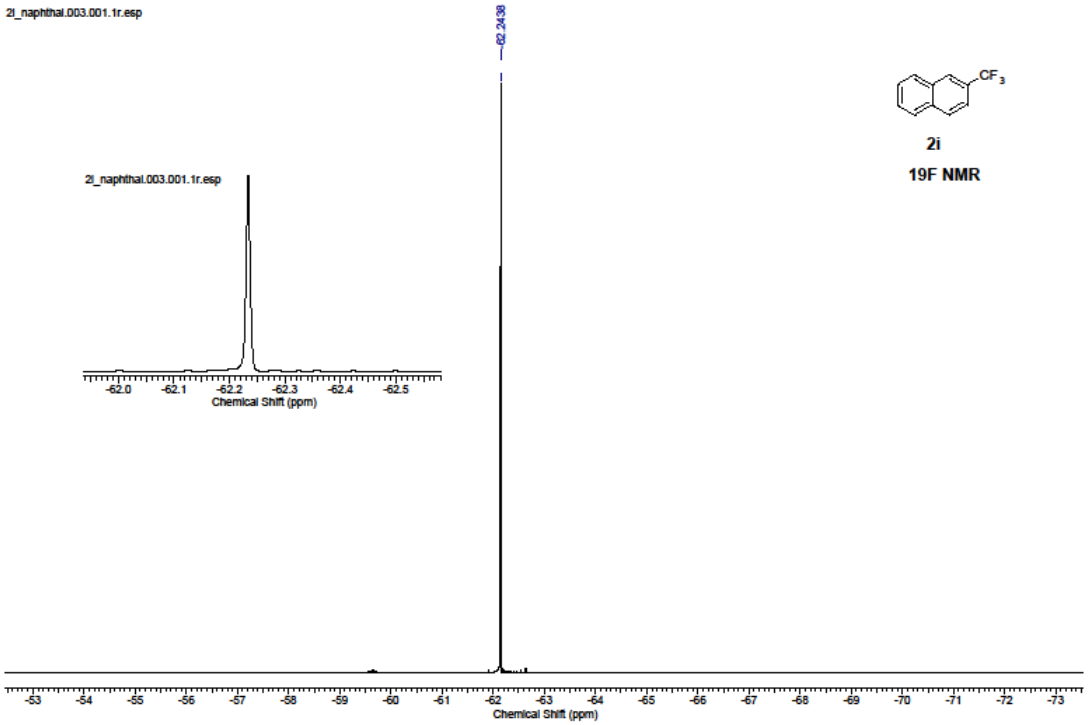

2h_Mes.001.001.1r.esp
6.9065
2.4631
2.4545
2.4460
2.3012
2h_Mes.001.001.1r.esp
Chemical Shift (ppm)
CF3
2h
1H NMR
Chemical Shift (ppm)

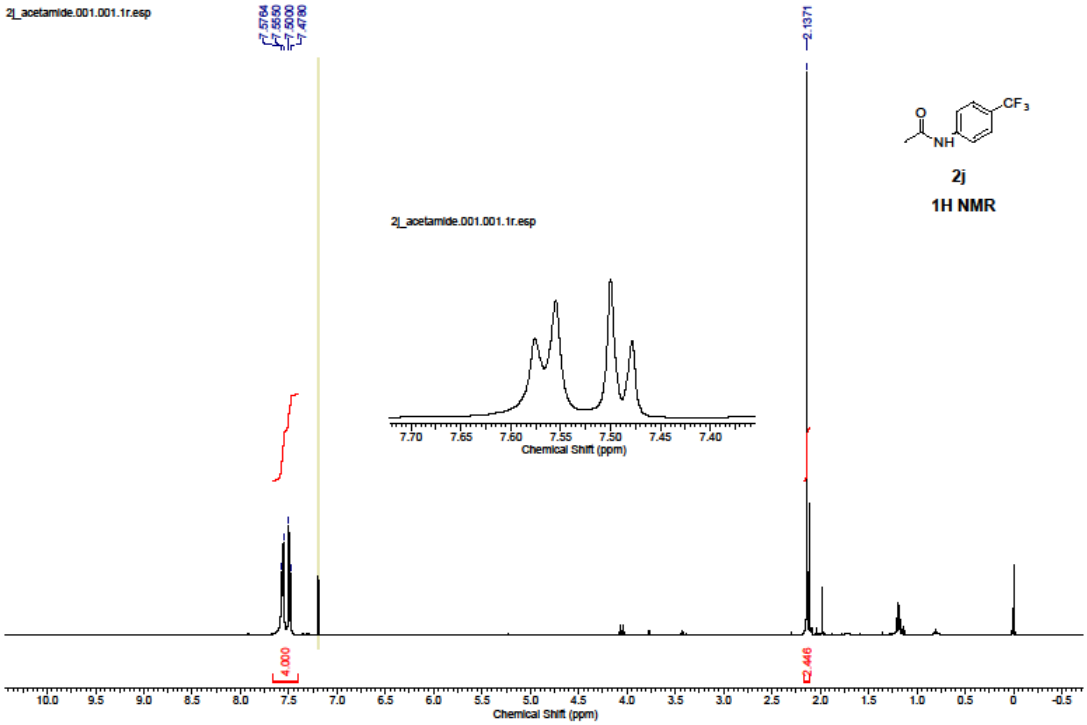

2h_Mes.002.001.1r.esp
140.8275
137.2504
130.8227
29.6999
21.3217
21.2822
20.8321
2h_Mes.002.001.1r.esp
Chemical Shift (ppm)
CF3
2h
13C NMR
Chemical Shift (ppm)

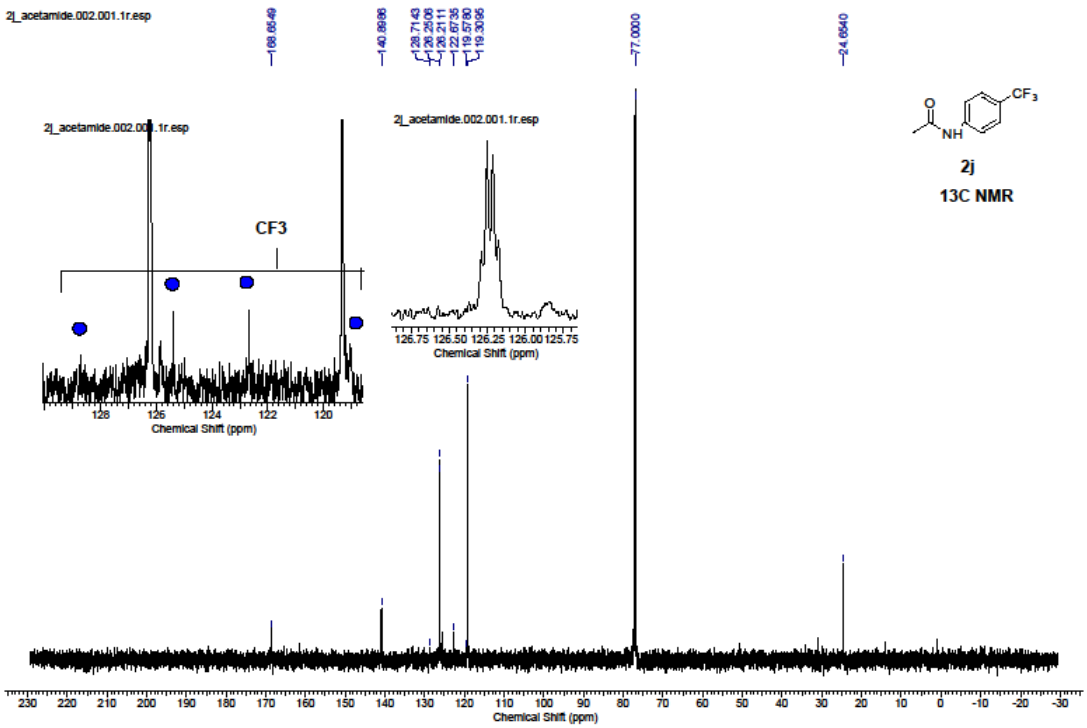

2h_Mes.003.001.1r.esp
-53.6899
-53.6990
-53.7081
2h_Mes.003.001.1r.esp
-53.60
-53.65
-53.70
-53.75
-53.80
-53.85
Chemical Shift (ppm)
CF3
2h
19F NMR
-51.0
-51.5
-52.0
-52.5
-53.0
-53.5
-54.0
-54.5
-55.0
-55.5
-56.0
-56.5
-57.0
-57.5
-58.0
-58.5
-59.0
-59.5
-60.0
Chemical Shift (ppm)

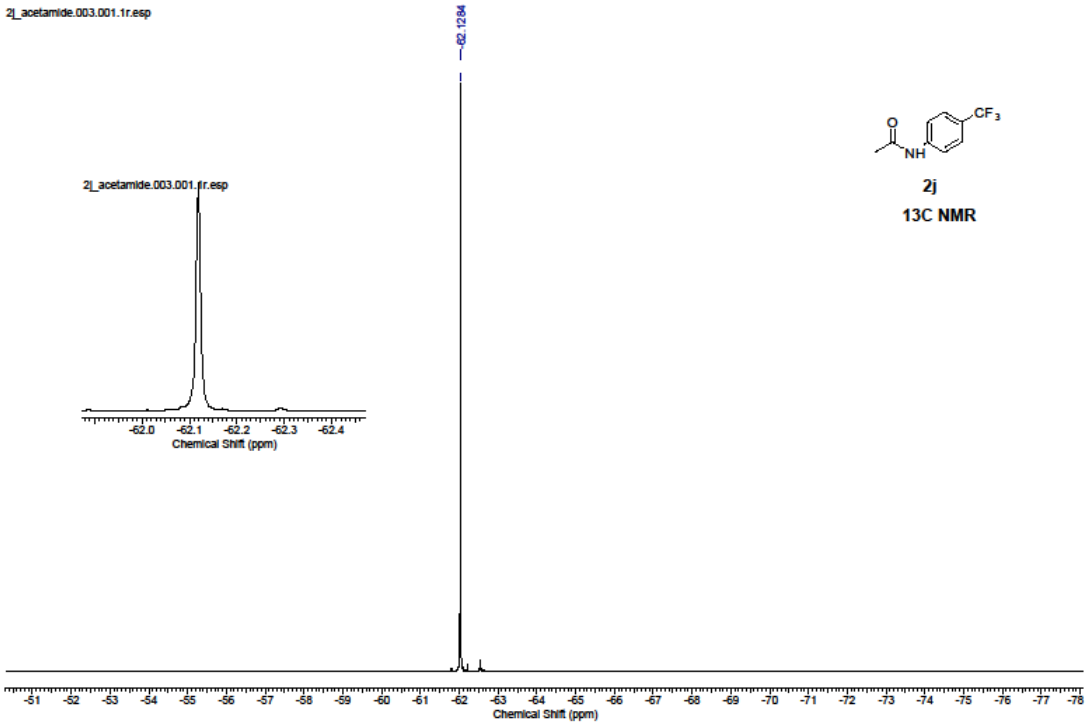

2i_naphthal.001.001.1r.esp
8.1699
8.1687
7.9775
7.9616
7.9561
7.9084
7.8470
7.8457
7.6523
7.6189
7.6134
7.6085
7.2700
2i_naphthal.001.001.1r.esp
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
Chemical Shift (ppm)
CF3
2i
1H NMR
1.000
1.070
3.020
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

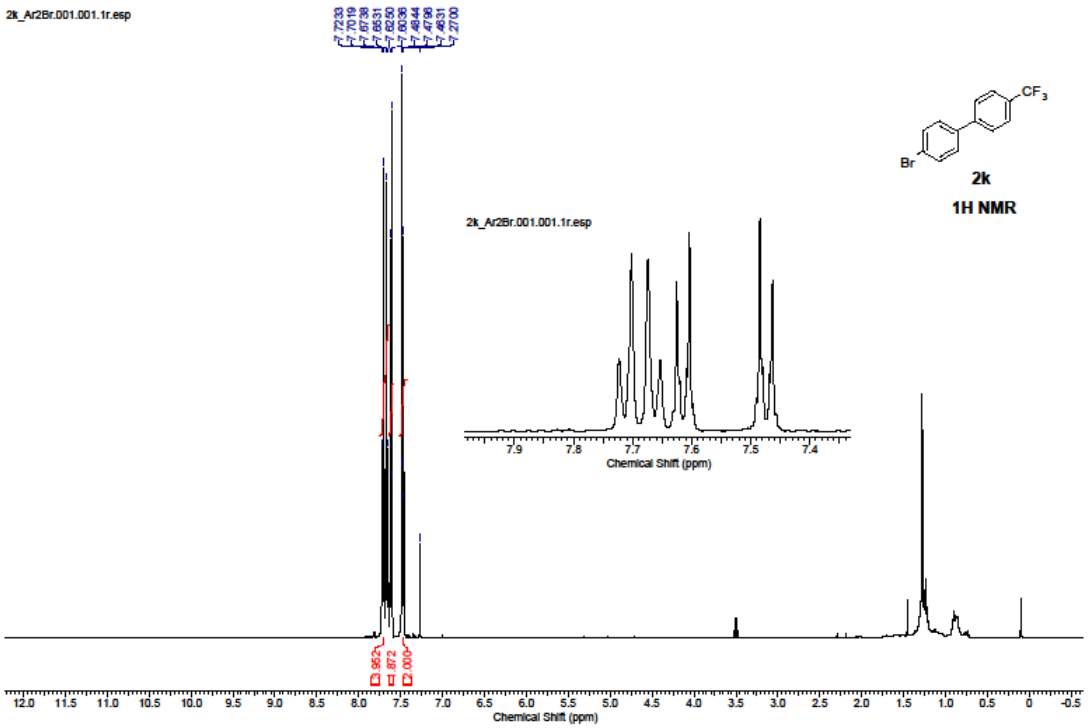

2i_naphthal.002.001.1r.esp
134.5419
132.1690
128.9691
128.7932
128.0352
127.8457
127.1350
125.7373
125.6425
125.5951
123.0367
121.4416
121.3784
77.3159
77.0000
76.6841
CF3
2i
13C NMR
2i_naphthal.002.001.1r.esp
135 130 125 120
Chemical Shift (ppm)
2i_naphthal.002.001.1r.esp
126.00 125.75 125.50 125.25
Chemical Shift (ppm)
2i_naphthal.002.001.1r.esp
121.75 121.50 121.25 121.00
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

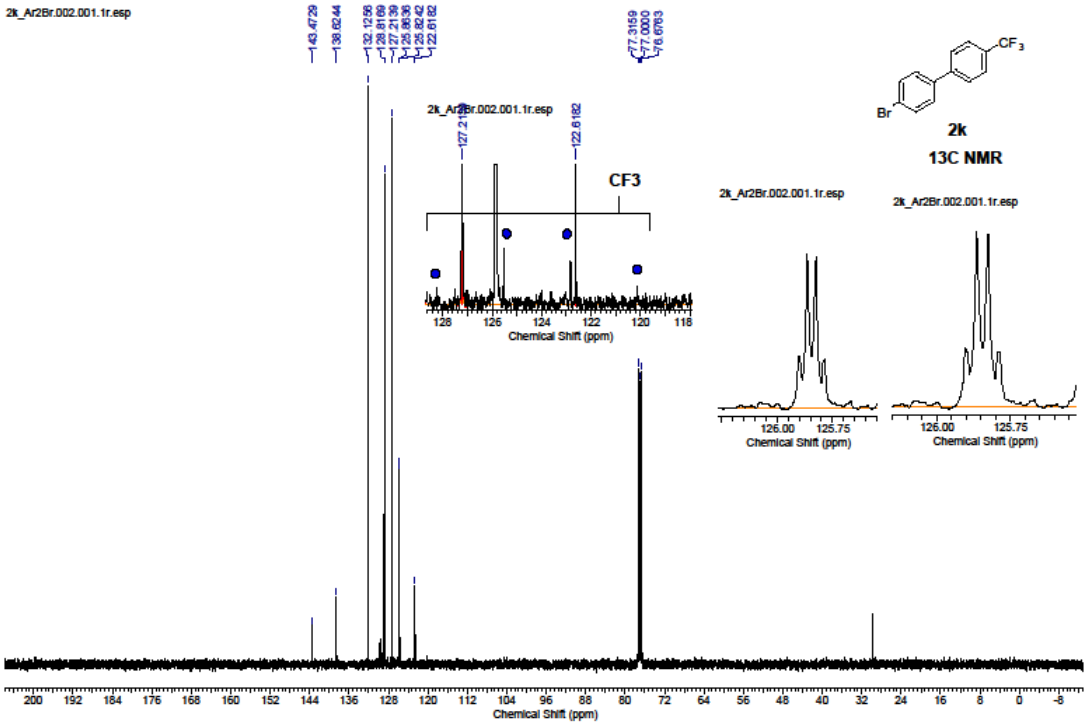

2i_naphthal.003.001.1r.esp
-62.2438
CF3
2i
19F NMR
2i_naphthal.003.001.1r.esp
-62.0 -62.1 -62.2 -62.3 -62.4 -62.5
Chemical Shift (ppm)
-53 -54 -55 -56 -57 -58 -59 -60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72 -73
Chemical Shift (ppm)

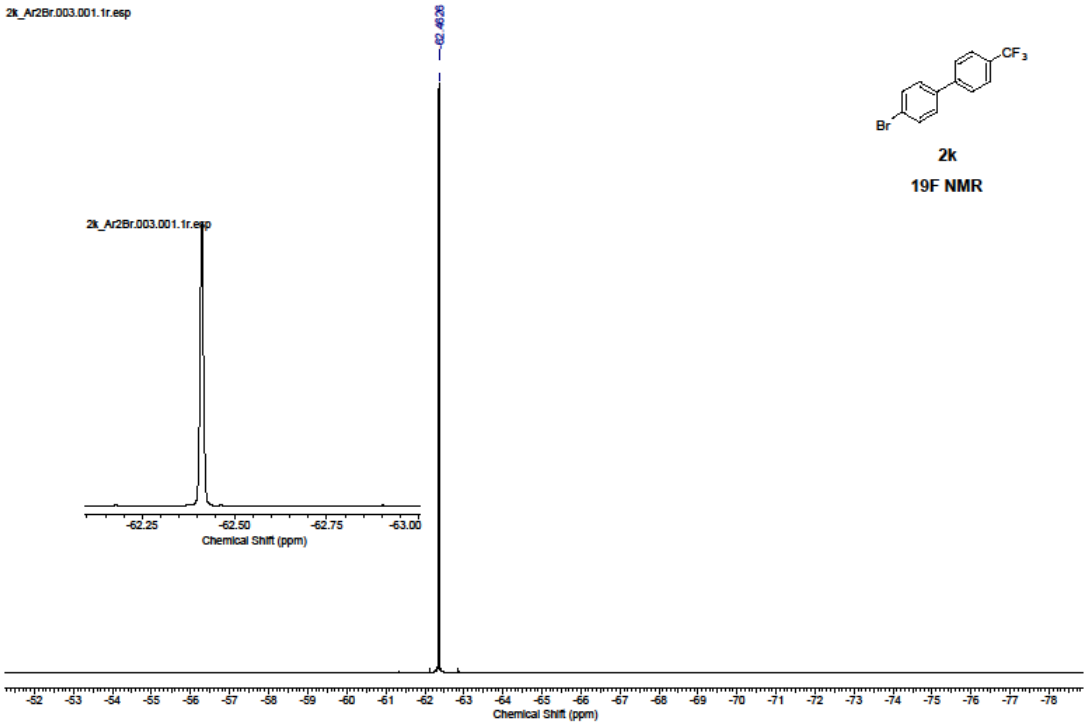

2j
1H NMR
Chemical Shift (ppm)

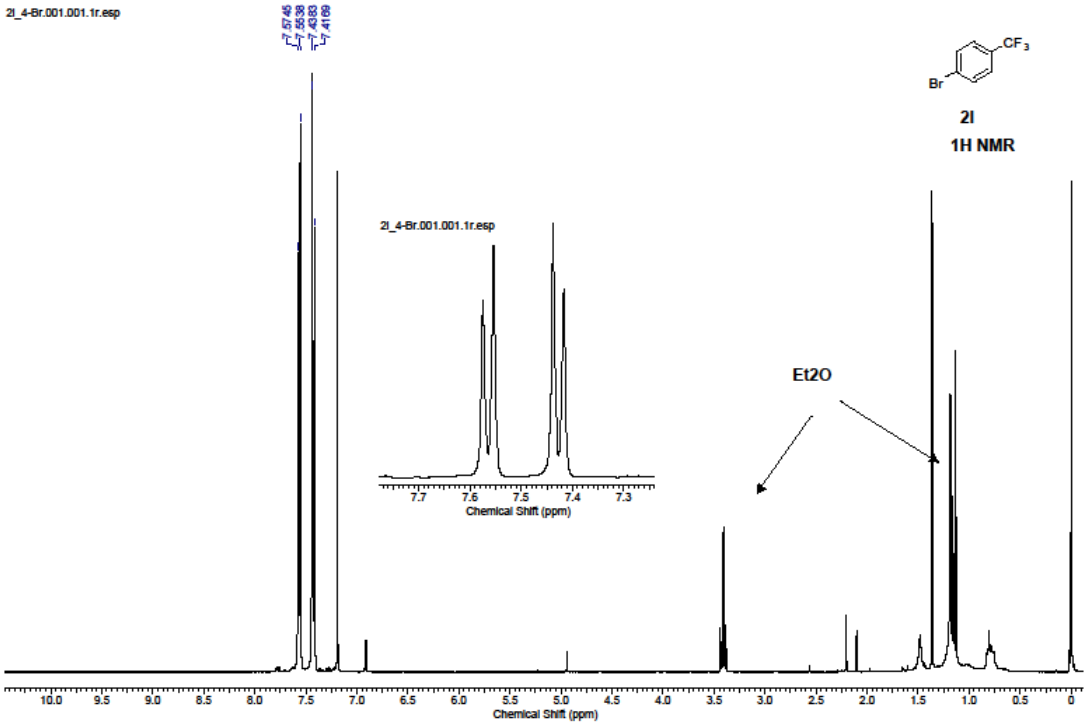

2j
13C NMR
CF3
Chemical Shift (ppm)

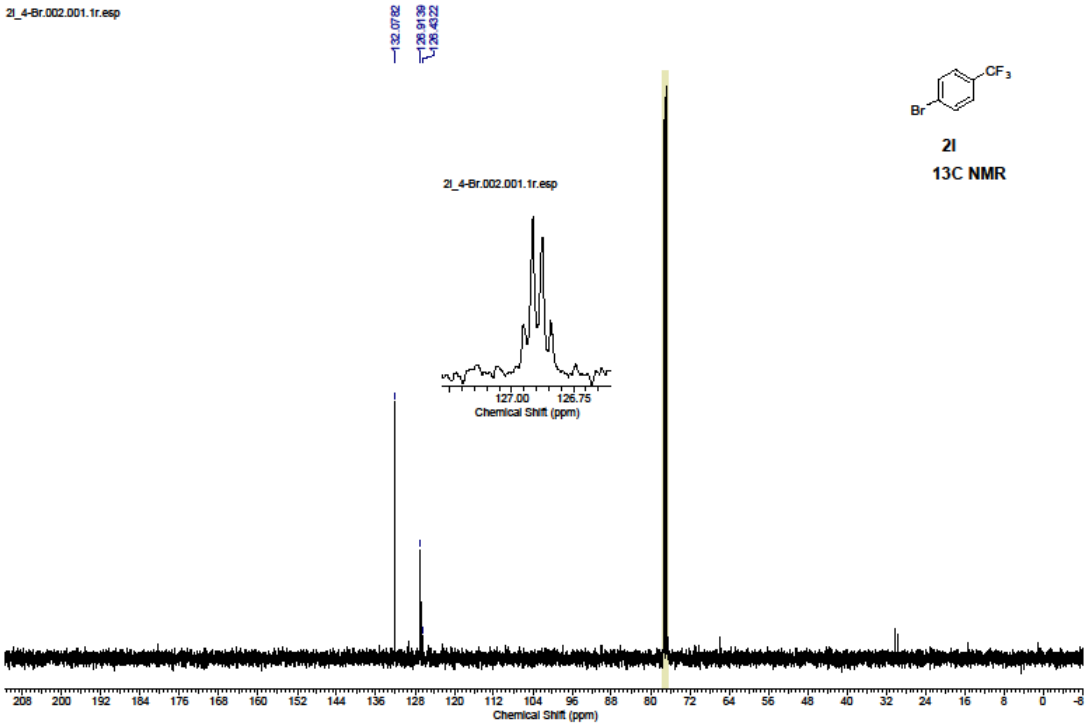

2j_acetamide.003.001.1r.esp
-62.1284
2j_acetamide.003.001.1r.esp
-62.0 -62.1 -62.2 -62.3 -62.4
Chemical Shift (ppm)
-51 -52 -53 -54 -55 -56 -57 -58 -59 -60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72 -73 -74 -75 -76 -77 -78
Chemical Shift (ppm)
O
NH
CF3
2j
13C NMR

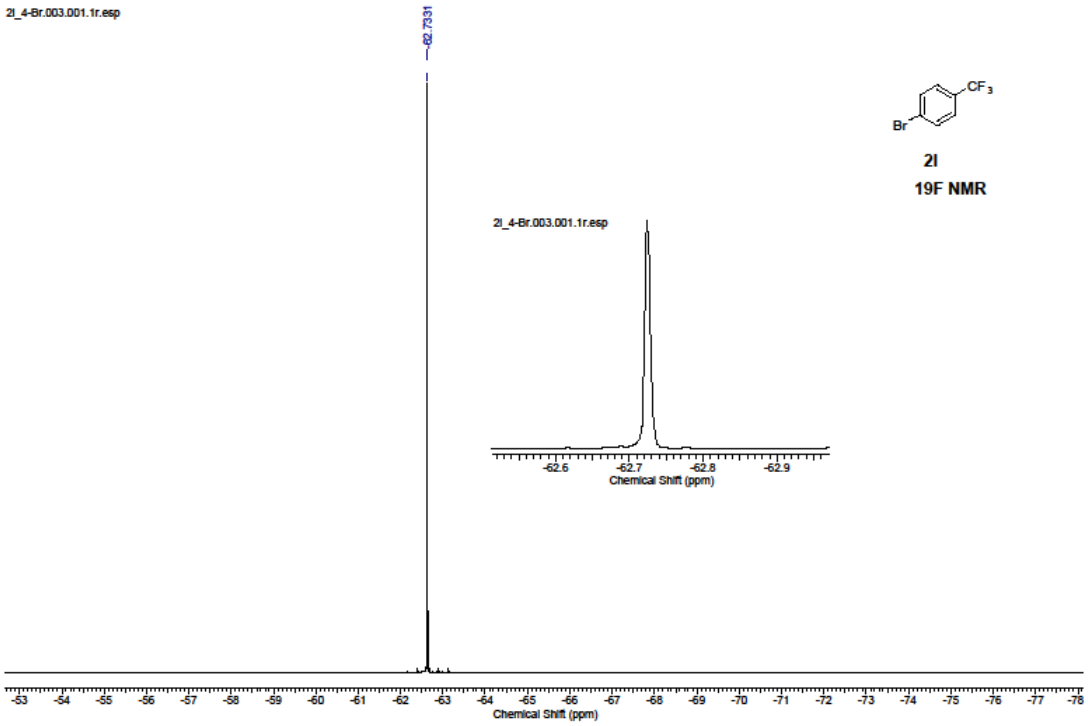

2k_Ar2Br.001.001.1r.esp
7.7233
7.7019
7.6738
7.6531
7.6250
7.6036
7.4844
7.4796
7.4631
7.2700
2k_Ar2Br.001.001.1r.esp
7.9 7.8 7.7 7.6 7.5 7.4
Chemical Shift (ppm)
1.962
1.872
2.000
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)
Br
CF3
2k
1H NMR


2k_Ar2Br.002.001.1r.esp
143.4729
138.6244
132.1266
128.8169
127.2139
125.8836
125.8242
122.6182
77.3159
77.0000
76.6763
CF3
Chemical Shift (ppm)
CF3
Br
2k
13C NMR


2k_Ar2Br.003.001.1r.esp
62.4626
Chemical Shift (ppm)
CF3
Br
2k
19F NMR

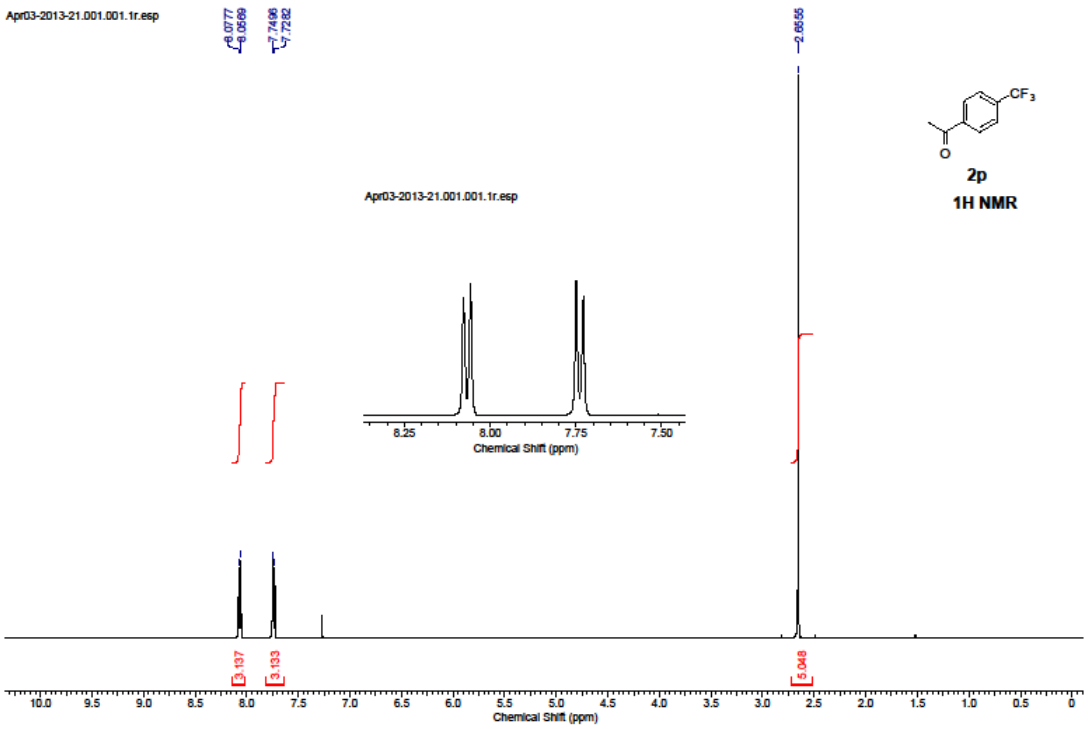

2l_4-Br.001.001.1r.esp
7.5746
7.5538
7.4363
7.4169
CF3
Br
2l
1H NMR
2l_4-Br.001.001.1r.esp
7.7
7.6
7.5
7.4
7.3
Chemical Shift (ppm)
Et2O
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


2l_4-Br.002.001.1r.esp
132.0782
126.9139
126.4322
CF3
Br
2l
13C NMR
2l_4-Br.002.001.1r.esp
127.00
126.75
Chemical Shift (ppm)
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)



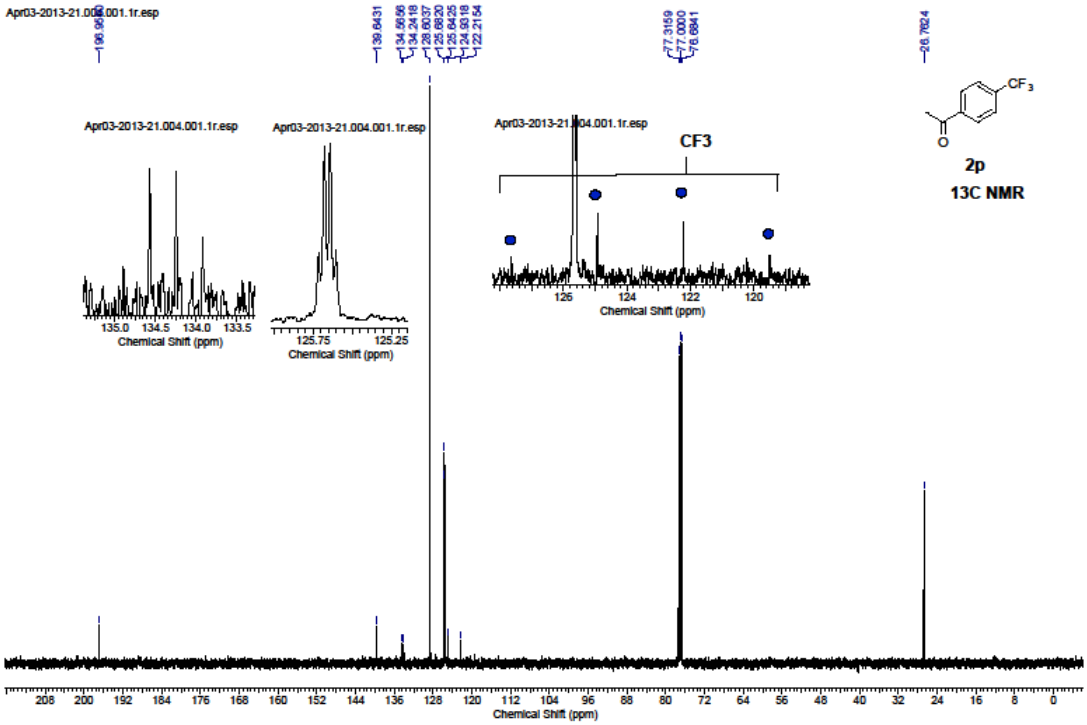
2l

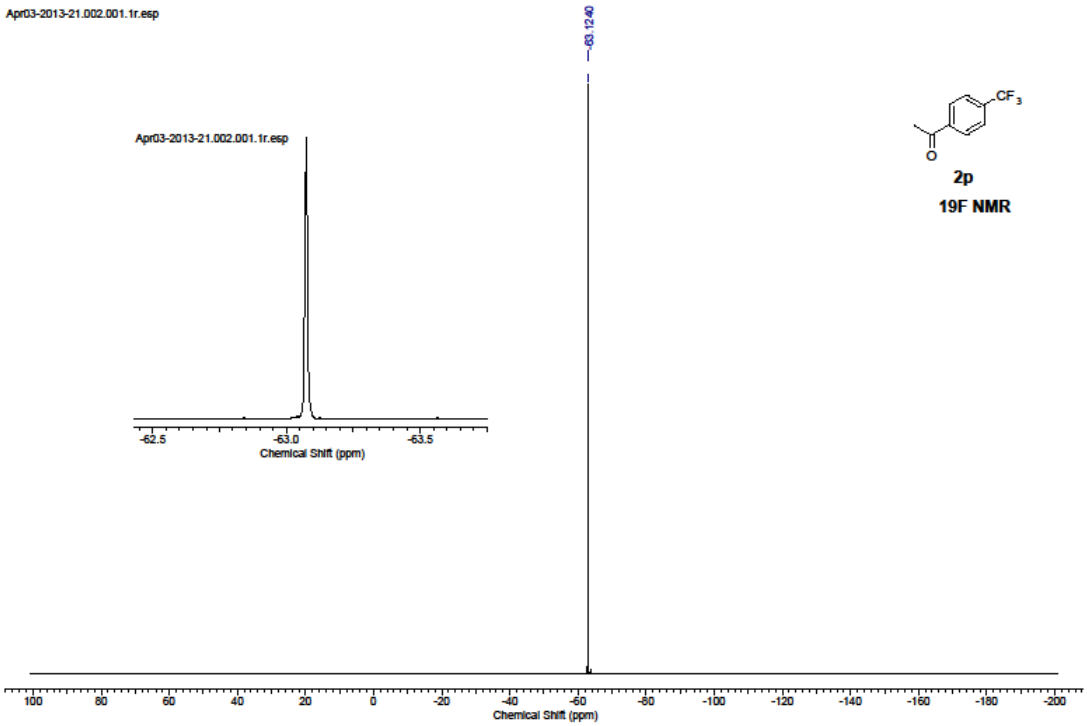
19F NMR

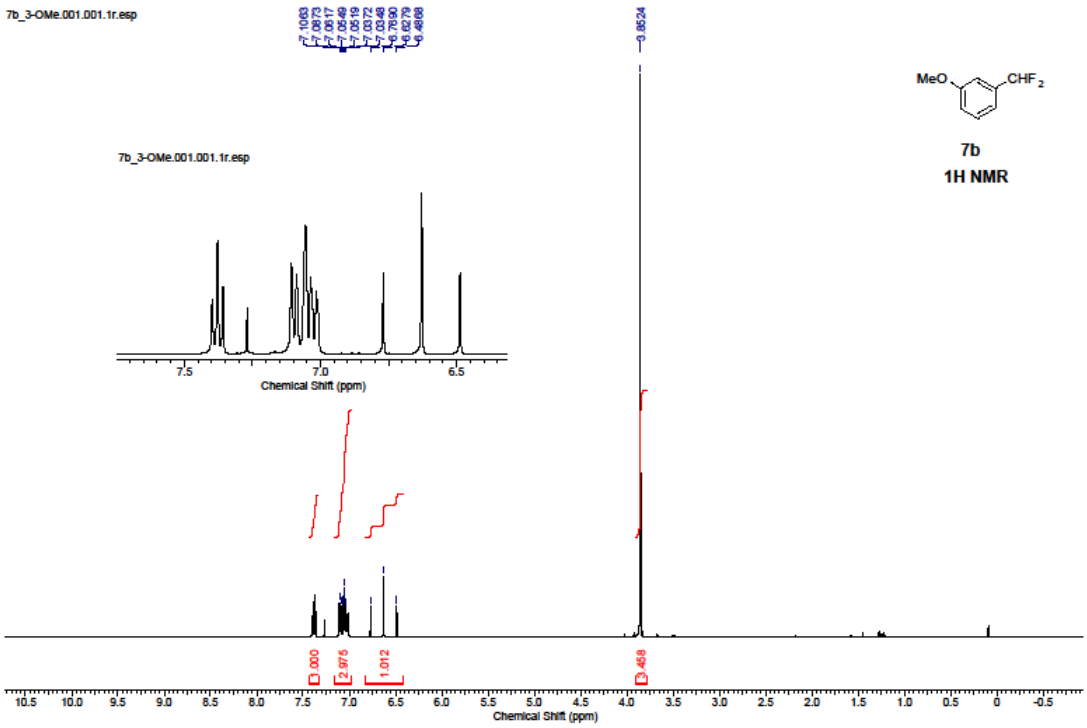


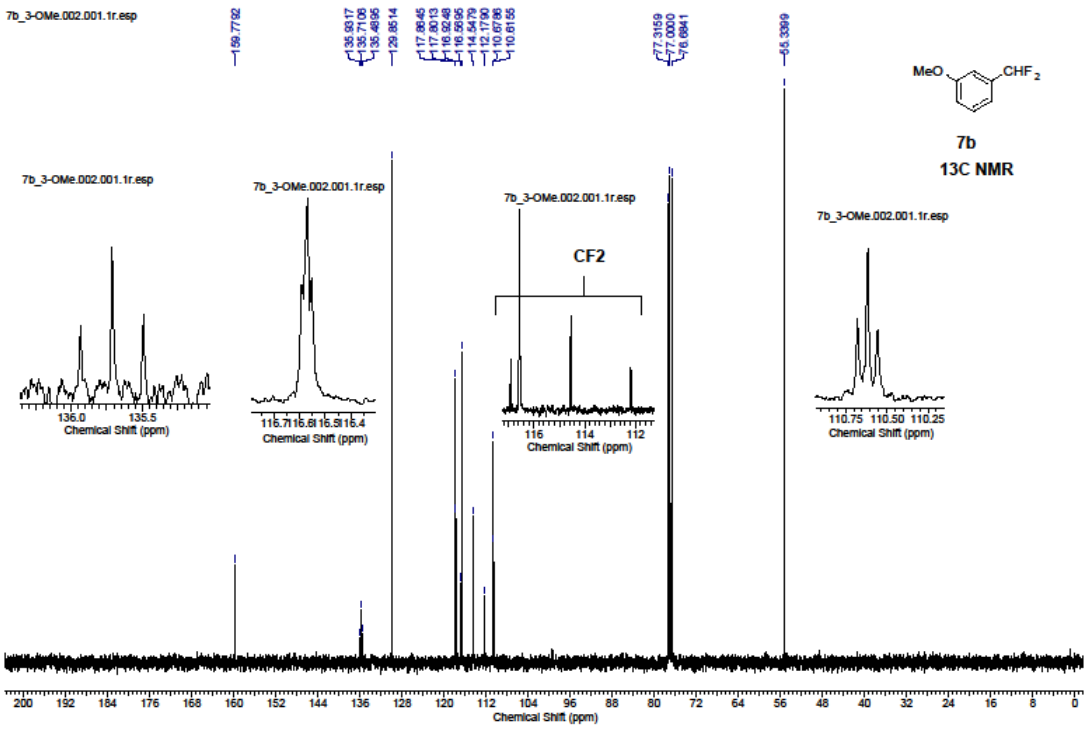
2p

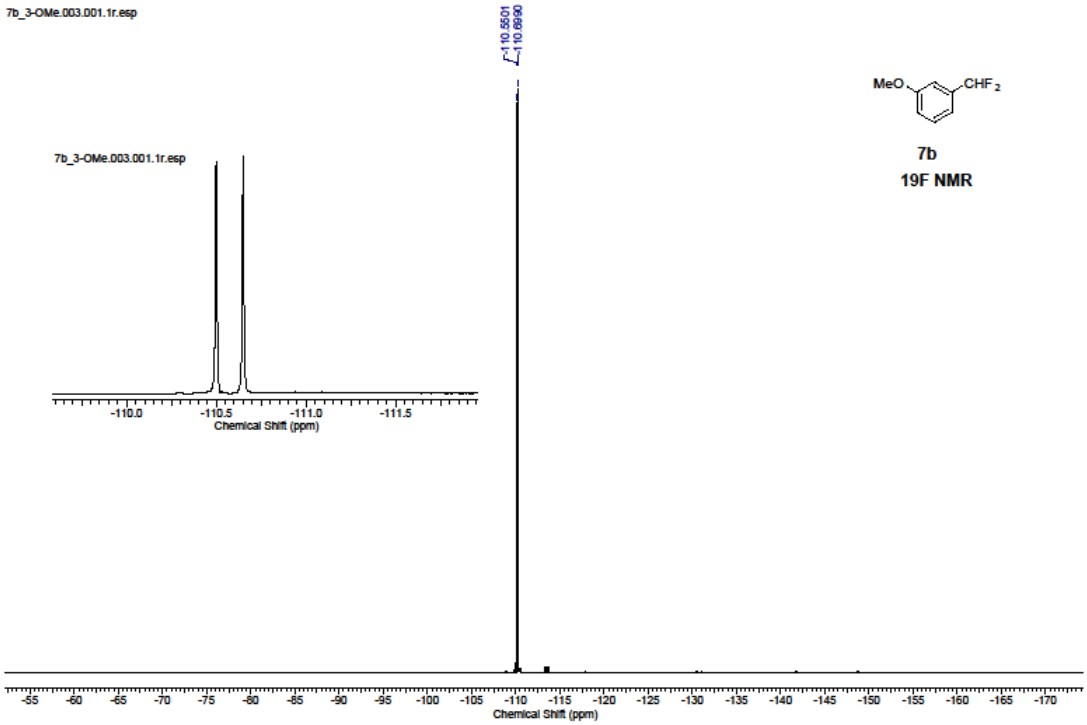
1H NMR

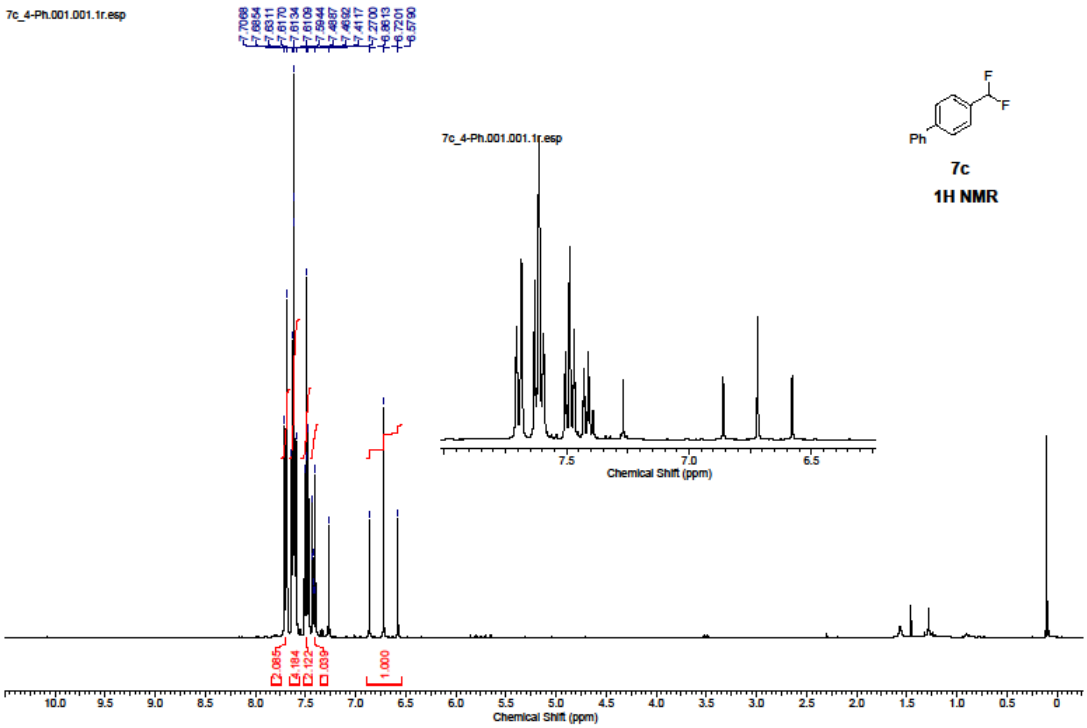

Apr03-2013-21.004.001.1r.esp
CF3
2p
13C NMR
Chemical Shift (ppm)

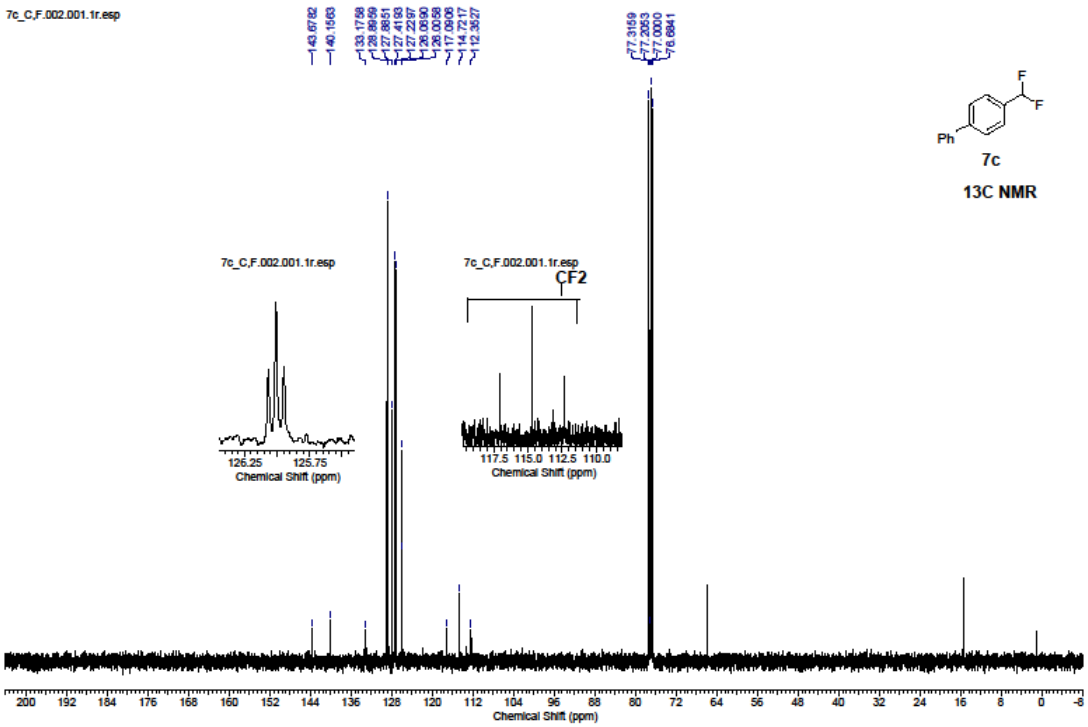

Apr03-2013-21.002.001.1r.esp
2p
19F NMR
Chemical Shift (ppm)

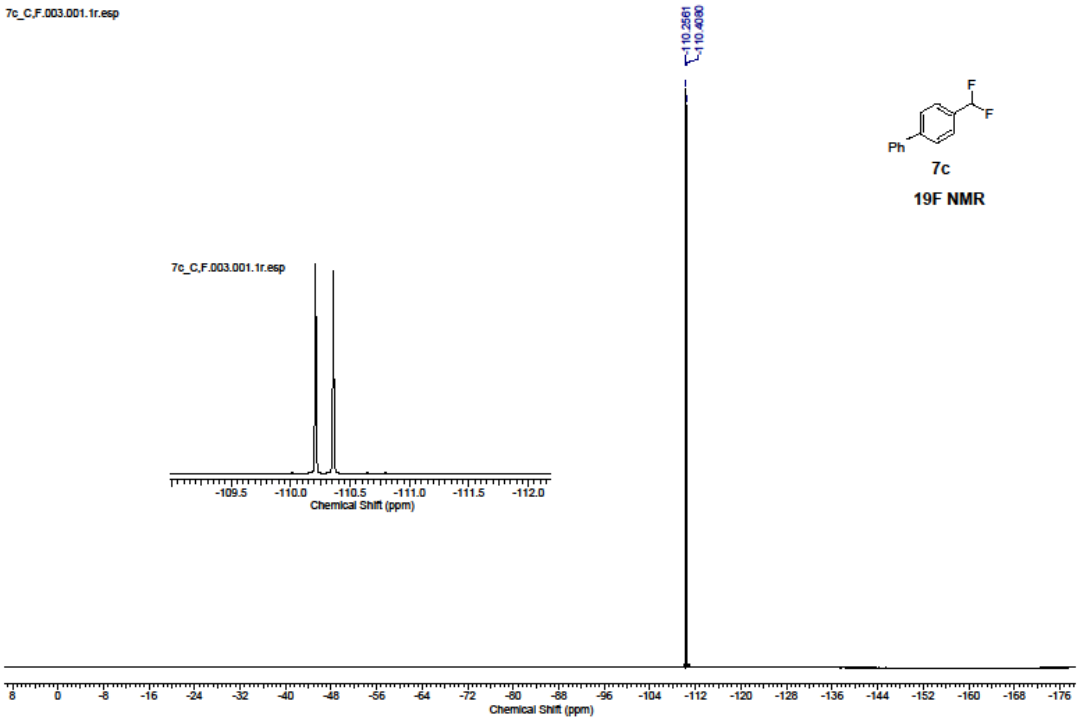

7b_3-OMe.001.001.1r.esp
MeO
CHF2
7b
1H NMR
Chemical Shift (ppm)

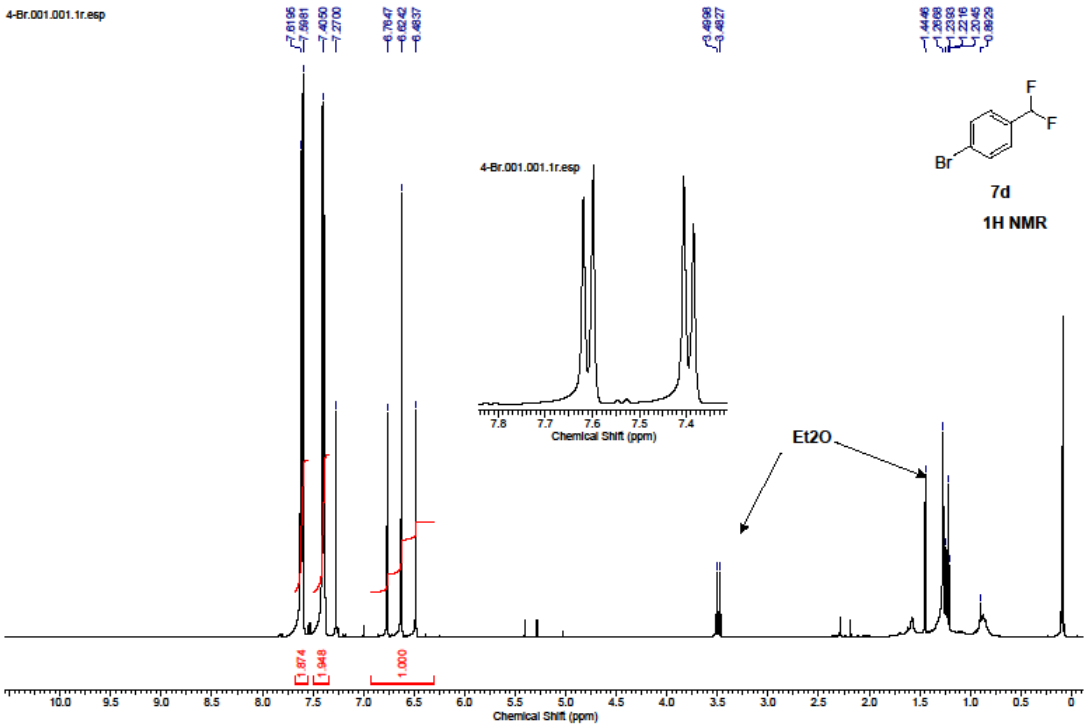

7b_3-OMe.002.001.1r.esp
MeO
CHF2
7b
13C NMR
CF2
Chemical Shift (ppm)

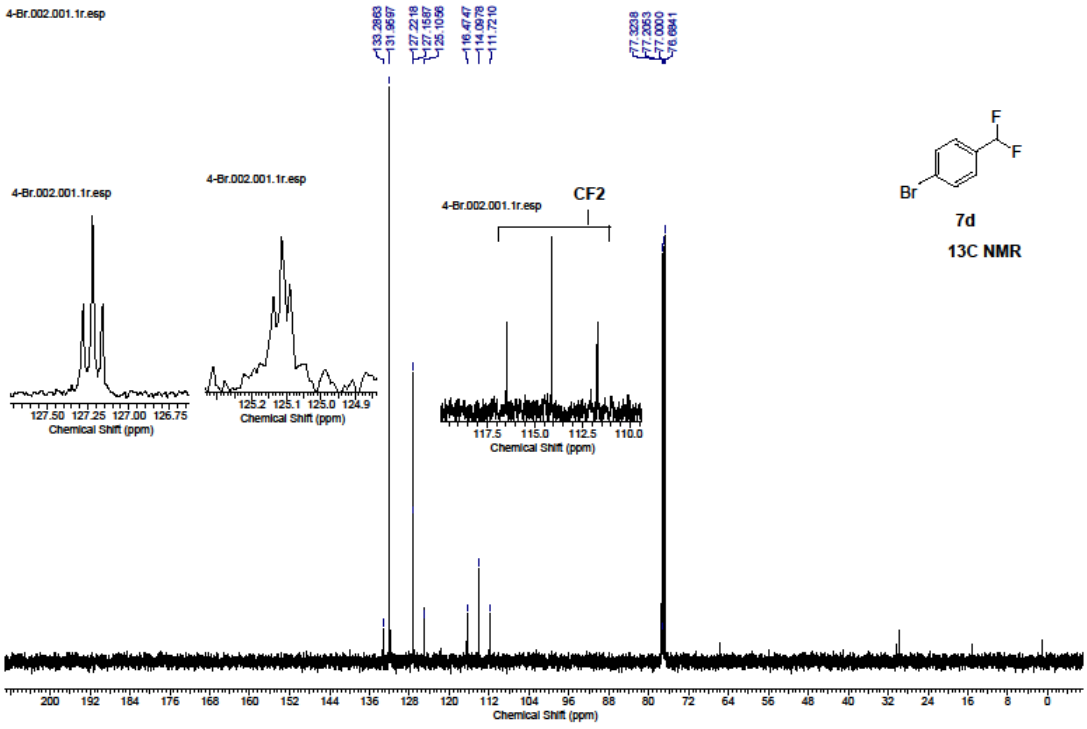

7b_3-OMe.003.001.1r.esp
-110.5501
-110.6990
MeO
CHF2
7b
19F NMR
7b_3-OMe.003.001.1r.esp
-110.0
-110.5
-111.0
-111.5
Chemical Shift (ppm)
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170
Chemical Shift (ppm)

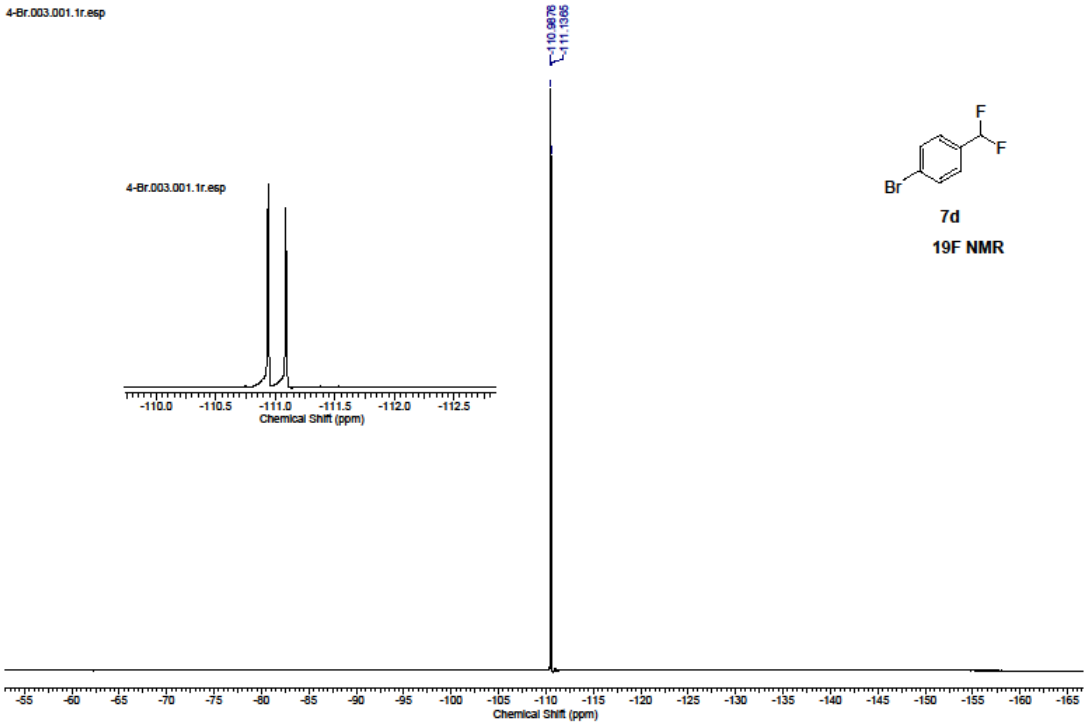

7c_4-Ph.001.001.1r.esp
7.7068
7.6834
7.6511
7.6170
7.6134
7.6109
7.5944
7.4887
7.4692
7.4117
7.2700
6.8613
6.7201
6.5790
F
F
Ph
7c
1H NMR
7c_4-Ph.001.001.1r.esp
7.5
7.0
6.5
Chemical Shift (ppm)
0.85
4.84
1.22
0.39
1.000
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

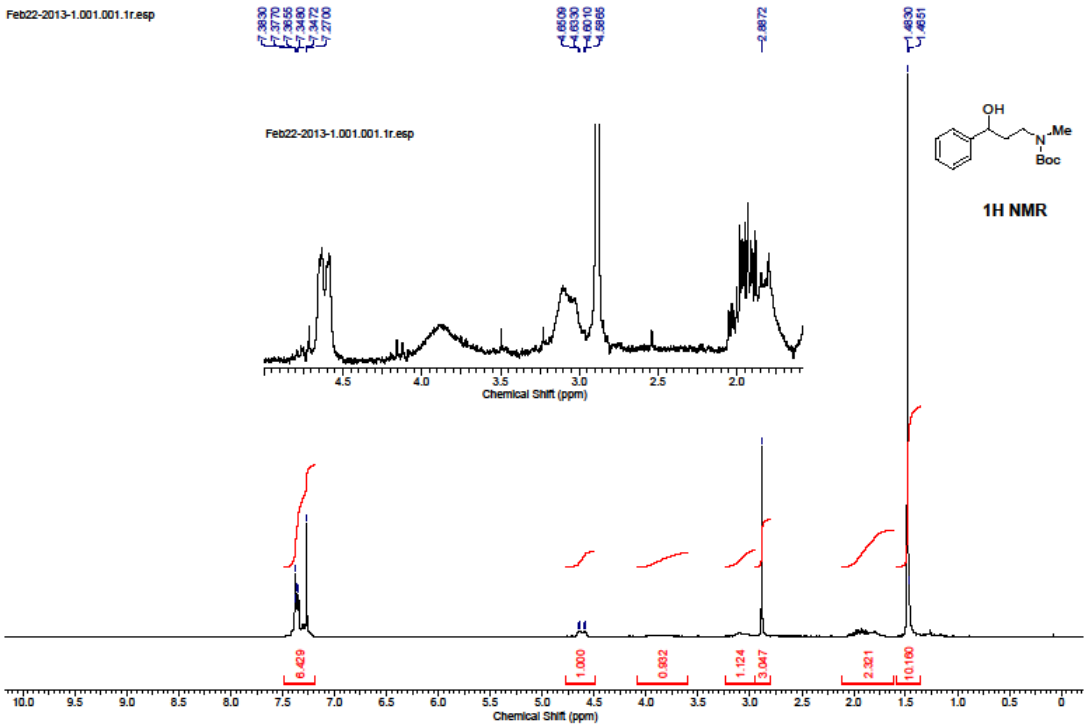

7c_C,F.002.001.1r.esp
143.6782
140.1563
133.1798
128.9899
127.8851
127.4183
127.2297
126.8580
126.0058
117.0906
114.7217
112.3527
77.3159
77.2053
77.0000
76.6841
F
F
Ph
7c
13C NMR
7c_C,F.002.001.1r.esp
126.25
125.75
Chemical Shift (ppm)
7c_C,F.002.001.1r.esp
CF2
117.5 115.0 112.5 110.0
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

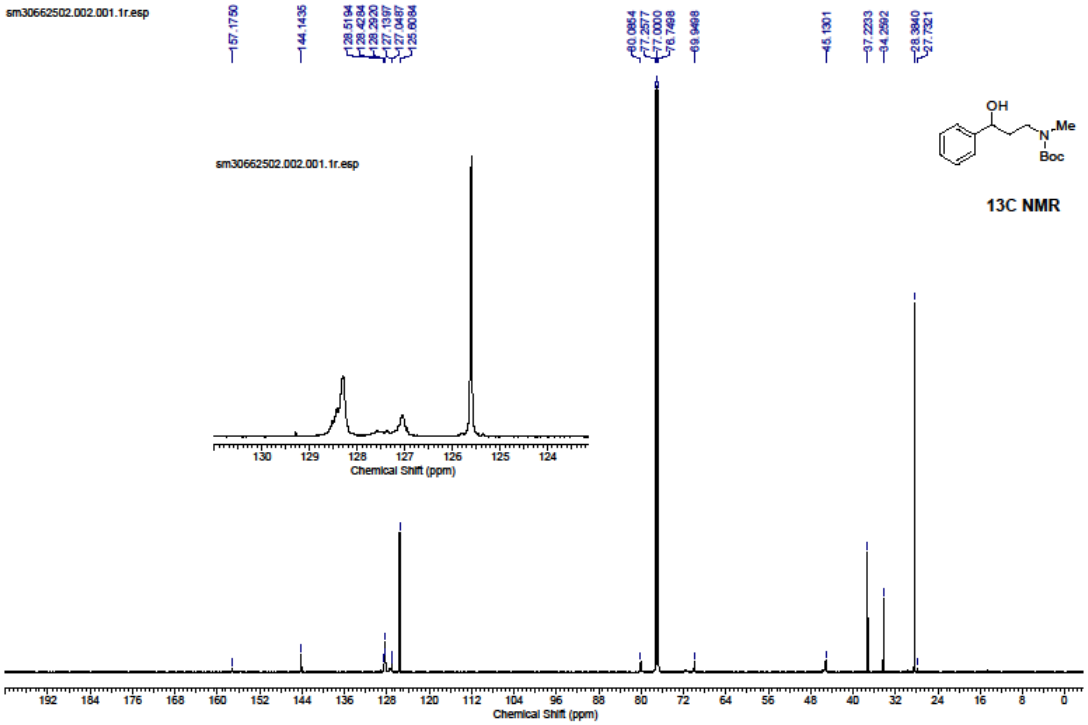

7c_C,F.003.001.1r.esp
110.2561
110.4090
F
F
Ph
7c
19F NMR
7c_C,F.003.001.1r.esp
-109.5 -110.0 -110.5 -111.0 -111.5 -112.0
Chemical Shift (ppm)
8 0 -8 -16 -24 -32 -40 -48 -56 -64 -72 -80 -88 -96 -104 -112 -120 -128 -136 -144 -152 -160 -168 -176
Chemical Shift (ppm)

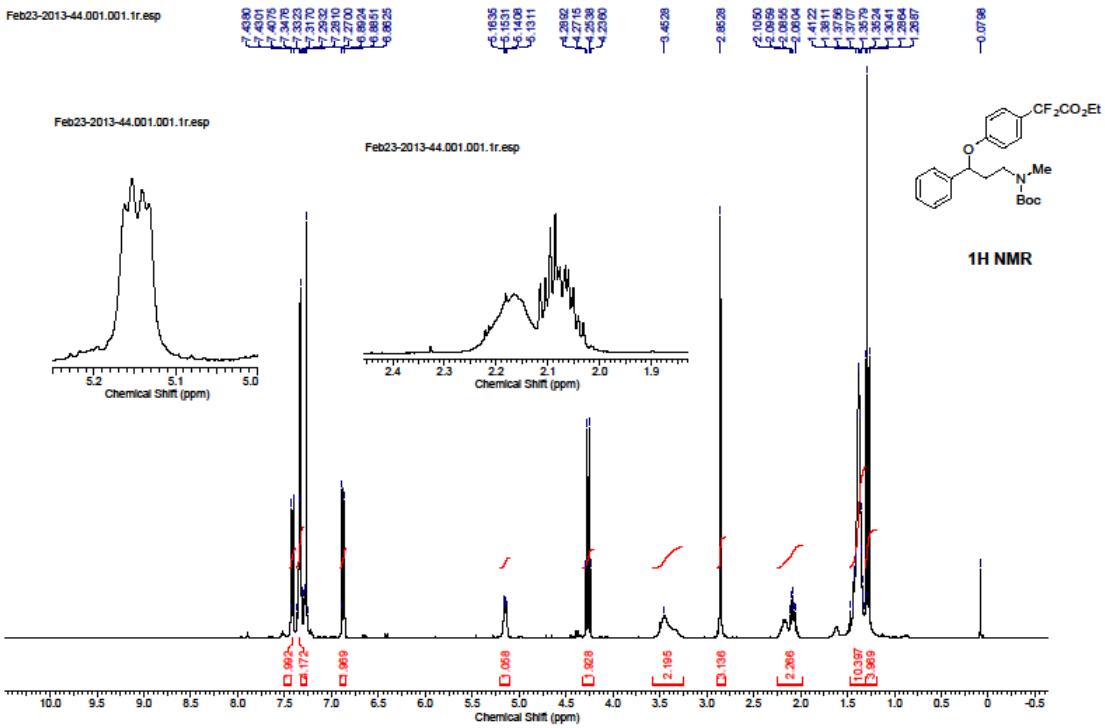

4-Br.001.001.1r.esp
7.8195
7.5981
7.4050
7.2700
6.7647
6.6242
6.4837
3.4998
3.4827
1.4446
1.2868
1.2393
1.2216
1.2045
0.8929
F
F
Br
7d
1H NMR
4-Br.001.001.1r.esp
Et2O
1.874
1.948
1.000
Chemical Shift (ppm)

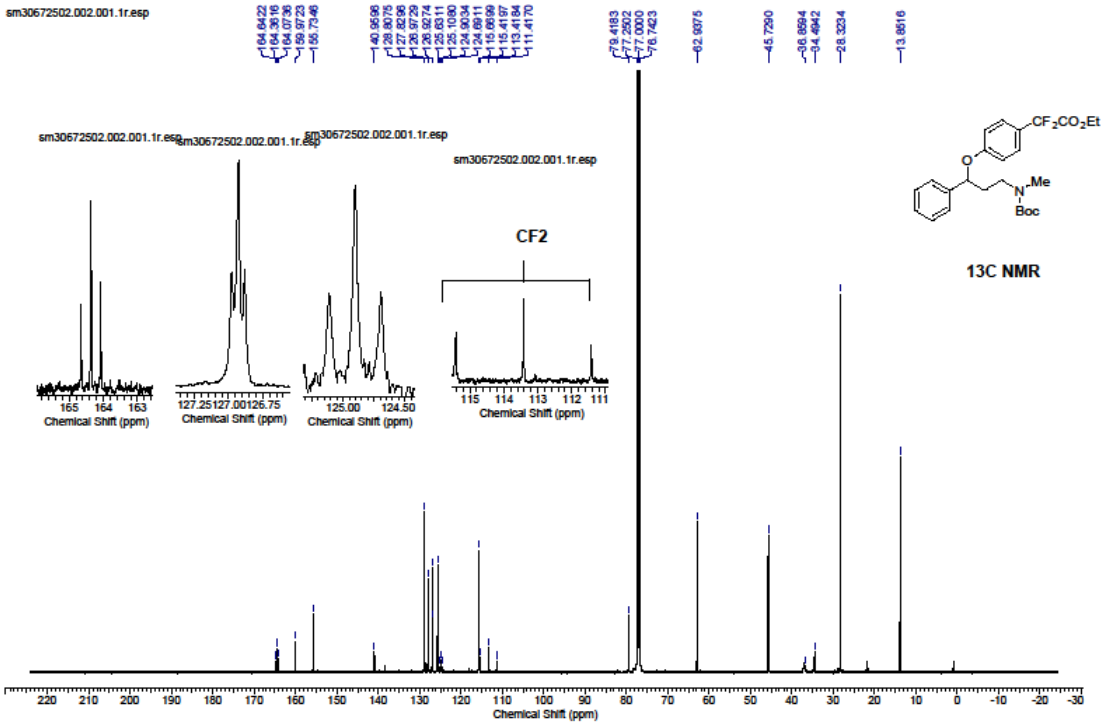

4-Br.002.001.1r.esp
133.2863
131.9597
127.2218
127.1587
125.1056
116.4747
114.0678
111.7210
77.3238
77.2063
77.0000
76.6941
F
F
Br
7d
13C NMR
CF2
Chemical Shift (ppm)

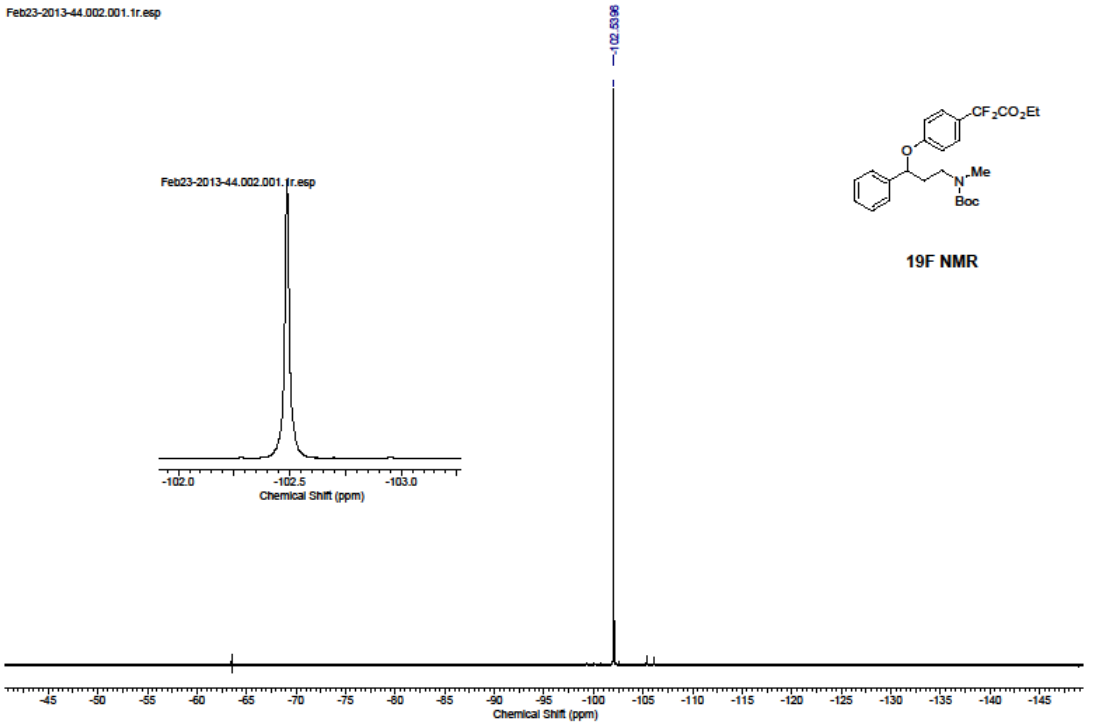

4-Br.003.001.1r.esp
-110.9878
-111.1365
4-Br.003.001.1r.esp
-110.0
-110.5
-111.0
-111.5
-112.0
-112.5
Chemical Shift (ppm)
F
F
Br
7d
19F NMR
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
Chemical Shift (ppm)

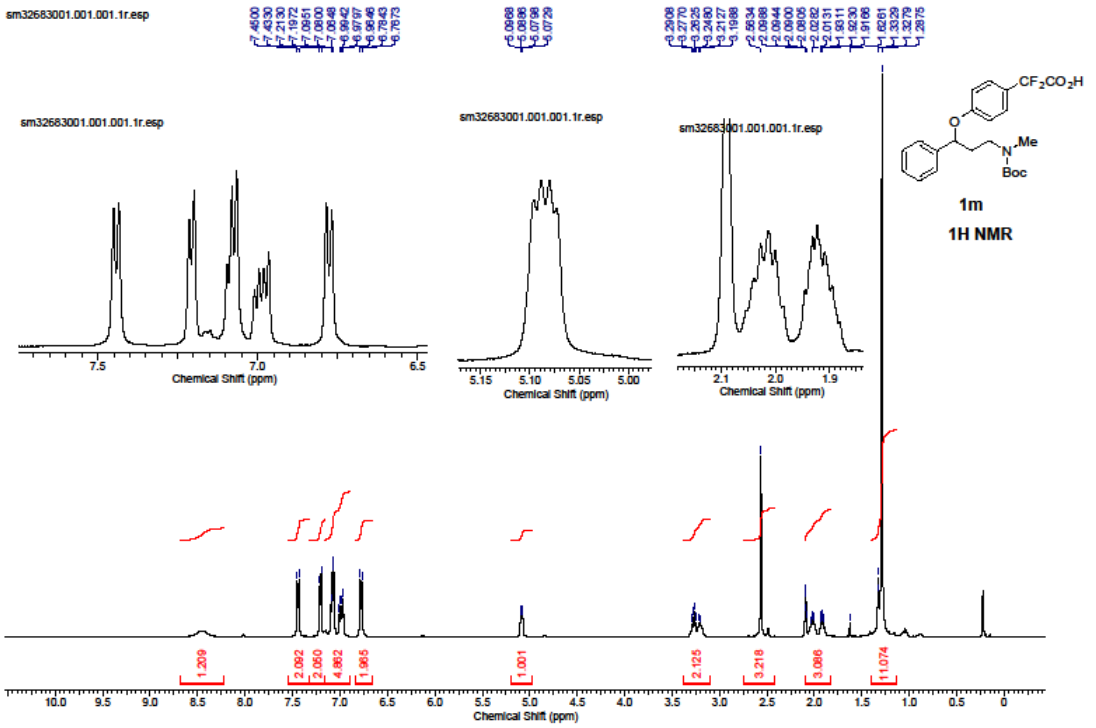

Feb22-2013-1.001.001.1r.esp
7.3830
7.3770
7.3655
7.3480
7.3472
7.2700
4.6509
4.6330
4.6010
4.5865
2.8872
1.4830
1.4651
Feb22-2013-1.001.001.1r.esp
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)
OH
N
Me
Boc
1H NMR
6.429
1.000
0.882
1.124
3.047
2.321
10.160
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

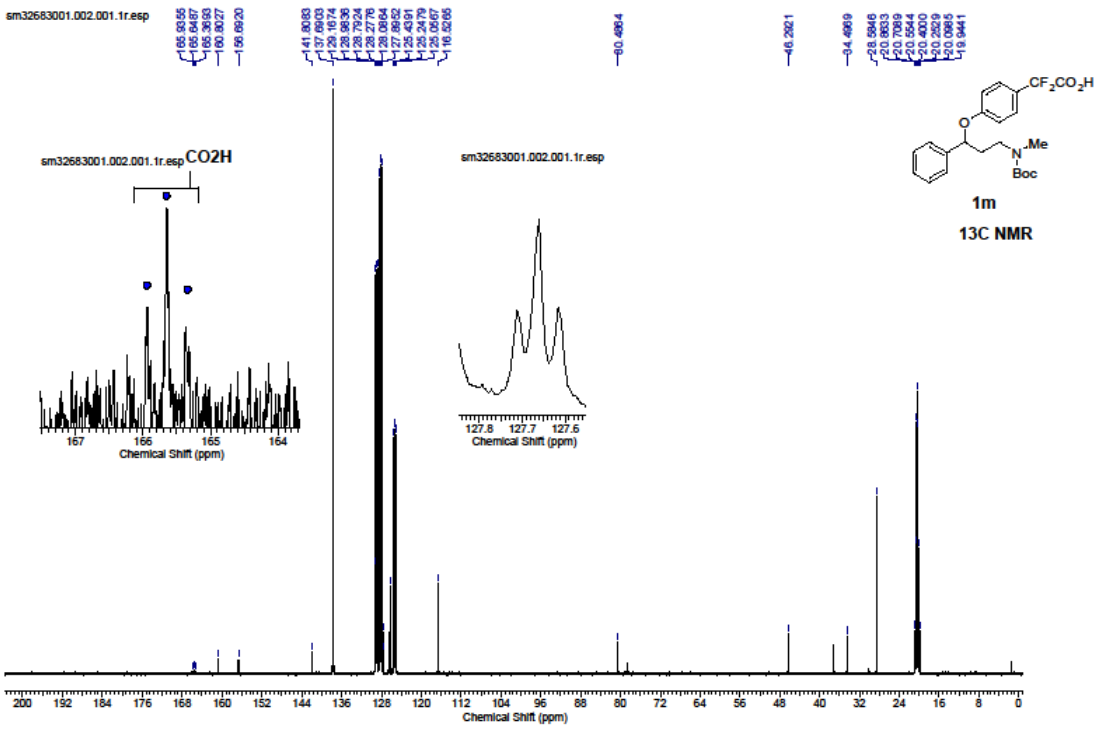

sm30662502.002.001.1r.esp
OH
N
Me
Boc
13C NMR
Chemical Shift (ppm)

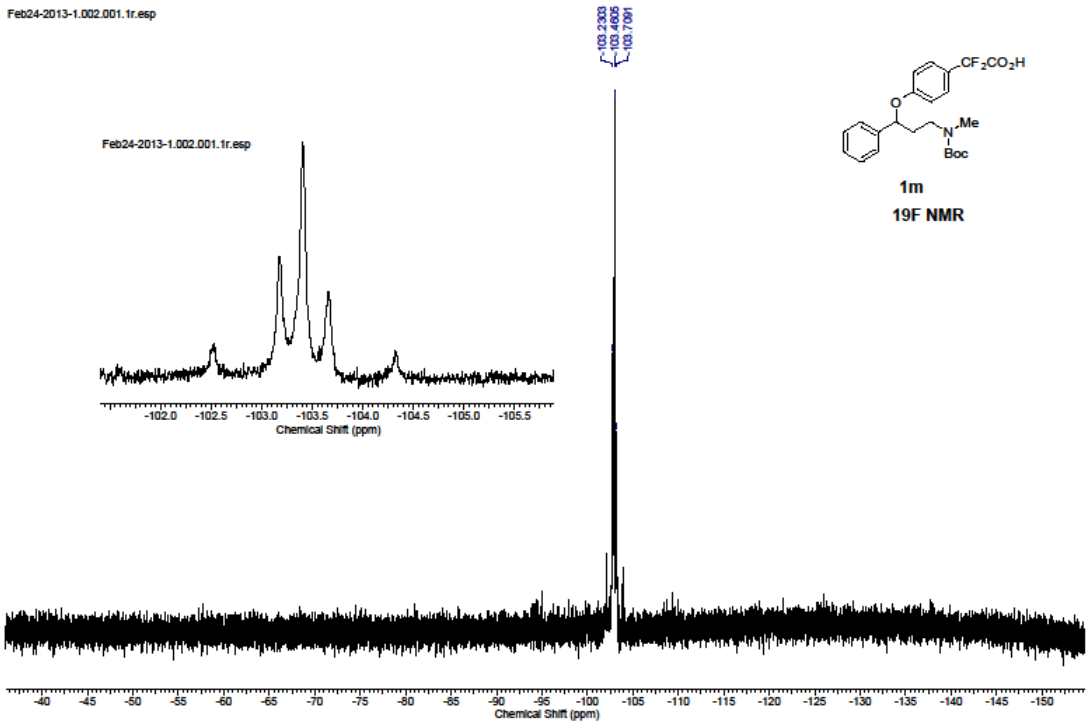

Feb23-2013-44.001.001.1r.esp
CF2CO2Et
O
N
Me
Boc
1H NMR
Chemical Shift (ppm)

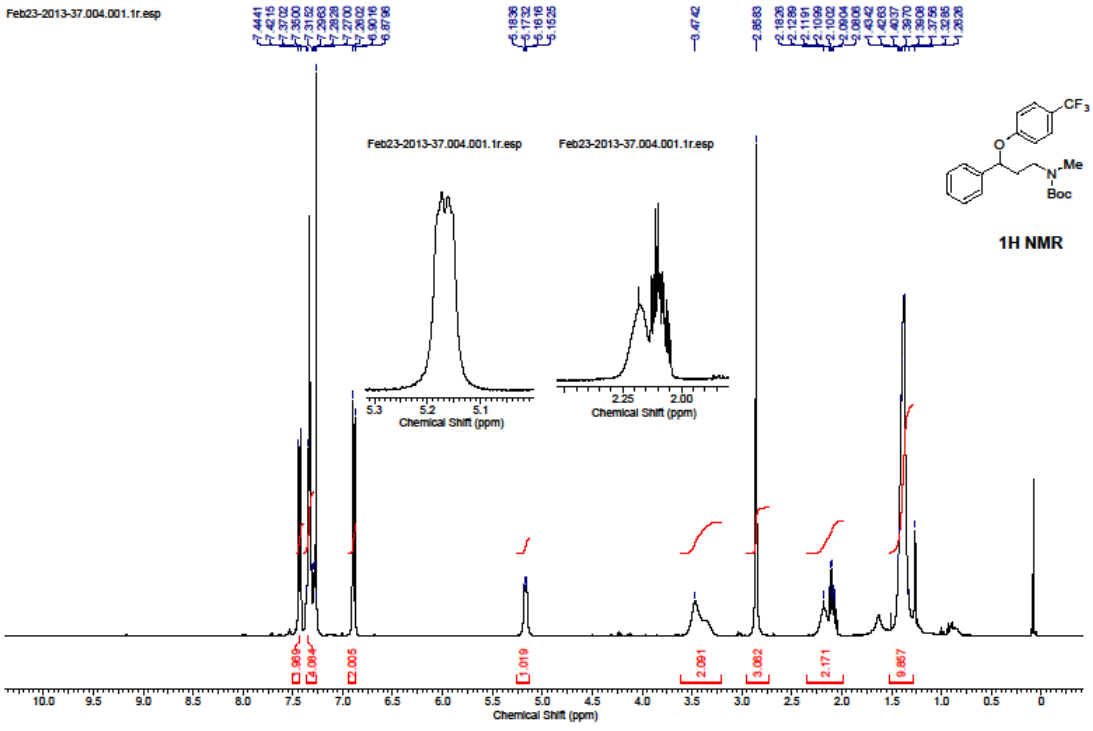

sm30672502.002.001.1r.esp
CF2
13C NMR
Chemical Shift (ppm)

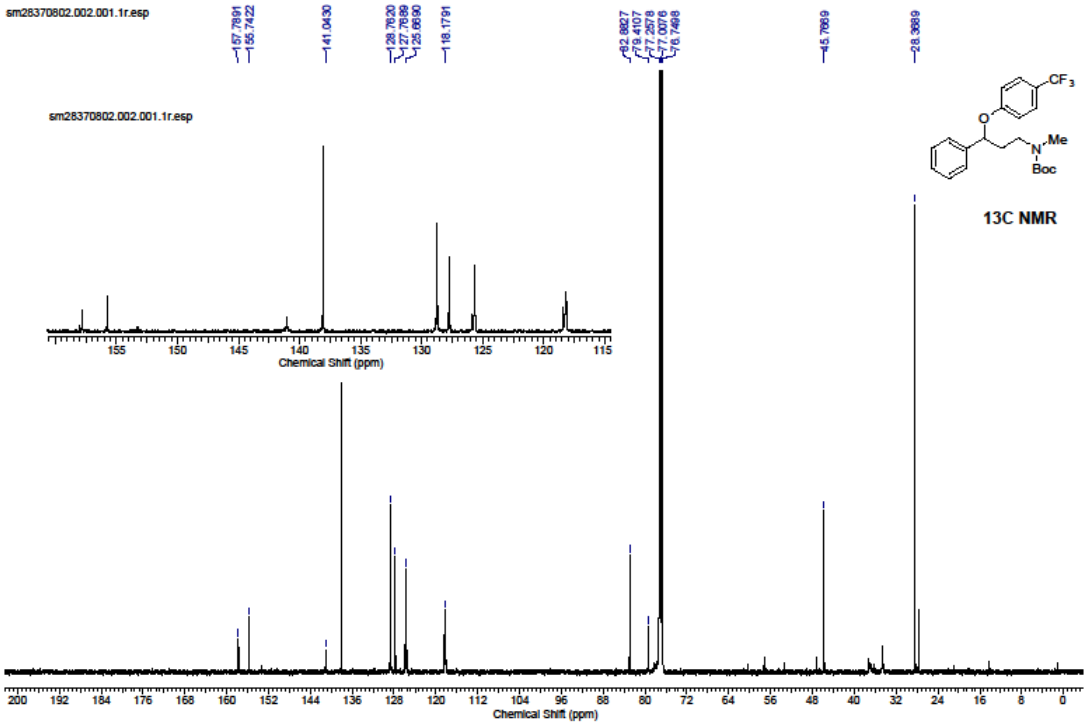

Feb23-2013-44.002.001.1r.esp
19F NMR
Chemical Shift (ppm)

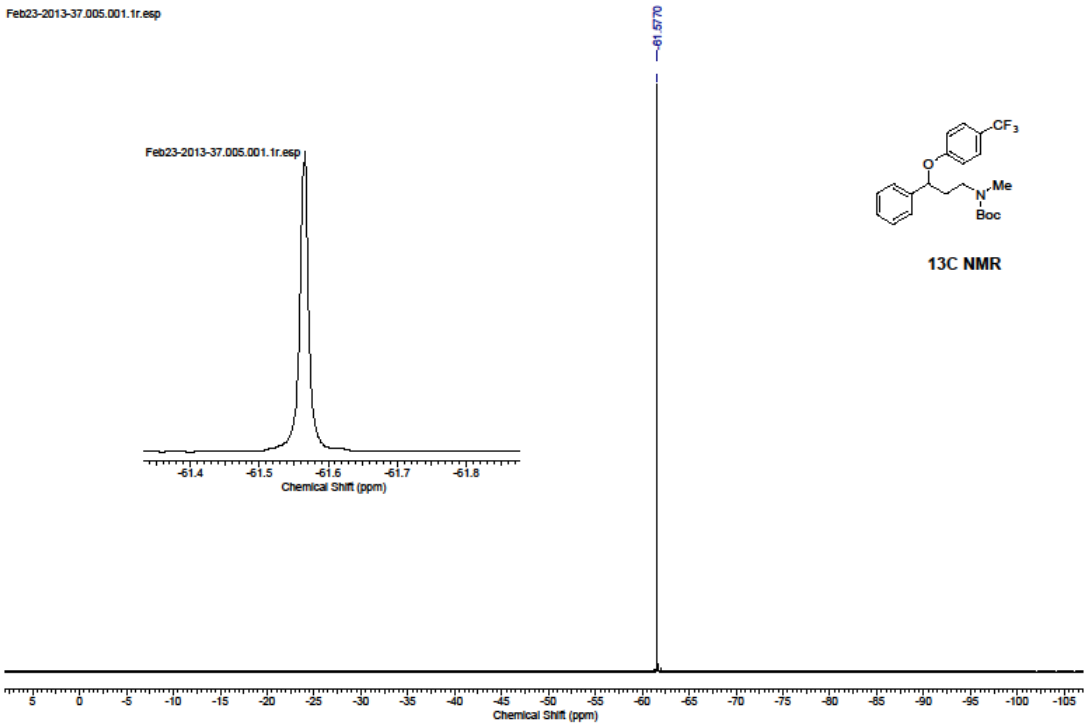

sm32683001.001.001.1r.esp
Chemical Shift (ppm)
1m
1H NMR

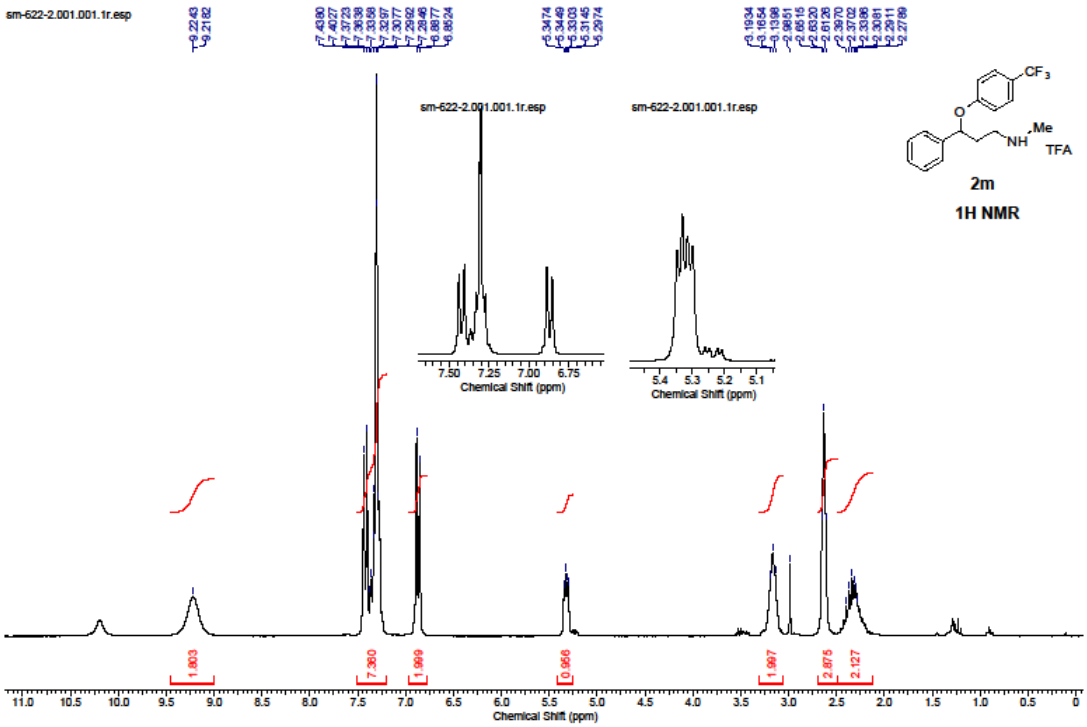

sm32683001.002.001.1r.esp
CO2H
Chemical Shift (ppm)
1m
13C NMR

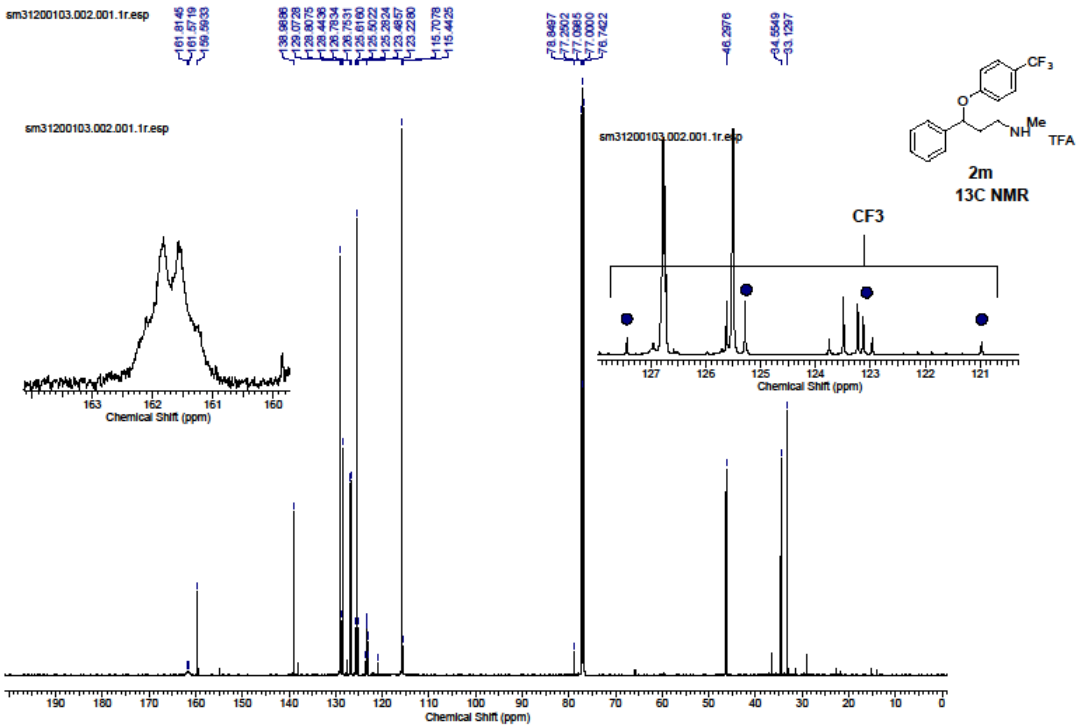

Feb24-2013-1.002.001.1r.esp
-103.2303
-103.4605
-103.7091
Feb24-2013-1.002.001.1r.esp
CF2CO2H
O
N
Me
Boc
1m
19F NMR
-102.0 -102.5 -103.0 -103.5 -104.0 -104.5 -105.0 -105.5
Chemical Shift (ppm)
-40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
Chemical Shift (ppm)

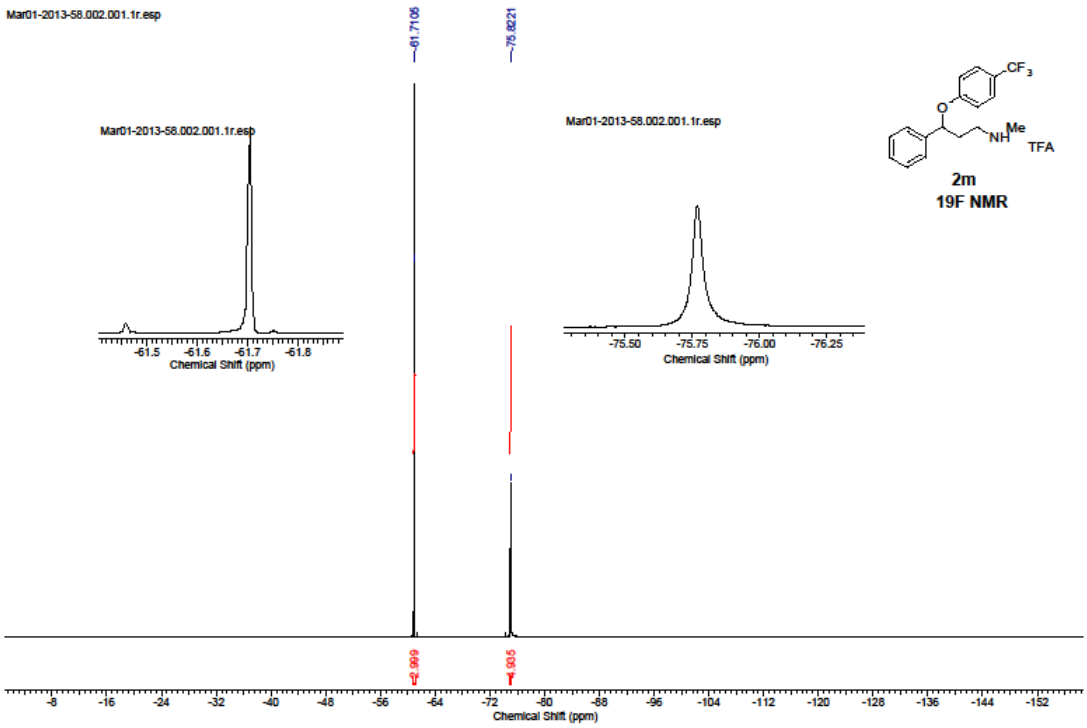

Feb23-2013-37.004.001.1r.esp
7.4441
7.4215
7.3732
7.3500
7.3152
7.2963
7.2828
7.2700
7.2602
6.9016
6.8786
6.1836
6.1732
6.1616
6.1525
3.4742
2.8583
2.1826
2.1289
2.1191
2.1099
2.1022
2.0904
2.0806
1.4342
1.4263
1.4037
1.3970
1.3906
1.3756
1.3286
1.2626
Feb23-2013-37.004.001.1r.esp
Feb23-2013-37.004.001.1r.esp
5.3 5.2 5.1
Chemical Shift (ppm)
2.25 2.00
Chemical Shift (ppm)
CF3
O
N
Me
Boc
1H NMR
0.969
0.984
2.000
1.019
2.091
3.092
2.171
9.887
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


sm28370802.002.001.1r.esp
157.7891
155.7422
141.0430
128.7820
127.7689
125.8690
118.1791
82.8827
79.4107
77.2578
77.0076
76.7466
45.7869
28.3889
sm28370802.002.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
CF3
O
N
Me
Boc
13C NMR


Feb23-2013-37.005.001.1r.esp
61.5770
Feb23-2013-37.005.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
CF3
O
N
Me
Boc
13C NMR


sm-622-2.001.001.1r.esp
sm-622-2.001.001.1r.esp
sm-622-2.001.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
2m
1H NMR
TFA


sm31200103.002.001.1r.esp
sm31200103.002.001.1r.esp
sm31200103.002.001.1r.esp
CF3
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
2m
13C NMR
TFA


Mar01-2013-58.002.001.1r.esp
-61.7106
-75.8221
Mar01-2013-58.002.001.1r.esp
Chemical Shift (ppm)
Mar01-2013-58.002.001.1r.esp
Chemical Shift (ppm)
CF3
O
NH
Me
TFA
2m
19F NMR
2.999
1.935
Chemical Shift (ppm)